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New Methods to Prepare Complex Macrocyclic Peptidomimetics Directly from Unprotected
Peptides

A dissertation submitted in partial satisfaction of the
requirements for the degree Doctor of Philosophy
in Chemistry

by

Kenneth Victor Lawson

2014

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ABSTRACT OF THE DISSERTATION

New Methods to Prepare Complex Macrocyclic Peptidomimetics Directly from Unprotected Peptides

by

Kenneth Victor Lawson

Doctor of Philosophy in Chemistry

University of California, Los Angeles, 2014

Professor Patrick G. Harran, Chair

Chapter one provides a brief overview of existing methods to prepare template-constrained macrocyclic peptides. This includes precedent from our laboratory describing a multi-functional electrophile which, in three conserved steps, forms composite macrocycles directly from unprotected oligopeptides. This lipophilic reagent was designed to offset the limiting characteristics of peptides, while imparting favorable conformational definition and an ability to passively diffuse through cellular membranes. This chapter also describes a new route to synthesize the processing reagent on scale, which enabled further study of the electrophilic reactivity of this species with two prototypical peptides.

Using the asymmetric synthesis described in chapter 1 we prepared a pilot library of composite macrocyclic peptidomimetics and screened it for antibacterial activity in a high-throughput format. Chapter 2 described preparation of a library consisting of 383 compound pools from which single compounds that inhibit *S. aureus* and *B. subtilis* were isolated. Moreover, we were

able to successfully establish an initial structure-activity relationship profile of the active constituent and moderately improve its antibacterial activity through iterative re-synthesis, purification and re-screening.

Chapter three describes the utility of a simplified, readily prepared lipophilic reagent to synthesize template constrained macrocyclic peptides via palladium catalyzed cinnamylation of imidazoles, carboxylates, amines, and phenols present in natural amino acids. This strategy is uniquely powerful. No protecting groups were used and subtle changes in reaction conditions had a marked effect the chemoselectivity of cyclization. This allowed the selective, divergent synthesis of isomeric macrocyclic peptides. We showed that conformation constraints, imparted by the template stabilized the secondary structure of longer peptide sequences (10 to 12 amino acids) and enhanced in vitro proteolytic stability relative their acyclic congeners.

Chapter four describes the utility of our lipophilic reagent, harboring a latent cinnamylation, to participate in Friedel-Crafts macrocyclization with tripeptide Trp-Trp-Tyr. In a single reaction eight unique macrocycles were generated from electrophilic substitution of tryptophan and tyrosine. The product distribution as a function of multiple Lewis- and Brønsted acids was investigated, as well as rearrangements induced from ionization of the corresponding tyrosine-linked macrocyclic ether. A bridged macrocyclic pyrroloindoline was isolated and the solution conformation was determined by two-dimensional NMR methods and molecular mechanics simulations. Chapter five expands the scope of this method. Using our processing reagent, a pilot library composed of thirty composite macrocycles was prepared from functionally diverse tryptophan containing oligopeptides. We anticipate this method to prepare diverse composite macrocycles has the potential to target surfaces involved in protein-protein interaction.

The dissertation of Kenneth Victor Lawson is approved.

Neil K. Garg

Curtis D. Eckhert

Patrick G. Harran, Committee Chair

University of California, Los Angeles

2014

For my family and friends who have been extraordinarily supportive of my academic pursuits.

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LIST OF ABBREVIATIONS

Bn	benzyl
Boc	<i>tert</i> -Butoxycarbonyl
Cbz	benzyloxycarbonyl
COSY	Correlation Spectroscopy
DBU	1,8-Diazobicyclo[5.4.0]undec-7-ene
DMF	Dimethylformamide
DMSO	Dimethylsulfoxide
<i>dr</i>	Diastereomeric ratio
<i>ee</i>	Enantiomeric excess
equiv	Equivalents
ESI	Electrospray ionization
HMBC	Heteronuclear Multiple Bond Correlation
HMQC	Heteronuclear Multiple Quantum Coherence
HPLC	High performance liquid chromatography
HRMS	High resolution mass spectrometry
HSQC	Heteronuclear Single Quantum Coherence
Hz	Hertz
LCMS	Liquid chromatography – mass spectrometry
mol	mole
NMR	Nuclear magnetic resonance
NOE	Nuclear Overhauser Effect
pHPLC	Preparative High performance liquid chromatography

quant.	Quantitative
ROESY	Rotating frame Nuclear Overhauser Effect Spectroscopy
TBAF	Tetrabutylammonium fluoride
TBTU	O-(Benzotriazol-1-yl)-N,N,N',N'-tetramethyluronium tetrafluoroborate
TFA	Trifluoroacetic acid
TFE	2,2,2-Trifluoroethanol
THF	Tetrahydrofuran
TLC	Thin-layer chromatography
UV	Ultraviolet

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PUBLICATIONS

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PRESENTATIONS

- 2012 Lawson, Kenneth V.*; Rose, Tristan E. Harran, Patrick, G.; New methods to generate complex peptidomimetics. Poster Presentation, ACS National Meeting, San Diego, CA, United States, March 22, 2012.
- 2010 Lawson, Kenneth V.*; Harran, Patrick, G.; Synthetic Approaches towards the Epidithiodiketopiperazine Class of Fungal Metabolites. Poster Presentation, ACS National Meeting, San Francisco, CA, United States, March 21-25, 2010.
- 2007 Lawson, Kenneth V.*; Spence, John D. Synthetic Approaches Towards mono-azacalix[4]arene and Synthesis of di-Azacalix[8]arene. Oral Presentation, 19th Undergraduate ACS Regional Meeting, Sonoma, CA, May 5, 2007.
- 2006 Lawson, Kenneth V.*; Spence, John D. Synthetic Approaches Towards mono-azacalix[4]arene. Poster Presentation, 231st ACS National Meeting, Atlanta, GA, United States, March 26-30, 2006

AWARDS

- | | |
|---|------------|
| UCLA Travel Award (243rd ACS National Meeting, San Diego, CA) | March 2012 |
| ACS Organic Division Travel Award (239th ACS National Meeting, San Francisco, CA) | March 2010 |
| National Science Foundation - Research for Undergraduates Fellowship | June 2006 |

Chapter 1 - Towards synthetic emulations of natural product biosynthesis

1.1. Introduction

Advances in pharmaceutical and biological research have revealed numerous protein-protein interactions underlying poorly treated diseases.^{1,2,3} The relatively large, shallow, solvent exposed surfaces involved in these interactions are difficult to modulate using traditional 'drug-like' small molecules. Consequently, there is considerable need for new synthetic methods to prepare complex molecules able to modulate protein-protein interactions for therapeutic intervention or to interrogate their biological roles. Peptides presenting complimentary recognition motifs represent a logical starting point to develop molecules able to bind these surfaces avidly and selectively. However the poor pharmacological properties of peptides have precluded their application in vivo.⁴ Nature has evolved numerous strategies to mitigate these problems, including the incorporation of recognition domains into complex, conformationally constrained macrocyclic scaffolds (Figure 1A). These macrocyclic natural products are abundant and often feature sophisticated biological activity which is not present in their acyclic progenitors.^{5,6} Synthetic methods to systematically access comparable 'macrocycle space' could be uniquely valuable.^{7,8}

Numerous methods have been developed to prepare peptide macrocycles, including: head-to-tail lactamization^{9,10}, internal disulfide bonding¹¹, ring-closing metathesis¹², azide-alkyne cycloaddition^{13,14}, and others. Many of these methods have been applied to the discovery of biological active compounds and pharmaceutical leads, however each relies on a unique set of reactive amino acid monomers and protecting group strategies. The direct modification of unprotected, unmodified peptides is significantly less developed.

An alternative strategy is to incorporate short peptides into macrocyclic scaffolds through the use of templates or scaffolds. Degrado^{15,16} Boger¹⁷, and others^{18,19,20,21} have demonstrated the utility of so-called 'template-constrained' macrocyclic peptides (Figure 1B).

Their work established that conformation can be controlled by the template, which can have a

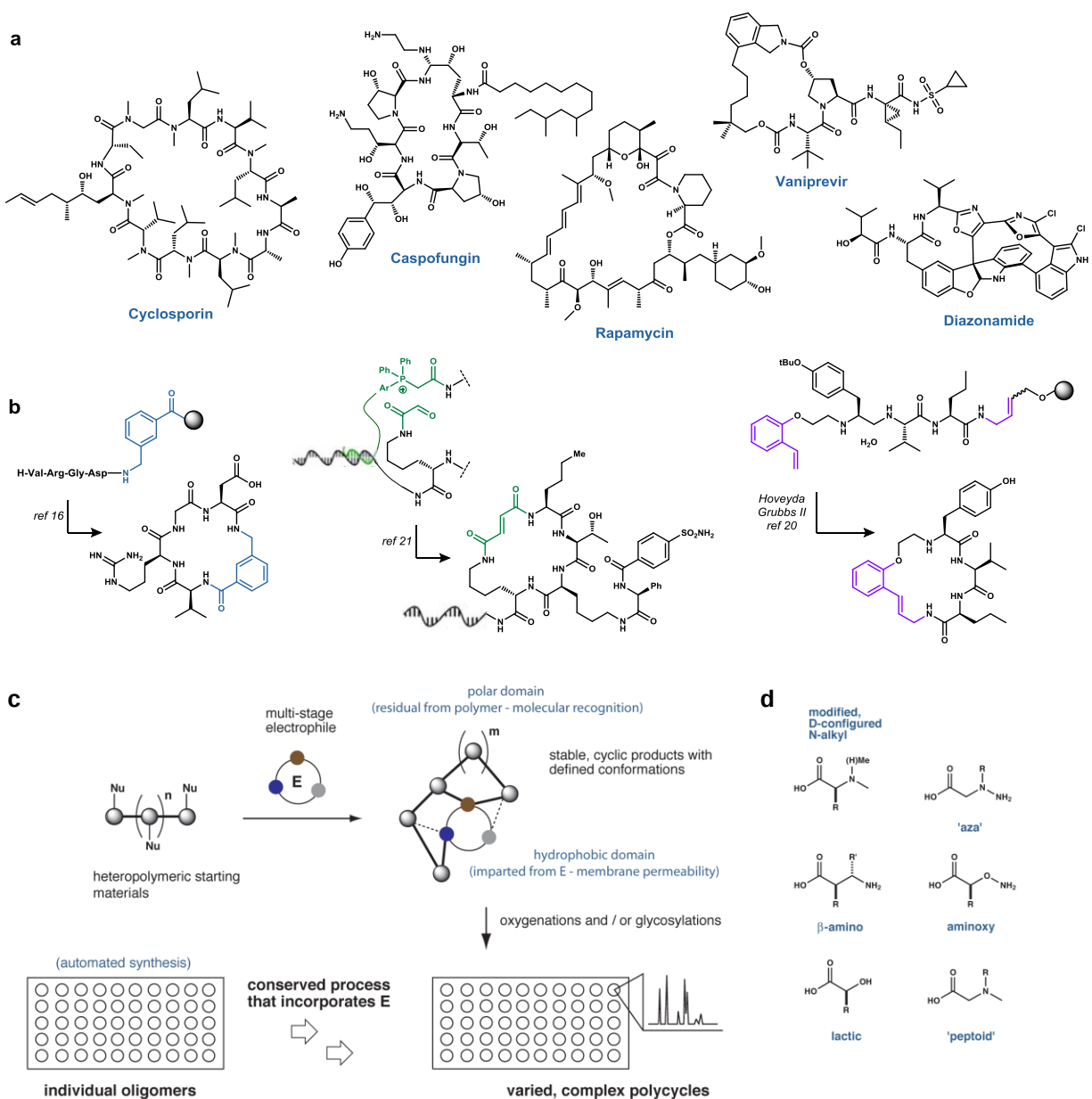


Figure 1. A. Examples of macrocyclic natural products and therapeutic agents with diverse biological activities. **B.** Examples of existing methods to incorporate peptides into macrocycles through reacting partners incorporated into non-peptidic templates **C.** Machine-made peptides and related oligomers can be incrementally reacted with template **E** to afford products with defined conformations and improved pharmacological properties. **D.** The set of potential starting materials for these exercises is vast.

marked affect on the polarity, geometry, and overall function of the peptide domain. Recently these strategies have been coupled with biosynthetic techniques, including phage display²² and

DNA templated synthesis²¹ (Figure 1B), to prepare large libraries of macrocyclic peptidomimetics.

Our templates (e.g. **E**, Figure 1C) were designed to mimic post-translational peptide modification and secondary metabolism.²³ These templates incorporate multiple latent reactive sites able to sequentially engage peptides; first bi-molecularly to form a stable peptide-template linkage, then multiple times intramolecularly to form structurally complex template-constrained macrocycles in a conserved reaction sequence. The end-result would be a *sequence dependent* remodeling of synthetic peptides. The goal from each polymer is not one product, but rather a mixture of isolable isomeric shape variants, each poised to display recognition elements in a unique ensemble of three dimensional conformations. These products would ideally possess characteristics making them valuable as biological probes and leads for drug development, including the ability to traverse lipid membranes and resist metabolic degradation.

1.2. Background

Two embodiments of **E** have been reported by Harran and co-workers previously. The first, compound **1**, featured two electrophilic motifs designed to react in series with functional groups common to peptides and related polyamides. For example the aldehyde of **1** is able to form a Schiff base with the N-terminus of Gly-Tyr-NHBu (Figure 2A). Following conditions developed by Van Leusen, condensation of the incipient imine with *p*-fluorophenyltosylmethyl isocyanide **3** in the presence of base affords 2,3,4-trisubstituted imidazole **4** - effectively incorporating the aldehyde of **1** and peptide N-terminus into a stable heterocycle. The vinylaryl carbinol is now poised to engage nucleophiles intramolecularly via intermediate metal π -allyl species.²⁴ Ideally a variety of nucleophiles presented by peptides could participate; namely phenols, imidazoles, indoles, and amines. These studies found the phenol of tyrosine to react selectively (e.g. **5**).²⁵ This two-step process proved general with numerous macrocyclic ethers prepared in good yield.

A second-generation reagent was envisioned to build added functionality within the core design of **1**.²³ Post cyclization, the goal was to unveil additional reactive intermediates to further

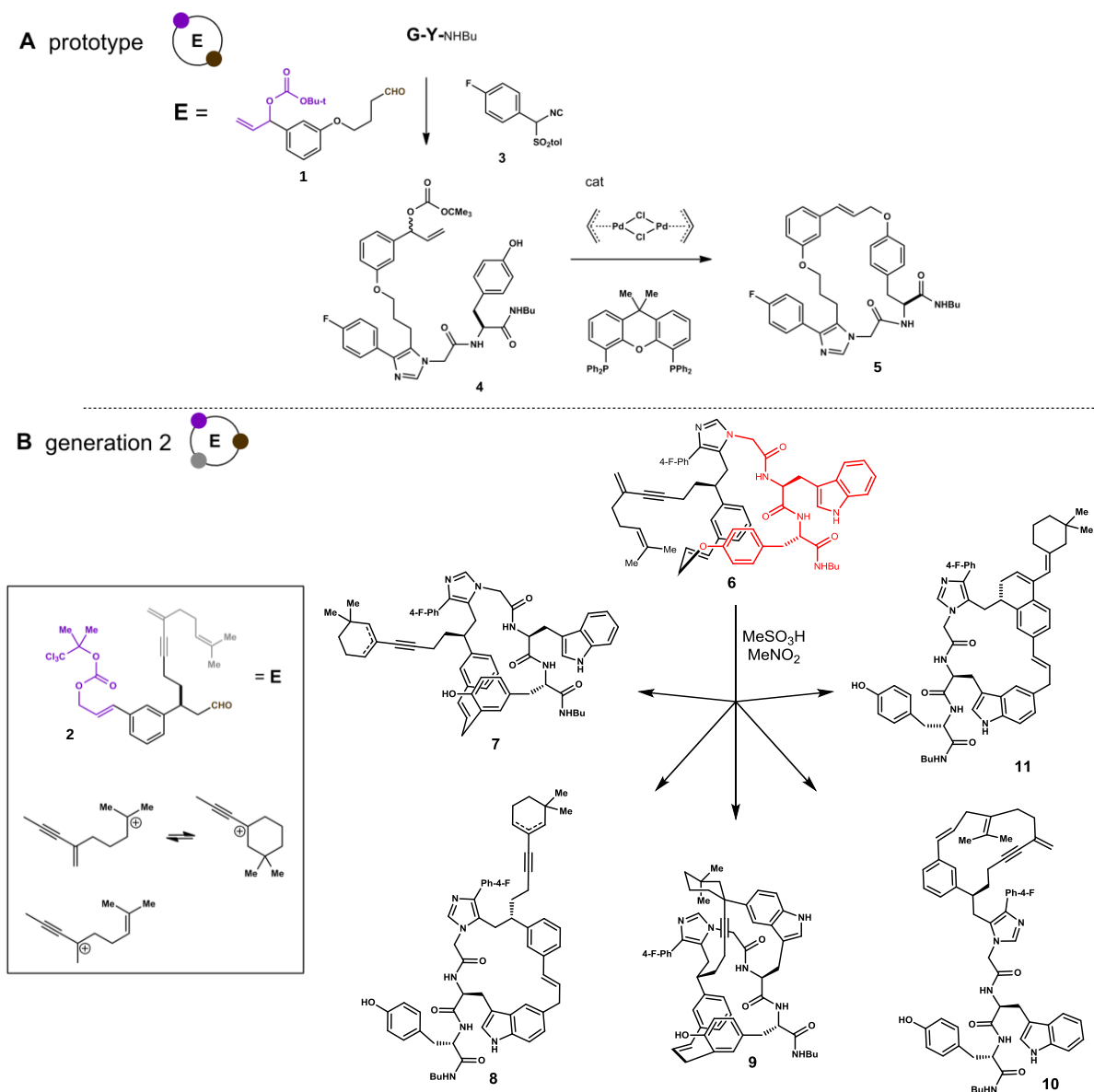


Figure 2. A. The earliest design for **E** was compound **1**, a molecule having two reactive positions. This substance can be incorporated into a range of unprotected peptides to form macrocyclic composites. **B.** Template **2** retains the reactive functionality, of **1** but also harbors a dieneyne appendage. This substance is able to transform linear peptides into diverse sets of polycyclic products (e.g. **7** - **11**) in three steps.

diversify and stabilize products. Inspired by terpene biosynthesis, reagent **2** harbors an unsaturated hydrocarbon motif which can be activated following the two-step macrocyclization

process. The diene-yne appendage was designed to react divergently with the peptide domain to provide an array of composite macrocycles from a single reaction. These isomers would vary in shape and uniquely display recognition groups in three dimensions. Furthermore this reactivity would ideally be dependent on the constitution of the starting oligomer, with bonding dependent on the proximity and nature of the functional groups present in the peptide.

An example of this process is depicted in Figure 2B. The product obtained from Van Leusen imidazole synthesis of **2** and Gly-Trp-Tyr-NHBu was converted to cinnamyl ether **6** by treatment with Pd-Xantphos complex. Exposure of **6** to anhydrous methanesulfonic acid in nitromethane promoted a series of carbocationic rearrangements within the hydrocarbon template, generating products **7** - **11**. In each, the cinnamyl ether had rearranged to form stable C-C bonded macrocycles. This likely occurs via an intermediate cinnamyl cation which undergoes Friedel-Crafts alkylation with adjacent aryl residues. Concomitantly, protonation of the diene-yne appendage promotes skeletal rearrangements (Figure 2B, inset). Notably, product **9** is derived from transannular electrophilic aromatic substitution of the proximal tryptophan residue. This *ansa* bridge imparts further conformational definition the peptide.

As a pilot study three oligopeptides, GWY, WWY and GGY were processed using reagent **2**. Product mixtures were synthesized as described above and fractionated by preparative HPLC. An average of 10-12 product fractions were separated from each sequence and reconstituted in DMSO to provide 10mM stock solutions (total isomer concentration). Fractions were assayed for hippocampal neurogenesis *in vivo*.

A description of assay protocols and resulting data are described below - adapted from Zhao, H. D.; Negash, L.; Wei, Q.; LaCour, T. G.; Estill, S. J.; Capota, E.; Pieper, A. A.; Harran, P. G. *J. Am. Chem. Soc.* **2008**, *130*, 13864 (Reference 23):

Isolated HPLC fractions were diluted (10^3 fold) in artificial cerebrospinal fluid and infused intracerebroventricularly at a constant rate into the left lateral ventricle of adult C57BL/J6 mice by means of an implanted Alzet osmotic minipump. Mice were awake and unconstrained during

the infusion, and administered daily intraperitoneal injections of bromo deoxyuridine (BrdU, 50 mg/kg) as a marker of cell divisions. After infusion was complete (7 days), mice were transcardially perfused and brain tissue stained with antibodies against BrdU. Hippocampal neurogenesis was evaluated by light microscopy contralateral to the side of pump implantation (Fig. 3A) to avoid artifacts from tissue damage. Every fifth section through the rostral-caudal extent of the hippocampus was analyzed, and the total number of BrdU+ cells was normalized against the volume of the dentate gyrus. Similarly infused recombinant fibroblast growth factor (FGF – 0.04 mg/ Kg / day) served as a positive control (Fig. 3B).

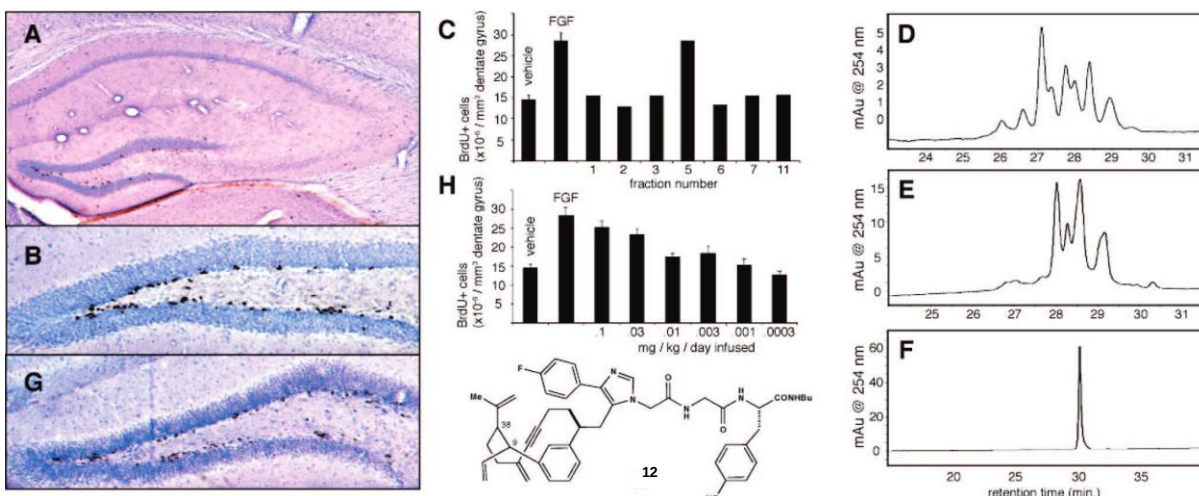


Figure 3. **A)** Normally proliferating cells (anti BrdU, black dots) in the subgranular zone of the mouse hippocampal dentate gyrus (DG, lower left). **B)** Magnified DG from a mouse infused with FGF (0.04 mg/kg/d for 7d) showing increased BrdU incorporation. **C)** In vivo screening of products derived from processing GGY with **6** identified a chromatography fraction (#5) that elicits BrdU incorporation comparably to FGF. HPLC analysis of this fraction (**D**) showed it contained several products. These were divided into three pools by HPLC and re-screened *in vivo*. The active fraction (**E**) was resolved into components, one of which (**F**) retained the majority of neurogenesis activity and was assigned structure **17**. (~1:1 mixture of isomers, stereochemistry at C9 and C38 unassigned). Isolated **12** elicits marked BrdU incorporation in the DG when infused at 0.1 mg/kg/d for 7d (**G**) and its activity is dose dependent (**H**).

Pools derived from each of the processed peptides displayed activity in this format. Fractions derived from GGY elicited the most robust and selective response (Fig 3C). This fraction contained several products (Fig. 3D) which were fractionated into three pools and re-screened. A single fraction retained the observed activity. HPLC analysis showed it was composed of four major products (Figure 3E). Each was chromatographed to homogeneity. A single fraction (Figure 3F) retained the majority of neurogenesis activity. The structure of the active constituent was subsequently assigned as *meta*-cyclophane **12**. Pure **12** reproducibly

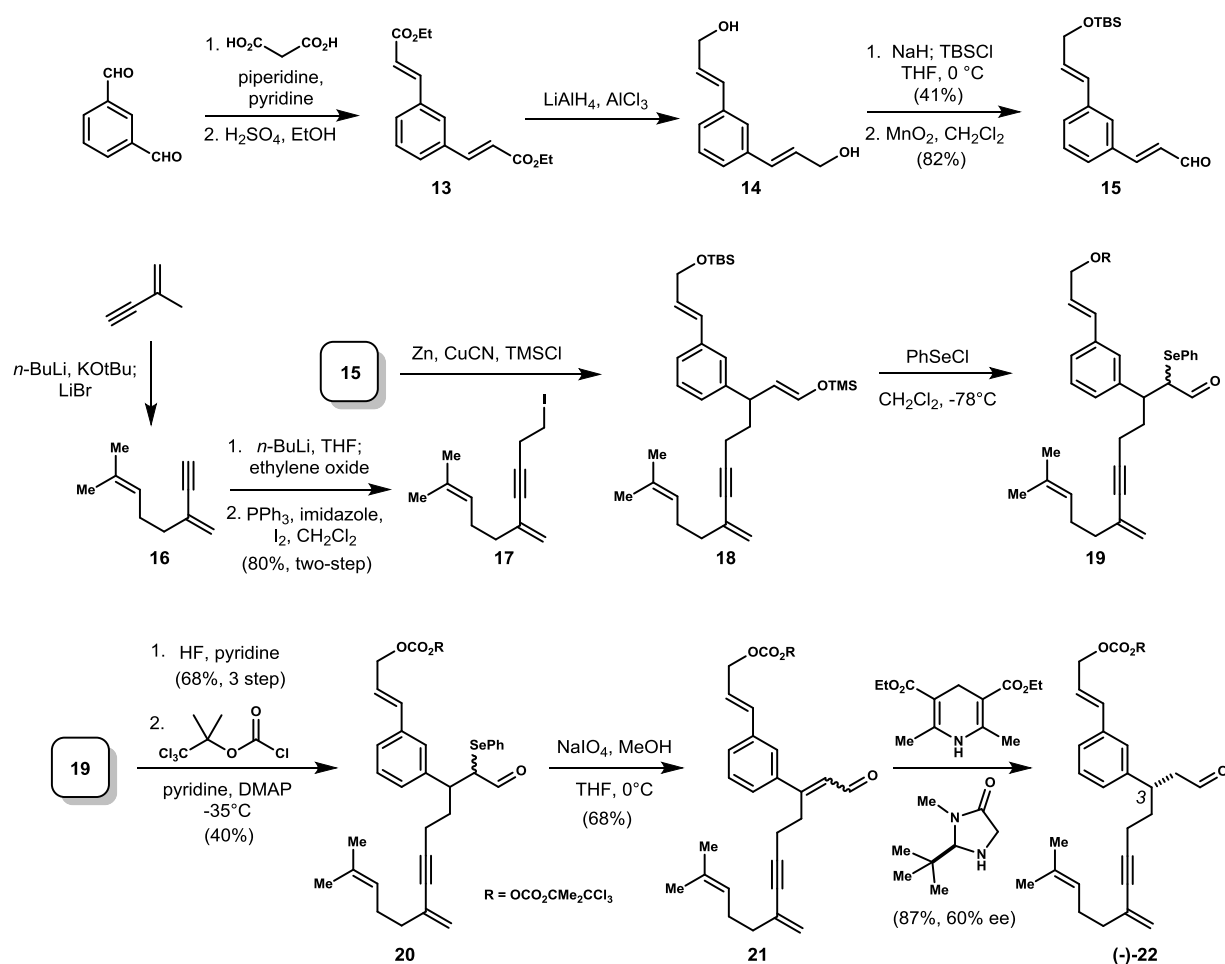
elicited marked (Figure 3G) and selective neural cell proliferation in the hippocampal dentate gyrus and its activity was dose dependent in a dilution series (Figure 3H).

Isolation of **12** was a milestone for the project, showing that we could track and purify a trace constituent from our chemistry. Iterative purification and re-screening of increasingly homogenous product fractions minimized the probability of isolating false positives. Time-intensive structure determination was limited to active components.

1.3. Asymmetric synthesis of processing reagent on scale.²⁶

Inspired by the utility of the initial screening library, our attention turned to expanding the screening sets derived from the second generation processing reagent. This required us to further our understanding of the reactivity and scope of the acid-promoted carbocationic rearrangements. The studies performed above utilized scalemic **2** (~60% ee) and required separation of diastereomers following ligation with peptides. A more scalable, selective synthesis of **2** was desirable.

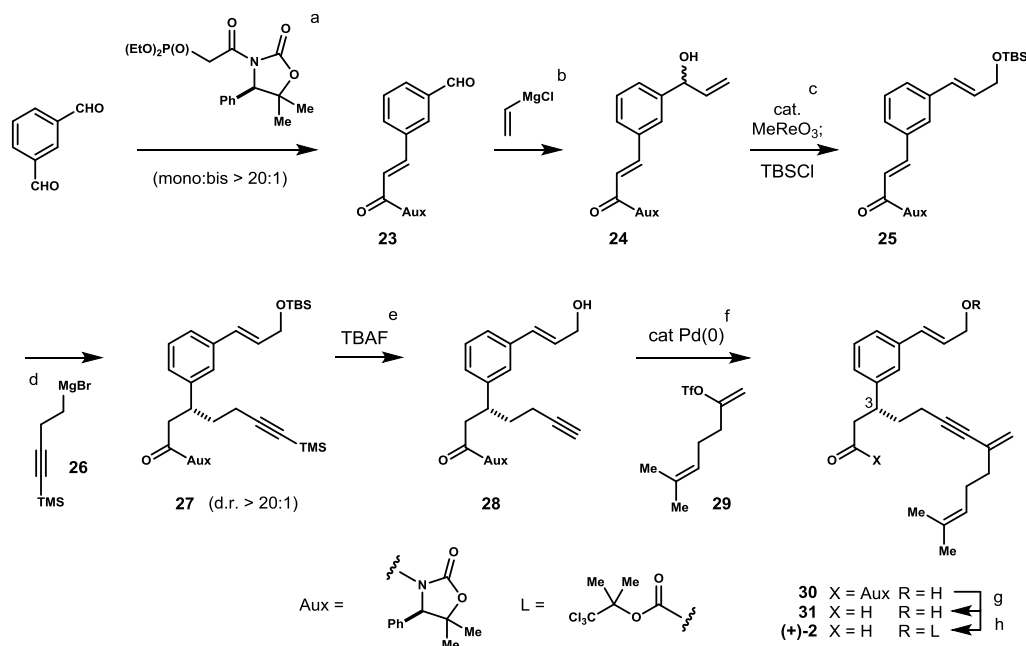
The initial synthesis of **2** relied upon copper promoted 1,4-addition of homopropargylic organozinc species **17** to cinnamaldehyde **15** (Scheme 1).²⁷ The resultant trimethylsilyl enol ether was parlayed (1. PhSeCl; 2. HF/pyridine; 3. CCl₃C(Me)₂CO₂Cl, DMAP, pyridine; 4. NaIO₄) into isomeric enals **21**. Subsequent chiral imidazolidinone-catalyzed conjugate reduction²⁸ afforded **2**. The conjugate reduction required high catalyst loads to proceed at a useful rate and provided **2** in moderate enantiomeric excess (60% ee). This was inconvenient because oily substance **2** could not be further resolved via crystallization.²⁹ Furthermore, attempts to selectively monosilate diol **14** were unsuccessful. The nearly statistical mixtures of starting material and mono-/di-silyl ethers required chromatographic separation which reduced the scalability of the route at an early stage.



Scheme 1. The original synthetic route to **2** utilized an organocatalytic conjugate reduction of **21** to induce asymmetry at *C3*. Unfortunately the reaction proceeded with only moderate enantioselectivity. Reagents & Conditions: see reference 27.

To circumvent these limitations and to provide flexible, scalable access to optically active **2** and congeners, an alternate synthesis was developed. Commercial isophthalaldehyde was desymmetrized³⁰ via controlled olefination employing (*R*)-(-)-phenylglycine derived phosphonoacetyl oxazolidinone **22** (Scheme 1).³¹ Adduct **23** was then treated with vinyl magnesium chloride to generate a mixture of diastereoisomeric aryl vinyl carbinols **24**. MeReO_3 catalyzed allylic alcohol transposition³² followed by in situ silylation with TBSCl afforded a single isomer of cinnamyl ether **25**. Homopropargylic Grignard reagent **26**³³ was added conjugately to the acrylimide in **25** affording **27** in high yield and diastereomeric excess. After degradation of the silicon groups in **27** with TBAF, the terminal alkyne in **28** participated smoothly in a

Sonogashira cross-coupling reaction with methylheptenone derived enol triflate **29**.³⁴ The resultant diene-yne containing imide **30** was reduced with a 2-fold excess of (*i*-Bu)₂AlH in toluene to afford aldehyde **31**, from which target **2** was derived via acylation with 2,2,2-trichloro-1,1-dimethylethyl chloroformate.



Scheme 2. Reagents & Conditions: a) isophthalaldehyde (2 equiv.), LiCl, iPr₂NEt, MeCN, rt, 48h, (74% from (4*R*)-5,5-Dimethyl-4-phenyloxazolidin-2-one); b) vinylmagnesium chloride, toluene, -78 °C; c) MeReO₃ (3 mol%), toluene, rt, 12h; TBSCl (1.2 equiv), imidazole, rt, 45 min (79 % from **23**); d) **26** (1.2 equiv.), CuI, Me₂S/THF, -40 °C → -20 °C, 96%; e) TBAF, THF, -10 °C, 1h, 95%; f) **29**, Pd(PPh₃)₂Cl₂ (2.5 mol%), CuI (5 mol %), iPr₂NH, 0 °C → rt, THF, 1h, 61 %; g) (*i*-Bu)₂AlH (3 equiv.), toluene, -78 °C; h) CCl₃C(Me)₂CO₂Cl (1.4 equiv), DMAP, pyridine, DCM, -40 °C, 2h (52 % from **30**).

The above route entailed eight linear steps, proceeded in 17 % overall yield and provided **2** in 91% e.e.^{35,36} It gave access to our target in up to 10 g batches without incident and had the added benefit of introducing the diene-yne appendage incrementally in two segments, wherein both could be controllably varied in future iterations. To simplify its use, aldehyde **2** was stored a 0.3M solution in DMF at -20 °C. Under these conditions only slight decomposition, comparable to that of a neat sample, was observed after storage for over six months.

1.4. Investigation of scope and reactivity of acid-promoted rearrangements.

With a scalable route to **2** established, we further investigated the cationic rearrangements that occur as the final step in our processing sequence. Moreover, electronic and steric properties of arene nucleophiles that would effecting participate in the chemistry were ill defined. We first attempted to simultaneously probe these two issues.

Peptides **32** and **33** we chosen for study. These sequences harbored pi-basic aromatics, namely thiophene, anisole, oxazole, and 5-hydroxindole that had not been examined. Furthermore, we anticipated the 3-oxazolyl-indole motif present in **32** would reduce available conformation degrees of freedom in the substrate. The resulting product distribution would be informative.

Following protocols described above, condensation of **32** and **33** with aldehyde **2** followed by cycloaddition with TosMIC reagent **3** provided N-terminal imidazole ligation products. These cyclized upon treatment with catalytic amounts of Pd/xantphos complex.²⁷ Notable, cyclic ethers derived **33** were isolated as a 2:1 mixture of branched and linear alkylation products **35** and **36**. Branched ethers had not been observed from Pd-catalyzed cinnamylation of tyrosine. Branched regiochemistry was confirmed by COSY correlations between H¹-H^{1'} (²J_{gem} = 1.0 Hz), H²-H³ (³J_{HH} = 6.3 Hz), and H¹/H^{1'}-H² (³J_{cis} = 10.5 Hz, ³J_{trans} = 17.0 Hz) indicative of a terminal olefin (Figure 3C). The macrocyclic ether linkage was assigned by a diagnostic HMBC correlation between the methine H³ and the phenolic carbon (C⁶) resonance observed at δ 153 ppm (Figure 4D). The macrocyclic linkages in **34** and **35** were assigned analogously.

A mixture of branched and linear alkylation products would be inconsequential in subsequent acidolysis reactions. Interestingly, however **36** slowly underwent thermal aryl Claisen rearrangement selectively to the indole 4-position forming stable C-C bonded macrocycle **37**.³⁷ This process was complete, as observed by NMR, at 70 °C within 12 hours in MeCN-d₃ (Figure 5B). This rearrangement was also accelerated under the macrocyclization

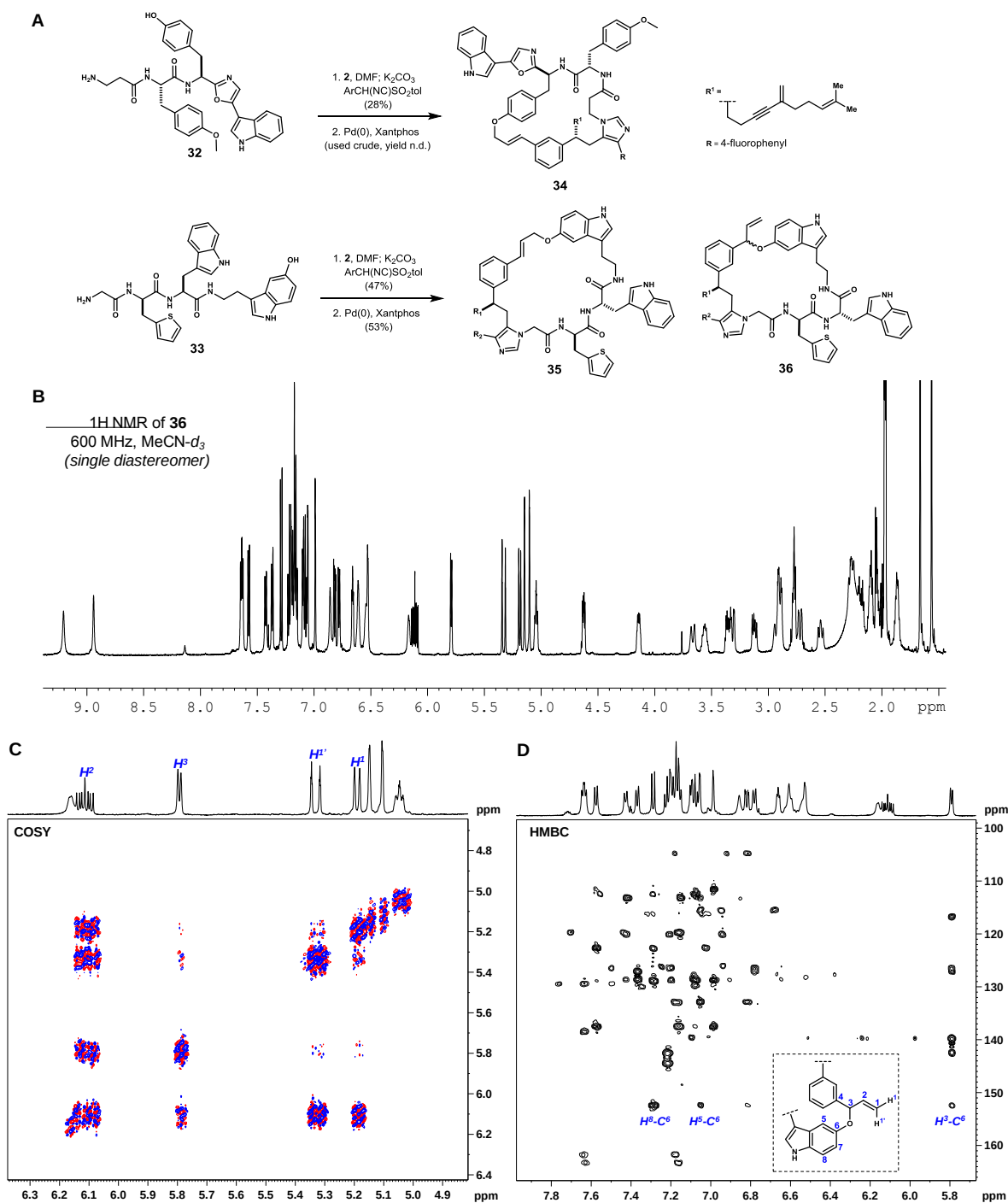


Figure 4. A. Synthesis of macrocycles **34-36**. Conditions: 1) **2**, K_2CO_3 (5 eq.), DMF (0.1 M), 2h, rt; **3**, 12h; 2) $[Pd(C_3H_5)Cl]_2$ (4 mol%), xantphos (10 mol%), DMF/THF (5 mM), rt, 2h. **B.** 1H NMR ($MeCN-d_3$, 600 MHz) of **36** isolated by preparative HPLC (C18, $MeCN/H_2O$). **C.** Olefinic region of COSY spectra reveal presence of branched allylic ether. **D.** Key HMBC correlation of **36** are indicative of macrocyclic linkage.

conditions leading to considerable degradation of **36** at extended reaction times. Catalyst poisoning with aqueous NaCN and cold-storage was essential to halt this process.

rearrangements were limited to aromatic substitutions of the 5-hydroxyindole and rearrangements within the framework of **2**.

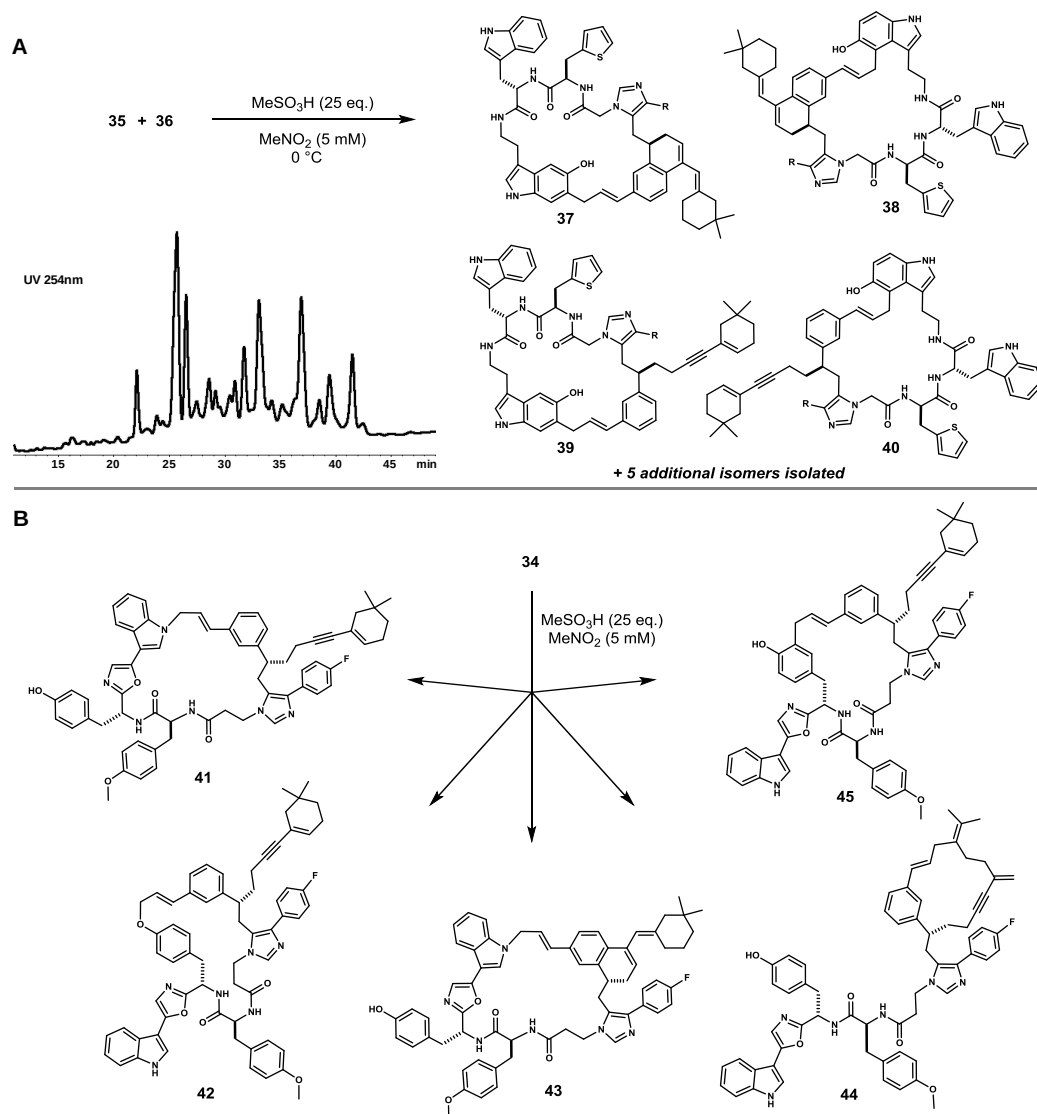


Figure 5. A. Treatment of **35** and **36** with dry acid promotes a series of cationic rearrangements. Nine compounds including **37** - **40** were purified to homogeneity by preparative HPLC (C18, MeCN/H₂O, 0.1% HCO₂H). *Inset:* HPLC chromatogram of reaction mixture at 2 hours. *Conditions:* MeSO₃H (25 eq.), MeNO₂ (5 mM), 0 °C, 2h. **B.** Acidolysis of macroether **34** afforded isomeric macrocycles **41** - **45**. Numerous additional products were observed by HPLC, but were not present in sufficient quantity for characterization or could not be purified to homogeneity. *Conditions:* MeSO₃H (25 eq.), MeNO₂ (5 mM), 0 °C, 2h.

Novel reactivity was observed from acidolysis of indole-oxazole **34**. Indole N-alkylation proceeded to form 24-membered macrocycles **41** and **43** wherein the diene-yne had cyclized to form cyclohexene and dihydronaphthalene groups respectively. These products were the first examples of cinnamyl ion migration to form larger ring macrocycles. Products **42** and **44** provide

insight into the relative kinetics of cinnamyl and diene-yne isomerization. *meta*-Cyclophane **44** is derived from nucleophilic addition of the trisubstituted olefin to the cinnamyl cation. Conversely, product **42** retained an intact cinnamyl ether and cyclized diene-yne, suggesting cyclohexene formation and cinnamyl ionization occur at similar rates.

1.5. Discussion and Conclusion

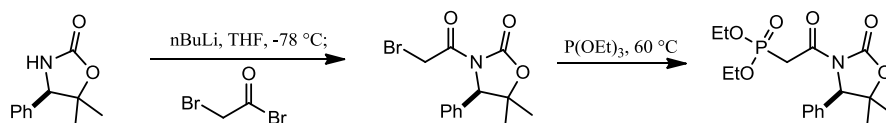
A scalable route to **2** was developed which enabled further study of its electrophilic reactivity in the context peptide macrocycles. All acidolysis products isolated had undergone 6-*exo* cyclization of the diene-yne appendage. Previous studies, processing Trp-Trp-Tyr, identified a single example of the cyclohexene reacting further to alkylate Trp₂ to form an *ansa*-bridged macrocycle. No analogous transannular Friedel-Crafts alkylations were observed from acidolysis of macrocycles **34** and **35/36** demonstrating the limited scope of this diene-yne reactivity. Further cyclization to form the dihydronaphthalene motif, likely prevents additional engagement with the peptide domain due to geometrical constraints. Modification of this reactive appendage to mitigate rapid, small-ring formations would likely be beneficial.

The entropic cost associated with the large-ring forming cationic rearrangements observed in these systems is potentially offset by starting from macrocyclic precursors. This is evidenced by the unresolvable reaction mixtures obtained from acidolysis of the acyclic carbonates which are presumably able to access analogous carbocationic intermediates following carbonate decomposition. The novel indole N-alkylated macrocycles **41** and **43** uniquely demonstrate the ability of cinnamyl cation migration to form ring-expanded macrocycles. Ionization of the ether C-O bond likely proceeds conformational relaxation in these systems. The presence of ring expanded products suggest intermediate cinnamyl cations may be poised to engage aromatic nucleophiles in large-ring forming reactions directly from acyclic material. This observation greatly influenced the direction of our subsequent research (see chapters 4 and 5).

Chapter 1 - Supporting Information

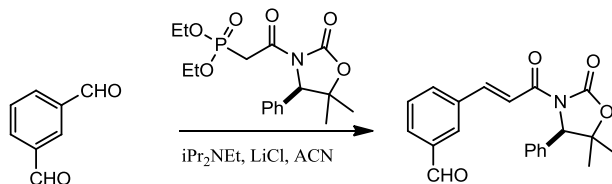
General Experimental Procedures. All reactions were performed in flame-dried glassware under a positive pressure of argon, unless otherwise noted. Air- and moisture-sensitive liquids were transferred via syringe or stainless steel cannula. Analytical thin-layer chromatography was performed using glass plates pre-coated with silica gel (0.25 mm, 60 Å pore size, 230-400 mesh, Silicycle Inc.) impregnated with a fluorescent indicator and visualized by exposure to ultraviolet light (254 nm) and/or stained by submersion in basic aqueous KMnO_4 , acidic *p*-anisaldehyde in ethanol, or aqueous ceric ammonium molybdate followed by heating with a heat gun. Flash-column chromatography was performed employing silica gel (60-Å pore size, 40-60 μm , Silicycle Inc.) or utilizing pre-packed silica gel cartridges (60-Å pore size, 40-60 μm , Silicycle Inc.) with an automated flash chromatography system equipped with a binary gradient pump, UV-Vis detector, and fraction collector. Commercial reagents were used as received. Tetrahydrofuran (THF), toluene, and acetonitrile were dried by passing through alumina towers according to Pangborn, et al.¹ The concentration of commercial solution *n*-butyllithium was determined by titration against standard solutions of diphenylacetic acid.²

Experimental Procedures.



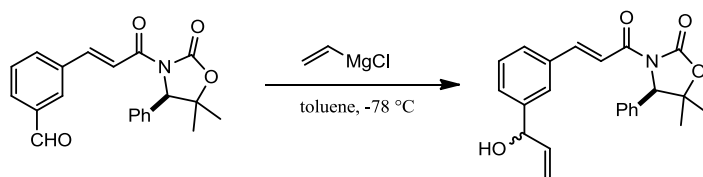
Diethyl {2-[(4R)-4-Phenyl-2-oxo-1,3-oxazolidin-3-yl]-2-oxoethyl}-phosphonate (20). To a solution of (*R*)-(-)-5,5-dimethyl-4-phenyl-2-oxazolidinone (62.09 g, 324.7 mmol) in THF (1.3 L) at -78 °C was added *n*-BuLi (2.5 M in hexane, 132.5 mL, 331.2 mmol) dropwise over 30 minutes. The resulting solution was stirred 30 min at this temperature prior to the addition of bromoacetyl bromide (65.5 g, 325 mmol) over 3 minutes via syringe. After stirring an addition 45 minutes the solution was allowed to slowly warm to 0 °C and sat. NH_4Cl (300 mL) is added. The organic layer is separated and washed with sat. NH_4Cl and brine, dried over Na_2SO_4 and concentrated. This material was taken up in triethylphosphite (670 mL) and heated to 60 °C for 2h then concentrated under reduced pressure. The resulting dark viscous oil was taken up in ethyl acetate (2.0 L) and washed sequentially with water and brine, dried over Na_2SO_4 and concentrated to give an amber oil. This material is used without further purification. ¹H NMR (CDCl_3 , 400 MHz): δ 7.28-7.39 (m, 3H), 7.16-7.22 (m, 2H), 5.07 (s, 1H), 4.09-4.17 (m, 4H), 3.98 (dd, J_{HP} = 22.5 Hz, J_{HH} = 13.7 Hz, 1H), 3.66 (dd, J_{HP} = 22.5 Hz, J_{HH} = 13.7 Hz, 1H), 1.62 (s, 3H), 1.30 (t, J = 7.1 Hz, 1H), 1.27 (t, J = 7.1 Hz, 1H), 0.99 (t, J = 7.1 Hz, 1H). ¹³C NMR (CDCl_3 , 100 MHz): δ 164.6 (d, J_{CP} = 6.8 Hz), 153.2,

135.8, 128.8, 128.6, 126.5, 82.7, 67.3, 62.8 (d, J_{CP} = 6.0 Hz), 34.6 (d, J_{CP} = 129 Hz), 28.8, 23.6, 16.32 (d, J_{CP} = 1.7 Hz), 16.26 (d, J_{CP} = 1.7 Hz).



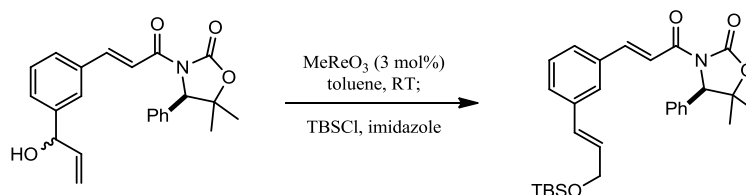
(*R,E*)-3-(3-(5,5-dimethyl-2-oxo-4-phenyloxazolidin-3-yl)-3-oxoprop-1-en-1-yl)benzaldehyde (23).

Diisopropylethylamine (62.2 mL, 357 mmol) was added to a solution of keto-phosphonate **20** (119 g, 324 mmol) and LiCl (15.1 g, 357.2 mmol) at room temperature. This mixture was stirred for 5 minutes prior to the addition of isophthalaldehyde (87.1 g, 649.4 mmol) in one portion. After stirring overnight, water (500 mL) was added and the mixture was extracted with EtOAc (1.0 L). The organic phase was washed with sat. NH_4Cl , sat. NaHCO_3 , and brine, dried over Na_2SO_4 and concentrated in vacuo. Purification by flash chromatography (SiO_2 , gradient 70:15:10 $\rightarrow$ 45:15:40 hexanes: CHCl_3 : Et_2O) gave aldehyde **23** (83.5 g, 74 % over 3 steps) as a white solid. ^1H NMR (CDCl_3 , 400 MHz): δ 10.05 (s, 1H), 8.10 (d, J = 15.7 Hz, 1H), 8.05 (d, J = 0.6, 1H), 7.92 (dd, J = 7.6, 1.3 Hz, 1H), 7.86 (d, J = 7.8 Hz, 1H), 7.80 (d, J = 15.7 Hz, 1H), 7.57 (app t, J = 7.7 Hz, 1H), 7.30-7.45 (m, 3H), 7.15-7.25 (m, 2H), 5.21 (s, 1H), 1.66 (s, 3H), 1.04 (s, 3H). ^{13}C NMR (CDCl_3 , 100 MHz): δ 191.7, 164.6, 153.3, 144.5, 136.9, 136.2, 135.5, 133.9, 131.0, 129.9, 129.7, 128.9, 128.7, 126.4, 119.0, 82.7, 67.3, 29.0, 23.8. HRMS (ESI) Calculated for $\text{C}_{21}\text{H}_{19}\text{NO}_4$ $[\text{M}+\text{Na}]^+$: 372.1206, found 372.1207.

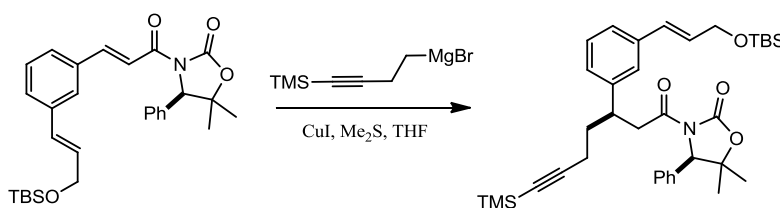


(4*R*)-3-((*E*)-3-(3-(1-hydroxyallyl)phenyl)acryloyl)-5,5-dimethyl-4-phenyloxazolidin-2-one (24). To a solution of aldehyde **23** (5.0 g, 14.3 mmol) in toluene (190 mL) at $-78\text{ }^\circ\text{C}$ was added dropwise vinylmagnesium chloride (1.6 M in THF, 10.3 mL, 16.47 mmol) over 45 minutes maintaining an internal temperature $< -65\text{ }^\circ\text{C}$. The mixture was stirred an additional 4h at this temperature and quenched with saturated NH_4Cl (50 mL). The organic layer was separated, diluted with ethyl acetate (100 mL) and washed sequentially with sat. NH_4Cl , water, and brine. The solution was dried over Na_2SO_4 , filtered and concentrated to give a crude yellow foam which was used in the next step without further purification. An analytically pure sample was obtained by flash chromatography (SiO_2 , gradient 15 $\rightarrow$ 40%

EtOAc/hexanes). ^1H NMR (CDCl_3 , 400 MHz): δ 8.00 (d, J = 15.7 Hz, 1H), 7.76 (d, J = 15.7 Hz, 1H), 7.58 (s, 1H), 7.53 (dd, J = 7.2, 1.6 Hz, 1H), 7.30-7.45 (m, 5H), 7.25-7.05 (m, 2H), 6.03 (ddd, J = 16.8, 10.3, 5.9 Hz, 1H), 5.36 (ddd, J = 16.8, 1.2, 1.2 Hz, 1H), 5.15-5.25 (m, 3H), 2.09 (s, 1H), 1.64 (s, 3H), 1.03 (s, 3H). ^{13}C NMR (CDCl_3 , 100 MHz): δ 165.1, 153.3, 146.4, 143.4, 140.0, 136.3, 134.8, 129.1, 128.9, 128.7, 128.6, 127.9, 126.6, 117.4, 115.6, 82.5, 75.0, 74.9, 67.3, 29.0, 23.8. HRMS (ESI) Calculated for $\text{C}_{23}\text{H}_{23}\text{NO}_4$ $[\text{M}+\text{Na}]^+$: 400.1519, found 400.1521.

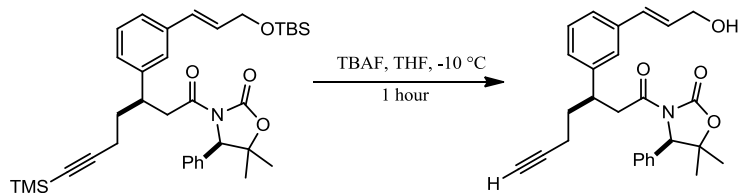


(R)-3-((R)-3-(3-((E)-3-((tert-butyldimethylsilyl)oxy)prop-1-en-1-yl)phenyl)acryloyl)-5,5-dimethyl-4-phenyloxazolidin-2-one (25). Methyltrioxorhenium (107 mg, 0.430 mmol) was added in one portion to a solution of allylic alcohol **24** (5.40 g, 14.32 mmol) in toluene (115 mL). After complete consumption of starting material (typically 12 h), as monitored by HPLC, imidazole (2.92 g, 43.0 mmol) was added followed by TBSCl (2.59 g, 17.2 mmol). After 1h the mixture was diluted with EtOAc (200 mL) and washed sequentially with sat. NH_4Cl , NaHCO_3 , and brine, dried over Na_2SO_4 and concentrated. Cinnamyl silyl ether **25** (5.56 g, 79 % from **23**) was obtained as an off-white foam. ^1H NMR (CDCl_3 , 400 MHz): δ 8.01 (d, J = 15.7 Hz, 1H), 7.76 (d, J = 15.7 Hz, 1H), 7.58 (s, 1H), 7.30-7.50 (m, 6H), 7.20 (d, J = 6.8 Hz, 2H), 6.61 (dt, J = 15.8, 1.6 Hz, 1H), 6.33 (dt, J = 15.8, 4.9 Hz, 1H), 5.21 (s, 1H), 4.37 (dd, 4.9, 1.6 Hz, 2H), 1.65 (s, 3H), 1.03 (s, 3H), 0.95 (s, 9H), 0.12 (s, 6H). ^{13}C NMR (CDCl_3 , 100 MHz): 165.1, 153.3, 146.5, 137.9, 136.3, 134.8, 130.4, 129.1, 129.0, 128.9, 128.6, 128.5, 127.4, 126.7, 117.3, 82.5, 67.3, 63.7, 29.0, 26.0, 23.8, 18.5. HRMS (ESI) Calculated for $\text{C}_{29}\text{H}_{37}\text{NO}_4\text{Si}$ $[\text{M}+\text{Na}]^+$: 514.2384, found 514.2394.

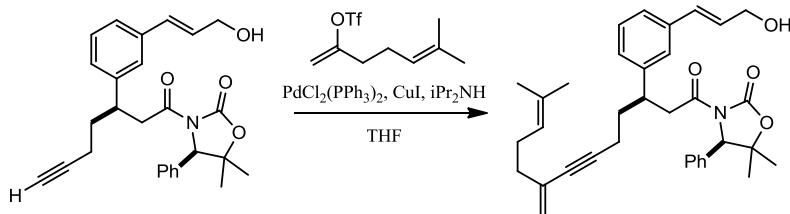


(R)-3-((R)-3-(3-((E)-3-((tert-butyldimethylsilyl)oxy)prop-1-en-1-yl)phenyl)-7-(trimethylsilyl)hept-6-ynoyl)-5,5-dimethyl-4-phenyloxazolidin-2-one (27). Grignard reagent **26** was prepared by addition of 4-bromo-1-trimethylsilyl-1-butyne (16.4 g, 80 mmol) in THF (80 mL) to magnesium filings (2.92 g, 120 mmol); initial addition of 8 mL followed by dropwise addition of the remainder via syringe pump over 1 h. The solution was warmed to reflux for 15 min, cooled to room temperature, diluted with 80 mL THF and

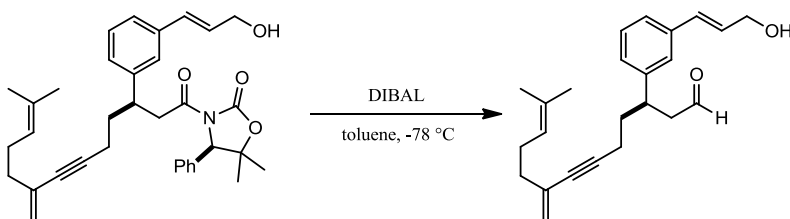
titrated against a standard solution of menthol in THF containing 1,10-phenanthroline as an indicator ($c = 0.50$ M). Copper(I) iodide (10.11 g, 53.1 mmol) was dissolved in THF (90 mL) and dimethylsulfide (22 mL), cooled to -78 °C and stirred for 15 min. The Grignard reagent (101 mL) was added via cannula over 10 minutes, and the mixture was stirred for 10 minutes at -78 °C, then 10 minutes at -40 °C. A pre-cooled solution of **25** (22.53g, 45.8 mmol) in THF (60 mL) was added over 10 minutes, and stirring continued at -40 °C for 30 min and then at -20 °C for 4h. The reaction was quenched with saturated NH_4Cl (25 mL) and diluted with H_2O (150 mL). The aqueous phase was extracted with EtOAc, and the combined organic phase was washed with H_2O , brine, dried over MgSO_4 , and concentrated. The residue was freed from copper salts by repeated trituration with 1:1 hexane:EtOAc and filtration through short plugs of silica gel. Compound **27** (27.30 g, 96%, single diastereoisomer by ^1H NMR) was used without purification. ^1H NMR (CDCl_3 , 400 MHz): δ 7.28-7.38 (m, 3H), 7.18-7.24 (m, 3H), 7.05-7.10 (m, 3H), 6.55 (dt, $J = 15.8, 1.7$ Hz, 1H), 6.27 (dt, $J = 15.8, 5.0$ Hz, 1H), 4.87 (s, 1H), 4.35 (dd, $J = 5.0, 1.7$ Hz, 2H), 3.67 (dd, $J = 16.2, 9.6$ Hz, 1H), 3.27 (dddd, $J = 10.0, 9.6, 5.4, 4.9$ Hz, 1H), 3.09 (dd, $J = 16.2, 5.4$ Hz, 1H), 1.75-2.12 (m, 4H), 1.34 (s, 3H), 0.95 (s, 9H), 0.90 (s, 3H), 0.12 (brs, 15H). ^{13}C NMR (CDCl_3 , 100 MHz): δ 171.5, 153.4, 143.1, 137.4, 136.4, 129.5, 129.4, 129.0, 128.8, 128.7, 126.9, 126.1, 124.9, 106.7, 85.1, 82.5, 67.1, 64.0, 41.5, 41.2, 35.4, 28.7, 26.1, 25.8, 23.7, 18.6, 18.1, 0.3, -5.0. HRMS (ESI) Calculated for $\text{C}_{36}\text{H}_{51}\text{NO}_4\text{Si}_2$ $[\text{M}+\text{Na}]^+$: 640.3249, found 640.3243.



(R)-3-((R)-3-(3-((E)-3-hydroxyprop-1-en-1-yl)phenyl)hept-6-ynoyl)-5,5-dimethyl-4-phenyloxazolidin-2-one (28). To a solution of **27** (24.40 g, 39.48 mmol) in THF (400 mL) at -10 °C was added tetrabutylammonium fluoride (1.0M/THF, 98.70 mL, 98.71 mmol) over 15 min. The resulting orange solution was stirred for 1h at this temperature then diluted with EtOAc (500 mL) and washed with sat. NH_4Cl , and brine, dried over Na_2SO_4 and concentrated by rotary evaporation. The crude oil was taken up in chloroform (100 mL) and filtered through a plug of silica with 1:1 ethyl acetate:hexanes (1.0 L). The filtrate was concentrated to give **28** (16.25 g, 95 %) as an orange foam. ^1H NMR (CDCl_3 , 400 MHz): δ 7.24-7.34 (m, 3H), 7.14-7.24 (m, 3H), 7.02-7.1 (m, 3H), 6.54 (dt, $J = 15.9, 1.4$ Hz, 1H), 6.31 (dt, $J = 15.9, 5.6$ Hz, 1H), 4.86 (s, 1H), 4.24 (dd, $J = 5.6, 1.4$ Hz, 2H), 3.63 (dd, $J = 16.2, 9.3$ Hz, 1H), 3.24-3.34 (m, 1H), 3.08 (dd, $J = 16.2, 5.7$ Hz, 1H), 2.65 (brs, 1H), 1.70-2.05 (m, 5H), 1.30 (s, 3H), 0.88 (s, 3H). ^{13}C NMR (CDCl_3 , 100 MHz): δ 171.3, 153.3, 143.0, 137.1, 136.2, 130.5, 129.1, 128.9, 128.8, 128.7, 128.6, 127.0, 126.0, 124.9, 83.7, 82.5, 69.1, 66.9, 63.3, 41.5, 40.8, 35.0, 28.5, 23.5, 16.5. HRMS (ESI) Calculated for $\text{C}_{27}\text{H}_{29}\text{NO}_4$ $[\text{M}+\text{Na}]^+$: 454.1989, found 454.1992.

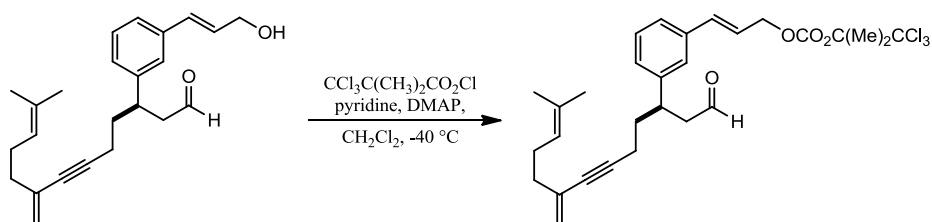


(R)-3-((R)-3-(3-((E)-3-hydroxyprop-1-en-1-yl)phenyl)-12-methyl-8-methylenetridec-11-en-6-ynoyl)-5,5-dimethyl-4-phenyloxazolidin-2-one (30). A mixture of PdCl₂(PPh₃)₂ (641mg, 0.913 mmol), CuI (349 mg, 1.83 mmol), diisopropylamine (12.8 mL, 91.3 mmol) and vinyl triflate **29** (11.31 g, 43.8 mmol) in argon-sparged THF (40 mL) and DMF (10 mL) was cooled to 0 °C, and a solution of alkyne (**28**) (15.75 g, 36.5 mmol) in THF (50 mL) was added over 10 min. The reaction was allowed to warm to room temperature and stir an additional 1h. The reaction mixture was diluted with EtOAc, washed with H₂O, brine, dried over MgSO₄ and concentrated. Purification by flash chromatography (SiO₂, gradient 0 → 50% EtOAc/hexanes) gave diene-yne **30** (12.04 g, 61%) as a light brown oil. ¹H NMR (CDCl₃, 300 MHz): δ 7.28-7.38 (m, 3H), 7.20-7.24 (m, 3H), 7.04-7.14 (m, 3H), 6.57 (brd, *J* = 15.9 Hz, 1H), 6.34 (td, *J* = 15.9, 5.6 Hz, 1H), 5.19 (d, *J* = 1.3 Hz, 1H), 5.11 (d, *J* = 1.3 Hz, 1H), 5.05-5.10 (m, 1H), 4.87 (s, 1H), 4.29 (d, *J* = 5.6 Hz, 2H), 3.66 (dd, *J* = 16.1, 9.4 Hz, 1H), 3.23-3.36 (m, 1H), 3.10 (dd, *J* = 16.1, 5.4 Hz, 1H), 1.76-2.23 (m, 9H), 1.67 (s, 3H), 1.59 (s, 3H), 1.33 (s, 3H), 0.91 (s, 3H). ¹³C NMR (CDCl₃, 75 MHz): δ 171.4, 153.3, 143.2, 137.0, 136.3, 132.1, 131.8, 131.1, 129.0, 128.9, 128.8, 128.7, 127.3, 126.6, 126.1, 124.9, 123.6, 119.9, 89.2, 82.5, 81.6, 67.0, 63.7, 41.6, 41.1, 37.7, 35.5, 28.6, 26.9, 25.8, 23.6, 17.8, 17.5. HRMS (ESI) Calculated for C₃₅H₄₁NO₄ [M+Na]⁺: 562.2933, found 562.2912.



(R,E)-3-(3-(3-hydroxyprop-1-en-1-yl)phenyl)-12-methyl-8-methylenetridec-11-en-6-ynal (31). A solution of 1-acyl-oxazolidin-2-one **30** (8.84 g, 16.4 mmol) in toluene (160 mL) was cooled to -78 °C and diisobutylaluminum hydride (49 mL, 1.0 M/hexanes) was added. After stirring 20 min at this temperature, 10 % (w/v) aqueous Rochelle's salt (100 mL) was added and the reaction was warmed to rt, stirred for 15 min, and filtered through Celite. The aqueous filtrate was extracted with EtOAc and the combined organic phase was washed with brine, dried over Na₂SO₄ and concentrated. The partially solidified residue was reconstituted in Et₂O and treated with pentane to induce crystallization. After chilling, the mixture was

filtered and the cake washed with cold 2:1 pentane:Et₂O to recover the chiral auxiliary (1.503 g, 48%) as colorless needles. The filtrate was concentrated to give **31** (5.49 g) as a light brown oil, which was used without purification. An aliquot was purified for characterization (preparative TLC eluent 1:1:1 hexane:DCM:EtOAc). ¹H NMR (CDCl₃, 400 MHz): δ 9.66 (t, *J* = 1.8 Hz, 1H), 7.30-7.24 (m, 3H), 7.23-7.20 (m, 1H), 6.60 (brd, *J* = 15.9 Hz, 1H), 6.36 (dt, *J* = 15.9, 5.6 Hz, 1H), 5.23 (d, *J* = 1.1 Hz, 1H), 5.16 (d, *J* = 1.1 Hz, 1H), 5.14-5.08 (m, 1H), 4.32 (dd, *J* = 5.6, 1.0 Hz, 2H), 3.40-3.30 (m, 1H), 2.75 (dt, *J* = 7.1, 1.8 Hz, 2H), 2.26-2.06 (m, 7H), 1.97-1.76 (m, 2H), 1.69 (s, 3H), 1.62 (s, 3H). ¹³C NMR (CDCl₃, 75 MHz): δ 201.5, 143.1, 137.3, 132.2, 131.8, 131.0, 129.2, 129.0, 127.0, 125.9, 125.1, 123.5, 120.1, 89.0, 81.9, 63.7, 50.1, 39.0, 37.8, 35.4, 26.9, 25.8, 17.9, 17.4.



(*R,E*)-3-(3-(12-methyl-8-methylene-1-oxotridec-11-en-6-yn-3-yl)phenyl)allyl (1,1,1-trichloro-2-methylpropan-2-yl) carbonate (2**).** A solution of alcohol **31** (5.49 g, 15.7 mmol) in DCM (160 mL) was cooled to -40 °C. A solution of pyridine (2.0 mL, 25 mmol) and DMAP (230 mg, 1.9 mmol) in DCM (50 mL) was added, followed by dropwise addition of 1,1-dimethyl-2,2,2-trichloroethyl chloroformate (5.25 g, 21.9 mmol) in DCM (50 mL). The reaction was stirred for 2 h, diluted with EtOAc (700 mL), washed with cold sat. NaHCO₃, H₂O, brine, dried over MgSO₄ and concentrated. Purification by flash chromatography (SiO₂, 15% EtOAc/hexanes) afforded **2** as a colorless oil (4.75 g, 52% from **30**). ¹H NMR (CDCl₃, 500 MHz): δ 9.66 (t, *J* = 1.9 Hz, 1H), 7.10-7.32 (m, 4H), 6.67 (brd, *J* = 15.8 Hz, 1H), 6.30 (dt, *J* = 15.8, 6.6 Hz, 1H), 5.23 (s, 1H), 5.15 (s, 1H), 5.08-5.14 (m, 1H), 4.78 (d, *J* = 6.7 Hz, 2H), 3.33-3.42 (m, 1H), 2.75 (dt, *J* = 7.5, 1.9 Hz, 2H), 2.07-2.29 (m, 6H), 1.96 (s, 6H), 1.75-1.95 (m, 2H), 1.69 (s, 3H), 1.62 (s, 3H). ¹³C NMR (CDCl₃, 125 MHz): δ 201.3, 152.4, 143.2, 136.6, 135.1, 132.2, 131.8, 129.2, 127.6, 126.1, 125.4, 123.5, 122.7, 120.2, 105.6, 90.1, 88.9, 81.9, 68.6, 50.1, 39.0, 37.8, 35.4, 26.9, 25.8, 21.3 (2), 17.9, 17.4. [α]_D²⁰ = +29.0 (*c* 0.56, CHCl₃).

Indole-oxazole composite macrocycles **41-45**:

All work related contained within the oxazole-indole series was performed by Tristan E. Rose. Tabulated spectroscopic data and synthetic methods related to these compounds will be described elsewhere.

Synthesis of composite macrocycles of Gly-Thi-Trp-5HTA:

Peptide Synthesis:

H-Gly-Trp-Thi-5-Hydroxytryptamine was prepared by attachment of Fmoc-5-hydroxytryptamine to 2-Chlorotritylchloride resin (100-200 mesh, 0.84 mmol/g) via the phenolic oxygen as follows: A solution of Fmoc-5-hydroxytryptamine (398 mg, 1.00 mmol) in dichloromethane (10 ml) was added to a flask containing 2-Chlorotritylchloride resin (840 mg, 1.00 mmol) followed by $i\text{Pr}_2\text{NEt}$ (174 μL , 1.00 mmol). The mixture was agitated for 10 minutes then an addition aliquot of $i\text{Pr}_2\text{NEt}$ (261 μL , 1.50 mmol) was added and the mixture was agitated for an addition 2 hours. Methanol (500 μL) was added and the resin was mixed for an addition 15 minutes, then filtered through a sintered glass funnel. The resin was washed with CH_2Cl_2 (3x), DMF (3x), CH_3OH (3x), and dried under high vacuum. The substitution was estimated by mass. Chain elongation was performed as described above. Fmoc-deprotection was achieved with 20% piperidine in DMF (2 x 30 min). The reaction vessel was washed with DMF (3x) and CH_2Cl_2 (2x). The vessel was then charged with the appropriate Fmoc-amino acid (4 equiv) and TBTU (4 equiv) followed by DMF (10-20 ml) and $i\text{Pr}_2\text{NEt}$ (10 eq). The resin was agitated for 2 hours, drained, and washed with DMF (3X). Cleavage from the resin was achieved with 1:1:8 AcOH:TFE: CH_2Cl_2 for 2 hours.

NMR methods:

NMR spectra were recorded on Bruker Avance (300, 500 or 600 MHz), DRX (500 MHz) and ARX (400 MHz) spectrometers. Data for ^1H NMR spectra are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration), and are referenced to a residual protonated solvent peak.¹ ^{13}C resonances are reported in terms of chemical shift (δ ppm) as referenced to the residual DMSO peak. For mass-limited samples, solvent magnetic susceptibility matched Shigemi tubes were used with a sample volume of ~ 300 μL . Optimization of on-axis shims was accomplished using the TopShim automated tool within Bruker Topspin™ 2.1. Optimization of off-axis shims was performed manually.² ^1H 90° transmitter pulse lengths were calibrated by back calculation from the 360° or 180° null.³ The pulse width or power level for soft pulses and shaped pulses were calculated using the Shape Tool within TopSpin™ 2.1. ^1H - ^1H COSY spectra were recorded using a phase sensitive, gradient enhanced double-quantum-filtered experiment, using States-TPPI acquisition.⁴ TOCSY spectra were recorded using a sensitivity improved, phase sensitive experiment using a 60ms DIPSI-2 pulse train for homonuclear Hartman-Hahn transfer.⁵ NOESY spectra were recorded using a phase sensitive

¹ Gottlieb, H.E.; Kotlyar, V.; Nudelman, A., *J. Org. Chem.*, **1997**, 62, 7512-7515.

² Berger, S.; Braun, S., *200 and More NMR Experiments*, Wiley-VCH, Weinheim, **2004**, 6-11.

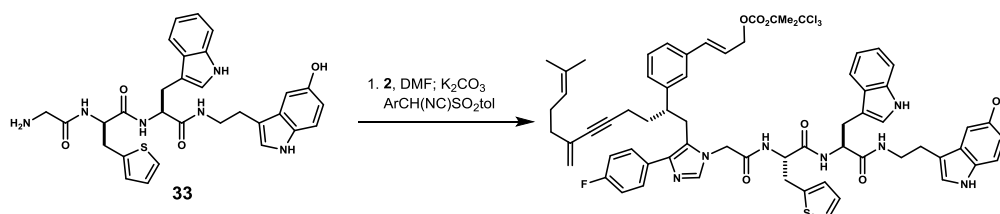
³ a) Claridge, T.D.W., *High-Resolution NMR Techniques in Organic Chemistry*, Pergamon, Oxford, **1999**, 94-97. b) Berger, S.; Braun, S., *200 and More NMR Experiments*, Wiley-VCH, Weinheim, **2004**, 15-17.

⁴ a) Hurd, R.E., *J. Magn. Reson.*, **1990**, 87, 422-428. b) Brereton, I.M.; Crozier, S.; Field, J.; Doddrell, D.M., *J. Magn. Reson.*, **1991**, 93, 54-62. c) Shaw, A.A.; Salaun, C.; Dauphin, J.F.; Ancian, B., *J. Magn. Reson. Ser. A*, **1996**, 120, 110-115.

⁵ Cavanagh, J.; Rance, M., *J. Magn. Reson.*, **1990**, 88, 72-85.

experiment with selection gradients during the mixing time.⁶ ROESY spectra were recorded using a phase sensitive experiment with selection gradients and water suppression with excitation sculpting.⁷ Carbon chemical shifts were measured from 2D plots of either HSQC spectra for protonated carbons or HMBC spectra for non-protonated carbons. ^1H - ^{13}C HSQC spectra were recorded using a sensitivity improved phase sensitive experiment using an adiabatic shape pulse for ^{13}C inversion, and ^{13}C decoupling during acquisition.⁸ Experimental parameters were optimized for $^1J_{\text{CH}} = 145\text{ Hz}$. ^1H - ^{13}C HMBC spectra were recorded using a gradient selected experiment with a two-fold J-filter optimized for $^1J_{\text{CH}} = 125\text{--}165\text{ Hz}$. Experimental parameters were optimized for long range $^nJ_{\text{CH}} = 8\text{ Hz}$.

Imidazole S1 -



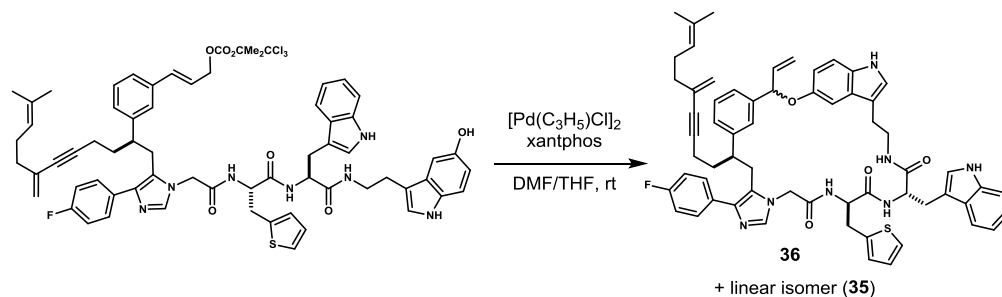
To a solution of Gly-Thi-Trp-5HTA (1.36 g, 2.23 mmol, 1.2 eq.) in DMF (12.5 mL) was added Cs_2CO_3 (1.94g, 5.95 mmol, 3.2 equiv) followed by a 0.3M solution of **1** in DMF (6.2 ml, 1.86 mmol, 1 eq.) and mixed for 4 hours to induce imine formation. Solid (*para*-fluorophenyl)tosylmethylisocyanate (445 mg, 2.23 mmol, 1.2 equiv) was added directly to the reaction vessel and the resulting solution was stirred overnight. The reaction was filtered and the DMF removed in vacuo. The crude residue purified by column chromatography (dry loading, SiO_2 , 0-10% MeOH/ CHCl_3) to afford imidazole **S1** (993 mg, 47%). ^1H NMR ($\text{MeOH}-d_4$, 600 MHz): δ 7.86 (s, 1H), 7.5 (d, $J = 7.9\text{ Hz}$, 1H), 7.25-7.34 (m, 5H), 7.11-7.17 (m, 3H), 7.04-7.10 (m, 3H), 6.95-7.03 (m, 5H), 6.88 (d, $J = 2.1\text{ Hz}$, 1H), 6.82-6.86 (m, 2H), 6.74-6.80 (m, 3H), 6.65 (dd, $J = 8.6, 2.3\text{ Hz}$, 1H), 6.5 (d, $J = 16\text{ Hz}$, 1H), 6.16 (dt, $J = 15.9, 6.4\text{ Hz}$, 1H), 4.98-5.10 (m, 4H), 4.63-2.73 (m, 3H), 5.45-4.63 (m, 2H), 4.37 (d, $J = 16.8\text{ Hz}$, 1H), 4.22 (d, $J = 16.9\text{ Hz}$, 1H), 3.20-3.40 (m, 6H), 2.99-3.20 (m, 4H), 2.73-2.89 (m, 3H), 2.53-2.70 (m, 3H), 1.93-2.11 (m, 7H), 1.9 (s, 6H), 1.70-1.80 (m, 2H), 1.62 (s, 3H), 1.52 (s, 3H). ^1H NMR ($\text{MeCN}-d_3$, 150 MHz): 171.9, 170.9, 167.7, 161.0, 152.3, 149.7, 142.8, 138.5, 137.5, 136.6, 136.2, 134.4, 131.8, 131.7, 131.5, 131.0, 129.1, 129.1, 128.4, 128.0, 127.5, 127.2, 126.6, 126.4, 126.3, 125.9, 124.9, 124.3, 123.4, 123.2, 122.9, 122.3, 121.2, 118.9, 118.6, 118.1, 114.8, 114.7, 111.3, 111.0, 111.0, 110.9, 109.4, 105.4, 102.2, 89.5, 88.7, 81.2, 78.1, 68.2, 54.7, 54.5, 46.7, 44.3, 39.8, 37.4, 33.7, 31.4, 30.4, 27.7, 26.5, 24.7, 24.5, 20.2, 16.6. MS (ESI) Calculated for $\text{C}_{67}\text{H}_{69}\text{Cl}_3\text{FN}_7\text{O}_4\text{S}$ $[\text{M}+\text{H}]^+$: 1240.4, found 1240.8.

⁶ Wagner, R.; Berger, S., *J. Magn. Reson.*, **1996**, 123 A, 119-121.

⁷ a) Bax, A.; Davis, D.G., *J. Magn. Reson.*, **1985**, 63, 207-213. b) Hwang, T.L.; Shaka, A.J., *J. Magn. Reson., Series A*, **1995**, 112, 275-279.

⁸ Palmer, A.G. III; Cavanagh, J.; Wright, P.E.; Rance, M., *J. Magn. Reson.*, **1991**, 93, 151-170. b) Kay, L.E.; Keifer, P.; Saarinen, T., *J. Am. Chem. Soc.*, **1992**, 114, 10663-10665. c) Schleucher, J.; Schwendinger, M.; Sattler, M.; Schmidt, P.; Schedletsky, O.; Glaser, S.J.; Sorensen, O.W.; Griesinger, C., *J. Biomol. NMR* **4**, **1994**, 301-306.

Gly-Thi-Trp-5HTA Macrocycles **35-36** -



To a solution of imidazole **S1** (146 mg, 0.118 mmol) in degassed DMF (30 ml, 5 mM) was added catalyst solution (3.5 ml, 0.04 mol% $[\text{PdCl}(\text{C}_3\text{H}_5)]_2$, 0.10 mol% xantphos). The reaction was allowed to stir at room temperature for two hours as monitored by HPLC-MS (C18, MeCN/H₂O, 0.1%TFA). The reaction was diluted with EtOAc (200 ml) and washed with 0.1M NaCN (aq), H₂O (3x) and brine. The organic layer was dried over Na₂SO₄, filtered and solvent removed in vacuo. The macrocyclic ethers were purified by preparative HPLC (Waters Sunfire C18, 30x150mm, MeCN/H₂O, 0.1% TFA) and lyophilized to provide **35** and **36** (34 mg, 53 %). For characterization analytical samples each isomer were isolated. For subsequent reactions a mixture of macrocyclic ether isomers **35** and **36** was employed.

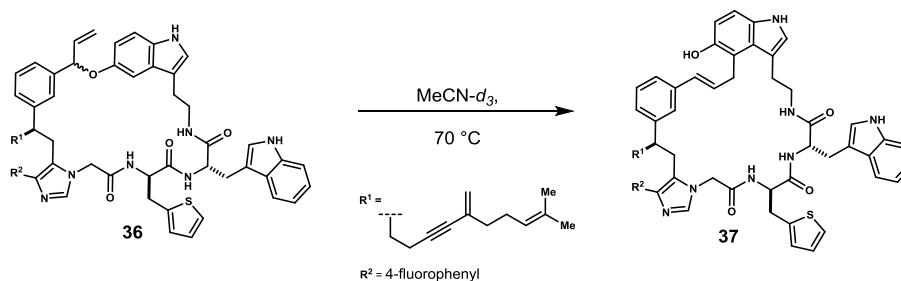
The solution of catalyst was prepared as follows: An oven-dried, serum-topped vial was placed in a glove bag and charged with $[\text{PdCl}(\text{C}_3\text{H}_5)]_2$ (14 mg, 0.038 mmol) and xantphos (55 mg, 0.095 mmol). The vial is sealed, removed from the glove bag, and degassed THF (7.0 ml) was added, followed by degassed DMF (7.0 ml). The resulting yellow solution was stirred under argon for 30 minutes.

Data for **35** - ¹H NMR (MeCN-*d*₃, 600 MHz): δ 9.12 (s, 1H), 8.93 (s, 1H), 7.67-7.71 (m, 1H), 7.56 (d, J = 8.3 Hz, 1H), 7.38 (d, J = 8.2 Hz, 1H), 7.38 (br. s, 1H), 7.3 (d, J = 8.5 Hz, 1H), 7.24 (s, 1H), 7.22 (br. d, J = 7.9 Hz, 1H), 7.14-7.19 (m, 3H), 7.11-7.14 (m, 2H), 7.09 (d, J = 7.7 Hz, 1H), 7.06 (d, J = 6.8 Hz, 1H), 7.03 (d, J = 2.3 Hz, 1H), 7.01 (d, J = 2.4 Hz, 1H), 6.91 (br. d, J = 8.2 Hz, 1H), 6.86 (dd, J = 8.8, 2.4 Hz, 1H), 6.70-6.75 (m, 2H), 6.65-6.68 (m, 2H), 6.63 (br. d, J = 7.6 Hz, 1H), 6.51 (dt, J = 16.4, 5.2 Hz, 1H), 6.4 (d, J = 6.2 Hz, 1H), 5.11-5.13 (m, 1H), 5.05-5.07 (m, 1H), 5.01-5.05 (m, 1H), 4.88 (ddd, J = 14.8, 5.3, 1.5 Hz, 1H), 4.83 (ddd, J = 14.8, 5.4, 1.4 Hz, 1H), 4.54 (ddd, J = 8.1, 8.1, 5.6 Hz, 1H), 4.31 (ddd, J = 10.0, 5.7, 4.4 Hz, 1H), 4.21 (d, J = 17.6 Hz, 1H), 3.63 (d, J = 17.5 Hz, 1H), 3.41-3.48 (m, 1H), 3.32-3.40 (m, 1H), 3.25 (dd, J = 14.7, 5.4 Hz, 1H), 2.91 (dddd, J = 15.4, 10.7, 5.6, 5.6 Hz, 1H), 2.70-2.82 (m, 4H), 2.52 (dd, J = 15.6, 9.5 Hz, 1H), 1.99-2.10 (m, 6H), 1.91-1.95 (m, 2H), 1.82-1.90 (m, 2H), 1.73-1.82 (m, 1H), 1.66 (s, 3H), 1.56 (s, 3H). ¹H NMR (MeCN-*d*₃, 150 MHz): 171.5, 170.6, 169.8, 152.4, 144.3, 142.4, 139.6, 139.5, 138.4, 138.3, 137.4, 132.9, 132.8, 132.8, 129.8, 129.3, 128.8, 128.6, 128.5, 128.0, 127.5, 127.0, 126.3, 125.9, 124.4, 124.2, 123.9, 122.5, 120.5, 119.9, 119.6, 116.6, 116.1, 115.9, 115.3, 113.1, 113.0, 112.3,

111.4, 104.7, 90.1, 82.4, 82.3, 57.4, 54.3, 48.0, 45.7, 40.1, 38.2, 34.7, 32.1, 31.0, 27.4, 25.8, 25.4, 17.9, 17.7. MS (ESI) Calculated for $C_{62}H_{62}FN_7O_4S$ $[M+H]^+$: 1020.5, found 1020.6

Data for **36** - 1H NMR (MeCN- d_3 , 600 MHz): δ 9.21 (s, 1H), 8.94 (s, 1H), 7.64 (d, J = 5.5 Hz, 1H), 7.63 (d, J = 5.7 Hz, 1H), 7.58 (d, J = 8.2 Hz, 1H), 7.43 (d, J = 8.5 Hz, 1H), 7.38 (d, J = 7.4 Hz, 1H), 7.29 (d, J = 9.1 Hz, 1H), 7.14-7.24 (m, 6H), 7.04-7.12 (m, 4H), 6.99 (br. s, 1H), 6.86 (br. s, 1H), 6.82 (dd, J = 8.8, 2.2 Hz, 1H), 6.78 (d, J = 7.7 Hz, 1H), 6.66 (dd, J = 4.5, 4.5 Hz, 1H), 6.61 (br. s, 1H), 6.51-6.57 (m, 2H), 6.15-6.19 (m, 1H), 6.11 (ddd, J = 17.0, 10.6, 6.3 Hz, 1H), 5.79 (d, J = 6.4 Hz, 1H), 5.33 (d, J = 17.2 Hz, 1H), 5.19 (d, J = 10.2 Hz, 1H), 5.15 (br. s, 1H), 5.11 (br. s, 1H), 5.02-5.07 (m, 1H), 4.60-4.65 (m, 1H), 4.11-4.17 (m, 1H), 3.66 (d, J = 17.7 Hz, 1H), 3.56 (ddd, J = 18.0, 13.6, 6.9 Hz, 1H), 3.28-3.39 (m, 3H), 3.12 (dd, J = 14.9, 8.5 Hz, 1H), 2.86-2.97 (m, 4H), 2.75-2.81 (m, 3H), 2.72 (dd, J = 15.6, 2.6 Hz, 1H), 2.21-2.33 (m, 2H), 2.19 (ddd, J = 17.0, 6.1, 6.1 Hz, 1H), 2.07-2.13 (m, 3H), 2.02-2.05 (m, 3H), 1.83-1.90 (m, 2H), 1.66 (s, 3H), 1.56 (s, 3H). Spectra for the remaining branched diastereomer is below. Stereochemistry of the vinylphenyl methine was not determined. MS (ESI) Calculated for $C_{62}H_{62}FN_7O_4S$ $[M+H]^+$: 1020.5, found 1020.6

Ortho-Aryl Claisen product **37** -



An analytical sample of **36** (~ 1 mg) in MeCN- d_3 was heated to 70 °C using the Bruker variable temperature unit. Slow conversion to **37** was observed by 1H NMR. The reaction was removed and heated to 70°C in an oil bath for 12 hours. The reaction was periodically monitored by NMR for conversion. The macrocyclic linkage was assigned by TOCSY/HMBC correlation. 1H NMR (MeCN- d_3 , 600 MHz): δ 9.21 (s, 1H), 8.97 (s, 1H), 7.68-7.74 (m, 2H), 7.56 (d, J = 7.8 Hz, 1H), 7.42 (br. s, 1H), 7.4 (d, J = 8.2 Hz, 1H), 7.13-7.23 (m, 6H), 7.05-7.12 (m, 3H), 6.95-7.04 (m, 3H), 6.75-6.81 (m, 2H), 6.65-6.71 (m, 2H), 6.63 (d, J = 2.8 Hz, 1H), 6.57 (d, J = 7.7 Hz, 1H), 6.39 (d, J = 3.8 Hz, 1H), 6.13 (d, J = 16.3 Hz, 1H), 5.12 (d, J = 1.7 Hz, 1H), 5.06 (d, J = 1.7 Hz, 1H), 4.99-5.03 (m, 1H), 4.55 (ddd, J = 7.7, 7.7, 5.2 Hz, 1H), 4.18 (ddd, J = 9.7, 4.9, 4.0 Hz, 1H), 4.03 (d, J = 17.3 Hz, 1H), 3.92 (dd, J = 17.0, 3.2 Hz, 1H), 3.84 (dd, J = 16.8, 5.5 Hz, 1H), 3.42-3.53 (m, 1H), 3.35 (d, J = 17 Hz, 1H), 3.31 (dd, J = 14.9, 4.9 Hz, 1H), 3.19 (dd, J = 15.0, 7.7 Hz, 1H), 3.13 (dd, J = 15.3, 3.8 Hz, 1H), 3.01 (ddd, J = 15.1, 9.3, 6.0 Hz, 1H), 2.84-2.93 (m, 2H), 2.81 (dd, J = 15., 9.9 Hz, 1H), 2.74 (dd, J = 15.8, 4.8 Hz, 1H), 2.45 (dd, J = 15.6, 9.6 Hz, 1H), 2.13 (ddd, J = 17.1, 5.7 Hz, 1H), 1.82-1.95 (m, 2H), 1.74-1.82 (m, 1H), 1.65 (s, 3H), 1.54 (s, 3H). MS (ESI) Calculated for $C_{62}H_{62}FN_7O_4S$ $[M+H]^+$: 1020.5, found 1020.5.

35

36

MeSO₃H (25 eq.)
 MeNO₂ (5 mM)
 0 °C

37 - 40
 (+ additional isomeric compounds, spectra/partial characterization below)

R¹ =

R² = 4-fluorophenyl

Fraction numbers annotated on spectra below indicate relative compound retention of iterative purifications. For example, Fraction 2-3 (product **38**) was contained in the second fraction of the first purification and purified a second time to reach homogeneity (Fraction 3 on second column). Products **37-40** were unambiguously characterized by a combination of hetero-/homonuclear correlation spectroscopy. An addition six isomers were partially assigned as indicated on copies of the respective NMR. These partial assignments indicated no substitution the Thi and Trp amino acids and were therefore of limited interest. Compound **37** was characterized by John MacMillan and co-workers (UT Southwestern).

Tabulated data for **38** - ^1H NMR (MeOD- d_4 , 600 MHz): δ 8.73 (s, 1H), 7.58 (br. t, J = 4.6 Hz, 1H), 7.52 (d, J = 7.9 Hz, 1H), 7.31 (d, J = 8.1 Hz, 1H), 7.24 (dd, J = 5.2, 1.1 Hz, 1H), 7.07 (dd, J = 7.5, 7.5 Hz, 1H), 7.00-7.05 (m, 4H), 6.95 (br. d, J = 8.1 Hz, 1H), 6.92 (s, 1H), 6.87-6.92 (m, 2H), 6.85-6.87 (m, 1H), 6.83 (d, J = 8.1 Hz, 1H), 6.71 (d, J = 8.7 Hz, 1H), 6.45 (dt, J = 15.5, 5.6 Hz, 1H), 6.18 (d, J = 15.7 Hz, 1H), 5.54 (s, 1H), 5.16-2.53 (m, 1H), 4.97 (s, 1H), 4.52 (dd, J = 7.2, 7.2 Hz, 1H), 4.47 (dd, J = 14.0, 7.2 Hz, 1H), 4.37

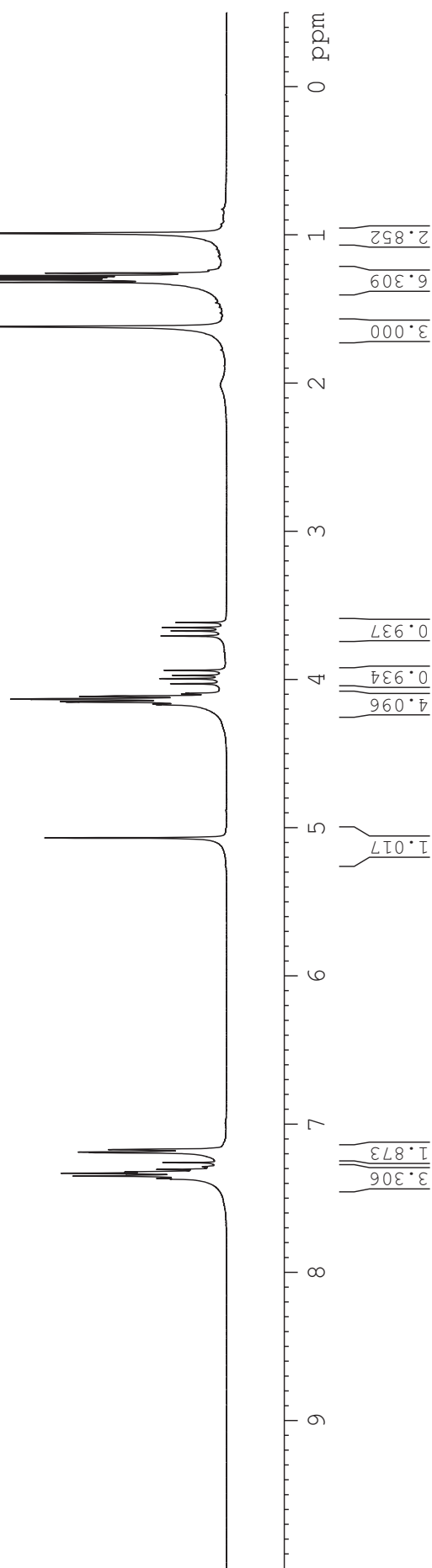
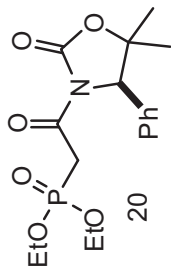
(dd, $J = 10.0, 3.6$ Hz, 1H), 3.88 (br. d, $J = 4.9$ Hz, 2H), 3.44-3.52 (m, 1H), 3.31-3.38 (m, 1H), 3.23 (dd, $J = 14.6, 7.5$ Hz, 1H), 3.09-3.11 (m, 1H), 2.93 (ddd, $J = 15.4, 10.4, 5.2$ Hz, 1H), 2.77-2.86 (m, 11H), 2.38 (d, $J = 16.6$ Hz, 1H), 2.09-2.18 (m, 2H), 1.96-2.06 (m, 1H), 1.93 (d, $J = 13.4$ Hz, 1H), 1.83 (d, $J = 13.2$ Hz, 1H), 1.55-1.64 (m, 2H), 0.76 (s, 3H), 0.73 (s, 3H). MS (ESI) Calculated for $C_{62}H_{62}FN_7O_4S$ $[M+H]^+$: 1020.5, found 1020.2

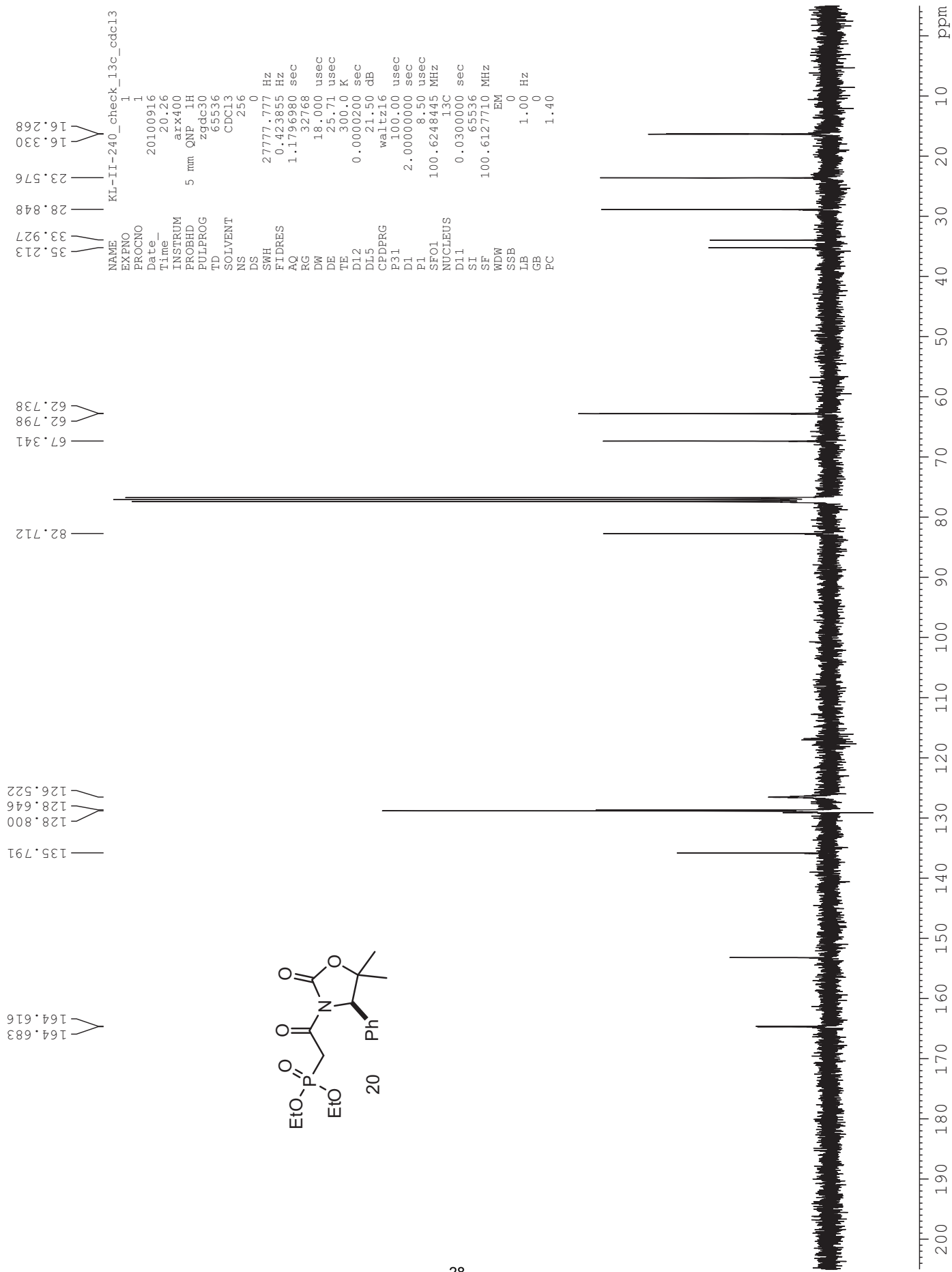
Tabulated data for **39** - 3/1 mixture of olefin isomers - 1H NMR (MeOD- d_4 , 600 MHz): δ 8.34 (s, 1H), 7.52-7.58 (m, 2H), 7.22-7.29 (m, 4H), 7.14 (app t, $J = 7.6$ Hz, 1H), 7.02-7.07 (m, 2H), 6.99 (app t, $J = 7.5$ Hz, 1H), 6.92 (d, $J = 4.7$ Hz, 1H), 6.8 (s, 1H), 6.77 (br. t, $J = 4.8$ Hz, 1H), 6.54-6.62 (m, 2H), 6.41-6.48 (m, 3H), 5.67-5.71 (m, 0.65 H, major isomer), 5.49-5.51 (m, 0.35 H, minor isomer), 4.47-4.57 (m, 2H), 4.20-4.34 (m, 2H), 3.76 (dd, $J = 15.4, 4.2$ Hz, 1H), 3.48-3.54 (m, 2H), 3.45 (dd, $J = 15.0, 7.5$ Hz, 1H), 3.03 (dd, $J = 14.9, 8.4$ Hz, 1H), 2.73-2.85 (m, 3H), 2.56-2.68 (m, 2H), 2.48 (dd, $J = 15.7, 8.3$ Hz, 1H), 2.18 (dd, $J = 14.6, 11.0$ Hz, 1H), 2.02-2.07 (m, 1H), 1.91-1.98 (m, 1H), 1.72-1.82 (m, 2H), 1.54-1.58 (m, 1H), 1.34-1.44 (m, 2H), 1.24-1.31 (m, 2H), 0.93 (s, 1H, minor isomer), 0.92 (s, 1H, minor isomer), 0.86 (br. s, 4H, major isomer). MS (ESI) Calculated for $C_{62}H_{62}FN_7O_4S$ $[M+H]^+$: 1020.5, found 1020.2

Tabulated data for **40** - 3/1 mixture of olefin isomers - 1H NMR (MeOD- d_4 , 600 MHz): δ 8.46 (br. s, 1H), 7.96 (s, 1H), 7.54 (m, 1H), 7.58 (d, $J = 8.1$ Hz, 1H), 7.53 (m, 1H), 7.44-7.51 (m, 2H), 7.28-7.33 (m, 2H), 7.19-7.25 (m, 3H), 7.05-7.09 (m, 2H), 7.02-7.05 (m, 2H), 7.01 (br. s, 1H), 6.96-7.01 (m, 2H), 6.92 (br. s, 1H), 6.87 (dd, $J = 5.2, 3.7$ Hz, 1H), 6.8 (br. d, $J = 3$ Hz, 1H), 6.71 (d, $J = 8.5$ Hz, 1H), 6.6 (br. d, $J = 7.1$ Hz, 1H), 6.53 (dt, $J = 15.4, 5.9$ Hz, 1H), 6.35 (d, $J = 15.4$ Hz, 1H), 5.66-5.70 (m, 0.75 H major isomer), 5.48-5.50 (m, 0.25 H minor isomer), 4.69 (d, $J = 17$ Hz, 1H), 4.46-4.51 (m, 1H), 4.38 (dd, $J = 10.6, 3.6$ Hz, 1H), 4.18-4.27 (m, 1H), 3.91 (dd, $J = 15.9, 5.6$ Hz, 1H), 3.87 (dd, $J = 16.1, 5.2$ Hz, 1H), 3.43-3.50 (m, 2H), 3.24-3.28 (m, 1H), 3.2 (dd, $J = 14.8, 7.3$ Hz, 1H), 3.14 (dd, $J = 15.4, 3.5$ Hz, 1H), 2.94-3.08 (m, 2H), 2.74-2.87 (m, 3H), 1.99-2.05 (m, 2H), 1.72-1.84 (m, 3H), 1.57-1.69 (m, 6H), 1.22-1.31 (m, 3H). MS (ESI) Calculated for $C_{62}H_{62}FN_7O_4S$ $[M+H]^+$: 1020.5, found 1020.2

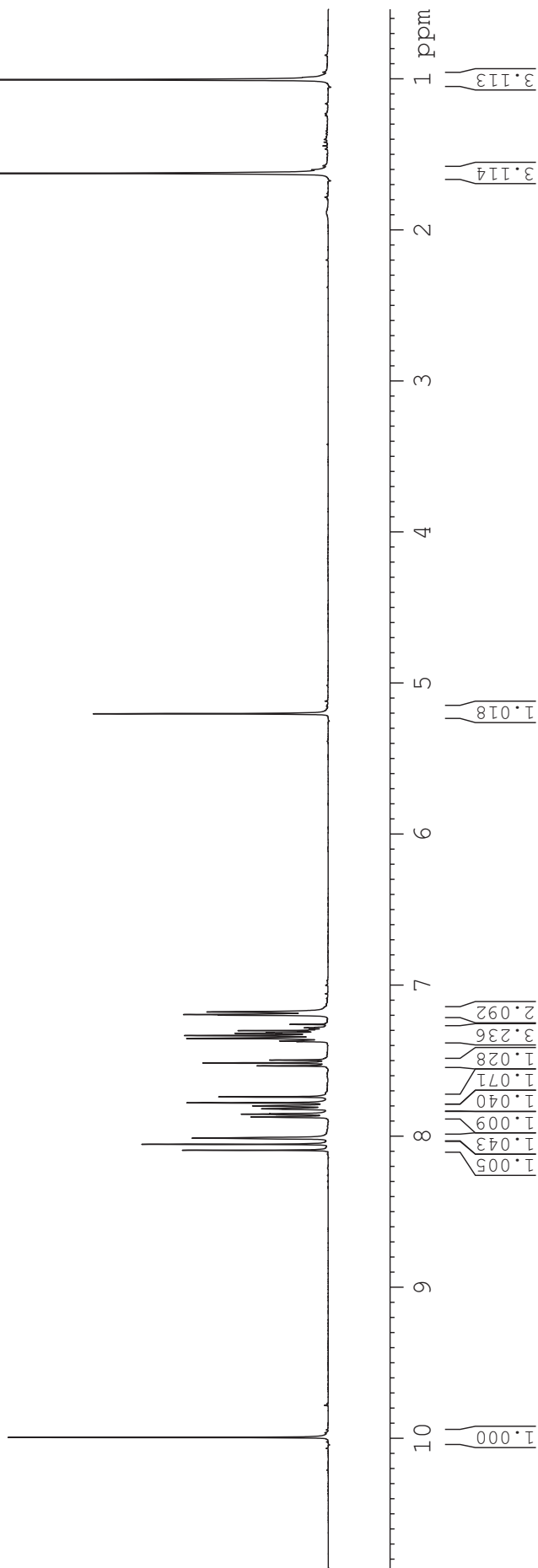
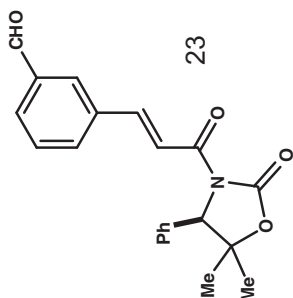
KL-II-240_check_1h_cdcl3

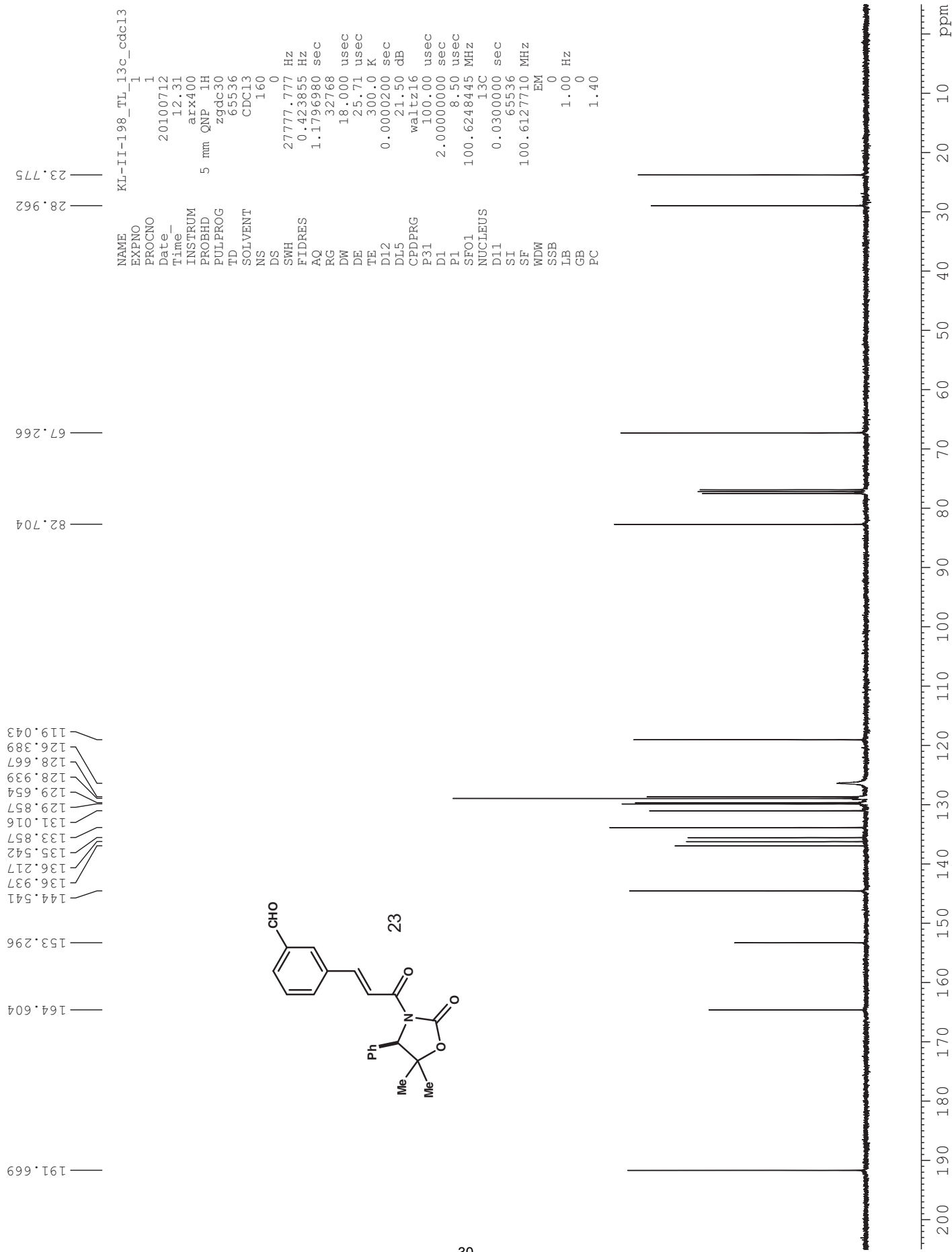
NAME
EXPNO 1
PROCNO 1
Date_ 20100916
Time_ 20.12
INSTRUM arx400
PROBHD 5 mm QNP 1H
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 8
DS 0
SWH 8064.516 Hz
FIDRES 0.123055 Hz
AQ 4.0632820 sec
RG 512
DW 62.000 usec
DE 88.57 usec
TE 300.0 K
D1 2.00000000 sec
P1 7.50 usec
SFO1 400.1324008 MHz
NUCLEUS 1H
SI 65536
SF 400.1300173 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

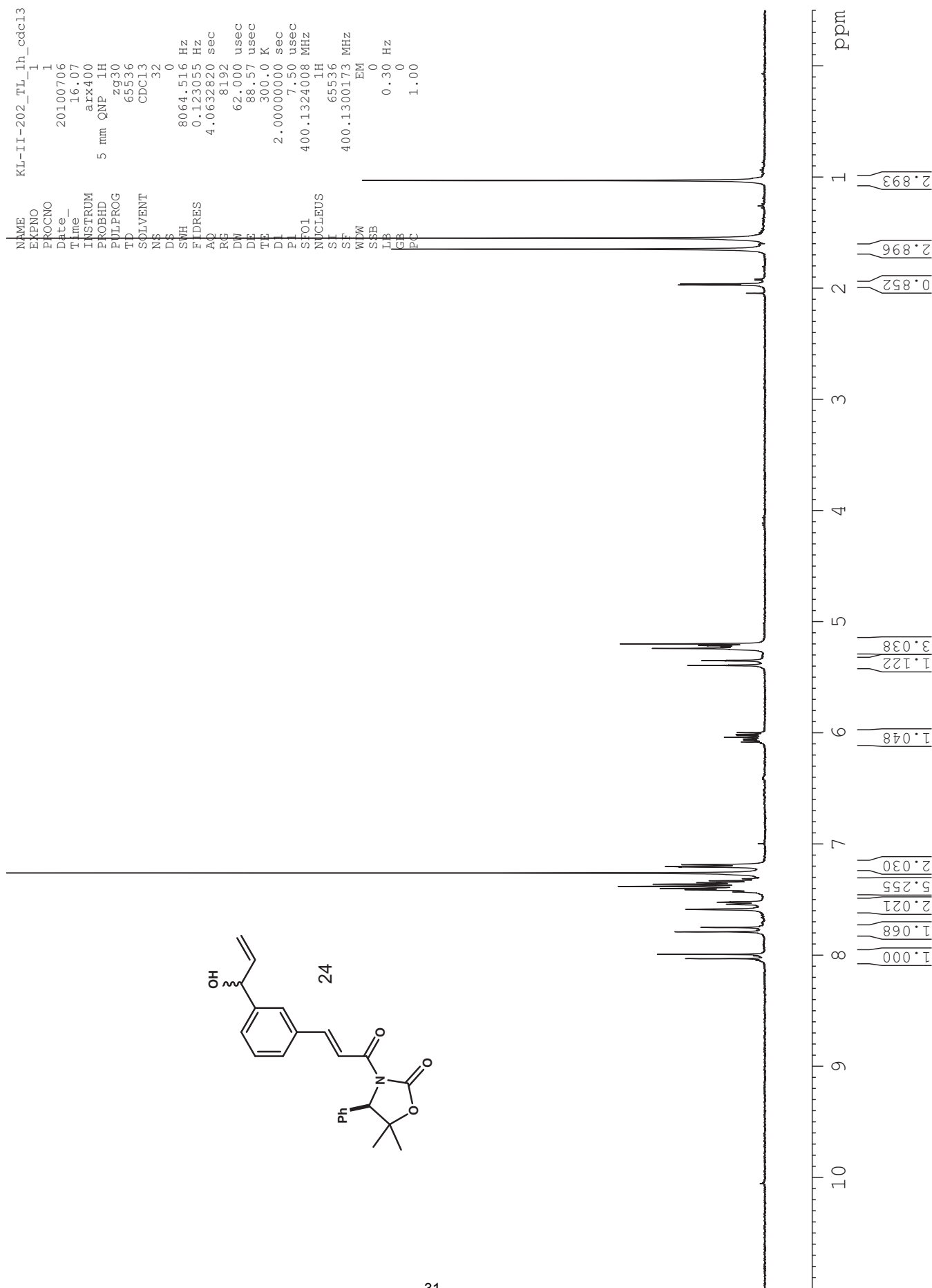


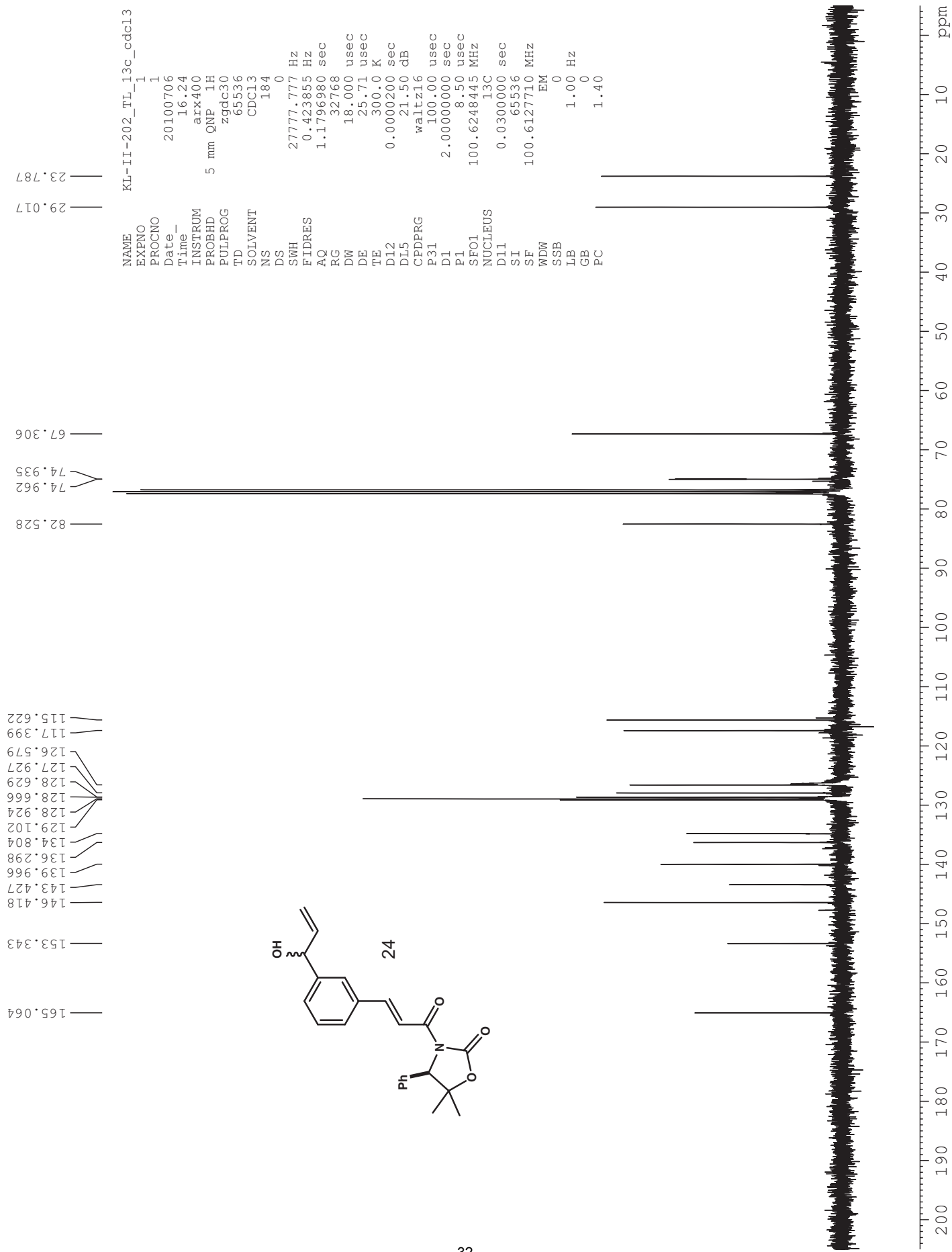


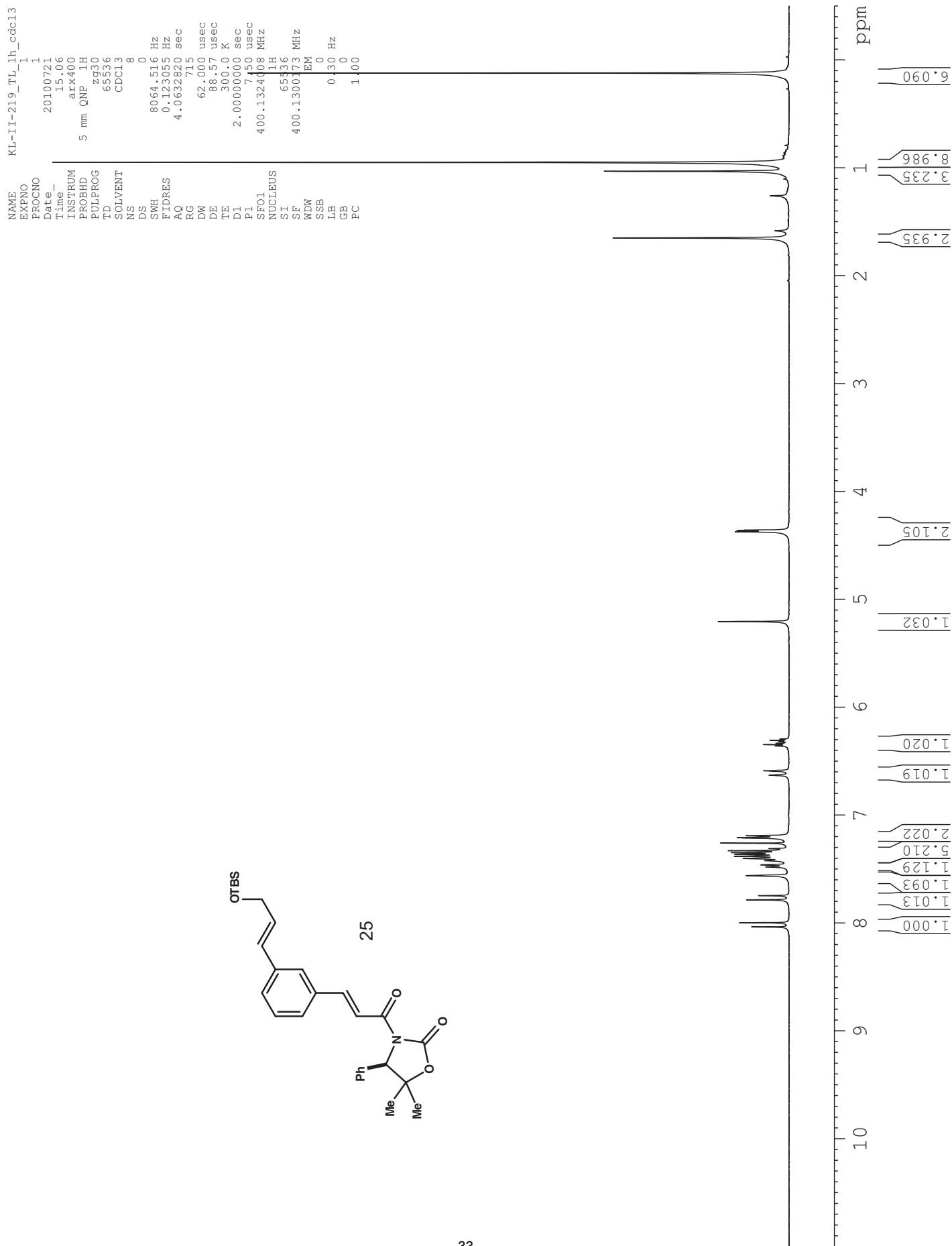
NAME KL-II-198_TL_1h_cdc13
EXPNO 1
PROCNO 1
Date_ 20100712
Time_ 12.21
INSTRUM arx400
PROBHD 5 mm QNP 1H
PULPROG zg30
TD 65536
SOLVENT CDC13
NS 8
DS 0
SWH 8064.516 Hz
FIDRES 0.123055 Hz
AQ 4.0632820 sec
RG 256
DW 62.000 usec
DE 88.57 usec
TE 300.0 K
D1 2.00000000 sec
P1 7.50 usec
SFO1 400.1324008 MHz
NUCLEUS 1H
SI 65536
SF 400.1300173 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

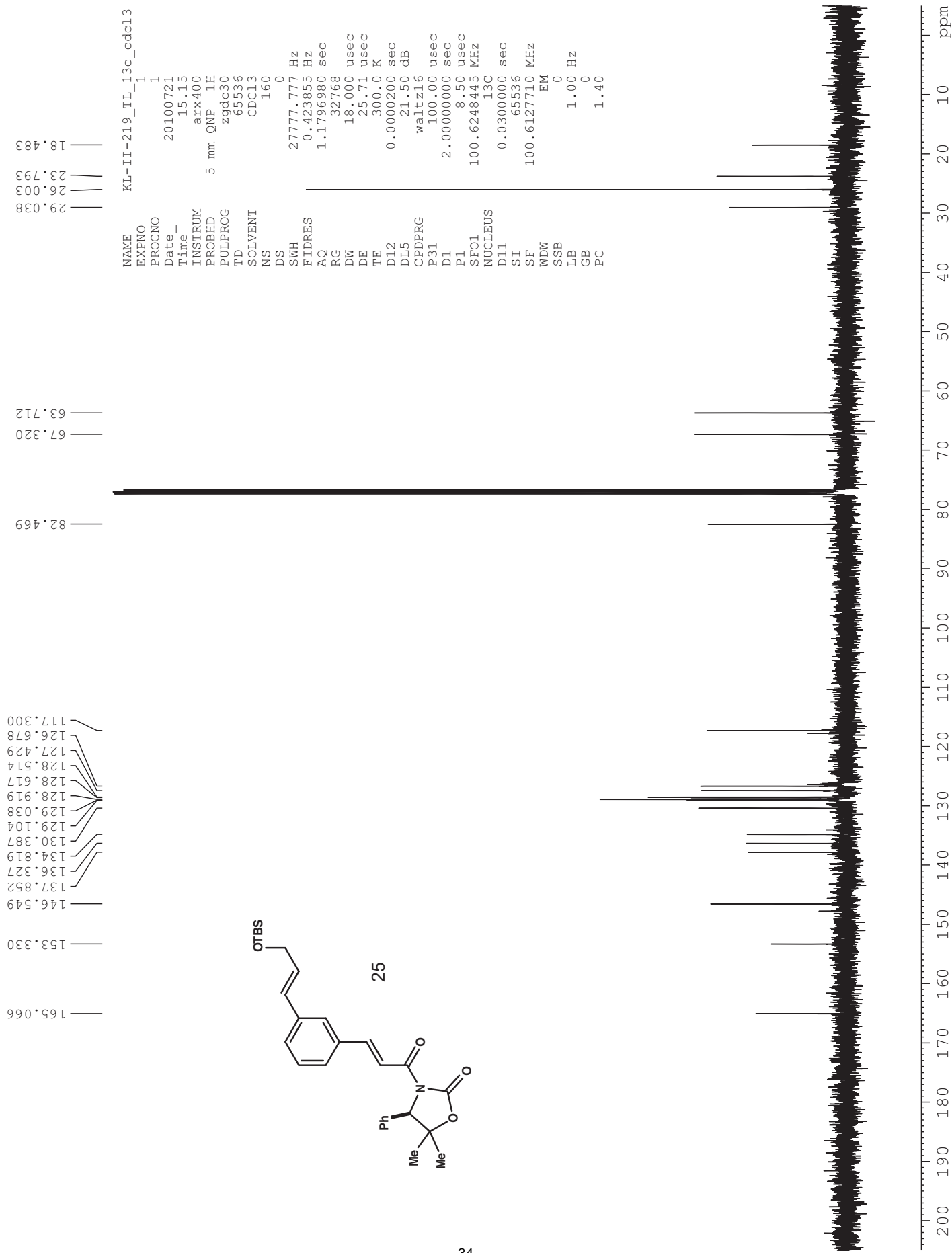


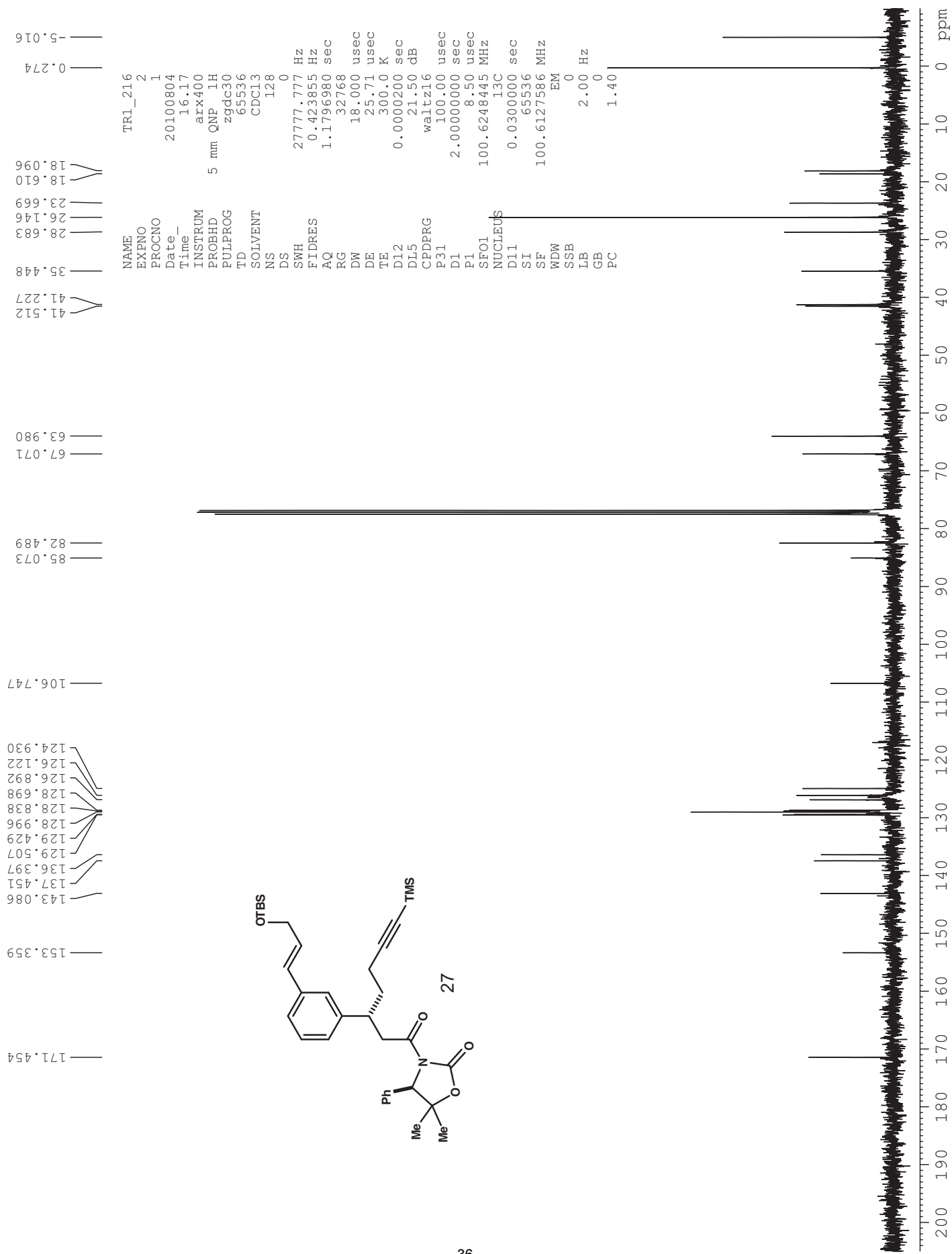






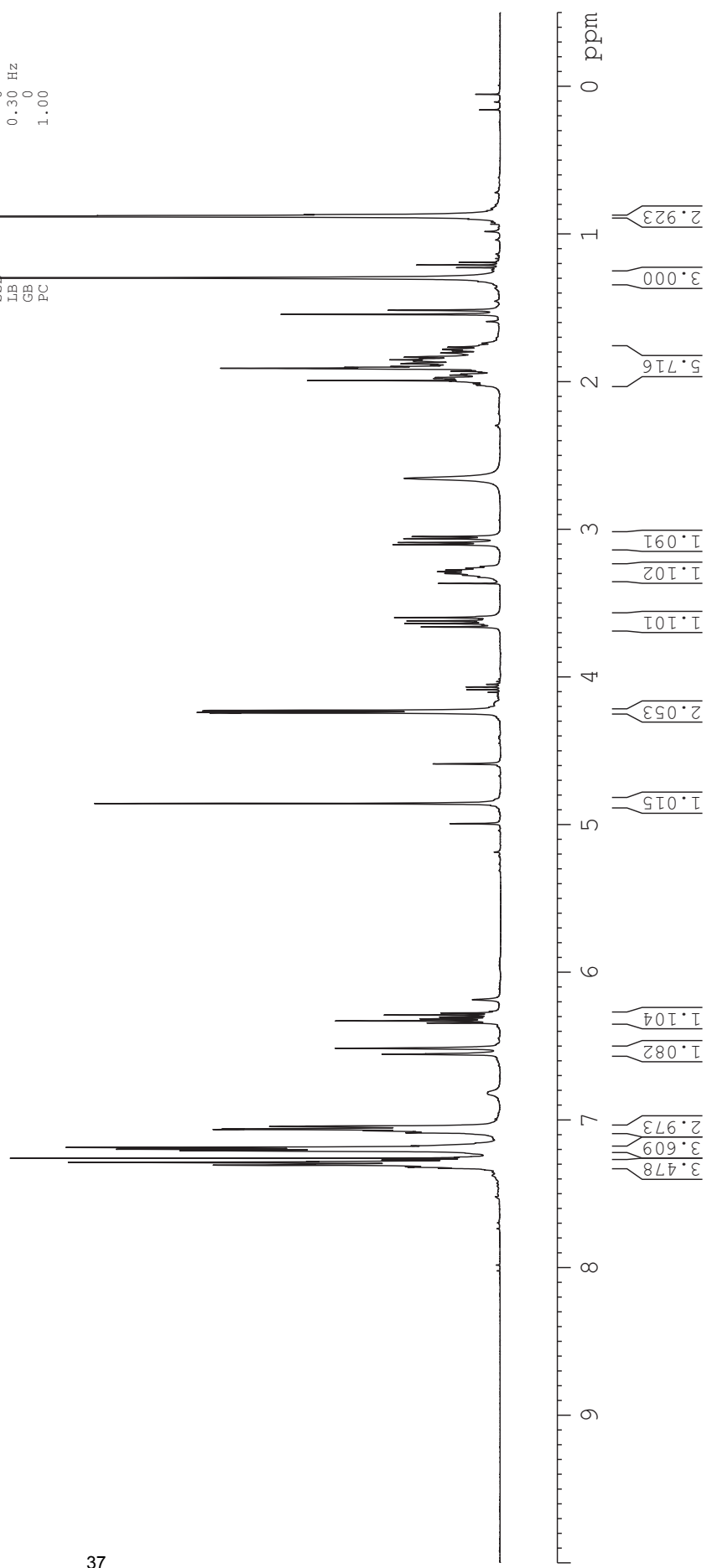
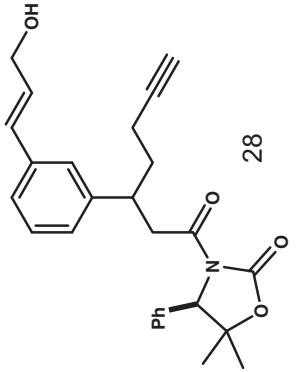


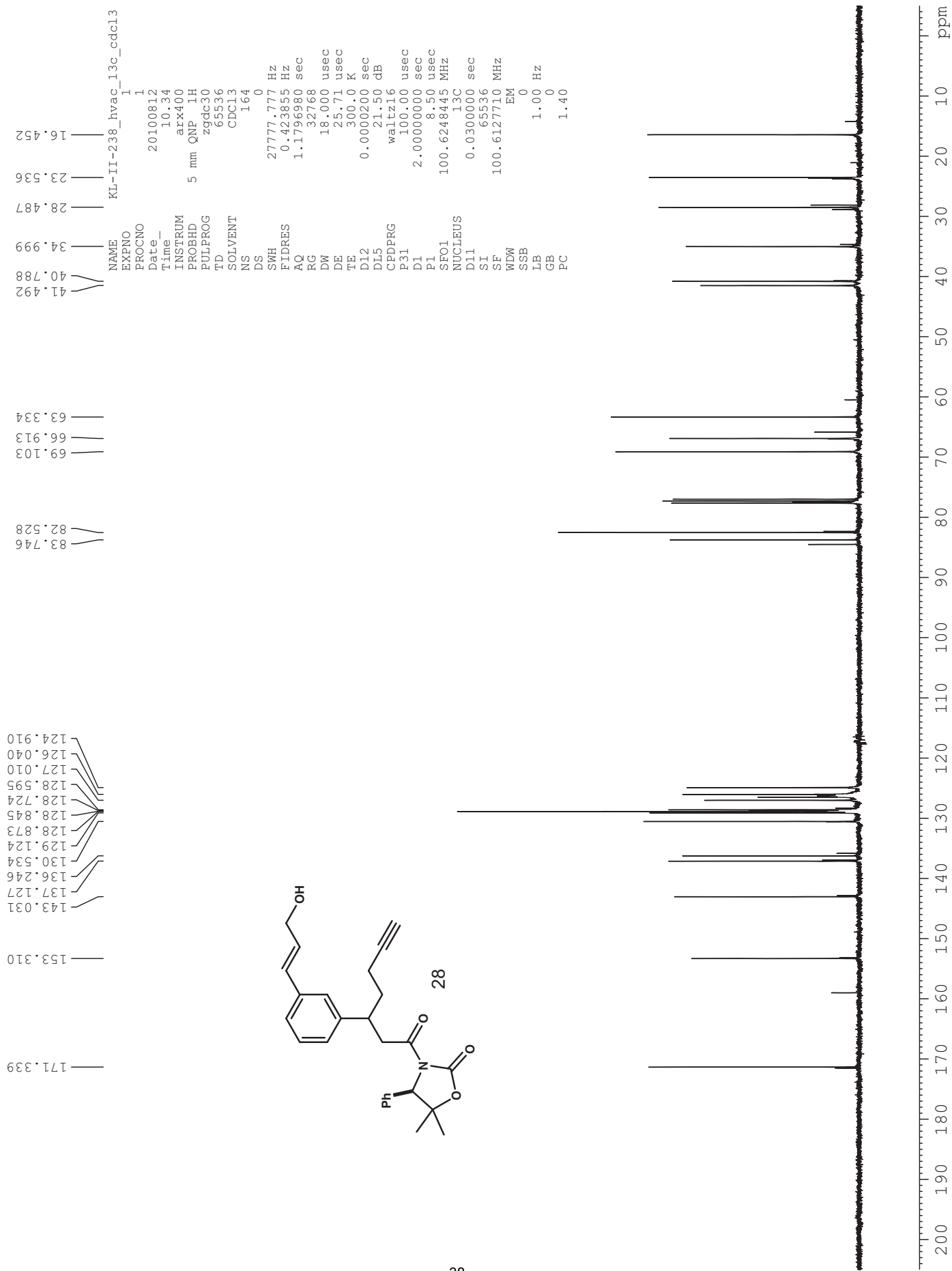




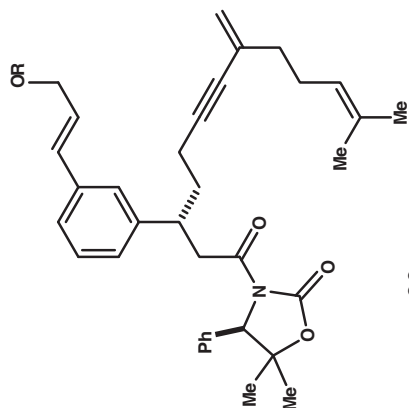
KL-II-238_plug_1h_cdcl3

NAME
EXPNO 1
PROCNO 1
Date_ 20100812
Time_ 10.25
INSTRUM arx400
PROBHD 5 mm QNP 1H
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 8
DS 0
SWH 8064.516 Hz
FIDRES 0.123055 Hz
AQ 4.0632820 sec
RG 90
DW 62.000 usec
DE 88.57 usec
TE 300.0 K
D1 2.00000000 sec
P1 7.50 usec
SFO1 400.1324008 MHz
NUCLEUS 1H
SI 65536
SF 400.1300173 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



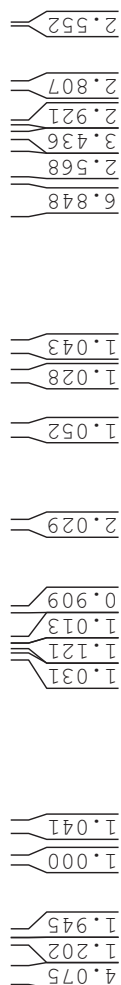


NAME TR1-226
EXPNO 1
PROCNO 1
Date_ 20100903
Time 15.17
INSTRUM advance500
PROBHD 5 mm bb-Z z800
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 64
DS 0
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2769001 sec
RG 71.8
DW 50.000 usec
DE 6.00 usec
TE 296.4 K
D1 2.00000000 sec
MCPRST 0.00000000 sec
MCPRK 0.01500000 sec
===== CHANNEL f1 =====
NUC1 1H
P1 12.25 usec
PL1 0.00 dB
SF01 500.3330020 MHz
SI 32768
SF 500.3300220 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.00



30

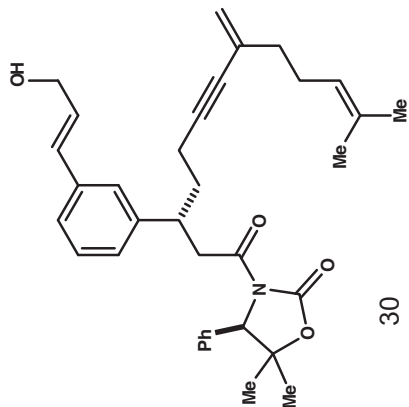
ppm



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153.348
143.235
137.006
136.317
132.101
131.843
131.075
128.959
128.893
128.826
128.672
127.281
126.560
126.147
124.945
123.590
119.936

89.151
82.508
81.583
67.013
63.737

41.585
41.144
37.743
35.497
28.623
26.852
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23.616
17.840
17.452

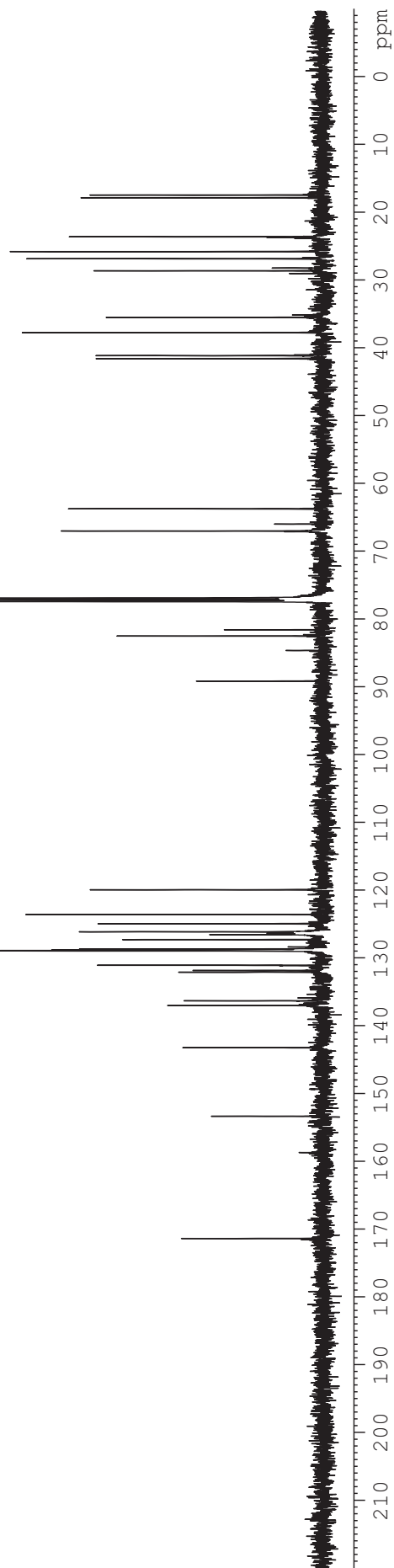


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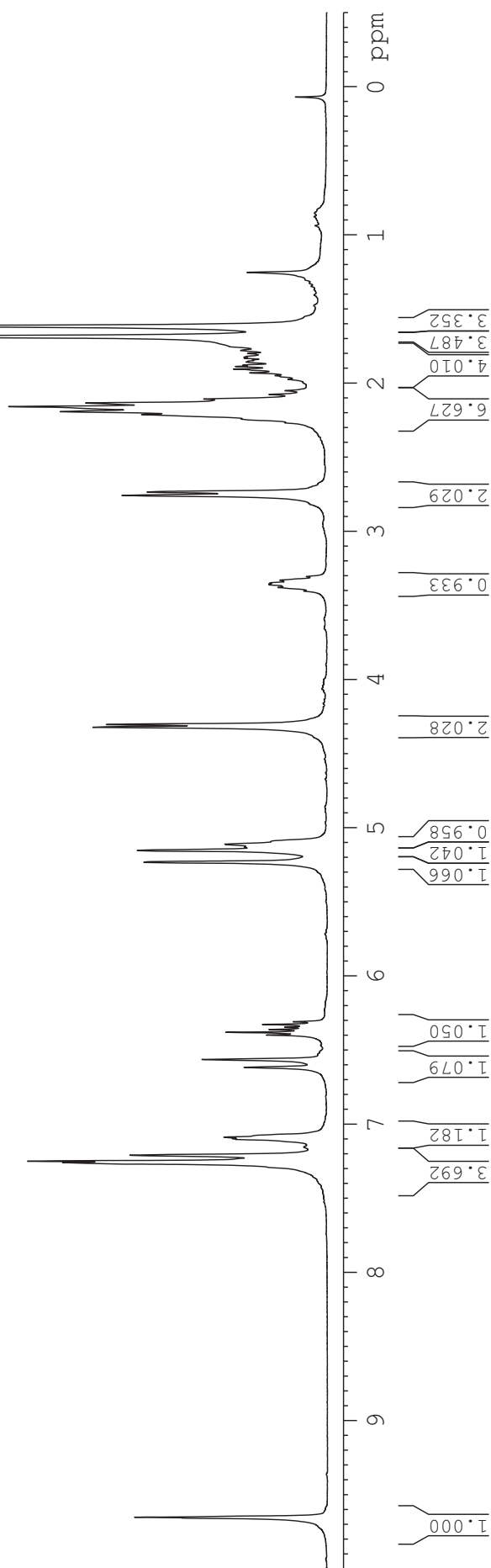
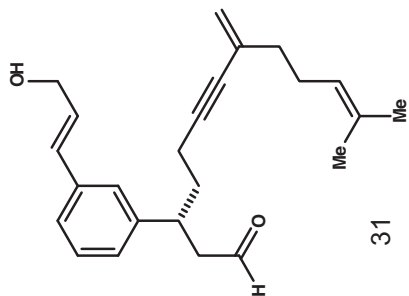
NAME          TRI-226
EXPNO         2
PROCNO        1
Date_         20100903
Time          15.28
INSTRUM       advance500
PROBHD        5 mm bb-z z800
PULPROG       zgdc30
TD            65536
SOLVENT       CDCl3
NS            129
DS            0
SWH           32679.738 Hz
FIDRES        0.498653 Hz
AQ            1.0027661 sec
RG            4096
DE            15.300 usec
TE            296.7 K
D1            2.00000000 sec
d11           0.03000000 sec
MCREST        0.00000000 sec
MCWRK         0.01500000 sec

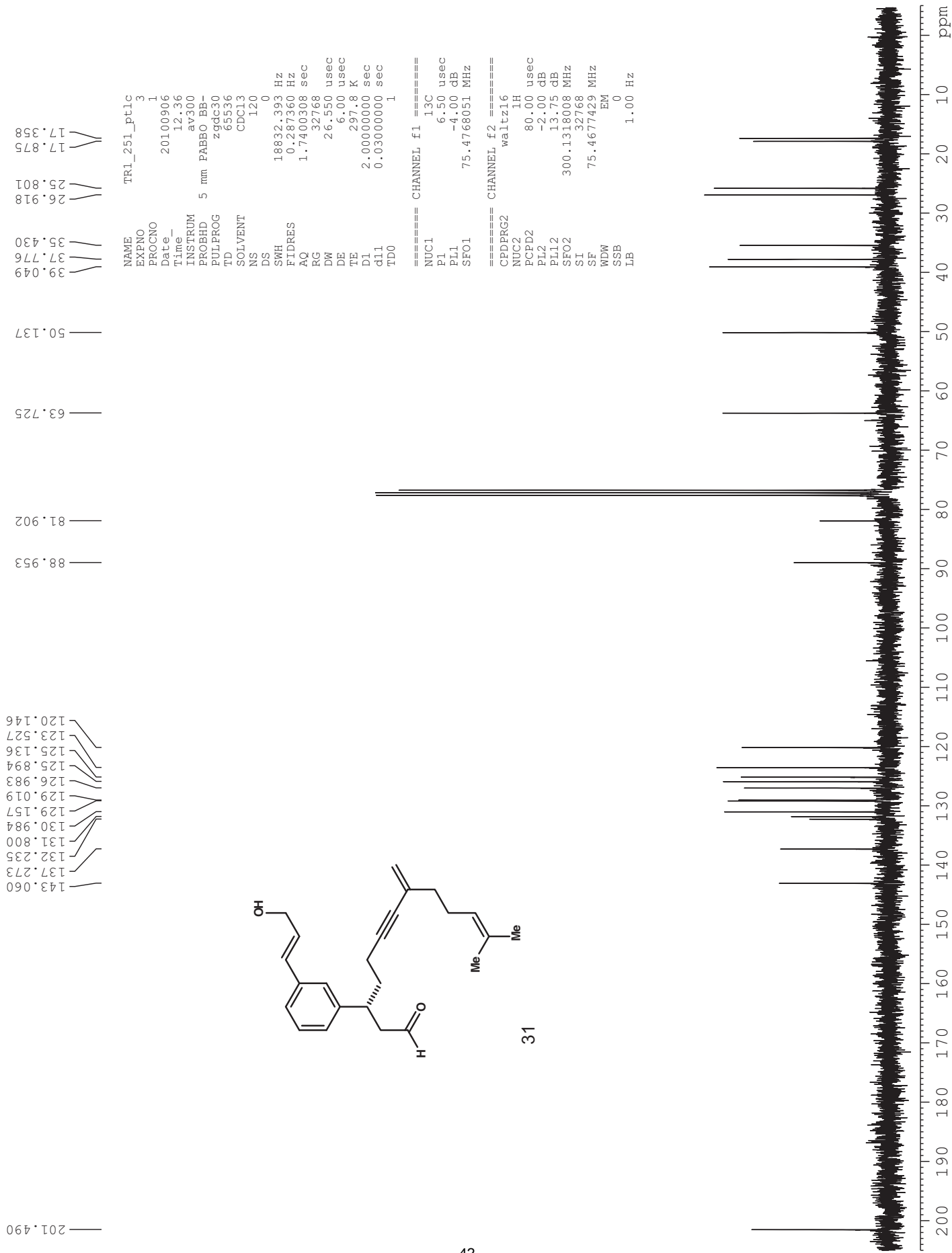
===== CHANNEL f1 =====
NUC1          13C
P1            6.20 usec
PL1           0.00 dB
SFO1          125.8231939 MHz

===== CHANNEL f2 =====
CPDPRG2       waltz16
NUC2          1H
PCPD2         100.00 usec
PL2           120.00 dB
PL12          16.10 dB
SFO2          500.3320013 MHz
SI            65536
SF            125.8080724 MHz
WDW           EM
SSB           0
  
```

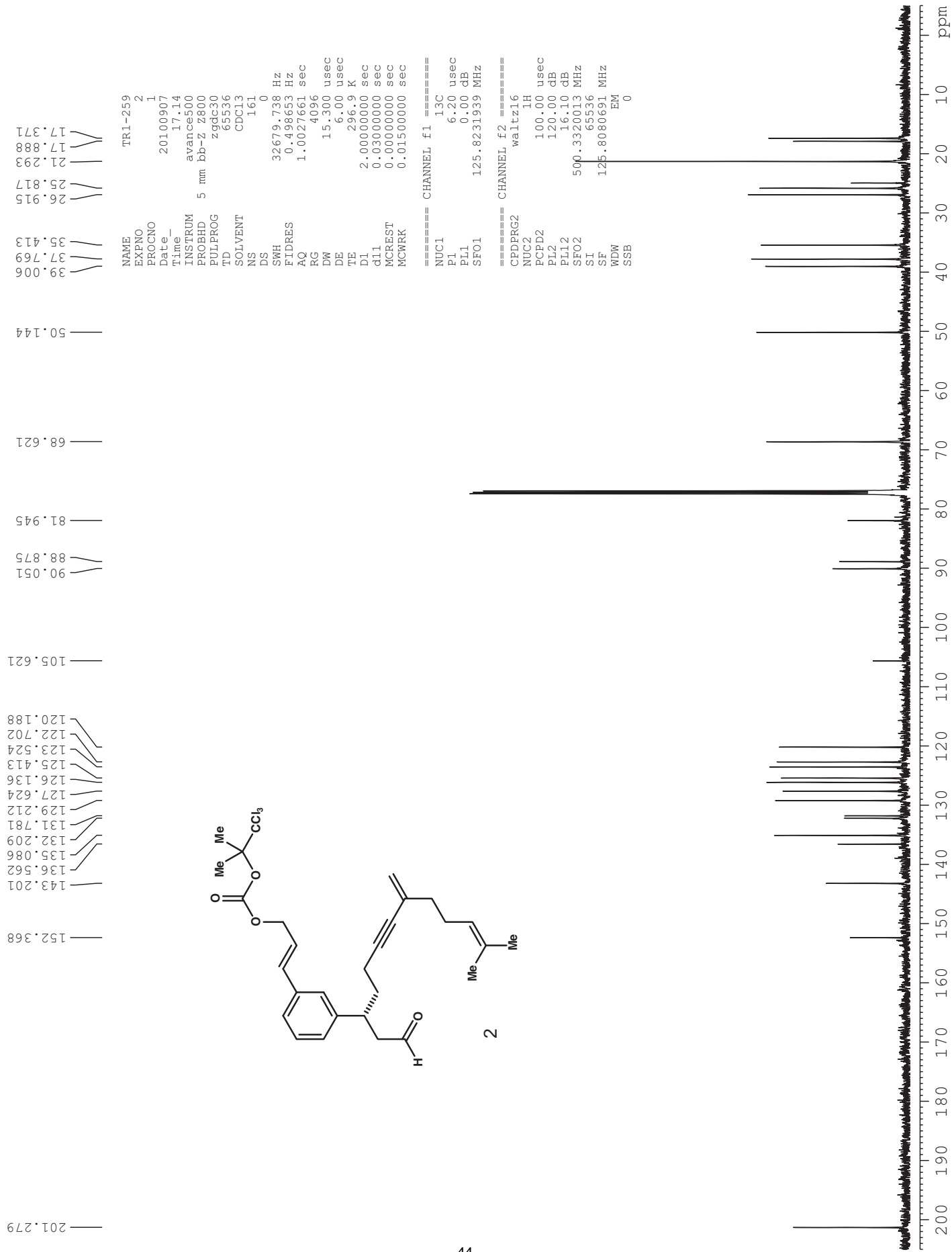


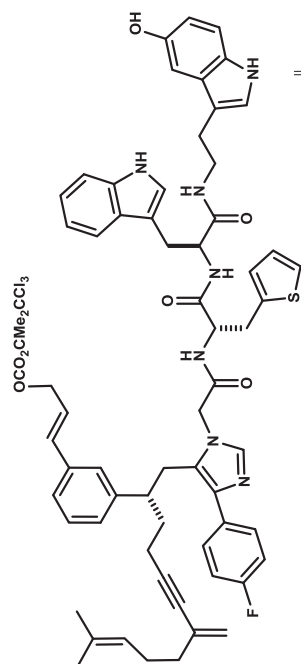
NAME TRI_251_pt1c
EXPNO 2
PROCNO 1
Date 20100906
Time_ 12.28
INSTRUM av300
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDC13
NS 8
DS 0
SWH 5995.204 Hz
FIDRES 0.091480 Hz
AQ 5.4657526 sec
RG 90.5
DW 83.400 usec
DE 6.00 usec
TE 297.5 K
D1 2.00000000 sec
TD0 1
===== CHANNEL f1 =====
NUC1 1H
P1 14.00 usec
PL1 -2.00 dB
SFO1 300.1318008 MHz
SI 65536
SF 300.1300124 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40







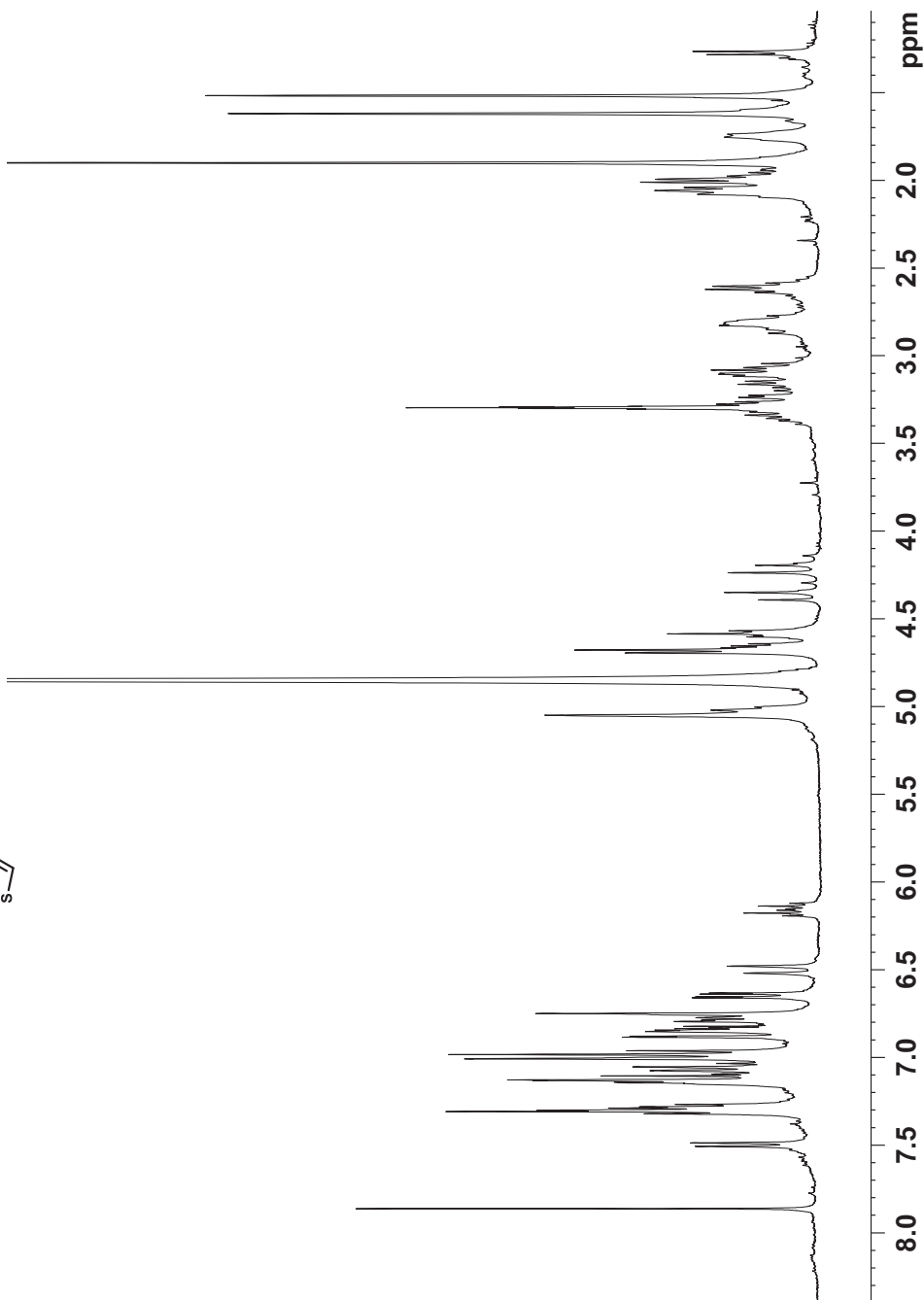


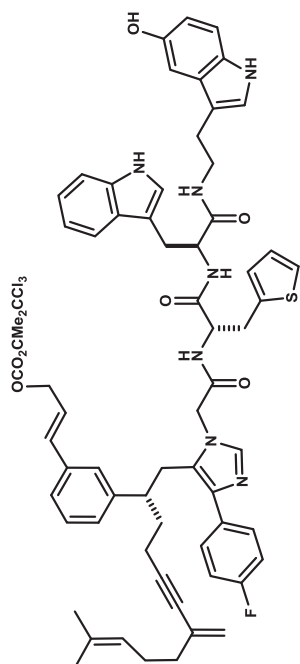


Current Data Parameters
NAME KL-II-292_c1f23_1h_meod
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20100921
Time_ 14.53
INSTRUM arx400
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 65536
SOLVENT MeOD
NS 8
DS 0
SWH 8064.516 Hz
FIDRES 0.123055 Hz
AQ 4.0632820 sec
RG 512
DW 62.000 usec
DE 88.57 usec
TE 300.0 K
D1 2.00000000 sec
P1 7.50 usec
SFO1 400.1324008 MHz
NUCLEUS 1H

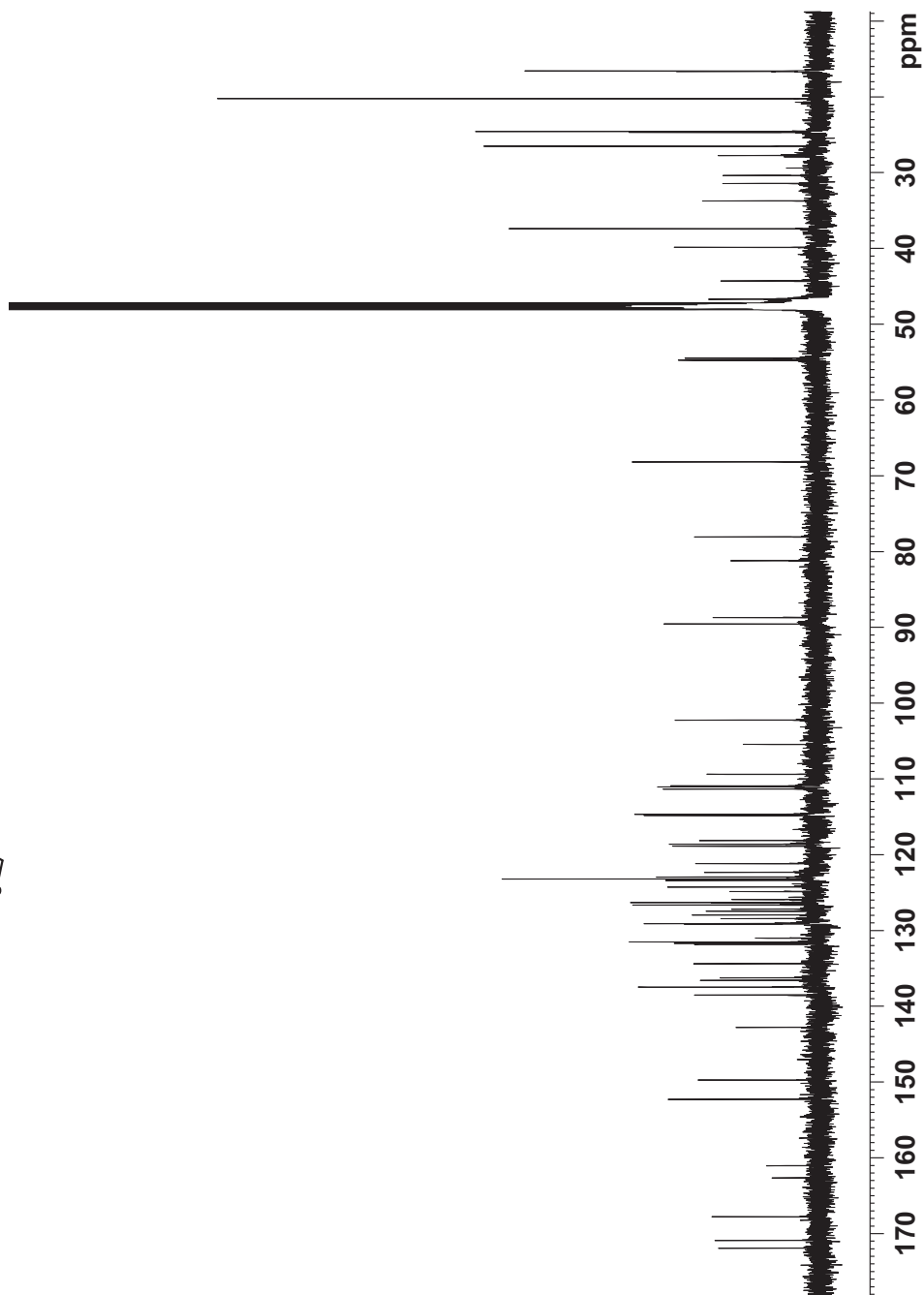
F2 - Processing parameters
SI 65536
SF 400.1300173 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

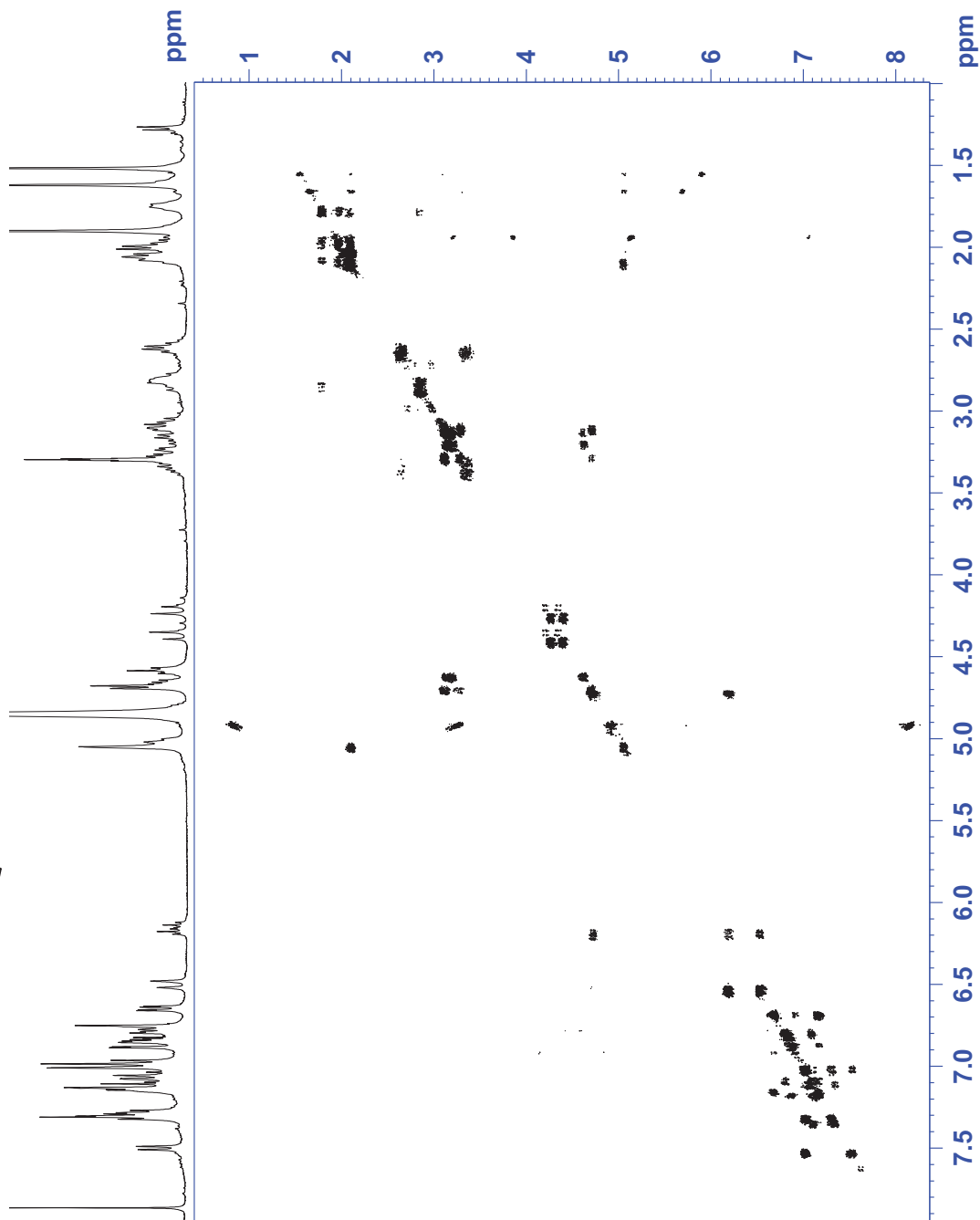




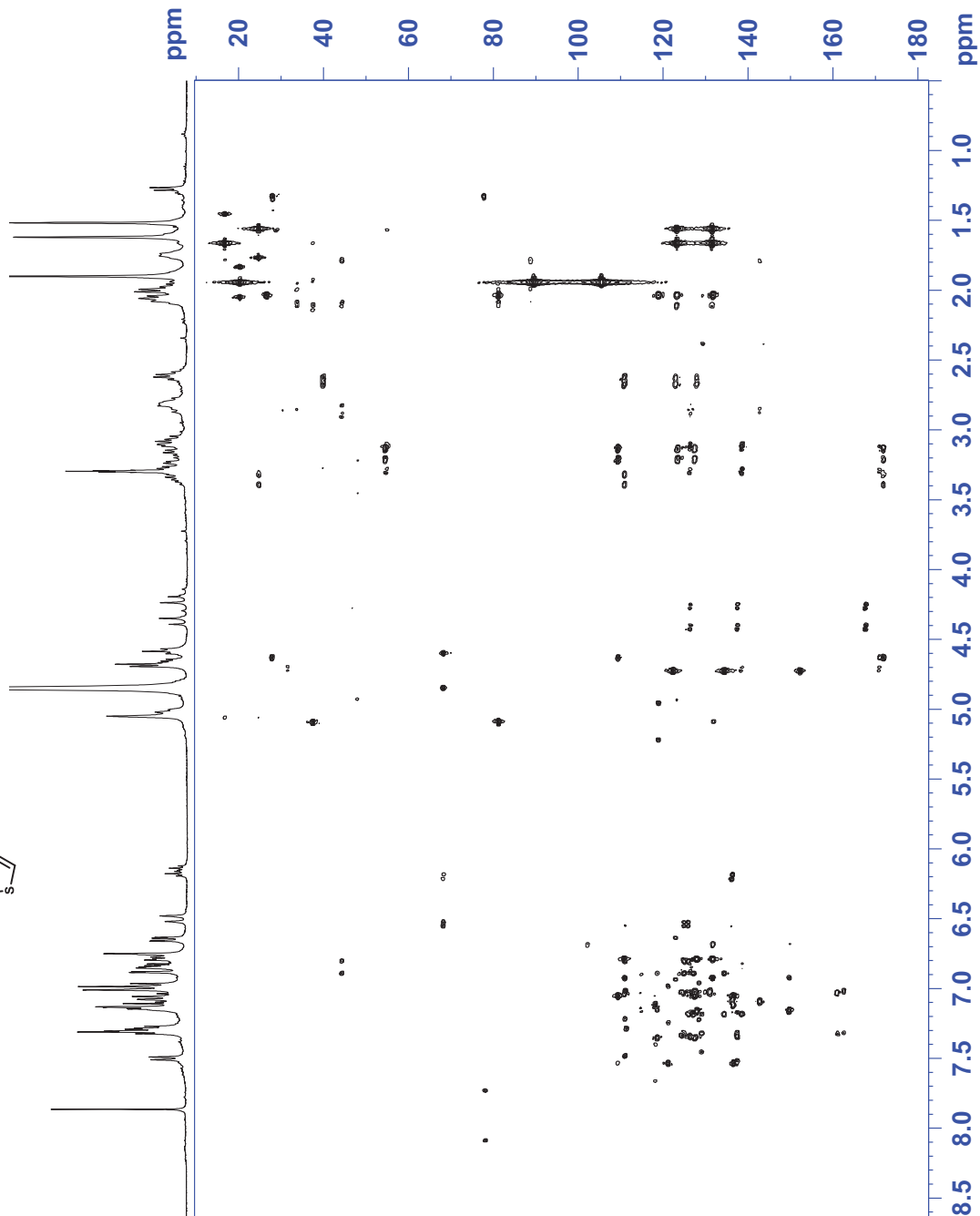
Current Data Parameters
 NAME KL-II-292_clf23_13c_meod
 EXPNO 1
 PROCNO 1

F2 - Processing parameters
 SI 65536
 SF 150.9028090 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.00





F1 - Acquisition parameters		F2 - Processing parameters		F1 - Processing parameters	
TD	356	SI	2048	SI	2048
SFO1	600.1327 MHz	SF	600.1300000 MHz	SCF	600.1300000 MHz
FFRDS	21.046506 Hz	WDW	SINE	WDW	States-TFPI
SW	8.978 ppm	SSB	0	SSB	600.1300000 MHz
States-TFPI		LB	0 Hz	LB	0
FFMODE		GB	0	GB	0 Hz
		PC	1.00	PC	0



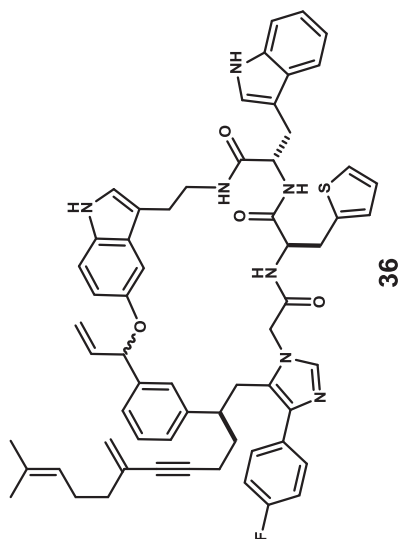
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Current Data Parameters
NAME      KL-II-292_c1f23_2d_1h_meod
EXPNO     4
PROCNO    1
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F1 - Acquisition parameters

TD	256
SFO1	150.9179 MHz
FIDRES	117.903725 Hz
SW	199.999 ppm
EnMODE	QE

F2 - Processing parameters	
SI	2048
SF	600.130000 MHz
WDW	QSINE
SSB	2
LB	0 Hz
GB	0
PC	1.00

```
F1 - Processing parameters
SI      2048
WC2     QF
SF      150.9028090 MHz
WDW      2
SSB      USER
LB       0 Hz
GB       0
```

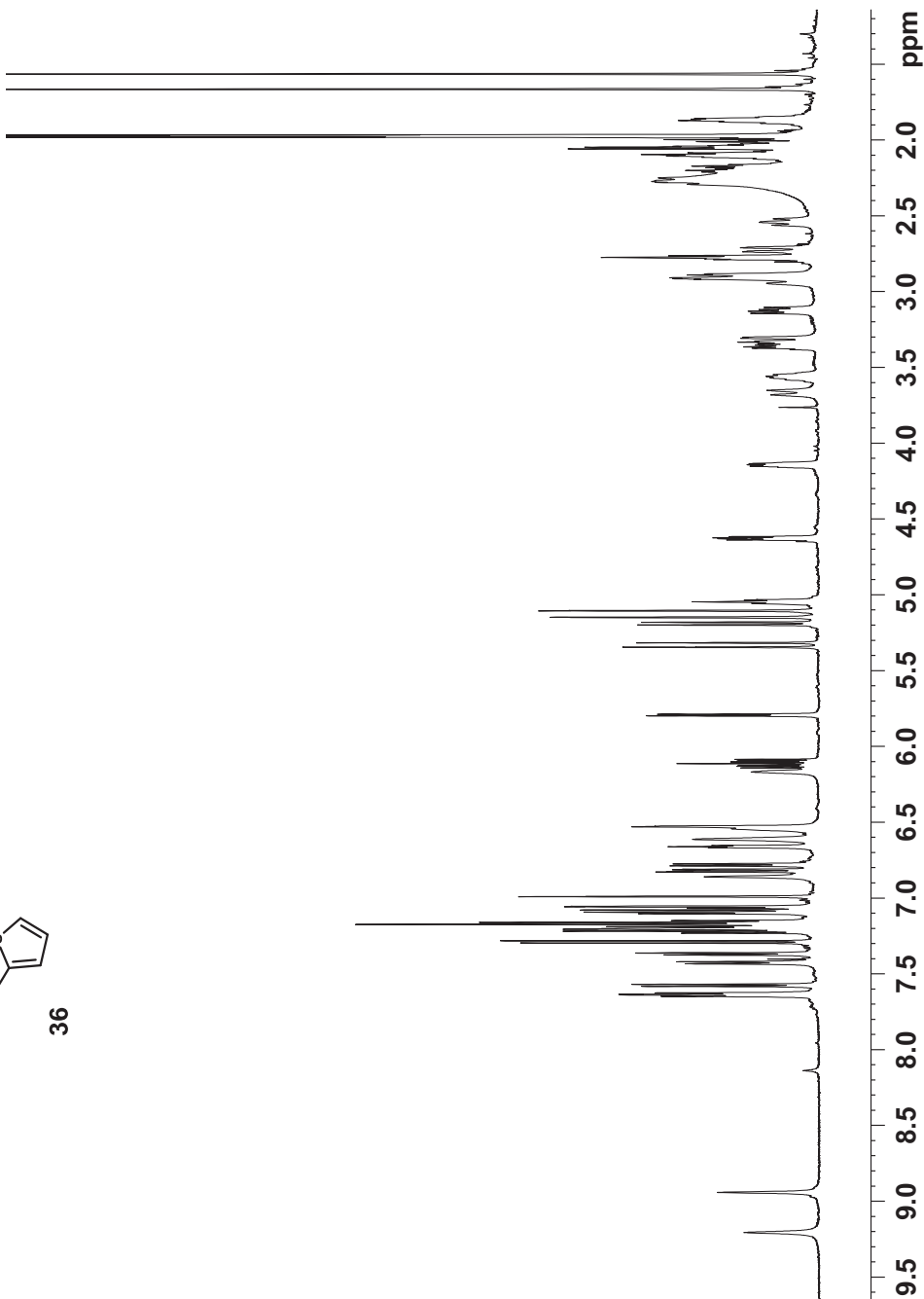


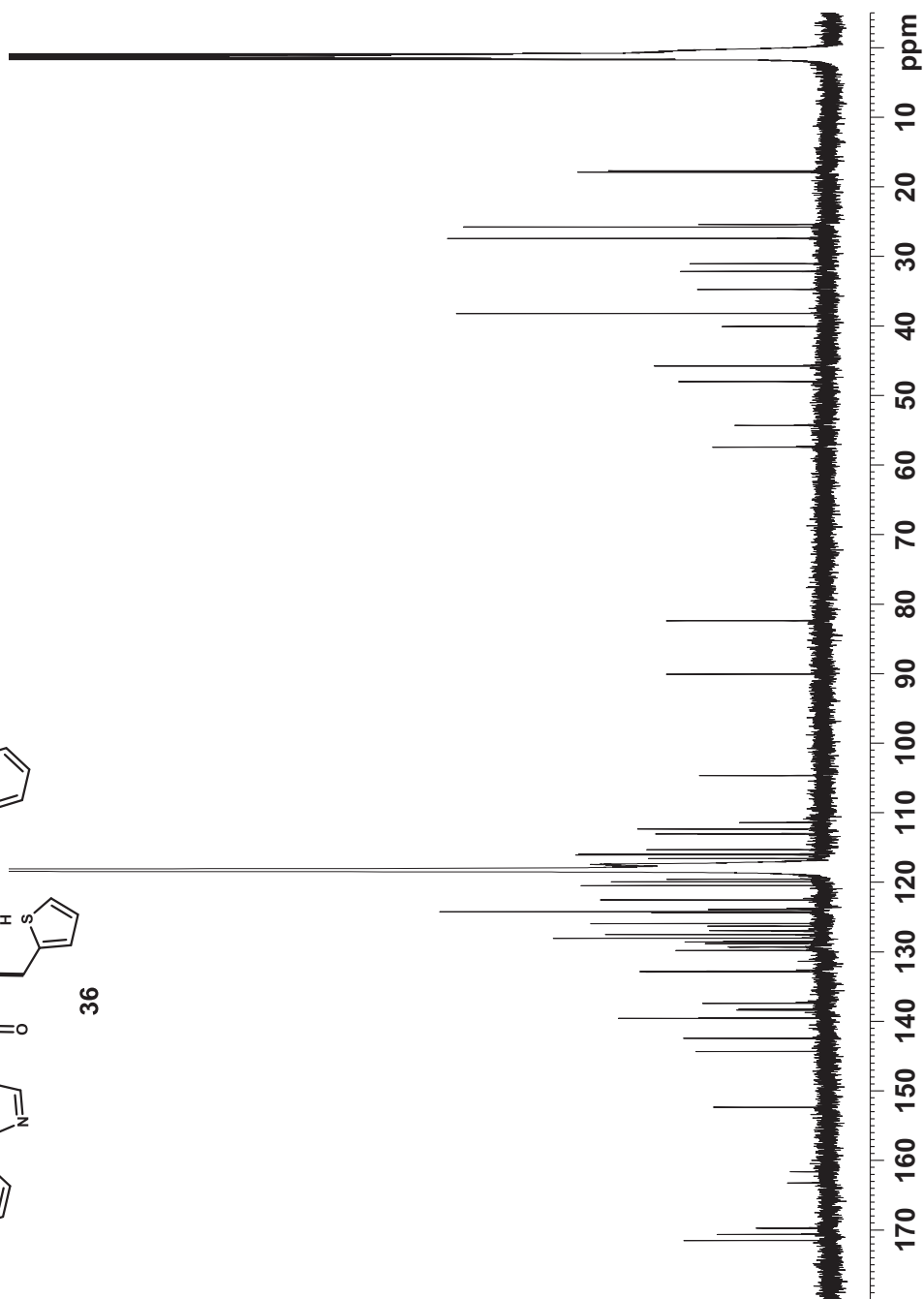
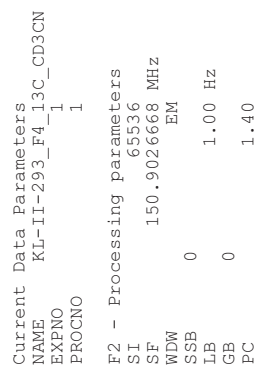
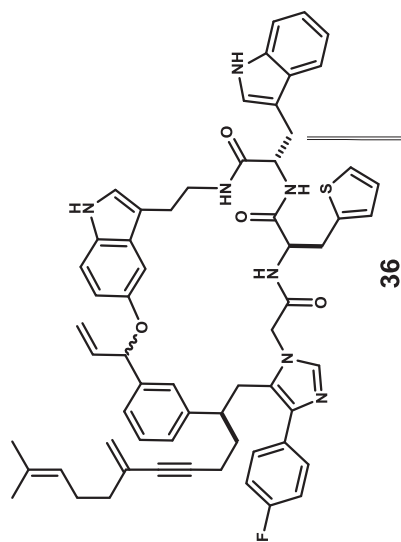
Current Data Parameters
 NAME KL-II-293_f4_1h_cd3cn
 EXPNO 6
 PROCNO 1

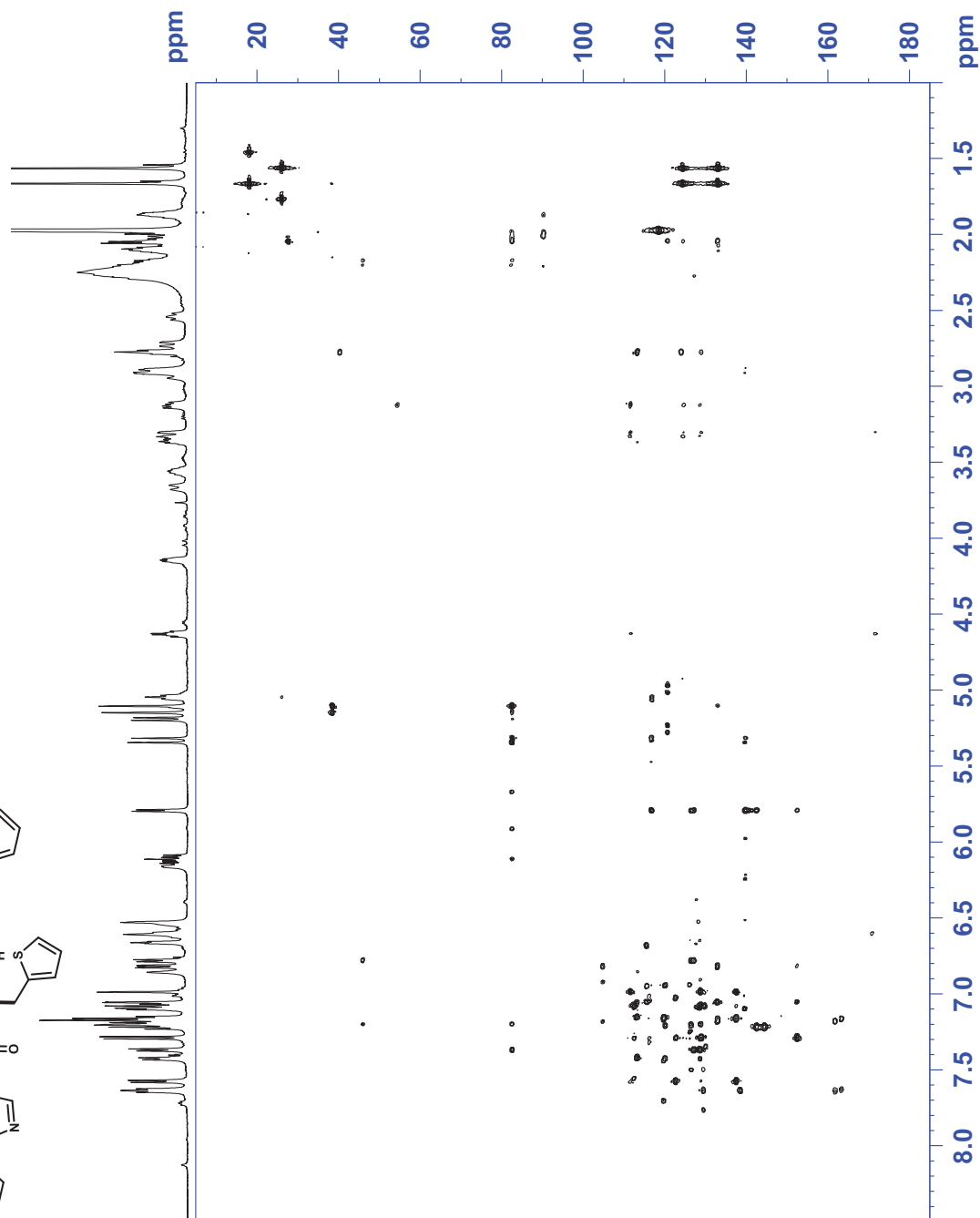
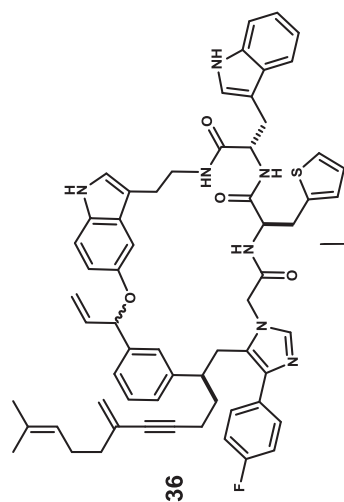
F2 - Acquisition Parameters
 Date_ 20100923
 Time_ 17.17
 INSTRUM AV600
 PROBHD 5 mm TBI 1H-BB
 PULPROG zg30
 TD 65536
 SOLVENT CD3CN
 NS 25
 DS 0
 SWH 12376.237 Hz
 FIDRES 0.188846 Hz
 AQ 2.6476543 sec
 RG 362
 DW 40.400 usec
 DE 6.00 usec
 TE 294.0 K
 D1 2.00000000 sec
 TD0 1

===== CHANNEL f1 =====
 NUC1 1H
 P1 8.60 usec
 PL1 -2.00 dB
 PL1W 39.81071854 W
 SFO1 600.1336008 MHz

F2 - Processing parameters
 SI 65536
 SF 600.1300000 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00





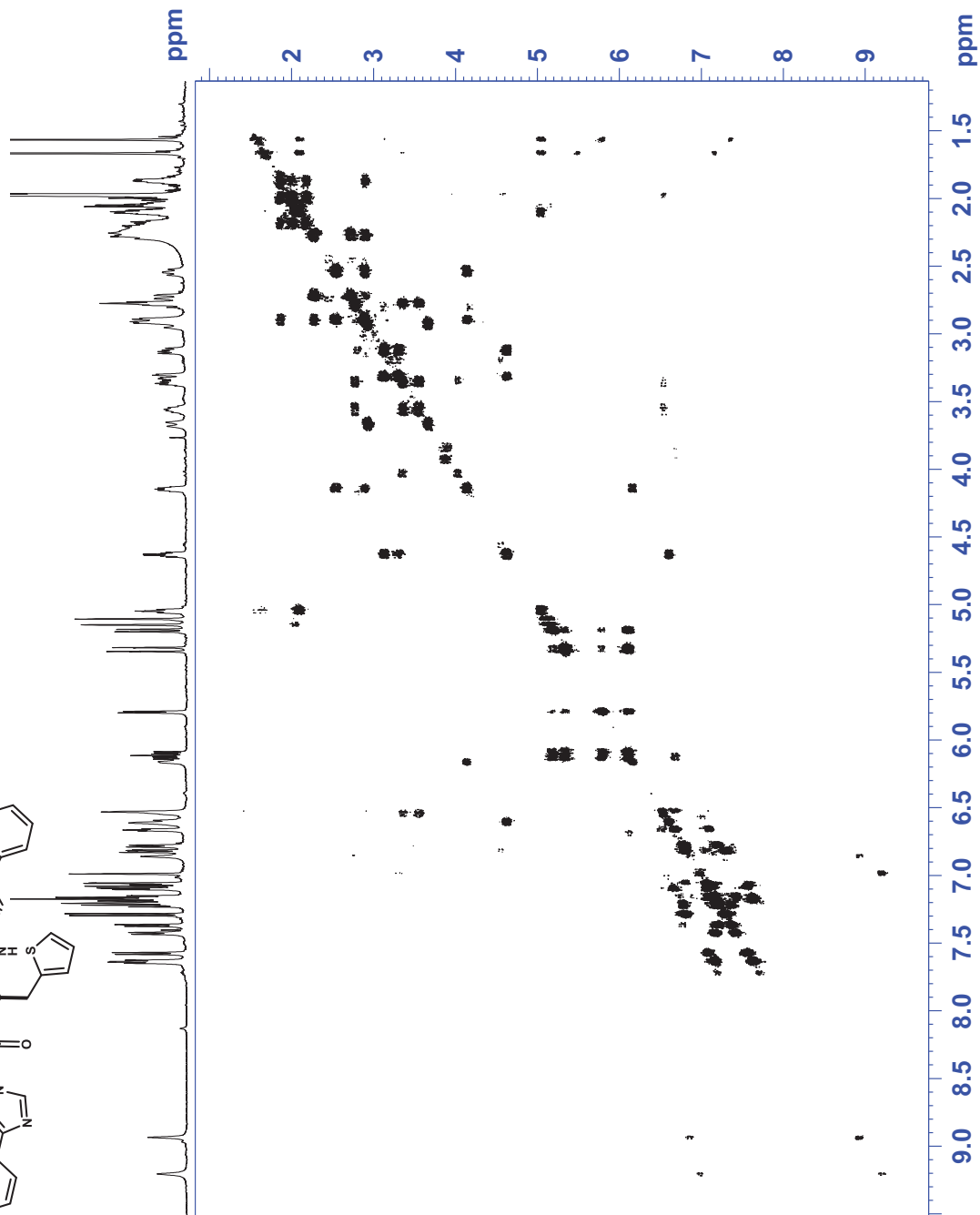
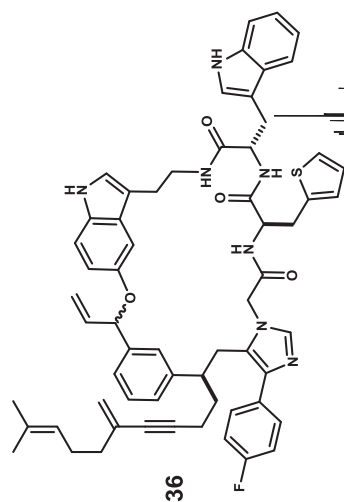


Current Data Parameters
NAME KL-II-293_F4_hmbc_cd3cn
EXPNO 2
PROCNO 1

F1 - Acquisition parameters
TD 256
SF01 150.9179 MHz
FIDRES 117.904610 Hz
SW 200.000 ppm
FMODE QF

F2 - Processing parameters
SI 2048
SF 600.1300000 MHz
WDW QF
SSB 2
LB 0 Hz
GB 0
PC 1.00

F1 - Processing parameters
SI 2048
MC2 QF
SF 150.9026367 MHz
WDW QF
SSB 2
LB 0 Hz
GB 0



Current Data Parameters
 NAME KL-II-292_F4_2d_cd3cn
 EXPNO 3
 PROCNO 1

F1 - Acquisition parameters
 TD 256

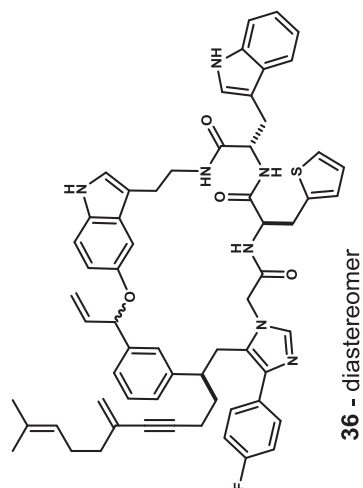
SF01 600.1332 MHz
 FIDRES 24.660667 Hz
 SW 10.520 ppm
 F1MODE States-TPPI

F2 - Processing parameters
 SI 2048

SF 600.1300000 MHz
 WDW SINE
 SSB 0
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 2048

MC2 States-TPPI
 SF 600.1300000 MHz
 WDW TRAP
 SSB 0
 LB 0 Hz
 GB 0

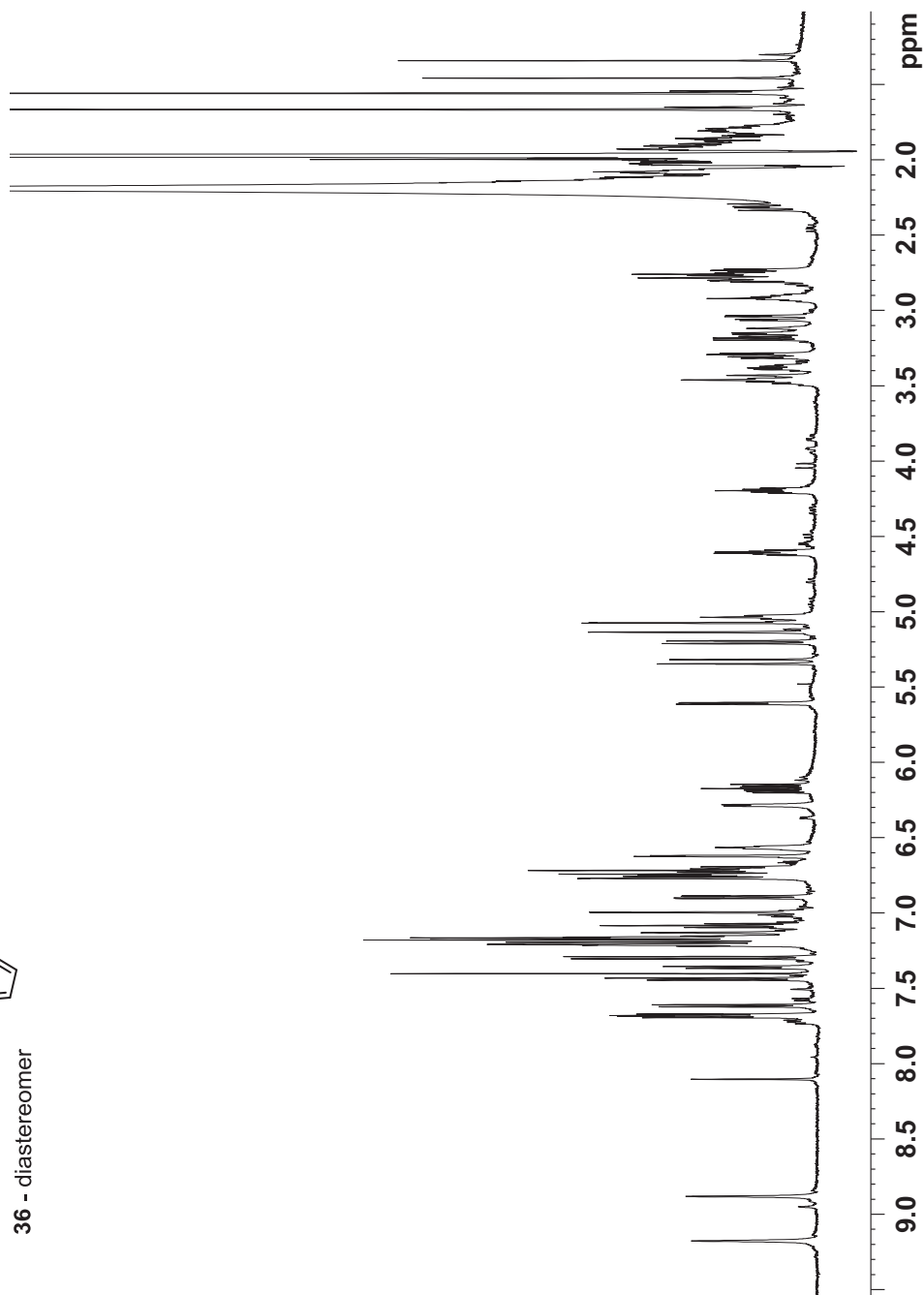


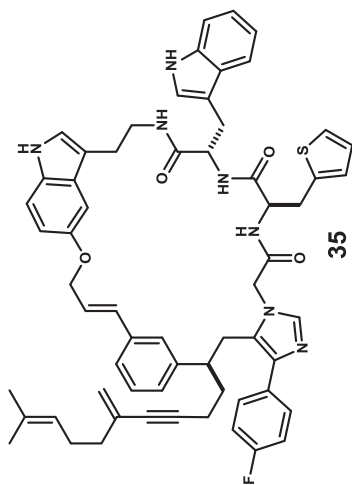
Current Data Parameters
NAME KL-11-293_f5_1h_cd3cn
EXPNO 6
PROCNO 1

F2 - Acquisition Parameters
Date_ 20100923
Time 17.26
INSTRUM AV600
PROBHD 5 mm TBI 1H-BB
PULPROG zg30
TD 65536
SOLVENT CD3CN
NS 121
DS 0
SWH 12376.237 Hz
FIDRES 0.188846 Hz
AQ 2.6476543 sec
RG 256
DE 40.400 usec
TE 294.0 K
D1 2.0000000 sec
TD0 1

===== CHANNEL f1 =====
NUC1 1H
P1 8.60 usec
PL1 -2.00 dB
PL1W 39.81071854 W
SF01 600.1336008 MHz

F2 - Processing parameters
SI 65536
SF 600.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



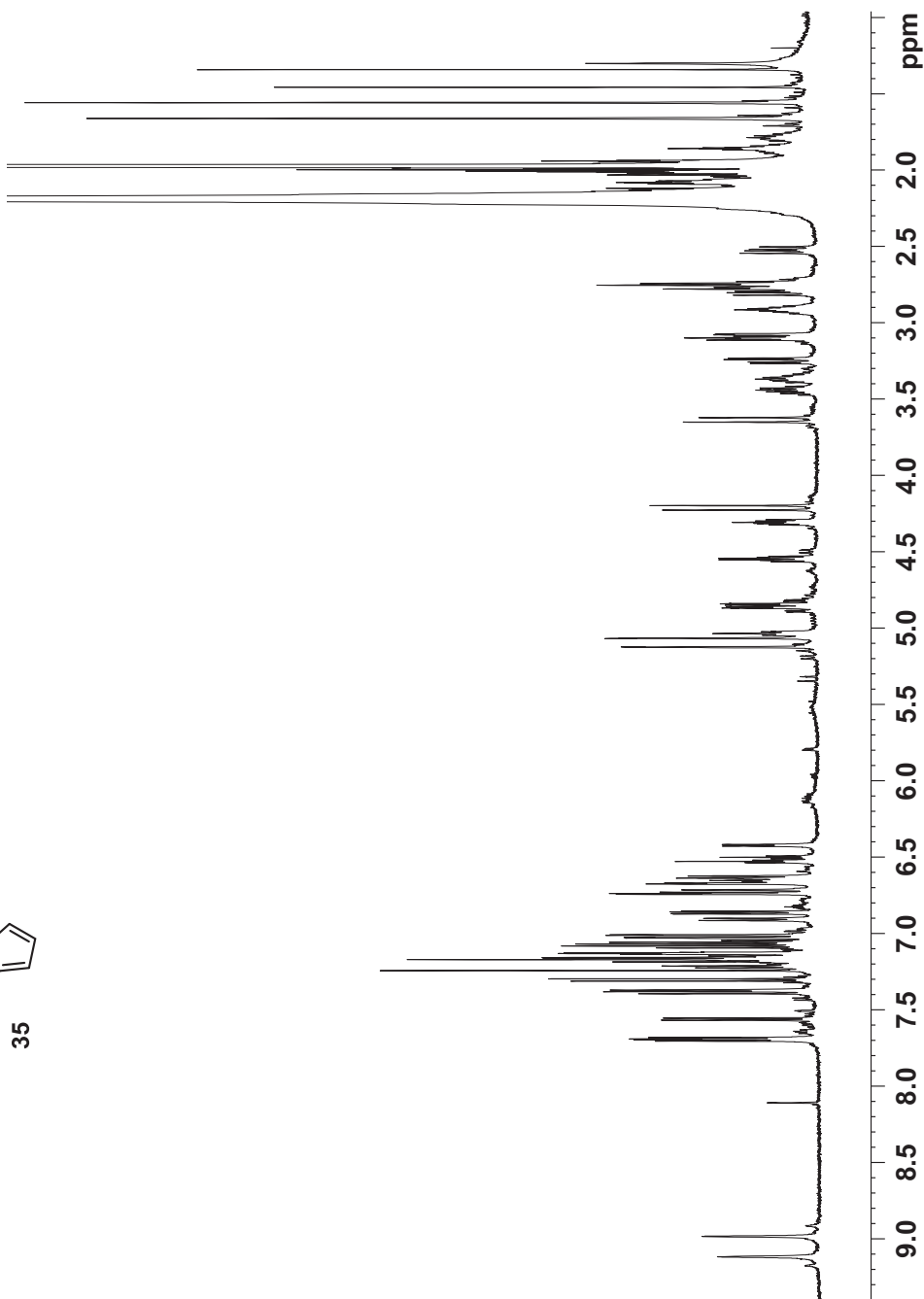


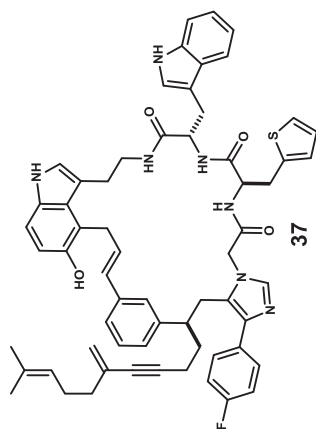
Current Data Parameters
 NAME KL-II-293_F2_1h_cd3cn
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20100929
 Time_ 17.46
 INSTRUM AV600
 PROBHD 5 mm TBI 1H-BB
 PULPROG zg30
 TD 65536
 SOLVENT CD3CN
 NS 51
 DS 0
 SWH 12376.237 Hz
 FIDRES 0.188846 Hz
 AQ 2.6476543 sec
 RG 228.1
 DW 40.400 usec
 DE 6.00 usec
 TE 294.0 K
 D1 2.00000000 sec
 TD0 1

===== CHANNEL f1 =====
 NUC1 1H
 P1 8.60 usec
 PL1 -2.00 dB
 PL1W 39.81071854 W
 SFO1 600.1336008 MHz

F2 - Processing parameters
 SI 65536
 SF 600.1300000 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00



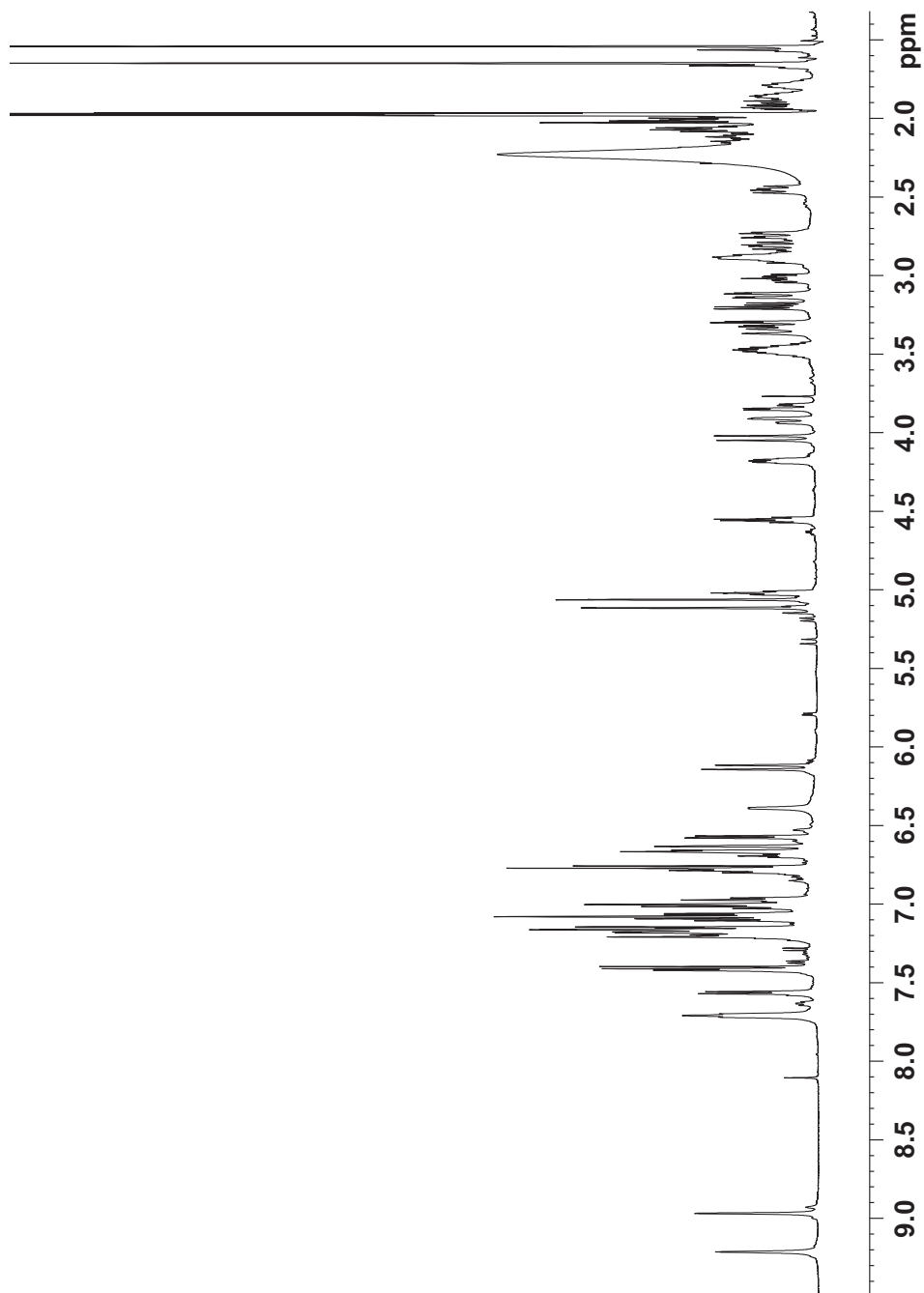


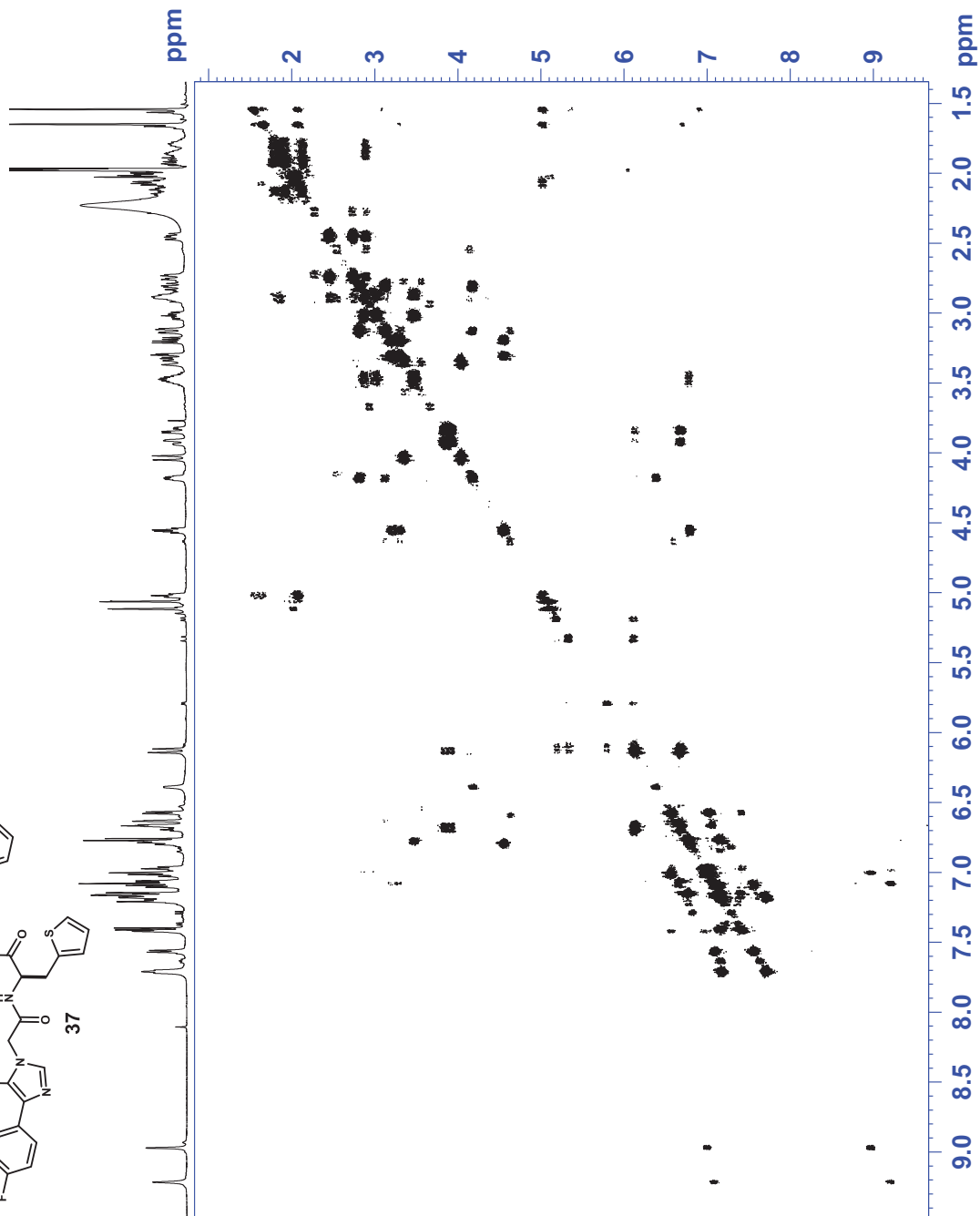
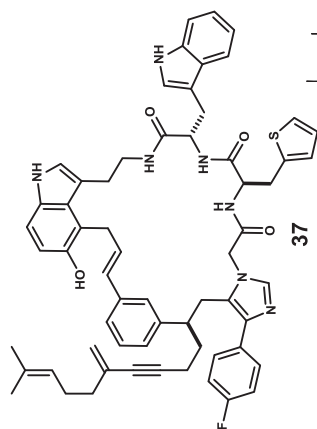
Current Data Parameters
NAME KL-II-293_F4heat12h_1h_cd3cn
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20100930
Time_ 19.04
INSTRUM AV600
PROBHD 5 mm TBI 1H-BB
PULPROG zg
TD 65536
SOLVENT CD3CN
NS 16
DS 0
SWH 6009.615 Hz
FIDRES 0.091699 Hz
AQ 5.4525952 sec
RG 228.1
DW 83.200 usec
DE 6.00 usec
TE 293.9 K
D1 2.0000000 sec
TD0 1

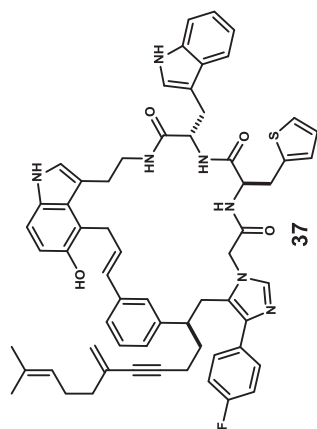
==== CHANNEL f1 =====
NUC1 1H
P1 8.60 usec
PL1 -2.00 dB
PL1W 39.81071854 W
SFO1 600.1330006 MHz

F2 - Processing parameters
SI 65536
SF 600.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



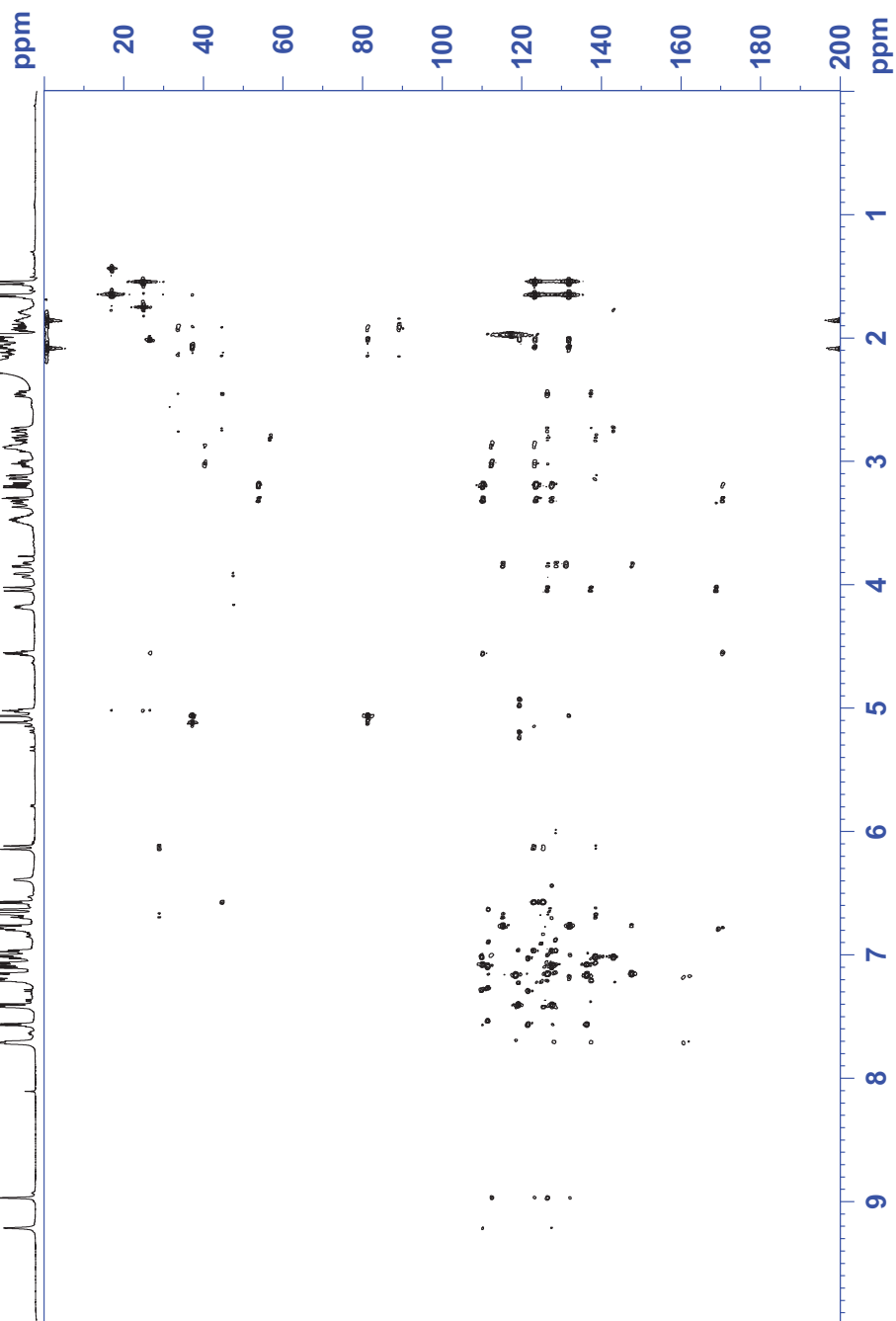


Current Data Parameters
 NAME K1-II-293_F4heat12h_1h_cd3cn
 EXPNO 3
 PROCNO 1
 F1 - Acquisition parameters
 TD 256
 SFO1 600.133 MHz
 FIDRES 23.475060 Hz
 SW 10.014 ppm
 FMODE States-TPPI
 F2 - Processing parameters
 SI 2048
 SF 600.1300000 MHz
 WDW SINE
 SSB 0 Hz
 LB 0
 GB 0
 PC 1.00
 F1 - Processing parameters
 SI 2048
 MC2 States-TPPI
 SF 600.1300000 MHz
 WDW QSINE
 SSB 0 Hz
 LB 0
 GB 0



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Current Data Parameters
 NAME K1-II-293_F4heat12h_1h_cd3cn
 EXPNO 4
 PROCNO 1
 F1 - Acquisition parameters
 TD 256
 SFO1 150.9179 MHz
 FIDRES 117.904610 Hz
 SW 200.000 ppm
 FMODE QF
 F2 - Processing parameters
 SI 2048
 SF 600.1300000 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00
 F1 - Processing parameters
 SI 2048
 MC2 QF
 SF 150.9028090 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0



Fraction 2-1

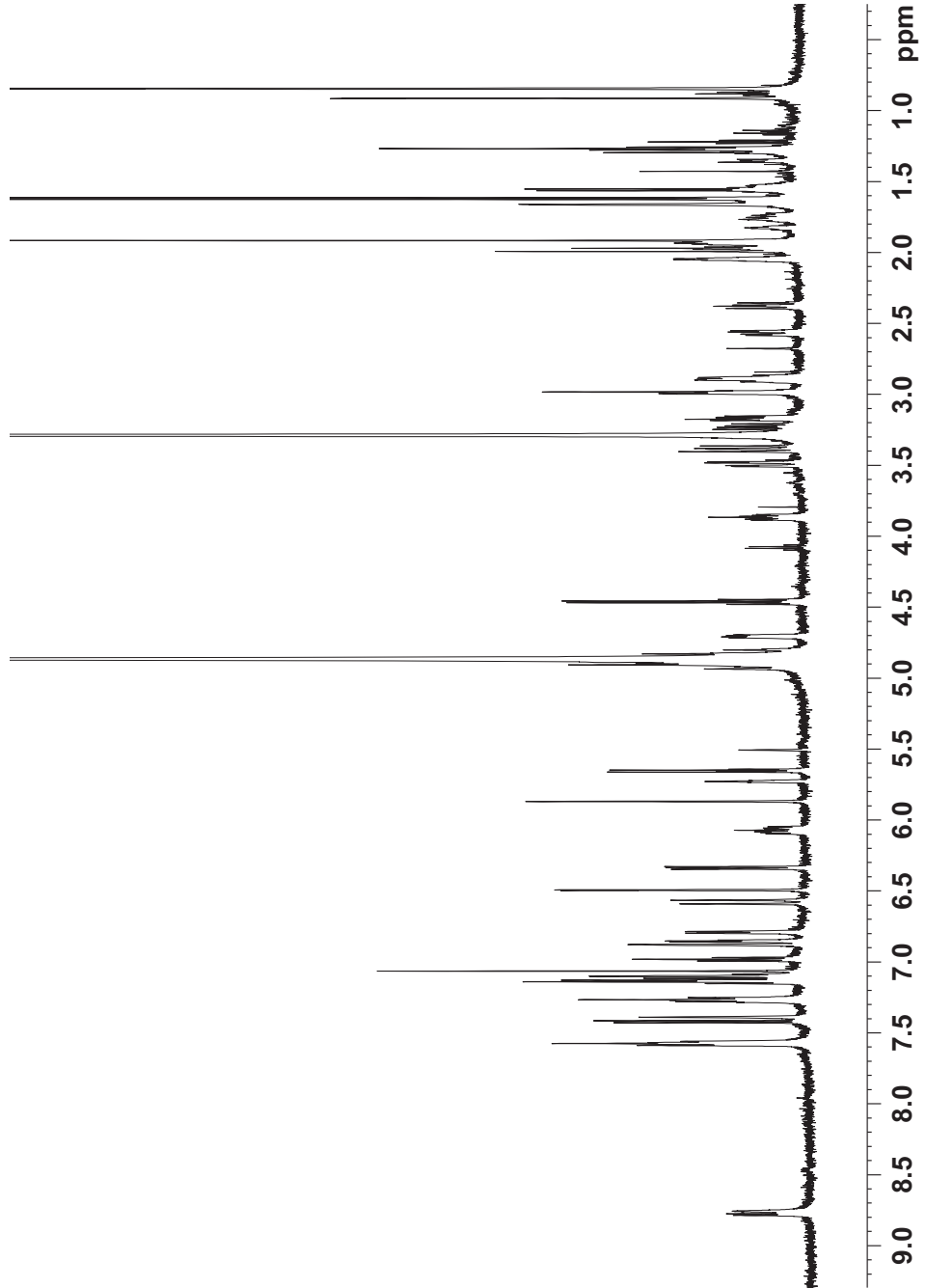
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Current Data Parameters
NAME      KL-III-108-2-1
EXPNO     1
PROCNO    1

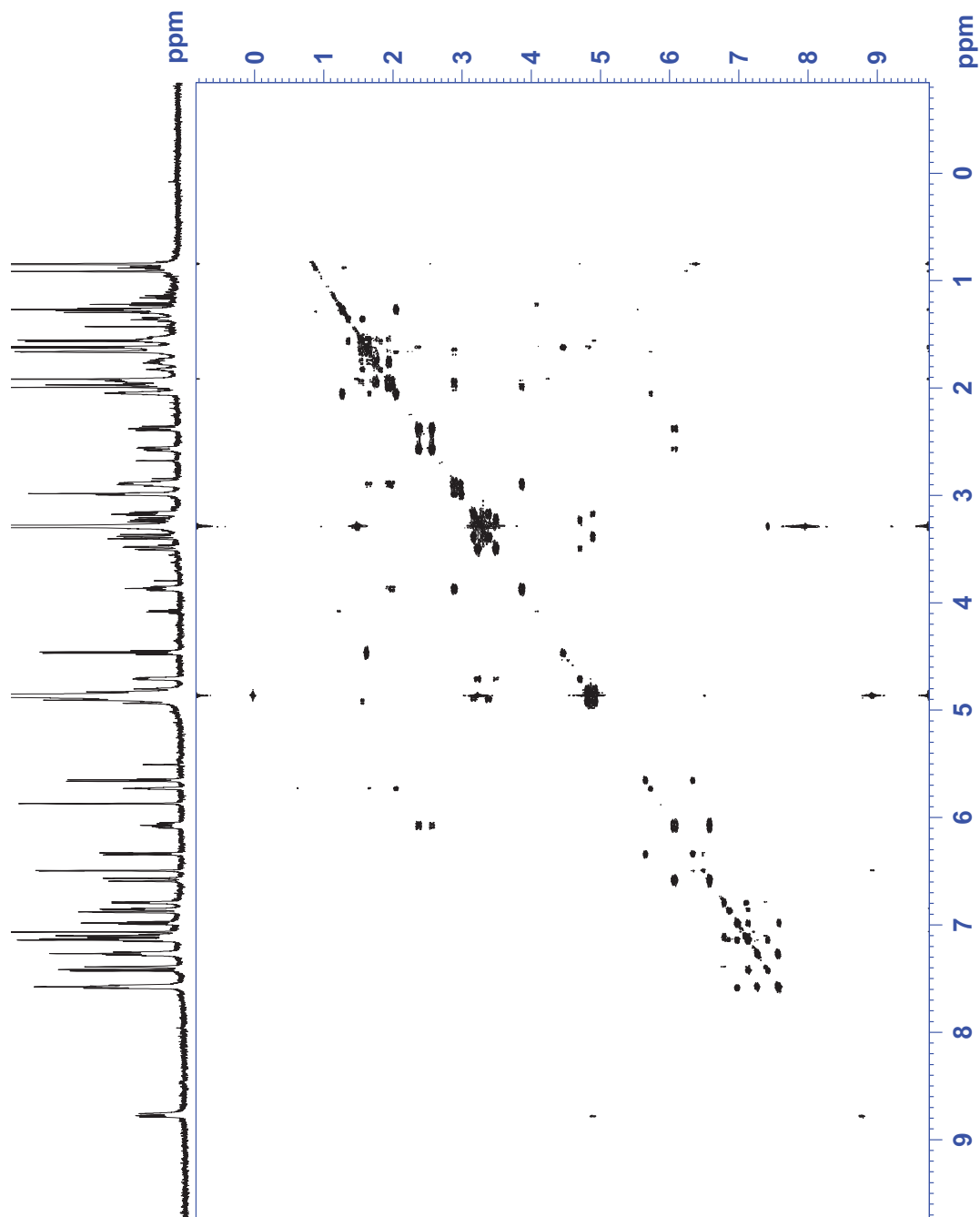
F2 - Acquisition Parameters
Date_     20110513
Time      18.32
INSTRUM   av600
PROBHD    5 mm TBI5
PULPROG   zg30
TD         65536
SOLVENT   MeOD
NS         37
DS         0
SWH        12376.237 Hz
FIDRES     0.188846 Hz
AQ         2.6476543 sec
RG         362
DW         40.400 usec
DE         6.50 usec
TE         294.4 K
D1         2.00000000 sec
TD0        1

===== CHANNEL f1 =====
NUC1       1H
P1         10.40 usec
PL1        -2.00 dB
PL1W       39.81071854 W
SFO1       600.1336008 MHz

F2 - Processing parameters
SI         65536
SF         600.1300273 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00
  
```



Fraction 2-1



```

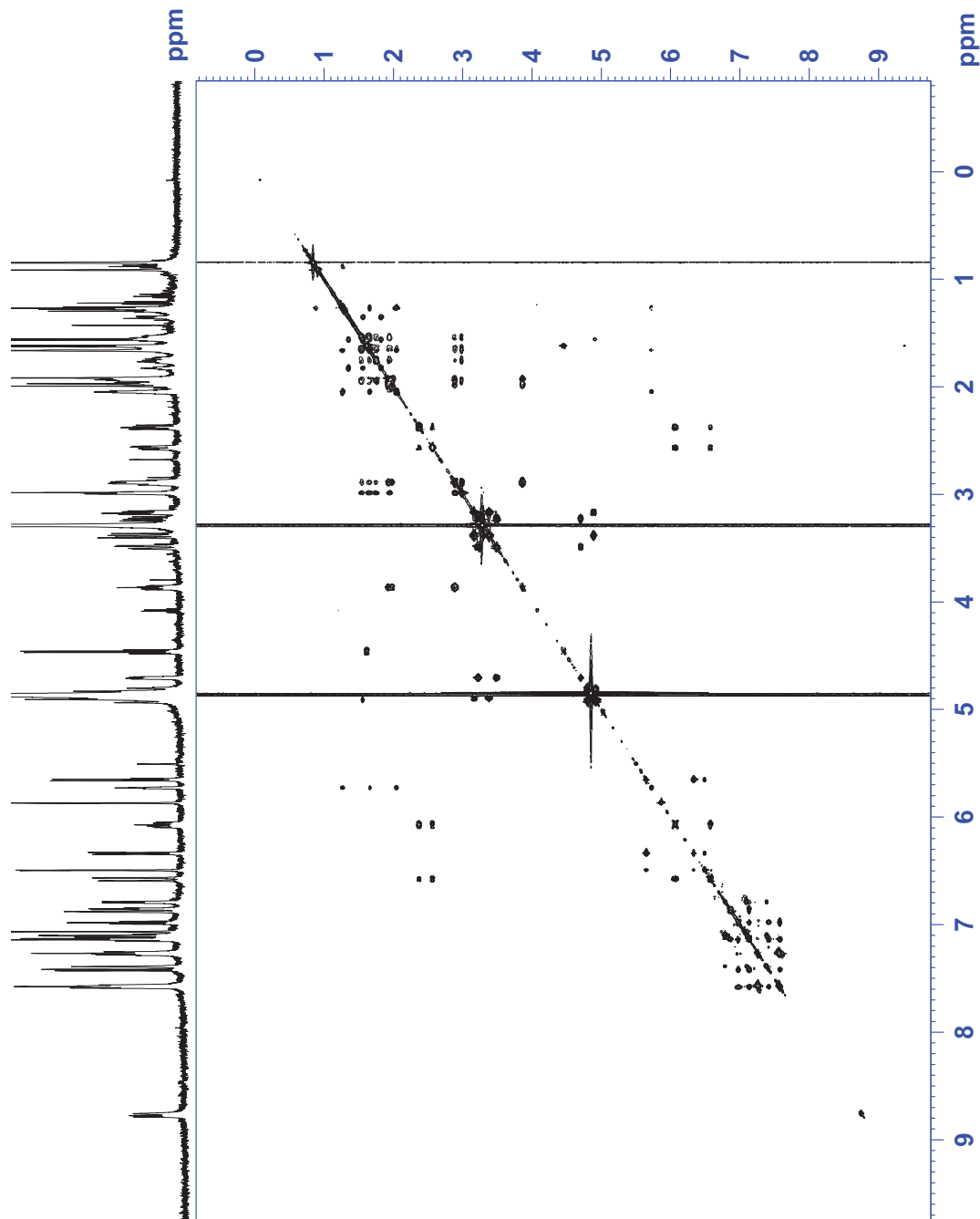
Current Data Parameters
NAME      KL-III-108-2-1
EXPNO     3
PROCNO    1

F1 - Acquisition parameters
TD         600
SFO1       600.1327 MHz
FIDRES     10.602201 Hz
SW         10.600 ppm
FMODE      States-TPPI

F2 - Processing parameters
SI         2048
SF         600.1300273 MHz
WDW        QSINE
SSB         2
LB          0 Hz
GB          0
PC          1.00

F1 - Processing parameters
SI         2048
MC2        States-TPPI
SF         600.1300273 MHz
WDW        USER
SSB         2
LB          0 Hz
GB          0
  
```

Fraction 2-1



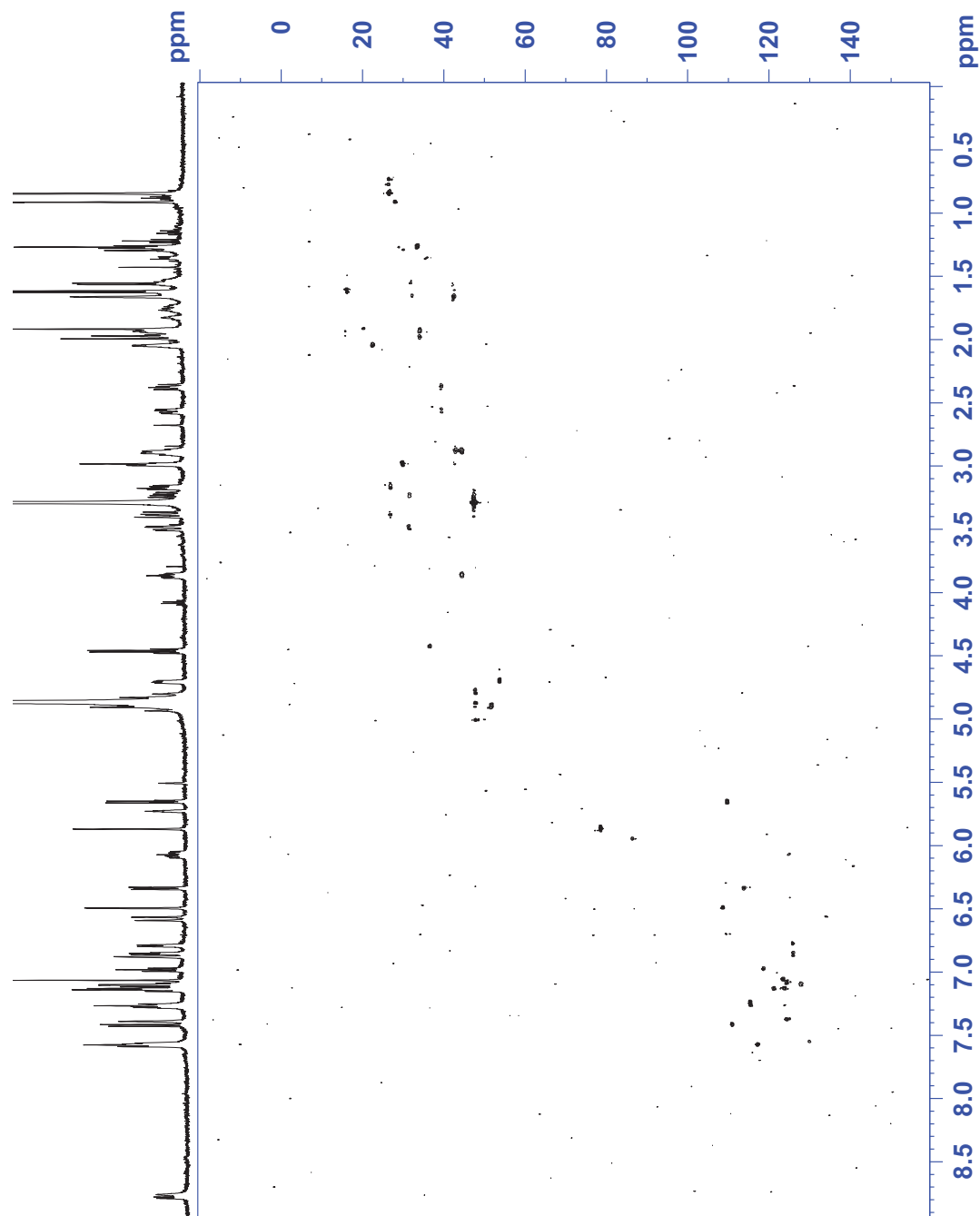
Current Data Parameters
NAME KL-III-108-2-1
EXPNO 4
PROCNO 1

F1 - Acquisition parameters
TD 600
SF01 600.1327 MHz
FIDRES 10.602203 Hz
SW 10.600 ppm
FnMODE Echo-Antiecho

F2 - Processing parameters
SI 1024
SF 600.1300273 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0
PC 1.00

F1 - Processing parameters
SI 1024
MC2 echo-antiecho
SF 600.1300273 MHz
WDW USER
SSB 2
LB 0 Hz
GB 0

Fraction 2-1



Current Data Parameters
 NAME KL-III-108-2-1
 EXPNO 5
 PROCNO 1

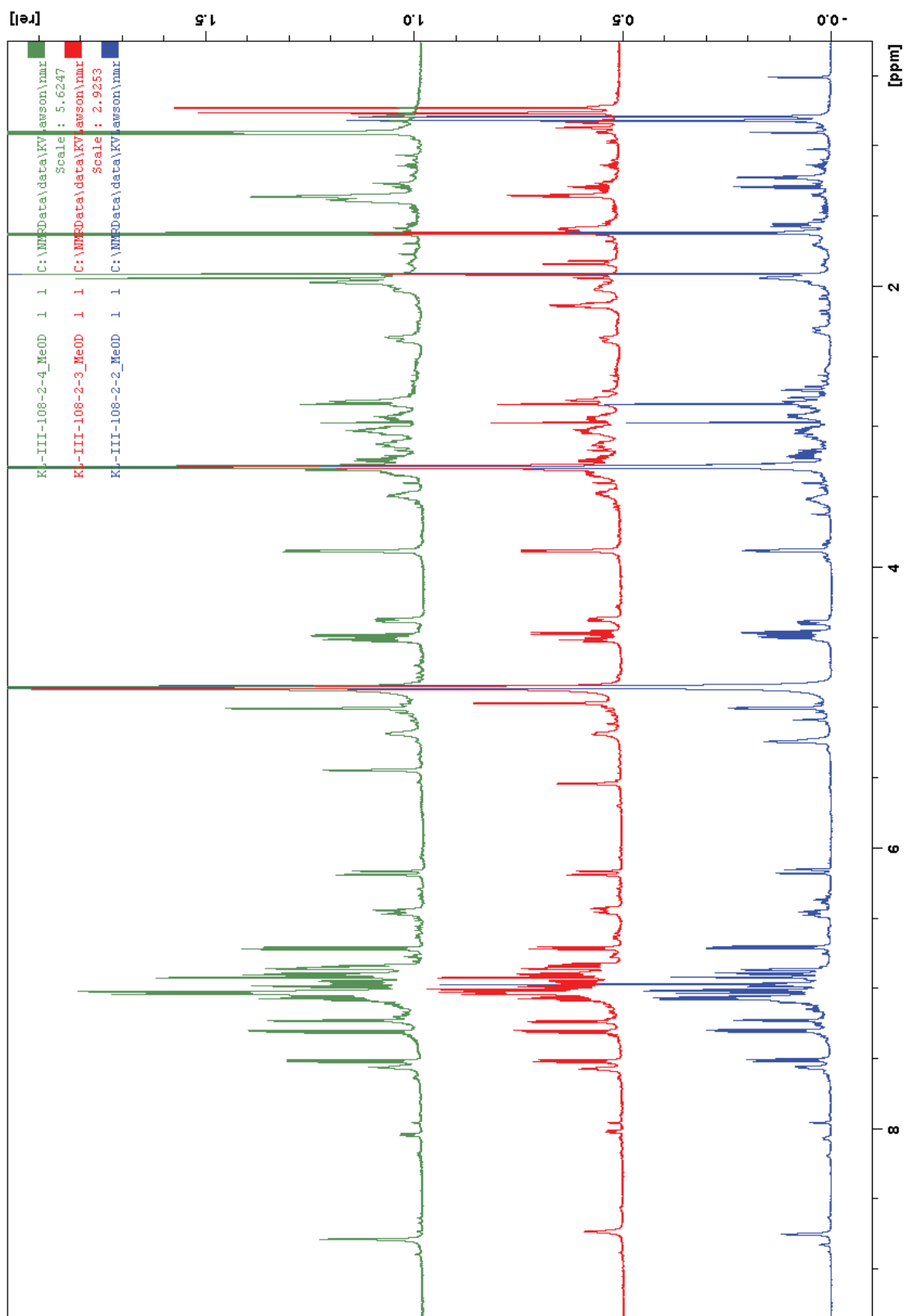
F1 - Acquisition parameters
 TD 256
 SF01 150.9134 MHz
 FIDRES 106.110962 Hz
 SW 180.000 ppm
 FMODE Echo-Antiecho

F2 - Processing parameters
 SI 2048
 SF 600.1300273 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.40

F1 - Processing parameters
 SI 2048
 MC2 echo-antiecho
 SF 150.9028800 MHz
 WDW TRAP
 SSB 2
 LB 0 Hz
 GB 0

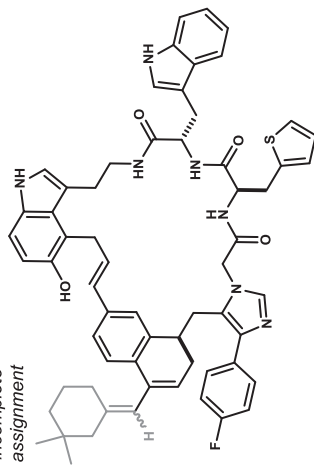
Fractions 2-2, 2-3, and 2-3 exhibit nearly identical ^1H NMR spectra (overlay below), but distinct by HPLC analysis. Fraction 2-3 was unambiguously assigned as dihydronaphthalene **38**. The related fractions are likely olefin isomers featuring the same C-C connectivity.

Figure: ^1H NMR (600 MHz, $\text{MeCN-}d_3$). Fraction 2-4 (green, top), Fraction 2-3 (product **39**, red, middle) and Fraction 2-4 (blue, bottom).



Fraction 2-2

incomplete
assignment



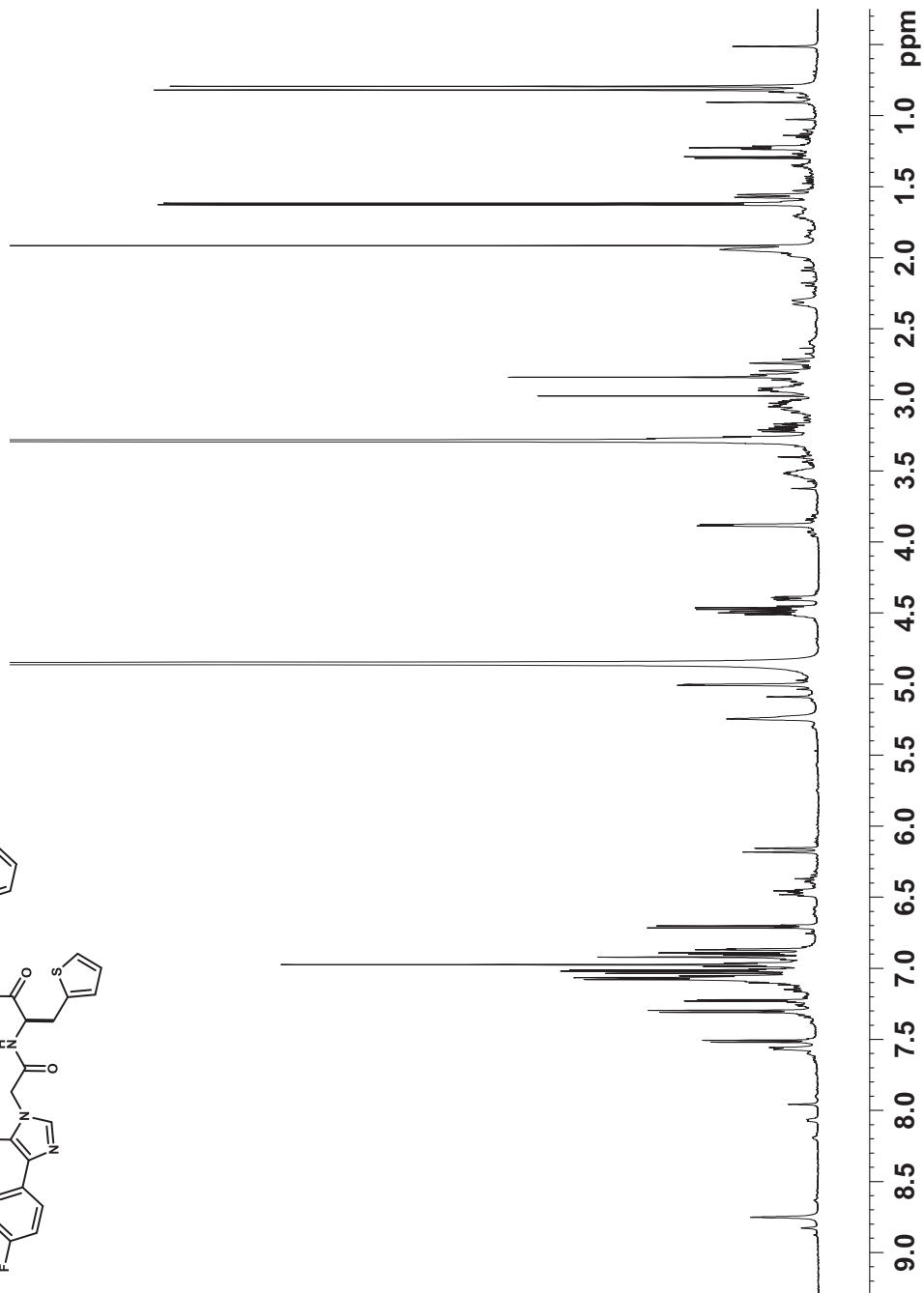
```

Current Data Parameters
NAME      KL-III-108-2-2 MeOD
EXPNO     1
PROCNO    1

F2 - Acquisition Parameters
Date_     20110504
Time      18.02
INSTRUM   av600
PROBHD    5 mm TBI5
PULPROG   zg30
TD         65536
SOLVENT   MeOD
NS         837
DS         0
SWH        12376.237 Hz
FIDRES     0.188846 Hz
AQ         2.6476543 sec
RG         362
DW         40.400 usec
DE         6.50 usec
TE         295.8 K
D1         2.00000000 sec
TD0        1

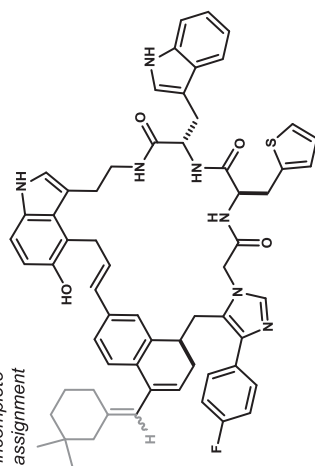
===== CHANNEL f1 =====
NUC1       1H
P1         8.60 usec
PL1        -2.00 dB
PL1W       39.81071854 W
SFO1       600.1336008 MHz

F2 - Processing parameters
SI         65536
SF         600.1300273 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00
  
```



Fraction 2-2

incomplete
assignment

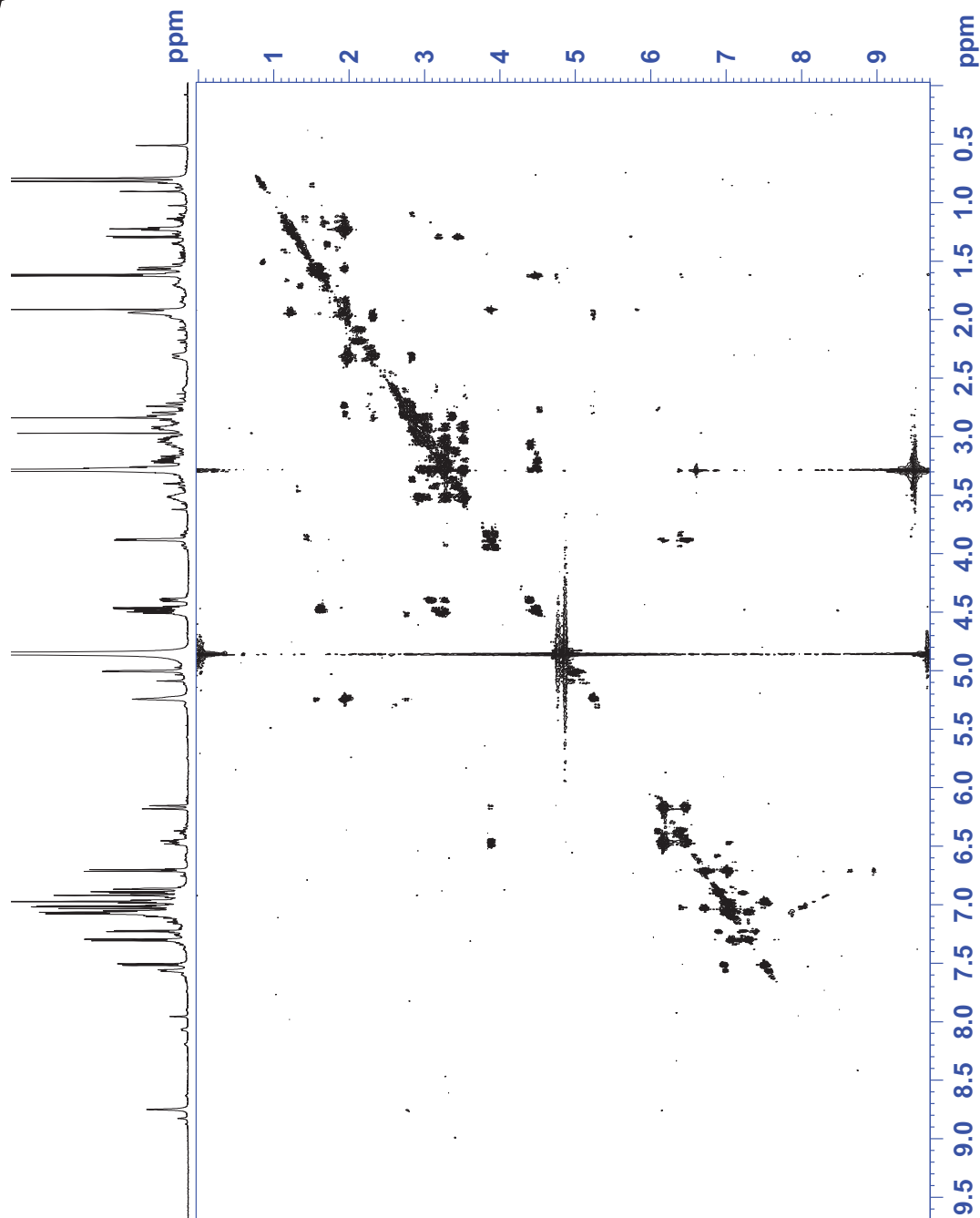


Current Data Parameters
NAME KL-III-108-2-2 MeOD
EXPNO 3
PROCNO 1

F1 - Acquisition parameters
TD 256
SFO1 600.1329 MHz
FIDRES 22.816883 Hz
SW 9.733 ppm
FMODE States-TPPI

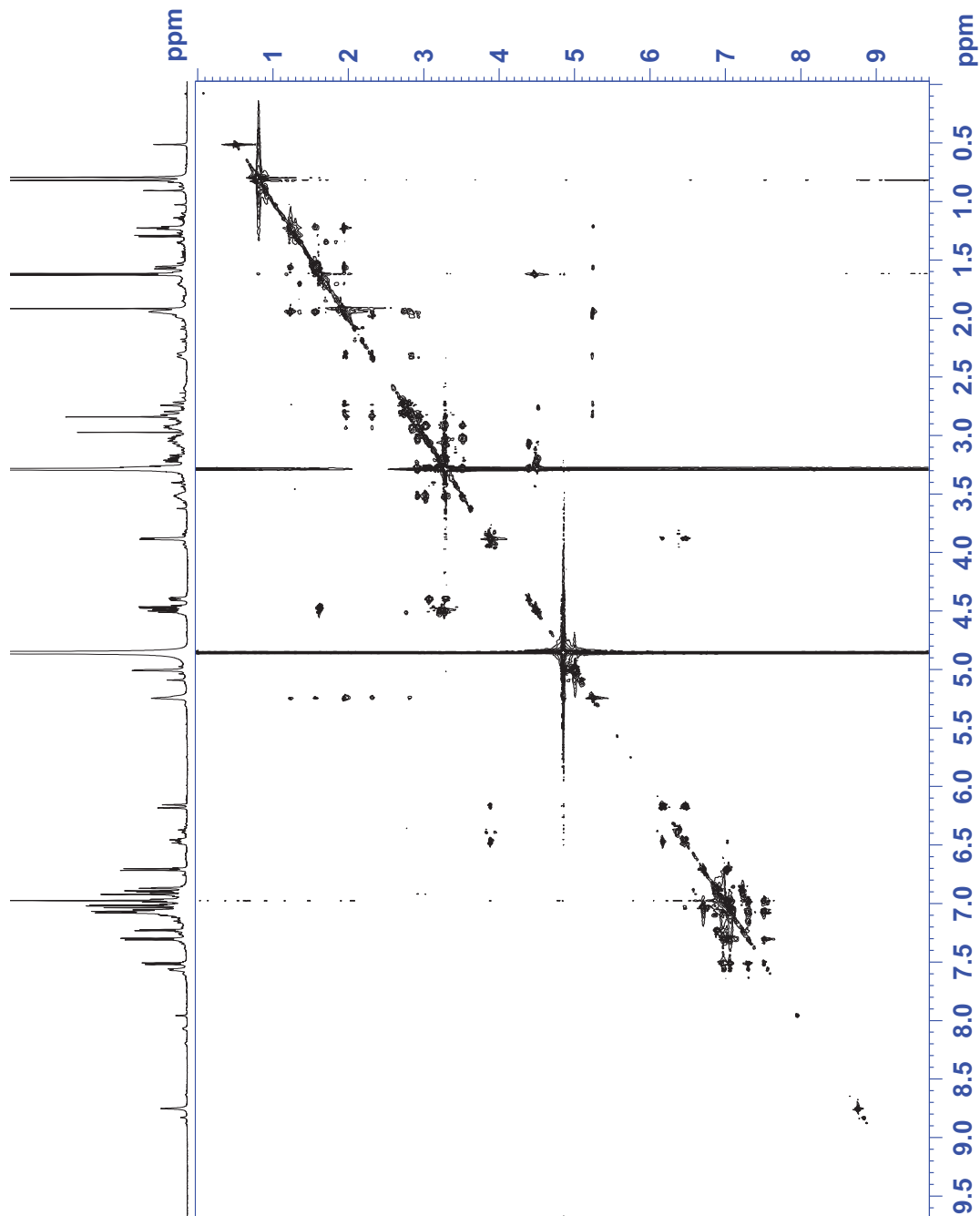
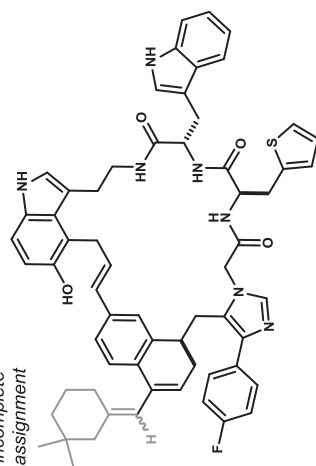
F2 - Processing parameters
SI 2048
SF 600.1300273 MHz
WDW QSI
SSB 2
LB 0 Hz
GB 0
PC 1.00

F1 - Processing parameters
SI 2048
MC2 States-TPPI
SF 600.1300273 MHz
WDW QSI
SSB 2
LB 0 Hz
GB 0



Fraction 2-2

incomplete
assignment



Current Data Parameters
NAME KL-III-108-2-2_MeOD
EXPNO 4
PROCNO 1

F1 - Acquisition parameters
TD 256

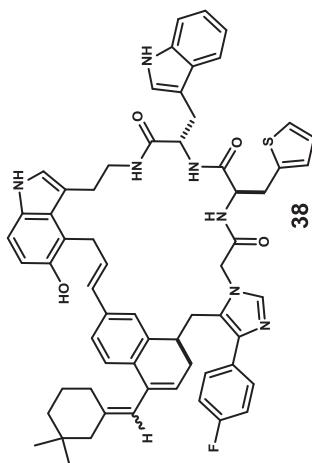
SFO1 600.1329 MHz
FIDRES 22.816883 Hz
SW 9.733 ppm
FMODE Echo-Antiecho

F2 - Processing parameters
SI 1024
SF 600.1300273 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0

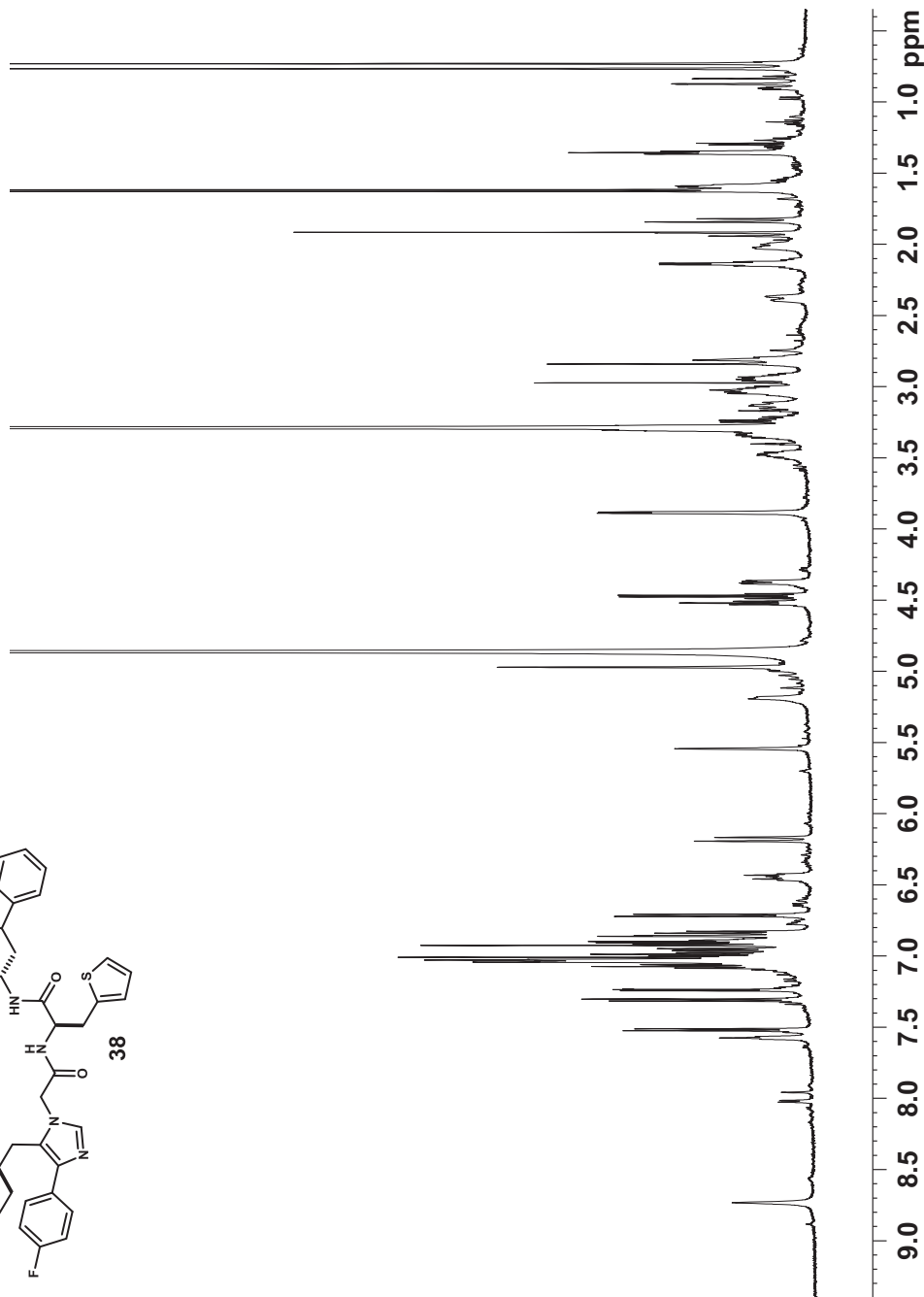
PC 1.00

F1 - Processing parameters
SI 1024
MC2 echo-antiecho
SF 600.1300273 MHz
WDW USER
SSB 2
LB 0 Hz
GB 0

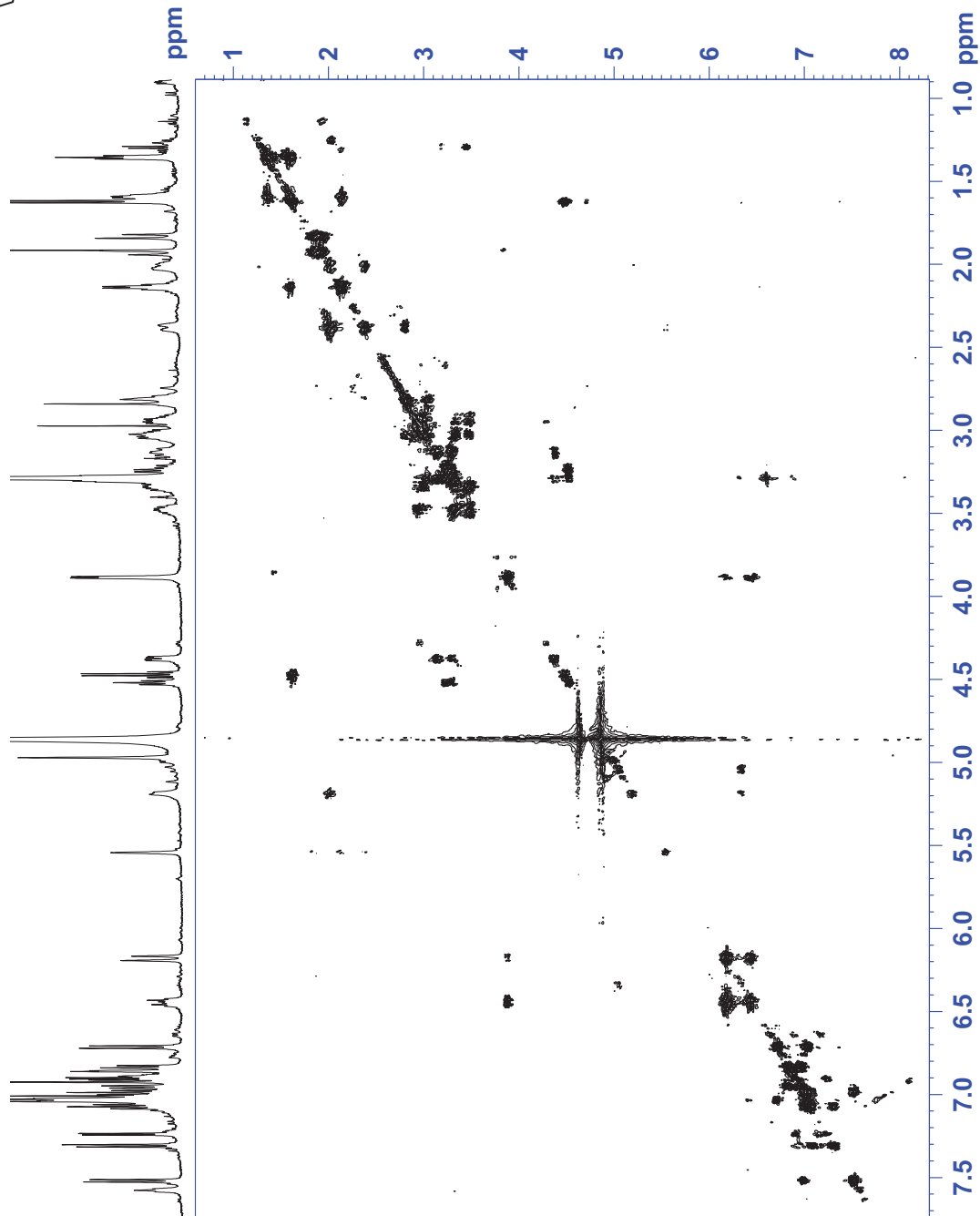
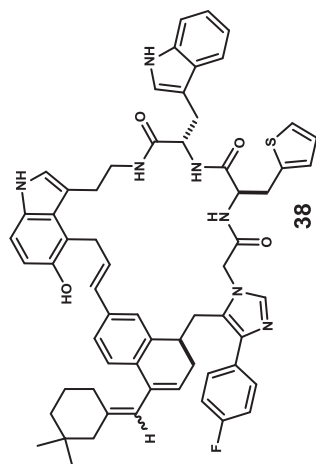
Fraction 2-3 (Product 38)



Current Data Parameters
 NAME KL-III-108-2-3 MeOD
 EXPNO 1
 PROCNO 1
 F2 - Acquisition Parameters
 Date_ 20110503
 Time_ 17.40
 INSTRUM av600
 PROBHD 5 mm TBI5
 PULPROG zg30
 TD 65536
 SOLVENT MeOD
 NS 293
 DS 0
 SMH 12376.237 Hz
 FIDRES 0.188846 Hz
 AQ 2.6476543 sec
 RG 362
 DW 40.400 usec
 DE 6.50 usec
 TE 294.7 K
 D1 2.00000000 sec
 TD0 1
 ===== CHANNEL f1 =====
 NUC1 1H
 P1 8.60 usec
 PL1 -2.00 dB
 PL1W 39.81071854 W
 SFO1 600.1336008 MHz
 F2 - Processing parameters
 SI 65536
 SF 600.1300273 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00



Fraction 2-3 (Product 38)



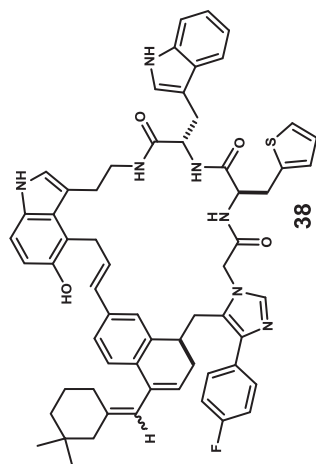
Current Data Parameters
 NAME KL-III-108-2-3_MeOD
 EXPNO 3
 PROCNO 1

F1 - Acquisition parameters
 TD 256
 SFO1 600.1329 MHz
 FIDRES 22.605614 Hz
 SW 9.643 ppm
 FnmODE States-TPPI

F2 - Processing parameters
 SI 2048
 SF 600.1300273 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 2048
 MC2 States-TPPI
 SF 600.1300273 MHz
 WDW USER
 SSB 2
 LB 0 Hz
 GB 0

Fraction 2-3 (Product 38)

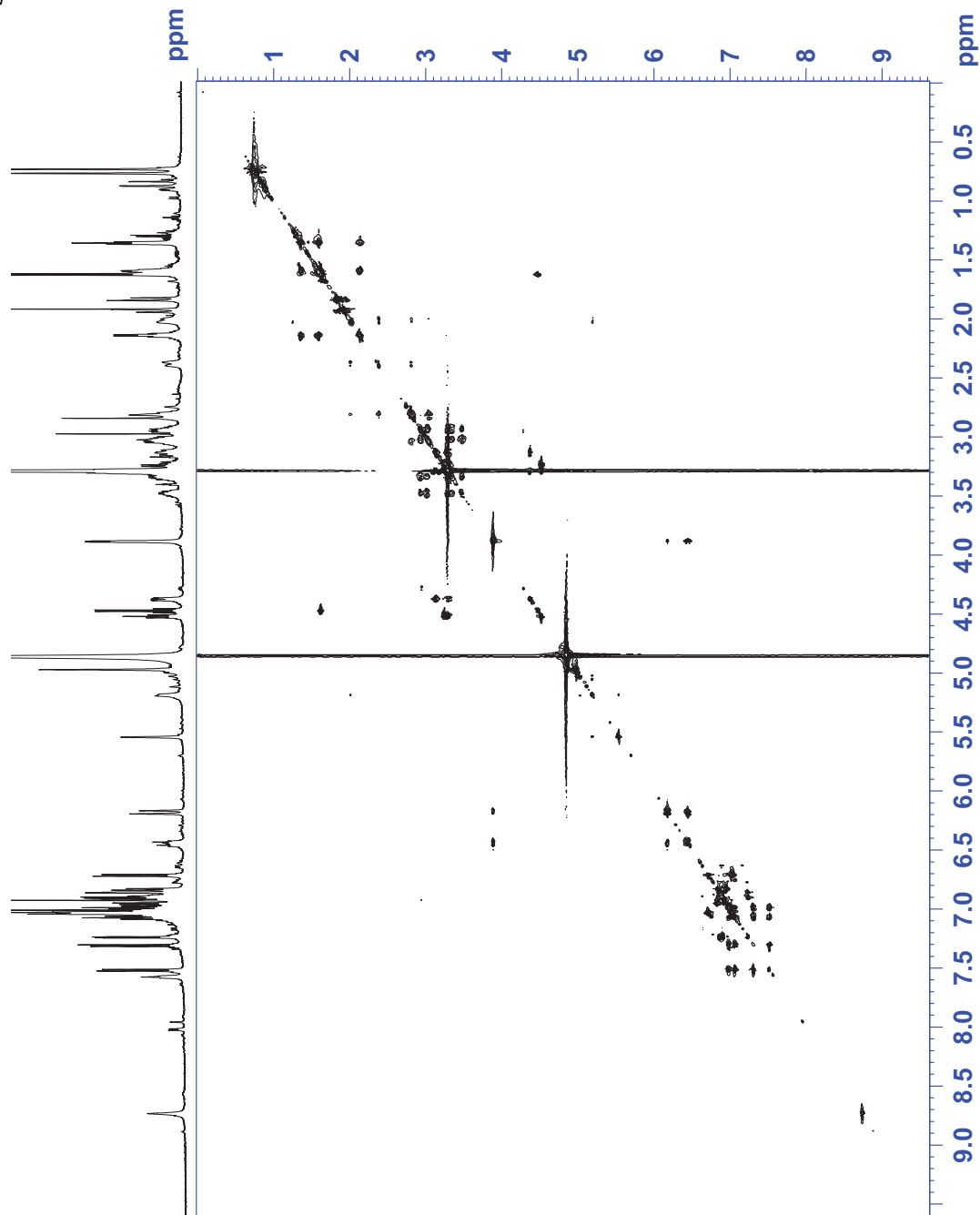


Current Data Parameters
 NAME KL-III-108-2-3 MeOD
 EXPNO 4
 PROCNO 1

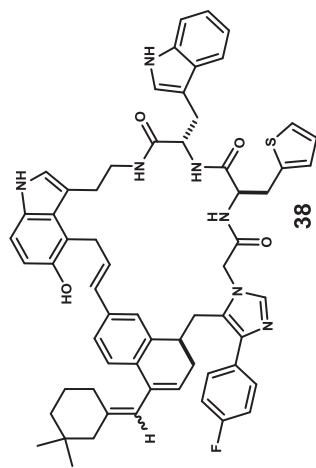
F1 - Acquisition parameters
 TD 256
 SFO1 600.1329 MHz
 FIDRES 22.605614 Hz
 SW 9.643 ppm
 F1MODE Echo-Antiecho

F2 - Processing parameters
 SI 1024
 SF 600.1300273 MHz
 WDW QSINE
 LB 2
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 1024
 MC2 echo-antiecho
 SF 600.1300273 MHz
 WDW QSINE
 LB 2
 GB 0



Fraction 2-3 (Product 38)

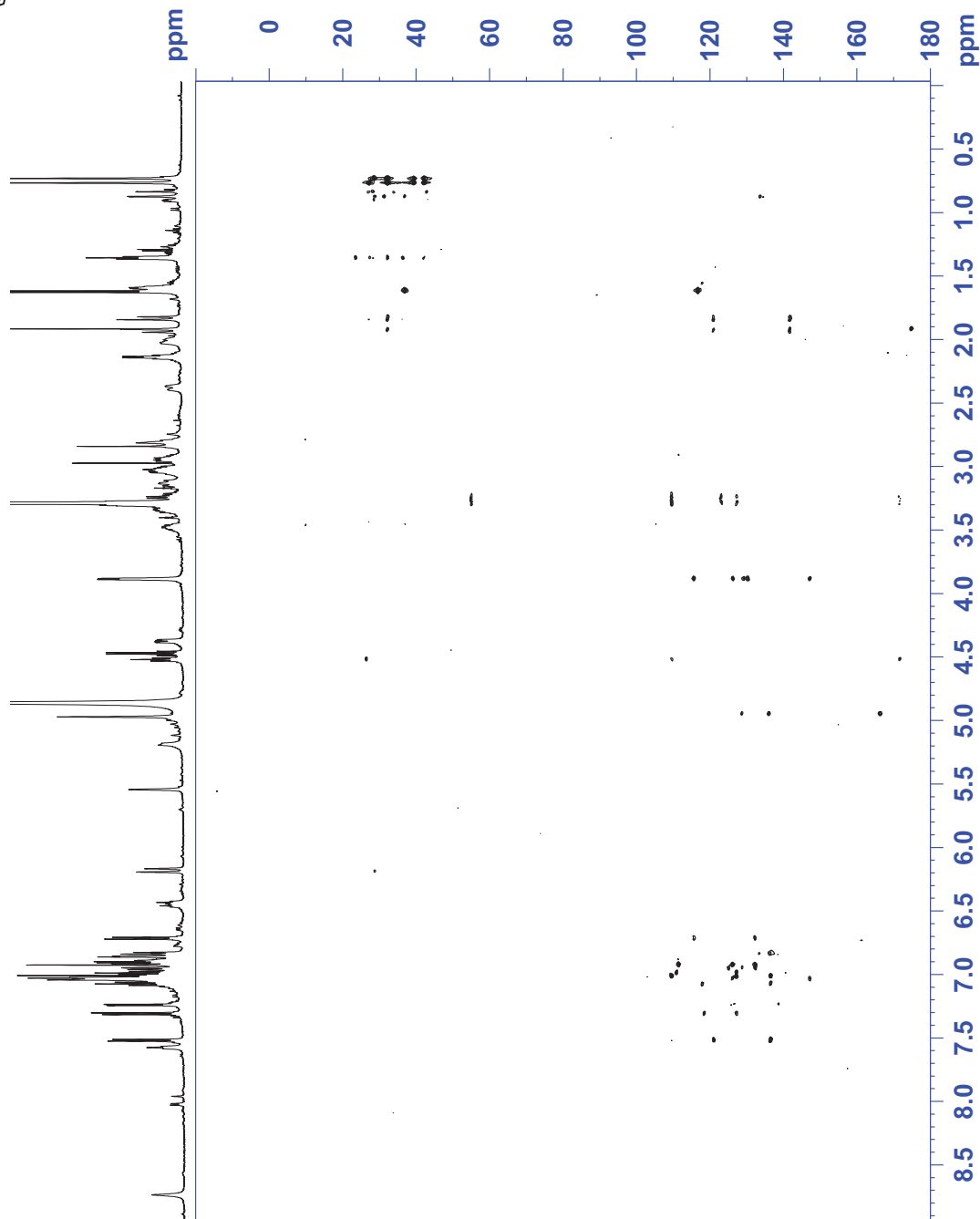


Current Data Parameters
 NAME KL-III-108-2-3 MeOD
 EXPNO 6
 PROCNO 1

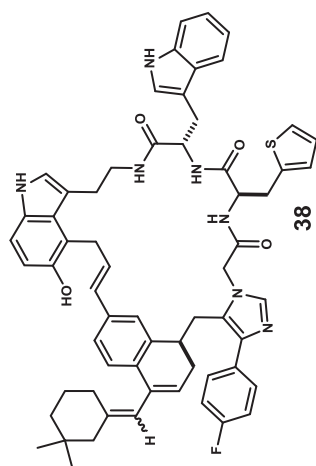
F1 - Acquisition parameters
 TD 256
 SF01 150.9149 MHz
 FIDRES 117.902252 Hz
 SW 200.000 ppm
 F1MODE QF

F2 - Processing parameters
 SI 1024
 SF 600.1300273 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 1024
 MC2 QF
 SF 150.9028090 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0



Fraction 2-3 (Product 38)

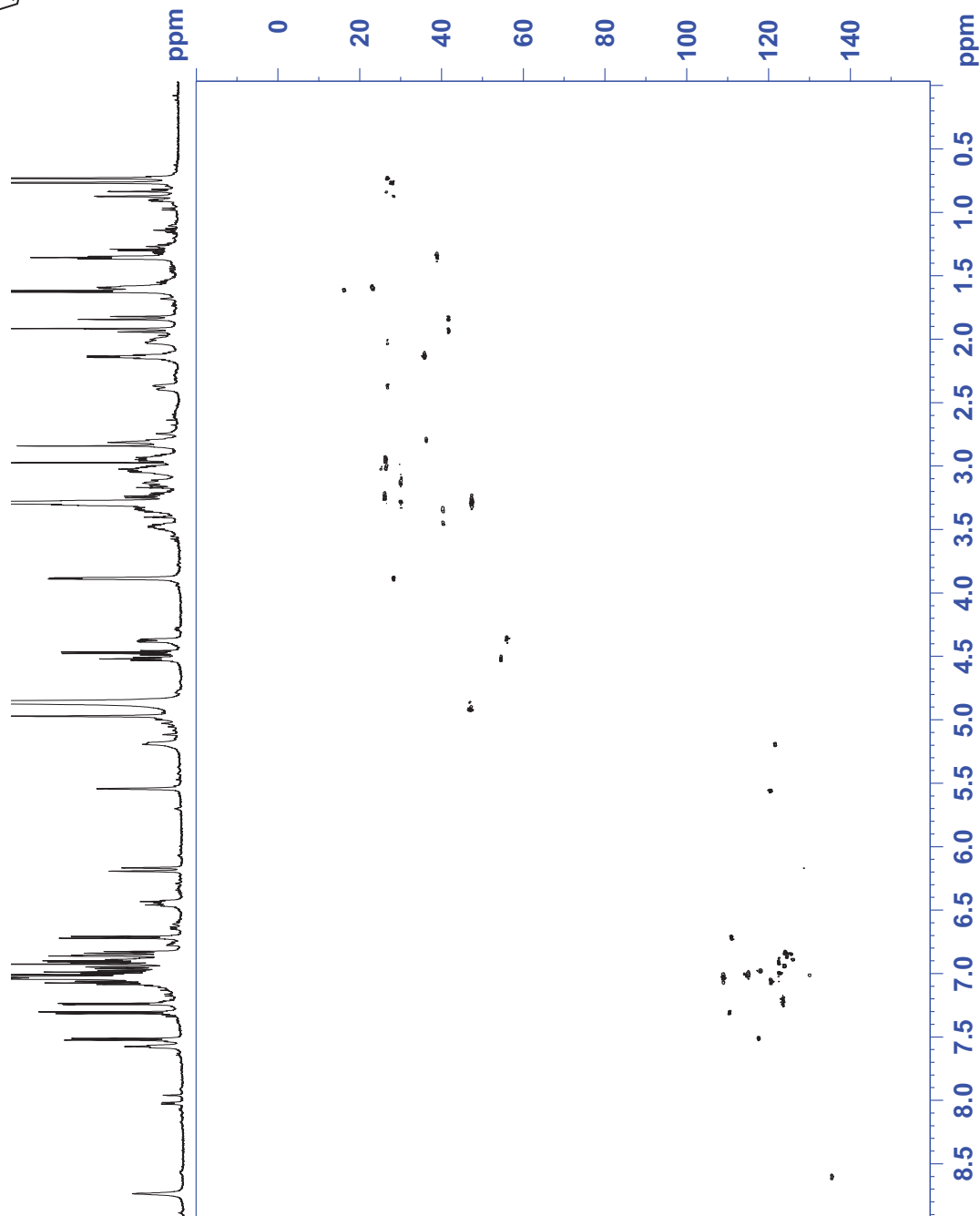


Current Data Parameters
 NAME KL-III-108-2-3 MeOD
 EXPNO 7
 PROCNO 1

F1 - Acquisition parameters
 TD 256
 SFO1 150.9134 MHz
 FIDRES 106.110962 Hz
 SW 180.000 ppm
 F1MODE Echo-Antiecho

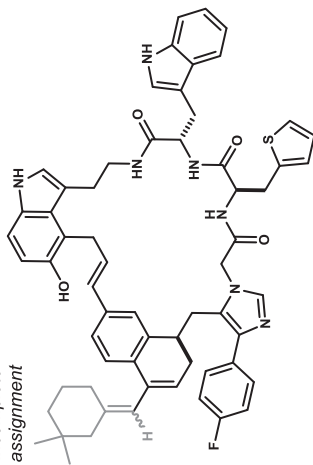
F2 - Processing parameters
 SI 2048
 SF 600.1300273 MHz
 WDW QSI
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.40

F1 - Processing parameters
 SI 2048
 MC2 echo-antiecho
 SF 150.9028800 MHz
 WDW QSI
 SSB 2
 LB 0 Hz
 GB 0



Fraction 2-4

incomplete
assignment



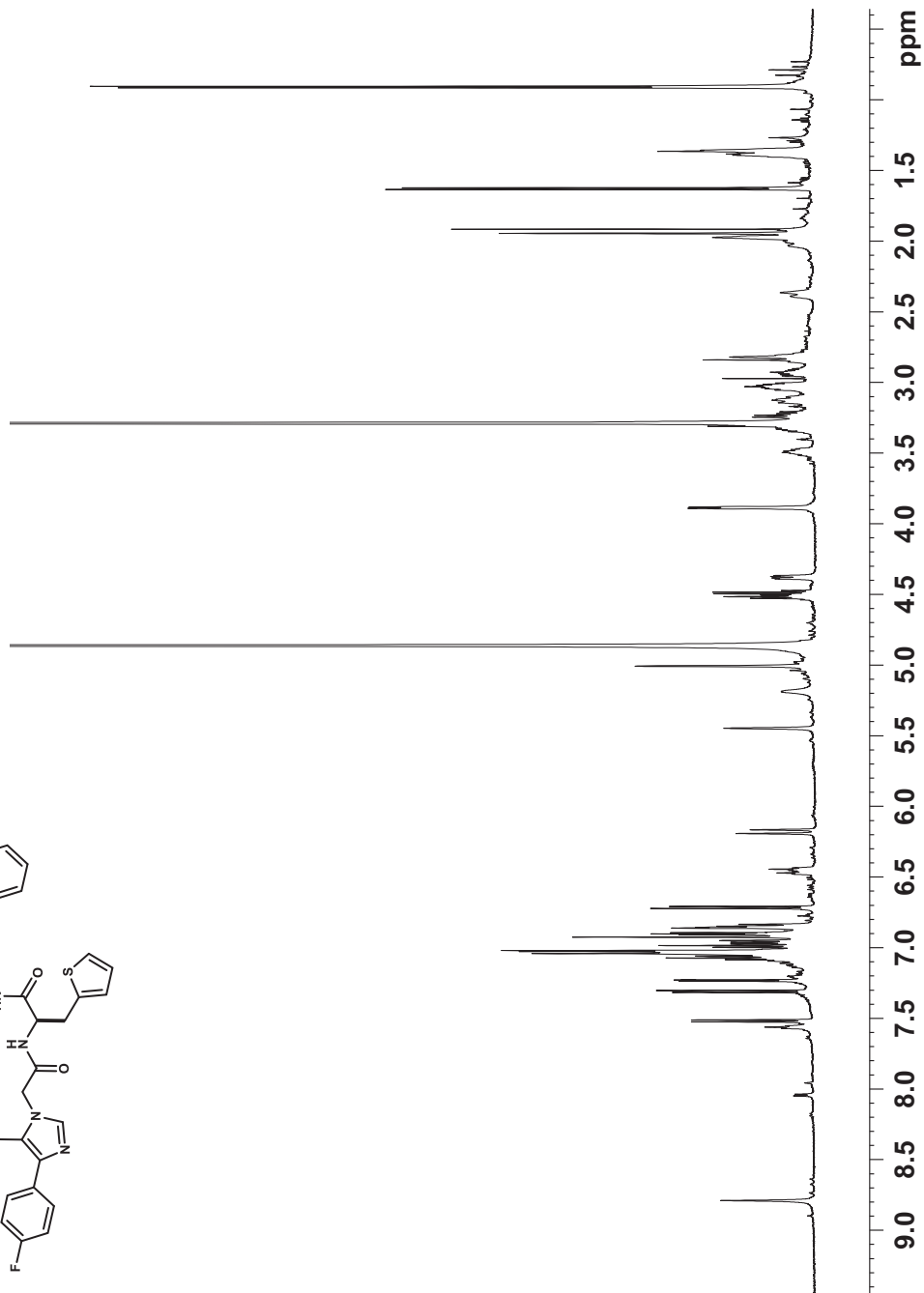
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Current Data Parameters
NAME      KL-III-108-2-4 MeOD
EXPNO     1
PROCNO    1

F2 - Acquisition Parameters
Date_     20110502
Time      21.03
INSTRUM   av600
PROBHD    5 mm TBI5
PULPROG   zg30
TD         65536
SOLVENT    MeOD
NS         112
DS         0
SWH        12376.237 Hz
FIDRES     0.188846 Hz
AQ         2.6476543 sec
RG         362
DW         40.400 usec
DE         6.50 usec
TE         294.8 K
D1         2.00000000 sec
TD0        1

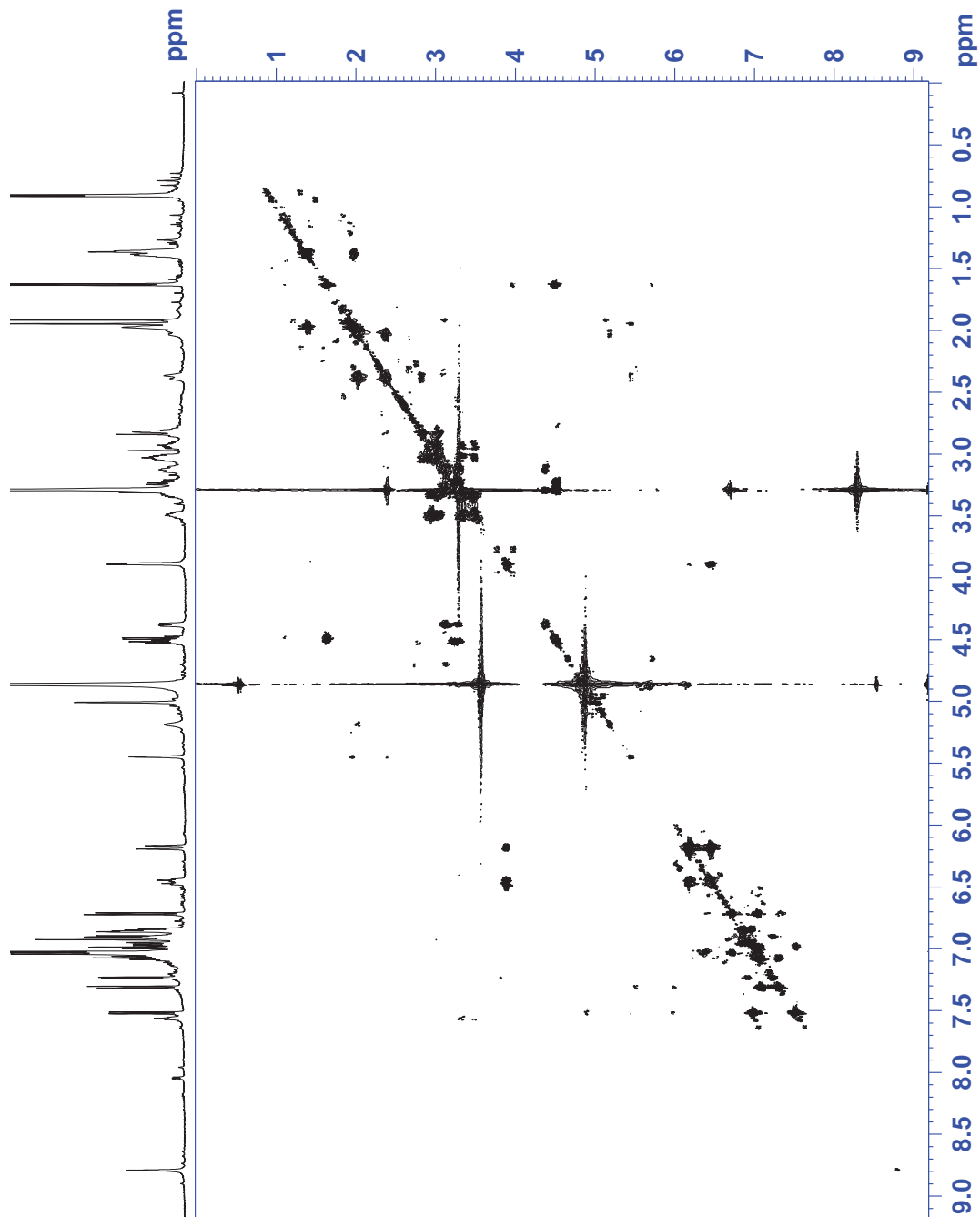
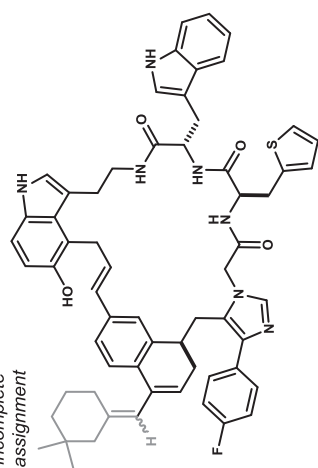
===== CHANNEL f1 =====
NUC1       1H
P1         8.60 usec
PL1        -2.00 dB
PL1W       39.81071854 W
SFO1       600.1336008 MHz

F2 - Processing parameters
SI         65536
SF         600.1300273 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00
    
```



Fraction 2-4

incomplete
assignment



Current Data Parameters
NAME KL-III-108-2-4 MeOD
EXPNO 3
PROCNO 1

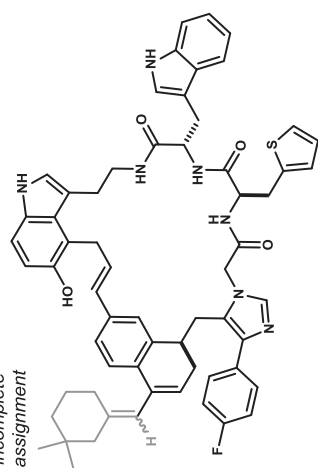
F1 - Acquisition parameters
TD 256
SF01 600.1328 MHz
FIDRES 21.798269 Hz
SW 9.299 ppm
FMODE States-TPPI

F2 - Processing parameters
SI 2048
SF 600.1300273 MHz
WDW QSI
SSB 2
LB 0 Hz
GB 0
PC 1.00

F1 - Processing parameters
SI 2048
MC2 States-TPPI
SF 600.1300273 MHz
WDW TRAP
SSB 2
LB 0 Hz
GB 0

Fraction 2-4

incomplete
assignment

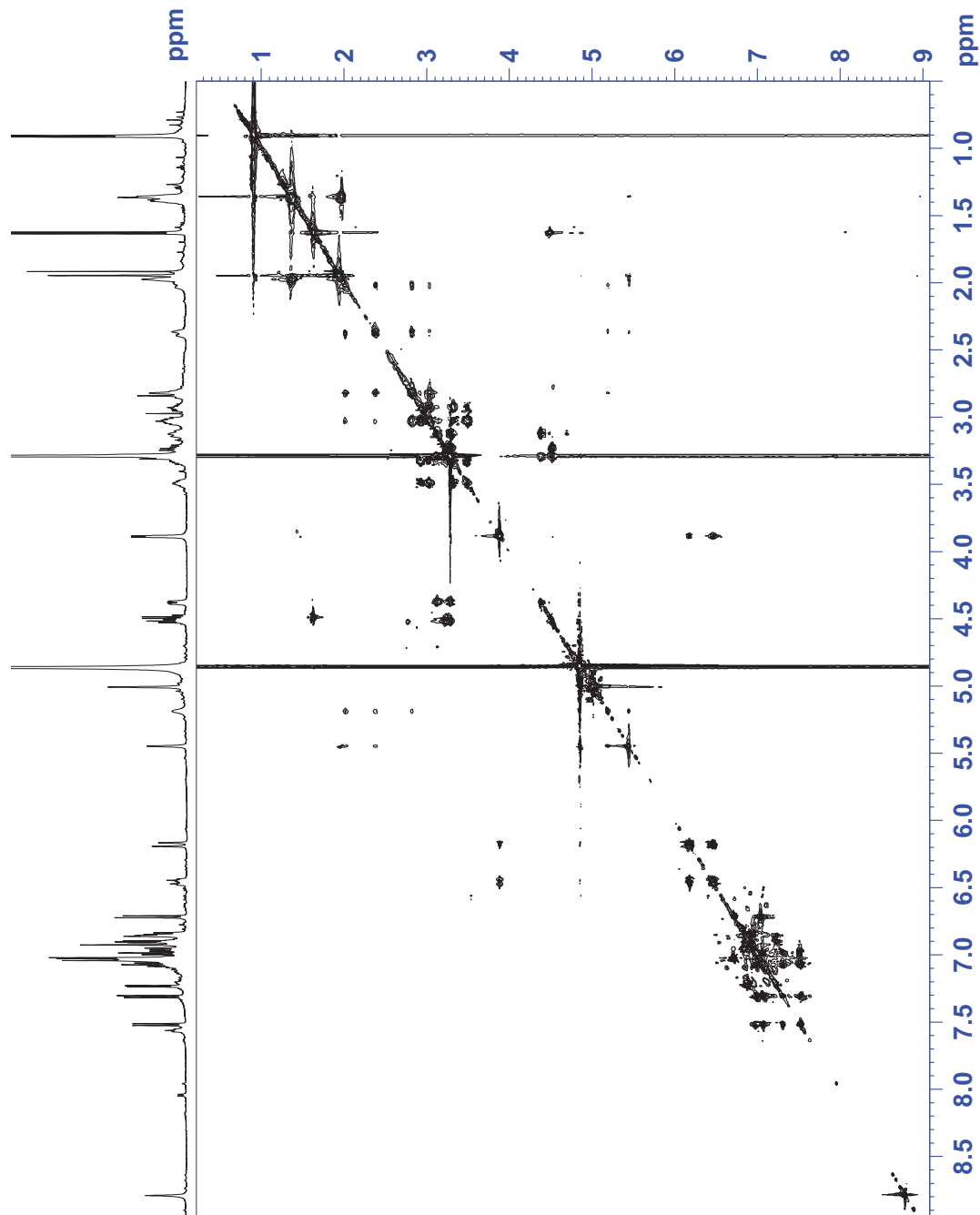


Current Data Parameters
NAME KL-III-108-2-4_MeOD
EXPNO 4
PROCNO 1

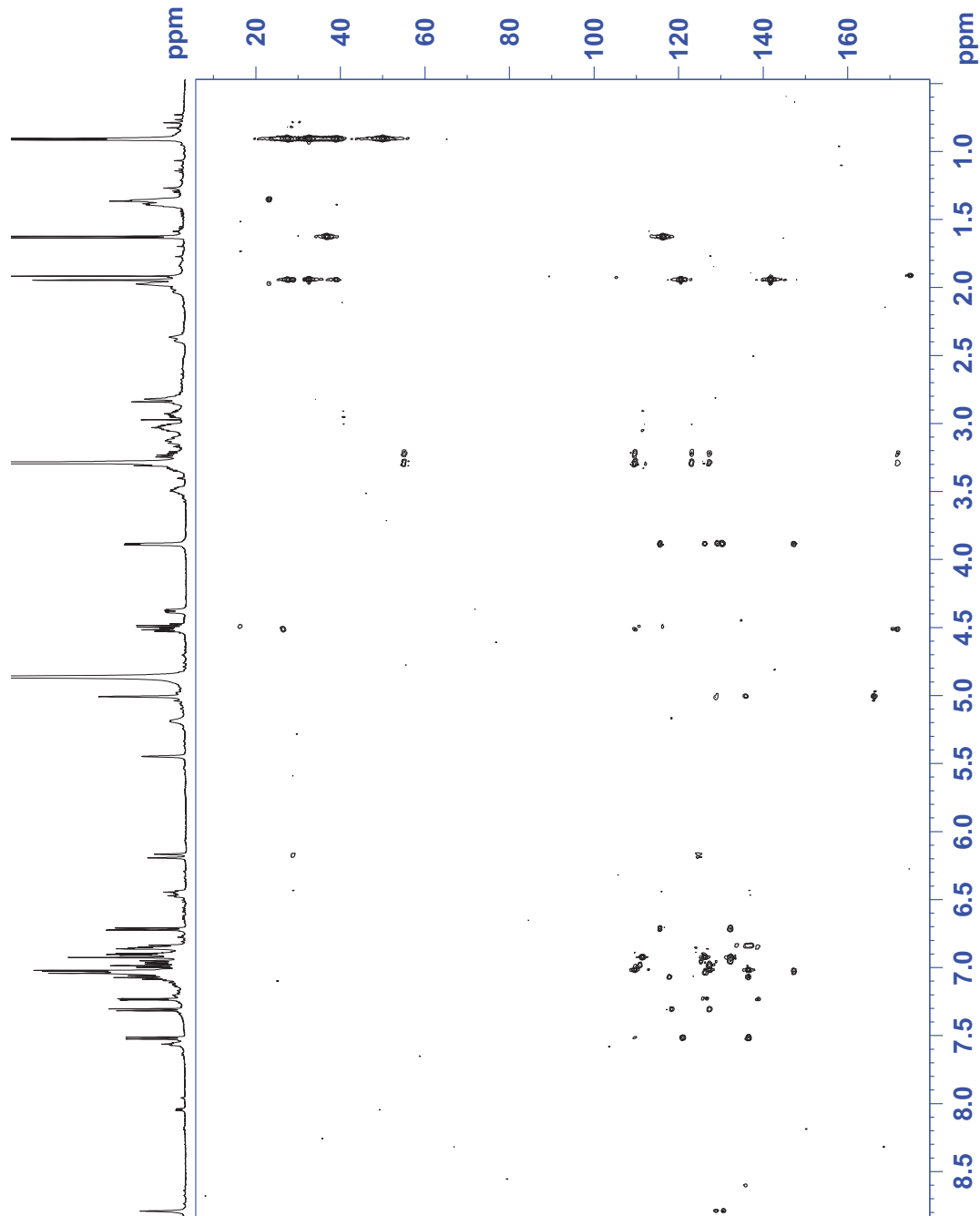
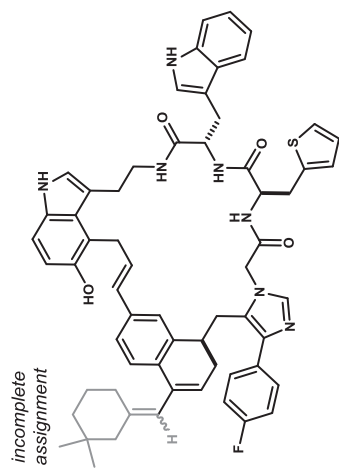
F1 - Acquisition parameters
TD 256
SF01 600.1328 MHz
FIDRES 21.798269 Hz
SW 9.299 ppm
F1MODE Echo-Antiecho

F2 - Processing parameters
SI 1024
SF 600.1300273 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0
PC 1.00

F1 - Processing parameters
SI 1024
MC2 echo-antiecho
SF 600.1300273 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0



Fraction 2-4



Current Data Parameters
NAME KL-III-108-2-4 MeOD
EXPNO 6
PROCNO 1

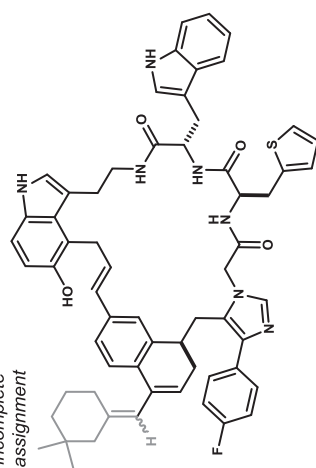
F1 - Acquisition parameters
TD 256
SF01 150.9149 MHz
FIDRES 117.902252 Hz
SW 200.000 ppm
FMODE QF

F2 - Processing parameters
SI 1024
SF 600.1300273 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0
PC 1.00

F1 - Processing parameters
SI 1024
MC2 QF
SF 150.9028090 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0

Fraction 2-4

incomplete
assignment

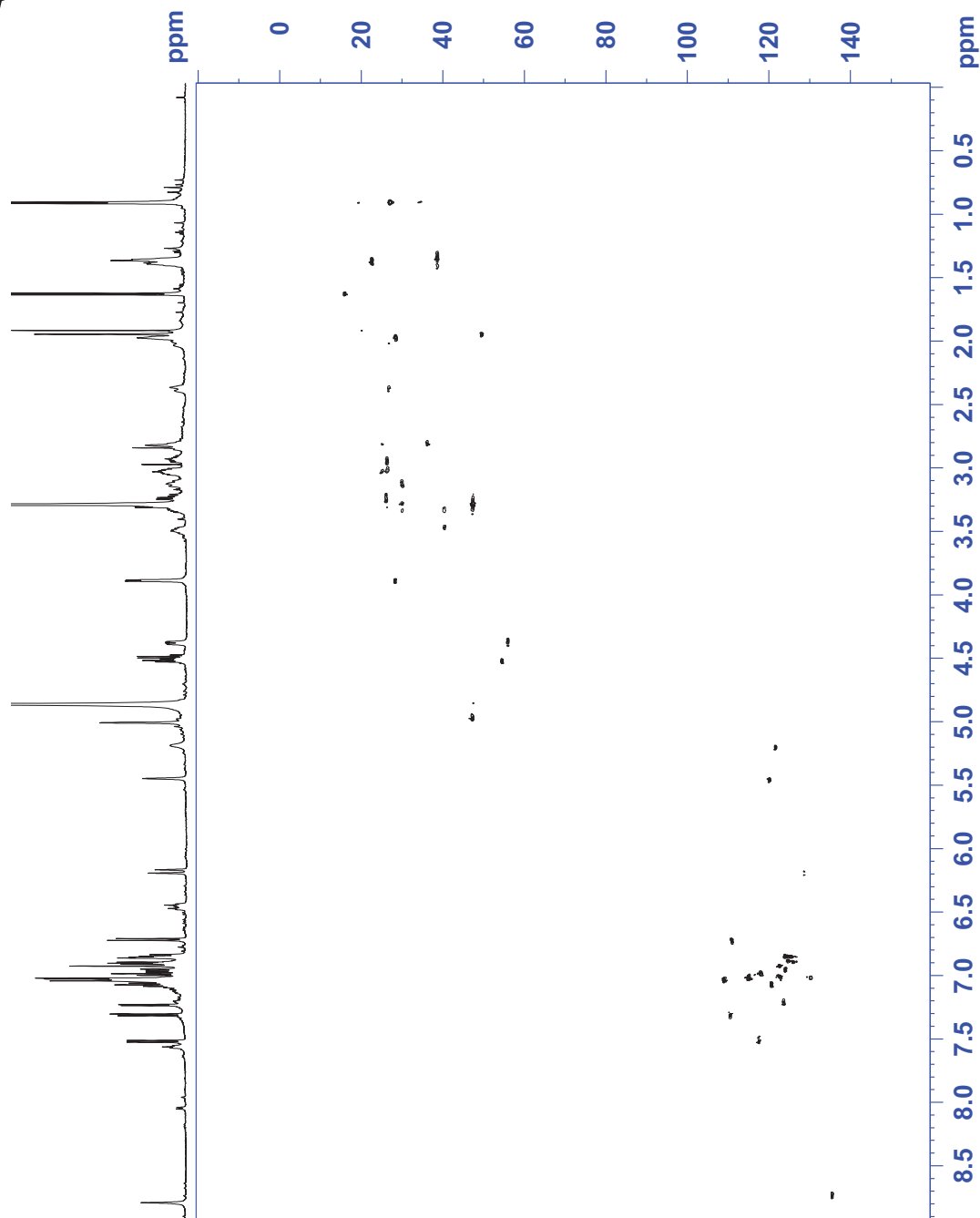


Current Data Parameters
NAME KL-III-108-2-4 MeOD
EXPNO 7
PROCNO 1

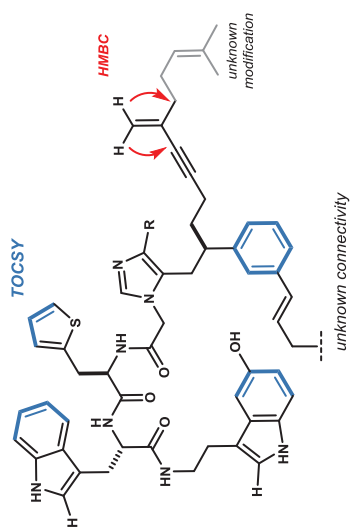
F1 - Acquisition parameters
TD 256
SFO1 150.9134 MHz
FIDRES 106.110962 Hz
SW 180.000 ppm
FMODE Echo-Antiecho

F2 - Processing parameters
SI 2048
SF 600.1300273 MHz
WDW QSI
SSB 2
LB 0 Hz
GB 0
PC 1.40

F1 - Processing parameters
SI 2048
MC2 echo-antiecho
SF 150.9028800 MHz
WDW USER
SSB 2
LB 0 Hz
GB 0



Fraction 3-5-1

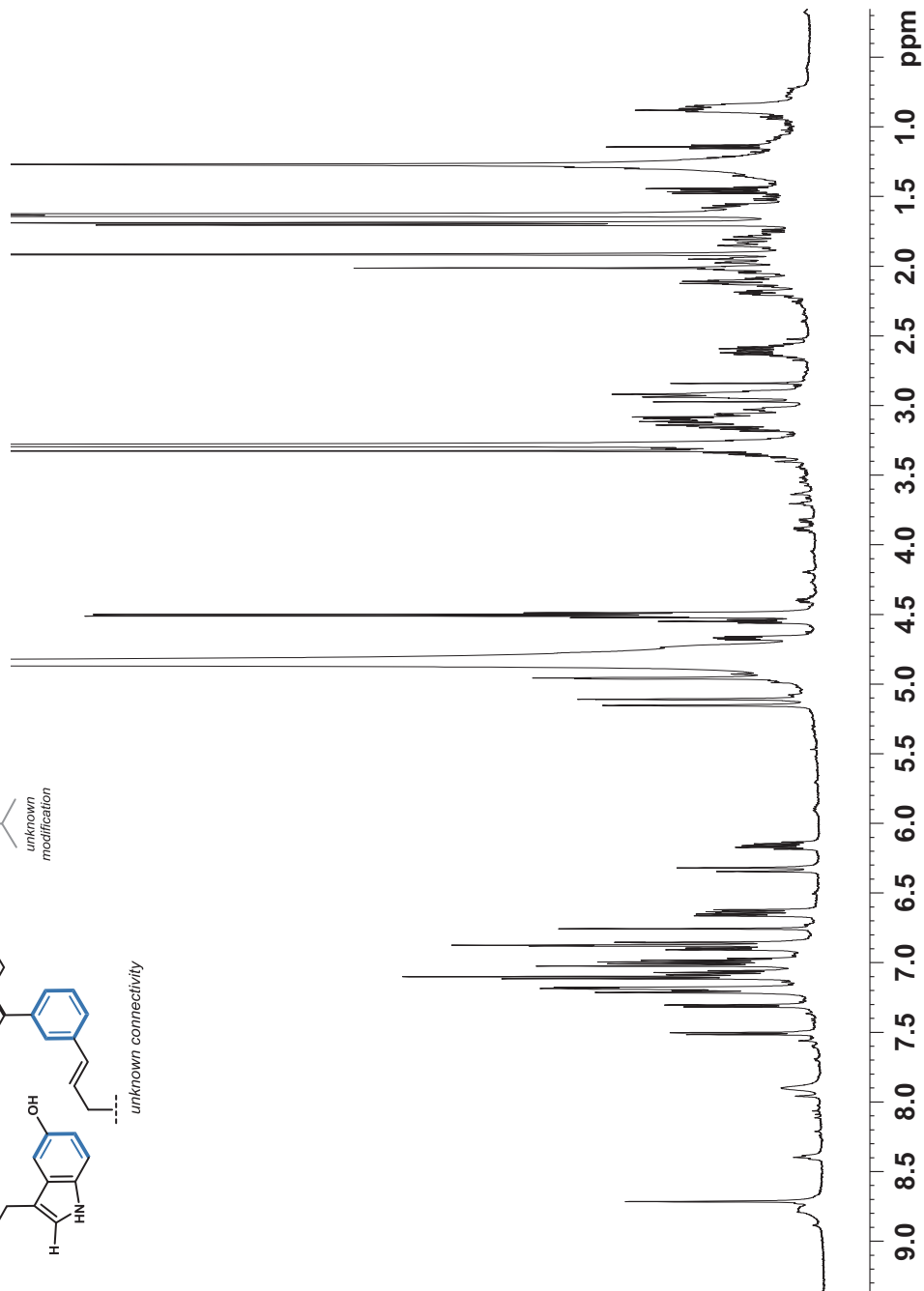


Current Data Parameters
NAME KL-III-108-3-5-1
EXPNO 5
PROCNO 1

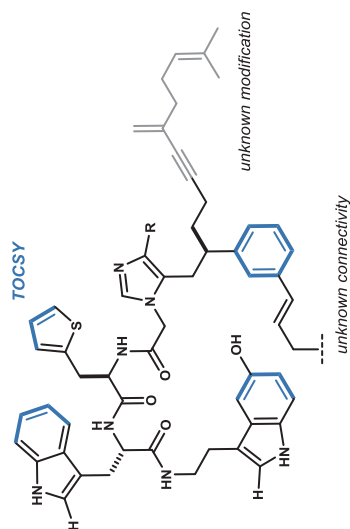
F2 - Acquisition Parameters
Date_ 20110603
Time 9.49
INSTRUM av600
PROBHD 5 mm TBI5
PULPROG zg
TD 65536
SOLVENT MeOD
NS 368
DS 0
SWH 12376.237 Hz
FIDRES 0.188846 Hz
AQ 2.6476543 sec
RG 362
DW 40.400 usec
DE 6.50 usec
TE 295.1 K
D1 2.00000000 sec
TD0 1

===== CHANNEL f1 =====
NUC1 1H
P1 10.60 usec
PL1 -2.00 dB
PL1W 39.81071854 W
SFO1 600.1336008 MHz

F2 - Processing parameters
SI 65536
SF 600.1300273 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



Fraction 3-5-1

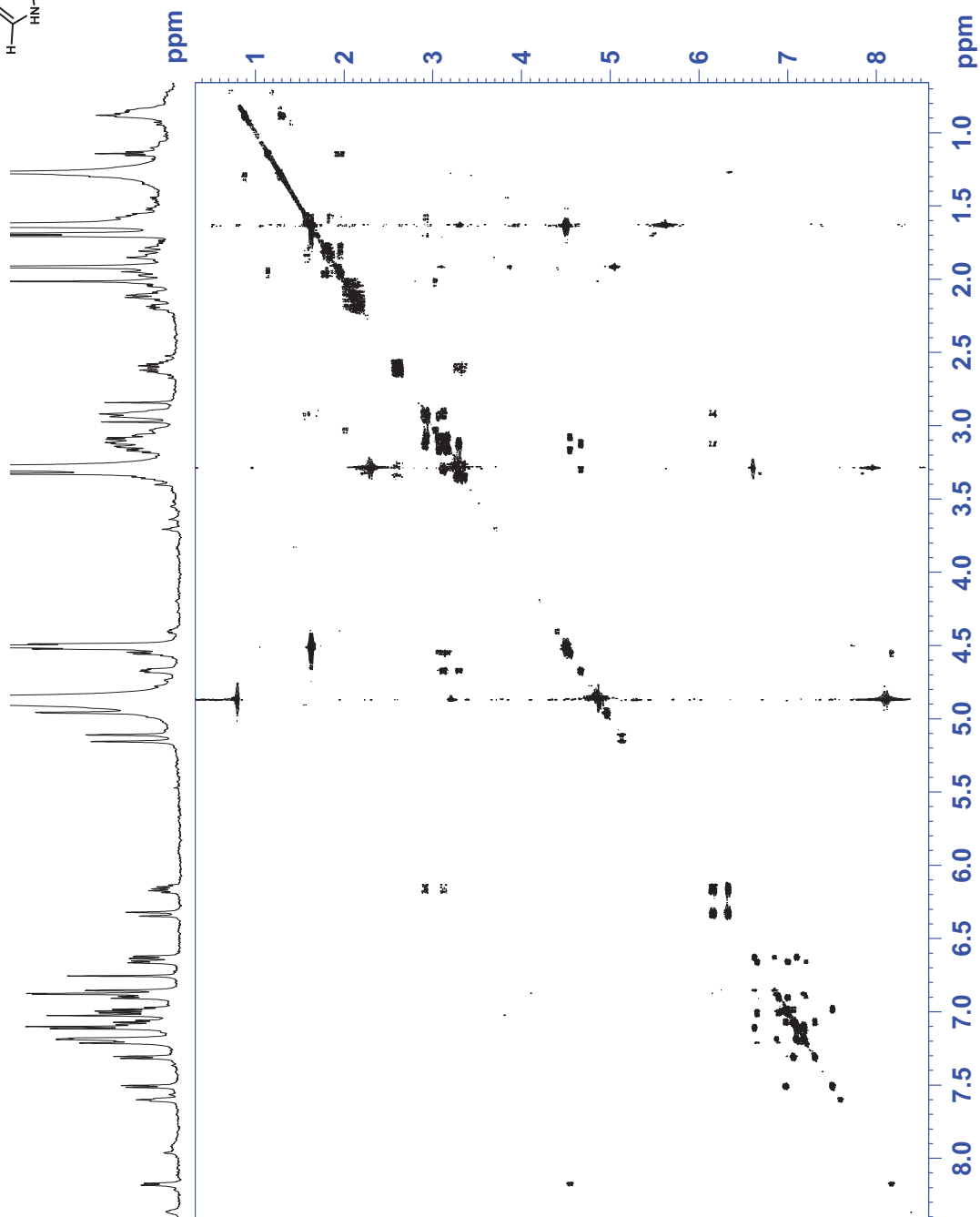


Current Data Parameters
 NAME K1-III-108-3-5-1
 EXPO 2
 PROCNO 1

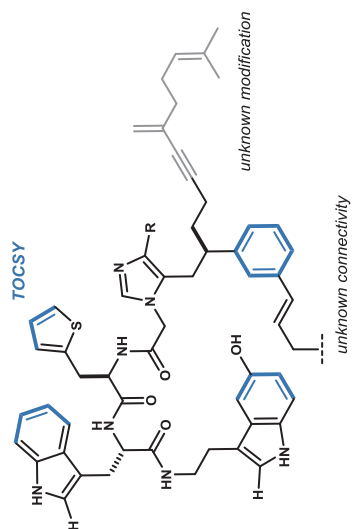
F1 - Acquisition parameters
 TD 512
 SFO1 600.1327 MHz
 FIDRES 10.523297 Hz
 SW 8.978 ppm
 F1MODE States-TPPI

F2 - Processing parameters
 SI 2048
 SF 600.1300273 MHz
 WDW QSI
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 2048
 MC2 States-TPPI
 SF 600.1300273 MHz
 WDW USER
 SSB 2
 LB 0 Hz
 GB 0



Fraction 3-5-1

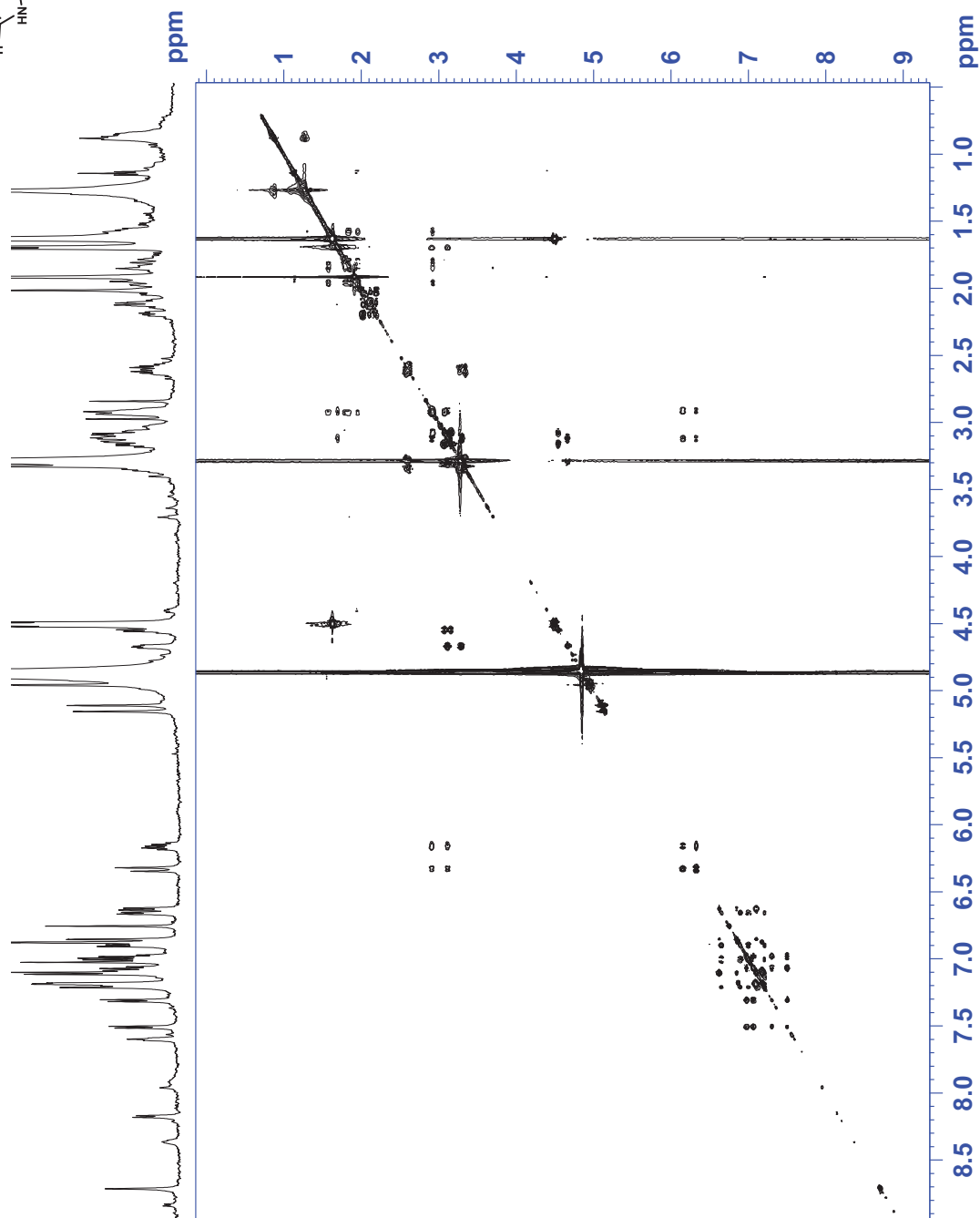


Current Data Parameters
 NAME KL-III-108-3-5-1
 EXNO 3
 PROCNO 1

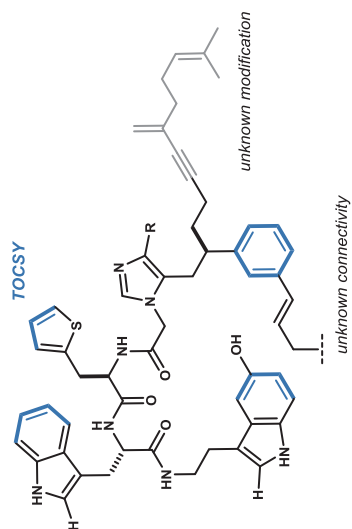
F1 - Acquisition parameters
 TD 512
 SFO1 600.1327 MHz
 FIDRES 12.424457 Hz
 SW 10.600 ppm
 FqMODE Echo-Antiecho

F2 - Processing parameters
 SI 1024
 SF 600.1300273 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 1024
 MC2 echo-antiecho
 SF 600.1300273 MHz
 WDW USER
 SSB 2
 LB 0 Hz
 GB 0



Fraction 3-5-1



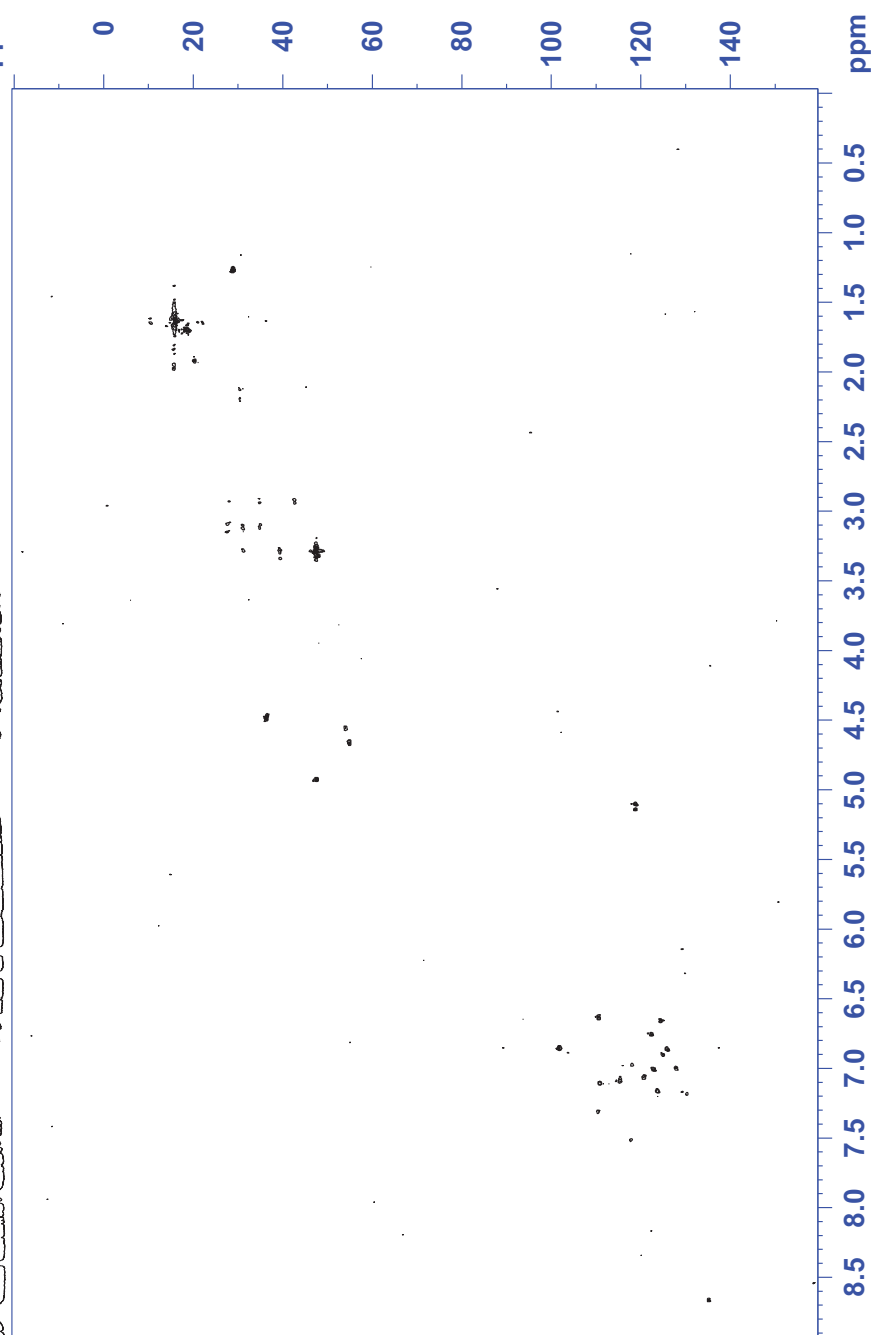
Current Data Parameters
 NAME KL-III-108-3-5-1
 EXNO 4
 PROCNO 1

F1 - Acquisition parameters
 TD 256
 SFO1 150.9134 MHz
 FIDRES 106.110962 Hz
 SW 180.000 ppm
 FnMODE Echo-Antiecho

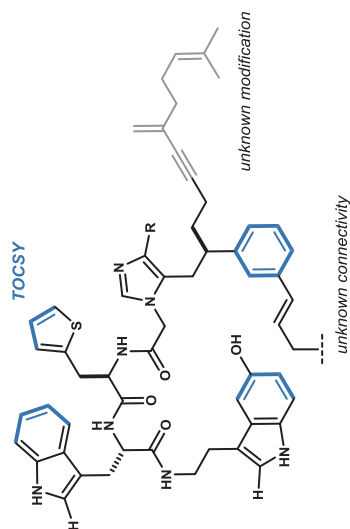
F2 - Processing parameters
 SI 2048
 SF 600.1300273 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.40

F1 - Processing parameters
 SI 2048
 MC2 echo-antiecho
 SF 150.9028800 MHz
 WDW TRAP
 SSB 2
 LB 0 Hz
 GB 0

ppm



Fraction 3-5-1

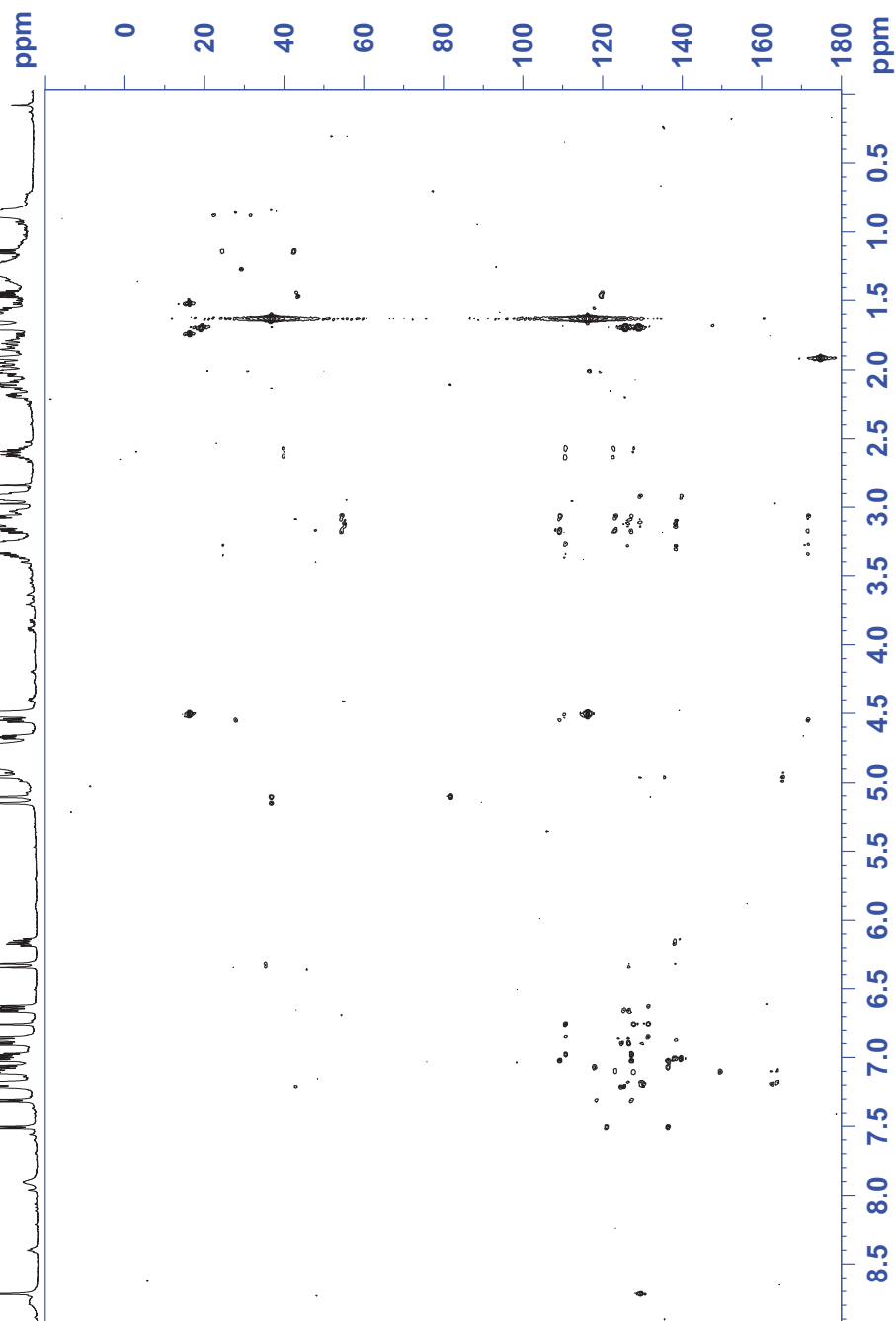


Current Data Parameters
 NAME K1-III-108-3-5-1
 EXPNO 7
 PROCNO 1

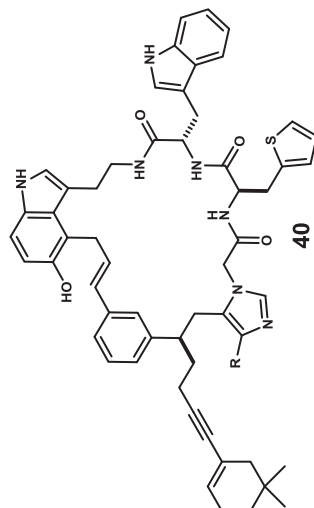
F1 - Acquisition parameters
 TD 256
 SF01 150.9149 MHz
 FIDRES 117.902252 Hz
 SW 200.000 ppm
 FMODE QF

F2 - Processing parameters
 SI 1024
 SF 600.1300273 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 1024
 MC2 QF
 SF 150.9028090 MHz
 WDW TRAP
 SSB 2
 LB 0 Hz
 GB 0



Fraction 4-1 (Product **40**)



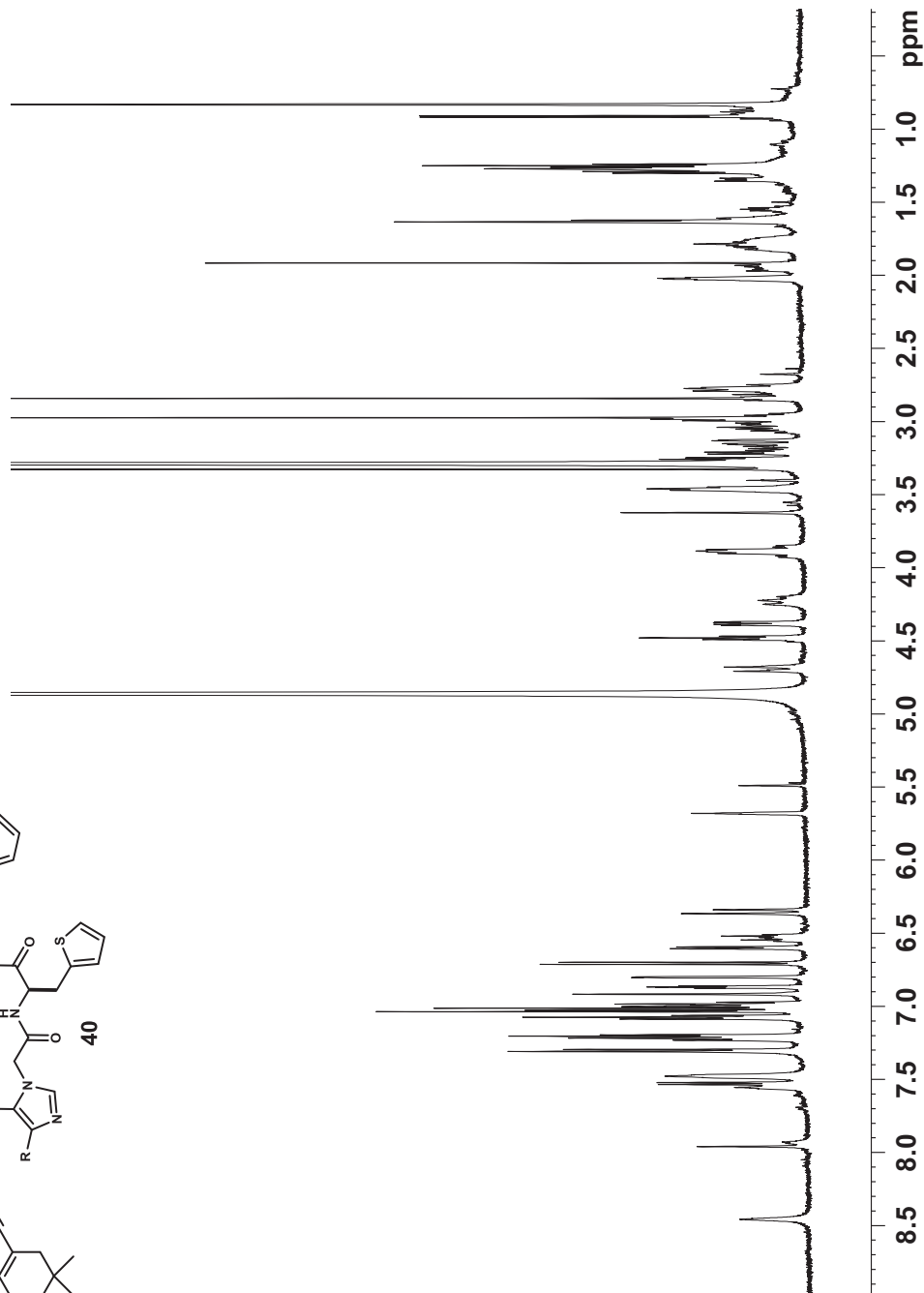
```

Current Data Parameters
NAME      KL-III-108-4-1 MeOD
EXPNO     1
PROCNO    5

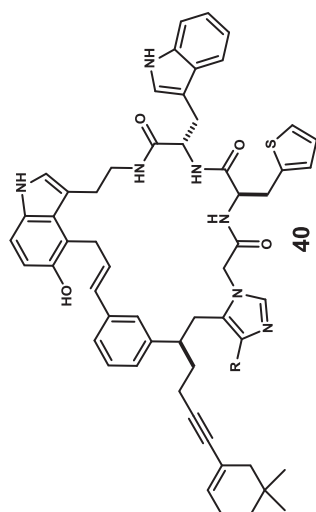
F2 - Acquisition Parameters
Date_     20110420
Time      21.14
INSTRUM   av600
PROBHD    5 mm TBI5
PULPROG   zg30
TD         65536
SOLVENT   MeOD
NS         179
DS         0
SWH        12376.237 Hz
FIDRES     0.188846 Hz
AQ         2.6476543 sec
RG         456.1
DW         40.400 usec
DE         6.50 usec
TE         294.6 K
D1         2.00000000 sec
TD0        1

===== CHANNEL f1 =====
NUC1       1H
P1         8.60 usec
PL1        -2.00 dB
PL1W       39.81071854 W
SFO1       600.1336008 MHz

F2 - Processing parameters
SI         65536
SF         600.1300273 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00
    
```



Fraction 4-1 (Product **40**)

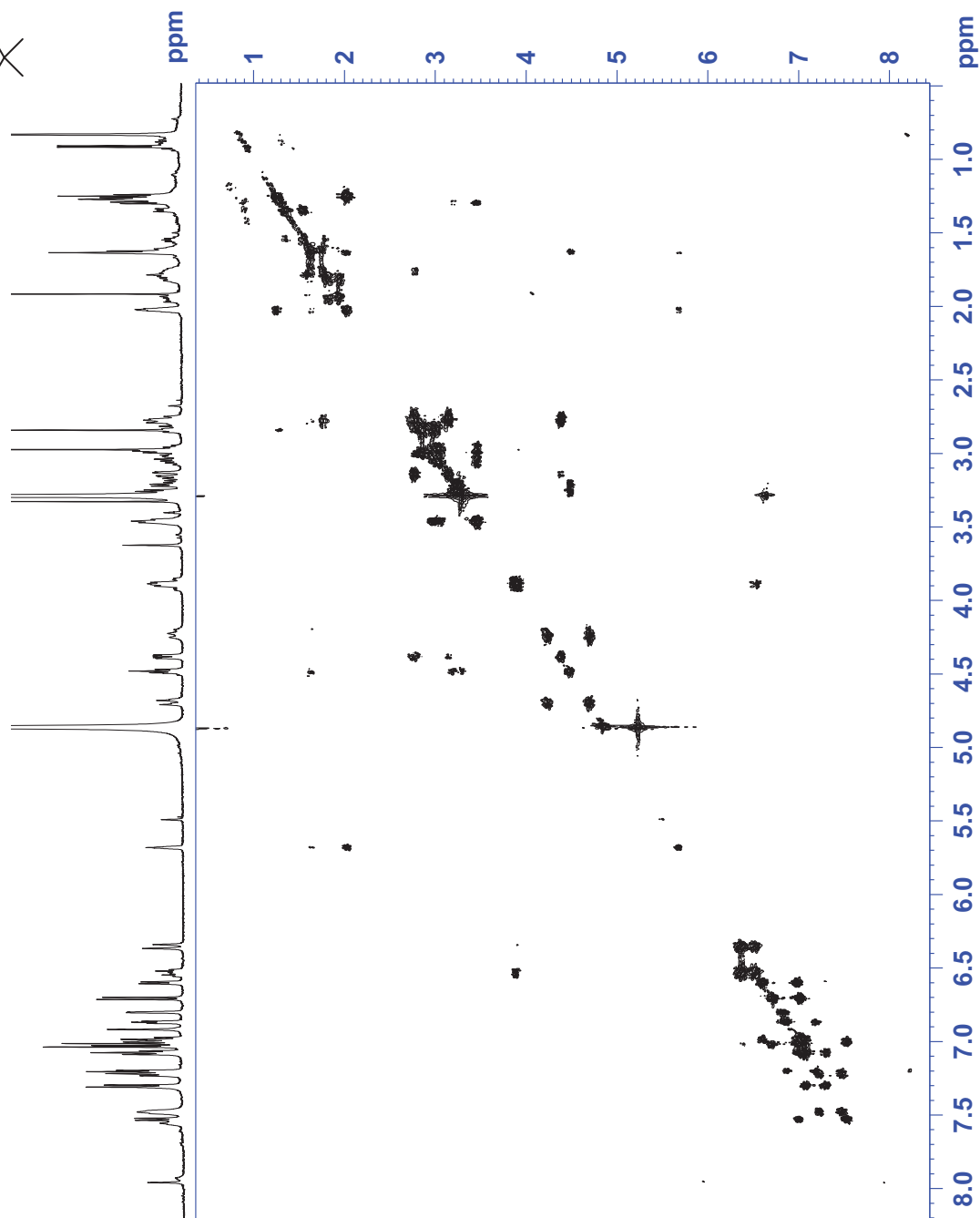


Current Data Parameters
 NAME KL-III-108-4-1 MeOD
 EXPNO 3
 PROCNO 999

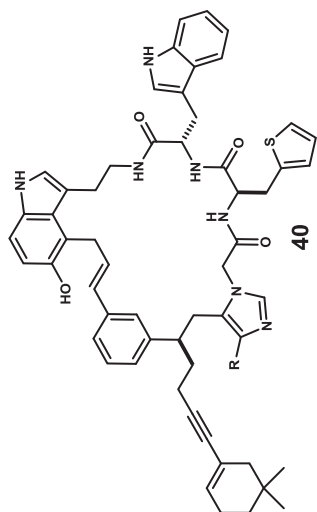
F1 - Acquisition parameters
 TD 256
 SFO1 600.133 MHz
 FIDRES 23.475060 Hz
 SW 10.014 ppm
 FMODE States-TPFI

F2 - Processing parameters
 SI 2048
 SF 600.1300273 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 2048
 MC2 States-TPFI
 SF 600.1300273 MHz
 WDW TRAP
 SSB 2
 LB 0 Hz
 GB 0



Fraction 4-1 (Product 40)

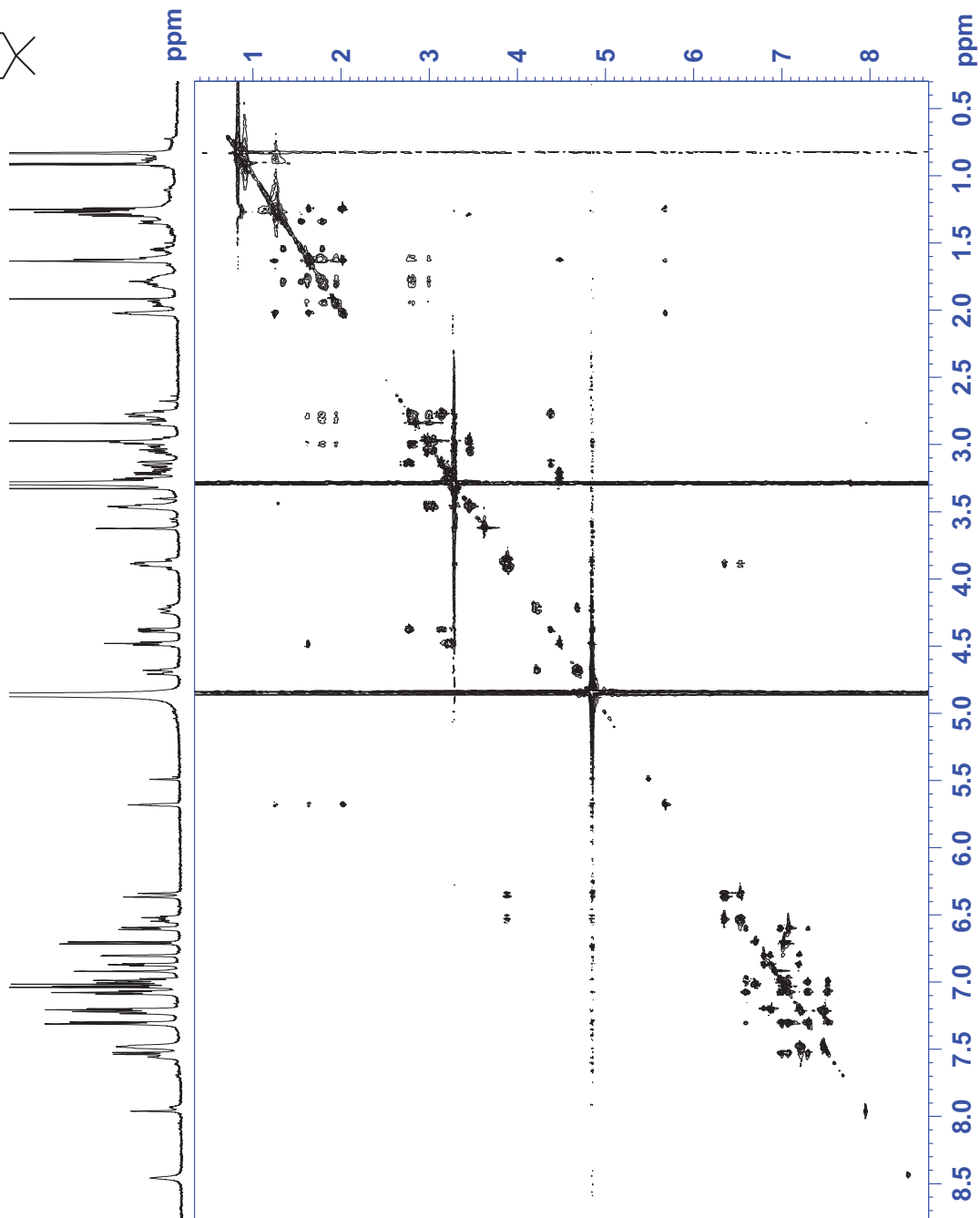


```
Current Data Parameters
NAME      KL-III-108-4-1 MeOD
EXPNO     7
PROCNO    5
```

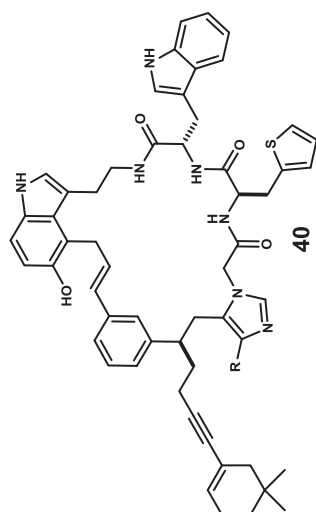
F1 - Acquisition parameters	
TD	256
SFO1	600.1327 MHz
FIDRES	21.046606 Hz
SW	8.978 ppm
FnMODE	Echo-Antiecho

F2 - Processing parameters	
SI	1024
SF	600.130273 MHz
WDW	QSIGNE
SSB	2
LB	0 Hz
GB	0
PC	1.00

F1 - Processing parameters	
SI	1024
MC2	echo-antiecho
SF	600.1300273 MHz
WDW	USER
SSB	2
LB	0 Hz
GB	0



Fraction 4-1 (Product **40**)

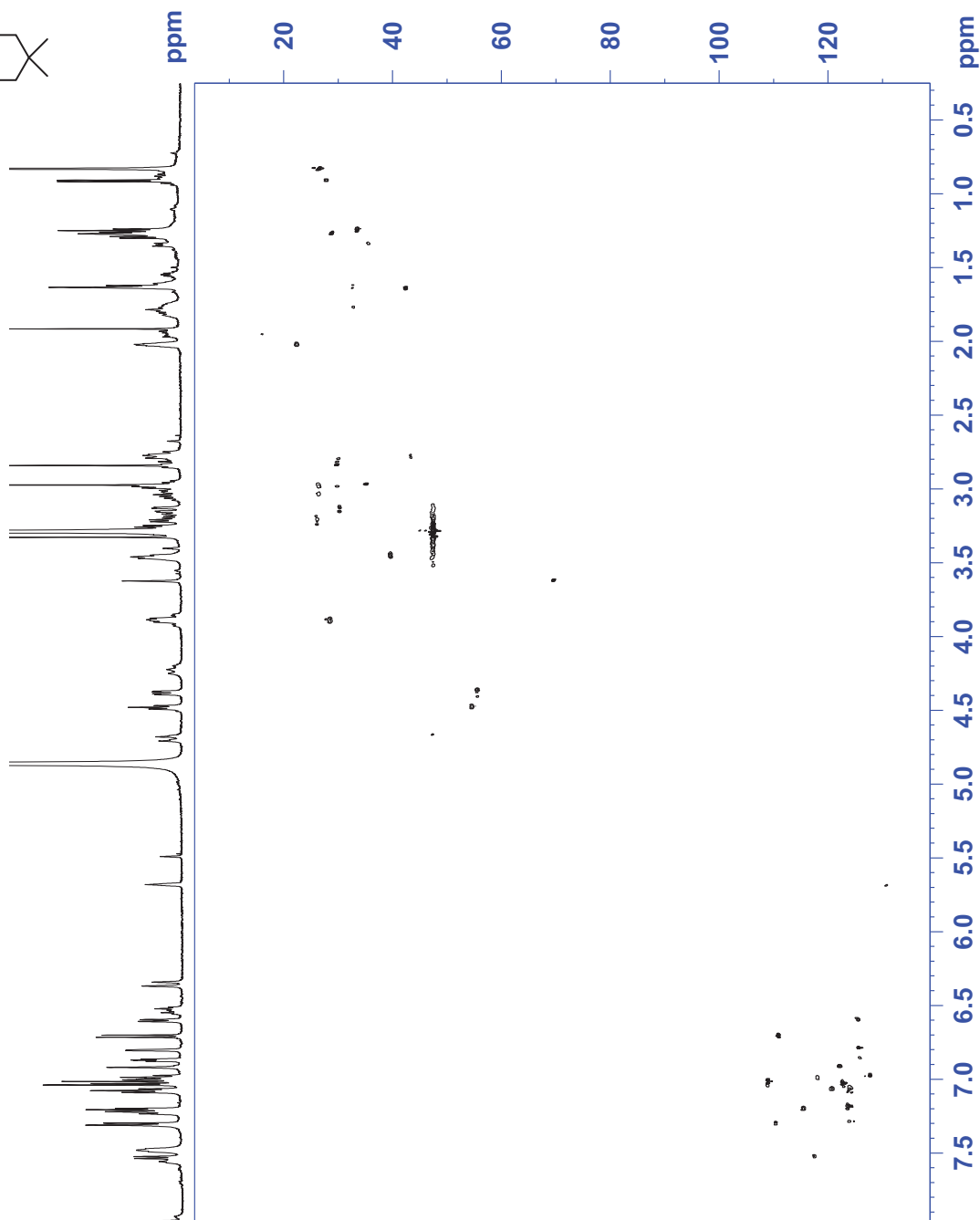


Current Data Parameters
 NAME KL-III-108-4-1 MeOD
 EXPNO 8
 PROCNO 1

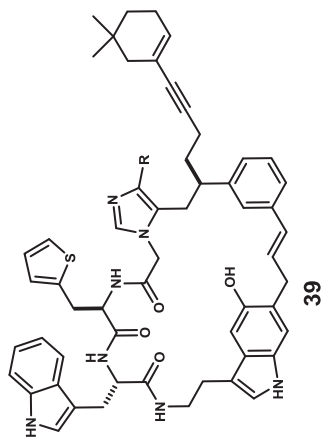
F1 - Acquisition parameters
 TD 256
 SFO1 150.9134 MHz
 FIDRES 106.110962 Hz
 SW 180.000 ppm
 F1MODE Echo-Antiecho

F2 - Processing parameters
 SI 2048
 SF 600.1300273 MHz
 WDW QSI
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.40

F1 - Processing parameters
 SI 2048
 MC2 echo-antiecho
 SF 150.9028800 MHz
 WDW QSI
 SSB 2
 LB 0 Hz
 GB 0



Fraction 5-2



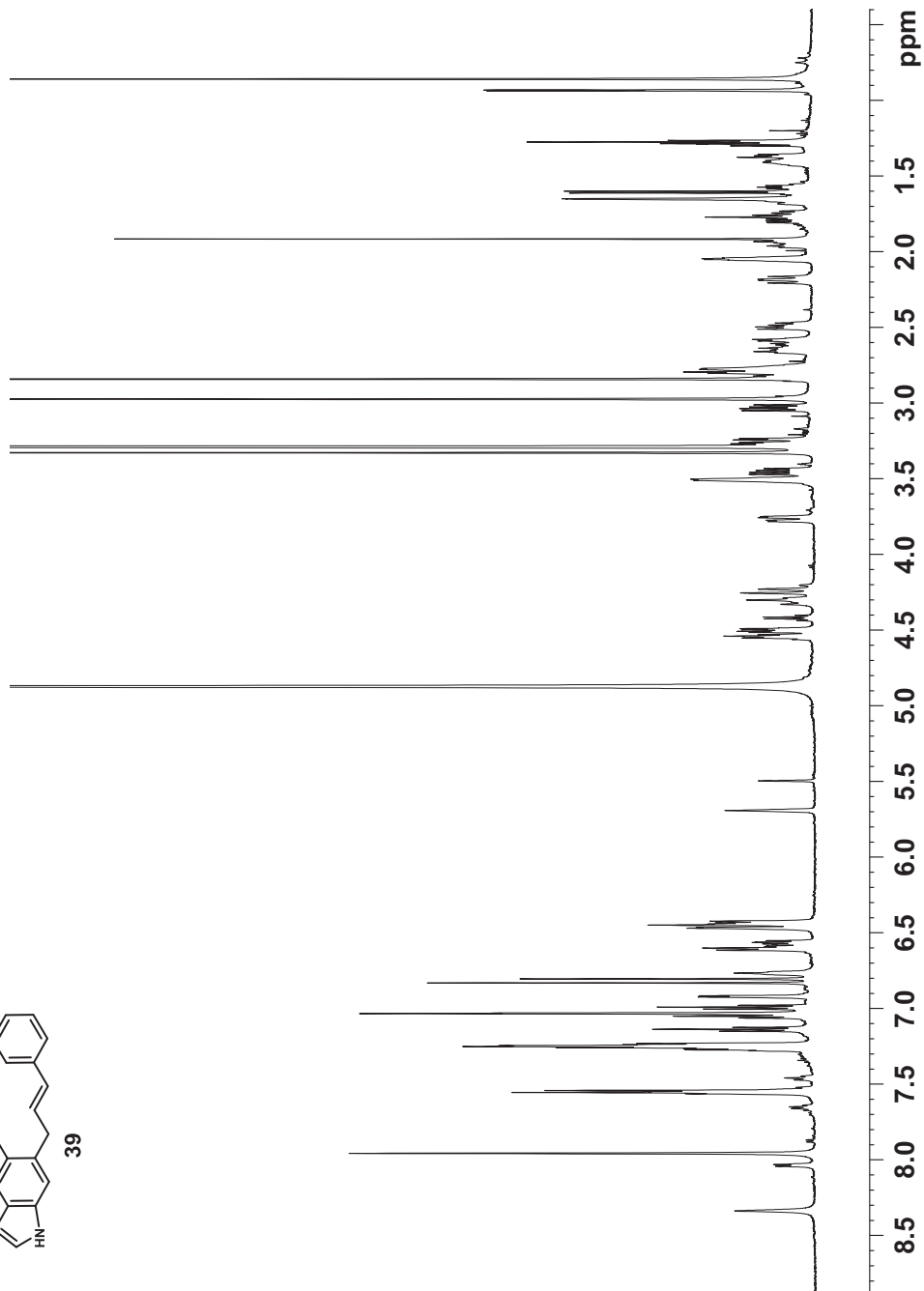
```

Current Data Parameters
NAME      KL-III-108-5-2 MeOD
EXPNO     1
PROCNO    1

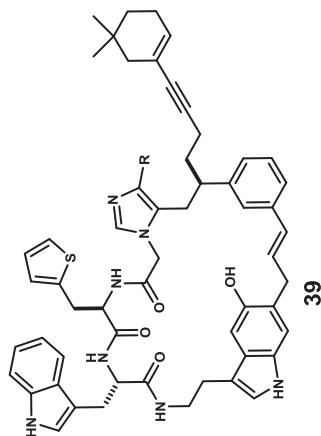
F2 - Acquisition Parameters
Date_     20110415
Time      17.09
INSTRUM   av600
PROBHD    5 mm TBI5
PULPROG   zg30
TD         65536
SOLVENT   MeOD
NS         128
DS         0
SWH        12376.237 Hz
FIDRES     0.188846 Hz
AQ         2.6476543 sec
RG         362
DW         40.400 usec
DE         6.50 usec
TE         293.6 K
D1         2.00000000 sec
TD0        1

===== CHANNEL f1 =====
NUC1       1H
P1         8.60 usec
PL1        -2.00 dB
PL1W       39.81071854 W
SFO1       600.1336008 MHz

F2 - Processing parameters
SI         65536
SF         600.1300273 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00
  
```



Fraction 5-2 (Product 39)



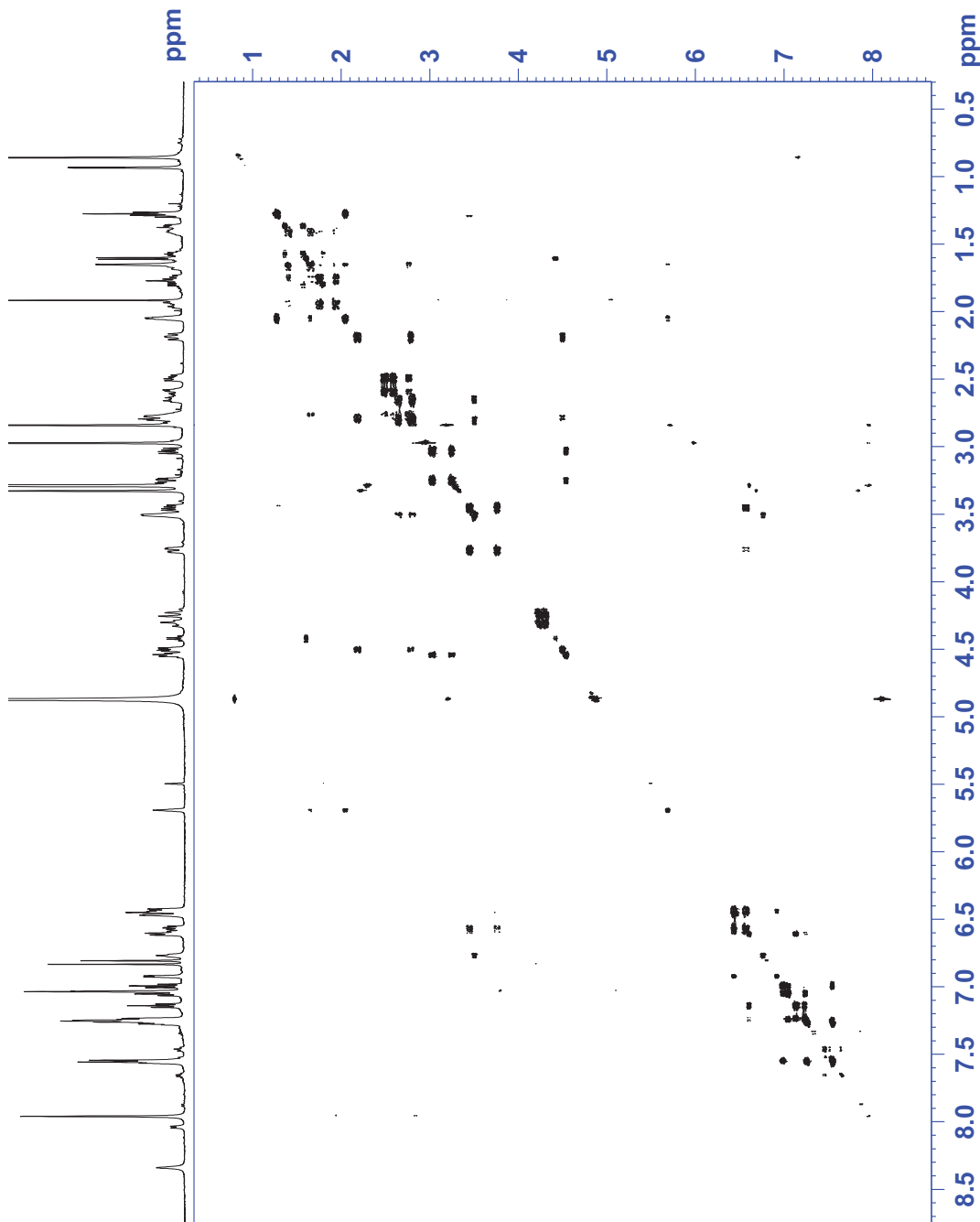
39

Current Data Parameters
 NAME KL-III-108-5-2 MeOD
 EXPNO 5
 PROCNO 1

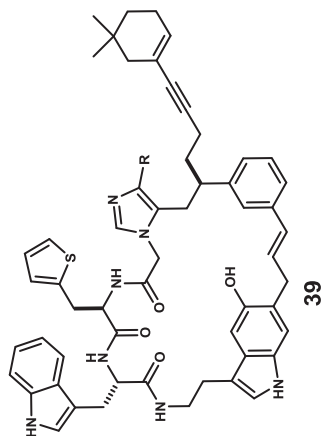
F1 - Acquisition parameters
 TD 512
 SFO1 600.1327 MHz
 FIDRES 10.523297 Hz
 SW 8.978 ppm
 F2 - Processing parameters

SI 2048
 SF 600.1300273 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 2048
 MC2 States-TPPI
 SF 600.1300273 MHz
 WDW USER
 SSB 2
 LB 0 Hz
 GB 0



Fraction 5-2 (Product 39)

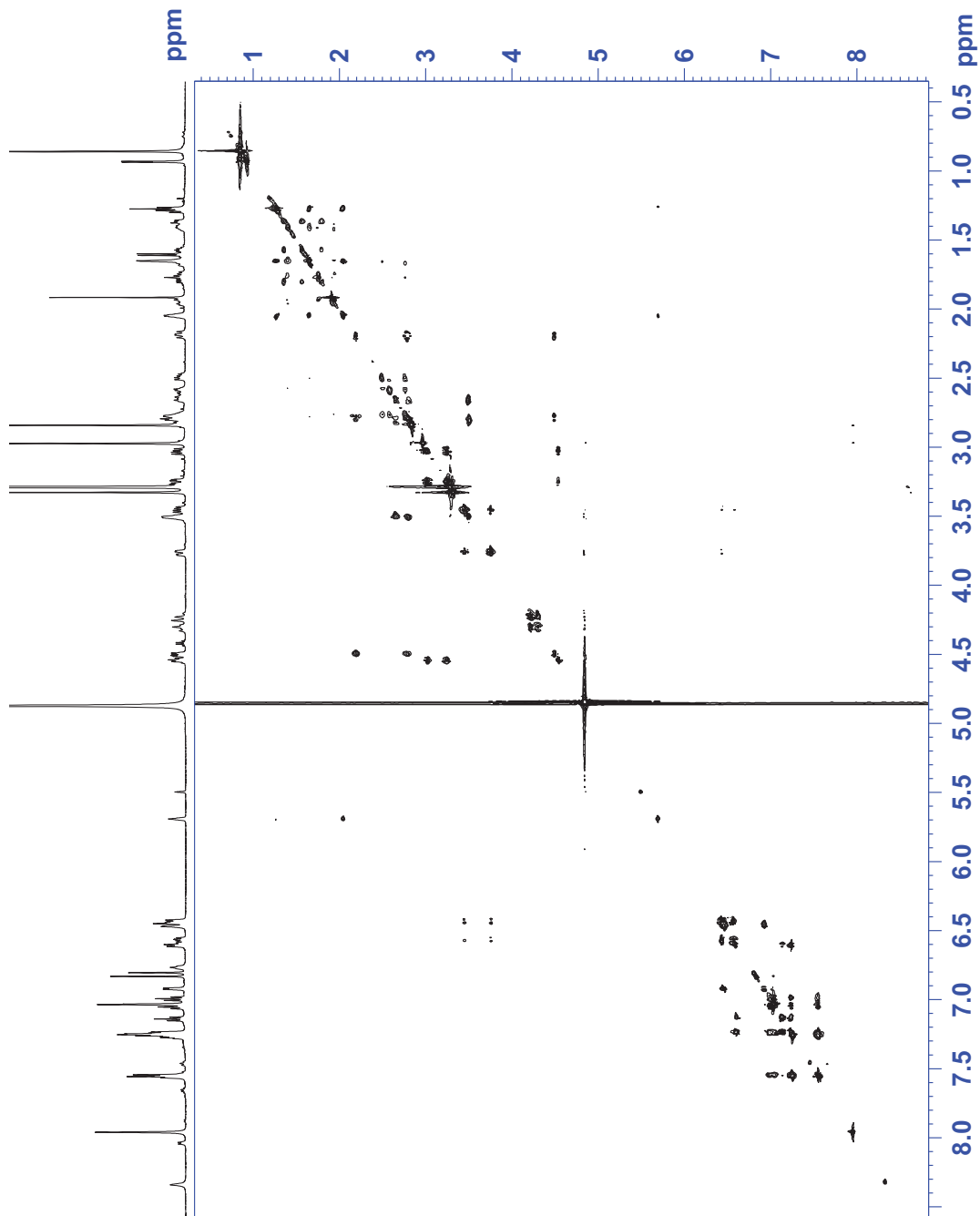


Current Data Parameters
 NAME KL-III-108-5-2 MeOD
 EXPNO 12
 PROCNO 1

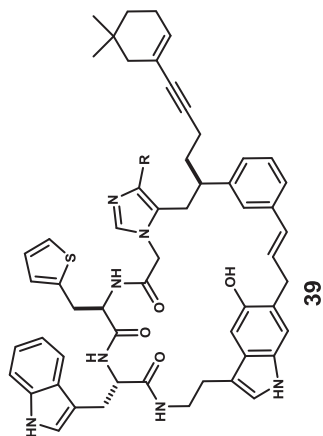
F1 - Acquisition parameters
 TD 256
 SFO1 600.1327 MHz
 FIDRES 24.848913 Hz
 SW 10.600 ppm
 FMODE Echo-Antiecho

F2 - Processing parameters
 SI 1024
 SF 600.1300273 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 1024
 MC2 echo-antiecho
 SF 600.1300273 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0



Fraction 5-2 (Product 39)

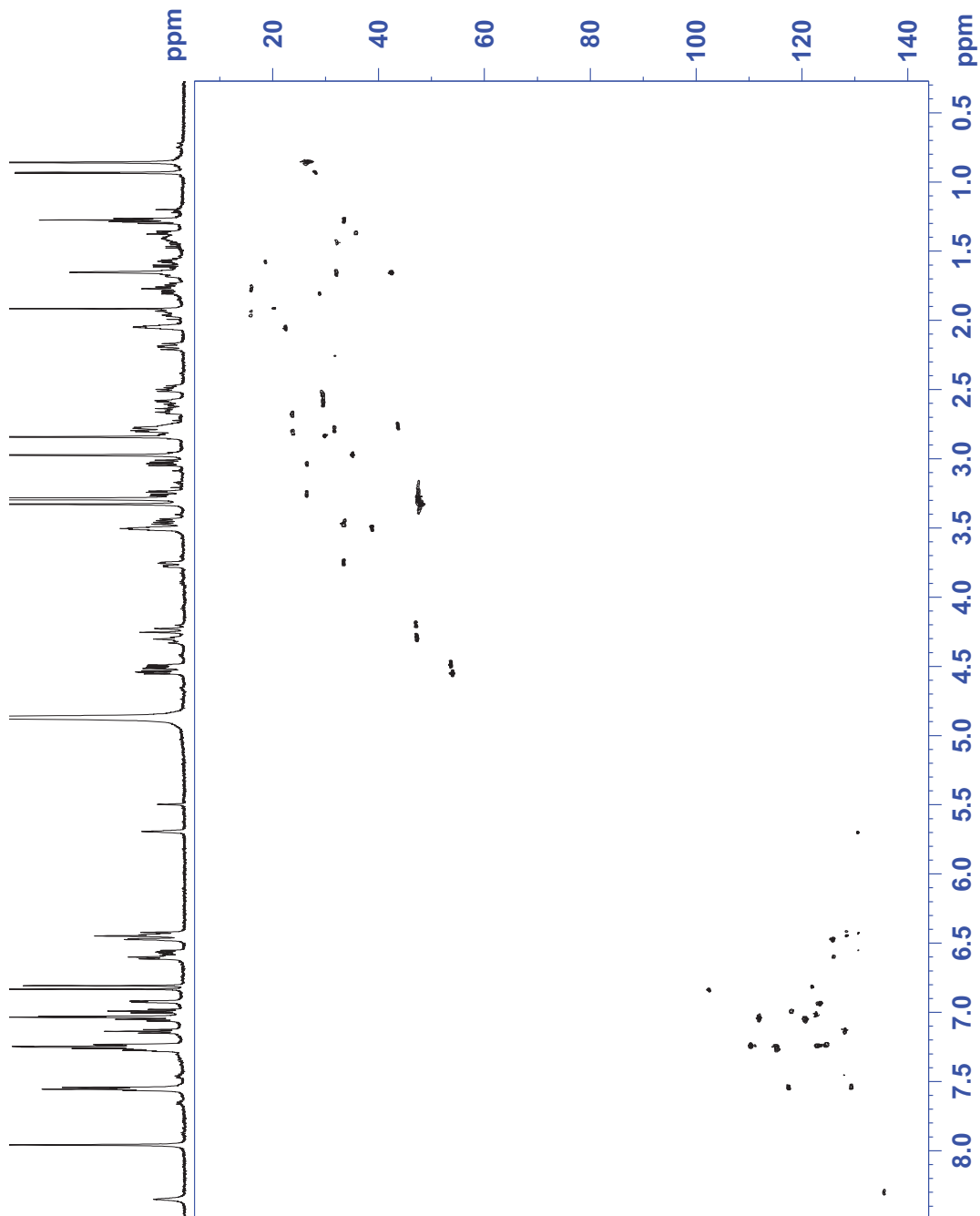


Current Data Parameters
 NAME KL-III-108-5-2_MeOD_3
 EXPNO 6
 PROCNO 1

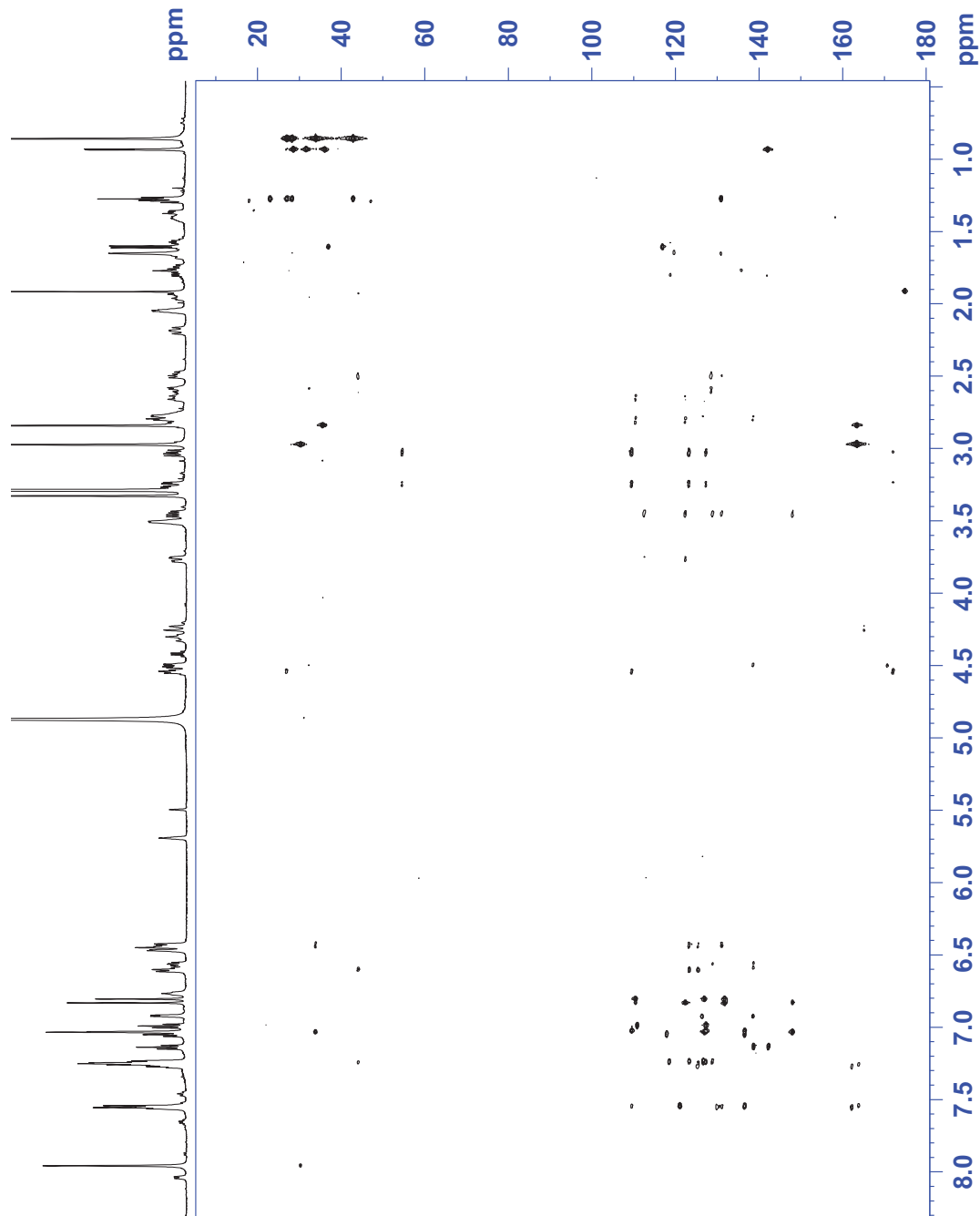
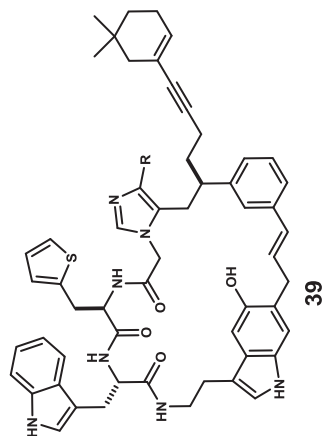
F1 - Acquisition parameters
 TD 248
 SFO1 150.9134 MHz
 FIDRES 109.53397 Hz
 SW 180.000 ppm
 F1MODE Echo-Antiecho

F2 - Processing parameters
 SI 2048
 SF 600.1300273 MHz
 WDW QSI
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.40

F1 - Processing parameters
 SI 2048
 MC2 echo-antiecho
 SF 150.9028800 MHz
 WDW USER
 SSB 2
 LB 0 Hz
 GB 0



Fraction 5-2 (Product 39)



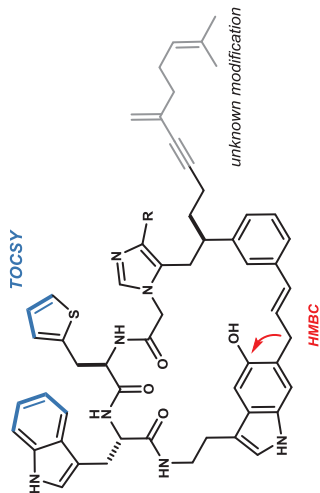
Current Data Parameters
 NAME KL-III-108-5-2 MeOD
 EXPNO 9
 PROCNO 1

F1 - Acquisition parameters
 TD 256
 SFO1 150.9171 MHz
 FIDRES 117.904022 Hz
 SW 200.000 ppm
 FqMODE QF

F2 - Processing parameters
 SI 1024
 SF 600.1300273 MHz
 WDW QF
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 1024
 MC2 QF
 SF 150.9028090 MHz
 WDW QF
 SSB 2
 LB 0 Hz
 GB 0

Fraction 6-2 (incomplete assignment)



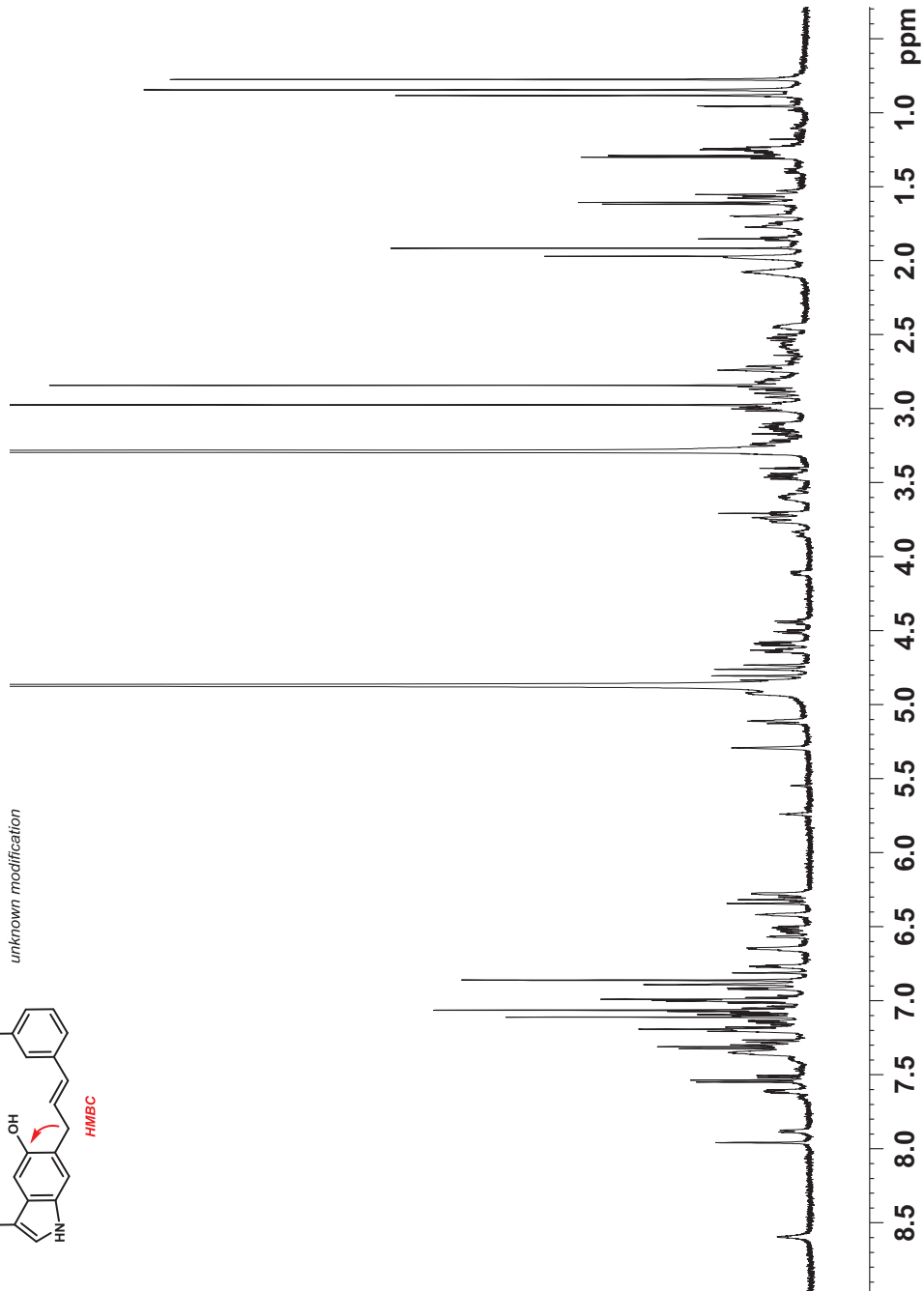
```

Current Data Parameters
NAME      KL-III-108-6-2
EXPNO     1
PROCNO    1

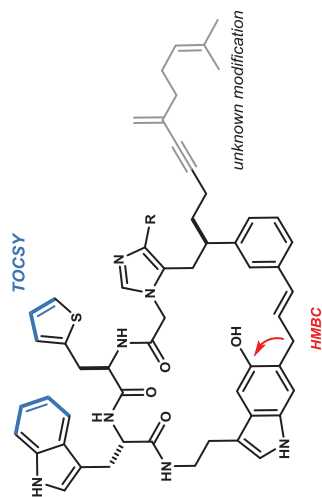
F2 - Acquisition Parameters
Date_     20110514
Time      18.39
INSTRUM   av600
PROBHD    5 mm TBI5
PULPROG   zg30
TD         65536
SOLVENT   MeOD
NS         36
DS         0
SWH        12376.237 Hz
FIDRES     0.188846 Hz
AQ         2.6476543 sec
RG         362
DW         40.400 usec
DE         6.50 usec
TE         294.0 K
D1         2.00000000 sec
TD0        1

===== CHANNEL f1 =====
NUC1       1H
P1         10.40 usec
PL1        -2.00 dB
PL1W       39.81071854 W
SFO1       600.1336008 MHz

F2 - Processing parameters
SI         65536
SF         600.1300273 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00
  
```



Fraction 6-2

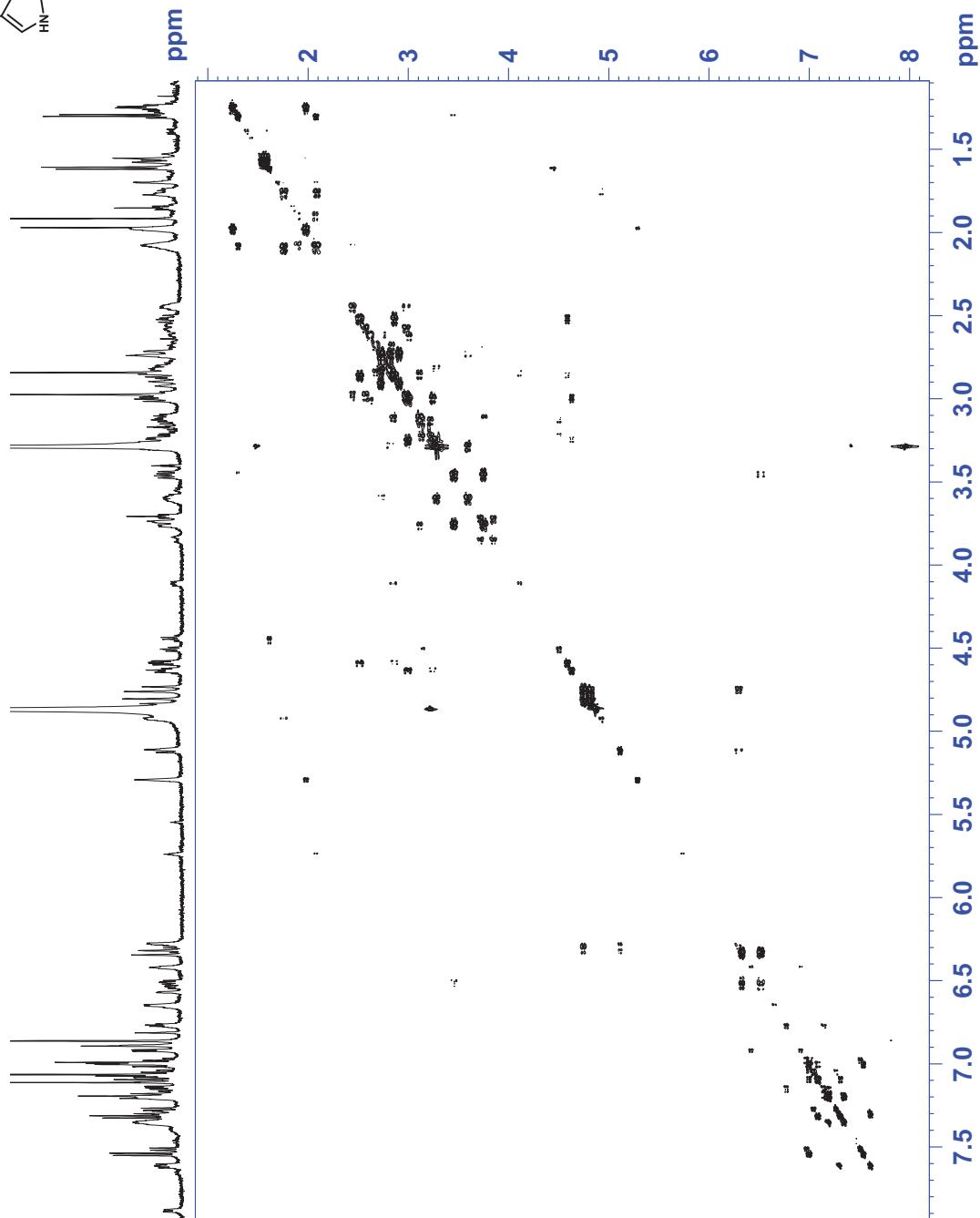


Current Data Parameters
 NAME KL-III-108-6-2
 EXPNO 3
 PROCNO 1

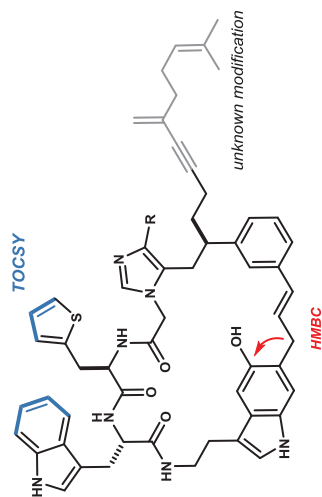
F1 - Acquisition parameters
 TD 600
 SF01 600.1327 MHz
 FIDRES 10.602201 Hz
 SW 10.600 ppm
 FnmODE States-TPPI

F2 - Processing parameters
 SI 2048
 SF 600.1300273 MHz
 WDW QSI
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 2048
 MC2 States-TPPI
 SF 600.1300273 MHz
 WDW QSI
 SSB 2
 LB 0 Hz
 GB 0



Fraction 6-2

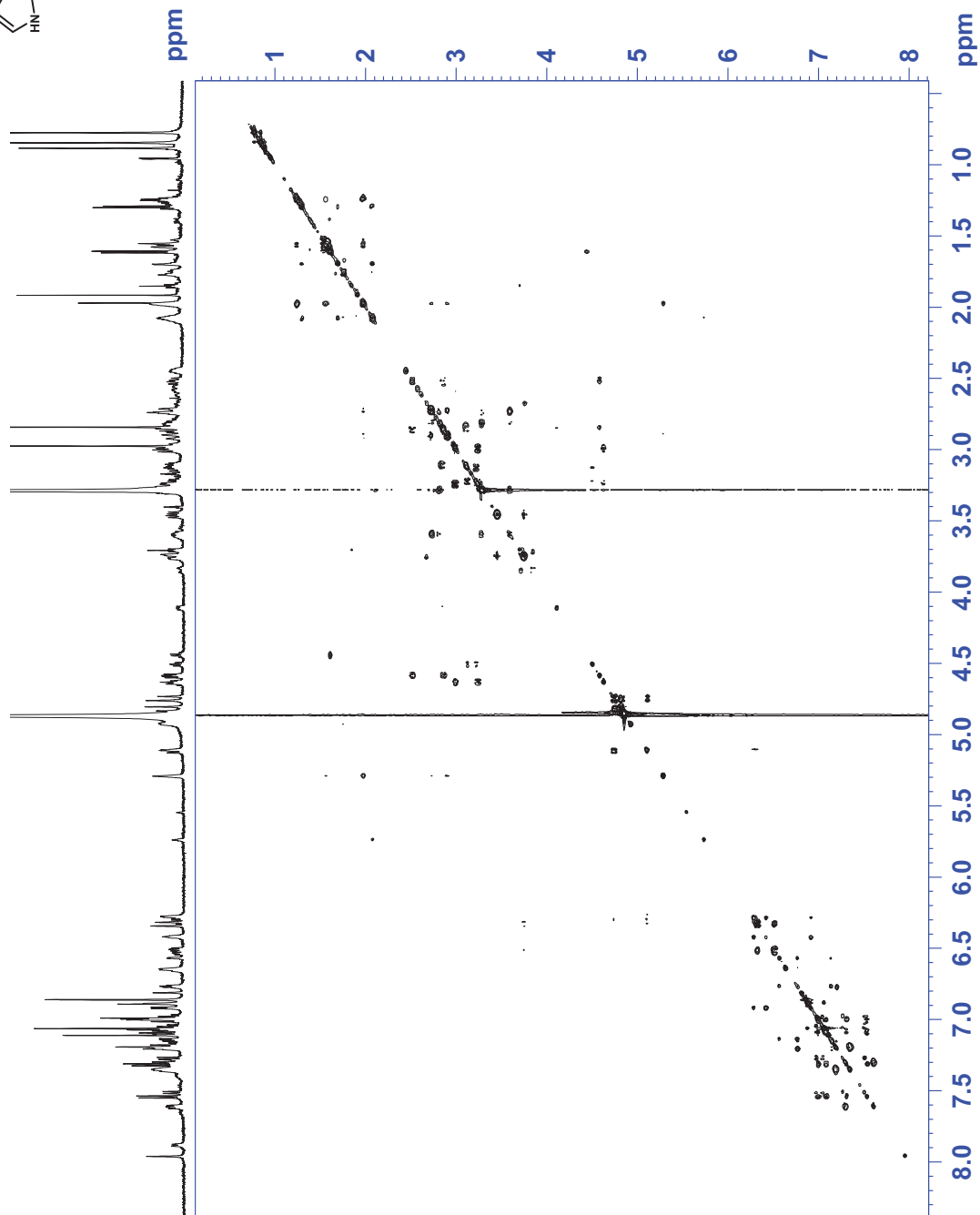


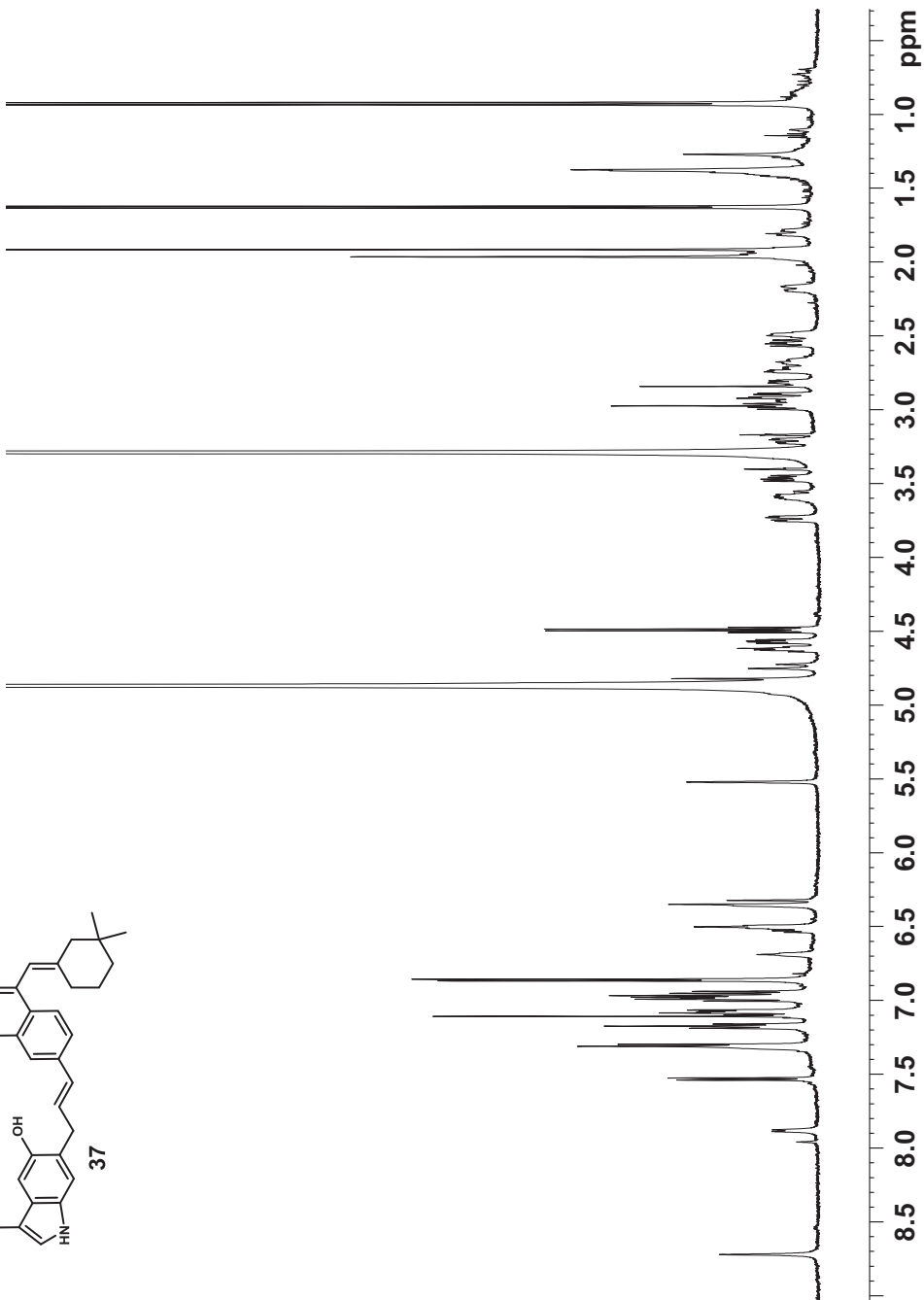
Current Data Parameters
 NAME KL-III-108-6-2
 EXPNO 4
 PROCNO 1

F1 - Acquisition parameters
 TD 600
 SFO1 600.1327 MHz
 FIDRES 10.602203 Hz
 SW 10.600 ppm
 F1MODE Echo-Antiecho

F2 - Processing parameters
 SI 1024
 SF 600.1300273 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 1024
 MC2 echo-antiecho
 SF 600.1300273 MHz
 WDW USER
 SSB 2
 LB 0 Hz
 GB 0





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- [35] Enantiomeric excess of **1** is determined via HPLC analysis of diastereoisomeric imidazolidines formed by reaction with (*R,R*)-*N,N'*-dimethyl-1,2-diphenyl ethylene diamine. Reaction with racemic **1** serves as a standard. See: (a) Mangeney, P.; Alexakis, A.; Normant, J. F. *Tetrahedron Lett.* **1988**, *29*, 2677. (b) Cuvinot, D.; Mangeney, P.; Alexakis, A.; Normant, J. F.; Lellouche, J. P. *J. Org. Chem.* **1989**, *54*, 2420.
- [36] Absolute stereochemistry at C-3 in **1** is assigned as *R* by analogy to outcomes in ref. 6. Material prepared in this work shows $[\alpha]_D^{20} = +29.0$ (*c* 0.56, CHCl₃). This is signed opposite to previously synthesized **1**, which was drawn incorrectly in our previous communication.
- [37] The observed regioselectivity is consistent with reported thermal [3,3] sigmatropic rearrangements of 5-allyloxyindoles: M. Julia and J.-Y. Lallemand, *Bull. Soc. Chim. Fr.*, **1973**, 2046; Cannon, J. G.; Roufos, I. *J. Heterocyclic Chem.* **1990**, *27*, 2093; Moody, C. J. *J. Chem. Soc. Perkin Trans. I* **1984**, 1333

Chapter 2 - Composite macrocyclic peptidomimetics display antibacterial activity against *S. aureus*

2. Introduction

*Introduction adapted from Lawson, K.V; Rose, T.E.; Harran, P.G
NIH Application Number: 1 R01 AI097490-01*

Modern antibiotics have been an unparalleled success. So much so that our ability to treat infectious disease is often taken for granted.^{1,2} However, after decades of use, resistance is widespread, rendering numerous of these compounds obsolete. More than 70% of hospital-acquired infections are now recalcitrant to at least one class of small molecule antibiotic – and resistance is no longer confined to health care institutions.³ In the United States, community associated methicillin-resistant *Staphylococcus aureus* (MRSA) is the leading cause of soft tissue infections.⁴ Vancomycin (Figure 1), often a last line of defense against multi-drug resistant bacteria, has begun to lose potency.^{5,6} The need to develop new, broadly efficacious antibiotics is widely recognized.⁷ At the same time, the rate of new antimicrobials reaching the

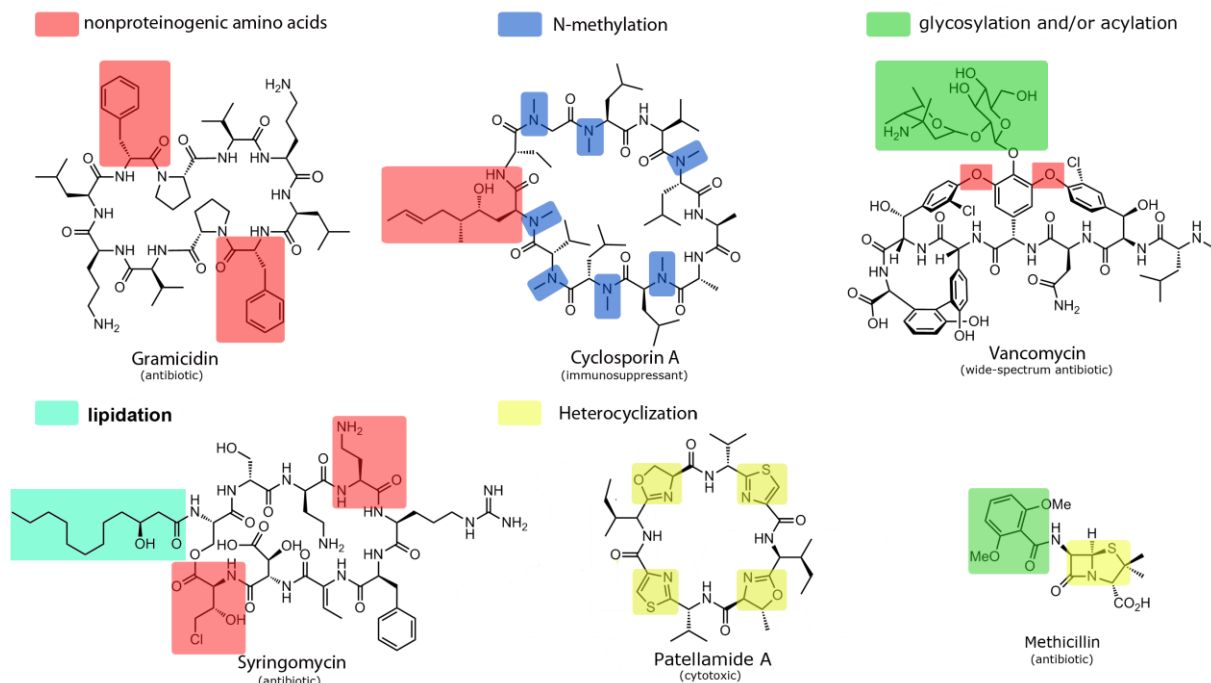


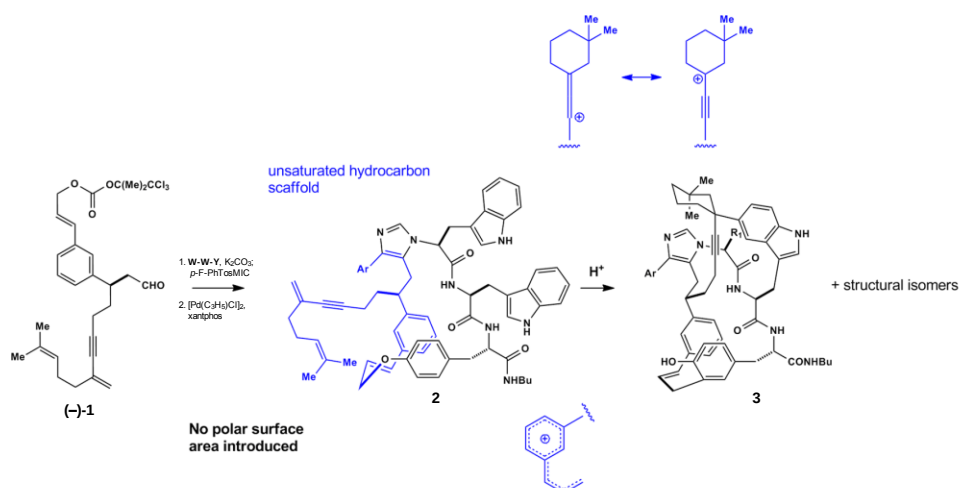
Figure 1. Non-ribosomal peptides are a diverse family of clinically useful antimicrobial natural products. In general, the materials are characterized by large ring structures incorporating non-proteinogenic amino acid residues, imbedded and/or peripheral heterocycles and often harbor lipid and/or carbohydrate modifications.

clinic is in steady decline.^{8,9} This is, in part, due to a lack of innovative technology to address the structural complexity of current antibiotics – the majority of which derive from intricate natural products.¹⁰ Whether the commercial material is natural or a semi-synthetic derivative, fermentation-based production methods inherently limit the range of accessible chemical diversity.^{11,12,13,14}

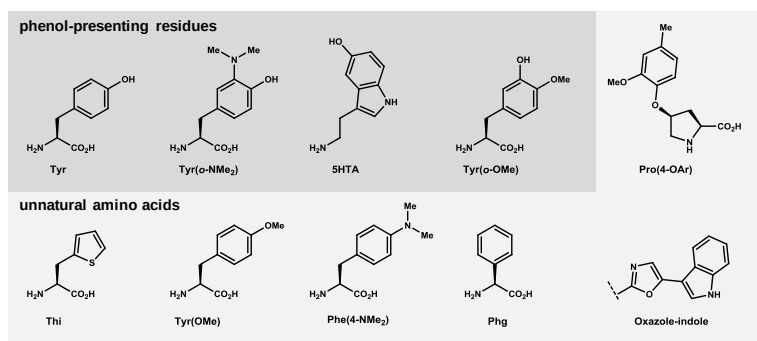
A promising source of novel antibiotics are the non-ribosomal peptides (Figure 1). Many well-known antibiotics are derived biosynthetically from peptides, such as the β -lactams, the glycopeptides vancomycin, teicoplanin, and telavancin, the lipopeptide daptomycin, as well as the cyclosporins, lantibiotics, and gramicidin.¹⁵ Inspired by how nature assembles these materials, we are developing synthetic processes that operate similarly. Using this technology, we are building a platform for antibiotic discovery. In short processing sequences, we transform machine-made peptides and related oligomers into complex polycyclic derivatives. These are rich in stereochemistry and diverse in shape. End-products retain molecular recognition elements in the biopolymer, yet display that functionality as part of stable, conformationally defined structures having improved pharmacological properties.

We have previously described the utility of aldehyde **1** to prepare diverse mixtures of conformationally constrained peptidomimetics which mirror the complexity of NRP natural products. This process involves three steps wherein electrophilic functionality present in **1** was sequentially promoted to react with unprotected peptide first bimolecularly, then intramolecularly to form constrained composites of **1** and the peptide. A typical example of this process is depicted in Figure 2A. Tripeptide WWY was ligated to **1** at the N-terminus using TosMIC methodology. Treatment of this adduct with catalytic Pd⁰ decomposes the cinnamyl carbonate and the resultant electrophilic Pd-cinnamyl is captured by the pendent tyrosyl phenol to afford macroether **2**. Reagent **1** sheds its oxygenation during these events to become solely unsaturated hydrocarbon in the product. Compound **2** is a unique cyclopeptide, yet the value of **1** in assembling such structures is the options it makes available for further modifications.

A



B



C

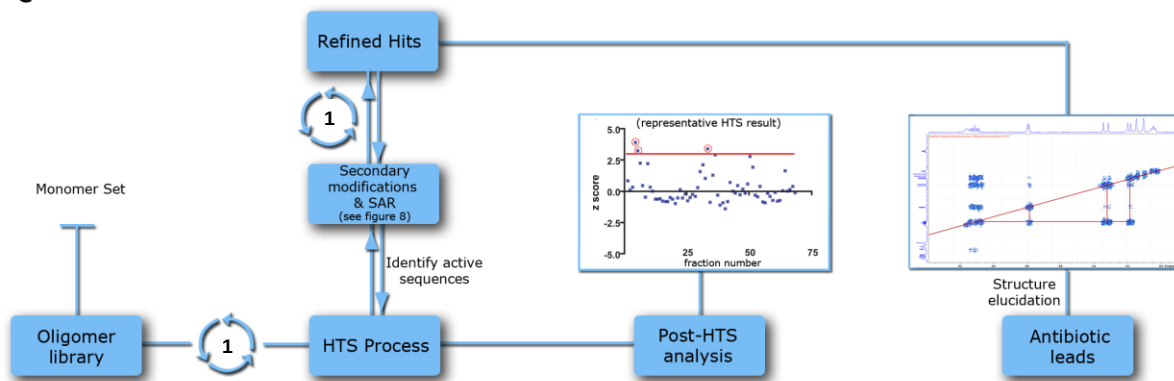


Figure 2. A. Scaffold (-)-1 is joined with WWY in two steps to afford macrocycle **2** followed by treatment with anhydrous acid. Product **3** is a result of noncanonical aryl Claisen rearrangement of the cinnamyl ether in **2** with simultaneous cyclization of its dienyl appendage to an alkynyl cyclohexene. B. Representative monomer set amenable to our process. C. Schematic flow of data and materials from a starting monomer set to antibiotic lead compounds.

Treatment with anhydrous acid initiates a number of competing/sequential isomerizations via carbocationic rearrangements. In the case of **2**, we convert a 23-membered cyclic ether into polycycle **13** wherein non-canonical aryl Claisen rearrangement has occurred alongside

installation of a novel *ansa* bridge - likely via a side-chain propargylic cation engaging the proximal tryptophan residue in a transannular electrophilic aromatic substitution. Additionally structurally unique isomeric products having 21, 19 and 15-membered macrocycles (see chapter 1) are also obtained from this single reaction.

The power of this process lies in its ability to rapidly produce structurally diverse macrocyclic composite peptides. We have characterized thoroughly individual products from this synthetic sequence to gain understanding of the chemistry. In future iterations full structure elucidations will be guided by biological screening after iterative SAR of the peptide domain has identified refined lead compounds. A schematic of this process is shown in Figure 2C. This study aims to expand the library size and interface with high-throughput screening for antibacterial activity. We believe this therapeutic area is well matched to the structural types generated in this work.

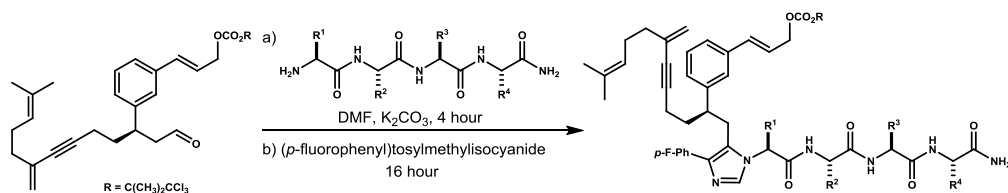
2.1. Materials and Methods

2.2.1. Van Leusen imidazole synthesis

Reactions were conducted in disposable reaction vials and mixed with an oscillating platform. Each vessel was charged with ~0.25 mmol peptide (1.2 equiv), K₂CO₃ (1.0 mmol, 4 equiv.) and diluted with anhydrous DMF (1.66 mL, 0.15 M). To this solution was added a 0.3M solution of **1** in DMF (833 μ L, 1 equiv.) and mixed for 4 hours to induce imine formation. Solid (*para*-fluorophenyl)tosylmethylisocyanate (0.3 mmol, 1.2 equiv) was added directly to the reaction vessel and the resulting solutions was mixed overnight. Each reaction was syringe filtered (0.45 μ M) into 16x100mm tubes and the solvent removed by centrifugal evaporation. The crude products were reconstituted in DMF (1.5 mL) and purified by mass-guided automated HPLC/MS (Table 1). Fractions were evaporated to dryness, reconstituted in methanol, and appropriate

Table 1. Typical preparative HPLC gradient.

Method	20-100%B (12min grad.)
Column	Sunfire C18 30x150mm
Solvent A	H ₂ O (0.1% TFA)
Solvent B	MeOH (0.1% TFA)
Injection Vol.	750 μ L (2 injections)



A

	(entered)						(entered)		
	Mol. Weight	Amt (mg)	Amt (mmol)	Reagent (mL)	TosMIC (mg)	K ₂ CO ₃ (mg)	Theo. Yield	Isol. Yield (mg)	% Yield
A1	449.5	103	0.229	0.95	79.2	126.7	256.3	63.5	24.78%A1
A2	475.6	99	0.208	0.87	72.0	115.1	232.9	65.6	28.17%A2
A3	643.8	123	0.191	0.80	66.1	105.6	213.7	26.4	12.35%A3
A4	636.7	131	0.206	0.86	71.2	113.7	230.1	30.2	13.12%A4
A5	603.7	109	0.181	0.75	62.4	99.8	202.0	23.5	11.64%A5
A6	513.6	98	0.191	0.80	66.0	105.5	213.4	14.6	6.84%A6
B1	544.6	100	0.184	0.77	63.5	101.5	205.4	23.8	11.59%B1
B2	584.6	107	0.183	0.76	63.3	101.2	204.7	23.4	11.43%B2
B3	485.6	113	0.233	0.97	80.5	128.7	260.3	81.7	31.39%B3
B4	433.5	99	0.228	0.95	79.0	126.3	255.5	15.7	6.15%B4
B5	591.7	106	0.179	0.75	62.0	99.0	200.4	28.0	13.97%B5
B6	497.6	100	0.201	0.84	69.5	111.1	224.8	49.7	22.11%B6
C1	555.7	108	0.194	0.81	67.2	107.4	217.4	28.9	13.29%C1
C2	617.7	100	0.162	0.67	56.0	89.5	181.1	0.0	0.00%C2
C3	492.6	111	0.225	0.94	77.9	124.6	252.1	13.1	5.20%C3
C4	574.6	107	0.186	0.78	64.4	102.9	208.3	54.0	25.93%C4
C5	540.6	115	0.213	0.89	73.6	117.6	238.0	25.2	10.59%C5
C6	527.6	106	0.201	0.84	69.5	111.1	224.7	34.7	15.44%C6
D1	531.6	110	0.207	0.86	71.6	114.4	231.5	0.0	0.00%D1
D2	527.6	102	0.193	0.81	66.9	106.9	216.3	15.9	7.35%D2
D3	581.7	100	0.172	0.72	59.5	95.0	192.3	37.7	19.60%D3
D4	584.7	100	0.171	0.71	59.2	94.6	191.3	37.9	19.81%D4
D5	584.7	141	0.241	1.00	83.4	133.3	269.8	25.7	9.53%D5
D6	497.6	120	0.241	1.00	83.4	133.3	269.8	71.4	26.47%D6
Avg/Total				20.08	1.7g			35.9	15.76%
				2.23g					

B

(N-Term)	AA1	AA2	AA3	AA4
A1	Gly	Val	Ile	Tyr
A2	Gly	D-Ala	Thi	Tyr(OMe)
A3	Thi	Tyr	Phg	Tyr(OMe)
A4	D-Trp	D-Tyr	D-Phg	D-His
A5	Ile	D-Tyr	D-Tyr	D-Phe
A6	Ser	D-Tyr	Ile	Phg
B1	Ile	D-His	Asn	Tyr
B2	D-His	Asn	D-Tyr	Thi
B3	Gly	Me-Phe	His	Leu
B4	Val	Gly	Tyr	Pro
B5	Trp	Gln	Pro	Tyr
B6	Gly	Tyr	D-Pro	Tyr
C1	Met	D-Pro	Phe	Tyr
C2	Asn	D-Trp	His	Tyr
C3	D-Val	Tyr	D-Val	Asn
C4	D-Ala	D-Trp	His	Tyr
C5	D-Phg	Gln	Val	Tyr
C6	Leu	Tyr	D-Phe	Ser
D1	D-His	Ile	Tyr	Thr
D2	Phg	Thr	Tyr	Leu
D3	Trp	His	D-Leu	Gln
D4	Phe	Pro	Trp	His
D5	D-Phe	D-Trp	D-Ala	Tyr
D6	Gly	D-Leu	Phe	Tyr

C

Sample ID	MW (product)	Reinj.	Purity (%)
KL-IV-71-A1	1118.59	X	95A1
KL-IV-71-A2	1144.61	X	95A2
KL-IV-71-A3	1312.80	X	85A3
KL-IV-71-A4	1305.75	X	85A4
KL-IV-71-A5	1272.76	X	85A5
KL-IV-71-A6	1182.64	X	90A6
KL-IV-71-B1	1213.65	X	80B1
KL-IV-71-B2	1253.70	X	20B2
KL-IV-71-B3	1154.64	X	95B3
KL-IV-71-B4	1102.56	X	95B4
KL-IV-71-B5	1260.72	X	90B5
KL-IV-71-B6	1166.60	X	>95B6
KL-IV-71-C1	1224.75	X	95C1
KL-IV-71-C2	1286.71		C2
KL-IV-71-C3	1161.62	X	90C3
KL-IV-71-C4	1243.68	X	90C4
KL-IV-71-C5	1209.66	X	85C5
KL-IV-71-C6	1196.66	X	90C6
KL-IV-71-D1	1200.65		D1
KL-IV-71-D2	1196.66	X	90D2
KL-IV-71-D3	1250.72	X	60D3
KL-IV-71-D4	1253.73	X	90D4
KL-IV-71-D5	1253.72	X	90D5
KL-IV-71-D6	1166.64	x	>95D6

Figure 3. Sample set of imidazole syntheses performed in a MiniBlock® 24-well reactor. **A.** Sample spreadsheet of reagent/stoichiometry calculations and yields. Yield denoted as 0% if desired product was not detected by LC/MS **B.** Sequences corresponding to A1-D6. **C.** Purity

fractions were combined into tared 16x100mm tubes and evaporated. The purity was re-analyzed via HPLC/MS. An example spreadsheet is shown in Figure 3.

2.1.2. Pd-catalyzed macrocyclization

Compounds purified by preparative HPLC were treated with silica bound tetraalkylammonium carbonate (Si-CO₃, Silicycle, 0.59 mmol/g, 2 equiv.) for 30 minutes in DMF, and re-concentrated to remove residual TFA prior to cyclization. The Pd-catalyzed macrocyclizations were performed in 24-well format using a MiniBlock® fitted with an inert atmosphere manifold. Reactions were performed in 10 mL filter tubes as follows. To a solution of imidazole (0.05 mmol) in degassed DMF (10 mL, 5 mM) was added catalyst solution (735 μ L, 0.04 mol% [PdCl(C₃H₅)₂], 0.10 mol% xantphos). The reaction was allowed to stir at room temperature for two hours and 50 mg Si-Thiol (Silicycle) was added to the reaction tube and mixed for 5 minutes. The solutions were filtered and collected in 16x100mm tubes and evaporated. The crude solutions were used without further purification.

The solution of catalyst was prepared as follows: An oven-dried, serum-topped vial was placed in a glove bag and charged with [PdCl(C₃H₅)₂] (14 mg, 0.038 mmol) and xantphos (55 mg, 0.095 mmol). The vial is sealed, removed from the glove bag, and degassed THF (7.0 mL) was added, followed by degassed DMF (7.0 mL). The resulting yellow solution was stirred under argon for 30 minutes.

2.1.3. Acid treatment

The crude macrocycles were dissolved in CH₃NO₂ (5 mM, based on mass of acyclic imidazole) and CH₃SO₃H (15 equiv.) was added via micropipette. The reaction was stirred for two hours then quenched with saturated NaHCO₃. The reaction was diluted with EtOAc and transferred to a separatory funnel. The organic layer was washed with water and brine then dried over Na₂SO₄ and evaporated in vacuo. The crude acidolysis mixture was reconstituted in

DMSO and fractionated by preparative HPLC. The fractions were evaporated, dissolved in methanol and transferred into pre-weighed 0.5dr vials and evaporated to dryness.

2.1.4. Antibacterial Screening

A detailed SOP for the primary screen is described in the appendix. Following fractionation the library was prepared as 10 mM stock solutions in DMSO and arrayed in 96-well plates. DMSO solutions were transferred into 384-well plates and diluted to 1.0 mM with DMSO. These solutions were pin tool transferred (0.5 μ M) to plates containing sterile culture media for a final concentration of 10 μ M with 1% DMSO present in final assay volume.

The primary library was initially assayed for antibacterial activity against *Burkholderia oklahomensis* (C6786), *Escherichia coli* (BW25113), *Staphalococcus aureus* at 10 μ M final compound concentration. Each strain was grown in liquid culture to OD₆₀₀ = 0.6, diluted 1000-fold, and seeded into assay plates in a class II biosafety cabinet. Microplates were sealed for biocontainment and incubated at 37°C. Optical density (OD₆₀₀) was measured every 60 minutes for 24 hours and data was obtained as growth curves. Growth inhibition was evaluated from the slope of growth within the logarithmic phase for each compound. Compounds displaying favorable activity were selected for further investigation. Chloramphenicol served as positive control for all screens. The dynamic range of the assay was confirmed using dilution series of doxycycline.

2.2. Results

2.2.1. Library Construction

Adapting our previous described protocols to parallel high-throughput synthesis required considerable optimization. Liquid-liquid extractions following the Van Leusen imidazole synthesis and Pd-catalyzed macrocyclization were readily obviated. Purification of the acyclic imidazoles was achieved via mass-guided automated preparative HPLC. A methanol/water

mobile phase was utilized to reduce cost. A set of 24 crude imidazole reaction mixtures (e.g. Figure 3) could be purified in 6 hours. Yields for the imidazole synthesis ranged from 0 to 30 % and was highly dependent to amino acid at the terminal position. As a result, β -branched amino acids were typically not employed at the N-terminus. This compromise improved average yields to approximately 30%.

Catalyst removal following macrocyclization was achieved with thiol impregnated silica gel, obviating a second chromatographic purification. Aqueous work-up following acidolysis was required which proved technically challenging when conducted in parallel. Similarly, due to the complicated acidolysis reaction mixtures, manual preparative HPLC fraction collection was required.

The pilot library was derived from sequences composed of 3-5 amino acids. Peptides were prepared using Fmoc-based automated solid phase synthesis techniques.¹⁶ Assembly was performed on Rink polystyrene resin, providing C-terminal carboxamides upon cleavage.¹⁷ Each sequence contained at least one phenol-presenting residue selected from those shown in Figure 2B or a histidine residue. The remaining positions were filled randomly with residues chosen from the same set shown and natural and D-configured amino acids. Cysteine was not included due to its oxidative lability. The initial screening set consisted of 383 fractions derived from 35 sequences (Table 2). An average of 11 fractions were isolated from each peptide.

Table 2. List of peptides processed to construct primary screening library.

Entry	Sequence	Entry	Sequence	Entry	Sequence
1	Val-Trp-Tyr-Phe	13	Phe-Tyr-Tyr	25	Tyr(OMe)-Trp-Tyr(o-NMe ₂)
2	Val-Ala-Tyr-Val	14	Ala-Val-Tyr(o-OMe)	26	Gly-D-Leu-D-Tyr-Ala
3	Gly-Trp-Tyr-Trp	15	Leu-Phe-Tyr(o-OMe)	27	Ac-Gly-Orn(H)-Dap(CO ₂ C ₆ H ₁₃)-Tyr
4	Ala-Phe-Trp-Tyr	16	Gly-MePhe-Tyr	28	Gly-Ser-Tyr-Trp
5	Ala-Phe-Tyr-Val	17	D-Leu-D-Tyr-D-His	29	D-Ile-Trp-Tyr-D-Ala
6	Ile-Trp-Tyr-5HTA	18	D-Leu-Phe(NMe ₂)-Tyr(o-NMe ₂)	30	Gly-Gly-Phg-Tyr(o-NMe ₂)
7	Gly-Leu-5HTA	19	Gly-Phe-Tyr-D-His	31	Gly-Tyr-Leu-5HTA
8	Val-D-Val-D-Leu-Tyr-Thi	20	D-Ala-D-Phe-His-Phg	32	D-Leu-Ile-Tyr(o-OMe)
9	D-Val-D-Tyr-Tyr(o-OMe)-Tyr	21	B-Ala-Tyr(OMe)-Tyr-oxazole-indole	33	Phe(NMe ₂)-Tyr(OMe)-Tyr
10	Tyr(OMe)-D-Leu-Tyr(o-NMe ₂)-D-Ala	22	B-Ala-Pro(4-OAr)-Trp-Tyr	34	Val-Pro-Tyr(o-OMe)-Tyr
11	Ala-D-Val-D-Pro-His	23	Ser-Tyr(OMe)-Tyr-Ile-oxazole	35	D-Val-Pro-Tyr(o-NMe ₂)
12	Ser-Tyr-D-Pro	24	Gly-Trp-Pro-Tyr-Leu-NHMe		

Library Statistics:

- 383 member library
- 35 sequences (average ~11 fractions/peptide sequence)
- Fraction quantities:
 - average: 1.24 mg
 - median: 0.76 mg

2.2.2. Screening

The primary bacterial growth inhibition screen of the 383 compounds was performed against gram negative *B. oklahomensis*, *E. coli*, and gram positive *S. aureus* at 10 μ M substrate concentration. No active fractions were identified against *B. oklahomensis* or *E. coli*. However, fractions derived from tetrapeptide Ala-D-Val-D-Pro-His, suppressed growth of *S. aureus* at 10 μ M. The exponential growth phase was delayed 12 hours relative to vehicle (Figure 4C). The observed activity was confirmed in a repeat assays.

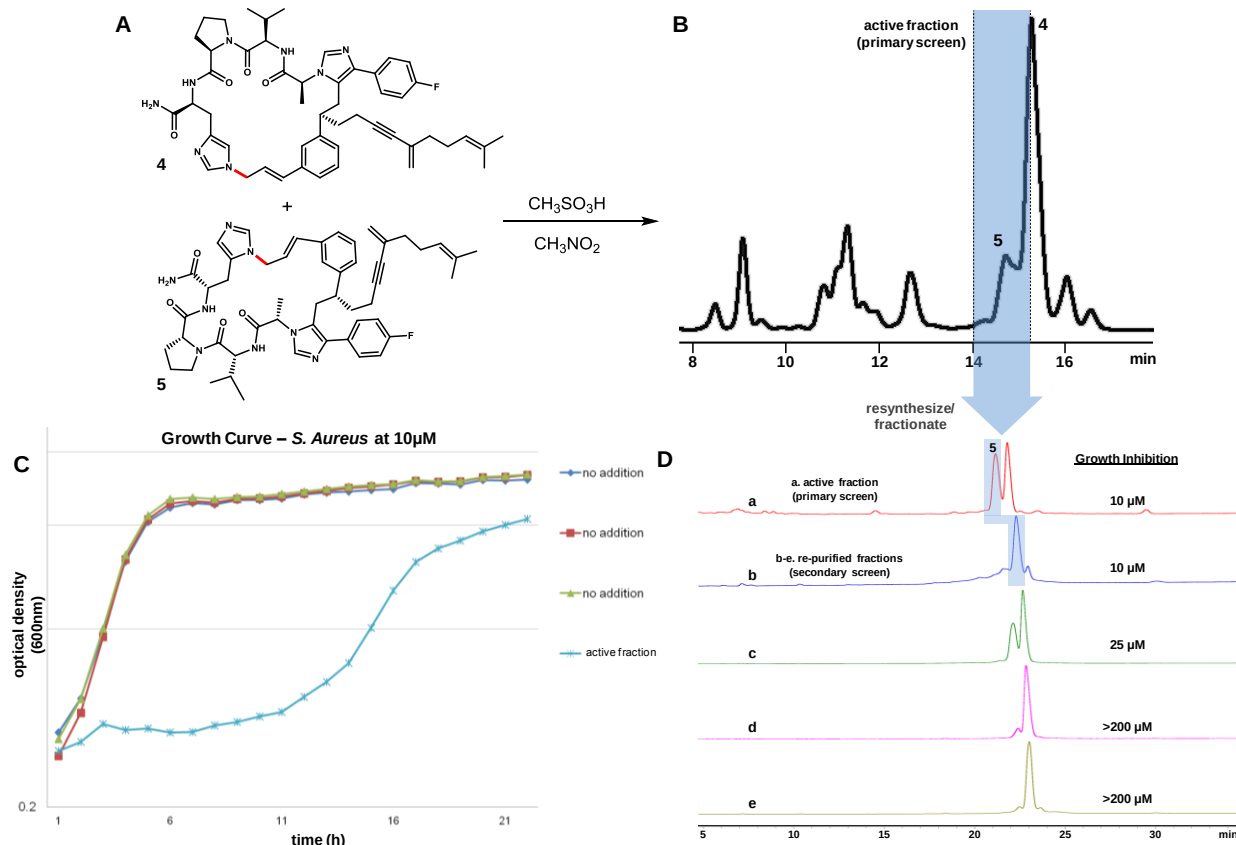


Figure 4. A) Acidolysis of Isomeric macrocycle derived from Pd-catalyzed macrocyclization of Ala-D-Val-D-Pro-His. B) Crude HPLC chromatogram of acidolysis reaction. All peaks represent isomeric compounds (UV254 nm, MeCN/H₂O, C18). C) Indicated fraction (a) inhibits growth of *S. aureus* at 10 μM . D) HPLC chromatograms of re-purified sequential fraction the preparative HPLC. A single component (5) retains observed activity. Indicated concentration for complete growth inhibition at 15 hours – end point assay.

HPLC analysis of the active fraction revealed it was predominantly composed of **4** and **5** – unconsumed starting materials to the acidolysis reaction (Figure 4). These regioisomeric macrocycles differ in the position of cinnamyl linkage. The major and minor products arise from the cinnamylation of the imidazole N^I and N^{II} positions respectively. In contrast to the tyrosyl ethers derived from Pd-catalyzed macrocyclization, the cinnamyl-histidine C-N bond is not prone to acid-catalyzed ionization. Cationic isomerizations are thereby limited to the dien-yne moiety and a reduced rate starting material consumption was common for His-alkylated macrocycles.

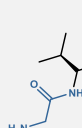
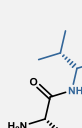
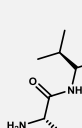
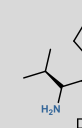
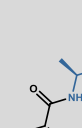
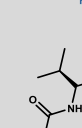
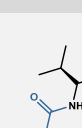
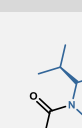
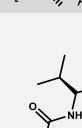
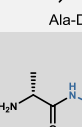
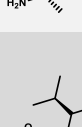
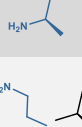
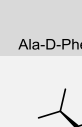
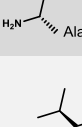
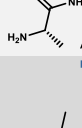
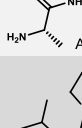
To minimize potential false negatives associated with screening compound mixtures and confirm no additional fractions were active against *S. aureus*, Ala-D-Val-D-Pro-His was re-synthesized and processed with **1**. Acidolysis products were fractionated to single components

and screened using an 8-point dilution series (range: 1.5 - 200 μ M). Only fractions composed of **5** inhibited bacterial growth with an IC₅₀ of $\sim$ 12.5 μ M. The major regioisomeric macrocycle **4**, derived the Pd-catalysis, showed no growth inhibition up to 200 μ M. Also, only the unreacted macrocycles were active indicating protolytic modification of the dien-yne appendage was not tolerated.

We next examined modifications of the peptide sequence. A set of 18 related sequences were prepared and processed with **1** (Table 3). Sequences were designed to systematically mutate single amino acid positions to build an initial SAR profile. Acidolysis products were fractionated to single components to minimize the need for re-purification and secondary screens. Isolated compounds were screened at 10 and 20 μ m as described for the primary assay.

Only limited modification of the first residue was tolerated. Truncation, oxygenation, and stereochemical modification resulted no observed growth inhibition (entries 2-4). The A1G mutated sequence (entry 1) showed a moderate reduction in activity, delaying growth for 10 hours at 20 μ M (Figure 4A). N-methylation and V2A mutation at position 2 was not tolerated (entries 7-9). Replacement of Val2 with (2,4-dimethoxy)phenylalanine resulted in multiple, sequential fractions which inhibited growth at 20 μ M (entry 10 and Figure 5A). Replacement of D-Val with D-Thr at position 2 resulted in slightly improved activity with growth inhibition observed at 10 μ M (entry 6, Figure 5B). All modifications of the proline residue resulted in reduced activity. Only replacement with α -aminoisobutyric acid displayed growth inhibition at 20 μ M. Replacement of the His4 with histamine briefly delayed growth at 20 μ M (entry 16). Stereochemical inversion at this position led to slightly enhanced activity with growth inhibition observed at 10 μ M (entry 17). These compounds retained activity when screened in the same format against *B. subtilis*.

Table 3. Antibacterial activities of secondary screening set.

Entry	Sequence	Inhib.	Entry	Sequence	Inhib.	Entry	Sequence	Inhib.
1	 Gly-D-Val-D-Pro-His	20 μ M	7	 Ala-Val-D-Pro-His	–	13	 Ala-D-Val-Sar-His	–
2	 D-Val-D-Pro-His	–	8	 Ala-D-Ala-D-Pro-His	–	14	 Ala-D-Val-D-Hyp-His	–
3	 Ser-D-Val-D-Pro-His	–	9	 Ala-D-(NMe)Val-D-Pro-His	–	15	 Ala-D-Val-Pro-His	–
4	 D-Ala-D-Val-D-Pro-His	–	10	 Ala-D-Phe(3,4-OMe)-D-Pro-His	20 μ M	16	 Ala-D-Val-D-Pro-Histamine	20 μ M
5	 Ac-Orn-D-Val-D-Pro-His	–	11	 Ala-D-Val-Alb-His	20 μ M	17	 Ala-D-Val-D-Pro-D-His	10 μ M
6	 Ala-D-Thr-D-Pro-His	10 μ M	12	 Ala-D-Val-Hyp-His	–	18	 Ala-D-Thr-D-Pro-D-Tyr	–

Modified residues depicted in blue. Fractions derived from each sequence were screened at 10 and 20 μ M. The concentration at which the sequence inhibited growth of *S. aureus* relative to control is indicated.

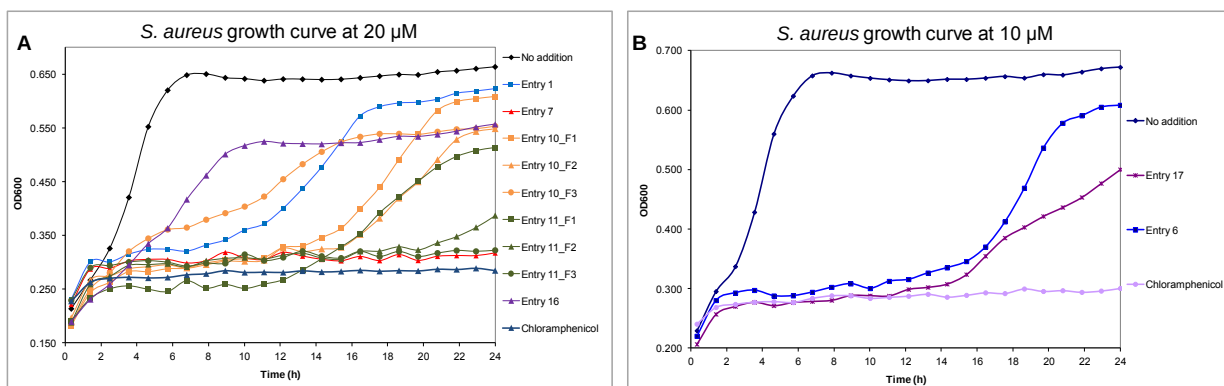


Figure 5. Bacterial growth curve for select Table 3 entries. **A.** Growth curves at 20 μ M substrate concentration. Repeat table entries represent unique fractions from acidolysis which exhibits growth inhibition. **B.** Growth curves at 10 μ M substrate concentration.

With an initial SAR profile of the peptide domain established we sought to investigate activity relationships of the hydrophobic domain imparted from **1**. As discussed above, an unmodified dien-yne appendage was a requisite for antibacterial activity. The *p*-fluorophenylimidazole motif was invariant within the screening library. To determine if this motif was essential for bioactivity we prepared an oxidized analog of our reagent (**6**, Figure 6). This allowed the imidazole motif to be replaced with an amide bond while retaining the core functionality of **1**. Following a three-step amidation-macrocyclization-acidolysis sequence (Figure 6), purified fractions were arrayed and screened. No fractions inhibited *S. aureus* growth up to 200 μ M, suggested the *p*-fluorophenylimidazole motif was a determinant for antibacterial activity.

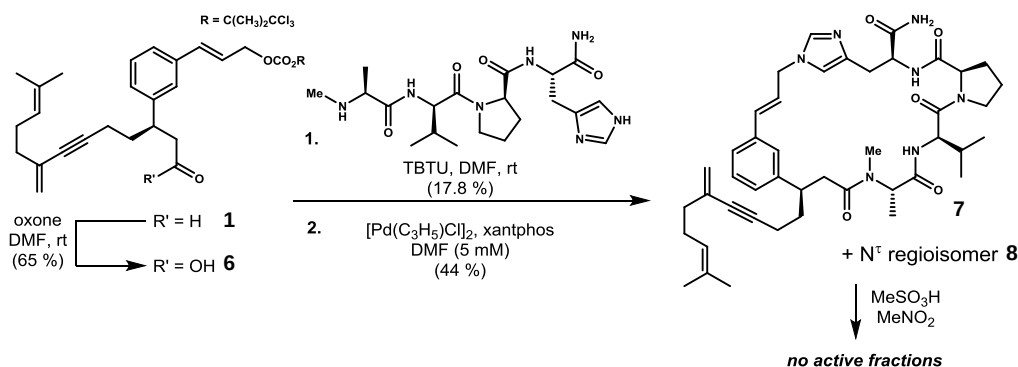


Figure 6. Reprocessing Me-Ala-D-Val-D-Pro-His with reagent **6**. Conditions: a) oxone, DMF, rt; b) **6** (1 eq.), peptide (1 eq.), TBTU (1.2 equiv), iPr_2NEt (4 eq.), rt; c) $[Pd(C_3H_5)Cl]_2$ (4 mol %)/xantphos (10 mol %), DMF (5 mM); d) $MeSO_3H$ (15 equiv.), $MeNO_2$ (5 mM).

2.3 Discussion and Conclusions

This initial follow-up set shows systematic modification of the peptidyl domain provides useful SAR data in the context of these discovery efforts. The hit-rate of the secondary library was greatly increased over that from random sequences. Multiple modifications aimed towards synergistic activity gains were not investigated, but would likely be beneficial. Of particular interest was the regiochemical dependence of cinnamyl alkylation on antibacterial activity. Although compounds derived from the secondary library were not fully characterized spectroscopically, the active component in each was derived from the minor product of the Pd-

catalyzed macrocyclization. Subsequent studies (chapter 3) reveal the ratio of N^+ and N^+ alkylation is consistent across numerous sequences. The marked activity relationship with this relatively minor structural variation suggests a general bacterial membrane pore-forming mechanism of action, common to amphipathic cationic antimicrobial peptides, may not be operative.^{18,19} Future work on the lead series identified in these studies is certainly warranted.

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Chapter 3 - Preparation of template-constrained macrocyclic peptides via Palladium-catalyzed allylic alkylation of natural amino acids

adapted in part from

Template-constrained macrocyclic peptides prepared from native, unprotected precursors

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3.1. Introduction

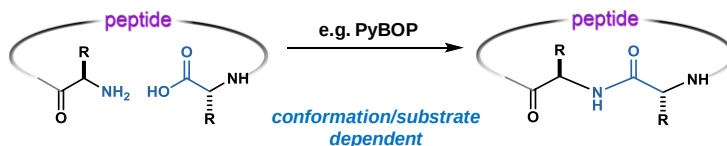
Synthetic peptides and peptidomimetics play wide ranging roles in pharmacology and drug discovery. Interest in these substances continues to grow, particularly as medicinal chemistry pushes further into control of cellular signaling events mediated by protein-protein interactions (PPIs).^{1,2,3} The subset of so-called 'druggable' PPIs include those mediated by consensus peptides, where binding determinants are localized within defined motifs.^{4,5,6,7,8} Experimental data as well as computational / bioinformatic efforts^{9,10,11} to identify 'short linear motifs' within signaling proteins suggest the number of druggable PPIs has been underestimated.^{12,13} Considerable opportunity exists for new chemistry in this area.¹⁴ Synthetic peptides that target 'hot spots' on protein surfaces are a logical entry to drug discovery programs.^{15,16,17,18,19} However, native peptides generally have poor pharmacological properties.²⁰ Modifications that offset those limitations while stably recapitulating protein-binding conformations are of considerable interest.^{14,21,22,23}

Ring-forming reactions are prominent among alterations found to improve the stability and performance of peptides.^{24,25,26,27} Relative to their acyclic counterparts, cyclic peptides have more defined conformations and are less prone to aggregate.²⁸ Head-to-tail lactamization is the most common method to synthesize cyclic peptides.^{29,30,31} Internal disulfide bonding is also used^{32,33}, as are newer techniques such as ring-closing olefin metathesis³⁴ and catalyzed

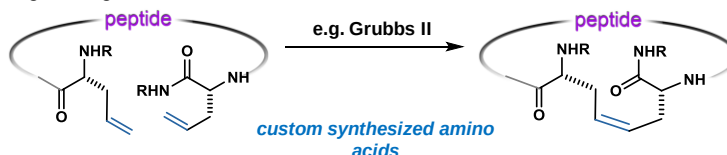
cycloaddition of azides to alkynes.^{35,36,37} These procedures rely on judicious use of protecting groups and/or tailored amino acid residues (Fig 1 A).^{38,39} Careful attention must be paid to substrate conformational biases to avoid competing oligomerization. Moreover, lactamization of peptides shorter than five residues can be particularly difficult.^{29,40}

A. Established Methods for Peptide Cyclization:

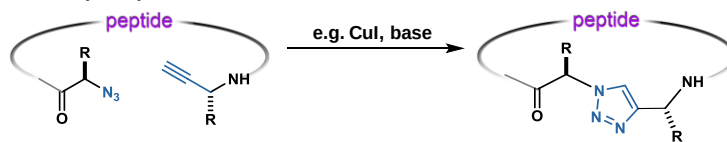
Peptide bond formation



Ring closing olefin metathesis



Azide-alkyne cycloaddition



B. Current Work: Templated Macrocyclization Catalyzed by Palladium(0)

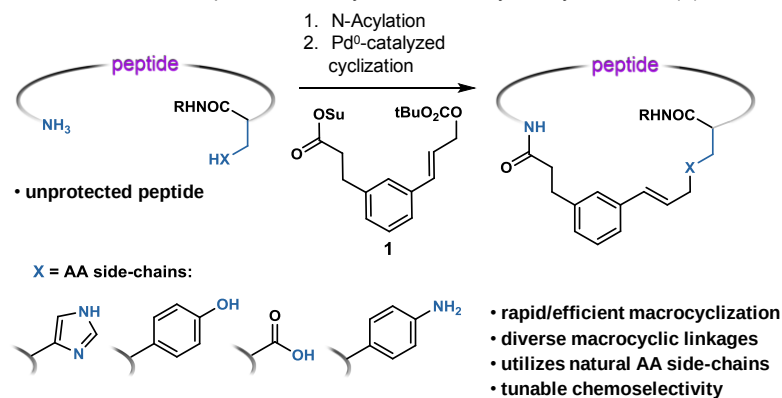


Figure 1. A. Existing methods for peptide cyclization can be sensitive to substrate conformational preferences and/or require tailored amino acid residues. B. The template-based cyclizations described here are catalyzed allylic substitutions. They engage native peptide functionality and proceed largely independent of oligomer length and composition.

An alternate method to incorporate short epitopes into rings is through the use of scaffolds. Degrado⁴¹, Boger⁴² and others have shown the utility of such template-constrained cyclic peptides^{43,44}, and how polarity and geometry of the template can influence shape and

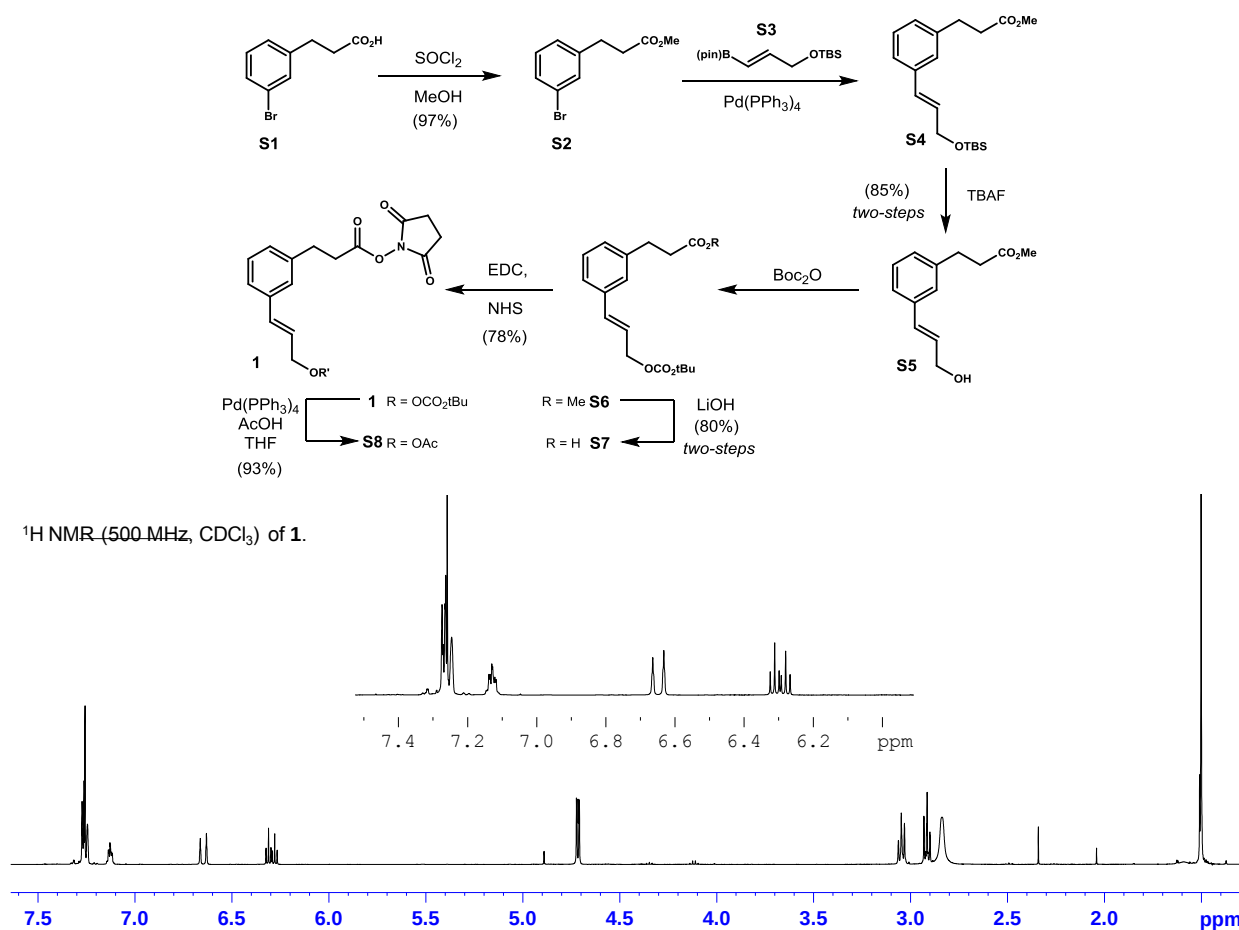
function of the peptide domain.⁴⁵ Our laboratory has also explored templates for forming macrocyclic peptides.^{46,47} In this work templates were designed as multiply reactive inserts. Stepwise engagement with a variety of peptides gave novel composite products. The resultant structures varied in shape, possessed defined conformations and increased solubility.

The large ring forming reaction in these processes was an allylic substitution catalyzed by palladium(0). We observed that decomposition of a cinnamyl carbonate within the template could capture pendant tryosine residues to form cyclic ethers.⁴⁶ This result followed from catalysis pioneered by Tsuji and Trost. Palladium catalyzed substitution of allylic leaving groups (a.k.a. the 'Tsuji-Trost reaction') is a versatile and well-studied process.^{48,49} Mechanistically it involves intermediate palladium π -allyl complexes that function as electrophiles. The chemistry occurs under mild conditions and is amenable to ligand-induced regio- and stereocontrol. It has been applied broadly, including in numerous instances to form large carbocyclic and heterocyclic rings.^{50,51,52,53} That said, when we simplified our templates to further study the catalysis in the context of cyclic peptide synthesis, we discovered a combination of scope and functional group tolerance that was remarkable. We describe those results here.

We show that intramolecular palladium-catalyzed cinnamylation of heteroatom nucleophiles can operate within highly functionalized native peptides. The nucleophile in the macrocyclization can be an amine, a carboxylic acid, a phenol, an imidazole and/or an aniline. Chemoselectivity is predictable and in many cases switchable. With one type of exception (vide infra), the reaction is catalyzed by a commercial complex of palladium(0), namely $\text{Pd}(\text{PPh}_3)_4$. No exotic or costly ligand sphere for the metal is necessary. No protecting groups are used in any substrate. Reactions proceed rapidly and in high yield at room temperature and, thus far, independent of product ring size and composition.

3.2. Results and Discussion

Template **1** (Figure 1B) is reminiscent of a lignan monomer. It is a simplified, achiral form of a structure we described previously.⁴⁶ The intent was to study large ring-forming reactions involving palladium π -allyl intermediates generated from the cinnamyl carbonate in this molecule. Compound **1** was synthesized in six steps and 51% overall yield from commercial 3-(3-bromophenyl)propionic acid (Scheme 1). Multi-gram batches of solid **1** were prepared and stored at room temperature without incident. Procedures using this material were designed to be simple. It's active ester acylated peptidyl amines in neutral DMF at room temperature. The resultant adducts reacted with catalytic amounts of commercial $\text{Pd}(\text{PPh}_3)_4$ in argon-sparged DMF, also at room temperature.



Scheme 1. Synthetic route to **1**. (conditions: see supporting information).

Initial experiments served to probe catalyzed cycloetherification of tyrosine residues (Figure 1B, $\text{XH} = \text{PhOH}$). Attention focused on how ring size, solvent, additives and substrate

concentration affected reaction rate and efficiency. As these experiments progressed, we observed a much greater functional group tolerance than expected. Moreover, residues such as aspartic acid, glutamic acid and histidine would participate as nucleophiles in the cyclization, as would a free carboxy or amino terminus under appropriate conditions. Chemoselectivity was both predictable and tunable. In two steps beginning with **1** and an unprotected peptide, we could achieve any one of several cyclization modes including head-to-tail, side chain-to-tail and side chain-to-side chain. Peptides up to eleven residues long were readily transformed into templated macrocycles.

3.2.1. Impact of solvent, substrate concentration and base additives on catalyzed cycloetherification of tyrosyl phenols.

Linear substrate **2** (Figure 2A) was chosen to evaluate affects of solvent and additives on catalyzed internal etherification of its tyrosyl phenol. *N*-Acylation of synthetic Ala-Trp-Thr-Tyr with *N*-hydroxysuccinimide **1** gave adduct **2** in 72% yield. Exposure of **2** to 5 mol % Pd(PPh₃)₄ in deoxygenated DMF (5 mM in **2**) at room temperature caused rapid conversion to cyclic ether **4** in 91% HPLC assay yield (78% when isolated by preparative HPLC). Reaction monitoring showed complete conversion to product within 15 minutes (Figure 2B). No dimeric or oligomeric materials were detected in the experiment. As illustrated in Table 1, the catalysis proceeded efficiently in several polar aprotic solvents. The use of water as co-solvent was tolerated (entry 5), but it slowed the reaction rate ~30-fold and resulted in formation of an unidentified side-product (~15%).

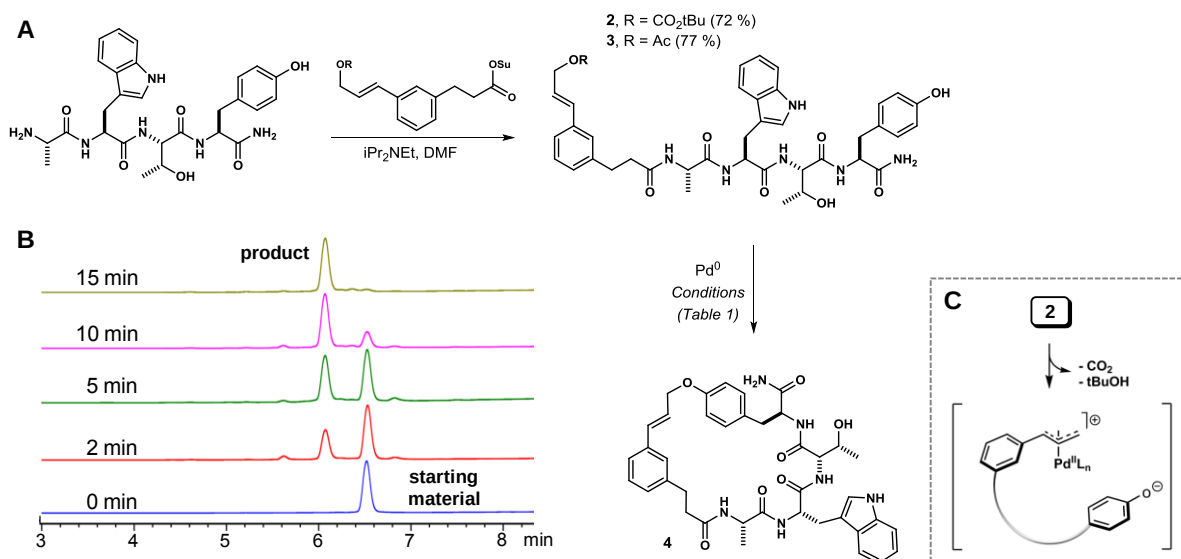


Figure 2. **A.** Catalyzed cycloetherification of substrates derived from templates **1** or **S8** and model peptide Ala-Trp-Thr-Tyr. **B.** HPLC analyses (C18, 40→100% MeCN/H₂O 0.1%TFA, 10 min, monitoring @ 254 nm) of samples taken from reaction of **2** with 5 mol% Pd(PPh₃)₄ (Table 1, entry 1) at the indicated time points. **C.** Partial schematic of internally ion-paired pi-allyl palladium(II) complex putatively generated from **2** via oxidative addition of Pd(0).

In neat DMF, contact ion pairing of transient intermediates within the catalytic cycle may explain the rapid reaction rate and high product yield.^{54,55} Consistent with literature precedent, *tert*-butoxide formed from decomposition of the cinnamyl carbonate following oxidative addition of Pd⁰ to the allylic C-O sigma bond likely deprotonates the proximal phenol, resulting in a new, more product-like (i.e cyclic, Figure 2C) metal ion pair. Reductive elimination or displacement of palladium would follow, leading to product. Electrostatic pre-organization of amphoteric peptides has been discussed previously.^{56,57} The inner salts invoked here as intermediates formed at low concentration would likewise be expected to offset entropic costs associated with ring formation.^{57,58} It is also consistent with a general lack of oligomeric products formed in the catalysis (vide infra), which can limit other peptide cyclization methods.^{40,59,60} Increasing the concentration 20-fold to 0.1M (Table 1, entry 2) led to only a slight reduction in yield.

Table 1. Media and additive effects on the palladium catalyzed synthesis of macrocyclic ether **4** from precursors **2** and **3**.

Entry	Substrate	Solvent/additive	Yield (%) ^a
1	2	DMF (5 mM)	91 (78)
2	2	DMF (100 mM)	84
3	2	THF (5 mM)	77
4	2	DMSO (5 mM)	91
5	2	1:1 DMF/H ₂ O (5 mM)	57
6	3	DMF (5 mM) ^b	nr
7	3	DMF (5 mM), Cs ₂ CO ₃ (2 equiv.)	88
8	2	1:1 DMF/100mM PBS (pH=5.5, 5mM) ^b	nr
9	2	1:1 DMF/100mM PBS (pH=7.4, 5mM) ^c	70
10	2	1:1 DMF/100mM PBS (pH=8.5, 5mM)	89

Reactions were run for 2h at room temperature in argon sparged media containing 5 mol % Pd(PPh₃)₄. ^aYield determined by HPLC assay. Isolated yield in parentheses. ^bNo conversion at 16h. ^c16h reaction time. PBS = phosphate buffered solution. nr = no reaction

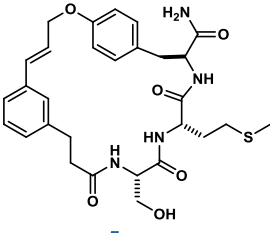
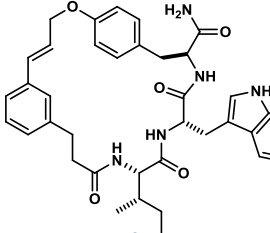
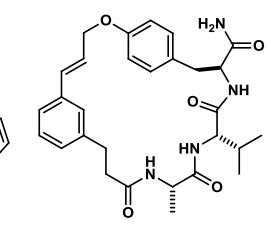
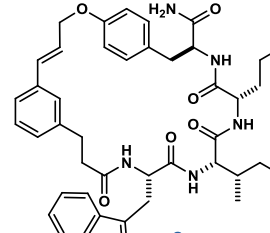
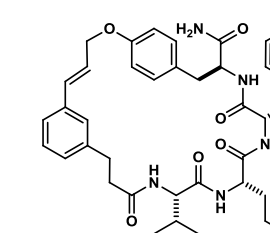
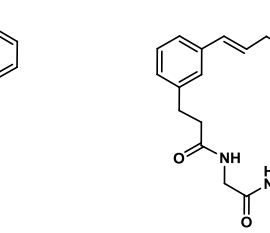
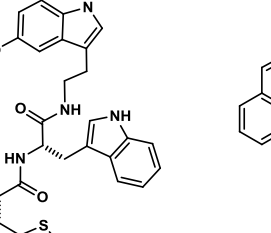
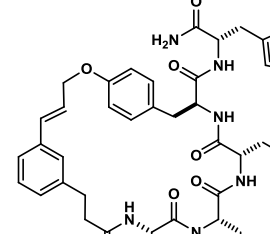
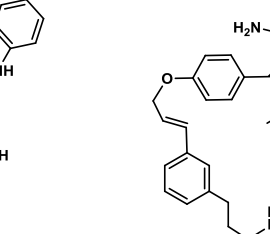
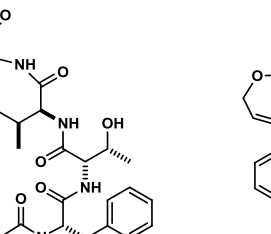
When cinnamyl acetate **3** (Figure 2) was subjected to identical cyclization conditions, conversion to **4** was not observed even upon prolonged heating (Table 1, entry 6). We speculated that, unlike the situation for **2**, acetate ion liberated by oxidative addition of Pd⁰ to **3** was insufficiently basic to propagate a catalytic cycle involving a tyrosyl phenoxide. Consistent with this hypothesis, addition of Cs₂CO₃ (2 equiv., Table 1, entry 7) rescued the reaction, promoting rapid conversion of **3** to cinnamyl ether **4**. Under buffered aqueous conditions, the cyclization rate was pH dependent. No conversion of **2** to **4** was observed when an equal mixture of DMF and pH 5.5 phosphate buffer was used as solvent (entry 8). Increasing the buffer pH to 7.4 induced a sluggish reaction. Complete conversion to **4** required 16 hours. However, at pH 8.5 the reaction was complete within 2 hours and **4** was formed in 89% HPLC assay yield. Taken together, data in Fig. 2C suggested 5 mM solutions of carbonate substrate in neat DMF (no additives) would be the most convenient to further evaluate the scope of the macrocyclization. Substrate solubility and reaction rate would be generally highest.

3.2.2. Evaluating the scope of catalyzed cycloetherification.

To define the range of macrocycles available through catalyzed cinnamylation of phenols, a set of unprotected, L-amino acid derived peptides were prepared as C-terminal

carboxamides. Peptides ranged from three to five residues long and each possessed a free N-terminus and a tyrosine residue in the sequence. All functional groups present in natural amino acids were represented in the set, with the exception of thiols (cysteine) to avoid complications from oxidative lability.

Table 2. Macrocyclic ethers obtained in two steps from template **1** and the indicated unprotected peptides (listed above product). Isolated yield of palladium catalyzed cyclization step indicated in parentheses. For conditions see Table 1, Entry 1. 5HTA = 5-hydroxytryptamine.

Ser-Met-Tyr	Ile-Trp-Tyr	Ala-Val-Tyr	Trp-Ile-Gln-Tyr
 5 (80 %)	 6 (72 %)	 7 (78 %)	 8 (81 %)
Val-Met-Phe-Tyr	Gly-Thi-Trp-5HTA	Ile-Ala-Arg-Tyr	
 9 (73 %)	 10 (75 %)	 11 (84 %)	
Ile-Met-Ser-Tyr-Trp	Ala-Phe-Thr-Ile-Tyr	Gly-Ser-Phe-Asn-Tyr	
 12 (73 %)	 13 (85 %)	 14 (74 %)	

Acylation of each peptide with template **1** was achieved by mixing in DMF in the presence of (i-Pr)₂NEt (see Table S1). Treatment of these products with 5 mol % Pd(PPh₃)₄

gave macrocyclic cinnamyl ethers **5-9** and **11-14** (Table 2) in high isolated yields (72-85%). No branched phenylallyl ethers were detected in these experiments. Polar functional groups including alcohols, amides and guanidines were well tolerated. Notably, efficient macroetherification was not restricted to tyrosine. 5-Hydroxyindole, incorporated as commercial 5-hydroxytryptamine, was equally competent as a nucleophile, affording macrocycle **10** in 75% yield. For each product, the macrocyclic ether linkage was assigned by NMR, wherein a diagnostic HMBC correlation between the cinnamyl methylene protons and the phenolic carbon resonance ($\sim \delta$ 155 ppm) was observed.

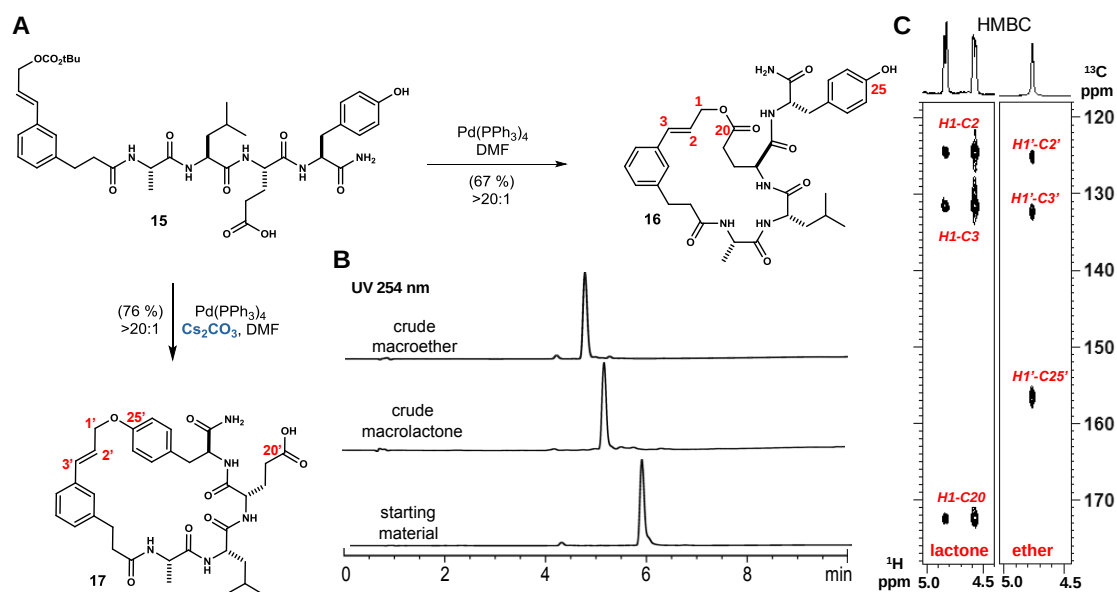


Figure 3. A. Cyclization chemoselectivity in a sequence containing both tyrosine and glutamic acid residues is high and base-dependent. B. HPLC analyses for the conversion of **15** to **16** or **17**: (a) starting material **15**, (b) after 1h in the presence of $\text{Pd(PPh}_3)_4$ (5 mol % in DMF) or (c) after 1h in the presence of $\text{Pd(PPh}_3)_4$ (5 mol % in DMF) and Cs_2CO_3 (2 equiv.). C. Key HMBC correlations used to assign connectivity within **16** (left) and **17** (right). Yields in parentheses refer to material isolated by preparative HPLC.

When the sequence Ala-Leu-Glu-Tyr was acylated with **1** and the product (**15**, Figure 3A) treated with $\text{Pd(PPh}_3)_4$, HMBC analysis of the resultant product did not reveal the anticipated cinnamyl ether. Rather, it indicated cyclization had formed macro lactone **16** (67% isolated yield) from cinnamylation of glutamic acid. This connectivity was assigned based on HMBC correlation between the cinnamyl methylene protons (H1 , Figure 3C) and Glu-C20 (δ 171.6 ppm). No other products were observed by HPLC (Figure 3B). We were cognizant that **16**

could form from **15**, yet expected this compound to be susceptible to re-ionization by palladium(0). However, consistent with the inertness of cinnamyl acetate **3** to Pd(PPh₃)₄ in the absence of base (Figure 2C, entry 6), macrolactone **16** proved stable and isolable. Re-subjecting **16** to the reaction conditions did not result in isomerization to cyclic ether **17**.

In contrast, when **15** was treated with 5 mol % Pd(PPh₃)₄ in the presence of Cs₂CO₃, macrocyclic ether **17** was formed exclusively and isolated in good yield (Figure 3B). Lactone **16** was not observable by HPLC during the course of the reaction. The absence or presence of Cs₂CO₃ was a convenient means to select for a 26-membered or 21-membered ring product. Such tunable outcomes bode well for preparing structurally distinct macrocycles from a single peptide sequence.

Catalyzed internal esterification proved an excellent method for head-to-tail macrolactonizations. Substrates prepared from **1** and peptides harboring a free carboxy terminus underwent the reaction readily. For example, treatment of Gly-Val-Trp-OH and Phe-Ile-Hyp-OH with **1** followed by Pd(PPh₃)₄ efficiently produced macrolactones **21** and **22** (Table 3), respectively. Branched allylic ester **22** was isolated as a ~1:1 mixture of diastereomers. No cinnamyl linkage was detected in this instance, an atypical outcome rationalized in terms of added geometric constraints imposed by the hydroxyproline residue.

Next examined were histidine containing substrates. Compound **18**, derived from **1** and Val-Gln-Tyr-His, was recovered unchanged after exposure to Pd(PPh₃)₄ for extended reaction times. Stable ligation of palladium by histidine containing peptides has been reported.^{61,62,63} To mitigate suspected catalyst poisoning, we turned to a less labile/dynamic ligand sphere for the metal. When a pre-catalyst generated from [Pd(C₃H₅Cl)]₂ (4 mol%) and the chelating bis-phosphine xantphos (10 mol%) was employed⁶⁴, complete consumption of **18** was observed within 30 minutes (Figure 4A,B). Two regioisomeric products were obtained in a ~5:1 ratio and 75% combined yield. HMBC correlations from the cinnamyl methylene *H1* to C28 and C30 confirmed the major product as histidine *N*29-alkylated macrocycle **20** (Figure 4C). The minor

product was determined to be its *N*31-alkylated regioisomer. Neutral imidazole is a weak nucleophile in solution.⁶⁵ A more nucleophilic imidazolate ion may be formed in this reaction. However, competition from the tyrosyl phenol was not observed despite possessing a similar pKa to the histidine imidazole.⁶⁶ Alternatively, the propensity for azoles to ligate palladium may sustain proximity to the π -allyl complex, thereby favoring imidazole allylation.⁶² As observed for substrate **15**, chemoselectivity was switchable upon the addition of base.

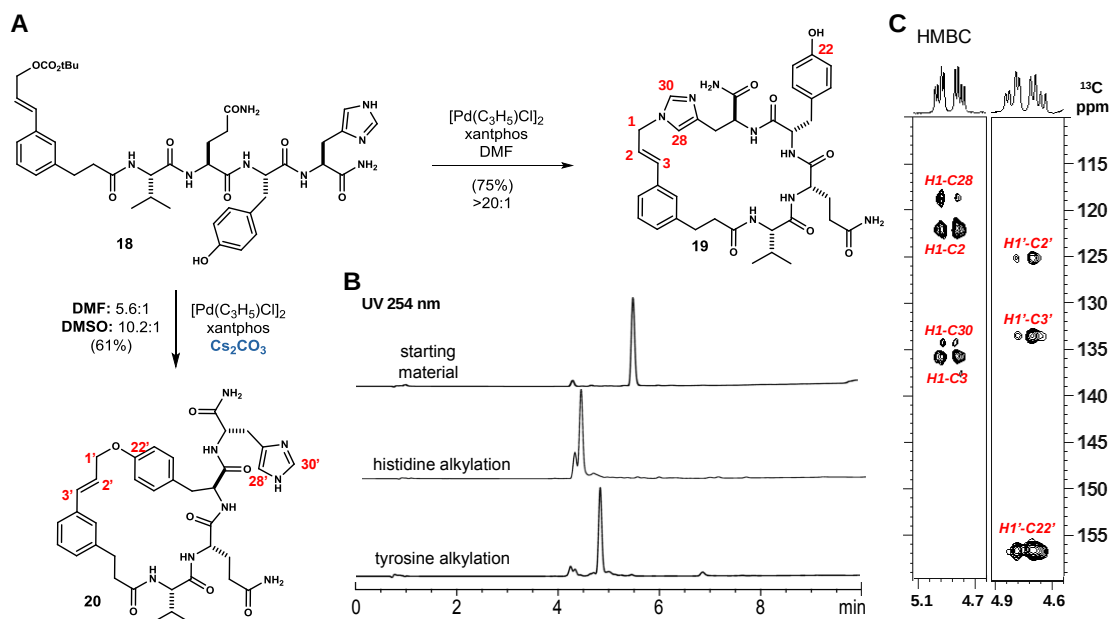


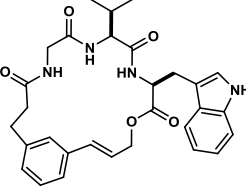
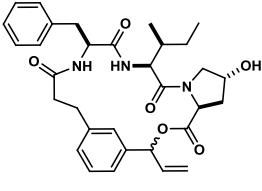
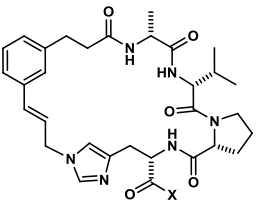
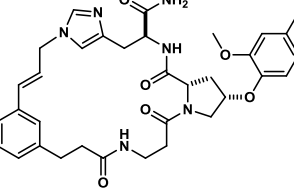
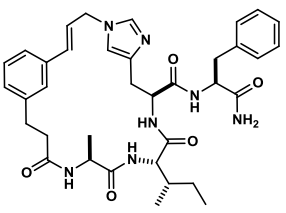
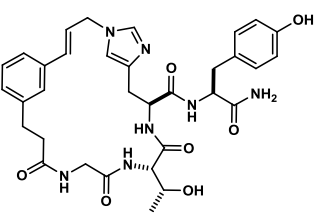
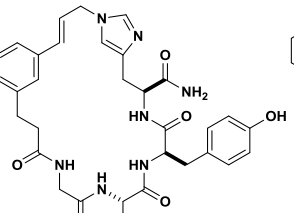
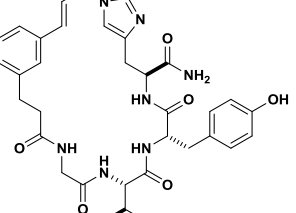
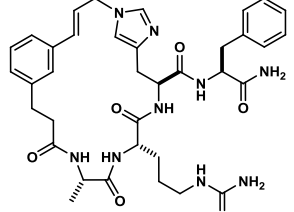
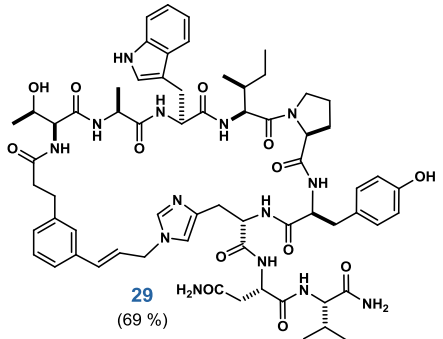
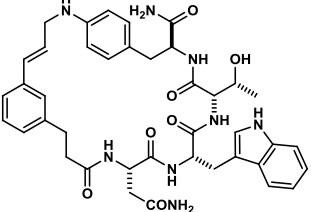
Figure 4. **A.** Cyclization chemoselectivity in sequences containing both tyrosine and histidine residues is high and base-dependent. **B.** HPLC analyses for the conversion of **18** to **19** or **20**: (a) starting material **18**, (b) after 30 min in the presence of $[\text{Pd}(\text{C}_3\text{H}_5)\text{Cl}]_2$ (4 mol %)/xantphos (10 mol % in DMF) or (c) after 30 min in the presence of $[\text{Pd}(\text{C}_3\text{H}_5)\text{Cl}]_2$ (4 mol %)/xantphos (10 mol % in DMSO) and Cs_2CO_3 (2 equiv.). **C.** Key HMBC correlations used to assign connectivity within **19** (left) and **20** (right). Note: **19** is formed as a ~5:1 mixture (see HPLC trace) of histidine N-alkylation regioisomers. The major isomer is drawn. Yields in parentheses refer to material isolated by preparative HPLC.

Treatment of **18** with $[\text{Pd}(\text{C}_3\text{H}_5)\text{Cl}]_2$ /xantphos and Cs_2CO_3 (2 equiv.) in DMF afforded macrocyclic ether **20** in a 5.7:1 ratio relative to regioisomers **19**. Changing the reaction solvent to DMSO improved the selectivity to 10.2:1 (Figure 4), likely due to the increased solubility of Cs_2CO_3 in DMSO.⁶⁷

A set of peptides was prepared to examine the generality of histidine-based macrocyclization (Table 2). In each case, treatment with $[\text{Pd}(\text{C}_3\text{H}_5)\text{Cl}]_2$ /xantphos afforded

exclusively histidine alkylated macrocycles in high yield. Where possible, tyrosine alkylation was not detected regardless of resultant ring size or stereochemistry (e.g. Table 3 **25a-c** and **29**). Histidine alkylation also occurred in preference to macrolactone formation in the presence of free carboxylic acids (see **23**). The presence of an carboxylic acid would theoretically preclude an intermediate imidazolate species. It is possible initial macrolactone formation precedes allyl migration to form a more stable cinnamyl-imidazole. Other polar functional groups including amides, alcohols, and guanidines were well tolerated. Sequences containing both histidine and residues displaying primary amines (i.e. Lys or Orn) were unique in that cyclization was unselective and low yielding. Only the combination of histidine caused this result with amines, which likely could be managed using orthogonal protection schemes.

Table 3. Novel macrocycles obtained from templated cyclization of oligomers (drawn above product) containing carboxylic acids, imidazoles, and anilines. Isolated yield of palladium catalyzed cyclization step indicated in parentheses. For conditions see Table 1, Entry 1.

Gly-Val-Trp-OH	Phe-Ile-Hyp-OH	D-Ala-D-Val-D-Pro-His-X	β -Ala-Pro(4-OAr)-His
 21 (74 %)	 22 (71 %)	 23 X = OH (69 %) 24 X = NH ₂ (77 %)	 26 (81 %)
Ala-Ile-His-Phe	Gly-Thr-His-Tyr	Gly-Thr-(D)Tyr-His	Gly-Thr-Tyr-His
 27 (71 %)	 25a (73 %)	 25b (n.d.)	 25c (n.d.)
Ala-Arg-His-Phe	Thr-Ala-Trp-Ile-Pro-Tyr-His-Asn-Val	Asn-Trp-Thr-Phe(4-NH ₂)	
 28 (76 %)	 29 (69 %)	 30 (77 %)	

In other settings, amines were useful and competent reaction partners in Pd⁰-catalyzed cinnamylation.⁶⁸ Moreover, use of the xantphos ligand was no longer necessary. For example, acylation of Fmoc-Val-Orn-Met-Tyr with template **1** followed by treatment with piperidine gave adduct **31** (Figure 5A). Exposure of this material to 5 mol % Pd(PPh₃)₄ resulted in exclusive cinnamylation of the N-terminus to afford **33** (>95% HPLC peak area purity). This product was readily assigned by TOCSY correlations. Uniquely, **32** shows ¹H-¹H correlations from the cinnamyl methylene to Val-H^N, H^α, and H^β (Figure 5B). Analogous to previous examples, chemoselectivity was sensitive to added base. The addition of 3 equiv.

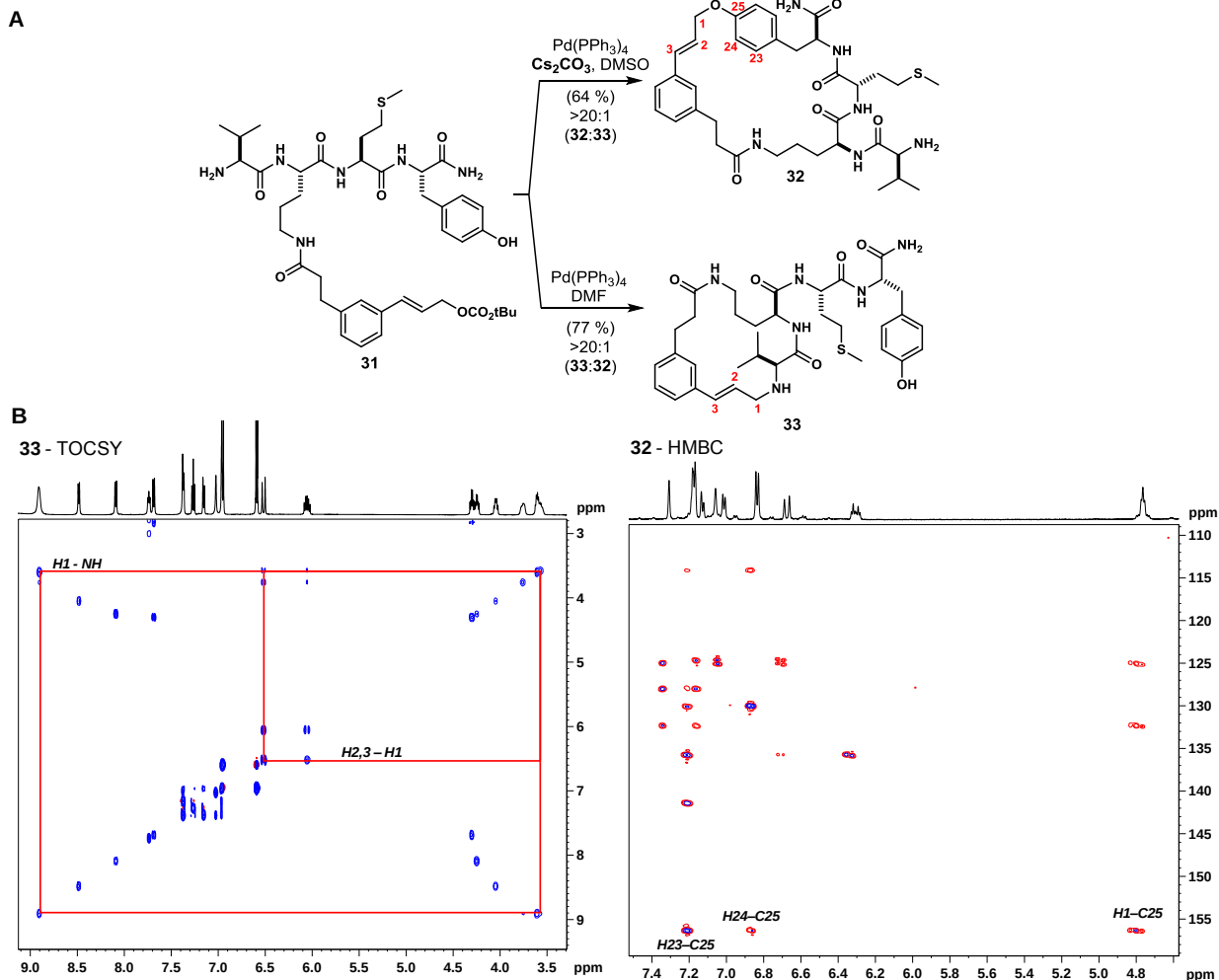


Figure 5. A. Cyclization chemoselectivity in a sequence containing a tyrosine residue and a free N-terminus is high and base-dependent. Conditions: For **32**; Pd(PPh₃)₄ (5 mol %), Cs₂CO₃ (3 equiv.), DMSO (5 mM in **31**). For **33**; Pd(PPh₃)₄ (5 mol %), DMF (5 mM in **31**). Yields in parentheses refer to material isolated by preparative HPLC. **B.** Characterization of **32** and **33** - key TOCSY (**33**) and HMBC (**32**) correlations

Cs₂CO₃ and use of DMSO as solvent provided cinnamyl ether **32** as the sole cyclization product. Under the same conditions, substrate **34** derived from **1** and Orn-Thr-Tyr gave macrocyclic ether **35** in 80% yield. The primary amine and secondary alcohol were unaffected.

We next examined a third type of nitrogen nucleophile in the cyclization reaction. Sequences were prepared containing the non-proteinogenic amino acid 4-aminophenylalanine, which is readily available and utilized as a tyrosine isostere.^{69,70} Peptides Ser-Phe-Phe(4-NH₂) and Asn-Trp-Thr-Phe(4-NH₂) were mixed independently with **1**, which selectively acylated their N-termini. Exposure of the products to 5 mol % Pd(PPh₃)₄ rapidly formed macrocyclic aryl amines **37** and **30** in high yield (Figure 6 and Table 3). Aniline alkylated macrocycles showed

moderate oxidative lability upon storage. This could be alleviated by acetylation of the aniline N-H with Ac_2O . (**37a**, Figure 6C). Experiments are ongoing to determine selectivity in aniline-based macrocyclizations when other potentially competing functional groups are present.

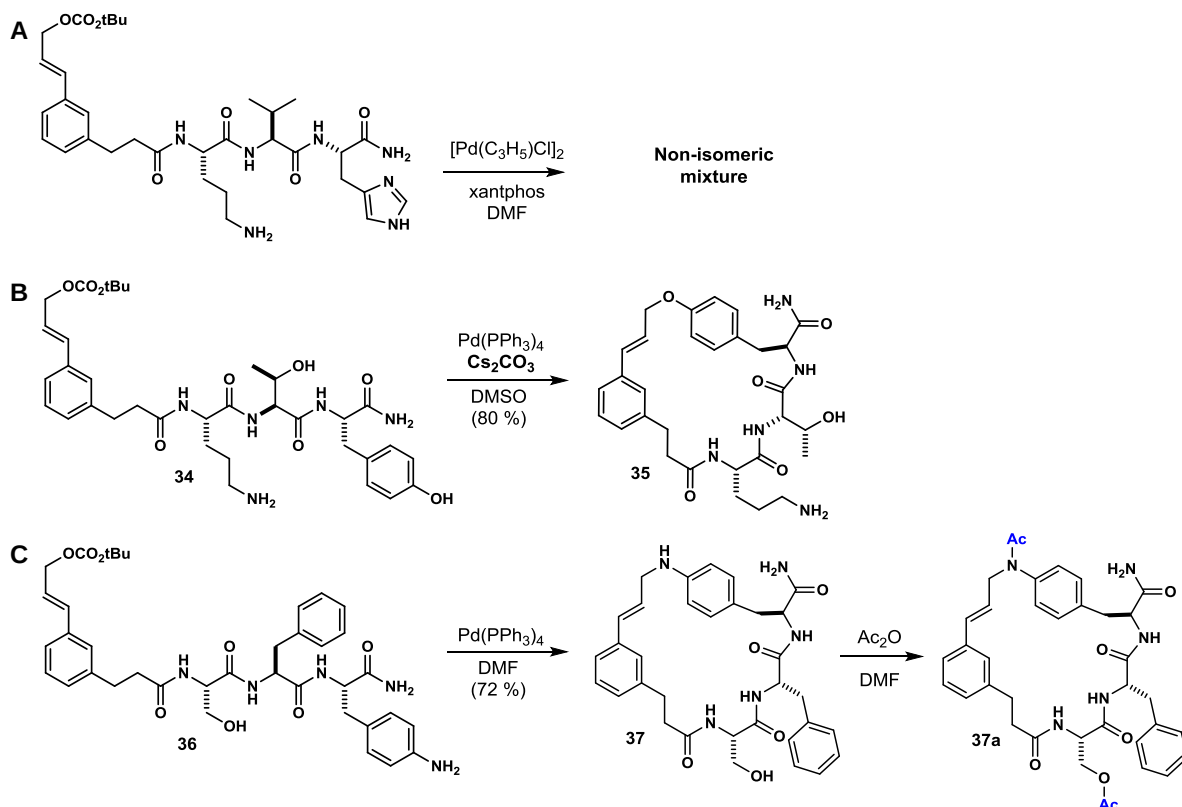


Figure 6. A. Sequences containing histidine and primary amines form non-isomeric mixtures up treatment with Pd^0 . B. In the presence of base, primary amines do not interfere with tyrosyl cyclizations. Conditions: $\text{Pd}(\text{PPh}_3)_4$ (5 mol %), Cs_2CO_3 (3 equiv.), DMSO (5 mM in **34**). C. A sequence containing p-aminophenylalanine cyclizes readily in the absence of base. Conditions: $\text{Pd}(\text{PPh}_3)_4$ (5 mol %), DMF (5 mM in **36**). Yields in parentheses refer to material isolated by preparative HPLC.

3.2.3. Reversibility of Pd-catalyzed macrocyclization.

As described above, Pd-catalyzed cyclization of VQYH in the absence of exogenous base affords only the histidine alkylated macrocycles. There is potential for His- and Tyr alkylation products to re-enter the catalytic cycle by oxidative insertion into the cinnamyl-N or O-bonds respectively. If this were to occur a thermodynamic distribution of products would be anticipated. Under these conditions equilibration was not observed. Re-subjecting **19** or **20** to $[\text{Pd}(\text{C}_3\text{H}_5)\text{Cl}]_2/\text{xantphos}$ did not reveal any interconversion of macrocyclic products (Figure 7A). Similarly, treatment of **4** with $\text{Pd}(\text{PPh}_3)_4$ (5 mol%) would irreversibly form **3** if oxidative

insertion/ionization of cinnamyl-tyrosyl C-O bond was operative (Figure 7B). These data suggest a kinetic product distribution formed when competitive tyrosine-histidine alkylation was possible.

Uniquely, the macrolactone C-O bond of **16** was isomerized to the more stable tyrosyl macrocycle upon treatment with Pd⁰ in the presence of Cs₂CO₃ (2 equiv.). This isomerization was not reversible resulting in complete conversion to **17**.

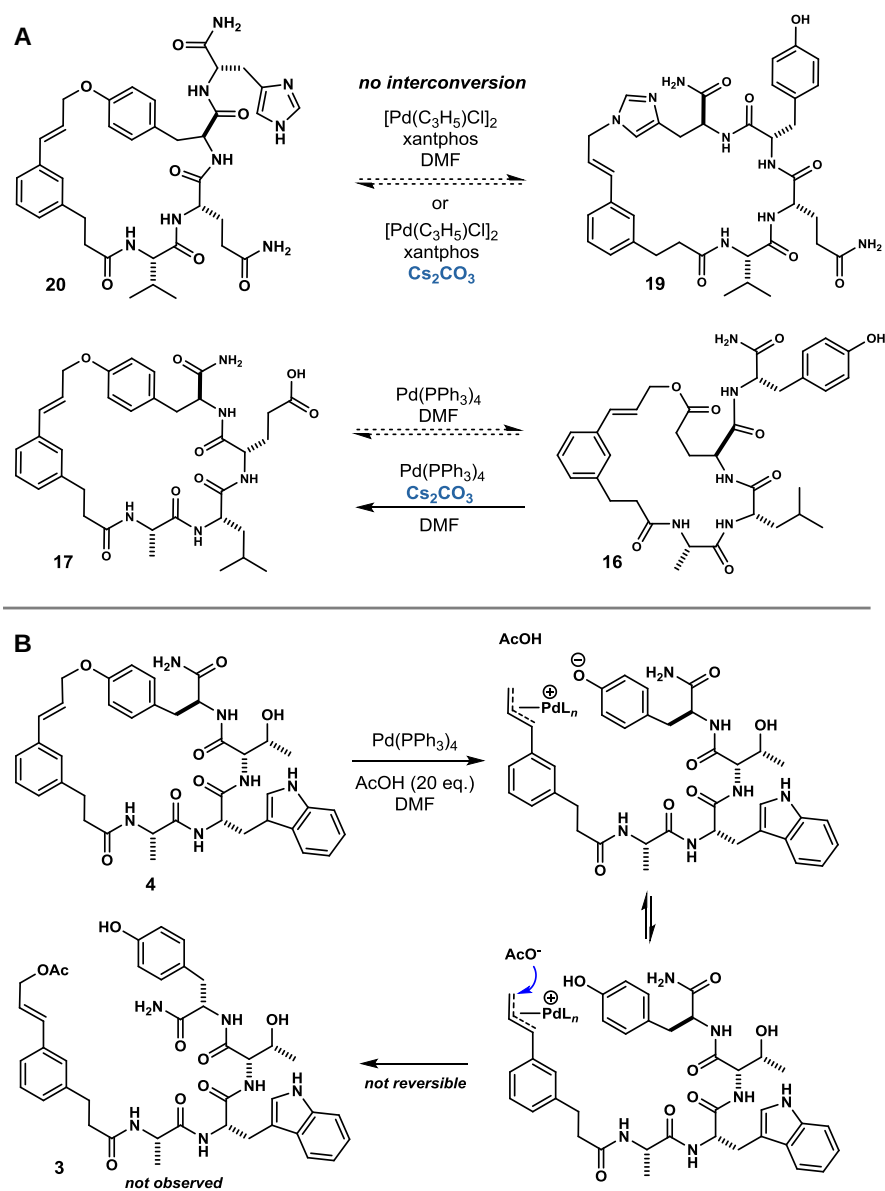


Figure 7. A. Resubjecting histidine or tyrosine alkylated macrocyclic products to Pd⁰ does not result in isomeric macrocyclic products. Macrolactone **16** isomerizes to **17** when exposed to Pd⁰ in the presence of Cs₂CO₃. **B.** Treatment of **4** with Pd(PPh₃)₄ (5 mol%) in the presence of AcOH (20 eq.) does not afford **3**.

3.2.4. Longer sequences undergo efficient macrocyclization.

Nascent secondary structure elements in longer peptides can assist or hinder cyclization attempts, depending upon how they influence access to the transition state for intramolecular reaction. Hinderance is common and oligomeric by-products often form as a result.^{59,60} High dilution⁷⁰, pseudo-dilution on solid-support⁷¹ and conformationally restrained pseudoprolines^{72,73} are used to improve cyclization efficiency. Techniques such as helical peptide ‘stapling’, based on ring-closing olefin metathesis, require folding of the helical element for efficient cyclization.⁷⁴ To begin testing the utility of palladium π -allyl chemistry for cyclizing longer sequences, we prepared octa- and dodecapeptides WLQMTGFY and AFSVPGVWISYV. Acylation of these materials with template **1** followed by treatment of the products with 5 mol % Pd(PPh₃)₄ gave macrocyclic cinnamyl ethers **39** and **38**, respectively. As observed for shorter sequences, the cyclization reactions were rapid and efficient at room temperature. The 38- and 47-membered ring products were readily isolated by preparative HPLC and characterized. Competing dimerization or oligomerization was not observed.

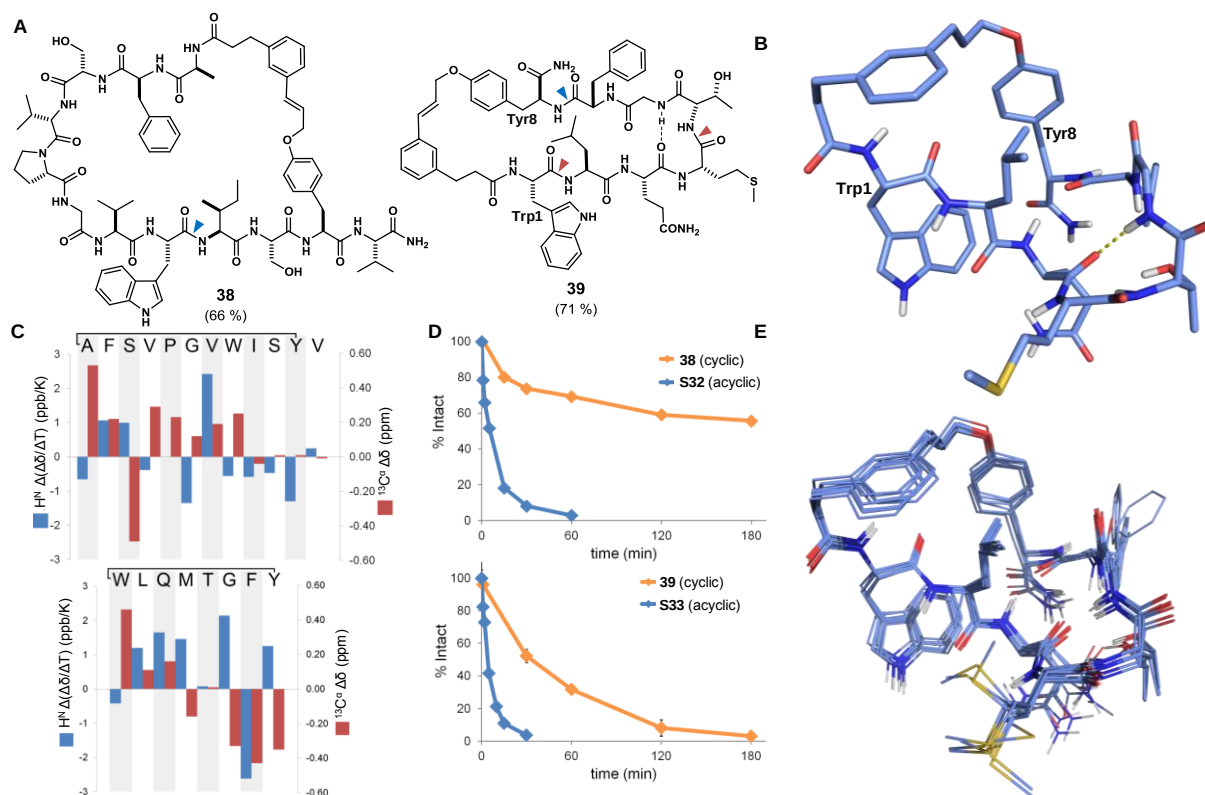
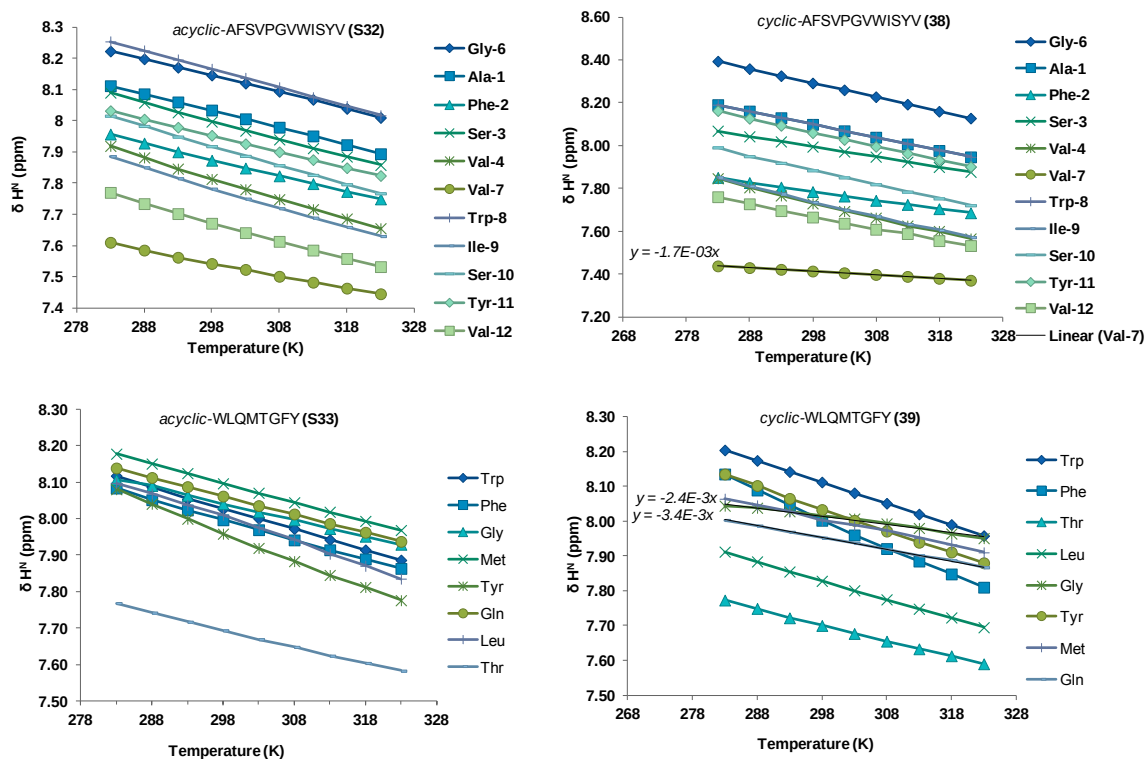


Figure 8. Conformational analysis and proteolytic stability of **38** and **39**. **A.** Planar structures of macrocycles **38** and **39**. Hydrogen bond H^N -Gly⁶-Gln³ in **39** was inferred from analysis of backbone amide chemical shift temperature dependence. $\blacktriangle$ Denotes primary α -chymotrypsin cleavage site, $\blacktriangleleft$ denotes secondary cleavage sites. **B.** Lowest energy conformation of compound **39** determined from NMR analyses in DMSO-*d*₆:H₂O (9:1). **C.** Comparison of NMR metrics for backbone amide solvent exposure ($H^N \Delta(\Delta\delta/\Delta T)_{cyclic-linear}$) and backbone conformation ($^{13}C^\alpha \Delta\delta_{cyclic-linear}$) between macrocycles **38** (top), **39** (bottom) and their respective linear precursors **S32** and **S33**. **D.** Macrocycle **38** exhibited greater stability against proteolysis by α -chymotrypsin in comparison to **S32** (top). Analogous stability was observed for macrocycle **39** over **S33** (bottom). **E.** Ensemble of ten low energy conformers of **39**. Core macrocycle rmsd = 0.36 Å.

These impressive results prompted us to investigate whether we had inadvertently chosen sequences poised to cyclize. Both **38** and **39** harbor potential turn inducing motifs centered at proline and glycine, respectively, which may accelerate the rate of ring closure. To explore this possibility, we utilized NMR to probe conformational preferences of macrocycles **38** and **39** relative to their linear precursors **S32** and **S33**.^{75,76} Comparison of $^{13}C^\alpha$ shifts, expressed as $\Delta\delta_{cyclic-linear}$ in Figure 8C and E, revealed distinct differences in the backbone conformations of linear and cyclic structures.^{77,78} These data imply that the linear precursors do not tightly occupy a product-like conformation, perhaps sampling an ensemble of states under these conditions. Differences were further evidenced by changes in the temperature dependence of backbone H^N chemical shifts following cyclization (Figure 9).^{79,80} Notably, Val⁷ and Gly⁶ in macrocycles **38** and **39**, respectively, showed a temperature dependence of greater than -3 ppb/K, suggestive of

internal hydrogen bonding at these positions.^{75,81} Similar interactions were not observed in the linear precursors, wherein a smaller temperature dependence was measured at the same positions; these comparisons are illustrated in Figure 5C as $\Delta(\Delta\delta/\Delta T)_{\text{cyclic-linear}}$. It appears that a product-like conformation of the linear precursor need not predominate in order for the palladium catalyzed cyclization to occur. Also, the G6A mutant of **8** cyclized readily. (Figure 10)

A



B

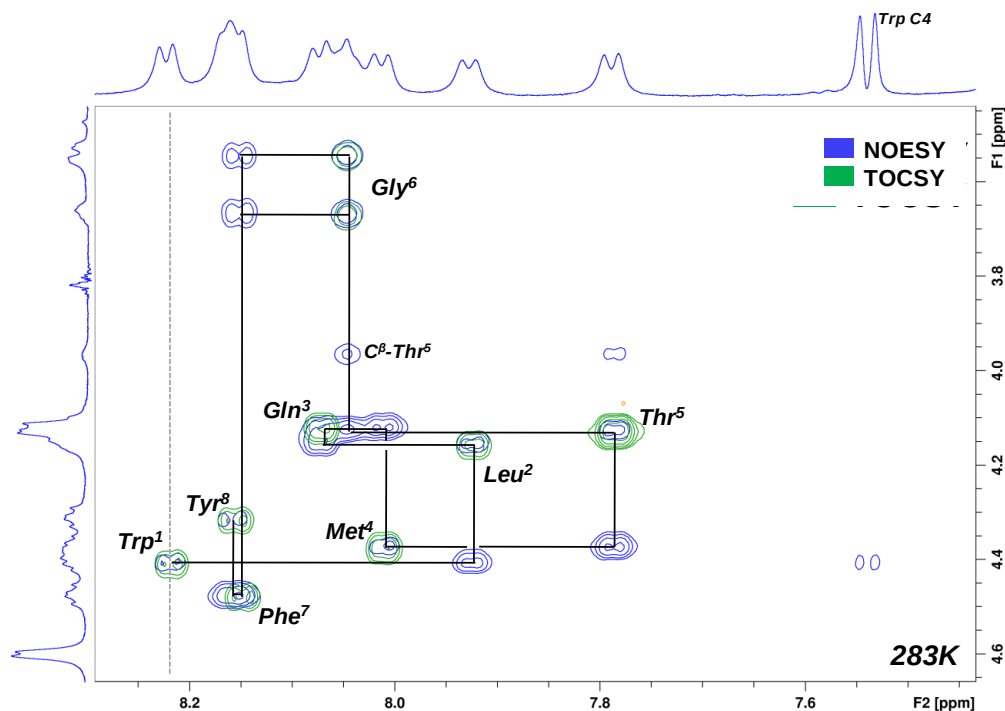


Figure 9. A. Temperature dependence of backbone ^1H chemical shifts for **S32**, **S33**, **38**, and **39** recorded in 9:1 $\text{DMSO-}d_6$, H_2O . Linear regression equation shown for residues exhibiting reduced chemical shift temperature dependence. B. Overlay of TOCSY and NOESY spectra of **39** ($\text{DMSO-}d_6/\text{D}_2\text{O}$, 9/1, 600 MHz). For full NOESY assignment see supporting information.

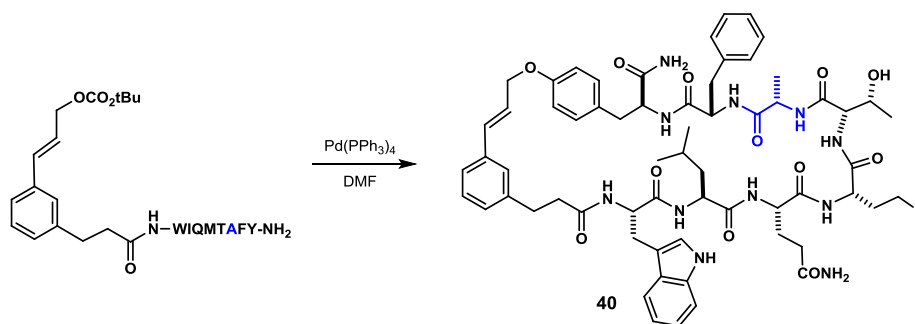


Figure 10. Cyclization of G6A mutant of **39** – Efficient cyclization can be achieved in the absence of turn-inducing residues.

3.2.5. Template 1 stabilizes secondary structure and enhances proteolytic stability *in vitro*.

Based on NMR evidence for internal hydrogen bonding, we next examined if templated macrocycle **39** exhibited a defined conformation in solution. Complete resonance annotations from NMR spectra acquired in 9:1 DMSO- d_6 :H₂O facilitated assignment of 80 intramolecular NOEs and 13 dihedral angle restraints. Sequential H^N NOEs within the triad Met⁴-Thr-Gly⁶ indicated the presence of a beta turn. Transannular NOEs between Leu² and Phe⁷, and between Gln³ and the C-terminus were indicative of the ring structure. Distance and angle constrained molecular mechanics calculations identified a tight ensemble of low energy conformers. The global energy minimum and an overlay of conformers of similar energy are shown Figure 5A and B. The region Gln³-Met-Thr-Gly-Phe⁷ occupies a type I β -turn, consistent with the observed Gly⁶ H^N temperature coefficient (-2.4 ppb/K, Figure 9). These data indicate a well-ordered core macrocycle and stabilization of the peptide domain, despite potential flexibility of the template.

Restricted conformational mobility is one means by which folded polypeptides evade enzymatic degradation.^{82,83,84} Accordingly, we examined the extent to which macrocycles **38** and **39** were protected against proteolytic degradation by α -chymotrypsin *in vitro*. As expected, linear compound **S33** was degraded rapidly, with primary cleavage occurring between Phe⁷ and Tyr⁸. Corresponding macrocycle **39** was 8.7-fold more stable in this assay (Figure 8D), and was

cleaved at the same site. Macrocycle **38** also exhibited resistance to proteolysis, although product inhibition precluded accurate determination of its half-life and comparison to linear counterpart **S32**. Enzymatic hydrolysis between Trp⁸ and Ile⁹ was invariant between cyclic **38** and the linear material. These preliminary results are encouraging and imply enhanced proteolytic stability observed for conventional cyclic peptides will be a feature of macrocycles derived from template **1** as well. Investigation of additional pharmacological properties of composite peptide macrocycles are ongoing.

3.2.6. *Template-stabilized α -helical motifs*

We are currently investigating whether palladium catalyzed allylation can be employed to stabilize other secondary structure elements. Methods to stabilize short alpha-helical domains present at protein-protein interfaces are of considerable interest, with numerous strategies having been employed.^{74,35,85,86} Recently all-hydrocarbon peptide stapling utilizing ring closing olefin metathesis of alpha-alkenyl alanine residues has been shown to stabilize known helical protein binding domains and confer favorable pharmacological properties.^{87,28} This strategy relies on a hydrophobic media to aid conformation pre-organization and facilitate interaction of reactive residues. The catalysts employed are sensitive to polar functional groups which are often masked with protecting groups during cyclization.

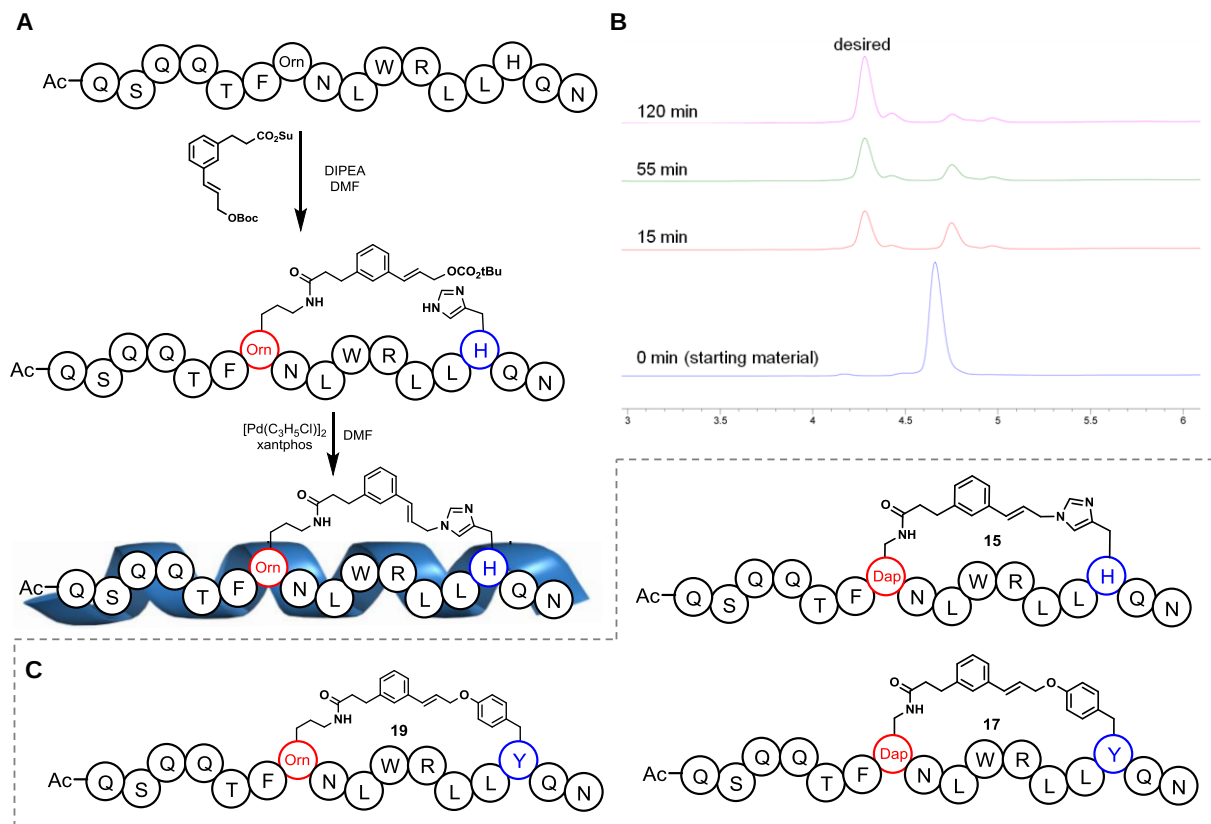


Figure 11. **A.** Cyclization of 16-residue peptide related to the biologically relevant p53-MDM2 interaction. **B.** Time-course analysis of macrocyclization depicted in A. **C.** Additional examples of *i, i+7* stapled peptides. Yields not determined.

The flexibility and versatility of our method may provide a powerful complement to these existing stapling strategies. The geometry, length, flexibility, and polarity of the staple can be optimized by systematic modification of reacting residues and template structure. By harnessing the inherent reactivity of native peptides, we may also be able to utilize biotic peptides. We have demonstrated the efficacy of our method to generate *i, i+7* cyclized peptides relevant to the p53-MDM2 interaction (e.g. Ac-QSQQTForN(L)WRL(L)LHQN, Figure 11). The functional group complexity of these longer peptide sequences does not reduce the cyclization efficiency (Figure 11B). Additional examples (Figure 11C) show how the length and flexibility of the staple may be tuned by modification of the reacting amino acid residues. While these data demonstrate the utility of Pd-catalyzed allylations to prepare long-chain macrocyclic peptides, the investigation of the pharmacological and conformational properties of these composite peptide macrocycles is ongoing.

3.2.7. Solid-phase synthesis of template constrained peptide macrocycles.

We next examined the potential of **1** to prepare macrocyclic peptides on solid support. Our strategy employed differentially histidine monomers which could be selectively deprotected following ligation of **1**. This strategy would selectively unveil reacting partners and thus overcome the intrinsic chemoselectivities described above. We chose Fmoc-His(Mmt)-OH which may be deprotected with weakly acidic solutions - AcOH:TFE:CH₂Cl₂ (1:1:8 v/v). Importantly, these conditions do not decompose the cinnamyl carbonate of **1** or remove other standard side-chain protecting groups commonly employed in Fmoc-SPPS.

Tetrapeptide Orn-Gln-His-Phe was chosen to evaluate the efficacy of this approach. This would expand the scope as the primary amine side-chain of ornithine is not compatible with the solution phase histidine alkylations described above. Following acylation with **1**, the Mmt protecting group was removed by treatment with AcOH:TFE:CH₂Cl₂ for two hours (Figure 12A). The optimal deprotection time was determined prior to installment of **1** by LC/MS analysis of test cleavages for the presence of the 4-methoxytritylcation. Following deprotection, treatment with [Pd(C₃H₅)Cl]₂/xantphos and subsequent cleavage from solid-support provided the desired histidine-alkylated macrocycle in good purity (Figure 12B).

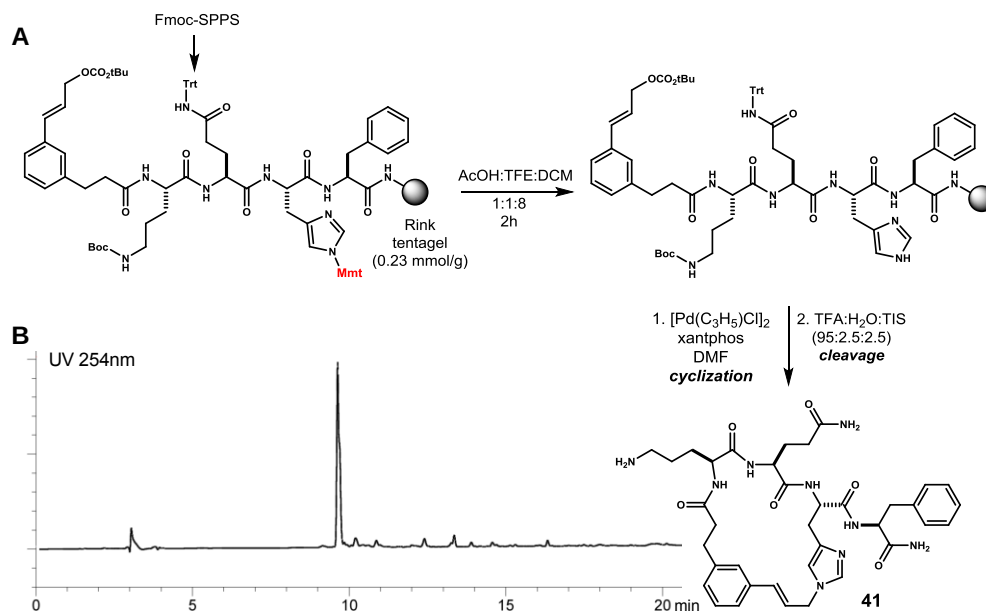


Figure 12. A. Solid-phase macrocyclization of Orn-Gln-His-Phe-NH₂(Rink). Conditions: a) AcOH, TFE, DCM (1:1:8); b) [Pd(C₃H₅)Cl]₂ (8 mol%), xantphos (20 mol%), DMF(degassed), 2h; c) TFA:H₂O:TIS (95:2.5:2.5), 1h. **B.** Crude HPLC analyses of **41** after cleavage. (C18, UV254 nm). TIS = triisopropylsilane, TFE = trifluoroethanol, Mmt = *p*-methoxytrityl

To examine the potential of this strategy to prepare stabilized helical motifs we prepared decapeptide OrnAVQRHEHAF. This sequence contains participating residues at *i,i*+7 relative positions (Orn1/His8) which would potentially be located on the same face of an alpha-helical conformation and represents a common peptide 'stapling' strategy. Following the three step deprotection-cyclization-cleavage protocol the desired cyclic decapeptide was isolated as a white solid following ether precipitation.

With the success of this model study our attention turned to biologically relevant α -helical motifs. Extensive work by Walensky and coworkers has demonstrated the utility of stapled peptides to interrogate biological process related to the Bcl-2 family proteins.^{88,89} To allow ready comparison to these existing techniques we investigated the utility of our approach to prepare cyclic peptides encompassing the BH3 domain of Mcl-1. A set of six sequence were chosen based on existing binding data.⁸⁸ To evaluate the effect of staple length a mixture of *i,i*+3 and *i,i*+7 staple positions were chosen. Sequences were prepared in parallel by standard Fmoc-SPPS techniques as their N-terminal acetate utilizing highly acid labile Lys(Mtt) side-chain

protecting strategy to allow selective amine deprotection and ligation with **1**. The acid sensitivity of the Mtt group was considerably reduced when incorporated into the peptide sequence and attached to solid support. As such, iterative treatment with TFA:TIS:DCM (3:2:95 v/v) was required for complete side-chain protecting group removal of participating Lys and His residues.

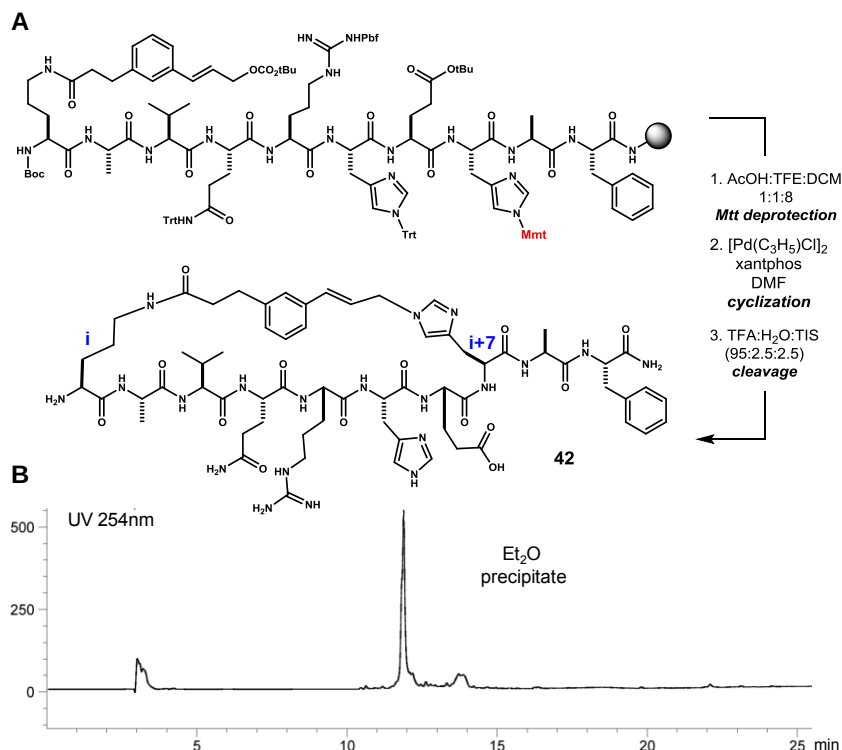
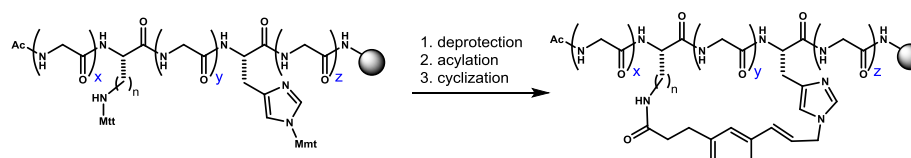


Figure 13. A. Solid-phase macrocyclization of Orn(γ -1)AVQRHEHAF-NH₂(Rink). Conditions: a) AcOH, TFE, DCM (1:1:8); b) [Pd(C₃H₅)Cl]₂ (8 mol%), xantphos (20 mol%), DMF(degassed), 2h; c) TFA:H₂O:TIS (95:2.5:2.5), 1h. **B.** Crude HPLC analyses for the conversion of # to #. (C18, UV254 nm). TIS = triisopropylsilane, TFE = trifluoroethanol, Mmt = *p*-methoxytrityl

Unfortunately, analysis of the completed peptides prior to ligation with **1**, revealed the desired peptides were formed in low purity. Adjusting coupling times, reagents, pre-activation of amino acids resulted in only a moderately improved purity. The source of side products was unclear. In spite of the poor peptide purity, each sequence was coupled with **1** and cyclized as described above. In each case the desired macrocycles were observed by LC/MS, but with substantial impurities, indicative of the low purity observed from the starting sequence. The macrocycles were isolated by iterative preparative HPLC. Characterization was limited to mass spectral analysis as only low-milligram quantities of each were isolated. While these data

indicate promise for Pd-catalyzed allylations to prepare long-chain macrocyclic peptides on solid-support, refined protocols for parallel peptide synthesis are necessary to make this a viable method. An alternative strategy to deblock participating residues, such as nucleophilic or basic cleavage, would be beneficial.

General Strategy:



Attempted sequences:

```

1 . K A L K T L R H V G D G V Q R N H E T A F
2 . K A L E T L R R V K D G V H R N H E T A F
3 . K A L E T L R R V G D G V K R N H H T A F
4 . K A L E T L R H V G D G V Q K N H E T A F
5 . K A L E T L R R V G D K V Q R N H E H A F
6 . K A L H T L R R V G K G V Q R N H E T A F

```

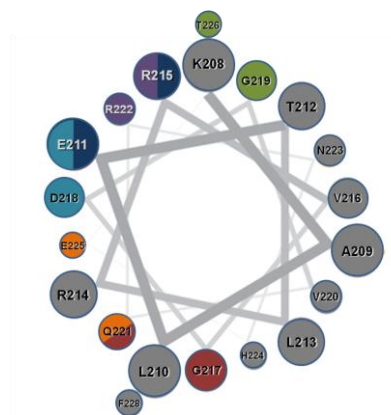


Figure 14. Solid-phase synthesis of stabilized alpha-helical peptide related to the BH3 domain of Mcl-1. Staple positions denoted with red characters. Coloration of helical represents stapled positions.

3.3. Conclusions

We have described methods to convert unmodified, unprotected linear peptides directly to stable macrocycles using **1** as a scaffold. Non-natural amino acids are not required. The catalyzed ring forming reaction is uniquely versatile and operates independent of product ring size and composition. Side chain functional groups present in tyrosine, histidine, glutamic acid and aspartic acid participate in the cyclization, as do a free carboxy or amino terminus under appropriate conditions. Alcohols, guanidines, carboxamides and thioethers neither participate nor interfere with the catalysis. The chemistry is well suited to probe consensus peptide binding sites, to generate peptide-based positive controls for assay development, to stabilize and protect elements of secondary structure (i.e. turns, helices) and to create prototype leads for

medicinal chemistry programs targeting protein/protein interactions. Simple procedures, mild reaction conditions, high yields and tunable chemoselectivity provide for myriad possibilities. The chemistry compares favorably to other methods for peptide cyclization. The ready availability of peptides commercially will hopefully facilitate additional research by others.

Chapter 3 - Supporting Information

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General:

Unless stated otherwise, reactions were performed under an argon atmosphere in flame-dried glassware. Tetrahydrofuran (THF) was deoxygenated and dried by passing through an activated alumina solvent drying system. Anhydrous *N,N*-dimethylformamide (EMD DriSolv®) was used without further purification.

Purification of acidolysis products employed an Agilent 1100/1200 HPLC system equipped with G1361A preparative pumps, a G1314A autosampler, a G1314A VWD, and a G1364B automated fraction collector. Analytical HPLC was performed using the same system, but with a G1312A binary pump. Mass spectra were recorded using an Agilent 6130 LC/MS system equipped with an ESI source.

NMR methods:

NMR spectra were recorded on Bruker Avance (500 or 600 MHz) spectrometers. Data for ^1H NMR spectra are reported as: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration), and are referenced to a residual DMSO-*d*₆ (2.50ppm). ^{13}C resonances are reported in terms of chemical shift (δ ppm) as referenced to DMSO-*d*₆ (39.52 ppm). For mass-limited samples, solvent magnetic susceptibility matched Shigemi tubes were used with a sample volume of ~300 μL . Optimization of on-axis shims was accomplished using the TopShim automated tool within Bruker Topspin™ 2.1. Optimization of off-axis shims was performed manually,¹ or with TopShim3D in the case of samples containing H₂O. ^1H 90° transmitter pulse lengths were calibrated by back calculation from the 360° null.² The pulse width or power level for soft pulses and shaped pulses were calculated using the Shape Tool within TopSpin™ 2.1.

COSY spectra were recorded using a phase sensitive, gradient enhanced double-quantum-filtered experiment,³ or magnitude mode gradient enhanced experiment with presaturation using the States-TPPI method. Data were typically recorded as a matrix of 2048 x 512 complex points and 2 transients per increment. Data were apodized with a $\pi/3$ -shifted sine-bell in the F1 dimension truncated at 10%, and with an untruncated $\pi/3$ -shifted sine-bell in the F2 dimension. Zero filling was applied in F2 to give a symmetrical matrix of 4K x 4K real points following mirror image linear prediction in F1 (64 coefficients) to 256 points.

TOCSY spectra were recorded using a phase sensitive experiment implementing preservation of equivalent pathways.⁴ A 60ms DIPSI-2 or MLEV pulse train was used for homonuclear Hartman-Hahn transfer.⁵ Data were typically recorded as a matrix of 2048 x 256 complex points and 2 or 8 transients per increment. Data were apodized with a $\pi/3$ -shifted squared sine-bell in the F1 dimension truncated at

¹ Berger, S.; Braun, S., *200 and More NMR Experiments*, Wiley-VCH, Weinheim, **2004**, 6-11.

² a) Claridge, T.D.W., *High-Resolution NMR Techniques in Organic Chemistry*, Pergamon, Oxford, **1999**, 94-97. b) Berger, S.; Braun, S., *200 and More NMR Experiments*, Wiley-VCH, Weinheim, **2004**, 15-17.

³ a) Hurd, R.E., *J. Magn. Reson.*, **1990**, 87, 422-428. b) Brereton, I.M.; Crozier, S.; Field, J.; Doddrell, D.M., *J. Magn. Reson.*, **1991**, 93, 54-62. c) Shaw, A.A.; Salaun, C.; Dauphin, J.F.; Ancian, B., *J. Magn. Reson. Ser. A*, **1996**, 120, 110-115.

⁴ Wagner, R.; Berger, S., *J. Magn. Reson.*, **1996**, 123 A, 119-121.

⁵ Cavanagh, J.; Rance, M., *J. Magn. Reson.*, **1990**, 88, 72-85.

10%, and with an untruncated $\pi/2$ -shifted squared sine-bell in the F2 dimension. Zero filling was applied in F2 to give a symmetrical matrix of 4K x 4K real points following mirror image linear prediction in F1 (64 coefficients) to 128 points.

NOESY spectra were recorded using a phase sensitive experiment with selection gradients during the mixing time. A 300ms mixing time was used for qualitative structural assignment. Data were typically recorded as a matrix of 4096 x 256 complex points and 8 transients per increment. Data were apodized with a $\pi/3$ -shifted squared sine-bell in the F1 dimension truncated at 10%, and with an untruncated $\pi/2$ -shifted squared sine-bell in the F2 dimension. Zero filling was applied in F2 to give a symmetrical matrix of 4K x 4K real points following forward linear prediction in F2 (32 coefficients) to 64 points, and mirror image linear prediction in F1 (64 coefficients) to 128 points.

Carbon chemical shifts were measured from 2D plots of either HSQC spectra for protonated carbons or HMBC spectra for non-protonated carbons. ^1H - ^{13}C HSQC spectra were recorded using a sensitivity improved phase sensitive experiment using an adiabatic shape pulse for ^{13}C inversion, and ^{13}C decoupling during acquisition.⁶ Experimental parameters were optimized for $^1J_{\text{CH}} = 145\text{Hz}$. ^1H - ^{13}C HMBC spectra were recorded using a gradient selected experiment with a J -filter element optimized for $^1J_{\text{CH}} = 125\text{-}165\text{Hz}$. Experimental parameters were optimized for long range $^nJ_{\text{CH}} = 8\text{Hz}$.

Solution conformation of compound **39**:

The solution conformation of **39** was determined from NMR spectra acquired in 9:1 DMSO- d_6 :H₂O and in 9:1 DMSO- d_6 :D₂O. All spectra were recorded on a Bruker AV-600 spectrometer equipped with an inverse triple resonance probe. Except for variable temperature experiments used for the determination of backbone NH temperature coefficients, all spectra were recorded at 283K. Water suppression was achieved with presaturation for COSY experiments, and with excitation sculpting for 1D- ^1H , TOCSY and NOESY experiments. Sequence specific ^1H assignments were determined by standard methods for unlabeled polypeptides employing TOCSY and NOESY data.⁷ Temperature dependence of backbone H^{N} chemical shifts was determined from 1D- ^1H experiments and confirmed by COSY experiments.

Distance restraints were obtained from a ^1H - ^1H NOESY experiment using a 150ms mixing time and 2s interscan delay. Data were calibrated to the fixed reference distance Trp $\text{H}^{\epsilon 1}$ - $\text{H}^{\text{Z}2}$ (H18-H20, page 4) of 2.82Å.⁸ Volume integrals were grouped into bins, and classified as strong (<2.5Å), medium (<3.5 Å) or weak (<4.5 Å), based on the relationship of r^{-6} assuming linear buildup and the isolated spin pair approximation. Backbone phi angle restraints were derived from $^3J_{\text{HNHa}}$ coupling constants measured from 1D- ^1H and DQF-COSY experiments conducted in 9:1 DMSO- d_6 :H₂O, and were restrained to $\pm 40^\circ$ of the

⁶ Palmer, A.G. III; Cavanagh, J.; Wright, P.E.; Rance, M., *J. Magn. Reson.*, **1991**, 93, 151-170. b) Kay, L.E.; Keifer, P.; Saarinen, T., *J. Am. Chem. Soc.*, **1992**, 114, 10663-10665. c) Schleucher, J.; Schwendinger, M.; Sattler, M.; Schmidt, P.; Schedletsky, O.; Glaser, S.J.; Sorensen, O.W.; Griesinger, C., *J. Biomol. NMR* **4**, **1994**, 301-306.

⁷ Cavanagh, J.; Fairbrother, W.J.; Palmer, A.G. III; Rance, M.; Skelton, N.J., *Protein NMR Spectroscopy, 2nd Edition: Principles and Practice*. Elsevier Academic Press: San Diego, 2007; chapter 10.

⁸ Bye, E.; Mostad, A.; Romming, C., *Acta. Chem. Scand.*, **1973**, 27, 471-484.

predicted angle(s) derived the Karplus equation.⁹ Side chain chi-1 torsion restraints were derived from analysis of $^3J_{\text{HaHb}}$ coupling constants measured from 1D- ^1H and E.COSY experiments conducted in 9:1 DMSO- d_6 :D $_2$ O. Stereospecific assignment of β -methylenes was made by analysis of H^{N} - H^{b} NOEs, where possible, and chi-1 angles were restrained to $\pm 60^\circ$ of the predicted angle(s).

Structure calculations were carried out using Macromodel v9.8 (Schrödinger, Inc., San Diego, CA) using the OPLS-2005 force field with implicit GB/SA aqueous solvation and a constant dielectric ($\epsilon = 1.0$). Distance and dihedral restraints were introduced as pseudoenergy terms comprising a flat bottomed harmonic potential of $100\text{kJ}/\text{\AA}^2$, and 1000kJ/mol , respectively. An initial model was generated by a 10,000 step mixed Monte-Carlo long range, low-mode conformational search. Ambiguous NOEs were manually refined based on this initial model. The final structure calculation was carried out in the same manner. Redundant conformers were filtered within a heavy atom RMSD cutoff of $1.0\text{\AA}$, and the top 10 structures selected for the ensemble.

Tabulated NOEs and coupling constants for macrocycle 39 in DMSO- d_6 :H $_2$ O (9:1):

<i>Residue</i>	$^3J_{\text{H}^{\text{N}}\text{H}^{\text{a}}}$ (Hz)	$^3J_{\text{H}^{\text{a}}\text{H}^{\text{b}_1}}$ (Hz)	$^3J_{\text{H}^{\text{a}}\text{H}^{\text{b}}}$ (Hz)
Trp ¹	7.5	5.7 (<i>pro-S</i>)	8.3 (<i>pro-R</i>)
Leu ²	7.0	nd	nd
Gln ³	7.3	5.8 (<i>pro-S</i>)	8.9 (<i>pro-R</i>)
Met ⁴	7.9	4.6 (<i>pro-R</i>)	7.9 (<i>pro-S</i>)
Thr ⁵	7.4	3.8	-
Gly ⁶	na	-	-
Phe ⁷	7.7	4.4 (<i>pro-R</i>)	9.5 (<i>pro-S</i>)
Tyr ⁸	9.1	4.0 (<i>pro-S</i>)	9.6 (<i>pro-R</i>)

⁹ Wang, A.C.; Bax, A., *J. Am. Chem. Soc.*, **1996**, 118(10), 2483–2494.

Tabulated NOEs for macrocycle 39

atom A	atom B	volume integral	bin	calc'd structure
18	20	1.00	Ref (2.82Å)	3.0
13	26	1.43	m	4.0
13	23	0.34	m	3.7
13	9	0.22	w	3.4
13	7	0.09	w	4.6
13	15	1.19	m	2.9
13	15'	2.07	m	3.5
13	11	4.69	s	2.3
13	29	0.25	w	3.9
23	14	0.69	m	4.0
23	15'	0.60	m	3.9
23	15	0.66	m	2.4
17	14	0.63	m	3.6
17	15'	0.70	m	2.6
17	15	0.74	m	3.7
17	26	0.20	w	3.8
23	26	0.20	w	3.3
14	26	3.32	s	2.2
15'	26	0.58	m	3.7
15	26	0.69	m	3.7
26	33	1.21	m	4.0
26	30	0.26	w	4.9
26	31	0.35	w	4.5
27	33	3.58	s	2.1
27	30	0.66	w	4.8
27	31	1.92	m	2.3
28	33	1.64	m	2.5
28	40	0.45	m	3.8
28	55	0.27	w	4.0
31	33	0.33	w	3.8
30	33	0.31	w	4.9
33	35	1.87	m	2.5
33	35'	1.40	m	2.9
33	36	1.18	m	4.4
34	40	3.43	s	2.1
34	36	1.75	m	3.2
35	38	0.23	w	2.0
35'	38	0.21	w	3.5
36	38	1.73	m	3.3
36	71	0.63	m	3.5
42	46	0.69	m	3.9
42'	46	0.78	m	3.5
40	46	0.93	m	3.0
40	43	0.66	m	3.7
40	36	0.50	m	3.9
40	42	2.18	m	2.0
40	42'	1.77	m	3.1
41	46	4.56	s	2.9
41	43	0.63	m	2.5
46	52	1.75	m	2.3
46	50	1.15	m	2.6
46	49	1.43	m	2.7
46	43	0.24	w	4.8
47	49	2.14	m	2.6
49	52	0.66	w	4.4
49	55	0.19	w	4.9
50	52	0.53	m	2.6
50	55	0.23	w	2.5
52	55	0.79	m	1.9
52	48	0.87	m	3.7
53'	55	1.74	m	3.3
55	57'	2.02	m	2.5
55	57	2.68	s	2.4
57'	59	1.13	m	3.0
57	59	1.65	m	3.3
56	59	1.03	m	2.3
63	65'	0.99	m	3.7
63	65	2.22	m	2.5
71	63	0.68	m	2.3
64	71	2.52	s	3.2
64	67	2.55	m	3.1
71	65'	0.59	m	4.0
65'	67	2.80	s	2.4
65	67	2.62	s	2.5
63	55	3.13	s	2.6
3	5	1.37	m	3.2
3	9	2.52	s	3.0
2	5	1.19	m	3.7
2	9	2.47	s	2.9

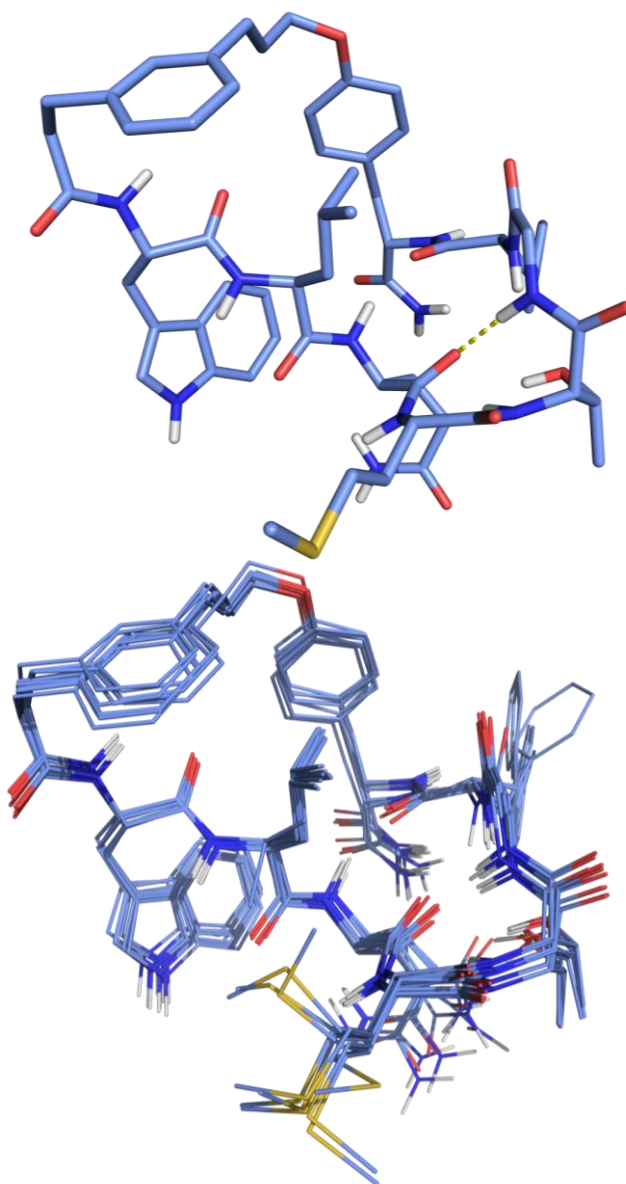
1	5	0.22	w	5.0
1	9	0.29	w	4.1

Total NOE restraints

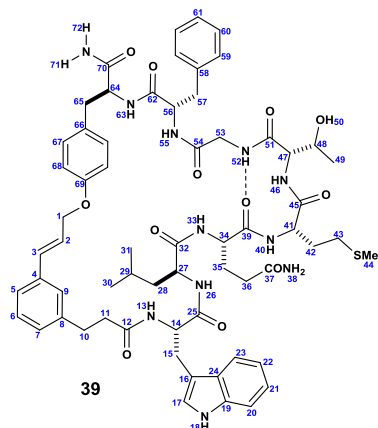
all (80)
intraresidue (42)
sequential ($|i - j| = 1$) (31)
non-sequential, long-range ($|i - j| > 1$) (7)

RMSD (Å) pairwise averaged over ensemble
Heavy atoms 0.76
Core macrocycle 0.36
All atoms 0.95

Constraint violations
No. of NOEs. $> 0.5\text{Å}$ 4
Sum of violations $> 0.5\text{Å}$ (Å) 2.22
Max. NOE violation (Å) 0.66



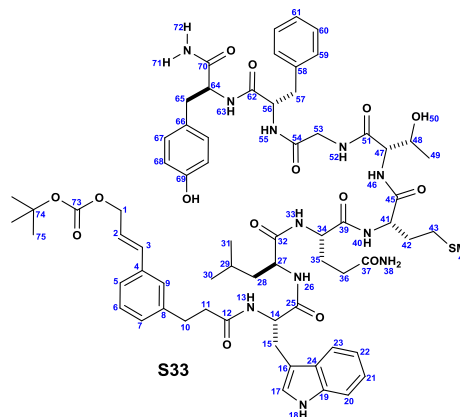
Resonance assignment for WLQMTGFY



reson	¹³ C	¹ H
1	67.94	4.61
2	124.76	6.40
3	132.25	6.64
4	136.28	-
5	123.67	7.24
6	128.30	7.22
7	127.90	7.03
8	141.64	-
9	126.36	7.22
10	33.42	2.71
11	39.02	2.39
12	172.47	-
13	-	8.11
14	56.70	4.43
15	27.06	2.91, 3.10
16	110.05	-
17	122.96	7.07
18	-	10.74
19	135.91	-
20	111.18	7.31
21	121.03	7.03
22	118.40	6.96
23	118.25	7.53
24	127.29	-
25	172.51	-
26	-	7.83
27	51.52	4.15
28	40.25	1.42
29	21.47	1.42
30	21.47	0.75
31	22.96	0.78
32	172.16	-
33	-	8.01
34	52.62	4.14
35	27.11	1.78,1.91
36	31.27	1.94,2.09
37	174.45	-
38	-	6.74,7.27
39	171.86	-
40	-	7.95
41	51.99	4.39
42	31.20	1.80,1.93
43	29.45	2.35,2.41

reson	¹³ C	¹ H
44	14.57	1.90
45	171.65	-
46	-	7.70
47	58.59	4.14
48	66.56	3.98
49	19.69	1.01
50	-	5.07
51	171.61	-
52	-	8.01
53	41.93	3.58,3.67
54	170.93	-
55	-	8.08
56	53.98	4.47
57	37.33	2.69,2.98
58	137.75	-
59	129.31	7.17
60	128.56	7.22
61	128.72	7.19
62	168.83	-
63	-	8.00
64	54.35	4.33
65	36.55	2.74,2.94
66	129.95	-
67	129.92	7.14
68	114.38	6.85
69	157.07	-
70	171.24	-
71	-	7.07
72	-	7.25

9:1 DMSO-*d*₆:H₂O (600 MHz)

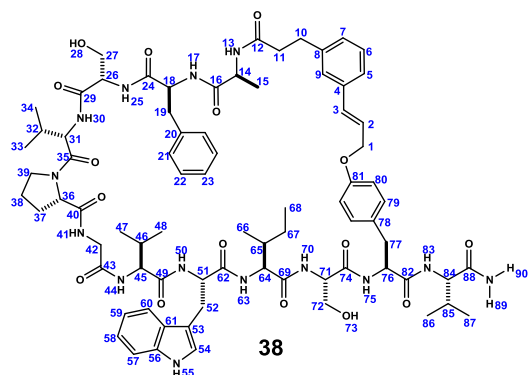


reson.	¹³ C	¹ H
1	-	4.63
2	-	6.28
3	-	6.57
4	-	-
5	-	7.23
6	-	7.23
7	-	6.99
8	-	-
9	-	7.18
10	-	2.65
11	-	2.34
12	-	-
13	-	8.03
14	53.70	4.51
15	-	2.88, 3.09
16	-	-
17	-	7.06
18	-	10.71
19	-	-
20	-	7.31
21	-	7.06
22	-	6.96
23	-	7.56
24	-	-
25	-	-
26	-	8.02
27	51.41	4.25
28	-	1.43
29	-	1.52
30	-	0.79
31	-	0.83
32	-	-
33	-	8.07
34	52.40	4.21
35	-	1.71
36	-	2.12
37	-	-
38	-	6.78, 7.30
39	-	-
40	-	8.10
41	52.15	4.40
42	-	1.81, 1.94
43	-	2.38, 2.44

reson	¹³ C	¹ H
44	-	1.96
45	-	-
46	-	7.70
47	58.62	4.15
48	-	3.97
49	-	1.01
50	-	n/o
51	-	-
52	-	8.05
53	42.17	3.63, 3.68
54	-	-
55	-	8.00
56	54.45	4.41
57	-	2.68, 2.91
58	-	-
59	-	7.13
60	-	7.20
61	-	7.15
62	-	-
63	-	7.97
64	54.60	4.29
65	-	2.70, 2.88
66	-	-
67	-	7.01
68	-	6.63
69	-	-
70	-	-
71	-	7.01
72	-	7.20
73	-	-
74	-	-
75	-	1.40

9:1 DMSO-*d*₆:H₂O (600 MHz)

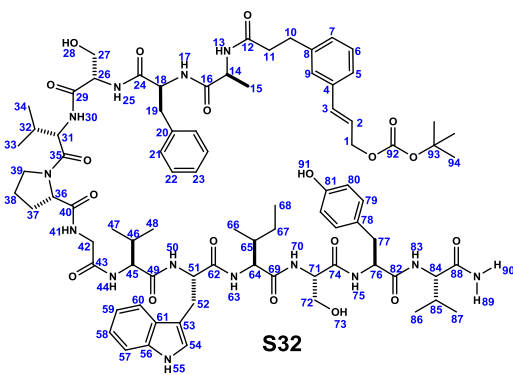
Resonance assignment for AFSVPGVWISYV



reso n.	¹³ C	¹ H
1		4.59
2		6.40
3		6.65
4		-
5		7.23
6		7.24
7		7.08
8		-
9		7.24
10		2.40
11		2.76
12		-
13		8.10
14	49.17	4.05
15		1.02
16		-
17		7.79
18	54.07	4.46
19		2.80, 3.09
20		-
21		7.15
22		7.18
23		7.17
24		-
25		8.00
26	55.23	4.31
27		3.58
28	n/o	-
29		-
30		7.73
31	55.61	4.33
32		1.96
33		0.81
34		0.86
35		-
36	60.15	4.23
37		1.77, 2.03
38		1.77, 1.90
39		3.53, 3.66
40		-
41		8.29
42	42.30	3.54, 3.77
43		-
44		7.41
45	57.89	4.08
46		1.92
47		0.71
48		0.73

9:1 DMSO-*d*₆:H₂O (600 MHz)

reson.	¹³ C	¹ H
49		-
50		8.10
51	53.78	4.52
52		2.91, 3.07
53		-
54		7.08
55		10.64
56		-
57		7.29
58		7.02
59		6.93
60		7.51
61		-
62		-
63		7.74
64	57.19	4.11
65		1.60
66		0.70
67		0.97, 1.31
68		0.65
69		-
70		7.88
71	55.23	4.28
72		3.52
73		n/o
74		-
75		8.06
76	54.65	4.54
77		2.76, 3.00
78		-
79		7.13
80		6.79
81		-
82		-
83		7.67
84	57.97	4.06
85		1.95
86		0.81
87		0.83
88		-
89		7.08
90		7.33



reson.	¹³ C	¹ H
1		4.63
2		6.31
3		6.60
4		-
5		7.25
6		7.22
7		7.08
8		-
9		7.26
10		2.37
11		2.74
12		-
13		8.11
14	48.68	4.12
15		1.04
16		-
17		7.96
18	53.85	4.48
19		2.76, 3.03
20		-
21		7.18
22		7.20
23		7.15
24		-
25		8.09
26	55.72	4.32
27		3.55
28		n/o
29		-
30		7.92
31	55.32	4.32
32		1.96
33		0.81
34		0.86
35		-
36	59.92	4.24
37		1.78, 2.02
38		1.78, 1.89
39		3.46, 3.49
40		-
41		8.22
42	42.14	3.63, 3.70
43		-
44		7.61
45	57.74	4.12
46		1.90
47		0.71
48		0.74

9:1 DMSO-*d*₆:H₂O (600 MHz)

reson.	¹³ C	¹ H
49		-
50		8.26
51	53.53	4.53
52		2.91, 3.06
53		-
54		7.08
55		10.72
56		-
57		7.29
58		7.03
59		6.94
60		7.54
61		-
62		-
63		7.89
64	57.23	4.16
65		1.65
66		0.73
67		0.99, 1.33
68		0.73
69		-
70		8.02
71	55.22	4.28
72		3.48, 3.51
73		n/o
74		-
75		8.03
76	54.64	4.42
77		2.71, 2.92
78		-
79		6.98
80		6.58
81		-
82		-
83		7.77
84	57.98	4.03
85		1.92
86		0.79
87		0.81
88		-
89		7.14
90		7.36
91		n/o
92		-
93		-
94		1.39

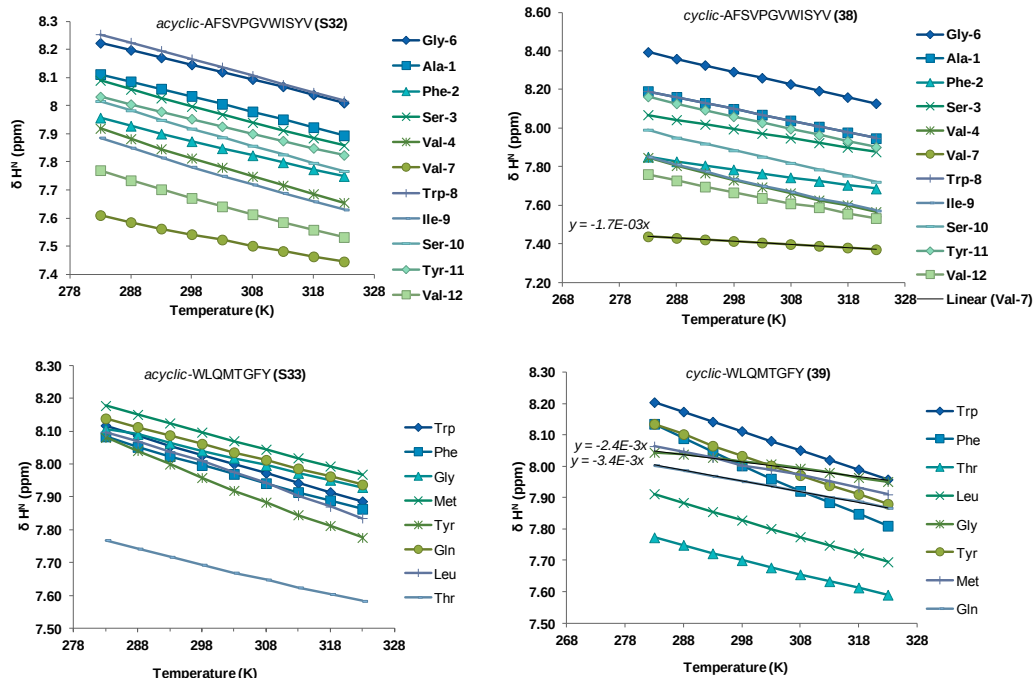
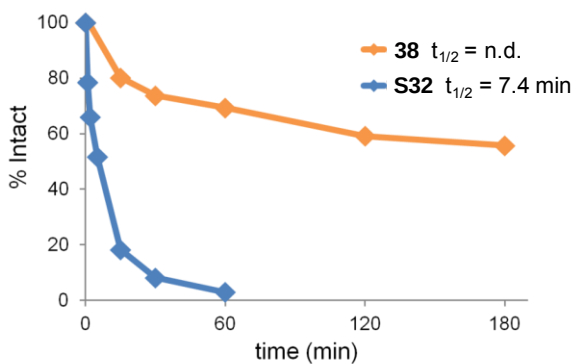


Figure S1. Temperature dependence of backbone $^1\text{H}^{\text{N}}$ chemical shifts for **S32**, **S33**, **38**, and **39**.

Proteolytic degradation assay:

Stock solutions of α -chymotrypsin (bovine type II, 61.75 U/mg) were freshly prepared in 1mM HCl, and diluted into assay buffer (56 mM Tris pH 7.8, 560 μ M CaCl_2 , 0.1%v Tween-80) just prior to addition of the substrate. Reactions were conducted in silanized glass vials. The reaction was initiated by addition of DMSO stock solution (50 μ M) of the macrocycle **39** or linear precursor **S33** to give a final substrate concentration of 5 μ M, 50 μ g/mL α -chymotrypsin, and 10%v DMSO. Control reactions contained BSA instead of α -chymotrypsin. Aliquots were removed in triplicate at 1, 2, 5, 10, 15 and 30min (acyclic) or 1, 15, 30, 60, 120, and 180 min (cyclic), and diluted 1:1 with *N,N*-DMF containing 1%v TFA, which resulted in a pH < 2. Time course data were obtained by HPLC-MS or HPLC-UV analysis and quantification against external calibration curves. Compound **38** was assayed in the same manner, except that Tween-80 was omitted from the reaction buffer and the initial substrate and enzyme concentrations were 50 μ M and 5 μ g/mL, respectively. No loss was observed in control reactions. Kinetic constants were determined by least squares fitting to the first order rate law $[S] = c + A(1 - e^{-kt})$ using the Solver tool in Microsoft Excel. Half lives were calculated as $0.693/k$. α -Chymotrypsin cleavage sites were determined by purification of products from short reaction times, and analysis by HPLC-MS (Agilent 6130) for linear precursors **S32** and **S33** and by infusion ESI-MS/MS (Bruker Solarix) for macrocycles **38** and **39**.



Analytical HPLC conditions for 38:

Column: Agilent Eclipse XBD C18, 4.6x150mm, 5µm

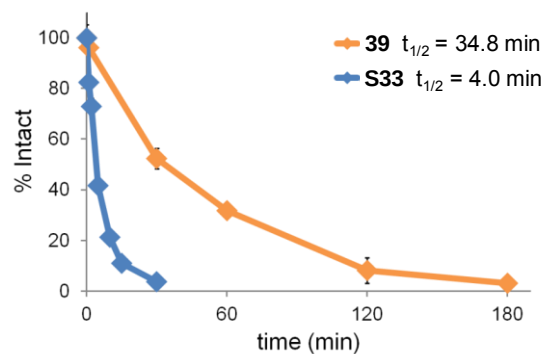
Solvent A: H₂O + 0.1%v TFA

Solvent B: ACN + 0.1%v TFA

Injection Vol.: 40µL

Flow rate: 1.00 ml/min

Time (min)	%B
0.0	30
1.0	30
11.0	100
12.0	30
17.0	30



Analytical HPLC Conditions for 39:

Column: Agilent SB-Aq, 4.6x50mm, 1.8µm

Solvent A: H₂O + 0.1%v TFA

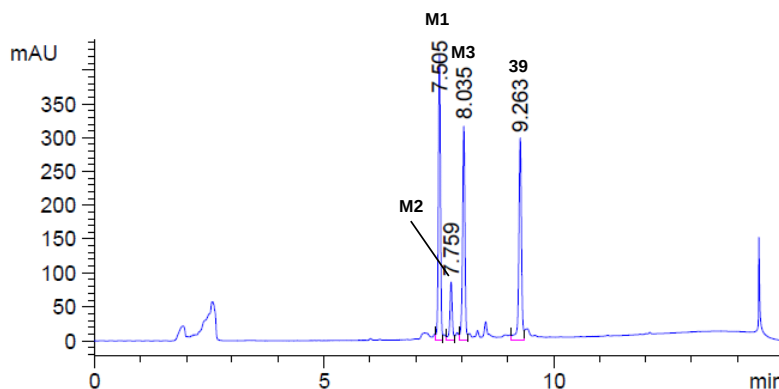
Solvent B: ACN + 0.1%v TFA

Injection Vol.: 40µL

Flow rate: 1.00 ml/min

Time (min)	%B
0.0	30
0.5	30
4.5	100
4.6	30
7.0	30

ESI-MS/MS data for proteolysis of 39



Preparative HPLC Conditions for 39:

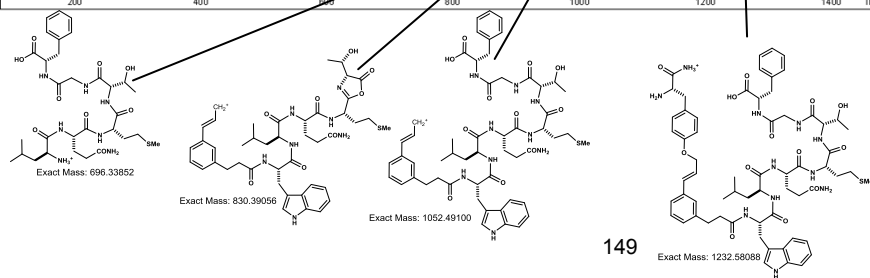
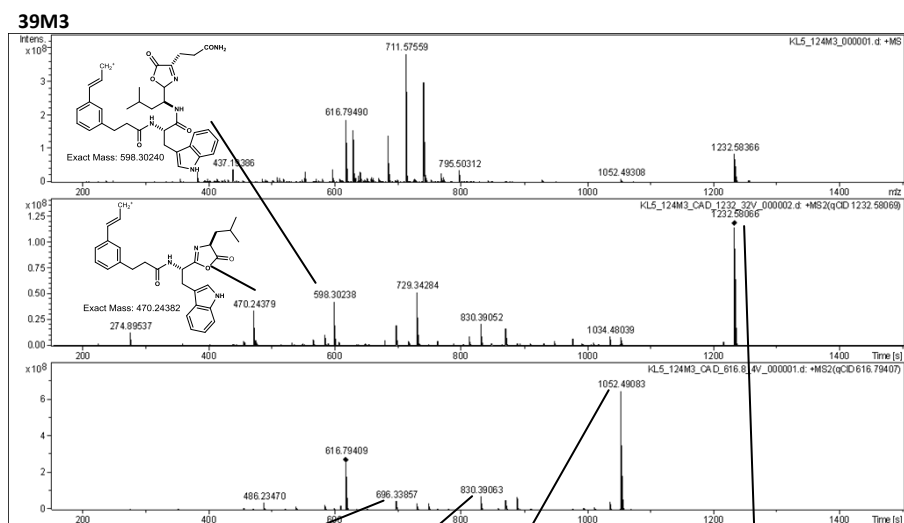
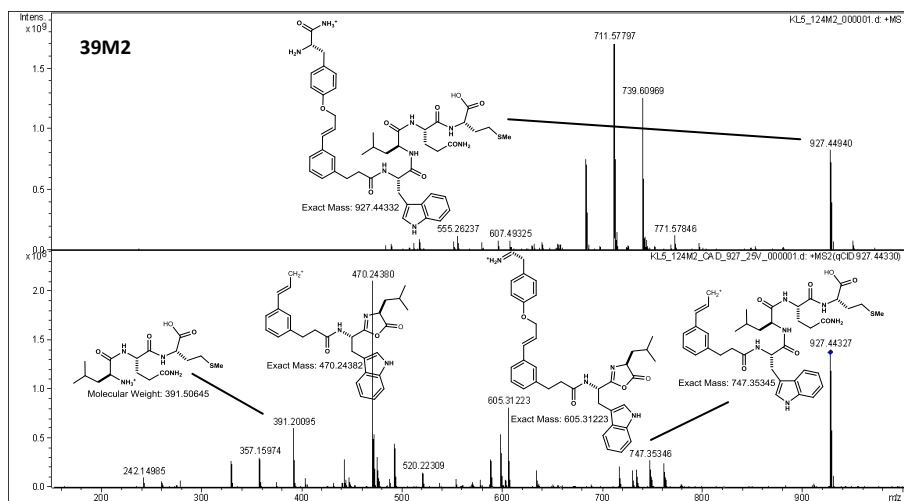
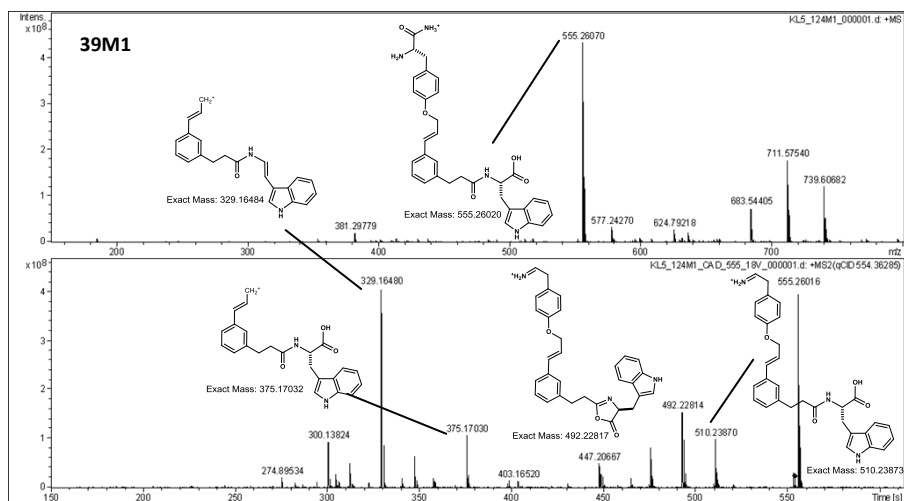
Column: Waters Sunfire, 10x250mm, 5µm

Solvent A: H₂O + 0.1%v TFA

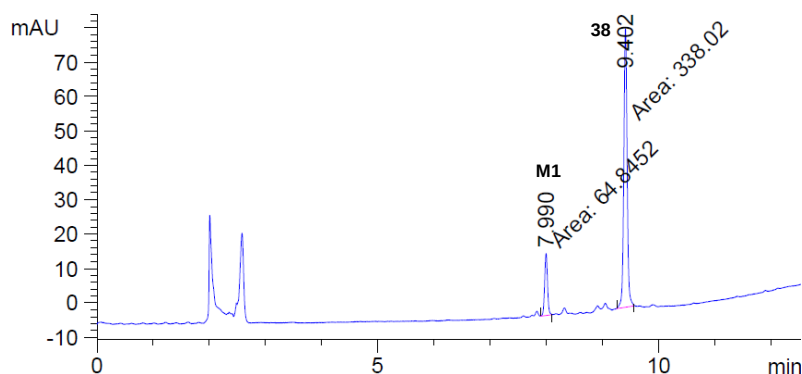
Solvent B: ACN + 0.1%v TFA

Flow rate: 7.0 ml/min

Time (min)	%B
0.0	20
2.0	20
12.0	100
13.0	20
15.0	20



ESI-MS/MS data for proteolysis of 38



Preparative HPLC Conditions for 38:

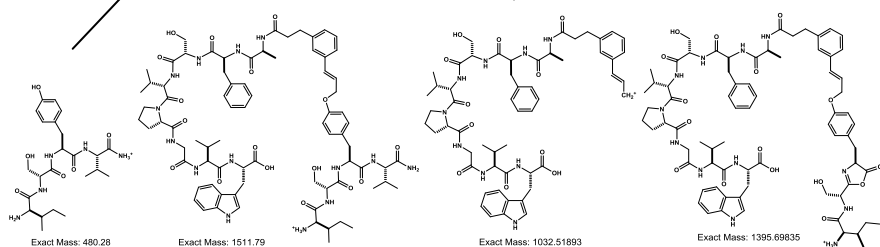
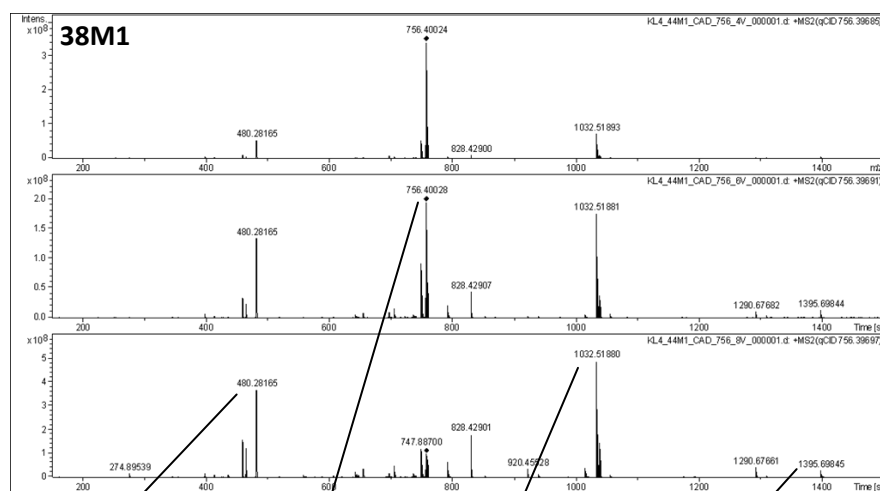
Column: Waters Sunfire, 10x250mm, 5µm

Solvent A: H₂O + 0.1%v TFA

Solvent B: ACN + 0.1%v TFA

Flow rate: 7.0 ml/min

Time (min)	%B
0.0	20
2.0	20
12.0	100
13.0	20
15.0	20



Peptide Synthesis:

C-terminal carboxamide peptides were synthesized manually using standard Fmoc solid phase synthesis protocols on Rink Amide MBHA resin (200-400 mesh, 0.70 mmol/g, 1% DVB) on 0.25-0.50 mmol scale using a fritted glass reaction vessel. Fmoc-deprotection was achieved with 20% piperidine in DMF (2 x 30 min). The reaction vessel was washed with DMF (3x) and CH₂Cl₂ (2x). The vessel was then charged with the appropriate Fmoc-amino acid (4 equiv) and TBTU (4 equiv) followed by DMF (10-20 ml) and iPr₂NEt (10 eq). The resin was agitated for 2 hours, drained, and washed with DMF (3X). After all coupling were completed the resin was cleaved with TFA/thioanisole/water/TIPS (90:2.5:5:2.5) for 2 hours. The cleaved resin was removed by filtration and the filtrate was concentrated under vacuum. The peptide was precipitated with ether and isolated by centrifugation. The peptide pellet was repeated washed with Et₂O to ensure complete removal of cleavage reagents. Fmoc-4-(Boc-amino)-L-phenylalanine was used to prepare 4-aminophenylalanine containing peptides.

C-terminal carboxylate peptides were prepared on Wang Resin (0.84 mmol/g). The first amino acid (2.5 equiv) was pre-activated with DIC (2.5 equiv) in DMF (5-10 ml) and then added the pre-swelled resin (1 equiv) and DMAP (0.1 equiv) in DMF (5-10 ml). The resin suspension was agitated for 3 hours. The subsequent Fmoc deprotections, couplings, and resin cleavage were performed as described above.

H-Gly-Trp-Thi-5-Hydroxytryptamine was prepared by attachment of Fmoc-5-hydroxytryptamine to 2-Chlorotritylchloride resin (100-200 mesh, 0.84 mmol/g) via the phenolic oxygen as follows: A solution of Fmoc-5-hydroxytryptamine (398 mg, 1.00 mmol) in dichloromethane (10 ml) was added to a flask containing 2-Chlorotritylchloride resin (840 mg, 1.00 mmol) followed by iPr₂NEt (174 μ l, 1.00 mmol). The mixture was agitated for 10 minutes then an addition aliquot of iPr₂NEt (261 μ l, 1.50 mmol) was added and the mixture was agitated for an addition 2 hours. Methanol (500 μ L) was added and the resin was mixed for an addition 15 minutes, then filtered through a sintered glass funnel. The resin was washed with CH₂Cl₂ (3x), DMF (3x), CH₃OH (3x), and dried under high vacuum. The substitution was estimated by mass. Chain elongation was performed as described above. Cleavage from the resin was achieved with 1:1:8 AcOH:TFE:CH₂Cl₂ for 2 hours.

Synthesis of 1:

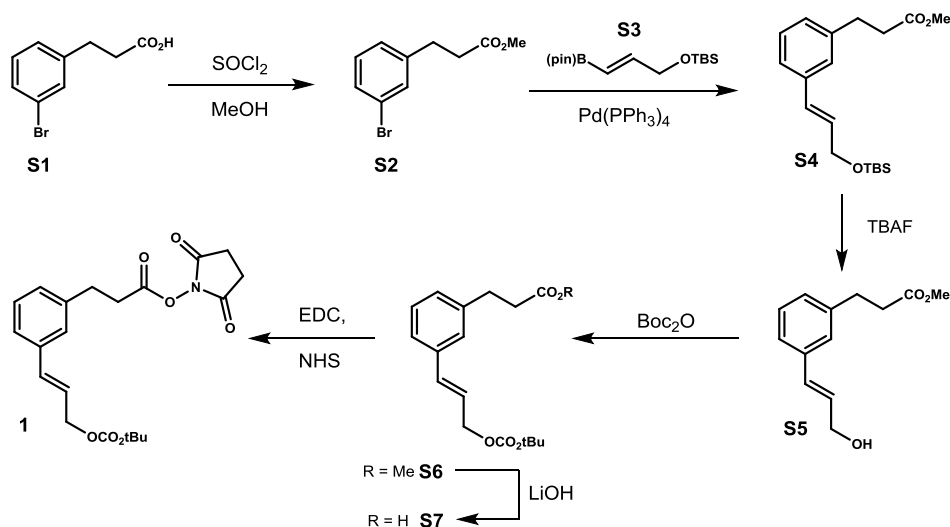


Figure S2. Synthetic route to 1.

methyl 3-(3-bromophenyl)propanoate (S2). To a solution of 3-bromophenylpropanoic acid **S1** (11.52 g, 50.29 mmol) in anhydrous methanol (200 ml) was added dropwise thionyl chloride (7.18 g, 60.35 mmol) over 30 minutes and allowed to stir for 18h at room temperature. Rotary evaporation gave crude ester **S2** as a colorless oil. Purification by column chromatography (SiO₂, 15% EtOAc/hexanes) afforded **S2** (11.80 g, 97%). ¹H NMR (CDCl₃, 500 MHz): δ 7.29-7.35 (m, 2H), 7.08-7.15 (m, 2H), 3.67 (s, 3H), 2.90 (t, *J* = 7.7 Hz, 2H), 2.62 (t, *J* = 7.7 Hz, 2H). ¹³C NMR (CDCl₃, 125 MHz): δ 172.9, 142.9, 131.4, 130.1, 129.4, 127.0, 122.5, 51.7, 35.3, 30.5. MS (ESI) Calculated for C₁₁H₁₁BrO₂ [M+H]⁺: 243.0, found 242.6.

(E)-methyl 3-(3-(3-((tert-butyldimethylsilyloxy)prop-1-en-1-yl)phenyl)propanoate (S4). To a solution of **S2** (11.80 g, 48.54 mmol) in 4:1 THF/H₂O (160 ml) was added boronic ester **S3** (17.38g, 58.25 mmol) followed by K₂CO₃ (20.13 g, 145.62 mmol). The resulting suspension was degassed by bubbling Argon through the stirred suspension with a needle for 30 minutes. Following addition of Pd(PPh₃)₄ (1.68 g, 1.45 mmol) the reaction was heated to 75 °C in an oil bath for 48h or until complete consumption of **S4** determined by HPLC/UV at 220 nm. The reaction was cooled, diluted with EtOAc (250 ml) and washed sequentially water, and brine. The organic layer was dried over Na₂SO₄, filtered and evaporated to give crude **S3** as an amber viscous oil which was used without further purification. ¹H NMR (CDCl₃, 500 MHz): δ 7.19-7.25 (m, 3H), 7.04-7.08 (m, 1H), 6.56 (dt, *J* = 15.9, 1.7 Hz, 1H), 6.27 (dt, *J* = 15.9, 5.0 Hz, 1H), 4.34 (dd, *J* = 5.0, 1.7 Hz, 2H), 3.67 (s, 3H), 2.94 (t, *J* = 7.9 Hz, 2H), 2.63 (t, *J* = 7.9 Hz, 2H), 0.94 (s, 9H), 0.11 (s, 6H). ¹³C NMR (CDCl₃, 125 MHz): δ 173.4, 140.7, 137.3, 129.32, 129.27, 128.7, 127.3, 126.4, 124.4, 63.9, 51.7, 35.7, 30.9, 26.0, 18.5, -5.1. MS (ESI) Calculated for C₁₉H₃₀O₃Si [M+Na]⁺: 357.2, found 357.4.

(E)-methyl 3-(3-(3-hydroxyprop-1-en-1-yl)phenyl)propanoate (S5). To a solution of **S4** (16.06 g, 48.0 mmol) in THF (160 ml) at room temperature was added TBAF (1.0M/THF, 64.9 ml, 64.9 mmol). The

resulting orange solution was allowed to stir for 2 hours. The reaction mixture was transferred to a separatory funnel, diluted with EtOAc (250 ml) and washed sequentially with sat. NH_4Cl and brine. The organic layer was dried over Na_2SO_4 , filtered, and evaporated in vacuo to give crude **S5** as a viscous amber oil. Purification by column chromatography (SiO_2 , gradient 30-65% EtOAc/hexanes) provides pure cinnamyl alcohol **S5** as a colorless oil (8.95 g, 85%). ^1H NMR (CDCl_3 , 400 MHz): δ 7.16-7.25 (m, 3H), 7.02-7.1 (m, 1H), 6.57 (dt, J = 16.0, 1.3 Hz, 1H), 6.33 (dt, 16.0, 5.7 Hz, 1H), 4.29 (dd, J = 3.7, 3.7 Hz, 2H), 3.65 (s, 3H), 2.92 (t, J = 7.9 Hz, 2H), 2.61 (t, J = 7.9 Hz, 2H), 2.29 (br. s, 1H). ^{13}C NMR (CDCl_3 , 100 MHz): δ 173.4, 140.8, 137.0, 130.8, 128.8, 127.6, 126.5, 124.4, 63.5, 51.7, 35.6, 30.8. MS (ESI) Calculated for $\text{C}_{13}\text{H}_{16}\text{O}_3$ $[\text{M}+\text{Na}]^+$: 243.1, found 243.0.

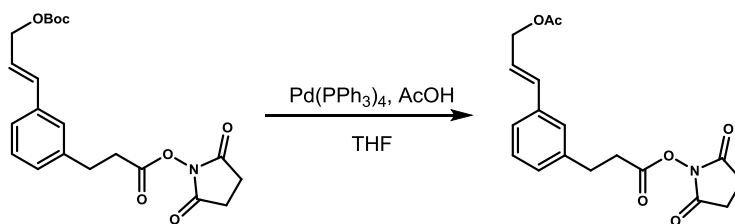
(E)-methyl 3-(3-(3-((tert-butoxycarbonyl)oxy)prop-1-en-1-yl)phenyl)propanoate (S6). To a solution of **S5** (7.5 g, 34.1 mmol) in CH_2Cl_2 (175 ml) at room temperature was added NaOH (15 wt% aqueous, 35 ml) followed by tetrabutylammonium bisulfate (347 mg, 1.02 mmol). Diterbutyldicarbonate (11.15 g, 51.1 mmol) was subsequently added in one portion and the mixture was allowed to stir overnight at room temperature. The reaction mixture was diluted with CH_2Cl_2 (200 ml) and washed with water and brine. The colorless crude oil obtained (**S6**) was used without further purification. ^1H NMR (CDCl_3 , 500 MHz): δ 7.20-7.25 (m, 3H), 7.06-7.12 (m, 1H), 6.63 (br. d, J = 15.9 Hz, 1H), 6.27 (dt, J = 15.9, 6.4 Hz, 1H), 4.70 (dd, J = 6.4, 1.2 Hz, 2H), 3.66 (s, 3H), 2.93 (t, J = 7.9 Hz, 2H), 2.62 (t, J = 7.9 Hz, 2H), 1.49 (s, 9H). ^{13}C NMR (CDCl_3 , 125 MHz): δ 173.3, 153.4, 140.9, 136.4, 134.3, 128.8, 128.1, 126.7, 124.7, 123.0, 82.2, 67.5, 51.7, 35.6, 30.8, 27.8. MS (ESI) Calculated for $\text{C}_{18}\text{H}_{24}\text{O}_5$ $[\text{M}+\text{Na}]^+$: 343.2, found 343.2.

(E)-3-(3-(3-((tert-butoxycarbonyl)oxy)prop-1-en-1-yl)phenyl)propanoic acid (S7). Crude methyl ester **S6** (10.92 g, 34.1 mmol) was dissolved in THF (170 ml) and aqueous LiOH (1.0 M, 52.0 ml) was added. The reaction was stirred for 4 hours at room temperature. The reaction was then diluted with EtOAc (300 ml) and 1.0 M HCl was added until the aqueous layer has a pH < 2. The organic layer was separated and washed with water and brine, dried over Na_2SO_4 , filtered and the solvent was removed by rotary evaporation to give **S7** (8.4 g, 80% over 2 steps) as an oil which was >95% pure by HPLC/UV. ^1H NMR (CDCl_3 , 500 MHz): δ 7.21-7.27 (m, 3H), 7.08-7.13 (m, 1H), 6.64 (d, J = 15.9 Hz, 1H), 6.29 (dt, J = 15.8, 6.4 Hz, 1H), 4.71 (br. d, J = 6.3 Hz, 2H), 2.95 (t, J = 7.9 Hz, 2H), 2.7 (t, J = 7.8 Hz, 1H), 1.5 (s, 9H). ^{13}C NMR (CDCl_3 , 125 MHz): δ 178.0, 153.4, 140.5, 136.5, 134.3, 128.9, 128.1, 126.7, 124.8, 123.1, 82.3, 67.4, 35.3, 30.5, 27.8. MS (ESI-Neg) Calculated for $\text{C}_{17}\text{H}_{22}\text{O}_5$ $[\text{M}-\text{H}]^-$: 305.1, found 305.2.

(E)-2,5-dioxopyrrolidin-1-yl 3-(3-(3-((tert-butoxycarbonyl)oxy)prop-1-en-1-yl)phenyl)propanoate (1).

To a solution of **S7** (5.9 g, 19.3 mmol) in CH_2Cl_2 (60 ml, 0.35 M) at room temperature was added N-hydroxysuccinimide (2.66g, 23.11 mmol) followed by EDC-HCl (4.06 g, 21.18 mmol). The reaction was stirred for 3 hours then transferred to a separatory funnel and washed sequentially with 1N HCl, H_2O and brine. The organic layer was dried over Na_2SO_4 , filtered and concentrated to give an amber oil. Purification by column chromatography (SiO_2 , 35% EtOAc/hexane) afforded succinimidyl ester **1** as a

white solid (6.09 g, 15.1 mmol, 78 %). Analytically pure crystals may be obtained by slow evaporation from THF/hexanes (2:1). ^1H NMR (CDCl_3 , 500 MHz): δ 7.24-7.28 (m, 3H), 7.11-7.15 (m, 1H), 6.65 (br. d, J = 15.9 Hz, 1H), 6.3 (dt, J = 15.9, 6.4 Hz, 1H), 4.72 (dd, J = 6.4, 1.3 Hz, 2H), 3.05 (t, J = 7.8 Hz, 2H), 2.92 (t, J = 7.8 Hz, 2H), 2.84 (br. s, 4H), 1.5 (s, 9H). ^{13}C NMR (CDCl_3 , 125 MHz): δ 169.0, 167.8, 153.4, 139.4, 136.7, 134.1, 129.0, 128.0, 126.7, 125.1, 123.3, 82.2, 67.4, 32.6, 30.4, 27.8, 25.6. IR (neat) ν = 2947, 1820, 1781, 1732, 1370, 1269, 1252, 1211, 1160, 1068, 972, 930, 793 cm^{-1} . MS (ESI) Calculated for $\text{C}_{21}\text{H}_{25}\text{NO}_7$ $[\text{M}+\text{Na}]^+$: 426.2, found 426.2.



(E)-2,5-dioxopyrrolidin-1-yl 3-(3-(3-(3-acetoxyprop-1-en-1-yl)phenyl)propanoate (S8). A solution of **1** (558 mg, 1.38 mmol, 1 equiv.) and AcOH (1.97 mL, 34.5 mmol, 25 equiv.) in THF (20 mL) was sparged with argon for 15 minutes. The septa was removed briefly to allow the addition of $\text{Pd}(\text{PPh}_3)_4$ (40 mg, 0.035 mmol, 2.5 mol%). The reaction was stirred for 4 hours then diluted with EtOAc and transferred to a separatory funnel. The organic layer was washed with saturated aq. NaHCO_3 , H_2O , and brine, dried over Na_2SO_4 and evaporated to give a yellow solid. Purification by column chromatography (SiO_2 , gradient 20-60% EtOAc/Hexane) afforded the title compound (443 mg, 1.28 mmol, 93 %) as a off-white solid. NMR (CDCl_3 , 500 MHz): δ 7.22-7.25 (m, 3H), 7.08-7.12 (m, 1H), 6.61 (dt, J = 16.0, 1.1 Hz, 1H), 6.27 (dt, J = 16.0, 6.4 Hz, 1H), 4.7 (dd, J = 6.4, 1.3 Hz, 2H), 3.02 (t, J = 7.8 Hz, 2H), 2.89 (t, J = 7.7 Hz, 2H), 2.79 (br. s, 4H), 2.08 (s, 3H). ^{13}C NMR (CDCl_3 , 125 MHz): δ 170.8, 169.2, 167.9, 139.5, 136.6, 133.8, 129.0, 128.0, 126.6, 125.0, 123.6, 65.0, 32.5, 30.3, 25.6, 21.0. MS (ESI) Calculated for $\text{C}_{18}\text{H}_{19}\text{NO}_6$ $[\text{M}+\text{Na}]^+$: 368.1, found 368.1

Coupling of **1** to acyclic peptides:

General Procedure A. An oven-dried, screw-capped scintillation vial was charged with appropriate peptide (0.2 mmol) and N-hydroxysuccinimide ester **1** (0.20 mmol) followed by addition of anhydrous DMF (2 mL, 0.10 M) and $i\text{Pr}_2\text{NEt}$ (0.8 mmol, 4 equiv.). The reaction was allowed to stir at room temperature until complete conversion as monitored by LC/MS. The solvent is removed under reduced pressure and purified as described below. Compounds purified by preparative HPLC were treated with silica bound tetraalkylammonium carbonate (Si-CO_3 , Silicycle, 0.59 mmol/g, 2 equiv.) for 30 minutes in DMF, and re-concentrated to scavenge residual TFA prior to cyclization.

Palladium-catalyzed macrocyclization:

General Procedure B. An oven-dried vial was charged with acyclic peptide (0.05 mmol) and sealed with a septa. The vial was flushed with Argon followed by addition of argon-sparged anhydrous DMF (10 ml, 5 mM). After complete dissolution of the peptide, $\text{Pd}(\text{PPh}_3)_4$ (0.0025 mmol, 5 mol %) in 1:1 THF:DMF (0.5 ml) was added and the reaction was allowed to stir at room temperature for two hours or until complete conversion of starting material as monitored by LC/MS. The solvent is removed under reduced pressure. The resulting residue is reconstituted in DMSO and purified by preparative HPLC as indicated below.

General Procedure C. A solution of catalyst was prepared as follows: An oven-dried, serum-topped vial was placed in a glove bag and charged with $[\text{PdCl}(\text{C}_3\text{H}_5)]_2$ (14 mg, 0.038 mmol) and xantphos (55 mg, 0.095 mmol). The vial is sealed, removed from the glove bag, and degassed THF (7.0 ml) was added, followed by degassed DMF (7.0 ml). The resulting yellow solution was stirred under argon for 30 minutes.

To a solution of acyclic peptide (0.05 mmol) in degassed DMF (10 ml, 5 mM) was added catalyst solution (735 μL , 0.04 mol% $[\text{PdCl}(\text{C}_3\text{H}_5)]_2$, 0.10 mol% xantphos). The reaction was allowed to stir at room temperature for two hours or until complete conversion of starting material as monitored by LC/MS. The solvent is removed under reduced pressure. The resulting residue is reconstituted in DMSO and purified by preparative HPLC as indicated below.

General Procedure D. As described in general procedure B with the addition of Cs_2CO_3 . An oven-dried vial was charged with acyclic peptide (0.05 mmol) and Cs_2CO_3 (0.10 mmol, 2 equiv) and sealed with a septa. The vial was flushed with Argon followed by addition of argon-sparged anhydrous DMF or DMSO (10 ml, 5 mM). After complete dissolution of the peptide, $\text{Pd}(\text{PPh}_3)_4$ (0.0025 mmol, 5 mol %) in 1:1 THF:DMF (0.5 ml) was added and the reaction was allowed to stir at room temperature for two hours or until complete conversion of starting material as monitored by LC/MS. The solvent is removed under reduced pressure. The resulting residue is reconstituted in DMSO and purified by preparative HPLC as indicated below.

Solid-supported macrocyclizations. Peptide synthesis was performed as described above on Tentagel Rink amide resin (0.23 mmol/g) on 0.05 mmol scale. Prior to final Fmoc-deblocking the His(Mmt) side chain was removed by treatment with 1:1:8 AcOH:TFE: CH_2Cl_2 (8 mL). After two hours the vessel was drained and washed with CH_2Cl_2 (2x), DMF (2x), CH_2Cl_2 (2x). Following Fmoc- deprotection the N-terminus was acylation with **1** (3 equiv.) and iPr_2NEt (8 equiv.) The resin was washed, shrunk with methanol and dried under high vacuum.

The dried resin was transferred to a serum capped vial and sparged with argon. Degassed DMF (10 ml) was added and the resin allowed to swell for 10 minutes. $[\text{Pd}(\text{C}_3\text{H}_5)\text{Cl}]_2/\text{xantphos}$ (8 mol%/20 mol%) catalyst solution (see general procedure C) was added and the resin gently stirred for two hours. The resin was washed with DMF (2x), CH_2Cl_2 (2x), shrunk with methanol and dried under high vacuum. The

macrocycle was cleaved by treatment with TFA:TIS:H₂O (95:2.5:2.5) for 1 hour. Cleaved macrocycles were analyzed by HPLC-MS (C18, MeCN/H₂O, 0.1%TFA).

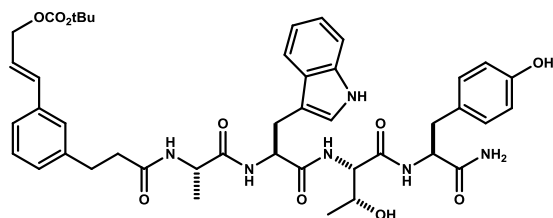
Summary of acylation of macrocyclization efficiency.

Peptide Sequence	Yield % (acylation)	Cyclization Procedure	Yield % (cyclization)	Peptide Sequence	Yield % (acylation)	Cyclization Procedure	Yield % (cyclization)
S M Y	71	B	80	A V P H	78	C	77
I W Y	65	B	72	G Thi W 5HT	57	B	75
A V Y	67	B	78	A F S V P G V W I S Y V	72	B	66
A W T Y	72	B	78	T A W I P Y H N V	64	C	69
V M F Y	59	B	73	W L Q M T G F Y	64	B	71
W I Q Y	70	B	81	B-Ala-P(4-Ar)- H	78	C	81
L A R Y	66	B	84	G T H Y	68	C	73
I M S Y W	77	B	73	A R H F	63	C	76
A F T I Y	67	B	85	A I H F	72	C	71
G S F N Y	80	B	74	V Q Y H	56	C	75
S F F(4-NH₂)	62	B	72	V Q Y H	-	C ^a	68
A L E Y	68	B	67	H-V O M Y	62	D ^a	64
A L E Y	-	D	76	H-V O M Y	-	B	77
FLHyp- OH	57	B	71	N W T F(4-NH₂)	61	B	77
GVW- OH	61	B	74	Orn T Y	97	D ^a	80
AVP H -OH	74	C	69				

^aDMSO Solvent.

Data for acyclic peptides:

Acyclic-Ala-Trp-Thr-Tyr (2):

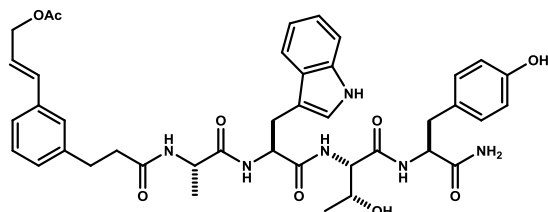


Following general procedure A, the corresponding compound was prepared from H-AWTY-NH₂ (•TFA, 163 mg, 0.250 mmol), diisopropylethylamine (174 μ L, 0.999 mmol) and reagent **1** (101 mg, 0.250 mmol). The product was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 40-100%

CH₃CN/H₂O with 0.1% TFA. The fractions collected were combined and lyophilized (149 mg, 0.180 mmol, 72%). ¹H NMR (DMSO-d₆, 600 MHz): δ 10.76 (s, 1H), 9.13 (br s, 1H), 8.05 (d, J = 7.9 Hz, 1H), 7.99 (d, J = 7.3 Hz, 1H), 7.75 (d, J = 8.1 Hz, 1H), 7.67 (d, J = 7.7 Hz, 1H), 7.52 (d, J = 7.9 Hz, 1H), 7.22-7.31 (m, 4H), 7.19 (dd, J = 7.6, 7.6 Hz, 1H), 7.10 (app s, 2H), 7.60 (d, J = 7.4 Hz, 1H), 6.96-7.02 (m, 3H), 6.89 (dd, 7.4, 7.4 Hz, 1H), 6.57-6.63 (m, 3H), 6.30 (dt, 15.9, 6.3 Hz, 1H), 4.63 (d, J = 5.8 Hz, 2H), 4.52 (ddd, J = 8.2, 8.2, 4.8 Hz, 1H), 4.33 (ddd, J = 8.2, 8.2, 5.2 Hz, 1H), 4.24 (dq, J = 7.1, 7.1 Hz, 1H), 4.16 (dd, J = 7.9, 4.1 Hz, 1H), 3.89-3.96 (m, 1H), 3.12 (dd, J = 15.0, 4.2 Hz, 1H), 2.95 (dd, J = 14.8, 9.0 Hz, 1H), 2.90 (dd, J = 14.0, 4.9 Hz, 1H), 2.65-2.78 (m, 3H), 2.28-2.41 (m, 2H), 1.39 (s, 9H), 1.08 (d, J = 6.8 Hz, 3H), 0.90 (d, J

= 6.4 Hz, 3H). ^{13}C NMR (DMSO- d_6 , 150 MHz): δ 173.2, 172.8, 171.7, 171.6, 169.6, 156.1, 153.1, 142.1, 136.3, 136.2, 133.8, 130.3, 128.9, 128.4, 128.1, 127.7, 126.7, 124.6, 123.9, 123.6, 121.1, 118.7, 118.5, 115.2, 111.5, 110.3, 81.8, 67.2, 66.9, 58.3, 54.6, 53.8, 48.4, 36.9, 36.9, 31.2, 27.7, 19.3, 18.4. MS (ESI) Calculated for $\text{C}_{44}\text{H}_{54}\text{N}_6\text{O}_{10}$ $[\text{M}-\text{OCO}_2\text{tBu}]^+$: 709.3, found 709.0.

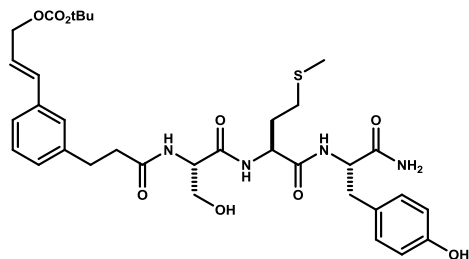
Acyclic-Ala-Trp-Thr-Tyr (3):



Following general procedure A, the corresponding compound was prepared from H-AWTY-NH₂ ($\bullet$ TFA, 195 mg, 0.299 mmol), diisopropylethylamine (208 μL , 1.19 mmol) and reagent **S8** (103 mg, 0.299 mmol). The product was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 40-100%

$\text{CH}_3\text{CN}/\text{H}_2\text{O}$ with 0.1% TFA. The fractions collected were combined and lyophilized (177 mg, 0.230 mmol, 77%). ^1H NMR (DMSO- d_6 , 500 MHz): δ 10.77 (d, J = 1.9 Hz, 1H), 9.13 (br. s, J = Hz, 1H), 8.05 (d, J = 7.5 Hz, 1H), 7.99 (d, J = 7.3 Hz, 1H), 7.75 (d, J = 8.1 Hz, 1H), 7.67 (d, J = 8.1 Hz, 1H), 7.54 (d, J = 7.9 Hz, 1H), 7.18-7.32 (m, 5H), 7.09-7.13 (m, 2H), 7.07 (br. d, J = 7.3 Hz, 1H), 6.98-7.04 (m, 3H), 6.9 (dd, J = 7.4 Hz, 1H), 6.58-6.64 (m, 3H), 6.31 (dy, J = 15.9, 6.1 Hz, 1H), 4.65 (br. d, J = 6.1 Hz, 2H), 4.53 (ddd, J = 8.3, 8.3, 4.6 Hz, 1H), 4.34 (ddd, J = 8.2, 8.2, 5.3 Hz, 1H), 4.25 (dq, J = 7.2, 7.2 Hz, 1H), 4.18 (dd, J = 8.2, 4.2 Hz, 1H), 3.90-3.97 (m, 1H), 3.13 (dd, J = 15.1, 4.4 Hz, 1H), 2.97 (dd, J = 15.2, 8.7 Hz, 1H), 2.91 (dd, J = 14.1, 5.1 Hz, 1H), 2.66-2.79 (m, 3H), 2.28-2.43 (m, 2H), 2.03 (s, 3H), 1.1 (d, J = 7.1 Hz, 3H), 0.92 (d, J = 6.6 Hz, 3H). ^{13}C NMR (DMSO- d_6 , 125 MHz): δ 173.4, 172.9, 171.9, 171.7, 170.6, 169.8, 156.2, 142.2, 136.5, 136.4, 133.6, 130.5, 129.1, 128.4, 128.3, 127.8, 126.8, 124.7, 124.1, 124.0, 121.3, 118.9, 118.7, 115.4, 111.7, 110.4, 67.0, 64.8, 58.4, 54.7, 53.9, 48.6, 37.1, 37.0, 31.4, 27.5, 21.2, 19.5, 18.6. MS (ESI) Calculated for $\text{C}_{41}\text{H}_{48}\text{N}_6\text{O}_9$ $[\text{M}+\text{H}]^+$: 769.3, found 769.2.

Acyclic-Ser-Met-Tyr (S9):

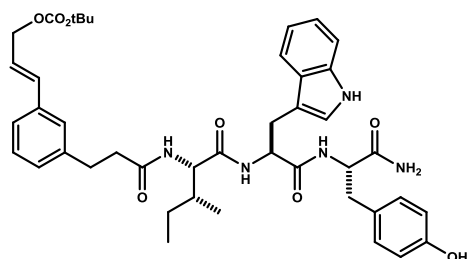


Following general procedure A, the corresponding compound was prepared from H-SMY-NH₂ ($\bullet$ TFA, 20 mg, 0.039 mmol), diisopropylethylamine (27 μL , 0.156 mmol) and reagent **1** (16 mg, 0.039 mmol). The product was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 40-

100% $\text{CH}_3\text{CN}/\text{H}_2\text{O}$ with 0.1% TFA. The fractions collected were combined and lyophilized (19 mg, 0.028 mmol, 71%). ^1H NMR (DMSO- d_6 , 400 MHz): δ 9.14 (br s, 1H), 8.28 (d, J = 6.8 Hz, 1H), 8.04 (d, J = 7.9 Hz, 1H), 7.77 (d, J = 8.4 Hz, 1H), 7.18-7.29 (m, 3H), 7.12 (br s, 1H), 7.08 (d, J = 7.08 Hz, 1H), 7.06 (br s, 1H), 6.95 (d, J = 8.4 Hz, 2H), 6.57-6.63 (m, 3H), 6.31 (dt, J = 16, 6.3 Hz, 1H), 4.64 (dd, 6.3, 1.0 Hz, 2H), 4.34 (ddd, J = 7.0, 7.0, 6.8 Hz, 1H), 4.23 (ddd, J = 9.8, 8.7, 4.6 Hz, 1H), 4.89 (ddd, J = 8.6, 7.1, 4.7 Hz, 1H), 3.57 (dd, J = 10.3, 6.1 Hz, 1H), 3.47 (dd, J = 10.3, 6.9

Hz, 1H), 2.91 (dd, $J = 14.0, 4.5$ Hz, 1H), 4.77 (t, $J = 8$ Hz, 2H), 2.54-5.62 (m, 1H), 2.41-2.48 (m, 4H), 2.30-2.37 (m, 1H), 2.23-2.29 (m, 1H), 1.95 (s, 3H), 1.39 (s, 9H). ^{13}C NMR (DMSO- d_6 , 150 MHz): δ 173.4, 172.0, 171.5, 170.9, 156.1, 153.1, 142.1, 136.2, 133.8, 130.2, 128.9, 128.4, 128.2, 126.7, 124.6, 123.6, 115.2, 81.8, 67.2, 62.1, 55.0, 54.6, 53.0, 40.8, 36.9, 36.8, 31.3, 31.2, 29.6, 27.7, 14.8. MS (ESI) Calculated for $\text{C}_{34}\text{H}_{46}\text{N}_4\text{O}_9\text{S}$ $[\text{M}-\text{OCO}_2\text{tBu}]^+$: 569.2, found 568.9.

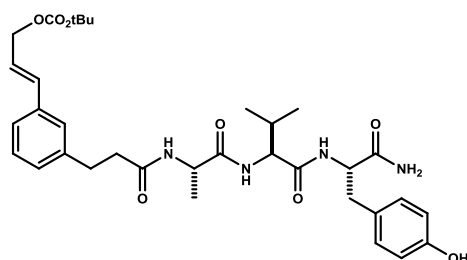
Acyclic-Ile-Trp-Tyr (S10):



Following general procedure A, the corresponding compound was prepared from H-IWY-NH₂ ($\bullet$ TFA, 203 mg, 0.342 mmol), diisopropylethylamine (238 μL , 1.37 mmol) and reagent **1** (138 mg, 0.342 mmol). The product was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 40-

100% $\text{CH}_3\text{CN}/\text{H}_2\text{O}$ with 0.1% TFA. The fractions collected were combined and lyophilized (171 mg, 0.222 mmol, 65%). ^1H NMR (DMSO- d_6 , 500 MHz): δ 10.78 (d, $J = 1.4$ Hz, 1H), 9.12 (s, 1H), 8.02 (d, $J = 7.8$ Hz, 1H), 7.82 (d, $J = 8.6$ Hz, 1H), 7.74 (d, $J = 8.1$ Hz, 1H), 7.51 (d, $J = 8$ Hz, 1H), 7.26-7.30 (m, 2H), 7.17-7.25 (m, 3H), 7.06-7.10 (m, 2H), 7.00-7.05 (m, 1H), 6.92-6.97 (m, 3H), 6.57-6.64 (m, 3H), 6.31 (dt, $J = 15.9, 6.3$ Hz, 1H), 4.65 (d, $J = 6.1$ Hz, 2H), 4.48 (ddd, $J = 8.3, 8.3, 4.9$ Hz, 1H), 4.62 (ddd, $J = 7.8, 7.8, 5.9$ Hz, 1H), 4.11 (ddd, $J = 8.2, 8.2$ Hz, 1H), 3.02 (ddd, $J = 14.9, 4.5$ Hz, 1H), 2.89 (ddd, $J = 14.9, 8.9$ Hz, 1H), 2.67-2.84 (m, 4H), 2.36 (ddd, $J = 14.5, 8.6, 5.9$ Hz, 1H), 1.52-1.62 (m, 1H), 1.41 (s, 9H), 1.32-1.39 (m, 1H), 1.15-1.26 (m, 1H), 0.83-0.95 (m, 1H), 0.69 (t, $J = 7.3$ Hz, 3H), 0.64 (d, $J = 6.9$ Hz, 3H). ^{13}C NMR (DMSO- d_6 , 150 MHz): δ 172.9, 171.7, 171.5, 171.2, 161.8, 156.1, 153.1, 142.0, 136.3, 136.1, 133.8, 130.4, 128.9, 128.4, 128.0, 127.6, 126.7, 124.5, 123.7, 123.5, 121.1, 118.6, 118.5, 115.2, 111.5, 110.3, 81.8, 67.2, 57.2, 54.3, 53.8, 40.8, 37.1, 36.8, 36.6, 31.3, 27.7, 24.5, 24.3, 15.5, 11.2. MS (ESI) Calculated for $\text{C}_{43}\text{H}_{53}\text{N}_5\text{O}_8$ $[\text{M}-\text{OCO}_2\text{tBu}]^+$: 650.3, found 649.9.

Acyclic-Ala-Val-Tyr (S11):

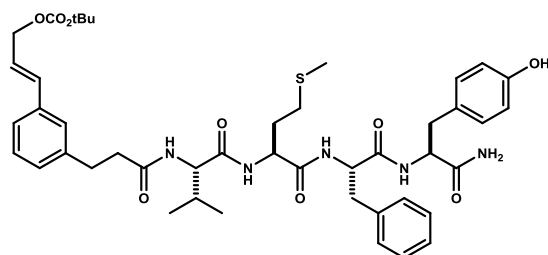


Following general procedure A, the corresponding compound was prepared from H-AVY-NH₂ ($\bullet$ TFA, 18 mg, 0.039 mmol), diisopropylethylamine (27 μL , 0.155 mmol) and reagent **1** (16 mg, 0.039 mmol). The product was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 40-

100% $\text{CH}_3\text{CN}/\text{H}_2\text{O}$ with 0.1% TFA. The fractions collected were combined and lyophilized (17 mg, 0.026 mmol, 17%). ^1H NMR (DMSO- d_6 , 400 MHz): δ 9.11 (br s, 1H), 8.04 (d, $J = 7.3$ Hz, 1H), 7.92 (s, 1H), 7.45 (d, $J = 8.6$ Hz, 1H), 7.70 (d, $J = 8.9$ Hz), 7.26 (br s, 1H), 7.22-7.26 (m, 2H), 7.20 (app t, $J = 7.5$ Hz, 1H), 7.08 (d, $J = 7.4$ Hz, 1H), 7.00 (br s, 1H), 6.95 (d, $J = 8.3$ Hz, 1H), 6.56-6.63 (m, 2H), 6.31 (dt, $J = 15.8, 6.3$ Hz, 1H), 4.64 (d, $J = 6.06$ Hz, 2H), 4.26-4.36 (m, 2H), 4.03 (dd, $J = 8.4, 6.7$ Hz, 1H), 2.83 (dd, $J = 13.9, 5.2$ Hz, 1H), 2.76 (t, $J = 7.7$ Hz, 2H), 2.66 (dd, $J = 14.0, 8.9$

Hz), 2.34-2.44 (m, 1H), 1.88 (dddd, $J = 13.3, 6.6, 6.6, 6.6$ Hz, 1H), 1.39 (s, 9H), 1.10 (d, $J = 7.2$ Hz, 3H), 0.71 (d, $J = 6.4$ Hz, 6H). ^{13}C NMR (DMSO- d_6 , 150 MHz): δ 173.2, 172.7, 171.6, 170.7, 156.1, 153.1, 142.0, 136.2, 133.8, 130.3, 128.9, 128.4, 128.1, 126.7, 124.6, 123.6, 115.1, 81.8, 67.2, 58.2, 54.1, 48.4, 40.8, 37.1, 36.9, 31.2, 30.7, 27.7, 19.4, 18.3, 18.2. MS (ESI) Calculated for $\text{C}_{34}\text{H}_{46}\text{N}_4\text{O}_8$ $[\text{M}-\text{OCO}_2\text{tBu}]^+$: 521.3, found 521.0.

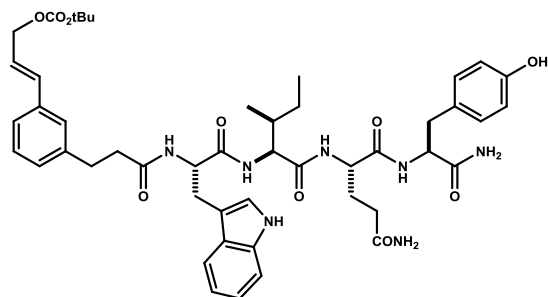
Acyclic-Val-Met-Phe-Tyr (S12):



Following general procedure A, the corresponding compound was prepared from H-VMFY-NH₂ ($\bullet$ TFA, 149 mg, 0.222 mmol), diisopropylethylamine (155 μL , 0.887 mmol) and reagent **1** (89 mg, 0.222 mmol). The product was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 40-100% $\text{CH}_3\text{CN}/\text{H}_2\text{O}$

with 0.1% TFA. The fractions collected were combined and lyophilized (111 mg, 0.131 mmol, 59%). ^1H NMR (DMSO- d_6 , 600 MHz): δ 9.13 (s, 1H), 8.00 (d, $J = 7.7$ Hz, 1H), 7.92 (d, $J = 7.9$ Hz, 1H), 7.83-7.90 (m, 2H), 7.27 (s, 1H), 7.10-7.25 (m, 9H), 7.08 (d, $J = 7.2$ Hz, 1H), 7.03 (s, 1H), 6.97 (d, $J = 8.1$ Hz, 2H), 6.57-6.65 (m, 2H), 6.30 (dt, $J = 16.0, 6.0$ Hz, 1H), 4.63 (d, $J = 6.1$ Hz, 2H), 4.45 (ddd, $J = 8.2, 8.2, 4.8$ Hz, 1H), 4.22-4.35 (m, 2H), 4.07 (dd, $J = 7.5, 7.5$ Hz, 1H), 2.9 (dd, $J = 14.0, 4.2$ Hz, 1H), 2.64-2.88 (m, 6H), 2.48-2.56 (m, 1H), 2.26-2.44 (m, 3H), 1.95 (d, 3H), 1.74-1.90 (m, 2H), 1.64-1.73 (m, 1H), 1.39 (s, 9H), 0.69 (d, $J = 6.6$ Hz, 6H). ^{13}C NMR (DMSO- d_6 , 150 MHz): δ 173.0, 172.0, 171.5, 171.1, 170.7, 156.1, 153.1, 142.0, 137.9, 136.2, 133.8, 130.4, 129.4, 128.9, 128.4, 128.3, 128.0, 126.7, 126.5, 124.6, 123.6, 115.2, 81.8, 67.2, 58.2, 54.4, 54.1, 52.2, 37.7, 37.2, 36.8, 32.0, 31.3, 30.5. MS (ESI) Calculated for $\text{C}_{45}\text{H}_{59}\text{N}_5\text{O}_9\text{S}$ $[\text{M}+\text{Na}]^+$: 868.4, found 868.9.

Acyclic-Trp-Ile-Gln-Tyr (S13):

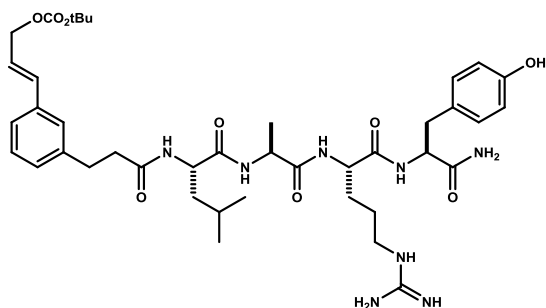


Following general procedure A, the corresponding compound was prepared from H-WIQY-NH₂ ($\bullet$ TFA, 77 mg, 0.107 mmol), diisopropylethylamine (74 μL , 0.427 mmol) and reagent **1** (43 mg, 0.107 mmol). The product was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 40-100% $\text{CH}_3\text{CN}/\text{H}_2\text{O}$ with 0.1% TFA. The fractions collected were combined

and lyophilized (67 mg, 0.075 mmol, 70%). ^1H NMR (DMSO- d_6 , 400 MHz): δ 10.73 (s, 1H), 9.12 (br s, 1H), 8.02-8.06 (m, 2H), 7.90 (d, $J = 8.1$ Hz, 1H), 7.79 (d, $J = 7.9$ Hz, 1H), 7.57 (d, $J = 7.9$ Hz, 1H), 7.30 (br s, 1H), 7.18-7.25 (m, 3H), 7.14 (dd, $J = 7.7, 7.7$ Hz, 1H), 6.99-7.06 (m, 3H), 6.91-6.99 (m, 4H), 6.478 (br s, 1H), 6.58 (d, $J = 7.9$ Hz, 2H), 6.56 (d, $J = 15.3$ Hz, 1H), 6.29 (dt, $J = 16.0, 6.2$ Hz, 1H), 4.62 (d, $J = 6.2$ Hz, 2H), 4.58 (ddd, $J = 9.3, 9.3, 4.7$ Hz, 1H), 4.30 (ddd, $J = 7.6, 7.6, 7.6$ Hz, 1H), 4.20 (ddd, $J = 7.7, 7.7,$

7.7 Hz, 1H), 4.14 (dd, $J = 7.7, 7.7$ Hz, 1H), 3.07 (dd, $J = 14.7, 4.1$ Hz, 1H), 2.87 (dd, $J = 14.6, 9.5$ Hz, 1H), 2.82 (dd, $J = 14.0, 5.3$ Hz, 1H), 2.60-2.66 (m, 2H), 2.32 (dd, $J = 7.7, 7.7$ Hz, 1H), 2.03-2.08 (m, 1H), 1.81 (dddd, $J = 13.8, 6.4, 6.4, 6.4$ Hz, 1H), 1.64-1.74 (m, 2H), 1.39 (s, 9H), 0.97-1.07 (m, 1H), 0.76 (t, $J = 7.3$ Hz, 3H), 0.75 (d, $J = 6.8$ Hz, 3H). ^{13}C NMR (DMSO- d_6 , 150 MHz): δ 174.3, 173.1, 172.0, 171.7, 171.2, 171.0, 156.1, 153.1, 142.0, 136.3, 136.1, 133.8, 130.3, 128.9, 128.2, 128.0, 127.7, 126.7, 124.5, 123.9, 123.6, 121.1, 118.9, 118.5, 115.2, 111.5, 110.5, 81.8, 67.2, 57.4, 54.4, 53.6, 52.7, 40.4, 37.2. MS (ESI) Calculated for $\text{C}_{48}\text{H}_{61}\text{N}_7\text{O}_{10}$ $[\text{M}-\text{OCO}_2\text{tBu}]^+$: 778.4, found 777.9.

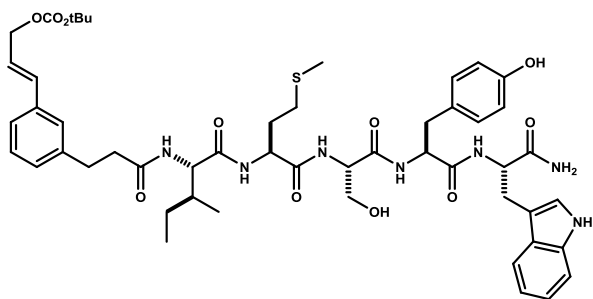
Acyclic-Ile-Ala-Arg-Tyr (S14):



Following general procedure A, the corresponding compound was prepared from H-LARY-NH₂ ($\bullet$ 3TFA, 88 mg, 0.102 mmol), diisopropylethylamine (71 μL , 0.408 mmol) and reagent **1** (41 mg, 0.102 mmol). The product was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 20-100% CH₃CN/H₂O with 0.1% TFA. The fractions collected were combined

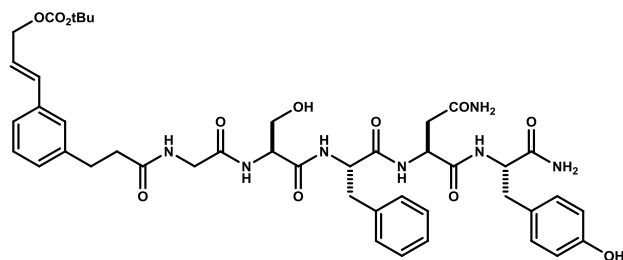
and lyophilized (54 mg, 0.067 mmol, 67%). ^1H NMR (DMSO- d_6 , 600 MHz): δ 8.06 (d, $J = 6.8$ Hz, 1H), 7.94-7.99 (m, 2H), 7.88 (d, $J = 7.7$ Hz, 1H), 7.73 (d, $J = 7.9$ Hz, 1H), 7.55 (dd, $J = 5.5, 5.5$ Hz, 1H), 7.31 (s, 1H), 7.22-7.27 (m, 2H), 7.19 (dd, $J = 7.7, 7.7$ Hz, 1H), 7.07 (d, $J = 7.4$ Hz, 1H), 7.04 (s, 1H), 6.95 (d, $J = 8.5$ Hz, 2H), 6.56-6.62 (m, 3H), 6.30 (dt, $J = 16.2, 6.5$ Hz, 1H), 4.63 (d, $J = 6.2$ Hz, 2H), 4.29 (ddd, $J = 8.1, 8.1, 5.4$ Hz, 1H), 4.24 (dq, $J = 7.8, 7.8$ Hz, 1H), 4.12-4.20 (m, 2H), 2.99-3.05 (m, 2H), 2.80-2.87 (m, 2H), 2.72-2.79 (m, 2H), 2.65-2.69 (m, 1H), 2.55 (d, $J = 4.7$ Hz, 1H), 2.43-2.49 (m, 2H), 2.35-2.42 (m, 1H), 1.59 (dddd, $J = 14.3, 6.7, 6.7, 6.7$ Hz, 1H), 1.43-1.51 (m, 1H), 1.39 (s, 9H), 1.31-1.37 (m, 2H), 1.15 (d, $J = 7.3$ Hz, 3H), 0.78 (d, $J = 6.4$ Hz, 3H), 0.72 (d, $J = 6.6$ Hz, 3H). ^{13}C NMR (DMSO- d_6 , 150 MHz): δ 173.1, 172.6, 172.6, 171.9, 171.1, 161.9, 159.0 (TFA, q, $J = 34.5$ Hz), 157.1, 156.1, 153.1, 141.9, 136.2, 133.8, 130.4, 128.9, 128.4, 128.0, 126.7, 124.5, 123.6, 116.6 (TFA, q, $J = 295$ Hz), 115.2, 81.8, 67.2, 54.3, 52.6, 51.2, 48.7, 40.9, 40.7, 37.1, 36.8, 31.2, 29.3, 27.7, 25.1, 24.3, 23.4, 21.7, 18.0. MS (ESI) Calculated for $\text{C}_{41}\text{H}_{60}\text{N}_8\text{O}_9$ $[\text{M}+\text{H}]^+$: 809.4, found 809.0.

Acyclic-Ile-Met-Ser-Tyr-Trp (S15):

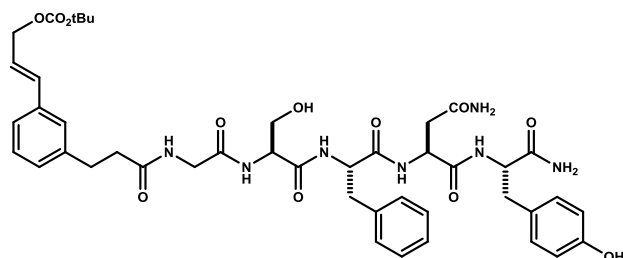


Following general procedure A, the corresponding compound was prepared from H-IMSYW-NH₂ ($\bullet$ TFA, 211 mg, 0.292 mmol), diisopropylethylamine (204 μL , 1.17 mmol) and reagent **1** (118 mg, 0.292 mmol). The product was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 40-100% CH₃CN/H₂O with 0.1% TFA. The fractions

Acyclic-Ala-Phe-Thr-Ile-Tyr (S16):

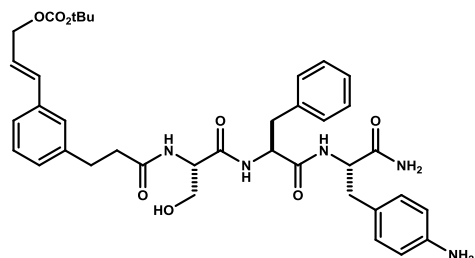


gradient of 40-100% CH₃CN/H₂O with 0.1% TFA. The fractions collected were combined and lyophilized (26 mg, 0.029 mmol, 67%). ¹H NMR (DMSO-d₆, 400 MHz): δ 8.00 (d, J = 8.28 Hz, 1H), 7.99 (d, J = 7.92 Hz, 1H), 7.87 (d, J = 8.1 Hz, 1H), 7.75 (d, J = 7.9 Hz, 1H), 7.69 (d, J = 8.1 Hz, 1H), 7.16-7.26 (m, 7H), 7.11-7.15 (m, 1H), 7.10 (br s, 1H), 7.07 (d, J = 7.9 Hz, 1H), 7.03 (br s, 1H), 6.95 (d, J = 8.9 Hz, 2H), 6.56-6.62 (m, 3H), 6.30 (dt, J = 15.8, 6.2 Hz, 1H), 4.63 (dd, J = 6.0, 0.9 Hz, 2H), 4.53 (ddd, J = 8.8, 8.8, 4.3 Hz, 1H), 4.25-4.35 (m, 2H), 4.21 (dq, J = 7.2, 7.2 Hz), 4.10 (dd, J = 7.7, 6.4 Hz, 1H), 3.95-4.02 (m, 1H), 3.03 (dd, J = 14.2, 4.1 Hz, 1H), 2.85-2.90 (m, 1H), 2.80 (dd, J = 14.1, 9.9 Hz, 1H), 2.70-2.76 (m, 2H), 2.61 (dd, J = 13.9, 9.5 Hz, 1H), 2.29-2.42 (m, 2H), 1.62-1.71 (m, 1H), 1.39 (s, 9H), 1.11-1.21 (m, 1H), 1.06 (d, J = 7.0 Hz, 3H), 0.99 (d, J = 6.6 Hz, 3H), 0.67-0.74 (m, 6H). ¹³C NMR (DMSO-d₆, 150 MHz): δ 173.2, 172.6, 171.6, 171.3, 170.7, 170.3, 156.1, 153.1, 142.0, 138.1, 136.2, 133.8, 130.2, 129.6, 129.0, 128.4, 128.3, 128.2, 126.7, 126.5, 124.6, 123.6, 115.2, 81.8, 67.2, 67.0, 58.0, 57.7, 54.5, 54.1, 48.4, 40.8, 37.3, 36.9, 36.88, 36.80, 36.1, 31.2, 27.7, 24.1, 19.5, 18.4, 15.6, 11.6. MS (ESI) Calculated for C₄₈H₆₄N₆O₁₁ [M+H]⁺: 901.5, found 901.0.

Acyclic-Gly-Ser-Phe-Asn-Tyr (S17):

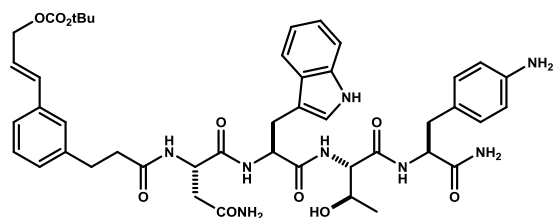
Following general procedure A, the corresponding compound was prepared from H-GSFNY-NH₂ (•TFA, 120 mg, 0.172 mmol), diisopropylethylamine (119 μ L, 0.686 mmol) and reagent **1** (69 mg, 0.172 mmol). The product was isolated by preparative HPLC (Waters Sunfire C18

30x150 mm) using a gradient of 40-100% CH₃CN/H₂O with 0.1% TFA. The fractions collected were combined and lyophilized (120 mg, 0.137 mmol, 80%). ¹H NMR (DMSO-d₆, 600 MHz): δ 8.14 (d, J = 6.6 Hz, 1H), 8.08-8.12 (m, 1H), 8.02 (d, J = 7.1 Hz, 1H), 7.89-7.94 (m, 2H), 7.87 (d, J = 7.2 Hz, 1H), 7.40 (app. s, 1H) 7.34 (app s, 1H) 7.06-7.30 (m, 10H), 7.93-7.99 (m, 3H), 7.56-7.63 (m, 3H), 6.31 (dt, J = 15.7, 6.6 Hz, 1H), 4.64 (d, J = 4.9 Hz, 2H), 4.41-4.50 (m, 2H), 4.18-4.26 (2H), 4.67-4.73 (m, 2H), 3.43-3.50 (m, 2H), 2.97 (d, J = 12.7 Hz, 1H), 2.92 (d, J = 13.2 Hz, 1H), 2.72-2.80 (m, 3H), 2.39-2.57 (m, 3H), 2.35 (dd, J = 15.1, 5.1 Hz, 1H), 1.39 (s, 9H). ¹³C NMR (DMSO-d₆, 100 MHz): δ 173.2, 172.2, 172.0, 171.2, 170.7, 170.3, 169.5, 153.1, 142.1, 138.0, 136.2, 133.8, 130.3, 129.5, 129.0, 128.3, 126.8, 124.5, 123.6, 115.2, 81.8, 67.2, 61.9, 55.4, 54.8, 54.4, 50.2, 42.4, 37.3. MS (ESI) Calculated for C₄₄H₅₅N₇O₁₂ [M+H]⁺: 874.4, found 874.0

Acyclic-Ser-Phe-Phe(4-NH₂) (S18):

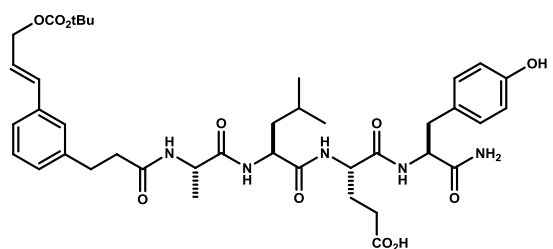
Following general procedure A, the corresponding compound was prepared from H-SFF(4-NH₂)-NH₂ (•2TFA, 170 mg, 0.265 mmol), diisopropylethylamine (185 μ L, 1.06 mmol) and reagent **1** (107 mg, 0.265 mmol). The product was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 30-100% CH₃CN/H₂O with 0.1% TFA. The fractions

collected were combined and lyophilized (115 mg, 0.164 mmol, 62%). ¹H NMR (DMSO-d₆, 500 MHz): δ 8.08 (d, J = 7.7 Hz, 1H), 8.05 (d, J = 8.1 Hz, 1H), 7.97 (d, J = 7.7 Hz, 1H), 7.22-7.28 (m, 3H), 7.16-7.28 (m, 4H), 7.12-7.15 (m, 4H), 7.1 (d, J = 8.5 Hz, 2H), 7.07 (d, J = 7.6 Hz, 1H), 6.6 (d, J = 15.8 Hz, 1H), 6.31 (dt, J = 16.1, 6.2 Hz, 1H), 6.64 (dd, J = 6.1, 1.0 Hz, 2H), 4.32-4.38 (m, 2H), 4.28 (ddd, J = 6.8, 6.8, 6.8 Hz, 1H), 3.41-3.50 (m, 2H), 3 (dd, J = 13.7, 4.8 Hz, 1H), 2.92 (dd, J = 14.1, 4.5 Hz, 1H), 2.68-2.78 (m, 4H), 2.34-2.45 (m, 2H), 1.39 (s, 9H). ¹³C NMR (DMSO-d₆, 100 MHz): δ 173.0, 172.6, 172.1, 171.5, 170.4, 157.2, 153.3, 142.1, 136.5, 136.3, 133.9, 130.7, 129.1, 128.4, 127.8, 126.9, 124.7, 124.1, 123.8, 121.3, 119.0, 118.6, 118.3, 115.9, 111.7, 110.6, 82.0, 67.4, 67.0, 58.5, 54.5, 54.0, 52.7, 40.9, 40.6. MS (ESI) Calculated for C₃₈H₄₇N₅O₈ [M+H]⁺: 702.3, found 702.3.

Acyclic-Asn-Trp-Thr-Phe(4-NH₂) (S19):

Following general procedure A, the corresponding compound was prepared from H-NWTF(4-NH₂)-NH₂ (•2TFA, 162 mg, 0.200 mmol), diisopropylethylamine (140 μ L, 0.801 mmol) and reagent **1** (81 mg, 0.200 mmol). The product was isolated by preparative HPLC

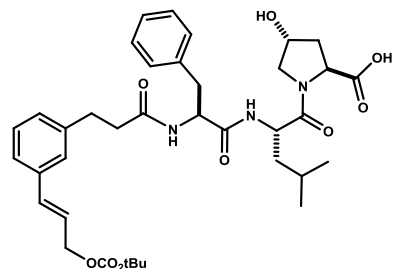
(Waters Sunfire C18 30x150 mm) using a gradient of 30-100% CH₃CN/H₂O with 0.1% TFA. The fractions collected were combined and lyophilized (106 mg, 0.122 mmol, 61%). ¹H NMR (DMSO-d₆, 500 MHz): δ 10.8 (d, J = 1.9 Hz, 1H), 8.09 (d, J = 7.8 Hz, 1H), 8.06 (d, J = 7.8 Hz, 1H), 7.9 (d, J = 8.3 Hz, 1H), 7.77 (d, J = 8.3 Hz, 1H), 7.52 (d, J = 7.8 Hz, 1H), 7.4 (br. s, J = Hz, 1H), 7.33 (br. s, J = Hz, 1H), 7.24-7.31 (m, 5H), 7.21 (dd, J = 7.8, 7.8 Hz, 1H), 7.11-7.19 (m, 4H), 7.08 (br. d, J = 7.3 Hz, 1H), 7.01 (dd, J = 7.1, 7.1 Hz, 1H), 6.97 (br. s, J = Hz, 1H), 6.91 (dd, J = 7.4, 7.4 Hz, 1H), 6.62 (d, J = 16 Hz, 1H), 6.32 (dt, J = 15.9, .62 Hz, 1H), 4.65 (dd, J = 6.3, 1.1 Hz, 2H), 4.56 (dq, J = 7.3, 7.3 Hz, 1H), 4.5 (ddd, J = 5.1, 5.1, 4.5 Hz, 1H), 4.41 (ddd, J = 8.5, 8.5, 5.2 Hz, 1H), 4.12 (dd, J = 8.0, 4.50 Hz, 1H), 3.92 (dddd, J = 12.5, 6.2, 6.2, 6.2 Hz, 1H), 3.15 (dd, J = 14.7, 4.0 Hz, 1H), 3.07 (dd, J = 13.9, 4.9 Hz, 1H), 2.98 (dd, J = 15.0, 8.7 Hz, 1H), 2.82 (dd, J = 13.8, 8.7 Hz, 1H), 2.66-2.76 (m, 2H), 2.44-2.54 (m, 1H), 2.27-2.39 (m, 3H), 1.41 (s, 9H). ¹³C NMR (DMSO-d₆, 100 MHz): δ 173.1, 172.3, 172.0, 171.9, 171.7, 170.0, 153.3, 142.2, 137.5, 136.5, 136.3, 133.9, 131.8, 130.9, 129.1, 128.5, 127.8, 126.9, 124.7, 124.1, 123.8, 122.5, 121.3, 118.8, 118.7, 111.7, 110.3, 82.0, 67.4, 67.1, 59.1, 54.4, 54.1, 50.1, 37.5, 37.2, 31.4, 27.85, 27.78, 27.5, 19.7. MS (ESI) Calculated for C₄₅H₅₆N₈O₁₀ [M+H]⁺: 869.4, found 869.3.

Acyclic-Ala-Leu-Glu-Tyr (15):

Following general procedure A, the corresponding compound was prepared from H-ALEY-NH₂ (•TFA, 183 mg, 0.301 mmol), diisopropylethylamine (210 μ L, 1.205 mmol) and reagent **1** (122 mg, 0.301 mmol). The product was isolated by flash chromatography (SiO₂, gradient 0-10% CH₃OH/CHCl₃). The fractions collected were

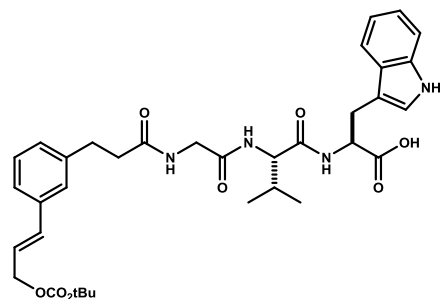
combined and concentrated under reduced pressure (160 mg, 0.205 mmol, 68%). ¹H NMR (DMSO-d₆, 400 MHz): δ 8.04 (d, J = 6.8 Hz, 1H), 7.96 (d, J = 7.2 Hz, 1H), 7.82 (d, J = 7.1 Hz, 1H), 7.72 (d, J = 8.1 Hz, 1H), 7.17-7.30 (m, 4H), 7.08 (d, J = 7.0 Hz, 1H), 7.02 (s, 1H), 6.96 (d, J = 7.7 Hz, 2H), 6.56-6.64 (m, 3H), 6.31 (dt, J = 15.8, 6.2 Hz, 1H), 4.64 (d, J = 5.3 Hz, 2H), 4.12-4.31 (m, 4H), 2.72-2.83 (m, 3H), 2.62-2.68 (m, 1H), 2.49-2.54 (m, 1H), 2.44-2.48 (m, 2H), 2.36-2.43 (m, 2H), 2.11-2.20 (m, 2H), 1.78-1.88 (m, 1H), 1.64-1.74 (m, 1H), 1.51-1.59 (m, 1H), 1.35-1.46 (m, 10H), 1.12 (d, J = 7.1 Hz, 3H), 0.84 (d, J = 6.4 Hz, 3H), 0.79 (d, J = 6.2 Hz, 3H). ¹³C NMR (DMSO-d₆, 150 MHz): δ 174.3, 173.0, 172.8, 172.3, 171.7, 170.9, 156.1, 153.1, 142.1, 136.2, 133.8, 130.3, 128.9, 128.4, 128.0, 126.7, 124.5, 123.6, 115.2, 81.8,

Acyclic-Phe-Leu-Hyp (S21):

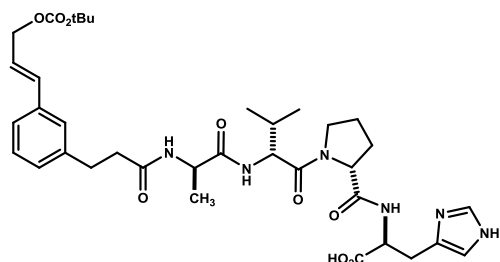


mmol, 57%). ¹H NMR (DMSO-d₆, 500 MHz): δ 8.10 (d, J = 8.3 Hz, 1H), 8.01 (d, J = 8.6 Hz, 1H), 7.12-7.26 (m, 8H), 7.00 (d, J = 7.4 Hz, 1H), 6.60 (d, J = 15.9 Hz, 1H), 6.31 (dt, J = 15.9, 6.3 Hz, 1H), 4.65 (dd, J = 6.1, 1.1 Hz, 2H), 4.50-4.55 (m, 2H), 4.31-4.37 (m, 1H), 3.59 (dd, J = 10.2, 4.6 Hz, 1H), 3.50-3.56 (m, 1H), 2.96 (dd, J = 13.9, 4.0 Hz, 1H), 2.60-2.72 (m, 3H), 2.29-2.35 (m, 2H), 2.07 (ddd, J = 11.9, 8.0, 2.5 Hz, 1H), 1.89 (ddd, J = 12.8, 8.0, 4.8 Hz, 1H), 1.62 (dddd, J = 13.4, 13.4, 6.9, 6.9 Hz, 1H), 1.41 (s, 9H), 0.86-0.89 (m, 6H). ¹³C NMR (DMSO-d₆, 125 MHz): δ 171.7, 171.5, 170.8, 153.3, 142.2, 138.4, 136.3, 133.9, 129.6, 129.1, 128.4, 126.9, 126.6, 124.6, 123.7, 82.0, 69.4, 67.4, 58.2, 55.1, 54.0, 49.0, 40.7, 38.1, 37.6, 37.2, 31.4, 27.8, 24.4, 23.6, 22.1. MS (ESI) Calculated for C₃₇H₄₉N₃O₉ [M-OCO₂tBu]⁺: 562.3, found 562.4.

Acyclic-Gly-Val-Trp (S22):

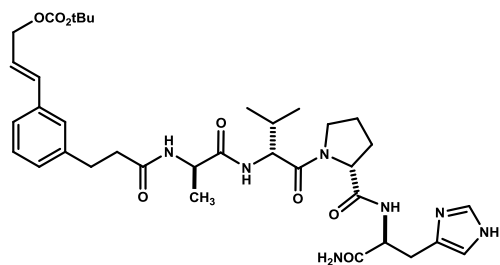


8.23 (d, J = 7.7 Hz, 1H), 8.09 (d, J = 6.0 Hz, 1H), 7.72 (d, J = 9.2 Hz, 1H), 7.51 (d, J = 8.4 Hz, 1H), 7.28-7.32 (m, 2H), 7.20-7.27 (m, 2H), 7.09-7.15 (m, 2H), 7.03 (dd, J = 7.6, 7.6 Hz, 1H), 6.95 (dd, J = 7.1, 7.1 Hz, 1H), 6.62 (d, J = 16.0 Hz, 1H), 6.32 (dt, 16.0, 6.3 Hz, 1H), 4.65 (dd, J = 6.1, 1.2 Hz, 2H), 4.43 (ddd, J = 7.9, 7.9, 5.5 Hz, 1H), 4.24 (dd, J = 9.0, 6.6 Hz, 1H), 3.66-3.76 (m, 2H), 3.15 (dd, J = 14.7, 5.3 Hz, 1H), 3.01 (dd, J = 14.7, 8.3 Hz, 1H), 2.71-2.82 (m, 2H), 2.40-2.46 (m, 2H), 1.94 (dddd, J = 13.4, 6.8, 6.8, 6.8 Hz, 1H), 1.41 (s, 9H), 0.82 (d, J = 6.7 Hz, 3H), 0.77 (d, J = 6.9 Hz, 3H). ¹³C NMR (DMSO-d₆, 125 MHz): δ 173.7, 172.2, 171.3, 169.2, 153.3, 142.2, 136.5, 136.3, 133.9, 129.1, 128.5, 127.7, 126.9, 124.7, 124.1, 123.8, 121.3, 118.8, 118.6, 111.8, 110.3, 82.0, 67.4, 57.5, 53.5, 42.4, 37.1, 31.4, 27.8, 27.5, 19.6, 18.3. MS (ESI) Calculated for C₃₅H₄₄N₄O₈ [M-OCO₂tBu]⁺: 531.3, found 531.3.

Acyclic-Ala-Val-Pro-His-OH (S23):

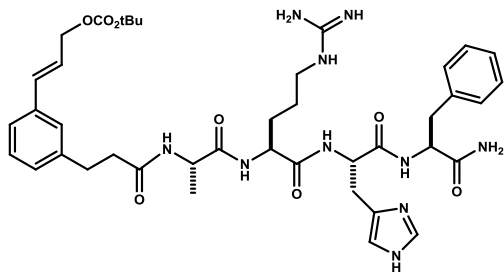
Following general procedure A, the corresponding compound was prepared from H-A(D-)V(D-)PH-OH ($\cdot$ 2TFA, 155 mg, 0.289 mmol), diisopropylethylamine (201 μ L, 1.16 mmol) and reagent **1** (117 mg, 0.289 mmol). The product was isolated by flash chromatography (SiO₂, gradient 0-10% CH₃OH/CHCl₃). The fractions collected were combined and concentrated under reduced pressure (152 mg, 0.214 mmol,

74%). ¹H NMR (DMSO-d₆, 500 MHz): δ ~3:1 mixture of rotamers; major: δ 8.97 (d, J = 1.2 Hz, 1H), 8.29 (d, J = 8.2 Hz, 1H), 8.08 (d, J = 8.7 Hz, 1H), 8 (d, J = 7.8 Hz, 1H), 7.36 (s, 1H), 7.29 (s, 1H), 7.17-7.26 (m, 2H), 7.09 (d, J = 7.8 Hz, 1H), 6.62 (d, J = 16 Hz, 1H), 6.32 (dt, J = 15.9, 6.2 Hz, 1H), 4.65 (d, J = 6.1 Hz, 2H), 4.52 (ddd, J = 9.6, 8.7, 4.6 Hz, 1H), 4.37 (dddd, J = 6.2, 6.2, 6.2, 6.2 Hz, 1H), 4.24-4.32 (m, 1H), 3.58-3.70 (m, 1H), 3.45-3.57 (m, 1H), 3.14 (dd, J = 15.0, 4.1 Hz, 1H), 2.95 (dd, J = 15.1, 9.9 Hz, 1H), 2.32-2.47 (m, 2H), 1.87-1.99 (m, 2H), 1.69-1.80 (m, 2H), 1.50-1.58 (m, 1H), 1.4 (s, 9H), 1.13 (d, J = 7 Hz, 3H), 0.85 (d, J = 6.8 Hz, 3H), 0.79 (d, J = 6.7 Hz, 3H). ¹³C NMR (DMSO-d₆, 100 MHz): δ 172.7, 172.3, 171.8, 171.4, 170.2, 153.3, 142.2, 136.3, 134.2, 133.9, 129.9, 129.1, 128.5, 126.8, 124.7, 123.7, 118.5, 117.5, 116.1, 82.0, 67.4, 59.8, 55.9, 55.5, 51.3, 48.3, 37.0, 31.4, 30.6, 29.8, 27.8, 27.0, 24.7, 19.6, 19.5, 18.6. MS (ESI) Calculated for C₃₆H₅₀N₆O₉ [M+H]⁺: 711.4, found 711.4.

Acyclic-Ala-Val-Pro-His-NH₂ (S24):

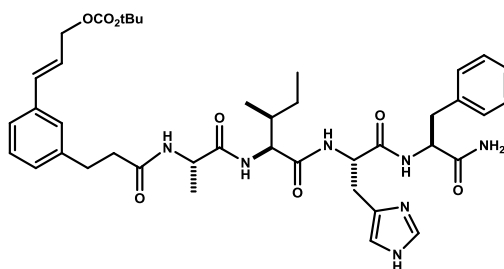
Following general procedure A, the corresponding compound was prepared from H-A(D-)V(D-)H-NH₂ ($\cdot$ 2TFA, 175 mg, 0.327 mmol), diisopropylethylamine (228 μ L, 1.307 mmol) and reagent **1** (132 mg, 0.327 mmol). The product was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 20-100% CH₃CN/H₂O with 0.1%

TFA. The fractions collected were combined and lyophilized (181 mg, 0.255 mmol, 78%). ¹H NMR (DMSO-d₆, 500 MHz): δ 8.94 (d, J = 1.2 Hz, 1H), 8.53 (d, J = 8.7 Hz, 1H), 8.06 (d, J = 8 Hz, 1H), 7.91 (d, J = 8.2 Hz, 1H), 7.37 (s, 1H), 7.21-7.33 (m, 5H), 7.11 (d, J = 7.3 Hz, 1H), 6.64 (d, J = 15.9 Hz, 1H), 6.33 (dt, J = 15.9, 6.3 Hz, 1H), 4.67 (dd, J = 6.3, 1.1 Hz, 2H), 4.49 (ddd, J = 9.4, 9.4, 4.3 Hz, 1H), 4.33 (dq, J = 7.2, 7.2 Hz, 1H), 4.24 (dd, J = 8.3, 8.3 Hz, 1H), 4.2 (dd, J = 7.1, 7.1 Hz, 1H), 3.75-3.82 (m, 1H), 3.52 (ddd, J = 9.5, 7.4, 7.2 Hz, 1H), 3.22 (dd, J = 15.2, 4.3 Hz, 1H), 2.88 (dd, J = 15.2, 10.1 Hz, 1H), 2.79 (t, J = 7.7 Hz, 2H), 2.36-2.47 (m, 2H), 1.86-2.01 (m, 3H), 1.72-1.83 (m, 1H), 1.59 (ddd, J = 13.8, 13.8, 7.0 Hz, 1H), 1.42 (s, 9H), 1.12 (d, J = 6.7 Hz, 3H), 0.86 (d, J = 6.8 Hz, 3H), 0.85 (d, J = 6.6 Hz, 3H). ¹³C NMR (DMSO-d₆, 100 MHz): δ 172.3, 172.1, 171.8, 171.2, 170.3, 152.8, 141.6, 135.8, 133.6, 133.4, 129.9, 128.6, 128.0, 126.3, 124.2, 123.2, 116.7, 81.5, 66.9, 59.8, 55.8, 51.3, 48.5, 47.7, 36.5, 30.8, 30.1, 28.9, 27.3, 26.3, 24.7, 18.8. MS (ESI) Calculated for C₃₆H₅₁N₇O₈ [M+H]⁺: 710.4, found 710.4.

Acyclic-Ala-Arg-His-Phe-NH₂ (S25):

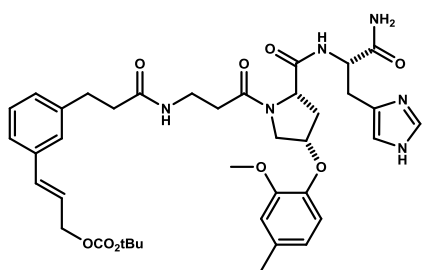
Following general procedure A, the corresponding compound was prepared from H-ARHF-NH₂ (•4TFA, 54 mg, 0.055 mmol), diisopropylethylamine (38 μ L, 0.219 mmol) and reagent **1** (22 mg, 0.055 mmol). The product was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 10-100% CH₃CN/H₂O with 0.1% TFA. The

fractions collected were combined and lyophilized (28 mg, 0.035 mmol, 63%). ¹H NMR (DMSO-d₆, 500 MHz): δ 8.94 (d, J = 1.2 Hz, 1H), 8.03-8.11 (m, 4H), 7.63 (dd, J = 5.6 Hz, 1H), 7.59 (br. s, 1H), 7.20-7.29 (m, 9H), 7.15-7.19 (m, 1H), 7.09 (br. d, J = 7.4 Hz, 1H), 6.62 (br. d, J = 15.9 Hz, 1H), 6.32 (dt, J = 16.0, 6.3 Hz, 1H), 4.65 (dd, J = 6.1, 1.1 Hz, 2H), 4.53 (ddd, J = 7.8, 7.8, 5.9 Hz, 1H), 4.41 (ddd, J = 8.6, 8.2, 4.9 Hz, 1H), 4.23 (dq, J = 7.0, 7.0 Hz, 1H), 4.17 (ddd, J = 7.8, 7.8, 5.6 Hz, 1H), 2.98-3.07 (m, 4H), 2.97 (dd, J = 15.7, 8.0 Hz, 1H), 2.74-2.85 (m, 3H), 2.35-2.46 (m, 2H), 1.57-1.60 (m, 1H), 1.43-1.53 (m, 2H), 1.41 (s, 9H), 1.12 (d, J = 7.2 Hz, 3H). ¹³C NMR (DMSO-d₆, 100 MHz): δ 173.4, 173.2, 172.0, 171.8, 169.9, 157.3, 153.3, 142.2, 138.0, 136.3, 134.2, 133.9, 129.6, 129.5, 129.1, 128.6, 128.5, 126.9, 126.8, 124.7, 123.8, 118.2, 117.4, 115.9, 82.0, 67.4, 54.4, 52.7, 51.9, 48.8, 40.9, 37.9, 37.0, 31.3, 29.1, 27.8, 27.5, 25.5, 18.4. MS (ESI) Calculated for C₄₁H₅₆N₁₀O₈ [M+H]⁺: 816.4, found 817.2.

Acyclic-Ala-Ile-His-Phe-NH₂ (S26):

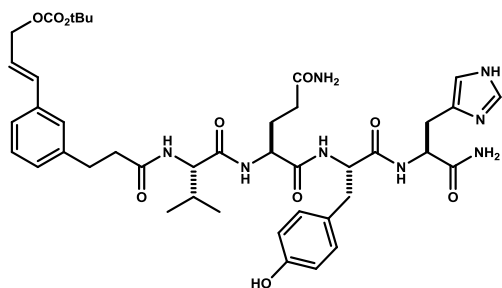
Following general procedure A, the corresponding compound was prepared from H-AIHF-NH₂ (•2TFA, 44 mg, 0.062 mmol), diisopropylethylamine (43 μ L, 0.247 mmol) and reagent **1** (25 mg, 0.062 mmol). The product was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 20-100% CH₃CN/H₂O with 0.1%

TFA. The fractions collected were combined and lyophilized (34 mg, 0.044 mmol, 72%). ¹H NMR (DMSO-d₆, 500 MHz): δ 8.94 (d, J = 1.6 Hz, 1H), 8.16 (d, J = 8.1 Hz, 1H), 8.04 (d, J = 7.4 Hz, 1H), 7.99 (d, J = 7.8 Hz, 1H), 7.76 (d, J = 8.4 Hz, 1H), 7.51 (br. s, 1H), 7.27-7.29 (m, 2H), 7.18-7.26 (m, 6H), 7.14-7.18 (m, 2H), 7.1 (br. d, J = 7.4 Hz, 1H), 6.62 (d, J = 16 Hz, 1H), 6.32 (dt, J = 16.0, 6.2 Hz, 1H), 4.65 (dd, J = 6.3, 1.2 Hz, 2H), 4.58 (ddd, J = 7.9, 7.9, 6.1 Hz, 1H), 4.41 (ddd, J = 8.3, 8.3, 5.1 Hz, 1H), 4.29 (dq, J = 7.0, 7.0 Hz, 1H), 4.07 (t, J = 7.6 Hz, 1H), 2.95-3.00 (m, 2H), 2.91 (dd, J = 15.4, 8.0 Hz, 1H), 2.75-2.85 (m, 3H), 2.36-2.45 (m, 2H), 1.59-1.66 (m, 1H), 1.41 (s, 9H), 1.27-1.34 (m, 1H), 1.1 (d, J = 7 Hz, 3H), 0.94-1.04 (m, 1H), 0.74 (t, J = 7.4 Hz, 3H), 0.69 (d, J = 6.7 Hz, 3H). ¹³C NMR (DMSO-d₆, 100 MHz): δ 173.2, 172.9, 171.8, 171.4, 170.0, 153.3, 142.2, 138.0, 136.3, 134.2, 133.9, 129.6, 129.6, 129.1, 128.5, 128.5, 126.9, 126.8, 124.7, 123.8, 117.3, 82.0, 67.4, 57.4, 54.3, 51.8, 48.5, 37.9, 37.1, 36.9, 31.4, 27.8, 27.5, 24.7, 18.3, 15.7, 11.5. MS (ESI) Calculated for C₄₁H₅₅N₇O₈ [M+H]⁺: 774.4, found 774.2.

Acyclic- β -Ala-Pro[4-(2-methoxy-4-methylphenoxy)]-His (S27):

Following general procedure A, the corresponding compound was prepared from H-(β -)AP(4-OAr)H-NH₂ ($\cdot$ 2TFA, 112 mg, 0.163 mmol), diisopropylethylamine (114 μ L, 0.653 mmol) and reagent **1** (66 mg, 0.163 mmol). The product was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 30-100% CH₃CN/H₂O with 0.1% TFA. The fractions collected were combined and lyophilized (95 mg, 0.127 mmol, 78%). ¹H NMR

(DMSO-d₆, 500 MHz): 5:1 mixture of rotamers. Major: δ 8.86 (d, J = 0.9 Hz, 1H), 8.14 (d, J = 8.7 Hz, 1H), 7.91 (d, J = 5.7 Hz, 1H), 7.33 (br. s, 1H), 7.25-7.31 (m, 2H), 7.17-7.24 (m, 3H), 7.06-7.10 (m, 2H), 6.75-6.82 (m, 2H), 6.64 (br. d, J = 8.3 Hz, 1H), 6.59 (d, J = 16 Hz, 1H), 6.3 (dt, J = 15.9, 6.3 Hz, 1H), 4.76-4.80 (m, 1H), 4.64 (d, J = 6.4 Hz, 2H), 4.51 (ddd, J = 9.2, 9.2, 4.6 Hz, 1H), 4.29 (dd, J = 9.9, 3.9 Hz, 1H), 3.71-3.73 (m, 1H), 3.7 (s, 3H), 3.19-3.29 (m, 3H), 2.93 (dd, J = 15.5, 9.7 Hz, 1H), 2.77 (t, J = 7.7 Hz, 2H), 2.26-2.53 (m, 6H), 2.23 (s, 3H), 1.99 (dt, J = 13.0, 3.1 Hz, 1H), 1.4 (s, 9H). ¹³C NMR (DMSO-d₆, 100 MHz): δ 172.4, 172.0, 171.9, 171.8, 153.3, 150.6, 143.8, 142.1, 136.3, 133.9, 132.9, 130.5, 129.0, 128.6, 126.9, 124.7, 123.7, 121.3, 118.8, 116.9, 113.8, 82.0, 78.2, 67.4, 59.7, 55.9, 52.3, 51.7, 37.3, 35.1, 34.7, 31.4, 27.8, 26.5, 21.2. MS (ESI) Calculated for C₃₉H₅₀N₆O₉ [M+H]⁺: 747.4, found 747.3.

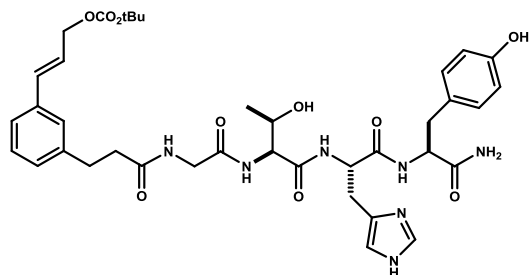
Acyclic-Val-Gln-Tyr-His-NH₂ (18):

Following general procedure A, the corresponding compound was prepared from H-VQYH-NH₂ ($\cdot$ 2TFA, 170 mg, 0.220 mmol), diisopropylethylamine (153 μ L, 0.88 mmol) and reagent **1** (89 mg, 0.220 mmol). The product was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 20-100% CH₃CN/H₂O with 0.1% TFA. The fractions collected were combined and lyophilized (103 mg,

0.123 mmol, 56%). ¹H NMR (DMSO-d₆, 500 MHz): δ 8.94 (d, J = 1.4 Hz, 1H), 8.19 (d, J = 8.3 Hz, 1H), 8.11 (d, J = 7.3 Hz, 1H), 7.91 (d, J = 7.8 Hz, 2H), 7.32 (br. s, J = Hz, 1H), 7.18-7.30 (m, 5H), 7.14 (br. s, J = Hz, 1H), 7.1 (br. d, J = 7.3 Hz, 1H), 6.96 (d, J = 8.4 Hz, 2H), 6.83 (br. s, J = Hz, 1H), 6.57-6.63 (m, 3H), 6.31 (dt, J = 16.0, 6.2 Hz, 1H), 4.65 (dd, J = 6.4, 1.2 Hz, 2H), 4.46 (ddd, J = 8.2, 8.2, 5.5 Hz, 1H), 4.32 (ddd, J = 8.1, 8.1, 5.0 Hz, 1H), 4.16 (ddd, J = 8.0, 8.0, 5.7 Hz, 1H), 4.04-4.09 (m, 1H), 3.1 (dd, J = 15.3, 5.2 Hz, 1H), 2.89 (dd, J = 15.4, 8.6 Hz, 1H), 2.74-2.86 (m, 3H), 2.68 (dd, J = 14.1, 9.1 Hz, 1H), 2.50-2.58 (m, 1H), 2.39-2.46 (m, 1H), 2.00-2.12 (m, 2H), 1.75-1.90 (m, 2H), 1.61-1.70 (m, 1H), 1.4 (s, 9H), 0.73 (d, J = 6.7 Hz, 6H). ¹³C NMR (DMSO-d₆, 100 MHz): δ 174.6, 172.4, 172.0, 171.9, 171.8, 171.6, 156.3, 153.3, 142.1, 136.3, 134.1, 133.9, 130.4, 129.9, 129.1, 128.5, 127.9, 126.8, 124.7, 123.7, 117.3,

115.4, 82.0, 67.4, 58.6, 55.0, 52.7, 51.9, 37.0, 31.8, 31.5, 30.7, 28.1, 27.8, 27.3, 19.6, 18.7. MS (ESI) Calculated for $C_{42}H_{56}N_8O_{10}$ $[M+H]^+$: 833.4, found 833.2.

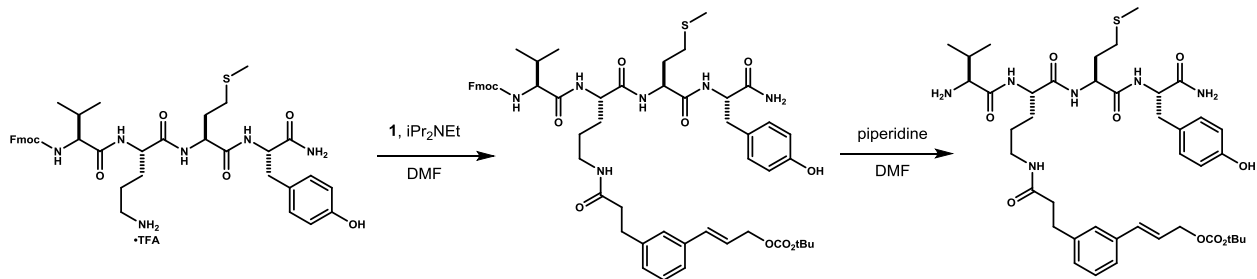
Acyclic-Gly-Thr-His-Tyr-NH₂ (S29):



Following general procedure A, the corresponding compound was prepared from H-GTHY-NH₂ ($\cdot 2$ TFA, 37 mg, 0.053 mmol), diisopropylethylamine (37 μ L, 0.210 mmol) and reagent **1** (21 mg, 0.053 mmol). The product was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 20-100% CH₃CN/H₂O with 0.1% TFA. The fractions collected were combined and

lyophilized (27 mg, 0.036 mmol, 68%). ¹H NMR (DMSO-d₆, 500 MHz): δ 8.92 (d, J = 1.4 Hz, H), 8.2 (t, J = 5.9 Hz, H), 8.15 (d, J = 8 Hz, H), 7.95 (d, J = 7.8 Hz, H), 7.8 (d, J = 8 Hz, H), 7.44 (br. s, H), 7.24-7.30 (m, H), 7.22 (t, J = 7.5 Hz, H), 7.15 (br. s, H), 7.1 (br. d, J = 7.3 Hz, H), 7.01 (d, J = 8.5 Hz, H), 6.59-6.65 (m, H), 6.32 (dt, J = 16.1, 6.3 Hz, H), 4.65 (dd, J = 6.3m 1.1 Hz, H), 4.54 (ddd, J = 8.0, 8.0, 5.4 Hz, H), 4.3 (ddd, J = 8.3, 8.3, 5.2 Hz, H), 4.19 (dd, J = 8.0, 4.5 Hz, H), 3.94 (dddd, J = 6.5, 6.5, 6.5, 4.7 Hz, H), 3.71-3.81 (m, H), 3.06 (dd, J = 15.3, 5.1 Hz, H), 2.93 (dd, J = 15.3, 8.3 Hz, H), 2.87 (dd, J = 13.7, 4.9 Hz, H), 2.76-2.81 (m, H), 2.69 (dd, J = 14.0, 8.9 Hz, H), 2.40-2.47 (m, H), 1.41 (s, H), 0.99 (d, J = 6.4 Hz, H). ¹³C NMR (DMSO-d₆, 100 MHz): δ 173.6, 172.5, 170.5, 170.0, 169.9, 156.3, 153.3, 142.2, 136.4, 134.2, 133.9, 130.5, 129.6, 129.1, 128.5, 128.1, 126.9, 124.7, 123.8, 117.5, 115.4, 82.0, 67.4, 66.9, 58.6, 55.0, 52.1, 42.6, 37.1, 31.8, 31.3, 27.8, 27.2, 20.0. MS (ESI) Calculated for $C_{38}H_{49}N_7O_{10}$ $[M+H]^+$: 764.4, found 764.1.

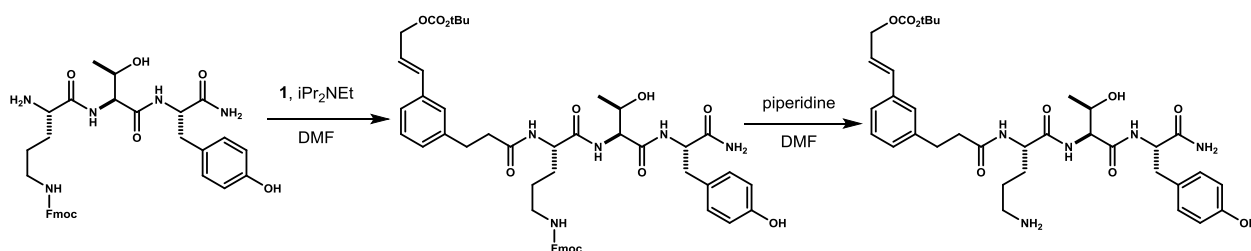
Acyclic-Val-Orn-Met-Tyr (S30):



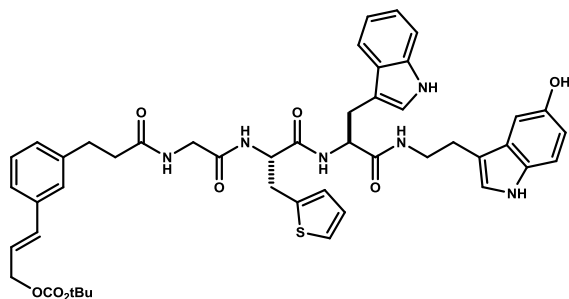
Following general procedure A, the corresponding compound was prepared from Fmoc-VOMY -NH₂ ($\cdot 1$ TFA, 94 mg, 0.110 mmol), diisopropylethylamine (76 μ L, 0.440 mmol) and reagent **1** (22 mg, 0.110 mmol). The reaction mixture was evaporated under reduced pressure. The resulting residue was treated with 20% piperidine/DMF (8 ml) for two hours and evaporated. The product was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 30-100% CH₃CN/H₂O with 0.1% TFA. The fractions collected were combined and lyophilized (56 mg, 0.069 mmol, 62%). ¹H NMR (DMSO-d₆, 500 MHz): δ 8.49 (d, J = 7.7 Hz, 1H), 8.14 (d, J = 8.4 Hz, 1H), 8.03-8.09 (m, 3H), 7.84 (dd, J = 5.7, 5.7 Hz,

1H), 7.77 (d, J = 8.1 Hz, 1H), 7.4 (br. s, J = Hz, 1H), 7.19-7.29 (m, 3H), 7.09 (br. d, J = 7.4 Hz, 1H), 7.05 (br. s, J = Hz, 1H), 6.98 (d, J = 8.6 Hz, 2H), 6.58-6.64 (m, 3H), 6.31 (dt, J = 15.9, 6.3 Hz, 1H), 4.65 (dd, J = 6.3, 1.2 Hz, 2H), 4.25-4.37 (m, 3H), 3.56-3.62 (m, 1H), 2.96-3.09 (m, 2H), 2.84 (dd, J = 13.9, 5.2 Hz, 1H), 2.75-2.80 (m, 2H), 2.68 (dd, J = 14.1, 8.6 Hz, 1H), 2.30-2.42 (m, 4H), 1.96-2.06 (m, 4H), 1.80-1.89 (m, 1H), 1.67-1.76 (m, 1H), 1.55-1.64 (m, 1H), 1.31-1.51 (m, 12H), 0.9 (d, J = 2.4 Hz, 3H), 0.89 (d, J = 2.7 Hz, 3H). ¹³C NMR (DMSO-d₆, 100 MHz): δ 173.3, 171.8, 171.5, 170.9, 168.2, 156.3, 153.3, 142.3, 136.3, 133.9, 130.6, 129.1, 128.5, 128.1, 126.9, 124.7, 123.8, 115.3, 82.0, 67.4, 57.6, 54.4, 52.8, 52.5, 38.5, 37.5, 37.3, 32.6, 31.5, 30.4, 29.8, 27.8, 18.7, 18.1, 15.0. MS (ESI) Calculated for C₄₁H₆₀N₆O₉S [M+H]⁺: 813.4, found 813.2.

Acyclic-Orn-Thr-Tyr (S35):

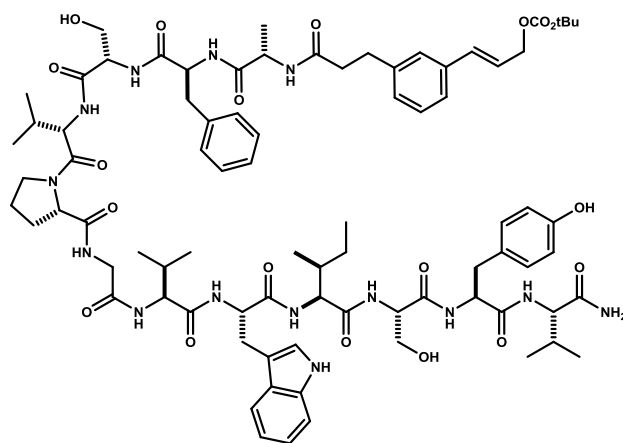


Following general procedure A, the corresponding compound was prepared from Orn(Fmoc)-Thr-Tyr-NH₂ (•1TFA, 109 mg, 0.15 mmol), diisopropylethylamine (52 μL, 0.30 mmol) and reagent **1** (60 mg, 0.15 mmol). The reaction mixture was evaporated under reduced pressure. The resulting residue was treated with DBU (1 equiv.) and Si-Thiol (Silicycle, 1.22 g/mmol) in DMF (1 ml) for one hour. The product was filtered and purified by preparative HPLC (Waters Xbridge C18 19x250 mm) using a gradient of 30-100% CH₃CN/H₂O with 0.1% TFA. The fractions collected were combined and evaporated (116 mg, 0.145 mmol, 97%). ¹H NMR (DMSO-d₆, 500 MHz): δ 9.20 (br s, 1H), 8.14 (d, J = 8.2 Hz, 1H), 7.86 (d, J = 8.3 Hz, 1H), 7.71 (d, J = 8.2 Hz, 1H), 7.65-7.70 (m, 3H), 7.42 (br s, 1H), 7.30 (br s, 1H), 7.27 (br d, J = 7.6 Hz, 1H), 7.24 (dd, J = 7.6, 7.3 Hz, 1H), 7.16 (br s, 1H), 7.11 (br d, J = 7.3 Hz, 1H), 7.01 (d, J = 8.4 Hz, 2H), 6.64 (d, J = 15.9 Hz, 1H), 6.63 (d, J = 8.4 Hz, 2H), 6.34 (dt, J = 15.9, 6.2 Hz, 1H), 4.67 (d, J = 6.1 Hz, 2H), 4.38-4.43 (m, 1H), 4.36 (ddd, J = 8.1, 8.0, 5.3 Hz, 1H), 4.18 (dd, J = 8.2, 4.2 Hz, 1H), 3.96-4.02 (m, 1H), 2.91 (dd, J = 14.0, 5.0 Hz, 1H), 2.80 (dd, J = 9.0, 6.8 Hz, 2H), 2.66-2.78 (m, 3H), 2.45 (dd, J = 8.3, 6.8 Hz, 2H), 1.63-1.72 (m, 1H), 1.46-1.54 (m, 3H), 1.43 (s, 9H), 0.97 (d, J = 6.3 Hz, 3H). ¹³C NMR (DMSO-d₆, 100 MHz): δ 173.1, 171.6, 169.4, 155.8, 152.8, 141.7, 135.9, 133.4, 130.1, 128.7, 128.0, 127.7, 126.4, 124.3, 123.4, 114.9, 81.6, 66.9, 66.4, 58.1, 54.1, 51.6, 38.5, 36.7, 31.0, 28.8, 27.4, 23.5, 19.4. MS (ESI) Calculated for C₃₅H₄₅N₅O₉ [M+H]⁺: 684.4, found 684.2.

Acyclic-Gly-Thi-Trp-5HT (S31):

Following general procedure A, the corresponding compound was prepared from H-GThiW-5HT-NH₂ ($\bullet$ TFA, 52 mg, 0.091 mmol), diisopropylethylamine (63 μ L, 0.363 mmol) and reagent **1** (37 mg, 0.091 mmol). The product was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 40-100% CH₃CN/H₂O with 0.1% TFA. The fractions collected

were combined and lyophilized (45 mg, 0.052 mmol, 57%). ¹H NMR (DMSO-d₆, 600 MHz): δ 10.75 (s, 1H), 10.42 (s, 1H), 8.08-8.14 (m, 2H), 7.85 (t, J = 5.6 Hz, 1H), 7.55 (d, J = 7.9 Hz, 1H), 7.30 (d, J = 8.1 Hz, 1H), 7.22-7.27 (m, 3H), 7.20 (t, J = 7.5 Hz, 1H), 7.06-7.11 (m, 3H), 7.02 (dd, J = 7.4, 7.4 Hz, 1H), 6.96-6.98 (m, 1H), 6.94 (dd, J = 7.4, 7.4 Hz, 1H), 6.85 (dd, J = 4.7, 4.0 Hz, 1H), 6.80-6.83 (m, 2H), 6.59 (d, J = 16.2 Hz, 1H), 6.57 (dd, J = 8.6, 2.2 Hz, 1H), 6.29 (dt, J = 16.0, 6.3 Hz, 1H), 4.63 (d, J = 6.4 Hz, 2H), 4.44-4.52 (m, 2H), 3.74 (dd, J = 16.5, 5.7 Hz, 1H), 3.62 (dd, J = 16.3, 5.6 Hz, 1H), 3.21-3.27 (m, 2H), 3.18 (dd, J = 15.1, 4.3 Hz, 1H), 3.11 (dd, J = 14.5, 5.4 Hz, 1H), 2.96-3.01 (m, 2H), 2.78 (t, J = 7.7 Hz, 1H), 2.62 (t, J = 7.7 Hz, 1H), 2.40-2.45 (m, 2H), 1.40 (s, 9H). ¹³C NMR (DMSO-d₆, 150 MHz): δ 172.3, 171.2, 170.4, 169.5, 153.1, 150.5, 142.1, 139.7, 136.4, 136.2, 133.7, 131.1, 129.0, 128.3, 128.1, 127.7, 127.0, 126.8, 126.6, 124.8, 124.5, 123.9, 123.7, 123.4, 121.2, 118.8, 118.6, 112.0, 111.60, 111.57, 111.0, 110.3, 102.5, 81.8, 67.2, 54.2, 54.1, 42.4, 37.0, 31.9. MS (ESI) Calculated for C₄₇H₅₂N₆O₈S [M+H]⁺: 861.4, found 861.3.

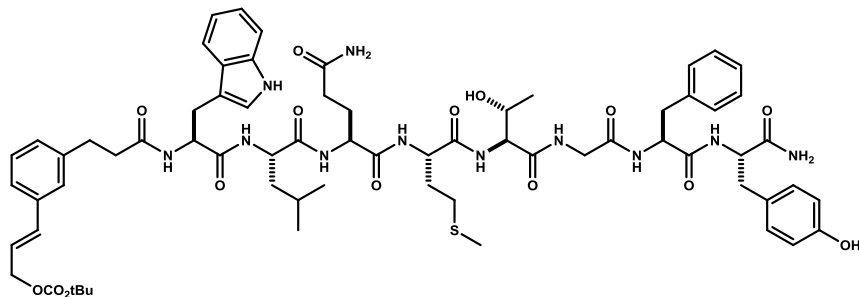
Acyclic-Ala-Phe-Ser-Val-Pro-Gly-Val-Trp-Ile-Ser-Tyr-Val (S32):

Following general procedure A, the corresponding compound was prepared from H-AFSVPGVWISYV-NH₂ ($\bullet$ TFA, 75 mg, 0.052 mmol), diisopropylethylamine (36 μ L, 0.209 mmol) and reagent **1** (21 mg, 0.052 mmol). The product was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 30-100% CH₃CN/H₂O with 0.1% TFA. The fractions collected were combined and lyophilized (61 mg, 0.038 mmol, 72%). ¹H NMR (DMSO-d₆, 600 MHz):

δ 10.68 (s, 1H), 8.18 (d, J = 8 Hz, 1H), 8.09 (dd, J = 5.6 Hz, 1H), 8.02 (d, J = 7.6 Hz, 1H), 7.91-7.98 (m, 3H), 7.89 (d, J = 8.1 Hz, 1H), 7.84 (d, J = 8.7 Hz, 1H), 7.79 (d, J = 8.7 Hz, 1H), 7.71 (d, J = 9.1 Hz, 1H), 7.56 (d, J = 8.9 Hz, 1H), 7.53 (d, J = 8.2 Hz, 1H), 7.16-7.28 (m, 9H), 7.10-7.15 (m, 1H), 7.04-7.09 (m, 3H), 7 (t, J = 7.4 Hz, 1H), 6.96 (d, J = 8.3 Hz, 2H), 6.92 (t, J = 7.5 Hz, 1H), 6.6 (d, J = 16 Hz, 1H), 6.56 (d, J = 8.1 Hz, 2H), 6.3 (dt, J = 16.0, 6.3 Hz, 1H), 4.63 (d, J = 6.1 Hz, 2H), 4.55 (ddd, J = 8.4, 8.4, 8.4 Hz, 1H),

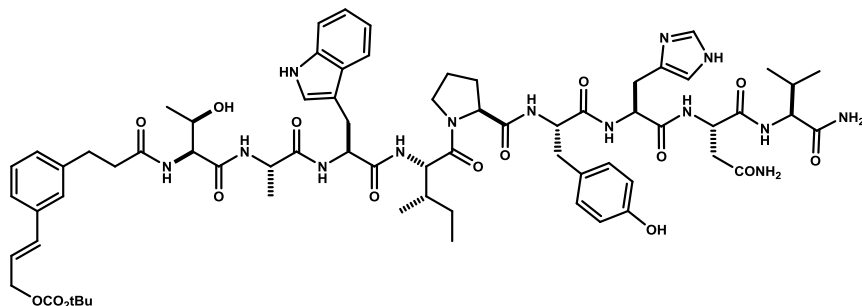
4.63 (ddd, $J = 8.7, 8.7, 4.2$ Hz, 1H), 6.06 (ddd, $J = 8.0, 8.0, 5.0$ Hz, 1H), 4.12-4.36 (m, 4H), 4.14-4.23 (m, 3H), 4.06 (dd, $J = 8.8, 6.7$ Hz, 1H), 3.71 (dd, $J = 16.5, 5.8$ Hz, 1H), 3.61-3.66 (m, 1H), 3.44-3.60 (m, 5H), 3.06 (dd, $J = 14.3, 3.9$ Hz, 1H), 3.01 (dd, $J = 13.9, 3.7$ Hz, 1H), 2.84-2.93 (m, 2H), 2.67-2.79 (m, 4H), 1.84-2.03 (m, 5H), 1.73-1.81 (m, 2H), 1.61-1.69 (m, 1H), 1.39 (s, 9H), 1.32-1.38 (m, 1H), 1.04 (d, $J = 7$ Hz, 3H), 0.96-1.03 (m, 1H), 0.87 (d, $J = 6.4$ Hz, 3H), 0.70-0.83 (m, 21H). ^{13}C NMR (DMSO- d_6 , 150 MHz): δ 173.1, 172.4, 172.3, 171.64, 171.56, 171.1, 171.03, 171.00, 170.9, 170.2, 170.05, 170.01, 168.8, 156.1, 153.1, 142.0, 138.0, 136.3, 136.2, 133.8, 130.3, 129.6, 128.9, 128.34, 128.26, 127.9, 127.6, 126.7, 126.5, 124.6, 123.9, 123.7, 121.1, 118.7, 118.5, 115.2, 111.5, 110.3, 81.8, 67.2, 62.1, 62.0, 59.89, 57.90, 57.7, 57.1, 56.0, 55.3, 55.2, 54.7, 53.9, 53.7, 48.6, 47.4, 42.4, 37.6, 37.2, 36.9, 36.6, 31.1, 31.0, 30.7, 30.4, 29.5, 27.7, 24.7, 24.5, 19.6, 19.6, 19.5, 18.4, 18.2. MS (ESI) Calculated for $\text{C}_{83}\text{H}_{114}\text{N}_{14}\text{O}_{19}$ $[\text{M}+2\text{H}]^{2+}$: 806.4, found 806.2.

Acyclic-Trp-Leu-Gln-Met-Thr-Gly-Phe-Tyr (S33):



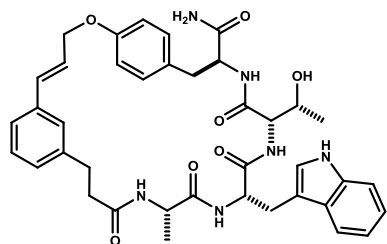
Following general procedure A, the corresponding compound was prepared from H-WLQMTGFY-NH₂ ($\bullet$ TFA, 83 mg, 0.072 mmol), diisopropylethylamine (50 μL , 0.287 mmol) and reagent **1**

(29 mg, 0.072 mmol). The product was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 40-100% $\text{CH}_3\text{CN}/\text{H}_2\text{O}$ with 0.1% TFA. The fractions collected were combined and lyophilized (61 mg, 0.046 mmol, 64%). ^1H NMR (DMSO- d_6 , 500 MHz): δ 10.74 (d, $J = 1.6$ Hz, 1H), 7.97-8.10 (m, 7H), 7.73 (d, $J = 8.1$ Hz, 1H), 7.59 (d, $J = 7.8$ Hz, 1H), 7.29 (d, $J = 8.2$ Hz, 1H), 7.11-7.26 (m, 10H), 7.08 (d, $J = 2.6$ Hz, 1H), 6.97-7.05 (m, 5H), 6.95 (t, $J = 7.9$ Hz, 1H), 6.78 (br. s, $J =$ Hz, 1H), 6.62 (d, $J = 8.4$ Hz, 2H), 6.58 (d, $J = 16.1$ Hz, 1H), 6.3 (dt, $J = 16.1, 6.2$ Hz, 1H), 4.64 (dd, $J = 6.3, 1.1$ Hz, 2H), 4.55 (ddd, $J = 8.6, 8.6, 4.6$ Hz, 1H), 4.46 (ddd, $J = 8.7, 8.7, 4.7$ Hz, 1H), 4.41 (ddd, $J = 8.4, 8.4, 4.8$ Hz, 1H), 4.27-4.33 (m, 2H), 4.23 (dq, $J = 7.7, 7.7$ Hz, 1H), 4.18 (dd, $J = 8.0, 3.9$ Hz, 1H), 3.91-3.97 (m, 1H), 3.68 (dd, $J = 17.0, 5.4$ Hz, 1H), 3.62 (dd, $J = 16.7, 5.2$ Hz, 1H), 3.08 (dd, $J = 14.6, 4.2$ Hz, 1H), 2.93 (dd, $J = 13.7, 4.4$ Hz, 1H), 2.83-2.91 (m, 2H), 2.60-2.72 (m, 4H), 2.30-2.46 (m, 4H), 2.06-2.13 (m, 2H), 1.98 (s, 3H), 1.81-1.96 (m, 2H), 1.70-1.81 (m, 2H), 1.49-1.61 (m, 1H), 1.36-1.46 (m, 11H), 0.85 (d, $J = 6.4$ Hz, 3H), 0.81 (d, $J = 6.6$ Hz, 3H). ^{13}C NMR (DMSO- d_6 , 125 MHz): δ 174.3, 173.3, 172.4, 172.1, 171.8, 171.7, 171.6, 171.0, 170.7, 169.0, 156.2, 153.3, 142.2, 138.1, 136.5, 136.3, 133.9, 130.6, 129.7, 129.1, 128.5, 128.4, 128.3, 127.9, 126.9, 126.7, 124.6, 124.1, 123.7, 121.2, 119.0, 118.6, 115.3, 111.7, 110.6, 82.0, 67.4, 67.1, 58.7, 54.7, 54.5, 53.7, 52.6, 52.3, 51.5, 42.4, 41.3, 38.0, 37.3, 37.3, 32.2, 31.9, 31.4, 30.0, 28.2, 28.1, 27.8, 24.6, 23.5, 22.2, 20.0, 15.1. MS (ESI) Calculated for $\text{C}_{68}\text{H}_{89}\text{N}_{11}\text{O}_{15}\text{S}$ $[\text{M}+\text{H}]^+$: 1332.6, found 1332.2.

Acyclic-Thr-Ala-Trp-Ile-Pro-Tyr-His-Asn-Val (S34):

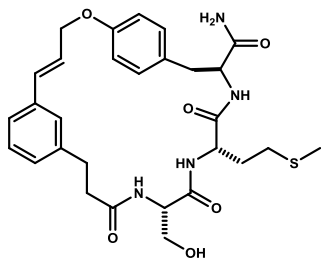
Following general procedure A, the corresponding compound was prepared from H-TAWIPYHNV-NH₂ ($\cdot$ 2TFA, 196 mg, 0.148 mmol), diisopropylethylamine (103 μ L, 0.591 mmol) and reagent

1 (60 mg, 0.148 mmol). The product was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 30-100% CH₃CN/H₂O with 0.1% TFA. The fractions collected were combined and lyophilized (131 mg, 0.095 mmol, 64%). ¹H NMR (DMSO-d₆, 500 MHz): δ 10.76 (s, 1H), 8.92 (s, 1H), 8.31 (d, J = 7.1 Hz, 1H), 8.18 (d, J = 7.7 Hz, 1H), 7.89-7.98 (m, 2H), 7.84 (d, J = 7.2 Hz, 1H), 7.77-7.81 (m, 2H), 7.47 (d, J = 7.9 Hz, 1H), 7.44 (s, 1H), 7.38 (s, 1H), 7.33 (s, 1H), 7.25-7.29 (m, 2H), 7.16-7.24 (m, 2H), 7.04-7.09 (m, 3H), 6.90-7.03 (m, 4H), 6.91 (d, J = 7.3 Hz, 1H), 6.56-6.62 (m, 3H), 6.29 (dt, J = 15.8, 6.2 Hz, 1H), 4.63 (dd, J = 6.2, 0.9 Hz, 2H), 4.49-4.61 (m, 3H), 4.18-4.32 (m, 5H), 4.04-4.08 (m, 1H), 3.9 (ddd, J = 10.0, 10.0, 5.7 Hz, 1H), 3.50-3.56 (m, 1H), 3.41-3.47 (m, 1H), 3.00-3.10 (m, 2H), 2.86-2.97 (m, 2H), 2.75-2.82 (m, 2H), 2.41-2.57 (m, 5H), 2 (dq, J = 13.5, 6.8 Hz, 1H), 1.82-1.91 (m, 1H), 1.59-1.75 (m, 4H), 1.41-1.48 (m, 1H), 1.39 (s, 9H), 0.92 (d, J = 6.2 Hz, 3H), 0.71-0.81 (m, 12H). ¹³C NMR (DMSO-d₆, 125 MHz): δ 173.0, 172.2, 172.0, 171.9, 171.5, 171.3, 171.2, 170.3, 170.2, 169.8, 161.8, 156.1, 153.1, 142.0, 136.3, 136.1, 134.0, 133.8, 130.3, 129.3, 128.9, 128.4, 128.0, 127.7, 126.7, 124.5, 123.9, 123.6, 121.1, 118.7, 118.5, 117.3, 116.7, 115.2, 114.8, 112.9, 111.5, 110.0, 81.8, 67.2, 66.9, 59.6, 58.3, 57.9, 54.9, 53.5, 51.6, 50.3, 48.6, 37.1, 36.9, 36.4, 31.3, 30.4, 29.2, 27.7, 24.5, 24.4, 24.3, 19.8, 19.6, 18.4, 17.8, 15.3, 11.1. MS (ESI) Calculated for C₇₀H₉₄N₁₄O₁₆ [M+H]⁺: 1387.7, found 1387.4.

Data for macrocyclic compounds:**Cyclic-Ala-Trp-Thr-Tyr (4):**

Following general procedure B, the corresponding compound was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 35-100% CH₃CN/H₂O with 0.1% TFA. The fractions collected were combined and lyophilized (8 mg, 0.011 mmol, 78%). ¹H NMR (DMSO-d₆, 500 MHz): δ 10.81 (d, J = 1.8 Hz, 1H), 8.1 (d, J = 7.5 Hz, 1H), 8.01 (d, J = 7.4 Hz, 1H), 7.68 (d, J = 8.1 Hz, 1H), 7.51 (d, J = 8.1 Hz, 1H), 7.25-7.36 (m, 3H), 7.06-7.22 (m, 5H), 6.89-7.05 (m, 3H), 6.79 (d, J = 8.7 Hz, 2H), 6.61 (d, J = 8.3 Hz, 2H), 6.53 (d, J = 15.9 Hz, 1H), 2.28 (dt, J = 16.0, 5.7 Hz, 1H), 4.15 (d, J = 5.4 Hz, 2H), 4.31-4.42 (m, 3H), 4.07-4.14 (m, 1H), 3.91-3.99 (m, 1H), 2.86-3.16 (m, 4H), 2.65-2.80 (m, 3H), 2.23-3.38 (m, 1H),

0.94 (d, $J = 7.5$ Hz, 3H), 0.86 (d, $J = 6.4$ Hz, 3H). ^{13}C NMR (DMSO- d_6 , 125 MHz): δ 173.6, 173.4, 172.9, 172.1, 169.9, 156.2, 141.8, 136.5, 132.7, 130.4, 130.3, 128.9, 128.5, 128.3, 127.8, 126.0, 125.7, 124.8, 124.2, 121.3, 118.7, 115.4, 115.1, 111.8, 110.2, 68.2, 67.0, 66.6, 58.4, 54.6, 49.0, 36.1, 30.7, 27.5, 19.5, 18.1. MS (ESI) Calculated for $\text{C}_{39}\text{H}_{44}\text{N}_6\text{O}_7$ $[\text{M}+\text{H}]^+$: 709.3, found 709.0.

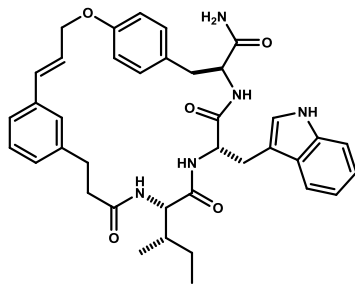


Cyclic-Ser-Met-Tyr (5):

Following general procedure B, the corresponding compound was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 35-100% $\text{CH}_3\text{CN}/\text{H}_2\text{O}$ with 0.1% TFA. The fractions collected were combined and lyophilized (15 mg, 0.026 mmol, 80%). ^1H NMR (DMSO- d_6 , 600 MHz): δ 7.96 (d, $J = 8.2$ Hz, 1H), 7.92 (d, $J = 7.9$ Hz, 1H), 7.75 (d, $J = 7.9$ Hz, 1H), 7.37 (s, 1H), 7.24 (s, 1H), 7.13-7.21 (m, 2H), 7.04-7.11 (m, 3H),

7.00 (d, $J = 8.1$ Hz, 1H), 6.81 (d, $J = 8.46$ Hz, 2H), 6.60 (d, $J = 15.9$, 1H), 6.36 (dt, $J = 16.1$, 5.7 Hz, 1H), 4.77 (d, $J = 5.5$ Hz, 2H), 4.21-4.31 (m, 2H), 4.14 (ddd, $J = 6.9$, 6.9, 6.9 Hz, 1H), 3.12 (dd, $J = 10.6$, 5.3 Hz, 1H), 3.06 (d, $J = 10.9$, 6.9 Hz, 1H), 2.89 (app d, $J = 14.2$ Hz, 1H), 2.68-2.84 (m, 3H), 2.55-2.64 (m, 1H), 2.27-2.39 (m, 3H), 1.96 (s, 1H), 1.74-1.82 (m, 1H), 1.58-1.66 (m, 1H). ^{13}C NMR (DMSO- d_6 , 150 MHz): δ 173.3, 171.8, 171.2, 170.2, 156.8, 141.4, 136.2, 132.8, 130.3, 130.0, 128.8, 128.6, 126.0, 125.6, 124.5, 115.0, 68.0, 62.2, 54.7, 54.1, 52.1, 36.4, 35.3, 31.9, 30.7, 29.7, 14.9. MS (ESI) Calculated for $\text{C}_{29}\text{H}_{36}\text{N}_4\text{O}_6\text{S}$ $[\text{M}+\text{H}]^+$: 569.2, found 569.2.

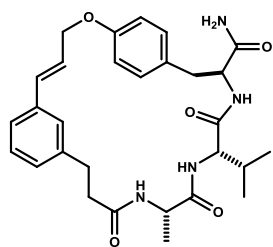
Cyclic-Ile-Trp-Tyr (6):



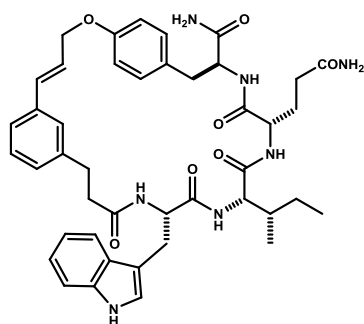
Following general procedure B, the corresponding compound was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 35-100% $\text{CH}_3\text{CN}/\text{H}_2\text{O}$ with 0.1% TFA. The fractions collected were combined and lyophilized (12 mg, 0.019 mmol, 72%).

^1H NMR (DMSO- d_6 , 500 MHz): 10.8 (d, $J = 1.8$ Hz, 1H), 7.81 (d, $J = 8.3$ Hz, 1H), 7.59 (d, $J = 7.8$ Hz, 1H), 7.52 (br. s, $J =$ Hz, 1H), 7.36 (d, $J = 8.5$ Hz, 1H), 7.31 (br. d, $J = 7.9$ Hz, 1H), 7.19 (br. s, $J =$ Hz, 1H), 7.09-7.06

(m, 3H), 6.92-7.07 (m, 6H), 6.8 (d, $J = 8.7$ Hz, 2H), 6.68 (d, $J = 16$ Hz, 1H), 6.51 (dt, $J = 15.8$, 6.4 Hz, 1H), 4.66-4.77 (m, 2H), 4.54 (ddd, $J = 8.3$, 8.3, 5.6 Hz, 1H), 4.24 (ddd, $J = 8.2$, 8.2, 4.8 Hz, 1H), 3.84 (app. dd, $J = 8.0$, 6.9 Hz, 1H), 2.95 (ddd, $J = 15.0$, 5.4 Hz, 1H), 2.68-2.90 (m, 6H), 2.27-2.35 (m, 1H), 1.11-1.19 (m, 1H), 0.57-0.71 (m, 2H), 0.26-0.31 (m, 3H), 0.08 (d, $J = 6.7$ Hz, 3H). ^{13}C NMR (DMSO- d_6 , 125 MHz): δ 173.9, 171.6, 171.4, 170.9, 157.2, 140.9, 136.7, 136.5, 134.3, 130.6, 129.9, 129.1, 128.7, 127.7, 125.8, 125.6, 125.3, 124.2, 121.3, 119.0, 118.6, 114.7, 111.8, 110.4, 68.5, 56.8, 54.6, 53.0, 38.2, 36.7, 34.9, 30.9, 27.1, 23.8, 15.1, 11.3. MS (ESI) Calculated for $\text{C}_{38}\text{H}_{43}\text{N}_5\text{O}_5$ $[\text{M}+\text{H}]^+$: 650.3, found 650.0

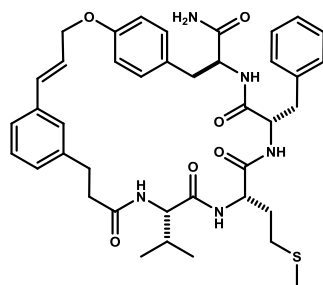
Cyclic-Ala-Val-Tyr (7):

Following general procedure B, the corresponding compound was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 35-100% CH₃CN/H₂O with 0.1% TFA. The fractions collected were combined and lyophilized (10 mg, 0.020 mmol, 78%). ¹H NMR (DMSO-d₆, 600 MHz): δ 7.82 (d, J = 8.9 Hz, 1H), 7.69 (d, J = 8.8 Hz, 1H), 7.52 (d, J = 7.1 Hz, 1H), 7.22 (s, 1H), 7.15-7.20 (m, 3H), 7.08 (s, 1H), 7.00-7.05 (m, 3H), 6.78 (d, J = 8.5 Hz, 2H), 6.64 (d, J = 16.0 Hz, 1H), 6.31 (dt, J = 15.8, 6.0 Hz, 1H), 4.74 (d, J = 5.8 Hz, 2H), 5.82 (ddd, J = 9.8, 9.8, 2.9 Hz, 1H), 4.74 (dq, J = 7.0, 7.0 Hz, 1H), 3.93 (dd, J = 8.6, 8.6 Hz, 1H), 2.81-2.89 (m, 2H), 2.71-2.79 (m, 2H), 2.53-2.60 (m, 1H), 2.21-2.27 (m, 1H), 1.81 (dddd, J = 13.5, 6.5, 6.5, 6.5 Hz, 1H), 1.38 (d, J = 6.8 Hz, 3H), 0.63 (d, J = 6.6 Hz, 6H). ¹³C NMR (DMSO-d₆, 150 MHz): δ 173.5, 172.2, 171.3, 170.9, 157.0, 141.4, 136.0, 133.2, 130.0, 129.7, 128.8, 128.8, 125.9, 125.5, 125.0, 114.9, 68.2, 58.4, 53.3, 47.9, 36.4, 35.8, 31.1, 29.9, 19.5, 19.4, 18.4. MS (ESI) Calculated for C₂₉H₃₆N₄O₅ [M+H]⁺: 521.3, found 521.2.

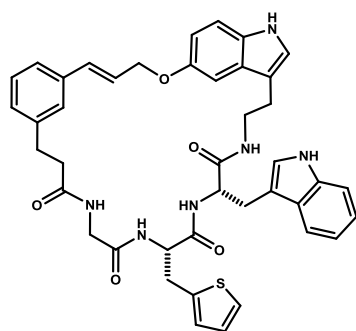
Cyclic-Trp-Ile-Gln-Tyr (8):

Following general procedure B, the corresponding compound was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 35-100% CH₃CN/H₂O with 0.1% TFA. The fractions collected were combined and lyophilized (11 mg, 0.014 mmol, 81%). ¹H NMR (DMSO-d₆, 500 MHz): δ 10.76 (d, J = 1.9 Hz, 1H), 8.22 (d, J = 7.8 Hz, 1H), 7.83 (d, J = 7.5 Hz, 1H), 7.79 (d, J = 7.8 Hz, 1H), 7.53 (d, J = 7.8 Hz, 1H), 7.37 (br. s, 1H), 7.27-7.34 (m, 2H), 7.16-7.25 (m, 3H), 7.08-7.15 (m, 3H), 6.99-7.08 (m, 4H), 6.95 (t, J = 7.4 Hz, 1H), 6.81 (d, J = 8.7 Hz,

2H), 6.73 (br. s, 1H), 6.61 (d, J = 16 Hz, 1H), 6.35 (dt, J = 15.9, 5.6 Hz, 1H), 4.69-4.79 (m, 2H), 4.38 (ddd, J = 9.6, 7.8, 4.4 Hz, 1H), 4.32 (ddd, J = 10.8, 7.7, 3.1 Hz, 1H), 4.2 (dd, J = 8.0, 5.7 Hz, 1H), 4.12 (ddd, J = 7.9, 7.9, 5.1 Hz, 1H), 3.14 (dd, J = 15.0, 4.3 Hz, 1H), 2.85-2.96 (m, 2H), 2.74-2.83 (m, 1H), 2.63-2.74 (m, 2H), 2.30-2.41 (m, 2H), 1.99-2.15 (m, 1H), 1.78-1.93 (m, 1H), 1.57-1.73 (m, 2H), 1.17-1.31 (m, 1H), 0.89-1.01 (m, 1H), 0.64-0.74 (m, 6H). ¹³C NMR (DMSO-d₆, 125 MHz): δ 174.3, 174.0, 172.5, 171.83, 171.81, 170.8, 157.0, 142.2, 136.6, 136.5, 132.7, 130.4, 130.2, 129.0, 128.1, 127.7, 126.6, 125.6, 124.7, 123.7, 121.4, 118.8, 118.7, 115.0, 111.8, 110.9, 68.1, 56.6, 54.8, 54.6, 52.6, 37.8, 36.9, 36.7, 32.0, 30.9, 28.0, 27.5, 24.5, 15.6, 11.8. MS (ESI) Calculated for C₄₃H₅₁N₇O₇ [M+H]⁺: 778.4, found 778.0.

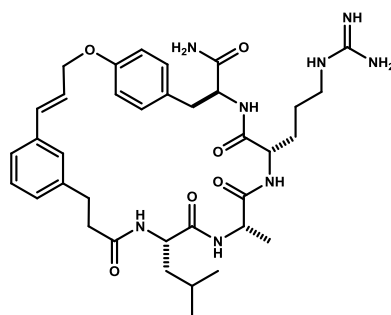
Cyclic-Val-Met-Phe-Tyr (9):

Following general procedure B, the corresponding compound was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 35-100% CH₃CN/H₂O with 0.1% TFA. The fractions collected were combined and lyophilized (9 mg, 0.012 mmol, 73%). ¹H NMR (DMSO-d₆, 600 MHz): δ 8.24 (d, J = 8.6 Hz, 1H), 8.04 (d, J = 7.0 Hz, 1H), 7.82 (d, J = 8.9 Hz, 1H), 7.39-7.43 (m, 2H), 7.09-7.22 (m, 11H), 7.01 (d, J = 6.7 Hz, 1H), 6.82 (d, J = 8.7 Hz, 2H), 6.72 (d, J = 15.7 Hz, 1H), 6.53 (ddd, J = 16.0, 6.6, 4.9 Hz, 1H), 4.74-4.85 (m, 2H), 4.32-4.41 (m, 2H), 4.09-4.16 (m, 2H), 3.13 (dd, J = 13.8, 4.8 Hz, 1H), 2.94 (dd, J = 14.0, 2.5 Hz, 1H), 2.77-2.85 (m, 4H), 2.65 (dd, J = 13.9, 11.6 Hz, 1H), 2.26-2.40 (m, 3H), 1.97 (s, 3H), 1.66-2.04 (m, 3H), 0.254 (d, J = 6.9 Hz, 3H), 0.17 (d, J = 6.7 Hz, 3H). ¹³C NMR (DMSO-d₆, 100 MHz): δ 173.5, 171.5, 171.4, 170.8, 170.1, 156.7, 140.8, 137.0, 136.2, 132.3, 130.0, 129.8, 129.5, 128.5, 128.2, 127.8, 126.2, 125.7, 124.9, 124.6, 114.2, 67.8, 56.7, 54.6, 53.0, 52.4, 48.6, 36.9, 36.8, 34.8, 31.1, 30.4, 29.3, 18.7, 16.2, 14.4. MS (ESI) Calculated for C₄₀H₄₉N₅O₆S [M+H]⁺: 728.3, found 728.2.

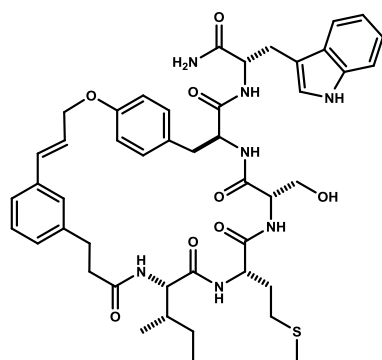
Cyclic-Gly-Thi-Trp-5HT (10):

Following general procedure B, the corresponding compound was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 35-100% CH₃CN/H₂O with 0.1% TFA. The fractions collected were combined and lyophilized (16 mg, 0.021 mmol, 69%). ¹H NMR (DMSO-d₆, 500 MHz): δ 10.79 (s, 1H), 10.60 (s, 1H), 8.57 (d, J = 7.6 Hz, 1H), 8.47 (t, J = 5.5 Hz, 1H), 7.87 (d, J = 8.5 Hz, 1H), 7.81 (t, J = 5.9 Hz, 1H), 7.53-7.56 (m, 2H), 7.48 (d, J = 7.9 Hz, 1H), 7.46 (d, J = 7.9 Hz, 1H), 7.32-7.37 (m, 2H), 7.30 (d, J = 7.7 Hz, 1H), 7.23-7.27 (m, 2H), 7.22 (d, J

= 7.7 Hz, 1H), 7.19 (d, J = 2.0 Hz, 1H), 7.15-7.18 (m, 2H), 7.10 (d, J = 1.9 Hz, 1H), 7.03 (d, J = 1.9 Hz, 1H), 7.03 (d, J = 7.9 Hz, 2H), 6.96 (dd, J = 7.4, 7.4 Hz, 1H), 6.84 (dd, J = 5.0, 3.3 Hz, 1H), 6.78-6.80 (m, 1H), 6.76 (d, J = 16.1 Hz, 1H), 6.71 (dd, J = 8.7, 2.3 Hz, 1H), 6.38 (dt, J = 16.0, 6.1 Hz, 1H), 4.52 (ddd, J = 9.2, 9.2, 4.6 Hz, 1H), 4.28 (ddd, J = 10.5, 7.6, 3.7 Hz, 1H), 3.82 (dd, J = 15.8, 5.4 Hz, 1H), 3.49 (dd, J = 15.7, 5.8 Hz, 1H), 3.42-3.46 (m, 1H), 3.30 (dd, J = 14.6, 4.7 Hz, 1H), 3.08-3.16 (m, 2H), 2.99-3.07 (m, 1H), 2.87-2.95 (m, 2H), 2.75 (ddd, J = 14.5, 10.6, 5.2 Hz, 1H), 2.65-2.71 (m, 1H), 2.62 (ddd, J = 15.3, 10.5, 5.8 Hz, 1H), 2.28 (ddd, J = 15.4, 8.4, 6.6 Hz, 1H). ¹³C NMR (DMSO-d₆, 125 MHz): δ 173.4, 171.4, 170.5, 151.4, 142.5, 140.1, 137.0, 136.5, 133.8, 132.0, 129.0, 128.3, 127.84, 127.80, 127.3, 127.1, 126.7, 126.1, 125.0, 123.9, 123.8, 121.4, 121.3, 118.83, 118.77, 112.8, 112.5, 111.84, 111.77, 110.9, 103.7, 68.9, 55.9, 54.3, 43.4, 36.9, 31.3, 30.5, 27.8. MS (ESI) Calculated for C₄₂H₄₂N₆O₅S [M+H]⁺: 743.3, found 743.2.

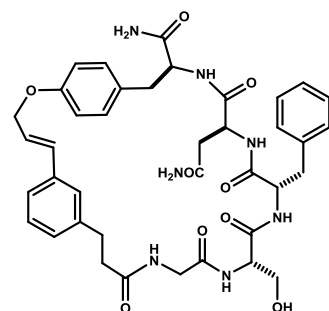
Cyclic- Ile-Ala-Arg-Tyr (11):

Following general procedure B, the corresponding compound was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 35-100% CH₃CN/H₂O with 0.1% TFA. The fractions collected were combined and lyophilized (13 mg, 0.019 mmol, 84%). ¹H NMR (DMSO-d₆, 600 MHz): δ 8.01 (d, J = 7.4 Hz, 1H), 7.83 (d, J = 7.0 Hz, 1H), 7.72 (d, J = 8.1 Hz, 1H), 7.62 (d, J = 7.1 Hz, 1H), 7.44 (dd, J = 5.8, 5.8 Hz, 1H), 7.31 (br s, 1H), 7.21-7.25 (m, 1H), 7.19 (dd, J = 7.5, 7.5 Hz, 1H), 7.07-7.12 (m, 4H), 7.05 (d, J = 7.6 Hz, 1H), 6.81 (d, J = 8.5 Hz, 2H), 6.60 (d, J = 16.3 Hz, 1H), 6.34 (dt, J = 16.1, 5.4 Hz, 1H), 4.71 (d, J = 5.3 Hz, 2H), 4.35 (ddd, J = 11.2, 8.3, 3.0 Hz, 1H), 4.05-4.15 (m, 3H), 2.96-3.03 (m, 3H), 2.85 (ddd, J = 13.8, 7.1, 7.1 Hz, 1H), 2.72 (ddd, J = 13.8, 6.8, 6.8 Hz, 1H), 2.64 (dd, J = 13.9, 11.4 Hz, 1H), 2.41-2.45 (m, 2H), 1.54-1.62 (m, 1H), 1.28-1.46 (m, 6H), 1.00 (d, J = 7.2 Hz, 3H), 0.76 (d, J = 6.1 Hz, 3H), 0.72 (d, J = 6.2 Hz, 3H). ¹³C NMR (DMSO-d₆, 125 MHz): δ 173.7, 172.7, 172.6, 172.5, 171.6, 158.9, 158.6, 141.9, 136.6, 132.6, 132.5, 130.4, 130.1, 128.9, 128.4, 126.9, 125.7, 124.3, 117.8, 115.4, 115.0, 68.2, 54.3, 52.6, 51.8, 48.8, 40.9, 36.8, 36.5, 30.9, 29.3, 25.3, 24.5, 23.4, 21.8, 18.5. MS (ESI) Calculated for C₃₆H₅₀N₈O₆ [M+H]⁺: 691.4, found 691.3.

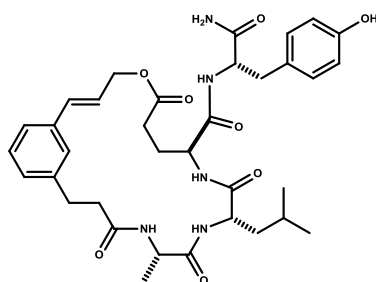
Cyclic-Ile-Met-Ser-Tyr-Trp (12):

Following general procedure B, the corresponding compound was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 35-100% CH₃CN/H₂O with 0.1% TFA. The fractions collected were combined and lyophilized (18 mg, 0.027 mmol, 73%). ¹H NMR (DMSO-d₆, 500 MHz): δ 10.79 (s, 1H), 8.11 (d, J = 7.5 Hz, 1H), 7.97 (d, J = 8.1 Hz, 1H), 7.89 (d, J = 8.2 Hz, 1H), 7.81 (d, J = 7.5 Hz, 1H), 7.58 (d, J = 8.0 Hz, 1H), 7.55 (d, J = 7.2 Hz, 1H), 7.30 (d, J = 8.0 Hz, 1H), 7.17-7.24 (m, 4H), 7.11-7.16 (m, 4H), 7.01-7.08 (m, 2H), 6.97 (dd, J = 7.3, 7.3 Hz), 6.83 (d, J = 8.6 Hz, 2H), 6.56 (d, J = 15.9 Hz, 1H), 6.39 (dt, J = 16.1, 5.5 Hz, 1H), 4.76 (d, J = 5.2 Hz, 2H), 4.43 (ddd, J = 8.5, 8.5, 5.2 Hz, 1H), 4.22-4.33 (m, 3H), 4.10 (dd, J = 8.4, 6.0 Hz, 1H), 3.55 (dd, J = 10.4, 6.0 Hz, 1H), 3.49 (dd, J = 10.5, 6.7 Hz, 1H), 3.16 (dd, J = 14.7, 4.9 Hz, 1H), 2.82-2.96 (m, 3H), 2.70-2.77 (m, 1H), 2.50-2.60 (m, 2H), 2.40-2.46 (m, 1H), 2.27-2.39 (m, 1H), 1.92 (s, 3H), 1.71-1.89 (m, 2H), 1.60-1.69 (m, 1H), 1.12-1.20 (m, 1H), 0.85-0.95 (m, 1H), 0.56-0.62 (m, 6H). ¹³C NMR (DMSO-d₆, 125 MHz): δ 173.8, 172.3, 171.49, 171.48, 171.3, 171.1, 157.1, 141.8, 136.7, 136.5, 132.7, 130.6, 130.2, 128.9, 128.6, 127.8, 126.2, 125.6, 124.7, 123.9, 121.3, 118.9, 118.8, 114.9, 111.7, 110.7, 68.1, 61.9, 57.7, 55.7, 55.2, 54.0, 52.2, 36.9, 36.4, 36.3, 32.0, 31.0, 29.6, 28.1, 24.5, 15.9, 14.9, 11.4. MS (ESI) Calculated for C₄₆H₅₇N₇O₈S [M+H]⁺: 868.4, found 868.0.

Cyclic-Gly-Ser-Phe-Asn-Tyr (14):

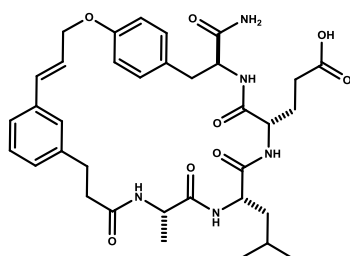


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Cyclic-Ala-Leu-Glu-Tyr (16):

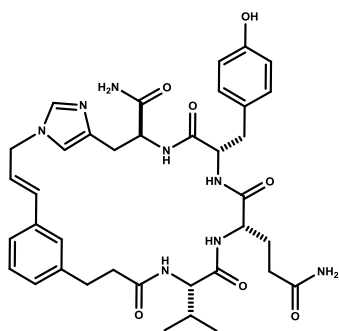
Following general procedure B, the corresponding compound was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 35-100% CH₃CN/H₂O with 0.1% TFA. The fractions collected were combined and lyophilized (17 mg, 0.026 mmol, 67%). ¹H NMR (DMSO-d₆, 600 MHz): δ 8.03 (d, J = 5.8 Hz, 1H), 7.99 (d, J = 7.2 Hz, 1H), 7.93 (d, J = 9.1 Hz, 1H), 7.45 (d, J = 7.9 Hz, 1H), 7.35-7.42 (m, 2H), 7.12-7.19 (m, 2H), 6.98-7.06 (m, 2H), 6.96 (d, J = 8.1 Hz, 2H),

6.59 (d, J = 8.2 Hz, 2H), 6.54 (d, J = 16.6 Hz, 1H), 6.33 (dt, J = 15.9, 4.6 Hz, 1H), 4.80-4.87 (m, 1H), 4.54-4.61 (m, 1H), 4.13-4.35 (m, 4H), 2.78-2.92 (m, 2H), 2.61-2.71 (m, 1H), 2.22-2.40 (m, 3H), 1.64-1.74 (m, 1H), 1.62-1.61 (m, 1H), 1.32-1.46 (m, 2H), 0.99 (d, J = 6.2 Hz, 3H), 0.85 (d, J = 6.2 Hz, 3H), 0.81 (d, J = 7.0 Hz, 3H). ¹³C NMR (DMSO-d₆, 150 MHz): δ 173.1, 172.6, 172.4, 172.3, 171.6, 170.7, 156.1, 141.7, 136.4, 131.6, 130.4, 128.7, 128.4, 128.0, 125.5, 124.4, 123.9, 115.2, 63.4, 54.2, 51.6, 51.5, 48.4, 37.2, 34.1, 30.0, 29.9, 27.9, 24.5, 23.2, 22.1, 19.2. MS (ESI) Calculated for C₃₅H₄₅N₅O₈ [M+H]⁺: 664.3, found 664.2.

Cyclic-Ala-Leu-Glu-Tyr (17):

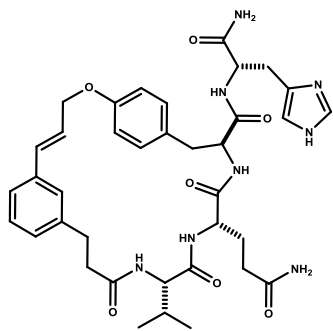
Following general procedure B, the corresponding compound was isolated by preparative HPLC (Waters Xbridge RP18 20x250 mm) using a gradient of 35-100% CH₃CN/H₂O with 0.1% TFA. The fractions collected were combined and lyophilized (11 mg, 0.160 mmol, 76%). ¹H NMR (DMSO-d₆, 600 MHz): δ 12.04 (s, 1H), 8.1 (d, J = 6.9 Hz, 1H), 7.82 (d, J = 7.8 Hz, 1H), 7.71 (d, J = 8 Hz, 1H), 7.56 (d, J = 7.2 Hz, 1H), 7.31 (br. s, J =

Hz, 1H), 7.17-7.22 (m, 3H), 7.02-7.13 (m, 4H), 6.83 (d, J = 8.6 Hz, 2H), 6.65 (d, J = 16 Hz, 1H), 6.37 (dt, J = 16.0, 5.6 Hz, 1H), 4.76 (d, J = 5.1 Hz, 2H), 4.32 (ddd, J = 10.9, 8.1, 3.1 Hz, 1H), 4.18 (dt, J = 7.6, 7.6 Hz, 1H), 4.02-4.13 (m, 2H), 2.96 (ddd, J = 14.2, 2.8 Hz, 1H), 2.76-2.82 (m, 2H), 2.67 (ddd, J = 14.3, 10.9 Hz, 1H), 2.36-2.42 (m, 1H), 2.11-2.23 (m, 2H), 1.79-1.89 (m, 1H), 1.66-1.76 (m, 1H), 1.57 (dddd, J = 13.3, 13.3, 6.7, 6.7 Hz, 1H), 1.40-1.48 (m, 2H), 1.03 (d, J = 7.2 Hz, 3H), 0.84 (d, J = 6.6 Hz, 3H), 0.81 (d, J = 6.6 Hz, 3H). ¹³C NMR (DMSO-d₆, 150 MHz): δ 173.9, 172.6, 172.2, 171.85, 171.8, 170.9, 156.6, 141.4, 136.0, 132.4, 132.3, 130.2, 128.3, 127.9, 126.0, 125.4, 124.3, 114.5, 67.7, 54.0, 51.6, 51.1, 48.9, 40.1, 36.3, 35.6, 30.2, 29.6, 26.7, 23.5, 22.9, 21.2, 17.3. MS (ESI) Calculated for C₃₅H₄₅N₅O₈ [M+H]⁺: 664.3, found 664.3.

Cyclic-Val-Gln-Tyr-His (19):

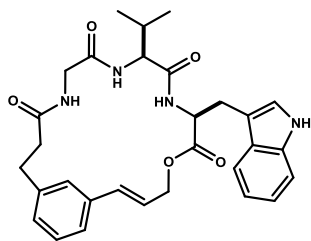
Following general procedure C, the corresponding compound was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 35-100% CH₃CN/H₂O with 0.1% TFA. The fractions collected were combined and lyophilized (14mg, 0.020 mmol, 75%). ¹H NMR (DMSO-d₆, 500 MHz): δ 9.16 (br. s, J = Hz, 1H), 9.02 (s, 1H), 8.31 (br. s, J = Hz, 1H), 8.1 (d, J = 8.3 Hz, 1H), 7.93 (d, J = 6.9 Hz, 1H), 7.73 (d, J = 5.6 Hz, 1H), 7.26-7.36 (m, 4H), 7.21 (d, J = 7.5 Hz, 1H), 7.15 (br. d, J = 7.8 Hz, 1H), 7.11 (br. d, J = 7.5 Hz, 1H), 7.01 (br. s, J = Hz, 1H), 6.97 (d, J = 8.6 Hz,

2H), 6.81 (br. s, J = Hz, 1H), 6.75 (d, J = 15.6 Hz, 1H), 6.59 (d, J = 8.4 Hz, 2H), 6.38 (dt, J = 15.4, 7.0 Hz, 1H), 4.92 (dd, J = 14.9, 5.9 Hz, 1H), 4.88 (dd, J = 14.9, 7.3 Hz, 1H), 4.47 (ddd, J = 10.6, 8.5, 3.4 Hz, 1H), 4.28 (ddd, J = 8.9, 7.9, 5.0 Hz, 1H), 3.99 (ddd, J = 7.8, 5.7, 5.7 Hz, 1H), 3.82-3.88 (m, 1H), 3.16 (dd, J = 15.2, 3.1 Hz, 1H), 2.86-2.94 (m, 2H), 2.79-2.85 (m, 2H), 2.74 (dd, J = 14.3, 9.4 Hz, 1H), 2.54-2.63 (m, 1H), 2.45-2.5 (m, 1H), 1.98-2.13 (m, 2H), 1.92 (ddd, J = 13.6, 12.5, 6.8 Hz, 1H), 1.77 (ddd, J = 13.8, 13.8, 7.0 Hz, 1H), 1.65 (ddd, J = 14.6, 14.6, 7.6 Hz, 1H), 0.67 (dd, J = 6.7, 2.0 Hz, 6H). ¹³C NMR (DMSO-d₆, 125 MHz): δ 174.0, 173.1, 173.0, 172.2, 172.1, 171.1, 155.7, 141.4, 135.7, 135.5, 134.8, 134.3, 130.7, 130.1, 129.0, 128.4, 125.6, 125.5, 122.2, 118.2, 114.9, 59.0, 54.7, 53.9, 51.1, 50.1, 35.9, 35.6, 31.1, 30.6, 29.0, 26.6, 26.4, 18.2. MS (ESI) Calculated for C₃₇H₄₆N₈O₇ [M+H]⁺: 715.4, found 715.0

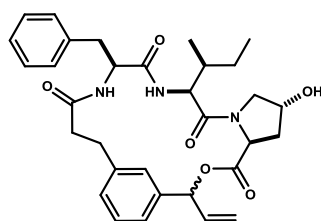
Cyclic-Val-Gln-Tyr-His (20):

Following general procedure C, the corresponding compound was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 35-100% CH₃CN/H₂O with 0.1% TFA. The fractions collected were combined and lyophilized (12 mg, 0.017 mmol, 68%). ¹H NMR (DMSO-d₆, 500 MHz): δ 8.95 (d, J = 1.1 Hz, 1H), 8.28 (d, J = 8.3 Hz, 1H), 7.92 (d, J = 6.9 Hz, 1H), 7.85 (d, J = 7.6 Hz, 1H), 7.50-7.55 (m, 2H), 7.34-7.38 (m, 2H), 7.28 (br. s, J = Hz, 2H), 7.14-7.17 (m, 2H), 7.13 (d, J = 8.7 Hz, 2H), 7.00-7.04 (m, 1H), 6.84 (d, J = 8.7 Hz, 2H), 6.81 (br. s, J = Hz, 1H), 6.67 (d, J =

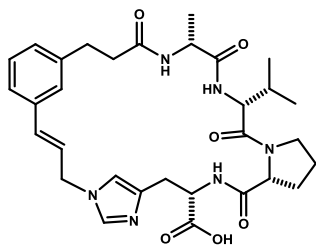
16 Hz, 1H), 6.55 (ddd, J = 15.9, 6.6, 5.6 Hz, 1H), 4.78 (dd, J = 14.5, 4.9 Hz, 1H), 4.7 (dd, J = 14.5, 6.9 Hz, 1H), 4.52 (ddd, J = 8.2, 8.2, 5.5 Hz, 1H), 4.26 (ddd, J = 10.0, 7.0, 2.4 Hz, 1H), 4.15 (ddd, J = 7.5, 7.5, 7.5 Hz, 1H), 3.94 (dd, J = 8.6, 6.7 Hz, 1H), 3.11 (dd, J = 15.5, 5.4 Hz, 1H), 2.92 (dd, J = 15.3, 8.2 Hz, 1H), 2.80-2.88 (m, 3H), 2.65 (dd, J = 14.1, 11.7 Hz, 1H), 2.33-2.42 (m, 1H), 1.96-2.09 (m, 2H), 1.71-1.80 (m, 1H), 1.55-1.64 (m, 1H), 1.42 (ddd, J = 13.4, 13.4, 6.7 Hz, 1H), 0.21 (d, J = 7.1 Hz, 3H), 0.19 (d, J = 7.8 Hz, 3H). ¹³C NMR (DMSO-d₆, 125 MHz): δ 174.5, 172.2, 171.9, 171.5, 171.0, 157.2, 141.0, 136.7, 134.14, 134.07, 130.6, 129.9, 129.6, 129.2, 128.7, 125.7, 125.4, 125.2, 117.3, 114.9, 68.4, 57.2, 55.5, 52.0, 51.8, 36.3, 34.4, 32.2, 31.8, 30.6, 27.4, 26.9, 19.1, 18.2. MS (ESI) Calculated for C₃₇H₄₆N₈O₇ [M+H]⁺: 715.4, found 715.4

Cyclic-Gly-Val-Trp (21):

Following general procedure B, the corresponding compound was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 35-100% CH₃CN/H₂O with 0.1% TFA. The fractions collected were combined and lyophilized (21 mg, 0.039 mmol, 74%). ¹H NMR (DMSO-d₆, 500 MHz): δ 10.82 (s, 1H), 8.31 (d, J = 7.2 Hz, 1H), 8.18 (dd, J = 6.8, 4.3 Hz, 1H), 7.55 (d, J = 8.3 Hz, 1H), 7.47 (d, J = 8.3 Hz, 1H), 7.27-7.31 (m, 2H), 8.10-7.18 (m, 3H), 7.00-7.05 (m, 2H), 6.95 (dd, J = 7.8, 7.8 Hz, 1H), 6.58 (d, J = 15.9 Hz, 1H), 6.11 (dt, J = 16.0, 5.3 Hz, 1H), 4.79 (ddd, J = 13.9, 5.0, 1.3 Hz, 1H), 4.40-4.48 (m, 2H), 4.02-4.48 (m, 2H), 4.02-4.14 (m, 3H), 3.57 (dd, J = 17.3, 3.9 Hz, 1H), 3.20 (dd, J = 14.8, 5.9 Hz, 1H), 3.10 (dd, J = 14.9, 9.1 Hz, 1H), 2.91-2.97 (m, 1H), 2.82 (ddd, J = 14.7, 8.9, 1.9 Hz, 1H), 2.59 (ddd, J = 15.2, 9.8, 2.1 Hz, 1H), 2.32 (ddd, J = 15.2, 8.9, 2.5 Hz, 1H), 1.90-1.98 (m, 1H), 0.69 (d, J = 6.8 Hz, 3H), 0.60 (d, J = 7.0 Hz, 3H). ¹³C NMR (DMSO-d₆, 125 MHz): δ 172.3, 171.6, 171.0, 169.4, 141.9, 136.5, 136.4, 131.4, 128.3, 128.2, 127.3, 125.4, 123.9, 123.5, 123.2, 120.9, 118.4, 117.9, 111.3, 110.0, 64.4, 57.1, 53.4, 42.2, 35.4, 30.6, 29.6, 26.3, 19.3, 17.0. MS (ESI) Calculated for C₃₀H₃₄N₄O₅ [M+H]⁺: 531.3, found 531.3.

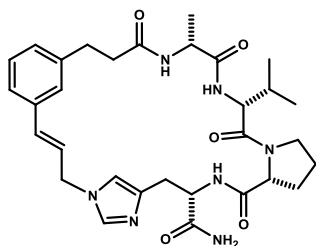
Cyclic-Phe-Leu-Hyp (22):

Following general procedure B, the corresponding compound was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 35-100% CH₃CN/H₂O with 0.1% TFA. The fractions collected were combined and lyophilized (16 mg, 0.029 mmol, 71%). ¹H NMR (DMSO-d₆, 500 MHz, mix of diastereomers): δ 8.35 (d, J = 7.6 Hz, 1H), 8.28 (d, J = 8.3 Hz, 1H), 8.13 (d, J = 8.4 Hz, 1H), 7.32-7.37 (m, 3H), 7.12-7.29 (m, 1H), 6.98-7.10 (m, 4H), 6.83 (ddd, J = 16.0, 9.0, 4.1 Hz, 1H), 6.65 (d, J = 16.2 Hz, 1H), 6.59 (d, J = 16.2 Hz, 1H), 6.12 (ddd, J = 16.2, 6.0, 4.0 Hz, 1H), 5.28 (ddd, J = 12.5, 3.9, 1.7 Hz, 1H), 5.02 (ddd, J = 14.1, 3.8, 1.7 Hz, 1H), 4.32-4.57 (m, 10H), 3.94-3.60 (m, 4H), 3.13 (dd, J = 14.2, 4.5 Hz, 2H), 2.94-3.07 (m, 3H), 2.64-2.73 (m, 3H), 2.50-2.58 (m, 2H), 2.38-2.46 (m, 2H), 2.24-2.34 (m, 2H), 2.07-2.21 (m, 2H), 1.88 (ddd, J = 13.7, 10.2, 4.1 Hz, 1H), 1.62-1.72 (m, 1H), 1.53 (ddd, J = 14.3, 12.4, 3.4 Hz, 1H), 1.32-1.43 (m, 1H), 1.18-1.29 (m, 3H), 1.06 (ddd, J = 14.2, 10.9, 3.4 Hz, 1H), 0.85 (d, J = 6.7 Hz, 3H), 0.83 (d, J = 6.4 Hz, 3H), 0.74 (d, J = 6.4 Hz, 3H), 0.53 (d, J = 6.6 Hz, 3H). MS (ESI) Calculated for C₃₂H₃₉N₃O₆ [M+H]⁺: 562.3, found 562.3.

Cyclic-Ala-Val-Pro-His-OH (23):

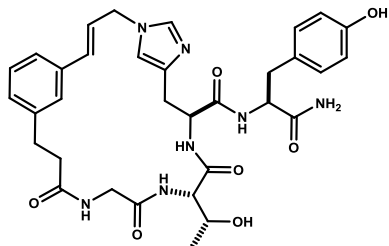
Following general procedure C, the corresponding compound was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 35-100% CH₃CN/H₂O with 0.1% TFA. The fractions collected were combined and lyophilized (16 mg, 0.029 mmol, 69%). ¹H NMR (DMSO-d₆, 500 MHz): δ 9.05 (s, 1H), 8.12 (d, J = 7.9 Hz, 1H), 8.04 (d, J = 7.7 Hz, 1H), 7.48 (s, 1H), 7.43 (d, J = 8.9 Hz, 1H), 7.16-7.27 (m, 3H), 7.09-7.14 (m, 1H),

6.66 (d, J = 15.9 Hz, 1H), 6.34 (dt, J = 16.0, 6.6 Hz, 1H), 4.84-4.98 (m, 2H), 4.22-4.30 (m, 2H), 4.18 (dd, J = 8.5, 3.6 Hz, 1H), 4.09 (t, J = 8.9 Hz, 1H), 3.55-3.63 (m, 1H), 3.48-3.46 (m, 1H), 3.05-3.18 (m, 2H), 2.9 (ddd, J = 14.7, 9.9, 4.3 Hz, 1H), 2.7 (ddd, J = 11.2, 6.4, 4.4 Hz, 1H), 2.61 (ddd, J = 15.0, 10.2, 4.1 Hz, 1H), 2.33-2.41 (m, 1H), 1.60-1.86 (m, 3H), 1.13 (d, J = 7.1 Hz, 3H), 0.79 (d, J = 6.6 Hz, 3H), 0.57 (d, J = 6.7 Hz, 3H). ¹³C NMR (DMSO-d₆, 125 MHz): δ 172.5, 172.13, 172.07, 171.5, 170.5, 141.9, 135.9, 135.4, 135.0, 130.9, 129.0, 129.0, 127.1, 124.2, 122.6, 120.4, 60.0, 56.0, 51.4, 50.9, 48.6, 47.4, 35.3, 30.6, 29.9, 29.5, 26.0, 24.6, 19.5, 18.6, 18.5. MS (ESI) Calculated for C₃₁H₄₀N₆O₆ [M+H]⁺: 593.3, found 593.1

Cyclic-Ala-Val-Pro-His-NH₂ (24):

Following general procedure C, the corresponding compound was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 35-100% CH₃CN/H₂O with 0.1% TFA. The fractions collected were combined and lyophilized (74 mg, 0.13 mmol, 77%). ¹H NMR (DMSO-d₆, 500 MHz): δ 9.08 (d, J = 1.4 Hz, 1H), 8.17 (d, J = 8.3 Hz, 1H), 8.03 (d, J = 8.0 Hz, 1H), 7.67 (d, J = 8.9 Hz, 1H), 7.40 (s, 1H), 7.34 (br. s, 1H), 7.21-7.29 (m,

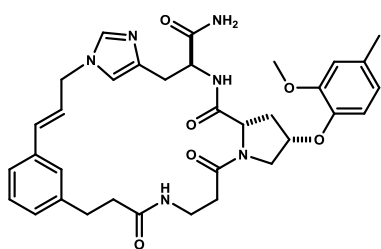
2H), 7.11-7.20 (m, 3H), 6.56 (d, J = 16.0 Hz, 1H), 6.35 (dt, J = 16.0, 6.2 Hz, 1H), 4.89-5.00 (m, 2H), 4.25-4.36 (m, 2H), 4.11-4.19 (m, 2H), 3.53-3.61 (m, 1H), 3.29-3.37 (m, 1H), 3.03-3.13 (m, 2H), 2.79-2.89 (m, 1H), 2.65-2.73 (m, 1H), 2.48-2.55 (m, 1H), 2.40 (ddd, J = 15.0, 6.5, 6.5 Hz, 1H), 1.79-1.88 (m, 1H), 1.63-1.77 (n, 2H), 1.52-1.62 (m, 1H), 1.12 (d, J = 7.0 Hz, 3H), 0.75 (d, J = 6.7 Hz, 3H), 0.71 (d, J = 6.6 Hz, 1H). ¹³C NMR (DMSO-d₆, 125 MHz): δ 172.6, 172.2, 172.1, 171.6, 170.7, 142.1, 135.9, 135.1, 134.5, 130.7, 129.0, 128.5, 127.8, 124.1, 123.3, 120.4, 60.4, 56.1, 51.9, 50.6, 49.1, 48.2, 47.5, 35.7, 30.8, 29.9, 29.3, 26.4, 24.9, 19.6, 18.6, 18.0. MS (ESI) Calculated for C₃₁H₄₁N₇O₅ [M+H]⁺: 592.3, found 592.3

Cyclic-Gly-Thr-His-Tyr-NH₂ (25):

Following general procedure C, the corresponding compound was isolated by preparative HPLC (Waters Xbridge RP18 20x250 mm) using a gradient of 25-100% CH₃CN/H₂O with 0.1% TFA. The fractions collected were combined and lyophilized (24 mg, 0.038 mmol, 73%). ¹H NMR (DMSO-d₆, 500 MHz): δ 8.99 (br. s, 1H), 8.14 (t, J = 5.9 Hz, 2H), 8.05 (d, J = 8.3 Hz, 1H), 7.96 (d, J = 7.7 Hz, 1H), 7.73 (d, J = 8.2

Hz, 1H), 7.54 (br. s, 1H), 7.4 (br. s, 1H), 7.36 (br. s, 1H), 7.19-7.22 (m, 2H), 7.16 (br. d, $J = 7.6$ Hz, 1H), 7.08 (br. d, $J = 7.6$ Hz, 1H), 7 (d, $J = 8.5$ Hz, 2H), 6.74 (d, $J = 15.7$ Hz, 1H), 6.61 (d, $J = 8.1$ Hz, 2H), 6.49 (dt, $J = 15.6, 7.1$ Hz, 1H), 4.92 (dd, $J = 14.8, 6.4$ Hz, 1H), 4.8 (dd, $J = 14.8, 7.3$ Hz, 1H), 4.53 (ddd, $J = 8.5, 8.5, 3.8$ Hz, 1H), 4.28 (ddd, $J = 8.7, 8.7, 4.7$ Hz, 1H), 4.63 (dd, $J = 7.6, 4.0$ Hz, 1H), 3.92 (dq, $J = 6.2, 6.2$ Hz, 1H), 3.8 (dd, $J = 15.6, 5.6$ Hz, 1H), 3.75 (dd, $J = 16.6, 6.2$ Hz, 1H), 3.05 (dd, $J = 15.5, 3.6$ Hz, 1H), 2.81-2.94 (m, 4H), 2.67 (dd, $J = 13.8, 9.3$ Hz, 1H), 2.34-2.41 (m, 1H), 1.04 (d, $J = 6.4$ Hz, 3H). ^{13}C NMR (DMSO- d_6 , 125 MHz): δ 173.7, 172.2, 170.5, 170.1, 169.9, 156.3, 142.3, 136.8, 136.0, 134.7, 130.6, 130.2, 129.5, 128.8, 128.2, 125.6, 125.4, 122.3, 120.2, 115.4, 67.2, 58.6, 55.1, 51.5, 51.0, 42.0, 37.1, 35.4, 29.9, 26.9, 20.2. MS (ESI) Calculated for $\text{C}_{33}\text{H}_{39}\text{N}_7\text{O}_7$ $[\text{M}+\text{H}]^+$: 646.3, found 646.1.

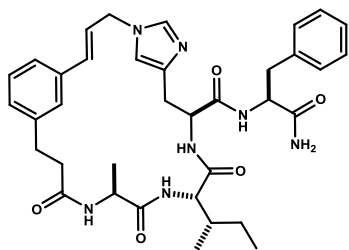
Cyclic- β -Ala-Pro[4-(2-methoxy-4-methylphenoxy)]-His (26):



Following general procedure C, the corresponding compound was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 35-100% $\text{CH}_3\text{CN}/\text{H}_2\text{O}$ with 0.1% TFA. The fractions collected were combined and lyophilized (57 mg, 0.091 mmol, 81%). ^1H NMR (DMSO- d_6 , 500 MHz): δ 8.85 (d, $J = 1.2$ Hz, 1H), 7.78 (d, $J = 7.5$ Hz, 1H), 7.65 (t, $J = 5.7$ Hz, 1H), 7.21-7.31 (m, 5H), 7.15-7.20 (m, 2H),

6.83 (d, $J = 8$ Hz, 1H), 6.78 (d, $J =$ Hz, 1H), 6.66-6.74 (m, 2H), 6.38 (dt, $J = 15.7, 7.0$ Hz, 1H), 4.89 (dd, $J = 14.8, 6.4$ Hz, 1H), 4.70-4.75 (m, 1H), 4.59 (dd, $J = 14.7, 7.3$ Hz, 1H), 4.35-4.42 (m, 2H), 3.71 (s, 3H), 3.67-3.70 (m, 1H), 3.34 (br. d, $J = 11.3$ Hz, 1H), 3.17 (m, 1H), 3.07 (d, $J = 6.4$ Hz, 2H), 2.92-3.00 (m, 1H), 2.84-2.90 (m, 1H), 2.78-2.83 (m, 1H), 2.27-2.41 (m, 3H), 2.25 (s, 3H), 2.15-2.23 (m, 2H), 1.85-2.00 (m, 2H). ^{13}C NMR (DMSO- d_6 , 125 MHz): δ 171.5, 171.2, 171.0, 170.6, 150.1, 143.4, 142.6, 141.3, 136.1, 134.6, 132.5, 132.2, 129.1, 128.5, 126.7, 124.9, 122.2, 120.8, 118.8, 118.1, 113.4, 77.9, 58.7, 55.4, 52.7, 50.9, 50.3, 36.7, 34.4, 33.8, 33.5, 31.4, 20.7. MS (ESI) Calculated for $\text{C}_{34}\text{H}_{40}\text{N}_6\text{O}_6$ $[\text{M}+\text{H}]^+$: 629.3, found 629.3

Cyclic-Ala-Ile-His-Phe-NH₂ (27):

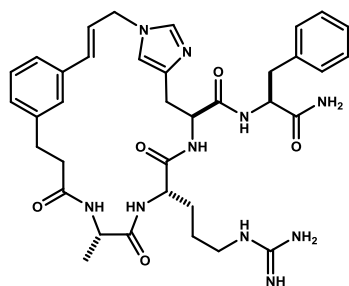


Following general procedure C, the corresponding compound was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 35-100% $\text{CH}_3\text{CN}/\text{H}_2\text{O}$ with 0.1% TFA. The fractions collected were combined and lyophilized (25 mg, 0.032 mmol, 71%). ^1H NMR (DMSO- d_6 , 500 MHz): δ 9.04 (d, $J = 1.5$ Hz, 1H), 8.12 (d, $J = 8.6$ Hz, 1H), 8 (d, $J = 5.7$ Hz, 1H), 7.86 (d, $J = 8.1$ Hz, 1H), 7.75 (d, $J = 7.3$ Hz, 1H),

7.59 (br. s, 1H), 7.55 (br. s, 1H), 7.44 (br. s, 1H), 7.14-7.25 (m, 7H), 7.1 (d, $J = 7.7$ Hz, 1H), 7.06 (d, $J = 7.7$ Hz, 1H), 6.71-6.82 (m, 2H), 4.85-4.96 (m, 2H), 4.61 (ddd, $J = 8.3, 9.3, 3.8$ Hz, 1H), 4.44 (ddd, $J = 8.1, 8.1, 5.0$ Hz, 1H), 4.14 (dq, $J = 6.7, 6.7$ Hz, 1H), 3.86 (t, $J = 7.6$ Hz, 1H), 2.87-3.04 (m, 4H), 2.81 (ddd, $J = 13.8, 8.3$ Hz, 1H), 2.70-2.77 (m, 1H), 2.40-2.46 (m, 2H), 1.52-1.62 (m, 1H), 1.36-1.46 (m, 1H), 1 (d, $J = 7$

Hz, 3H), 0.74 (t, J = 7.5 Hz, 3H), 0.75 (d, J = 6.8 Hz, 3H). ^{13}C NMR (DMSO- d_6 , 125 MHz): δ 173.2, 173.1, 172.0, 171.8, 170.2, 142.1, 137.8, 136.2, 136.1, 134.8, 130.5, 129.7, 129.5, 128.7, 128.5, 126.8, 126.1, 124.6, 123.1, 119.8, 57.9, 54.2, 51.2, 51.1, 48.8, 38.2, 36.1, 34.5, 29.9, 27.3, 25.1, 18.4, 15.8, 11.4. MS (ESI) Calculated for $\text{C}_{36}\text{H}_{45}\text{N}_7\text{O}_5$ $[\text{M}+\text{H}]^+$: 656.3, found 656.2

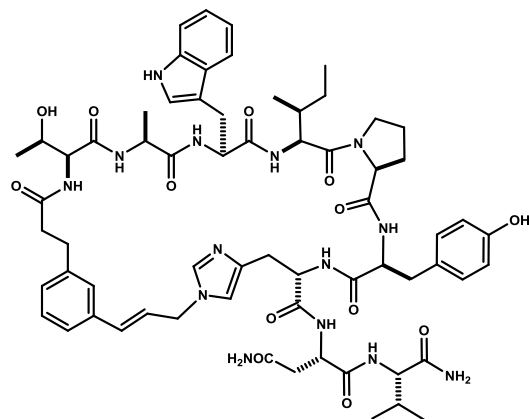
Cyclic-Ala-Arg-His-Phe-NH₂ (28):



Following general procedure C, the corresponding compound was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 35-100% $\text{CH}_3\text{CN}/\text{H}_2\text{O}$ with 0.1% TFA. The fractions collected were combined and lyophilized (36 mg, 0.044 mmol, 76%). ^1H NMR (DMSO- d_6 , 500 MHz): δ 9.03 (s, 1H), 8.11-8.14 (m, 2H), 7.97 (d, J = 6.2 Hz, 1H), 7.96 (d, J = 7.7 Hz, 1H), 7.7 (br. s, 1H), 7.48 (br. s, 1H), 7.38-7.41 (m, 2H), 7.28 (br. s, 1H), 7.14-7.25 (m, 7H), 7.1 (d, J = 7.4 Hz, 1H),

7.04 (d, J = 7.6 Hz, 1H), 6.8 (ddd, J = 15.7, 7.9, 5.6 Hz, 1H), 6.74 (d, J = 15.7 Hz, 1H), 4.91 (dd, J = 14.6, 5.2 Hz, 1H), 4.86 (dd, J = 14.8, 8.0 Hz, 1H), 4.57 (ddd, J = 8.7, 8.7, 3.5 Hz, 1H), 4.41 (ddd, J = 8.5, 8.5, 4.9 Hz, 1H), 4.05 (dq, J = 7.2, 7.2 Hz, 1H), 3.91-3.96 (m, 1H), 2.96-3.03 (m, 5H), 2.88 (dd, J = 15.6, 9.4 Hz, 1H), 2.79 (dd, J = 13.8, 8.9 Hz, 1H), 2.71 (dd, J = 15.0, 7.8 Hz, 1H), 2.34-2.41 (m, 2H), 1.40-1.52 (m, 4H), 1.09 (d, J = 7 Hz, 3H). ^{13}C NMR (DMSO- d_6 , 125 MHz): δ 173.5, 173.4, 172.3, 172.1, 170.2, 157.1, 142.1, 137.9, 136.3, 136.3, 134.8, 130.4, 129.7, 129.4, 128.7, 128.6, 126.9, 126.1, 124.5, 123.0, 119.7, 117.6, 115.3, 54.3, 52.9, 51.1, 51.0, 49.0, 40.9, 38.1, 34.4, 29.7, 28.7, 27.5, 25.6, 18.1. MS (ESI) Calculated for $\text{C}_{36}\text{H}_{46}\text{N}_{10}\text{O}_5$ $[\text{M}+\text{H}]^+$: 699.4, found 699.2

Cyclic-Thr-Ala-Trp-Ile-Pro-Tyr-His-Asn-Val (29):

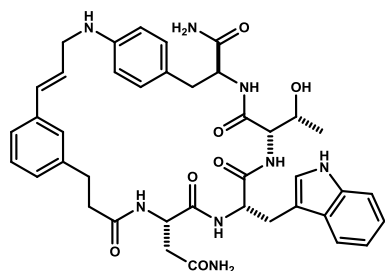


Following general procedure C, the corresponding compound was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 35-100% $\text{CH}_3\text{CN}/\text{H}_2\text{O}$ with 0.1% TFA. The fractions collected were combined and lyophilized (25 mg, 0.020 mmol, 69%). ^1H NMR (DMSO- d_6 , 500 MHz): δ 10.8 (d, J = 1.7 Hz, 1H), 9.04 (s, 1H), 8.33 (d, J = 7.2 Hz, 1H), 8.18 (d, J = 7.3 Hz, 1H), 7.98 (d, J = 6 Hz, 1H), 7.89 (d, J = 7.8 Hz, 1H), 7.73-7.82 (m, 2H), 7.54 (d, J = 8.7 Hz, 1H), 7.40-7.48 (m, 3H), 7.28-7.32 (m, 2H), 7.12-7.21 (m, 6H), 7.08-7.11 (m, 2H),

7.00-7.05 (m, 3H), 6.94 (t, J = 7.3 Hz, 1H), 6.63 (d, J = 15.9 Hz, 1H), 6.44 (dt, J = 15.9, 6.5 Hz, 1H), 4.9 (d, J = 6.1 Hz, 2H), 4.53-4.61 (m, 2H), 4.25-4.40 (m, 4H), 4.06-4.16 (m, 3H), 3.99 (dq, J = 6.9, 6.9 Hz, 1H), 3.37-3.44 (m, 1H), 3.14 (ddd, J = 15.6, 15.6, 4.8 Hz, 1H), 2.89-3.03 (m, 2H), 2.63-2.66 (m, 3H), 2.50-2.60 (m, 2H), 2.28-2.31 (m, 1H), 2.02 (dddd, J = 13.3, 6.7, 6.7, 6.7 Hz, 1H), 1.84-1.92 (m, 1H), 1.58-1.75

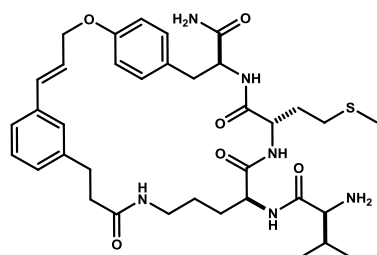
(m, 3H), 1.37-1.47 (m, 1H), 1.04 (d, $J = 7.2$ Hz, 3H), 0.94-1.01 (m, 1H), 0.93 (d, $J = 6$ Hz, 3H), 0.8 (d, $J = 7.3$ Hz, 3H), 0.79 (d, $J = 6.7$ Hz, 3H), 0.7 (d, $J = 7.3$ Hz, 3H). ^{13}C NMR (DMSO- d_6 , 125 MHz): δ 173.1, 172.7, 172.4, 172.4, 172.1, 171.7, 171.5, 171.3, 170.7, 170.2, 170.1, 142.2, 138.4, 136.5, 136.0, 135.1, 135.0, 130.1, 129.4, 128.9, 128.5, 127.7, 126.75, 126.70, 125.1, 123.9, 123.0, 121.3, 120.3, 118.8, 118.6, 117.7, 115.4, 111.8, 110.5, 67.1, 60.3, 58.5, 58.0, 55.5, 54.9, 54.6, 51.7, 50.7, 50.5, 49.8, 47.5, 37.5, 37.1, 36.8, 36.5, 31.8, 30.7, 29.4, 27.6, 27.4, 24.6, 24.5, 20.2, 19.8, 18.0, 17.9, 15.7, 11.3. MS (ESI) Calculated for $\text{C}_{65}\text{H}_{84}\text{N}_{14}\text{O}_{13}$ $[\text{M}+\text{H}]^+$: 1269.6, found 1269.4

Cyclic-Asn-Trp-Thr-Phe(4-NH₂) (30):



Following general procedure B, the corresponding compound was isolated by preparative HPLC (Waters Xbridge RP18 20x250 mm) using a gradient of 35-100% $\text{CH}_3\text{CN}/\text{H}_2\text{O}$ with 0.1% TFA. The fractions collected were combined and lyophilized (48 mg, 0.064 mmol, 77%). ^1H NMR (DMSO- d_6 , 500 MHz): δ 10.81 (d, $J = 1.4$ Hz, 1H), 8.31 (d, $J = 6.1$ Hz, 1H), 7.9 (d, $J = 5.8$ Hz, 1H), 7.55 (d, $J = 7.3$ Hz, 1H), 7.45-7.52 (m, 1H), 7.28 (d, $J = 8.1$ Hz, 1H), 7.19-7.25 (m, 4H), 7.17 (d, $J = 7.5$ Hz, 1H), 7.08-7.14 (m, 2H), 6.99-7.08 (m, 4H), 6.89-6.96 (m, 1H), 6.51 (d, $J = 15.9$ Hz, 1H), 6 (dt, $J = 15.7, 6.5$ Hz, 1H), 4.41 (ddd, $J = 6.6, 6.6, 6.6$ Hz, 1H), 4.33 (ddd, $J = 5.9, 5.9, 5.9$ Hz, 1H), 4.26 (ddd, $J = 10.9, 7.9, 3.0$ Hz, 1H), 3.89-3.98 (m, 2H), 3.81-3.88 (m, 2H), 3.03-3.11 (m, 3H), 2.63-2.80 (m, 3H), 2.26-2.45 (m, 4H), 0.7 (d, $J = 6.1$ Hz, 3H). ^{13}C NMR (DMSO- d_6 , 125 MHz): δ 173.8, 173.1, 172.6, 172.4, 172.0, 170.5, 142.1, 136.6, 136.3, 130.5, 129.1, 128.5, 127.8, 126.4, 125.0, 124.5, 121.4, 119.4, 118.8, 118.7, 118.5, 117.1, 114.8, 112.5, 111.8, 109.7, 66.6, 59.9, 55.2, 54.8, 51.4, 36.8, 36.7, 36.4, 30.6, 27.1, 19.4. MS (ESI) Calculated for $\text{C}_{40}\text{H}_{46}\text{N}_8\text{O}_7$ $[\text{M}+\text{H}]^+$: 751.4, found 751.2.

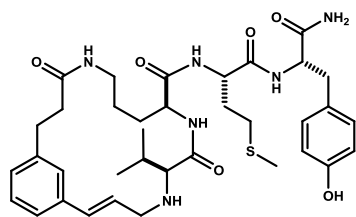
Cyclic-Val-Orn-Met-Try (32):



Following general procedure C, the corresponding compound was isolated by preparative HPLC (Waters Xbridge RP18 20x250 mm) using a gradient of 20-100% $\text{CH}_3\text{CN}/\text{H}_2\text{O}$ with 0.1% TFA. The fractions collected were combined and lyophilized (12 mg, 0.017 mmol, 64%). ^1H NMR (DMSO- d_6 , 500 MHz): δ 8.38 (d, $J = 7.9$ Hz, 1H), 8.11 (d, $J = 8.3$ Hz, 1H), 7.97-8.04 (m, 4H), 7.72 (dd, $J = 5.2, 5.2$ Hz, 1H), 7.55 (s, 1H), 7.31 (s, 1H), 7.15-7.20 (m, 3H), 7.13 (br. d, $J = 7.6$ Hz, 1H), 7.06 (br. s, $J =$ Hz, 1H), 7.01 (br. d, $J = 7.4$ Hz, 1H), 6.83 (br. d, $J = 8.1$ Hz, 2H), 6.67 (d, $J = 15.9$ Hz, 1H), 6.31 (dt, $J = 15.9, 6.0$ Hz, 1H), 4.73-4.81 (m, 2H), 4.29-4.38 (m, 2H), 4.21-4.27 (m, 1H), 3.52-3.58 (m, 1H), 2.95-3.02 (m, 1H), 2.84-2.94 (m, 2H), 2.71-2.72 (m, 2H), 2.62 (dd, $J = 12.9, 12.2$ Hz, 1H), 2.31-2.37 (m, 2H), 2.21-2.22 (n, $J =$ Hz, 1H), 1.93-2.01 (n, $J =$ Hz, 4H), 1.86-1.93 (n, $J =$ Hz, 1H), 1.71 (ddd, $J = 15.1, 15.1, 7.7$ Hz, 1H), 1.42-1.50 (m, 1H), 1.31-1.40 (m, 2H), 1.20-1.28 (m, 1H), 0.88 (d, $J = 7$ Hz, 6H). ^{13}C NMR (DMSO- d_6 , 125 MHz): δ 173.6,

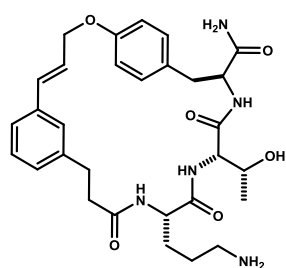
171.8, 171.32, 171.28, 168.1, 157.0, 142.1, 136.5, 133.0, 130.8, 130.7, 129.0, 128.7, 125.8, 125.7, 125.4, 114.8, 67.7, 57.6, 55.3, 52.6, 52.0, 38.5, 37.9, 37.2, 33.6, 31.8, 30.4, 29.5, 25.8, 18.7, 18.2, 15.0. MS (ESI) Calculated for $C_{36}H_{50}N_6O_6S$ $[M+H]^+$: 695.4, found 695.2

Cyclic-Val-Orn-Met-Try (33):



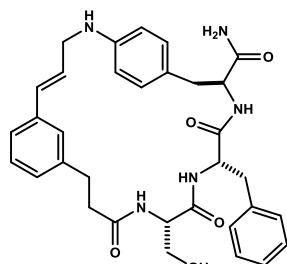
Following general procedure C, the corresponding compound was isolated by preparative HPLC (Waters Xbridge RP18 20x250 mm) using a gradient of 25-100% CH_3CN/H_2O with 0.1% TFA. The fractions collected were combined and lyophilized (12 mg, 0.017 mmol, 77%). 1H NMR ($DMSO-d_6$, 500 MHz): δ 8.91 (br. s, J = Hz, 2H), 8.48 (d, J = 7 Hz, 1H), 8.09 (d, J = 8.2 Hz, 1H), 7.74 (dd, J = 6.6, 5.3 Hz, 1H), 7.68 (d, J = 8.1 Hz, 1H), 7.35-7.39 (m, 2H), 7.27 (t, J = 7.9 Hz, 1H), 7.15 (br. d, J = 7.9 Hz, 1H), 7.02 (br. s, J = Hz, 1H), 6.93-6.97 (m, 3H), 6.59 (d, J = 8.6 Hz, 2H), 6.52 (br. d, J = 15.7 Hz, 1H), 6.05 (dt, J = 15.4, 7.7 Hz, 1H), 4.3 (ddd, J = 8.3, 8.3, 5.3 Hz, 1H), 4.25 (ddd, J = 8.8, 8.8, 4.6 Hz, 1H), 4.01-4.07 (m, 1H), 3.71-3.79 (m, 1H), 3.52-3.64 (m, 2H), 3 (ddd, J = 14.7, 14.7, 7.7 Hz, 1H), 2.75-2.89 (m, 4H), 2.65 (dd, J = 13.8, 8.6 Hz, 1H), 2.40-2.47 (m, 1H), 2.35-2.39 (m, 1H), 2.25-2.34 (m, 2H), 2.04 (ddd, J = 13.8, 12.2, 6.9 Hz, 1H), 1.98 (s, 3H), 1.79-1.87 (m, 1H), 1.63-1.72 (m, 1H), 1.30-1.39 (m, 1H), 1.10-1.25 (m, 3H), 0.95 (d, J = 6.9 Hz, 3H), 0.91 (d, J = 6.7 Hz, 3H). ^{13}C NMR ($DMSO-d_6$, 125 MHz): δ 172.6, 171.1, 170.6, 170.4, 166.0, 155.9, 141.1, 138.5, 134.5, 130.2, 129.3, 129.0, 128.4, 127.6, 122.0, 117.3, 114.8, 62.0, 53.9, 53.5, 51.6, 48.6, 36.6, 36.0, 34.8, 32.0, 30.6, 30.0, 29.1, 28.4, 27.0, 18.2, 17.9. MS (ESI) Calculated for $C_{36}H_{50}N_6O_6S$ $[M+H]^+$: 695.4, found 695.4

Cyclic-Orn-Thr-Try (35):

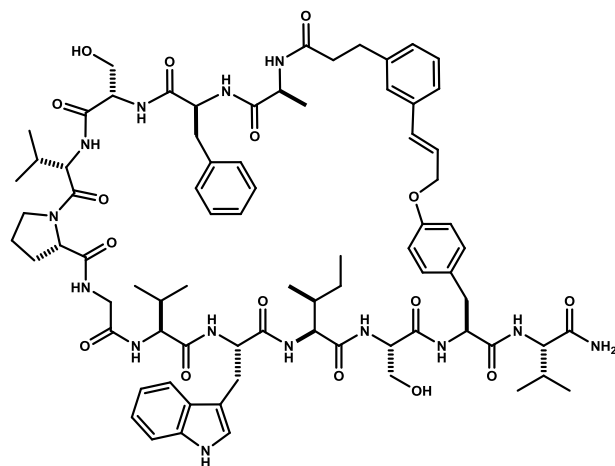


Following general procedure D, the corresponding compound was isolated by preparative HPLC (Waters Xbridge RP18 20x250 mm) using a gradient of 10-70% CH_3CN/H_2O with 0.1% TFA. The fractions collected were combined and lyophilized (22 mg, 0.033 mmol, 80%). 1H NMR ($DMSO-d_6$, 600 MHz): δ 7.90 (d, J = 8.3 Hz, 1H), 7.90 (d, J = 8.3 Hz, 1H), 7.64 (d, J = 7.8 Hz, 1H), 7.53 (br s, 3H), 7.37 (s, 1H), 7.20-7.22 (m, 2H), 7.41 (br s, 1H), 7.19 (br s, 1H), 7.13 (d, J = 8.6 Hz, 2H), 7.04-7.08 (m, 1H), 6.85 (d, J = 8.6 Hz, 2H), 6.66 (d, J = 15.9 Hz, 1H), 6.46 (dt, J = 15.9, 5.8 Hz, 1H), 4.78 (d, J = 5.8 Hz, 2H), 4.34 (ddd, J = 10.6, 8.3, 2.8 Hz, 1H), 4.21 (ddd, J = 8.3, 8.1, 5.3 Hz, 1H), 4.14 (dd, J = 7.8, 5.2 Hz, 1H), 3.94 (tdd, J = 6.3, 5.9, 5.2 Hz, 1H), 2.88 (ddd, J = 14.7, 6.8, 4.5 Hz, 1H), 2.82 (ddd, J = 14.7, 10.1, 4.1 Hz, 1H), 3.00 (dd, J = 14.2, 2.8 Hz, 1H), 2.74 (dd, J = 14.2, 10.6 Hz, 1H), 2.69 (14.5, 10.1, 4.5 Hz, 1H), 2.48-2.55 (m, 2H), 2.37 (ddd, J = 14.5, 6.8, 4.1 Hz, 1H), 1.31-1.39 (m, 1H), 1.06-1.20 (m, 3H), 1.01 (d, J = 6.3 Hz, 3H). ^{13}C NMR ($DMSO-d_6$, 125 MHz): δ 172.9, 171.1, 170.7, 169.3, 156.4, 140.9, 135.8, 132.8, 129.9, 129.6, 128.4, 128.2, 125.0, 124.9, 124.2, 114.4, 67.7, 65.6, 57.8, 53.8, 51.0, 37.8, 35.7, 34.4, 29.9, 29.4, 22.5, 19.1.

MS (ESI) Calculated for $C_{30}H_{39}N_5O_6$ $[M+H]^+$: 566.3, found 566.2.

Cyclic-Ser-Phe-Phe(4-NH₂) (37):

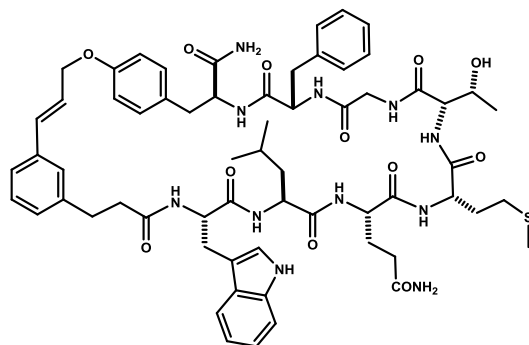
Following general procedure B, the corresponding compound was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 35-100% CH₃CN/H₂O with 0.1% TFA. The fractions collected were combined and lyophilized (13 mg, 0.023 mmol, 72%). ¹H NMR (DMSO-d₆, 500 MHz): δ 7.99 (d, J = 8.7 Hz, 1H), 7.77 (d, J = 7.8 Hz, 1H), 7.71 (d, J = 7.6 Hz, 1H), 7.10-7.25 (m, 8H), 7.08 (br s, 1H), 6.96-7.02 (m, 2H), 6.66 (br s, 1H), 6.45 (d, J = 15.7 Hz, 1H), 6.16 (dt, J = 15.9, 5.8 Hz, 1H), 4.78 (ddd, J = 8.2, 8.2, 4.9 Hz, 1H), 4.31 (ddd, J = 11.3, 8.6, 2.9 Hz, 1H), 4.09 (ddd, J = 6.2, 6.2, 6.2 Hz, 1H), 3.88 (d, J = 4.9 Hz, 2H), 3.1-3.2 (m, 2H), 3.00 (dd, J = 13.8, 4.8 Hz, 1H), 2.84 (dd, J = 14.5, 2.6 Hz, 1H), 2.67-2.78 (m, 3H), 2.48-2.57 (m, 1H), 2.27-2.35 (m, 1H). ¹³C NMR (DMSO-d₆, 125 MHz): δ 173.6, 172.1, 171.0, 170.2, 141.6, 138.0, 136.7, 130.1, 129.8, 128.7, 128.5, 128.4, 126.7, 126.2, 124.4, 62.3, 54.9, 54.4, 54.1, 37.5, 36.9, 35.8, 31.0. MS (ESI) Calculated for C₃₃H₃₇N₅O₅ [M+H]⁺: 584.3, found 584.3.

Cyclic-Ala-Phe-Ser-Val-Pro-Gly-Val-Trp-Ile-Ser-Tyr-Val (38):

Following general procedure B, the corresponding compound was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 35-100% CH₃CN/H₂O with 0.1% TFA. The fractions collected were combined and lyophilized (10 mg, 0.007 mmol, 66%). ¹H NMR (DMSO-d₆, 600 MHz): δ 10.67 (s, 1H), 8.24 (dd, J = 5.87 Hz, 1H), 8.09 (dd, J = 7.7 Hz, 1H), 8.02-8.08 (m, 3H), 8.01 (d, J = 7.9 Hz, 1H), 7.91 (d, J = 7.4 Hz, 1H), 7.77 (d, J = 8.1 Hz, 1H), 7.69-7.75 (m, 2H), 7.56-7.61 (m, 1H), 7.49-7.55 (m, 2H), 7.38 (d, J = 8.7 Hz, 1H), 7.31 (s, 1H), 7.23-7.28 (m, 3H), 7.13-7.22 (m, 5H), 7.10-7.13 (m, 3H), 7.05-7.09 (m, 3H), 6.99 (dd, J = 7.6, 7.6 Hz, 1H), 6.91 (dd, J = 7.5, 7.5 Hz, 1H), 6.78 (d, J = 8.3 Hz, 2H), 6.65 (d, J = 15.9 Hz, 1H), 6.42 (dt, J = 15.9, 5.8 Hz, 1H), 4.58 (d, J = 5.5 Hz, 2H), 4.53 (ddd, J = 8.5, 8.5, 5.4 Hz, 1H), 4.44-4.50 (m, 2H), 4.27-4.34 (m, 3H), 4.25 (dd, J = 7.6, 5.5 Hz, 1H), 4.14-4.20 (m, 2H), 4.05-4.13 (m, 3H), 3.75 (dd, J = 16.7, 6.1 Hz, 1H), 3.62-6.72 (m, 1H), 3.46-3.60 (m, 4H), 3.01-3.07 (m, 1H), 2.98 (dd, J = 13.7, 3.0 Hz, 1H), 2.87 (dd, J = 15.1, 9.6 Hz, 1H), 2.32-2.43 (m, 2H), 1.85-2.03 (m, 5H), 1.70-1.79 (m, 2H), 1.55-1.63 (m, 1H), 1.28-1.37 (m, 1H), 1.62 (d, J = 7 Hz, 3H), 0.94-1.0 (m, 1H), 0.85 (d, J = 6.6 Hz, 3H), 0.78-0.83 (m, 9H), 0.73 (d, J = 6.4 Hz, 3H), 0.63-0.72 (m, 6H), 0.67 (d, J = 6.8 Hz, 3H). ¹³C NMR (DMSO-d₆, 150 MHz, from HMBC/HSQC): δ 173.2, 172.45, 172.4, 172.3, 171.9, 171.4, 171.1, 171.07, 171.02, 170.5, 170, 169.9, 168.9, 157.1, 141.9, 137.9, 136.3, 133.2, 132.3, 131.6, 130.3, 129.1, 129, 127.9, 127.85, 127.8, 126.1, 126, 124.8, 124.1, 123.5, 120.7, 118.2, 118, 114.2, 111.1, 110.3, 67.9, 61.6, 61.5, 59.6,

57.9, 57.6, 56.8, 55.6, 54.9, 53.8, 53.6, 53.3, 48.7, 47, 42.3, 37.2, 37.1, 37, 36.4, 36.1, 30.6, 30.2, 29.3, 27.3, 24.5, 24.2, 22.1, 19.3, 19.1, 17.8, 17.5, 15.2, 11.1. MS (ESI) Calculated for $C_{78}H_{104}N_{14}O_{16}$ $[M+H]^+$: 1493.8, found 1493.7

Cyclic-Trp-Leu-Gln-Met-Thr-Gly-Phe-Tyr (39):

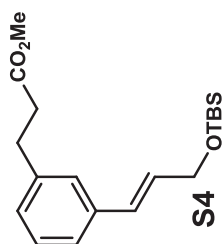


Following general procedure B, the corresponding compound was isolated by preparative HPLC (Waters Sunfire C18 30x150 mm) using a gradient of 35-100% CH_3CN/H_2O with 0.1% TFA. The fractions collected were combined and lyophilized (21 mg, 0.017 mmol, 71%). 1H NMR ($DMSO-d_6$, 500 MHz): δ 10.76 (d, J = 1.9 Hz, 1H), 8.11 (d, J = 7.8 Hz, 1H), 8.04-8.09 (m, 2H), 8.02 (d, J = 7.4 Hz, 1H), 7.96 (t, J = 5.4 Hz, 1H), 7.92 (d, J = 7.8 Hz,

1H), 7.81 (d, J = 7.9 Hz, 1H), 7.71 (d, J = 7.9 Hz, 1H), 7.55 (d, J = 7.8 Hz, 1H), 7.3 (d, J = 7.9 Hz, 1H), 7.23-7.27 (m, 3H), 7.17-7.23 (m, 6H), 7.12-7.17 (m, 3H), 7.06-7.10 (m, 2H), 7.01-7.05 (m, 2H), 6.95 (t, J = 7.5 Hz, 1H), 6.86 (d, J = 8.7 Hz, 2H), 6.72 (br. s, J = Hz, 1H), 6.66 (d, J = 15.9 Hz, 1H), 6.43 (dt, J = 15.9, 5.8 Hz, 1H), 4.61 (d, J = 5.4 Hz, 2H), 4.52 (ddd, J = 8.9, 8.9, 4.6 Hz, 1H), 4.45 (ddd, J = 8.4, 8.4, 5.0 Hz, 1H), 4.4 (ddd, J = 8.1, 8.1, 5.0 Hz, 1H), 4.35 (ddd, J = 8.9, 8.9, 4.0 Hz, 1H), 4.13-4.25 (m, 3H), 3.93-3.99 (m, 1H), 3.69 (dd, J = 17.1, 5.7 Hz, 1H), 3.56 (dd, J = 16.8, 5.2 Hz, 1H), 3.1 (dd, J = 14.9, 4.8 Hz, 1H), 2.99 (dd, J = 13.8, 4.2 Hz, 1H), 2.87-2.96 (m, 2H), 2.64-2.78 (m, 4H), 2.31-2.45 (m, 4H), 1.85-1.98 (m, 5H), 1.69-1.83 (m, 2H), 1.00 (d, J = 6.4 Hz, 3H), 0.75-0.86 (m, 6H). ^{13}C NMR ($DMSO-d_6$, 125 MHz): δ 174.2, 173.4, 172.3, 172.3, 172.1, 171.53, 171.51, 171.3, 170.7, 168.8, 157.3, 142.1, 138.2, 136.6, 136.5, 132.7, 130.7, 130.4, 129.7, 129.1, 128.5, 128.2, 127.8, 126.8, 126.7, 125.4, 124.6, 123.9, 121.3, 118.8, 118.7, 114.7, 111.8, 110.6, 68.4, 67.1, 58.8, 54.6, 54.5, 54.2, 52.9, 52.4, 51.6, 42.3, 41.0, 38.0, 37.2, 37.1, 32.2, 31.9, 31.3, 29.9, 29.2, 27.6, 24.5, 23.6, 22.0, 20.0, 15.0. MS (ESI) Calculated for $C_{63}H_{79}N_{11}O_{12}S$ $[M+H]^+$: 1214.6, found 1214.2.

Cyclic and Acyclic Ac-QSQQTFXNLWRLXQN (p53-MDM2 peptides): Peptides were prepared as described above in a 24-well MiniBlock parallel reactor. Cyclization was achieved using standard procedure C. $^1\text{H}/^{13}\text{C}$ NMR spectra for the side-chain acylated linear peptides are below. Full homo-/heteronuclear correlation data for entry 1 and 2 are included. Characterization of macrocycles corresponding to entries 3 and 4 is incomplete. Yields refer to material isolated by preparative HPLC.

entry	N-term															C-Term	acylation		cyclization	
																	amt (mg)	yield (%)	amt (mg)	yield (%)
1	Ac-Q	S	Q	Q	T	F	Dap	N	L	W	R	L	L	His	Q	N	93	28	29.6	33
2	Ac-Q	S	Q	Q	T	F	Orn	N	L	W	R	L	L	His	Q	N	98	45	50.2	41
3	Ac-Q	S	Q	Q	T	F	Dap	N	L	W	R	L	L	Tyr	Q	N	119	39	53.2	n.d.
4	Ac-Q	S	Q	Q	T	F	Orn	N	L	W	R	L	L	Tyr	Q	N	88	49	49	n.d.



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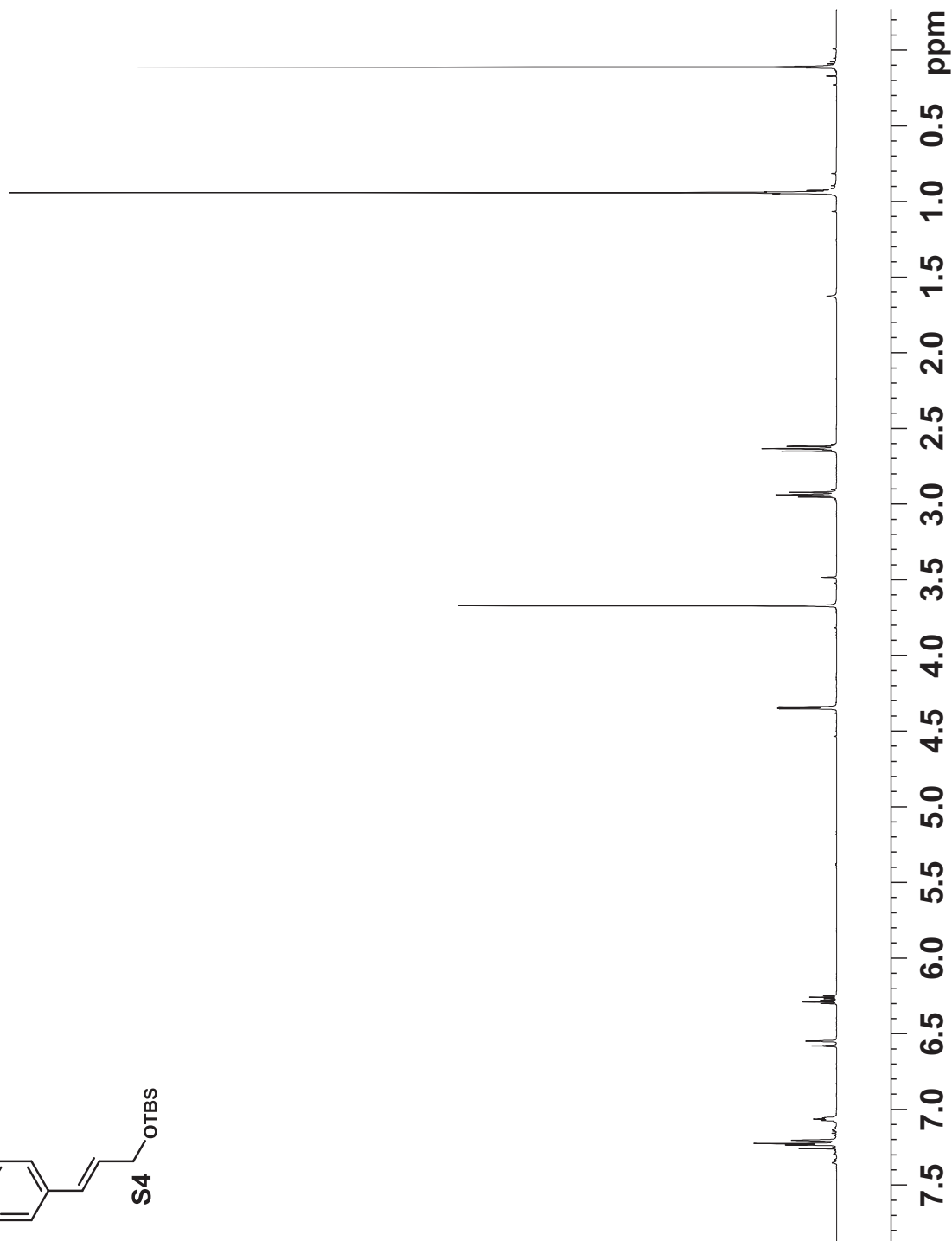
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PROCNO    1

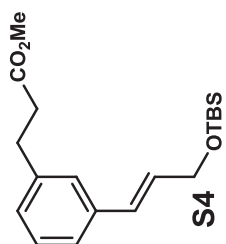
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RG         11
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DE         10.00 usec
TE         296.0 K
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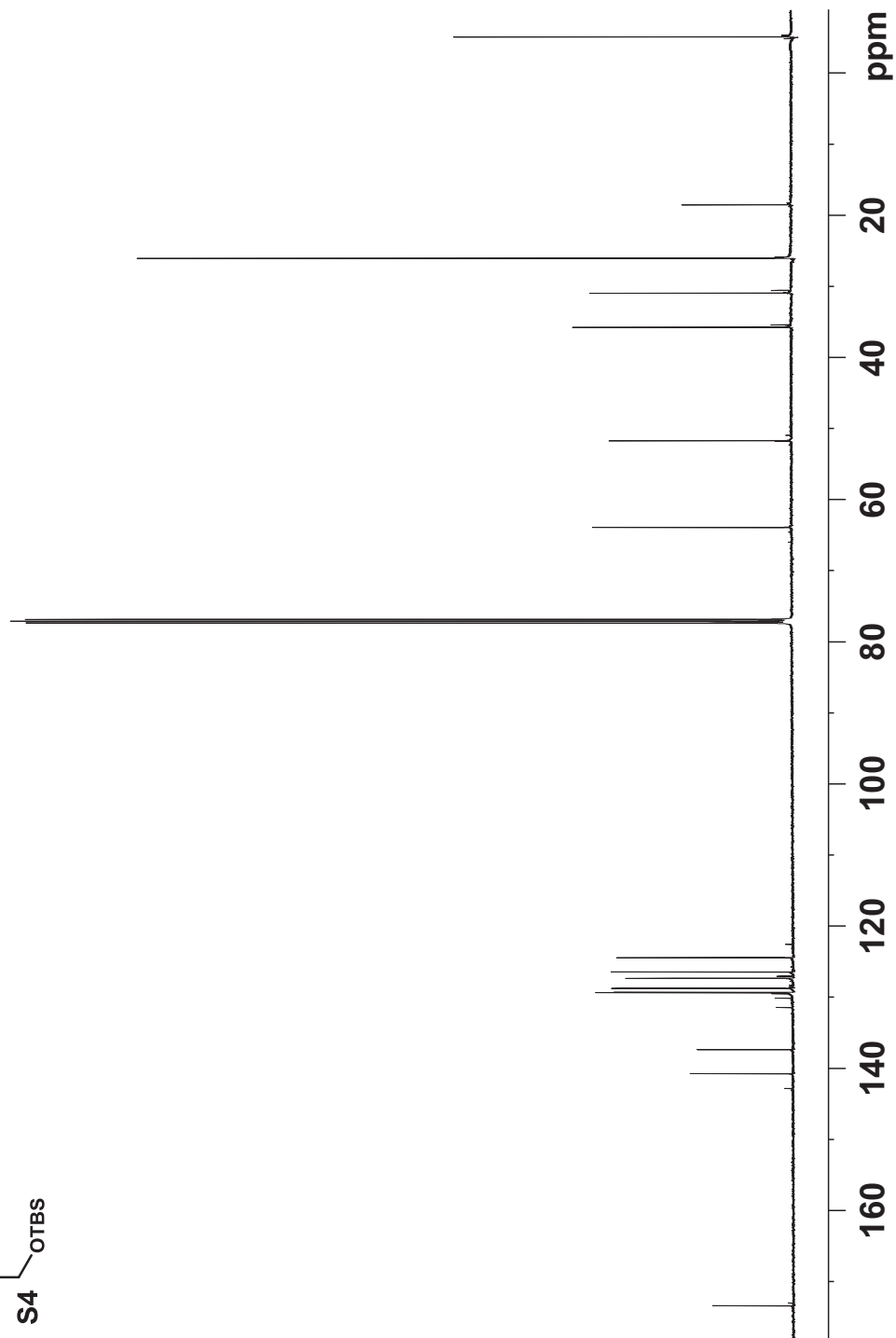
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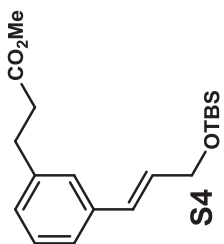
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Current Data Parameters
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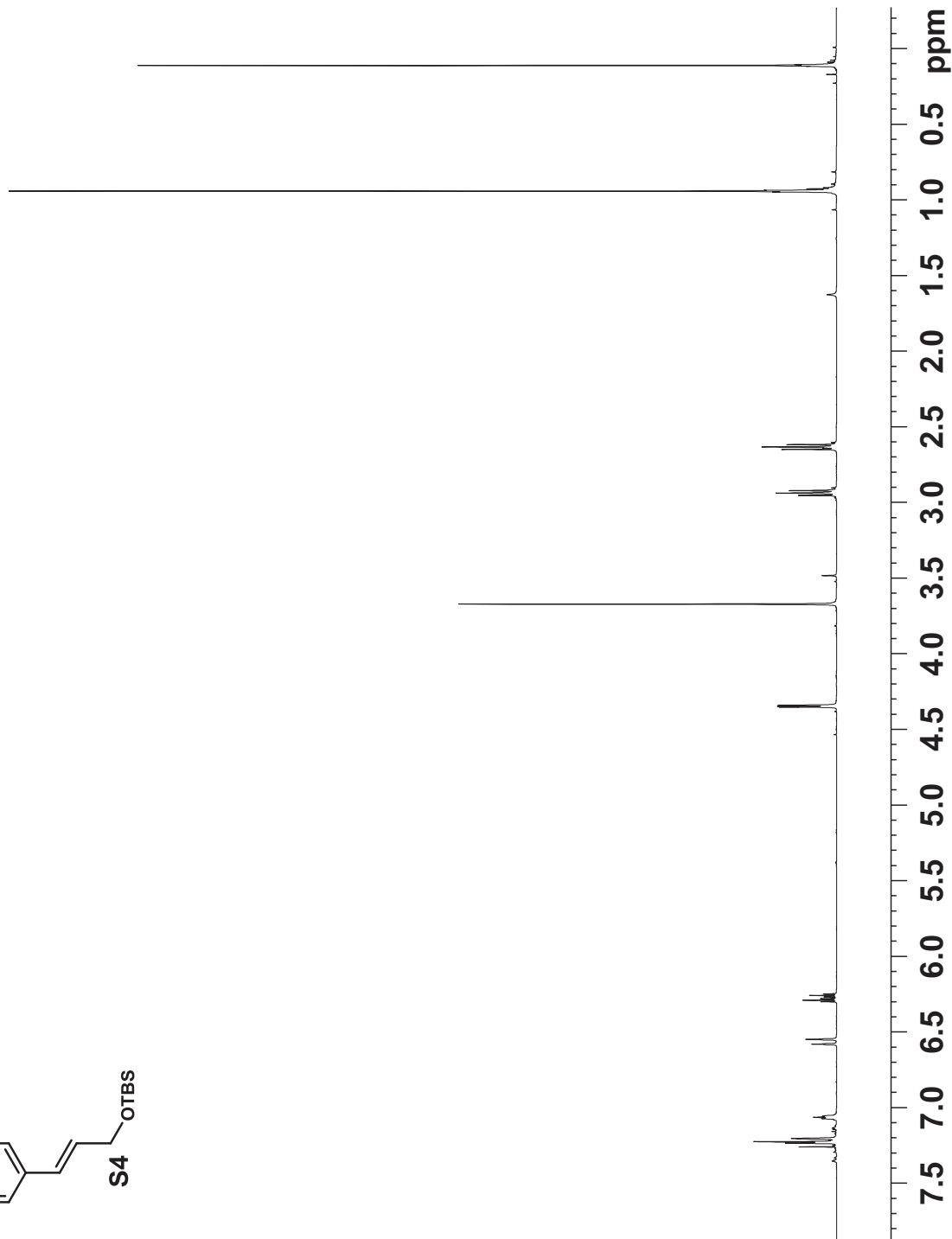
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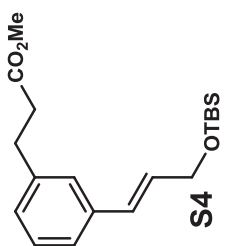
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NS         8
DS         0
SWH        10000.000 Hz
FIDRES     0.152588 Hz
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RG         11
DW         50.000 usec
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TE         296.0 K
D1         2.00000000 sec
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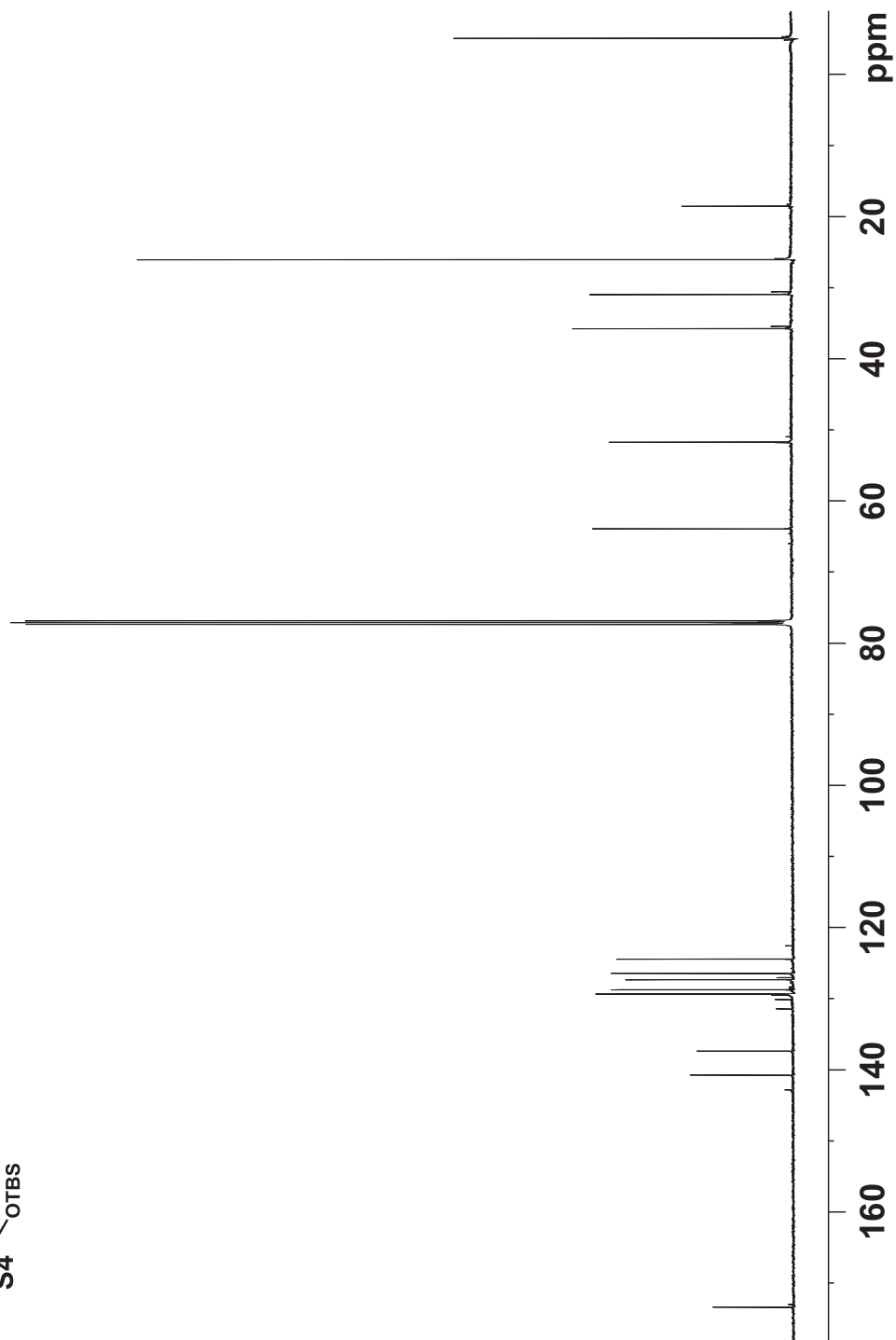
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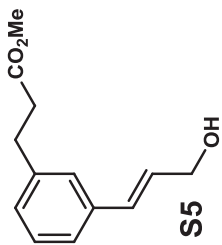
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Current Data Parameters
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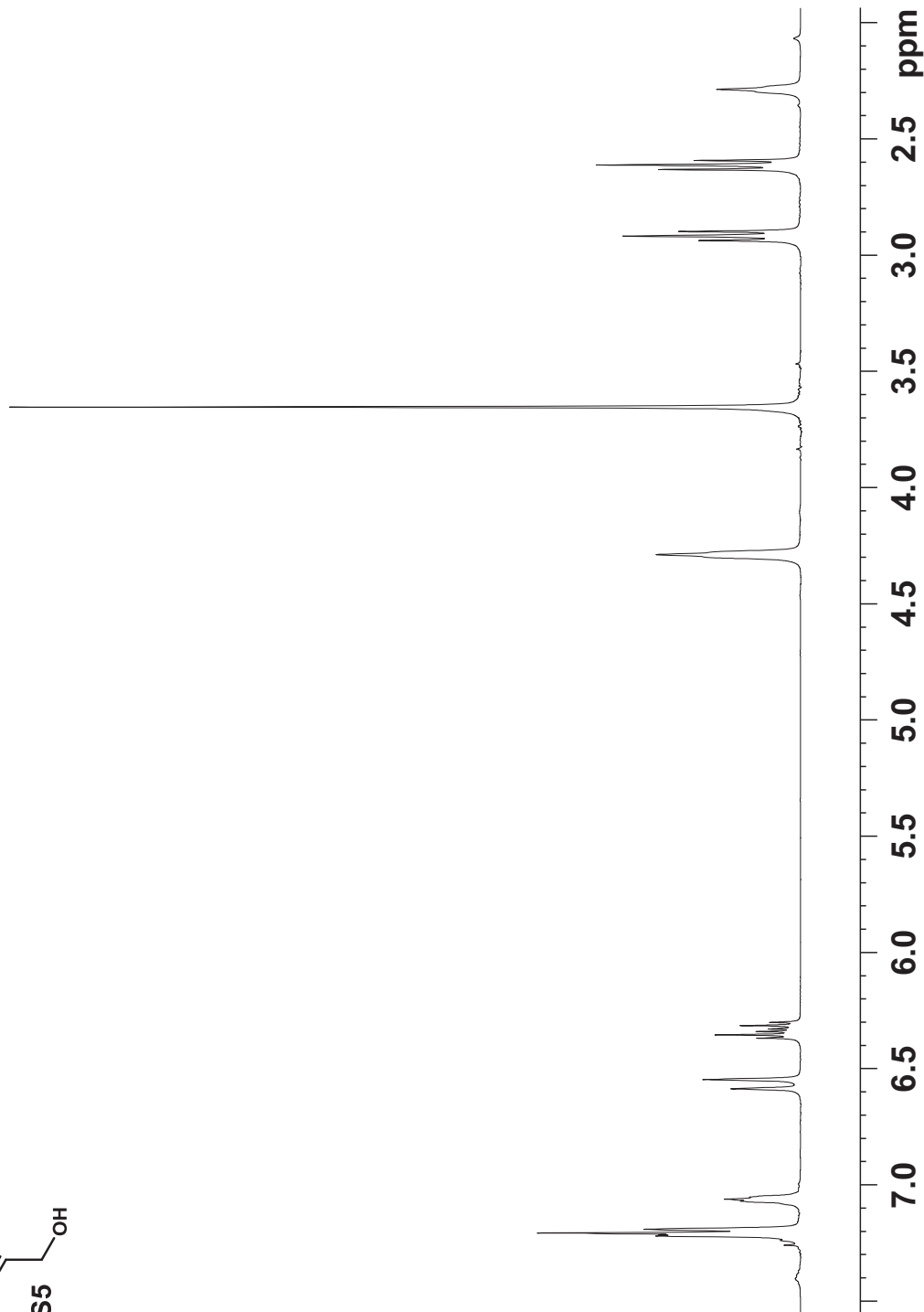


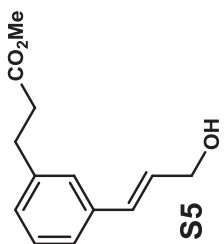


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 SOLVENT CDCl3
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 DS 0
 SWH 8064.516 Hz
 FIDRES 0.123055 Hz
 AQ 4.0632820 sec
 RG 180
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 DE 88.57 usec
 TE 300.0 K
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 P1 9.00 usec
 SFO1 400.1324008 MHz
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F2 - Processing parameters
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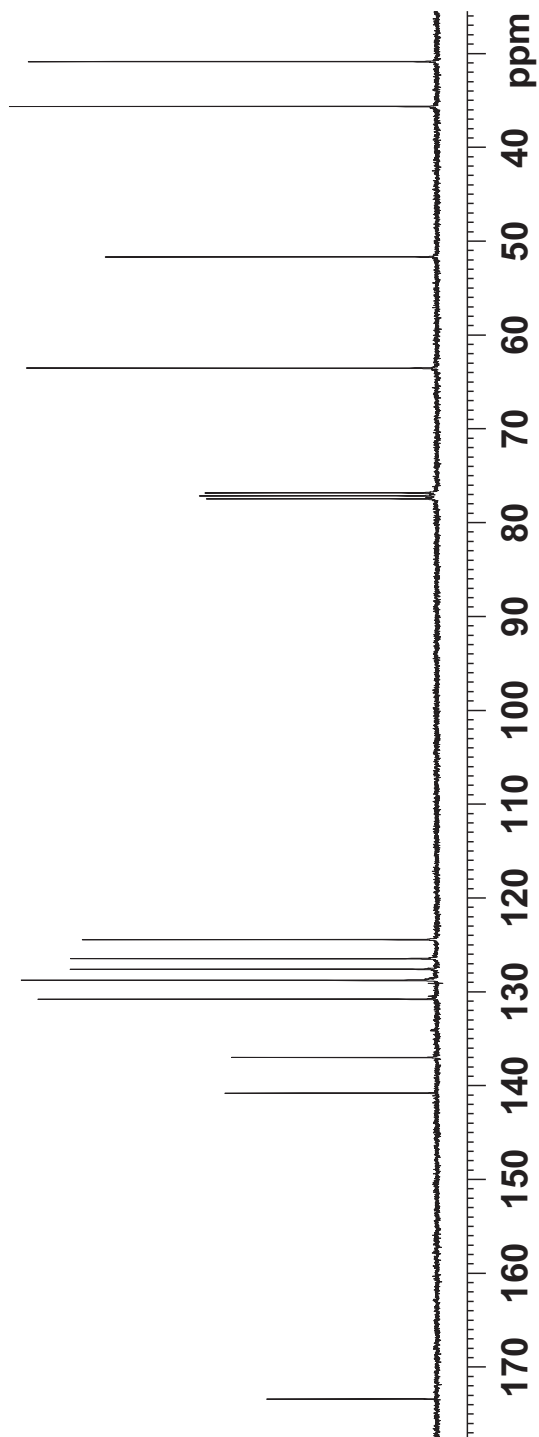


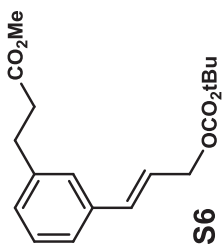


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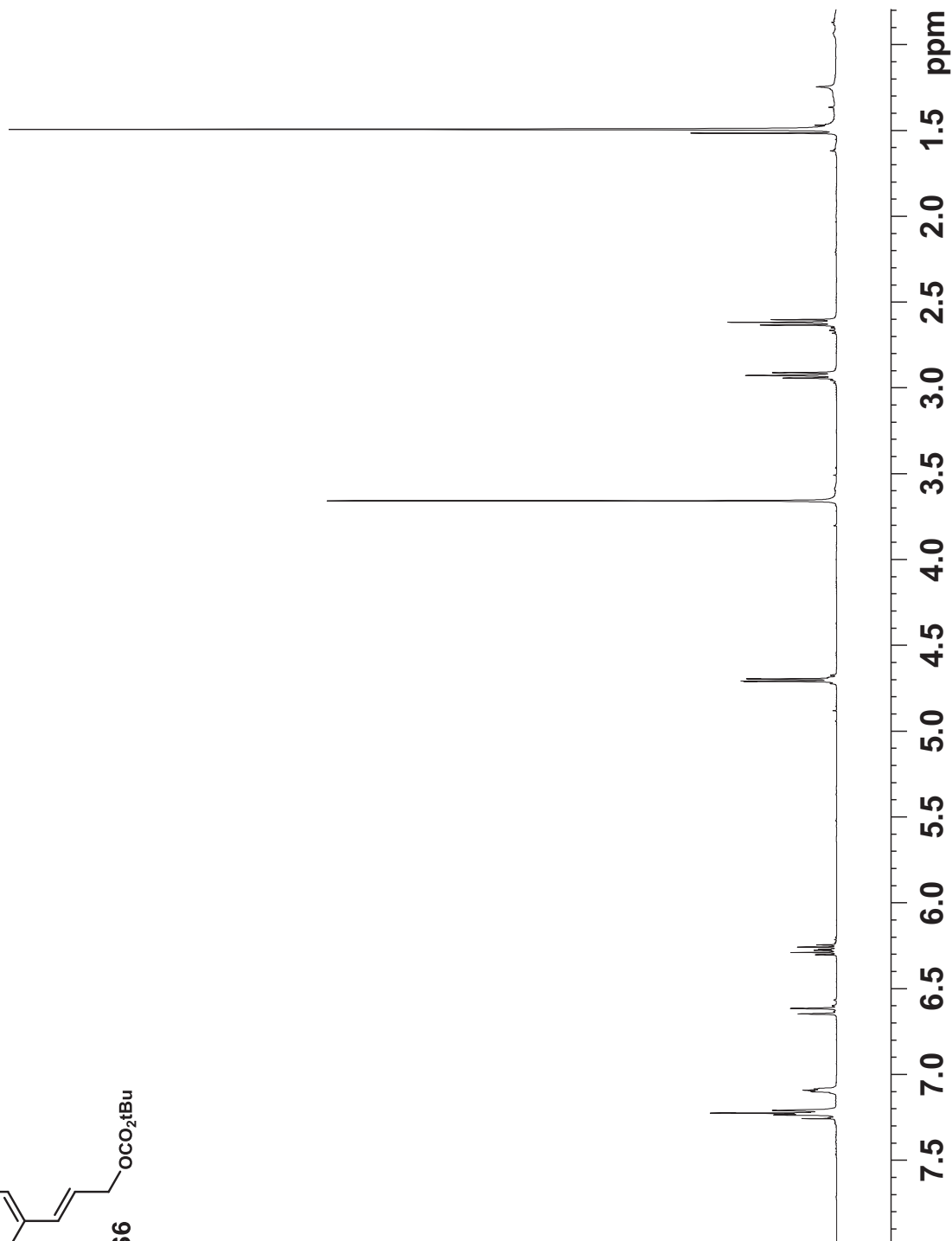
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RG            29.99
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DE            10.00 usec
TE            296.0 K
D1            2.00000000 sec
TD0           1

===== CHANNEL f1 =====
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P1            10.00 usec
PLW1          13.50000000 W
SFO1          500.1330008 MHz

F2 - Processing parameters
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SF            500.1300146 MHz
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SSB           0
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PC            1.00

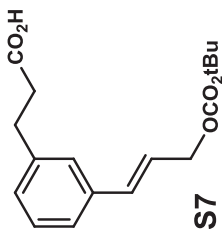
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F2 - Processing parameters





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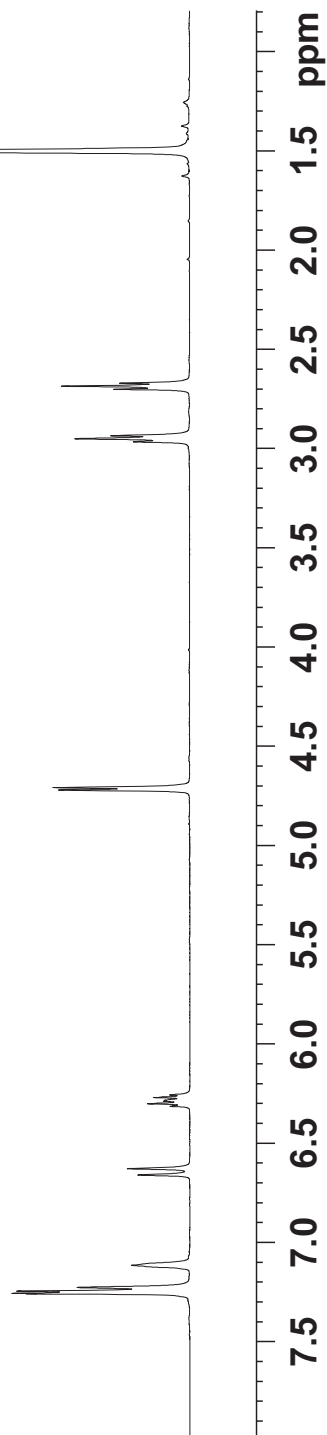
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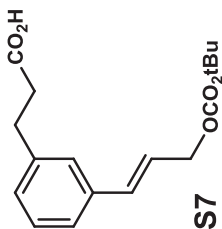
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NUC1          1H
P1            10.00 usec
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F2 - Processing parameters
SI            65536
SF            500.1300146 MHz
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Current Data Parameters
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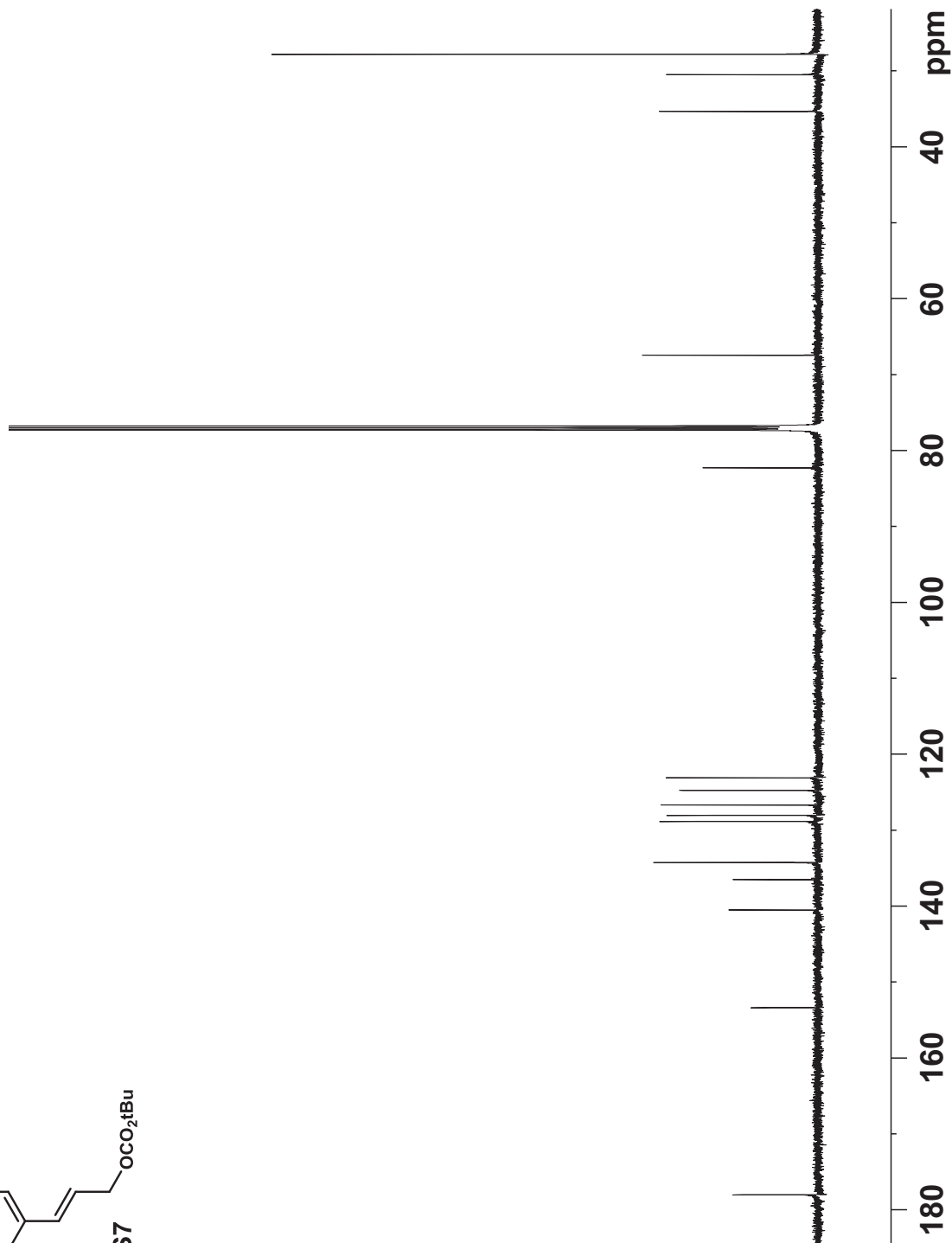
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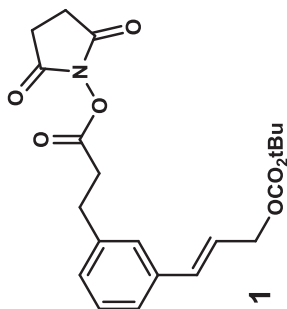
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PLW13         0.13500001 W

F2 - Processing parameters
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```





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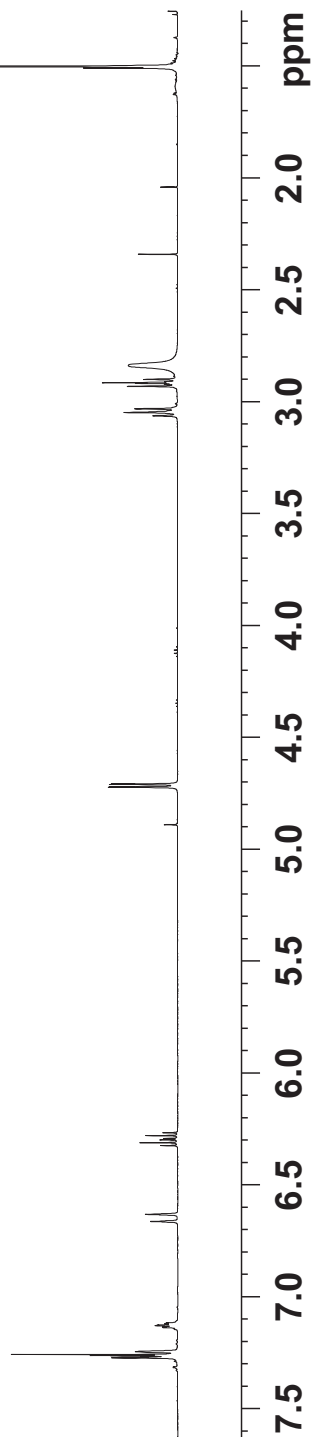
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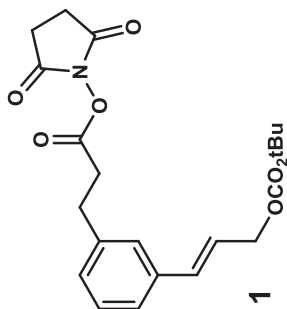
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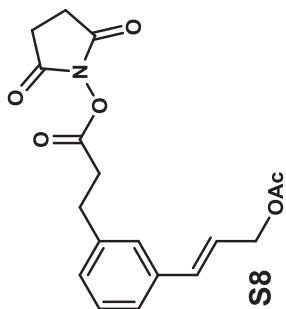
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GB         0
PC         1.00

```







```

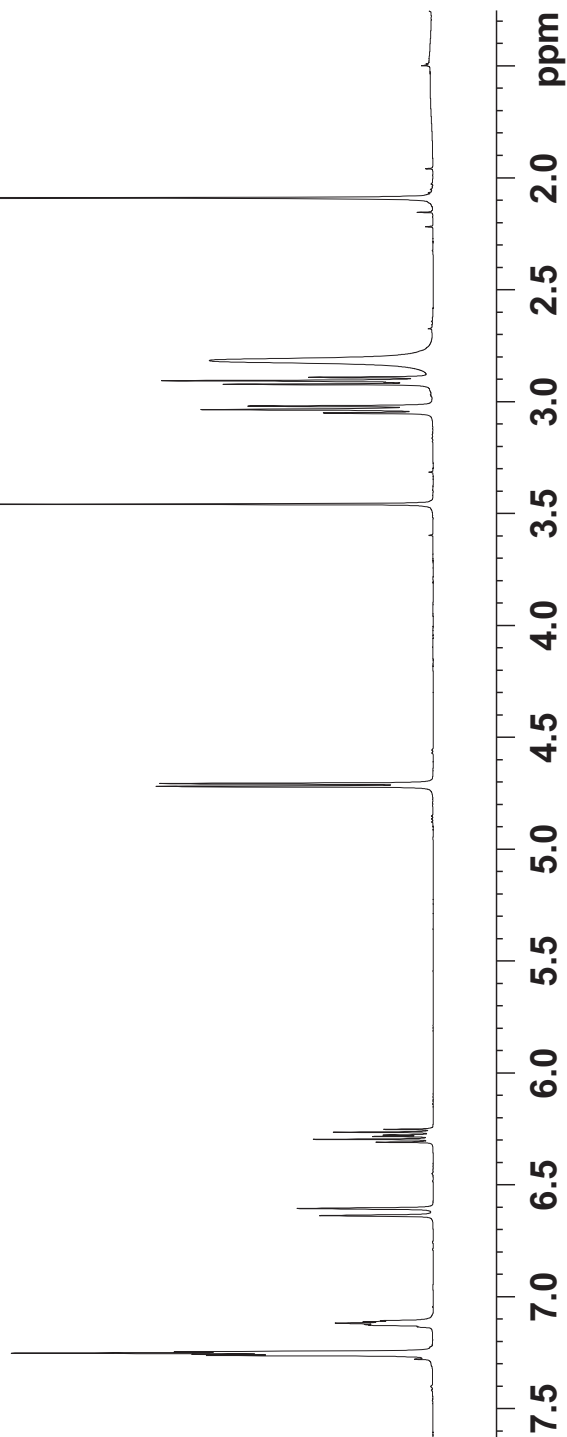
Current Data Parameters
NAME          H1_OAC
EXPNO         1
PROCNO        1

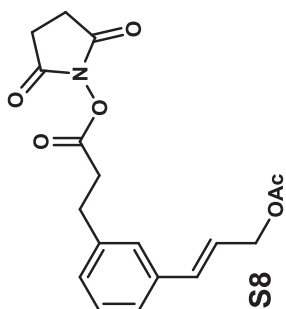
F2 - Acquisition Parameters
Date_         20130424
Time_         12.07
INSTRUM       av500
PROBHD        5 mm DCH 13C-1
PULPROG       zg30
TD            65536
SOLVENT       CDC13
NS            8
DS            0
SWH           10000.000 Hz
FIDRES        0.152588 Hz
AQ            3.276799 sec
RG            11
DW            50.000 usec
DE            10.00 usec
TE            298.0 K
D1            2.0000000 sec
TD0           1

===== CHANNEL f1 =====
SFO1          500.130008 MHz
NUC1          1H
P1            10.00 usec
PL1           13.5000000 W

F2 - Processing parameters
SI            65536
SF            500.1300146 MHz
WDW           EM
SSB           0
LB            0.30 Hz
GB            0
PC            1.00

```





```

Current Data Parameters
NAME          HI_OAC
EXPNO         2
PROCNO        1

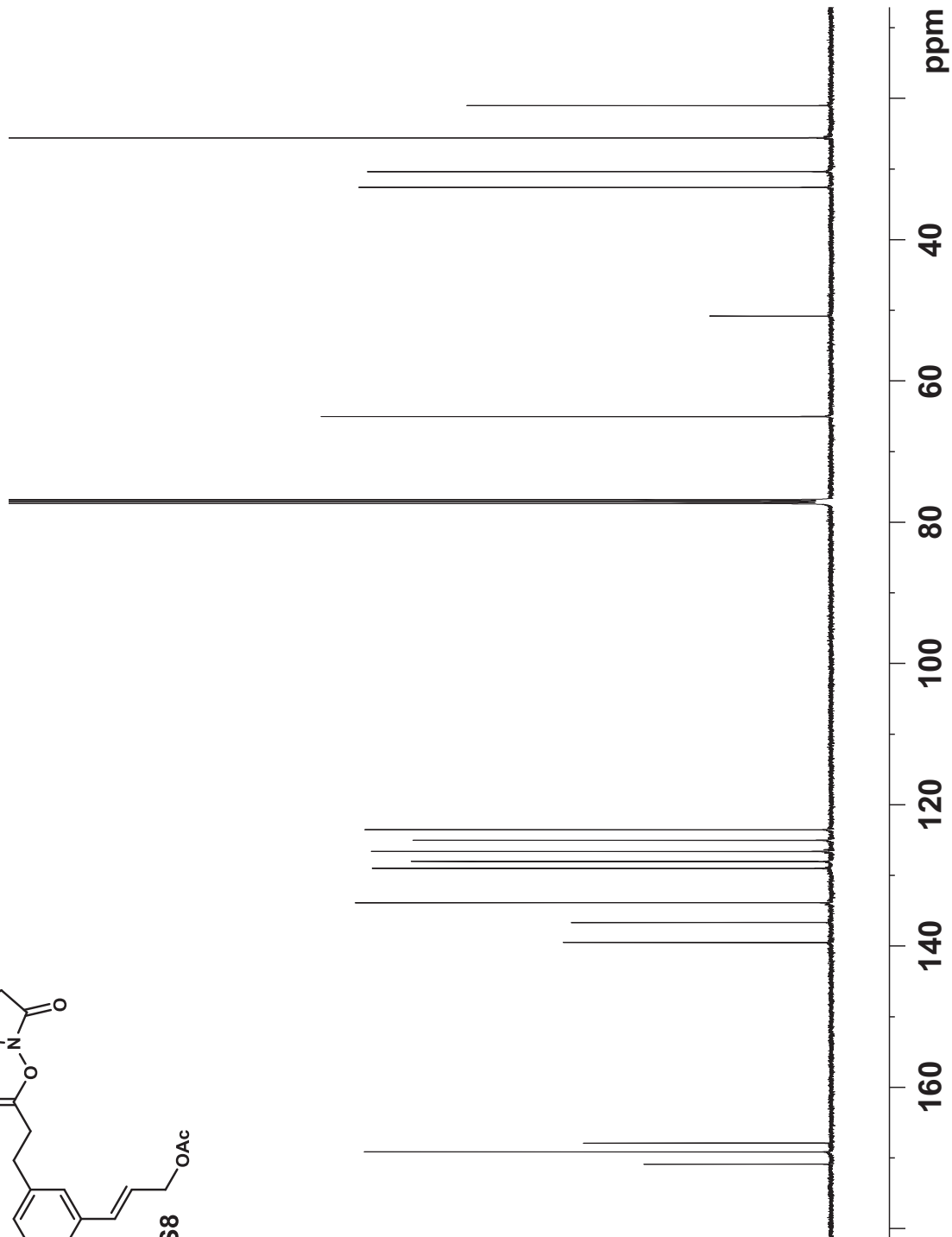
F2 - Acquisition Parameters
Date_         20130424
Time_         12.09
INSTRUM       av500
PROBHD        5 mm DCH 13C-1
PULPROG       zgpg30
TD            65536
SOLVENT       CDC13
NS            31
DS            2
SWH           31250.000 Hz
FIDRES        0.476837 Hz
AQ           1.0485760 sec
RG           202.91
DW           16.000 usec
DE           18.00 usec
TE           298.0 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0          1

===== CHANNEL f1 =====
SFO1         125.772511 MHz
NUC1         13C
P1           9.63 usec
PLW1        23.00000000 W

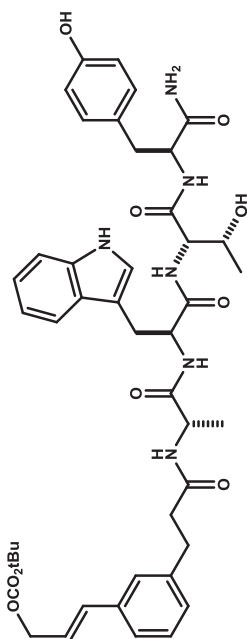
===== CHANNEL f2 =====
SFO2         500.1330008 MHz
NUC2         1H
CPDPRG2      waltz16
PCPD2        80.00 usec
PLW2        13.50000000 W
PLW12       0.21094000 W
PLW13       0.13500001 W

F2 - Processing parameters
SI           131072
SF           125.7577892 MHz
WDW          EM
SSB          0
LB           1.00 Hz
GB           0
PC           1.00

```



Acyclic-Ala-Trp-Thr-Tyr (2):



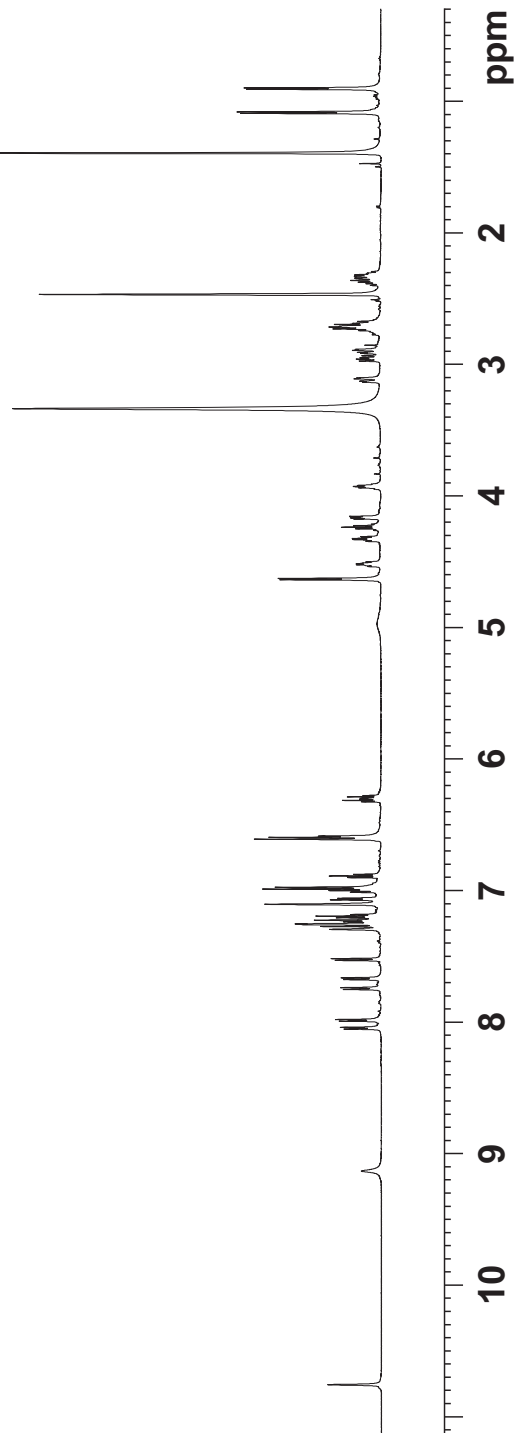
```

Current Data Parameters
NAME          KL-4-38
EXPNO         1
PROCNO        1

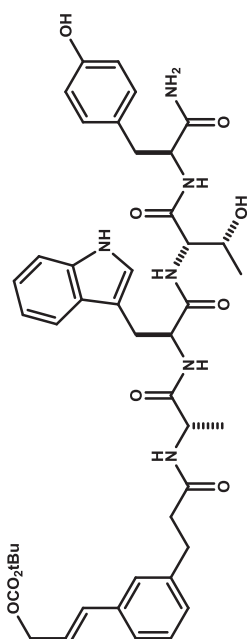
F2 - Acquisition Parameters
Date_         20111012
Time_         18.07
INSTRUM       av600
PROBHD        5 mm BB5
PULPROG       zg30
TD            65536
SOLVENT       DMSO
NS            8
DS            0
SWH           12376.237 Hz
FIDRES        0.188846 Hz
AQ            2.6476543 sec
RG            181
DW            40.400 usec
DE            6.50 usec
TE            295.2 K
D1            2.0000000 sec
TD0           1

===== CHANNEL f1 =====
NUC1          1H
P1            14.00 usec
PL1           -1.00 dB
PL1W          31.62277603 W
SFO1          600.1336008 MHz

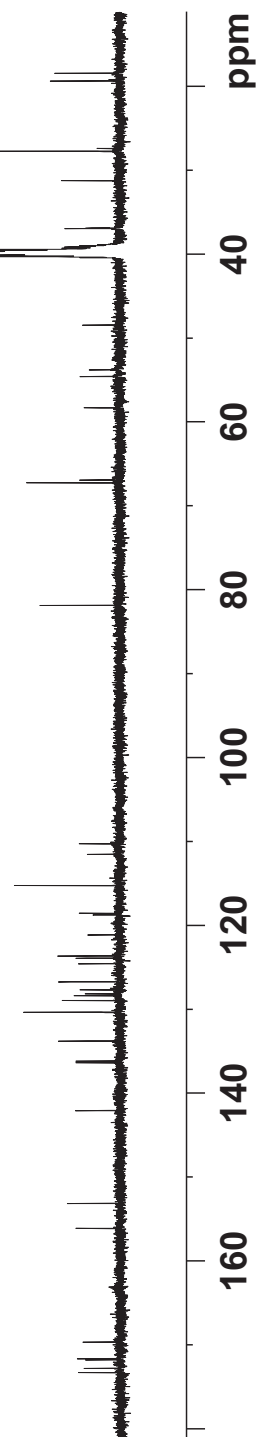
F2 - Processing parameters
SI            65536
SF            600.1300273 MHz
WDW           EM
SSB           0
LB            0.30 Hz
GB            0
PC            1.00
  
```



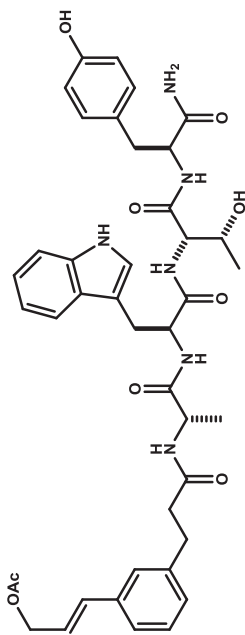
Acyclic-Ala-Trp-Thr-Tyr (2):



Current Data Parameters
NAME KL-4-38
EXPNO 2
PROCNO 1
F2 - Processing parameters
SI 65536
SF 150.9028319 MHz
WDW 0 EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40



Acyclic-Ala-Trp-Thr-Tyr (3):



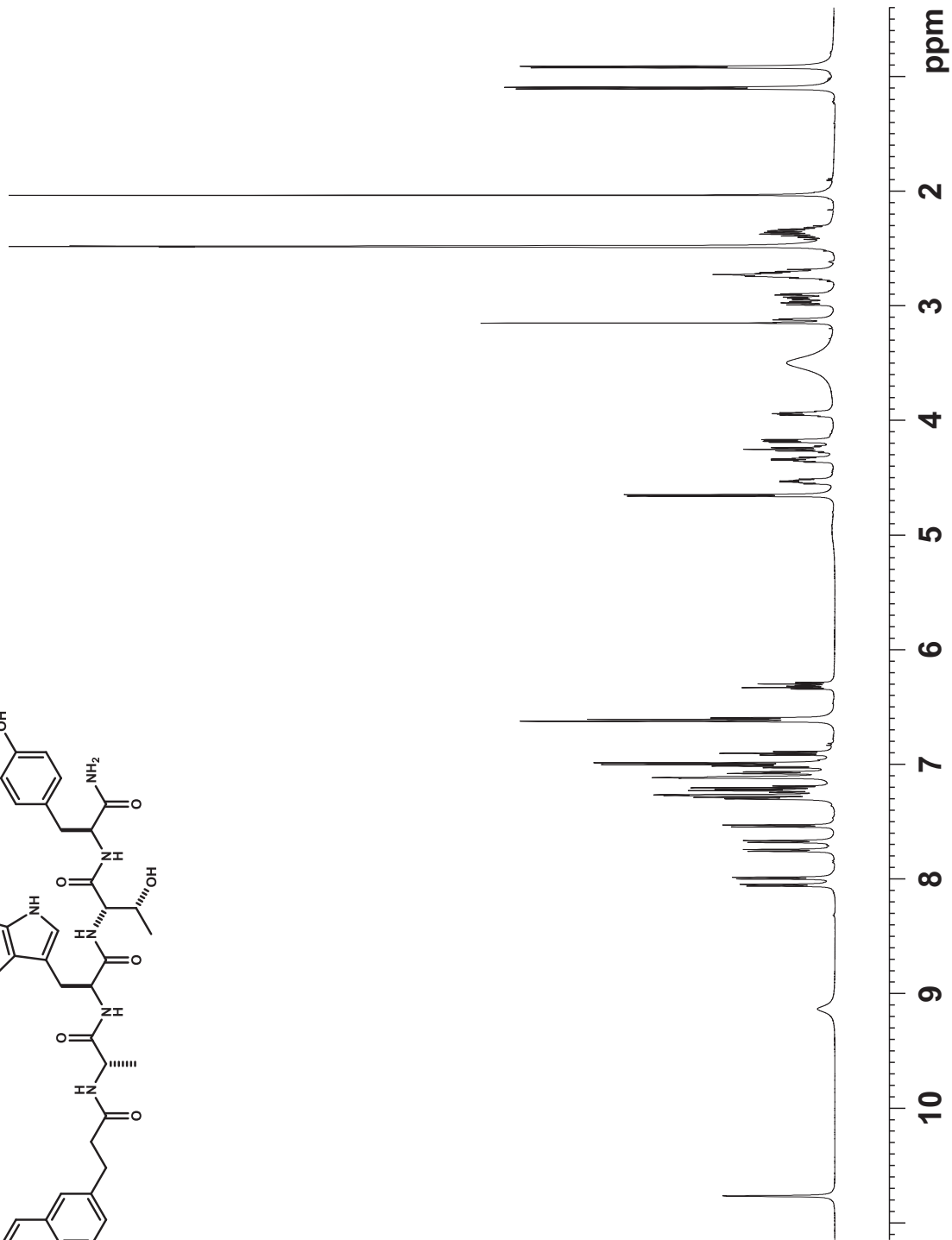
```

Current Data Parameters
NAME      KI-5-144b
EXPNO     1
PROCNO    1

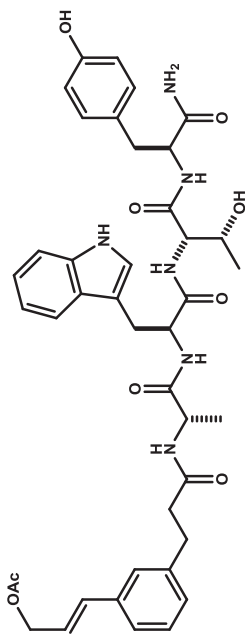
F2 - Acquisition Parameters
Date_     20130321
Time      18.13
INSTRUM   av500
PROBHD    5 mm DCH 13C-1
PULPROG   zg30
TD         65536
SOLVENT   DMSO
NS         8
DS         0
SWH        10000.000 Hz
FIDRES     0.152588 Hz
AQ         3.2767999 sec
RG         11
DW         50.000 usec
DE         10.00 usec
TE         298.0 K
D1         2.00000000 sec
TD0        1

===== CHANNEL f1 =====
SFO1      500.1330008 MHz
NUC1      1H
P1         10.00 usec
PLW1      13.50000000 W

F2 - Processing parameters
SI         65536
SF         500.1300146 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00
    
```



Acyclic-Ala-Trp-Thr-Tyr (3):



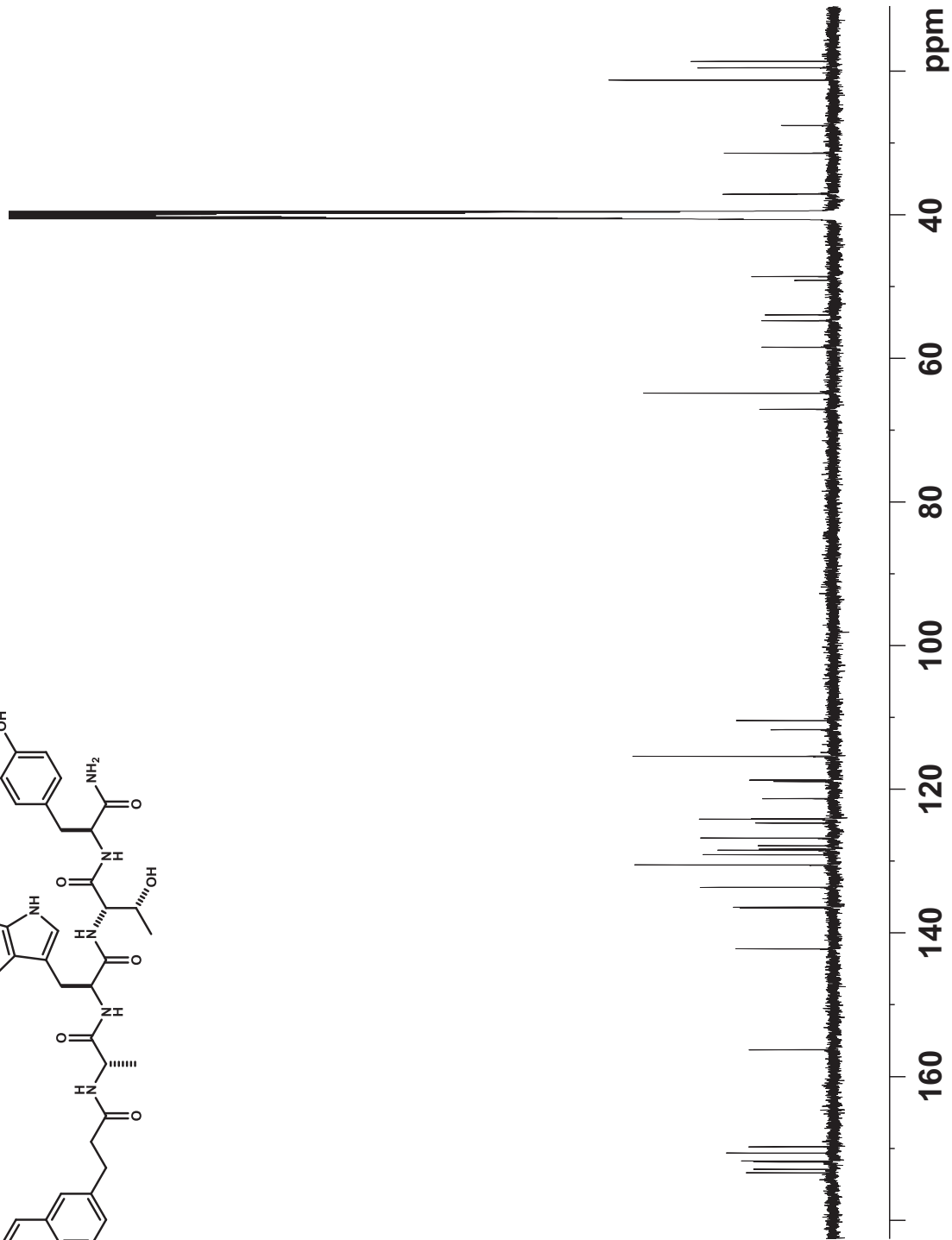
Current Data Parameters
NAME KL-5-144b
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20130321
Time 18.16
INSTRUM av500
PROBHD 5 mm DCH 13C-1
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 92
DS 2
SWH 31250.000 Hz
FIDRES 0.476837 Hz
AQ 1.0485760 sec
RG 202.91
DW 16.000 usec
DE 18.00 usec
TE 298.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

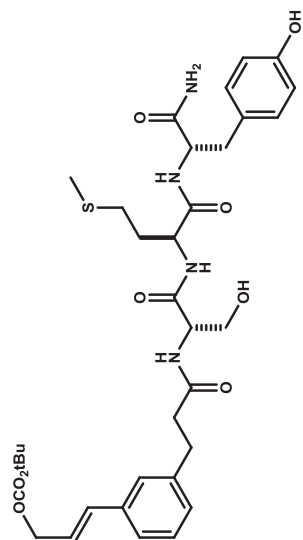
===== CHANNEL f1 =====
SFO1 125.7722511 MHz
NUC1 13C
P1 9.63 usec
PLW1 23.00000000 W

===== CHANNEL f2 =====
SFO2 500.1330008 MHz
NUC2 1H
PCPD2 waltz16
PCPD2 80.00 usec
PLW2 13.50000000 W
PLW12 0.21094000 W
PLW13 0.13500001 W

F2 - Processing parameters
SI 131072
SF 125.7577892 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40



Acyclic-Ser-Met-Tyr (S9):



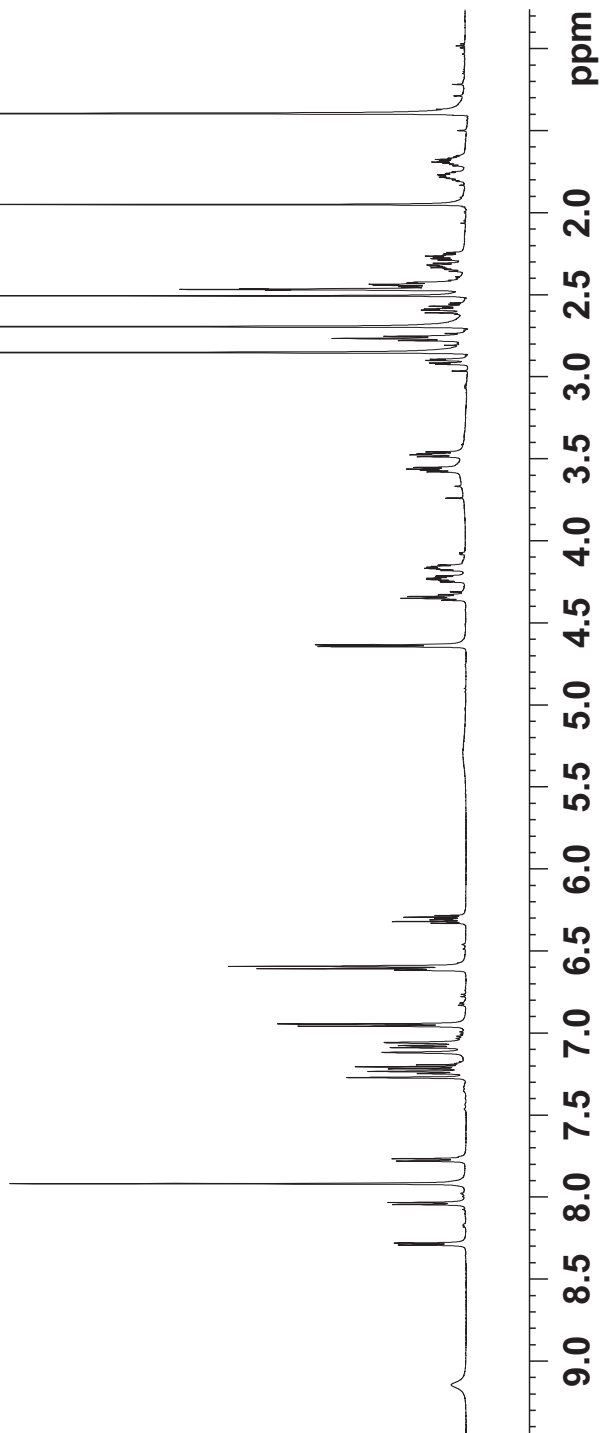
```

Current Data Parameters
NAME      KL-III-288
EXPNO     1
PROCNO    1

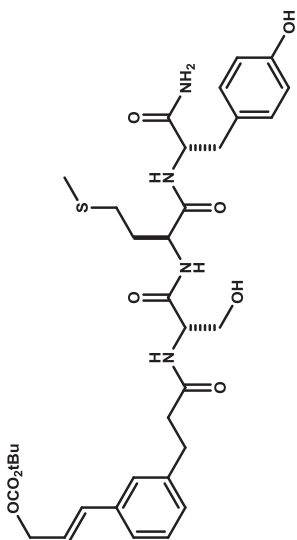
F2 - Acquisition Parameters
Date_     20110831
Time      15.21
INSTRUM   av600
PROBHD    5 mm BB5
PULPROG   zg30
TD         65536
SOLVENT   DMSO
NS         8
DS         0
SWH        12376.237 Hz
FIDRES     0.188846 Hz
AQ         2.6476543 sec
RG         114
DW         40.400 usec
DE         6.50 usec
TE         294.6 K
D1         2.0000000 sec
TD0        1

===== CHANNEL f1 =====
NUC1       1H
P1         14.00 usec
PL1        -1.00 dB
PL1W       31.62277603 W
SFO1       600.1336008 MHz

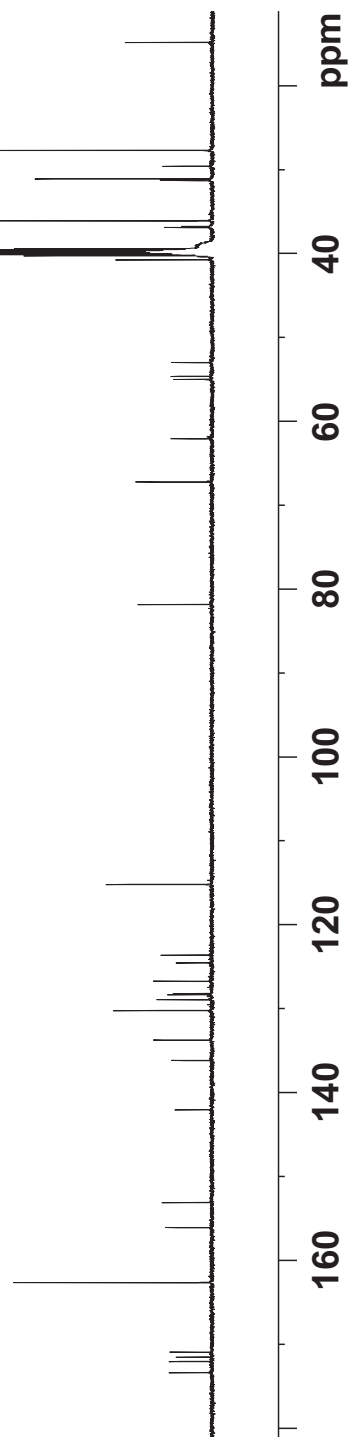
F2 - Processing parameters
SI         65536
SF         600.1300273 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00
  
```



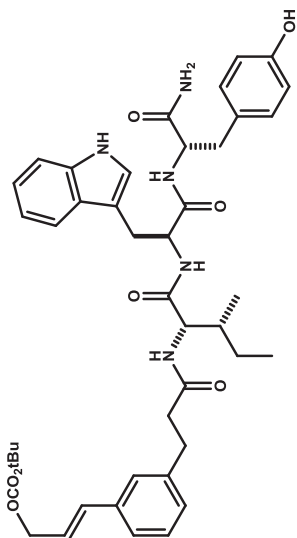
Acyclic-Ser-Met-Tyr (S9):



Current Data Parameters
NAME KL-III-288
EXPNO 2
PROCNO 1
F2 - Processing parameters
SI 65536
SF 150.9028319 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40



Acyclic-Ile-Trp-Tyr (S10):

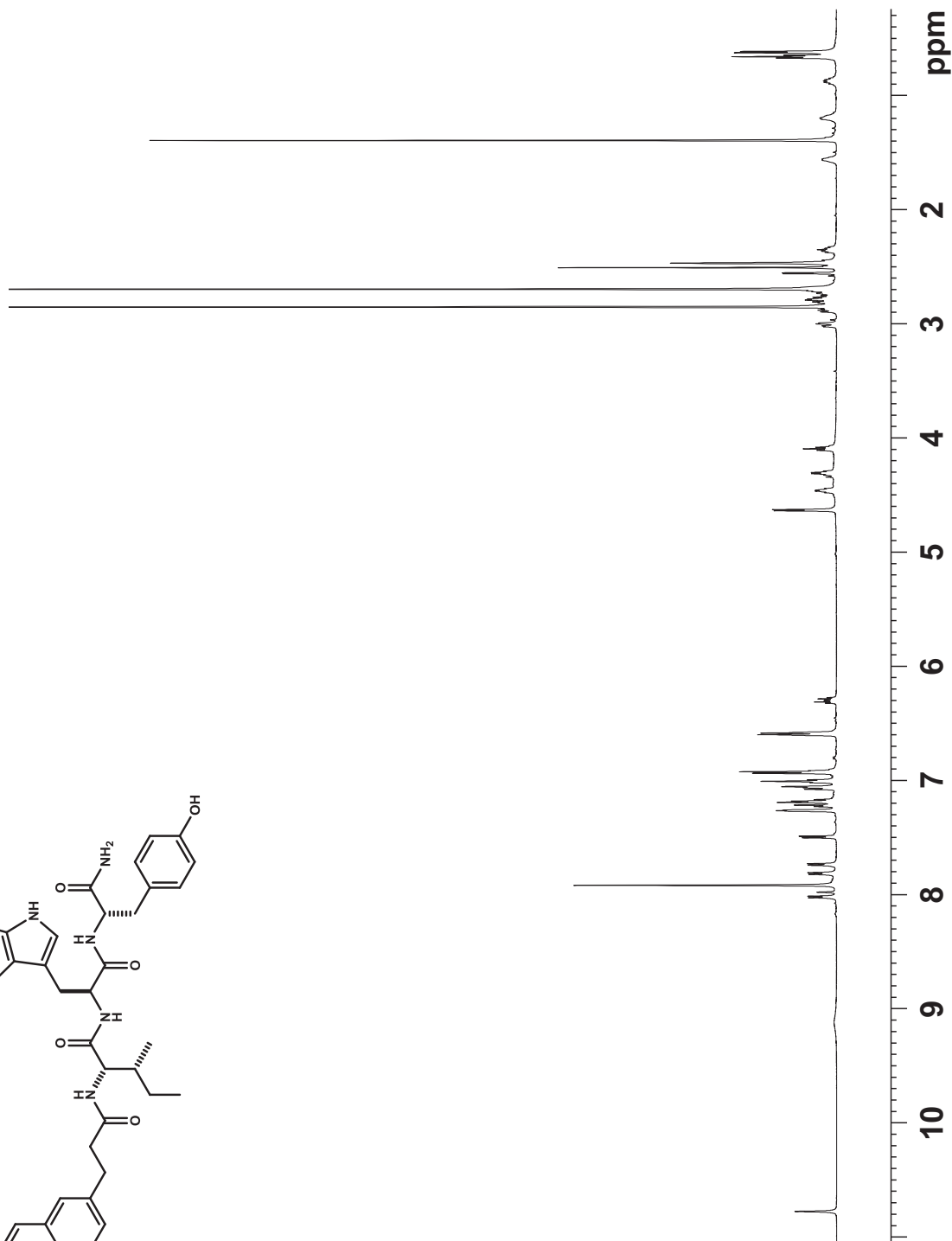


Current Data Parameters
NAME KL-III-287
EXPNO 1
PROCNO 1

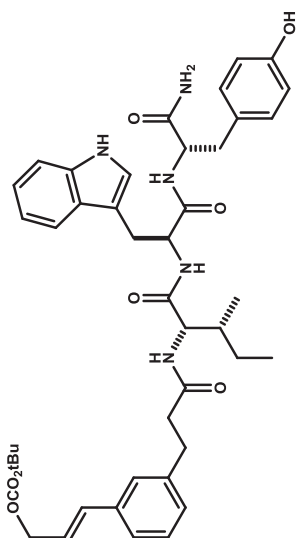
F2 - Acquisition Parameters
Date_ 20110828
Time_ 18.29
INSTRUM 5 mm BB5
PROBHD zg30
PULPROG 65536
TD 8
SOLVENT DMSO
NS 0
DS 12376.237 Hz
SWH 0.188846 Hz
FIDRES 2.6476543 sec
AQ 90.5
RG 40.400 usec
DE 6.50 usec
TE 294.1 K
D1 2.0000000 sec
TD0 1

===== CHANNEL f1 =====
NUC1 1H
P1 14.00 usec
PL1 -1.00 dB
PL1W 31.62277603 W
SFO1 600.1336008 MHz

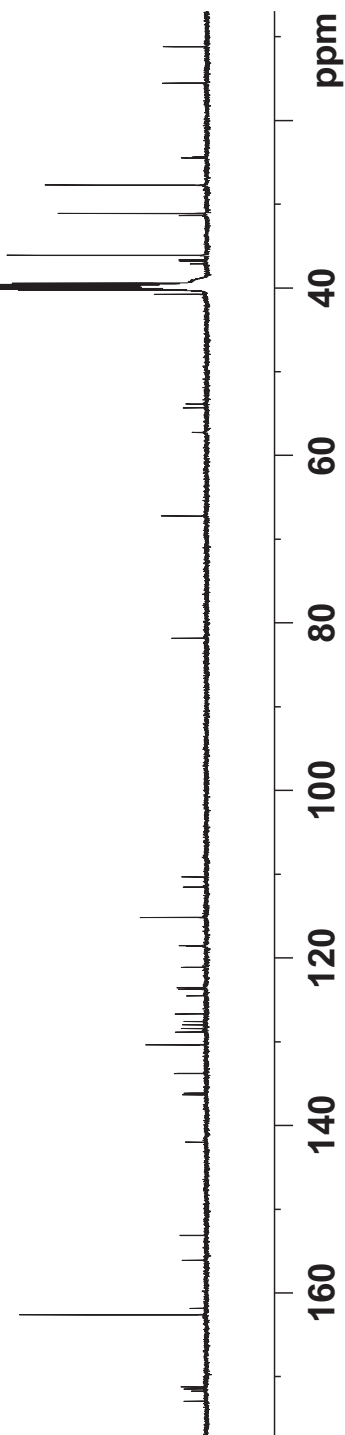
F2 - Processing parameters
SI 65536
SF 600.1300273 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



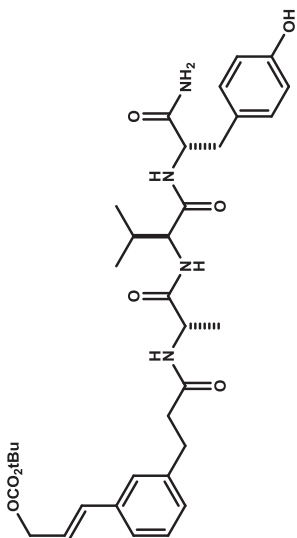
Acyclic-Ile-Trp-Tyr (S10):



Current Data Parameters
NAME KL-III-287
EXPNO 2
PROCNO 1
F2 - Processing parameters
SI 65536
SF 150.9028319 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40



Acyclic-Ala-Val-Tyr (S11):

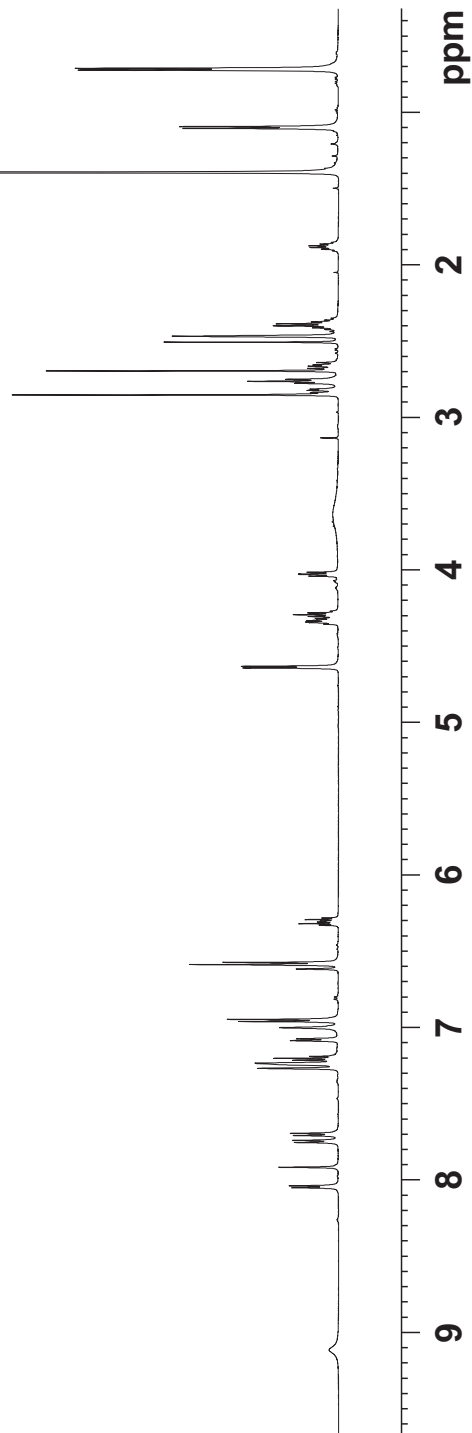


Current Data Parameters
NAME KL-III-286
EXPNO 1
PROCNO 1

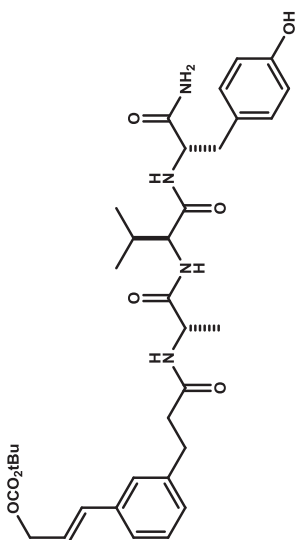
F2 - Acquisition Parameters
Date_ 20110829
Time_ 13.37
INSTRUM 5 mm BB5
PROBHD zg30
PULPROG 65536
TD 1
SOLVENT DMSO
NS 8
DS 0
SWH 12376.237 Hz
FIDRES 0.188846 Hz
AQ 2.6476543 sec
RG 114
DW 40.400 usec
DE 6.50 usec
TE 294.3 K
D1 2.0000000 sec
TD0 1

===== CHANNEL f1 =====
NUC1 1H
P1 14.00 usec
PL1 -1.00 dB
PL1W 31.62277603 W
SFO1 600.1336008 MHz

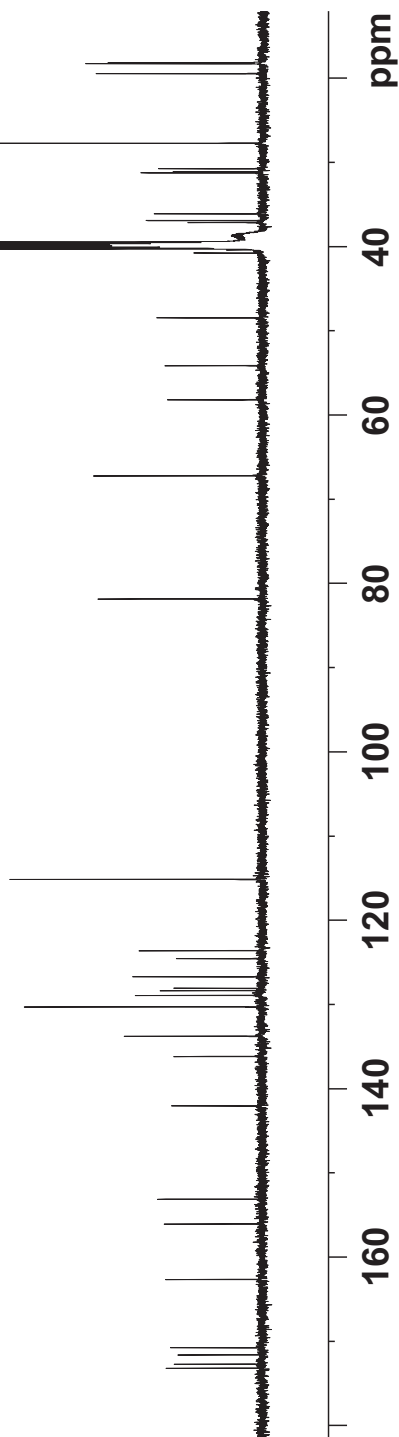
F2 - Processing parameters
SI 65536
SF 600.1300273 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



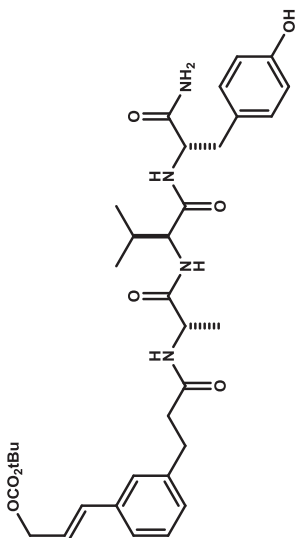
Acyclic-Ala-Val-Tyr (S11):



Current Data Parameters
NAME KL-III-286
EXPNO 2
PROCNO 1
F2 - Processing parameters
SI 65536
SF 150.9028319 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40



Acyclic-Ala-Val-Tyr (S11):

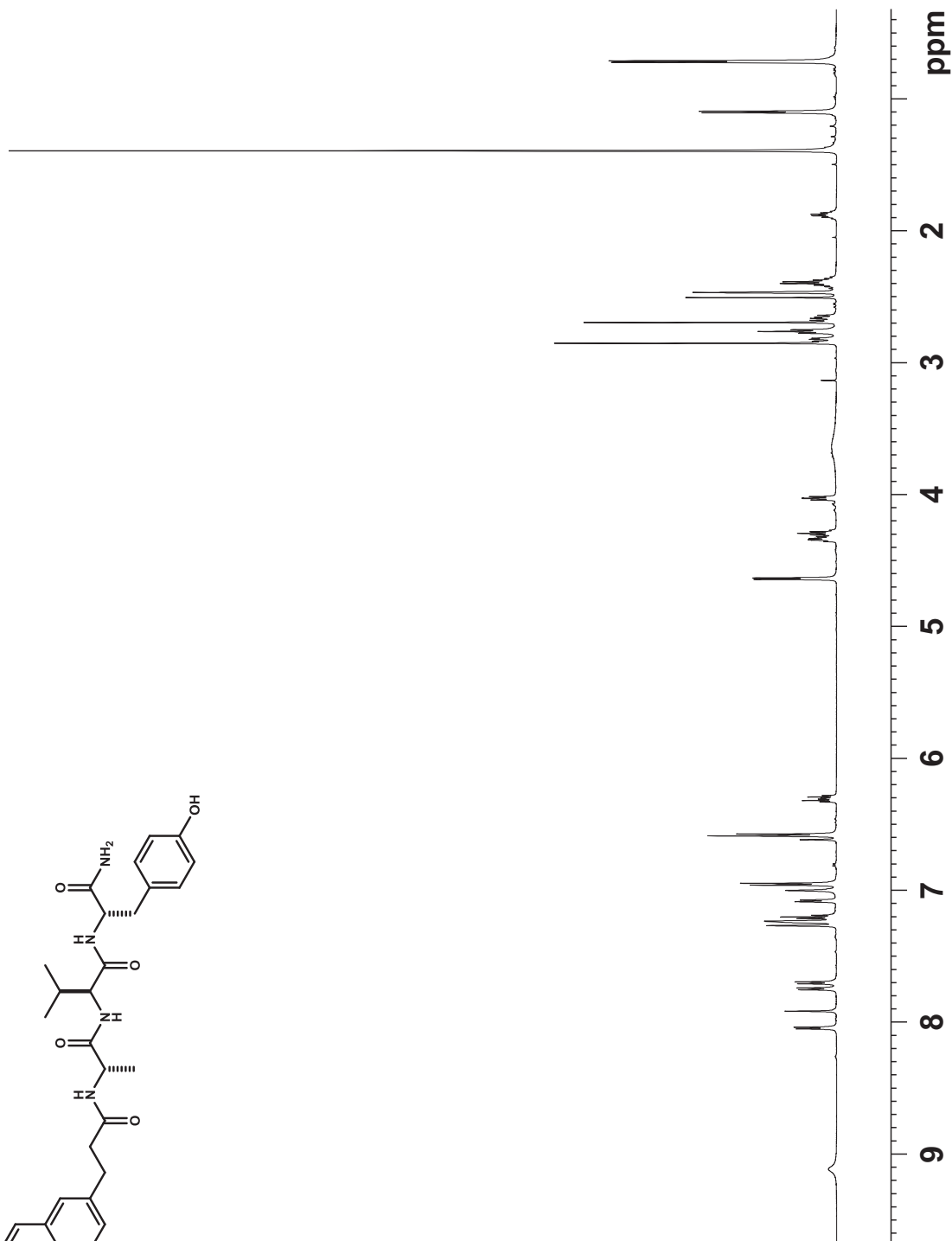


Current Data Parameters
NAME KL-III-286
EXPNO 1
PROCNO 1

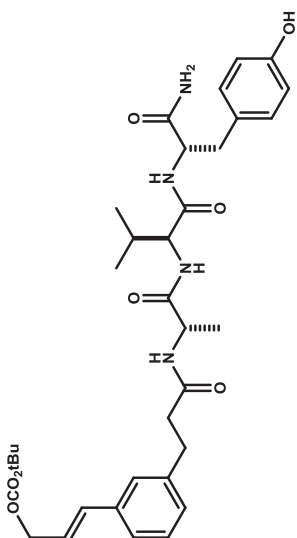
F2 - Acquisition Parameters
Date_ 20110829
Time_ 13.37
INSTRUM 5 mm BB5
PROBHD zg30
PULPROG 65536
TD 1
SOLVENT DMSO
NS 8
DS 0
SWH 12376.237 Hz
FIDRES 0.188846 Hz
AQ 2.6476543 sec
RG 114
DW 40.400 usec
DE 6.50 usec
TE 294.3 K
D1 2.0000000 sec
TD0 1

===== CHANNEL f1 =====
NUC1 1H
P1 14.00 usec
PL1 -1.00 dB
PL1W 31.62277603 W
SFO1 600.1336008 MHz

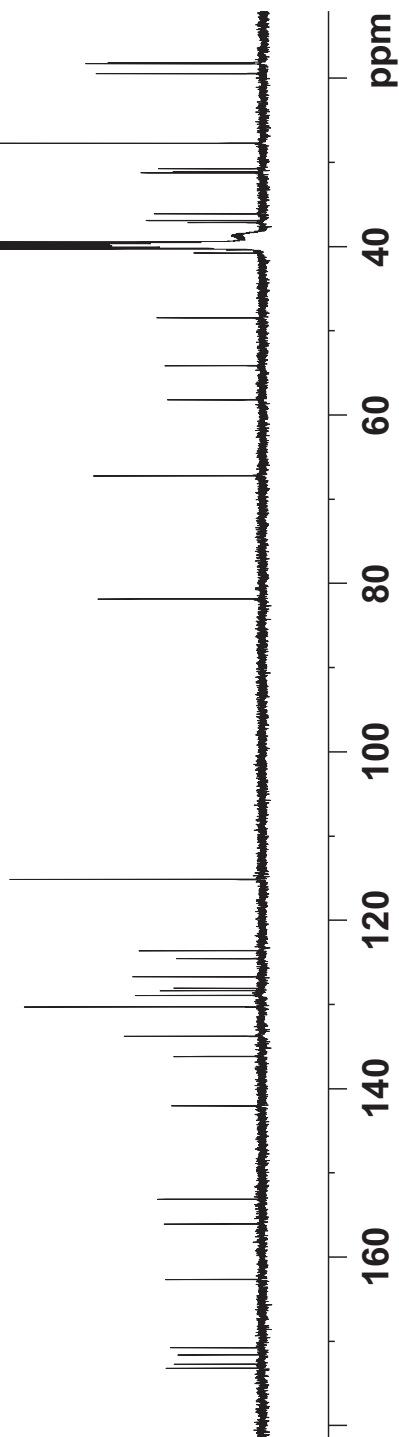
F2 - Processing parameters
SI 65536
SF 600.1300273 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



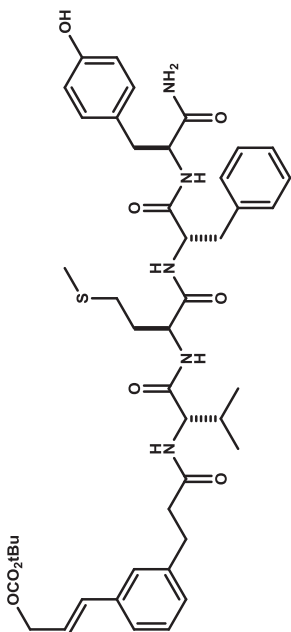
Acyclic-Ala-Val-Tyr (S11):



Current Data Parameters
NAME KL-III-286
EXPNO 2
PROCNO 1
F2 - Processing parameters
SI 65536
SF 150.9028319 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40



Acyclic-Val-Met-Phe-Tyr (S12):

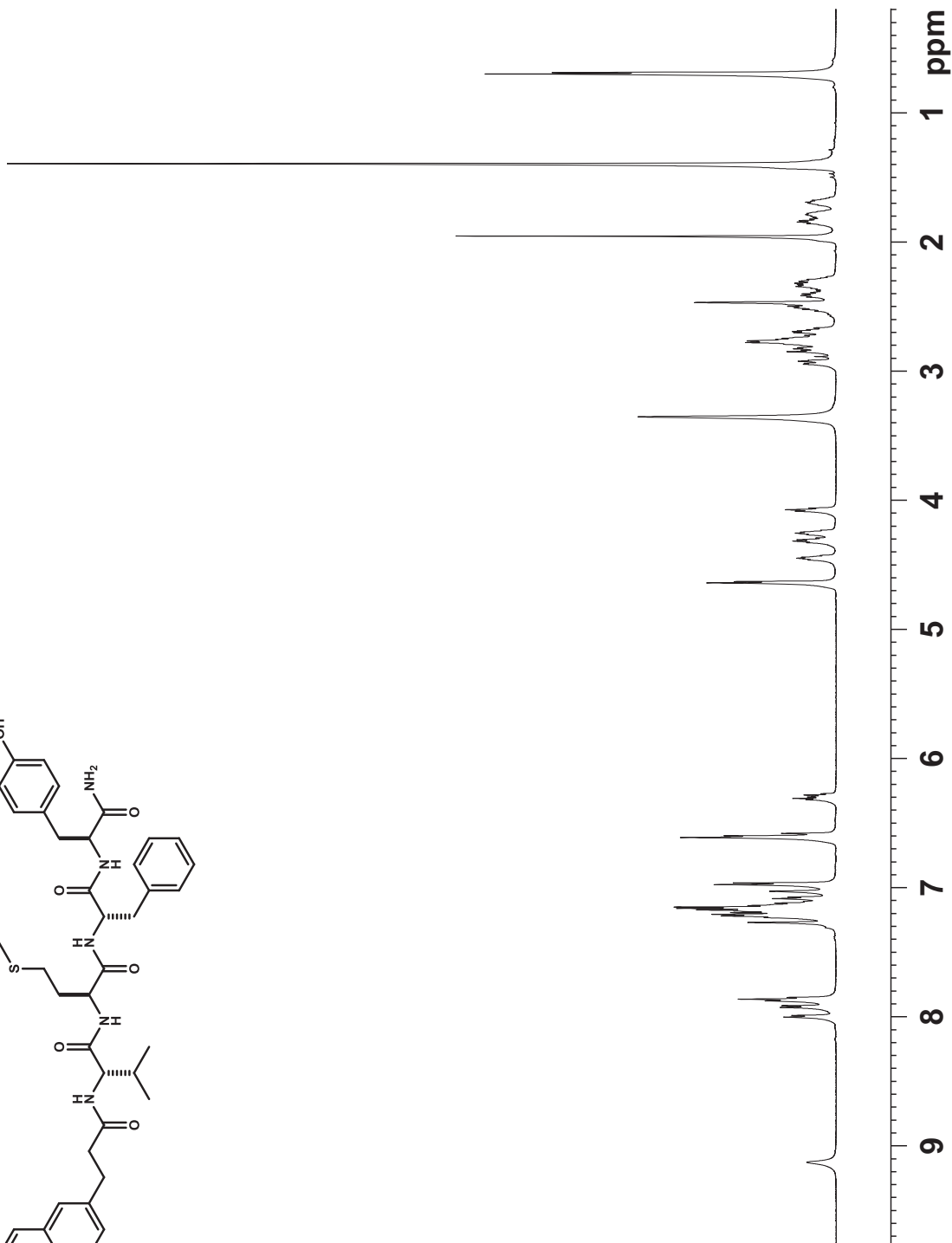


Current Data Parameters
NAME KL-4-39
EXPNO 2
PROCNO 1

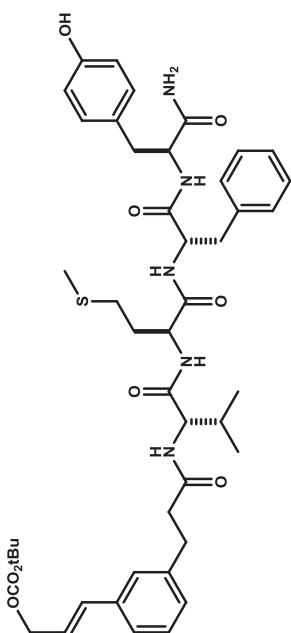
F2 - Acquisition Parameters
Date_ 20111010
Time_ 19.06
INSTRUM av600
PROBHD 5 mm BB5
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 2
DS 0
SWH 12376.237 Hz
FIDRES 0.188846 Hz
AQ 2.6476543 sec
RG 90.5
DW 40.400 usec
DE 6.50 usec
TE 294.7 K
D1 2.00000000 sec
TD0 1

===== CHANNEL f1 =====
NUC1 1H
P1 14.00 usec
PL1 -1.00 dB
PL1W 31.62277603 W
SF01 600.1336008 MHz

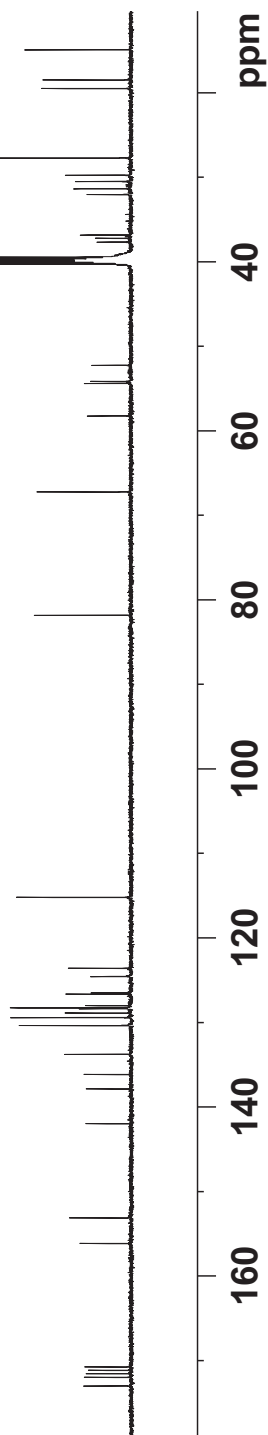
F2 - Processing parameters
SI 65536
SF 600.1300273 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



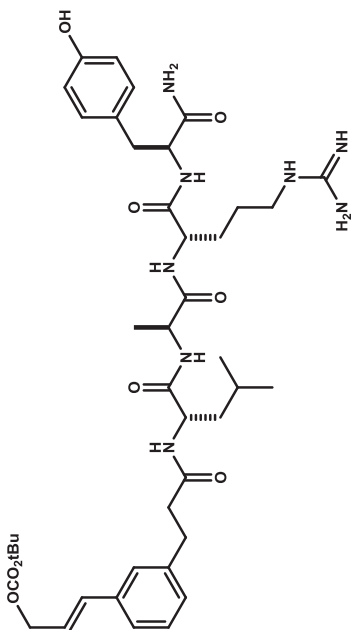
Acyclic-Val-Met-Phe-Tyr (S12):



Current Data Parameters
NAME KL-4-39
EXPNO 3
PROCNO 1
F2 - Processing parameters
SI 65536
SF 150.9028319 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40



Acyclic-Leu-Ala-Arg-Tyr (S14):



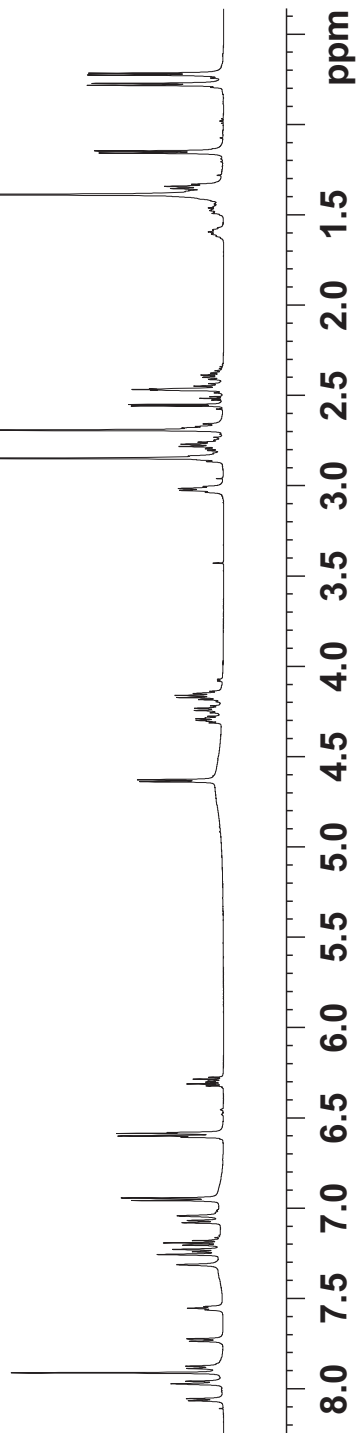
```

Current Data Parameters
NAME          KL-4-8
EXPNO         1
PROCNO        1

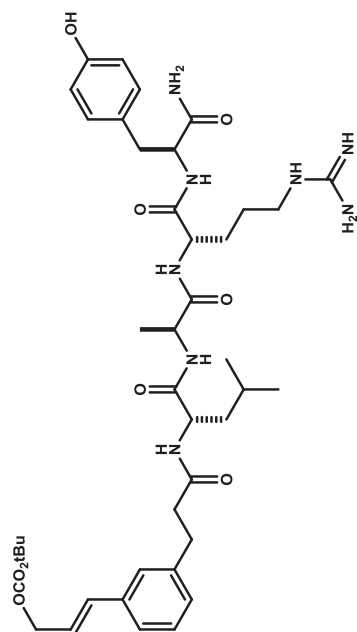
F2 - Acquisition Parameters
Date_         20110926
Time_         17.17
INSTRUM       av600
PROBHD        5 mm BB5
PULPROG       zg30
TD            65536
SOLVENT       DMSO
NS            8
DS            0
SWH           12376.237 Hz
FIDRES        0.188846 Hz
AQ            2.6476543 sec
RG            45.3
DW            40.400 usec
DE            6.50 usec
TE            295.3 K
D1            2.0000000 sec
TD0           1

===== CHANNEL f1 =====
NUC1          1H
P1            14.00 usec
PL1           -1.00 dB
PL1W          31.62277603 W
SFO1          600.1336008 MHz

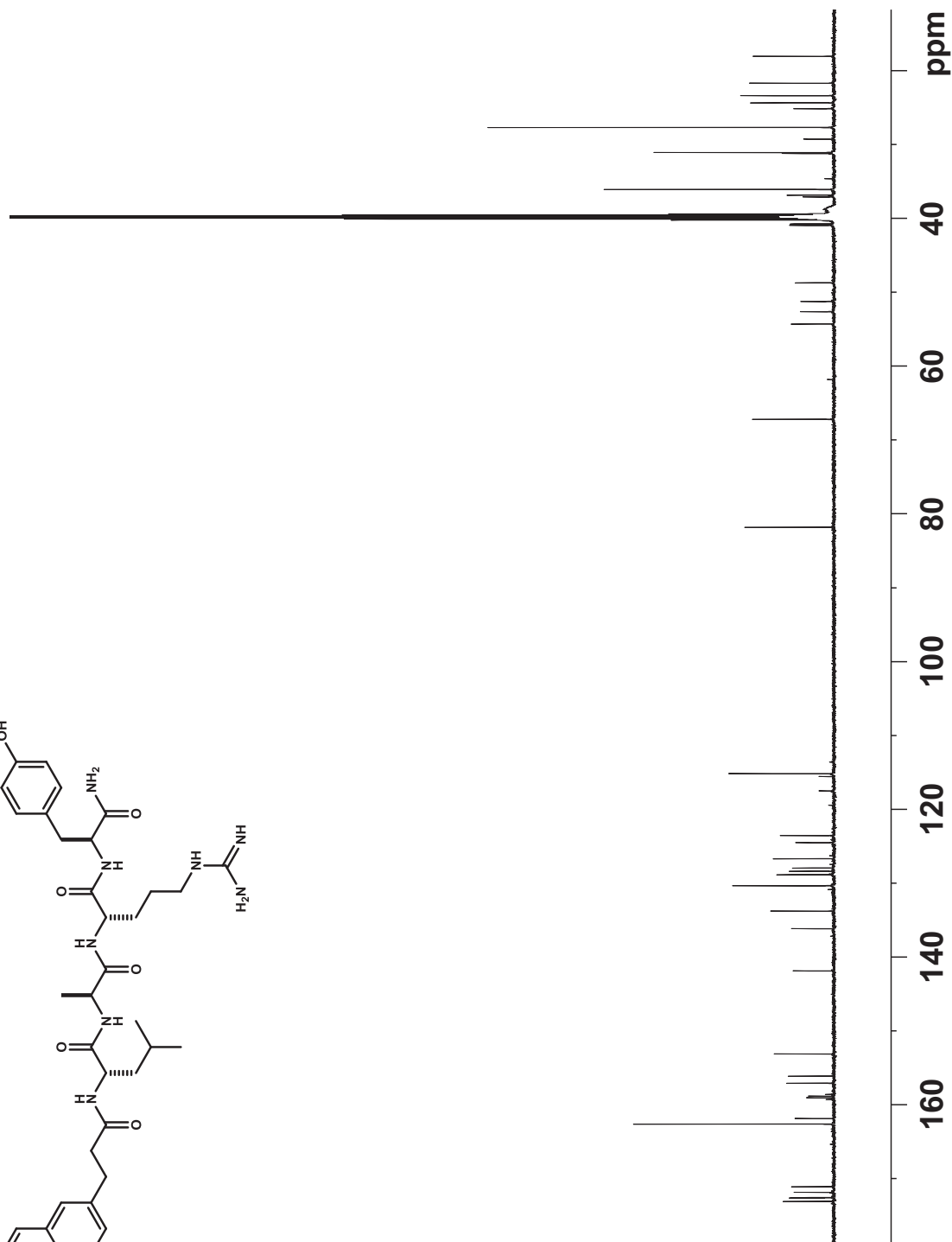
F2 - Processing parameters
SI            65536
SF            600.1300273 MHz
WDW           EM
SSB           0
LB            0.30 Hz
GB            0
PC            1.00
  
```



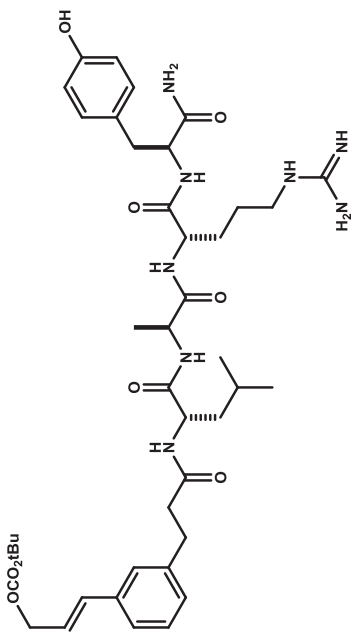
Acyclic-Leu-Ala-Arg-Tyr (S14):



Current Data Parameters
NAME KL-4-8
EXPNO 2
PROCNO 1
F2 - Processing parameters
SI 65536
SF 150.9028319 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40



Acyclic-Leu-Ala-Arg-Tyr (S14):



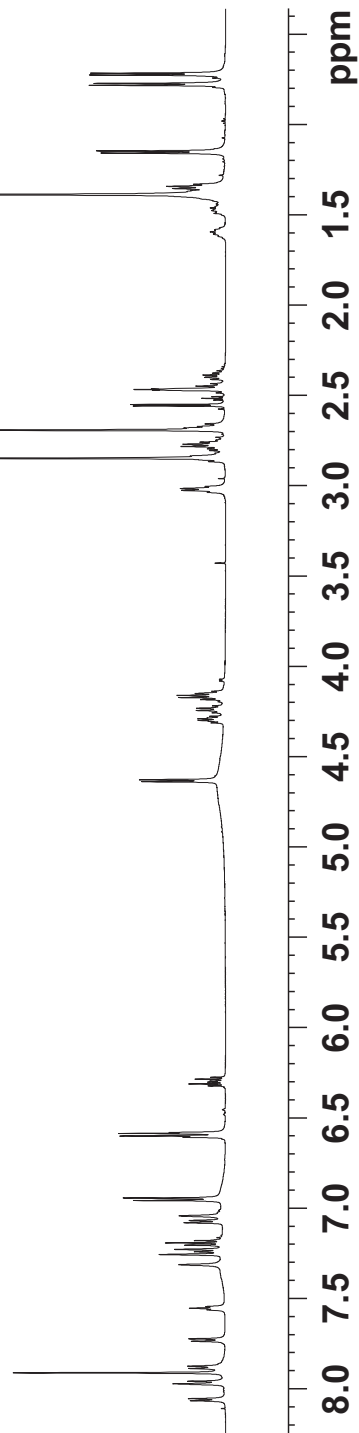
```

Current Data Parameters
NAME          KL-4-8
EXPNO         1
PROCNO        1

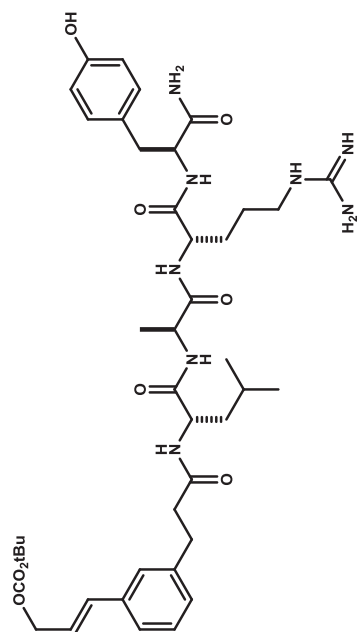
F2 - Acquisition Parameters
Date_         20110926
Time_         17.17
INSTRUM       av600
PROBHD        5 mm BB5
PULPROG       zg30
TD            65536
SOLVENT       DMSO
NS            8
DS            0
SWH           12376.237 Hz
FIDRES        0.188846 Hz
AQ            2.6476543 sec
RG            45.3
DW            40.400 usec
DE            6.50 usec
TE            295.3 K
D1            2.0000000 sec
TD0           1

===== CHANNEL f1 =====
NUC1          1H
P1            14.00 usec
PL1           -1.00 dB
PL1W          31.62277603 W
SFO1          600.1336008 MHz

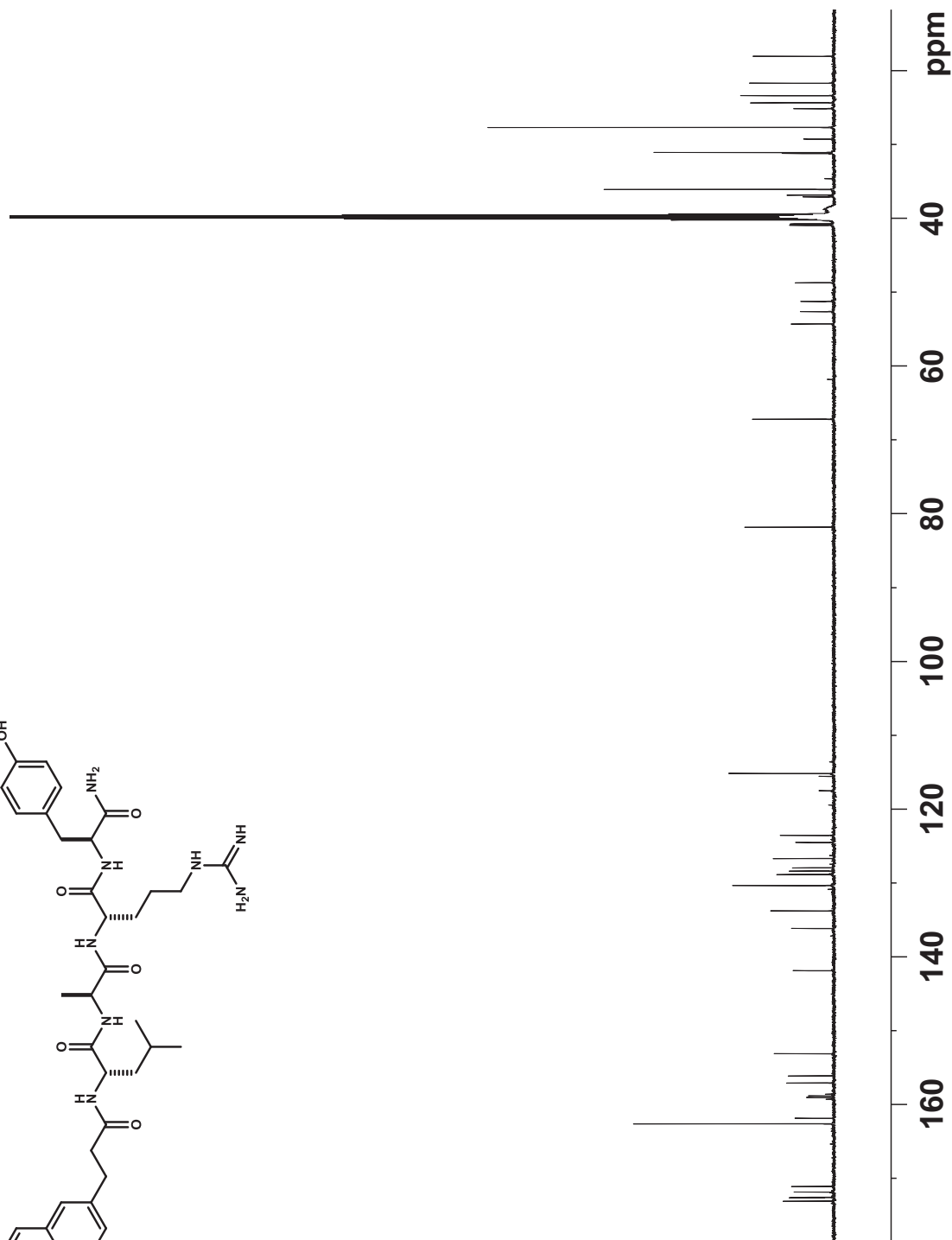
F2 - Processing parameters
SI            65536
SF            600.1300273 MHz
WDW           EM
SSB           0
LB            0.30 Hz
GB            0
PC            1.00
  
```



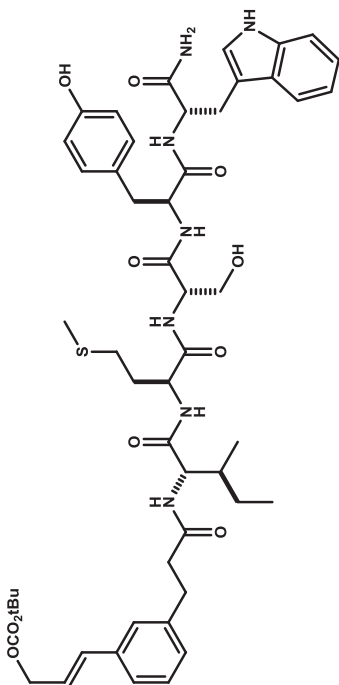
Acyclic-Leu-Ala-Arg-Tyr (S14):



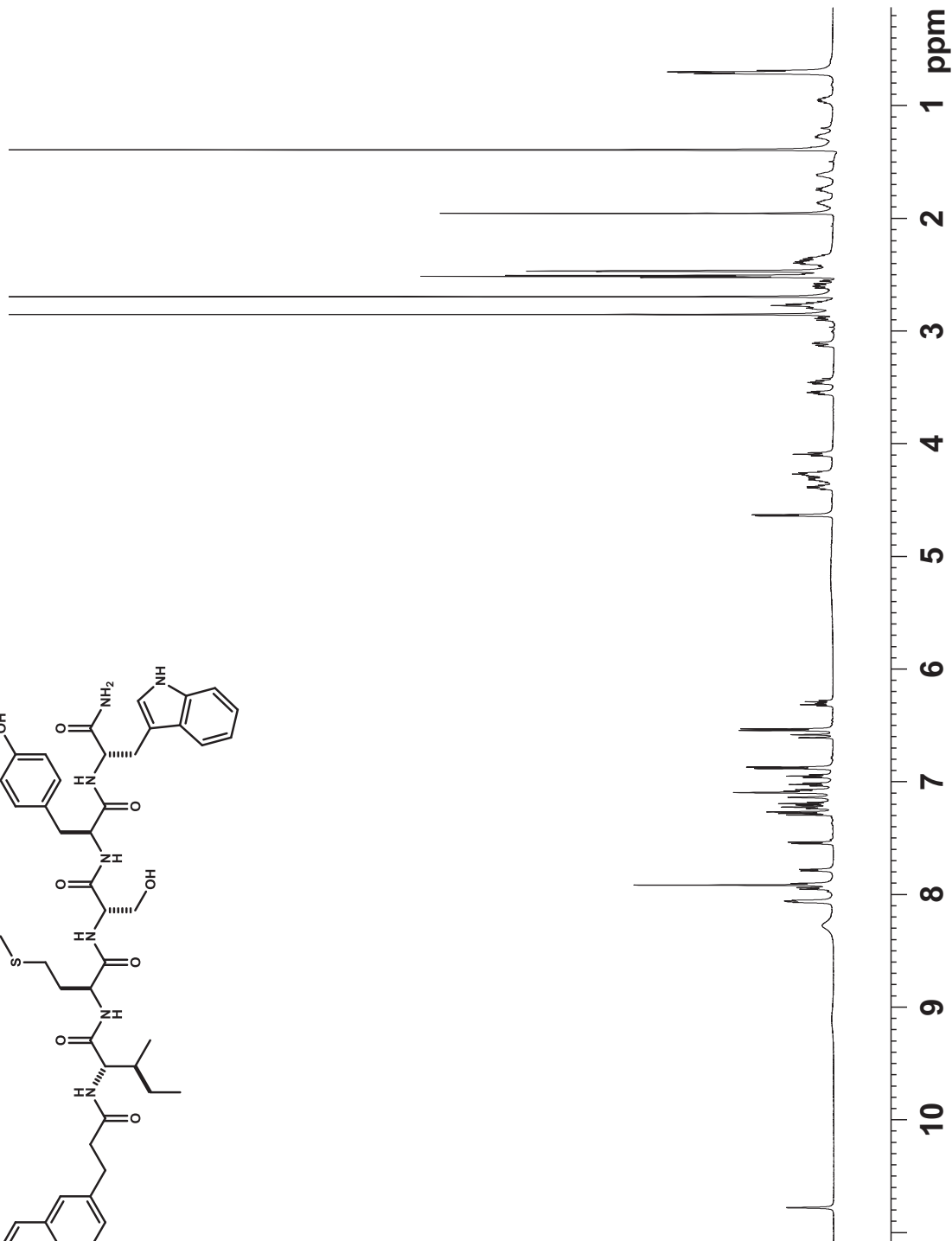
Current Data Parameters
NAME KL-4-8
EXPNO 2
PROCNO 1
F2 - Processing parameters
SI 65536
SF 150.9028319 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40



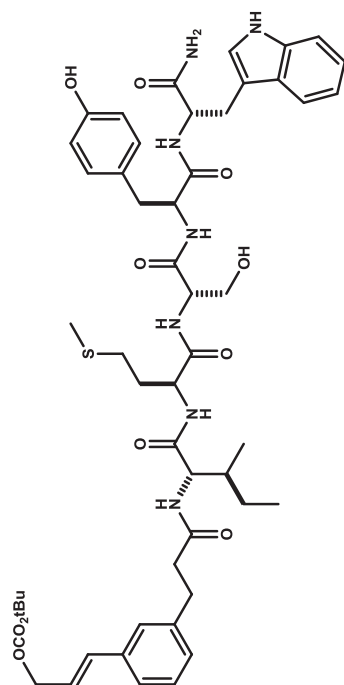
Acyclic-Ile-Met-Ser-Tyr-Trp (S15):



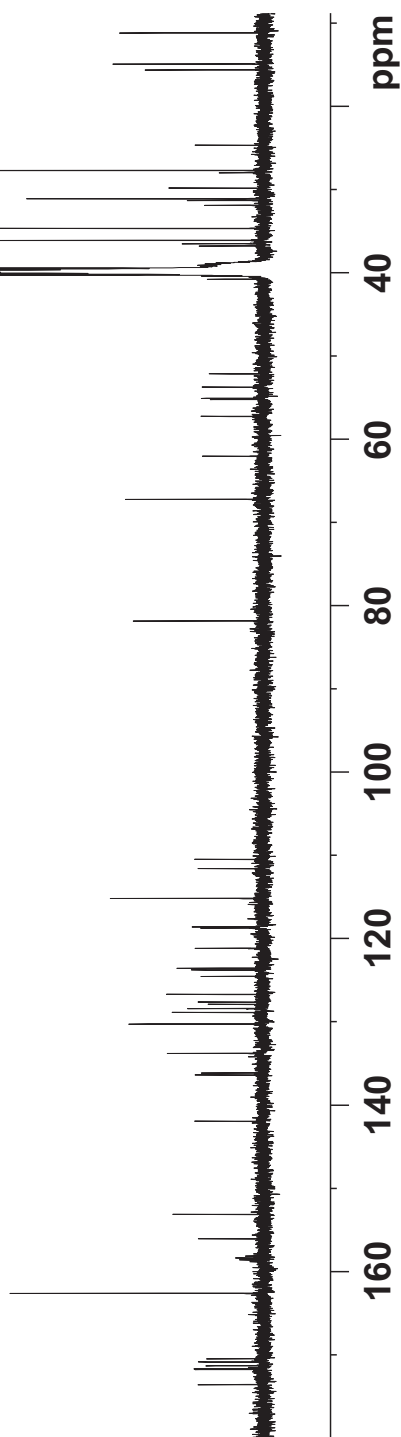
Current Data Parameters
NAME KL-III-289
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20110829
Time_ 14.51
INSTRUM av600
PROBHD 5 mm BB5
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 8
DS 0
SWH 12376.237 Hz
FIDRES 0.188846 Hz
AQ 2.6476543 sec
RG 128
DW 40.400 usec
DE 6.50 usec
TE 294.5 K
D1 2.0000000 sec
TD0 1
===== CHANNEL f1 =====
NUC1 1H
P1 14.00 usec
PL1 -1.00 dB
PL1W 31.62277603 W
SFO1 600.136008 MHz
F2 - Processing parameters
SI 65536
SF 600.1300273 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



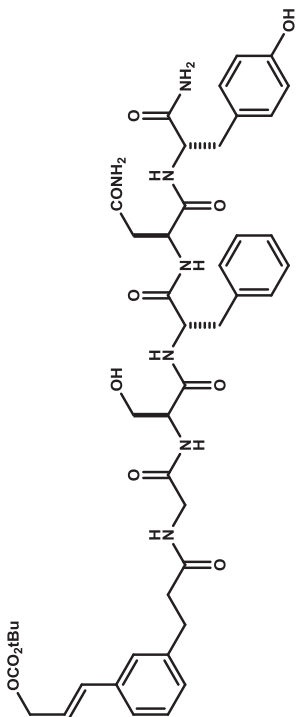
Acyclic-Ile-Met-Ser-Tyr-Trp (S15):



Current Data Parameters
NAME KL-III-289
EXPNO 2
PROCNO 1
F2 - Processing parameters
SI 65536
SF 150.9028319 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40



Acyclic-Ala-Phe-Thr-Ile-Tyr (S16):

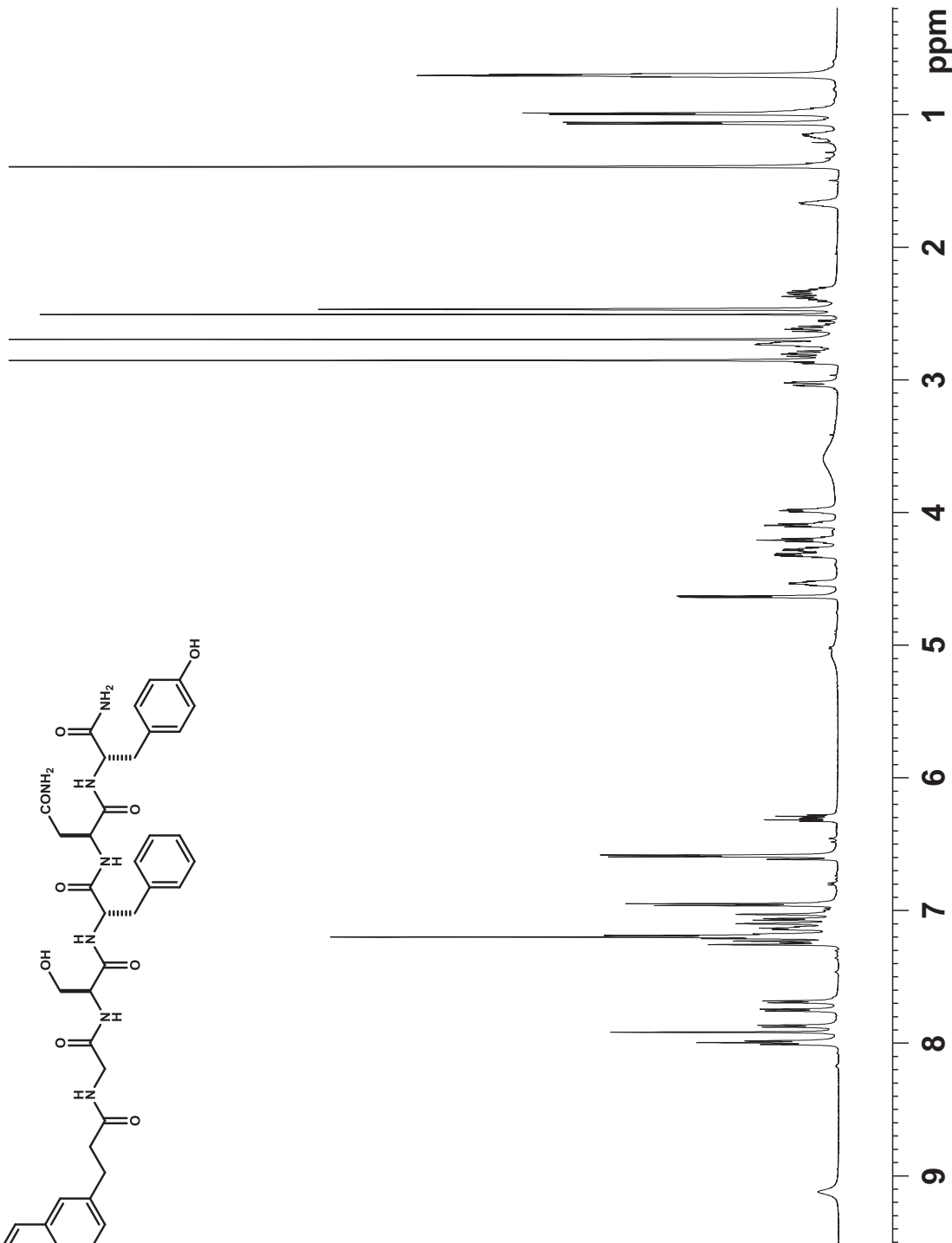


Current Data Parameters
NAME KL-III-279
EXPNO 1
PROCNO 1

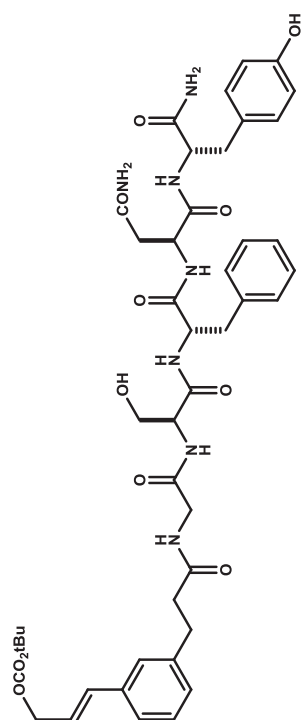
F2 - Acquisition Parameters
Date_ 20110829
Time_ 16.16
INSTRUM av600
PROBHD 5 mm BB5
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 8
DS 0
SWH 12376.237 Hz
FIDRES 0.188846 Hz
AQ 2.6476543 sec
RG 114
DW 40.400 usec
DE 6.50 usec
TE 294.2 K
D1 2.0000000 sec
TD0 1

===== CHANNEL f1 =====
NUC1 1H
P1 14.00 usec
PL1 -1.00 dB
PL1W 31.62277603 W
SFO1 600.1336008 MHz

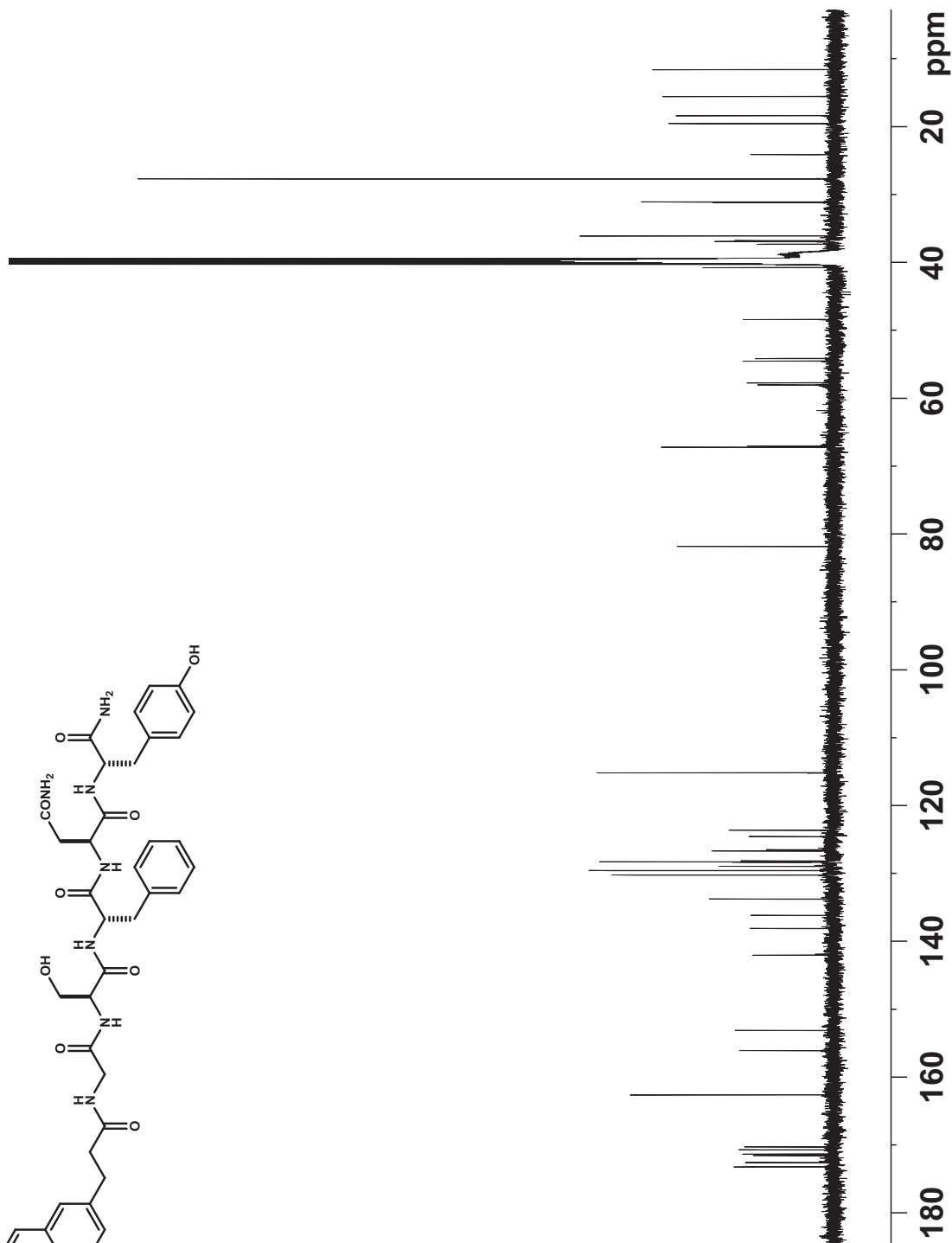
F2 - Processing parameters
SI 65536
SF 600.1300273 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



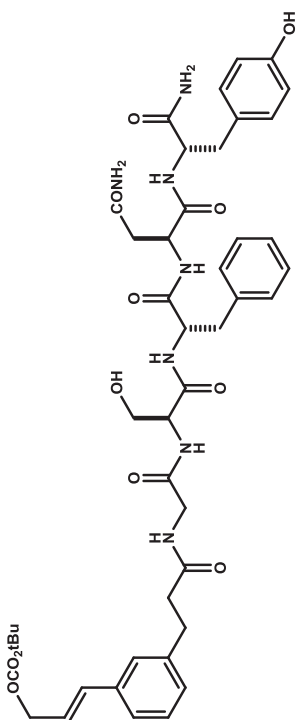
Acyclic-Ala-Phe-Thr-Ile-Tyr (S16):



Current Data Parameters
 NAME KL-III-279
 EXPNO 2
 PROCNO 1
 F2 - Processing parameters
 SI 65536
 SF 150.9028319 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40



Acyclic-Gly-Ser-Phe-Asn-Tyr (S17):



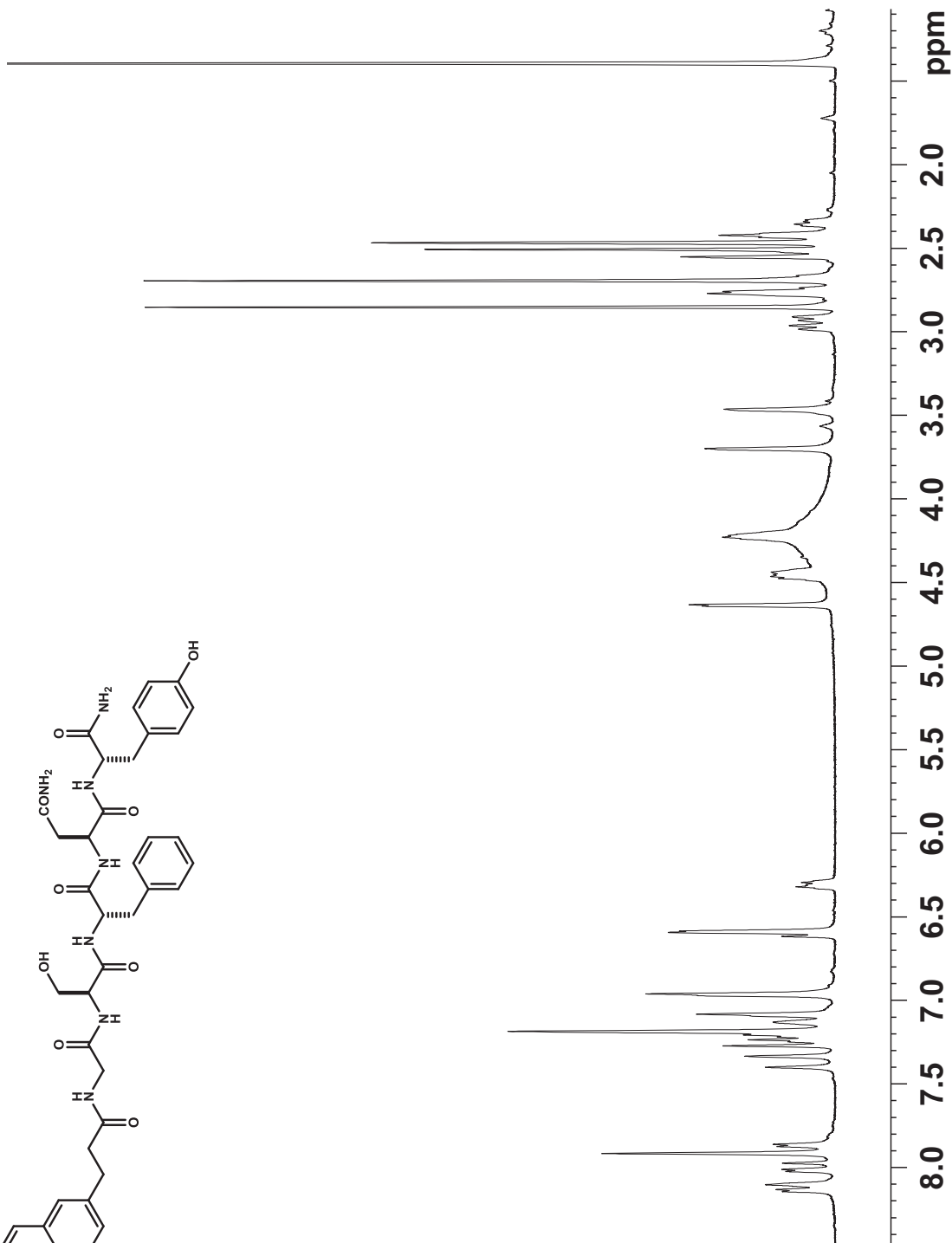
```

Current Data Parameters
NAME      KL-III-278
EXPNO     1
PROCNO    1

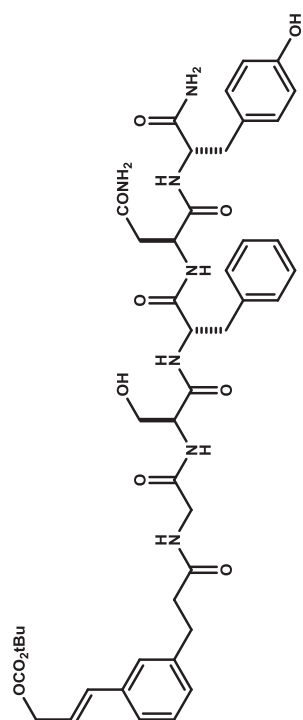
F2 - Acquisition Parameters
Date_     20110830
Time      16.05
INSTRUM   av600
PROBHD    5 mm BB5
PULPROG   zg30
TD         65536
SOLVENT   DMSO
NS         8
DS         0
SWH        12376.237 Hz
FIDRES     0.188846 Hz
AQ         2.6476543 sec
RG         128
DW         40.400 usec
DE         6.50 usec
TE         294.7 K
D1         2.0000000 sec
TD0        1

===== CHANNEL f1 =====
NUC1       1H
P1         14.00 usec
PL1        -1.00 dB
PL1W       31.62277603 W
SFO1       600.1336008 MHz

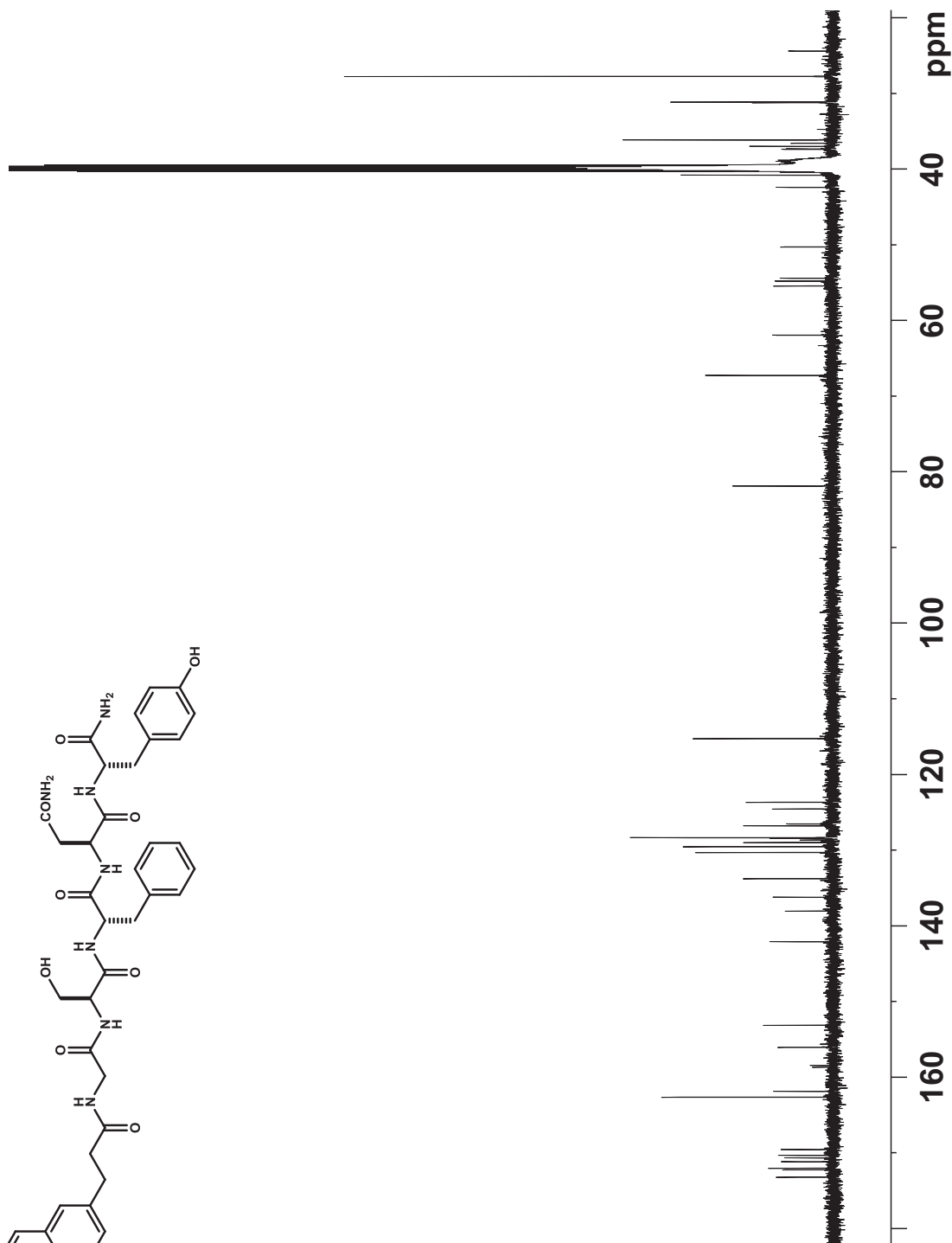
F2 - Processing parameters
SI         65536
SF         600.1300273 MHz
WDW        EM
SSB        0
LB         0 Hz
GB         0
PC         1.00
  
```

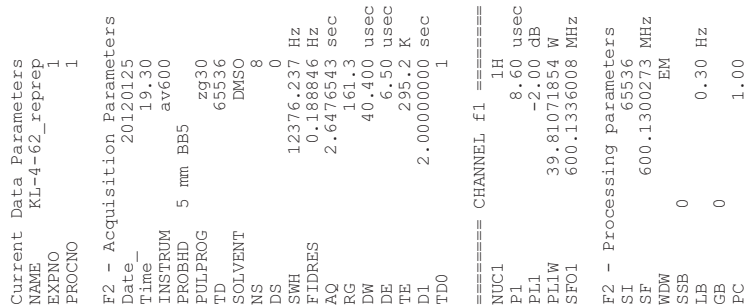


Acyclic-Gly-Ser-Phe-Asn-Tyr (S17):

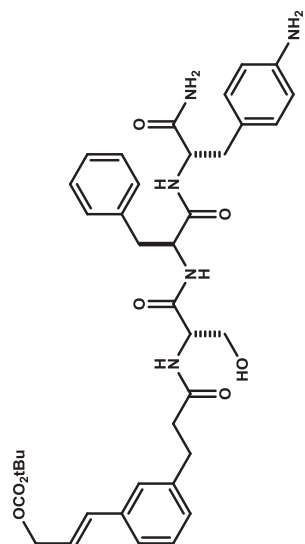


Current Data Parameters
NAME KL-III-278
EXPNO 2
PROCNO 1
F2 - Processing parameters
SI 65536
SF 150.9028319 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

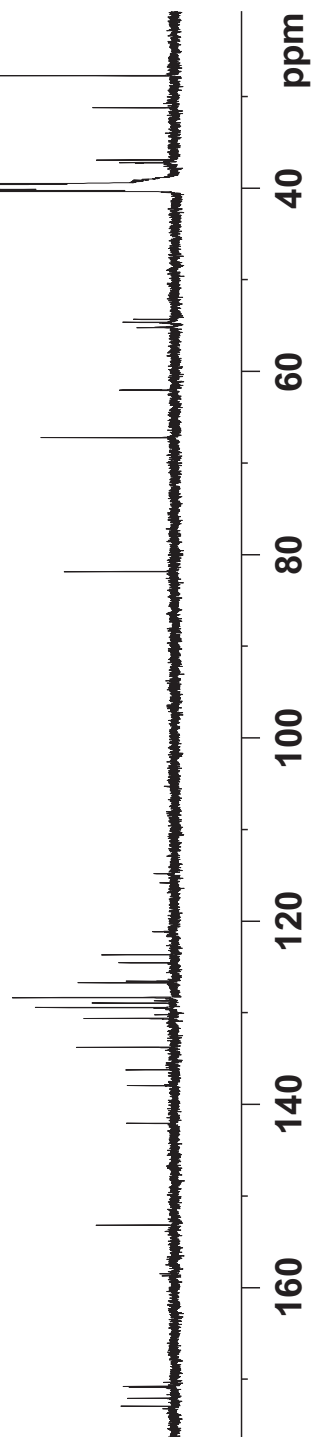


CCCC(=O)Oc1ccc(cc1)/C=C/C2=CC=CC=C2C(=O)N[C@@H](CCC(=O)N[C@@H](Cc3ccccc3)C(=O)N[C@@H](Cc4ccc(N)cc4)C(=O)O)C(=O)O

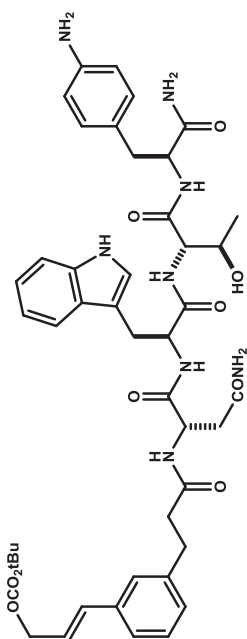
Acyclic-Ser-Phe-Phe(4-NH₂) (S18):



Current Data Parameters
NAME KL-4-62
EXPNO 2
PROCNO 1
F2 - Processing parameters
SI 65536
SF 150.9028319 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40



Acyclic-Asn-Trp-Thr-Phe(4-NH₂) (S19):



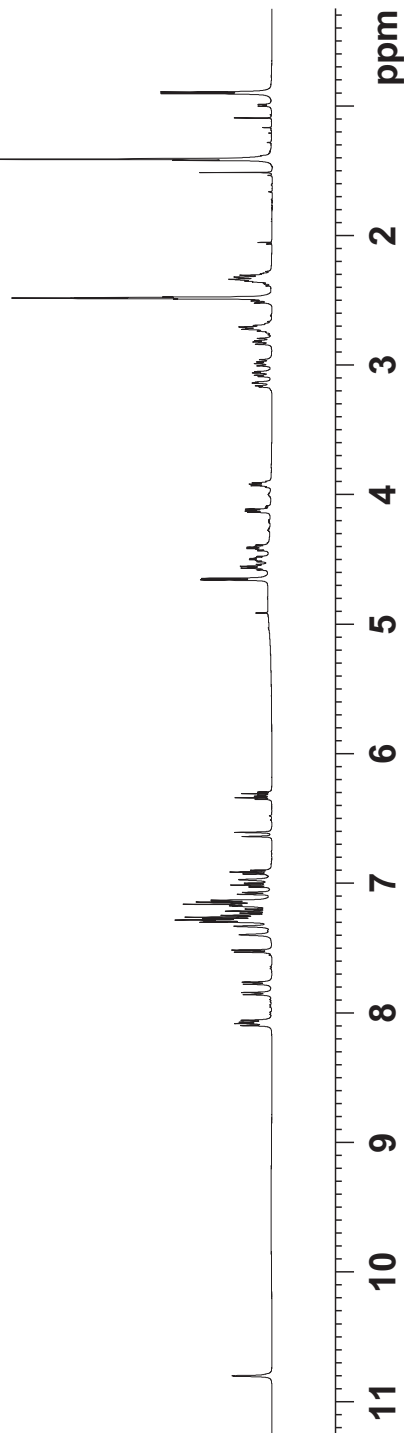
```

Current Data Parameters
NAME          KL-5-127
EXPNO         1
PROCNO        1

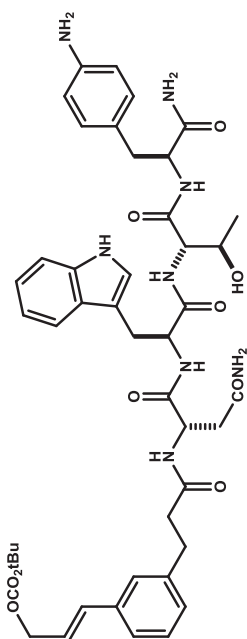
F2 - Acquisition Parameters
Date_         20130209
Time_         15:55
INSTRUM       av500
PROBHD        5 mm DCH 13C-1
PULPROG       zg30
TD            65536
SOLVENT       DMSO
NS            8
DS            0
SWH           10000.000 Hz
FIDRES        0.152588 Hz
AQ            3.2767999 sec
RG            11
DW            50.000 usec
DE            10.00 usec
TE            298.0 K
D1            2.00000000 sec
TD0           1

===== CHANNEL f1 =====
SF01          500.130008 MHz
NUC1          1H
P1            10.00 usec
PLW1          13.50000000 W

F2 - Processing parameters
SI            65536
SF            500.1300146 MHz
WDW           EM
SSB           0
LB            0.30 Hz
GB            0
PC            1.00
  
```



Acyclic-Asn-Trp-Thr-Phe(4-NH₂) (S19):



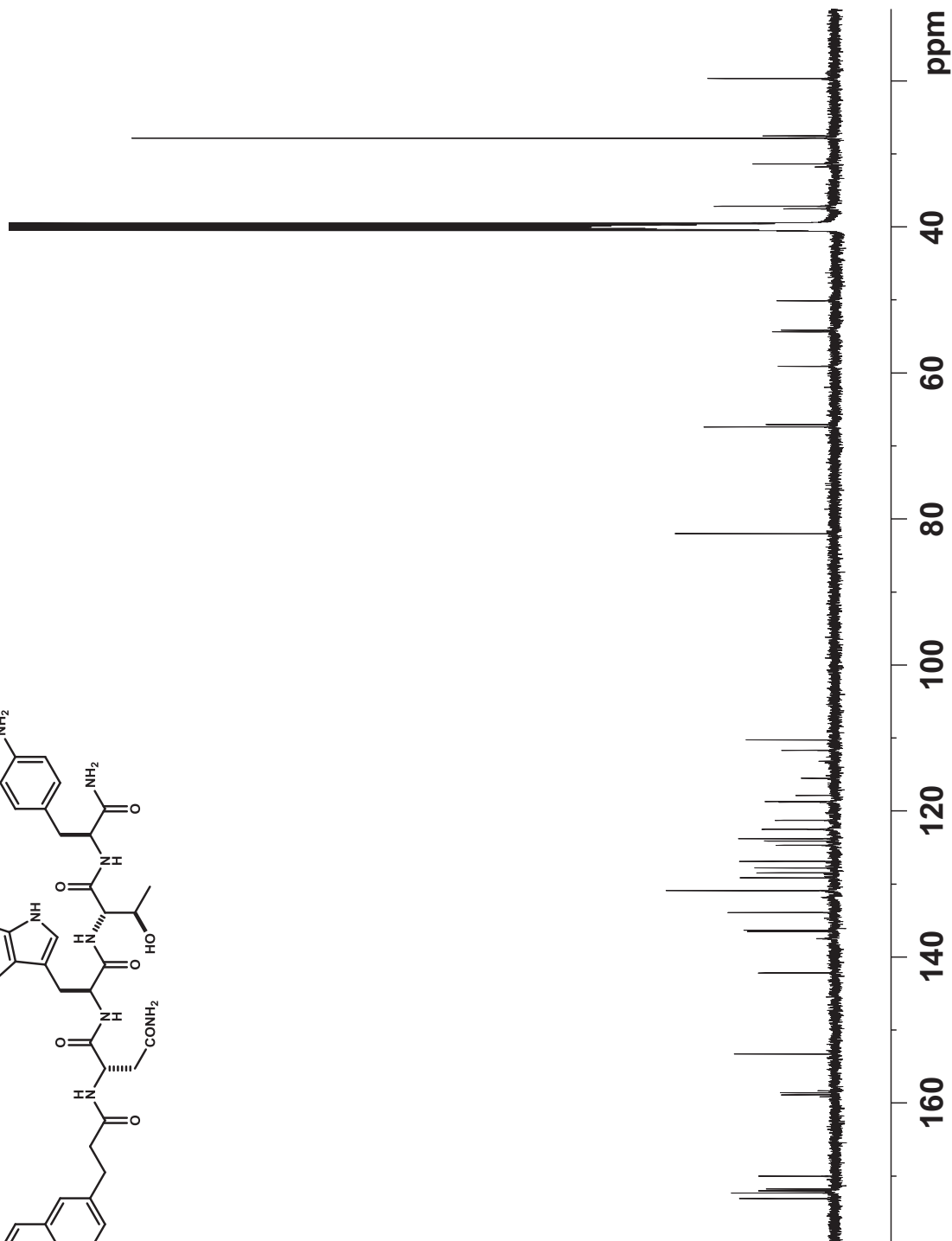
Current Data Parameters
 NAME KL-5-127
 EXPNO 2
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20130209
 Time_ 15:58
 INSTRUM av500
 PROBD 5 mm DCH 13C-1
 PULPROG zgpg30
 TD 65536
 SOLVENT DMSO
 NS 66
 DS 2
 SWH 31250.000 Hz
 FIDRES 0.476837 Hz
 AQ 1.0485760 sec
 RG 202.91
 DW 16.000 usec
 DE 18.00 usec
 TE 298.0 K
 D1 2.00000000 sec
 D11 0.03000000 sec
 TD0 1

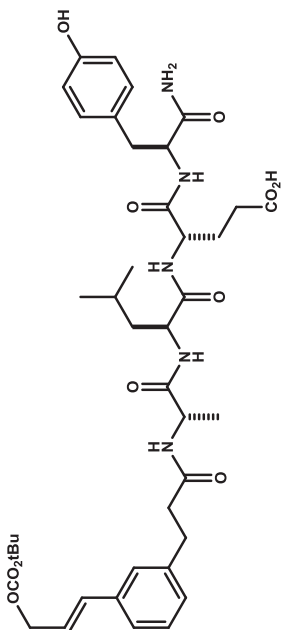
===== CHANNEL f1 =====
 SFO1 125.772511 MHz
 NUC1 13C
 P1 9.63 usec
 PLW1 23.00000000 W

===== CHANNEL f2 =====
 SFO2 500.1330008 MHz
 NUC2 1H
 CPDPRG2 waltz16
 FCPD2 80.00 usec
 PLW2 13.50000000 W
 PLW12 0.21094000 W
 PLW13 0.13500001 W

F2 - Processing parameters
 SI 131072
 SF 125.7577892 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40



Acyclic-Ala-Leu-Glu-Tyr (15):



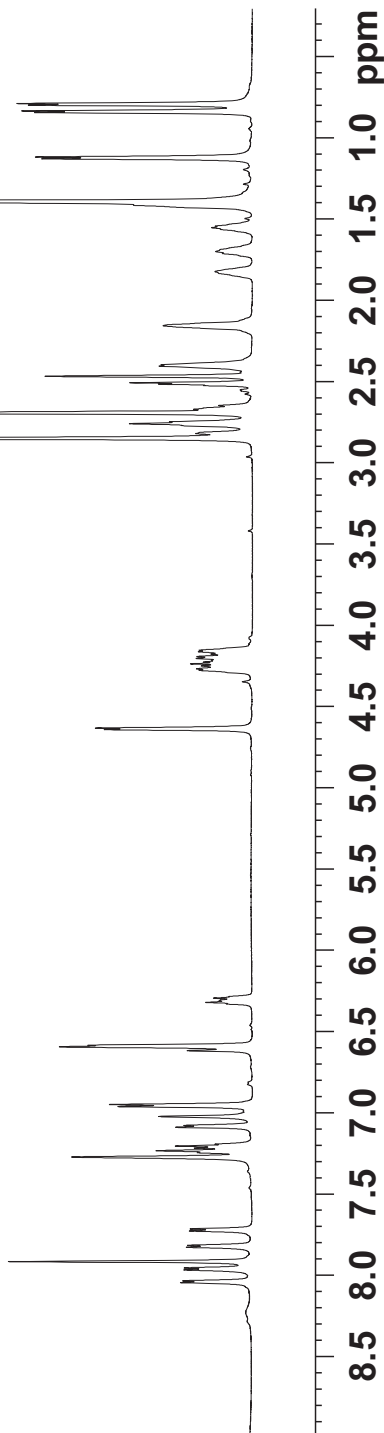
```

Current Data Parameters
NAME      KL-III-283
EXPNO     1
PROCNO    1

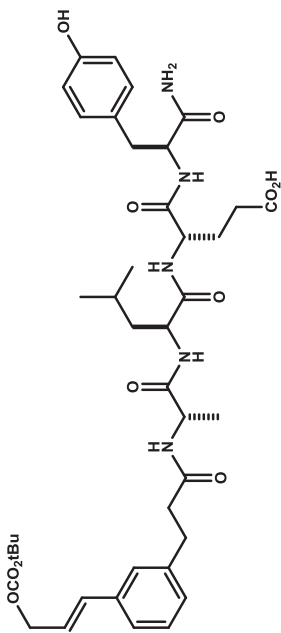
F2 - Acquisition Parameters
Date_     20110830
Time      17.22
INSTRUM   av600
PROBHD    5 mm BB5
PULPROG   zg30
TD         65536
SOLVENT   DMSO
NS         8
DS         0
SWH        12376.237 Hz
FIDRES     0.188846 Hz
AQ         2.6476543 sec
RG         71.8
DW         40.400 usec
DE         6.50 usec
TE         294.7 K
D1         2.00000000 sec
TD0        1

===== CHANNEL f1 =====
NUC1       1H
P1         14.00 usec
PL1        -1.00 dB
PL1W       31.62277603 W
SFO1       600.1336008 MHz

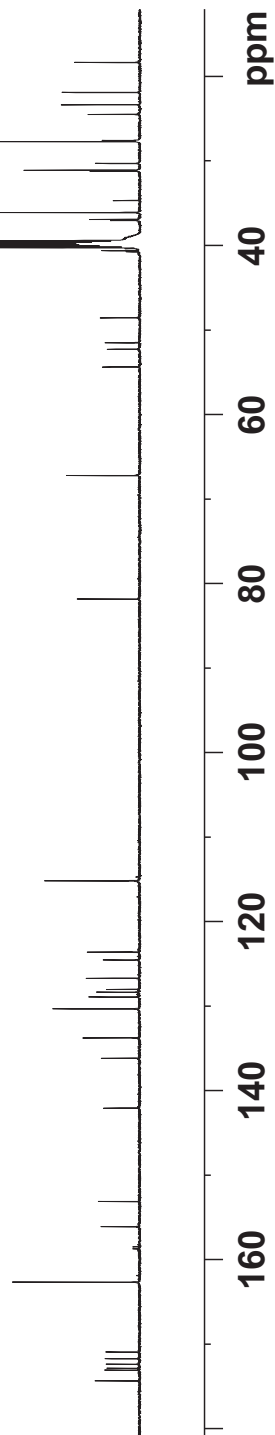
F2 - Processing parameters
SI         65536
SF         600.1300273 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00
  
```



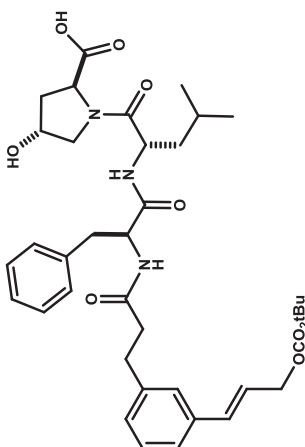
Acyclic-Ala-Leu-Glu-Tyr (15):



Current Data Parameters
 NAME KL-III-283
 EXPNO 2
 PROCNO 1
 F2 - Processing parameters
 SI 65536
 SF 150.9028319 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40



Acyclic-Phe-Leu-Hyp (S21):

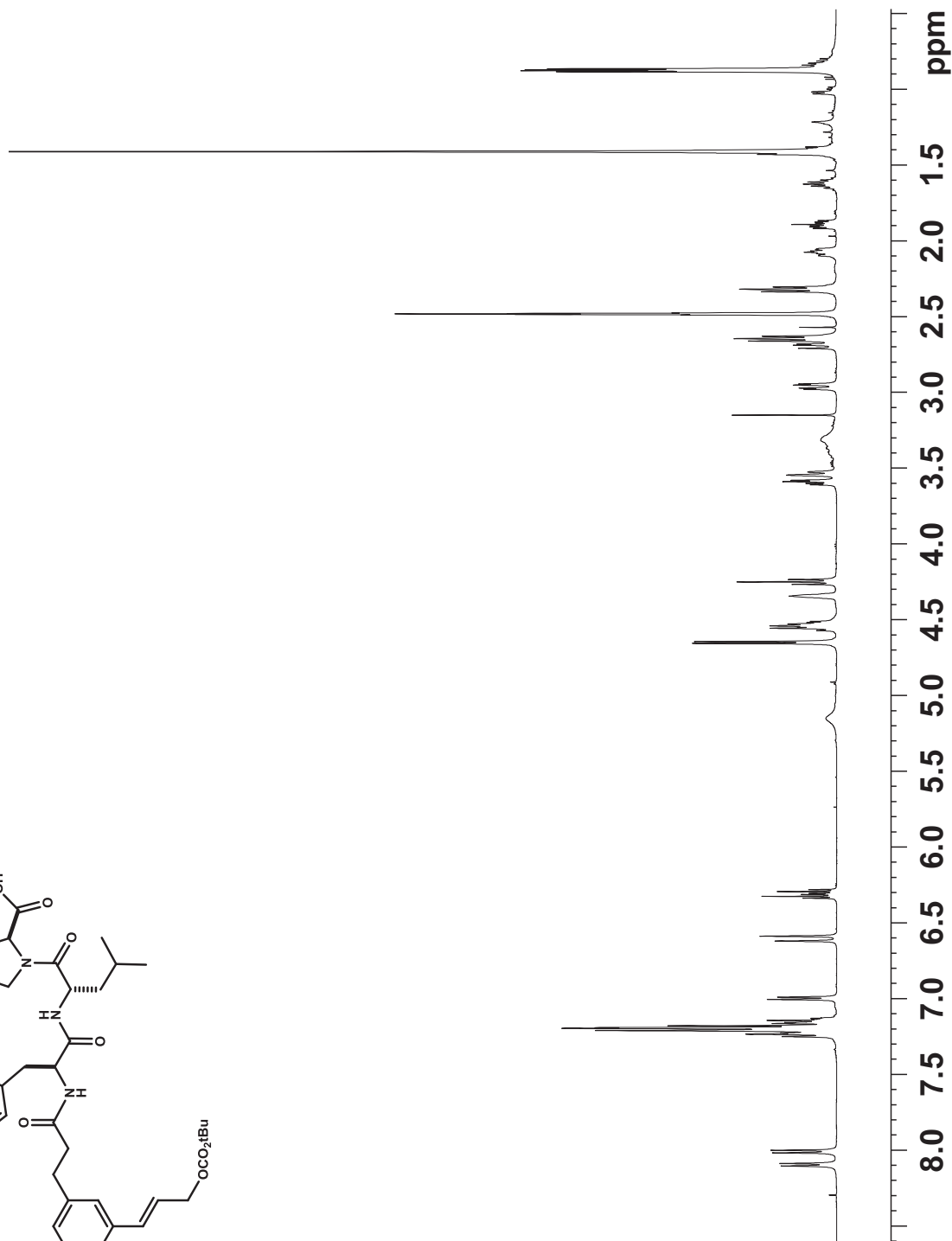


Current Data Parameters
NAME KL-5-11
EXPNO 1
PROCNO 1

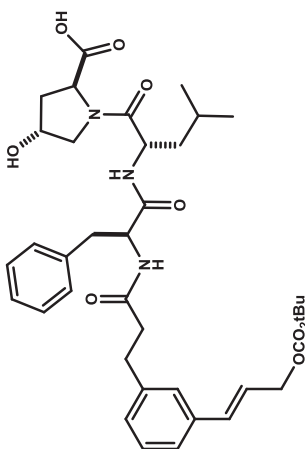
F2 - Acquisition Parameters
Date_ 20120821
Time_ 17.09
INSTRUM av500
PROBHD 5 mm DCH 13C-1
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 8
DS 0
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2767999 sec
RG 129.78
DW 50.000 usec
DE 10.00 usec
TE 298.0 K
D1 2.0000000 sec
TD0 1

===== CHANNEL f1 =====
NUC1 1H
P1 10.00 usec
PLW1 13.5000000 W
SFO1 500.1330008 MHz

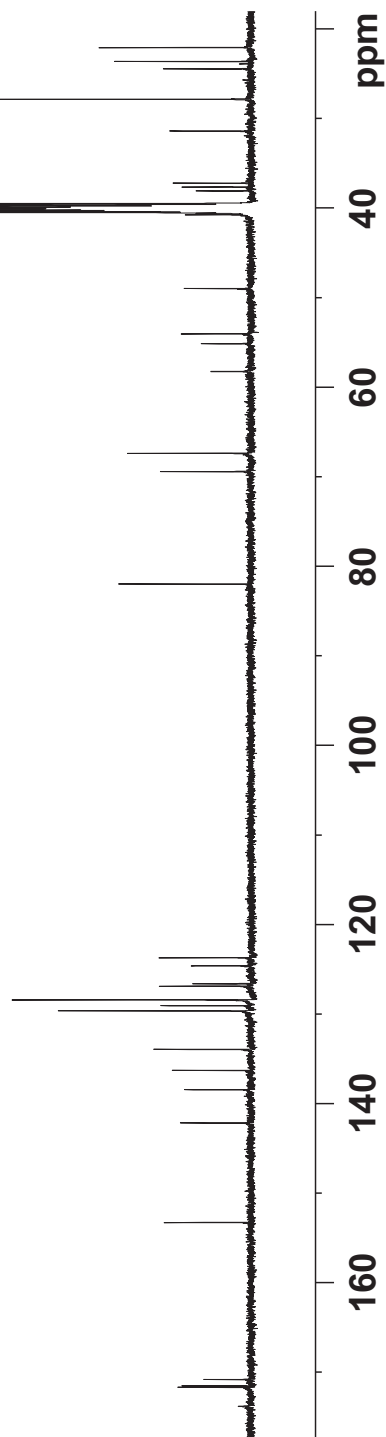
F2 - Processing parameters
SI 65536
SF 500.1300146 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



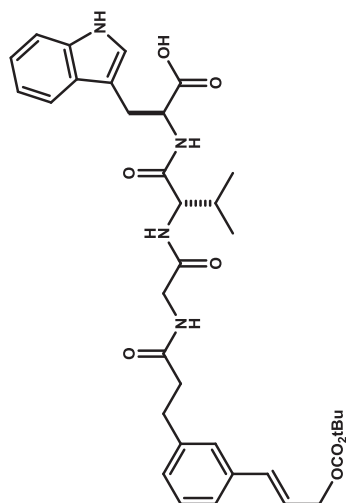
Acyclic-Phe-Leu-Hyp (S21):



Current Data Parameters
NAME KL-5-11
EXPNO 2
PROCNO 1
F2 - Processing parameters
SI 131072
SF 125.7577892 MHz
WDW 0 EM
LB 1.00 Hz
GB 0
PC 1.40



Acyclic-Gly-Val-Trp (S22):



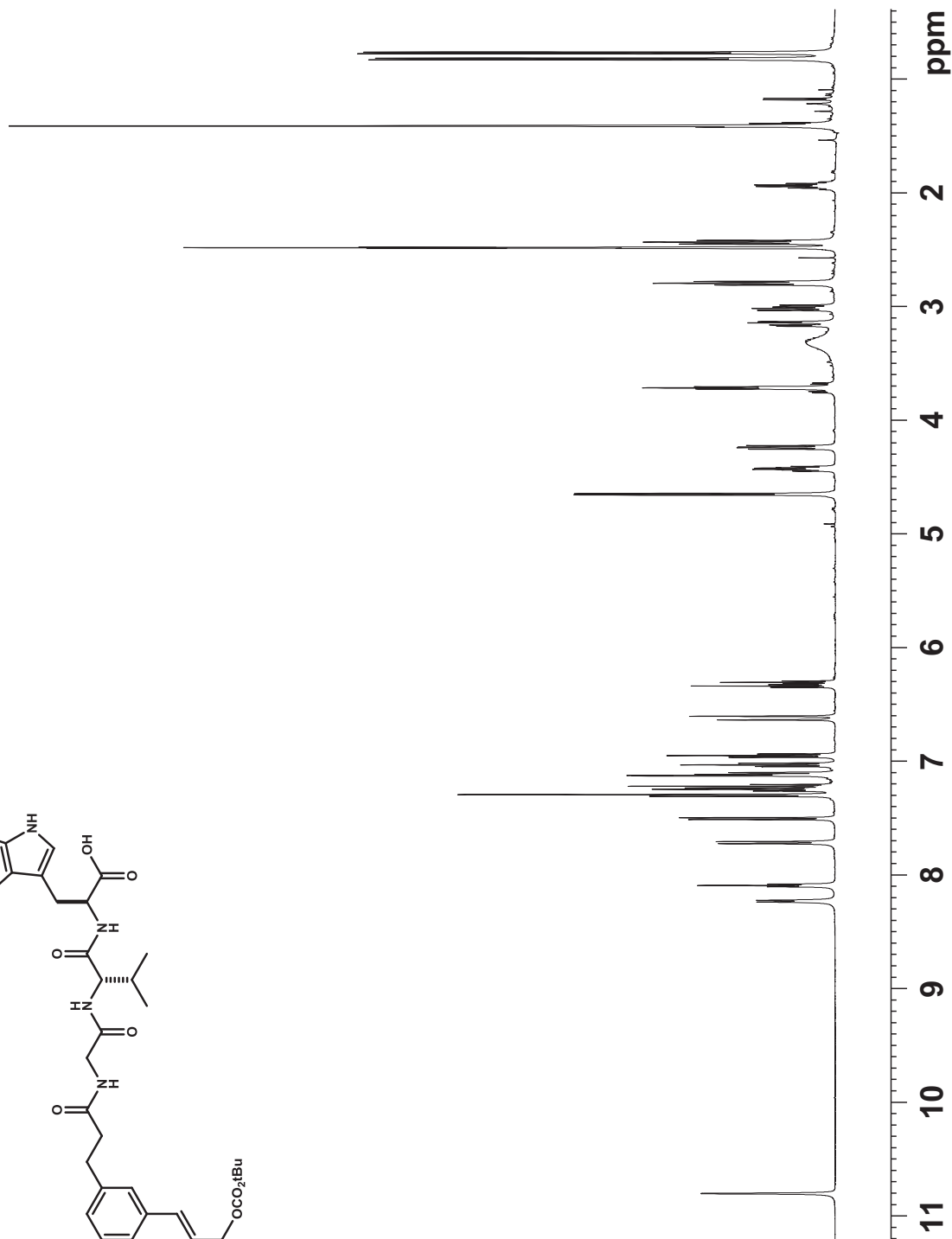
```

Current Data Parameters
NAME          KL-4-188
EXPNO         1
PROCNO        1

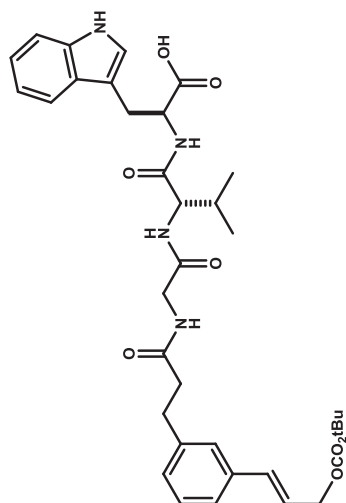
F2 - Acquisition Parameters
Date_         20120821
Time_         19.01
INSTRUM       av500
PROBHD        5 mm DCH 13C-1
PULPROG       zg30
TD            65536
SOLVENT       DMSO
NS            8
DS            0
SWH           10000.000 Hz
FIDRES        0.152588 Hz
AQ            3.2767999 sec
RG            145.12
DW            50.000 usec
DE            10.00 usec
TE            298.0 K
D1            2.00000000 sec
TD0           1

===== CHANNEL f1 =====
NUC1          1H
P1            10.00 usec
PLW1          13.50000000 W
SFO1          500.1330008 MHz

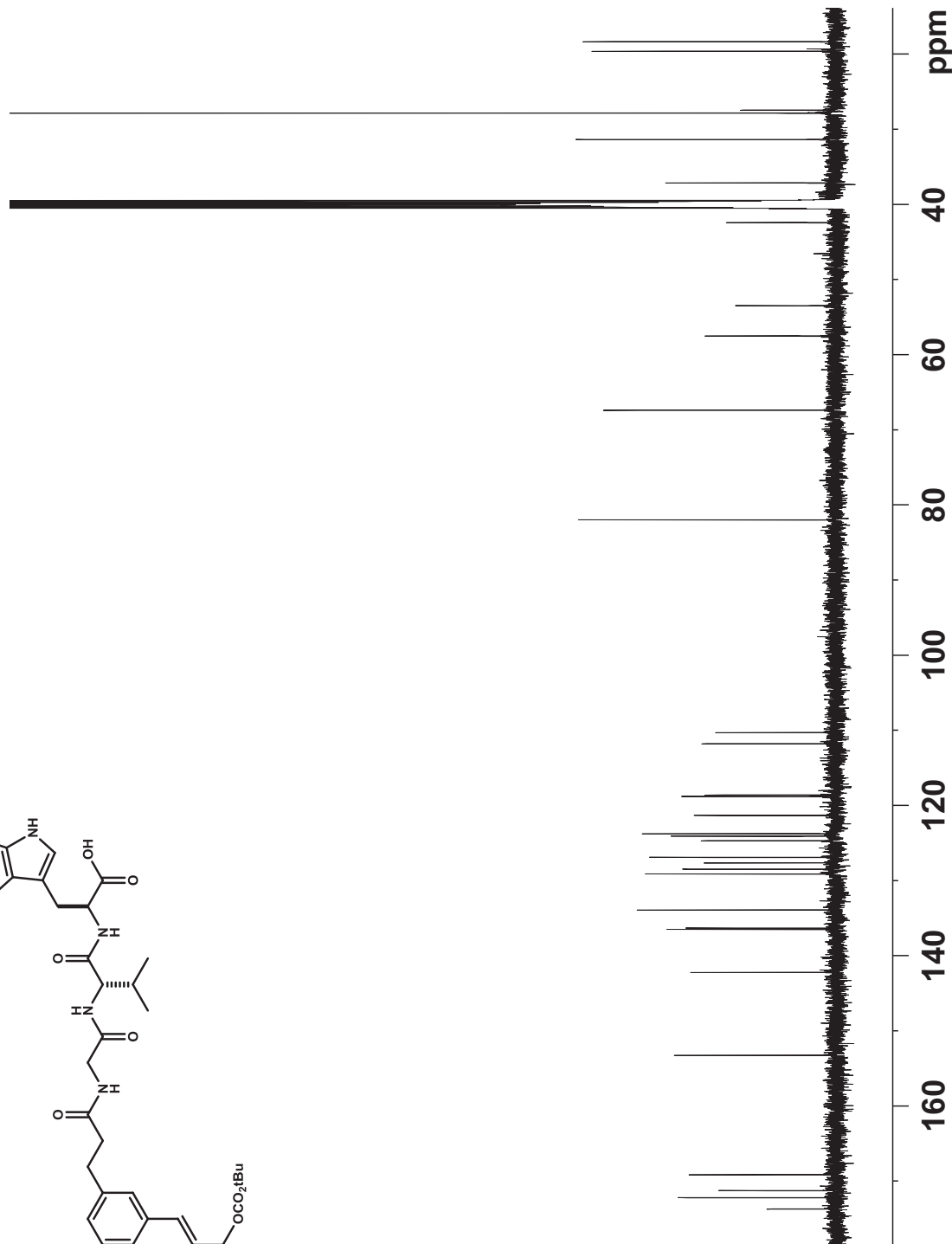
F2 - Processing parameters
SI            65536
SF            500.1300146 MHz
WDW           EM
SSB           0
LB            0 Hz
GB            0
PC            1.00
    
```



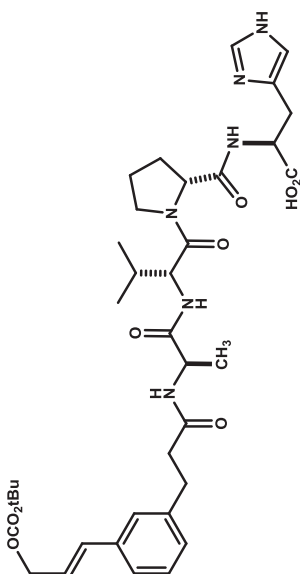
Acyclic-Gly-Val-Trp (S22):



Current Data Parameters
NAME KL-4-188
EXPNO 2
PROCNO 1
F2 - Processing parameters
SI 131072
SF 125.7577892 MHz
WDW 0 EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40



Acyclic-Ala-Val-Pro-His-OH (S23):



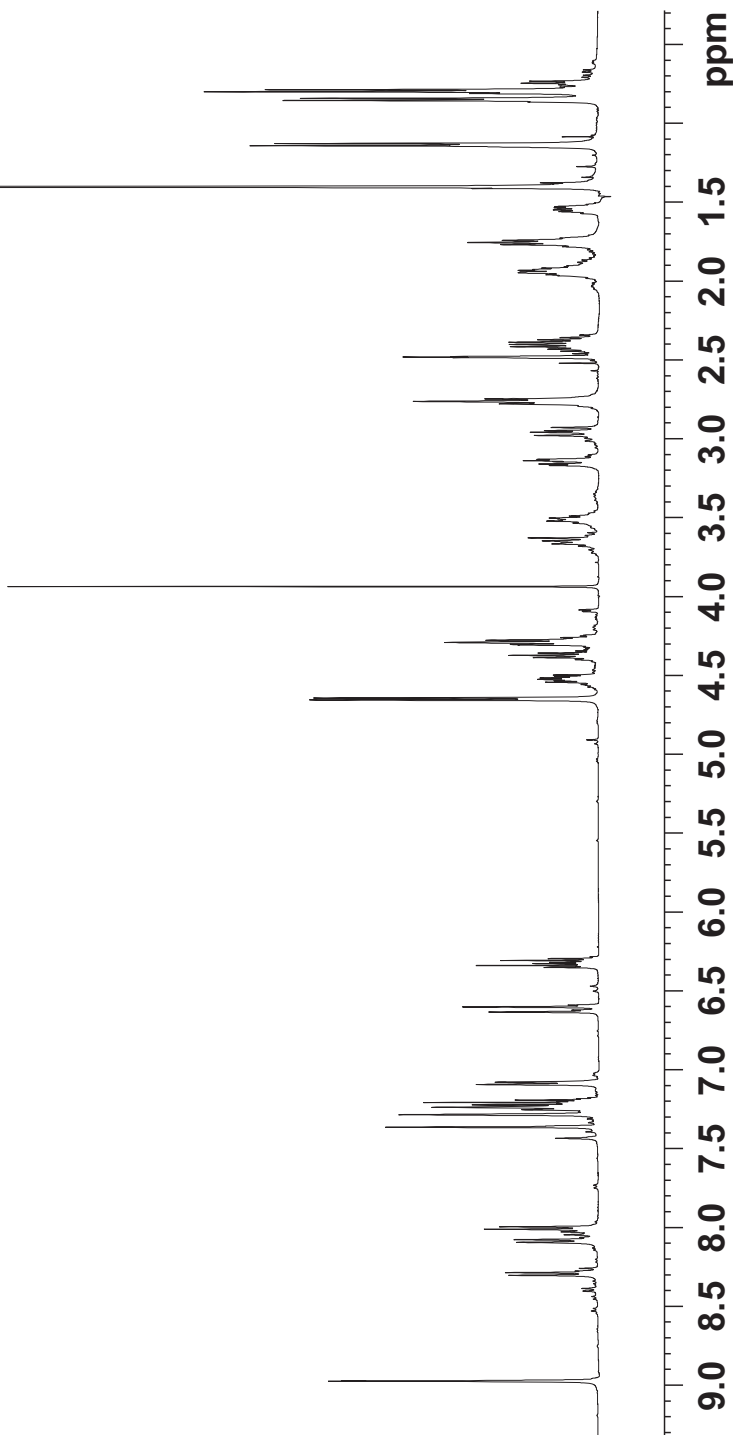
```

Current Data Parameters
NAME          KL-4-161
EXPNO         2
PROCNO        1

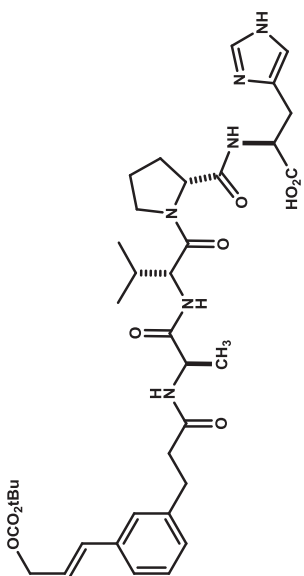
F2 - Acquisition Parameters
Date_         20120329
Time_         17.31
INSTRUM       av500
PROBHD        5 mm DCH 13C-1
PULPROG       zg30
TD            65536
SOLVENT       DMSO
NS            8
DS            0
SWH           10000.000 Hz
FIDRES        0.152588 Hz
AQ            3.276799 sec
RG            11
DW            50.000 usec
DE            10.00 usec
TE            296.0 K
D1            2.0000000 sec
TD0           1

===== CHANNEL f1 =====
NUC1          1H
P1            10.00 usec
PLW1          13.5000000 W
SFO1          500.1330008 MHz

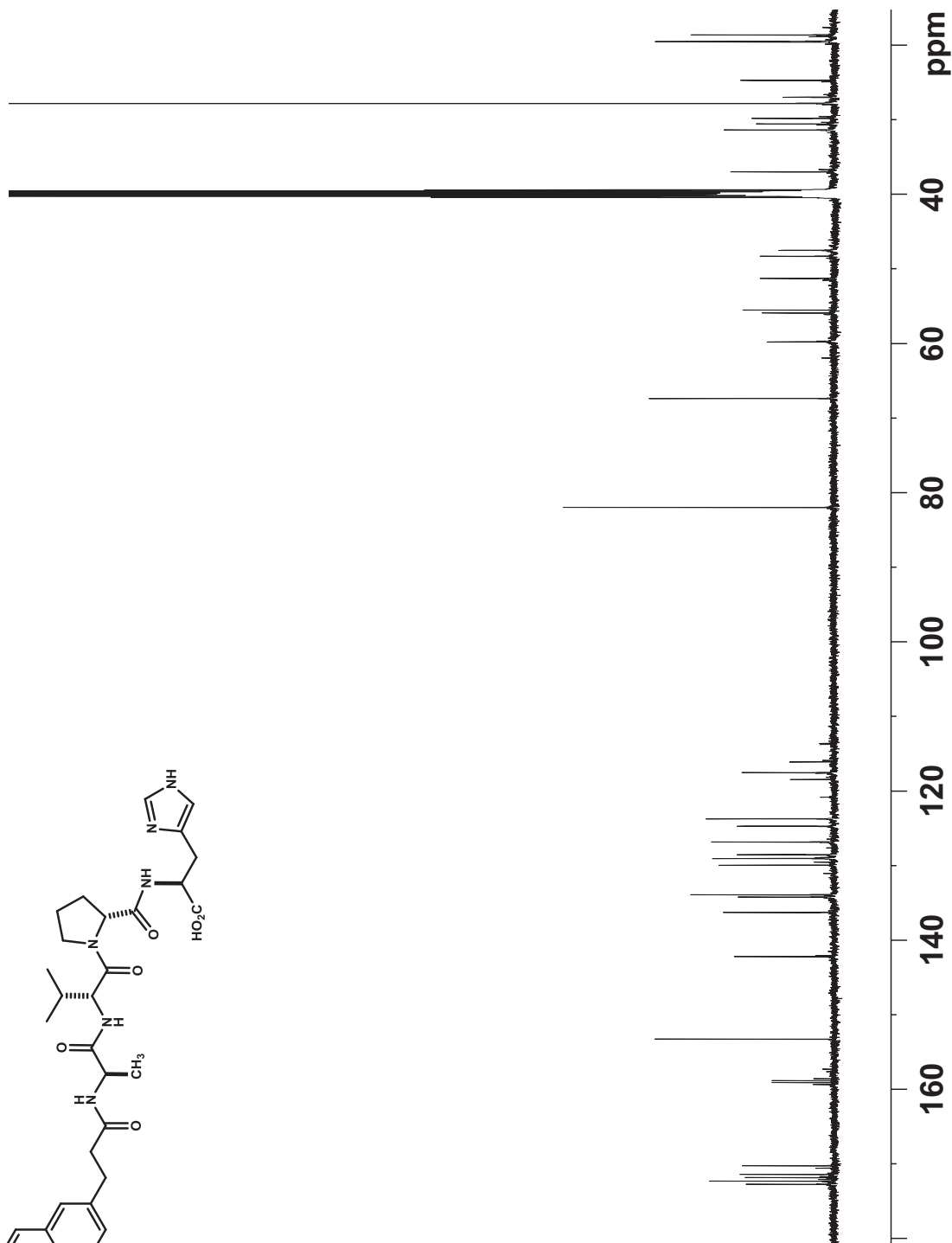
F2 - Processing parameters
SI            65536
SF            500.1300146 MHz
WDW           EM
SSB           0
LB            0.30 Hz
GB            0
PC            1.00
  
```

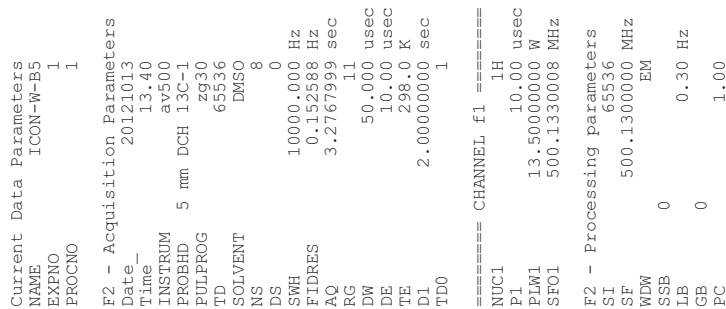


Acyclic-Ala-Val-Pro-His-OH (S23):

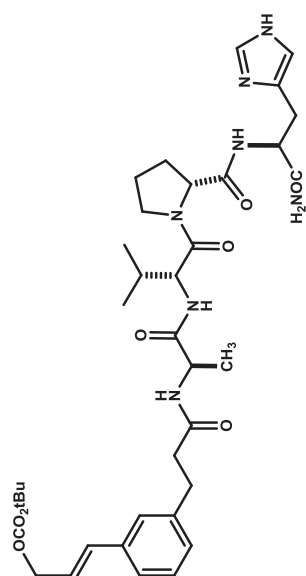


Current Data Parameters
NAME KL-4-161
EXPNO 1
PROCNO 1
F2 - Processing parameters
SI 131072
SF 125.7577892 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

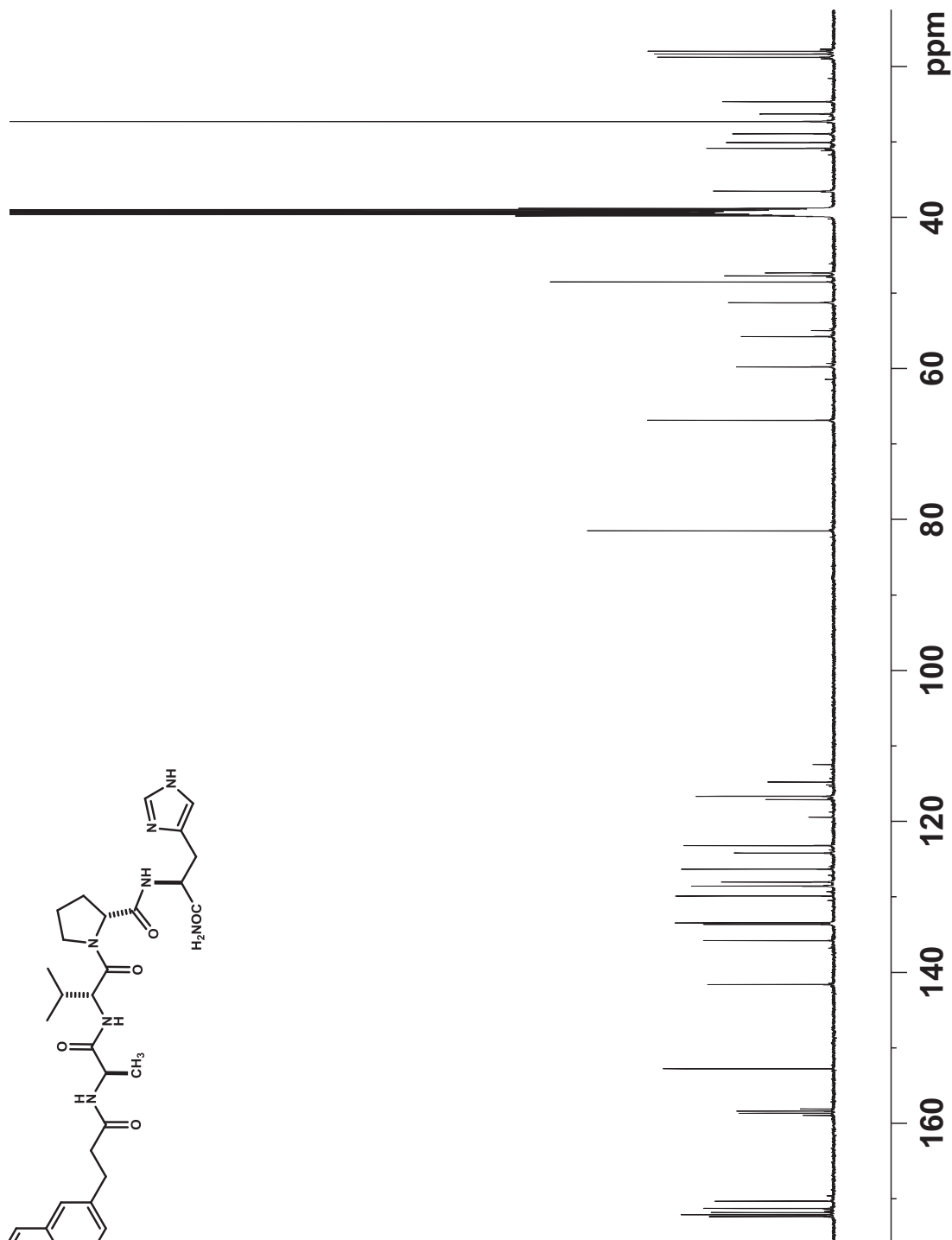


CCCCC(=O)N[C@@H](C)C(=O)N[C@@H](C)C(=O)N[C@@H](C)C(=O)N1CCCC1C(=O)N[C@@H](Cc2c[nH]cn2)C(=O)O

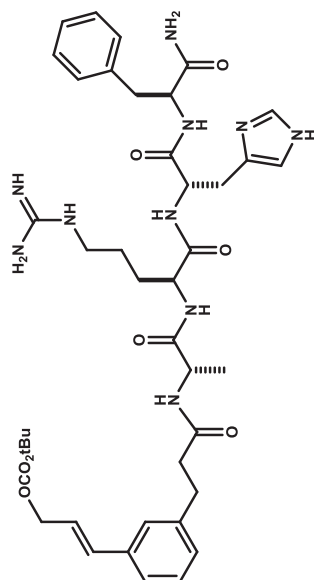
Acyclic-Ala-Val-Pro-His-NH₂ (S24):



Current Data Parameters
 NAME ICON-W-B5
 EXPNO 2
 PROCNO 1
 F2 - Processing parameters
 SI 131072
 SF 125.7578519 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40



Acyclic-Ala-Arg-His-Phe-NH₂ (S25):



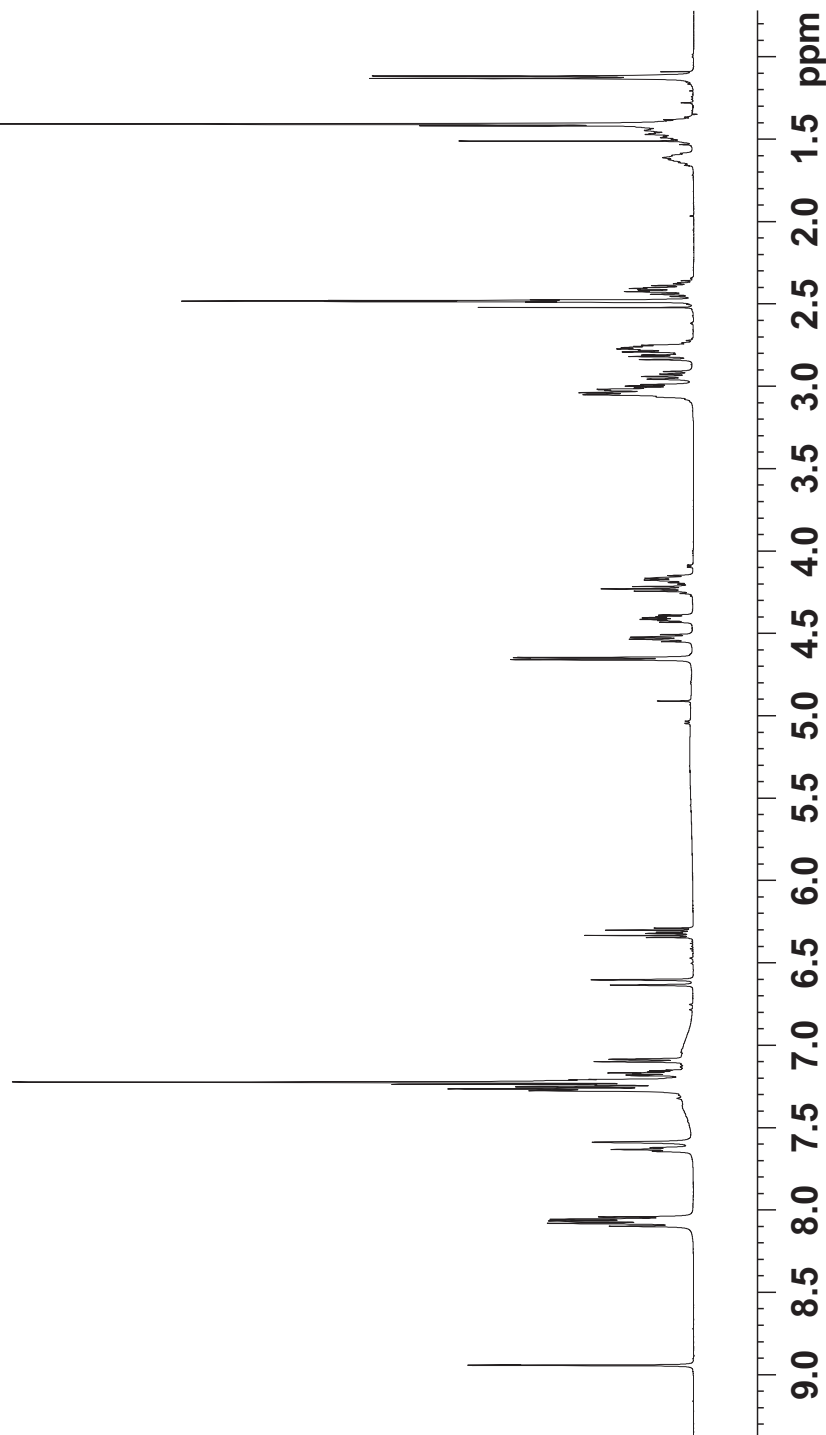
```

Current Data Parameters
NAME      HIS_A5
EXPNO     10
PROCNO    1

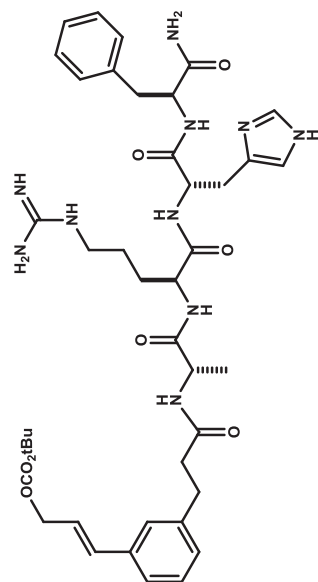
F2 - Acquisition Parameters
Date_     20121130
Time_     17.23
INSTRUM   av500
PROBHD    5 mm DCH 13C-1
PULPROG   zg30
TD        65536
SOLVENT   DMSO
NS         8
DS         0
SWH        10000.000 Hz
FIDRES     0.152588 Hz
AQ         3.2767999 sec
RG         11
DW         50.000 usec
DE         10.00 usec
TE         298.0 K
D1         2.00000000 sec
TD0        1

===== CHANNEL f1 =====
SFO1      500.130008 MHz
NUC1       1H
P1         10.00 usec
PLW1      13.50000000 W

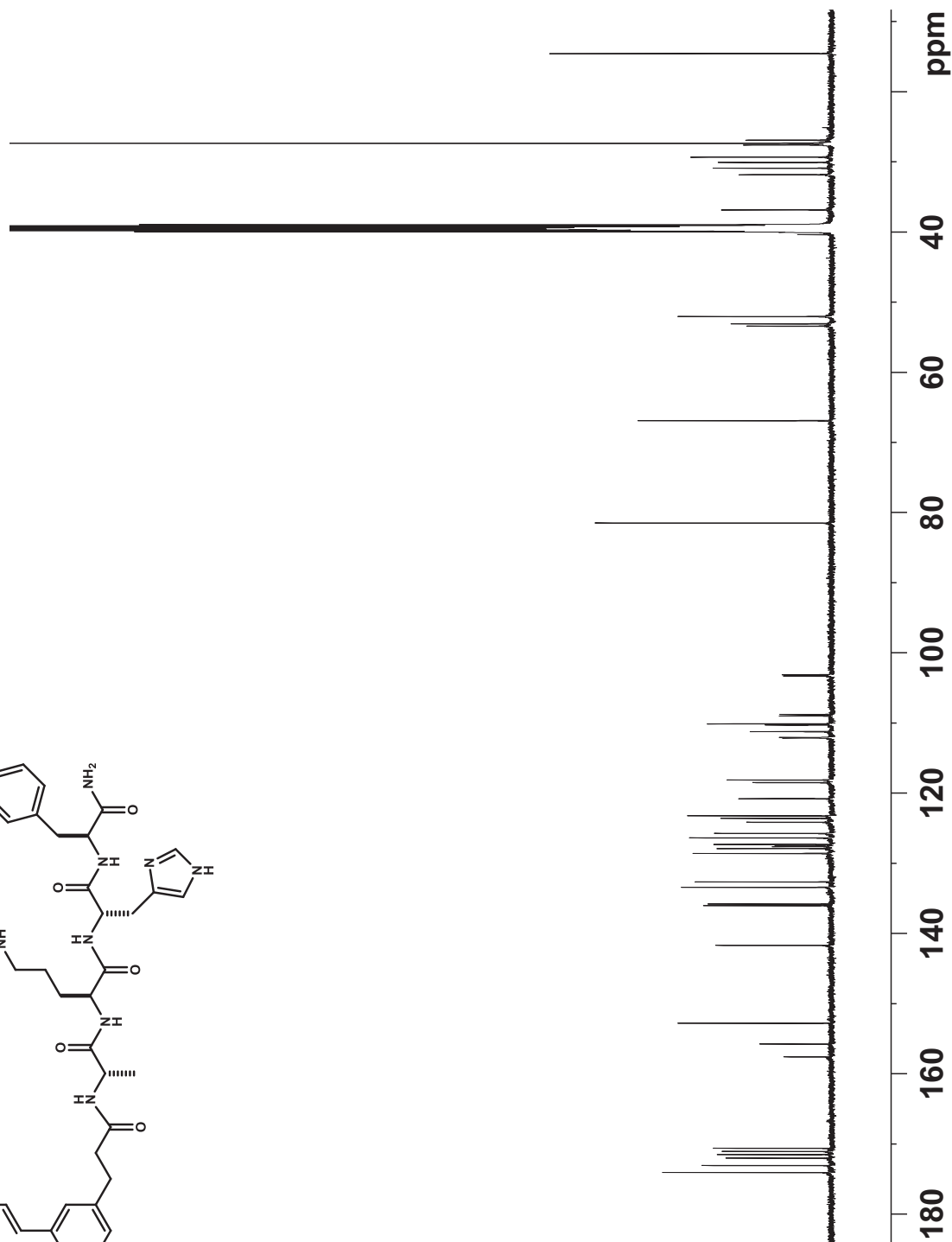
F2 - Processing parameters
SI         65536
SF         500.1300146 MHz
WDW        EM
SSB         0
LB         0.30 Hz
GB         0
PC         1.00
  
```



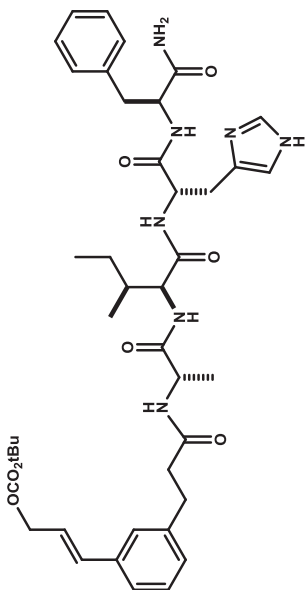
Acyclic-Ala-Arg-His-Phe-NH₂ (S25):



Current Data Parameters
NAME ICON-W-A5
EXPNO 2
PROCNO 1
F2 - Processing parameters
SI 131072
SF 125.7578519 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40



Acyclic-Ala-Ile-His-Phe-NH₂ (S26):



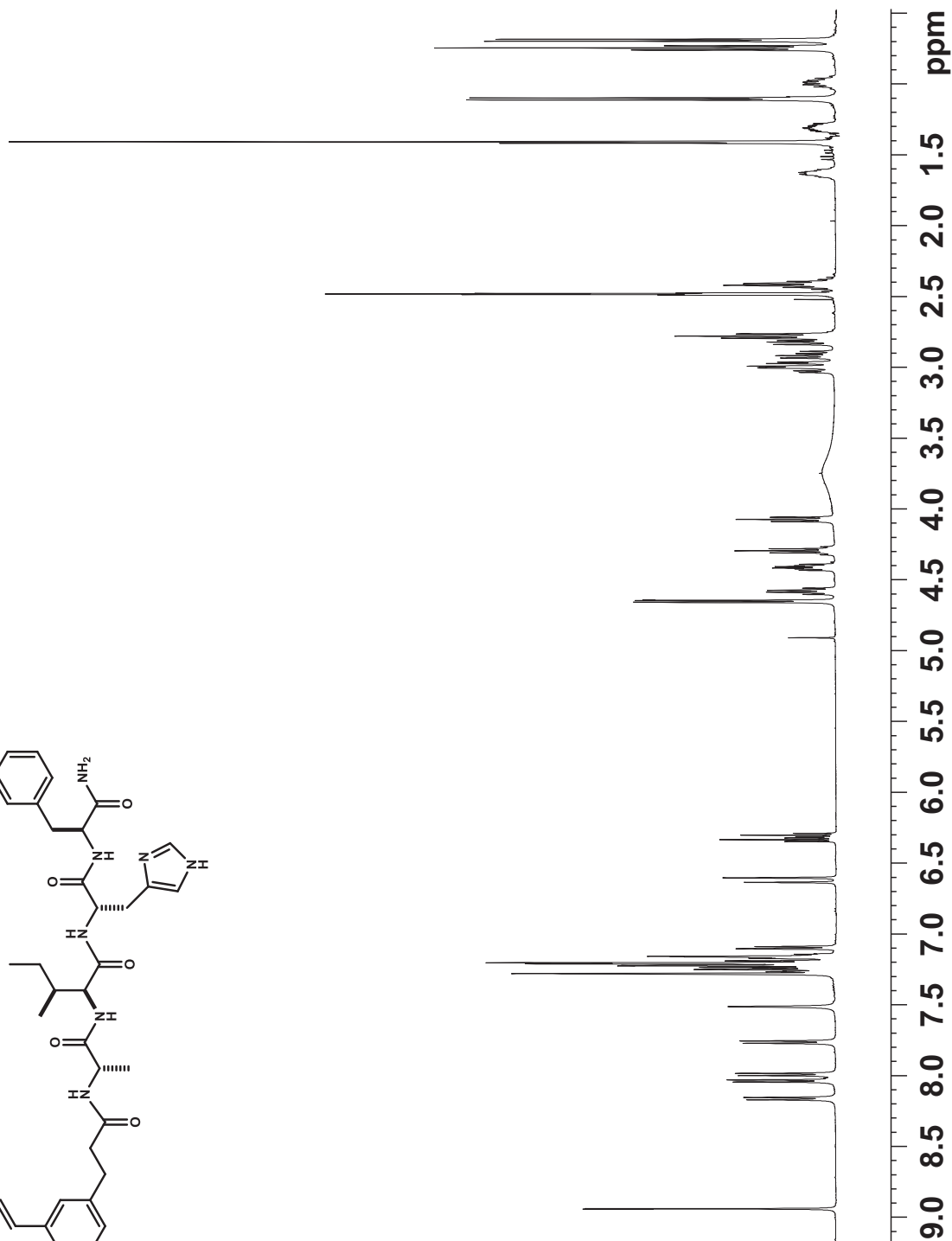
```

Current Data Parameters
NAME      HIS_A6
EXPNO     10
PROCNO    1

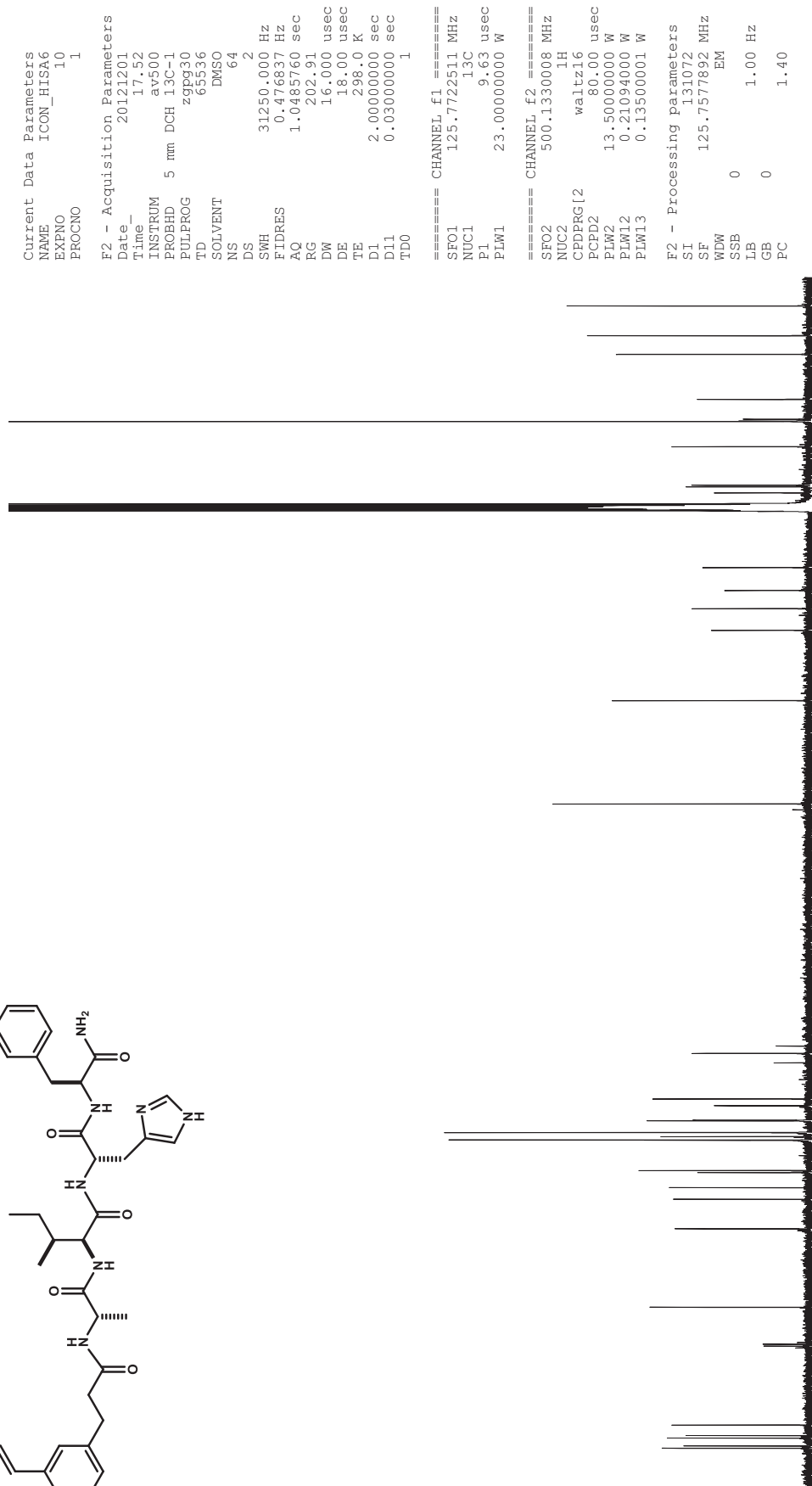
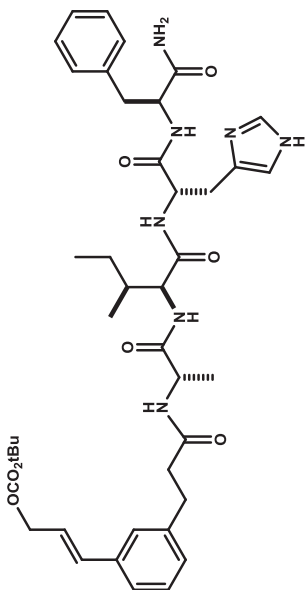
F2 - Acquisition Parameters
Date_     20121130
Time      17.41
INSTRUM   av500
PROBHD    5 mm DCH 13C-1
PULPROG   zg30
TD        65536
SOLVENT   DMSO
NS         8
DS         0
SWH        10000.000 Hz
FIDRES     0.152588 Hz
AQ         3.2767999 sec
RG         11
DW         50.000 usec
DE         10.00 usec
TE         298.0 K
D1         2.00000000 sec
TD0        1

===== CHANNEL f1 =====
SF01      500.1300008 MHz
NUC1       1H
P1         10.00 usec
PLW1      13.50000000 W

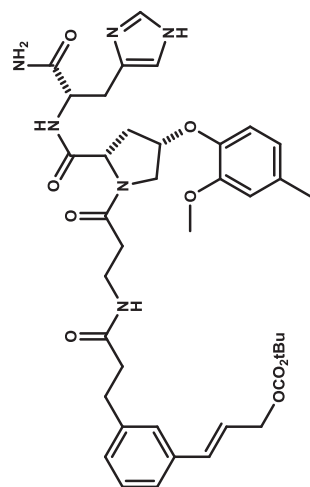
F2 - Processing parameters
SI         65536
SF         500.1300146 MHz
WDW        EM
SSB         0
LB          0.30 Hz
GB          0
PC          1.00
  
```



Acyclic-Ala-Ile-His-Phe-NH₂ (S26):



Acyclic- β -Ala-Pro[4-(2-methoxy-4-methylphenoxy)]-His (S27):



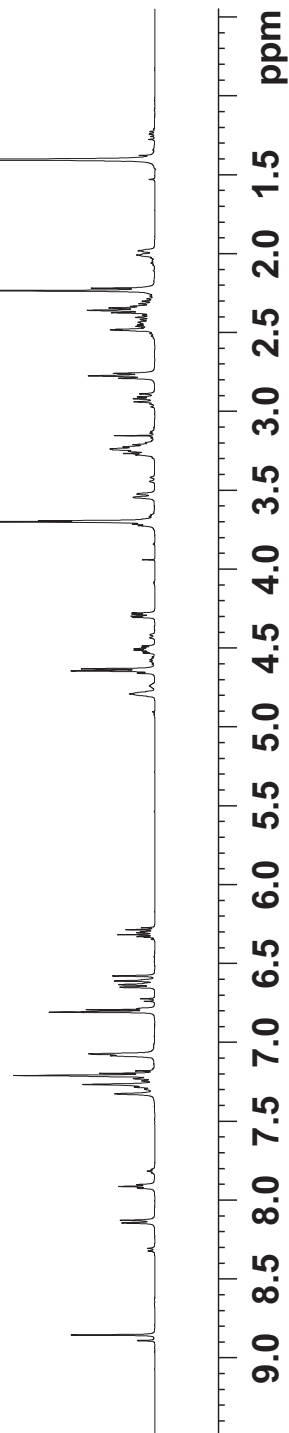
```

Current Data Parameters
NAME      KL-4-205
EXPNO     1
PROCNO    1

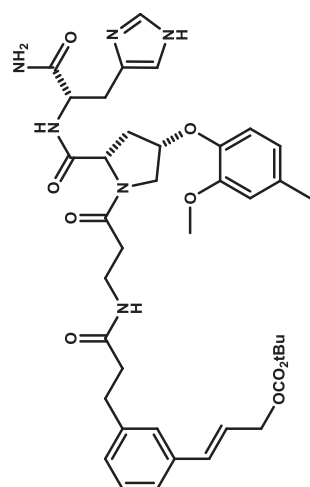
F2 - Acquisition Parameters
Date_     20120507
Time      19.27
INSTRUM   av500
PROBHD    5 mm DCH 13C-1
PULPROG   zg30
TD         65536
SOLVENT   DMSO
NS         8
DS         0
SWH        10000.000 Hz
FIDRES     0.152588 Hz
AQ         3.2767999 sec
RG         29.99
DW         50.000 usec
DE         10.00 usec
TE         296.0 K
D1         2.00000000 sec
TD0        1

===== CHANNEL f1 =====
NUC1       1H
P1         10.00 usec
PLW1       13.50000000 W
SFO1       500.1330008 MHz

F2 - Processing parameters
SI          65536
SF          500.1300146 MHz
WDW         EM
SSB         0
LB          0.30 Hz
GB          0
PC          1.00
    
```

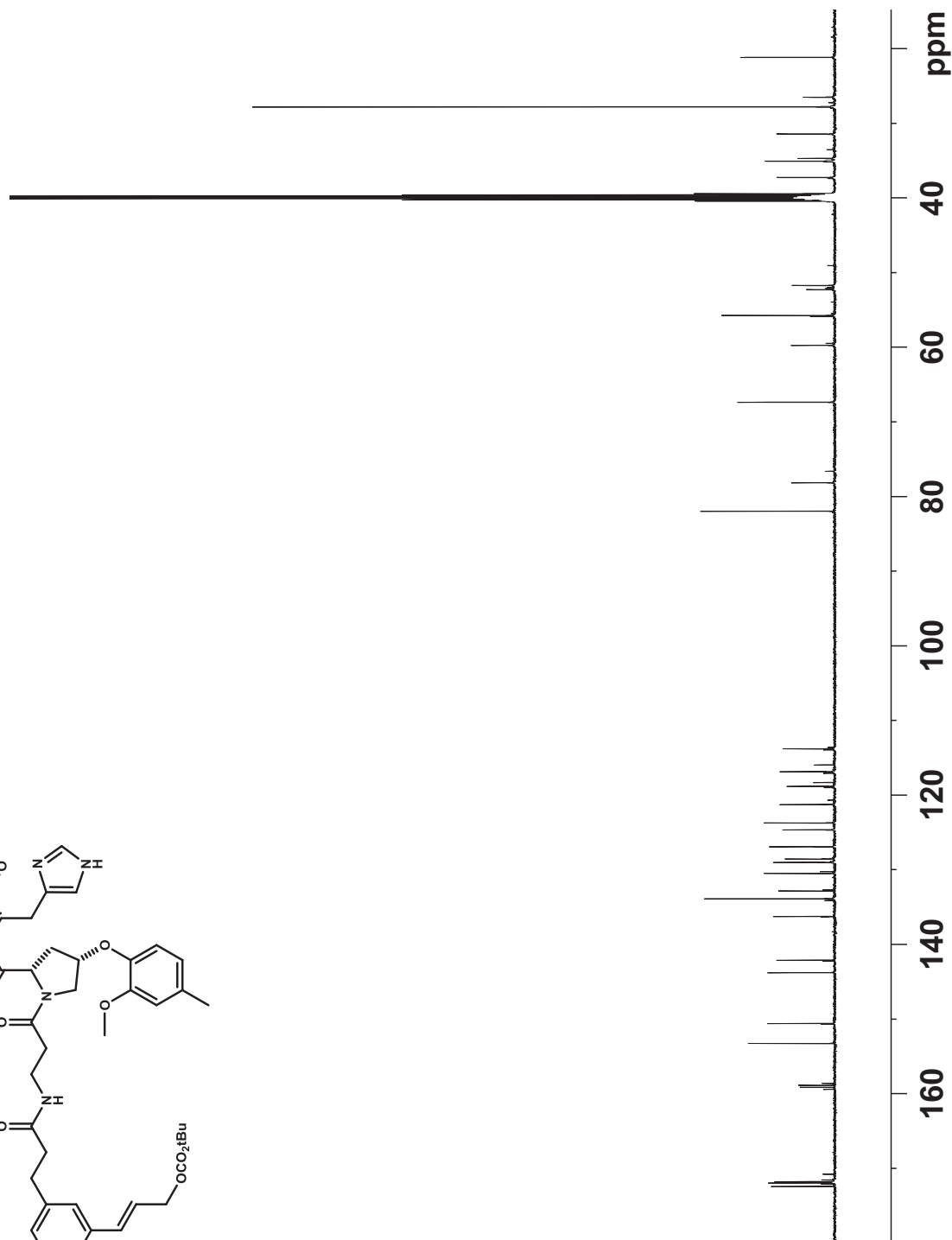


Acyclic- β -Ala-Pro[4-(2-methoxy-4-methylphenoxy)]-His (S27):

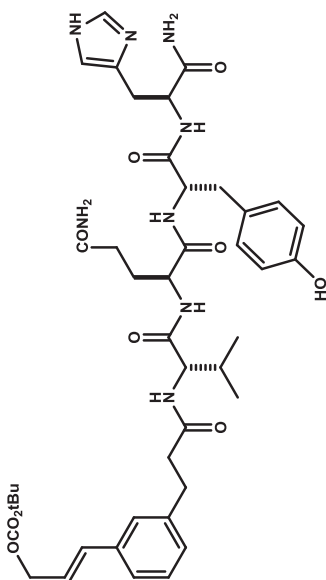


Current Data Parameters
NAME KL-4-205
EXPNO 2
PROCNO 1

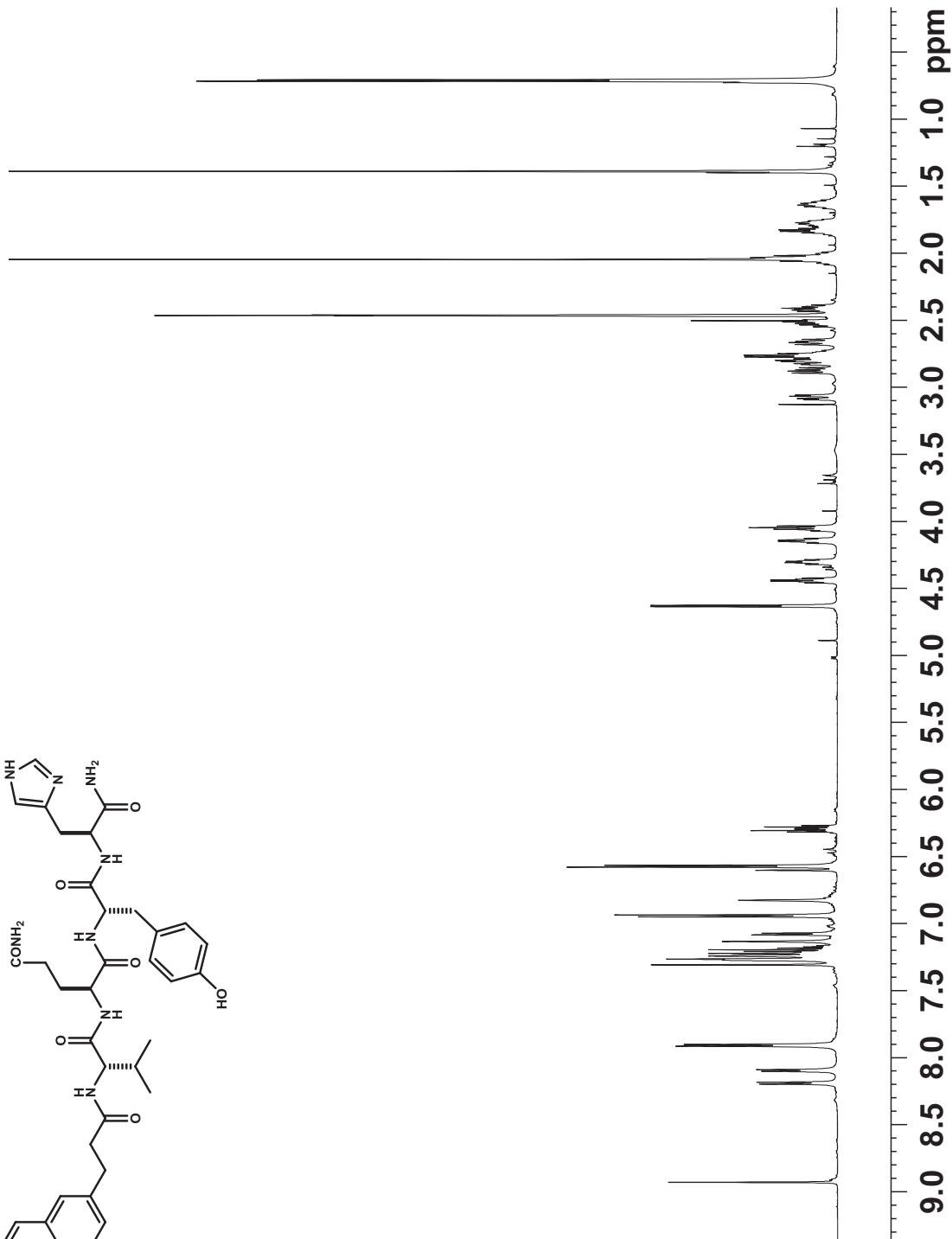
F2 - Processing parameters
SI 131072
SF 125.7577892 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40



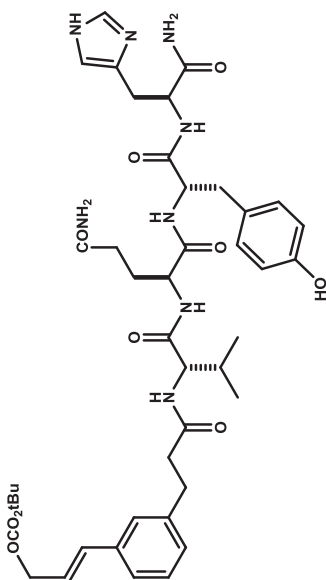
Acyclic-Val-Gln-Tyr-His-NH₂ (18):



Current Data Parameters
 NAME KL-5-151_AV600
 EXPNO 2
 PROCNO 1
 F2 - Acquisition Parameters
 Date_ 20130429
 Time_ 17.41
 INSTRUM 5 mm TBI5
 PROBHD zgpr
 PULPROG 65536
 TD 1
 SOLVENT DMSO
 NS 32
 DS 0
 SWH 12376.237 Hz
 FIDRES 0.188846 Hz
 AQ 2.6476543 sec
 RG 90.5
 DW 40.400 usec
 DE 6.50 usec
 TE 293.9 K
 D1 2.00000000 sec
 D12 0.00002000 sec
 TD0 1
 ===== CHANNEL f1 =====
 NUC1 1H
 P1 9.75 usec
 PL1 -2.00 dB
 PL9 52.20 dB
 PL1W 39.81071854 W
 PL9W 0.00015136 W
 SFO1 600.1320825 MHz
 F2 - Processing parameters
 SI 65536
 SF 600.1300273 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 FC 1.40



Acyclic-Val-Gln-Tyr-His-NH₂ (18):



```

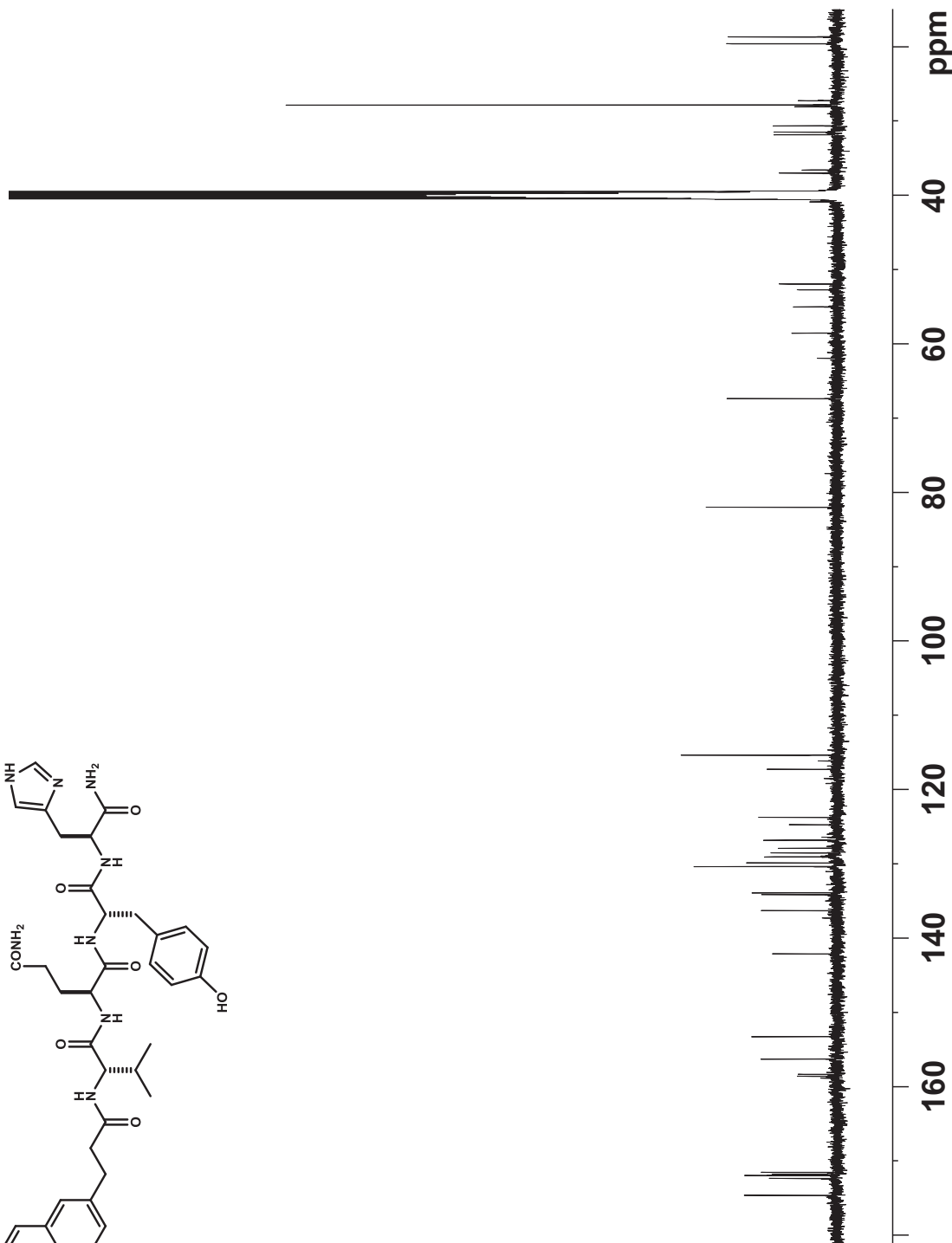
Current Data Parameters
NAME          KL-5-151
EXPNO         3
PROCNO        1

F2 - Acquisition Parameters
Date_         20130424
Time_         15.43
INSTRUM       av500
PROBHD        5 mm DCH 13C-1
PULPROG       zgpg30
TD            65536
SOLVENT       DMSO
NS            126
DS            2
SWH           31250.000 Hz
FIDRES        0.476837 Hz
AQ            1.0485760 sec
RG            202.91
DW            16.000 usec
DE            18.00 usec
TE            298.0 K
D1            2.0000000 sec
D11           0.0300000 sec
TD0           1

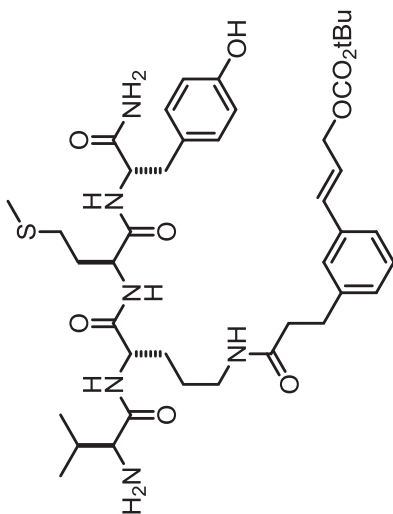
===== CHANNEL f1 =====
SFO1          125.772511 MHz
NUC1          13C
P1            9.63 usec
PLW1          23.0000000 W

===== CHANNEL f2 =====
SFO2          500.1330008 MHz
NUC2          1H
CPDPRG2       waltz16
PCPD2         80.00 usec
PLW2          13.5000000 W
PLW12         0.2109400 W
PLW13         0.13500001 W

F2 - Processing parameters
SI            131072
SF            125.7577892 MHz
WDW           EM
SSB           0
LB            1.00 Hz
GB            0
PC            1.40
  
```



Acyclic-Val-Orn-Met-Tyr (S30):



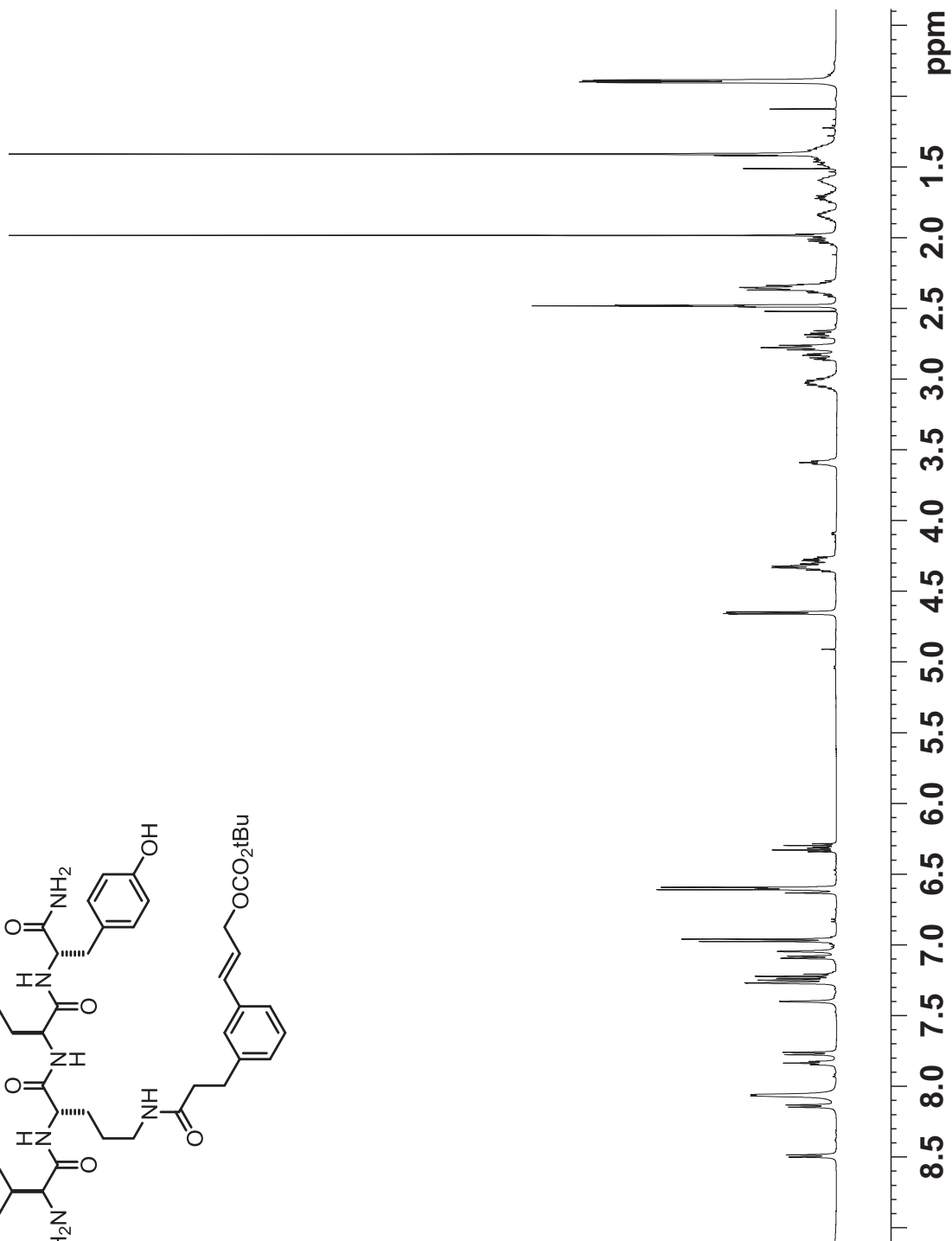
```

Current Data Parameters
NAME      KL-5-153_deprot
EXPNO     1
PROCNO    1

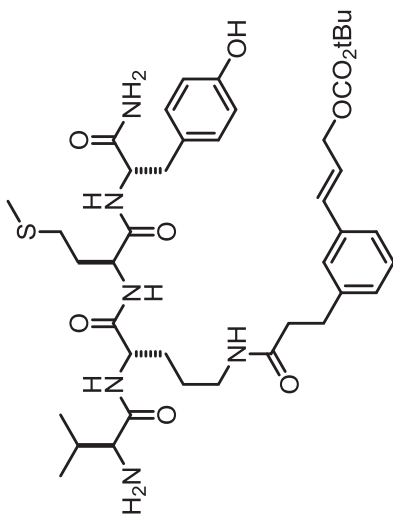
F2 - Acquisition Parameters
Date_     20130409
Time_     12.12
INSTRUM   av500
PROBHD    5 mm DCH 13C-1
PULPROG   zg30
TD         65536
SOLVENT   DMSO
NS         8
DS         0
SWH        10000.000 Hz
FIDRES     0.152588 Hz
AQ         3.276799 sec
RG         11
DW         50.000 usec
DE         10.00 usec
TE         298.0 K
D1         2.0000000 sec
TD0        1

===== CHANNEL f1 =====
SF01      500.130008 MHz
NUC1       1H
P1         10.00 usec
PLW1      13.5000000 W

F2 - Processing parameters
SI         65536
SF         500.1300146 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00
  
```



Acyclic-Val-Orn-Met-Tyr (S30):



```

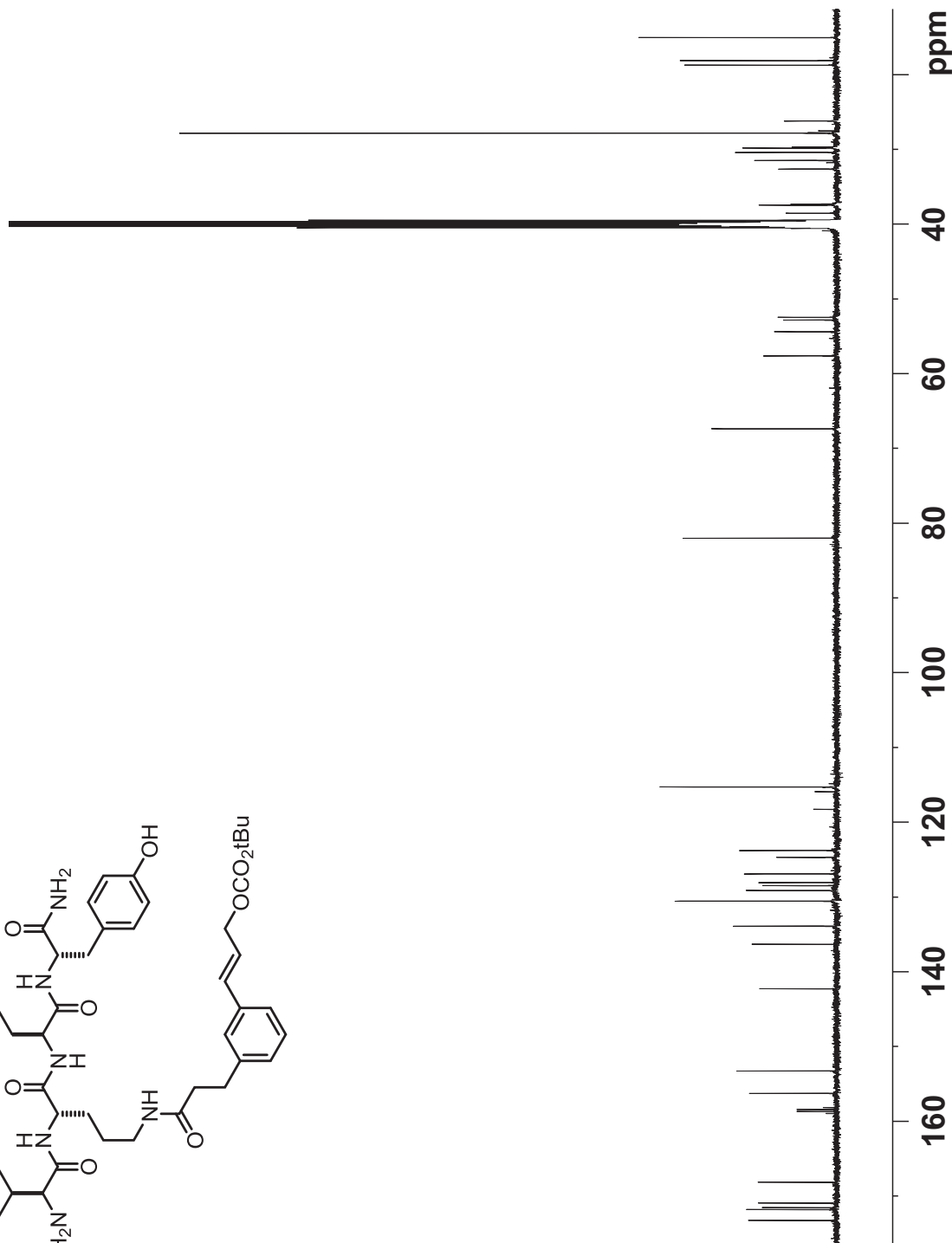
Current Data Parameters
NAME      KL-5-153_deprot
EXPNO     2
PROCNO    1

F2 - Acquisition Parameters
Date_     20130409
Time_     12.15
INSTRUM   av500
PROBHD    5 mm DCH 13C-1
PULPROG   zgpg30
TD        65536
SOLVENT   DMSO
NS        85
DS        2
SWH       31250.000 Hz
FIDRES    0.476837 Hz
AQ        1.0485760 sec
RG        202.91
DW        16.000 usec
DE        18.00 usec
TE        298.0 K
D1        2.00000000 sec
D11       0.03000000 sec
TD0       1

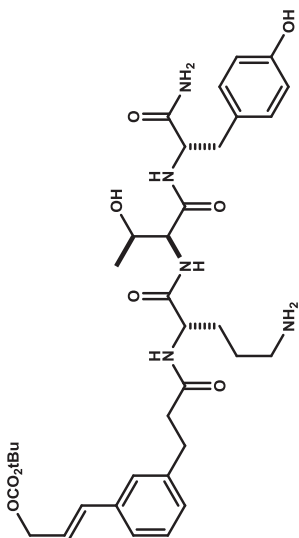
===== CHANNEL f1 =====
SFO1      125.772511 MHz
NUC1      13C
P1        9.63 usec
PLW1      23.00000000 W

===== CHANNEL f2 =====
SFO2      500.1330008 MHz
NUC2      1H
CPDPRG2   waltz16
PCPD2     80.00 usec
PLW2      13.50000000 W
PLW12     0.21094000 W
PLW13     0.13500001 W

F2 - Processing parameters
SI        131072
SF        125.7577892 MHz
WDW       EM
SSB       0
LB        1.00 Hz
GB        0
PC        1.40
  
```



Acyclic-Orn-Thr-Tyr (S35):



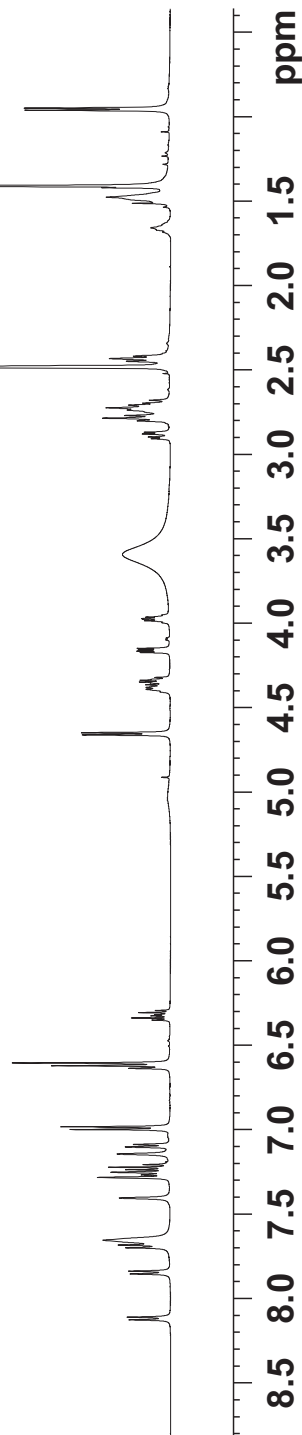
```

Current Data Parameters
NAME          TR4-128
EXPNO         1
PROCNO        1

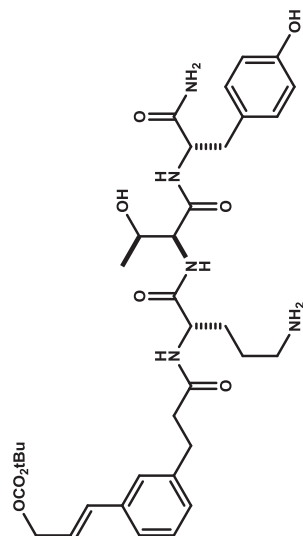
F2 - Acquisition Parameters
Date_         20130322
Time_         20:59
INSTRUM       av500
PROBHD        5 mm DCH 13C-1
PULPROG       zg30
TD            65536
SOLVENT       DMSO
NS            8
DS            0
SWH           10000.000 Hz
FIDRES        0.152588 Hz
AQ            3.276799 sec
RG            11
DW            50.000 usec
DE            10.00 usec
TE            298.0 K
D1            2.0000000 sec
TD0           1

===== CHANNEL f1 =====
SF01          500.130008 MHz
NUC1          1H
P1            10.00 usec
PLW1         13.5000000 W

F2 - Processing parameters
SI            65536
SF           500.1300146 MHz
WDW           EM
SSB           0
LB            0.10 Hz
GB            0
PC            1.00
  
```



Acyclic-Orn-Thr-Tyr (S35):



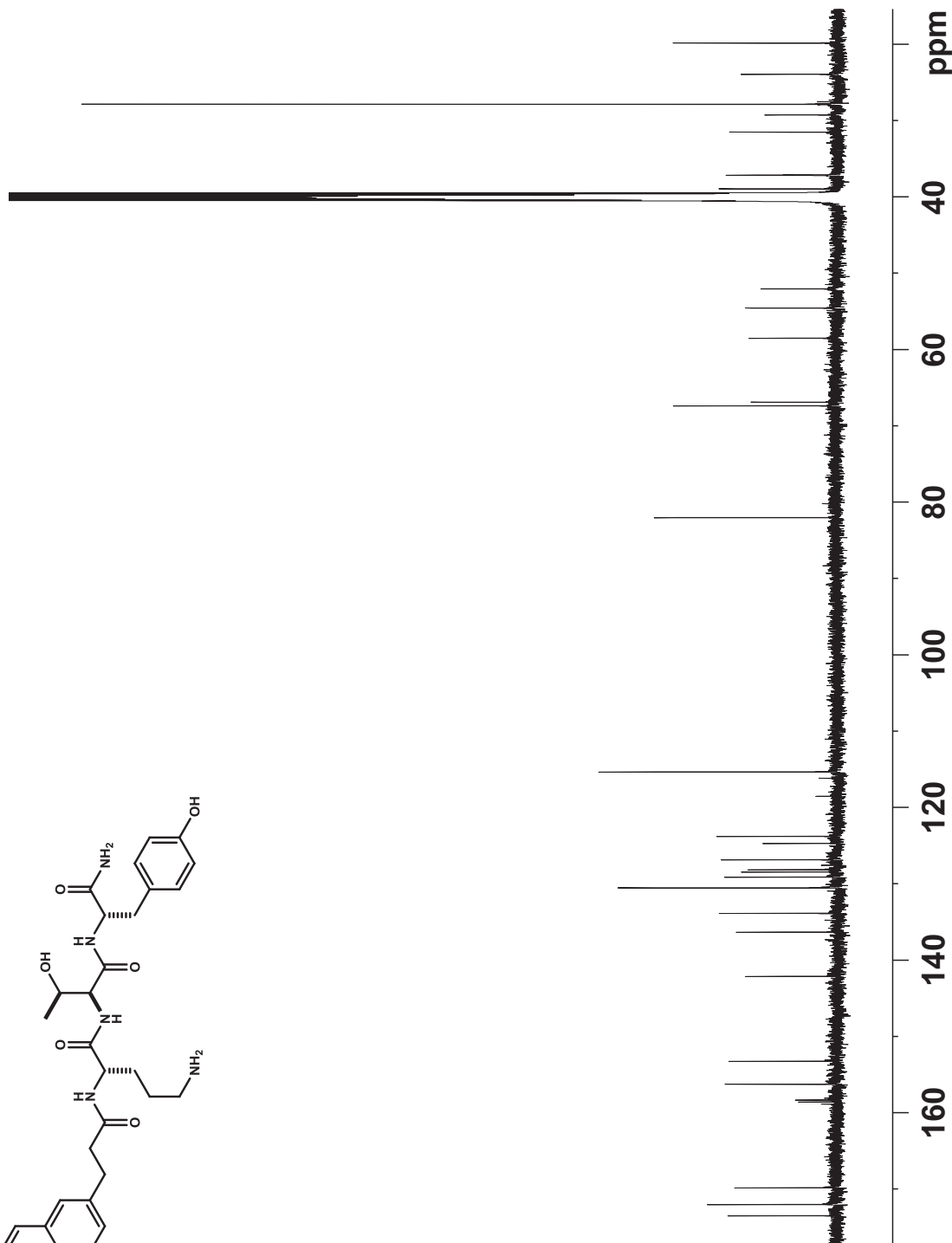
Current Data Parameters
 NAME TR4-l28
 EXPNO 2
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20130322
 Time_ 21.02
 INSTRUM av500
 PROBHD 5 mm DCH 13C-1
 PULPROG zgpg30
 TD 65536
 SOLVENT DMSO
 NS 128
 DS 2
 SWH 31250.000 Hz
 FIDRES 0.476837 Hz
 AQ 1.0485760 sec
 RG 15.53
 DW 16.000 usec
 DE 18.00 usec
 TE 298.0 K
 D1 2.00000000 sec
 D11 0.03000000 sec
 TD0 1

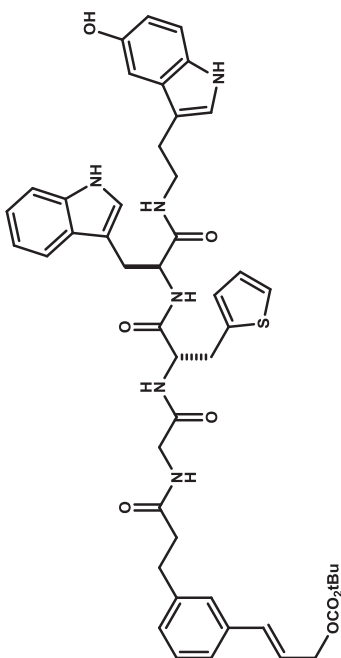
===== CHANNEL f1 =====
 SFO1 125.772511 MHz
 NUC1 13C
 P1 9.63 usec
 PLW1 23.00000000 W

===== CHANNEL f2 =====
 SFO2 500.1330008 MHz
 NUC2 1H
 CPDPRG2 waltz16
 FCPD2 80.00 usec
 PLW2 13.50000000 W
 PLW12 0.21094000 W
 PLW13 0.13500001 W

F2 - Processing parameters
 SI 131072
 SF 125.7577892 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.00



Acyclic-Gly-Thi-Trp-5HT (S31):



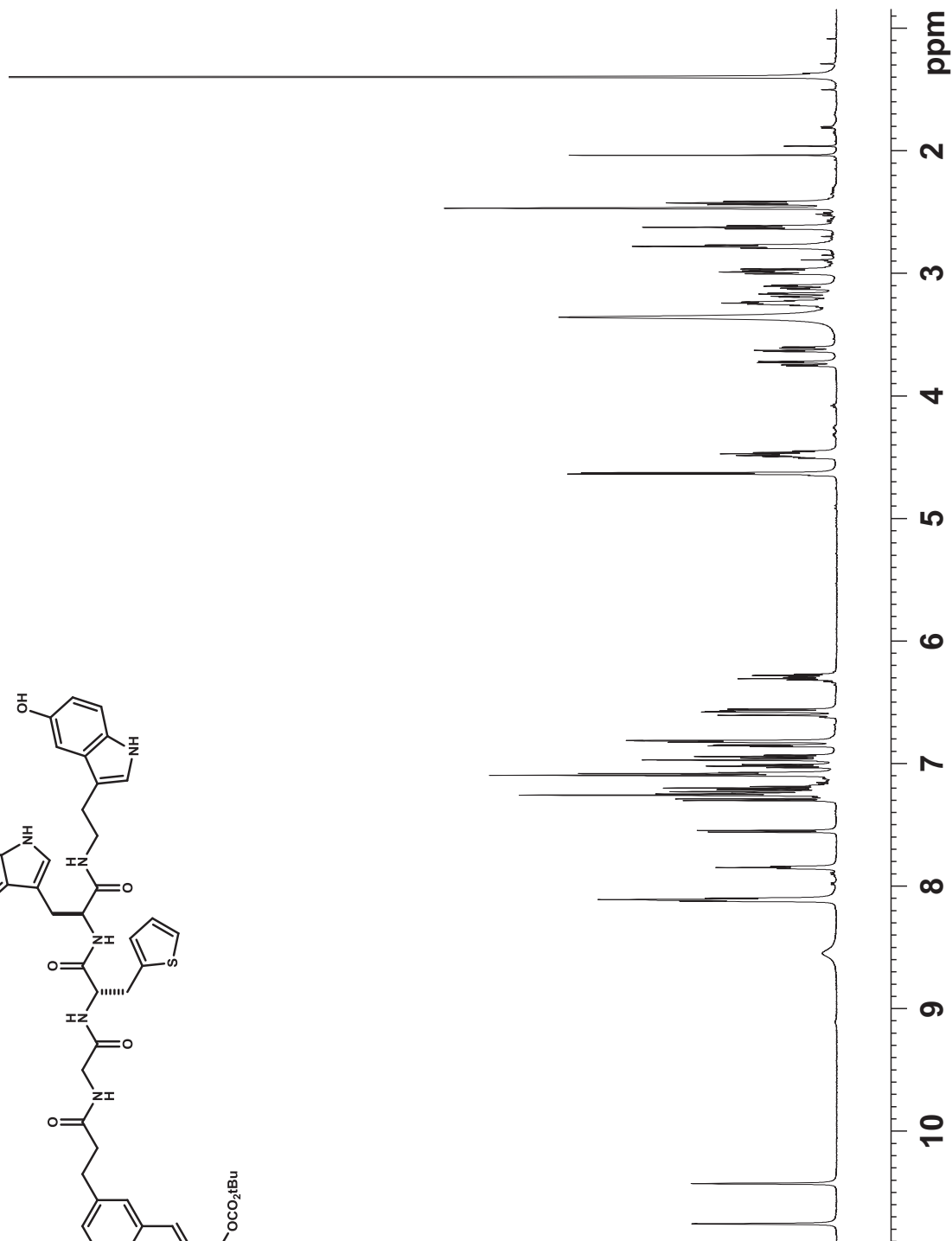
```

Current Data Parameters
NAME          KL-4-46
EXPNO         2
PROCNO        1

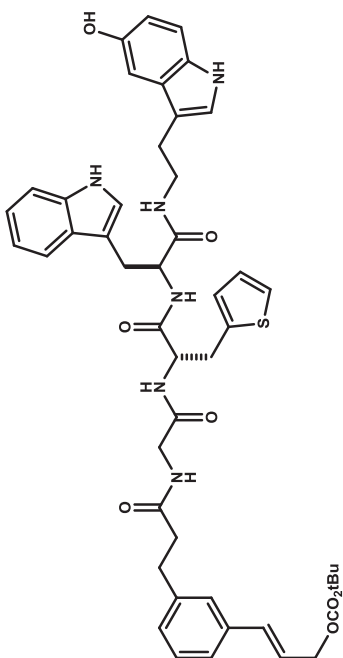
F2 - Acquisition Parameters
Date_         20111012
Time_         15.55
INSTRUM       av600
PROBHD        5 mm BB5
PULPROG       zg30
TD            65536
SOLVENT       DMSO
NS            4
DS            0
SWH           12376.237 Hz
FIDRES        0.188846 Hz
AQ            2.6476543 sec
RG            90.5
DW            40.400 usec
DE            6.50 usec
TE            300.5 K
D1            2.0000000 sec
TD0           1

===== CHANNEL f1 =====
NUC1          1H
P1            14.00 usec
PL1           -1.00 dB
PL1W          31.62277603 W
SFO1          600.1336008 MHz

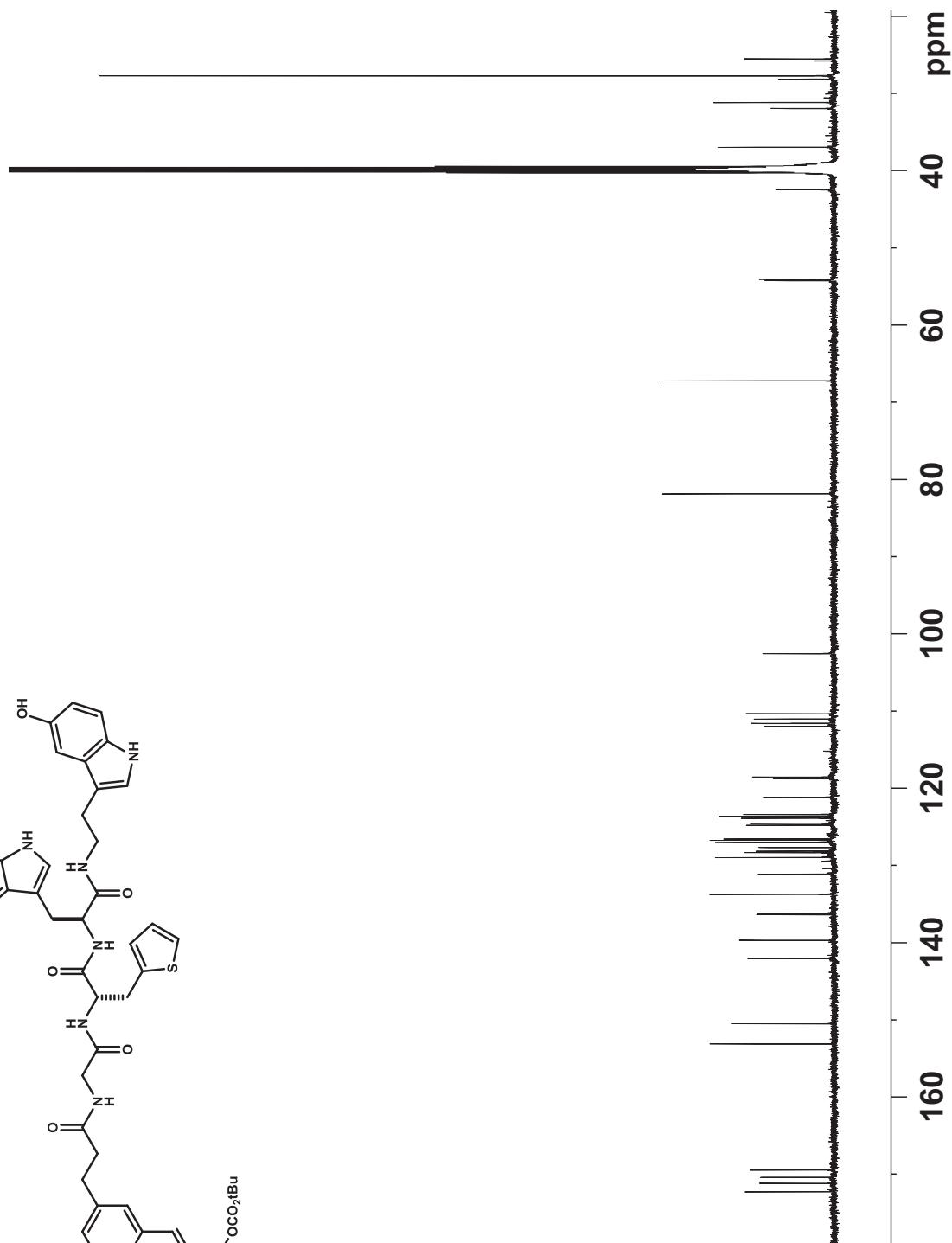
F2 - Processing parameters
SI            65536
SF            600.1300273 MHz
WDW           EM
SSB           0
LB            0.30 Hz
GB            0
PC            1.00
  
```



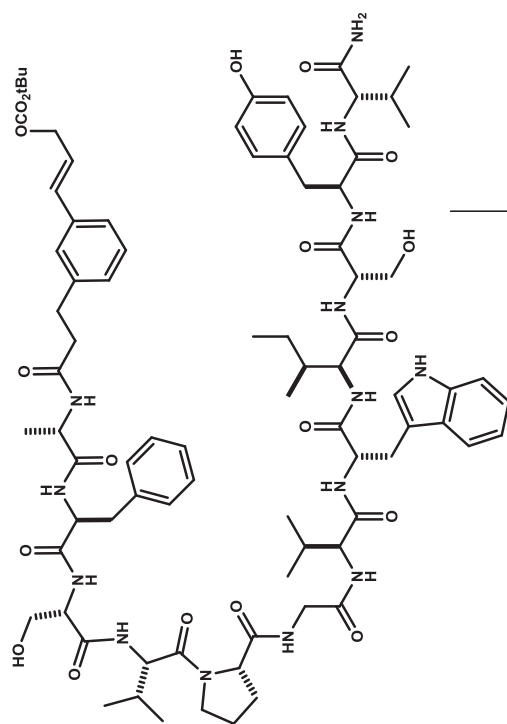
Acyclic-Gly-Thi-Trp-5HT (S31):



Current Data Parameters
NAME KL-4-46
EXPNO 3
PROCNO 1
F2 - Processing parameters
SI 65536
SF 150.9028319 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40



Acyclic-Ala-Phe-Ser-Val-Pro-Gly-Val-Trp-Ile-Ser-Tyr-Val (S32):



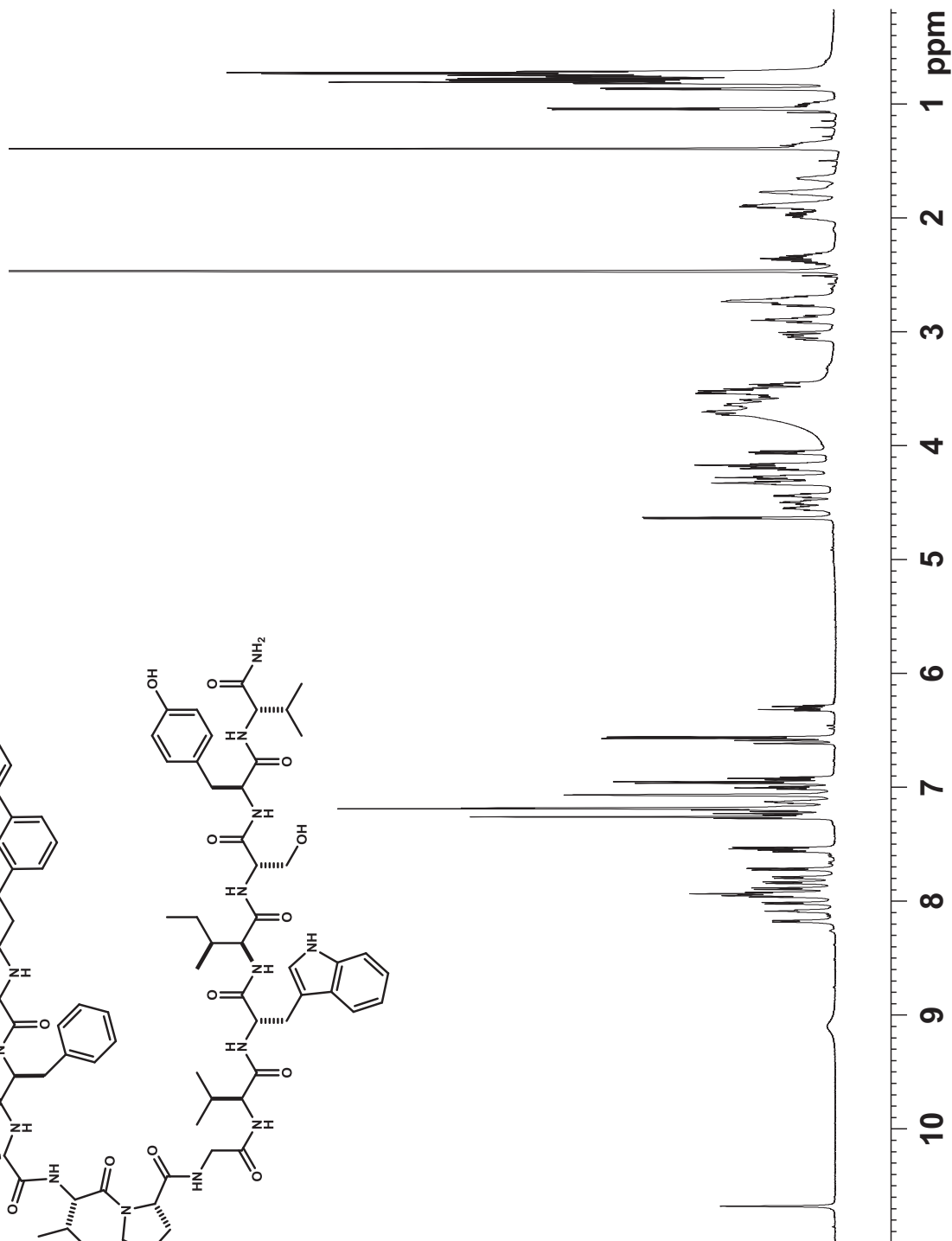
```

Current Data Parameters
NAME      KL-4-7_prep
EXPNO     1
PROCNO    1

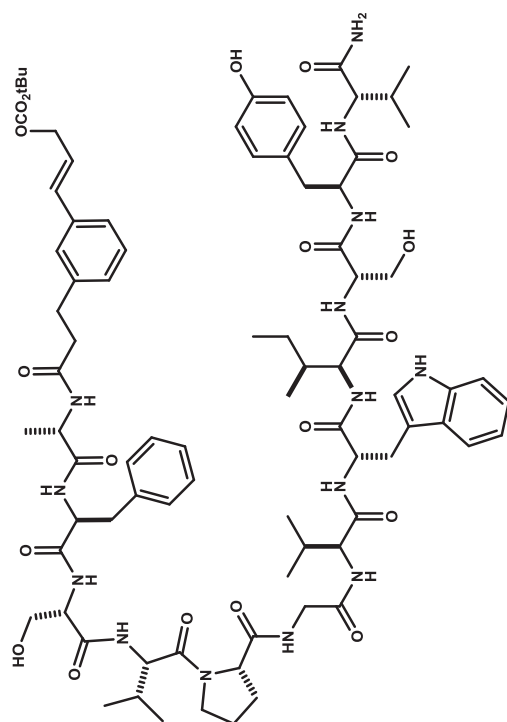
F2 - Acquisition Parameters
Date_     20110923
Time      14.35
INSTRUM   av600
PROBHD    5 mm TBI5
PULPROG   zg30
TD         65536
SOLVENT    DMSO
NS         8
DS         0
SWH        12376.237 Hz
FIDRES     0.188846 Hz
AQ         2.6476543 sec
RG         114
DW         40.400 usec
DE         6.50 usec
TE         294.3 K
D1         2.0000000 sec
TD0        1

===== CHANNEL f1 =====
NUC1       1H
P1         9.10 usec
PL1        -2.00 dB
PL1W       39.81071854 W
SFO1       600.1336008 MHz

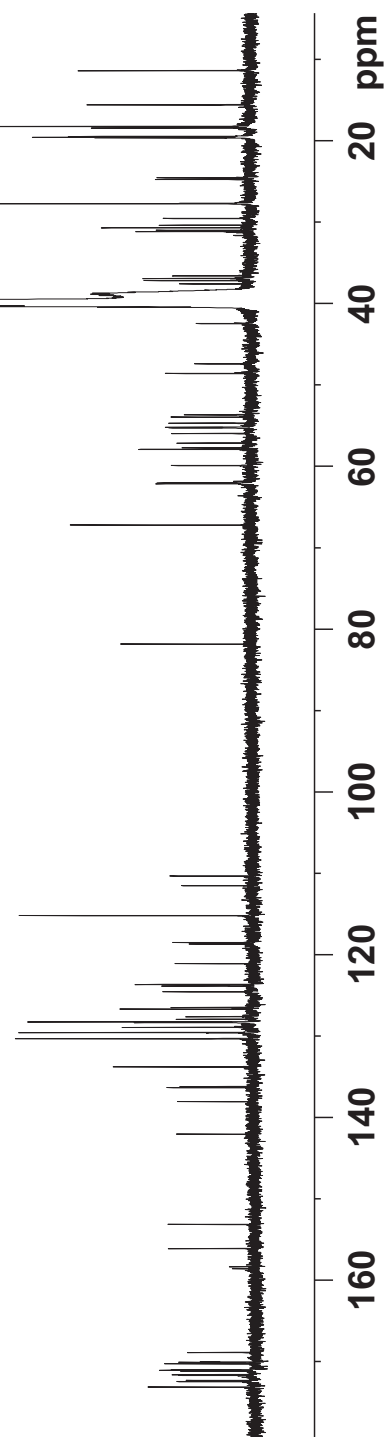
F2 - Processing parameters
SI         65536
SF         600.1300273 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00
  
```



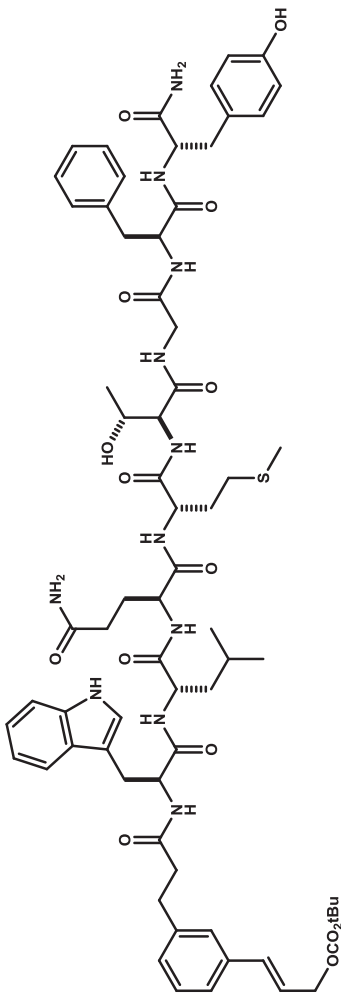
Acyclic-Ala-Phe-Ser-Val-Pro-Gly-Val-Trp-Ile-Ser-Tyr-Val (S32):



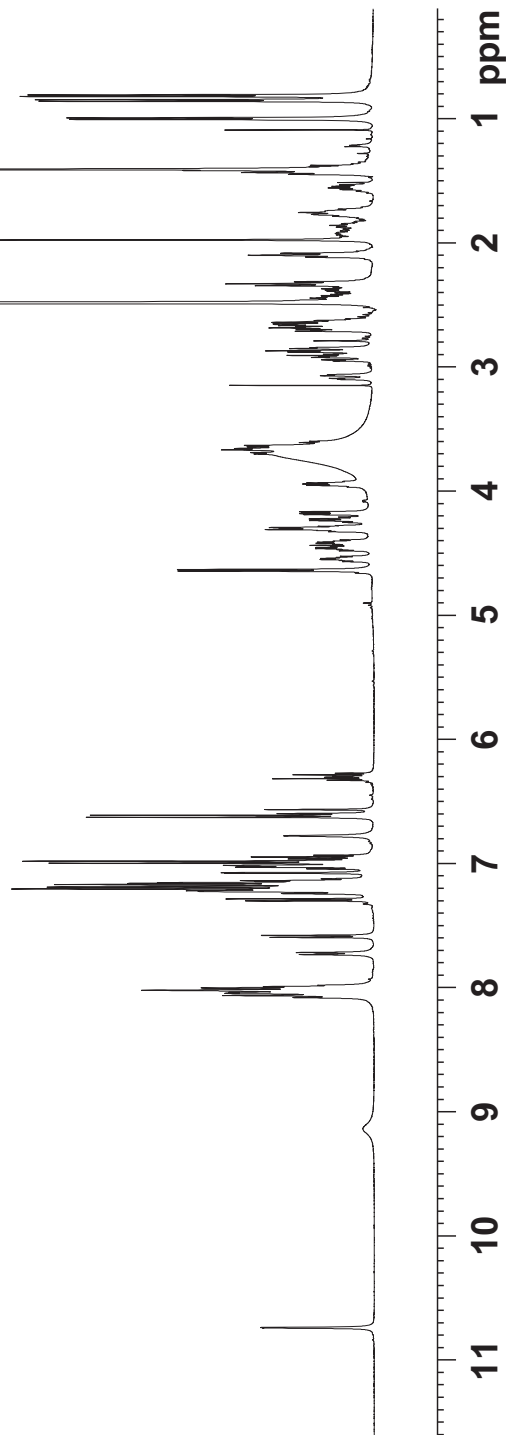
Current Data Parameters
NAME KL-4-7_prep
EXPNO 3
PROCNO 1
F2 - Processing parameters
SI 65536
SF 150.9028319 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40



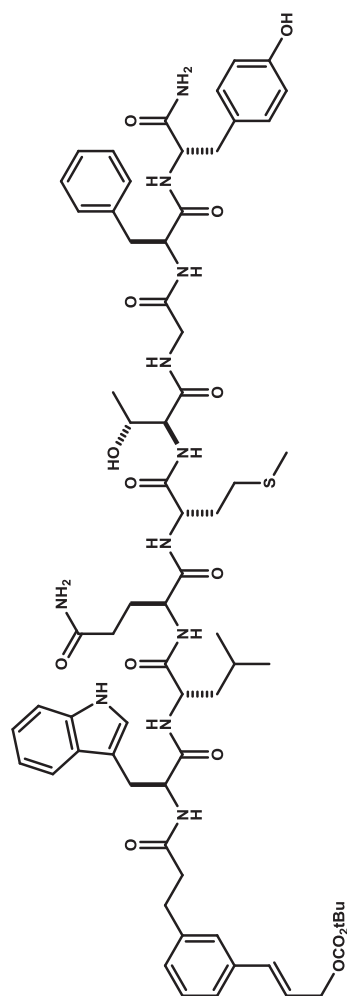
Acyclic-Trp-Leu-Gln-Met-Thr-Gly-Phe-Tyr (S33):



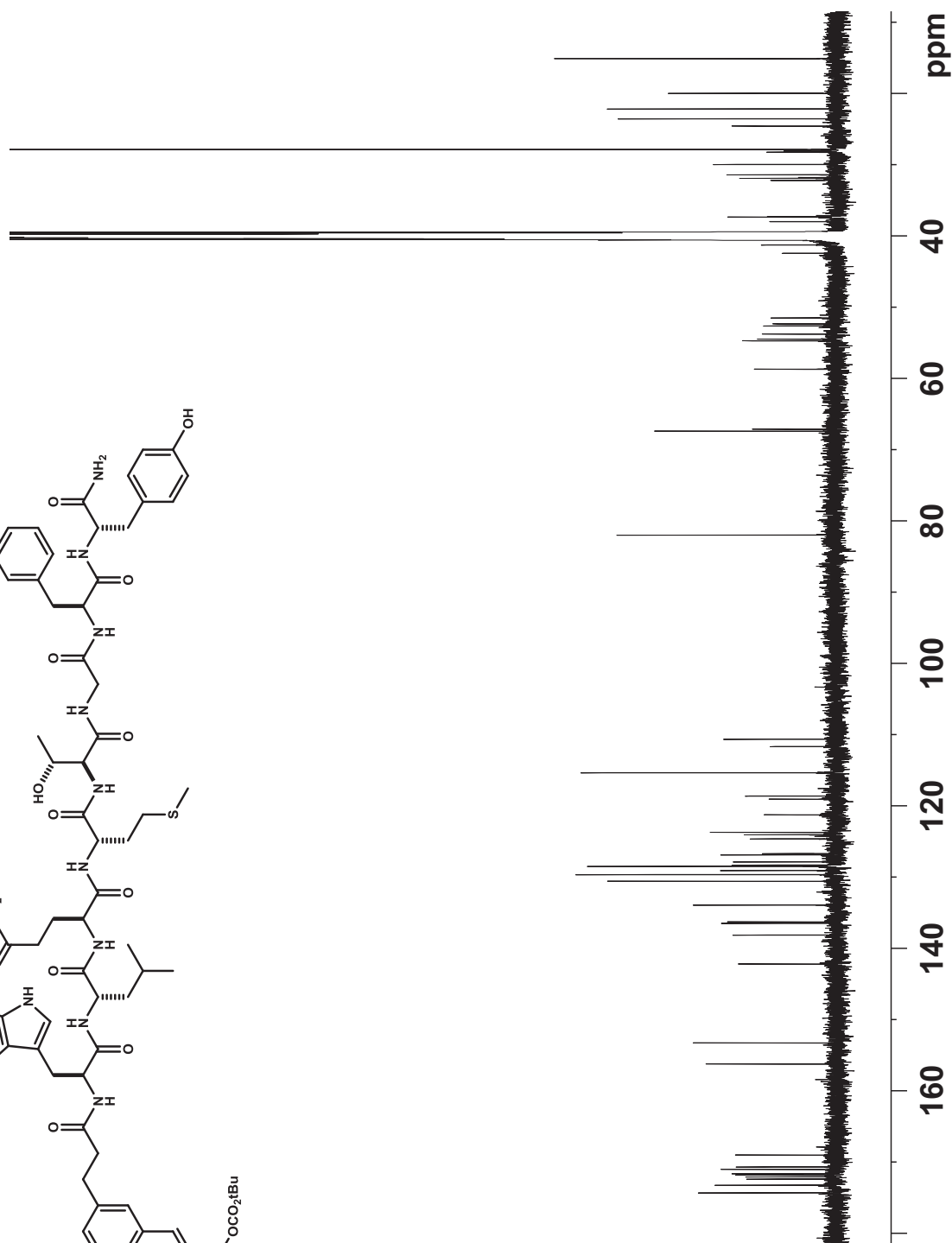
Current Data Parameters
NAME KL-4-15d_F21
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20120730
Time_ 12.13
INSTRUM av500
PROBHD 5 mm DCH-1
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 8
DS 0
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2767999 sec
RG 202.91
DW 50.000 usec
DE 10.00 usec
TE 296.0 K
D1 2.00000000 sec
TD0 1
===== CHANNEL f1 =====
NUC1 1H
P1 10.00 usec
PLW1 13.50000000 W
SFO1 500.1330008 MHz
F2 - Processing parameters
SI 65536
SF 500.1300146 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



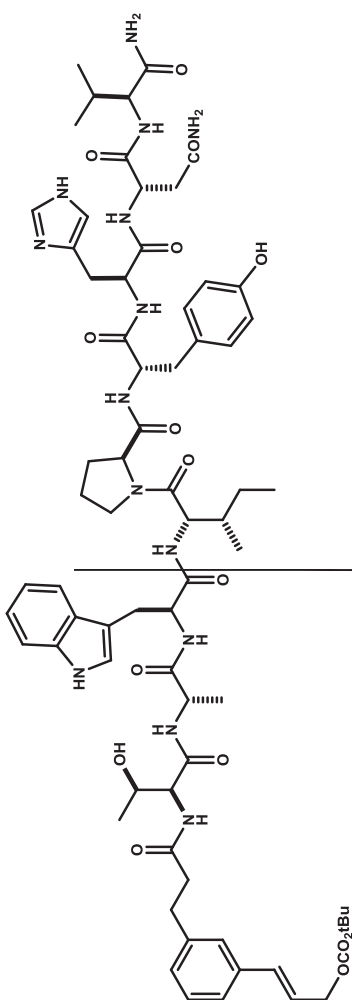
Acyclic-Trp-Leu-Gln-Met-Thr-Gly-Phe-Tyr (S33):



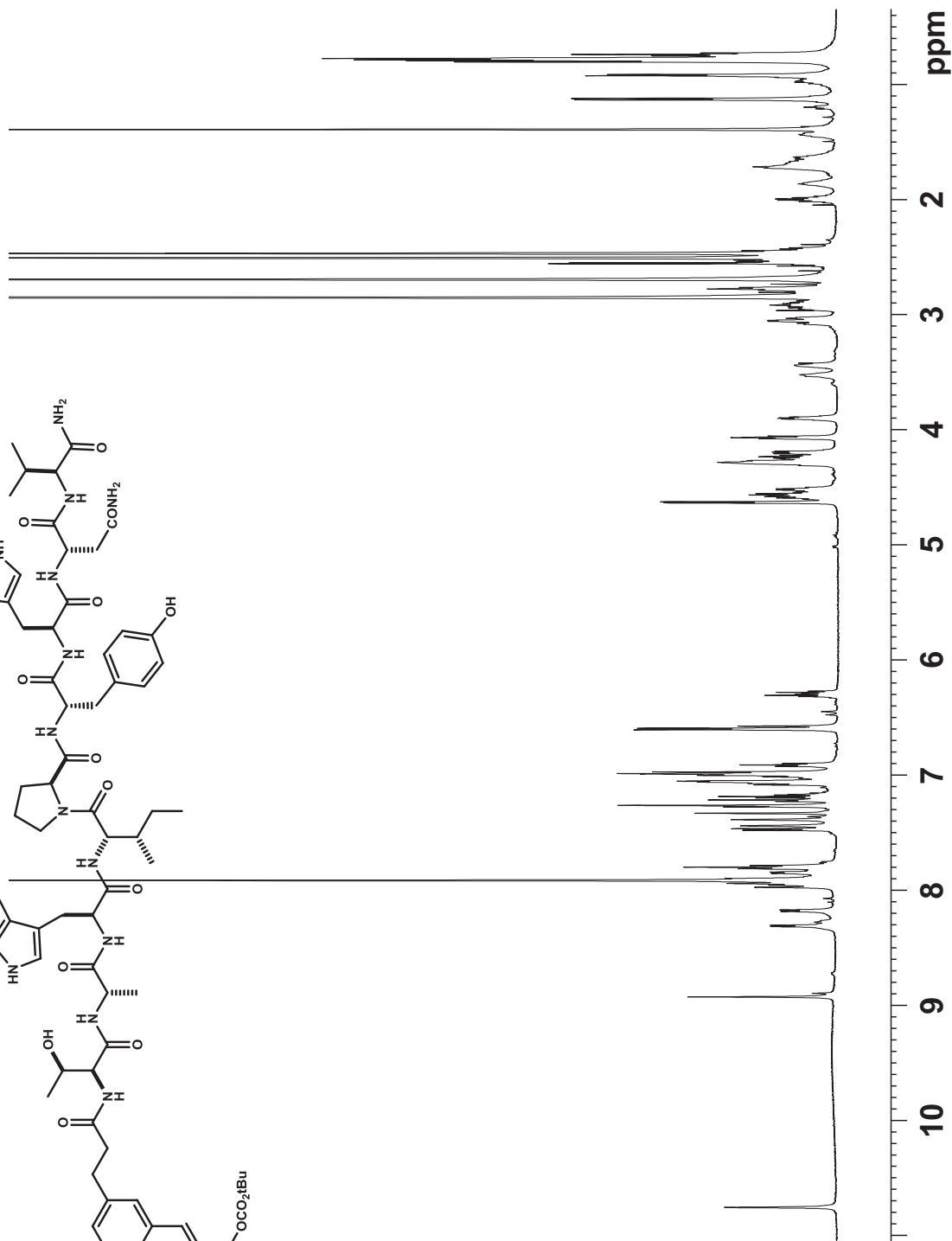
Current Data Parameters
NAME KL-4-15d_F21
EXPNO 2
PROCNO 1
F2 - Processing parameters
SI 131072
SF 125.7577892 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40



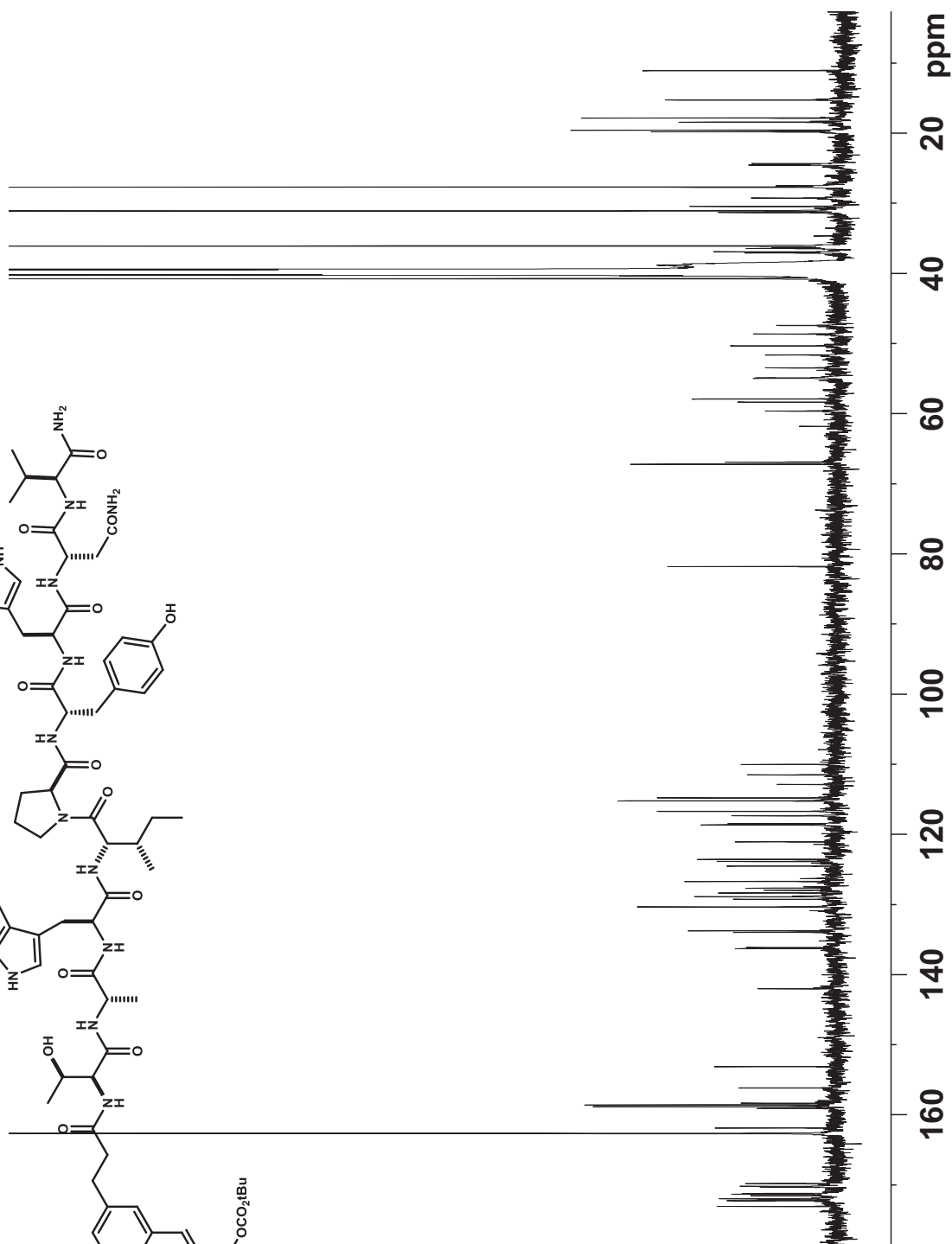
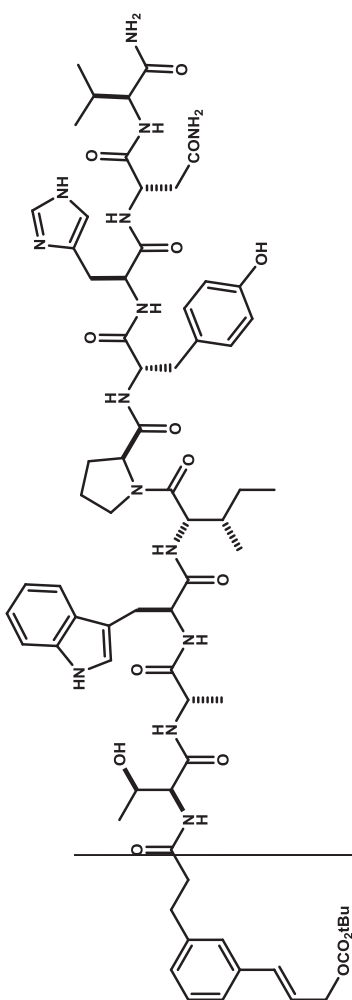
Acyclic-Thr-Ala-Trp-Ile-Pro-Tyr-His-Asn-Val (S34):



Current Data Parameters
 NAME KL-III-284
 EXPNO 1
 PROCNO 1
 F2 - Acquisition Parameters
 Date_ 20110829
 Time_ 17.20
 INSTRUM av600
 PROBHD 5 mm BB5
 PULPROG zg30
 TD 65536
 SOLVENT DMSO
 NS 8
 DS 0
 SWH 12376.237 Hz
 FIDRES 0.188846 Hz
 AQ 2.6476543 sec
 RG 90.5
 DW 40.400 usec
 DE 6.50 usec
 TE 294.5 K
 D1 2.00000000 sec
 TD0 1
 ===== CHANNEL f1 =====
 NUC1 1H
 P1 14.00 usec
 PL1 -1.00 dB
 PL1W 31.62277603 W
 SFO1 600.1336008 MHz
 F2 - Processing parameters
 SI 65536
 SF 600.1300273 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00

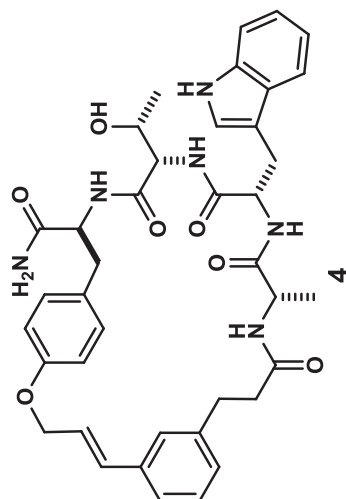


Acyclic-Thr-Ala-Trp-Ile-Pro-Tyr-His-Asn-Val (S34):



Current Data Parameters
NAME KL-III-284
EXPNO 2
PROCNO 1
F2 - Processing parameters
SI 65536
SF 150.9028319 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40

Cyclic-Ala-Trp-Thr-Tyr (4):



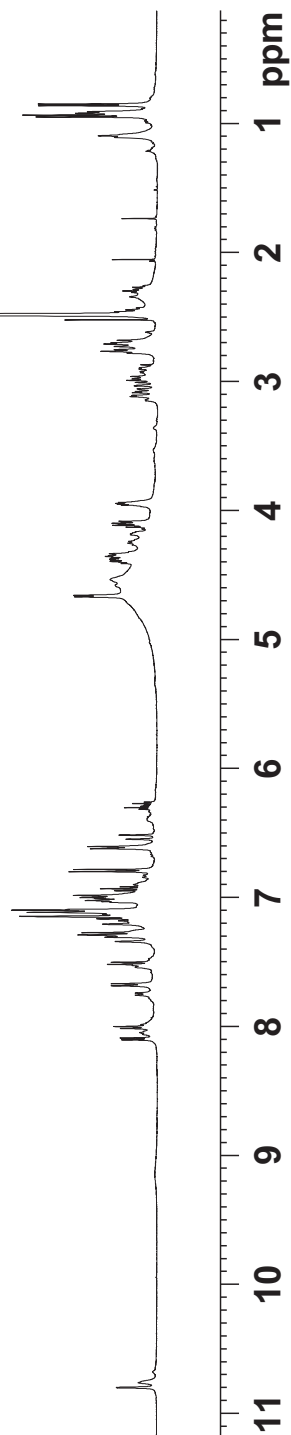
```

Current Data Parameters
NAME      KL-4-55_CHECK
EXPNO     1
PROCNO    1

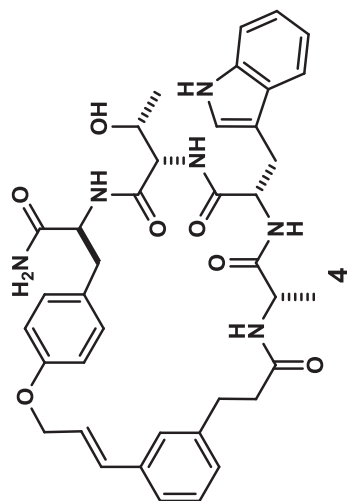
F2 - Acquisition Parameters
Date_     20111019
Time      19.56
INSTRUM   av500
PROBHD    5 mm DCH 13C-1
PULPROG   zg30
TD         65536
SOLVENT   DMSO
NS         8
DS         0
SWH        10000.000 Hz
FIDRES     0.152588 Hz
AQ         3.2767999 sec
RG         22.82
DW         50.000 usec
DE         10.00 usec
TE         301.0 K
D1         2.00000000 sec
TD0        1

===== CHANNEL f1 =====
NUC1       1H
P1         10.00 usec
PLW1       13.50000000 W
SFO1       500.1330008 MHz

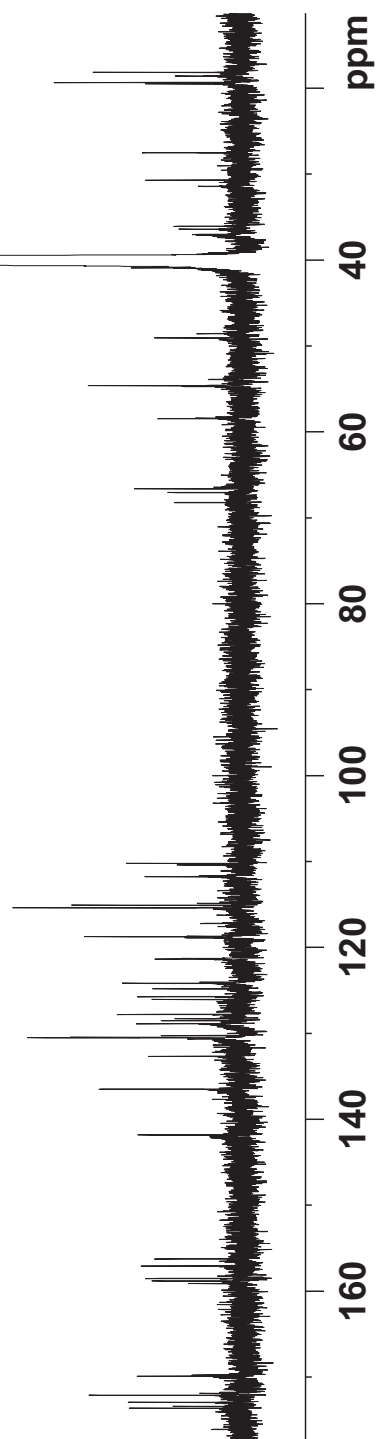
F2 - Processing parameters
SI          65536
SF          500.1300146 MHz
WDW         EM
SSB         0
LB          0.30 Hz
GB          0
PC          1.00
  
```



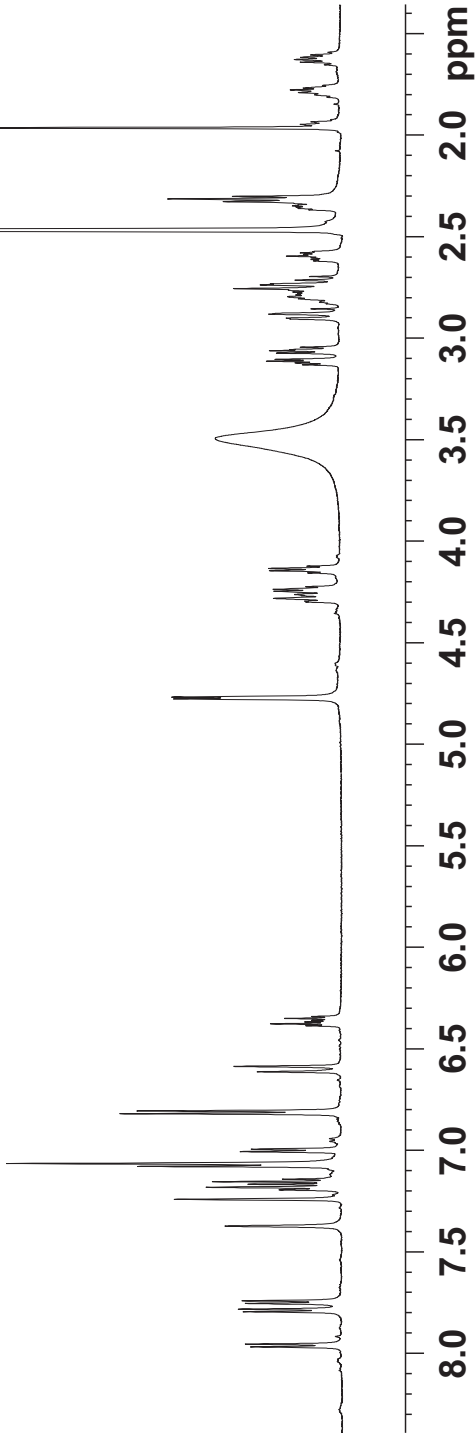
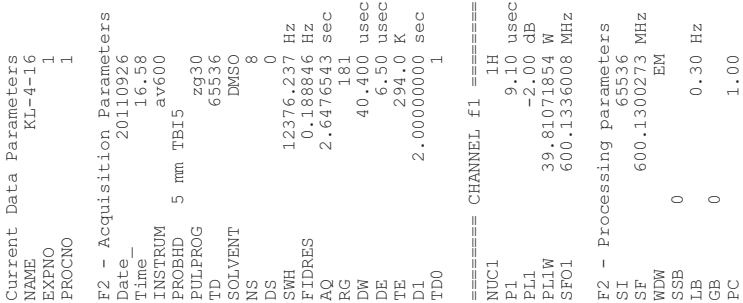
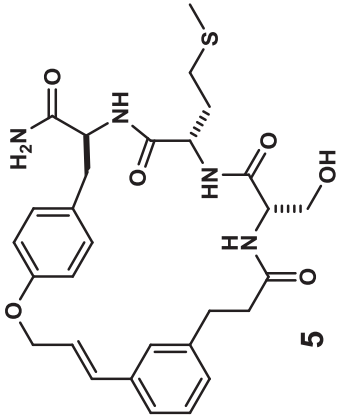
Cyclic-Ala-Trp-Thr-Tyr (4):



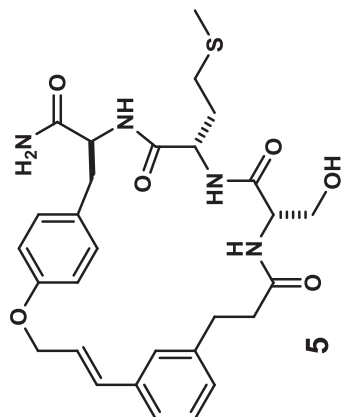
Current Data Parameters
NAME KL-4-55_CHECK
EXPNO 2
PROCNO 1
F2 - Processing parameters
SI 131072
SF 125.7577892 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.00



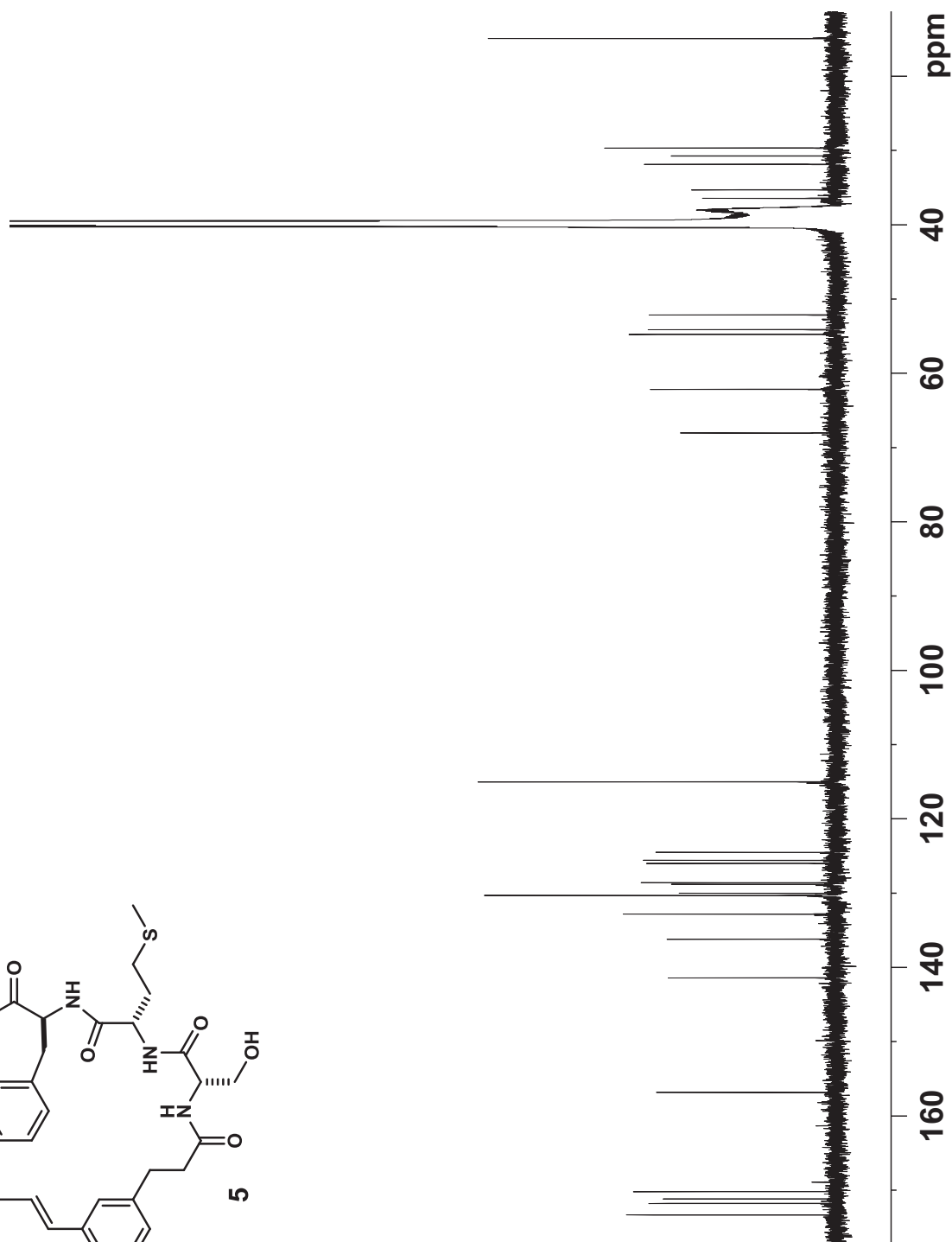
Cyclic-Ser-Met-Tyr (5):



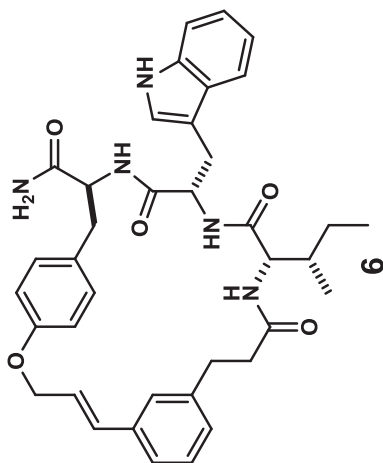
Cyclic-Ser-Met-Tyr (5):



Current Data Parameters
NAME KL-4-16
EXPNO 3
PROCNO 1
F2 - Processing parameters
SI 65536
SF 150.9028319 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40



Cyclic-Ile-Trp-Tyr (6):



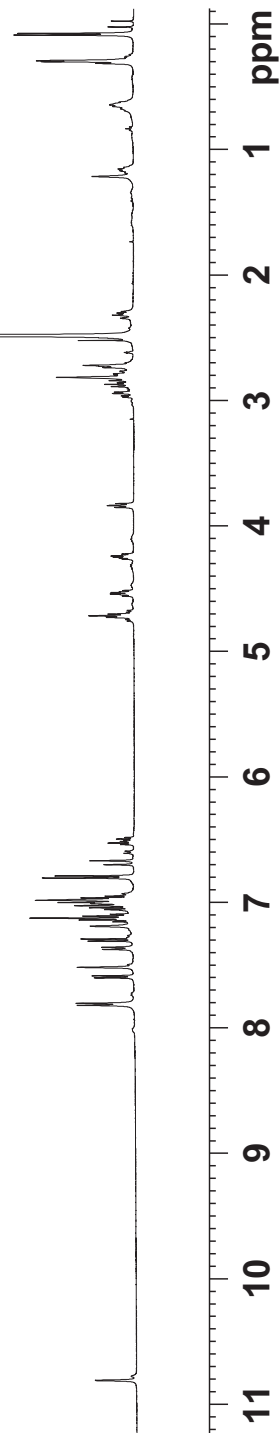
```

Current Data Parameters
NAME          IWY-Cy
EXPNO         2
PROCNO        1

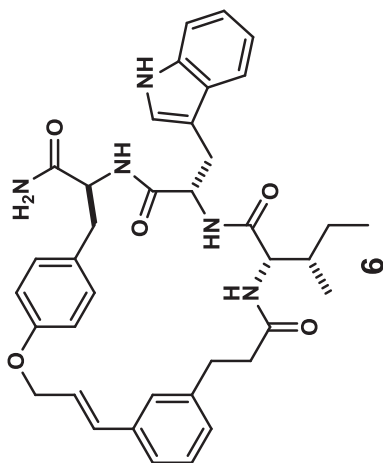
F2 - Acquisition Parameters
Date_         20130509
Time_         11:10
INSTRUM       av500
PROBHD        5 mm DCH 13C-1
PULPROG       zgpr
TD            65536
SOLVENT       DMSO
NS            8
DS            0
SWH           10000.000 Hz
FIDRES        0.152588 Hz
AQ            3.2767999 sec
RG            11
DW            50.000 usec
DE            10.00 usec
TE            298.0 K
D1            2.00000000 sec
D12           0.00002000 sec
TD0           1

===== CHANNEL f1 =====
SFO1          500.1317204 MHz
NUC1          1H
P1            10.00 usec
PLW1          13.50000000 W
PLW9          0.00005400 W

F2 - Processing parameters
SI            65536
SF            500.1300146 MHz
WDW           EM
SSB           0
LB            0.30 Hz
GB            0
PC            1.00
  
```



Cyclic-Ile-Trp-Tyr (6):



```

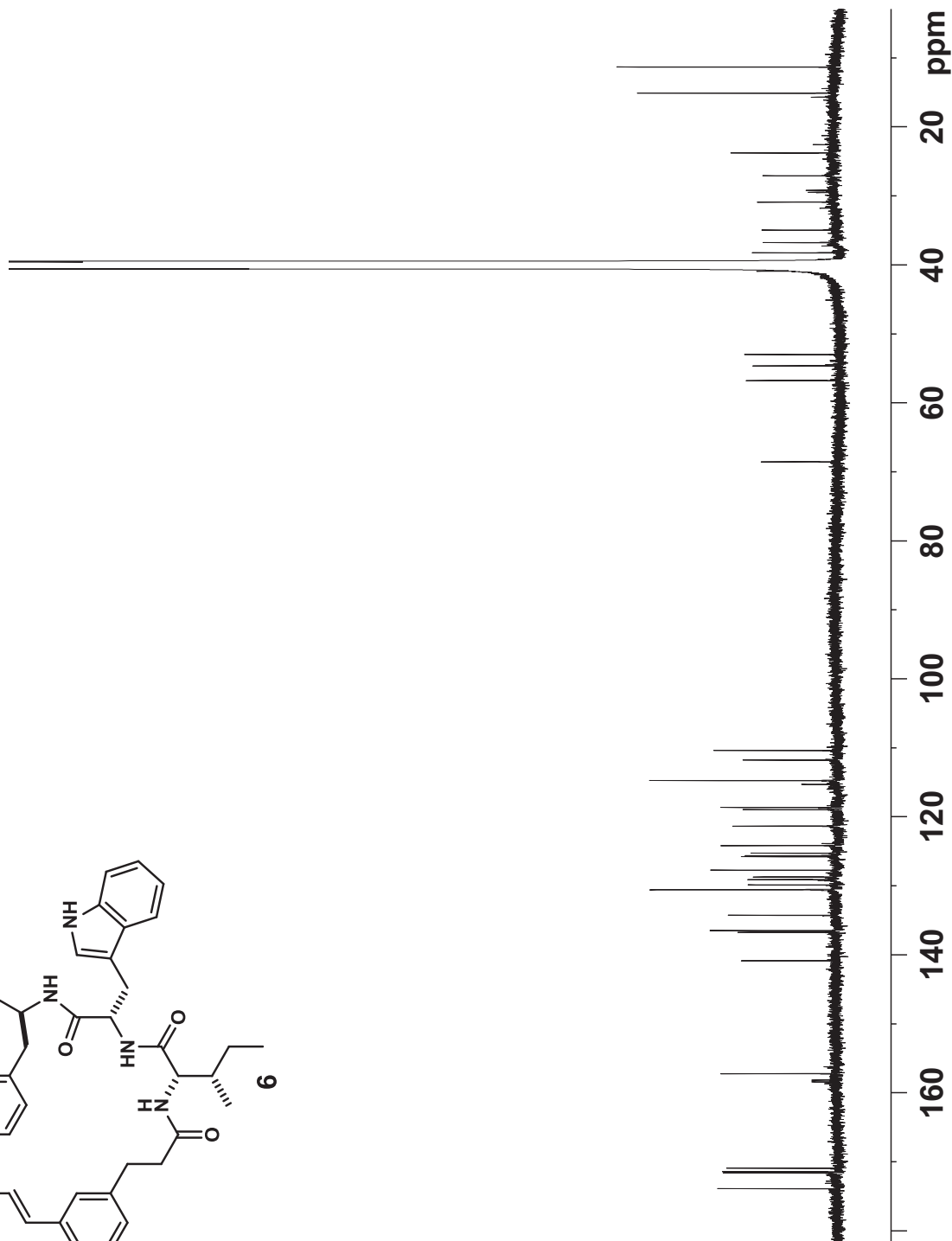
Current Data Parameters
NAME          IWY-Cy
EXPNO         6
PROCNO        1

F2 - Acquisition Parameters
Date_         20130518
Time_         3.28
INSTRUM       av500
PROBHD        5 mm DCH 13C-1
PULPROG       zgpg30
TD            65536
SOLVENT       DMSO
NS            8192
DS            2
SWH           31250.000 Hz
FIDRES       0.476837 Hz
AQ           1.0485760 sec
RG           202.91
DW           16.000 usec
DE           18.00 usec
TE           298.0 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0          1

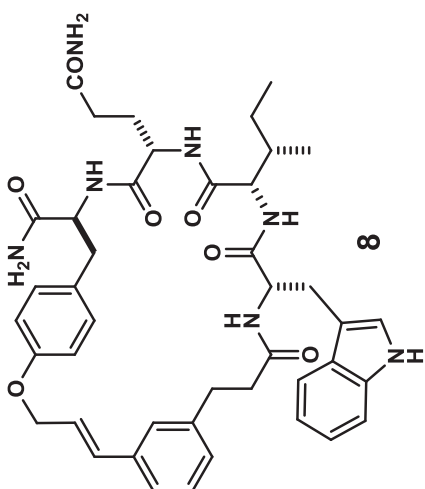
===== CHANNEL f1 =====
SFO1         125.772511 MHz
NUC1         13C
P1           9.63 usec
PLW1         23.00000000 W

===== CHANNEL f2 =====
SFO2         500.1330008 MHz
NUC2         1H
CPDPRG2      waltz16
PCPD2        80.00 usec
PLW2         13.50000000 W
PLW12        0.21094000 W
PLW13        0.13500001 W

F2 - Processing parameters
SI           131072
SF           125.7577892 MHz
WDW          EM
SSB          0
LB           1.00 Hz
GB           0
PC           1.00
  
```



Cyclic-Trp-Ile-Gln-Tyr (8):

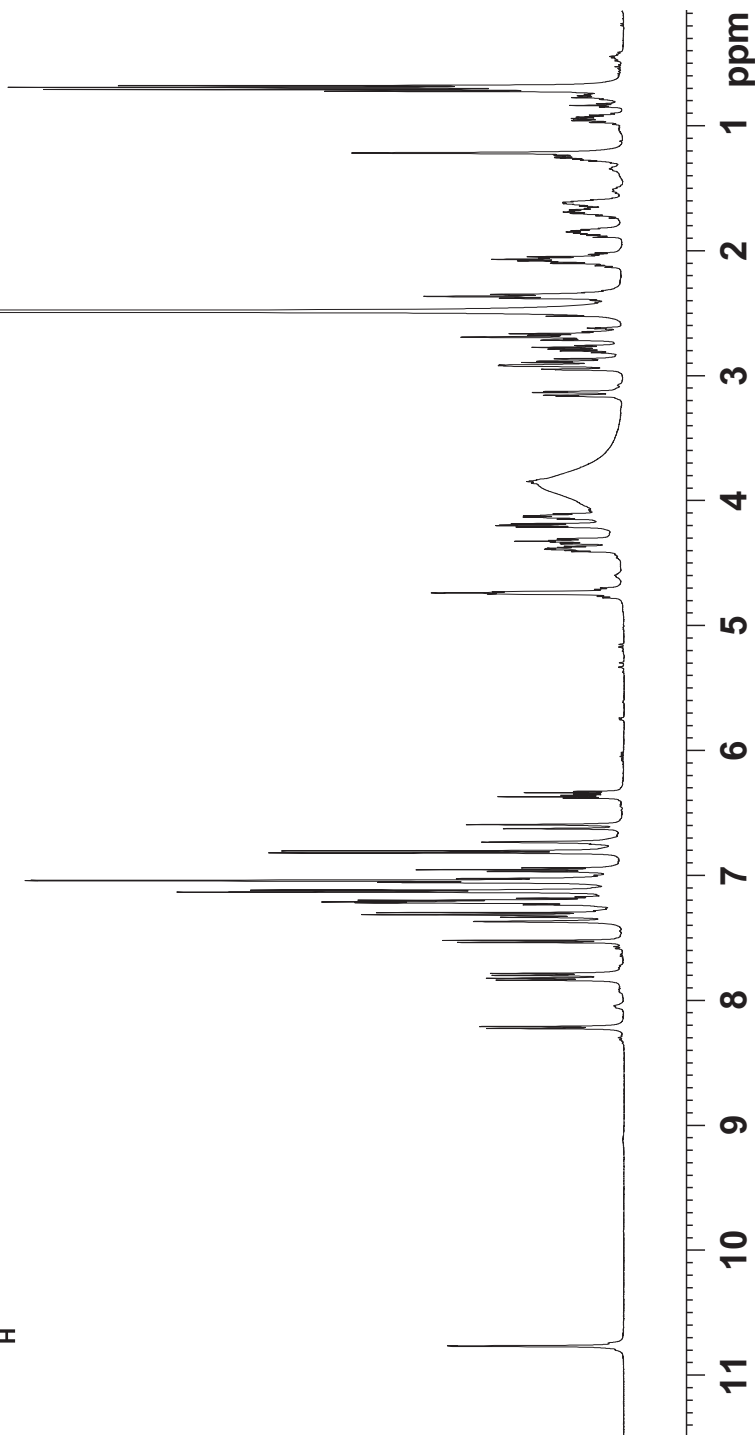


Current Data Parameters
NAME KL-5-117b
EXPNO 3
PROCNO 1

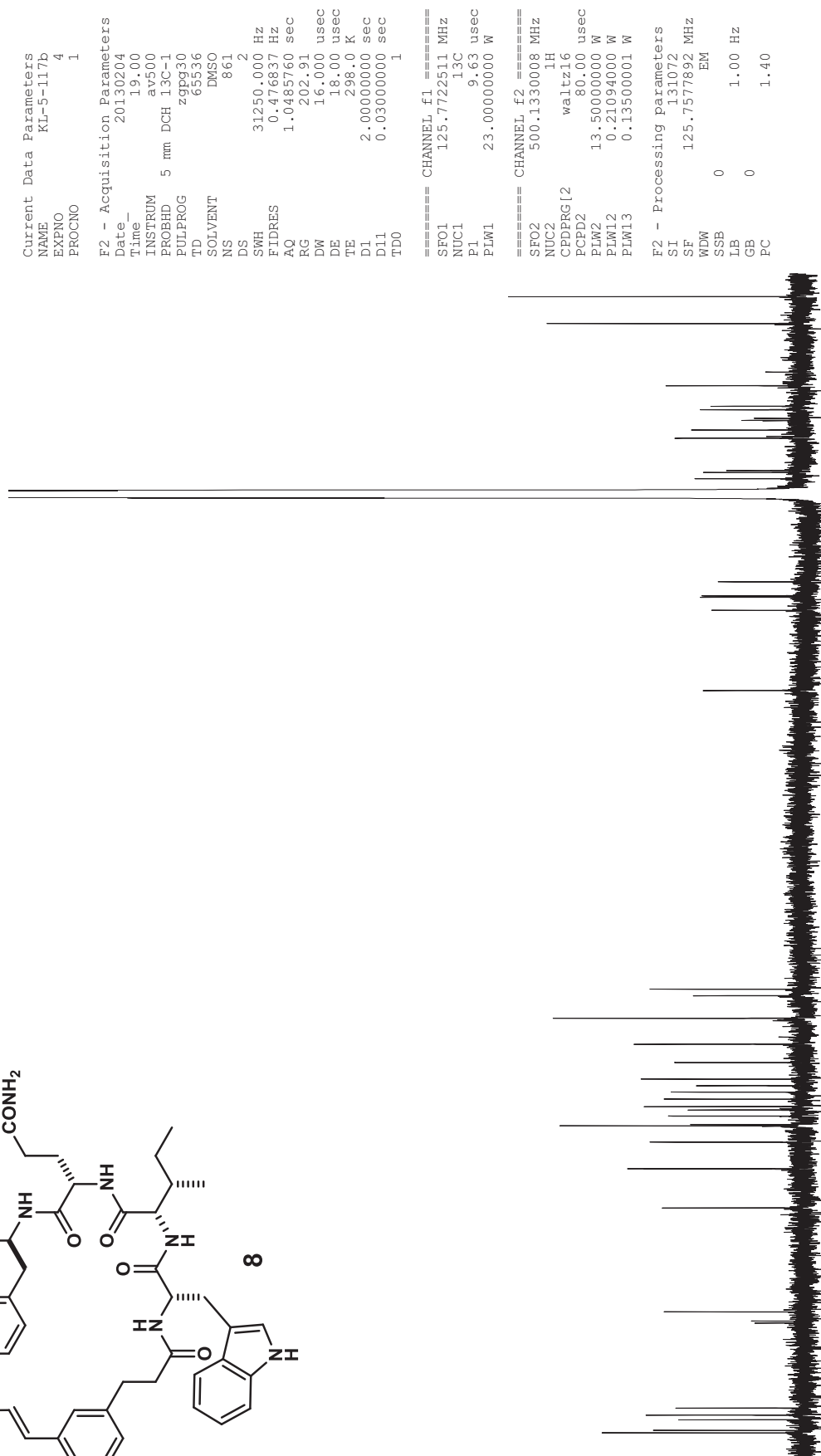
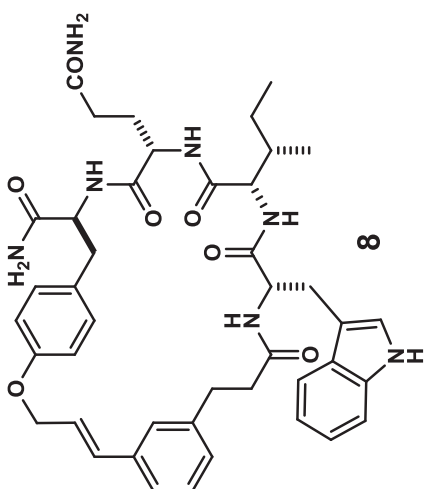
F2 - Acquisition Parameters
Date_ 20130204
Time_ 18.16
INSTRUM av500
PROBHD 5 mm DCH 13C-1
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 64
DS 0
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2767999 sec
RG 11
DW 50.000 usec
DE 10.00 usec
TE 298.0 K
D1 2.00000000 sec
TD0 1

===== CHANNEL f1 =====
SFO1 500.1330008 MHz
NUC1 1H
P1 10.00 usec
PLW1 13.50000000 W

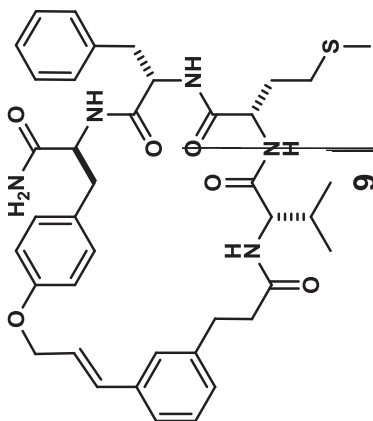
F2 - Processing parameters
SI 65536
SF 500.1300146 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



Cyclic-Trp-Ile-Gln-Tyr (8):



Cyclic-Val-Met-Phe-Tyr (9):

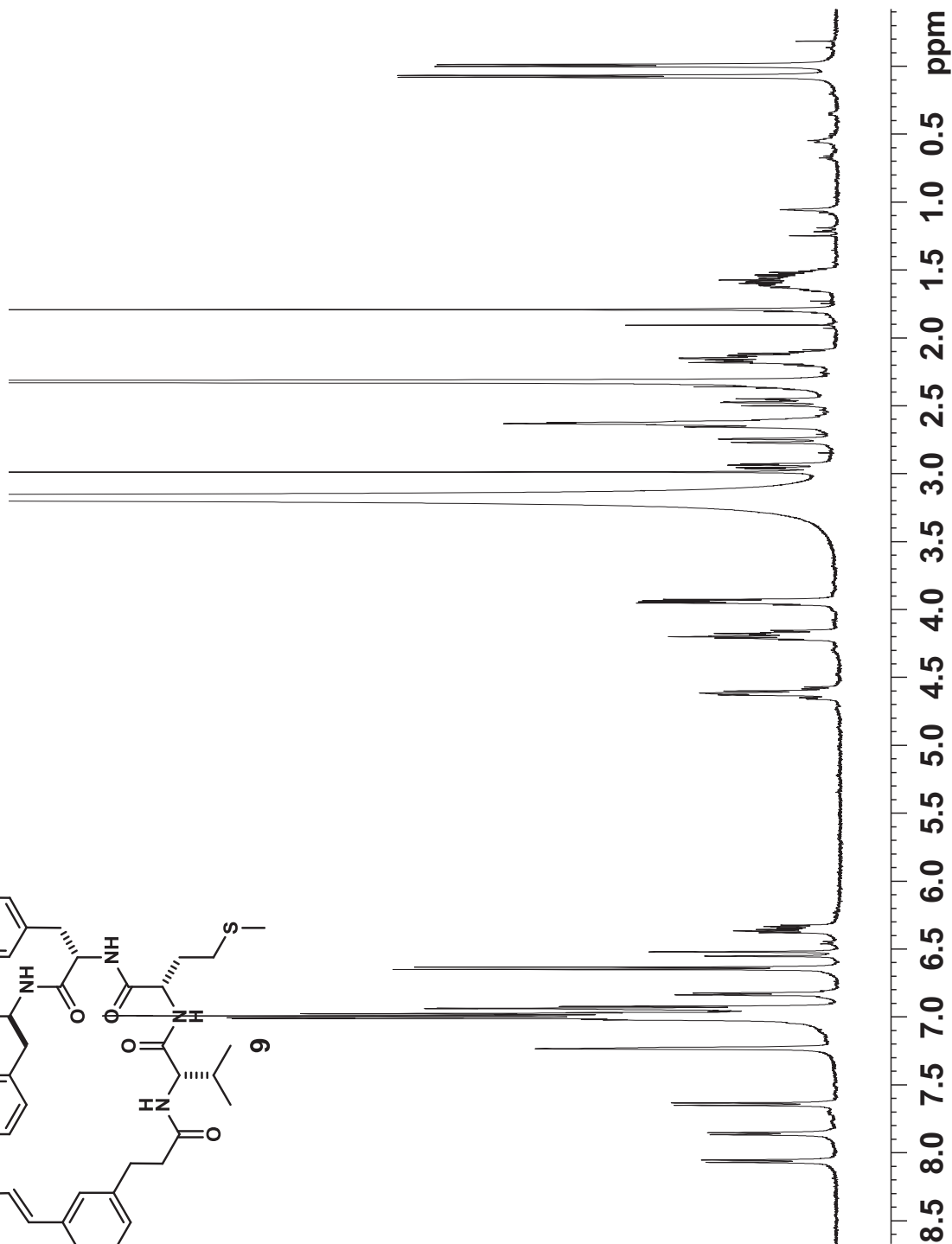


Current Data Parameters
NAME KL-4-56_ICON
EXPNO 1
PROCNO 1

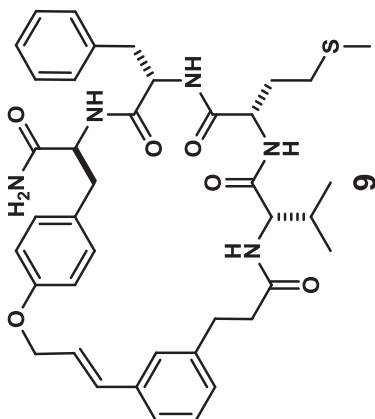
F2 - Acquisition Parameters
Date_ 20120827
Time_ 22.07
INSTRUM av500
PROBHD 5 mm DCH 13C-1
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 8
DS 0
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2767999 sec
RG 28.6
DW 50.000 usec
DE 10.00 usec
TE 298.0 K
D1 2.0000000 sec
TD0 1

===== CHANNEL f1 =====
NUC1 1H
P1 10.00 usec
PLW1 13.5000000 W
SFO1 500.1330008 MHz

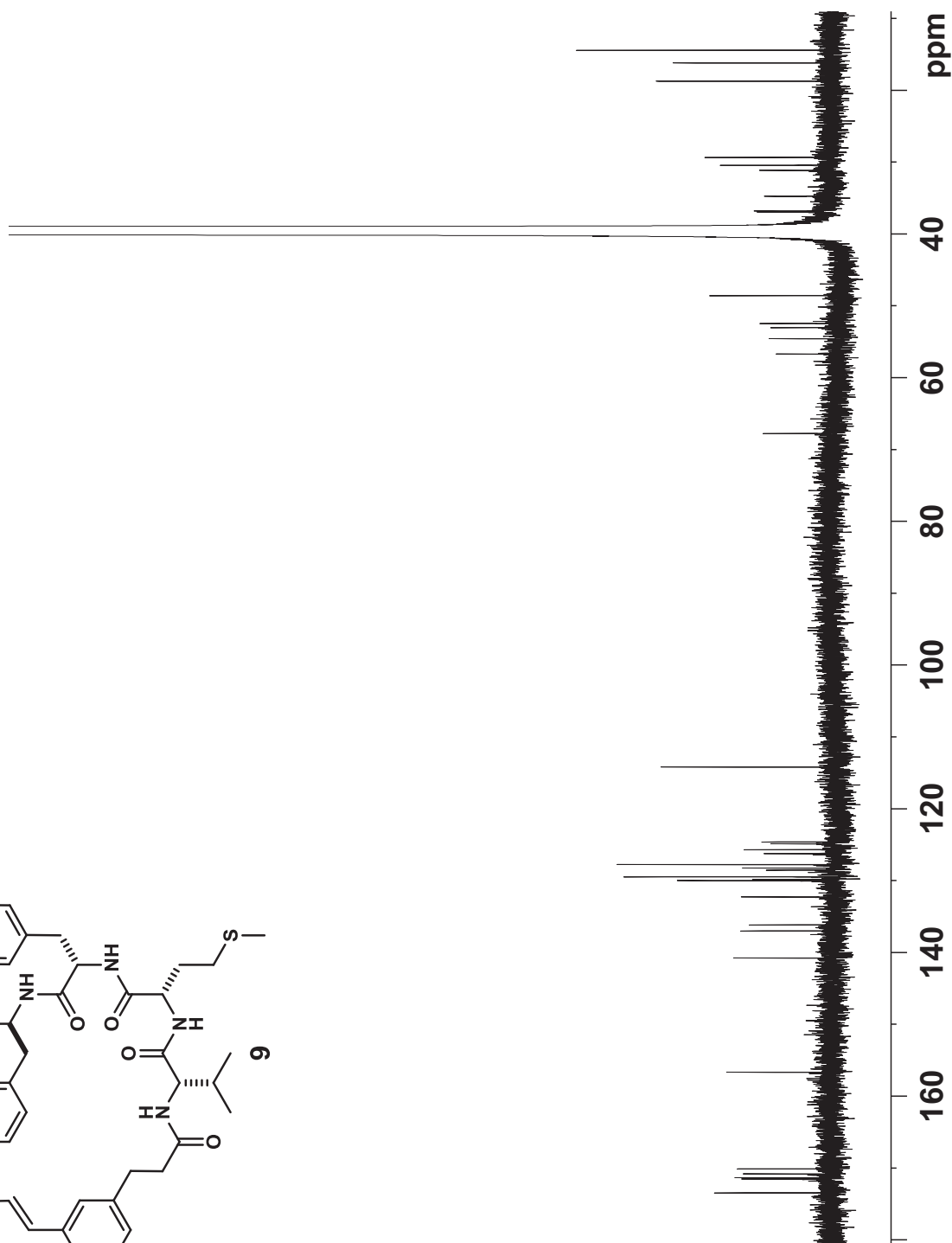
F2 - Processing parameters
SI 65536
SF 500.1300950 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



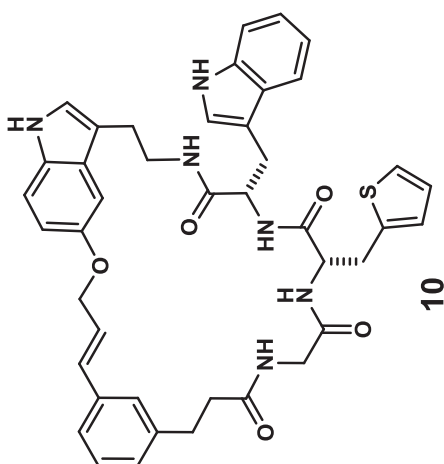
Cyclic-Val-Met-Phe-Tyr (9):



Current Data Parameters
NAME KL-4-56_ICON
EXPNO 2
PROCNO 1
F2 - Processing parameters
SI 131072
SF 125.7578519 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40



Cyclic-Gly-Thi-Trp-5HT (10):



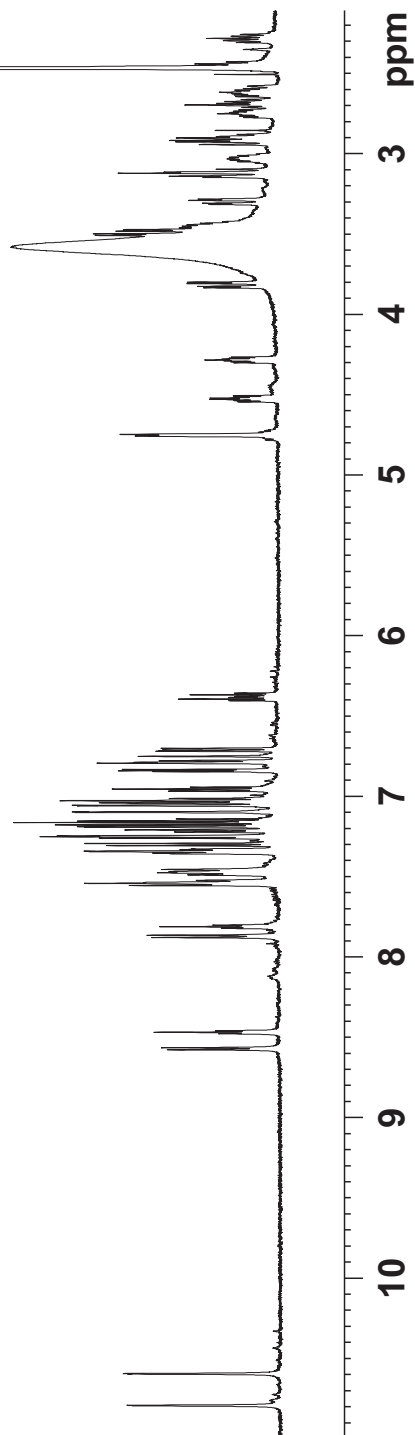
```

Current Data Parameters
NAME      KI-4-171B
EXPNO     1
PROCNO    1

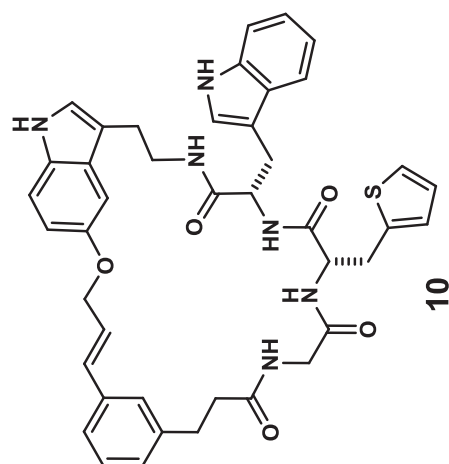
F2 - Acquisition Parameters
Date_     20120409
Time      19.19
INSTRUM   av600
PROBHD    5 mm TBI5
PULPROG   zg30
TD         65536
SOLVENT   DMSO
NS         8
DS         0
SWH        12376.237 Hz
FIDRES     0.188846 Hz
AQ         2.6476543 sec
RG         181
DW         40.400 usec
DE         6.50 usec
TE         294.6 K
D1         2.0000000 sec
TD0        1

===== CHANNEL f1 =====
NUC1       1H
P1         9.10 usec
PL1        -2.00 dB
PL1W       39.81071854 W
SFO1       600.1336008 MHz

F2 - Processing parameters
SI         65536
SF         600.1300273 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00
  
```



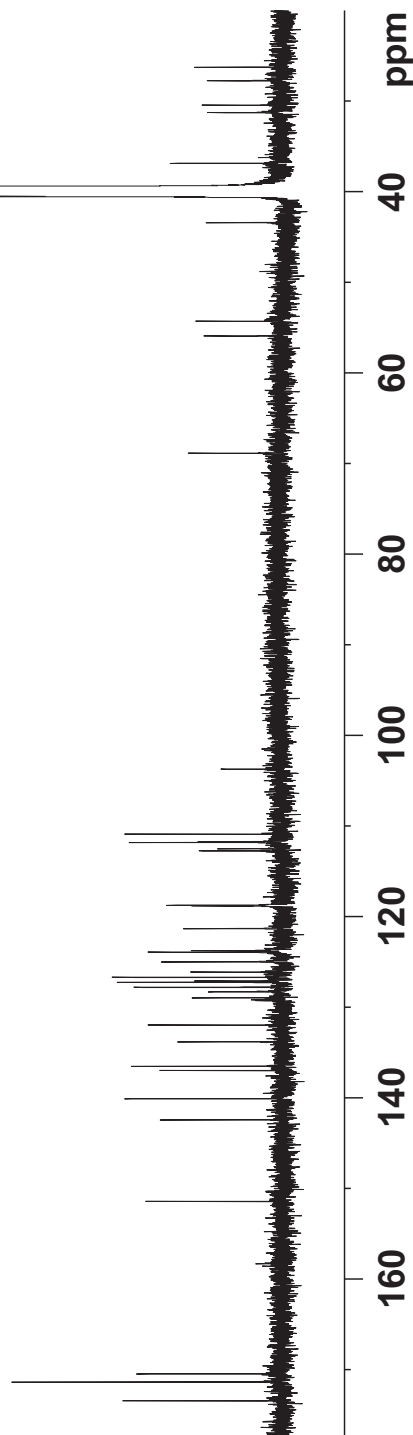
Cyclic-Gly-Thi-Trp-5HT (10):

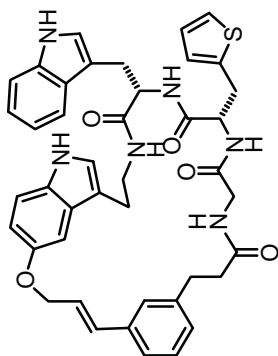
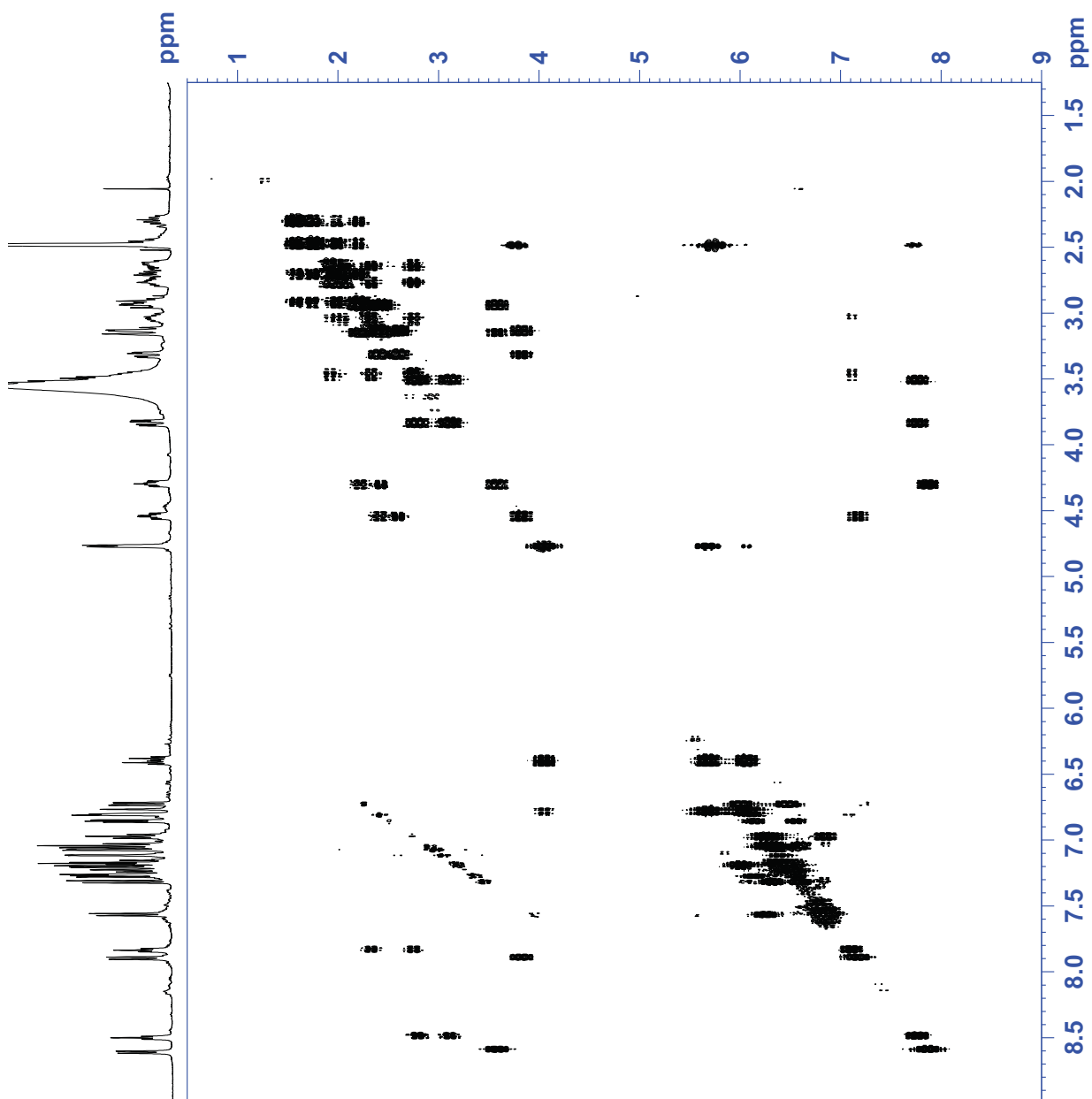


Current Data Parameters
 NAME KL-4-171A_500A
 EXPNO 2
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20120411
 Time_ 18.26
 INSTRUM av500
 PROBHD 5 mm DCH 13C-1
 PULPROG zgpg30
 TD 65536
 SOLVENT DMSO
 NS 600
 DS 2
 SWH 31250.000 Hz
 FIDRES 0.476837 Hz
 AQ 1.0485760 sec
 RG 202.91
 DW 16.000 usec
 DE 18.00 usec
 TE 296.0 K
 D1 2.0000000 sec
 d11 0.0300000 sec
 DELTA 1.8999998 sec
 TD0 1
 SF01 125.7722511 MHz
 NUC1 13C
 P1 9.63 usec
 PL1 23.0000000 W
 SF02 500.1330008 MHz
 NUC2 1H
 CPDPRG12 waltz16
 PCPD2 80.00 usec
 PLW2 13.5000000 W
 PLW12 0.2109400 W
 PLW13 0.1350000 W

F2 - Processing parameters
 SI 131072
 SF 125.7577892 MHz
 EM
 WDW 0
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40



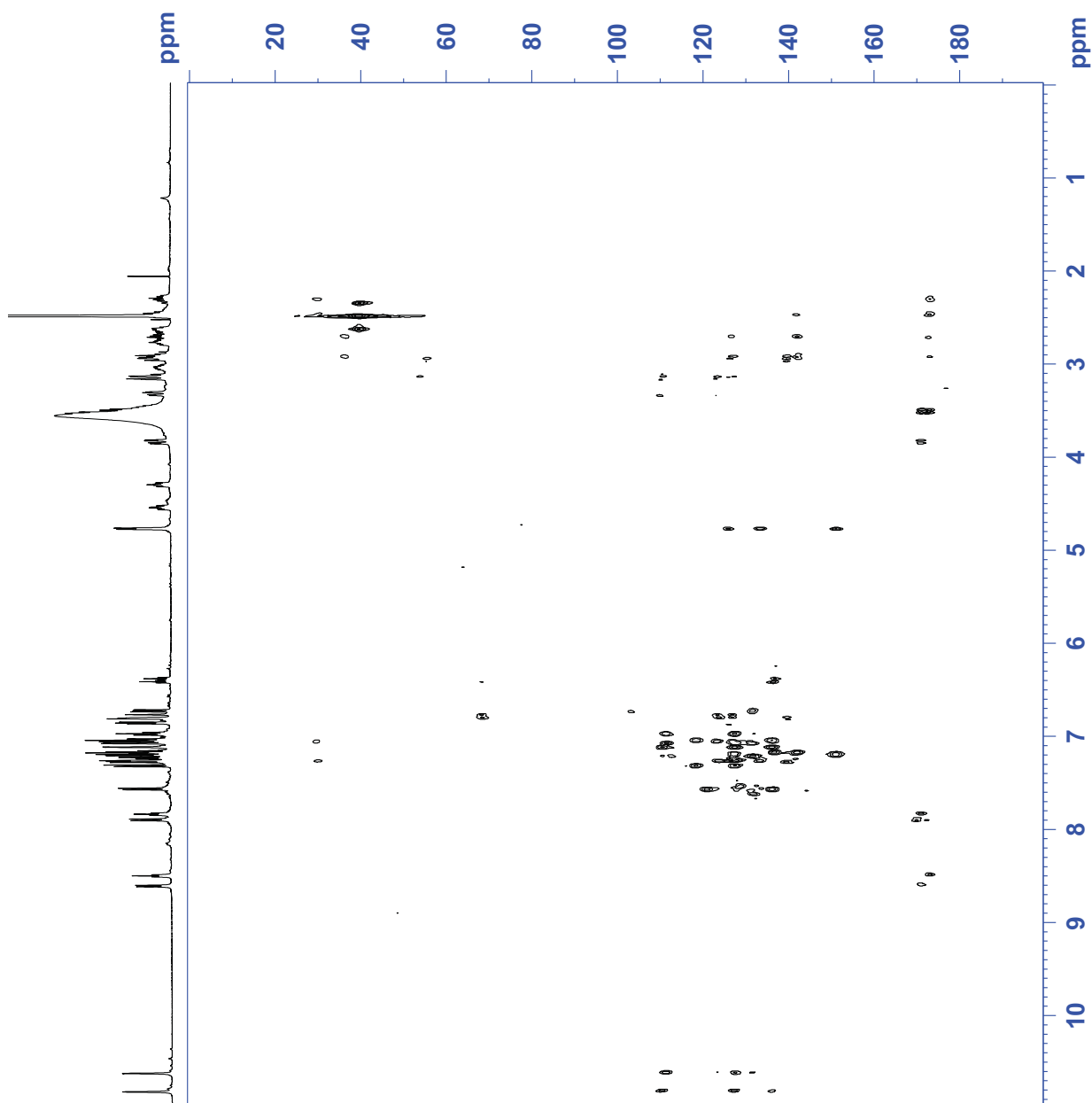


Current Data Parameters
 NAME KL-4-171A_500A
 EXPNO 5
 PROCNO 1

F1 - Acquisition parameters
 TD 256
 SFO1 500.1328 MHz
 FIDRES 19.536423 Hz
 SW 10.000 ppm
 FnmODE States-TPPI

F2 - Processing parameters
 SI 2048
 SF 500.1300135 MHz
 WDW SINE
 SSB 1
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 2048
 MC2 States-TPPI
 SF 500.1303720 MHz
 WDW QSINE
 SSB 1
 LB 0 Hz
 GB 0



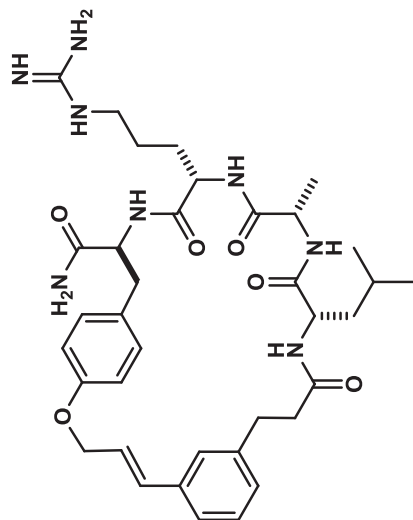
Current Data Parameters
 NAME KL-4-171A_500A
 EXPNO 6
 PROCNO 1

F1 - Acquisition parameters
 TD 162
 SFO1 125.7704 MHz
 FIDRES 155.271286 Hz
 SW 199.999 ppm
 FnmODE QF

F2 - Processing parameters
 SI 2048
 SF 500.1300135 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 2048
 MC2 QF
 SF 125.7578472 MHz
 WDW 2
 SSB 0 Hz
 LB 0
 GB 0

Cyclic- Leu-Ala-Arg-Tyr (11):



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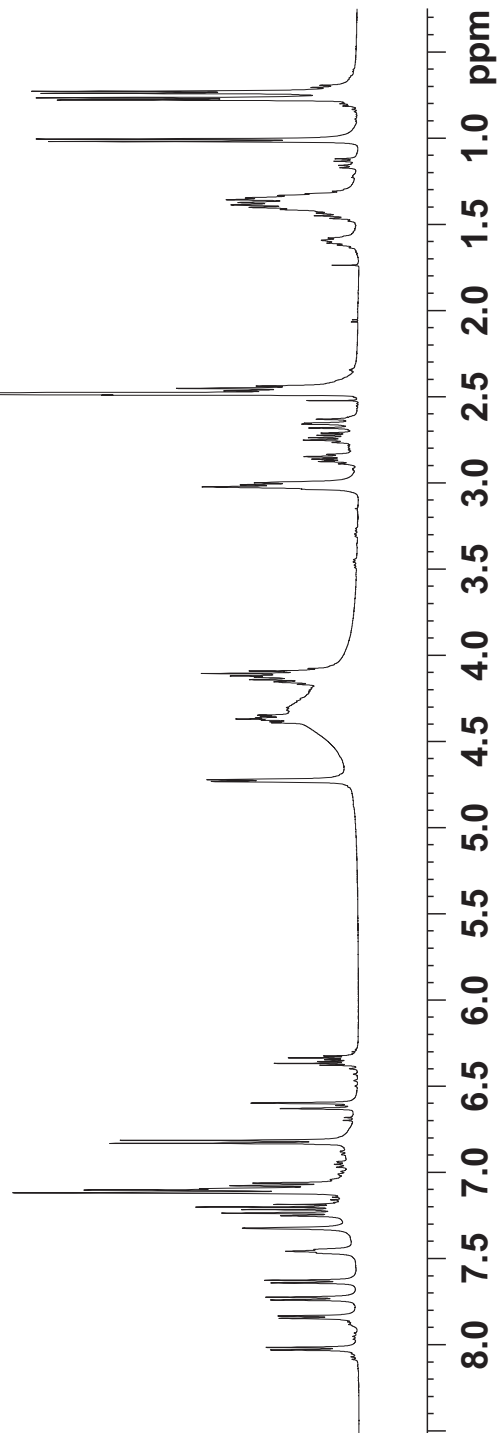
```

Current Data Parameters
NAME      KL-4-51_CHECK
EXPNO     1
PROCNO    1

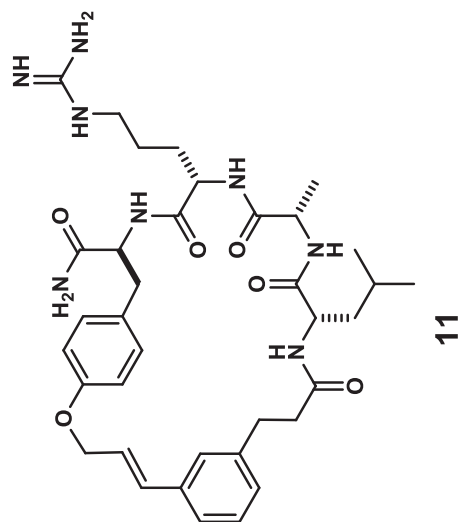
F2 - Acquisition Parameters
Date_     20111019
Time      19.37
INSTRUM   av500
PROBHD    5 mm DCH 13C-1
PULPROG   zg30
TD         65536
SOLVENT   DMSO
NS         8
DS         0
SWH        10000.000 Hz
FIDRES     0.152588 Hz
AQ          3.2767999 sec
RG          22.82
DW          50.000 usec
DE          10.00 usec
TE         301.0 K
D1         2.00000000 sec
TD0        1

===== CHANNEL f1 =====
NUC1       1H
P1         10.00 usec
PLW1       13.50000000 W
SFO1       500.1330008 MHz

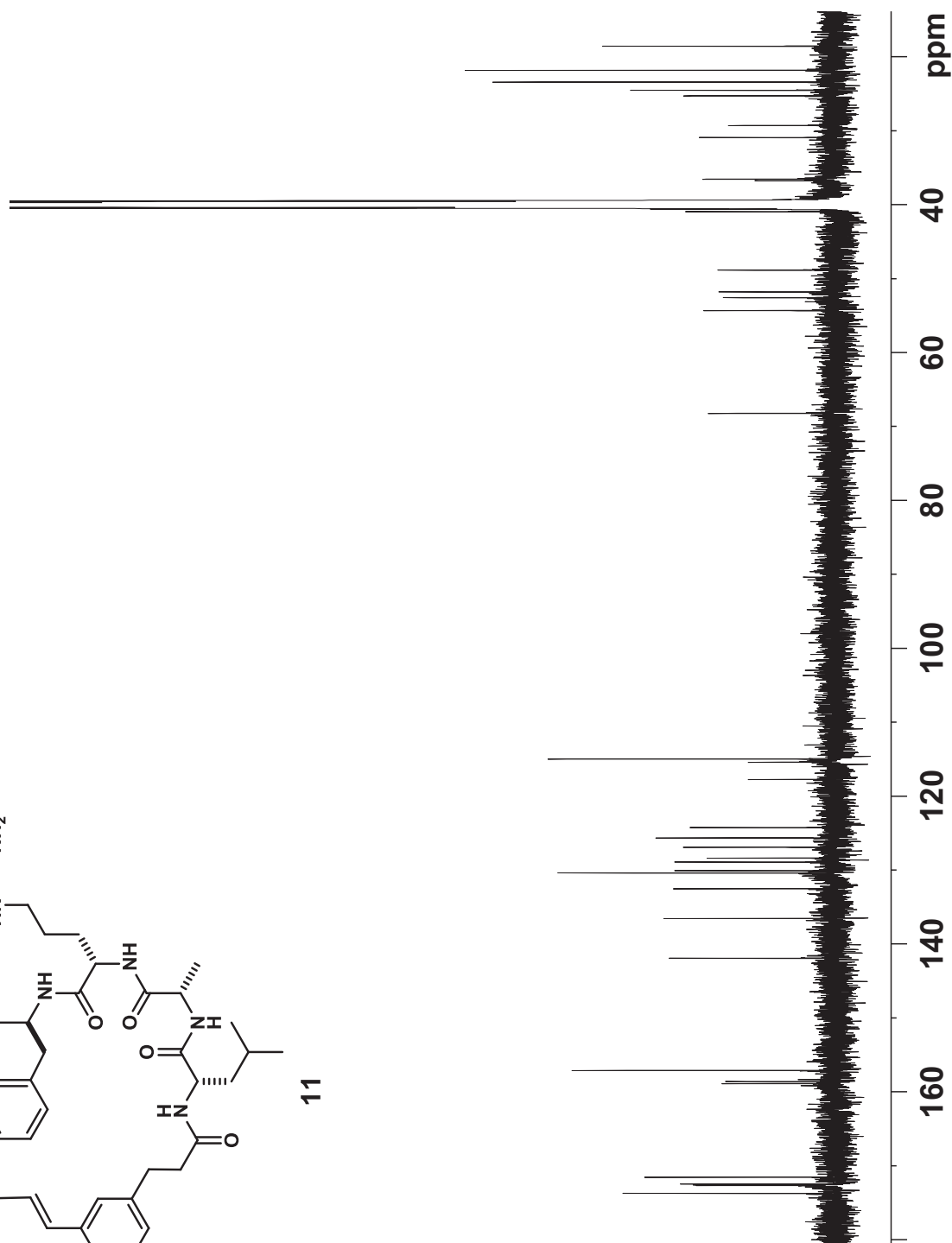
F2 - Processing parameters
SI         65536
SF         500.1300146 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00
  
```



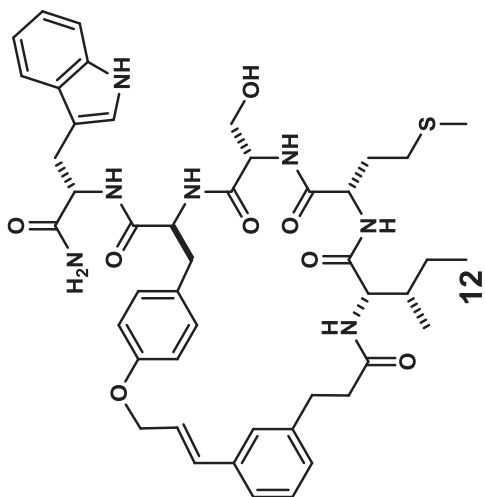
Cyclic- Leu-Ala-Arg-Tyr (11):



Current Data Parameters
NAME KL-4-51_CHECK
EXPNO 2
PROCNO 1
F2 - Processing parameters
SI 131072
SF 125.7577892 MHz
WDW 0 EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.00



Cyclic-Ile-Met-Ser-Tyr-Trp (12):



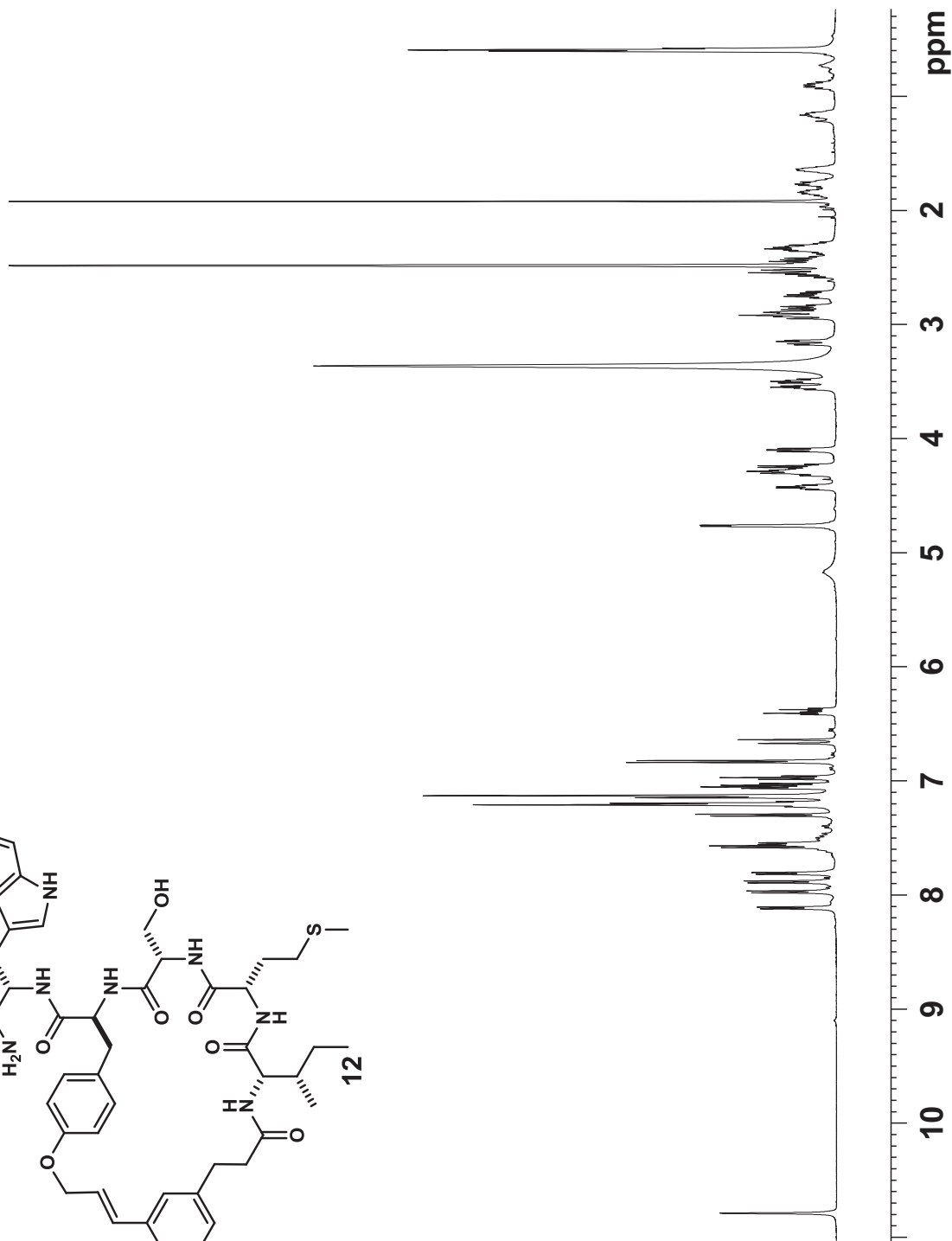
```

Current Data Parameters
NAME          KL-4-57
EXPNO         1
PROCNO        1

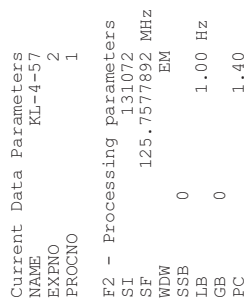
F2 - Acquisition Parameters
Date_         20111019
Time_         19.25
INSTRUM       av500
PROBHD        5 mm DCH 13C-1
PULPROG       zg30
TD            65536
SOLVENT       DMSO
NS            8
DS            0
SWH           10000.000 Hz
FIDRES        0.152588 Hz
AQ            3.2767999 sec
RG            20.17
DW            50.000 usec
DE            10.00 usec
TE            301.0 K
D1            2.00000000 sec
TD0           1

===== CHANNEL f1 =====
NUC1          1H
P1            10.00 usec
PLW1          13.50000000 W
SFO1          500.1330008 MHz

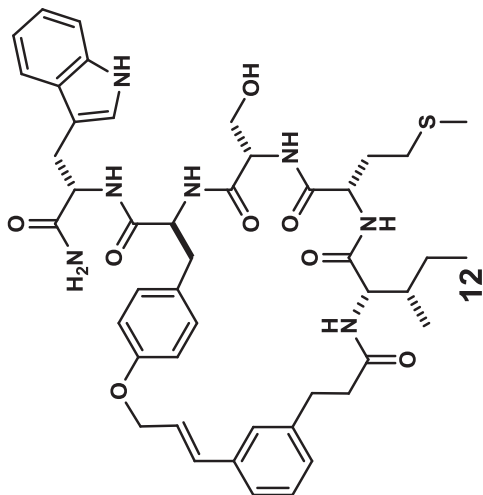
F2 - Processing parameters
SI            65536
SF            500.1300146 MHz
WDW           EM
SSB           0
LB            0.30 Hz
GB            0
PC            1.00
  
```



Chemical structure of compound 12, a macrocyclic peptide derivative. The structure features a 12-membered ring with an indole side chain, a hydroxymethyl group, a methylthiomethyl group, and a long side chain containing a trans-vinyl ether and a terminal phenyl group. The number 12 is shown in a large, bold font.



Cyclic-Ile-Met-Ser-Tyr-Trp (12):



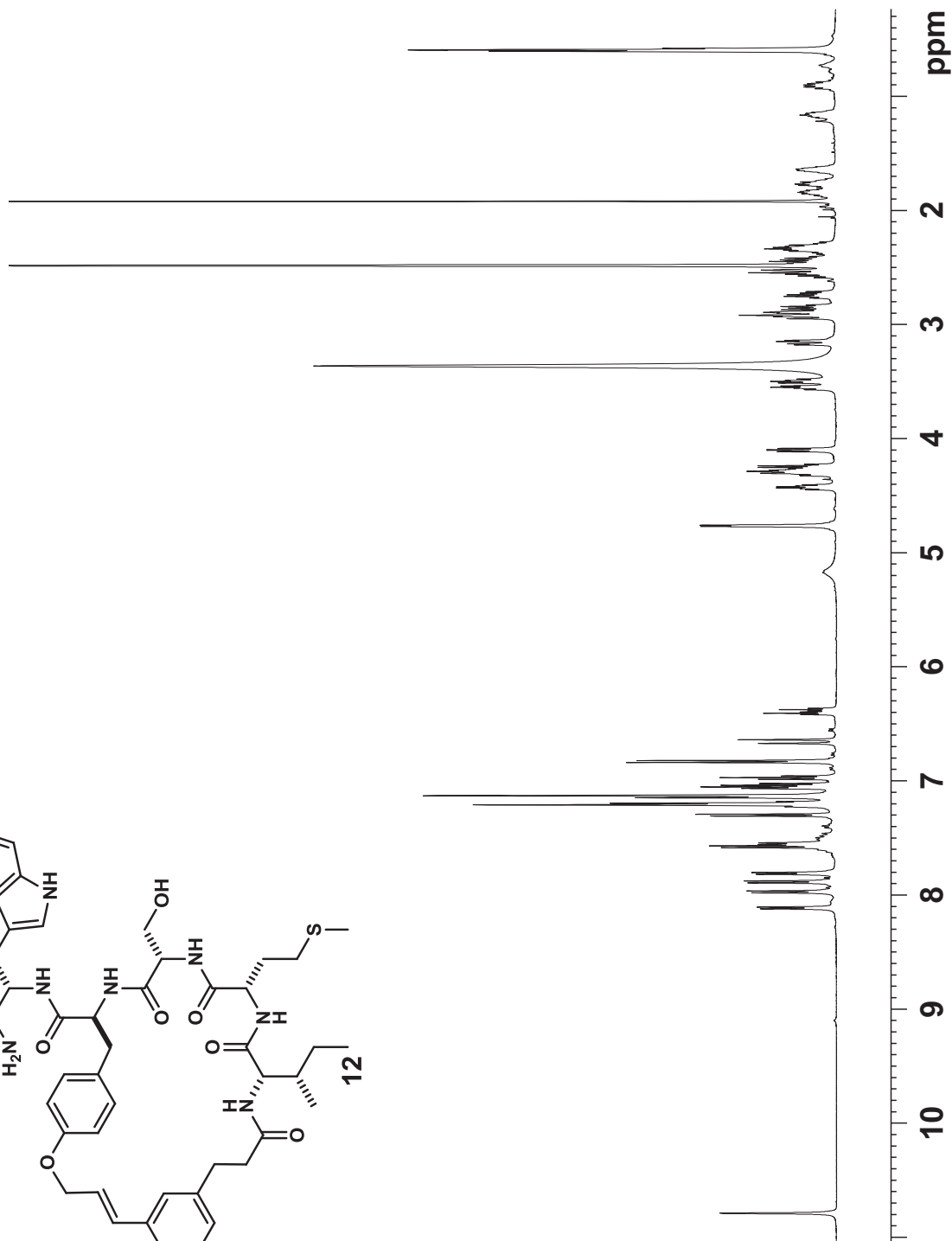
```

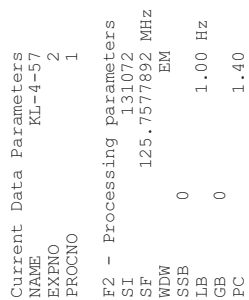
Current Data Parameters
NAME          KL-4-57
EXPNO         1
PROCNO        1

F2 - Acquisition Parameters
Date_         20111019
Time_         19.25
INSTRUM       av500
PROBHD        5 mm DCH 13C-1
PULPROG       zg30
TD            65536
SOLVENT       DMSO
NS            8
DS            0
SWH           10000.000 Hz
FIDRES        0.152588 Hz
AQ            3.2767999 sec
RG            20.17
DW            50.000 usec
DE            10.00 usec
TE            301.0 K
D1            2.00000000 sec
TD0           1

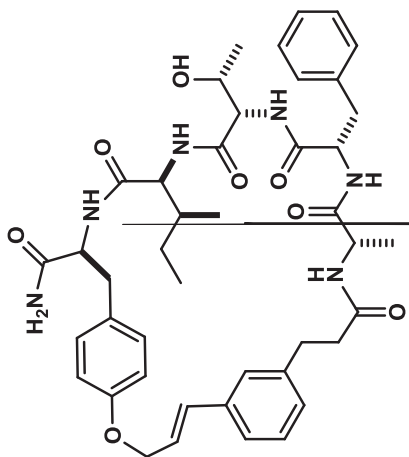
===== CHANNEL f1 =====
NUC1          1H
P1            10.00 usec
PLW1          13.50000000 W
SFO1          500.1330008 MHz

F2 - Processing parameters
SI            65536
SF            500.1300146 MHz
WDW           EM
SSB           0
LB            0.30 Hz
GB            0
PC            1.00
  
```



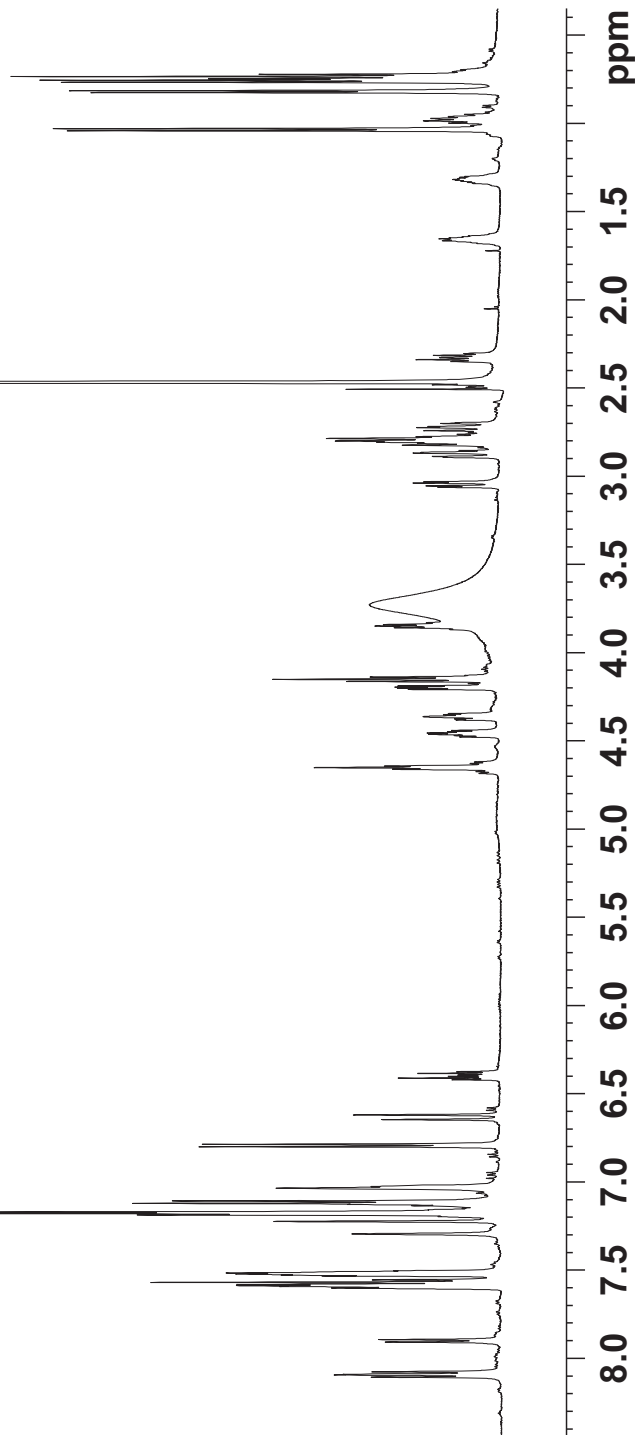


Cyclic- Ala-Phe-Thr-Ile-Tyr (13):

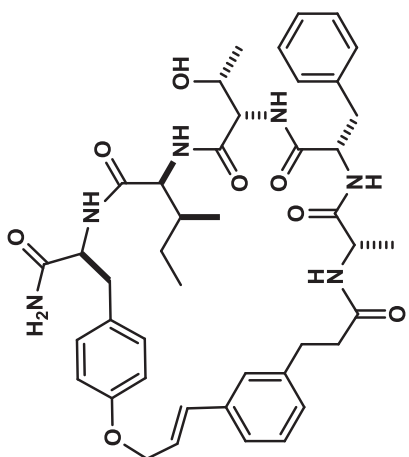


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Current Data Parameters
 NAME KL-4-48
 EXPNO 1
 PROCNO 1
 F2 - Acquisition Parameters
 Date_ 20111007
 Time_ 10.20
 INSTRUM av600
 PROBHD 5 mm TBI5
 PULPROG zg30
 TD 65536
 SOLVENT DMSO
 NS 8
 DS 0
 SWH 12376.237 Hz
 FIDRES 0.188846 Hz
 AQ 2.6476543 sec
 RG 181
 DW 40.400 usec
 DE 6.50 usec
 TE 295.8 K
 D1 2.0000000 sec
 TD0 1
 ===== CHANNEL f1 =====
 NUC1 1H
 P1 9.10 usec
 PL1 -2.00 dB
 PL1W 39.81071854 W
 SFO1 600.136008 MHz
 F2 - Processing parameters
 SI 65536
 SF 600.1300273 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00

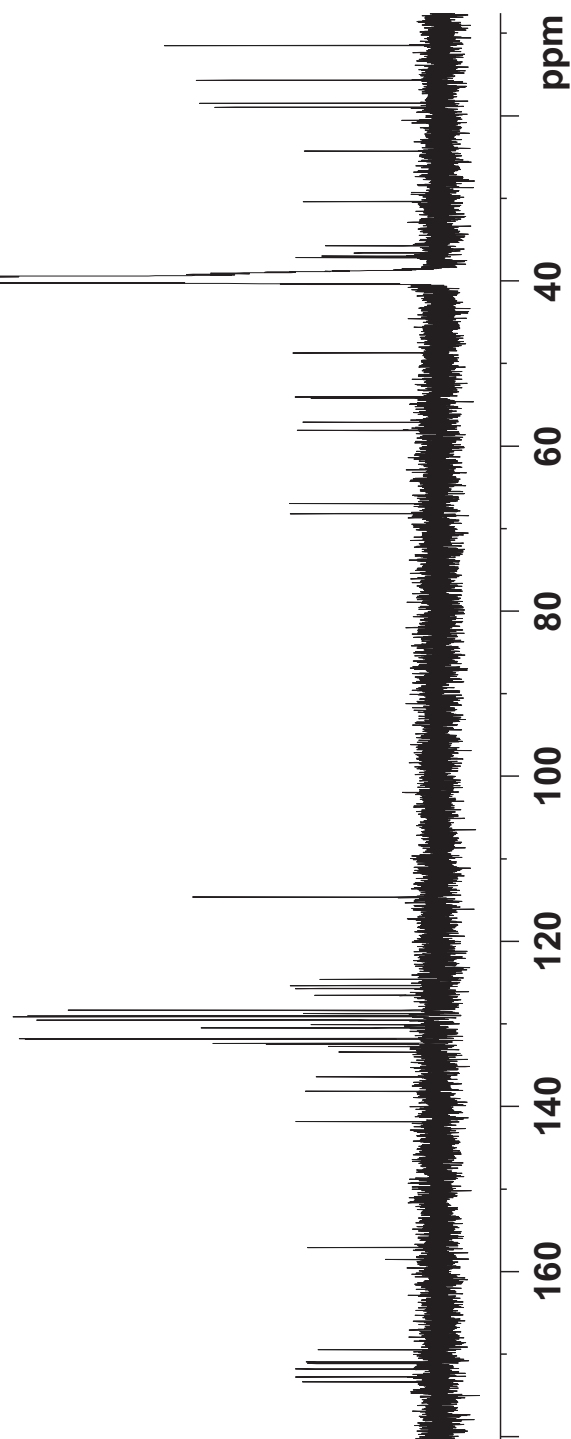


Cyclic- Ala-Phe-Thr-Ile-Tyr (13):

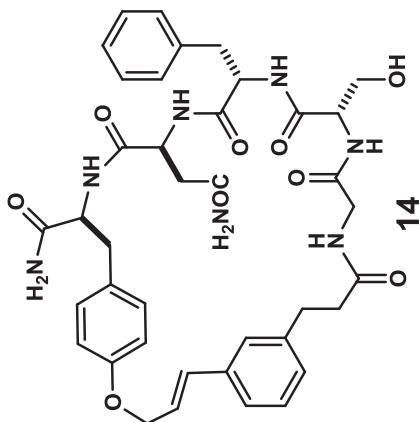


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Current Data Parameters
NAME KL-4-48
EXPNO 3
PROCNO 1
F2 - Processing parameters
SI 65536
SF 150.9028319 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40



Cyclic-Gly-Ser-Phe-Asn-Tyr (14):



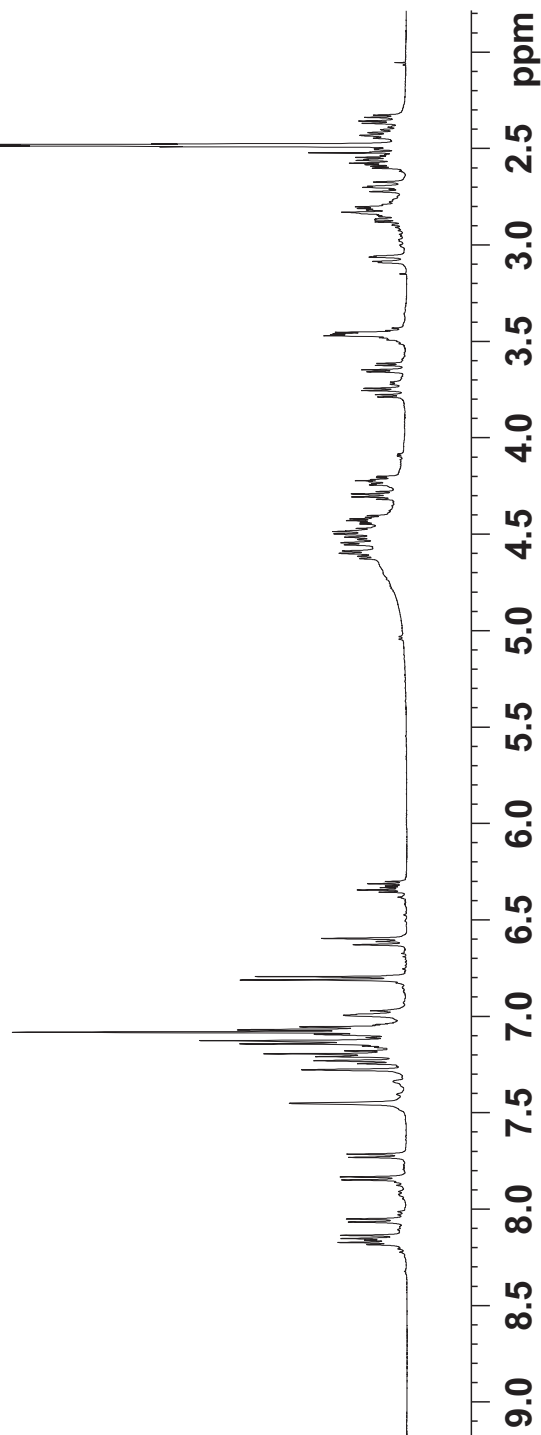
```

Current Data Parameters
NAME      KL-4-58
EXPNO     1
PROCNO    1

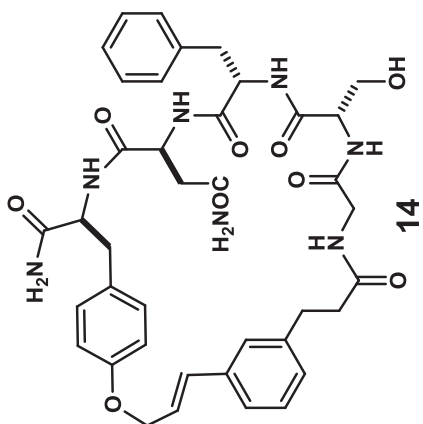
F2 - Acquisition Parameters
Date_     20111019
Time      19.11
INSTRUM   av500
PROBHD    5 mm DCH 13C-1
PULPROG   zg30
TD         65536
SOLVENT    DMSO
NS         4
DS         0
SWH        10000.000 Hz
FIDRES     0.152588 Hz
AQ         3.2767999 sec
RG         60.32
DW         50.000 usec
DE         10.00 usec
TE         301.0 K
D1         2.00000000 sec
TD0        1

===== CHANNEL f1 =====
NUC1       1H
P1         10.00 usec
PLW1       13.50000000 W
SFO1       500.1330008 MHz

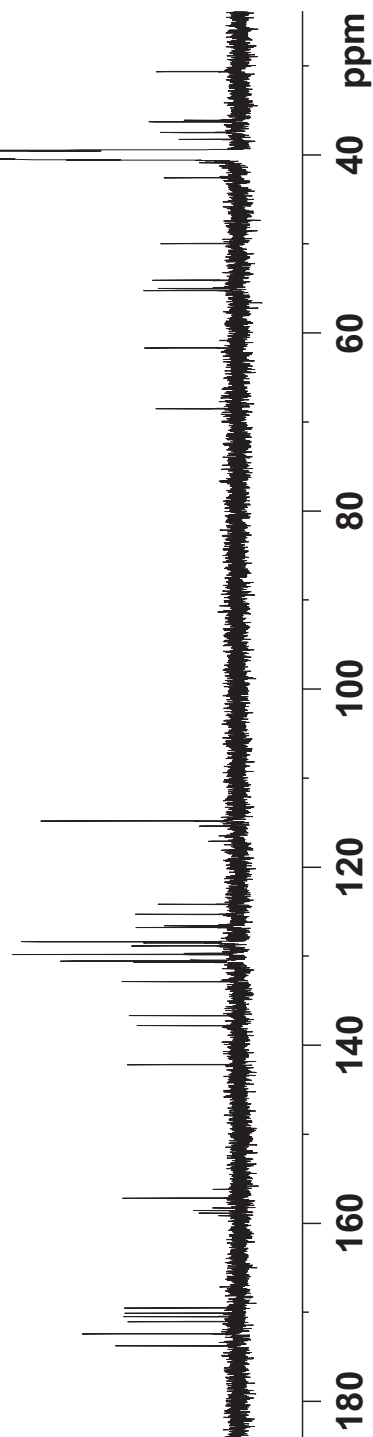
F2 - Processing parameters
SI         65536
SF         500.1300146 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00
  
```



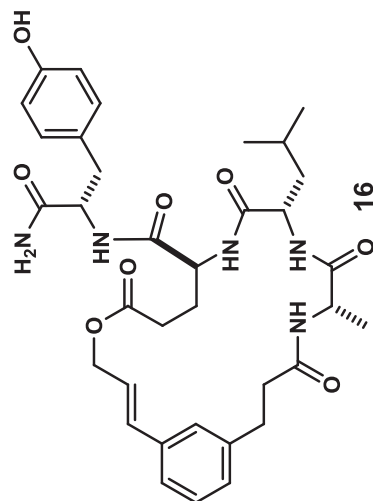
Cyclic-Gly-Ser-Phe-Asn-Tyr (14):



Current Data Parameters
NAME KL-4-58
EXPNO 2
PROCNO 1
F2 - Processing parameters
SI 131072
SF 125.7577892 MHz
WDW 0 EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40



Cyclic-Ala-Leu-Glu-Tyr (16):



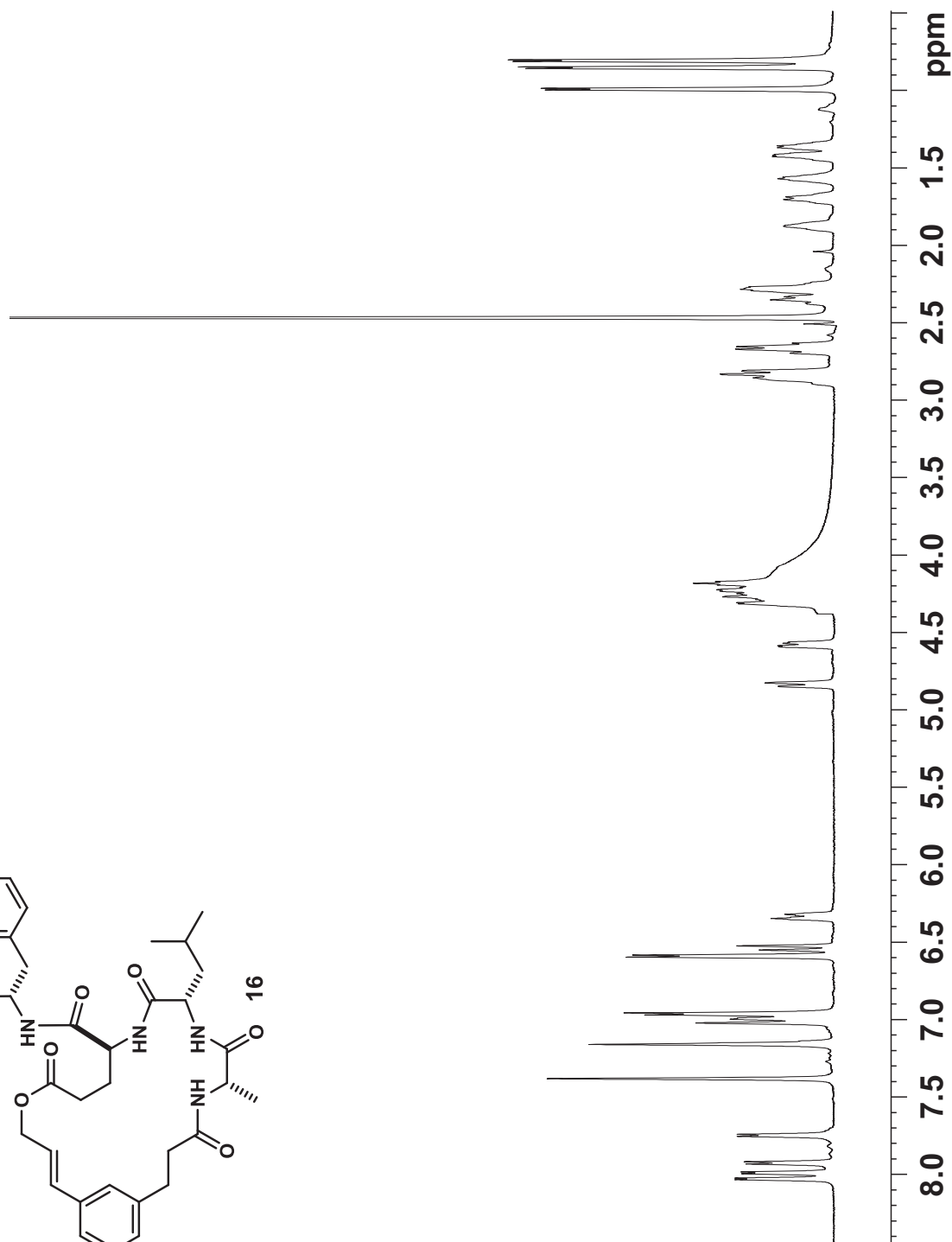
```

Current Data Parameters
NAME      KL-4-50_f92
EXPNO     1
PROCNO    1

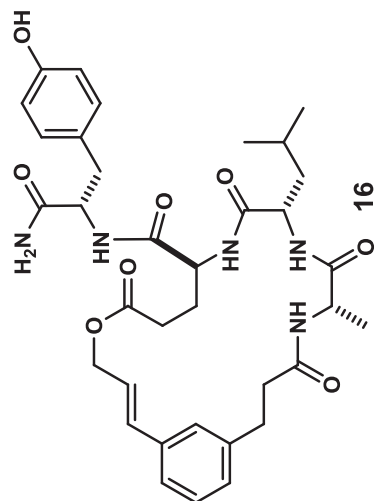
F2 - Acquisition Parameters
Date_     20111008
Time      19.54
INSTRUM   av600
PROBHD    5 mm TBI5
PULPROG   zg30
TD         65536
SOLVENT    DMSO
NS         8
DS         0
SWH        12376.237 Hz
FIDRES     0.188846 Hz
AQ         2.6476543 sec
RG         181
DW         40.400 usec
DE         6.50 usec
TE         295.7 K
D1         2.0000000 sec
TD0        1

===== CHANNEL f1 =====
NUC1       1H
P1         9.10 usec
PL1        -2.00 dB
PL1W       39.81071854 W
SFO1       600.1336008 MHz

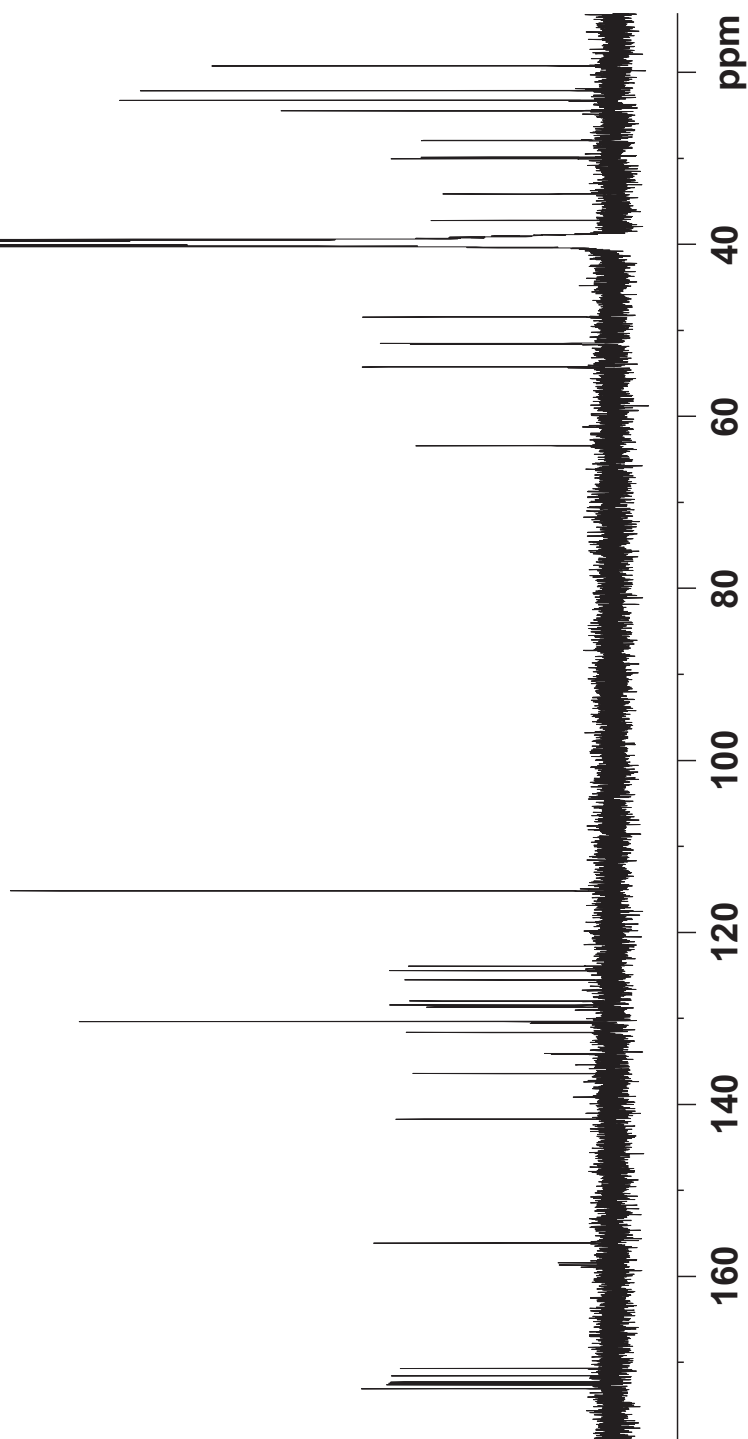
F2 - Processing parameters
SI         65536
SF         600.1300273 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00
    
```

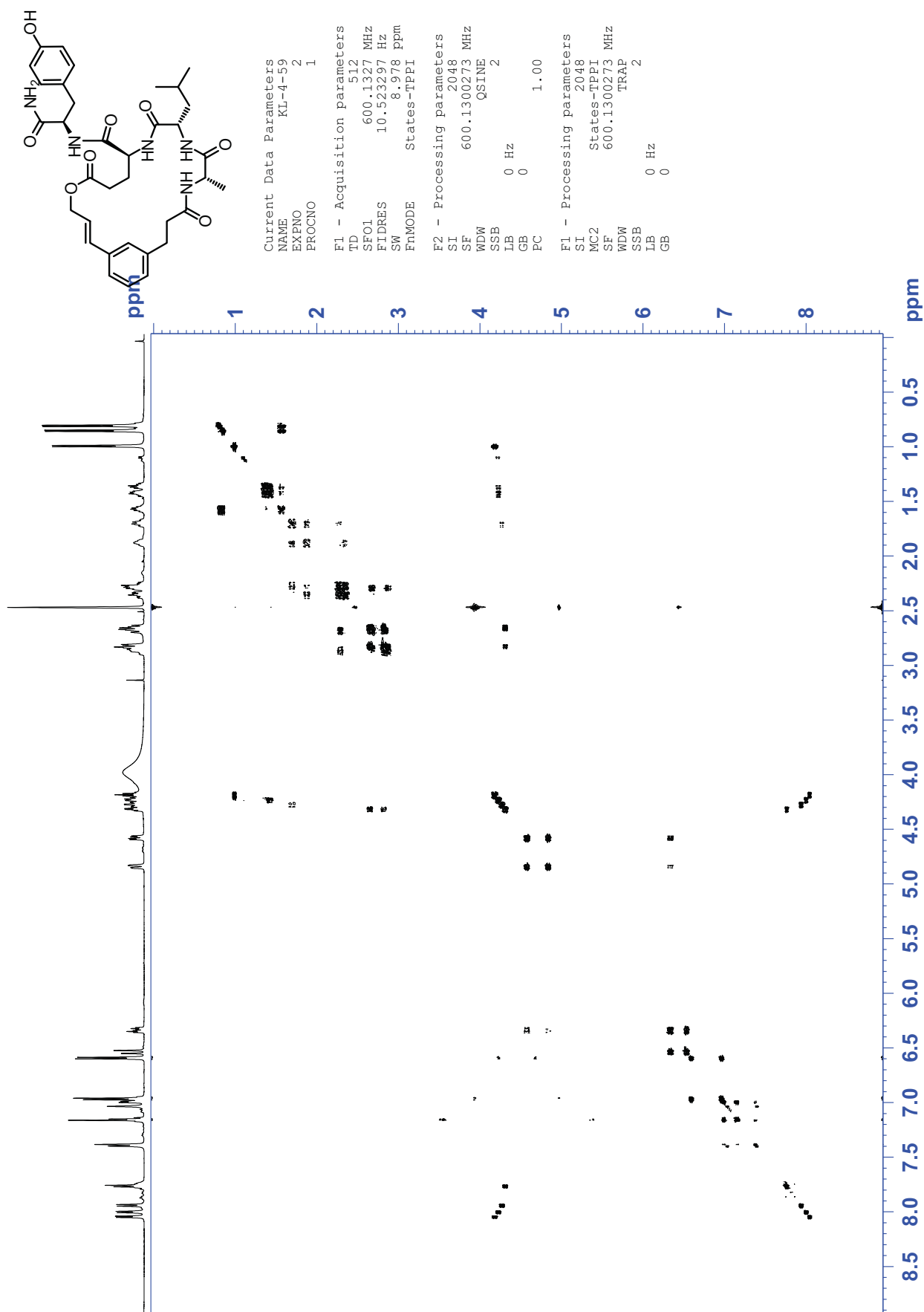


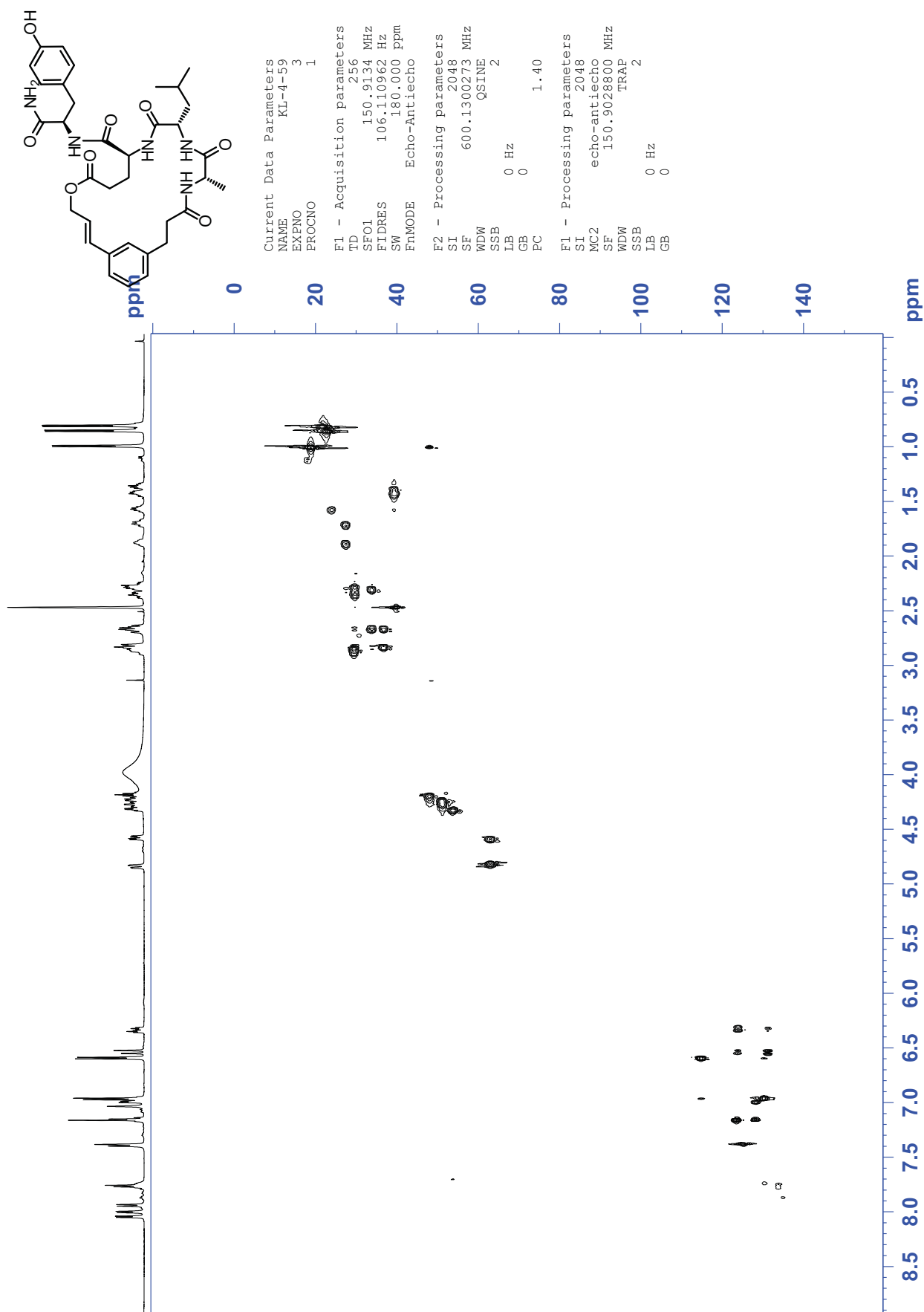
Cyclic-Ala-Leu-Glu-Tyr (16):

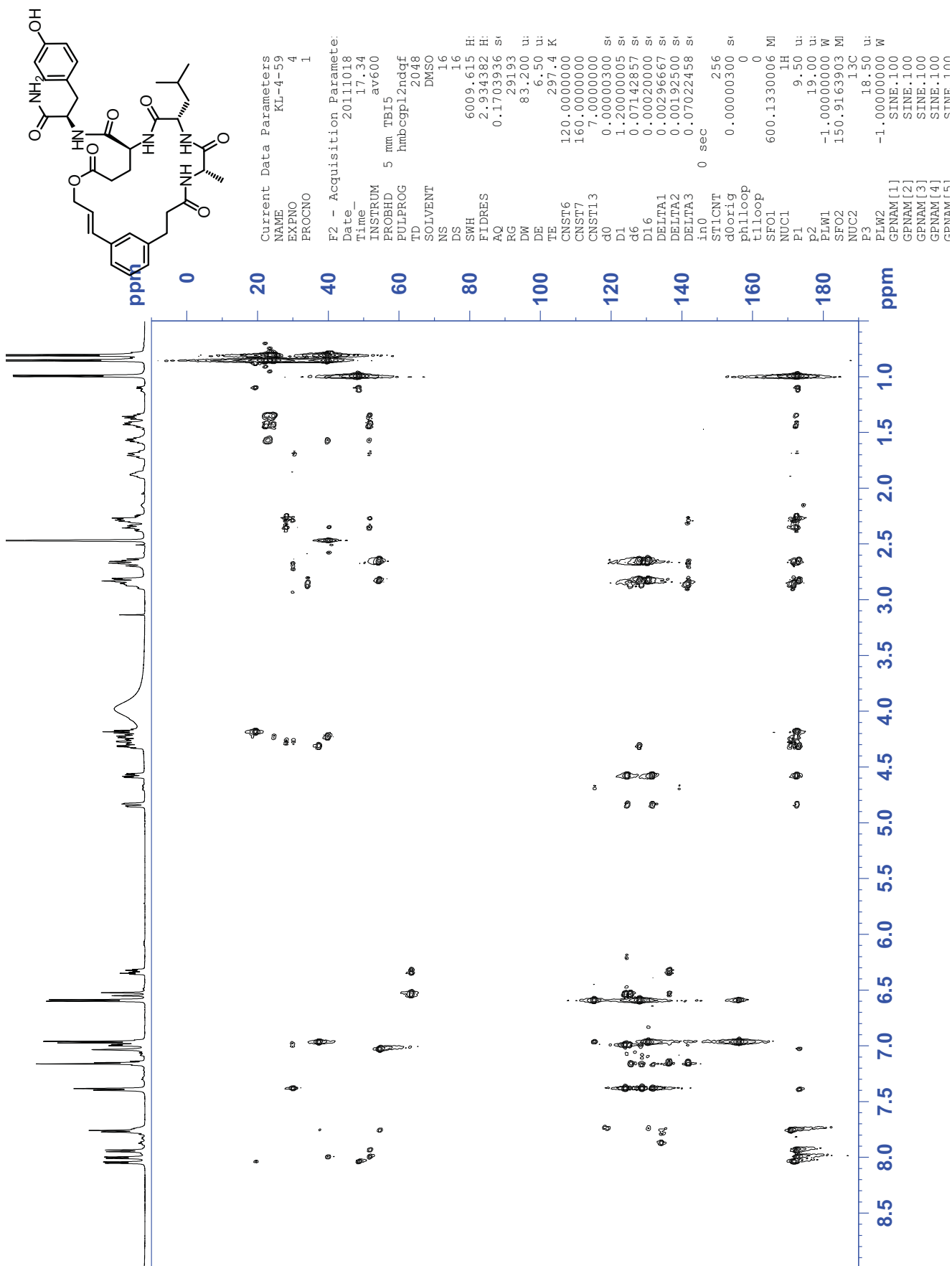


Current Data Parameters
NAME KL-4-59
EXPNO 7
PROCNO 1
F2 - Processing parameters
SI 65536
SF 150.9028319 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

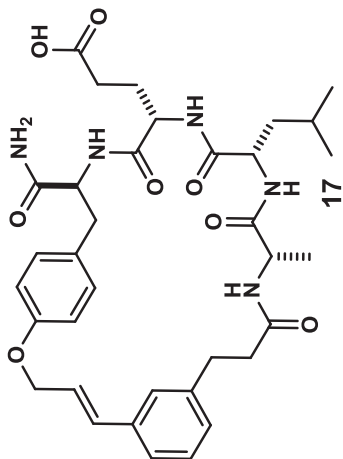








Cyclic-Ala-Leu-Glu-Tyr (17):



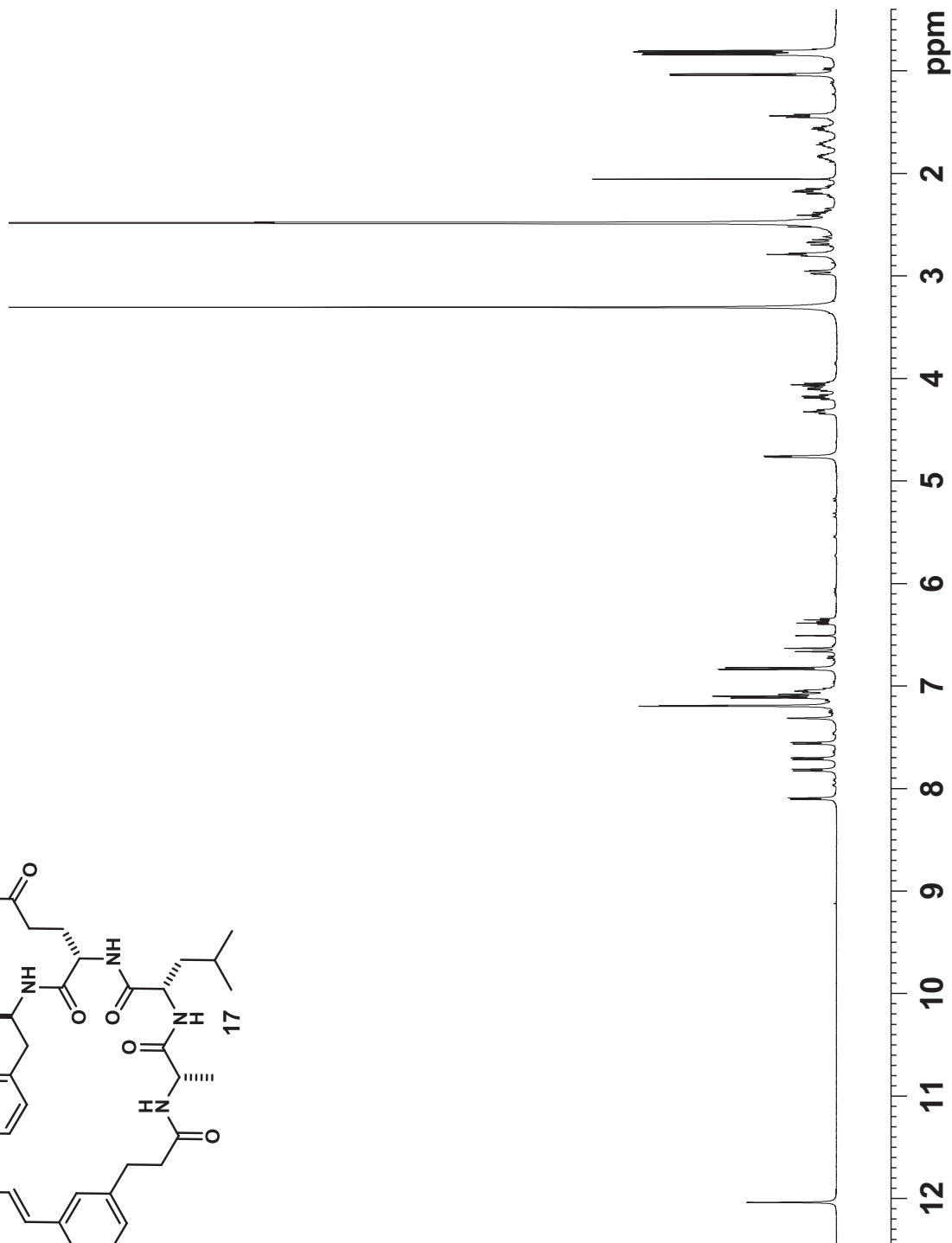
```

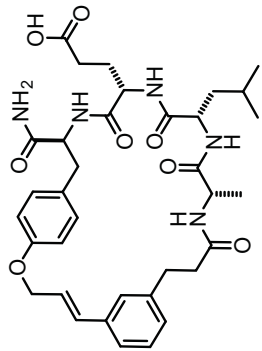
Current Data Parameters
NAME      KL-5-149_F5_AV500
EXPNO     1
PROCNO    1

F2 - Acquisition Parameters
Date_     20130326
Time_     17.19
INSTRUM   av500
PROBHD    5 mm DCH 13C-1
PULPROG   zg30
TD        65536
SOLVENT   DMSO
NS         8
DS         0
SWH        10000.000 Hz
FIDRES     0.152588 Hz
AQ         3.2767999 sec
RG         14.01
DW         50.000 usec
DE         10.00 usec
TE         298.0 K
D1         2.00000000 sec
TD0        1

===== CHANNEL f1 =====
SFO1      500.130008 MHz
NUC1       1H
P1         10.00 usec
PLW1      13.50000000 W

F2 - Processing parameters
SI         65536
SF         500.1300146 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00
    
```





Current Data Parameters	
NAME	KL-5-149_F5_AV501
EXPNO	3
PROCNO	1

F2 - Acquisition Paramete:

Date_ 20130326

Time 17.21

INSTRUM	av500
PROBUD	F --- DCU 12C 1

PROBHD 5 mm DCH 13C-1
BIIT PROC 05/20/2006

PULPROG	cosygmfph
TD	4096

T.D	SOLVENT
4096	DMSO

SOLVENT	DMSO
NS	2

DS
N 85498.534 H:
SWH

FIDRES
1.342415 H:

AQ	0.3724629 s
0.3724629 s	0.3724629 s

RG	202.91
DW	00.033

DW	90.933	u:
DE	10.00	u:

DE	10.00	u:
TE	298.0	K

TH	298.0	K
D0	0.00007880	S

D0	0.00000000	s'
D1	2.00000000	s'

D13 0.00000400 S

D16	0.00020000	s'
-----	------------	----

```
IN0 0.00018180 s'
```

CHARTER	£1	-----
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```
===== CHANNEL f1 =====
SF01          500 1327507 M
```

SF01 500.1327507 M
NUC1 ¹H

NUCL
P1
IH
9.50 u:

P1	9.30	u:
P2	19.00	u:

PLW1	13.50000000	W
PLW2	13.50000000	W

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```
===== GRADIENT CHANNEL =====
```

GPNAM[1]	SMSQ10.100
GPNAM[2]	SMSQ10.100
GPNAM[3]	SMSQ10.100
GPNAM[4]	SMSQ10.100
GPNAM[5]	SMSQ10.100
GPNAM[6]	SMSQ10.100
GPNAM[7]	SMSQ10.100
GPNAM[8]	SMSQ10.100
GPNAM[9]	SMSQ10.100
GPNAM[10]	SMSQ10.100
GPNAM[11]	SMSQ10.100
GPNAM[12]	SMSQ10.100
GPNAM[13]	SMSQ10.100
GPNAM[14]	SMSQ10.100
GPNAM[15]	SMSQ10.100
GPNAM[16]	SMSQ10.100
GPNAM[17]	SMSQ10.100
GPNAM[18]	SMSQ10.100
GPNAM[19]	SMSQ10.100
GPNAM[20]	SMSQ10.100
GPNAM[21]	SMSQ10.100
GPNAM[22]	SMSQ10.100
GPNAM[23]	SMSQ10.100
GPNAM[24]	SMSQ10.100
GPNAM[25]	SMSQ10.100
GPNAM[26]	SMSQ10.100
GPNAM[27]	SMSQ10.100
GPNAM[28]	SMSQ10.100
GPNAM[29]	SMSQ10.100
GPNAM[30]	SMSQ10.100
GPNAM[31]	SMSQ10.100
GPNAM[32]	SMSQ10.100
GPNAM[33]	SMSQ10.100
GPNAM[34]	SMSQ10.100
GPNAM[35]	SMSQ10.100
GPNAM[36]	SMSQ10.100
GPNAM[37]	SMSQ10.100
GPNAM[38]	SMSQ10.100
GPNAM[39]	SMSQ10.100
GPNAM[40]	SMSQ10.100
GPNAM[41]	SMSQ10.100
GPNAM[42]	SMSQ10.100
GPNAM[43]	SMSQ10.100
GPNAM[44]	SMSQ10.100
GPNAM[45]	SMSQ10.100
GPNAM[46]	SMSQ10.100
GPNAM[47]	SMSQ10.100
GPNAM[48]	SMSQ10.100
GPNAM[49]	SMSQ10.100
GPNAM[50]	SMSQ10.100
GPNAM[51]	SMSQ10.100
GPNAM[52]	SMSQ10.100
GPNAM[53]	SMSQ10.100
GPNAM[54]	SMSQ10.100
GPNAM[55]	SMSQ10.100
GPNAM[56]	SMSQ10.100
GPNAM[57]	SMSQ10.100
GPNAM[58]	SMSQ10.100
GPNAM[59]	SMSQ10.100
GPNAM[60]	SMSQ10.100
GPNAM[61]	SMSQ10.100
GPNAM[62]	SMSQ10.100
GPNAM[63]	SMSQ10.100
GPNAM[64]	SMSQ10.100
GPNAM[65]	SMSQ10.100
GPNAM[66]	SMSQ10.100
GPNAM[67]	SMSQ10.100
GPNAM[68]	SMSQ10.100
GPNAM[69]	SMSQ10.100
GPNAM[70]	SMSQ10.100
GPNAM[71]	SMSQ10.100
GPNAM[72]	SMSQ10.100
GPNAM[73]	SMSQ10.100
GPNAM[74]	SMSQ10.100
GPNAM[75]	SMSQ10.100
GPNAM[76]	SMSQ10.100
GPNAM[77]	SMSQ10.100
GPNAM[78]	SMSQ10.100
GPNAM[79]	SMSQ10.100
GPNAM[80]	SMSQ10.100
GPNAM[81]	SMSQ10.100
GPNAM[82]	SMSQ10.100
GPNAM[83]	SMSQ10.100
GPNAM[84]	SMSQ10.100
GPNAM[85]	SMSQ10.100
GPNAM[86]	SMSQ10.100
GPNAM[87]	SMSQ10.100
GPNAM[88]	SMSQ10.100
GPNAM[89]	SMSQ10.100
GPNAM[90]	SMSQ10.100
GPNAM[91]	SMSQ10.100
GPNAM[92]	SMSQ10.100
GPNAM[93]	SMSQ10.100
GPNAM[94]	SMSQ10.100
GPNAM[95]	SMSQ10.100
GPNAM[96]	SMSQ10.100
GPNAM[97]	SMSQ10.100
GPNAM[98]	SMSQ10.100
GPNAM[99]	SMSQ10.100
GPNAM[100]	SMSQ10.100

```

GPNAM[2]      SMSQ10.100
CD71          10.00

```

GPZ1	10.00	0%
GPZ2	20.00	0%

GPZ2	20.00	20
P16	1000.00	11

9TH 00.000T

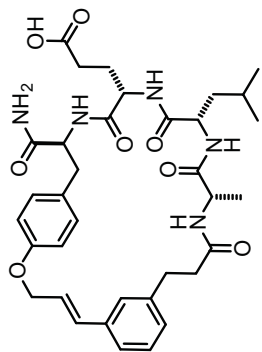
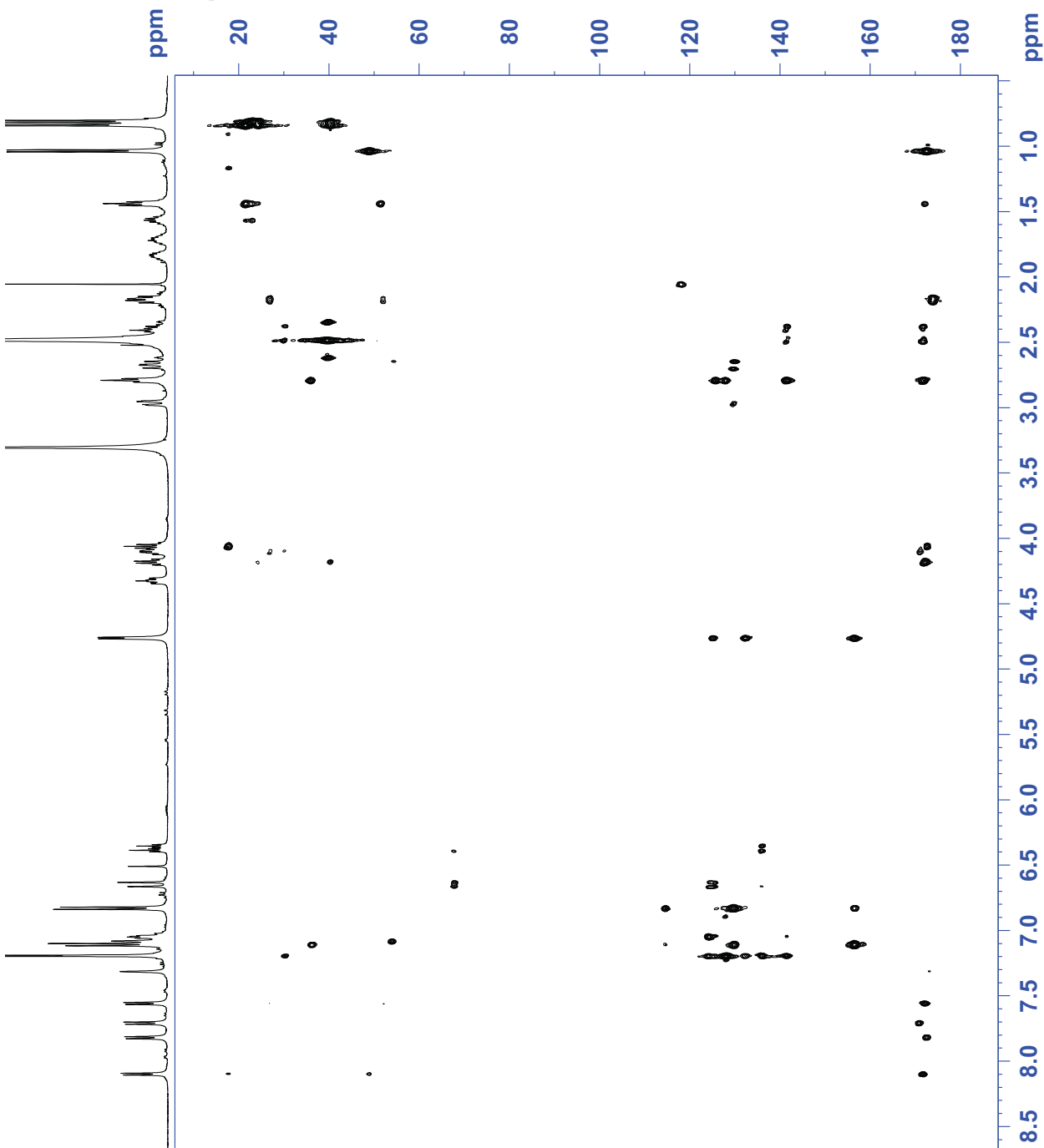
F1 - Acquisition paramete:

TD	256
Acquisition Parameters:	

500.1328 MI
SF01

FIDRES 21.486525 H:

MS 10.998 pl



Current Data Parameters
 NAME KL-S-149_F5_AV501
 EXPNO 5
 PROCNO 1

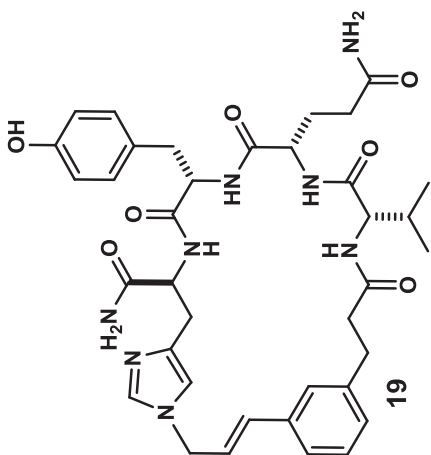
F2 - Acquisition Parameters
 Date_ 20130326
 Time_ 17.57
 INSTRUM av500
 PROBHD 5 mm DCH 13C-1
 PULPROG hmbcpg12ndqf
 TD 2048
 SOLVENT DMSO
 NS 2
 DS 16
 SWH 6009.615 H:
 FIDRES 2.934382 H:
 AQ 0.1703936 s:
 RG 202.91
 DW 83.200 u:
 DE 10.00 u:
 TE 298.0 K
 CNST6 120.0000000
 CNST7 160.0000000
 CNST13 7.0000000
 D0 0.00000300 s:
 D1 1.50000000 s:
 D6 0.07142857 s:
 D16 0.00020000 s:
 IN0 0.00001990 s:

===== CHANNEL f1 =====
 SFO1 500.1330008 M
 NUC1 1H
 P1 9.50 u:
 P2 19.00 u:
 PLW1 13.50000000 W

===== CHANNEL f2 =====
 SFO2 125.7703648 M
 NUC2 13C
 P3 9.63 u:
 PLW2 23.01399994 W

===== GRADIENT CHANNEL =====
 GPNAM[1] SMSQ10.100
 GPNAM[2] SMSQ10.100

Cyclic-Val-Gln-Tyr-His (19):



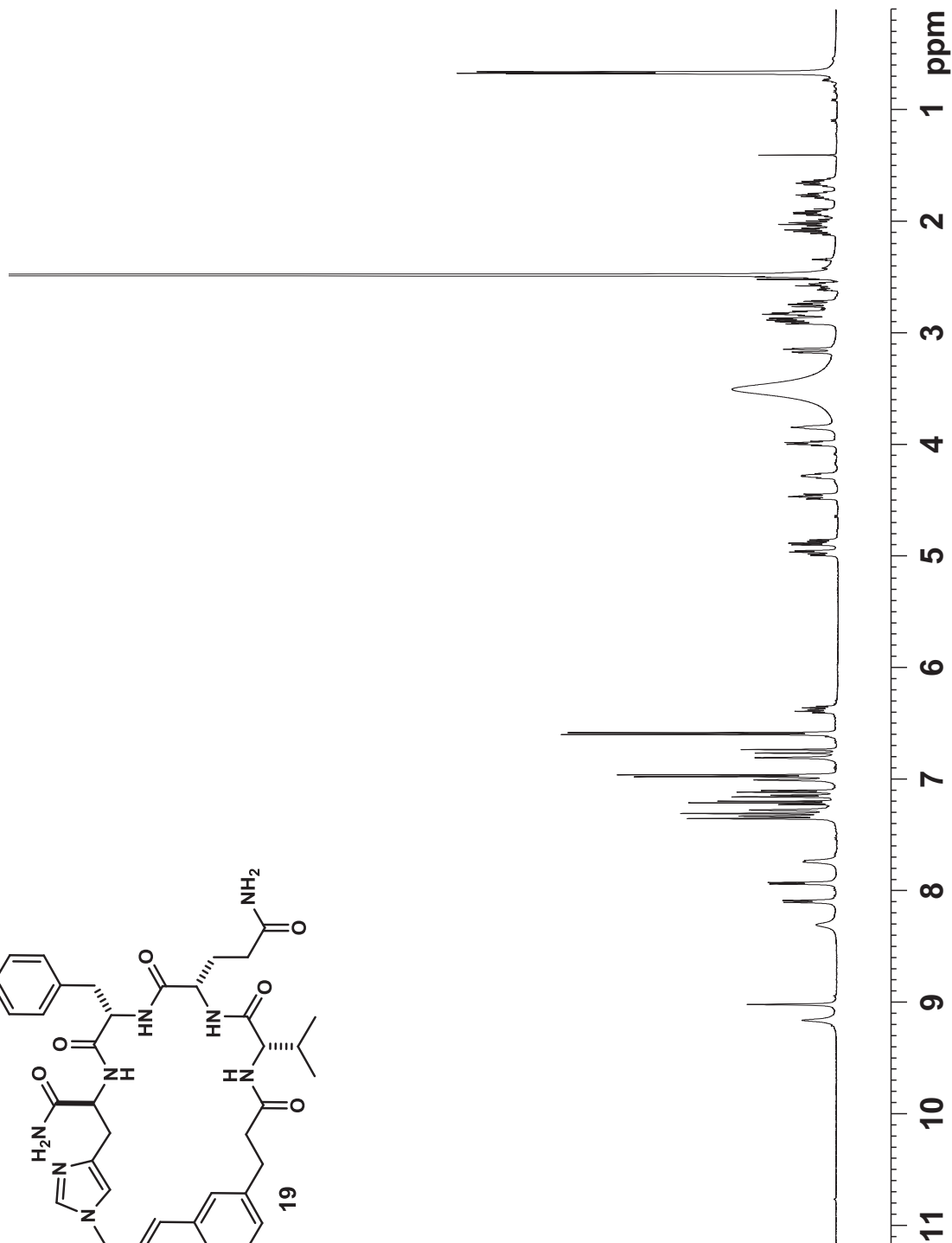
```

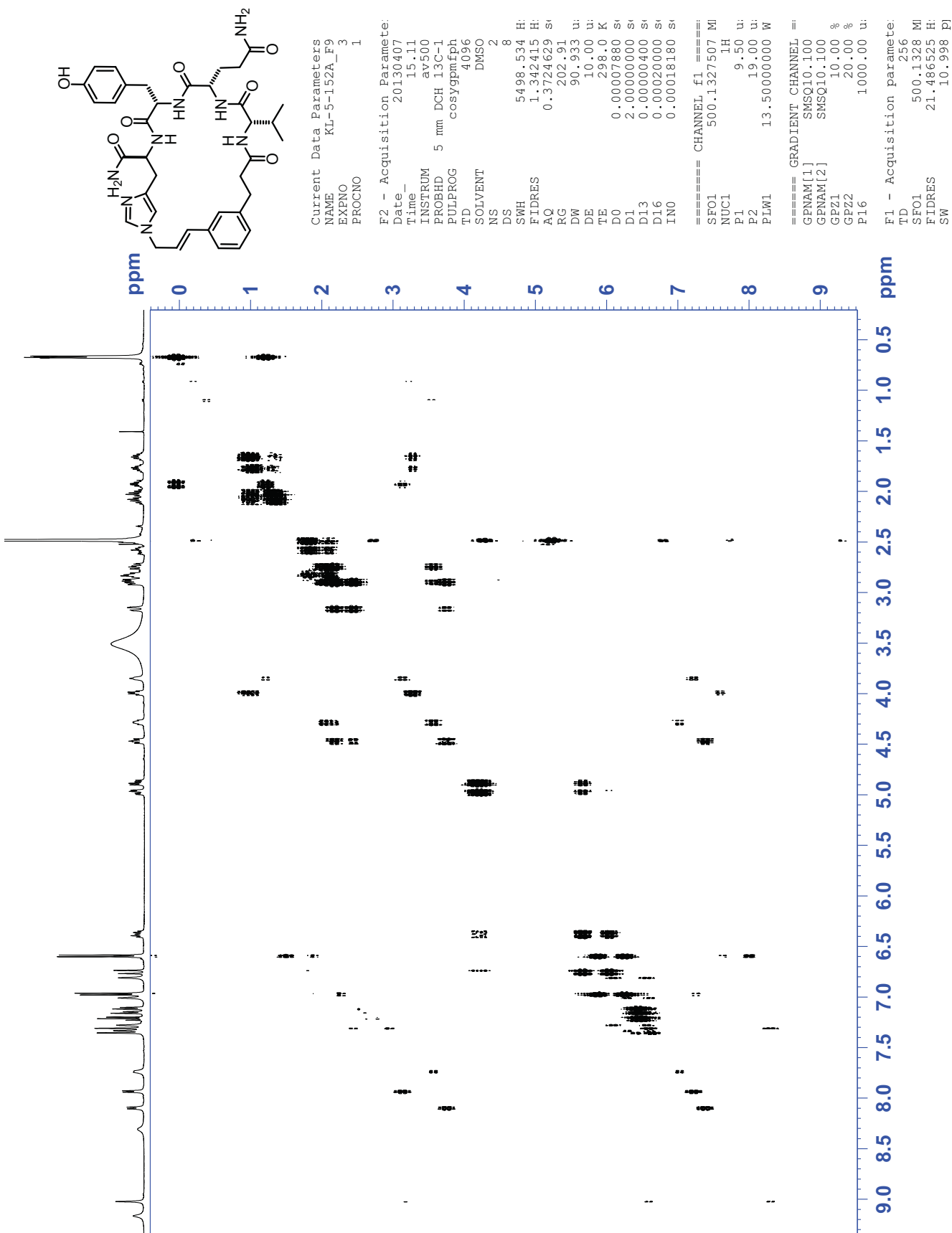
Current Data Parameters
NAME      KL-5-152A_F9
EXPNO     1
PROCNO    1

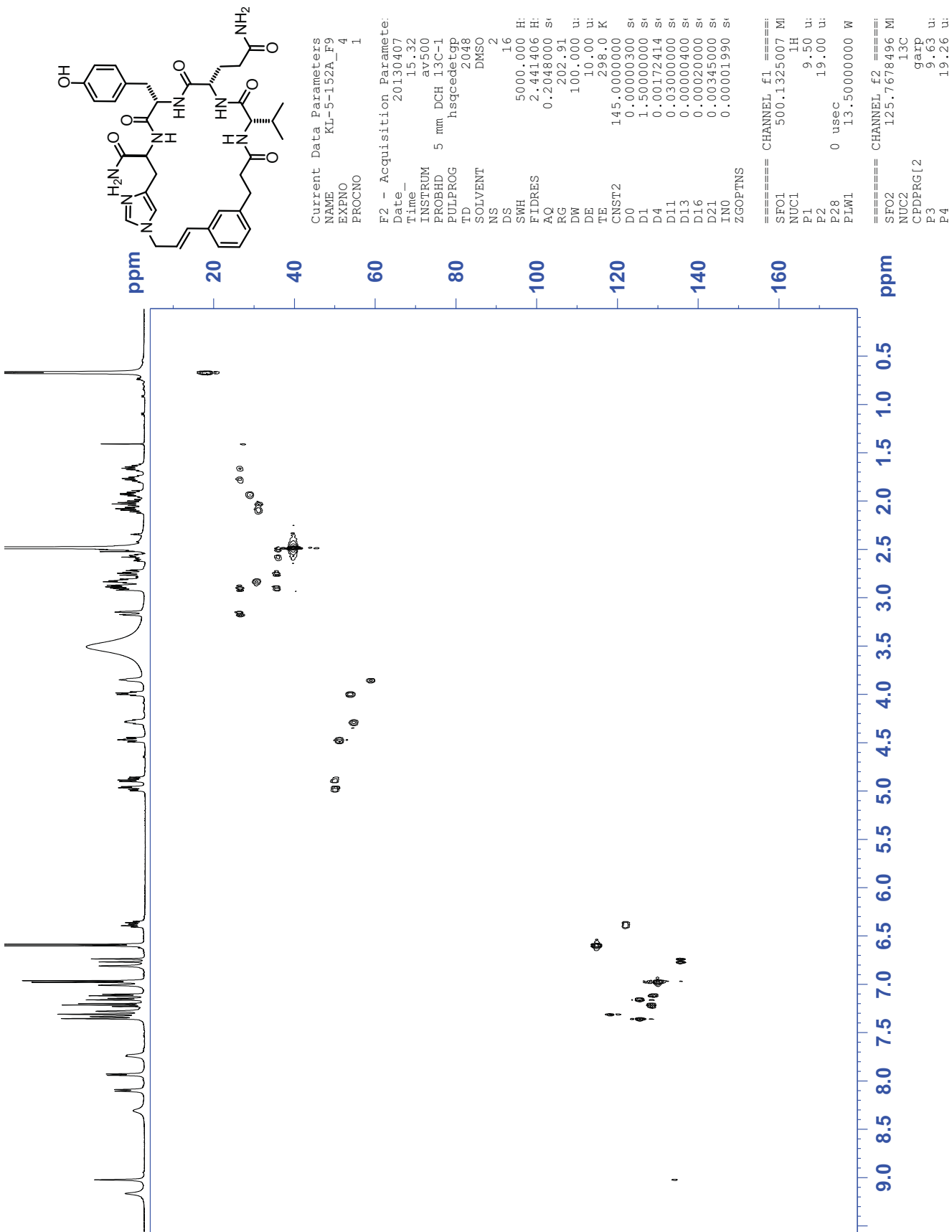
F2 - Acquisition Parameters
Date_     20130407
Time      15.08
INSTRUM   av500
PROBHD    5 mm DCH 13C-1
PULPROG   zg30
TD        65536
SOLVENT   DMSO
NS         8
DS         0
SWH        10000.000 Hz
FIDRES     0.152588 Hz
AQ         3.276799 sec
RG         11
DW         50.000 usec
DE         10.00 usec
TE         298.0 K
D1         2.0000000 sec
TD0        1

===== CHANNEL f1 =====
SFO1      500.130008 MHz
NUC1       1H
P1         10.00 usec
PLW1      13.5000000 W

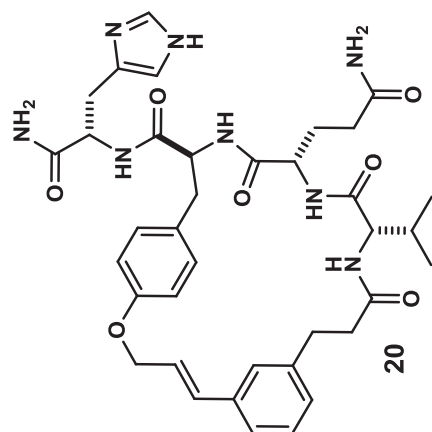
F2 - Processing parameters
SI         65536
SF         500.1300146 MHz
WDW        EM
SSB         0
LB         0.30 Hz
GB         0
PC         1.00
    
```







Cyclic-Val-Gln-Tyr-His (20):

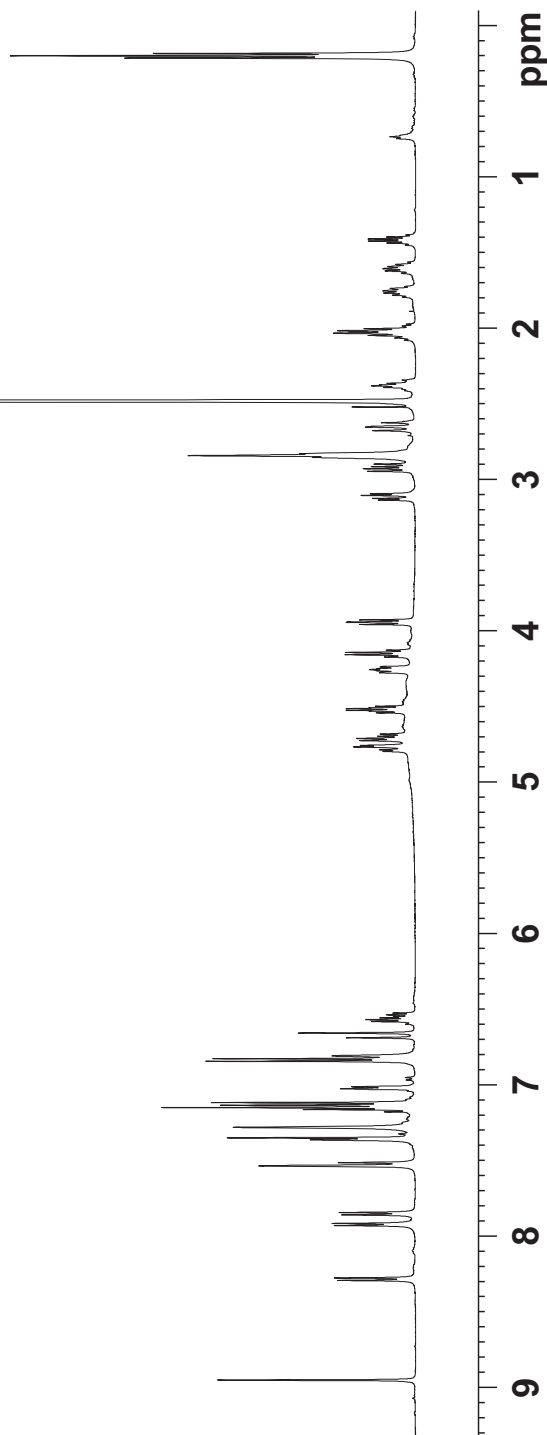


Current Data Parameters
NAME KL-5-159B
EXPNO 1
PROCNO 1

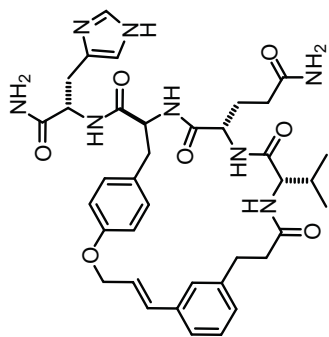
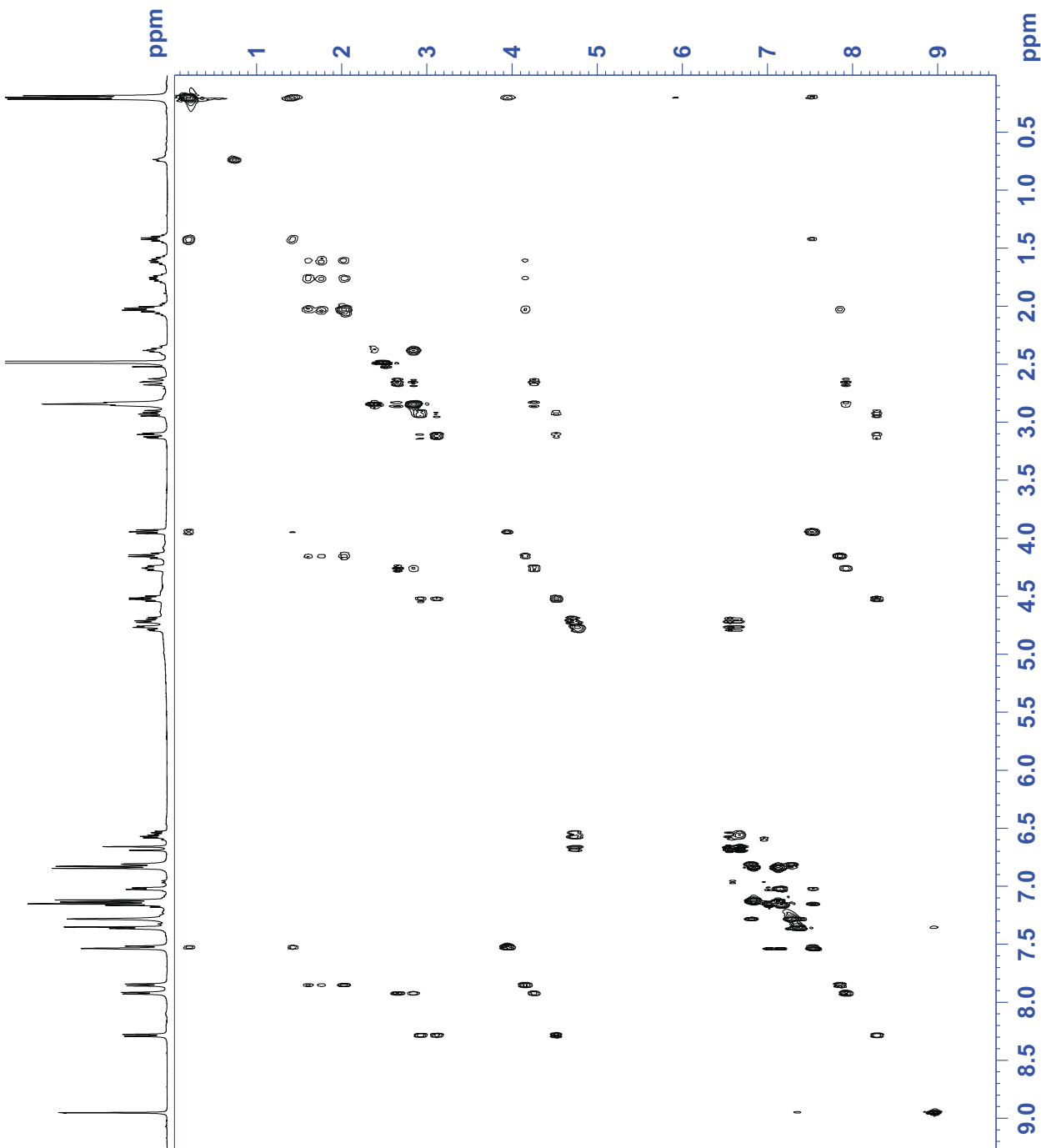
F2 - Acquisition Parameters
Date_ 20130416
Time_ 19.50
INSTRUM av500
PROBHD 5 mm DCH 13C-1
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 8
DS 0
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2767999 sec
RG 28.6
DW 50.000 usec
DE 10.00 usec
TE 298.0 K
D1 2.0000000 sec
TD0 1

===== CHANNEL f1 =====
SFO1 500.130008 MHz
NUC1 1H
P1 10.00 usec
PLW1 13.5000000 W

F2 - Processing parameters
SI 65536
SF 500.1300146 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



[illegible]



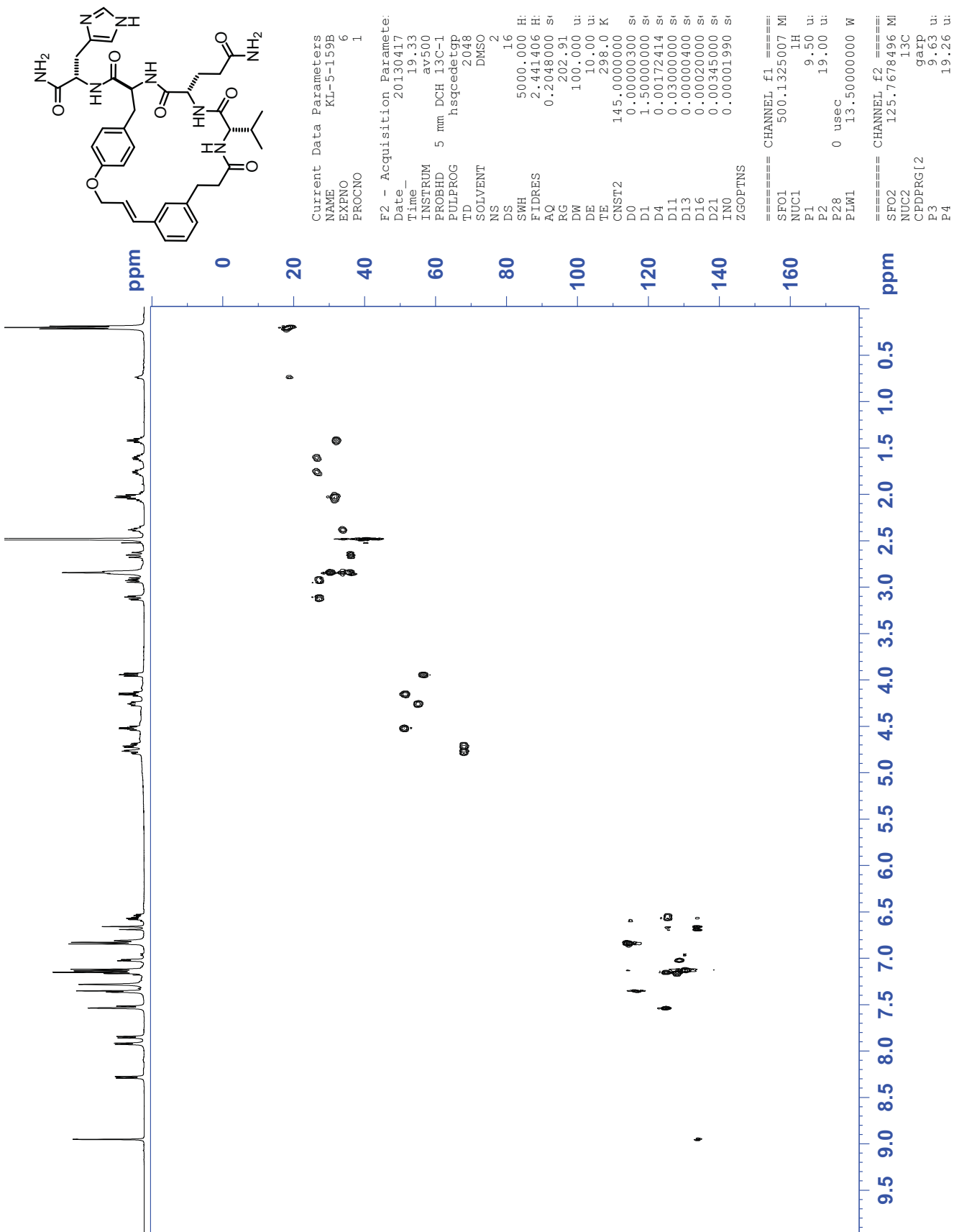
Current Data Parameters
 NAME KL-5-159B
 EXPNO 5
 PROCNO 1

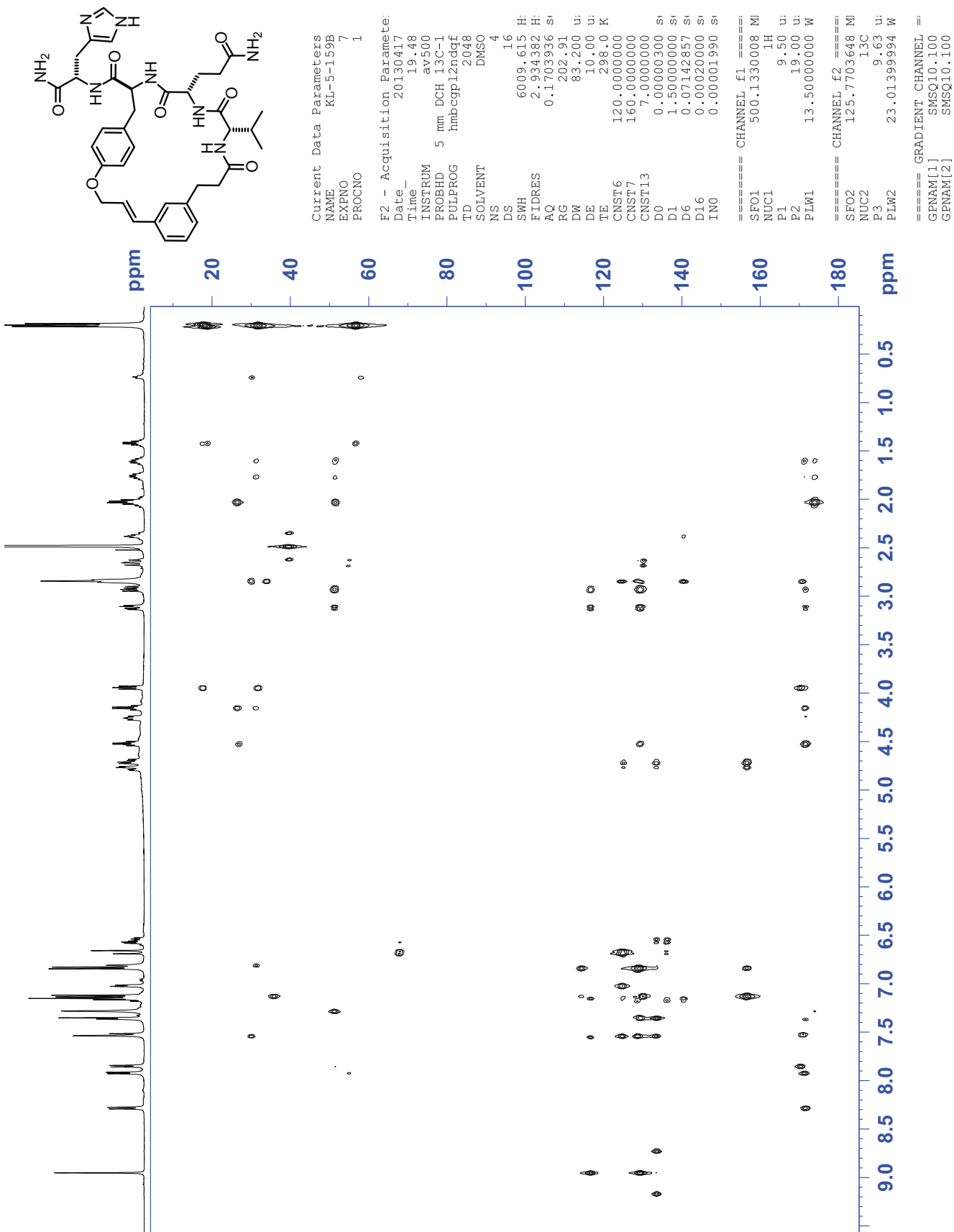
F2 - Acquisition Parameters:

Date_ 20130417
 Time_ 19.13
 INSTRUM av500
 PROBHD 5 mm DCH 13C-1
 PULPROG mlevetgp.js
 TD 2048
 SOLVENT DMSO
 NS 2
 DS 8
 SWH 6009.615 H:
 FIDRES 2.934382 H:
 AQ 0.1703936 s:
 RG 37.94
 DW 83.200 u:
 DE 10.00 u:
 TE 298.0 K
 D0 0.00000300 s:
 D1 2.00000000 s:
 D9 0.06000000 s:
 D11 0.03000000 s:
 D12 0.00002000 s:
 D16 0.00020000 s:
 INO 0.00016660 s:
 L1 24

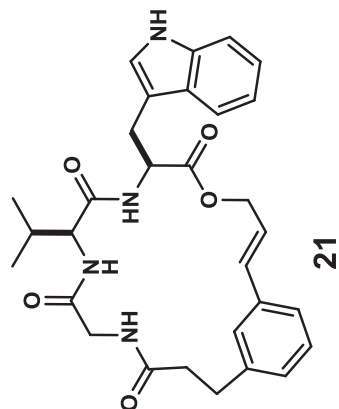
===== CHANNEL f1 =====
 SFO1 500.1330008 MHz
 NUC1 1H
 P1 9.50 u:
 P2 19.00 u:
 F5 26.68 u:
 P6 40.00 u:
 P7 80.00 u:
 PLW1 2500.00 u:
 PLW10 13.50000000 W
 PLW10 0.84375000 W

===== GRADIENT CHANNEL =====
 GPNAM[1] SINE.100
 GPNAM[2] SINE.100
 GPZ1 30.00 %





Cyclic-Gly-Val-Trp (21):

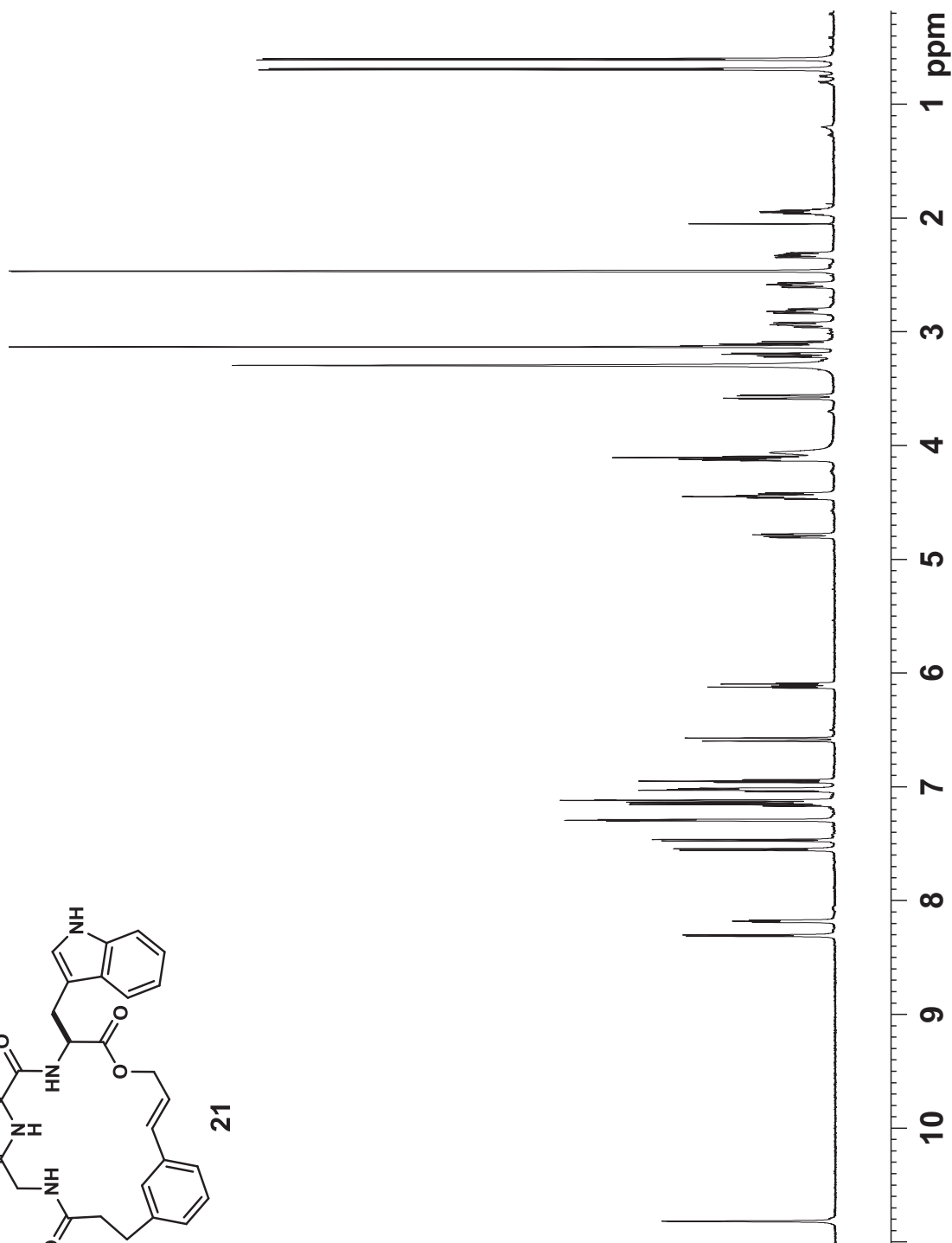


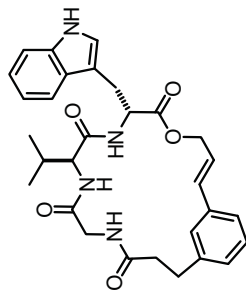
Current Data Parameters
NAME KL-4-189
EXPNO 3
PROCNO 1

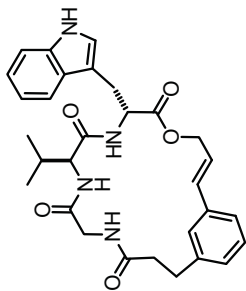
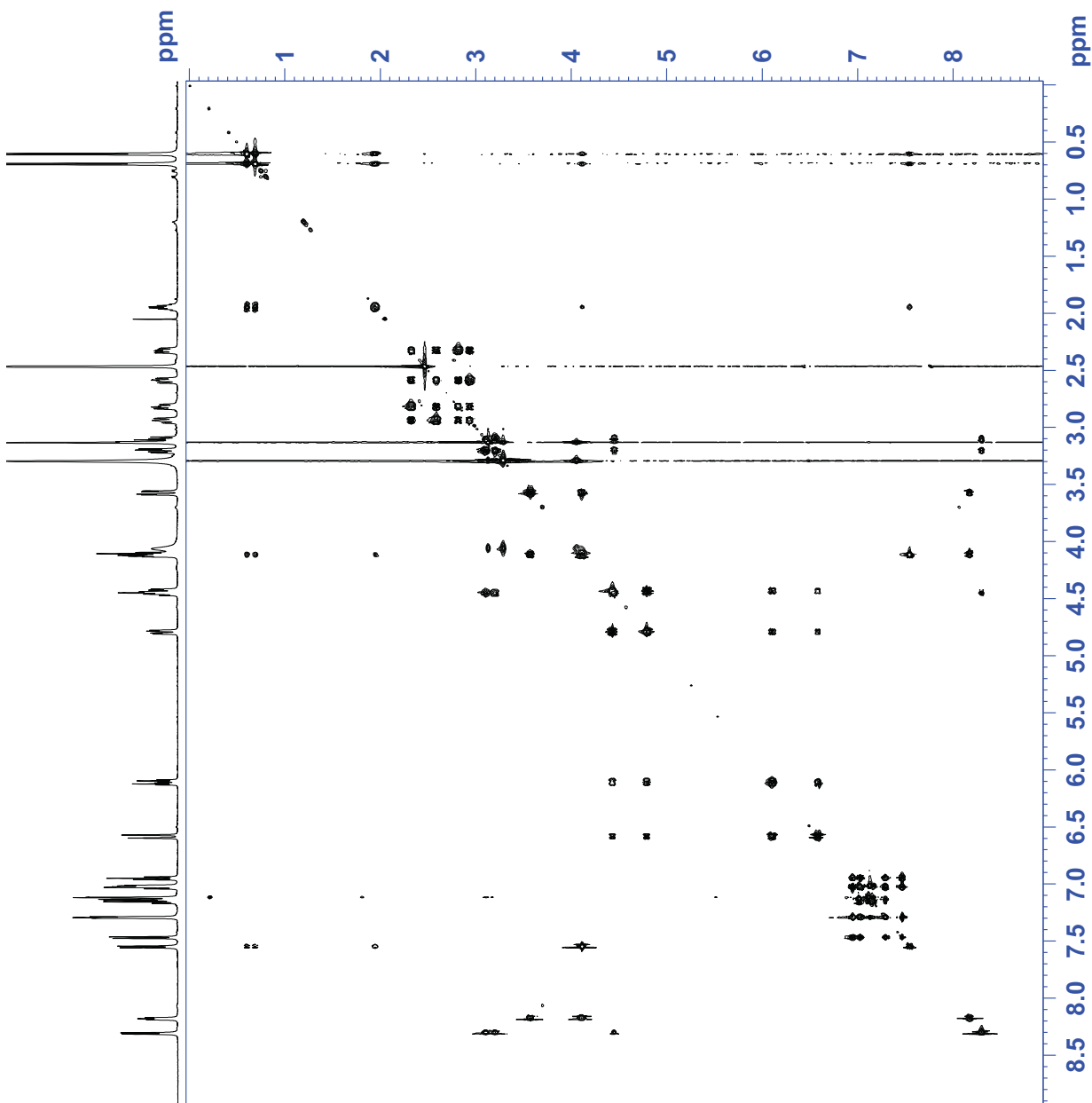
F2 - Acquisition Parameters
Date_ 20120423
Time_ 11.12
INSTRUM av600
PROBHD 5 mm TBI5
PULPROG zg
TD 65536
SOLVENT DMSO
NS 8
DS 0
SWH 12376.237 Hz
FIDRES 0.188846 Hz
AQ 2.6476543 sec
RG 181
DW 40.400 usec
DE 6.50 usec
TE 295.7 K
D1 2.0000000 sec
TD0 1

===== CHANNEL f1 =====
NUC1 1H
P1 9.50 usec
PL1 -2.00 dB
PL1W 39.81071854 W
SFO1 600.1336008 MHz

F2 - Processing parameters
SI 65536
SF 600.1300273 MHz
WDW EM
SSB 0
LB 0 Hz
GB 0
PC 1.00





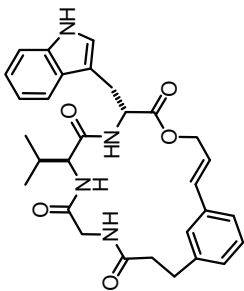
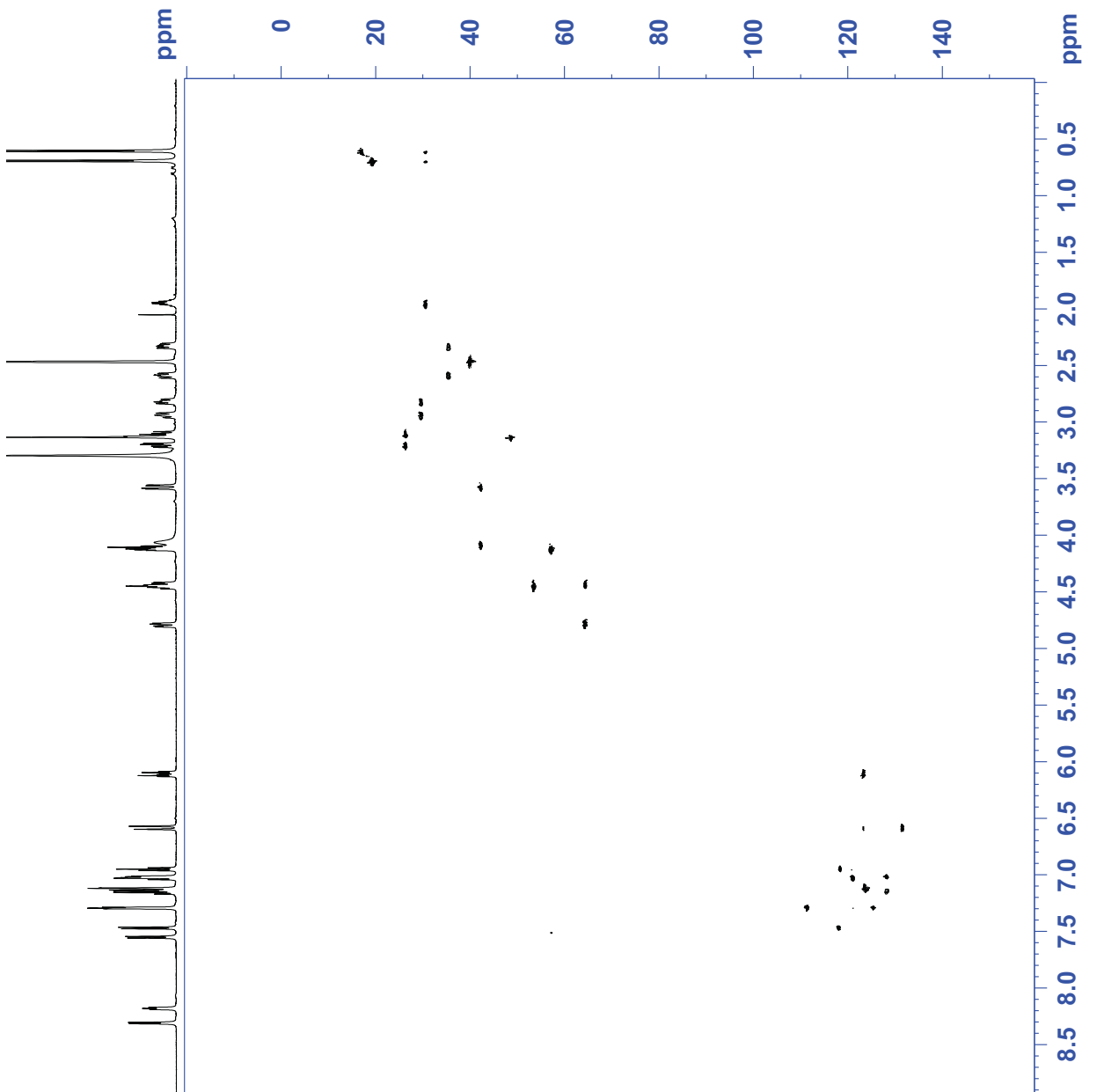


Current Data Parameters
 NAME KL-4-189
 EXPNO 5
 PROCNO 1

F1 - Acquisition parameters
 TD 600
 SFO1 600.1327 MHz
 FIDRES 10.602203 Hz
 SW 10.600 ppm
 FnMODE Echo-Antiecho

F2 - Processing parameters
 SI 1024
 SF 600.1300273 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

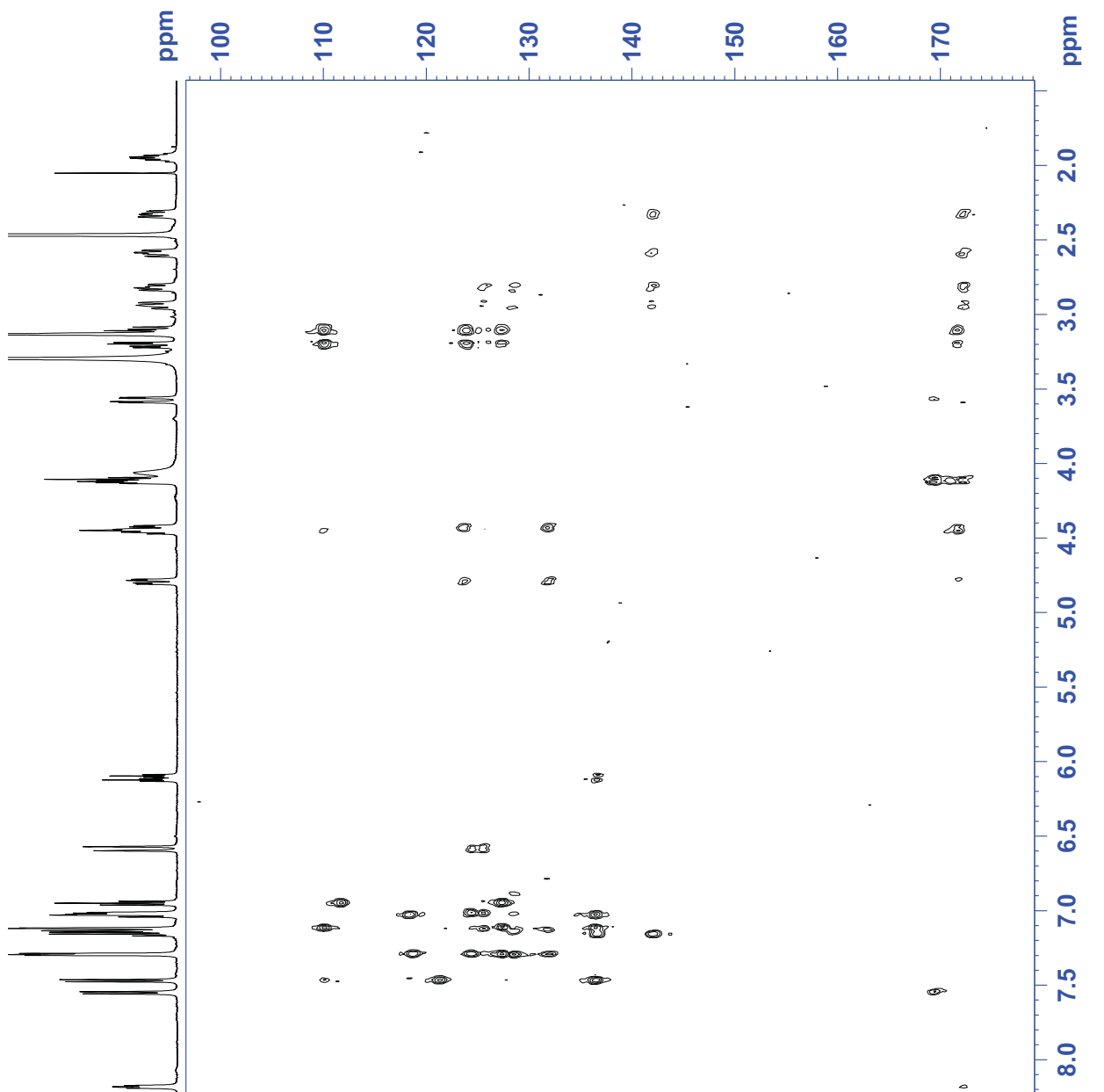
F1 - Processing parameters
 SI 1024
 MC2 echo-antiecho
 SF 600.1300273 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0



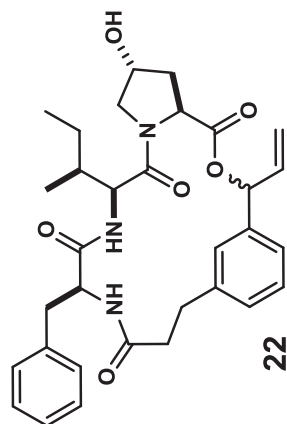
Current Data Parameters
 NAME KL-4-189
 EXPNO 6
 PROCNO 1

F2 - Acquisition Parameters

Date_ 20120423
 Time_ 12.11
 INSTRUM 5 mm TBI5
 PROBHD hsqcetgpsisp
 PULPROG 2048
 TD DMSO
 SOLVENT 8
 NS 16
 DS 16
 SWH 5387.931 Hz
 FIDRES 2.630826 Hz
 AQ 0.1900544 sec
 RG 26008
 DW 92.800 usec
 DE 6.00 usec
 TE 295.8 K
 CNST2 145.0000000
 d0 0.00000300 sec
 D1 1.20000005 sec
 d4 0.00172414 sec
 d11 0.03000000 sec
 D16 0.00020000 sec
 D24 0.00086200 sec
 DELTA 0.00127500 sec
 DELTA1 0.00120659 sec
 DELTA2 0.00097414 sec
 in0 0 sec
 cm1 1.00



Cyclic-Phe-Leu-Hyp (22):



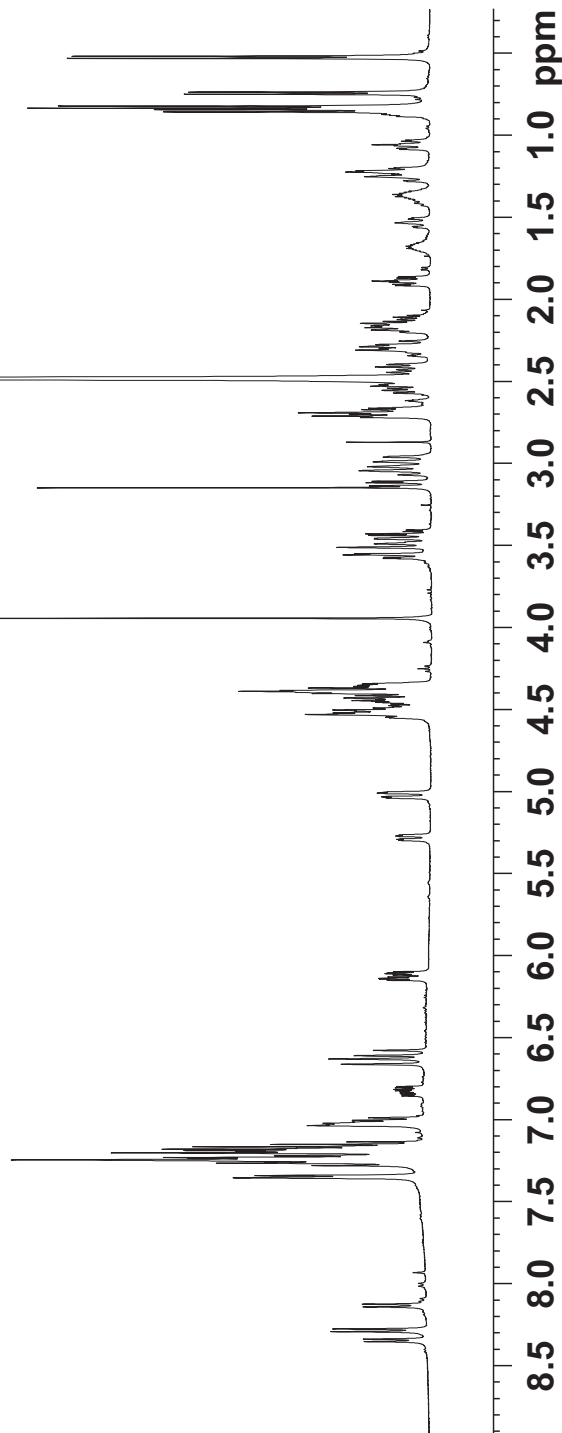
```

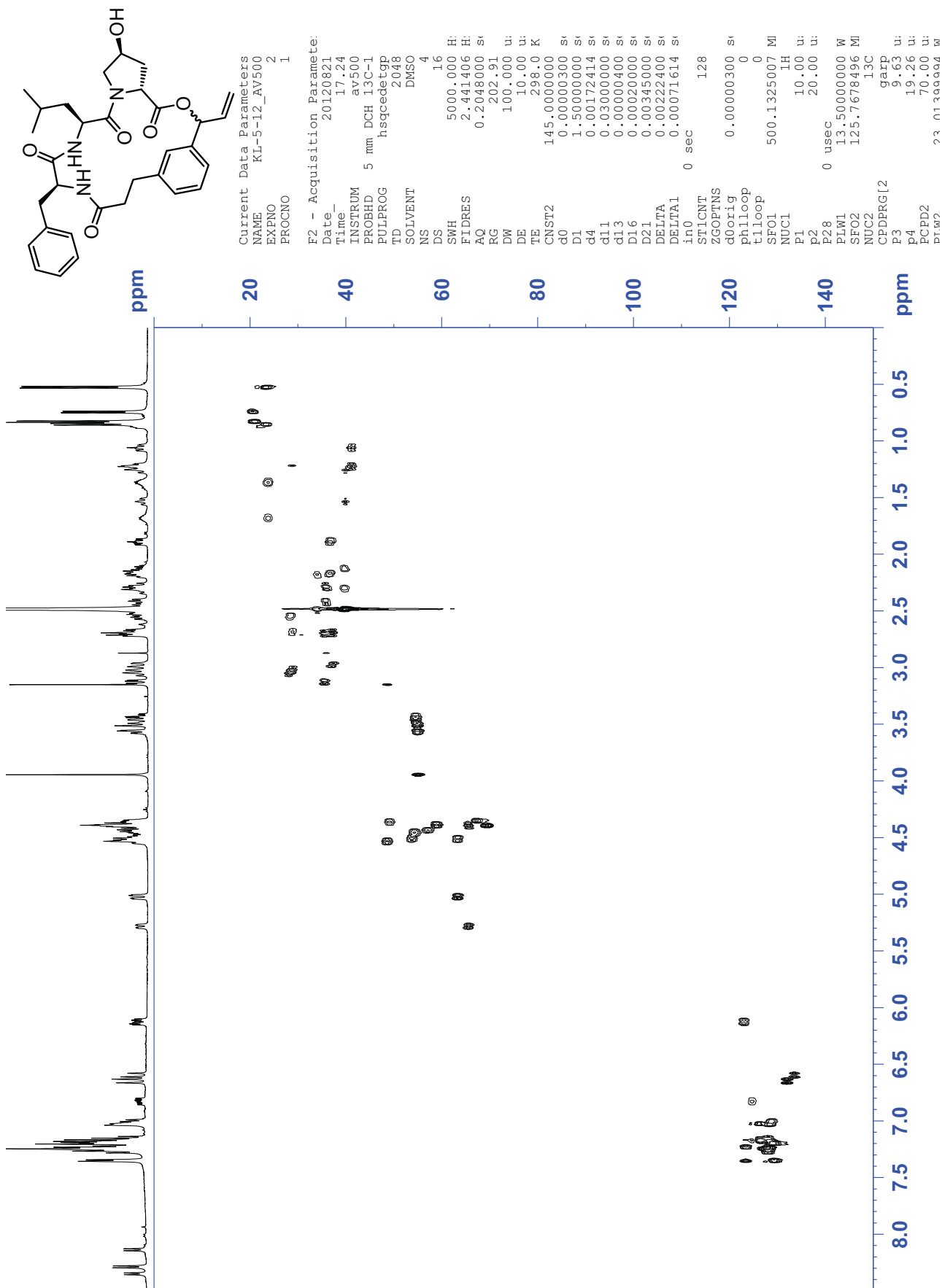
Current Data Parameters
NAME      KL-5-12_AV500
EXPNO     1
PROCNO    1

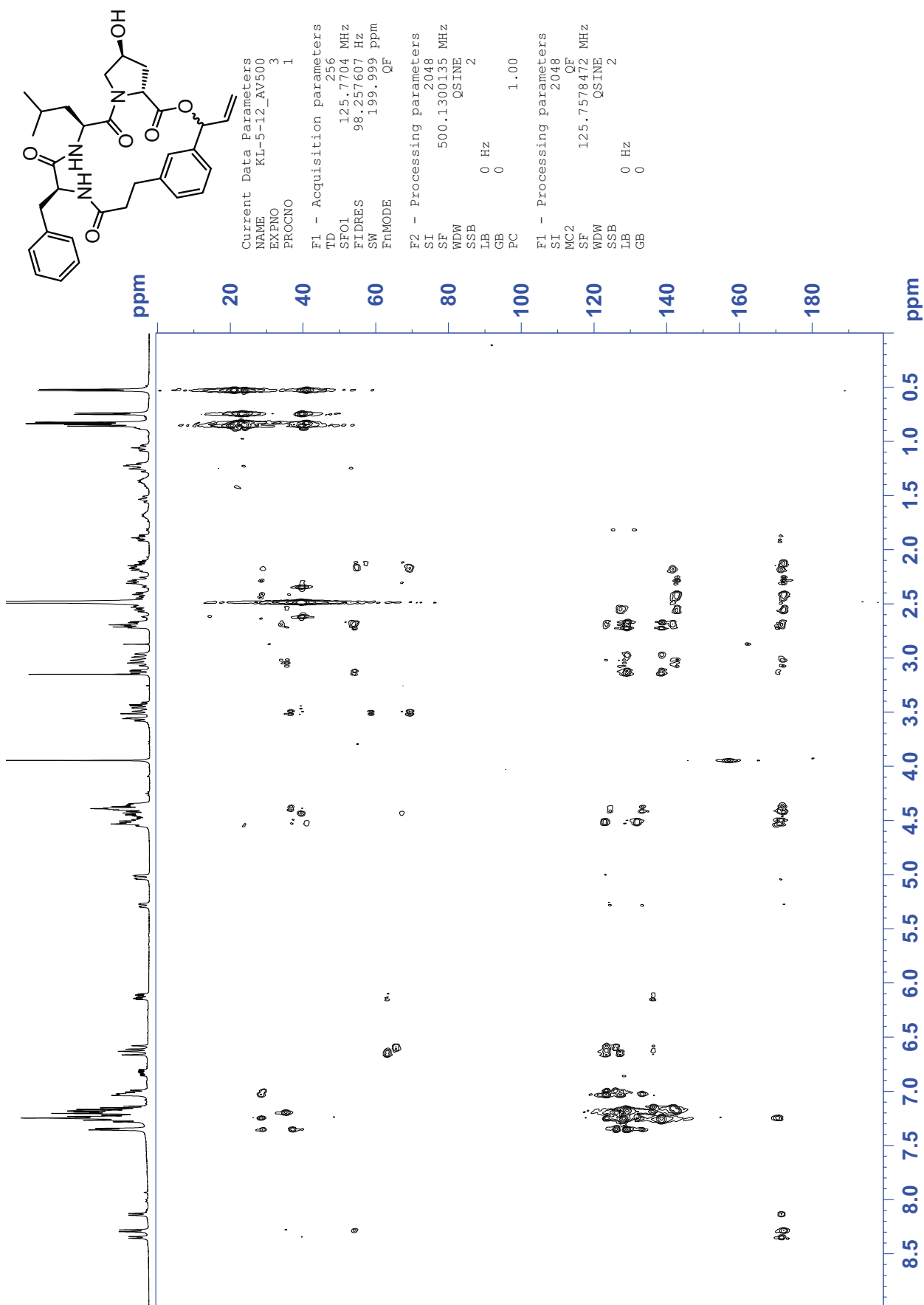
F2 - Acquisition Parameters
Date_     20120821
Time      17:22
INSTRUM   av500
PROBHD    5 mm DCH 13C-1
PULPROG   zg30
TD         65536
SOLVENT   DMSO
NS         8
DS         0
SWH        10000.000 Hz
FIDRES     0.152588 Hz
AQ         3.2767999 sec
RG         202.91
DM         50.000 usec
DE         10.00 usec
TE         298.0 K
D1         2.00000000 sec
TD0        1

===== CHANNEL f1 =====
NUC1       1H
P1         10.00 usec
PLW1       13.50000000 W
SFO1       500.1330008 MHz

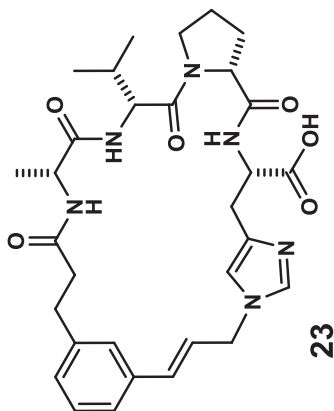
F2 - Processing parameters
SI         65536
SF         500.1300146 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00
    
```







Cyclic-Ala-Val-Pro-His-OH (23):



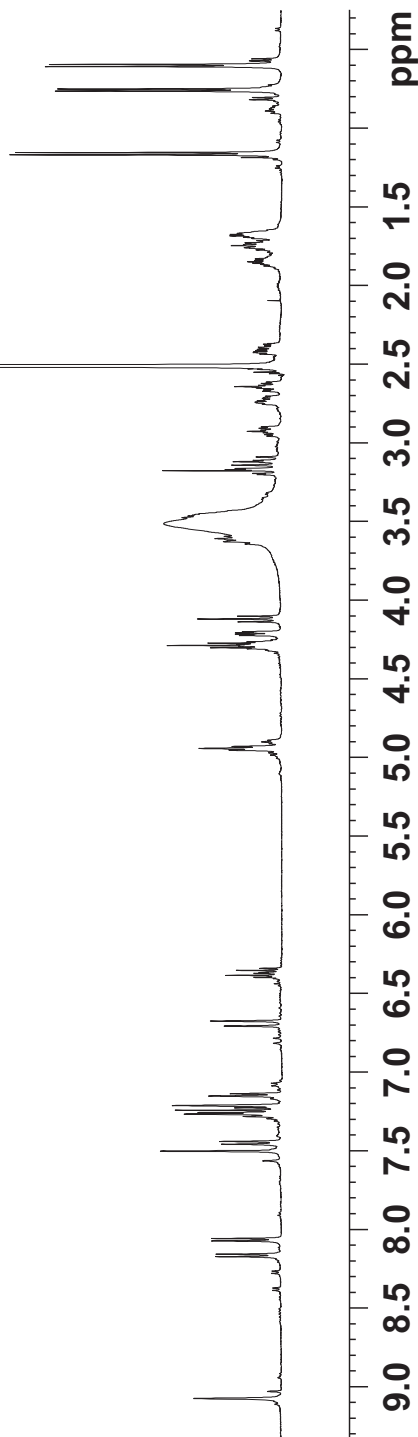
```

Current Data Parameters
NAME      KL-4-183_F14_ICON
EXPNO     1
PROCNO    1

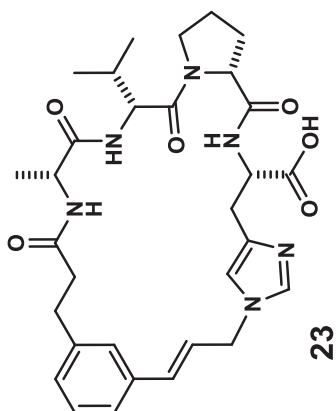
F2 - Acquisition Parameters
Date_     20120827
Time_     20.16
INSTRUM   av500
PROBHD    5 mm DCH 13C-1
PULPROG   zg30
TD         65536
SOLVENT   DMSO
NS         8
DS         0
SWH        10000.000 Hz
FIDRES     0.152588 Hz
AQ         3.2767999 sec
RG         11
DW         50.000 usec
DE         10.00 usec
TE         298.0 K
D1         2.00000000 sec
TD0        1

===== CHANNEL f1 =====
NUC1       1H
P1         10.00 usec
PLW1       13.50000000 W
SFO1       500.1330008 MHz

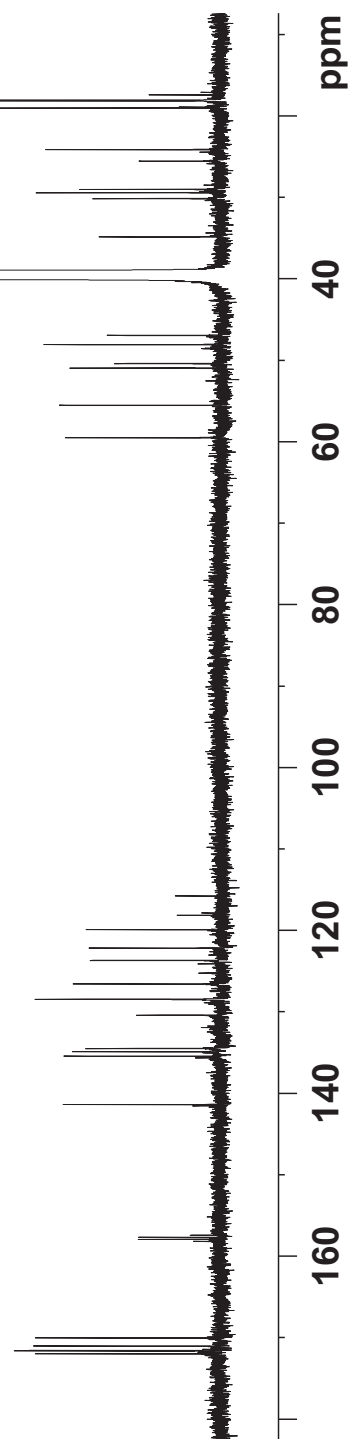
F2 - Processing parameters
SI         65536
SF         500.1300000 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00
  
```

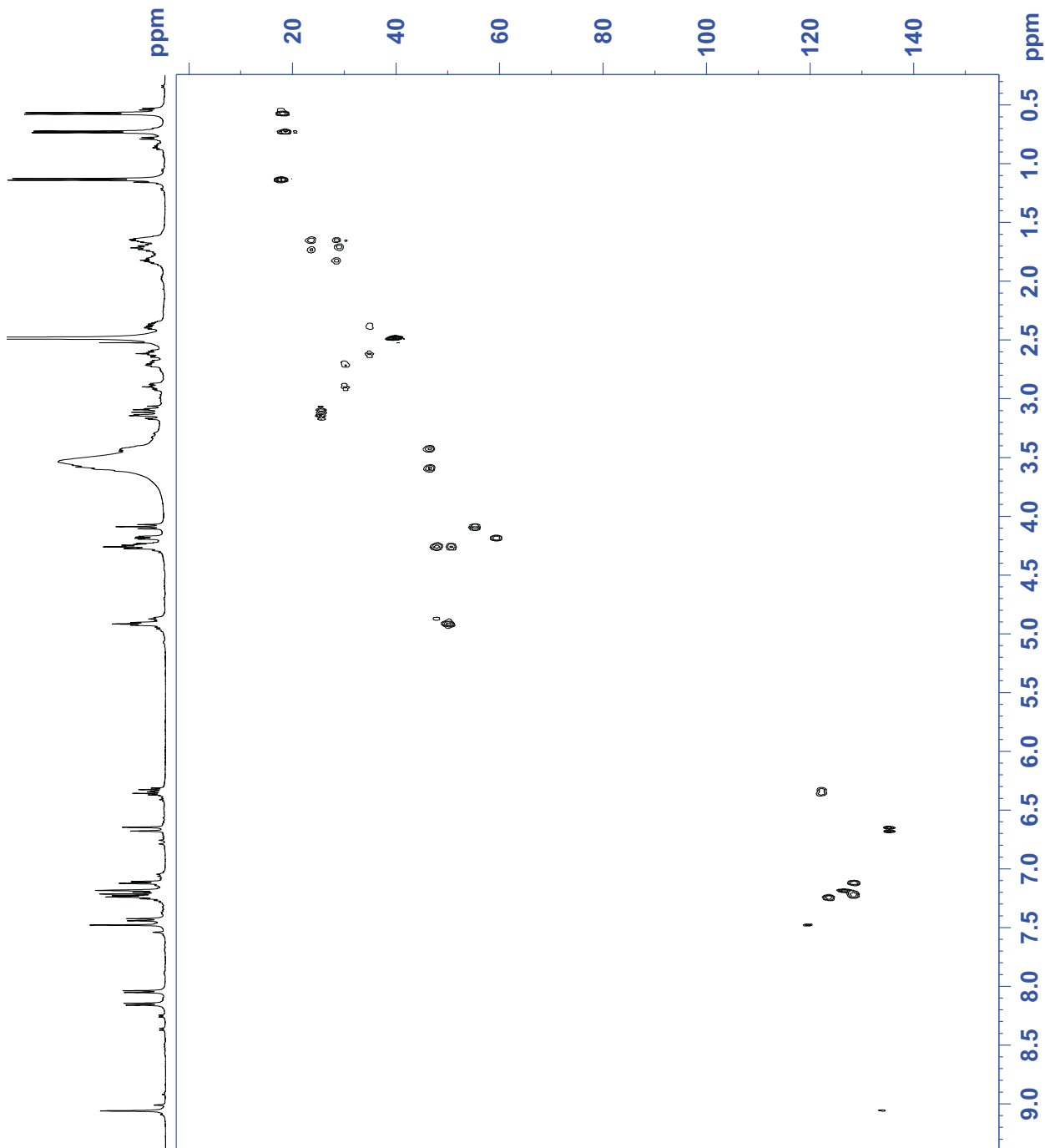


Cyclic-Ala-Val-Pro-His-OH (23):



Current Data Parameters
NAME KL-4-183_F14-ICON
EXPNO 2
PROCNO 1
F2 - Processing parameters
SI 131072
SF 125.7578519 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40





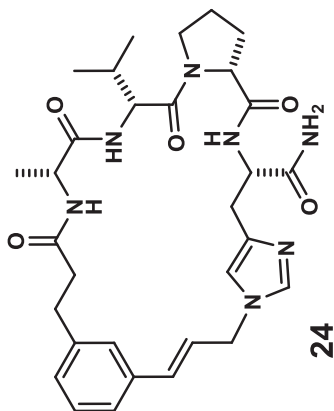
Current Data Parameters
NAME KL-4-183_F14
EXPNO 5
PROCNO 1

F1 - Acquisition parameters
TD 256
SFO1 125.7678 MHz
FIDRES 98.255890 Hz
SW 200.000 ppm
FMODE Echo-Antiecho

F2 - Processing parameters
SI 2048
SF 500.1300135 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0
PC 1.00

F1 - Processing parameters
SI 2048
MC2 echo-antiecho
SF 125.7578472 MHz
WDW TRAP
SSB 2
LB 0 Hz
GB 0

Cyclic-Ala-Val-Pro-His-NH₂ (24):



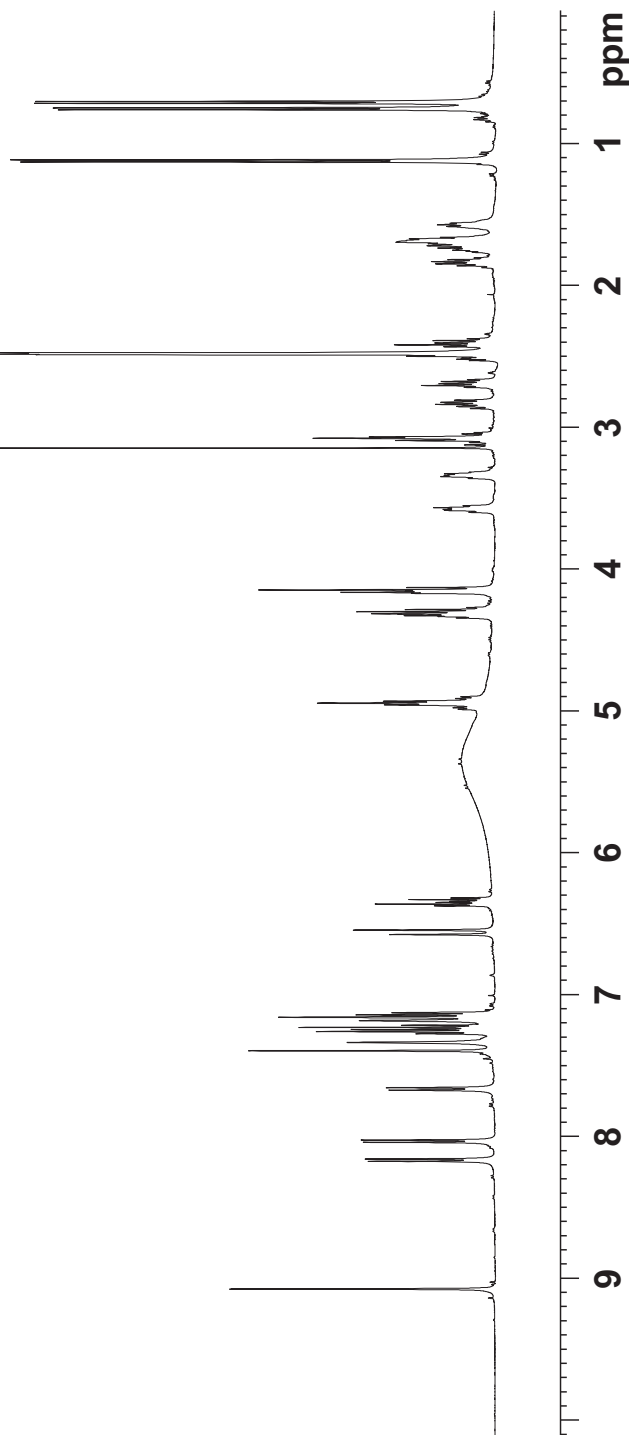
```

Current Data Parameters
NAME      KL-4-206A_F22
EXPNO     1
PROCNO    1

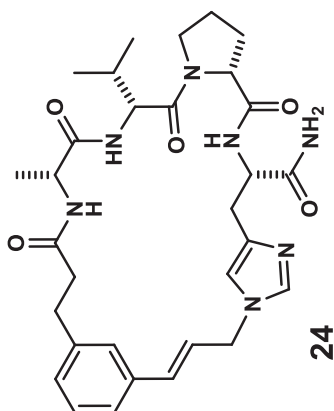
F2 - Acquisition Parameters
Date_     20120731
Time      12.41
INSTRUM   av500
PROBHD    5 mm DCH 13C-1
PULPROG   zg30
TD         65536
SOLVENT   DMSO
NS         8
DS         0
SWH        10000.000 Hz
FIDRES     0.152588 Hz
AQ         3.2767999 sec
RG         202.91
DW         50.000 usec
DE         10.00 usec
TE         296.0 K
D1         2.00000000 sec
TD0        1

===== CHANNEL f1 =====
NUC1       1H
P1         10.00 usec
PLW1       13.50000000 W
SFO1       500.1330008 MHz

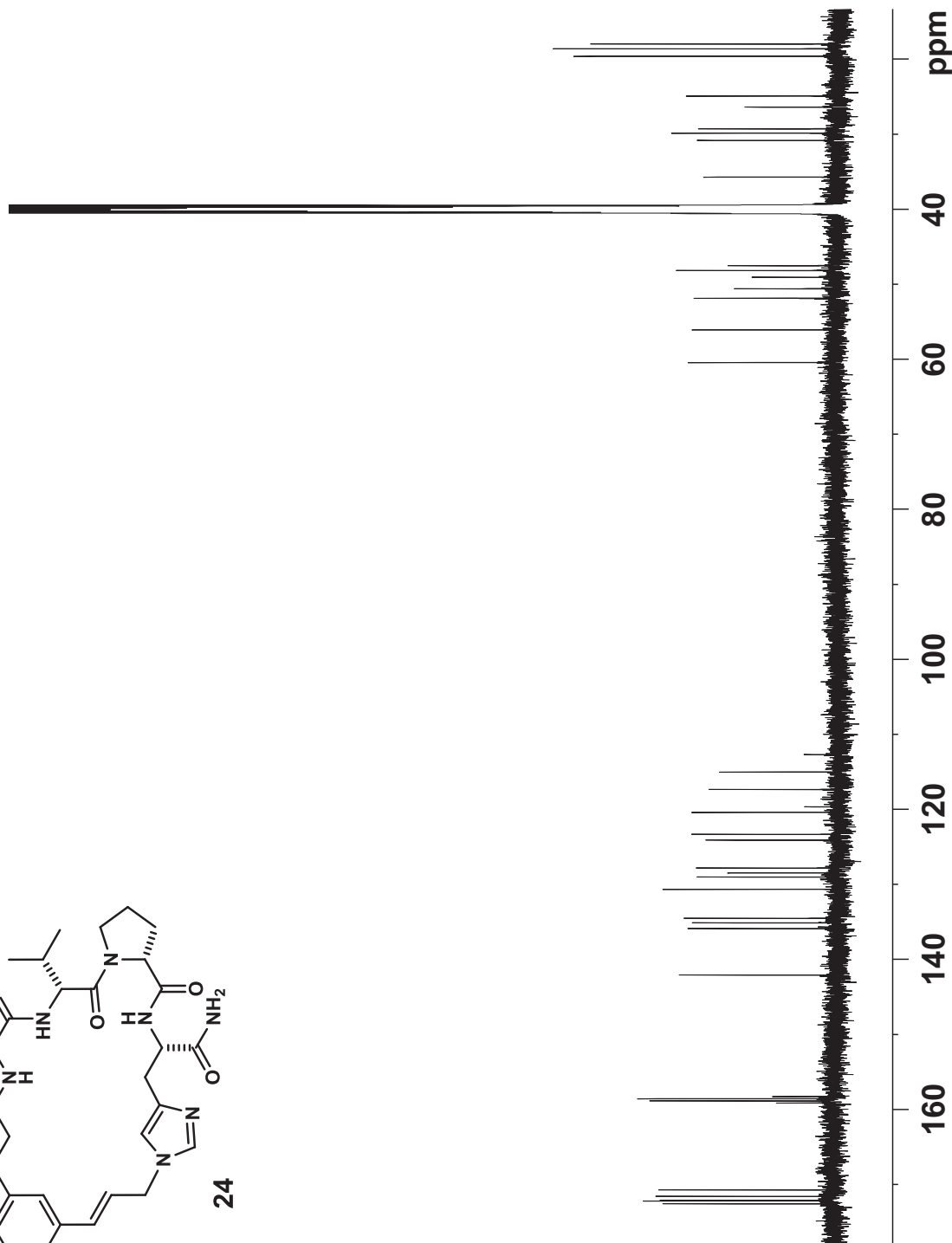
F2 - Processing parameters
SI         65536
SF         500.1300146 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00
    
```

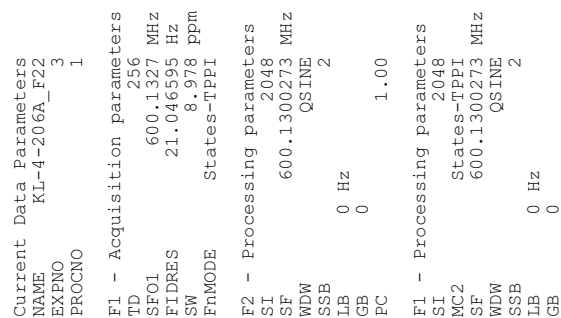


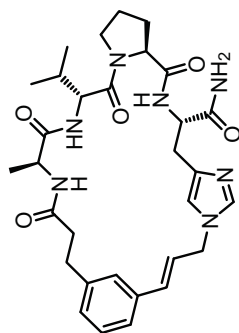
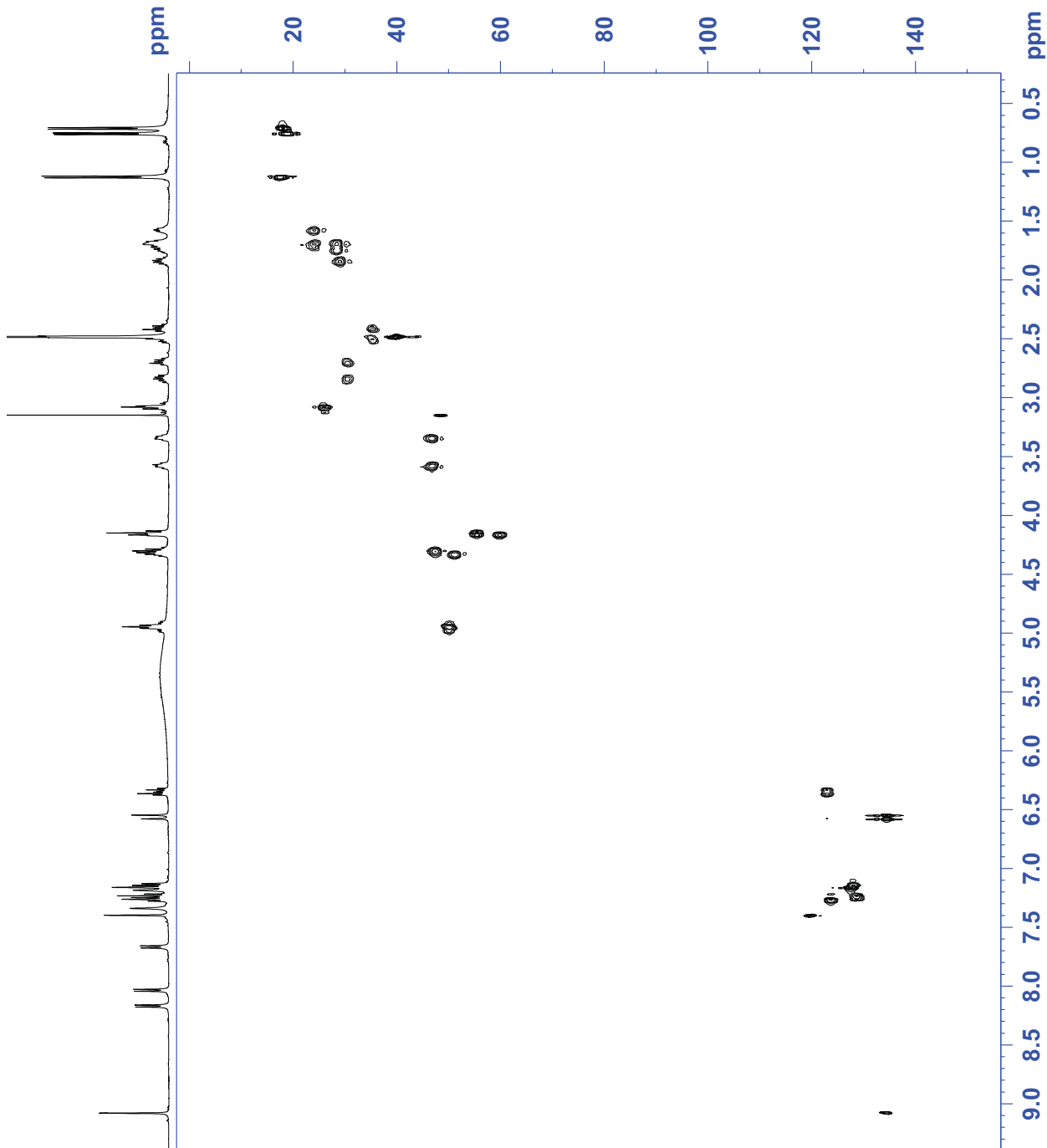
Cyclic-Ala-Val-Pro-His-NH₂ (24):



Current Data Parameters
 NAME KL-4-206A_F22
 EXPNO 5
 PROCNO 1
 F2 - Acquisition Parameters
 Date_ 20120821
 Time_ 19.30
 INSTRUM av500
 PROBHD 5 mm DCH 13C-1
 PULPROG zgpg30
 TD 65536
 SOLVENT DMSO
 NS 128
 DS 2
 SWH 31250.000 Hz
 FIDRES 0.476837 Hz
 AQ 1.0485760 sec
 RG 202.91
 DW 16.000 usec
 DE 18.00 usec
 TE 298.0 K
 d11 2.0000000 sec
 0.03000000 sec
 DELTA 1.8999998 sec
 TD0 1
 SF01 125.772511 MHz
 NUC1 13C
 P1 9.63 usec
 PLW1 23.00000000 W
 SF02 500.1330008 MHz
 NUC2 1H
 CPDPRG12 waltz16
 PCPD2 80.00 usec
 PLW2 13.50000000 W
 PLW12 0.21094000 W
 PLW13 0.13500001 W
 F2 - Processing parameters
 SI 131072
 SF 125.7577892 MHz
 EM
 WDW 0
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40







Current Data Parameters
 NAME KL-4-206A_F22
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters

Date_ 20120731
 Time_ 12.41
 INSTRUM av500
 PROBHD 5 mm DCH 13C-1
 PULPROG zg30
 TD 65536
 SOLVENT DMSO
 NS 8
 DS 0
 SWH 10000.000 Hz
 FIDRES 0.152588 Hz
 AQ 3.2767999 sec
 RG 202.91
 DW 50.000 usec
 DE 10.00 usec
 TE 296.0 K
 D1 2.00000000 sec
 TD0 1

===== CHANNEL f1 =====

NUC1 1H
 P1 10.00 usec
 PLW1 13.5000000 W
 SFO1 500.1330008 MHz

F2 - Processing parameters

SI 65536
 SF 500.1300146 MHz
 WDW EM
 SSB 0
 LB 0
 GB 0
 PC 1.00



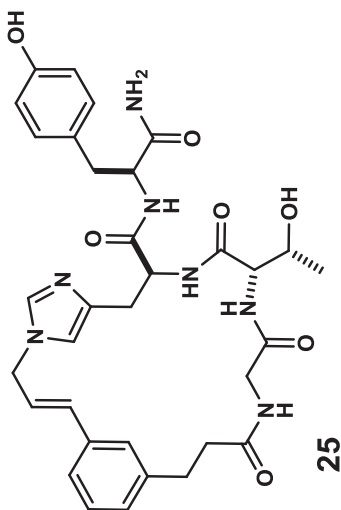
F1 - Acquisition parameters	
TD	220
SF01	125.7704 MHz
FIDRES	114.336121 Hz
SW	199.999 ppm
EnMODE	QF

F2 - Processing parameters	
SI	2048
SF	500.1300135 MHz
WDW	QSINE
SSB	2
LB	0 Hz
GB	0
PC	1.00

F1 - Processing parameters	
SI	2048
MC2	QF
SF	125.7578472 MHz
WDW	QSINE
SSB	2
LB	0 Hz
GB	0



Cyclic-Gly-Thr-His-Tyr-NH₂ (25):



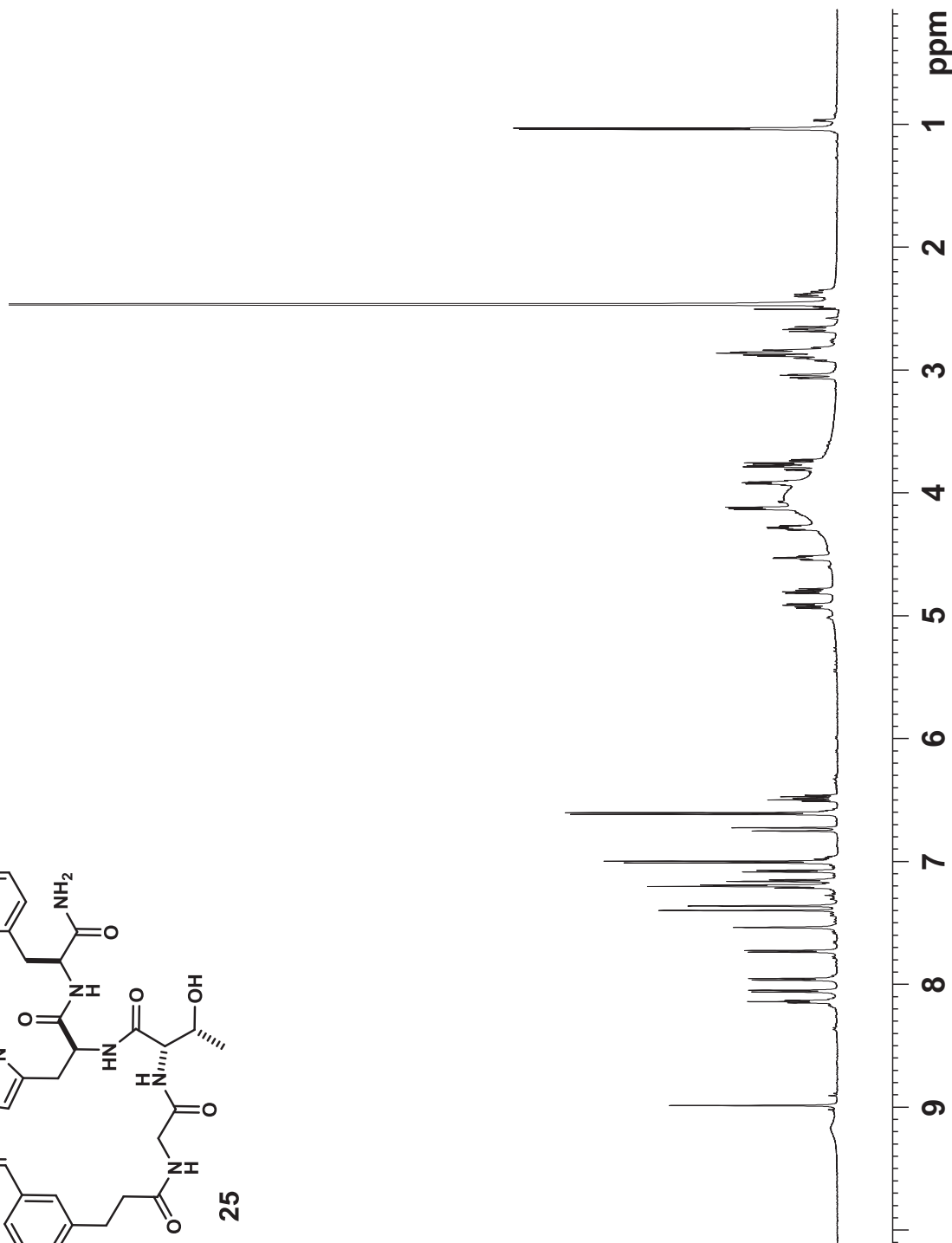
```

Current Data Parameters
NAME      His_A2_F17
EXPNO     1
PROCNO    1

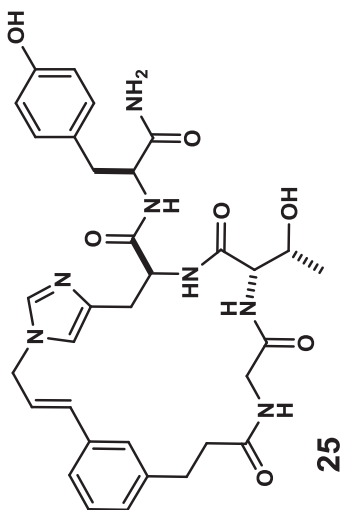
F2 - Acquisition Parameters
Date_     20121207
Time      17.19
INSTRUM   av600
PROBHD    5 mm TBI5
PULPROG   zg30
TD         65536
SOLVENT   DMSO
NS         16
DS         0
SWH        12376.237 Hz
FIDRES     0.188846 Hz
AQ         2.6476543 sec
RG         256
DW         40.400 usec
DE         6.50 usec
TE         294.0 K
D1         2.0000000 sec
TD0        1

===== CHANNEL f1 =====
NUC1       1H
P1         9.10 usec
PL1        -2.00 dB
PL1W       39.81071854 W
SFO1       600.1336008 MHz

F2 - Processing parameters
SI         65536
SF         600.1300273 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00
    
```



Cyclic-Gly-Thr-His-Tyr-NH₂ (25):



```

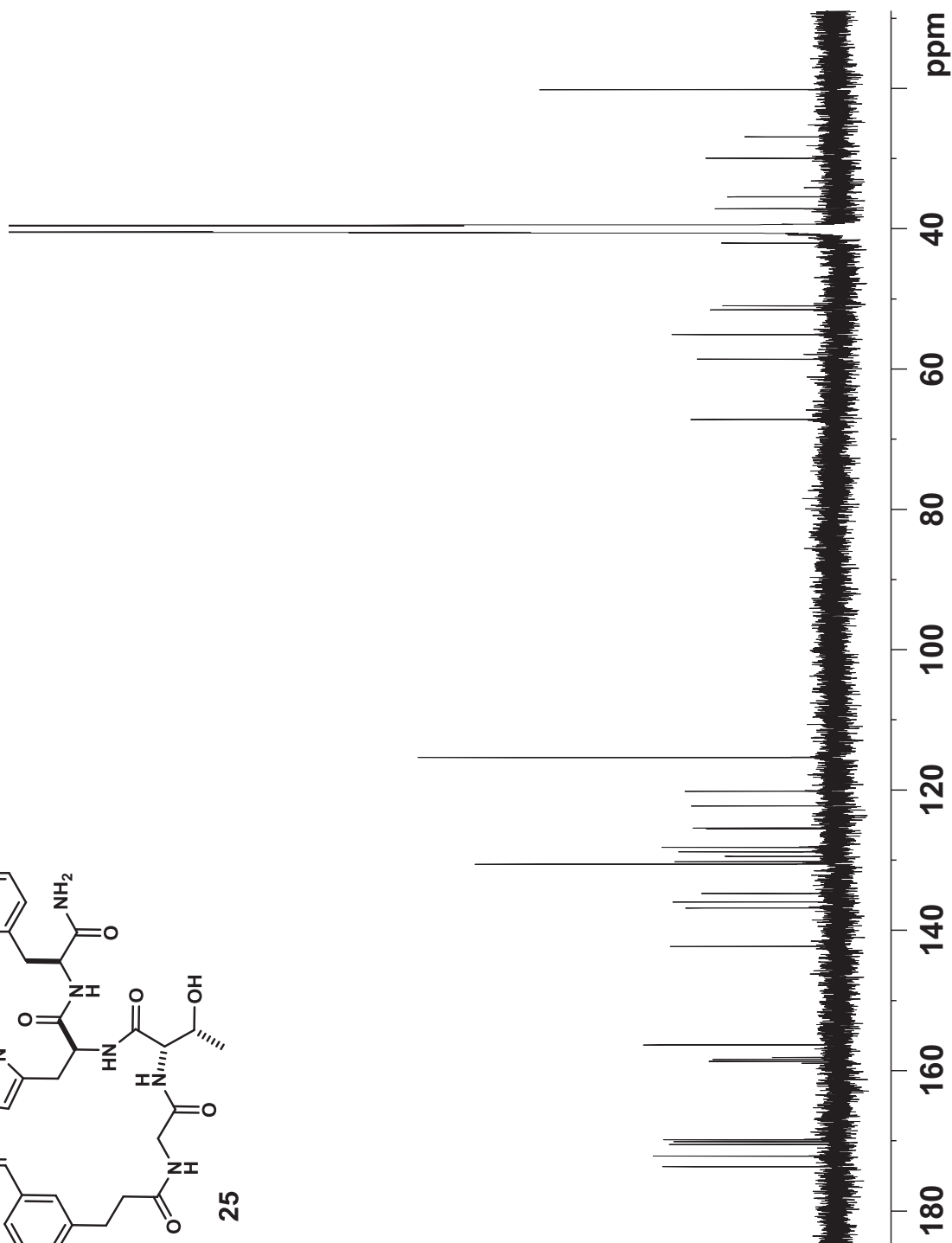
Current Data Parameters
NAME      His_A2_F17
EXPNO     6
PROCNO    1

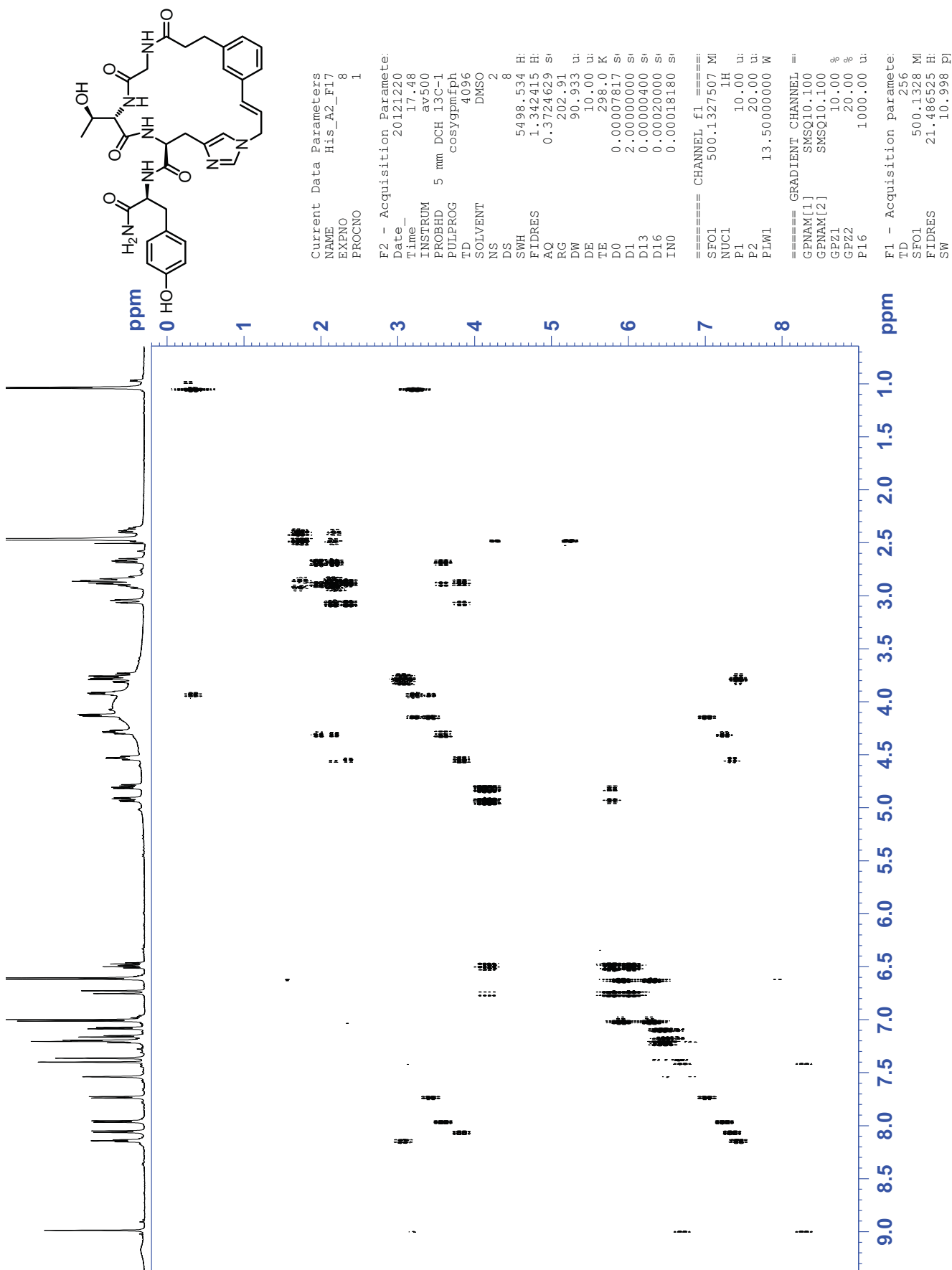
F2 - Acquisition Parameters
Date_     20121220
Time      17.18
INSTRUM   av500
PROBHD    5 mm DCH 13C-1
PULPROG   zgpg30
TD        65536
SOLVENT   DMSO
NS        256
DS        2
SWH        31250.000 Hz
FIDRES     0.476837 Hz
AQ         1.0485760 sec
RG         202.91
DW         16.000 usec
DE         18.00 usec
TE         298.0 K
D1         2.00000000 sec
D11        0.03000000 sec
TD0        1

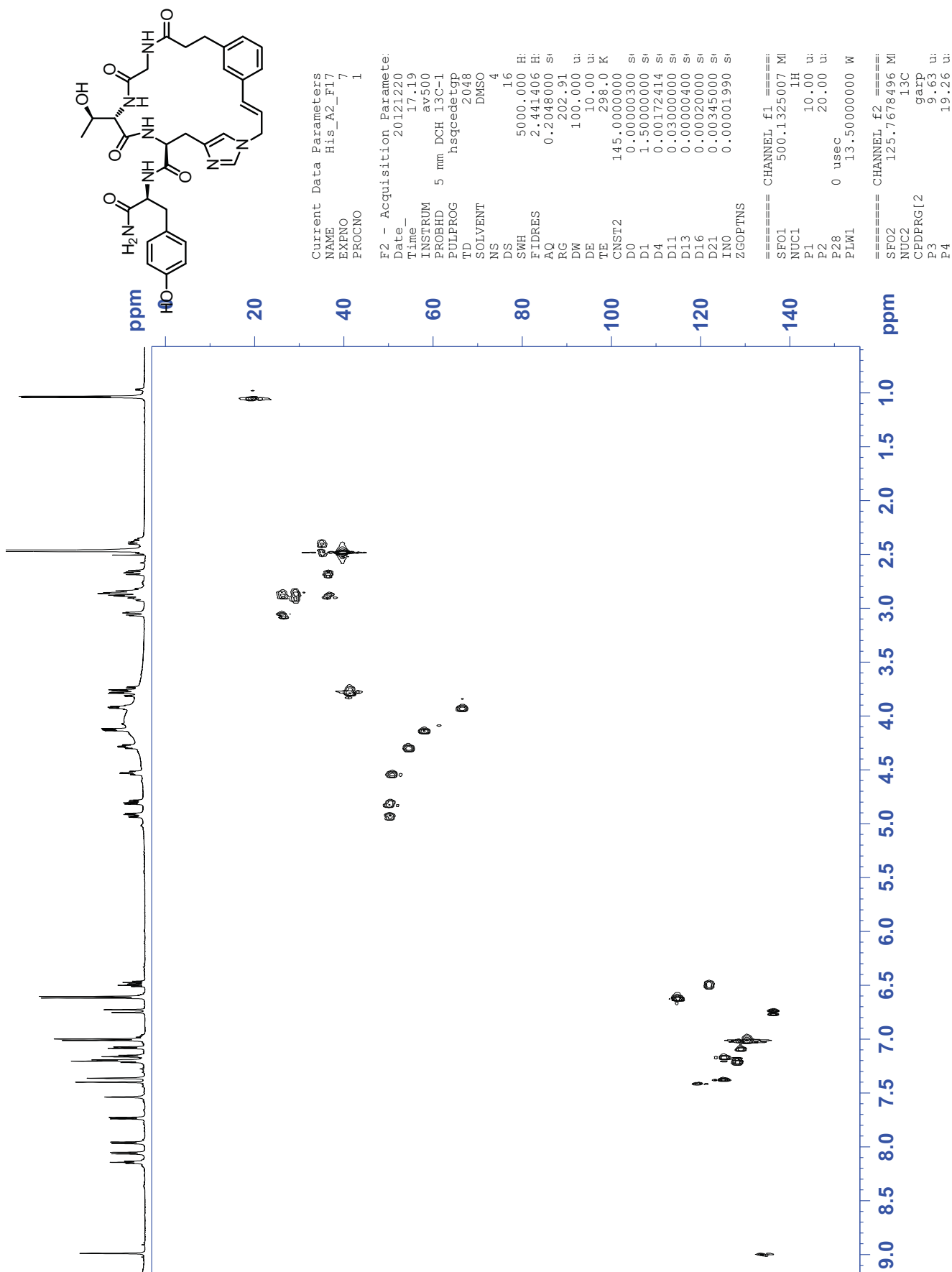
===== CHANNEL f1 =====
SFO1      125.772511 MHz
NUC1      13C
P1        9.63 usec
PLW1      23.00000000 W

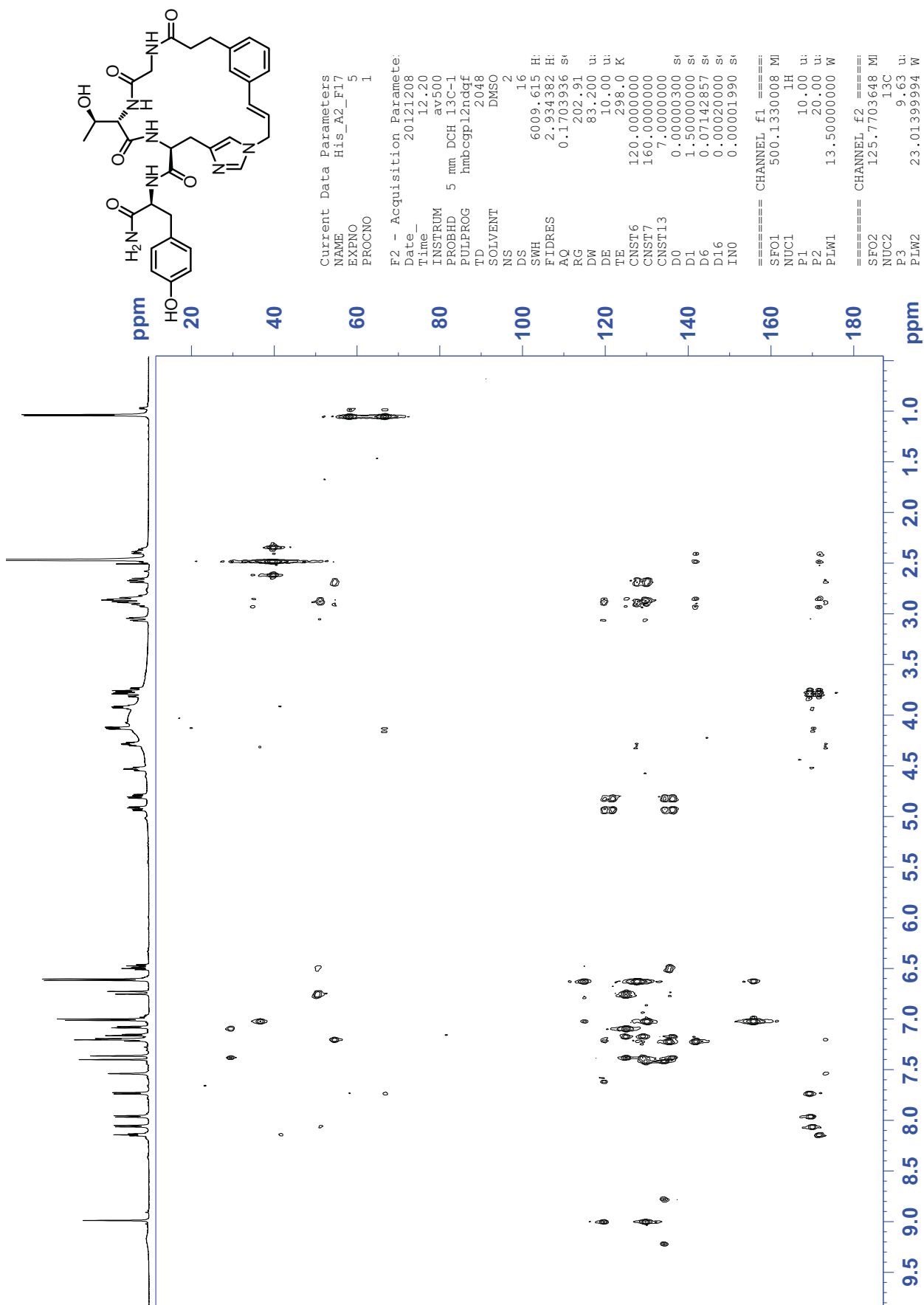
===== CHANNEL f2 =====
SFO2      500.1330008 MHz
NUC2      1H
CPDPRG2   waltz16
PCPD2     80.00 usec
PLW2      13.50000000 W
PLW12     0.21094000 W
PLW13     0.13500001 W

F2 - Processing parameters
SI         131072
SF         125.7577892 MHz
WDW        EM
SSB        0
LB         1.00 Hz
GB         0
PC         1.40
    
```

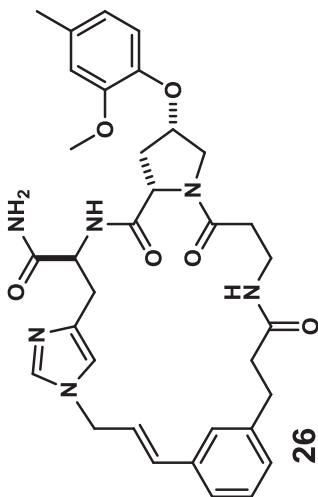








Cyclic- β -Ala-Pro[4-(2-methoxy-4-methylphenoxy)]-His (26):



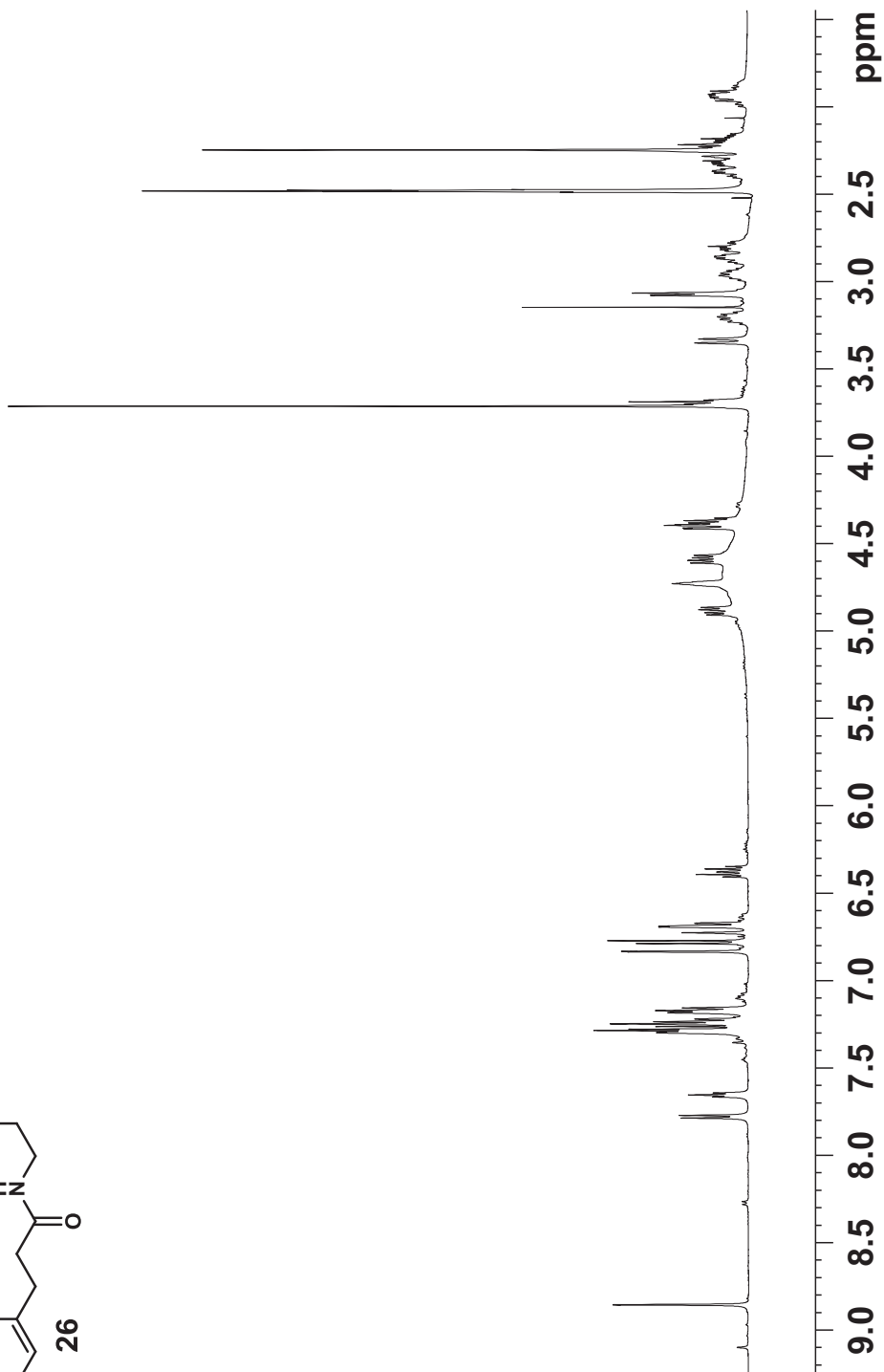
```

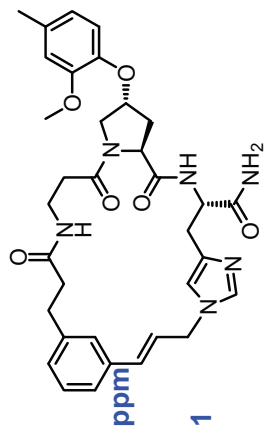
Current Data Parameters
NAME      KL-4-221B_F7
EXPNO     2
PROCNO    1

F2 - Acquisition Parameters
Date_     20120731
Time      19.30
INSTRUM   av500
PROBHD    5 mm DCH 13C-1
PULPROG   zg30
TD         65536
SOLVENT    DMSO
NS         8
DS         0
SWH        10000.000 Hz
FIDRES     0.152588 Hz
AQ          3.2767999 sec
RG          180.61
DW          50.000 usec
DE          10.00 usec
TE          296.0 K
D1          2.00000000 sec
TD0        1

===== CHANNEL f1 =====
NUC1       1H
P1          10.00 usec
PLW1       13.50000000 W
SFO1       500.1330008 MHz

F2 - Processing parameters
SI          65536
SF          500.1300146 MHz
WDW         EM
SSB         0
LB          0.30 Hz
GB          0
PC          1.00
    
```





```
Current Data Parameters
NAME      KL-4-221B_F7
EXPNO     4
PROCNO    1
```

F2 - Acquisition Paramete:

Date_ 20120731

Time- 19.33

INSTRUM
av500

PROBHD 5 mm DCH 13C-1

PULPROG cosygpmfph

TD 4096

SOLVENT	DMSO
0	0
1	1
2	2
3	3
4	4
5	5
6	6
7	7
8	8
9	9
10	10
11	11
12	12
13	13
14	14
15	15
16	16
17	17
18	18
19	19
20	20
21	21
22	22
23	23
24	24
25	25
26	26
27	27
28	28
29	29
30	30
31	31
32	32
33	33
34	34
35	35
36	36
37	37
38	38
39	39
40	40
41	41
42	42
43	43
44	44
45	45
46	46
47	47
48	48
49	49
50	50
51	51
52	52
53	53
54	54
55	55
56	56
57	57
58	58
59	59
60	60
61	61
62	62
63	63
64	64
65	65
66	66
67	67
68	68
69	69
70	70
71	71
72	72
73	73
74	74
75	75
76	76
77	77
78	78
79	79
80	80
81	81
82	82
83	83
84	84
85	85
86	86
87	87
88	88
89	89
90	90
91	91
92	92
93	93
94	94
95	95
96	96
97	97
98	98
99	99

NS 20

DS 8

5498.534 H: SWH

FIDRES 1.342415 H:

AQ	0.3724629	st
DC	0.44331	

RG	44.31	...
DW	00.033	...

DW	90.933	u:
DE	10.00	u:

DE	10.00	u:
FE	296.0	K

$$\frac{d\theta}{dt} = -0.00001273 \text{ K s}^{-1}$$

d0	-0.000012/3	s'
d1	2.000000000	s'

d1	2.00000000	s
d13	0.00000040	s

D15	0.000000000	S'
D16	0.000200000	S'

DELTA	0.00020000	S'
DELTA	0.00120400	S'

```

in0 0 sec

```

ST1CNT	128
--------	-----

d0orig	-0.00001273	s
--------	-------------	---

ph1loop 0 0

t1loop	0
cfo1	500 1 3 3 7 5 0 7 80

SF01 500.1327507 MI

NUC1	1H
P1	10 00 "

	10.00 u:	20.00 u:
p1		
p2		

p2 20.00 u:
PLW1 13.50000000 W

```
PLWI      T3.50000000 W
GPNAM[1]  SMSO10.100
```

GPNAM[1]	SMSQ10.100
GPNAM[2]	SMSQ10.100

GPNAM[Z]	SM5Q10.100	%
GPZ1	10.00	%

GPZ2	20.00	%
GPZ1	4.00	%

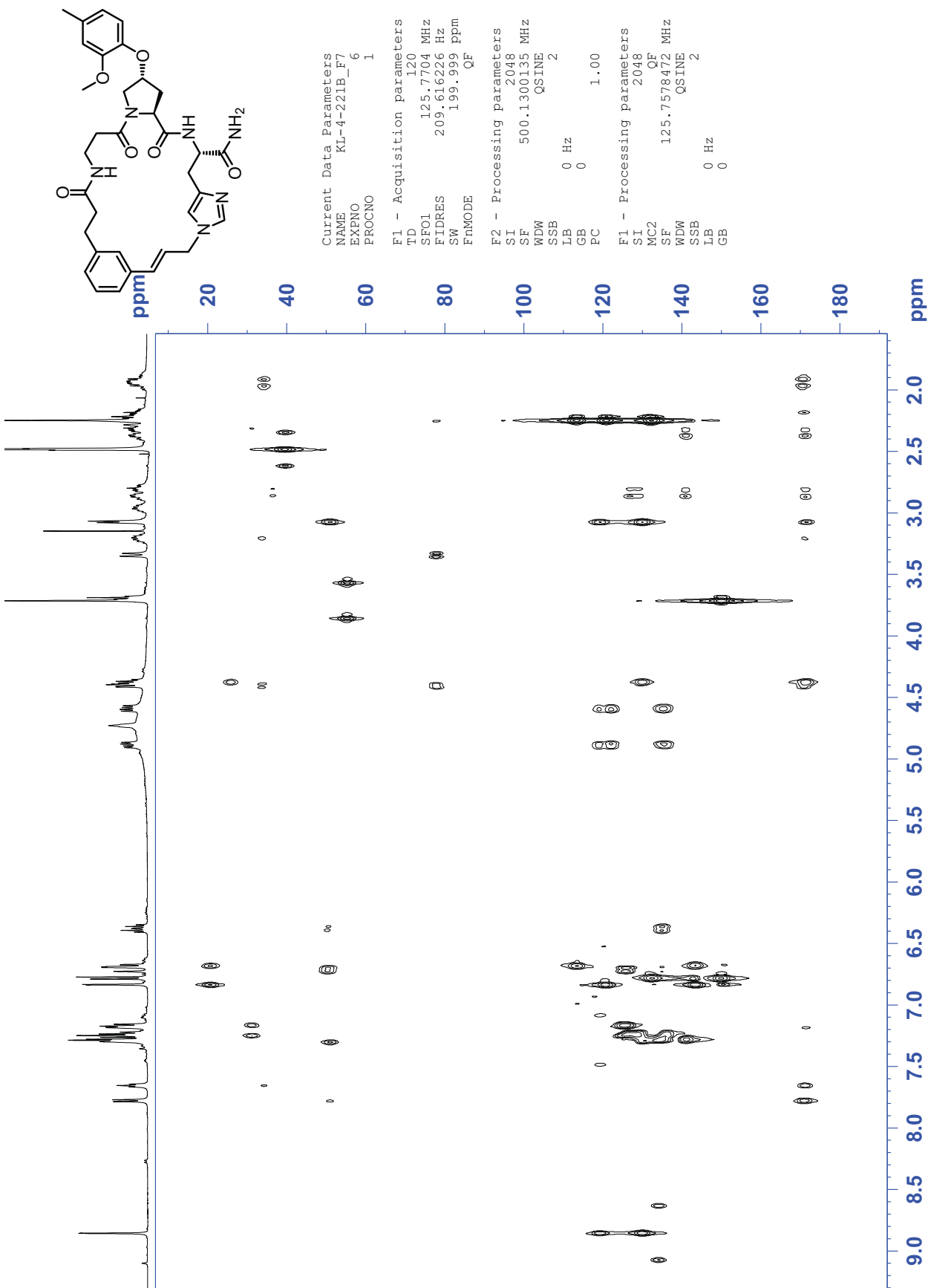
P16 1000.00 u;

F1 - Acquisition paramete:

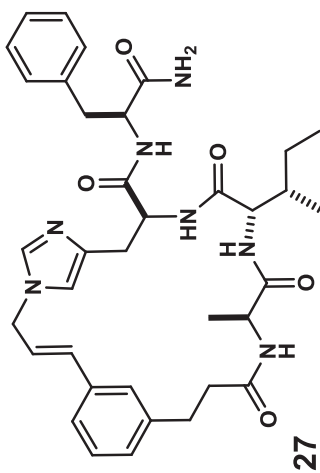
TD	256
----	-----

SFO1 500.1328 Ml

FIDRES 19.536423 H:



Cyclic-Ala-Ile-His-Phe-NH₂ (27):



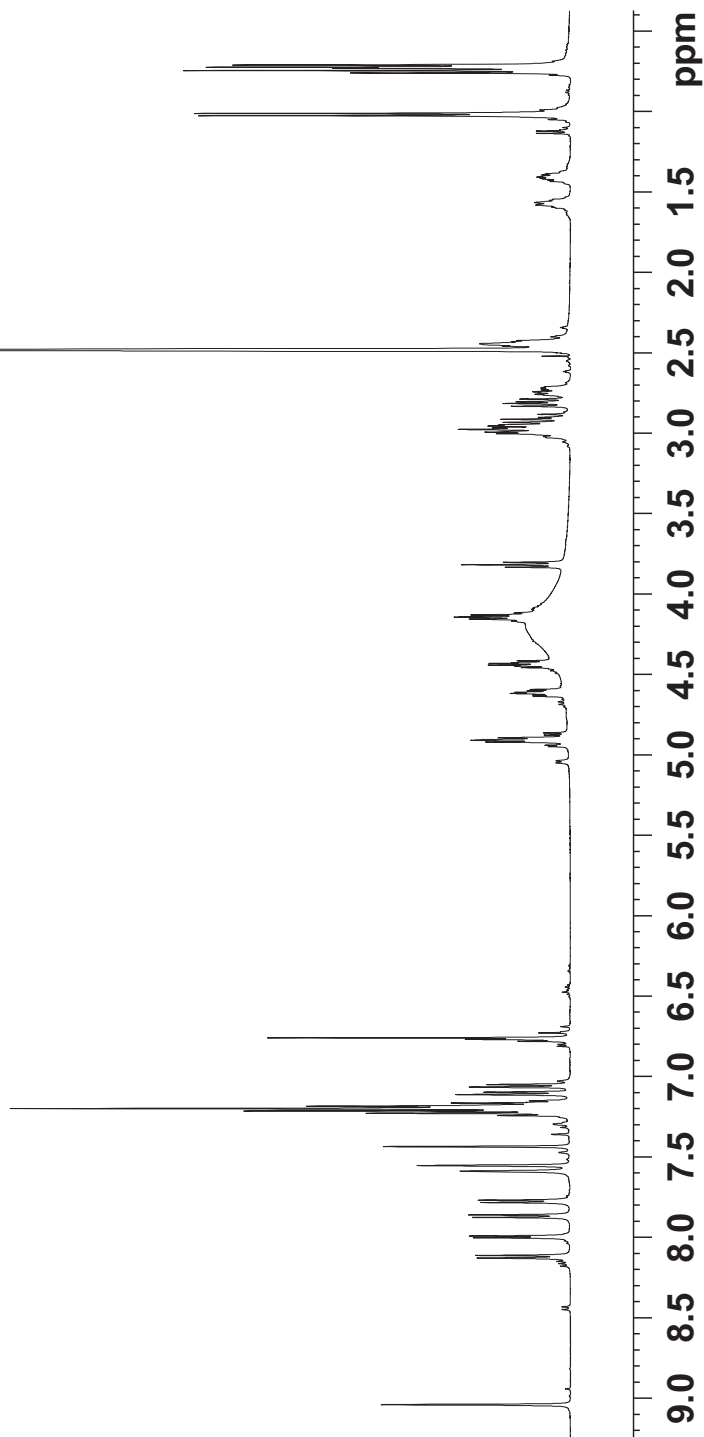
```

Current Data Parameters
NAME   HisA6_cycleF33
EXPNO   1
PROCNO   1

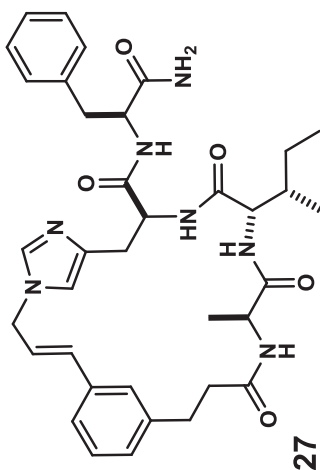
F2 - Acquisition Parameters
Date_   20121208
Time_   12.49
INSTRUM  av500
PROBHD   5 mm DCH 13C-1
PULPROG  zg30
TD       65536
SOLVENT  DMSO
NS       8
DS       0
SWH      10000.000 Hz
FIDRES   0.152588 Hz
AQ       3.2767999 sec
RG       24.37
DW       50.000 usec
DE       10.00 usec
TE       298.0 K
D1       2.0000000 sec
TD0      1

===== CHANNEL f1 =====
SFO1     500.130008 MHz
NUC1     1H
P1       10.00 usec
PLW1     13.5000000 W

F2 - Processing parameters
SI       65536
SF       500.1300146 MHz
WDW      EM
SSB      0
LB       0.30 Hz
GB       0
PC       1.40
    
```



Cyclic-Ala-Ile-His-Phe-NH₂ (27):



```

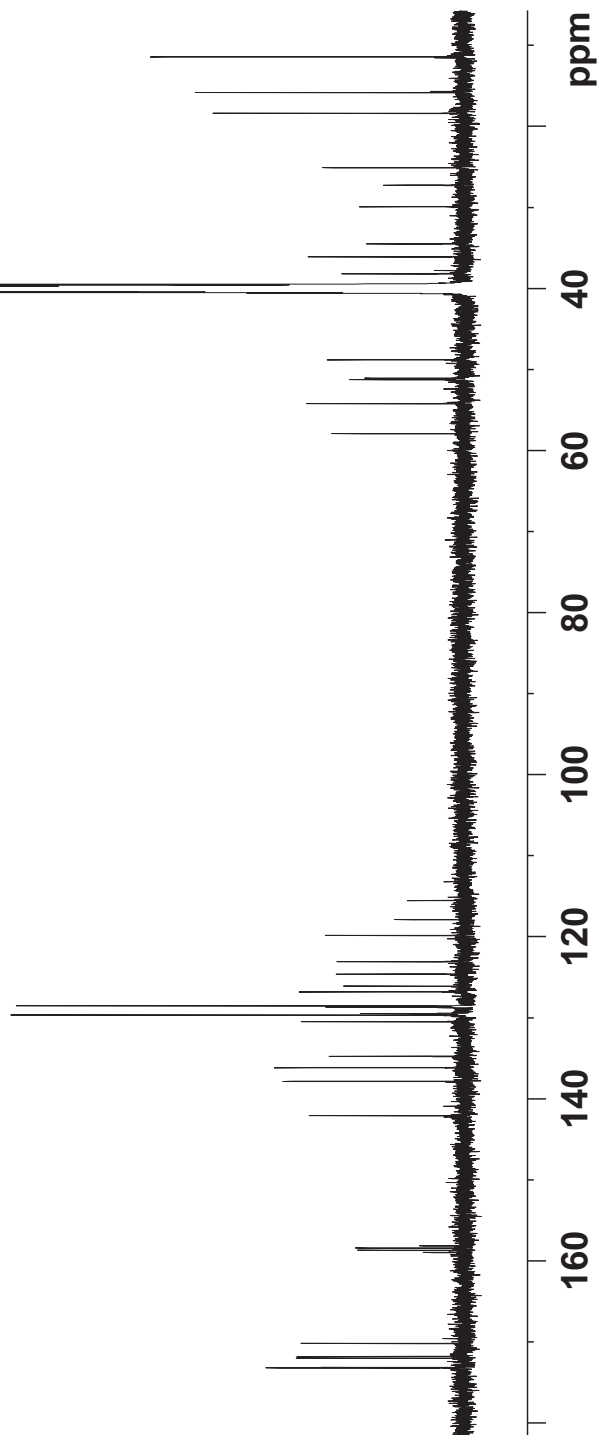
Current Data Parameters
NAME      HisA6_cycleF33
EXPNO     2
PROCNO    1

F2 - Acquisition Parameters
Date_     20121208
Time_     12.50
INSTRUM   av500
PROBHD    5 mm DCH 13C-1
PULPROG   zgpg30
TD        65536
SOLVENT   DMSO
NS         186
DS         2
SWH        31250.000 Hz
FIDRES     0.476837 Hz
AQ         1.0485760 sec
RG         202.91
DW         16.000 usec
DE         18.00 usec
TE         298.0 K
D1         2.00000000 sec
D11        0.03000000 sec
TD0        1

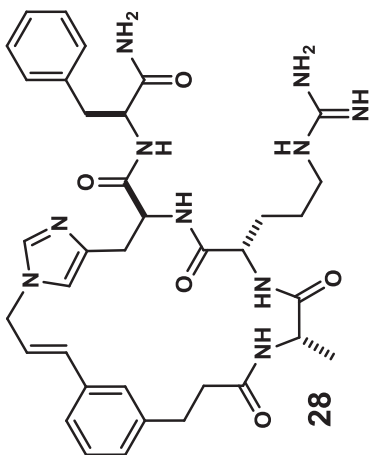
===== CHANNEL f1 =====
SFO1      125.772511 MHz
NUC1       13C
P1         9.63 usec
PLW1      23.00000000 W

===== CHANNEL f2 =====
SFO2      500.1330008 MHz
NUC2       1H
CPDPRG2   waltz16
PCPD2      80.00 usec
PLW2      13.50000000 W
PLW12     0.21094000 W
PLW13     0.13500001 W

F2 - Processing parameters
SI         131072
SF         125.7577892 MHz
WDW        EM
SSB        0
LB         1.00 Hz
GB         0
PC         1.40
    
```



Cyclic-Ala-Arg-His-Phe-NH₂ (28):



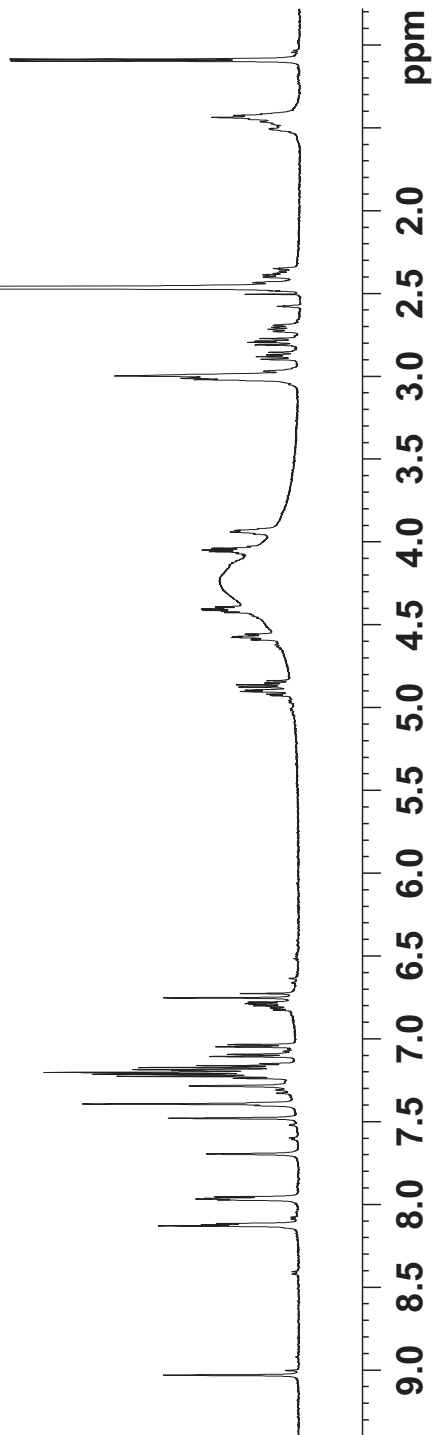
```

Current Data Parameters
NAME      His_A5_F24
EXPNO     1
PROCNO    1

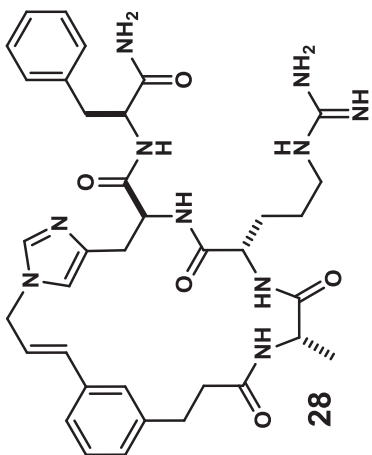
F2 - Acquisition Parameters
Date_     20121207
Time_     17.25
INSTRUM   av600
PROBHD    5 mm TBI5
PULPROG   zg30
TD        65536
SOLVENT   DMSO
NS         16
DS         0
SWH        12376.237 Hz
FIDRES     0.188846 Hz
AQ         2.6476543 sec
RG         256
DW         40.400 usec
DE         6.50 usec
TE         294.1 K
D1         2.0000000 sec
TD0        1

===== CHANNEL f1 =====
NUC1       1H
P1         9.10 usec
PL1        -2.00 dB
PL1W       39.81071854 W
SFO1       600.136008 MHz

F2 - Processing parameters
SI         65536
SF         600.1300273 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00
  
```



Cyclic-Ala-Arg-His-Phe-NH₂ (28):



```

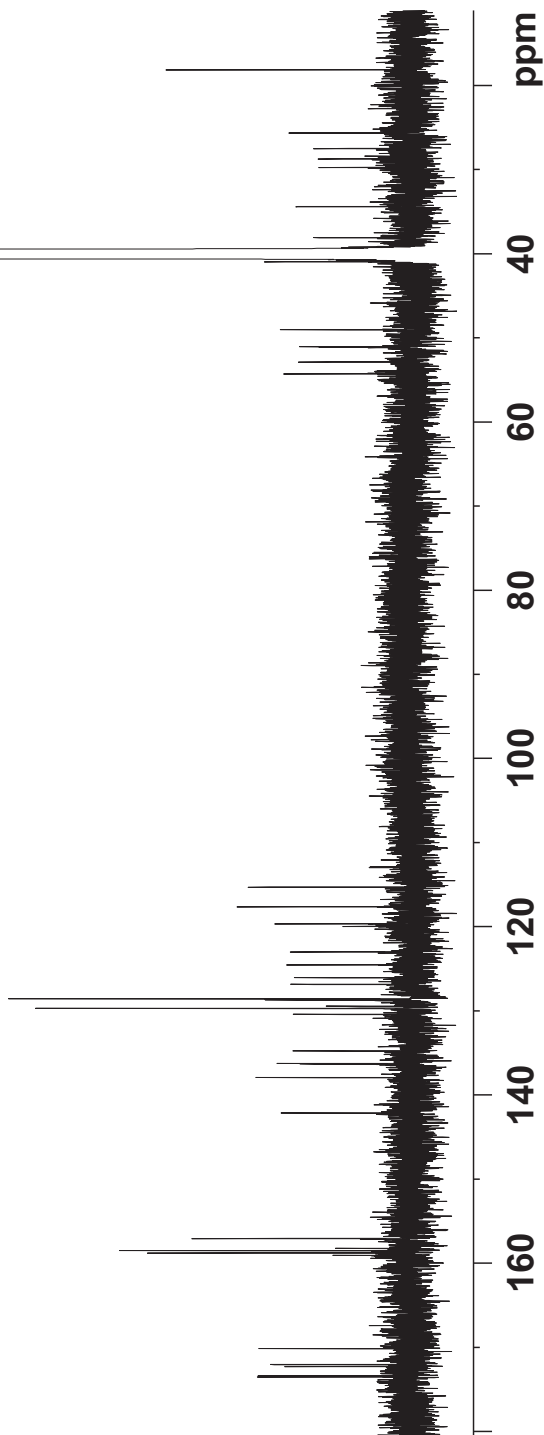
Current Data Parameters
NAME      His_A5_F24
EXPNO     2
PROCNO    1

F2 - Acquisition Parameters
Date_     20130122
Time      10.40
INSTRUM   av500
PROBHD    5 mm DCH 13C-1
PULPROG   zgpg30
TD        65536
SOLVENT   DMSO
NS         472
DS         2
SWH        31250.000 Hz
FIDRES     0.476837 Hz
AQ         1.0485760 sec
RG         202.91
DW         16.000 usec
DE         18.00 usec
TE         298.0 K
D1         2.00000000 sec
D11        0.03000000 sec
TD0        1

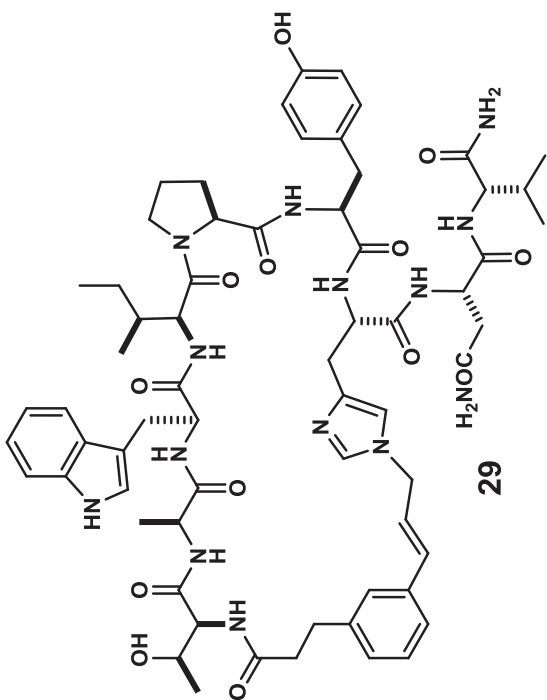
===== CHANNEL f1 =====
SFO1      125.772511 MHz
NUC1       13C
P1         9.63 usec
PLW1      23.00000000 W

===== CHANNEL f2 =====
SFO2      500.1330008 MHz
NUC2       1H
CPDPRG2   waltz16
PCPD2     80.00 usec
PLW2      13.50000000 W
PLW12     0.21094000 W
PLW13     0.13500001 W

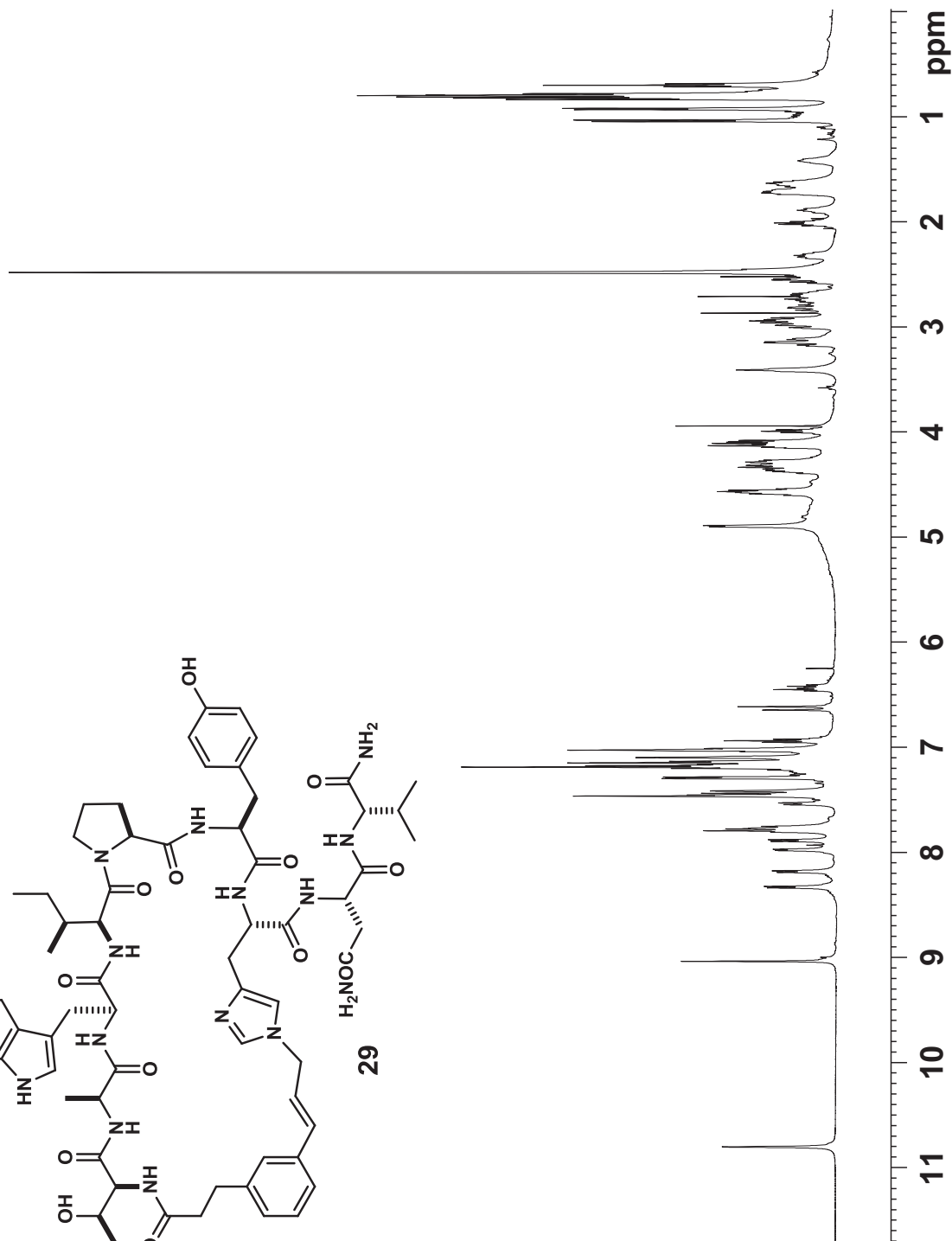
F2 - Processing parameters
SI         131072
SF         125.7577892 MHz
WDW        0
SSB        0
LB         1.00 Hz
GB         0
PC         1.40
  
```



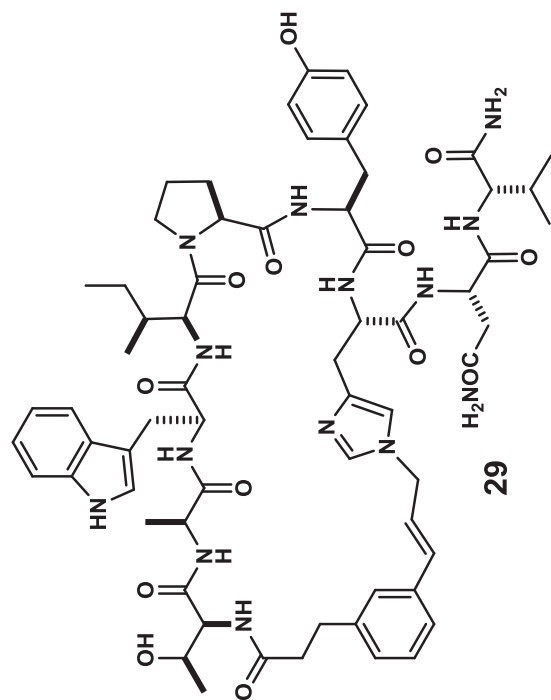
Cyclic-Thr-Ala-Trp-Ile-Pro-Tyr-His-Asn-Val (29):



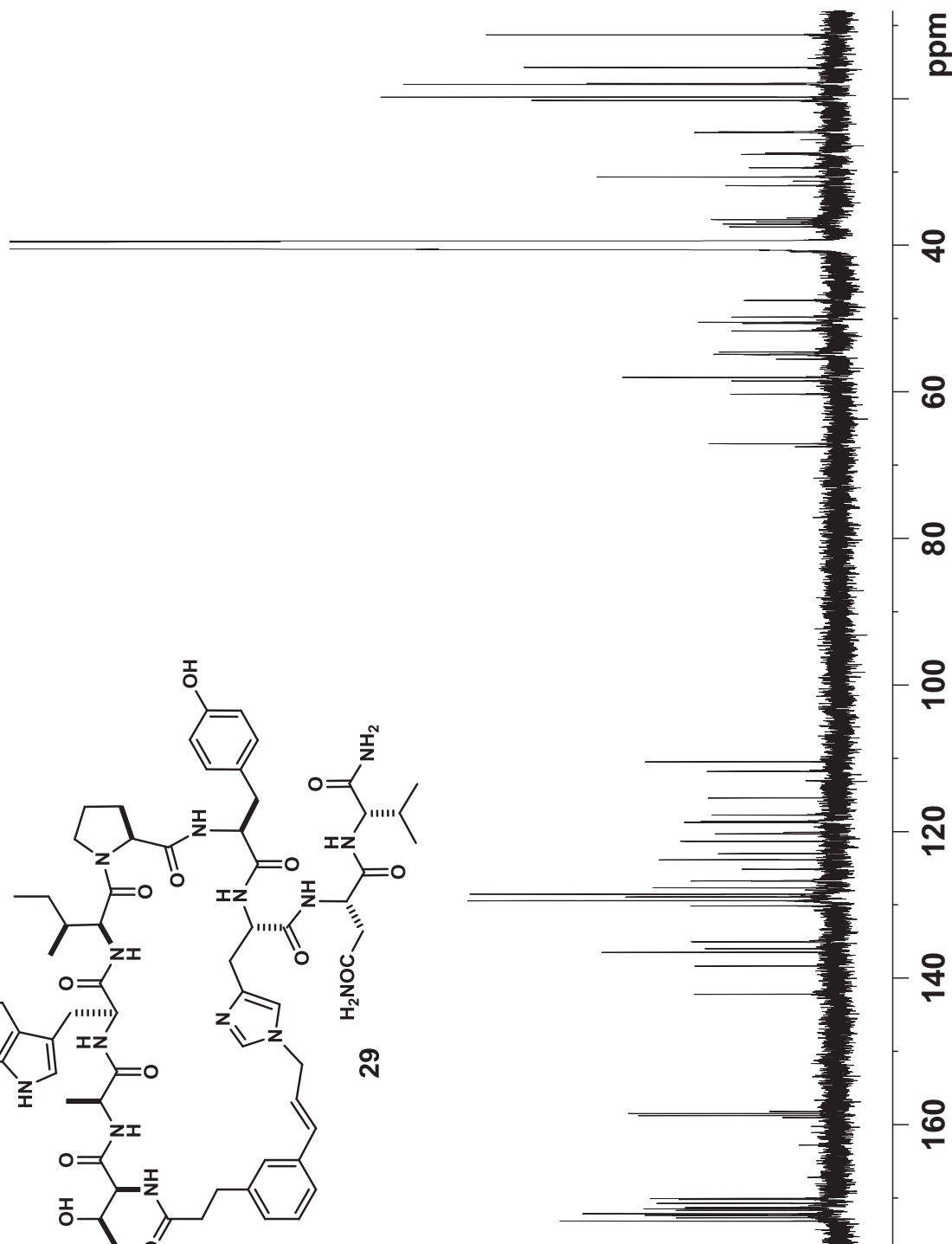
Current Data Parameters
NAME K1-4-184B
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20120419
Time_ 19.16
INSTRUM av500
PROBHD 5 mm DCH 13C-1
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 8
DS 0
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.276799 sec
RG 160.04
DW 50.000 usec
DE 10.00 usec
TE 296.0 K
D1 2.0000000 sec
TD0 1
===== CHANNEL f1 =====
NUC1 1H
P1 10.00 usec
PLW1 13.5000000 W
SFO1 500.1330008 MHz
F2 - Processing parameters
SI 65536
SF 500.1300146 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

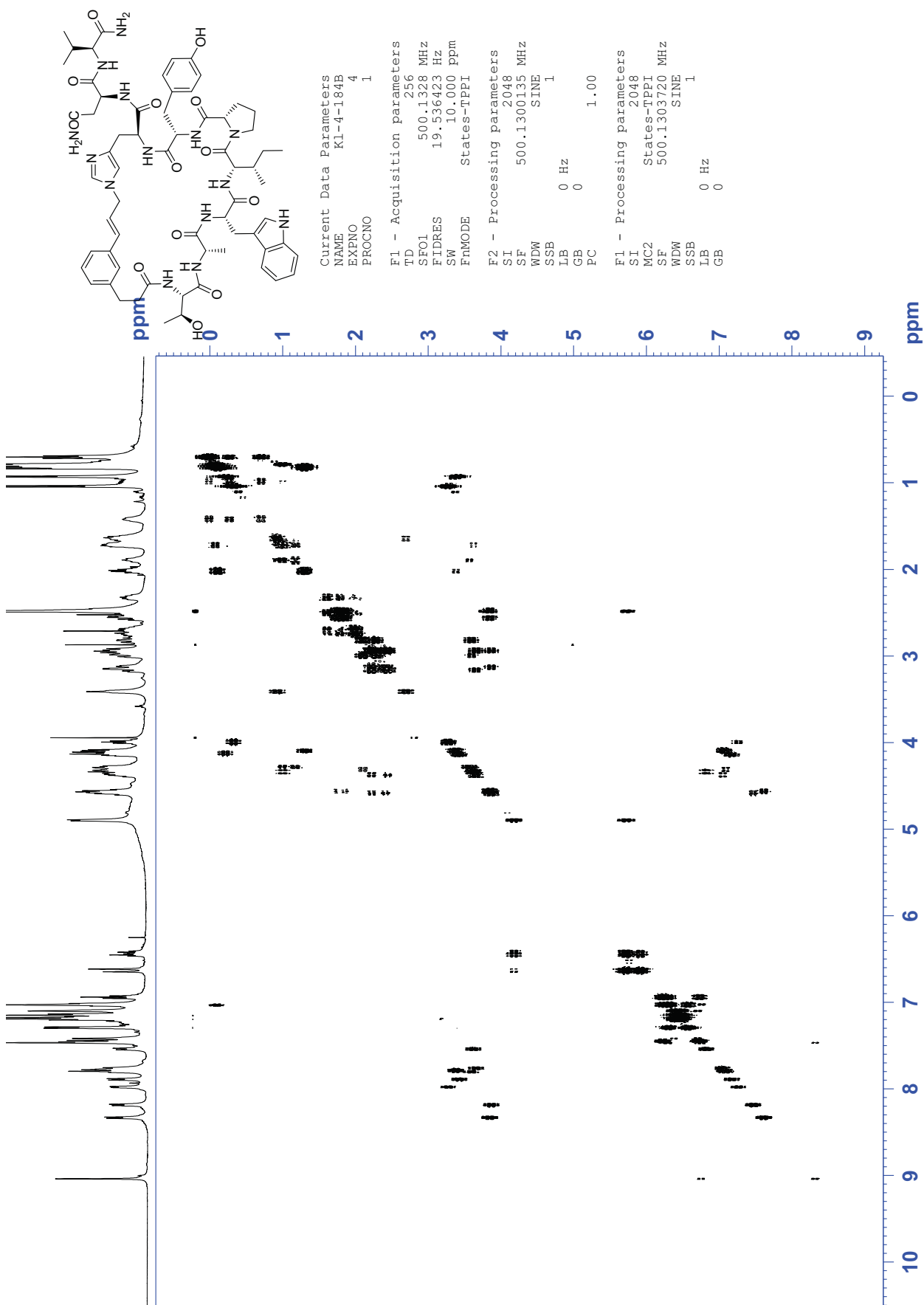


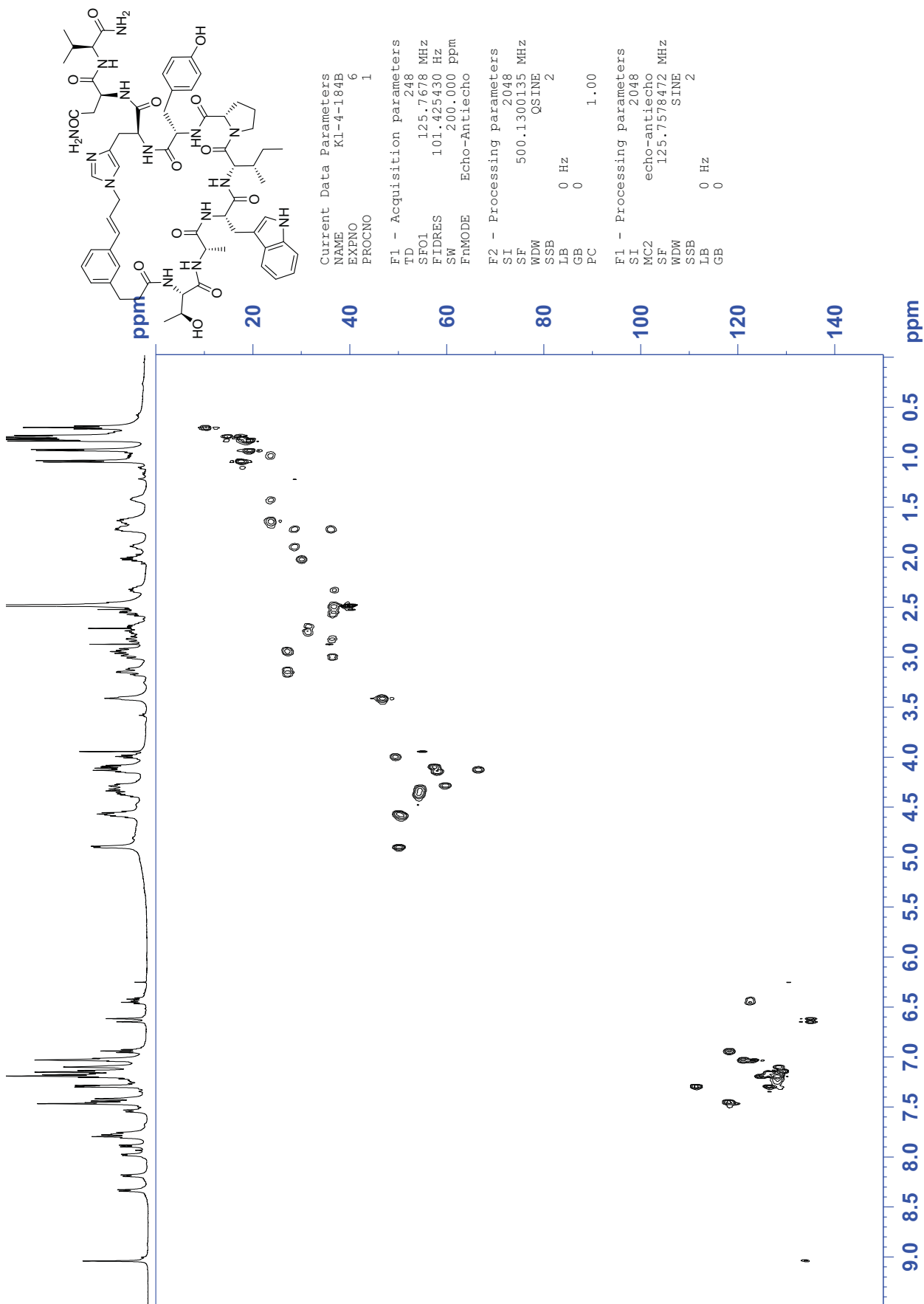
Cyclic-Thr-Ala-Trp-Ile-Pro-Tyr-His-Asn-Val (29):



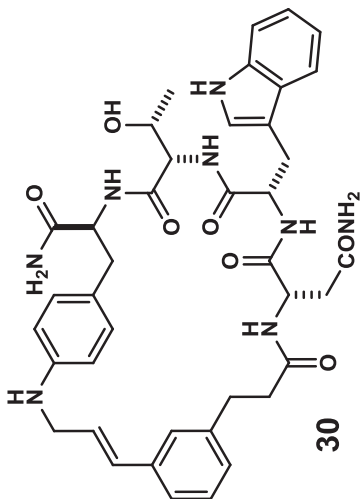
Current Data Parameters
 NAME K1-4-184B
 EXPNO 2
 PROCNO 1
 F2 - Acquisition Parameters
 Date_ 20120419
 Time_ 19:18
 INSTRUM av500
 PROBHD 5 mm DCH 13C-1
 PULPROG zgpg30
 TD 65536
 SOLVENT DMSO
 NS 272
 DS 2
 SWH 31250.000 Hz
 FIDRES 0.476837 Hz
 AQ 1.0485760 sec
 RG 202.91
 DW 16.000 usec
 DE 18.00 usec
 TE 296.0 K
 D1 2.00000000 sec
 d11 0.03000000 sec
 DELTA 1.89999998 sec
 TD0 1
 SF01 125.7722511 MHz
 NUC1 13C
 P1 9.63 usec
 PLW1 23.00000000 W
 SF02 500.1330008 MHz
 NUC2 1H
 CPDPRG12 waltz16
 PCPD2 80.00 usec
 PLW2 13.50000000 W
 PLW12 0.21094000 W
 PLW13 0.13500001 W
 F2 - Processing parameters
 SI 131072
 SF 125.7577892 MHz
 EM
 WDW 0
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40







Cyclic-Asn-Trp-Thr-Phe(4-NH₂) (30):



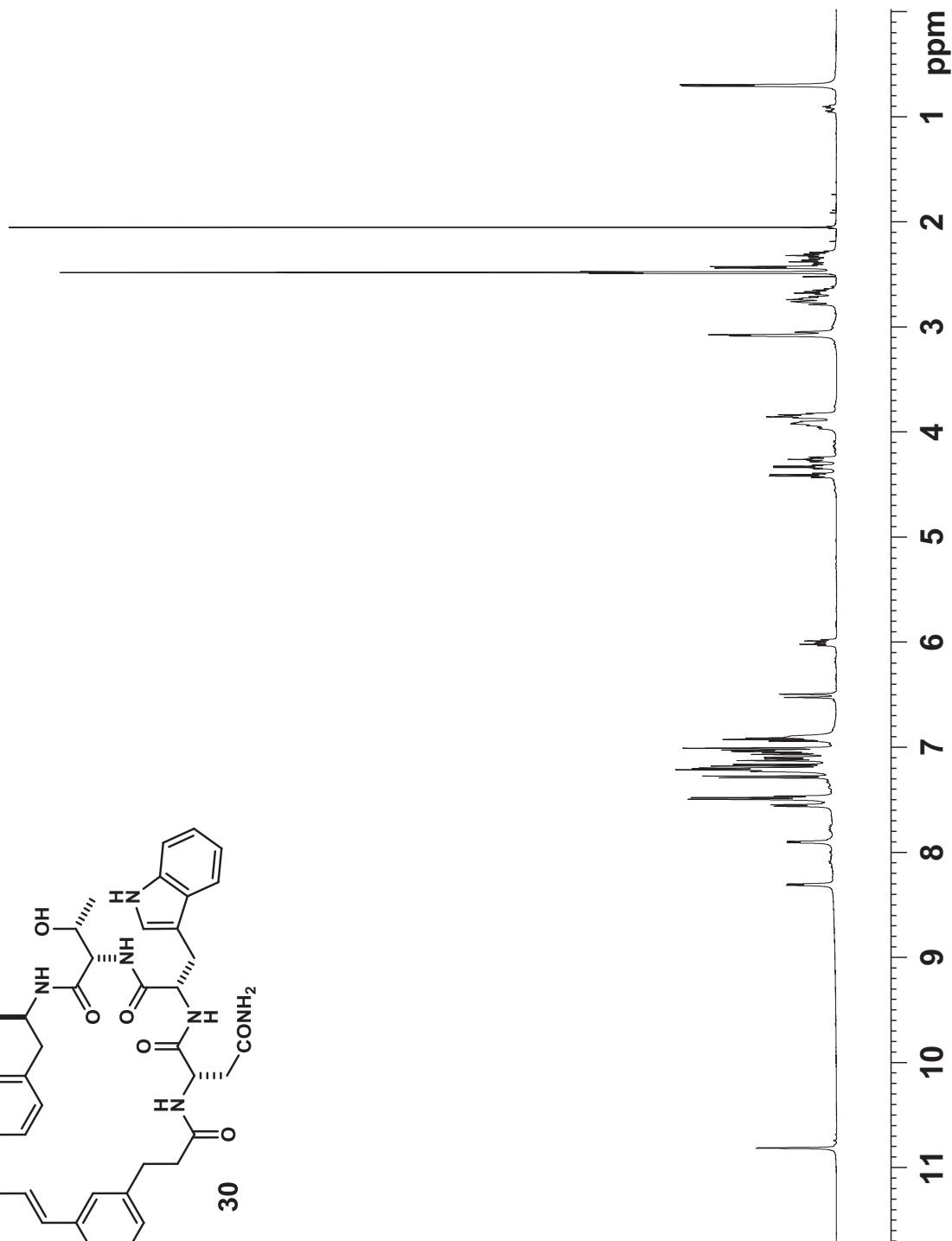
```

Current Data Parameters
NAME      KL-5-158
EXPNO     1
PROCNO    1

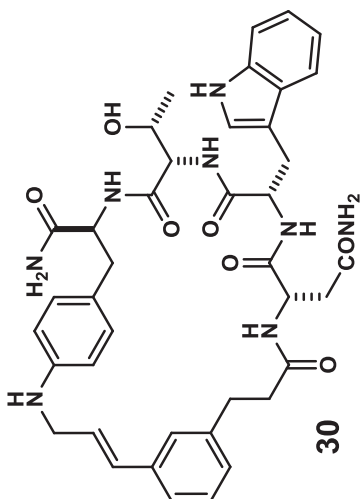
F2 - Acquisition Parameters
Date_     20130416
Time      19.41
INSTRUM   av500
PROBHD    5 mm DCH 13C-1
PULPROG   zg30
TD        65536
SOLVENT   DMSO
NS         8
DS         0
SWH        10000.000 Hz
FIDRES     0.152588 Hz
AQ         3.2767999 sec
RG         11
DW         50.000 usec
DE         10.00 usec
TE         298.0 K
D1         2.0000000 sec
TD0        1

===== CHANNEL f1 =====
SFO1      500.130008 MHz
NUC1      1H
P1         10.00 usec
PLW1      13.5000000 W

F2 - Processing parameters
SI         65536
SF         500.1300146 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00
  
```



Cyclic-Asn-Trp-Thr-Phe(4-NH₂) (30):



```

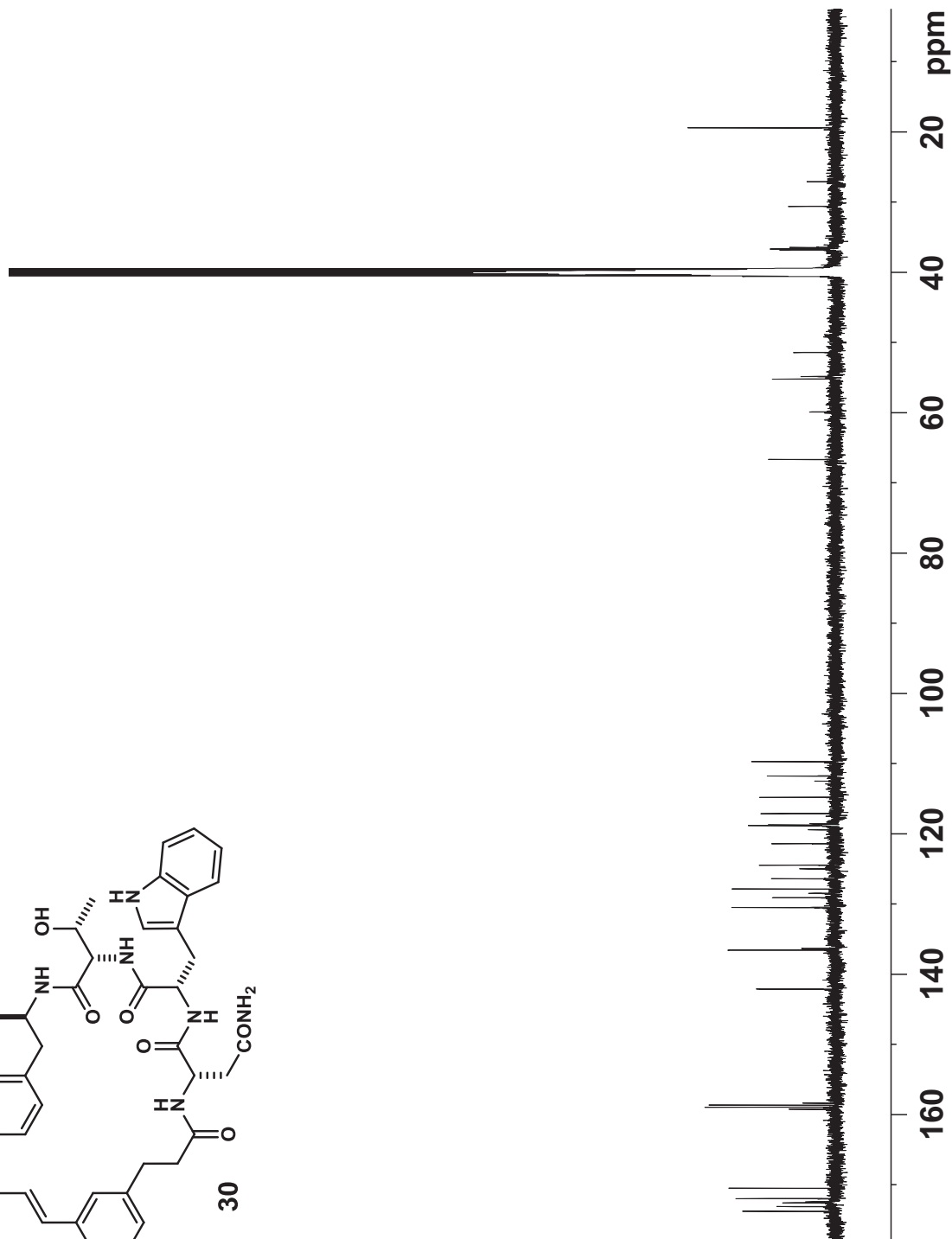
Current Data Parameters
NAME          KL-5-158
EXPNO         2
PROCNO        1

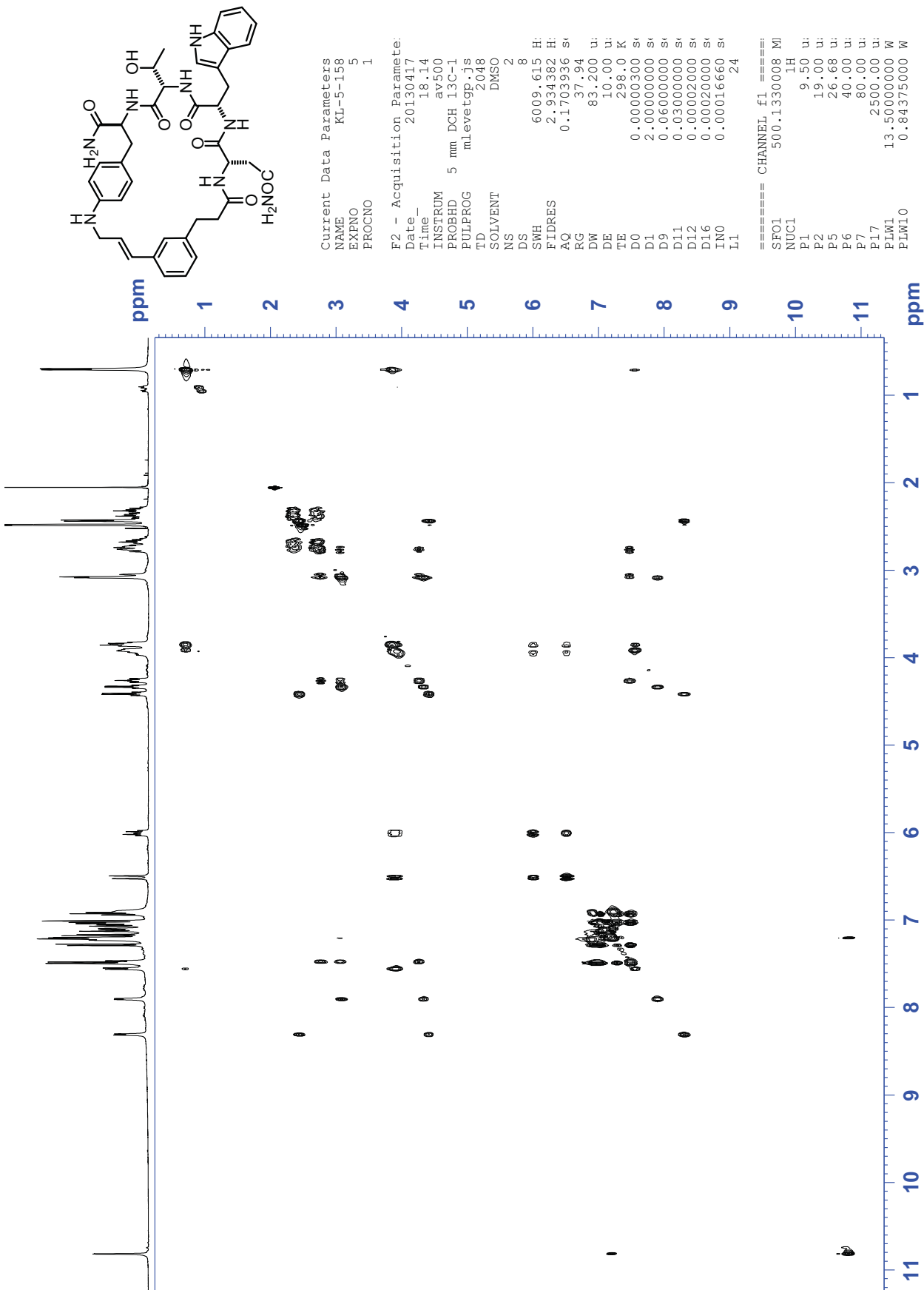
F2 - Acquisition Parameters
Date_         20130416
Time_         19.45
INSTRUM       av500
PROBHD        5 mm DCH 13C-1
PULPROG       zgpg30
TD            65536
SOLVENT       DMSO
NS            82
DS            2
SWH           31250.000 Hz
FIDRES        0.476837 Hz
AQ            1.0485760 sec
RG            202.91
DW            16.000 usec
DE            18.00 usec
TE            298.0 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0           1

===== CHANNEL f1 =====
SFO1          125.772511 MHz
NUC1          13C
P1            9.63 usec
PLW1          23.00000000 W

===== CHANNEL f2 =====
SFO2          500.1330008 MHz
NUC2          1H
CPDPRG2       waltz16
PCPD2         80.00 usec
PLW2          13.50000000 W
PLW12         0.21094000 W
PLW13         0.13500001 W

F2 - Processing parameters
SI            131072
SF            125.7577892 MHz
WDW           EM
SSB           0
LB            1.00 Hz
GB            0
PC            1.40
  
```





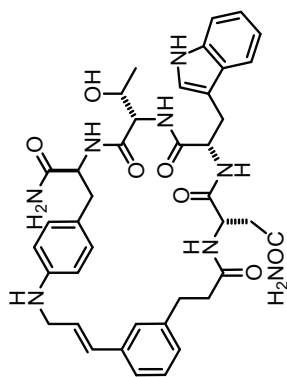
Current Data Parameters
 NAME KL-5-158
 EXPNO 5
 PROCNO 1

F2 - Acquisition Parameters

Date_ 20130417
 Time_ 18.14
 INSTRUM av500
 PROBHD 5 mm DCH 13C-1
 PULPROG mlevetgp.js
 TD 2048
 SOLVENT DMSO
 NS 2
 DS 8
 SWH 6009.615 H:
 FIDRES 2.934382 H:
 AQ 0.1703936 s:
 RG 37.94
 DW 83.200 u:
 DE 10.00 u:
 TE 298.0 K
 D0 0.00000300 s:
 D1 2.00000000 s:
 D9 0.06000000 s:
 D11 0.03000000 s:
 D12 0.00002000 s:
 D16 0.00020000 s:
 INO 0.00016660 s:
 L1 24

===== CHANNEL f1 =====
 SFO1 500.1330008 MHz
 NUC1 1H
 P1 9.50 u:
 P2 19.00 u:
 P5 26.68 u:
 P6 40.00 u:
 P7 80.00 u:
 PL17 2500.00 u:
 PLW1 13.50000000 W
 PLW10 0.84375000 W

===== GRADIENT CHANNEL =====
 GPNAM[1] SINE.100
 GPNAM[2] SINE.100
 GPZ1 30.00 %



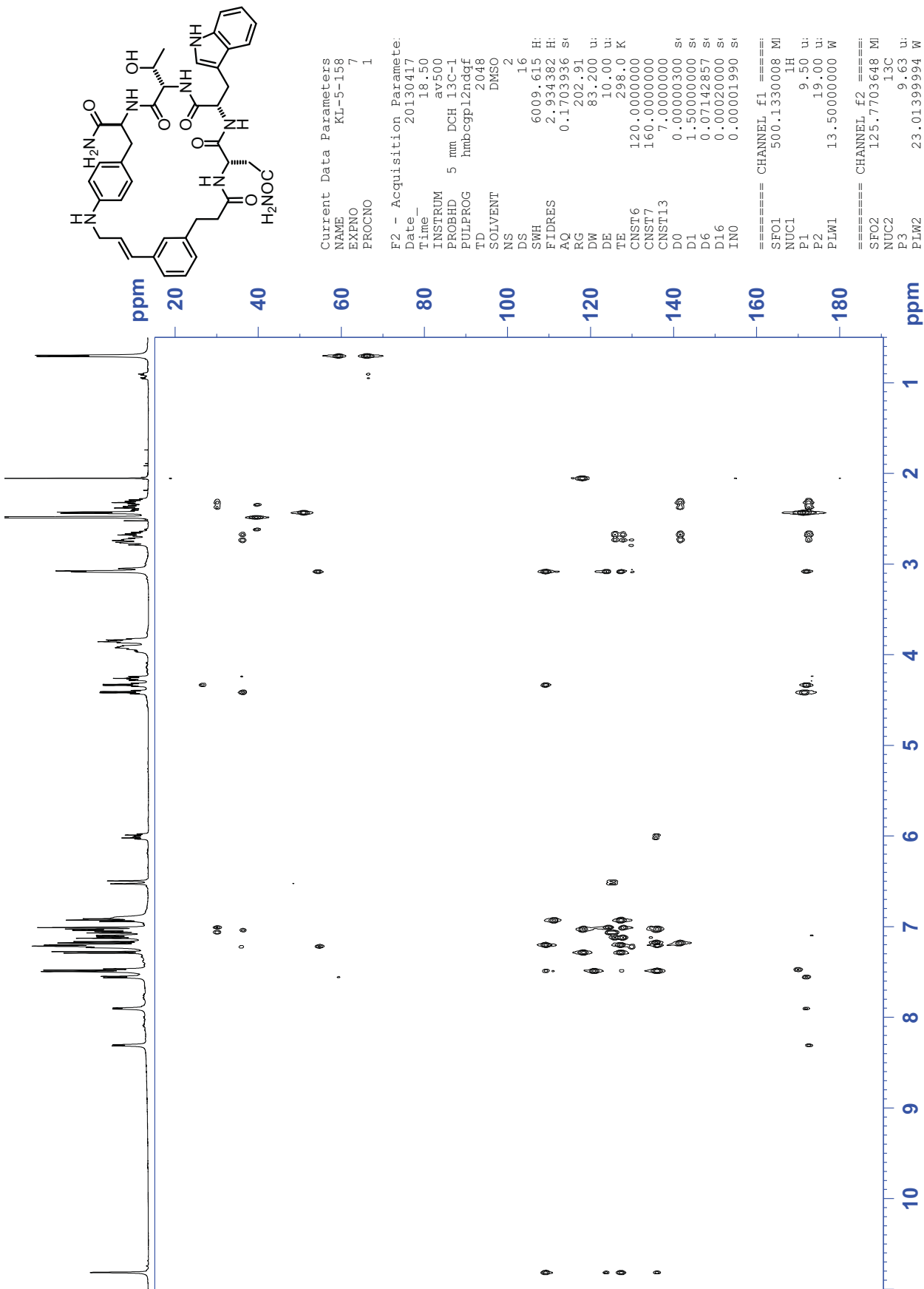
Current Data Parameters	
NAME	KL-5-158
EXPNO	6
PROCNO	1

F2 - Acquisition Paramete:

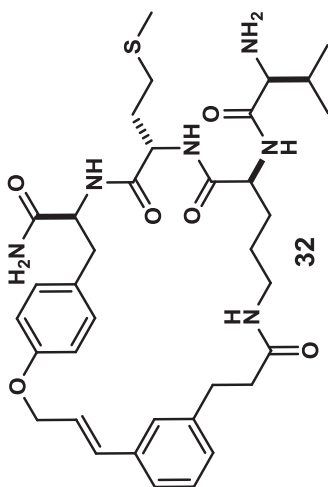
Date_	20130417
Time	18:34
INSTRUM	av500
PROBHD	5 mm DCH 13C-1
PULPRG	hsqcetgpp
TD	2048
SOLVENT	DMSO
NS	2
DS	16
SWH	5000.000 Hz
FIDRES	2.441406 Hz
AQ	0.2048000 s
RQ	202.91
DW	100.000 u:
DE	10.00 u:
TE	298.0 K
CNCSNT2	145.00000000
D0	0.00000300 s
D1	1.50000000 s
D4	0.00172414 s
D11	0.03000000 s
D13	0.00000400 s
D16	0.00020000 s
D21	0.00345000 s
INO	0.00001990 s
ZGPTNS	

```
===== CHANNEL f1 =====
SFO1      500.1325007 M
NUC1      1H
P1         9.50 u:
P2        19.00 u:
P28
PLW1      0 usec
          13.50000000 W
```

```
===== CHANNEL f2 =====
SF02      125.7678496 MHz
NUC2      13C
CPDPRG[2  garp
P3         9.63 u;
P4        19.26 u;
```



Cyclic-Val-Orn-Met-Try (32):



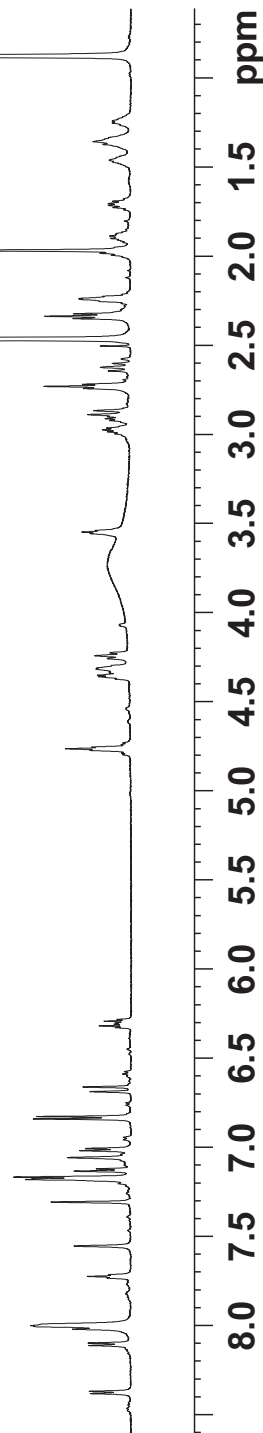
```

Current Data Parameters
NAME      KL-5-156C_AV600
EXPNO     1
PROCNO    1

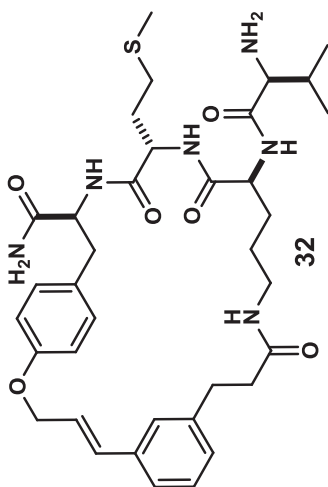
F2 - Acquisition Parameters
Date_     20130411
Time      20.12
INSTRUM   av600
PROBHD    5 mm TBI5
PULPROG   zg30
TD        65536
SOLVENT   DMSO
NS         8
DS         0
SWH        12376.237 Hz
FIDRES     0.188846 Hz
AQ         2.6476543 sec
RG         181
DW         40.400 usec
DE         6.50 usec
TE         294.1 K
D1         2.0000000 sec
TD0        1

===== CHANNEL f1 =====
NUC1       1H
P1         9.75 usec
PL1        -2.00 dB
PL1W       39.81071854 W
SFO1       600.136008 MHz

F2 - Processing parameters
SI         65536
SF         600.1300273 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.40
  
```



Cyclic-Val-Orn-Met-Try (32):



```

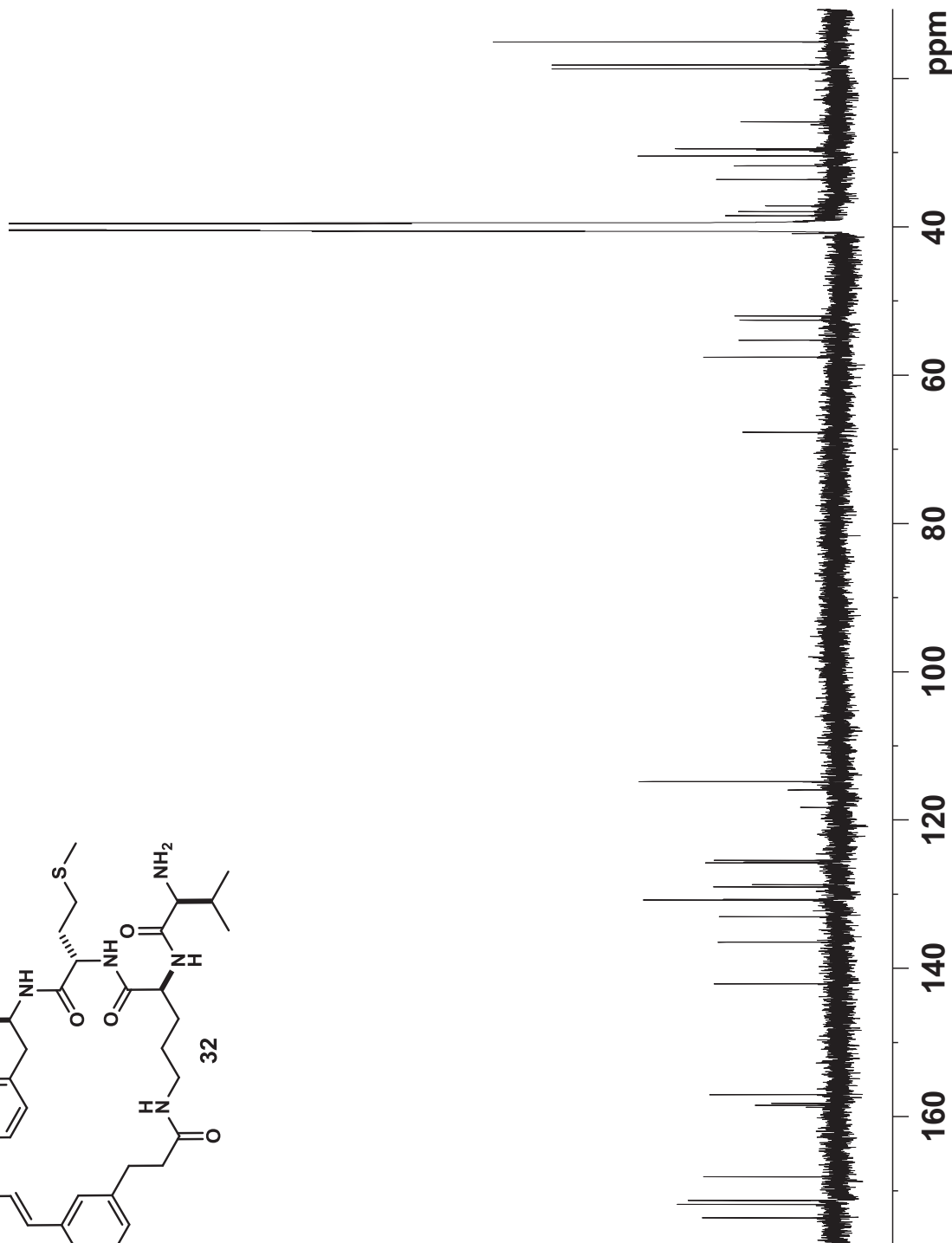
Current Data Parameters
NAME          KI-5-156C
EXPNO         4
PROCNO        1

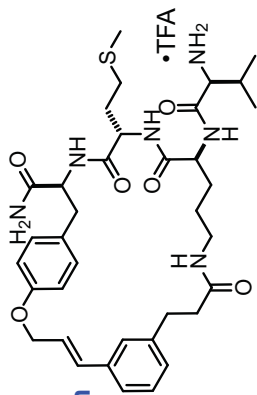
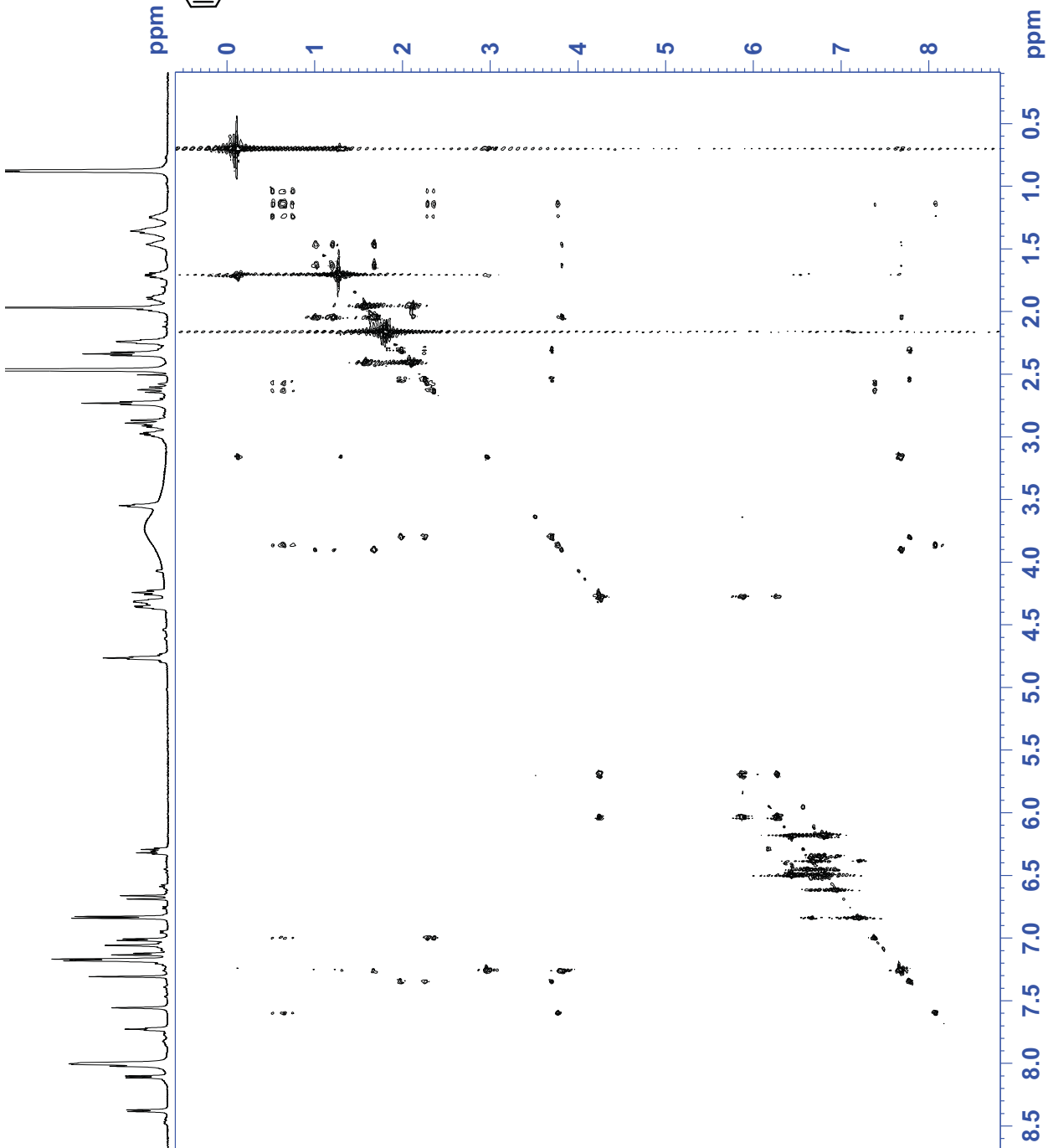
F2 - Acquisition Parameters
Date_         20130425
Time_         19.49
INSTRUM       av500
PROBHD        5 mm DCH 13C-1
PULPROG       zgpg30
TD            65536
SOLVENT       DMSO
NS            487
DS            2
SWH           31250.000 Hz
FIDRES        0.476837 Hz
AQ            1.0485760 sec
RG            202.91
DW            16.000 usec
DE            18.00 usec
TE            298.0 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0           1

===== CHANNEL f1 =====
SFO1          125.772511 MHz
NUC1          13C
P1            9.63 usec
PLW1          23.00000000 W

===== CHANNEL f2 =====
SFO2          500.1330008 MHz
NUC2          1H
CPDPRG2       waltz16
PCPD2         80.00 usec
PLW2          13.50000000 W
PLW12         0.21094000 W
PLW13         0.13500001 W

F2 - Processing parameters
SI            131072
SF            125.7577892 MHz
WDW           EM
SSB           0
LB            1.00 Hz
GB            0
PC            1.40
  
```



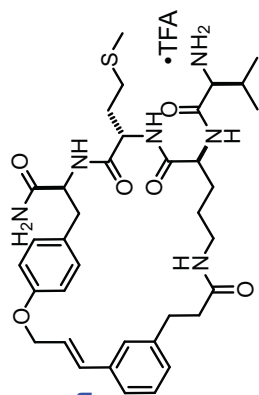
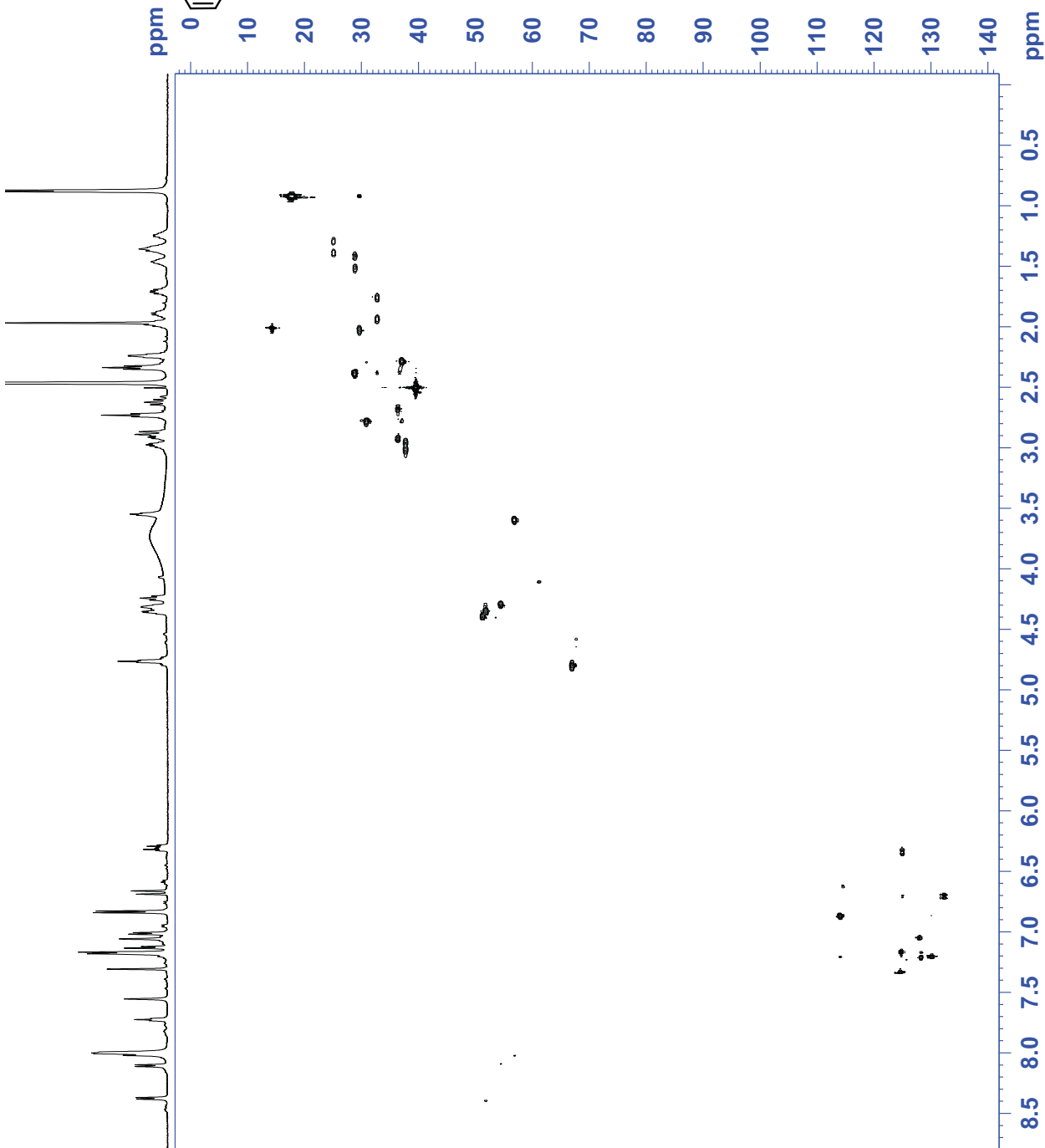


Current Data Parameters
 NAME KL-S-156C_AV600
 EXPNO 3
 PROCNO 1

F1 - Acquisition parameters
 TD 600
 SFO1 600.133 MHz
 FIDRES 10.002216 Hz
 SW 10.000 ppm
 FMODE Echo-Antiecho

F2 - Processing parameters
 SI 1024
 SF 600.1300273 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 1024
 MC2 echo-antiecho
 SF 600.1300273 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0



Current Data Parameters
 NAME KL-S-156C_AV600
 EXPNO 5
 PROCNO 1

F1 - Acquisition parameters
 TD 512

SFO1 150.9134 MHz
 FIDRES 47.160427 Hz
 SW 160.000 ppm

FMODE Echo-Antiecho

F2 - Processing parameters

SI 4096

SF 600.130051 MHz

WDW EM

SSB 0

LB 1.00 Hz

GB 0

PC 1.40

F1 - Processing parameters

SI 4096

MC2 echo-antiecho

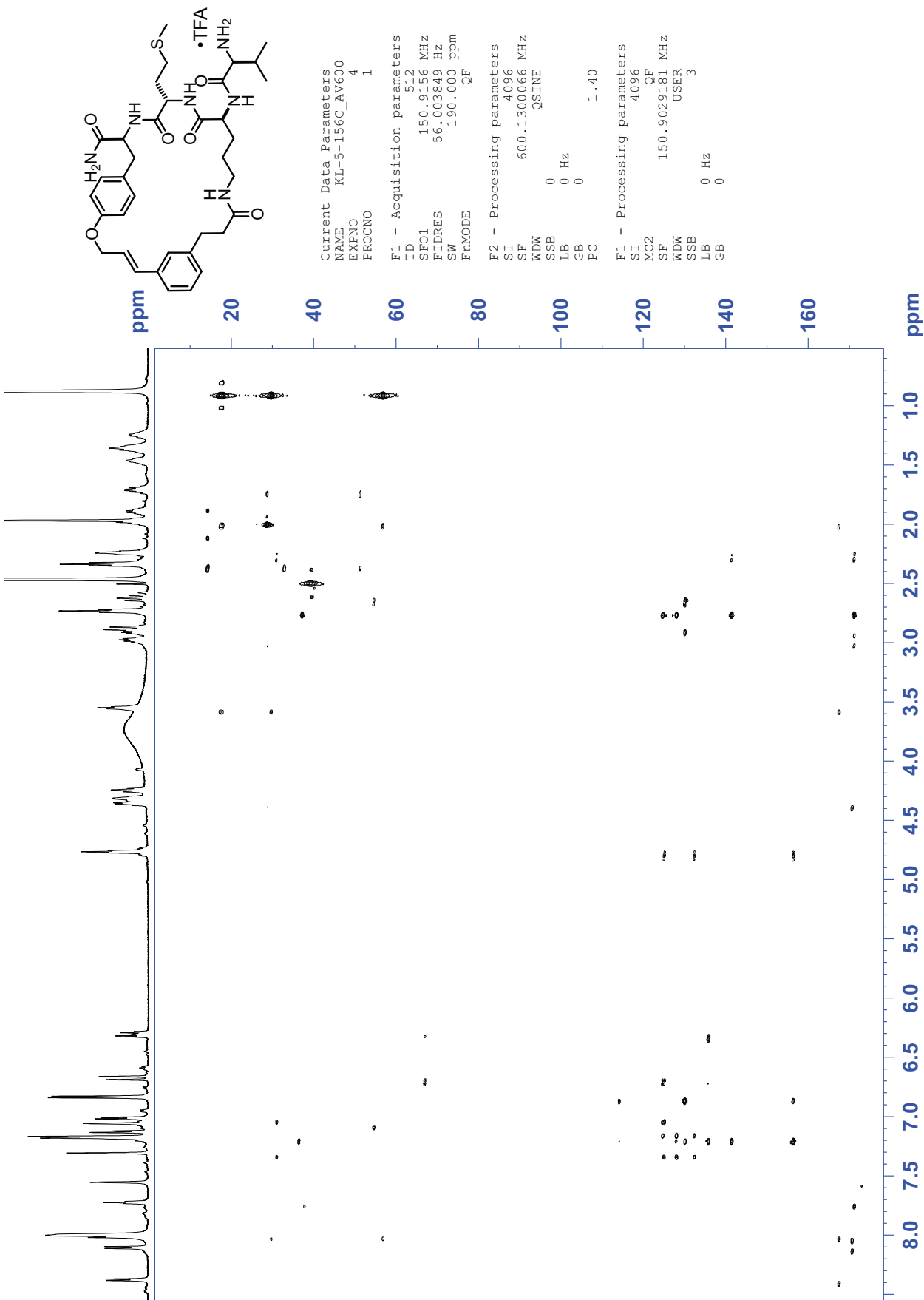
SF 150.902931 MHz

WDW TRAP

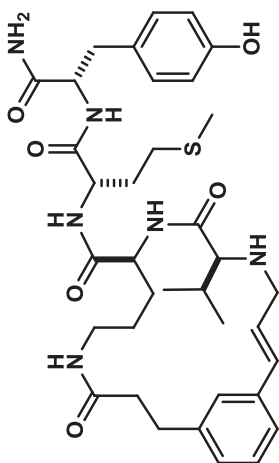
SSB 2

LB 0 Hz

GB 0



Cyclic-Val-Orn-Met-Try (33):



33

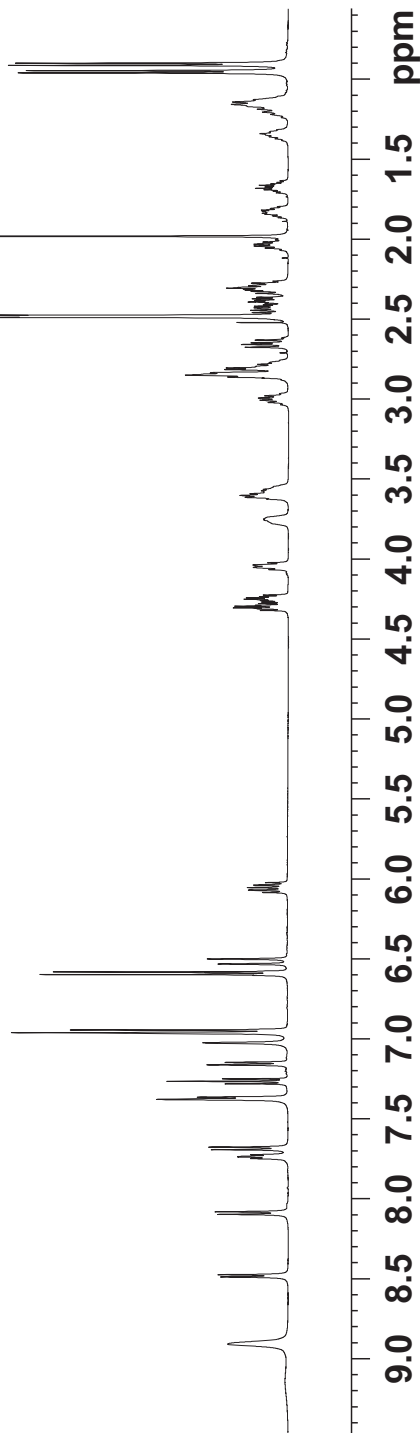
```

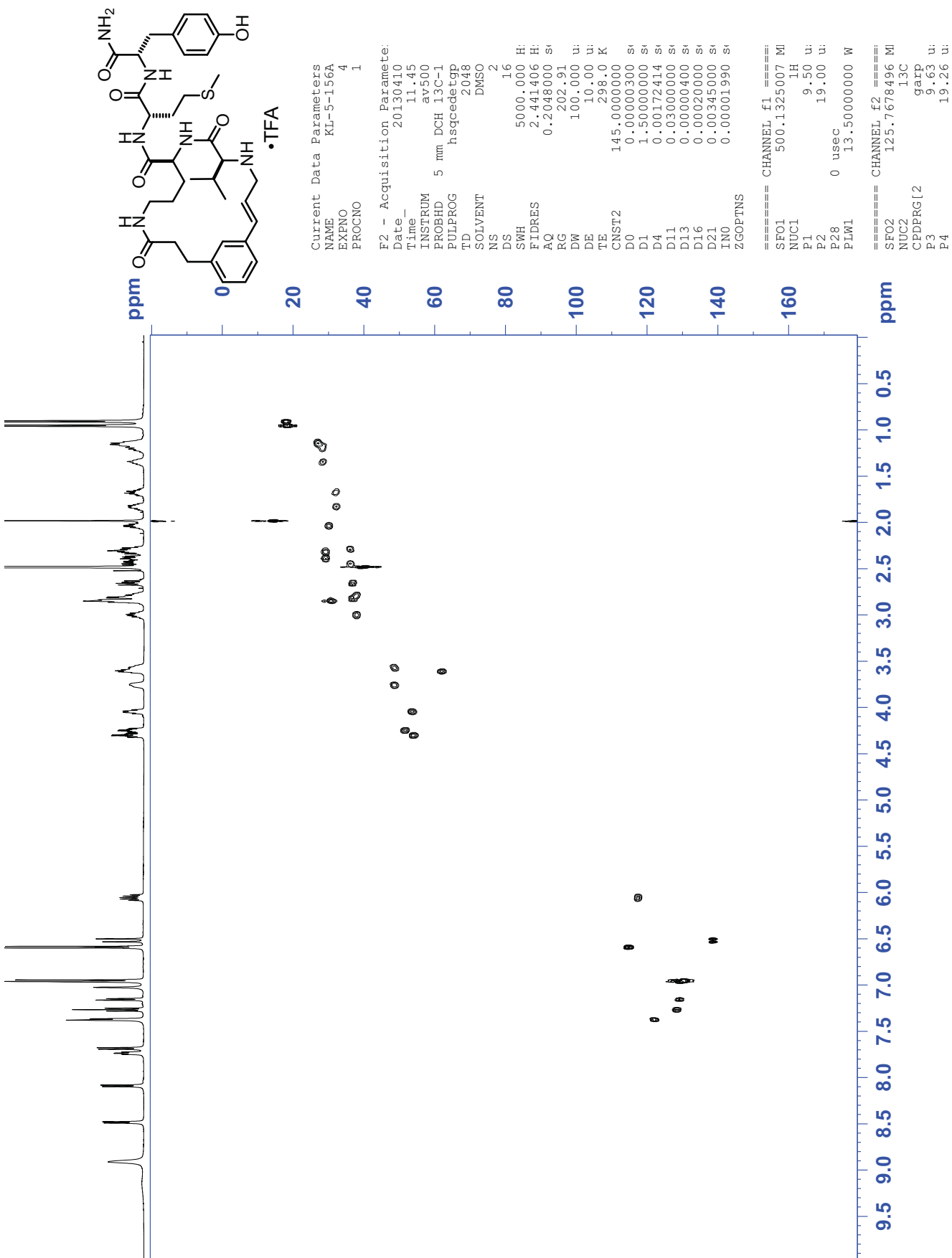
Current Data Parameters
NAME      KI-5-156A
EXPNO     1
PROCNO    1

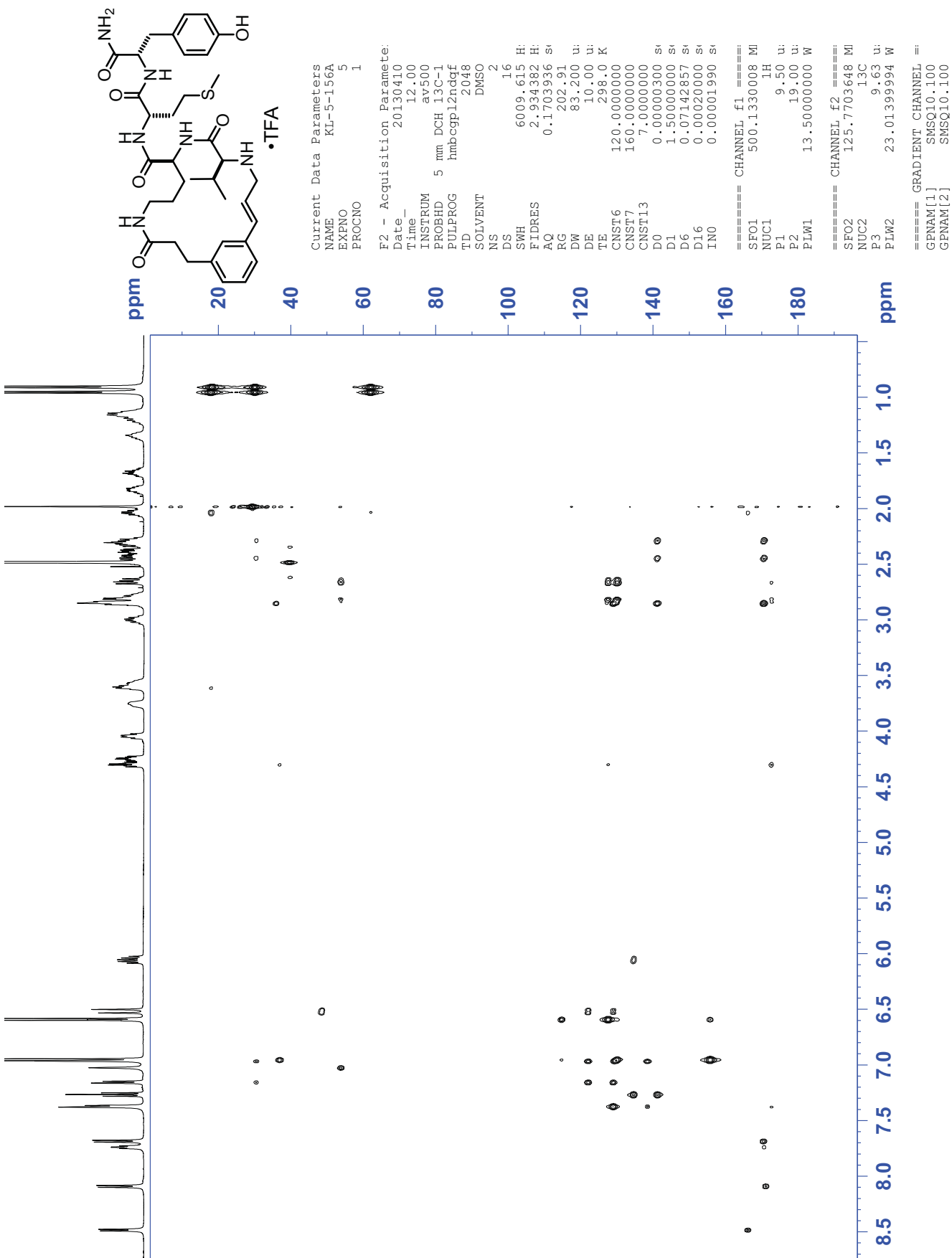
F2 - Acquisition Parameters
Date_     20130410
Time      11:40
INSTRUM   av500
PROBHD    5 mm DCH 13C-1
PULPROG   zg30
TD         65536
SOLVENT   DMSO
NS         8
DS         0
SWH        10000.000 Hz
FIDRES     0.152588 Hz
AQ         3.2767999 sec
RG         72.5
DW         50.000 usec
DE         10.00 usec
TE         298.0 K
D1         2.00000000 sec
TD0        1

===== CHANNEL f1 =====
SFO1      500.1330008 MHz
NUC1       1H
P1         10.00 usec
PLW1      13.50000000 W

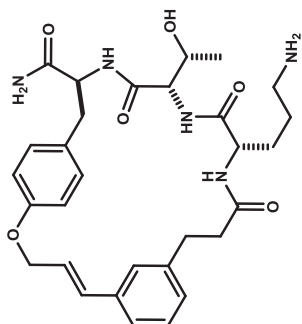
F2 - Processing parameters
SI         65536
SF         500.1300146 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00
    
```







Cyclic-Orn-Thr-Try (35):



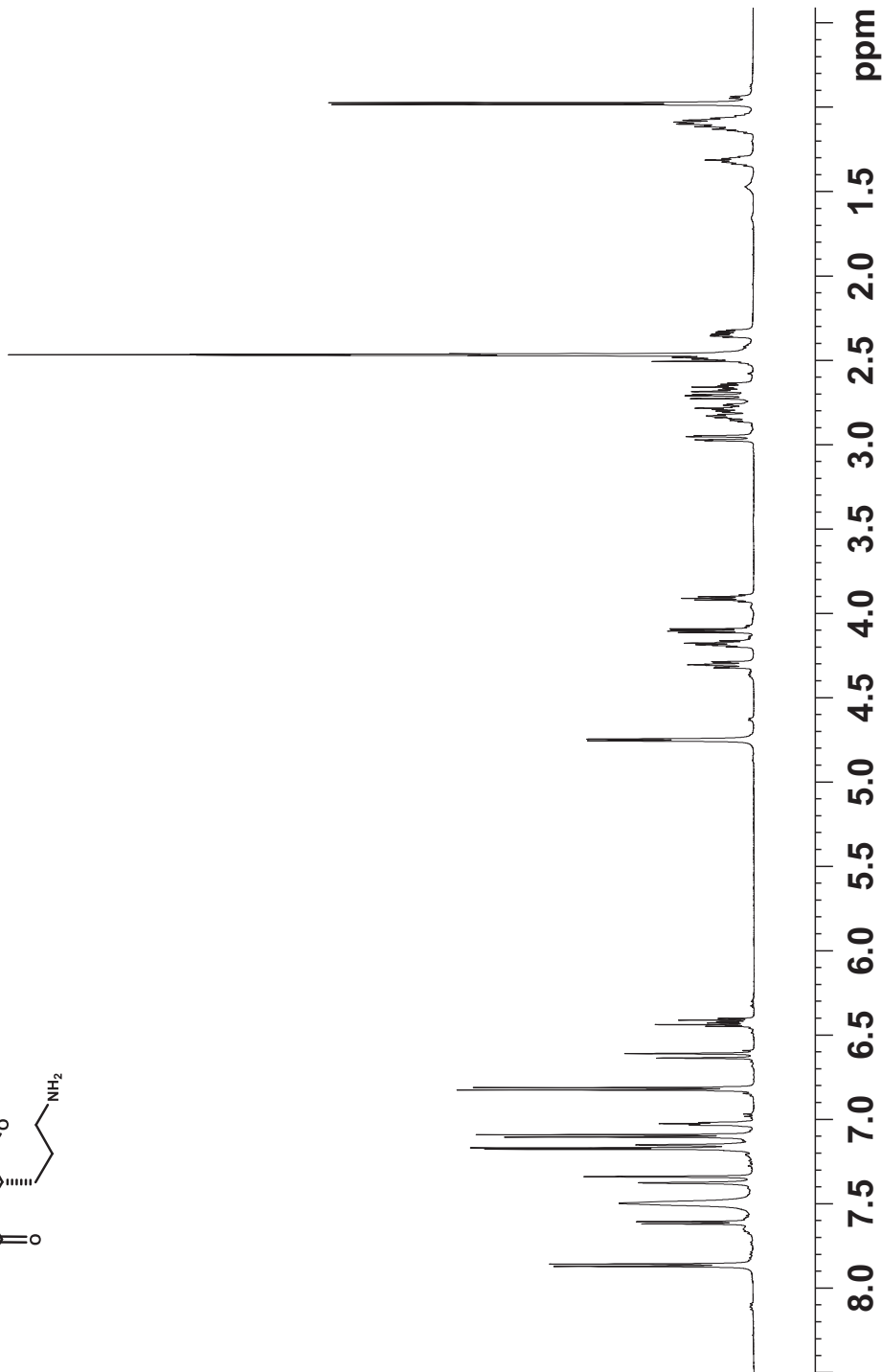
```

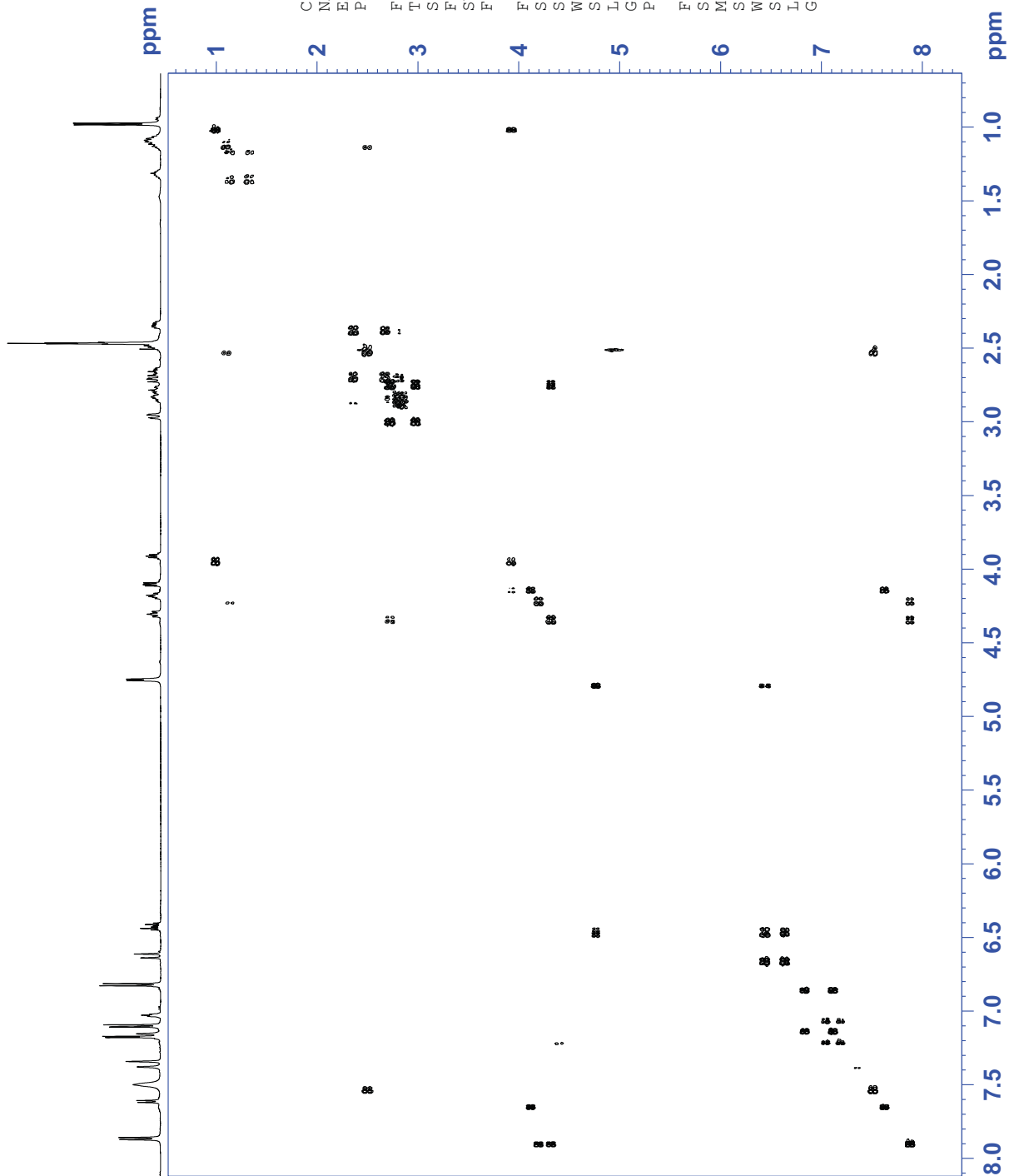
Current Data Parameters
NAME      TR4-169A 2
EXPNO     4
PROCNO    1

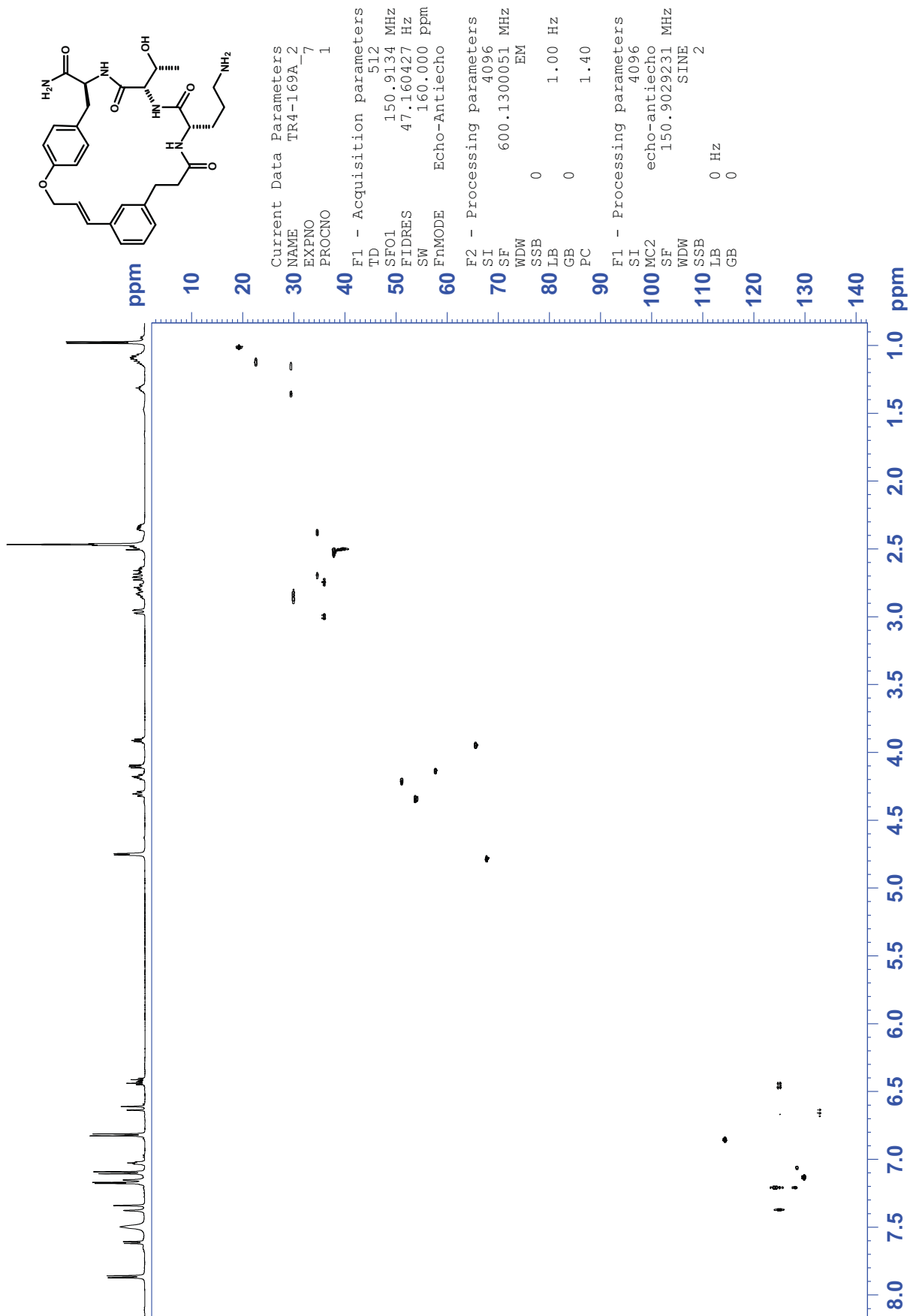
F2 - Acquisition Parameters
Date_     20130428
Time      18.14
INSTRUM   av600
PROBHD    5 mm TBI5
PULPROG   zgpg
TD         65536
SOLVENT    DMSO
NS         8
DS         0
SWH        6009.615 Hz
FIDRES     0.091699 Hz
AQ         5.4525952 sec
RG         64
DW         83.200 usec
DE         6.50 usec
TE         298.0 K
D1         2.00000000 sec
D12        0.00002000 sec
TD0        1

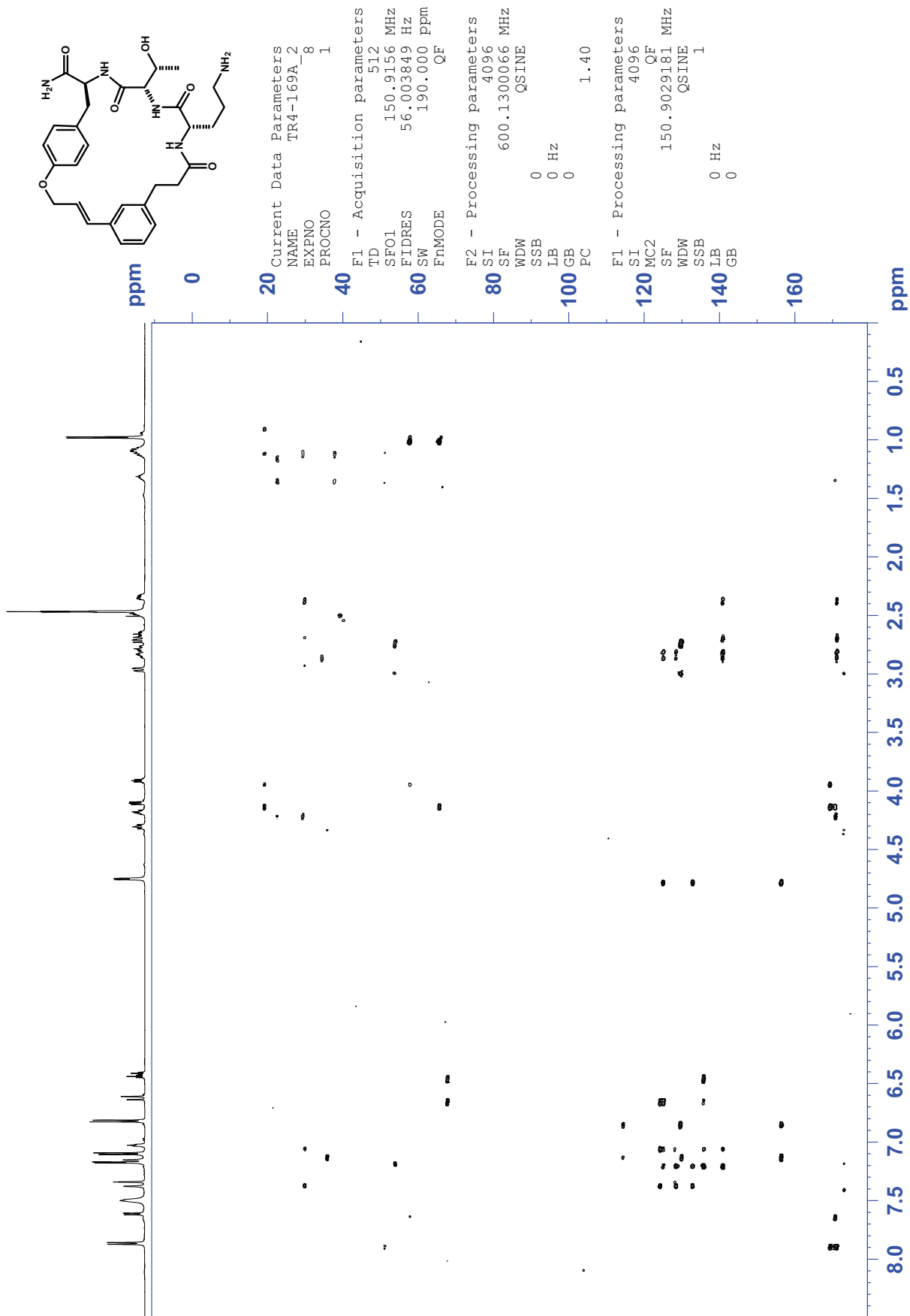
===== CHANNEL f1 =====
NUC1       1H
P1         9.70 usec
PL1        -2.00 dB
PL9        52.24 dB
PL1W       39.81071854 W
PL9W       0.00014997 W
SFO1       600.1321531 MHz

F2 - Processing parameters
SI         65536
SF         600.1300273 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00
    
```

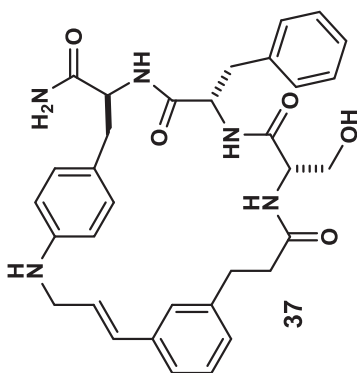








Cyclic-Ser-Phe-Phe(4-NH₂) (37):



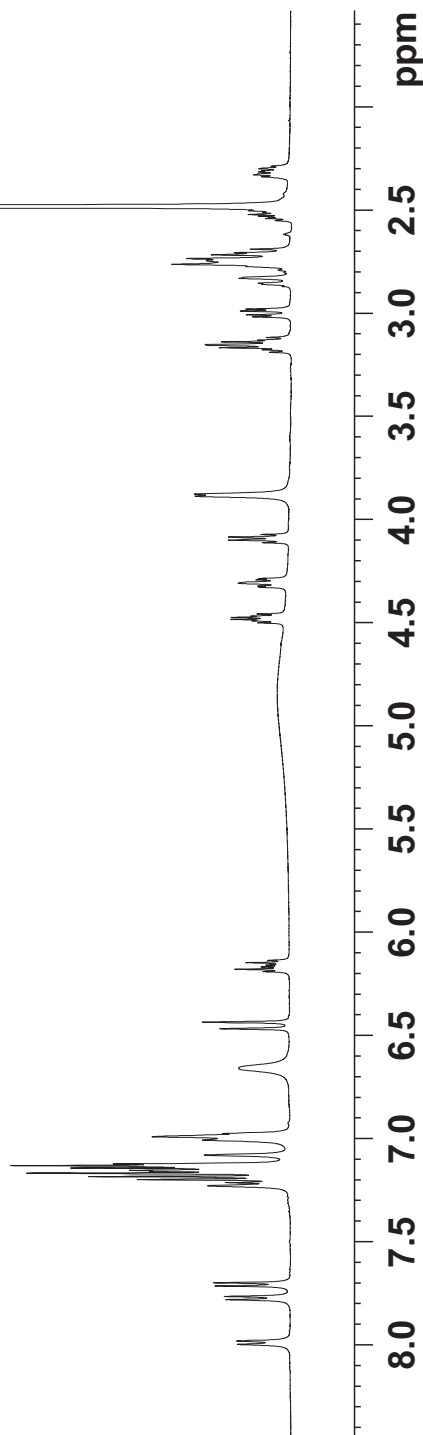
```

Current Data Parameters
NAME          KL-5-10
EXPNO         1
PROCNO        1

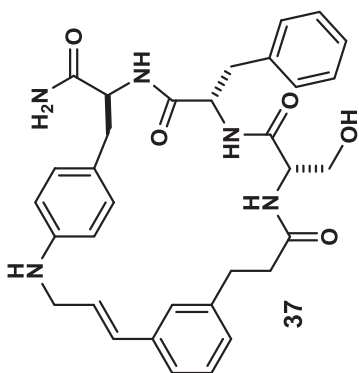
F2 - Acquisition Parameters
Date_         20120815
Time_         12.06
INSTRUM       av500
PROBHD        5 mm DCH 13C-1
PULPROG       zg30
TD            65536
SOLVENT       DMSO
NS            8
DS            0
SWH           10000.000 Hz
FIDRES        0.152588 Hz
AQ            3.2767999 sec
RG            202.91
DW            50.000 usec
DE            10.00 usec
TE            298.0 K
D1            2.00000000 sec
TD0           1

===== CHANNEL f1 =====
NUC1          1H
P1            10.00 usec
PLW1          13.50000000 W
SFO1          500.1330008 MHz

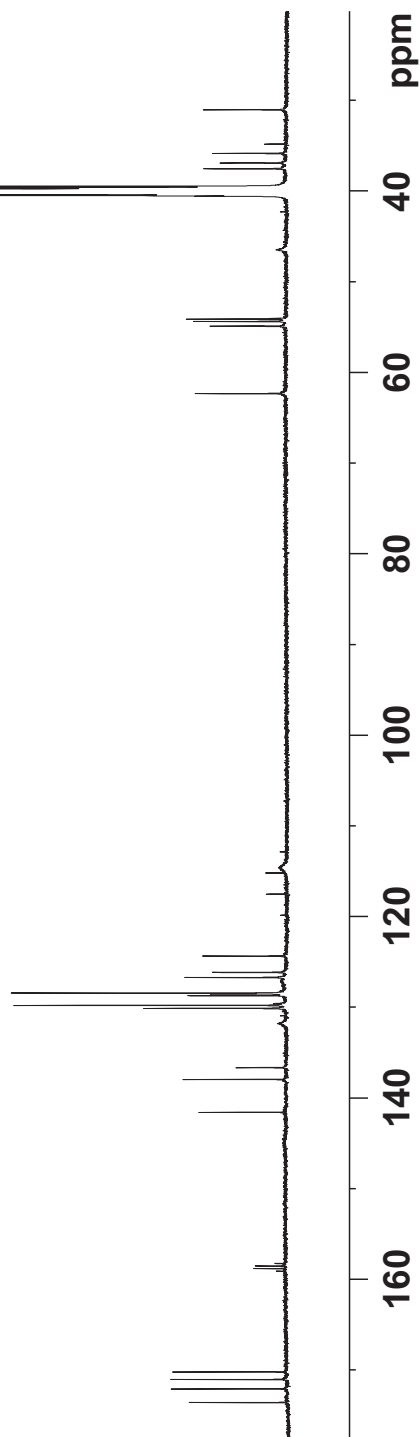
F2 - Processing parameters
SI            65536
SF            500.1300146 MHz
WDW           EM
SSB           0
LB            0.30 Hz
GB            0
PC            1.00
  
```

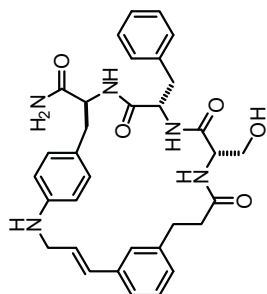
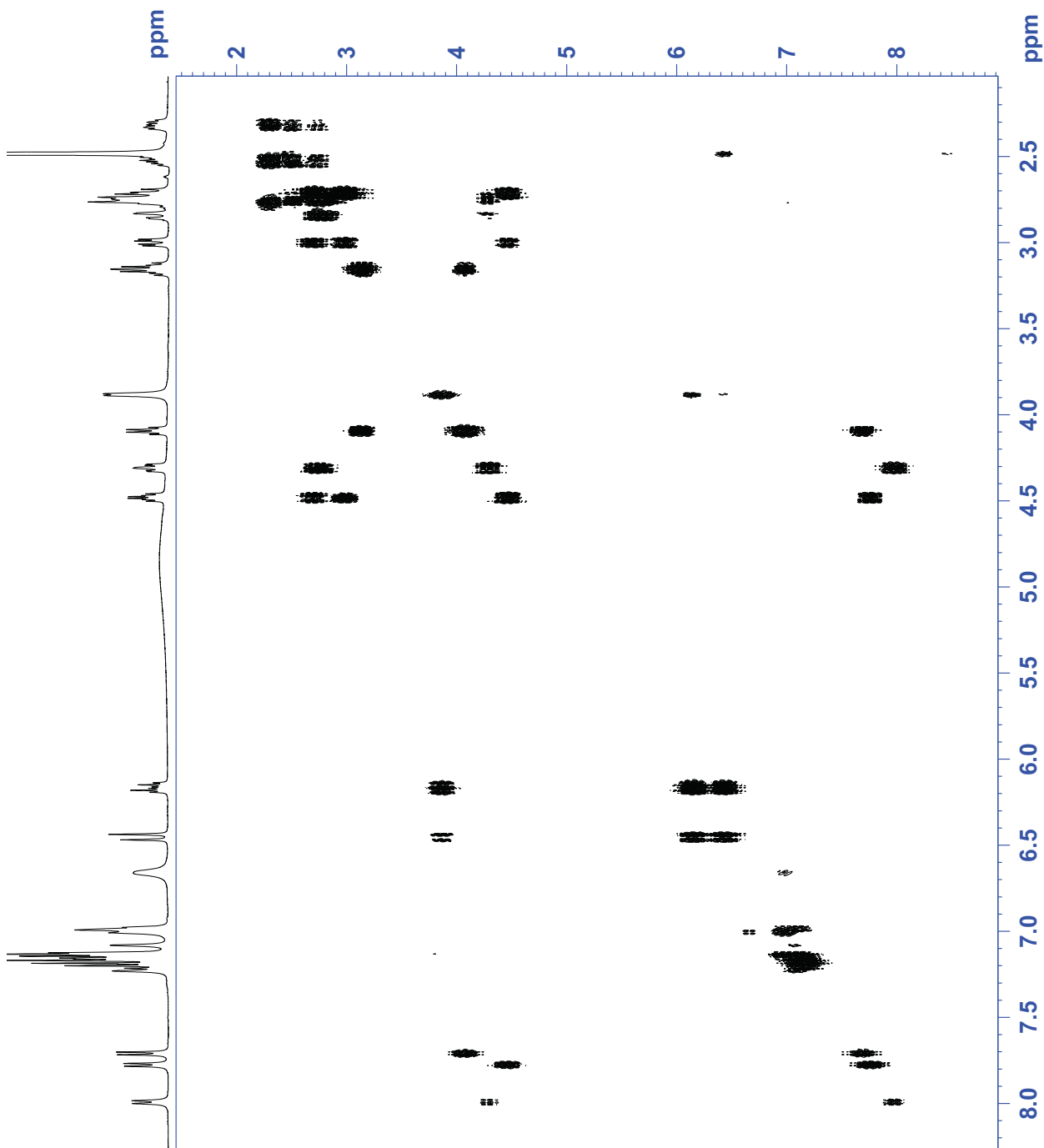


Cyclic-Ser-Phe-Phe(4-NH₂) (37):



Current Data Parameters
NAME KL-5-10
EXPNO 12
PROCNO 1
F2 - Processing parameters
SI 131072
SF 125.7577892 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40



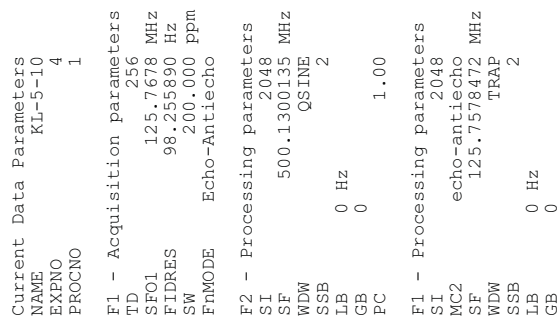


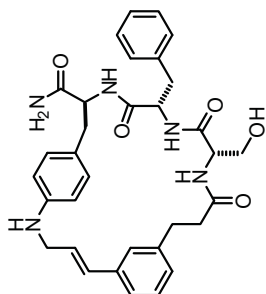
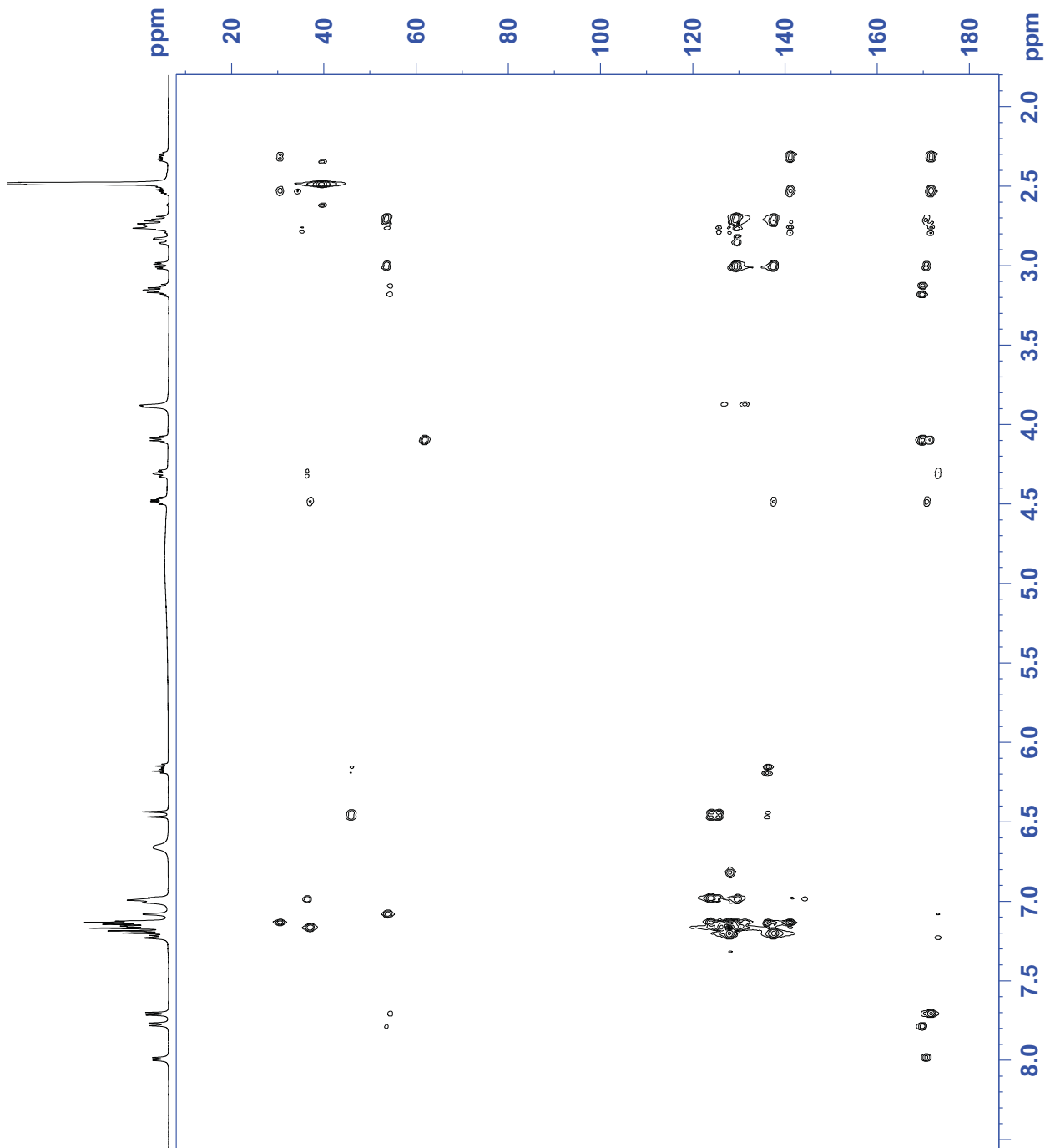
Current Data Parameters
 NAME KL-5-10
 EXPNO 3
 PROCNO 1

F1 - Acquisition parameters
 TD 256
 SFO1 500.1328 MHz
 FIDRES 19.536423 Hz
 SW 10.000 ppm
 FMODE States-TpPI

F2 - Processing parameters
 SI 2048
 SF 500.1300135 MHz
 SINE
 WDW 1
 SSB 0 Hz
 LB 0
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 2048
 MC2 States-TpPI
 SF 500.1300216 MHz
 SINE
 WDW 1
 SSB 0 Hz
 LB 0
 GB 0

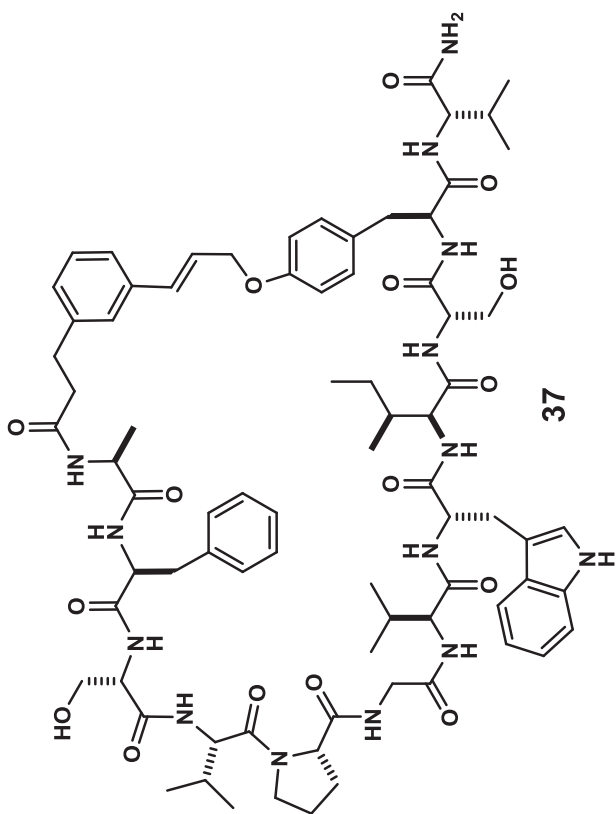




Current Data Parameters
 NAME KL-5-10
 EXPNO 9
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20120816
 Time_ 19.26
 INSTRUM av500
 PROBHD 5 mm DCH 13C-1
 PULPROG hmbcgp1zndqf
 TD 2048
 SOLVENT DMSO
 NS 4
 DS 16
 SWH 6009.615 H:
 FIDRES 2.934382 H:
 AQ 0.1703936 s:
 RG 202.91
 DW 83.200 u:
 DE 10.00 u:
 TE 298.0 K
 CNST6 120.0000000
 CNST7 160.0000000
 CNST13 7.0000000
 d0 0.00000300 s:
 d1 1.50000000 s:
 d6 0.07142857 s:
 d16 0.00020000 s:
 DELTA1 0.00296667 s:
 DELTA2 0.00192500 s:
 DELTA3 0.07022458 s:
 in0 0 sec
 STICNT 256
 d0orig 0.00000300 s:
 phloop 0
 tloop 500.1330008 M:
 SFO1 1H
 NUC1 13C
 P1 10.00 u:
 P2 20.00 u:
 PLW1 13.50000000 W
 SFO2 125.7703648 M:
 NUC2 13C
 P3 9.63 u:
 PLW2 23.01399994 W
 GPNAM[1] SMSQ10.100

Cyclic-Ala-Phe-Ser-Val-Pro-Gly-Val-Trp-Ile-Ser-Tyr-Val (38):



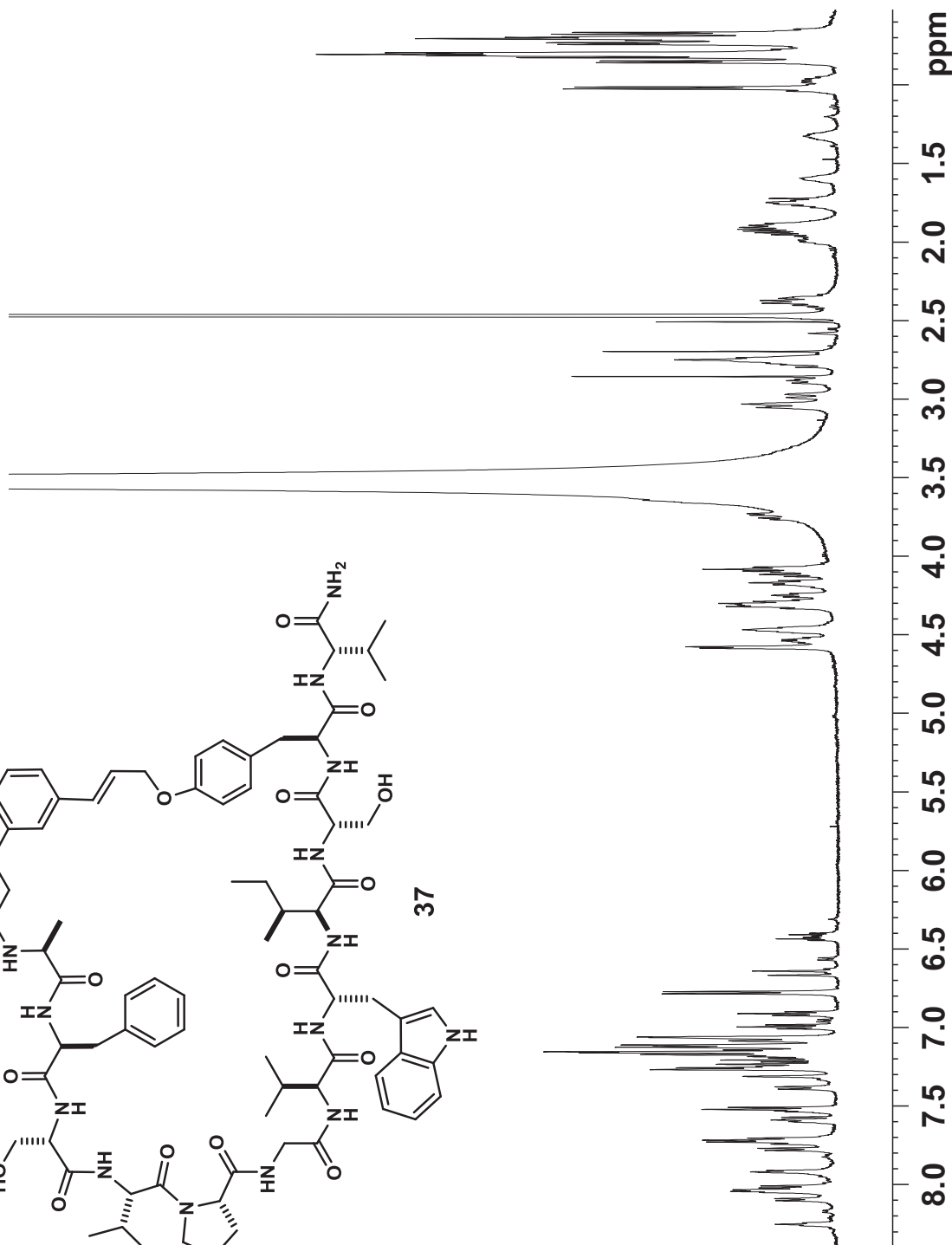
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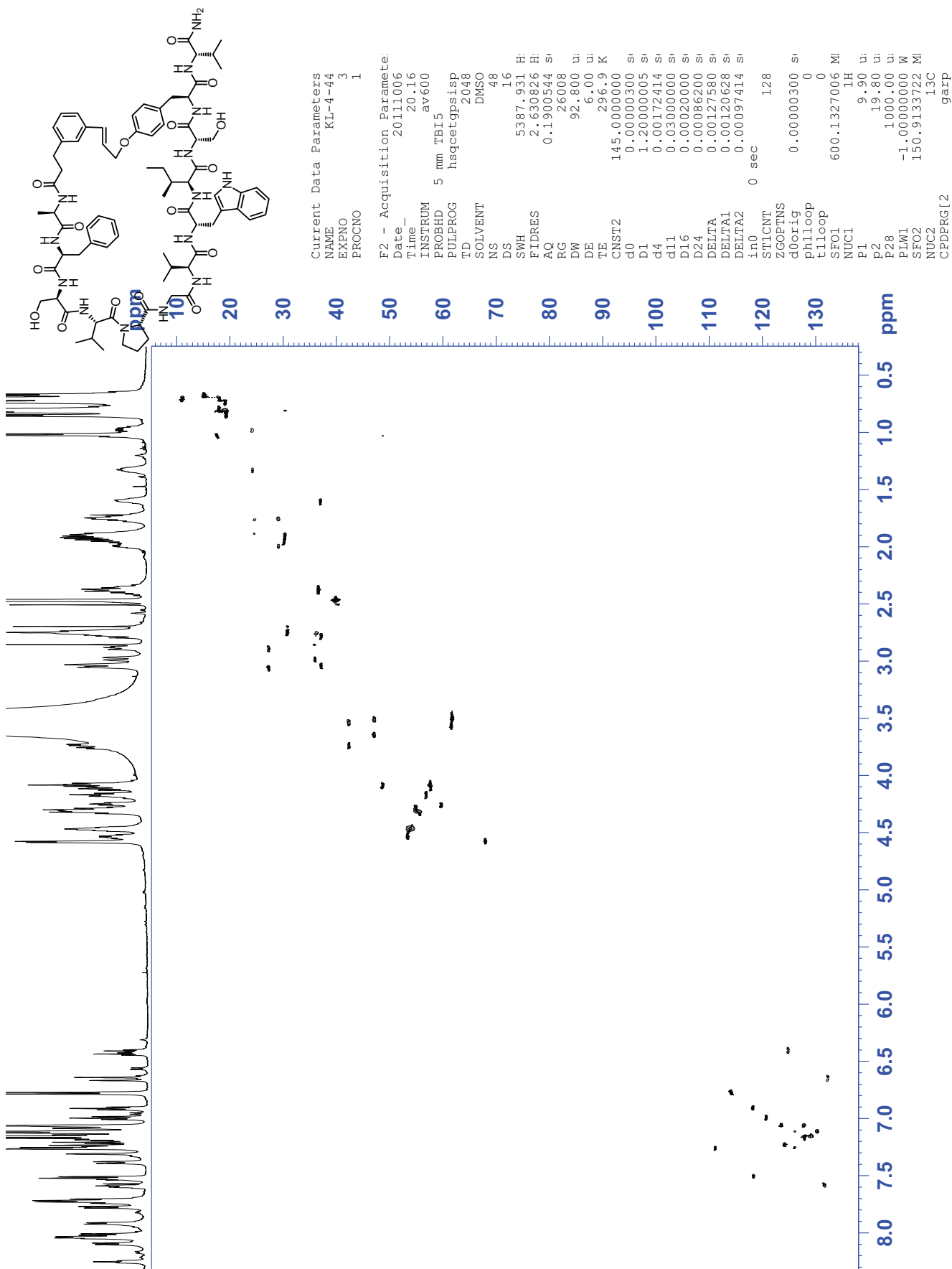
Current Data Parameters
NAME          KL-4-44
EXPNO         1
PROCNO        1

F2 - Acquisition Parameters
Date_         20111006
Time_         18.36
INSTRUM       5 mm TBI5
PROBHD        zg30
PULPROG       65536
TD            8
SOLVENT       DMSO
NS            8
DS            0
SWH           12376.237 Hz
FIDRES        0.188846 Hz
AQ            2.6476543 sec
RG            181
DW            40.400 usec
DE            6.50 usec
TE            295.8 K
D1            2.0000000 sec
TD0           1

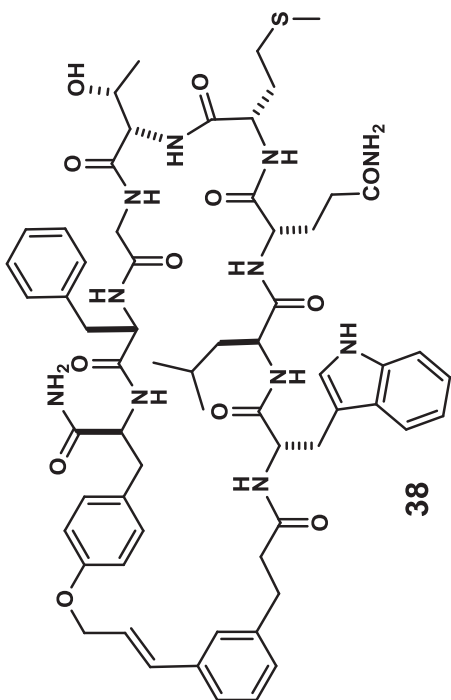
===== CHANNEL f1 =====
NUC1          1H
P1            9.10 usec
PL1           -2.00 dB
PL1W          39.81071854 W
SFO1          600.1336008 MHz

F2 - Processing parameters
SI            65536
SF            600.1300273 MHz
WDW           EM
SSB           0
LB            0.30 Hz
GB            0
PC            1.00
  
```





Cyclic-Trp-Leu-Gln-Met-Thr-Gly-Phe-Tyr (39):

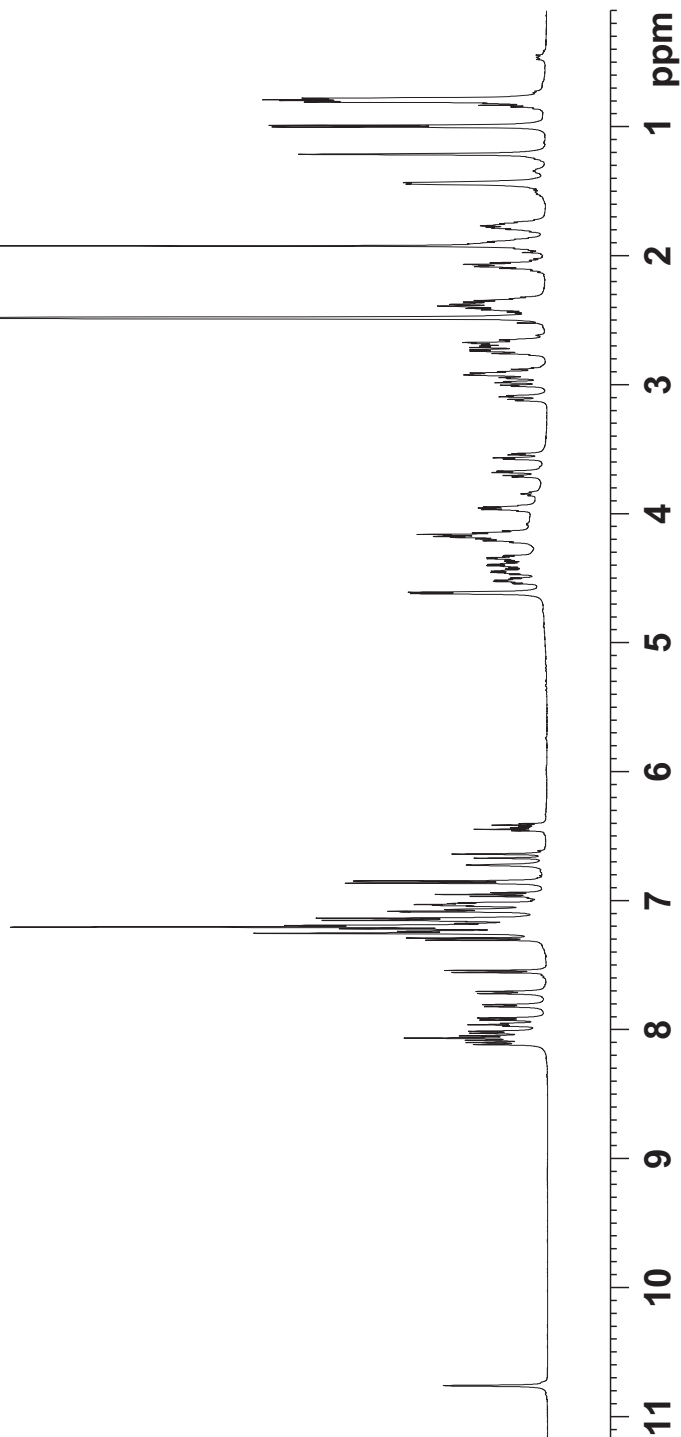


Current Data Parameters
NAME KL-5-124
EXPNO 1
PROCNO 1

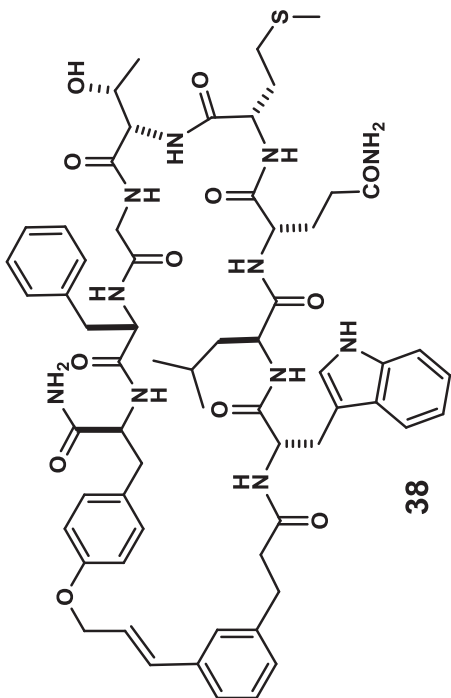
F2 - Acquisition Parameters
Date_ 20130201
Time_ 11:51
INSTRUM av500
PROBHD 5 mm DCH 13C-1
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 8
DS 0
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2767999 sec
RG 22.82
DW 50.000 usec
DE 10.00 usec
TE 298.0 K
D1 2.00000000 sec
TD0 1

===== CHANNEL f1 =====
SFO1 500.130008 MHz
NUC1 1H
P1 10.00 usec
PLW1 13.50000000 W

F2 - Processing parameters
SI 65536
SF 500.1300146 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



Cyclic-Trp-Leu-Gln-Met-Thr-Gly-Phe-Tyr (39):



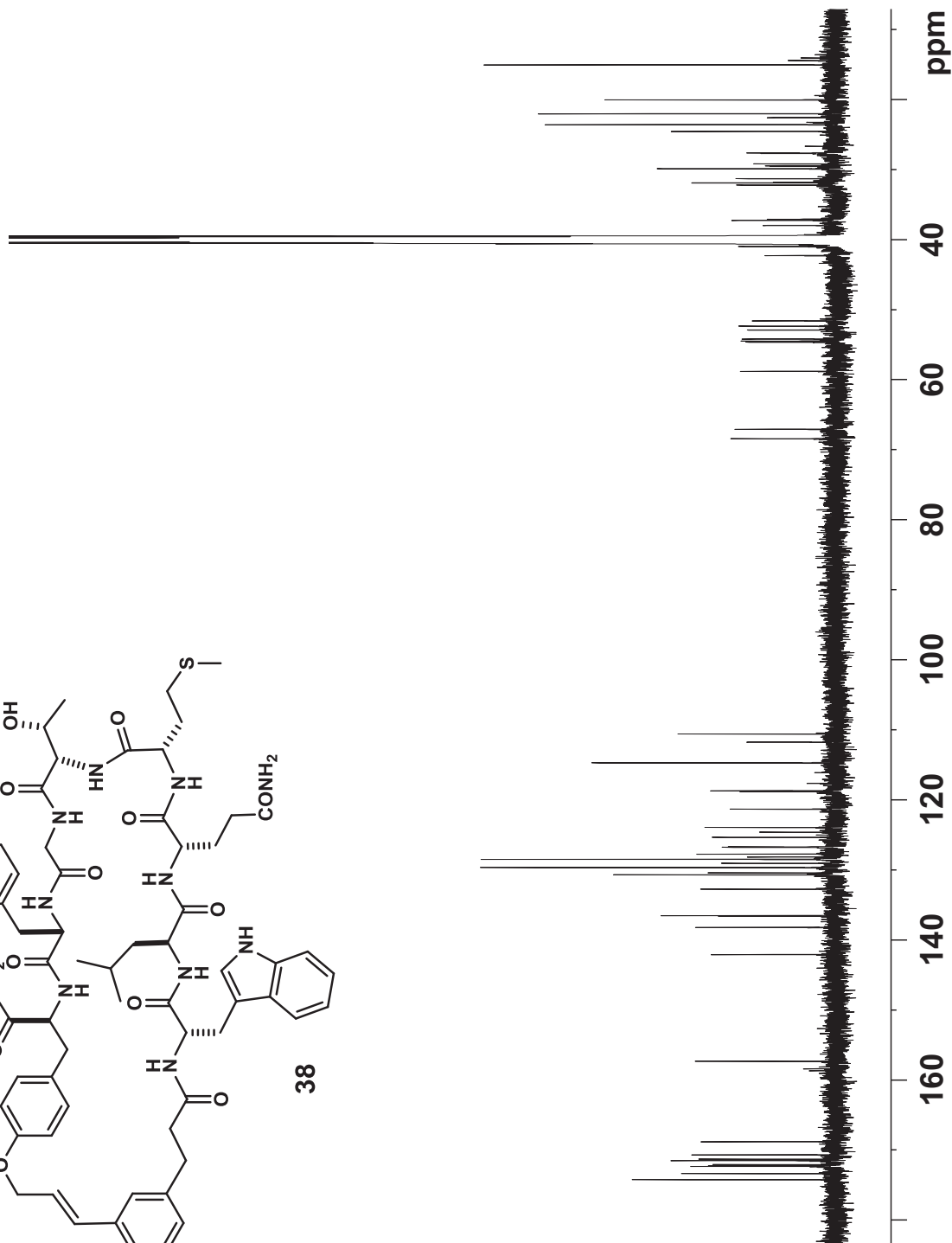
Current Data Parameters
NAME KL-5-124
EXPNO 2
PROCNO 1

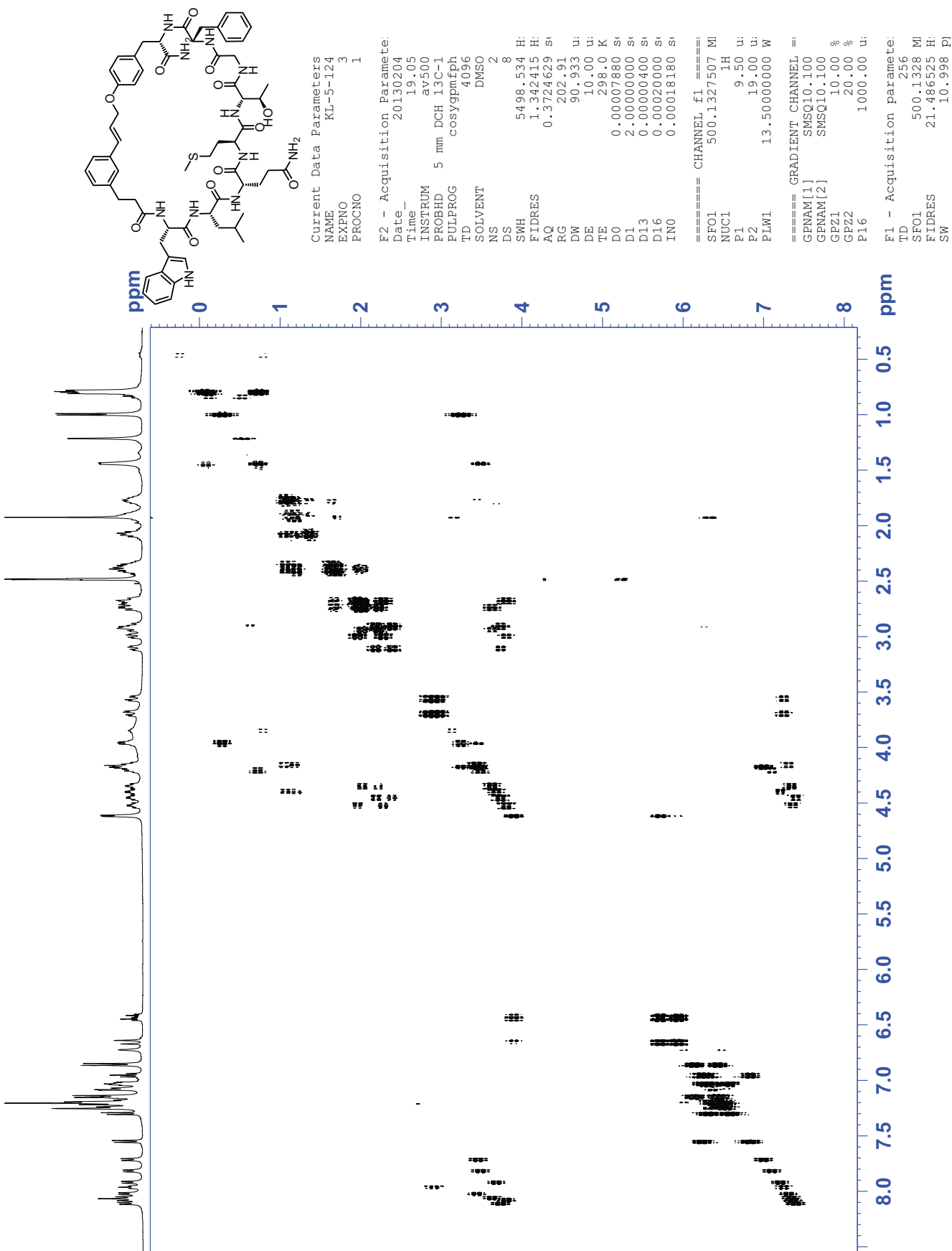
F2 - Acquisition Parameters
Date_ 20130201
Time_ 11:53
INSTRUM av500
PROBHD 5 mm DCH 13C-1
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 162
DS 2
SWH 31250.000 Hz
FIDRES 0.476837 Hz
AQ 1.0485760 sec
RG 202.91
DW 16.000 usec
DE 18.00 usec
TE 298.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

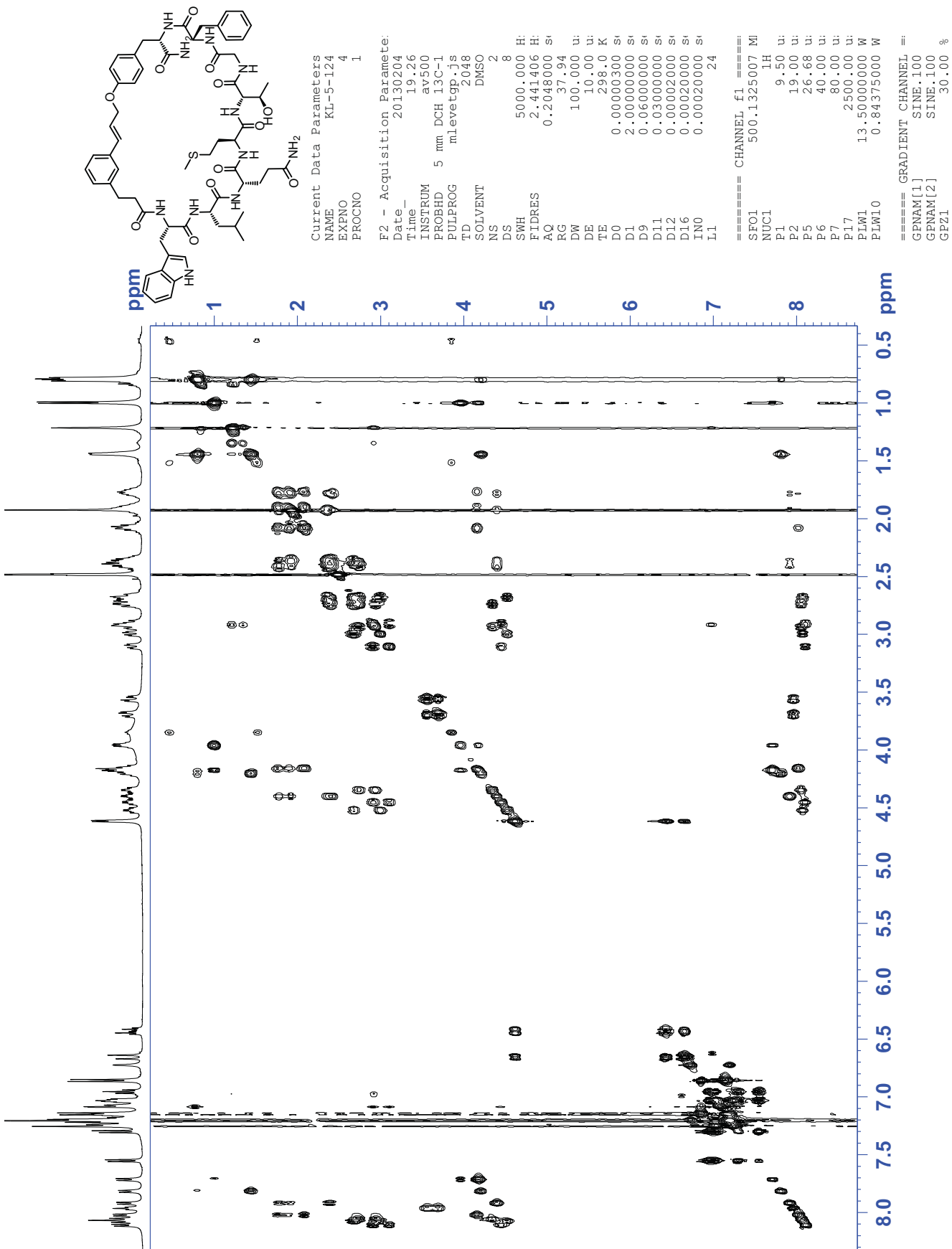
===== CHANNEL f1 =====
SFO1 125.772511 MHz
NUC1 13C
P1 9.63 usec
PLW1 23.00000000 W

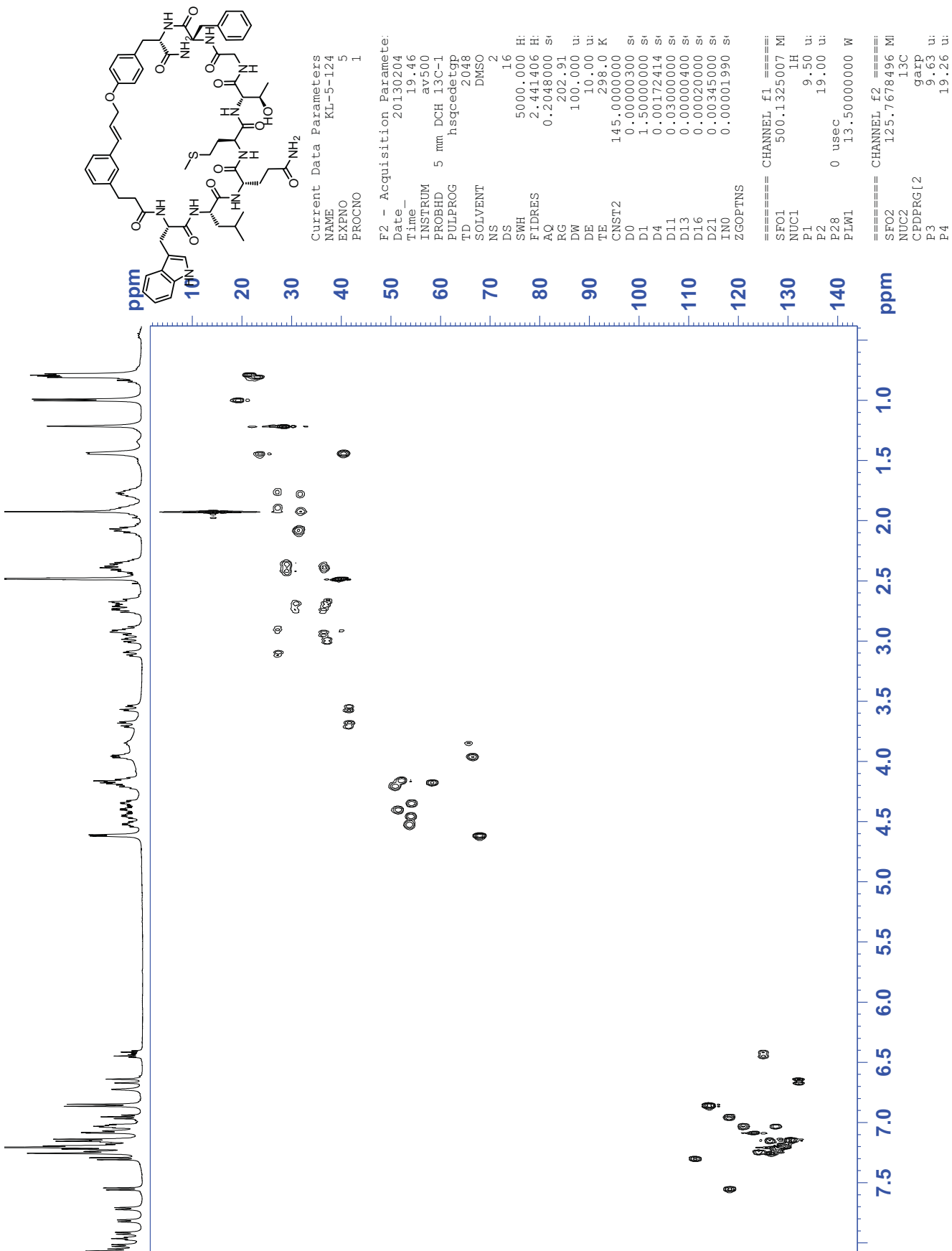
===== CHANNEL f2 =====
SFO2 500.1330008 MHz
NUC2 1H
CPDPRG2 waltz16
PCPD2 80.00 usec
PLW2 13.50000000 W
PLW12 0.21094000 W
PLW13 0.13500001 W

F2 - Processing parameters
SI 131072
SF 125.7577892 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40









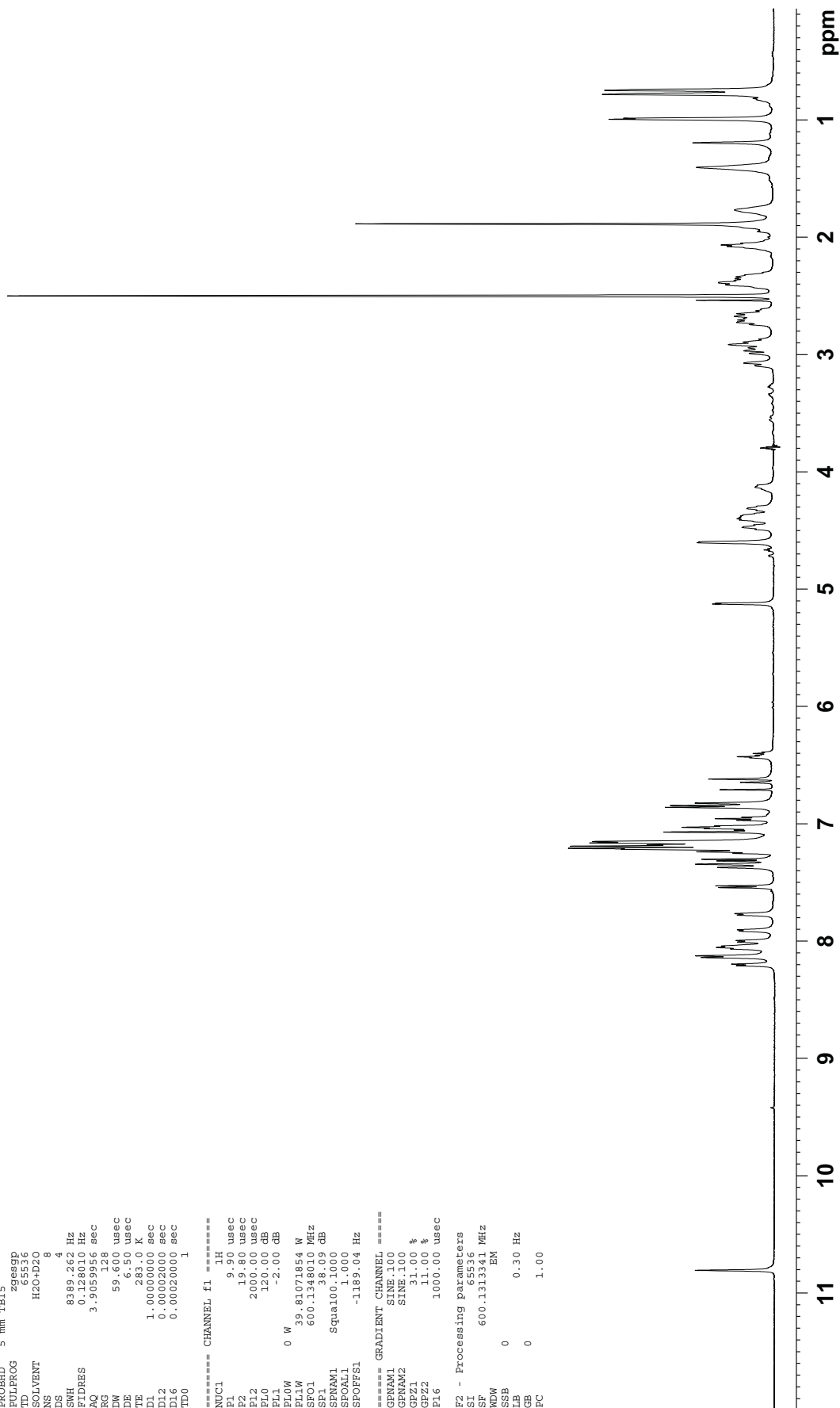
Compound 39

Current Data Parameters
NAME KJ5-124
EXPNO 24
PROCNO 1

F2 - Acquisition Parameters
Date_ 20130314
Time 21.43
INSTRUM 5 mm TBI5
PROBHD zgpg3p
PULPROG zgpg3p
TD 65536
SOLVENT H2O/D2O
NS 8
DS 4
SWH 8389.262 Hz
FIDRES 0.128010 Hz
AQ 3.9059956 sec
RG 128
DM 59.600 usec
DE 26.50 usec
TE 300.2 K
D1 1.00002000 sec
D12 0.00002000 sec
D16 0.00020000 sec
TD0 1

===== CHANNEL f1 =====
NUC1 1H
P1 9.90 usec
P2 19.80 usec
P3 200.00 usec
PL2 120.00 dB
PL1 -2.00 dB
PL0 0 W
PLW 39.81071854 W
SFO1 600.1348010 MHz
SF1 38.09 dB
SFOA1 Squal00.1000
SFOAL1 1.000
SFOFFS1 -1189.04 Hz
===== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPZ1 31.00 %
GPZ2 11.00 %
P16 1000.00 usec

F2 - Processing parameters
SI 65536
SF 600.1313341 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



Compound 39

Current Data Parameters
 NAME KLS-124 mulder
 EXPNO 6
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20130322
 Time_ 13:29
 INSTRUM spect
 PROBD 5 mm QXI 1H Z-
 PULPROG ecos3ch
 TD 2048
 SOLVENT D2O
 NS 12
 DS 32
 SWH 2540.650 Hz
 FIDRES 1.240552 Hz
 AQ 0.403084 sec
 RG 256
 DW 196.800 usec
 DE 6.00 usec
 TE 300.0 K
 d0 0.00018361 sec
 d1 2.00000000 sec
 d13 0.00000400 sec
 INO 0.00039360 sec
 MCREST 0 sec
 MCWRC 1.00000000 sec
 STCNT 0

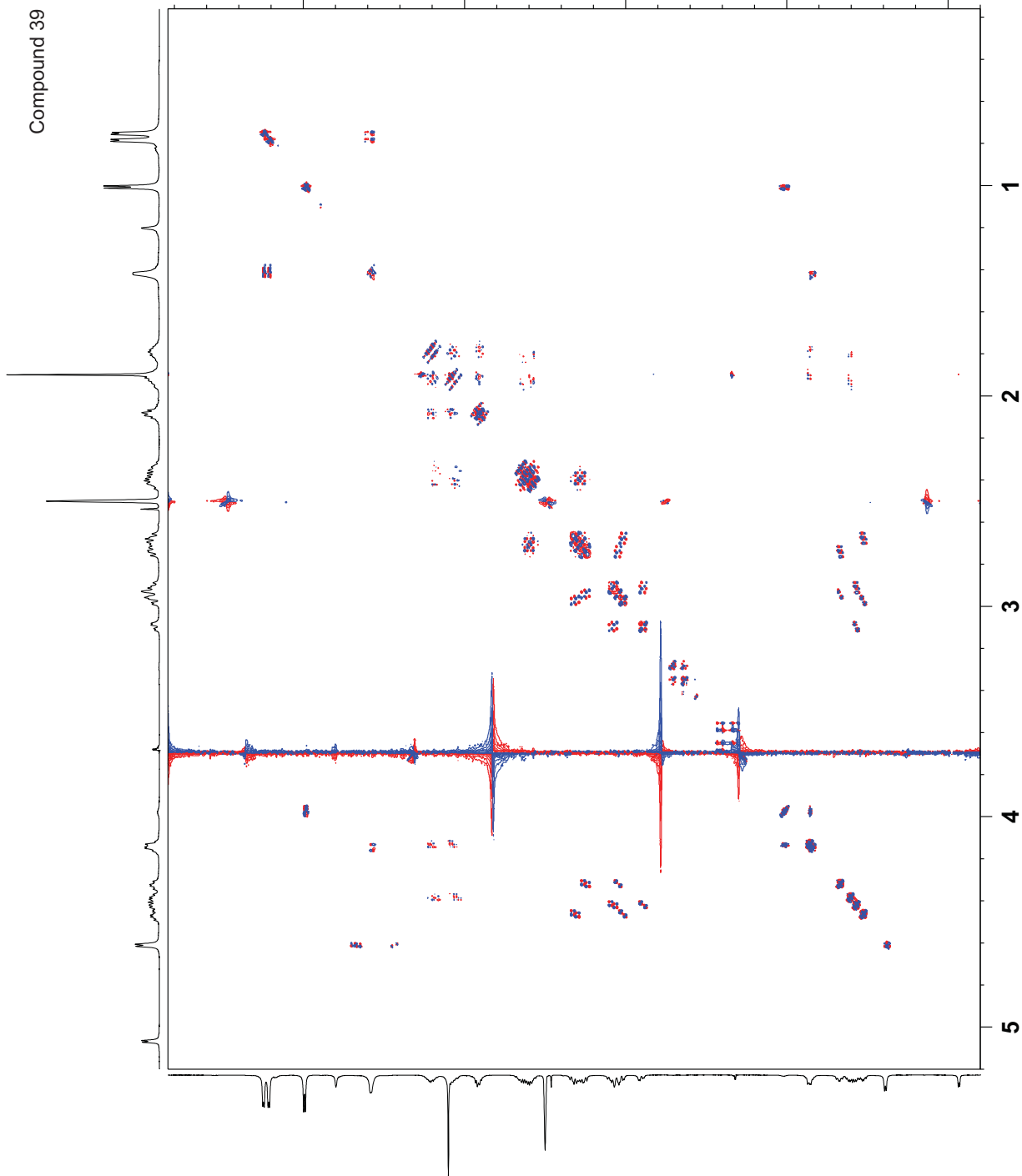
===== CHANNEL f1 =====
 NUC1 1H
 P1 10.20 usec
 PL1 -3.00 dB
 SFO1 500.0913502 MHz

F1 - Acquisition parameters
 TD 900
 SFO1 500.0914 MHz
 FIDRES 2.822945 Hz
 SW 5.080 ppm
 FMODE States-TpPI

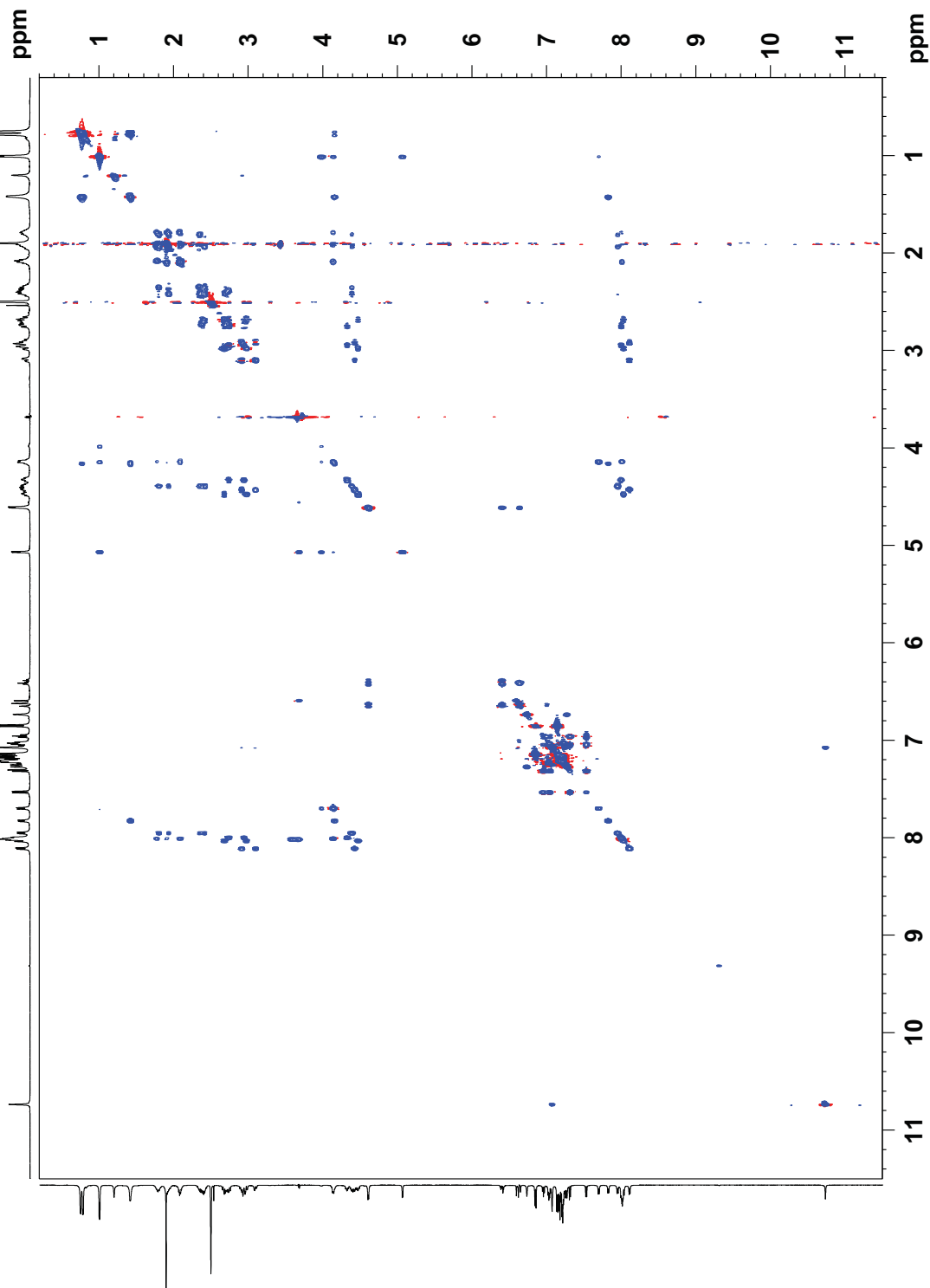
F2 - Processing parameters
 SI 4096
 SF 500.0900073 MHz
 WDW QSI
 SSB 3
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 4096
 MC2 States-TpPI
 SF 500.0900024 MHz
 WDW 3
 SSB 0 Hz
 LB 0
 GB 0

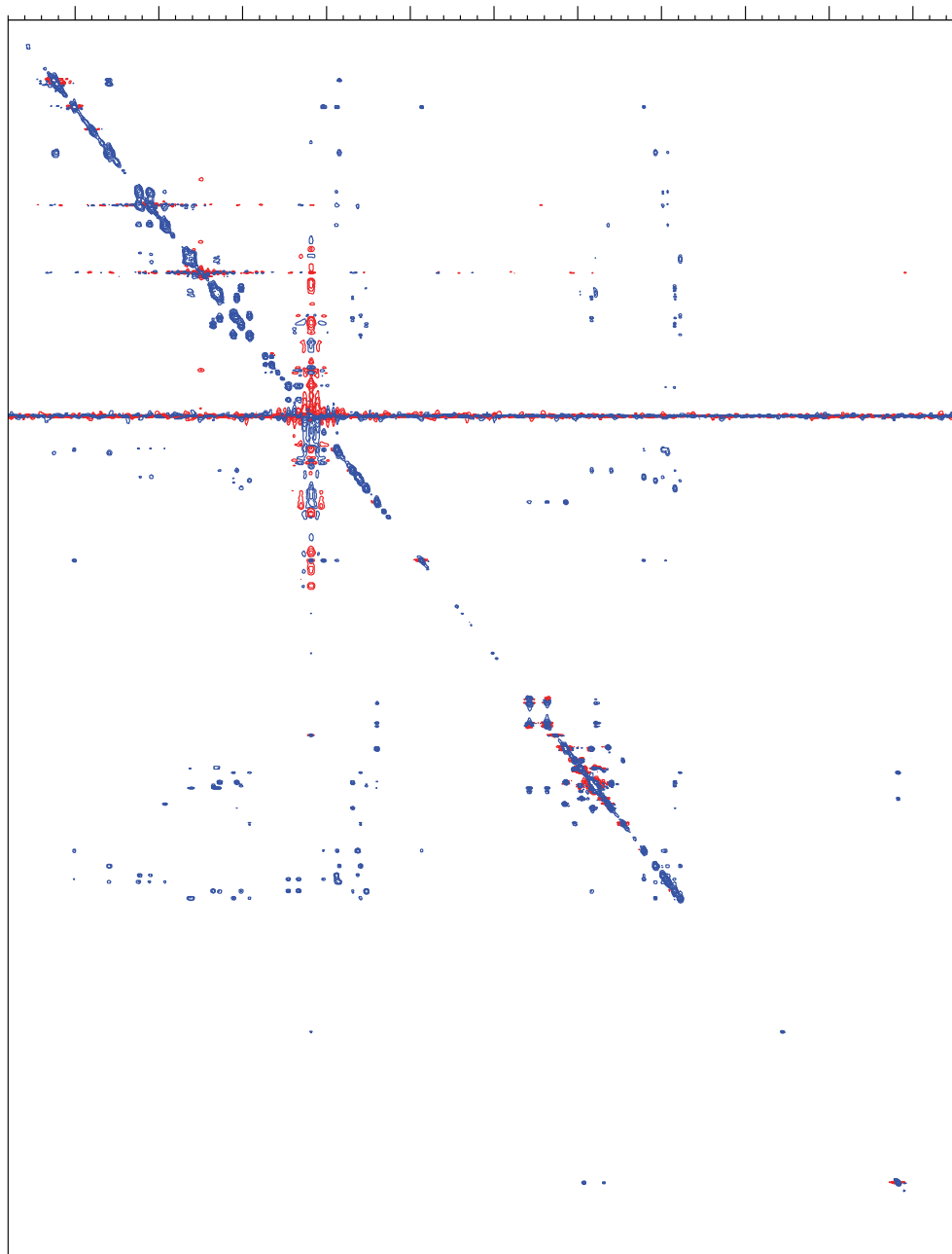
ppm 1 2 3 4 5 ppm



Compound 39

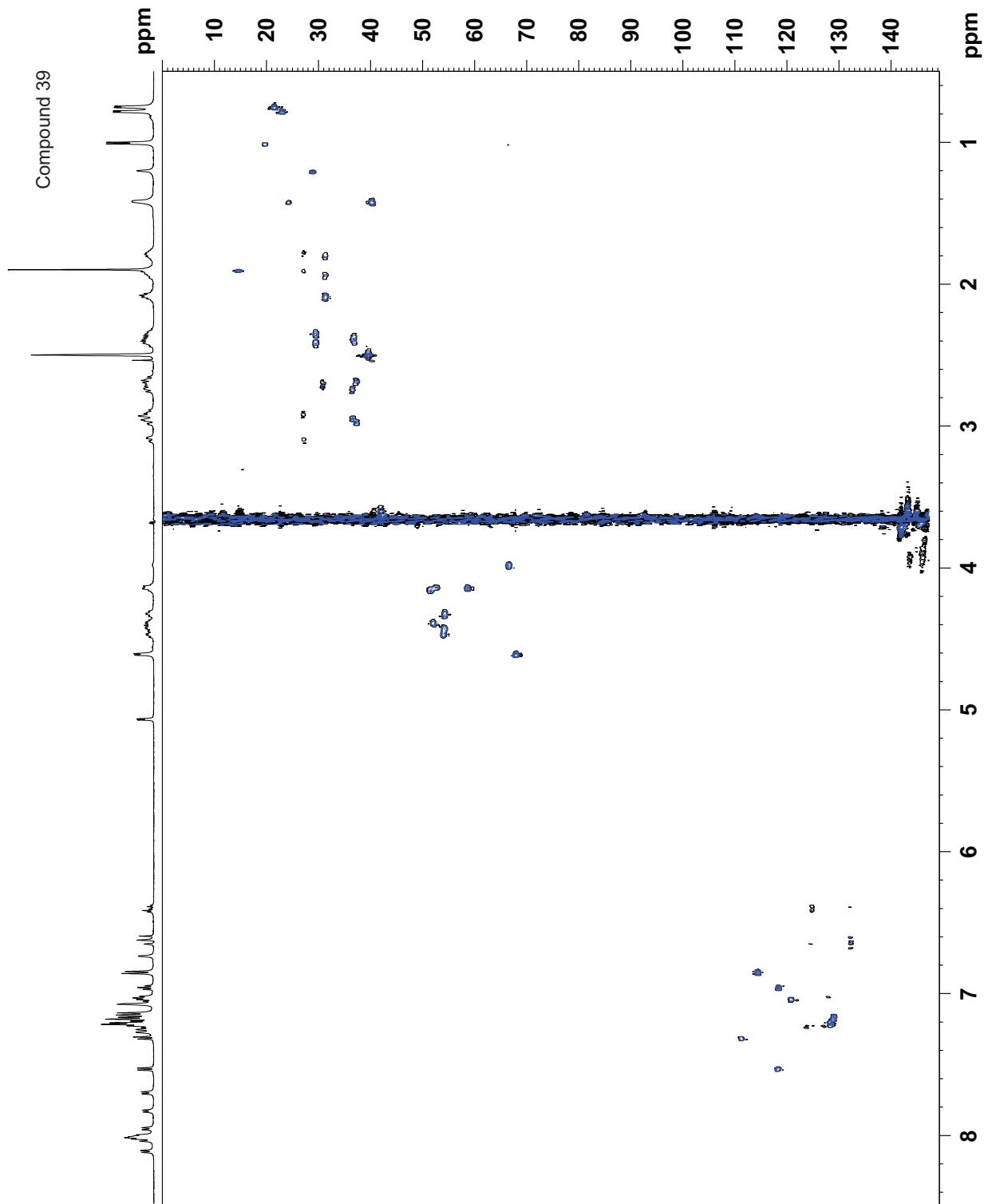


ppm



ppm

Current Data Parameters	
NAME	KU5-124
EXPNO	47
PROCNO	1
F2 - Acquisition Parameters	
Date_	20130316
Time	22.44
INSTRUM	av600
PROBHD	5 mm WB15
PULPROG	hoesyessgph
PCPDPRG2	h16
SOLVENT	H2O-D2O
DS	16
NS	24
SMH	8389.26162 Hz
FFIDRES	2.046160 Hz
RG	0.2441716 sec
RG	322.5
DE	59.600 usec
DE	6.50 usec
TE	280.0 K
DO	0.0004670 sec
DO	2.0000000 sec
DD	0.15000001 sec
DD11	0.03000000 sec
DD12	0.0002000 sec
DD16	0.0002000 sec
DD16	0.0002000 sec
INNO	0.00011920 sec
===== CHANNEL f1 =====	
NUC1	1H
P1	10.23 usec
P2	20.46 usec
PL1	3000.00 usec
PL2	120.00 usec
PL1	2.00 dB
PL2	2.00 dB
W	39.81071854 W
PL1W	600.1348010 MHz
SPF1	43.82 dB
SPF1	1000.000
SPFNAM1	Sqal100.1000
SPFOFF1	1.000
SPFOFS1	-1176.04 Hz
===== GRADIENT CHANNEL =====	
NAME1	SINE-100
GENAM2	SINE-100
GENP2	31.00 %
GENP2	11.00 %
PL16	1000.00 usec
F1 - Acquisition parameters	
TD	512
SSFO1	600.13468 MHz
FFIDRES	16.385277 Hz
SW	13.979 ppm
PRNAME	States-TpFI
F2 - Processing parameters	
SI	4096
SP	600.1313334 MHz
WDW	QSI
SSS	2.5
LB	0 Hz
LB	0
PC	1.00
F1 - Processing parameters	
SI	4096
SP	States-TpFI
WDW	600.1313355 MHz
SSS	2.5
LB	0 Hz
LB	0



```

Current Data Parameters
NAME          KLS-124
EXPNO         21
PROCNO        1

F2 - Acquisition Parameters
Date_         20110114
Time          18.55
PROBHD        5 mm TBS1
PULPROG       zgpg30
TD            65536
SOLVENT       H2O+d2o
DS            16
SNH           5165.285 Hz
FIDRES        2.522114 Hz
AQ            0.192608 sec
RG            96.800 usec
DE            6.00 usec
TE            298.0 K
DST2          145.000000 sec
D1            0.00000000 sec
D4            0.00172414 sec
D11           0.00000000 sec
D12           0.00000000 sec
D14           0.00000000 sec
D24           0.00086200 sec
IN0           0.00002070 sec
ZSOPNTS

===== CHANNEL f1 =====
NUC1          1H
P1            9.90 usec
PL1           19.80 dB
P2            9.90 usec
PL2           19.80 dB
PL1W          39.81071854 W
SFO1          600.1339609 MHz

===== CHANNEL f2 =====
CPDPRG2       garrp
NUC2          13C
P3            19.52 usec
PL3           19.80 dB
P4            19.52 usec
PL4           19.80 dB
PCPD2         65.00 usec
PL0           120.00 dB
PL2           120.00 dB
PL2W          150.35617065 W
PL12W         13.55567932 W
SFO2          150.9137722 MHz
SFOAL3        C13P80.0.5.20.1
SFOFFS3       0.500 Hz

===== GRADIENT CHANNEL =====
GENAM1        SINE.100
GENAM2        SINE.100
GEZ1          80.00 %
GEZ2          20.10 %
F16           1000.00 usec

F1 - Acquisition Parameters
TD            65536
SOLVENT       H2O+d2o
FIDRES        142.876572 Hz
SN            160.000 Ppm
FMODE         Echo-Antiecho

F2 - Processing Parameters
SI            4096
SF            600.131329 MHz
WDW           EM
SS            0
LB            1.00 Hz
GB            0
PC            1.40

F1 - Processing Parameters
SI            4096
SF            150.9032019 MHz
WDW           EM
SS            0
PC            1.40
  
```


Compound 39

Current Data Parameters
NAME KL5-124
EXPNO 23
PROCNO 1

F2 - Acquisition Parameters
Date_ 20130116
Time_ 19:37
INSTRUM av600
PROBHD 5 mm TB15
PULPROG hmcgplbndqf
TD 2048
SOLVENT H2O-D2O
NS 24
DS 4
SWH 6887.052 Hz
FIDRES 3.362818 Hz
AQ 0.1487348 sec
RG 26008
DE 72.600 usec
TE 300.2 K
CNSST2 145.000000
CNSST13 7.000000
D0 0.00000300 sec
D1 1.00000000 sec
D2 0.00344828 sec
D6 0.07142857 sec
D16 0.00020000 sec
IN0 0.00001745 sec

===== CHANNEL f1 =====
NUC1 1H
P1 9.90 usec
PL1 19.80 dB
PL1W 39.81071854 W
SFO1 600.1347710 MHz

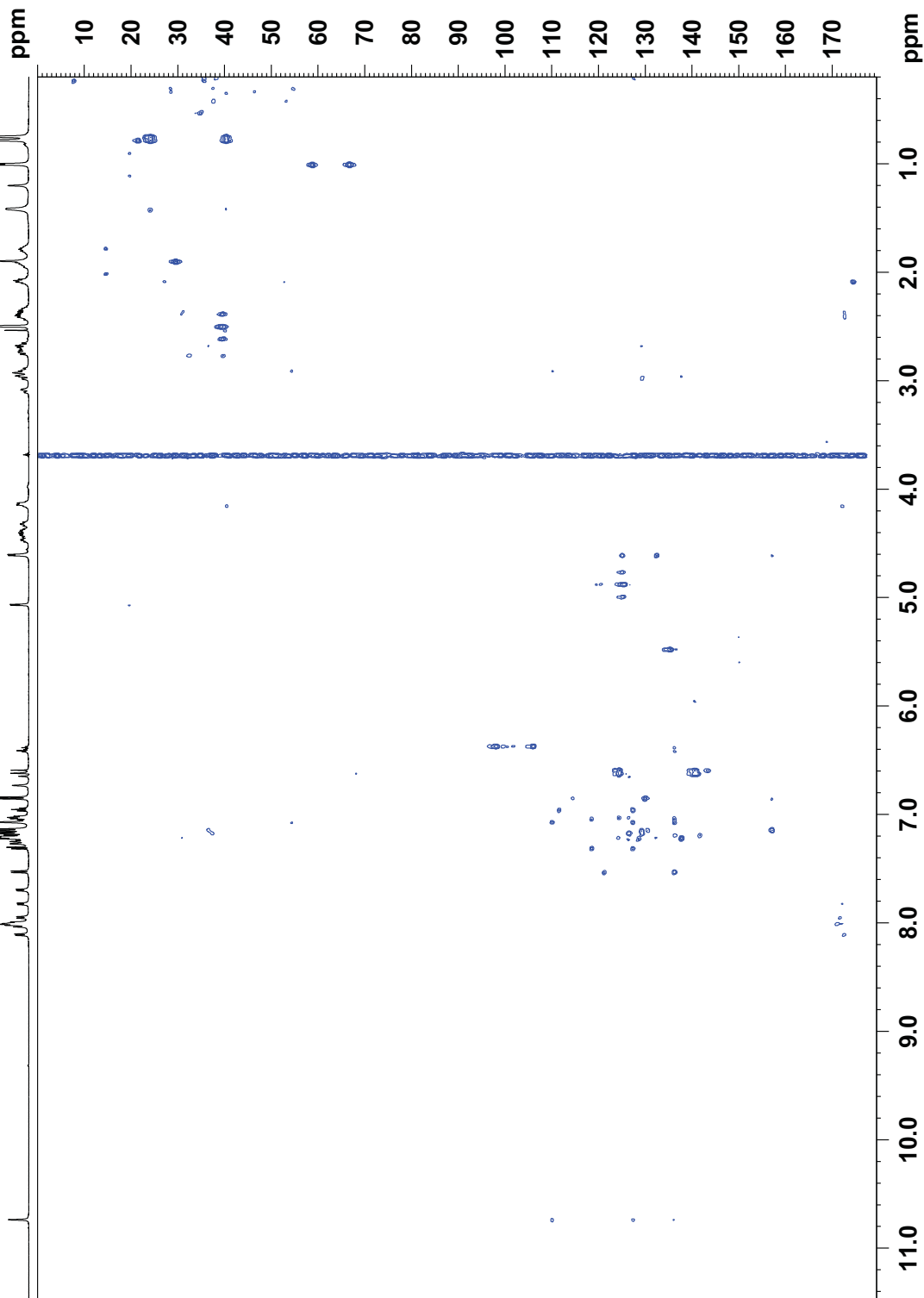
===== CHANNEL f2 =====
NUC2 13C
P3 19.52 usec
PL2 -3.00 dB
PL2W 150.35617065 W
SFO2 150.9156357 MHz

===== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPNAM3 SINE.100
GPZ1 50.00 %
GPZ2 30.00 %
GPZ3 40.10 %
F16 1000.00 usec

F1 - Acquisition parameters
TD 197
SFO1 150.9156 MHz
FIDRES 145.553146 Hz
SW 190.000 PPM
FHM00 QF

F2 - Processing parameters
SI 4096
SF 600.1313342 MHz
WDW 0
SSB 0 Hz
LB 0
GB 0
PC 1.40

F1 - Processing parameters
SI 4096
MC2 QF
SF 150.9031854 MHz
WDW 2
SSB



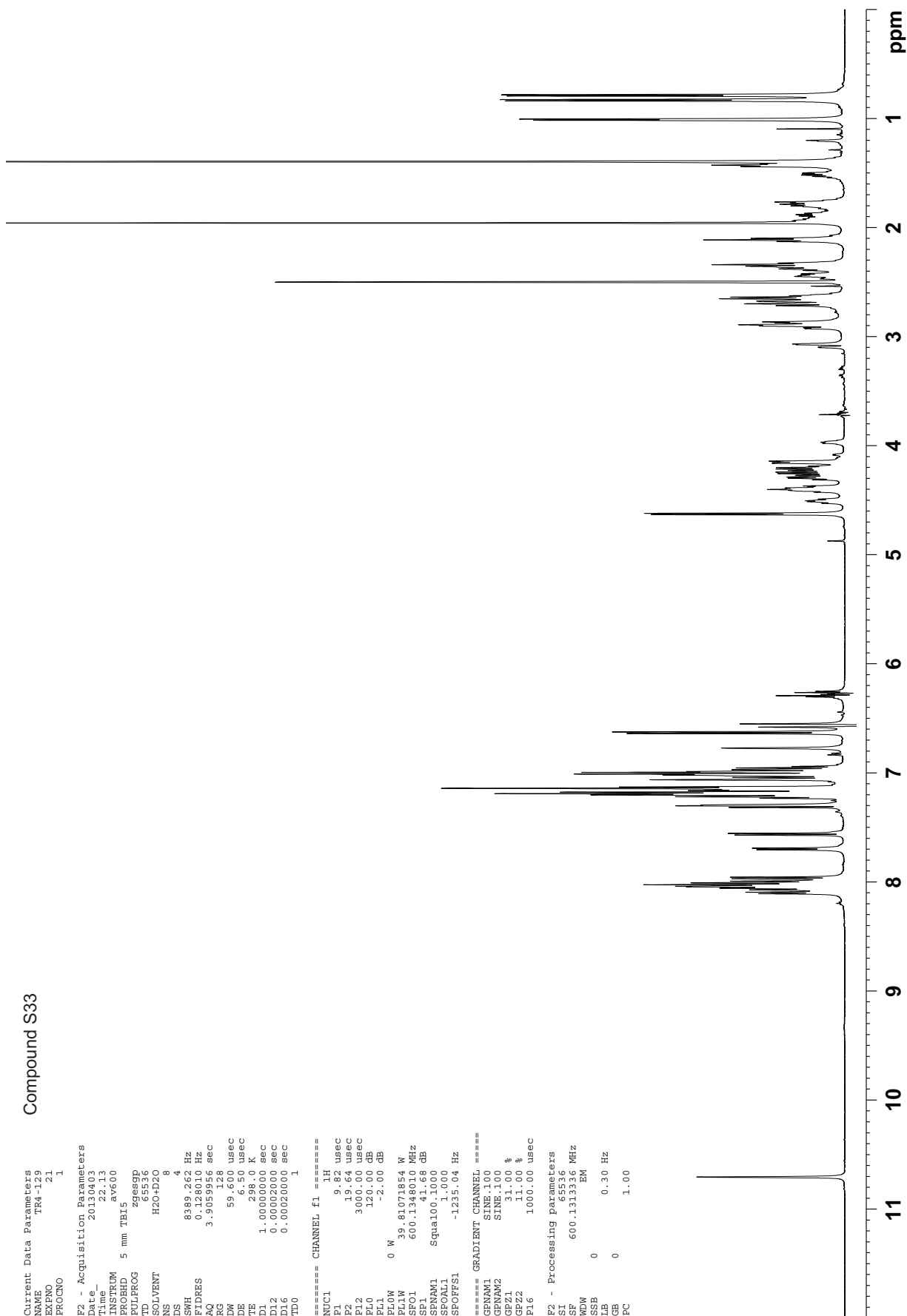
Compound S33

Current Data Parameters
NAME IR4-121
EXPNO 21
PROCNO 1

F2 - Acquisition Parameters
Date_ 20130403
Time 22.13
INSTRUM av600
PROBHD 5 mm TBI5
PULPROG zgpg30
TD 65536
SOLVENT H2O/D2O
NS 8
DS 4
SWH 8389.262 Hz
FIDRES 0.128010 Hz
AQ 3.9059956 sec
RG 128
DM 59.600 usec
DE 26.50 usec
TE 300.2 K
D1 1.00002000 sec
D12 0.00002000 sec
D16 0.00020000 sec
TD0 1

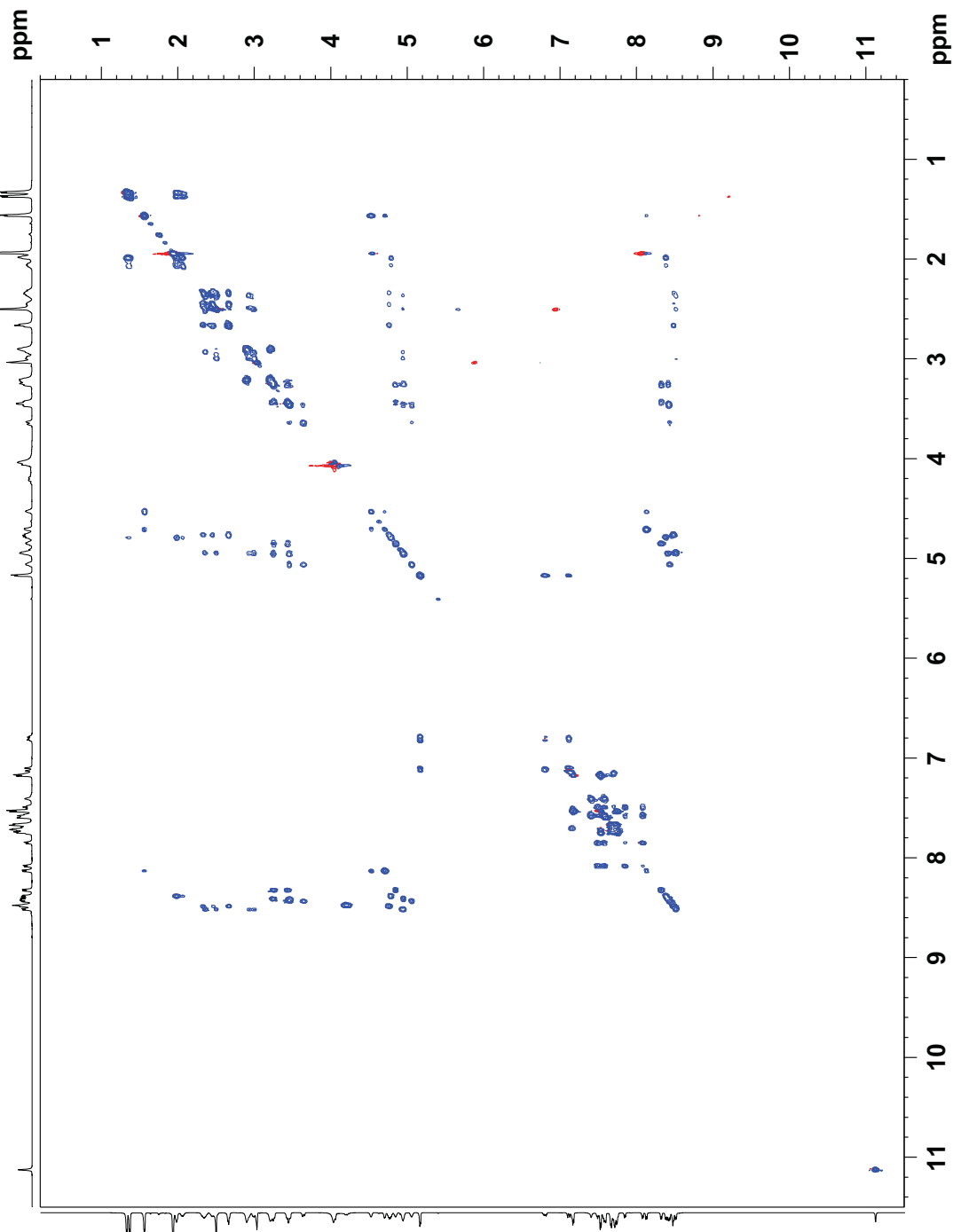
===== CHANNEL f1 =====
NUC1 1H
P1 9.82 usec
P2 19.64 usec
P3 300.00 usec
P4 120.00 dB
P5 -2.00 dB
P6 0 W
P7 39.81071854 W
P8 600.1348010 MHz
P9 41.68 dB
P10 Squal100.1000
P11 1.000
P12 -1235.04 Hz
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P999
P1000

F2 - Processing parameters
SI 65536
SF 600.1313336 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



```

===== CURRENT DATA PARAMETERS =====
NAME          VALUE
TR4-129
EXRNO         1
PROCNO        1
===== F2 - Acquisition Parameters =====
Time         20130326
Time         22.05
FREQID       17600
PROBHD       5 mm TB15
PULPROG      zgpg30
MAGPROG      zgpg30
TD           2048
AQ           0.000192 sec
SFO           400.131920 MHz
RG           1
RG2           1
RG3           1
RG4           1
RG5           1
RG6           1
RG7           1
RG8           1
RG9           1
RG10          1
RG11          1
RG12          1
RG13          1
RG14          1
RG15          1
RG16          1
RG17          1
RG18          1
RG19          1
RG20          1
RG21          1
RG22          1
RG23          1
RG24          1
RG25          1
RG26          1
RG27          1
RG28          1
RG29          1
RG30          1
RG31          1
RG32          1
RG33          1
RG34          1
RG35          1
RG36          1
RG37          1
RG38          1
RG39          1
RG40          1
RG41          1
RG42          1
RG43          1
RG44          1
RG45          1
RG46          1
RG47          1
RG48          1
RG49          1
RG50          1
RG51          1
RG52          1
RG53          1
RG54          1
RG55          1
RG56          1
RG57          1
RG58          1
RG59          1
RG60          1
RG61          1
RG62          1
RG63          1
RG64          1
RG65          1
RG66          1
RG67          1
RG68          1
RG69          1
RG70          1
RG71          1
RG72          1
RG73          1
RG74          1
RG75          1
RG76          1
RG77          1
RG78          1
RG79          1
RG80          1
RG81          1
RG82          1
RG83          1
RG84          1
RG85          1
RG86          1
RG87          1
RG88          1
RG89          1
RG90          1
RG91          1
RG92          1
RG93          1
RG94          1
RG95          1
RG96          1
RG97          1
RG98          1
RG99          1
RG100         1
===== CHANNEL f1 =====
NUC1          1H
P1            10.21 usec
PC            1.00
PR            10.21 usec
PL            10.21 usec
PT            10.21 usec
PS            2.48 usec
PD            2.48 usec
PE            2.48 usec
PF            2.48 usec
PG            2.48 usec
PH            2.48 usec
PI            2.48 usec
PJ            2.48 usec
PK            2.48 usec
PL            2.48 usec
PM            2.48 usec
PN            2.48 usec
PO            2.48 usec
PP            2.48 usec
PQ            2.48 usec
PR            2.48 usec
PS            2.48 usec
PT            2.48 usec
PU            2.48 usec
PV            2.48 usec
PW            2.48 usec
PX            2.48 usec
PY            2.48 usec
PZ            2.48 usec
QA            2.48 usec
QB            2.48 usec
QC            2.48 usec
QD            2.48 usec
QE            2.48 usec
QF            2.48 usec
QG            2.48 usec
QH            2.48 usec
QI            2.48 usec
QJ            2.48 usec
QK            2.48 usec
QL            2.48 usec
QM            2.48 usec
QN            2.48 usec
QO            2.48 usec
QP            2.48 usec
QQ            2.48 usec
QR            2.48 usec
QS            2.48 usec
QT            2.48 usec
QU            2.48 usec
QV            2.48 usec
QW            2.48 usec
QX            2.48 usec
QY            2.48 usec
QZ            2.48 usec
RA            2.48 usec
RB            2.48 usec
RC            2.48 usec
RD            2.48 usec
RE            2.48 usec
RF            2.48 usec
RG            2.48 usec
RH            2.48 usec
RI            2.48 usec
RJ            2.48 usec
RK            2.48 usec
RL            2.48 usec
RM            2.48 usec
RN            2.48 usec
RO            2.48 usec
RP            2.48 usec
RQ            2.48 usec
RS            2.48 usec
RT            2.48 usec
RU            2.48 usec
RV            2.48 usec
RW            2.48 usec
RX            2.48 usec
RY            2.48 usec
RZ            2.48 usec
SA            2.48 usec
SB            2.48 usec
SC            2.48 usec
SD            2.48 usec
SE            2.48 usec
SF            2.48 usec
SG            2.48 usec
SH            2.48 usec
SI            2.48 usec
SJ            2.48 usec
SK            2.48 usec
SL            2.48 usec
SM            2.48 usec
SN            2.48 usec
SO            2.48 usec
SP            2.48 usec
SQ            2.48 usec
SR            2.48 usec
SS            2.48 usec
ST            2.48 usec
SU            2.48 usec
SV            2.48 usec
SW            2.48 usec
SX            2.48 usec
SY            2.48 usec
SZ            2.48 usec
TA            2.48 usec
TB            2.48 usec
TC            2.48 usec
TD            2.48 usec
TE            2.48 usec
TF            2.48 usec
TG            2.48 usec
TH            2.48 usec
TI            2.48 usec
TJ            2.48 usec
TK            2.48 usec
TL            2.48 usec
TM            2.48 usec
TN            2.48 usec
TO            2.48 usec
TP            2.48 usec
TQ            2.48 usec
TR            2.48 usec
TS            2.48 usec
TT            2.48 usec
TU            2.48 usec
TV            2.48 usec
TW            2.48 usec
TX            2.48 usec
TY            2.48 usec
TZ            2.48 usec
UA            2.48 usec
UB            2.48 usec
UC            2.48 usec
UD            2.48 usec
UE            2.48 usec
UF            2.48 usec
UG            2.48 usec
UH            2.48 usec
UI            2.48 usec
UJ            2.48 usec
UK            2.48 usec
UL            2.48 usec
UM            2.48 usec
UN            2.48 usec
UO            2.48 usec
UP            2.48 usec
UQ            2.48 usec
UR            2.48 usec
US            2.48 usec
UT            2.48 usec
UU            2.48 usec
UV            2.48 usec
UW            2.48 usec
UX            2.48 usec
UY            2.48 usec
UZ            2.48 usec
VA            2.48 usec
VB            2.48 usec
VC            2.48 usec
VD            2.48 usec
VE            2.48 usec
VF            2.48 usec
VG            2.48 usec
VH            2.48 usec
VI            2.48 usec
VJ            2.48 usec
VK            2.48 usec
VL            2.48 usec
VM            2.48 usec
VN            2.48 usec
VO            2.48 usec
VP            2.48 usec
VQ            2.48 usec
VR            2.48 usec
VS            2.48 usec
VT            2.48 usec
VU            2.48 usec
VV            2.48 usec
VW            2.48 usec
VX            2.48 usec
VY            2.48 usec
VZ            2.48 usec
WA            2.48 usec
WB            2.48 usec
WC            2.48 usec
WD            2.48 usec
WE            2.48 usec
WF            2.48 usec
WG            2.48 usec
WH            2.48 usec
WI            2.48 usec
WJ            2.48 usec
WK            2.48 usec
WL            2.48 usec
WM            2.48 usec
WN            2.48 usec
WO            2.48 usec
WP            2.48 usec
WQ            2.48 usec
WR            2.48 usec
WS            2.48 usec
WT            2.48 usec
WU            2.48 usec
WV            2.48 usec
WW            2.48 usec
WX            2.48 usec
WY            2.48 usec
WZ            2.48 usec
XA            2.48 usec
XB            2.48 usec
XC            2.48 usec
XD            2.48 usec
XE            2.48 usec
XF            2.48 usec
XG            2.48 usec
XH            2.48 usec
XI            2.48 usec
XJ            2.48 usec
XK            2.48 usec
XL            2.48 usec
XM            2.48 usec
XN            2.48 usec
XO            2.48 usec
XP            2.48 usec
XQ            2.48 usec
XR            2.48 usec
XS            2.48 usec
XT            2.48 usec
XU            2.48 usec
XV            2.48 usec
XW            2.48 usec
XX            2.48 usec
XY            2.48 usec
XZ            2.48 usec
YA            2.48 usec
YB            2.48 usec
YC            2.48 usec
YD            2.48 usec
YE            2.48 usec
YF            2.48 usec
YG            2.48 usec
YH            2.48 usec
YI            2.48 usec
YJ            2.48 usec
YK            2.48 usec
YL            2.48 usec
YM            2.48 usec
YN            2.48 usec
YO            2.48 usec
YP            2.48 usec
YQ            2.48 usec
YR            2.48 usec
YS            2.48 usec
YT            2.48 usec
YU            2.48 usec
YV            2.48 usec
YW            2.48 usec
YX            2.48 usec
YZ            2.48 usec
ZA            2.48 usec
ZB            2.48 usec
ZC            2.48 usec
ZD            2.48 usec
ZE            2.48 usec
ZF            2.48 usec
ZG            2.48 usec
ZH            2.48 usec
ZI            2.48 usec
ZJ            2.48 usec
ZK            2.48 usec
ZL            2.48 usec
ZM            2.48 usec
ZN            2.48 usec
ZO            2.48 usec
ZP            2.48 usec
ZQ            2.48 usec
ZR            2.48 usec
ZS            2.48 usec
ZT            2.48 usec
ZU            2.48 usec
ZV            2.48 usec
ZW            2.48 usec
ZX            2.48 usec
ZY            2.48 usec
ZZ            2.48 usec
===== GRADIENT CHANNEL =====
NAME          VALUE
G1            0 N
G2            39.8107184 N
G3            2.5417963 N
G4            600.1348010 MHz
G5            600.1348010 MHz
G6            1000.0000000 dB
G7            1000.0000000 dB
G8            1000.0000000 dB
G9            1000.0000000 dB
G10           1000.0000000 dB
G11           1000.0000000 dB
G12           1000.0000000 dB
G13           1000.0000000 dB
G14           1000.0000000 dB
G15           1000.0000000 dB
G16           1000.0000000 dB
G17           1000.0000000 dB
```



Compound S33

```

Current Data Parameters
NAME      TR4-129
EXPNO     22
PROCNO    1

F2 - Acquisition Parameters
Date_     20130403
Time      22.20
INSTRUM   spect
PROBHD    5 mm TBS1
PULPROG   zgpg30
TD         65536
SOLVENT   H2O-D2O
NS         16
DS         4
SWH        8389.262 Hz
FIDRES     2.048160 Hz
AQ          0.247156 sec
RG          655.36
DE          59.600 usec
TE          298.2 K
D1          0.0000000 sec
D2          0.0000000 sec
D3          0.0000001 sec
D4          0.0300000 sec
D5          0.0000000 sec
D6          0.0000000 sec
D7          0.0000000 sec
D8          0.0000000 sec
D9          0.0000000 sec
D10         0.0000000 sec
D11         0.0000000 sec
D12         0.0000000 sec
D13         0.0000000 sec
D14         0.0000000 sec
D15         0.0000000 sec
D16         0.0000000 sec
IN0         0.00011920 sec

===== CHANNEL f1 =====
NUC1        13C
P1          9.82 usec
PL1         19.64 usec
PL2         19.64 usec
PL3         19.64 usec
PL4         19.64 usec
PL5         19.64 usec
PL6         19.64 usec
PL7         19.64 usec
PL8         19.64 usec
PL9         19.64 usec
PL10        19.64 usec
PL11        19.64 usec
PL12        19.64 usec
PL13        19.64 usec
PL14        19.64 usec
PL15        19.64 usec
PL16        19.64 usec
PL17        19.64 usec
PL18        19.64 usec
PL19        19.64 usec
PL20        19.64 usec
PL21        19.64 usec
PL22        19.64 usec
PL23        19.64 usec
PL24        19.64 usec
PL25        19.64 usec
PL26        19.64 usec
PL27        19.64 usec
PL28        19.64 usec
PL29        19.64 usec
PL30        19.64 usec
PL31        19.64 usec
PL32        19.64 usec
PL33        19.64 usec
PL34        19.64 usec
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PL40        19.64 usec
PL41        19.64 usec
PL42        19.64 usec
PL43        19.64 usec
PL44        19.64 usec
PL45        19.64 usec
PL46        19.64 usec
PL47        19.64 usec
PL48        19.64 usec
PL49        19.64 usec
PL50        19.64 usec
PL51        19.64 usec
PL52        19.64 usec
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PL64        19.64 usec
PL65        19.64 usec
PL66        19.64 usec
PL67        19.64 usec
PL68        19.64 usec
PL69        19.64 usec
PL70        19.64 usec
PL71        19.64 usec
PL72        19.64 usec
PL73        19.64 usec
PL74        19.64 usec
PL75        19.64 usec
PL76        19.64 usec
PL77        19.64 usec
PL78        19.64 usec
PL79        19.64 usec
PL80        19.64 usec
PL81        19.64 usec
PL82        19.64 usec
PL83        19.64 usec
PL84        19.64 usec
PL85        19.64 usec
PL86        19.64 usec
PL87        19.64 usec
PL88        19.64 usec
PL89        19.64 usec
PL90        19.64 usec
PL91        19.64 usec
PL92        19.64 usec
PL93        19.64 usec
PL94        19.64 usec
PL95        19.64 usec
PL96        19.64 usec
PL97        19.64 usec
PL98        19.64 usec
PL99        19.64 usec
PL100       19.64 usec

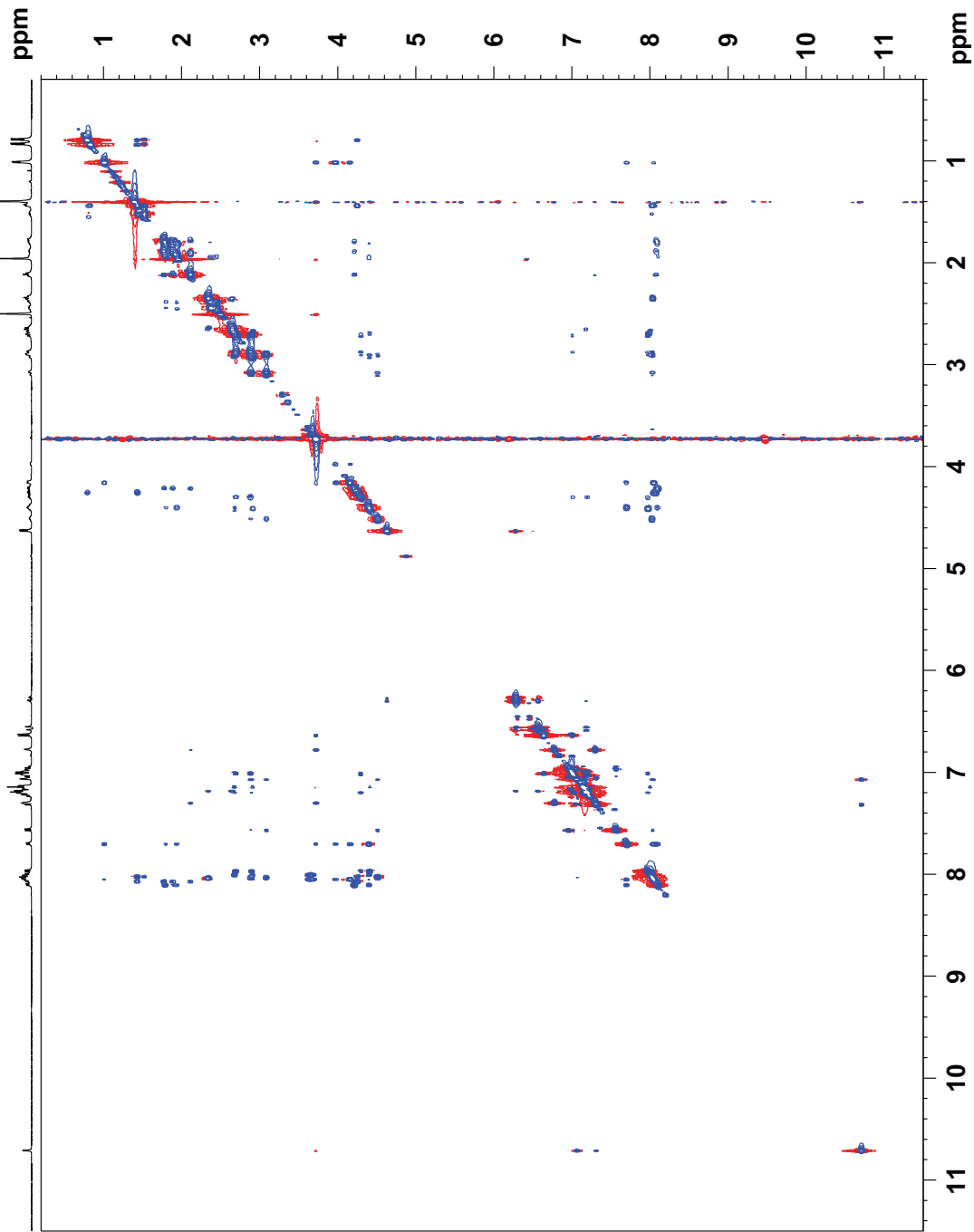
===== GRADIENT CHANNEL =====
GPNAM1     SINE.100
GPNAM2     SINE.100
GPD1       31.00 %
GPD2       31.00 %
GPD3       31.00 %
GPD4       31.00 %
GPD5       31.00 %
GPD6       31.00 %
GPD7       31.00 %
GPD8       31.00 %
GPD9       31.00 %
GPD10      31.00 %
GPD11      31.00 %
GPD12      31.00 %
GPD13      31.00 %
GPD14      31.00 %
GPD15      31.00 %
GPD16      31.00 %
GPD17      31.00 %
GPD18      31.00 %
GPD19      31.00 %
GPD20      31.00 %
GPD21      31.00 %
GPD22      31.00 %
GPD23      31.00 %
GPD24      31.00 %
GPD25      31.00 %
GPD26      31.00 %
GPD27      31.00 %
GPD28      31.00 %
GPD29      31.00 %
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GPD31      31.00 %
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GPD38      31.00 %
GPD39      31.00 %
GPD40      31.00 %
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GPD67      31.00 %
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GPD73      31.00 %
GPD74      31.00 %
GPD75      31.00 %
GPD76      31.00 %
GPD77      31.00 %
GPD78      31.00 %
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GPD80      31.00 %
GPD81      31.00 %
GPD82      31.00 %
GPD83      31.00 %
GPD84      31.00 %
GPD85      31.00 %
GPD86      31.00 %
GPD87      31.00 %
GPD88      31.00 %
GPD89      31.00 %
GPD90      31.00 %
GPD91      31.00 %
GPD92      31.00 %
GPD93      31.00 %
GPD94      31.00 %
GPD95      31.00 %
GPD96      31.00 %
GPD97      31.00 %
GPD98      31.00 %
GPD99      31.00 %
GPD100     31.00 %

F1 - Acquisition Parameters
Date_     20130403
Time      22.20
INSTRUM   spect
PROBHD    5 mm TBS1
PULPROG   zgpg30
TD         65536
SOLVENT   H2O-D2O
NS         16
DS         4
SWH        8389.262 Hz
FIDRES     2.048160 Hz
AQ          0.247156 sec
RG          655.36
DE          59.600 usec
TE          298.2 K
D1          0.0000000 sec
D2          0.0000000 sec
D3          0.0000001 sec
D4          0.0300000 sec
D5          0.0000000 sec
D6          0.0000000 sec
D7          0.0000000 sec
D8          0.0000000 sec
D9          0.0000000 sec
D10         0.0000000 sec
D11         0.0000000 sec
D12         0.0000000 sec
D13         0.0000000 sec
D14         0.0000000 sec
D15         0.0000000 sec
D16         0.0000000 sec
IN0         0.00011920 sec

===== GRADIENT CHANNEL =====
GPNAM1     SINE.100
GPNAM2     SINE.100
GPD1       31.00 %
GPD2       31.00 %
GPD3       31.00 %
GPD4       31.00 %
GPD5       31.00 %
GPD6       31.00 %
GPD7       31.00 %
GPD8       31.00 %
GPD9       31.00 %
GPD10      31.00 %
GPD11      31.00 %
GPD12      31.00 %
GPD13      31.00 %
GPD14      31.00 %
GPD15      31.00 %
GPD16      31.00 %
GPD17      31.00 %
GPD18      31.00 %
GPD19      31.00 %
GPD20      31.00 %
GPD21      31.00 %
GPD22      31.00 %
GPD23      31.00 %
GPD24      31.00 %
GPD25      31.00 %
GPD26      31.00 %
GPD27      31.00 %
GPD28      31.00 %
GPD29      31.00 %
GPD30      31.00 %
GPD31      31.00 %
GPD32      31.00 %
GPD33      31.00 %
GPD34      31.00 %
GPD35      31.00 %
GPD36      31.00 %
GPD37      31.00 %
GPD38      31.00 %
GPD39      31.00 %
GPD40      31.00 %
GPD41      31.00 %
GPD42      31.00 %
GPD43      31.00 %
GPD44      31.00 %
GPD45      31.00 %
GPD46      31.00 %
GPD47      31.00 %
GPD48      31.00 %
GPD49      31.00 %
GPD50      31.00 %
GPD51      31.00 %
GPD52      31.00 %
GPD53      31.00 %
GPD54      31.00 %
GPD55      31.00 %
GPD56      31.00 %
GPD57      31.00 %
GPD58      31.00 %
GPD59      31.00 %
GPD60      31.00 %
GPD61      31.00 %
GPD62      31.00 %
GPD63      31.00 %
GPD64      31.00 %
GPD65      31.00 %
GPD66      31.00 %
GPD67      31.00 %
GPD68      31.00 %
GPD69      31.00 %
GPD70      31.00 %
GPD71      31.00 %
GPD72      31.00 %
GPD73      31.00 %
GPD74      31.00 %
GPD75      31.00 %
GPD76      31.00 %
GPD77      31.00 %
GPD78      31.00 %
GPD79      31.00 %
GPD80      31.00 %
GPD81      31.00 %
GPD82      31.00 %
GPD83      31.00 %
GPD84      31.00 %
GPD85      31.00 %
GPD86      31.00 %
GPD87      31.00 %
GPD88      31.00 %
GPD89      31.00 %
GPD90      31.00 %
GPD91      31.00 %
GPD92      31.00 %
GPD93      31.00 %
GPD94      31.00 %
GPD95      31.00 %
GPD96      31.00 %
GPD97      31.00 %
GPD98      31.00 %
GPD99      31.00 %
GPD100     31.00 %

F1 - Processing Parameters
SI         4096
SF         600.131313 MHz
WDW        SINE
SSB        1.00
PC         1.00

F1 - Processing Parameters
SI         4096
SF         600.131313 MHz
WDW        SINE
SSB        1.00
PC         1.00
  
```



Compound S33

```

Current Data Parameters
NAME      TR4-129
EXPNO     17
PROCNO    1

F2 - Acquisition Parameters
Date_     20130326
Time      23:30
INSTRUM   spect
PROBHD    5 mm TBS15 av600
PULPROG   zgpg30
TD         65536
SOLVENT   H2O-D2O
NS         16
DS         4
SWH        4921.260 Hz
FIDRES     2.402959 Hz
AQ         0.2081256 sec
RG          327.899
DE         101.600 usec
TE         283.1 K
CPDPRG2   garp
NUC1       13C
P1         9.90 usec
P2         19.80 usec
P3         19.80 usec
P4         100.00 usec
PL1        -2.00 dB
PL2        19.80 dB
PL3        19.80 dB
PL4        100.00 usec
PL1W       39.81071854 W
SFO1       600.1340570 MHz

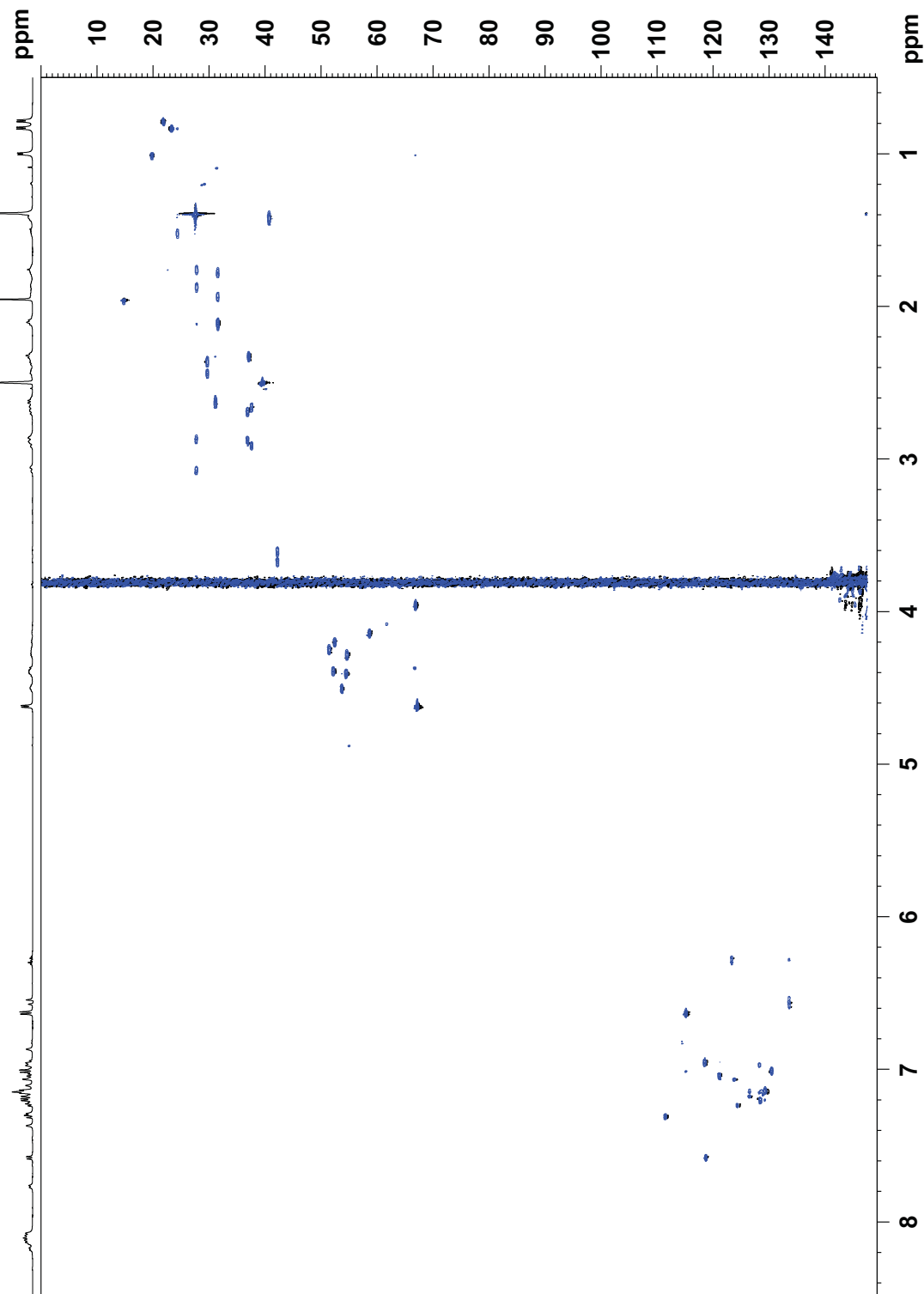
===== CHANNEL f2 =====
CPDPRG2    garp
NUC2        13C
P1         19.52 usec
P2         19.52 usec
P3         19.52 usec
P4         100.00 usec
PL1        65.00 usec
PL2        120.00 dB
PL3        -3.00 dB
PL4        7.45 dB
PL1W       0 W
PL2W       150.35617065 W
PL3W       13.55567932 W
PL4W       150.3137222 MHz
SFO2       150.9134411 MHz
SFO3       C13P80.0.5.20.1
SFOAL3     0 Hz
SFOFFS3    0.500

===== GRADIENT CHANNEL =====
GPNAM1     SINE.100
GPNAM2     SINE.100
GZ1        20.10 $
GZ2        20.10 $
GZ3        1000.00 usec

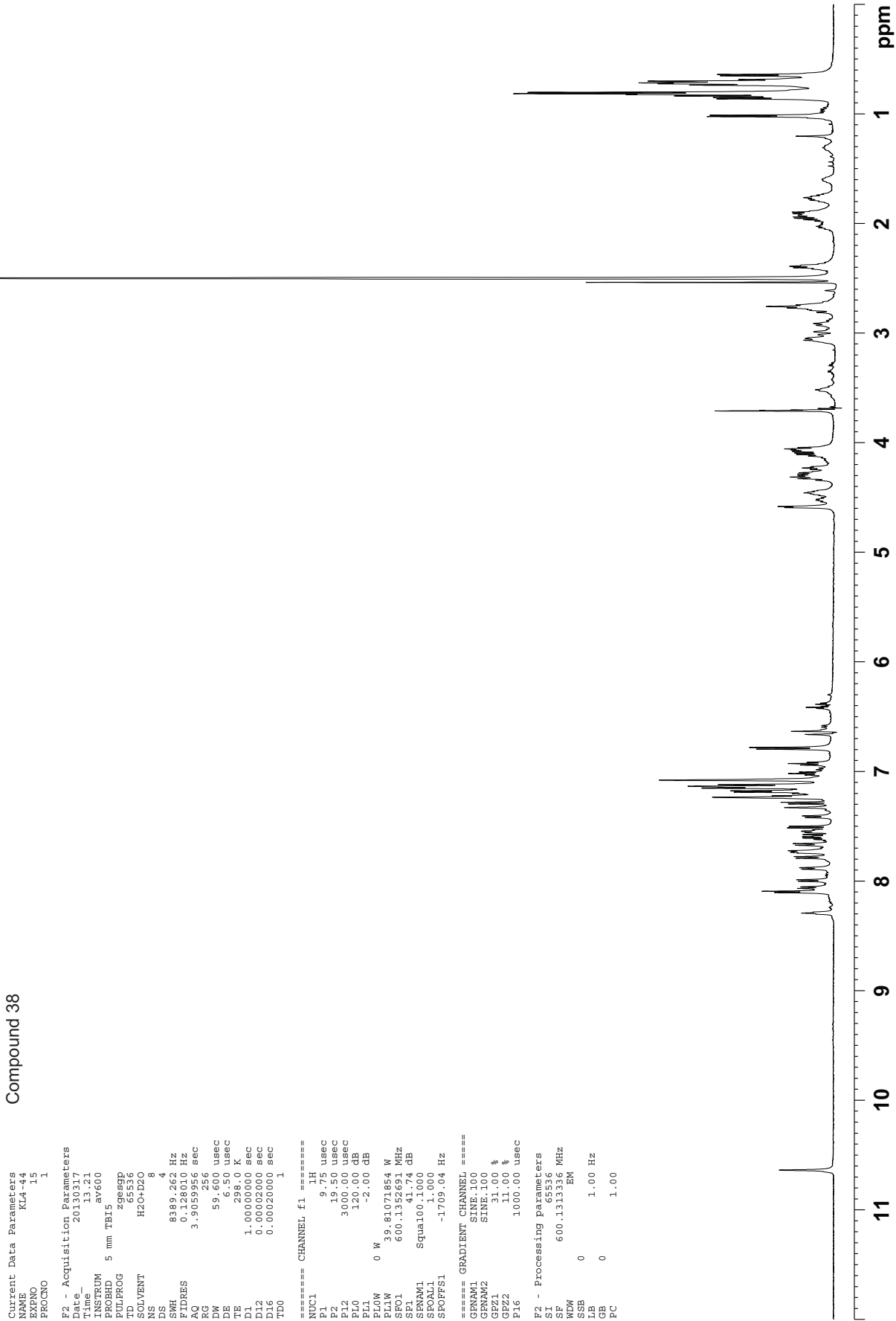
F1 - Acquisition parameters
P1         150.9134 MHz
SFO1       150.9134 MHz
FIDRES     47.160427 Hz
SN         160.000 Ppm
P2         Echo-Antiecho

F2 - Processing parameters
SI         4096
SF         600.1313271 MHz
RG          327.899
SSB        0
LB         1.00 Hz
PC         1.40

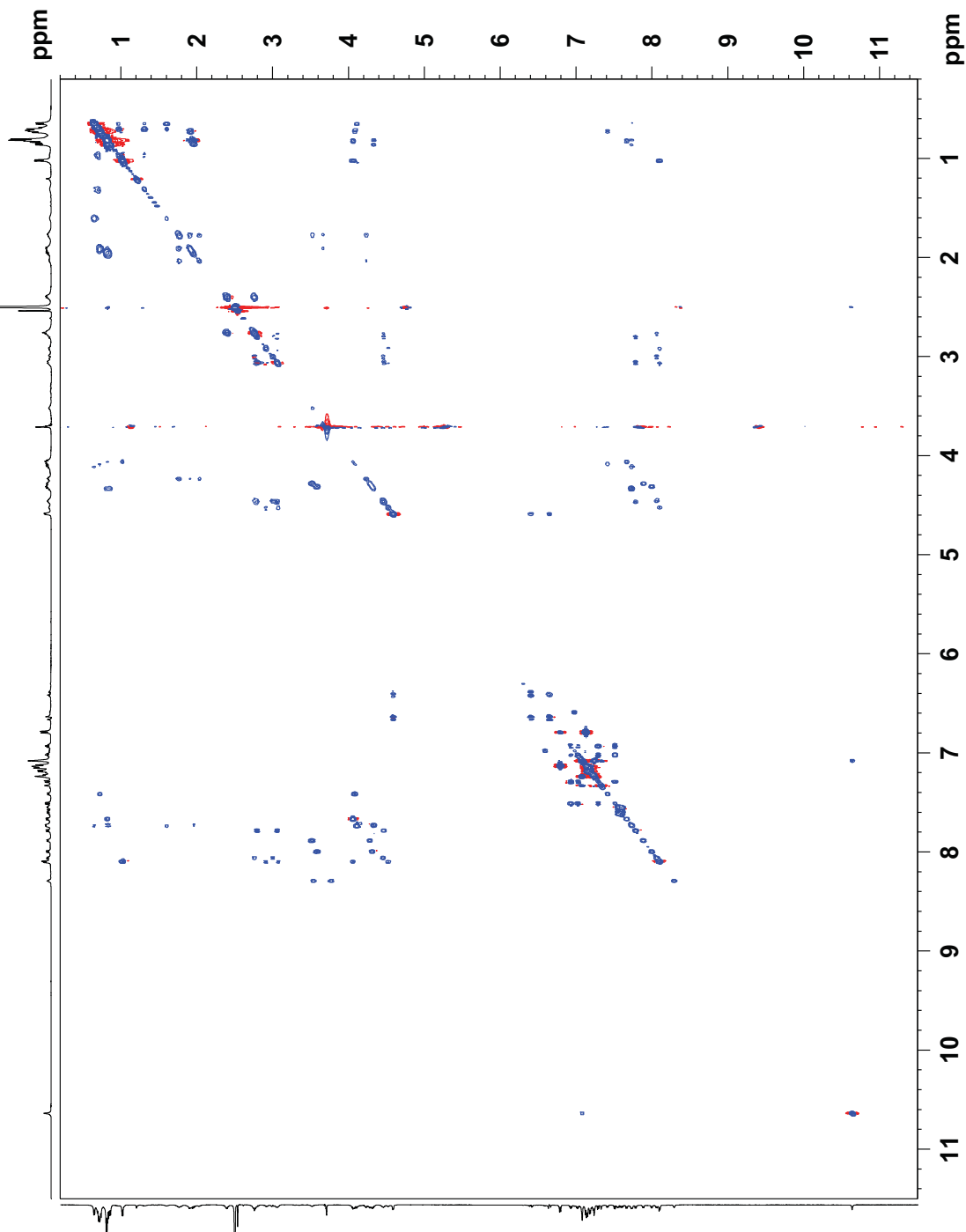
F1 - Processing parameters
SI         4096
MC2        echo-antiecho
SF         150.9031701 MHz
RG          327.899
SSB        2.5
  
```



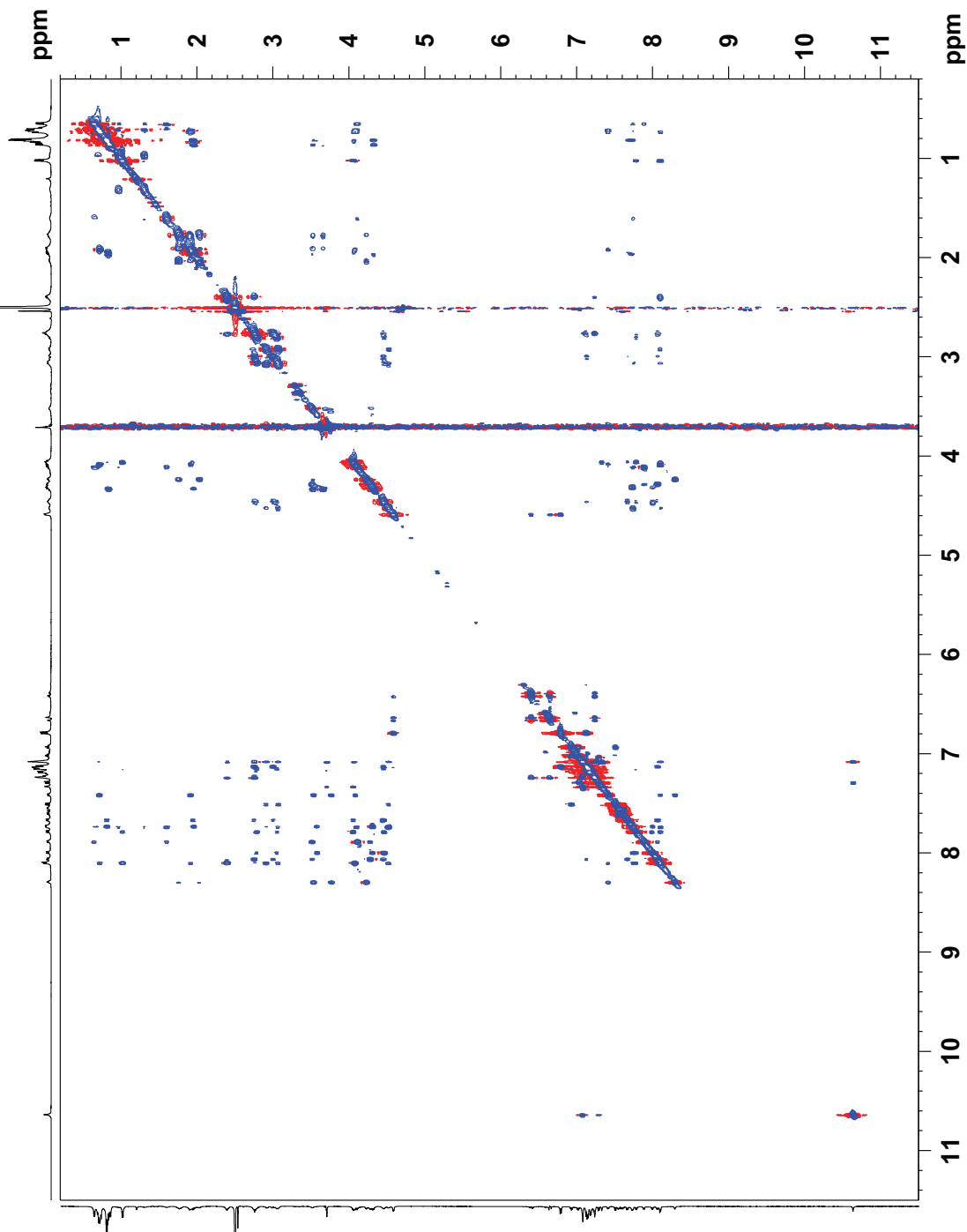
Compound 38



Compound 38



Compound 38



```

Current Data Parameters
NAME          KL4-44
EXPNO         16
PROCNO        1

F2 - Acquisition Parameters
Date_         20130317
Time          13.24
INSTRUM       spect
PROBHD        5 mm Tais
PULPROG       noesyzgpgph
TD            4096
SOLVENT       H2O-D2O
DS            16
SNH           8189.262 Hz
FIDRES        2.048160 Hz
AQ            0.2441716 sec
RG            655.5
DE            59.600 usec
TE            298.0 K
D0            0.0000000 sec
D1            2.0000000 sec
D8            0.30000001 sec
D11           0.03000000 sec
D12           0.0002000 sec
SFO1          600.1352691 MHz
SFO2          101.2532000 MHz
SFO3          400.1463000 MHz
SFO4          1.000
SPOFFS1       -1710.14 Hz

===== CHANNEL f1 =====
NUC1           13C
P1            9.75 usec
P2            19.50 usec
PL1           3000.00 usec
PL2           120.00 dB
PL3           -2.00 dB
PL4           0 W
PL1W          39.81071854 W
SFO1          600.1352691 MHz
SFO2          101.2532000 MHz
SFO3          400.1463000 MHz
SFO4          1.000
SPOFFS1       -1710.14 Hz

===== GRADIENT CHANNEL =====
GPM1          SINE.100
GPM2          SINE.100
GP21          31.00 %
GP22          11.00 %
P16           1000.00 usec

F1 - Acquisition Parameters
TD            256
INSTRUM       spect
PROBHD        5 mm Tais
PULPROG       zgpg30
SN            13.979 Ppm
PMDRPG        States-TPPI

F2 - Processing parameters
SI            4096
SF            600.1313328 MHz
SFO1          600.1313328 MHz
SSB           0 SINE
PC            1.00

F1 - Processing parameters
SI            4096
SF            101.2532000 MHz
SFO1          101.2532000 MHz
SSB           0 SINE
  
```


Compound S32

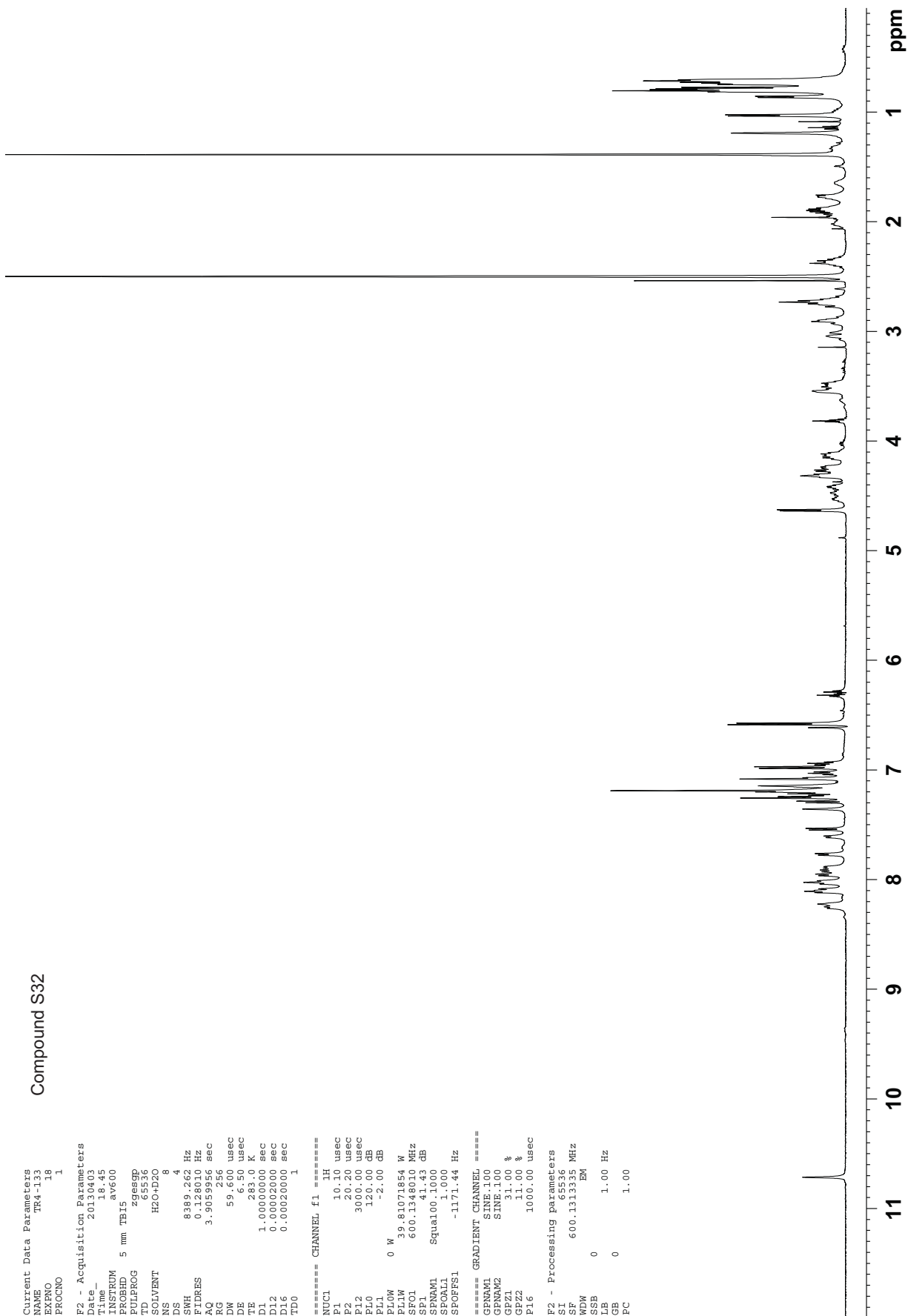
```

Current Data Parameters
NAME      IR4-13
EXPNO     18
PROCNO    1

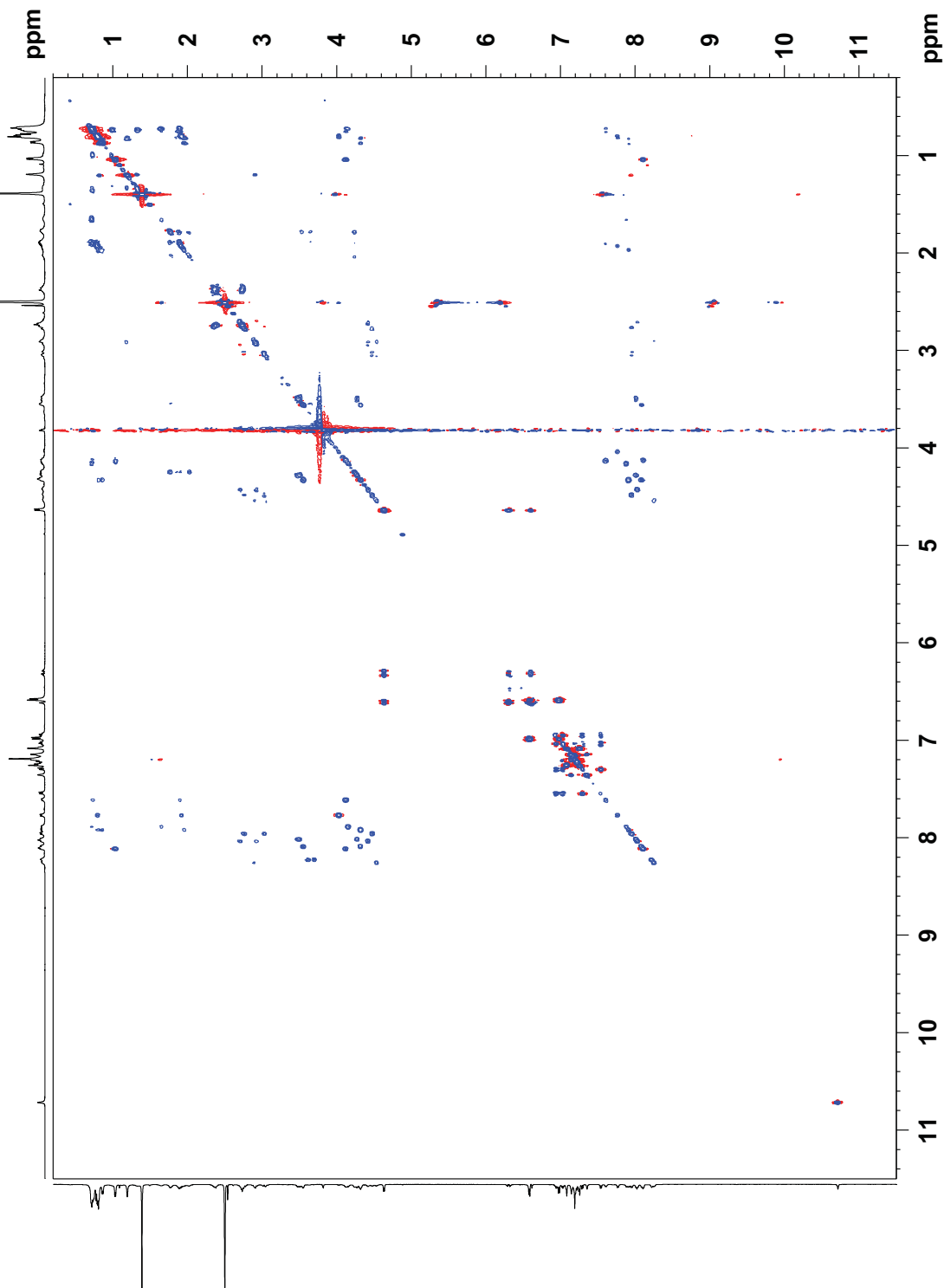
F2 - Acquisition Parameters
Date_     20130403
Time      18.45
INSTRUM   av600
PROBHD    5 mm TBI5
PULPROG   zgpg3p
TD        65536
SOLVENT   H2O/D2O
NS         8
DS         4
SWH        8389.262 Hz
FIDRES     0.128010 Hz
AQ         3.9059956 sec
RG         256
DW         59.600 usec
DE         6.50 usec
TE         300.2 K
D1         1.00000000 sec
D12        0.00002000 sec
D16        0.00020000 sec
TD0        1

===== CHANNEL f1 =====
NUC1       1H
P1         10.10 usec
P2         20.20 usec
PL1        300.00 usec
PL2        12.00 usec
PL3        -2.00 dB
PL4        0 W
PL5        39.81071854 W
PL6        600.1348010 MHz
SFO1       41.43 dB
SFO2       Squal100.1000
SFO3       1.000
SFO4       -1171.44 Hz
===== GRADIENT CHANNEL =====
GPNAM1     SINE.100
GPNAM2     SINE.100
GP21       31.00 %
GP22       11.00 %
P16        1000.00 usec

F2 - Processing parameters
SI         65536
SF         600.1313335 MHz
WDW        EM
SSB        0
LB         1.00 Hz
GB         0
PC         1.00
  
```



Compound S32

[illegible]

[illegible]

```

===== CHANNEL f1 =====
SF01 500.1330008 MHz
NUC1 1H
P1 10.00 usec
PLW1 13.5000000 W

F2 - Processing parameters
SI 65536
SF 500.1300146 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.40

```

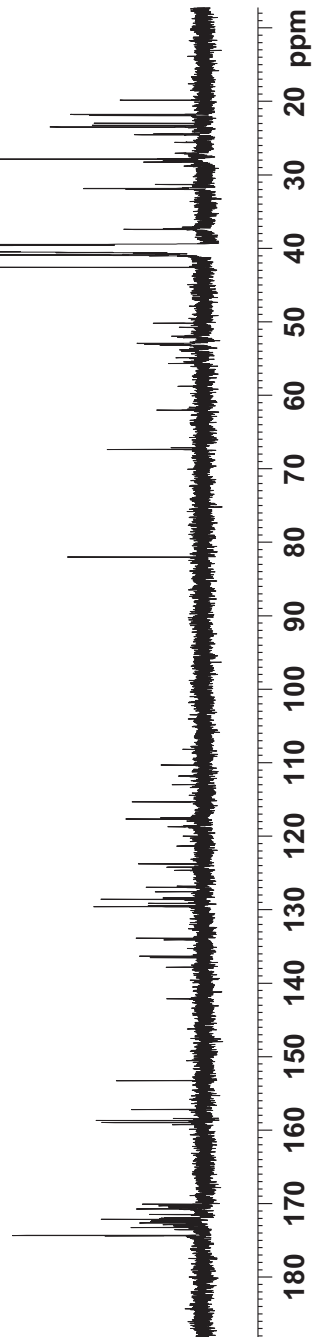


Chemical structures of various 1,2,3,4-tetrahydrophthalazine derivatives, labeled 1a through 1j. The structures show a central tetrahydrophthalazine core substituted with various side chains including amides, alcohols, and aromatic groups.

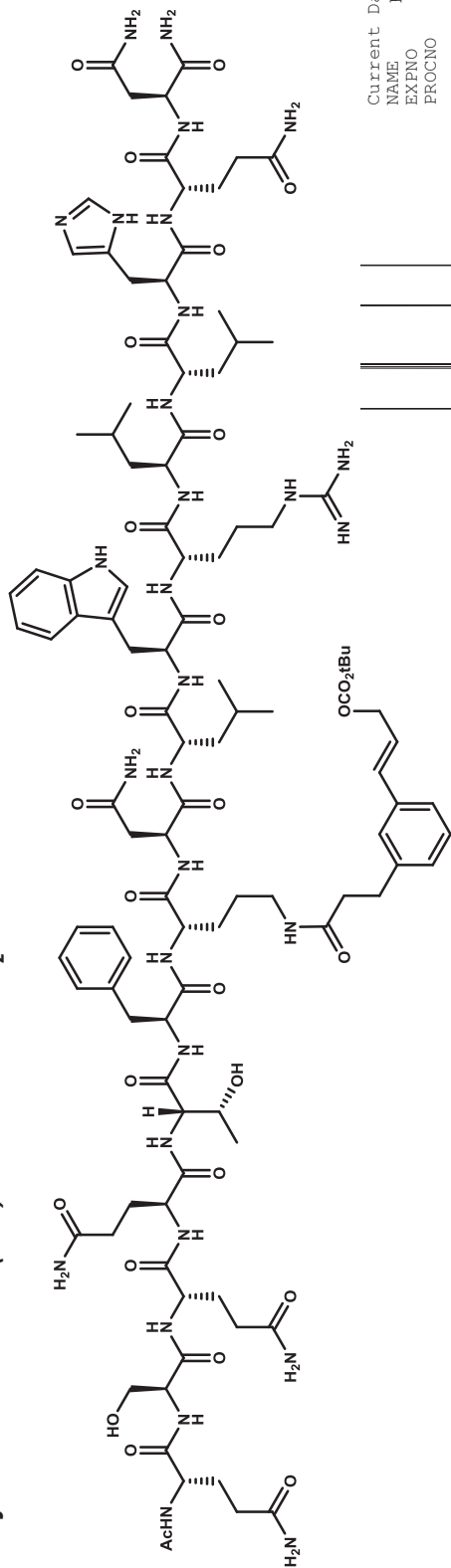
F2 - Acquisition Parameters	
Date_	20121206
Time	17.06
INSTRUM	av500
PROBHD	5 mm DCH 13C-1
PULPROG	zgpg30
TD	65536
SOLVENT	DMSO
NS	125
DS	2
SWH	31250.000 Hz
FIDRES	0.476837 Hz
AQ	1.0485760 sec
RG	202.91
RGW	16.0000 usec
DE	18.00 usec
TE	298.0 K
D1	2.0000000 sec
D11	0.0300000 sec
TD0	1

```
===== CHANNEL f2 =====
500.1330008 MHz
NUC2                                1H
SFO2                                waltz16
CPDPRG[2]                          80.00 usec
PCPD2                               13.5000000 W
PLW2                                0.21094000 W
PLW12                               0.21094000 W
PLW13                               0.13500001 W
```

F2 - Processing parameters	
SI	131072
SF	125.7577892 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0



Acyclic - Ac-QSQQTF(Orn)NLWRLLHQN-NH₂

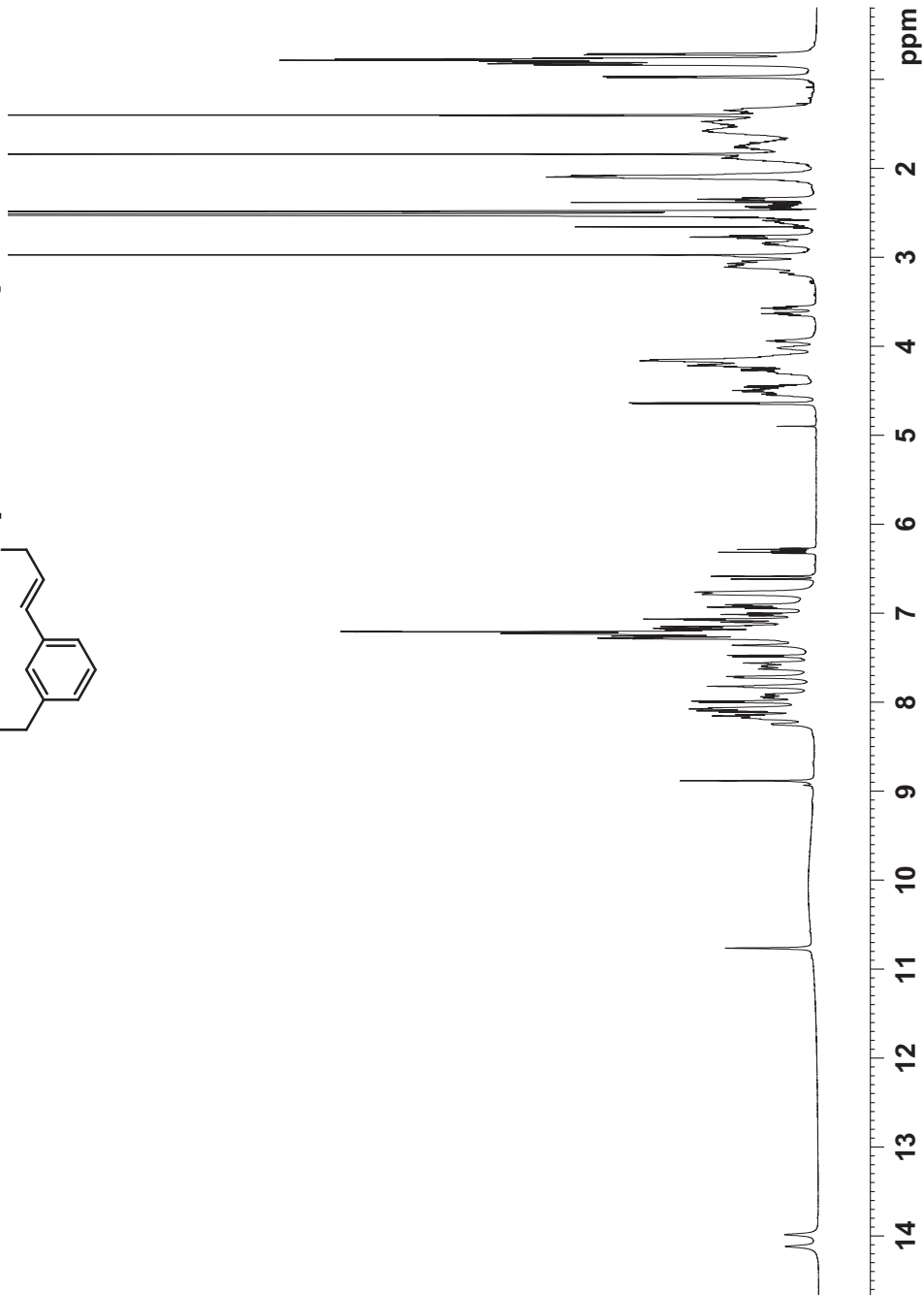


Current Data Parameters
NAME p53_A2_acyclic
EXPNO 10
PROCNO 1

F2 - Acquisition Parameters
Date_ 20121206
Time_ 17.19
INSTRUM av500
PROBHD 5 mm DCH 13C-1
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 8
DS 0
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2767999 sec
RG 11
DW 50.000 usec
DE 10.00 usec
TE 298.0 K
D1 2.0000000 sec
TD0 1

===== CHANNEL f1 =====
SFO1 500.1330008 MHz
NUC1 1H
P1 10.00 usec
PLW1 13.5000000 W

F2 - Processing parameters
SI 65536
SF 500.1300146 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



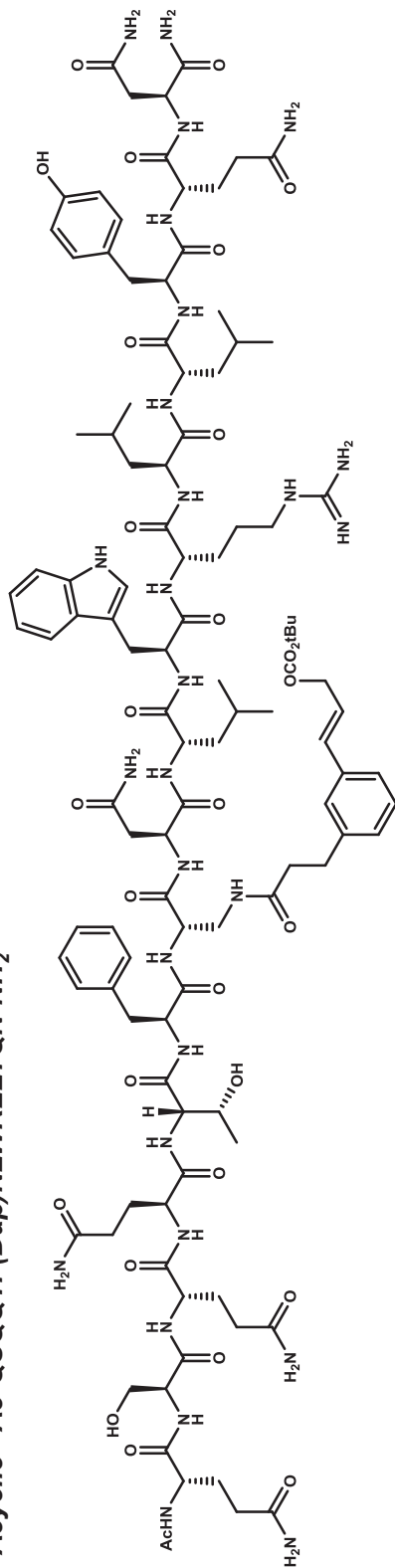
The chemical structure is a complex molecule featuring a central benzene ring. Attached to the benzene ring is a side chain containing a carboxylate group (CO₂iBu) and a long alkyl chain. The molecule also includes several amide groups (NH-C=O), amine groups (NH₂), and a hydroxyl group (OH). The structure is highly branched and contains multiple stereocenters, indicated by wedge and dash bonds. The molecule is labeled with 'Current' and 'D' at the top right.

```
===== CHANNEL f2 =====
SFO2      500.1330008 MHz
NUC2      1H
CPDPRG[2]  waltz16
PCPD2      80.00 usec
PLW2      13.50000000 W
PLW1      0.21094000 W
PLW13     0.13500001 W

F2 - Processing parameters
SI         131072
SF         125.7577892 MHz
SSB        EM
WDW        EM
SSB        0
LB         1.00 Hz
GB         0
```



Acyclic - Ac-QSQQTF(Dap)NLWRLLYQN-NH₂

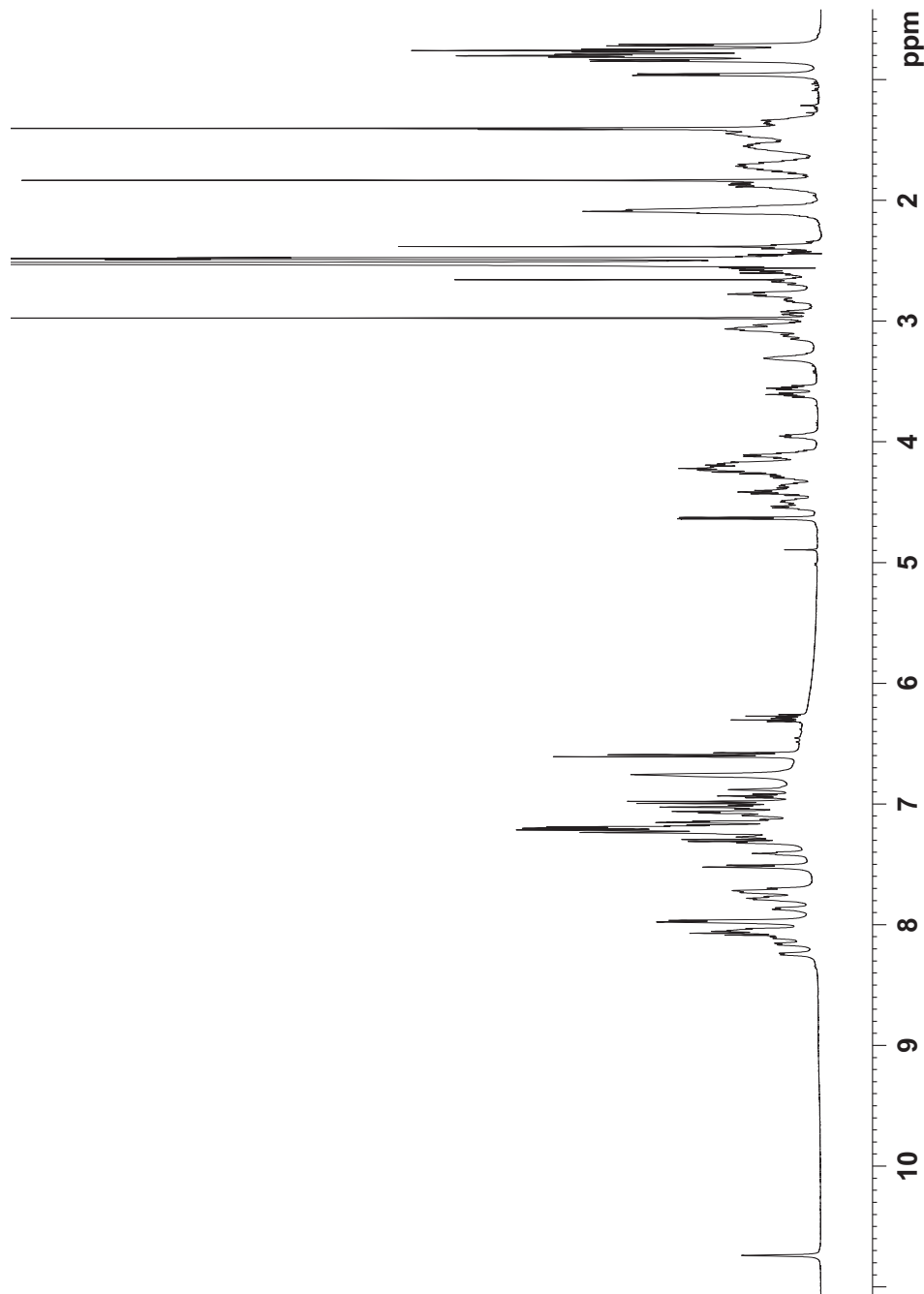


Current Data Parameters
 NAME p53_A3_acyclic
 EXPNO 10
 PROCNO 1

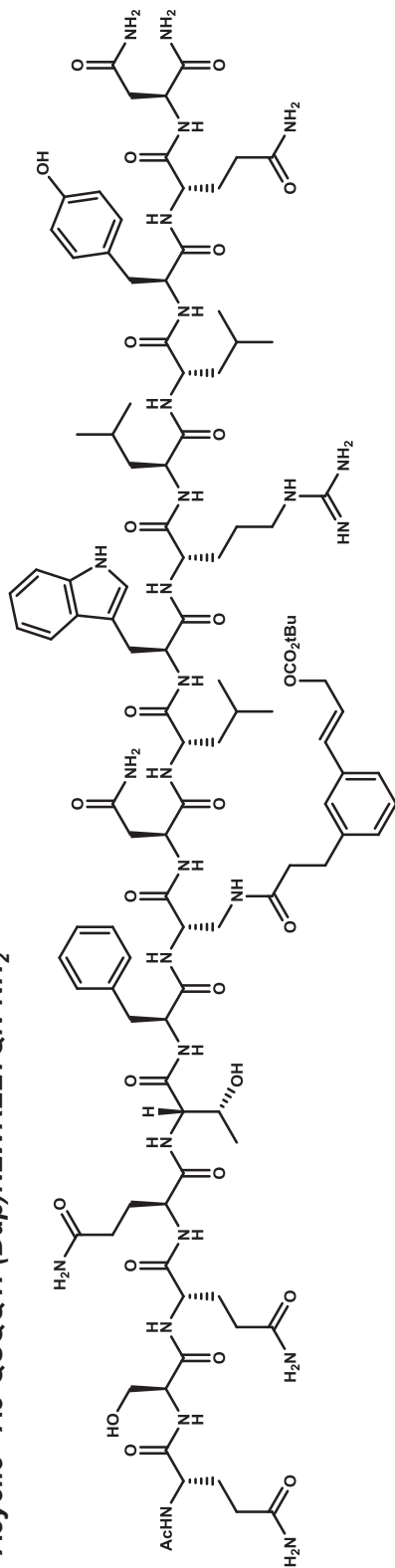
F2 - Acquisition Parameters
 Date_ 20121206
 Time_ 18.17
 INSTRUM av500
 PROBHD 5 mm DCH 13C-1
 PULPROG zg30
 TD 65536
 SOLVENT DMSO
 NS 8
 DS 0
 SWH 10000.000 Hz
 FIDRES 0.152588 Hz
 AQ 3.276799 sec
 RG 20.17
 DW 50.000 usec
 DE 10.00 usec
 TE 298.0 K
 D1 2.0000000 sec
 TD0 1

===== CHANNEL f1 =====
 SFO1 500.130008 MHz
 NUC1 1H
 P1 10.00 usec
 PLW1 13.5000000 W

F2 - Processing parameters
 SI 65536
 SF 500.1300146 MHz
 WDW EM
 SSB 0
 LB 0
 GB 0
 PC 1.00



Acyclic - Ac-QSQQTF(Dap)NLWRLLYQN-NH₂



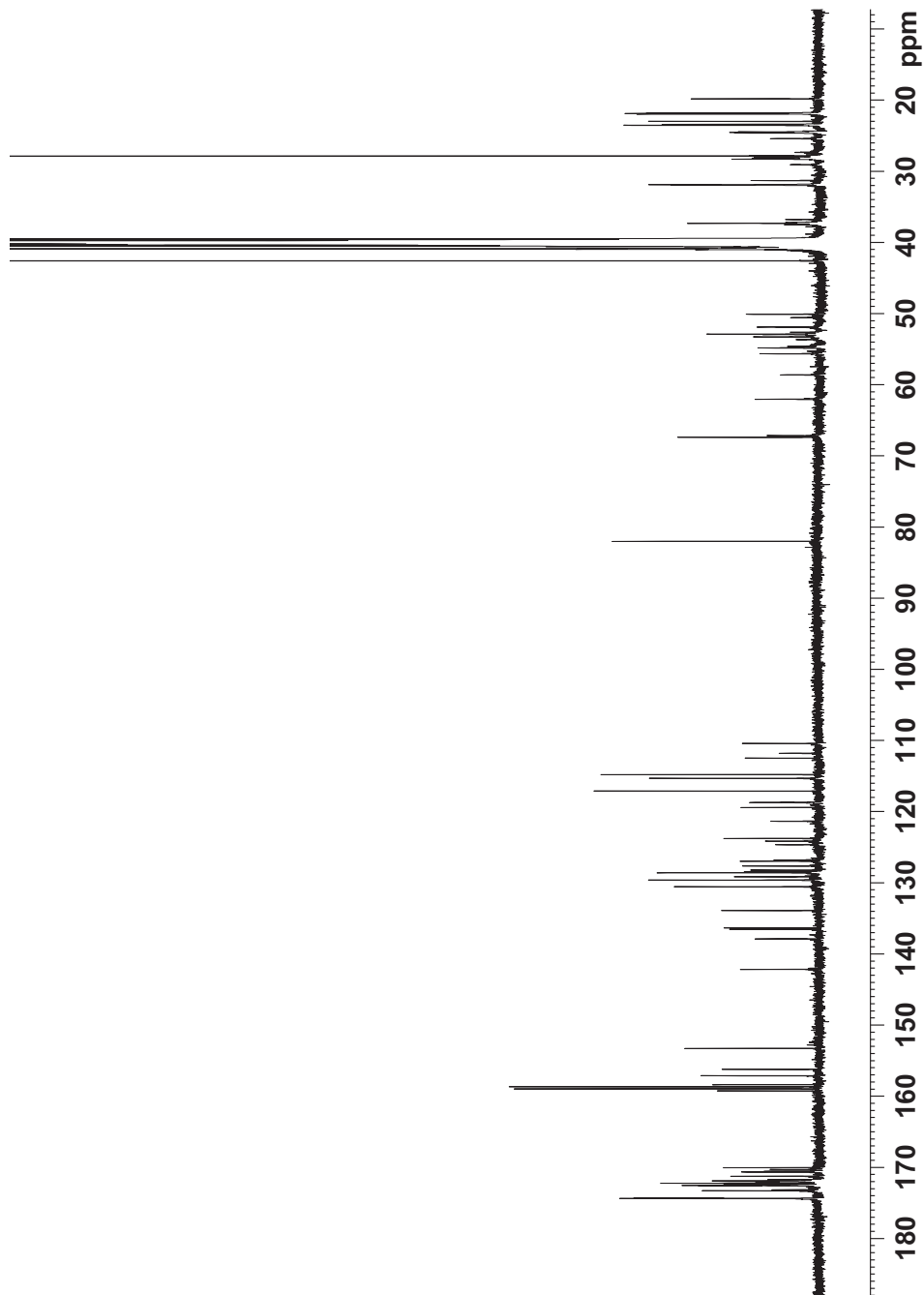
Current Data Parameters
NAME p53_A3_acyclic
EXPNO 11
PROCNO 1

F2 - Acquisition Parameters
Date_ 20121206
Time_ 19.12
INSTRUM av500
PROBHD 5 mm DCH 13C-1
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 1024
DS 2
SWH 31250.000 Hz
FIDRES 0.476837 Hz
AQ 1.0485760 sec
RG 202.91
DW 16.000 usec
DE 18.00 usec
TE 298.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

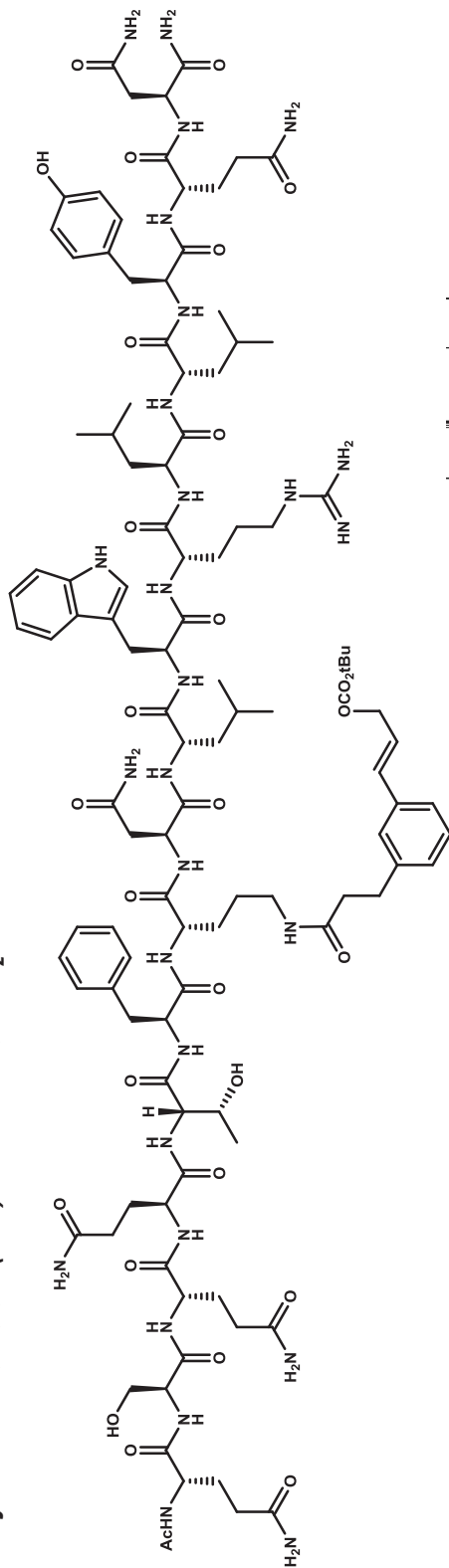
===== CHANNEL f1 =====
SFO1 125.7722511 MHz
NUC1 13C
P1 9.63 usec
PLW1 23.00000000 W

===== CHANNEL f2 =====
SFO2 500.1330008 MHz
NUC2 1H
PCPD2 waltz16
PLW2 13.50000000 W
PLW12 0.21094000 W
PLW13 0.13500001 W

F2 - Processing parameters
SI 131072
SF 125.7577892 MHz
WDW EM
SSB 0
LB 0
GB 1.00 Hz



Acyclic - Ac-QSQQTF(Orn)NLWRLLYQN-NH₂

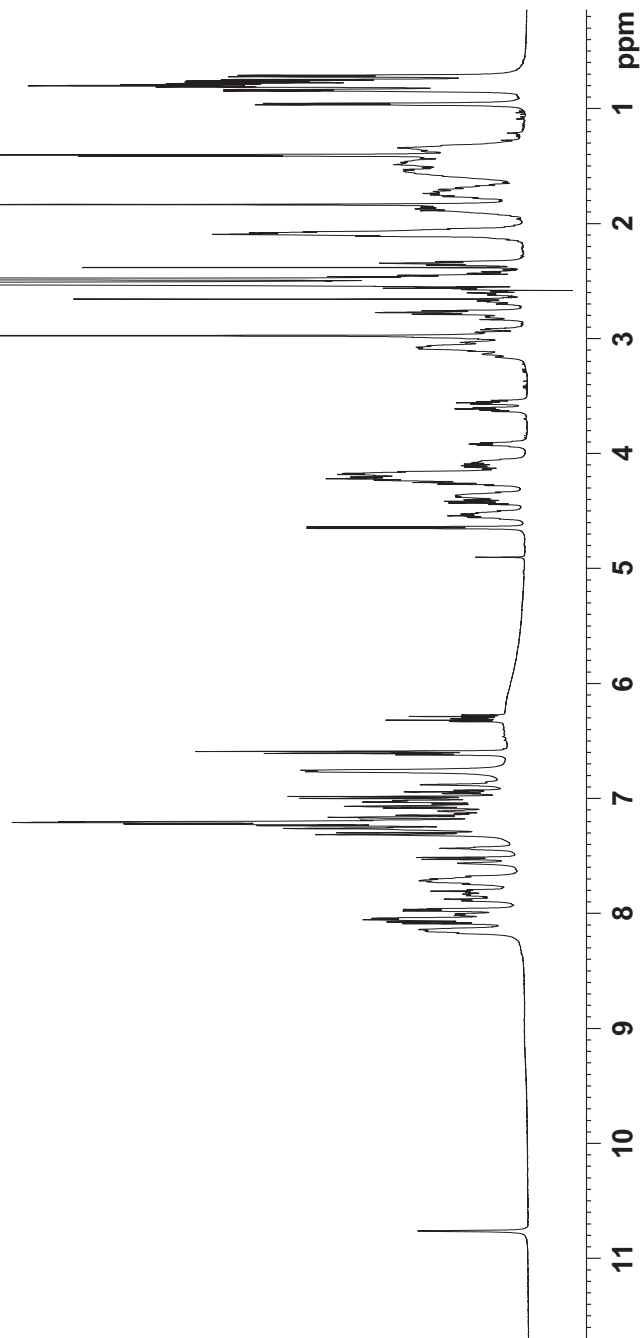


Current Data Parameters
NAME p53_A4_acyclic
EXPNO 10
PROCNO 1

F2 - Acquisition Parameters
Date_ 20121206
Time 19.15
INSTRUM av500
PROBHD 5 mm DCH 13C-1
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 8
DS 0
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2767999 sec
RG 20.17
DW 50.000 usec
DE 10.00 usec
TE 298.0 K
D1 2.0000000 sec
TD0 1

===== CHANNEL f1 =====
SFO1 500.130008 MHz
NUC1 1H
P1 10.00 usec
PLW1 13.5000000 W

F2 - Processing parameters
SI 65536
SF 500.1300146 MHz
WDW EM
SSB 0
LB 0
GB 0
PC 1.00

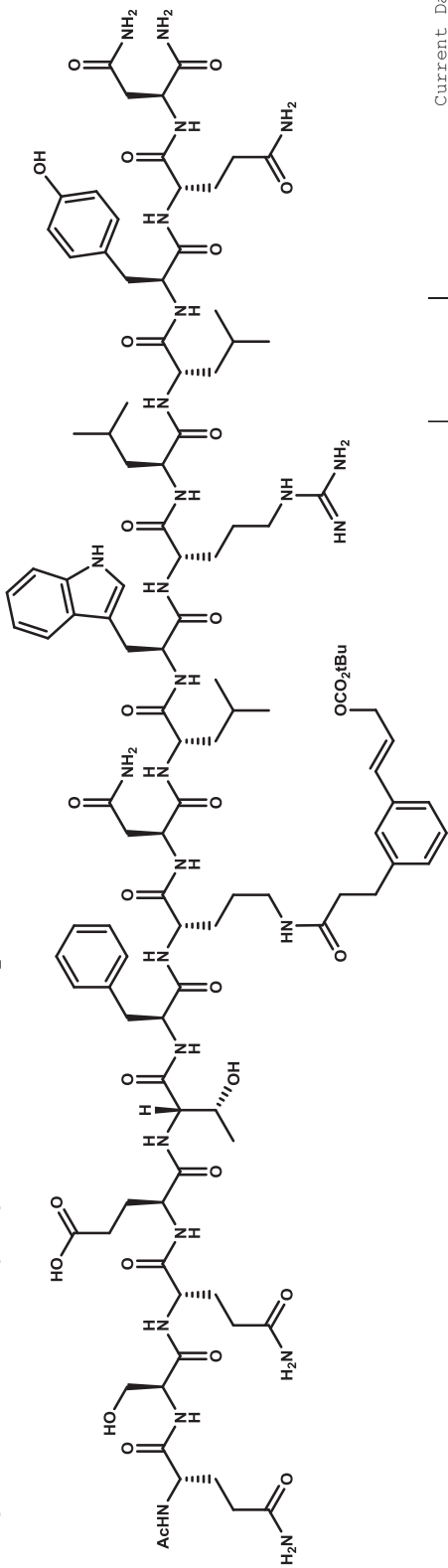


[illegible]

F2 - Processing parameters	
SI	131072
SF	125.7577892 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0



Acyclic - Ac-QSQETF(Orn)NLWRLLYQN-NH₂



Current Data	Parameters
NAME	p53_B6_acy
EXPNO	1
PROCNO	1

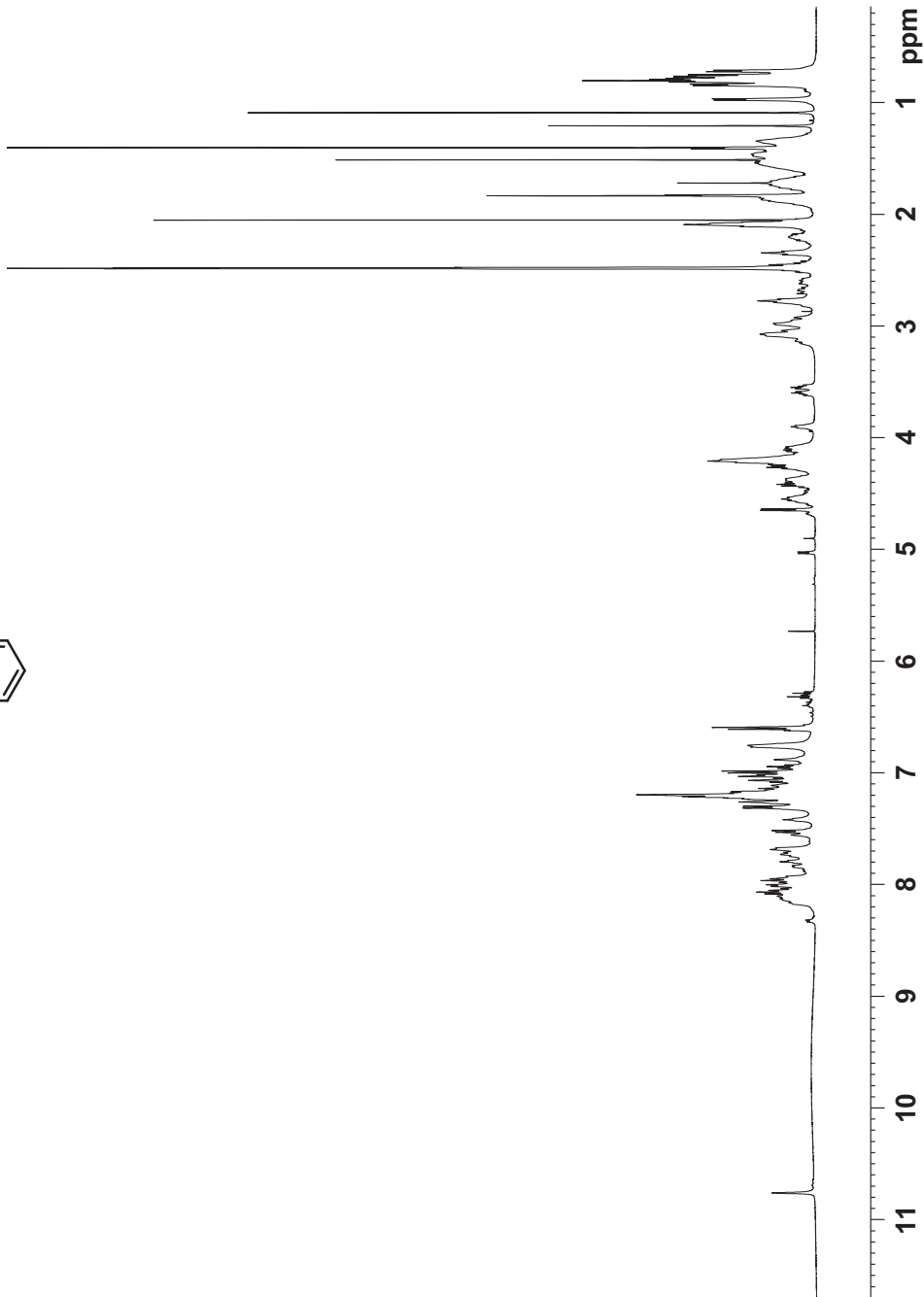
F2 - Acquisition Parameters

Date	20130509
Time	11.27
INSTRUM	av500
PROBHD	5 mm DCH 13C-1
PULPROG	zg30
TD	65536
SOLVENT	DMSO
NS	8
DS	0
SWH	10000.000 Hz
FIDRES	0.152588 Hz
AQ	3.2767999 sec
RG	22.82
DW	50.000 usec
DE	10.00 usec
TE	298.0 K
D1	2.0000000 sec
TD0	1

```
===== CHANNEL f1 =====
SFO1      500.1330008 MHz
NUC1              1H
P1                  10.00 usec
PLW1      13.50000000 W
```

F2 - Processing parameters

SI	65536	
SF	500.1300146	MHz
WDW		EM
SSB	0	
LB		0.30 Hz
GB	0	
PC		1.00

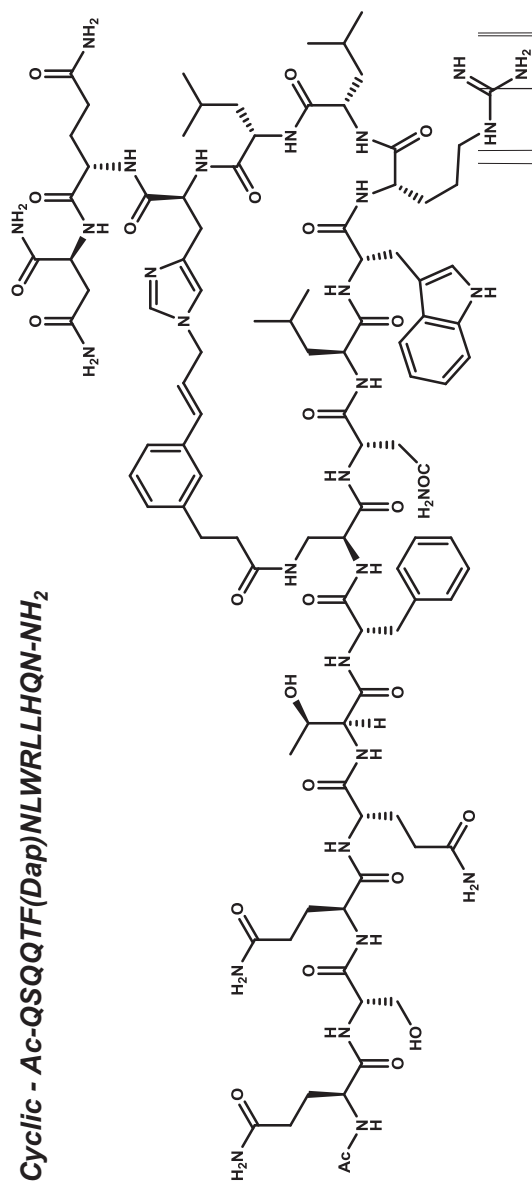


The chemical structure is a complex molecule featuring a central chain with multiple amide, ester, and hydroxyl groups. The structure includes several aromatic and heterocyclic systems, including a benzene ring, a pyridine ring, and a quinoline ring. The molecule is highly functionalized, with numerous amide and ester groups, and a central chain that is highly branched and contains multiple stereocenters. The structure is a complex derivative of a natural product, likely a peptide or a related compound, and is highly functionalized with various groups, including amide, ester, and hydroxyl groups. The molecule is highly branched and contains multiple stereocenters, making it a complex and highly functionalized compound.

F2 - Processing parameters	
SI	131072
SF	125.7577892 MHz
WDW	EM



Cyclic - Ac-QSQQTF(Dap)NLWRLHQN-NH₂



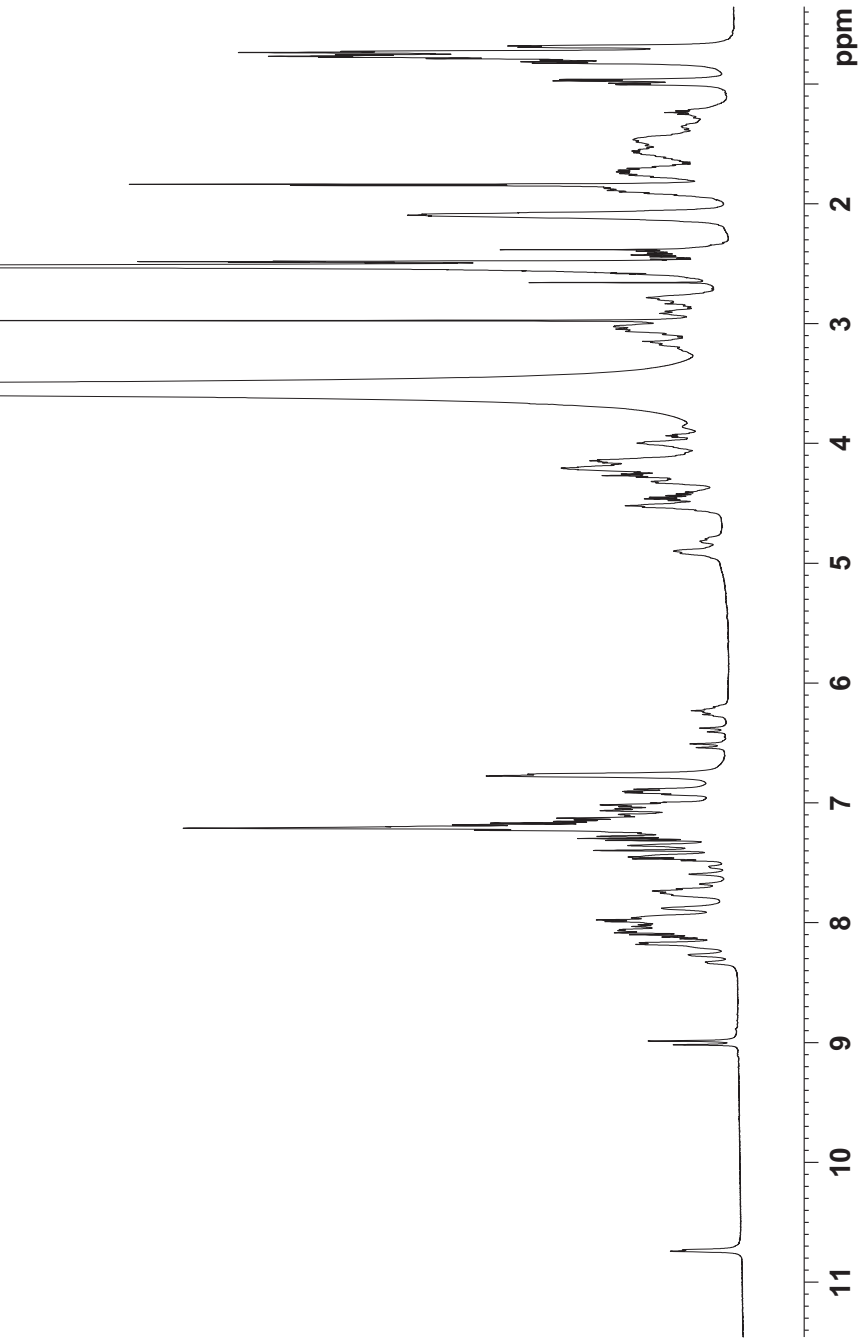
```

Current Data Parameters
NAME      p53_A1_cycle
EXPNO     3
PROCNO    1

F2 - Acquisition Parameters
Date_     20130122
Time      18.59
INSTRUM   av500
PROBHD    5 mm DCH 13C-1
PULPROG   zg
TD         65536
SOLVENT    DMSO
NS         8
DS         0
SWH        10000.000 Hz
FIDRES     0.152588 Hz
AQ         3.276799 sec
RG         11
DW         50.000 usec
DE         10.00 usec
TE         298.0 K
D1         2.0000000 sec
TD0        1

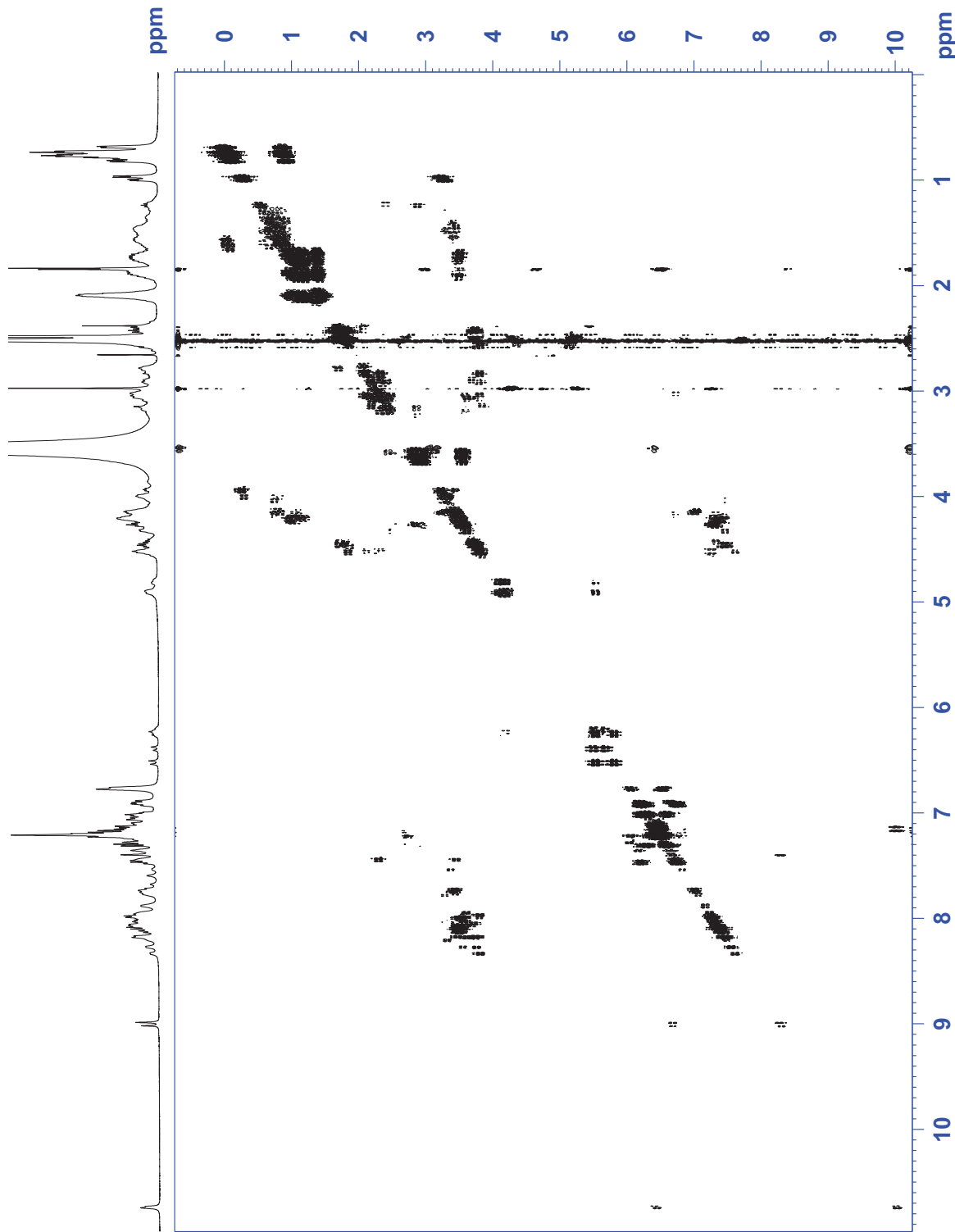
===== CHANNEL f1 =====
SFO1      500.1330008 MHz
NUC1      1H
P1         10.00 usec
PLW1      13.50000000 W

F2 - Processing parameters
SI         65536
SF         500.1300146 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.40
    
```



Cyclic - Ac-QSQQTF(Dap)NLWRLHQN-NH₂

COSY



```

Current Data Parameters
NAME      p53_A1_cycle
EXPNO     4
PROCNO    1

F2 - Acquisition Parameters
Date_     20130122
Time      19.03
INSTRUM   av500
PROBHD    5 mm DCH 13C-1
PULPROG   cosygpmfph
TD         4096
SOLVENT   DMSO
NS         4
DS         8
SWH        5498.534 Hz
FIDRES     1.342415 Hz
AQ         0.3724629 sec
RG         202.91
DE         90.933 usec
TE         10.00 usec
D0         298.0 K
D1         0.00007817 sec
D13        2.00000000 sec
D16        0.00000400 sec
IN0        0.00020000 sec

===== CHANNEL f1 =====
SF01      500.1327507 MHz
NUC1       1H
P1         10.00 usec
P2         20.00 usec
PLW1      13.50000000 W

===== GRADIENT CHANNEL =====
GPNAM[1]   SMSQ10.100
GPNAM[2]   SMSQ10.100
GP21       10.00 %
GP22       20.00 %
P16        1000.00 usec

F1 - Acquisition parameters
TD         256
SF01      500.1328 MHz
FIDRES     21.486525 Hz
SW         10.998 ppm
F0MODE     States-TPPI

F2 - Processing parameters
SI         2048
SF         500.1300135 MHz
WDW        SINE
SSB        0 Hz
LB         0
GB         0
PC         1.00

F1 - Processing parameters
SI         2048
MC2        States-TPPI
SF         500.1303720 MHz
WDW        SINE
SSB        0 Hz
LB         0
GB         0
    
```

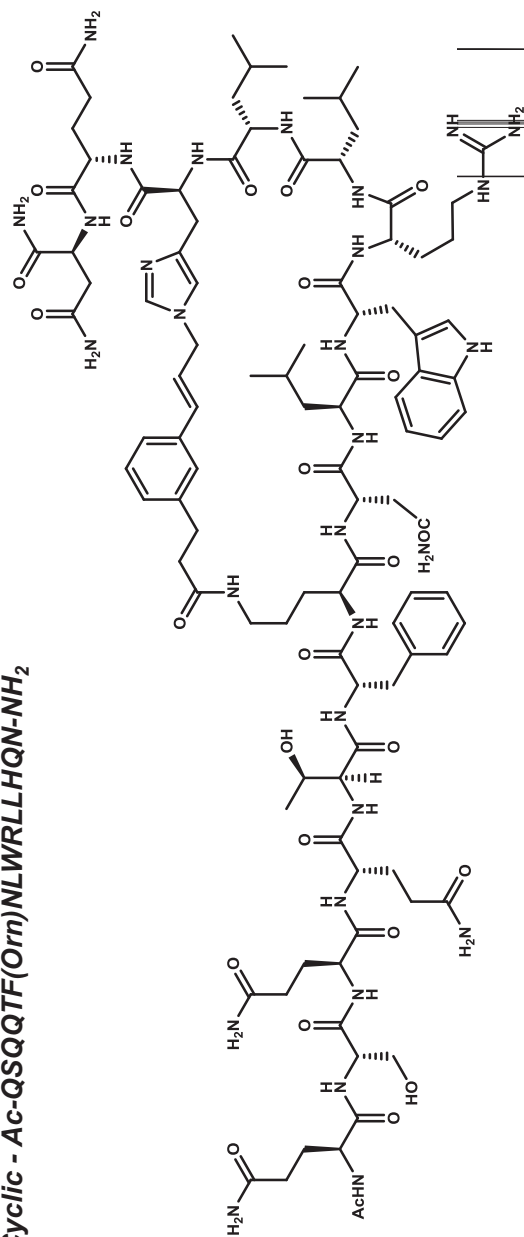
TOCSY



HMBC



Cyclic - Ac-QSQQTF(Orn)NLWRLLHQN-NH₂

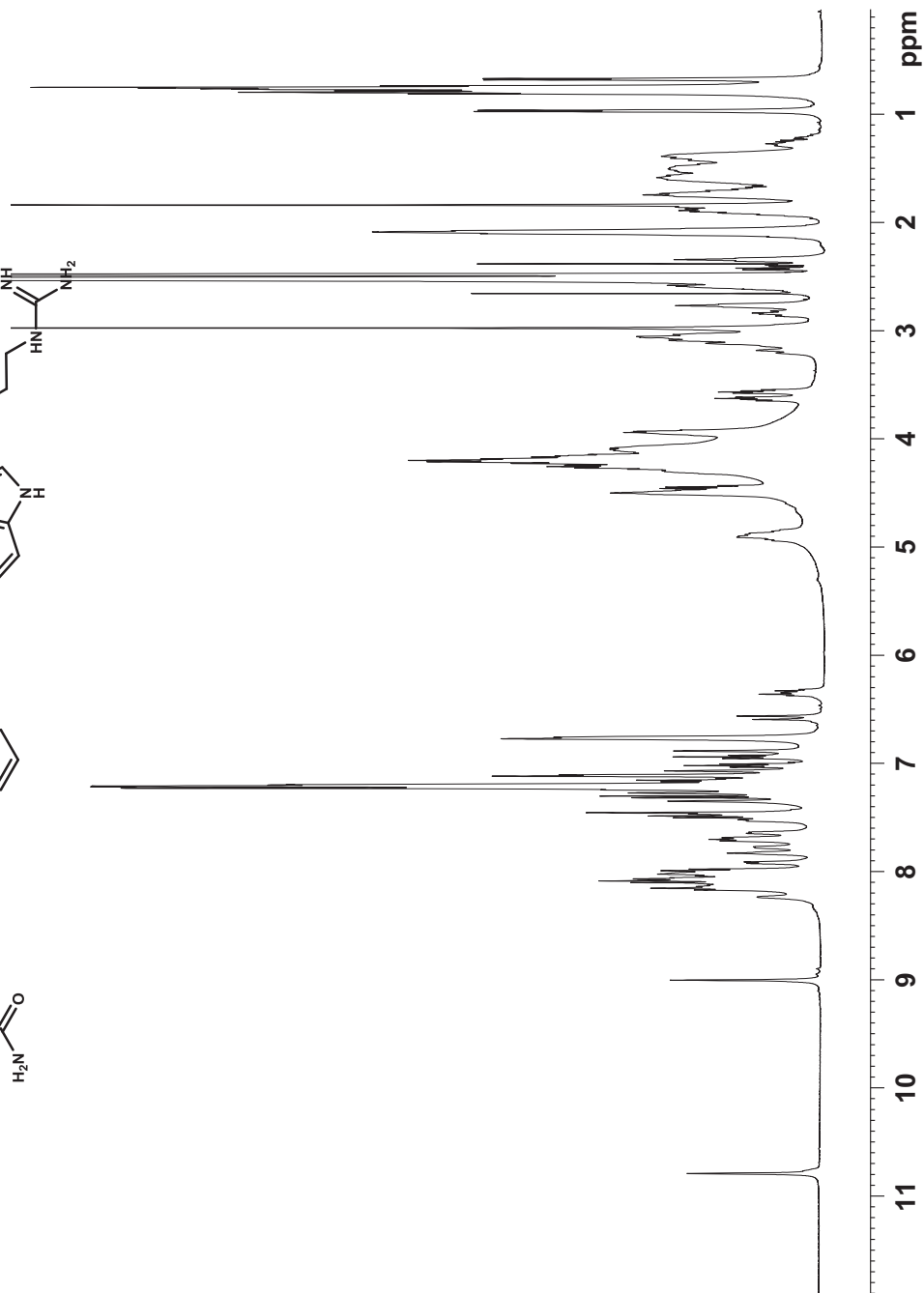


Current Data Parameters
NAME p53_A2b_cycle
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20121211
Time 17.15
INSTRUM av500
PROBHD 5 mm DCH 13C-1
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 64
DS 0
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2767999 sec
RG 11
DW 50.000 usec
DE 10.00 usec
TE 298.0 K
D1 2.0000000 sec
TD0 1

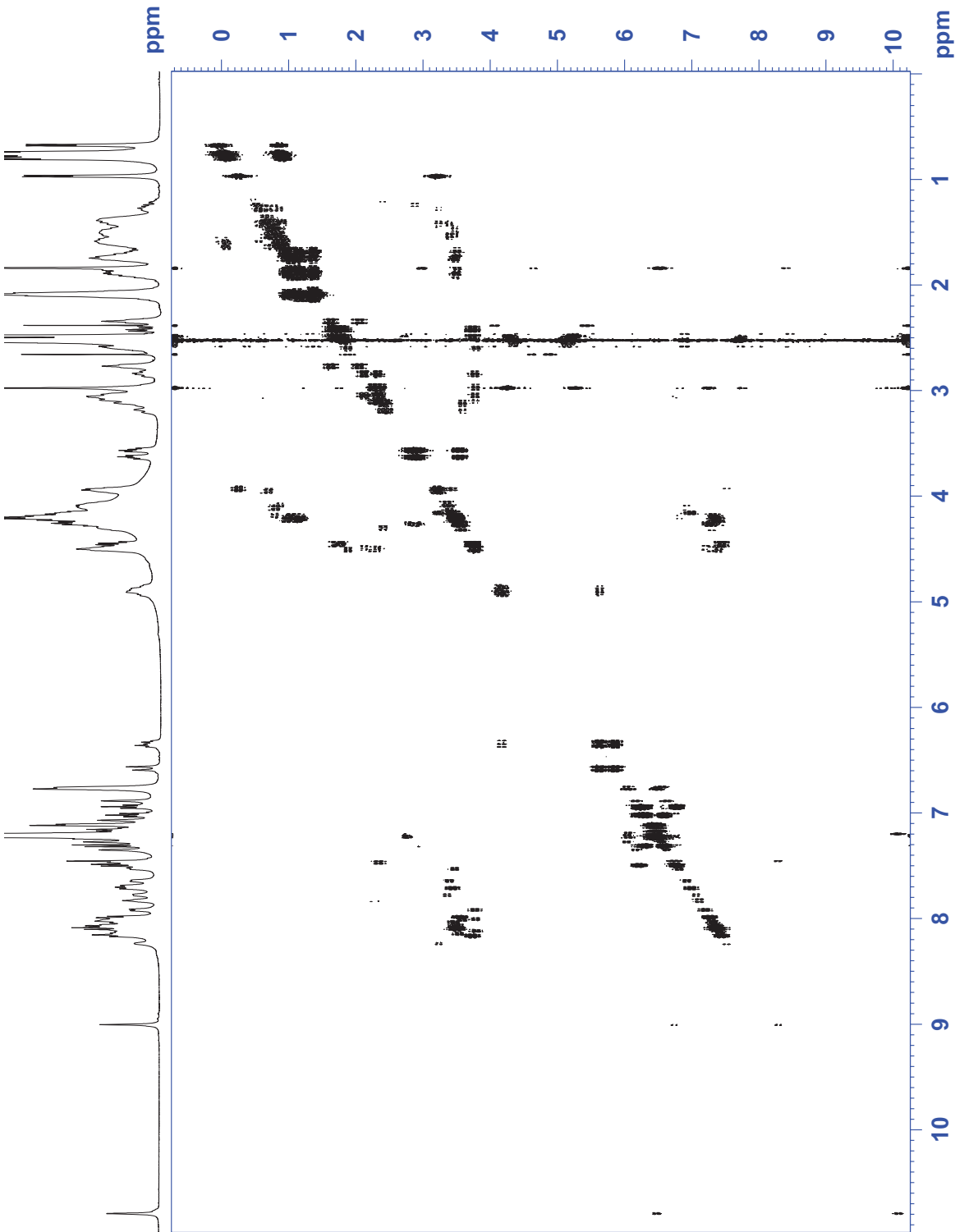
==== CHANNEL f1 =====
SFO1 500.1300008 MHz
NUC1 1H
P1 10.00 usec
PLW1 13.50000000 W

F2 - Processing parameters
SI 65536
SF 500.1300146 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.40



Cyclic - Ac-QSQQTF(Orn)NLWRLLHQN-NH₂

COSY



Current Data Parameters
NAME p53_A2b_cycle
EXPNO 3
PROCNO 1

F2 - Acquisition Parameters
Date_ 20121211
Time_ 17.15
INSTRUM av500
PROBHD 5 mm DCH 13C-1
PULPROG cosygpmph
TD 4096
SOLVENT DMSO
NS 2
DS 8
SWH 5498.534 Hz
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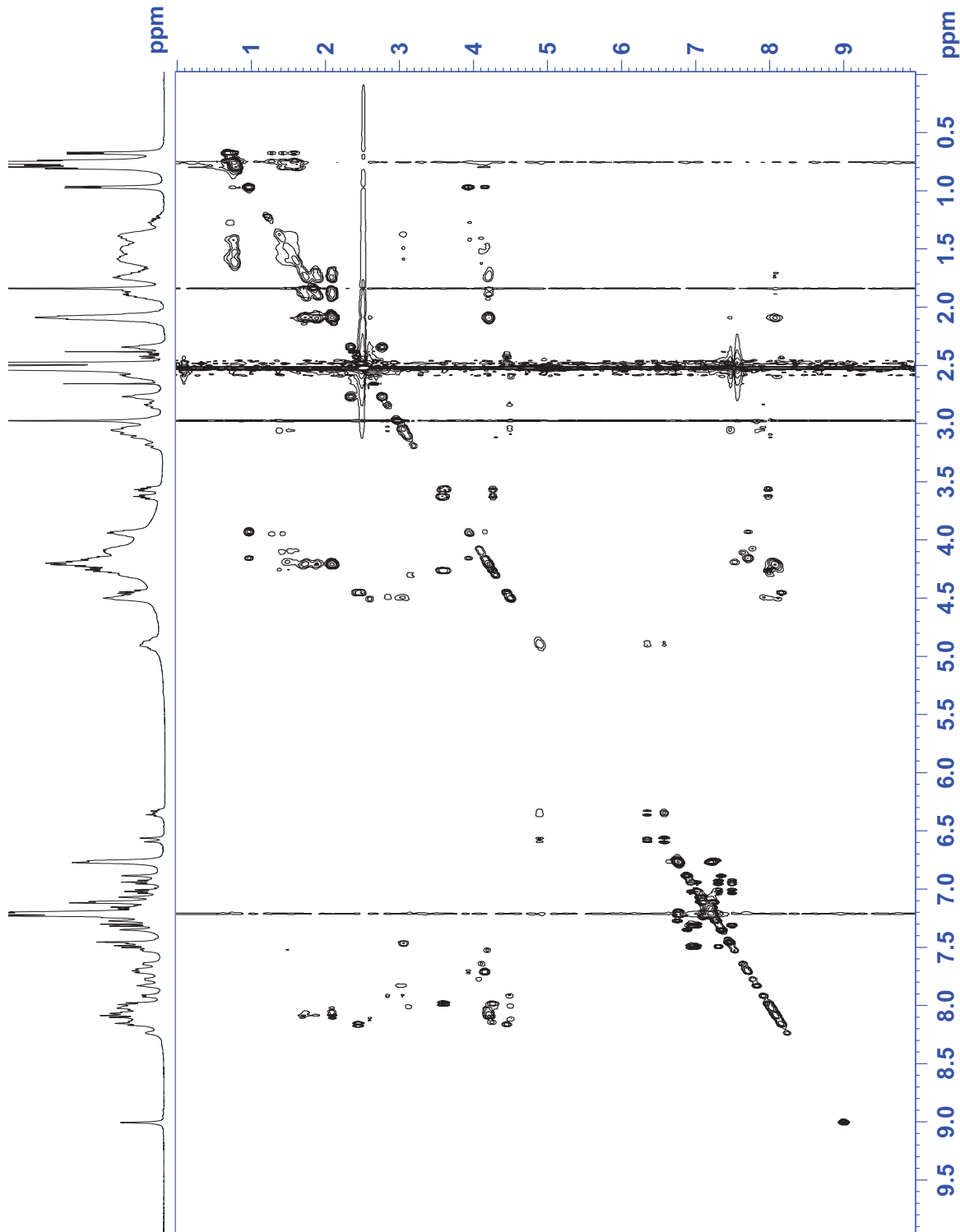
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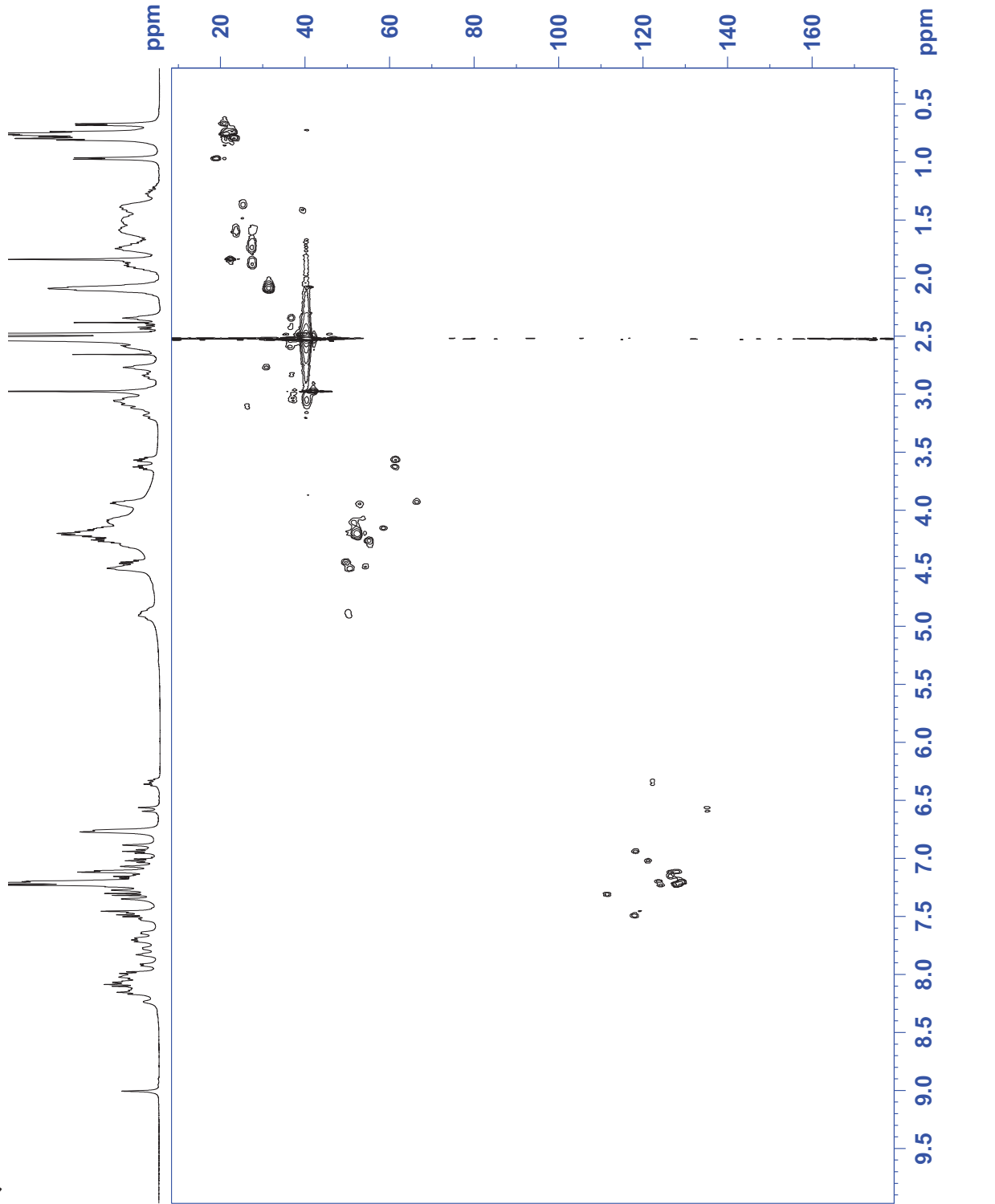
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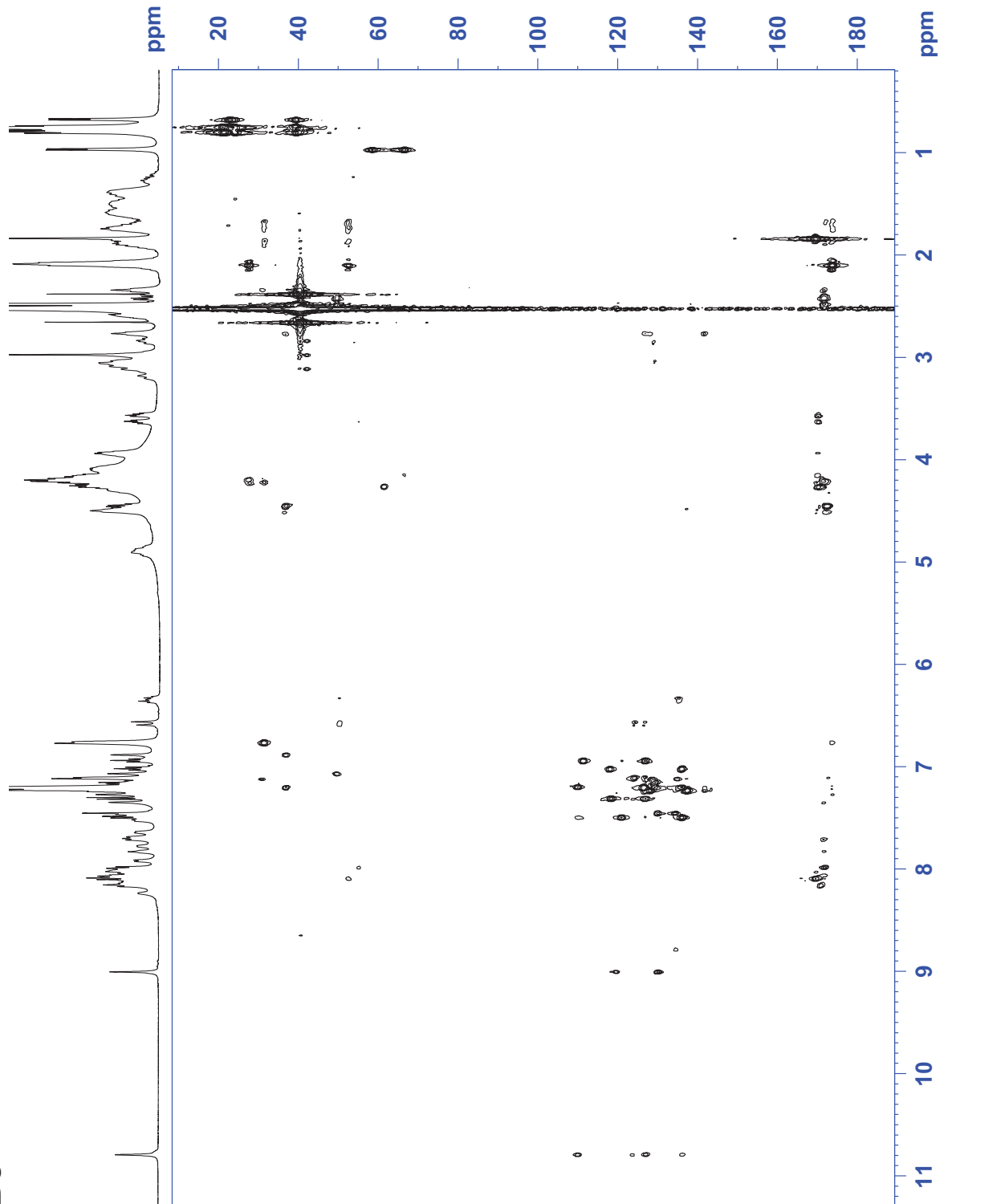
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Chapter 4 - Diverse macrocyclic peptidomimetics through Friedel-Crafts alkylations of tryptophan and tyrosine

adapted in part from

Template-induced macrocycle diversity through large-ring forming alkylations of tryptophan

Kenneth V. Lawson, Tristan E. Rose, Patrick G. Harran

Tetrahedron **2013**, 69 (36), 7683-7691

4.1. Introduction

As opportunities in biological research and drug discovery expand, there is considerable need for synthetic methods that form new types of complex small molecules.¹ Conventional screening libraries often fail to produce viable lead structures when challenged with demanding targets.² These include receptors with relatively large, dynamic, or solvent exposed ligand binding sites and protein-protein interaction surfaces.³ Recent drug discovery efforts aimed at such targets⁴ have benefited from biophysical studies highlighting 'hot spots' within these larger binding motifs.⁵ Focused libraries that incorporate structures able to interact selectively and avidly with such sites would be valuable. Molecules that recapitulate the three-dimensional display of functional groups found in native binding partners while possessing favorable pharmacological properties would be ideal.

Peptides are intrinsically relevant to this goal. They are a logical starting point to identify ligands for protein surfaces.⁶ However, peptides frequently exhibit poor bioavailability and limited stability in vivo.⁷ Numerous strategies have been developed to mitigate these problems, including the incorporation of D-configured⁸ and non-proteinogenic amino acids,⁹ pseudo-peptide bonds and conformational constraints.^{10,11} Each of these features is seen in peptide-derived macrocyclic natural products, which often possess markedly different properties relative

to their acyclic precursors. With macrocycles as a central theme, we have sought to expand upon existing methods for large ring formation.

In a previous report, we outlined elements of a program aimed at systematically generating complex peptidomimetics.¹² These experiments used designed templates (Fig. 1B) to form composite structures with peptides.¹³ Our current templates capitalize on reactivity of the cinnamyl cation, and transiently formed palladium complexes thereof, to efficiently promote large ring-forming substitution reactions involving aromatic rings and heteroatom nucleophiles. While numerous methods exist to prepare peptidic macrocycles, most require tailored reacting partners.^{14,15} Our template chemistry exploits reactivity inherent to a subset of natural amino acid side chains.

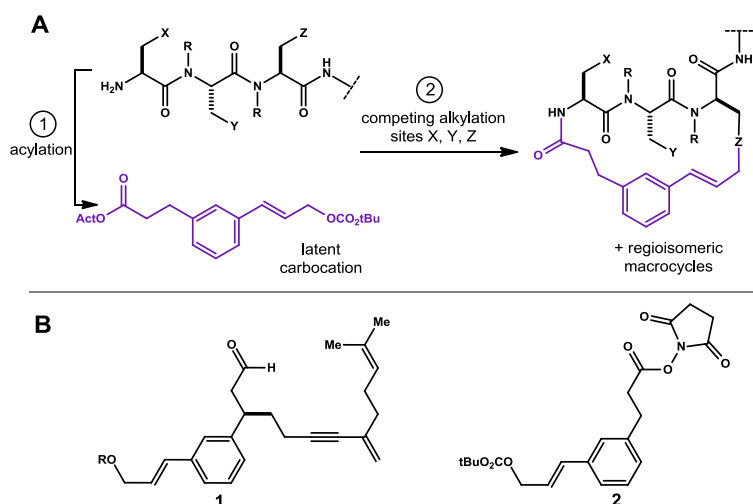


Figure 1. A) Current template designs (purple) utilize a cinnamyl mixed carbonate as a latent electrophile. Competing reactions with side-chain nucleophiles provide isomeric macrocycles of varying shape, B) prototypical templates **1** and **2** (this work). R = CO₂CMe₂CCl₃

For example, we used the allylic carbonate in template **1** (Fig. 1B) to form macrocyclic ethers by engaging the phenol of tyrosine in palladium catalyzed substitution reactions.^{12,16} In the context of peptides harboring other aromatic residues, we observed that acid treatment caused these ethers to rearrange, wherein the cinnamyl unit migrated to adjacent tryptophan residues forming stable carbon-carbon bonded products. This was an exciting discovery. To

probe this reactivity in greater detail, and in systems not complicated by competing rearrangements of the diene-yne appendage in **1**, we synthesized template **2**.¹⁷ Using simple, straightforward chemistry, composites of **2** participate in remarkable reactions that alter the structure and properties of linear peptide motifs (*vide infra*).

Towards the goal of rapidly accessing diverse, natural product-like structures, we demonstrate use of **2** in a divergent process to prepare mixtures of macrocyclic products displaying a peptidic binding epitope.¹⁸ In two synthetic steps, template **2** transforms a peptide harboring multiple nucleophilic side-chains (X, Y, Z Fig. 1A) into constitutionally isomeric macrocycles through competing reaction pathways. The resulting products differ in core ring size and conformation, each dictating a unique display of side chains.¹⁹ The structural diversity derived from this process arises from the nature of the starting peptide and the reactivity of the template. Processes of this kind have potential to create composite macrocycles with inherent complementarity to protein surfaces.

4.2. Results and Discussion

4.2.1. Preparation of Cyclic and Acyclic Acidolysis Precursors

Template **2** was prepared from commercial 3-(3-bromophenyl)propionic acid in 6 steps and 51% overall yield.¹⁷ This material acylated the N-terminus of synthetic Trp-Trp-Tyr-NH₂

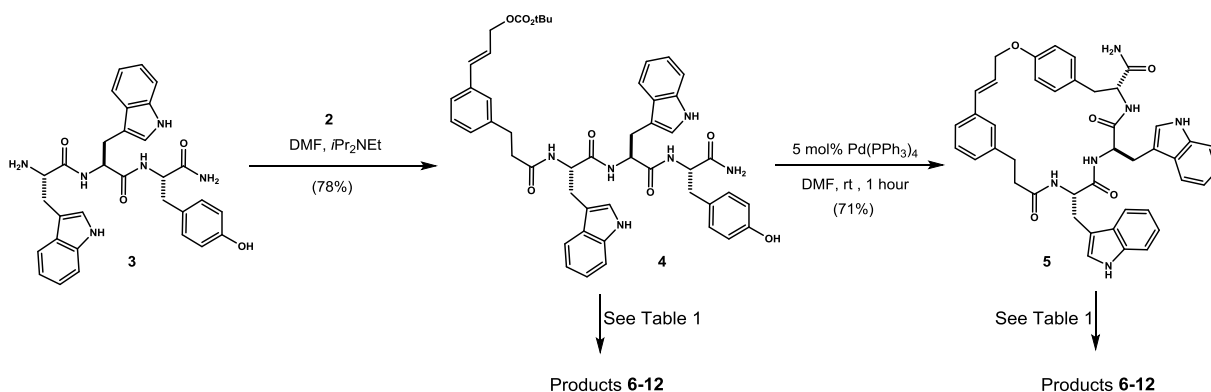


Figure 2. Reaction conditions: a) H-Trp-Trp-Tyr • TFA (1 eq.), template **2** (1 eq.), *i*Pr₂NEt (4 eq.), DMF (0.1M). b) Pd(PPh₃)₄ (5 mol %), DMF (5 mM, degassed).

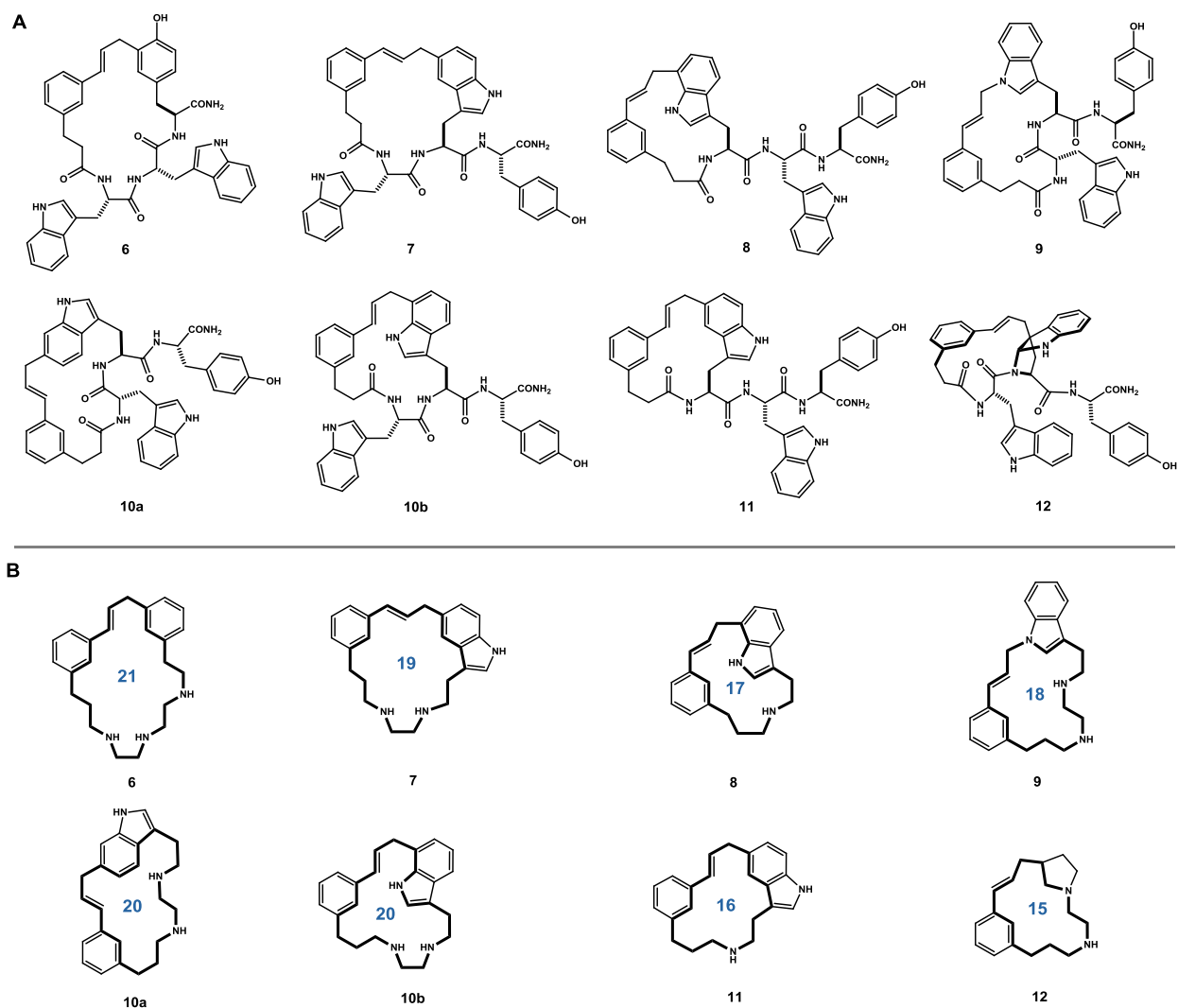


Figure 3. A) Products obtained and fully characterized from acidolyses of **4** and **5**. For conditions and relative yields see Table 1. B) Macrocyclic core structures **6-12** have, to our knowledge, not been reported in the literature.

without incident, providing composite product **4** in good yield (Fig. 2). Analogous to previous work, exposure of **4** to 5 mol% $\text{Pd}(\text{PPh}_3)_4$ catalyzed efficient macrocyclization to give tyrosine *O*-linked cinnamyl ether **5**. Treatment of **5** with 15 equiv. methanesulfonic acid in anhydrous nitromethane at room temperature provided a mixture of three isolable products (Fig. 3A and 5B). These proved to be analogous to the four macrocyclic core structures observed previously from reactions of template **1** with Trp-Trp-Tyr-NH₂.¹² Close inspection of HPLC-MS ion chromatograms indicated the presence of five additional minor isomers (vide infra). Combined,

those eight products accounted for >95% of the total peak area (HPLC-UV at 254 nm). This confirmed that template **2** was an excellent model for further study.

4.2.2. Purification and Characterization

Acidolysis products **6-12** were readily separated by reverse phase preparative HPLC (Fig. 5). From macrocyclic ether **5**, we initially isolated only **6**, **7**, and **11** in sufficient quantities for NMR analyses. Upon refining the reaction conditions (see Sect. 2.3 and Table 1), initially trace components **8**, **9**, **10** and **12** were also isolated. Compounds **6-9**, **11** and **12** were each

Entry	Substrate	Promoter	Equiv.	Temp	Solvent	Compound %						
						6	7	8	9	10	11	12
1	5	MeSO ₃ H	5	rt	MeNO ₂	74	4	3	3	1	12	3
2	5	MeSO ₃ H	15	0 °C	MeNO ₂	71	6	3	2	2	13	3
3	5	MeSO ₃ H	15	rt	MeNO ₂	63	7	4	3	2	17	4
4	5	MeSO ₃ H	25	-20 °C	MeNO ₂	58	10	4	3	2	20	4
5 ^a	5	MeSO ₃ H	5	-20 °C	MeNO ₂	95	<1	<1	<1	<1	4	<1
6	5	MeSO ₃ H	15	rt	CH ₂ Cl ₂	N/A ^b	-	-	-	-	-	-
7 ^a	5	CF ₃ SO ₃ H	15	rt	CH ₂ Cl ₂	N/A ^b	-	-	-	-	-	-
8	5	TFA	50%v	rt	CH ₂ Cl ₂	3	24	8	15	3	34	13
9	5	TFA	15	rt	CH ₂ Cl ₂	95	<1	<1	<1	<1	4	<1
10	5	Sc(OTf) ₃	1	rt	MeNO ₂	61	3	6	2	1	22	5
11	4	MeSO ₃ H	15	rt	MeNO ₂	12	16	6	9	5	40	12
12	4	TFA	50%v	rt	CH ₂ Cl ₂	32	17	7	7	1	28	8
13 ^a	4	TFA	15	rt	CH ₂ Cl ₂	21	14	6	7	5	35	11
14	4	CF ₃ SO ₃ H	1	rt	MeNO ₂	N/A ^b	-	-	-	-	-	-
15	4	HCO ₂ H	50%v	rt	H ₂ O	NR	-	-	-	-	-	-
16 ^c	4	Tf ₂ NH	2	rt	MeNO ₂	4	14	5	8	6	38	24
17	4	Sc(OTf) ₃	1	rt	MeNO ₂	9	1	9	<1	<1	68	13

Table 1. Effect of substrate and acid promoter on product distribution in rearrangement reactions of cyclic ether **5** and direct large-ring closure reactions of acyclic mixed carbonate **4**. Reaction conditions: substrate (5 mM) in indicated solvent, 2 hours unless otherwise noted. ^a16 hour reaction time. ^bDecomposition to non-isomeric products observed. ^c30 minute reaction time.

obtained in >95% purity. Only fraction **10** was isolated as a mixture of closely related regioisomers **10a** and **10b**, which were characterized together.

The planar structures of compounds **6-12** (Fig. 3A) were determined by complete assignment of their proton and carbon connectivities on the basis of homo- and heteronuclear correlations obtained from 2D and selective 1D NMR experiments (see supplementary information). Structural elucidation involved 1) sequential assignment of the peptide backbone, 2) correlation of backbone atoms to their corresponding side chain aromatic ring, and 3) determination of the connectivity of the cinnamyl moiety to an aromatic side chain.

In this model peptide, complete resonance assignment of the peptide was required to differentiate between the two tryptophan residues. Sequential assignment of the amide backbone was made by H^N -C(O) and H^α -C(O) correlations observed by HMBC,²⁰ or by $H_i^\alpha - H_{i+1}^N$ NOE where ambiguities arose from weak correlations or overlapping carbonyl resonances.²¹ Assignment of residue specific H^N - H^α - H^β spin systems from TOCSY spectra was then possible,²² and connectivity of H^β to the aromatic portion of the side chain was established from reciprocal HMBC correlations.

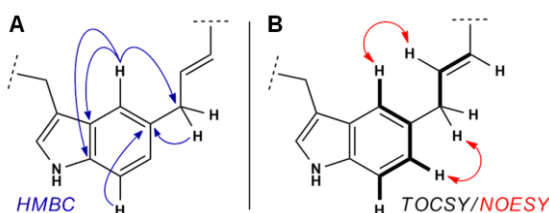


Figure 4. Connectivity of macrocycles was determined from A) HMBC or B) TOCSY and NOESY/ROESY correlations, as illustrated for tryptophan indole C5 alkylation products **7** and **11**.

The ansa bridge motif arising from electrophilic aromatic substitution causes a characteristic loss of one proton relative to the parent 1H spin system of the aromatic amino acid side chains which was apparent by TOCSY. The precise position of substitution was deduced from careful analysis of $^{2,3,4}J_{CH}$ correlations observed in HMBC experiments (e.g. Fig. 4A). In general, heteronuclear correlations from the cinnamyl methylene to aromatic resonances of the substituted ring, and the reciprocal thereof, allowed unambiguous structural assignment. In cases where HMBC correlations were either unclear or not observed, the connectivity of the cinnamyl unit was inferred from NOE correlations between the two proximal spin systems observed by TOCSY (Fig. 4B).

The isomeric products obtained from acidolysis of macrocyclic ether **5** comprised three of the four outcomes anticipated from previous work. We obtained compound **6**, arising from rearrangement of the *O*-linked macrocyclic ether to the phenolic *ortho* position, as the

predominant product. The next most abundant outcomes derived from alkylation of tryptophan at indole C5. Substitution of Trp1 (**11**) and Trp2 (**7**) at indole C5 comprised 17% and 7% of the product mixture, respectively. The absence of branched isomers observed previously from alkylation at indole C2 likely reflects a subtle difference between the conformational preferences of templates **1** and **2**.¹²

4.2.3. Unprecedented large ring-forming Friedel-Crafts alkylations

We next investigated what role the cinnamyl ether in **5** played in the formation of carbon-carbon bonded isomers. Acid promoted rearrangement of cyclic ether **5** to isomers **6-12** is, for this substrate, a set of competing ring contractions. It was possible that starting from a pre-organized cyclic template like **5** was necessary to observe such outcomes. Large ring-forming Friedel-Crafts alkylations are virtually absent from the literature.^{23,24} To test this idea, we

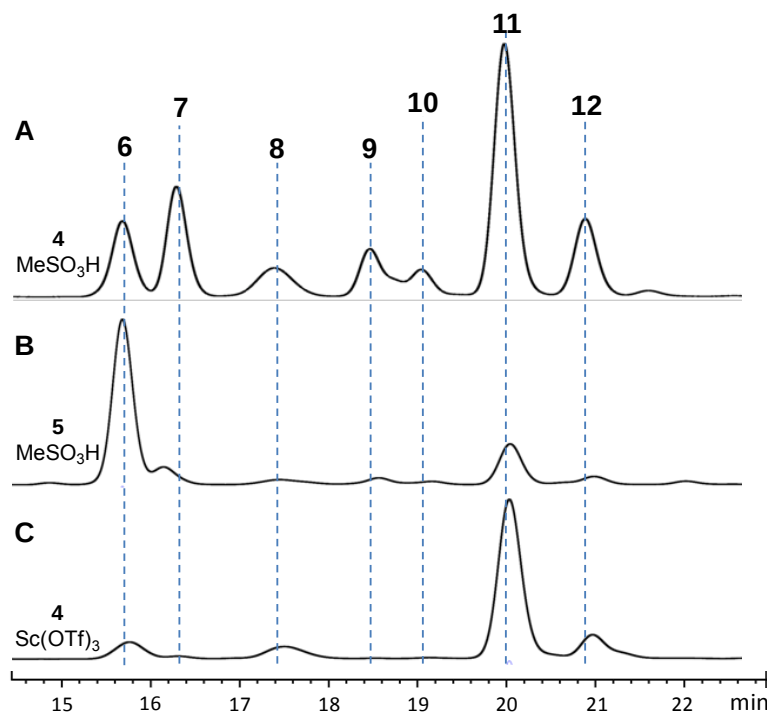


Figure 5. HPLC traces of large-ring forming reactions: A) **4** with MeSO₃H (conditions: Table 1, entry 11), B) **5** with MeSO₃H (conditions: Table 1, entry 3), C) **4** with Sc(OTf)₃ (conditions: Table 1, entry 17). Conditions: RP-C18, MeCN/H₂O, 0.1% TFA (see supplementary information).

subjected acyclic mixed carbonate **4** to the same reaction conditions that caused isomerizations of **5**. Remarkably, the reaction afforded a mixture of products that co-chromatographed with those derived from **5**, varying only in their relative abundance (Fig. 5A). From this more evenly distributed mixture, minor products **8**, **9**, **10a/b**, and **12** were readily isolated and characterized. Structure elucidation by NMR methods led to the assignment of five novel macrocycles arising from alkylation of tryptophan at indole N1, C3, C6 and C7. Products of C5 alkylation of Trp1 (**11**) and Trp2 (**7**) were obtained as the major products, consistent with the relatively high reactivity of this position observed in rearrangement of **5**, and in related bimolecular reactions.²⁵ Tyrosine alkylation product **6**, the major product from **5**, now comprised only 12% of the product mixture. Lesser products arising from alkylation at C7 of Trp1 (**8**) and Trp2 (**10b**), C6 of Trp2 (**10a**), and N1 of Trp2 (**9**) were also obtained. Product **12**, comprising the final 12% of the mixture, was determined to be a macrocyclic pyrroloindoline arising from indole C3 alkylation of Trp2 and trapping of the resultant indolium ion by the proximal amide nitrogen (Fig. 6).²⁶

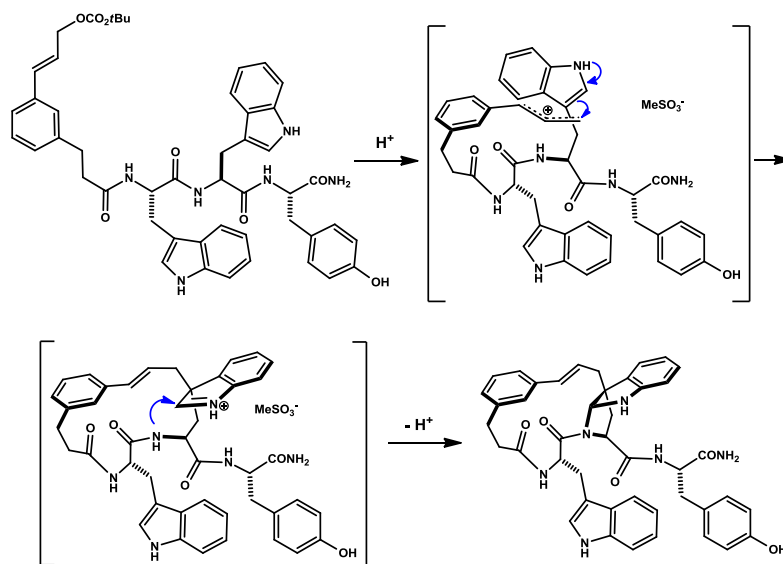


Figure 6. Plausible mechanism for the formation of **12** involving initial alkylation of C3 of tryptophan followed by internal capture of the incipient iminium ion.

Template **2** illustrates the utility of the cinnamyl cation to access diverse macrocycles by direct engagement of aromatic amino acid side chains. From a single reaction, we isolated eight unique macrocyclic cores comprising 15, 16, 17, 18, 19, 20 and 21-membered rings (see Fig. 3B). Isomeric structures **6-12** exhibit varying polarity as evidenced by their elution order in HPLC, and distinct conformations as evidenced by large chemical shift differences observed between conserved motifs (see supplementary information). These results bode well for accessing molecular diversity by template-induced macrocyclization of oligomers containing other π -basic aromatic residues.

4.2.4. Affects of acid catalyst, solvent and pre-cyclization

Counterion and solvent effects are known to perturb the reaction rate and product distributions of Friedel-Crafts alkylation and rearrangement reactions.²⁷ Accordingly, we examined alternative conditions to promote large ring-forming reactions of mixed carbonate **4** and cyclic cinnamyl ether **5**.

The nature of the acidic counterion was examined using a range of Brønsted and Lewis acids in both polar and non-polar solvents, the results of which are summarized in Table 1. Strong organic acids, including methanesulfonic acid and trifluoroacetic acid (TFA) were superior in promoting clean conversion to products **6-12** by ring contractions of **5** (entries 1-10) and direct large-ring formations from **4** (entries 11-17). Weaker acids, such as aqueous acetic acid (not shown) and formic acid, returned only starting material. Using methanesulfonic acid, but changing the solvent from MeNO₂ to CH₂Cl₂, led to intractable decomposition of **4** as observed by HPLC-MS. Consistent with previous studies by Olah and others, nitromethane likely stabilizes ion-paired intermediates along the reaction pathway.²⁸ In CH₂Cl₂, stoichiometric amounts of TFA reacted only slowly, whereas higher concentrations of TFA rapidly converted both **4** and **5** to well-distributed mixtures comparable to those seen in reactions of **4** with methanesulfonic acid in nitromethane. Superacids showed mixed results. Stoichiometric triflic

acid caused decomposition of **4** to non-isomeric products, even in MeNO₂ solvent. On the other hand, two equivalents of bistriflimide caused rapid reaction of **4**, and doubled the relative abundance of pyrroloindoline **12**. Lewis acids also efficiently promoted these reactions. Relative to Brønsted acids, metal triflates such as Sc(OTf)₃ enhanced the conversion of acyclic precursor **4** to Trp1 indole C5 alkylation product **11** (see Fig. 5C and Fig. S2). The product distribution from reactions of **4** is tunable with choice of acid promoter and solvent.

Under certain reaction conditions, significantly different product distributions were observed when starting from cyclic ether **5** relative to **4**. Reaction of **5** with dilute TFA in CH₂Cl₂ at room temperature (entry 9, Table 1), while sluggish, selectively formed tyrosine alkylation product **6**, exhibiting a prominent reversal of selectivity relative to that of **4** (entry 13).²⁹ This selectivity was lost at high concentrations of TFA. Similar trends were observed with methanesulfonic acid. Using only 5 equivalents of methanesulfonic acid in nitromethane at -20 °C, **6** was formed in a 20:1 ratio relative to all other isomers. These dramatic differences appear to reflect the influence of conformational pre-organization in **5** on the resulting reaction pathways.

One way to rationalize these results is in terms of a qualitative least motion argument.³⁰ All else considered equal, the conformationally pre-organized template in **5** rearranges more selectively, with the cinnamyl unit migrating to electron rich positions adjacent to the original attachment site.³¹ In contrast, ionization of acyclic carbonate **4** occurs in the context of a complex ensemble of peptide conformations, providing ample opportunity for the solvated cinnamyl ion pair to approach multiple internal reactive sites, wherein less selectivity is manifest and a more diverse mixture results.³² The attenuated selectivity observed from **5** in higher concentrations of acid may reflect accelerated ion pair return or altered solvation thereby permitting relaxation away from the cyclic conformation and leading to products by similar pathways as **4**.³³

While the initial acidolysis conditions using methanesulfonic acid gave a desirable, evenly-distributed product mixture, there are reasons to perturb this outcome. To retain tractability in biological screening exercises, a mixture should optimally contain an equal concentration of products so as to minimize the incidence of false negatives. Conversely, in the event that a single component becomes desirable as a result of either structure or function, it may be possible to enhance its abundance by subtle changes in reaction conditions, rather than undertaking a target-oriented synthesis. We have shown this is possible by biasing the template-induced macrocyclization towards the 15-membered macrocyclic pyrroloindoline **12**, 16-membered ring **11**, or 21-membered ring **6**. Cyclic cinnamyl ether **5** was essential in this regard. While we were successful in biasing the product distribution in favor of initially abundant compounds **6**, **11** or **12**, it is not yet clear this can be accomplished for minor constituents to the same degree. Further experiments on a variety of substrates are ongoing.

4.2.5. Scope of selective tyrosine ortho-alkylation

With conditions established which strongly favor intraresidue O-C_{ortho} migration, we prepared a set of macrocyclic ethers derived from **2** and set of peptides with varied functional groups. For example, treatment of macroether **13** with 15 equivalents of trifluoroacetic acid in CH₂Cl₂ provided tyrosine ortho-alkylated macrocycle **14** in 69% isolated yield. Polar functionality including alcohols, thioethers, and guanidines were well-tolerated in peptides possessing three to five amino acids (Table 2). These data bode well for the application of this method in more complex setting or library construction efforts.

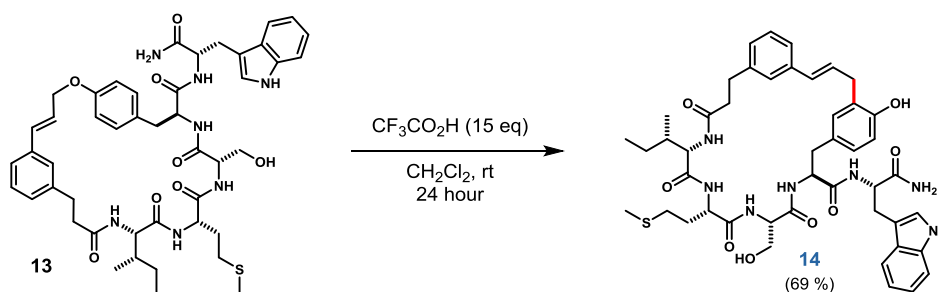


Figure 7. TFA promoted O-C_{ortho} migration within LMSYW derived macroether.

Table 2. Macrocytes derived from TFA promoted O-C_{ortho} migrations. The indicated unprotected peptides precursors are listed above product. Isolated yield from preparative HPLC indicated in parentheses.

Ile-Trp-Tyr	Ala-Val-Tyr	Trp-Ile-Gln-Tyr
15 (77 %)	16 (84 %)	17 (74 %)

Under these conditions intraresidue cinnamyl migration is strongly favored and in the case of Trp-Trp-Tyr the product distribution is greatly altered relative to acidolysis of the corresponding acyclic carbonate. In other settings, where 1,3 migration is not a possible migratory pathway, the relative distribution from cationic rearrangements in cyclic vs acyclic precursors is unclear. To investigate one such scenario, macrolactone **19** was prepared from Pd-catalyzed cyclization of Gly-Val-Trp-OH with template **2**. Macrolactone **19** possesses numerous indole nucleophilic sites at varied distance from the ionizable C-O bond. However, acidolysis of **19** has no discernible effect on product distribution when compared to acidolysis of acyclic carbonate **18** under identical conditions. This data suggests pre-organization in a macrocyclic conformation only effects product distribution where directly adjacent sites are apt to capture the forming electrophile (e.g. tyrosine O-C_{ortho} migration).

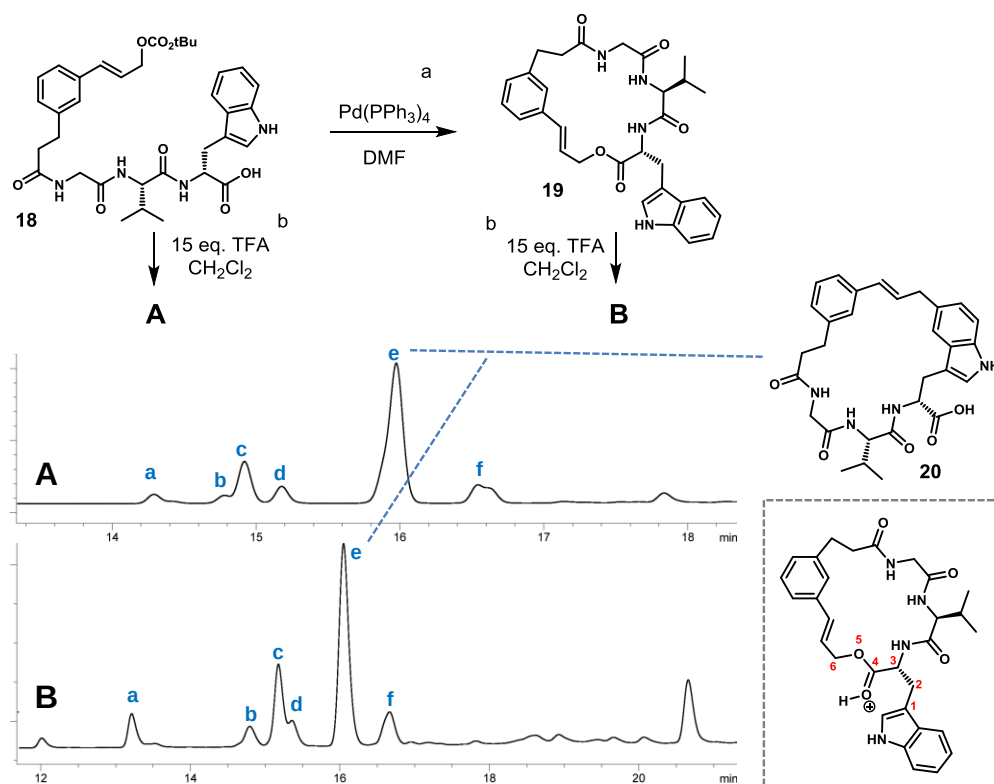


Figure 8. Comparison to acidolysis of acyclic carbonate **18** and macrolactone **19**. The major product of acidolysis is **20** from both **18** and **19**. Inset: Nucleophilic indolyl positions vary in distance from ionizing bond. Conditions: a) Pd(PPh₃)₄ (5 mol%), DMF (5 mM), 1h; b) 15 eq. TFA, CH₂Cl₂ (5 mM), 48h. Chromatograms A and B recorded on different instrument.

4.2.6. Deuterium labeling - Mass spectrometry assay

The process of isolation and characterization of individual products derived from divergent acidolyses becomes challenging with increasingly sophisticated templates. Accordingly, we sought to develop sensitive analytical means to assess product distribution and the efficiency of large ring formations. In principle, perdeuteration of selected aromatic amino acid side-chains would provide a characteristic molecular mass shift upon electrophilic aromatic substitution by loss of ²H⁺ upon re-aromatization (Fig. 9A). The high sensitivity of HPLC-MS would allow analytical separation of small-scale reactions. Successful aromatic substitution of the ²H labeled amino acid would result in a molecular mass of [M-1].³⁴ To examine the viability of this approach, the tripeptide Trp-Trp-Tyr was again employed as a model substrate to allow comparison with the structures determined by NMR (vide supra). Isotopologues Trp(*d*₅)-Trp-Tyr

and Trp-Trp(*d*₅)-Tyr were synthesized using solution-phase chemistry to incorporate Fmoc-Trp(*d*₅)-OH in high isotopic purity.³⁵ Subsequent acylation with template **2** afforded acyclic mixed carbonates **21** and **22** (Fig. 9B). After purification, MS analysis showed > 95 % average ²H incorporation at positions indicated in Figure 7B.

Acidolyses of **21** and **22** under the standard conditions with MeSO₃H proceeded to product mixtures which were, by HPLC-UV, identical to that observed with unlabeled substrate **4**. To avoid potential complications arising from scrambling of the labeling pattern, reactions were analyzed at partial and full conversion, and also under Lewis acidic conditions. The rate of product formation appeared to outcompete scrambling.³⁶ As anticipated, alkylation of Trp1(*d*₅) leading to products **8** and **11** was revealed as [M-1] by HPLC-MS analysis of the reaction of **21**. This characteristic mass signature was also observed for products **7**, **10a** and **10b** arising from alkylation of Trp2(*d*₅) in the reaction of **22**. While complete retention of deuterium was observed as expected for product **12**, an unexpected loss of two deuterium was found for Trp2 *N*-alkylated product **9** from the acidolysis of **22**. Whether this loss is mechanism based or due to increased exchange rate in the product is not yet known. *N*-alkylation of indole may accelerate deuterium/hydrogen exchange by enhancing the basic character of the resulting aromatic system.³⁷ Although this non-diagnostic outcome limits the accuracy of deuterium labeling in probing macrocycle connectivity, this result remains characteristic of substitution at Trp2.

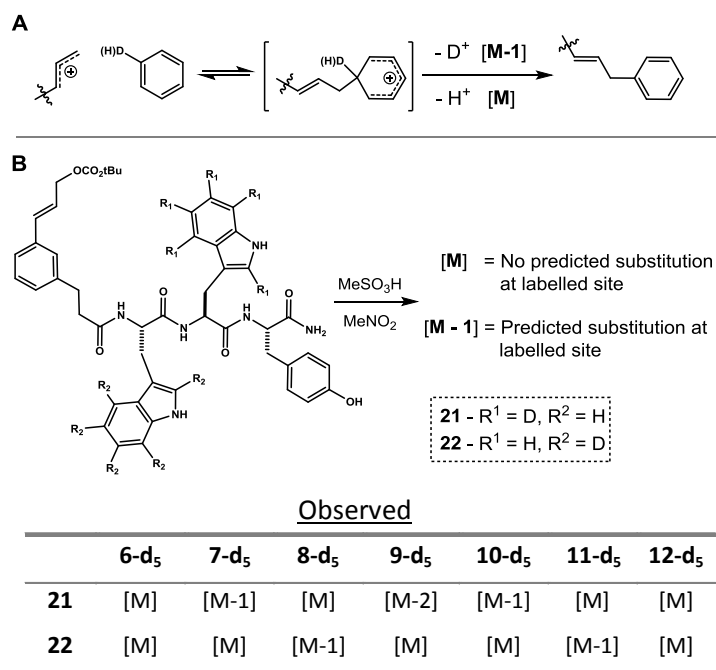


Figure 9. Selectively deuterated substrates permit sensitive detection of electrophilic substitution events by crude HPLC/MS analyses.

These data demonstrate the utility of deuterium labeled tryptophan in predicting large ring structures arising from aromatic substitution using templates such as **2** without the need for purification and characterization. This analytical approach may be particularly useful when investigating peptide sequences harboring multiple aromatic amino acids, where spectral overlap can complicate structural assignment. Future development of electrophilic templates incorporating novel or multiple reactive centers may also benefit from similar mass spectrometry-based pre-screens in the search for unique structures.

4.2.7. Stereochemical assignment and NMR solution structure of pyrroloindoline **12**

Macrocyclic pyrroloindoline **12** bears structural resemblance to a large family of natural products possessing these motifs.³⁸ To our knowledge **12** is the first example possessing an all carbon quaternary center at the core 5,5 ring juncture (Fig. 10A). A number of both naturally and synthetically derived pyrroloindolines have been studied spectroscopically and computationally

in an effort to characterize the stability and conformational equilibria of this ring system.³⁹ Intrigued by this heterocyclic motif in the context of macrocycle **12**, we further examined its structure and three-dimensional conformation using NMR.

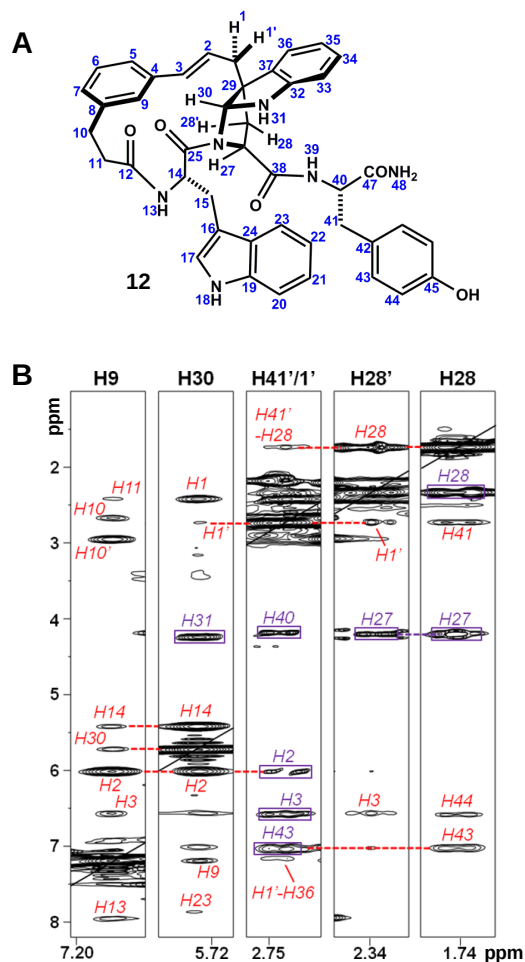


Figure 10. a) Numbering scheme used in the annotation of spectra for **12**. b) Selected slices from 2D-NOESY of compound **12** highlighting intrasidue (purple boxes) and key long-range (red) correlations. Black lines denote the diagonal.

The conformation of **12** in solution appeared to be relatively homogenous. The core pyrroloindoline was clearly observed as a methine, weakly split by the adjacent H31, with a carbon chemical shift of 81.1ppm characteristic of an aminal. Heteronuclear correlations codified connectivity of the cinnamyl moiety at bridging quaternary center C29. As anticipated,

the 5,5 ring juncture was formed with the thermodynamically preferred *cis* relationship, which was readily established from NOE correlation of methine H30 to the geminal pair H1/1'. Spectral

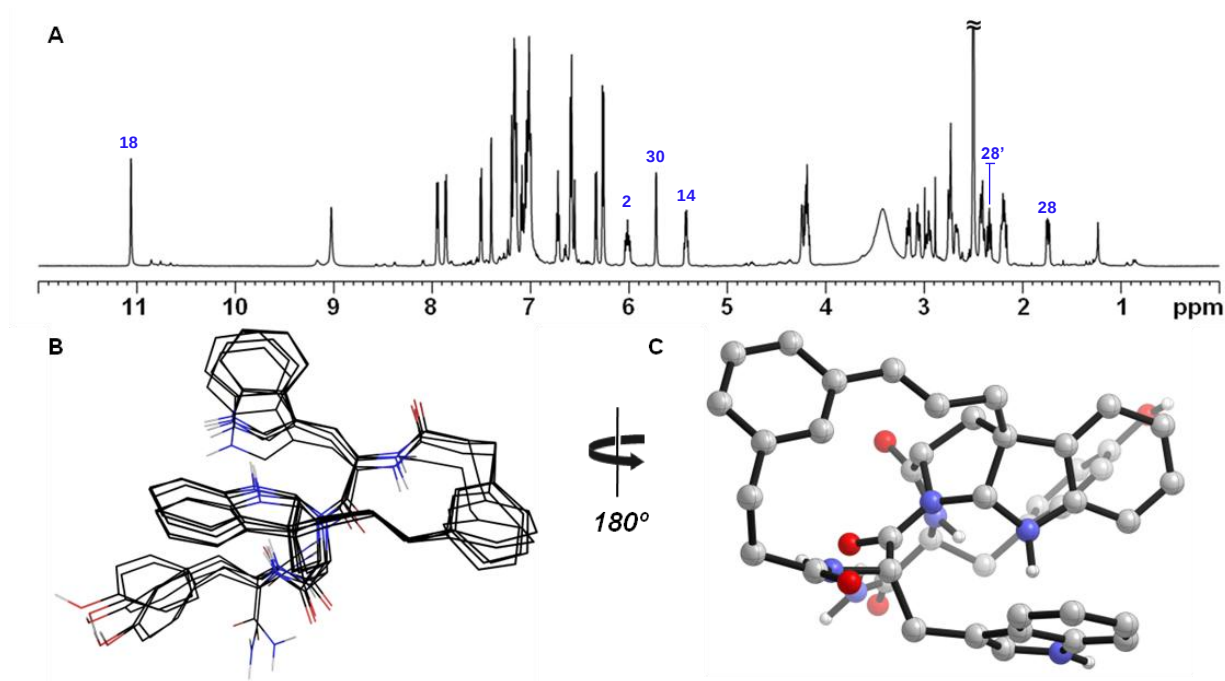


Figure 11. a) ^1H NMR spectrum of compound **12** ($\text{DMSO}-d_6$, 600 MHz) b) Overlay of the five lowest energy conformers calculated using NOE distance constrained molecular mechanics simulation and c) the lowest energy conformer obtained from this analysis. Spectral annotations correspond to numbering scheme in Figure 10A.

overlap in the aliphatic region, and of H27, H31 and H41 frustrated the use of correlations to H1/1' in assigning the ansa bridge stereochemistry relative to the 27S stereocenter, preserved from L-tryptophan. Stereospecific assignment of the geminal pair H28/28' was tenuous, with no significant difference observed by NOE to H30. Analysis of $^3J_{27-28}$ and $^3J_{27-28'}$ suggested an *endo* orientation of H28', which appeared contradictory to their relative chemical shift in comparison to related systems.³⁹ We viewed a distinct possibility that the macrocyclic motif and/or tyrosine residue could distort this pyrrolidine ring, leading to atypical *J*-values.⁴⁰ A single unambiguous long-range NOE from H2 to H27 led to the tentative assignment of the C38-*endo* 27S,29R,30R stereochemistry, as shown. Careful analysis of selective 1D-NOESY, 2D-NOESY and 2D-ROESY spectra obtained in DMSO or DMSO/D₂O supported this configuration, revealing seven prominent long-range correlations. Notably, strong NOEs within the tetrad H14, H30, H9 and H2

indicated arrangement of these positions along the interior of the macrocycle. An initial model generated from a conformational search incorporating these constraints facilitated assignment of 29 additional long-range NOEs, and calculation of a refined structural ensemble (Fig. 11B) showing agreement with experimental NOEs (see Table S4).

The solution structure revealed several notable features induced by template **2**. Planarity of the cinnamyl unit was retained, as evidenced by strong NOE of H3 to H5, and H2 to H9, thereby limiting the overall conformational flexibility of the 15-membered ring. The Trp1 side chain appeared to populate a single rotamer resulting in a close proximity of the indole ring to the benzene ring of the pyrroloindoline, which was supported by NOE observed between H20 and H33. While side chain torsions were indirectly restrained by long-range NOEs, the calculated rotamer preferences of Trp1 (g^2t^3) and Tyr3 (t^2g^3) agreed only loosely with observed coupling constants ($\pm 30^\circ$), suggesting potential motional averaging at these side chains.⁴¹

The bridged pyrroloindoline motif formed from cyclization of Trp2 onto the backbone effectively acts as a proline mimic. The backbone amide at this position retains the *trans* conformation, and the highly puckered *endo* pyrroloindoline induces a turn conformation, analogously to proline, yielding a potential hydrogen bond between the Trp1-C(O) and Tyr3 carboxamide. The anomalous *J*-values associated with H28/28' were rectified on basis of long-range NOEs from H28 to H43 and H44 indicating a *syn* relationship of H28 to the C-terminal tyrosine residue, though details of the pyrrolidine ring conformer were not revealed from these force field calculations.⁴¹ These data suggest that compound **12** occupies a relatively ordered conformation in solution that is enforced by both the macrocyclic and pyrroloindoline motifs.

4.3. Conclusion

In this pilot study, we have demonstrated a template-based approach to form composite macrocyclic peptidomimetics by unique large ring-forming Friedel-Crafts alkylations of tryptophan and tyrosine. A single reaction efficiently accessed eight macrocyclic structures. The

product distribution showed a strong dependence on acid promoter and substrate geometry. Rearrangement within a conformationally pre-organized tyrosine *O*-linked cinnamyl macrocyclic ether favored alkylation *ortho* to the phenol. By reducing the concentration of acid, this product was formed in 20:1 ratio relative to all other isomers. The ability to enhance the formation of specific isomers by tuning the reaction conditions allows rapid access to individual constituents for further study. It should be emphasized that, any one of products **6-12** could likely be selectively synthesized *de novo* utilizing established methodologies.⁴²

The peptide domain was found to be conformationally restricted as a result of template-induced macrocycle formation. This was demonstrated in the NMR solution structure of novel *endo*-pyrroloindoline **12** possessing an all-carbon quaternary center at ansa bridgehead C29. These results suggest that the divergent reactivity of templates such as **2** is an effective means of accessing molecular diversity. Isomeric products inherently possess the same primary peptide sequence, but likely vary substantially in their spatial display of side chains. Products derived from **2**, formed from carbon-carbon sigma bonding, also display improved physicochemical properties. These macrocycles have polar surface area comparable to the linear peptide, but much improved solubility in organic solvents and minimal propensity to aggregate.

We believe divergent strategies such as those described herein will prove valuable in a broader context of preparing structurally complex peptidomimetics. The particular utility of template **2** is demonstrated by the ability to transform a single peptide, Trp-Trp-Tyr, in two steps into eight isomeric macrocycles that would be otherwise time consuming to prepare. Rapid, efficient synthesis of diverse, composite macrocyclic peptidomimetics has the potential to identify small molecules effective against challenging targets where traditional libraries are often unsuccessful. We anticipate methods to generate shape diversity will prove valuable in efforts to recapitulate key motifs within larger folded polypeptides and to target surfaces involved in protein-protein interactions.

Chapter 4 - Supporting Information

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General

Reactions were performed under ambient atmosphere, unless otherwise noted. Dichloromethane was deoxygenated and dried by passing through an activated alumina solvent drying system. Anhydrous *N,N*-dimethylformamide (EMD DriSolv®) was used without further purification. Nitromethane was dried over 4Å molecular sieves for at least 24 hr before use. Methanesulfonic acid ($\geq 99.5\%$, Sigma Aldrich) was used without further purification. Column chromatography was performed on silica gel 60 (SiliCycle, 240-400 mesh). Thin layer chromatography (TLC) utilized pre-coated plates (Sorbent Technologies, silica gel 60 PF254, 0.25 mm) visualized with UV 245 nm, iodine, or basic potassium permanganate stain.

Purification of acidolysis products employed an Agilent 1100/1200 HPLC system equipped with G1361A preparative pumps, a G1314A autosampler, a G1314A VWD, and a G1364B automated fraction collector. Analytical HPLC was performed using the same system, but with a G1312A binary pump. Mass spectra were recorded using an Agilent 6130 LC/MS system equipped with an ESI source.

NMR methods:

NMR spectra were recorded on Bruker Avance (300, 500 or 600 MHz), DRX (500 MHz) and ARX (400 MHz) spectrometers. Data for ^1H NMR spectra are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration), and are referenced to a residual protonated solvent peak.¹ ^{13}C resonances are reported in terms of chemical shift (δ ppm) as referenced to the residual DMSO peak. For mass-limited samples, solvent magnetic susceptibility matched Shigemi tubes were used with a sample volume of $\sim 300\ \mu\text{L}$. Optimization of on-axis shims was accomplished using the TopShim automated tool within Bruker Topspin™ 2.1. Optimization of off-axis shims was performed manually.² ^1H 90° transmitter pulse lengths were calibrated by back calculation from the 360° or 180° null.³ The pulse width or power level for soft pulses and shaped pulses were calculated using the Shape Tool within TopSpin™ 2.1. ^1H - ^1H COSY spectra were recorded using a phase sensitive, gradient enhanced double-quantum-filtered experiment, using States-TPPI acquisition.⁴ TOCSY spectra were recorded using a sensitivity improved, phase sensitive experiment using a 60ms DIPSI-2 pulse train for homonuclear Hartman-Hahn transfer.⁵ NOESY spectra were recorded using a phase sensitive experiment with selection gradients during the mixing time.⁶ ROESY spectra were recorded using a phase sensitive experiment with selection gradients and water suppression with excitation sculpting.⁷ Carbon chemical shifts were measured from 2D plots of either HSQC spectra for protonated carbons or

¹ Gottlieb, H.E.; Kotlyar, V.; Nudelman, A., *J. Org. Chem.*, **1997**, 62, 7512-7515.

² Berger, S.; Braun, S., *200 and More NMR Experiments*, Wiley-VCH, Weinheim, **2004**, 6-11.

³ a) Claridge, T.D.W., *High-Resolution NMR Techniques in Organic Chemistry*, Pergamon, Oxford, **1999**, 94-97. b) Berger, S.; Braun, S., *200 and More NMR Experiments*, Wiley-VCH, Weinheim, **2004**, 15-17.

⁴ a) Hurd, R.E., *J. Magn. Reson.*, **1990**, 87, 422-428. b) Brereton, I.M.; Crozier, S.; Field, J.; Doddrell, D.M., *J. Magn. Reson.*, **1991**, 93, 54-62. c) Shaw, A.A.; Salaun, C.; Dauphin, J.F.; Ancian, B., *J. Magn. Reson. Ser. A*, **1996**, 120, 110-115.

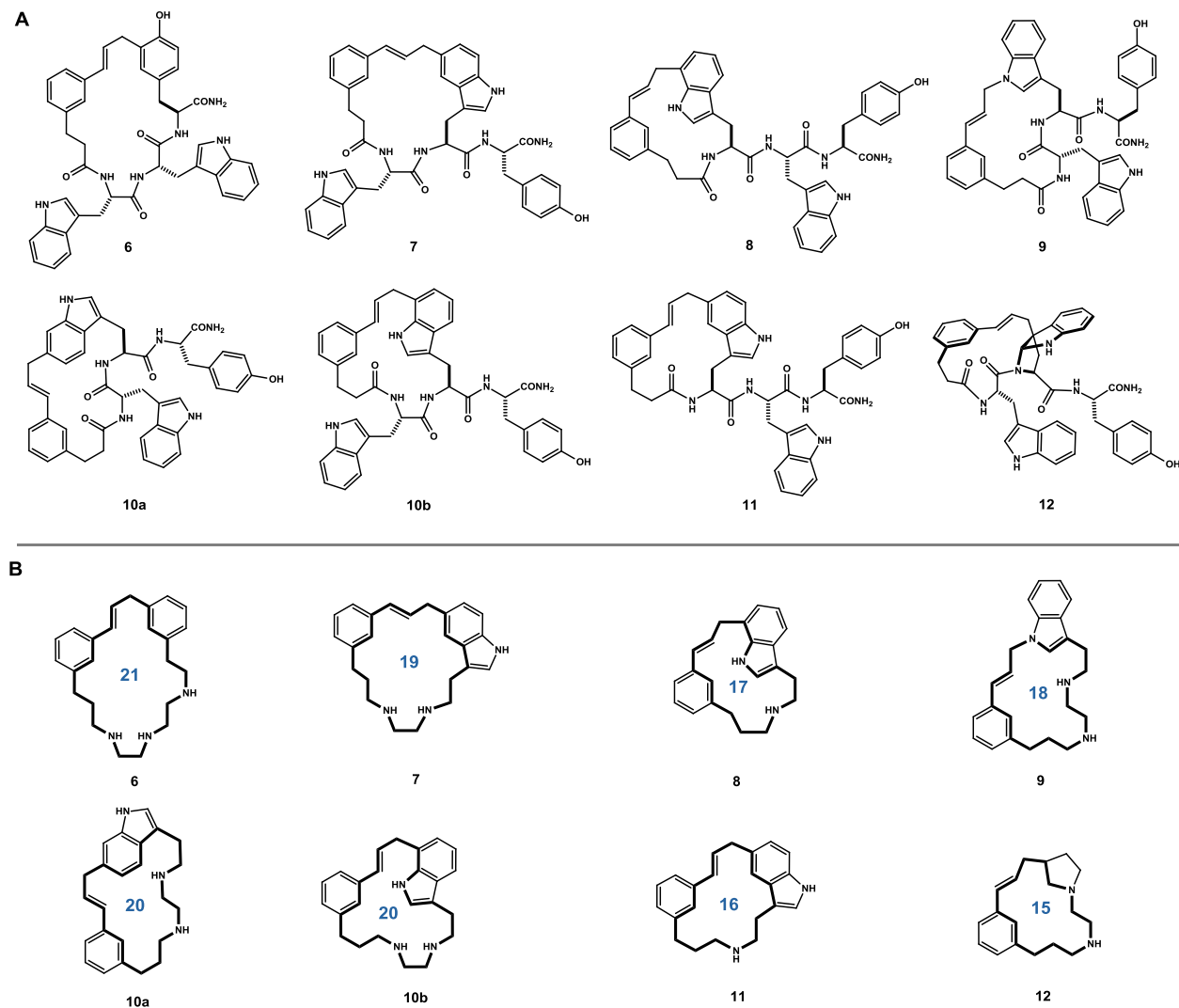
⁵ Cavanagh, J.; Rance, M., *J. Magn. Reson.*, **1990**, 88, 72-85.

⁶ Wagner, R.; Berger, S., *J. Magn. Reson.*, **1996**, 123 A, 119-121.

⁷ a) Bax, A.; Davis, D.G., *J. Magn. Reson.*, **1985**, 63, 207-213. b) Hwang, T.L.; Shaka, A.J., *J. Magn. Reson., Series A*, **1995**, 112, 275-279.

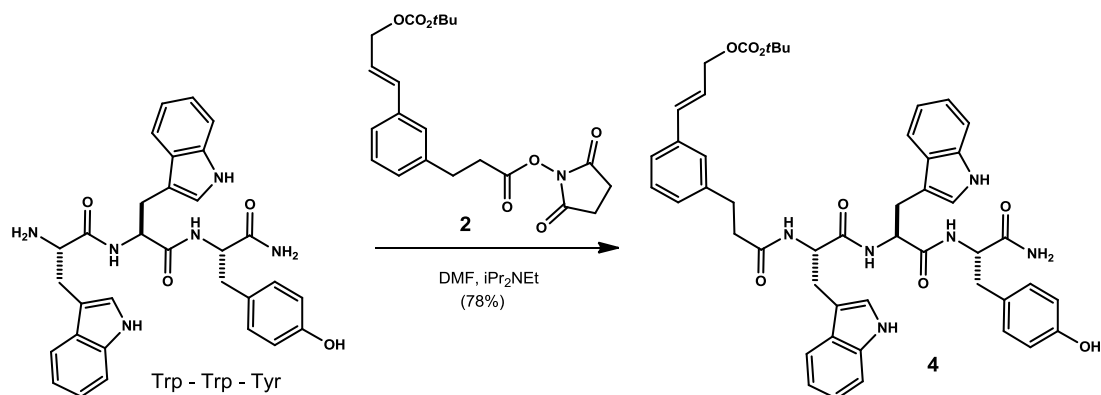
HMBC spectra for non-protonated carbons. ^1H - ^{13}C HSQC spectra were recorded using a sensitivity improved phase sensitive experiment using an adiabatic shape pulse for ^{13}C inversion, and ^{13}C decoupling during acquisition.⁸ Experimental parameters were optimized for $^1J_{\text{CH}} = 145\text{Hz}$. ^1H - ^{13}C HMBC spectra were recorded using a gradient selected experiment with a two-fold J-filter optimized for $^1J_{\text{CH}} = 125\text{-}165\text{Hz}$. Experimental parameters were optimized for long range $^nJ_{\text{CH}} = 8\text{Hz}$.

Figure S1. a) Products **6-12** derived from acidolysis of Trp-Trp-Tyr. **b)** Core macrocyclic substructures of **6-12**.



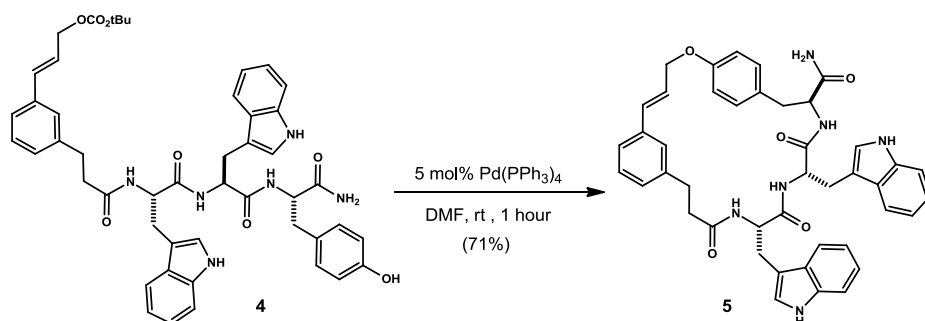
⁸ Palmer, A.G. III; Cavanagh, J.; Wright, P.E.; Rance, M., *J. Magn. Reson.*, **1991**, 93, 151-170. b) Kay, L.E.; Keifer, P.; Saarinen, T., *J. Am. Chem. Soc.*, **1992**, 114, 10663-10665. c) Schleucher, J.; Schwendinger, M.; Sattler, M.; Schmidt, P.; Schedletzky, O.; Glaser, S.J.; Sorensen, O.W.; Griesinger, C., *J. Biomol. NMR* **4**, **1994**, 301-306.

Acylation of Trp-Trp-Tyr with template 2



An oven-dried, screw-capped scintillation vial was charged with Trp-Trp-Tyr•TFA (343 mg, 0.515 mmol) and N-hydroxysuccinimide ester **2** (208 mg, 0.515 mmol) followed by addition of anhydrous DMF (10 ml) and *i*Pr₂NEt (359 μ l, 2.06 mmol). The reaction was allowed to stir at room temperature for 3 hours. The DMF was removed by rotary evaporation and the residue was dissolved in MeCN/CHCl₃ (1:3) and purified by column chromatography (SiO₂, gradient 0-10% MeOH/CHCl₃) to give **4** as a white solid (337 mg, 0.402 mmol, 78%). ¹H NMR (DMSO-d₆, 600 MHz): δ 10.79 (br. s, 1H), 10.7 (br. s, 1H), 9.13 (br. s, 1H), 8.07 (d, *J* = 6.8 Hz, 1H), 8.01 (d, *J* = 7.4 Hz, 1H), 7.82 (d, *J* = 8.7 Hz, 1H), 7.56 (d, *J* = 7.6 Hz, 1H), 7.49 (d, *J* = 7.6 Hz, 1H), 7.26-7.31 (m, 2H), 7.11-7.25 (m, 4H), 6.99-7.08 (m, 5H), 6.90-6.99 (m, 5H), 6.62 (d, *J* = 8.1 Hz, 2H), 6.56 (d, *J* = 15.7 Hz, 1H), 6.28 (dt, *J* = 15.4, 7.4 Hz, 1H), 4.60-4.64 (m, 2H), 4.42-4.53 (m, 2H), 4.31-4.37 (m, 1H), 3.01-3.07 (m, 2H), 2.93 (dd, *J* = 12.1, 11.3 Hz, 1H), 2.79-7.86 (m, 2H), 2.71 (dd, *J* = 10.2, 10.2 Hz, 1H), 2.56-2.62 (m, 2H), 1.4 (s, 9H). ¹³C NMR (DMSO-d₆, 150 MHz): δ 173.0, 172.6, 172.1, 171.5, 170.4, 157.2, 153.3, 142.1, 136.5, 136.3, 133.9, 130.7, 129.1, 128.4, 127.8, 126.9, 124.7, 124.1, 123.8, 121.3, 119.0, 118.6, 118.3, 115.9, 111.7, 110.6, 82.0, 67.4, 67.0, 58.5, 54.5, 54.0, 52.7, 40.9, 40.6. MS (ESI) Calculated for C₄₈H₅₂N₆O₈ [M+H]⁺: 841.4, found 841.1.

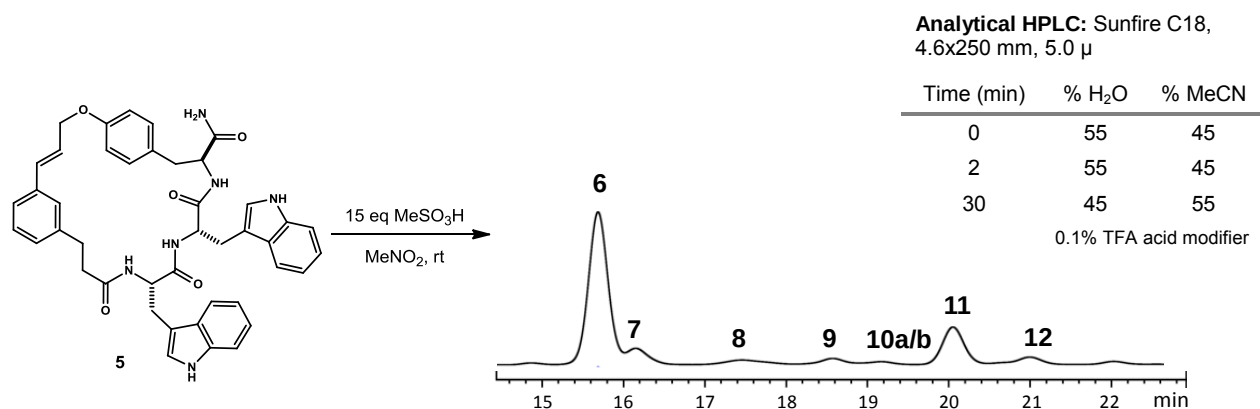
Palladium-catalyzed macrocyclization



A solution of acyclic carbonate **4** (109 mg, 0.130 mmol) in DMF (26 ml, 5mM) was sparged with Argon for 15 minutes. The septa was removed briefly to allow the addition of $\text{Pd(PPh}_3)_4$ (8 mg, 0.0065 mmol, 5 mol %). The mixture was stirred for 1 hour at which point analysis by HPLC/UV showed complete conversion of **4** to **5**. Silica bound thiol (Si-Thiol, silicycle, 1.29 mmol/gram, ~25 mg) was added to the reaction mixture, mixed for 5 minutes, and filtered (syringe filter, 0.45 μ). DMF was removed by rotary evaporation with a high vacuum oil pump. The residual oil was taken up in $\text{CHCl}_3/\text{MeCN}$ and purified by column chromatography (SiO_2 , gradient 0-10% $\text{MeOH}/\text{CHCl}_3$) to give **5** as a white solid (67 mg, 0.092 mmol, 71%).

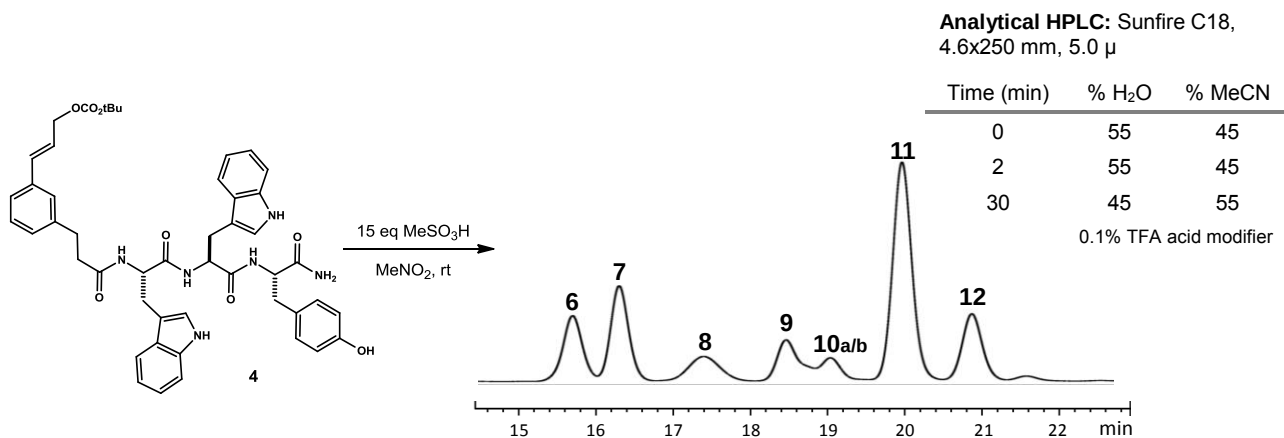
^1H NMR (DMSO-d_6 , 500 MHz): δ 10.7 (d, J = 2.0 Hz, 1H), 10.64 (d, J = 2.0 Hz, 1H), 7.99 (d, J = 8.1 Hz, 1H), 7.83 (d, J = 7.9 Hz, 1H), 7.51 (d, J = 8.0 Hz, 1H), 7.48 (d, J = 7.8 Hz, 1H), 7.46 (d, J = 8.0 Hz, 1H), 7.28 (br. d, J = 3.7 Hz, 1H), 7.26 (br. d, J = 3.9 Hz, 1H), 7.10-7.13 (m, 3H), 6.99-7.10 (m, 6H), 6.90-6.96 (m, 3H), 6.74 (d, J = 8.9 Hz, 2H), 6.6 (d, J = 2.5 Hz, 1H), 6.47 (br. d, J = 16.1 Hz, 1H), 6.21 (dt, J = 15.9, 5.9 Hz, 1H), 4.68 (dd, J = 15.3, 6.3 Hz, 1H), 4.6 (dd, J = 14.3, 5.6 Hz, 1H), 4.51 (ddd, J = 7.6, 7.6, 5.9 Hz, 1H), 4.34 (ddd, J = 10.9, 8.1, 2.8 Hz, 1H), 4.22 (app q, J = 7.5 Hz, 1H), 3.02 (dd, J = 14.8, 5.5 Hz, 1H), 2.92 (dd, J = 13.8, 2.6 Hz, 1H), 2.84 (dd, J = 14.7, 6.0 Hz, 1H), 2.70-2.77 (m, 4H), 2.59 (dd, J = 14.8, 7.8 Hz, 1H), 2.42-2.47 (m, 1H). ^{13}C NMR (DMSO-d_6 , 125 MHz): δ 173.8, 171.9, 171.4, 171.2, 157.0, 141.6, 136.4, 136.3, 133.4, 130.6, 130.3, 128.8, 127.9, 127.8, 126.1, 125.4, 124.8, 124.1, 124.0, 121.3, 121.2, 118.9, 118.8, 118.6, 115.1, 111.69, 111.65, 110.5, 110.3, 68.2, 54.8, 54.1, 53.5, 36.8, 36.3, 35.8, 31.2, 30.6. MS (ESI) Calculated for $\text{C}_{43}\text{H}_{42}\text{N}_6\text{O}_5$ $[\text{M}+\text{H}]^+$: 723.3, found 723.0.

Acidolysis of macrocycle 5



Tyrosine macroether (**5**) (80 mg, 0.11 mmol) was suspended in dry nitromethane (22 ml, 5 mM) under argon atmosphere, and treated with methanesulfonic acid (108 μ l, 1.66 mmol, 15 eq.) at room temperature, which caused complete dissolution of the starting material. After 2 hours the reaction was partitioned between EtOAc and saturated NaHCO₃. The organic phase was washed with saturated NaHCO₃ (x2) and brine, then dried over Na₂SO₄ and concentrated. The product mixture was reconstituted in N,N-DMF and purified by semi-preparative RP-HPLC (Sunfire C18, 5 μ , 10x250 mm, gradient: 41-48% MeCN/H₂O, 0.1% TFA, 21 minutes). Fractions were pooled and evaporated under reduced pressure.

Acidolysis of acyclic carbonate 4



Acyclic cinnamyl carbonate (**4**) (330 mg, 0.39 mmol) was suspended in dry nitromethane (78 ml, 5 mM) under argon atmosphere, and treated with methanesulfonic acid (382 μ l, 5.89 mmol, 15 eq.) at room temperature, which caused complete dissolution of the starting material. After 2 hours the reaction was partitioned between EtOAc and saturated NaHCO₃. The organic phase was washed with saturated NaHCO₃ (x2) and brine, then dried over Na₂SO₄ and concentrated. The product mixture was reconstituted in N,N-DMF and purified by semi-preparative RP-HPLC (Sunfire C18, 5 μ , 10.0x250 mm, gradient: 41-

48% MeCN/H₂O, 0.1% TFA, 21 minutes). Fractions were pooled and evaporated under reduced pressure.

Screening acidolysis conditions

The tyrosine macroether or acyclic cinnamyl carbonate (~5 mg) in a 1 dr vial was dissolved or suspended in indicated solvent (5 mM) under ambient atmosphere, and treated with acid. All reactions were stopped at two hours unless otherwise noted in the table below. MeSO₃H/CF₃CO₂H was transferred to the reaction vial via a micropipet using polypropylene tips. Bistriflimide was weighed under an Argon atmosphere and a 10 mM solution in anhydrous MeNO₂ was prepared and transferred to the reaction vessel via syringe. Volumetric solutions of 50% TFA, HCO₂H or AcOH in their respective solvents were prepared and transferred to a reaction vessel containing acidolysis substrate. Metal triflates were weighed under ambient atmosphere and transferred to a suspension of acidolysis substrate. Sc(OTf)₃ uniquely promoted complete dissolution of substrate/acid in the reaction media. Other metal triflates were heterogeneous throughout the reaction which resulted in increased reaction time (16 hours). Reactions performed below ambient temperatures were performed in a cool aluminum block and the temperature was equilibrated for 30 minutes prior to addition of acid. Aliquots for HPLC/MS analysis were removed and quenched with a methanolic solution of Et₃N, evaporated under high vacuum, and reconstituted in DMSO prior to injection. Relative yields were determined by integration at UV 254 nm and were not standardized.

Entry	Substrate	Promoter	Equiv.	Temp	Solvent	Compound %						
						6	7	8	9	10a/b	11	12
1	A	MeSO ₃ H	5	rt	CH ₃ NO ₂	74	4	3	3	1	12	3
2	A	MeSO ₃ H	15	0 °C	CH ₃ NO ₂	71	6	3	2	2	13	3
3	A	MeSO ₃ H	15	rt	CH ₃ NO ₂	63	7	4	3	2	17	4
4	A	MeSO ₃ H	25	-20 °C	CH ₃ NO ₂	58	10	4	3	2	20	4
5	A	MeSO ₃ H	5	-20 °C	CH ₃ NO ₂	95	<1	<1	<1	<1	4	<1
6	A	MeSO ₃ H	15	rt	CH ₂ Cl ₂	N/A ^a	-	-	-	-	-	-
7	A	CF ₃ SO ₃ H	15	rt	CH ₂ Cl ₂	N/A ^a	-	-	-	-	-	-
8	A	TFA	50%v	rt	CH ₂ Cl ₂	3	24	8	15	3	34	13
9	A	TFA	15	rt	CH ₂ Cl ₂	95	<1	<1	<1	<1	4	<1
10	A	Sc(OTf) ₃	1	rt	CH ₃ NO ₂	61	3	6	2	1	22	5
11	B	MeSO₃H	15	rt	CH₃NO₂	12	16	6	9	5	40	12
12	B	TFA	50%v	rt	CH ₂ Cl ₂	32	17	7	7	1	28	8
13	B	TFA	15	rt	CH ₂ Cl ₂	21	14	6	7	5	36	11
14	B	CF ₃ SO ₃ H	1	rt	CH ₃ NO ₂	N/A ^a	-	-	-	-	-	-
15	B	HCO ₂ H	50 %v	rt	H ₂ O	-	-	-	-	-	-	-
16	B	Tf ₂ NH	2	rt	CH ₃ NO ₂	5	14	5	8	6	38	24
17	B	Sc(OTf) ₃	1	rt	CH ₃ NO ₂	9	1	9	<1	<1	68	13

Table S1. Effect of substrate and acid promoter on product distribution

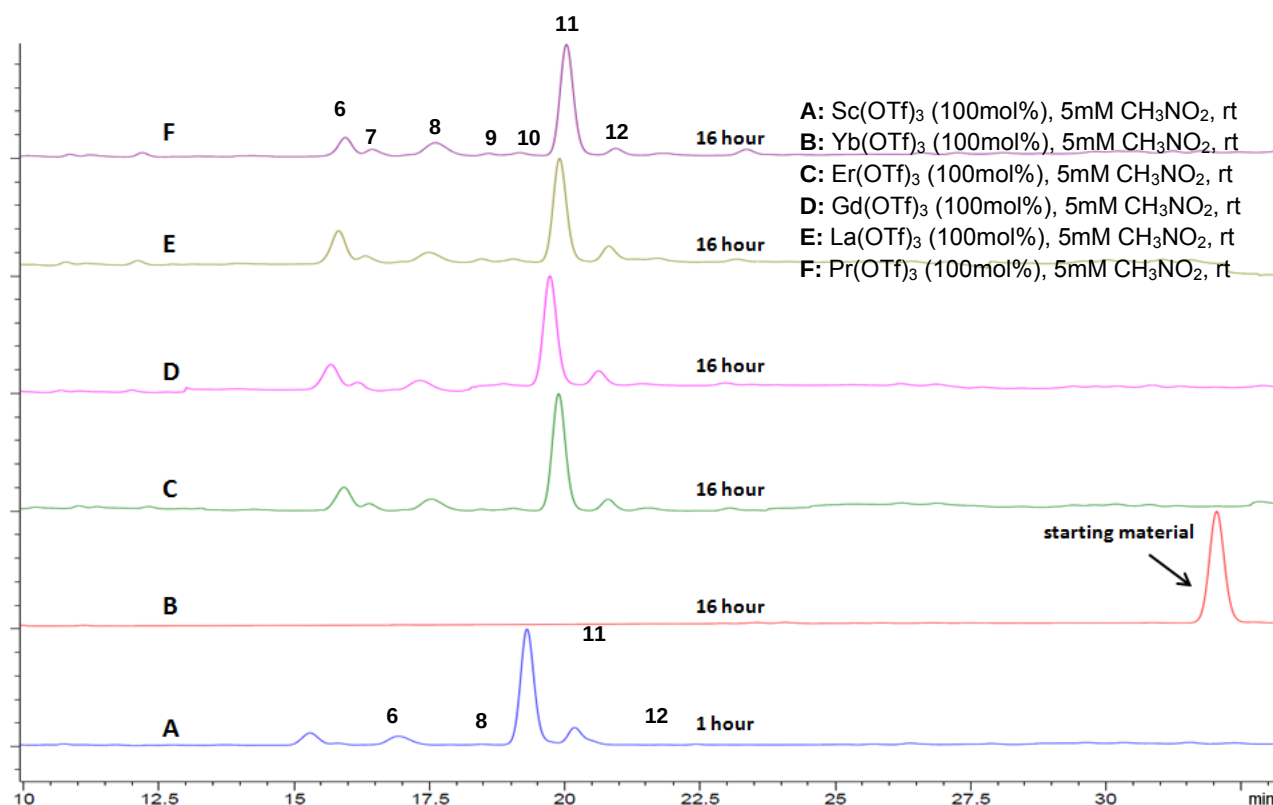
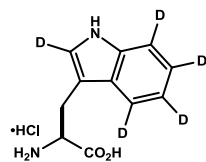


Figure S2. Analytical HPLC of the reaction of various metal triflates with acyclic carbonate **4**. Little perturbation of product distribution was observed. HPLC conditions: Sunfire C18, 4.6x250 mm, 5.0 μ . 45-55% MeCN/H₂O, 0.1% TFA, 35 minute run time.

Acidolysis of selectively deuterated Trp-Trp-Tyr



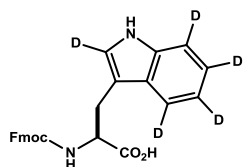
L-Tryptophan(*d*₅)·HCl: Prepared according to Oba, et al.⁹ To a degassed solution of H-Trp-OH (3.0 g, 14.7 mmol) in D₂O (20.0 ml) was added mercaptoacetic acid (0.4 ml, 5.9 mmol) followed by 4M DCl (30 wt% in D₂O). The solution was heated to 100 °C (oil bath) for 5 hours then cooled to room temperature and extracted with EtOAc.

The aqueous layer was lyophilized to give a white powder which was re-subjected to the conditions above. The DCl/D₂O solution of Trp(*d*₅) was diluted with H₂O (250 ml) and lyophilized to give a white powder (3.01 g, 14.4 mmol, 98%). Analysis by MS (ESI+) showed > 95 % average incorporation at each position (~ 75% *d*₅). The percent deuterium at each position was determined by ¹H NMR.¹⁰ The residual Ar-H signals were integrated relative to C α -H to give C2-²H (98%), C4-²H (90%), C5-²H (97%), C6-²H (98%), C7-²H (96%). ¹H NMR (DMSO-*d*₆, 500 MHz): δ 7.58 (s, 0.10H), 7.34 (s, 0.04H), 7.25 (s, 0.02H),

⁹ Oba, Y., Kato, S., Ojika, M., Inouye, S. *Tetrahedron Lett.*, **2002**, 43, 2389-2392

¹⁰ Bhat, B., Harrison, D. M., Lamont, H.M., *Tetrahedron*, **1993**, 49, 10663-10668

7.06 (s, 0.03H), 6.98 (s, 0.02H), 4.09 (t, $J = 6.0$ Hz, 1H), 3.29 (d, $J = 6.3$ Hz, 2H). MS (ESI) Calculated for $C_{11}H_7D_5N_2O_2$ $[M+H]^+$: 210.1, found 210.1.



Fmoc-L-Trp(d_5)-OH: To a suspension of H-Trp(d_5)-OH (1.79 g, 8.53 mmol) in sat. aq. $NaHCO_3$ (25 ml) and THF (25 ml) was added Fmoc-OSu (3.45 g, 10.24 mmol, 1.2 equiv.) in one portion. The reaction was stirred for 2 hours at room temperature. The THF was evaporated by rotary evaporation to give a white aqueous suspension was diluted with sat. $NaHCO_3$ (25 ml) and extracted with diethyl ether (2X) to remove excess Fmoc-OSu. The aqueous layer was acidified with 1.0N HCl to pH < 3 and extracted with EtOAc (2X) to give Fmoc-L-Trp(d_5)-OH as a tan solid (3.09 g, 7.17 mmol, 84%). MS analysis showed no loss of isotopic purity. 1H NMR ($DMSO-d_6$, 600 MHz): mixture of rotamers. δ 12.67 (s, 1H), 10.82 (s, 1H), 7.84 (br. d, $J = 7.6$ Hz, 2H), 7.68 (d, $J = 8.1$ Hz, 1H), 7.64 (d, $J = 7.6$ Hz, 1H), 7.61 (d, $J = 7.6$ Hz, 1H), 7.32-7.40 (m, 2H), 7.28 (ddd, $J = 7.6, 7.6, 0.7$ Hz, 1H), 7.24 (ddd, $J = 7.6, 7.6, 0.7$ Hz, 1H), 4.12-4.23 (m, 4H), 3.17 (dd, $J = 14.6, 4.5$ Hz, 1H), 3.00 (dd, $J = 14.6, 9.9$ Hz, 1H). MS (ESI) Calculated for $C_{26}H_{17}D_5N_2O_4$ $[M+H]^+$: 432.2, found 432.1.

Peptide synthesis:

Peptides were prepared using solution phase techniques with the Fmoc- protection strategy. Couplings were performed with O-(benzotriazol-1-yl)- N,N,N',N' -tetramethyluronium tetrafluoroborate (TBTU) (1.2 equivalent), Fmoc-AA-OH (1.2 eq), iPr_2NEt (5 eq.) in DMF (0.1M). Coupling were complete within 2 hours and diluted with EtOAc and washed sequentially with 1.0N HCl, sat. $NaHCO_3$, H_2O and brine. Fmoc deprotection was performed was achieved with DBU (1.0 eq) in THF (0.2M) in the presence of octanethiol (5 equiv).¹¹ After deprotection, the unprotected peptide was precipitated with Et_2O and pelleted by centrifugation. The peptide was repeatedly suspended in Et_2O and collected by centrifugation to completely remove residual octanethiol and DBU. After final deprotection the peptide was purified via reverse-phase HPLC (C18, MeCN/ H_2O , 0.1%TFA). Fractions were pooled and lyophilized. Under these coupling/purification conditions no significant loss of isotopic purity was observed.

¹¹ Sheppeck, J.E. II; Kar, H.; Hong, H., *Tetrahedron Lett.*, **2000**, 41, 5329–5333.

Acidolysis of Trp-Trp(*d*₅)-Tyr

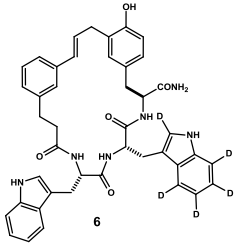
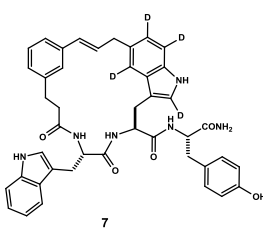
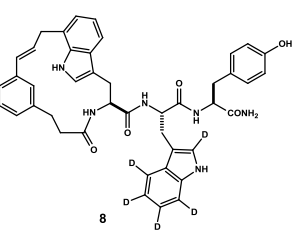
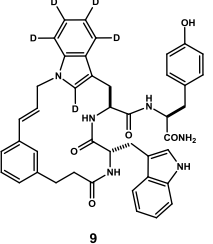
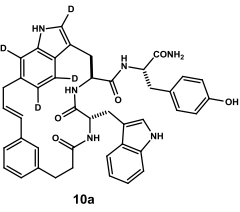
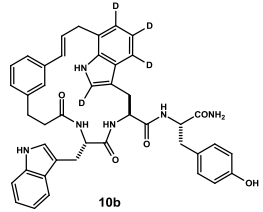
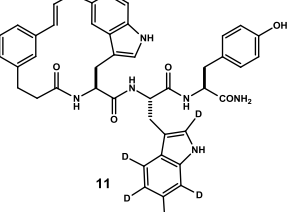
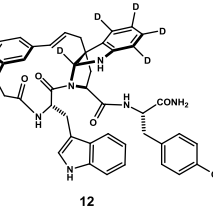
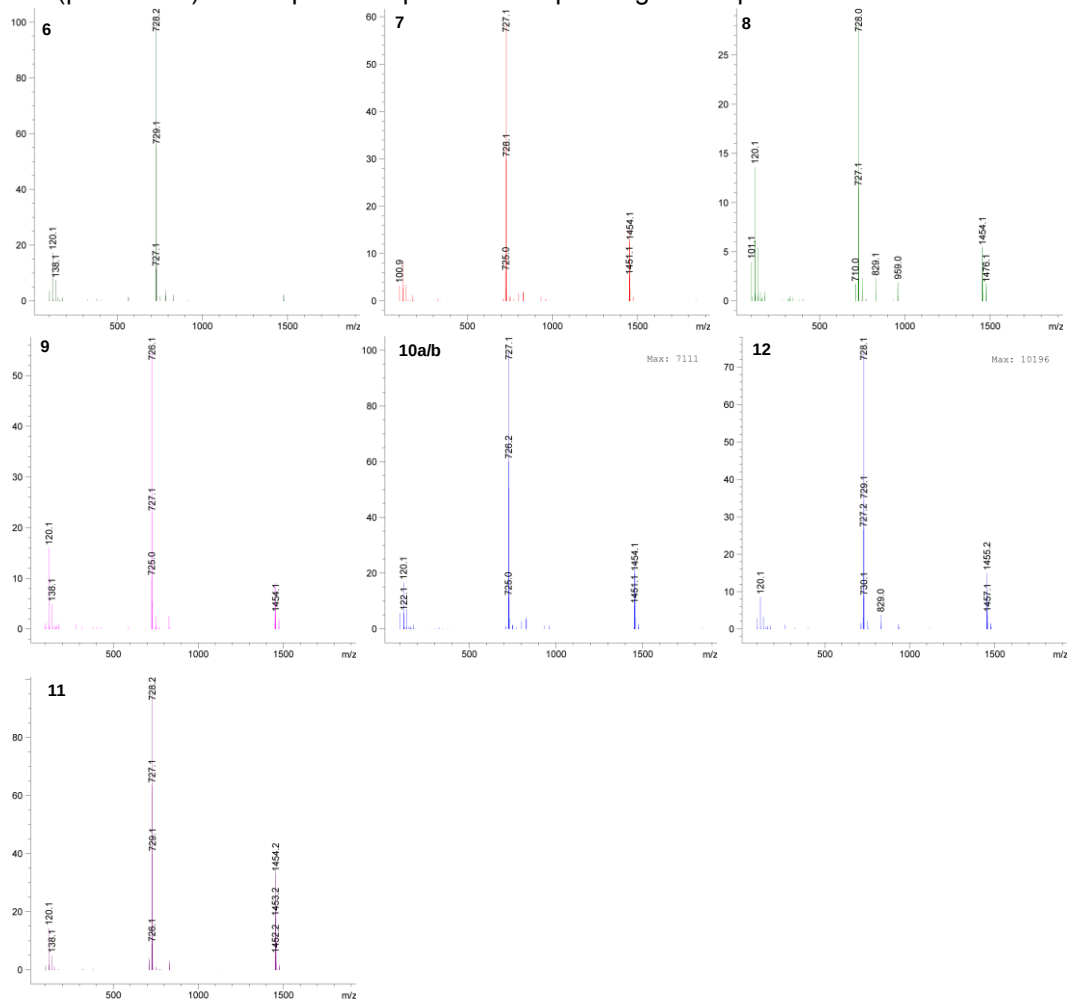
Structure				
Formula	C ₄₃ H ₃₇ D ₅ N ₆ O ₅	C ₄₃ H ₃₈ D ₄ N ₆ O ₅	C ₄₃ H ₃₇ D ₅ N ₆ O ₅	C ₄₃ H ₃₇ D ₅ N ₆ O ₅
Predicted mass [M+1]	728.35	727.35	728.35	728.35
Observed mass	728.2	727.1	728.0	726.1
Structure				
Formula	C ₄₃ H ₃₈ D ₄ N ₆ O ₅	C ₄₃ H ₃₈ D ₄ N ₆ O ₅	C ₄₃ H ₃₇ D ₅ N ₆ O ₅	C ₄₃ H ₃₇ D ₅ N ₆ O ₅
Predicted mass [M+1]	727.35	727.35	728.35	728.35
Observed mass	727.1	727.1	728.1	728.2

Table S2. MS analysis of acidolysis products derived from **13**.

ESI (pos. mode) mass spectra of peaks corresponding to compounds **6-12** derived from acidolysis of **13**.



Acidolysis of Trp(*d*₅)-Trp-Tyr

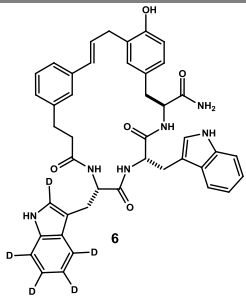
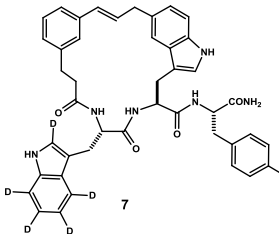
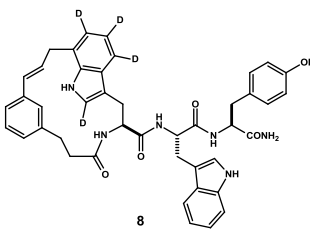
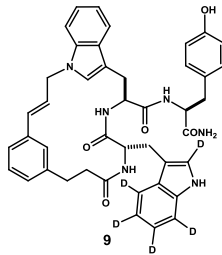
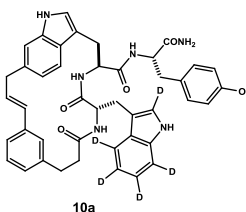
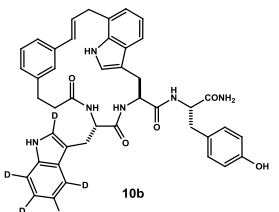
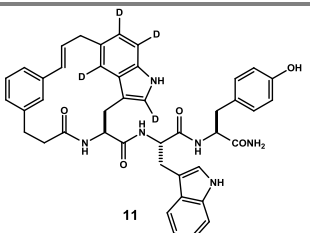
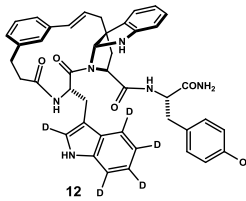
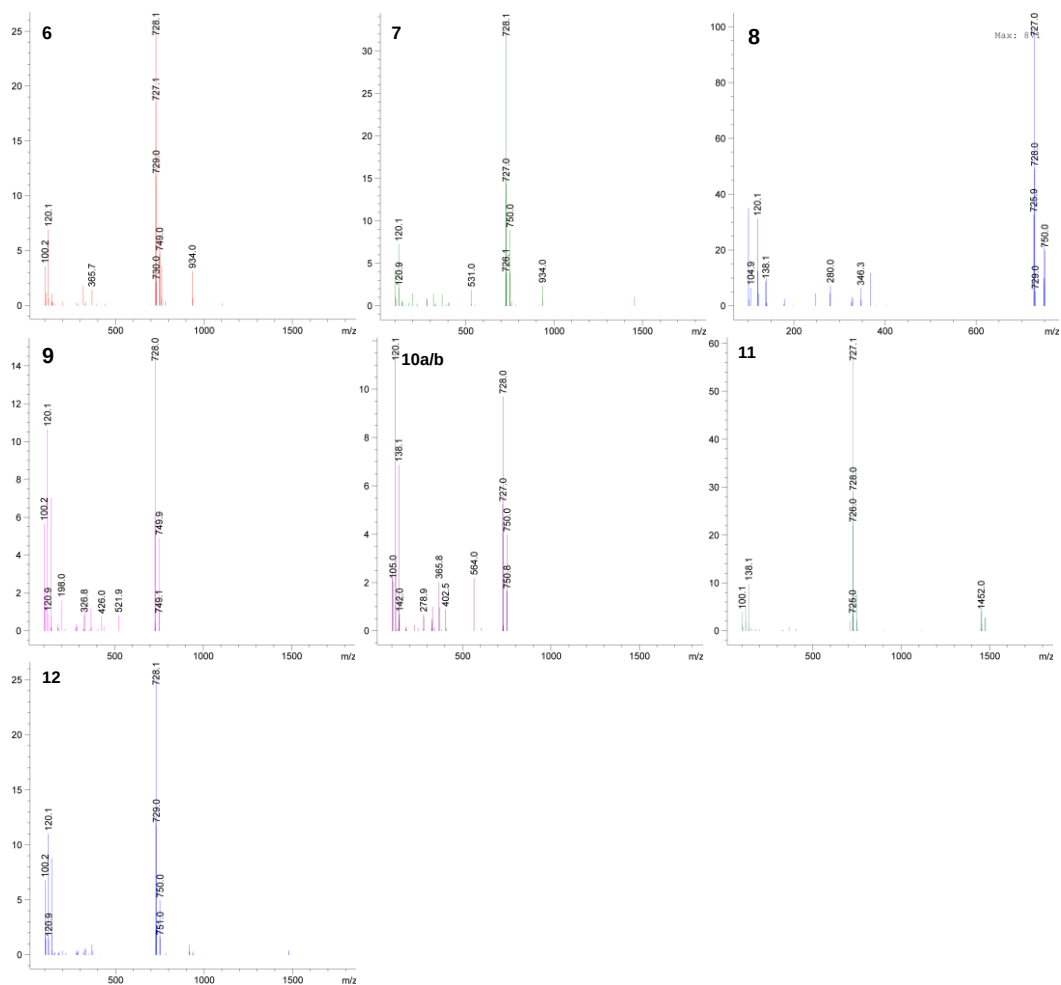
Structure				
	6	7	8	9
Formula	C ₄₃ H ₃₇ D ₅ N ₆ O ₅	C ₄₃ H ₃₇ D ₅ N ₆ O ₅	C ₄₃ H ₃₈ D ₄ N ₆ O ₅	C ₄₃ H ₃₇ D ₅ N ₆ O ₅
Predicted mass [M+1]	728.35	728.35	727.35	728.35
Observed mass	728.1	728.1	727.0	728.0
Structure				
	10a	10b	11	12
Formula	C ₄₃ H ₃₇ D ₅ N ₆ O ₅	C ₄₃ H ₃₇ D ₅ N ₆ O ₅	C ₄₃ H ₃₈ D ₄ N ₆ O ₅	C ₄₃ H ₃₇ D ₅ N ₆ O ₅
Predicted mass [M+1]	728.35	728.35	727.35	728.35
Observed mass	728.0	728.0	727.1	728.1

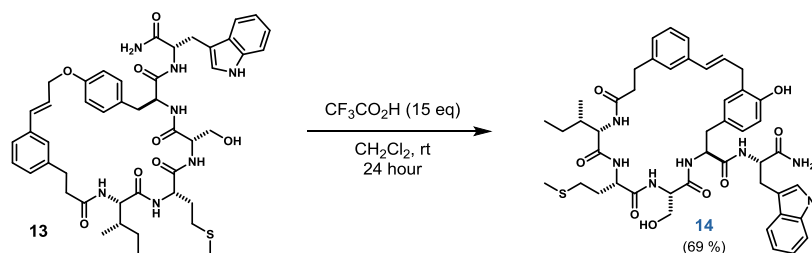
Table S2. MS analysis of acidolysis products derived from **14**.

ESI (pos. mode) mass spectra of peaks corresponding to compounds **6-12** derived from acidolysis of **14**.

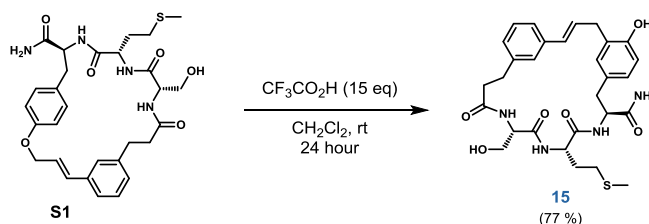


Selective O-*C*_{ortho} acidolyses:

The macrocyclic ether starting materials were characterized in chapter 4.

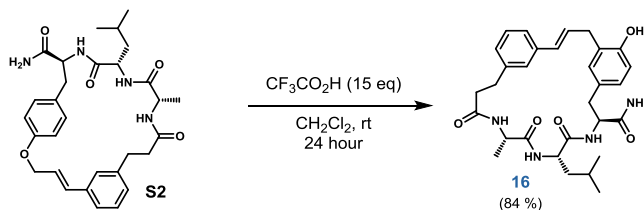


Cyclic-Ile-Met-Ser-Tyr-Trp (14) - To a solution of macrocycle **13** (5.2 mg, 5.9 μmol) in CH_2Cl_2 (1.2 ml) was added $\text{CF}_3\text{CO}_2\text{H}$ (6.3 μl , 82.5 μmol , 15 equiv.). The reaction was stirred at room temperature for 24 hours at which point HPLC shows complete consumption of macrocyclic ether. The reaction was concentrated without heating, reconstituted in DMSO (400 μL) and purified by preparative reverse phase HPLC (C18, XBridge RP18, 19x250mm). Concentration afforded 3.6 mg (69 %). The product was characterized by mass and ^1H NMR analysis for loss of symmetry about tyrosine. ^1H NMR (DMSO- d_6 , 500 MHz): δ 10.77 (d, J = 2 Hz, 1H), 9.15 (s, 1H), 8.08 (d, J = 6.8 Hz, 1H), 7.97 (d, J = 8.8 Hz, 1H), 7.94 (d, J = 8.1 Hz, 1H), 7.63 (d, J = 7.2 Hz, 1H), 7.55 (d, J = 8.1 Hz, 1H), 7.38 (br. s, 1H), 7.29 (d, J = 7.9 Hz, 1H), 7.08-7.20 (m, 5H), 7.00-7.05 (m, 2H), 6.94-6.99 (m, 3H), 6.87 (dd, J = 8.3, 1.9 Hz, 1H), 6.66 (d, J = 8.4 Hz, 1H), 6.41 (d, J = 15.9 Hz, 1H), 6.31 (dt, J = 15.9, 6.8 Hz, 1H), 5.24 (dd, J = 5.4, 5.4 Hz, 1H), 4.4 (ddd, J = 8.2, 8.2, 5.3 Hz, 1H), 4.34 (ddd, J = 6.4, 6.4, 6.4 Hz, 1H), 4.23-4.31 (m, 2H), 4.03 (dd, J = 8.4, 6.1 Hz, 1H), 3.63 (ddd, J = 10.9, 5.5, 5.5 Hz, 1H), 3.57 (ddd, J = 11.0, 5.5, 5.5 Hz, 1H), 3.48 (dd, J = 15.6, 6.2 Hz, 1H), 3.25-3.30 (m, 1H), 3.14 (dd, J = 14.6, 5.1 Hz, 1H), 2.9 (dd, J = 14.9, 8.6 Hz, 1H), 2.74-2.84 (m, 3H), 2.49-2.59 (m, 3H), 2.33-2.45 (m, 3H), 1.94 (s, 3H), 1.83-1.90 (m, 1H), 1.74-1.82 (m, 1H), 1.65-1.76 (m, 1H), 1.17-1.25 (m, 2H), 0.95-1.03 (m, 1H), 0.66-0.74 (m, 6H). (ESI) Calculated for $\text{C}_{46}\text{H}_{57}\text{N}_7\text{O}_8\text{S}$ $[\text{M}+\text{H}]^+$: 868.4, found 868.7

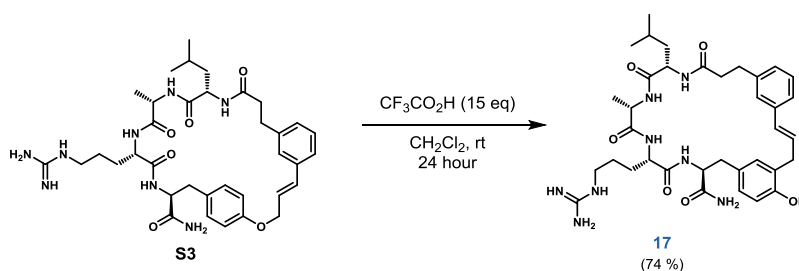


Cyclic-Ser-Met-Tyr (15) - To a solution of macrocycle **S1** (3.3 mg, 5.8 μmol) in CH_2Cl_2 (1.16 ml) was added $\text{CF}_3\text{CO}_2\text{H}$ (6.7 μl , 87.0 μmol , 15 equiv.). The reaction was stirred at room temperature for 24 hours at which point HPLC shows complete consumption of macrocyclic ether. The reaction was concentrated without heating, reconstituted in DMSO (400 μL) and purified by preparative reverse phase HPLC (C18,

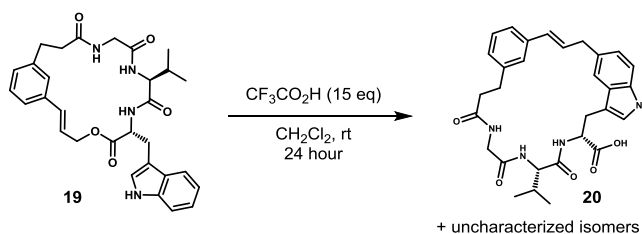
XBridge RP18, 19x250mm). Concentration afforded 2.5 mg (77 %). The product was characterized by mass and ^1H NMR analysis for loss of symmetry about tyrosine. ^1H NMR (DMSO- d_6 , 500 MHz): δ 9.1 (s, 1H), 8.06 (d, J = 8.1 Hz, 1H), 7.98 (d, J = 8.7 Hz, 1H), 7.45 (d, J = 7.6 Hz, 1H), 7.39 (br. s, 1H), 7.2 (br. d, J = 7.9 Hz, 1H), 7.15 (dd, J = 7.6, 7.6 Hz, 1H), 7.1 (br. s, 1H), 7.03 (br. s, 1H), 6.98-7.02 (m, 2H), 6.84 (dd, J = 8.2, 2.0 Hz, 1H), 6.64 (d, J = 8.1 Hz, 1H), 6.41 (dt, J = 15.8, 6.6 Hz, 1H), 6.21 (d, J = 15.6 Hz, 1H), 4.39 (ddd, J = 9.5, 9.5, 3.7 Hz, 1H), 4.21 (ddd, J = 8.3, 5.6, 5.6 Hz, 1H), 4.16 (ddd, J = 7.8, 7.8, 5.2 Hz, 1H), 3.47-3.50 (m, 2H), 3.31-3.42 (m, 1H), 2.95 (ddd, J = 13.8, 9.9, 3.3 Hz, 1H), 2.86 (dd, J = 13.6, 3.8 Hz, 1H), 2.71 (ddd, J = 11.9, 9.3, 2.4 Hz, 1H), 2.64 (dd, J = 13.7, 10.7 Hz, 1H), 2.51-2.59 (m, 1H), 2.33-2.40 (m, 1H), 2.11-2.23 (m, 2H), 1.94 (s, 3H), 1.7 (ddd, J = 14.9, 11.5, 6.5 Hz, 1H), 1.5 (m, 1H). (ESI) Calculated for $\text{C}_{29}\text{H}_{36}\text{N}_4\text{O}_6$ $[\text{M}+\text{H}]^+$: 569.2, found 569.5



Cyclic-Ala-Leu-Tyr (16) - To a solution of macrocycle **S2** (1.1 mg, 2.1 μmol) in CH_2Cl_2 (0.41 ml) was added $\text{CF}_3\text{CO}_2\text{H}$ (2.4 μl , 31 μmol , 15 equiv.). The reaction was stirred at room temperature for 24 hours at which point HPLC shows complete consumption of macrocyclic ether. The reaction was concentrated without heating, reconstituted in DMSO (400 μL) and purified by preparative reverse phase HPLC (C18, XBridge RP18, 19x250mm). Concentration afforded 0.9 mg (84 %). The product was characterized by mass and ^1H NMR analysis for loss of symmetry about tyrosine. ^1H NMR (DMSO- d_6 , 500 MHz): δ 9.09 (s, 1H), 7.98 (d, J = 7.8 Hz, 1H), 7.75 (d, J = 8.7 Hz, 1H), 7.35 (d, J = 8.6 Hz, 1H), 7.25 (br. s, 1H), 7.12-7.19 (m, 3H), 7.02 (br. s, 1H), 6.96-7.01 (m, 2H), 6.84 (dd, J = 8.3, 2.0 Hz, 1H), 6.65 (d, J = 8.6 Hz, 1H), 6.27-6.37 (m, 2H), 4.42 (ddd, J = 9.3, 9.3, 4.0 Hz, 1H), 4.26 (dq, J = 7.1, 7.1 Hz, 1H), 3.82 (dt, J = 7.9 Hz, 1H), 2.89-2.97 (m, 1H), 2.82 (dd, J = 13.9, 3.8 Hz, 1H), 2.64-2.74 (m, 2H), 2.36-2.43 (m, 2H), 1.62 (app dq, J = 6.8, 6.8 Hz, 1H), 0.99 (d, J = 7 Hz, 3H), 0.49 (t, J = 6.7 Hz, 6H). (ESI) Calculated for $\text{C}_{30}\text{H}_{38}\text{N}_4\text{O}_5$ $[\text{M}+\text{H}]^+$: 534.3, found 534.6



Cyclic-Leu-Ala-Arg-Tyr (14) - To a solution of macrocycle **S3** (6.0 mg, 8.7 μmol) in CH_2Cl_2 (1.74 ml) was added $\text{CF}_3\text{CO}_2\text{H}$ (9.9 μl , 130 μmol , 15 equiv.). The reaction was stirred at room temperature for 24 hours at which point HPLC shows complete consumption of macrocyclic ether. The reaction was concentrated without heating, reconstituted in DMSO (400 μL) and purified by preparative reverse phase HPLC (C18, XBridge RP18, 19x250mm). Concentration afforded 4.4 mg (74 %). The product was characterized by mass and ^1H NMR analysis for loss of symmetry about tyrosine. ^1H NMR (DMSO- d_6 , 500 MHz): δ 9.18 (br. s, H), 8.08 (d, J = 7.6 Hz, H), 7.88 (d, J = 8.1 Hz, H), 7.84 (d, J = 6.3 Hz, H), 7.75 (d, J = 7.9 Hz, H), 7.42 (dd, J = 5.7, 5.7 Hz, H), 7.32 (br. s, H), 7.27 (br. s, H), 7.16 (dd, J = 7.6, 7.6 Hz, H), 7.04-7.11 (m, H), 7 (br. d, J = 7.5 Hz, H), 6.94 (br. s, H), 6.89 (dd, J = 8.2, 1.8 Hz, H), 6.69 (d, J = 8.1 Hz, H), 6.41 (d, J = 15.7 Hz, H), 6.32 (dt, J = 15.7, 6.8 Hz, H), 4.29 (ddd, J = 8.5, 8.5, 4.1 Hz, H), 4.21 (ddd, J = 8.0, 8.0, 5.0 Hz, H), 4.04-4.12 (m, H), 3.97 (dd, J = 15.9, 6.7 Hz, H), 3.29 (dd, J = 15.6, 6.5 Hz, H), 3.03 (dd, J = 12.8, 6.5 Hz, H), 2.9 (dd, J = 14.2, 3.7 Hz, H), 2.74-2.84 (m, H), 2.66 (dd, J = 14.2, 9.2 Hz, H), 2.53 (ddd, J = 14.6, 7.3, 7.3 Hz, H), 2.4 (ddd, J = 14.0, 6.9, 6.9 Hz, H), 1.61-1.71 (m, H), 1.48-1.58 (m, H), 1.30-1.45 (m, H), 1.12 (d, J = 7.4 Hz, H), 0.77 (d, J = 6.1 Hz, H), 0.7 (d, J = 6.1 Hz, H). (ESI) Calculated for $\text{C}_{36}\text{H}_{50}\text{N}_8\text{O}_6$ $[\text{M}+\text{H}]^+$: 691.4, found 691.7

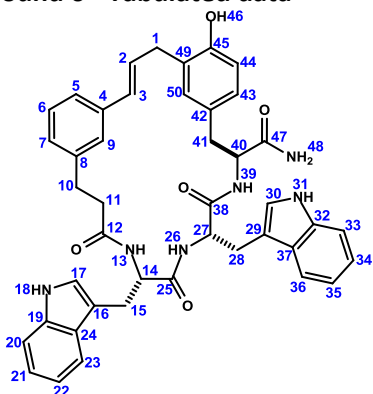


Cyclic-Leu-Ala-Arg-Tyr (14) - To a solution of macrocycle **S3** (2.4 mg, 4.5 μmol) in CH_2Cl_2 (0.90 ml) was added $\text{CF}_3\text{CO}_2\text{H}$ (5.2 μl , 68 μmol , 15 equiv.). The reaction was stirred at room temperature for 24 hours at which point HPLC shows complete consumption of macrocyclic ether. The reaction was concentrated without heating, reconstituted in DMSO (400 μL) and purified by preparative reverse phase HPLC (C18, XBridge RP18, 19x250mm). Yield not determined. The macrocyclic linkage was assigned by a combination of TOCSY, COSY, HSQC. ^1H NMR (DMSO- d_6 , 500 MHz): δ 12.58 (s, 1H), 10.75 (d, J = 2 Hz, 1H), 8.31 (d, J = 7.6 Hz, 1H), 8.11 (t, J = 5.9 Hz, 1H), 7.49-7.56 (m, 2H), 7.27 (br. s, 1H), 7.21 (d, J = 8.3 Hz, 1H), 7.13-7.18

(m, 3H), 7.06-7.10 (m, 2H), 6.97-7.00 (m, 1H), 6.89 (dd, J = 8.2, 1.6 Hz, 1H), 6.48-6.56 (m, 1H), 6.4 (d, J = 15.6 Hz, 1H), 4.46 (ddd, J = 8.0, 8.0, 5.5 Hz, 1H), 4.25 (dd, J = 9.0, 5.8 Hz, 1H), 3.84 (dd, J = 16.5, 6.6 Hz, 1H), 3.49-3.57 (m, 4H), 3.09 (dd, J = 14.5, 5.5 Hz, 1H), 2.99 (dd, J = 14.2, 7.8 Hz, 1H), 2.76-2.91 (m, 3H), 2.38-2.44 (m, 1H), 1.99 (dddd, J = 13.2, 13.2, 6.6, 6.6 Hz, 1H), 0.78 (d, J = 6.5 Hz, 3H), 0.71 (d, J = 6.9 Hz, 3H). (ESI) Calculated for C₃₀H₃₄N₄O₅ [M+H]⁺: 531.3, found 531.6

Tabulated data for compounds 6 - 12:

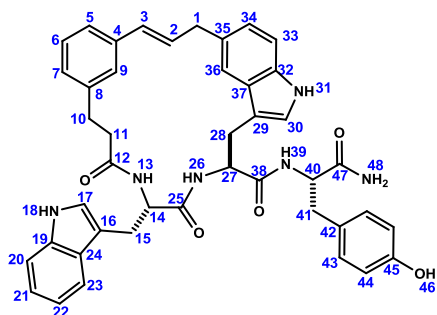
Compound 6 - Tabulated data



Atom #	¹³ C	¹ H	Key correlations
1	31.9	3.31-3.42 (m, 2H)	TOCSY→2,3 HMBC→45, 2, 3, 49
2	128.7	6.34 (dt, J = 15.7, 6.6 Hz, 1H)	TOCSY→1, 3 HMBC→3, 4
3	130.8	6.22 (br. d, J = 15.9 Hz, 1H)	TOCSY→1, 2 HMBC→2, 5
4	137.2	-	-
5	123.0	7.02 (m, 1H) overlap	HMBC→7
6	128.1	7.04 (m, 1H) overlap	HMBC→4,8
7	128.0	7.03 (m, 1H) overlap	HMBC→5
8	141.2	-	-
9	126.0	7.08 (m, 1H) overlap	HMBC→7, 5
10	30.4	2.57 (ddd, J = 11.6, 8.3, 2.7 Hz, 1H), 2.84 (m, 1H) overlap	TOCSY→10', 11, 11'
11	36.0	2.23 (ddd, J = 12.3, 8.3, 3.2 Hz, 1H), 2.38 (ddd, J = 12.4, 9.3, 3.1 Hz, 1H)	HMBC→12, 8, 7
12	171.6	-	TOCSY→11', 10, 10,
13	-	7.91 (d, J = 8.4 Hz, 1H)	HMBC→12, 8
14	53.2	4.37 (m, 1H) overlap	-
15	26.9	2.92-3.02 (m, 1H), 2.69-2.72 (m, 1H) overlap	HMBC→12
16	110.4	-	TOCSY→13, 15, 15'
17	123.5	6.94 (m, 1H), overlap	HMBC→16, 25, 15
18	-	10.68 (d, J = 1.8 Hz, 1H)	TOCSY→15', 13
19	136.0	-	HMBC→16, 17, 24, 14
20	111.3	7.29 (br. d, J = 6.3 Hz, 1H)	-
21	120.8	7.02 (m, 1H) overlap	HMBC→16
22	118.1	6.91 (m, 1H) overlap	HMBC→16, 19, 24, 20
23	118.0	7.48 (br. d, J = 8.0 Hz, 1H)	-
24	127.5	-	-
25	171.3	-	-
26	-	7.46 (d, J = 7.5 Hz, 1H)	TOCSY→21 HMBC→22, 24
27	53.6	4.34 (m, 1H) overlap	COSY→20, 22 HMBC→19, 23
28	27.3	2.96 (m, 1H) overlap, 2.72 (m, 1H) overlap	COSY→22, 21 HMBC→20, 24
29	109.6	-	COSY→22 HMBC→16, 24, 19
30	123.2	6.71 (s, 1H) overlap	-
31	-	10.69 (d, J = 1.8 Hz, 1H)	TOCSY→27, 28, 28'
32	136.0	-	HMBC→25
			TOCSY→26 HMBC→38, 29, 28
			COSY→27 HMBC→27, 29, 38, 37, 30
			-
			HMBC→29
			HMBC→32, 29, 37
			-

33	111.3	7.28 (br. d, J = 6.4 Hz, 1H)	COSY→34 HMBC→35
34	120.7	7.03 (m, 1H) overlap	COSY→33 HMBC→36, 32
35	118.0	6.89 (m, 1H) overlap	COSY→36 HMBC→33, 37
36	118.1	7.43 (br. d, J = 8.1 Hz, 1H)	COSY→35 HMBC→29, 34, 32, 38
37	127.4	-	-
38	120.7	-	-
39	-	7.98 (d, J = 8.2 Hz, 1H)	TOCSY→40 HMBC→38
40	53.2	4.39 (m, 1H)	TOCSY→41, 41', 39
41	36.3	2.73 (m, 1H) overlap, 2.84 (m, 1H) overlap	HMBC→47, 41
42	127.7	-	HMBC→50, 42, 43, 40
43	127.5	6.9 (m, 1H) overlap	HMBC→45, 50
44	114.7	6.7 (d, J = 6.3 Hz, 1H)	HMBC→45 (weak), 43
45	153.4	-	-
46	-	9.13	-
47	173.4	-	-
48	-	7.04, 7.30	HMBC→47
49	125.6	-	-
50	131.1	7.07 (br. s, 1H) overlap	TOCSY→44 HMBC→45, 43

Compound 7 - Tabulated data

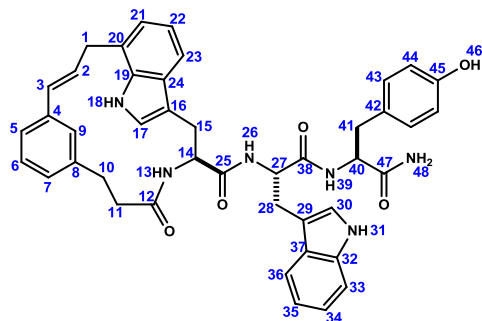


Atom #	¹³ C	¹ H	Key correlation
1	37.7	3.57 (d, J = 6.4 Hz, 2H)	HMBC 1→3,21,22,23
2	129.4	6.47 (dt, J = 15.6, 6.4 Hz, 1H)	COSY 2→1 HMBC 2→4
3	130.6	6.27 (d, J = 15.6 Hz, 1H)	HMBC 3→4,5,9
4	136.9	-	-
5	123.1	7.13 - 7.17 (m, 1H) overlap	HMBC 5→3,7,9
6	127.8	7.13 - 7.17 (m, 1H) overlap	HMBC 6→4,8
7	127.0	6.97 - 7.00 (m, 1H) overlap	HMBC 7→5,8,9
8	141.2	-	-
9	124.7	7.13 - 7.17 (m, 1H) overlap	HMBC 9→7
10	29.3	2.64 (dd, J = 13.4, 8.0 Hz, 1H), 2.93 - 2.99 (m, 1H) overlap	HMBC 10→8,12
11	35.0	2.22 (dd, J = 13.6, 7.7 Hz, 1H), 2.45-2.52 (m, 1 H) obscured	HMBC 11→8,12
12	170.3	-	-
13	-	7.92 (d, J = 8.1 Hz, 1H)	HMBC 13→12,14 TOCSY 13→14,15
14	52.5	4.56 - 4.62 (m, 1H) overlap	-
15	28.2	2.70 - 2.76 (m, 1H) overlap, 2.86 - 2.94 (m, 1H) overlap	HMBC 15→16
16	109.2	-	-
17	123.8	6.96 - 6.99 (m, 1H) overlap	HMBC 17→16,19
18	-	10.72 (s, 1H) or 10.63 (s, 1H)*	-
19	134.7	-	-

20	110.7	7.25 (d, J = 8.7 Hz, 1H) overlap	HMBC 20→22,24
21	121.9	6.93 (d, J = 8.7 Hz, 1H)	HMBC 21→1,19,23 COSY 21→20
22	129.1	-	-
23	117.0	7.52 (s, 1H)	HMBC 23→1,16,21,22,24
24	127.4	-	-
25	171.1	-	-
26	-	8.30 (d, J = 7.4 Hz, 1H)	TOCSY 26→27,28
27	53.8	4.56 - 4.62 (m, 1H) overlap	HMBC 27→38
28	28.0	2.89 - 2.94 (m, 1H) overlap, 3.08 (dd, J = 14.2, 7.2 Hz, 1H)	HMBC 28→29
29	109.9	-	-
30	123.2	6.81 (br s, 1H)	HMBC 30→32,37
31	-	10.72 (s, 1H) or 10.63 (s, 1H)*	-
32	135.6	-	-
33	110.6	7.27 (d, J = 8.4 Hz, 1H) overlap	HMBC 33→35,37
34	120.4	6.99-7.03 (m, 1H) overlap	HMBC 34→32,36
35	117.6	6.89 (dd, J = 7.4, 7.4 Hz, 1H)	HMBC 35→33,37
36	118.3	7.56 (d, J = 7.9 Hz, 1H)	HMBC 36→29,36 COSY 36→35
37	127.1	-	-
38	170.7	-	-
39	-	7.71 (d, J = 7.6 Hz, 1H)	HMBC 39→38,40,41
40	53.7	4.37 (dd, J = 13.8, 7.6 Hz, 1H)	HMBC 40→38,47
41	36.5	2.70-2.76 (m, 1H) overlap, 2.87-2.93 (m, 1H) overlap	HMBC 41→42,43,47 TOCSY 41→42
42	127.5	-	-
43	129.8	6.97 - 7.00 (m, 2H) overlap	HMBC 43→41,42,45
44	114.5	6.63 (d, J = 8.0 Hz, 2H)	COSY 44→43 HMBC 44→42
45	155.5	-	-
46	-	9.17 (br s, 1H)	HMBC 46→44,45
47	172.4	-	-
48	-	7.05 (s, 1H), 7.26 (s, 1H) overlap	HMBC 48→47

* indole N-H not assigned

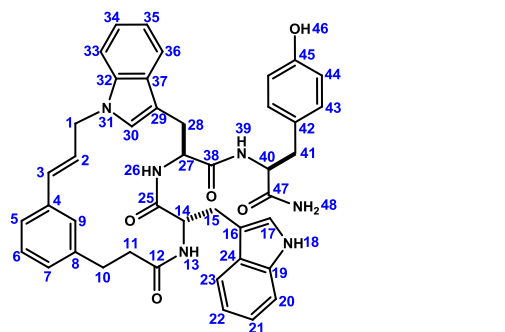
Compound 8 - Tabulated data



Atom #	¹³ C	¹ H	Key correlations
1	34.0	3.47 (br d, J = 17.4 Hz, 1H), 3.92 (dd, J = 17.4, 5.5 Hz, 1H)	HMBC 1→2,3,19,20,21
2	126.8	6.13 (ddd, J = 16.4, 5.5, 2.8 Hz, 1H)	-
3	132.0	4.61 (br d, J = 16.4 Hz, 1H)	HMBC 3→5,9
4	137.3	-	-
5	120.1	7.18 (d, J = 7.7 Hz, 1H) overlap	HMBC 5→3,9
6	127.6	7.06 (dd, J = 7.7, 7.7 Hz, 1H) overlap	HMBC 6→8,4
7	126.2	6.83 (d, J = 7.7 Hz, 1H) overlap	HMBC 7→10
8	142.2	-	-
9	127.3	5.62 (s, 1H)	HMBC 9→5,3,10,7

10	26.9	2.32 (dd, H = 14.9, 7.3 Hz, 1H), 3.05 (dd, J = 14.9, 11.9 Hz, 1H)	HMBC 10→8,12
11	34.3	2.07 (dd, J = 15.5, 11.9 Hz, 1H), 2.24 (dd, J = 15.5, 7.3 Hz, 1H)	HMBC 11→8,12
12	171.9	-	-
13	-	8.05 (d, J = 7.8 Hz, 1H)	HMBC 13→12
14	53.6	4.36 (ddd, J = 12.8, 7.8, 3.1 Hz, 1H)	-
15	26.7	2.75 (dd, J = 13.9, 12.8 Hz, 1H), 3.23 (dd, J = 13.9, 3.1 Hz, 1H)	HMBC 15→16,17
16	109.6	-	-
17	124.7	7.19 (d, J = 2.4 Hz, 1H) overlap	-
18	-	10.28 (br s, 1H)	HMBC 18→17,19
19	135.7	-	-
20	123.5	-	-
21	121.5	6.93 (d, J = 6.8 Hz, 1H)	HMBC 21→1
22	118.3	6.97-7.01 (m, 1H) overlap	HMBC 22→20,24
23	117.1	7.68 (d, J = 7.8 Hz, 1H)	TOCSY 23→22,21
24	126.1	-	-
25	172.3	-	-
26	-	8.18 (d, J = 7.4 Hz, 1H)	TOCSY 26→27,28 HMBC 26→25
27	53.5	4.52 (ddd, J = 8.5, 7.4, 5.0 Hz, 1H)	HMBC 27→29,37
28	27.0	3.05 (dd, J = 14.9, 8.5 Hz, 1H), 3.15 (dd, J = 14.9, 5.0 Hz, 1H)	HMBC 28→29,30
29	109.7	-	-
30	1232.0	7.14 (d, J = 2.0 Hz, 1H)	HMBC 30→29,32,37
31	-	10.84 (br d, J = 2.0 Hz, 1H)	HMBC 31→30
32	135.8	-	-
33	111.0	7.32 (d, J = 7.4 Hz, 1H) overlap	-
34	120.6	7.06 (dd, J = 7.4, 7.4 Hz, 1H) overlap	HMBC 34→32,36
35	118.2	6.97-7.01 (m, 1H) overlap	HMBC 35→33,37
36	118.1	7.56 (d, J = 7.8 Hz, 1H)	TOCSY 36→33,34,35
37	127.1	-	-
38	170.8	-	-
39	-	7.84 (d, J = 8.0 Hz, 1H)	TOCSY 39→40,41 HMBC 39→38
40	53.6	4.40 (ddd, J = 8.0, 7.9, 5.7 Hz, 1H)	HMBC 40→38,47
41	36.6	2.77 (dd, 13.8, 7.9 Hz, 1H), 2.89 (dd, J = 13.8, 5.7 Hz, 1H)	HMBC 41→47
42	127.4	-	-
43	129.9	7.02 (d, J = 8.5 Hz, 2H)	HMBC 43→41,45
44	114.6	6.66 (d, J = 8.5 Hz, 2H)	HMBC 44→42,45 COSY 44→43
45	155.6	-	-
46	-	9.15 (br s, 1H)	-
47	172.5	-	-
48	-	7.09 (br s, 1H), 7.31 (br s, 1H) overlap	HMBC 48→47

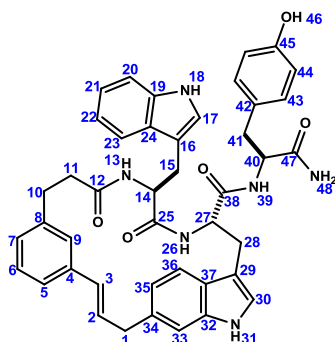
Compound 9 - Tabulated data



Atom #	¹³ C	¹ H	Key correlations
1	46.5	4.93 (br. dd, J = 16.7, 3.9 Hz, 1H), 4.78 (dd, J = 16.3, 6.9 Hz, 1H)	TOCSY→2, 3 HMBC→2, 3, 4
2	125.3	6.11 (ddd, J = 15.8, 6.8, 4.8 Hz, 1H)	TOCSY→3, 1 HMBC→3, 1, 4
3	131.2	6.22 (br. d, J = 16.9 Hz, 1H)	TOCSY→2, 1 HMBC→2, 1, 4
4	136.1	-	-
5	125.2	7.12 (m, 1H) overlap	HMBC→7, 9
6	125.1	7.15 (m, 1H) overlap	COSY→7 HMBC→8, 4
7	127.8	6.94 (m, 1H) overlap	COSY→6 HMBC→9, 5
8	142.0	-	-
9	124.2	7.09 (m, 1H) overlap	HMBC→7
10	28.6	2.46 (m, 1H), 2.96 (dd, J = 13.2, 13.2 Hz, 1H)	COSY→10', 11, 11' HMBC→8, 12, 7, 9
11	35.0	2.06 (m, 1H), 2.38 (m, 1H)	COSY→11', 10, 10' HMBC→12, 10, 8
12	170.5	-	-
13	-	7.67 (d, J = 8.5 Hz, 1H)	TOCSY→15, 15' COSY→14, HMBC→12
14	52.3	4.69 (ddd, J = 7.9, 7.9, 4.6 Hz, 1H)	COSY→15', 13 HMBC→15, 16, 25
15	28.7	3.11 (dd, J = 14.3, 4.3 Hz, 1H), 2.83 (ddd, J = 14.7, 7.7 Hz, 1H)	TOCSY→13 COSY→14, 15', HMBC→14, 16, 17, 24
16	109.8	-	-
17	123.6	6.96 (m, 1H) overlap	COSY→18 HMBC→16, 19, 24
18	-	10.65 (d, J = 1.9 Hz, 1H)	COSY→17 HMBC→16, 17, 24, 19
19	135.9	-	-
20	110.6	7.23 (d, J = 8.2 Hz, 1H)	COSY→21 HMBC→22, 24
21	120.4	6.95 (m, 1H)	COSY→22, 20 HMBC→23, 19
22	117.6	6.85 (dd, J = 7.1, 7.1 Hz, 1H)	COSY→23, 21 HMBC→20, 24
23	118.4	7.52 (d, J = Hz, 1H)	COSY→22 HMBC→16, 19, 21
24	127.7	-	-
25	171.3	-	-
26	-	8.49 (d, J = 8.5 Hz, 1H)	TOCSY→27, 28, 28' HMBC→25
27	53.1	4.63 (ddd, J = 11.4, 8.5, 2.1 Hz, 1H)	TOCSY→28, 28', 26 HMBC→28, 29
28	27.8	2.88 (m, 1H), 3.03 (br. d, J = 14.0 Hz, 1H)	HMBC→29, 37, 30
29	111.3	-	-
30	125.2	7.16 (s, 1H) overlap	HMBC→1
31	-	-	-
32	136.4	-	-
33	109.6	7.42 (d, J = 8.1 Hz, 1H) overlap	COSY→34 HMBC→37, 35
34	121.3	7.08 (m, 1H) overlap	COSY→33 HMBC→36, 32
35	118.5	7.01 (m, 1H) overlap	COSY→35, 34 HMBC→37, 33
36	118.7	7.60 (d, J = 7.9 Hz, 1H)	COSY→35 HMBC→29, 34, 32
37	127.8	-	-
38	171.9	-	-
39	-	7.94 (d, J = 7.9 Hz, 1H)	TOCSY→41, 41' COSY→40
40	54.0	4.44 (ddd, J = 7.8, 7.8, 6.0 Hz, 1H)	HMBC→38
41	37.2	2.78 (dd, J = 13.9, 7.8 Hz, 1H), 2.91 (m, 1H) overlap	COSY→41, 41', 39 HMBC→42, 41, 47
			TOCSY→39 COSY→40 HMBC→40,

42	128.1	-	47, 42, 43
43	130.6	7.03 (m, 2H) overlap	-
44	115.1	6.64 (d, J = 8.5 Hz, 2H)	COSY→44 HMBC→45, 44
45	156.1	-	COSY→43 HMBC→45, 42
46	-	9.16 (s, 1H)	-
47	172.7	-	HMBC→44, 45
48	-	7.08 (m, 1H) overlap, 7.42 (br. s)	-
			HMBC→47

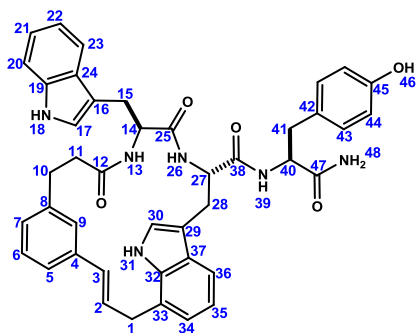
Compound 10a - Tabulated data



Atom #	¹³ C	¹ H	Key correlation
1	34.1	3.53-3.59 (m, 1H), 3.76-3.81 (m, 1H)	-
2	127.9	6.40 (ddd, J = 16.1, 5.5, 5.5 Hz, 1H)	COSY 2→1,3 HMBC 2→4,33 ROESY 2→5
3	129.1	5.78 (d, J = 16.1 Hz, 1H)	HMBC 3→5 ROESY 3→9
4	137.0	-	-
5	121.5	7.23-7.26 (m, 1H)	COSY 5→6 HMBC 5→3
6	127.7	7.10-7.13 (m, 1H)	HMBC 6→4,8 COSY 6→7
7	126.7	6.88-6.91 (m, 1H)	-
8	141.9	-	-
9	125.4	6.50 (br s, 1H)	HMBC 9→3,5 TOCSY 9→5,6,7 ROESY 9→2,3,11
10	27.4	2.37-2.45 (m, 1H), 3.02-3.11 (m, 1H)	HMBC 10→8
11	33.9	2.08-2.17 (m, 1H), 2.30-2.38 (m, 1H)	TOCSY 11→10 HMBC 11→12
12	170.0	-	-
13	-	7.37 (d, J = 8.1 Hz, 1H)	ROESY 13→11,14 HMBC 13→12
14	52.2	4.52-4.57 (m, 1H)	TOCSY 14→13,15 ROESY 14→26
15	28.4	2.87-2.92 (m, 1H), 3.10-3.15 (m, 1H)	HMBC 15→16
16	109.4	-	-
17	123.3	6.98-7.01 (m, 1H)	HMBC 17→16,19
18	-	10.66-10.69 (m, 1H)	HMBC 18→19,24 TOCSY 18→17 ROESY 18→20
19	135.4	-	-
20	110.7	7.25-7.28 (m, 1H)	-
21	120.2	6.98-7.02 (m, 1H)	HMBC 21→19
22	117.7	6.86-6.91 (m, 1H), 6.98-7.02 (m, 1H)	HMBC 22→24
23	118.3	7.52 (d, J = 7.7 Hz, 1H)	HMBC 23→19,21
24	127.6	-	-
25	-	-	-
26	-	8.31 (d, J = 8.6 Hz, 1H)	HMBC 26→25
27	52.8	4.61 (ddd, J = 12.3, 8.6, 2.9 Hz, 1H)	TOCSY 27→26,28 ROESY 27→39
28	27.7	2.80-2.86 (m, 1H), 3.14-3.18 (m, 1H)	ROESY 28→36

29	109.7	-	-
30	124.0	7.20 (d, J = 1.7 Hz, 1H)	HMBC 30→29,32,37 ROESY 30→27,28
31	-	10.54 (br s, 1H)	ROESY 31→1,2,3 COSY 31→30
32	134.9	-	-
33	122.0	-	-
34	120.9	6.86-6.89 (m, 1H)	ROESY 34→1 HMBC 34→1
35	118.1	6.90-6.95 (m, 1H)	-
36	116.6	7.57 (d, J = 8.0 Hz, 1H)	HMBC 36→32,34
37	126.7	-	-
38	-	-	-
39	-	7.92 (d, J = 7.7 Hz, 1H)	TOCSY 39→40,41
40	53.6	4.49-4.54 (m, 1H)	HMBC 40→42,47 ROESY 40→48
41	36.8	2.81-2.87 (m, 1H), 2.94-2.99 (m, 1H)	HMBC 41→47
42	127.4	-	-
43	129.9	7.05-7.09 (m, 2H)	HMBC 43→45,41
44	114.6	6.66-6.69 (m, 2H)	HMBC 44→42,45
45	155.7	-	-
46	-	9.17-9.19 (m, 1H)	HMBC 46→45
47	172.6	-	-
48	-	7.11 (br s, 1H), 7.48 (br s, 1H)	TOCSY 48→48'

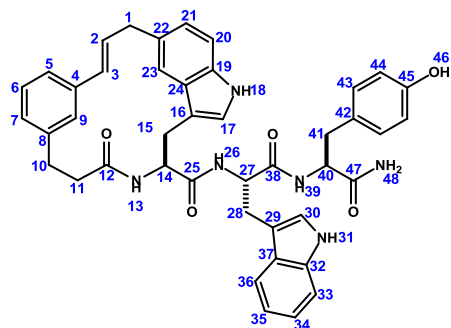
Compound 10b - Tabulated data



Atom #	¹³ C	¹ H	Key correlations
1	37.7	3.41-3.47 (m, 1H), 3.51-3.57 (m, 1H)	HMBC 1→33,34,35 ROESY 1→33,35
2	131.4	6.46 (ddd, J = 15.8, 4.9, 4.9 Hz, 1H)	COSY 2→1,3
3	129.8	5.39 (d, J = 15.8 Hz, 1H)	ROESY 3→9
4	137.0	-	-
5	121.0	7.23-7.26 (m, 1H)	-
6	127.7	7.09-7.13 (m, 1H)	HMBC 6→4,8
7	126.8	6.86-6.89 (m, 1H)	-
8	141.9	-	-
9	125.8	6.38 (br s, 1H)	TOCSY 9→5,6,7 ROESY 9→10,11
10	27.7	2.38-2.45 (m, 1H), 2.95-3.02 (m, 1H)	-
11	34.0	2.09-2.17 (m, 1H), 2.31-2.40 (m, 1H)	-
12	169.8	-	-
13	-	7.12-7.15 (m, 1H)	ROESY 13→11
14	52.7	4.42-4.46 (m, 1H)	TOCSY 14→13,15 ROESY 15→26,27
15	27.8	2.94-3.00 (m, 1H), 3.27-3.34 (m, 1H)	-
16	109.1	-	-
17	123.6	6.91 (br s, 1H)	HMBC 17→16,19,24
18	-	10.62 (br s, 1H)	COSY 18→17 ROESY 18→20 HMBC 18→16,19,24

19	135.5	-	-
20	110.7	7.23-7.26 (m, 1H)	HMBC 20→24 COSY 20→21
21	120.2	6.96-7.00 (m, 1H)	-
22	117.7	6.84 (dd, J = 8.0, 7.0 Hz, 1H)	-
23	118.2	7.40 (d, J = 8.0 Hz, 1H)	ROESY 23→15 TOCSY 23→20,21,22
24	127.9	-	-
25	-	-	-
26	-	8.28 (d, J = 8.9 Hz, 1H)	-
27	54.5	4.71-4.76 (m, 1H)	TOCSY 27→26,28 ROESY 27→39
28	28.4	2.88-2.94 (m, 1H), 3.12-3.17 (m, 1H)	HMBC 28→29
29	109.6	-	-
30	123.3	7.12 (br s, 1H)	ROESY 30→28 HMBC 30→37
31	-	10.68 (br s, 1H)	TOCSY 31→30 ROESY 31→33
32	136.2	-	-
33	111.3	7.07 (s, 1H)	HMBC 33→1,35,37 ROESY 33→1
34	131.1	-	-
35	120.1	6.77 (d, J = 8.1 Hz, 1H)	HMBC 35→1,33,37 ROESY 35→1
36	118.7	7.78 (d, J = 8.1 Hz, 1H)	HMBC 36→32,34 ROESY 36→27,28
37	125.6	-	-
38	171.7	-	-
39	-	8.14 (d, J = 7.7 Hz, 1H)	HMBC 39→38 TOCSY 39→40,41
40	53.8	4.52-4.56 (m, 1H)	HMBC 40→47
41	36.8	2.81-2.87 (m, 1H), 2.94-2.99 (m, 1H)	HMBC 41→42,43,47
42	127.4	-	-
43	129.9	7.05-7.09 (m, 2H)	HMBC 43→41,45
44	114.6	6.66-6.69 (m, 2H)	HMBC 44→42,45
45	155.7	-	-
46	-	9.17-9.19 (m, 1H)	HMBC 46→45
47	172.5	-	-
48	-	7.07 (br s, 1H), 7.44 (br s, 1H)	TOCSY 48→48'

Compound 11 - Tabulated data

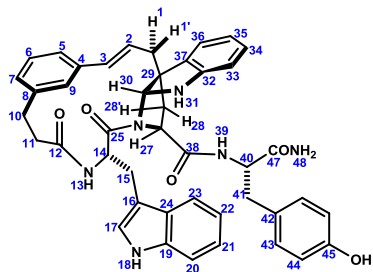


Atom #	¹³ C	¹ H	Key correlations
1	36.0	3.58 (m, 2H)	TOCSY→2, 3 HMBC→2, 3, 22
2	130.0	6.23 (m, 1H)	TOCSY→1, 3 HMBC→1, 4
3	132.7	6.55 (d, J = 15.7 Hz, 1H)	TOCSY→2, 1 HMBC→1, 4, 9
4	138.3	-	-
5	124.8	7.08 (m, 1H) overlap	HMBC→3, 7, 9
6	128.5	7.21 (dd, J = 7.4, 7.4 Hz, 1H)	HMBC→8, 4
7	127.9	7.04 (m, 1H) overlap	HMBC→9, 7
8	142.7	-	-
9	124.5	7.41 (s, 1H)	HMBC→5, 3
10	29.1	2.56 (app. dd, J = 13.8, 5.7 Hz, 1H), 3.24 (app. t, J = 13.0	COSY→10', 11 HMBC→8, 9, 7

		Hz, 1H)	
11	35.7	2.21-2.34 (m, 2H)	COSY→10, 10' HMBC→8, 12
12	172.6	-	-
13	-	8.49 (d, J = 6.0 Hz, 1H)	TOCSY→15, 15' COSY→14 HMBC→12
14	54.6	4.29 (m, 1H), overlap	COSY→13, 15, 15' HMBC→16, 15, 25
15	27.1	2.98 (m, 1H) overlap, 2.66 (m, 1H) overlap	COSY→15', 14 HMBC→16, 14, 24, 17, 25
16	111.1	-	-
17	123.8	6.8 (s, 1H)	HMBC→19, 24, 16
18	-	10.82 (s, 1H) or 10.57 (s, 1H)*	-
19	135.1	-	-
20	111.4	7.25 (d, J = 8.2 Hz, 1H)	TOCSY→23 COSY→21 HMBC→24, 22
21	122.2	6.96 (m, 1H) overlap	COSY→20 HMBC→19
22	130.8	-	-
23	125.1	7.08 (m, 1H) overlap	TOCSY→21, 20 HMBC→21, 19
24	127.5	-	-
25	171.8	-	-
26	-	7.47 (d, J = 6.8 Hz, 1H)	TOCSY→28 COSY→27 HMBC→25
27	53.9	4.37 (m, 1H) overlap	COSY→26, 28 HMBC→28, 29, 38
28	27.1	2.98 (m, 1H) overlap, 2.82 (m, 1H) overlap	TOCSY→26 COSY→27 HMBC→27, 29, 37, 30, 38
29	110.2	-	-
30	123.6	7.0 (m, 1H) overlap	HMBC→37, 29
31	-	10.82 (s, 1H) or 10.57 (s, 1H)*	-
32	136.3	-	-
33	111.3	7.29 (d, J = 7.9 Hz, 1H)	TOCSY→35, 36 COSY→34 HMBC→37, 35
34	120.9	7.01 (m, 1H), overlap	TOCSY→36 COSY→33, 35 HMBC→32, 36
35	118.4	6.92 (m, 1H), overlap	TOCSY→33 COSY→34, 36 HMBC→37, 33
36	118.4	7.44 (d, J = 7.7 Hz, 1H)	TOCSY→33, 34 COSY→35 HMBC→29, 34, 32
37	127.6	-	-
38	171.3	-	-
39	-	7.77 (d, J = 7.9 Hz, 1H)	TOCSY→41, 41' COSY→40 HMBC→38
40	54.0	4.28 (m, 1H) overlap	COSY→39, 41 HMBC→42, 41, 47
41	36.6	2.85 (m, 1H) overlap, 2.66 (m, 1H) overlap	TOCSY→39 COSY→40 HMBC→42, 40, 43
42	128.3	-	-
43	130.4	6.94 (m, 2H), overlap	COSY→44 HMBC→45, 41
44	115	6.61 (d, J = 7.7 Hz, 2H)	COSY→43 HMBC→45
45	156.1	-	-
46	-	9.16 (s, 1H)	HMBC→45, 44
47	173.3	-	-
48	-	7.10 (s, 1H) overlap, 7.02 (s, 1H) overlap	HMBC→47

* indole N-H not assigned

Compound 12 - Tabulated data



Atom #	¹³ C	¹ H	Key correlations
1 (pro-R)	39.0	2.42 (dd, J = 13.5, 6.4 Hz, 1H)	HMBC 1→28,29,30,37
1' (pro-S)		2.73 (dd, J = 13.5, 9.5 Hz, 1H)	
2	125.3	6.02 (ddd, J = 15.6, 9.0, 6.8 Hz, 1H)	TOCSY 2→1,3 HMBC 2→4
3	132.1	6.57 (d, J = 15.6 Hz, 1H) overlap	HMBC 3→1,4
4	136.8	-	
5	124.1	7.01-7.04 (m, 1H) overlap	
6	128.2	7.13-7.18 (m, 1H) overlap	HMBC 6→4,8
7	127.0	6.99-7.02 (m, 1H) overlap	
8	140.5	-	
9	124.6	7.19 (s, 1H) overlap	HMBC 9→5,3,7
10	30.6	2.64-2.70 (m, 1H), 2.92-2.99 (m, 1H)	HMBC 10→8,11,12
11	37.5	2.15-2.23 (m, 1H) overlap, 2.38-2.45 (m, 1H)	HMBC 11→8,12
12	171.2	-	
13	-	7.96 (d, J = 8.4 Hz, 1H)	
14	49.8	5.39-5.45 (m, 1H)	HMBC 14→25
15	29.9	3.06 (dd, J = 14.2, 5.7 Hz, 1H), 3.16 (dd, J = 14.2, 7.8 Hz, 1H)	HMBC 15→16
16	109.4	-	
17	124.0	7.40 (br s, 1H)	HMBC 17→19,24
18	-	11.07 (br s, 1H)	
19	135.9	-	
20	111.5	7.51 (d, J = 8.1 Hz, 1H)	HMBC 20→24
21	121.3	7.14-7.18 (m, 1H) overlap	
22	118.8	7.09 (dd, J = 7.8, 7.2 Hz, 1H)	TOCSY 22→20,21,23 HMBC 22→24
23	118.4	7.86 (d, J = 7.8 Hz, 1H)	COSY 23→22 HMBC 23→16,19,20,21,24
24	126.9	-	
25	171.3	-	
26	-	-	
27	62.4	4.22 (dd J = 10.3, 6.1 Hz, 1H) overlap	HMBC 27→29,38
28 (pro-S)	40.0	1.74 (dd, J = 13.2, 6.1 Hz, 1H)	HMBC 28→38,29 NOESY 28→41,43,44
28' (pro-S)		2.34 (dd, J = 13.2, 10.3 Hz, 1H)	NOESY 28'→2,3
30	81.1	5.73 (s, 1H)	HMBC 30→27,29
31	-	4.25 (br s, 1H)	NOESY 31→33
32	146.6	-	
33	109.3	6.34 (d, J = 7.7 Hz, 1H)	HMBC 33→37
34	127.9	7.00-7.04 (m, 1H) overlap	
35	119.0	6.72 (dd, J = 7.8, 7.2 Hz, 1H)	HMBC 35→37
36	121.7	7.02-7.06 (m, 1H) overlap	HMBC 36→32
37	134.8	-	
38	169.7	-	
39	-	6.99-7.02 (m, 1H) overlap	HMBC 39→38
40	53.4	4.16-4.20 (m, 1H) overlap	HMBC 40→47 TOCSY 40→39
41	37.3	2.18 (dd, J = 13.6, 9.2 Hz, 1H) overlap, 2.74 (dd, J = 13.6, 5.0 Hz, 1H) overlap	HMBC 41→42,43,47

42	127.2	-	
43	129.8	6.59 (d, J = 8.3 Hz, 2H)	
44	114.4	6.26 (d, J = 8.3 Hz, 2H)	HMBC 44→42
45	155.3	-	
46	-	9.04 (br s, 1H)	HMBC 46→44
47	172.4	-	
48	-	7.18 (br s, 2H)	HMBC 48→47

Solution structure:

The solution conformation of pyrroloindoline **7** was determined from NMR spectra of **7** acquired in DMSO to permit the observation of exchangeable protons. ROESY was also acquired in DMSO:D₂O (9:1) to resolve potential signal overlap arising from exchangeable protons. The relative stereochemistry of the pyrroloindoline ring juncture was determined by careful analysis of long range inter-residue correlations observed by NOESY and ROESY (see text). Distance restraints were obtained from pairs of NOE correlations from a 100ms ¹H-¹H NOESY experiment. The fixed reference distance H18-H20 (2.8Å)¹² was corroborated by distance H30-H31¹³ and all geminal pairs, suggesting sufficiently linear NOE buildup for stratification of the larger dataset. Volume integrals were grouped into bins, and classified as strong (<2.5Å), medium (<3.5 Å) and weak (<4.5 Å), based on the relationship of r^{-6} . An initial model was generated by a Mixed Monte-Carlo low-mode conformational search incorporating 7 key long-distance NOE distance restraints. From this model, an additional 29 NOEs were defined, and prochiral methylenes H1 (pro-*R*), H1' (pro-*S*) and H28 (pro-*S*), H28' (pro-*R*) were defined. Equivalent NOE correlations arising from unassigned prochiral methylenes at C10, C11, C15 and C41, where present, were assigned the weaker of the two restraint bins. No torsional constraints were utilized. Structure calculations were carried out using Macromodel 9.8 (Schrödinger, Inc., San Diego, CA) using the OPLS-2005 force field with implicit GB/SA solvation and a constant dielectric ($\epsilon = 1.0$). A 5,000 step restrained Mixed Monte-Carlo low-mode conformational search was used. Amide bonds rotations were not restrained. Redundant conformers were filtered within a heavy atom RMSD cutoff of 1.0Å, which converged to 5 structures within 11kcal/mol of the global minimum. The global minimum was located 150 times.

¹² Bye, E.; Mostad, A.; Romming, C., *Acta. Chem. Scand.*, **1973**, 27, 471-484.

¹³ Flippen, J., *Acta Cryst.*, **1978**, B34, 995-997.

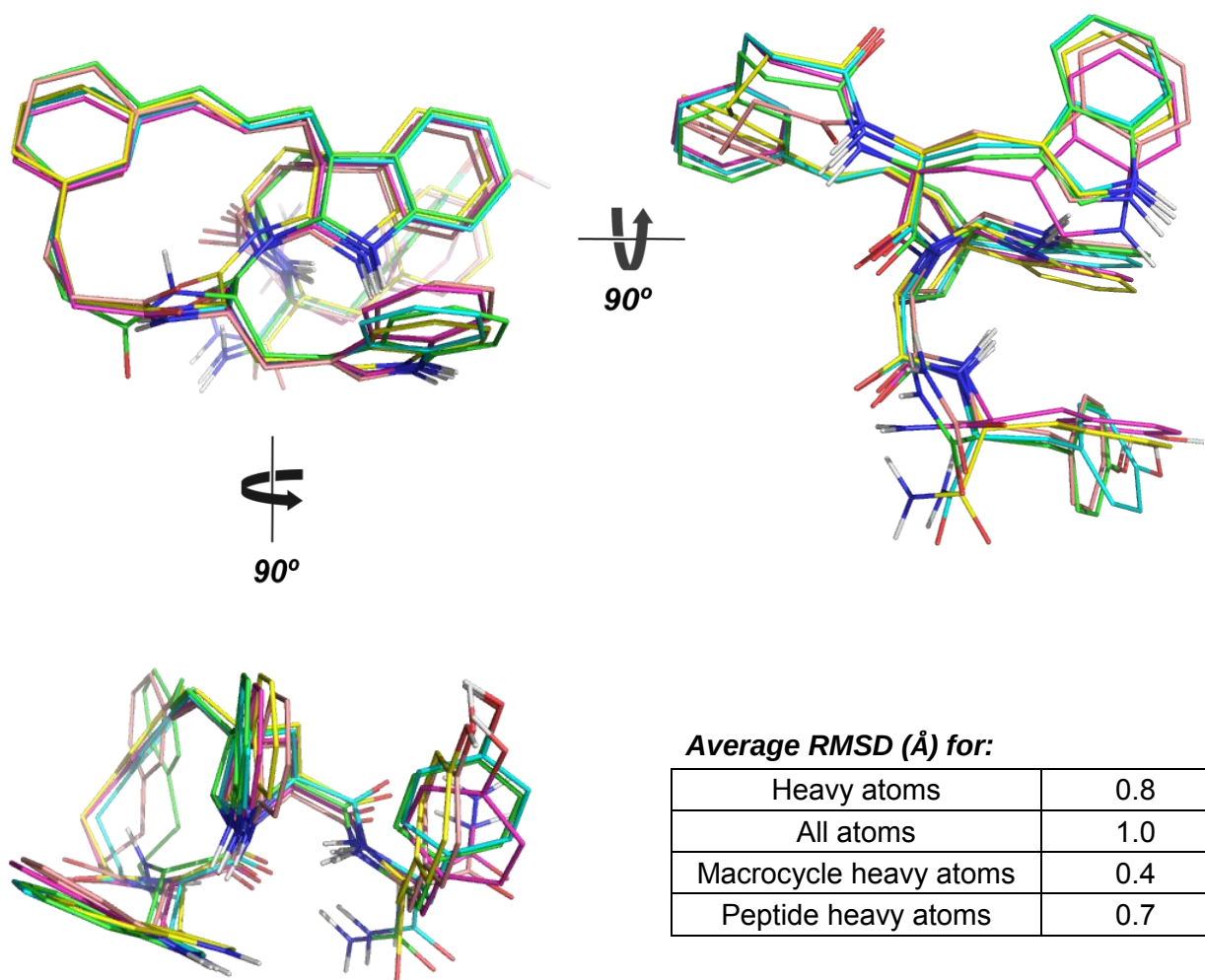
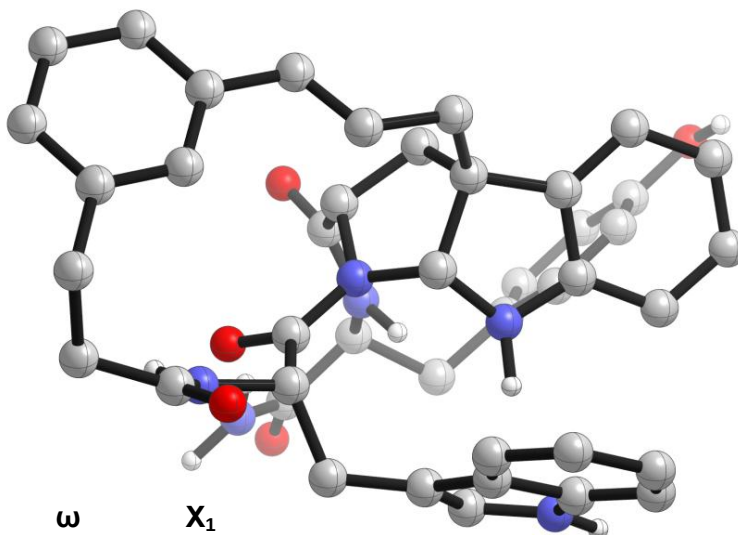


Figure S3. Conformational ensemble and average RMSDs of pyrroloindoline **12** derived from constrained simulations using 36 distances measured by NOE. Rendered with PyMol.



Residue	ϕ	ψ	ω	X_1
Trp1	-149°	137°	-149°	-160°
PyrInd2	-71°	-27°	178°	-17°
Tyr3	-96°	111°	n/a	-71°

Figure S4. Lowest energy conformational and peptide torsional angles of pyrroloindoline **12**. Rendered with CYLview.¹⁴

Table S2. Internuclear distances determined from NOESY, and distances from calculated solution conformation.

	Long range ¹⁵	prelim. calc. ¹⁶	final calc. ¹⁷	NOE correlation ¹⁸	avg. Integration	r exp. (Å) ¹⁹	bin ²⁰	r calc. (Å) ²¹
1 ²²	n			18↔20	0.8	2.8	m	2.9
2	n			1↔1'	15.7	1.7	s	1.7
3	y			1↔3	0.9	2.8	m	3.6
4	y			1'↔3	1.5	2.6	s	2.5
5	y		y	1↔30	1.2	2.7	m	2.8
6	y		y	1'↔30	0.3	3.4	m	3.8
7	y		y	1'↔36	1.8	2.5	s	2.7
8	y		y	1↔36	0.8	2.9	m	3.0
9	n			2↔3	28.2	1.6	s	3.1
10	y	y	y	2↔14	0.8	2.9	m	2.5

¹⁴ "CYLview, 1.0b; Legault, C. Y., Université de Sherbrooke, 2009 (<http://www.cylview.org>)"

¹⁵ Correlation which is greater than three bonds, and which is not geometrically fixed due to small rings, etc.

¹⁶ Distance restraints used in generating a preliminary model (see text).

¹⁷ Long range correlations used in final calculation of solution conformation.

¹⁸ See numbering scheme, above.

¹⁹ Internuclear distance calculated from experiment NOE

²⁰ Bins were defined as strong (s, <2.5 Å), medium (m, <3.5 Å) and weak (w, <4.5 Å)

²¹ Internuclear distance measured from lowest energy conformer.

²² Reference distance (2.82 Å). Bye, E.; Mostad, A.; Romming, C., *Acta. Chem. Scand.*, **1973**, 27, 471-484.

11	y		y	2↔27	0.4	3.2	m	3.6
12	y	y	y	2↔30	3.7	2.2	s	2.2
13	y	y	y	2↔9	5.2	2.1	s	2.0
14	y	y	y	3↔5	2.2	2.4	s	2.4
15	y		y	3↔27	0.2	3.5	m	3.2
16	y		y	3↔28'	0.9	2.8	m	3.0
17	y		y	10↔7	0.2	3.6	m	3.6
18	y		y	10'↔7	0.6	2.9	m	2.4
19	y		y	10↔9	0.6	3.0	m	3.7
20	y		y	10'↔9	1.8	2.5	s	2.6
21	n			10↔10'	20.4	1.7	s	1.7
22	n			10↔11	2.9	2.3	s	2.4
23	n			10↔11'	4.3	2.2	s	2.6
24	n			10'↔11	1.6	2.5	m	2.6
25	n			10'↔11'	1.7	2.5	m	3.1
26	y			11↔9	0.2	3.5	m	4.1
27	y			11'↔9	0.4	3.2	m	3.6
28	n			11↔11'	25.6	1.6	s	1.8
29	y			13↔9	0.6	3.0	m	3.5
30	y			13↔10	0.5	3.1	m	4.3
31	y			13↔10'	0.2	3.8	w	4.5
32	y		y	13↔11	1.0	2.7	m	3.3
33	y		y	13↔11'	4.6	2.1	s	2.2
34	y		y	13↔15	0.8	2.8	m	3.2
35	y		y	13↔15'	0.5	3.1	m	3.4
36	y		y	13↔27	0.1	3.9	w	4.2
37	y	y	y	14↔9	0.5	3.0	m	2.8
38	y		y	14↔17	0.4	3.2	m	4.1
39	y		y	14↔23	1.2	2.7	m	2.9
40	y		y	14↔31	0.6	3.0	m	3.5
41	y		y	17↔15	0.3	3.3	m	3.6
42	y		y	17↔15'	0.6	3.0	m	2.4
43	y		y	17↔41	0.3	3.4	m	3.6
44	n			17↔18	2.5	2.4	s	2.6
45	y		y	20↔33	0.2	3.7	m	3.5
46	y			23↔15	0.5	3.1	m	2.8
47	y			23↔15'	0.2	3.6	m	4.3
48	y			23↔31	0.2	3.7	m	4.4
49	n			28↔28'	15.1	1.7	s	1.7
50	y			28↔36	0.7	2.9	m	3.5
51	y			28'↔36	0.2	3.5	m	3.5

52	y		y	28↔39	0.6	3.0	m	3.0
53	y		y	28↔43	0.6	3.0	m	2.9
54	y		y	28↔44	0.2	3.5	m	3.5
55	y			28↔41'	0.9	2.8	m	4.7 ²³
56	y	y	y	30↔9	0.6	3.0	m	3.8
57	y		y	30↔13	0.1	3.8	w	4.4
58	y	y	y	30↔14	9.2	1.9	s	1.9
59	y		y	30↔15	0.2	3.6	m	3.9
60	y		y	30↔15'	0.2	3.7	w	4.0
61	y		y	30↔17	0.1	3.9	w	4.1
62	y		y	30↔23	0.2	3.5	m	3.5
63	y			30↔28	0.2	3.6	m	4.0
64	y			30↔28'	0.2	3.7	m	4.2
65	n			30↔31	2.4	2.4	s	2.4
66	y			30↔33	0.2	3.7	m	4.5
67	n			31↔33	1.0	2.7	m	2.6
68	n			41↔41'	14.7	1.8	s	1.7
69	y			41↔43	1.3	2.6	m	2.5
70	y			41'↔43	1.3	2.6	s	2.5

²³ Anomalous distance. Violates constraint from NOE measured distance.

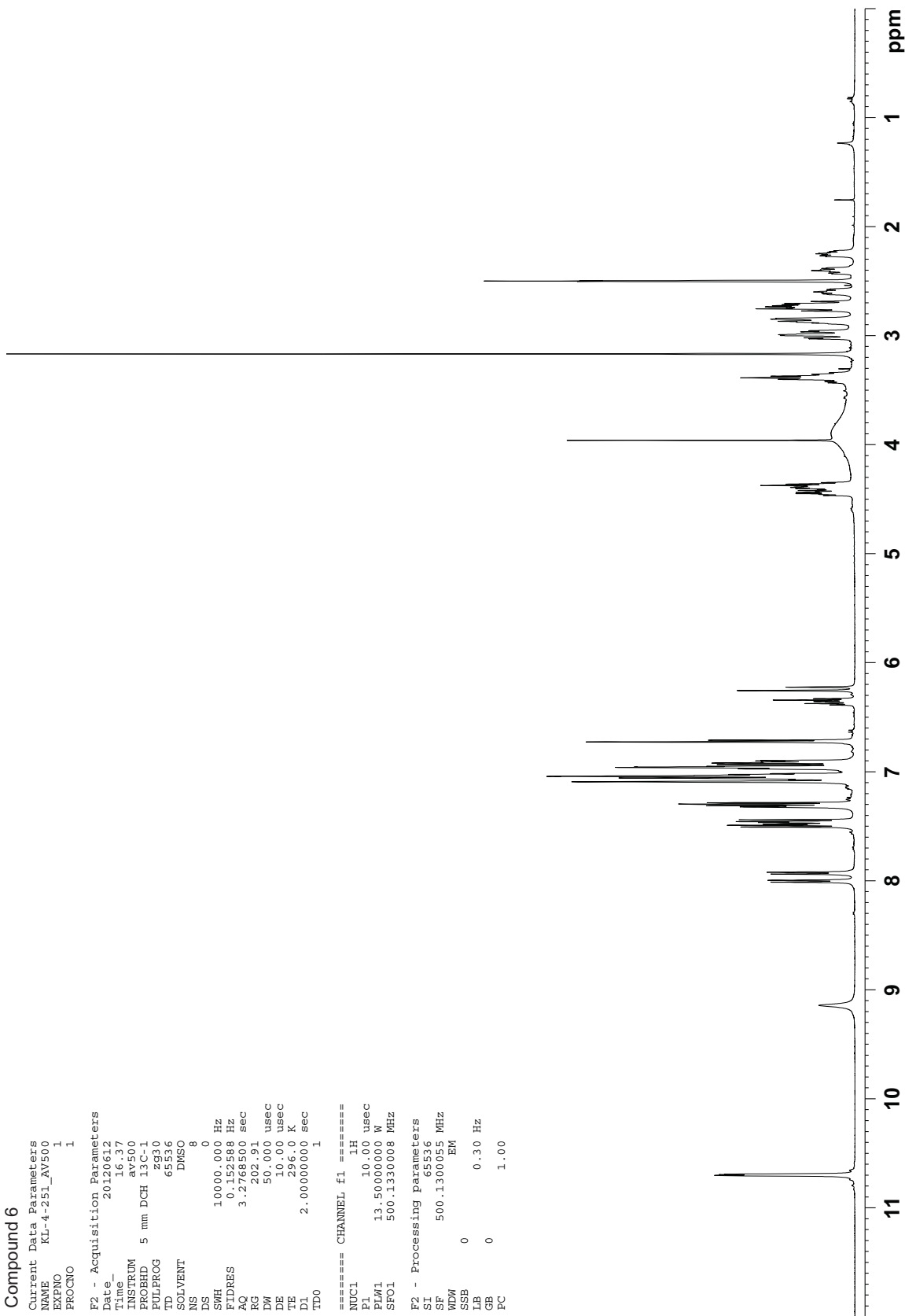
Compound 6

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PROCNO 1

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PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 8
DS 0
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2768500 sec
RG 202.91
DM 50.000 usec
DE 10.00 usec
TE 296.0 K
D1 2.00000000 sec
TD0 1

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P1 10.00 usec
PLW1 13.50000000 W
SFO1 500.1330008 MHz

F2 - Processing parameters
SI 65536
SF 500.1300055 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



Compound 6

Current Data Parameters
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EXPNO 5
PROCNO 1

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Time_ 18:50
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PROBHD 5 mm DCH 13C-1
PULPROG cosygmfph
TD 2048
SOLVENT DMSO
NS 2
DS 8
SWH 5498.534 Hz
FIDRES 2.684831 Hz
AQ 0.1862815 sec
RG 202.91
DW 90.933 usec
DE 10.00 usec
TE 296.0 K
DO 0.00008724 sec
D1 2.00000000 sec
D13 0.00000400 sec
D16 0.00020000 sec
IN0 0.00019995 sec

===== CHANNEL f1 =====

NUC1 1H
P1 10.00 usec
P2 20.00 usec
PLW1 13.50000000 W
SFO1 500.1327507 MHz

===== GRADIENT CHANNEL =====

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GENAW2 SMSQ10.100
GFZ1 10.00 %
GFZ2 20.00 %
F16 1000.00 usec

F1 - Acquisition parameters

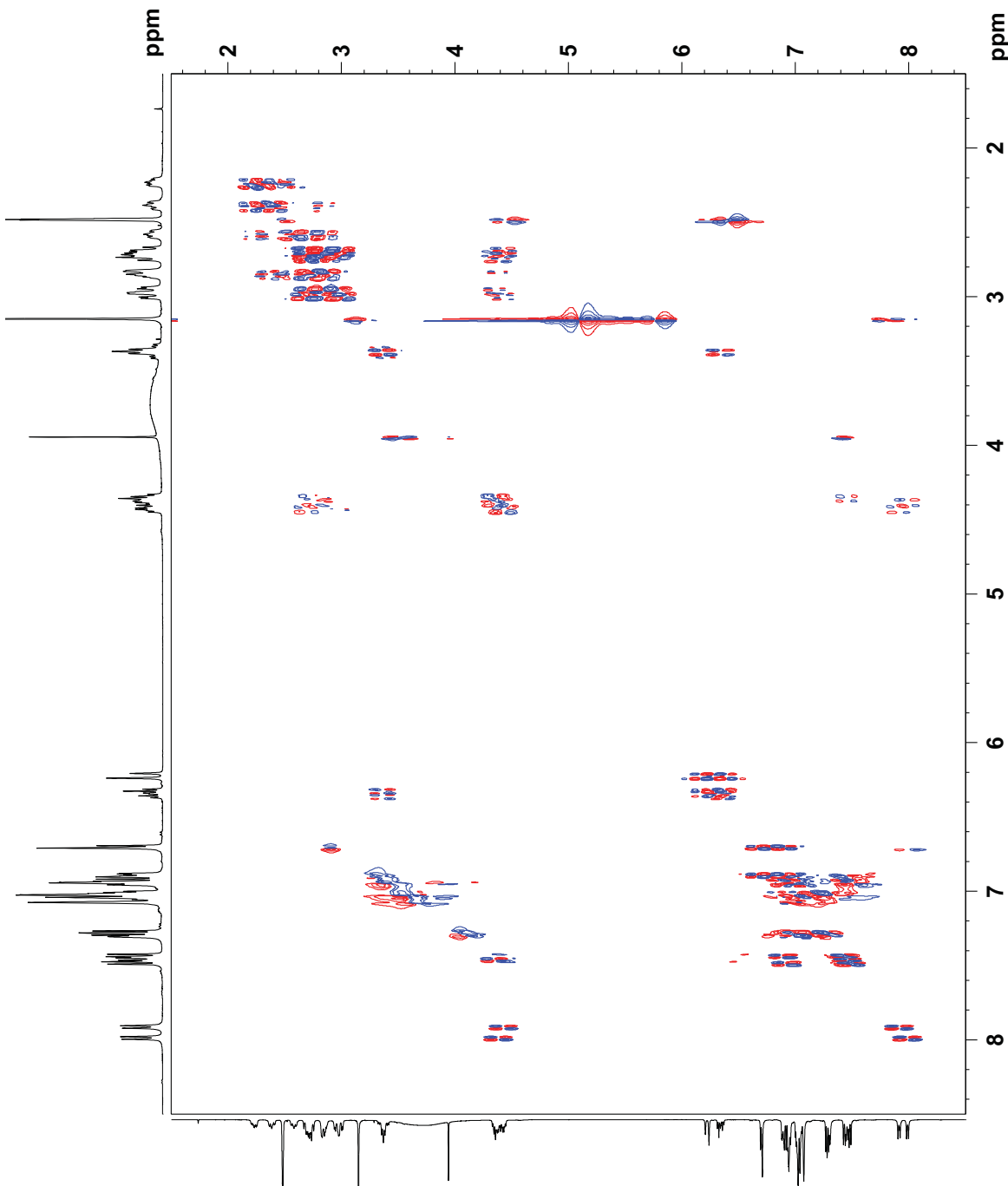
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SW 10.800 ppm
PRMODE States-TpPI

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WDW SINE
SSB 2
LB 0 Hz
GB 0
PC 1.00

F1 - Processing parameters

SI 4096
MC2 States-TpPI
SF 500.1300168 MHz
WDW SINE
SSB 2
LB 0 Hz
GB 0



Compound 6

Current Data Parameters
NAME KL-4-251_AV500
EXPNO 8
PROCNO 1

F2 - Acquisition Parameters
Date_ 20120613
Time_ 19.41
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PROBHD 5 mm DCH 13C-1
PULPROG mlevetgp.js
TD 2048

SOLVENT DMSO
NS 2
DS 8
SWH 5151.099 Hz
FIDRES 2.515185 Hz
AQ 0.1988425 sec
RG 979.31
RW 11.067 usec
DE 296.0 usec
TE 296.0 usec
D0 0.00000300 sec
D1 2.00000000 sec
D9 0.06000000 sec
D11 0.03000000 sec
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D16 0.00020000 sec
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L1 24

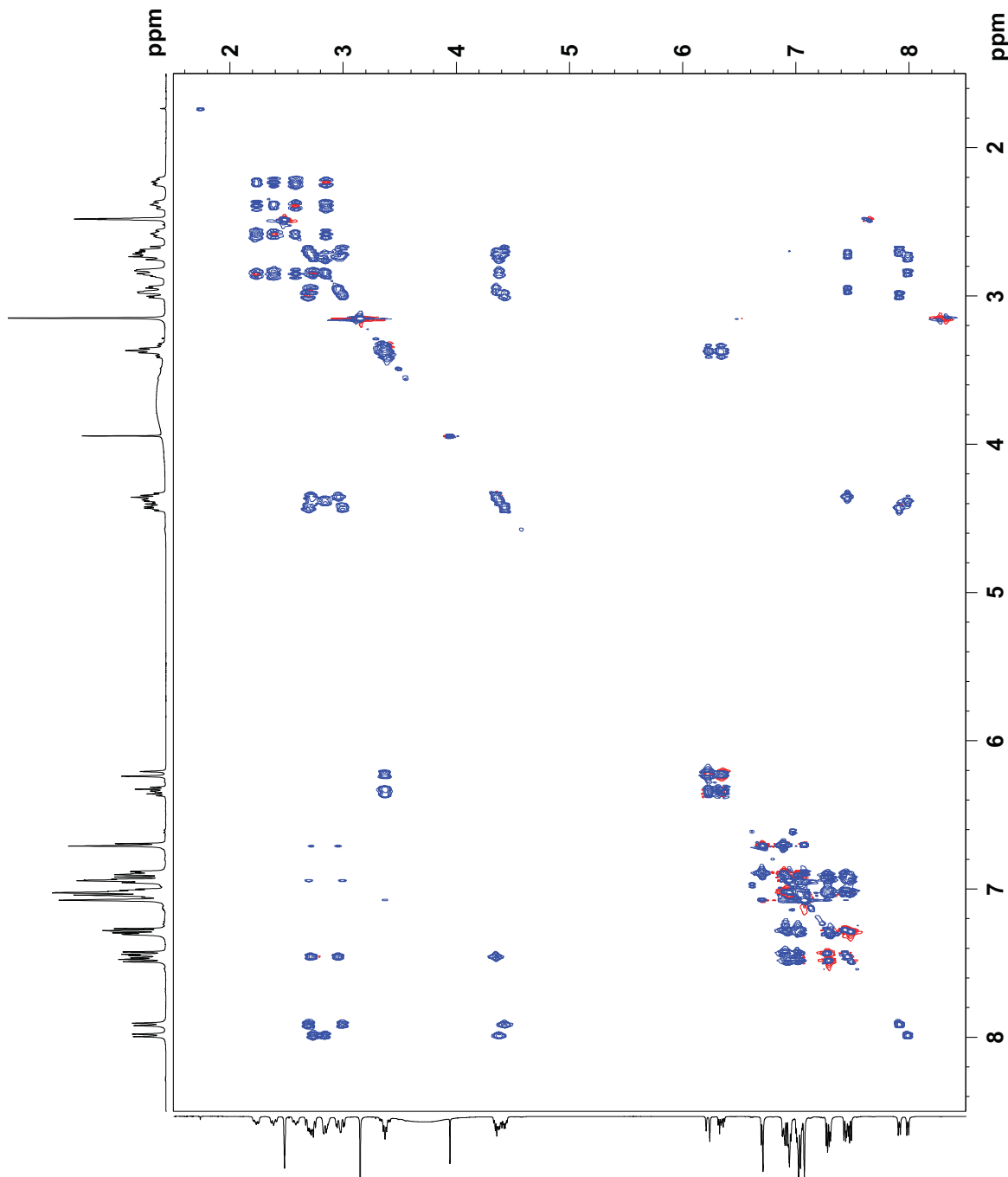
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P2 20.00 usec
P5 26.68 usec
P6 40.00 usec
P7 250.00 usec
PL1 13.50000000 W
PL10 0.84375000 W
SF01 500.1324246 MHz

===== GRADIENT CHANNEL =====
GENAM1 SINE.100
GENAM2 SINE.100
GPZ1 30.00 %
GPZ2 30.00 %
P16 1000.00 usec

F1 - Acquisition parameters
TD 256
SF01 500.1324 MHz
FIDRES 20.121468 Hz
SWH 10.299 Ppm
FMODE Echo-Antiecho

F2 - Processing parameters
SI 4096
SF 500.1300135 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0
PC 1.00

F1 - Processing parameters
SI 4096
MC2 echo-antiecho
SF 500.1300135 MHz
WDW
SSB 2
LB 0 Hz
GB 0



Compound 6

Current Data Parameters
NAME KL-4-251_AV500
EXPNO 6
PROCNO 1

F2 - Acquisition Parameters
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Time 19:00
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PROBHD 5 mm BBO 13C-1
PULPROG hmczgpg130
TD 2048
SOLVENT DMSO

NS 2
DS 16
SWH 6009.615 Hz
FIDRES 2.1764436 sec
AQ 0.1704436 sec
RG 202.91
DW 83.200 usec
DE 10.00 usec
TE 296.0 K
TEST6 120.0000000
CNS17 160.0000000
CNS13 7.0000000
D0 0.0000300 sec
D1 2.0000000 sec
D6 0.07142857 sec
D7 0.0000000 sec
IN0 0.0001990 sec

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NUC1 1H
P1 10.00 usec
PL1 2.00 dB
RF1 13.5000000 MHz
SP01 500.1330008 MHz

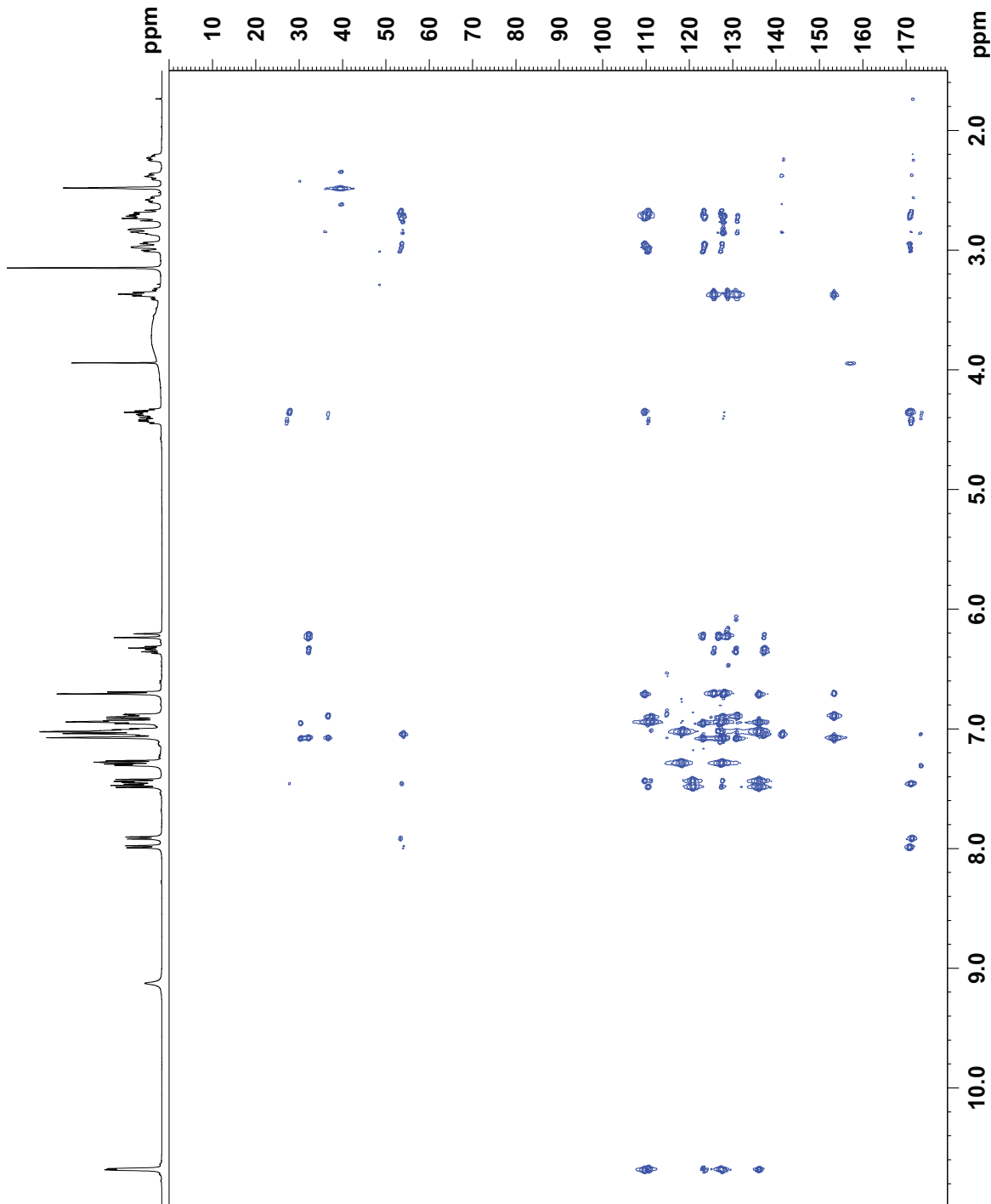
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NUC2 13C
P2 23.0139563 usec
PL2 19.00 dB
RF2 125.7703648 MHz
SP02 125.7703648 MHz

===== GRADIENT CHANNEL =====
GPM1 SMSQ10.100
GPM2 SMSQ10.100
GPM3 SMSQ10.100
GPM4 SMSQ10.100
GPM5 SMSQ10.100
GPM6 SMSQ10.100
GPZ1 50.00 %
GPZ2 50.00 %
GPZ3 45.00 %
GPZ4 15.00 %
GPZ5 -10.00 %
GPZ6 -5.00 %
P16 1000.00 usec

F1 - Acquisition Parameters
F1 125.7704 MHz
F2 125.7704 MHz
FIDRES 98.257607 Hz
SW 199.999 ppm
FMODE QF

F2 - Processing parameters
SI 4096
SF 500.1300135 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0

F1 - Processing parameters
SI 4096
MC2 QF
F1F2 125.7578472 MHz
WDW
SSB 2
LB 0 Hz
GB 0



Compound 6

Current Data Parameters
NAME KL-4-251_AV500
EXPNO 7
PROCNO 1

F2 - Acquisition Parameters

Date_ 20120613
Time_ 19.20
INSTRUM av500
PROBHD 5 mm DCH 13C-1
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 2
DS 16
SWH 5000.000 Hz
FIDRES 2.441406 Hz
AQ 0.200331 sec
RG 102.91
DM 100.000 usec
DE 10.00 usec
TE 296.0 K
CNS12 145.0000000
DO 0.0000300 sec
D1 0.0001000 sec
D4 0.00172414 sec
D11 0.03000000 sec
D13 0.00000400 sec
D16 0.00020000 sec
D21 0.00345000 sec
SFO1 500.1325007 MHz
ZGPG1NS

===== CHANNEL f1 =====

NUC1 1H
P1 10.00 usec
P2 20.00 usec
P2S 0 usec
PL1 13.50000000 W
SFO1 500.1325007 MHz

===== CHANNEL f2 =====

CPDPRG2 garp
NUC2 13C
P4 9.26 usec
P4S 0 usec
PCPD2 70.00 usec
PLM2 23.01399994 W
PLM12 0.43557000 W
SFO2 125.7678496 MHz

===== GRADIENT CHANNEL =====

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GENAM2 SMSQ10.100
GP21 80.00 %
GP22 20.10 %
P16 1000.00 usec

F1 - Acquisition parameters

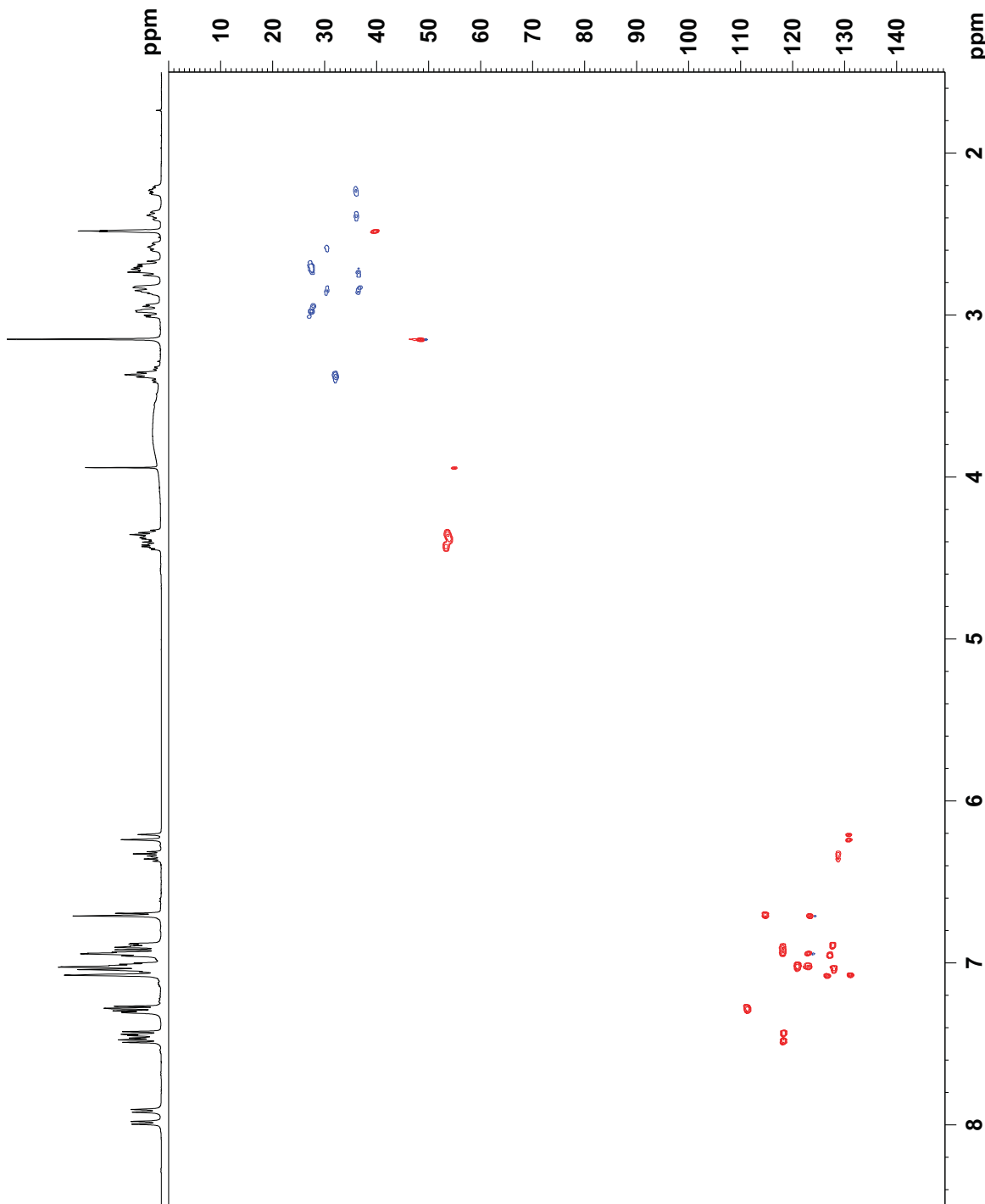
TD 256
SFO1 125.7678 MHz
FIDRES 98.255890 Hz
SW 200.000 PPM
PRMODE Echo-Antiecho

F2 - Processing parameters

SI 4096
SF 500.1300135 MHz
WDW QSI
SSB 2
GB 0 Hz
GB 0

F1 - Processing parameters

SI 4096
MC2 echo-antiecho
WDW 125.7578472 MHz
SSB 2
LB 0 Hz
GB 0



Compound 7

Current Data Parameters

NAME KL-4-103-4-1
EXPNO 2
PROCNO 1

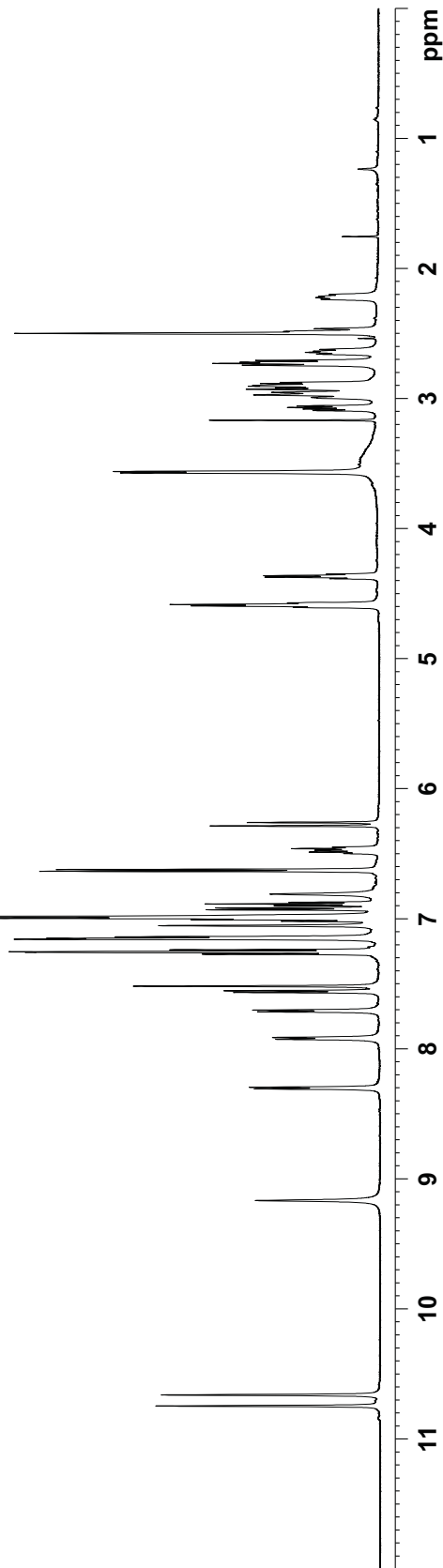
F2 - Acquisition Parameters

Date_ 20120209
Time 15:11
INSTRUM spect
PROBHD 5 mm TB15
PULPROG zg
TD 65536
SOLVENT DMSO
NS 8
DS 0
SWH 12376.237 Hz
FIDRES 0.188846 Hz
AQ 2.6477044 sec
RG 90.5
DM 40.400 usec
DE 6.50 usec
TE 294.4 K
D1 2.00000000 sec
TD0 1

===== CHANNEL f1 =====
NUC1 1H
P1 9.40 usec
PL1 -2.00 dB
PL1W 39.81071854 W
SFO1 600.1336008 MHz

F2 - Processing parameters

SI 65536
SF 600.1300078 MHz
WDW EM
SSB 0
LB 0 Hz
GB 0
PC 1.00



Compound 7

Current Data Parameters

NAME KL-4-103-4-1
EXPNO 3
PROCNO 1

F2 - Acquisition Parameters

Date_ 20120209
Time_ 19.35
INSTRUM 5 mm TBI-5
PROBHD 5 mm TBI-5
PULPROG casy2dmpfb
TD 4096
SOLVENT DMSO
NS 4
DS 4
SWH 5397.93 Hz
FIDRES 1.315113 Hz
AQ 0.3801588 sec
RG 181
DM 92.800 usec
DE 6.50 usec
TE 298.4 K
D1 0.0002000 sec
D13 2.0000000 sec
D16 0.0000400 sec
D16 0.0002000 sec
IN0 0.00018560 sec

===== CHANNEL f1 =====

NUC1 1H
P1 9.40 usec
P2 18.80 usec
PL1 -2.00 dB
PL1W 39.81071854 W
SFO1 600.1327006 MHz

===== GRADIENT CHANNEL =====

GENAM1 SINE.100
GENAM2 SINE.100
GP21 10.00 %
GP22 20.00 %
P16 1000.00 usec

F1 - Acquisition parameters

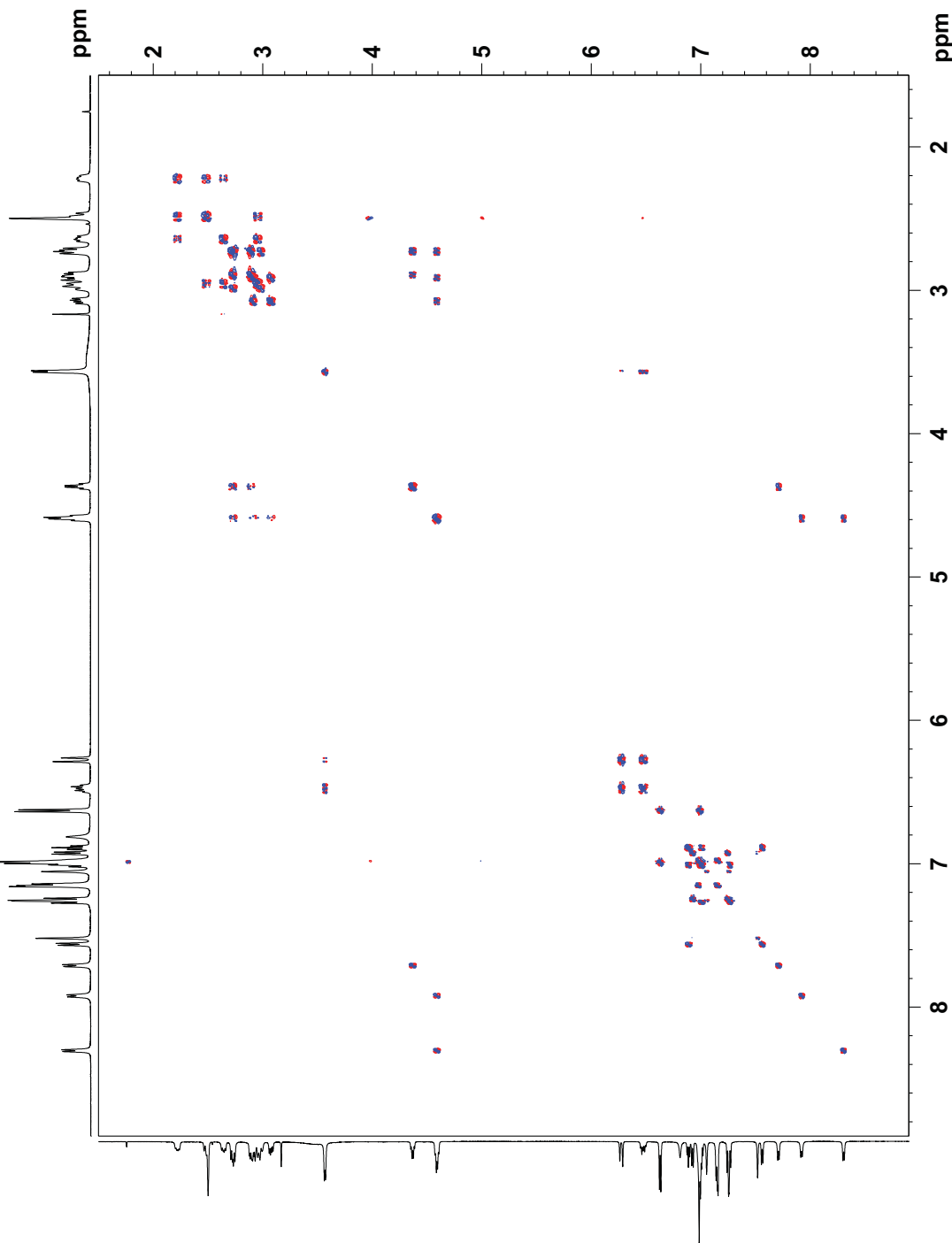
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SFO1 600.1327 MHz
FIDRES 10.52327 Hz
SFO2 600.1327006 MHz
P2MODE States-TPI

F2 - Processing parameters

SI 8192
SF 600.1300115 MHz
WDW 600.1300115 MHz
SSB 0 Hz
GB 0

F1 - Processing parameters

SI 8192
SF 600.1300115 MHz
WDW 600.1300115 MHz
SSB 0 Hz
GB 0



Current Data Parameters	
NAME	KL-4-103-4-1
EXPNO	4
PROCNO	1

	NS	DS	SMH	FIFDES	RAQ	DD	DW	DE	TE	TT	DO	DD	DS	DZ	DJ	D10	D11	D12	D16	L1	L3
	4	16																			
			5530.974 Hz	1.303535 Hz	0.3703284 sec	128	90.4400 usec	6.50 usec	234.4 K			0.00003300 sec	1.20000005 sec	0.23000000 sec	0.30000000 sec	0.00000000 sec	0.00022000 sec	0.00023000 sec	0.0015720 sec		34

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===== GRADIENT CHANNEL =====
GPNAM1      SINE.100
GPNAM2      SINE.100
GPZ1        30.00 %
GPZ2        30.00 %
P16         100.00 used
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F1 - Processing parameters	
SI	4096
MC2	echo-antiecho
SF	600.1300034 MHz
WDW	
SSB	2
LB	0 Hz
GB	0



Compound 7

Current Data Parameters
NAME: KL-4-103-4-1
EXPNO: 1
PROCNO: 1

F2 - Acquisition Parameters

Date_ 20120209
Time_ 22.07
INSTRUM S mm WB5AV600
PROBHD 5mm QNP 1H/13
PULPROG zgpg30
TD 2048
SOLVENT DMSO
DS 16
SWH 5187.331 Hz
FIDRES 2.50824 Hz
AQ 0.1526008 sec
RG 26008
DM 92.800 usec
TE 296.2 K
CNS2 145.0000000
DO 0.0000300 sec
D1 0.0000000 sec
D11 0.0300000 sec
D16 0.0020000 sec
DE 0.0000000 sec
IN 0.0001840 sec
ZGPGFNS

===== CHANNEL f1 =====

NUC1 1H
P1 9.40 usec
PL1 18.50 usec
PL2 100.00 usec
PL3 -2.00 dB
PL4 39.81071854 W
PL1W 600.1327006 MHz
SFO1 600.1327006 MHz

===== CHANNEL f2 =====

CPDPRG2 garp
P3 18.50 usec
PL3 37.00 usec
PL4 1500.00 usec
PL5 1500.00 usec
PL6 150.00 dB
PL7 -3.00 dB
PL8 7.91 dB
PL9 0 W
PL10 150.13617065 W
PL11 12.19330025 W
PL12 150.9133722 MHz
SFO2 150.9133722 MHz
SFO3 150.9133722 MHz
WURST WURST
SFOAL3 0 Hz
SFOFFS3 0.500

===== GRADIENT CHANNEL =====

GP1 100
GP2 100
GP3 0 %
GP4 0 %
GP5 0 %
GP6 0 %
GP7 0 %
GP8 0 %
GP9 0 %
GP10 0 %
GP11 0 %
GP12 0 %
GP13 0 %
GP14 0 %
GP15 0 %
GP16 0 %
GP17 0 %
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GP90 0 %
GP91 0 %
GP92 0 %
GP93 0 %
GP94 0 %
GP95 0 %
GP96 0 %
GP97 0 %
GP98 0 %
GP99 0 %
GP100 0 %

F1 - Acquisition Parameters

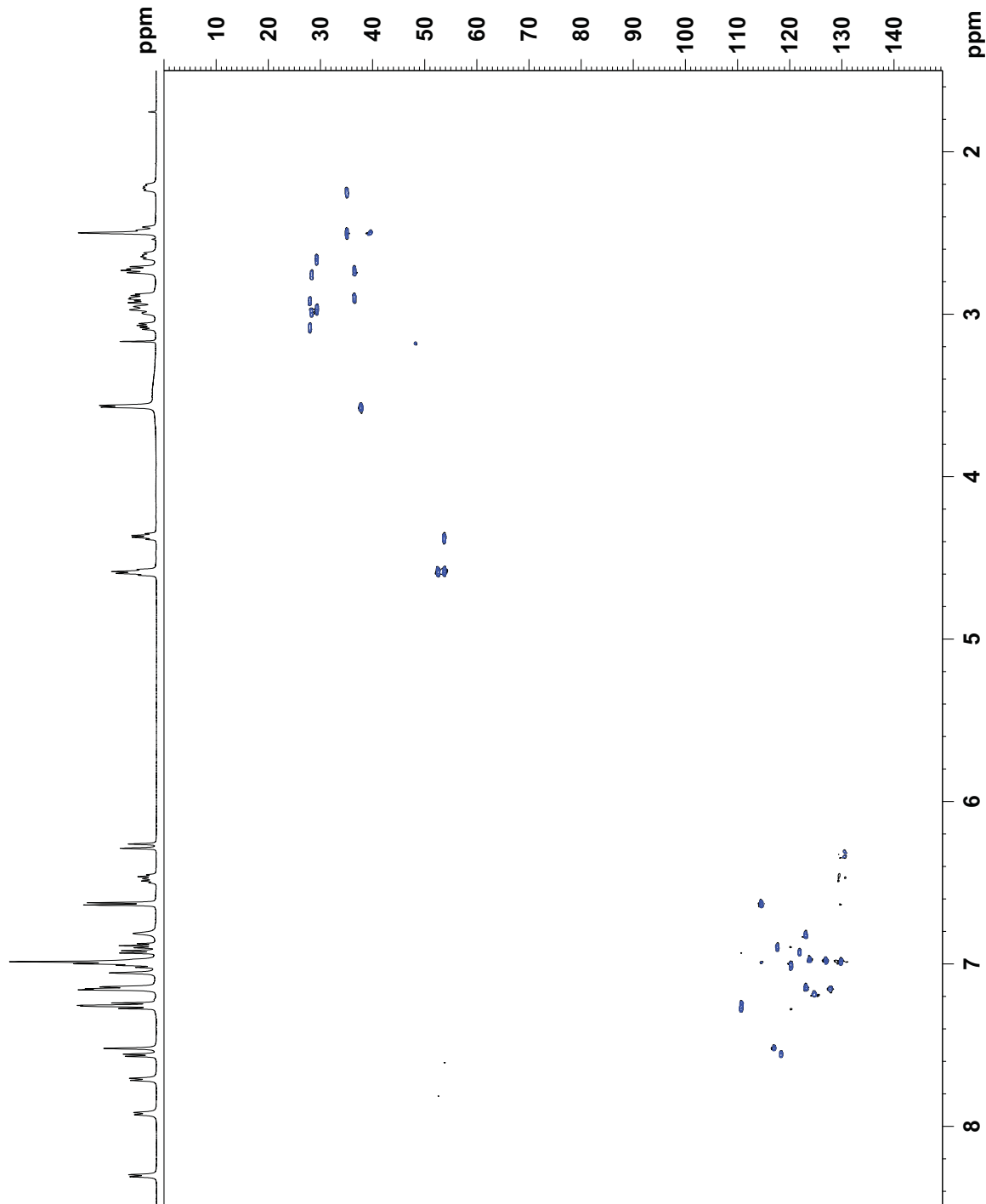
TD 65536
FIDRES 160.256 Hz
AQ 0.1526008 sec
RG 26008
DM 92.800 usec
TE 296.2 K
CNS2 145.0000000
DO 0.0000300 sec
D1 0.0000000 sec
D11 0.0300000 sec
D16 0.0020000 sec
DE 0.0000000 sec
IN 0.0001840 sec
ZGPGFNS

F2 - Processing parameters

SI 4096
SF 600.1300071 MHz
WDW 2
SSB 0 Hz
GB 0
PC 1.40

F1 - Processing parameters

SI 4096
SF 150.9029377 MHz
WDW 2
SSB 0 Hz
GB 0



Compound 8

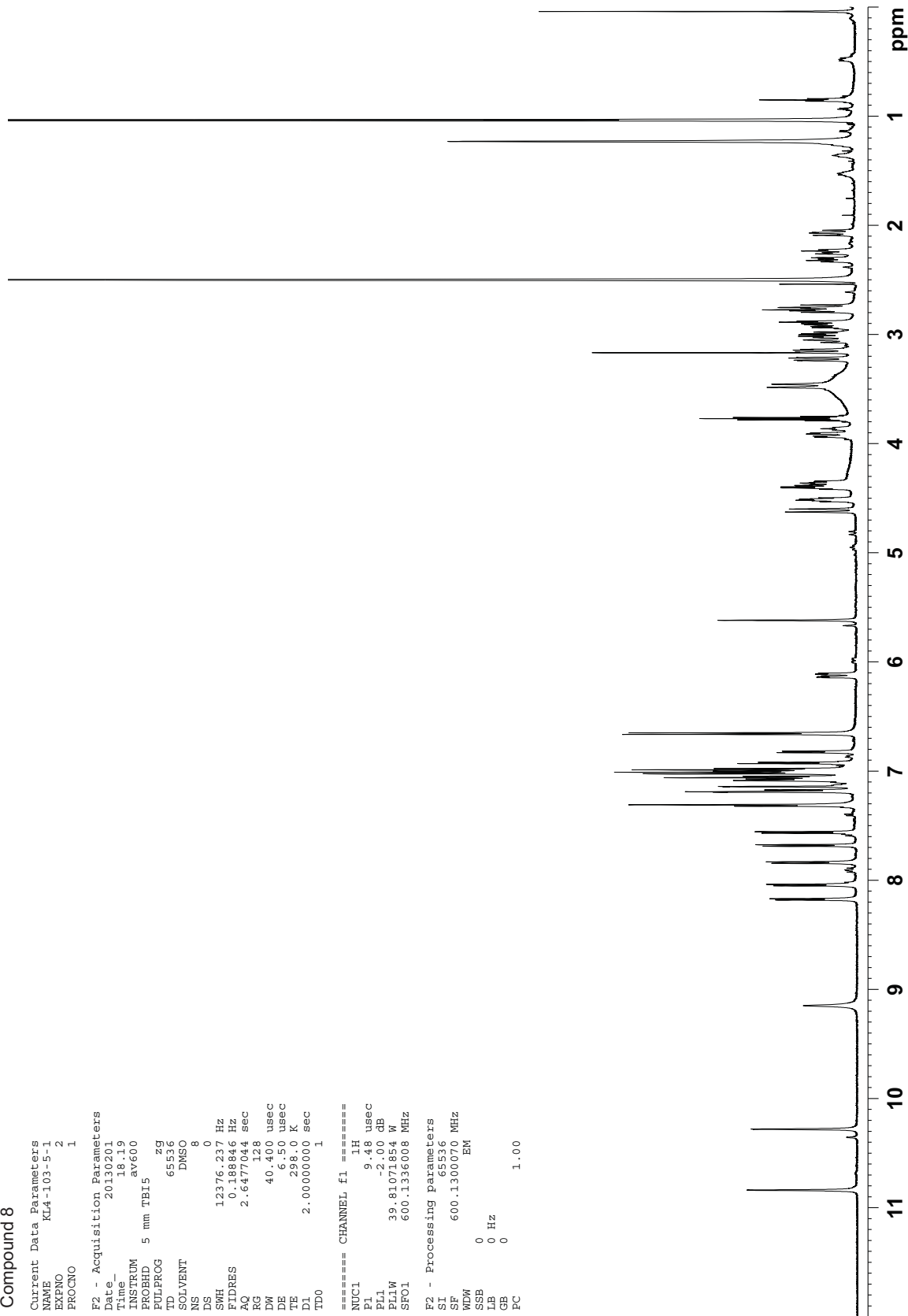
```

Current Data Parameters
NAME      KLA-103-5-1
EXPNO     2
PROCNO    1

F2 - Acquisition Parameters
Date_     20130201
Time      18.15
INSTRUM   spect
PROBHD    5 mm TB15
PULPROG   zg
TD         65536
SOLVENT    DMSO
NS         8
DS         0
SWH        12376.237 Hz
FIDRES     0.188846 Hz
AQ         2.6477044 sec
RG         128
DM         40.400 usec
DE         6.50 usec
TE         298.0 K
D1         2.00000000 sec
TD0        1

===== CHANNEL f1 =====
NUC1       1H
P1         9.48 usec
PL1        -2.00 dB
PL1W       39.81071854 W
SFO1       600.1336008 MHz

F2 - Processing parameters
SI         65536
SF         600.1300070 MHz
WDW        EM
SSB        0
LB         0 Hz
GB         0
PC         1.00
  
```



Compound 8

Current Data Parameters
NAME KL4-103-5-1
EXPNO 5
PROCNO 1

F2 - Acquisition Parameters
Date_ 20130201
Time_ 18.23
INSTRUM av600
PROBHD 5 mm TBI5
PULPROG cosygmph
TD 2048
SOLVENT DMSO
NS 16
DS 7788.162 Hz
SWH 3.802814 Hz
FIDRES 0.1315316 sec
AQ 128
RG 64.200 usec
DW 6.50 usec
DE 298.0 K
TE 0.00005213 sec
DO 1.50000000 sec
D1 0.00000400 sec
D13 0.00020000 sec
D16 0.00012840 sec
IN0

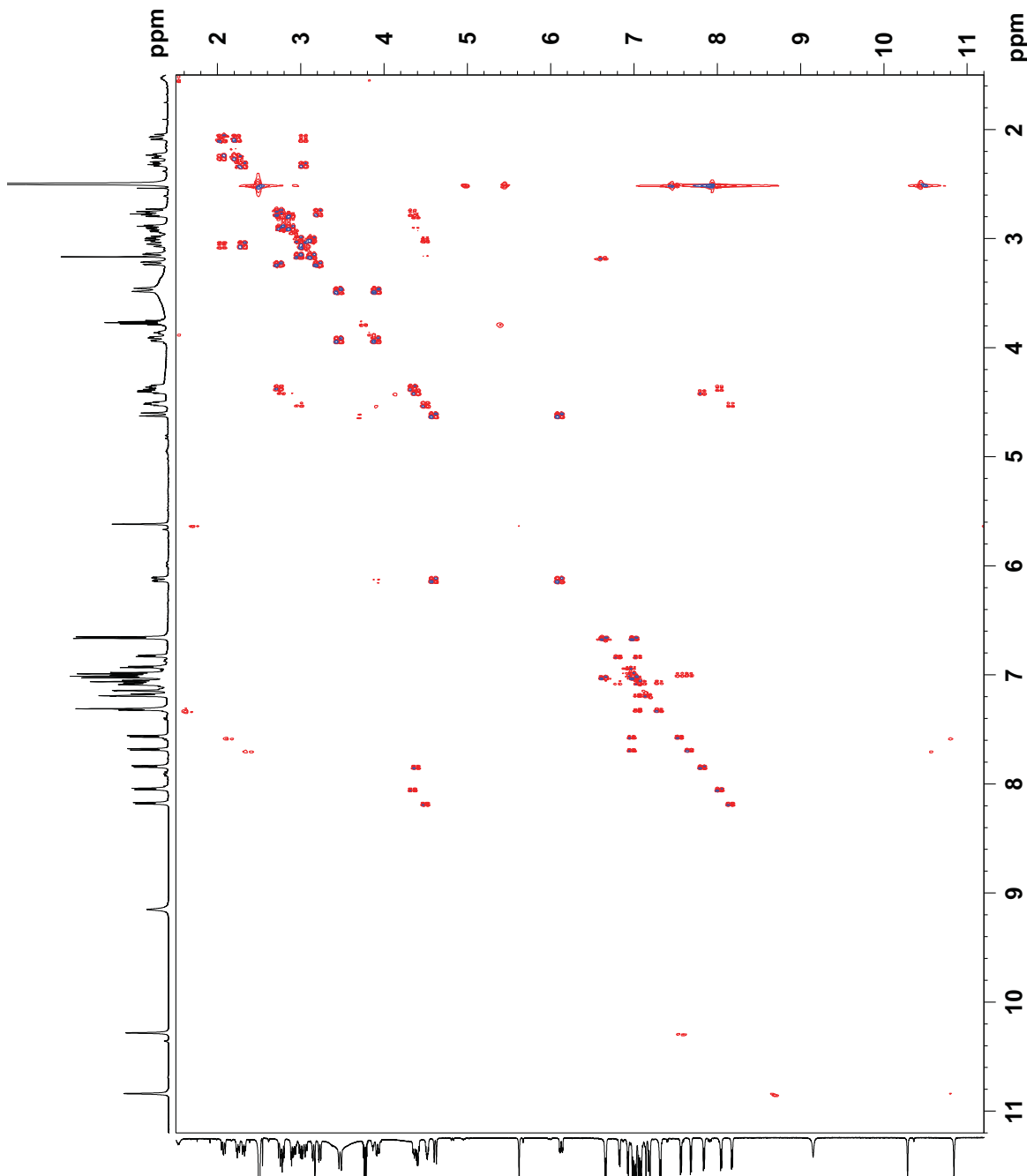
===== CHANNEL f1 =====
NUC1 1H
P1 9.48 usec
P2 18.96 usec
PL1 2.00 dB
PL1W 39.81071654 W
SF01 600.1339008 MHz

===== GRADIENT CHANNEL =====
GENAM1 SINE.100
GENAM2 SINE.100
GEZ1 10.00 %
GEZ2 20.00 %
P16 1000.00 usec

F1 - Acquisition parameters
TD 512
SF01 600.1339 MHz
FIDRES 15.211266 Hz
SW 12.977 ppm
FMODE States-TpPI

F2 - Processing parameters
SI 4096
SF 600.1300014 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0
PC 1.00

F1 - Processing parameters
SI 4096
MC2 States-TpPI
SF 600.1300177 MHz
WDW
SSB 2
LB 0 Hz
GB 0



Compound 8

Current Data Parameters
NAME KL4-103-5-1
EXPNO 6
PROCNO 1

F2 - Acquisition Parameters

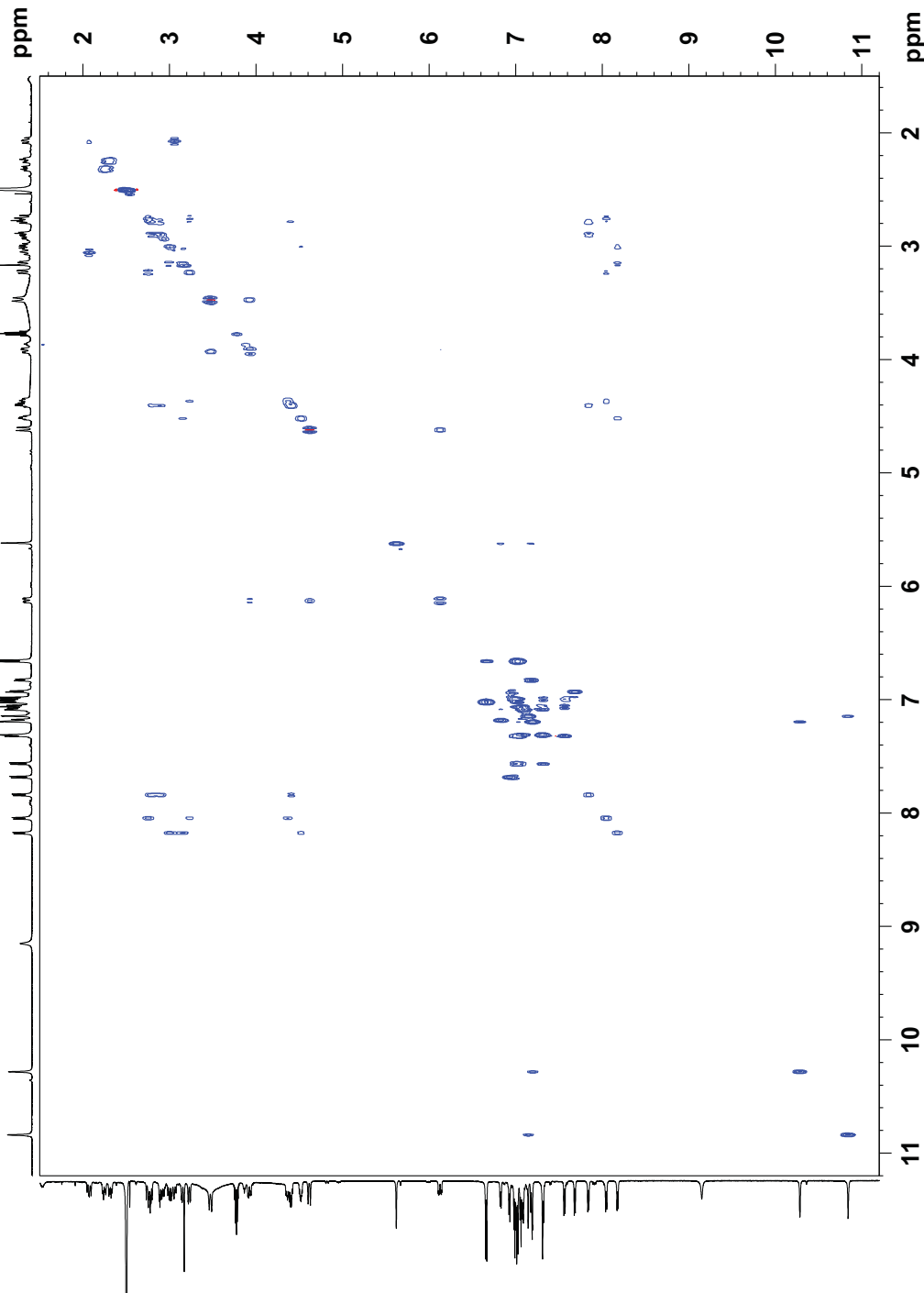
Date_ 20130201
Time_ 18:43
INSTRUM 5 mm QNP1H
PROBHD zgpg30
PULPROG zgpg30
TD 2048
SOLVENT DMSO
NS 8
DS 16
SWH 7708.16 Hz
F2 382814 Hz
AQ 0.131516 sec
RG 456.1
DW 64.200 usec
DE 6.50 usec
TE 300.2 K
D1 0.000200 sec
D11 1.50000000 sec
D9 0.06000000 sec
D11 0.03000000 sec
D16 0.00020000 sec
D20 0.00010000 sec
ZS 0.00010000 sec
ZB 0.00010000 sec
ZC 0.00010000 sec
ZD 0.00010000 sec
ZG 0.00010000 sec
ZJ 0.00010000 sec
ZK 0.00010000 sec
ZL 0.00010000 sec
ZM 0.00010000 sec
ZN 0.00010000 sec
ZO 0.00010000 sec
ZP 0.00010000 sec
ZQ 0.00010000 sec
ZR 0.00010000 sec
ZS 0.00010000 sec
ZT 0.00010000 sec
ZU 0.00010000 sec
ZV 0.00010000 sec
ZW 0.00010000 sec
ZX 0.00010000 sec
ZY 0.00010000 sec
ZZ 0.00010000 sec
L1 14

===== CHANNEL f1 =====
NUC1 1H
P1 9.18 usec
PL1 18.96 usec
P2 40.00 usec
PL2 -2.00 dB
P3 10.51 dB
PL3 39.81071854 W
P4 2.23552000 W
PL4 600.1336008 MHz
SFO1 600.1336008 MHz
===== GRADIENT CHANNEL =====
GPM1 SINE.100
GPM2 SINE.100
GPM3 SINE.100
GPM4 SINE.100
GPM5 SINE.100
GPM6 SINE.100
GPM7 SINE.100
GPM8 SINE.100
GPM9 SINE.100
GPM10 SINE.100
GPM11 SINE.100
GPM12 SINE.100
GPM13 SINE.100
GPM14 SINE.100
GPM15 SINE.100
GPM16 SINE.100
GPM17 SINE.100
GPM18 SINE.100
GPM19 SINE.100
GPM20 SINE.100
GPM21 SINE.100
GPM22 SINE.100
GPM23 SINE.100
GPM24 SINE.100
GPM25 SINE.100
GPM26 SINE.100
GPM27 SINE.100
GPM28 SINE.100
GPM29 SINE.100
GPM30 SINE.100
GPM31 SINE.100
GPM32 SINE.100
GPM33 SINE.100
GPM34 SINE.100
GPM35 SINE.100
GPM36 SINE.100
GPM37 SINE.100
GPM38 SINE.100
GPM39 SINE.100
GPM40 SINE.100
GPM41 SINE.100
GPM42 SINE.100
GPM43 SINE.100
GPM44 SINE.100
GPM45 SINE.100
GPM46 SINE.100
GPM47 SINE.100
GPM48 SINE.100
GPM49 SINE.100
GPM50 SINE.100
GPM51 SINE.100
GPM52 SINE.100
GPM53 SINE.100
GPM54 SINE.100
GPM55 SINE.100
GPM56 SINE.100
GPM57 SINE.100
GPM58 SINE.100
GPM59 SINE.100
GPM60 SINE.100
GPM61 SINE.100
GPM62 SINE.100
GPM63 SINE.100
GPM64 SINE.100
GPM65 SINE.100
GPM66 SINE.100
GPM67 SINE.100
GPM68 SINE.100
GPM69 SINE.100
GPM70 SINE.100
GPM71 SINE.100
GPM72 SINE.100
GPM73 SINE.100
GPM74 SINE.100
GPM75 SINE.100
GPM76 SINE.100
GPM77 SINE.100
GPM78 SINE.100
GPM79 SINE.100
GPM80 SINE.100
GPM81 SINE.100
GPM82 SINE.100
GPM83 SINE.100
GPM84 SINE.100
GPM85 SINE.100
GPM86 SINE.100
GPM87 SINE.100
GPM88 SINE.100
GPM89 SINE.100
GPM90 SINE.100
GPM91 SINE.100
GPM92 SINE.100
GPM93 SINE.100
GPM94 SINE.100
GPM95 SINE.100
GPM96 SINE.100
GPM97 SINE.100
GPM98 SINE.100
GPM99 SINE.100
GPM100 SINE.100

F1 - Acquisition Parameters
TD 128
SFO1 600.1336 MHz
F2 600.1336 MHz
SWH 7708.16 Hz
SF 600.1336 MHz
FWD 12.377 ppm
FMODE Echo-Antiecho

F2 - Processing parameters
SI 4096
SF 600.1336 MHz
WDW 600.1336 MHz
SSB 0 Hz
LB 0 Hz
GB 0
PC 1.00

F1 - Processing parameters
SI 4096
SF 600.1336 MHz
WDW 600.1336 MHz
SSB 0 Hz
LB 0 Hz
GB 0



Compound 8

Current Data Parameters
NAME ML4-103-5-1
EXPNO 8
PROCNO 1

F2 - Acquisition Parameter
Date_ 20130201
Time_ 20.33
INSTRUM 5 mm WB15 av600
PROBHD 5 mm WB15
PULPROG hmczgpcdscf
TD 2048
SOLVENT DMSO

NS 18
DS 24
SWH 7183.908 Hz
FIDRES 0.1425908 Hz
AQ 0.1425908 sec
RG 26008
DW 69.600 us
DE 6.00 us
TE 297.9 K
TEMT6 125.0000000
CNSRT7 165.0000000
CNSRT13 8.0000000
D0 0.0000300 sec
D1 1.20000005 sec
D6 0.06250000 sec
D16 0.00020000 sec
RG 0.00021745 sec

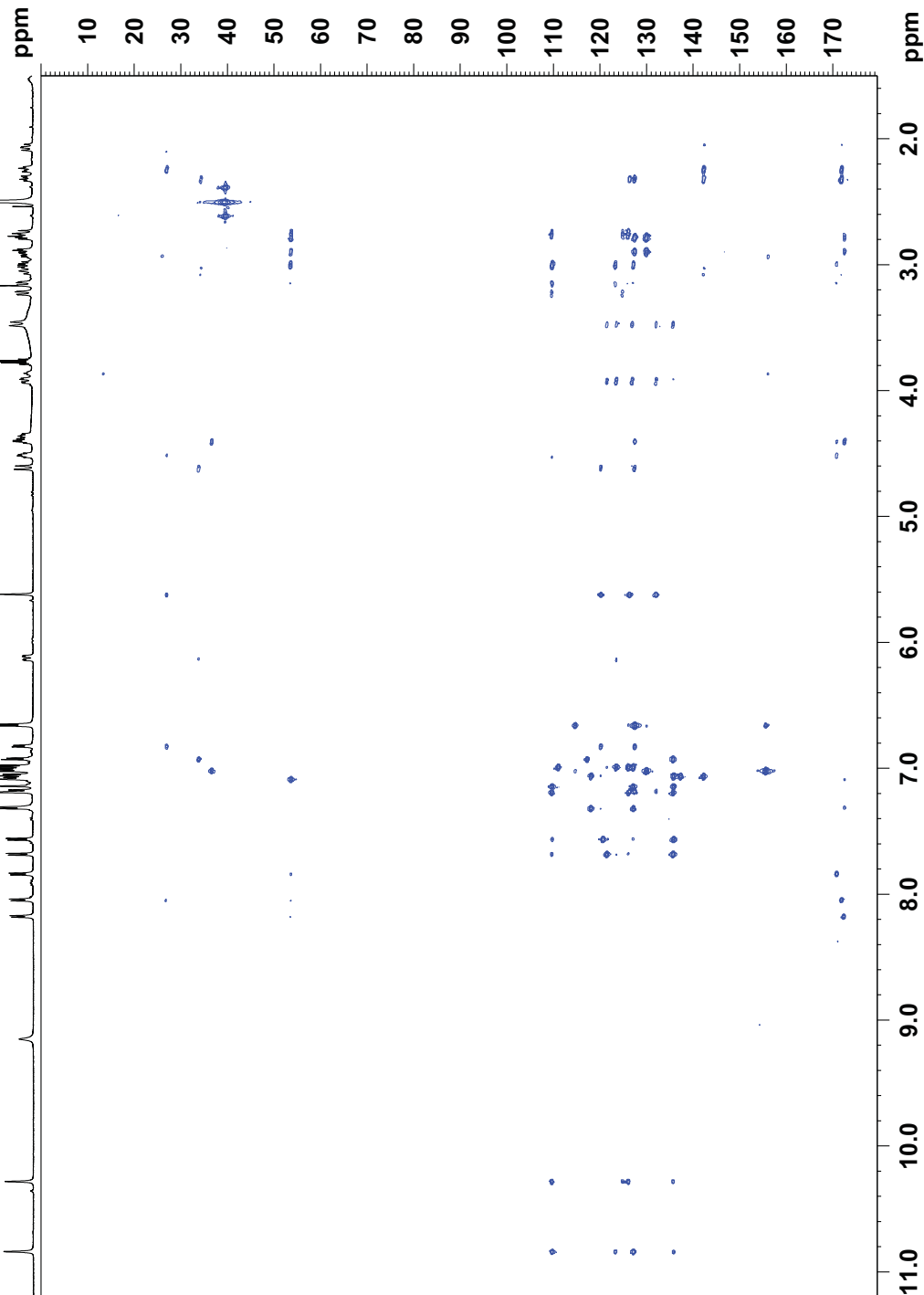
===== CHANNEL f1 =====
NUC1 1H
P1 9.48 us
P2 18.96 us
PL1 18.96 us
PL2 3.00 us
PLW 39.81071854 W
SFO1 600.1333007 MHz

===== CHANNEL f2 =====
NUC2 13C
P1 18.96 us
P2 3.00 us
PL1 18.96 us
PL2 3.00 us
PLW 150.35617065 W
SFO2 150.9156357 MHz

===== GRADIENT CHANNEL =====
GNAME1 SINE.100
GNAME2 SINE.100
GNAME3 SINE.100
GNAME4 SINE.100
GNAME5 SINE.100
GNAME6 SINE.100
GPR1 50.00 %
GPR2 50.00 %
GPR3 40.10 %
GPR4 15.00 %
GPR5 -10.00 %
GPR6 -5.00 %
PL6 1000.00 us

F1 - Acquisition parameter
TD 512
SFO1 150.9156 MHz
FIDRES 56.003849 Hz
SW 190.000 PF
RG 0.0000000
FMODE QF

F2 - Processing parameters
SI 4096
SF 600.1300061 MHz
WDW SS
SSB COSINE
LB 0 Hz



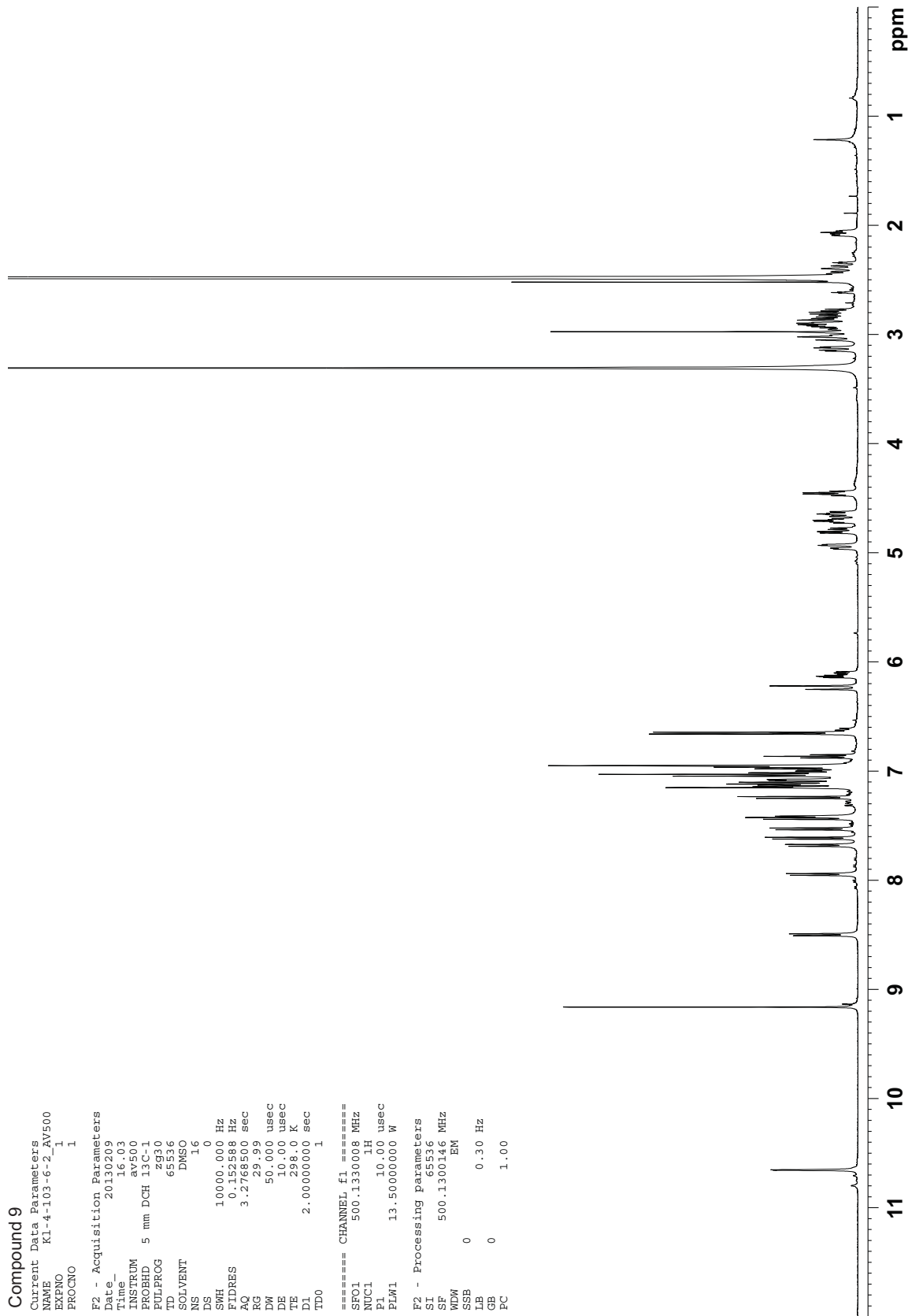
Compound 9

Current Data Parameters
NAME K1-4-103-6-2_AV500
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20130209
Time 16:03
INSTRUM avn60
PROBHD 5 mm DCH 13C1
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 16
DS 0
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2768500 sec
RG 29.99
DM 50.000 usec
DE 10.00 usec
TE 298.0 K
D1 2.00000000 sec
TD0 1

===== CHANNEL f1 =====
SFO1 500.1330008 MHz
NUC1 1H
P1 10.00 usec
PLW1 13.50000000 W

F2 - Processing parameters
SI 65536
SF 500.1300146 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



Compound 9

Current Data Parameters
 NAME KL-4-103-6-2
 EXPNO 3
 PROCNO 1

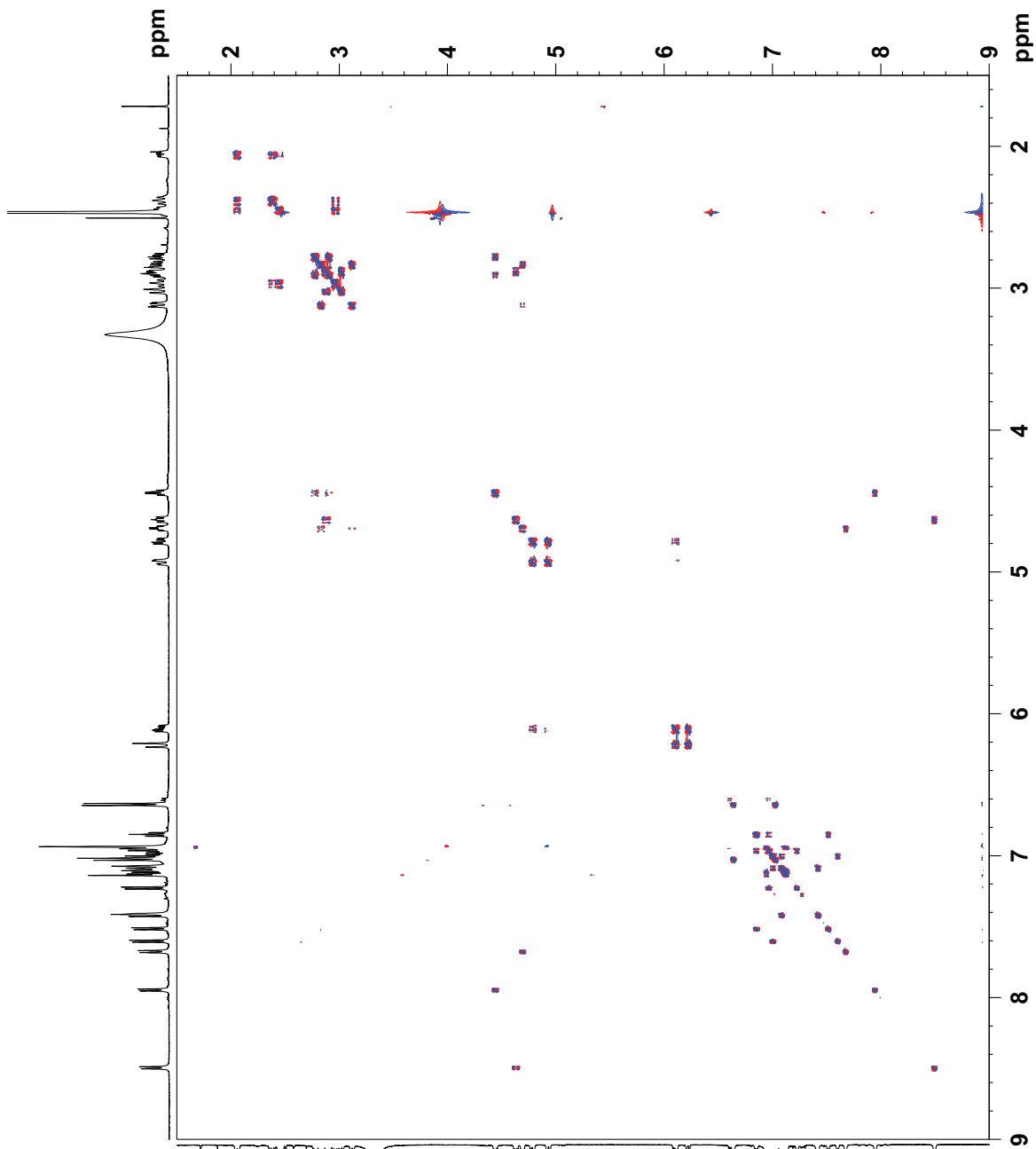
F2 - Acquisition Parameters
 Date_ 20120214
 Time_ 18.39
 INSTRUM av600
 PROBDH 5 mm TBI5
 PULPROG cosygpmfph
 TD 4096
 SOLVENT DMSO
 NS 2
 DS 4
 SWH 5387.931 Hz
 FIDRES 1.315413 Hz
 AQ 0.3801588 sec
 RG 181
 DW 92.800 usec
 DE 6.50 usec
 TE 294.8 K
 D0 0.00008090 sec
 D1 2.00000000 sec
 D13 0.00000400 sec
 D16 0.00020000 sec
 IN0 0.00018560 sec

===== CHANNEL f1 =====
 NUC1 1H
 P1 9.35 usec
 P2 18.70 usec
 PL1 -2.00 dB
 PL1W 39.81071854 W
 SF01 600.1327006 MHz
 ===== GRADIENT CHANNEL =====
 GENAM1 SINE.100
 GENAM2 SINE.100
 GPX1 0 %
 GPY1 0 %
 GPZ1 0 %
 GPX2 10.00 %
 GPY2 20.00 %
 GPZ2 1000.00 usec
 PL6

F1 - Acquisition Parameters
 TD 512
 SF01 600.1327 MHz
 FIDRES 10.523297 Hz
 SW 8.978 ppm
 FMODE States-TpPI

F2 - Processing parameters
 SI 2048
 SF 600.1300273 MHz
 WDW QSI
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 2048
 MC2 States-TpPI
 SF 600.1300273 MHz
 WDW SSB
 LB 0 Hz
 GB 0



Compound 9

Current Data Parameters
NAME KI-4-103-6-2_AV500
EXPNO 4
PROCNO 1

F2 - Acquisition Parameters
Date_ 20120203
Time 11.59
INSTRUM av600

PROBHD 5 mm TB15
PULPROG mlevpgr-jr
TD 4096
SOLVENT DMSO
NS 2

DS 16
SWH 5530.974 Hz
FIDRES 1.350335 Hz
AQ 0.3703284 sec

RG 128
DM 90.400 usec
DE 6.50 usec
TE 294.5 K

D0 0.0000000 sec
D1 1.20000005 sec
D2 0.60000000 sec

D11 0.03000000 sec
D12 0.00002000 sec
D16 0.00020000 sec
IN0 0.00015720 sec
L1 24

===== CHANNEL f1 =====
NUC1 1H
P1 9.00 usec
P2 19.40 usec

P5 26.68 usec
P6 40.00 usec
P7 80.00 usec
P17 2500.00 usec
PL1 -2.00 dB

PL10 9.54 dB
PL1W 39.81071854 W
PLOW 2.79254389 W
SFO1 600.1327006 MHz

===== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GENAM2 SINE.100
GPZ1 30.00 %

GPZ2 30.00 %
P16 1000.00 usec
F1 - Acquisition parameters

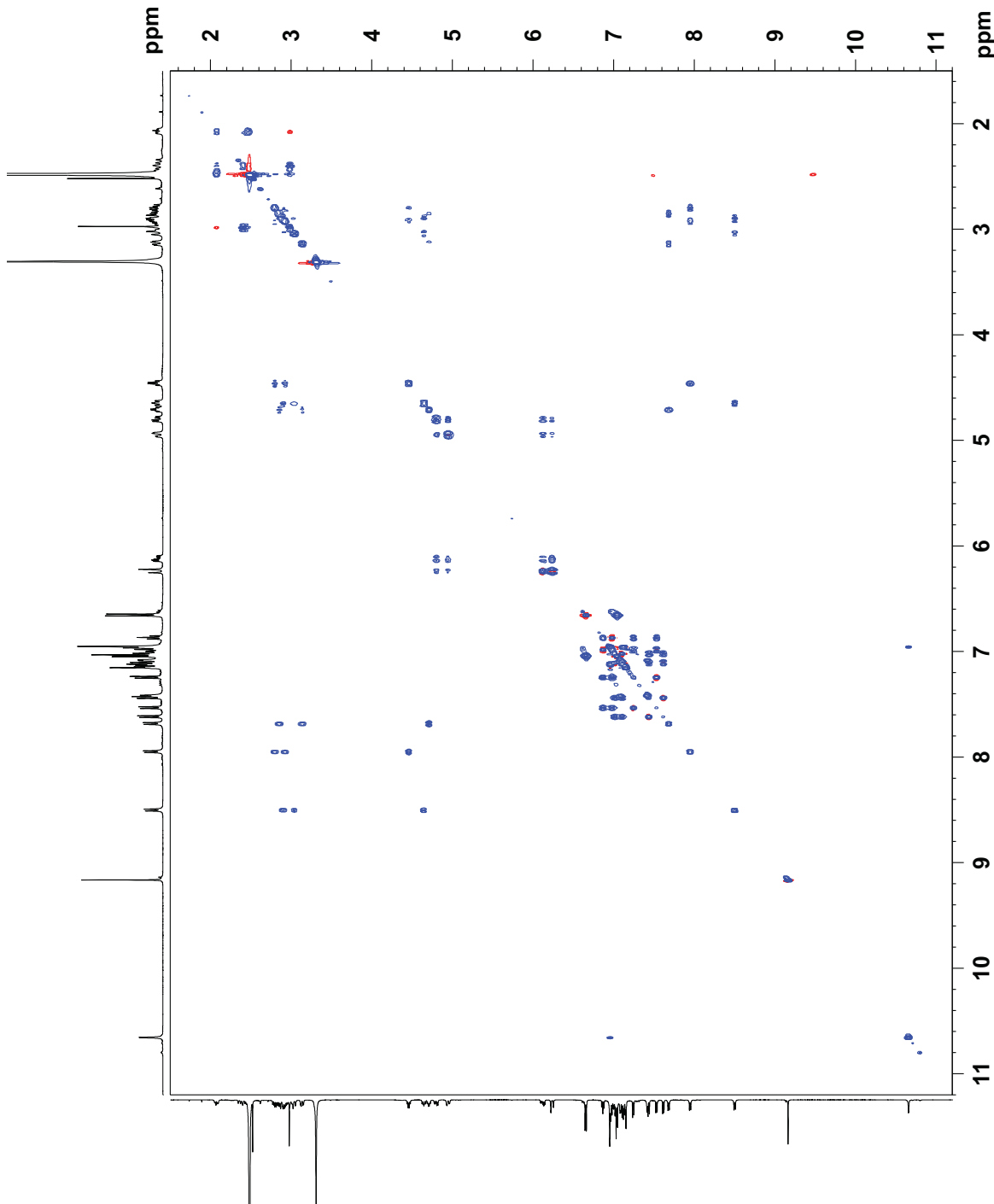
TD 600
SFO1 600.1327006 MHz
FIDRES 1.0402201 Hz
SW 10.10600 ppm

FMODE Echo-Antiecho
F2 - Processing parameters
SI 4096
SF 600.1300067 MHz

SSB 2
LB 0 Hz
GB 0
PC 1.00

F1 - Processing parameters
SI 4096
MC2 echo-antiecho
SF 600.1300046 MHz

WDW 2
SSB 0 Hz
LB 0
GB 0



[illegible]

Compound 10a/b

Current Data Parameters

NAME KLS-116-7-1
EXPNO 12
PROCNO 1

F2 - Acquisition Parameters

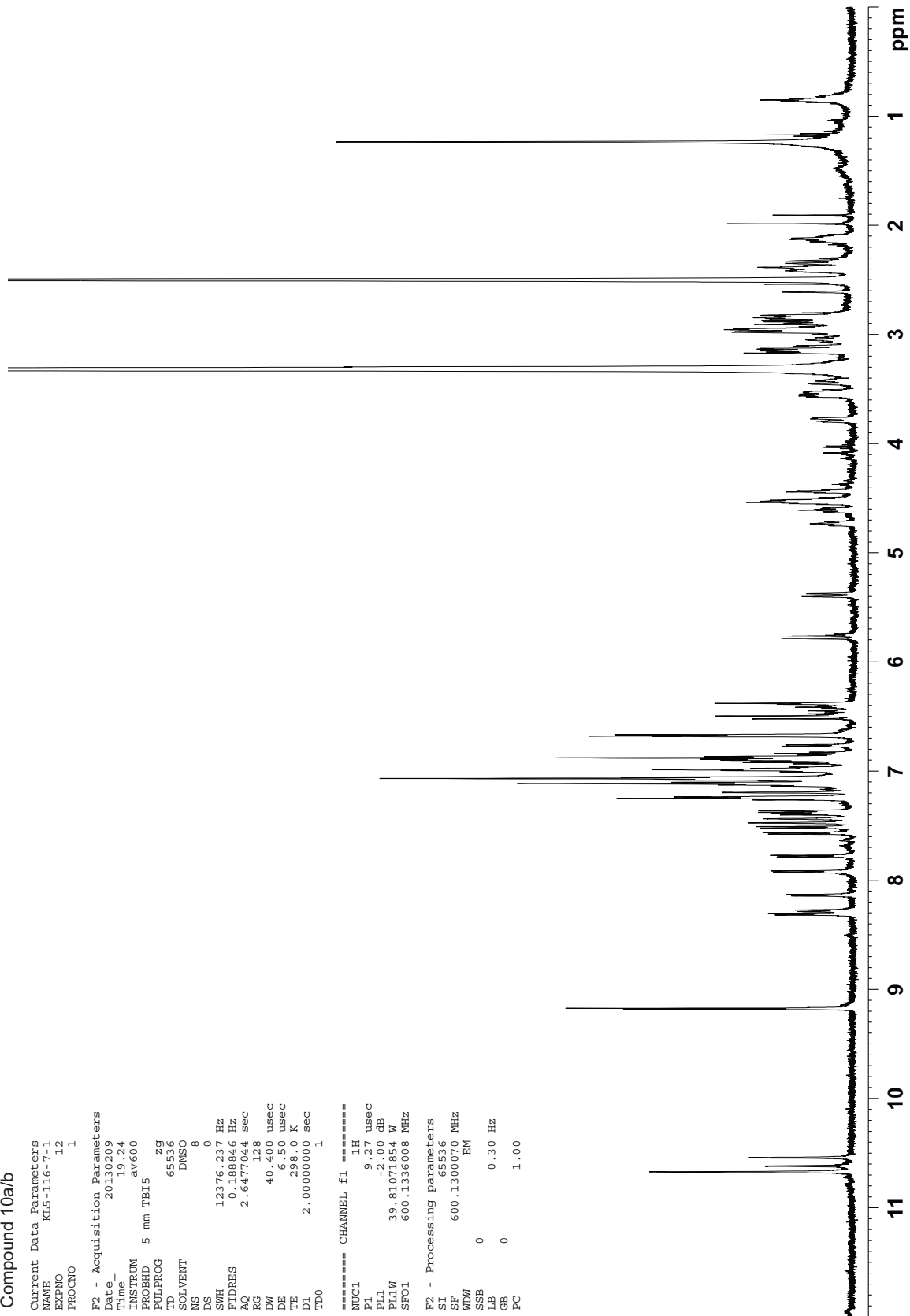
Date_ 20130209
Time 15:24
INSTRUM av600
PROBHD 5 mm TB15
PULPROG zg
TD 65536
SOLVENT DMSO
NS 8
DS 0
SWH 12376.237 Hz
FIDRES 0.188846 Hz
AQ 2.6477044 sec
RG 128
DM 40.400 usec
DE 6.50 usec
TE 298.0 K
D1 2.00000000 sec
TD0 1

===== CHANNEL f1 =====

NUC1 1H
P1 9.27 usec
PL1 -2.00 dB
PL1W 39.81071854 W
SFO1 600.1336008 MHz

F2 - Processing parameters

SI 65536
SF 600.1300070 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



Compound 10a/b

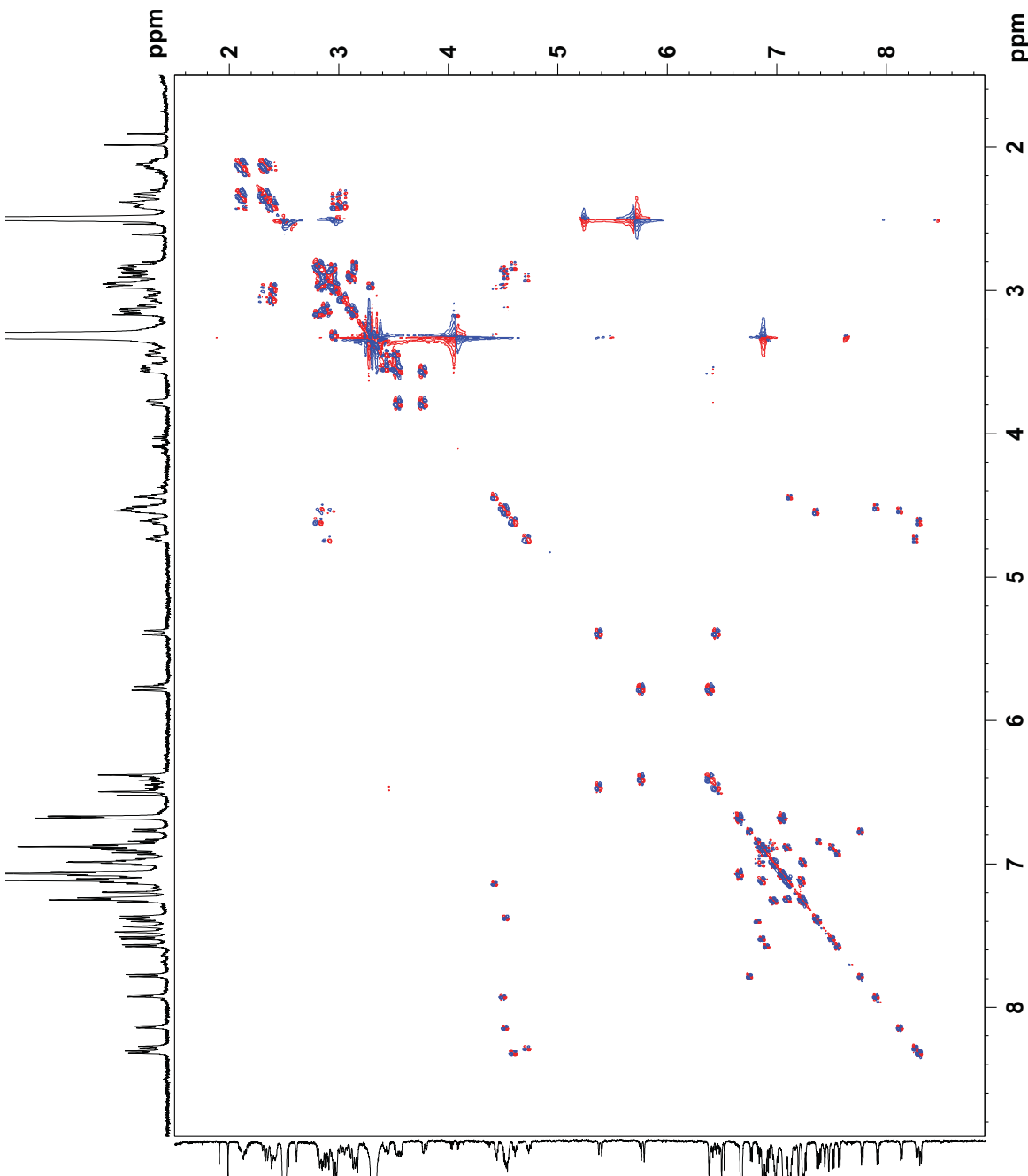
Current Data Parameters
NAME KL5-116-7-1
EXPNO 5
PROCNO 1

F2 - Acquisition Parameters
Date_ 20130207
Time_ 19.26
INSTRUM av600
PROBHD 5 mm TBI5
PULPROG cosygpmfph
TD 2048
SOLVENT DMSO
NS 8
DS 16
SWH 6887.052 Hz
FIDRES 3.362818 Hz
AQ 0.1487348 sec
RG 128
DE 72.600 usec
TE 298.0 K
D0 0.00006068 sec
D1 1.50000000 sec
D13 0.00000400 sec
D16 0.00020000 sec
IN0 0.00014520 sec

===== CHANNEL f1 =====
NUC1 1H
P1 9.36 usec
P2 18.72 usec
PL1 -2.00 dB
PL1W 39.81071854 W
SF01 600.1333007 MHz
===== GRADIENT CHANNEL =====
GENM1 SINE.100
GENM2 SINE.100
GPX1 0 %
GPY1 0 %
GPZ1 0 %
GPZ2 10.00 %
PI6 20.00 %
PI6 1000.00 usec

F1 - Acquisition parameters
TD 512
SF01 600.1333 MHz
FIDRES 13.451260 Hz
SW 11.476 ppm
FMODE States-TpPI
F2 - Processing parameters
SI 4096
SF 600.1300026 MHz
WDW QSI
SSB 2
LB 0 Hz
GB 0
PC 1.00

F1 - Processing parameters
SI 4096
MC2 States-TPPI
SF 600.1300177 MHz
WDW
SSB 2
LB 0 Hz
GB 0



Compound 10a/b

Current Data Parameters

NAME KL5-116-7-1
EXPNO 6
PROCNO 1

F2 - Acquisition Parameters

Date_ 20081217
Time 21:27
INSTRUM av600
PROBHD 5 mm TB15
PULPROG dpsi2etgpsi
TD 2048

SOLVENT DMSO

NS 8
DS 16
SWH 7788.16 Hz

FIDRES 3.802812 Hz

AQ 0.1315316 sec

RG 456.1

DW 64.200 usec

DE 6.50 usec

TE 298.0 K

D0 0.0000300 sec

D1 1.5000000 sec

D2 0.0500000 sec

D3 0.1500000 sec

D16 0.0002000 sec

D20 0.00001000 sec

D21 0.00001000 sec

IN0 0.00012840 sec

L1 14

===== CHANNEL f1 =====

NUC1 1H

P1 9.16 usec

P2 18.70 usec

P6 40.00 usec

PL1 -2.00 dB

PL10 10.62 dB

PL1W 39.81071854 W

PL1OW 2.17770982 W

SFO1 600.1336008 MHz

===== GRADIENT CHANNEL =====

GP1M1 SINE 100

GP1M2 SINE 100

GF21 30.00 %

GF22 30.00 %

P16 1000.00 usec

F1 - Acquisition parameters

TD 512

RG 600.1336008 MHz

FIDRES 15.211256 Hz

SW 12.977 ppm

FMODE Echo-Antiecho

F2 - Processing parameters

SI 4096

SF 600.1300046 MHz

WDW QSINE

SSB 2

GB 0

PC 1.00

F1 - Processing parameters

SI 4096

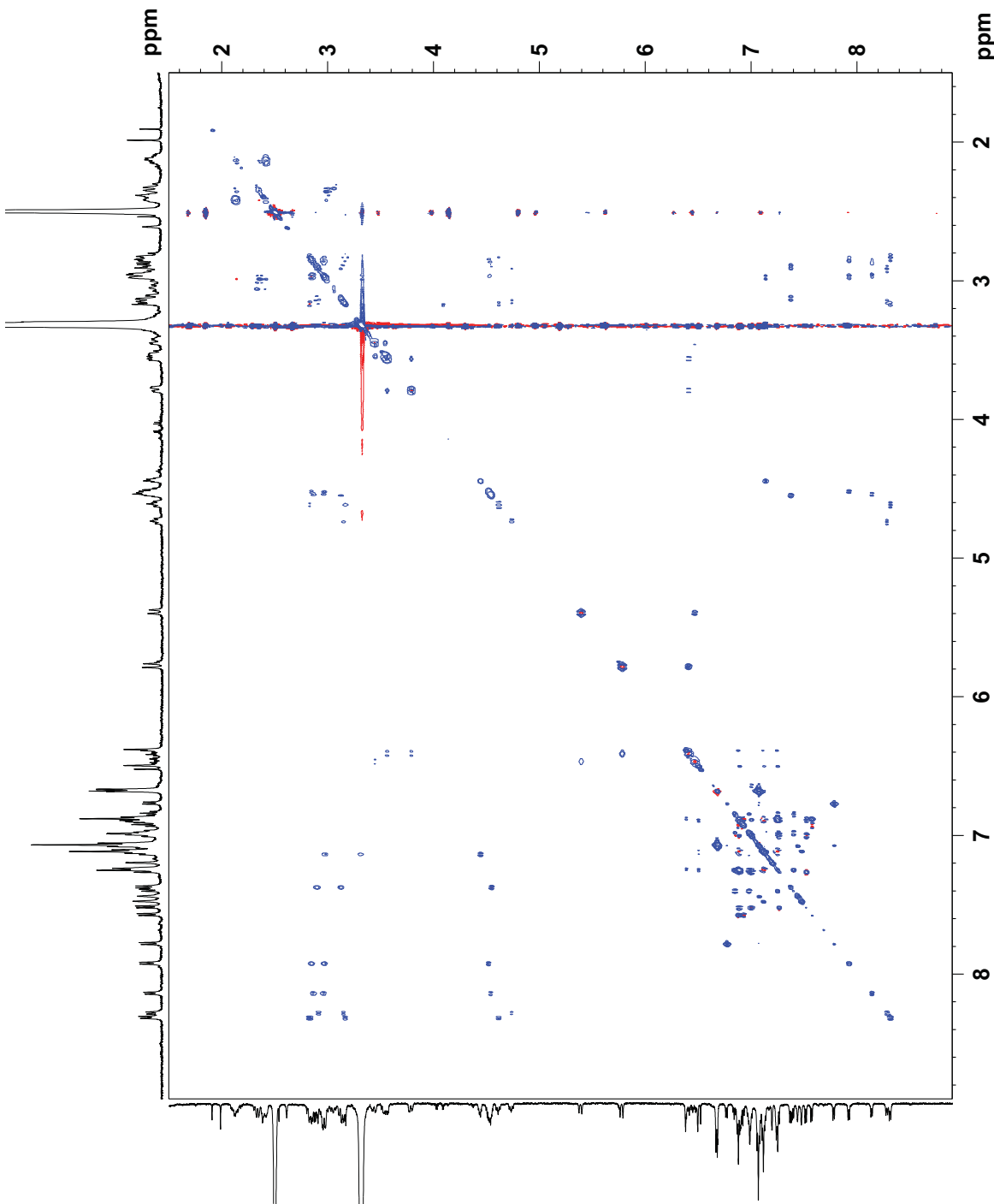
MC2 echo-antiecho

SF 600.1300036 MHz

WDW QSINE

SSB 2

GB 0



Compound 10a/b

Current Data Parameters
NAME KL5-116-7-1
EXPNO 27
PROCNO 1

F2 - Acquisition Parameters
Date_ 20130209
Time 21.39
INSTRUM 5 mm WB15 AV600
PROBHD 5 mm WB15
PULPROG zacesysgph
TD 2048

SOLVENT DMSO
NS 16
DS 16
SWH 7798.162 Hz
FIDRES 3.802814 Hz
AQ 0.1315316 sec
RG 13004
DW 64.200 usec
DE 6.50 usec
TE 298.0 K

DELTA 0.00000000 sec
D1 1.50000000 sec
D12 0.00020000 sec
D16 0.00020000 sec
IN0 0.00012840 sec

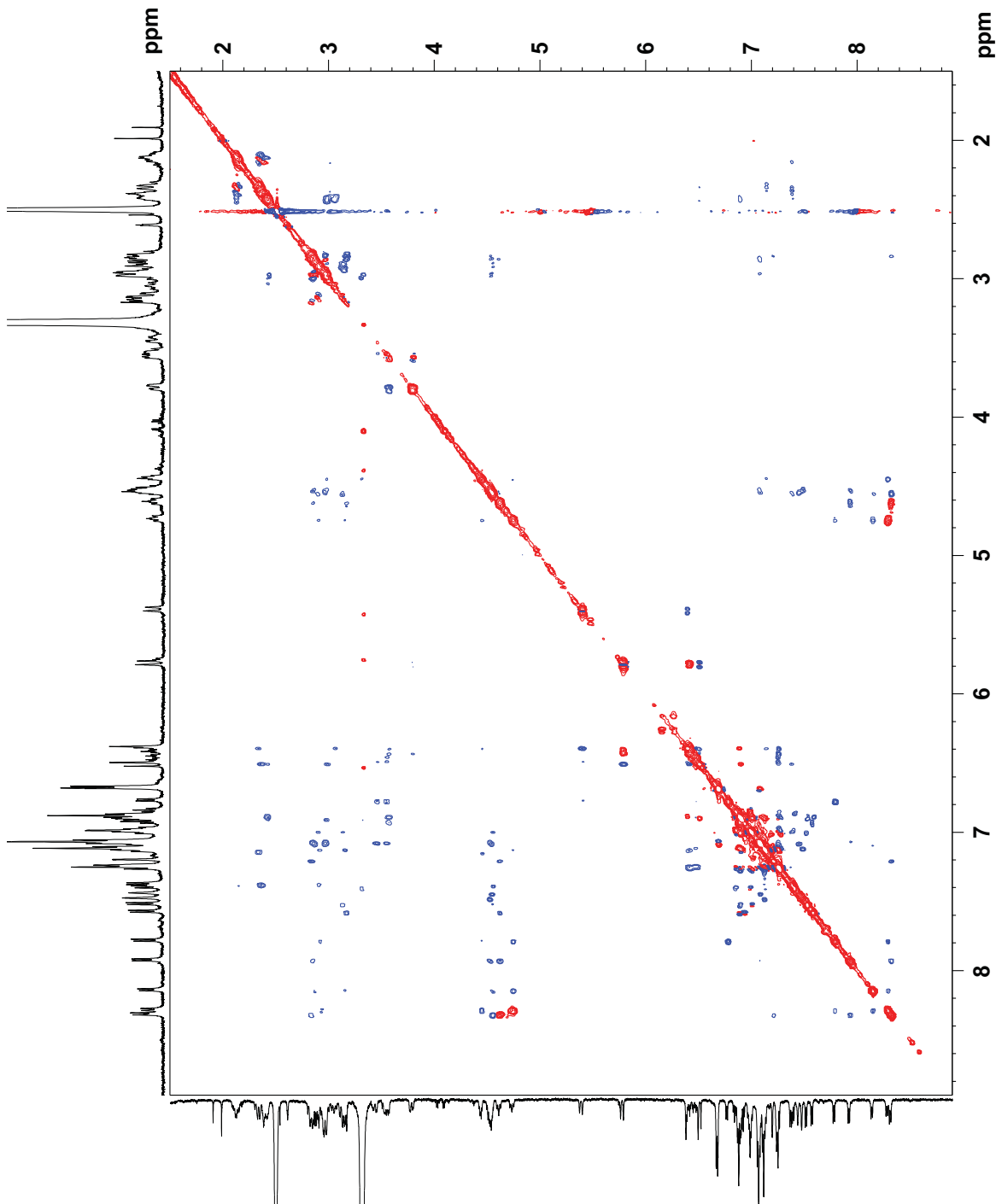
===== CHANNEL f1 =====
NUC1 1H
P1 9.27 usec
P2 18.54 usec
P15 200000.00 usec
P40 2000.00 usec
PL0 12.00 dB
PL1 2.00 dB
PL11 18.66 dB
PLOW 0 W
PL1W 39.81071854 W
PL1W 0.34197944 W
SFO1 600.1339008 MHz
SFO2 600.1339008 MHz
SFNMI0 Squalo0.1000
SFOAL10 0.500
SPOFFS10 -1901.00 Hz

===== GRADIENT CHANNEL =====
GSP1 100
GPM12 SINE.100
GF21 31.00 %
GF22 11.00 %
P16 1000.00 usec

F1 - Acquisition Parameters
TD 512
SFO1 600.1339 MHz
FIDRES 15.211282 Hz
SW 12.977 ppm
PRMODE States-TPII

F2 - Processing parameters
SI 4096
SF 600.1300000 MHz
WDW 2
SSB 0 Hz
LB 0
GB 0
PC 1.00

F1 - Processing parameters
SI 4096
MC2 States-TPII
NMW 600.1300000 MHz
SSB 2
LB 0 Hz
GB 0



Compound 10a/b

Current Data Parameters
NAME KLS-116-7-1
EXPNO 10
PROCNO 1

F2 - Acquisition Parameters
Date_ 20130209
Time 5.13
INSTRUM av600
PROBHD 5 mm TBS
PULPROG hmczgplndrf
TD 2048
SOLVENT DMSO

NS 72
DS 64
SWH 6987.064 Hz
AQ 3.362918 Hz
FIDRES 0.1487348 sec
RG 26008
RW 72.600 usec
DE 6.00 usec
TE 298.0 K
CNS12 145.000000
CNS13 7.0000000
D0 0.0000300 sec
D1 1.0000000 sec
D2 0.00344828 sec
D6 0.07142857 sec
D8 0.0000000 sec
D9 0.0000000 sec
IN0 0.0001745 sec

===== CHANNEL f1 =====
NUC1 1H
P1 9.32 usec
PL1 1.44 usec
PL12 -2.00 dB
PL1W 39.81071854 W
PL1W 600.1334507 MHz
SFO1 600.1334507 MHz

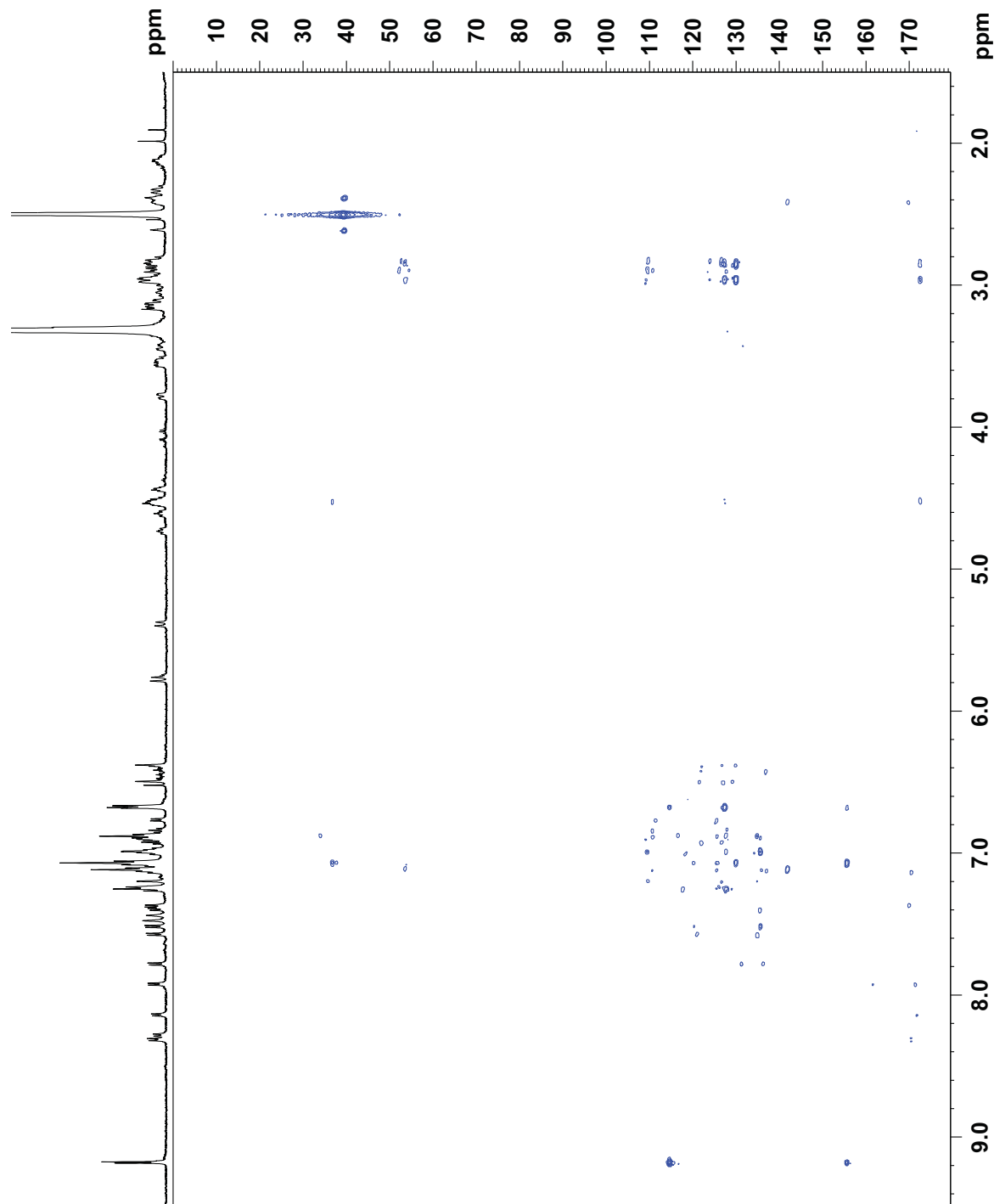
===== CHANNEL f2 =====
NUC2 13C
P2 18.50 usec
PL2 -3.00 dB
PL2W 150.35617065 W
PL2W 150.9156357 MHz
SFO2 150.9156357 MHz

===== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPNAM3 SINE.100
GPD1 50.00 %
GPD2 30.00 %
GPD3 40.10 %
PL6 1000.00 usec

F1 - Acquisition Parameters
TD 512
SFO1 150.9156 MHz
FIDRES 56.003849 Hz
AQ 0.0000000 sec
PULPROG hmczgplndrf
PRMODE QP

F2 - Processing parameters
SI 4096
SF 600.1300066 MHz
WDW HANN
SSB 0 Hz
LB 0
GB 0
PC 1.40

F1 - Processing parameters
SI 4096
SF 150.9029181 MHz
WDW HANN
SSB 0 Hz
LB 3
GB 0



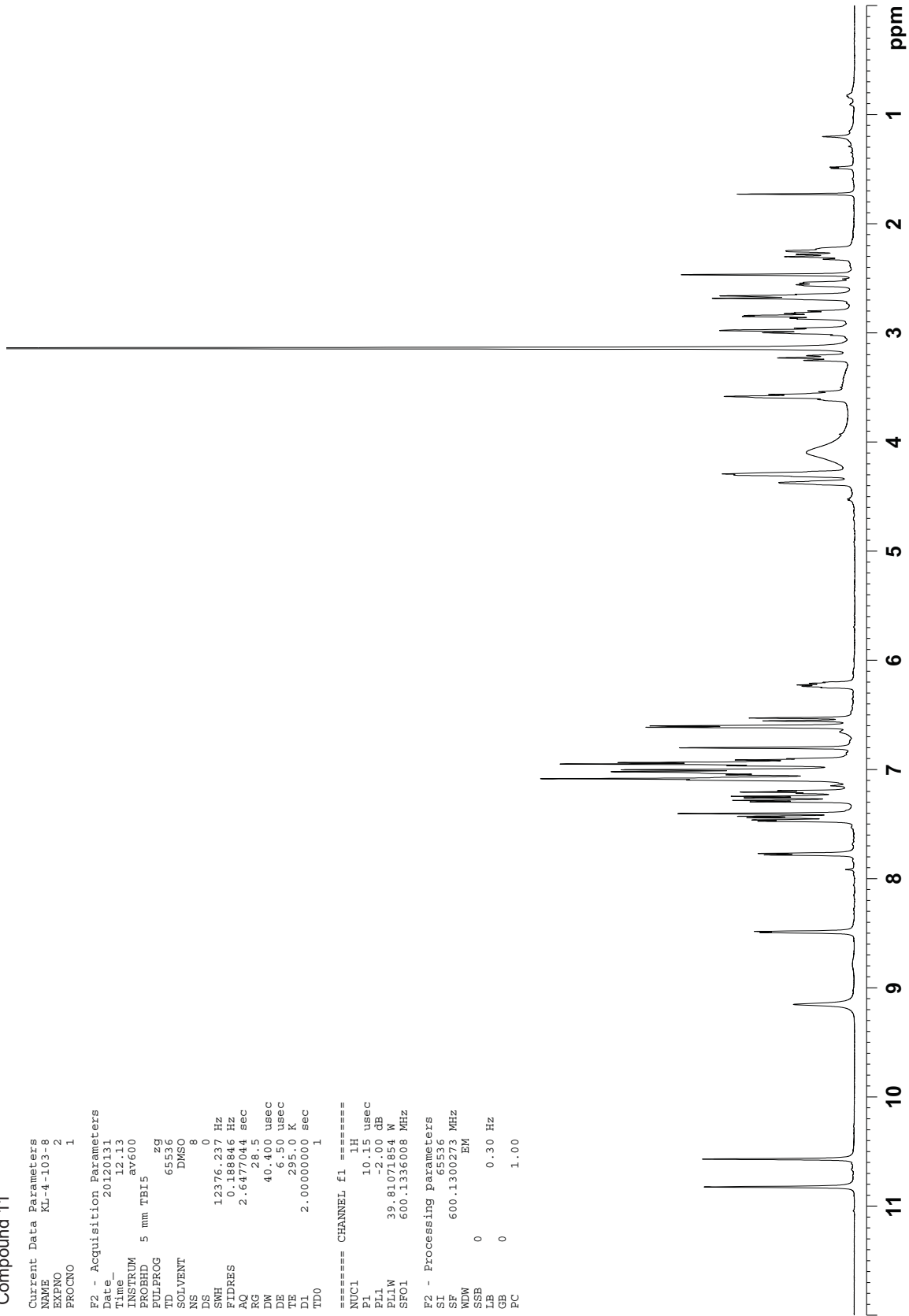
Compound 11

Current Data Parameters
 NAME KL-4-103-8
 EXPNO 2
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20120131
 Time 12.13
 INSTRUM spect
 PROBRD 5 mm TB15
 PULPROG zg
 TD 65536
 SOLVENT DMSO
 NS 8
 DS 0
 SWH 12376.237 Hz
 FIDRES 0.188846 Hz
 AQ 2.6477044 sec
 RG 28.5
 DW 40.400 usec
 DE 6.50 usec
 TE 295.0 K
 D1 2.00000000 sec
 TD0 1

===== CHANNEL f1 =====
 NUC1 1H
 P1 10.15 usec
 PL1 -2.00 dB
 PL1W 39.81071854 W
 SFO1 600.1336008 MHz

F2 - Processing parameters
 SI 65536
 SF 600.1300273 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00



Compound 11

Current Data Parameters
NAME KL-4-103-8
EXPNO 3
PROCNO 1

F2 - Acquisition Parameters
Date_ 20120131
Time 12.16
INSTRUM av600
PROBHD 5 mm TBI5
PULPROG cosygmph
TD 4096
SOLVENT DMSO
NS 2
DS 4
SWH 5387.931 Hz
FIDRES 1.315413 Hz
AQ 0.3801588 sec
RG 181
DW 92.800 usec
DE 6.50 usec
TE 295.0 K
D0 0.00007988 sec
D1 2.00000000 sec
D13 0.00000400 sec
D16 0.00020000 sec
IN0 0.00018560 sec

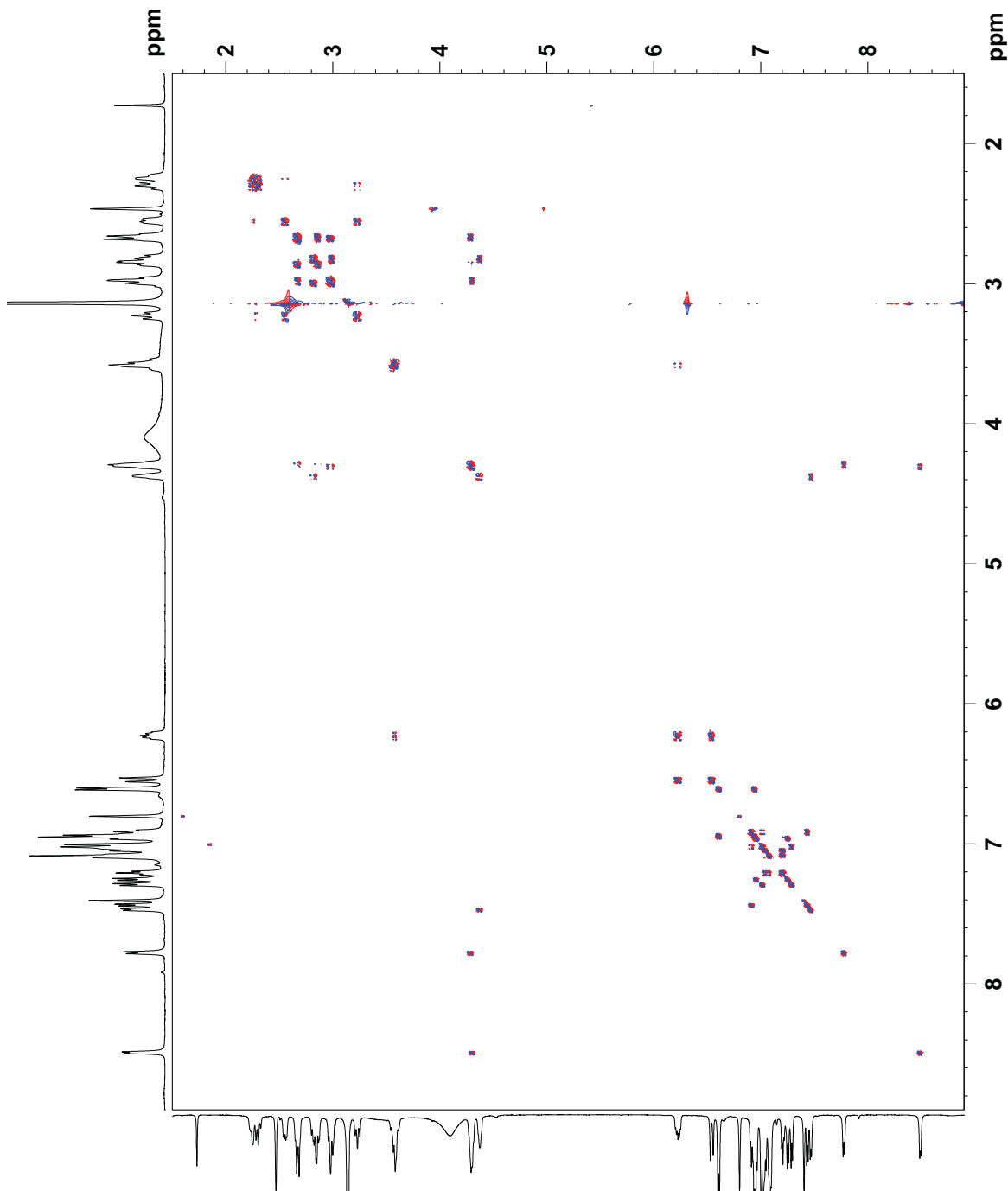
===== CHANNEL f1 =====
NUC1 ¹H
P1 10.15 usec
PL1 2.30 dB
PL1W 39.81071854 W
SFO1 600.1327006 MHz

===== GRADIENT CHANNEL =====
GENAM1 SINE 100
GENAM2 SINE 100
GP21 10.00 %
GP22 20.00 %
P16 1000.00 usec

F1 - Acquisition Parameters
TD 512
SF01 600.1327 MHz
FIDRES 10.523297 Hz
SW 8.978 ppm
FMODE States-TpPI

F2 - Processing parameters
SI 2048
SF 600.1300273 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0
PC 1.00

F1 - Processing parameters
SI 2048
MC2 States-TpPI
SF 600.1300273 MHz
WDW
SSB 2
LB 0 Hz
GB 0



Compound 11

Current Data Parameters
 NAME KL-4-103-8
 EXPNO 7
 PROCNO 1

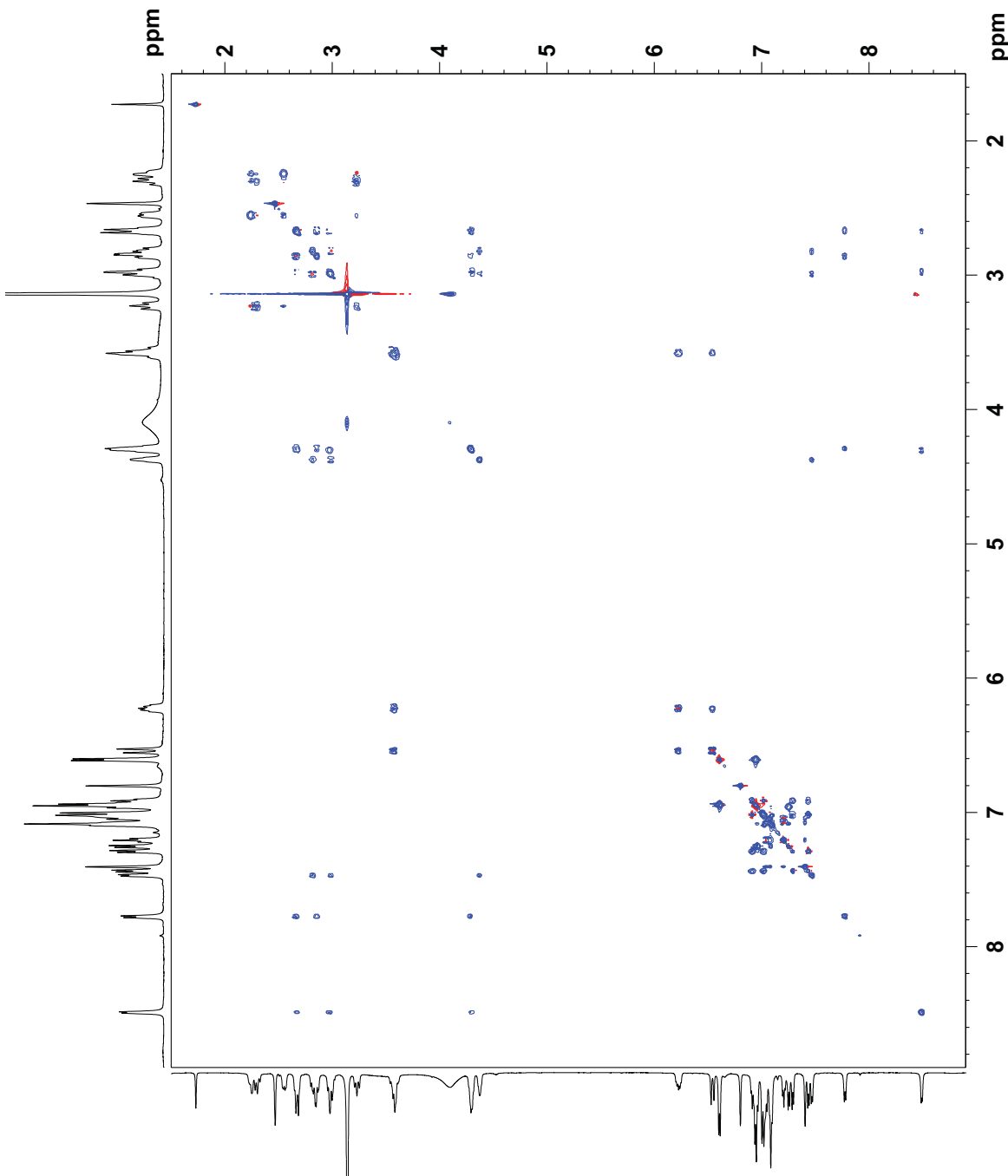
F2 - Acquisition Parameters
 Date_ 20120202
 Time 11.13
 INSTRUM 5 mm TBI5 av600
 FREQID 4096
 PULPROG mlevuprog
 TD 4096
 SOLVENT DMSO
 NS 2
 DS 16
 SWH 5530.974 Hz
 FIDRES 1.350335 Hz
 AQ 0.3703284 sec
 RG 128
 DW 90.400 usec
 DE 29.50 usec
 TE 300.2 K
 D0 0.00000300 sec
 D1 1.20000005 sec
 D9 0.06000000 sec
 D11 0.03000000 sec
 D12 0.00002000 sec
 D16 0.00020000 sec
 IN0 0.00015720 sec
 L1 24

===== CHANNEL f1 =====
 NUC1 ¹H
 P1 10.50 usec
 P2 21.00 usec
 P5 26.68 usec
 P6 40.00 usec
 P7 80.00 usec
 P17 2500.00 usec
 PL1 -2.00 dB
 PL10 9.54 dB
 PL1W 39.81071854 W
 PL10W 2.79254589 W
 SFO1 600.1327006 MHz

===== GRADIENT CHANNEL =====
 GENAM1 SINE.100
 GENAM2 SINE.100
 GEZ1 30.00 %
 GEZ2 30.00 %
 PL6 1000.00 usec

F1 - Acquisition Parameters
 SI 600
 SF 600.132703 MHz
 FIDRES 10.602203 Hz
 SW 10.600 ppm
 FMODE Echo-Antiecho
 F2 - Processing parameters
 SI 1024
 SF 600.1300273 MHz
 WDW Hanning
 SSB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 1024
 MC2 echo-antiecho
 SF 600.1300273 MHz
 WDW Hanning
 SSB 0 Hz
 GB 0



```
Current Data Parameters
NAME          KL5-126-5
EXPNO         10
PROCNO        1
```

```
F2 - Acquisition Parameters
Date_      20130214
Time_      20.02
INSTRUM    av600
PROBD      5 mm TBI5
PULPROG    roesyegpph
```

SOLVENT	DMSO
NS	8
OS	16
SWH	7183.908 Hz
FIDRES	3.507768 Hz
AQ	0.1425908 sec
RNO	5792.6
DEW	69.600 usec
OW	6.50 usec
TTE	298.0 K
D1	0.00005978 sec
D12	1.50000000 sec
D16	0.0002000 sec
TV	0.0002000 sec
VS	0.0013000

```
===== CHANNEL f1 =====
NUC1
P1      9.14 usec
P2     18.28 usec
P15    20000.00 usec
P40    2000.00 usec
P10    120.00 dB
P11     -2.00 dB
P11    18.78 dB
```

U W	39.81071854 W
PLW	0.33265951 W
PLLIW	600.1336008 MHz
SSFO1	38.78 dB
SP10	Squa100.1000
SPNMA10	0.500
SPOAL10	-1601.48 Hz
SPOFS10	

```
===== GRADIENT CHANNEL =====
GPNAME1      SINE.100
GPNAME2      SINE.100
GPZ1         31.00 %
GPZ2         11.00 %
P16          100.00 used
```

F1 - Acquisition parameters	
ITD	554
SFO1	600.1336 MHz
FIDRES	12.967337 Hz
SW	11.971 ppm

```
F2 - Processing parameters
SI      4096
SF      600.130000 MHz
WDW      QSINE
SSB      2
```

LB	0 Hz	
GB	0	
PC	1.00	

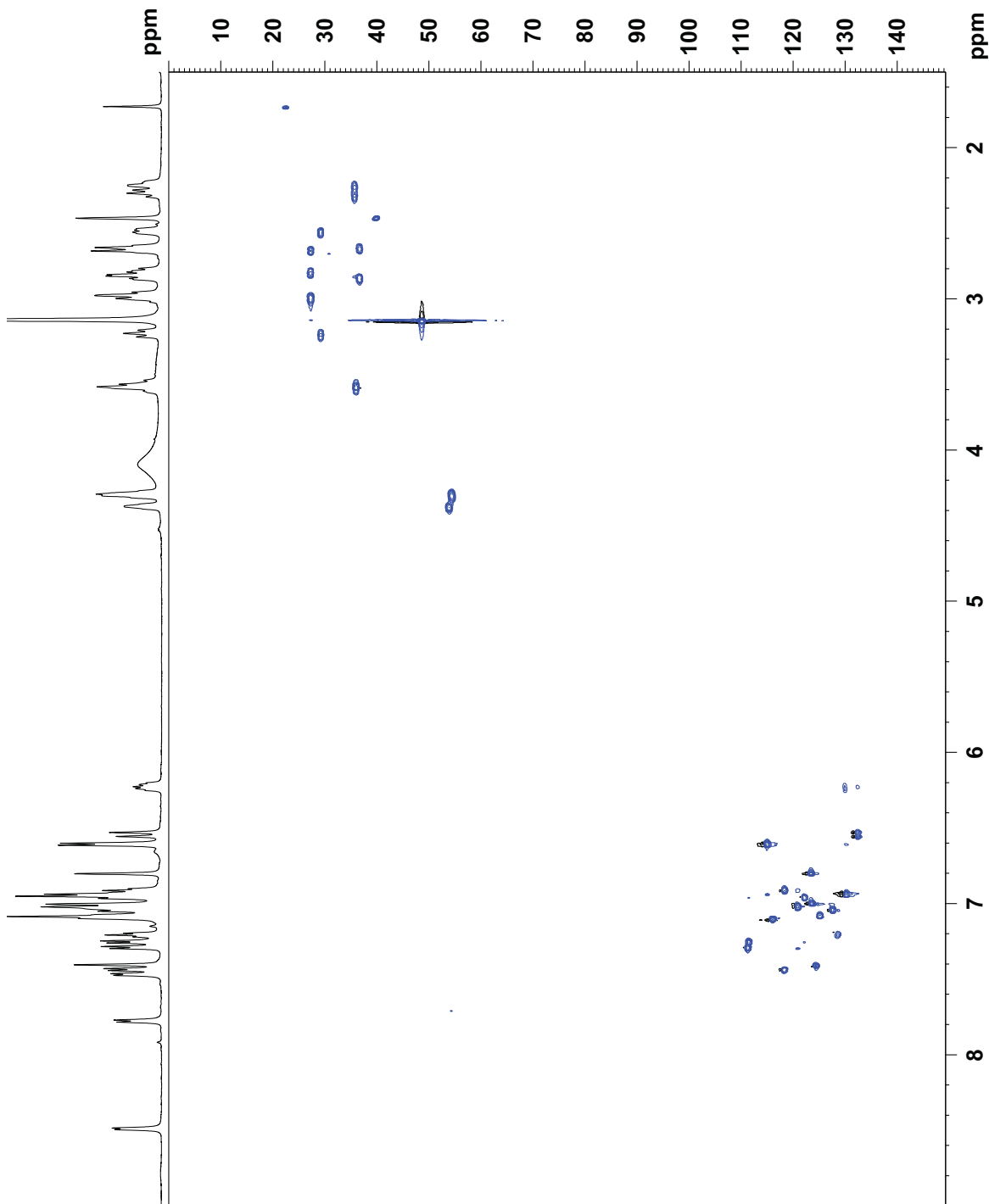
SF	600.130000 MHz
WDW	
SSB	2
LB	0 Hz
GB	0



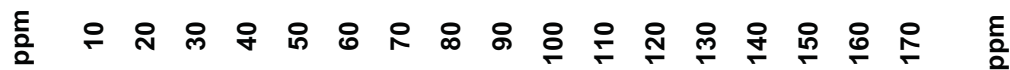
Compound 11

```

Current Data Parameters
NAME      KL-4-101-8
EXPNO     1
PROCNO    1
F2 - Acquisition Parameters
Date_     20120131
Time      12:58
INSTRUM   S
PROBHD    5 mm BBO
PULPROG   zgpg30
TD         65536
SOLVENT   DMSO
NS         16
DS         4
SWH        5387.931 Hz
FIDRES     2.63026 Hz
AQ         0.19398 sec
RG          26008
DM          92.800 usec
TE          296.2 K
CNS12      145.000000
DO         0.0000300 sec
D1         1.1500000 sec
D4         0.0172014 sec
D11        0.0300000 sec
D16        0.0020000 sec
DELTA      0.0150000 sec
ZG30PTS    0.00001840 sec
===== CHANNEL f1 =====
NUC1       1H
P1         10.15 usec
P2         20.30 usec
P3         10.15 usec
PL1        -2.00 dB
PL2        -3.00 dB
PL1W       39.81071854 W
SFO1       600.1327066 MHz
===== CHANNEL f2 =====
CPDPRG2    garp
NUC2       13C
P1         18.50 usec
P2         37.00 usec
P3         1500.00 usec
P4         1500.00 usec
PL1        -2.00 dB
PL2        -3.00 dB
PL12       0 W
PL12W      150.35617065 W
PL2W       12.19330025 W
SFO2       150.9133722 MHz
SFO3       150.9133722 MHz
SFO4       150.9133722 MHz
SFOAL3     MURF.ret
SFOAL3     0 Hz
SFOFFS3    0.500
===== GRADIENT CHANNEL =====
GPRM1      SINE.100
GPRM2      SINE.100
GPRM3      SINE.100
GPZ1       20.10 %
GPZ2       20.10 %
GPZ3       20.10 %
F1 - Acquisition parameters
TD          256
SFO1       150.9134 MHz
FIDRES     1.0618000000000000
SM         106180.000 DPM
F2 - Processing parameters
SI         4096
SF         600.1300273 MHz
WDW         EM
SSB         0 Hz
GB          0
PC          1.40
F1 - Processing parameters
SI         4096
SF         150.9134 MHz
WDW         EM
SSB         0 Hz
GB          0
  
```



Current Data Parameters	
NAME	VALUE
NAME	KZ-4-103-8
PROJNO	1
EXPNO	5
PROCNO	1
F2 - Acquisition Parameters	
Date_	20120331
Time	17.00
INSTRUM	AW60
PROBHD	5 mm TB15
PULPROG	hmcg30ldrf
PCPDPRG2	hmcg30ldrf
SOLVENT	DMSO
NS	24
DS	4
SWH	6009.615 Hz
FIDRES	2.934382 Hz
AQ	0.1704342 sec
RG	327.500
DE	83.240 usec
TE	6.50 usec
TD	120.0098.0 K
NUC1	129.0000000
CHN1	160.0000000
CHN2	160.0000000
CHN3	1.7000000
CHN4	1.2000000 sec
D1	0.07142857 sec
D6	0.07142857 sec
D16	0.00200000 sec
D17	0.00200000 sec
IN0	0.00166325 sec
===== CHANNEL f1 =====	
NUC1	10.15 usec
P1	20.30 usec
PL1	39.81 -2.00 dB
PL2	39.81 -2.00 dB
PL3	150.963903 MHz
PL4	150.963903 MHz
PL5	150.963903 MHz
PL6	150.963903 MHz
PL7	150.963903 MHz
PL8	150.963903 MHz
PL9	150.963903 MHz
PL10	150.963903 MHz
PL11	150.963903 MHz
PL12	150.963903 MHz
PL13	150.963903 MHz
PL14	150.963903 MHz
PL15	150.963903 MHz
PL16	150.963903 MHz
PL17	150.963903 MHz
PL18	150.963903 MHz
PL19	150.963903 MHz
PL20	150.963903 MHz
PL21	150.963903 MHz
PL22	150.963903 MHz
PL23	150.963903 MHz
PL24	150.963903 MHz
PL25	150.963903 MHz
PL26	150.963903 MHz
PL27	150.963903 MHz
PL28	150.963903 MHz
PL29	150.963903 MHz
PL30	150.963903 MHz
PL31	150.963903 MHz
PL32	150.963903 MHz
PL33	150.963903 MHz
PL34	150.963903 MHz
PL35	150.963903 MHz
PL36	150.963903 MHz
PL37	150.963903 MHz
PL38	150.963903 MHz
PL39	150.963903 MHz
PL40	150.963903 MHz
PL41	150.963903 MHz
PL42	150.963903 MHz
PL43	150.963903 MHz
PL44	150.963903 MHz
PL45	150.963903 MHz
PL46	150.963903 MHz
PL47	150.963903 MHz
PL48	150.963903 MHz
PL49	150.963903 MHz
PL50	150.963903 MHz
PL51	150.963903 MHz
PL52	150.963903 MHz
PL53	150.963903 MHz
PL54	150.963903 MHz
PL55	150.963903 MHz
PL56	150.963903 MHz
PL57	150.963903 MHz
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PL59	150.963903 MHz
PL60	150.963903 MHz
PL61	150.963903 MHz
PL62	150.963903 MHz
PL63	150.963903 MHz
PL64	150.963903 MHz
PL65	150.963903 MHz
PL66	150.963903 MHz
PL67	150.963903 MHz
PL68	150.963903 MHz
PL69	150.963903 MHz
PL70	150.963903 MHz
PL71	150.963903 MHz
PL72	150.963903 MHz
PL73	150.963903 MHz
PL74	150.963903 MHz
PL75	150.963903 MHz
PL76	150.963903 MHz
PL77	150.963903 MHz
PL78	150.963903 MHz
PL79	150.963903 MHz
PL80	150.963903 MHz
PL81	150.963903 MHz
PL82	150.963903 MHz
PL83	150.963903 MHz
PL84	150.963903 MHz
PL85	150.963903 MHz
PL86	150.963903 MHz
PL87	150.963903 MHz
PL88	150.963903 MHz
PL89	150.963903 MHz
PL90	150.963903 MHz
PL91	150.963903 MHz
PL92	150.963903 MHz
PL93	150.963903 MHz
PL94	150.963903 MHz



Compound 12

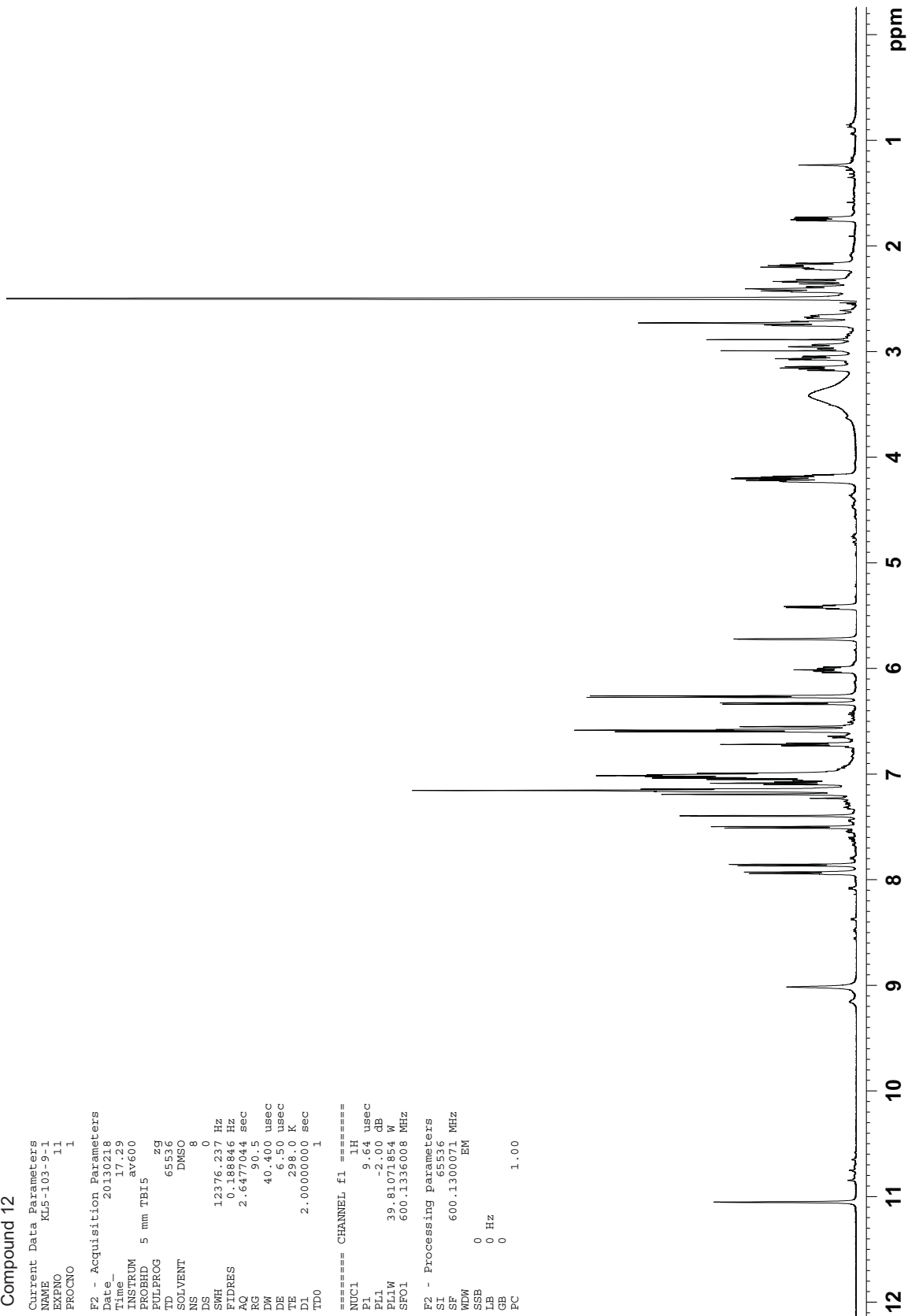
```

Current Data Parameters
NAME      KLS-103-9-1
EXPNO     11
PROCNO    1

F2 - Acquisition Parameters
Date_     20130216
Time      17:23
INSTRUM   spect
PROBHD    5 mm TB15
PULPROG   zg
TD         65536
SOLVENT   DMSO
NS         8
DS         0
SWH        12376.237 Hz
FIDRES     0.188846 Hz
AQ         2.6477044 sec
RG         90.5
DM         40.400 usec
DE         6.50 usec
TE         298.0 K
D1         2.00000000 sec
TD0        1

===== CHANNEL f1 =====
NUC1       1H
P1         9.64 usec
PL1        -2.00 dB
PL1W       39.81071854 W
SFO1       600.1336008 MHz

F2 - Processing parameters
SI         65536
SF         600.1300071 MHz
WDW        EM
SSB        0
LB         0 Hz
GB         0
PC         1.00
  
```



Compound 12

Current Data Parameters
NAME KL-4-103-9-1_KL
EXPNO 3
PROCNO 1

F2 - Acquisition Parameters
Date_ 20120203
Time_ 11.17
INSTRUM av600
PROBHD 5 mm TBI5
PULPROG cosygpmfph
TD 4096
SOLVENT DMSO
NS 2
DS 4
SWH 5387.931 Hz
FIDRES 1.315413 Hz
AQ 0.3801588 sec
RG 181
DE 92.800 usec
TE 294.5 K
D0 0.0008045 sec
D1 2.0000000 sec
D13 0.0000040 sec
D16 0.0002000 sec
INO 0.00018560 sec

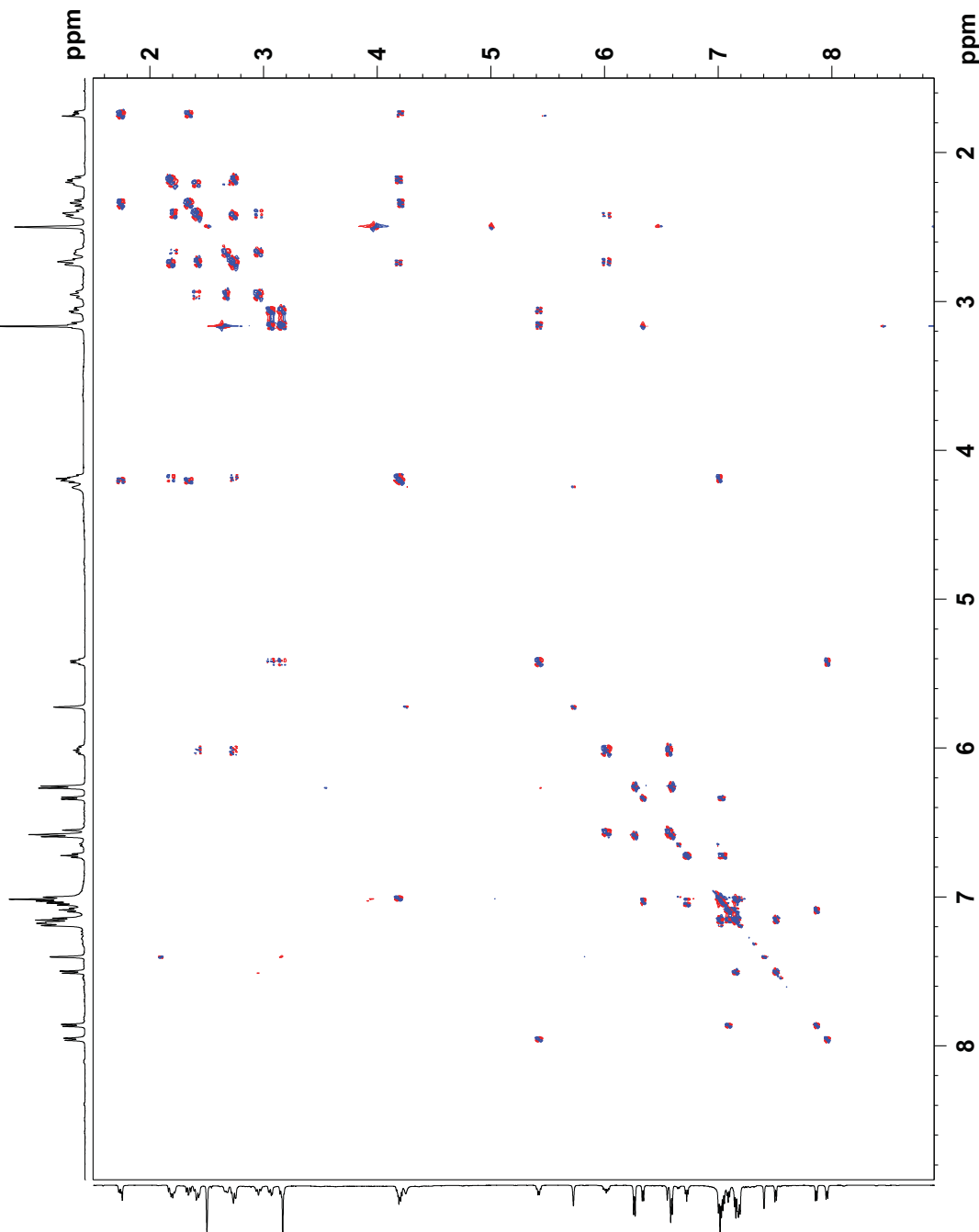
===== CHANNEL f1 =====
NUC1 ¹H
P1 9.70 usec
PL1 19.40 dB
RF1 -2.00 dB
PC1W 39.81071854 W
SFO1 600.1327006 MHz

===== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPNAM2 SINE.100
GP21 10.00 %
GP22 20.00 %
P16 1000.00 usec

F1 - Acquisition parameters
TD 512
SFO1 600.1327 MHz
FIDRES 10.523297 Hz
SW 8.978 ppm
FMODE States-TpPI

F2 - Processing parameters
SI 4096
SF 600.1300099 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0
PC 1.00

F1 - Processing parameters
SI 4096
MC2 States-TpPI
SF 600.1300058 MHz
WDW
SSB 2
LB 0 Hz
GB 0



Compound 12

Current Data Parameters
 NAME KL-4-103-9-1_KL
 EXPNO 4
 PROCNO 1

F2 - Acquisition Parameter
 Date 20120203
 Time 11.59
 INSTRUM av600
 PROBD 5 mm TBI5
 PULPROG mlevetgp.js
 TD 4096
 SOLVENT DMSO
 NS 2
 DS 16

SWH 5530.974 Hz
 FIDRES 1.350335 Hz
 AQ 0.3703284 se
 RG 128
 DW 90.400 us
 DE 6.50 us
 TE 294.5 K

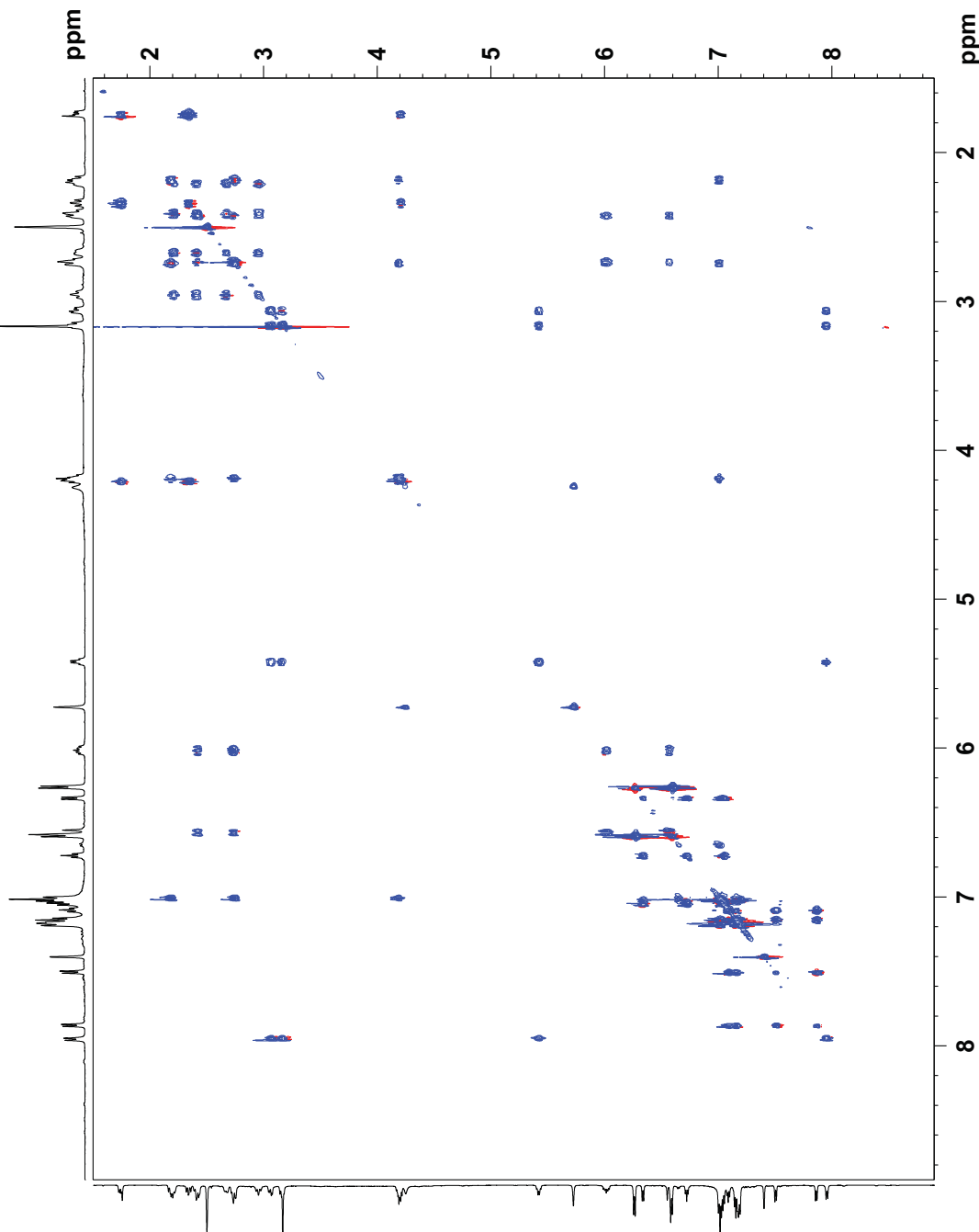
D0 0.00000300 se
 D1 1.20000005 se
 D9 0.06000000 se
 D11 0.03000000 se
 D12 0.00002000 se
 D16 0.00020000 se
 INO 0.00015720 se
 L1 24

===== CHANNEL f1 =====
 NUC1 ¹H
 P1 9.70 us
 P2 19.40 us
 P5 26.68 us
 P6 40.00 us
 P7 80.00 us
 P17 2500.00 us
 PL1 -2.50 dB
 PL0 -2.50 dB
 PL10 39.81071854 W
 PL1W 2.79254389 W
 PL1W 600.1327006 MH
 SF01 600.1327006 MH

===== GRADIENT CHANNEL ==
 GENAM1 SINE 100
 GENAM2 SINE 100
 GP21 30.00 %
 GP22 30.00 %
 PL6 1000.00 us

F1 - Acquisition parameter
 TD 600
 SF01 600.1327 MH
 FIDRES 10.602203 Hz
 SW 10.600 pp
 FMODE Echo-Antiecho

F2 - Processing parameters
 SI 4096
 SF 600.1300067 MH
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00



```
Current Data Parameters
NAME          KL5-103-9-1
EXPNO         40
PROCNO        1
```

```
F2 - Acquisition Parameters
Date_      20130222
Time       23.22
INSTRUM    av600
PROBHD     5 mm TR15
```

PULPROG	noesyestph	
TD	2048	
SOLVENT	DMSO	
NS	16	
DS	16	
SWH	7788.162 Hz	
FIDRES	3.802814 Hz	
RG	0.1315316 sec	
AQ	322.5	
DD	64.200 usec	
DE	6.50 usec	
TE	296.0 K	
DO	0.00005004 sec	
D1	4.00000000 sec	
D8	0.10000000 sec	
D11	0.30000000 sec	
D12	0.03002000 sec	
D16	0.00020000 sec	
IN0	0.00012844 sec	

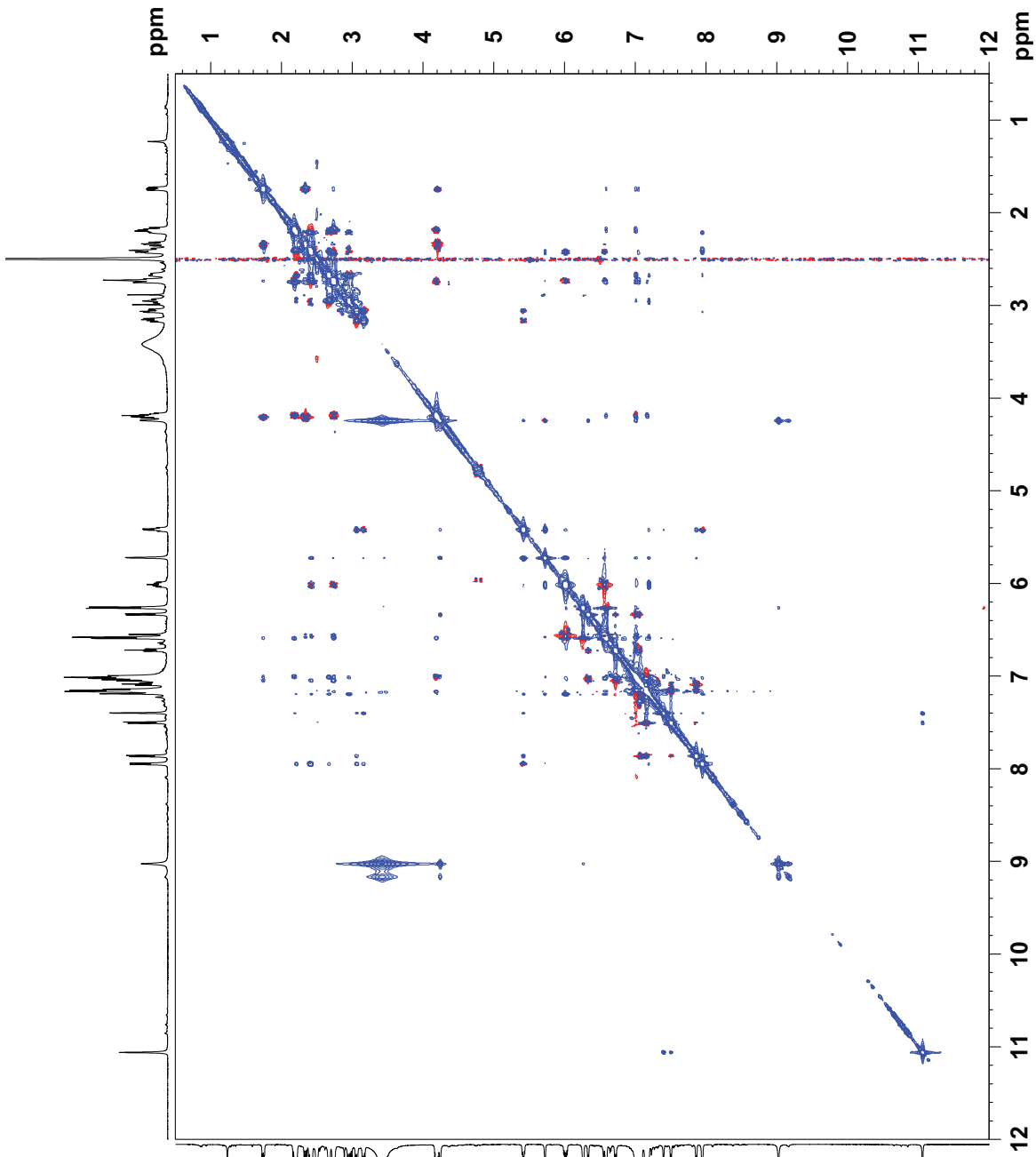
```
===== CHANNEL f1 =====
NUC1      1H      11.12 usec
P1        22.24 usec
P2        2000.00 usec
P3        120.00 dB
P4        -2.00 dB
P5
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P819
P820
P821
P822
P823
P824
P825
P826
P827
P828
P82
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```

===== GRADIENT CHANNEL =====
GPNAM1      SINE.100
GPNAM2      SINE.100
GPX1        0 0
GPX2        0 0
GPY1        0 0
GPY2        0 0
GPZ1        31.00 0
GPZ2        11.00 0
P16         1000.00 usec

```

F1 - Acquisition parameters		F2 - Processing parameters	
FT	512	SI	4096
SFO1	600.1336 MHz	SF	600.1300067 MHz
FIDRES	15.21254 Hz	WDW	QSIGNE
SW	12.977 ppm		2
PRNAME	States-1p1		0 Hz
			0
			1.00



Compound 12

Current Data Parameters
NAME KL5-103-9-1
EXPNO 39
PROCNO 1

F2 - Acquisition Parameters

Date_ 20130222
Time_ 21.13
INSTRUM av600
PROBHD 5 mm TBI5
PULPROG roesyessgph
TD 2048
SOLVENT DMSO
NS 8
DS 16
SWH 7788.162 Hz
FIDRES 3.802814 Hz
AQ 0.1315316 sec
RG 2896.3
DW 64.200 usec
DE 6.50 usec
TE 296.0 K
D0 0.00005312 sec
D1 1.50000000 sec
D12 0.00020000 sec
D16 0.00020000 sec
IN0 0.00012840 sec

===== CHANNEL f1 =====

NUC1 1H
P1 11.12 usec
P2 22.24 usec
P15 200000.00 usec
P40 2000.00 usec
PL0 120.00 dB
PL1 -2.00 dB
PL11 17.08 dB
PL0W 0 W
PL1W 39.81071854 W
PL1W 0.49203953 W
SFO1 600.1336008 MHz
SFO10 37.08 dB
SFO100 Squal100.1000
SFOAL10 0.500
SFOFFS10 -1548.00 Hz

===== GRADIENT CHANNEL =====

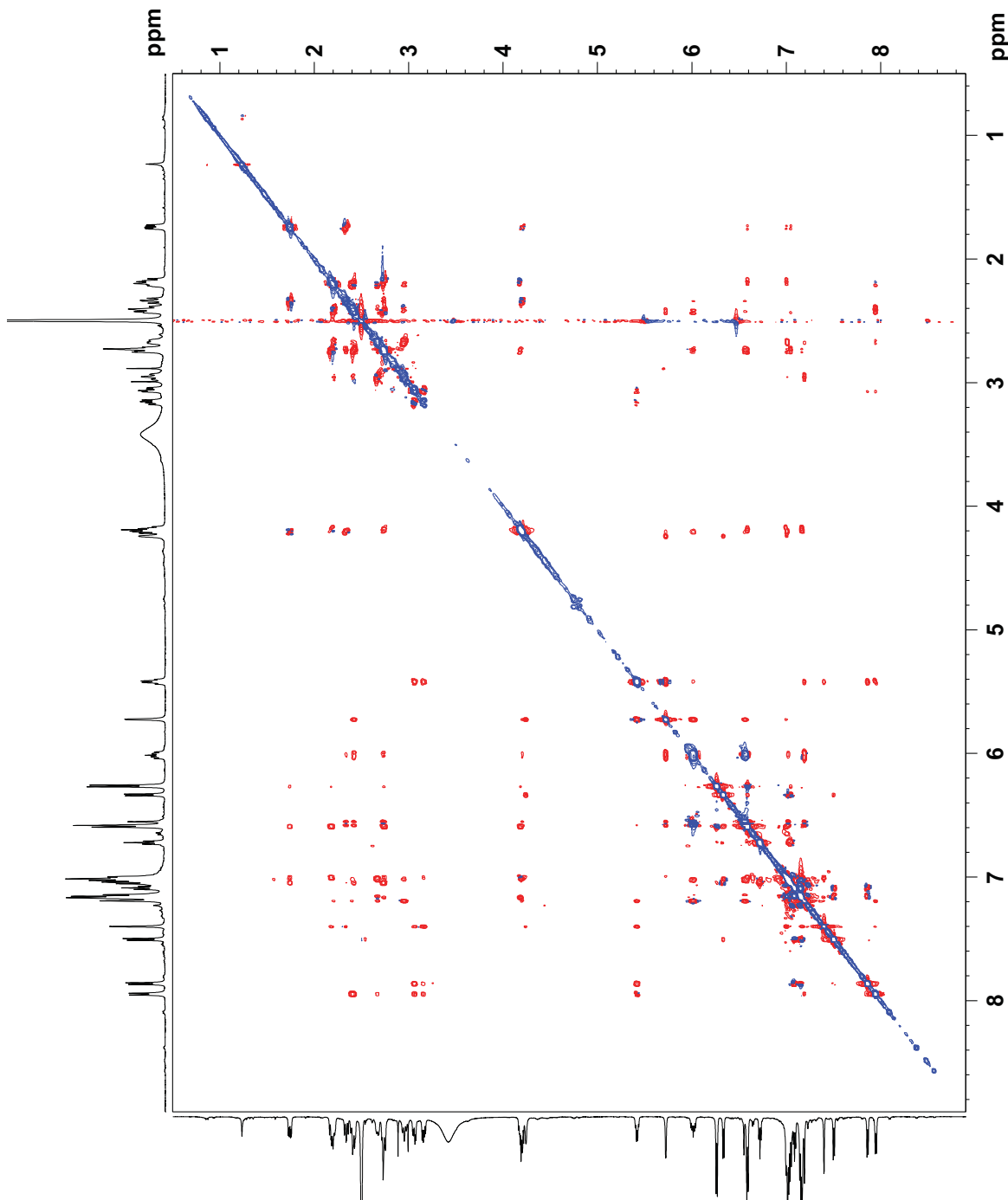
GENM1 SINE.100
GENM2 SINE.100
GEX1 0 %
GEX2 0 %
GPY1 0 %
GPY2 0 %
GPZ1 31.00 %
GPZ2 11.00 %
PI6 1000.00 usec

F1 - Acquisition parameters

TD 512
SFO1 600.1336 MHz
FIDRES 15.211274 Hz
SW 12.977 ppm
FMODE States-TpPI

F2 - Processing parameters

SI 4096
SF 600.1300060 MHz
WDW QSI
SSB 2.5
LB 0 Hz
GB 0
PC 1.00



Compound 12

Current Data Parameters
 NAME KL5-103-9-1
 EXPNO 48
 PROCNO 1

F2 - Acquisition Parameters

Date_ 20130223
 Time_ 18.19
 INSTRUM av600
 PROBHD 5 mm TBI5
 PULPROG roesyessgph
 TD 2048
 SOLVENT DMSO
 NS 8
 DS 16
 SWH 7788.162 Hz
 FIDRES 3.802814 Hz
 AQ 0.1315316 sec
 RG 2896.3
 DW 64.200 usec
 DE 6.50 usec
 TE 298.0 K
 D0 0.00005287 sec
 D1 1.50000000 sec
 D12 0.00002000 sec
 D16 0.00020000 sec
 INO 0.00012840 sec

===== CHANNEL f1 =====

NUC1 1H
 P1 11.52 usec
 P2 23.04 usec
 P15 200000.00 usec
 P40 2000.00 usec
 PL0 120.00 dB
 PL1 -2.00 dB
 PL11 16.77 dB
 PLOW 0 W
 PLW 39.81071854 W
 PL1W 0.52844518 W
 SF01 600.1336008 MHz
 SFO1 600.1336008 MHz
 SFNM10 Squa100.1800
 SFOL10 0.500
 SFOFS10 -1397.00 Hz

===== GRADIENT CHANNEL =====

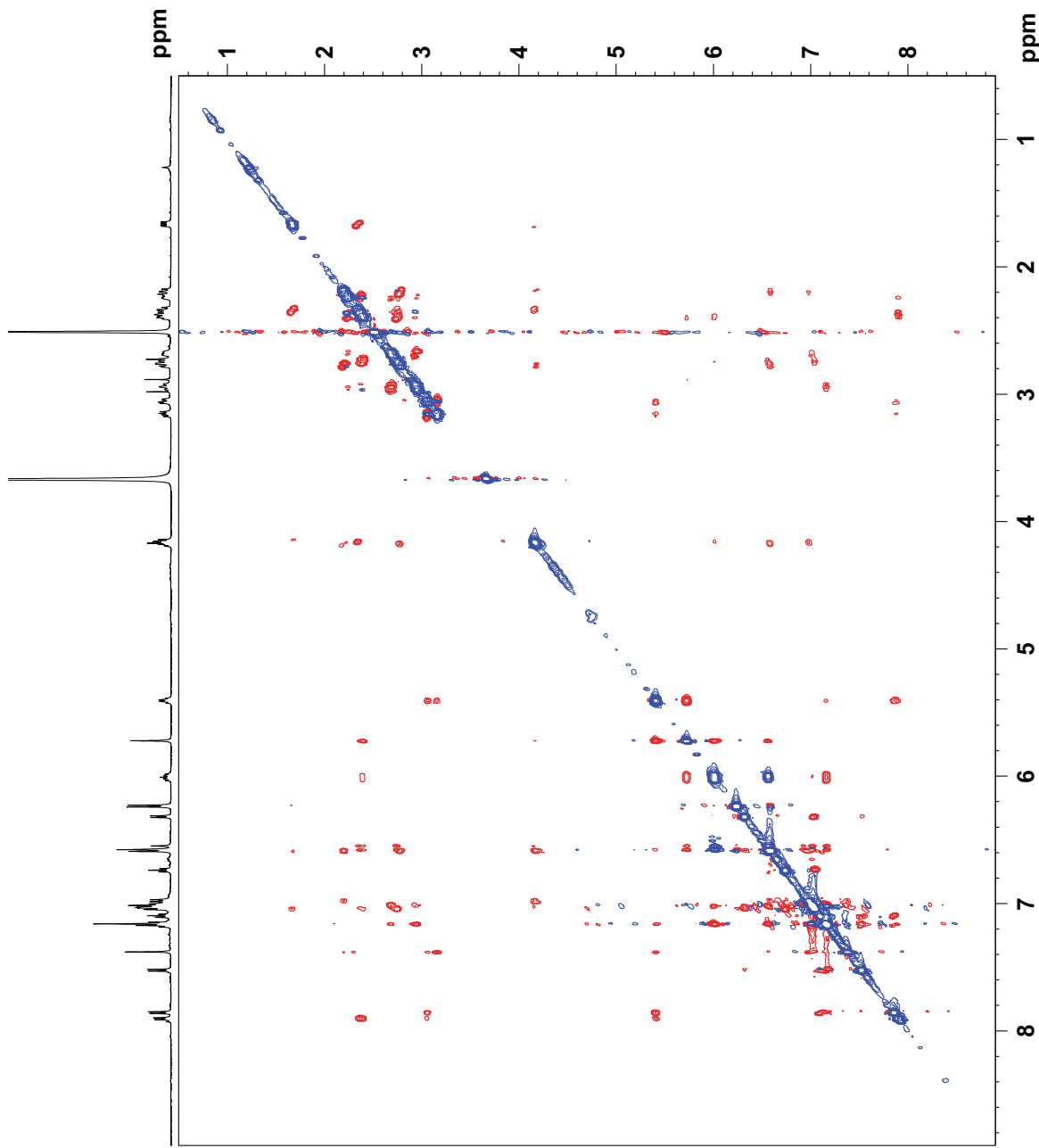
GENAM1 SINE.100
 GENAM2 SINE.100
 GPX1 0 %
 GPX2 0 %
 GPY1 0 %
 GPY2 0 %
 GPZ1 31.00 %
 GPZ2 11.00 %
 P16 1000.00 usec

F1 - Acquisition parameters

TD 264
 SF01 600.1336 MHz
 FIDRES 29.500652 Hz
 SW 12.977 ppm
 FnmODE States-TpPI

F2 - Processing parameters

SI 8192
 SF 600.1300000 MHz
 WDW QSI
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00



Compound 12

Current Data Parameters
NAME KL-4-103-9-1_KL
EXPNO 5
PROCNO 1

F2 - Acquisition Parameters
Date_ 20120203
Time 12.34
INSTRUM 5 mm WB15 av600
PROBHD 5 mm WB15 av600
PULPROG hsqcztgssisp
TD 2048
SOLVENT DMSO
NS 16
DS 16
SWH 5397.931 Hz
FIDRES 2.000000 sec
AQ 0.1901044 sec
RG 26008
DW 92.800 usec
DE 6.00 usec
TE 295.7 K
TEST2 145.000000 sec
D0 0.0000300 sec
D1 1.20000005 sec
D4 0.00172414 sec
D11 0.03000000 sec
D16 0.00200000 sec
DELTA 0.0065240 sec
TNO 0.00001940 sec
Z30PTNS

===== CHANNEL f1 =====
NUC1 1H
P1 9.70 usec
P2 19.70 usec
P3 18.50 usec
P4 37.00 usec
PL1 -2.00 dB
PL1W 39.81071854 W
SFO1 600.1327006 MHz
===== CHANNEL f2 =====
CEPRG2 garp
NUC2 13C
P3 18.50 usec
P4 37.00 usec
PL1 1500.00 usec
PL2 1500.00 usec
PL2W 1500.00 usec
PL2 130.00 dB
PL2 3.00 dB
PL2 7.91 dB
PL2W 0 W
PL2W 150.35617065 W
PL2W 150.35617065 W
SFO2 150.9133722 MHz
SFO3 6.35 dB
SRNAM3 Wurst.ret
SFOALL3
SPOFFS3 0 Hz

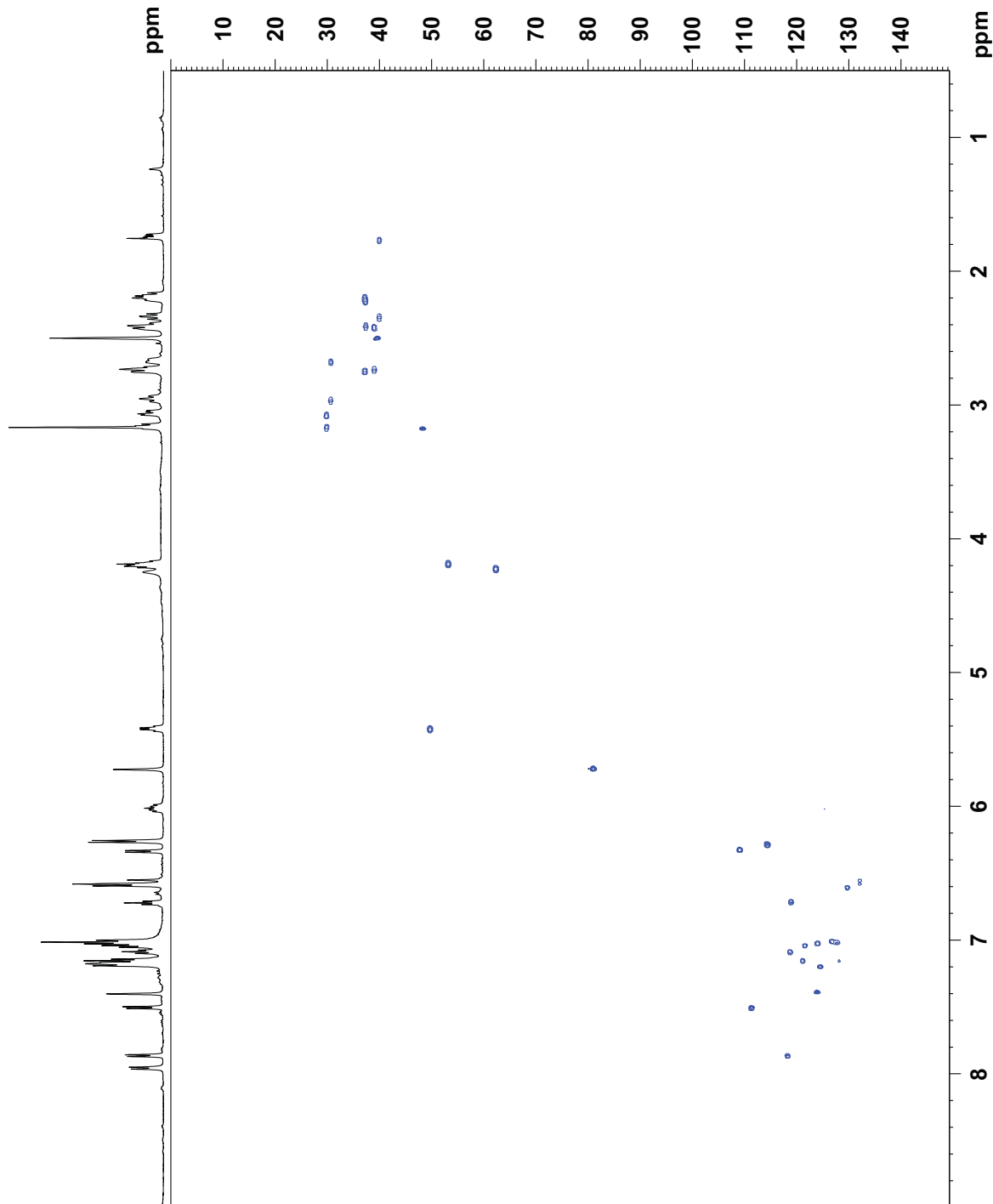
===== GRADIENT CHANNEL =====
GRNAM1 SINE.100
GRNAM2 SINE.100
GFX1 0 %
GFX2 0 %
GFX1 0 %
GFX2 0 %
GFX1 80.00 %
GFX2 20.10 %
PL6 1000.00 usec

F1 - Acquisition Parameters
Date_ 20120203
Time 12.34
INSTRUM 5 mm WB15 av600
PROBHD 5 mm WB15 av600
PULPROG hsqcztgssisp
TD 2048
SOLVENT DMSO
NS 16
DS 16
SWH 5397.931 Hz
FIDRES 2.000000 sec
AQ 0.1901044 sec
RG 26008
DW 92.800 usec
DE 6.00 usec
TE 295.7 K
TEST2 145.000000 sec
D0 0.0000300 sec
D1 1.20000005 sec
D4 0.00172414 sec
D11 0.03000000 sec
D16 0.00200000 sec
DELTA 0.0065240 sec
TNO 0.00001940 sec
Z30PTNS

===== GRADIENT CHANNEL =====
GRNAM1 SINE.100
GRNAM2 SINE.100
GFX1 0 %
GFX2 0 %
GFX1 0 %
GFX2 0 %
GFX1 80.00 %
GFX2 20.10 %
PL6 1000.00 usec

F1 - Acquisition Parameters
Date_ 20120203
Time 12.34
INSTRUM 5 mm WB15 av600
PROBHD 5 mm WB15 av600
PULPROG hsqcztgssisp
TD 2048
SOLVENT DMSO
NS 16
DS 16
SWH 5397.931 Hz
FIDRES 2.000000 sec
AQ 0.1901044 sec
RG 26008
DW 92.800 usec
DE 6.00 usec
TE 295.7 K
TEST2 145.000000 sec
D0 0.0000300 sec
D1 1.20000005 sec
D4 0.00172414 sec
D11 0.03000000 sec
D16 0.00200000 sec
DELTA 0.0065240 sec
TNO 0.00001940 sec
Z30PTNS

F2 - Processing Parameters
SF 600.1300061 MHz
SF 409.500 MHz
SSB COSINE
LB 0 Hz



```
Current Data Parameters
NAME      KL-4-103-9-1_KL
EXPNO     9
PROCNO    1
```

```

F2 - Acquisition Parameters
-----
Date_      20120204
Time       15.46
INSTRUM    av600
PROBHD     5 mm TBI5
PULPROG    hmbcgp12ndqf
ID         2048
SOLVENT     DMSO

```

[illegible]

```
===== CHANNEL f1 =====
NUC1      1H
P1        9.70 usec
P2        19.40 usec
PL1       -2.00 dB
PL1W      39.81071854 W
SF01      600.1330006 MHz
```

```
===== CHANNEL f2 =====
NUC2      13C
P3        18.50 usec
PL2       -3.00 dB
PL2W      150.35617065 W
SF02      150.9163903 MHz
```

=====		GRADIENT CHANNEL	=====
GFENAM1	SINE, 1.00		
GFENAM2	SINE, 1.00		
GFENAM3	SINE, 1.00		
GFENAM4	SINE, 1.00		
GFENAM5	SINE, 1.00		
GFENAM6	SINE, 1.00		
GPZ1	50.00	φ	
GPZ2	30.00	φ	
GPZ3	40.10	φ	
GPZ4	15.00	φ	
GPZ5	-10.00	φ	
GPZ6	-5.00	φ	
PI6	1000.00	usec	

F1 - Acquisition parameters	
TD	256
SFO1	150.9164 MHz
FIDRES	117.903427 Hz
SW	200.000 ppm
FnMODE	OF

F2 - Processing parameters	
SI	4096
SSF	600.130083 MHz
WDW	QSIGNE
SSB	2
LB	0 Hz
GB	0
PC	1.00

F1 - Processing parameters	
SI	4096
MC2	QF
SF	150.9029037 MHz
WDW	
SSSB	2
LB	0 Hz
GB	0



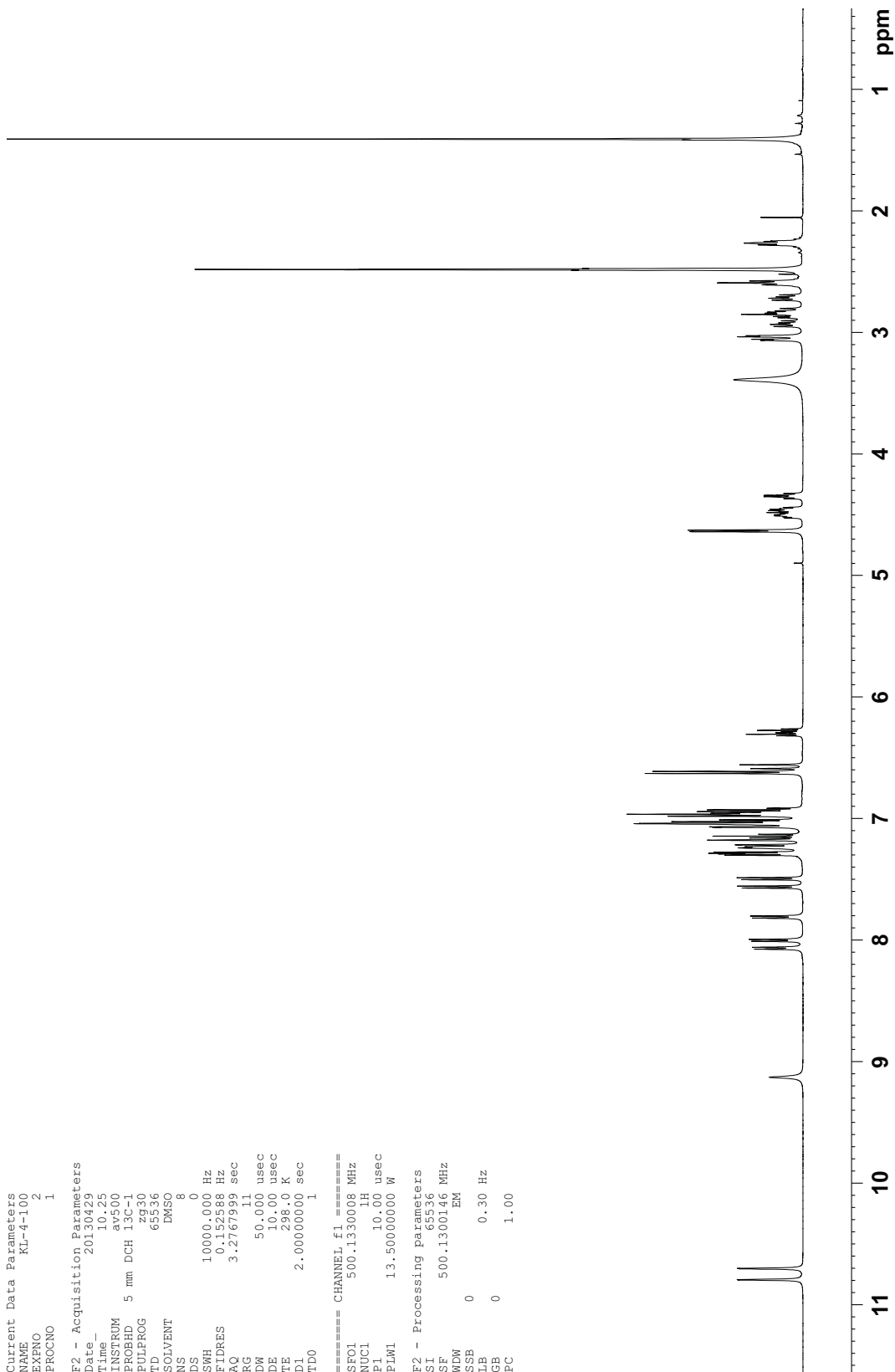
Compound 4

Current Data Parameters
NAME KL-4-100
EXNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20130429
Time_ 10.25
INSTRUM av500
PROBHD 5 mm DCH 13C-1
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 8
DS 0
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.276799 sec
RG 11
DW 50.000 usec
DE 10.00 usec
TE 298.0 K
D1 2.0000000 sec
TD0 1

===== CHANNEL f1 =====
SFO1 500.1330008 MHz
NUC1 1H
P1 10.00 usec
PLW1 13.5000000 W

F2 - Processing parameters
SI 65536
SF 500.1300146 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



Compound 4

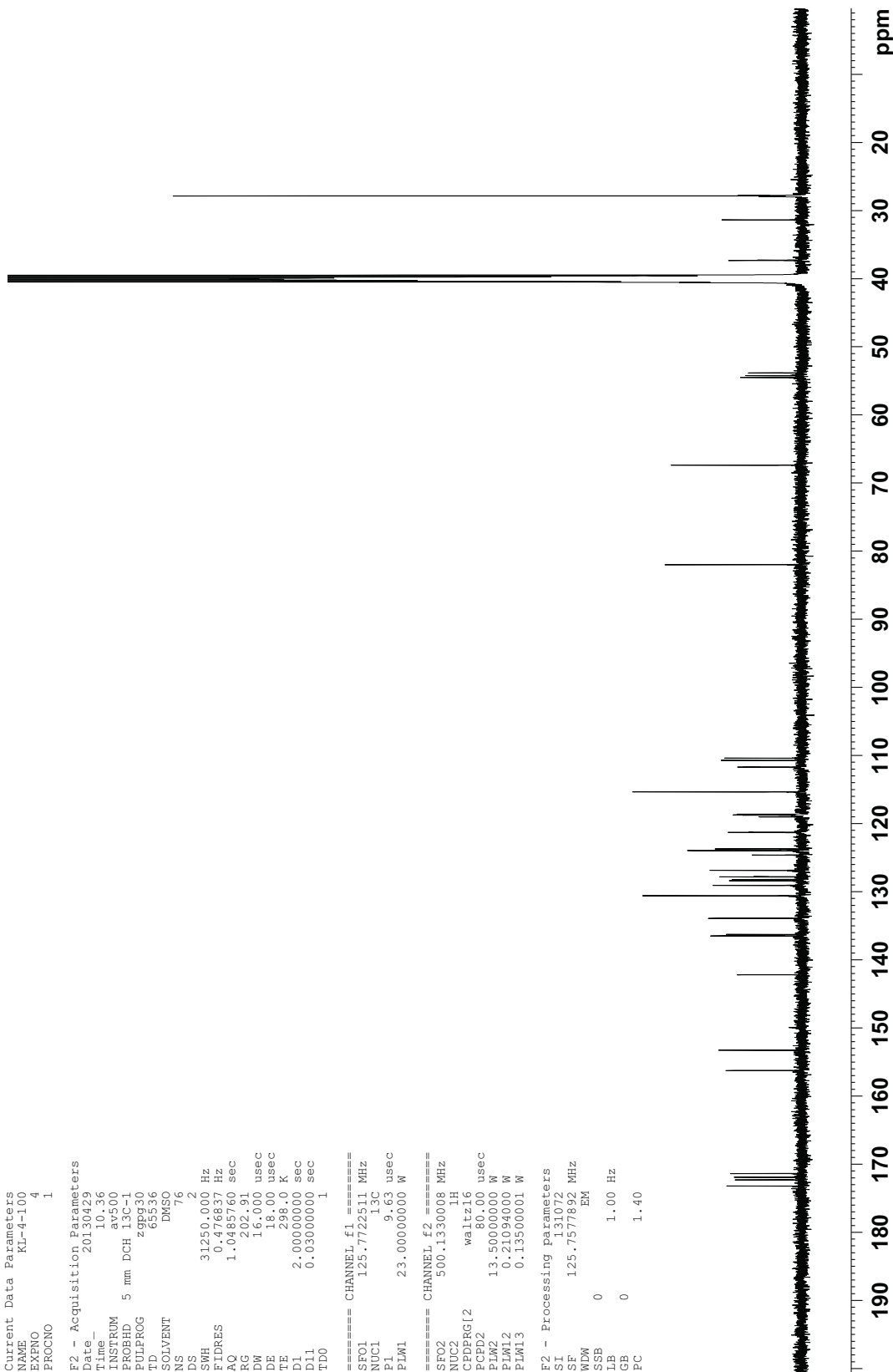
Current Data Parameters
NAME KL-4-100
EXNO 4
PROCNO 1

F2 - Acquisition Parameters
Date_ 20130429
Time_ 10.36
INSTRUM av500
PROBHD 5 mm DCH 13C-1
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 76
DS 2
SWH 31250.000 Hz
FIDRES 0.476837 Hz
AQ 1.0485760 sec
RG 202.91
DW 16.000 usec
DE 18.00 usec
TE 298.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

===== CHANNEL f1 =====
SFO1 125.7722511 MHz
NUC1 13C
P1 9.63 usec
PLW1 23.00000000 W

===== CHANNEL f2 =====
SFO2 500.1330008 MHz
NUC2 1H
CFDPRG12 waltz16
PCPD2 80.00 usec
PLW2 13.50000000 W
PLW12 0.21094000 W
PLW13 0.13500001 W

F2 - Processing parameters
SI 32768
SF 125.7577892 MHz
RG 0
SSB 0
LB 1.00 Hz
GB 0
PC 1.40



Compound 5

Current Data Parameters
NAME WWY-Cy_AV500
EXPNO 8
PROCNO 1

F2 - Acquisition Parameters

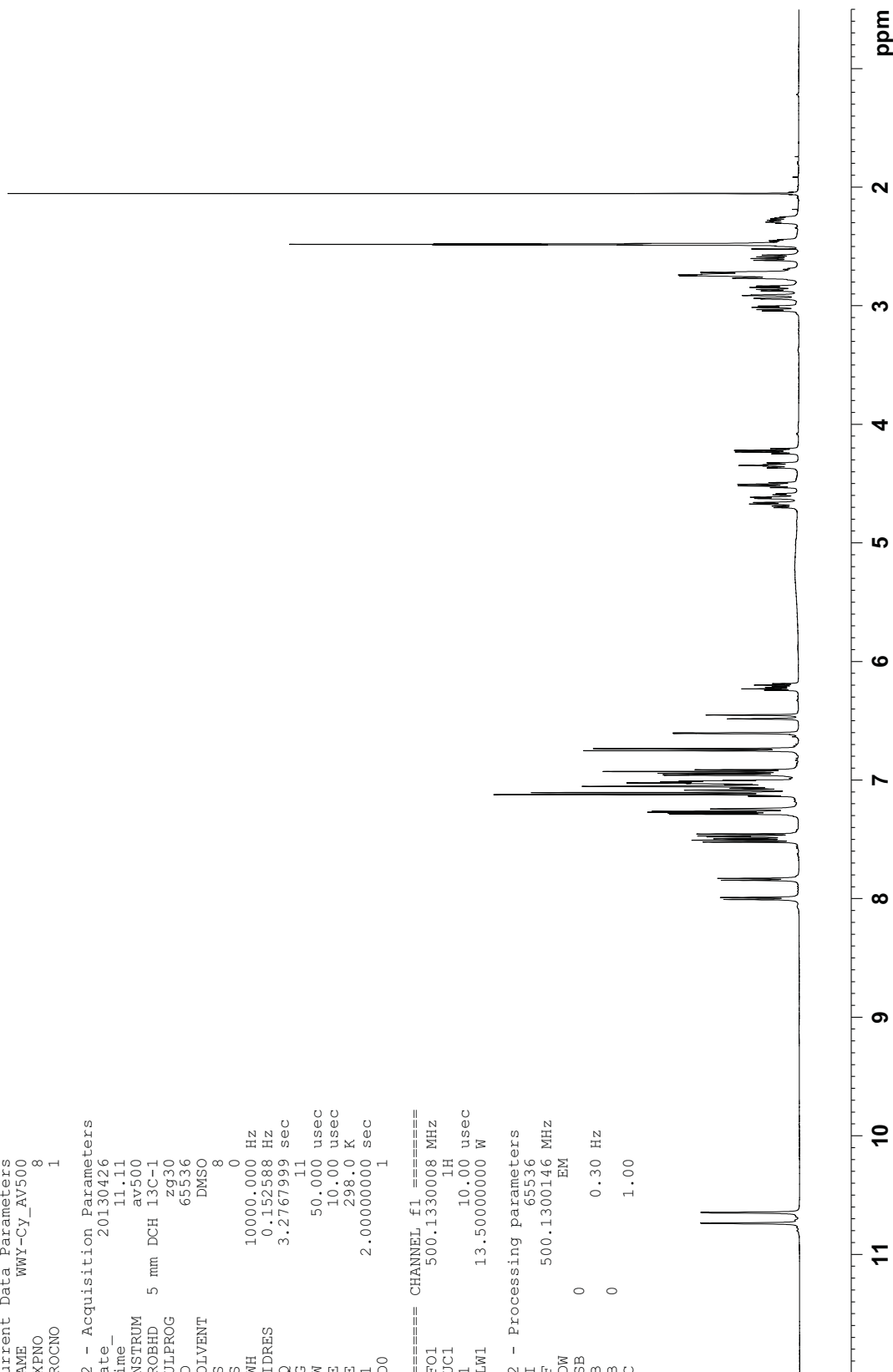
Date_ 20130426
Time 11.11
INSTRUM av500
PROBHD 5 mm DCH 13C-1
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 8
DS 0
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2767999 sec
RG 11
DW 50.000 usec
DE 10.00 usec
TE 298.0 K
D1 2.00000000 sec
TD0 1

===== CHANNEL f1 =====

SFO1 500.1330008 MHz
NUC1 1H
P1 10.00 usec
PLW1 13.50000000 W

F2 - Processing parameters

SI 65536
SF 500.1300146 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



Compound 5

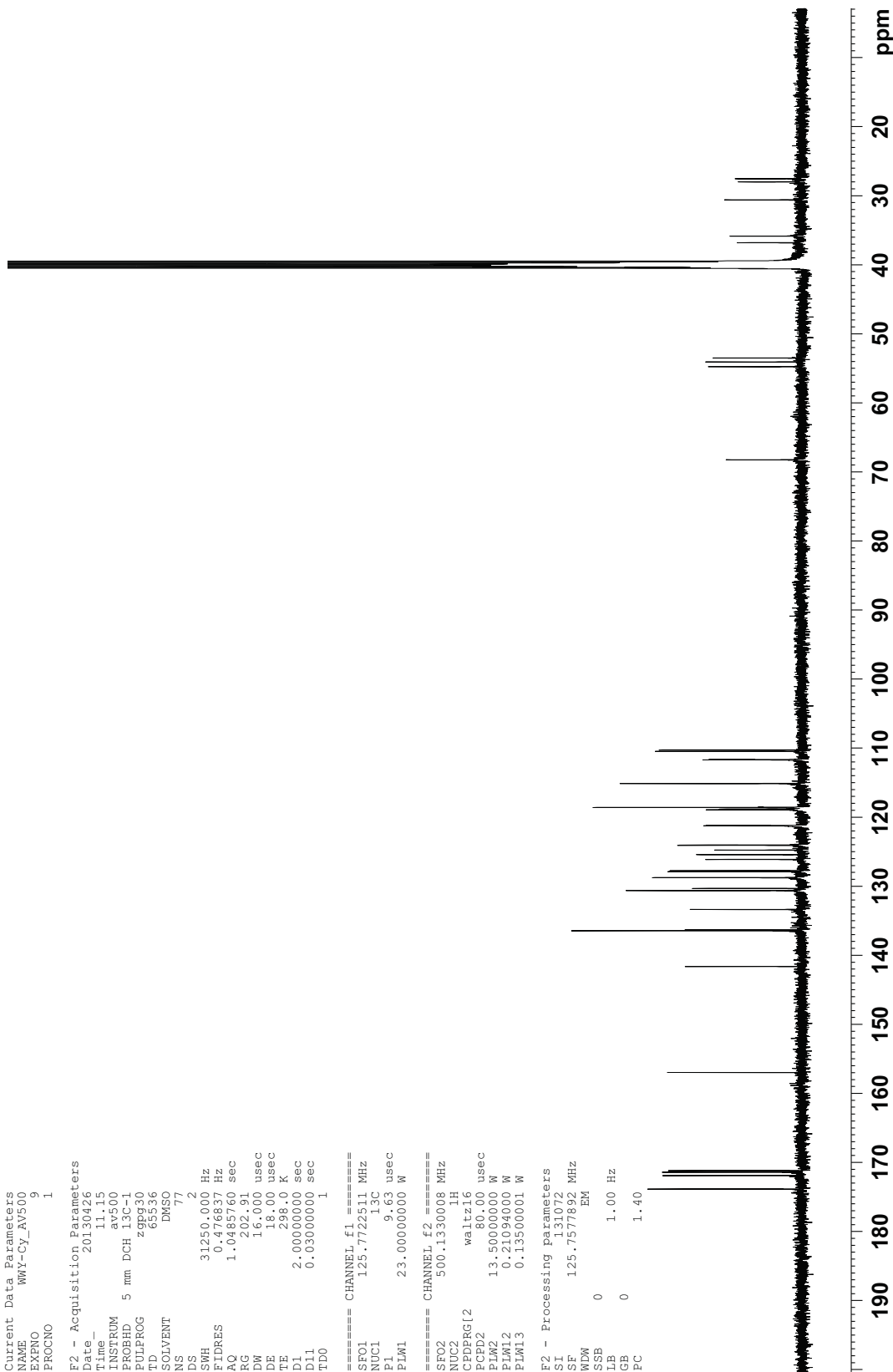
Current Data Parameters
NAME WXY-Cy_AV500
EXNO 9
PROCNO 1

F2 - Acquisition Parameters
Date_ 20130426
Time_ 11.15
INSTRUM av500
PROBHD 5 mm DCH-1
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 77
DS 2
SWH 31250.000 Hz
FIDRES 0.476837 Hz
AQ 1.0485760 sec
RG 202.91
DW 16.000 usec
DE 18.00 usec
TE 298.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

===== CHANNEL f1 =====
SFO1 125.7722511 MHz
NUC1 13C
P1 9.63 usec
PLW1 23.00000000 W

===== CHANNEL f2 =====
SFO2 500.1330008 MHz
NUC2 1H
CFDPRGf2 waltz16
PCPD2 80.00 usec
PLW2 13.50000000 W
PLW12 0.21094000 W
PLW13 0.13500001 W

F2 - Processing parameters
SI 32768
SF 125.7577892 MHz
RG 655
RES 0
SSB 0
LB 1.00 Hz
GB 0
PC 1.40



Compound 5

Current Data Parameters
NAME WWY-Cy_AV500
EXPNO 6
PROCNO 1

F2 - Acquisition Parameters
Date_ 20130305
Time 14:50
INSTRUM spect
PROBHD 5 mm DCH 13C-1
PULPROG mlevetgp.js
TD 2048
SOLVENT DMSO
NS 2
DS 8
SWH 5000.000 Hz
FIDRES 2.441406 Hz
AQ 0.2048000 sec
RG 37.94
RG2 100.000 usec
TE 298.0 K
D0 0.00000300 sec
D1 2.00000000 sec
D9 0.06000000 sec
D11 0.03000000 sec
D12 0.00000000 sec
D16 0.00000000 sec
IN0 0.00020000 sec
L1

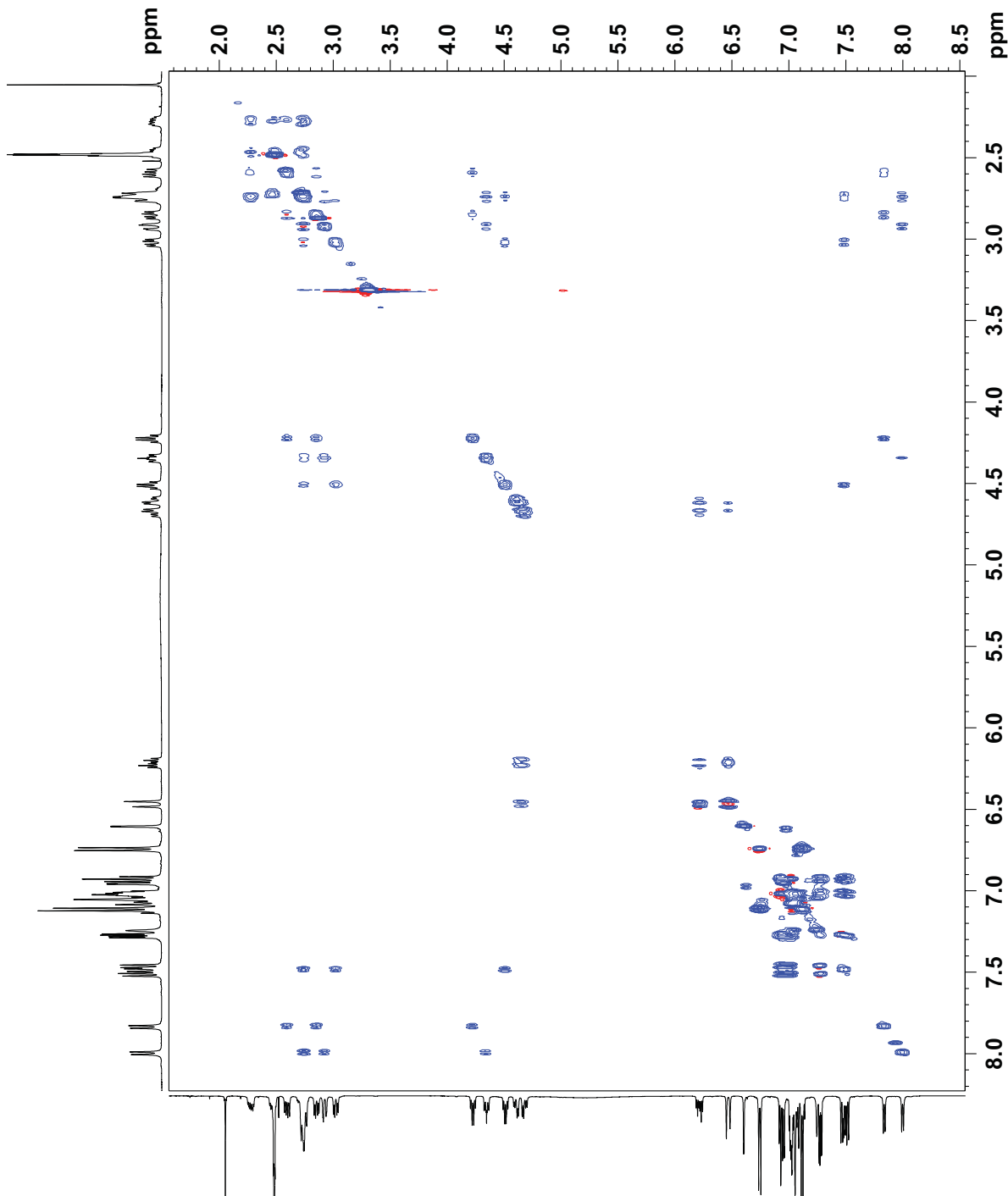
===== CHANNEL f1 =====
SF01 500.1325007 MHz
NUC1 13C
P1 9.10 usec
P2 19.00 usec
P5 26.68 usec
P6 40.00 usec
P7 80.00 usec
P17 2500.00 usec
PL1 13.40000000 W
PL10 0.84375000 W

===== GRADIENT CHANNEL =====
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPZ1 30.00 %
GPZ2 30.00 %
P16 1000.00 usec

F1 - Acquisition parameters
TD 256
SF01 500.1325 MHz
FIDRES 19.31326 Hz
SFO2 500.130135 MHz
F1MODE Echo-Antiecho

F2 - Processing parameters
SI 2048
SF 500.1300135 MHz
WDW QSIH2
SSB 0 Hz
LB 0
GB 0
PC 1.00

F1 - Processing parameters
SI 2048
SF 500.130135 MHz
WDW QSIH2
SSB 0 Hz
LB 0
GB 0



Compound 5

Current Data Parameters
NAME WW-Cy_AV500
EXPNO 4
PROCNO 1

F2 - Acquisition Parameters
Date_ 20130305
Time 15:20
INSTRUM spect
PROBHD 5 mm DCH 13C-1
PULPROG hsqcdegtp
TD 2048
SOLVENT DMSO
NS 2
DS 16
SNR 5000.000 Hz
FIDRES 2.4465 Hz
AQ 0.2048000 sec
RG 202.91
DW 100.000 usec
TE 300.2 K
CNS2 145.0000000
D0 0.0000300 sec
D1 1.5000000 sec
D11 0.0000000 sec
D13 0.0000400 sec
D16 0.0002000 sec
DELTA 7.0000000 sec
IN0 0.0001990 sec
ZCOPTNS

===== CHANNEL f1 =====
NUC1 13C
P1 9.50 usec
F2 19.00 usec
PL1 13.50000000 W

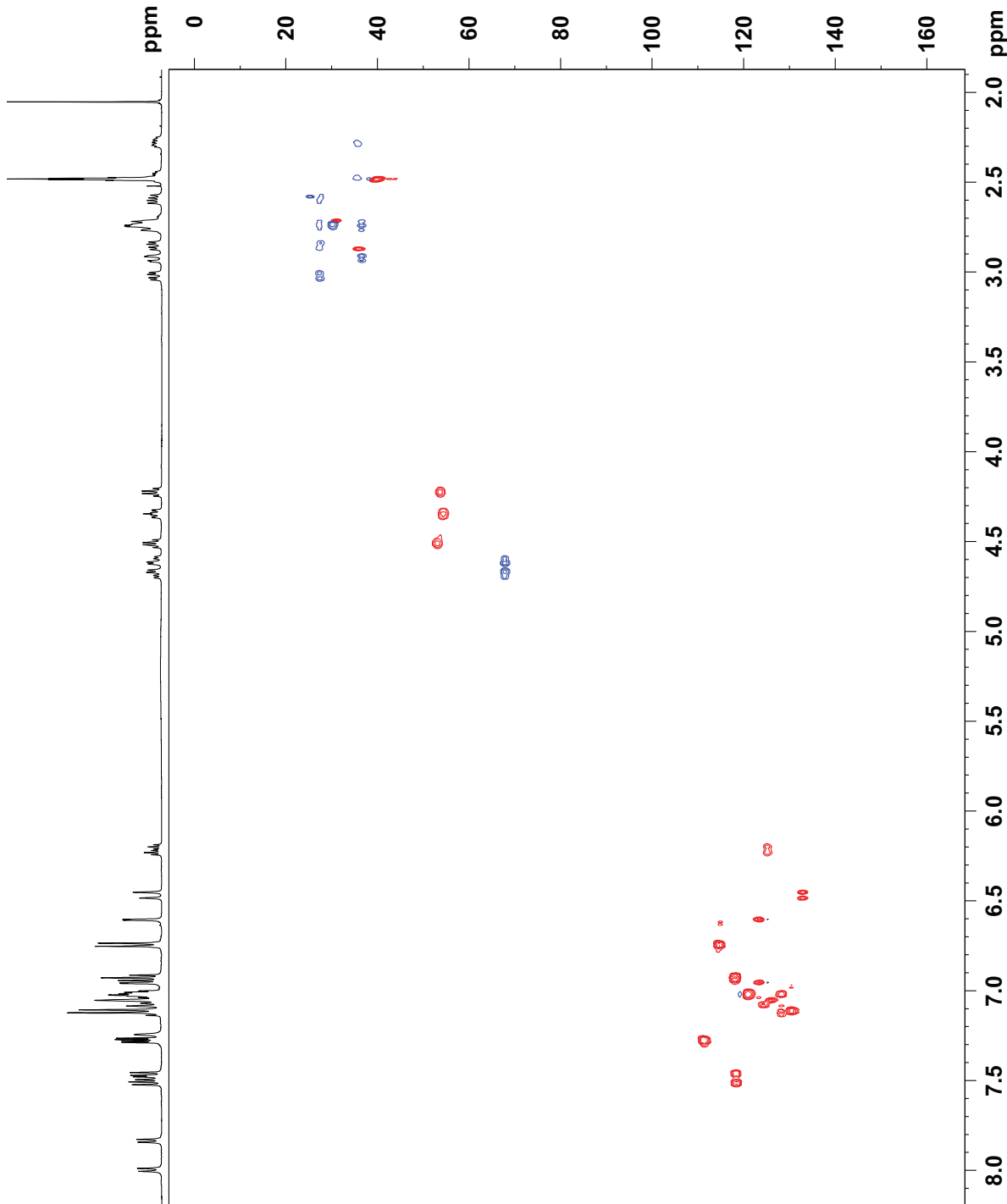
===== CHANNEL f2 =====
NUC2 13C
P2 9.53 usec
PL2 23.01399994 W
PLW2 0.43557000 W

===== GRADIENT CHANNEL =====
GPM1[1] SMSQ10.100
GPM1[2] SMSQ10.100
GPM2[1] 80.00 %
GPM2[2] 80.00 %
P16 1000.00 usec

F1 - Acquisition Parameters
TD 65536
FIDRES 125.7258 MHz
FIDRES 98.146988 Hz
SN 199.778 ppm
FMODE Echo-Antiecho

F2 - Processing Parameters
SI 2048
SF 500.1300135 MHz
AQ 0.2048 sec
SSB 2
LB 0 Hz
GB 0
PC 1.00

F1 - Processing Parameters
SI 2048
MC2 echo-antlecho
CSTPRG2 g3gpgp
NORM COSYPPTRAP
SSB 2
LB 0 Hz
GB 0



Compound 5

Current Data Parameters
NAME WW-CY_AV500
EXPNO 5
PROCNO 1

F2 - Acquisition Parameters
Date_ 20130305
Time 15:35
PULPROG zgpg30
PROBHD 5 mm DCH 13C-1
PULPROG hmbcpg12ndqf
TD 2048
SOLVENT DMSO
NS 2
DS 16
SNR 6009.615 Hz
F2 125.7704 MHz
AQ 0.703936 sec
RG 202.91
DW 83.200 usec
DE 15.00 usec
TE 298.0 K
CNS16 120.0000000
CNS17 160.0000000
CNS18 120.0000000
CNS19 0.0000000
CNS20 1.500000000 sec
D1 0.07142857 sec
D6 0.07142857 sec
D16 0.00220000 sec
IN0 0.00001990 sec

===== CHANNEL f1 =====
SFO1 500.1330008 MHz
NUC1 13C
P1 9.50 usec
PL1 19.00 usec
PLW1 13.50000000 W

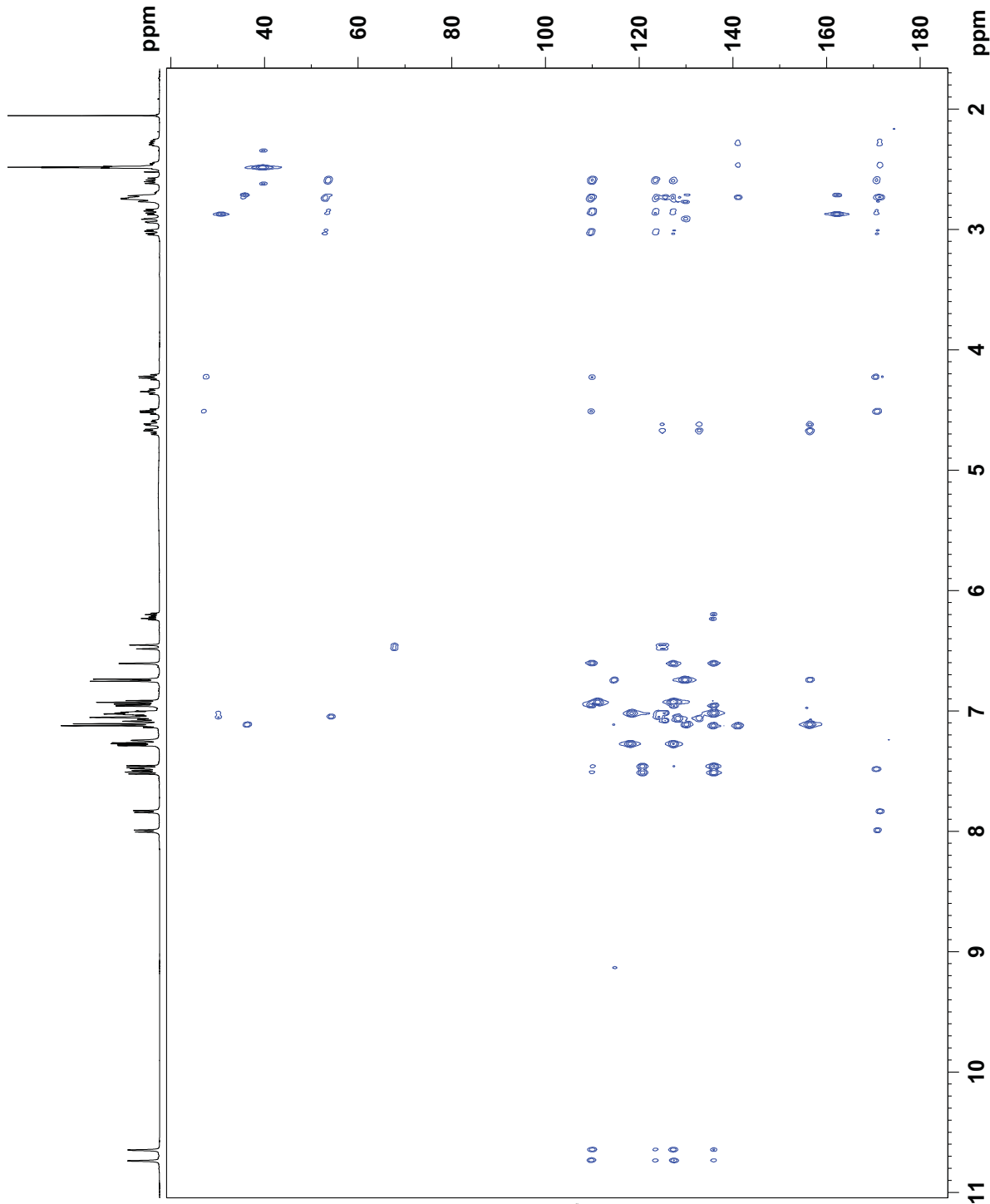
===== CHANNEL f2 =====
SFO2 125.7703648 MHz
NUC2 13C
P2 13.00 usec
PLW2 23.0139994 W

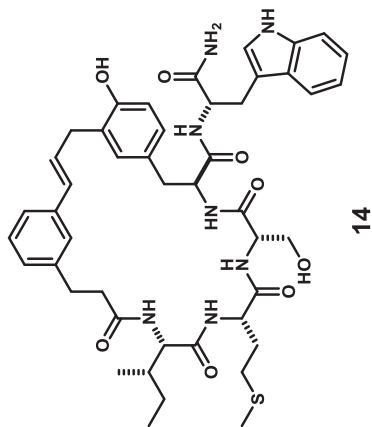
===== GRADIENT CHANNEL =====
GPM11 50.00 %
GPM12 50.00 %
GPM13 50.00 %
GPM14 50.00 %
GPM15 50.00 %
GPM16 50.00 %
GPM17 50.00 %
GPM18 50.00 %
GPM19 50.00 %
GPM20 50.00 %
GPM21 50.00 %
GPM22 30.00 %
GPM23 40.00 %
GPM24 40.00 %
GPM25 -10.00 %
GPM26 -5.00 %
PL6 1000.00 usec

F1 - Acquisition parameters
TD 256
SFO1 125.7704 MHz
F2 500.1330008 MHz
SN 199.774 PPM
F1MODE QF

F2 - Processing parameters
SI 2048
SF 500.1300135 MHz
WDW QF
SS 2
LB 0
GB 0
PC 1.00

F1 - Processing parameters
SI 2048
MC2 QF
SF 125.7578472 MHz
WDW N
SSB 1
LB 0
GB 0



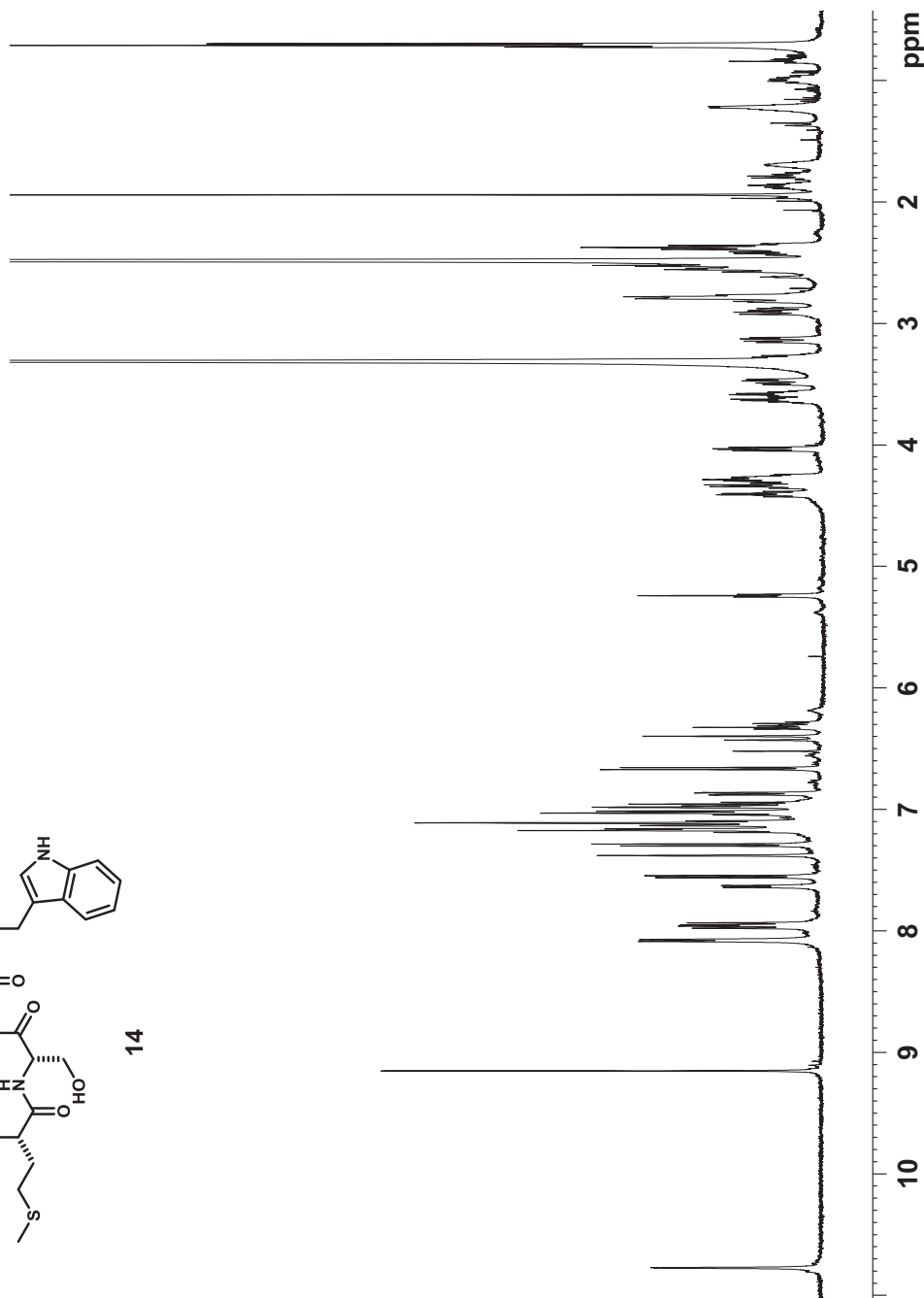


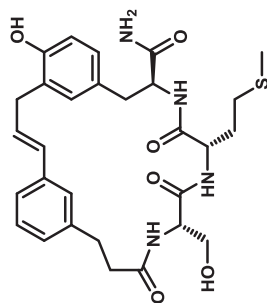
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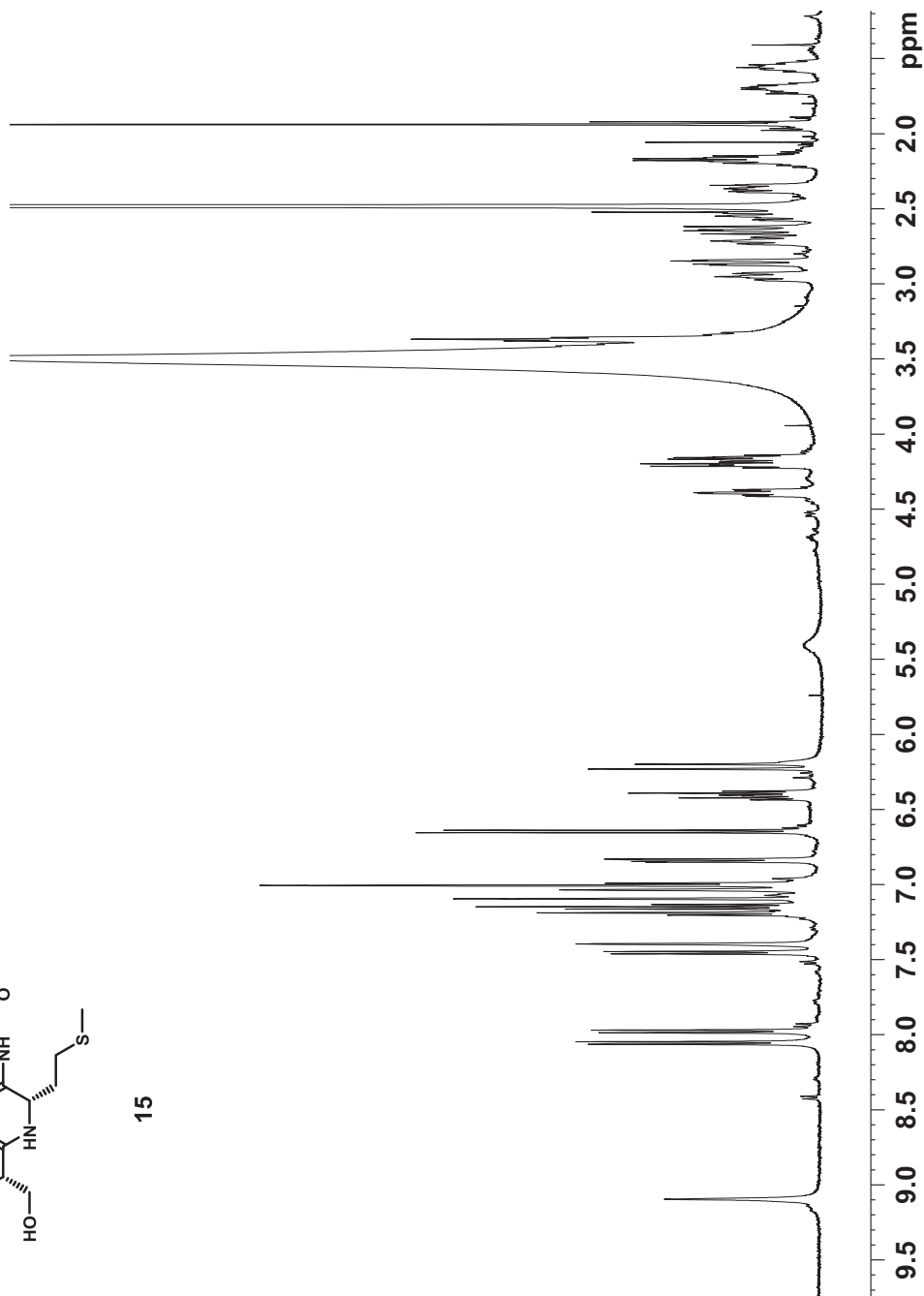
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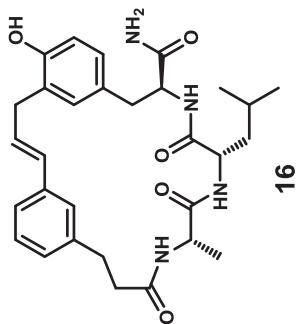
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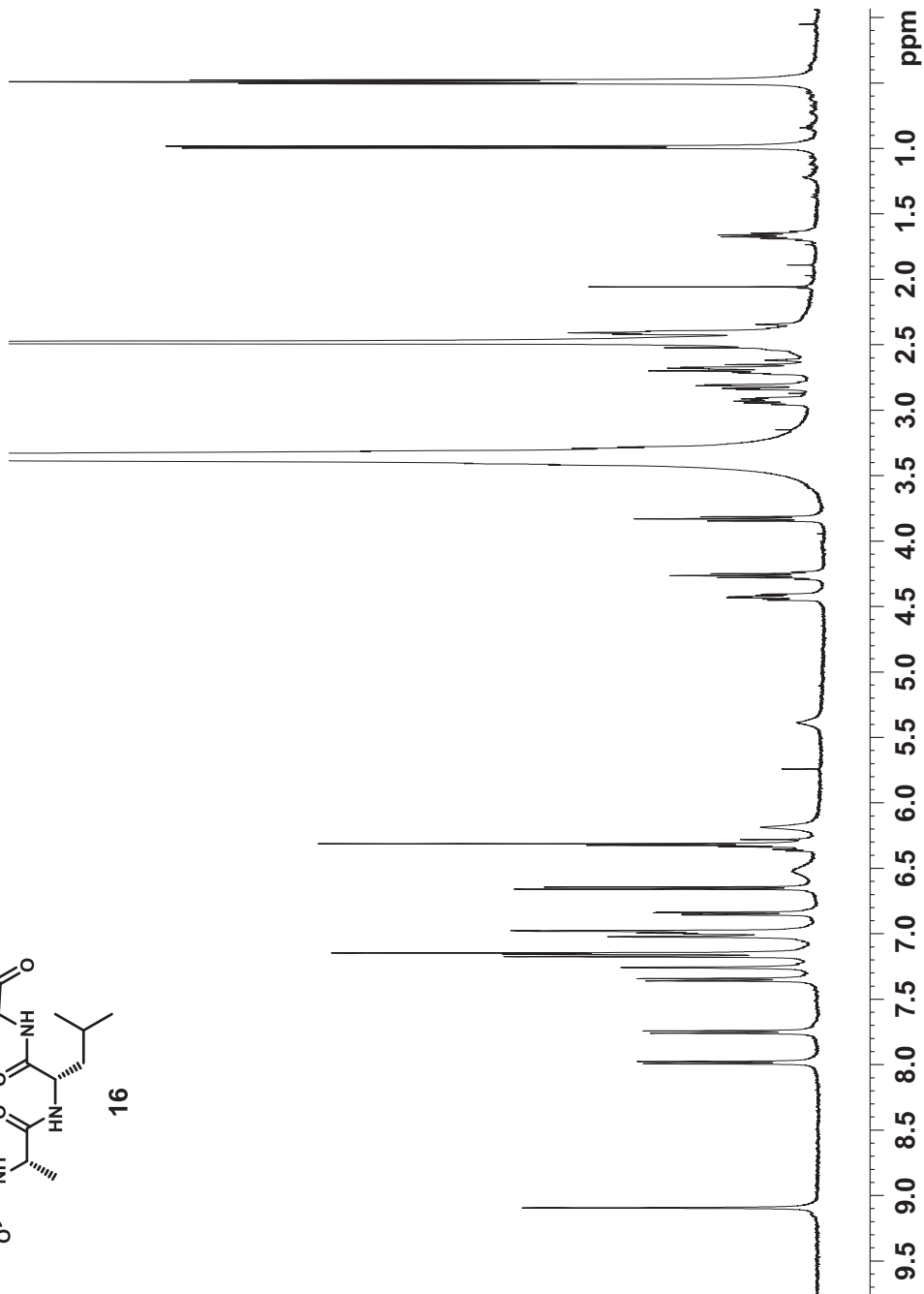
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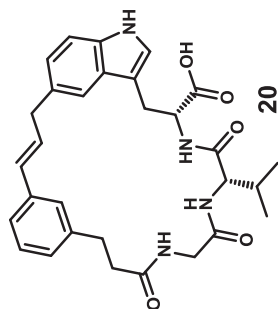
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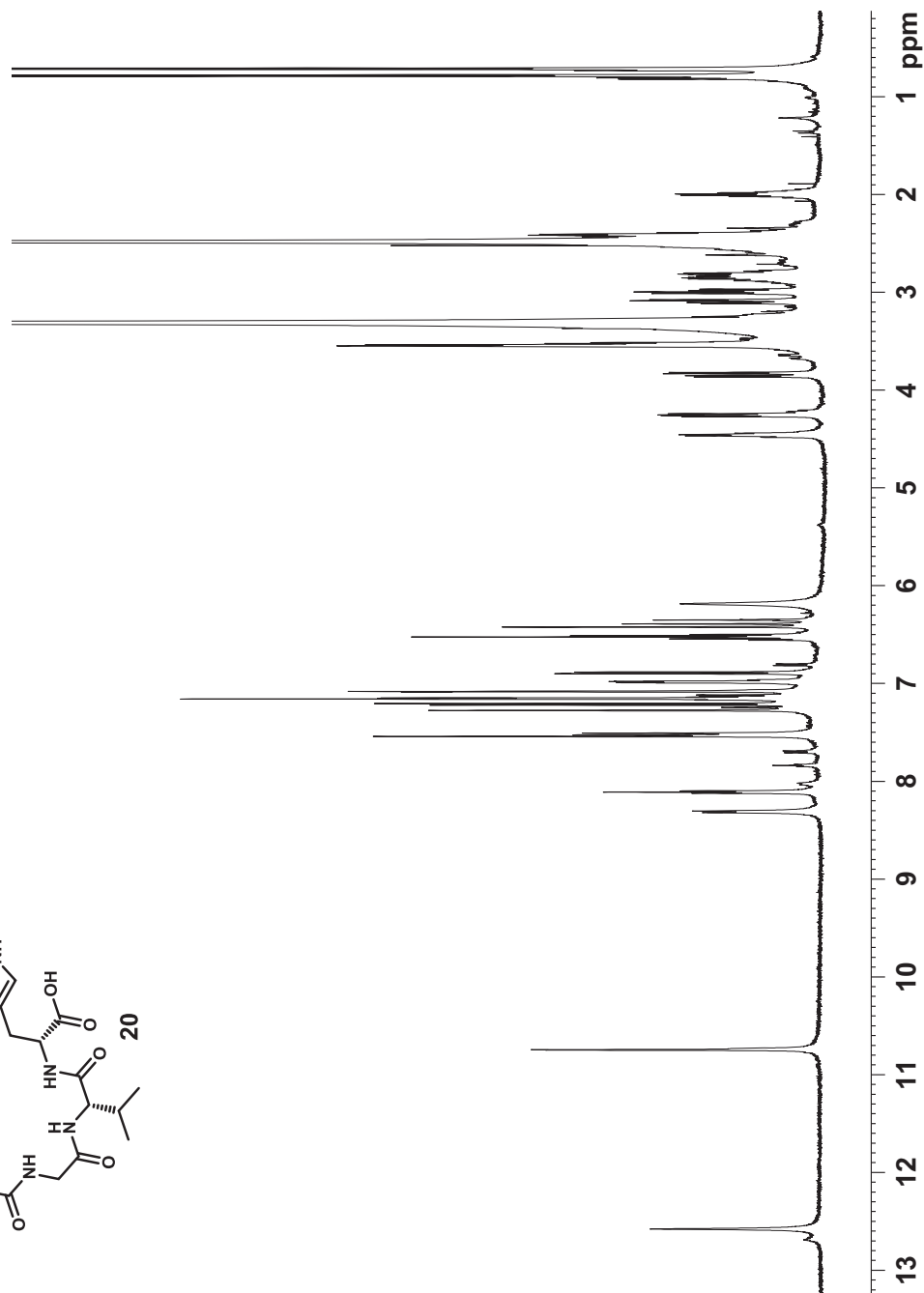


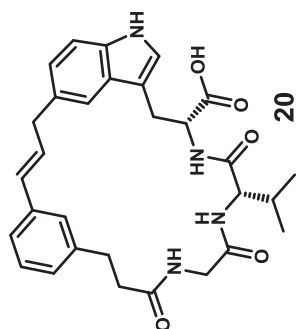
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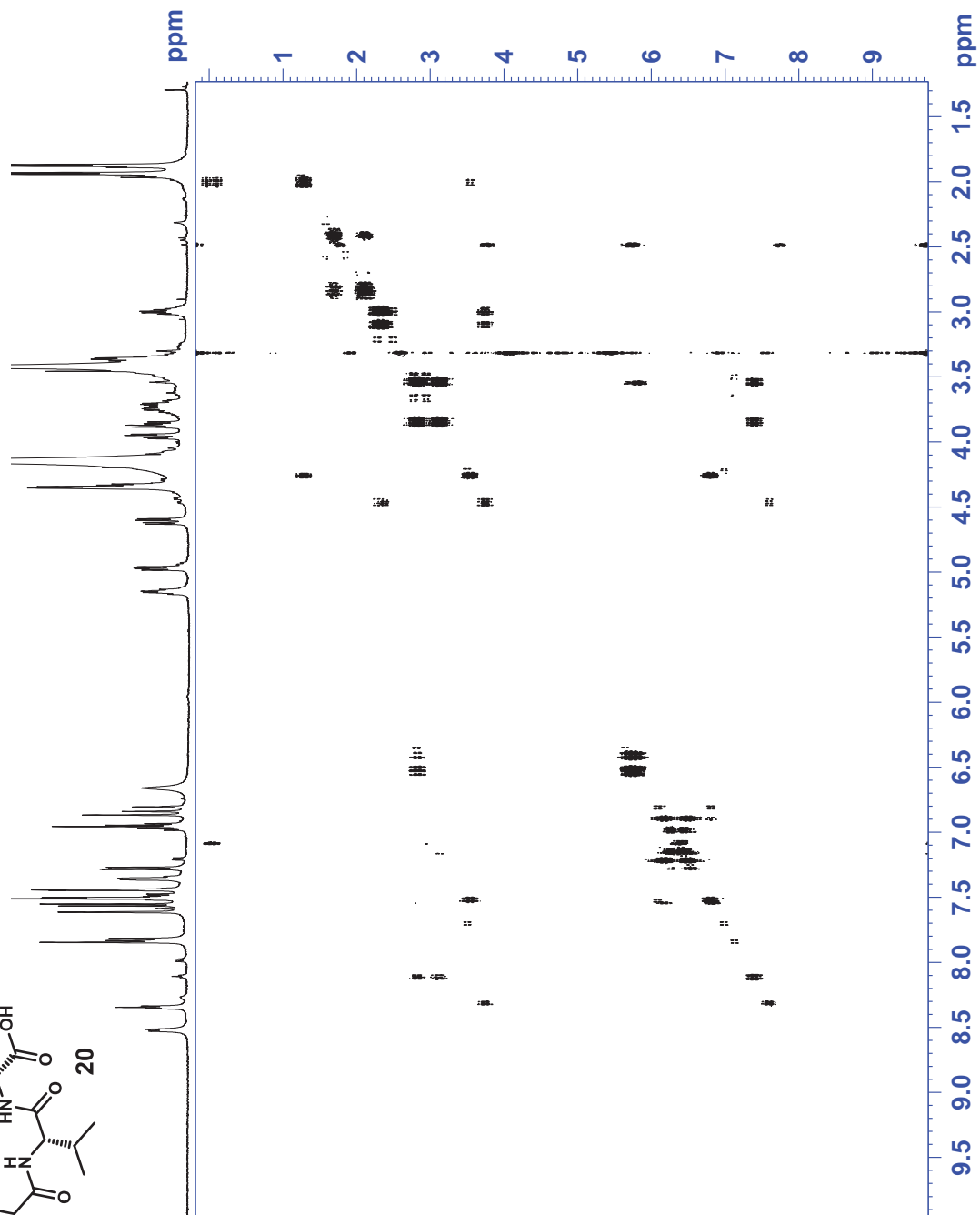
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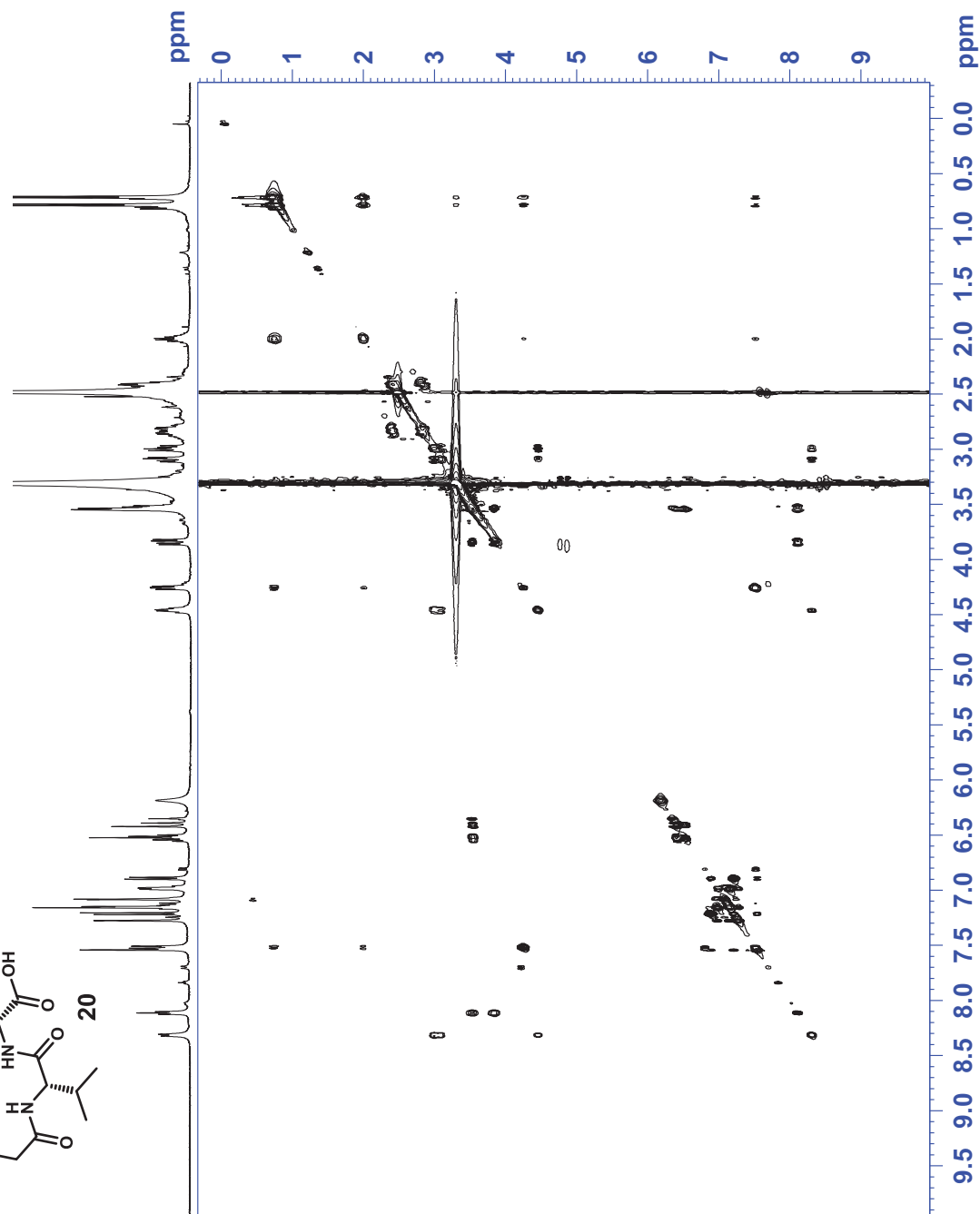
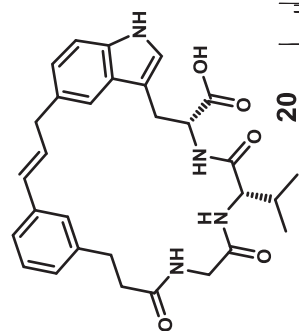
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GB 0
PC 1.00





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 EXPNO 3
 PROCNO 1
 F1 - Acquisition parameters
 TD 286
 SF01 500.1308 MHz
 FIDRES 19.536423 Hz
 SW 10.000 ppm
 FhMODE States-TpPI
 F2 - Processing parameters
 SI 2048
 SF 500.1300135 MHz
 WDW SINE
 SSB 1
 LB 0 Hz
 GB 0
 PC 1.00
 F1 - Processing parameters
 SI 2048
 MC2 States-TpPI
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 WDW GM
 SSB 1
 LB 0 Hz
 GB 0



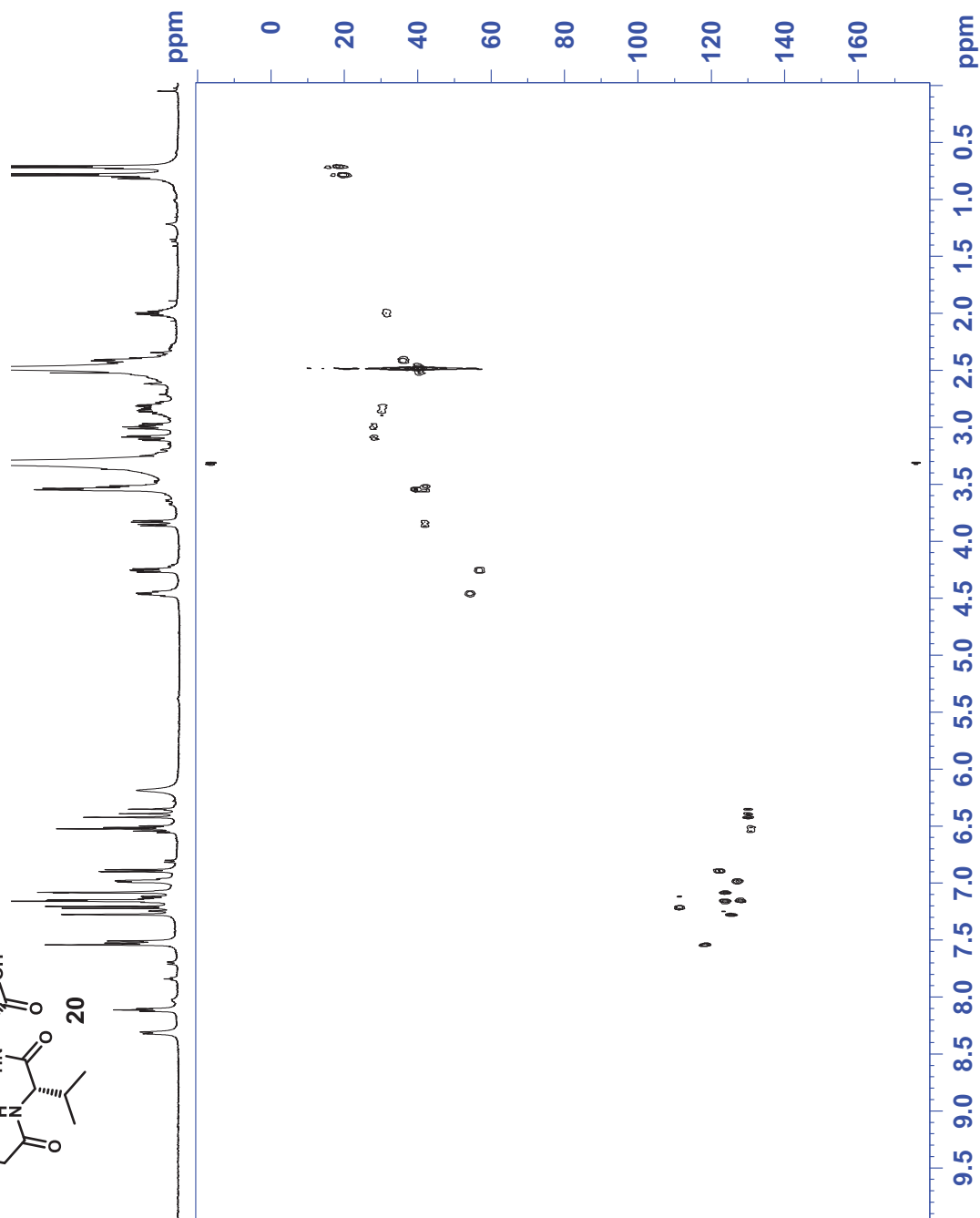
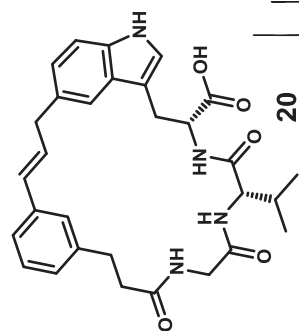


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 PROCNO 1

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 FIDRES 20.121468 Hz
 SW 10.299 ppm
 FMODE Echo-Antiecho

F2 - Processing parameters
 SI 2048
 SF 500.1300135 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 2048
 MC2 echo-antiecho
 SF 500.1300135 MHz
 WDW TRAP
 SSB 2
 LB 0 Hz
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Current Data Parameters
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 PROCNO 1

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 FIDRES 138.969650 Hz
 SW 200.000 ppm
 FnmODE Echo-Antiecho

F2 - Processing parameters
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 SSB 2
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F1 - Processing parameters
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 MC2 echo-antiecho
 SF 125.7578472 MHz
 WDW QSINE
 SSB 2
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reaction times (16h). The anomalous loss of two mass units [M-2] from acidolysis of **13** to form labeled **9** could not be observed with Sc(OTf)₃ as **9** is formed in only trace quantities under these conditions.

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Chapter 5 - Macrocycle shape diversity through large-ring forming Friedel-Crafts alkylations

5.1. Introduction

Small molecules are powerful tools to interrogate biological processes. As drugs discovery efforts expand to increasingly challenging targets, including expanded, shallow ligand binding surfaces and protein-protein interfaces, identifying potent and selective small molecule ligands has become an increasingly difficult challenge.¹⁻⁵ Natural products have been a rich source of biologically active compounds.⁶⁻⁸ These frequently feature complex molecular architectures beyond the structural space occupied by traditional screening libraries and are often uniquely capable of modulating challenging biological targets.⁹ So-called diversity oriented synthesis (DOS) of natural product-like libraries has become an area of considerable interest.¹⁰⁻¹³ A structural motif often observed in medicinally valuable natural products is the macrocycle.^{7,9,14-17} Despite renewed enthusiasm for this structural class serving as therapeutic leads, general methods to generate macrocycle diversity are lacking.¹⁷

We are interested in methods to prepare diverse composite macrocyclic peptidomimetics in short reaction sequences beginning with unprotected peptides.¹⁸ In this regard, nature produces extraordinary structural diversity via modification of tryptophan.^{19,20} In fact, tryptophan is a unique amino acid in this regard; there are multiple, potentially competing nucleophilic sites on the indole nucleus (Figure 1). We have exploited this promiscuity in the context of large-ring forming reactions.²¹

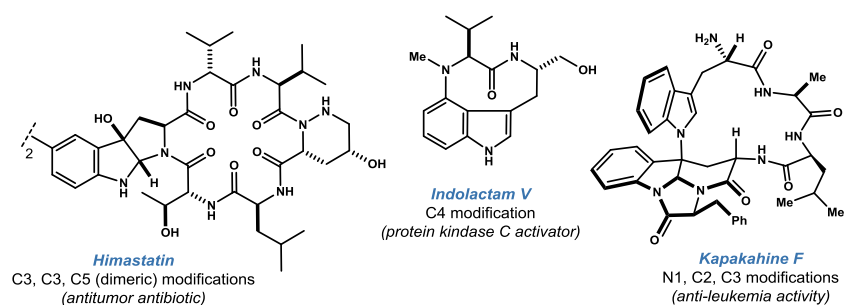


Figure 1. Natural products derived from modification of tryptophan

We have recently described an electrophilic reagent able to directly engage electron rich aromatic amino acids via large-ring forming Friedel-Crafts alkylations.²² Reactions proceeded rapidly and efficiently to form macrocyclic composites of **1** and peptides containing tyrosine and 4-aryloxyprolines (Figure 2A). Additionally, reaction of **1** with Trp-Trp-Tyr provided a mixture of diverse macrocycles via promiscuous alkylation of indole (Figure 2B).²³ Here we examine the scope and functional group tolerance of this method and identify numerous novel macrocyclic substructures. A pilot macrocycle library has been prepared and fully characterized. Statistical measures were utilized to assess diversity with respect to commercial screening libraries and to evaluate shape diversity amongst isomeric macrocycles.²⁴⁻²⁶

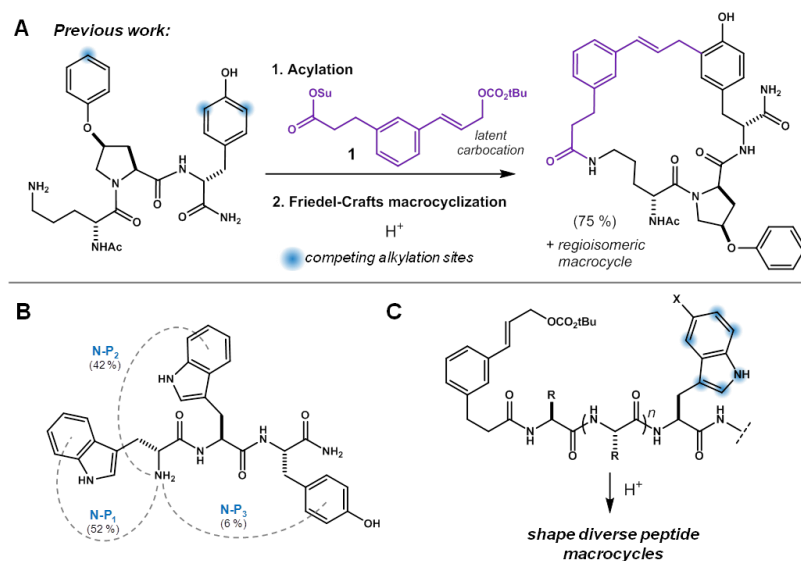


Figure 2. **A.** Competitive large-ring forming Friedel-Crafts alkylations of 4-aryloxyproline and tyrosine. **B.** Friedel-Crafts macrocyclization of Trp-Trp-Tyr with **1** provide a mixture of N-P₁₋₃ alkylated macrocycles **C.** This-work: Divergent reactivity of substituted tryptophan derivatives provide mixtures of shape diverse macrocyclic peptidomimetics.

5.2. Results and Discussion

Initial experiments were designed to investigate the scope of Friedel-Crafts macrocyclization employing template **1**. The efficiency of peptide macrocyclization methodologies are notoriously susceptible to changes in peptide composition, length, and stereochemistry.²⁷⁻²⁹ Importantly, our method is largely insensitive to these parameters. In spite of employing reactive carbocationic intermediates, basic, acidic, and nucleophilic residues were well tolerated. Turn-inducing residues were not required and peptides containing 3-5 amino acids cyclized efficiently, an outcome difficult to achieve via direct lactamization.²⁷ Tryptophan 5-substitution had notable effect on product distribution and macrocycle diversity in these systems.

5.2.1. Preparation, Isolation and Characterization of Isomeric Macrocycles

From the onset we chose to incorporate 5-substituted tryptophan derivatives. In preliminary studies alkylation of this position was dominant.²³ We hypothesized blocking this position would temper indole reactivity and provide a more uniform distribution of isomeric

macrocycles. We employed SIW(5-Br)A as a model tetrapeptide to investigate the effect of 5-bromo substitution. N-terminal acylation of SIW(5-Br)A with template **1** provided seco-composite **2** (Figure 3A). Exposure of **2** to 75 mM methansulfonic acid in nitromethane at room temperature provided a mixture of five isomeric macrocycles. These could be readily resolved by HPLC (Figure 3B). Together these products accounted for ~90 % total peak area indicating this reaction proceeded efficiently. Also, these reactions were remarkably fast; complete conversion was observed within 15 minutes.

Individual acidolysis products were resolved by preparative HPLC and their structures determined by 2D homo- and heteronuclear correlation NMR spectroscopy. Products **3** - **7** were identified as five novel macrocyclic substructures with 19, 20, 21, 23-membered rings. The major product **6** (51%) is derived from alkylation of indole-C6 with minor constituents arising from substitution at *N1* (13%), *C2* (13%), *C3* (19%), and *C4* (4%). Alkylation of *C3* induced pyrroloindoline formation by trapping of the intermediate indolium ion with the proximal amine. This product was isolated as a single diastereomer which was assigned as the *endo*-pyrroloindoline by diastereotopic proton assignment of the Trp- β -CH₂ and *syn* NOE to the cinnamyl methylene as previously described.²³ Natural occurring indole alkaloids commonly possess the pyrroloindoline motif. However this all carbon quaternary macrocyclic ring juncture appears to be unique to this chemistry.

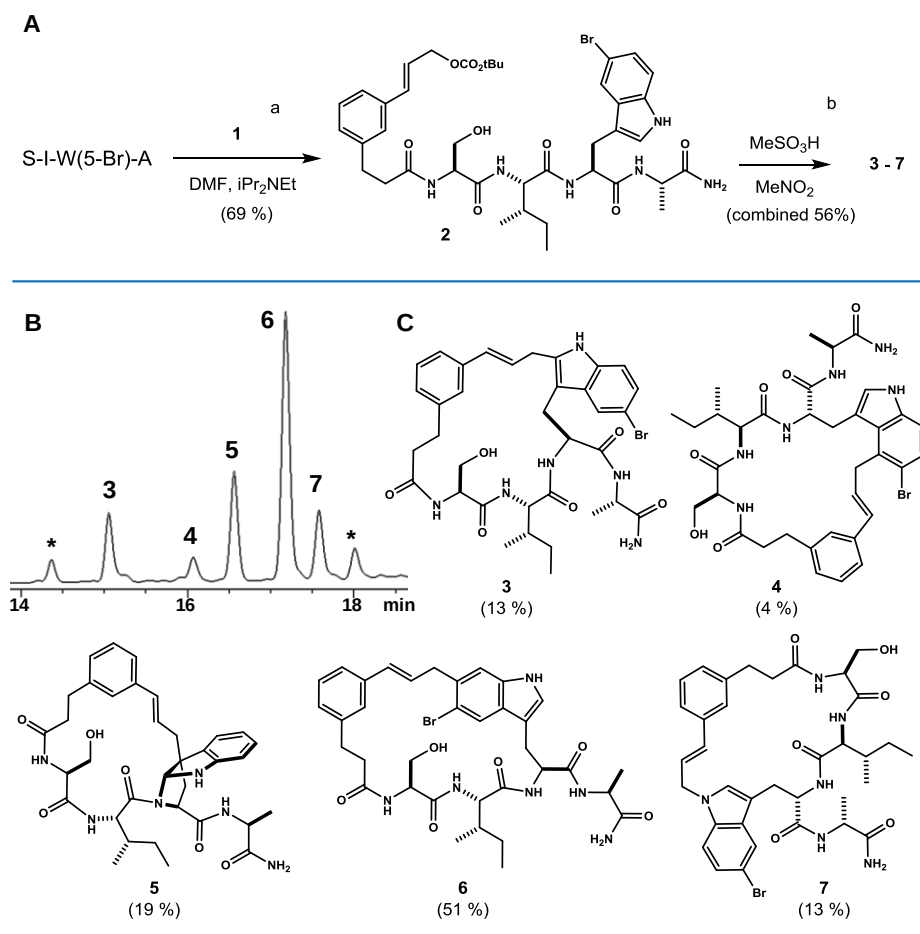
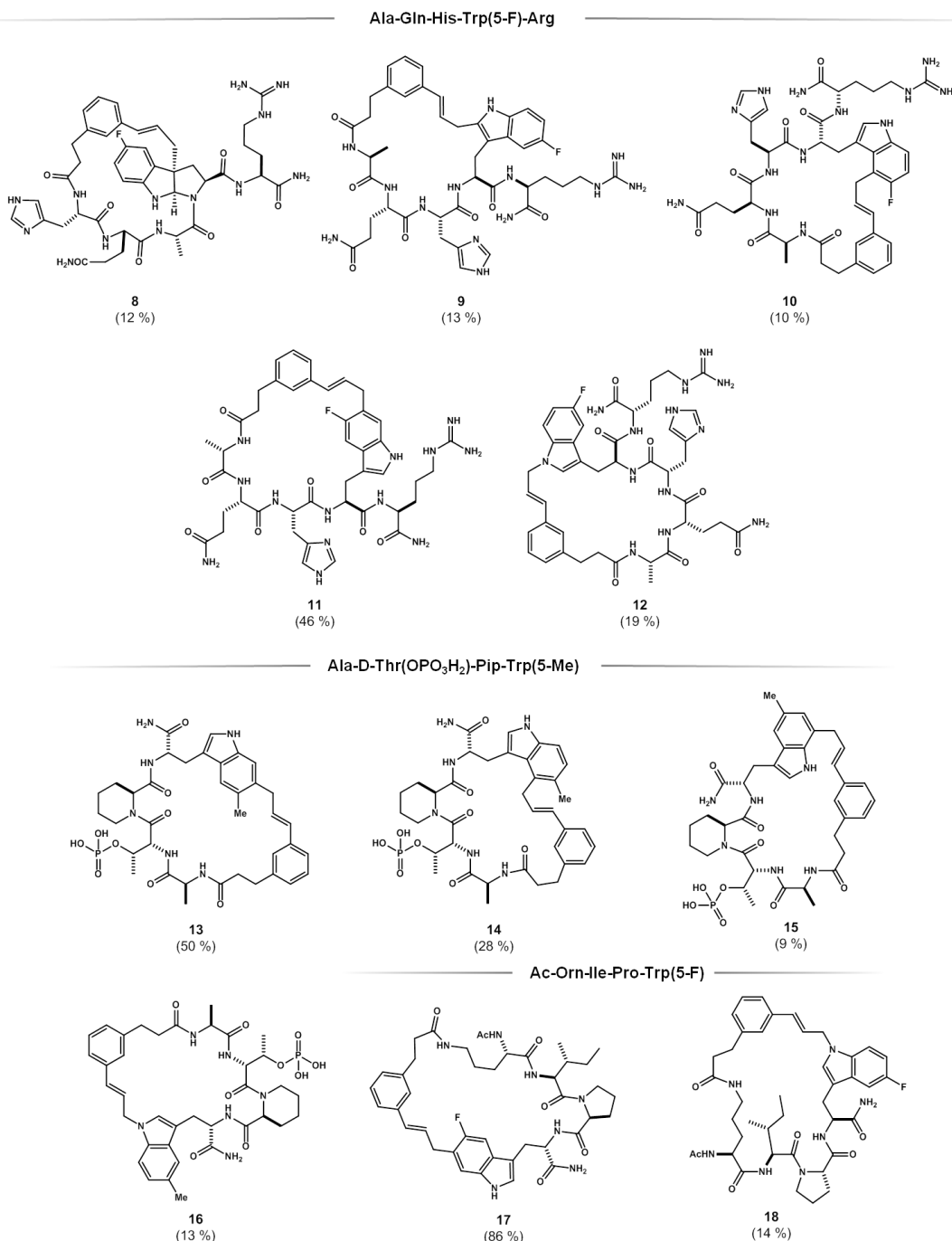


Figure 3. A. Divergent macrocyclization of SIW(5-Br)A with reagent **1**. conditions: a) peptide (1 eq.), **1** (1 eq.), $i\text{Pr}_2\text{NEt}$ (4 eq.), DMF (50 mM), rt; b) MeSO_3H (15 eq.), MeNO_2 (5 mM in **2**), rt, 2h. **B.** Macrocycles **3-7** obtained by acidolysis of **2**. Products isolated by preparative HPLC (inset, C18, $\text{MeCN}/\text{H}_2\text{O}$); combined isolated yield 56%. Yields in parentheses represent relative isomer ratio derived from chromatogram integration at 254 nm. Asterisk denotes non-isomeric products – not isolated.

5.2.2. Investigation of function group compatibility.

Cyclization of SIW(5-Br)A demonstrated the compatibility of this method with alcohols. No alkylation or elimination of Ser(β -OH) was observed. There remained potential that the carbocationic intermediates generated in this chemistry would not be compatible with basic or strongly nucleophilic functional groups present in natural amino acids due to competing heteroatom alkylation. To evaluate this possibility we processed pentapeptide AQHW(5-F)R with template **1**. Cyclization proceeded efficiently to provide composite macrocycles **8 - 12**

Table 1. Composite macrocycles obtained in two steps from template **1** and the indicated unprotected peptides (listed above product). Percentages in parentheses are product ratios determined by HPLC-UV (254 nm).



arising solely from tryptophan alkylation (Table 1). No arginine or histidine alkylation was observed. Analogous to previous examples, Indole C3 alkylation exclusively formed the *endo*-pyrroloindoline (**8**) suggesting a general mechanism of stereoiduction may be operative.

Phosphorylated peptides play a central role in many biological process and numerous phosphorylation dependent binding epitopes have been exploited for therapeutic applications.³⁰ This functionality has been scarcely reported in macrocyclic peptidomimetics, partly due to incompatibility with many cyclization strategies. We prepared Ala-D-pThr-Pip-Trp(5-Br) featuring an isostere for pSer/Thr-Pro motif commonly recognized by phosphorylation dependent peptidylprolyl isomerases.³¹⁻³⁴ The phosphate ester was well tolerated. Following acylation with **1**, acidolysis with MeSO₃H cleanly afforded macrocycles **13** - **16** derived from alkylation at indole *N1*, *C4*, *C6*, and *C7*. No elimination or alteration of the phosphothreonine residue was observed. Interestingly, products derived from *C2* and *C3* alkylation were not isolated. This was again observed from acidolysis of Orn-Ile-Pro-Trp(5-F) acylated with **1** on the side-chain amino group of ornithine. Product **17** comprised 86% of the reaction mixture and only a single additional indole N-alkylated regioisomer was isolated (**18**).

The perturbed product distribution may be due to geometric constraint imparted from the pipecolate and proline residues. The above data suggest the relative rates of indole alkylation are not governed solely by the electronics of the indole nucleus, which would presumably favor *C3* alkylation. Rather, strain associated with the macrocyclic transition states leading to discrete regioisomeric products plays an important role and will likely be dependent on peptide composition.

5.2.3. Effect of Trp C5-substitution on Product Distribution

Product mixtures generated in these processes would ideally be composed of an evenly-distributed collection of composite macrocycles. This would maximize chemical space coverage and alleviate common issues associated with biological screening of compound mixtures. Conversely, the ability to enhance the abundance of specific isomers may become valuable as specific components are identified by screening exercises. It appeared likely this could be achieved by electronic perturbation of indole moiety. To investigate this possibility we compared

the relative alkylation rates of Phe-Trp-Thr congeners **19** and **20**, possessing moderately electron-donating and withdrawing groups respectively.

Acylation of **19** with template **1** followed by treatment with MeSO₃H afforded a mixture of three isomeric macrocycles (Figure 3). Alkylation of C4 (49%) was favored, with minor products derived from substitution of C2 (31%) and C3 (20%). Conversely, products derived from acidolysis of 5-fluorotryptophan containing peptide **20** were more evenly distributed. Alkylation of every available indole position was observed, though C4-alkylation remained dominant (Figure 4B). *Full spectral assignment of compounds derived from these sequences is ongoing. Assignment of the putative C6-alkylated macrocycle derived from **20** is complicated by slow interconversion of conformations on the NMR time scale at temperatures up to 70°C.*

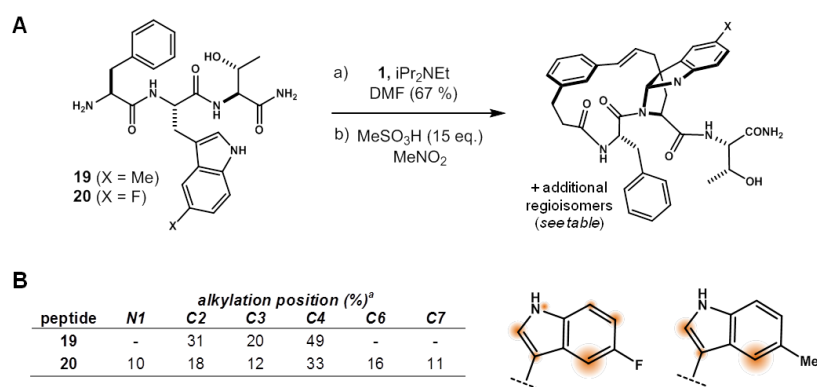


Figure 4. Comparison of product distribution from acidolysis of homologous peptides **19** and **20**. **A.** Ligation of **19** and **20** with **1** followed by acidolysis affords sets of isomeric macrocycles. Alkylation at C3 affords pyrroloindoline products shown. Conditions: a) peptide (1 eq.), **1** (1 eq.), iPr₂NEt (4 eq.), DMF (50 mM), rt; b) MeSO₃H (15 eq.), MeNO₂ (5 mM in **2**), rt, 2h. **B.** Comparison of product distribution. Table and Indole heat map proportional to percentage of substitution determined by HPLC (UV 254 nm).

This initial data demonstrate that subtle electronic perturbation of the indole nucleus can effect product distribution within homologous sequences. Although a more even distribution of composite macrocycles was observed from Trp(5-F) containing peptide **20**, the major product remained constant. This is further evidence that peptide composition has a considerable effect of product distribution in these systems, rather than the electronic predisposition of the indole

moiety. This bias for C4-alkylation was not observed in sequences described above featuring either electron withdrawing Trp(5-F), Trp(5-Br) or electron releasing Trp(5-Me).

5.2.4. Additional Nucleophiles

We next sought to explore the reactivity of additional nucleophilic aromatic amino acids. Thiophenylalanine is a commonly employed isostere for phenylalanine and the electronic character of thiophene is well-suited to react with **1**. As such, we prepared tripeptide Thr-Gln-Thi and investigated its propensity to engage **1** in large-ring forming reactions. Acylation of Thr-Gln-Thi with **1** followed by treatment with MeSO₃H afforded two isomeric macrocycles as observed by HPLC-MS. The major isomer resulted from alkylation of the thiophene 4-position (**22**, 71%). Surprisingly, NMR analysis of the minor isomer indicated the thiophene moiety was also 2,4-disubstituted. Despite what appeared to be similar structures the minor isomer exhibited a stark difference in polarity on hydrophobic stationary phase as well as distinct ¹H NMR spectroscopic characteristics, specifically with respect to the threonine residue. Full spectral assignment revealed an unambiguous HMBC correlation from Thr-H^β to the carbonyl carbon of the reagent. The anticipated analogous ThrH^α HMBC correlation was absent, suggesting an N-O acyl migration had occurred to form macrolactone **21**. Furthermore, The ThrH^N resonance integrated to 3H, presumably isolated as the TFA ammonium salt following preparative HPLC.

Although thiophene did not react with **1** precisely as anticipated, a new mechanism resulting in added structural diversity was identified. This atypical N- to O- migration is mechanistically intriguing. Presumably protonation of the carbonyl oxygen precedes nucleophilic attack of the β-hydroxyl group. The resulting macrolactone is likely not thermodynamically favored. However, protonation of the α-amine may render the reaction irreversible under these conditions. Alternatively, macrolactone **21** may occupy a conformation which precludes the reverse O- to N- migration.

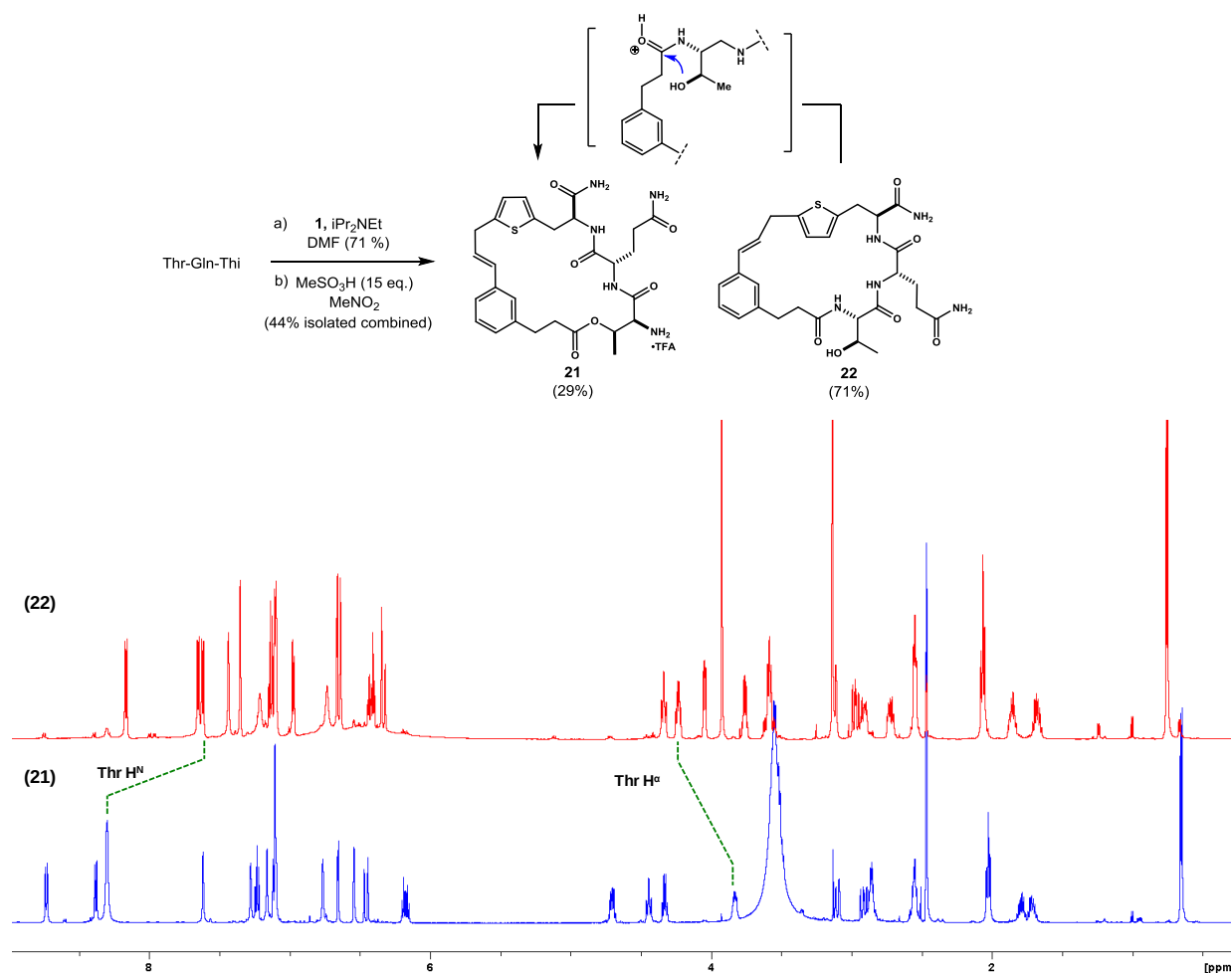


Figure 5. A. Acylation and Thr-Gln-Thi with **1** and subsequent Friedel-Crafts macrocyclization affords **21** and **22**. Conditions: a) peptide (1 eq.), **1** (1 eq.), $i\text{Pr}_2\text{NEt}$ (4 eq.), DMF (50 mM), rt; b) MeSO_3H (15 eq.), MeNO_2 (5 mM), rt, 2h. **B.** Comparison of ^1H NMR (600 MHz, $\text{DMSO}-d_6$) of macrocycles **21** and **22**.

Following the successful macrocyclization of thiophene containing oligopeptides, we explored the reactivity of benzothiophene in these systems. Analogous to indole, electrophilic substitution of benzothiophene typically occur on the heterocyclic ring, but are generally less regioselective. As such we anticipated a broad, diverse product distribution. Surprisingly HPLC-MS analysis of the product mixture derived from the acidolysis of Arg-Glu-Val-BnThi (**23**), revealed predominantly a single isomeric macrocycle. A combination of homo- and heteronuclear correlation spectroscopy identified this product to be **24**, derived from alkylation of arginine. This macrocycle showed an unique HMBC correlation from the cinnamyl methylene the guanidyl carbon at $\delta \sim 155$ ppm. Also distinctive to this linkage was an extended $^1\text{H}-^1\text{H}$

TOCSY correlation of the cinnamyl protons to the guanidyl H^N (Figure 6). Alkylation of arginine was not anticipated. Arginine was unreactive in previous examples (Table 1). Also sequences containing arginine (e.g. Gly-Ser-Pro-Arg) without an aromatic nucleophile resulted in a complex mixture of non-isomeric products, indicative of sequences which lack a competent nucleophile. Additional studies are necessary elucidate the factors leading to **24**. Potentially, intermediate alkylation of neighboring residues within Arg-Glu-Val-BnThi followed by cinnamyl transposition may aid in the formation of **24**. Also the proximity of Arg to the electrophilic center may play a role, though overall reaction efficiency has not correlated with the distance of the nucleophile to the cinnamyl moiety thus far.

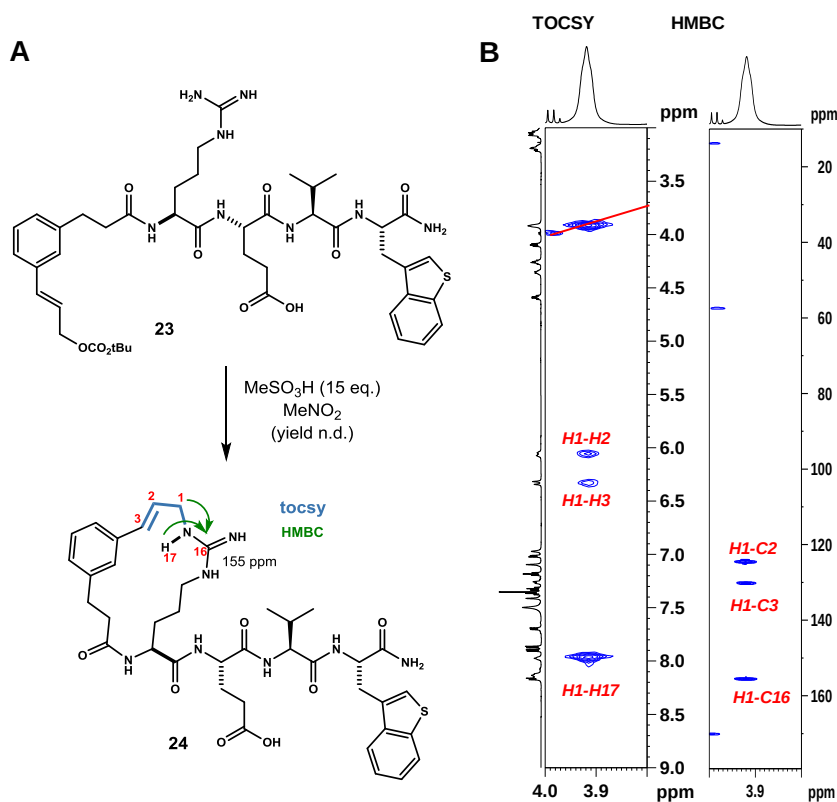


Figure 6. A. Acid treatment of **23** afford arginine alkylated macrocycle **24**. Conditions: MeSO₃H (15 eq.), MeNO₂ (5 mM), rt, 2h. B. Key TOCSY and HMBC indicating presence of cinnamyl guanidine.

5.2.5. Assessing molecular and shape diversity of macrocyclic peptidomimetics

Macrocycles are uniquely capable of recapitulating the larger interaction surfaces which often define challenging biological targets. Macrocycles occupy chemical space outside of typical descriptors of 'drug-likeness' while retaining favorable pharmacokinetic properties.^{9,15} Macrocycle diversity can be divided into two measures; 1. Chemical diversity displayed on the scaffold, and 2. Topological diversity of the macrocyclic core, including three-dimensional shape and volume. To evaluate the chemical space coverage of the composite peptide macrocycles generated from this method, we performed principle component analysis (PCA) on a set of 27 macrocycles, derived from the seven sequences described above. For comparison a set of 40 top-selling drugs, 60 diverse natural products and 20 molecules available from commercial vendors were similarly evaluated. According to protocols described by Tan and co-workers, an established set of 20 calculated and physicochemical descriptors was utilized.^{12,25} Linear combination of these descriptors reduced the data set to three principle components (presented as unitless axes) which represent 69% of original data set. This treatment allows variation across the 20 original descriptors to be readily visualized with minimal loss of information.

The composite macrocycle library occupied distinct chemical space relative to commercial libraries and top-selling drugs, but was largely encompassed by the diverse set of natural products (Figure 7A). The descriptors which differentiate the macrocycle library from the reference set can be elucidated from analysis of the PCA component loadings (see *supplemental information*). The increased molecular weight, number hydrogen bond donors and acceptors, and total polar surface area shift the macrocycle library left along the *x-axis* relative to the drug and commercial reference set. Considerably more overlap was observed along the *y-axis*, likely due to similarities in calculated measures of hydrophobicity, such as water solubility and membrane permeability.

The macrocycle library exhibited only a moderate shift from the N-terminal acetates of the peptides from which they were derived. This is likely due to homology across empirical measures of stereochemical diversity and heteroatom content. Also, the lipophilic template

imparts little additional polar surface area. The shift up along the *y*-axis of the macrocycles was likely due to a predicted decrease in aqueous solubility and a considerable reduction in rotatable bonds from macrocyclization.

The clustering of isomeric macrocycles within these PCA data sets is noteworthy. Considerable homology was observed amongst the physicochemical descriptors chosen, with only slight component shifts arising from variation in macrocyclic ring size as well as additional stereochemistry and hydrophobicity arising from pyrroloindoline formation. This highlights the deficiency of PCA to evaluate chemical space of conformationally complex peptidomimetics where minor modification can manifest substantial conformational perturbation (and thereby structural diversity). We anticipate variation in macrocycle shape will correlate with conformational change of the peptide, which will in turn allow unique interactions with molecular targets. We utilized three-dimensional descriptors of molecular shape to better evaluate diversity amongst isomeric macrocycles.

We chose to evaluate shape variation within macrocycles **3** - **7** derived from Ser-Ile-Trp(5-Br)-Ala. Low energy conformations were calculated using a macrocycle specific meta-sampling protocol consisting of a large scale low-mode conformation search followed by a stochastic dynamics simulated annealing and minimization. Conformations were generated from 5000 simulation cycles using the OPLS2005 force-field using an aqueous solvation model. Three principle moments of inertia (PMI) were calculated for unique conformations (1.0 rmsd) within 3.0 kcal/mol of the lowest energy conformation. Normalized ratios (I_1/I_3 , I_2/I_3) were plotted with vertices (0,1), (0.5, 0.5), and (1,1) representing a rod, disc, and sphere respectively (Figure 7B). Macrocycles derived from Ser-Ile-Trp(5-Br)-Ala exhibit broad shape diversity. In general these macrocycles lie away from the rod-disc axis where established drugs and commercial libraries have been shown to occupy.^{24,37} Although there is partial overlap across isomeric macrocycles, three of the five isomers occupy largely unique regions of the chart. The

macrocyclic pyrroloindoline **5** lies primarily on the disc-sphere axis and occupies a relatively narrow area of the chart, likely due to reduced conformational mobility within 3.0 kcal/mol.

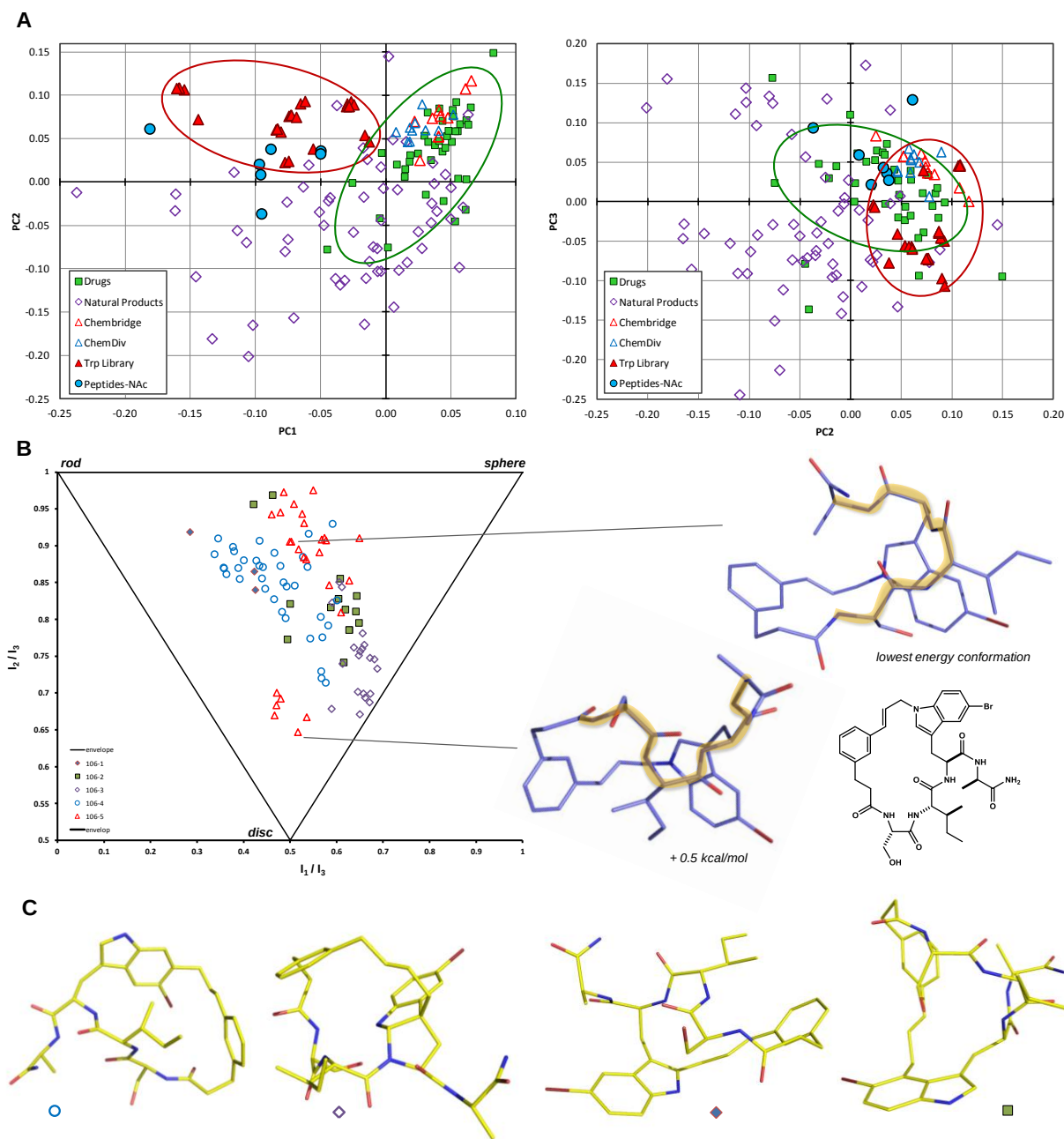


Figure 6. A. Principle component analysis identified unique chemical space of macrocycle library. B. Graphical analysis of molecule shape from normalized principle moments of inertia. Conformations were plotted within 3.0 kcal/mol of the lowest energy conformer obtained from macrocycle-specific conformation search. C. Analysis of lowest-energy conformation show unique orientations of peptide domain.

Interestingly the indole N-alkylated macrocycle **7** occupied two distinct molecular shape regions of the chart. One conformation lies largely along the rod-sphere axis and the second

nearer the disc vertex. This illustrates the propensity of peptidic macrocycles to occupy multiple, distinct low-energy conformations. Analysis of their structures revealed that they differ by inversion of the phenyl group around the metacyclophane. These conformations exhibit distinct orientations of the peptide (highlighted), suggesting shape analysis may be a good surrogate to identify conformational changes within the peptide. Analysis of the low-energy conformations of the remaining macrocycles **3** - **7** shown in Figure 7C provides additional empirical evidence that the isomeric macrocycles display the peptide domain in unique conformations.

5.3. Conclusion

Lead optimization in medicinal chemistry generally follows multiple stages of synthetic divergence to access chemical diversity around lead structures. This strategy is difficult to recapitulate in macrocycle space due to a lack of broadly applicable, divergent methods to prepare macrocycles. In this study, we have demonstrated a method to rapidly access diverse macrocyclic peptidomimetics. Our method utilizes an electrophilic reagent to engage substituted tryptophan residues present in oligopeptides via large-ring forming Friedel-Crafts alkylations. These reactions proceed rapidly at room temperature and exploit the divergent reactivity of indole to provide mixtures of isomeric composite macrocycles. A broad range of functional groups present in native or modified amino acids were tolerated, including guanidines, alcohols, amides, and phosphates.

The distribution of isomeric macrocycles from these processes appear to be highly sequence dependent. Turn-inducing residues strongly favored specific isomeric outcomes in certain sequences. Furthermore, we have demonstrated the ability to enhance the formation of specific isomers within homologous sequences by subtle modification of the tryptophan residues. This macrocyclization method is unique in its ability to generate diversity in a single divergent reaction. We anticipate this will allow rapid access to chemical space around macrocyclic scaffolds. From seven sequences we prepared 30 compounds with 19 novel

macrocyclic substructures ranging from 16 to 27 membered rings (*see supporting information*). Principle component analysis identified unique chemical space coverage of the macrocycle library relative to commercial libraries and currently marketed drugs. Calculated principle moments of inertia revealed substantial shape diversity amongst macrocycles derived from a common oligopeptide. This method has the unique potential to prepare isomeric macrocycles displaying defined peptide conformation which we anticipate will be valuable in screening efforts targeting exposed protein surfaces involved in protein-protein interactions.

Chapter 5 - Supporting Information

General

Reactions were performed under ambient atmosphere, unless otherwise noted. Dichloromethane was deoxygenated and dried by passing through an activated alumina solvent drying system. Anhydrous *N,N*-dimethylformamide (EMD DriSolv®) was used without further purification. Nitromethane was dried over 4Å molecular sieves for at least 24 hr before use. Methanesulfonic acid (≥99.5%, Sigma Aldrich) was used without further purification. Column chromatography was performed on silica gel 60 (SiliCycle, 240-400 mesh). Thin layer chromatography (TLC) utilized pre-coated plates (Sorbent Technologies, silica gel 60 PF254, 0.25 mm) visualized with UV 245 nm, iodine, or basic potassium permanganate stain.

Purification of acidolysis products employed an Agilent 1100/1200 HPLC system equipped with G1361A preparative pumps, a G1314A autosampler, a G1314A VWD, and a G1364B automated fraction collector. Analytical HPLC was performed using the same system, but with a G1312A binary pump. Mass spectra were recorded using an Agilent 6130 LC/MS system equipped with an ESI source.

NMR methods:

NMR spectra were recorded on Bruker Avance (300, 500 or 600 MHz), DRX (500 MHz) and ARX (400 MHz) spectrometers. Data for ¹H NMR spectra are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration), and are referenced to a residual protonated solvent peak.¹ ¹³C resonances are reported in terms of chemical shift (δ ppm) as referenced to the residual DMSO peak. For mass-limited samples, solvent magnetic susceptibility matched Shigemi tubes were used with a sample volume of ~300 μL. Optimization of on-axis shims was accomplished using the TopShim automated tool within Bruker Topspin™ 2.1. Optimization of off-axis shims was performed manually.² ¹H 90° transmitter pulse lengths were calibrated by back calculation from the 360° or 180° null.³ The pulse width or power level for soft pulses and shaped pulses were calculated using the Shape Tool within TopSpin™ 2.1. ¹H-¹H COSY spectra were recorded using a phase sensitive, gradient enhanced double-

¹ Gottlieb, H.E.; Kotlyar, V.; Nudelman, A., *J. Org. Chem.*, **1997**, 62, 7512-7515.

² Berger, S.; Braun, S., *200 and More NMR Experiments*, Wiley-VCH, Weinheim, **2004**, 6-11.

³ a) Claridge, T.D.W., *High-Resolution NMR Techniques in Organic Chemistry*, Pergamon, Oxford, **1999**, 94-97. b) Berger, S.; Braun, S., *200 and More NMR Experiments*, Wiley-VCH, Weinheim, **2004**, 15-17.

quantum-filtered experiment, using States-TPPI acquisition.⁴ TOCSY spectra were recorded using a sensitivity improved, phase sensitive experiment using a 60ms DIPSI-2 pulse train for homonuclear Hartman-Hahn transfer.⁵ NOESY spectra were recorded using a phase sensitive experiment with selection gradients during the mixing time.⁶ ROESY spectra were recorded using a phase sensitive experiment with selection gradients and water suppression with excitation sculpting.⁷ Carbon chemical shifts were measured from 2D plots of either HSQC spectra for protonated carbons or HMBC spectra for non-protonated carbons. ¹H-¹³C HSQC spectra were recorded using a sensitivity improved phase sensitive experiment using an adiabatic shape pulse for ¹³C inversion, and ¹³C decoupling during acquisition.⁸ Experimental parameters were optimized for ¹J_{CH} = 145Hz. ¹H-¹³C HMBC spectra were recorded using a gradient selected experiment with a two-fold J-filter optimized for ¹J_{CH} = 125-165Hz. Experimental parameters were optimized for long range ⁿJ_{CH} = 8Hz.

Peptide Synthesis:

C-terminal carboxamide peptides were synthesized manually using standard Fmoc solid phase synthesis protocols on Rink Amide MBHA resin (200-400 mesh, 0.70 mmol/g, 1% DVB) on 0.25-0.50 mmol scale using a fritted glass reaction vessel. Fmoc-deprotection was achieved with 20% piperidine in DMF (2 x 30 min). The reaction vessel was washed with DMF (3x) and CH₂Cl₂ (2x). The vessel was then charged with the appropriate Fmoc-amino acid (4 equiv) and TBTU (4 equiv) followed by DMF (10-20 ml) and iPr₂NEt (10 eq). The resin was agitated for 2 hours, drained, and washed with DMF (3X). After all coupling were completed the resin was cleaved with TFA/thioanisole/water/TIPS (90:2.5:5:2.5) for 2 hours. The cleaved resin was removed by filtration and the filtrate was concentrated under vacuum. The peptide was precipitated with ether and isolated by centrifugation. The peptide pellet was repeatedly washed with Et₂O to ensure complete removal of cleavage reagents. Fmoc-D-Thr(PO(OBzl)OH)-OH was used to prepare phosphothreonine containing peptides.

⁴ a) Hurd, R.E., *J. Magn. Reson.*, **1990**, 87, 422-428. b) Brereton, I.M.; Crozier, S.; Field, J.; Doddrell, D.M., *J. Magn. Reson.*, **1991**, 93, 54-62. c) Shaw, A.A.; Salaun, C.; Dauphin, J.F.; Ancian, B., *J. Magn. Reson. Ser. A*, **1996**, 120, 110-115.

⁵ Cavanagh, J.; Rance, M., *J. Magn. Reson.*, **1990**, 88, 72-85.

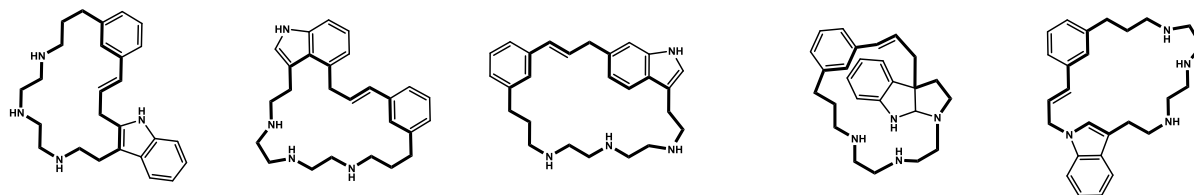
⁶ Wagner, R.; Berger, S., *J. Magn. Reson.*, **1996**, 123 A, 119-121.

⁷ a) Bax, A.; Davis, D.G., *J. Magn. Reson.*, **1985**, 63, 207-213. b) Hwang, T.L.; Shaka, A.J., *J. Magn. Reson., Series A*, **1995**, 112, 275-279.

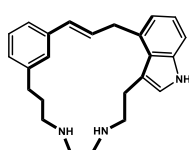
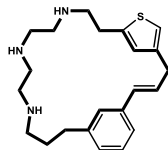
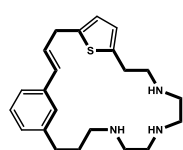
⁸ Palmer, A.G. III; Cavanagh, J.; Wright, P.E.; Rance, M., *J. Magn. Reson.*, **1991**, 93, 151-170. b) Kay, L.E.; Keifer, P.; Saarinen, T., *J. Am. Chem. Soc.*, **1992**, 114, 10663-10665. c) Schleucher, J.; Schwendinger, M.; Sattler, M.; Schmidt, P.; Schedletzky, O.; Glaser, S.J.; Sorensen, O.W.; Griesinger, C., *J. Biomol. NMR* **4**, **1994**, 301-306.

Summary of novel macrocyclic core structures:

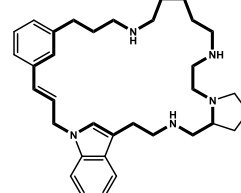
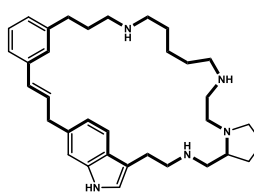
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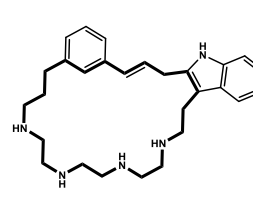
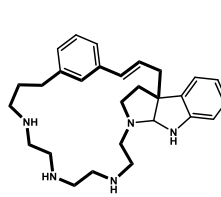
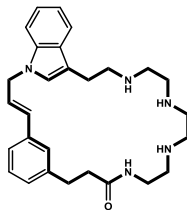
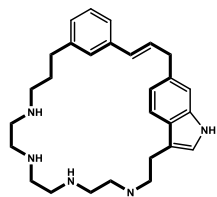
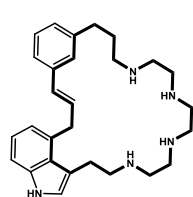
Thr-Gln-Thi



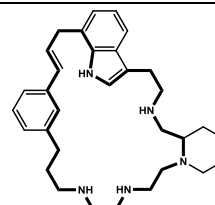
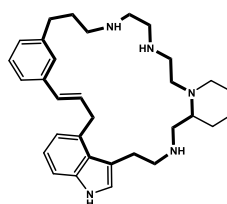
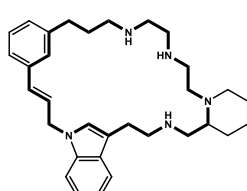
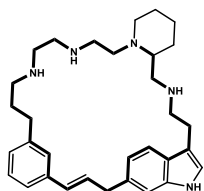
Orn-Ile-Pro-Trp(5-F)



His-Gln-Ala-Trp(5-F)-Arg



Ala-D-Thr-Pip-Trp(5-Me)



Principle Component Analysis

Principle component analysis was performed according to procedures described by Tan and co-workers.¹

Importance of Components:

	PC1	PC2	PC3	PC4	PC5	PC6	PC7
Standard deviation	7.3440	6.3702	5.2038	4.6741	3.3081	2.5645	2.0725
Proportion of Variance	0.3077	0.2315	0.0155	0.1246	0.0624	0.0375	0.0245
Cumulative Proportion	0.3077	0.5392	0.6937	0.8183	0.8808	0.9183	0.9428
	PC8	PC9	PC10	PC11	PC12	PC13	PC14
Standard deviation	1.7949	1.3462	1.1385	1.0053	0.9144	0.7524	0.7341
Proportion of Variance	0.0184	0.0103	0.0074	0.0058	0.0048	0.0032	0.0031
Cumulative Proportion	0.9611	0.9715	0.9789	0.9846	0.9894	0.9926	0.9957

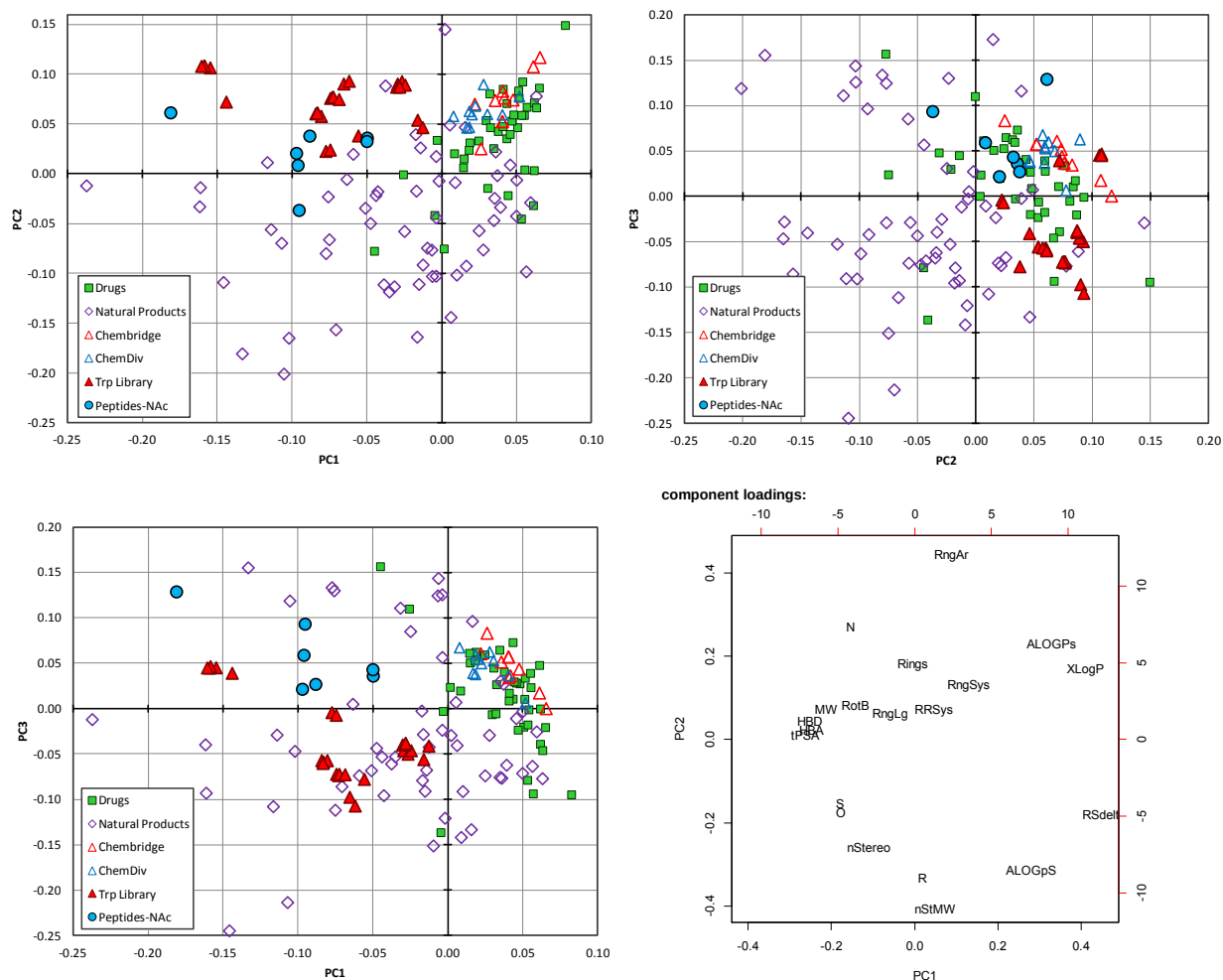
List of Drugs (PCA):

Abilify	Crestor	Lipitor	Topamax
Aciphex	Cymbalta	Nexium	Toprol
Actos	Diovan	Norvasc	Tricor
Adderall	Effexor	Plavix	Valtrex
Ambien	Flonase	Prevacid	Wellbutrin
Avandia	Fosamax	Protonix	Zetia
Benazepril	Imitrex	Risperdal	Zocor
Celebrex	Lamictal	Serevent	Zoloft
Concerta	Levaquin	Seroquel	Zyprexa
Coreg	Lexapro	Singulair	Zyrtec

List of Natural Products (PCA):

Actinonin	BrevetoxinB	Discodermolide	Lactacystin	Quinine	Talaromycin B
Adriamycin	Calicheamicin G1	Duocarmycin A	Lipstatin	Radicicol	Taxol
Amphotericin B	Calyculin A	Echinocandin B	Midecamycin A1	Rapamycin	Telomestatin
Apoptolidin	Cephameycin C	Epothilone A	Mizoribine	Rifamycin B	Thienamycin
Arglabin	Coformycin	Erythromycin A	Monensin	Salicylhalamide A	Trapoxin B
Artemisinin	Colchicine	FK506	Mycobactin S	Spergualin	Trichostatin
Avermectin B1a	Compactin	Forskolin	Penicillin G	Spongistatin1	Validamycin
Bestatin	Cyclosporin A	Fumagillin	Phorbol MA	SQ26180	Vancomycin
Bleomycin	Cytochalasin B	Geldanamycin	Plaunotol	Staurosporine	Vincristine
Brefeldin A	Daptomycin	Ginkgolide B	Pseudomonic Acid A	Streptomycin	Zaragozic Acid A

Summary of PCA data:



General Procedure A - Acylation of unprotected peptides with 1.

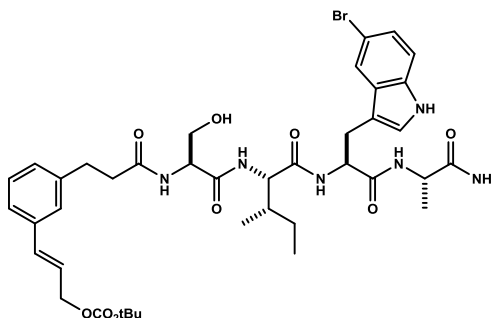
An oven-dried, screw-capped scintillation vial was charged with unprotected peptide (0.5 mmol) and N-hydroxysuccinimide ester **2** (0.5 mmol, 1 eq.) followed by addition of anhydrous DMF (10 ml) and *i*Pr₂NEt (2.0 mmol). The reaction was allowed to stir at room temperature for 3 hours. The DMF was removed by rotary evaporation and the residue was dissolved in DMSO (1 ml) and purified by reverse-phase HPLC (C18, MeCN/H₂O, 0.1% TFA) to give the acyclic carbonate as a white solid.

General Procedure B - Acidolysis of cinnamyl carbonates.

The acyclic cinnamyl carbonate (0.25 mmol) was suspended in dry nitromethane (50 ml, 5 mM) under argon atmosphere, and treated with methanesulfonic acid (250 μ l, 3.75 mmol, 15 eq.) at room temperature, which caused complete dissolution of the starting material. After 2 hours the reaction was partitioned between quenched by addition of *i*Pr₂NEt (18 equiv). The solvent was

removed under reduced pressure and product mixture was reconstituted in N,N-DMF and purified by semi-preparative RP-HPLC (Sunfire C18, 5.0 μ , 10.0x250 mm, MeCN/H₂O, 0.1% TFA). Fractions were pooled and evaporated under reduced pressure.

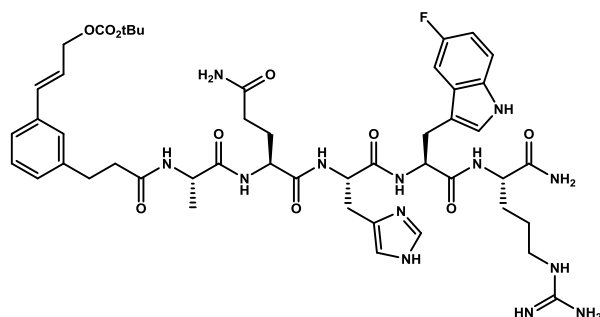
Tabulated data for acyclic peptides:



Acyclic - Ser-Ile-Trp(5-Br)-Ala (2): Following the general procedure A with 125 mg SIW(5-Br)-A. Isolation by preparative HPLC afforded **2** (118 mg, 62%).

¹H NMR (DMSO-d₆, 500 MHz): δ 11.00 (d, J = 2.5 Hz, 1H), 7.96 (d, J = 7.8 Hz, 1H), 7.89 (d, J = 8.3 Hz, 1H), 7.84 (d, J = 7.5 Hz, 1H), 7.83 (d, J = 7.9 Hz, 1H), 7.74 (d, J = 1.8 Hz, 1H), 7.26-7.30 (m, 1H), 7.26 (br. s, 1H), 7.23-7.24 (m, 1H), 7.21 (t, J = 7.6 Hz, 1H), 7.17 (d, J = 2.3 Hz, 1H), 7.14 (d, J = 2 Hz, 1H), 7.13 (d, J = 2 Hz, 1H), 7.10 (br. d, J = 7.5 Hz, 1H), 7.07 (br. s, 1H), 6.99 (br. s, 1H), 6.61 (d, J = 15.9 Hz, 1H), 6.32 (dt, J = 15.6, 6.2 Hz, 1H), 4.65 (dd, J = 6.3, 6.2 Hz, 2H), 4.50 (ddd, J = 9.2, 8.2, 5.0 Hz, 1H), 4.41 (app q, J = 6.7 Hz, 1H), 4.15 (dddd, J = 7.2, 7.2, 7.2, 7.2 Hz, 1H), 4.07 (dd, J = 7.8, 6.2 Hz, 1H), 3.56 (dd, J = 10.4, 6.0 Hz, 1H), 3.51 (dd, J = 10.4, 6.3 Hz, 1H), 3.11 (dd, J = 14.9, 4.8 Hz, 1H), 2.85 (dd, J = 14.7, 9.4 Hz, 1H), 2.78 (app t, J = 7.9 Hz, 2H), 2.43-2.49 (m, 3H), 1.60-2.49 (m, 1H), 1.41 (s, 9H), 1.19 (d, J = 7.0 Hz, 3H), 1.08-1.16 (m, 1H), 0.90-1.00 (m, 1H), 0.65 (d, J = 6.7 Hz, 3H). ¹³C NMR (DMSO-d₆, 125 MHz): δ 174.4, 172.1, 171.3, 171.3, 171.2, 153.3, 142.2, 136.3, 135.2, 133.9, 129.5, 129.1, 128.5, 126.9, 126.0, 124.7, 123.8, 121.2, 113.7, 111.5, 110.3, 82.0, 67.4, 62.2, 58.0, 55.0, 53.6, 48.7, 37.1, 36.7, 31.4, 27.85, 27.78, 27.6, 24.3, 18.6, 15.7, 11.7.

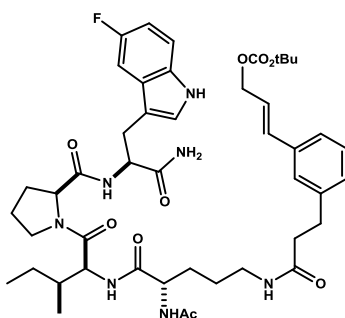
MS (ESI) Calculated for C₄₀H₅₃BrN₆O₉ [M+H]⁺: 841.1, found 841.4.



Acyclic - Ala-Gln-His-Trp(5-F)-Arg (S1): Following the general procedure A with 115 mg AQHW95-F)R. Isolation by preparative HPLC afforded **S1** (122 mg, 81%).

^1H NMR (DMSO- d_6 , 500 MHz): δ 10.98 (d, J = 2.3 Hz, 1H), 8.96 (d, J = 1.2 Hz, 1H), 8.24 (d, J = 7.9 Hz, 1H), 8.06-8.16 (m, 4H), 7.74 (t, J = 5.7 Hz, 1H), 7.39 (dd, J = 16.0, 2.5 Hz, 1H), 7.36 (br. s, 1H), 7.23-7.34 (m, 7H), 7.09-7.14 (m, 2H), 6.87-6.93 (m, 2H), 6.65 (d, J = 15.9 Hz, 1H), 6.35 (dt, J = 16.0, 6.2 Hz, 1H), 4.68 (dd, J = 6.5, 1.0 Hz, 2H), 4.52-4.60 (m, 2H), 4.18-4.28 (m, 2H), 4.16 (ddd, J = 7.9, 5.6 Hz, 1H), 3.03-3.17 (m, 4H), 2.94 (dd, J = 15.9, 15.9, 9 Hz, 2H), 2.75-2.84 (m, 2H), 2.39-4.29 (m, 2H), 2.04-2.17 (m, 2H), 1.80-1.91 (m, 1H), 1.65-1.79 (m, 2H), 1.45-1.55 (m, 2H), 1.43 (s, 9H), 1.15 (d, J = 7.0 Hz, 3H). ^{13}C NMR (DMSO- d_6 , 125 MHz): δ 174.1, 173.1, 172.7, 171.6, 171.4, 171.3, 169.8, 157.6, 156.8, 155.8, 152.8, 141.7, 135.8, 133.7, 133.4, 132.7, 129.3, 129.1, 128.6, 128.0, 127.5, 127.4, 126.4, 125.9, 124.2, 123.3, 117.7, 116.8, 115.3, 115.2, 112.2, 112.1, 109.9, 109.9, 81.5, 66.9, 55.0, 53.4, 52.4, 52.2, 51.5, 48.3, 36.6, 31.3, 30.8, 29.1, 27.3, 25.0, 17.9.

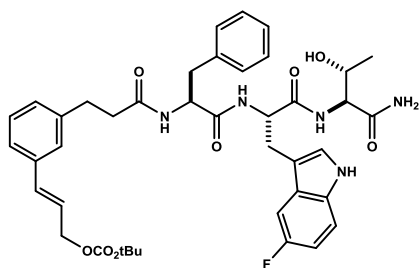
MS (ESI) Calculated for $\text{C}_{48}\text{H}_{64}\text{FN}_{13}\text{O}_{10}$ $[\text{M}+\text{H}]^+$: 1002.5, found 1002.7.



Acyclic - Orn-Ile-Pro-Trp(5-F) (S2): Following the general procedure A with 86 mg OIPW(5-F). Isolation by preparative HPLC afforded **S2** (78 mg, 60%).

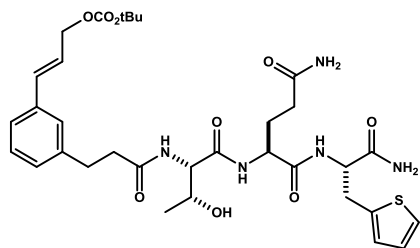
^1H NMR (DMSO- d_6 , 500 MHz): δ 10.93 (d, J = 2.5 Hz, 1H), 7.97 (d, J = 8.3 Hz, 1H), 7.89 (d, J = 8.4 Hz, 1H), 7.83 (t, J = 5.6 Hz, 1H), 7.28-7.37 (m, 5H), 7.22-7.27 (m, 3H), 7.11 (br. d, J = 7.3 Hz, 1H), 7.04 (br. s, 1H), 6.89 (ddd, J = 9.1, 9.1, 2.5 Hz, 1H), 6.64 (d, J = 16.0 Hz, 1H), 6.34 (dt, J = 16.0, 6.2 Hz, 1H), 4.68 (dd, J = 6.2, 1.1 Hz, 2H), 4.38 (ddd, J = 7.0, 7.0, 7.0 Hz, 1H), 4.26-

4.35 (m, 3H), 3.74 (ddd, $J = 9.6, 6.6, 6.6$ Hz, 1H), 3.53 (ddd, $J = 9.6, 5.7, 6.0$ Hz, 1H), 2.96-3.10 (m, 4H), 2.80 (app t, $J = 7.8$ Hz, 2H), 2.37 (app t, $J = 7.8$ Hz, 2H), 1.93-2.03 (m, 1H), 1.70-1.91 (m, 6H), 1.47-1.60 (m, 2H), 1.44 (s, 9H), 1.27-2.39 (m, 2H), 1.00-1.08 (m, 1H), 0.84 (d, $J = 6.8$ Hz, 3H), 0.81 (t, $J = 7.4$ Hz, 1H). ^{13}C NMR (DMSO- d_6 , 125 MHz): δ 173.0, 171.7, 171.2, 171.1, 170.2, 169.2, 155.7, 152.8, 141.8, 135.8, 133.4, 132.7, 128.6, 128.0, 127.7, 127.7, 126.4, 125.8, 124.2, 123.3, 112.1, 112.0, 110.32, 110.28, 108.9, 108.7, 103.3, 103.1, 81.5, 67.0, 66.9, 59.5, 54.5, 53.3, 51.9, 47.2, 38.1, 36.9, 36.1, 31.0, 29.6, 28.9, 27.3, 25.8, 24.4, 24.1, 22.5, 14.9, 10.8. MS (ESI) Calculated for $\text{C}_{46}\text{H}_{62}\text{FN}_7\text{O}_9$ $[\text{M}+\text{H}]^+$: 876.5, found 876.5.



Acyclic - Phe-Trp(5-F)-Thr (S3): Following the general procedure A with 91 mg FW(5-F)T. Isolation by preparative HPLC afforded **S3** (72 mg, 63%).

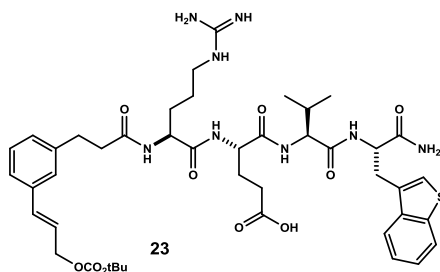
^1H NMR (DMSO- d_6 , 500 MHz): δ 10.97 (d, $J = 2.2$ Hz, 1H), 8.29 (d, $J = 7.8$ Hz, 1H), 8.08 (d, $J = 8.1$ Hz, 1H), 7.80 (d, $J = 8.6$ Hz, 1H), 7.41 (dd, $J = 10.2, 2.4$ Hz, 1H), 7.32 (dd, $J = 8.8, 4.5$ Hz, 1H), 7.29 (d, $J = 2.2$ Hz, 1H), 7.26 (br. d, $J = 7.8$ Hz, 1H), 7.23 (br. s, 1H), 7.21 (br. s, 1H), 7.2 (br. s, 1H), 7.14-7.18 (m, 4H), 7.09 (br. s, 1H), 7.01 (d, $J = 8.1$ Hz, 1H), 6.9 (ddd, $J = 9.0, 9.0, 2.3$ Hz, 1H), 6.63 (d, $J = 15.7$ Hz, 1H), 6.33 (dt, $J = 15.9, 6.2$ Hz, 1H), 4.67 (dd, $J = 6.3, 1.1$ Hz, 2H), 4.63 (ddd, $J = 8.6, 8.0, 4.9$ Hz, 1H), 4.54 (ddd, $J = 9.9, 8.4, 4.0$ Hz, 1H), 4.16 (dd, $J = 8.7, 3.2$ Hz, 1H), 4.08 (dddd, $J = 6.2, 6.2, 6.2, 3.4$ Hz, 1H), 3.17 (dd, $J = 15.0, 4.6$ Hz, 1H), 3.02 (dd, $J = 15.3, 9.3$ Hz, 1H), 2.97 (dd, $J = 13.7, 4.0$ Hz, 1H), 2.71 (dd, $J = 13.9, 16.0$ Hz, 1H), 2.65 (app t, $J = 7.9$ Hz, 2H), 2.23-2.38 (m, 2H), 1.4 (s, 9H), 1.02 (d, $J = 6.4$ Hz, 3H). ^{13}C NMR (DMSO- d_6 , 125 MHz): δ 172.0, 171.5, 171.4, 171.3, 157.6, 155.8, 152.8, 141.7, 137.9, 135.8, 133.4, 132.7, 129.1, 128.6, 127.9, 127.6, 127.5, 126.4, 126.1, 125.9, 124.1, 123.2, 112.14, 112.06, 110.2, 110.2, 109.0, 108.8, 103.3, 103.1, 81.5, 66.9, 66.3, 58.0, 53.7, 53.5, 37.4, 36.7, 30.9, 27.3, 19.9. MS (ESI) Calculated for $\text{C}_{41}\text{H}_{48}\text{FN}_5\text{O}_8$ $[\text{M}+\text{H}]^+$: 758.4, found 758.8.



Acyclic - Thr-Gln-Thi (S4): Following the general procedure A with 300 mg Thr-Gln-Thi. Isolation by preparative HPLC afforded **S4** (257 mg, 50%).

^1H NMR (DMSO- d_6 , 500 MHz): δ 8.09 (d, J = 7.0 Hz, 1H), 7.89 (d, J = 8.3 Hz, 1H), 7.79 (d, J = 7.9 Hz, 1H), 7.28 (br. s, 1H), 7.25 (d, J = 5.1 Hz, 1H), 7.13-7.25 (m, 4H), 7.07-7.12 (m, 2H), 6.87 (d, J = 4.7, 3.8 Hz, 1H), 6.82-6.86 (m, 1H), 6.68 (br. s, 1H), 6.61 (d, J = 15.9 Hz, 1H), 6.30 (dt, J = 16.0, 6.2 Hz, 1H), 4.04 (d, J = 5.9 Hz, 2H), 4.32 (ddd, J = 8.6, 8.6, 4.7 Hz, 1H), 4.2 (dd, J = 7.7, 4.1 Hz, 1H), 4.17 (ddd, J = 7.7, 7.7, 5.2 Hz, 1H), 3.96 (ddd, J = 10.6, 6.1, 6.1 Hz, 1H), 3.24 (dd, J = 14.9, 4.2 Hz, 1H), 3.04 (dd, J = 14.9, 9.1 Hz, 1H), 2.76-2.84 (m, 2H), 2.45-2.60 (m, 3H), 1.99-2.12 (m, 2H), 1.81-1.90 (m, 1H), 1.67-1.76 (m, 1H), 1.4 (s, 9H), 0.97 (d, J = 6.1 Hz, 3H).
 ^{13}C NMR (DMSO- d_6 , 125 MHz): δ 174.3, 172.5, 172.5, 171.4, 170.9, 153.1, 142.0, 140.0, 136.2, 133.8, 128.9, 128.4, 127.0, 126.7, 126.3, 124.6, 124.5, 123.7, 81.8, 67.2, 66.8, 58.8, 54.4, 53.2, 36.9, 31.8, 31.6, 31.3, 27.7, 27.6, 19.8.

MS (ESI) Calculated for $\text{C}_{33}\text{H}_{45}\text{N}_5\text{O}_9\text{S}$ $[\text{M}+\text{H}]^+$: 688.4, found 688.2.



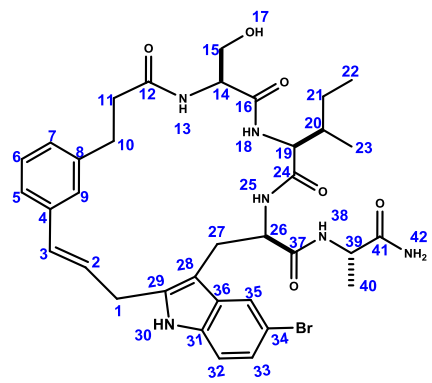
Acyclic - Arg-Glu-Val-BnThi (S5): Following the general procedure A with 344 mg Arg-Gly-Val-BnThi. Isolation by preparative HPLC afforded **S4** (257 mg, 46%).

^1H NMR (DMSO- d_6 , 500 MHz): δ 8.12 (d, J = 8.3 Hz, 1H), 8.06 (d, J = 7.9 Hz, 1H), 8.05 (d, J = 7.5 Hz, 1H), 7.91 (br. d, J = 7.6 Hz, 1H), 7.88 (br. d, J = 7.5 Hz, 1H), 7.74 (br. d, J = 8.7 Hz, 1H), 7.31-7.44 (d, J = Hz, 5H), 7.24-7.30 (m, 3H), 7.22 (m, 1H), 7.07-7.11 (t, J = Hz, 2H), 6.62 (m, 1H), 6.32 (d, J = 15.9, 6.2 Hz, 1H), 4.65 (dt, J = 6.3, 1.2 Hz, 2H), 4.6 (dd, J = 8.4, 8.4, 5.6 Hz, 1H), 4.24-4.30 (ddd, J = Hz, 2H), 4.1 (m, 1H), 3.21 (dd, J = 15.0, 5.0 Hz, 1H), 2.97-3.09 (dd, J = Hz, 3H), 2.69 (m, 2H), 2.44 (ddd, J = 14.5, 12.6, 6.7 Hz, 1H), 2.15-2.29 (m, 2H), 1.82-1.94 (m, 2H), 1.68-1.79 (m, 1H), 1.55-1.65 (m, 1H), 1.32-1.48 (m, 13H), 0.76 (d, J = 6.7 Hz, 3H), 0.75 (d,

J = 6.7 Hz, 3H). ^{13}C NMR (DMSO- d_6 , 125 MHz): δ 174.5, 173.1, 172.1, 172.0, 171.5, 171.2, 157.1, 153.3, 142.1, 139.9, 139.2, 136.3, 133.9, 132.5, 129.1, 128.5, 126.9, 124.74, 124.69, 124.5, 123.83, 123.78, 123.2, 122.3, 82.0, 67.4, 58.2, 52.44, 52.40, 37.1, 31.5, 31.0, 30.7, 27.8, 27.7, 25.4, 19.6, 18.4.

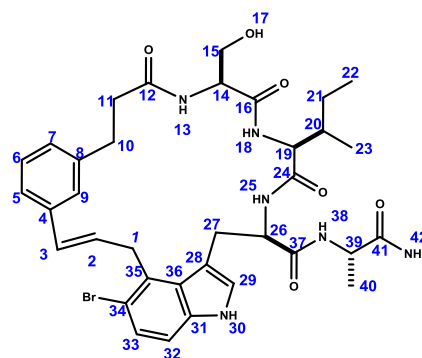
MS (ESI) Calculated for $\text{C}_{44}\text{H}_{60}\text{N}_8\text{O}_{10}\text{S}$ $[\text{M}+\text{H}]^+$: 893.4, found 893.1.

Spectral assignments for macrocycles:



Ato m #	^{13}C	^1H	key correlation
1	29.6	3.62-3.68 (m, 1H), 3.70-3.76 (m, 1H)	HMBC 1→29, 28
2	126.7	6.53-6.60 (m, 1H) overlap	COSY 2→1
3	131.4	6.53-6.60 (m, 1H) overlap	
4	136.8	-	
5	123.6	7.16-7.20 (m, 1H) overlap	
6	127.9	7.17-7.21 (m, 1H) overlap	
7	127.4	7.02-7.06 (m, 1H)	HMBC 7→5
8	141.4	-	
9	125.3	7.31 (br s, 1H) overlap	HMBC 9→3,5
10	29.9	2.68-2.75 (m, 1H), 3.02-3.10 (m, 1H) overlap	HMBC 10→7,8,9
11	35.1	2.41 (ddd, J = 14.9, 9.2, 2.2 Hz, 1H), 2.58-2.65 (m, 1H)	
12	171.5	-	
13	-	8.11 (d, J = 8.4 Hz, 1H)	
14	55.3	4.25 (ddd, J = 8.4, 5.5, 5.5 Hz, 1H)	
15	61.4	3.46-3.54 (m, 2H)	
16	169.4	-	
17	-	not observed	
18	-	7.29-7.32 (m, 1H) overlap	HMBC 18→16
19	56.6	4.06 (dd, J = 8.0, 6.6 Hz, 1H)	
20	37.3	1.60-1.69 (m, 1H)	

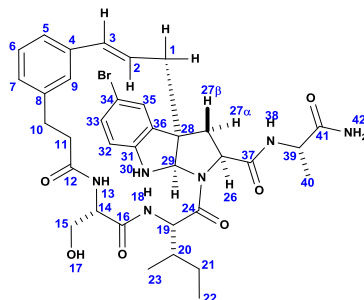
21	23.4	0.88-0.98 (m, 1H), 1.22-1.33 (m, 1H)	
22	10.9	0.71 (t, J = 7.4 Hz, 3H)	
23	15.0	0.68 (d, J = 6.7 Hz, 3H)	
24	170.3	-	
25	-	8.25 (d, J = 8.8 Hz, 1H)	
26	53.6	4.60 (ddd, J = 9.0, 8.8, 5.9 Hz, 1H)	HMBC 26→28
27	26.1	2.91 (dd, J = 14.4, 9.4 Hz, 1H), 3.04-3.10 (m, 1H) overlap	HMBC 27→28,29,36
28	105.9	-	
29	136.6	-	
30	-	10.94 (s, 1H)	
31	133.6	-	
32	112.3	7.17 (d, J = 8.6 Hz, 1H)	HMBC 32→36
33	122.4	7.06 (dd, J = 8.6, 1.9 Hz, 1H)	HMBC 33→31,34, TOCSY 33→32,35
34	110.6	-	
35	120.1	7.70 (d, J = 1.9 Hz, 1H)	HMBC 35→28,31,33,34
36	130.1	-	
37	170.6	-	
38	-	7.84 (d, J = 7.5 Hz, 1H)	
39	18.3	1.20 (d, J = 7.1 Hz, 3H)	
40	47.9	4.17 (dq, J = 7.1, 7.1 Hz, 1H)	
41	173.5	-	
42	-	7.00 (br s, 1H), 7.20 (br s, 1H)	TOCSY 42→42', HMBC 42→41



4

Atom #	¹³ C	¹ H	key correlation
1	34.9	3.93-3.99 (m, 1H), 4.23-4.28 (m, 1H) overlap	COSY 1→1', HMBC 1→34,35,36
2	128.4	6.45 (ddd, J = 16.06, 6.0, 5.5 Hz, 1H)	HMBC 2→4
3	129.8	6.20 (br d, J = 16.0 Hz, 1H)	HMBC 3→4
4	137.0	-	
5	122.9	7.00 (br d, J = 7.5 Hz, 1H)	HMBC 5→3
6	127.9	7.10 (dd, J = 7.5, 7.5 Hz, 1H)	HMBC 6→4,8, TOCSY 6→5,7,9

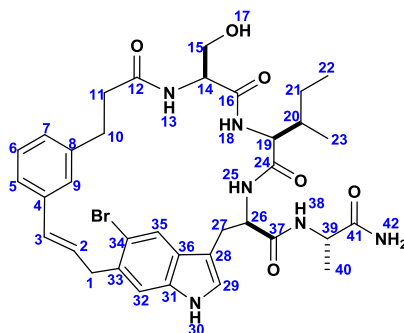
7	127.3	6.99 (br d, J = 7.5 Hz, 1H) overlap	
8	141.3	-	
9	124.6	7.22 (br s, 1H)	HMBC 9→3
10	28.9	2.68-2.74 (m, 1H) overlap, 3.01-3.05 (m, 1H) overlap	HMBC 10→7,8,9,12
11	34.3	2.48-2.53 (m, 1H) obscured, 2.66-2.72 (m, 1H) overlap	HMBC 11→9,12
12	171.5	-	
13	-	8.10 (d, J = 8.3 Hz, 1H)	HMBC 13→12, COSY 13→14
14	56.1	4.23-4.27 (m, 1H) overlap	HMBC 14→15,16
15	62.0	3.50-3.55 (m, 1H), 3.60 (ddd, J = 11.0, 5.7, 5.7 Hz, 1H)	HMBC 15→16
16	169.3	-	
17	-	4.90 (dd, J = 5.7, 5.7 Hz, 1H)	HMBC 17→14,15
18	-	7.34 (d, J = 8.3 Hz, 1H)	HMBC 18→16, COSY 18→19
19	56.3	4.30 (dd, J = 8.3, 7.4 Hz, 1H)	COSY 19→20, HMBC 19→24
20	37.1	1.65-1.72 (m, 1H)	COSY 20→21,23
21	23.9	0.98-1.06 (m, 1H), 1.39-1.48 (m, 1H)	
22	10.9	0.79 (t, J = 7.3 Hz, 3H)	COSY 22→21
23	14.8	0.80 (d, J = 6.6 Hz, 3H)	
24	170.2	-	
25	-	8.34 (d, J = 7.3 Hz, 1H)	HMBC 25→24, COSY 25→26
26	54.3	4.61 (ddd, J = 7.8, 7.8, 7.3 Hz, 1H)	HMBC 26→28, COSY 26→27
27	29.1	3.09-3.14 (m, 2H)	HMBC 27→28
28	109.6	-	
29	126.1	7.06 (d, J = 2.5 Hz, 1H)	HMBC 29→28,31,36
30	-	11.06 (d, J = 2.5 Hz, 1H)	
31	135.6	-	
32	111.8	7.18 (d, J = 8.6 Hz, 1H)	HMBC 32→31,34,36
33	124.6	7.26 (d, J = 8.6 Hz, 1H)	HMBC 33→31
34	114.9	-	
35	129.7	-	
36	126.6	-	
37	169.5	-	
38	-	7.78 (d, J = 7.6 Hz, 1H)	HMBC 38→37
39	18.1	4.16 (dq, J = 7.6, 7.0 Hz, 1H)	
40	47.8	1.14 (d, J = 7.0 Hz, 1H)	
41	173.3	-	
42	-	6.90 (br s, 1H), 6.91 (br s, 1H)	HMBC 42→41



5

Atom #	¹³ C	¹ H	key correlation
1	39.5	2.51-2.55 (m, 2H)	HMBC 1→28,29
2	124.1	6.18 (ddd, J = 15.7, 8.2, 7.0 Hz, 1H)	COSY 2→1, HMBC 2→4
3	134.3	6.57 (d, J = 15.7 Hz, 1H)	
4	136.8	-	
5	124.4	7.03 (br d, J = 7.6 Hz, 1H)	HMBC 5→3, TOCSY 5→6,7,9
6	128.0	7.16 (dd, J = 7.6, 7.6 Hz, 1H)	HMBC 6→4,8
7	127.5	7.01 (br d, J = 7.6 Hz, 1H)	
8	141.4	-	
9	124.5	7.38 (br s, 1H)	HMBC 9→3
10	29.8	2.75 (apt dd, J = 14.0, 9.8 Hz, 1H), 3.02 (apt dd, J = 14.0, 10.7 Hz, 1H)	HMBC 10→7,9,12
11	35.8	2.31-2.36 (m, 1H) overlap, 2.47-2.54 (m, 1H) overlap	
12	171.3	-	
13	-	7.98 (d, J = 7.9 Hz, 1H)	HMBC 13→12
14	54.7	4.35 (ddd, J = 7.9, 7.0, 5.4 Hz, 1H)	COSY 14→13
15	61.5	3.54 (dd, J = 10.7, 7.0 Hz, 1H), 3.60 (dd, J = 10.7, 5.4 Hz, 1H)	COSY 15→14
16	170.2	-	
17	-	not observed	
18	-	8.03 (d, J = 6.1 Hz, 1H)	HMBC 18→16
19	55.6	4.23 (dd, J = 9.1, 6.1 Hz, 1H)	HMBC 19→24
20	36.4	1.71-1.77 (m, 1H) overlap	COSY 20→19
21	24.1	1.18-1.25 (m, 1H), 1.66-1.73 (m, 1H) overlap	
22	11.0	0.89 (t, J = 7.5 Hz, 3H)	COSY 22→21
23	14.8	0.99 (d, J = 6.8 Hz, 3H)	COSY 23→20
24	172.3	-	
25	-	-	
26	60.3	4.42 (dd, J = 8.7, 6.3 Hz, 1H)	COSY 26→27, HMBC 26→24
27	38.3	2.09 (dd, J = 13.0, 6.3 Hz, 1H), 2.32-2.37 (m, 1H) overlap	HMBC 27→26,28,29,37
28	56.8	-	
29	80.8	6.35 (s, 1H)	HMBC 29→1,24,27,31,36
30	-	not observed	

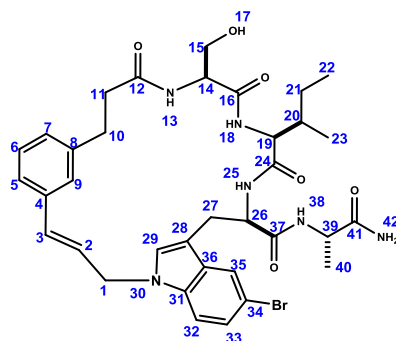
31	147.8	-	
32	111.1	6.50 (d, J = 8.3 Hz, 1H)	HMBC 32→34,36
33	130.6	7.14 (dd, J = 8.3, 2.1 Hz, 1H)	HMBC 33→31
34	108.8	-	
35	124.9	7.31 (d, J = 2.1 Hz, 1H)	HMBC 35→31
36	136.7	-	
37	169.4	-	
38	-	7.33 (d, J = 7.1 Hz, 1H)	
39	47.4	3.98 (dq, J = 7.1, 6.8 Hz, 1H)	HMBC 39→41
40	17.9	0.83 (d, J = 6.8 Hz, 3H)	COSY 40→39, HMBC 40→41
41	173.3	-	
42	-	6.90 (br s, 1H), 7.38 (br s, 1H)	HMBC 42→41, TOCSY 42→42'



6

Atom #	13C	1H	key correlation
1	38.0	3.68 (apt d, J = 4.1 Hz, 2H)	
2	129.0	6.38 (ddd, J = 16.0, 5.9, 5.9 Hz, 1H)	HMBC 2→4
3	129.4	6.16 (br d, J = 16.0 Hz, 1H)	HMBC 3→5,9
4	136.8	-	
5	123.1	7.18 (d, J = 8.0 Hz, 1H) overlap	
6	127.6	7.16 (dd, J = 8.0, 8.0 Hz, 1H) overlap	HMBC 6→4,9
7	126.8	6.97 (br d, J = 8.0 Hz, 1H)	
8	140.6	-	
9	124.4	7.03 (br s, 1H)	HMBC 9→3,5,7,10
10	29.3	2.78 (ddd, J = 14.8, 7.8, 3.5 Hz, 1H), 2.83-2.89 (m, 1H) overlap	
11	34.7	2.32 (ddd, J = 14.9, 7.8, 3.5 Hz, 1H), 2.50-2.56 (m, 1H)	HMBC 11→12

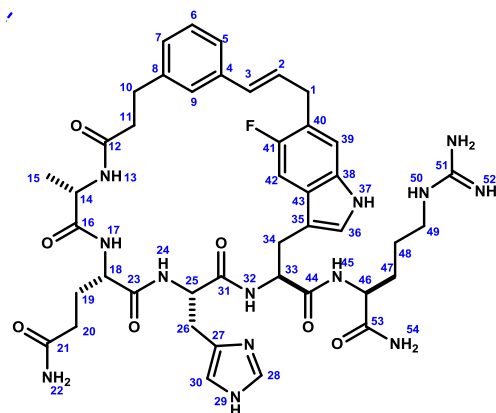
12	171.4	-	
13	-	7.46 (d, J = 7.4 Hz, 1H)	
14	53.9	4.12 (apt dd, J = 11.9, 6.0 Hz, 1H)	
15	61.6	3.03 (dd, J = 10.8, 6.0 Hz, 1H), 2.84-2.89 (m, 1H) overlap	
16	not observed	-	
17	-	not observed	
18	-	7.38-7.42 (m, 1H) overlap	
19	56.8	4.03 (dd, J = 7.9, 6.4 Hz, 1H)	HMBC 19→24
20	35.8	1.72-1.80 (m, 1H)	
21	23.4	0.99-1.08 (m, 1H), 1.30-1.38 (m, 1H)	
22	10.5	0.80 (t, J = 7.4 Hz, 3H)	
23	14.8	0.84 (d, J = 6.8 Hz, 3H)	
24	170.0	-	
25	-	7.38-7.42 (m, 1H) overlap	
26	52.9	4.62 (apt dd, J = 14.4, 7.5 Hz, 1H)	HMBC 26→37
27	26.5	3.08-3.12 (m, 1H) obscured	HMBC 27→28,37
28	108.8	-	
29	125.0	7.15 (br s, 1H) overlap	HMBC 29→28,31,36
30	-	10.69 (br s, 1H)	HMBC 30→31
31	135.4	-	
32	113.0	7.32 (s, 1H)	HMBC 32→1,36
33	130.0	-	
34	113.6	-	
35	121.7	7.83 (s, 1H)	HMBC 35→28,31,33,34
36	127.4	-	
37	170.3	-	
38	-	7.60 (br s, 1H)	
39	47.6	4.29 (qd, J = 7.1, 7.0 Hz, 1H)	HMBC 39→37,41
40	17.6	1.23 (d, J = 7.1 Hz, 3H)	HMBC 40→41
41	173.4	-	
42	-	6.82 (br s, 1H), 7.06 (br s, 1H)	



7

Atom #	¹³ C	¹ H	key correlation
1	47.5	4.83-4.90 (m, 2H)	HMBC 1→2,3,29,31
2	124.7	6.59-6.67 (m, 1H) overlap	HMBC 2→4
3	132.6	6.59-6.67 (m, 1H) overlap	
4	136.2	-	
5	124.5	7.16-7.20 (m, 1H) overlap	HMBC 5→3
6	127.9	7.20 (dd, J = 7.5, 7.3 Hz, 1H) overlap	HMBC 6→4,8
7	128.1	7.04 (ddd, J = 7.3, 1.5, 1.5 Hz, 1H)	
8	141.5	-	
9	124.7	7.41 (br s, 1H)	HMBC 9→3, TOCSY 9→5,6,7
10	29.6	2.70-2.76 (m, 1H), 2.94-3.00 (m, 1H) overlap	HMBC 10→7,8,9
11	34.7	2.42 (ddd, J = 14.5, 8.5, 2.7 Hz, 1H), 2.46-2.51 (m, 1H) obscured	HMBC 11→8
12	171.4	-	
13	-	7.87 (d, J = 7.4 Hz, 1H)	
14	54.5	4.22-4.27 (m, 1H) overlap	HMBC 14→16
15	61.4	3.34-3.40 (m, 2H) obscured	HMBC 15→16
16	170.0	-	
17	-	not observed	HMBC 18→16
18	-	7.70 (d, J = 8.0 Hz, 1H)	HMBC 19→24
19	57.1	4.01 (dd, J = 8.0, 7.1 Hz, 1H)	
20	35.9	1.60-1.68 (m, 1H)	
21	23.6	0.95-1.02 (m, 1H), 1.27-1.34 (m, 1H)	
22	10.7	0.73 (dd, J = 7.6, 7.6 Hz, 3H) overlap	
23	15.0	0.72 (d, J = 7.1 Hz, 3H) overlap	
24	171.2	-	
25	-	7.98 (d, J = 8.2 Hz, 1H)	HMBC 25→24,27
26	52.2	4.56 (ddd, J = 8.6, 8.2, 4.8 Hz, 1H)	HMBC 26→37, COSY 26→25,27
27	26.5	2.99-3.94 (m, 2H) overlap	
28	109.2	-	
29	128.6	7.35 (s, 1H)	HMBC 29→1,27,31,36
30	-	-	
31	134.5	-	
32	111.4	7.44 (d, J = 8.7 Hz, 1H)	HMBC 32→34,36
33	123.1	7.21 (dd, J = 8.7, 1.9 Hz, 1H)	HMBC 33→31,35
34	111.1	-	
35	120.9	7.78 (d, J = 1.9 Hz, 1H)	HMBC 35→31,33
36	129.3	-	
37	170.9	-	
38	-	7.94 (d, J = 7.3 Hz, 1H)	HMBC 38→37
39	47.8	4.21 (dq, J = 7.3, 7.2 Hz, 1H)	HMBC 39→41
40	18.1	1.17 (d, J = 7.2 Hz, 1H)	HMBC 40→39

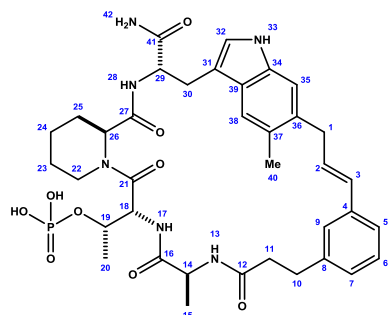
41	173.8	-	
42	-	7.02 (br s, 1H), 7.32 (br s, 1H)	



11

Atom #	¹³ C	¹ H	TOCSY/COSY	HMBC
1	32.4	3.62, 3.49	2, 3	2, 39, 40, 41
2	129.3	6.38	1, 3	3, 1, 4
3	129.9	6.28	1, 2	2, 1, 4
4	136.95	-	-	-
5	124.1	7.15		7, 9
6	128.3	7.18		4, 8
7	127.6	6.99		9
8	141.1	-	-	-
9	124.5	7.10		7
10	30.2	2.81, 2.70	10, 11, 11'	8, 12, 9, 7
11	35.4	2.47, 2.29	11', 10, 10'	8, 12
12	121.2	-	-	-
13	-	8.05	14, 15	12
14	47.74	4.10	15, 13	15, 16
15	17.6	0.84	14, 13	14, 16
16	172.3	-	-	-
17	-	7.84	18-20, 19	16
18	52.3	3.96	18-20, 19	19, 20, 23
19	27.3	1.77, 1.56		20, 21
20	30.9	1.96	18, 19	19, 21
21	173.94	-	-	-
22		7.20		21
23	171.2	-	-	-
24	-	7.54	25	23
25	50.7	4.43	26	26, 27

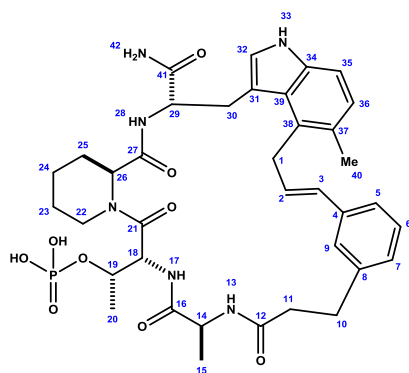
26	27.1	3.06, 2.92	25, 24	25, 27, 30
27	128.9	-	-	-
28	134.0	8.93		27, 30
29		not observed (imidazole N-H)		
30	116.81	7.28		27, 28
31	170.0	-	-	-
32		8.06	33, 34	31
33	53.7	4.58	34	34
34	27.7	3.15, 2.84	33, 32	33, 35
35	109.8	-	-	-
36	125.7	7.17	37	
37	-	10.81	36	35, 36, 38
38	133.09	-	-	-
39	112.8	7.20		41
40	120.1	-	-	-
41	155.3	-	-	-
42	103.8	7.56		35, 41, 38
43	133.04	-	-	-
44	172.2	-	-	-
45	-	8.38	46, 47-49	44
46	52.2	4.23	47	47
47	28.89	1.73, 1.59		46
48	25.07	1.48	49	46, 49
49	40.3	3.11	48	47, 48, 51
50	-	not observed (guanidine N-H)	-	-
51	156.9	-		
52		not observed (guanidine N-H)	-	-
53	173.3	-	-	-
54	-	7.36, 7.13		53



13

Atom #	¹³ C	¹ H	TOCSY/COSY	HMBC
1	36.20	3.60 (dd, J = 16.2, 5.1 Hz, 1H), 3.45 (dd, J = 15.6, 7.1 Hz, 1H)	2, 3	2, 3
2	130.08	6.31 (dt, J = 16.0, 6.1 Hz, 1H)	1, 3	1, 4
3	128.51	6.20 (d, J = 15.9 Hz, 1H)	2, 1	1, 9, 4
4	136.79			
5	123.93	7.14 (m, 1H) overlap		9
6	128.15	7.15 (m, 1H) overlap	7	4, 8
7	126.79	6.96 (m, 1H) overlap		
8	141.02			
9	124.78	7.14 (m, 1H) overlap		5
10	30.98	2.63 (m, 2H)	11	8, 7, 9
11	37.38	2.26 (m, 2H)	10	12
12	171.20			
13		8.19 (d, J = 7.9 Hz, 1H)	14, 15	14
14	47.49	4.24 (dq, J = 7.3, 7.3 Hz, 1H)	15, 13	15
15	17.20	1.02 (d, J = 7.2 Hz, 3H)	14, 13	14
16	171.28			
17		7.37 (d, J = 7.9 Hz, 1H)	18, 19, 20	
18	51.38	4.85 (m, 1H) overlap	17, 19, 20	19, 20, 21
19	71.42	4.34 (m, 1H) overlap	18, 20, 17	21
20	17.31	1.02 (d, J = 6.1 Hz, 1H)	19	20
21	166.99			
22	43.07	3.35 (ddd, J = 12.6, 12.6, 2.6 Hz, 1H), 3.82 (br. d, J = 12.1 Hz, 1H)		
23	24.20	1.50 (m, 2H)	22	
24	19.80	1.26 (m, 1H), 2.30 (m, 1H) overlap		
25	27.10	1.50 (m, 1H), 2.30 (m, 1H) overlap	26, 25', 24	27
26	51.50	4.86 (m, 1H) overlap	25	
27	170.72			
28		7.66 (d, J = 7.7 Hz, 1H)	29, 30	
29	54.40	4.29 (m, 1H)	28, 30	30
30	27.74	3.01 (dd, J = 14.3, 2.0, 1H), 2.89 (app t, J = 13.0 hz, 1H)	29, 28	29, 39, 31, 32

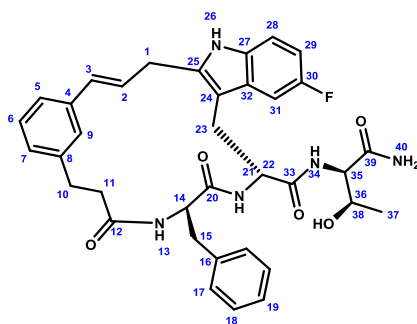
31	109.67			
32	123.97	7.14 (m, 1H) overlap		
33		10.56 (d, J = 1.7 Hz, 1H)		31, 34, 32, 39
34	135.06			
35	111.86	7.10 (s, 1H)		37
36	130.87			
37	125.61			
38	119.09	7.56 (s, 1H)		40, 31, 34, 36
39	125.81			
40	19.14	2.34 (s, 3H)		38, 36, 37
41	174.00			
42		6.97 (m, 1H) overlap, 7.52 (br. s, 1H)		41



14

Atom #	¹³ C	¹ H	TOCSY/COSY	HMBC
1	32.15	3.8 (m, 2H)	2, 3	38, 37, 2
2	128.75	6.43 (dt, J = 15.3, 6.8 Hz, 1H)	1, 3	1
3	128.80	6.3 (dt, J = 15.8 Hz, 1H)	1, 2	1, 9, 5
4	136.08			
5	124.51	6.94 (dt, J = 7.7 Hz, 1H)	6, 9	9, 7
6	127.88	7.08 (m, 1H) overlap	5, 7	4, 8
7	127.44	6.90 (dt, J = 7.6 Hz, 1H)	6, 9	9, 5, 10
8	140.20			
9	123.80	7.28 (s, 1H)	5, 6, 7	7
10	35.26	2.75 (m, 1H) overlap, 2.22 (m, 1H)	11	9, 8, 7, 11
11	30.78	2.74 (m, 1H) overlap	10	10
12	170.94			
13		7.81 (s, 1H)	14, 15	12, 14
14	47.77	4.12 (dq, J = 7.0, 7.0 Hz, 1H)	15, 13	15, 16
15	17.55	0.71 (d, J = 6.8 Hz, 3H)	14, 13	14, 16
16	171.52			
17		8.29 (d, J = 4.5 Hz, 1H)	18, 19, 20	16

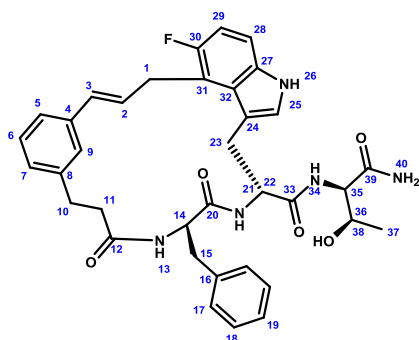
18	52.71	4.69 (app t, J = 6.2 Hz, 1H)	19, 17, 20	19, 21
19	71.25	4.39 (dddd, J = 9.6, 6.3, 6.3, 6.3 Hz, 1H)	18, 20, 17	18, 21
20	17.57	1.15 (d, J = 6.2 Hz, 3H)	19, 18, 17	
21	168.01			
22	43.25	3.08 (t, J = 12.1 Hz, 1H), 4.01 (m, 1H) overlap	22', 23, 23'	23
23	24.73	1.55 (m, 1H) overlap, 1.39 (m, 1H) overlap	22, 22'	
24	25.91	1.41 (m, 1H) overlap, 2.23 (m, 1H) overlap	25	
25	20.10	1.34 (m, 1H) overlap, 1.56 (m, 1H) overlap	26	
26	51.86	5.09 (d, J = 2.04 Hz, 1H)	25, 24, 23, 22	25, 24, 27
27	169.06			
28		7.98 (, J = 9.1 Hz, 1H)	29, 30, 30'	27
29	52.09	4.94 (dddd, J = 9.1, 9.1, 5.0 Hz, 1H)	28, 30	
30	29.74	3.68 (dd, J = 14.9, 9.5 Hz, 1H), 2.89 (dd, J = 15.1, 4.3 Hz, 1H)	29, 30', 28	29, 31, 32, 41
31	110.00			
32	122.80	7.20 (s, H)	33	31, 39, 34
33		10.78 (d, J = 2.0 Hz, 1H)	22	31, 32, 39, 34
34	135.45			
35	109.05	7.05 (m, H)	30	37
36	123.87	6.83 (d, J = 7.3 Hz, 1H)	35	38, 34, 40
37	125.09			
38	128.95			
39	135.31			
40	18.68	2.31 (s, 3H)		37, 36, 38
41	172.67			
42		7.73 (br. s), 7.07 (br. s)		29, 41



Peptide 19 - C2

Atom #	13C	1H	TOCSY/COSY	HMBC
1	30.04	3.57 (dd, J = 15.3, 7.2 Hz, 1H), 3.80 (dd, J = 15.3, 6.3 Hz, 1H)	2, 3	25, 24, 2, 3
2	127.55	6.07 (dt, J = 15.6, 6.9 Hz, 1H)	1	1, 4
3	131.01	6.43 (d, J = 15.9 Hz, 1H)	1	1, 4, 5, 9
4	136.80	-	-	-

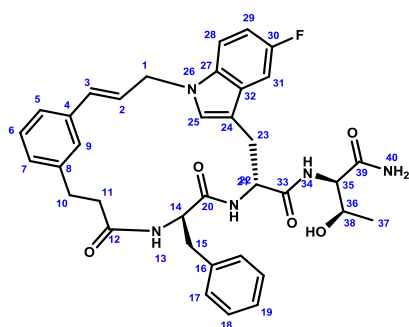
5	123.62	7.10 (m, 1H) overlap		9
6	127.90	7.13 (m, 1H) overlap		4
7	124.02	7.1 (m, 1H) overlap		5, 9
8	141.20	-	-	-
9	124.99	6.98 (br. s, 1)		5
10	30.36	2.62 (m, 1H) overlap, 2.88 (ddd, J = 13.7, 11.0, 5.6 Hz, 1H)	11	8, 9
11	35.82	1.98 (ddd, J = 14.0, 7.6, 3.1 Hz, 1H), 2.40 (ddd, J = 13.6, 11.0, 2.6 Hz, 1H)	10	8, 12
12	171.15	-	-	-
13	-	8.07 (d, J - 8.9 Hz, 1H)	14, 15, 15'	12
14	52.65	4.75 (ddd, J - 9.3, 9.5, 3.8 Hz, 1H)	15, 15', 13	15
15	38.01	2.98 (m, 1H) overlap , 2.65 (m, 1H) overlap	14, 13	14, 16, 17
16	138.10	-	-	-
17	129.47	7.16 (m, 1H) overlap		18
18	127.73	7.17 (m, 1H) overlap		16, 17
19	128.04	7.14 (m, 1H) overlap		
20	172.05			
21	-	8.59 (d, J = 7.8 Hz, 1H)	22, 23	20
22	54.09	4.66 (ddd, J = 10.2, 7.6, 5.1 Hz, 1H)	23, 21	23
23	26.16	3.07 (dd, J - 15.1, 5.2 Hz, 1H), 2.97 (m, 1H) overlap	22, 21	22, 24, 32
24	106.41	-	-	-
25	136.40	-	-	-
26	-	10.91 (s, 1H)		24, 32, 25, 27
27	131.80	-	-	-
28	111.20	7.18 (m, 1H) overlap	29	30
29	108.40	6.81 (ddd, J = 9.3, 9.3, 2.5 Hz, 1H)	28, 31	27, 30 (weak)
30	156.60			
31	103.40	7.24 (dd, J = 10.3, 2.7 Hz, 1H)	29, 28	27, 30
32	129.00	-		
33	172.07	-		
34	-	7.73 (d, J = 8.7 Hz, 1H)	35, 36	33
35	57.77	4.13 (dd, J = 8.7, 2.9 Hz, 1H)	36, 37	36, 39
36	66.16	4.07 (m, 1H)	35, 37	
37	19.50	1.05 (d, J = 6.4 Hz, 3H)	35, 36	35, 36
38		4.96 (d, J = 4.9 Hz, 1H)	35, 36, 37	35, 36, 37
39	172.04	-		
40	-	6.93 (m, 1H) overlap		39



Peptide 19 - C4

Atom #	¹³ C	¹ H	TOCSY/COSY	HMBC
1	27.76	3.76 (dd, J = 16.6, 5.9 Hz, 1H), 3.90 (br. d, J = 16.0 Hz, 1H)	2, 3	2, 3, 31
2	130.04	6.07 (d, J = 15.8 Hz, 1H)	1, 3	1, 31
3	128.84	6.35 (dt, J = 16.0, 5.5 Hz, 1H)	2, 1	1, 9, 5, 30, 32
4	136.48	-	-	-
5	122.9	7.00 (m, 1H) overlap		9
6	127.8	7.06 (m, 1H) overlap		4, 8
7	127.12	6.93 (m, 1H) overlap		9
8	141.28	-		
9	125.81	6.99 (br. s, 1H)		7, 5
10	29.63	2.91 (m, 1H) overlap, 2.52 (m, 1H) overlap	11	11, 8, 9, 7, 12
11	35.72	2.32 (app t, 13.5 Hz, 1H), 2.08 (m, 1H) overlap	10	10, 8, 12
12	170.66	-		
13	-	8.1 (d, J = 8.9 Hz, 1H)	14, 15, 15'	12
14	52.61	4.82 (ddd, J = 9.7, 9.7, 4.1 Hz, 1H)	13, 15	15
15	38.02	2.89 (m, 1H) overlap, 2.64 (dd, J = 13.3, 10.5 Hz, 1H)	14, 13	14, 16, 17
16	137.74	-	-	-
17	128.79	7.21 (m, 1H) overlap		
18	127.6	7.21 (m, 1H) overlap		
19	127.6	7.15 (m, 1H) overlap		17
20	171.06	-	-	-
21	-	8.62 (d, J = 6.6 Hz, 1H)	22, 23	20
22	53.19	4.66 (m, 1H)		
23	29.10	3.30 (m, 1H) overlap, 3.06 (br. d, J = 13.4 Hz, 1H)		22 (weak), 24
24	110.63	-		
25	125.8	7.13 (m, 1H) overlap		27
26	-	10.96 (br. s, 1H)	25	24, 25, 27
27	132.95	-		
28	110.0	7.18 (m, 1H) overlap	29	30, 32
29	108.8	6.89 (m, 1H) overlap	28	27, 30, 31
30	154.46	-	-	-

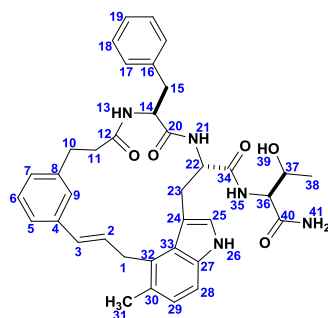
31	115.6	-	-	-
32	125.8	-	-	-
33	170.67	-	-	-
34	-	7.74 (d, J = 8.3 Hz, 1H)	35, 36	33
35	57.76	4.08 (dd, J = 8.7, 3.0 Hz, 1H)	36, 37	36
36	65.82	4.02 (m, 1H)	35	
37	19.80	0.99 (d, J = 6.4 Hz, 3H)	36, 35	35, 36
38	-	4.9 (d, J = 5.1 Hz, 1H)	35, 36, 37	35, 36, 37
39	171.73	-	-	-
40	-	7.03 (m, 1H) overlap		39



Peptide 19 - N1

Atom #	¹³ C	¹ H	TOCSY/COSY	HMBC
1	46.6	4.95 (ddd, J = 16.4, 4.7, 1.6 Hz, 1H), 4.83 (dd, J = 16.4, 6.9 Hz, 1H)	2, 3	2, 3, 25
2	125.5	6.07 (ddd, J = 15.8, 7.1, 4.5 Hz, 1H)	3, 1	3, 1, 4
3	131	6.22 (br d, J = 15.9 Hz, 1H)	2, 1	2, 1, 4
4	135.7	-	-	-
5	124.7	7.11 (m, 1H) overlap		9, 7
6	127.8	7.15 (m, 1H) overlap		8, 4
7	128.2	6.96 (m, 1H) overlap		9
8	142	-	-	-
9	124.5	6.92 (m, 1H) overlap		7
10	29.1	2.46 (m, 1H) overlap, 2.95 (m, 1H) overlap	11	8, 11, 7, 9, 12
11	35.5	2.08 (ddd, J = 15.1, 7.2, 2.4 Hz, 1H), 2.40 (ddd, J = 15.2, 11.6, 2.3 Hz, 1H)	10	8, 10, 12
12	170.64	-	-	-
13	-	7.68 (d, J = 8.5 Hz, 1H)	14, 15	12
14	52.6	4.71 (m, 1H) overlap	13, 15, 15'	
15	38.9	2.70 (dd, J = 13.6, 8.0 Hz, 1H), 3.02 (dd, J = 13.6, 4.1 Hz, 1H)	13, 14	14, 16, 17, 20
16	137.3	-	-	-
17	129.4	7.08 (m, 1H) overlap		15
18	127.8	7.15 (m, 1H) overlap		16

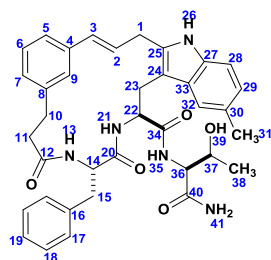
19	126.4	7.11 (m, 1H) overlap		17
20	170.6	-		
21	-	8.60 (d, J = 8.7 Hz, 1H)	22, 23	20
22	52.6	4.74 (m, 1H) overlap	23, 21	23
23	27.2	3.10 (br. d, J = 14.8 Hz, 1H), 2.90 (m, 1H) overlap	21, 22	22, 24, 25
24	110.8	-	-	-
25	128.1	7.28 (s, 1H)		1, 32, 28
26				
27	132.6	-	-	-
28	110.9	7.45 (dd, J = 7.8, 4.5 Hz, 1H)	29, 31	32
29	109.22	6.94 (m, 1H) overlap	28, 31	27, 30
30	157	-		
31	103.8	7.51 (dd J = 9.9, 2.4 Hz, 1H)	29, 28	27, 30
32	127.83	-	-	-
33	171.88	-	-	-
34	-	7.96 (d, J = 8.8 Hz, 1H)	35, 36	33
35	58.01	4.21 (dd, J = 8.8, 3.1 Hz, 1H)	36, 34	36
36	66.39	4.10 (m, 1H)	34, 35, 37	
37	19.98	1.07 (d, J = 6.4 Hz, 3H)	36	35, 36
38	-	not observed O-H		
39	172.19	-	-	-
40	-	7.2 (br. s, 2H)		39



Peptide 20 - C4

Atom #	¹³ C	¹ H	key correlation
1	32.0	3.82-3.91 (m, 2H)	
2	128.9	6.37 (dt, J = 16.0, 5.4 Hz, 1H)	HMBC 2→4,32, COSY 2→1
3	129.6	6.07 (d, J = 16.0 Hz, 1H)	HMBC 3→5,9
4	136.7	-	
5	123.0	7.02 (d, J = 8.0 Hz, 1H)	
6	127.7	7.09 (dd, J = 8.0, 8.0 Hz, 1H) overlap	HMBC 6→4,8
7	126.8	6.94 (d, J = 8.0 Hz, 1H) overlap	
8	141.1	-	

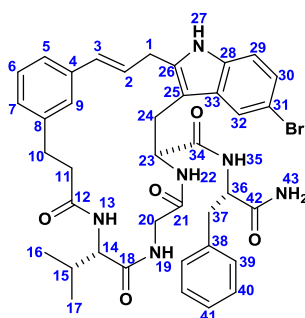
9	125.3	7.07 (br s, 1H) overlap	
10	29.7	2.54-2.59 (m, 1H) obscured, 2.91-2.97 (m, 1H) overlap	HMBC 10→7,9,12
11	35.9	2.09-2.15 (m, 1H), 2.33-2.39 (m, 1H) overlap	HMBC 11→8,12
12	170.6	-	
13	-	7.94 (d, J = 9.1 Hz, 1H)	HMBC 13→12
14	52.5	4.80-4.88 (m, 1H)	
15	37.9	2.66-2.72 (m, 1H), 2.92-2.97 (m, 1H) overlap	HMBC15→16,17
16	137.7	-	
17	128.8	7.23-7.24 (m, 2H) overlap	HMBC 17→15
18	127.5	7.23-7.25 (m, 2H) overlap	
19	125.6	7.14-7.19 (m, 1H)	
20	171.0	-	
21	-	8.44-8.48 (m, 1H)	HMBC 21→20
22	53.4	4.63-4.70 (m, 1H)	
23	29.5	3.14-3.19 (m, 1H), 3.39 (dd, J = 13.9, 9.9 Hz, 1H)	HMBC 23→24
24	109.5	-	
25	123.3	7.06-7.08 (m, 1H) overlap	HMBC 25→24,27,33
26	-	10.66 (br s, 1H)	COSY 26→25, HMBC 26→24,25,27,33
27	135.4	-	
28	109.2	7.12 (d, J = 8.3 Hz, 1H) overlap	HMBC 28→30,33
29	123.6	6.91 (d, J = 8.3 Hz, 1H)	HMBC 29→27,31,32
30	125.2	-	
31	18.4	2.34 (s, 3H)	HMBC 31→29,30,32
32	128.4	-	
33	126.0	-	
34	170.7	-	
35	-	7.59 (d, J = 8.4 Hz, 1H)	
36	57.6	4.13 (dd, J = 8.4, 3.0 Hz, 1H)	HMBC 36→40
37	65.8	4.04-4.09 (m, 1H)	
38	19.6	1.05 (d, J = 6.2 Hz, 1H)	COSY 38→37, HMBC 38→36,37
39	-	not observed	
40	171.6	-	
41	-	6.87 (br s, 1H), 6.95 (br s, 1H) overlap	



Peptide 19 - C2

Atom #	¹³ C	¹ H	key correlation
1	29.8	3.56 (dd, J = 15.6, 6.9 Hz, 1H), 3.78 (dd, J = 15.6, 5.9 Hz, 1H)	HMBC 1→24,25
2	127.8	6.08 (apt dt, J = 15.7, 6.8 Hz, 1H)	COSY 2→1, HMBC 2→4
3	130.3	6.40 (d, J = 15.7 Hz, 1H)	
4	136.6	-	
5	123.9	7.09-7.12 (m, 1H) overlap	
6	127.8	7.14 (dd, J = 7.4, 7.4 Hz, 1H) overlap	
7	127.1	6.95 (br d, J = 7.4 Hz, 1H)	HMBC 7→5
8	141.0	-	
9	124.4	6.98-7.00 (m, 1H) overlap	
10	30.0	2.59-2.65 (m, 1H) overlap, 2.06-2.92 (m, 1H)	HMBC 10→8
11	35.8	2.00 (ddd, J = 14.0, 7.7, 3.1 Hz, 1H), 2.37-2.42 (m, 1H) overlap	
12	171.0	-	
13	-	8.08 (d, J = 8.8 Hz, 1H)	TOCSY 13→14,15, HMBC 13→12
14	52.5	4.79 (ddd, J = 9.4, 9.4, 3.8 Hz, 1H)	
15	38.2	2.61-2.66 (m, 1H) overlap, 2.97-3.02 (m, 1H) overlap	HMBC 15→16
16	137.6	-	
17	129.1	7.17-7.19 (m, 2H) overlap	HMBC 17→19
18	127.4	7.17-7.20 (m, 2H) overlap	HMBC 18→16
19	125.7	7.12-7.15 (m, 1H) overlap	HMBC 19→17
20	172.0	-	
21	-	8.62 (d, J = 7.6 Hz, 1H)	TOCSY 21→22,23, HMBC 21→20
22	54.2	4.67 (ddd, J = 10.6, 7.6, 4.6 Hz, 1H)	
23	26.0	3.02 (dd, J = 14.9, 10.6 Hz, 1H), 3.10 (dd, J = 14.9, 4.6 Hz, 1H) overlap	HMBC 23→24,25
24	105.3	-	
25	133.9	-	
26	-	10.64 (s, 1H)	HMBC 26→24,25,33
27	133.3	-	
28	109.9	7.11 (d, J = 8.3 Hz, 1H) overlap	HMBC 28→30,33
29	121.6	6.83 (dd, J = 8.3, 1.3 Hz, 1H)	HMBC 29→32,31
30	126.3	-	
31	21.1	2.39 (s, 3H)	HMBC 31→29,30,32

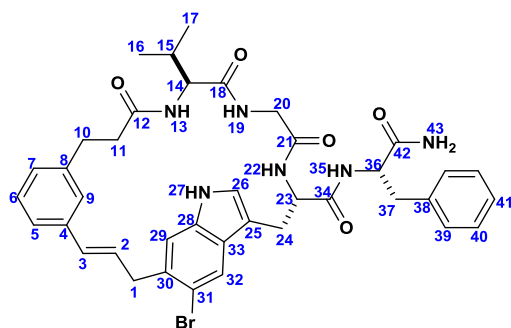
32	117.6	7.30 (br s, 1H)	HMBC 32→29,31
33	129.0	-	
34	171.9	-	
35	-	7.66 (d, J = 8.5 Hz, 1H)	HMBC 35→34
36	57.5	4.16 (dd, J = 8.5, 3.1 Hz, 1H)	HMBC 36→40
37	66.0	4.08-4.13 (m, 1H) overlap	
38	19.7	1.08 (d, J = 6.4 Hz, 3H)	HMBC 38→36,37
39	-	not observed	
40	171.8	-	
41	-	6.98-7.00 (m, 1H) overlap, 7.10-7.12 (m, 1H) overlap	HMBC 41→40, TOCSY 41→41'



VGW(5-Br)-C2

Atom #	13C	1H	key correlation
1	28.3	3.53 (dd, J = 17.2, 5.9 Hz, 1H), 3.81 (dd, J = 17.2, 5.9 Hz, 1H)	HMBC 1→25,26
2	127.6	6.56 (ddd, J = 16.0, 5.9, 5.9 Hz, 1H)	HMBC 2→4, COSY 2→1
3	130.2	6.37 (br d, J = 16.0 Hz, 1H)	
4	136.9	-	
5	123.0	7.26 (d, J = 7.9 Hz, 1H) overlap	HMBC 5→9,3
6	127.97	7.18 (dd, J = 7.9, 7.9 Hz, 1H) overlap	HMBC 6→4,8
7	127.95	6.99 (d, J = 7.9 Hz, 1H) overlap	
8	140.7	-	
9	124.9	7.20 (s, 1H) overlap	
10	29.8	2.73-2.78 (m, 1H) overlap, 2.89-2.96 (m, 1H) overlap	HMBC 10→9
11	34.0	2.34-2.40 (m, 1H), 2.72-2.79 (m, 1H) overlap	TOCSY 11→11',10
12	171.3	-	
13	-	7.78 (d, J = 9.1 Hz, 1H)	TOCSY 13→14,15,16,17, HMBC 13→12
14	58.0	3.92 (dd, J = 9.1, 6.0 Hz, 1H)	HMBC 14→18
15	29.1	1.92-1.98 (m, 1H)	
16	17.6	0.76 (d, J = 3.7 Hz, 3H)	
17	19.0	0.77 (d, J = 3.7 Hz, 3H)	

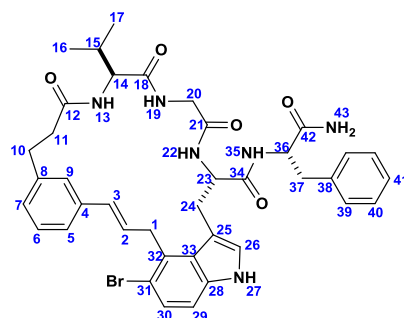
18	170.8	-	
19	-	6.97 (dd, J = 8.0, 2.9 Hz, 1H) overlap	
20	41.1	3.12 (dd, J = 16.7, 2.9 Hz, 1H), 3.76 (dd, J = 16.7, 8.0 Hz, 1H)	TOCSY 20→19, HMBC 20→18,21
21	167.6	-	
22	-	8.04-8.08 (m, 1H) overlap	HMBC 22→21
23	53.1	4.51-4.56 (m, 1H)	HMBC 23→34
24	26.7	2.72-2.79 (m, 1H) overlap, 2.96-3.00 (m, 1H) obscured	HMBC 24→25,26,33,34
25	106.6	-	
26	136.4	-	
27	-	11.00 (s, 1H)	
28	134.1	-	
29	112.3	7.21 (d, J = 8.5 Hz, 1H) overlap	HMBC 29→31
30	122.5	7.12 (dd, J = 8.5, 1.6 Hz, 1H)	HMBC 30→28,31
31	110.7	-	
32	120.0	7.73 (d, J = 1.6 Hz, 1H)	HMBC 32→25,28,30,31
33	129.8	-	
34	171.1	-	
35	-	8.04-8.08 (m, 1H) overlap	HMBC 35→34
36	53.5	4.49 (ddd, J = 9.0, 8.0, 5.0 Hz, 1H)	HMBC 36→34,38,42
37	37.3	2.86 (dd, J = 13.7, 9.0 Hz, 1H), 3.05 (dd, J = 13.7, 5.0 Hz, 1H)	HMBC 37→38,39
38	137.5	-	
39	129.0	7.22 (d, J = 7.7 Hz, 2H) overlap	
40	127.9	7.26 (dd, J = 7.7, 7.7 Hz, 2H) overlap	HMBC 40→38
41	126.0	7.15-7.18 (m, 1H) overlap	
42	172.4	-	
43	-	7.15 (br s, 1H), 7.46 (br s, 1H)	HMBC 43→42, TOCSY 43→43'



VGW(5-Br)-C6

Atom #	¹³ C	¹ H	key correlation
1	38.3	3.61-3.67 (m, 1H) overlap, 3.69-3.75 (m, 1H) overlap	HMBC 1→3
2	129.0	6.40 (ddd, J = 16.0, 5.6, 5.6 Hz, 1H)	HMBC 2→4, COSY 2→1
3	129.1	6.08 (br d, J = 16.0 Hz, 1H)	HMBC 3→4,5,9
4	137.0	-	
5	122.6	7.21 (br d, J = 8.0 Hz, 1H)	HMBC 5→3,7,9
6	127.6	7.17 (dd, J = 8.0, 8.0 Hz, 1H) overlap	HMBC 6→8,4
7	126.7	6.99 (d, J = 8.0 Hz, 1H) overlap	
8	140.9	-	
9	124.5	6.99 (br s, 1H) overlap	HMBC 9→3,5,7
10	29.1	2.68-2.74 (m, 1H), 2.86-2.92 (m, 1H) overlap	HMBC 10→8
11	34.3	2.42-2.48 (m, 1H), 2.53-2.59 (m, 1H)	HMBC 11→8
12	170.9	-	
13	-	7.39 (d, J = 8.7 Hz, 1H)	HMBC 13→12
14	57.8	3.92 (dd, J = 8.7, 5.9 Hz, 1H)	COSY 14→13, HMBC 14→18
15	29.5	1.83-1.90 (m, 1H)	COSY 15→14
16	17.0	0.68 (d, J = 6.7 Hz, 3H) overlap	COSY 16→15
17	18.6	0.69 (d, J = 6.6 Hz, 3H) overlap	
18	170.3	-	
19	-	7.26-7.31 (m, 1H) overlap	
20	40.8	3.09-3.17 (m, 1H) overlap, 3.66-3.72 (m, 1H) overlap	HMBC 20→18,21
21	167.4	-	
22	-	7.75-7.86 (m, 1H) overlap	
23	54.8	4.50-4.56 (m, 1H) overlap	COSY 23→22
24	27.6	2.76-2.82 (m, 1H), 3.04-3.10 (m, 1H) overlap	
25	109.9	-	
26	124.4	7.13 (d, J = 2.1 Hz, 1H)	HMBC 26→25,28,33, COSY 26→27
27	-	10.71 (br s, 1H)	HMBC 27→25,26,28,33
28	135.1	-	
29	113.1	7.31 (s, 1H)	HMBC 29→1
30	129.6	-	

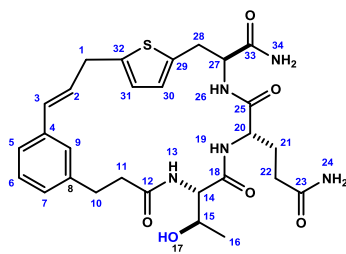
31	113.8	-	
32	121.9	8.00 (s, 1H)	HMBC 32→25,28,30,31
33	128.1	-	
34	170.5	-	
35	-	7.84 (d, J = 8.1 Hz, 1H) overlap	HMBC 35→34
36	53.1	4.56 (ddd, J = 8.5, 8.1, 5.4 Hz, 1H) overlap	HMBC 36→38,42
37	37.2	2.91 (dd, J = 13.9, 8.5 Hz, 1H) overlap, 3.10 (dd, J = 13.9, 5.4 Hz, 1H) overlap	HMBC 37→38,39
38	137.4	-	
39	128.6	7.25-7.28 (m, 2H) overlap	HMBC 39→41
40	127.5	7.25-7.28 (m, 2H) overlap	HMBC 40→38
41	125.5	7.16-7.20 (m, 1H) overlap	
42	172.1	-	
43	-	not observed	



VGW(5-Br)-C4

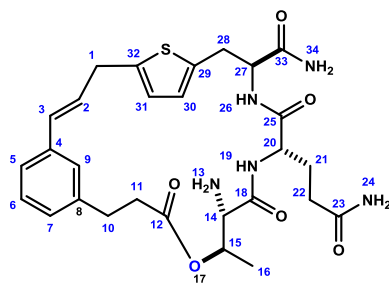
Atom #	¹³ C	¹ H	key correlation
1	34.9	3.93 (br dd, J = 16.6, 4.1 Hz, 1H), 4.03 (dd, J = 16.6, 6.3 Hz, 1H)	HMBC 1→31,33
2	128.2	6.42 (ddd, J = 16.0, 6.3, 4.1 Hz, 1H)	COSY 2→1, HMBC 2→4,5
3	129.8	6.13 (br d, J = 16.0 Hz, 1H)	
4	136.8	-	
5	123.1	6.99 (dd, J = 7.9 Hz, 1H) overlap	
6	127.90	7.14-7.19 (m, 1H) overlap	HMBC 6→8,4
7	127.30	7.09 (d, J = 7.9 Hz, 1H) overlap	HMBC 7→10
8	141.3	-	
9	124.62	7.28 (br s, 1H)	HMBC 9→10,5,7
10	29.3	2.68-2.75 (m, 1H) overlap, 2.96-3.03 (m, 1H) overlap	HMBC 10→7,8,9
11	34.3	2.40-2.47 (m, 1H), 2.69-2.77 (m, 1H) overlap	HMBC 11→8
12	171.7	-	
13	-	7.95 (d, J = 8.6 Hz, 1H)	TOCSY 13→14,15,16,17, HMBC 13→12

14	57.5	4.24 (dd, J = 8.6, 5.6 Hz, 1H)	HMBC 14→18
15	30.1	2.03-2.11 (m, 1H)	HMBC 15→18
16	17.3	0.78 (d, J = 6.9 Hz, 3H)	
17	19.1	0.82 (d, J = 6.9 Hz, 3H)	
18	171.0	-	
19	-	7.82-7.86 (m, 1H) overlap	HMBC 19→18
20	42.3	3.58 (dd, J = 16.4, 4.8 Hz, 1H), 3.78 (dd, J = 16.4, 6.1 Hz, 1H)	COSY 20→19, HMBC 20→18
21	168.2	-	
22	-	8.11 (d, J = 8.1 Hz, 1H)	HMBC 22→21
23	54.0	4.59 (ddd, J = 8.4, 8.1, 5.9 Hz, 1H)	HMBC 23→24
24	29.3	2.96-3.03 (m, 1H) overlap, 3.15 (dd, J = 14.7, 8.4 Hz, 1H)	HMBC 24→25,34
25	110.1	-	
26	125.5	6.90 (d, J = 2.2 Hz, 1H)	HMBC 26→25,33
27	-	11.05 (d, J = 2.2 Hz, 1H)	HMBC 27→25,26,28,33
28	135.6	-	
29	111.6	7.17 (d, J = 8.5 Hz, 1H) overlap	HMBC 29→31
30	124.55	7.25 (d, J = 8.5 Hz, 1H) overlap	
31	114.7	-	
32	129.5	-	
33	126.3	-	
34	170.0	-	
35	-	7.85 (d, J = 8.3 Hz, 1H)	HMBC 35→34
36	53.6	4.39 (ddd, J = 8.5, 8.3, 5.3 Hz, 1H)	HMBC 36→34,42
37	37.2	2.74-2.81 (m, 1H) overlap, 2.96-3.02 (m, 1H) overlap	HMBC 37→38,39,42
38	137.4	-	
39	128.9	7.18 (d, J = 7.7 Hz, 2H) overlap	HMBC 39→37
40	127.8	7.20-7.25 (m, 2H) overlap	
41	126.0	7.14-7.19 (m, 1H) overlap	
42	172	-	
43	-	6.99 (br s, 1H) overlap, 7.10 (br s, 1H) overlap	TOCSY 43→43', HMBC 43→42



22

Atom #	¹³ C	¹ H	TOCSY/COSY	HMBC
1	32.75	3.58 (m, 2H)	2, 3	
2	128.60	6.42 (dt, J = 15.7, 6.3 Hz, 1H)	3, 1	
3	130.49	6.34 (d, J = 15.8 Hz, 1H)	2, 1	
4	136.72			
5	123.83	7.09 (m, 1H)		
6	127.77	7.13 (t, J = 7.4 Hz, 1H)		
7	127.43	6.97 (d, J = 7.4 Hz, 1H)	9	
8	140.83			
9	124.82	7.35 (s, 1H)	7	
10	29.86	2.72 (m, 1H) overlap, 2.91 (m, 1H)	11	
11	34.57	2.55 (m, 1H) overlap	10	
12	171.38			
13		7.69 (d, J = 7.3 Hz, 1H)		
14	57.93	4.04 (dd, J = 7.1, 4.5 Hz, 1H)	13, 15, 16	
15	65.93	3.76 (dddd, J = 10.7, 6.3, 6.3, 6.3 Hz, 1H)	15, 14, 13	
16	18.38	0.75 (d, J = 6.4 Hz, 3H)	15, 14, 13	
17		not observed		
18	169.19			
19		7.62 (d, J = 7.8 Hz, 1H)	20, 21, 22	
20	51.67	4.23 (ddd, J = 8.0, 8.0, 5.2 Hz, 1H)	19, 21, 22	
21	27.78	1.86 (dddd, J = 13.8, 13.8, 7.4, 3.8 Hz, 1H)	20, 22	
22	30.93	2.06 (t, J = 7.8 Hz, 2H)	21	
23	173.79			
24		7.21 (br. s, 1H), 6.73 (br. s, 1H)	24-24'	
25	171.14			
26		8.16 (d, J = 8.4 Hz, 1H)	27, 28, 28'	
27	53.70	4.33 (ddd, J = 11.0, 8.6, 3.1 Hz, 1H)	26, 28, 28'	
28	31.69	2.97 (dd, J = 15.0, 10.8, 1H), 3.12 (m, 1H) overlap	27, 26	
29	138.13			
30	125.28	6.66 (d, J = 3.3 Hz, 1H)	31	
31	124.02	6.63 (d, J = 3.3 Hz, 1H)	30	
32	141.07			
33	172.51			
34		7.43 (br. s, 1H), 7.09 (br. s, 1H)	34, 34'	



21

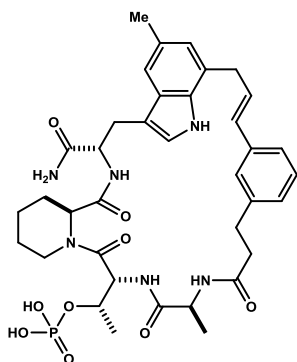
Atom #	¹³ C	¹ H	TOCSY/COSY	HMBC
1	32.27	3.53 (m, 2H)	2, 3	2, 3, 32, 31
2	138.30	6.17 (dt, J = 15.2, 7.6 Hz, 1H)	3, 1	1
3	13.03	6.45 (d, J = 15.7 Hz, 1H)	2, 1	1, 9
4	136.29			
5	125.06	7.11 (m, 1H) overlap		9
6	128.70	7.23 (m, 1H) overlap	8, 7	4, 8
7	12.57	7.10 (m, 1H) overlap		9
8	140.06			
9	124.00	7.1 (m, 1H) overlap		7
10	30.79	2.86 (m, 2H)	11	11, 8, 9, 12
11	35.85	2.55 (m, 2H)	10	10, 8, 12
12	171.41			
13		8.30 (m, 3H)	14, 15, 16	14, 15, 18
14	55.08	3.83 (m, 1H)	15, 13, 16	18
15	68.92	4.69 (dddd, J = 9.4, 6.3, 6.3, 6.3 Hz, 1H)	14, 16, 13	12, 14
16	16.40	0.65 (d, J = 6.4 Hz, 1H)	15, 14, 13	14, 15
17				
18	165.16			
19		8.73 (d, J = 8.2 Hz, 1H)	20	
20	51.83	4.33 (ddd, J = 7.4, 7.4, 7.4 Hz, 1H)	21, 22	
21	28.73	1.79 (dddd, J = 14.7, 7.7, 7.7, 7.7 Hz, 1H), 1.71 (dddd, J = 14.6, 7.7, 7.7, 7.7 Hz, 1H)	20, 22	22, 25, 23
22	30.94	2.03 (app. t, J = 8.1 Hz, 2H)	21, 20, 19	21, 23
23	173.46			
24		6.76 (br. s, 1H), 7.28 (br. s, 1H)		22
25	169.48			
26		8.38 (d, J = 8.7 Hz, 1H)	27, 28	25
27	53.42	4.44 (ddd, J = 11.1, 8.7, 2.4 Hz, 1H)	28, 26	28
28	32.24	3.10 (d, J = 13.1 Hz, 1H), 2.91 (dd, J = 15.1, 11.2 Hz, 1H)	27, 26	29, 30
29	137.70			

30	126.08	6.65 (d, J = 3.4 Hz, 1H)	31	29, 31
31	123.99	6.54 (d, J = 3.4 Hz, 1H)	30	32, 30
32	140.30			
33	172.50			
34		7.61 (br. s, 1H), 7.16 (br. s, 1H)		33

Tabulated ^1H NMR for macrocycles:

The following products have been assigned by key HMBC/HSQC/TOCY/COSY. Full spectral assignment, analogous to those above is ongoing.

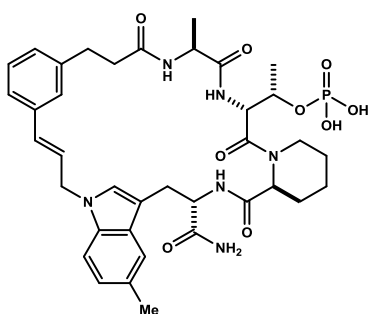
Cyclic Ala-(D-pThr)-Pip-Trp(5-Me) (**15**):



^1H NMR (DMSO- d_6 , 500 MHz): δ 10.51 (d, J = 1.8 Hz, 1H), 8.42 (d, J = 8.5 Hz, 1H), 7.7 (d, J = 7.2 Hz, 1H), 7.53 (s, 1H), 7.44 (s, 1H), 7.23 (d, J = 2.3 Hz, 1H), 7.15-7.20 (m, 2H), 7.11 (d, J = 7.7 Hz, 1H), 6.97 (br. s, 1H), 6.77 (s, 1H), 6.55 (d, J = 15.7 Hz, 1H), 6.51 (br. s, 1H), 6.2 (dt, J = 15.7, 6.6 Hz, 1H), 6.82-6.88 (m, 2H), 4.65-4.43 (m, 1H), 4.21-4.29 (m, 2H), 3.84 (d, J = 12.2 Hz, 1H), 3.8 (dd, J = 15.0, 7.1 Hz, 1H), 3.55 (dd, J = 15.1, 5.2 Hz, 1H), 3 (br. d, J = 12.1 Hz, 1H), 2.87 (t, J = 13.4 Hz, 1H), 2.64-2.72 (m, 2H), 2.36 (s, 3H), 2.19-2.34 (m, 3H), 1.41-

1.53 (m, 3H), 1.17-1.27 (m, 1H), 1.09 (d, J = 7.2 Hz, 3H), 0.98 (d, J = 6.4 Hz, 3H).

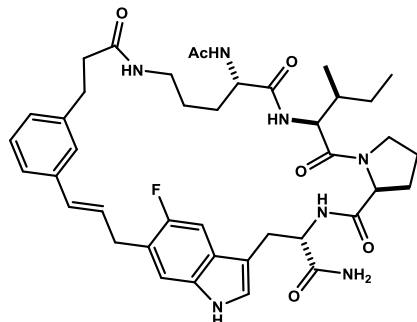
Cyclic Ala-(D-pThr)-Pip-Trp(5-Me) (**16**):



^1H NMR (DMSO- d_6 , 500 MHz): δ 8.38 (d, J = 8.3 Hz, 1H), 7.76 (d, J = 7.6 Hz, 1H), 7.55-7.61 (m, 2H), 7.28 (d, J = 7 Hz, 1H), 7.20-7.25 (m, 4H), 7.05-7.11 (m, 2H), 7.01 (s, 1H), 8.88 (d, J = 8.9 Hz, 1H), 6.5 (d, J = 16 Hz, 1H), 6.16 (dt, J = 16.0, 5.7 Hz, 1H), 4.90-5.01 (m, 1H), 4.89-4.92 (m, 2H), 4.84 (dd, J = 7.2, 4.0 Hz, 1H), 4.37-4.44 (m, 1H), 4.34 (ddd, J = 11.9, 7.6, 3.0 Hz, 1H), 4.23 (dq, J = 7.6, 7.6 Hz, 1H), 3.88 (d, J = 12.5 Hz, 1H), 3.15-

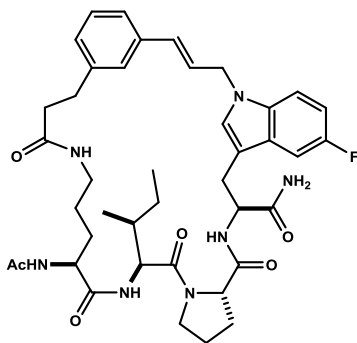
3.25 (m, 1H), 3.03 (dd, J = 14.4, 2.6 Hz, 1H), 2.9 (dd, J = 14.2, 12.5 Hz, 1H), 2.68-2.81 (m, 3H), 2.36 (s, 3H), 2.26 (ddd, J = 12.9, 11.8, 6.4 Hz, 1H), 2.17 (ddd, J = 13.0, 11.5, 4.7 Hz, 1H), 1.40-1.58 (m, 4H), 1.18-1.30 (m, 1H), 1.09 (d, J = 7.4 Hz, 3H), 0.99 (d, J = 6.4 Hz, 3H).

Cyclic Orn-Ile-Pro-Trp(5-F) (**17**):



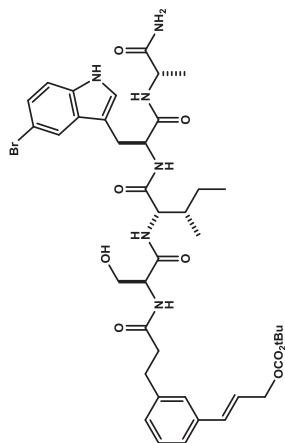
^1H NMR (DMSO- d_6 , 500 MHz): 10.82 (d, J = 1.9 Hz, H), 7.91 (d, J = 7.7 Hz, H), 7.81 (d, J = 8.4 Hz, H), 7.79 (d, J = 5.7 Hz, H), 7.44-7.52 (m, H), 7.79 (br. s, H), 7.21 (d, J = 6.4 Hz, H), 7.12-7.18 (m, H), 6.96-7.003 (m, H), 6.31 (dt, J = 15.8, 5.8 Hz, H), 6.3 (d, J = 15.9 Hz, H), 4.46 (ddd, J = 9.7, 8.0, 3.6 Hz, H), 4.22-4.29 (m, H), 4.17 (t, J = 8.2 Hz, H), 4.12 (dd, J = 8.3, 5.0 Hz, H), 3.69 (ddd, J = 9.5, 6.7, 6.7 Hz, H), 3.56 (d, J = 5.5 Hz, H), 3.44 (ddd, J = 9.4, 6.7, 6.4 Hz, H), 2.98-3.10 (m, H), 2.94 (dd, J = 14.9, 10.0 Hz, H), 2.75-2.85 (m, H), 2.69 (t, J = 15.6 Hz, H), 2.25 (t, J = 15.6 Hz, H), 1.88-1.99 (m, H), 1.78 (s, H), 1.61-1.76 (m, H), 1.42-1.55 (m, H), 1.19-1.33 (m, H), 0.96-1.08 (m, H), 0.85 (d, J = 6.8 Hz, H), 0.77 (t, J = 7.4 Hz, H).

Cyclic Orn-Ile-Pro-Trp(5-F) (**18**):



^1H NMR (DMSO- d_6 , 500 MHz): 8.06-8.11 (m, H), 7.99 (d, J = 8.6 Hz, H), 7.89 (d, J = 8 Hz, H), 7.69 (d, J = 5.7 Hz, H), 7.44 (t, J = 8.9, 4.5 Hz, H), 7.37 (dd, J = 10.1, 2.4 Hz, H), 7.34 (dd, J = Hz, H), 7.27 (s, H), 7.14-7.21 (br. s, H), 7.11 (m, H), 7.03-7.07 (br. s, H), 6.90-6.96 (m, H), 6.48 (m, H), 6.33 (d, J = 15.8, 6.0 Hz, H), 4.96 (dt, J = 16.6, 5.6 Hz, H), 4.87 (dd, J = 16.3, 5.6 Hz, H), 4.39 (dd, J = 10.8, 8.0, 3.1 Hz, H), 4.22-4.30 (ddd, J = Hz, H), 4.16 (dd, J = 8.2, 5.0 Hz, H), 3.50-3.64 (m, H), 3.44-3.52 (m, H), 3.28 (t, J = 7.1 Hz, H), 2.96-3.03 (m, H), 2.86 (dddd, J = 12.6, 12.6, 6.7, 6.7 Hz, H), 2.72 (t, J = 7.5 Hz, H), 2.52 (s, H), 2.20-2.31 (m, H), 1.81-1.93 (m, H), 1.65-1.75 (m, H), 1.55-1.64 (m, H), 1.38-1.53 (m, H), 1.26-1.35 (m, H), 1.13-1.25 (m, H), 0.93-1.05 (m, H), 0.81 (d, J = 6.7 Hz, H), 0.76 (d, J = 7.4 Hz, H).

(1) Kopp, F.; Stratton, C. F.; Akella, L. B.; Tan, D. S., A diversity-oriented synthesis approach to macrocycles via oxidative ring expansion, *Nat. Chem. Biol.* **2012**, 8, 358.



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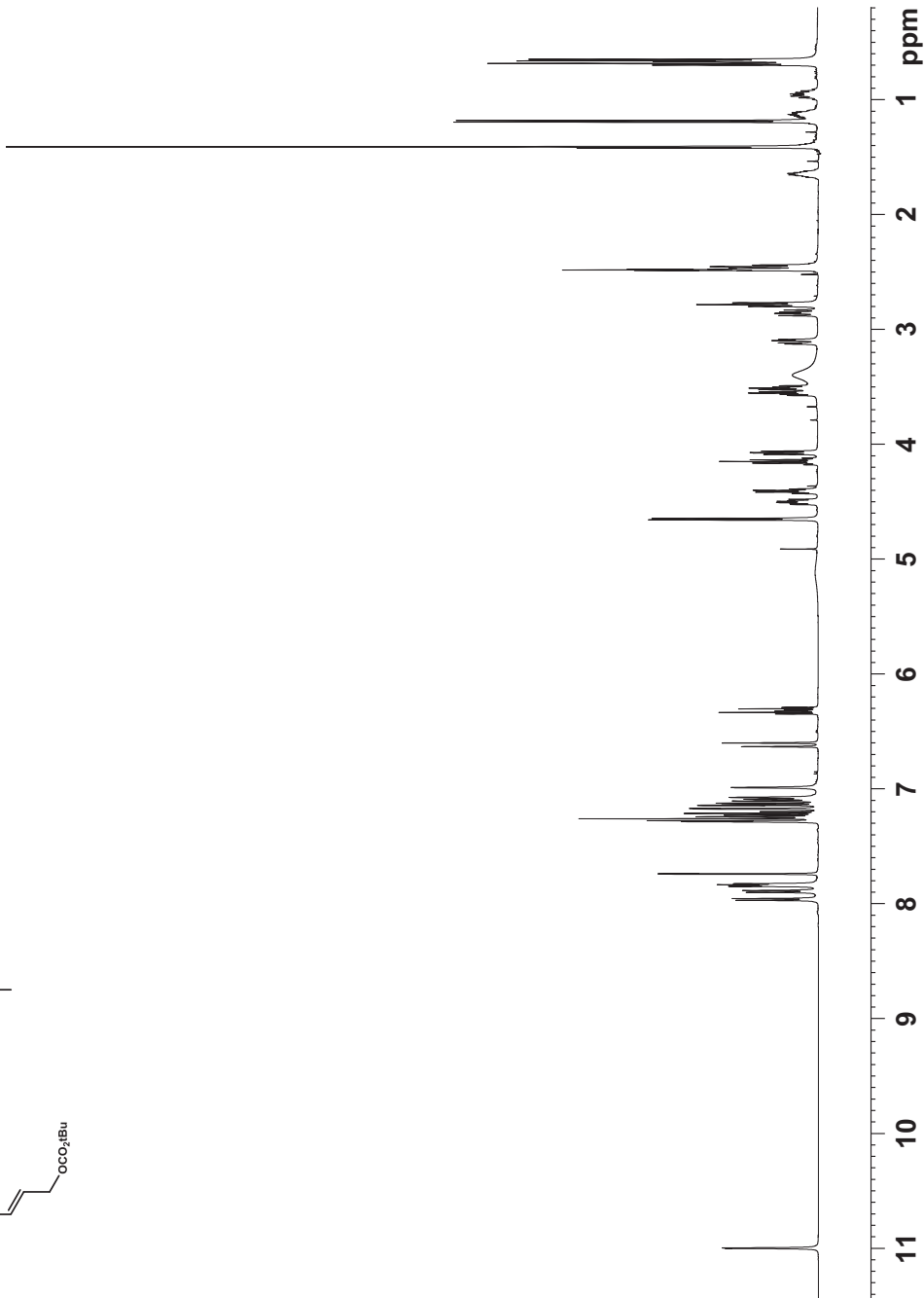
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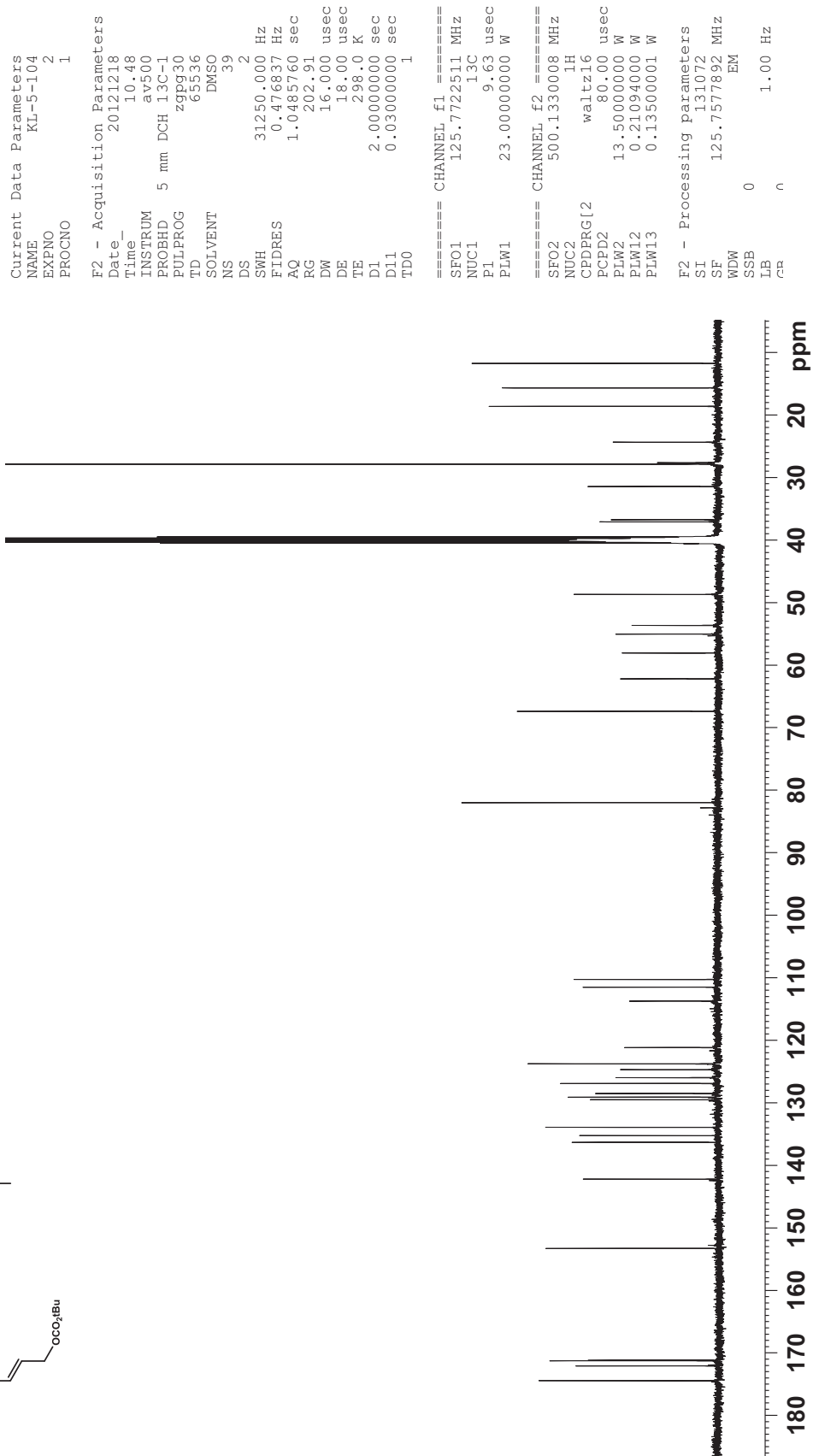
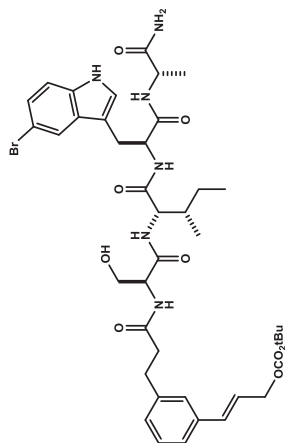
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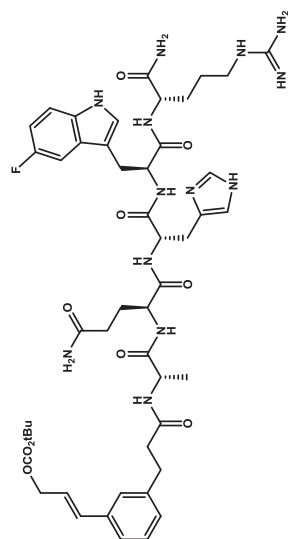
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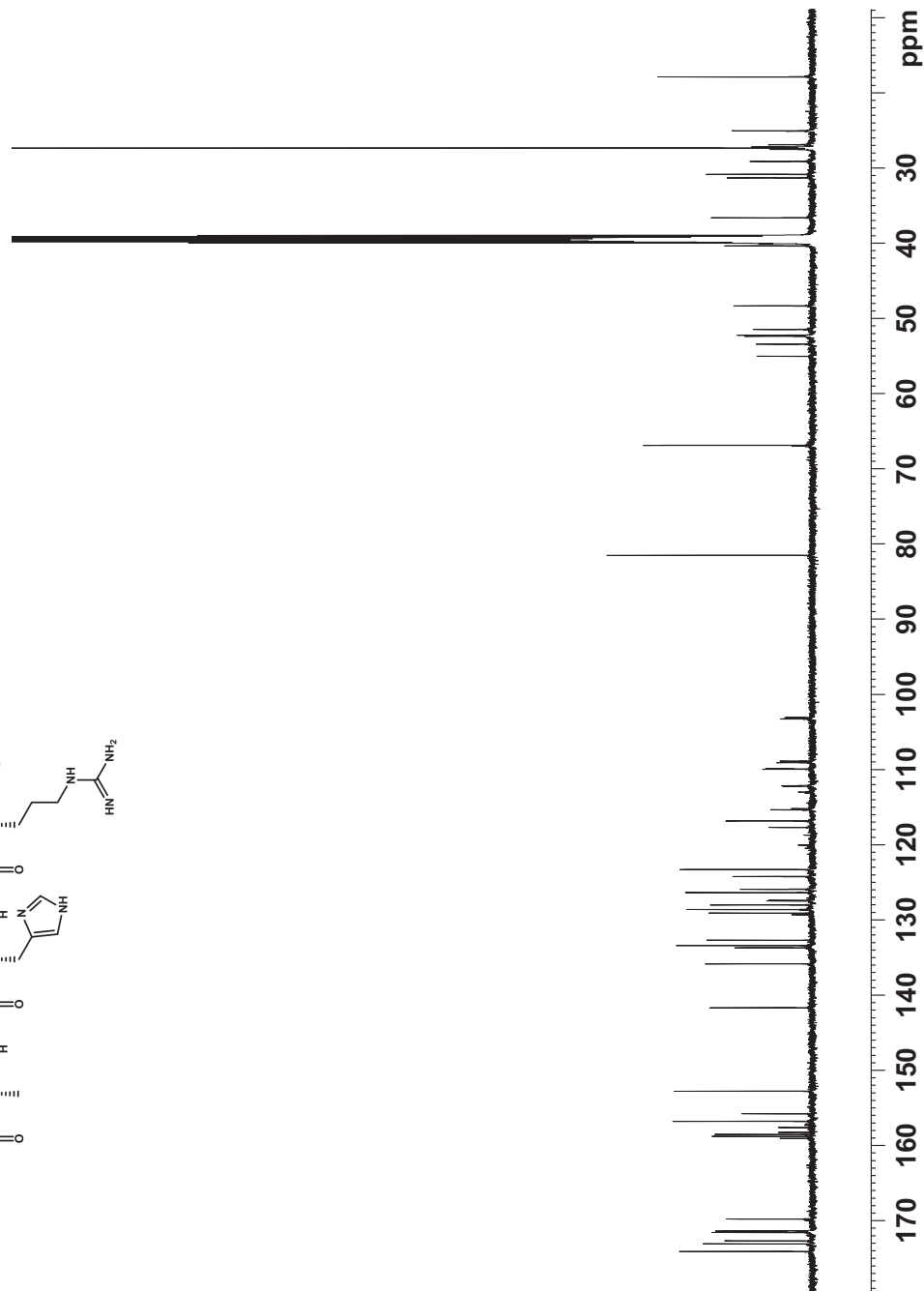
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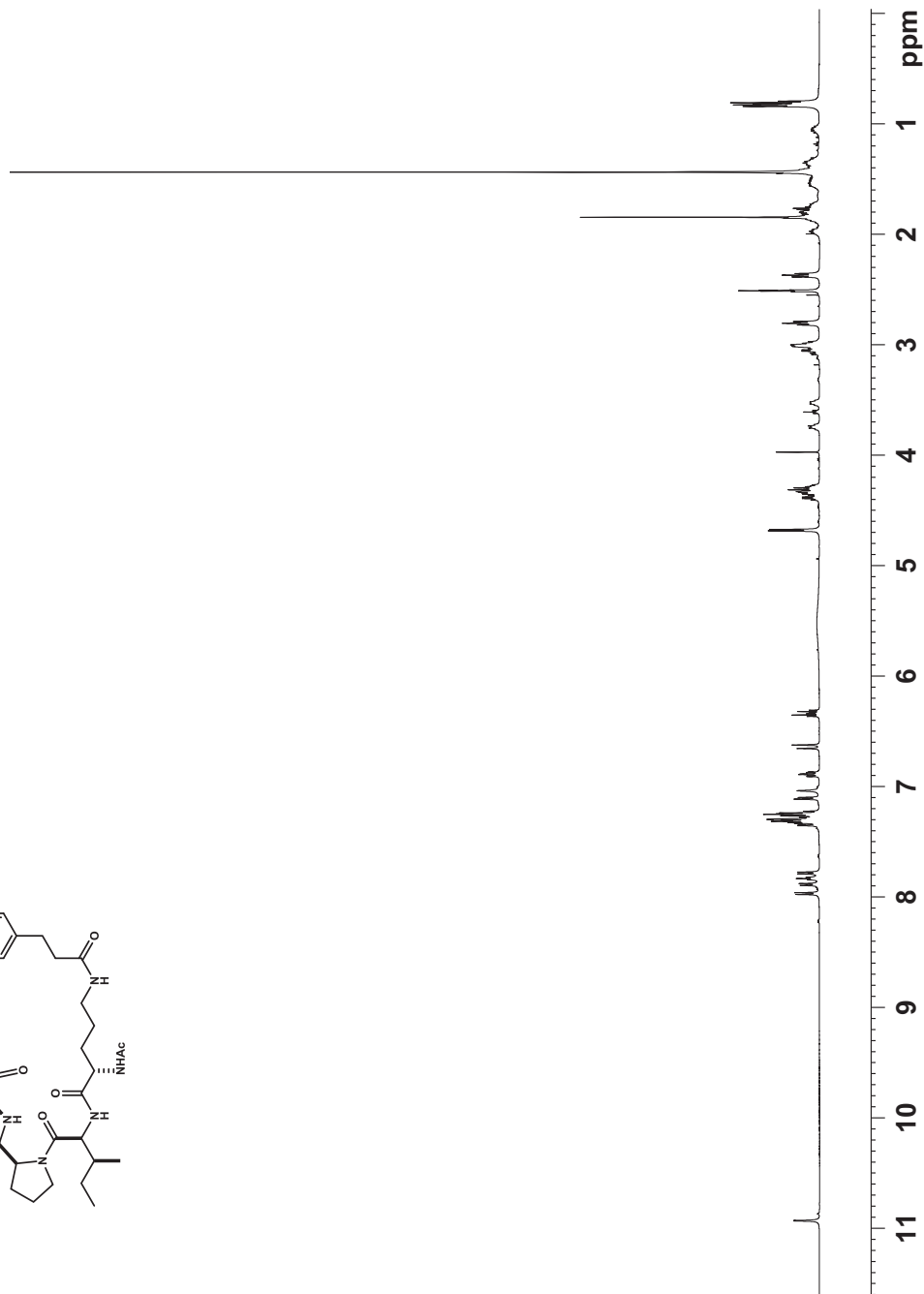






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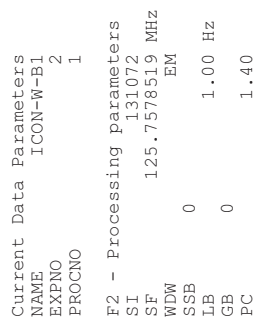


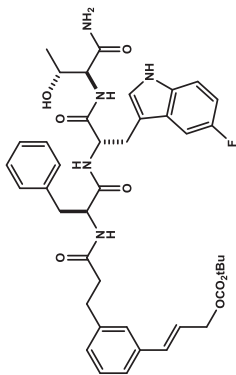


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D1	2.00000000 sec
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PLW1      13.50000000 W
STOF      500.1330008 MHz

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WDW        EM
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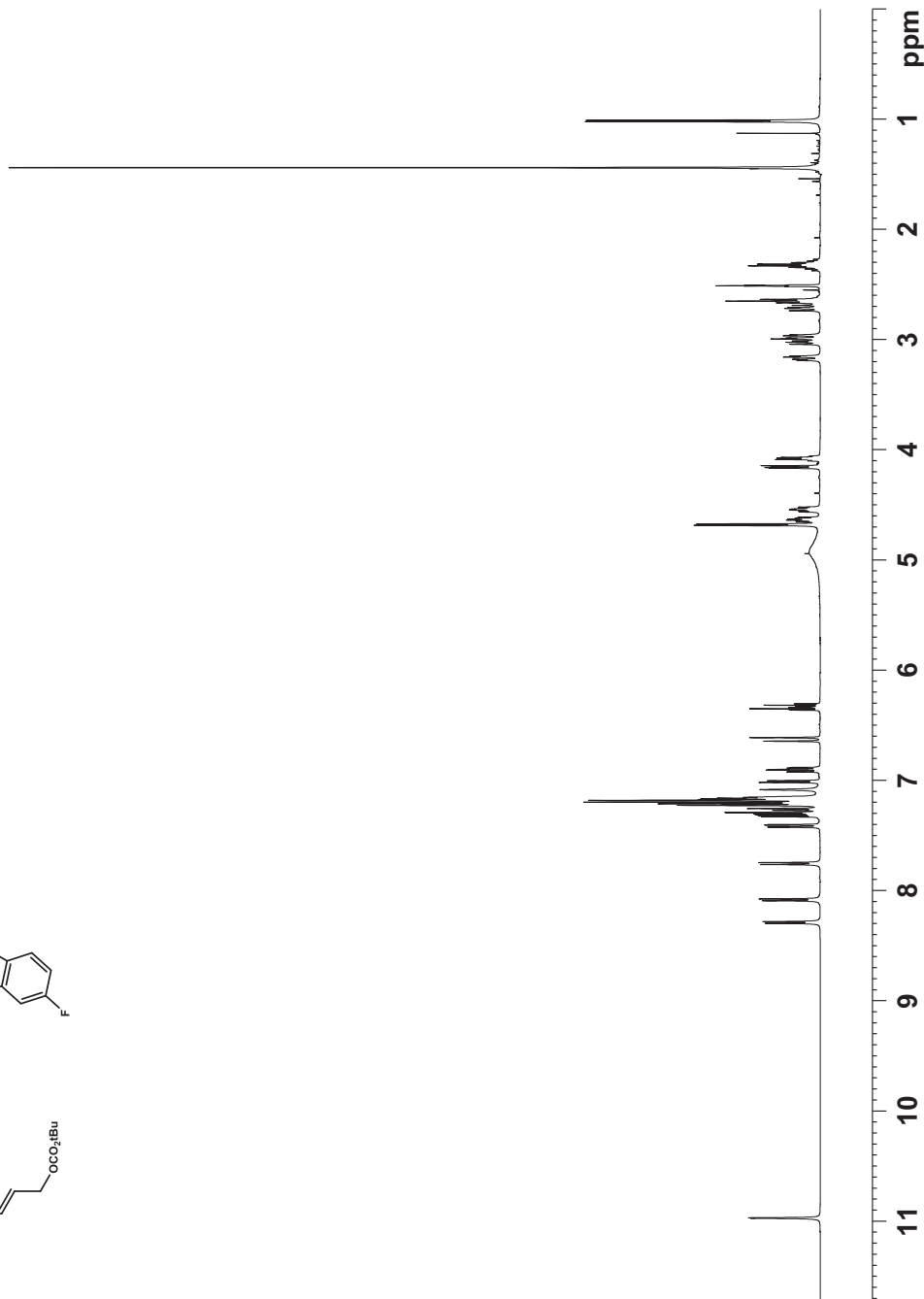
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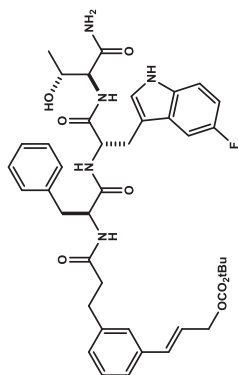
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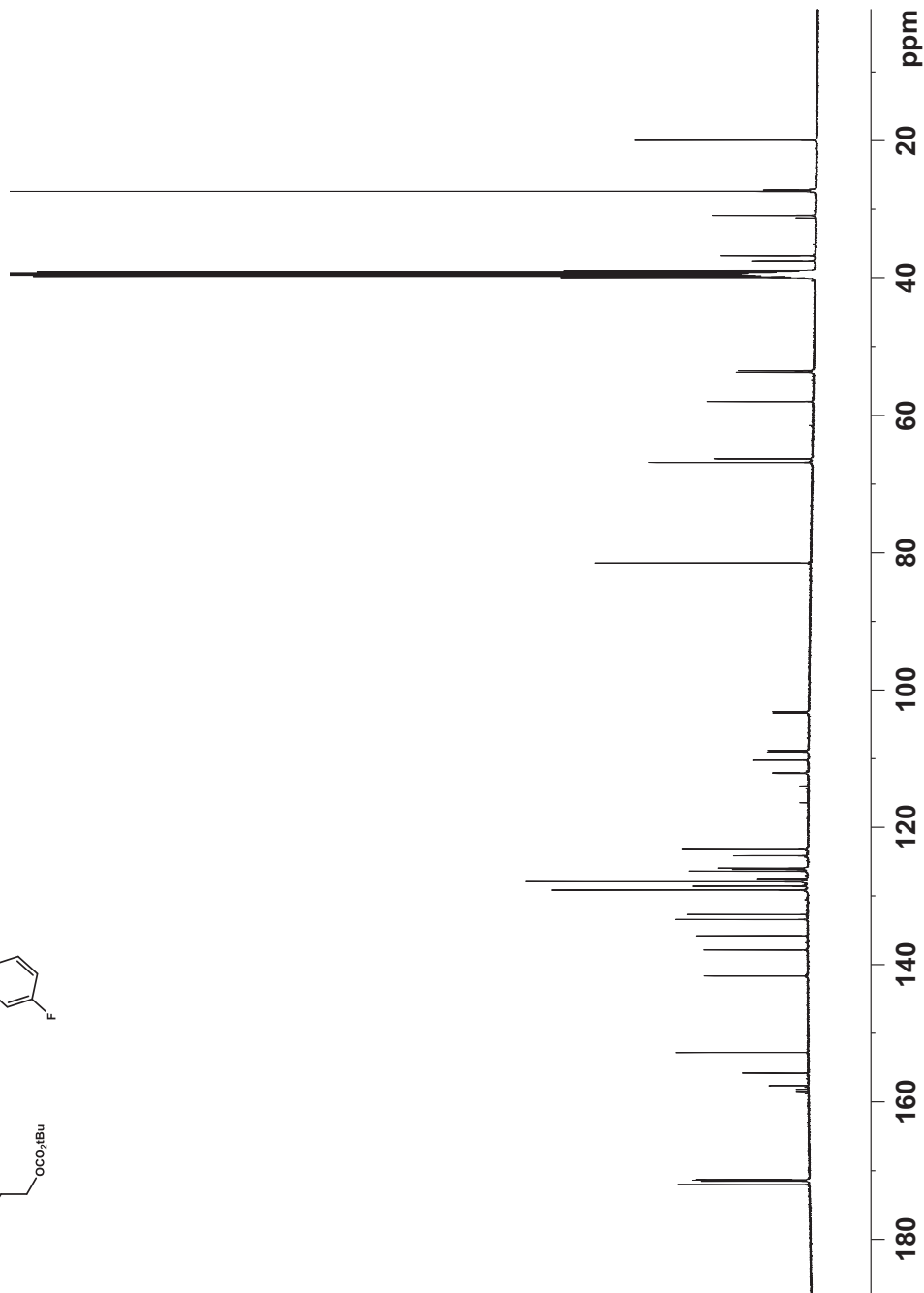
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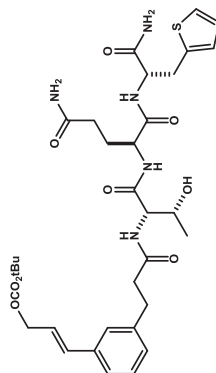
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Current Data Parameters
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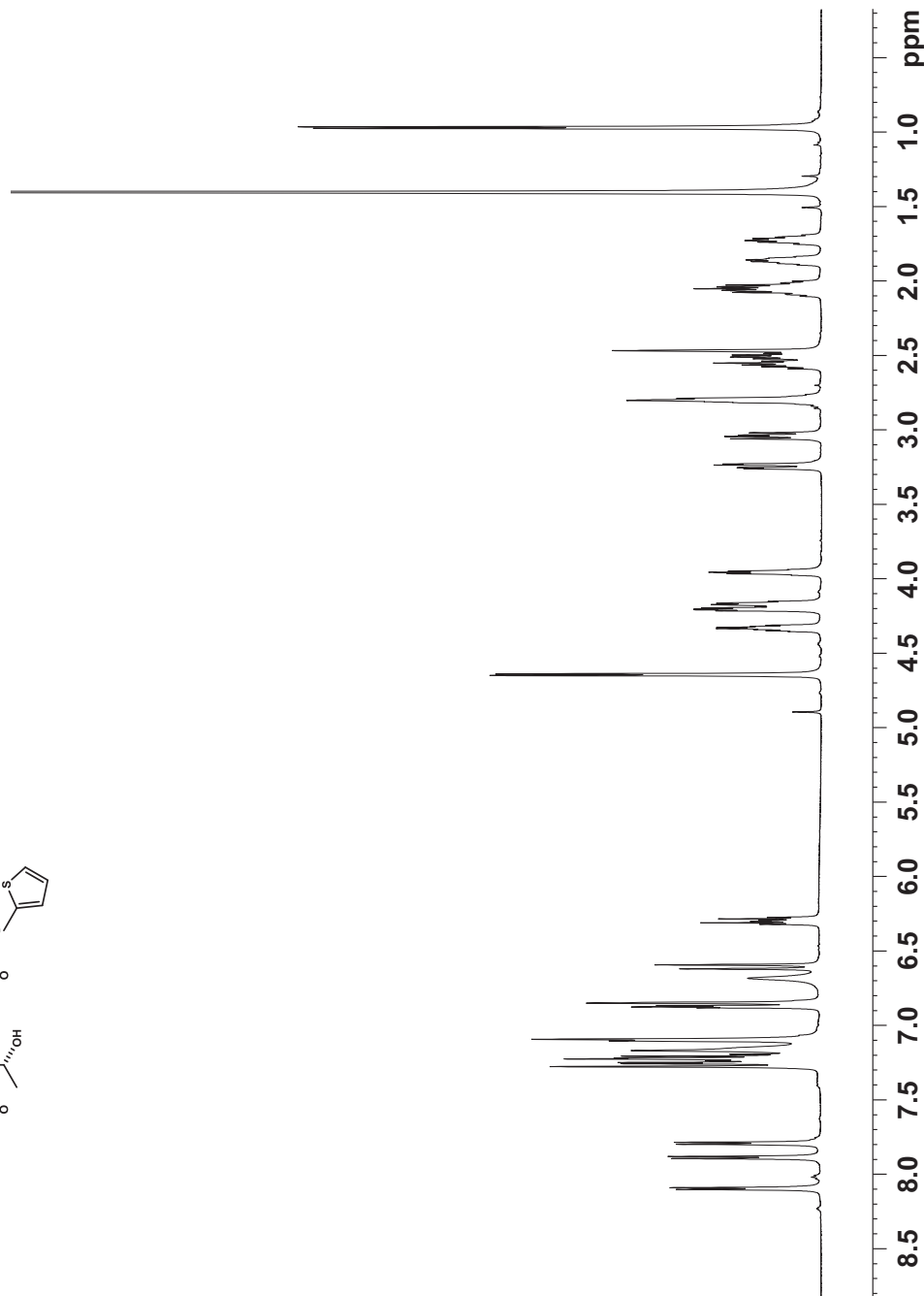
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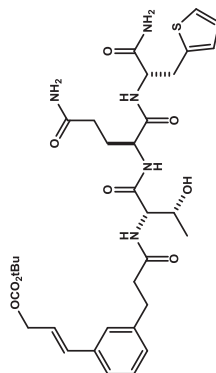
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DS            0
SWH           12376.237 Hz
FIDRES        0.188846 Hz
AQ            2.6476543 sec
RG            71.8
DW            40.400 usec
DE            6.50 usec
TE            310.0 K
D1            2.00000000 sec
TD0           1

===== CHANNEL f1 =====
NUC1          1H
P1            15.38 usec
PL1           -1.00 dB
PL1W          31.62277603 W
SFO1          600.1336008 MHz

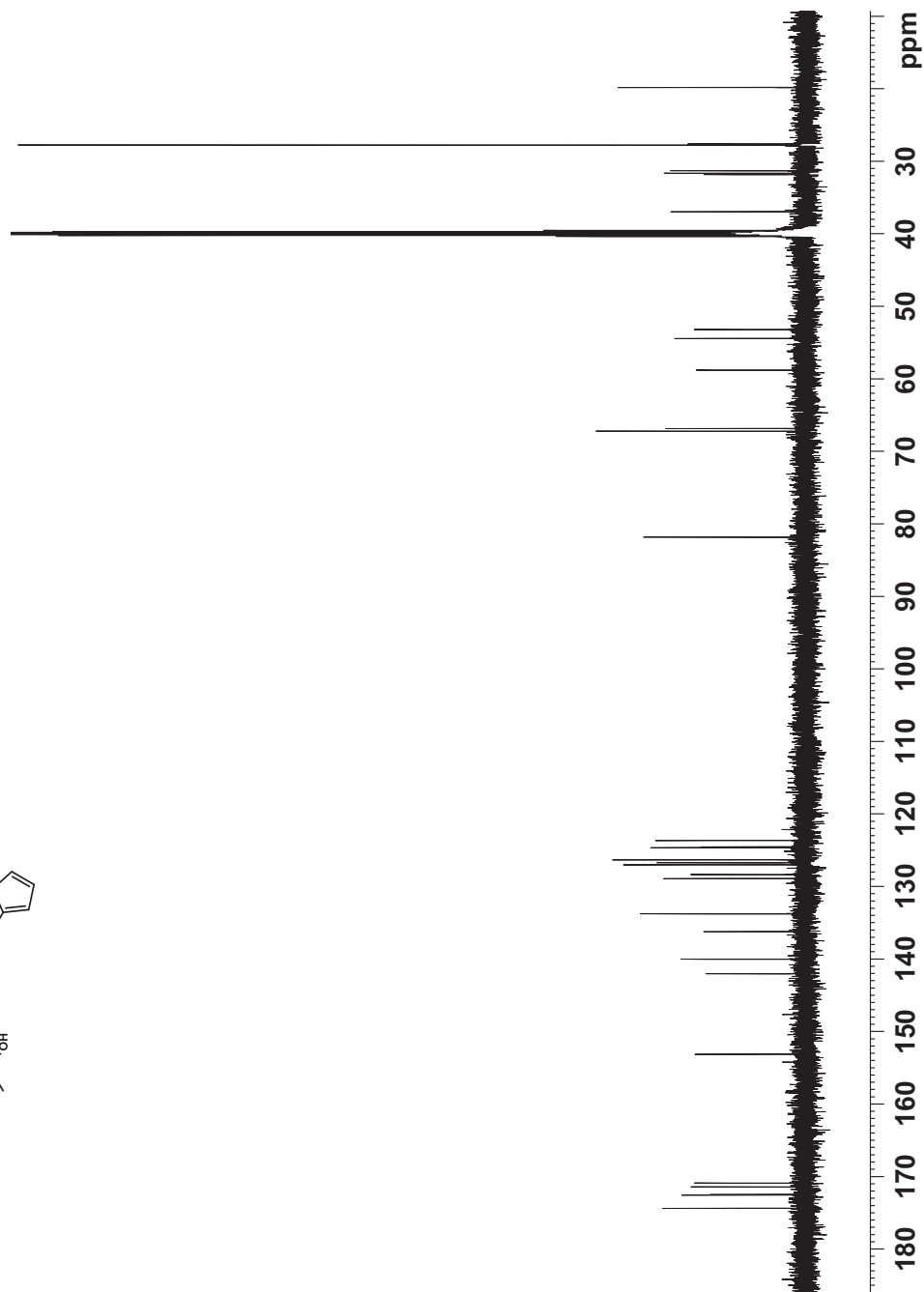
F2 - Processing parameters
SI            65536
SF            600.1300273 MHz
WDW           EM
SSB           0
LB            0.30 Hz
GB            0
PC            1.00

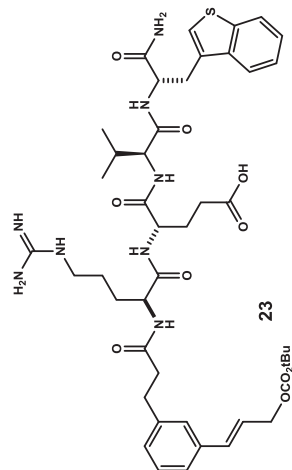
```





Current Data Parameters
 NAME KL-5-226
 EXPNO 2
 PROCNO 1
 F2 - Processing parameters
 SI 65536
 SF 150.9028319 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.00





```

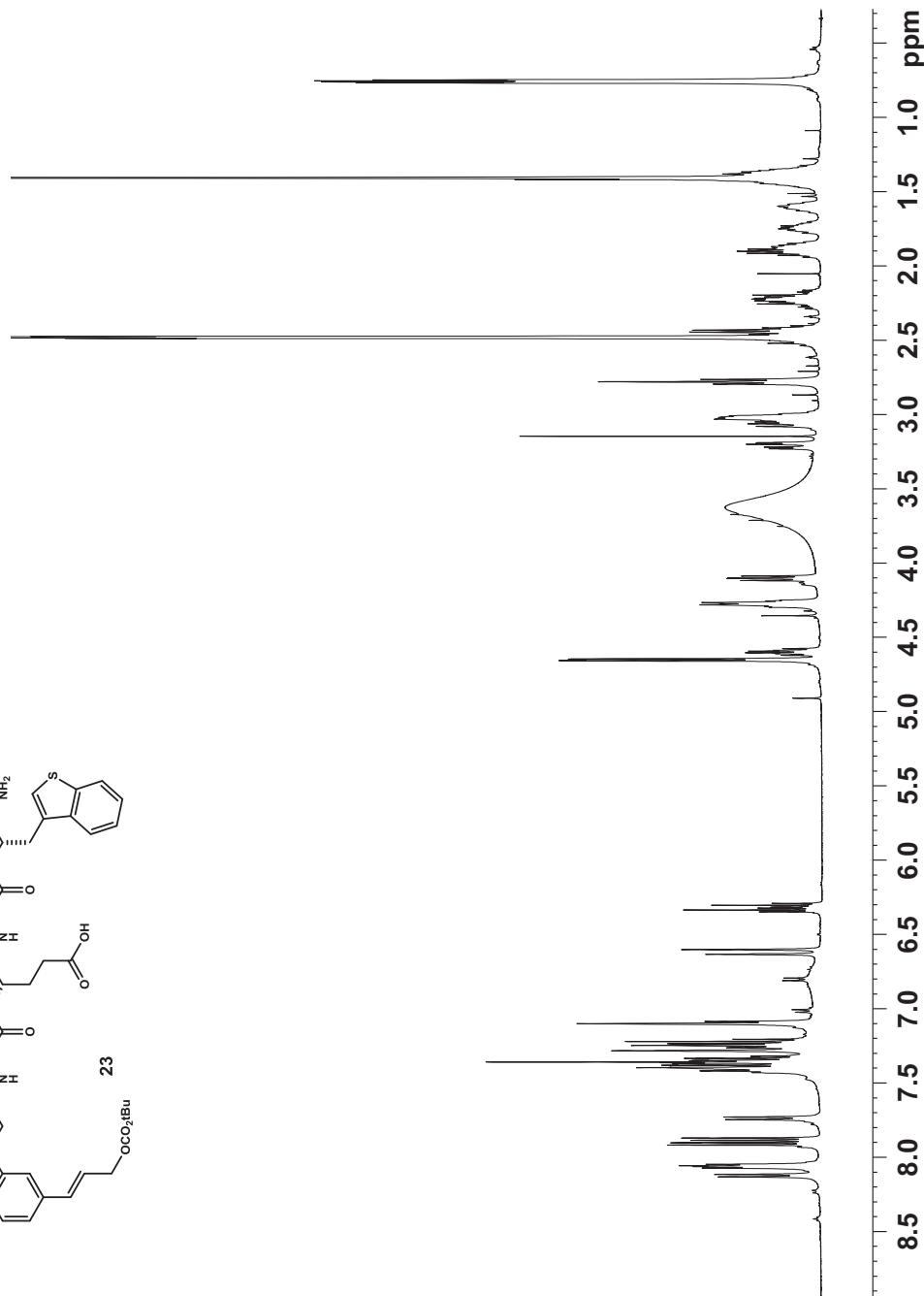
Current Data Parameters
NAME      KL-5-228
EXPNO     1
PROCNO    1

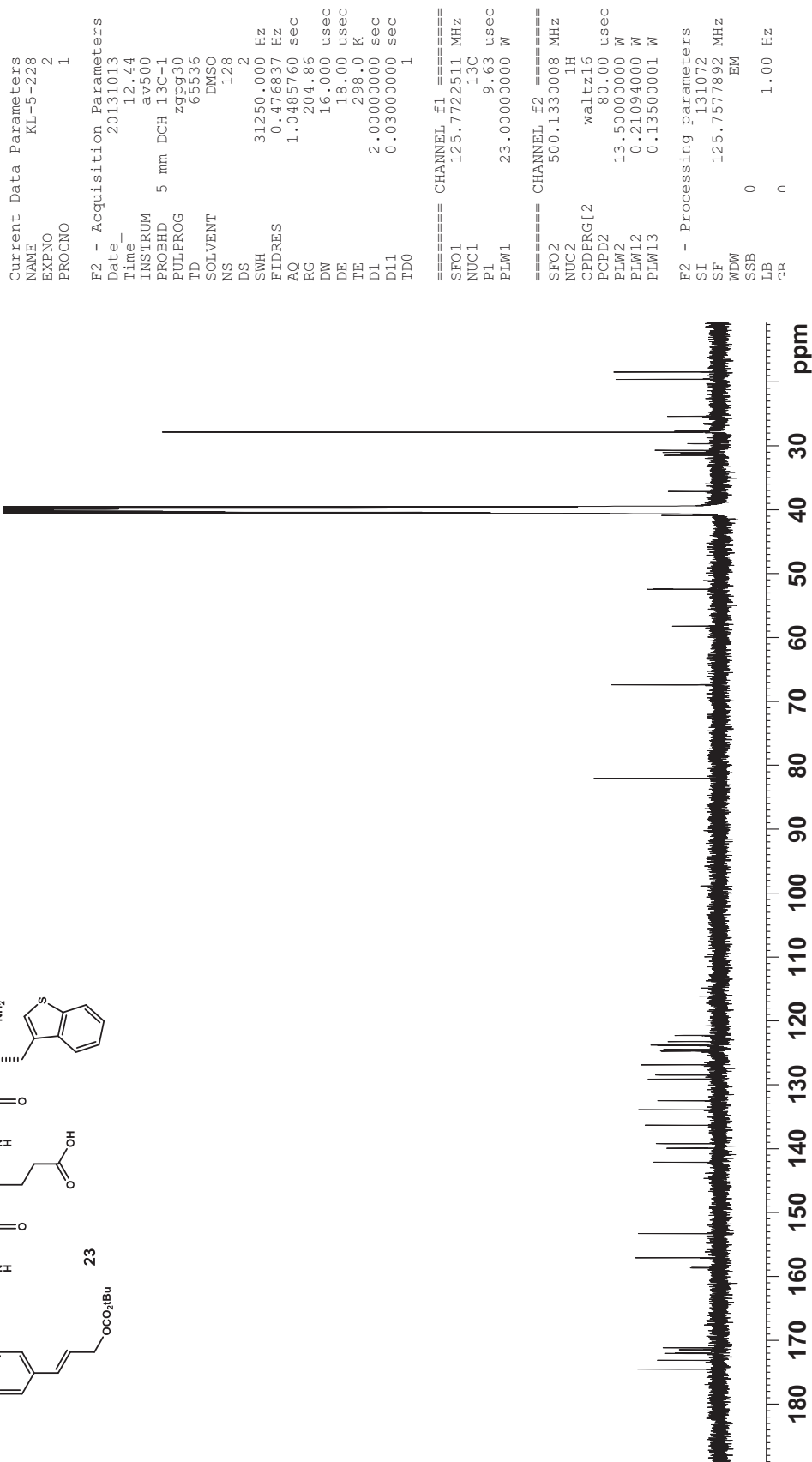
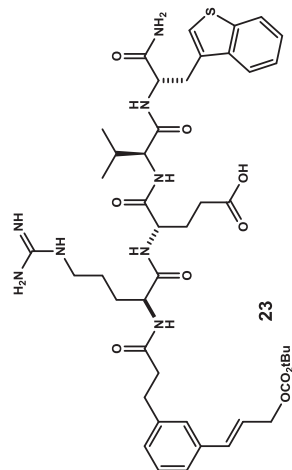
F2 - Acquisition Parameters
Date_     20131013
Time      12.42
INSTRUM   av500
PROBHD    5 mm DCH 13C-1
PULPROG   zg30
TD         65536
SOLVENT   DMSO
NS         8
DS         0
SWH        10000.000 Hz
FIDRES     0.152588 Hz
AQ         3.2767999 sec
RG         12.14
DW         50.000 usec
DE         10.00 usec
TE         298.0 K
D1         2.00000000 sec
TD0        1

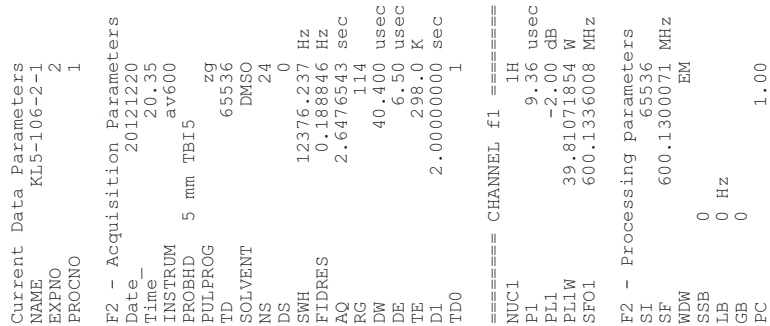
===== CHANNEL f1 =====
SFO1      500.1330008 MHz
NUC1       1H
P1         10.00 usec
PLW1      13.50000000 W

F2 - Processing parameters
SI         65536
SF         500.1300146 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00

```







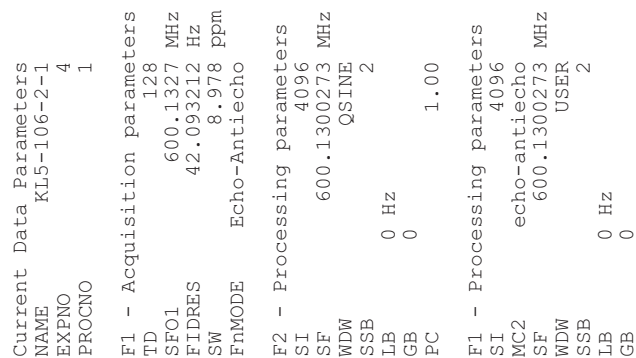


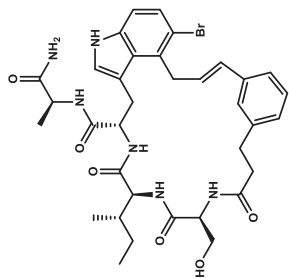
FF1 - Acquisition parameters	
TD	512
SF01	600.1327 MHz
FIDRES	10.523297 Hz
SW	8.978 ppm
EnMODE	States-TPPI

F2 - Processing parameters	
SI	2048
SF	600.130067 MHz
WDW	QSINE
SSB	2
LB	0 Hz
GB	0
PC	1.00

```
F1 - Processing parameters
SSI      2048
MC2      States-TPFI
SF        600.130058  MHz
WDW       QSINE
SSB       2
LB        0  Hz
GB        0
```





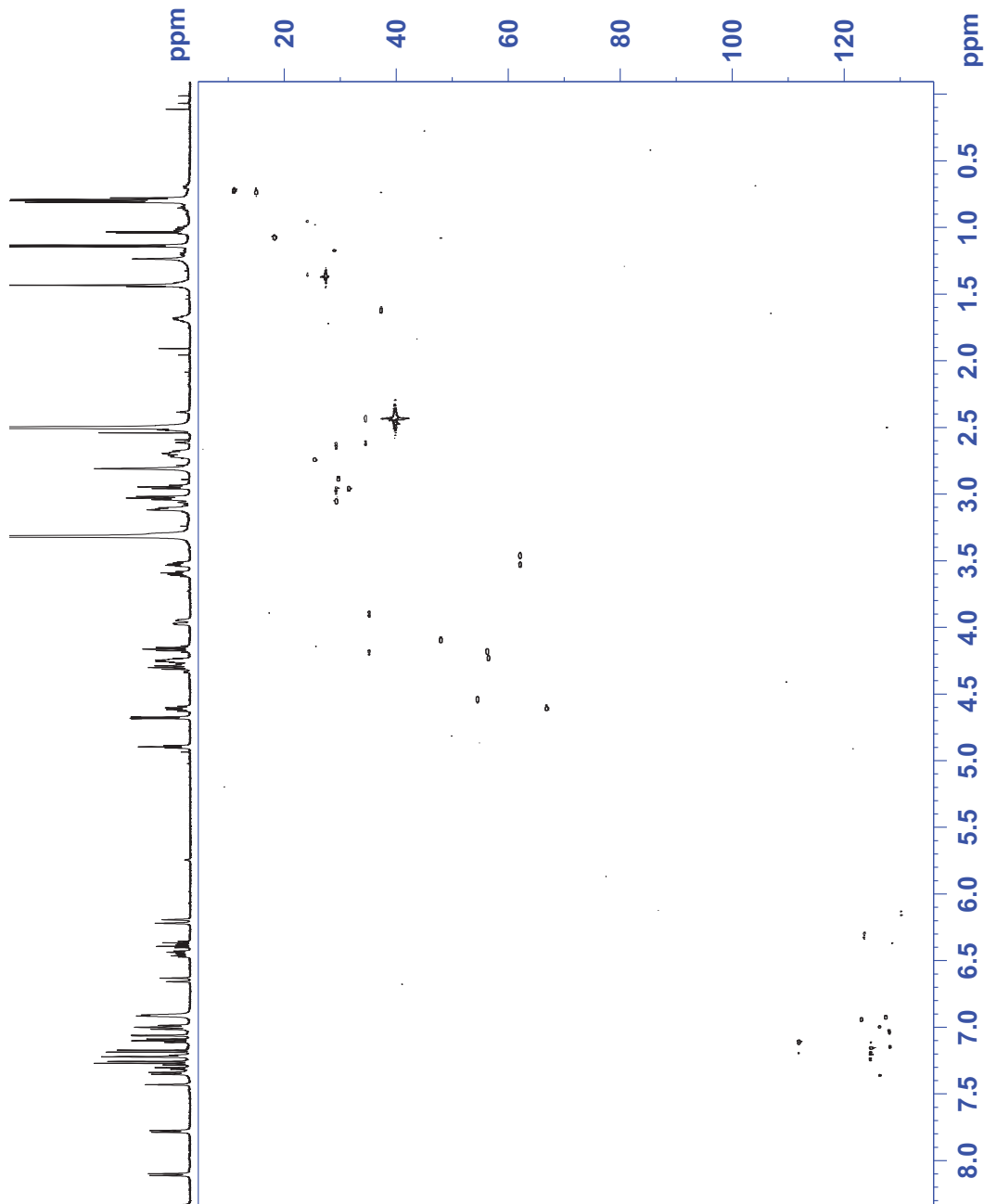


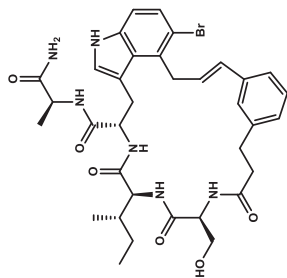
Current Data Parameters
 NAME KL5-106-2-1
 EXPNO 5
 PROCNO 1

F1 - Acquisition parameters
 TD 512
 SFO1 150.9134 MHz
 FIDRES 47.160427 Hz
 SW 160.000 ppm
 FnMODE Echo-Antiecho

F2 - Processing parameters
 SI 4096
 SF 600.1300450 MHz
 EM
 WDW 0
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

F1 - Processing parameters
 SI 4096
 MC2 echo-antiecho
 SF 150.902800 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0



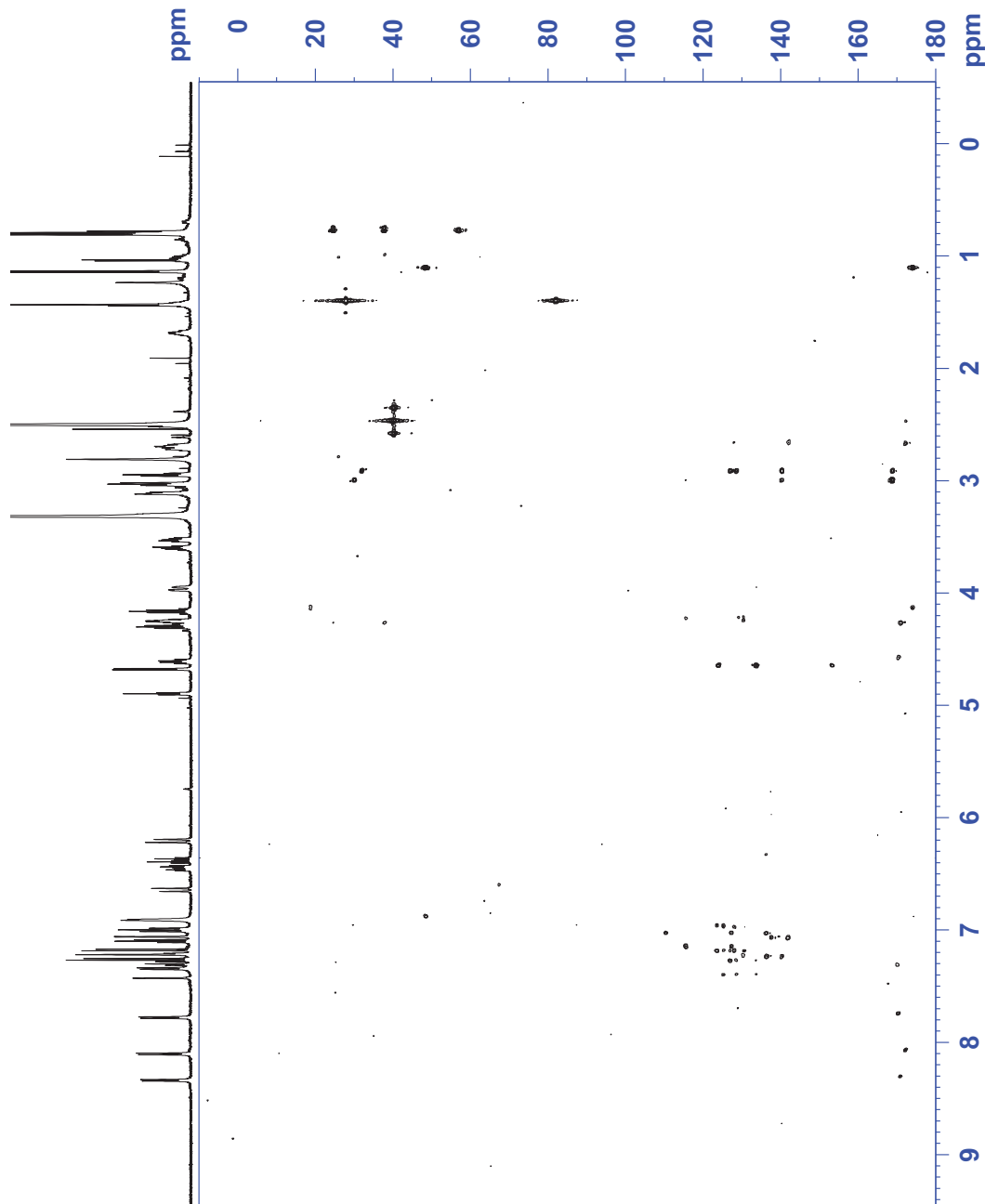


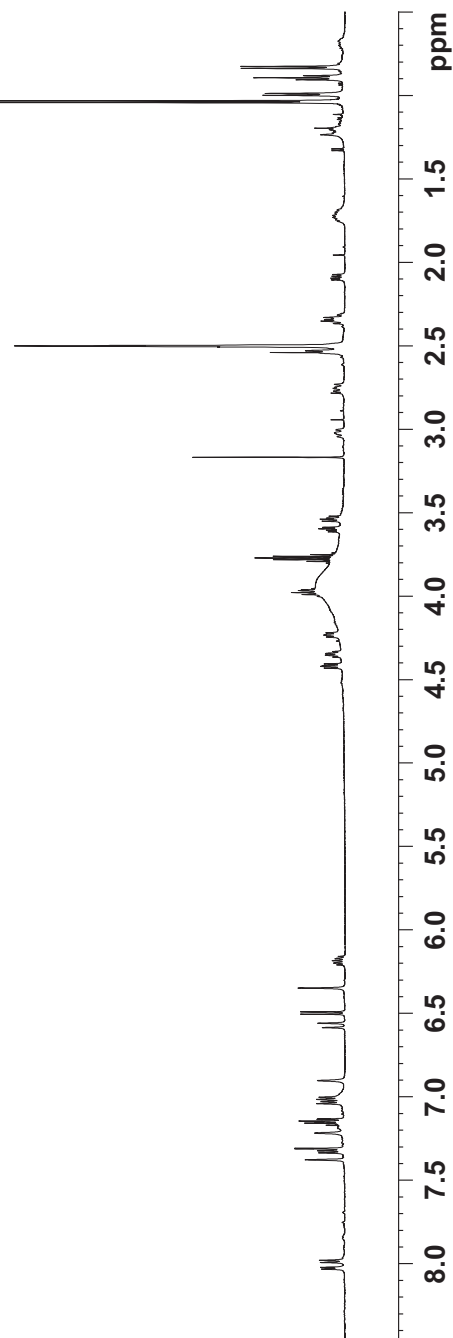
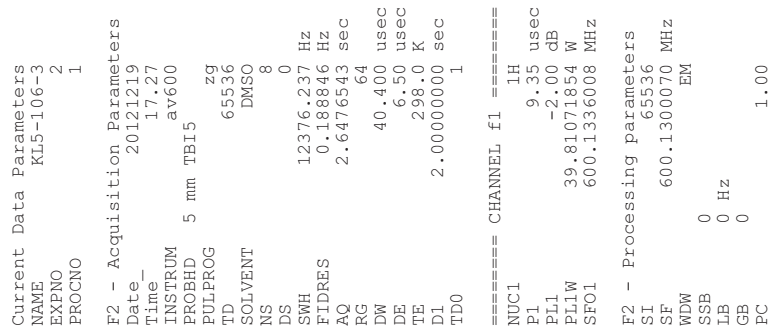
Current Data Parameters
 NAME KL5-106-2-1
 EXPNO 6
 PROCNO 1

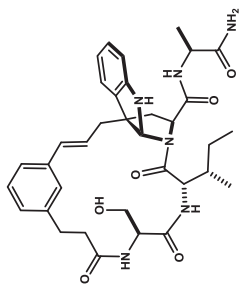
F1 - Acquisition parameters
 TD 256
 SFO1 150.9156 MHz
 FIDRES 112.007698 Hz
 SW 190.000 ppm
 FnmODE QF

F2 - Processing parameters
 SI 4096
 SF 600.1300273 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.40

F1 - Processing parameters
 SI 2048
 MC2 QF
 SF 150.9028090 MHz
 WDW USER
 SSB 2
 LB 0 Hz
 GB 0





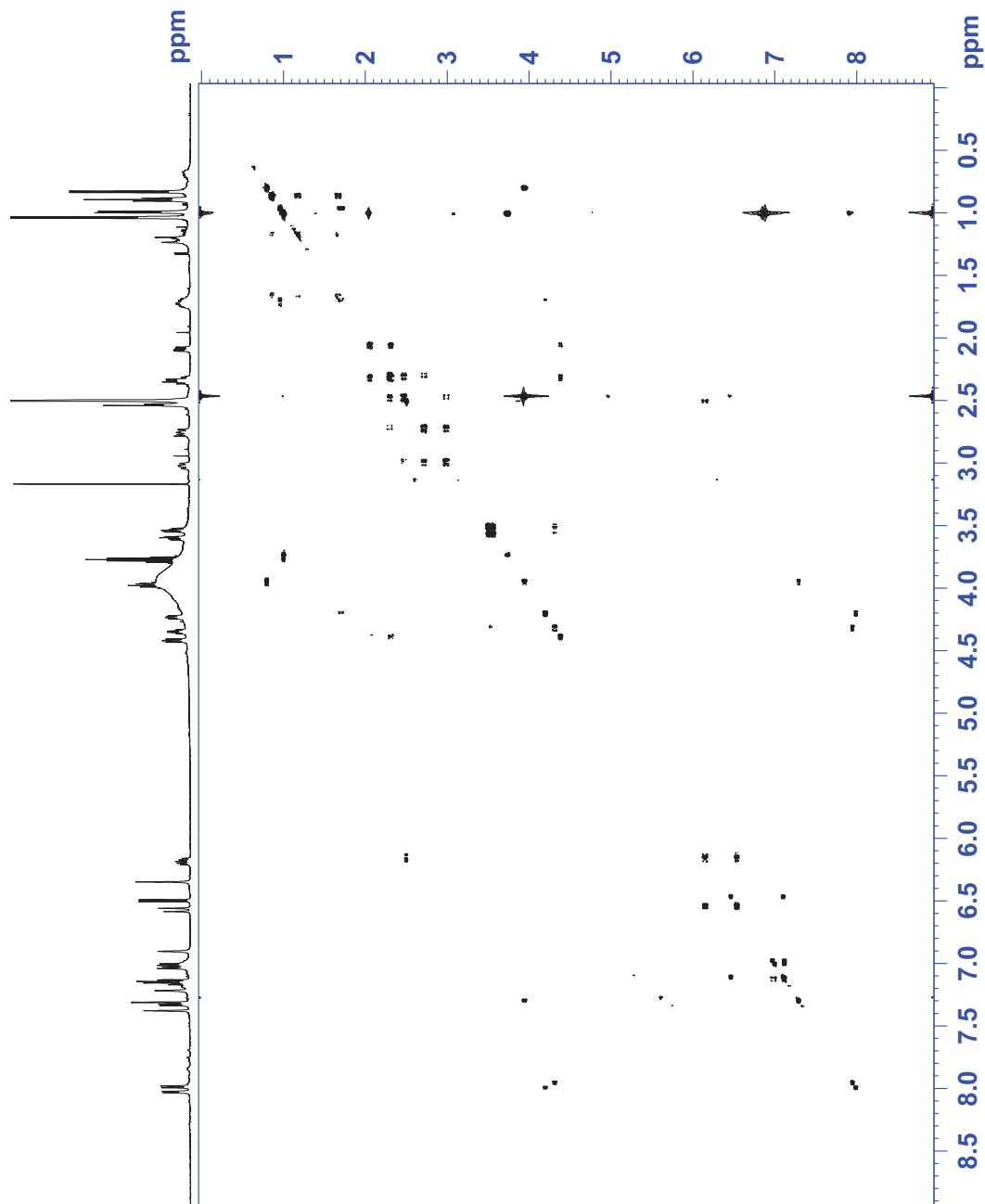


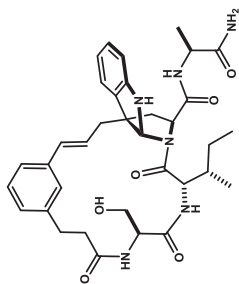
Current Data Parameters
 NAME KL5-106-3
 EXPNO 3
 PROCNO 1

F1 - Acquisition parameters
 TD 512
 SFO1 600.1327 MHz
 FIDRES 10.523297 Hz
 SW 8.978 ppm
 FnmODE States-TPPI

F2 - Processing parameters
 SI 2048
 SF 600.1300273 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 2048
 MC2 States-TPPI
 SF 600.1300273 MHz
 WDW USER
 SSB 2
 LB 0 Hz
 GB 0



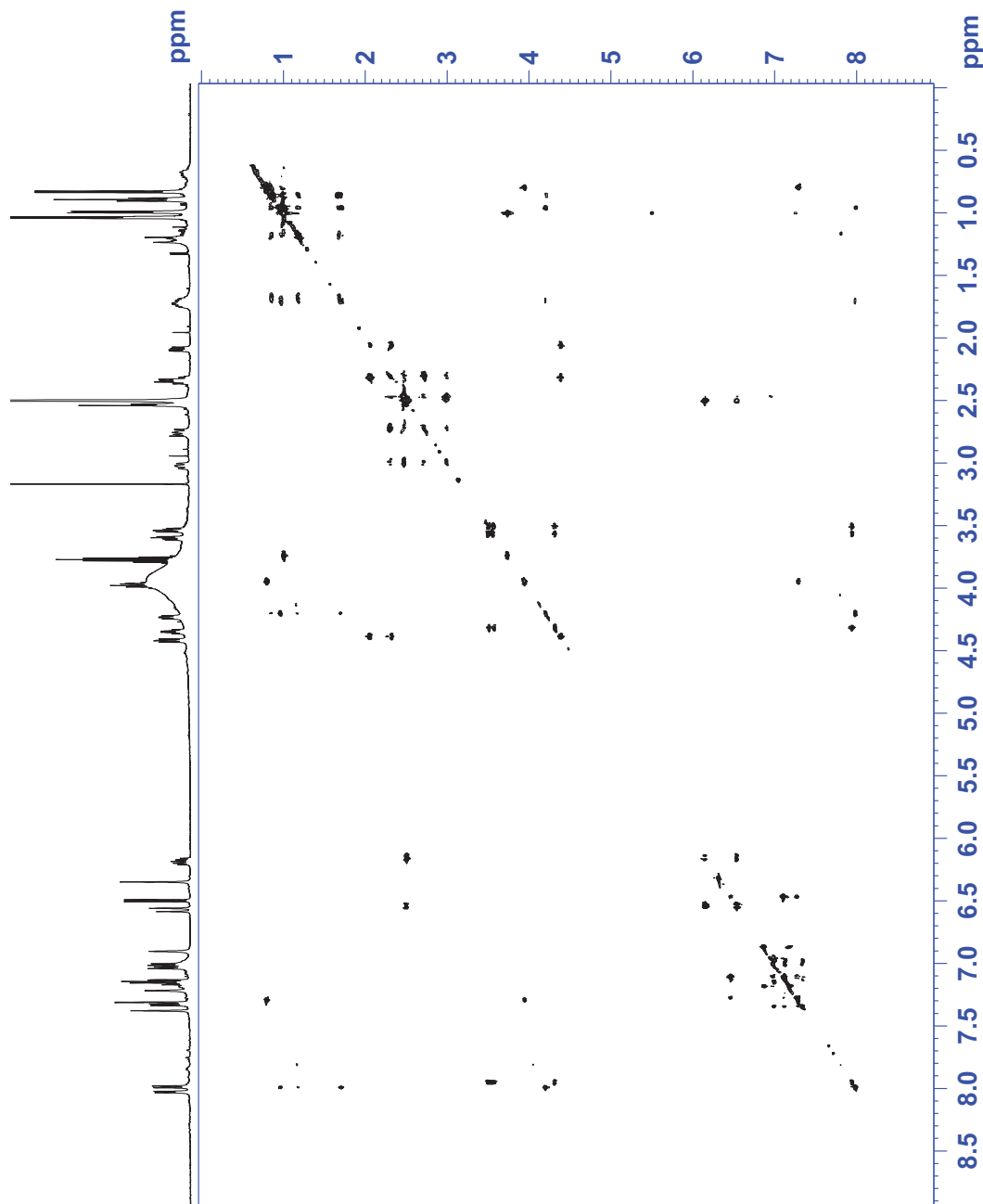


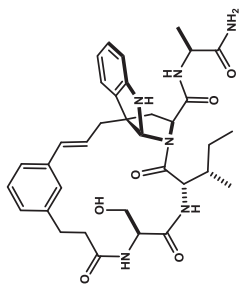
Current Data Parameters
 NAME KL5-106-3
 EXPNO 4
 PROCNO 1

F1 - Acquisition parameters
 TD 128
 SFO1 600.1327 MHz
 FIDRES 42.093212 Hz
 SW 8.978 ppm
 FnMODE Echo-Antiecho

F2 - Processing parameters
 SI 4096
 SF 600.1300273 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 4096
 MC2 echo-antiecho
 SF 600.1300273 MHz
 WDW USER
 SSB 2
 LB 0 Hz
 GB 0



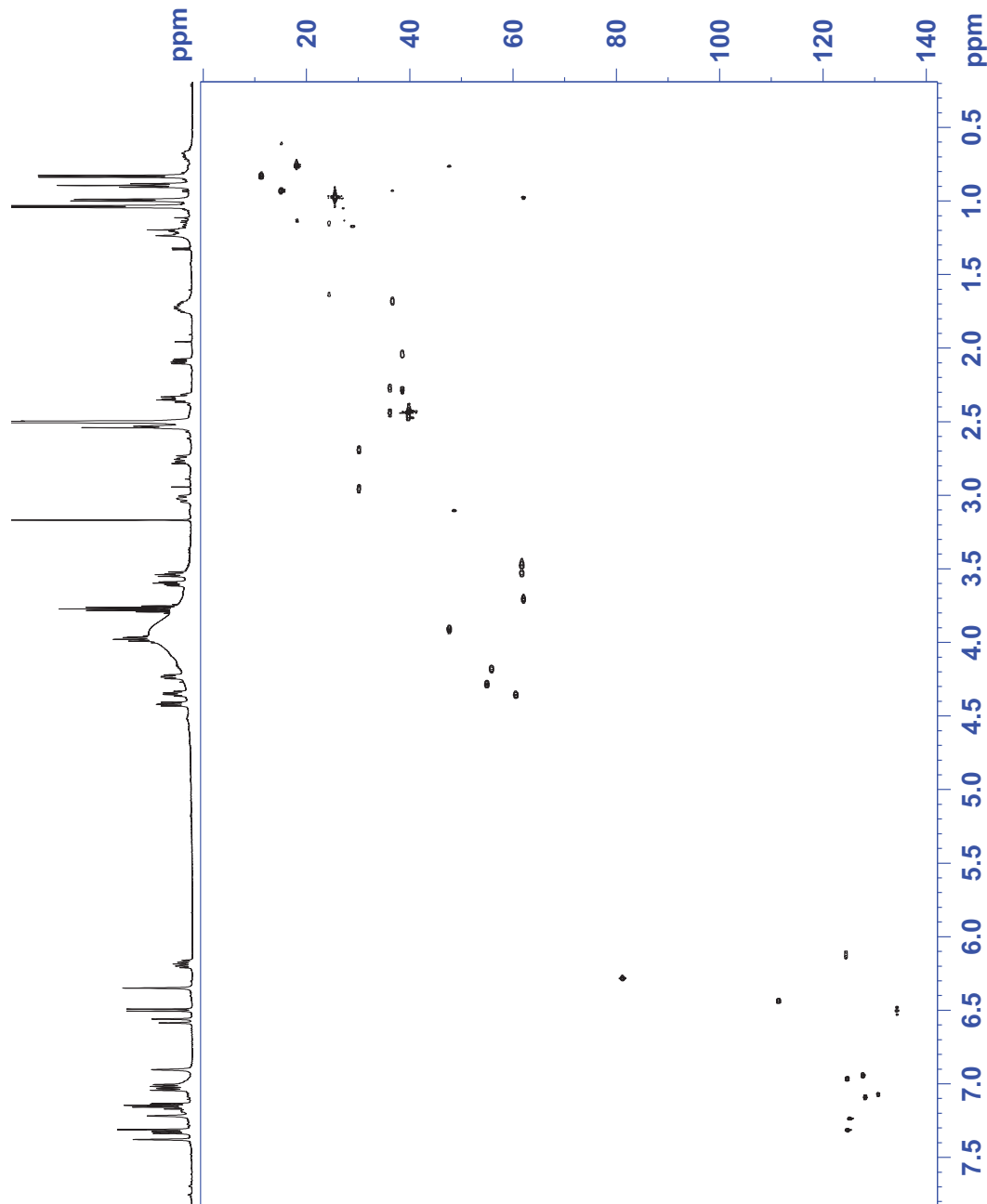


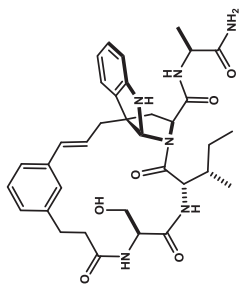
Current Data Parameters
 NAME KL5-106-3
 EXPNO 5
 PROCNO 1

F1 - Acquisition parameters
 TD 512
 SFO1 150.9134 MHz
 FIDRES 47.160427 Hz
 SW 160.000 ppm
 FnmODE Echo-Antiecho

F2 - Processing parameters
 SI 4096
 SF 600.1300450 MHz
 EM
 WDW 0
 SSB 1.00 Hz
 LB 0
 GB 1.40
 PC

F1 - Processing parameters
 SI 4096
 MC2 echo-antiecho
 SF 150.9028800 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0



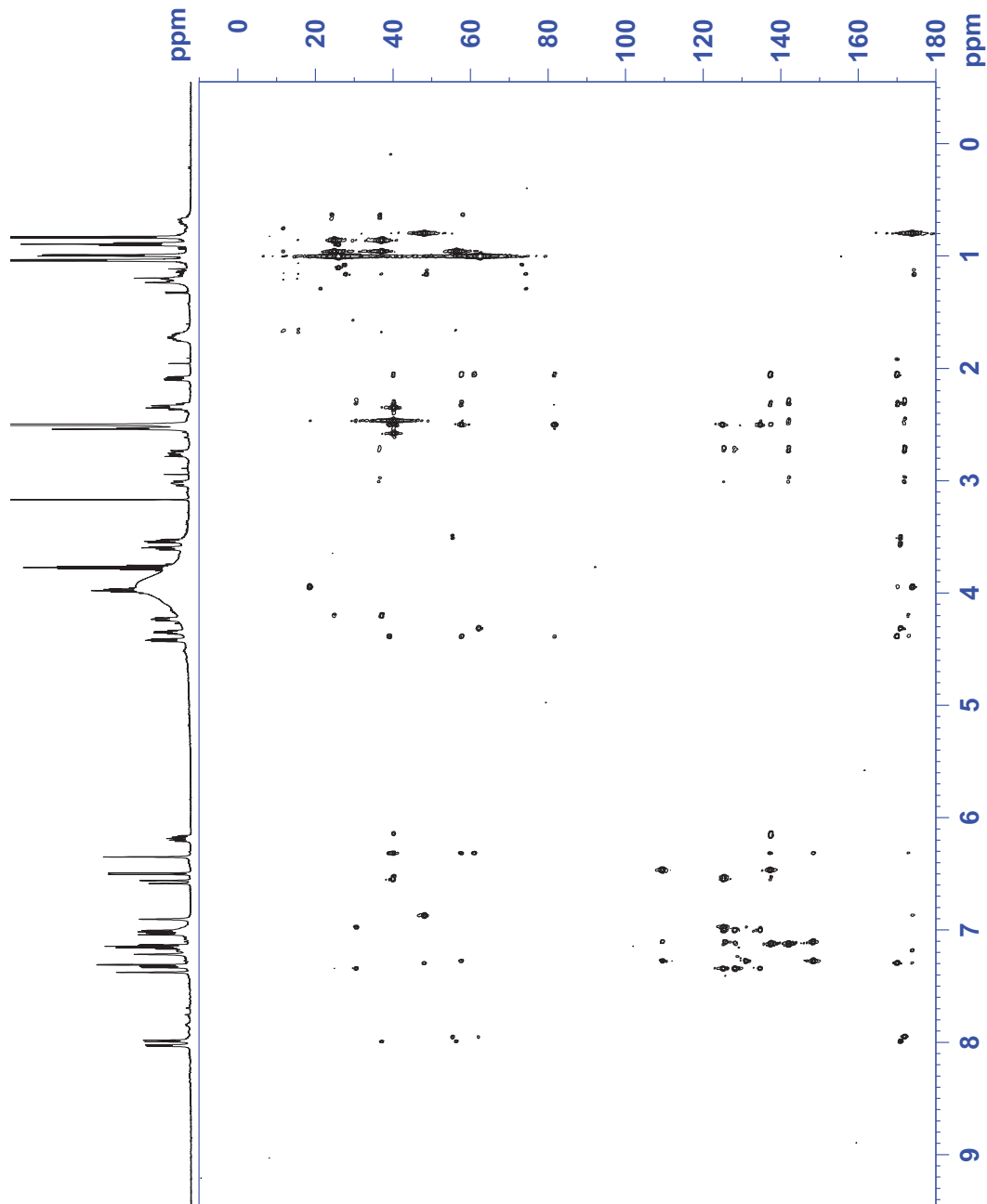


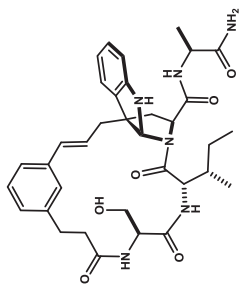
Current Data Parameters
 NAME KL5-106-3
 EXPNO 6
 PROCNO 1

F1 - Acquisition parameters
 TD 256
 SF01 150.9156 MHz
 FIDRES 112.007698 Hz
 SW 190.000 ppm
 FnmODE QF

F2 - Processing parameters
 SI 4096
 SF 600.1300273 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.40

F1 - Processing parameters
 SI 2048
 MC2 QF
 SF 150.9028090 MHz
 WDW TRAP
 SSB 2
 LB 0 Hz
 GB 0



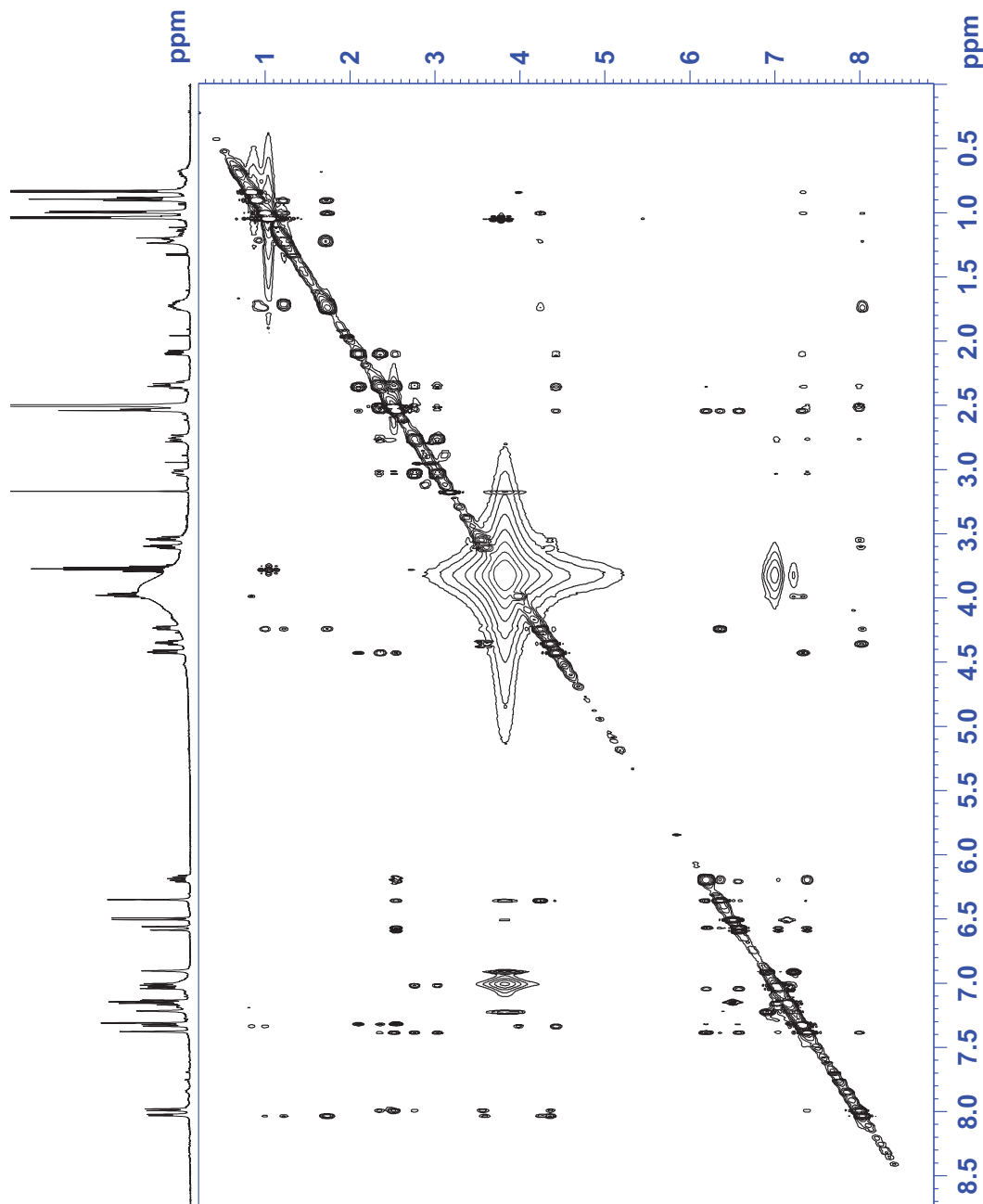


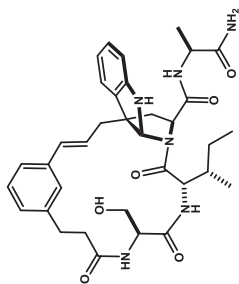
Current Data Parameters
 NAME KL5-106-3
 EXPNO 10
 PROCNO 1

F1 - Acquisition parameters
 TD 224
 SFO1 600.1328 MHz
 FIDRES 27.331724 Hz
 SW 10.202 ppm
 FnMODE States-TPPI

F2 - Processing parameters
 SI 1024
 SF 600.130000 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 1024
 MC2 States-TPPI
 SF 600.130000 MHz
 WDW SINE
 SSB 2
 LB 0 Hz
 GB 0



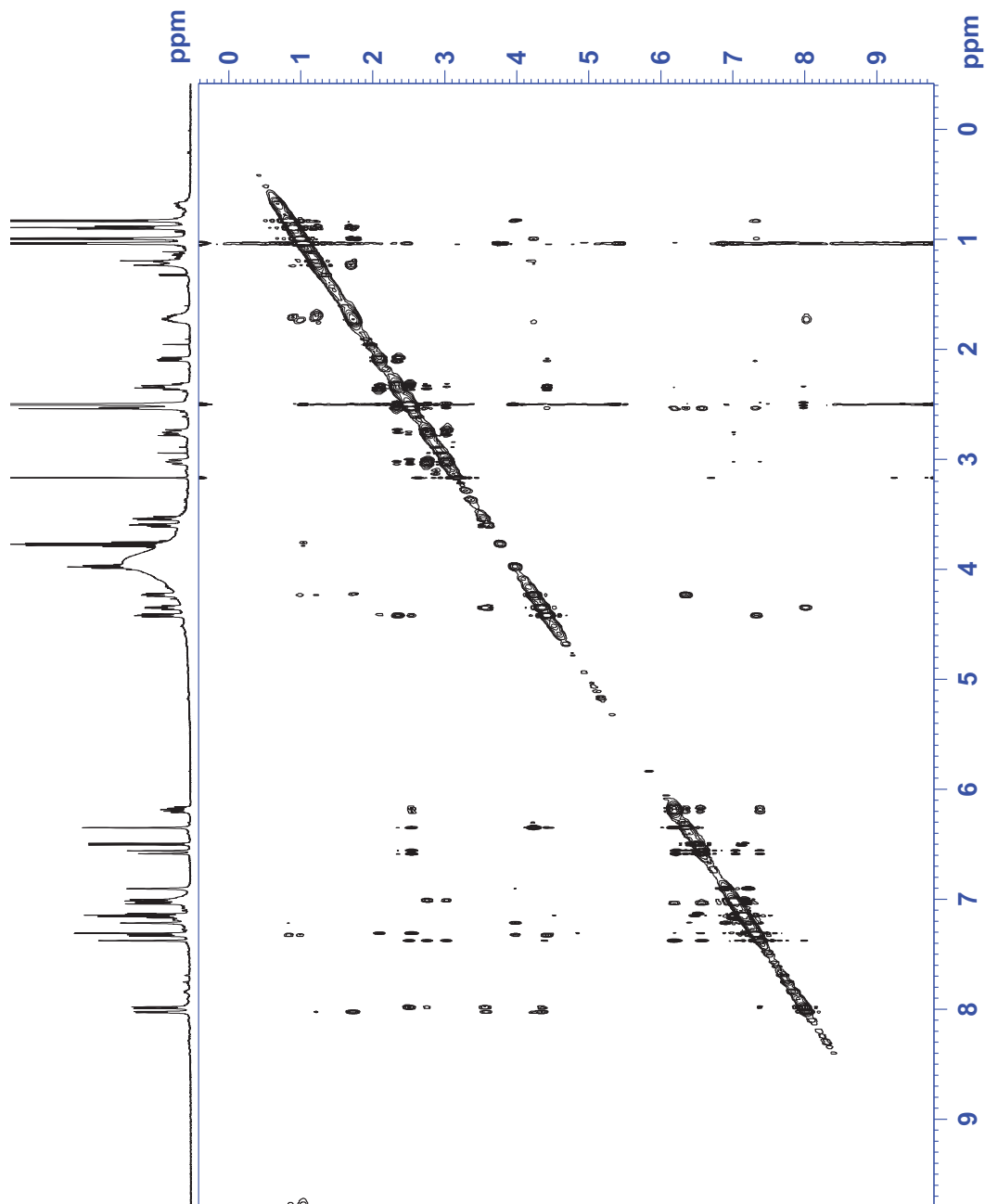


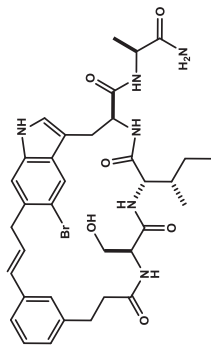
Current Data Parameters
 NAME KL5-106-3
 EXPNO 15
 PROCNO 1

F1 - Acquisition parameters
 TD 200
 SFO1 600.1328 MHz
 FIDRES 30.637295 Hz
 SW 10.210 ppm
 FnmODE States-TPPI

F2 - Processing parameters
 SI 2048
 SF 600.1300070 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 4096
 MC2 States-TPPI
 SF 600.1300070 MHz
 WDW TRAP
 SSB 2
 LB 0 Hz
 GB 0





340K

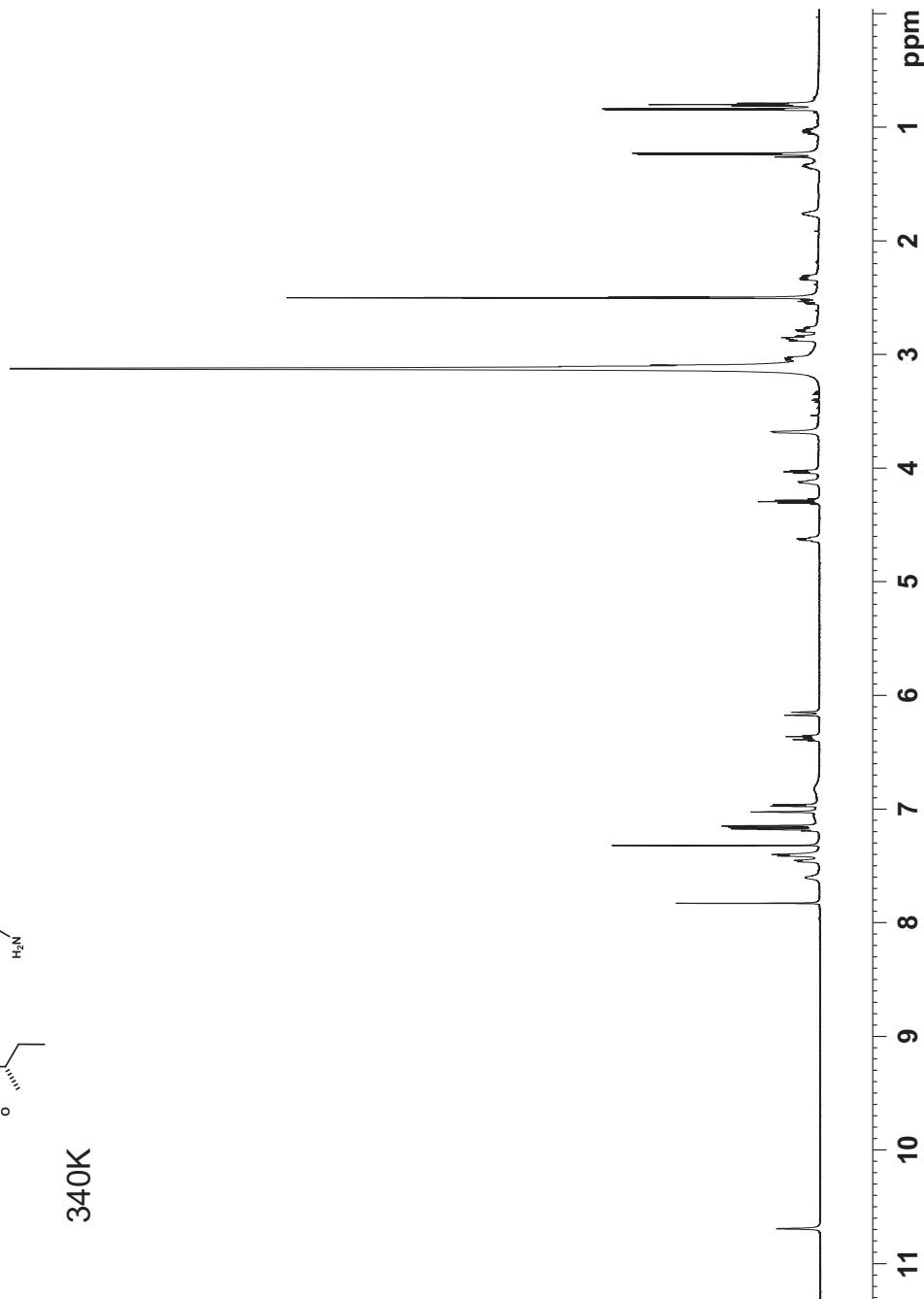
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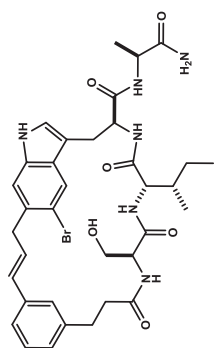
Current Data Parameters
NAME      KL5-106-4_AV600
EXPNO     22
PROCNO    1

F2 - Acquisition Parameters
Date_     20130104
Time_     18.26
INSTRUM   av600
PROBHD    5 mm BB5
PULPROG   zg
TD         65536
SOLVENT   DMSO
NS         8
DS         0
SWH        12376.237 Hz
FIDRES     0.188846 Hz
AQ         2.6476543 sec
RG         114
DW         40.400 usec
DE         6.50 usec
TE         340.0 K
D1         2.00000000 sec
TD0        1

===== CHANNEL f1 =====
NUC1       1H
P1         15.25 usec
PL1        -1.00 dB
PL1W       31.62277603 W
SFO1       600.1336008 MHz

F2 - Processing parameters
SI         65536
SF         600.1300069 MHz
WDW        EM
SSB        0
LB         0 Hz
GB         0
PC         1.00
  
```





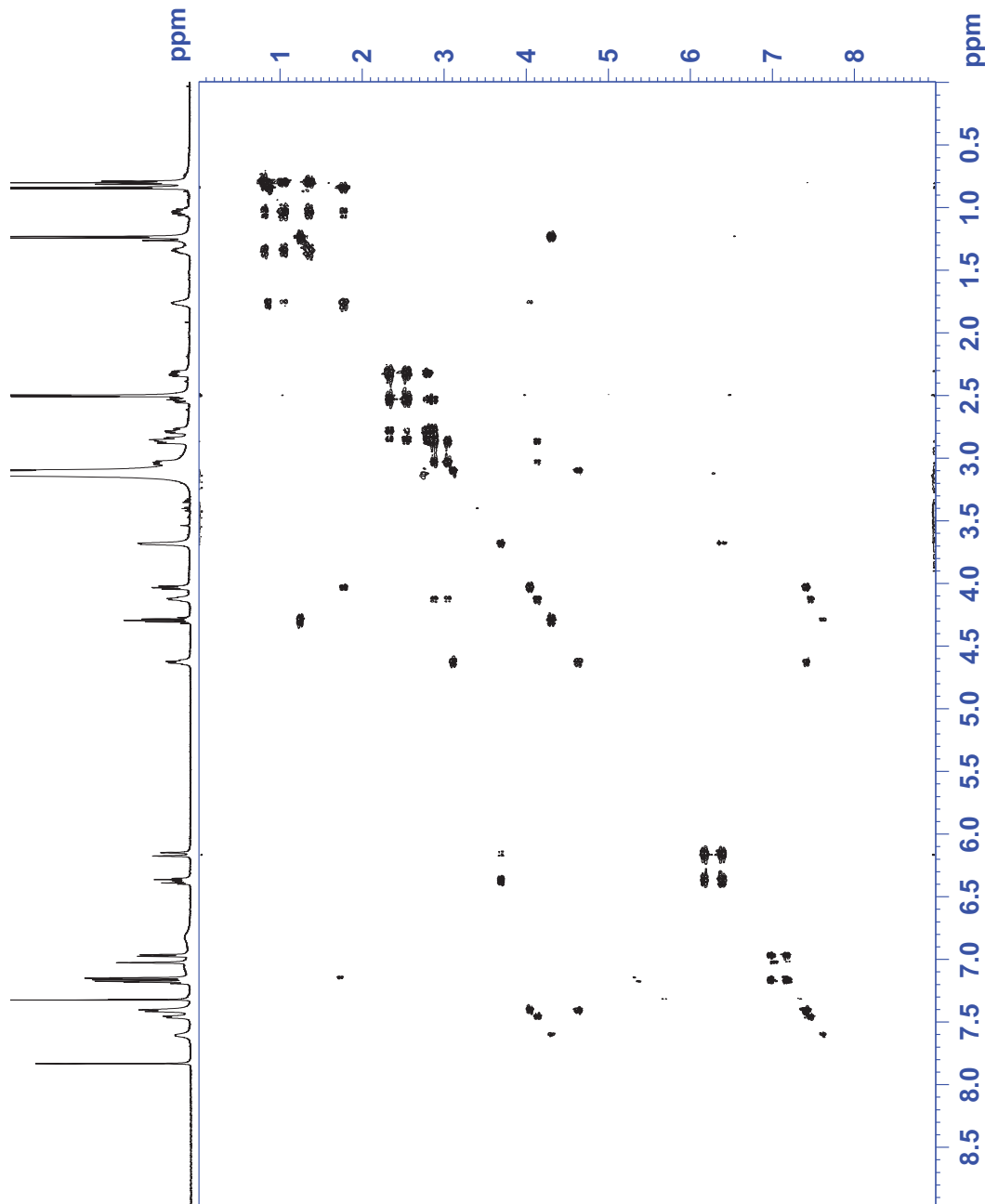
Current Data Parameters
 NAME KL5-106-4_AV600
 EXPNO 25
 PROCNO 1

F1 - Acquisition parameters
 TD 512
 SF01 600.1327 MHz
 FIDRES 10.523297 Hz
 SW 8.978 ppm
 FnMODE States-TPPI

F2 - Processing parameters
 SI 2048
 SF 600.1300102 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 2048
 MC2 States-TPPI
 SF 600.1299991 MHz
 WDW SINE
 SSB 2
 LB 0 Hz
 GB 0

340K



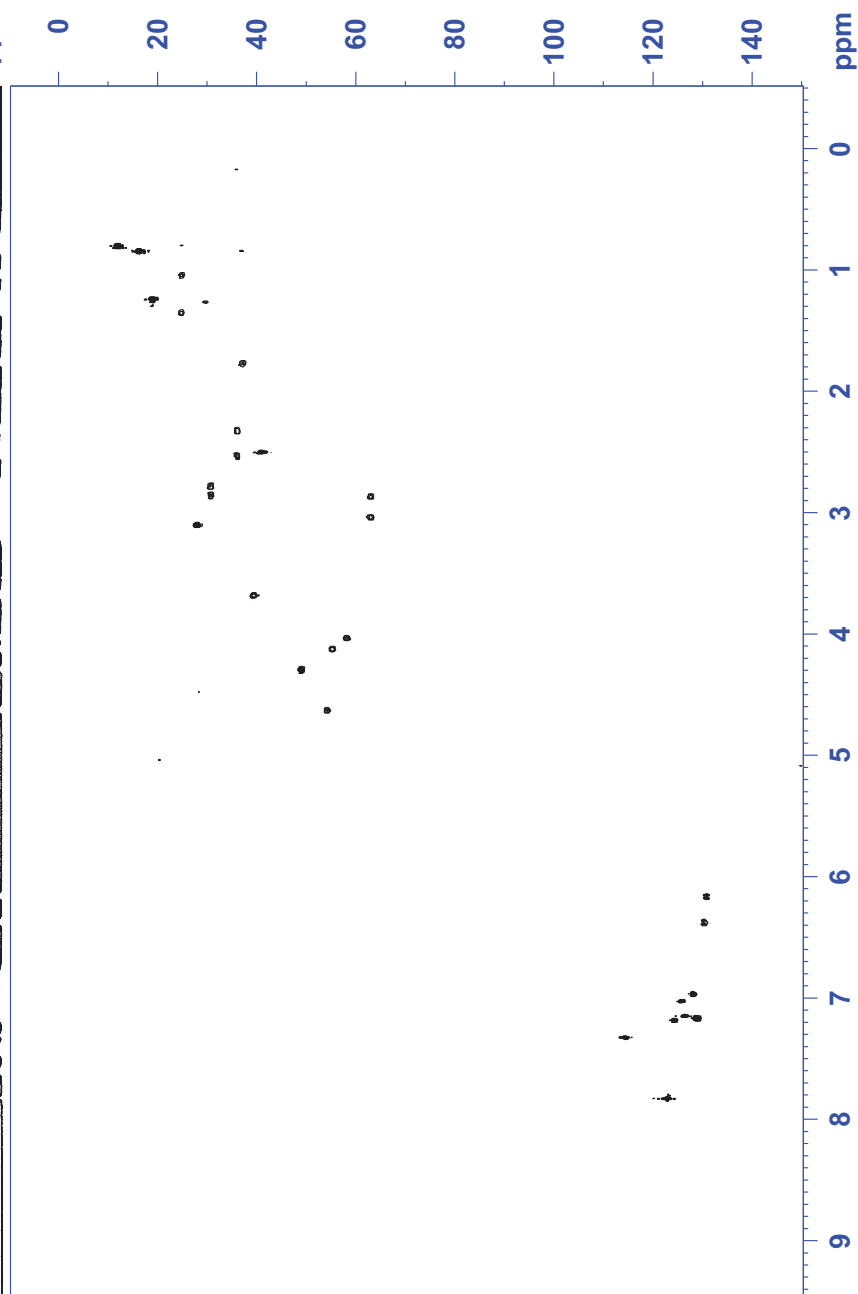
C[C@@H](CCC(=O)NCC(O)CNC(=O)c1ccc(cc1)/C=C/c2cc(Br)ccc2c3[nH]cnc3C(=O)N[C@H](C)C(N)=O)C(=O)N

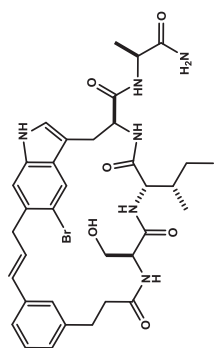
ppm

0

20

60





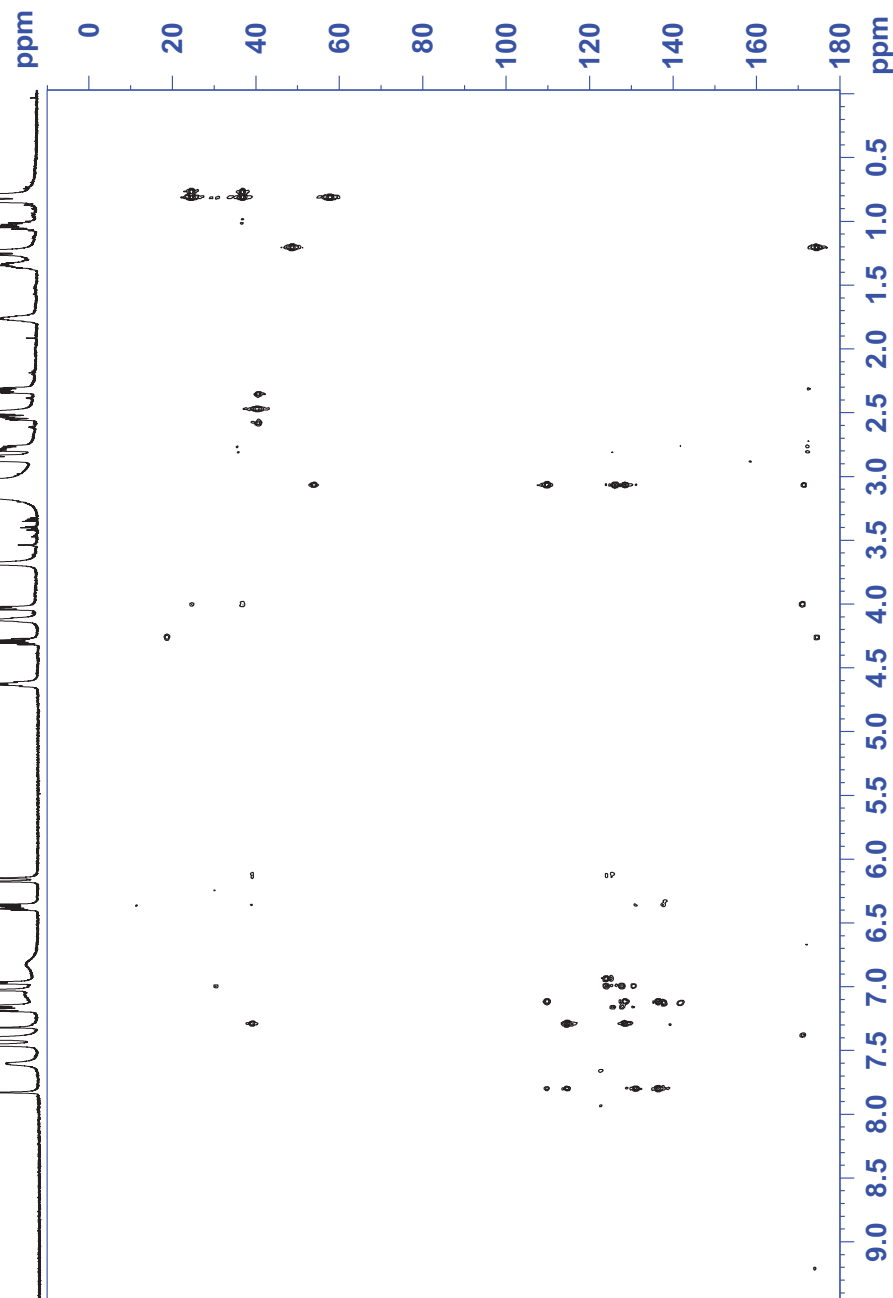
Current Data Parameters
 NAME KL5-106-4_AV600
 EXPNO 28
 PROCNO 1

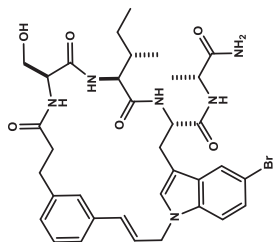
F1 - Acquisition parameters
 TD 210
 SFO1 150.9156 MHz
 FIDRES 136.542725 Hz
 SW 190.000 ppm
 FnmODE QF

F2 - Processing parameters
 SI 4096
 SF 600.1300273 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.40

F1 - Processing parameters
 SI 2048
 MC2 QF
 SF 150.9028090 MHz
 WDW USER
 SSB 2
 LB 0 Hz
 GB 0

340K



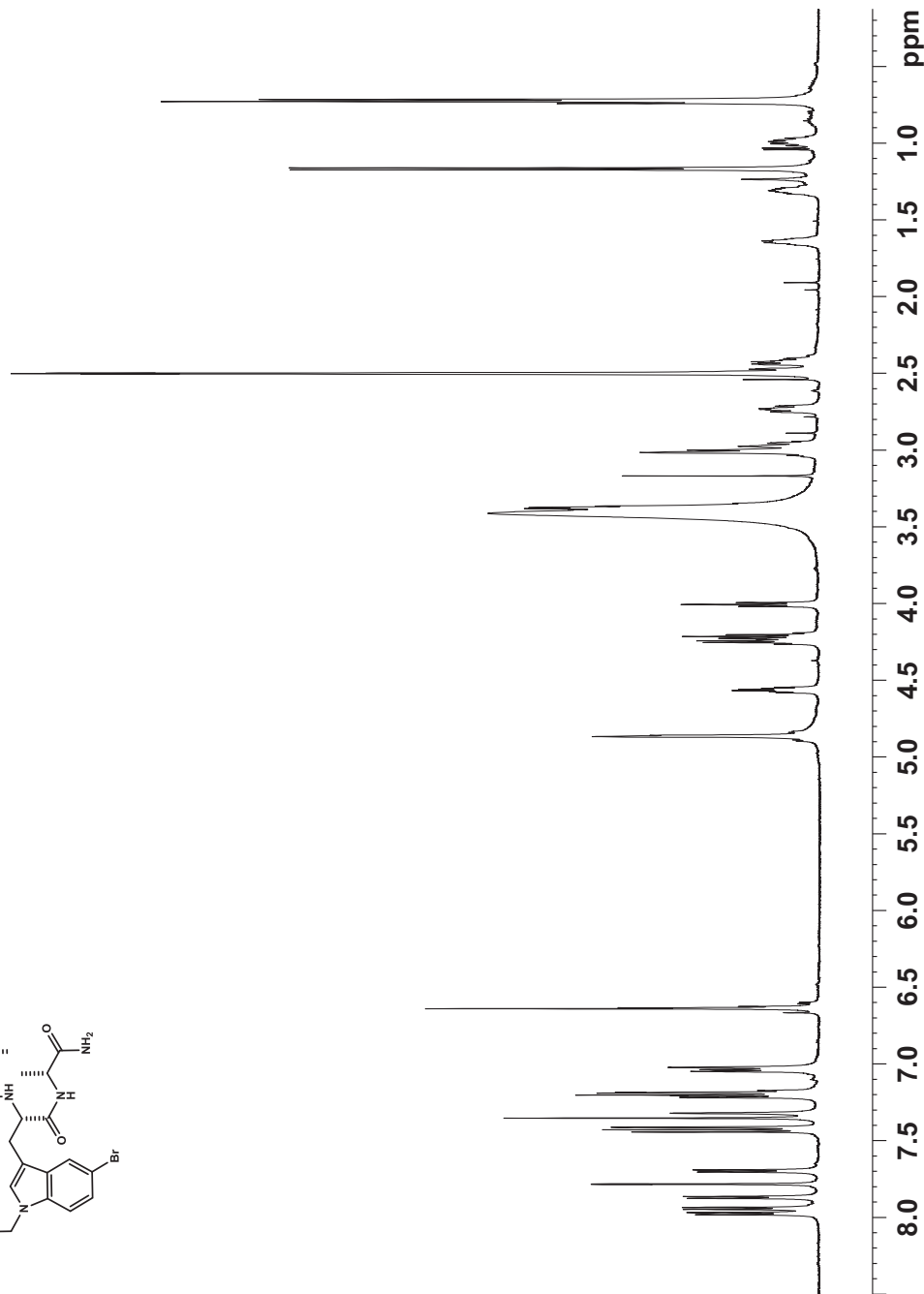


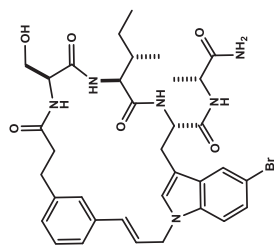
Current Data Parameters
NAME KL5-106-5-1
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20121221
Time_ 17.32
INSTRUM av600
PROBHD 5 mm TBI5
PULPROG zg
TD 65536
SOLVENT DMSO
NS 8
DS 0
SWH 12376.237 Hz
FIDRES 0.188846 Hz
AQ 2.6476543 sec
RG 114
DW 40.400 usec
DE 6.50 usec
TE 298.0 K
D1 2.00000000 sec
TD0 1

===== CHANNEL f1 =====
NUC1 1H
P1 9.23 usec
PL1 -2.00 dB
PL1W 39.81071854 W
SFO1 600.1336008 MHz

F2 - Processing parameters
SI 65536
SF 600.1300070 MHz
WDW EM
SSB 0
LB 0 Hz
GB 0
PC 1.00



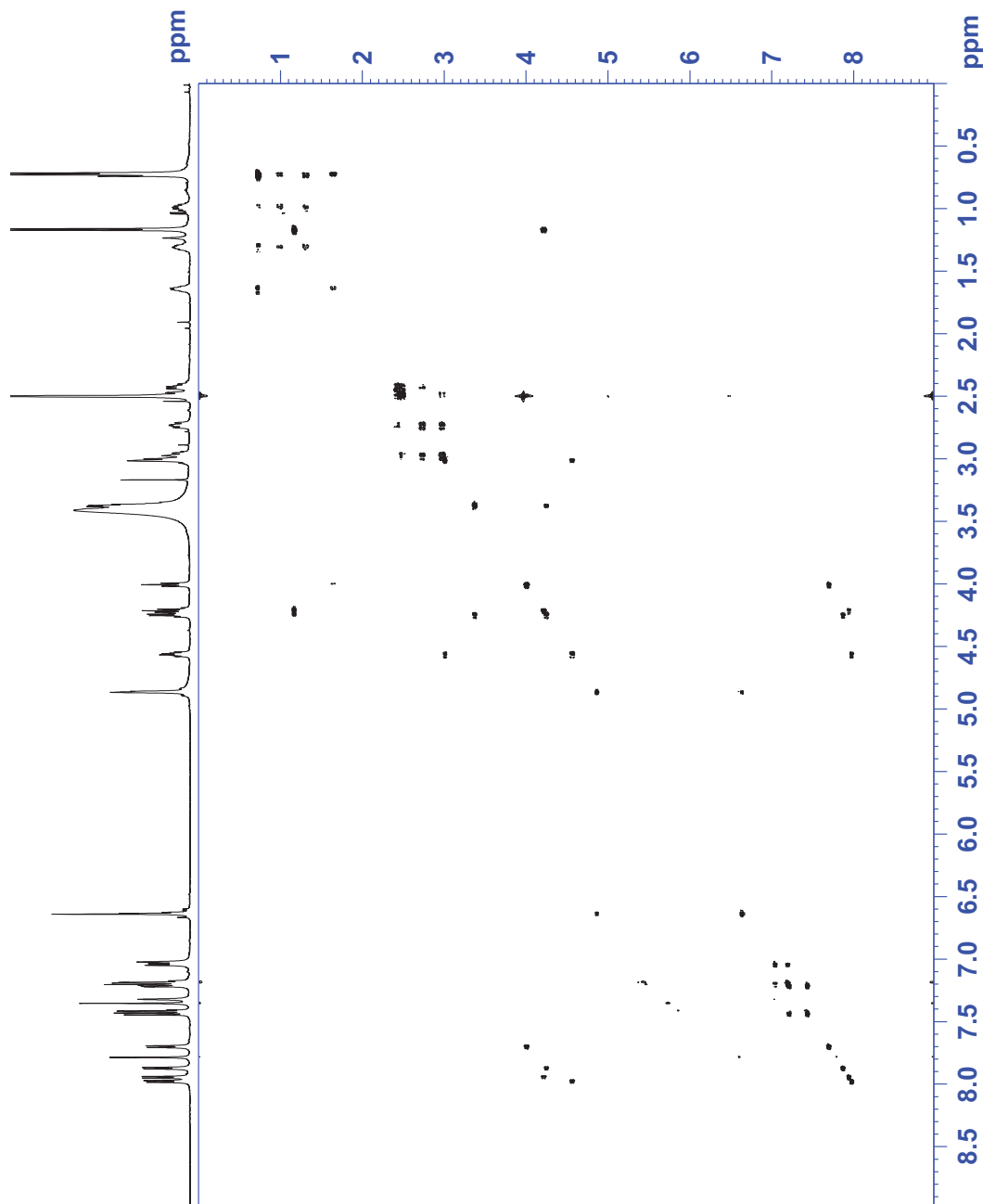


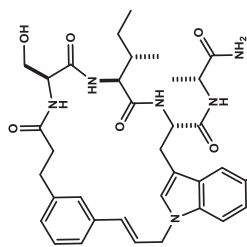
Current Data Parameters
 NAME KL5-106-5-1
 EXPNO 3
 PROCNO 1

F1 - Acquisition parameters
 TD 512
 SFO1 600.1327 MHz
 FIDRES 10.523297 Hz
 SW 8.978 ppm
 FnmODE States-TPPI

F2 - Processing parameters
 SI 2048
 SF 600.1300067 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 2048
 MC2 States-TPPI
 SF 600.1300058 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0



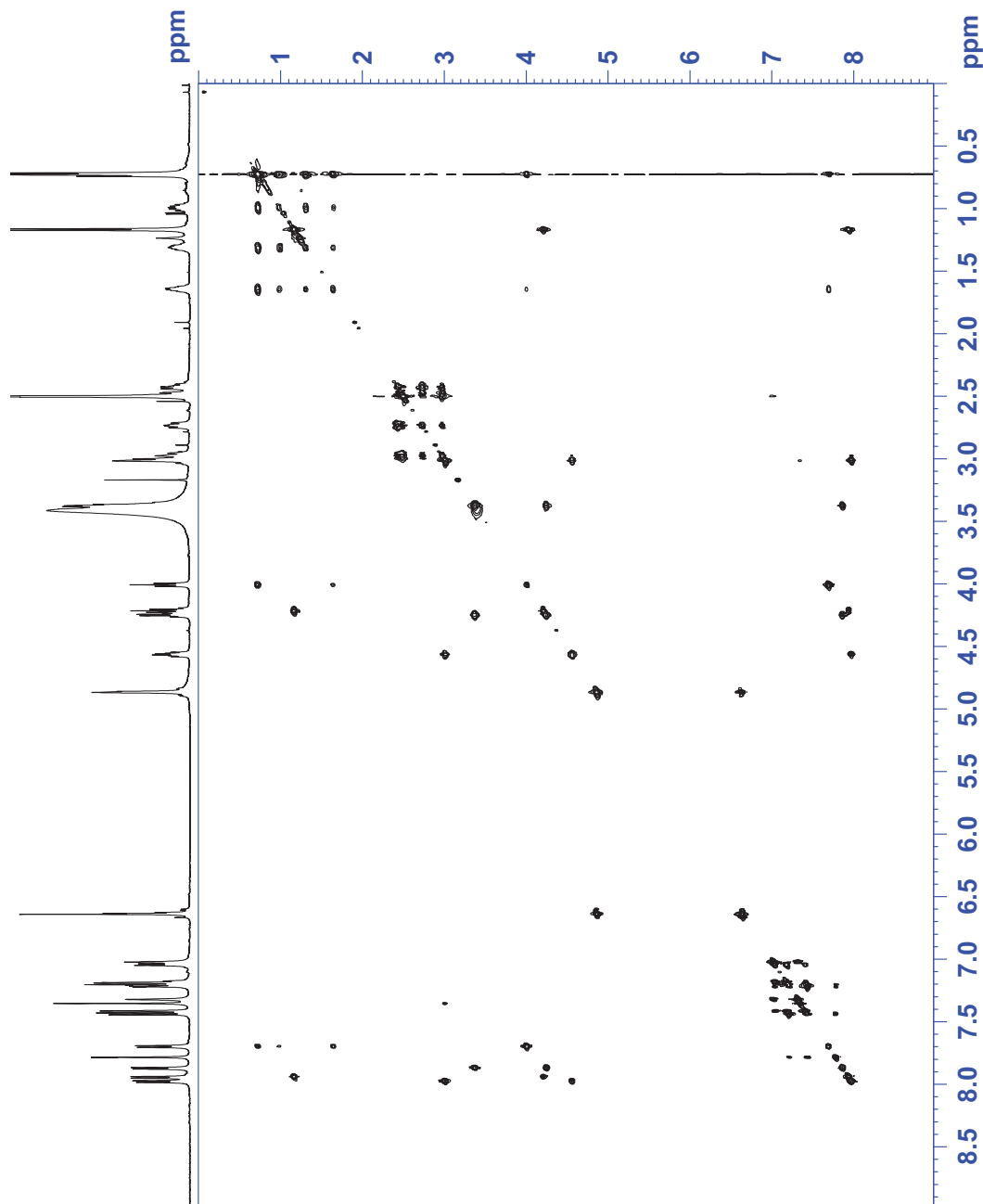


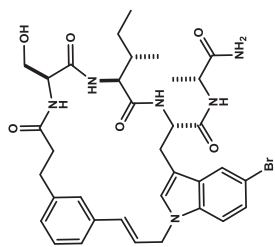
Current Data Parameters
 NAME KL5-106-5-1
 EXPNO 4
 PROCNO 1

F1 - Acquisition parameters
 TD 128
 SF01 600.1327 MHz
 FIDRES 42.093212 Hz
 SW 8.978 ppm
 FnmODE Echo-Antiecho

F2 - Processing parameters
 SI 4096
 SF 600.1300072 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 4096
 MC2 echo-antiecho
 SF 600.1300081 MHz
 WDW USER
 SSB 2
 LB 0 Hz
 GB 0



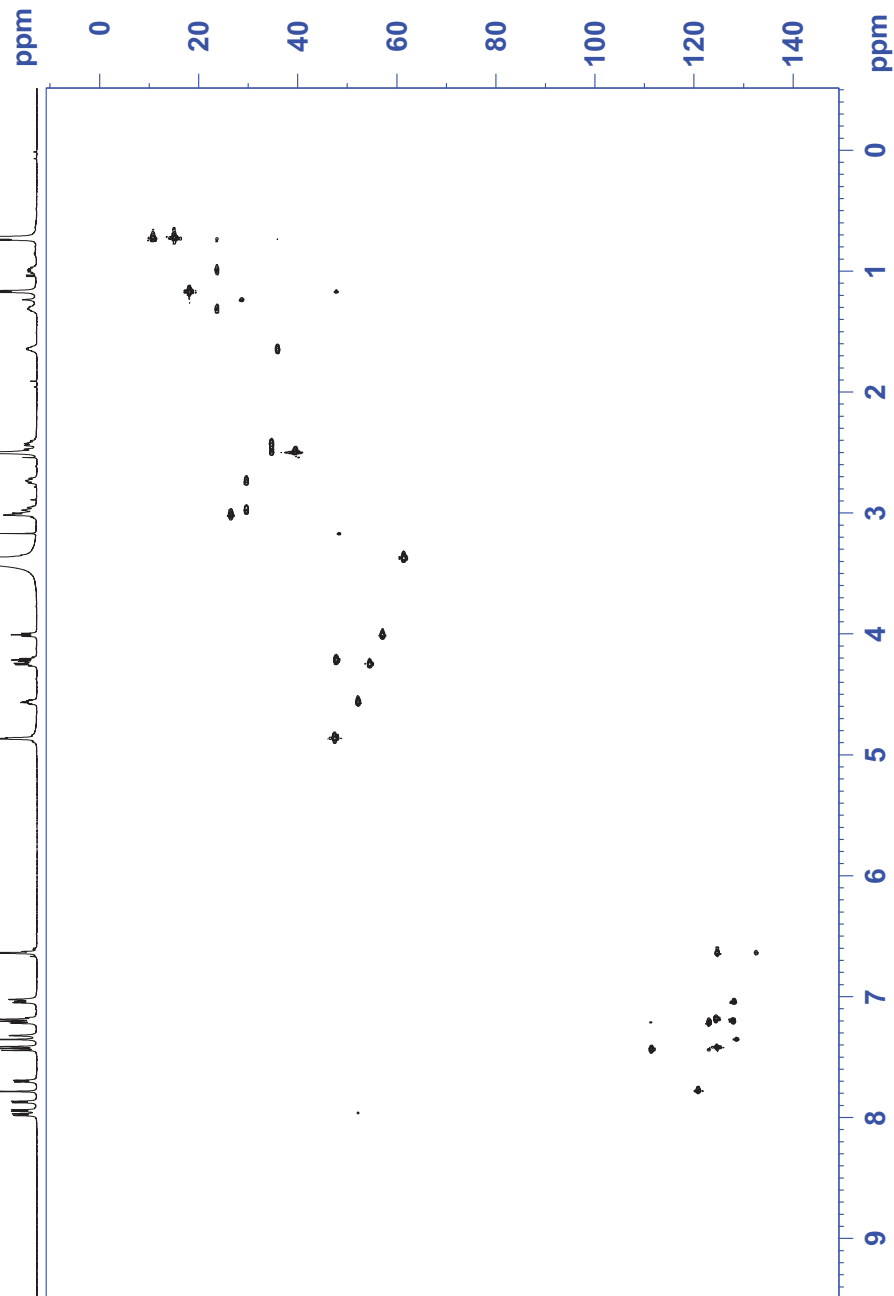


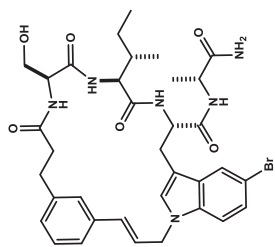
Current Data Parameters
 NAME KL5-106-5-1
 EXPNO 5
 PROCNO 1

F1 - Acquisition parameters
 TD 512
 SFO1 150.9134 MHz
 FIDRES 47.160427 Hz
 SW 160.000 ppm
 FnMODE Echo-Antiecho

F2 - Processing parameters
 SI 4096
 SF 600.1300053 MHz
 EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

F1 - Processing parameters
 SI 4096
 MC2 echo-antiecho
 SF 150.9029217 MHz
 WDW TRAP
 SSB 2
 LB 0 Hz
 GB 0



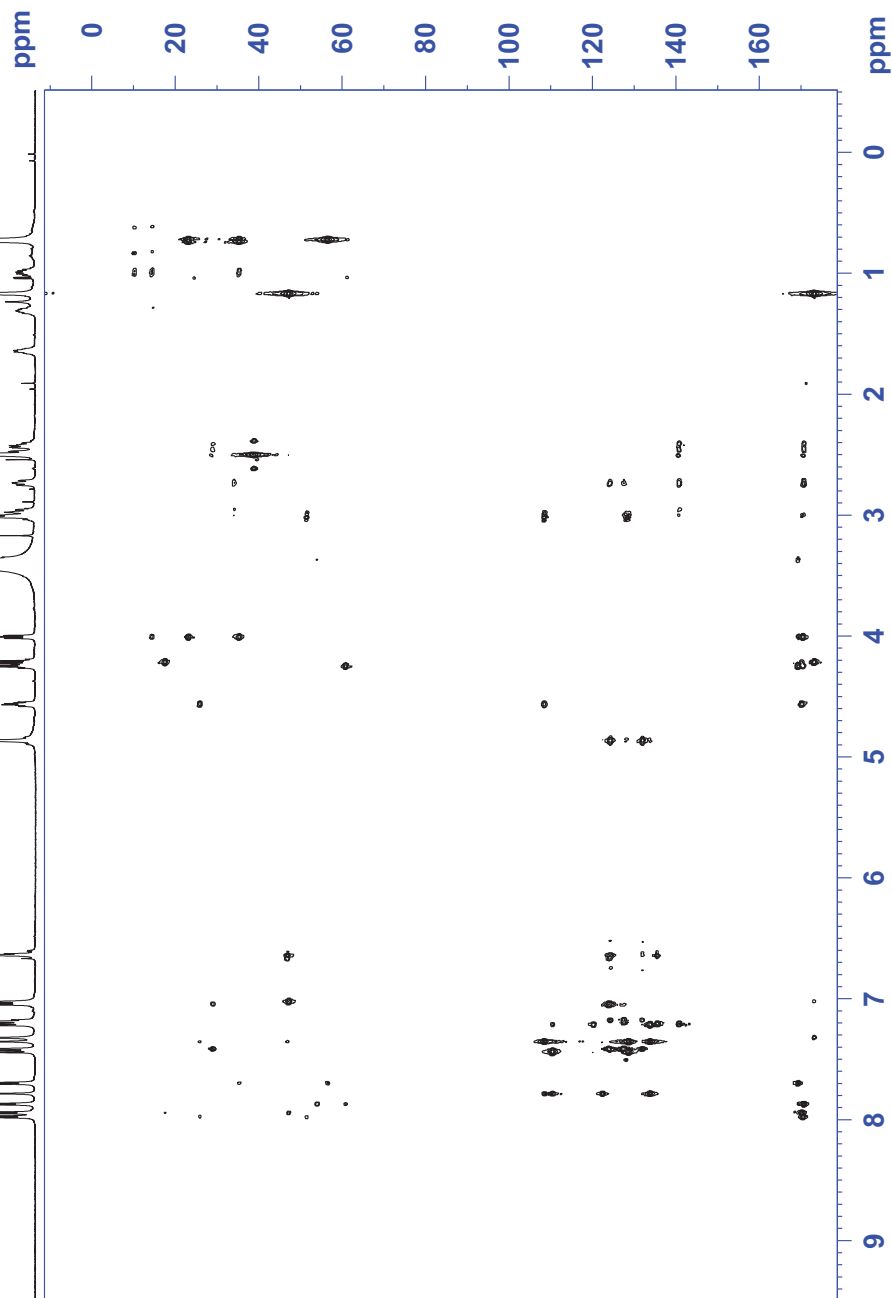


Current Data Parameters
 NAME KL5-106-5-1
 EXPNO 6
 PROCNO 1

F1 - Acquisition parameters
 TD 256
 SF01 150.9156 MHz
 FIDRES 112.007698 Hz
 SW 190.000 ppm
 FMODE QF

F2 - Processing parameters
 SI 4096
 SF 600.1300061 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.40

F1 - Processing parameters
 SI 2048
 MC2 QF
 SF 150.9030067 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0



```

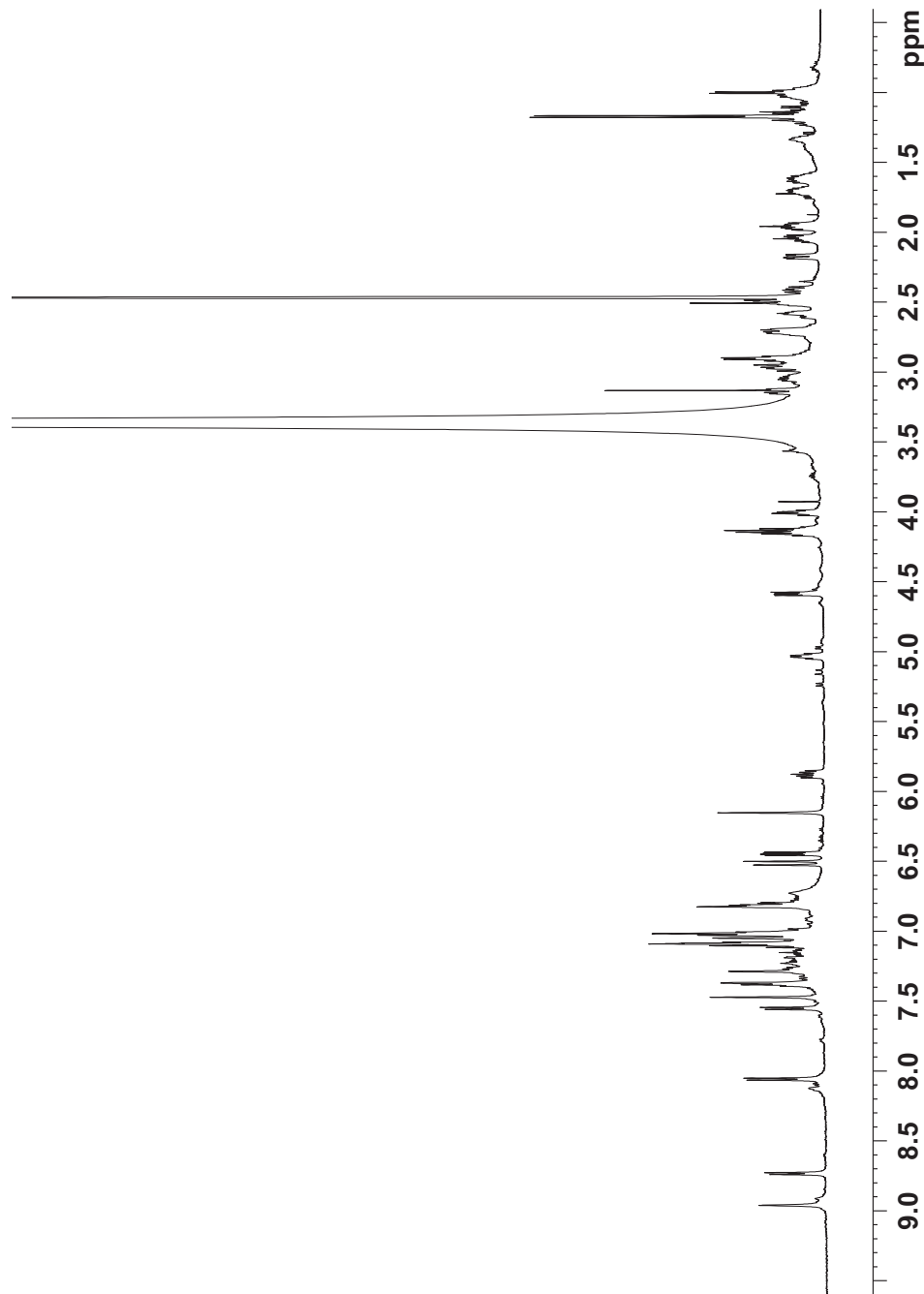
Current Data Parameters
NAME      W-A4-1-1
EXPNO     2
PROCNO    1

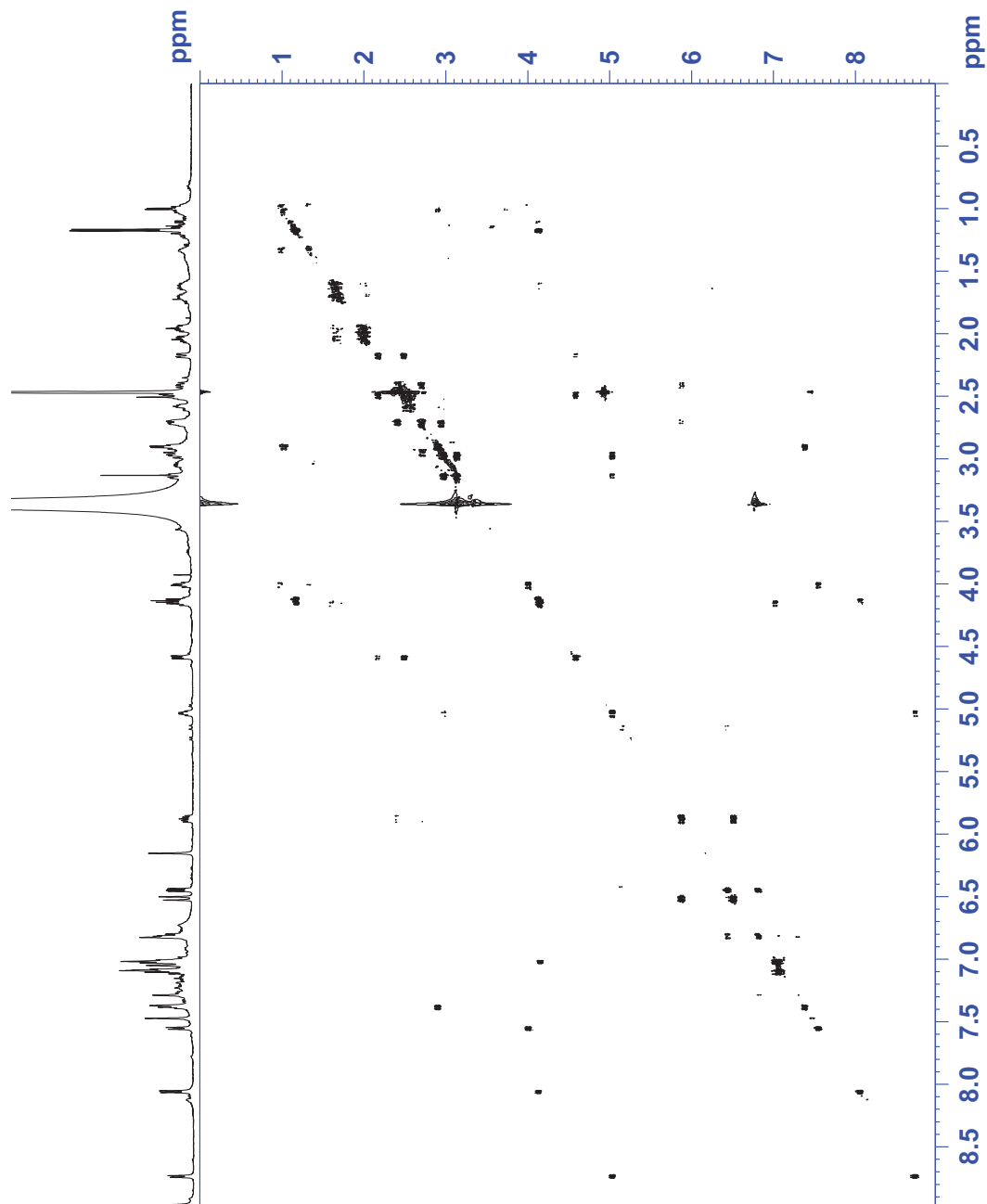
F2 - Acquisition Parameters
Date_     20121217
Time      16.32
INSTRUM   av600
PROBHD    5 mm TBI5
PULPROG   zg
TD         65536
SOLVENT   DMSO
NS         64
DS         0
SMH        12376.237 Hz
FIDRES     0.188846 Hz
AQ         2.6476543 sec
RG         181
DW         40.400 usec
DE         6.50 usec
TE         294.0 K
D1         2.00000000 sec
TD0        1

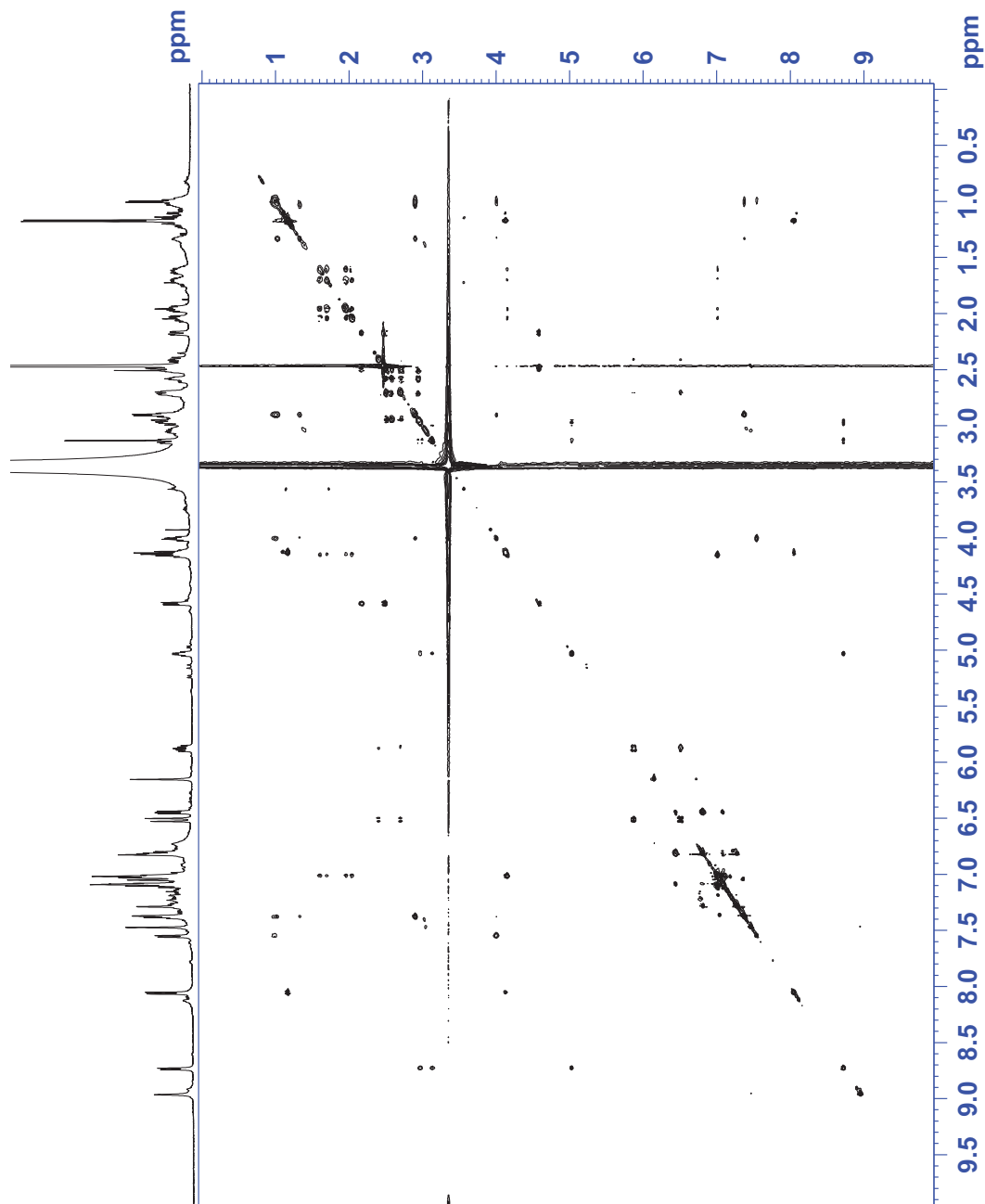
===== CHANNEL f1 =====
NUC1       1H
P1         10.00 usec
PL1        -2.00 dB
PL1W       39.81071854 W
SFO1       600.1336008 MHz

F2 - Processing parameters
SI         65536
SF         600.1300273 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00

```





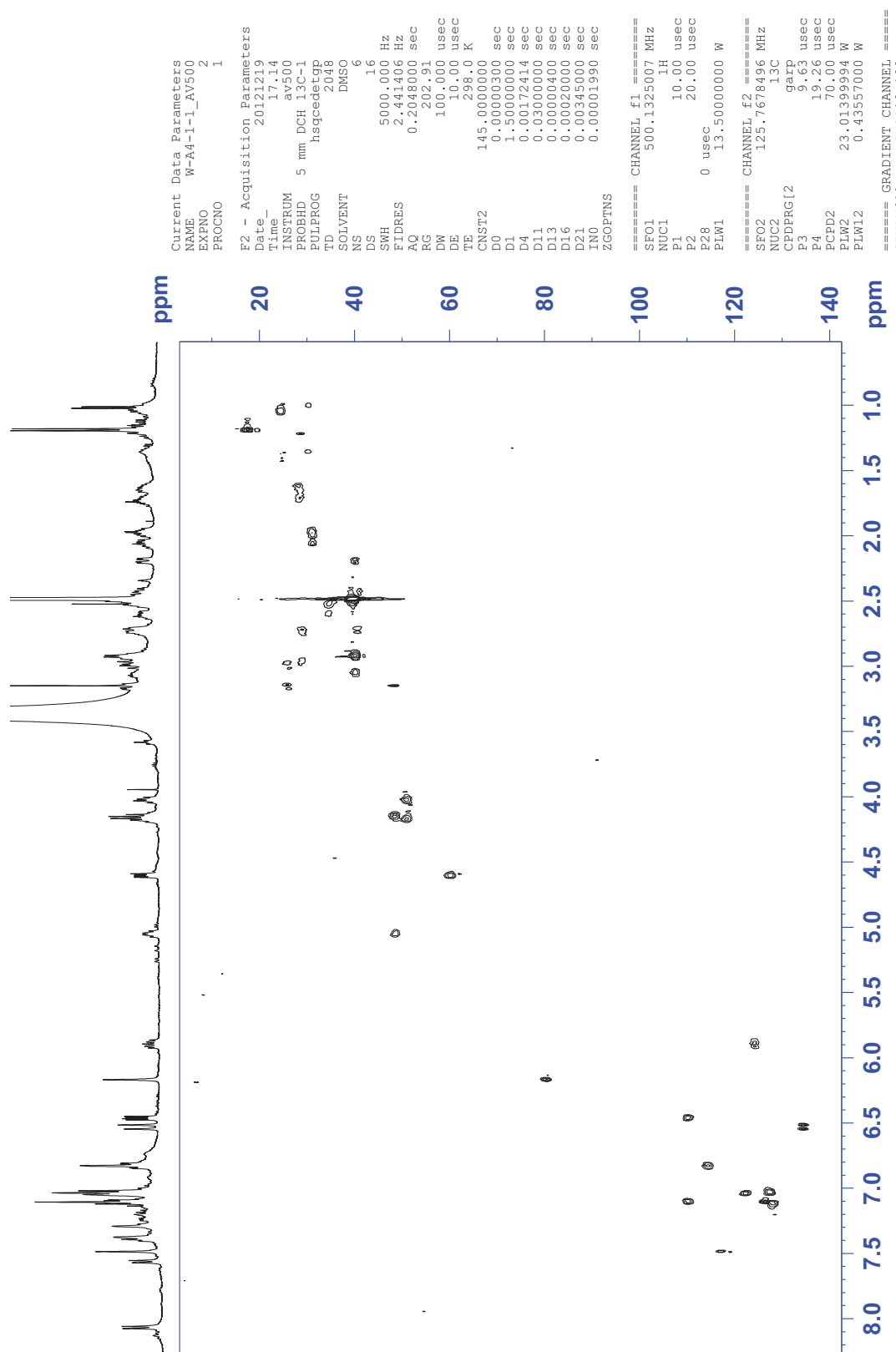


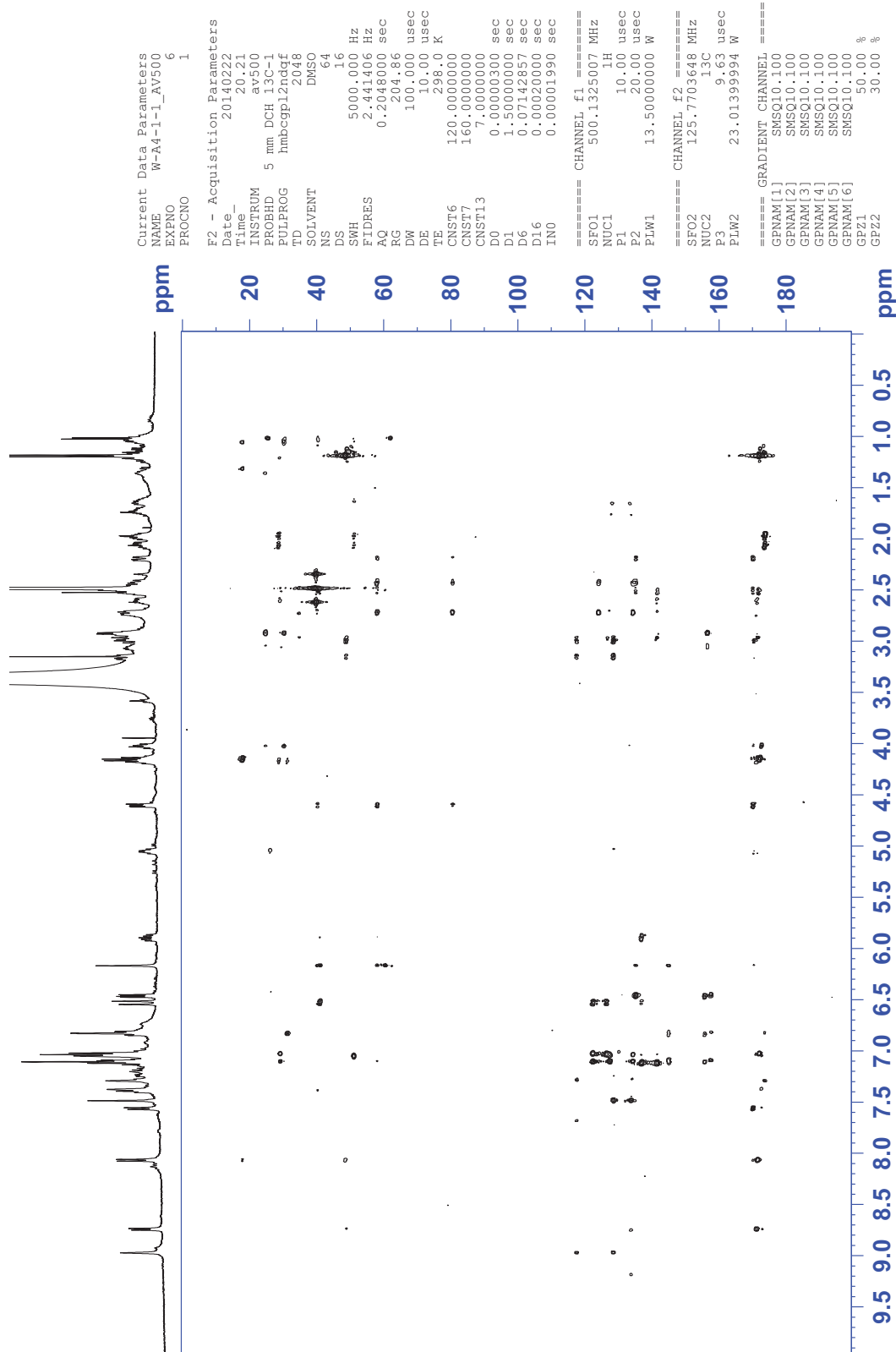
Current Data Parameters
NAME W-AA-1-1
EXPNO 4
PROCNO 1

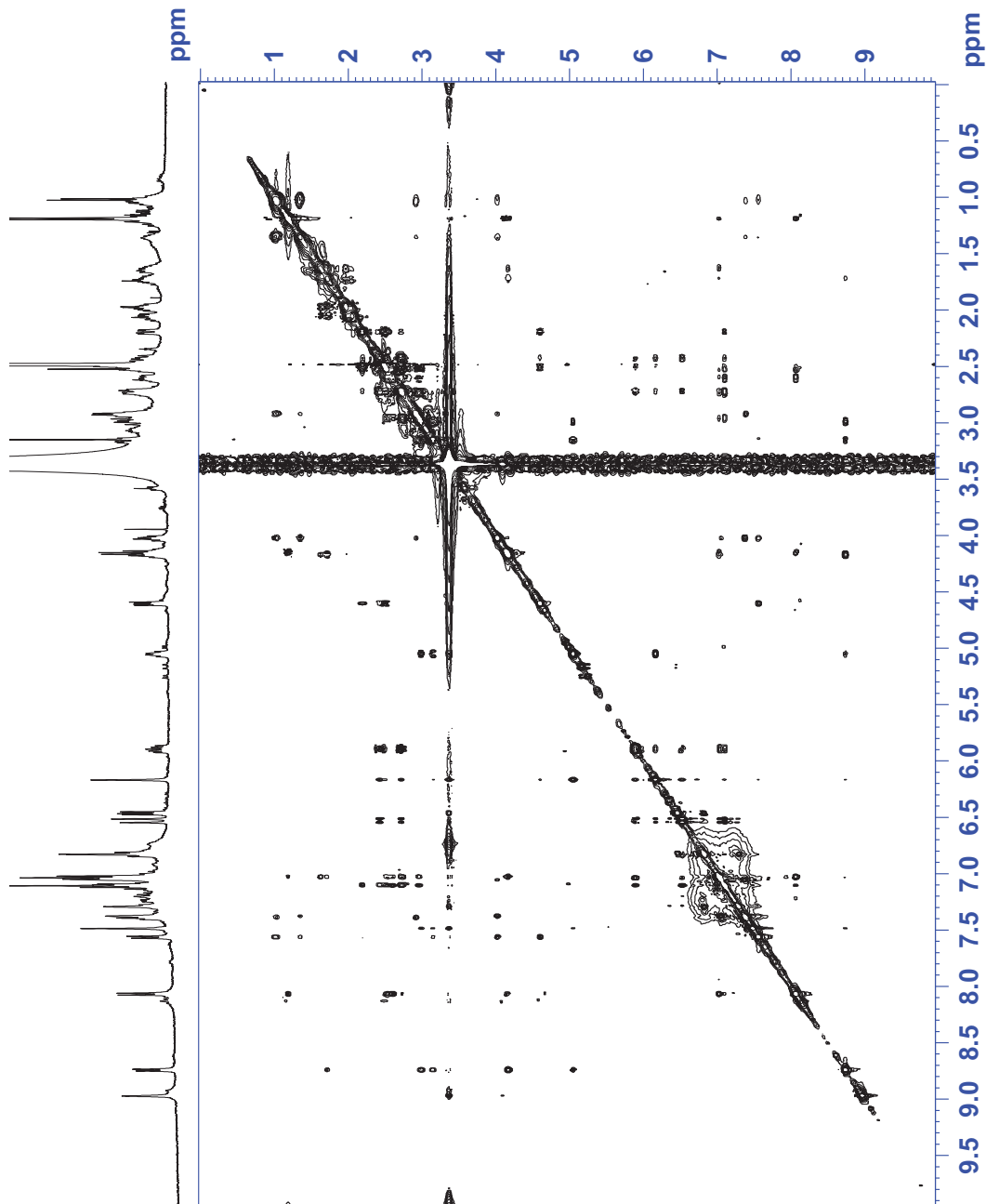
F1 - Acquisition parameters
TD 408
SF01 600.133 MHz
FIDRES 14.709142 Hz
SW 10.000 ppm
FnMODE Echo-Antiecho

F2 - Processing parameters
SI 1024
SF 600.1300273 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0
PC 1.00

F1 - Processing parameters
SI 1024
MC2 echo-antiecho
SF 600.1300273 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0







Current Data Parameters
NAME W-A4-1-1_AV500
EXPNO 7
PROCNO 1

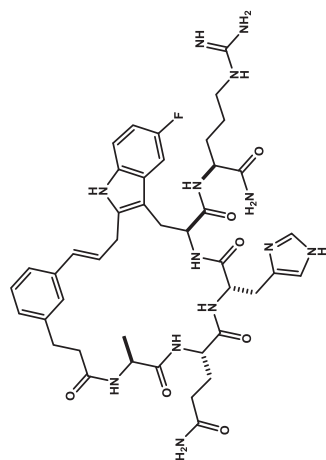
F2 - Acquisition Parameters
Date_ 20140223
Time_ 4.31
INSTRUM 5 mm DCH 13C-1
PROBHD noesypph
TD 2048
SOLVENT DMSO
NS 16
DS 8
SWH 5000.000 Hz
FIDRES 2.441406 Hz
AQ 0.2048000 sec
RG 26.58
DW 100.000 usec
DE 10.00 usec
TE 298.0 K
D0 0.00008727 sec
D1 2.00000000 sec
D8 0.20000000 sec
D16 0.00020000 sec
IN0 0.00020000 sec

===== CHANNEL f1 =====
SFO1 500.1325007 MHz
NUC1 1H
P1 10.00 usec
P2 20.00 usec
PLW1 13.50000000 W

===== GRADIENT CHANNEL =====
GPNAM[1] SINE.100
GP21 40.00 %
PL6 1000.00 usec

F1 - Acquisition parameters
TD 256
SFO1 500.1325 MHz
FIDRES 19.531250 Hz
SW 9.997 ppm
FMODE States-TPPI

F2 - Processing parameters
SI 2048
SF 500.1300135 MHz
WDW QSI
SSB 2
LB 0 Hz
GB 0



```

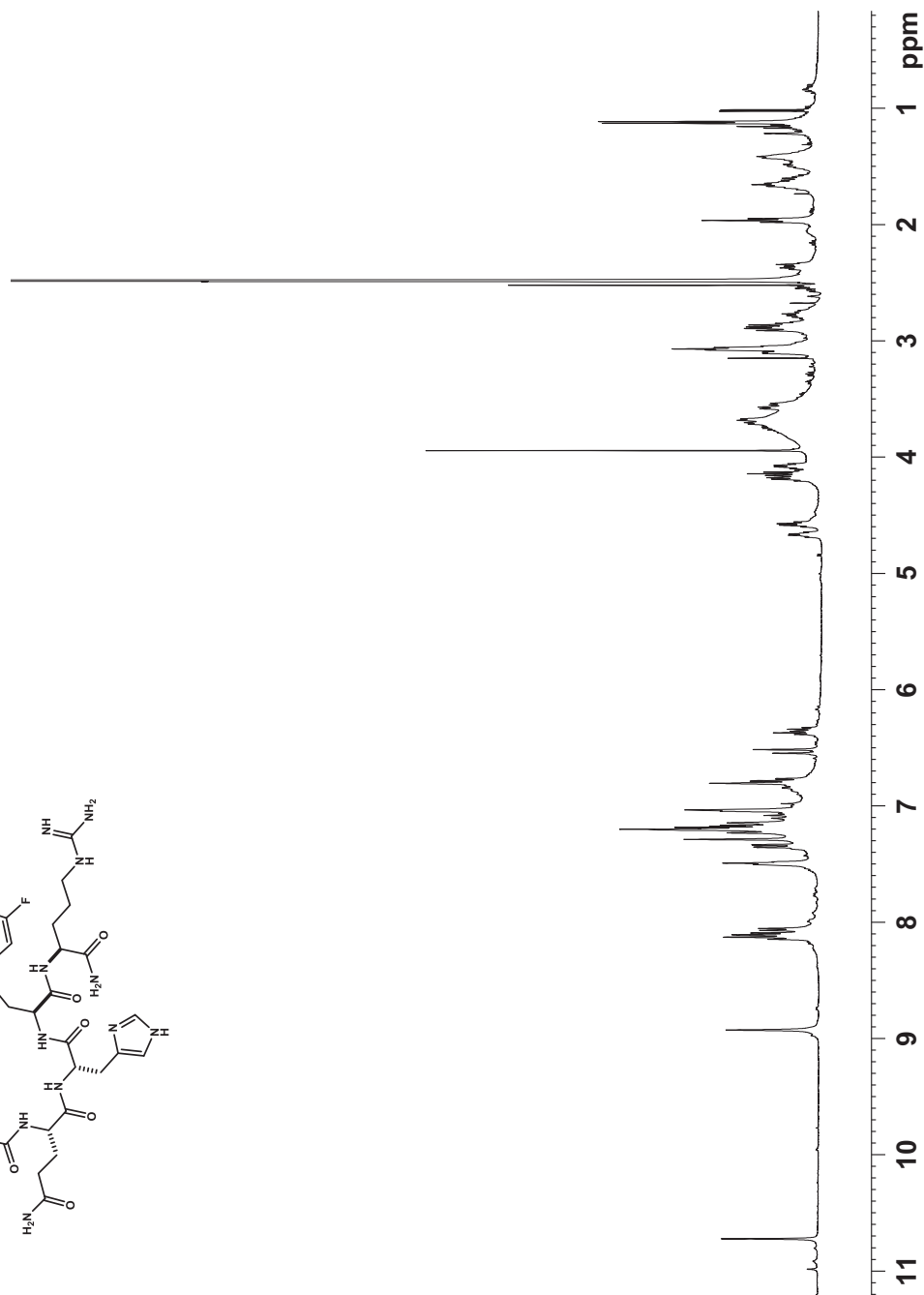
Current Data Parameters
NAME      W-A4-2
EXPNO     2
PROCNO    1

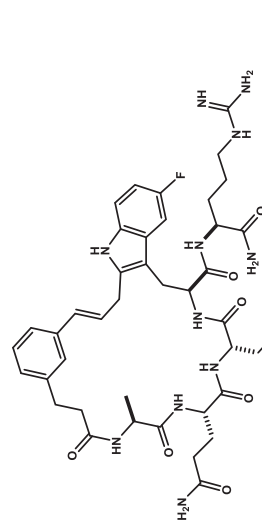
F2 - Acquisition Parameters
Date_     20121020
Time      15.18
INSTRUM   av500
PROBHD    5 mm DCH 13C-1
PULPROG   zg
TD         65536
SOLVENT   DMSO
NS         8
DS         0
SWH        10000.000 Hz
FIDRES     0.152588 Hz
AQ         3.2767999 sec
RG         9.65
DW         50.000 usec
DE         10.00 usec
TE         298.0 K
D1         2.00000000 sec
TD0        1

===== CHANNEL f1 =====
NUC1       1H
P1         10.00 usec
PLW1       13.50000000 W
SFO1       500.1330008 MHz

F2 - Processing parameters
SI         65536
SF         500.1300146 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00

```



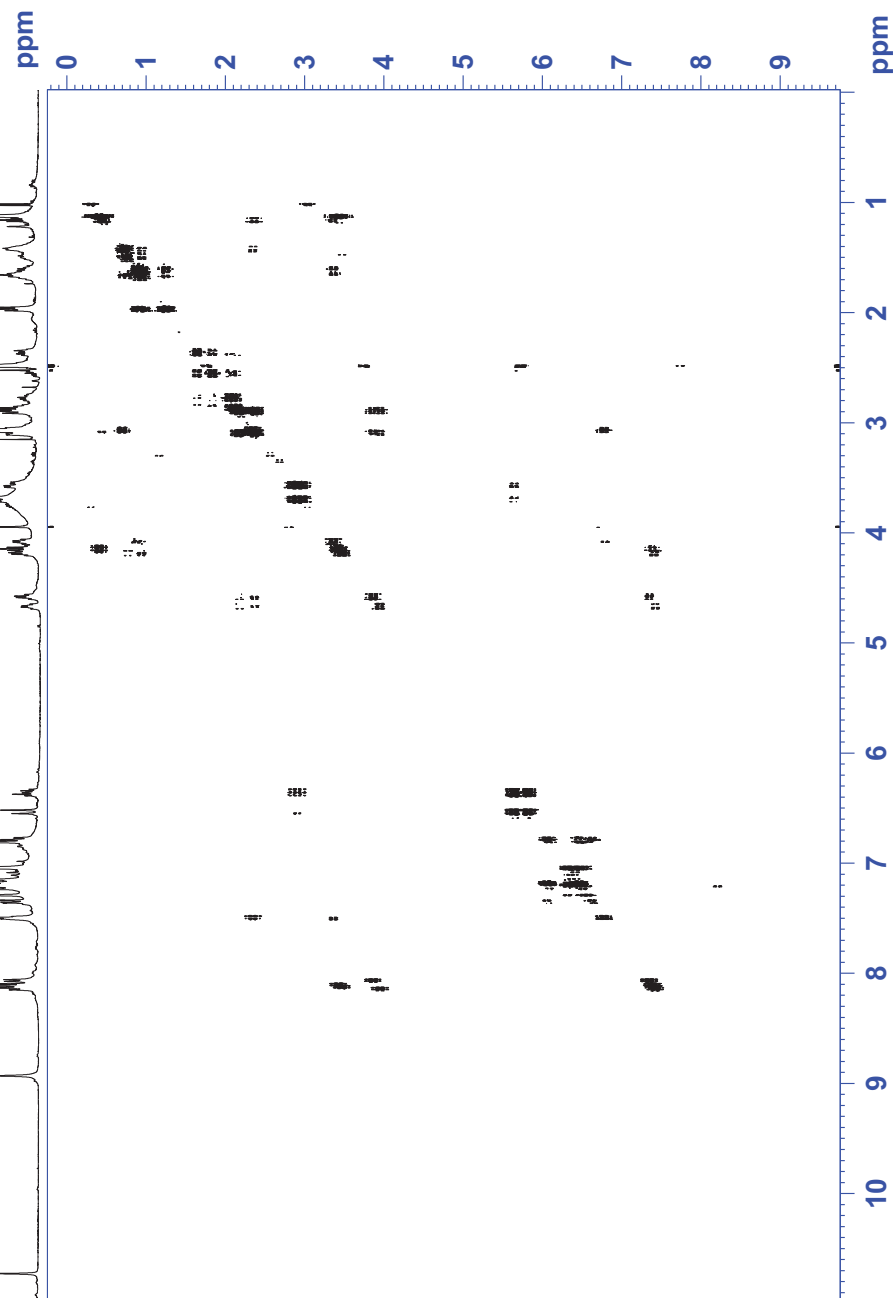


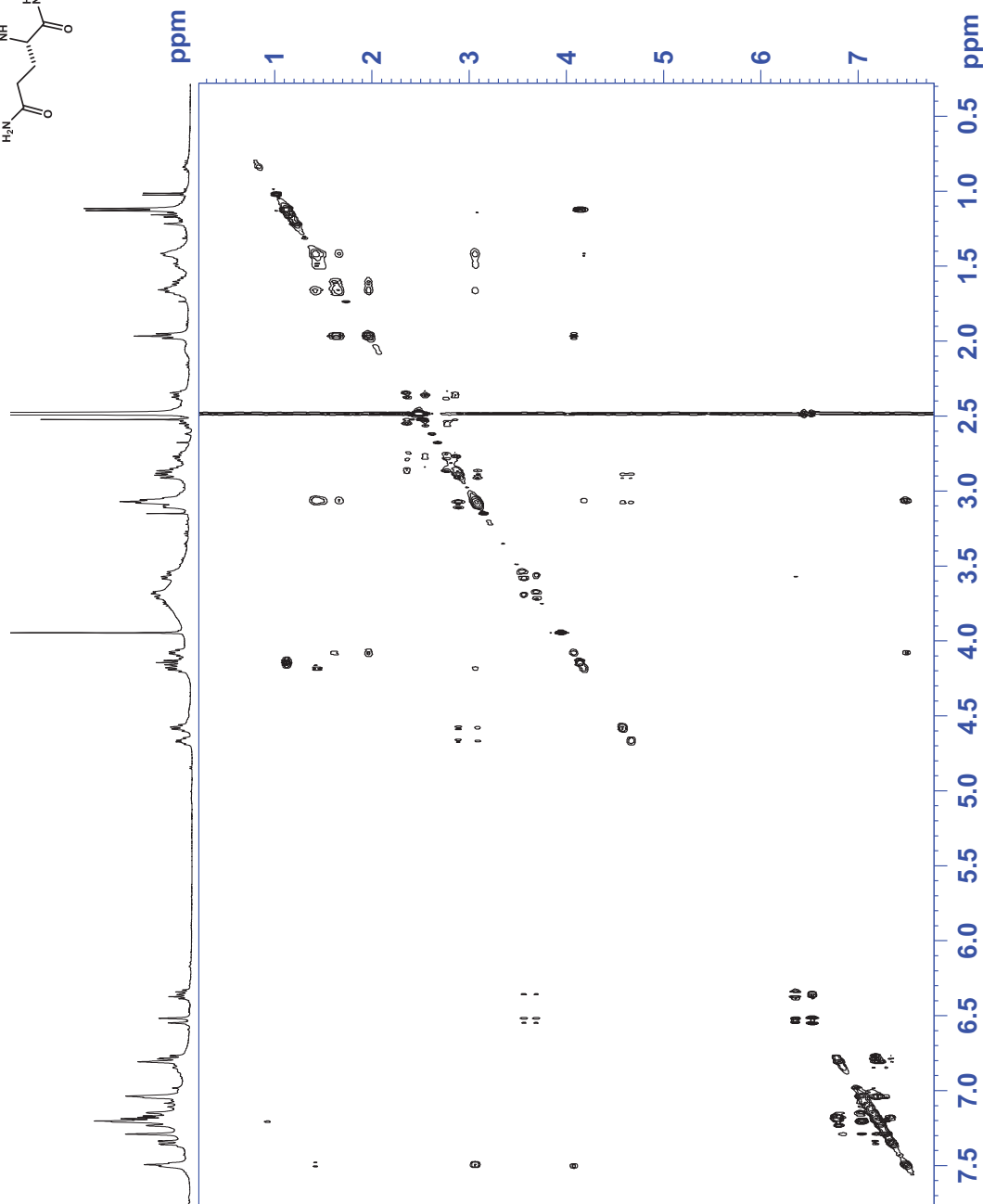
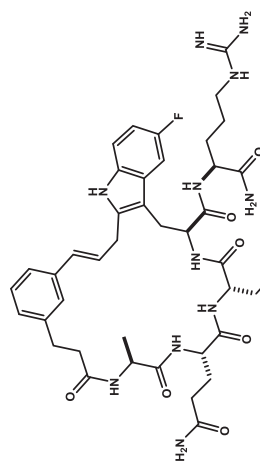
Current Data Parameters
NAME W-A4-2
EXPNO 3
PROCNO 1

F1 - Acquisition parameters
TD 256
SF01 500.1328 MHz
FIDRES 19.536423 Hz
SW 10.000 ppm
FnMODE States-TPPI

F2 - Processing parameters
SI 2048
SF 500.1300135 MHz
WDW SINE
SSB 1
LB 0 Hz
GB 0
PC 1.00

F1 - Processing parameters
SI 2048
MC2 States-TPPI
SF 500.1303720 MHz
WDW GM
SSB 1
LB 0 Hz
GB 0



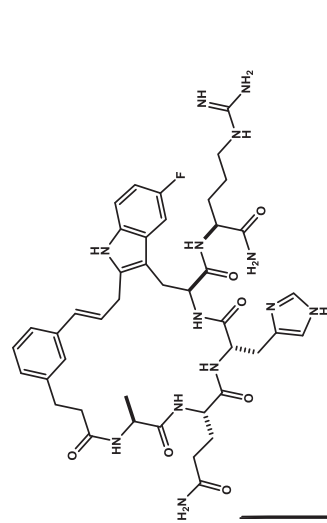


Current Data Parameters
NAME W-A4-2
EXPNO 4
PROCNO 1

F1 - Acquisition parameters
TD 256
SF01 500.132 MHz
FIDRES 15.629138 Hz
SW 8.000 ppm
FnMODE Echo-Antiecho

F2 - Processing parameters
SI 2048
SF 500.1300135 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0
PC 1.00

F1 - Processing parameters
SI 2048
MC2 echo-antiecho
SF 500.1300135 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0



Current Data Parameters
 NAME W-A4-2
 EXPNO 6
 PROCNO 1

F1 - Acquisition parameters
 TD 256
 SF01 125.7678 MHz
 FIDRES 98.255890 Hz
 SW 200.000 ppm
 FnMODE Echo-Antiecho

F2 - Processing parameters
 SI 2048
 SF 500.1300135 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 2048
 MC2 echo-antiecho
 SF 125.7578472 MHz
 WDW USER
 SSB 2
 LB 0 Hz
 GB 0

ppm

20

40

60

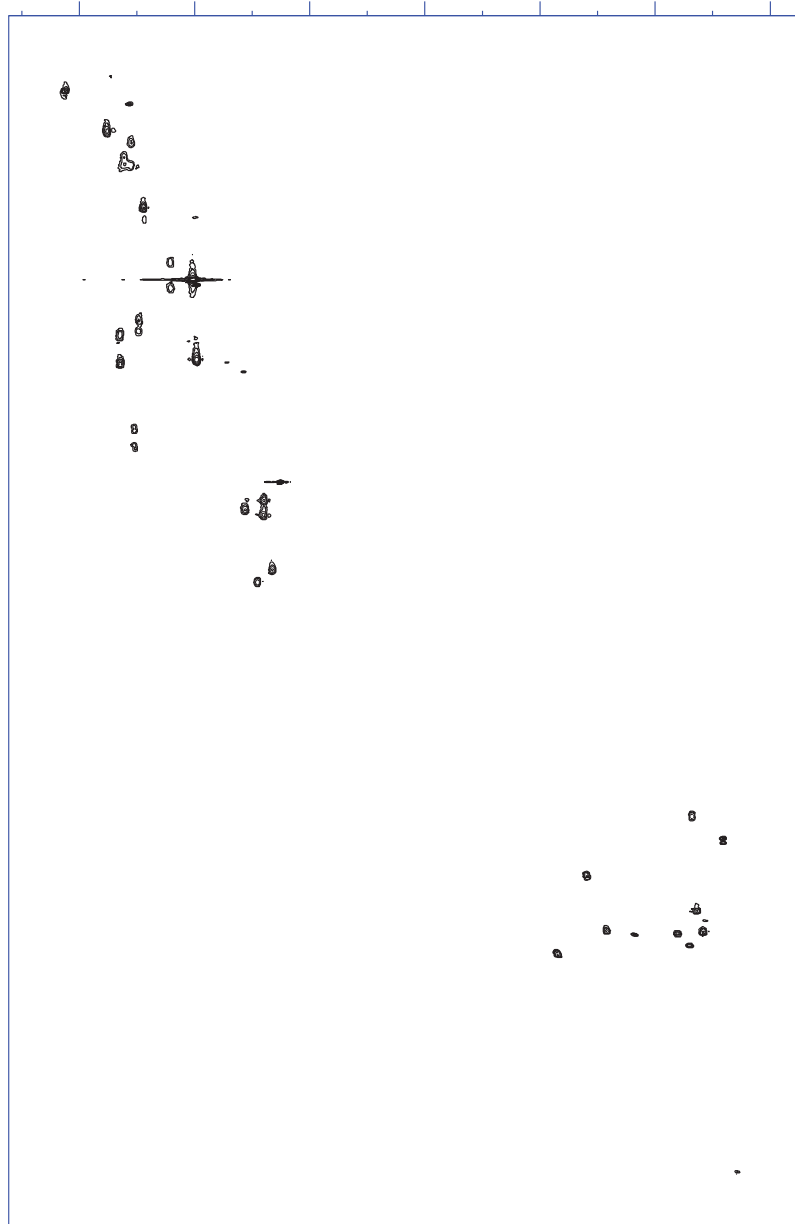
80

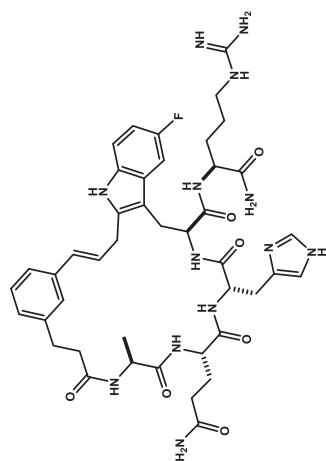
100

120

140

ppm



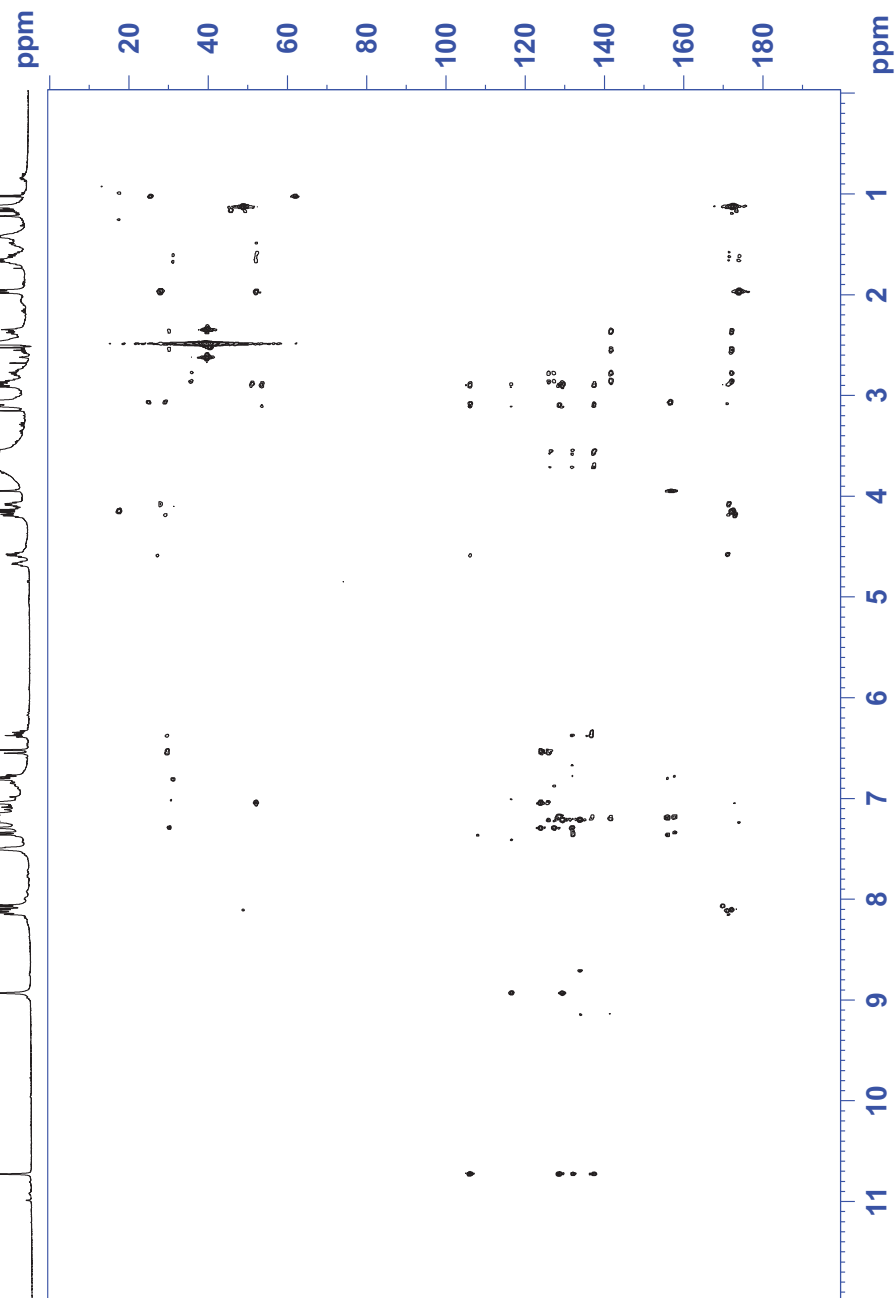


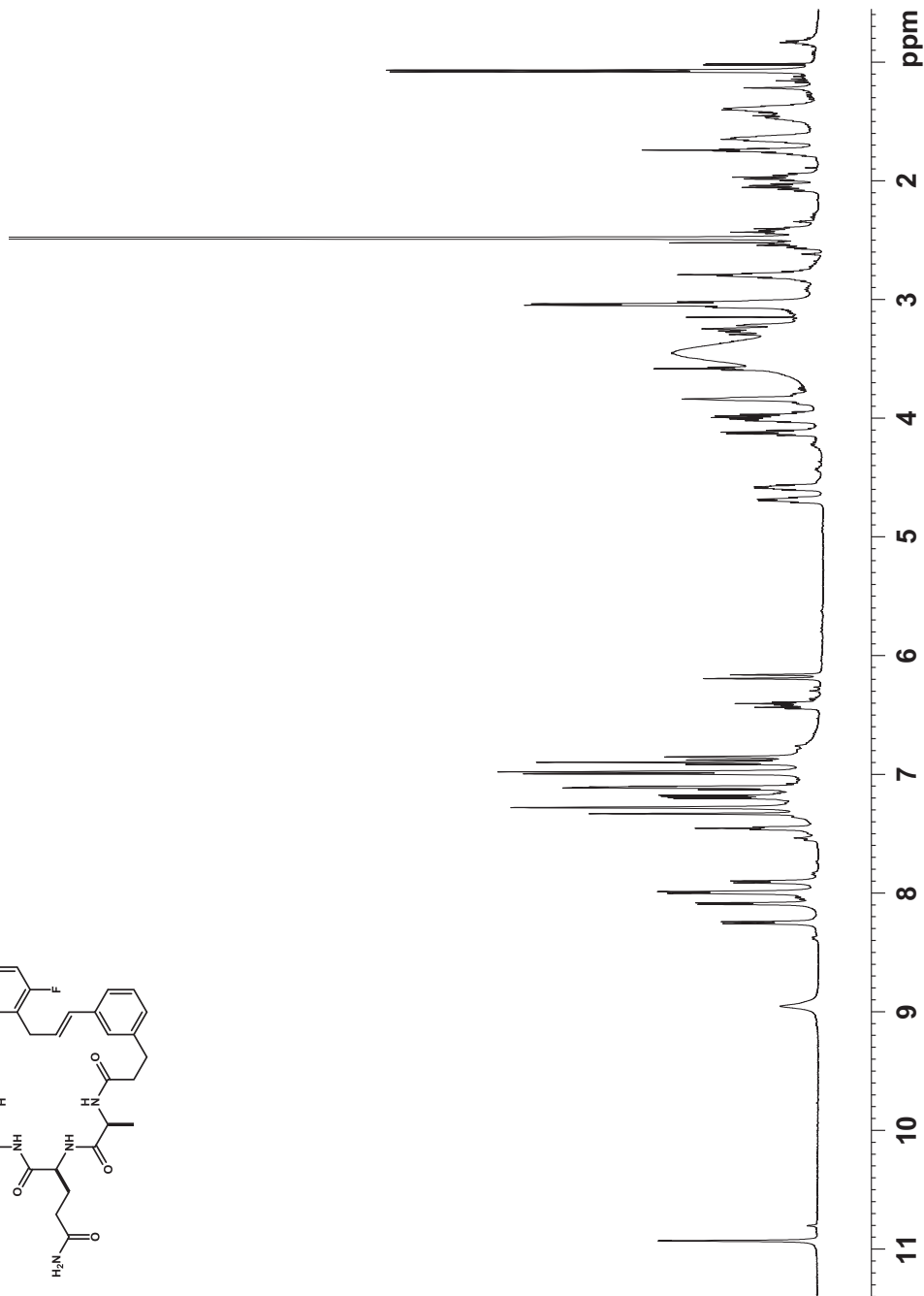
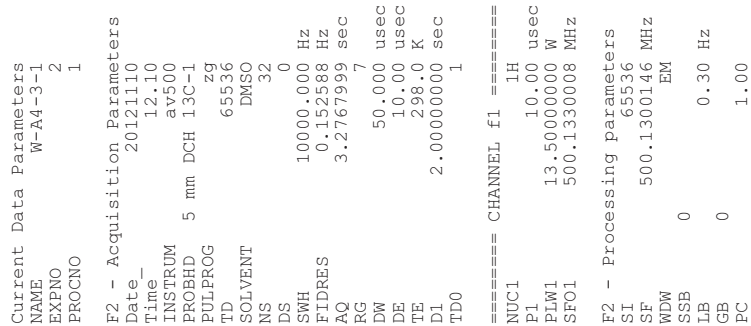
Current Data Parameters
 NAME W-A4-2
 EXPNO 7
 PROCNO 1

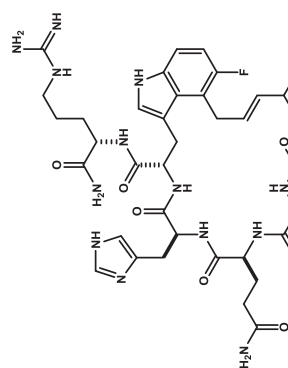
F1 - Acquisition parameters
 TD 256
 SF01 125.7704 MHz
 FIDRES 98.257607 Hz
 SW 199.999 ppm
 FnMODE QF

F2 - Processing parameters
 SI 2048
 SF 500.1300135 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 2048
 MC2 QF
 SF 125.7578472 MHz
 WDW USER
 SSB 2
 LB 0 Hz
 GB 0





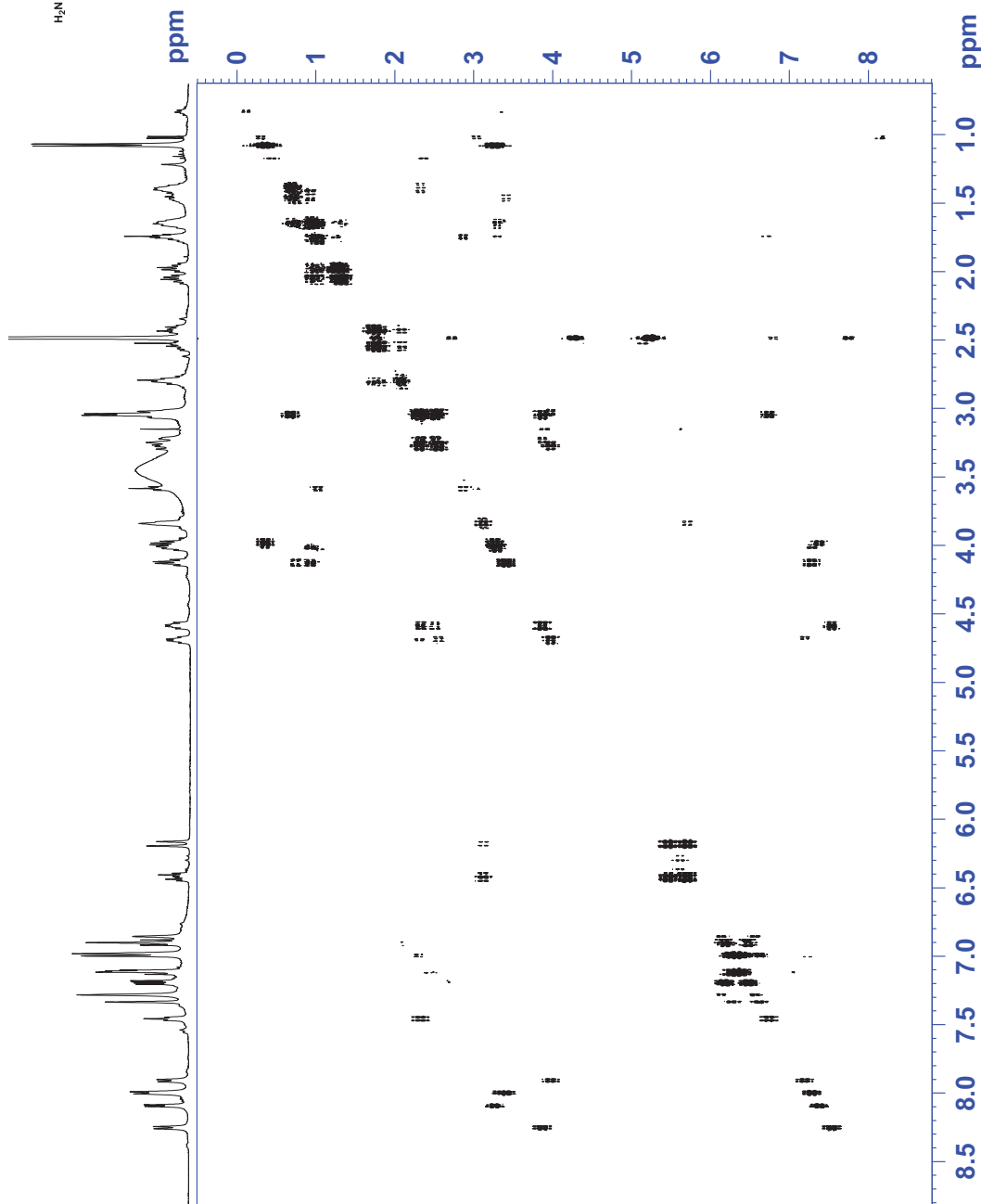


Current Data Parameters
 NAME W-AA-3-1
 EXPNO 3
 PROCNO 1

F1 - Acquisition parameters
 TD 256
 SFO1 500.1328 MHz
 FIDRES 21.490080 Hz
 SW 11.000 ppm
 FnMODE States-TPPI

F2 - Processing parameters
 SI 2048
 SF 500.1300135 MHz
 WDW SINE
 SSB 1
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 2048
 MC2 States-TPPI
 SF 500.1303720 MHz
 WDW GM
 SSB 1
 LB 0 Hz
 GB 0



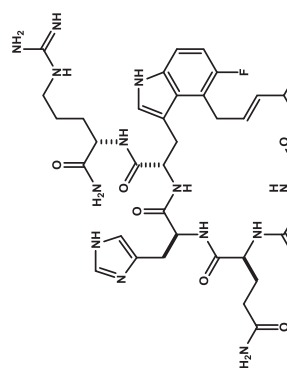


F1 - Acquisition parameters	
TD	256
SF01	500.1325 MHz
FIDRES	19.536406 Hz
SW	10.000 ppm
EnMODE	Echo-Antiecho

F2 - Processing parameters	
SI	2048
SF	500.1300135 MHz
WDW	QSINE
SSB	2
LB	0 Hz
GB	0
PC	1.00

F1 - Processing parameters	
SI	2048
MC2	echo-antiecho
SS	500.1300135 MHz
WDW	TRAP
SSB	2
LB	0 Hz
GB	0



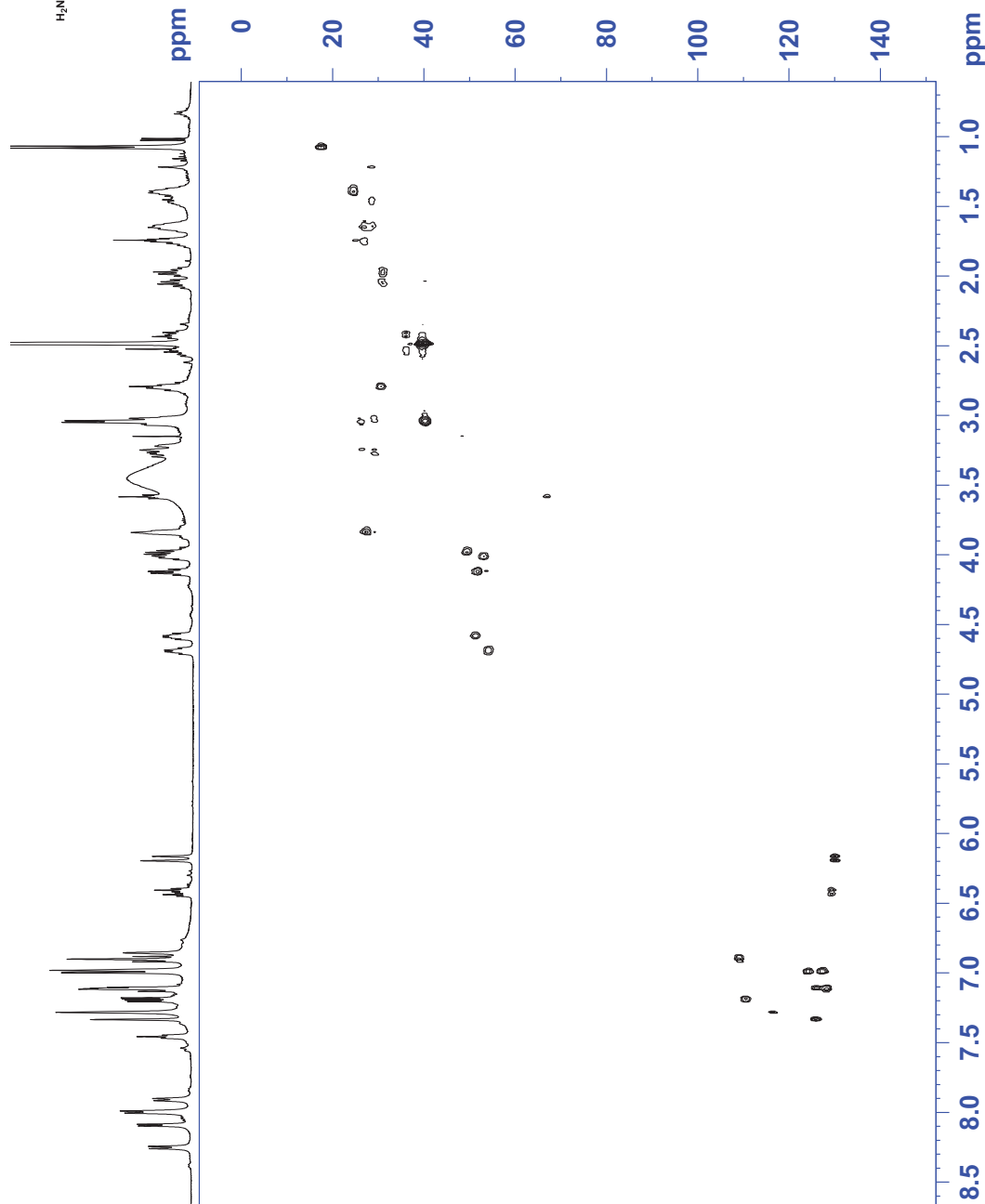


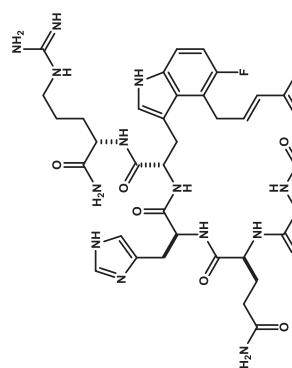
Current Data Parameters
 NAME W-AA-3-1
 EXPNO 5
 PROCNO 1

F1 - Acquisition parameters
 TD 256
 SFO1 125.7678 MHz
 FIDRES 98.255890 Hz
 SW 200.000 ppm
 FnmODE Echo-Antiecho

F2 - Processing parameters
 SI 2048
 SF 500.1300135 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 2048
 MC2 echo-antiecho
 SF 125.7578472 MHz
 WDW TRAP
 SSB 2
 LB 0 Hz
 GB 0



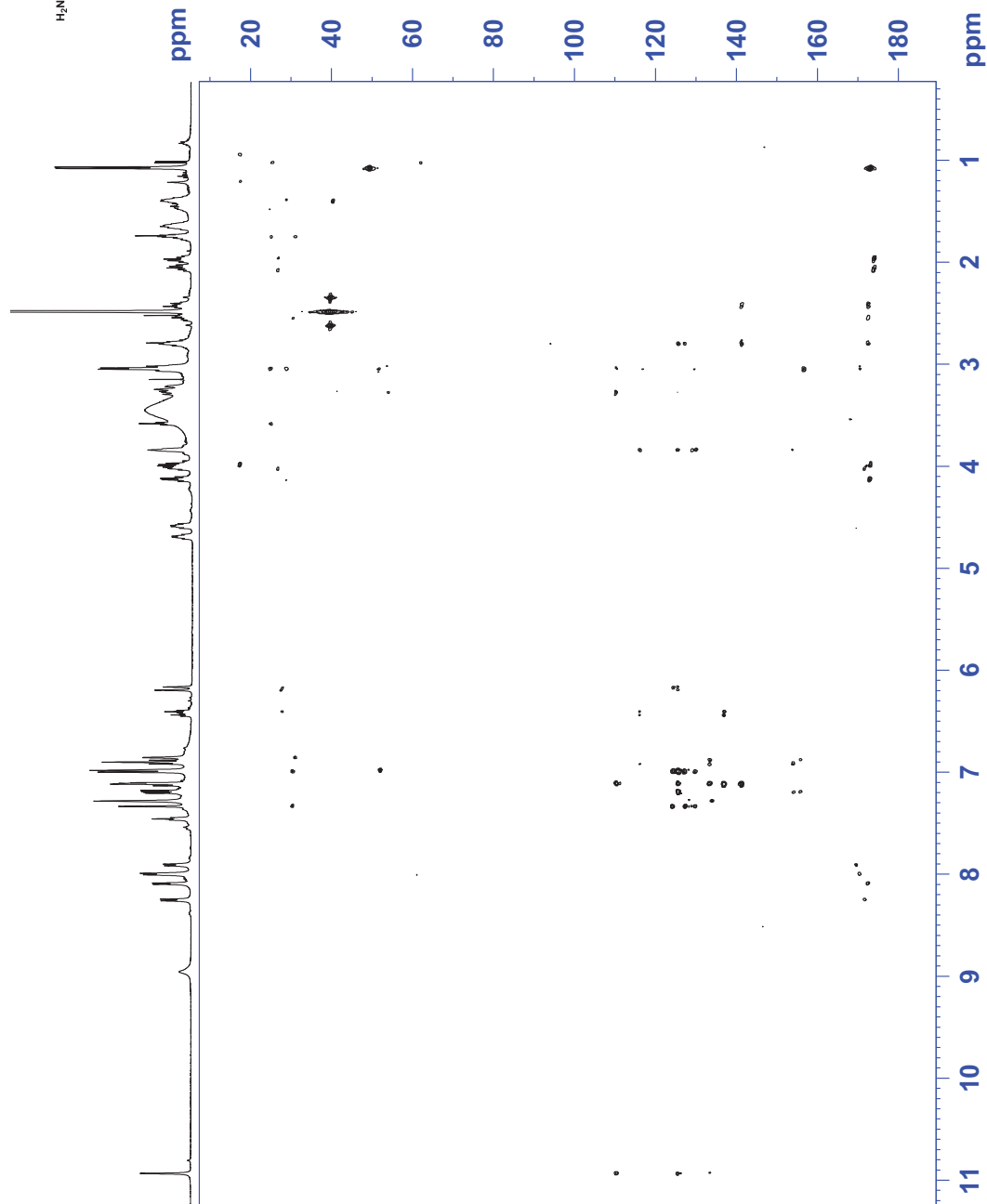


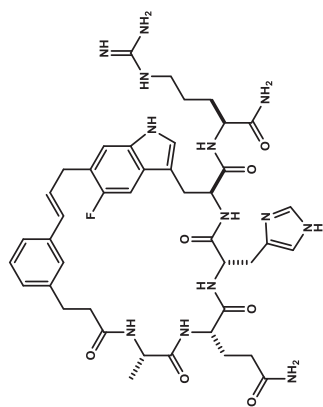
Current Data Parameters
NAME W-AA-3-1
EXPNO 6
PROCNO 1

F1 - Acquisition parameters
TD 256
SF01 125.7704 MHz
FIDRES 98.257607 Hz
SW 199.999 ppm
FnMODE QF

F2 - Processing parameters
SI 2048
SF 500.1300135 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0
PC 1.00

F1 - Processing parameters
SI 2048
MC2 QF
SF 125.7578472 MHz
WDW TRAP
SSB 2
LB 0 Hz
GB 0



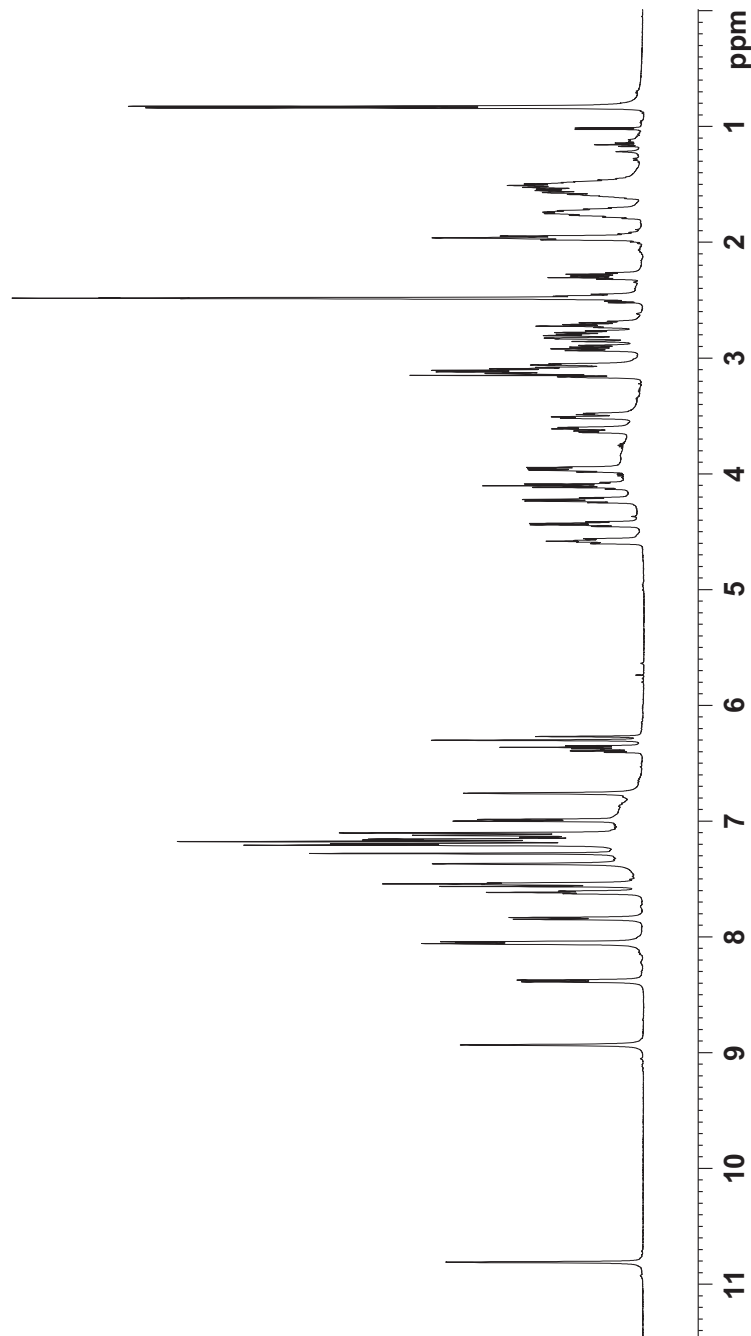


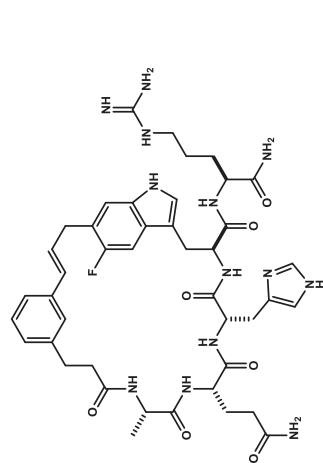
Current Data Parameters
NAME W-A4-4-17(2)
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20121023
Time_ 18.51
INSTRUM av500
PROBHD 5 mm DCH 13C-1
PULPROG zg
TD 65536
SOLVENT DMSO
NS 8
DS 0
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2767999 sec
RG 20.17
DW 50.000 usec
DE 10.00 usec
TE 298.0 K
D1 2.00000000 sec
TD0 1

===== CHANNEL f1 =====
NUC1 1H
P1 10.00 usec
PLW1 13.50000000 W
SFO1 500.1330008 MHz

F2 - Processing parameters
SI 65536
SF 500.1300146 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



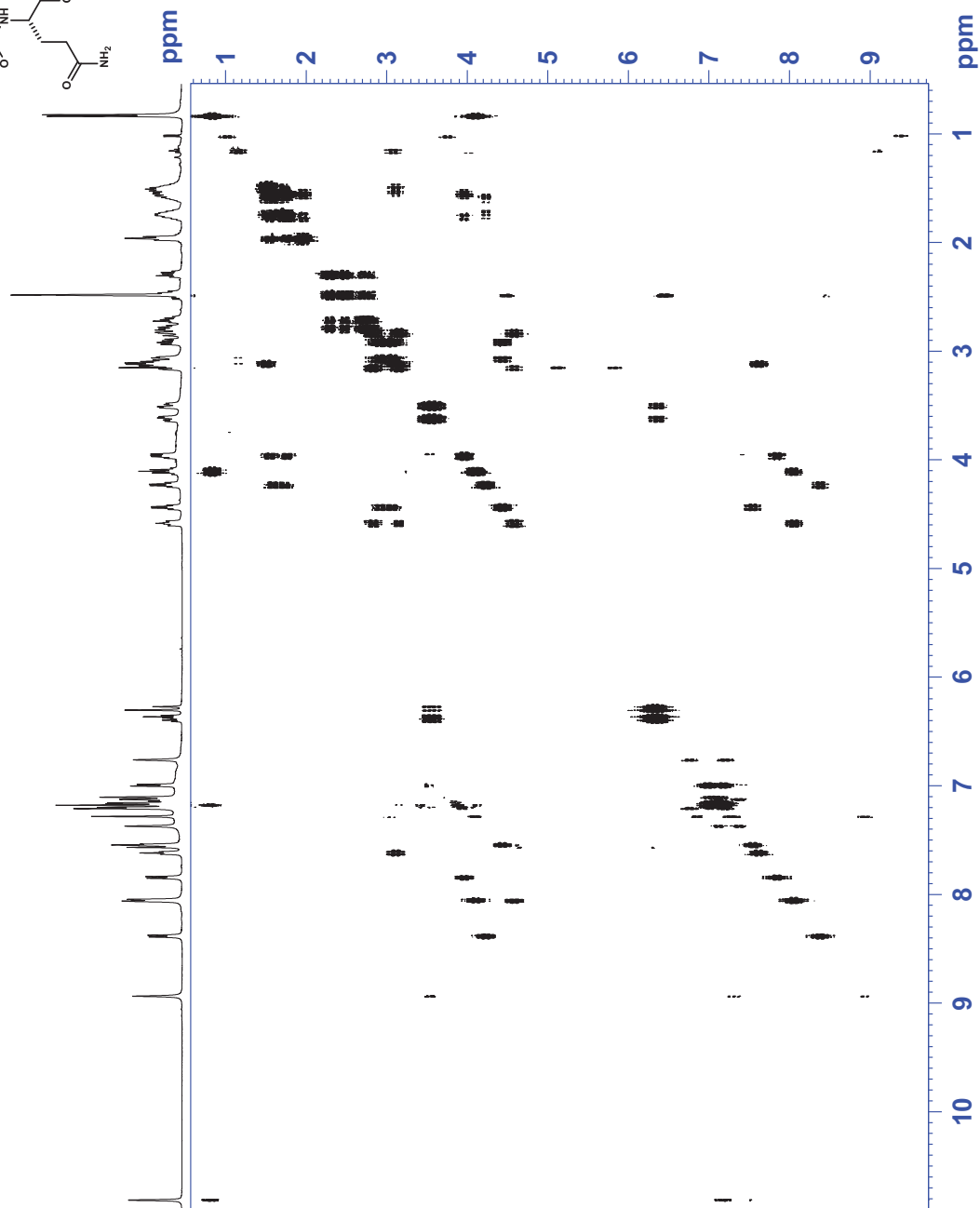


Current Data Parameters
NAME W-A4-4-17 (2)
EXPNO 3
PROCNO 1

F1 - Acquisition parameters
TD 256
SFOL 500.1328 MHz
FIDRES 19.536423 Hz
SW 10.000 ppm
FnMODE States-TPPI

F2 - Processing parameters
SI 2048
SF 500.1300135 MHz
WDW SINE
SSB 1
LB 0 Hz
GB 0
PC 1.00

F1 - Processing parameters
SI 2048
MC2 States-TPPI
SF 500.1300137 MHz
WDW GM
SSB 1
LB 0 Hz
GB 0





Current Data Parameters
NAME W-A4-4-17(2)

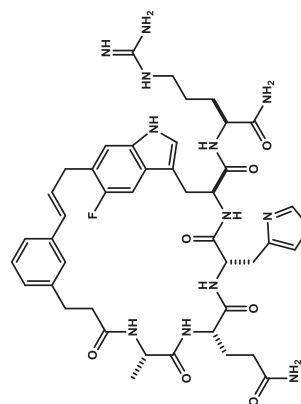
NAME	W	FF	F	1	7	(Z)	4
EXPNO							1
PROCNO							1

F1 - Acquisition parameters	
TD	256
SF01	500.1325 MHz
FIDRES	19.536406 Hz
SW	10.000 ppm
EnMODE	Echo-Antiecho

```
F2 - Processing parameters
SI      2048
SF      500.1300135 MHz
WDW     QSINE
SSB     2
LB      0 Hz
GB      0
PC      1.00
```

F1 - Processing parameters	
SI	2048
MC2	echo-antiecho
SS	500.1300135 MHz
WDW	TRAP
SSB	2
LB	0 Hz
GB	0





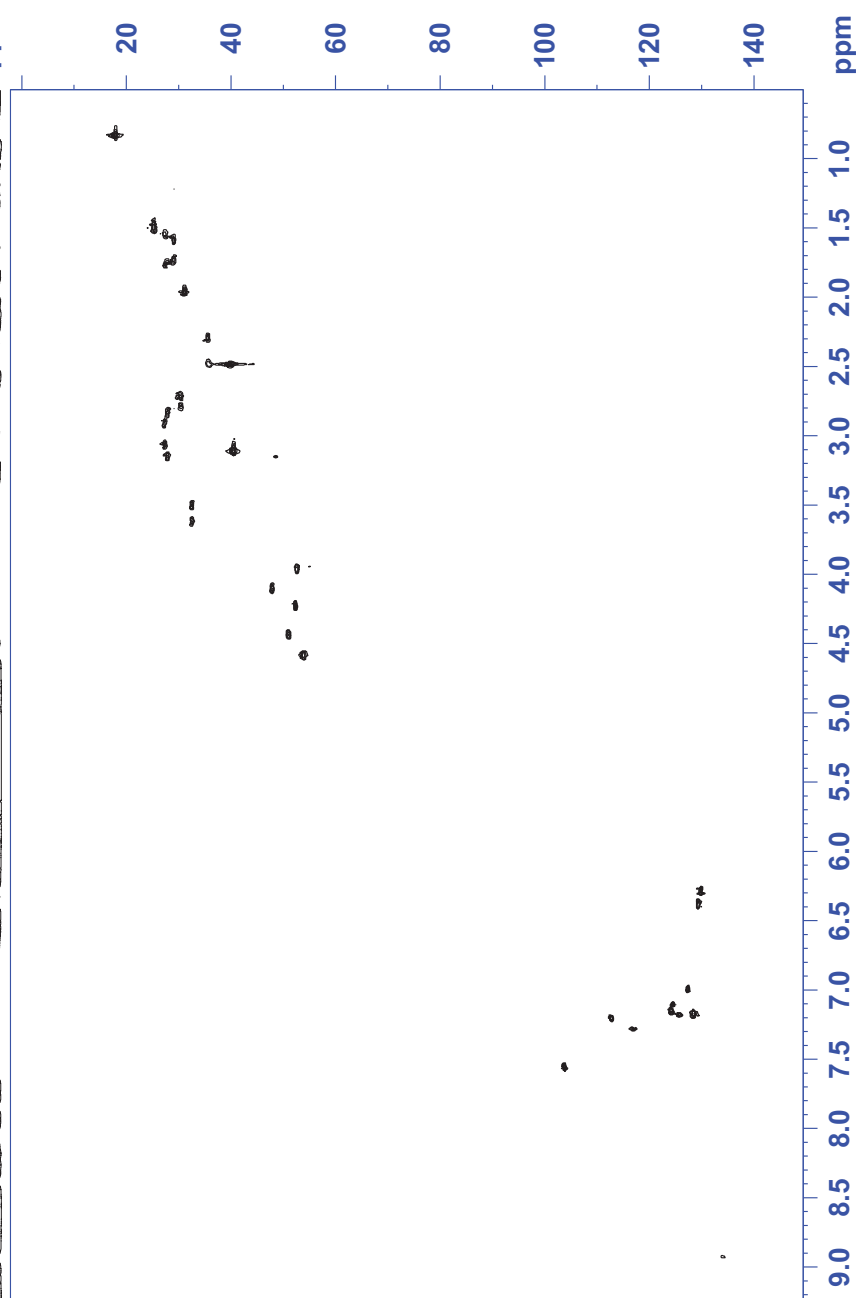
Current Data Parameters
NAME W-A4-4-17 (2)
EXPNO 5
PROCNO 1

F1 - Acquisition parameters
TD 256
SF01 125.7678 MHz
FIDRES 98.255890 Hz
SW 200.000 ppm
FnMODE Echo-Antiecho

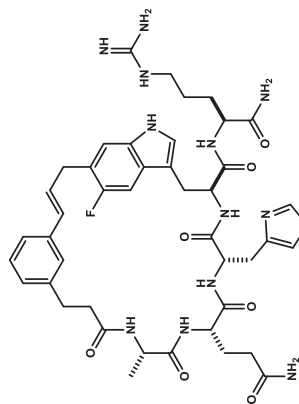
F2 - Processing parameters
SI 2048
SF 500.1300135 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0
PC 1.00

F1 - Processing parameters
SI 2048
MC2 echo-antiecho
SF 125.7578472 MHz
WDW TRAP
SSB 2
LB 0 Hz
GB 0

ppm



ppm

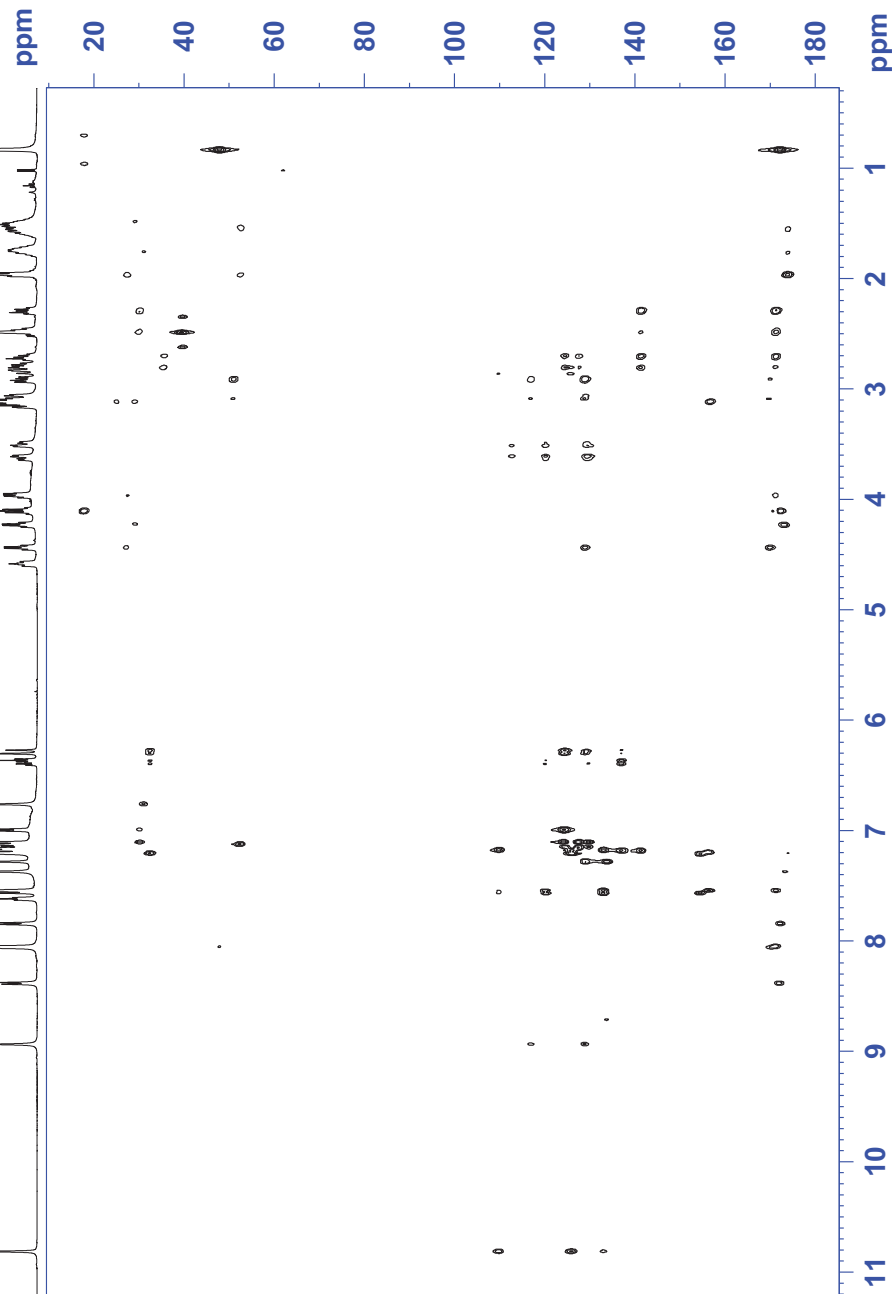


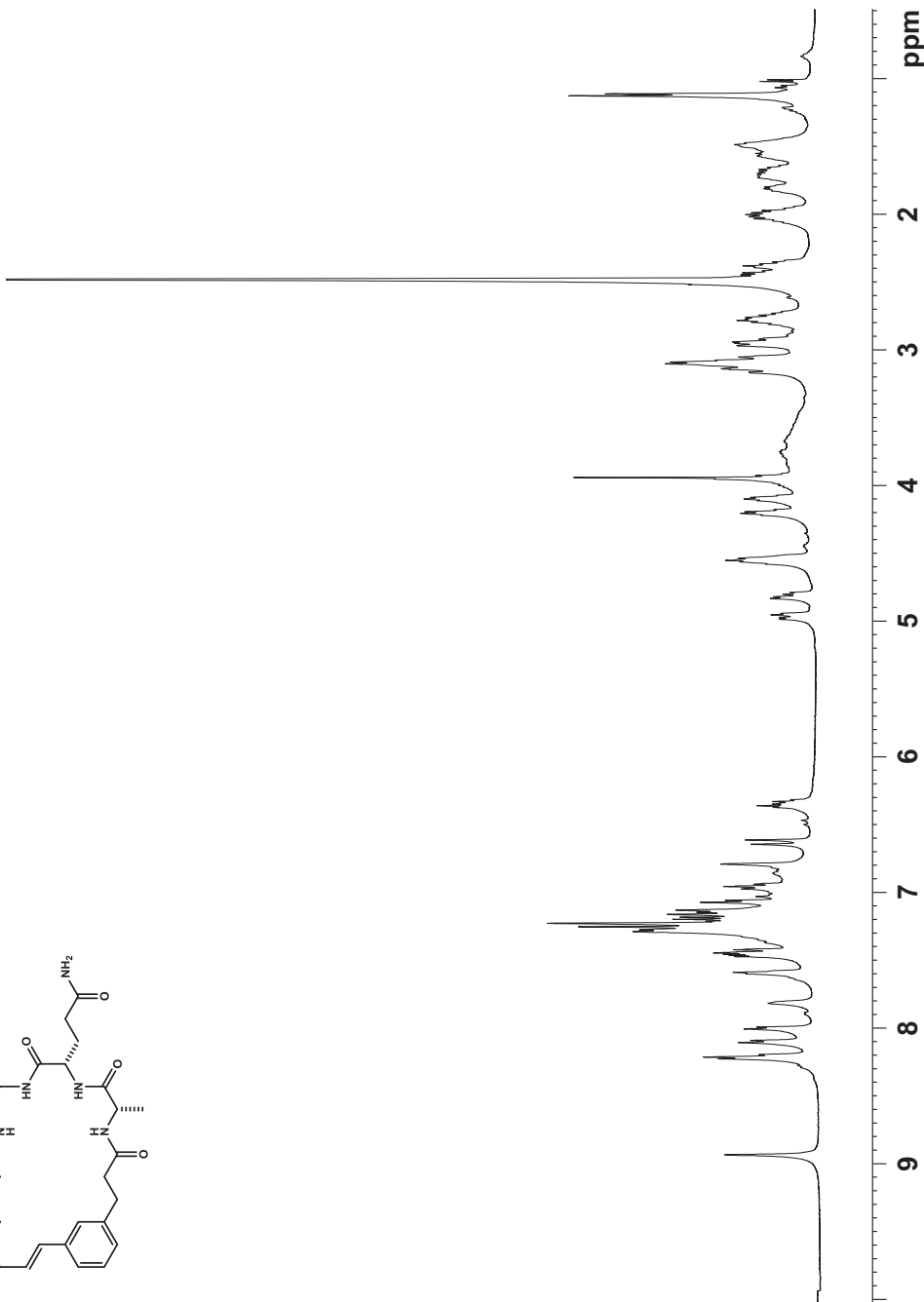
Current Data Parameters
NAME W-A4-4-17 (2)
EXPNO 6
PROCNO 1

F1 - Acquisition parameters
TD 256
SF01 125.7704 MHz
FIDRES 98.257607 Hz
SW 199.999 ppm
FnMODE QF

F2 - Processing parameters
SI 2048
SF 500.1300135 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0
PC 1.00

F1 - Processing parameters
SI 2048
MC2 QF
SF 125.7578472 MHz
WDW USER
SSB 2
LB 0 Hz
GB 0





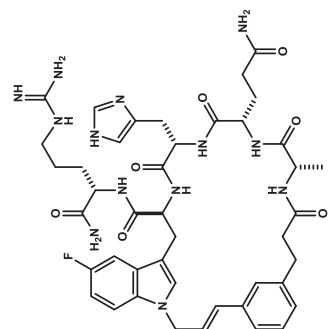
Current Data Parameters	
NAME	W-A4-5-1
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

F2 Acquisition Parameters	
Date	20121027
Time	17.23
INSTRUM	av500
PROBHD	5 mm DCH 13C-1
PULPROG	zg
TD	65536
SOLVENT	DMSO
NS	8
DS	0
SWH	100.000 MHz
FTIDFS	0.132588 Hz
AQ	3.2767999 sec
RG	7
DW	50.000 usec
DE	10.000 usec
TE	298.0 K
D1	2.00000000 sec
TD0	1

```
===== CHANNEL f1 =====
NUC1      1H
P1         10.00 usec
PLW1      13.50000000 W
SFO1      500.1330008 MHz
```

F2 - Processing parameters	
SI	65536
SF	500.1300146 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

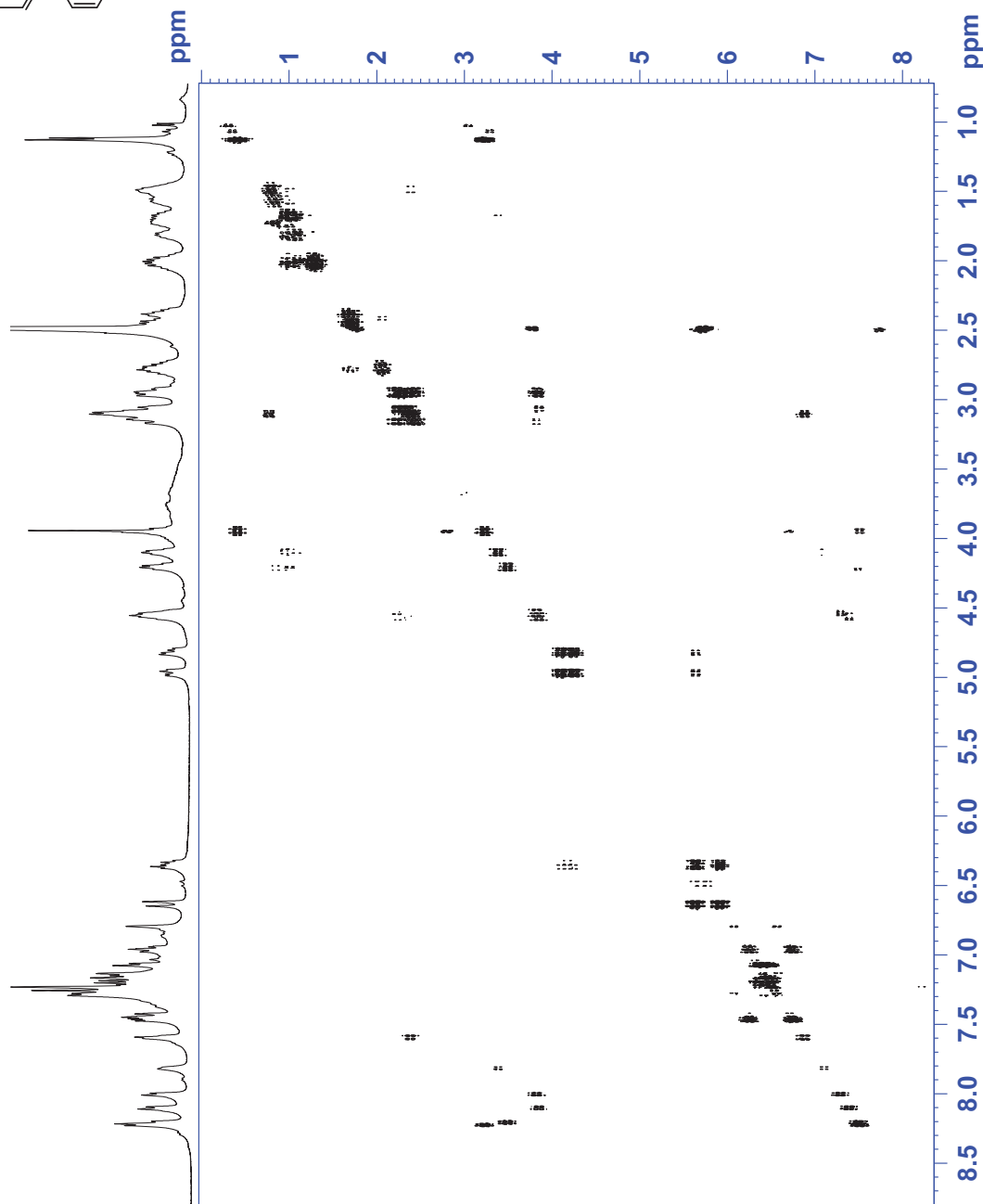


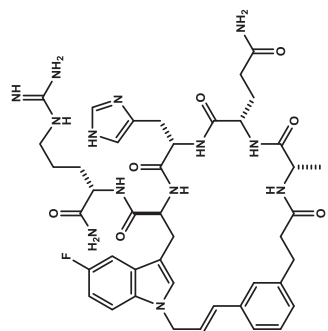
Current Data Parameters
 NAME W-AA-5-1
 EXPNO 3
 PROCNO 1

F1 - Acquisition parameters
 TD 256
 SFO1 500.1328 MHz
 FIDRES 19.536423 Hz
 SW 10.000 ppm
 FnMODE States-TPPI

F2 - Processing parameters
 SI 2048
 SF 500.1300135 MHz
 WDW SINE
 SSB 1
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 2048
 MC2 States-TPPI
 SF 500.1303720 MHz
 WDW GM
 SSB 1
 LB 0 Hz
 GB 0



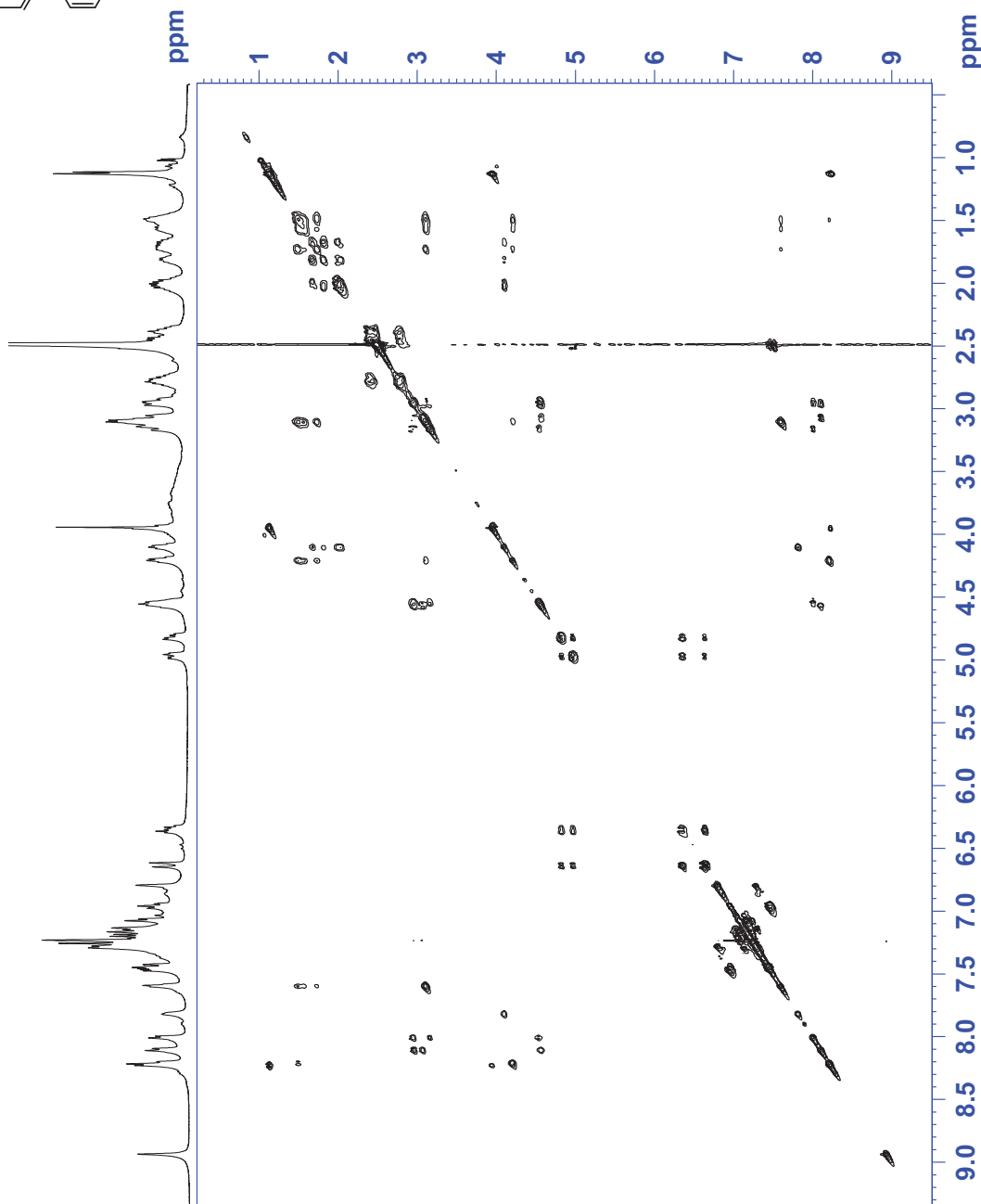


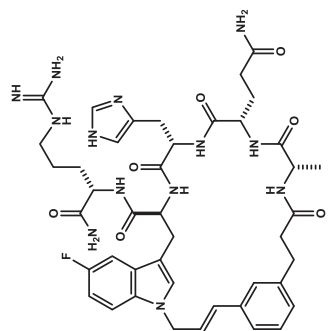
Current Data Parameters
 NAME W-AA-5-1
 EXPNO 4
 PROCNO 1

F1 - Acquisition parameters
 TD 256
 SFO1 500.1325 MHz
 FIDRES 19.536406 Hz
 SW 10.000 ppm
 FnmODE Echo-Antiecho

F2 - Processing parameters
 SI 2048
 SF 500.1300135 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 2048
 MC2 echo-antiecho
 SF 500.1300135 MHz
 WDW TRAP
 SSB 2
 LB 0 Hz
 GB 0



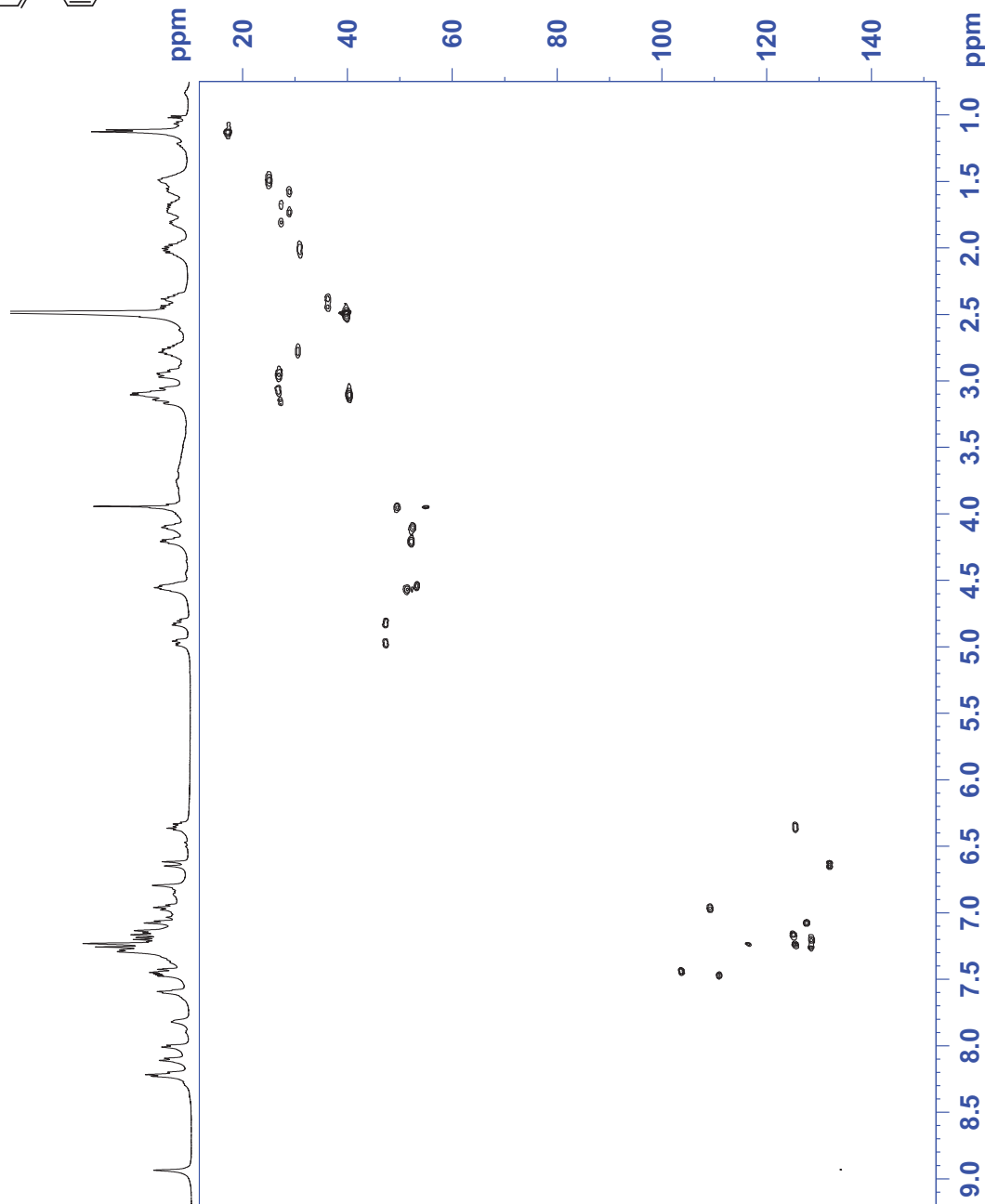


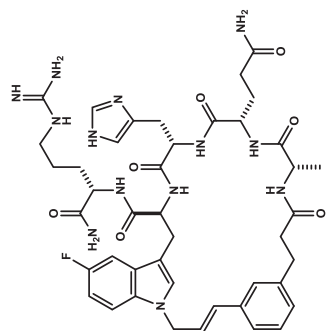
Current Data Parameters
 NAME W-A4-5-1
 EXPNO 5
 PROCNO 1

F1 - Acquisition parameters
 TD 256
 SF01 125.7678 MHz
 FIDRES 98.255890 Hz
 SW 200.000 ppm
 FnmODE Echo-Antiecho

F2 - Processing parameters
 SI 2048
 SF 500.1300135 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 2048
 MC2 echo-antiecho
 SF 125.7578472 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0



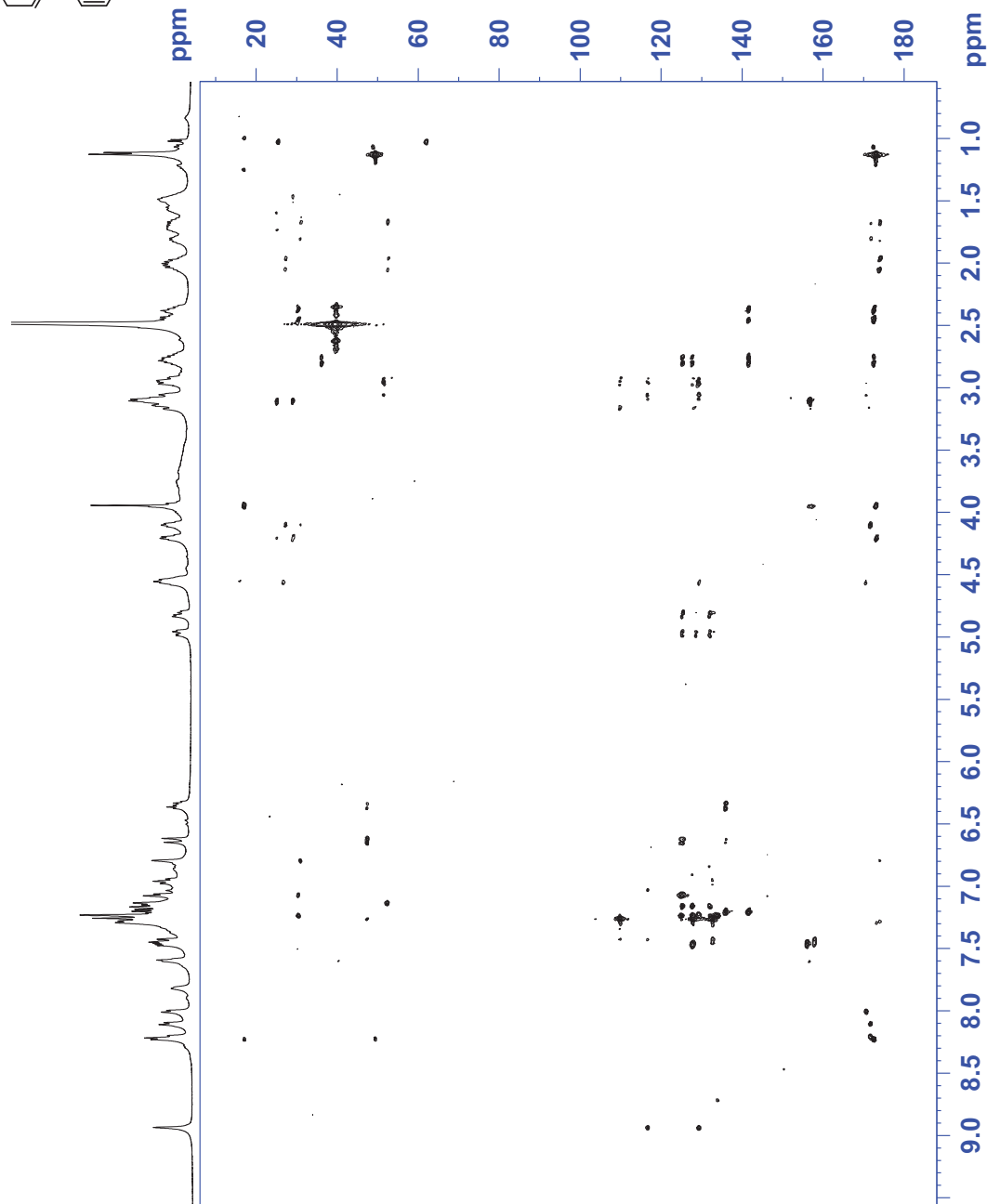


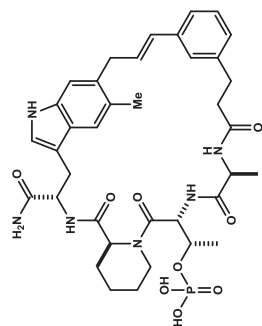
Current Data Parameters
 NAME W-A4-5-1
 EXPNO 6
 PROCNO 1

F1 - Acquisition parameters
 TD 256
 SFOL 125.7704 MHz
 FIDRES 98.257607 Hz
 SW 199.999 ppm
 FnmODE QF

F2 - Processing parameters
 SI 2048
 SF 500.1300135 MHz
 WDW QF
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 2048
 MC2 QF
 SF 125.7578472 MHz
 WDW QF
 SSB 2
 LB 0 Hz
 GB 0



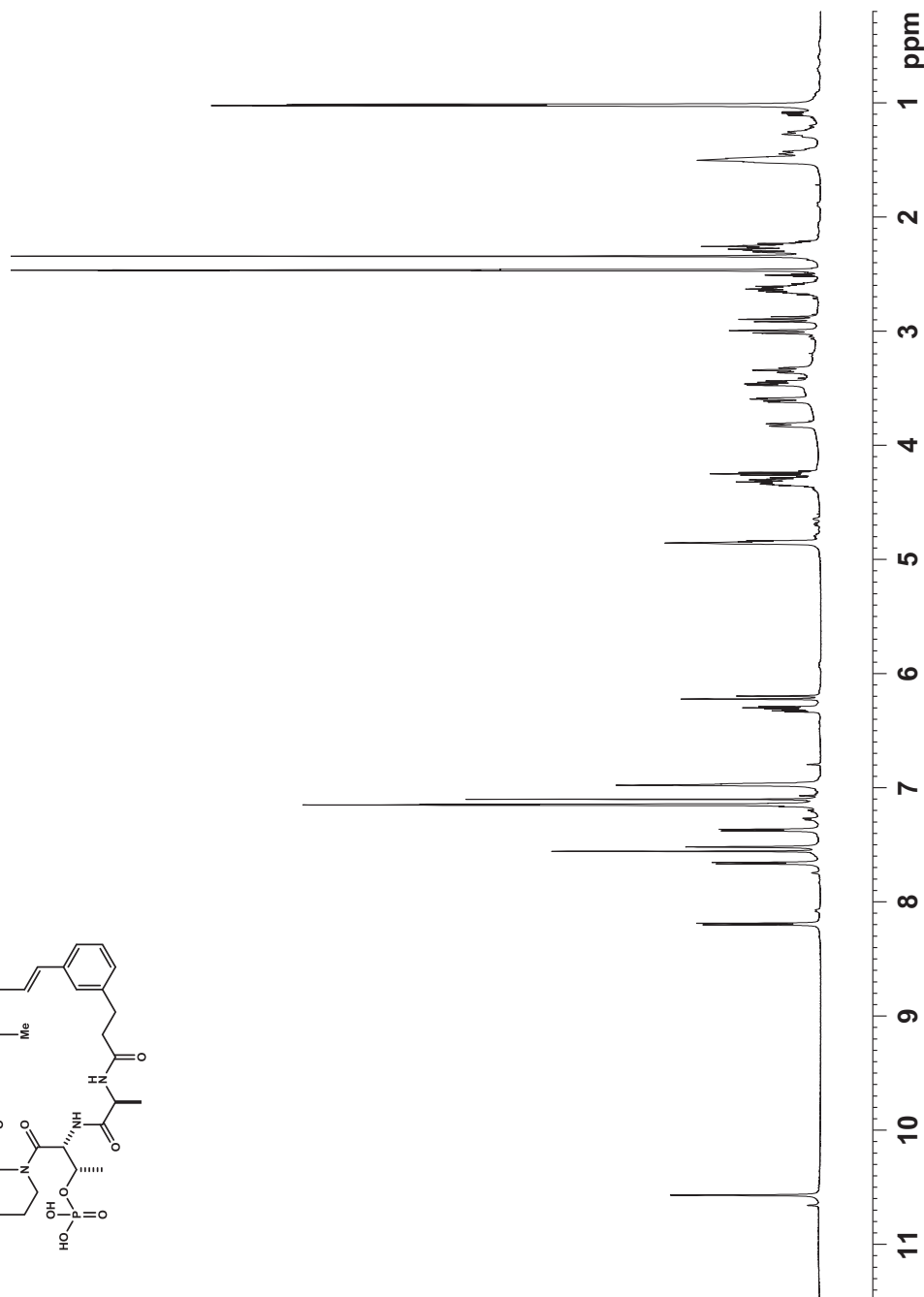


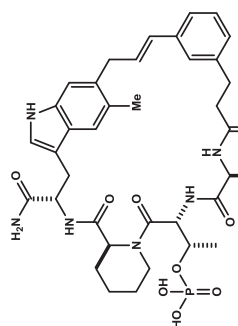
Current Data Parameters
 NAME KL-5-225-1m-1
 EXPNO 2
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20131013
 Time_ 17.07
 INSTRUM av600
 PROBHD 5 mm TBI5
 PULPROG zg
 TD 65536
 SOLVENT DMSO
 NS 8
 DS 0
 SMH 12376.237 Hz
 FIDRES 0.188846 Hz
 AQ 2.6476543 sec
 RG 574.7
 DW 40.400 usec
 DE 6.50 usec
 TE 294.6 K
 D1 2.00000000 sec
 TD0 1

===== CHANNEL f1 =====
 NUC1 1H
 P1 9.50 usec
 PL1 -2.00 dB
 PL1W 39.81071854 W
 SFO1 600.1336008 MHz

F2 - Processing parameters
 SI 65536
 SF 600.1300273 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00



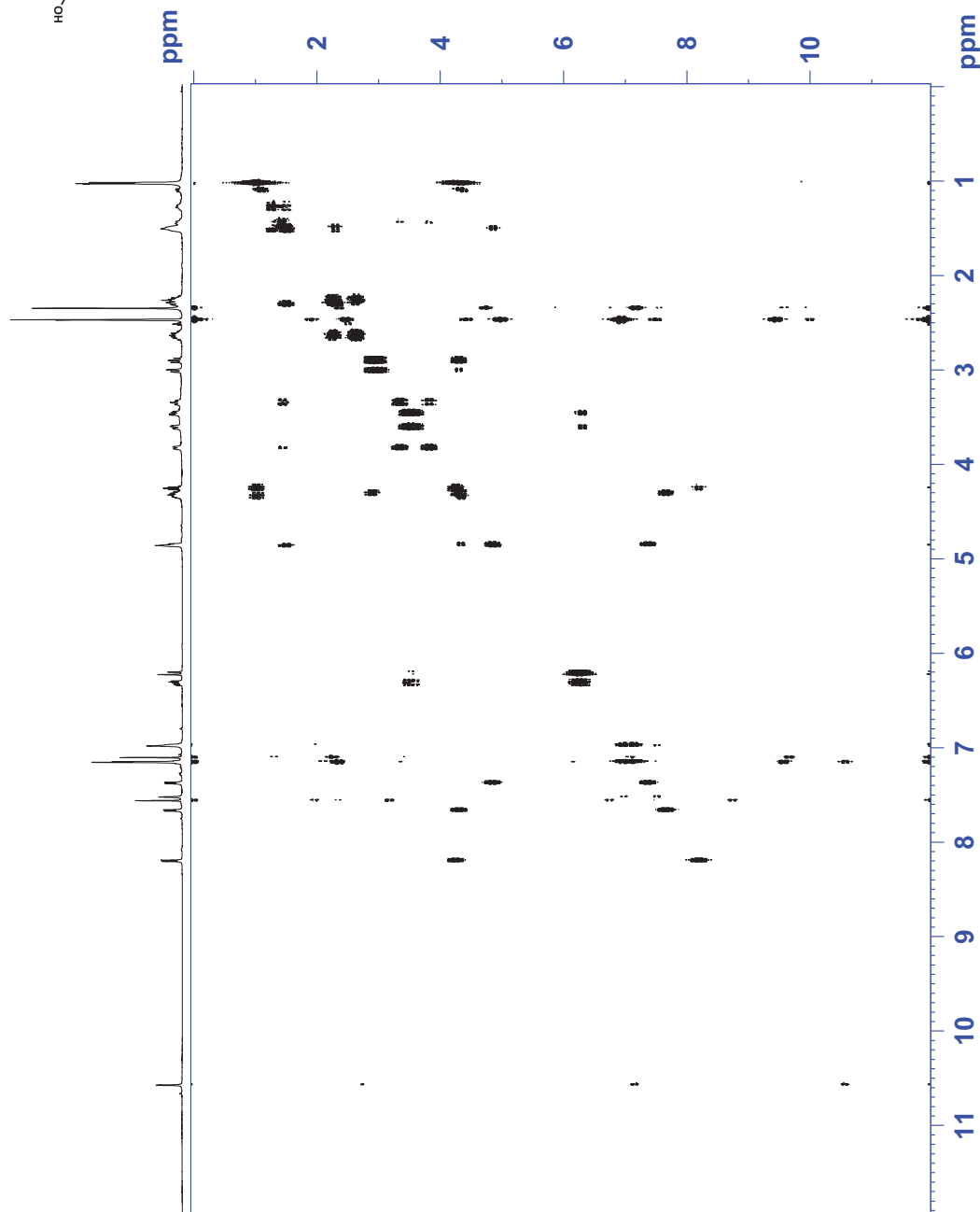


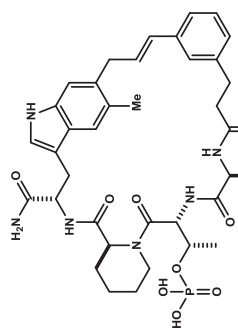
Current Data Parameters
 NAME KL-5-225-1m-1
 EXPNO 4
 PROCNO 1

F1 - Acquisition parameters
 TD 256
 SFO1 600.1336 MHz
 FIDRES 28.131262 Hz
 SW 12.000 ppm
 FnmODE States-TPPI

F2 - Processing parameters
 SI 2048
 SF 600.1300273 MHz
 WDW SINE
 SSB 1
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 2048
 MC2 States-TPPI
 SF 600.1300273 MHz
 WDW QSINE
 SSB 1
 LB 0 Hz
 GB 0



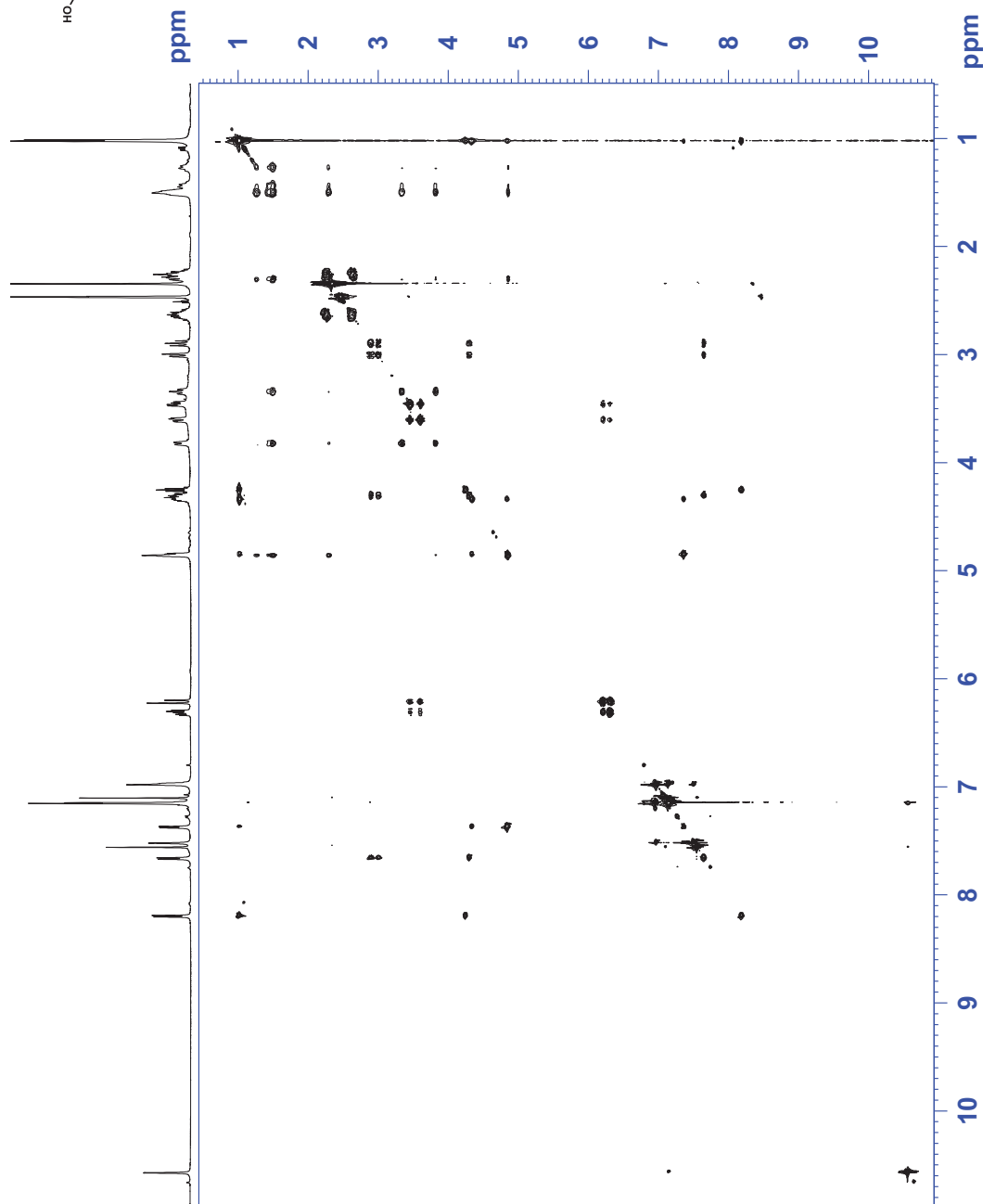


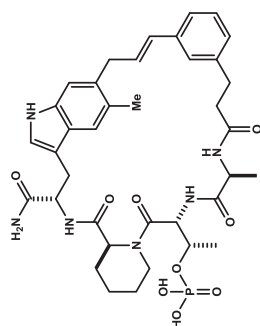
Current Data Parameters
 NAME KL-5-225-1m-1
 EXPNO 3
 PROCNO 1

F1 - Acquisition parameters
 TD 600
 SFO1 600.1336 MHz
 FIDRES 12.002672 Hz
 SW 12.000 ppm
 FnMODE Echo-Antiecho

F2 - Processing parameters
 SI 1024
 SF 600.1300273 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 1024
 MC2 echo-antiecho
 SF 600.1300273 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0



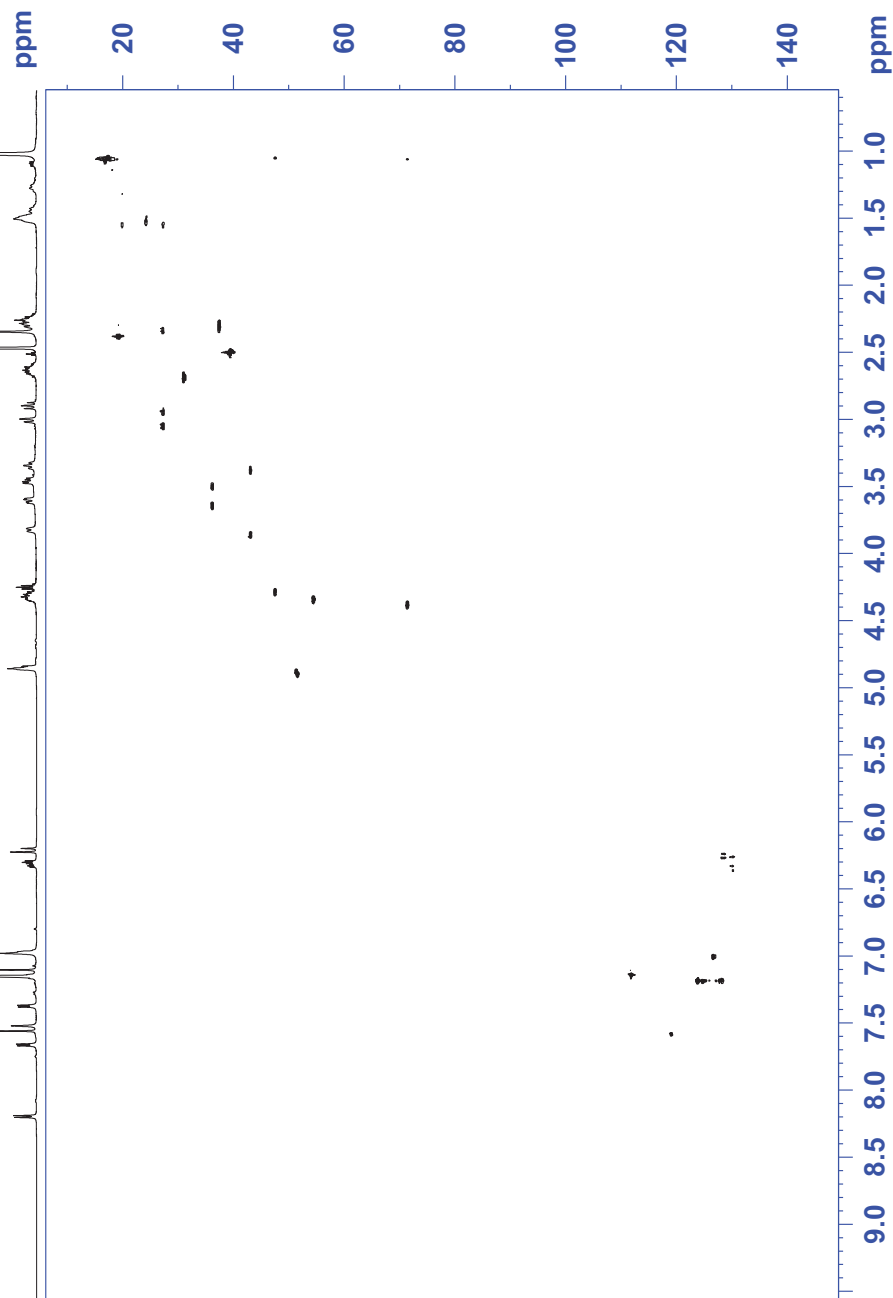


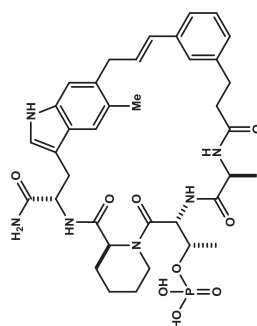
Current Data Parameters
 NAME KL-S-225-1m-1
 EXPNO 5
 PROCNO 1

F1 - Acquisition parameters
 TD 512
 SF01 150.9134 MHz
 FIDRES 47.160427 Hz
 SW 160.000 ppm
 FnMODE Echo-Antiecho

F2 - Processing parameters
 SI 4096
 SF 600.1300051 MHz
 EM
 WDW 0
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

F1 - Processing parameters
 SI 4096
 MC2 echo-antiecho
 SF 150.9029231 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0



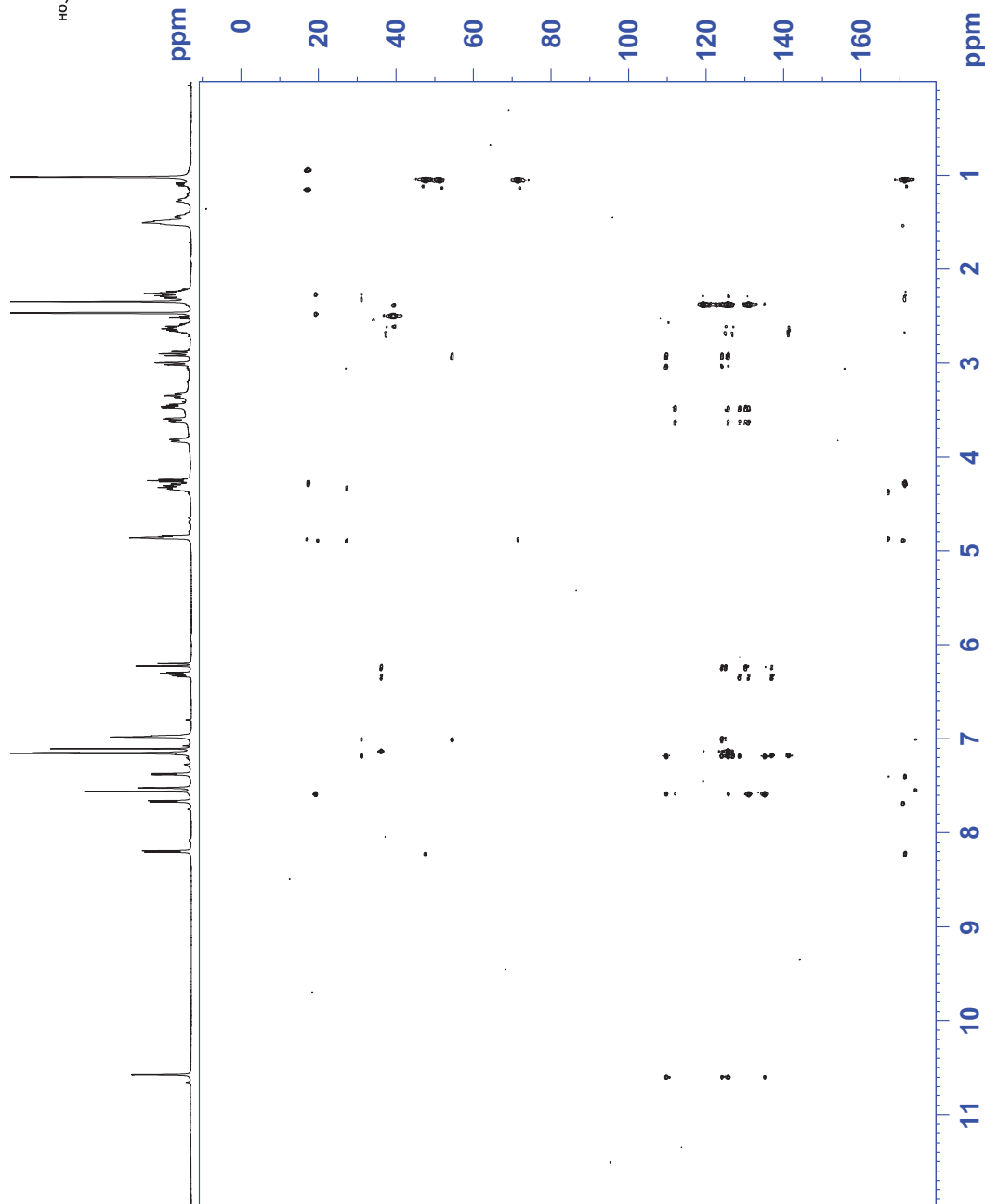


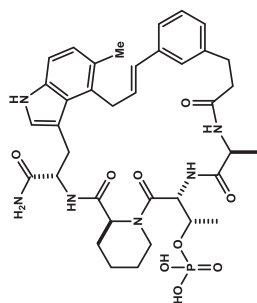
Current Data Parameters
 NAME KL-5-225-1m-1
 EXPNO 6
 PROCNO 1

F1 - Acquisition parameters
 TD 512
 SF01 150.9156 MHz
 FIDRES 56.003849 Hz
 SW 190.000 ppm
 FnmODE QF

F2 - Processing parameters
 SI 4096
 SF 600.1300066 MHz
 WDW QSINE
 SSB 0
 LB 0 Hz
 GB 0
 PC 1.40

F1 - Processing parameters
 SI 4096
 MC2 QF
 SF 150.9029181 MHz
 WDW QSINE
 SSB 3
 LB 0 Hz
 GB 0





```

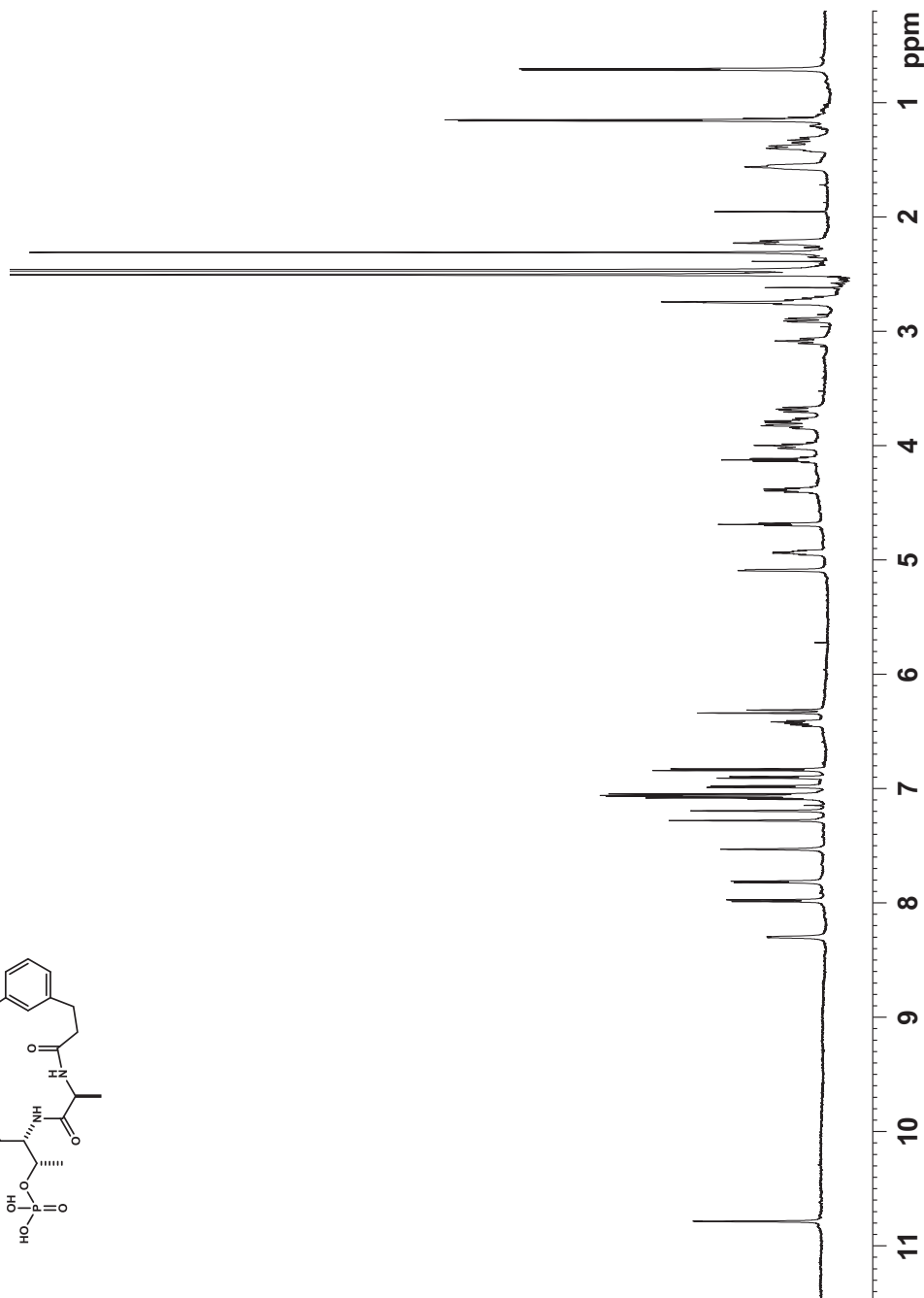
Current Data Parameters
NAME      KL-5-225-3-1
EXPNO     2
PROCNO    1

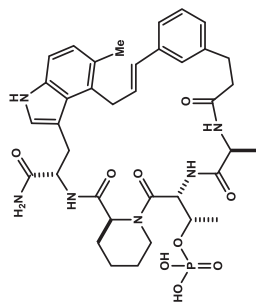
F2 - Acquisition Parameters
Date_     20131029
Time      20.40
INSTRUM   av600
PROBHD    5 mm TBI5
PULPROG   zg
TD         65536
SOLVENT   DMSO
NS         1
DS         0
SWH        12376.237 Hz
FIDRES     0.188846 Hz
AQ         2.6476543 sec
RG         812.7
DW         40.400 usec
DE         6.50 usec
TE         295.0 K
D1         2.00000000 sec
TD0        1

===== CHANNEL f1 =====
NUC1       1H
P1         9.75 usec
PL1        -2.00 dB
PL1W       39.81071854 W
SFO1       600.1336008 MHz

F2 - Processing parameters
SI         65536
SF         600.1300273 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00

```



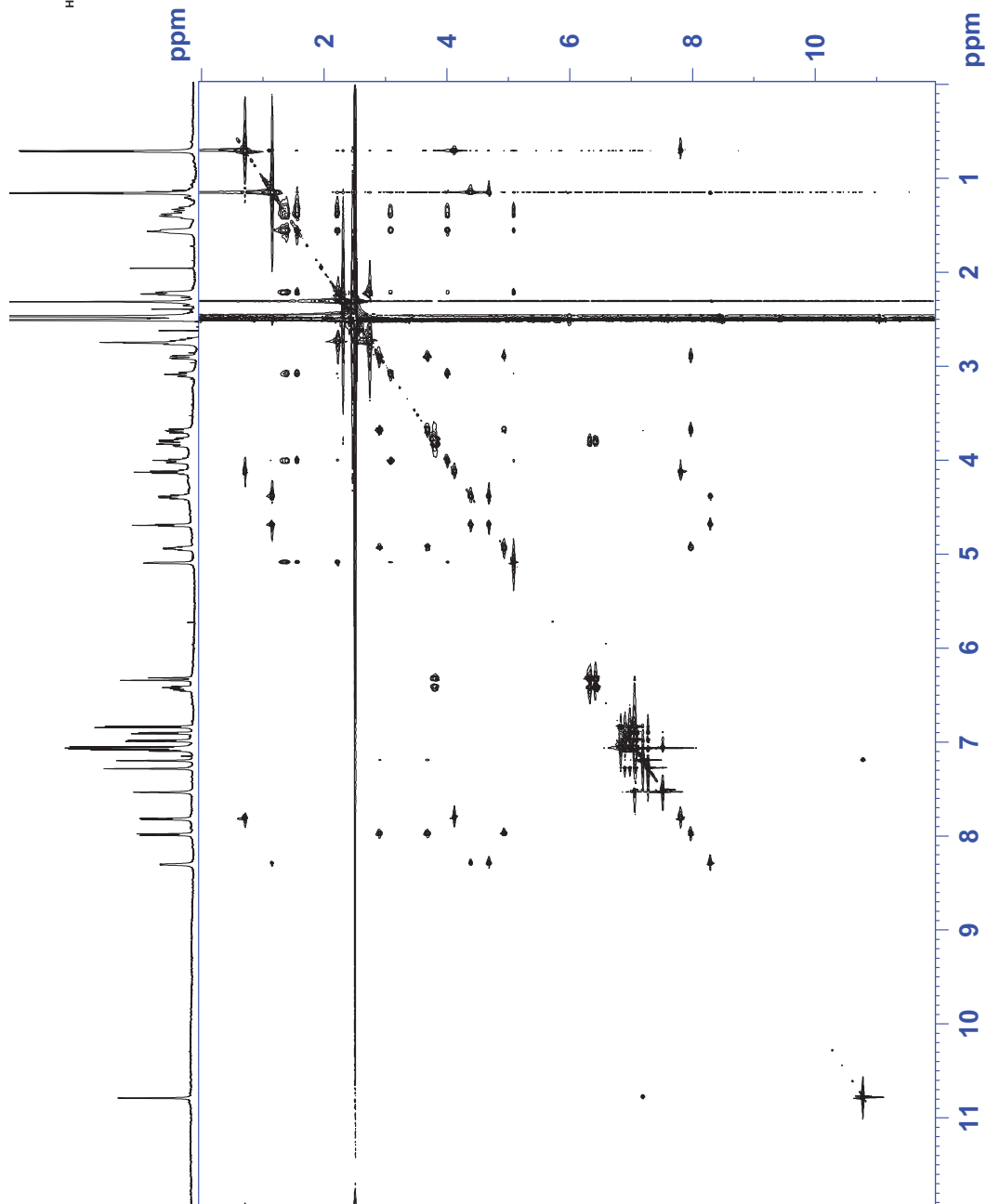


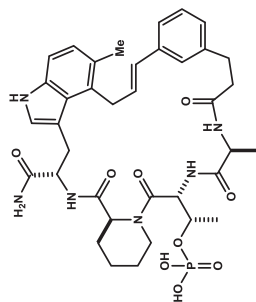
Current Data Parameters
 NAME KL-5-225-3-1
 EXPNO 3
 PROCNO 1

F1 - Acquisition parameters
 TD 600
 SF01 600.1336 MHz
 FIDRES 12.002672 Hz
 SW 12.000 ppm
 FnmODE Echo-Antiecho

F2 - Processing parameters
 SI 1024
 SF 600.1300273 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 1024
 MC2 echo-antiecho
 SF 600.1300273 MHz
 WDW TRAP
 SSB 2
 LB 0 Hz
 GB 0



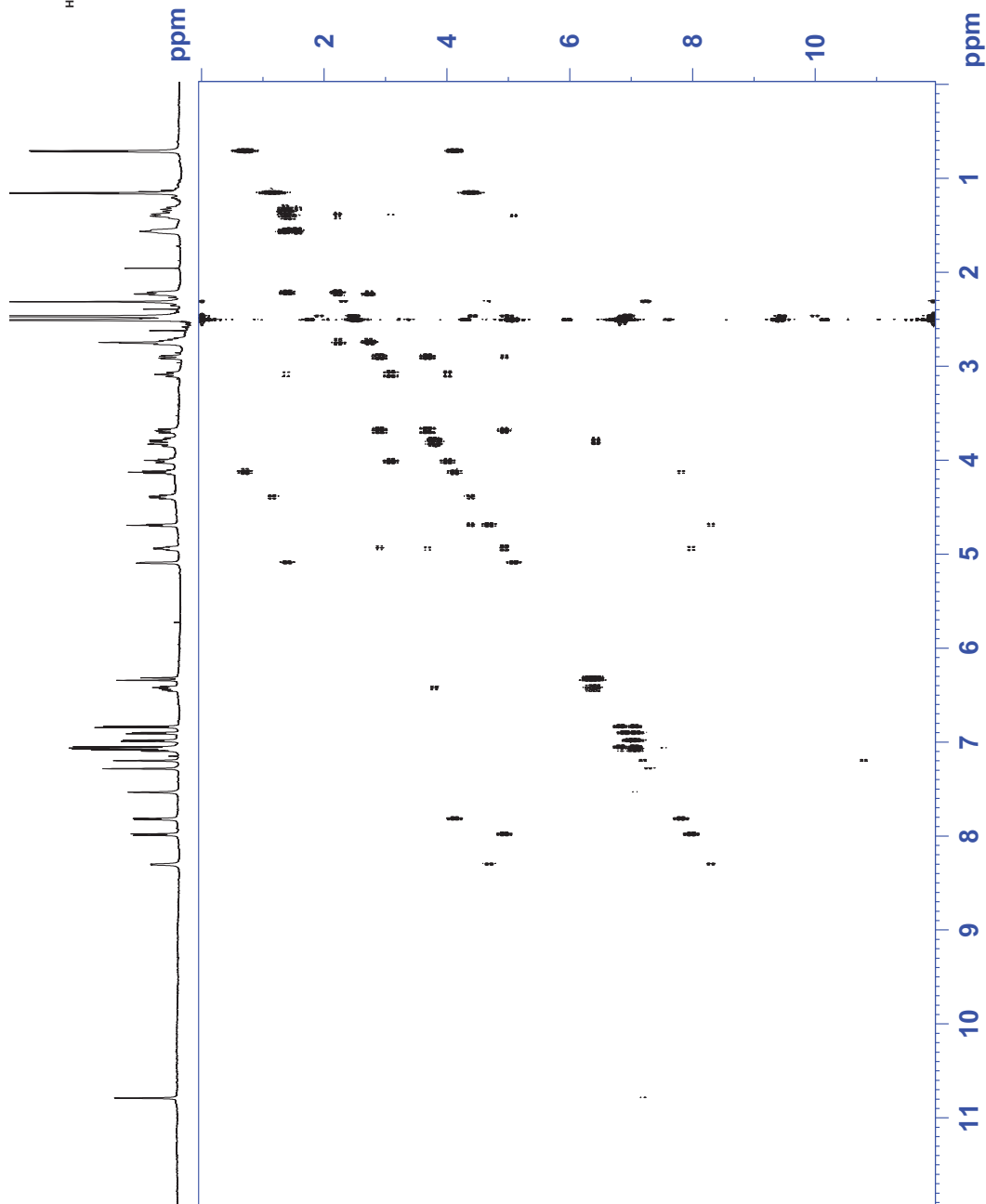


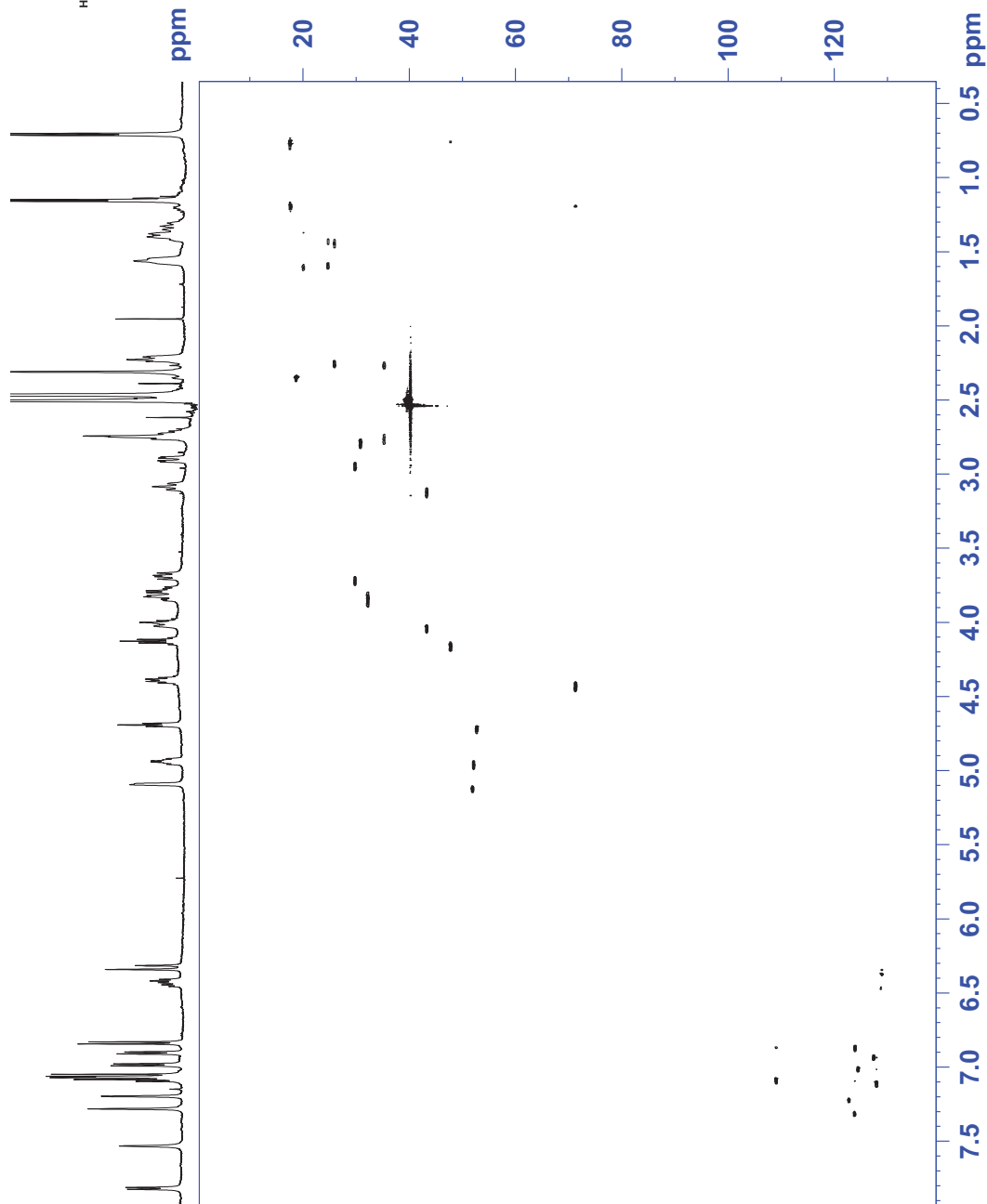
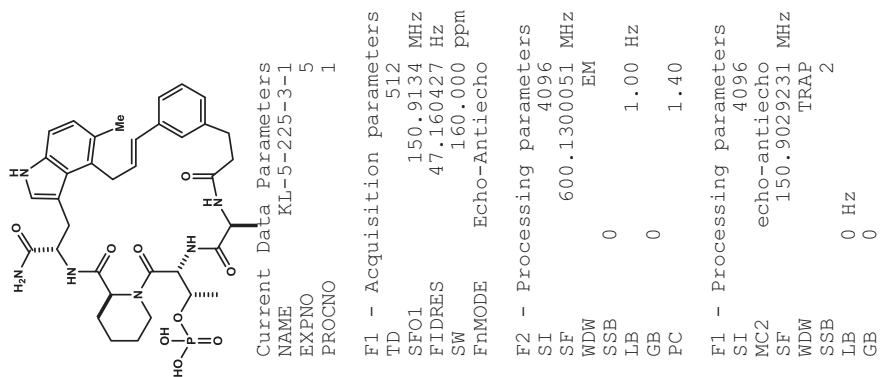
Current Data Parameters
 NAME KL-5-225-3-1
 EXPNO 4
 PROCNO 1

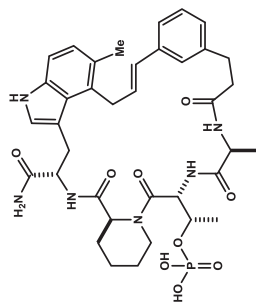
F1 - Acquisition parameters
 TD 256
 SF01 600.1336 MHz
 FIDRES 28.131262 Hz
 SW 12.000 ppm
 FnmODE States-TPPI

F2 - Processing parameters
 SI 2048
 SF 600.1300273 MHz
 SINE
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 2048
 MC2 States-TPPI
 SF 600.1300273 MHz
 WDW QSINE
 SSB 1
 LB 0 Hz
 GB 0





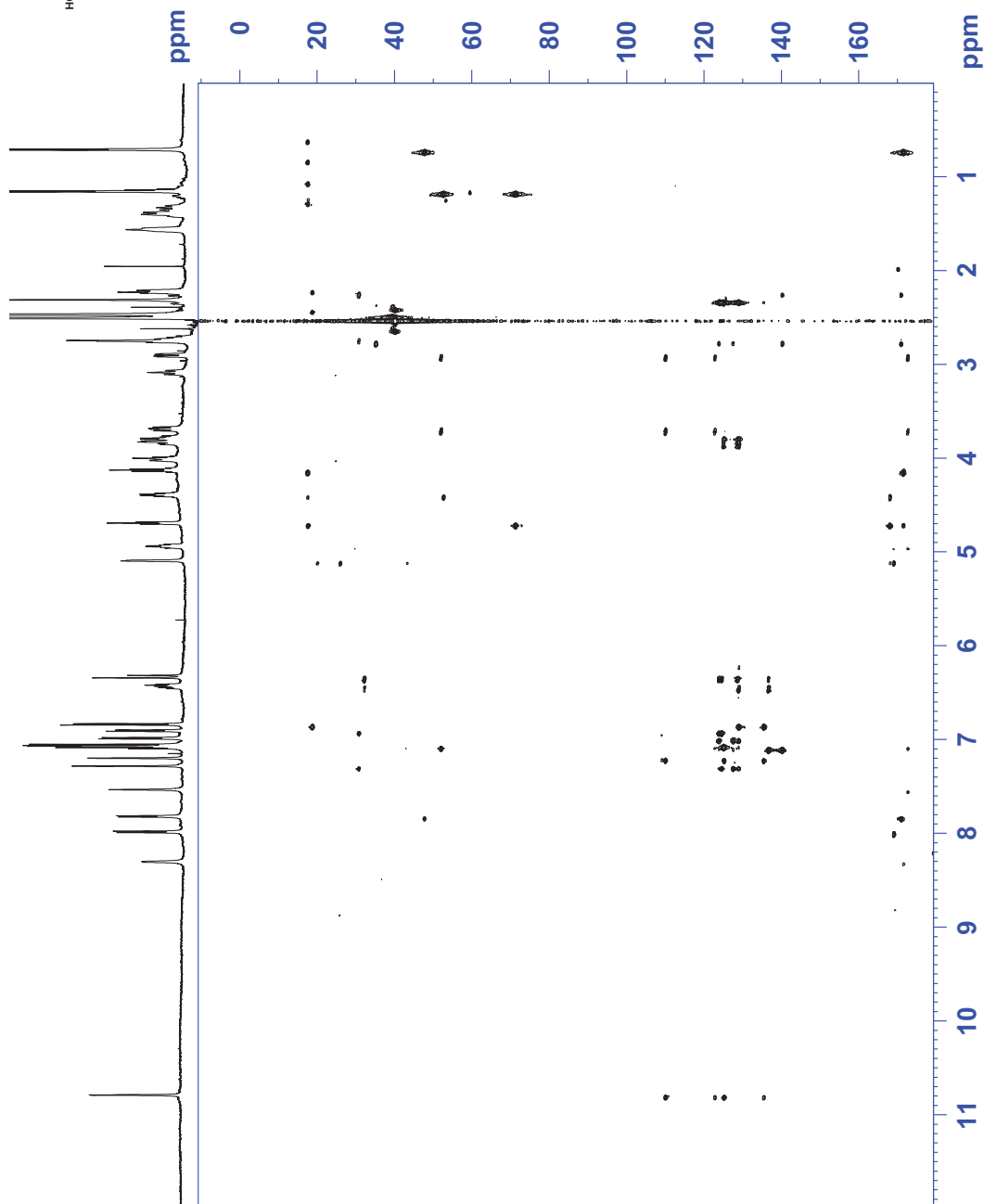


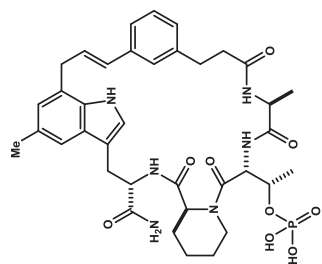
Current Data Parameters
 NAME KL-5-225-3-1
 EXPNO 6
 PROCNO 1

F1 - Acquisition parameters
 TD 512
 SFO1 150.9156 MHz
 FIDRES 56.003849 Hz
 SW 190.000 ppm
 FwMODE QF

F2 - Processing parameters
 SI 4096
 SF 600.1300066 MHz
 WDW QSINE
 SSB 0
 LB 0 Hz
 GB 0
 PC 1.40

F1 - Processing parameters
 SI 4096
 MC2 QF
 SF 150.9029181 MHz
 WDW TRAP
 SSB 3
 LB 0 Hz
 GB 0





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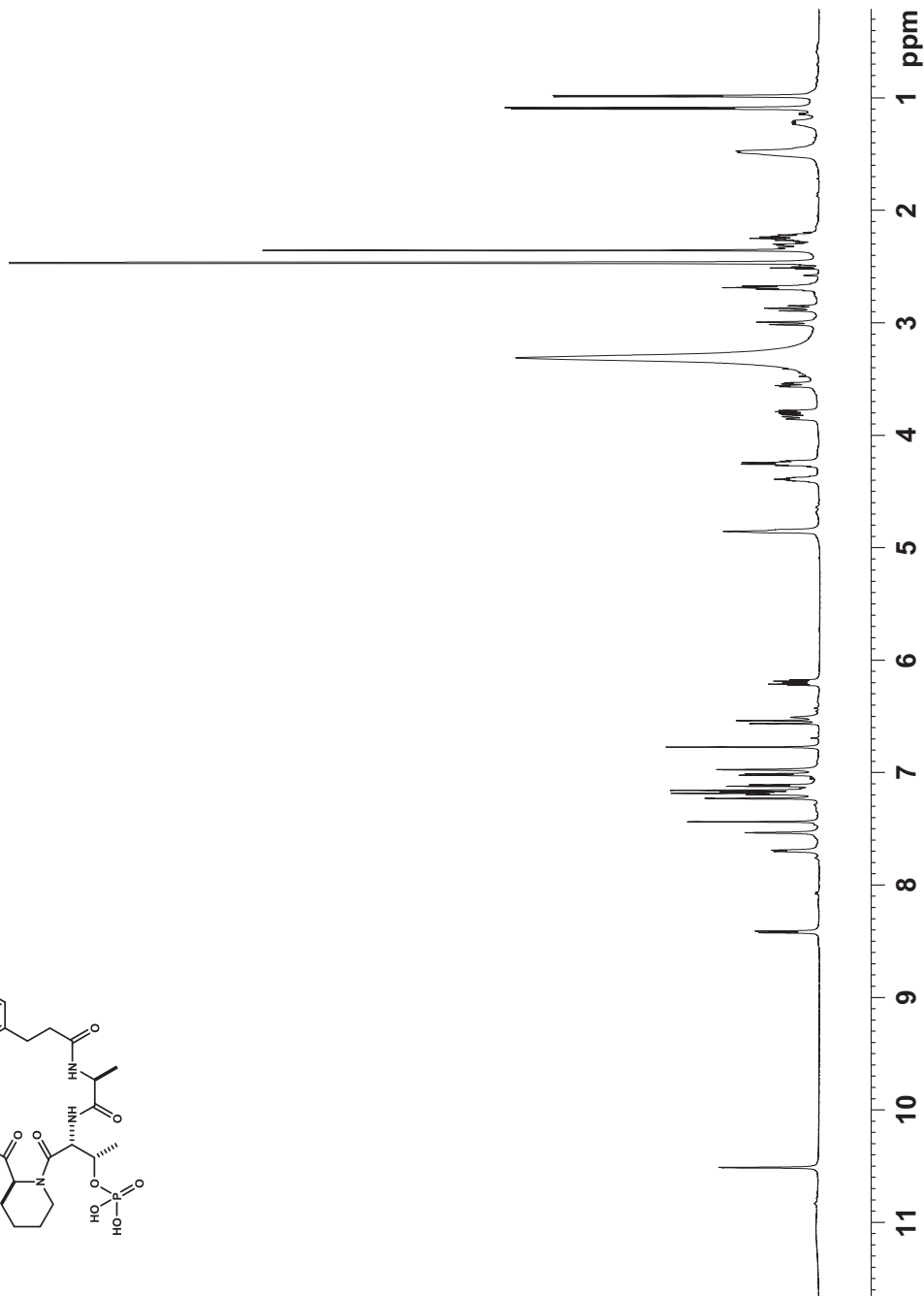
Current Data Parameters
NAME      KI-5-225-4-1
EXPNO     2
PROCNO    1

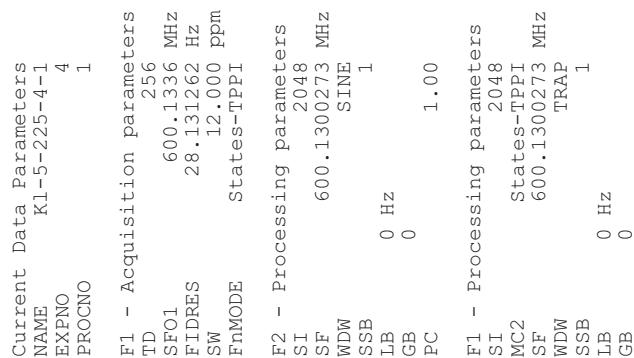
F2 - Acquisition Parameters
Date_     20131014
Time      18.31
INSTRUM   av600
PROBHD    5 mm TBI5
PULPROG   zg
TD         65536
SOLVENT   DMSO
NS         64
DS         0
SWH        12376.237 Hz
FIDRES     0.188846 Hz
AQ         2.6476543 sec
RG         574.7
DW         40.400 usec
DE         6.50 usec
TE         294.9 K
D1         2.00000000 sec
TD0        1

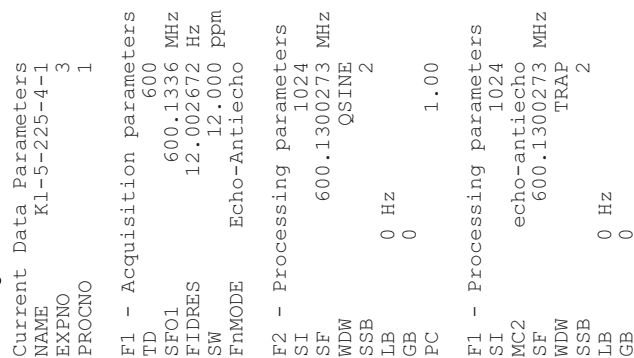
===== CHANNEL f1 =====
NUC1       1H
P1         9.60 usec
PL1        -2.00 dB
PL1W       39.81071854 W
SFO1       600.1336008 MHz

F2 - Processing parameters
SI         65536
SF         600.1300273 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00

```







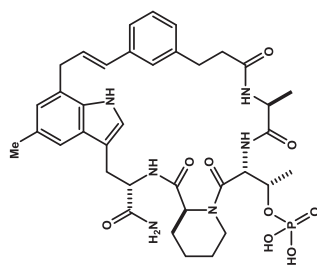


F1 - Acquisition parameters	
TD	512
SFO1	150.9134 MHz
FIDRES	47.160427 Hz
SW	160.000 ppm
PnMODE	Echo-Antiecho

F2 - Processing parameters	
SI	4096
SF	600.1300051 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	
PC	1.40

F1 - Processing parameters	
SI	4096
MC2	echo-antiecho
SF	150.9029231 MHz
WDW	SINE
SSB	2
LB	0 Hz
GB	0



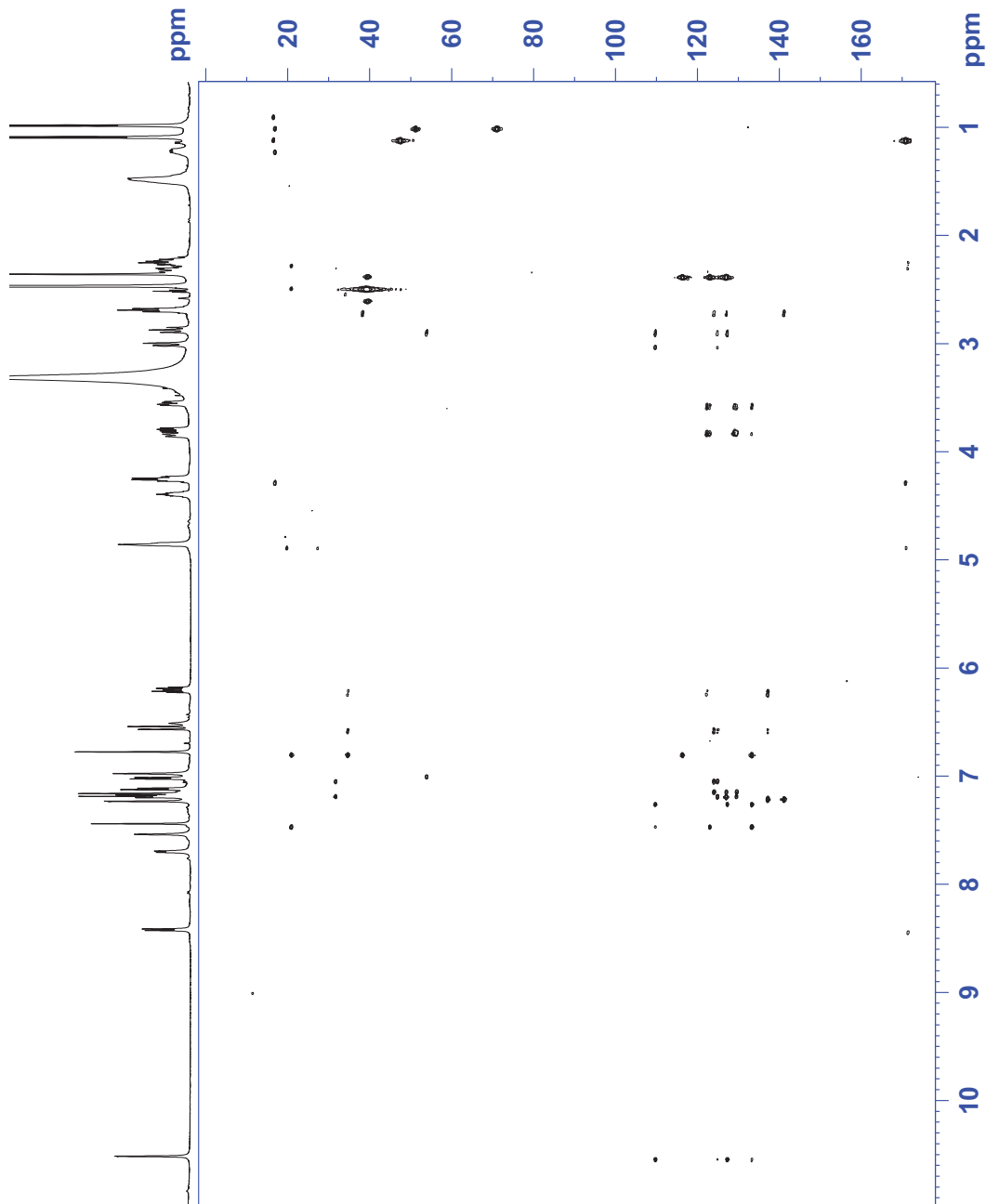


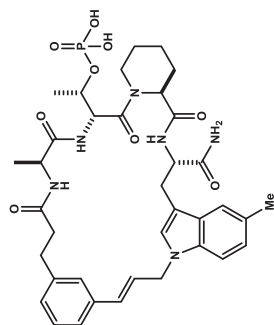
Current Data Parameters
 NAME K1-5-225-4-1
 EXPNO 6
 PROCNO 1

F1 - Acquisition parameters
 TD 512
 SF01 150.9156 MHz
 FIDRES 56.003849 Hz
 SW 190.000 ppm
 FnmODE QF

F2 - Processing parameters
 SI 4096
 SF 600.1300066 MHz
 WDW QSINE
 SSB 0
 LB 0 Hz
 GB 0
 PC 1.40

F1 - Processing parameters
 SI 4096
 MC2 QF
 SF 150.9029181 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0





```

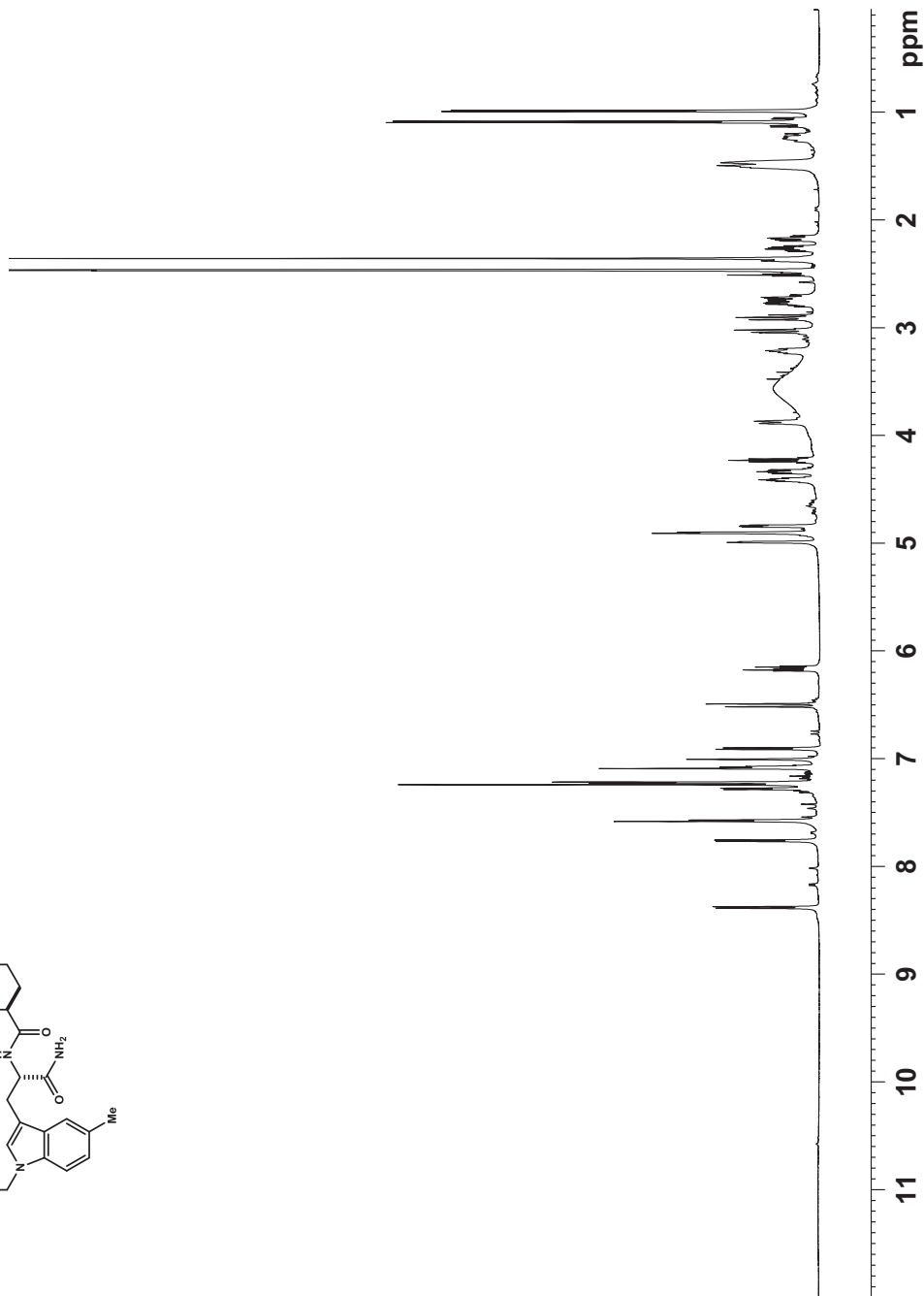
Current Data Parameters
NAME      KL-5-225-4-2
EXPNO     2
PROCNO    1

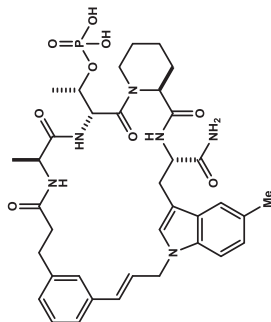
F2 - Acquisition Parameters
Date_     20131013
Time      20.56
INSTRUM   av600
PROBHD    5 mm TBI5
PULPROG   zg
TD         65536
SOLVENT   DMSO
NS         128
DS         0
SWH        12376.237 Hz
FIDRES     0.188846 Hz
AQ         2.6476543 sec
RG         574.7
DW         40.400 usec
DE         6.50 usec
TE         294.6 K
D1         2.00000000 sec
TD0        1

===== CHANNEL f1 =====
NUC1       1H
P1         9.50 usec
PL1        -2.00 dB
PL1W       39.81071854 W
SFO1       600.1336008 MHz

F2 - Processing parameters
SI         65536
SF         600.1300273 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00

```



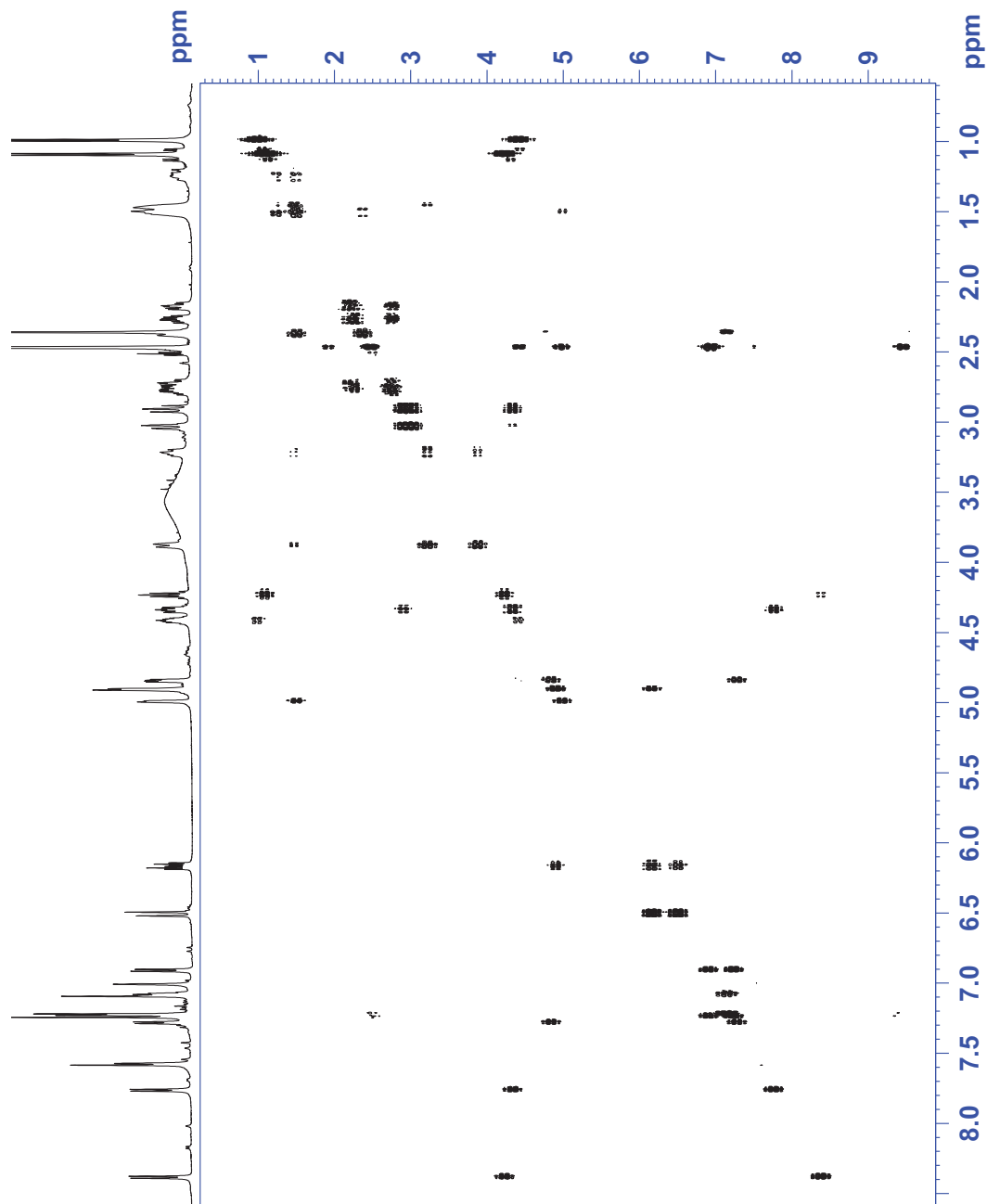


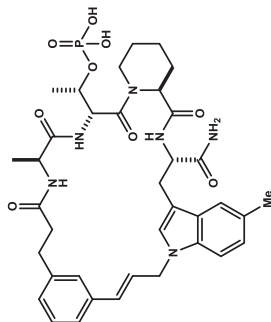
Current Data Parameters
 NAME KL-5-225-4-2
 EXPNO 4
 PROCNO 1

F1 - Acquisition parameters
 TD 256
 SFO1 600.1336 MHz
 FIDRES 28.131262 Hz
 SW 12.000 ppm
 FnmODE States-TPPI

F2 - Processing parameters
 SI 2048
 SF 600.1300273 MHz
 WDW SINE
 SSB 1
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 2048
 MC2 States-TPPI
 SF 600.1300273 MHz
 WDW QSINE
 SSB 1
 LB 0 Hz
 GB 0



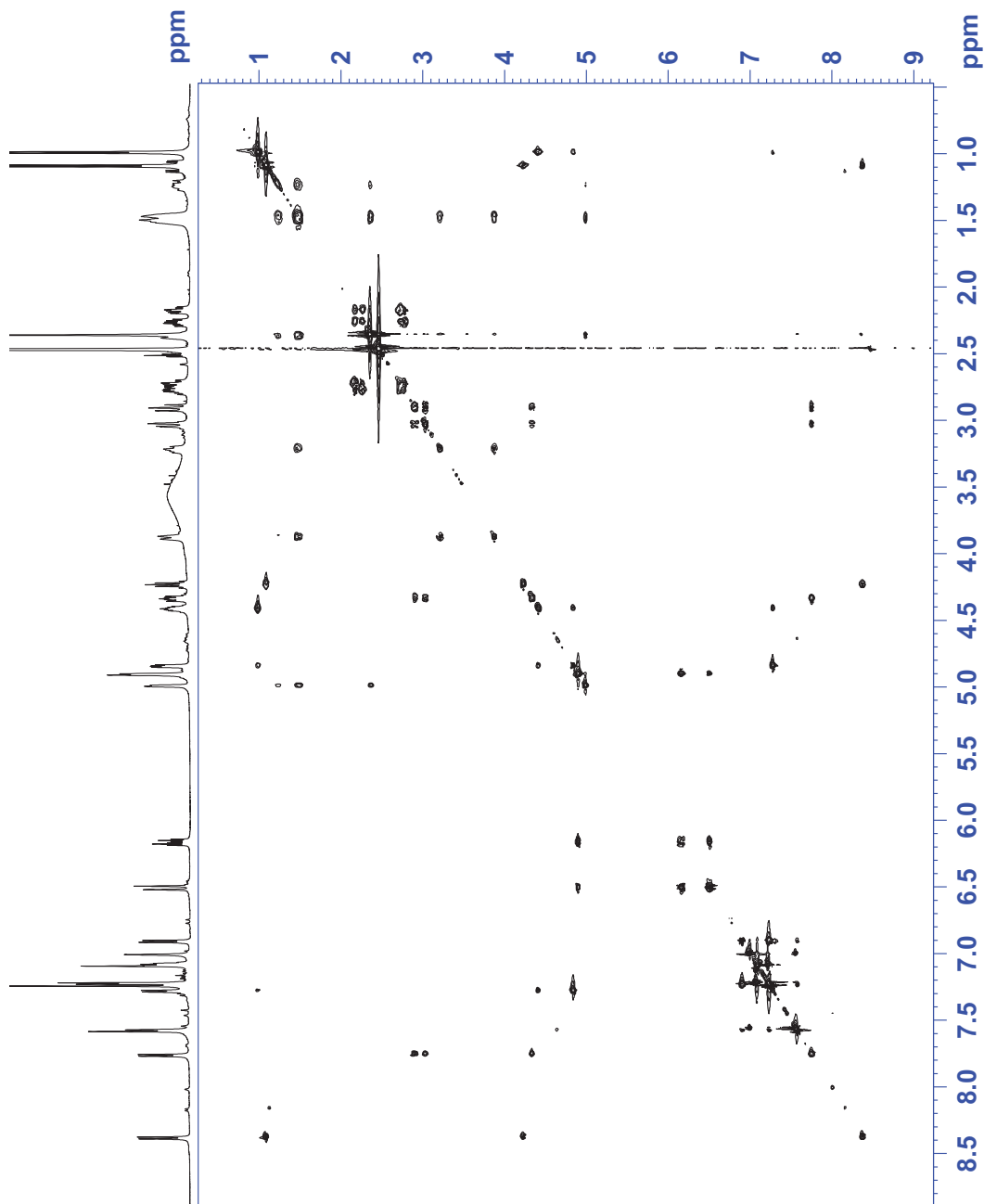


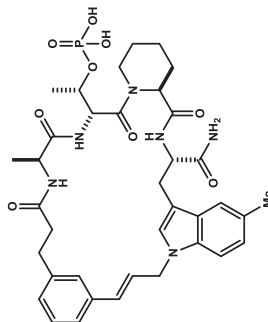
Current Data Parameters
 NAME KL-5-225-4-2
 EXPNO 3
 PROCNO 1

F1 - Acquisition parameters
 TD 600
 SF01 600.1336 MHz
 FIDRES 12.002672 Hz
 SW 12.000 ppm
 FnmODE Echo-Antiecho

F2 - Processing parameters
 SI 1024
 SF 600.1300273 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 1024
 MC2 echo-antiecho
 SF 600.1300273 MHz
 WDW USER
 SSB 2
 LB 0 Hz
 GB 0



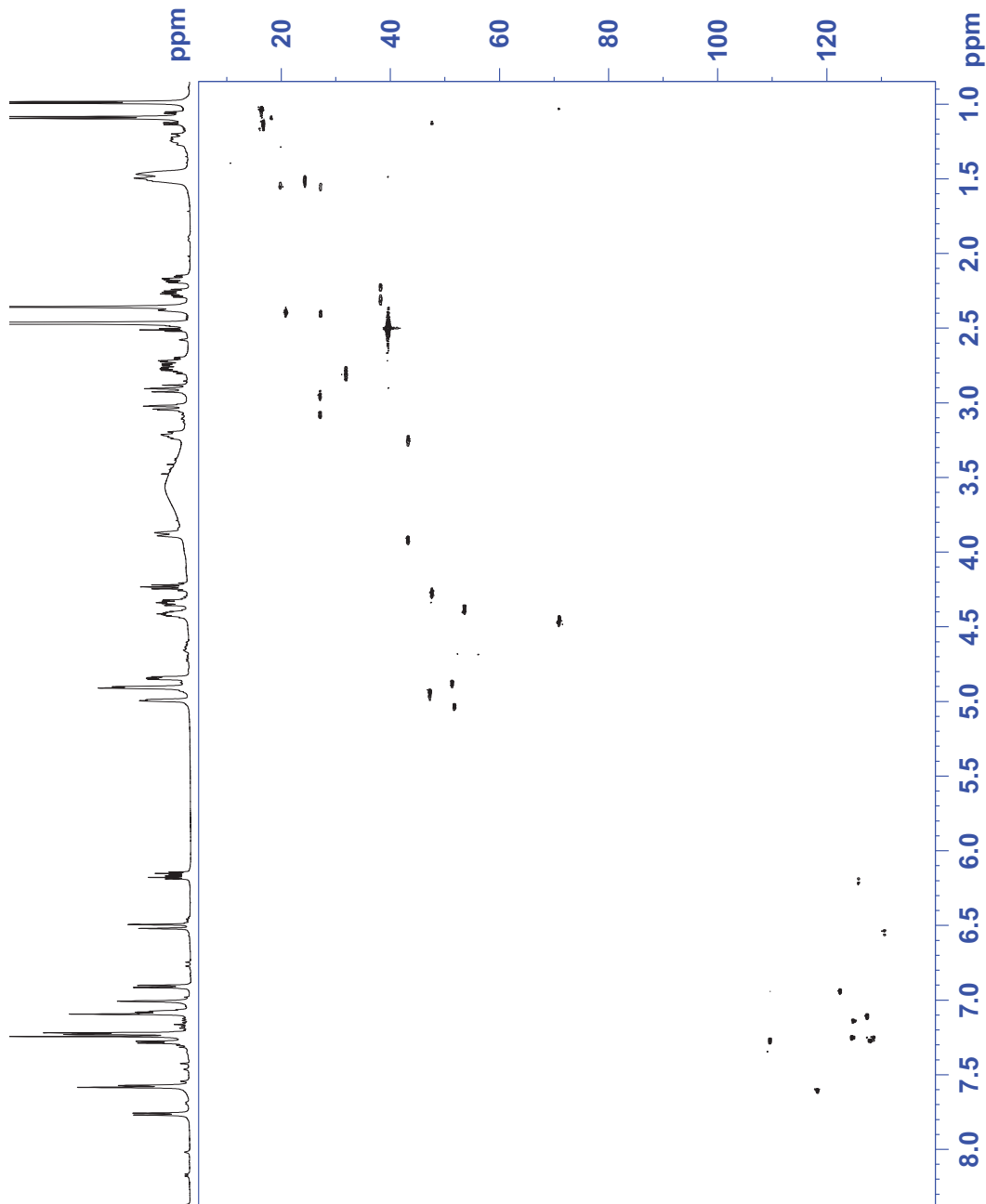


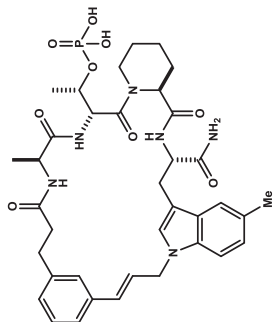
Current Data Parameters
 NAME KL-5-225-4-2
 EXPNO 5
 PROCNO 1

F1 - Acquisition parameters
 TD 512
 SF01 150.9134 MHz
 FIDRES 47.160427 Hz
 SW 160.000 ppm
 FnMODE Echo-Antiecho

F2 - Processing parameters
 SI 4096
 SF 600.1300051 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

F1 - Processing parameters
 SI 4096
 MC2 echo-antiecho
 SF 150.9029231 MHz
 WDW TRAP
 SSB 2
 LB 0 Hz
 GB 0



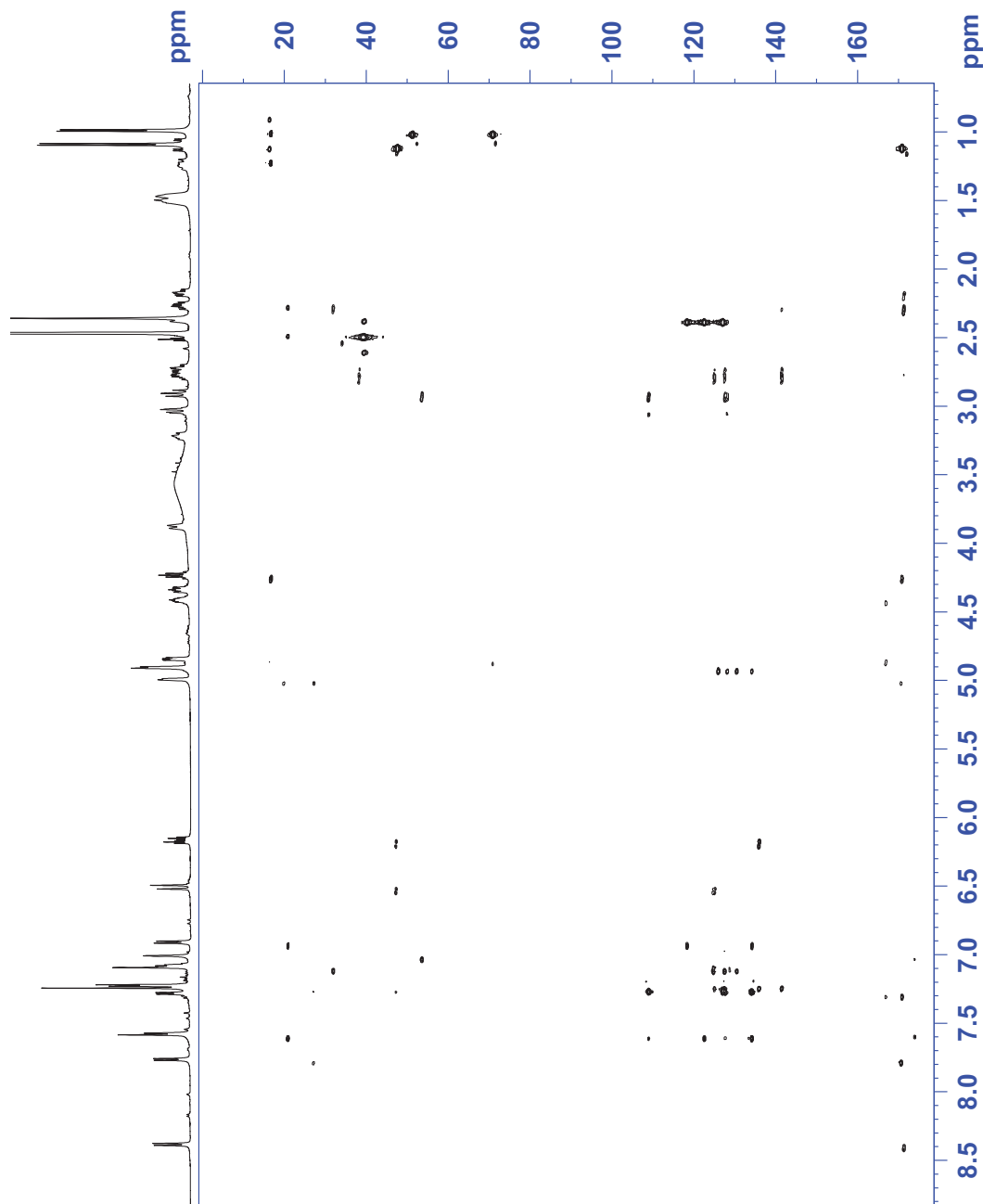


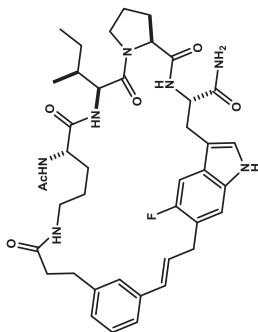
Current Data Parameters
 NAME KL-5-225-4-2
 EXPNO 6
 PROCNO 1

F1 - Acquisition parameters
 TD 512
 SFO1 150.9156 MHz
 FIDRES 56.003849 Hz
 SW 190.000 ppm
 FnmODE QF

F2 - Processing parameters
 SI 4096
 SF 600.1300066 MHz
 WDW QSINE
 SSB 0
 LB 0 Hz
 GB 0
 PC 1.40

F1 - Processing parameters
 SI 4096
 MC2 QF
 SF 150.9029181 MHz
 WDW TRAP
 SSB 3
 LB 0 Hz
 GB 0





```

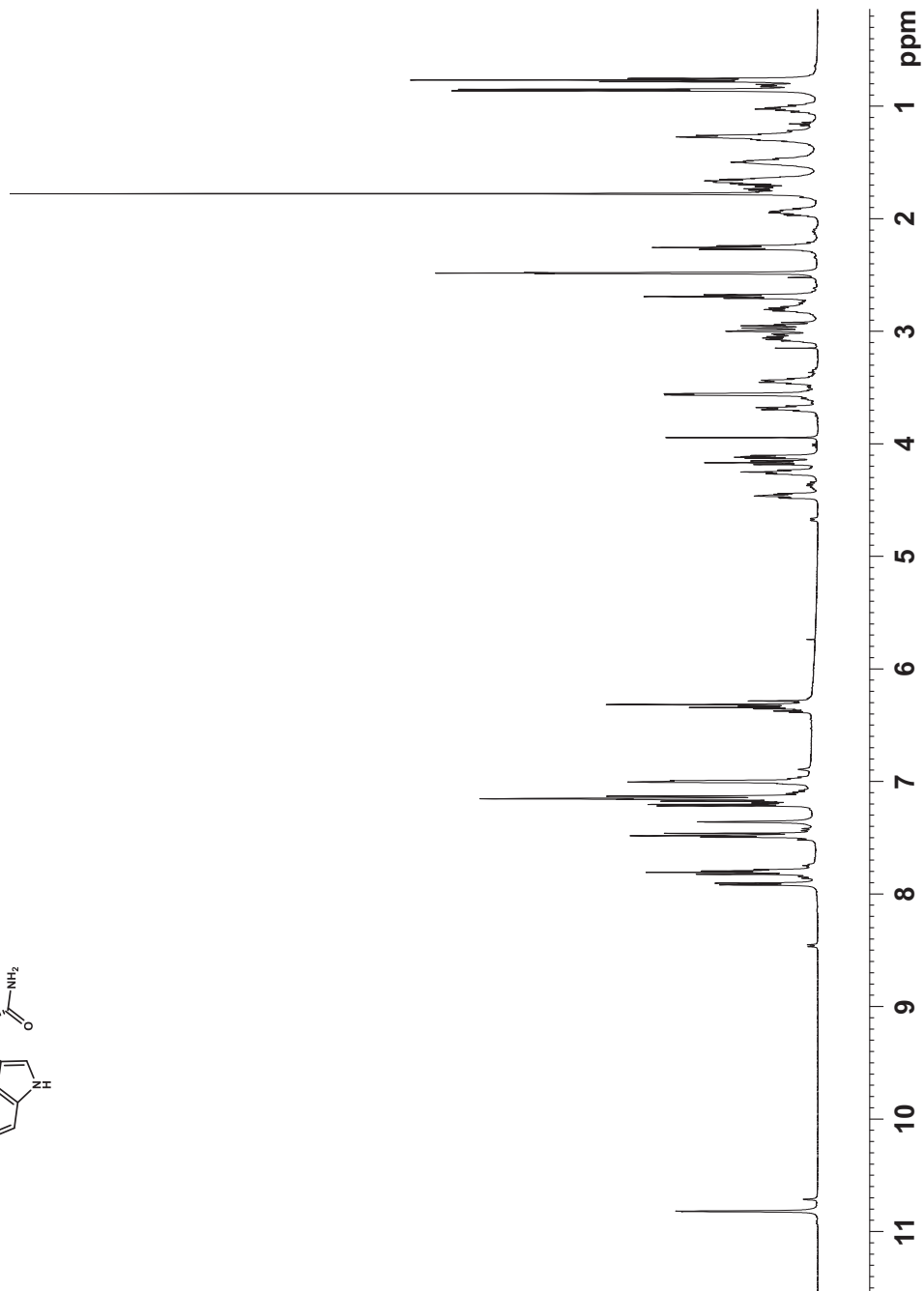
Current Data Parameters
NAME      W-B1-1a-4
EXPNO     2
PROCNO    1

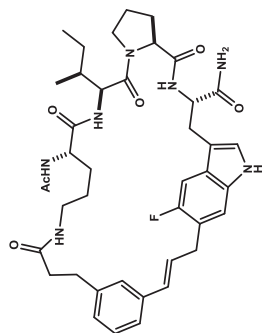
F2 - Acquisition Parameters
Date_     20121023
Time      17.17
INSTRUM   av500
PROBHD    5 mm DCH 13C-1
PULPROG   zg
TD         65536
SOLVENT   DMSO
NS         8
DS         0
SWH        10000.000 Hz
FIDRES     0.152588 Hz
AQ         3.2767999 sec
RG         7
DW         50.000 usec
DE         10.00 usec
TE         298.0 K
D1         2.00000000 sec
TD0        1

===== CHANNEL f1 =====
NUC1       1H
P1         10.00 usec
PLW1       13.50000000 W
SFO1       500.1330008 MHz

F2 - Processing parameters
SI         65536
SF         500.1300146 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00

```



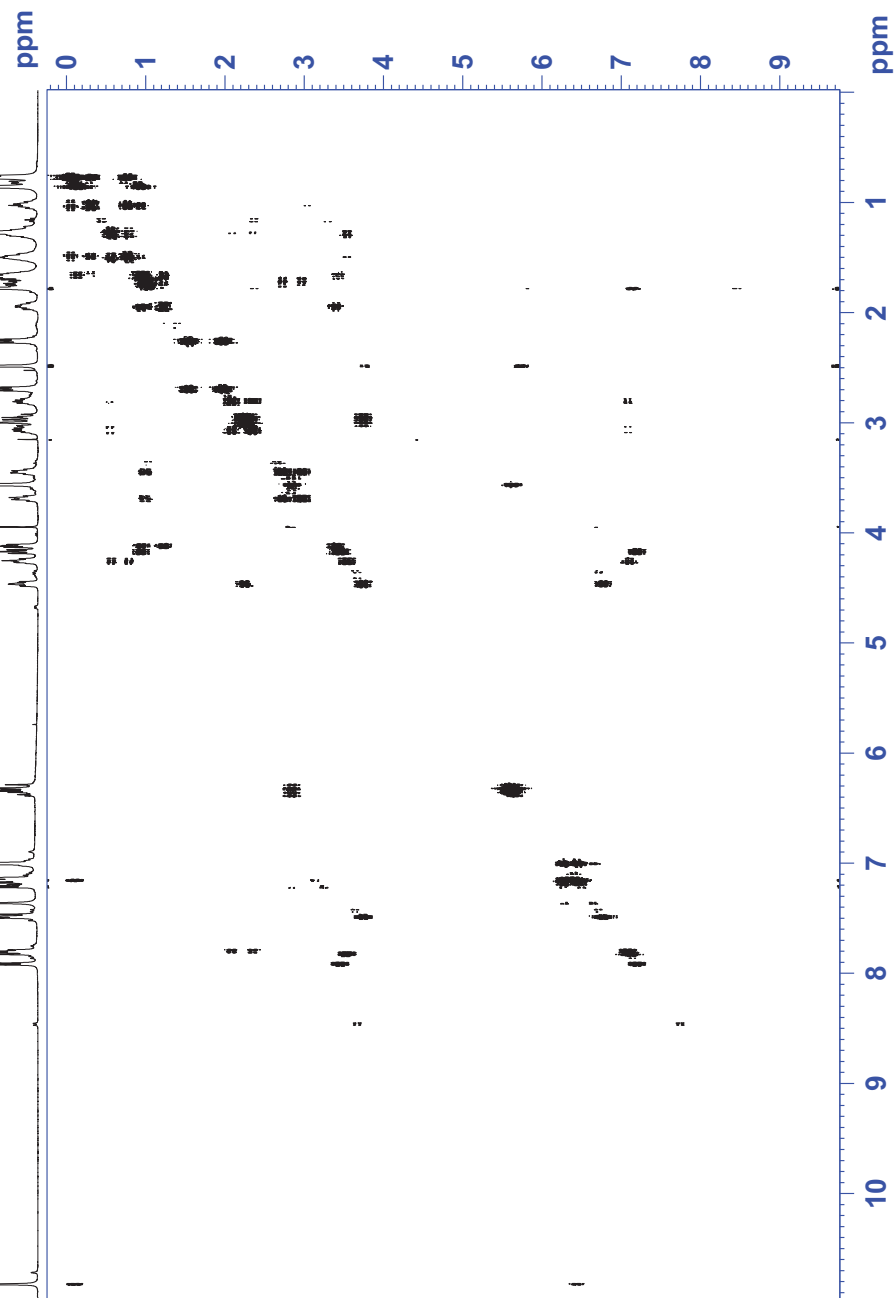


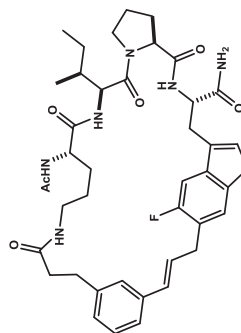
Current Data Parameters
 NAME W-BI-1a-4
 EXPNO 3
 PROCNO 1

F1 - Acquisition parameters
 TD 256
 SF01 500.1328 MHz
 FIDRES 19.536423 Hz
 SW 10.000 ppm
 FnMODE States-TPPI

F2 - Processing parameters
 SI 2048
 SF 500.1300135 MHz
 SINE
 WDW 1
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 2048
 MC2 States-TPPI
 SF 500.1303720 MHz
 WDW GM
 SSB 1
 LB 0 Hz
 GB 0





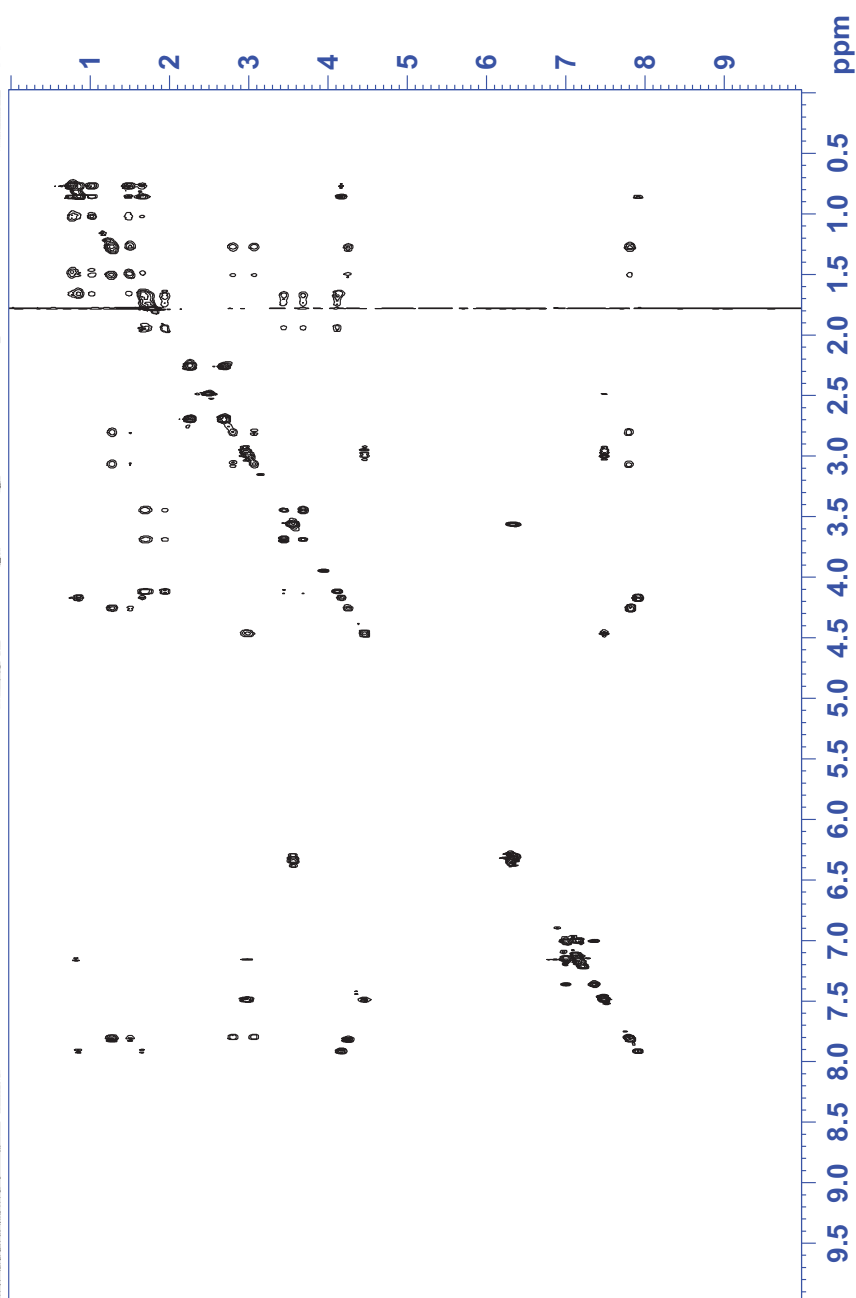
Current Data Parameters
 NAME W-B1-1a-4
 EXPNO 4
 PROCNO 1

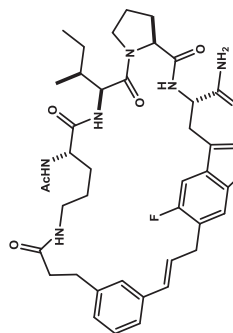
F1 - Acquisition parameters
 TD 256
 SF01 500.1325 MHz
 FIDRES 19.536406 Hz
 SW 10.000 ppm
 FnmODE Echo-Antiecho

F2 - Processing parameters
 SI 2048
 SF 500.1300135 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 2048
 MC2 echo-antiecho
 SF 500.1300135 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0

ppm



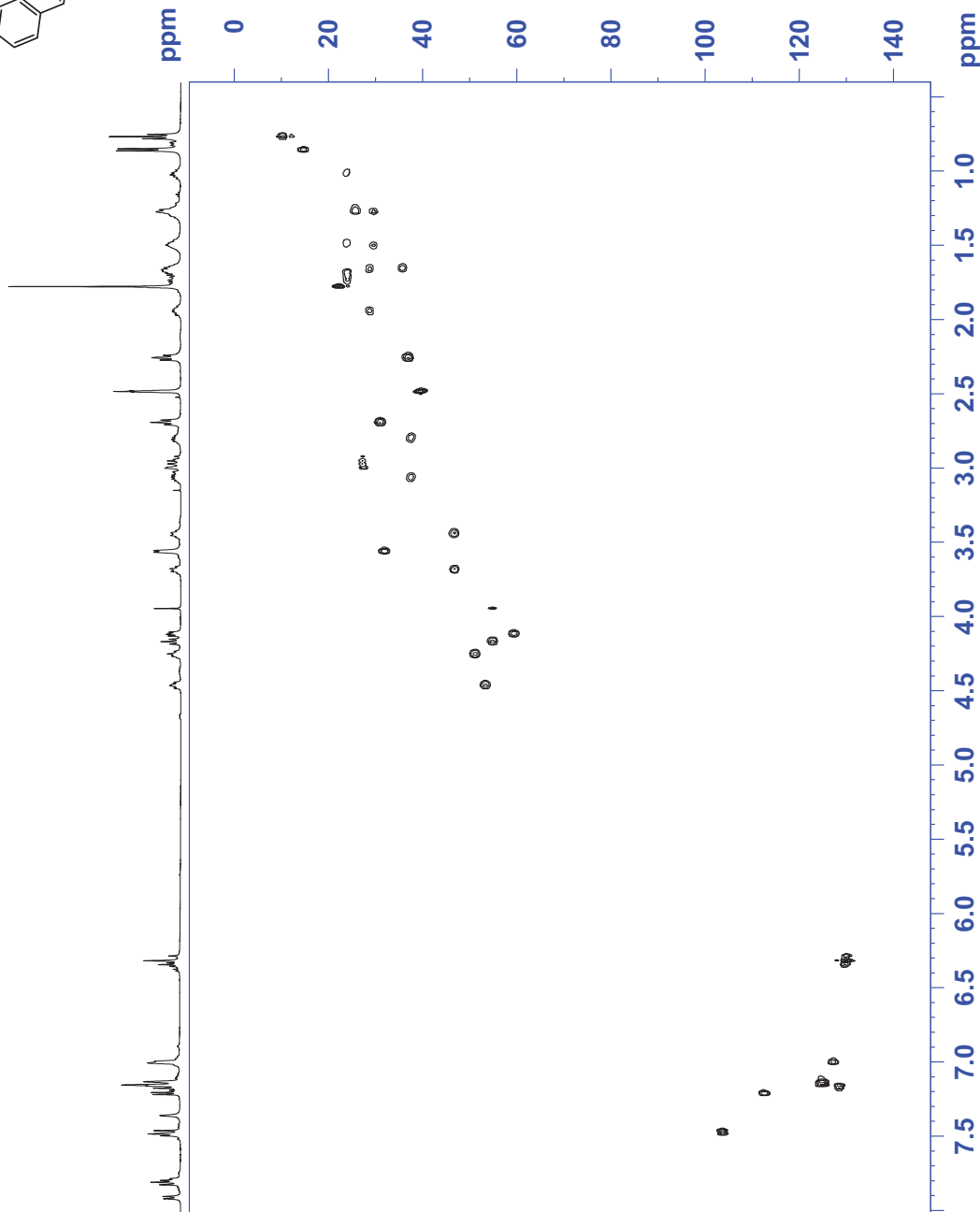


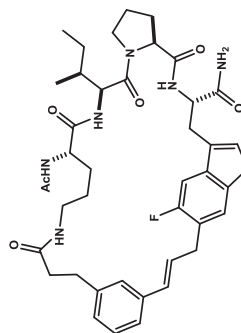
Current Data Parameters
NAME W-B1-1a-4
EXPNO 5
PROCNO 1

F1 - Acquisition parameters
TD 256
SF01 125.7678 MHz
FIDRES 98.255890 Hz
SW 200.000 ppm
FnMODE Echo-Antiecho

F2 - Processing parameters
SI 2048
SF 500.1300135 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0
PC 1.00

F1 - Processing parameters
SI 2048
MC2 echo-antiecho
SF 125.7578472 MHz
WDW USER
SSB 2
LB 0 Hz
GB 0



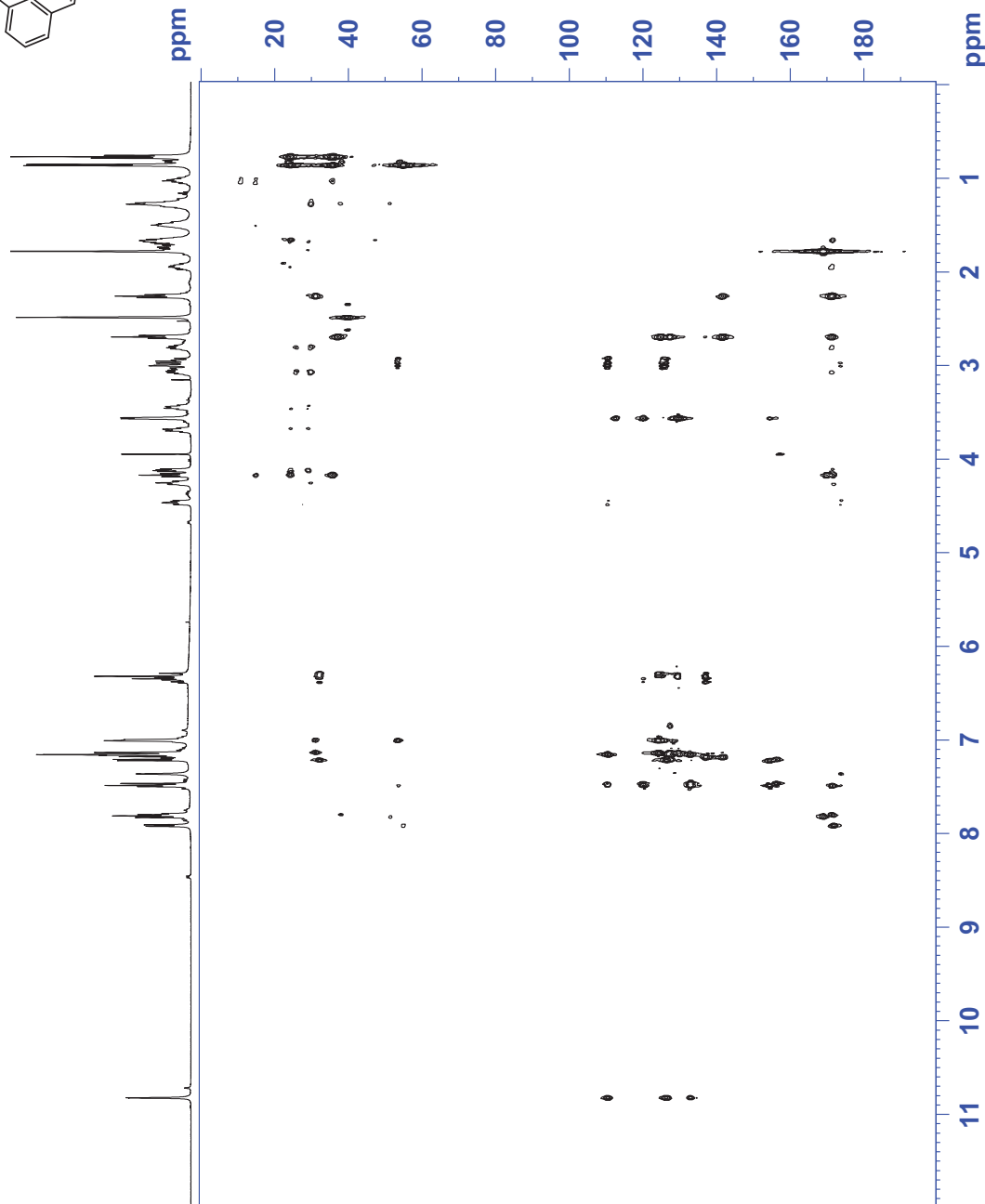


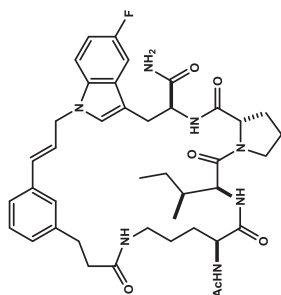
Current Data Parameters
 NAME W-B1-1a-4
 EXPNO 6
 PROCNO 1

F1 - Acquisition parameters
 TD 256
 SFO1 125.7704 MHz
 FIDRES 98.257607 Hz
 SW 199.999 ppm
 FMODE QF

F2 - Processing parameters
 SI 2048
 SF 500.1300135 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 2048
 MC2 QF
 SF 125.7578472 MHz
 WDW USER
 SSB 2
 LB 0 Hz
 GB 0





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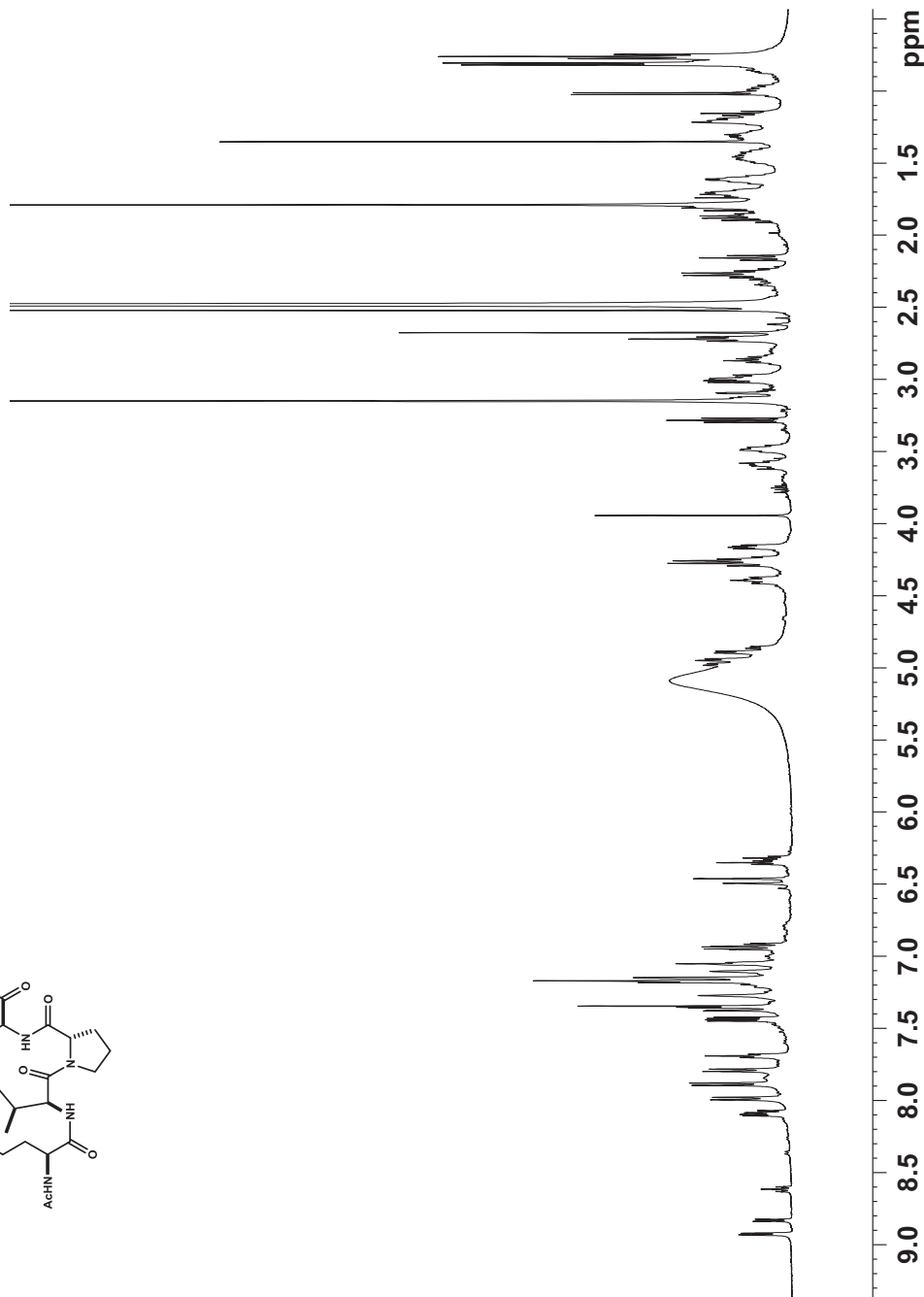
Current Data Parameters
NAME      W-B1-2
EXPNO     1
PROCNO    1

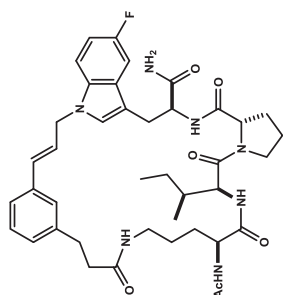
F2 - Acquisition Parameters
Date_     20121020
Time_     13.37
INSTRUM   av500
PROBHD    5 mm DCH 13C-1
PULPROG   zg30
TD        65536
SOLVENT   DMSO
NS         8
DS         0
SWH        10000.000 Hz
FIDRES     0.152588 Hz
AQ         3.2767999 sec
RG         15.53
DW         50.000 usec
DE         10.00 usec
TE         298.0 K
D1         2.00000000 sec
TD0        1

===== CHANNEL f1 =====
NUC1       1H
P1         10.00 usec
PLW1       13.50000000 W
SFO1       500.1330008 MHz

F2 - Processing parameters
SI         65536
SF         500.1300146 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00

```



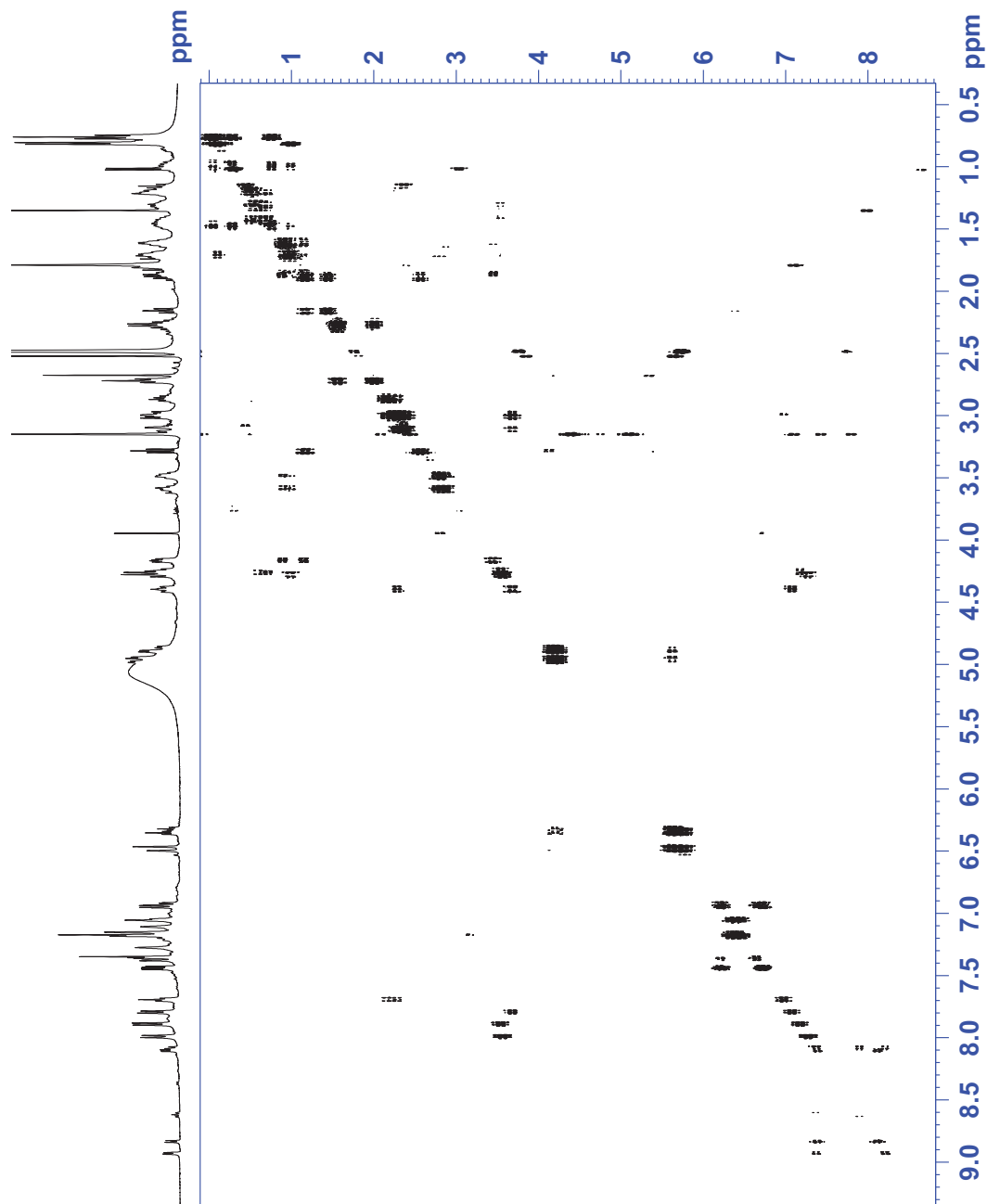


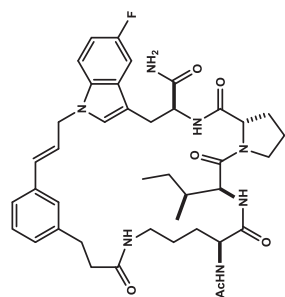
Current Data Parameters
 NAME W-B1-2
 EXPNO 3
 PROCNO 1

F1 - Acquisition parameters
 TD 256
 SFO1 500.1328 MHz
 FIDRES 19.536423 Hz
 SW 10.000 ppm
 FnmODE States-TPPI

F2 - Processing parameters
 SI 2048
 SF 500.1300135 MHz
 WDW SINE
 SSB 1
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 2048
 MC2 States-TPPI
 SF 500.1303720 MHz
 WDW GM
 SSB 1
 LB 0 Hz
 GB 0



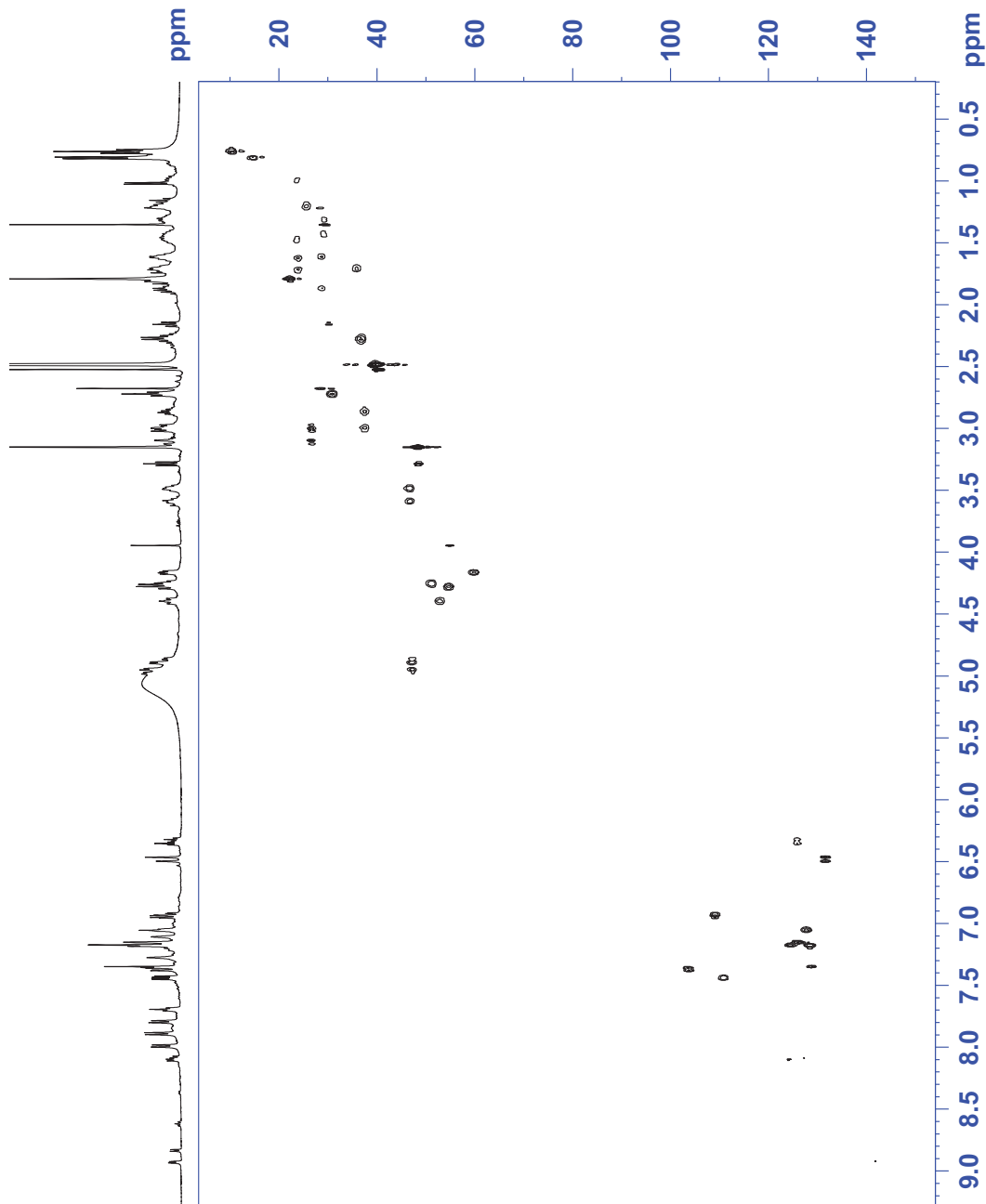


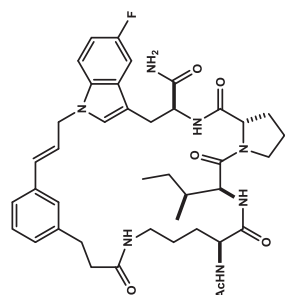
Current Data Parameters
 NAME W-B1-2
 EXPNO 4
 PROCNO 1

F1 - Acquisition parameters
 TD 256
 SF01 125.7678 MHz
 FIDRES 98.255890 Hz
 SW 200.000 ppm
 FnmODE Echo-Antiecho

F2 - Processing parameters
 SI 2048
 SF 500.1300135 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 2048
 MC2 echo-antiecho
 SF 125.7578472 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0



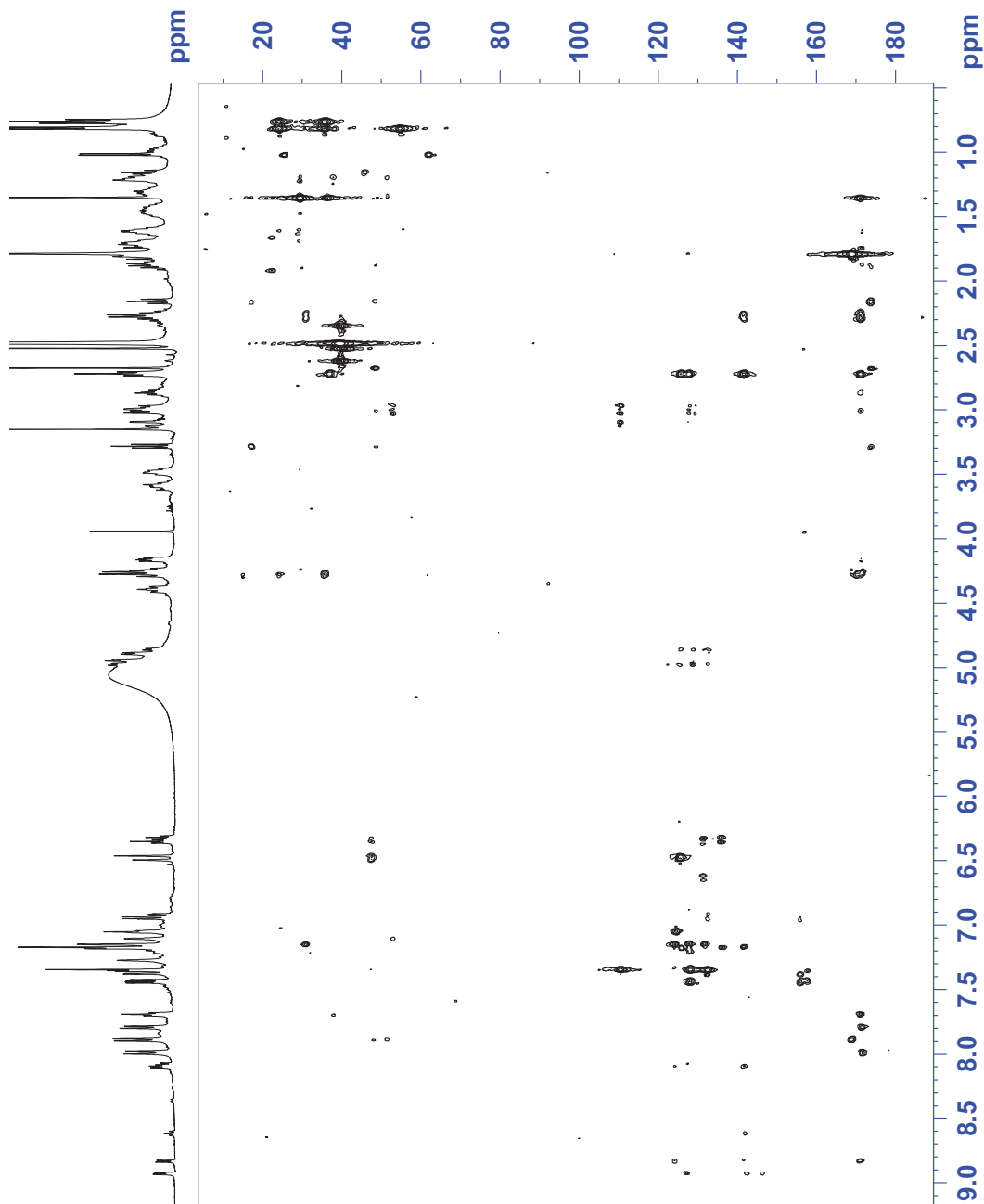


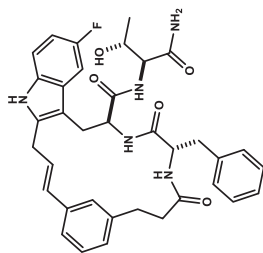
Current Data Parameters
 NAME W-B1-2
 EXPNO 5
 PROCNO 1

F1 - Acquisition parameters
 TD 256
 SF01 125.7704 MHz
 FIDRES 98.257607 Hz
 SW 199.999 ppm
 FnMODE QF

F2 - Processing parameters
 SI 2048
 SF 500.1300135 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 2048
 MC2 QF
 SF 125.7578472 MHz
 WDW USER
 SSB 2
 LB 0 Hz
 GB 0



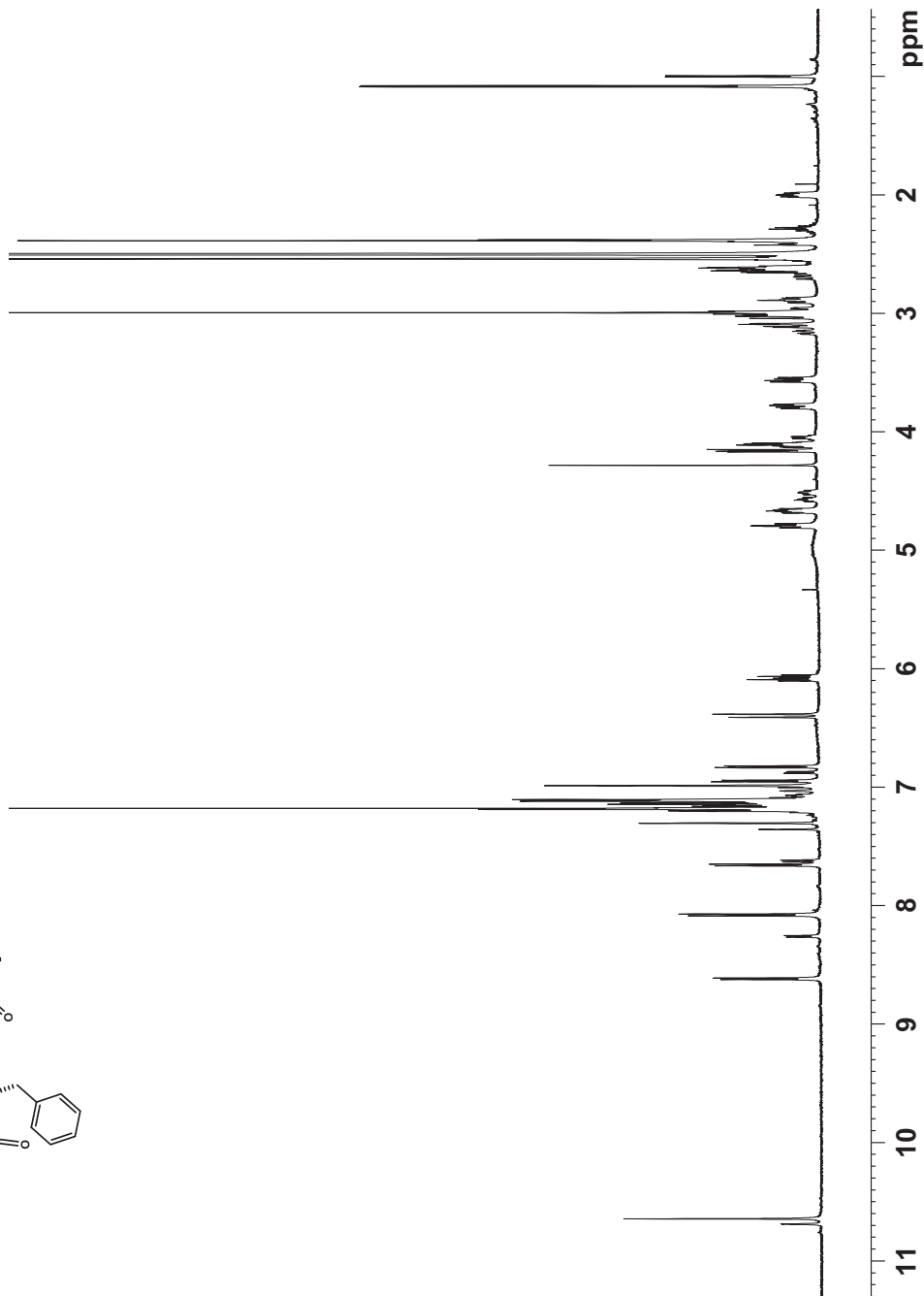


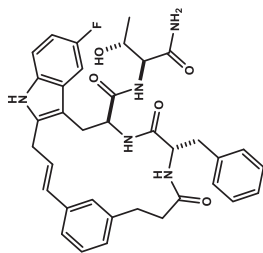
Current Data Parameters
 NAME KL-5-108-2_TROSE
 EXPNO 3
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20130110
 Time_ 18.39
 INSTRUM av600
 PROBHD 5 mm TBI5
 PULPROG zg
 TD 65536
 SOLVENT DMSO
 NS 8
 DS 0
 SWH 12376.237 Hz
 FIDRES 0.188846 Hz
 AQ 2.6476543 sec
 RG 114
 DW 40.400 usec
 DE 6.50 usec
 TE 298.0 K
 D1 2.00000000 sec
 TD0 1

==== CHANNEL f1 =====
 NUC1 1H
 P1 9.55 usec
 PL1 -2.00 dB
 PL1W 39.81071854 W
 SFO1 600.1336008 MHz

F2 - Processing parameters
 SI 65536
 SF 600.1300070 MHz
 WDW EM
 SSB 0
 LB 0.20 Hz
 GB 0
 PC 1.00



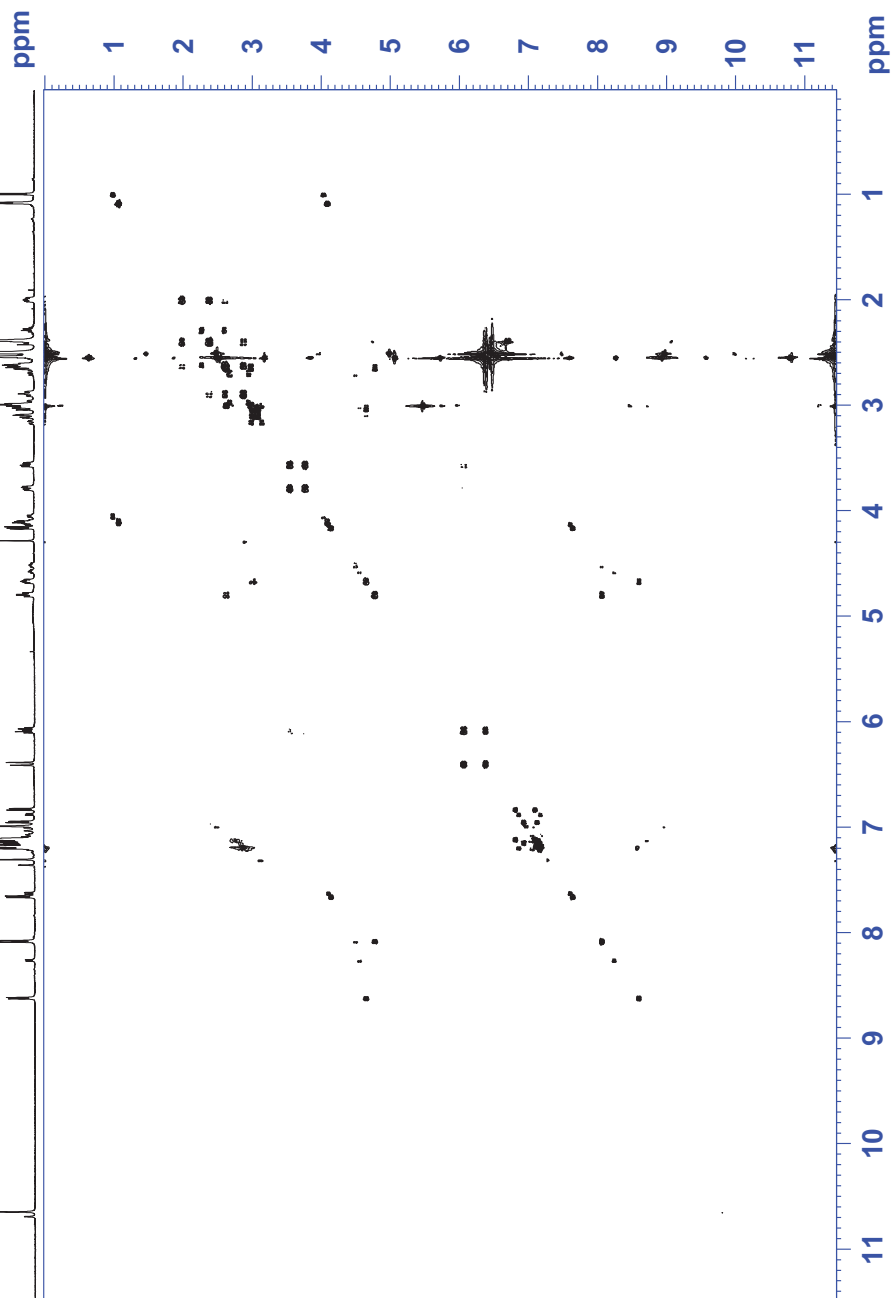


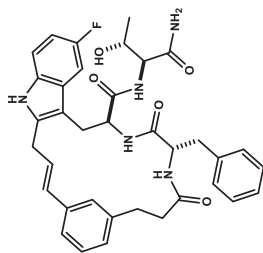
Current Data Parameters
 NAME KL-5-108-2_TROSE
 EXPNO 4
 PROCNO 1

F1 - Acquisition parameters
 TD 512
 SFO1 600.1335 MHz
 FIDRES 13.451290 Hz
 SW 11.476 ppm
 FnmODE States-TPPI

F2 - Processing parameters
 SI 4096
 SF 600.1300014 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 4096
 MC2 States-TPPI
 SF 600.1300177 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0



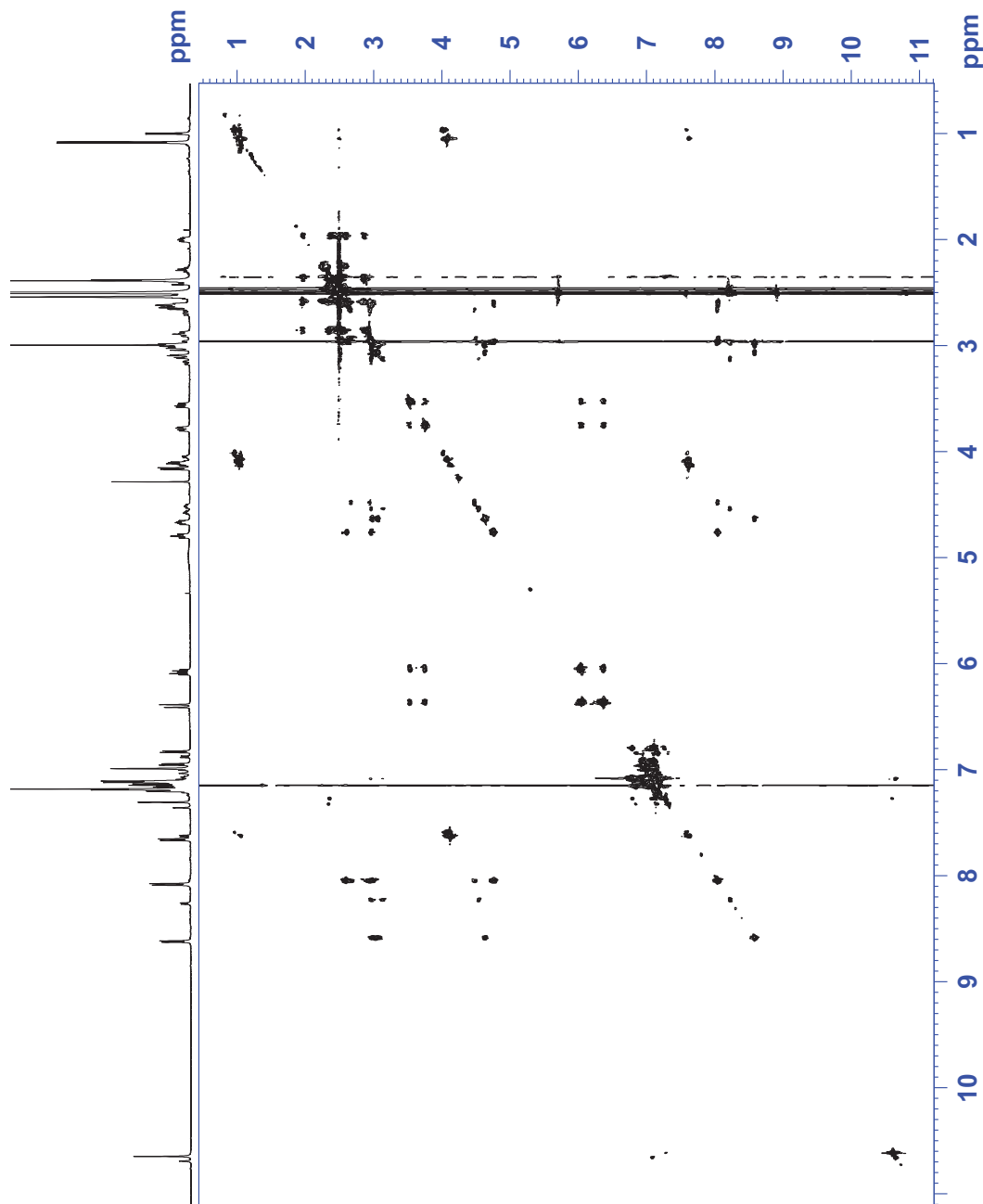


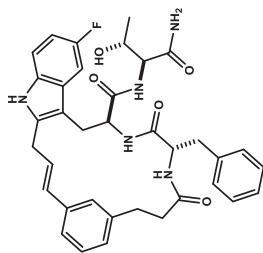
Current Data Parameters
NAME KL-5-108-2_TROSE
EXPNO 8
PROCNO 1

F1 - Acquisition parameters
TD 128
SFO1 600.1335 MHz
FIDRES 53.805161 Hz
SW 11.476 ppm
FnMODE Echo-Antiecho

F2 - Processing parameters
SI 4096
SF 600.1300273 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0
PC 1.00

F1 - Processing parameters
SI 4096
MC2 echo-antiecho
SF 600.1300273 MHz
WDW TRAP
SSB 2
LB 0 Hz
GB 0



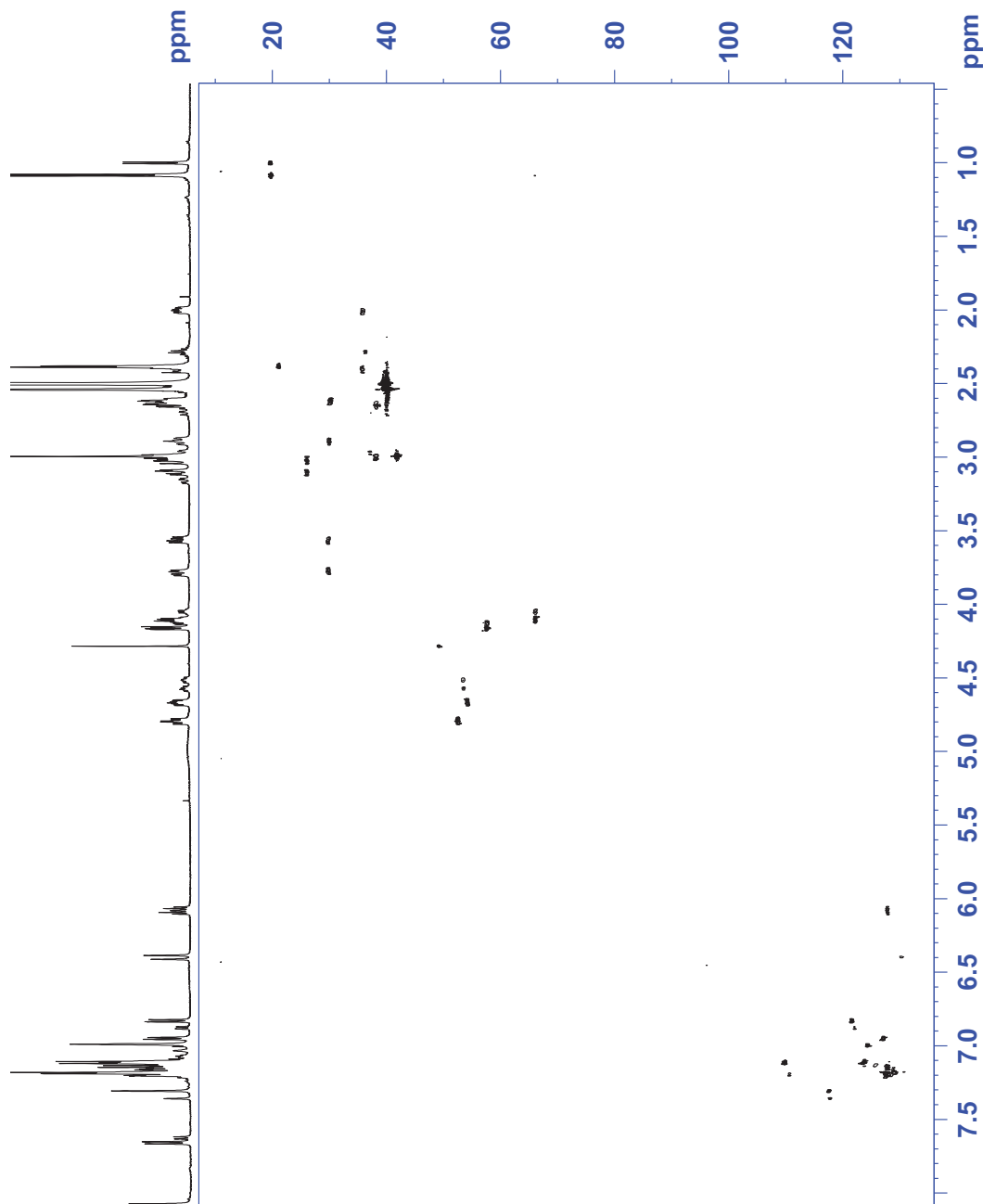


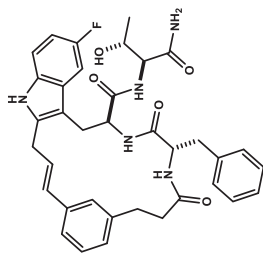
Current Data Parameters
 NAME KL-5-108-2_TROSE
 EXPNO 6
 PROCNO 1

F1 - Acquisition parameters
 TD 253
 SFO1 150.9134 MHz
 FIDRES 95.439285 Hz
 SW 160.000 ppm
 FnMODE Echo-Antiecho

F2 - Processing parameters
 SI 4096
 SF 600.1300051 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

F1 - Processing parameters
 SI 4096
 MC2 echo-antiecho
 SF 150.9029231 MHz
 WDW TRAP
 SSB 2
 LB 0 Hz
 GB 0



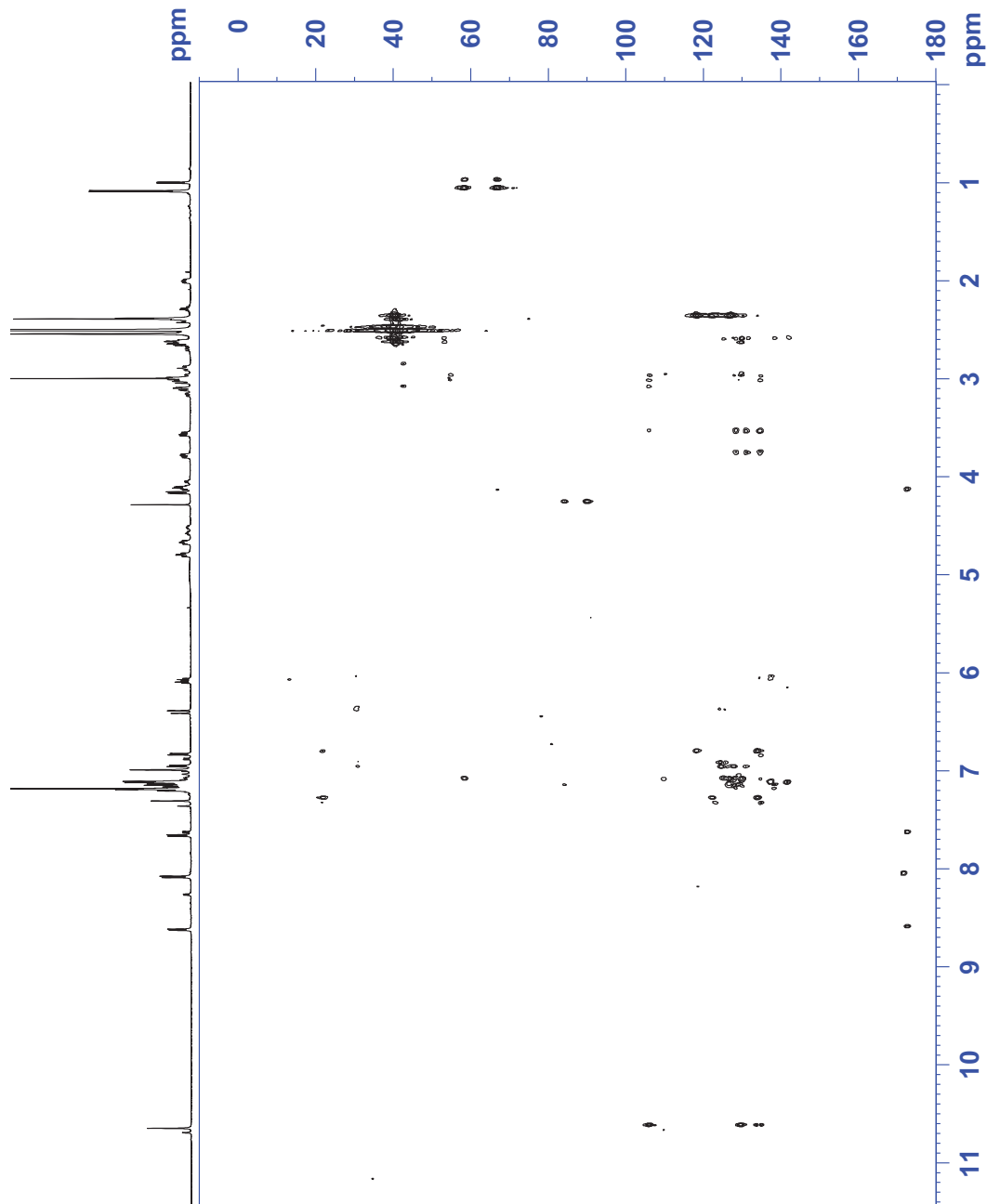


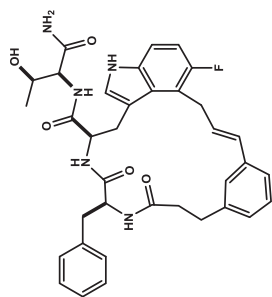
Current Data Parameters
 NAME KL-5-108-2_TROSE
 EXPNO 7

PROCNO 1
 F1 - Acquisition parameters
 TD 256
 SFO1 150.9156 MHz
 FIDRES 112.007698 Hz
 SW 190.000 ppm
 FnmODE QF

F2 - Processing parameters
 SI 4096
 SF 600.1300273 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.40

F1 - Processing parameters
 SI 2048
 MC2 QF
 SF 150.9028090 MHz
 WDW USER
 SSB 2
 LB 0 Hz
 GB 0



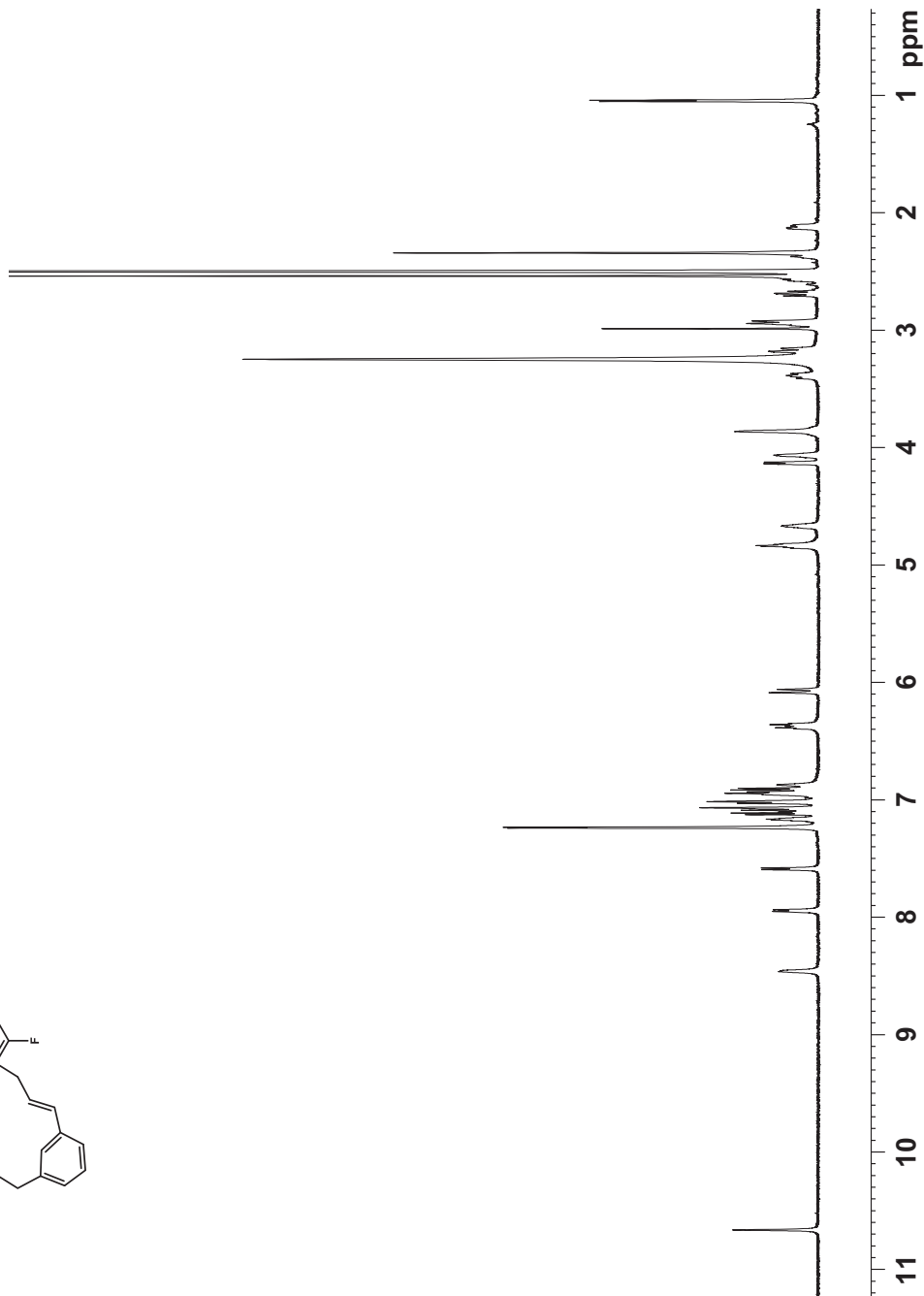


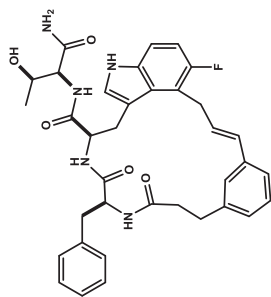
Current Data Parameters
 NAME KL-5-108-3-1_TROSE
 EXPNO 4
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20130113
 Time_ 17.25
 INSTRUM av600
 PROBHD 5 mm TBI5
 PULPROG zg
 TD 65536
 SOLVENT DMSO
 NS 8
 DS 0
 SWH 12376.237 Hz
 FIDRES 0.188846 Hz
 AQ 2.6476543 sec
 RG 128
 DW 40.400 usec
 DE 6.50 usec
 TE 320.0 K
 D1 2.00000000 sec
 TD0 1

==== CHANNEL f1 =====
 NUC1 1H
 P1 9.73 usec
 PL1 -2.00 dB
 PL1W 39.81071854 W
 SFO1 600.1336008 MHz

F2 - Processing parameters
 SI 65536
 SF 600.1300070 MHz
 WDW EM
 SSB 0
 LB 0 Hz
 GB 0
 PC 1.00



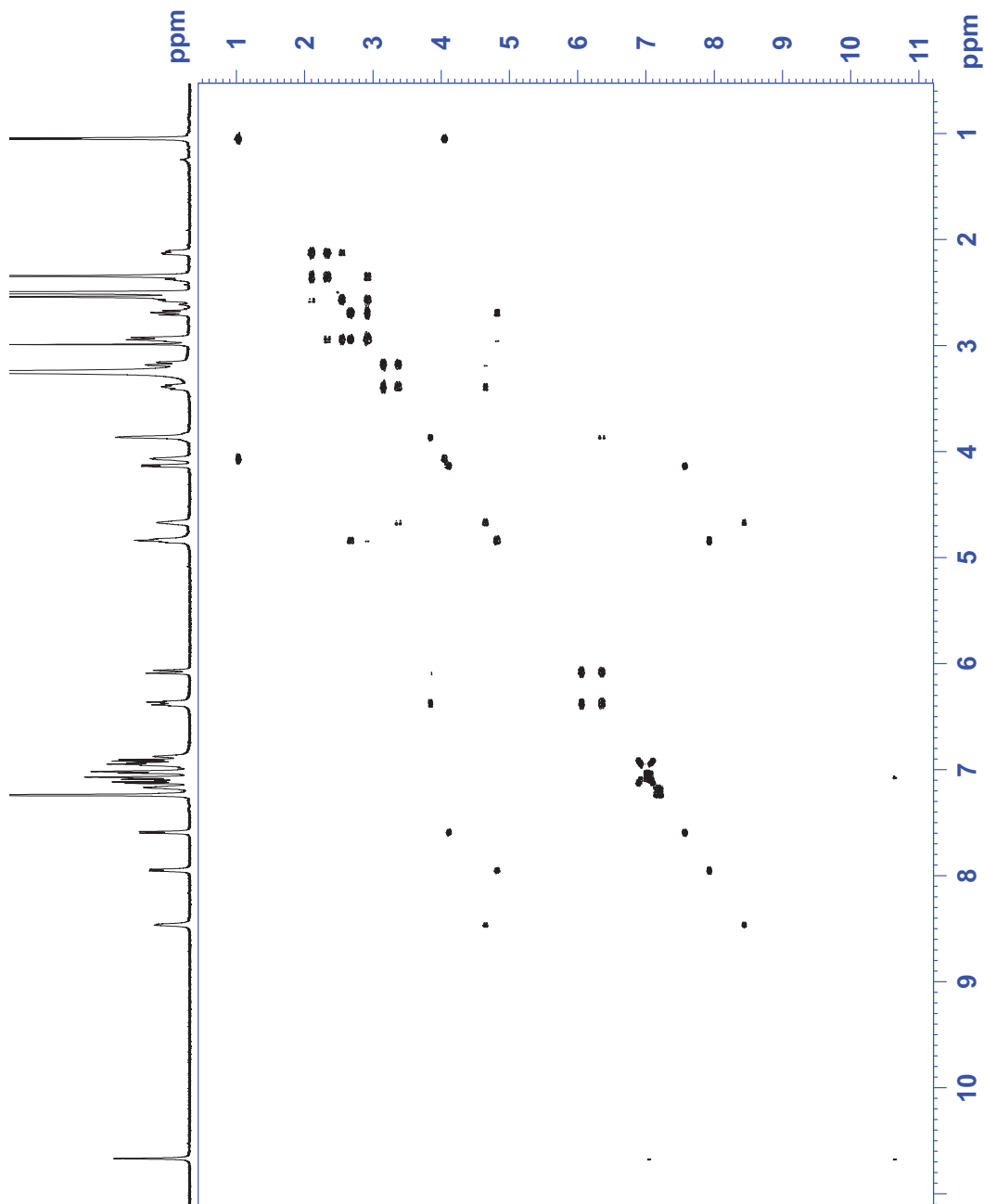


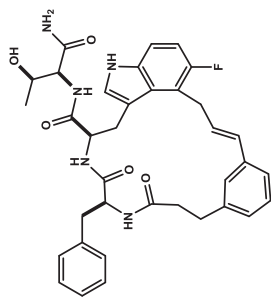
Current Data Parameters
 NAME KL-5-108-3-1_TROSE
 EXPNO 10
 PROCNO 1

F1 - Acquisition parameters
 TD 512
 SFO1 600.1335 MHz
 FIDRES 13.451290 Hz
 SW 11.476 ppm
 FnmODE States-TPPI

F2 - Processing parameters
 SI 4096
 SF 600.1300014 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 4096
 MC2 States-TPPI
 SF 600.1300177 MHz
 WDW TRAP
 SSB 2
 LB 0 Hz
 GB 0



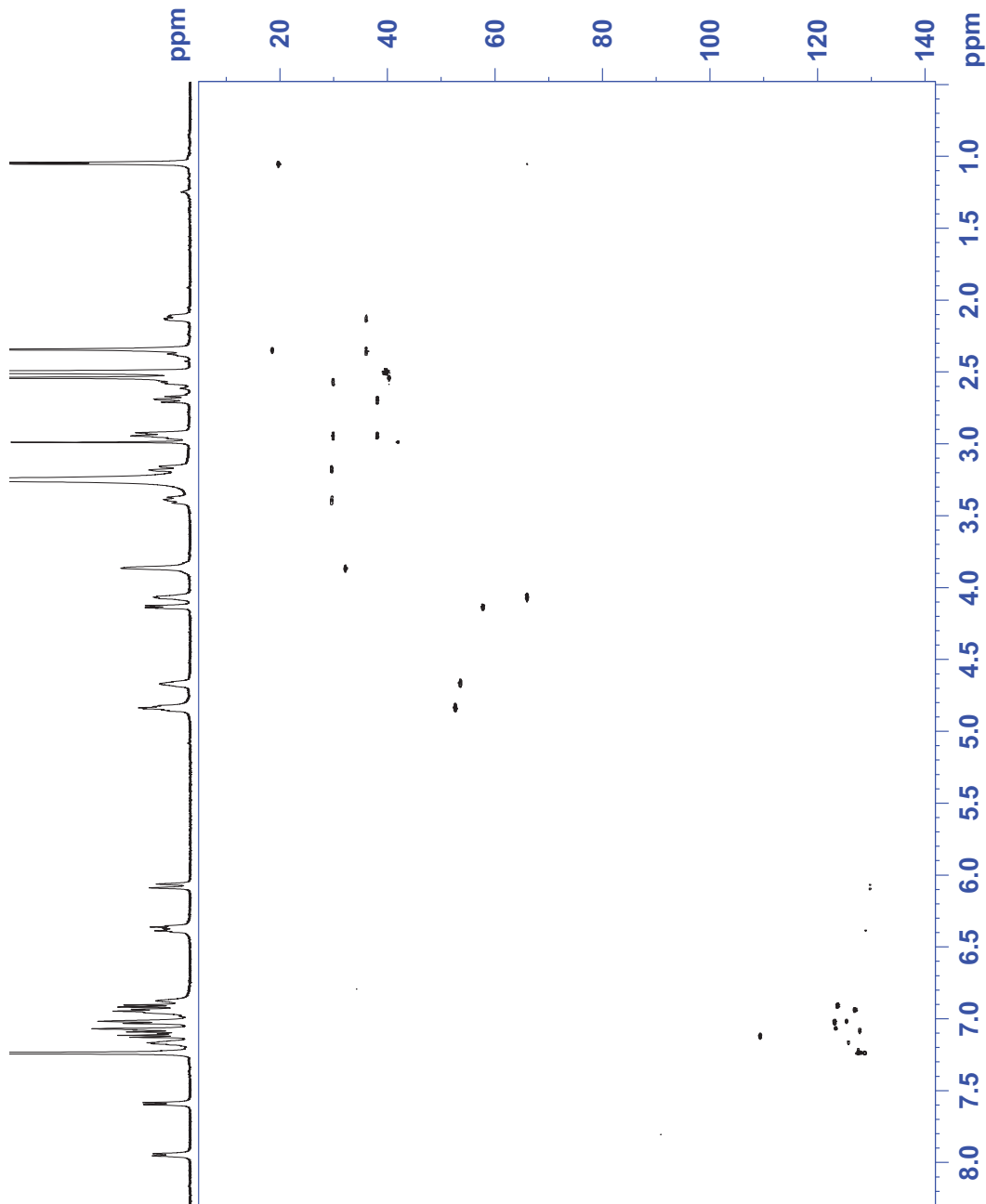


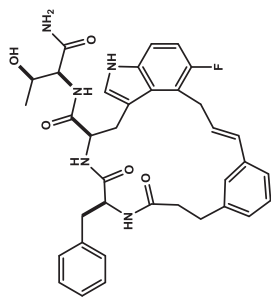
Current Data Parameters
 NAME KL-5-108-3-1_TROSE
 EXPNO 1
 PROCNO 1

F1 - Acquisition parameters
 TD 533
 SF01 150.9134 MHz
 FIDRES 45.302326 Hz
 SW 160.000 ppm
 FnMODE Echo-Antiecho

F2 - Processing parameters
 SI 4096
 SF 600.1300051 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

F1 - Processing parameters
 SI 4096
 MC2 echo-antiecho
 SF 150.9029231 MHz
 WDW TRAP
 SSB 2
 LB 0 Hz
 GB 0



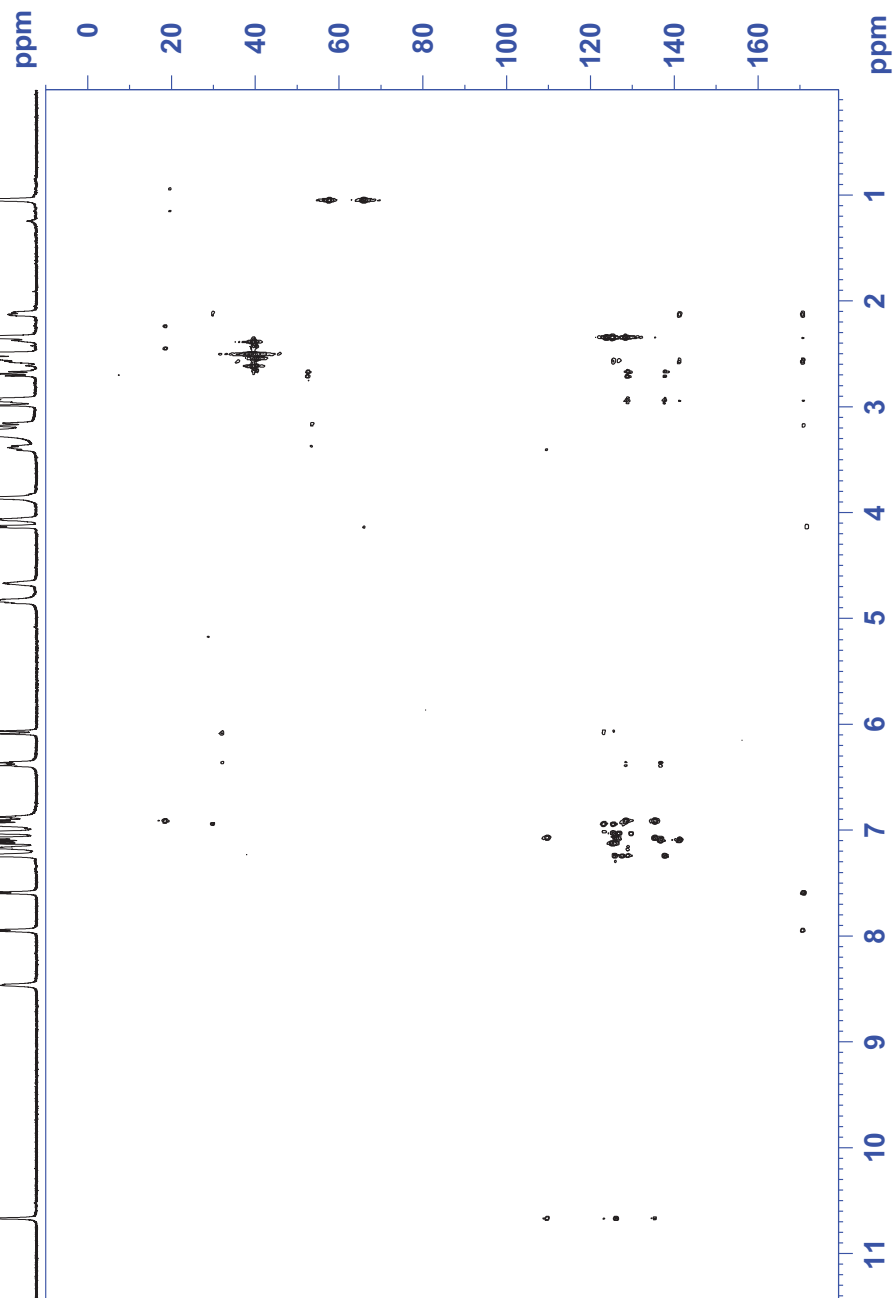


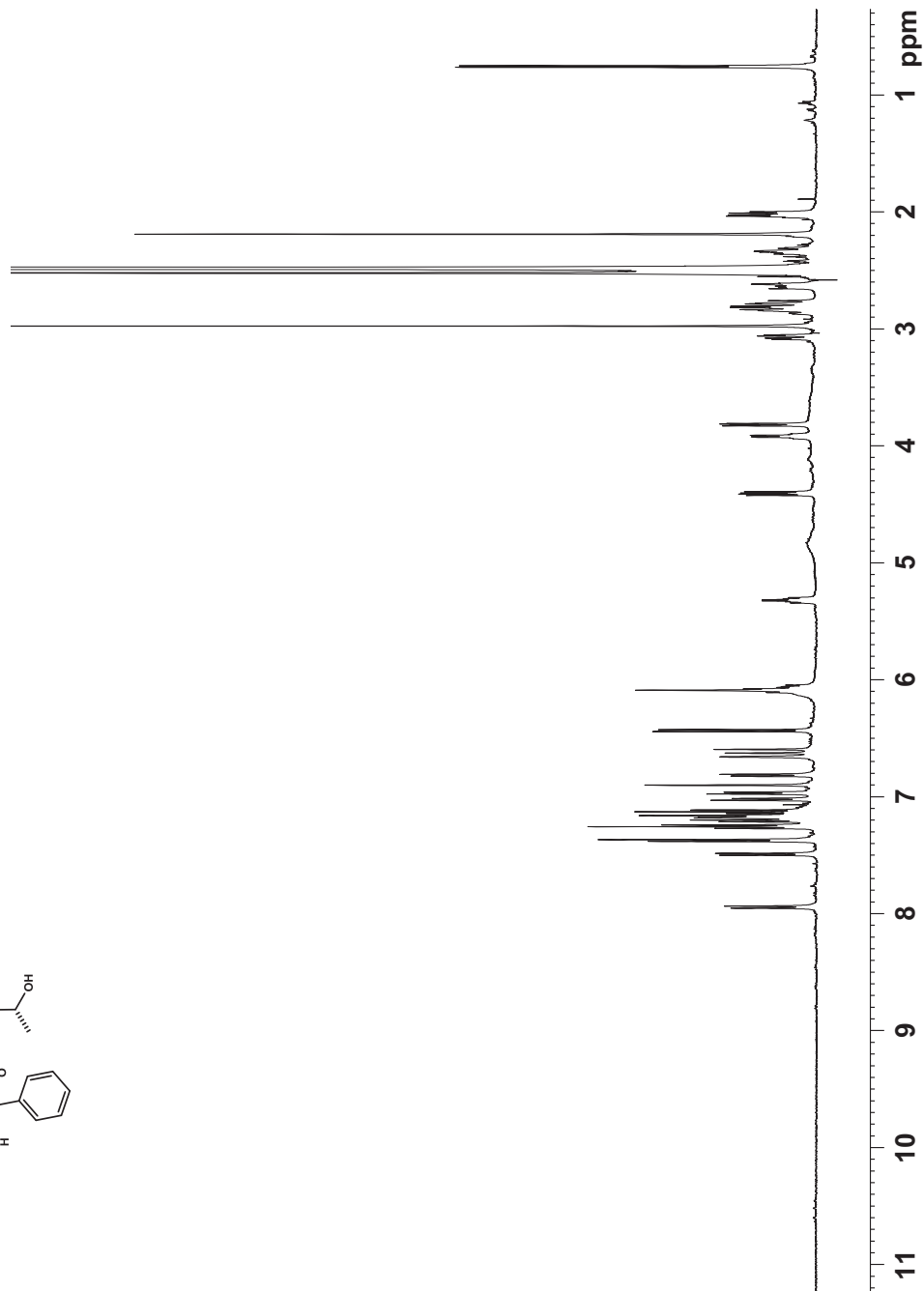
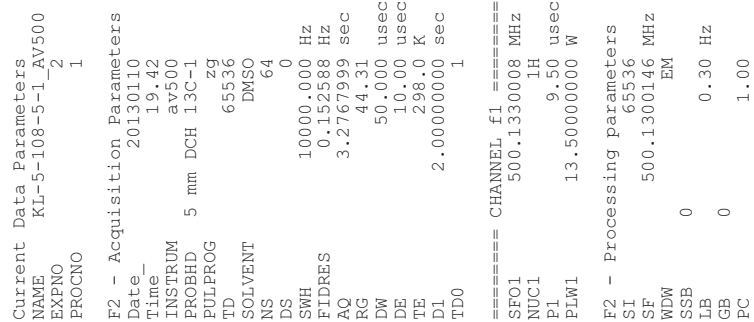
Current Data Parameters
 NAME KL-5-108-3-1_TROSE
 EXPNO 14
 PROCNO 1

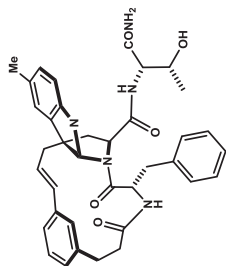
F1 - Acquisition parameters
 TD 256
 SF01 150.9156 MHz
 FIDRES 112.007698 Hz
 SW 190.000 ppm
 FnmODE QF

F2 - Processing parameters
 SI 4096
 SF 600.1300044 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.40

F1 - Processing parameters
 SI 4096
 MC2 QF
 SF 150.9029322 MHz
 WDW USER
 SSB 2
 LB 0 Hz
 GB 0







Current Data Parameters
 NAME KL-5-108-5-1_AV500
 EXFNO 3
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20130110
 Time_ 19.43
 INSTRUM av500
 PROBHD 5 mm DCH 13C-1
 PULPROG cosygmph
 TD 65536
 SOLVENT DMSO
 NS 4
 DS 8
 SWH 5498.534 Hz
 FIDRES 1.74245 Hz
 AQ 0.17245 sec
 RG 202.91
 DW 90.933 usec
 DE 10.00 usec
 TE 298.0 K
 D0 0.0007880 sec
 D1 0.0007880 sec
 D13 0.0000400 sec
 D16 0.0002000 sec
 INO 0.0001818 sec

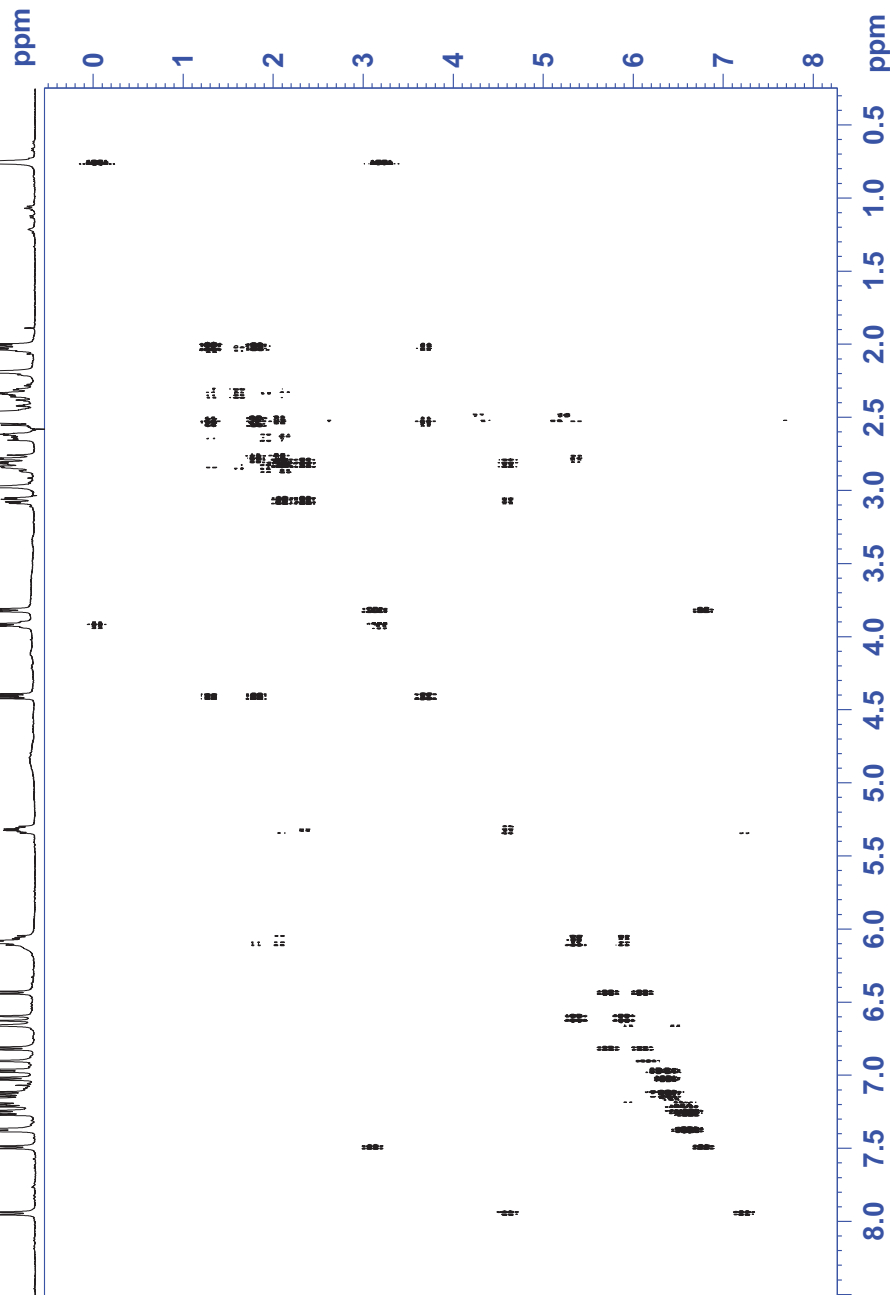
===== CHANNEL f1 =====
 SFO1 500.1327501 MHz
 NUC1 1H
 P1 9.50 usec
 PLW1 13.5000000 W

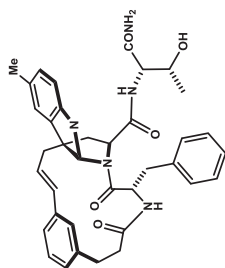
===== GRADIENT CHANNEL =====
 GPNAM[1] SMSQ10.100
 GPNAM[2] SMSQ10.100
 GP21 10.00 %
 GP22 20.00 %
 P16 1000.00 usec

F1 - Acquisition Parameters
 TD 256
 SFO1 500.1328 MHz
 FIDRES 21.486525 Hz
 SW 10.998 Ppm
 FMODE States-FFI

F2 - Processing parameters
 SI 2048
 SF 500.1300135 MHz
 SSB 1
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 65536
 SF 500.1300135 MHz
 SSB 1
 LB 0 Hz
 GB 0





Current Data Parameters
 NAME KL-5-108-5-1_AV500
 PROCNO 1

F2 - Acquisition Parameters

Time 20.24
 INSTRUM av500
 PROBD 5 mm DCH 13C-1
 PULPROG zgpg30
 TD 2048
 SOLVENT DMSO
 NS 4
 DS 4
 SWH 5000.000 Hz
 FIDRES 2.441406 Hz
 AQ 0.2048000 sec
 RG 327.680
 DW 100.000 usec
 DE 10.00 usec
 TE 298.0 K
 D0 0.0000000 sec
 D1 2.0000000 sec
 D2 0.0000000 sec
 D3 0.0600000 sec
 D4 0.0300000 sec
 D5 0.0300000 sec
 D6 0.0300000 sec
 D7 0.0300000 sec
 D8 0.0300000 sec
 D9 0.0300000 sec
 D10 0.0300000 sec
 D11 0.0300000 sec
 D12 0.0300000 sec
 D13 0.0300000 sec
 D14 0.0300000 sec
 D15 0.0300000 sec
 D16 0.0300000 sec
 D17 0.0300000 sec
 D18 0.0300000 sec
 D19 0.0300000 sec
 D20 0.0300000 sec
 D21 0.0300000 sec
 D22 0.0300000 sec
 D23 0.0300000 sec
 D24 0.0300000 sec
 L1 24

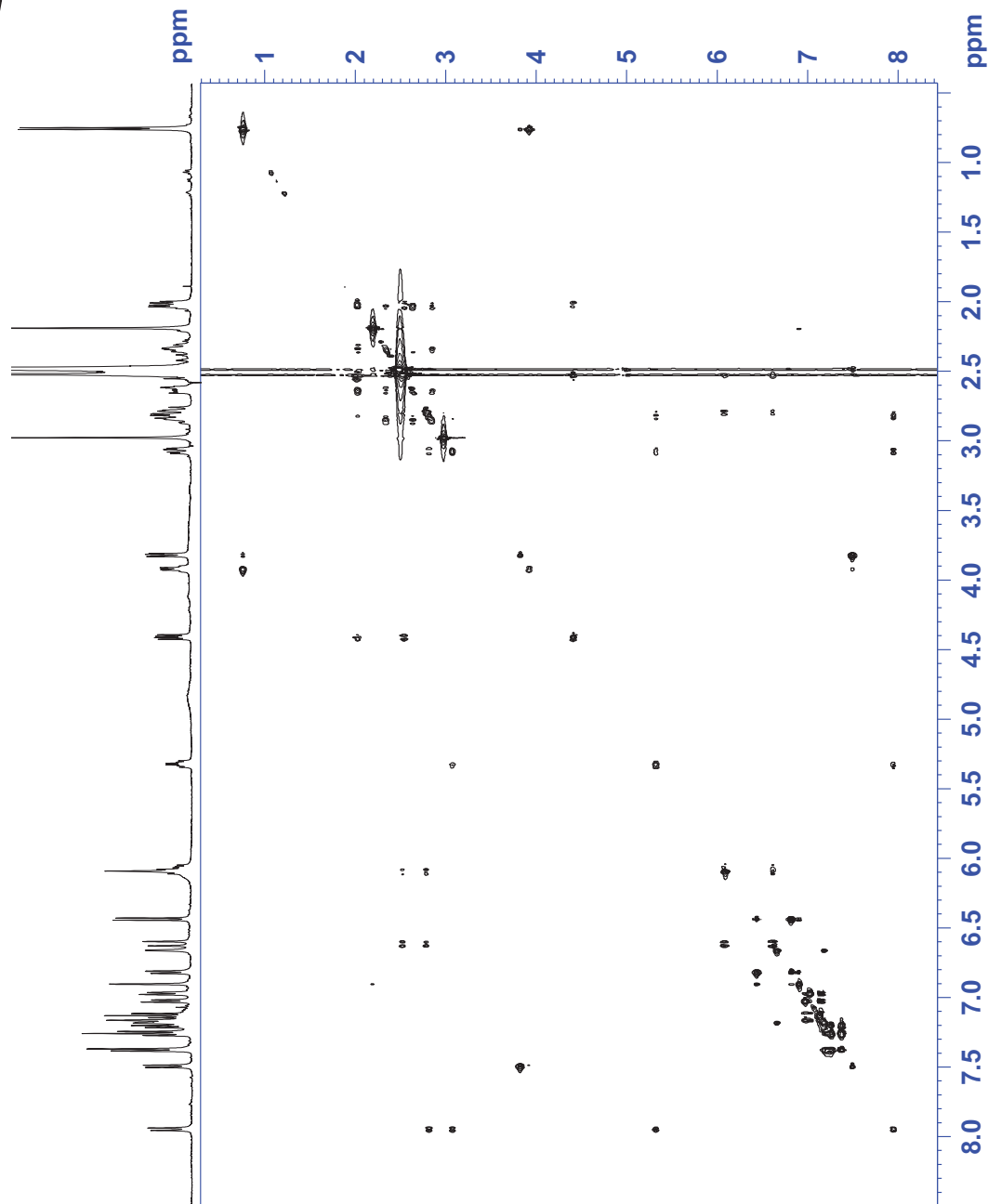
===== CHANNEL f1 =====
 SFO1 500.1325007 MHz
 NUC1 1H
 P1 9.00 usec
 P2 19.00 usec
 P3 19.00 usec
 P4 26.68 usec
 P5 26.68 usec
 P6 40.00 usec
 P7 40.00 usec
 P8 40.00 usec
 P9 40.00 usec
 P10 40.00 usec
 P11 40.00 usec
 P12 40.00 usec
 P13 40.00 usec
 P14 40.00 usec
 P15 40.00 usec
 P16 40.00 usec
 P17 2500.00 usec
 PLW1 13.50000000 W
 PLW10 0.84375000 W

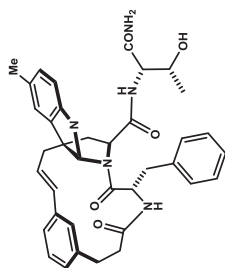
===== GRADIENT CHANNEL =====
 GPM1[1] SINE.100
 GPM1[2] SINE.100
 GPM2[1] SINE.100
 GPM2[2] SINE.100
 GPM3[1] SINE.100
 GPM3[2] SINE.100
 GPM4[1] SINE.100
 GPM4[2] SINE.100
 GPM5[1] SINE.100
 GPM5[2] SINE.100
 GPM6[1] SINE.100
 GPM6[2] SINE.100
 GPM7[1] SINE.100
 GPM7[2] SINE.100
 GPM8[1] SINE.100
 GPM8[2] SINE.100
 GPM9[1] SINE.100
 GPM9[2] SINE.100
 GPM10[1] SINE.100
 GPM10[2] SINE.100
 GPM11[1] SINE.100
 GPM11[2] SINE.100
 GPM12[1] SINE.100
 GPM12[2] SINE.100
 GPM13[1] SINE.100
 GPM13[2] SINE.100
 GPM14[1] SINE.100
 GPM14[2] SINE.100
 GPM15[1] SINE.100
 GPM15[2] SINE.100
 GPM16[1] SINE.100
 GPM16[2] SINE.100
 GPM17[1] SINE.100
 GPM17[2] SINE.100
 GPM18[1] SINE.100
 GPM18[2] SINE.100
 GPM19[1] SINE.100
 GPM19[2] SINE.100
 GPM20[1] SINE.100
 GPM20[2] SINE.100
 GPM21[1] SINE.100
 GPM21[2] SINE.100
 GPM22[1] SINE.100
 GPM22[2] SINE.100
 GPM23[1] SINE.100
 GPM23[2] SINE.100
 GPM24[1] SINE.100
 GPM24[2] SINE.100

F1 - Acquisition Parameters
 TD 256
 SFO1 500.1325 MHz
 FIDRES 19.51250 Hz
 SF 500.1325007 MHz
 FWHM 0.0000000 Hz
 F2 - Processing Parameters

SF 500.130135 MHz
 WDW 0 Hz
 SSB 0 Hz
 GB 0 Hz
 PC 1.00

F1 - Processing Parameters
 SI 2048
 MC2 echo-artlecho
 SF 500.130135 MHz
 WDW 0 Hz
 SSB 0 Hz
 GB 0 Hz





Current Data Parameters
 NAME RL-9-108-5-1_AVS00
 EXPNO 5
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20100521
 Time 21:05

INSTRUM 8 mm BBO avx00
 PULPROG zgpg30
 TD 2048

TD0 16
 NS 16
 DS 16

SWH 5000.16
 FIDRES 2.441406 Hz
 AQ 0.2048000 sec

RG 327.68
 DW 100.000 usec
 DE 10.00 usec

TE 300.2 K
 CNST2 145.0000000

D0 0.0000300 sec
 D1 0.0000300 sec

D2 0.0000300 sec
 D3 0.0000300 sec

D4 0.0000300 sec
 D5 0.0000300 sec

D6 0.0000300 sec
 D7 0.0000300 sec

D8 0.0000300 sec
 D9 0.0000300 sec

D10 0.0000300 sec
 D11 0.0000300 sec

D12 0.0000300 sec
 D13 0.0000300 sec

D14 0.0000300 sec
 D15 0.0000300 sec

D16 0.0000300 sec
 D17 0.0000300 sec

D18 0.0000300 sec
 D19 0.0000300 sec

D20 0.0000300 sec
 D21 0.0000300 sec

D22 0.0000300 sec
 D23 0.0000300 sec

D24 0.0000300 sec
 D25 0.0000300 sec

D26 0.0000300 sec
 D27 0.0000300 sec

D28 0.0000300 sec
 D29 0.0000300 sec

D30 0.0000300 sec
 D31 0.0000300 sec

D32 0.0000300 sec
 D33 0.0000300 sec

D34 0.0000300 sec
 D35 0.0000300 sec

D36 0.0000300 sec
 D37 0.0000300 sec

D38 0.0000300 sec
 D39 0.0000300 sec

D40 0.0000300 sec
 D41 0.0000300 sec

D42 0.0000300 sec
 D43 0.0000300 sec

D44 0.0000300 sec
 D45 0.0000300 sec

D46 0.0000300 sec
 D47 0.0000300 sec

D48 0.0000300 sec
 D49 0.0000300 sec

D50 0.0000300 sec
 D51 0.0000300 sec

D52 0.0000300 sec
 D53 0.0000300 sec

D54 0.0000300 sec
 D55 0.0000300 sec

D56 0.0000300 sec
 D57 0.0000300 sec

D58 0.0000300 sec
 D59 0.0000300 sec

D60 0.0000300 sec
 D61 0.0000300 sec

D62 0.0000300 sec
 D63 0.0000300 sec

D64 0.0000300 sec
 D65 0.0000300 sec

D66 0.0000300 sec
 D67 0.0000300 sec

D68 0.0000300 sec
 D69 0.0000300 sec

D70 0.0000300 sec
 D71 0.0000300 sec

D72 0.0000300 sec
 D73 0.0000300 sec

D74 0.0000300 sec
 D75 0.0000300 sec

D76 0.0000300 sec
 D77 0.0000300 sec

D78 0.0000300 sec
 D79 0.0000300 sec

D80 0.0000300 sec
 D81 0.0000300 sec

D82 0.0000300 sec
 D83 0.0000300 sec

D84 0.0000300 sec
 D85 0.0000300 sec

D86 0.0000300 sec
 D87 0.0000300 sec

D88 0.0000300 sec
 D89 0.0000300 sec

D90 0.0000300 sec
 D91 0.0000300 sec

D92 0.0000300 sec
 D93 0.0000300 sec

D94 0.0000300 sec
 D95 0.0000300 sec

D96 0.0000300 sec
 D97 0.0000300 sec

D98 0.0000300 sec
 D99 0.0000300 sec

D100 0.0000300 sec
 D101 0.0000300 sec

D102 0.0000300 sec
 D103 0.0000300 sec

D104 0.0000300 sec
 D105 0.0000300 sec

D106 0.0000300 sec
 D107 0.0000300 sec

D108 0.0000300 sec
 D109 0.0000300 sec

D110 0.0000300 sec
 D111 0.0000300 sec

D112 0.0000300 sec
 D113 0.0000300 sec

D114 0.0000300 sec
 D115 0.0000300 sec

D116 0.0000300 sec
 D117 0.0000300 sec

D118 0.0000300 sec
 D119 0.0000300 sec

D120 0.0000300 sec
 D121 0.0000300 sec

D122 0.0000300 sec
 D123 0.0000300 sec

D124 0.0000300 sec
 D125 0.0000300 sec

D126 0.0000300 sec
 D127 0.0000300 sec

D128 0.0000300 sec
 D129 0.0000300 sec

D130 0.0000300 sec
 D131 0.0000300 sec

D132 0.0000300 sec
 D133 0.0000300 sec

D134 0.0000300 sec
 D135 0.0000300 sec

D136 0.0000300 sec
 D137 0.0000300 sec

D138 0.0000300 sec
 D139 0.0000300 sec

D140 0.0000300 sec
 D141 0.0000300 sec

D142 0.0000300 sec
 D143 0.0000300 sec

D144 0.0000300 sec
 D145 0.0000300 sec

D146 0.0000300 sec
 D147 0.0000300 sec

D148 0.0000300 sec
 D149 0.0000300 sec

D150 0.0000300 sec
 D151 0.0000300 sec

D152 0.0000300 sec
 D153 0.0000300 sec

D154 0.0000300 sec
 D155 0.0000300 sec

D156 0.0000300 sec
 D157 0.0000300 sec

D158 0.0000300 sec
 D159 0.0000300 sec

D160 0.0000300 sec
 D161 0.0000300 sec

D162 0.0000300 sec
 D163 0.0000300 sec

D164 0.0000300 sec
 D165 0.0000300 sec

D166 0.0000300 sec
 D167 0.0000300 sec

D168 0.0000300 sec
 D169 0.0000300 sec

D170 0.0000300 sec
 D171 0.0000300 sec

D172 0.0000300 sec
 D173 0.0000300 sec

D174 0.0000300 sec
 D175 0.0000300 sec

D176 0.0000300 sec
 D177 0.0000300 sec

D178 0.0000300 sec
 D179 0.0000300 sec

D180 0.0000300 sec
 D181 0.0000300 sec

D182 0.0000300 sec
 D183 0.0000300 sec

D184 0.0000300 sec
 D185 0.0000300 sec

D186 0.0000300 sec
 D187 0.0000300 sec

D188 0.0000300 sec
 D189 0.0000300 sec

D190 0.0000300 sec
 D191 0.0000300 sec

D192 0.0000300 sec
 D193 0.0000300 sec

D194 0.0000300 sec
 D195 0.0000300 sec

D196 0.0000300 sec
 D197 0.0000300 sec

D198 0.0000300 sec
 D199 0.0000300 sec

D200 0.0000300 sec
 D201 0.0000300 sec

D202 0.0000300 sec
 D203 0.0000300 sec

D204 0.0000300 sec
 D205 0.0000300 sec

D206 0.0000300 sec
 D207 0.0000300 sec

D208 0.0000300 sec
 D209 0.0000300 sec

D210 0.0000300 sec
 D211 0.0000300 sec

D212 0.0000300 sec
 D213 0.0000300 sec

D214 0.0000300 sec
 D215 0.0000300 sec

D216 0.0000300 sec
 D217 0.0000300 sec

D218 0.0000300 sec
 D219 0.0000300 sec

D220 0.0000300 sec
 D221 0.0000300 sec

D222 0.0000300 sec
 D223 0.0000300 sec

D224 0.0000300 sec
 D225 0.0000300 sec

D226 0.0000300 sec
 D227 0.0000300 sec

D228 0.0000300 sec
 D229 0.0000300 sec

D230 0.0000300 sec
 D231 0.0000300 sec

D232 0.0000300 sec
 D233 0.0000300 sec

D234 0.0000300 sec
 D235 0.0000300 sec

D236 0.0000300 sec
 D237 0.0000300 sec

D238 0.0000300 sec
 D239 0.0000300 sec

D240 0.0000300 sec
 D241 0.0000300 sec

D242 0.0000300 sec
 D243 0.0000300 sec

D244 0.0000300 sec
 D245 0.0000300 sec

D246 0.0000300 sec
 D247 0.0000300 sec

D248 0.0000300 sec
 D249 0.0000300 sec

D250 0.0000300 sec
 D251 0.0000300 sec

D252 0.0000300 sec
 D253 0.0000300 sec

D254 0.0000300 sec
 D255 0.0000300 sec

D256 0.0000300 sec
 D257 0.0000300 sec

D258 0.0000300 sec
 D259 0.0000300 sec

D260 0.0000300 sec
 D261 0.0000300 sec

D262 0.0000300 sec
 D263 0.0000300 sec

D264 0.0000300 sec
 D265 0.0000300 sec

D266 0.0000300 sec
 D267 0.0000300 sec

D268 0.0000300 sec
 D269 0.0000300 sec

D270 0.0000300 sec
 D271 0.0000300 sec

D272 0.0000300 sec
 D273 0.0000300 sec

D274 0.0000300 sec
 D275 0.0000300 sec

D276 0.0000300 sec
 D277 0.0000300 sec

D278 0.0000300 sec
 D279 0.0000300 sec

D280 0.0000300 sec
 D281 0.0000300 sec

D282 0.0000300 sec
 D283 0.0000300 sec

D284 0.0000300 sec
 D285 0.0000300 sec

D286 0.0000300 sec
 D287 0.0000300 sec

D288 0.0000300 sec
 D289 0.0000300 sec

D290 0.0000300 sec
 D291 0.0000300 sec

D292 0.0000300 sec
 D293 0.0000300 sec

D294 0.0000300 sec
 D295 0.0000300 sec

D296 0.0000300 sec
 D297 0.0000300 sec

D298 0.0000300 sec
 D299 0.0000300 sec

D300 0.0000300 sec
 D301 0.0000300 sec

D302 0.0000300 sec
 D303 0.0000300 sec

D304 0.0000300 sec
 D305 0.0000300 sec

D306 0.0000300 sec
 D307 0.0000300 sec

D308 0.0000300 sec
 D309 0.0000300 sec

D310 0.0000300 sec
 D311 0.0000300 sec

D312 0.0000300 sec
 D313 0.0000300 sec

D314 0.0000300 sec
 D315 0.0000300 sec

D316 0.0000300 sec
 D317 0.0000300 sec

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 D319 0.0000300 sec

D320 0.0000300 sec
 D321 0.0000300 sec

D322 0.0000300 sec
 D323 0.0000300 sec

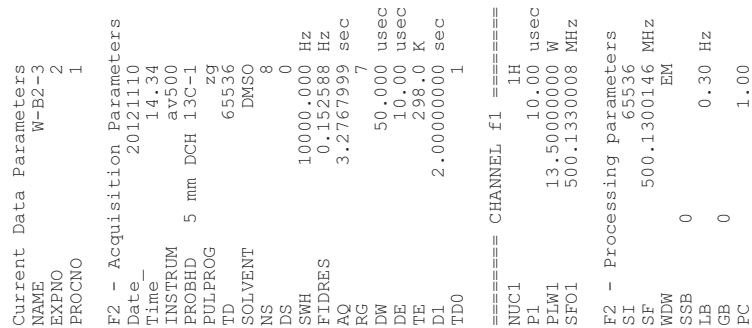
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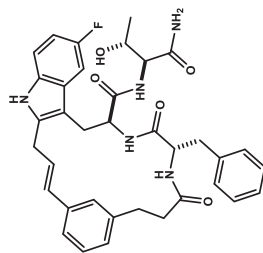
D326 0.0000300 sec
 D327 0.0000300 sec

D328 0.0000300 sec
 D329 0.0000300 sec

D330 0.0000300 sec
 D331 0.0000300 sec

D332 0.0000300 sec
 D333 0.0000300



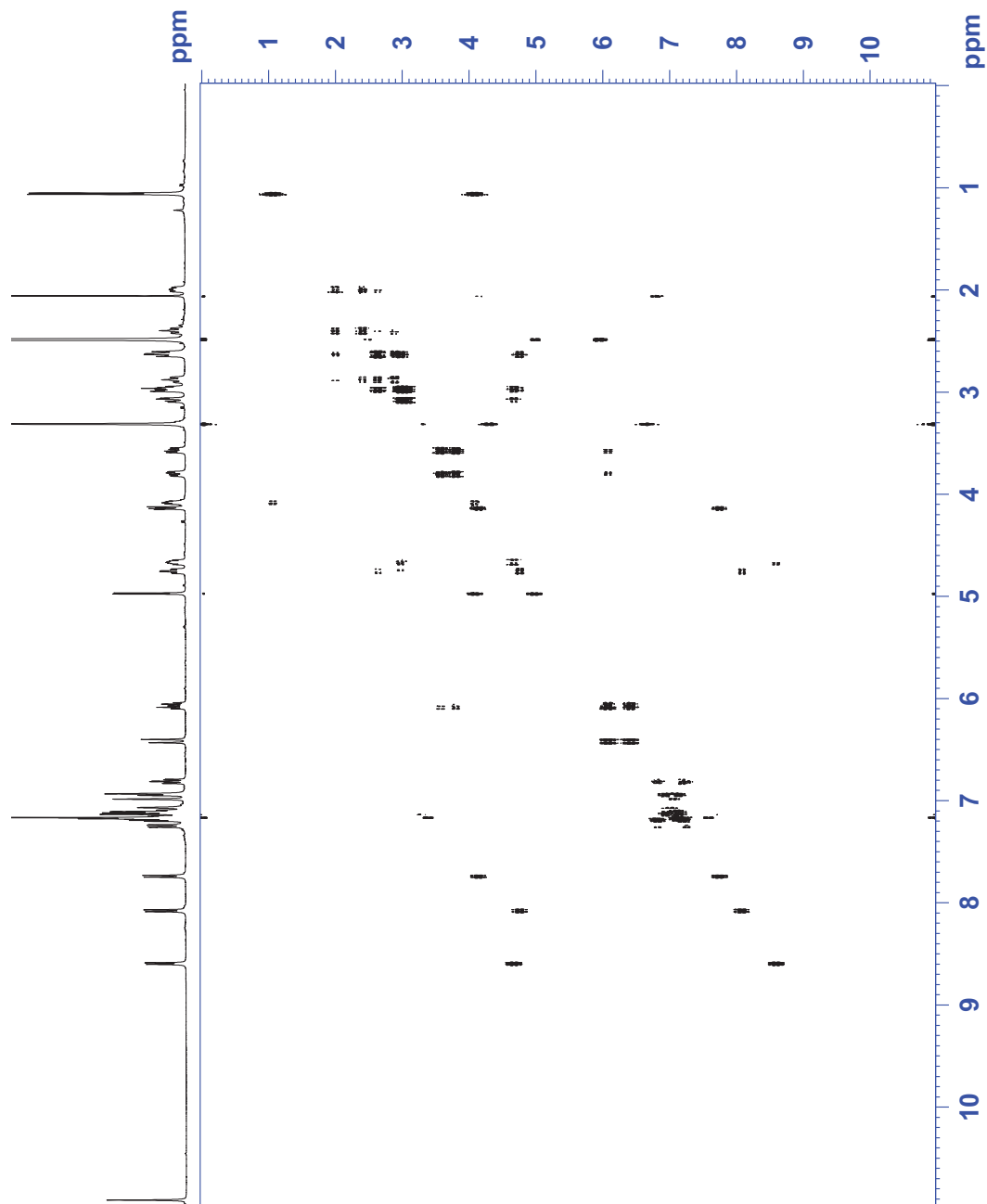


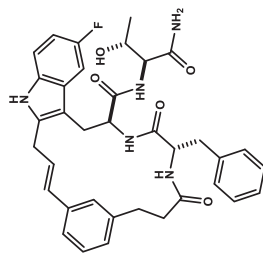
Current Data Parameters
 NAME W-B2-3
 EXPNO 3
 PROCNO 1

F1 - Acquisition parameters
 TD 256
 SFO1 500.1328 MHz
 FIDRES 21.490080 Hz
 SW 11.000 ppm
 FnmODE States-TPPI

F2 - Processing parameters
 SI 2048
 SF 500.1300135 MHz
 WDW SINE
 SSB 1
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 2048
 MC2 States-TPPI
 SF 500.1300112 MHz
 WDW GM
 SSB 1
 LB 0 Hz
 GB 0



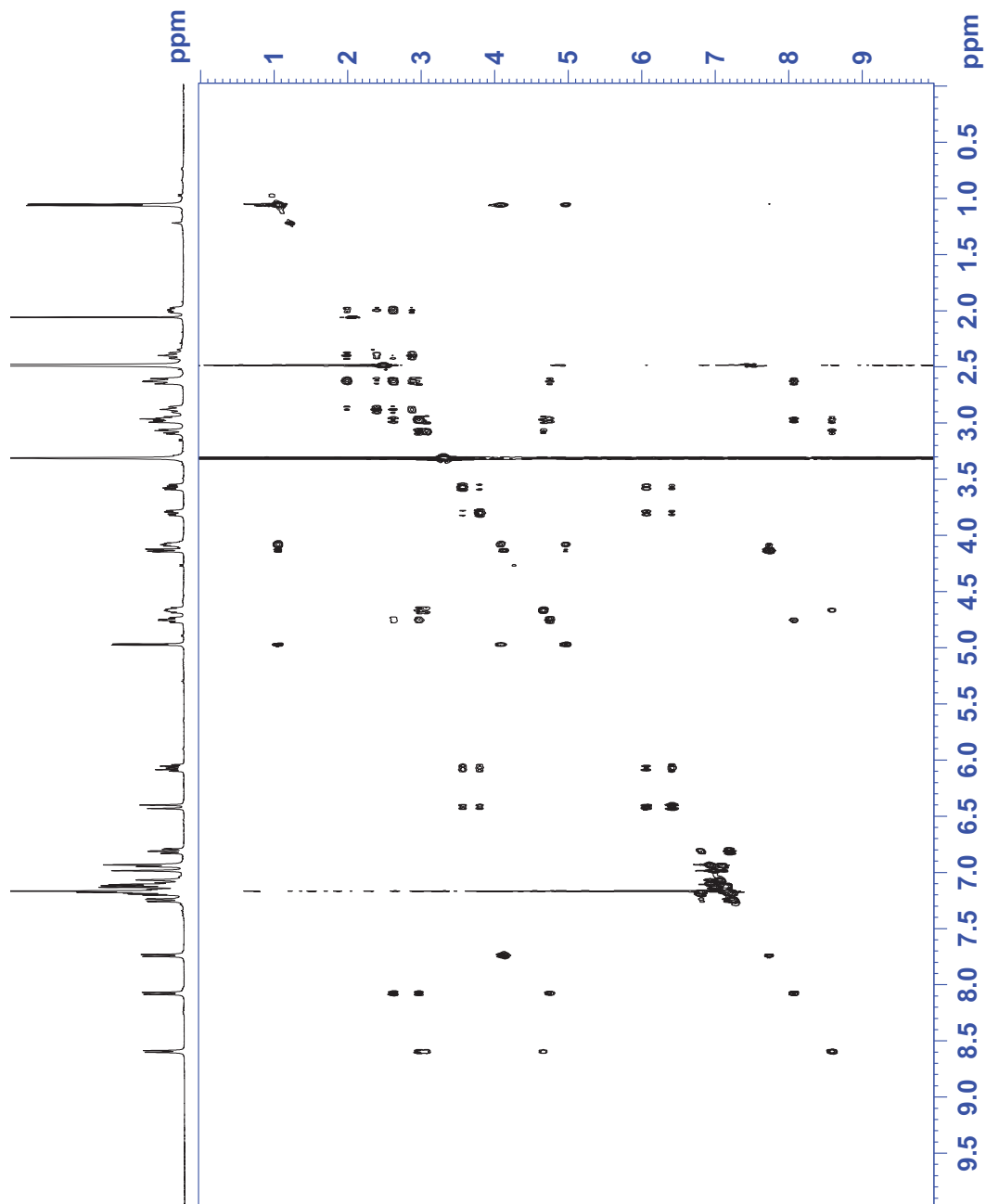


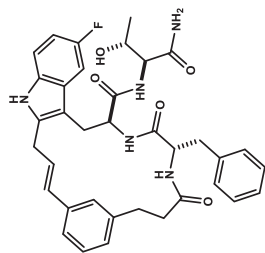
Current Data Parameters
 NAME W-B2-3
 EXPNO 4
 PROCNO 1

F1 - Acquisition parameters
 TD 256
 SF01 500.1325 MHz
 FIDRES 19.536406 Hz
 SW 10.000 ppm
 FnMODE Echo-Antiecho

F2 - Processing parameters
 SI 2048
 SF 500.1300135 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 2048
 MC2 echo-antiecho
 SF 500.1300135 MHz
 WDW TRAP
 SSB 2
 LB 0 Hz
 GB 0



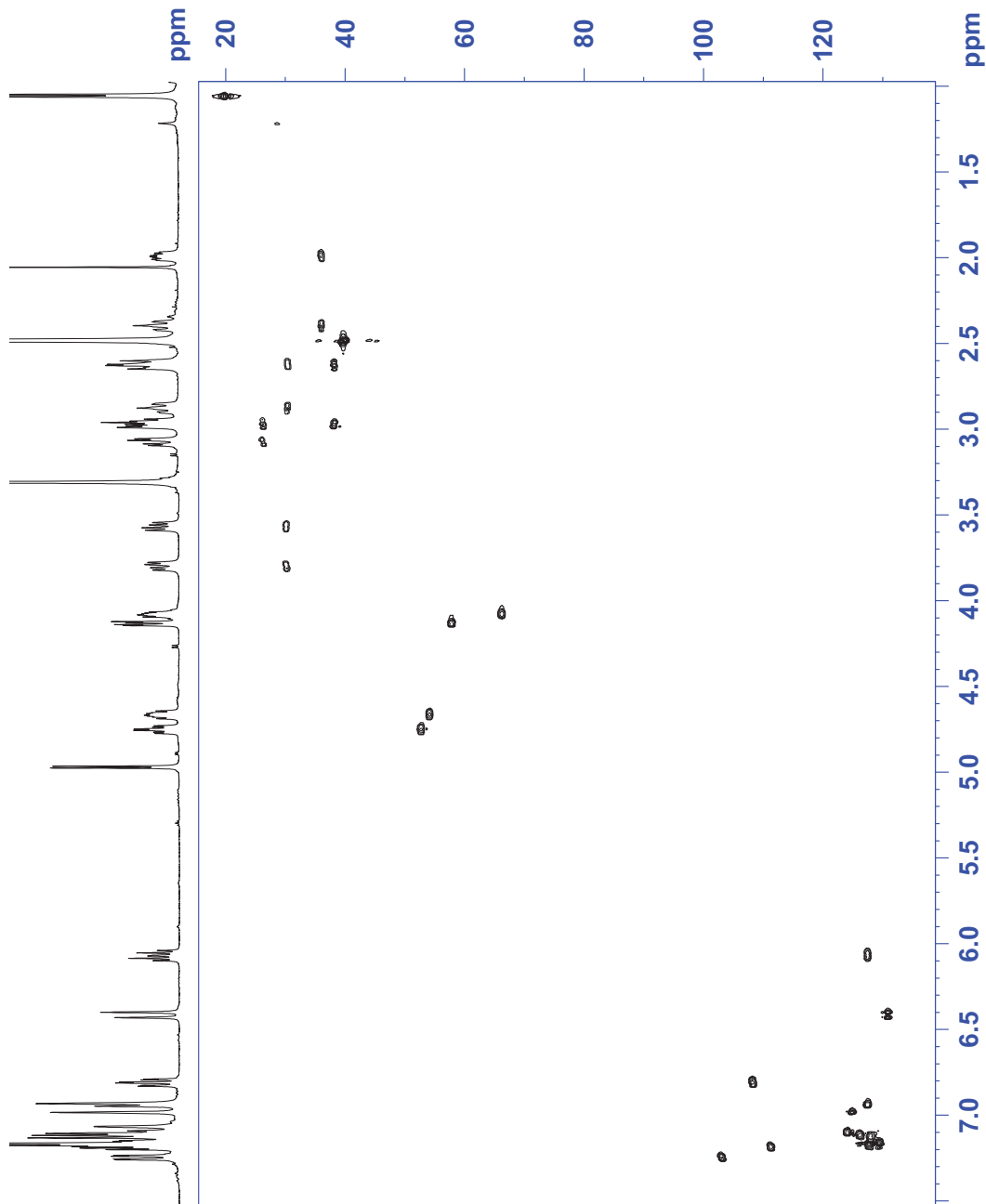


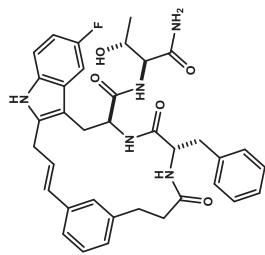
Current Data Parameters
NAME W-B2-3
EXPNO 5
PROCNO 1

F1 - Acquisition parameters
TD 256
SF01 125.7678 MHz
FIDRES 98.255890 Hz
SW 200.000 ppm
FnMODE Echo-Antiecho

F2 - Processing parameters
SI 2048
SF 500.1300135 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0
PC 1.00

F1 - Processing parameters
SI 2048
MC2 echo-antiecho
SF 125.7578472 MHz
WDW TRAP
SSB 2
LB 0 Hz
GB 0



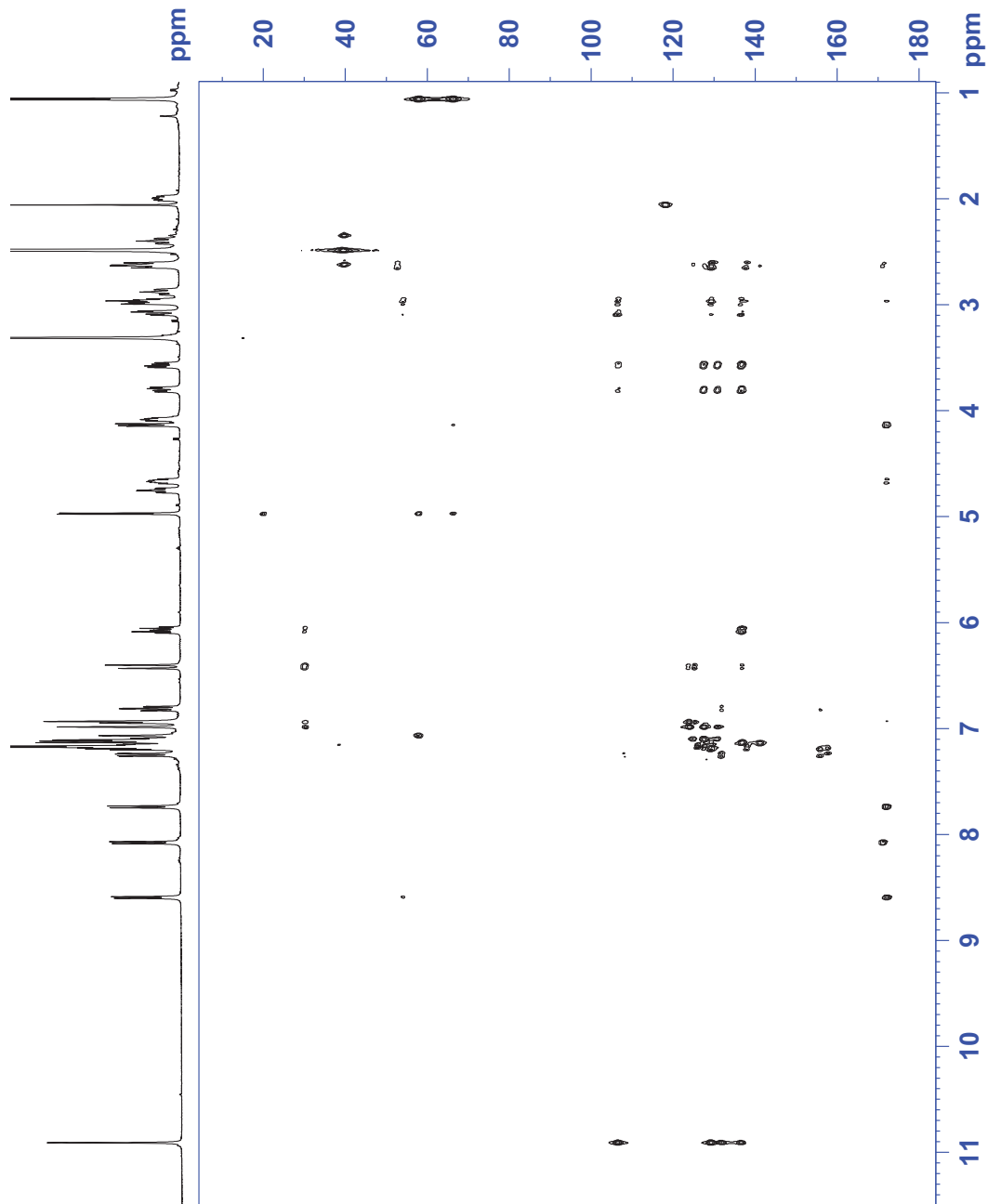


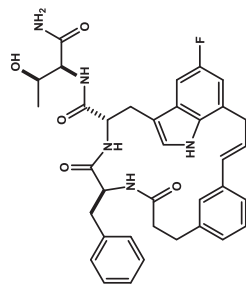
Current Data Parameters
 NAME W-B2-3
 EXPNO 6
 PROCNO 1

F1 - Acquisition parameters
 TD 256
 SF01 125.7704 MHz
 FIDRES 98.257607 Hz
 SW 199.999 ppm
 FnmODE QF

F2 - Processing parameters
 SI 2048
 SF 500.1300135 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 2048
 MC2 QF
 SF 125.7578472 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0





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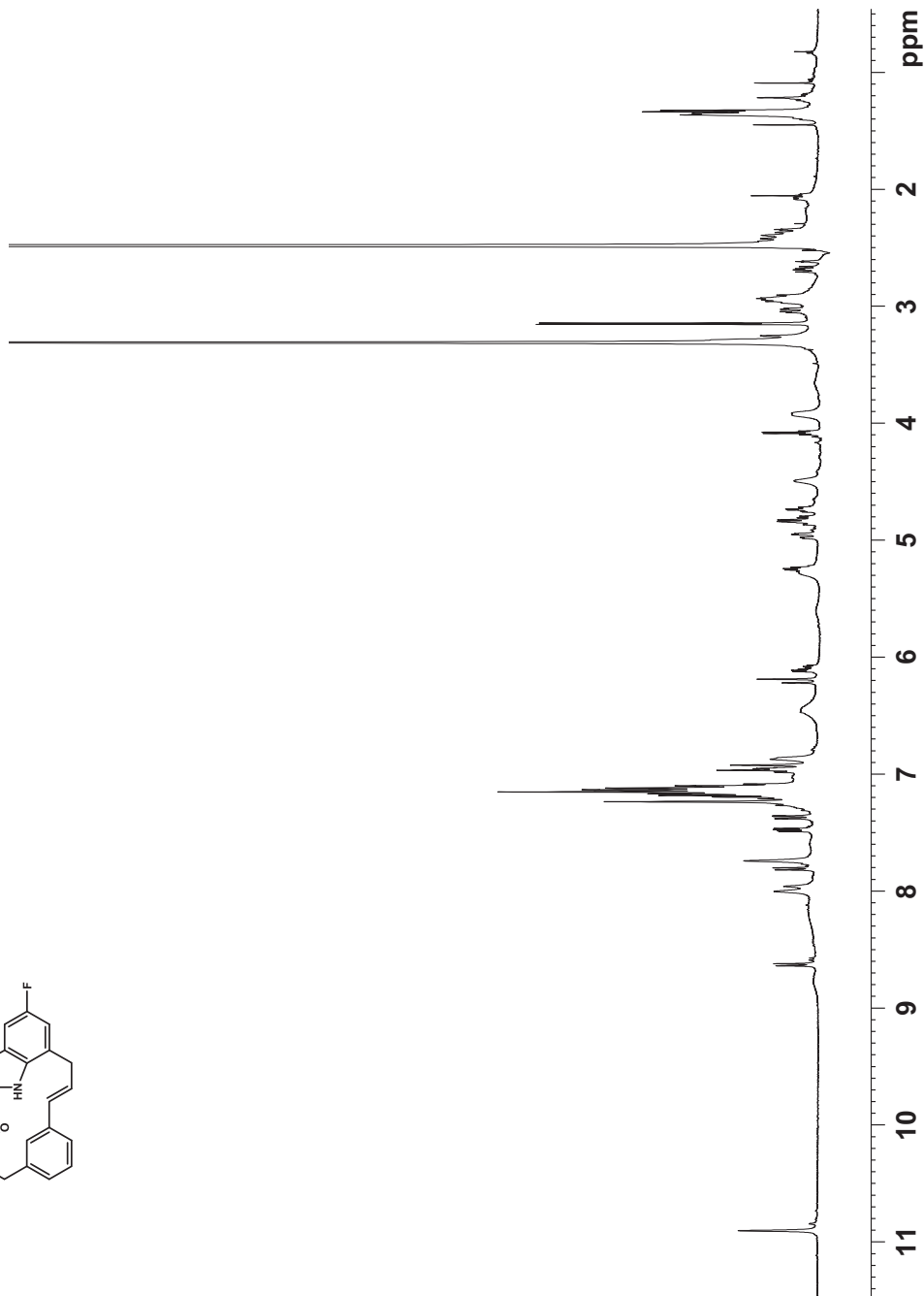
Current Data Parameters
NAME      W-B2-4
EXPNO     1
PROCNO    1

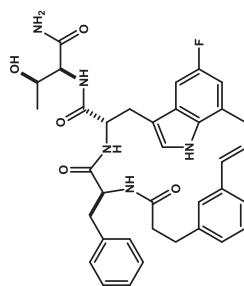
F2 - Acquisition Parameters
Date_     20121110
Time      15.59
INSTRUM   av500
PROBHD    5 mm DCH 13C-1
PULPROG   zg30
TD         65536
SOLVENT   DMSO
NS         8
DS         0
SWH        10000.000 Hz
FIDRES     0.152588 Hz
AQ         3.2767999 sec
RG         11
DW         50.000 usec
DE         10.00 usec
TE         298.0 K
D1         2.00000000 sec
TD0        1

===== CHANNEL f1 =====
NUC1       1H
P1         10.00 usec
PLW1       13.50000000 W
SFO1       500.1330008 MHz

F2 - Processing parameters
SI         65536
SF         500.1300146 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00

```



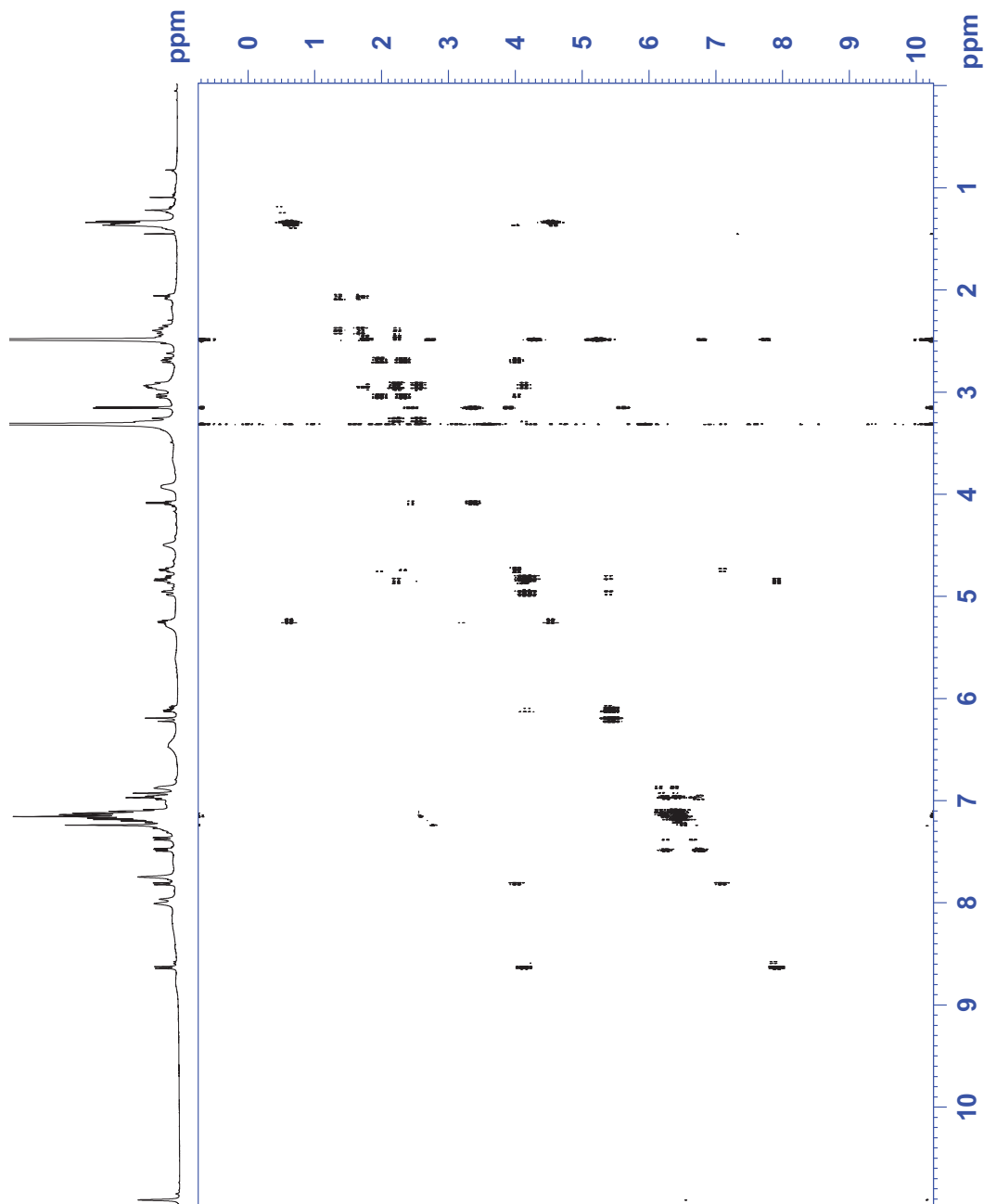


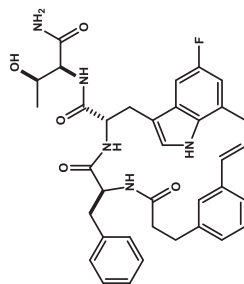
Current Data Parameters
NAME W-B2-4
EXPNO 3
PROCNO 1

F1 - Acquisition parameters
TD 256
SF01 500.1328 MHz
FIDRES 21.490080 Hz
SW 11.000 ppm
FnMODE States-TPPI

F2 - Processing parameters
SI 2048
SF 500.1300135 MHz
WDW SINE
SSB 1
LB 0 Hz
GB 0
PC 1.00

F1 - Processing parameters
SI 2048
MC2 States-TPPI
SF 500.1303720 MHz
WDW GM
SSB 1
LB 0 Hz
GB 0



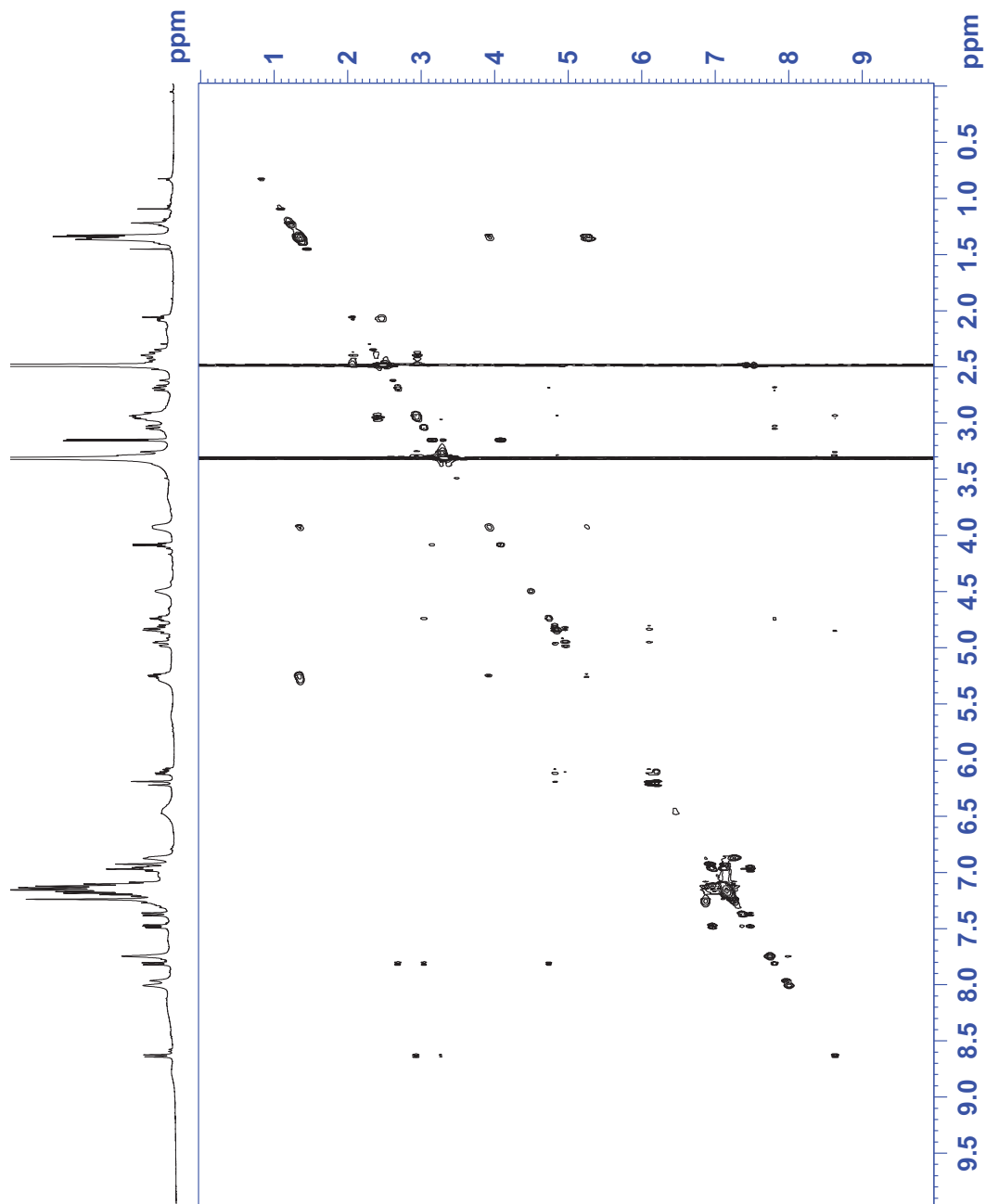


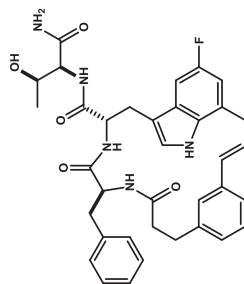
Current Data Parameters
 NAME W-B2-4
 EXPNO 4
 PROCNO 1

F1 - Acquisition parameters
 TD 256
 SF01 500.1325 MHz
 FIDRES 19.536406 Hz
 SW 10.000 ppm
 FnMODE Echo-Antiecho

F2 - Processing parameters
 SI 2048
 SF 500.1300135 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 2048
 MC2 echo-antiecho
 SF 500.1300135 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0



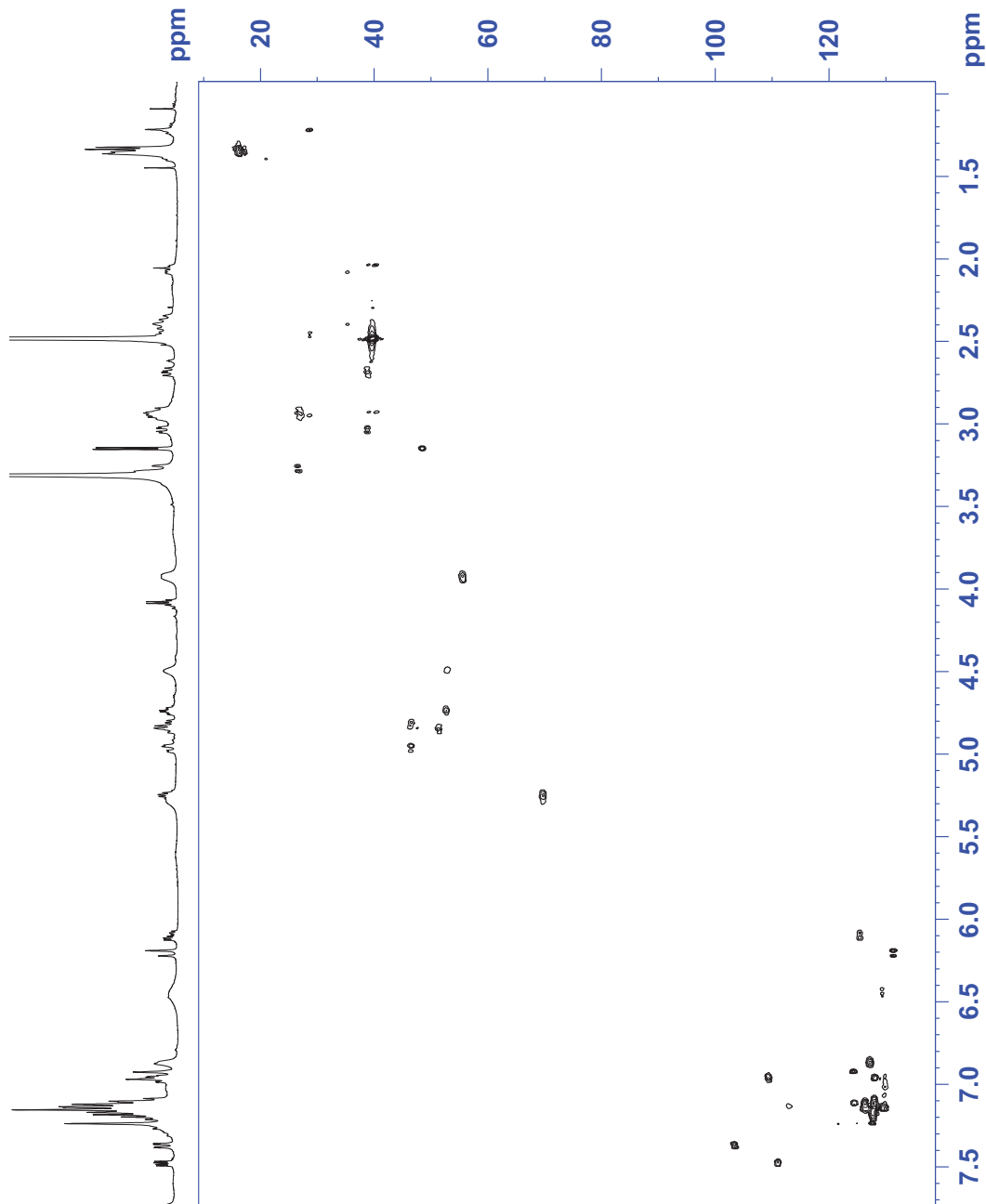


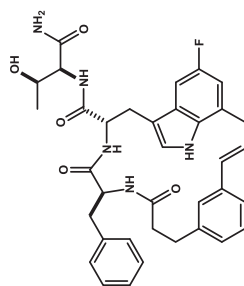
Current Data Parameters
 NAME W-B2-4
 EXPNO 5
 PROCNO 1

F1 - Acquisition parameters
 TD 256
 SF01 125.7678 MHz
 FIDRES 98.255890 Hz
 SW 200.000 ppm
 FnMODE Echo-Antiecho

F2 - Processing parameters
 SI 2048
 SF 500.1300135 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 2048
 MC2 echo-antiecho
 SF 125.7578472 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0



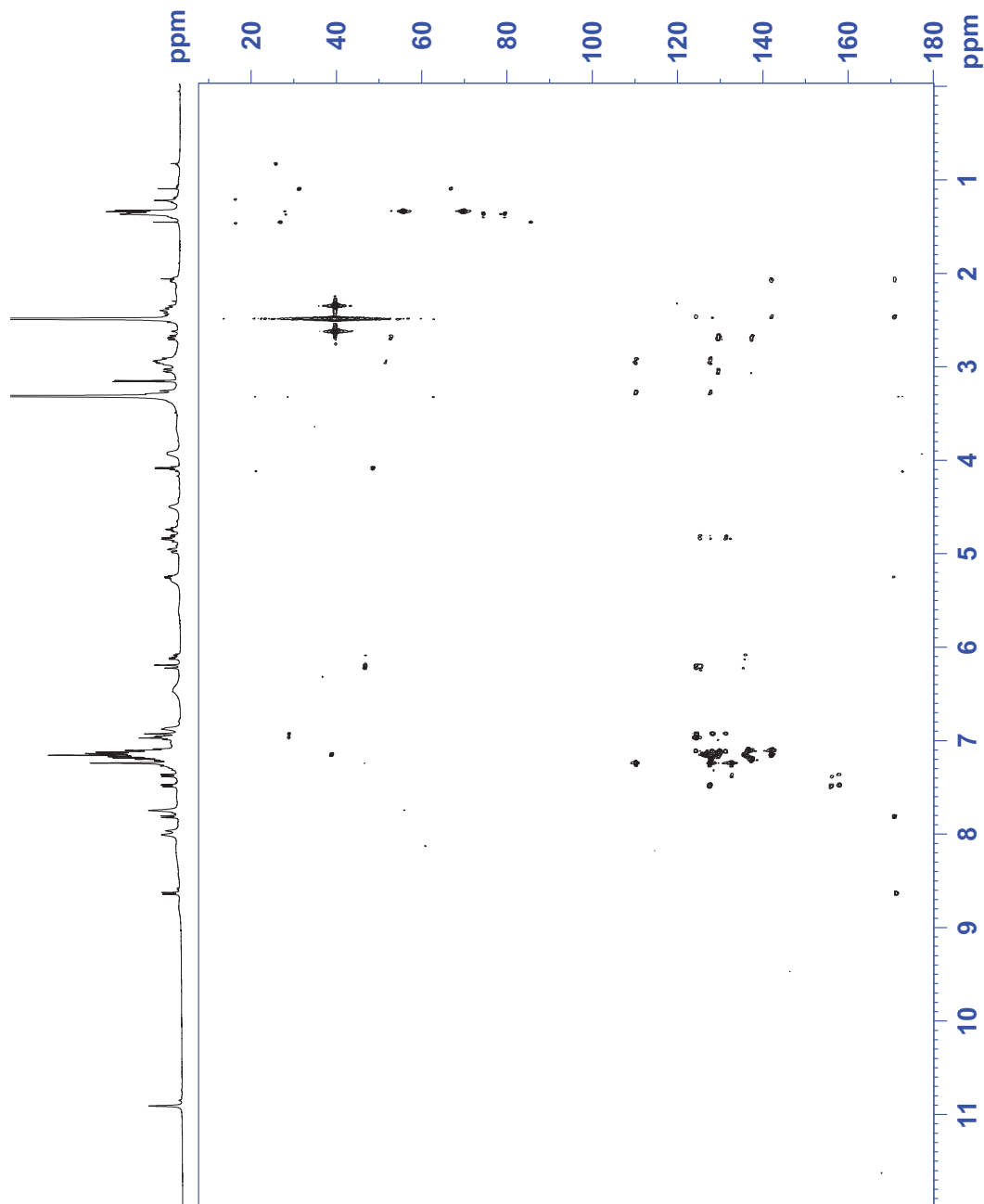


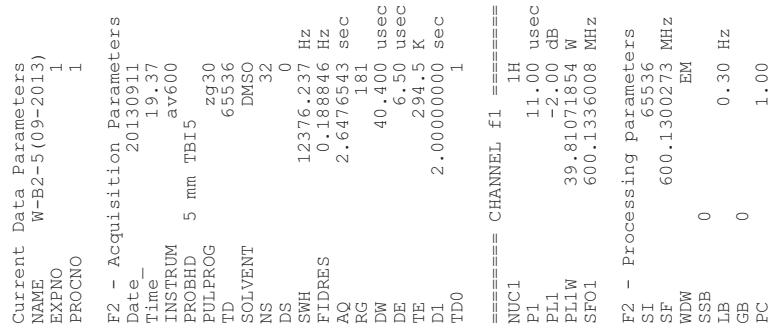
Current Data Parameters
NAME W-B2-4
EXPNO 6
PROCNO 1

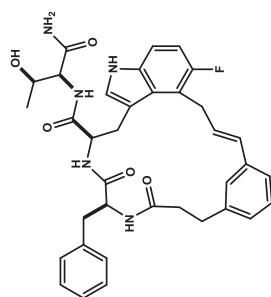
F1 - Acquisition parameters
TD 256
SFO1 125.7704 MHz
FIDRES 98.257607 Hz
SW 199.999 ppm
FnMODE QF

F2 - Processing parameters
SI 2048
SF 500.1300135 MHz
WDW QSI
SSB 2
LB 0 Hz
GB 0
PC 1.00

F1 - Processing parameters
SI 2048
MC2 QF
SF 125.7578472 MHz
WDW USER
SSB 2
LB 0 Hz
GB 0





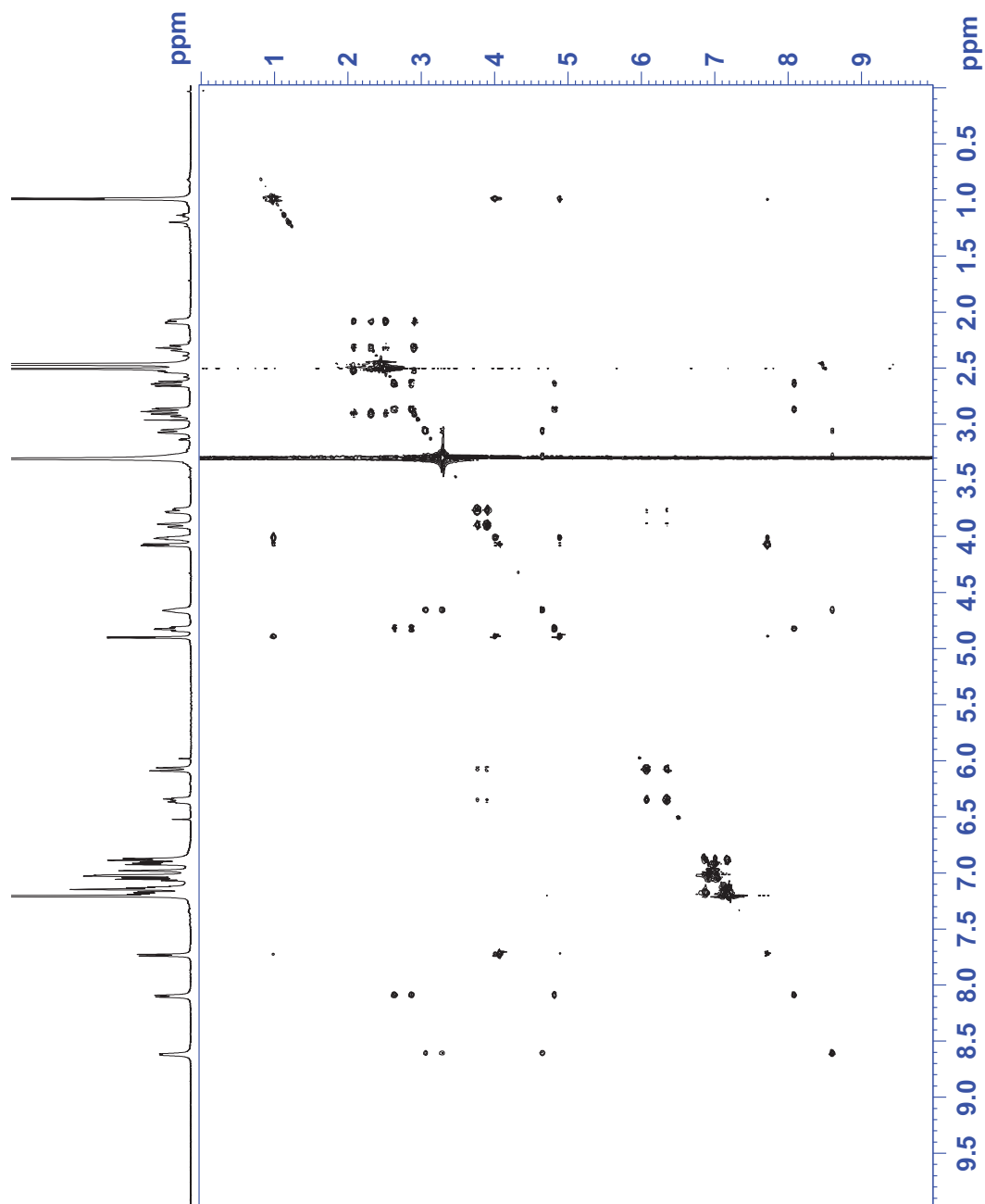


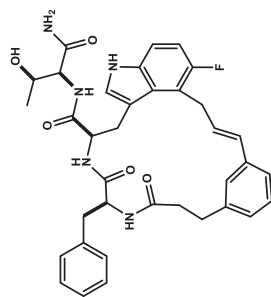
Current Data Parameters
 NAME W-B2-5 (09-2013)
 EXPNO 3
 PROCNO 1

F1 - Acquisition parameters
 TD 600
 SF01 600.1336 MHz
 FIDRES 12.002672 Hz
 SW 12.000 ppm
 FnMODE Echo-Antiecho

F2 - Processing parameters
 SI 1024
 SF 600.1300273 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 1024
 MC2 echo-antiecho
 SF 600.1300273 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0



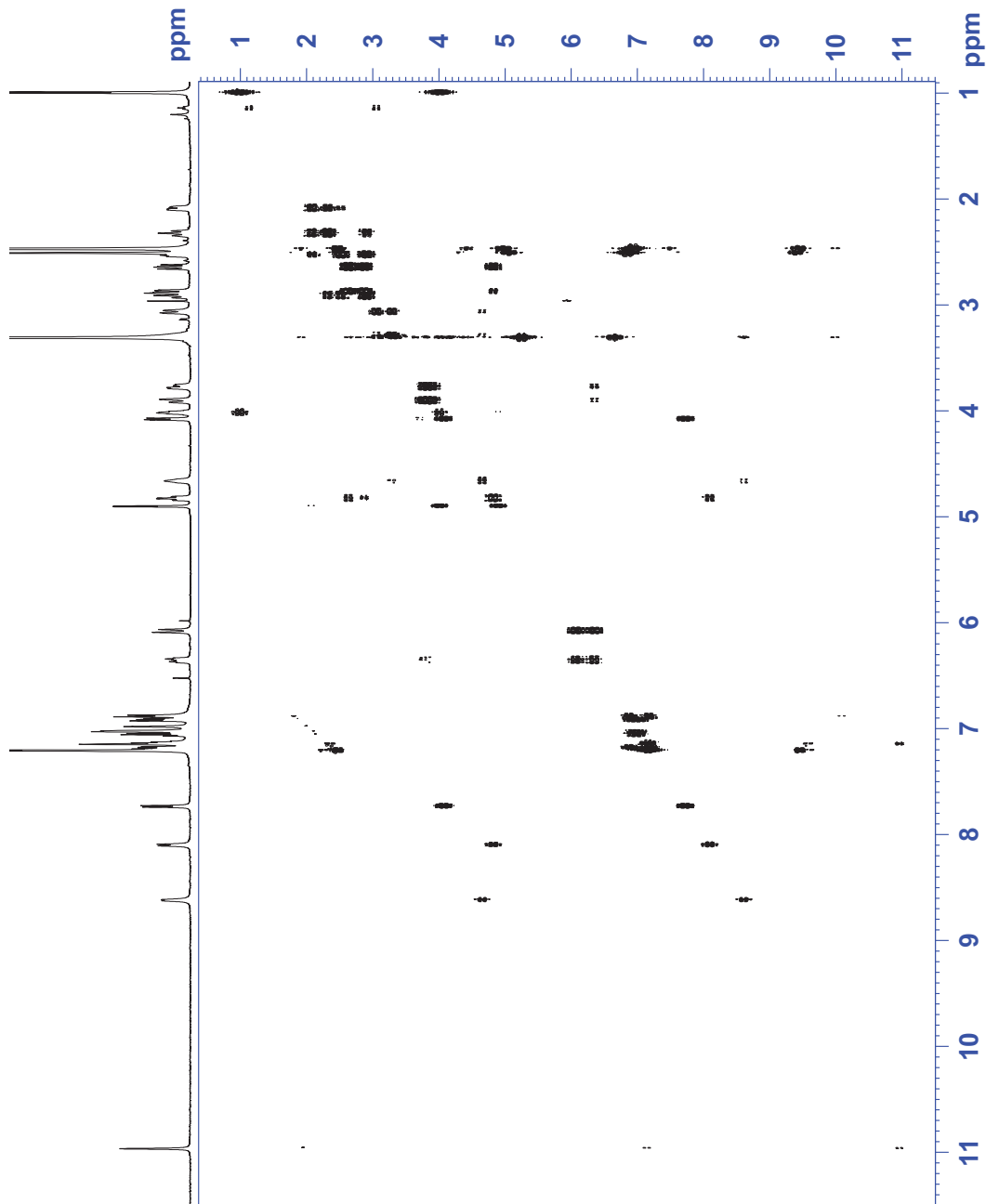


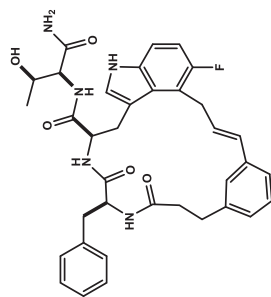
Current Data Parameters
NAME W-B2-5 (09-2013)
EXPNO 4
PROCNO 1

F1 - Acquisition parameters
TD 256
SF01 600.1336 MHz
FIDRES 28.131262 Hz
SW 12.000 ppm
FnMODE States-TPPI

F2 - Processing parameters
SI 2048
SF 600.1300273 MHz
WDW SINE
SSB 1
LB 0 Hz
GB 0
PC 1.00

F1 - Processing parameters
SI 2048
MC2 States-TPPI
SF 600.1300273 MHz
WDW TRAP
SSB 1
LB 0 Hz
GB 0



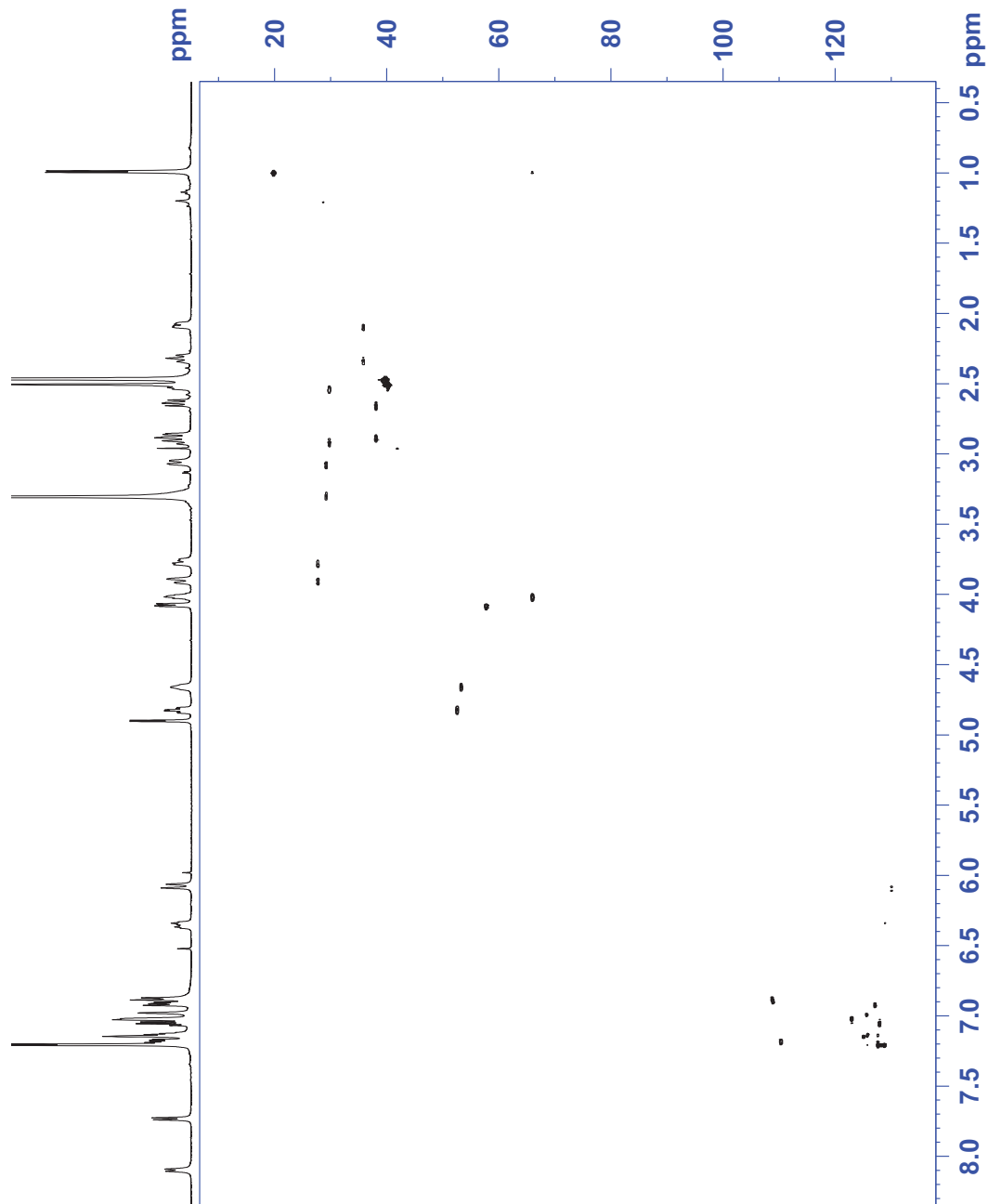


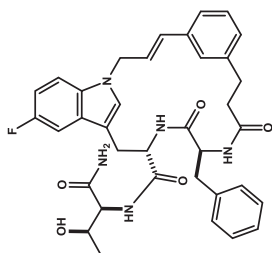
Current Data Parameters
 NAME W-B2-5 (09-2013)
 EXPNO 5
 PROCNO 1

F1 - Acquisition parameters
 TD 512
 SF 150.9134 MHz
 FIDRES 47.160427 Hz
 SW 160.000 ppm
 FnMODE Echo-Antiecho

F2 - Processing parameters
 SI 4096
 SF 600.1300200 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

F1 - Processing parameters
 SI 4096
 MC2 echo-antiecho
 SF 150.9029231 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0



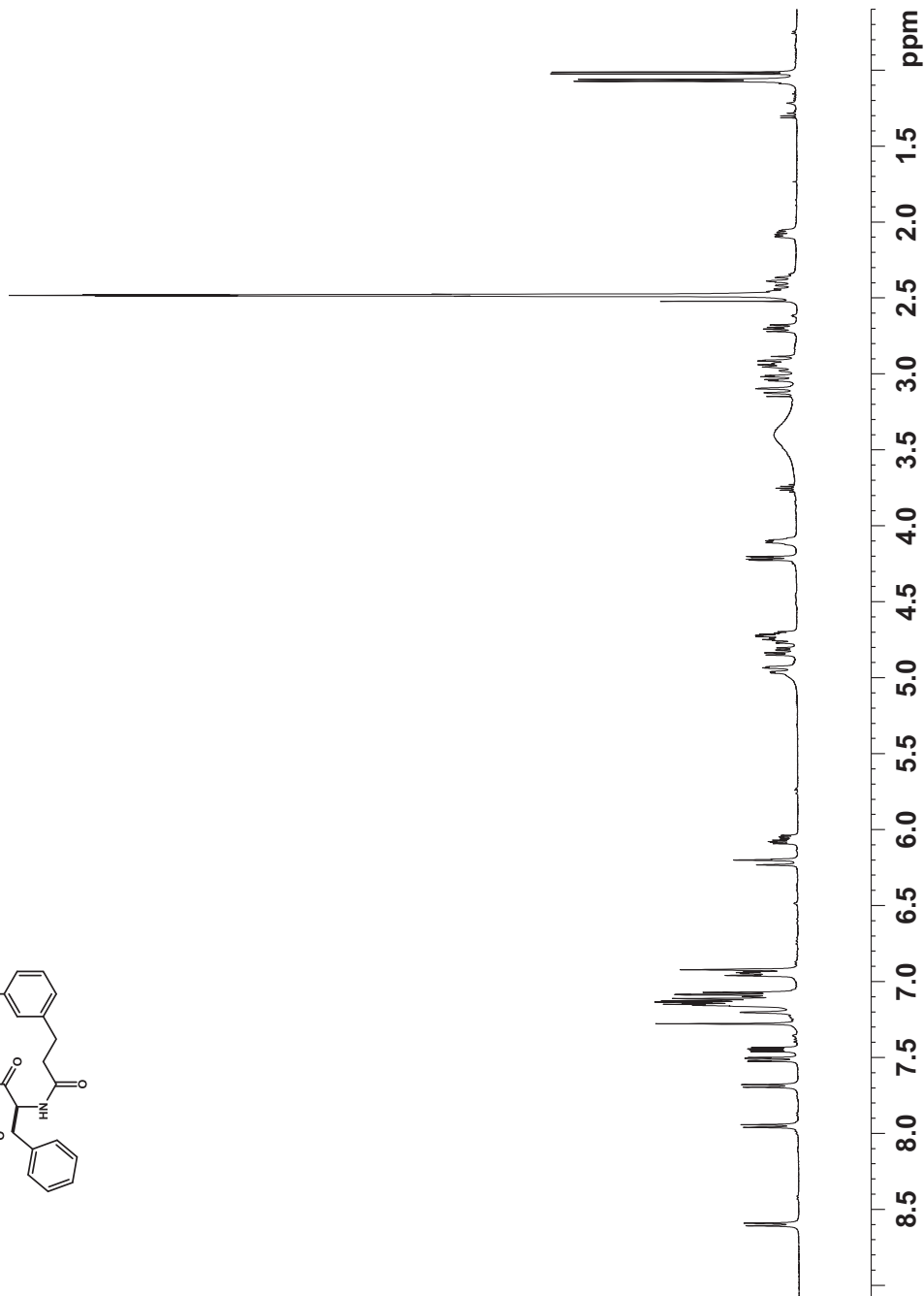


Current Data Parameters
NAME W-B2-7-2
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20121124
Time_ 15.05
INSTRUM av500
PROBHD 5 mm DCH 13C-1
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 8
DS 0
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.2767999 sec
RG 11
DW 50.000 usec
DE 10.00 usec
TE 298.0 K
D1 2.00000000 sec
TD0 1

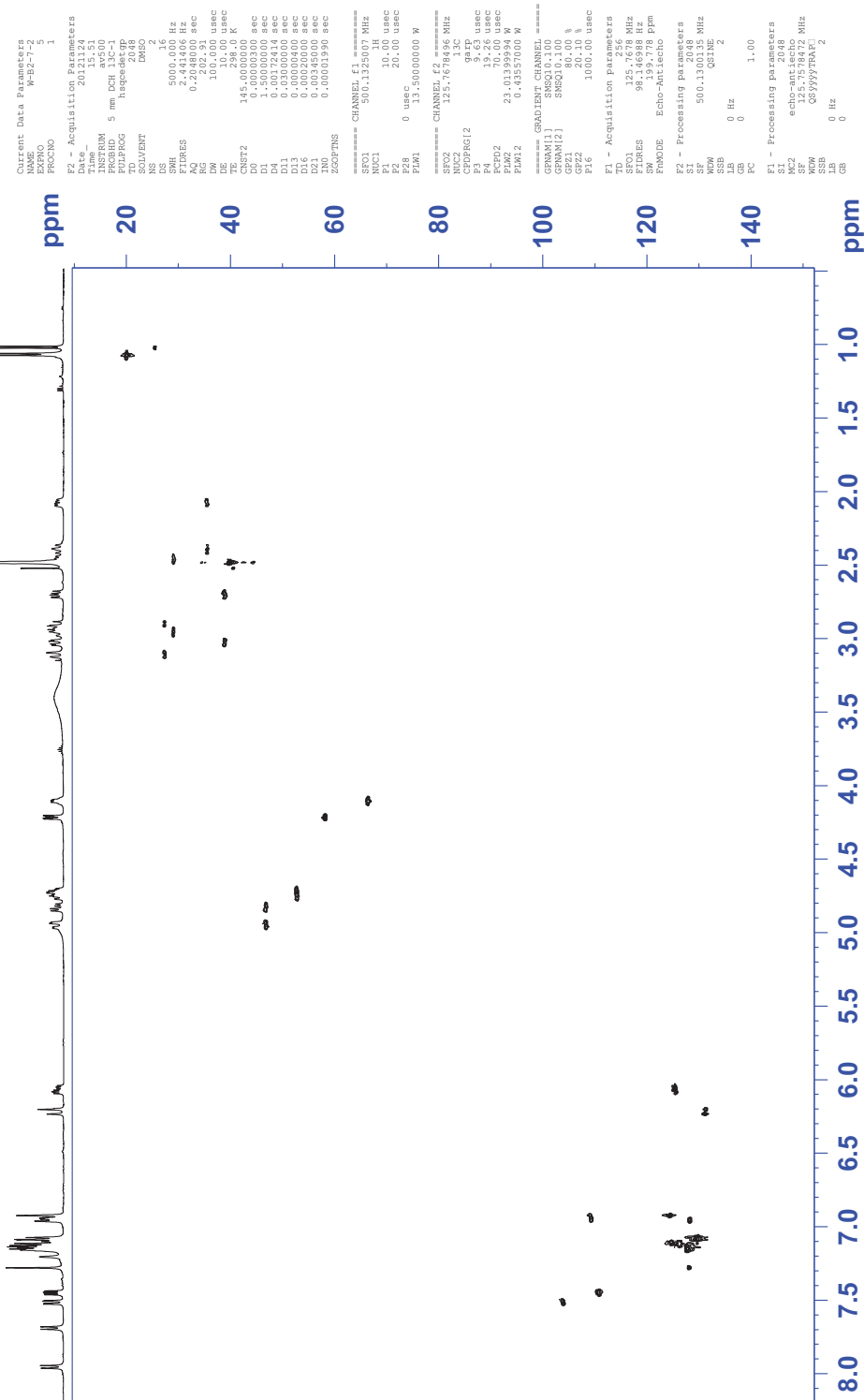
===== CHANNEL f1 =====
SFO1 500.130008 MHz
NUC1 1H
P1 10.00 usec
PLW1 13.50000000 W

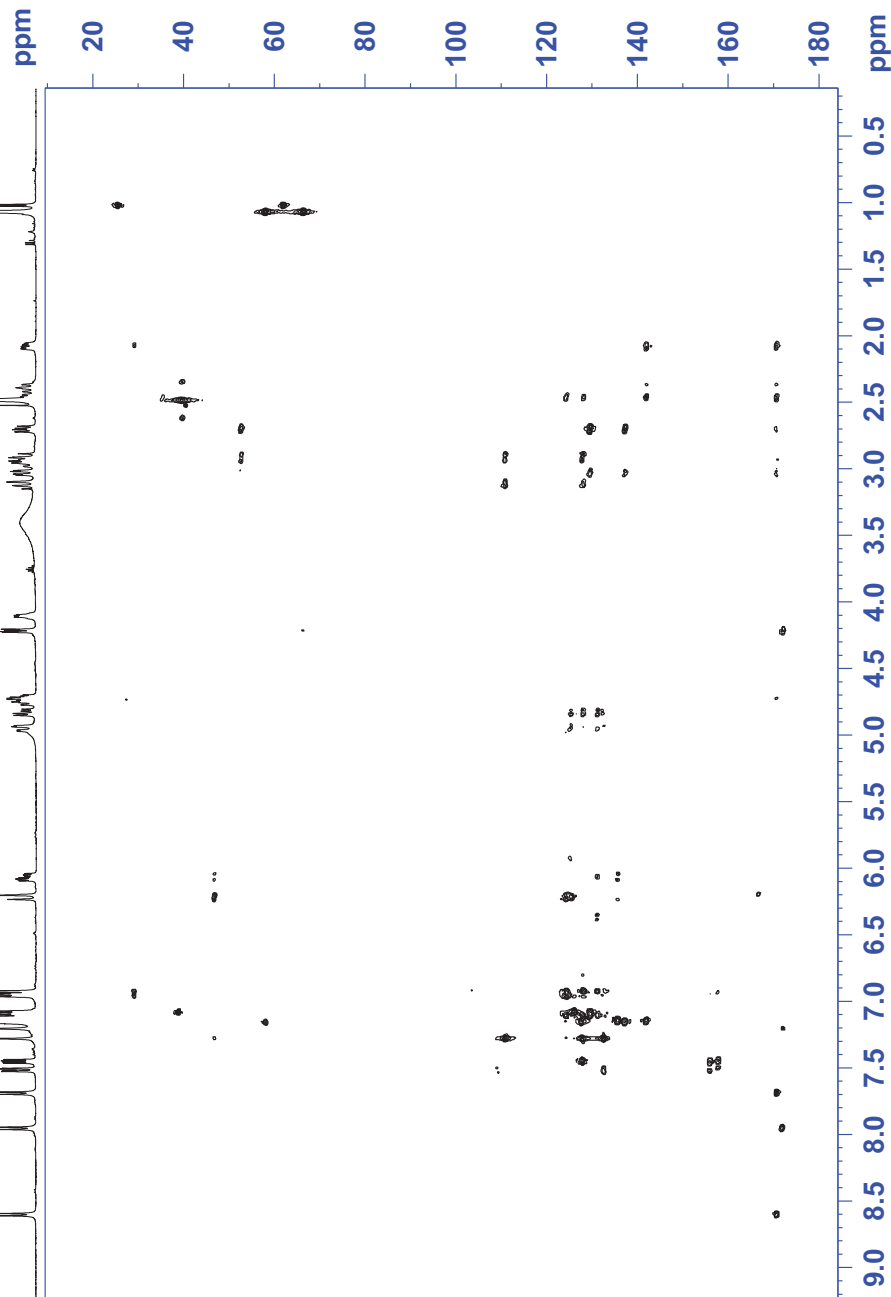
F2 - Processing parameters
SI 65536
SF 500.1300146 MHz
WDW EM
SSB 0
LB 0
GB 0
PC 1.00

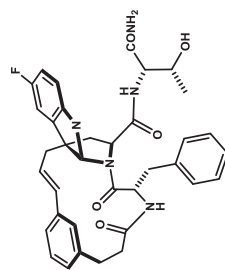










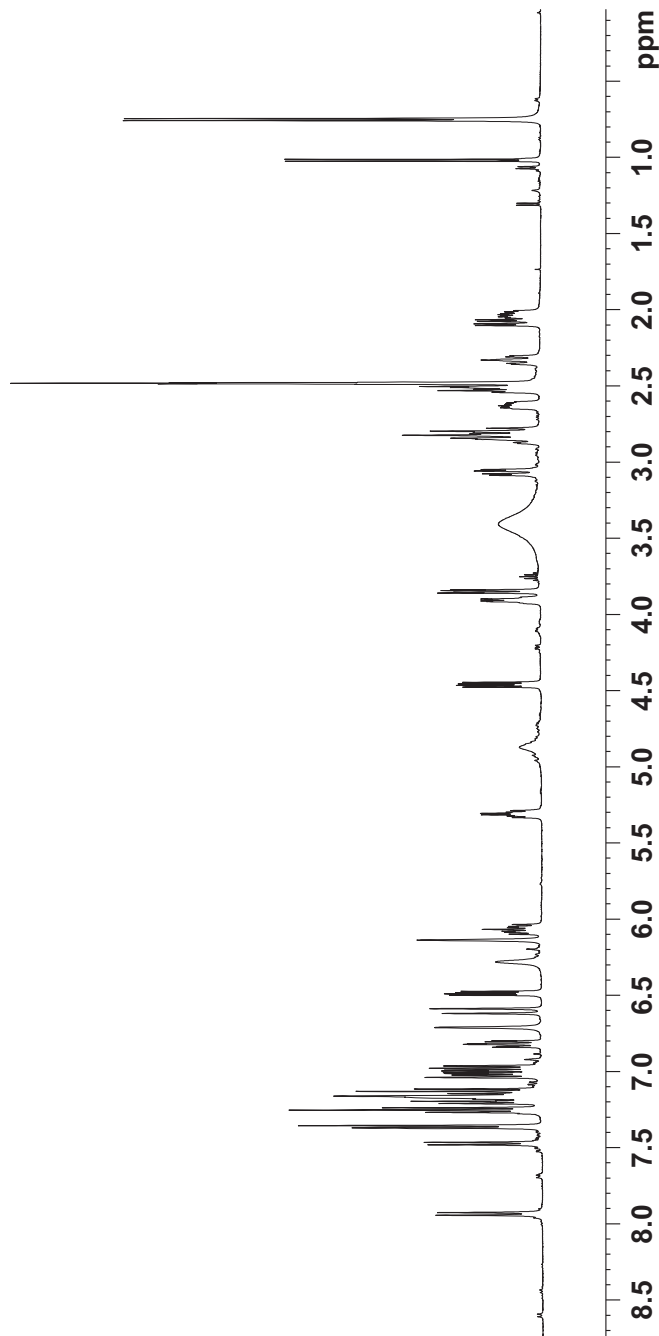


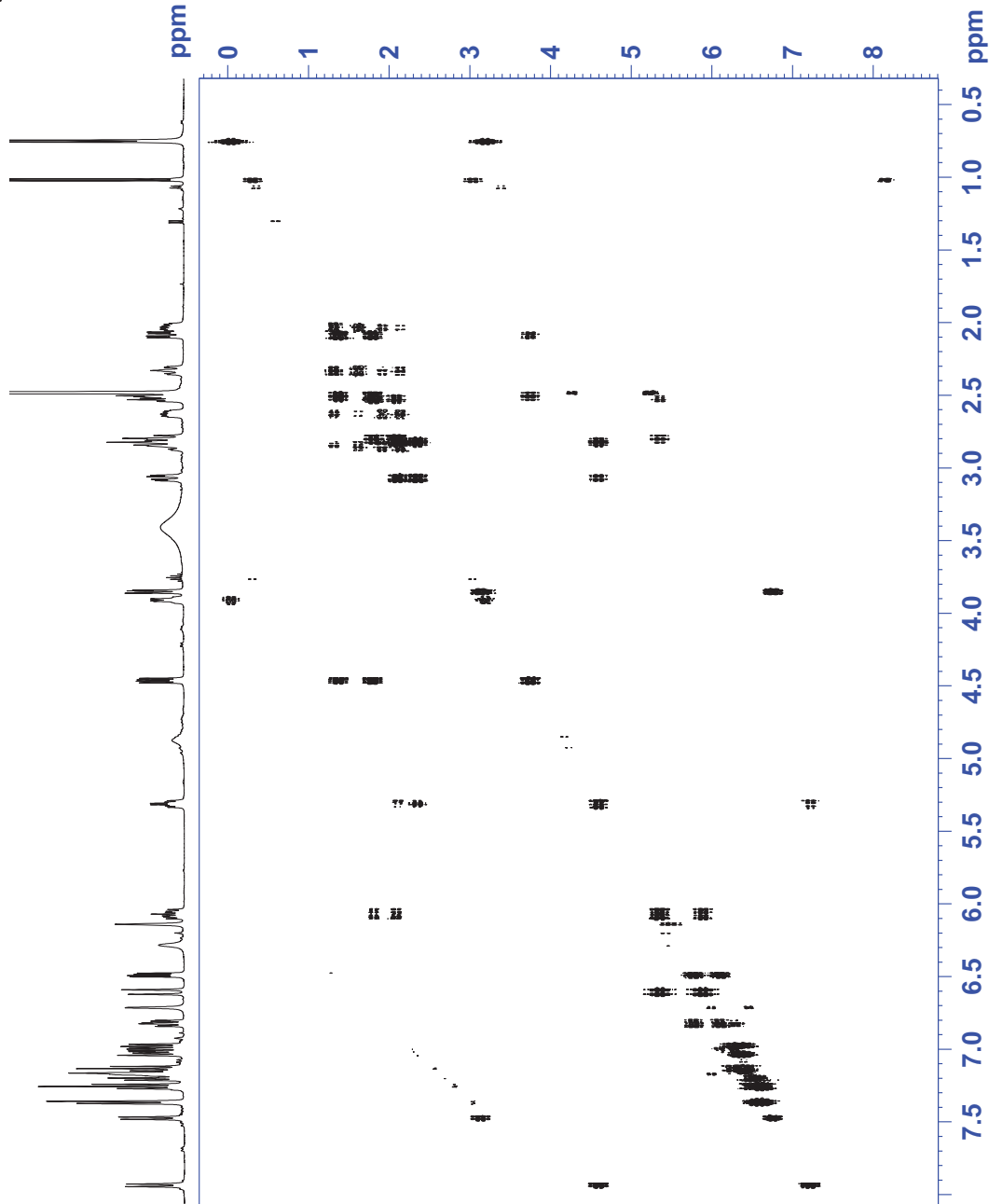
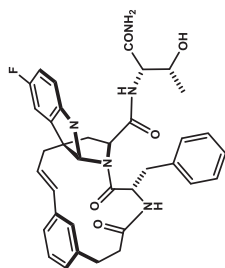
Current Data Parameters
NAME W-B2-7-3
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20121124
Time_ 16.44
INSTRUM av500
PROBHD 5 mm DCH 13C-1
PULPROG zg
TD 65536
SOLVENT DMSO
NS 16
DS 0
SWH 10000.000 Hz
FIDRES 0.152588 Hz
AQ 3.276799 sec
RG 7
DW 50.000 usec
DE 10.00 usec
TE 298.0 K
D1 2.00000000 sec
TD0 1

===== CHANNEL f1 =====
SFO1 500.1330008 MHz
NUC1 1H
P1 10.00 usec
PL1 13.50000000 W

F2 - Processing parameters
SI 65536
SF 500.1300146 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00





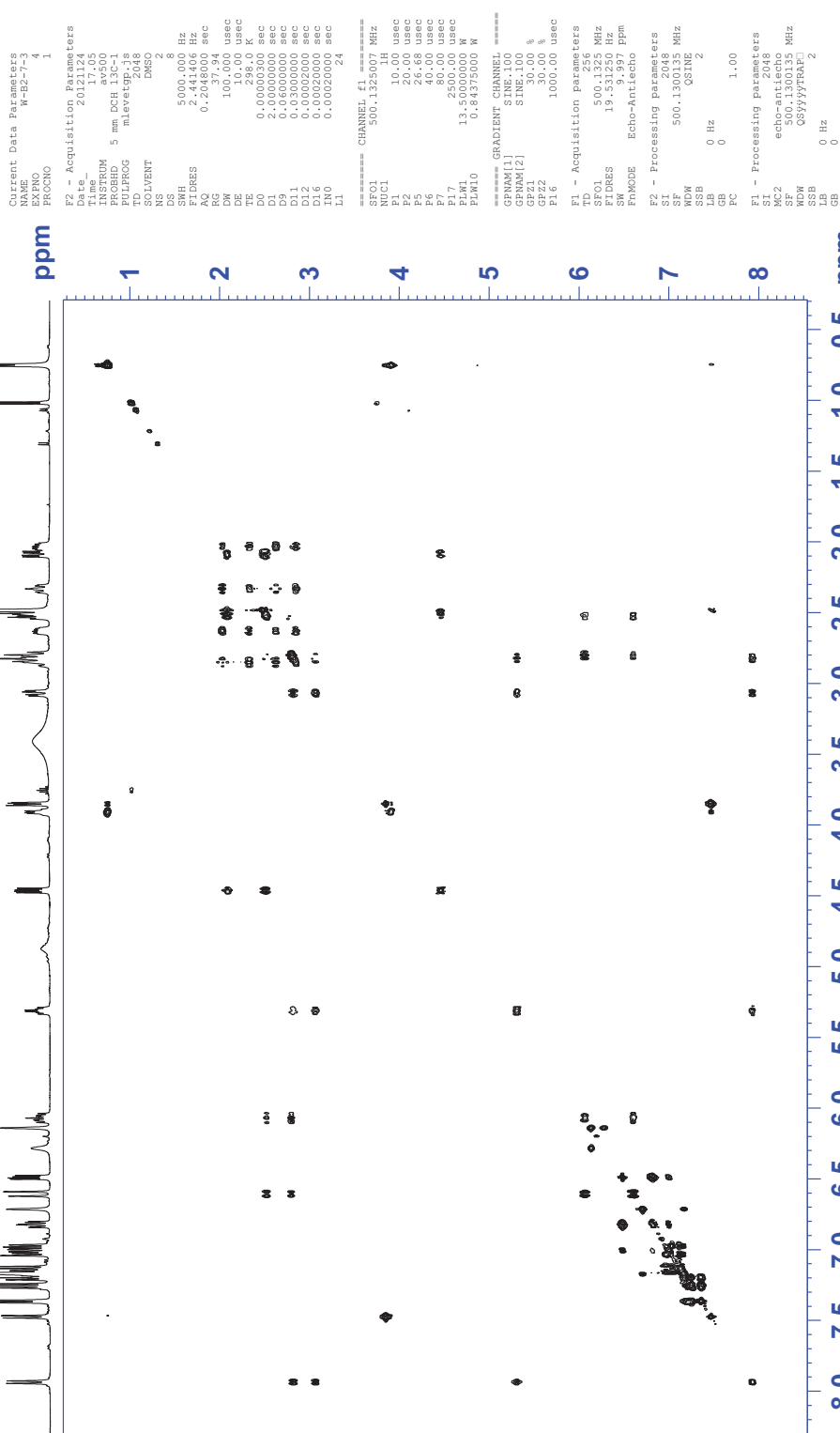
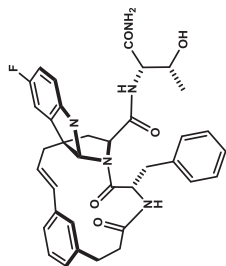
Current Data Parameters
NAME W-B2-7-3
EXPNO 1
PROCNO 1

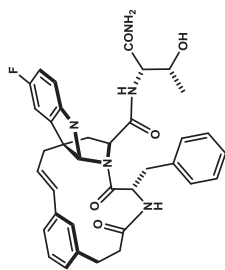
F2 - Acquisition Parameters
Date_ 20121124
Time 16:44
INSTRUM spect
PROBHD 5 mm DCH 13C-1
PULPROG cosygmfph
TD 4096
SOLVENT DMSO
NS 2
DS 2
SWH 5498.134 Hz
FIDRES 1.342415 Hz
AQ 0.3724629 sec
RG 202.91
DM 90.933 usec
DE 1.000 usec
TE 298.0
D0 0.00007817 sec
D1 2.00000000 sec
D13 0.0000400 sec
D16 0.00020000 sec
INO 0.00018180 sec
===== CHANNEL f1 =====
SFO1 500.1327507 MHz
NUC1 1H
P1 10.00 usec
P2 20.00 usec
PLW1 13.50000000 W
===== GRADIENT CHANNEL =====
GPNAM[1] SMSQ10.100
GPNAM[2] SMSQ10.100
GPZ1 10.00 %
GPZ2 2.00 %
P16 1000.00 usec

F1 - Acquisition Parameters
TD 256
SFO1 500.1327507 MHz
FIDRES 21.614228 MHz
RG 202.91
SW 10.998 ppm
FhMODE States-TPPI

F2 - Processing parameters
SI 2048
SF 500.1303720 MHz
WDW SINE
SSB 1
LB 0 Hz
GB 0
PC 1.00

F1 - Processing parameters
SI 2048
MC2 States-TPPI
SF 500.1303720 MHz
WDW SINE
SSB 1
LB 0 Hz
GB 0



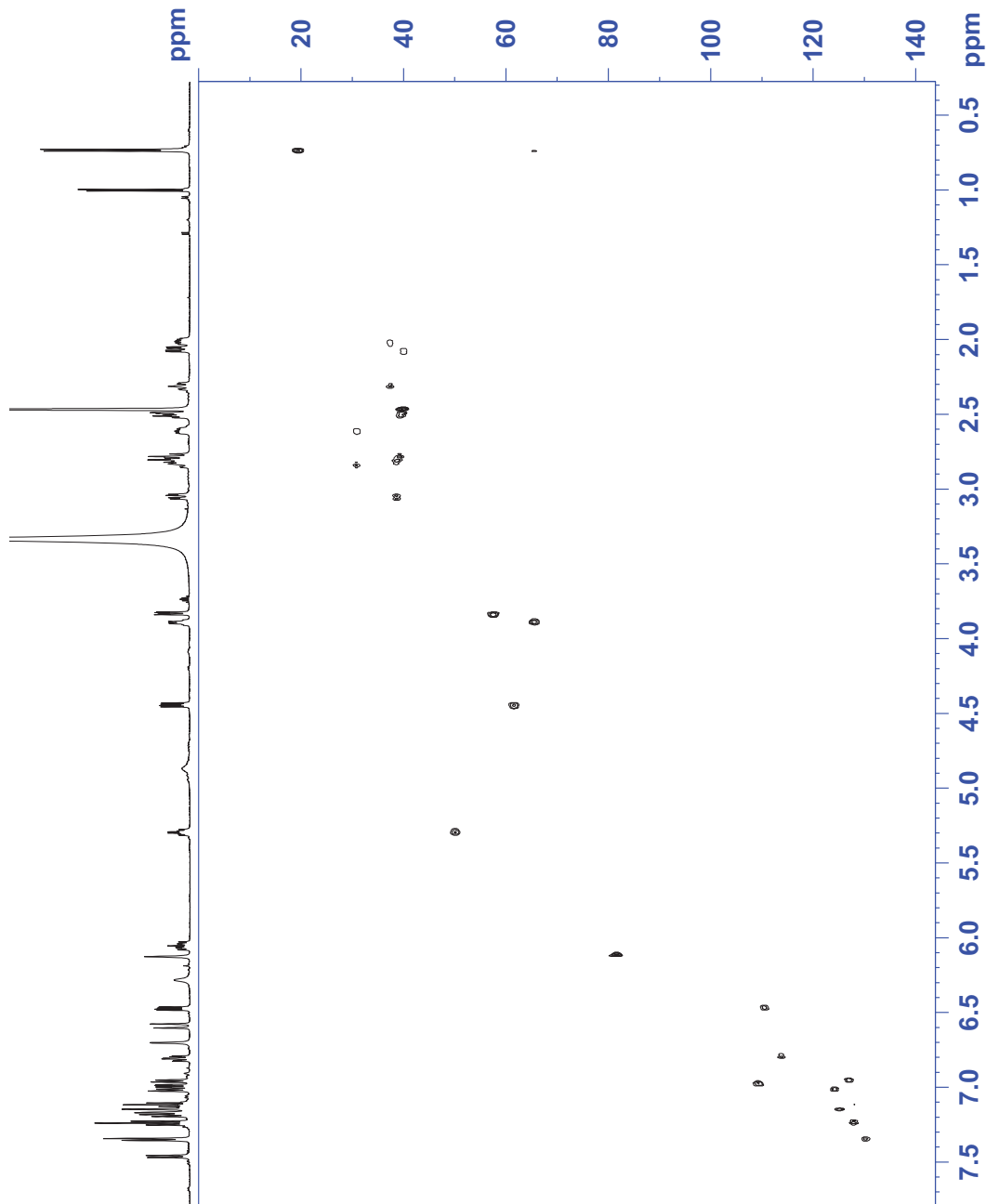


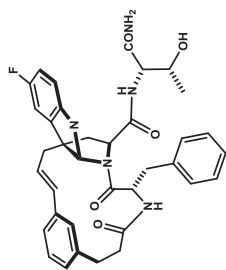
Current Data Parameters
 NAME W-B2-7-3_AV600
 EXPNO 2
 PROCNO 1

F1 - Acquisition parameters
 TD 256
 SF01 150.9134 MHz
 FIDRES 106.110962 Hz
 SW 180.000 ppm
 FnmODE Echo-Antiecho

F2 - Processing parameters
 SI 2048
 SF 600.1300273 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.40

F1 - Processing parameters
 SI 2048
 MC2 echo-antiecho
 SF 150.9028800 MHz
 WDW TRAP
 SSB 2
 LB 0 Hz
 GB 0



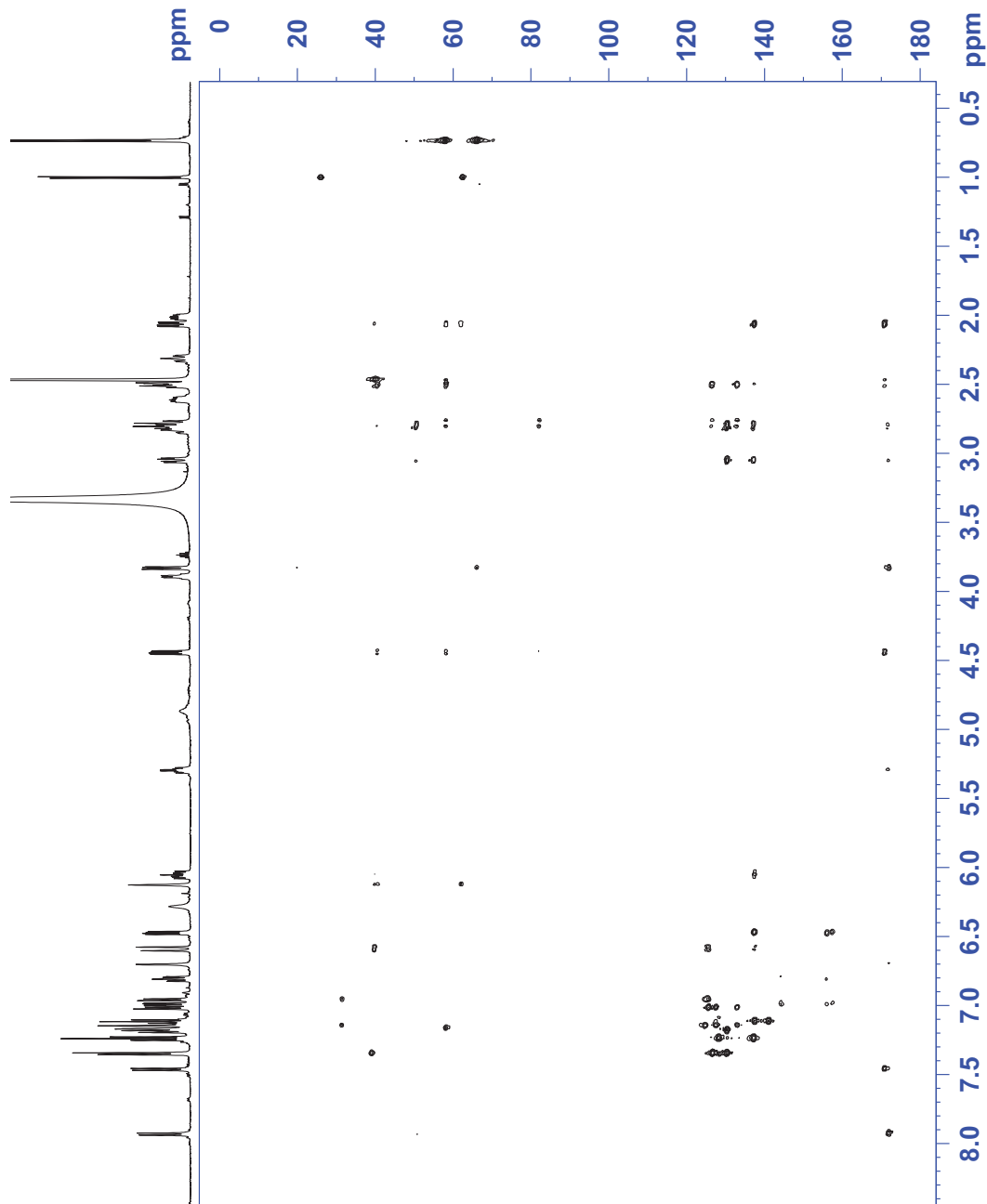


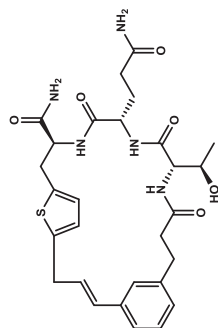
Current Data Parameters
 NAME W-B2-7-3_AV600
 EXPNO 3
 PROCNO 1

F1 - Acquisition parameters
 TD 256
 SFO1 150.9164 MHz
 FIDRES 117.903427 Hz
 SW 200.000 ppm
 FnmODE QF

F2 - Processing parameters
 SI 1024
 SF 600.1300273 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 1024
 MC2 QF
 SF 150.9028090 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0





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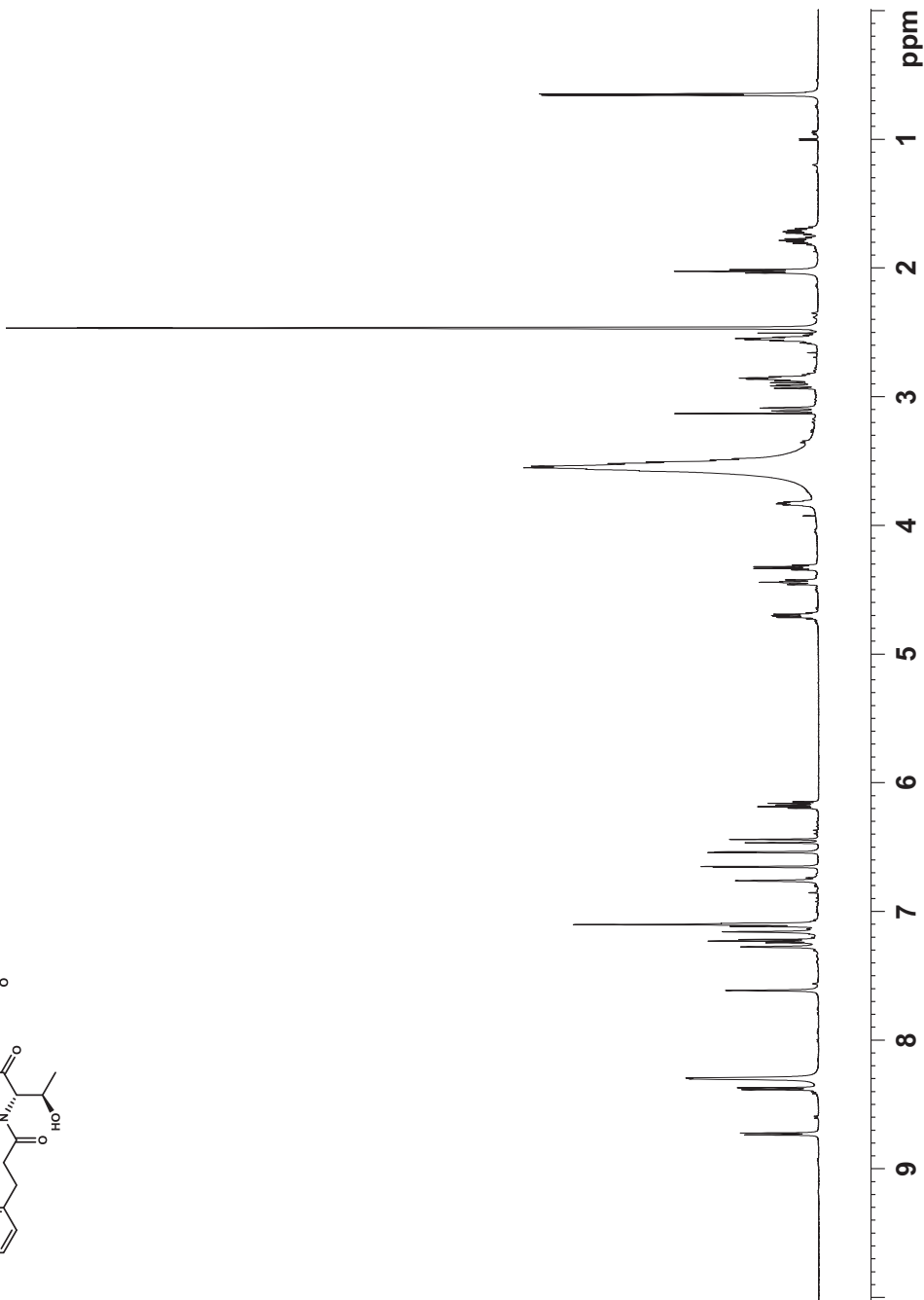
Current Data Parameters
NAME      KL-5-227-1-F37
EXPNO     1
PROCNO    1

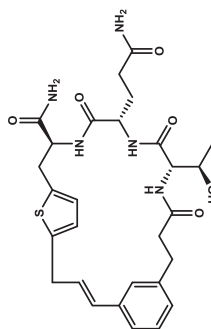
F2 - Acquisition Parameters
Date_     20131012
Time      17.47
INSTRUM   av600
PROBHD    5 mm TBI5
PULPROG   zg30
TD         65536
SOLVENT    DMSO
NS         14
DS         0
SWH        12376.237 Hz
FIDRES     0.188846 Hz
AQ         2.6476543 sec
RG         161.3
DW         40.400 usec
DE         6.50 usec
TE         294.7 K
D1         2.00000000 sec
TD0        1

===== CHANNEL f1 =====
NUC1       1H
P1         11.00 usec
PL1        -2.00 dB
PL1W       39.81071854 W
SFO1       600.1336008 MHz

F2 - Processing parameters
SI         65536
SF         600.1300273 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00

```



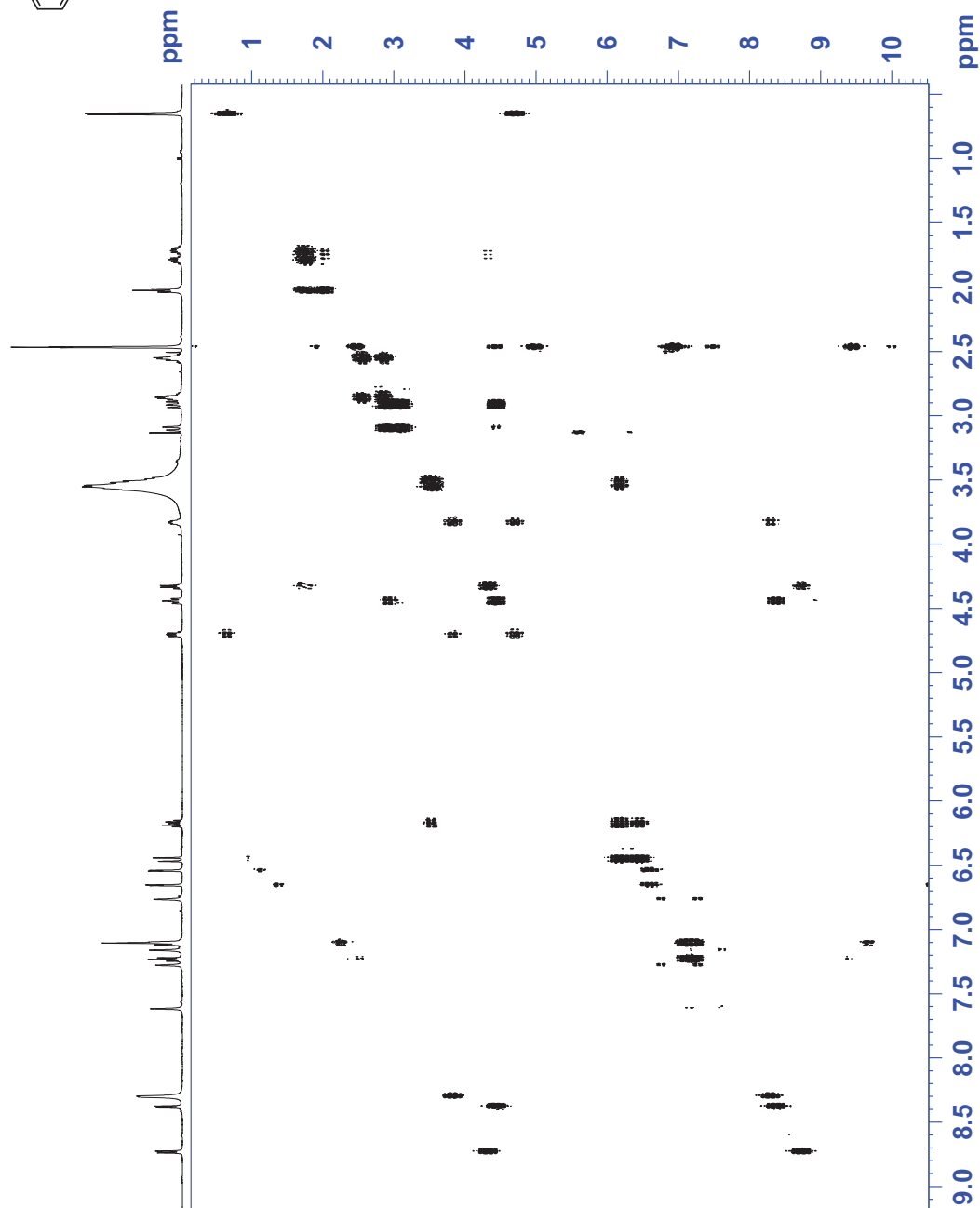


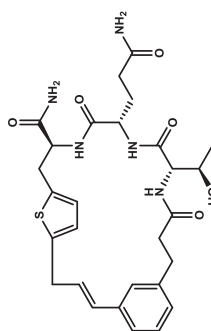
Current Data Parameters
 NAME KL-5-227-1-F37
 EXPNO 4
 PROCNO 1

F1 - Acquisition parameters
 TD 256
 SF01 600.1336 MHz
 FIDRES 28.131262 Hz
 SW 12.000 ppm
 FnmODE States-TPPI

F2 - Processing parameters
 SI 2048
 SF 600.1300273 MHz
 WDW SINE
 SSB 1
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 2048
 MC2 States-TPPI
 SF 600.1300273 MHz
 WDW SINE
 SSB 1
 LB 0 Hz
 GB 0



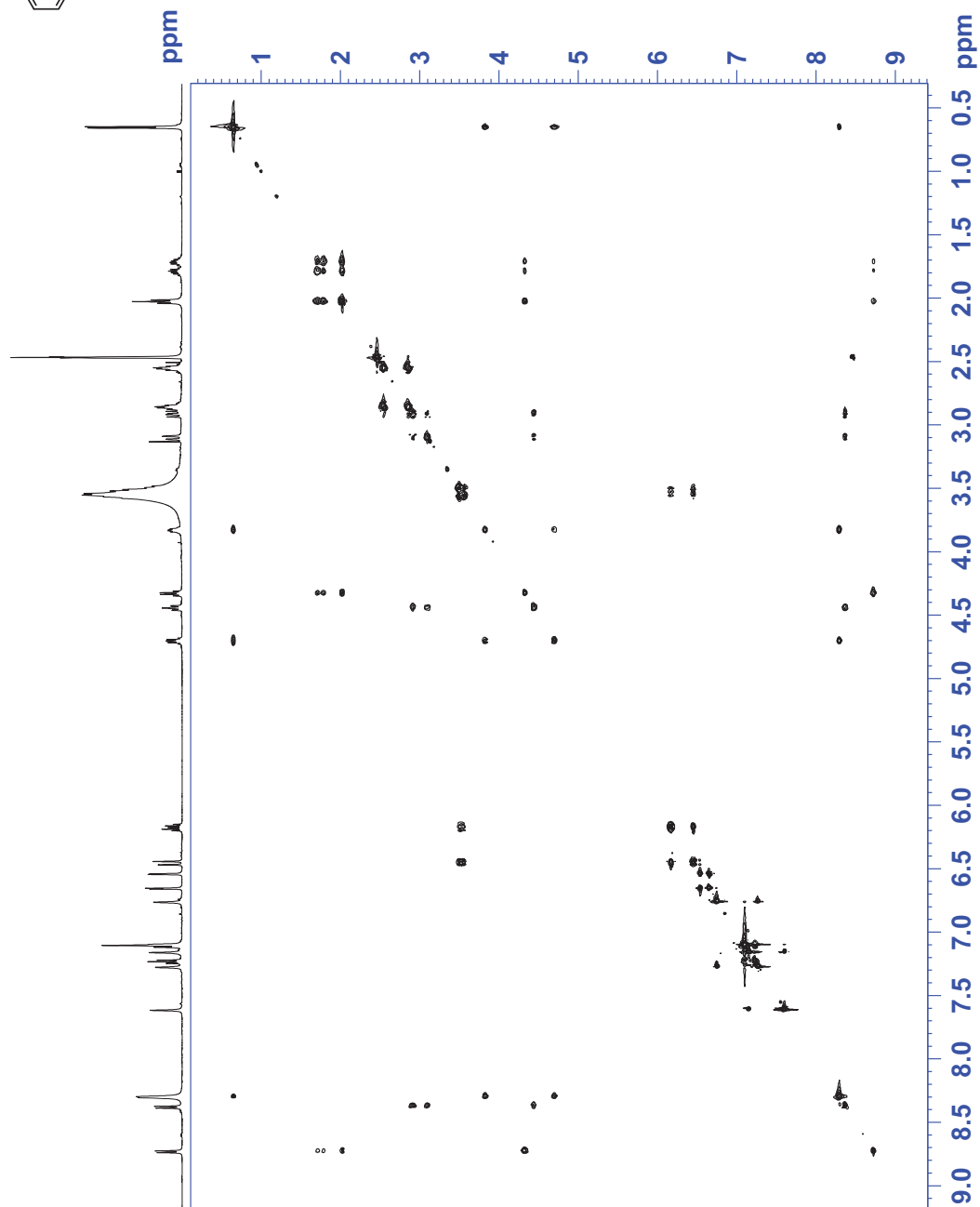


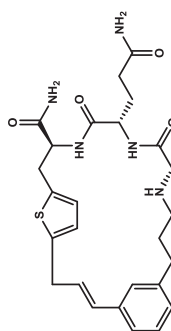
Current Data Parameters
 NAME KL-5-227-1-F37
 EXPNO 3
 PROCNO 1

F1 - Acquisition parameters
 TD 600
 SF01 600.1336 MHz
 FIDRES 12.002672 Hz
 SW 12.000 ppm
 FnmODE Echo-Antiecho

F2 - Processing parameters
 SI 1024
 SF 600.1300273 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 1024
 MC2 echo-antiecho
 SF 600.1300273 MHz
 WDW USER
 SSB 2
 LB 0 Hz
 GB 0



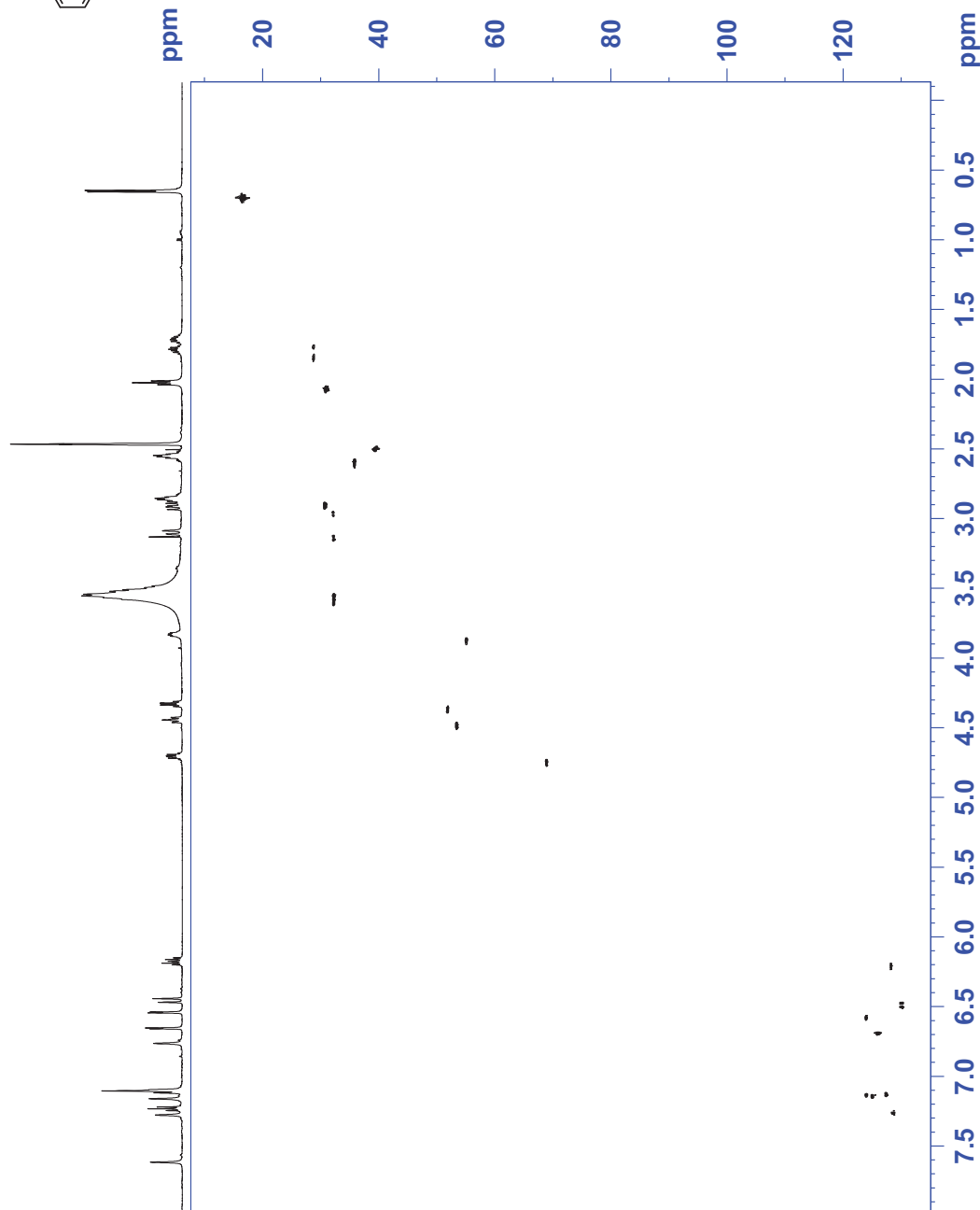


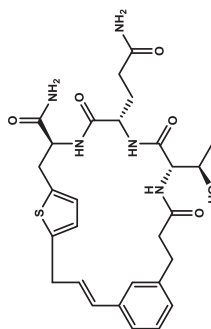
Current Data Parameters
 NAME KL-5-227-1-F37
 EXPNO 5
 PROCNO 1

F1 - Acquisition parameters
 TD 512
 SFO1 150.9134 MHz
 FIDRES 47.160427 Hz
 SW 160.000 ppm
 FnMODE Echo-Antiecho

F2 - Processing parameters
 SI 4096
 SF 600.1300051 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

F1 - Processing parameters
 SI 4096
 MC2 echo-antiecho
 SF 150.9029231 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0



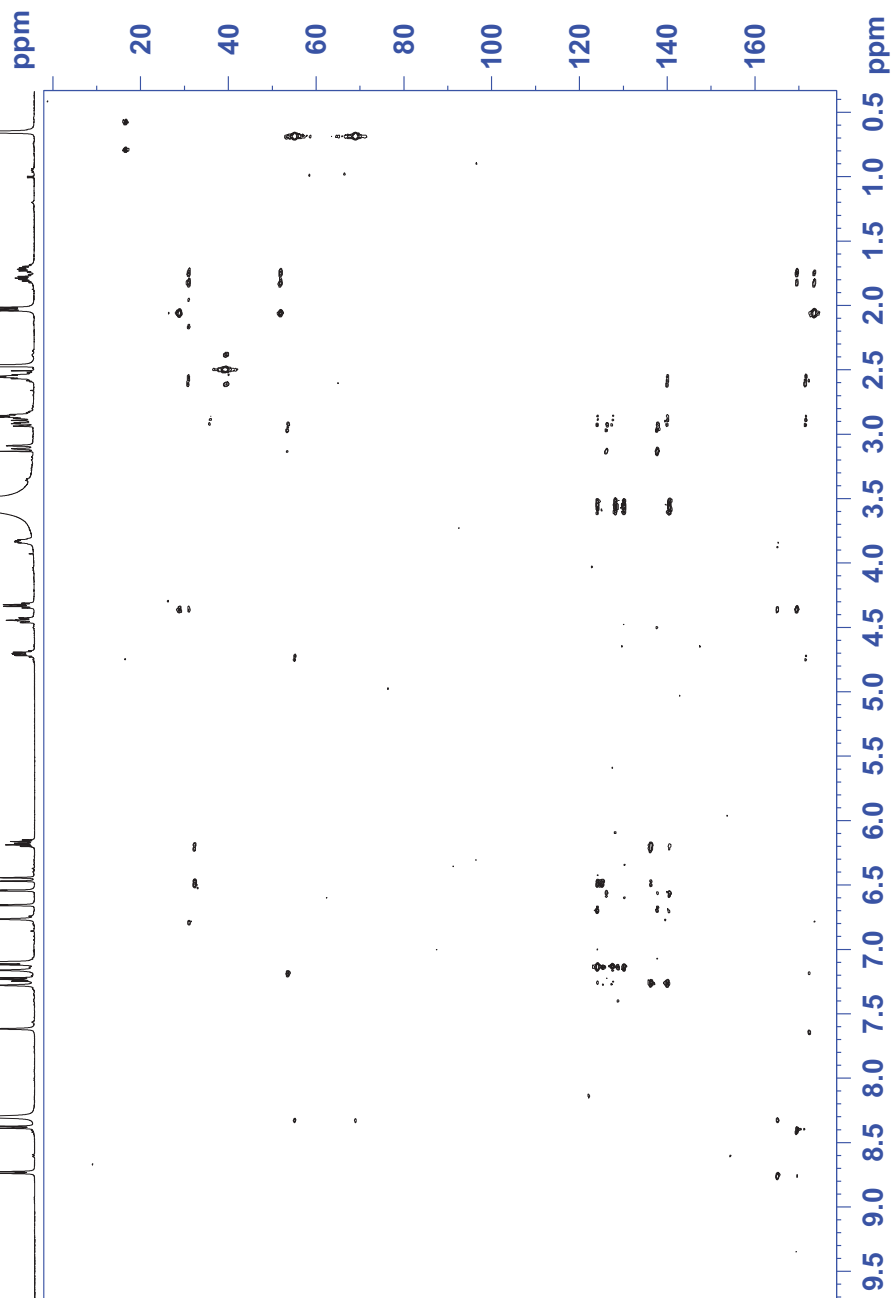


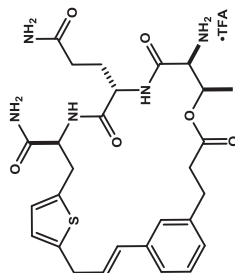
Current Data Parameters
 NAME KL-5-227-1-F37
 EXPNO 6
 PROCNO 1

F1 - Acquisition parameters
 TD 512
 SF01 150.9156 MHz
 FIDRES 56.003849 Hz
 SW 190.000 ppm
 FnmODE QF

F2 - Processing parameters
 SI 4096
 SF 600.1300066 MHz
 WDW QF
 SSB 0
 LB 0 Hz
 GB 0
 PC 1.40

F1 - Processing parameters
 SI 4096
 MC2 QF
 SF 150.9029181 MHz
 WDW USER
 LB 2
 SSB 0 Hz
 GB 0





```

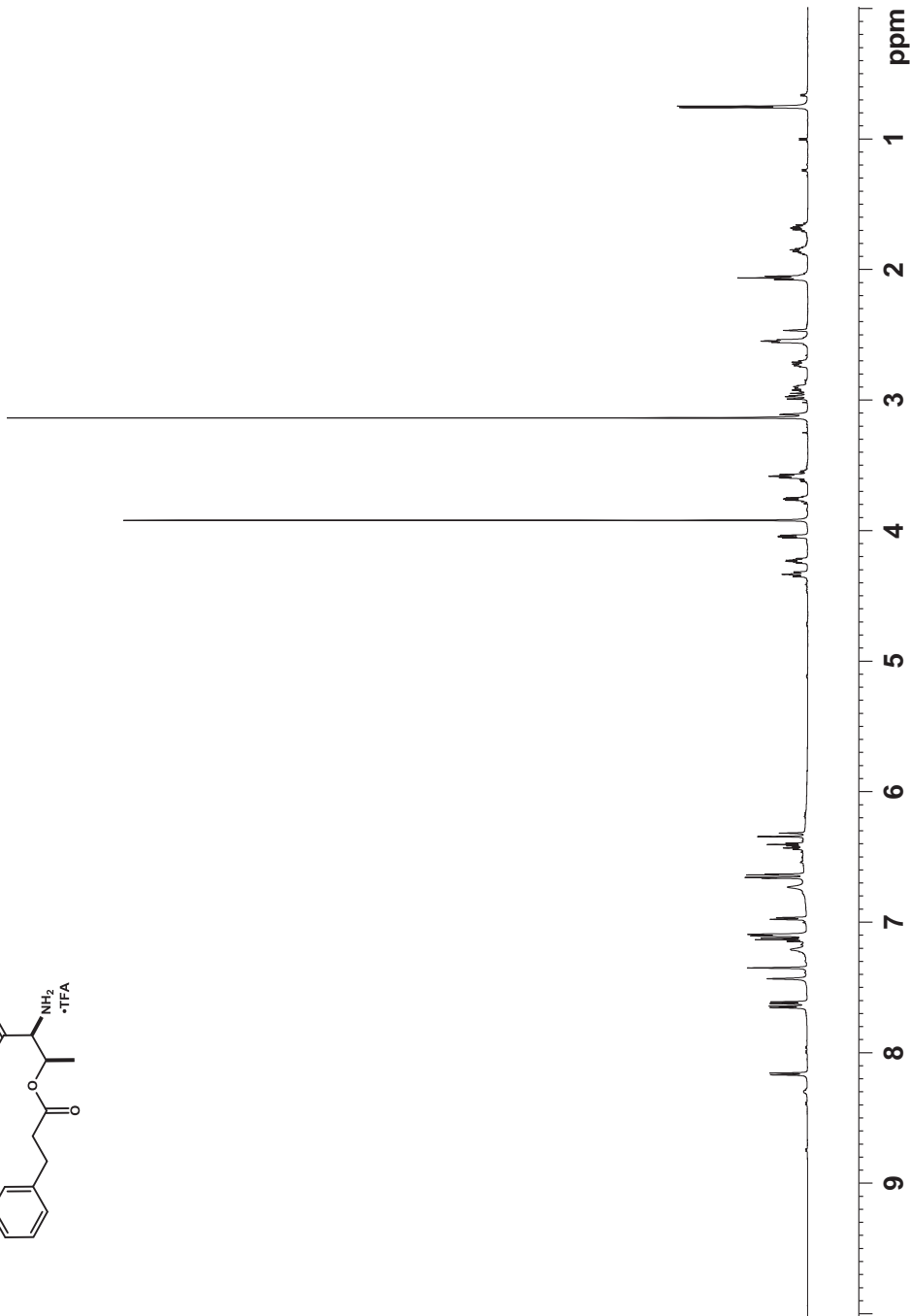
Current Data Parameters
NAME      KL-5-227-2-1
EXPNO     2
PROCNO    1

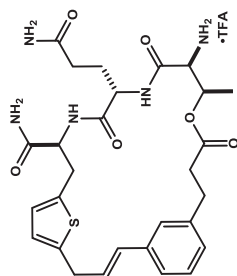
F2 - Acquisition Parameters
Date_     20131012
Time      14.18
INSTRUM   av600
PROBHD    5 mm TBI5
PULPROG   zg
TD         65536
SOLVENT    DMSO
NS         8
DS         0
SWH        12376.237 Hz
FIDRES     0.188846 Hz
AQ         2.6476543 sec
RG         18
DW         40.400 usec
DE         6.50 usec
TE         294.7 K
D1         2.0000000 sec
TD0        1

===== CHANNEL f1 =====
NUC1       1H
P1         10.60 usec
PL1        -2.00 dB
PL1W       39.81071854 W
SFO1       600.1336008 MHz

F2 - Processing parameters
SI         65536
SF         600.1300273 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00

```



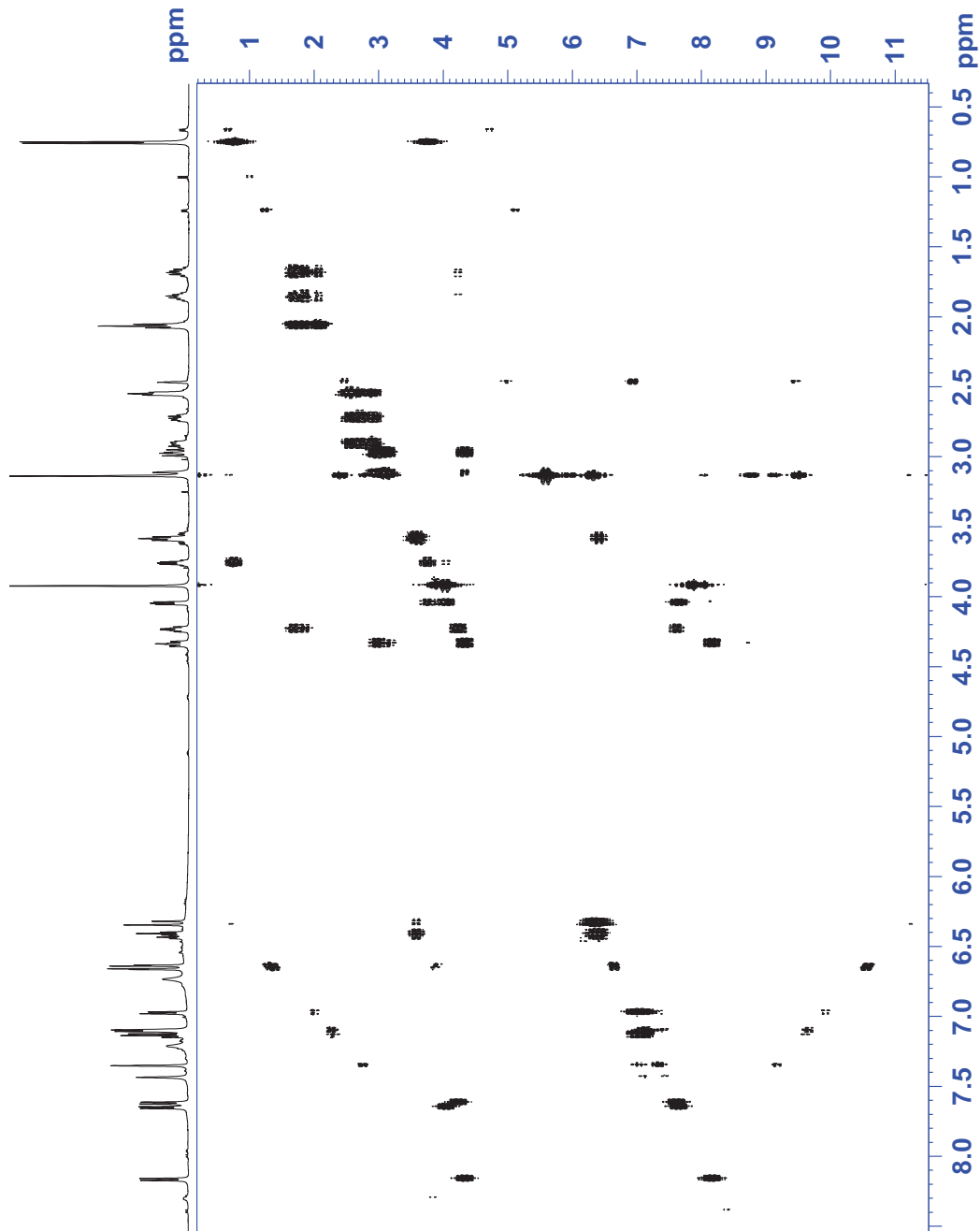


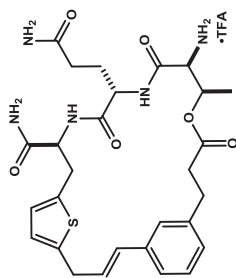
Current Data Parameters
 NAME KL-5-227-2-1
 EXPNO 4
 PROCNO 1

F1 - Acquisition parameters
 TD 256
 SFO1 600.1336 MHz
 FIDRES 28.131262 Hz
 SW 12.000 ppm
 F1MODE States-TPPI

F2 - Processing parameters
 SI 2048
 SF 600.1300273 MHz
 WDW SINE
 SSB 1
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 2048
 MC2 States-TPPI
 SF 600.1300273 MHz
 WDW QSINE
 SSB 1
 LB 0 Hz
 GB 0



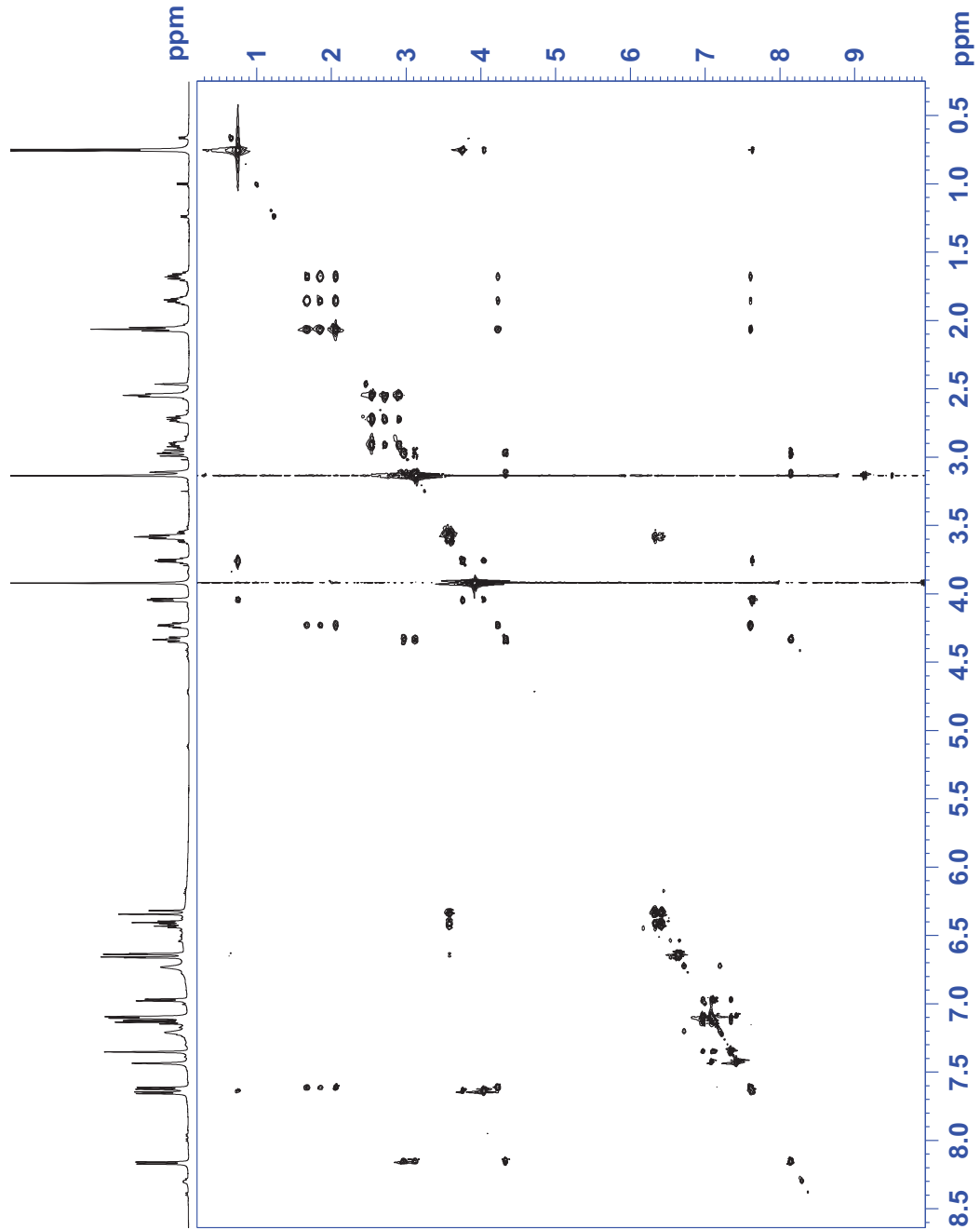


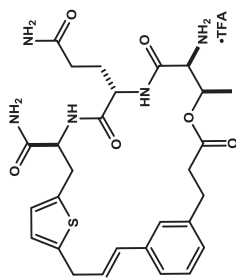
Current Data Parameters
 NAME KL-5-227-2-1
 EXPNO 3
 PROCNO 1

F1 - Acquisition parameters
 TD 600
 SFO1 600.1336 MHz
 FIDRES 12.002672 Hz
 SW 12.000 ppm
 FwMODE Echo-Antiecho

F2 - Processing parameters
 SI 1024
 SF 600.1300273 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 1024
 MC2 echo-antiecho
 SF 600.1300273 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0



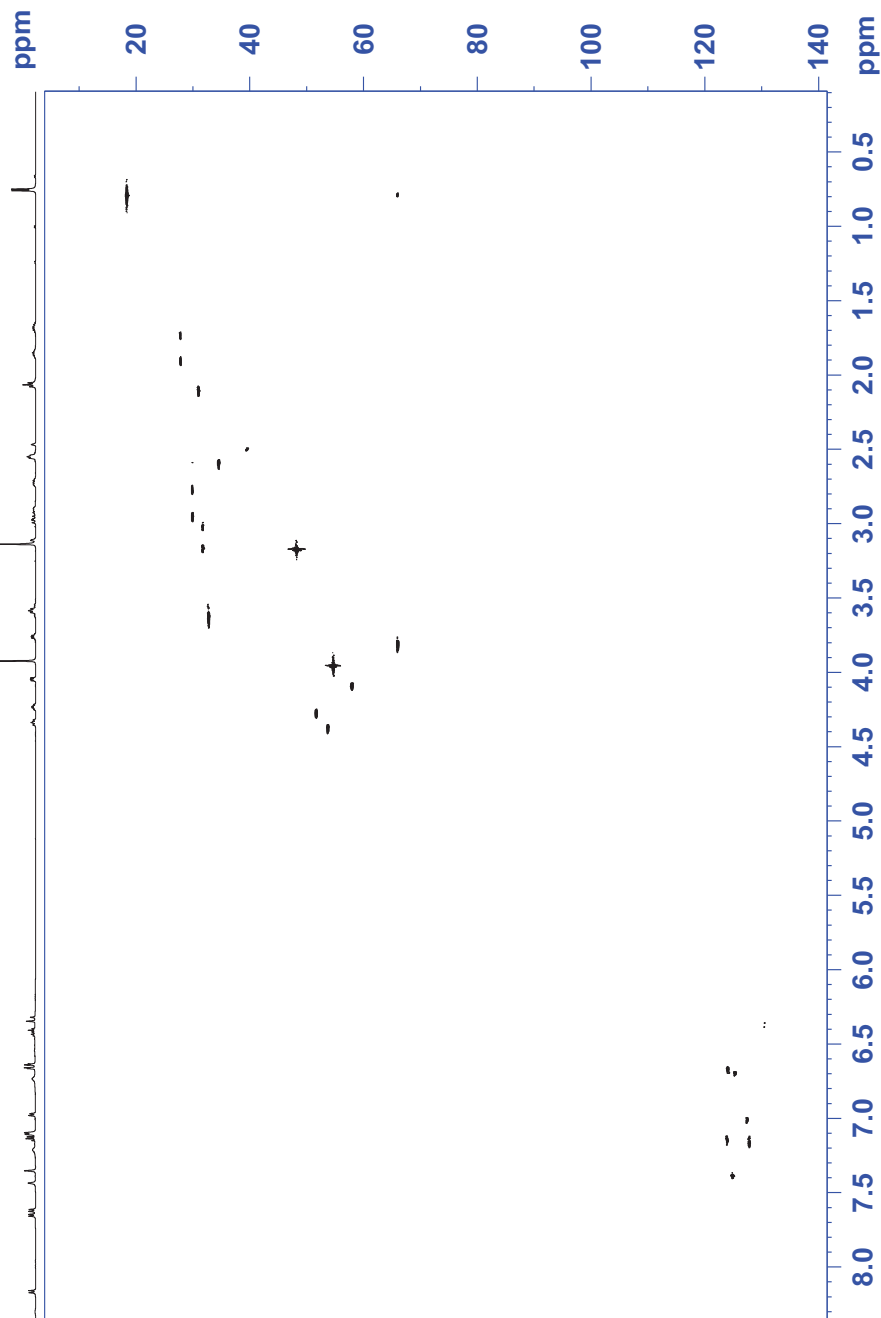


Current Data Parameters
 NAME KL-5-227-2-1
 EXPNO 5
 PROCNO 1

F1 - Acquisition parameters
 TD 512
 SFO1 150.9134 MHz
 FIDRES 47.160427 Hz
 SW 160.000 ppm
 FMODE Echo-Antiecho

F2 - Processing parameters
 SI 4096
 SF 600.130051 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

F1 - Processing parameters
 SI 4096
 MC2 echo-antiecho
 SF 150.9029231 MHz
 WDW SINE
 SSB 2
 LB 0 Hz
 GB 0





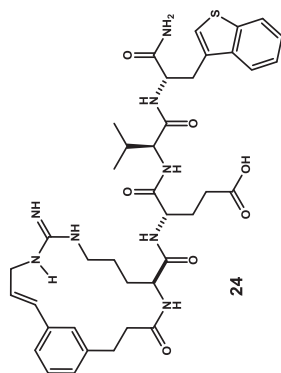
Current Data Parameters	
NAME	KL-5-227-2-1
EXPNO	6
PROCNO	1

F1 - Acquisition parameters	
TD	512
SFO1	150.9156 MHz
FIDRES	56.003849 Hz
SW	190.000 ppm
EnMODE	QF

F2 - Processing parameters	
SI	4096
SF	600.130066 MHz
WDW	QSINE
SSB	0
LB	0 Hz
GB	0
PC	1.40

F1 - Processing parameters	
SI	4096
MC2	QF
SSSF	150.9029181 MHz
WDW	QSSINE
SSB	3
LB	0 Hz
GB	0



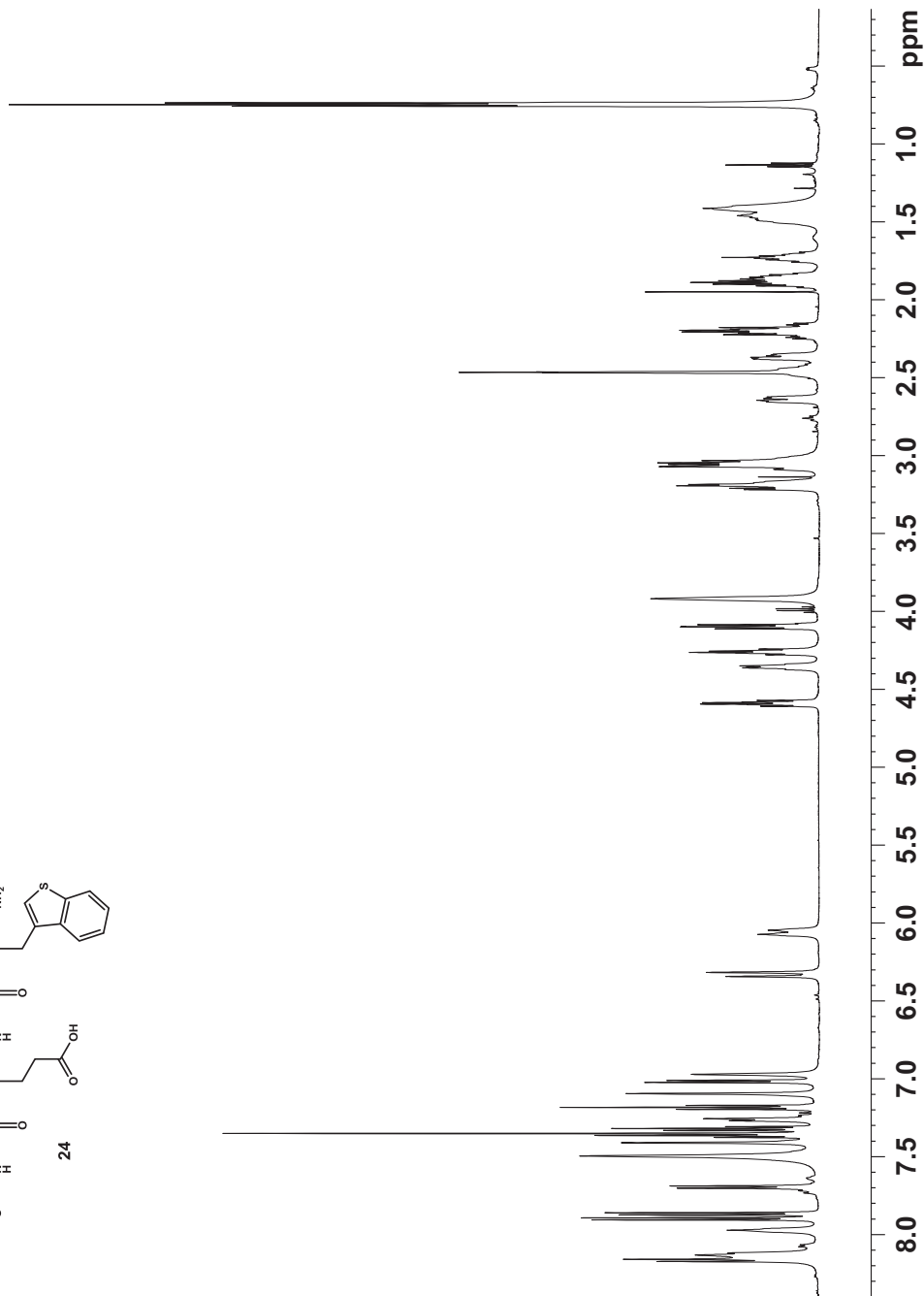


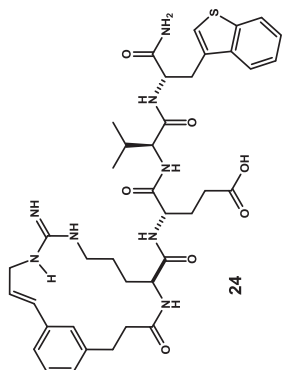
Current Data Parameters
 NAME KL-5-229-1
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20131109
 Time_ 19.17
 INSTRUM av600
 PROBHD 5 mm TBI5
 PULPROG zg30
 TD 65536
 SOLVENT DMSO
 NS 8
 DS 0
 SWH 12376.237 Hz
 FIDRES 0.188846 Hz
 AQ 2.6476543 sec
 RG 35.9
 DW 40.400 usec
 DE 6.50 usec
 TE 295.3 K
 D1 2.0000000 sec
 TD0 1

==== CHANNEL f1 =====
 NUC1 1H
 P1 9.50 usec
 PL1 -2.00 dB
 PL1W 39.81071854 W
 SFO1 600.1336008 MHz

F2 - Processing parameters
 SI 65536
 SF 600.1300273 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00





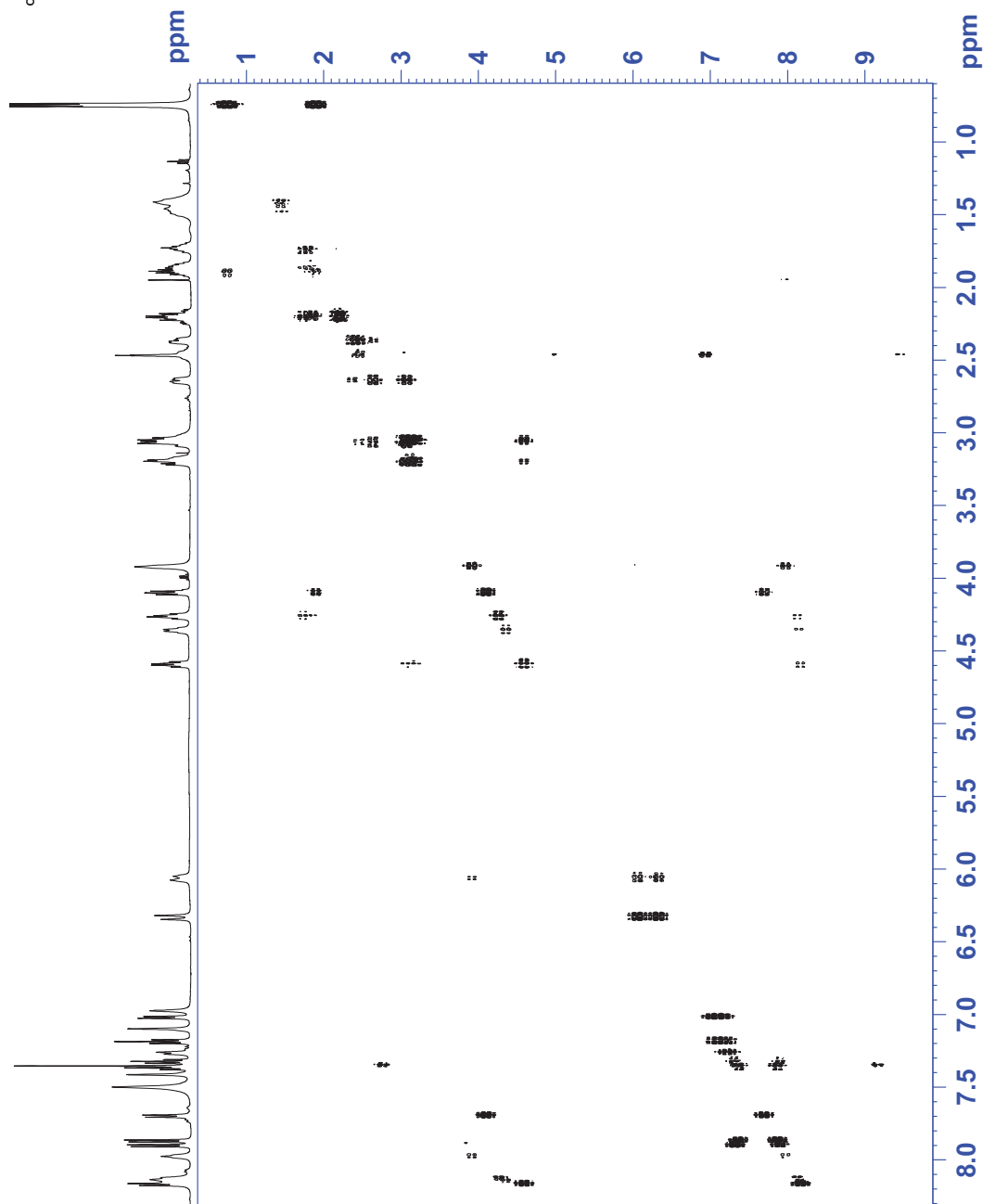
24

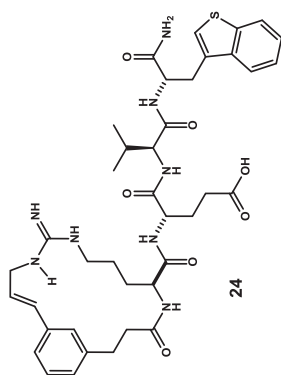
Current Data Parameters
 NAME KL-5-229-1
 EXPNO 4
 PROCNO 1

F1 - Acquisition parameters
 TD 256
 SFO1 600.1336 MHz
 FIDRES 28.131262 Hz
 SW 12.000 ppm
 FreqMODE States-TPPI

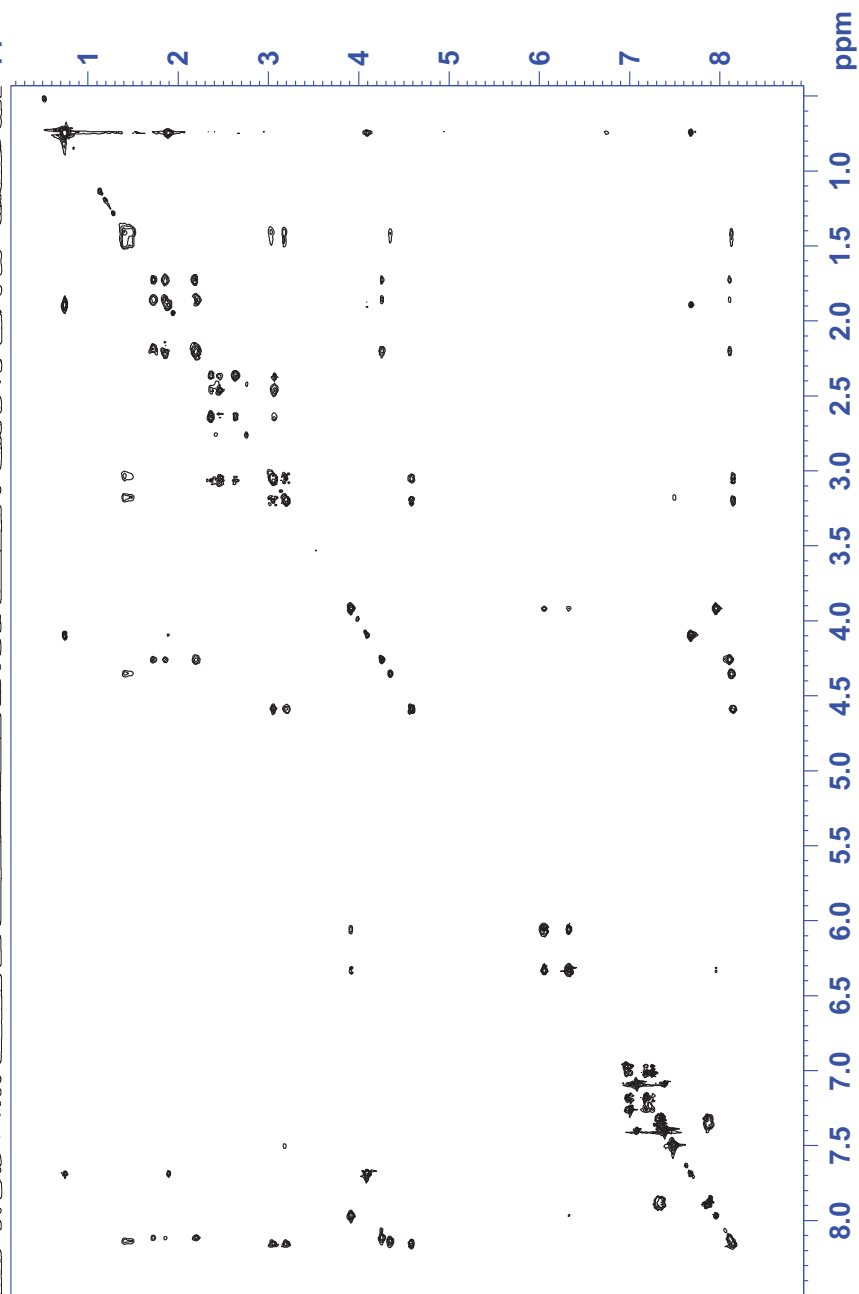
F2 - Processing parameters
 SI 2048
 SF 600.1300273 MHz
 WDW SINE
 SSB 1
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 2048
 MC2 States-TPPI
 SF 600.1300273 MHz
 WDW SSB
 LB 1
 GB 0 Hz
 PC 0





ppm

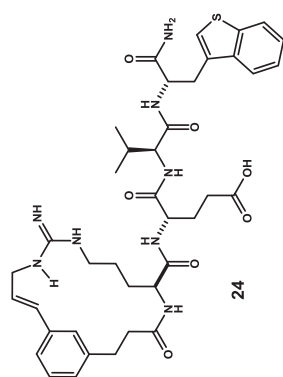


Current Data Parameters
 NAME KL-5-229-1
 EXPNO 3
 PROCNO 1

F1 - Acquisition parameters
 TD 400
 SFOL 600.1336 MHz
 FIDRES 18.004007 Hz
 SW 12.000 ppm
 FnmODE Echo-Antiecho

F2 - Processing parameters
 SI 1024
 SF 600.1300273 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0
 PC 1.00

F1 - Processing parameters
 SI 1024
 MC2 echo-antiecho
 SF 600.1300273 MHz
 WDW USER
 SSB 2
 LB 0 Hz
 GB 0

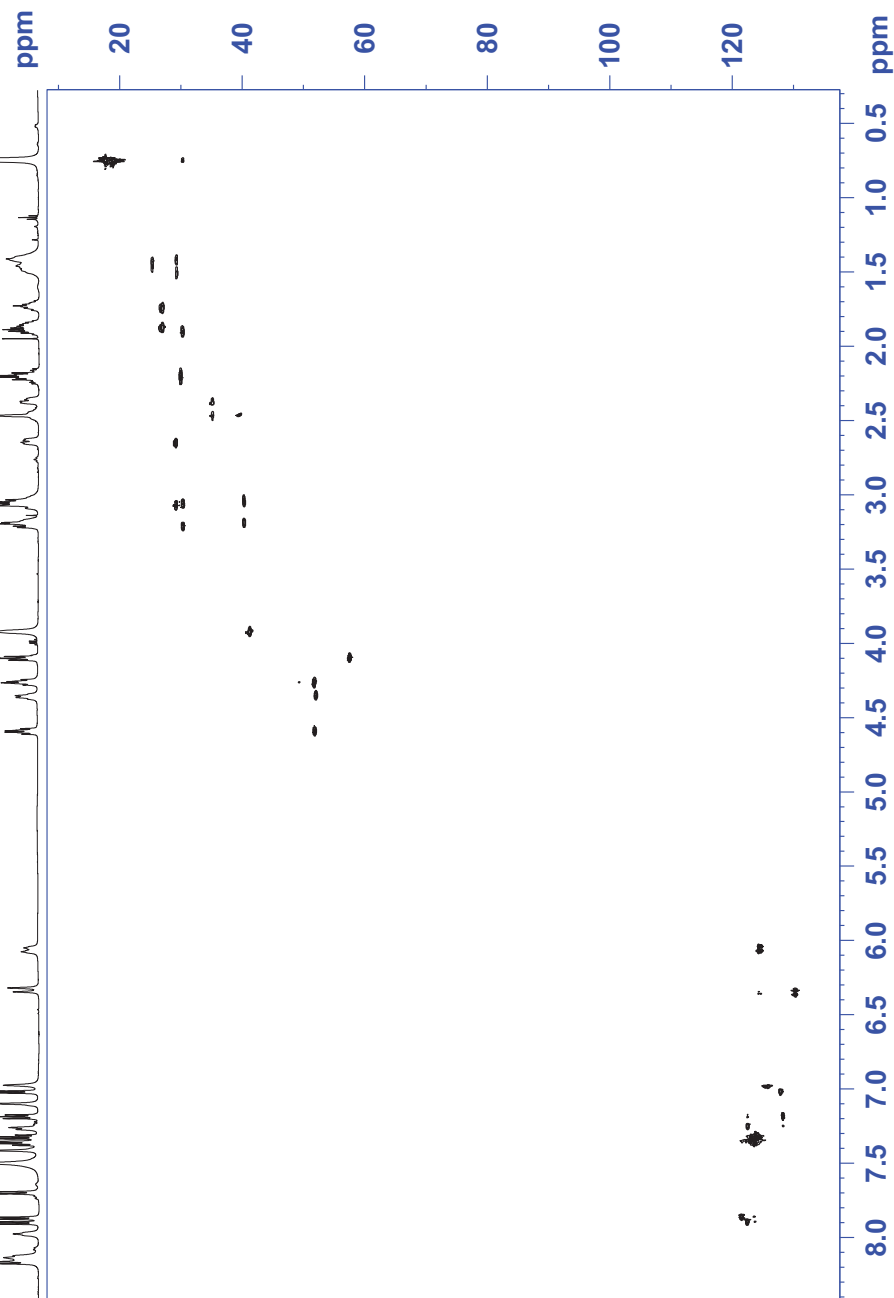


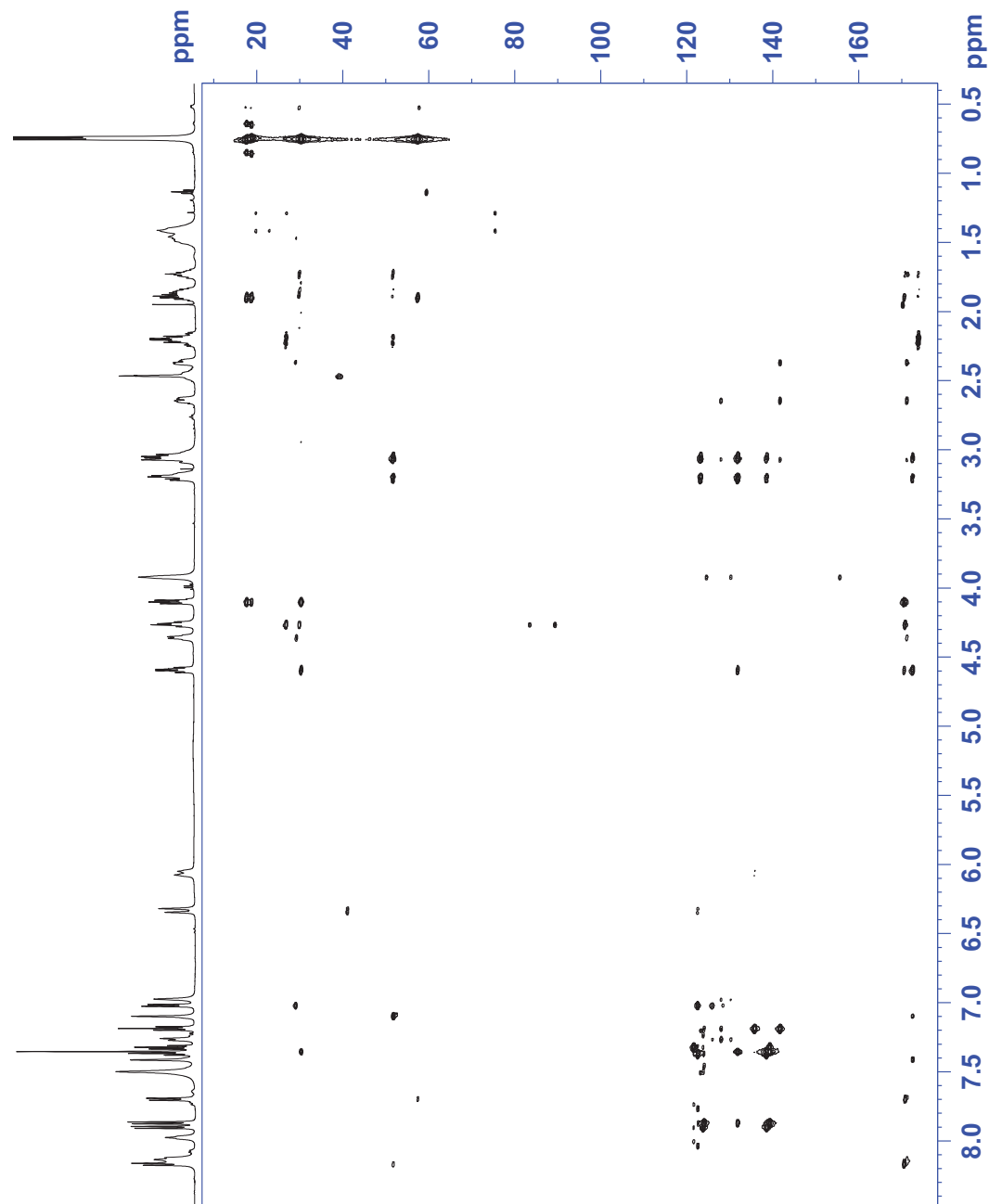
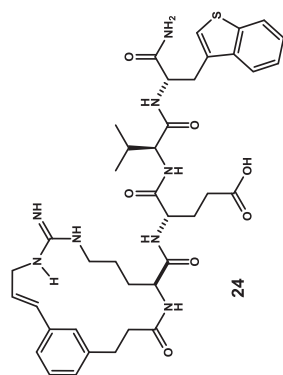
Current Data Parameters
 NAME KL-5-229-1
 EXPNO 5
 PROCNO 1

F1 - Acquisition parameters
 TD 512
 SF01 150.9134 MHz
 FIDRES 47.160427 Hz
 SW 160.000 ppm
 FnMODE Echo-Antiecho

F2 - Processing parameters
 SI 4096
 SF 600.1300282 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

F1 - Processing parameters
 SI 4096
 MC2 echo-antiecho
 SF 150.9029231 MHz
 WDW QSINE
 SSB 2
 LB 0 Hz
 GB 0





Current Data Parameters
 NAME KL-5-229-1
 EXPNO 6
 PROCNO 1

F1 - Acquisition parameters
 TD 512
 SFO1 150.9156 MHz
 FIDRES 56.003849 Hz
 SW 190.000 ppm
 FMODE QF

F2 - Processing parameters
 SI 4096
 SF 600.1300231 MHz
 WDW QSINE
 SSB 0
 LB 0 Hz
 GB 0
 PC 1.40

F1 - Processing parameters
 SI 4096
 MC2 QF
 SF 150.9029181 MHz
 WDW SINE
 SSB 3
 LB 0 Hz
 GB 0

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