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Santa Barbara

Total Synthesis and Structural Revision of (+)-Muironolide A and Late Stage Derivatization of Cyclic Imine Toxins

A dissertation submitted in partial satisfaction of the

requirements for the degree Doctor of Philosophy

in Chemistry

by

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June 2017

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Bachelor of Science in Chemistry, University of Kansas, June **2008**

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3. Young, K.; Xiao, Q.; Zakarian, A. Toward the Synthesis of Muironolide A: Synthesis and Structure of Heteroleptic Lanthanide-Terpyridine Complexes with 2-Oxo Amides. *Eur. J. Org. Chem.* **2015**, *11,* 2337-2341.
4. Xiao, Q.; Young, K.; Zakarian, A. An Efficient Synthesis of the Fully Elaborated Isoindolinone Unit of Muironolide A. *Org. Lett.* **2013**, *15,* 3314-3317.
5. 5. Rolfe, A.; Young, K.; Volp, K.; Schoenen, F.; Neuenswander, B.; Lushington, G. H.; Hanson, P. R. One-Pot, Three-Component, Domino Heck-aza-Michael Approach to

Libraries of Functionalized 1,1-Dioxido-1,2-benzisothiazoline-3-acetic Acids. *J. Comb. Chem.* **2009**, *11*, 732-738.

6. Rolfe, A.; Young, K.; Hanson, P. R. Domino Heck-aza-Michael reactions: a one-pot, sequential three-component approach to 1,1-dioxido-1,2-benzisothiazoline-3-acetic acid. *Eur. J. Org. Chem.*, **2008**, *31*, 5254-5262.

Awards

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Abstract

Total Synthesis and Structural Revision of (+)-Muironolide A

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In the Zakarian group, we are interested in the synthesis and application of marine natural products. Elucidating the biological properties of marine natural products is often hampered by a lack of its availability from natural sources in meaningful quantities. Therefore, chemical synthesis remains the most viable option for the production of these molecules. The syntheses of marine natural products frequently open opportunities to develop new synthetic methods, which push the boundaries of current state-of-the-art bond constructions.

Herein, we report the total synthesis and structural revision of (+)-muironolide A. Asymmetric intramolecular Diels-Alder reaction and late stage macrolactonization were the key transformations used for the synthesis of muironolide A, which led us to the reassignment of its structure as (−)-C21-*epi*-muironolide A.

The second portion describes the late stage derivatization of pinnatoxin compounds. The ultimate goal for pinnatoxin derivatives is introducing ^{18}F, ^{13}C and ^{3}H isotope labeling to probe cellular metabolism and biodistribution in biological systems. This

work builds upon a growing body of information that will provide an understanding of the full biological profile of the structurally complex pinnatoxin compounds.

The last portion of this thesis will focus on synthetic studies towards the synthesis of pteriatoxin A. A regioselective catalytic asymmetric dihydroxylation of pinnatoxin G is the featured method for the installment of the 1,2-diol moiety. Establishing this key step could secure a concise route for the total synthesis of pteriatoxin A.

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List of Abbreviations

Abbreviation, symbol, or chemical formula	Term
9-BBN	9-borabicyclo[3.3.1]nonane
[α]	specific rotation
α	alpha
AcOH	acetic acid
aq.	Aqueous
$AgBF_4$	silver tetrafluoroborate
$AgClO_4$	silver perchlorate
AgOTf	silver triflate
$AuCl_3$	gold(III) chloride
β	beta
BF_3 Et_2O	boron trifluoride diethyl etherate
Bn	benzyl
BnBr	benzyl bromide
Boc	*tert*-butyl carbonate
Boc_2O	di-*tert*-butyl dicarbonate
br	broad
brsm	based on recovery of starting material
$BrCCl_3$	bromotrichloromethane
BSA	bis(trimethylsilyl)acetamide

Bu	butyl
Bu_4NI	tetrabutylammonium iodide
Bz	benzoate
BzCl	benzoyl chloride
°C	degrees Celsius
c	concentration
^{13}C	carbon 13
calcd	calculated
CBz	benzyloxycarbonyl
CCl_4	carbon tetrachloride
$CDCl_3$	deuterochloroform
C_6D_6	deuterobenzene
CD_3OD	deuteromethanol
$CF_3CO_2CH_2CF_3$	2,2,2-trifluoroethyl trifluoroacetate
$(CF_3CO)_2O$	Trifluoroacetic anhydride
CH_2Cl_2	dichloromethane
CH_2O	formaldehyde
CH_3CN	acetonitirile
$C_2H_4Cl_2$	1,2-dichloroethane
$(COCl)_2$	oxalyl chloride
CrO_3	chromium(III) oxide
CSA	camphorsulfonic acid
Cs_2CO_3	cesium carbonate

CuBr	copper(I) bromide
$CuBr \cdot Me_2Br$	copper(I) bromide dimethyl sulfide complex
CuCl	copper(I) chloride
$Cu(OAc)_2$	copper(II) acetate
δ	chemical shift(s)
d (NMR)	doublet
d (time)	days
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCE	dichloroethane
DDQ	2,3-dichloro-5,6-dicyano-*p*-benzoquinone
DHP	dihydropyran
DIPEA	di-*iso*-propylethylamine
DIBAL	diisobutylaluminum hydride
DMAP	*N,N*-4-dimethylaminopyridine
DMF	dimethylformamide
DMP	Dess-Martin periodinane
DMPU	1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone
DMSO	Dimethyl sulfoxide
DPPA	diphenyl phosphoryl azide
DPEphos	(Oxydi-2,1-phenylene)bis(diphenylphosphine)
dr	diastereoseomeric ratio
DTMP	2,6-di-*tert*-butyl-4-methylpyridine

E	entgegen
EDCI	1-ethyl-3-(3-dimethylaminopropyl)-carbodiimidehydrochloride
ee	enantiomeric excess
EI	electron impact
equiv	equivalent
ESI	electrospray ionization
Et	ethyl
Et_3N	triethylamine
Et_2O	diethyl ether
EtOAc	ethyl acetate
EtOH	ethanol
Et_3SiH	triethylsilane
Et_3SiOTf	trimethylsilyl trifluoromethanesulfonate
Et_2Zn	diethyl zinc
$FeCl_3 \cdot 6H_2O$	iron(III) chloride hexahydrate
g	gram(s)
h	hour(s)
^1H	proton
HCl	hydrochloric acid
HF	hydrofluoric acid
$HfCl_4$	hafnium tetrachloride
HFIP	1,1,1,3,3,3-hexafluoroisopropanol

HMPA	hexamethylphosphoramide
H_2O	water
HOBt	*N*-hydroxybenzotriazole
HPLC	high performance liquid chromatography
HRMS	high resolution mass spectroscopy
H_2SO_4	sulfuric acid
Hünig's base	*N,N*-diisopropylethylamine
hν	light
Hz	hertz
ImH	imidazole
i	iso
I_2	iodine
i-Bu_2AlH	diisobutylaluminum hydride
$^{i}Pr_2NH$	di-*iso*-propylamine
$^{i}Pr_2NEt$	di-*iso*-propylethylamine (Hünig's Base)
$^{i}PrOH$	isopropanol or (2-propanol)
IR	Infrared Spectroscopy
KCN	potassium cyanide
KHMDS	potassium hexamethyldisilazane
K_2CO_3	potassium carbonate
KOH	potassium hydroxide
J	coupling constant

L	liter(s)
LDA	lithium diisopropylamide
$LiAlH_4$	lithium aluminum hydride
LiBr	lithium bromide
$LiBF_4$	lithium tetrafluoroborate
LiCl	lithium chloride
LiDBB	lithium di-tert-butyl biphenyl
LiOH	lithium hydroxide
LiOOH	lithium peroxide
m	multiplet
M	molarity
m/z	mass/charge
(M + Na)	molecular weight + sodium
MBz	*para*–methoxybenzoyl
mCPBA	*Meta*–chloroperoxybenzoic acid
Me	methyl
MeCN	acetonitrile
MeI	iodomethane
MeLi	methyl lithium
MeMgBr	methylmagnesium bromide
$MeNO_2$	nitromethane
MeO	methoxy

MeOH	methanol
$MeReO_3$	methyltrioxorhenium
Me_2CuLi	Gilman's reagent
Me_2S	dimethyl sulfide
$Me_3S^+I^-$	trimethylsulfonium iodide
Me_3SiCl	trimethylsilyl chloride
Me_3SiOK	potassium trimethylsilanolate
$(MeSO_2)_2O$	methanesulfonic anhydride
mg	milligram(s)
Mg	magnesium
MHz	megahertz
μL	microliter(s)
min	minute(s)
mL	milliliter(s)
mmol	millimole
mmHg	millimeters of mercury
MOM	methoxymethyl
MOMCl	chloromethyl methyl ether
MS	mass spectrometry
MsCl	methanesulfonyl chloride
MTO	methyltrioxorhenium
$Na(AcO)_3BH$	sodium triacetoxyborohydride

$NaBH_4$	sodium borohydride
$NaClO_2$	sodium chlorite
n-BuOLi	lithium *n*-butoxide
Na	sodium
NaH	sodium hydride
$NaHCO_3$	sodium bicarbonate
NaHMDS	sodium 1,1,1,3,3,3-hexamethylsilazane
NaH_2PO_4	sodium dihydrogen phosphate
$NaHSO_3$	sodium bisulfite
$NaIO_4$	sodium periodate
NaN_3	sodium azide
NaOAc	sodium acetate
NaOH	sodium hydroxide
NaO-*t*Bu	sodium tert-butoxide
$Na_2S_4 \cdot H_2O$	sodium sulfide hydrate
$Na_2S_8 \cdot 9H_2O$	sodium sulfide nonahydrate
Na_2SO_4	sodium sulfate
NBS	*N*-bromosuccinimide
NFSI	*N*-fluorobenzenesulfonimide
$NH_2OH \cdot HCl$	hydroxylamine hydrochloride
n-BuLi	*n*-butyllithium
NIS	*N*-iodosuccinimide

NMO	*N*-methylmorpholine-*N*-oxide
NMP	*N*-methyl-2-pyrrolidone
NMR	nuclear magnetic resonance
NOE	nuclear Overhauser effect
O_3	ozone
OsO_4	osmium(VIII) oxide
Pd/C	palladium(0) on charcoal
$Pd/CaCO_3$	palladium (0) on calcium carbonate Lindlar Catalyst
$Pd(PPh_3)_4$	tetrakis(triphenylphosphine)palladium (0)
$Pd_2(dba)_3$	tris(dibenzylideneacetone)dipalladium (0)
$[Pd(allyl)Cl]_2$	allylpalladium(II) chloride dimer
Ph	phenyl
Ph_2SiH_2	diphenylsilane
Ph_3As	triphenylarsine
$PhI(OAc)_2$	(diacetoxyiodo)benzene
PhMe	toluene
$[Ph_3P]_3RuCl_2$	dichlorotris(triphenylphosphine)ruthenium(II)
$Ph_3SiOReO_3$	triphenylsilyl perrhenate
PivCl	Pivaloyl chloride
PMe_3	trimethylphosphine
$POCl_3$	phosphorus(V) oxychloride
PPh_3	triphenylphosphine

PPh_3AuCl	chloro(triphenylphosphine)gold(I)
PMB	*para*–methoxybenzyl
PMP	*para*–methoxyphenyl
ppm	parts per million
PPTS	pyridinium *p*-toluenesulfonate
PTSA	*para*-toluenesulfonic acid
p-ABSA	4-acetamidobenzenesulfonyl azide
p-Tol	*para*–tolyl
p-TsOH	*para*–toluenesulfonic acid
PvCl	pivaloyl chloride
Py	pyridine
$[Rh(COD)Cl]_2$	chloro(1,5-cyclooctadiene)rhodium(I) dimer
$Rh_2(OAc)_4$	rhodium acetate
rt	room temperature
(*R*)-(*p*-tolyl)$_2$BINAP	(*R*)-(−)-*para*-toluenesulfinamide
s	singlet
SO_3	sulfur trioxide
TBAF	tetrabutylammonium fluoride
TBAI	tetrabutylammonium iodide
t-BuLi	*tert*-butyl lithium
t-BuOH	*tert*-butanol
TBD	1,5,7-triazabicyclo[4.4.0]dec-5-ene

TBDPS	*tert*-butyldiphenylsilyl
TBDPSCl	*tert*-butyl(chloro)diphenylsilane
TBS	*tert*-butyldimethylsilyl
TBSCl	*tert*-butyldimethylsilyl chloride
TEMPO	2,2,6,6-tetramethyl-1-piperidinyloxy, free radical
TES	triethylsilyl
TESCl	triethylsilyl chloride
TFA	trifluoroacetic acid
THF	tetrahydrofuran
$TiCl_4$	titanium(IV) chloride
TIPS	triisopropylsilyl
TIPSCl	chlorotriisopropylsilane
TMS	trimethylsilyl
TMSCl	trimethylsilyl chloride
$TMSCHN_2$	trimethylsilyldiazomethane
Ts	4-toluenesulfonyl
TsCl	4-toluenesulfonyl chloride
Zn	Zinc
$ZrCl_4$	zirconium tetrachloride

Chapter 1: Total Synthesis and Structural Revision of (+)-Muironolide A

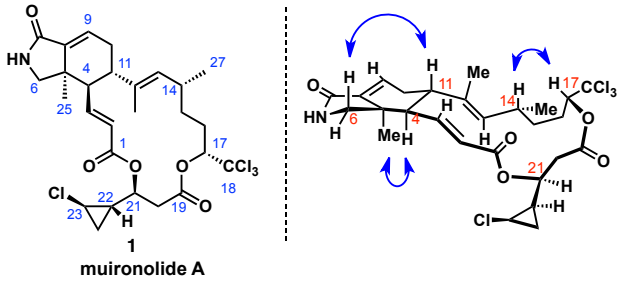
1.1: Introduction

In 2009, the Molinski group at the University of California, San Diego (UCSD) published a report of the isolation and characterization of muironolide A.[1] Muironolide A, a secondary metabolite, was isolated from the marine sponge *Phorbus* sp. Muironolide A most likely arose from heterogeneous microbial interactions with the marine sponge. These types of associations provide a diverse array of natural products. For example, this same sponge also produced known metabolites such as phorboxazoles A and B and phorbaside A.[2] State-of-the-art microcryobe NMR spectroscopy and degradation techniques were employed to elucidate the structure of muironolide A with only 90 μg of the material isolated from the natural source. From these structural studies, it was discovered that muironolide A possessed two unprecedented features: a hexahydro-1*H*-isoindolone ring and a trichlorocarbinol ester. Other notable features include a 16-membered macrocyclic diester and a chlorocyclopropane ketide (CCK). With exceedingly small amounts of sample available, some preliminary biological screening was performed, and muironolide A was shown to exhibit moderate activity towards HCT116 colon tumor cell line with IC_{50} = 96.5 μg/mL and antifungal activity against *Cryptococcus neoformans* MIC = 16 μg/mL. In order to unveil the full biological profile of **1** (Figure 1), more material was required. Extraction from natural sources was not feasible. Since 2009, the authors of the original isolation have not encountered the marine sponge *Phorbus*. The only option to access additional supply of muironolide A was through total synthesis.

1.2: Isolation and Characterization of Muironolide A

Marine sponge *Phorbus* was encountered off the western coast of Australia near the Muiron islands. Extraction and HPLC purification afforded 90 μg of muironolide A. Microcryobe NMR spectroscopy, Fourier Transform Mass Spectrometry (FTMS), circular dichroism (CD) and synthesis/chemical degradation techniques were employed to elucidate its structure. FTMS result showed a molecular formula of **1** as $C_{27}H_{33}Cl_4NO_5$ and *m/z* = 5.92.11869 $[M+H]^+$ to reveal 10 double bonds. Carbon-13 NMR showed three ester or amide groups. Circular dichroism (CD) spectrum established the absolute configuration of muironolide A based on Harada−Nakanishi nonempirical rule.

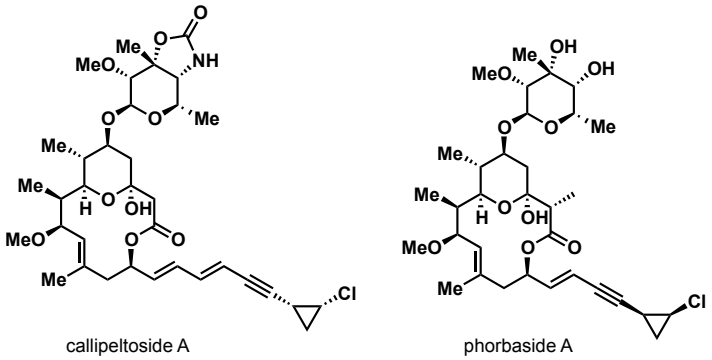
Figure 1. HMBC and NOESY Determination of Stereochemistry at C4, C5, C11, C14 and C17.



The relative stereochemistry of the northern portion of the diester was established through key NOE signals shown in Figure 1. Strong NOE correlation was observed between H11 and H6 (AB system J_{HH} = 8.8 Hz) positions of the γ-lactam. Also, H14 and H17 NOE signals indicated a *gauche*-turn conformation of the macrocycle. The stereochemistry at C21 adjacent to the chlorocyclopropyl ketide (CCK) fragment could not be resolved through NMR spectroscopic methods. NOESY or *J*-based methods could not relay the stereochemical information of the C4 stereocenter through the α,β-unsaturated ester to C21. Subjecting **1** to hydrolysis and esterification of the

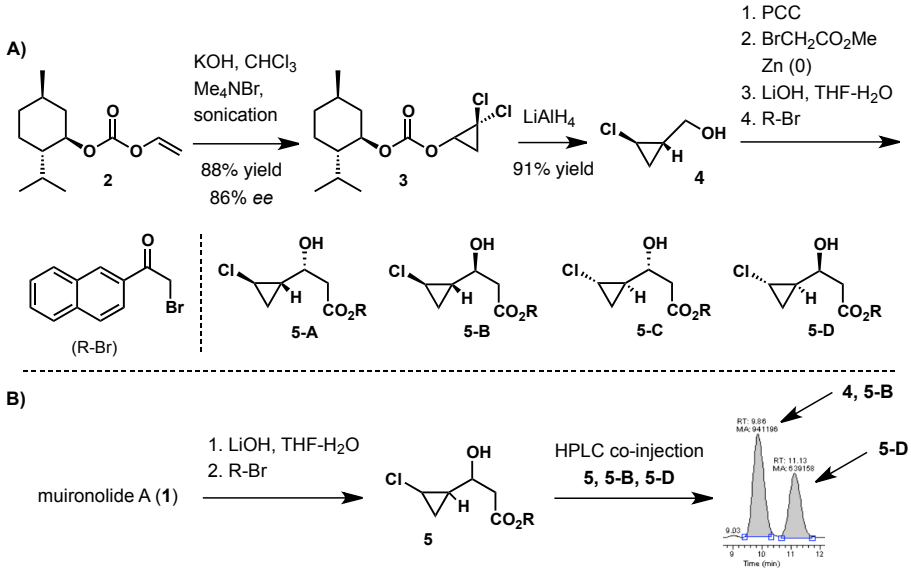
corresponding CCK fragment for HPLC trace analysis were performed to establish C23, C22 and C21 stereocenters.

Figure 2. Chlorocyclopropanes in Natural Products



Chlorocyclopropanes are present in other natural products such as phorbaside A[3] and callipeltosides A-C.[4] Molinski proposed that the stereochemistry at C22 and C23 positions of muironolide A have the same absolute configuration found in callipeltosides A-C but opposite to phorbaside A. Interestingly, phorbaside A was extracted from the same marine sponge *Phorbus* as muironolide A.

Scheme 1. Identification of CCK of **1** via Degradation, Synthesis and HPLC

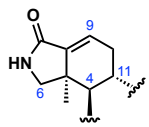


Efforts to confirm the stereochemistry of CCK **5** by HPLC traces prompted the synthesis of four synthetic CCK diastereomers shown in Scheme 1A. Sonication of chloroform solutions containing (−)-menthyl acrylate **2**, potassium hydroxide and tetramethylammonium bromide afforded dichlorocyclopropane **3** in 88% *ee*. Diastereoselective reduction of **3** was achieved with lithium aluminum hydride that provided *trans*-alcohol **4**. The configuration of the chlorocyclopropyl alcohol **4** matched the same compound that was reported by Olivo and coworkers.[5] Oxidation and treatment of the resulting aldehyde with zinc powder and methyl 2-bromoacetate completed the synthesis of the CCK fragment. A total of four isomers at C23, C22 and C21-positions were made from this synthesis. Further modifications to install a chromophore to aid in the HPLC analysis were necessary. Hydrolysis of the methyl ester and esterification with 2-bromo-1-(naphthalen-2-yl)ethanone were performed. Similarly, muironolide A was subjected to the same hydrolysis and esterification procedures. Then, the natural product derived CCK fragment **5** was spiked with samples **5-B** and **5-D**. The natural CCK **5** showed matching retention times with sample **5-B**. Therefore, they concluded that the natural CCK unit was the C23-(*R*), C22-(*S*) and C21-(*S*) isomer.

1.3: Synthetic Studies Towards Hexahydro-1*H*-Isoindolone Unit of Muironolide A

1.3.1: Molinski's Study Towards Hexahydro-1*H*-Isoindolone Unit

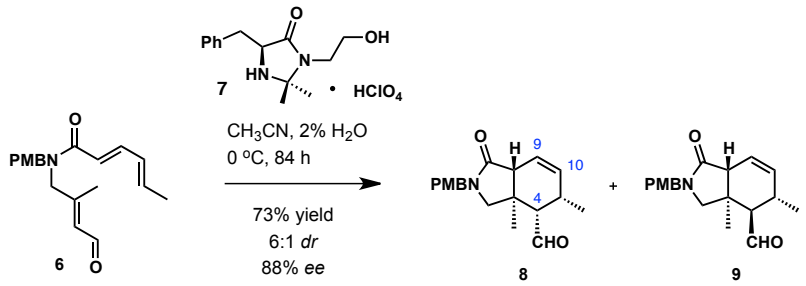
Figure 3. Hexahydro-1*H*-Isoindolone Unit of Muironolide A



Hexahydro-1*H*-Isoindolinone

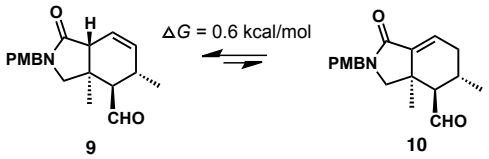
The hexahydro-1*H*-isoindolinone (referred to here as isoindolinone) bears three contiguous stereocenters on the C4, C5, and C11-positions and unsaturation at the α,β-positions of the amide. Asymmetric intramolecular Diels-Alder (IMDA) cycloaddition with MacMillan-type organocatalyst was used to construct the isoindolinone subunit from precursor **6** (Scheme 2).[6]

Scheme 2. Asymmetric Intramolecular Diels-Alder using Organocatalyst



Under optimized conditions, the treatment of amide **6** with 20 mol % of (*S*)-5-benzyl-3-(2-hydroxyethyl)-2,2-dimethylimidazolidin-4-one perchlorate (**7**) in a 2% water-acetonitrile solution at 0 °C for 84 h provided a 6:1 (**8**:**9**) mixture of diastereomers in 73% yield and 88% *ee*. Diastereomer **8** was converted to the desired isomer **9** with DBU. Attempts to isomerize the C9 and C10 double bond into conjugation were unsuccessful with a variety of different bases (NaOMe-MeOH, DBU-benzene, NaH-DMF). Conformational analysis provided some insight into the reluctance of this isomerization.

Figure 4. Conformational Analysis of Double Bond Isomers



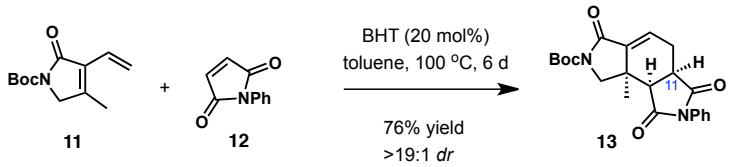
The double bond at the α,β-positions of **10** confers a strained half-chair conformation (Figure 4). Additionally, semiempirical calculations of enthalpies of formation showed

the β,γ-position (**9**) was more stable than the α,β-positions (**10**) by 0.6 kcal/mol (PM3). The authors suggested that one possible method to place the double into conjugation was through hydrogenation, α-selenation and oxidation/elimination.

1.3.3: Mitchell's Study Towards Hexahydro-1*H*-Isoindolone Unit

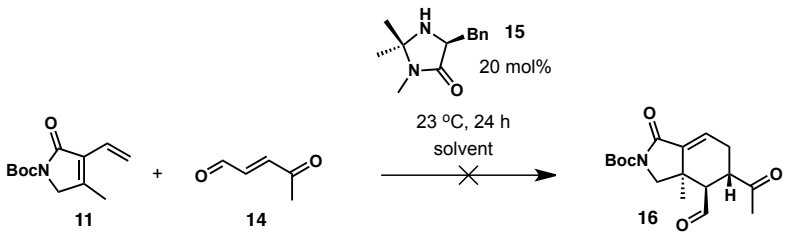
In 2013 and 2015, Mitchell reported a unique intermolecular Diels-Alder approach to the isoindolinone core of muironolide A.[7] In their study, an electronically deficient diene **11** underwent [4+2] cyclization with dienophile **12** to afford *endo* product **13** in 76% yield and > 19:1 dr.

Scheme 3. Mitchell's Intermolecular Diels-Alder Approach



Unfortunately, the stereocenter at the C11 position was epimeric from the desired configuration due to the cyclic restraint of the dienophile. Attempts with acyclic dienophile to correct the stereochemical configuration were unsuccessful. The treatment of α,β-unsaturated aldehyde **14** and diene **11** with Macmillan's organocatalyst provided no cycloaddition adduct.

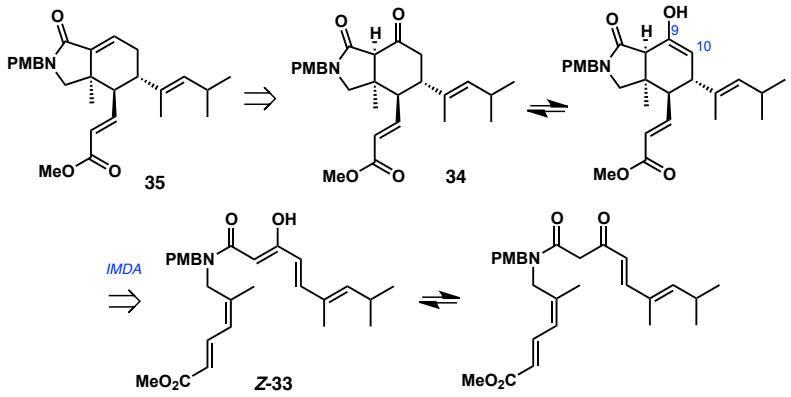
Scheme 4. Mitchell's Intermolecular Diels-Alder Reaction with Organocatalyst



1.3.4: Zakarian's Study Towards Hexahydro-1*H*-Isoindolone Unit

In 2013, we reported a study utilizing an intramolecular Diels-Alder (IMDA) reaction to access the isoindolinone subunit in an efficient manner.[8] We identified that compound **35** was structurally similar to the natural product and would serve as a suitable model to study the IMDA reaction.

Scheme 5. IMDA Strategy

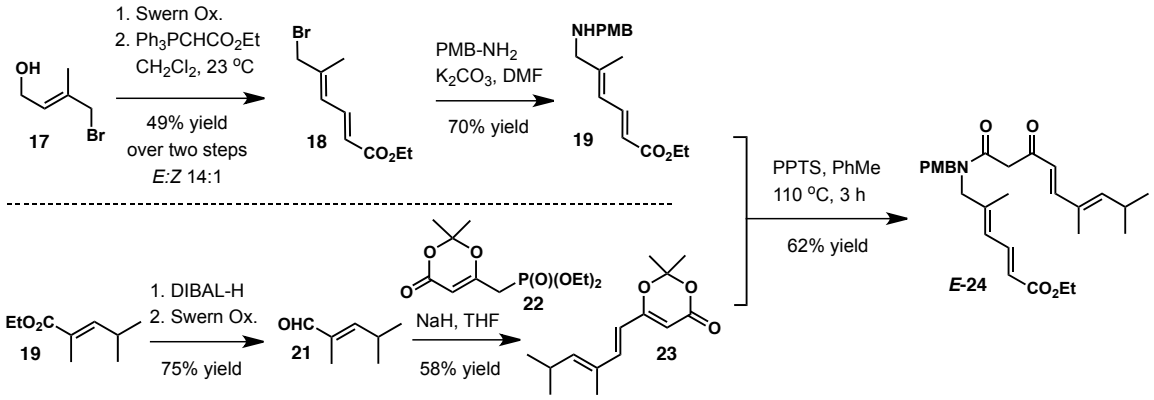


We envisioned that β-ketoamide ***Z*-33**, in the enol form, would undergo a cycloaddition or a double Michael addition to access **34**. The strategic placement of β-keto amide served two purposes in our synthetic design. First, the placement of the double bond between C9 and C10 after cycloaddition was inconsequential as this existed as the *enol*-tautomer. Also, the dicarbonyl functional group could chelate with a chiral Lewis acid to promote an asymmetric IMDA reaction. At the onset of our plan, we were aimed to test the influence of double bond geometry on the stereochemical outcome of the IMDA reaction with ***Z*-33** and ***E*-24** as substrates. This investigation started with substrate ***E*-24**.

The synthesis of ***E*-24** was completed in a four-step sequence. Swern oxidation of (*E*)-4-bromo-3-methylbut-2-en-1-ol **17**[9], Wittig olefination of the respective aldehyde and

direct exposure with PMB-amine (K_2CO_3, DMF) provided **19** in 34% overall yield. Dioxinone **23** was completed in three-steps by treatment of (*E*)-ethyl 2,4-dimethylpent-2-enoate **20** with *i*-Bu_2AlH, Swern oxidation to **21**, followed by olefination with Horner-Wadsworth-Emmons (HWE) reagent **22** provided **23** in 44% overall yield.[10,11] Direct coupling of amine **19** and dioxinone **23** in the presence of pyridinium *p*-toluenesulfonate in refluxing toluene afforded amide ***E*-24** in 62% yield.[12]

Scheme 6. Synthesis of ***E*-24** IMDA Precursor

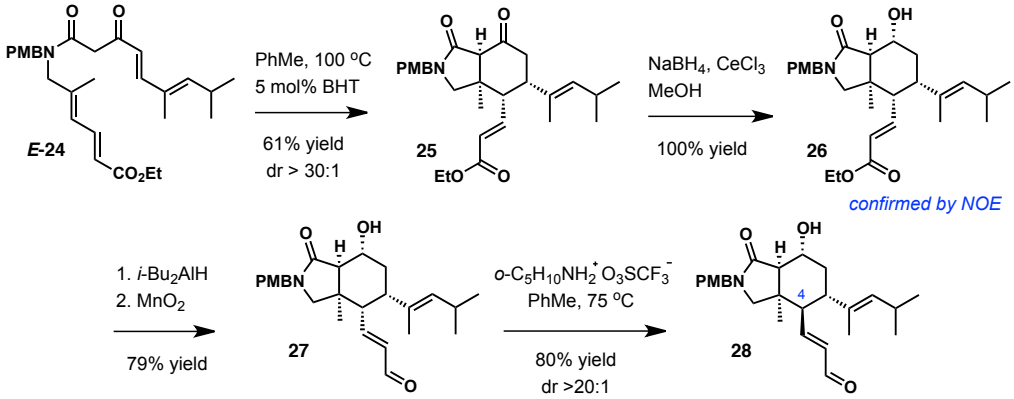


Upon heating of substrate ***E*-24** in toluene, a highly *endo*-selective IMDA product **25** was isolated in 61% yield and dr >30:1. The addition of any base additives (*e.g.*, triethyl amine, Cs_2CO_3, $LiN(SiMe_3)_2$, *n*-Bu_4NF)[13] did not accelerate the reaction rate but rather poor yields or decomposition products were isolated. Therefore this suggested a concerted cycloaddition was occurring rather than a double Michael addition.

After the Luche reduction ($NaBH_4$, $CeCl_3$) of the ketone, the relative stereochemistry of **26** was confirmed by NOE studies. The stereochemistry consistent with muironolide A could be obtained by epimerizing C4-position. Treatment of ester **26** with *i*-Bu_2AlH and MnO_2 provided unsaturated aldehyde **27** in 79% yield. Epimerization was performed in

the presence of piperidinium trifluoroacetate (toluene, 75 °C) to afford **28** in 80% yield and dr >20:1.[14]

Scheme 7. Highly *Endo*-Selective IMDA Reaction with ***E*-24**

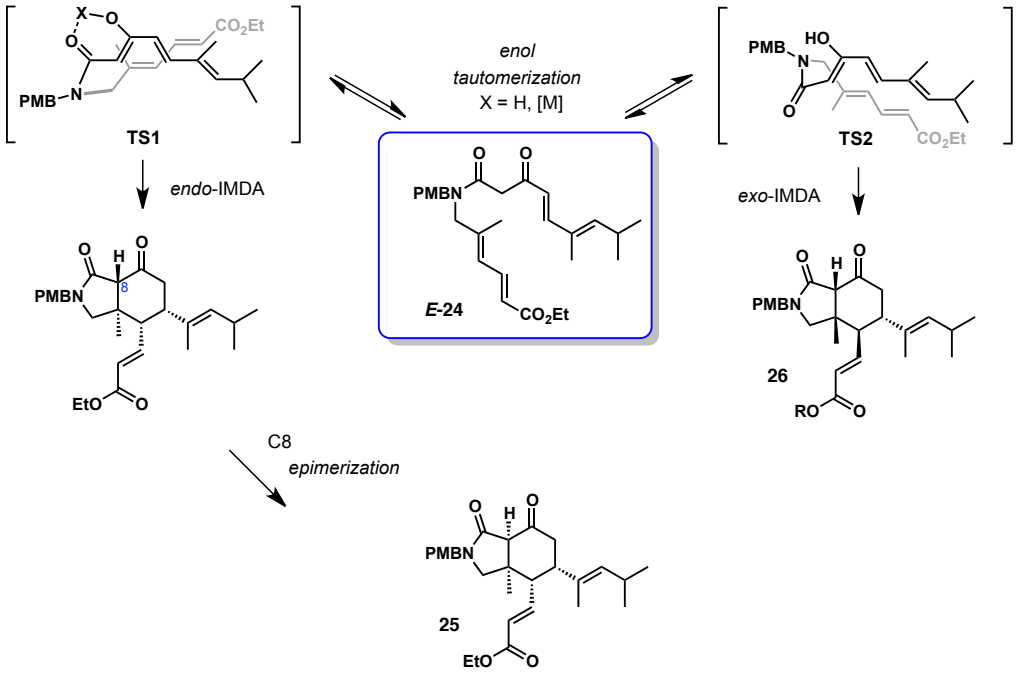


The stereochemical outcome of this key IMDA transformation deserves a comment. At the onset, the reactive enol form of ***E*-24** was hydrogen bond stabilized (**TS1**). This underwent an *endo*-selective cycloaddition reaction, followed by rapid C8 epimerization (Figure 5). We hypothesized that the origin of this highly diastereoselective transformation was based on hydrogen bond stabilization in the transition state (**TS1**) rather than stabilization gained from secondary orbital overlap (**TS2**). There was notable erosion in diastereoselectivity (~5:1 favoring *endo*) when ***E*-24** was trapped as a silyl ketene acetal, suggesting minor influences of secondary orbital overlap to the stereoselective outcome of this transformation. The IMDA reaction of ***Z*-33** was investigated next.

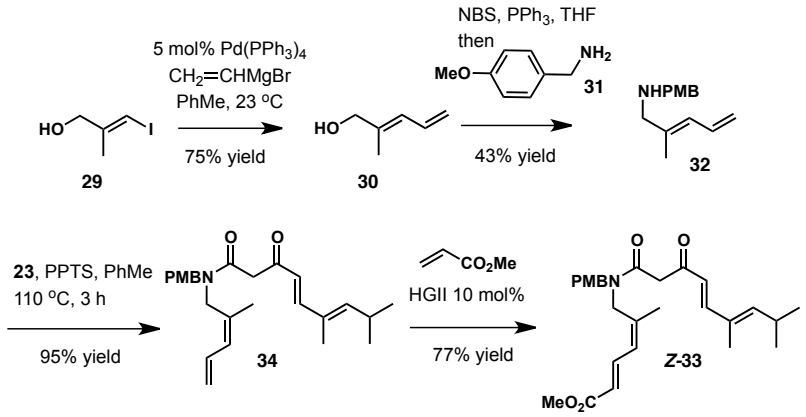
The synthesis of IMDA precursor ***Z*-33** began with Kumada coupling of iodide **29** with vinylmagnesium-bromide and $Pd(PPh)_4$, followed by a one-pot substitution of the hydroxyl group to PMB-amine **32** in 32% overall yield (Scheme 8).[15] Amide bond formation proceeded cleanly with pyridinium *p*-toluenesulfonate (PPTS) in refluxing

toluene for 3 h to provide rotamer **34** in 95% yield. Cross metathesis of methyl acrylate with diene **34** in the presence of Hoyveda-Grubbs II (HGII) catalyst (10 mol%) completed IMDA precursor ***Z*-33** in 81% yield.[16]

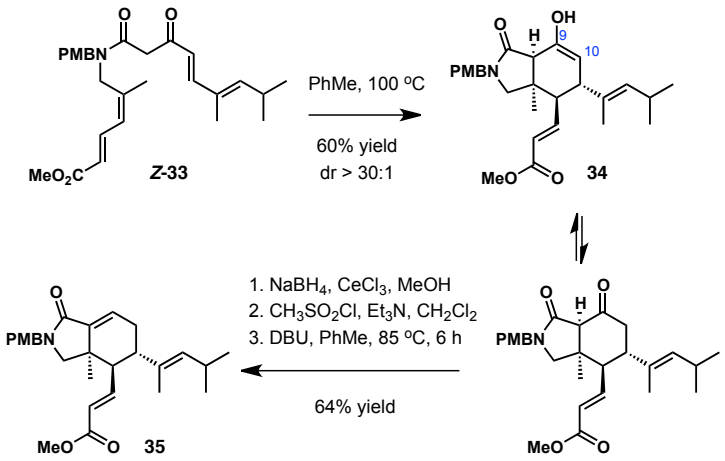
Figure 5. Rational for *Endo*-selective IMDA Reaction for *E*-Isomer



Scheme 8. Synthesis of *Z*-configured IMDA Precursor

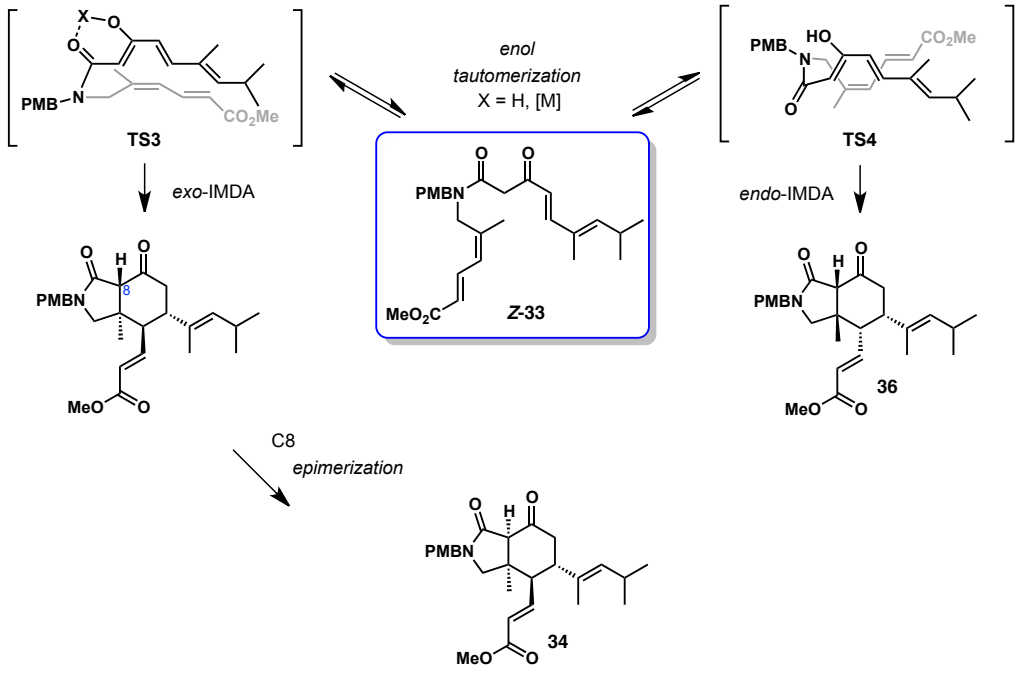


Scheme 9. Highly *Exo*-Selective IMDA Reaction with ***Z*-33**



Heating β-keto amide ***Z*-33** in toluene at 100 °C for 24 h, provided IMDA product **34** in 60% yield and dr > 30:1. NOE studies confirmed the relative stereochemistry at C4, C5 and C11 were consistent with the natural product.

Figure 6. Rational for *Exo*-selective IMDA Reaction for *Z*-Isomer



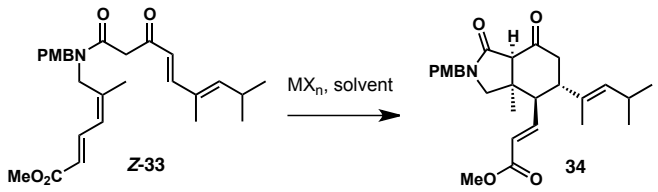
Three additional steps were required to complete the isoindolinone subunit. Luche reduction ($NaBH_4$, CeCl3) of the ketone followed mesylation of the corresponding

alcohol and mesylate elimination (DBU at 85 °C) provided isoindolinone **35** in 64% yield over three steps. The significance of this transformation was the ability to access the correct stereoconfiguration of the isoindolinone in one-step. This study represents the most concise entry to the isoindolinone core to-date.

1.3.5: Heteroleptic Lanthanide–Terpyridine Complexes with 2-Oxo Amides

The ultimate goal of the IMDA approach to access the isoindolinone core of muironolide A was to render this transformation stereoselective. Asymmetric catalysis with lanthanide complexes has increasing utility in organic synthesis.[17] Unique characteristics of lanthanides include high coordination numbers, stability and dynamic binding towards ligands that impart catalytic efficiency.[18]

Table 1. Lewis Acid Screening for IMDA Reaction

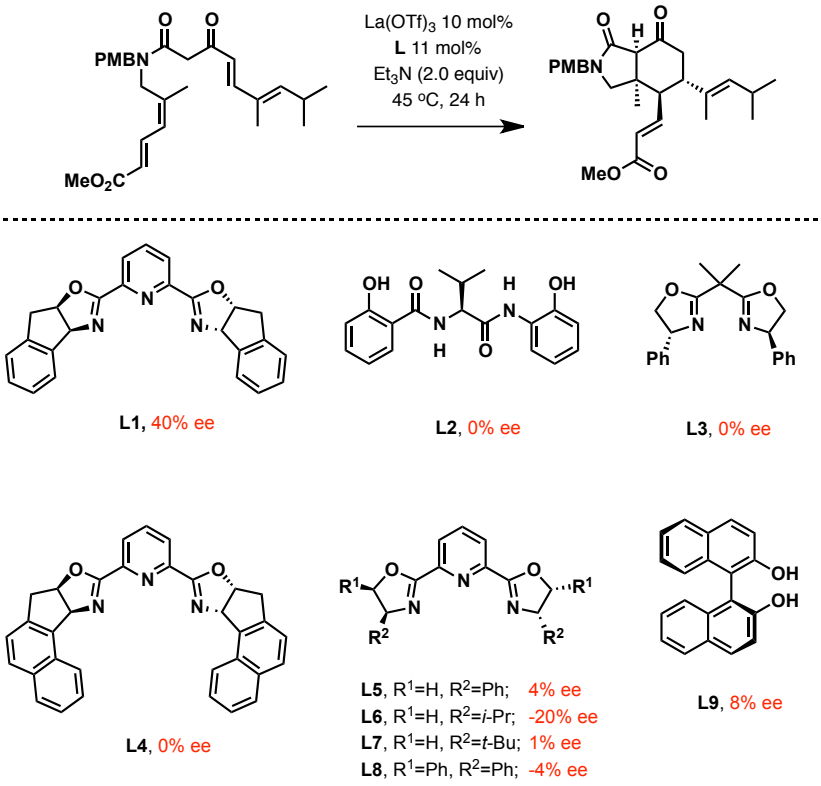


entry	MX_n	solvent	temp, °C	time, h	conv., %	dr
1	none	$CDCl_3$	61	40	16	>20:1
2	$Cu(OTf)_2$	$CDCl_3$	61	60	43	>20:1
3	$Fe(OAc)_2$	$CDCl_3$	61	70	36	4:1
4	$Zr(OPr\text{-}i)_4$	$CDCl_3$	61	70	35	14:1
5	$Yb(OTf)_3$	$CDCl_3$	61	17	76	>20:1
6	$Yb(OTf)_3$	CD_3CN	45	24	16	14:1
7	$Sc(OTf)_3$	CD_3CN	45	24	15	5:1
8	$Eu(OTf)_3$	$CDCl_3$	61	17	75	>20:1
9	$Eu(OTf)_3$	CD_3CN	75	3	72	7:1
10	$Eu(OTf)_3$	CD_3CN	45	24	62	5:1
11	$La(OTf)_3$	CD_3CN	45	24	90	4:1
12	$La(OTf)_3$	THF	45	24	90	20:1
13	$La(OTf)_3$	EtOAc	45	24	90	>20:1
14	$Dy(OTf)_3$	EtOAc	45	24	53	10:1

15	$Dy(NO_3)_3$	EtOAc	45	24	73	10:1

Initial screening of the IMDA reaction in the presence of catalytic amounts of metal salts revealed that La(III) salts were superior. Under optimized conditions, entries 13 and 15 (see Table 1), β-keto amide ***Z*-33** was converted to isoindolone **34** in the presence of either $La(OTf)_3$ or $Dy(NO_3)_3$ in ethyl acetate at 45 °C for 24 h with dr >20:1 and 10:1, respectively. Screening different D-block transition metals such as copper, iron and zirconium salts led to poor conversions (16-43%) and long reaction times (40-70 h) (entries 2-4).

Figure 7. Screening of Ligands for IMDA Reaction



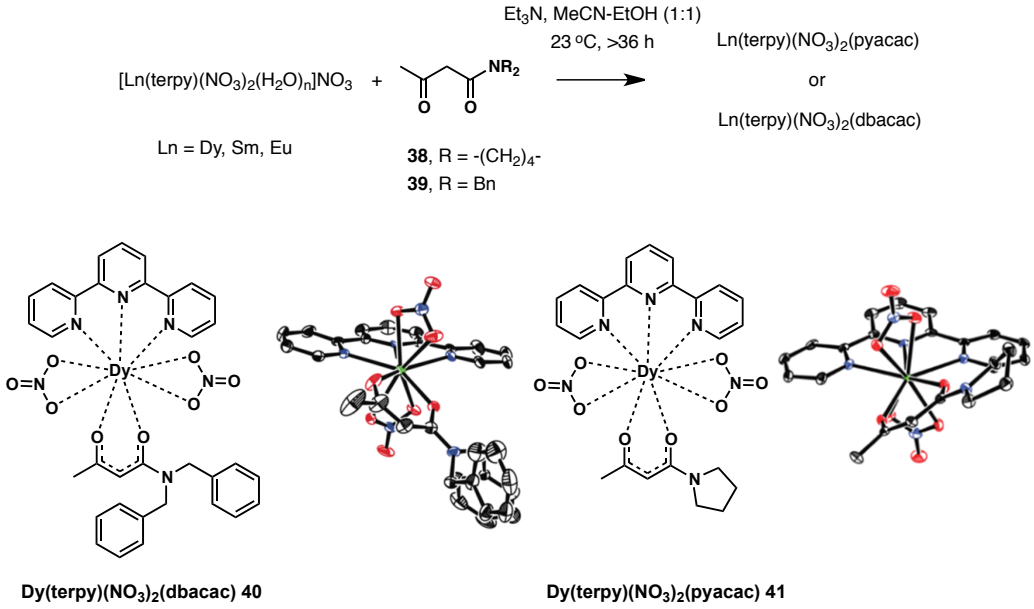
With optimized conditions at hand, we next turned our focus towards chiral ligands for asymmetric catalysts with lanthanide salts. The reaction conditions for each ligand

were individually optimized and **L1** provided the most satisfactory enantioselectivity at 40% *ee*.

At this point, we were inspired to explore unconventional ligands for the IMDA reaction. Our goal was to rationally design chiral ligands that were suitable for β-ketoamides. Inspiration first came from a report by Fukuda and co-workers, who reported crystal structures of heteroleptic lanthanum-terpyridine complexes with acetoacetate ($Ln(terpy)(acac)(NO_3)_2$).[19] Surprisingly, there was little literature precedence for chiral terpyridine (terpy) ligands with rare earth metals used in asymmetric synthesis. The only relevant application was modestly enantioselective cyclopropanation of styrene using chiral terpy ligand with Cu(II) or Rh(III) catalysts reported by Kwong *et. al*.[20] Other applications of non-chiral Ln(III)-terpy complexes range from the study of fluorescent emissions properties and application as photochemotherapeutic agents.[21]

At the onset, we chose to replace acac with unsymmetrical ligands such as pyrolidineamide **38** or *N,N*-dibenzyl-2-oxobutanamide **39** (Scheme 10). Known complexes of $[Ln(terpy)(NO_3)_2(H_2O)_n]NO_3$ were obtained by the treatment of $Ln(NO_3)_3 \bullet xH_2O$ with one equivalent of terpyridine in ethanol for one hour at room temperature followed by filtration. This bench-top stable complex was treated with three equivalents of β-keto amide, two equivalence of triethylamine in a 1:1 mixture of acetonitrile and ethanol. Slow evaporation at room temperature (~36 h) provided colorless crystals ranging from 10-50 μm. Crystal structures of this type were obtained through X-Ray diffraction for dysprosium, samarium and europium.

Scheme 10. Synthesis and X-Ray Structures of Ln-Terpyridine Complexes with β-Keto Amide Ligands.



The ORTEP drawing of $Dy(terpy)(NO_3)_2(pyacac)$ is shown in Scheme 10. As expected, the two nitrate groups occupy the axial positions above and below the plane occupied by terpy and pyacac ligands. Of note, while the majority of reported acac complexes with lanthanides contain more than two units of the ligand, in our case only one pyacac unit was present in the Dy complex.[22] This property was highly desirable for catalyst development because it was indicative of a more defined, unambiguous substrate binding. Both the terpyridine and pyacac ligands are nearly planar; the angle between the planes was approximately 33°. XRD structures with closely related complexes were also obtained for $Sm(terpy)(NO_3)_2(pyacac)$ and $Eu(terpy)(NO_3)_2(pyacac)$, with the angles between the planar terpyridine and pyacac ligands at 29° and 30°, respectively. With these compounds on-hand, we continued with a more complex, conformationally labile dibenzyl amide **39**. We were delighted that when $[Dy(terpy)(NO_3)_2(H_2O)_2]NO_3$ was treated with amide **39** in the presence of triethylamine, the resulting complex

$Dy(terpy)(NO_3)_2(dbacac)$ afforded crystals suitable for crystallographic analysis (Scheme 10).

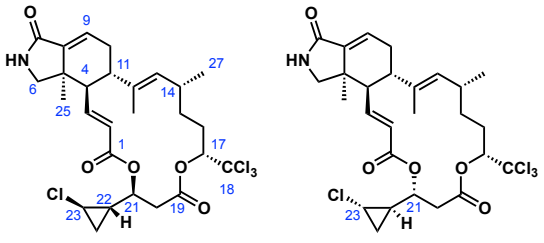
From these structures, we concluded that Ln(III)-terpy complexes could be excellent catalysts for the IMDA application, not only for its ability to generate the reactive enolate form of β-ketoamides but also for its well-defined and predictable metal-ligand geometry. In the future, these crystal structures could aid in the strategic placement of chiral groups on the terpyridine ligand to impart a chiral environment necessary for asymmetric catalysis

1.4: Total Synthesis and Structural Revision of (+)-Muironolide A

We reported the first enantioselective total synthesis of (+)-muironolide A (**44**).[23] Based on chemical synthesis and NMR studies, synthetic **1** did not match the characterization data of the natural substance. The synthesis of two C21, C22, C23-diastereomers (**43** and **44**) led to the discovery of the correct structure of muironolide A to be the C21-epimer (**44**) shown in Figure 8. The full characterization of **44** was in full agreement with that of natural muironolide A. However, the CD spectrum of **44** was found to be antipodal; therefore, we established the absolute configuration of the natural product to be (-)-muironolide A.

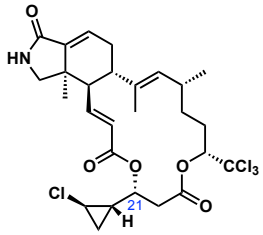
In this synthetic strategy, we envisioned a challenging late stage 16-membered macro-lactonization shown in Scheme 11. Concise reduction and dehydration steps completed the isoindolinone subunit. An asymmetric lanthanum catalyzed intramolecular Diels-Alder (IMDA) reaction was employed for the construction of the isoindoledione subunit.

Figure 8. Muironolide A and C21, C22 and C23-Diastereomers



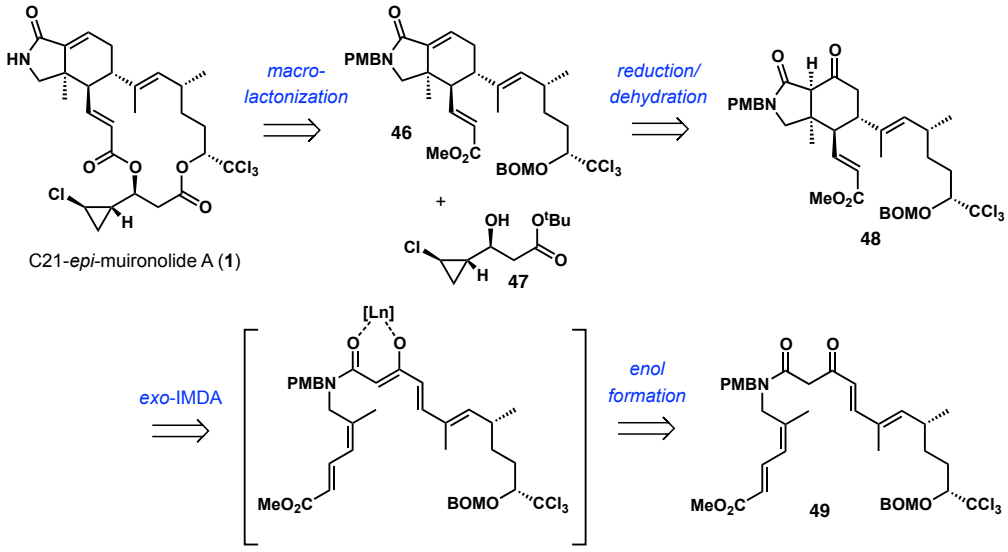
C21-*epi*-muironolide A (**1**)
original assignment

C22,C23-*epi*-muironolide A (**43**)



(+)-muironolide A (**44**)
revised structure

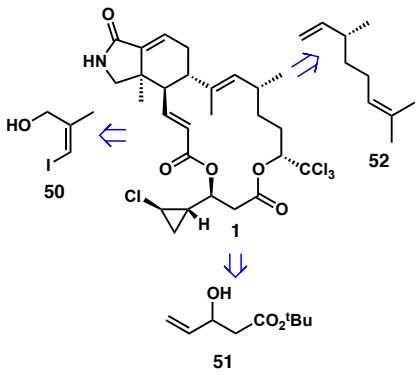
Scheme 11. Synthesis Plan for (+)-Muironolide A



Strategically, the natural product was divided into three segments (Figure 9). The synthesis of the eastern fragment started with (+)-β-citronellene **52**. The southern chlorocyclopropyl ketide (CCK) fragment had its origins from enzymatic resolution of β-

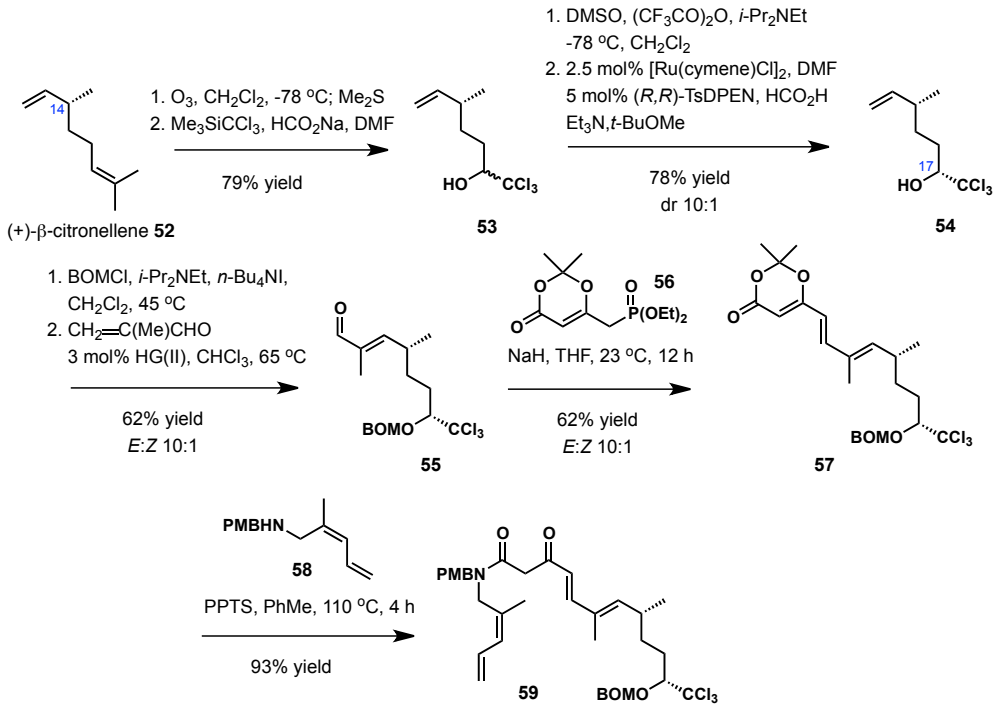
hydroxy pentenoate **51**. Finally, the synthesis of the western portion began from known iodo-alcohol **50**.

Figure 9. Three Key Starting Material Fragments



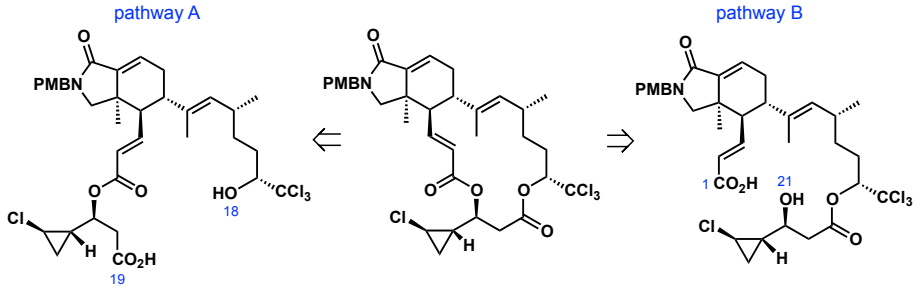
The preparation of the western fragment began by converting (+)-β-citronellene[24] to trichloromethyl carbinol **53** (Scheme 12). Selective ozonolysis and treatment of the resulting aldehyde with $TMSCCl_3$ and sodium formate afforded alcohol **53** in 79% yield in a 1:1 dr.[25]

Scheme 12. Synthesis of Eastern Fragment Starting From (+)-β-citronellene



No literature precedence existed for asymmetric trichloromethyl addition to aldehydes and our attempts were met without success. Therefore, the synthesis of **54** required oxidation (DMSO, $(CF_3CO)_2O$, *i*-Pr_2NEt) followed by an asymmetric Noyori reduction of the corresponding ketone with $[Ru(cymene)Cl]_2$ and (*R,R*)-TsDPEN to afforded **54** in 78% yield with a 10:1 dr.[26] Benzyloxymethyl (BOM) protection of **54** and cross metathesis with methacrolein in the presence of Hoveyda-Grubbs II catalyst (HGII) gave aldehyde **55** in 62% yield and an *E:Z* ratio of 10:1. Installment of dioxinone **56** through Horner-Wadsworth-Emmons (HWE) olefination with aldehyde **55** provided intermediate **57**. Thermolysis of the resulting dioxinone (PPTS, toluene, 110 °C) with amine **58** afforded amide **59** in 93% yield.[27]

Figure 10. Macrolactonization Strategy: Pathway A and Pathway B

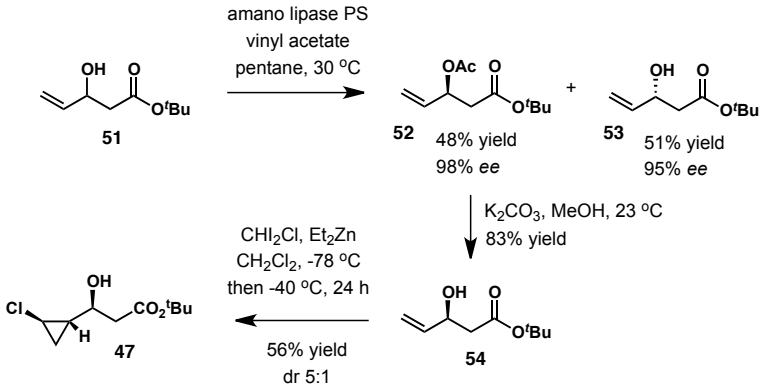


At this juncture, our synthetic plan for late stage macrolactonization was left flexible for ring closure through pathway A (positions 19, 18, Figure 10) or pathway B (positions 1, 21). Ultimately, both routes have been explored. Our investigation began with pathway A, which required early installment of the CCK fragment.

The chlorocyclopropyl ketide was prepared in three steps from *tert*-butyl 3-hydroxypent-4-enoate **51**.[28] Allylic acetate **52** was obtained through a robust and scalable enzymatic resolution with amano lipase PS and vinyl acetate in pentanes at 30 °C in 48%

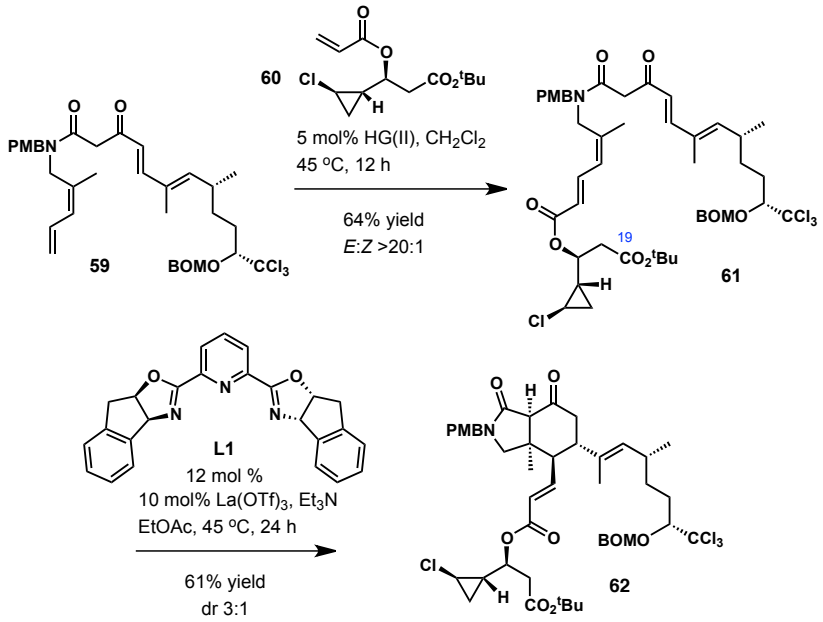
yield (50% theoretical yield) and 98% *ee*. Treatment of acetate **52** with potassium carbonate in methanol afforded allylic alcohol **54** in 83% yield.

Scheme 13. Synthesis of Chlorocyclopropyl Ketide (CCK)



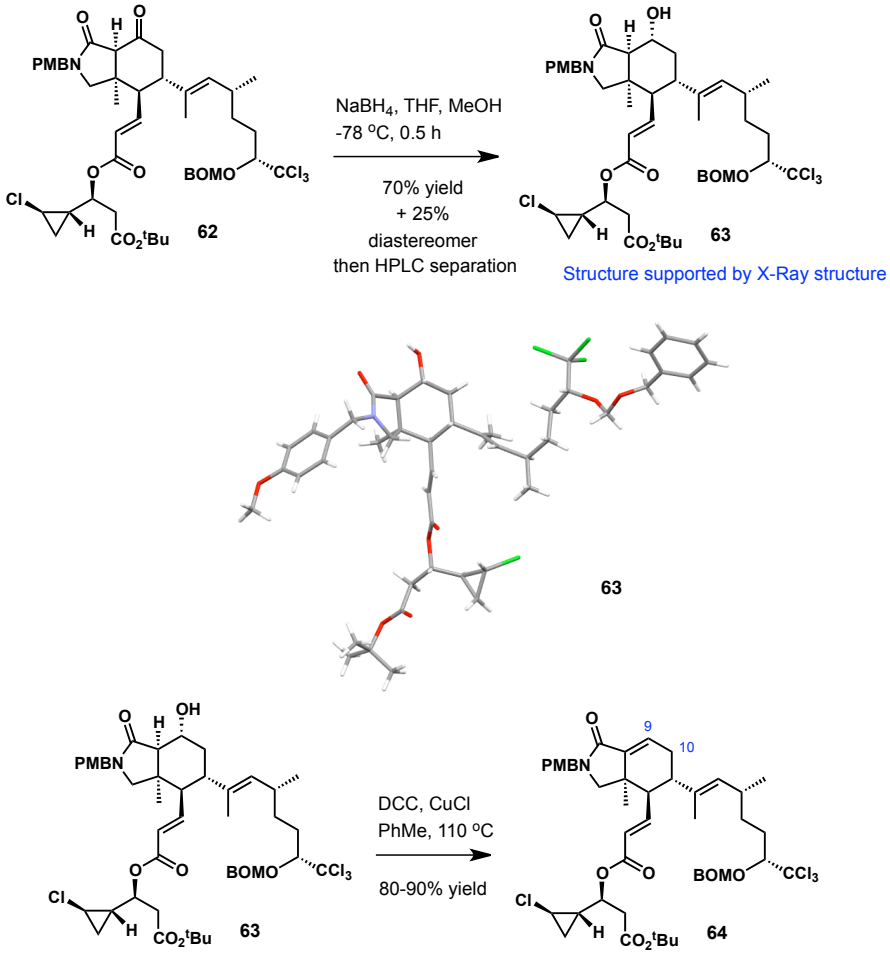
Treatment of allylic alcohol **54** with CHI_2Cl and diethyl zinc at -40 °C for 24 h afforded CCK fragment **47** in 56% yield in a dr of 5:1 (Scheme 13).[29] Acylation of intermediate **47** with acryloyl chloride and its cross metathesis with diene **59** (5 mol% HG(II), CH_2Cl_2, 45 °C, 12 h) provided IMDA precursor **61** in 64% yield with an *E:Z* of >20:1.

Scheme 14. Lanthanum Catalyzed IMDA Reaction



Optimized cycloaddition conditions required 12 mol% PYBOX ligand **L1**, 10 mol% $La(OTf)_3$ and Et_3N in ethyl acetate at 45 °C for 24 h, furnishing isoindoledione **62** in 61% yield as an inseparable 3:1 mixture of diastereomers (Scheme 14). The *exo* IMDA reaction pathway was preferred due to stabilization of the metal enolate in the transition state (as mentioned previously). The lanthanum enolate was expected to raise the HOMO energy of the diene system by increasing its electron density, which was favorable for the cycloaddition reaction.

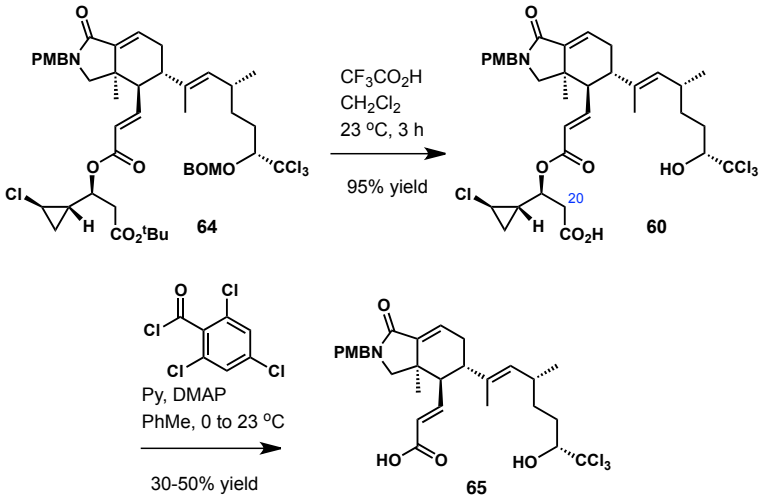
Scheme 15. Separation of Diastereomers by Preparative HPLC



The reduction of ketone **62** with sodium borohydride made the separation of the diastereomeric mixtures possible by preparative HPLC. The major diastereomer **63** was

isolated in 70% yield, and the minor diastereomer was isolated in 25% yield. A single crystal of **63** suitable for X-Ray analysis was obtained. This crystal structure unequivocally established all stereogenic centers present in muironolide A (Scheme 15). Dehydration with DCC and CuCl in refluxing toluene completed the isoindolinone subunit in 80-90% yield.[30] Other dehydration methods (MsCl/DBU, Burgess or Martin reagents) solely provided the C9-C10 double bond isomer (versus C8-C9 double bond). In preparation for macrolactonization, a one-pot deprotection of the *tert*-butyl ester and benzyloxymethyl (BOM) ether was achieved with trifluoroacetic acid in CH_2Cl_2 to reveal hydroxyl acid **60** in 95% yield (Scheme 16).

Scheme 16. Macrolactonization *via* Pathway A

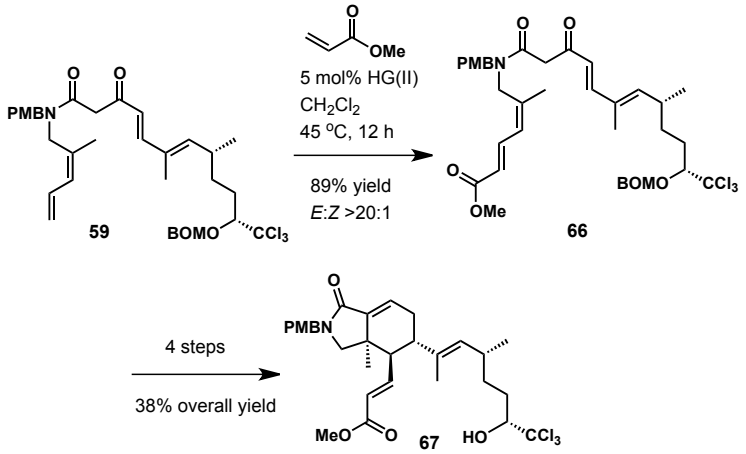


Conditions for macrolactonization using Yamaguchi reagent appeared to be the most promising.[31] However, hydroxyl acid **65** was isolated in 30-50% yield as a major product apparently arising from β-elimination of the CCK fragment. Therefore, our attention shifted towards macrolactonization through pathway B.

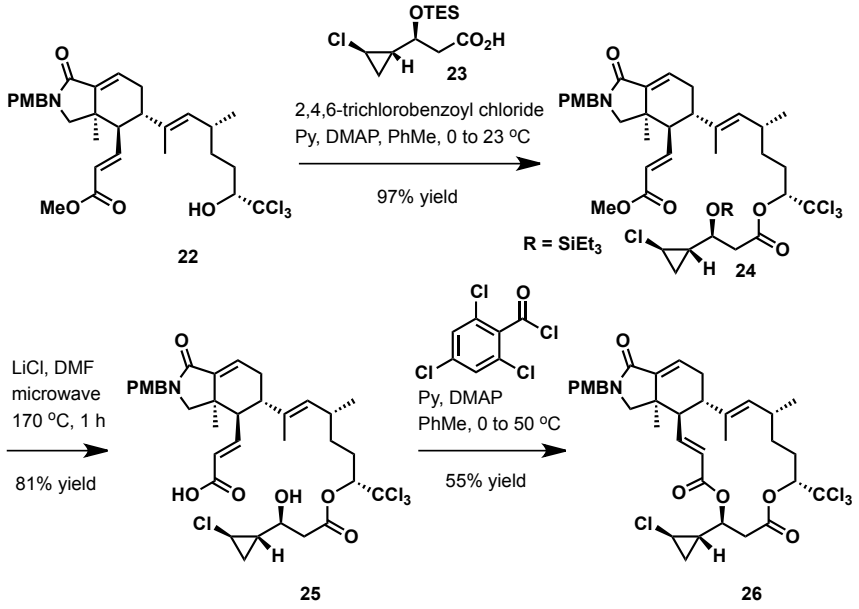
From a common diene intermediate (**59**), cross metathesis with methyl acrylate afforded IMDA precursor **66** in 89% yield and an *E:Z* of >20:1 (Scheme 17). The same

four-step sequence shown previously for the construction of the isoindolinone core and BOM-deprotection afforded alcohol **67** in 38% yield over 4 steps.

Scheme 17. Synthesis of Alcohol **67**



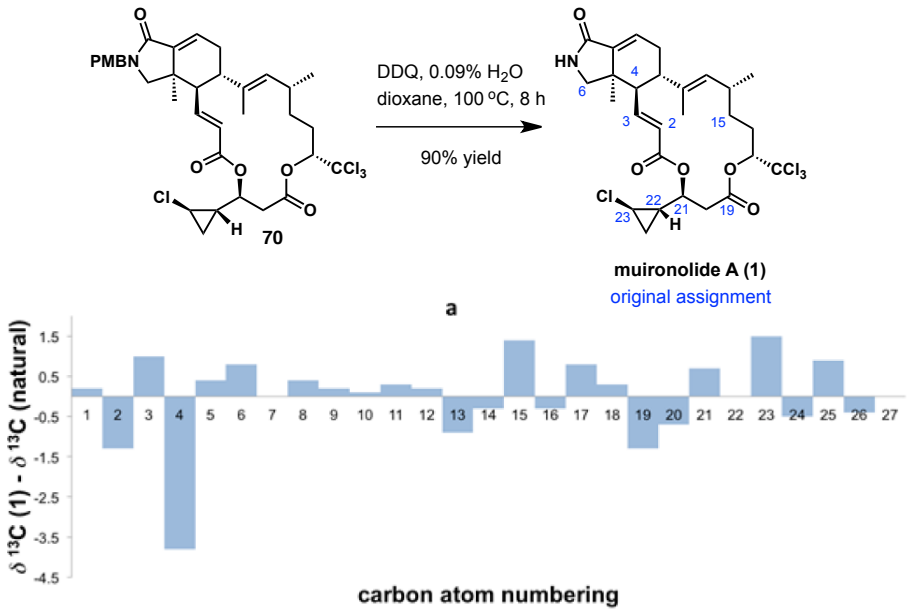
Scheme 18. Pathway B: Yamaguchi Protocol for Macrolactonization



Esterification of **67** with acid **23** was achieved through Yamaguchi's protocol to provide ester **69** in excellent yield. Simultaneous cleavage of methyl ester and silyl ether in the presence of LiCl in DMF with microwaved-assisted heating (170 °C for 1 h) afforded **61** in 81% yield. We were delighted when, under Yamaguchi conditions, hydroxyl acid **61**

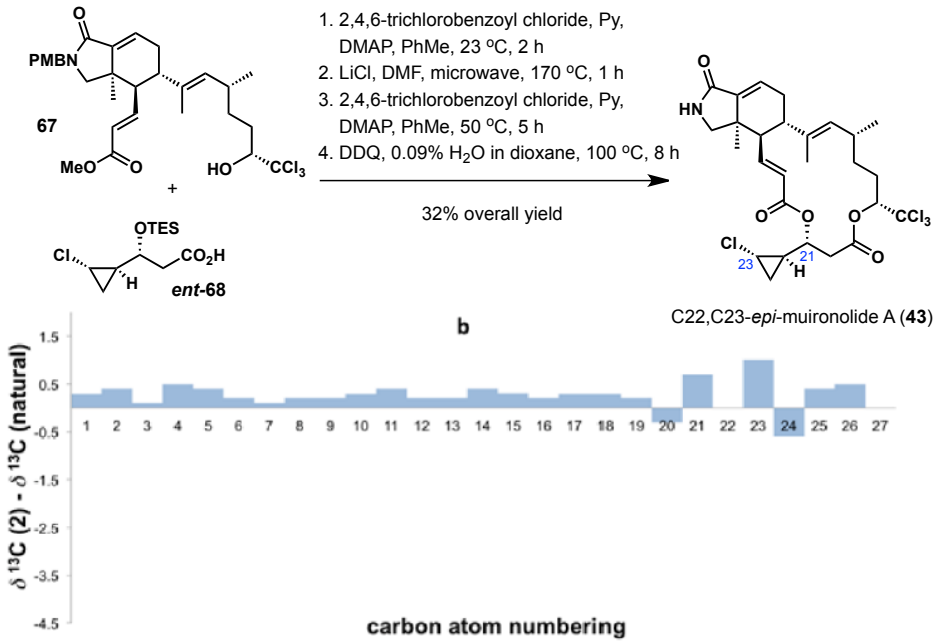
underwent macrolactonization at 50 °C to afford macrocycle **70** in 55% yield. The final steps of this synthesis consisted of oxidative deprotection of the *p*-methoxybenzyl (PMB) group with DDQ and controlled amounts of water (5 equiv.) in dioxanes at 100 °C. These conditions afforded **1** in 90% yield.[32]

Scheme 19. Completion of the Synthesis of C21-*epi*-Muironolide A



Unfortunately, ^{1}H NMR, ^{13}C NMR and HMBC data for **1** did not match the spectroscopic data of the natural compound. Graphical analysis of the differences in chemical shifts of the synthetic versus natural is shown in Scheme 19. This graph depicts carbon numbering of muironolide A (X-axis) *versus* differences in chemical shift denoted as $\Delta\delta$ (δ ^{13}C (**1**) - δ ^{13}C (natural)) on the Y-axis. Examination of this graph revealed the biggest discrepancies were confined to the macrocycle and the CCK units. We were confident in the relative stereocenters of C4, C5 and C11 through IMDA studies to form the isoindolinone subunit. It was hypothesized that a C21 epimer could have a drastic affect on the configuration of the macrocyclic diester. We could easily test this hypothesis since the CCK fragment had its origins in enzymatic resolution.

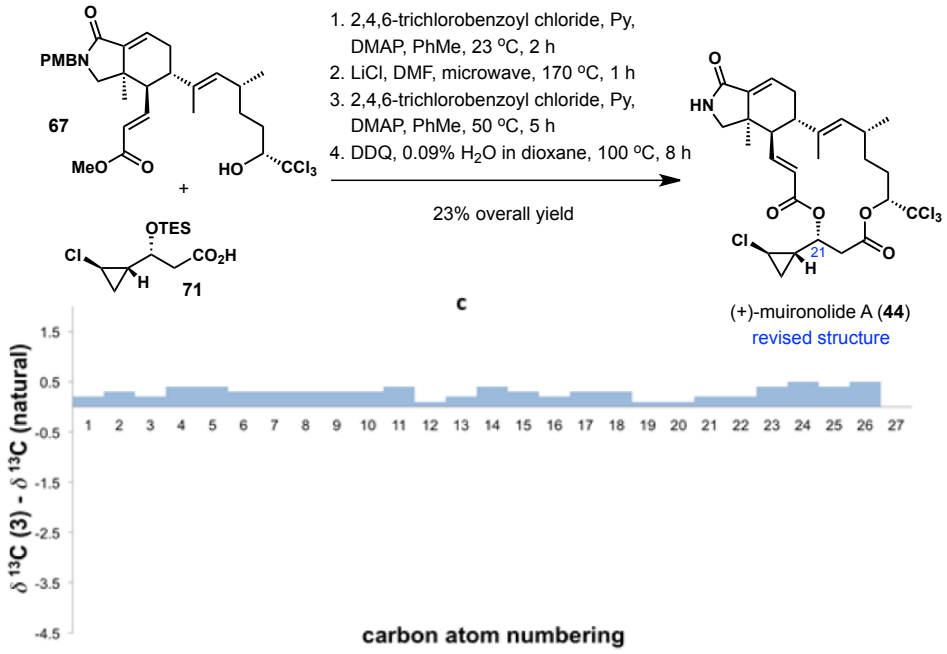
Scheme 20. Synthesis of C22, C23-*epi*-Muironolide A



Following the same four-step sequence with acid *ent*-**68** provided C22, C23-*epi*-muironolide A **43** in 32% overall yield (Scheme 20). Comparing $\Delta\delta$ in ^{13}C NMR spectra showed remarkable similarity of this synthetic product to the natural compound. The main differences were now confined to the C22 and C23 positions, thereby suggesting a *cis*-relationship between C21 and C22 rather than a *trans* configuration. Based on this evaluation, we conjectured that the CCK fragment would be the original C21 epimer **71**.

Again, the same four-step sequence was applied to **67** and **71**, and the synthesis of (+)-muironolide A was completed (**44**) in 23% yield (Scheme 21). All spectroscopic data of **44** was in full agreement with the natural product. The only deviation from physical data arose from the circular dichroism (CD) spectrum that showed synthetic muironolide was antipodal to the natural. Therefore we reassigned the absolute configuration to be (-)-muironolide A.

Scheme 21. Completion of the Synthesis of (+)-Muironolide A



Conclusion

We reported the first enantioselective total synthesis of (+)-muironolide A. We reassigned the stereochemistry as the C21-epimer and determined the absolute configuration of the natural product. Although, synthetic (+)-muironolide A was enantiomeric, material was sent to NCI60 (National Cancer Institute) to assay against 60 cell lines with data still pending. Current efforts towards the scale-up of muironolide A are ongoing and will be reported in due course.

Chapter 2: Late Stage Derivatization of Pinnatoxin Compounds

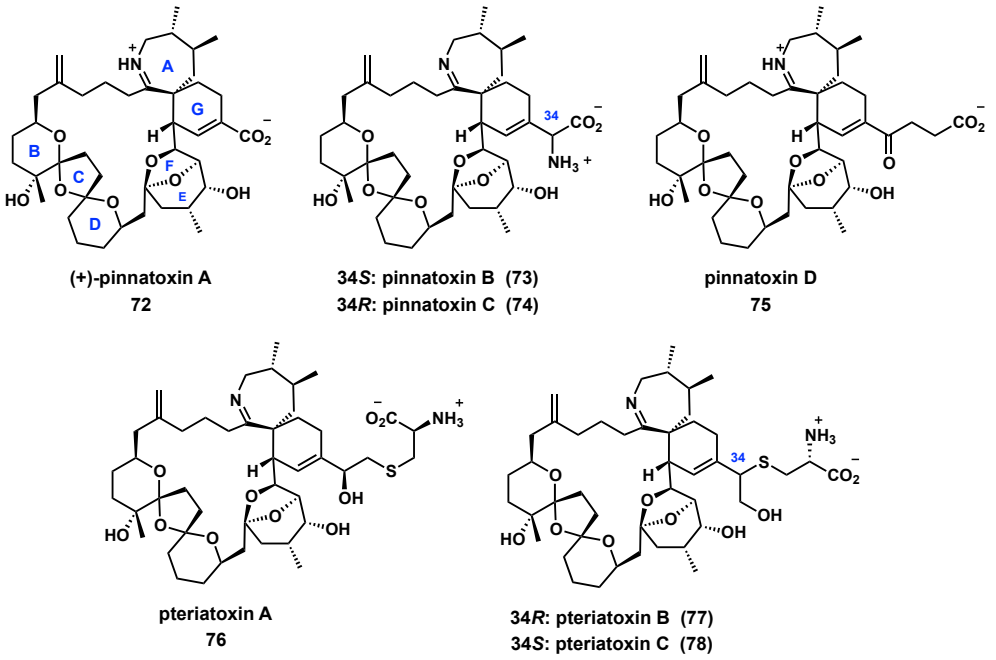
2.1: Background of Pinnatoxin and Cyclic Imine Toxins

Cyclic imine (CI) toxins are an important class of marine toxins with worldwide distribution. Dinoflagellates of a genus *K. selliformis, A. ostenfeldii, A. peruvianum* and *V. rogsum* are members of a phytoplankton specie that are attributed to the production and proliferation of CI toxins.[33] During favorable oceanic conditions, harmful algal blooms (HABs) are the source of toxic dinoflagellates that spread to aquatic life. Filter feeding bivalve mollusks (shellfish) that feed on toxic phytoplankton accumulate CI toxins in their digestive glands and edible tissues.[34] In turn, this poses a health risk to higher order predators either marine or terrestrial. Pinnatoxins and pteriatoxins represent the largest subgroups of known CI toxins. These compounds pose the highest risk to human health due to their potent oral toxicity.[35] Although there are no reports of fatal toxicity in humans, widespread shellfish poisoning attributed to CI toxins was reported in China and Japan.[36]

In 1994, Uemura and coworkers reported the isolation and characterization of pinnatoxins (PnTXs) from *Pinna muricata*, a bivalve mollusk.[37] Collection of 45 kg of this shellfish led to the isolation of pinnatoxin A (3.5 mg), pinnatoxin B and C (1.2 mg as a 1:1 mixture) and pinnatoxin D (2.0 mg) (Figure 11).[38] Bioassays *via* intraperitoneal (i.p.) injection in mice showed lethal toxicity of pinnatoxin A with LD_{99} = 180 μg/kg and pinnatoxin B and C with LD_{99} = 22 μg/kg.[39] Pinnatoxin D showed the lowest potency with LD_{99} = 400 μg/kg, however it showed strong toxicity against murine leukemia cell line P388 at IC_{50} = 2.5 μg/mL.[40] Pteriatoxins are the least studied members of the pinnatoxin family. Pteriatoxins A−C were isolated from bivalve *Pteria penguin* in 2001,

were found to be more potent by i.p. injection in mice (pteriatoxin A with LD_{99} = 100 μg/kg and pteriatoxins B and C (1:1 mixture) with LD_{99} = 8 μg/kg).[41]

Figure 11. Pinnatoxins and Pteriatoxins



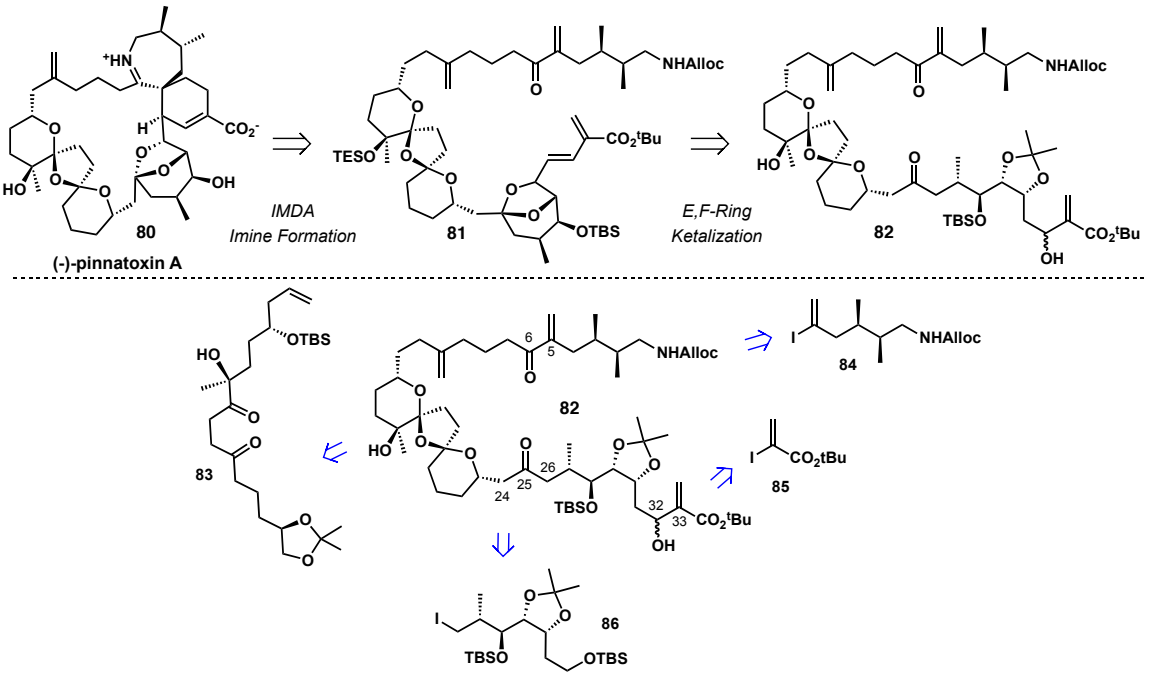
Currently, there are no regulations that mandate acceptable levels of CI toxins in seafood that are bound for human consumption.[42] One barrier to monitoring these marine toxins was the lack of access to highly pure standards.[43] Chemical purity of CI standards used in bioassays is a growing concern, as they are persistently not reported.[44] Methods employed for the extraction from natural sources heavily influence the purity of CI compounds that are used for testing. To address this problem, a reliable method to access these compounds is needed and one option is the direct and reliable chemical synthesis of these marine natural products. Additionally, very little was known about the biological mode of action (MOA), biodistribution, cellular metabolism and short/long-term effects of CI toxin exposure. Our goal was to build upon a growing body of knowledge to help answer these intriguing questions.

Pinnatoxins and related pteriatoxins are intriguing macrocycles containing a spiroimine AG-ring, BCD-dispiroketal and EF-bicycloketal rings. Varying the substituents at C34-position provided the different pinnatoxins A-D and related pteriatoxins A-C (Figure 11). Uemura proposed a biomimetic intramolecular Diels-Alder cycloaddition pathway for the construction of the 6,7-azaspiro-linked imine fragment (AG-ring) and the macrocycle. Feeding studies of *Alexandrium ostenfeldii* demonstrated that the polycyclic ether units of PnTX was made from linear polyketide synthesis and a glycine unit was incorporated intact to form the imine portion.[45] The first pioneering total synthesis of (-)-pinnatoxin A and related pteriatoxins A, B and C was reported by Kishi *et. al.* in 1998 and 2006, respectively.[46] Murai (2002),[47] Inoue-Hirama (2004),[48] Nakamura-Hashimoto (2008)[49] and Zakarian group (2008, 2011)[50] have also reported the total synthesis of PnTX A. A review of Kishi's synthesis, which established the stereochemistry of (-)-pinnatoxin A and pteriatoxins A-C, will be briefly summarized. Also, the Zakarian synthesis (2011) of pinnatoxin A and biological MOA, which is the prelude to this work, will be presented.

2.2: Kishi's Total Synthesis of (-)-Pinnatoxin A (1998)[51]

The synthesis of the unnatural enantiomer of pinnatoxin A was reported through a potentially biomimetic intramolecular Diels-Alder (IMDA) reaction pathway. Kishi and coworkers established the absolute stereochemistry of synthetic pinnatoxin A to be the antipode of the natural and confirmed the assignment of the relative stereochemistry of this stereo-rich natural product through their total synthesis. This synthesis, which remained the shortest sequence of 38 steps to-date, produced 1.0 mg of (-)-pinnatoxin A.

Figure 12. Kishi's Synthetic Strategy for (-)-Pinnatoxin A

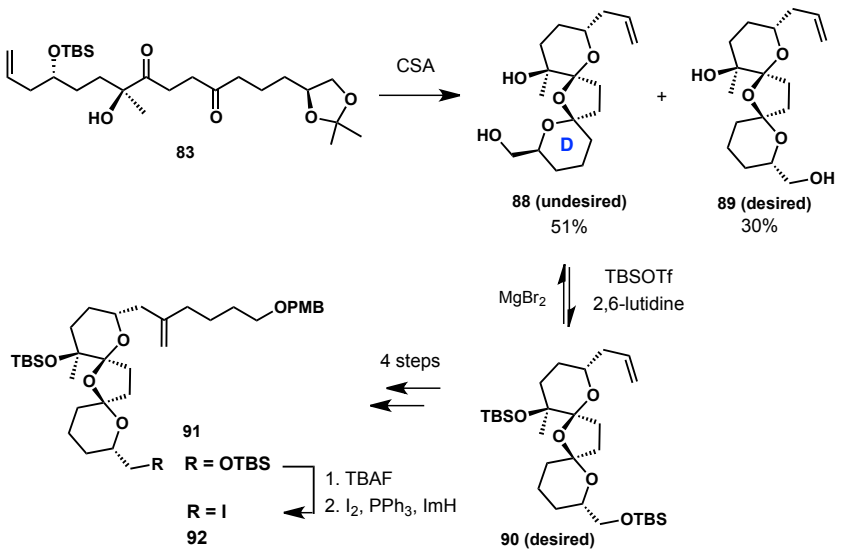


In this retrosynthetic analysis, the putative biomimetic intramolecular Diels-Alder reaction forged the quaternary stereogenic center of the spiroimine unit. Cyclic ketalization formed the EF-rings and dispiroketalization reaction assembled the BCD-bisketal rings under thermodynamic control. The synthesis of complex fragment **82** was achieved from four smaller fragments employing two dithiane umpolung strategies to form C24, C25 and C26 bonds and Nozaki-Hiyama-Kishi (NHK) reactions to form C5, C6 and C32, C33 bonds shown in Figure 12.

The synthesis of BCD-rings began with diketone **83**, which was prepared in 12 steps from 1-pentynol. The formation of the bis-spiroketal portion was made possible by treating diketone **83** with camphorsulfonic acid (CSA) in methanol to provide a 2:3 mixture favoring the desired isomer. The formation of undesired compound **88** was assisted by hydrogen bonding of the tertiary alcohol and the oxygen of the D-ring (see Murai and coworkers).[52] Disruption of hydrogen bonding by O-silylation with TBSOTf

fully converted the undesired tricyclic ketal **88** to more conformationally stable isomer **90** (Scheme 22).

Scheme 22. Bis-Ketalization to Form B,C,D-Rings

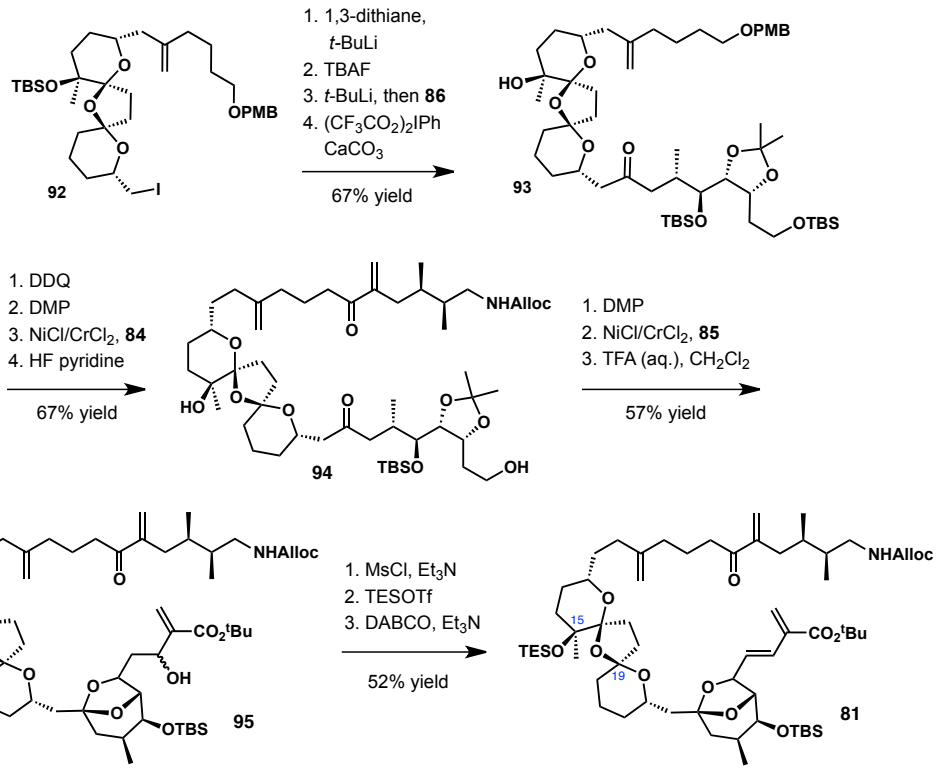


In preparation for dithiane coupling partner, *tert*-butyldimethylsilyl ether (TBS) was cleaved (TBAF) to produce the corresponding primary alcohol and subsequently converted to iodide **92** under standard Mitsanobu conditions. Iodide **92** was added to a solution of lithiated 1,3-dithiane (*t*-BuLi, 10% HMPA/THF) to form C24 and C25 bonds. After exposure with tetrabutylammonium fluoride (TBAF), this alkylation sequence was repeated with iodide **86** followed by oxidative deprotection of 1,3-dithiane ($PhI(CF_3CO_2)_2$, $CaCO_3$) delivering ketone **93** in 57% yield over four steps.

The first $NiCl_2/CrCl_2$ (NHK) mediated coupling to install alkyl amine **84**, began with *p*-methoxybenzyl (PMB) group removal, followed by Dess-Martin Periodinane (DMP) oxidation in 63% yield. The resulting aldehyde was treated with 1 mol% $NiCl_2/CrCl_2$ in DMF and vinyl iodide **84** that provided the corresponding allylic alcohol in 55% yield as a 1:1 diastereomeric mixture. En-route to the second NHK coupling, chemoselective *tert*-

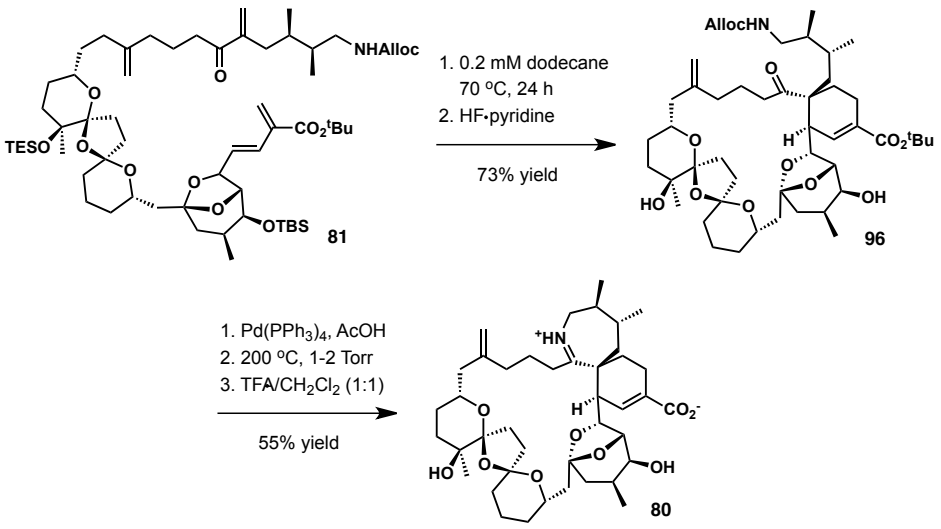
butyldimethylsilyl (TBS) group deprotection (HF pyridine) and DMP oxidation was performed. Increased amounts of catalyst loading at 33 mol% $NiCl_2/CrCl_2$ and bispyridinyl ligand were required to forge C32-C33 bond.

Scheme 23. Preparation of IMDA Precursor



Acetonide solvolysis mediated by trifluoroacetic acid (TFA) in aqueous dichloromethane allowed for formation of EF-ketal in 71% yield. IMDA precursor **81** was completed in three additional steps through mesylation, hydroxyl protection with triethylsilane (TES) followed mesylate elimination with DABCO (52% yield in three steps). It was noteworthy that during the EF-ring formation, C19 completely epimerized under acidic conditions (TFA, H_2O-CH_2Cl_2). However upon silylation (TES) of the tertiary alcohol at C15, the desired isomer of BCD-rings was obtained quantitatively.

Scheme 24. Completion of Synthesis of (-)-Pinnatoxin A



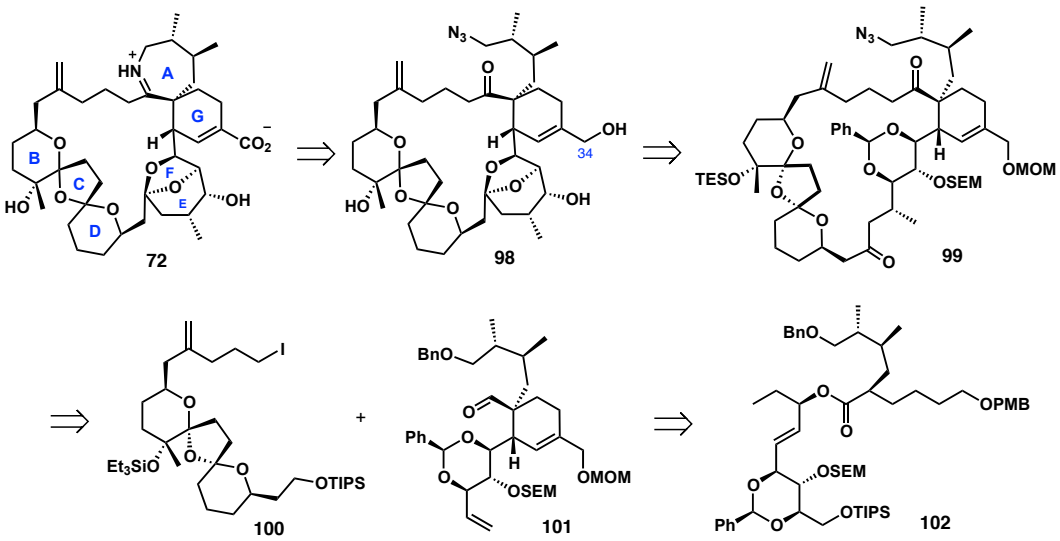
The *exo*/*endo* selectivity of the intramolecular Diels-Alder reaction was found to depend on the choice of solvent and amine substituent. For example, heating IMDA precursor **81** in toluene at 100 °C gave a 1:1:1 mixture of *exo*:*endo* product distribution. The formation of *endo* (undesired) product could be minimized using 2 mM dilution in dodecane at 70 °C that afforded 1.0:0.9:0.4 with ca. 5:1 *exo*:*endo* in 78% combined yield. After N-allylchloroformate cleavage ($Pd(PPh_3)_4$, AcOH), imine formation occurred under high temperature and pressure (200 °C, 1-2 Torr). Forcing conditions for imine cyclization was indicative of a high energy barrier between the imine and the amino ketone. The synthesis was completed by the cleavage of the *tert*-butyl ester to afford (-)-pinnatoxin A in 55% yield over three steps. Synthetic pinnatoxin A was found to be antipodal to the natural through the optical rotation measurement.

2.3: Zakarian's Total Synthesis of Pinnatoxin A (2011)[53]

Zakarian group first published the total synthesis of pinnatoxin A in 2008, however an improved synthesis and biological mode of action was later published in 2011, which

will be the focus of this segment. The impetus for the second-generation synthesis was to address two issues: the scalability of PnTX synthesis and confirming the hypothesis that toxicity of PnTXs is solely due to their potent action on nicotinic acetylcholine receptors.

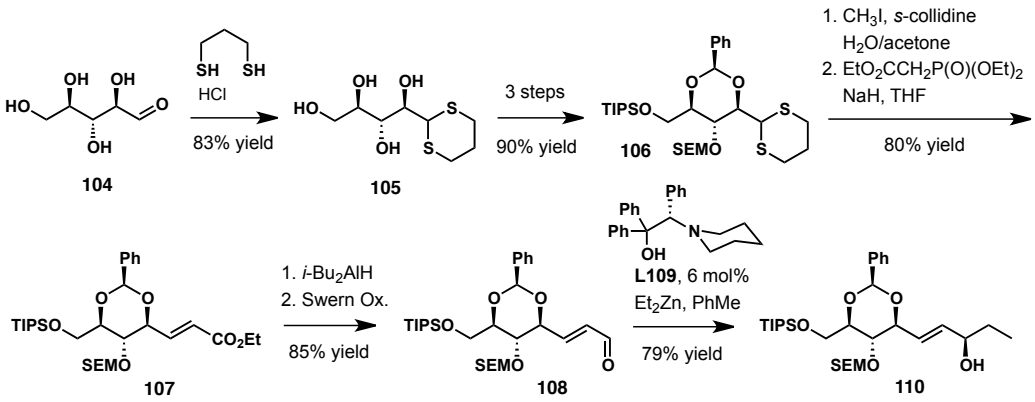
Figure 13. Zakarian's Retrosynthesis of Pinnatoxin A



PnTX A was accessed from azido triol **98** by oxidation of the allyl alcohol to the carboxylate at C34, followed spiroimine formation. Tandem deprotection and ketalization of substrate **99** formed the EF-rings. Direct alkyllithium addition, from lithium-iodide exchange of **100**, to aldehyde **101** united the two advanced fragments. Finally, central to this strategy was the use of the Ireland-Claisen rearrangement of ester **102** to form the C5 quaternary center in a diastereospecific fashion. The significance of this design was the recognition that further elaboration of azido triol **98** would allow one to access all of the pinnatoxins A-F and related pteriatoxins A-C.

Synthesis of aldehyde **101** began with dithioacetal formation of D-ribose followed by a three-step protocol for selective protection of the resulting tetraol. Cleavage of dithioacetal revealed the corresponding aldehyde and its olefination with Horner-Wadsworth-Emmons reagent gave α,β-unsaturated ester **107** in 80% yield.

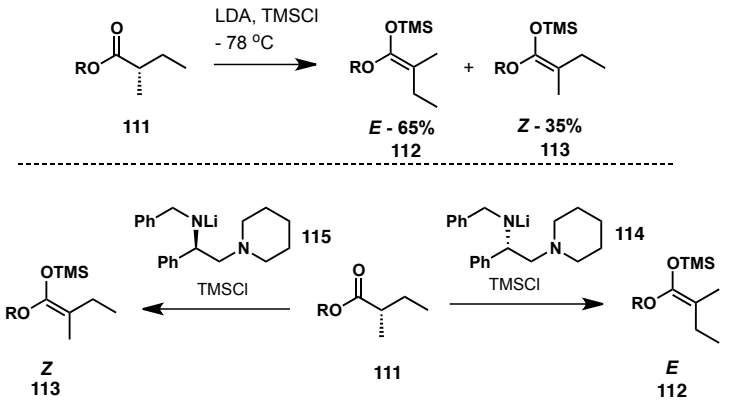
Scheme 25. Synthesis of Allylic Alcohol **110**



After reduction and oxidation to α,β-unsaturated aldehyde **108**, asymmetric ethylation with 6 mol% ligand **L109** and diethyl zinc afforded allylic alcohol **110** in 79% yield. Esterification, under Yamaguchi conditions, of alcohol **110** with carboxylic acid **116** (made in 11 steps from (*S*)-citronellic acid) provided ester **102** in 85% yield.

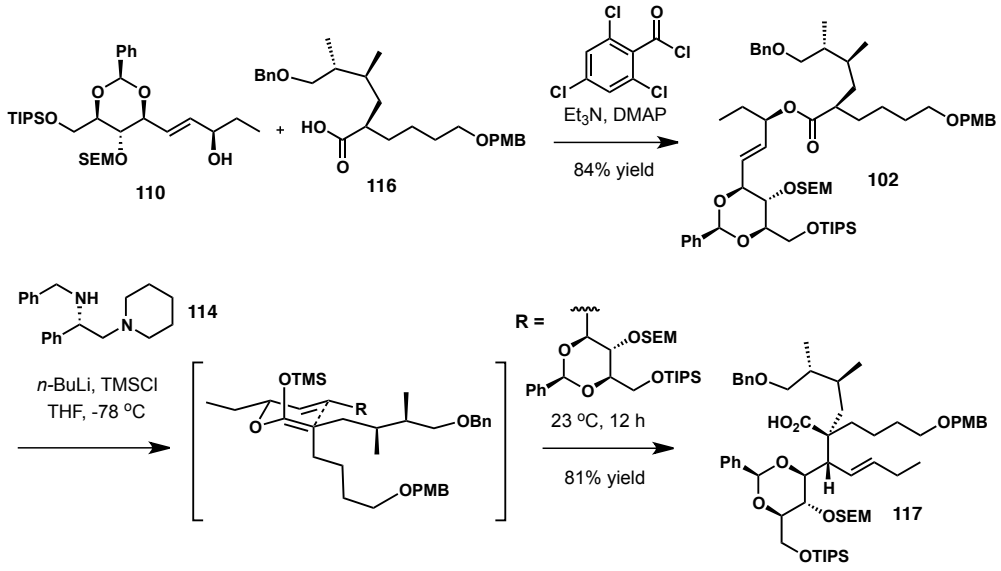
The key transformation in the synthesis was performed by a diastereospecific Ireland-Claisen rearrangement with lithium amide **114**. Traditional methods for this transformation gave an unwanted mixture of diastereomers at C5, which opened an opportunity to explore new methodology. It was well established that obtaining exclusive *E* and *Z* geometry during enolate formation was critical to high diastereocontrol. In model studies, using chiral α-branched esters, enolization with lithium diisopropyl amine (LDA) gave a mixture of *E* (65%) and *Z* (35%) isomers as shown in Scheme 26. However, in the presence of chiral lithium amide **115**, the chirality match between the ester and lithium reagent enabled exclusive formation of *Z*-enolate **113**. The chirality of lithium amide controls the *E* and *Z* geometries during the enolization event.

Scheme 26. Stereoselective Enolization with Chiral Lithium Amines



To demonstrate the utility of this transformation, a highly stereoselective *Z*-enolate formation was enabled by the chiral base **114** of α,α-branched ester **102**, where rearrangement to acid **117** was possible as a single diastereomer in 81% yield.

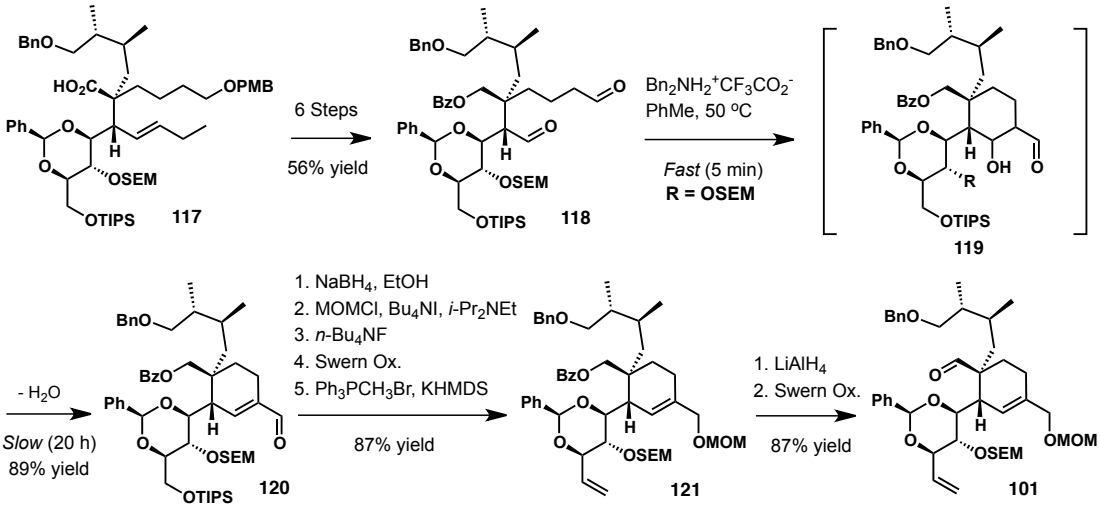
Scheme 27. Diastereoselective Ireland-Claisen Rearrangement



Formation of the G-ring required converting rearrangement product **117** to dialdehyde **118** in 6 steps. Treatment of the dialdehyde with dibenzylammonium trifluoroacetate rapidly formed aldol product **119**, followed by a slow dehydration step (~20 h) to complete α,β-unsaturated aldehyde **120** in 89% yield. Reduction of the allylic aldehyde

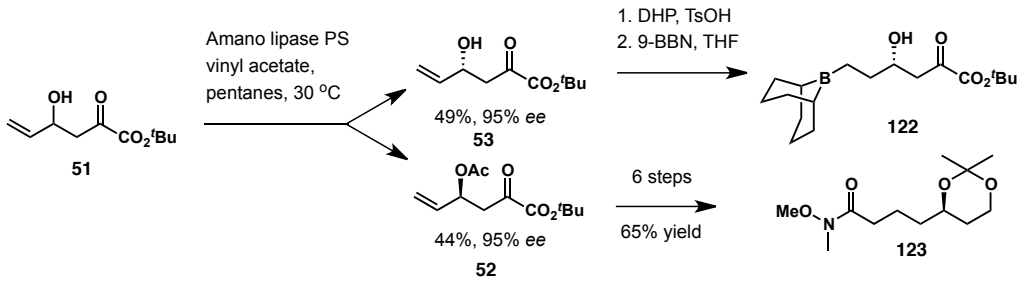
followed by protection of the resultant hydroxy group with methoxymethyl ether (MOM) was performed. Selective triisopropylsilyl (TIPS) deprotection, oxidation and Wittig olefination with the corresponding aldehyde afforded **121** in 87% yield over five steps. In two steps, aldehyde **101** was completed by $LiAlH_4$ reduction followed by Swern oxidation in 87% yield.

Scheme 28. Assembly of G-Ring and Completion of Aldehyde **101**



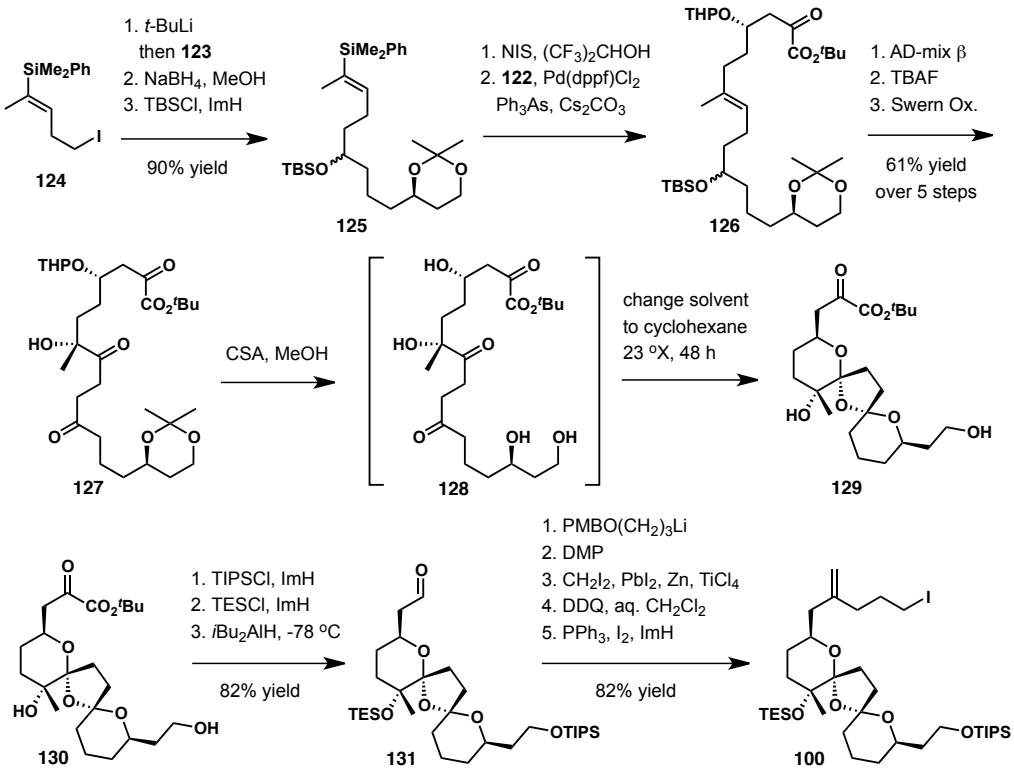
The synthesis of BCD-bisketal fragment started with an efficient enzymatic resolution of *tert*-butyl hydroxy-pentenoate **51** catalyzed by amano lipase PS, using vinyl acetate in pentanes. The produced free allylic alcohol was advanced to borane **122** in two steps, while the vinyl acetate was transformed to Weinreb amide **123** in six steps in 65% yield.

Scheme 29. Efficient Enzymatic Resolution for Synthesis of Ketal Precursors



Carbon extension with organolithium reagent, generated from lithium-iodide exchange of iodide **124**, coupled with Weinreb amide **123** afforded the resulting ketone. Stereoselective iodo-de-silylation, from silane **125**, allowed for its coupling with borane **122** under Suzuki-Miyaura conditions in the presence of $Pd(dppf)Cl_2$ and Ph_3As.

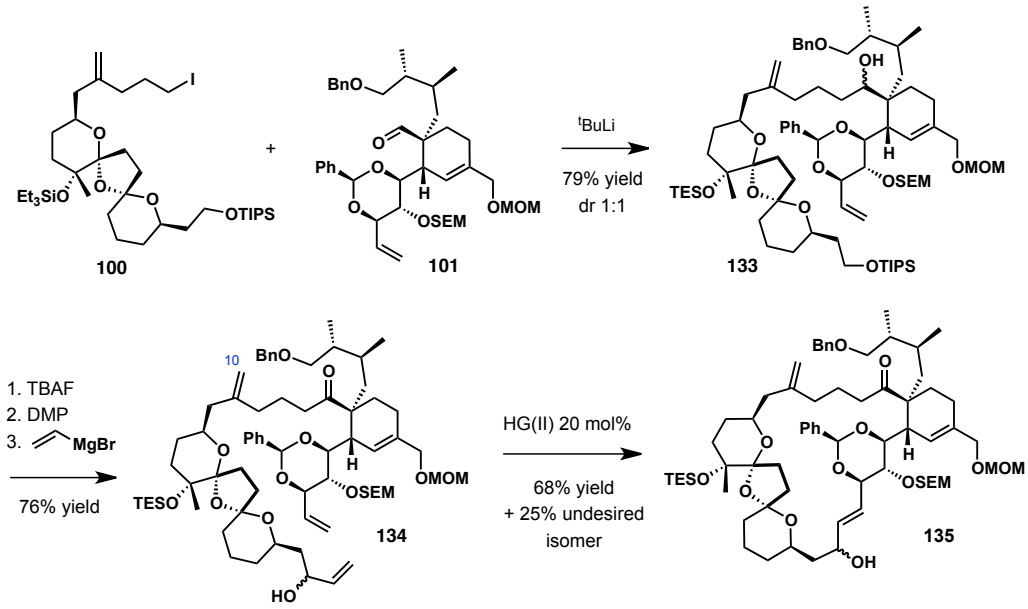
Scheme 30. Completion of Spiroketal Fragment **100**



Installation of tertiary alcohol by Sharpless asymmetric dihydroxylation with AD-mix β, followed by silyl group removal and oxidation to diketone completed ketal precursor **127** in 61% yield over five steps. The treatment of precursor **127** with camphorsulfonic acid in methanol revealed free tetraol intermediate **128**. The solvent displacement to cyclohexane was essential to trigger spiroketalization that was complete within 48 h producing the desired product under thermodynamic control. The completion of the spiroketal fragment was done in eight steps that began with silyl protection of the primary

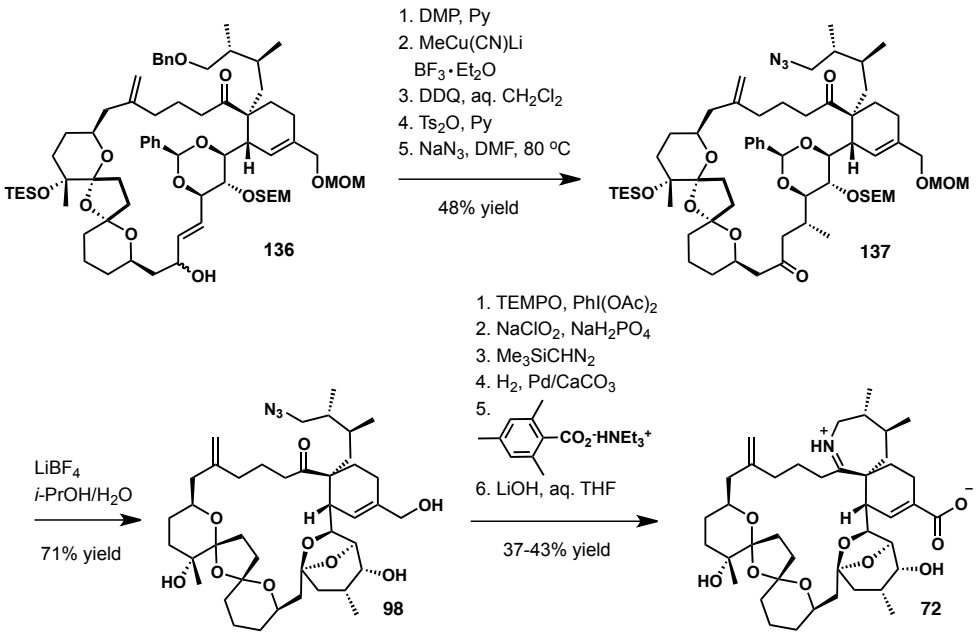
alcohol, reduction of the ester with *i*Bu_2AlH to aldehyde **131**. Alkylation, Dess-Martin Periodinane (DMP) oxidation, Peterson olefination, *para*-methoxybenzyl deprotection and iodo-de-hydroxylation concluded the bisketal fragment **100** in 67% yield. The two fragments could now be united by the addition of complex organolithium reagent derived from iodide **100**, through lithium-iodide exchange, to aldehyde **101** resulted in an inconsequential 1:1 mixture of diastereomers **133** in 75% yield.

Scheme 31. Fragment Coupling and Ring Closing Metathesis



The ring closing metathesis (RCM) precursor **134** was prepared in three steps with a 76% overall yield. The treatment of **134** with 20 mol% HGII catalyst provided a 3:1 mixture of isomers in 68% combined yield. Isolation of the minor isomer revealed an RCM product that formed between the allylic alcohol and the methylene group at C10. Ratios greater than 3:1 could not be obtained after screening different catalysts, temperatures and solvents. Oxidation to α,β-unsaturated ketone, stereoselective cuprate addition paved the way for a challenging one-pot deprotection and ketalization to form EF-rings.

Scheme 32. Completion of Total Synthesis of Pinnatoxin A



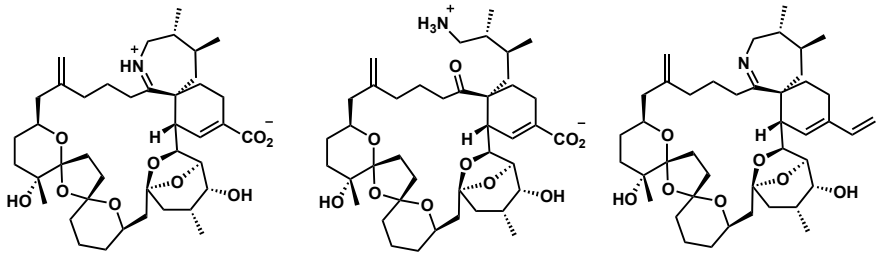
The synthesis of PnTX A was completed in six steps, where the allylic alcohol at C34 was converted to the methyl ester. Azide reduction to the primary amine and was followed by imine formation, which was accomplished with triethylammonium 2,4,6-trimethylbenzoate in toluene at 85 °C for 60 h. Hydrolysis of the methyl ester provided pinnatoxin A in 37-43% yield over six steps.

2.4: Binding Studies of Pinnatoxin A with Nicotinic Receptors (nAChRs)

With reproducible synthetic method to access high quality PnTX A, the mode of action (MOA) of this toxin could now be investigated. One clue was provided from the observation of mice after i.p. injection of PnTX A, which led to hyperactivity, spasms, respiratory distress and death (3-50 min) indicating CNS related mortality. Previous reports revealed that gymnodimine A and 13-desmethylspirolide C (related CI toxins) were potent antagonists towards nicotinic receptors (nAChRs). Together with these observations, PnTX A was conjectured to have similar activity against nAChRs.

The nAChRs are homo- or heteropentamers consisting of different subunits. There have been 17 identified nAChRs, and the stoichiometry of the subunits uniquely defines its function.[54] These ionotropic receptors are divided in two types based on protein sequences: neuronal-type and muscle-type.[55] Neuronal-types only contain α,β-subunits, while muscle-types contain α,β,δ,γ,ε-subunits.[56] Pinnatoxins A, G and pinnatoxin amino ketone derivative (PnTX AK) were used in binding studies with nAChRs.

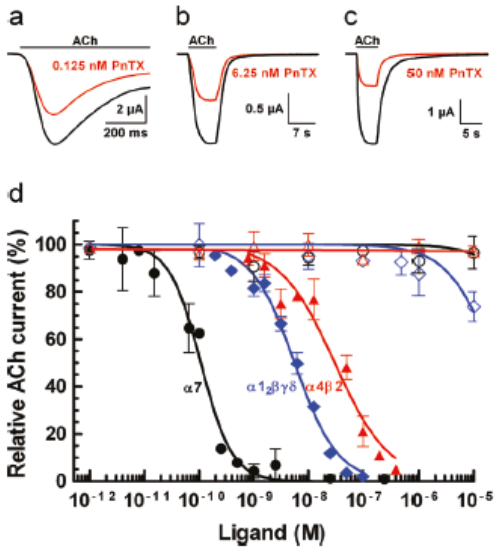
Figure 14. Pinnatoxins Tested for nAChRs Binding Studies



The dual-microelectrode voltage-clamp electrophysiology study on *Xenopus* oocytes expressing human neuronal α4β2 or α7 nAChRs subtypes was performed. Control experiments established EC_{50} values with 350 μM acetylcholine (ACh), a known agonist, which elicited currents from 1 – 3 μA at −60 mV holding membrane potential (n = 54 oocytes from five donors).

The perfusion of PnTX A at varying concentrations showed partial decrease in desensitization (competitive binding against ACh) shown in Figure 15A-C. Dramatic suppression of ACh-evoked currents were observed in a concentration-inhibition curve (Figure 15D) at pM and nM concentrations of PnTX A. Oocytes expressing human α7 nAChRs showed high degree of potency for PnTX A with IC_{50} = 0.107 nM, however PnTX G showed a lower potency with IC_{50} = 5.06 nM.

Figure 15. Electrophysiology Experiment of *Xenopus* Oocytes with PnTX A



Ach and PnTX A current effect on nAChRs at holding potential −60 mV. **(a)** human α7, **(b)** *Torpedo* $\alpha 1_2\beta\gamma\delta$, and **(c)** human α4β2 nAChRs before (black line) and after (red line) of addition of PnTX A. **(d)** Inhibition of ACh-evoked currents by PnTX A or PnTX AK of *Xenopus* oocytes in human α7 (solid circles, black curve) and α4β2 (solid triangles, red curve), or *Torpedo* $\alpha 1_2\beta\gamma\delta$ (solid diamonds, blue curve).

After attempting to washout PnTX A from the medium (10-15 min), PnTX A remained bound to nAChRs suggesting irreversible blocking action with nAChRs. Final evaluation of the potency of PnTX A was dependent on the receptor type and established an order of inhibition on nAChRs as α7 (human) > $\alpha 1_2\beta\gamma\delta$ (*Torpedo*) > α4β2 (human) ranging from 0.1 – 30.4 nM. The performance of PnTX AK analogue (opened form of the imine ring) showed no action on nAChRs subtypes in a range of concentrations. This indicated that the spiroimine component was the pharmacophore necessary for binding in nAChRs. Competitive binding studies were performed with radiotracers [^{125}I]α-bungarotoxin (α-BTX) and (±)-[^{3}H]epibatidine with PnTX A and showed high affinities

in *Torpedo* $\alpha 1_2\beta\gamma\delta$ and α7-5HT$_3$ (chimeric chicken neuronal nAChRs type) at 2.8 nM and 0.35 nM, respectively. Affinities for hetereopentameric neuronal nAChRs ($\alpha 3\beta 2$ and $\alpha 4\beta 2$) were less potent, and the order of potency was α7-5HT$_3$ > *Torpedo* $\alpha 1_2\beta\gamma\delta$ > $\alpha 3\beta 2$ = $\alpha 4\beta 2$.

2.5: Studies Towards ^{18}F, ^{13}C and ^{3}H Isotope Labeled PnTX Derivatives

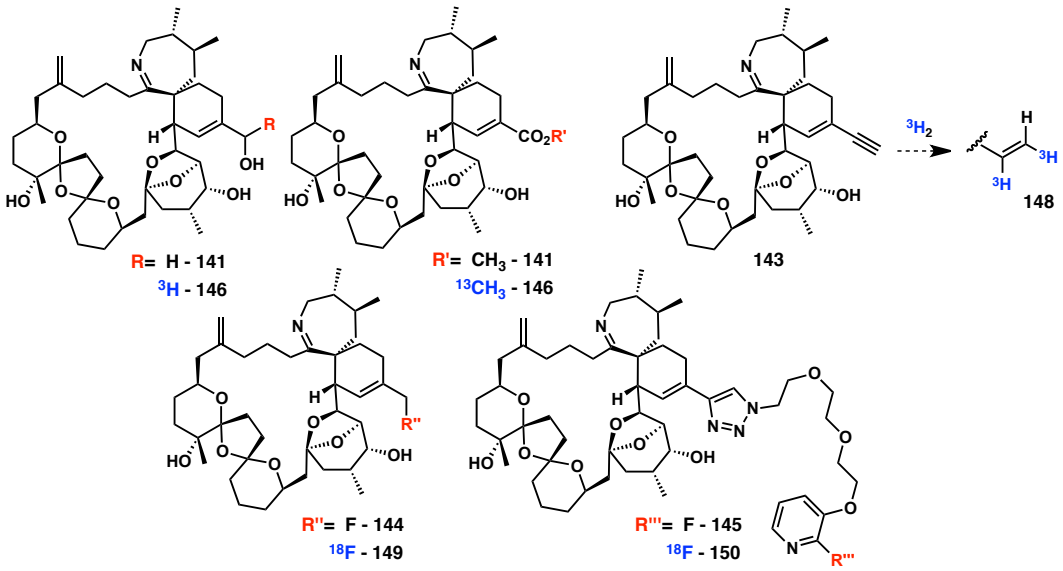
We proposed ^{18}F, ^{13}C and ^{3}H isotope labeled pinnatoxin derivatives (Figure 16) to probe biodistribution, cellular metabolomics and toxicological profile in biological systems.[57] Ultimately, information gained from these studies can be part of an effort to aid in the regulation of CI toxin levels in seafood, to understand short and long-term effects of CI exposure, and to utilize PnTX radiotracers as standards for drug discovery in nAChR related neurodegenerative diseases such as schizophrenia, Parkinson's and Alzheimer's.[58]

In 1935, Shoenheimer and Rittenberg first used isotopic labeling in their study of fat metabolism in mice with deuterium.[59] Since its inception, isotopically labeled bioactive molecules have been used heavily in areas such as drug discovery and oncology.[60] For more than two decades, radiotracers in animal models have accelerated drug discovery by gathering toxicological, metabolomics, fluxomics and excretion profiles in a rapid manner.[61] For example, drug metabolism and pharmacokinetic (DMPK) studies now utilize quantitative whole-body autoradiography (QWBA) for drug distribution of radiolabeled bioactive molecules in medicinal chemistry.[62]

^{18}F-labeled bioactive molecules are valuable tools for *in vivo* images that are detected by positron emissions tomography (PET).[63] Clear 3-D images are obtained that show the biodistribution of the radiotracer. For example, ^{18}F-nifene radiotracers were used to

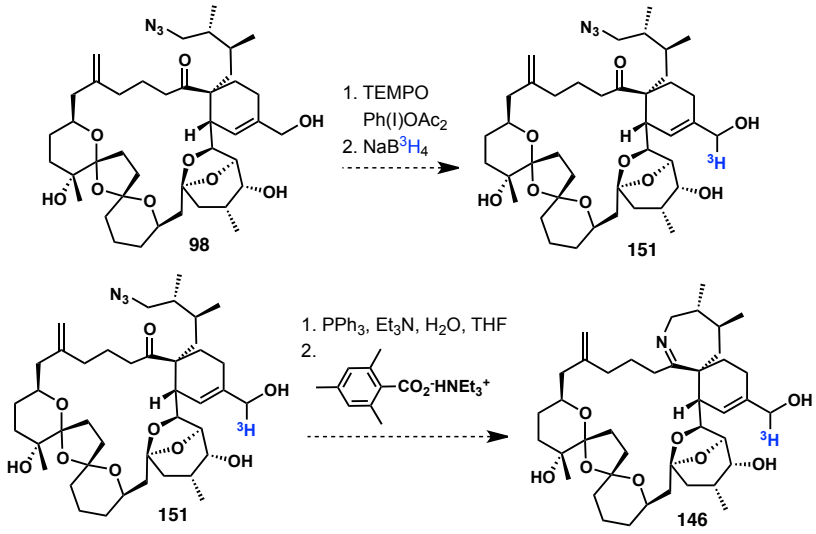
obtain PET images of $\alpha_4\beta_2$ nAChRs (thalamic and extrathalamic brain regions) in rhesus monkeys and exhibited potent binding properties at K_i=0.50 nM for this subtype.[64] Similarly, we wish to incorporate ^{18}F-radiolabeled pinnatoxin (derivative **149** and **150**) to acquire PET images in mice.

Figure 16. Targets of Derivatives Accessed from Azido triol



Additionally, ^{3}H and ^{13}C-labeling are also routinely used in metabolomics. With the advent of ultra-high resolution Fourier transform mass spectrometry (FT-MS); metabolites can be characterized accurately by mass to offer clues in cellular metabolic pathways.[65] We carefully selected different derivative candidates for isotopic labeling shown in Figure 16. Our initial goal was to develop a reliable synthetic method to access these derivatives and to fully characterization them. Additionally, we wanted to obtain the potency of each derivative against nAChRs to compare its binding properties against PnTX A prior to isotopic labeling.

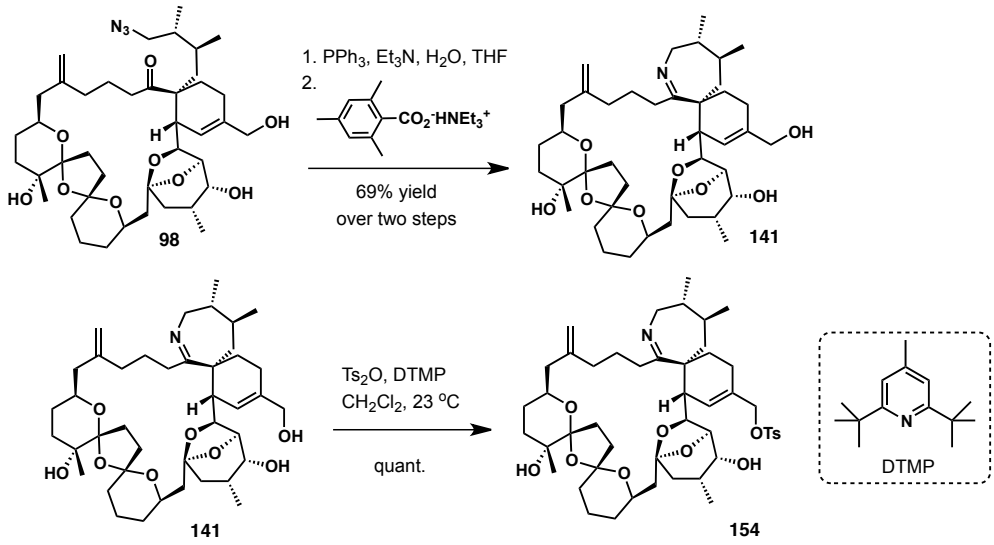
Scheme 33. Proposed Synthesis of [^{3}H]-PnTX-OH **146**



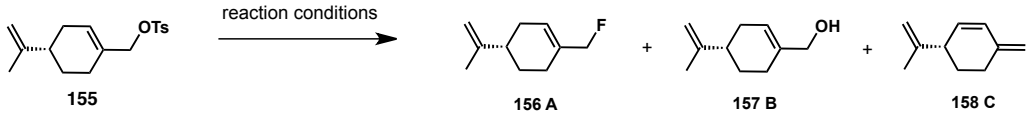
The proposed synthesis of [^{3}H]-PnTX-OH **146** (Scheme 33) would advance azido triol **98** to [^{3}H]-azido triol **151** by TEMPO/PhI(OAc)$_2$ oxidation and reduction with sodium borotritide.[66] Standard imine formation protocol would complete the synthesis of [^{3}H]-PnTX-OH **146** in four steps. The synthesis of PnTX-OH **141** could be rapidly accessed from azidotriol in two steps through Staudinger reduction (PPh_3, THF−H_2O, 55 °C, 36 h) of azide **98** (Scheme 34), followed by imine formation (69% yield over two steps). The completion of derivative **141** provided the necessary substrate to investigate the feasibility of synthesizing PnTX-F **144** through nucleophilic substitution of the corresponding tosylate.

Selective mono-tosylation of allylic alcohol **141** was achieved in the presence of *p*-toluenesulfonic anhydride (Ts_2O) and 2,6-di-*tert*-butyl-4-methyl pyridine (DTMP) in dichloromethane in quantitative yield (Scheme 34). Fluorine substitution conditions were screened with a model tosylate **155**, which was made in two steps from (*S*)-perillaldehyde. For each of the conditions, thermal and microwave assisted heating were performed.

Scheme 34. Synthesis of PnTX-OH and Selective Mono Tosylation



Scheme 35. Screening Conditions for Fluoro-de-Tosylation



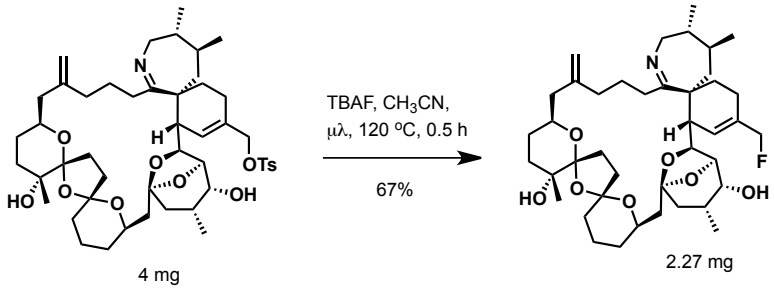
experiment	reaction conditions	results A:B:C %
1	KF, CH_3CN, reflux, 3 h	0:0:100
2	KF, CH_3CN, μλ, 85 °C, 0.5 h	0:0:100
3	KF, 18-crown-6 CH_3CN, reflux, 3 h	70:10:20
4	KF, 18-crown-6 CH_3CN, μλ, 120 °C, 0.5 h	60:10:20
5	TBAF, CH_3CN, reflux, 3 h	85:15:0
6	TBAF, CH_3CN μλ, 120 °C, 0.5 h	85:15:0
7	KF, 18-crown-6 CH_3CN, reflux, 3 h	80:5:10
8	KF, 18-crown-6 CH_3CN, μλ, 120 °C, 0.5 h	80:5:10
9	AgF, CH_3CN, μλ, 120 °C, 0.5 h	decomposition

The most promising reaction conditions are presented in entries 5-8. Tetrabutylammonium fluoride (TBAF) in refluxing acetonitrile provided allylic fluoride **156A** in 85% yield along with hydrolysis product **157B** (allylic alcohol).[67] Utilization of potassium fluoride and 18-crown-6 in acetonitrile also gave comparable yields (80%

yield),[68] however, elimination product **158C** was observed in both traditional oil bath and microwave assisted heating.

With these promising conditions at-hand, mono-tosylate **154** was subjected to the same reaction conditions (entries 5-8). The treatment of tosylate **154** with potassium fluoride and 18-crown-6 in refluxing acetonitrile only produced complex mixtures. We were delighted to find that in the presence of tetrabutylammonium fluoride in acetonitrile with microwave assisted heating at 120 °C for 30 min afforded 2.27 mg of fluoride **144** in 67% isolated yield (Scheme 36). It should be noted that yields of reactions on a 4 mg scale were calculated by ^{1}H NMR titration (see Supporting Information).

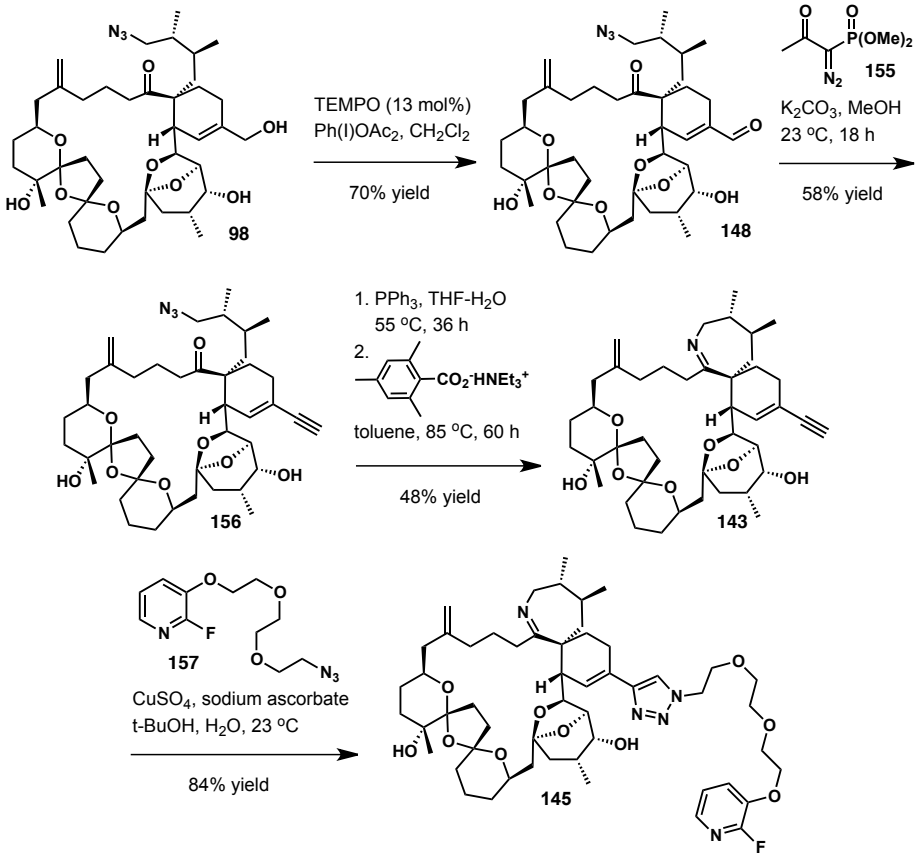
Scheme 36. Synthesis of Pinnatoxin-Fluoride



Our focus shifted towards our next target, pinnatoxin 2-fluropyridine **145**. The synthetic strategy was based on a reliable reaction pathway utilizing "click" chemistry to couple azide **157** with pinnatox-yne **143**. Pinnatox-yne **143** was made in four steps from azido triol. Selective oxidation at C34 with TEMPO/PhI(OAc)$_2$ in dichloromethane provided aldehyde **148** in 70% yield. Homologation of the corresponding aldehyde to alkyne **148** was possible with Ohira-Bestmann reagent **155** in potassium carbonate and methanol.[69] Standard conditions for imine formation began with reduction of the azide to the primary amine, followed by cyclization with triethylammonium 2,4,6-

trimethylbenzoate in toluene at 85 °C for 60 h provided pinnatox-yne **143** in 48% yield over two steps.

Scheme 37. Synthesis of Pinnatoxin 2-Fluoropyridine

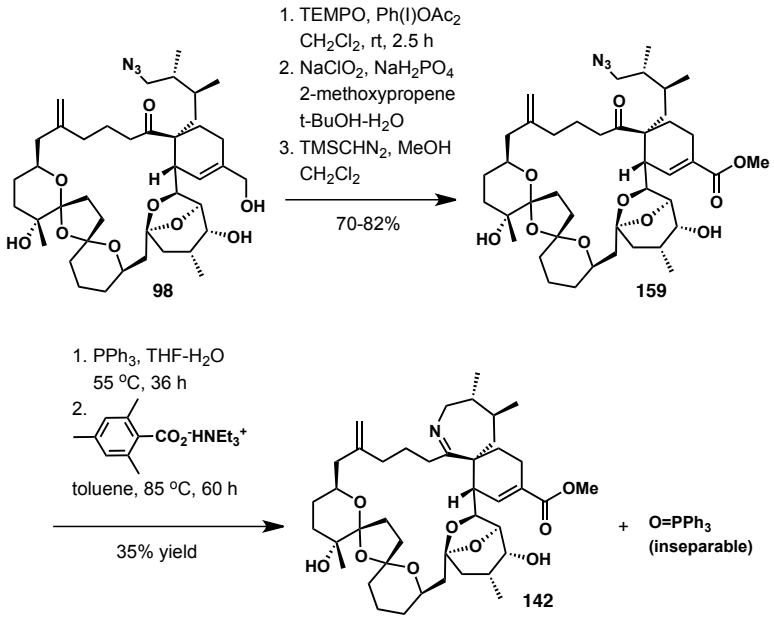


Prior to azide-alkyne cycloaddition chemistry, 3-(2-(2-(2-azidoethoxy)ethoxy)ethoxy-2-fluoropyridine **157** was prepared in four steps from triethylene glycol (TEG) and 2-nitropyridin-3-ol. [70] The copper catalyzed 1,3-dipolar azide-alkyne cycloaddition proceeded cleanly in the presence 20 mol% $CuSO_4$ and 40 mol% sodium ascorbate in aqueous *tert*-butanol at 23 °C for 12 h producing triazole **145** in 84% yield.[71]

The last target, pinnatoxin methyl ester **142**, was obtained in five steps. Oxidation to the methyl ester was accomplished by stepwise TEMPO/$Ph(I)OAc_2$ and Pinnick

oxidation to the carboxylic acid followed by methyl ester formation with trimethylsilyl diazomethane in 70-80% yield over three steps.

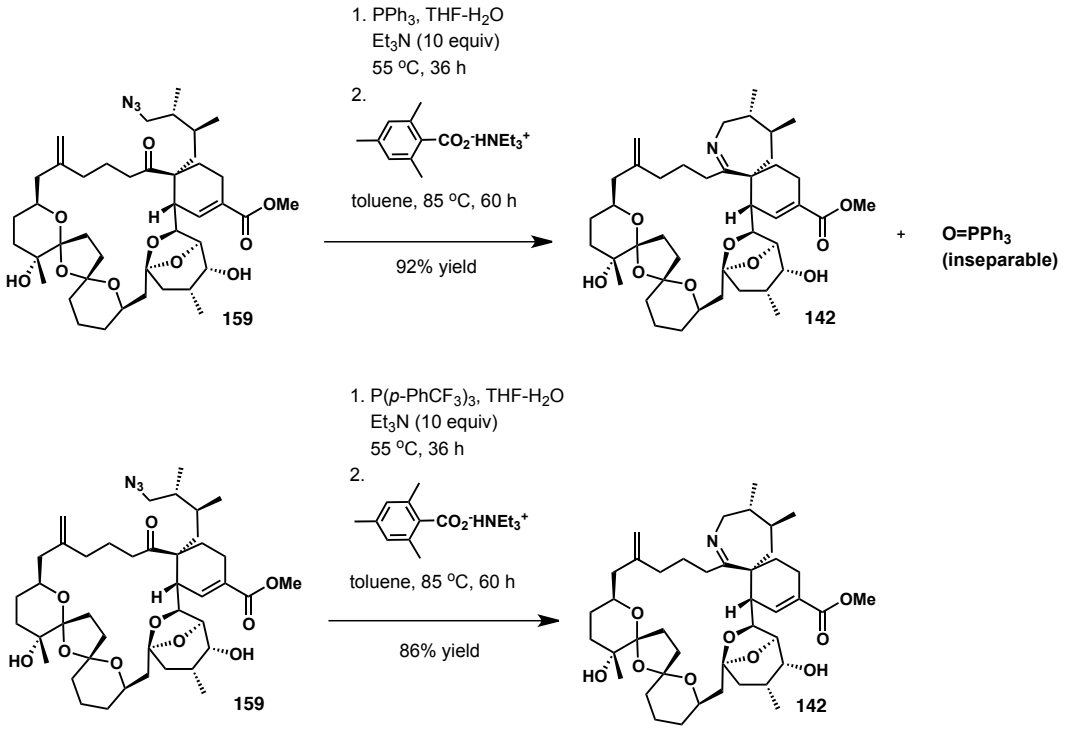
Scheme 38. Unoptimized Synthesis of Pinnatoxin Methyl Ester



Standard conditions for imine formation provided pinnatoxin methyl ester **142** in 35% yield as an inseparable mixture with triphenylphosphine oxide. To address the issue of this low yielding imine formation with the methyl ester functionality, we hypothesized that during the Staudinger reduction, the presence of the iminophosphorane intermediate was the culprit that led to unproductive reaction pathways. One way to circumvent this issue was shortening the lifespan of the iminophosphorane in the reaction mixture by expediting its hydrolysis with water. Triethylamine is known to accelerate the hydrolysis step in Staudinger azide reductions.[72] To test this hypothesis, azide **159** was treated with PPh_3, Et_3N, THF−H_2O at 55 °C. We observed full consumption of starting material in 8 h compared to 36 h without triethylamine. Under standard protocol, this crude reaction

mixture was submitted to cyclic imine formation that afforded pinnatoxin methyl ester **142** in 92% yield.

Scheme 39. Synthesis of Pinnatoxin Methyl Ester



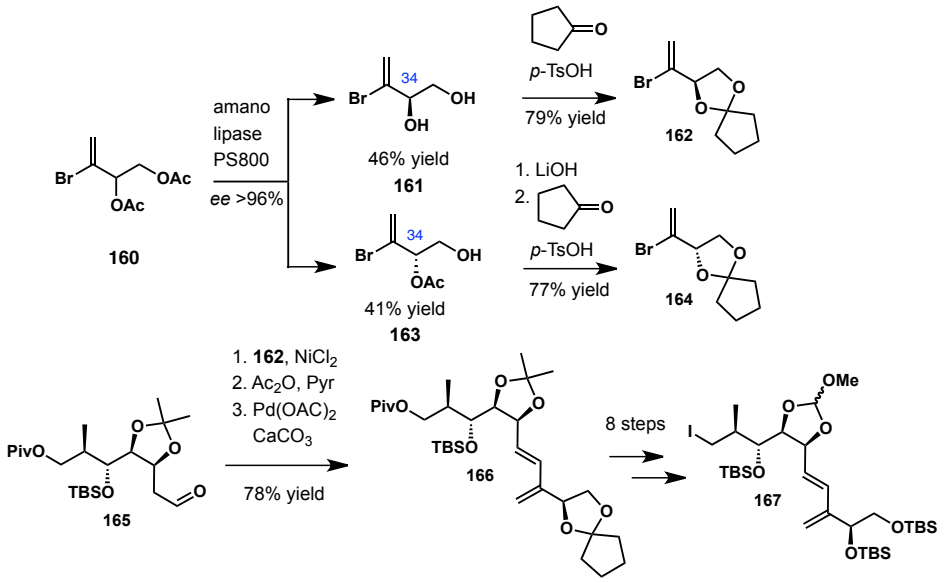
Although we were able to substantially improve the yield, triphenylphosphine oxide was still problematic during purification. We began screening various triarylphosphines for suitable reactivity and separation from its corresponding oxide. Excellent results came from Tris(4-(trifluoromethyl)-phenyl)-phosphine that afforded pure PnTX methyl ester **142** in 86% yield. Due to the decreased nucleophilic nature of this phosphine, the azide reduction required 36 h. We postulated that the rate-determining step was the formation of the iminophosphorane, followed by its rapid hydrolysis.

2.6: Kishi's Total Synthesis of Pteriatoxin A-C

Uemura and co-workers, in 2001, isolated PtTX A and PtTX B/C as an inseparable mixture from *Pteria penguin*, and they observed the same gross structure as PnTX A but

containing a cysteine residue. In 2006, Kishi reported the total synthesis[73] and stereochemistry[74] of pteriatoxins A, B and C (PrTX A−C). Their synthetic strategy heavily relied on previously published synthesis of pinnatoxin A discussed above. The purpose of Kishi's synthesis of PtTXs was to secure access to all possible stereoisomers at C34 and C2-positions to unequivocally identify each member of the PrTX family. Although PtTX B and C were isolated as a 1:1 mixture, they were able to identify distinct ^{1}H NMR signals for each isomer. The diagnostic NMR characteristics and HPLC traces established the stereochemistry as (34 *S*,2'*R*) PtTX A, (34*R*,2'*R*) PtTX B and (34*S*,2'*R*) PtTX C (Scheme 41).

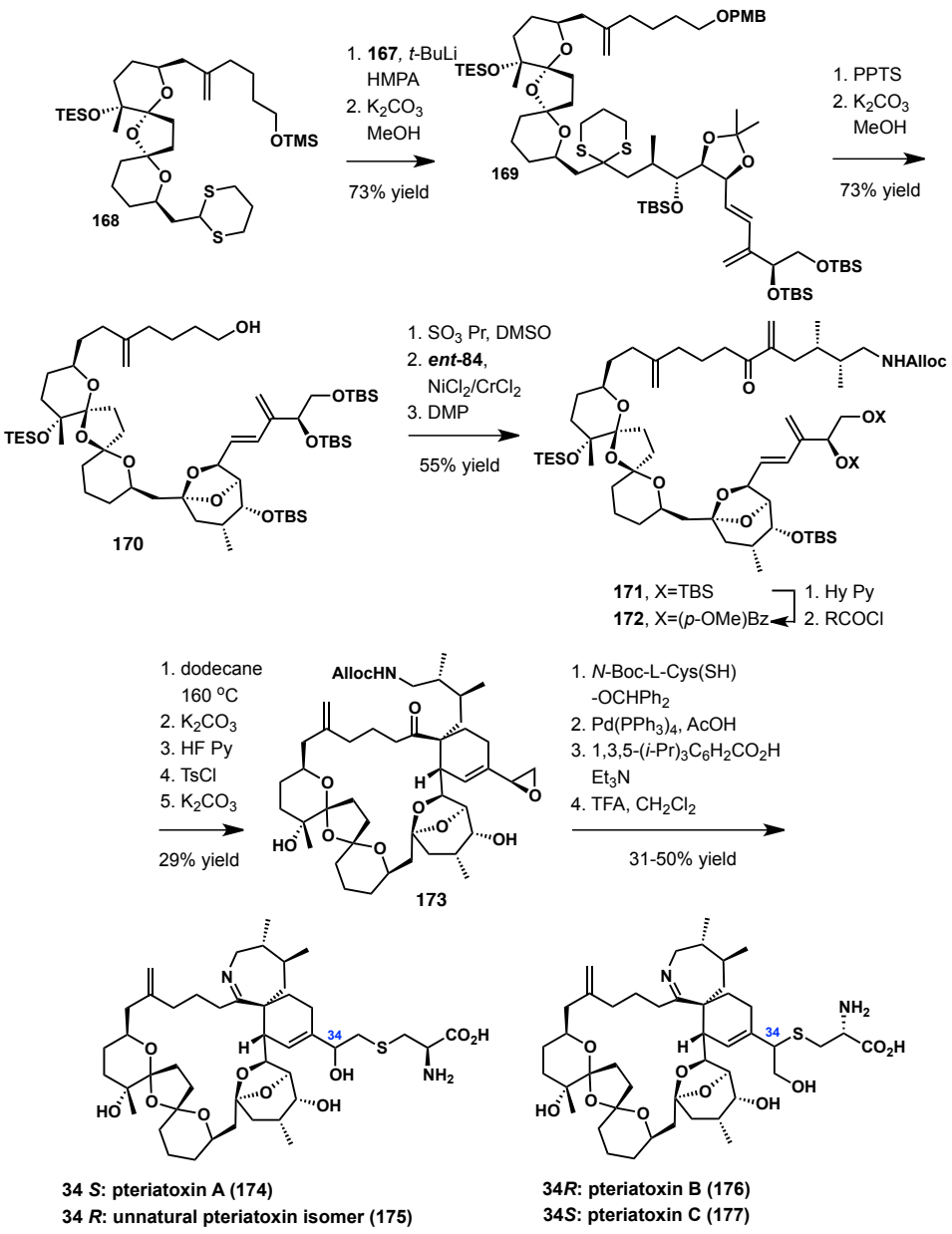
Scheme 40. Synthesis of C33−C35 Fragments through Enzymatic Resolution



Enzymatic resolution of **160** was the foundation in which all C34 isomers could be synthesized (Scheme 40). The other building blocks for the construction of the macrocyclic carbostructure are the same used for the synthesis of PnTX A. Hydrolysis with Amano lipase PS800 of diacetate **160** resolved two optically pure fragments (*ee* > 96%) and was subsequently converted to their respective dioxaspiranes. Vinyl bromide

162 was further elaborated to the diene functionality through NHK-coupling (Ni/Cr) with aldehyde **165**, acylation and Pd-mediated elimination in 78% yield.

Scheme 41. Synthesis of PtTX A−C



Alkylation of lithiated dithiane **168** with iodide **167** united the two complex fragments in high yield. After the formation of EF-rings, oxidation to the aldehyde of the C6 hydroxy group permitted the second Ni/Cr-mediated coupling with vinyl iodide ***ent*-84** and DMP

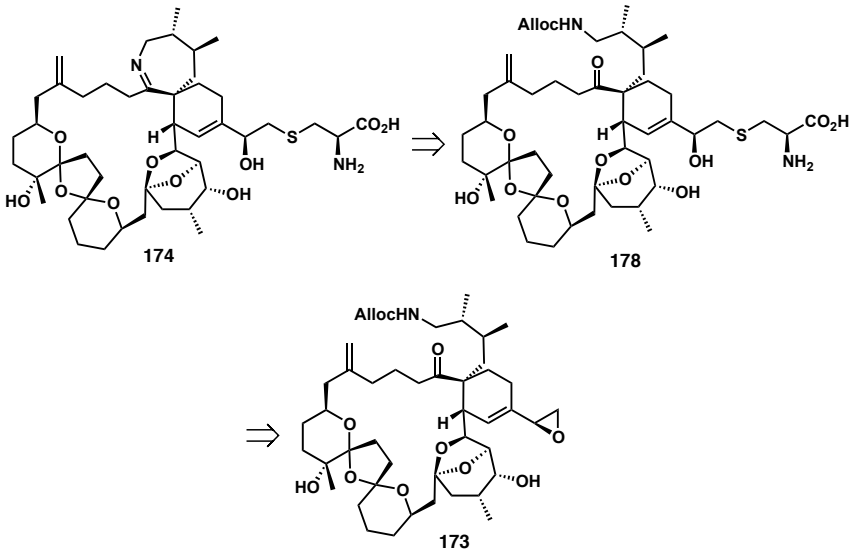
oxidation completed the IMDA precursor in 40% yield over five steps. Protecting group manipulation of the 1,2-diol to the *p*-methoxybenzoate provided the best *exo:endo* (ca. 2:1) selectivity for the desired *exo* intramolecular Diels-Alder product (dodecane, 160 °C) in 51% isolated yield. Introduction of cysteine residue was possible through epoxide **173** to provide two regioisomers, PtTX A and PtTX B, in an S_N2 fashion. Forcing conditions (200 °C) for imine cyclization used in the PnTX A synthesis was unsuccessful in this approach. The implication of weakly acidic conditions with sterically congested carboxylic acids (2,4,6-(i-Pr)$_3$C$_6$H$_2$CO$_2$H) and triethylamine delivered the requested cyclic imines in acceptable yields for PtTX A-C as well as the unnatural PrTX isomer (see Scheme 41).

2.7: Synthetic Studies Towards Pteriatoxin A

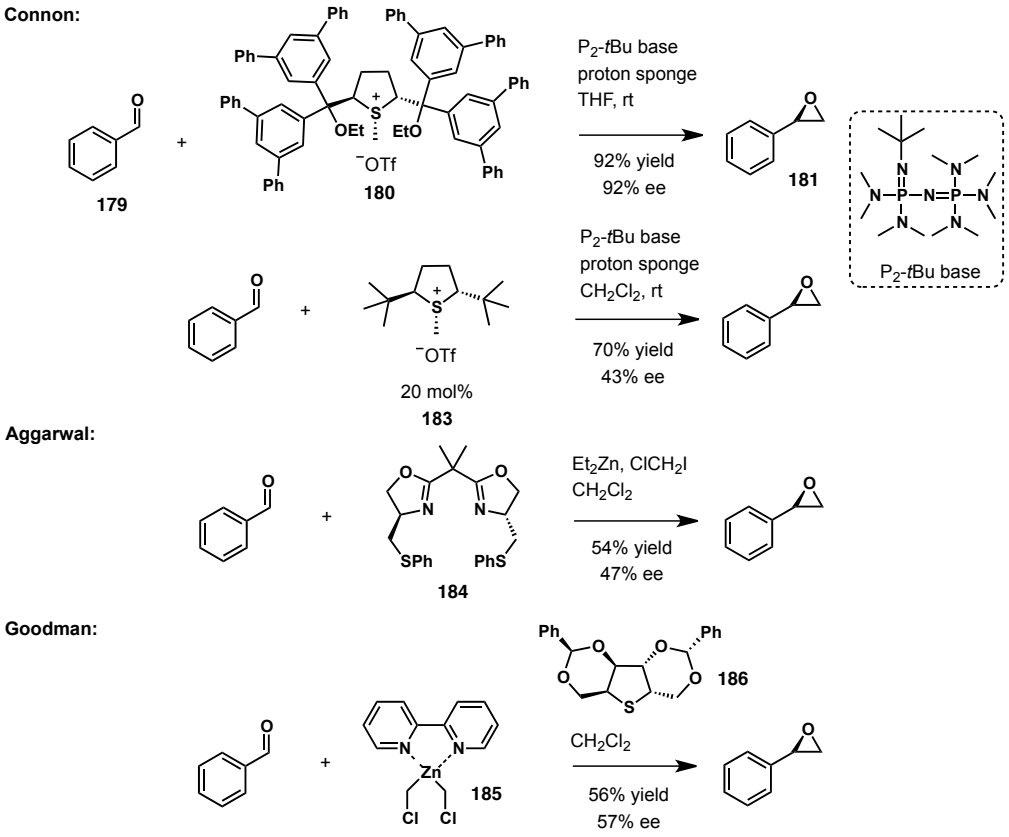
The landmark synthesis by Kishi required early C34 functionalization to access pteriatoxins A-C in 34 steps (longest linear steps). Our ultimate goal was to develop the synthesis of pteriatoxins by direct functionalization of pinnatoxin G. Concise synthetic approach to these molecules would allow establishing their bioactivity profile, which remained to be conclusively investigated.

Our first approach envisioned cysteine addition to chiral allylic epoxide **173** (Figure 17). At the onset, no literature precedence existed to access terminal chiral allylic epoxides from their corresponding aldehydes. Three reports by Connon, Aggarwal and Goodman reported asymmetric Corey-Chaykovsky epoxidation of benzaldehyde with chiral sulfur ylides shown in Scheme 42. Connon provided the most promising results with bulky ylide **180**, P$_2$-tBu base, proton sponge to afford styrene oxide in 92% yield and 92% *ee*.

Figure 17. Retrosynthesis of PrTX A via Cysteine Addition to Chiral Epoxide



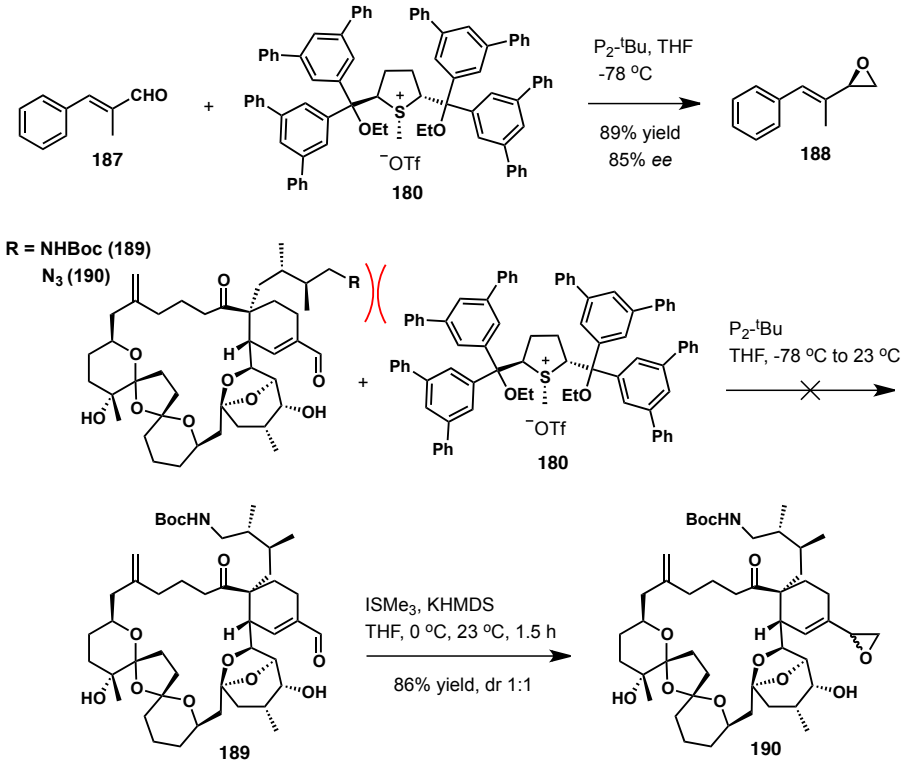
Scheme 42. Precedence for Asymmetric Corey-Chaykovsky Epoxidation



Performing Connon procedure on a suitable model containing the requisite α-branched and α,β-unsaturated aldehyde **187** afforded epoxide **188** in 89% yield and 85% *ee*

(Scheme 43). Application of this method with aldehyde **189** and **190** provided no epoxide but only moderate decomposition of the starting material. We hypothesized that the steric clash of the bulky aryl groups of the ylide with the sterically congested cyclohexenal prohibited this reaction. Next, we wanted to investigate the possibility of substrate (**189**) controlled asymmetric epoxidation with trimethylsulfonium iodide could be achieved. However, a 1:1 mixture of diastereomers (**190**) was obtained from trimethylsulfonium iodide and potassium bis(trimethylsilyl)amide (KHMDS). Unfortunately, the addition of cysteine residue to racemic epoxide would lead to four diastereomers. This route greatly deviated from our primary objective, which was the direct synthesis of pteriatoxin A. As an alternative approach, we envisioned chiral diols as another attractive precursor to all isomers of pteriatoxins.

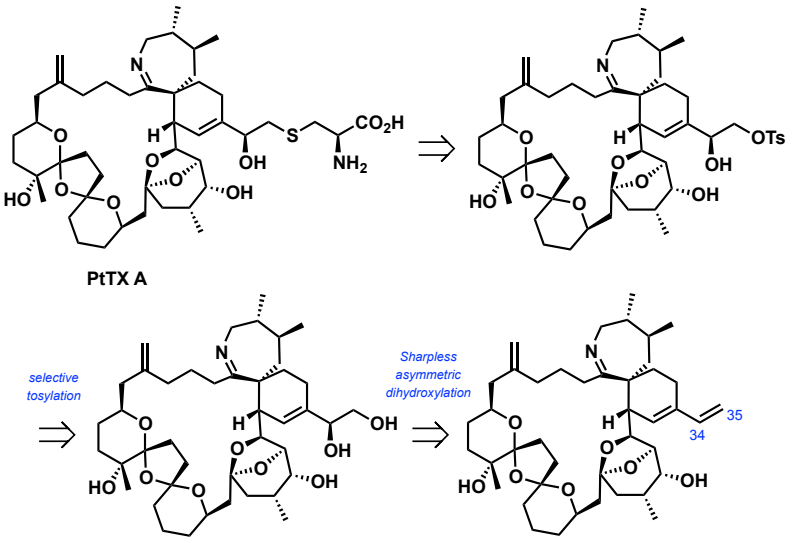
Scheme 43. Connon Procedure for Asymmetric Epoxidation



We investigated the feasibility of accessing PtTX A through a direct Sharpless asymmetric dihydroxylation of pinnatoxin G, followed by selective mono-tosylation and direct S_N2 addition with cysteine (Figure 18). The starting material was prepared in four steps from azido triol. Oxidation and Wittig olefination of the corresponding aldehyde with methyltriphenylphosphonium bromide, *n*-BuLi in THF at -78 °C to -10 °C provided azido triene **194** in 40-45% yield. Standard spiroimine formation provided PnTX G in 88-91% yield.

A review of literature suggested that we could tune the regioselectivity to favor dihydroxylation of the mono-substituted olefin (C34 and C35-positions). It was well documented that dihydroxylation of di- or tri-substituted olefins required the use of methanesulfonamide additive to the AD-mix. [75]

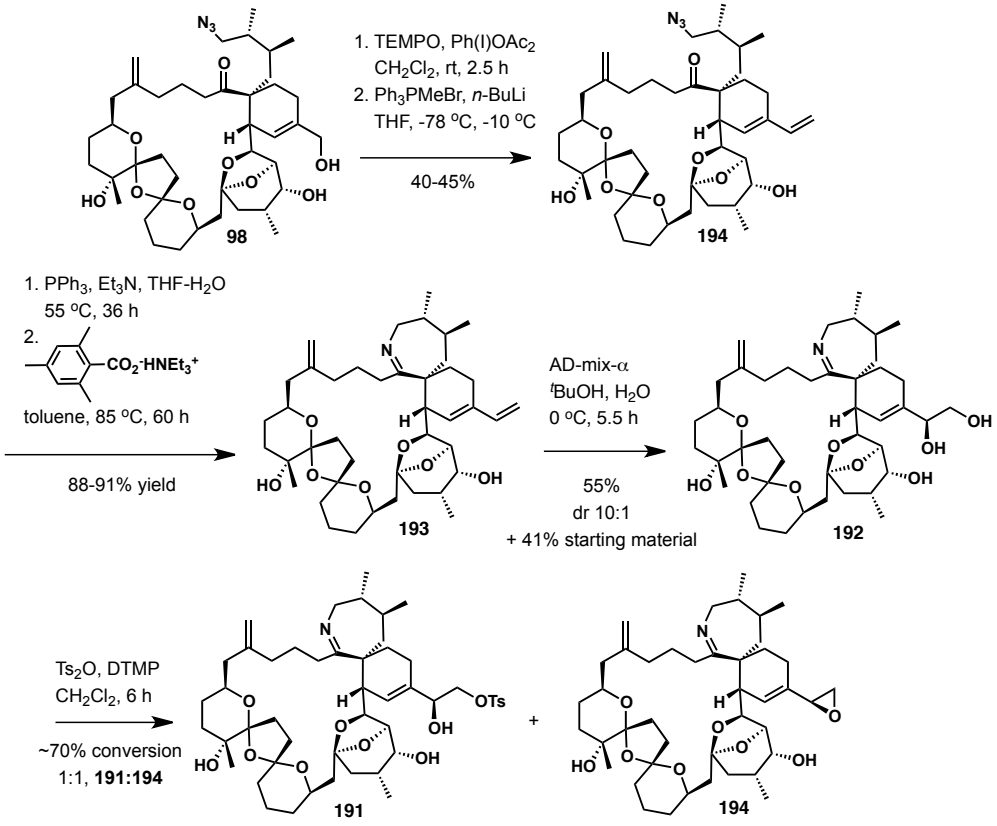
Figure 18. Retrosynthetic Plan for the Synthesis of Pteriatoxin A



In contrast, methanesulfonamide was shown to slow the reactivity with terminal olefins (1,1-disubstituted and mono-substituted olefins).[76] Additionally, the phthalazine ligand linker, as in $(DHQ)_2PHAL$, stabilizes substrates through π-π interactions. The π-π

stabilization between phthalazine and cyclohexene could provide the necessary preference needed for dihydroxylation of the C34-C35 double bond.

Scheme 44. Catalytic Asymmetric Dihydroxylation of Pinnatoxin G



We were delighted to see that regioselective dihydroxylation of PnTX G occurred in the presence of AD-mix-α, ^{t}BuOH−H_2O (1:1) at 0 °C (no sulfonamide additive) for 5.5 h afforded tetraol **192** in 55% yield and a 10:1 dr along with recovered starting material. Longer reaction times (16 h) under these conditions led to complex distribution of products and decomposition of the tetraol. Halting this reaction at 5.5 h provided clean tetraol in 55% yield along with recovered PnTX G in 31% yield. Tosylation of tetraol **192** (Ts_2O, DTMP, CH_2Cl_2, ~70% conversion) afforded a 1:1 mixture of mono-tosylate **191** and epoxide **194**. Purification of the tosylate through column chromatography resulted in

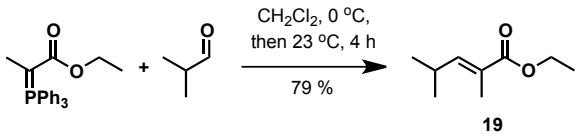
higher conversion to the epoxide. The future direction of the synthesis of PtTX A would be to investigate other possibilities of substitution of C35 hydroxyl group with cysteine.

Conclusion

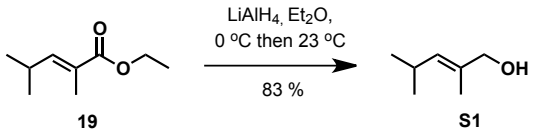
In 2011, the Zakarian laboratory established a robust and scalable synthesis of PnTX A. This was demonstrated in this work by producing almost 600 mg of an advanced azido triol intermediate, which can be converted to PnTX A in 6 steps, or PnTX G in 4 steps. The azido triol has been used as a starting material for the preparation of a variety of bioactive pinnatoxin derivatives. Competitive binding and electrophysiological data of these derivatives against nicotinic acetylcholine receptors are pending. In the future, ^{18}F, ^{13}C and ^{3}H isotope labeling of these derivatives can reveal biodistribution, cellular metabolism and short/long-term affect of pinnatoxin exposure. Also, a catalytic asymmetric dihydroxylation of pinnatoxin G secured a promising route to the synthesis of pteriatoxins. The culmination of this work will build upon a growing body of knowledge that will ultimately lead to the regulation of these toxins in contaminated shellfish.

Experimental Procedures

General Information. All reactions were carried out under an inert atmosphere of dry argon in oven or flame-dried glassware, unless the reaction procedure states otherwise. Tetrahydrofuran (THF) and ether (diethyl ether) were distilled from sodium-benzophenone in a continuous still under an atmosphere of argon. Dichloromethane, di-*iso*-propylamine and triethylamine were distilled from calcium hydride in a continuous still under and atmosphere of argon. Reaction temperatures were controlled by IKA ETS-D4 fuzzy thermo couples. Analytical thin-layer chromatography (TLC) was performed using pre-coated TLC plates with Silica Gel 60 F_{254} (EMD no. 5715-7) and visualized using combinations of UV, anisaldehyde, ceric ammonium molybdate (CAM), potassium permanganate, and iodine staining. Flash column chromatography was preformed using 40-63 mm silica gel (EMD, Geduran, no. 1.11567.9026) as the stationary phase. Proton nuclear magnetic resonance spectra were recorded at 400, 500, and 600 MHz on Varian Unity Inova. Carbon nuclear magnetic resonance spectra were recorded at 100 MHz, 125 MHz, and 150 MHz on Varian Unity Inova, and Varian Unity Inova spectrometers. All chemical shifts were reported in δ units relative to tetramethylsilane. Optical Rotations were measured on a Rudolph Autopol III polarimeter. High resolution mass spectral data were obtained by the Mass Spectrometry laboratory at the University of California, Santa Barbara.

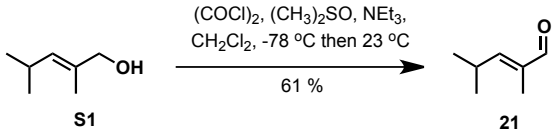


(*E*)-Ethyl 2,4-dimethylpent-2-enoate (19). Ethyl 2-(triphenylphosphoranylidene) propanoate (7.97 g, 22.0 mmol) in dry dichloromethane (25.0 mL) was cooled to 0 °C. Freshly distilled isobutyraldehyde (1.8 mL, 20.0 mmol) was added dropwise via syringe within 5 min. This mixture was warmed to 23 °C and stirred for an additional 4 h. The crude yellow mixture was concentrated and purified by column chromatography (silica, 10% diethyl ether – pentanes, then 30% diethyl ether – pentanes) to give the desired ester **19** (2.73 g, 17.5 mmol, 79% yield) as a clear liquid. ^{1}H NMR (500 MHz, $CDCl_3$); δ(ppm): 6.54 (dd, J = 9.7, 1.4 Hz, 1H), 4.16 (q, J = 7.1 Hz, 2H), 2.61 (dhept, J = 9.7, 6.7 Hz, 1H), 1.81 (d, J = 1.4 Hz, 3H), 1.29 – 1.26 (m, 3H), 1.00 (d, J = 6.7 Hz, 6H); ^{13}C NMR (500 MHz, $CDCl_3$); δ(ppm): 168.48, 148.68, 125.57, 60.34, 27.86, 21.91, 14.25, 12.21; HRMS-EI (*m*/*z*): [M+] calcd for $C_9H_{16}O_2$, 156.1150; found, 156.1156.



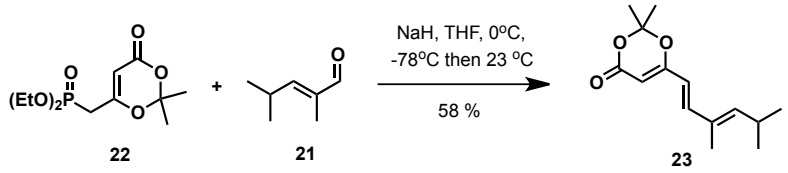
(*E*)-2,4-Dimethylpent-2-en-1-ol (S1). (*E*)-Ethyl 2,4-dimethylpent-2-enoate 5 (1.40 g, 8.96 mmol) in dry diethyl ether (10.0 mL) was added dropwise with a syringe over 5 min to a mixing solution of $LiAlH_4$ (0.850 g, 22.40 mmol) in diethyl ether (35.0 mL) at 0 °C. After stirring at 23 °C for 45 min, the solution was cooled to 0 °C. To the cooled mixture, H_2O (0.9 mL), 3 M NaOH (0.9 mL) and another portion of H_2O (2.6 mL) were added sequentially at 5 min intervals while stirring vigorously.

The resultant mixture was warmed to 23 °C and stirred for 3 h. The salts were filtered and washed with ether (3 x 10 mL), and the combined filtrate was dried with magnesium sulfate and evaporated. The crude clear mixture was purified by column chromatography (silica, 20% diethyl ether – pentanes, then 40% diethyl ether – pentanes) to give the desired alcohol **S1** (0.844 g, 7.39 mmol, 82% yield) as a clear liquid. ^{1}H NMR (500 MHz, $CDCl_3$); δ (ppm): 5.22 (ddd, J = 9.2, 2.6, 1.3 Hz, 1H), 3.97 (d, J = 4.3 Hz, 2H), 2.58 – 2.48 (m, 1H), 1.66 (d, J = 1.3 Hz, 3H), 1.40 (t, J = 5.3 Hz, 1H), 0.95 (d, J = 6.7 Hz, 6H); ^{13}C NMR (500 MHz, $CDCl_3$) ; δ(ppm): 133.93, 132.34, 76.75, 69.00, 26.80, 22.87, 13.57.



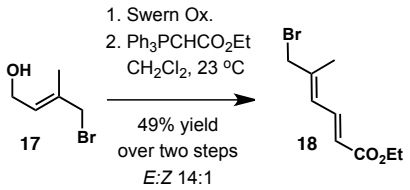
(*E*)-2,4-Dimethylpent-2-enal (21). Dimethylsulfoxide (1.1 mL, 16.1 mmol) was added dropwise to a solution of $(COCl)_2$ (0.7 mL, 8.04 mmol) in dry dichloromethane (10.0 mL) at -78 °C. After stirring for 15 min, (E)-2,4-dimethylpent-2-en-1-ol S1 (0.612 g, 5.36 mmol) in dry dichloromethane (7.0 mL) was added via syringe at -78 °C and stirred for 25 min. Triethylamine (3.4 mL, 24.1 mmol) was added over 5 min at -78 °C, and then the reaction mixture was warmed to 0 °C and stirred for an additional 25 min. The solution was diluted with diethyl ether (10 mL) and H_2O (10 mL) and stirred for 5 min. A 1:1 mixture of brine (10 mL) and 1 M HCl (10 mL) was added and the aquesous phase was extracted with diethyl ether (3 x 10 mL). The combined organic layers were washed with a mixture of brine (10 mL) and saturated aqueous sodium bicarbonate (10 mL), dried with sodium sulfate, and the crude clear mixture was purified by column chromatography (silica, 20% diethyl ether –

pentanes, then 40% diethyl ether – pentanes) to give the desired aldehyde **21** (0.367 g, 3.28 mmol, 61% yield) as a clear liquid. ^{1}H NMR (500 MHz, $CDCl_3$); δ (ppm): 9.34 (s, 1H), 6.26 (dd, J = 9.6, 1.3 Hz, 1H), 2.81 (dhept, J = 9.7, 6.7 Hz, 1H), 1.72 (d, J = 1.3 Hz, 3H), 1.06 (d, J = 6.7 Hz, 6H); ^{13}C NMR (500 MHz, $CDCl_3$) ; δ(ppm): 195.60, 161.15, 137.05, 28.16, 21.71, 9.05.



6-((1E,3E)-3,5-Dimethylhexa-1,3-dien-1-yl)-2,2-dimethyl-4H-1,3-dioxin-4-one (23). Diethyl ((2,2-dimethyl-4-oxo-4H-1,3-dioxin-6-yl)methyl)phosphinate **22** (3.07 g, 11.0 mmol) was dissolved in dry THF (23.0 mL) and added dropwise to a suspension of NaH (60% in mineral oil, 0.463 g, 11.0 mmol) in dry THF (23.0 mL) at 0 °C. The resulting solution was warmed to 23 °C and stirred for an additional 30 min. A solution of (E)-2,4-Dimethylpent-2-enal **21** (1.30 g, 11.6 mmol) in dry THF (23.0 mL) was added via cannula at -78 °C over 15 min. The reaction mixture was warmed to 23 °C and stirred for 12 h and then quenched with H_2O (5 mL), diluted with ethyl acetate (20 mL), and washed with brine (20 mL). The organic layer was dried with sodium sulfate and evaporated. The crude product was purified by column chromatography (silica, 10% ethyl acetate – hexanes) to give a white crystalline solid **23** (1.58 g, 6.68 mmol, 58%). ^{1}H NMR (500 MHz, $CDCl_3$); δ (ppm): 6.92 (d, J = 15.6 Hz, 1H), 5.87 (d, J = 15.6 Hz, 1H), 5.68 (d, J = 9.4 Hz, 1H), 5.28 (s, 1H), 2.67 (ddt, J = 13.3, 9.4, 6.6 Hz, 1H), 1.78 (d, J = 1.1 Hz, 3H), 1.69 (s, 6H), 0.99 (d, J = 6.6 Hz, 6H); ^{13}C NMR (125 MHz, CDCl3); δ(ppm): 164.11, 162.08, 148.89, 143.31, 130.80,

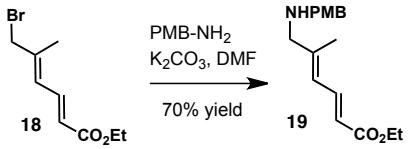
117.16, 106.10, 93.61, 27.96, 25.03, 22.45, 12.04; HRMS-ESI (m/z): [M+Na] calcd for $C_{14}H_{20}O_3Na$, 259.1310; found, 259.1298.



(2*E*,4*E*)-Ethyl 6-bromo-5-methylhexa-2,4-dienoate (18). The (*E*)-4-bromo-3-methyl but-2-en-1-ol was synthesized from isoprene according to a known procedure.[77] Dimethylsulfoxide (2.8 mL, 38.9 mmol) was added to a solution of oxalyl chloride (1.6 mL, 19.5 mmol) in dry dichloromethane (60.0 mL) at -78 °C. After 15 min, a solution of the (*E*)-4-bromo-3-methylbut-2-en-1-ol (2.14 g, 12.9 mmol) in dichloromethane (30.0 mL total with rinses) was added. The mixture was stirred for 45 min. Diisopropylethylamine (10.0 mL, 58.5 mmol) was added dropwise, and after 30 min the mixture was warmed to 0 °C and stirred for 25 min. The reaction mixture was quenched by adding 100 mL of 1 M aqueous HCl. The aqueous layer was extracted with dichloromethane (3 x 65 mL). The combined organic layers were washed with water and a saturated aqueous solution of sodium bicarbonate, dried with sodium sulfate, concentrated at 25 °C, and the residue was used directly in the next step.

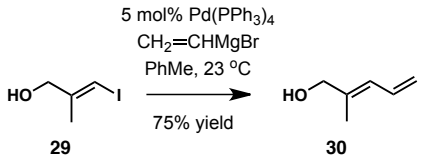
Ethyl 2-(triphenylphosphoranylidene)acetate (4.70 g, 13.5 mmol) was added to the solution of aldehyde in dichloromethane (40.0 mL) at 23 °C. The resultant mixture was stirred at the same temperature for 14 h, after which 5 g of silica gel were added. The mixture was concentrated and purified by column chromatography (silica, 5% ethyl acetate – hexanes) to give **18** as a yellow oil (1.48 g, 49%). ^{1}H NMR

(500 MHz, $CDCl_3$); δ (ppm): 7.48 (ddd, J = 15.2, 12.8, 11.6 Hz, 1H), 6.30 – 6.20 (m, 1H), 5.91 (dd, J = 15.2, 2.5 Hz, 1H), 4.24 – 4.17 (q, J = 7.1, 2H), 4.07 (s, 1H), 4.01 (s, 1H), 1.99 (dd, J = 14.1, 1.2 Hz, 3H), 1.28 (t, J = 7.1, 3H); ^{13}C NMR (125 MHz, CDCl3); δ(ppm): 166.87, 166.84, 139.39, 139.24, 127.29, 126.75, 122.84, 122.79, 60.43, 60.41, 50.79, 39.43, 14.27; HRMS-EI (m/z): [M+] calcd for $C_9H_{13}BrO_2$, 232.0099; found, 232.0108.

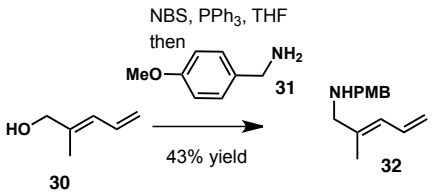


(2*E*,4*E*)-Ethyl 6-((4-methoxybenzyl)amino)-5-methylhexa-2,4-dienoate (19). K_2CO_3 (1.74 g, 12.6 mmol) was added to a mixture of 4-methoxybenzylamine (0.9 mL, 6.60 mmol) and (2*E*,4*E*)-ethyl 6-bromo-5-methylhexa-2,4-dienoate (1.48 g, 6.30 mmol) in dimethylformamide (20.0 mL) at 0 °C. The mixture was warmed to 23 °C and stirred for 2 h. The reaction mixture was diluted with H_2O and extracted with ethyl acetate (3 x 50 mL). The organic layer was washed with H_2O (3 x 20 mL) and brine, dried with sodium sulfate, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (silica, 20% to 30% ethyl acetate – hexanes) to afford **19** (0.960 g, 70%) as a yellow oil. ^1H NMR (600 MHz, $CDCl_3$); δ(ppm): 7.60 (dd, J = 15.2, 11.6 Hz, 1H), 7.23 (d, J = 8.5 Hz, 2H), 6.86 (d, J = 8.5 Hz, 2H), 6.19 (d, J = 11.6 Hz, 1H), 5.84 (d, J = 15.2 Hz, 1H), 4.20 (q, J = 7.1 Hz, 2H), 3.79 (s, 3H), 3.68 (s, 2H), 3.27 (s, 2H), 1.91 (s, 3H), 1.47 (s, 1H), 1.29 (t, J = 7.1 Hz, 3H); ^{13}C NMR (150 MHz, CDCl3); δ(ppm): 167.67, 158.85, 147.47, 140.52, 132.42, 129.45, 123.28, 120.28, 113.97, 60.36, 56.49, 55.43, 52.73,

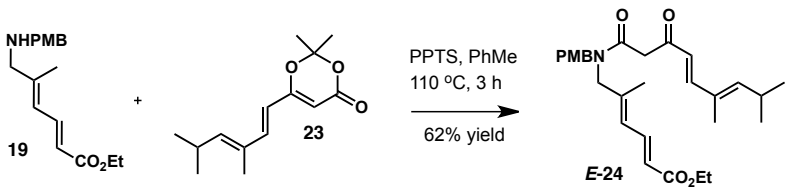
16.31, 14.51; HRMS-ESI (m/z): [M+Na] calcd for $C_{17}H_{23}NO_3Na$, 312.1576; found, 312.1564.



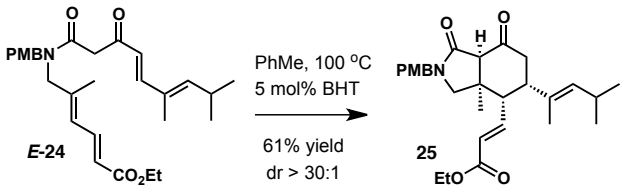
(*Z*)-2-Methylpenta-2,4-dien-1-ol (30). (*Z*)-3-Iodo-2-methylprop-2-en-1-ol 14 was synthesized from propargyl alcohol according to a known procedure.[78] Tetrakis(triphenylphosphine)palladium (0.292 g, 0.250 mmol) was added to a solution of vinyl iodide 13 (2.00 g, 10.0 mmol) in dry, degassed toluene (135.0 mL) at 0 °C. After stirring for 20 min, vinyl magnesium bromide (1.25 M in THF, 24.0 mL, 30.0 mmol) was added dropwise. The reaction mixture was stirred at 0 °C for 1 h and at room temperature for 30 min. The reaction was quenched by adding 20 ml of saturated aqueous ammonium chloride. The aqueous layer was extracted with diethyl ether (3 x 30 mL). The combined organic layers were washed with brine, dried with sodium sulfate, concentrated under reduced presuure at 10 °C, and the residue was purified by column chromatography on silica gel (silica, 30% diethyl ether – hexanes) to afford **30** (0.770 g, 75%) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$); δ (ppm): 6.63 (dt, J = 16.7, 10.6 Hz, 1H), 5.96 (d, J = 11.1 Hz, 1H), 5.17 (d, J = 16.7 Hz, 1H), 5.07 (d, J = 10.2 Hz, 1H), 4.27 (d, J = 5.9 Hz, 2H), 1.89 (s, 3H), 1.24 (s, 1H); ^{13}C NMR (125 MHz, CDCl3); δ (ppm): 137.57, 131.96, 128.37, 116.57, 61.26, 21.34; HRMS-EI (m/z): [M+] calcd for $C_6H_{10}O$, 98.0732; found, 98.0730.



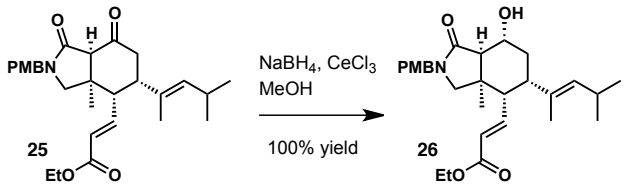
(*Z*)-N-(4-Methoxybenzyl)-2-methylpenta-2,4-dien-1-amine (32). N-Bromo-succimide (1.82 g, 10.2 mmol) was added to a stirred solution of triphenylphosphine (2.67 g, 10.2 mmol) and **30** (0.770 g, 7.80 mmol) in anhydrous THF (20.0 mL) at –10 °C over 2–3 min in small portions under argon. After 20 min, TLC showed a complete consumption of alcohol 14. 4-Methoxybenzylamine (2.0 mL, 15.6 mmol) was injected via a syringe in one portion. The temperature was raised to 23 °C and the mixture was stirred at 23 °C for 12 h. Hexane (10 mL) was added to the reaction mixture and stirred for 0.5 h. to precipitate triphenylphosphine oxide and succinimide. The solid was filtered and washed with 1 N HCl. Then the aqueous layer was neutralized by sodium bicarbonate solution and extracted with diethyl ether (3 x 20 mL). The combined organic layers were dried with anhydrous sodium sulfate and concentrated. The residue was purified by column chromatography on silica gel (silica, 60% ethyl acetate – hexanes) to afford **32** (0.730 g, 43%) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$); δ (ppm): 7.24 (d, J = 8.7 Hz, 2H), 6.87 (d, J = 8.7 Hz, 2H), 6.61 – 6.50 (m, 1H), 6.04 – 5.95 (m, 1H), 5.13 (ddd, J = 16.7, 1.3, 0.6 Hz, 1H), 5.00 (dd, J = 10.2, 1.8 Hz, 1H), 3.80 (s, 3H), 3.67 (s, 2H), 3.35 (s, 2H), 1.87 (s, 3H), 1.54 (bs, 1H); ^{13}C NMR (125 MHz, CDCl3); δ (ppm): 158.61, 137.28, 132.50, 132.42, 129.32, 128.75, 115.86, 113.74, 55.25, 52.43, 49.12, 22.56; HRMS-ESI (m/z): [M+H] calcd for $C_{14}H_{20}NO$, 218.1545; found, 218.1533.



(2*E*,4*E*)-Ethyl 6-((4*E*,6*E*)-*N*-(4-methoxybenzyl)-6,8-dimethyl-3-oxonona-4,6-dien amido)-5-methylhexa-2,4-dienoate (*E*-24). Pyridinium tosylate (4.3 mg, 0.0172 mmol) was added to a solution of 6-((1*E*,3*E*)-3,5-dimethylhexa-1,3-dienyl)-2,2-dimethyl-4*H*-1,3-dioxin-4-one **19** (40.0 mg, 0.172 mmol) and (2*E*,4*E*)-ethyl 6-(4-methoxybenzylamino)-5-methylhexa-2,4-dienoate (50.0 mg, 0.172 mmol) 12 in dry toluene (3.5 mL). The resulting solution was heated to reflux for 2 h. Toluene was evaporated and the crude product was purified by column chromatography (silica, 40% ethyl acetate – hexanes) to give **(*E*)-24** as a white crystalline solid (50.0 mg, 0.106 mmol, 62%). ^{1}H NMR (600 MHz, $CDCl_3$); δ (ppm): 7.56 (ddd, J = 2.4, 11.4, 16.8 Hz, 2H), 7.19 (dd, J = 8.4, 12.5 Hz, 1H), 7.12 – 7.04 (m, 1H), 6.87 (ddd, J = 3.3, 8.5, 20.3 Hz, 2H), 6.18 (d, J = 16.2 Hz, 1H), 6.04 (d, J = 11.6 Hz, 1H), 5.97 (t, J = 13.4, 13.4 Hz, 1H), 5.89 – 5.75 (m, 1H), 5.62 (d, J = 9.3, 1H), 5.30 (s, 1H), 5.04 (s, 1H), 4.53 (d, J = 5.1 Hz, 2H), 4.45 - 4.37 (m, 2H), 4.21 (qd, J = 5.2, 7.1, 7.1, 7.1 Hz, 3H), 4.07 (d, J = 13.3 Hz, 2H), 3.84 – 3.77 (m, 5H), 3.69 (s, 2H), 2.74 – 2.61 (m, 1H), 1.85 (d, J = 6.3 Hz, 3H), 4.45 – 4.37 (m, 3H), 1.33 – 1.23 (m, 3H), 1.04 – 0.97 (m, 6H). HRMS-ESI (m/z): [M+Na] calcd for $C_{28}H_{37}NO_5Na$, 490.2569; found, 490.2552.

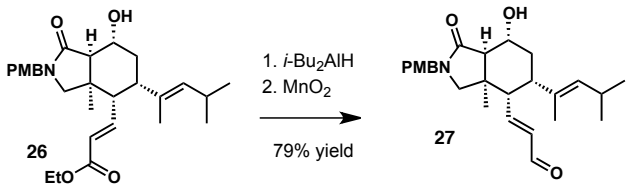


(*E*)-Ethyl 3-((3a*R*,4*S*,5*S*,7a*R*)-2-(4-methoxybenzyl)-3a-methyl-5-((*E*)-4-methyl pent-2-en-2-yl)-1,7-dioxooctahydro-1*H*-isoindol-4-yl)acrylate (25). (2*E*,4*E*)-Ethyl 6-((4*E*,6*E*)-*N*-(4-methoxybenzyl)-6,8-dimethyl-3-oxonona-4,6-dienamido)-5-methyl hexa-2,4-dienoate (***E*-24**) (8.2 mg, 17.5 μmol) and BHT (0.4 mg, 1.70 μmol) were dissolved in dry toluene (0.6 mL) and heated at reflux for 18 h. Toluene was evaporated and the crude product was purified by column chromatography (silica, 50% ethyl acetate – hexanes) to give **25** as a yellowish oil (7.0 mg, 15.0 μmol, 86%). ^{1}H NMR (500 MHz, $CDCl_3$); δ (ppm): 7.15 (t, J = 7.9 Hz, 2H), 6.84 (d, J = 8.5 Hz, 2H), 6.64 (dd, J = 15.3, 11.0 Hz, 1H), 5.62 (d, J = 15.3 Hz, 1H), 4.70 (t, J = 12.6 Hz, 1H), 4.53 (d, J = 14.4 Hz, 1H), 4.28 (d, J = 14.4 Hz, 1H), 4.19 – 4.11 (m, 2H), 3.77 (s, 3H), 3.22 (d, J = 10.2 Hz, 1H), 3.03 (s, 1H), 2.86 (d, J = 10.2 Hz, 1H), 2.55 – 2.48 (m, 2H), 2.46 – 2.30 (m, 3H), 1.46 (s, 3H), 1.24 (t, J = 7.1 Hz, 3H), 1.04 (s, 3H), 0.86 (d, J = 6.6 Hz, 3H), 0.78 (d, J = 6.6 Hz, 3H); ^{13}C NMR (500 MHz, $CDCl_3$) ; δ (ppm): 204.94, 168.38, 165.44, 159.46, 143.21, 135.09, 130.30, 129.88, 127.90, 125.55, 114.36, 62.73, 60.66, 57.39, 55.44, 48.38, 46.36, 43.34, 41.19, 39.35, 27.91, 27.28, 22.94, 22.92, 16.65, 14.42; HRMS-ESI (m/z): [M+Na] calcd for $C_{28}H_{37}NO_5Na$, 490.2569; found, 490.2565.



(*E*)-Ethyl 3-((3a*R*,4*S*,5*S*,7*R*,7a*R*)-7-hydroxy-2-(4-methoxybenzyl)-3a-methyl-5-((*E*)-4-methylpent-2-en-2-yl)-1-oxooctahydro-1*H*-isoindol-4-yl)acrylate (26). Sodium borohydride (8.0 mg, 20.0 μmol) was added to a solution of **25** (10.0 mg,

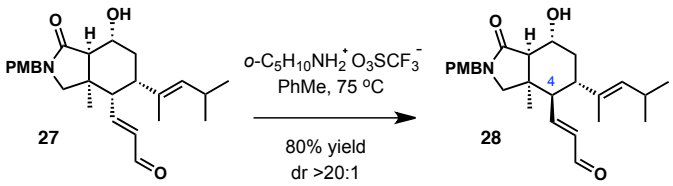
21.0 μmol) and $CeCl_3 \cdot 7H_2O$ (74.0 mg, 20.0 μmol) in dry MeOH (1.5 mL) at -78 °C for 20 min. Ammonium chloride (3 mL) and H_2O (10 mL) were added and the mixture was extracted with ethyl acetate (3 x 15 mL). The organic layers were combined, dried with sodium sulfate, and concentrated. Purification with column chromatography (silica, 60% ethyl acetate – hexanes) gave a yellowish oil **26** (10.0 mg, 21.0 μmol, 100%). ^{1}H NMR (500 MHz, $CDCl_3$); δ (ppm): 7.15 (d, J = 8.4 Hz, 2H), 6.92 (d, J = 8.4 Hz, 2H), 6.67 (dd, J = 15.4, 11.3 Hz, 1H), 5.58 (d, J = 15.4 Hz, 1H), 4.83 (d, J = 9.1 Hz, 1H), 4.44 (d, J = 14.4 Hz, 1H), 4.35 (d, J = 14.4 Hz, 1H), 4.14 (q, J = 7.1 Hz, 2H), 3.80 (s, 3H), 3.59 (td, J = 11.5, 4.6 Hz, 1H), 3.23 (d, J = 9.7 Hz, 1H), 3.04 (s, 1H), 2.68 (d, J = 9.6 Hz, 1H), 2.45 – 2.36 (m, 1H), 2.22 (dd, J = 11.2, 3.8 Hz, 1H), 2.15 (d, J = 12.5 Hz, 1H), 2.08 – 2.00 (m, 1H), 1.85 – 1.73 (m, 1H), 1.62 – 1.53 (m, 1H), 1.49 (s, 3H), 1.24 (t, J = 7.1 Hz, 3H), 0.90 (s, 3H), 0.87 (d, J = 6.6 Hz, 3H), 0.75 (d, J = 6.6 Hz, 3H); ^{13}C NMR (500 MHz, $CDCl_3$) ; δ (ppm): 176.07, 165.77, 159.41, 145.38, 134.36, 131.87, 129.79, 128.25, 123.64, 114.38, 71.68, 60.46, 56.33, 55.85, 55.45, 46.27, 46.03, 42.87, 39.69, 30.72, 27.97, 27.18, 23.07, 22.92, 16.52, 14.46; HRMS-ESI (m/z): [M+Na] calcd for $C_{28}H_{39}NO_5Na$, 492.2726; found, 492.2720.



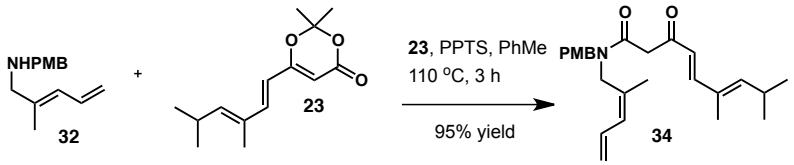
(*E*)-3-((3a*R*,4*S*,5*S*,7*R*,7a*R*)-7-Hydroxy-2-(4-methoxybenzyl)-3a-methyl-5-((*E*)-4-methylpent-2-en-2-yl)-1-oxooctahydro-1*H*-isoindol-4-yl)acrylaldehyde (27). Diiso- butylaluminum hydride (1 M in toluene, 0.2 mL, 0.200 mmol) was added

dropwise to a solution of ester **26** (10.0 mg, 21.0 μmol) in dry dichloromethane (1.0 mL) at -78 °C. After 20 min, a saturated solution of Rochelle's salt (5 mL) was added and then the mixture was diluted with ethyl acetate (20 mL). The mixture was stirred vigorously for 2 h at room temperature. The layers were separated and the aqueous layer was extracted with ethyl acetate (3 x 20 mL). The organic layers were dried with sodium sulfate, concentrated, and the residue was purified by column chromatography on silica gel (silica, 70% to 90% ethyl acetate – hexanes) to afford the expected allylic alcohol (8.0 mg, 80%).

Activated MnO_2 (80.0 mg) was added to a solution of the allylic alcohol in dry dichloromethane (1.5 mL). The mixture was stirred at room temperature for 12 h, and then directly submitted to purification by column chromatography (70% ethyl acetate – hexane) to give pure aldehyde **27** (7.0 mg 88% yield) as an oil. ^{1}H NMR (500 MHz, $CDCl_3$); δ (ppm): 9.45 (d, J = 7.8 Hz, 1H), 7.18 (d, J = 8.6 Hz, 2H), 6.89 (d, J = 8.6 Hz, 2H), 6.56 (dd, J = 15.4, 11.1 Hz, 1H), 5.92 (dd, J = 15.4, 7.8 Hz, 1H), 4.86 (d, J = 9.1 Hz, 1H), 4.47 – 4.43 (d, J = 14.4 Hz, 1H), 4.38 (d, J = 14.4 Hz, 1H), 3.81 (s, 3H), 3.67 – 3.59 (m, 1H), 3.27 (d, J = 9.7 Hz, 1H), 3.01 (s, 1H), 2.73 (d, J = 9.7 Hz, 1H), 2.44 – 2.33 (m, 2H), 2.23 (d, J = 8.0 Hz, 1H), 2.05 (d, J = 9.4 Hz, 1H), 1.91 – 1.85 (m, 1H), 1.49 (d, J = 0.9 Hz, 3H), 0.92 (s, 3H), 0.87 (d, J = 3.1 Hz, 3H), 0.75 (d, J = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$); δ (ppm): 193.02, 175.58, 159.28, 154.32, 134.92, 134.40, 131.43, 129.62, 127.89, 114.24, 71.33, 56.19, 55.98, 55.57, 55.27, 46.33, 45.87, 42.51, 39.45, 29.70, 27.83, 26.98, 22.99, 22.84; HRMS-ESI (m/z): [M+Na] calcd for $C_{26}H_{35}NO_4Na$, 448.2464; found, 448.2462.

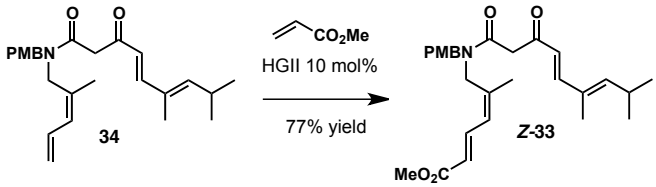


(28). Aldehyde **27** (2.5 mg, 5.80 μmol) was dissolved in dry toluene (1.0 mL) and piperidium trifluoroacetate (1.5 mg, 7.50 μmol) was added. The mixture was heated to 75 °C for 2.5 h, and then finally cooled to 23 °C. The solution was directly applied on a silica column (silica, 60% ethyl acetate – hexanes) to afford product **28** (2.0 mg, 47.0 μmol, 80%). ^{1}H NMR (500 MHz, $CDCl_3$); δ (ppm): 9.38 (d, J = 7.7 Hz, 1H), 7.15 (d, J = 8.6 Hz, 2H), 6.89 (d, J = 8.6 Hz, 2H), 6.23 (dd, J = 15.6, 10.3 Hz, 1H), 6.04 (dd, J = 15.5, 7.6 Hz, 1H), 4.97 (d, J = 9.1 Hz, 1H), 4.46 (d, J = 14.5 Hz, 1H), 4.35 (d, J = 14.4 Hz, 1H), 3.82 (s, 3H), 3.59 (dd, J = 13.9, 7.1 Hz, 1H), 3.28 (d, J = 9.5 Hz, 1H), 3.06 (s, 1H), 2.59 (d, J = 9.6 Hz, 1H), 2.39 (m, 1H), 2.28 (t, J = 10.9 Hz, 1H), 2.07 – 1.94 (m, 2H), 1.89 (d, J = 11.2 Hz, 1H), 1.44 (d, J = 1.1 Hz, 3H), 1.08 (s, 3H), 0.87 (d, J = 6.6 Hz, 3H), 0.77 (d, J = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$); δ (ppm): 192.77, 175.36, 159.28, 155.66, 135.95, 135.57, 131.87, 129.47, 127.87, 114.28, 70.10, 57.98, 55.28, 52.27, 49.82, 46.28, 45.94, 39.86, 35.96, 28.32, 26.70, 22.98, 22.75, 12.19; HRMS-ESI (m/z): [M+Na] calcd for $C_{26}H_{35}NO_4Na$, 448.2464; found, 448.2447.



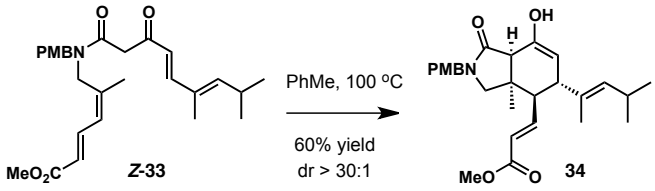
(4*E*,6*E*)-*N*-(4-Methoxybenzyl)-6,8-dimethyl-*N*-((*Z*)-2-methylpenta-2,4-dien-1-yl)-3-oxonona-4,6-dienamide (34). Pyridinium p-toluenesulfonate (35.0 mg, 0.138

mmol) was added to a solution of dioxinone **23** (0.326 g, 1.38 mmol) and amine **32** (0.300 g, 1.38 mmol) in toluene (25.0 mL), and the mixture was stirred and heated at reflux for 3 h. After cooling, the mixture was concentrated and the resultant red oil was purified by silica gel flash chromatography (silica, 20% ethyl acetate – hexanes) yielding the title compound **34** as a yellow oil (0.520 g, 95%). ^{1}H NMR (500 MHz, $CDCl_3$); δ (ppm): 7.30 – 7.15 (m, 1H), 7.10 – 7.03 (m, 2H), 6.88 – 6.80 (m, 2H), 6.46 – 6.14 (m, 1H), 6.07 – 6.00 (m, 1H), 5.83 – 5.73 (m, 1H), 5.59 (d, J = 10.0, 1H), 5.28 (d, J = 15.2, 1H), 5.22 – 4.90 (m, 2H), 4.48 (d, J = 3.5, 2H), 4.32 (s, 2H), 4.20 (d, J = 2.2, 2H), 3.97 – 9.92 (d, J = 7.0, 2H), 3.80 – 3.75 (m, 5H), 2.74 – 2.60 (m, 1H), 1.79 – 1.75 (m, 3H), 1.73 (d, J = 8.2, 3H), 1.03 – 0.95 (m, 6H). HRMS-ESI (m/z): [M+Na] calcd for $C_{25}H_{33}NO_3Na$, 418.2358; found, 418.2343.

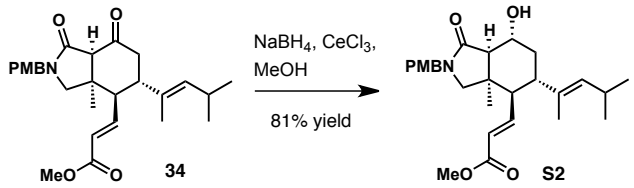


(2*E*,4*Z*)-Methyl 6-((4*E*,6*E*)-*N*-(4-methoxybenzyl)-6,8-dimethyl-3-oxonona-4,6-dienamido)-5-methylhexa-2,4-dienoate (*Z*-33). Alkene **34** (0.520 g, 1.31 mmol) and methyl acrylate (35.0 μL, 3.94 mmol) were dissolved in dichloromethane (35.0 mL), and Hoveyda-Grubbs second generation catalyst (20.0 mg, 33.0 μmol) was added in one portion. The reaction was stirred at 45 °C for 3 h and then concentrated. The residue was purified by column chromatography (silica, 20% to 30% ethyl acetate – hexanes) to give the desired product **(*Z*)-33** (0.480 g, 81%) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$); δ (ppm): 7.61 – 7.38 (m, 1H), 7.38 – 7.31 (m, 1H), 7.30 – 7.20 (m, 2H), 7.09 – 6.94 (m, 2H), 6.33 – 6.27 (m, 1H), 6.03 – 5.92 (m, 1H), 5.78 (d,

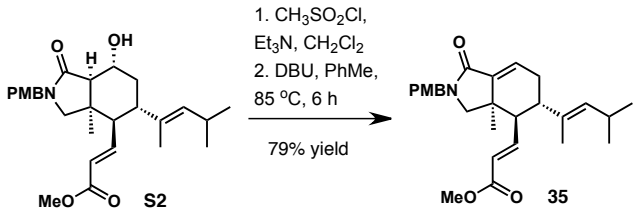
J = 9.4 Hz, 1H), 5.53 (s, 1H), 5.52 – 5.42 (m, 1H), 4.66 (d, J = 10.2 Hz, 2H), 4.49 (d, J = 3.57 Hz, 2H), 4.45 (d, J = 4.8 Hz, 2H) 4.22 (d, J = 9.61 Hz, 2H), 4.00 (s, 2H), 3.96 (dt, J = 4.3, 4.3, 8.1 Hz, 3H), 3.90 (s, 2H), 3.88 – 3.83 (m, 3H), 2.93 – 2.77 (m, 1H), 2.05 (s, 3H), 2.01 – 1.98 (d, J = 6.9 Hz, 3H), 1.97 – 1.91 (M, 3H), 1.17 (dd, J = 6.5, 10.5 Hz, 6H). HRMS-ESI (m/z): [M+Na] calcd for $C_{27}H_{35}NO_5Na$, 476.2413; found, 476.2403.



(*E*)-Ethyl 3-((3a*R*,4*R*,5*S*,7a*R*)-2-(4-methoxybenzyl)-3a-methyl-5-((*E*)-4-methyl pent-2-en-2-yl)-1,7-dioxooctahydro-1*H*-isoindol-4-yl)acrylate (34). A solution of ***Z*-33** (24.0 mg, 53.0 μmol) in toluene (1.8 mL) was heated at reflux for 18 h. After cooling, the mixture was concentrated and the resultant red oil was purified by silica gel flash chromatography (silica, 20% to 60% ethyl acetate – hexanes) yielding the title compound **34** as a yellow oil (14.4 mg, 60%). ^{1}H NMR (500 MHz, $CDCl_3$); δ (ppm): 7.15 (d, J = 8.6 Hz, 2H), 6.85 (d, J = 8.6 Hz, 2H), 6.36 (dd, J = 15.5, 9.8 Hz, 1H), 5.79 (d, J = 15.5 Hz, 1H), 4.95 (dd, J = 9.2, 1.0 Hz, 1H), 4.47 (d, J = 14.5 Hz, 1H), 4.34 (d, J = 14.7 Hz, 1H), 3.79 (s, 3H), 3.68 (s, 3H), 3.30 (d, J = 10.2 Hz, 1H), 2.97 (s, 1H), 2.62 (d, J = 10.2 Hz, 1H), 2.52 – 2.28 (m, 5H), 1.43 (d, J = 1.0 Hz, 3H), 1.15 (s, 3H), 0.85 (d, J = 6.6 Hz, 3H), 0.77 (d, J = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$); δ (ppm): 204.46, 168.56, 165.76, 159.21, 145.37, 137.07, 130.17, 129.53, 127.77, 124.57, 114.20, 63.88, 55.23, 52.19, 51.57, 49.53, 47.71, 46.10, 44.66, 42.75, 28.10, 26.78, 22.59, 22.57, 11.66; HRMS-ESI (m/z): [M+Na] calcd for $C_{27}H_{35}NO_5Na$, 476.2413; found, 476.2405.



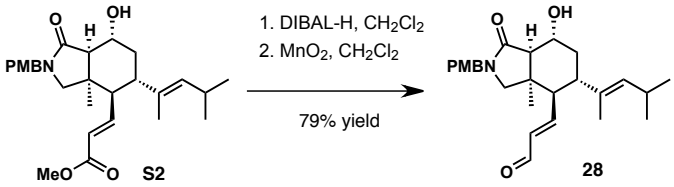
(*E*)-Ethyl 3-((3a*R*,4*R*,5*S*,7*R*,7a*R*)-7-hydroxy-2-(4-methoxybenzyl)-3a-methyl-5-((*E*)-4-methylpent-2-en-2-yl)-1-oxooctahydro-1*H*-isoindol-4-yl)acrylate (S2). Sodium borohydride (15.0 mg, 0.400 mmol) was added to a stirred solution of cerium(III) chloride heptahydrate (61.0 mg, 0.160 mmol) and **34** (37.0 mg, 81.0 μmol) in anhydrous methanol (4.0 mL) at –78 °C. After 40 min, saturated aqueous ammonium chloride (4 mL) was added. The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layers were washed with brine, dried with sodium sulfate, concentrated, and the residue was purified by column chromatography on silica gel (silica, 50% to 70% ethyl acetate – hexanes) to afford the desired alcohol **S2** (30.0 mg, 81%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$); δ (ppm): 7.14 (d, J = 8.6 Hz, 2H), 6.87 (d, J = 8.6 Hz, 2H), 6.34 (dd, J = 15.5, 10.5 Hz, 1H), 5.72 (d, J = 15.5 Hz, 1H), 4.93 (dd, J = 9.1, 1.1 Hz, 1H), 4.42 (d, J = 14.5 Hz, 1H), 4.33 (d, J = 14.4 Hz, 1H), 3.81 (s, 3H), 3.67 (s, 3H), 3.56 (ddd, J = 11.5, 9.7, 4.2 Hz, 1H), 3.24 (d, J = 9.8 Hz, 1H), 3.12 (s, 1H), 2.59 (d, J = 9.8 Hz, 1H), 2.43 – 2.34 (m, 1H), 2.10 (t, J = 11.0 Hz, 1H), 1.97 (m, 2H), 1.85 (ddd, J = 12.4, 4.0, 2.6 Hz, 1H), 1.42 (d, J = 1.1 Hz, 3H), 1.05 (s, 3H), 0.86 (d, J = 6.6 Hz, 3H), 0.76 (d, J = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$); δ (ppm): 175.52, 166.07, 159.21, 147.05, 135.66, 131.94, 129.50, 127.99, 123.84, 114.24, 70.14, 58.05, 55.25, 52.37, 51.46, 49.56, 46.13, 45.91, 39.73, 36.05, 28.23, 26.68, 22.77, 22.72, 12.30; HRMS-ESI (m/z): [M+Na] calcd for $C_{27}H_{37}NO_5Na$, 478.2569; found, 478.2548.



(*E*)-Ethyl 3-((3a*R*,4*R*,5*S*)-2-(4-methoxybenzyl)-3a-methyl-5-((*E*)-4-methylpent-2-en-2-yl)-1-oxo-2,3,3a,4,5,6-hexahydro-1*H*-isoindol-4-yl)acrylate (35). Methane sulfonyl chloride (25.0 μL, 0.330 mmol) was added to the solution of alcohol **S2** (30.0 mg, 66.0 μmol) and triethylamine (92.0 μL, 0.660 mmol) in dichloromethane (5.0 mL) at 0 °C. The mixture was stirred at 0 °C for 30 min. The reaction mixture was poured into a saturated aqueous solution of sodium bicarbonate and extracted with ethyl acetate. The combined organic leyers were washed with 1 M HCl, brine, dried over sodium sulfate, and filtered. The filtrate was concentrated under reduced pressure, and the residue was used directly in the next step.

The residue was dissolved in toluene (4.0 mL) and treated with 1,8-diazabicyclo(5.4.0)-undec-7-ene (93.0 μL, 0.660 mmol) at 25 °C. The reaction mixture was stirred at 80 °C for 6 h and then poured into a mixture of 1 M HCl and ethyl acetate. The organic layer was separated and washed with saturated aqueous solution of sodium bicarbonate, brine, then dried over sodium sulfate, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography on silica gel (silica, 30% ethyl acetate – hexanes) to afford **35** (23.0 mg, 79%) as an oil. ^{1}H NMR (500 MHz, $CDCl_3$); δ (ppm): 7.14 (d, J = 8.6 Hz, 2H), 6.84 (d, J = 8.7 Hz, 2H), 6.74 (dd, J = 5.7, 4.7 Hz, 1H), 6.56 (dd, J = 15.5, 10.3 Hz, 1H), 5.77 (d, J = 15.5 Hz, 1H), 4.99 (d, J = 9.2 Hz, 1H), 4.63 (d, J = 14.6 Hz, 1H), 4.17 (d, J = 14.6 Hz, 1H), 3.79 (s, 3H), 3.69 (s, 3H), 3.09 (d, J = 9.2 Hz, 1H), 2.55 (d, J = 9.2 Hz, 1H), 2.46 –

2.41 (m, 1H), 2.38 (d, J = 10.7 Hz, 1H), 2.20 – 2.13 (m, 2H), 1.96 (ddd, J = 10.7, 8.9, 5.7 Hz, 1H), 1.48 (d, J = 1.2 Hz, 3H), 1.14 (s, 3H), 0.88 (d, J = 6.6 Hz, 3H), 0.81 (d, J = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$); δ (ppm): 167.18, 166.21, 159.05, 148.05, 140.17, 135.89, 132.03, 129.52, 129.35, 128.40, 122.55, 114.07, 55.24, 53.83, 51.48, 49.84, 49.51, 46.06, 41.53, 29.28, 28.35, 26.84, 22.86, 22.72, 12.79; HRMS-ESI (m/z): [M+Na] calcd for $C_{27}H_{35}NO_4Na$, 460.2464; found, 460.2442.

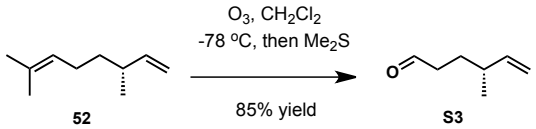


(*E*)-3-((3a*R*,4*R*,5*S*,7*R*,7a*R*)-7-Hydroxy-2-(4-methoxybenzyl)-3a-methyl-5-((*E*)-4-methylpent-2-en-2-yl)-1-oxooctahydro-1*H*-isoindol-4-yl)acrylaldehyde (28).

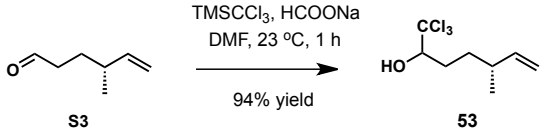
Diisobutylaluminum hydride (1 M in toluene, 0.2 mL, 0.200 mmol) was added dropwise to a solution of ester **S2** (4.0 mg, 8.80 μmol) in dry dichloromethane (1.0 mL) at -78 °C. After 20 min, a saturated solution of Rochelle's salt (5 mL) was added and then the mixture was diluted with ethyl acetate (20 mL). The mixture was stirred vigorously for 2 h at room temperature. The layers were separated and the aqueous layer was extracted with ethyl acetate (3 x 5 mL). The organic layers were dried with sodium sulfate, concentrated, and the residue was purified by column chromatography on silica gel (silica, 70% to 90% ethyl acetate – hexanes) to afford the expected allylic alcohol (4.0 mg, 99%).

Activated MnO_2 (40.0 mg) was added to a solution of the allylic alcohol in dry dichloromethane (1.0 mL). The mixture was stirred at room temperature for 12 h, and then directly submitted to purification by column chromatography (100% ethyl

acetate) to give pure aldehyde **28** as an oil (4.0 mg 95% yield). The ^{1}H and ^{13}C NMR data were identical to the material prepared previously for substrate **28**.

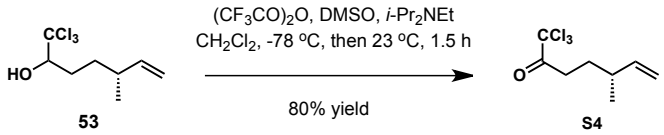


(*R*)-4-Methylhex-5-enal (S3). (*R*)-3,7-Dimethylocta-1,6-diene was prepared according to a described synthetic procedure.[79] Ozone was bubbled through a solution of citronellene **52** (3.00 g, 21.7 mmol) in CH_2Cl_2 (80 mL) at -78 °C for 3 h. The reaction was monitored by TLC, and once the starting material was consumed, dimethylsulfide (4.0 mL, 54.2 mmol) was added and the mixture was stirred at -30 °C for 1 h. The solution was warmed to 0 °C and fractionated directly by distillation at ~200 mm Hg to isolate pure product **S3** (2.06 g, 18.4 mmol, 85% yield), which was collected as the last fraction. $[\alpha]_D^{23}$ -6.7° (*c* 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 9.77 (t, *J*=1.7 Hz, 1H), 5.63 (ddd, *J*=17.1, 10.4, 7.8 Hz, 1H), 5.01-4.95 (m, 2H), 2.43 (dddd, *J*=8.4, 7.0, 3.0, 1.7 Hz, 2H), 2.15 (dddd, *J*=12.4, 8.1, 5.7, 1.2 Hz, 1H), 1.74-1.55 (m, 2H), 1.03 (d, *J*=6.7 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 202.5, 143.2, 113.7, 41.7, 37.4, 28.4, 20.1. HRMS-ESI (*m*/z): $[M+Na]^+$ calcd for $C_7H_{12}ONa$, 135.0786; found, 135.0789.



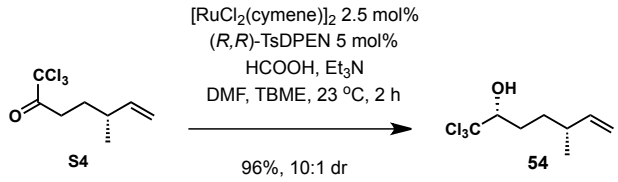
(5*R*)-1,1,1-Trichloro-5-methylhept-6-en-2-ol (53). Sodium formate (0.260 g, 3.87 mmol) and Me_3SiCCl_3 (11.1 g, 58.0 mmol) were added to a solution of (4*R*)-4-methylhex-5-enal **S3** (4.30 g, 38.7 mmol) in dry DMF (86 mL) at 23 °C and the

mixture was stirred for 1 h. A mixture of methanol and 1 M aqueous HCl (8 mL, 1:1, v/v) was added and the reaction mixture was stirred at 23 °C for 1 h. Water (10 mL) was added, the aqueous layer was separated and extracted with diethyl ether (4×10 mL). The combined organic phase was washed with brine and dried over Na_2SO_4, concentrated and the crude product was purified by column chromatography on silica gel (10% diethyl ether in pentanes) to afford the alcohol **53** (8.42 g, 36.4 mmol, 94% yield). $[\alpha]_D^{23}$ -2.2° (*c* 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 5.70 (dddd, *J*=17.4, 13.8, 10.3, 7.7 Hz, 1H), 5.08-4.89 (m, 2H), 4.06-3.94 (m, 1H), 2.64 (ddd, *J*=14.6, 5.7, 1.5 Hz, 1H), 2.26-2.15 (m, 1H), 2.14-2.01 (m, 1H), 1.74-1.55 (m, 2H), 1.52-1.41 (m, 1H), 1.05-1.03 (m, 3H): ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 143.9, 143.6, 113.5, 113.2, 104.9, 104.2, 83.2, 82.9, 37.6, 37.5, 32.9, 32.7, 29.4, 29.2, 20.4, 20.0. HRMS-ESI (*m*/z): $[M-H]^-$ calcd for $C_8H_{12}Cl_3O$, 228.9954; found, 228.9952.



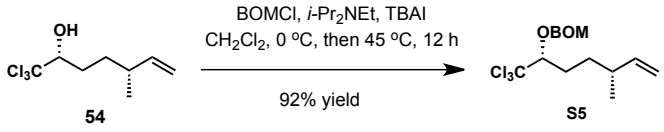
(*R*)-1,1,1-Trichloro-5-methylhept-6-en-2-one (S4). Trifluoroacetic anhydride (5.5 mL, 38.8 mmol) in CH_2Cl_2 (30 mL) was added to a solution of dimethyl sulfoxide (3.3 mL, 46.6 mmol) in CH_2Cl_2 (30 mL) dropwise at -78 °C over 5 min. The mixture was stirred at -78 °C for 10 min. A solution of (5*R*)-1,1,1-trichloro-5-methylhept-6-en-2-ol **53** (3.60 g, 15.5 mmol) in CH_2Cl_2 (15 mL) was added dropwise over 10 min at -78 °C and stirred for an additional 5 min. The reaction mixture was warmed to 23 °C and stirred for another 1 h. The solution was cooled to 0 °C and *i*-Pr_2NEt (13.5 mL, 77.7 mmol) was added dropwise. The mixture was warmed to 23 °C for 1 h. The solution was diluted with diethyl ether (4 mL) and washed with 1 M

HCl, and saturated aqueous $NaHCO_3$. The aqueous layers were extracted with diethyl ether (3x4 mL). The combined organic layer was washed with brine, dried over Na_2SO_4, concentrated under atmospheric conditions and purified by column chromatography on silica gel (10% diethyl ether in pentanes) to deliver trichloromethyl ketone **S4** (2.85 g, 12.4 mmol, 80% yield). $[\alpha]_D^{23}$ -3.6° (*c* 1.0, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ (ppm) 5.65 (ddd, *J*=17.2, 10.3, 7.9 Hz, 1H), 5.10-4.93 (m, 2H), 3.09-2.89 (m, 2H), 2.20 (p, *J*=7.0 Hz, 1H), 1.90-1.63 (m, 2H), 1.06 (d, *J*=6.7 Hz, 2H): ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 190.8, 142.9, 114.2, 37.5, 31.8, 31.2, 29.6, 20.2.



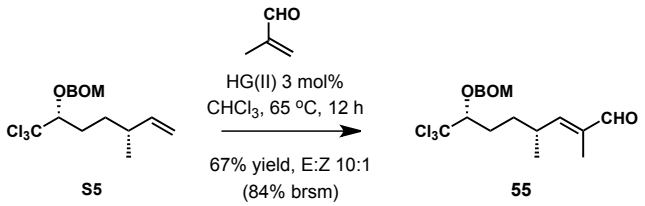
(2*R*,5*R*)-1,1,1-trichloro-5-methylhept-6-en-2-ol (54). Dichloro(*p*-cymene) ruthenium(II) dimer (0.150 g, 0.246 mmol) and Et_3N (69 μL, 0.492 mmol) were added to a solution of (1*R*,2*R*)-*N*-*p*-tosyl-1,2-diphenylethylenediamine (0.180 g, 0.492 mmol) in DMF (5.0 mL) at 23 °C and the mixture was stirred for 1 h. In parallel, formic acid (1.2 mL, 49.2 mmol) and Et_3N (2.7 mL, 19.7 mmol) were stirred at 23 °C for 10 min. A solution of substrate **S4** (2.26 g, 9.84 mmol) in *tert*-butyl methyl ether (20 mL) was added to the formic acid-triethylamine mixture, followed by the solution of the catalyst. After stirring at 23 °C for 3 h, water (20 mL) was added. The layers were separated and the aqueous phase was extracted with ethyl acetate (3x10 mL). The combined organic phase was washed with brine, dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on

silica gel (20% diethyl ether in pentanes) to afford the alcohol **54** (2.20 g, 9.44 mmol, 96% yield, dr 10:1). $[\alpha]_D^{23}$ +25.3° (*c* 1.0, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ (ppm) 5.71 (ddd, *J*=17.1, 10.3, 7.6 Hz, 1H), 5.02-4.95 (m, 2H), 3.99 (ddd, *J*=9.6, 5.6, 1.9 Hz, 1H), 2.21-2.17 (m, 1H), 2.11-2.02 (m, 2H), 1.69-1.56 (m, 2H), 1.51-1.39 (m, 1H), 1.04 (dd, *J*=6.8 Hz, 3H): ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 143.9, 113.2, 104.2, 83.2, 37.6, 32.9, 29.4, 20.1.

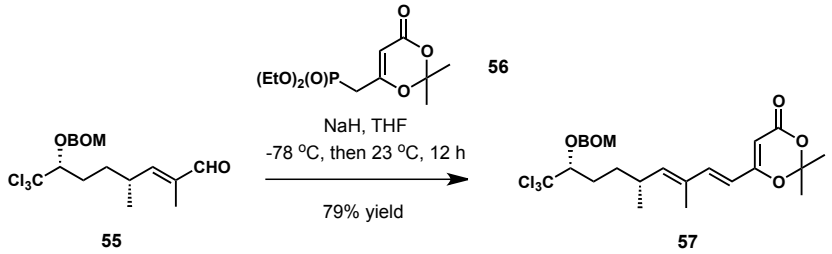


((((2*R*,5*R*)-1,1,1-Trichloro-5-methylhept-6-en-2-yl)oxy)methoxy)benzene (S5). Diisopropyl-ethylamine (13.8 mL, 79.0 mmol) was added to a solution of (2*R*,5*R*)-1,1,1-trichloro-5-methylhept-6-en-2-ol **54** (3.02 g, 13.2 mmol), benzyloxymethyl chloride (7.2 mL, 52.1 mmol), and tetrabutylammonium iodide (0.48 g, 1.30 mmol) in CH_2Cl_2 (13.0 mL) at 0 °C and the mixture was stirred for 15 min. The solution was then heated at 45 °C for 12 h. The crude mixture was cooled to 23 °C, water (13 mL) was added, and the resulting mixture was extracted with CH_2Cl_2 (3x15 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (10% ethyl acetate in hexanes) to afford **S5** (2.20 g, 9.44 mmol, 96% yield, dr 10:1). $[\alpha]_D^{23}$ +82.1° (*c* 1.0, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.37-7.36 (m, 4H), 7.33-7.31 (m, 1H), 5.72-5.64 (m, 1 H), 5.13-5.11 (m, 1H), 5.04-4.94 (m, 3H), 4.83 (d, *J*=11.9 Hz, 1H), 4.65 (d, 11.3 Hz, 1H), 4.00 (d, 8.5 Hz, 1H), 2.19-2.10 (m, 2H), 1.82-1.75 (m, 1H), 1.73-1.65 (m, 1H), 1.01 (d, *J*=6.7 Hz, 3H): ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 143.9, 137.3, 128.4, 127.8, 127.7, 113.2, 102.7, 97.1, 89.7, 70.6,

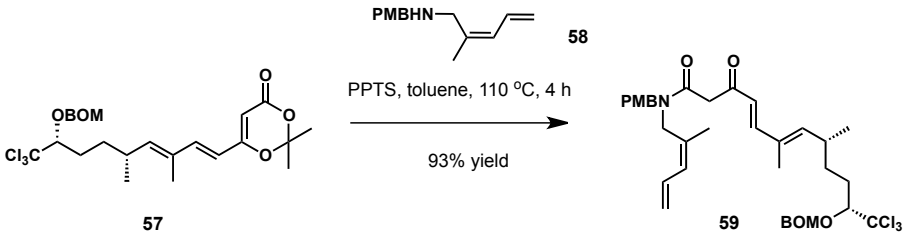
37.8, 32.8, 30.1, 20.4. HRMS-ESI (*m*/z): $[M+Na]^+$ calcd for $C_{16}H_{21}Cl_3O_2Na$, 373.0505; found, 373.0509.



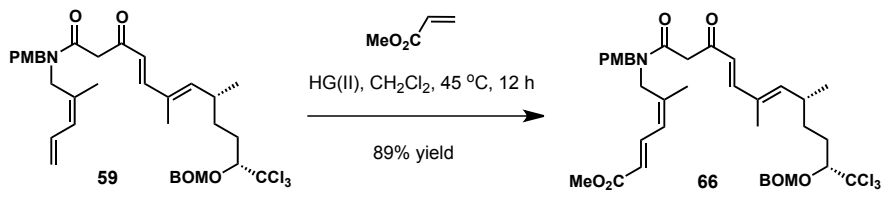
(4*R*,7*R*,*E*)-7-((Benzyloxy)methoxy)-8,8,8-trichloro-2,4-dimethyloct-2-enal (55). Hoveyda-Grubbs II catalyst (1,3-bis-(2,4,6,-trimethylphenyl)-2-imidazol idinylidene)-dichloro (*o*-isopropoxyphenylmethylene)ruthenium (28 mg, 44.3 μmol) was added to a degassed solution of **S5** (0.520 g, 1.48 mmol) and metacrolein (2.3 mL, 28.1 mmol) in CH_2Cl_2 (19.0 mL). The solution was heated at 65 °C for 10 h. The crude mixture was concentrated and immediately purified by column chromatography on silica gel (30% ethyl acetate in hexanes) to afford aldehyde **55** (0.390 g, 0.991 mmol, 67% yield, *E*:*Z* 10:1), along with recovered starting material (90 mg, 0.256 mmol, 17% yield). $[\alpha]_D^{23}$ +88.6° (*c* 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.37-7.36 (m, 4H), 7.33-7.31 (m, 1H), 5.72-5.64 (m, 1 H), 5.13-5.11 (m, 1H), 5.04-4.94 (m, 3H), 4.83 (d, *J*=11.9 Hz, 1H), 4.65 (d, 11.3 Hz, 1H), 4.00 (d, 8.5 Hz, 1H), 2.19-2.10 (m, 2H), 1.82-1.75 (m, 1H), 1.73-1.65 (m, 1H), 1.01 (d, *J*=6.7 Hz, 3H): ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 195.3, 158.9, 138.3, 137.1, 128.4, 127.9, 127.5, 102.3, 97.2, 89.5, 70.5, 33.4, 32.6, 30.0, 19.4, 9.3.



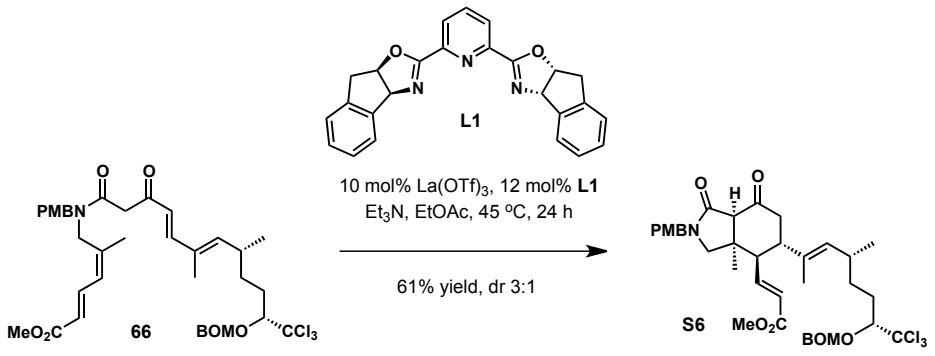
6-((1*E*,3*E*,5*R*,8*R*)-8-((Benzyloxy)methoxy)-9,9,9-trichloro-3,5-dimethylnona-1,3-dien-1-yl)-2,2-dimethyl-4*H*-1,3-dioxin-4-one (57). A solution of diethyl ((2,2-dimethyl-4-oxo-4*H*-1,3-dioxin-6-yl)methyl)phosphonate **56** (5.07 g, 18.1 mmol) in THF (40 mL) was added to a suspension of sodium hydride (60% in mineral oil, 0.673 g, 16.8 mmol) in THF (80 mL) at 0 °C. After stirring at 0 °C for 30 min, the mixture was warmed to 23 °C and stirred for an additional 30 min. This mixture was added via cannula into a solution of (4*R*,7*R*,*E*)-7-((benzyloxy)methoxy)-8,8,8-trichloro-2,4-dimethyloct-2-enal **55** (5.1 g, 13.0 mmol) in THF (140 mL) at -78 °C over 15 min. This solution was stirred at -78 °C for 30 min and then warmed to 23 °C and stirred for an additional 12 h. Brine (200 mL) was added, layers separated, and the aqueous layer was extracted with ethyl acetate (3x50 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (30% ethyl acetate in hexanes) to afford dioxinone **57** (5.3 g, 10.2 mmol, 79% yield) as the only isomer. $[\alpha]_D^{23}$ +34.3° (*c* 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.37-7.28 (m, 5H), 6.92 (d, *J*=15.6 Hz, 1H), 5.88 (d, *J*=9.8 Hz, 1H), 5.31 (s, 1H), 5.10 (d, *J*=7.2 Hz, 1H), 5.01 (d, *J*=7.3 Hz, 1H), 4.81 (d, *J*=11.8 Hz), 4.62 (d, *J*=11.8 Hz, 1H), 3.97 (dd, *J*=8.4, 2.3 Hz, 1H), 2.56 (m, 1H), 2.08-1.99 (m, 1H), 1.78 (d, *J*=1.2 Hz, 3H), 1.72 (d, *J*=4.4 Hz, 6H), 1.51-1.41 (m, 1H), 0.98 (d, *J*=6.6 Hz, 3H): ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 163.9, 162.0, 146.6, 142.8, 137.2, 132.1, 128.4, 127.8, 128.6, 117.6, 106.1, 102.5, 97.2, 93.9, 89.6, 70.6, 33.3, 33.2, 30.1, 25.1, 25.0, 20.2, 12.3. HRMS-ESI (*m*/z): $[M+Na]^+$ calcd for $C_{25}H_{31}Cl_3O_5Na$, 539.1135; found, 539.1131.



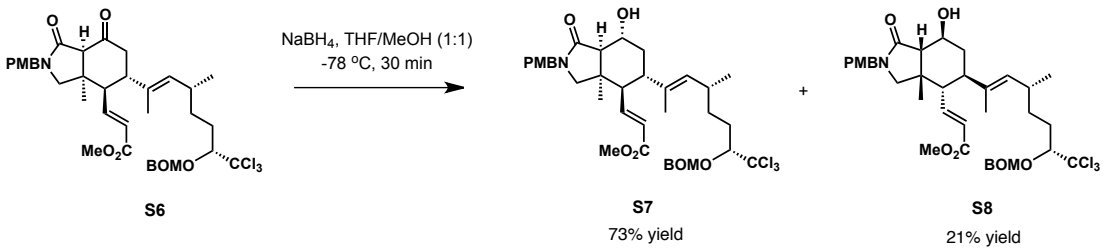
(4*E*,6*E*,8*R*,11*R*)-11-((Benzyloxy)methoxy)-12,12,12-trichloro-*N*-(4-methoxy benzyl)-6,8-dimethyl-*N*-((*Z*)-2-methylpenta-2,4-dien-1-yl)-3-oxododeca-4,6-dienamide (59). Pyridinium *p*-toluenesulfonate (43 mg, 0.343 mmol) was added to a stirring solution of amine **58** (0.812 g, 3.43 mmol) and dioxinone **57** (1.78 g, 3.43 mmol) in toluene (68 mL) in a sealed flask and heated at 110 °C for 4 h. The crude mixture was allowed to cool to room temperature and concentrated. The residue was purified by column chromatography on silica gel (20% ethyl acetate in hexanes) to afford the amide **59** (2.17 g, 3.19 mmol, 93% yield), which exists as a mixture of rotamers and tautomers as observed by NMR. ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.35 (dd, *J*=5.3, 3.1 Hz, 4H), 7.32-7.30 (m, 2H), 7.20 (dd, *J*=8.4, 4.4 Hz, 2H), 7.14-7.04 (m, 2H), 6.91-6.82 (m, 2H), 6.47-6.17 (m, 1H), 6.11-6.03 (m, 1H), 5.87-5.65 (m, 1H), 5.53 (d, *J*=9.8 Hz, 1H), 5.29 (d, *J*=15.3 Hz, 1H), 5.18 (dd, *J*=26.6, 17.3 Hz, 1H), 5.10 (dd, *J*=7.4, 1.8 Hz, 1H), 5.04-4.99 (m, 2H), 4.81 (dd, *J*=11.8, 2.0 Hz, 1H), 4.63 (dd, *J*=11.8, 1.9 Hz, 1H), 4.52 (s, 1H), 4.34 (s, 1H), 4.22 (d, *J*=6.1 Hz, 1H), 4.01-3.94 (m, 2H), 3.84-3.75 (m, 3H), 2.54 (tq, *J*=14.6, 7.1 Hz, 1H), 2.12-1.99 (m, 1H), 1.80-1.72 (m, 6H), 1.53-1.40 (m, 2H), 0.97 (td, *J*=7.7, 6.4, 4.7 Hz, 3H).



(2*E*,4*Z*)-Methyl 6-((4*E*,6*E*,8*R*,11*R*)-11-((benzyloxy)methoxy)-12,12,12-trichloro-*N*-(4-methoxy-benzyl)-6,8-dimethyl-3-oxododeca-4,6-dienamido)-5-methylhexa-2,4-dienoate (66). Hoveyda Grubbs II catalyst (0.102 g, 0.162 mmol) was added to a stirring degassed solution of methyl acrylate (1.2 mL, 13.0 mmol) and substrate **59** (2.2 g, 3.25 mmol) in CH_2Cl_2 (108 mL). The resulting solution was heated at 45 °C for 14 h. The crude mixture was cooled to room temperature and immediately concentrated. The residue was purified by column chromatography on silica gel (20% ethyl acetate in hexanes) to afford the amide **66** as a mixture of rotamers and tautomers (2.12 g, 2.88 mmol, 89% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.37-7.29 (m, 5H), 7.23-7.05 (m, 3H), 6.87 (dd, *J*=12.8, 8.4 Hz, 2H), 6.25-6.11 (m, 1H), 5.94-5.70 (m, 2H), 5.53 (d, *J*=9.8 Hz, 1H), 5.34 (s, 1H), 5.10 (d, *J*=7.2 Hz, 1H), 5.01 (d, *J*=7.2 Hz, 1H), 4.81 (d, *J*=11.9 Hz, 1H), 4.63 (d, *J*=11.9 Hz, 1H), 4.52 (s, 1H), 4.38-4.22 (m, 3H), 4.06 (d, *J*=6.5 Hz, 1H), 4.00-3.96 (m, 1H), 3.81 (d, *J*=3.0 Hz, 4H), 3.78-3.68 (m, 3H), 2.53 (dq, *J*=15.1, 7.8 Hz, 1H), 2.11-1.99 (m, 1H), 1.91-1.81 (m, 3H), 1.79-1.71 (m, 6H), 1.44 (ddd, *J*=14.9, 10.2, 6.2 Hz, 1H), 0.97 (dd, *J*=6.6, 4.7 Hz, 3H): HRMS-ESI (*m*/z): $[M+Na]^+$ calcd for $C_{38}H_{46}Cl_3NO_7Na$, 756.2238; found, 756.2257.

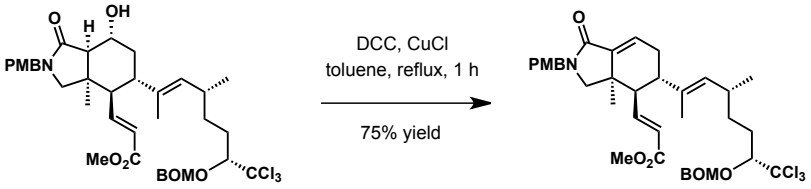


(*E*)-Methyl 3-((3a*R*,4*R*,5*S*)-5-((4*R*,7*R*,*E*)-7-((benzyloxy)methoxy)-8,8,8-trichloro-4-methyl-oct-2-en-2-yl)-2-(4-methoxybenzyl)-3a-methyl-1,7-dioxo octahydro-1*H*-isoindol-4-yl) acrylate (S6). Lanthanum(III) triflate (0.191 g, 0.325 mmol) was added to a solution of 2,6-bis((3a*S*,8a*R*)-8,8a-dihydro-3a*H*-indeno[1,2-*d*]oxazol-2-yl)pyridine **L1** (0.154 g, 0.390 mmol) in ethyl acetate (20 mL). After stirring at 23 °C for 1 h, the catalyst was added to **66** (2.39 g, 3.25 mmol) in ethyl acetate (88 mL). The resulting solution was capped and heated at 45 °C for 24 h. The reaction mixture was cooled, concentrated, and the residue was purified by chromatography on silica gel (80% ethyl acetate in hexanes) to afford product **S6** (1.45 g, 1.98 mmol, 61% yield, 3:1 dr). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.37-7.31 (m, 5H), 7.17 (dd, *J*=8.8, 2.2 Hz, 2H), 6.89-6.85 (m, 2H), 6.46-6.30 (m, 1H), 5.80 (dd, *J*=15.6, 1.7 Hz, 1H), 5.08 (d, *J*=7.2 Hz, 1H), 4.98 (dd, *J*=12.7, 7.2 Hz, 1H), 4.89 (ddd, *J*=19.3, 9.4, 1.6 Hz, 1H), 4.77 (t, *J*=11.4, 1H), 4.63 (t, *J*=11.2 Hz, 1H), 4.48 (d, *J*=14.6 Hz, 1H), 4.35 (dd, *J*=14.6, 2.4 Hz, 1H), 3.92 (ddd, *J*=10.1, 8.4, 2.4 Hz, 1H), 3.79 (d, *J*=2.1 Hz, 3H), 3.68 (d, *J*=1.5 Hz, 3H), 3.36-3.23 (m, 1H), 2.97 (d, *J*=2.6 Hz, 1H), 2.63 (dd, *J*=10.2, 5.5 Hz, 1H), 2.45-2.38 (m, 4H), 2.38-2.33 (m, 1H), 2.29-2.19 (m, 1H), 1.96 (qdd, *J*=10.8, 5.5, 2.5 Hz, 1H), 1.75-1.55 (m, 4H), 1.45 (dd, *J*=15.6, 1.3 Hz, 3H), 1.34-1.22 (m, 2H), 1.16 (s, 3H), 0.8 (dd, *J*=45.2, 6.6 Hz, 3H): ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 204.1, 168.4, 165.7, 159.2, 145.2, 137.2, 135.1, 131.9, 129.5, 128.4, 127.8, 127.5, 124.5, 114.2, 102.6, 97.1, 89.6, 70.5, 63.8, 55.2, 52.1, 51.5, 49.3, 47.9, 46.1, 44.6, 42.7, 33.4, 32.1, 30.1, 28.0, 20.5, 11.7. HRMS-ESI (*m*/z): $[M+Na]^+$ calcd for $C_{38}H_{46}Cl_3O_7NNa$, 756.2238; found, 756.2224.



(3a*R*,4*R*,5*S*,7*R*)-5-((4*R*,7*R*,*E*)-7-((Benzyloxy)methoxy)-8,8,8-trichloro-4-methyloct-2-en-2-yl)-7-hydroxy-2-(4-methoxybenzyl)-3a-methyl-4-((*E*)-prop-1-en-1-yl)octahydro-1*H*-isoindol-1-one (S7). Sodium borohydride (0.148 g, 3.99 mmol) was added to a solution of **S6** (2.45 g, 3.33 mmol) in MeOH and THF (1:1 v/v, 167 mL) at -78 °C. After stirring at -78 °C for 30 min, the reaction mixture was quenched with saturated aqueous NH_4Cl and warmed to 23 °C, and extracted with ethyl acetate. The combined organic phase was washed with brine, dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel (70% ethyl acetate in hexanes) to deliver products **S7** and **S8** as a mixture (2.40 g, 3.26 mmol, 98% yield). The mixture was separated by preparative HPLC (YMC Pak-Sil; 2% *i*-PrOH in toluene; flow rate = 50.0 mL/min; detection at 290 nm; t_1=27.8 min (**S8**); t_2= 37.0 min (**S7**); t_3=38.0 min (other isomers)) to provide **S7** as a white crystalline solid (1.82 g, 2.43 mmol, 73% yield), **S8** (0.55 g, 0.746 mmol, 22% yield), and a mixture of other isomers (0.140 g, 0.190 mmol, 6% yield). **S7** $[\alpha]_D^{23}$ +5.2° (*c* 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.33 (d, *J*=4.5 Hz, 5H), 7.17 (dd, *J*=17.1, 8.6 Hz, 2H), 6.88 (d, *J*=7.9 Hz, 2H), 6.34 (dd, *J*=15.5, 10.4 Hz, 1H), 5.73 (d, *J*=15.5 Hz, 1H), 5.07 (d, *J*=7.2 Hz, 1H), 4.99 (d, *J*=7.2 Hz, 1H), 4.89-4.82 (m, 1H), 4.78 (d, 11.9 Hz, 1H), 4.62 (d, *J*=11.9 Hz, 1H), 4.44 (d, *J*=14.6 Hz, 1H), 4.33 (d, *J*=14.5 Hz, 1H), 3.93 (dd, *J*=8.6, 2.3 Hz, 1H), 3.80 (s, 3H), 3.67 (s, 3H), 3.57 (d,

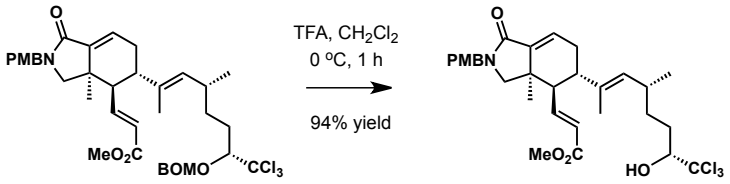
J=10.9 Hz, 1H), 3.25 (d, *J*=9.6 Hz, 1H), 2.60 (d, *J*=9.7 Hz, 1H), 2.25 (tt, *J*=8.4, 5.7 Hz, 1H), 2.10 (t, *J*=10.9 Hz, 1H), 2.04-1.92 (m, 3H), 1.81 (d, *J*=12.3 Hz, 1H), 1.78-1.56 (m, 3H), 1.43 (s, 3H), 1.31-1.24 (m, 1H), 1.06 (s, 3H): ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 165.9, 159.2, 146.9, 137.2, 133.7, 129.4, 128.4, 128.3, 127.7, 127.6, 123.8, 114.2, 102.6, 97.0, 89.6, 70.5, 55.2, 52.3, 51.4, 49.3, 45.9, 39.7, 33.6, 32.0, 30.2, 28.1, 20.6, 12.3. HRMS-ESI (*m*/z): $[M+Na]^+$ calcd for $C_{38}H_{48}Cl_3O_7NNa$, 758.2394; found, 758.2381.



S7 **S9**

(*E*)-Methyl 3-((3a*R*,4*R*,5*S*)-5-((4*R*,7*R*,*E*)-7-((benzyloxy)methoxy)-8,8,8-trichloro-4-methyloct-2-en-2-yl)-2-(4-methoxybenzyl)-3a-methyl-1-oxo-2,3,3a,4,5,6-hexahydro-1*H*-isoindol-4-yl)acrylate (S9). *N*,*N'*-Dicyclohexylcarbodiimide (0.463 g, 2.24 mmol) and CuCl (0.444 g, 4.48 mmol) were sequentially added to a stirring solution of substrate **S7** (0.330 g, 0.448 mmol) in dry toluene (22 mL). The reaction mixture was stirred at 110 °C for 1 h. The resulting mixture was cooled and saturated aqueous ammonium chloride (30 mL) was added. The mixture was stirred at 23 °C for 2 h. The aqueous layer was extracted with ethyl acetate (3x15 mL) and the combined organic phase was washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography (50% ethyl acetate in hexanes) to deliver product **S9** (0.216 g, 0.336 mmol, 75% yield). $[\alpha]_D^{23}$ -13.4° (*c* 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.33 (d, *J*=4.4 Hz,

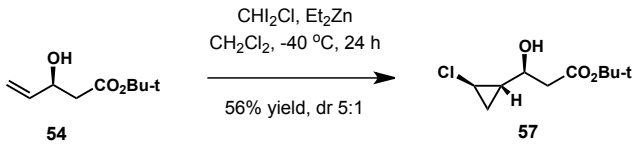
4H), 7.32-7.26 (m, 1H), 7.15 (d, 8.6 Hz, 2H), 6.85 (d, *J*=8.5 Hz, 2H), 6.73 (dd, *J*=7.6, 2.8 Hz, 1H), 6.73 (dd, *J*=7.6, 2.8 Hz, 1H), 5.77 (d, *J*=15.5 Hz, 1H), 5.08 (d, *J*=7.1 Hz, 1H), 5.00 (d, *J*=7.2 Hz, 1H), 4.92 (dd, *J*=9.5, 1.7 Hz, 1H), 4.79 (d, 11.8 Hz, 1H), 4.64-4.58 (m, 1H), 4.20 (d, *J*=14.6 Hz, 1H), 3.95 (dd, *J*=8.5, 2.2 Hz, 1H), 3.95 (dd, *J*=8.5, 2.2 Hz, 1H), 3.79 (s, 3H), 3.68 (s, 3H), 3.09 (d, *J*=9.2 Hz, 1H), 2.55 (d, *J*=9.1 Hz, 1H), 2.38 (t, *J*=10.7 Hz, 1H), 2.28 (ddd, *J*=14.6, 10.4, 6.9 Hz, 1H), 2.20-2.07 (m, 2H), 2.03-1.90 (m, 2H), 1.66 (dtdd, *J*=27.1, 24.9, 11.3, 6.6 Hz, 3H), 1.47 (s, 3H), 1.31 (ddt, *J*=10.4, 7.3, 3.0 Hz, 1H), 1.27-1.21 (m, 1H), 1.27-1.21 (m, 1H), 1.14 (s, 3H), 0.80 (d, *J*=6.6 Hz, 3H): ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 167.0, 166.1, 159.0, 147.8, 140.2, 137.2, 134.0, 133.8, 129.2, 128.4, 128.3, 127.8, 127.6, 122.5, 114.0, 102.6, 97.0, 89.6, 70.5, 55.2, 53.7, 51.4, 50.1, 49.4, 46.0, 41.5, 33.6, 32.2, 30.3, 29.4, 28.4, 20.7, 12.8. HRMS-ESI (*m*/z): $[M+Na]^+$ calcd for $C_{38}H_{46}Cl_3O_6NNa$, 740.2288; found, 740.2277.



S9 **67**

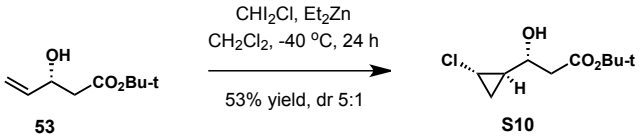
(*E*)-Methyl 3-((3a*R*,4*R*,5*S*)-2-(4-methoxybenzyl)-3a-methyl-1-oxo-5-((4*R*,7*R*, *E*)-8,8,8-trichlo-ro-7-hydroxy-4-methyloct-2-en-2-yl)-2,3,3a,4,5,6-hexahydro-1*H*-isoindol-4-yl)acrylate (67). Substrate **S9** (0.216 g, 0.300 mmol) was stirred in a solution of trifluoroacetic acid and CH_2Cl_2 (1:1, v/v, 30 mL) at 0 °C. After 10 min, the reaction mixture was warmed to 23 °C and stirred for additional 1 h. The crude mixture was concentrated, toluene (3x15 mL) was added, and the solution was concentrated again. The dilution-concentration using toluene was repeated three

times. The residue was purified by column chromatography (50% ethyl acetate in hexanes) to deliver alcohol **67** (0.170 g, 0.282 mmol, 94% yield). $[\alpha]_D^{23}$ -48.1° (*c* 1.0, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.14 (d, *J*=8.5 Hz, 2H), 6.85 (d, *J*=8.6 Hz, 2H), 6.78-6.72 (m, 1H), 6.57 (dd, *J*=15.5, 10.3 Hz, 1H), 5.79 (d, *J*=15.6 Hz, 1H), 4.98 (dd, *J*=9.5, 1.7 Hz, 1H), 4.61 (d, *J*=14.6 Hz, 1H), 4.19 (d, *J*=14.6 Hz, 1H), 3.95 (ddd, *J*=9.8, 5.6, 2.0 Hz, 1H), 3.80 (s, 3H), 3.69 (s, 3H), 3.09 (d, *J*=9.2 Hz, 1H), 2.95 (dd, *J*=5.6, 1.4 Hz, 1H), 2.56 (d, *J*=9.2 Hz, 1H), 2.41 (t, *J*=10.7 Hz, 1H), 2.34 (tt, *J*=8.2, 5.5 Hz, 1H), 2.24-2.10 (m, 2H), 2.07-1.94 (m, 2H), 1.73-1.61 (m, 2H), 1.59-1.51 (m, 1H), 1.50 (s, 1H), 1.33-1.23 (m, 1H), 1.15 (s, 3H), 0.86 (d, *J*=6.6 Hz, 3H): ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 167.1, 166.1, 159.0, 147.8, 140.2, 134.0, 133.9, 129.5, 129.2, 128.3, 122.6, 114.0, 104.3, 83.2, 55.2, 53.7, 51.5, 50.0, 49.5, 46.0, 41.6, 33.7, 32.1, 29.6, 29.4, 28.4, 20.9, 13.0. HRMS-ESI (*m*/z): $[M+Na]^+$ calcd for $C_{30}H_{38}Cl_3NO_5Na$, 620.1713; found, 620.1703.



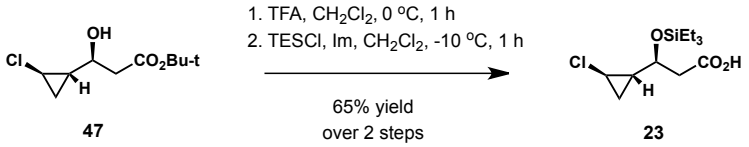
(*S*)-*tert*-Butyl 3-((1*S*,2*R*)-2-chlorocyclopropyl)-3-hydroxypropanoate (57). Diethylzinc (2.1 mL, 20.1 mmol) was added dropwise to a stirring solution of (*S*)-*tert*-butyl 3-hydroxypent-4-enoate **54**[80] (1.57 g, 9.11 mmol) in CH_2Cl_2 (46 mL) at -40 °C and the reaction mixture was stirred for 10 min. Diiodochloromethane[81] (3.8 mL, 40.1 mmol) was added dropwise and resulting mixture was stirred protected from light at -40 °C for 24 h. The reaction mixture was quenched with saturated aqueous sodium sulfite (20 mL) and allowed to warm to 23 °C and stirred for an additional 1 h. Aqueous 1 M solution of HCl was added in portions until precipitates dissolved,

the layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3x20 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography (2% ethyl acetate in dichloromethane) to deliver product **57** (1.13 g, 5.10 mmol, 56% yield). $[\alpha]_D^{23}$ -13.4° (*c* 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 3.61 (ddt, *J*=8.5, 6.4, 3.7 Hz, 1H), 3.11 (d, *J*=3.9 Hz, 1H), 3.06 (ddd, *J*=6.8, 4.9, 3.2 Hz, 1H), 2.61-2.44 (m, 2H), 1.37 (s, 9H), 1.47 (s, 9H), 1.38-1.28 (m, 1H), 1.03-0.91 (m, 2H): ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 171.9, 81.6, 68.4, 41.6, 30.1, 28.0, 27.3, 13.0. HRMS-ESI (*m*/z): $[M+Na]^+$ calcd for $C_{10}H_{17}ClO_3Na$, 243.0764; found, 243.0754.



(*R*)-*tert*-Butyl 3-((1*R*,2*S*)-2-chlorocyclopropyl)-3-hydroxypropanoate (S10). Diethylzinc (2.1 mL, 20.1 mmol) was added dropwise to a stirring solution of (*R*)-*tert*-butyl 3-hydroxypent-4-enoate **53** (1.57 g, 9.11 mmol) in CH_2Cl_2 (46 mL) at -40 °C and the reaction mixture was stirred for 10 min. Diiodochloromethane**Error! Bookmark not defined.** (3.8 mL, 40.1 mmol) was added dropwise and resulting mixture was protected from light and stirred at -40 °C for 24 h. The reaction mixture was quenched with saturated aqueous sodium sulfite (20 mL) and allowed to warm to 23 °C and stirred for an additional 1 h. Aqueous 1 M solution of HCl was added in portions until precipitates dissolved, the layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3x20 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography (2% ethyl acetate in dichloromethane) to deliver product **S10** (1.13

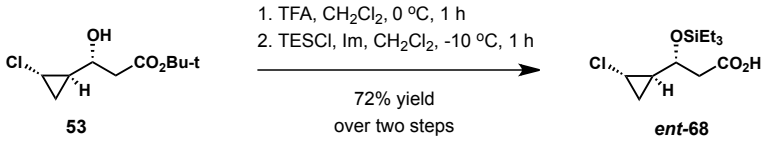
g, 5.10 mmol, 56% yield). $[\alpha]_D^{23}$ +12.8° (*c* 1.0, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 3.61 (ddt, *J*=8.5, 6.4, 3.7 Hz, 1H), 3.11 (d, *J*=3.9 Hz, 1H), 3.06 (ddd, *J*=6.8, 4.9, 3.2 Hz, 1H), 2.61-2.44 (m, 2H), 1.37 (s, 9H), 1.47 (s, 9H), 1.38-1.28 (m, 1H), 1.03-0.91 (m, 2H): ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 171.9, 81.6, 68.4, 41.6, 30.1, 28.0, 27.3, 13.0. HRMS-ESI (*m*/z): $[M+Na]^+$ calcd for $C_{10}H_{17}ClO_3Na$, 243.0764; found, 243.0763.



(*S*)-3-((1*S*,2*R*)-2-Chlorocyclopropyl)-3-((triethylsilyl)oxy)propanoic acid (23). Ester **47** (0.216 g, 0.300 mmol) was stirred in a solution of trifluoroacetic acid and CH_2Cl_2 (1:1, v/v, 30.0 mL) at 0 °C. After 10 min, the reaction mixture was warmed to 23 °C and stirred for another 1 h. The crude mixture was concentrated, toluene (3x15 mL) was added, and the solution was concentrated again. The dilution-concentration using toluene was repeated three times. This residue was used in the next step without purification.

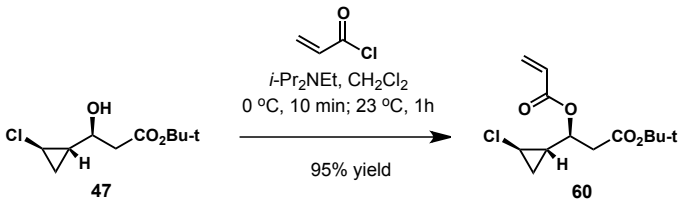
Chlorotriethylsilane (0.56 mL, 2.72 mmol) was added to a stirring solution of the hydroxyl acid and imidazole (0.231 g, 3.40 mmol) in CH_2Cl_2 (6.8 mL) at -10 °C. After stirring for 1 h, the reaction mixture was poured into aqueous acetate buffer (pH=4) and extracted with ethyl acetate (3x10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography (30% ethyl acetate in hexanes) to deliver product **23** (0.122 g, 0.442 mmol, 65% yield). $[\alpha]_D^{23}$ -50.2° (*c* 1.0, $CHCl_3$). ^1H NMR (500

MHz, $CDCl_3$) δ (ppm): 3.75 (q, *J*=6.3 Hz, 1H), 2.98 (dt, *J*=7.3, 3.5 Hz, 1H), 2.61 (d, *J*=6.1 Hz, 2H), 1.44 (dtd, *J*=9.9, 6.6, 3.2 Hz, 1H), 1.03-0.98 (m, 1H), 0.97-0.93 (m, 9H), 0.90 (dt, *J*=7.5, 6.4 Hz, 1H), 0.73-0.52 (m, 6H): ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 176.7, 69.5, 42.6, 30.6, 28.2, 13.2, 6.7, 4.8. HRMS-ESI (*m*/z): $[M-H]^-$ calcd for $C_{12}H_{22}ClO_3Si$, 277.1027; found, 277.1035.

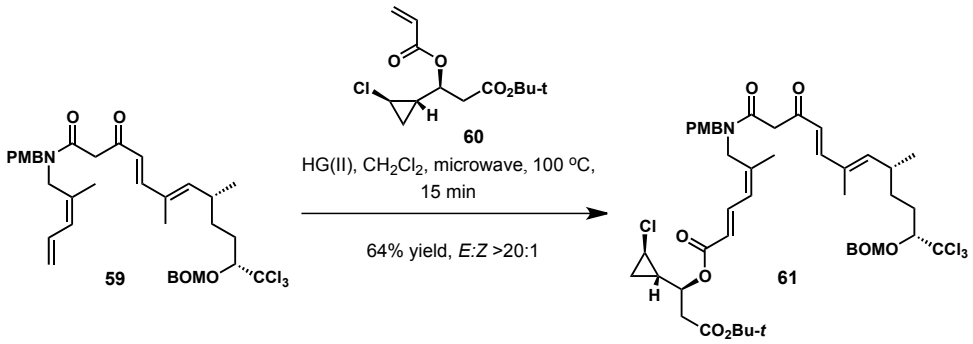


(*R*)-3-((1*R*,2*S*)-2-Chlorocyclopropyl)-3-((triethylsilyl)oxy)propanoic acid (*ent*-68). Substrate **53** (0.216 g, 0.300 mmol) was stirred in a solution of trifluoroacetic acid and CH_2Cl_2 (1:1, v/v, 30.0 mL) at 0 °C. After 10 min, the reaction mixture was warmed to 23 °C and stirred for another 1 h. The crude mixture was concentrated and toluene (3x15 mL) was added and concentrated in triplicate. This residue was used in the next step without purification. Chlorotriethylsilane (0.56 mL, 2.72 mmol) was added to a stirring solution of the hydroxy acid and imidazole (0.231 g, 3.40 mmol) in CH_2Cl_2 (6.8 mL) at -10 °C. After 1 h, the reaction mixture was poured into aqueous acetate buffer (~100 mM, pH 4) and extracted with ethyl acetate (3x10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography (30% ethyl acetate in hexanes) to deliver product ***ent*-68** (0.122 g, 0.442 mmol, 65% yield). $[\alpha]_D^{23}$ +47.4° (*c* 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 3.75 (q, *J*=6.3 Hz, 1H), 2.98 (dt, *J*=7.3, 3.5 Hz, 1H), 2.61 (d, *J*=6.1 Hz, 2H), 1.44 (dtd, *J*=9.9, 6.6, 3.2 Hz, 1H), 1.03-0.98 (m, 1H), 0.97-0.93 (m, 9H), 0.90 (dt, *J*=7.5, 6.4 Hz, 1H), 0.73-0.52 (m, 6H): ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 176.7, 69.5, 42.6, 30.6, 28.2, 13.2,

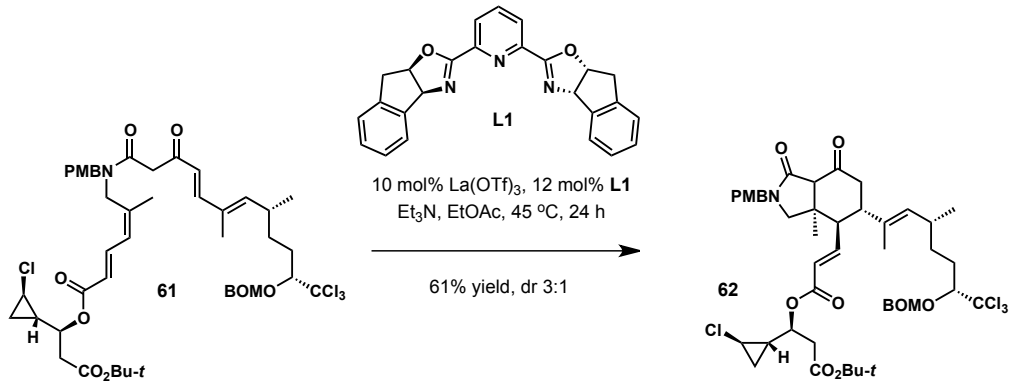
6.7, 4.8. HRMS-ESI (*m*/z): $[M-H]^-$ calcd for $C_{12}H_{22}ClO_3Si$, 277.1027; found, 277.1029.



(*S*)-3-(*tert*-butoxy)-1-((1*S*,2*R*)-2-chlorocyclopropyl)-3-oxopropyl acrylate (60). Acryloyl chloride (0.27 mL, 2.88 mmol) was added dropwise to a solution of alcohol **47** and diisopropylethylamine (0.63 mL, 3.60 mmol) in CH_2Cl_2 (4.0 mL) at 0 °C. After 10 min. the resulting mixture warmed to 23 °C and stirred for an additional 1 h. The solution was diluted with CH_2Cl_2 (4.0 mL) and washed with water (5 mL). The organic phase was washed successively with 1 M aqueous solution of HCl and saturated aqueous solution of $NaHCO_3$. The combined organic phase was washed with brine, dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography (20% ethyl acetate in hexanes) to deliver acrylate **60** (0.188 g, 0.684 mmol, 95% yield). $[\alpha]_D^{23}$ -76.2° (*c* 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 6.40 (dd, *J*=17.3, 1.4 H, 1H), 6.10 (dd, *J*=17.3, 10.4 Hz, 1H), 5.85 (dd, *J*=10.4, 1.3 Hz, 1H), 4.78 (td, *J*=8.4, 5.2 Hz, 1H), 3.15 (ddd, *J*=7.3, 4.0, 3.1 Hz, 1H), 2.79-2.47 (m, 2H), 1.48 (dddd, *J*=9.7, 8.6, 6.3, 3.2 Hz, 1H), 1.40 (s, 9H), 1.05 (ddd, *J*=9.9, 6.6, 4.0 Hz, 1H), 0.96 (dt, *J*=7.5, 6.4 Hz, 1H): ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 168.7, 165.1, 131.3, 128.1, 81.2, 71.6, 40.4, 30.8, 27.9, 25.9, 14.0. HRMS-ESI (*m*/z): $[M+Na]^+$ calcd for $C_{13}H_{19}ClO_4Na$, 297.0869; found, 297.0876.

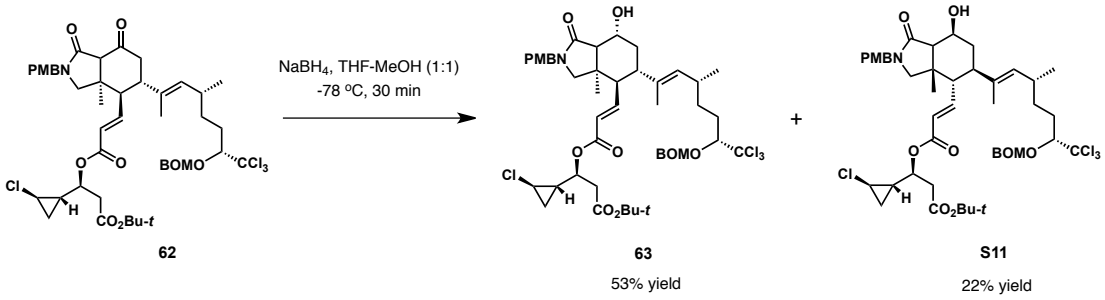


(2*E*,4*Z*)-(*S*)-3-(*tert*-Butoxy)-1-((1*S*,2*R*)-2-chlorocyclopropyl)-3-oxopropyl-6-((4*E*,6*E*,8*R*,11*R*) -11-((benzyloxy)methoxy)-12,12,12-trichloro-*N*-(4-methoxy benzyl)-6,8-dimethyl-3-oxododeca-4,6-dienamido)-5-methylhexa-2,4-dienoate (61). Hoveyda-Grubbs II catalyst (1,3-Bis-(2,4,6-trimethylphenyl)-2-imidazolidinylidene)dichloro(*o*-isopropoxyphenyl methy-lene)ruthenium (5.5 mg, 8.80 μmol) was added to a solution of acrylate **60** (73.0 mg, 0.265 mmol) and substrate **59** (0.120 g, 0.177 mmol) in CH_2Cl_2 (1.8 mL) contained in a microwave vial. The resulting solution was heated in the microwave at 100 °C (4 atm) for 15 min. The crude mixture was cooled to room temperature and concentrated. The residue was purified by column chromatography on silica gel (25% ethyl acetate in hexanes) to afford amide **61** (0.104 g, 0.113 mmol, 64% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.39-7.28 (m, 9H), 7.25-7.13 (m, 2H), 7.13-7.04 (m, 3H), 6.94-6.81 (m, 3H), 6.24-6.11 (m, 2H), 5.91-5.69 (m, 3H), 5.53 (d, *J*=9.9 Hz, 1H), 5.10 (d, *J*=7.2 Hz, 2H), 5.01 (d, *J*=7.2 Hz, 2H), 4.81 (d, *J*=11.9 Hz, 2H), 4.75 (ddd, *J*=11.0, 6.4, 2.1 Hz, 1H), 4.63 (d, *J*=11.9 Hz, 2H), 4.55-4.44 (m, 1H), 4.31 (dd, *J*=10.5, 6.5 Hz, 4H), 4.00-3.91 (m, 2H), 3.87-3.74 (m, 6H).



(*E*)-(*S*)-3-(*tert*-Butoxy)-1-((1*S*,2*R*)-2-chlorocyclopropyl)-3-oxopropyl 3-((3a*R*, 4*R*,5*S*)-5-((4*R*,7*R*,*E*)-7-((benzyloxy)methoxy)-8,8,8-trichloro-4-methyloct-2-en -2-yl)-2-(4-methoxybenz-yl)-3a-methyl-1,7-dioxooctahydro-1*H*-isoindol-4-yl) acrylate (62). Lanthanum(III) triflate (13 mg, 22.0 μmol) was added to a stirring solution of 2,6-bis((3a*S*,8a*R*)-8,8a-dihydro-3a*H*-indeno[1,2-*d*]oxazol-2-yl)pyr idine **L1** (8.7 mg, 22.0 μmol) in ethyl acetate (1.0 mL). After 1 h at 23 °C, the catalyst solution was added to **61** (0.100 g, 0.108 mmol) in ethyl acetate (4.6 mL). The resulting solution was capped and heated at 45 °C for 24 h. The reaction mixture was cooled, concentrated, and the residue was purified by chromatography on silica gel (80% ethyl acetate in hexanes) to afford product **62** as inseparable mixture of diastereomers (61.0 mg, 65.9 μmol, 61% yield, 3:1 dr). Major diastereomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.35-7.30 (m, 4H), 7.26-7.23 (m, 1H), 7.15 (d, *J*=8.6 Hz, 2H), 6.85 (d, *J*=8.6 Hz, 2H), 6.37 (dd, *J*=15.5, 2.7 Hz, 1H), 5.79 (d, *J*=15.4 Hz, 1H), 5.08 (d, *J*=7.2 Hz, 1H), 4.98 (d, *J*=7.2 Hz, 1H), 4.86 (d, *J*=9.3 Hz, 1H), 4.78 (d, *J*=11.9 Hz, 1H), 4.71-4.65 (m, 1H), 4.61 (d, *J*=11.8 Hz, 1H), 4.56-4.29 (m, 2H), 3.93 (dd, *J*=8.7, 2.3 Hz, 1H), 3.77 (s, 3H), 3.28 (d, *J*=10.3, 1H), 3.05 (dt, *J*=7.3, 3.8 Hz, 1H), 2.96 (d, *J*=8.6 Hz, 1H), 2.69-2.51 (m, 3H), 2.48-2.37 (m, 1H), 2.36-2.30 (m, 1H), 2.24 (ddd, *J*=13.6, 10.5, 6.8 Hz, 1H), 1.95 (tddd, *J*=19.5, 11.5, 5.1, 2.4 Hz, 1H),

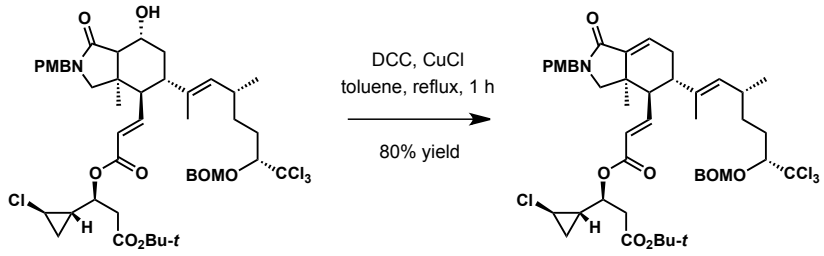
1.72-1.56 (m, 2H), 1.44 (s, 3H), 1.35 (s, 9H), 1.12 (s, 3H), 1.03 (ddd, *J*=10.1, 6.7, 3.9 Hz, 1H), 0.91 (ddt, *J*=10.6, 7.5, 6.4 Hz, 1H), 0.78 (d, *J*=6.6 Hz, 3H): minor diastereomer - ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.36-7.31 (m, 4H), 7.26-7.23 (m, 1H), 7.17 (d, *J*=8.5 Hz, 2H), 6.86 (d, *J*=6.4 Hz, 2H), 6.39 (dd, *J*=15.5, 2.2 Hz, 1H), 5.77 (d, *J*=15.5 Hz, 1H), 5.05 (d, *J*=7.2 Hz, 1H), 4.98 (d, *J*=7.2 Hz, 1H), 4.88 (d, *J*=7.5 Hz, 1H), 4.77 (d, *J*=11.9 Hz, 1H), 4.71-4.63 (m, 1H), 4.61 (d, *J*=11.8 Hz, 1H), 4.54-4.25 (m, 2H), 3.97 (dd, *J*=8.7, 2.4 Hz, 1H), 3.77 (s, 3H), 3.28 (d, *J*=10.3 Hz, 1H), 3.12-3.08 (m, 1H), 2.96 (d, *J*=8.6 Hz, 1H), 2.70-2.50 (m, 3H), 2.48-2.37 (m, 3H), 2.37-2.30 (m, 1H), 2.24 (ddd, *J*=13.6, 10.5, 6.8 Hz, 1H), 1.95 (ddddt, *J*=19.5, 14.1, 11.5, 5.3, 2.5 Hz, 1H), 1.72-1.55 (m, 2H), 1.44 (s, 3H), 1.38 (s, 9H), 1.17 (s, 3H), 1.03 (ddd, *J*=10.1, 6.7, 3.9 Hz, 1H), 0.91 (ddt, *J*=10.6, 7.5, 6.4 Hz, 1H), 0.83 (d, *J*=6.6 Hz, 3H).



62 → 63 (53% yield) + S11 (22% yield)

(*E*)-(*S*)-3-(*tert*-Butoxy)-1-((1*S*,2*R*)-2-chlorocyclopropyl)-3-oxopropyl 3-((3a*R*, 4*R*,5*S*,7*R*)-5-((4*R*,7*R*,*E*)-7-((benzyloxy) methoxy)-8,8,8-trichloro-4-methyloct-2-en-2-yl)-7-hydroxy-2-(4-methoxybenzyl)-3a-methyl-1-oxooctahydro-1*H*-iso indol-4-yl)acrylate (63). Sodium borohydride (12 mg, 0.324 mmol) was added to a solution of **62** (60 mg, 64.0 μmol) in methanol and THF (1:1 v/v, 3.2 mL) at -78 °C. After stirring for 20 min, the reaction mixture was quenched with saturated aqueous NH_4Cl solution and warmed to 23 °C and extracted with ethyl acetate. The combined

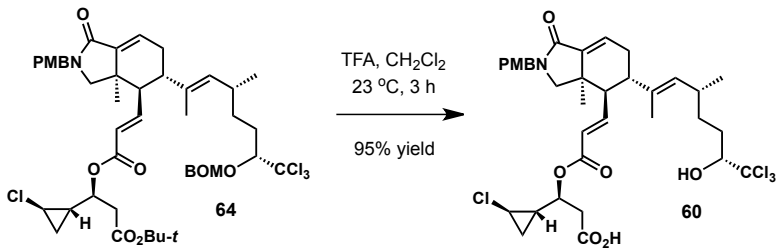
organic phase was washed with brine, dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel (70% ethyl acetate in hexanes) to deliver a mixture of products **63** and **S11**. Pure **63** was isolated by dissolving the mixture of products in 5% *i*-PrOH/hexane and separation by preparative HPLC (YMC Pak-Sil; 5% *i*-PrOH in hexane; flow rate = 20.0 mL/min; detection at 210 nm; t_1= 17.5 min; t_2= 20.0 min; t_3= 21.2 min) to provide major diastereomer **63** as a white solid (31 mg, 33.9 μmol, 53% yield) and minor diastereomer **S11** as a white solid (13 mg, 14.1 μmol, 22% yield). $[\alpha]_D^{23}$ -1.4° (*c* 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.33 (d, *J*=4.4 Hz, 4H), 7.28-7.25 (m, 1H), 7.15 (d, *J*=8.5 Hz, 2H), 6.87 (d, *J*=8.5 Hz, 2H), 6.38 (dd, *J*=15.4, 10.5 Hz, 1H), 5.72 (d, *J*=15.4 Hz, 1H), 5.08 (d, *J*=7.2 Hz, 1H), 4.99 (d, *J*=7.3 Hz, 1H), 4.86 (dd, *J*=9.5, 1.6 Hz, 1H), 4.79 (d, *J*=11.9 Hz, 1H), 4.73-4.67 (m, 1H), 4.62 (d, *J*=11.9 Hz, 1H), 4.38 (q, *J*=14.4 Hz, 2H), 3.94 (dd, *J*=8.6, 2.2 Hz, 1H), 3.80 (s, 3H), 3.57 (t, *J*=10.0 Hz, 1H), 3.24 (d, *J*=9.8 Hz, 1H), 3.05 (ddd, *J*=7.3, 4.0, 3.1 Hz, 1H), 2.64-2.50 (m, 3H), 2.64-2.50 (m, 1H), 2.26 (ddd, *J*=9.1, 7.3, 4.3 Hz, 1H), 2.10 (t, *J*=11.0 Hz, 1H), 2.05-1.92 (m, 3H), 1.85-1.77 (m, 1H), 1.75-1.56 (m, 2H), 1.44 (d, *J*=1.3 Hz, 3H), 1.44-1.37 (m, 1H), 1.36 (s, 9H), 1.33-1.24 (m, 1H), 1.02 (s, 3H), 0.99-0.89 (m, 1H), 0.78 (d, *J*=6.6 Hz, 3H): ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 175.4, 168.7, 164.8, 159.2, 148.0, 137.3, 134.0, 133.6, 129.6, 128.4, 127.9, 127.8, 127.6, 123.5, 114.2, 102.6, 97.0, 89.7, 81.1, 71.7, 70.5, 69.9, 58.0, 55.2, 52.3, 49.2, 46.4, 45.9, 40.4, 39.7, 35.8, 33.6, 32.1, 30.8, 30.3, 29.6, 28.1, 27.9, 26.9, 25.9, 20.9, 14.2, 12.1. HRMS-ESI (*m*/z): $[M+Na]^+$ calcd for $C_{47}H_{61}Cl_4NO_9Na$, 948.2998; found, 946.2687.



63 64

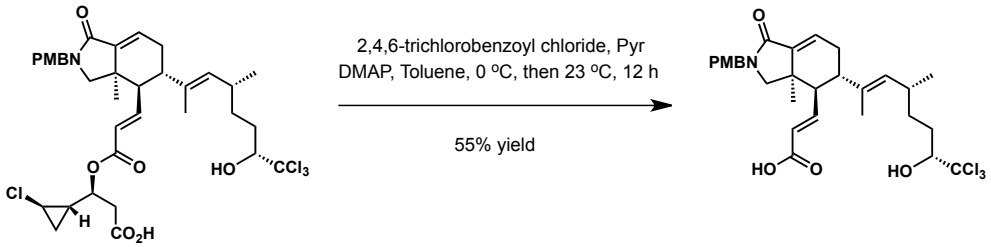
(*E*)-(*S*)-3-(*tert*-Butoxy)-1-((1*S*,2*R*)-2-chlorocyclopropyl)-3-oxopropyl 3-((3a*R*, 4*R*,5*S*)-5-((4*R*,7*R*,*E*)-7-((benzyloxy)methoxy)-8,8,8-trichloro-4-methyloct-2-en -2-yl)-2-(4-methoxybenzyl)-3a-methyl-1-oxo-2,3,3a,4,5,6-hexahydro-1*H*-iso indol-4-yl) acrylate (64). *N*,*N'*-Dicyclohexylcarbodiimide (6.7 mg, 32.0 μmol) and CuCl (6.3 mg, 14.0 μmol) were sequentially added to a solution of alcohol **63** (5.0 mg, 5.40 μmol) in toluene (0.3 mL). The reaction mixture was stirred at 110 °C for 20 min. The resulting mixture was cooled and saturated aqueous ammonium chloride (30 mL) was added. The mixture was stirred at 23 °C for 2 h. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3x2 mL). The combined organic phase was washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography (5% acetone in dichloromethane) to deliver product **64** (4.0 mg, 4.3 μmol, 80% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.33 (d, *J*=4.4 Hz, 4H), .28 (q, *J*=3.9 Hz, 1H), 7.14 (d, *J*=8.4 Hz, 2H), 6.84 (d, *J*=8.5 Hz, 2H), 6.73 (dd, *J*=7.8, 2.7 Hz, 1H), 6.58 (dd, *J*=15.5, 10.4 Hz, 1H), 5.76 (d, *J*=15.5 Hz, 5.08 (d, *J*=7.2 Hz, 1H), 5.00 (d, *J*=7.2 Hz, 1H), 4.93 (dd, *J*=9.5, 1.7 Hz, 1H), 4.79 (d, *J*=11.8 Hz, 1H), 4.72 (td, *J*=8.4, 5.4 Hz, 1H), 4.68-4.56 (m, 2H), 4.16 (d, *J*=14.6 Hz, 1H), 3.96 (dd, *J*=8.4, 2.3 Hz, 1H), 3.78 (s, 3H), 3.48 (dtd, *J*=10.7, 7.2, 4.1 Hz, 1H), 3.11-3.05 (m, 2H), 2.58 (qd, *J*=15.5, 6.7 Hz, 2H), 2.51 (d, *J*=9.2 Hz, 1H), 2.38 (t, 10.8 Hz, 1H), 2.29 (tt, *J*=8.5, 5.9 Hz, 1H), 2.21-2.13 (m,

1H), 2.08 (td, *J*=8.9, 8.4, 3.7 Hz, 1H), 2.02-1.90 (m, 3H), 1.73-1.65 (m, 3H), 1.65-1.57 (m, 1H), 1.47 (s, 3H), 1.45-1.40 (m, 1H), 1.35 (s, 9H), 1.28-1.22 (m, 2H), 1.12 (s, 3H), 1.04 (ddd, *J*=10.1, 6.5, 4.0 Hz, 1H), 0.93 (q, *J*=6.8 Hz, 1H), 0.82 (d, *J*=6.6 Hz, 3H).



(*S*)-3-((1*S*,2*R*)-2-chlorocyclopropyl)-3-(((*E*)-3-((3a*R*,4*R*,5*S*)-2-(4-methoxy benzyl)-3a-methyl-1-oxo-5-((4*R*,7*R*,*E*)-8,8,8-trichloro-7-hydroxy-4-methyloct-2-en-2-yl)-2,3,3a,4,5,6-hexahydro-1*H*-isoindol-4-yl)acryloyl)oxy)propanoic acid (60). Benzyloxymethyl ether **64** (29 mg, 31.0 μmol) was stirred in a solution of trifluoroacetic acid and CH_2Cl_2 (1:1, v/v, 2.6 mL) at 0 °C. After stirring for 10 min, the reaction mixture was warmed to 23 °C and stirred for 3 h. The crude mixture was concentrated and the residue was purified by column chromatography (10% methanol in chloroform) to deliver hydroxy acid **60** (21.5 mg, 29.5 μmol, 95% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.15 (d, *J*=7.8 Hz, 2H), 6.85 (d, *J*=8.0 Hz, 2H), 6.78 (t, *J*=5.2 Hz, 1H), 6.59 (dd, *J*=15.5, 10.2 Hz, 1H), 5.77 (d, *J*=15.5 Hz, 1H), 4.98 (d, *J*=9.3 Hz, 1H), 4.74 (q, *J*=7.2 Hz, 1H), 4.59 (d, *J*=14.5 Hz, 1H), 4.24 (d, *J*=14.4 Hz, 1H), 3.98 (d, *J*=10.1 Hz, 1H), 3.79 (s, 3H), 3.11 (d, *J*=9.0 Hz, 2H), 2.77-2.67 (m, 2H), 2.59 (d, *J*=9.3 Hz, 1H), 2.42 (t, *J*=10.6, 1H), 2.23-2.14 (m, 2H), 1.99 (ddd, *J*=11.5, 8.4, 5.6 Hz, 2H), 1.65-1.53 (m, 3H), 1.49 (d, *J*=5.4 Hz, 4H), 1.33-1.26 (m, 2H), 1.15

(s, 3H), 1.07 (ddd, *J*=10.3, 6.5, 4.0 Hz, 1H), 1.01 (d, *J*=6.3 Hz, 1H), 0.96 (q, *J*=6.8 Hz, 1H), 0.87 (t, *J*=8.6 Hz, 5H).

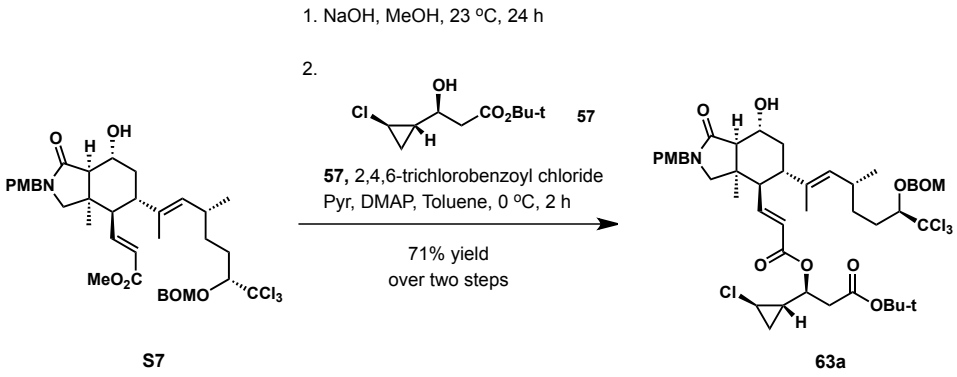


60 **65**

(*E*)-3-((3a*R*,4*R*,5*S*)-2-(4-Methoxybenzyl)-3a-methyl-1-oxo-5-((4*R*,7*R*,*E*)-8,8,8-trichloro-7-hydroxy-4-methyloct-2-en-2-yl)-2,3,3a,4,5,6-hexahydro-1*H*-iso indol-4-yl)acrylic acid (65). 2,4,6-trichlorobenzoyl chloride (0.26 mL, 1.64 mmol) was added to a solution of acid **60** (30 mg, 41.0 μmol) and pyridine (0.20 mL, 2.46 mmol) in toluene (2.7 mL) at 0 °C. After 45 min, 4-(dimethylamino)pyridine (20 mg, 0.164 mmol) was added to the reaction mixture at 0 °C. After 10 min, the reaction mixture was warmed to 50 °C and stirred for 5 h. Brine was added, layers separated, and the aqueous layer was extracted with ethyl acetate (3x5 mL). The combined organic layers were dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography (50% ethyl acetate in hexanes) to deliver product **65** (16 mg, 22.5 μmol, 55% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.17 (d, *J*=8.5 Hz, 2H), 6.86 (d, *J*=8.6 Hz, 2H), 6.72 (dd, *J*=7.9, 2.1 Hz, 1H), 6.63 (dd, *J*=16.0, 7.7 Hz, 1H), 5.70 (dd, *J*=16.1, 1.2 Hz, 1H), 5.39 (dd, *J*=8.2, 3.6 Hz, 1H), 4.83-4.81 (m, 1H), 4.69-4.47 (m, 2H), 4.22 (d, *J*=14.5 Hz, 1H), 3.80 (s, 3H), 3.20 (ddd, *J*=7.3, 4.1, 3.1 Hz, 1H), 2.97 (d, *J*=9.2 Hz, 1H), 2.89-2.79 (m, 2H), 2.72-2.62 (m, 2H), 2.62-2.52 (m, 1H), 2.44 (dd, *J*=14.0, 8.0 Hz, 1H), 2.08 (ddd, *J*=10.3, 6.0, 3.9 Hz, 1H), 1.85-1.76 (m, 2H), 1.71 (s, 3H), 1.60 (dddd, *J*=12.2, 6.9, 4.8, 1.8 Hz, 1H), 1.53 (tdd, *J*=9.9, 6.9, 4.8 Hz,

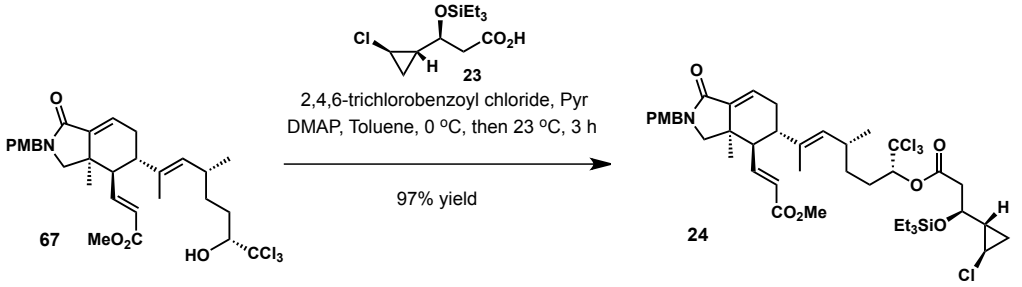
1H), 1.42-1.34 (m, 1H), 1.34-1.29 (m, 1H), 1.27 (s, 3H), 1.13 (ddt, *J*=10.2, 6.6, 3.0 Hz, 1H), 1.00-0.94 (m, 1H), 0.93 (d, *J*=6.8 Hz, 3H).

Chemical correlation of compounds S7 and 63a



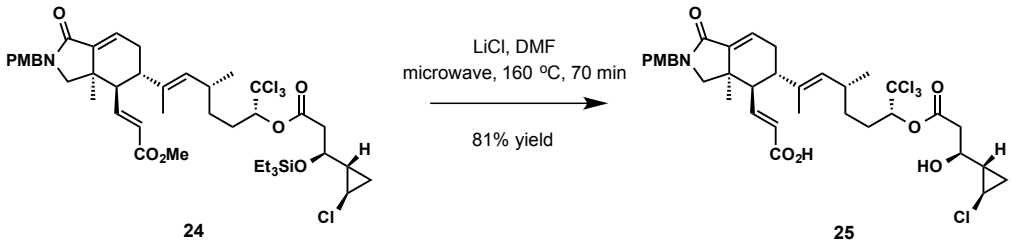
(*E*)-(*S*)-3-(*tert*-butoxy)-1-((1*S*,2*R*)-2-chlorocyclopropyl)-3-oxopropyl 3-((3a*R*, 4*R*,5*S*,7*R*)-5-((4*R*,7*R*,*E*)-7-((benzyloxy)methoxy)-8,8,8-trichloro-4-methyloct-2-en-2-yl)-7-hydroxy-2-(4-methoxybenzyl)-3a-methyl-1-oxooctahydro-1*H*-isoindol-4-yl)acrylate (63a). Sodium hydroxide (0.108 g, 2.71 mmol) was added to a solution of ester **S7** (20 mg, 27.1 μmol) in methanol and water (7:1, v/v, 2.7 mL) and the reaction mixture was stirred at 23 °C for 24 h. The reaction mixture was diluted with ether (3 mL) and 1 M aqueous HCl was added (3 mL). The layers were separated and the aqueous layer was extracted with diethyl ether (3x5 mL). The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated. 2,4,6-Trichlorobenzoyl chloride (5.4 μL, 34.5 μmol) was added to a solution of the resulting hydroxyl acid (10 mg, 13.8 μmol) and pyridine (6.7 μL, 82.9 μmol) in toluene (1.4 mL) at 0 °C. After 45 min, a solution of alcohol **57** (14 mg, 62.2 μmol) and 4-(dimethylamino)pyridine (17 mg, 0.138 mmol) in toluene (0.5 mL) was added at 0 °C. After 10 min, the reaction mixture was warmed to 23 °C and stirred for an

additional 1 h. Brine was added, layers separated, and the aqueous layer was extracted with ethyl acetate (3x5 mL), the combined organic layers were dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography (50% ethyl acetate in hexanes) to deliver product **63a** (9.6 mg, 10.4 μmol, 71% yield over two steps). This compound had ^1H and ^{13}C NMR data identical to those observed previously for compound **63** confirming its absolute and relative configuration.



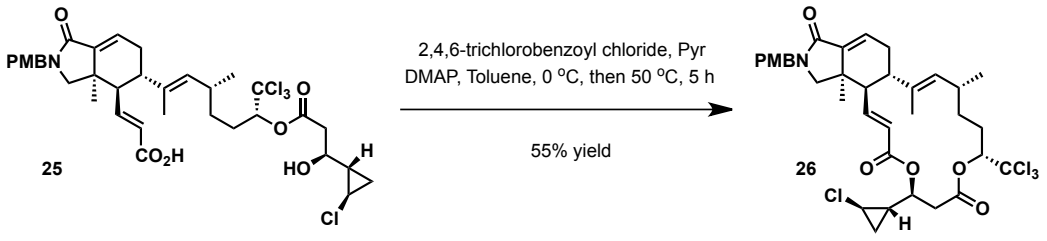
(*E*)-Methyl 3-((3a*R*,4*R*,5*S*)-2-(4-methoxybenzyl)-3a-methyl-1-oxo-5-((4*R*,7*R*, *E*)-8,8,8-trichlo-ro-7-(((*S*)-3-((1*S*,2*R*)-2-chlorocyclopropyl)-3-((triethylsilyl) oxy)propanoyl)oxy)-4-methyl-oct-2-en-2-yl)-2,3,3a,4,5,6-hexahydro-1*H*-iso indol-4-yl)acrylate (24). 2,4,6-Trichloro-benzoyl chloride (40 μL, 0.254 mmol) was added to a solution of acid **23** (34 mg, 0.122 mmol) and pyridine (49 μL, 0.611 mmol) in toluene (2.0 mL) at 0 °C. After 45 min, a solution of alcohol **67** (61 mg, 0.102 mmol) and 4-(dimethylamino)pyridine (31 mg, 0.254 mmol) in toluene (2.0 mL) was added at 0 °C. After another 10 min, the reaction mixture was warmed to 23 °C and stirred for an additional 1 h. Brine was added, layers separated, and the aqueous layer was extracted with ethyl acetate (3x5 mL). The combined organic layers were dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography (50% ethyl acetate in hexanes) to deliver **24** (84 mg, 98.4 μmol, 97% yield). $[\alpha]_D^{23}$ -39.5° (*c* 1.0, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.14 (d, *J*=8.5 Hz, 2H), 6.85 (d,

J=8.5 Hz, 2H), 6.75 (dd, *J*=7.3, 3.1 Hz, 1H), 6.56 (dd, *J*=15.5, 10.2 Hz, 1H), 5.78 (d, *J*=15.5 Hz, 1H), 5.46 (dd, *J*=10.1, 2.1 Hz, 1H), 4.96 (dd, *J*=9.5, 1.7 Hz, 1H), 4.62 (d, 14.6 Hz, 1H), 4.18 (d, *J*=14.6 Hz, 1H), 3.97-3.86 (m, 1H), 3.80 (s, 3H), 3.69 (s, 3H), 3.09 (d, *J*=9.2 Hz, 1H), 3.03-2.96 (m, 1H), 2.76-2.64 (m, 2H), 2.55 (d, *J*=9.2 Hz, 1H), 2.40 (t, *J*=10.7 Hz, 1H), 2.29 (qd, *J*=8.4, 5.6 Hz, 1H), 2.15 (ddt, *J*=12.4, 9.1, 4.1 Hz, 2H), 2.12-1.97 (m, 2H), 1.80-1.68 (m, 1H), 1.52-1.43 (m, 4H), 1.36 (ddd, *J*=13.4, 10.9, 5.4 Hz, 1H), 1.29-1.19 (m, 1H), 1.15 (s, 3H), 0.94 (t, *J*=7.9 Hz, 11H), 0.83 (d, *J*=6.6 Hz, 3H), 0.59 (q, *J*=7.8 Hz, 6H): ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 169.7, 167.0, 166.1, 159.0, 147.8, 140.2, 134.1, 133.7, 129.5, 129.2, 128.3, 122.62, 114.0, 99.9, 81.1, 68.0, 55.2, 53.7, 51.4, 50.1, 49.4, 46.0, 42.5, 41.5, 32.8, 32.0, 30.2, 29.4, 28.6, 28.4, 27.8, 20.7, 13.2, 12.8, 6.8, 4.8. HRMS-ESI (*m*/z): $[M+Na]^+$ calcd for $C_{42}H_{59}Cl_4NO_7Na$, 880.2712; found, 880.2703.



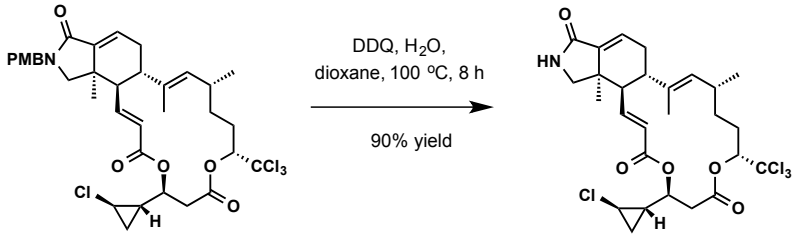
(*E*)-3-((3a*R*,4*R*,5*S*)-2-(4-Methoxybenzyl)-3a-methyl-1-oxo-5-((4*R*,7*R*,*E*)-8,8,8-trichloro-7-(((*S*)-3-((1*S*,2*R*)-2-chlorocyclopropyl)-3-hydroxypropanoyl)oxy)-4-methyloct-2-en-2-yl)-2,3,3a,4,5,6-hexahydro-1*H*-isoindol-4-yl)acrylic acid (25). Lithium chloride (2.48 g, 58.6 mmol) was added to a solution of substrate **24** (84 mg, 97.6 μmol) in DMF (5.0 mL) in a microwave vial. The vial was sealed and the mixture was heated in the microwave reactor at 160 °C for 70 min. The heterogeneous mixture was cooled to 23 °C, diluted with ethyl acetate (3 mL) and

water (5 mL), and stirred until all precipitates dissolved. The resulting solution was extracted with ethyl acetate (3x5 mL) and the combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography (50% ethyl acetate in hexanes) to deliver **25** (67 mg, 79.1 μmol, 81% yield) and a byproduct of only the triethylsilyl ether cleavage (hydroxy methyl ester) (13 mg, 17.4 μmol, 18% yield). $[\alpha]_D^{23}$ -3.1° (*c* 1.0, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.14 (d, *J*=8.6 Hz, 2H), 6.85 (d, *J*=8.6 Hz, 2H), 6.77 (t, *J*=5.1 Hz, 1H), 6.64 (dd, *J*=15.4, 10.3 Hz, 1H), 5.78 (d, *J*=15.5 Hz, 1H), 5.48 (dd, *J*=10.2, 2.2 Hz, 1H), 4.95 (d, *J*=9.2 Hz, 1H), 4.63 (d, *J*=14.6 Hz, 1H), 4.18 (d, *J*=14.6 Hz, 1H), 3.79 (s, 3H), 3.72 (td, *J*=7.2, 4.4 Hz, 1H), 3.16-3.04 (m, 2H), 2.79-2.68 (m, 2H), 2.57 (d, *J*=9.2 Hz, 1H), 2.44 (t, *J*=10.6 Hz, 1H), 2.34-2.27 (m, 1H), 2.17 (dt, *J*=9.5, 3.4 Hz, 2H), 2.08 (ddd, *J*=10.7, 6.5, 2.2 Hz, 1H), 2.03-1.98 (m, 1H), 1.75 (dtd, *J*=15.0, 10.3, 4.9 Hz, 1H), 1.50 (s, 3H), 1.40 (dtd, *J*=9.7, 6.7, 3.2 Hz, 1H), 1.32 (ddd, *J*=17.1, 8.2, 4.4 Hz, 2H), 1.24-1.19 (m, 1H), 1.15 (s, 3H), 1.06-0.97 (m, 2H), 0.88 (d, *J*=7.2 Hz, 1H), 0.85 (d, *J*=6.6 Hz, 3H): ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 170.8, 167.1, 159.0, 149.8, 140.1, 134.2, 133.5, 129.5, 128.1, 114.1, 99.7, 97.7, 81.2, 68.1, 60.3, 55.2, 53.8, 49.4, 46.1, 41.6, 40.9, 32.7, 31.9, 30.0, 29.6, 28.4, 27.4, 21.0, 20.7, 14.1, 13.2. HRMS-ESI (*m*/z): $[M-H]^-$ calcd for $C_{35}H_{42}Cl_4NO_7$, 728.1715; found, 728.1744.



(5a*S*,6*E*,8*R*,11*R*,15*S*,18*E*,19a*R*,19b*R*)-15-((1*S*,2*R*)-2-Chlorocyclopropyl)-2-(4-methoxybenzyl)-6,8,19b-trimethyl-11-(trichloromethyl)-5,5a,8,9,10,11,14,15-octahydro-1*H*-[1,5]dioxacyclo-hexadecino[9,10-*e*]isoindole-3,13,17(2*H*,19a*H*, 19b*H*)-trione (26). 2,4,6-Trichlorobenzoyl chloride (0.26 mL, 1.64 mmol) was added to a solution of acid **25** (30 mg, 41.0 μmol) and pyridine (0.20 mL, 2.46 mmol) in toluene (2.7 mL) at 0 °C. After 45 min, 4-(dimethylamino)pyridine (20 mg, 0.164 mmol) was added at 0 °C. After 10 min, the reaction mixture was warmed to 50 °C and stirred for 5 h. After cooling to room temperature, brine was added and the mixture was extracted with ethyl acetate (3x5 mL). The combined organic layers were dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography (50% ethyl acetate in hexanes) to deliver **26** (16 mg, 22.5 μmol, 55% yield). $[\alpha]_D^{23}$ +3.2° (*c* 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.17 (d, *J*=8.5 Hz, 2H), 6.86 (d, *J*=8.6 Hz, 2H), 6.72 (dd, *J*=7.9, 2.1 Hz, 1H), 6.63 (dd, *J*=16.0, 7.7 Hz, 1H), 5.70 (dd, *J*=16.1, 1.2 Hz, 1H), 5.39 (dd, *J*=8.2, 3.6 Hz, 1H), 4.83-4.81 (m, 1H), 4.69-4.47 (m, 2H), 4.22 (d, *J*=14.5 Hz, 1H), 3.80 (s, 3H), 3.20 (ddd, *J*=7.3, 4.1, 3.1 Hz, 1H), 2.97 (d, *J*=9.2 Hz, 1H), 2.89-2.79 (m, 2H), 2.72-2.62 (m, 2H), 2.62-2.52 (m, 1H), 2.44 (dd, *J*=14.0, 8.0 Hz, 1H), 2.08 (ddd, *J*=10.3, 6.0, 3.9 Hz, 1H), 1.85-1.76 (m, 2H), 1.71 (s, 3H), 1.60 (dddd, *J*=12.2, 6.9, 4.8, 1.8 Hz, 1H), 1.53 (tdd, *J*=9.9, 6.9, 4.8 Hz, 1H), 1.42-1.34 (m, 1H), 1.34-1.29 (m, 1H), 1.27 (s, 3H), 1.13 (ddt, *J*=10.2, 6.6, 3.0 Hz, 1H), 1.00-0.94 (m, 1H), 0.93 (d, *J*=6.8 Hz, 3H): ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 167.6, 166.9, 164.6, 159.1, 148.0, 141.1, 134.1, 130.6, 129.6, 129.2, 128.3, 123.4, 114.1, 99.6, 81.0, 71.6, 64.3, 55.2, 53.7, 49.7, 46.6, 46.0, 42.3,

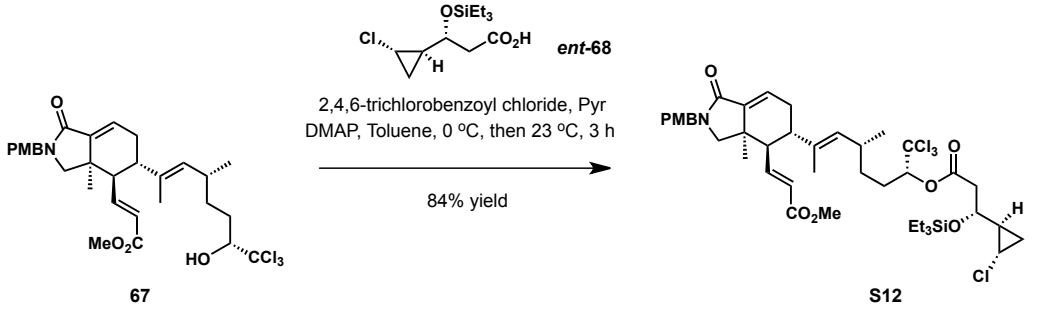
38.6, 32.7, 31.5, 31.4, 30.6, 30.4, 28.8, 26.8, 25.6, 20.9, 19.1, 19.0, 18.7, 14.2, 13.6. HRMS-ESI (*m*/z): $[M+Na]^+$ calcd for $C_{35}H_{41}Cl_4NO_6Na$, 734.1586; found, 734.1569.



26 **1**

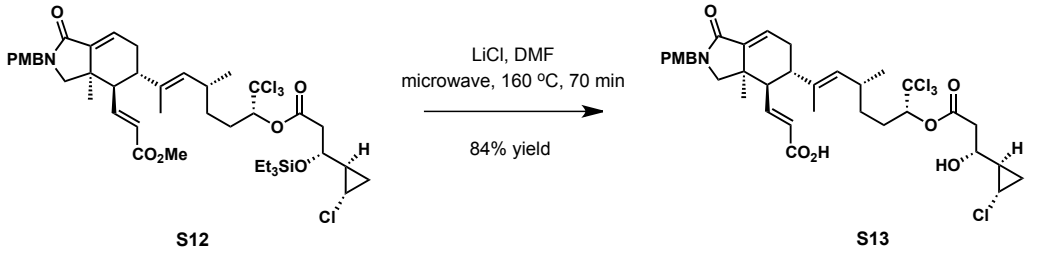
(5a*S*,6*E*,8*R*,11*R*,15*S*,18*E*,19a*R*,19b*R*)-15-((1*S*,2*R*)-2-Chlorocyclopropyl)-6,8,19b-trimethyl-11-(trichloromethyl)-5,5a,8,9,10,11,14,15-octahydro-1*H*-[1,5]dioxacyclohexadecino[9,10-*e*]isoindole-3,13,17(2*H*,19a*H*,19b*H*)-trione (1). 2,3-Dichloro-5,6-dicyano-*p*-benzoquinone (64 mg, 0.280 mmol) was added to a solution of substrate **26** (20 mg, 28.0 μmol) and water (2.5 μL (measured and injected with a 10 μL Hamilton syringe), 0.140 mmol) in 1,4-dioxane (2.8 mL). The solution was heated at 100 °C for 8 h. After cooling to 23 °C, CH_2Cl_2 (2.0 mL) was added followed by a mixture of saturated aqueous solutions of $Na_2S_2O_3$ and $NaHCO_3$ (1:1, 4.0 mL). The mixture was stirred at 23 °C for 30 min. The biphasic solution was extracted with ethyl acetate (3x4 mL). The combined organic layers were washed with brine and dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography (100% ethyl acetate) to deliver **1** (15.0 mg, 25.2 μmol, 90% yield). $[\alpha]_D^{23}$ +36.5° (*c* 1.0, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 6.74 (d, *J*=7.2 Hz, 1H), 6.72 (d, *J*=7.7 Hz, 1H), 5.76 (d, *J*=16.0 Hz, 1H), 5.63 (s, 1H), 5.40 (dd, *J*=8.1, 3.6 Hz, 1H), 4.86 (d, *J*=9.2 Hz, 1H), 4.66 (ddd, *J*=9.3, 7.5, 5.6 Hz, 1H), 3.25-3.18 (m, 1H), 3.14 (d, *J*=8.9 Hz, 1H), 2.87 (dd, *J*=7.9, 5.6 Hz, 3H), 2.77-2.69 (m, 1H), 2.65-2.56 (m, 1H), 2.48 (dd, *J*=14.1, 8.1 Hz, 1H), 2.14-2.02 (m, 1H), 1.91-

1.78 (m, 2H), 1.74 (d, *J*=1.6 Hz, 3H), 1.54 (tdd, *J*=14.3, 7.1, 4.5 Hz, 2H), 1.42 (s, 4H), 1.34 (ddd, *J*=13.7, 9.5, 5.2 Hz, 1H), 1.13 (ddd, *J*=10.2, 6.5, 4.1 Hz, 1H), 1.00-0.95 (m, 1H), 0.94 (d, *J*=6.8 Hz, 3H): ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 169.7, 167.6, 164.6, 147.9, 140.1, 134.0, 130.7, 130.2, 123.5, 99.6, 81.1, 71.5, 49.8, 46.5, 44.4, 38.7, 32.8, 31.5, 31.4, 30.5, 28.6, 26.8, 25.6, 19.0, 18.7, 14.2.



(*E*)-Methyl 3-((3a*R*,4*R*,5*S*)-2-(4-methoxybenzyl)-3a-methyl-1-oxo-5-((4*R*,7*R*, *E*)-8,8,8-trichlo-ro-7-(((*R*)-3-((1*R*,2*S*)-2-chlorocyclopropyl)-3-((triethylsilyl) oxy)propanoyl)oxy)-4-methyl-oct-2-en-2-yl)-2,3,3a,4,5,6-hexahydro-1*H*-iso indol-4-yl)acrylate (S12). 2,4,6-Trichloro-benzoyl chloride (39 μL, 0.246 mmol) was added to a solution of acid ***ent*-68** (33 mg, 0.118 mmol) and pyridine (48 μL, 0.590 mmol) in toluene (2.0 mL) at 0 °C. After 45 min, a solution of alcohol **67** (59 mg, 98.6 μmol) and 4-(dimethylamino)pyridine (30 mg, 0.246 mmol) in toluene (2.0 mL) was added at 0 °C. After another 10 min, the reaction mixture was warmed to 23 °C and stirred for an additional 1 h. Brine was added, layers separated, and the aqueous layer was extracted with ethyl acetate (3x5 mL). The combined organic layers were dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography (50% ethyl acetate in hexanes) to deliver **S12** (71 mg, 82.8 μmol, 84% yield). $[\alpha]_D^{23}$ -28.4° (*c* 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.15 (d,

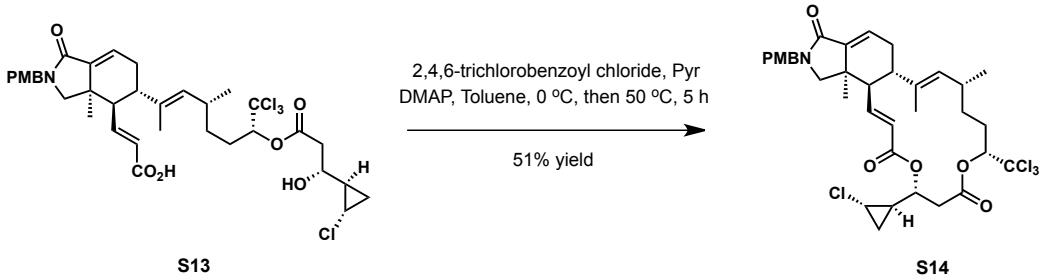
J=8.5 Hz, 2H), 6.85 (d, *J*=8.6 Hz, 2H), 6.74 (dd, *J*=7.4, 3.1 Hz, 1H), 6.56 (dd, *J*=15.6, 10.3 Hz, 1H), 5.78 (d, *J*=15.5 Hz, 1H), 5.45 (dd, *J*=10.0, 2.2 Hz, 1H), 4.97 (dd, 9.6, 1.6 Hz, 1H), 4.62 (d, *J*=14.6 Hz, 1H), 4.19 (d, *J*=14.6 Hz, 1H), 3.86 (q, *J*=6.0 Hz, 1H), 3.80 (s, 3H), 3.69 (s, 3H), 3.09 (d, *J*=9.1 Hz, 1H), 2.99 (dt, *J*=7.4, 3.7 Hz, 1H), 2.70 (dd, *J*=5.9, 1.2 Hz, 2H), 2.56 (d, *J*=9.2 Hz, 1H), 2.40 (t, *J*=10.7 Hz, 1H), 2.30 (tt, *J*=9.0, 5.7 Hz, 1H), 2.17 (dddd, *J*=19.7, 16.6, 9.7, 4.1 Hz, 2H), 2.12-1.97 (m, 2H), 1.80-1.68 (m, 1H), 1.55-1.43 (m, 3H), 1.36 (td, *J*=12.0, 11.1, 5.5 Hz, 1H), 1.29-1.18 (m, 1H), 1.15 (s, 3H), 0.94 (t, *J*=8.0 Hz, 10H), 0.83 (d, *J*=6.6 Hz, 3H), 0.60 (q, *J*=7.6 Hz, 6H): ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 169.9, 167.0, 166.1, 159.0, 147.8, 140.3, 134.2, 133.7, 129.5, 129.1, 128.3, 122.6, 114.0, 100.0, 81.2, 68.5, 55.2, 53.7, 51.4, 50.1, 49.4, 46.0, 42.4, 41.5, 33.0, 32.1, 30.5, 29.4, 28.6, 28.4, 28.0, 20.8, 13.2, 12.8, 6.8, 4.9. HRMS-ESI (*m*/z): $[M+Na]^+$ calcd for $C_{42}H_{59}Cl_4NO_7SiNa$, 880.2712; found, 880.2718.



S12 S13

(*E*)-3-((3a*R*,4*R*,5*S*)-2-(4-Methoxybenzyl)-3a-methyl-1-oxo-5-((4*R*,7*R*,*E*)-8,8,8-trichloro-7-(((*R*)-3-((1*R*,2*S*)-2-chlorocyclopropyl)-3-hydroxypropanoyl)oxy)-4-methyloct-2-en-2-yl)-2,3,3a,4,5,6-hexahydro-1*H*-isoindol-4-yl)acrylic acid (S13). Lithium chloride (1.95 g, 46.1 mmol) was added to a solution of substrate **S12** (66 mg, 76.7 μmol) in DMF (4.0 mL) in a microwave vial. The mixture was sealed and heated in a microwave reactor at 160 °C for 70 min. The heterogeneous mixture was

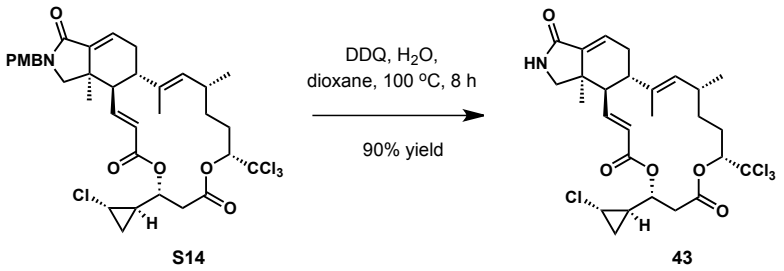
cooled to 23 °C and diluted with ethyl acetate (3 mL) and water (5 mL). The mixture was stirred until all precipitate dissolved. The resulting solution was extracted with ethyl acetate (3x5 mL) and the combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography (50% ethyl acetate in hexanes) to deliver **S13** (47 mg, 64.4 μmol, 84% yield) and a byproduct of only the triethylsilyl ether cleavage (hydroxy methyl ester) (6 mg, 7.7 μmol, 10% yield). $[\alpha]_D^{23}$ -3.1° (*c* 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.14 (d, *J*=8.6 Hz, 2H), 6.85 (d, *J*=8.6 Hz, 2H), 6.77 (t, *J*=5.1 Hz, 1H), 6.64 (dd, *J*=15.4, 10.3 Hz, 1H), 5.78 (d, *J*=15.5 Hz, 1H), 5.48 (dd, *J*=10.2, 2.2 Hz, 1H), 4.95 (d, *J*=9.2 Hz, 1H), 4.63 (d, *J*=14.6 Hz, 1H), 4.18 (d, *J*=14.6 Hz, 1H), 3.79 (s, 3H), 3.72 (td, *J*=7.2, 4.4 Hz, 1H), 3.16-3.04 (m, 2H), 2.79-2.68 (m, 2H), 2.57 (d, *J*=9.2 Hz, 1H), 2.44 (t, *J*=10.6 Hz, 1H), 2.34-2.27 (m, 1H), 2.17 (dt, *J*=9.5, 3.4 Hz, 2H), 2.08 (ddd, *J*=10.7, 6.5, 2.2 Hz, 1H), 2.03-1.98 (m, 1H), 1.75 (dtd, *J*=15.0, 10.3, 4.9 Hz, 1H), 1.50 (s, 3H), 1.40 (dtd, *J*=9.7, 6.7, 3.2 Hz, 1H), 1.32 (ddd, *J*=17.1, 8.2, 4.4 Hz, 2H), 1.24-1.19 (m, 1H), 1.15 (s, 3H), 1.06-0.97 (m, 2H), 0.88 (d, *J*=7.2 Hz, 1H), 0.85 (d, *J*=6.6 Hz, 3H): ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 170.8, 167.1, 159.0, 149.8, 140.1, 134.2, 133.5, 129.5, 128.1, 114.1, 99.7, 97.7, 81.2, 68.1, 60.3, 55.2, 53.8, 49.4, 46.1, 41.6, 40.9, 32.7, 31.9, 30.0, 29.6, 28.4, 27.4, 21.0, 20.7, 14.1, 13.2. HRMS-ESI (*m*/z): $[M-H]^-$ calcd for $C_{35}H_{42}Cl_4NO_7$, 728.1715; found, 728.1727.



S13 **S14**

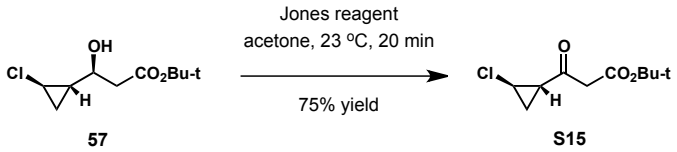
(5a*S*,6*E*,8*R*,11*R*,15*R*,18*E*,19a*R*,19b*R*)-15-((1*R*,2*S*)-2-Chlorocyclopropyl)-2-(4-methoxybenzyl)-6,8,19b-trimethyl-11-(trichloromethyl)-5,5a,8,9,10,11,14,15-octahydro-1*H*-[1,5]dioxacyclo-hexadecino[9,10-*e*]isoindole-3,13,17(2*H*,19a*H*, 19b*H*)-trione (S14). 2,4,6-Trichlorobenzoyl chloride (0.24 mL, 1.53 mmol) was added to a solution of acid **S13** (28 mg, 38.2 μmol) and pyridine (0.19 mL, 2.29 mmol) in toluene (2.5 mL) at 0 °C. After 45 min, 4-(dimethylamino)pyridine (19 mg, 0.153 mmol) was added to the reaction mixture at 0 °C. After another 10 min, the reaction mixture was warmed to 50 °C for 5 h. Brine was added to the resulting solution and the mixture was extracted with ethyl acetate (3x5 mL). The combined organic layers were dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography (50% ethyl acetate in hexanes) to deliver substrate **S14** (14 mg, 19.5 μmol, 51% yield). $[\alpha]_D^{23}$ +12.9° (*c* 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.18 (d, *J*=8.6 Hz, 2H), 6.86 (d, *J*=8.6 Hz, 2H), 6.71 (dd, *J*=7.9 2.6 Hz, 1H), 6.48 (dd, *J*=15.3, 11.1 Hz, 1H), 5.72 (d, *J*=15.3 Hz, 1H), 5.72 (d, *J*=15.3 Hz, 5.53 (dd, *J*=10.7, 2.4 Hz, 1H), 4.97-4.81 (m, 2H), 4.63 (d, *J*=14.6 Hz, 1H), 4.20 (d, *J*=14.6 Hz, 1H), 3.80 (s, 3H), 3.26-3.14 (m, 2H), 2.93-2.84 (m, 1H), 2.77 (dd, *J*=16.2, 2.6 Hz, 1H), 2.66 (d, *J*=8.8 Hz, 1H), 2.45-2.32 (m, 3H), 2.04 (dddd, *J*=12.9, 8.8, 6.5, 2.6 Hz, 1H), 1.99-1.87 (m, 2H), 1.69-1.58 (m, 1H), 1.53 (s, 3H), 1.42 (dddd, *J*=9.6, 6.5, 4.8, 2.1 Hz, 1H), 1.15 (s, 3H), 1.09 (tdt, *J*=11.6, 8.3, 3.8 Hz, 3H), 0.98 (dt, *J*=7.4, 6.4 Hz, 1H), 0.93 (d, *J*=6.5 Hz, 3H): ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 169.1, 167.1, 164.7, 159.1, 147.1, 140.9, 134.2, 131.6, 129.6, 129.2, 128.3, 125.0, 114.1, 99.6, 80.5, 71.5, 55.2, 54.1, 53.2, 46.7, 46.1, 42.3, 39.1, 31.6, 31.5, 31.1, 31.0, 28.4, 27.3, 25.6,

19.6, 18.5, 14.1. HRMS-ESI (*m*/z): $[M+Na]^+$ calcd for $C_{35}H_{41}Cl_4NO_6Na$, 734.1586; found, 734.1584.

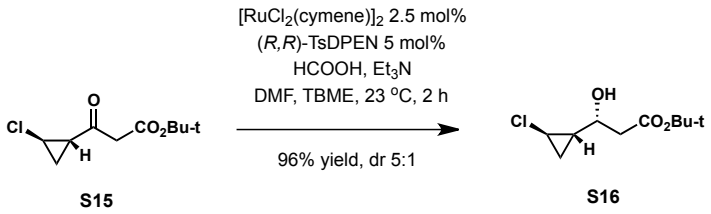


(5a*S*,6*E*,8*R*,11*R*,15*R*,18*E*,19a*R*,19b*R*)-15-((1*R*,2*S*)-2-Chlorocyclopropyl)-6,8,19b-trimethyl-11-(trichloromethyl)-5,5a,8,9,10,11,14,15-octahydro-1*H*-[1,5]dioxacyclohexadecino[9,10-*e*]isoindole-3,13,17(2*H*,19a*H*,19b*H*)-trione (43). 2,3-Dichloro-5,6-dicyano-*p*-benzoquinone (64.0 mg, 0.280 mmol) was added to a solution of substrate **S14** (16 mg, 22.4 μmol) and water (2.0 μL, (measured and injected with a 10 μL Hamilton syringe) 0.111 mmol) in 1,4-dioxane (2.2 mL). The solution was heated at 100 °C for 8 h. After cooling to 23 °C, CH_2Cl_2 (2.0 mL) was added followed by a mixture of saturated aqueous solutions of $Na_2S_2O_3$ and $NaHCO_3$ (1:1, 4.0 mL). The mixture was stirred at 23 °C for 30 min. The biphasic solution was extracted with ethyl acetate (3x4 mL). The combined organic layers were washed with brine and dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography (100% ethyl acetate) to deliver **43** (10 mg, 20.2 μmol, 90% yield). $[\alpha]_D^{23}$ +62.3° (*c* 1.0, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 6.73 (dd, *J*=8.0, 2.6 Hz, 1H), 6.55 (dd, 15.3, 11.1 Hz, 1H), 5.79 (d, *J*=15.2 Hz, 1H), 5.59-5.52 (m, 2H), 5.00-4.87 (m, 2H), 3.35 (d, *J*=8.7 Hz, 1H), 3.35 (d, *J*=8.7 Hz, 1H), 3.24 (dt, *J*=7.4, 3.6 Hz, 1H), 2.97-2.85 (m, 2H), 2.79 (dd, *J*=16.2, 2.4 Hz, 1H), 2.52-2.33 (m, 3H), 2.06 (dddd, *J*=14.6, 8.6, 6.4, 2.3 Hz, 1H), 1.94 (dddd, *J*=24.4, 16.5, 9.9, 4.4 Hz,

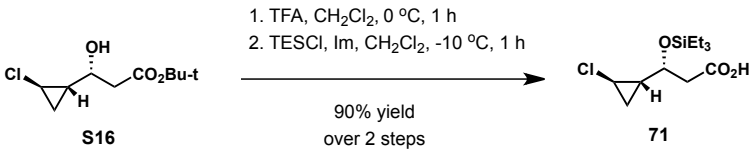
2H), 1.71 (qd, *J*=11.6, 10.3, 2.2 Hz, 1H), 1.57 (d, *J*=1.5 Hz, 3H), 1.49-1.41 (m, 1H), 1.30 (s, 3H), 1.23-1.15 (m, 1H), 1.14-1.05 (m, 2H), 1.00 (q, *J*=6.8 Hz, 1H), 1.00 (q, *J*=6.8 Hz, 3H): ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 169.8, 169.1, 164.7, 147.0, 139.9, 134.0, 131.8, 130.2, 125.2, 99.6, 80.6, 71.5, 54.1, 49.2, 46.6, 44.4, 39.1, 31.7, 31.6, 31.2, 31.0, 28.1, 27.3, 25.6, 19.6, 18.5, 14.1. HRMS-ESI (*m*/z): $[M+Na]^+$ calcd for $C_{27}H_{33}Cl_4NO_5Na$, 614.1011; found, 614.0989.



***tert*-Butyl 3-((1*S*,2*R*)-2-chlorocyclopropyl)-3-oxopropanoate (S15).** Jones reagent (2.0 M, 0.75 mL, 1.42 mmol) was added dropwise to a solution of alcohol **57** (0.210 g, 0.951 mmol) in acetone (9.5 mL). The mixture was stirred for 20 min at 23 °C. Methanol (4 mL) was added and stirring was continued for 30 min. After addition of water (4 mL), the mixture was extracted with diethyl ether (3x30 mL). The combined organic phase was washed with brine, dried over $MgSO_4$, concentrated and residue was purified by column chromatography on silica gel (30% diethyl ether in pentanes) to deliver keto ester **S15** (0.156 g, 0.713 mmol, 75%). $[\alpha]_D^{23}$ -14.3° (*c* 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 3.51 (s, 2H), 3.31 (ddd, *J*=7.6, 4.9, 2.8 Hz, 1H), 2.42 (ddd, *J*=8.9, 5.9, 2.7 Hz, 1H), 1.66 (dt, *J*=7.4, 5.8 Hz, 1H), 1.48 (s, 9H), 1.45-1.38 (m, 1H): ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 200.0, 165.7, 82.3, 51.7, 35.8, 30.8, 27.9, 21.0. HRMS-ESI (*m*/z): $[M+Na]^+$ calcd for $C_{10}H_{15}ClO_3Na$, 241.0607; found, 241.0605.

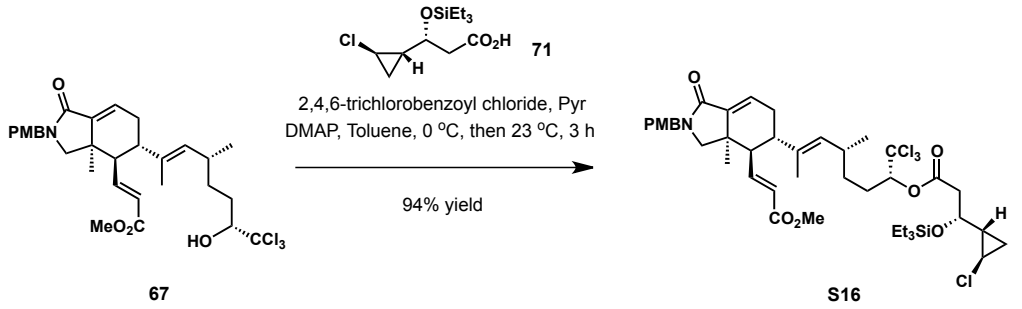


(*R*)-*tert*-Butyl 3-((1*S*,2*R*)-2-chlorocyclopropyl)-3-hydroxypropanoate (S16). Dichloro(*p*-cymene)ruthenium(II) dimer (11 mg, 17.8 μmol) and Et_3N (0.40 mL, 2.85 mmol) were added to a solution of (1*R*,2*R*)-(-)-*N*-*p*-tosyl-1,2-diphenylethylenediamine (13 mg, 35.6 μmol) in DMF (0.36 mL) at 23 °C. The mixture was stirred for 1 h. In parallel, a mixture of HCO_2H (0.18 mL, 7.13 mmol) and Et_3N (0.40 mL, 2.85 mmol) was prepared at 23 °C for 10 min. A solution of **S15** (0.156 g, 0.713 mmol) in *tert*-butyl methyl ether (1.4 mL) was added to the formic acid-triethylamine mixture followed by the solution of the preformed catalyst. The mixture was stirred at 23 °C for 3 h. Water (10 mL) was added, layers separated, and the aqueous layer extracted with ethyl acetate (3x10 mL). The combined organic phase was washed with brine, dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel (20% ethyl acetate in hexanes) to afford the alcohol **S16** (0.150 g, 0.684 mmol, 96% yield, dr 5:1). $[\alpha]_D^{23}$ -1.2° (*c* 1.0, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 3.74 (ddt, *J*=9.2, 6.2, 3.0 Hz, 1H), 3.06 (q, *J*=1.8 Hz, 1H), 2.98 (ddd, *J*=7.2, 3.8, 3.2 Hz, 1H), 2.64-2.34 (m, 2H), 1.47 (s, 9H), 1.31 (dtd, *J*=9.6, 6.4, 3.2 Hz, 1H), 1.14-1.04 (m, 1H), 0.99 (ddd, *J*=9.9, 6.3, 3.8 Hz, 1H): ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 171.9, 81.6, 68.4, 41.6, 30.1, 28.0, 27.3, 13.0. HRMS-ESI (*m*/z): $[M+Na]^+$ calcd for $C_{10}H_{17}ClO_3Na$, 243.0764; found, 243.0766.



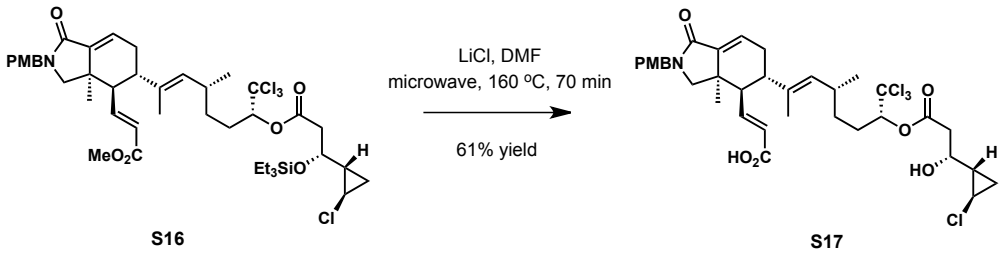
(*R*)-3-((1*S*,2*R*)-2-Chlorocyclopropyl)-3-((triethylsilyl)oxy)propanoic acid (71). Ester **S16** (0.111 g, 0.502 mmol) was stirred in a solution of trifluoroacetic acid and CH_2Cl_2 (1:1, v/v, 1.3 mL) at 0 °C. After 10 min, the reaction mixture was warmed to 23 °C and stirred for another hour. The mixture was concentrated, toluene was added (15 mL), and the solution was concentrated again. The dilution-concentration protocol was repeated trice. Chlorotriethylsilane (0.2 mL, 0.975 mmol) was added to a stirring solution of the resulting crude hydroxy acid (73.0 mg, 0.443 mmol) and imidazole (75.0 mg, 1.10 mmol) in CH_2Cl_2 (4.4 mL) at -10 °C. After 1 h, the reaction mixture was poured into acetate buffer (pH=4, 5 mL) and the aqueous layer was extracted with ethyl acetate (3x5 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated. To hydrolyze a residual amount of the silyl ester, a mixture of the crude oil and $NaHCO_3$ (0.186 g, 2.21 mmol) in methanol (2.0 mL) was stirred at 23 °C for 20 min. Water (20 mL) was added, the mixture was acidified with 1 M aqueous HCl to pH ~ 4, and then extracted with dichloromethane (3x6 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated, delivering **71** which was used without further purification (0.111 g, 0.398 mmol, 90% yield over two steps). $[\alpha]_D^{23}$ -40.2° (*c* 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 3.99 (q, *J*=6.0 Hz, 1H), 2.91 (dt, *J*=7.3, 3.6 Hz, 1H), 2.74-2.51 (m, 2H), 1.50-1.39 (m, 1H), 1.06-0.86 (m, 9H), 0.68-0.55 (m, 6H): ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 176.5, 68.1, 42.7, 30.2, 28.1,

13.0, 6.7, 4.9. HRMS-ESI (*m*/z): $[M+Na]^+$ calcd for $C_{12}H_{23}ClO_3SiNa$, 301.1003; found, 301.0997.



(*E*)-Methyl 3-((3a*R*,4*R*,5*S*)-2-(4-methoxybenzyl)-3a-methyl-1-oxo-5-((4*R*,7*R*, *E*)-8,8,8-trichlo-ro-7-(((*R*)-3-((1*S*,2*R*)-2-chlorocyclopropyl)-3-((triethylsilyl) oxy)propanoyl)oxy)-4-methyl-oct-2-en-2-yl)-2,3,3a,4,5,6-hexahydro-1*H*-iso indol-4-yl)acrylate (S16). 2,4,6-Trichloro-benzoyl chloride (0.14 mL, 0.917 mmol) was added to a solution of acid **71** (64 mg, 0.229 mmol) and pyridine (0.14 mL, 1.72 mmol) in toluene (4.6 mL) at 0 °C. After 45 min, a solution of alcohol **67** (0.164 g, 0.275 mmol) and 4-(dimethylamino)pyridine (70 mg, 0.573 mmol) in toluene (4.6 mL) was added at 0 °C. After 10 min, the reaction mixture was warmed to 23 °C and stirred for an additional 1 h. Brine was added, the layer were separated, and the aqueous layer was extracted with ethyl acetate (3x5 mL). The combined organic layers were dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography (50% ethyl acetate in hexanes) to deliver **S16** (0.184 g, 0.215 mmol, 94% yield). $[\alpha]_D^{23}$ -26.4° (*c* 1.0, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.15 (d, *J*=8.6 Hz, 2H), 6.85 (d, *J*=8.6 Hz, 2H), 6.75 (dd, *J*=7.4, 3.0 Hz, 1H), 6.56 (dd, *J*=15.5, 10.3 Hz, 1H), 5.78 (dd, *J*=15.6, 0.7 Hz, 1H), 5.46 (dd, *J*=10.1, 2.2 Hz, 1H), 4.97 (dd, *J*=9.6, 1.6 Hz, 1H), 4.62 (d, *J*=14.5 Hz, 1H), 4.19 (d, *J*=14.6 Hz, 1H), 4.05 (q, *J*=6.0 Hz, 1H), 3.80 (s, 3H), 3.69 (s, 3H), 3.09 (d, *J*=9.2 Hz, 1H), 2.93 (dt, *J*=7.3, 3.6 Hz,

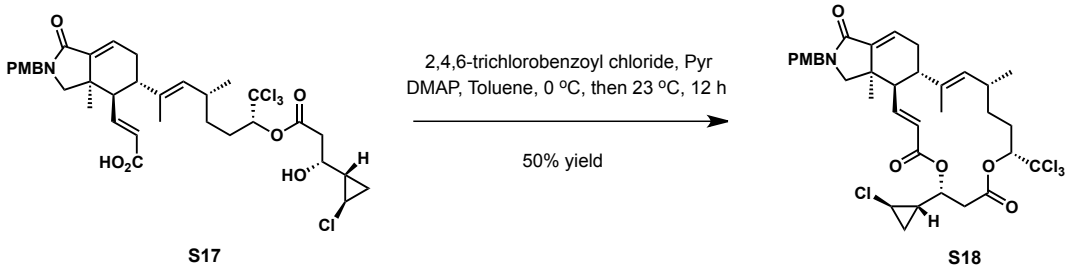
1H), 2.76-2.60 (m, 2H), 2.56 (d, *J*=9.2 Hz, 1H), 2.40 (t, *J*=10.7 Hz, 1H), 2.30 (dtt, *J*=9.7, 6.3, 3.9 Hz, 1H), 2.23-2.11 (m, 2H), 2.09-1.98 (m, 2H), 1.73 (dtd, *J*=14.9, 10.6, 4.9 Hz, 1H), 1.49 (s, 3H), 1.44 (ddd, *J*=9.9, 6.7, 5.6, 3.3 Hz, 1H), 1.36 (ddt, *J*=13.2, 10.8, 5.2 Hz, 1H), 1.30-1.19 (m, 2H), 1.15 (s, 3H), 1.04 (dt, *J*=7.2, 6.3 Hz, 1H), 0.94 (t, *J*=8.0 Hz, 9H), 0.84 (d, *J*=6.6 Hz, 3H), 0.59 (q, *J*=8.0 Hz, 6H): ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 169.7, 167.0, 166.0, 159.0, 147.7, 140.2, 134.2, 133.7, 129.5, 129.2, 128.3, 122.6, 114.0, 99.9, 81.1, 67.5, 55.2, 53.6, 51.4, 50.1, 49.4, 46.0, 42.5, 41.5, 33.0, 32.0, 30.2, 29.4, 28.6, 28.4, 28.1, 20.8, 13.1, 12.8, 6.7, 6.5, 5.7, 4.9. HRMS-ESI (*m*/z): $[M+Na]^+$ calcd for $C_{42}H_{59}Cl_4NO_7Na$, 880.2712; found, 880.2715.



S16 S17

(*E*)-3-((3a*R*,4*R*,5*S*)-2-(4-Methoxybenzyl)-3a-methyl-1-oxo-5-((4*R*,7*R*,*E*)-8,8,8-trichloro-7-(((*R*)-3-((1*S*,2*R*)-2-chlorocyclopropyl)-3-hydroxypropanoyl)oxy)-4-methyloct-2-en-2-yl)-2,3,3a,4,5,6-hexahydro-1*H*-isoindol-4-yl)acrylic acid (S17). Lithium chloride (5.29 g, 0.124 mol) was added to a solution of **S16** (0.179 g, 0.208 mmol) in DMF (10.4 mL) in a microwave vial. The vial was sealed and the mixture was heated in a microwave reactor at 160 °C for 70 min. The heterogeneous mixture was cooled to 23 °C and diluted with ethyl acetate (200 mL) and water (20 mL). The biphasic mixture was stirred until all solids dissolved. The layers were separated and the aqueous layer extracted with ethyl acetate (3x30 mL) and the combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated. The residue was

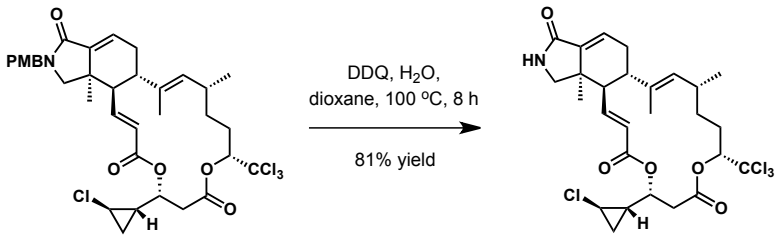
purified by column chromatography (50% ethyl acetate in hexanes) to deliver hydroxy acid **S17** (92 mg, 0.127 mmol, 61% yield) and a byproduct of only the triethylsilyl ether cleavage (hydroxy methyl ester) (27 mg, 37.4 μmol, 18% yield). $[\alpha]_D^{23}$ -30.1° (*c* 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.14 (d, *J*=8.5 Hz, 2H), 6.85 (d, *J*=8.6 Hz, 2H), 6.77 (q, *J*=5.2, 4.4 Hz, 1H), 6.69-6.57 (m, 1H), 5.78 (dd, *J*=15.8, 3.6 Hz, 1H), 5.48 (dd, *J*=10.2, 2.2 Hz, 1H), 4.95 (dd, *J*=9.2, 2.0 Hz, 1H), 4.63 (dd, *J*=14.7, 2.7 Hz, 1H), 4.18 (dd, *J*=14.7, 3.9 Hz, 1H), 3.86 (ddd, *J*=9.3, 6.4, 3.4 Hz, 1H), 3.79 (s, 3H), 3.09 (dd, *J*=9.4, 3.3 Hz, 1H), 3.00 (dt, *J*=7.3, 3.5 Hz, 1H), 2.82-2.67 (m, 2H), 2.57 (d, *J*=9.2 Hz, 1H), 2.44 (td, *J*=10.8, 4.9 Hz, 1H), 2.31 (tt, *J*=9.1, 6.4 Hz, 1H), 2.17 (dd, *J*=7.5, 4.9 Hz, 2H), 2.08-2.05 (m, 1H), 2.00 (ddt, *J*=14.7, 7.4, 2.9 Hz, 1H), 1.76 (dtd, *J*=13.9, 10.5, 5.1 Hz, 1H), 1.51 (s, 3H), 1.37 (dq, *J*=9.8, 3.3 Hz, 1H), 1.31 (ddd, *J*=11.4, 7.9, 5.5 Hz, 1H), 1.25 (t, *J*=7.1 Hz, 2H), 1.23-1.19 (m, 1H), 1.15 (s, 3H), 1.11 (q, *J*=6.8 Hz, 1H), 1.01 (ddd, *J*=9.9, 6.3, 3.8 Hz, 1H), 0.85 (d, *J*=6.8 Hz, 3H): ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 170.8, 167.1, 159.1, 149.9, 140.0, 137.8, 134.1, 133.6, 129.5, 129.0, 128.1, 125.2, 114.1, 99.7, 81.2, 67.4, 55.2, 53.8, 49.7, 49.4, 46.1, 41.6, 41.0, 32.7, 31.9, 29.9, 29.4, 28.4, 27.3, 21.4, 20.6, 13.4, 13.0. HRMS-ESI (*m*/z): $[M-H]^-$ calcd for $C_{35}H_{42}Cl_4NO_7$, 728.1715; found, 728.1695.



S17 S18

(5a*S*,6*E*,8*R*,11*R*,15*R*,18*E*,19a*R*,19b*R*)-15-((1*S*,2*R*)-2-Chlorocyclopropyl)-2-(4-methoxybenzyl)-6,8,19b-trimethyl-11-(trichloromethyl)-5,5a,8,9,10,11,14,15-

octahydro-1*H*-[1,5]dioxacyclo-hexadecino[9,10-*e*]isoindole-3,13,17(2*H*,19a*H*, 19b*H*)-trione (S18). 2,4,6-Trichlorobenzoyl chloride (0.68 mL, 4.37 mmol) was added to a solution of acid **S17** (80 mg, 0.109 mmol) and pyridine (0.53 mL, 2.29 mmol) in toluene (7.3 mL) at 0 °C. After 45 min, 4-(dimethylamino)pyridine (53 mg, 0.437 mmol) was added at 0 °C. After 10 min, the reaction mixture was kept at 23 °C for 12 h. Brine was added, the layers were separated, and the aqueous layer was extracted with ethyl acetate (3x10 mL). The combined organic layers were dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography (50% ethyl acetate in hexanes) to deliver **S18** (39 mg, 54.5 μmol, 50% yield). $[\alpha]_D^{23}$ +19.0° (*c* 1.0, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 7.16 (d, *J*=8.6 Hz, 2H), 6.85 (d, *J*=8.6 Hz, 2H), 6.71 (dd, *J*=8.0, 2.6 Hz, 1H), 6.46 (dd, *J*=15.3, 11.1 Hz, 1H), 5.70 (d, *J*=15.2 Hz, 1H), 5.53 (dd, *J*=10.8, 2.4 Hz, 1H), 5.01 (ddd, *J*=10.9, 8.8, 3.1 Hz, 1H), 4.85 (dd, *J*=8.9, 1.9 Hz, 1H), 4.65 (d, 14.6 Hz, 1H), 4.15 (d, *J*=14.6 Hz, 1H), 3.79 (s, 3H), 3.16 (d, *J*=9.0 Hz, 1H), 3.00-2.94 (m, 1H), 2.94-2.83 (m, 2H), 2.61 (d, *J*=8.9 Hz, 1H), 2.44-2.33 (m, 3H), 2.08-1.99 (m, 1H), 1.92 (dddd, *J*=19.5, 16.6, 10.0, 4.4 Hz, 2H), 1.69-1.59 (m, 1H), 1.53 (s, 3H), 1.41 (ddt, *J*=11.8, 6.4, 3.1 Hz, 1H), 1.24-1.19 (m, 2H), 1.12 (s, 3H), 1.06 (tdd, *J*=8.6, 6.3, 3.9 Hz, 2H), 0.92 (d, *J*=6.5 Hz, 3H): ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 169.0, 167.1, 164.6, 159.0, 147.2, 140.9, 134.0, 131.7, 129.6, 129.3, 128.3, 124.9, 114.0, 99.6, 80.5, 70.9, 55.2, 53.9, 53.1, 46.6, 46.1, 42.2, 39.5, 31.6, 31.5, 31.2, 29.6, 28.3, 27.3, 25.8, 19.6, 18.5, 15.1. HRMS-ESI (*m*/z): $[M+Na]^+$ calcd for $C_{35}H_{41}Cl_4NO_6Na$, 734.1586; found, 734.1566.



Muironolide A (44). 2,3-Dichloro-5,6-dicyano-*p*-benzoquinone (118 mg, 0.518 mmol) was added to a solution of **S18** (37 mg, 51.9 μmol) and water (4.7 μL (measured and injected into solution with a 10 μL Hamilton syringe), 0.259 mmol) in 1,4-dioxane (5.2 mL). The solution was heated at 100 °C for 8 h. After cooling to 23 °C, CH_2Cl_2 (2.0 mL) was added followed by a mixture of saturated aqueous solutions of $Na_2S_2O_3$ and $NaHCO_3$ (1:1, 4.0 mL). The mixture was stirred at 23 °C for 30 min. The layers were separated and the aqueous layer was extracted with ethyl acetate (3x10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography (100% ethyl acetate) to deliver muironolide A, **44** (21 mg, 35.3 μmol, 68% yield) and recovered starting material **S18** (6 mg, 8.4 μmol, 16%). The recovered starting material was resubmitted to the same reaction conditions shown above to deliver an additional amount of muironolide A, **44** (4 mg, 6.86 μmol, 82% yield) for a total of 25 mg (42.2 μmol, 81% overall yield). $[\alpha]_D^{23}$ +42.3° (*c* 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 6.72 (dd, *J*=8.0 2.6 Hz, 1H), 6.53 (dd, *J*=15.2, 11.1 Hz, 1H), 5.93 (s, 1H), 5.76 (d, *J*=15.3 Hz, 1H), 5.54 (dd, *J*=10.7, 2.5 Hz, 1H), 5.03 (ddd, *J*=11.3, 8.8, 3.0 Hz, 1H), 4.88 (dd, *J*=9.0, 1.8 Hz, 1H), 3.33 (d, *J*=8.8 Hz, 1H), 3.01-2.96 (m, 1H), 2.96-2.86 (m, 2H), 2.84 (d, *J*=8.7 Hz, 1H), 2.47-2.35 (m, 3H), 2.05 (ddd, *J*=14.6, 8.8, 6.3,

2.7 Hz, 1H), 2.00-1.86 (m, 2H), 1.74-1.66 (m, 1H), 1.56 (s, *J*=1.4 Hz, 3H), 1.46-1.39 (m, 1H), 1.28 (s, 3H), 1.25 (td, *J*=6.3, 2.1 Hz, 1H), 1.21-1.14 (m, 1H), 1.09 (dqd, *J*=11.8, 5.9, 4.9, 2.9 Hz, 2H), 0.94 (d, *J*=6.5 Hz, 3H): ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 170.0, 169.0, 164.6, 147.1, 140.0, 133.9, 131.8, 130.3, 125.1, 99.6, 80.6, 71.0, 54.0, 49.3, 46.6, 44.4, 39.5, 31.7, 31.6, 31.2, 30.4, 28.1, 27.3 25.8, 19.6, 18.5, 15.2. HRMS-ESI (*m*/z): $[M+Na]^+$ calcd for $C_{27}H_{33}Cl_4NO_5Na$, 614.1011; found, 614.1006.

^{1}H NMR data for natural muironolide A and synthetic compounds 1, 43, and 44.

position	natural, *d* (*J*)	synthetic **44**, *d* (*J*)	synthetic **1**, *d* (*J*)	synthetic **43**, *d* (*J*)
1				
2	5.77 (15.5)	5.76 (15.3)	5.76 (16.0)	5.79 (15.2)
3	6.53 (15.5, 11.6)	6.53 (15.2, 11.1)	6.72 (7.7)	6.73 (8.0, 2.6)
4	2.45 (11.6)	2.44 (11.8)	2.73	2.45 (11.8)
5				
6	3.33 (8.8)	3.33 (8.8)	3.14 (8.9)	3.35 (8.7)
6’	2.84 (8.8)	2.84 (8.7)	2.87 (8.3)	2.88 (8.7)
7				

8				
9	6.73 (7.8, 2.5)	6.72 (8.0, 2.6)	6.74 (7.2)	6.73 (8.0, 2.6)
10	1.92	1.93	1.81	1.94
10’	2.40	2.42	2.73	2.40
11	1.70 (11.6, 8.7, 2.8)	1.69 (11.7, 9.1, 3.1)	1.85 (11.4, 9.6)	1.71 (11.6, 10.3, 2.2)
12				
13	4.88 (9.12)	4.88 (9.0)	4.86 (9.2)	4.90 (9.5)
14	2.42	2.42	2.6	2.45
15	1.16	1.17	1.42	1.18
15’	1.05	1.09	1.34	1.11
16	1.95	1.93	1.54	1.96
16’	2.04	2.05	2.08	2.06
17	5.55 (10.8, 2.4)	5.54 (10.7, 2.5)	5.40 (8.1, 3.6)	5.55 (11.1, 2.1)
18				
19				
20	2.90	2.91	2.87	2.79

	(16.2, 3.0)	(16.2, 2.9)	(7.9, 5.6)	(16.2, 2.4)
20’	2.94	2.94	2.86	2.92
	(16.2, 3.0)	(16.2, 3.1)	(7.9, 5.6)	(16.1, 4.5)
21	5.03	5.03	4.66	4.93
	(11.6, 9.4, 3.2)	(11.3, 8.8, 3.0)	(9.3, 7.5, 5.6)	(11.5, 9.1, 2.4)
22	1.44 (9.4, 9.4, 6.3, 3.2)	1.43 (9.4, 6.4, 3.0)	1.54 (14.3, 7.1, 4.5)	1.44
23	2.98 (6.5, 3.7, 3.2)	2.98 (7.3, 3.8, 3.6)	3.22 (7.3, 3.6)	3.24 (7.5, 3.7)
24	1.09 (9.4, 6.5, 3.7)	1.09 (9.9, 6.4, 3.9)	0.98 (13.9, 7.0, 6.8)	1.00 (6.8)
24’	1.25 (6.5)	1.25 (6.9)	1.13 (10.2, 6.6, 4.1)	1.10
25	1.28	1.28	1.42	1.30
26	1.56	1.56	1.74	1.59
27		0.94 (6.5)	0.94 (6.8)	0.95 (6.5)

^{13}C NMR chemical shifts for natural muironolide A and synthetic compounds 1, 43, and 44.

position	natural, *d*	synthetic **44**, *d*	synthetic **1**, *d*	synthetic **43**, *d*
1	164.4	164.6	164.6	164.7
2	124.8	125.1	123.5	125.2
3	146.9	147.1	147.9	147.0
4	53.6	54.0	49.8	54.1
5	44.0	44.4	44.4	44.4
6	49.0	49.3	49.8	49.2
7	169.7	170.0	169.7	169.8
8	139.7	140.0	140.1	139.9
9	130.0	130.0	130.2	130.2
10	31.3	31.6	31.4	31.6
11	46.2	46.6	46.5	46.6
12	133.8	133.9	134.0	134.0
13	131.6	131.8	130.7	131.8
14	30.8	31.2	30.5	31.2
15	31.4	31.7	32.8	31.7
16	27.1	27.3	26.8	27.3
17	80.3	80.6	81.1	80.6

18	99.3	99.6	99.6	99.6
19	168.9	169.0	167.6	169.1
20	39.4	39.5	38.7	39.1
21	70.8	71.0	71.5	71.5
22	25.6	25.8	25.6	25.6
23	30.0	30.4	31.5	31.0
24	14.7	15.2	14.2	14.1
25	27.7	28.1	28.6	28.1
26	19.1	19.6	18.7	19.6
27		18.5	19.0	18.5

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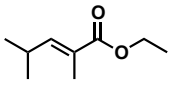
3 Number of Scans	4
4 Acquisition Date	2013-04-03T19:24:28
5 Spectrometer Frequency	499.86



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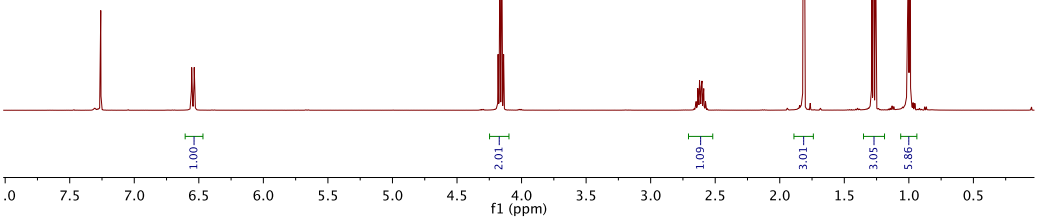

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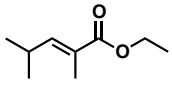

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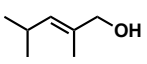
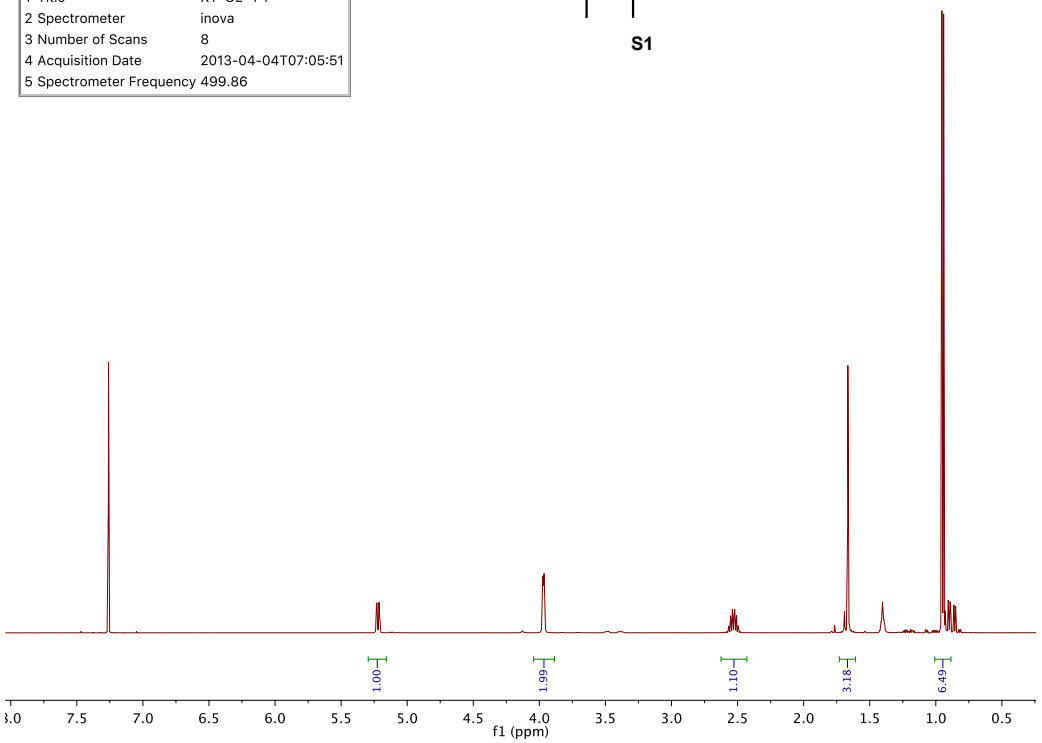


S1



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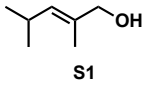

S1

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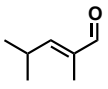

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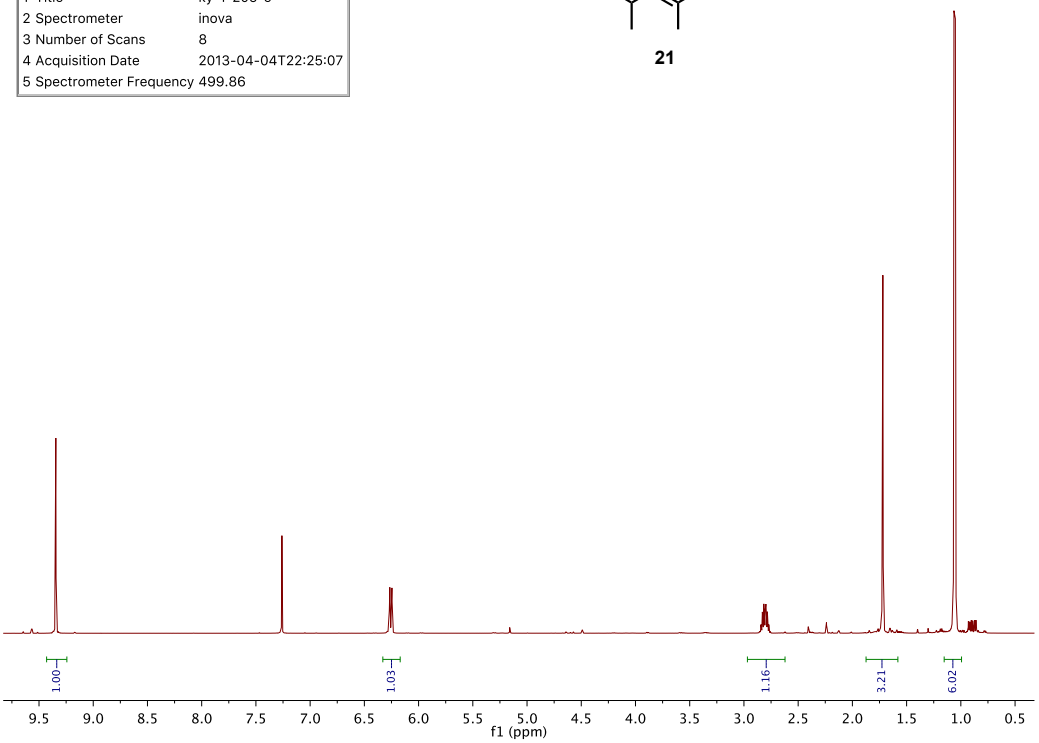

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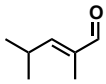

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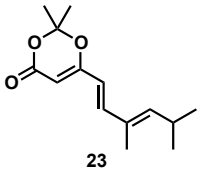

23

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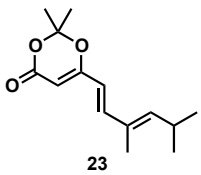

23

Parameter	Value
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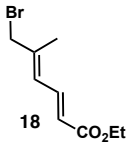

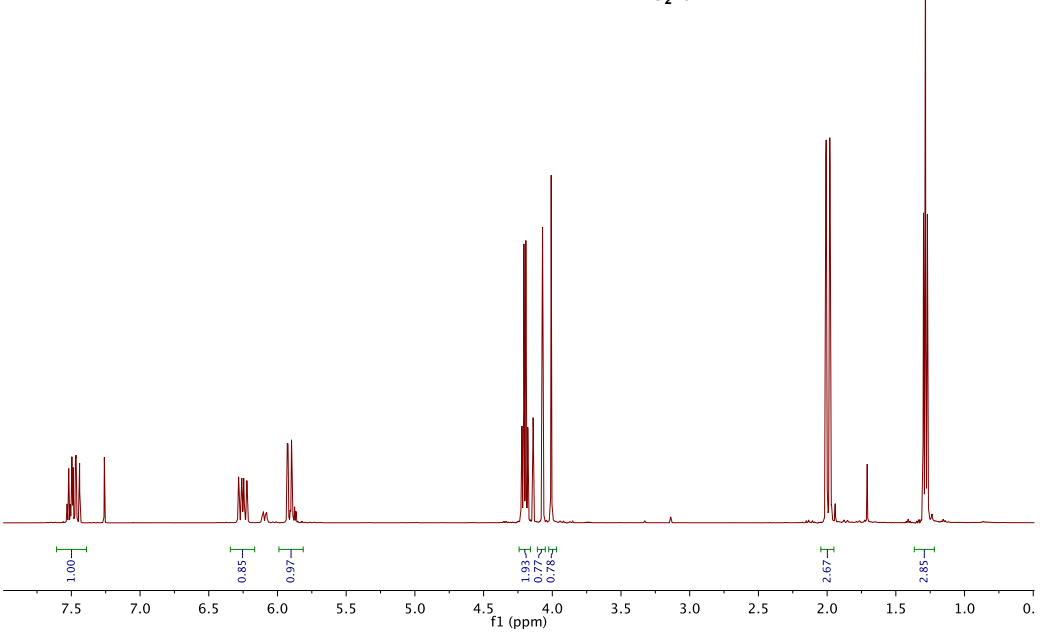

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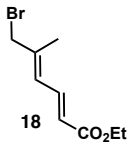
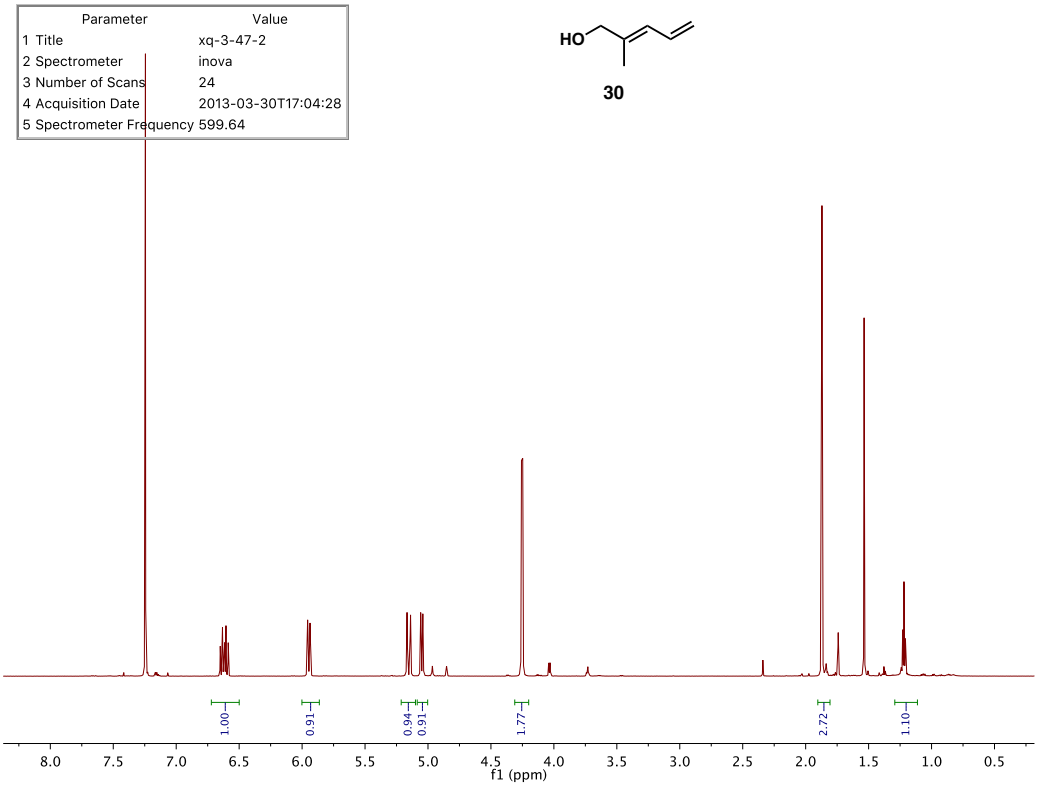
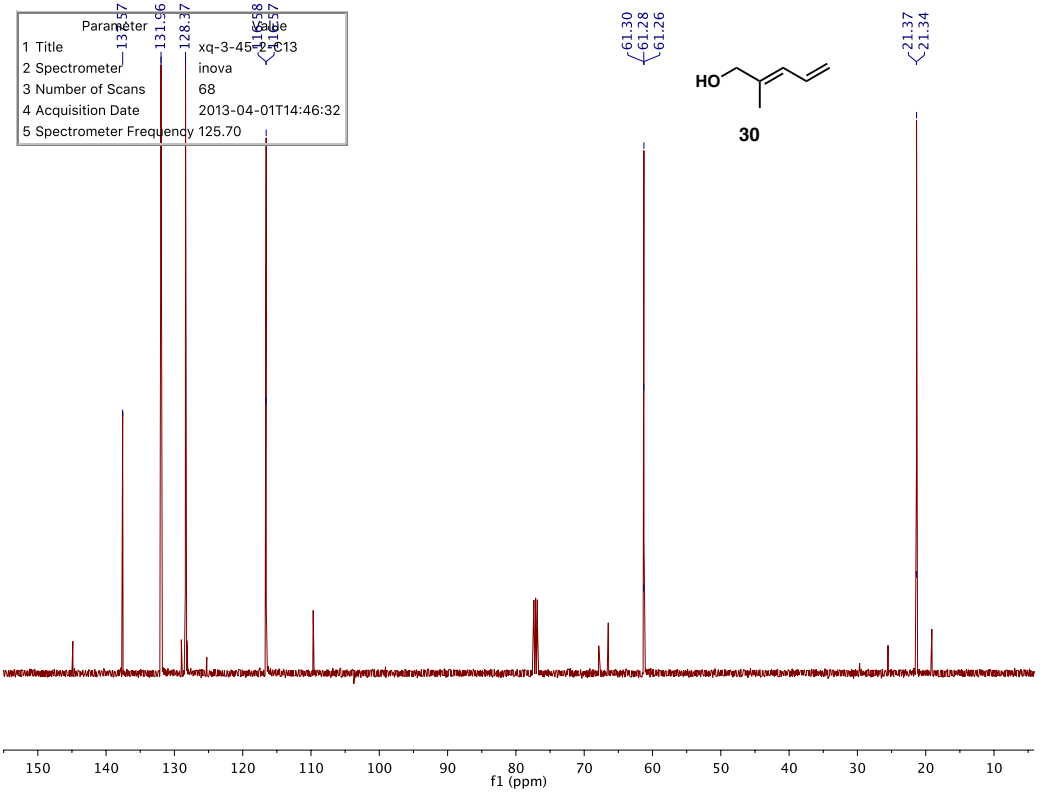
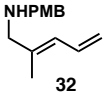
5 Spectrometer Frequency	125.70




Parameter Value
1 Title xq-3-47-2
2 Spectrometer inova
3 Number of Scans 24
4 Acquisition Date 2013-03-30T17:04:28
5 Spectrometer Frequency 599.64
HO
30
1.00
0.91
0.94
0.91
1.77
2.72
1.10
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

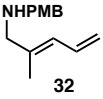

Parameter Value
1 Title xq-3-45-2-C13
2 Spectrometer inova
3 Number of Scans 68
4 Acquisition Date 2013-04-01T14:46:32
5 Spectrometer Frequency 125.70
137.57
131.96
128.37
114.58
114.57
61.30
61.28
61.26
21.37
21.34
HO
30
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

Parameter	Value
1 Title	xq-3-46-2
2 Spectrometer	inova
3 Number of Scans	16
4 Acquisition Date	2013-03-09T12:44:02
5 Spectrometer Frequency	499.86

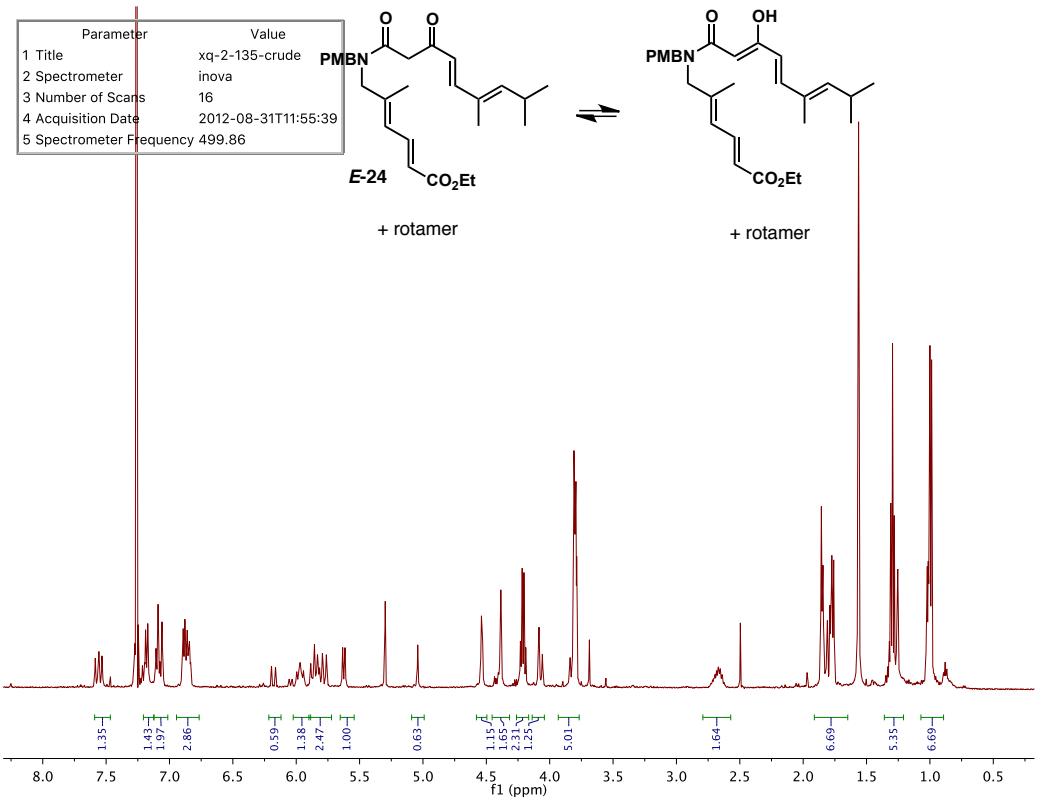


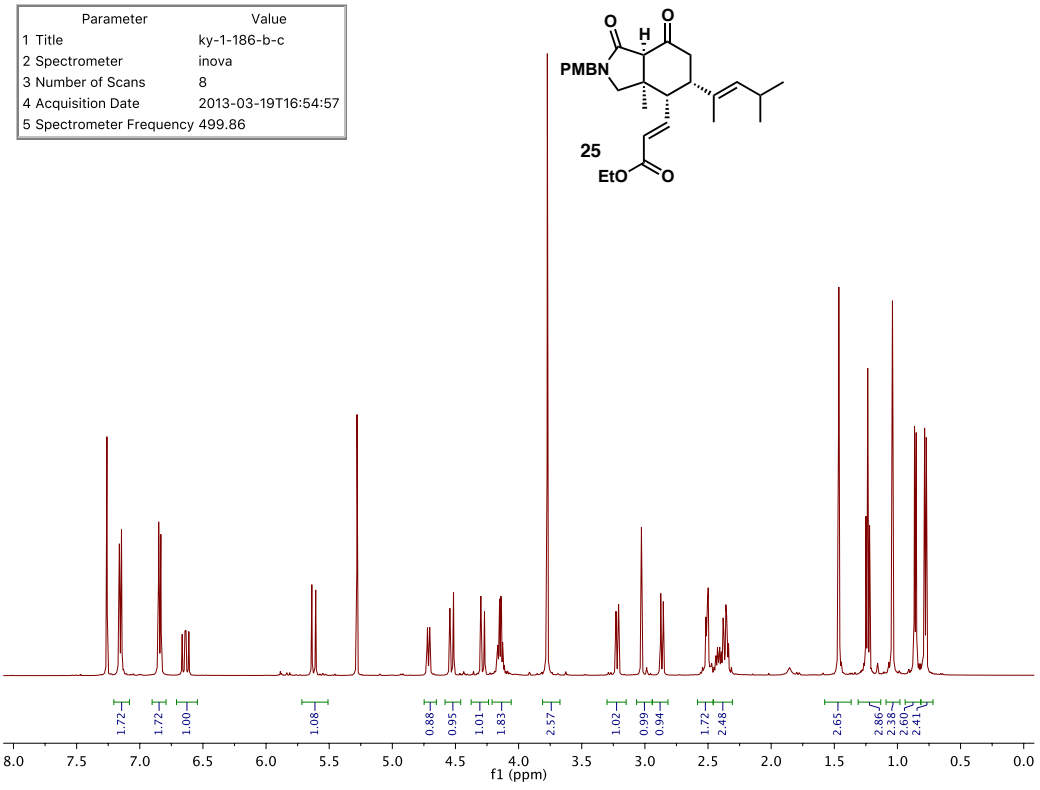
32

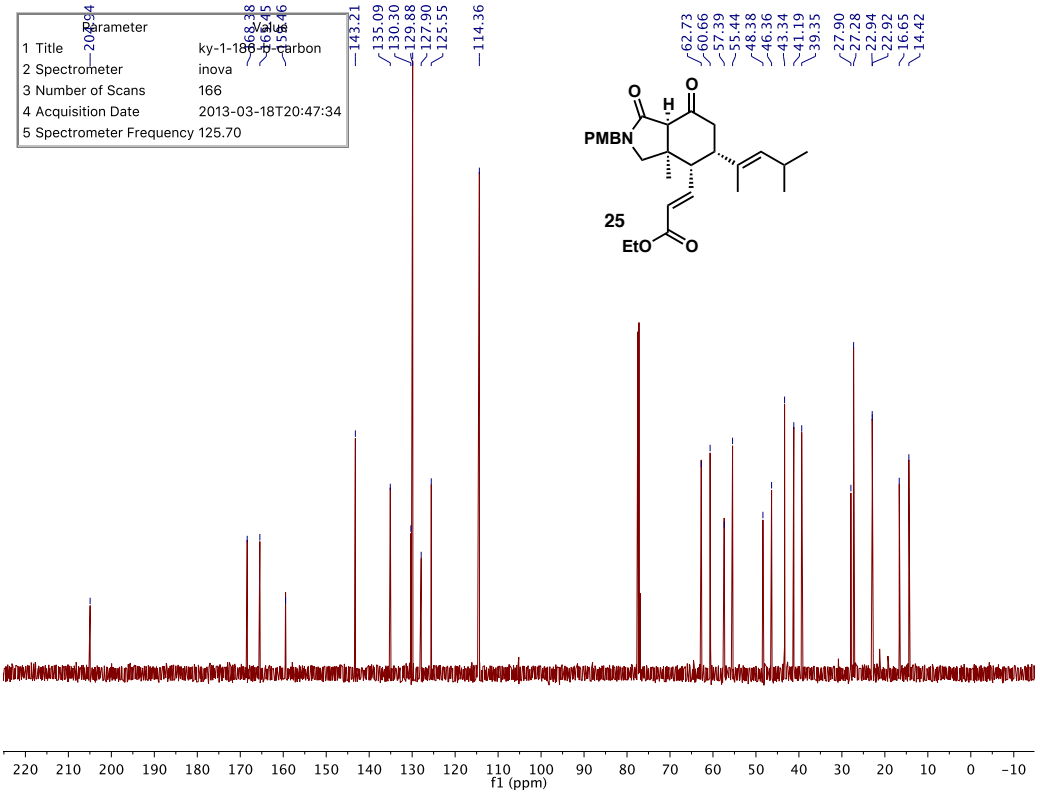
Parameter	Value
1 Title	xq-3-46-2-C13
2 Spectrometer	inova
3 Number of Scans	272
4 Acquisition Date	2013-03-09T12:44:43
5 Spectrometer Frequency	125.70

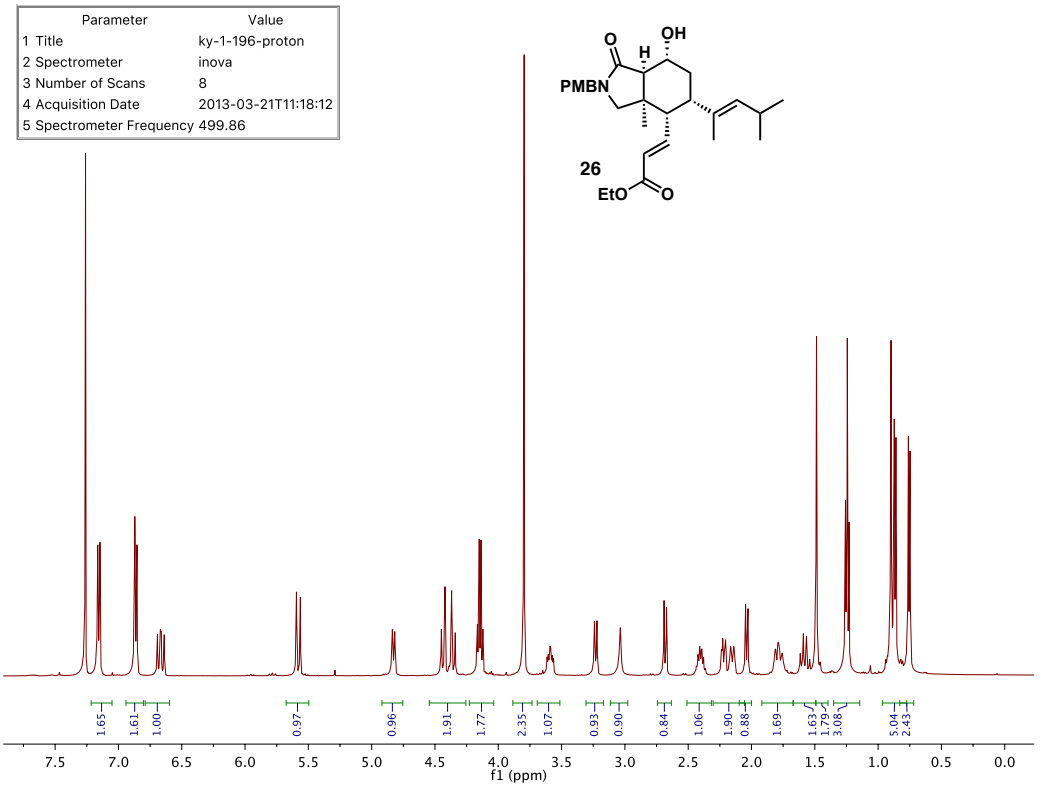


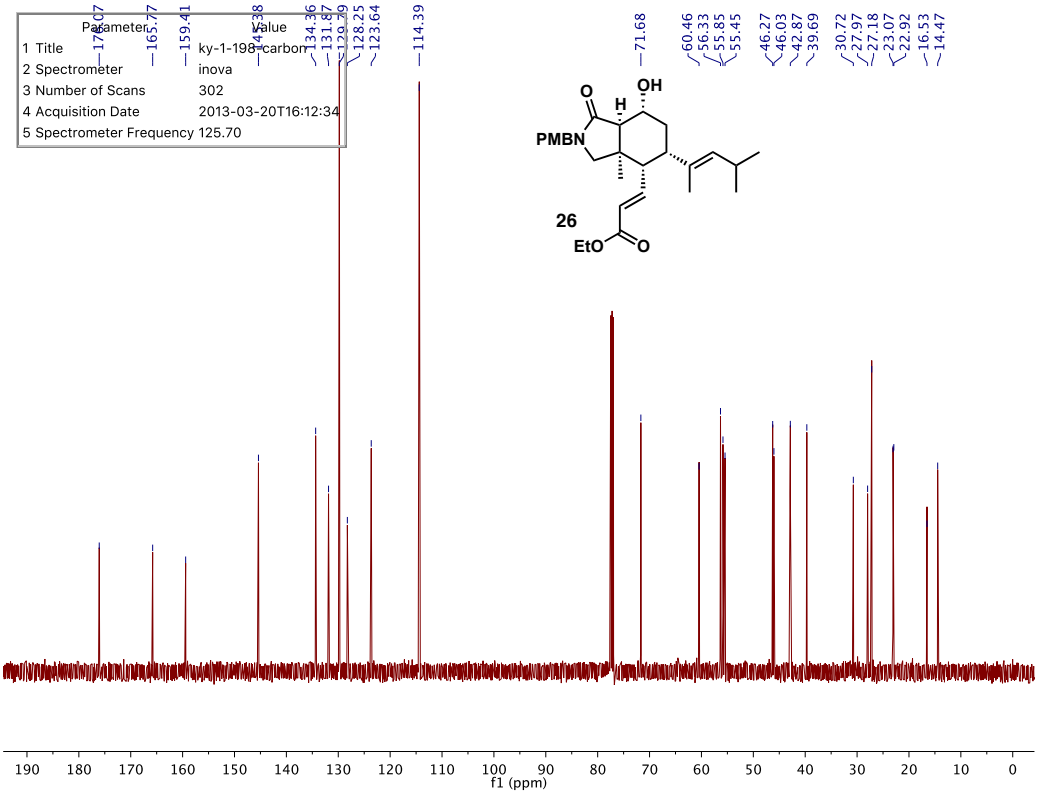
32

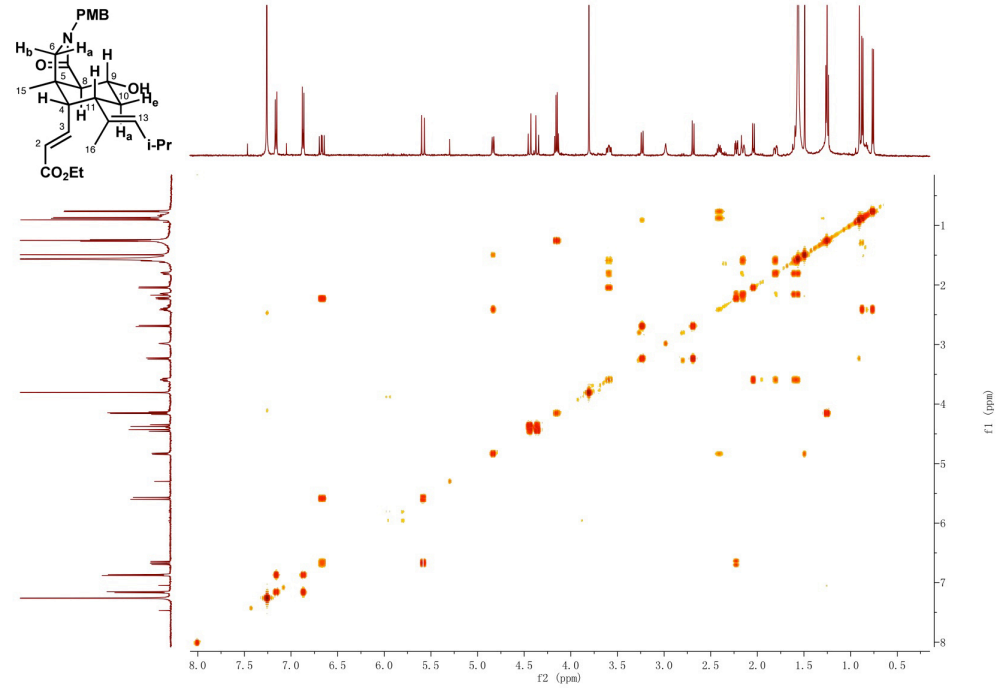

Parameter Value
1 Title xq-2-135-crude
2 Spectrometer inova
3 Number of Scans 16
4 Acquisition Date 2012-08-31T11:55:39
5 Spectrometer Frequency 499.86
PMBN
O
O
E-24
CO2Et
+ rotamer
PMBN
O
OH
CO2Et
+ rotamer
1.35
1.43
1.97
2.86
0.59
1.38
2.47
1.00
0.63
1.15
1.65
2.31
1.25
5.01
1.64
6.69
5.35
6.69
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

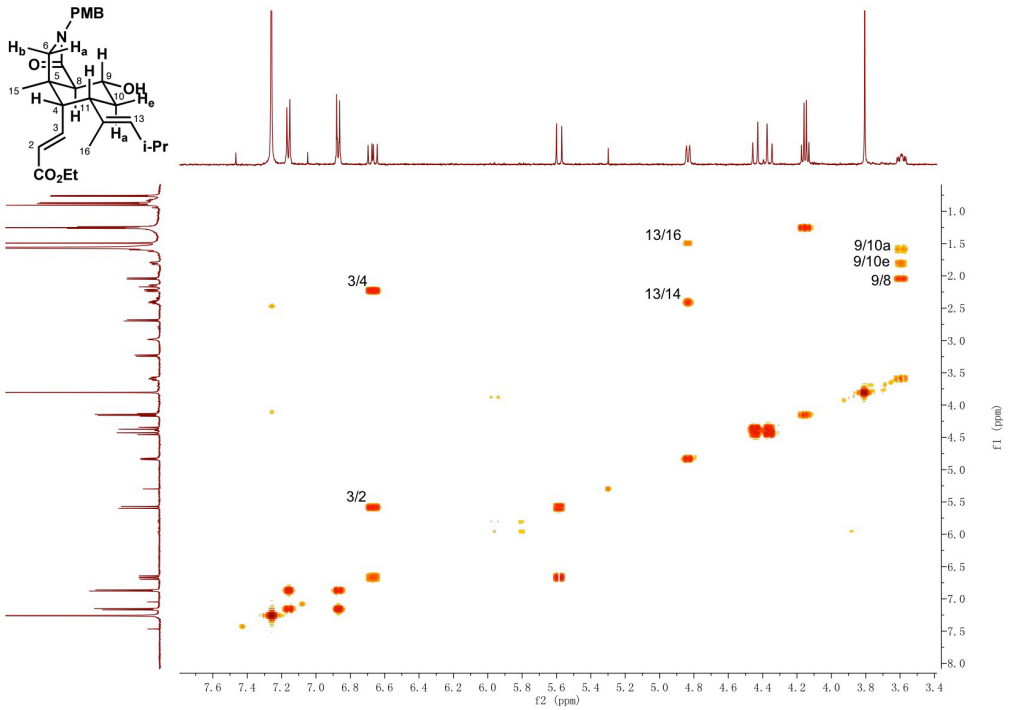

Parameter Value
1 Title ky-1-186-b-c
2 Spectrometer inova
3 Number of Scans 8
4 Acquisition Date 2013-03-19T16:54:57
5 Spectrometer Frequency 499.86
O
H
O
PMBN
25
EtO
O
1.72
1.72
1.00
1.08
0.88
0.95
1.01
1.83
2.57
1.02
0.99
0.94
1.72
2.48
2.65
2.86
2.38
2.66
2.41
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

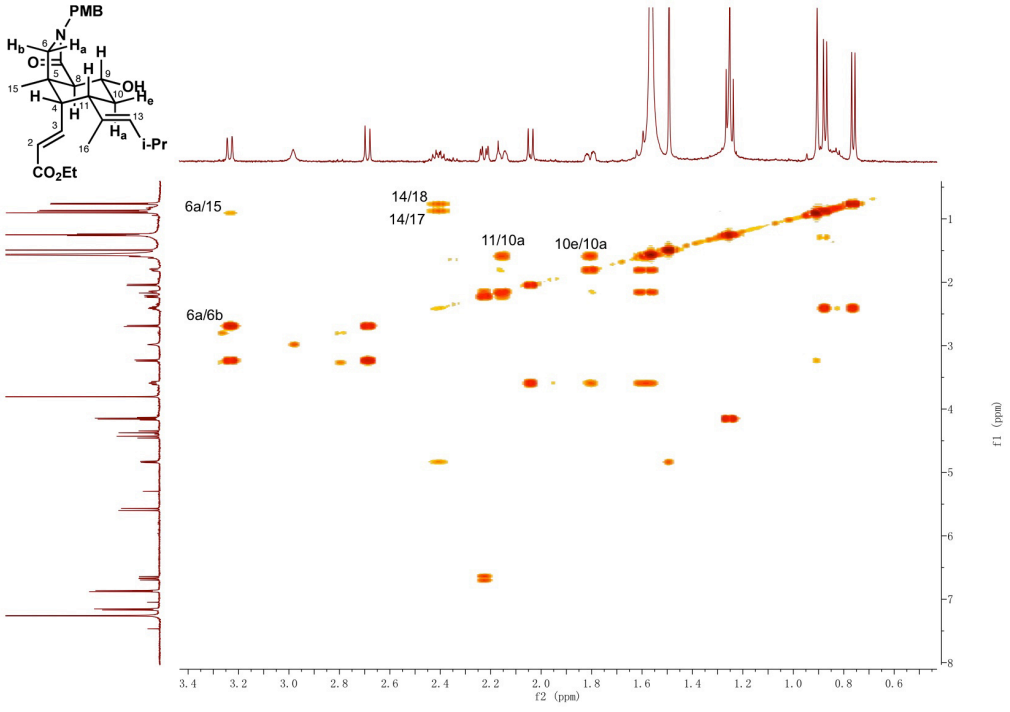

Parameter Value
1 Title ky-1-186-b-carbon
2 Spectrometer inova
3 Number of Scans 166
4 Acquisition Date 2013-03-18T20:47:34
5 Spectrometer Frequency 125.70
208.04
66.38
61.45
55.46
143.21
135.09
130.30
129.88
127.90
125.55
114.36
62.73
60.66
57.39
55.44
48.38
46.36
43.34
41.19
39.35
27.90
27.28
22.94
22.92
16.65
14.42
PMBN
25
EtO
f1 (ppm)

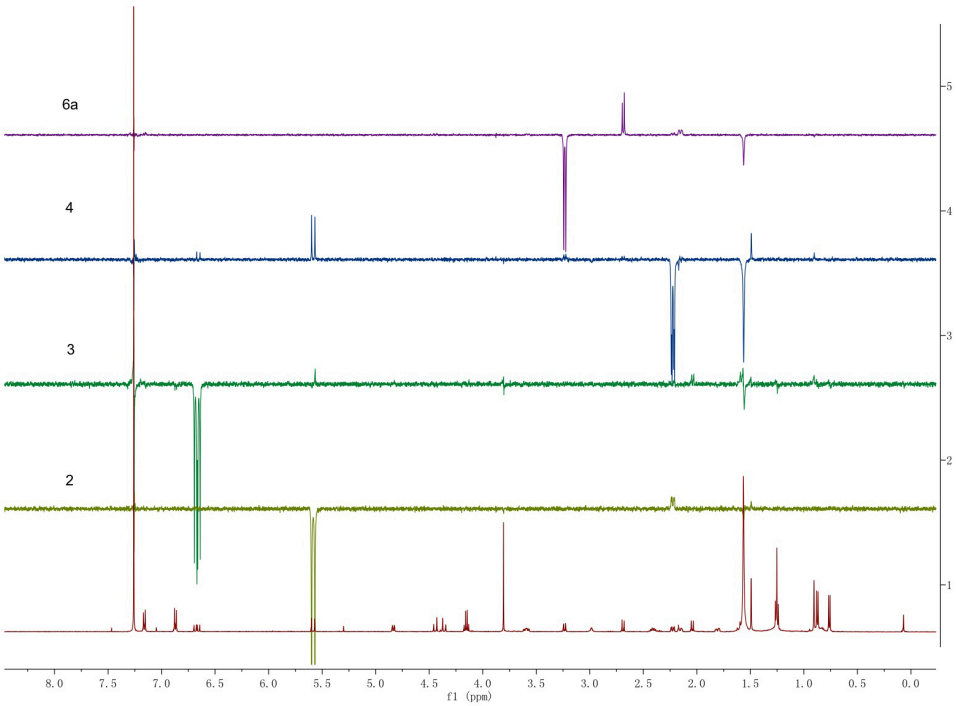

Parameter Value
1 Title ky-1-196-proton
2 Spectrometer inova
3 Number of Scans 8
4 Acquisition Date 2013-03-21T11:18:12
5 Spectrometer Frequency 499.86
PMBN
OH
26
EtO
1.65
1.61
1.00
0.97
0.96
1.91
1.77
2.35
1.07
0.93
0.90
0.84
1.06
1.90
0.88
1.69
1.63
1.79
3.08
5.04
2.43
f1 (ppm)

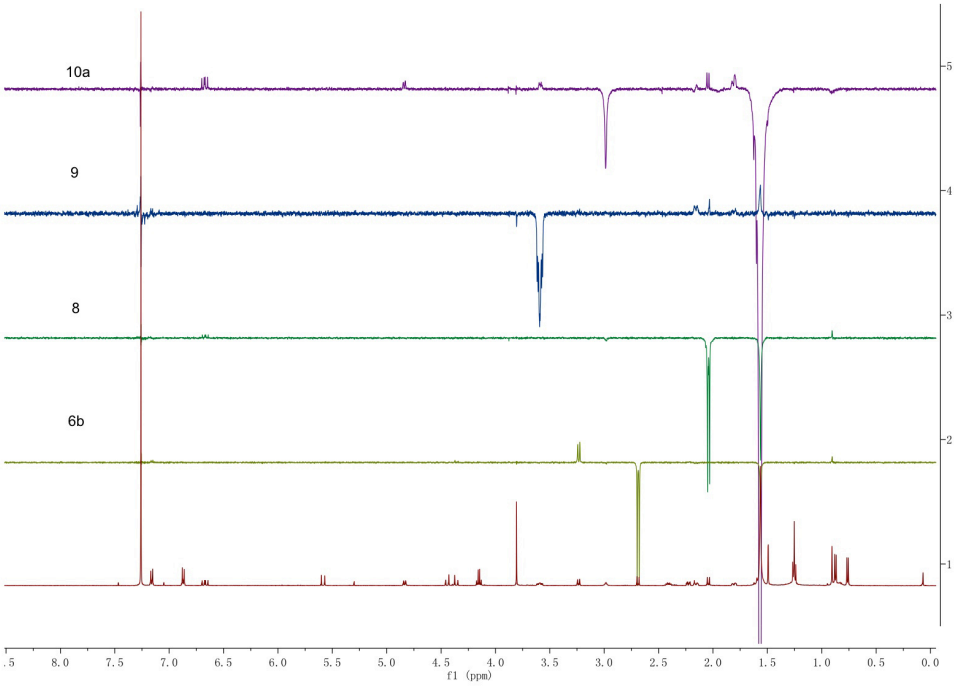

Parameter Value
1 Title ky-1-198-carbon
2 Spectrometer inova
3 Number of Scans 302
4 Acquisition Date 2013-03-20T16:12:34
5 Spectrometer Frequency 125.70
176.07
165.77
159.41
147.38
134.36
131.87
129.39
128.25
123.64
114.39
71.68
60.46
56.33
55.85
55.45
46.27
46.03
42.87
39.69
30.72
27.97
27.18
23.07
22.92
16.53
14.47
PMBN
OH
H
O
26
EtO
O
f1 (ppm)

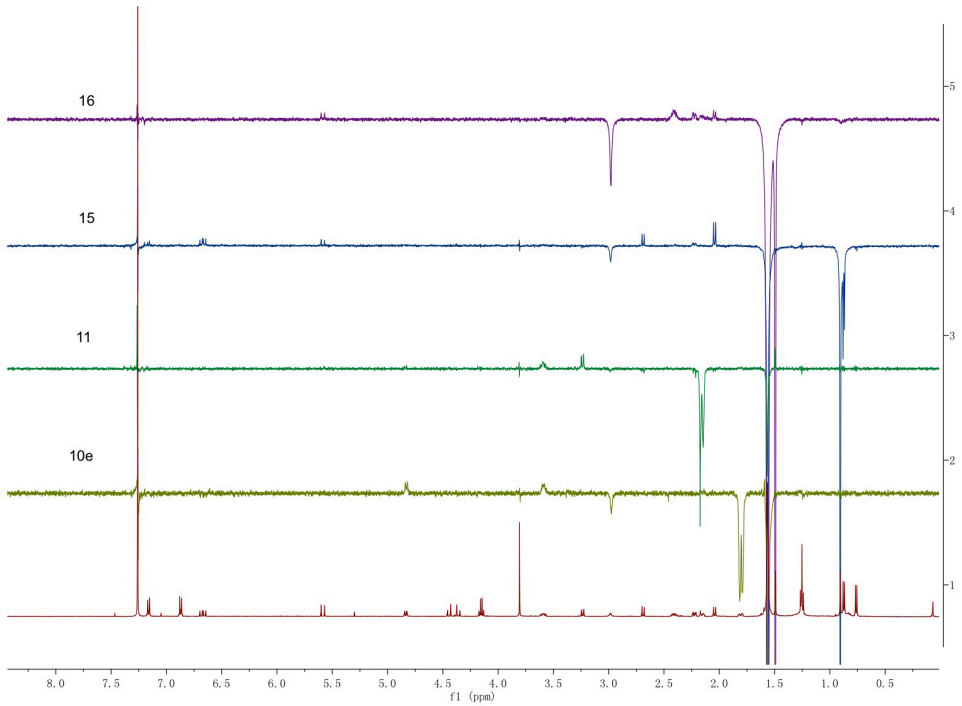

PMB
i-Pr
CO2Et
f2 (ppm)
f1 (ppm)


PMB
i-Pr
CO2Et
13/16
9/10a
9/10e
9/8
13/14
3/4
3/2
f2 (ppm)
f1 (ppm)

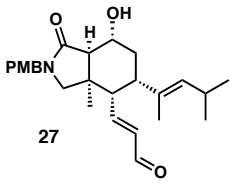

PMB
i-Pr
CO2Et
6a/15
14/18
14/17
11/10a
10e/10a
6a/6b
f2 (ppm)
f1 (ppm)


6a
4
3
2
f1 (ppm)

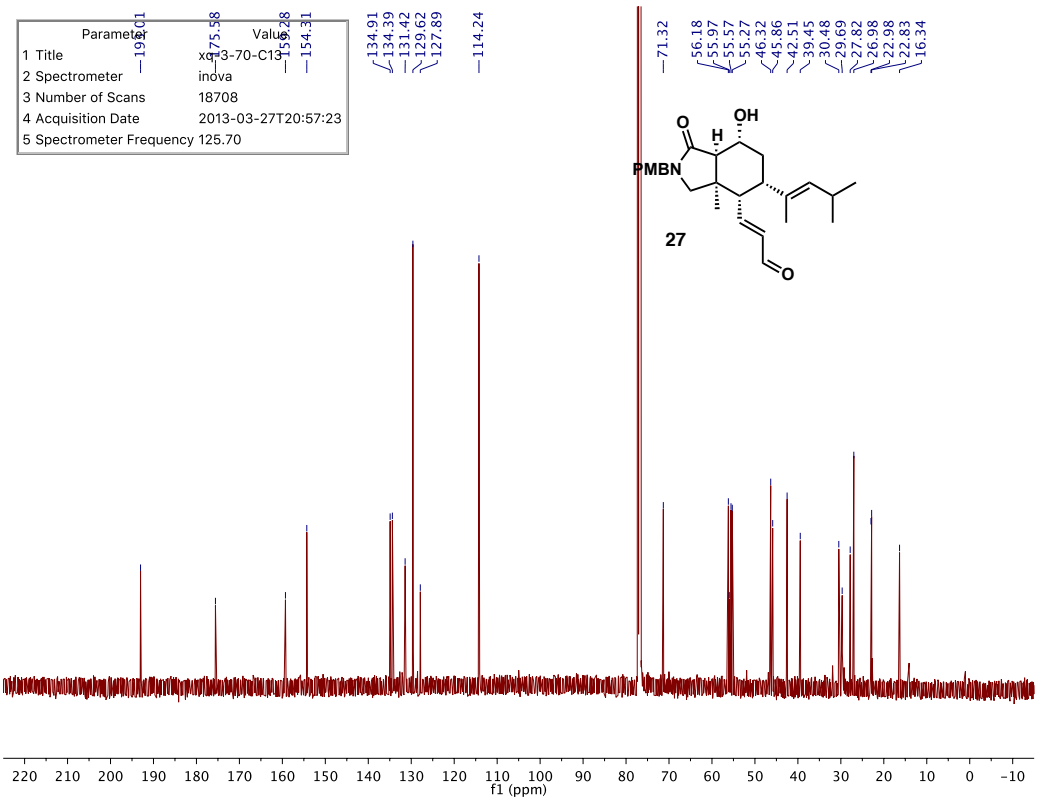

10a
9
8
6b
f1 (ppm)

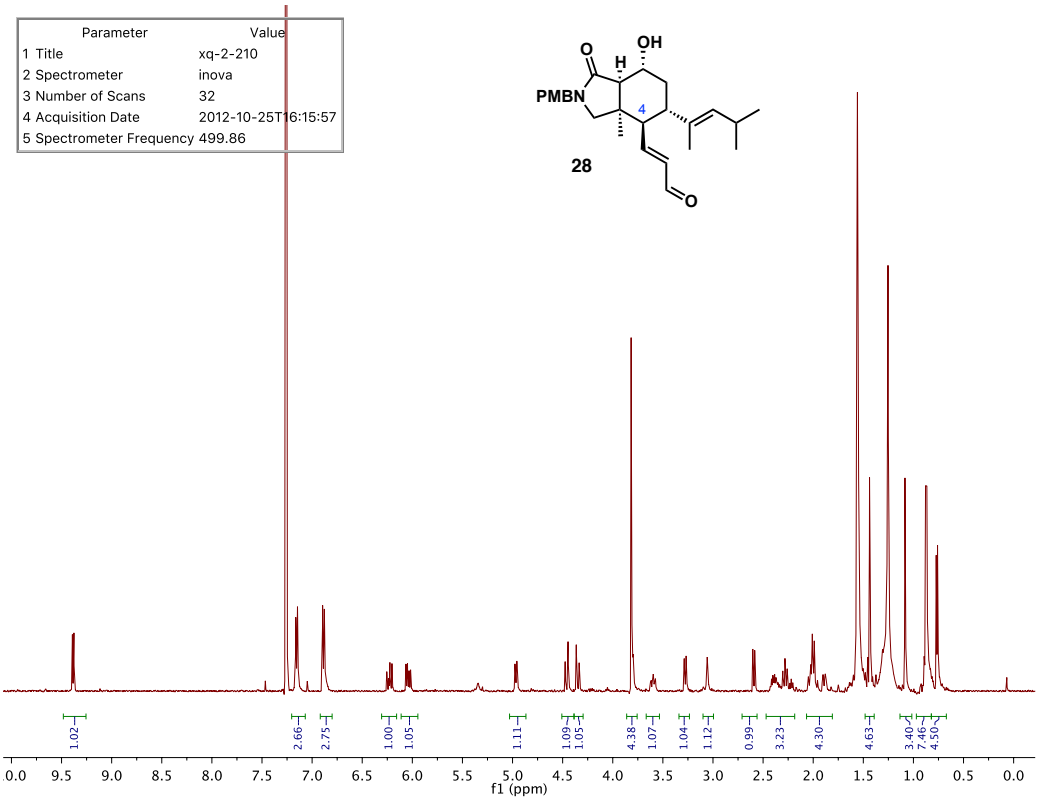


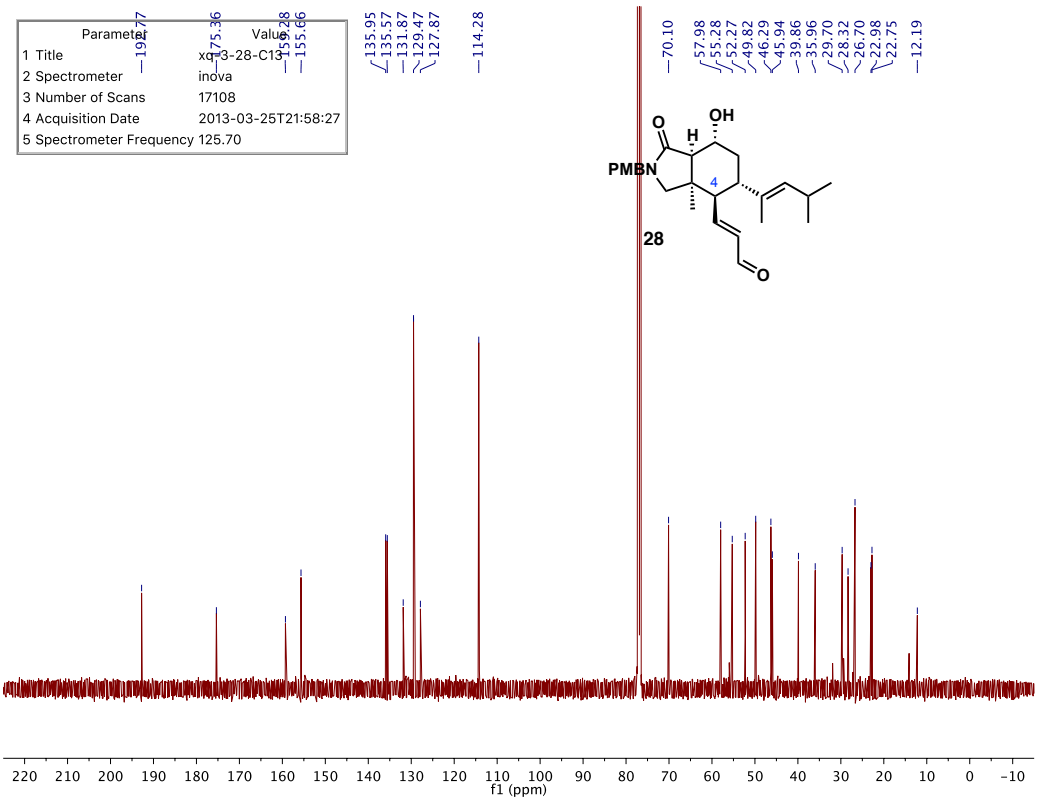
Parameter	Value
1 Title	xq-3-70
2 Spectrometer	inova
3 Number of Scans	32
4 Acquisition Date	2013-03-27T10:50:05
5 Spectrometer Frequency	499.86

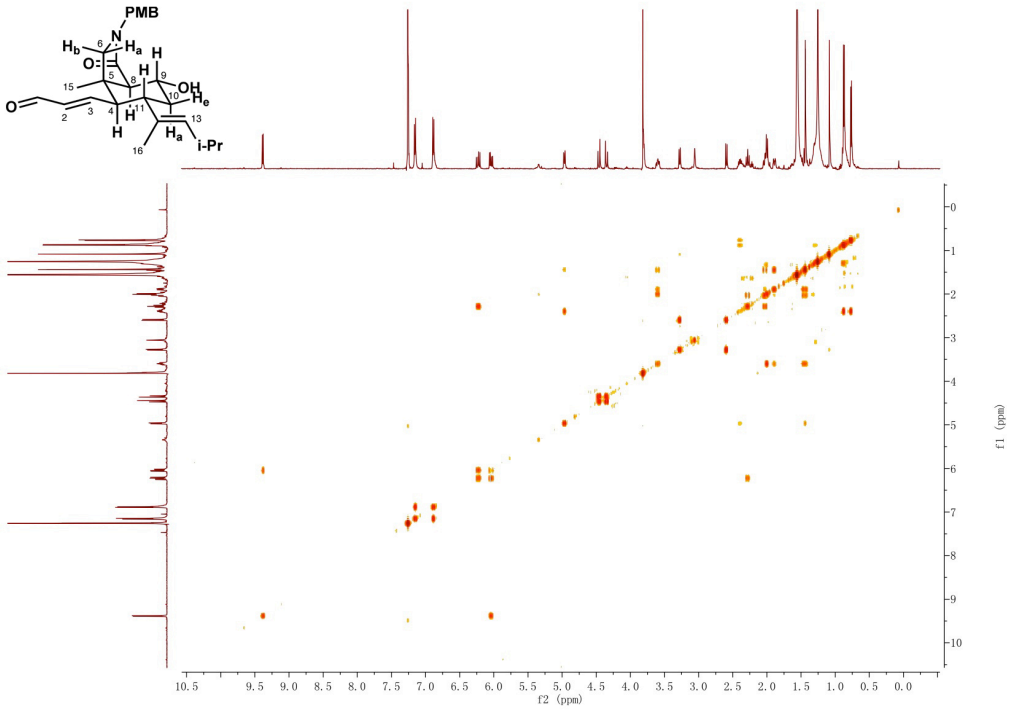


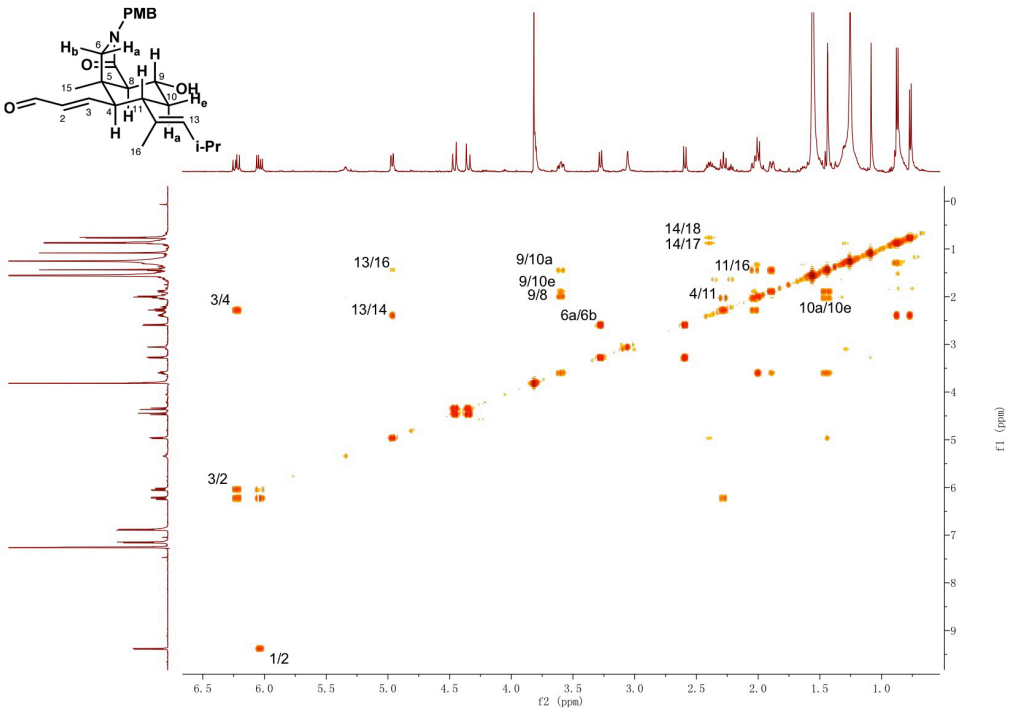
27

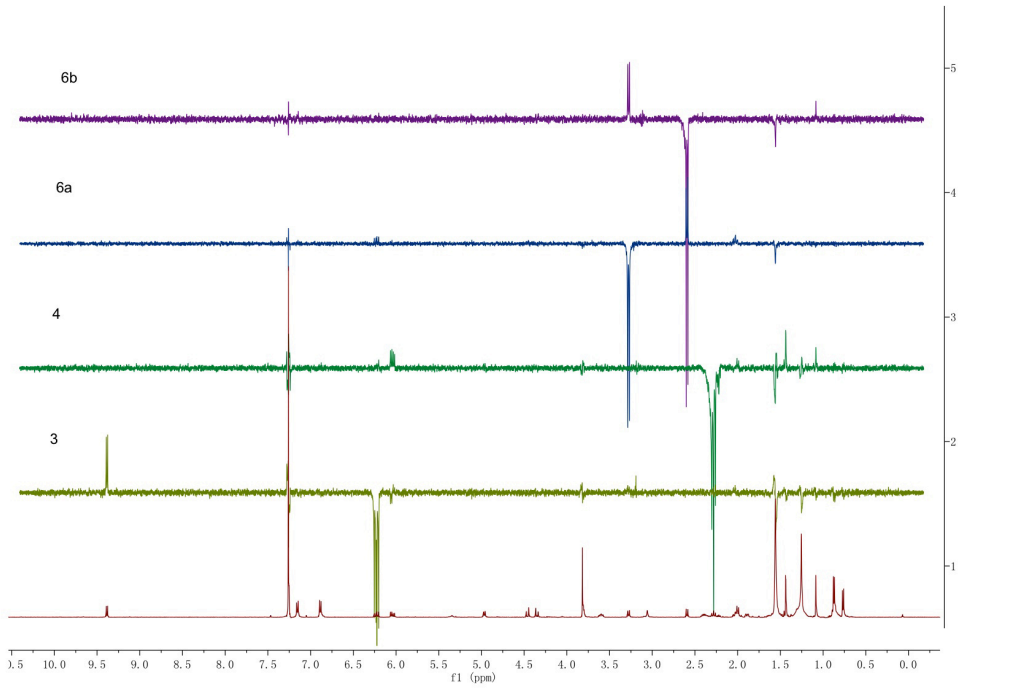

Parameter Value
1 Title xq-3-70-C13
2 Spectrometer inova
3 Number of Scans 18708
4 Acquisition Date 2013-03-27T20:57:23
5 Spectrometer Frequency 125.70
OH
O
H
PMBN
27
O
f1 (ppm)

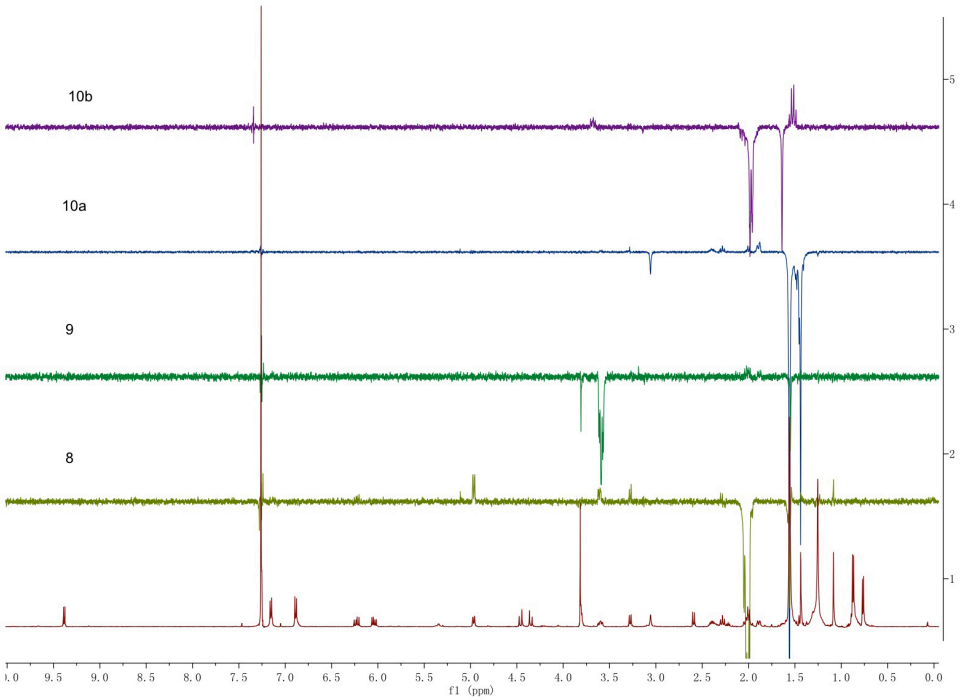

Parameter Value
1 Title xq-2-210
2 Spectrometer inova
3 Number of Scans 32
4 Acquisition Date 2012-10-25T16:15:57
5 Spectrometer Frequency 499.86
OH
O
H
PMBN
4
28
O
f1 (ppm)

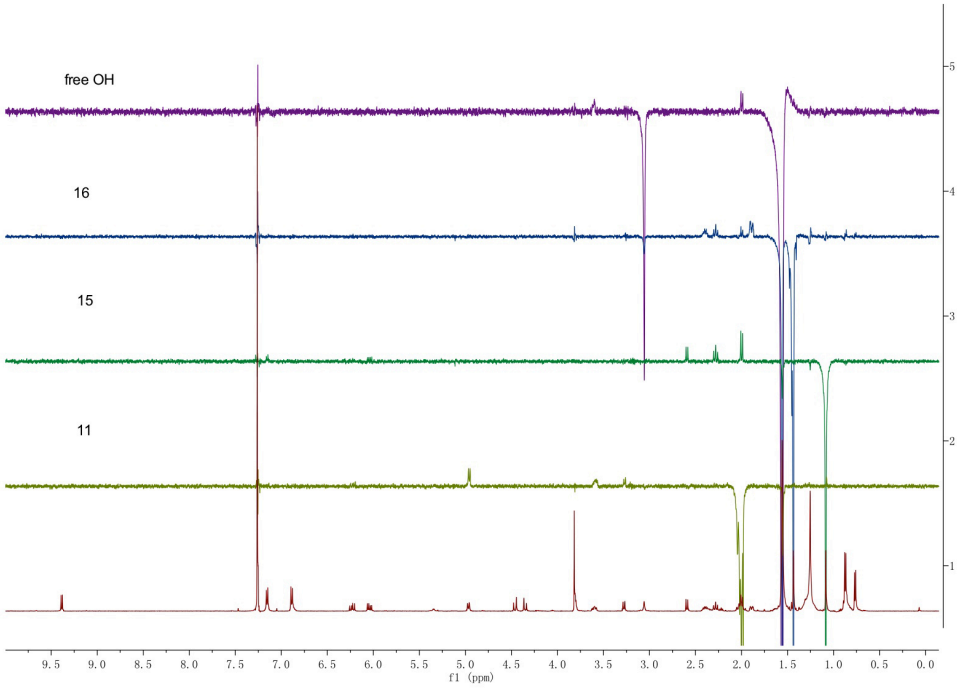

Parameter Value
1 Title xq-3-28-C13
2 Spectrometer inova
3 Number of Scans 17108
4 Acquisition Date 2013-03-25T21:58:27
5 Spectrometer Frequency 125.70
193.17
175.36
159.28
155.66
135.95
135.57
131.87
129.47
127.87
114.28
70.10
57.98
55.28
52.27
49.82
46.29
45.94
39.86
35.96
29.70
28.32
26.70
22.98
22.75
12.19
PMBN
OH
H
O
4
28
O
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


PMB
N
Hb
Ha
O
H
OH
He
i-Pr
O
H
Ha
10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f2 (ppm)
f1 (ppm)

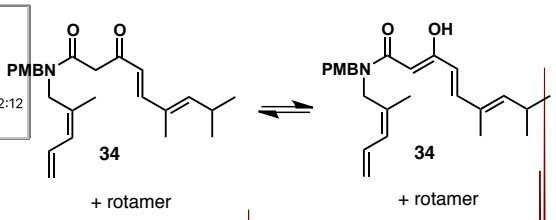

PMB
i-Pr
13/16
9/10a
9/10e
9/8
14/18
14/17
11/16
4/11
10a/10e
6a/6b
13/14
3/4
3/2
1/2
f2 (ppm)
f1 (ppm)


6b
6a
4
3
f1 (ppm)

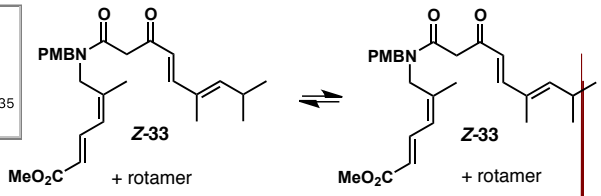

10b
10a
9
8
f1 (ppm)

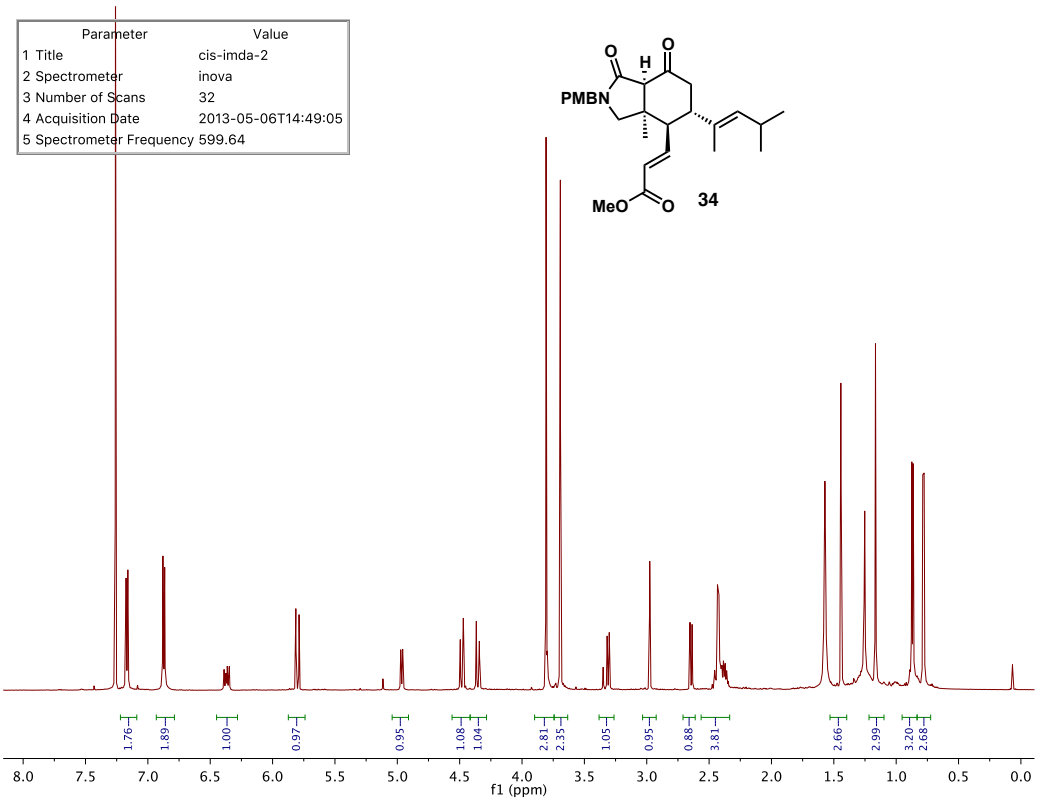

free OH
16
15
11
f1 (ppm)

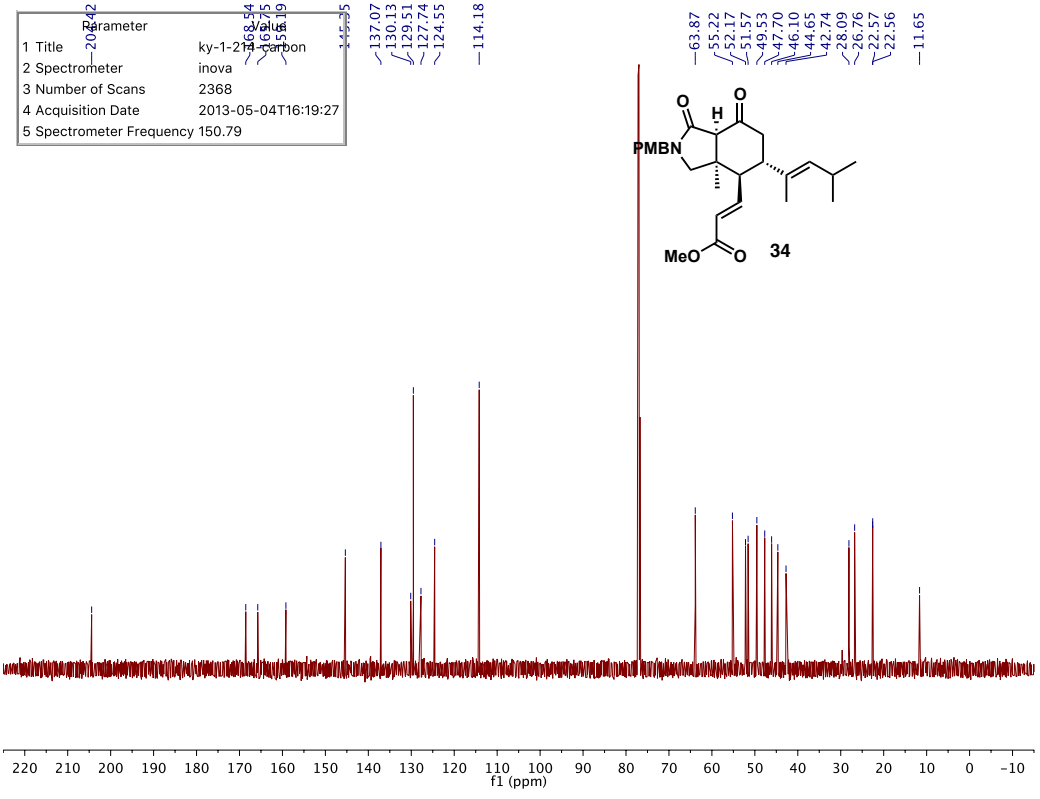
Parameter	Value
1 Title	xq-3-88
2 Spectrometer	inova
3 Number of Scans	8
4 Acquisition Date	2013-04-19T10:22:12
5 Spectrometer Frequency	499.86



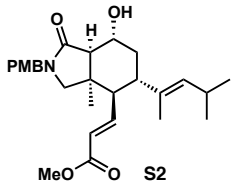
Parameter	Value
1 Title	xq-3-91
2 Spectrometer	inova
3 Number of Scans	16
4 Acquisition Date	2013-04-20T10:46:35
5 Spectrometer Frequency	499.86



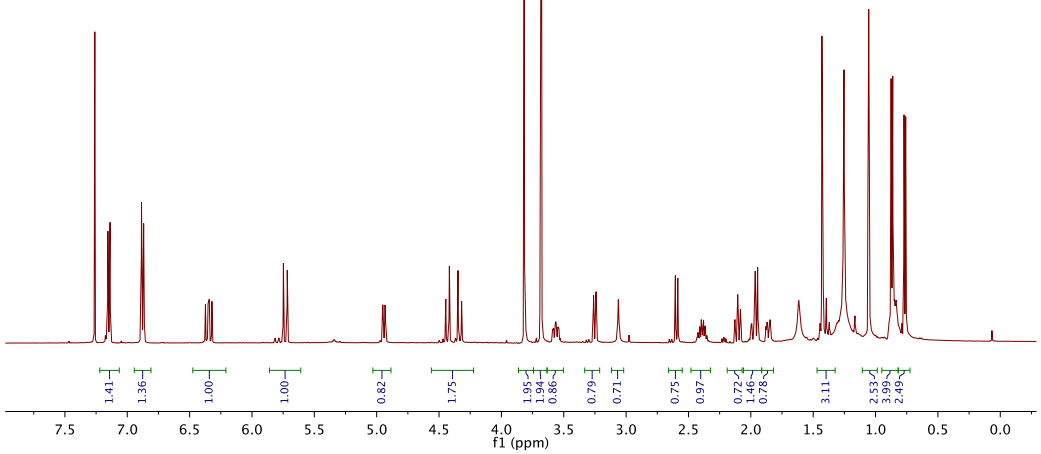

Parameter Value
1 Title cis-imda-2
2 Spectrometer inova
3 Number of Scans 32
4 Acquisition Date 2013-05-06T14:49:05
5 Spectrometer Frequency 599.64
PMBN
MeO
34
1.76
1.89
1.00
0.97
0.95
1.08
1.04
2.81
2.35
1.05
0.95
0.88
3.81
2.66
2.99
3.20
2.68
f1 (ppm)

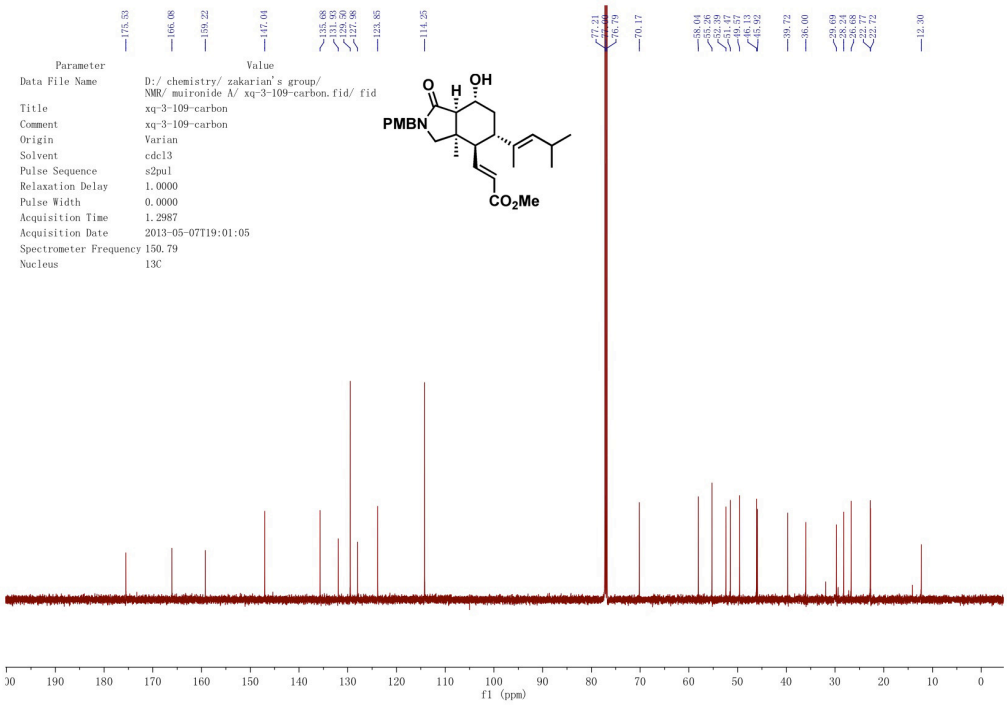

Parameter
1 Title ky-1-214-carbon
2 Spectrometer inova
3 Number of Scans 2368
4 Acquisition Date 2013-05-04T16:19:27
5 Spectrometer Frequency 150.79
20.42
68.54
66.75
55.19
145.35
137.07
130.13
129.51
127.74
124.55
114.18
63.87
55.22
52.17
51.57
49.53
47.70
46.10
44.65
42.74
28.09
26.76
22.57
22.56
11.65
PMBN
MeO
34
f1 (ppm)

Parameter	Value
1 Title	xq-3-109
2 Spectrometer	inova
3 Number of Scans	32
4 Acquisition Date	2013-05-07T17:17:51
5 Spectrometer Frequency	499.86

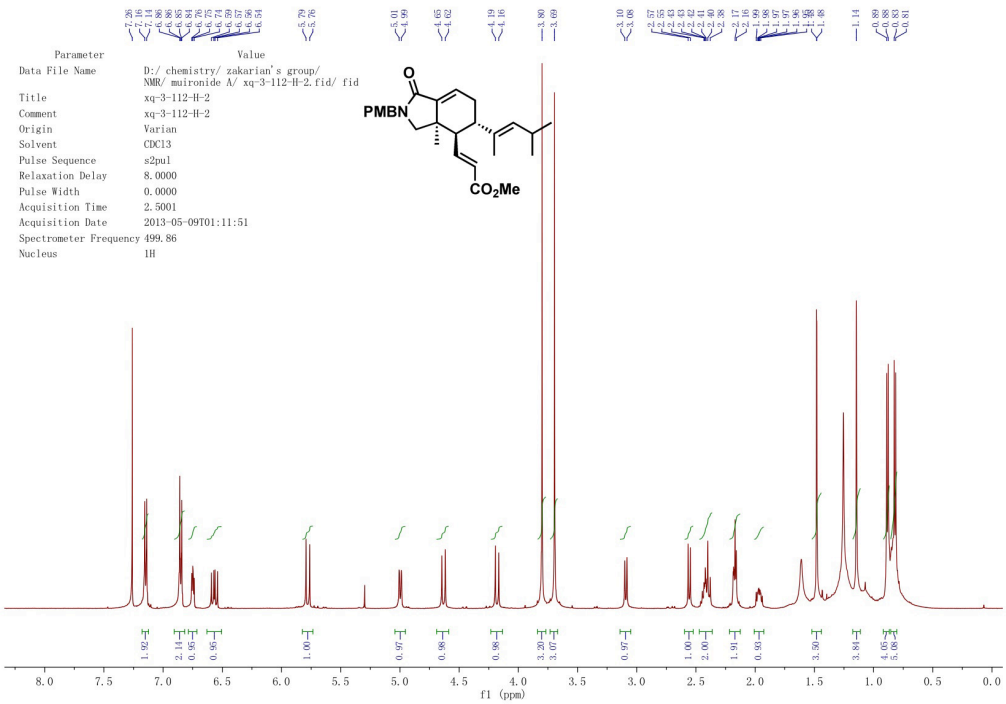


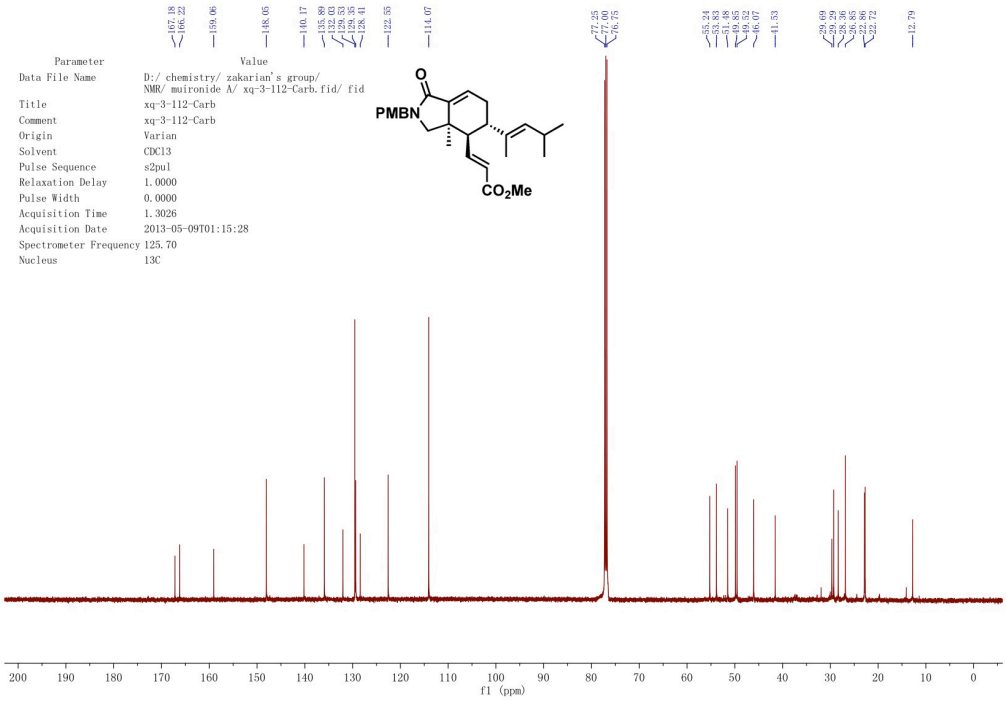
S2

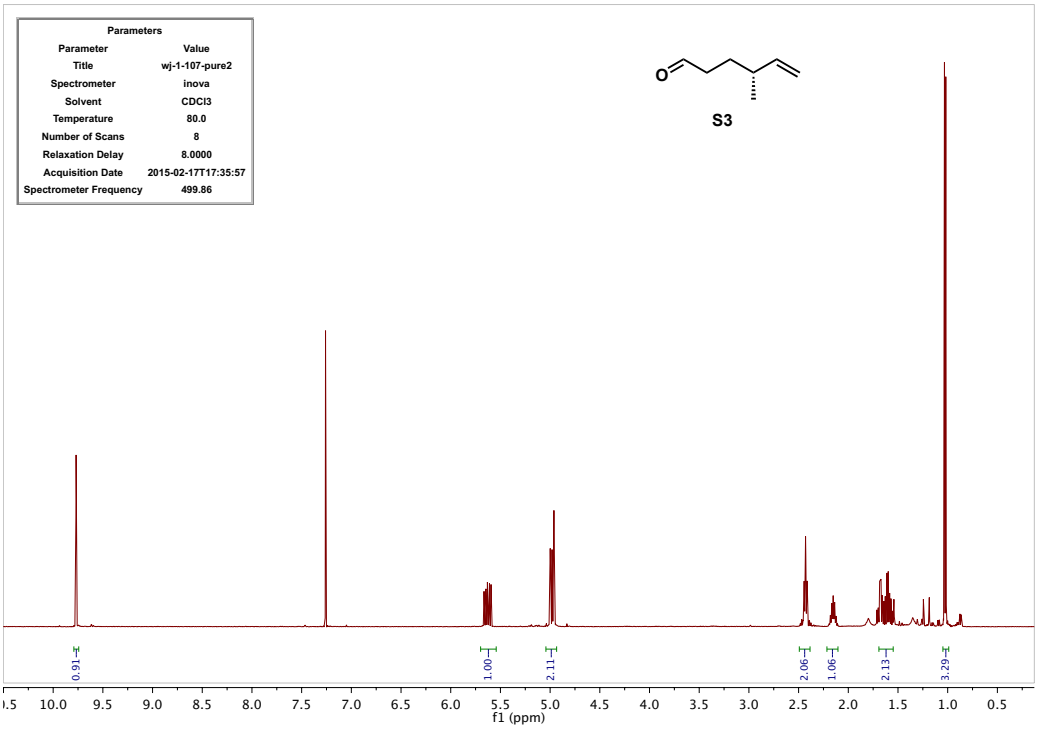


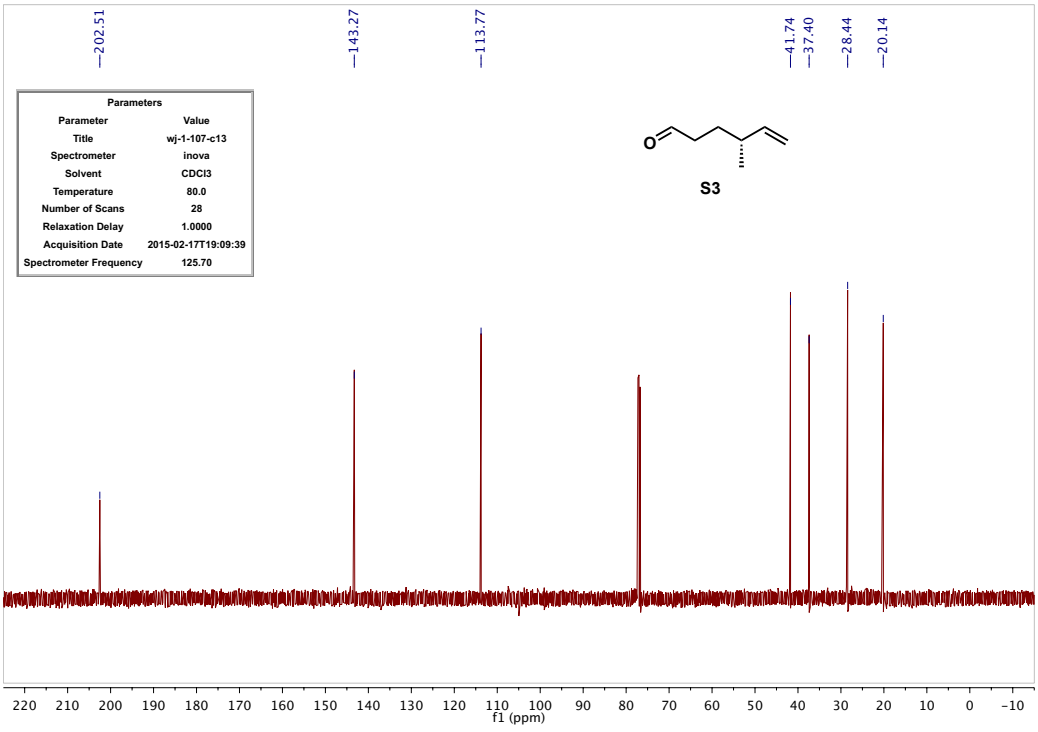


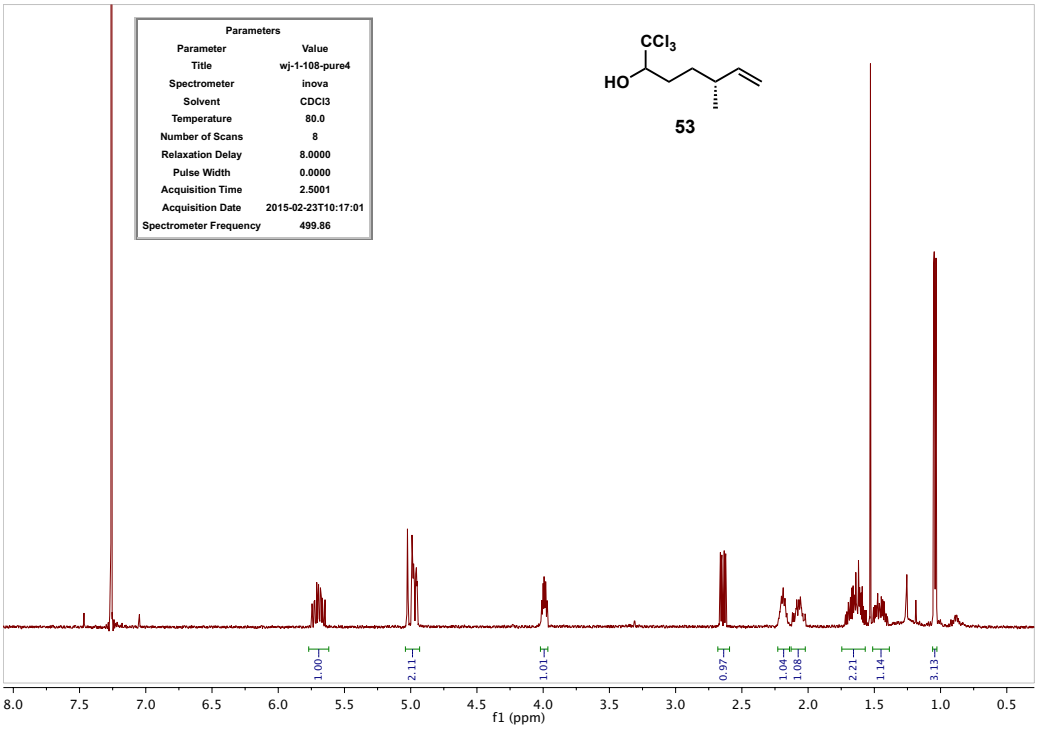
Parameter	Value
Data File Name	D:/ chemistry/ zakarian's group/ NMR/ muironide A/ xq-3-109-carbon.fid/ fid
Title	xq-3-109-carbon
Comment	xq-3-109-carbon
Origin	Varian
Solvent	cdcl3
Pulse Sequence	s2pul
Relaxation Delay	1.0000
Pulse Width	0.0000
Acquisition Time	1.2987
Acquisition Date	2013-05-07T19:01:05
Spectrometer Frequency	150.79
Nucleus	13C

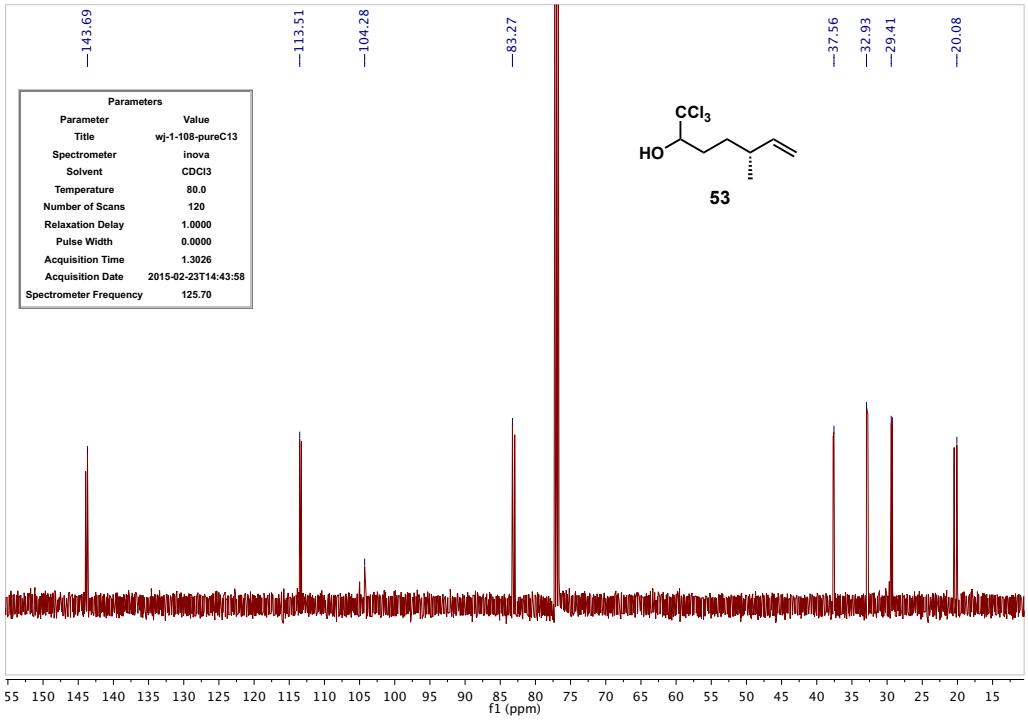

Parameter Value
Data File Name D:/ chemistry/ zakarian's group/ NMR/ muironide A/ xq-3-112-H-2.fid/ fid
Title xq-3-112-H-2
Comment xq-3-112-H-2
Origin Varian
Solvent CDCl3
Pulse Sequence s2pul
Relaxation Delay 8.0000
Pulse Width 0.0000
Acquisition Time 2.5001
Acquisition Date 2013-05-09T01:11:51
Spectrometer Frequency 499.86
Nucleus 1H
PMBN
CO2Me
f1 (ppm)

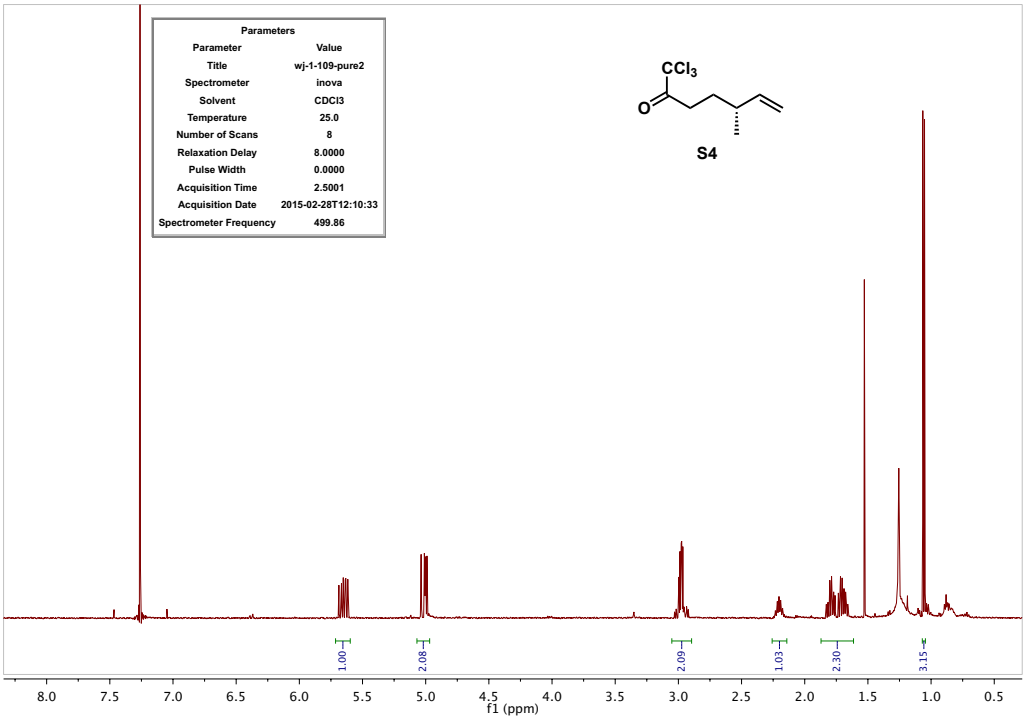

Parameter Value
Data File Name D:/ chemistry/ zakarian's group/ NMR/ muironide A/ xq-3-112-Carb.fid/ fid
Title xq-3-112-Carb
Comment xq-3-112-Carb
Origin Varian
Solvent CDCl3
Pulse Sequence s2pul
Relaxation Delay 1.0000
Pulse Width 0.0000
Acquisition Time 1.3026
Acquisition Date 2013-05-09T01:15:28
Spectrometer Frequency 125.70
Nucleus 13C
PMBN
CO2Me
f1 (ppm)

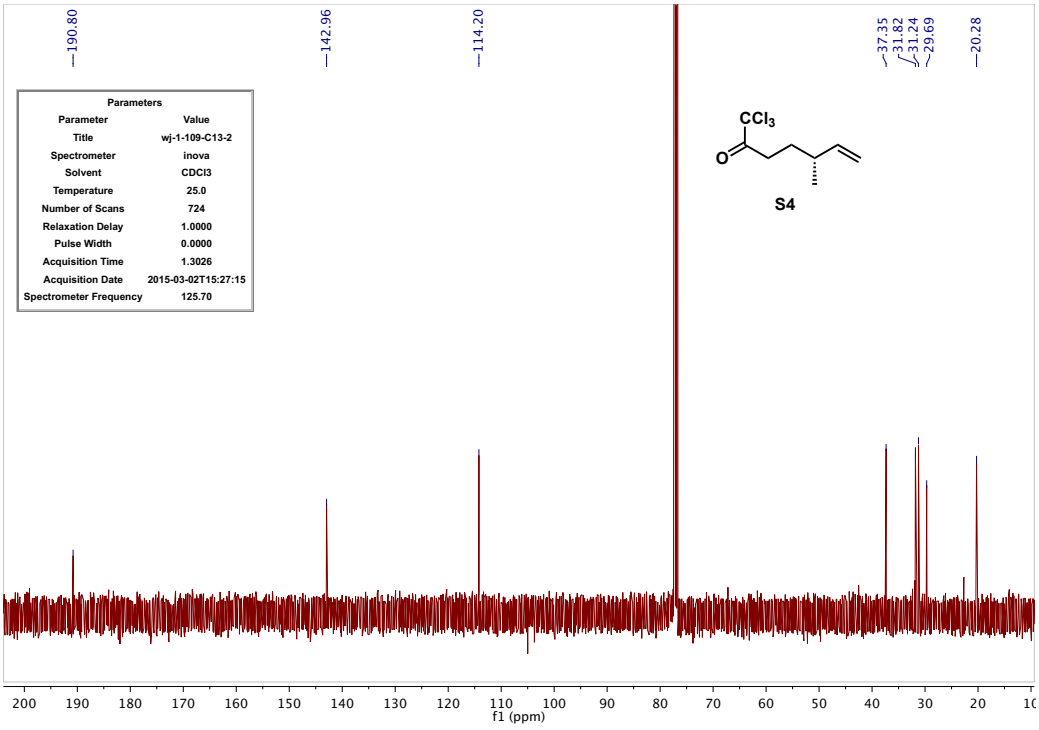

Parameters
Parameter Value
Title wj-1-107-pure2
Spectrometer inova
Solvent CDCl3
Temperature 80.0
Number of Scans 8
Relaxation Delay 8.0000
Acquisition Date 2015-02-17T17:35:57
Spectrometer Frequency 499.86
O
S3
0.91
1.00
2.11
2.06
1.06
2.13
3.29
f1 (ppm)

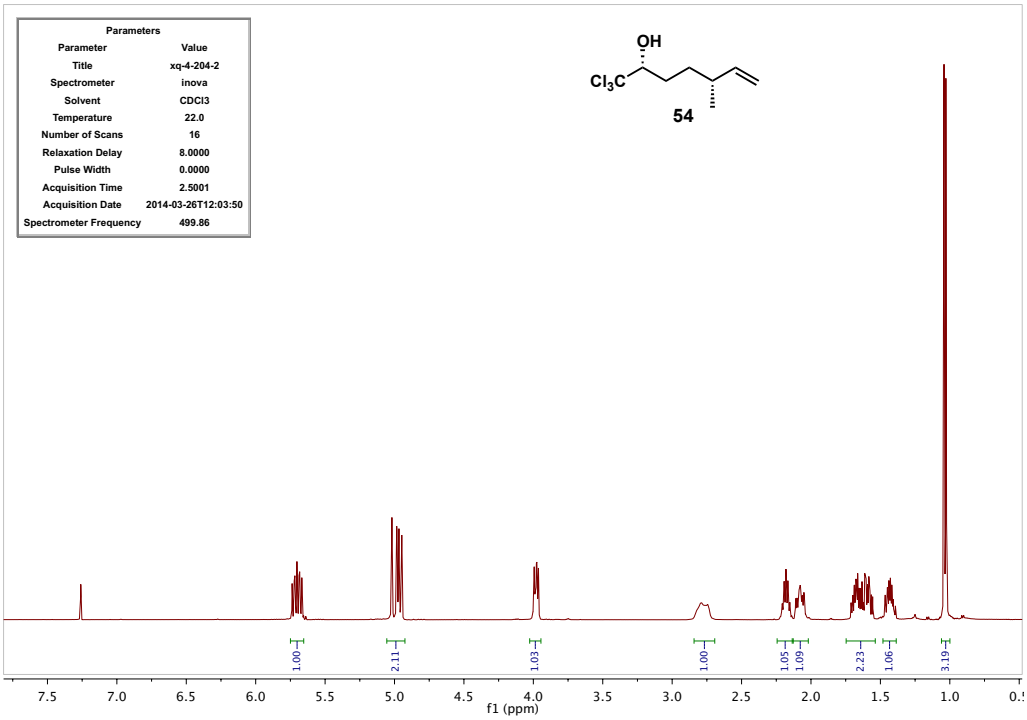

202.51
143.27
113.77
41.74
37.40
28.44
20.14
Parameters
Parameter Value
Title wj-1-107-c13
Spectrometer inova
Solvent CDCl3
Temperature 80.0
Number of Scans 28
Relaxation Delay 1.0000
Acquisition Date 2015-02-17T19:09:39
Spectrometer Frequency 125.70
O
S3
f1 (ppm)

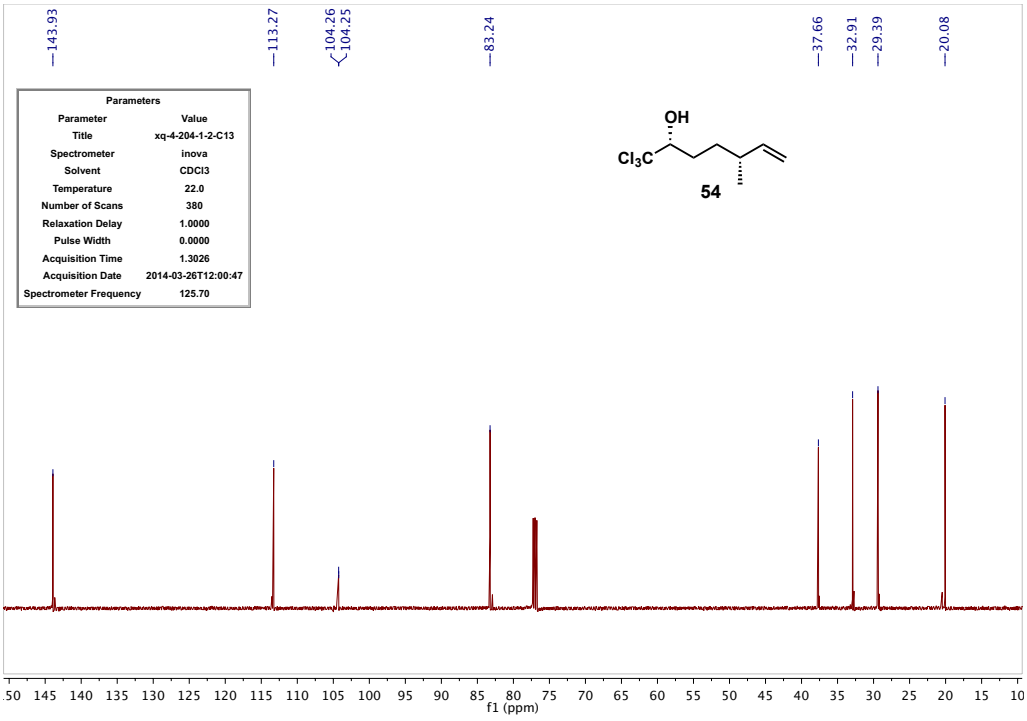

Parameters
Parameter Value
Title wj-1-108-pure4
Spectrometer inova
Solvent CDCl3
Temperature 80.0
Number of Scans 8
Relaxation Delay 8.0000
Pulse Width 0.0000
Acquisition Time 2.5001
Acquisition Date 2015-02-23T10:17:01
Spectrometer Frequency 499.86
CCl3
HO
53
1.00
2.11
1.01
0.97
1.04
1.08
2.21
1.14
3.13
f1 (ppm)

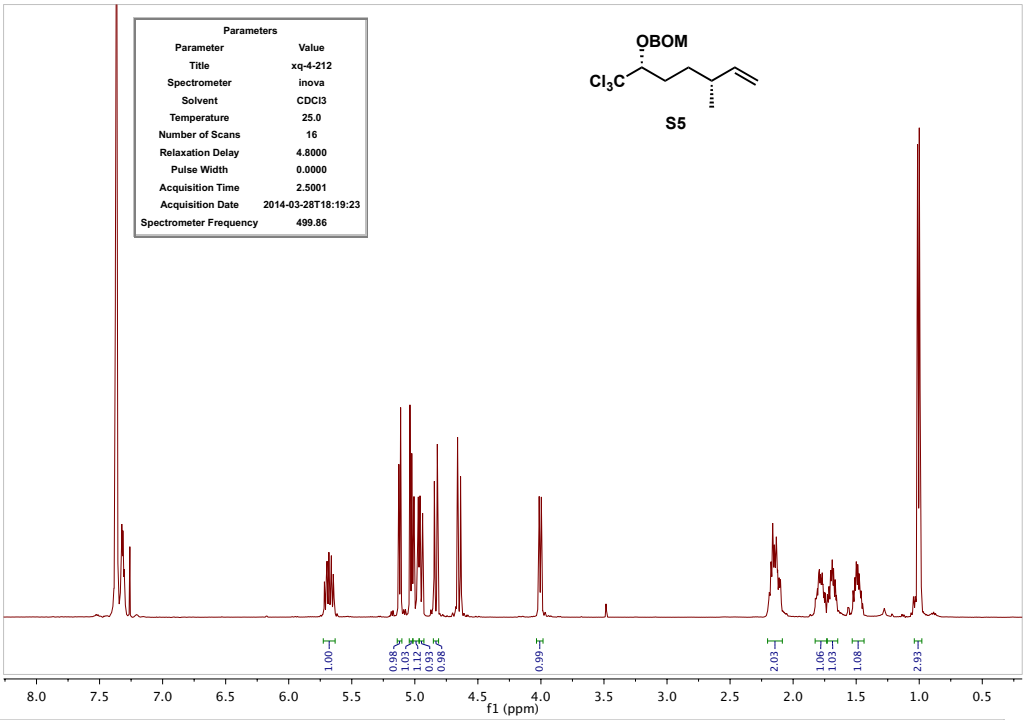

143.69
113.51
104.28
83.27
37.56
32.93
29.41
20.08
Parameters
Parameter Value
Title wj-1-108-pureC13
Spectrometer inova
Solvent CDCl3
Temperature 80.0
Number of Scans 120
Relaxation Delay 1.0000
Pulse Width 0.0000
Acquisition Time 1.3026
Acquisition Date 2015-02-23T14:43:58
Spectrometer Frequency 125.70
CCl3
HO
53
f1 (ppm)

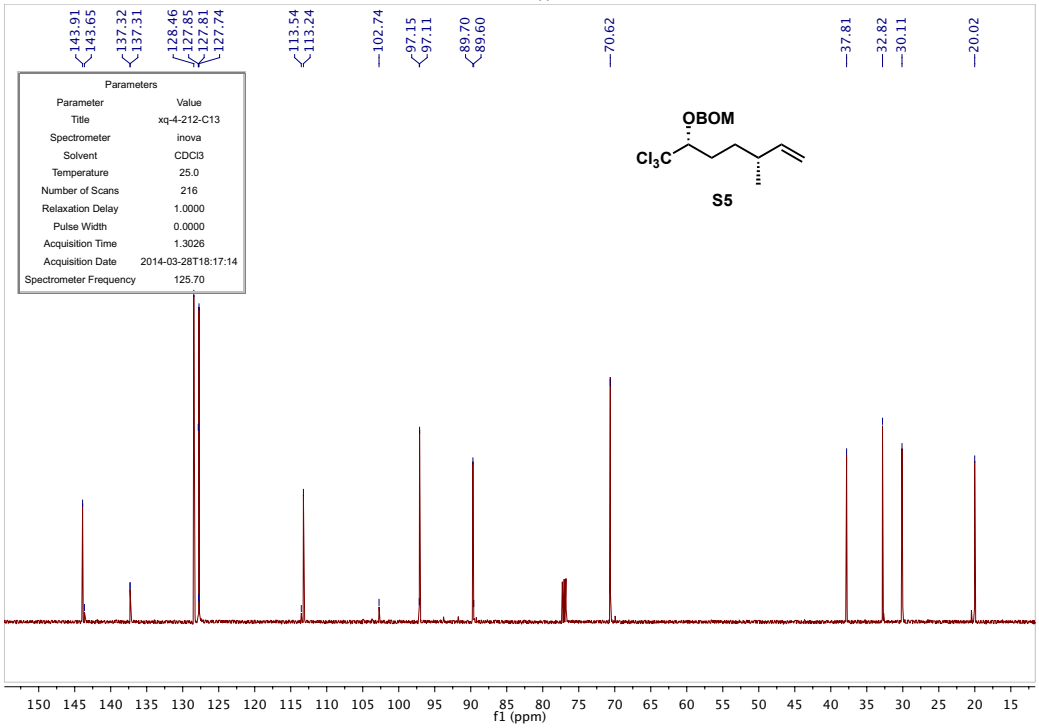

Parameters
Parameter Value
Title wj-1-109-pure2
Spectrometer inova
Solvent CDCl3
Temperature 25.0
Number of Scans 8
Relaxation Delay 8.0000
Pulse Width 0.0000
Acquisition Time 2.5001
Acquisition Date 2015-02-28T12:10:33
Spectrometer Frequency 499.86
CCl3
O
S4
1.00
2.08
2.09
1.03
2.30
3.15
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

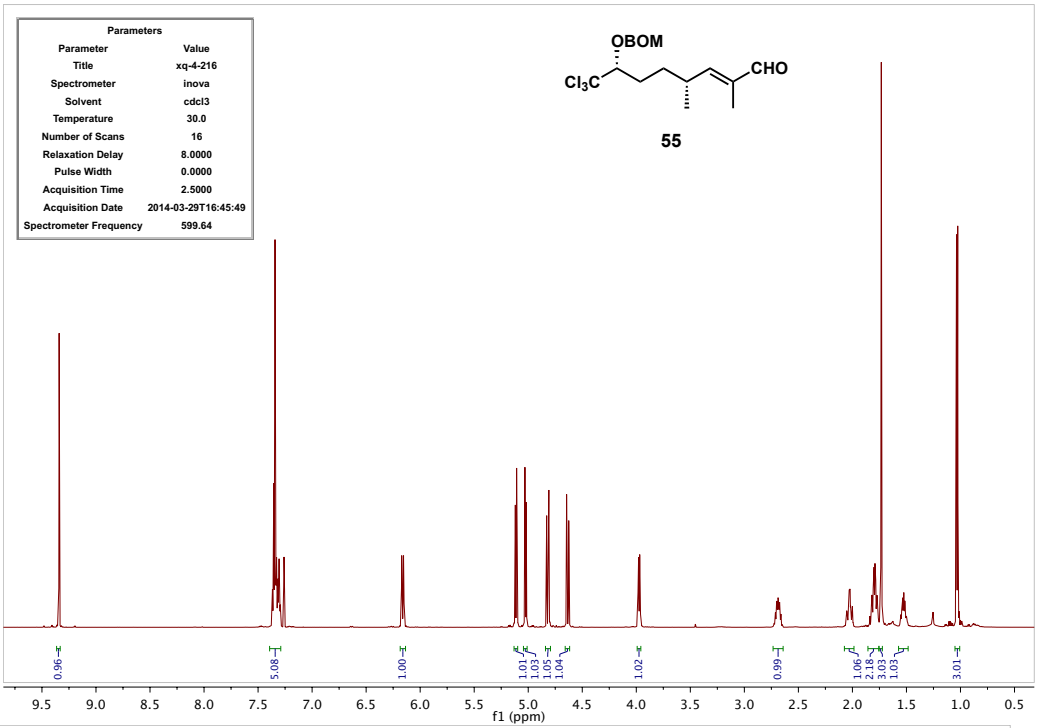

190.80
142.96
114.20
37.35
31.82
31.24
29.69
20.28
Parameters
Parameter Value
Title wj-1-109-C13-2
Spectrometer inova
Solvent CDCl3
Temperature 25.0
Number of Scans 724
Relaxation Delay 1.0000
Pulse Width 0.0000
Acquisition Time 1.3026
Acquisition Date 2015-03-02T15:27:15
Spectrometer Frequency 125.70
CCl3
O
S4
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

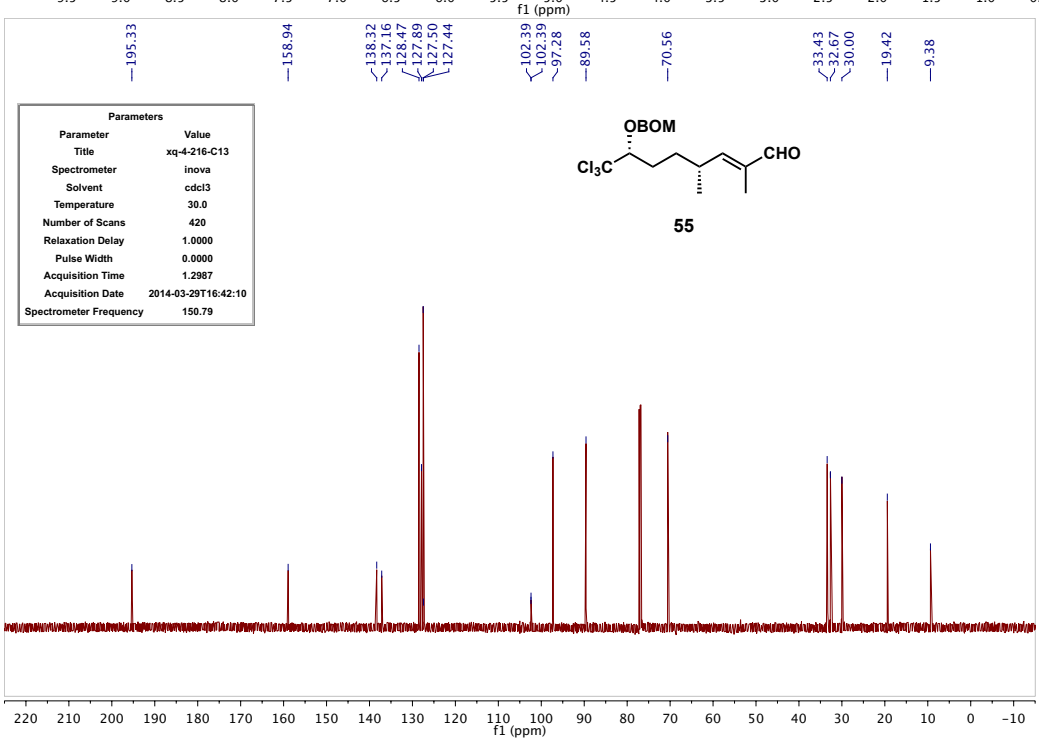

Parameters
Parameter Value
Title xq-4-204-2
Spectrometer inova
Solvent CDCl3
Temperature 22.0
Number of Scans 16
Relaxation Delay 8.0000
Pulse Width 0.0000
Acquisition Time 2.5001
Acquisition Date 2014-03-26T12:03:50
Spectrometer Frequency 499.86
OH
Cl3C
54
1.00
2.11
1.03
1.00
1.05
1.09
2.23
1.06
3.19
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0
f1 (ppm)

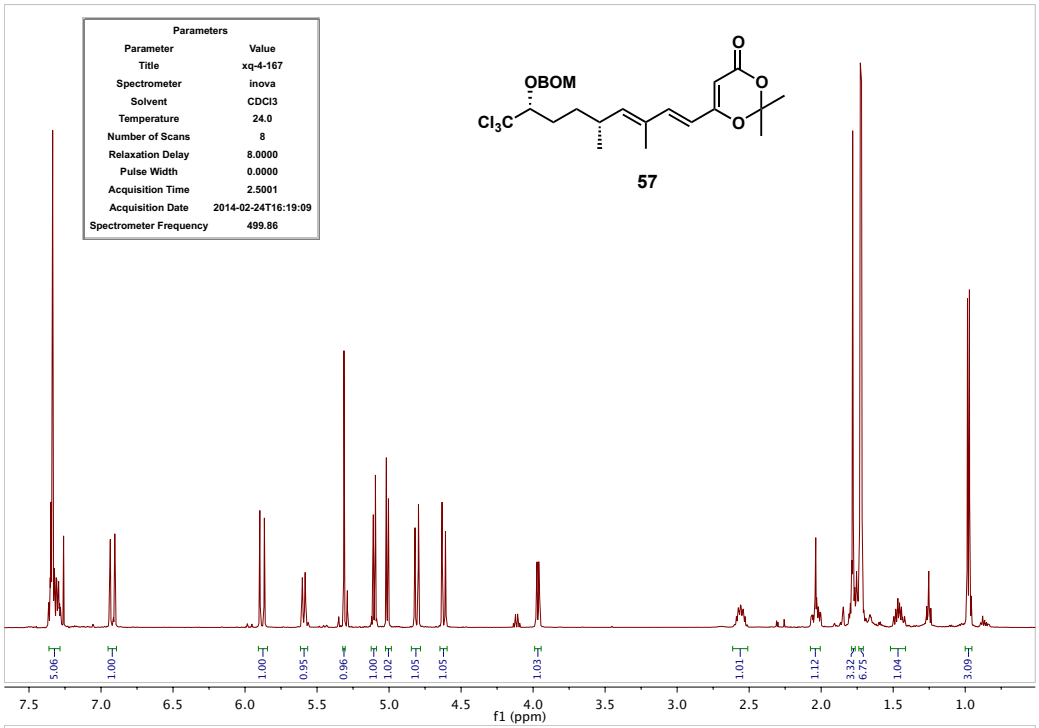

143.93
113.27
104.26
104.25
83.24
37.66
32.91
29.39
20.08
Parameters
Parameter Value
Title xq-4-204-1-2-C13
Spectrometer inova
Solvent CDCl3
Temperature 22.0
Number of Scans 380
Relaxation Delay 1.0000
Pulse Width 0.0000
Acquisition Time 1.3026
Acquisition Date 2014-03-26T12:00:47
Spectrometer Frequency 125.70
OH
Cl3C
54
150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10
f1 (ppm)

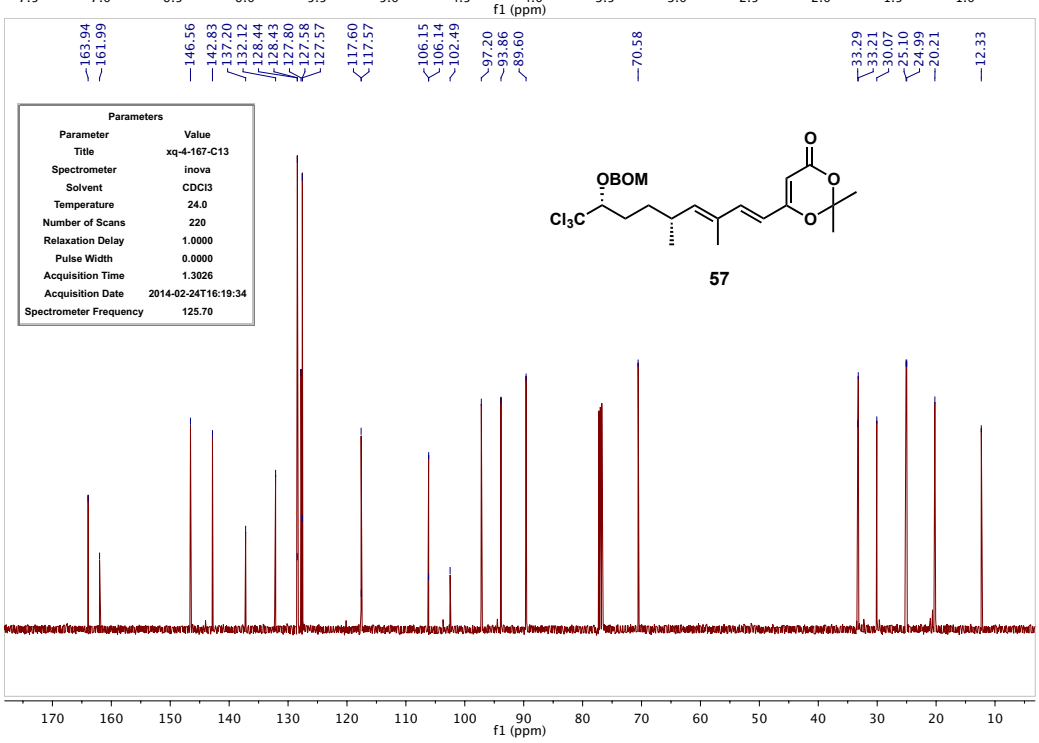

Parameters
Parameter Value
Title xq-4-212
Spectrometer inova
Solvent CDCl3
Temperature 25.0
Number of Scans 16
Relaxation Delay 4.8000
Pulse Width 0.0000
Acquisition Time 2.5001
Acquisition Date 2014-03-28T18:19:23
Spectrometer Frequency 499.86
OBOM
Cl3C
S5
1.00
0.98
1.03
1.12
0.93
0.98
0.99
2.03
1.06
1.03
1.08
2.93
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

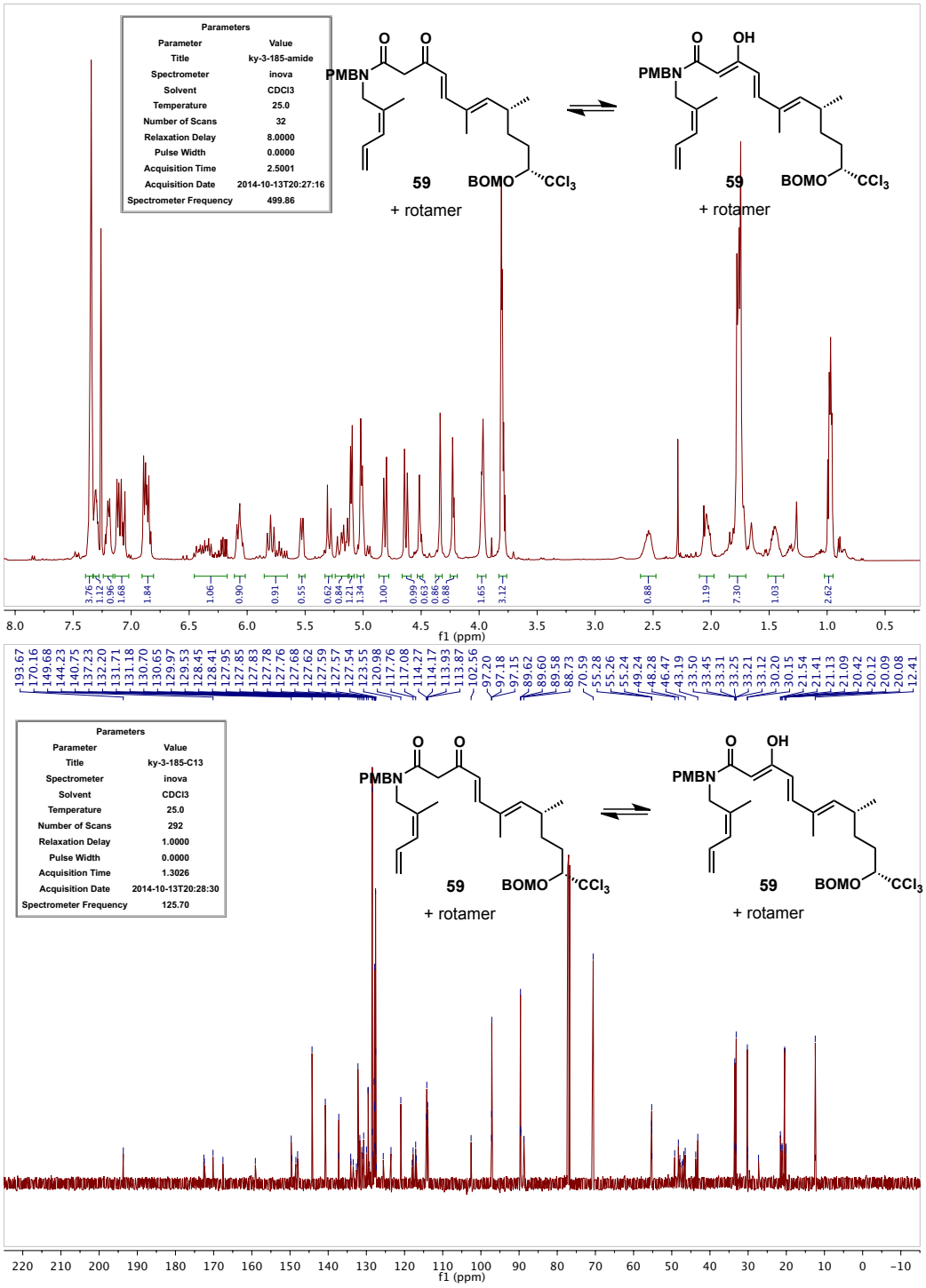

143.91
143.65
137.32
137.31
128.46
127.85
127.81
127.74
113.54
113.24
102.74
97.15
97.11
89.70
89.60
70.62
37.81
32.82
30.11
20.02
Parameters
Parameter Value
Title xq-4-212-C13
Spectrometer inova
Solvent CDCl3
Temperature 25.0
Number of Scans 216
Relaxation Delay 1.0000
Pulse Width 0.0000
Acquisition Time 1.3026
Acquisition Date 2014-03-28T18:17:14
Spectrometer Frequency 125.70
OBOM
Cl3C
S5
150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15
f1 (ppm)

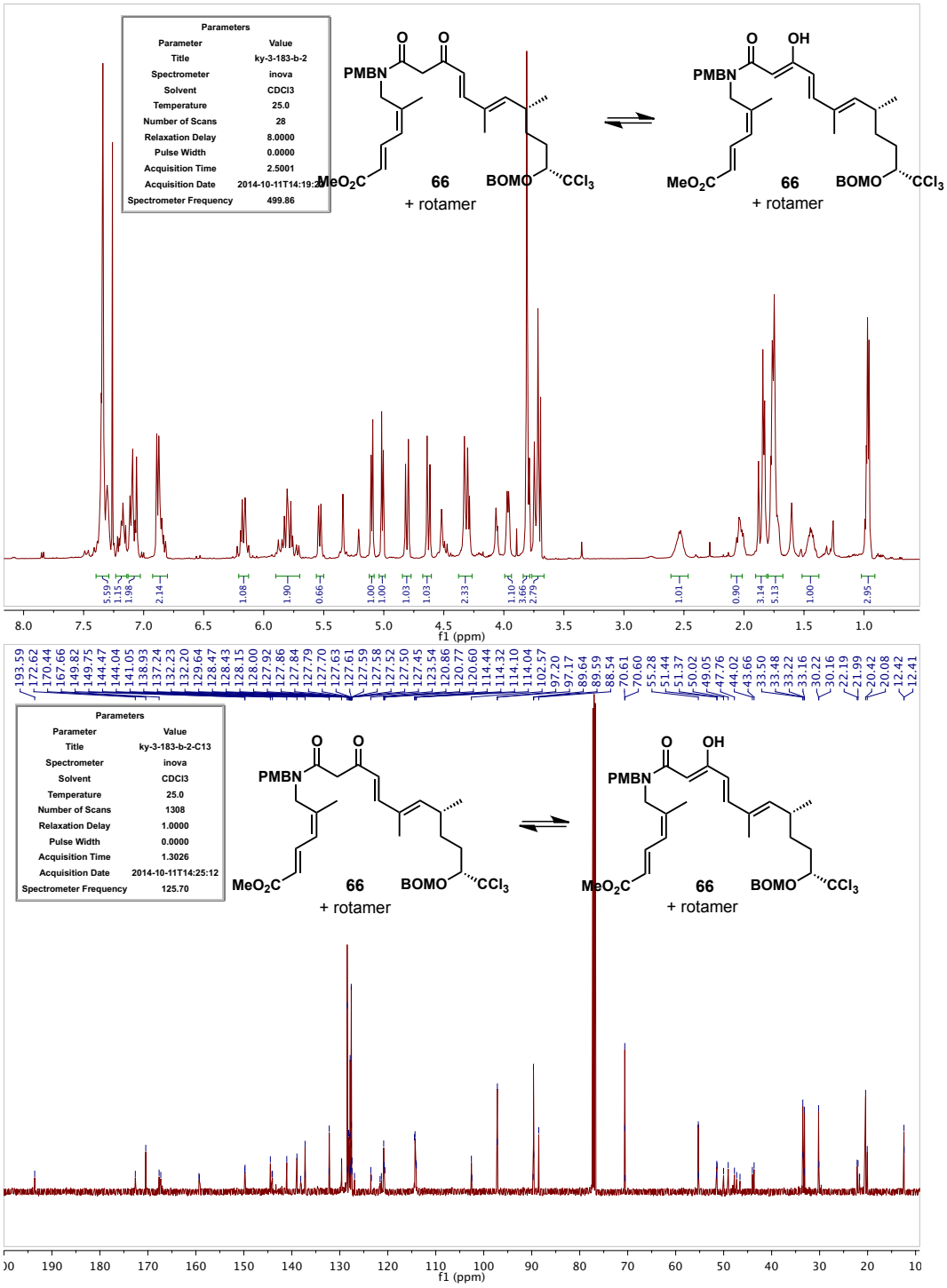

Parameters
Parameter Value
Title xq-4-216
Spectrometer inova
Solvent cdcl3
Temperature 30.0
Number of Scans 16
Relaxation Delay 8.0000
Pulse Width 0.0000
Acquisition Time 2.5000
Acquisition Date 2014-03-29T16:45:49
Spectrometer Frequency 599.64
OBOM
Cl3C
CHO
55
0.96
5.08
1.00
1.01
1.03
1.05
1.04
1.02
0.99
1.06
2.18
3.03
1.03
3.01
f1 (ppm)

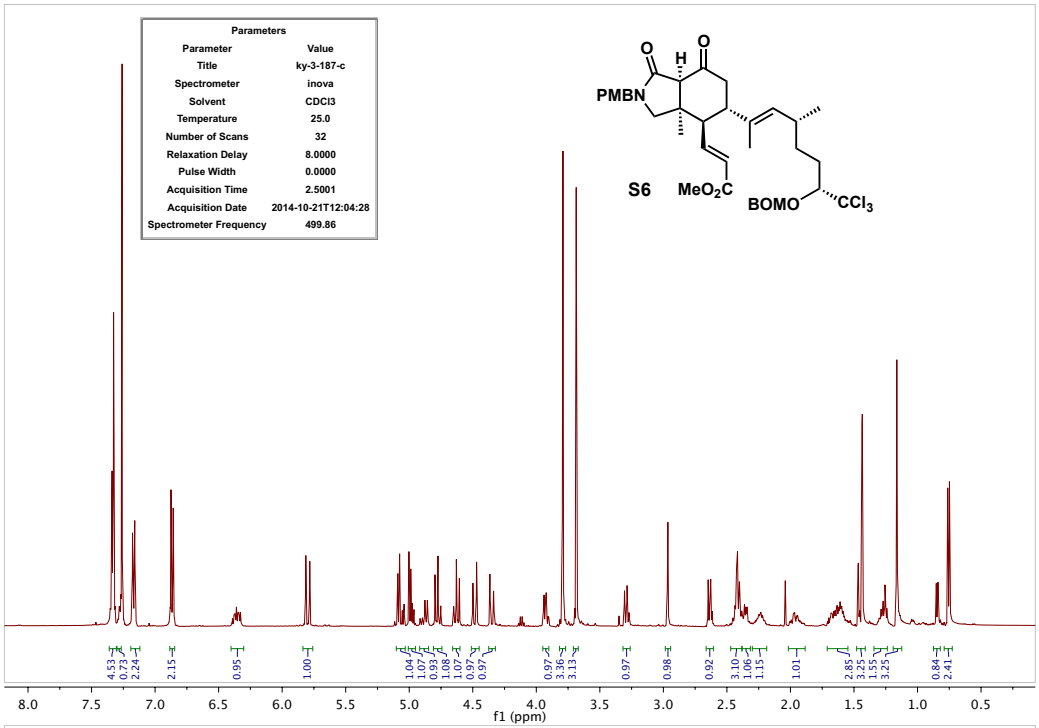

195.33
158.94
138.32
137.16
128.47
127.89
127.50
127.44
102.39
102.39
97.28
89.58
70.56
33.43
32.67
30.00
19.42
9.38
Parameters
Parameter Value
Title xq-4-216-C13
Spectrometer inova
Solvent cdcl3
Temperature 30.0
Number of Scans 420
Relaxation Delay 1.0000
Pulse Width 0.0000
Acquisition Time 1.2987
Acquisition Date 2014-03-29T16:42:10
Spectrometer Frequency 150.79
OBOM
Cl3C
CHO
55
f1 (ppm)

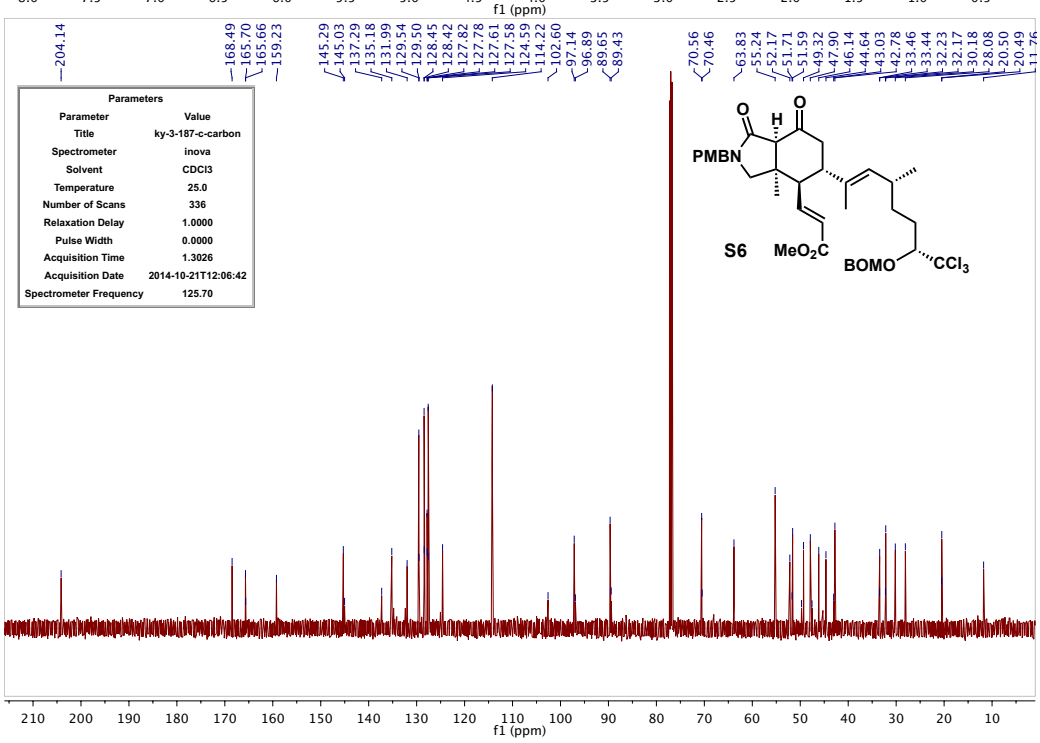

Parameters
Parameter Value
Title xq-4-167
Spectrometer inova
Solvent CDCl3
Temperature 24.0
Number of Scans 8
Relaxation Delay 8.0000
Pulse Width 0.0000
Acquisition Time 2.5001
Acquisition Date 2014-02-24T16:19:09
Spectrometer Frequency 499.86
OBOM
Cl3C
O
O
O
57
5.06
1.00
1.00
0.95
0.96
1.00
1.02
1.05
1.05
1.03
1.01
1.12
3.32
6.75
1.04
3.09
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

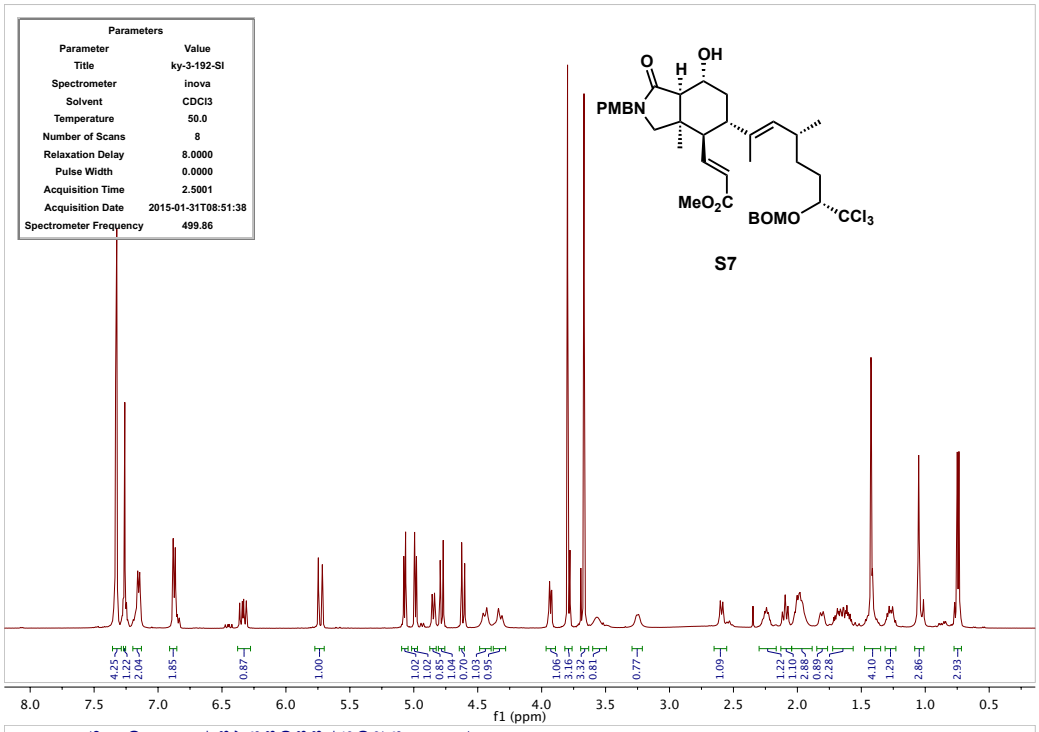

163.94
161.99
146.56
142.83
137.20
132.12
128.44
128.43
127.80
127.58
127.57
117.60
117.57
106.15
106.14
102.49
97.20
93.86
89.60
70.58
33.29
33.21
30.07
25.10
24.99
20.21
12.33
Parameters
Parameter Value
Title xq-4-167-C13
Spectrometer inova
Solvent CDCl3
Temperature 24.0
Number of Scans 220
Relaxation Delay 1.0000
Pulse Width 0.0000
Acquisition Time 1.3026
Acquisition Date 2014-02-24T16:19:34
Spectrometer Frequency 125.70
OBOM
Cl3C
O
O
O
57
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

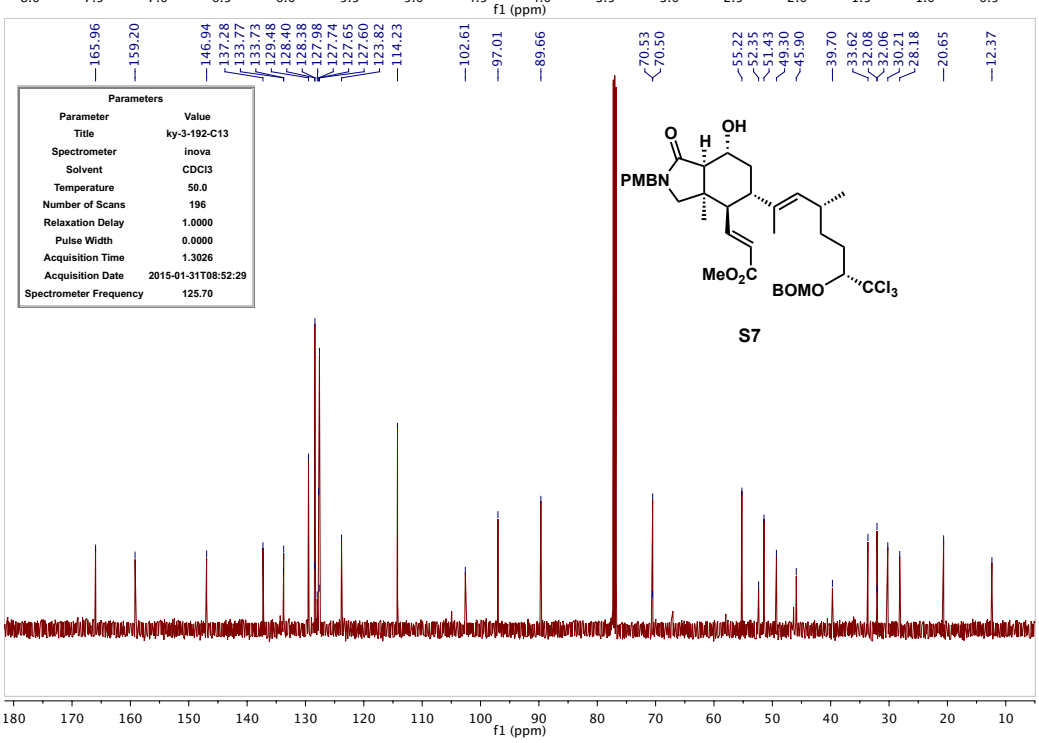

Parameters
Parameter Value
Title ky-3-185-amide
Spectrometer inova
Solvent CDCl3
Temperature 25.0
Number of Scans 32
Relaxation Delay 8.0000
Pulse Width 0.0000
Acquisition Time 2.5001
Acquisition Date 2014-10-13T20:27:16
Spectrometer Frequency 499.86
PMBN
O
O
59
BOMO
CCl3
+ rotamer
OH
f1 (ppm)
Parameters
Parameter Value
Title ky-3-185-C13
Spectrometer inova
Solvent CDCl3
Temperature 25.0
Number of Scans 292
Relaxation Delay 1.0000
Pulse Width 0.0000
Acquisition Time 1.3026
Acquisition Date 2014-10-13T20:28:30
Spectrometer Frequency 125.70

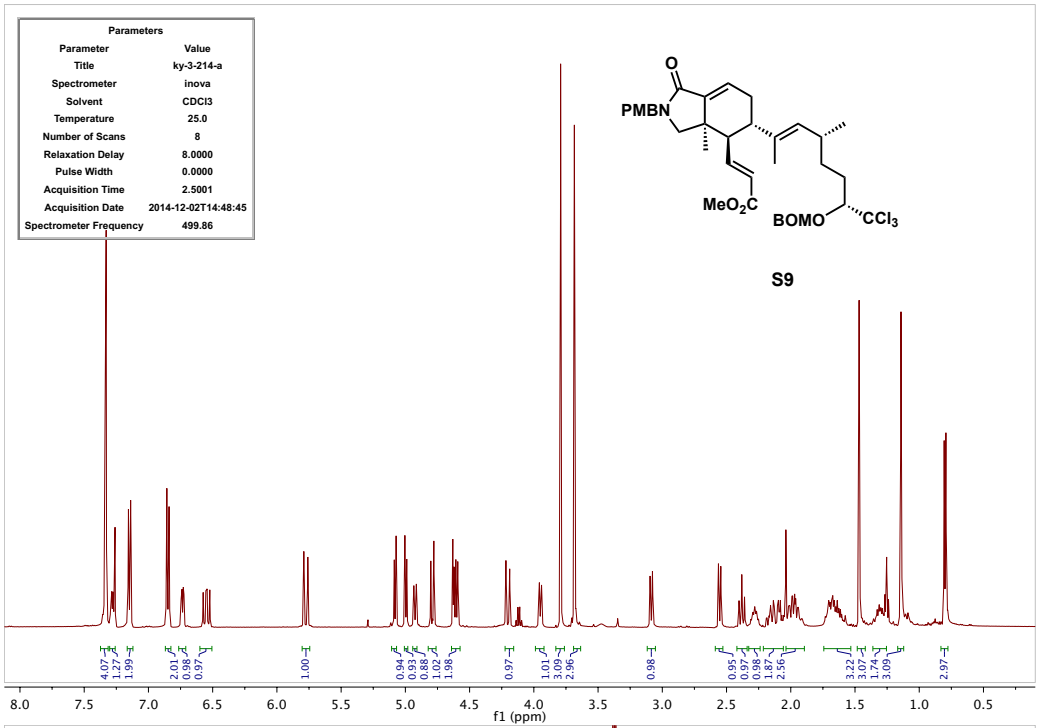

Parameters
Parameter Value
Title ky-3-183-b-2
Spectrometer inova
Solvent CDCl3
Temperature 25.0
Number of Scans 28
Relaxation Delay 8.0000
Pulse Width 0.0000
Acquisition Time 2.5001
Acquisition Date 2014-10-11T14:19:2
Spectrometer Frequency 499.86
PMBN
MeO2C
66
BOMO
CCl3
+ rotamer
OH
f1 (ppm)
Parameters
Parameter Value
Title ky-3-183-b-2-C13
Spectrometer inova
Solvent CDCl3
Temperature 25.0
Number of Scans 1308
Relaxation Delay 1.0000
Pulse Width 0.0000
Acquisition Time 1.3026
Acquisition Date 2014-10-11T14:25:12
Spectrometer Frequency 125.70

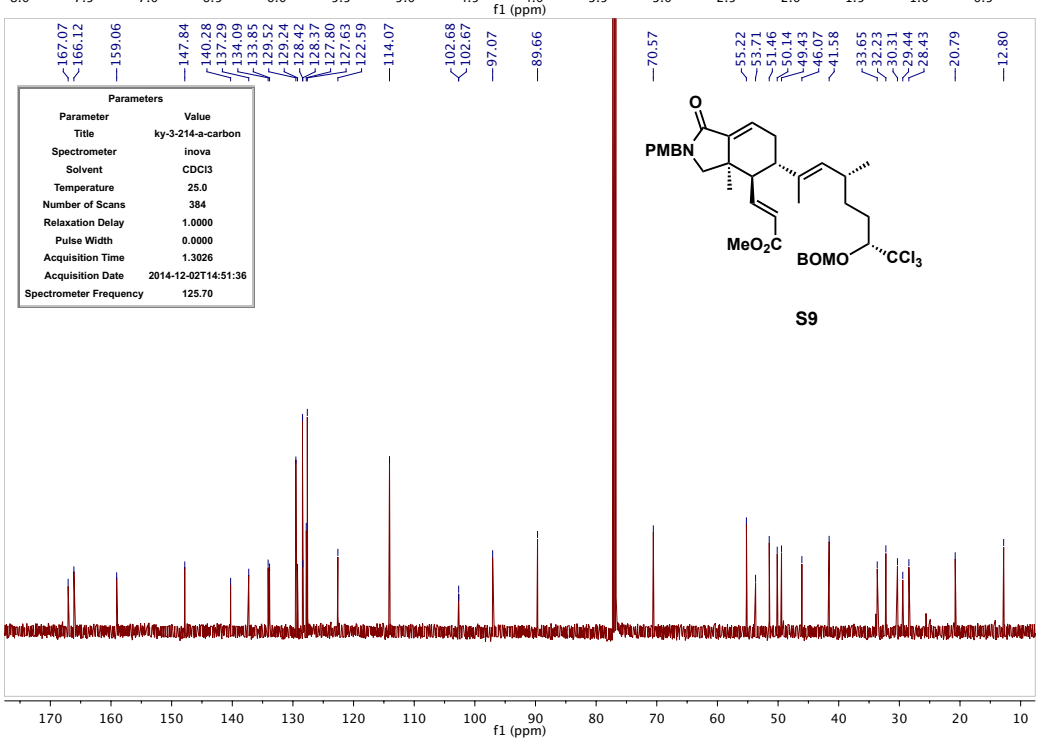

Parameters
Parameter Value
Title ky-3-187-c
Spectrometer inova
Solvent CDCl3
Temperature 25.0
Number of Scans 32
Relaxation Delay 8.0000
Pulse Width 0.0000
Acquisition Time 2.5001
Acquisition Date 2014-10-21T12:04:28
Spectrometer Frequency 499.86
PMBN
S6
MeO2C
BOMO
CCl3
f1 (ppm)

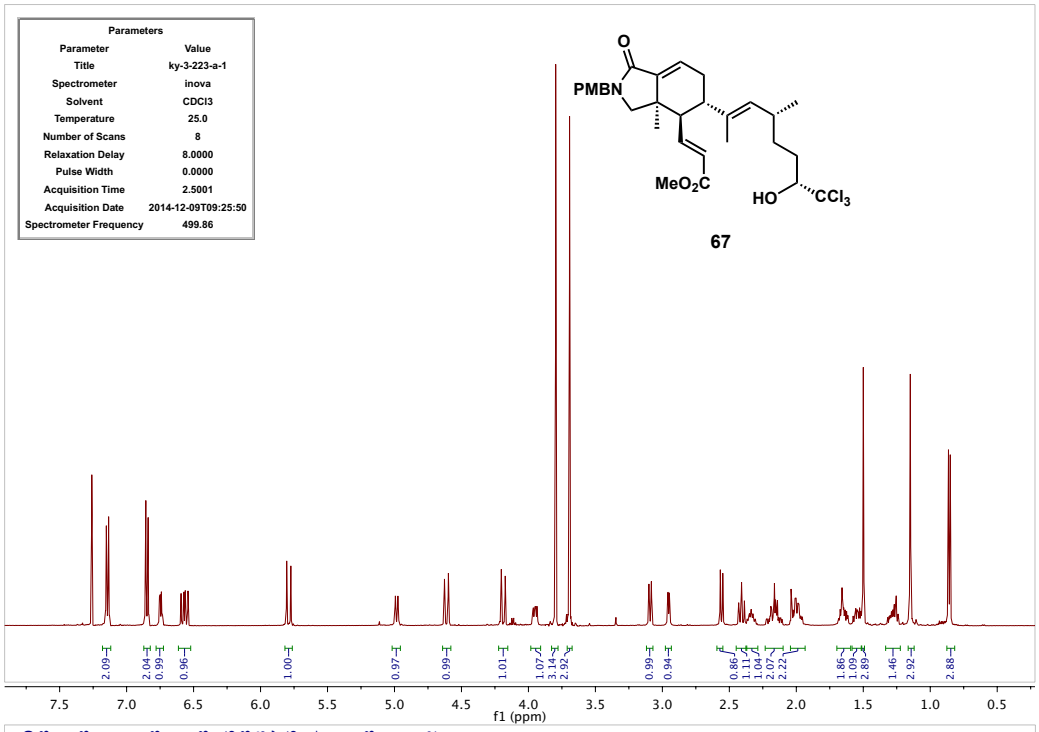

Parameters
Parameter Value
Title ky-3-187-c-carbon
Spectrometer inova
Solvent CDCl3
Temperature 25.0
Number of Scans 336
Relaxation Delay 1.0000
Pulse Width 0.0000
Acquisition Time 1.3026
Acquisition Date 2014-10-21T12:06:42
Spectrometer Frequency 125.70
PMBN
S6
MeO2C
BOMO
CCl3
f1 (ppm)

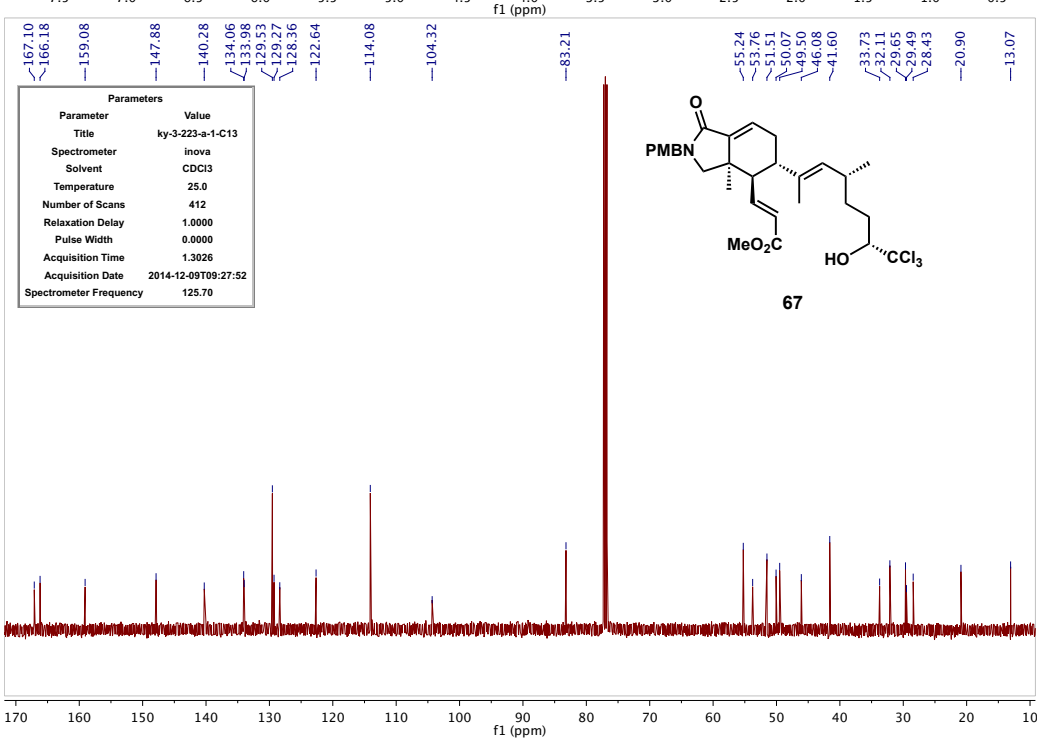

Parameters
Parameter Value
Title ky-3-192-SI
Spectrometer inova
Solvent CDCl3
Temperature 50.0
Number of Scans 8
Relaxation Delay 8.0000
Pulse Width 0.0000
Acquisition Time 2.5001
Acquisition Date 2015-01-31T08:51:38
Spectrometer Frequency 499.86
PMBN
OH
H
O
MeO2C
BOMO
CCl3
S7
f1 (ppm)

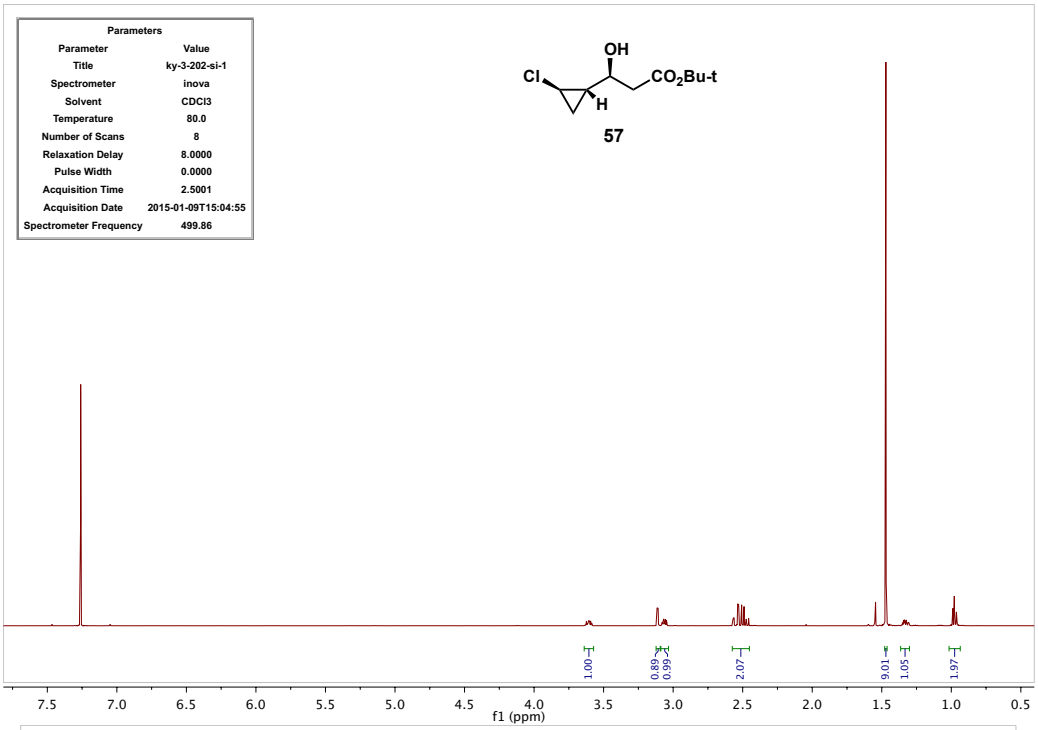

165.96
159.20
146.94
137.28
133.77
133.73
129.48
128.40
128.38
127.98
127.74
127.65
127.60
123.82
114.23
102.61
97.01
89.66
70.53
70.50
55.22
52.35
51.43
49.30
45.90
39.70
33.62
32.08
32.06
30.21
28.18
20.65
12.37
Parameters
Parameter Value
Title ky-3-192-C13
Spectrometer inova
Solvent CDCl3
Temperature 50.0
Number of Scans 196
Relaxation Delay 1.0000
Pulse Width 0.0000
Acquisition Time 1.3026
Acquisition Date 2015-01-31T08:52:29
Spectrometer Frequency 125.70
PMBN
OH
H
O
MeO2C
BOMO
CCl3
S7
f1 (ppm)

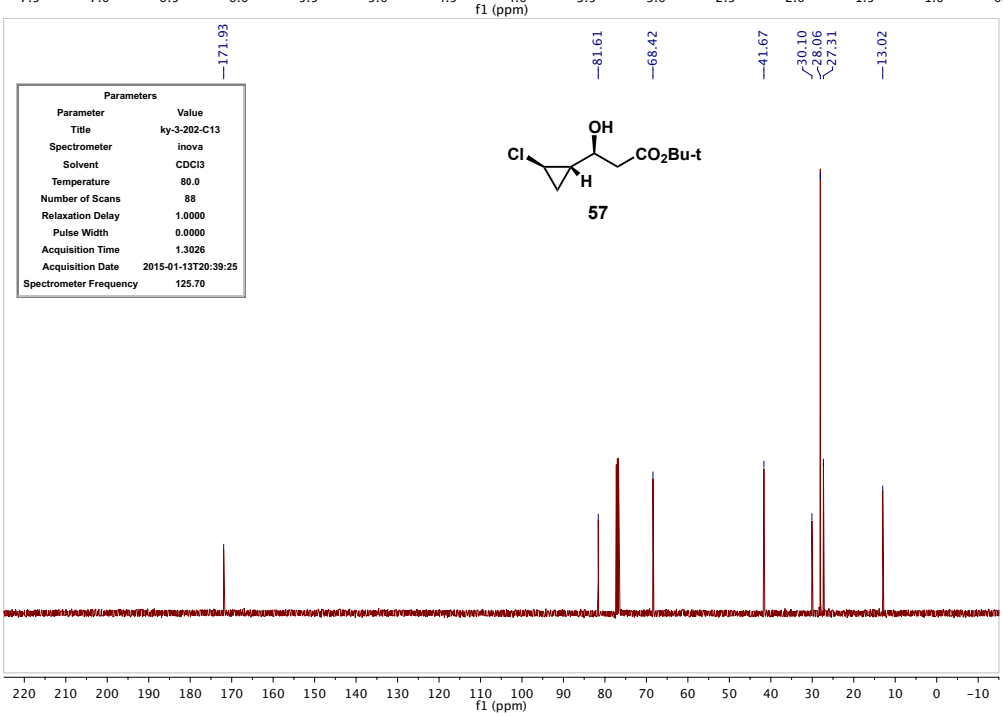

Parameters
Parameter Value
Title ky-3-214-a
Spectrometer inova
Solvent CDCl3
Temperature 25.0
Number of Scans 8
Relaxation Delay 8.0000
Pulse Width 0.0000
Acquisition Time 2.5001
Acquisition Date 2014-12-02T14:48:45
Spectrometer Frequency 499.86
PMBN
O
MeO2C
BOMO
CCl3
S9
f1 (ppm)

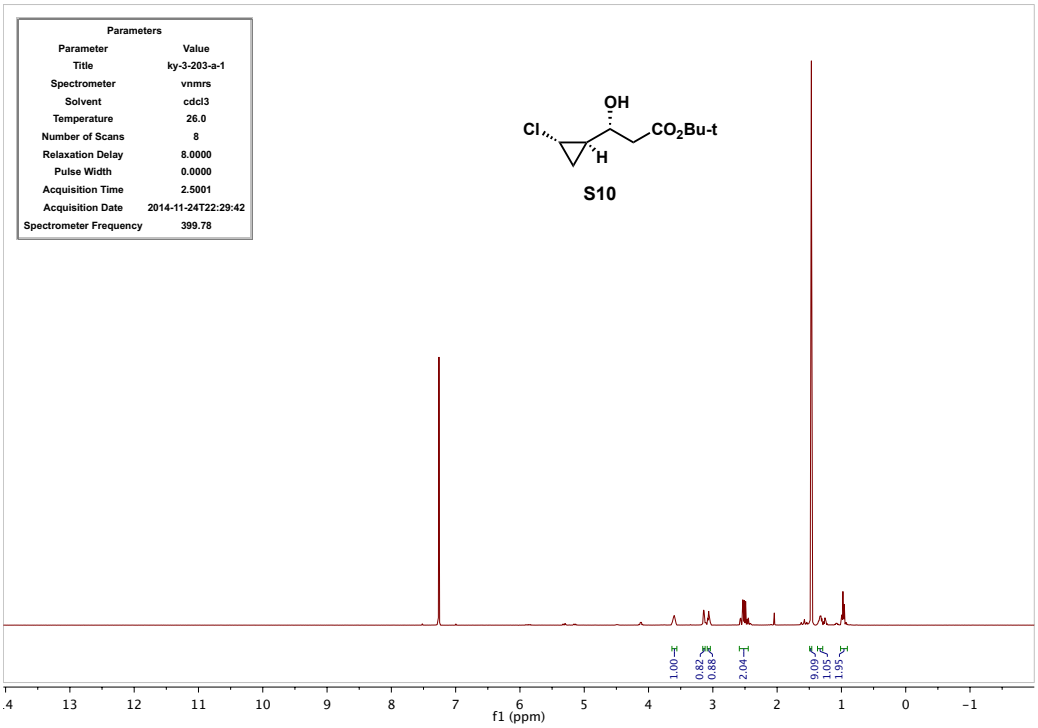

Parameters
Parameter Value
Title ky-3-214-a-carbon
Spectrometer inova
Solvent CDCl3
Temperature 25.0
Number of Scans 384
Relaxation Delay 1.0000
Pulse Width 0.0000
Acquisition Time 1.3026
Acquisition Date 2014-12-02T14:51:36
Spectrometer Frequency 125.70
PMBN
O
MeO2C
BOMO
CCl3
S9
f1 (ppm)

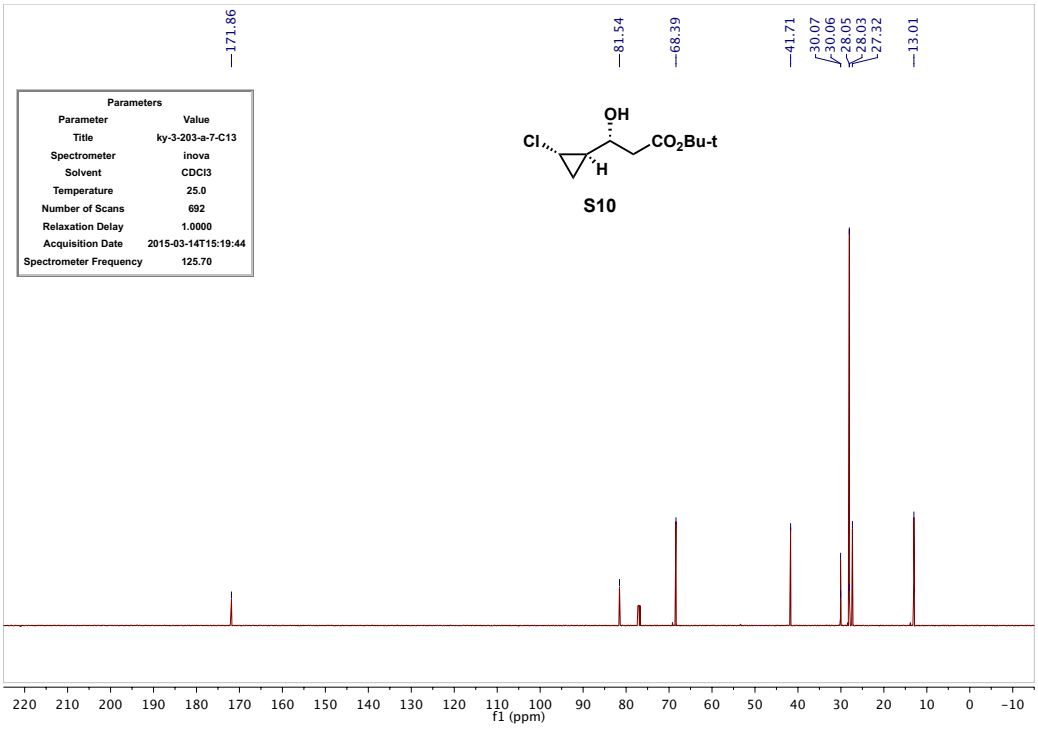

Parameters
Parameter Value
Title ky-3-223-a-1
Spectrometer inova
Solvent CDCl3
Temperature 25.0
Number of Scans 8
Relaxation Delay 8.0000
Pulse Width 0.0000
Acquisition Time 2.5001
Acquisition Date 2014-12-09T09:25:50
Spectrometer Frequency 499.86
PMBN
MeO2C
HO
CCl3
67
f1 (ppm)

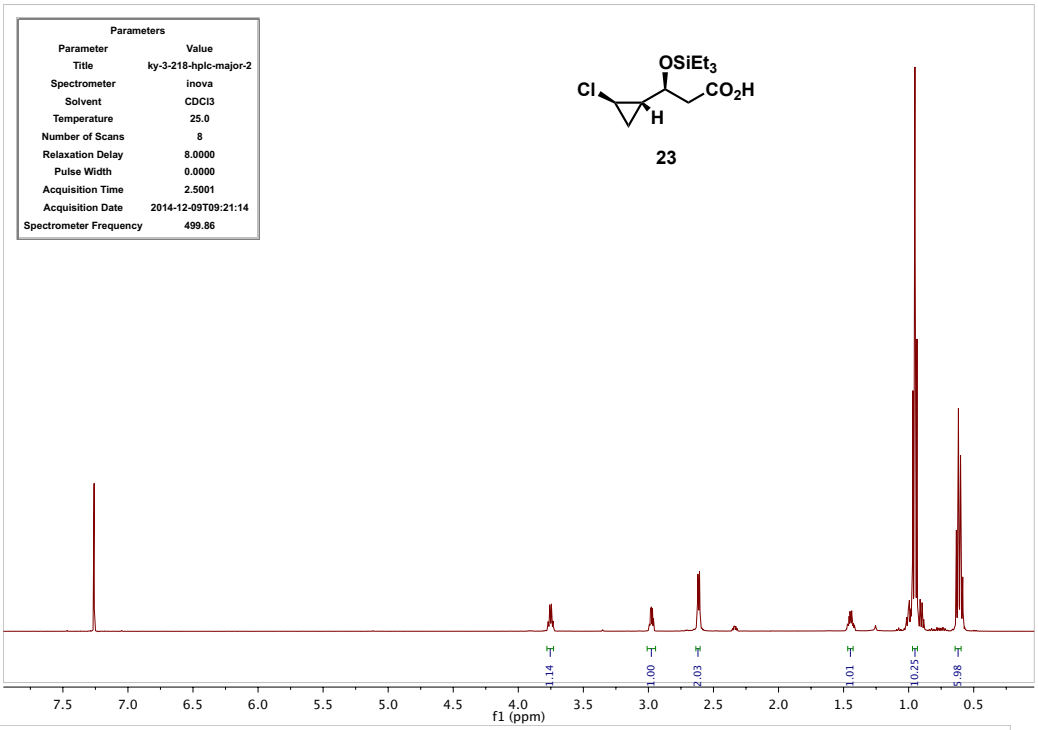

Parameters
Parameter Value
Title ky-3-223-a-1-C13
Spectrometer inova
Solvent CDCl3
Temperature 25.0
Number of Scans 412
Relaxation Delay 1.0000
Pulse Width 0.0000
Acquisition Time 1.3026
Acquisition Date 2014-12-09T09:27:52
Spectrometer Frequency 125.70
PMBN
MeO2C
HO
CCl3
67
f1 (ppm)

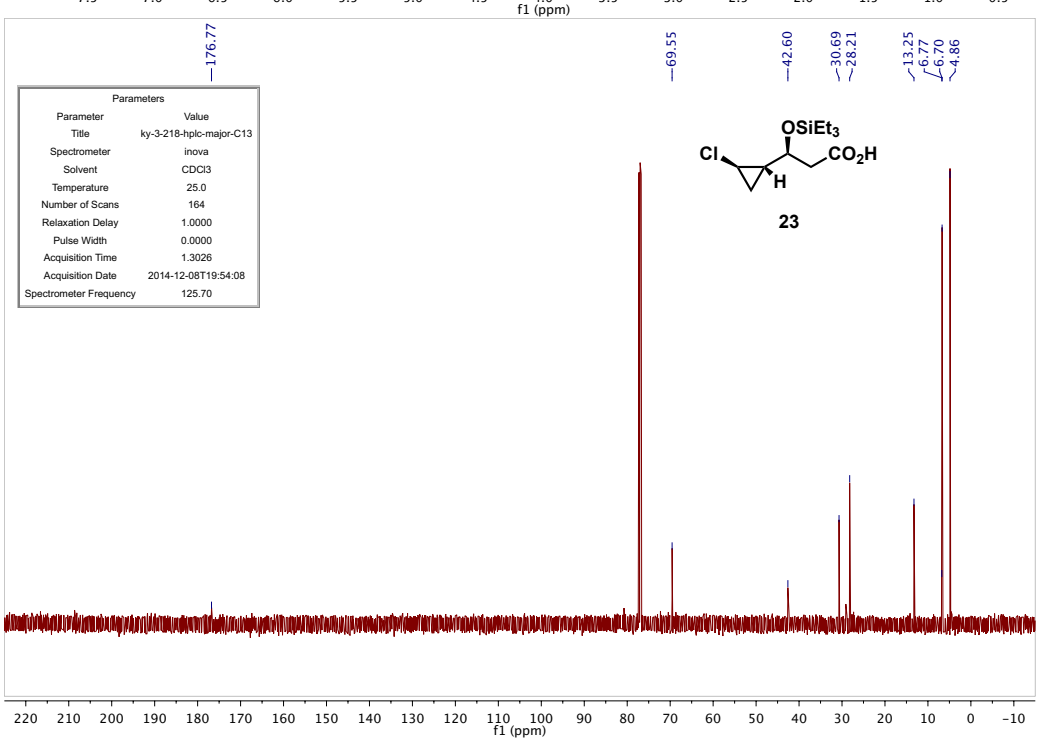

Parameters
Parameter Value
Title ky-3-202-si-1
Spectrometer inova
Solvent CDCl3
Temperature 80.0
Number of Scans 8
Relaxation Delay 8.0000
Pulse Width 0.0000
Acquisition Time 2.5001
Acquisition Date 2015-01-09T15:04:55
Spectrometer Frequency 499.86
OH
Cl
CO2Bu-t
H
57
1.00
0.89
0.99
2.07
9.01
1.05
1.97
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

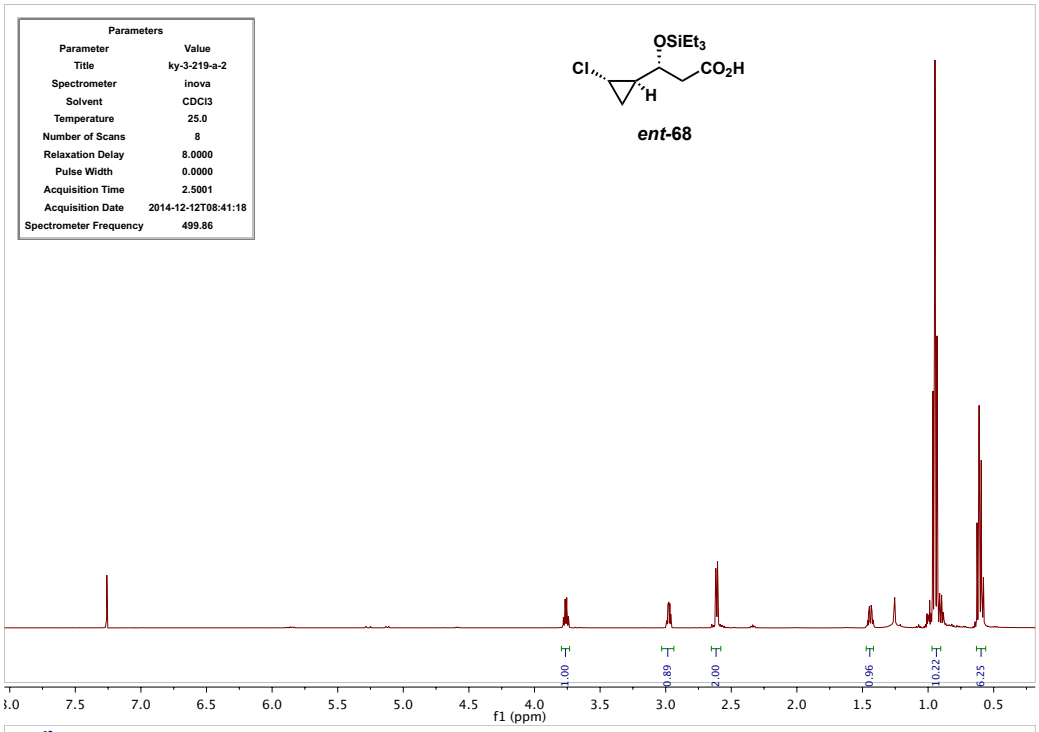

171.93
81.61
68.42
41.67
30.10
28.06
27.31
13.02
Parameters
Parameter Value
Title ky-3-202-C13
Spectrometer inova
Solvent CDCl3
Temperature 80.0
Number of Scans 88
Relaxation Delay 1.0000
Pulse Width 0.0000
Acquisition Time 1.3026
Acquisition Date 2015-01-13T20:39:25
Spectrometer Frequency 125.70
OH
Cl
CO2Bu-t
H
57
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

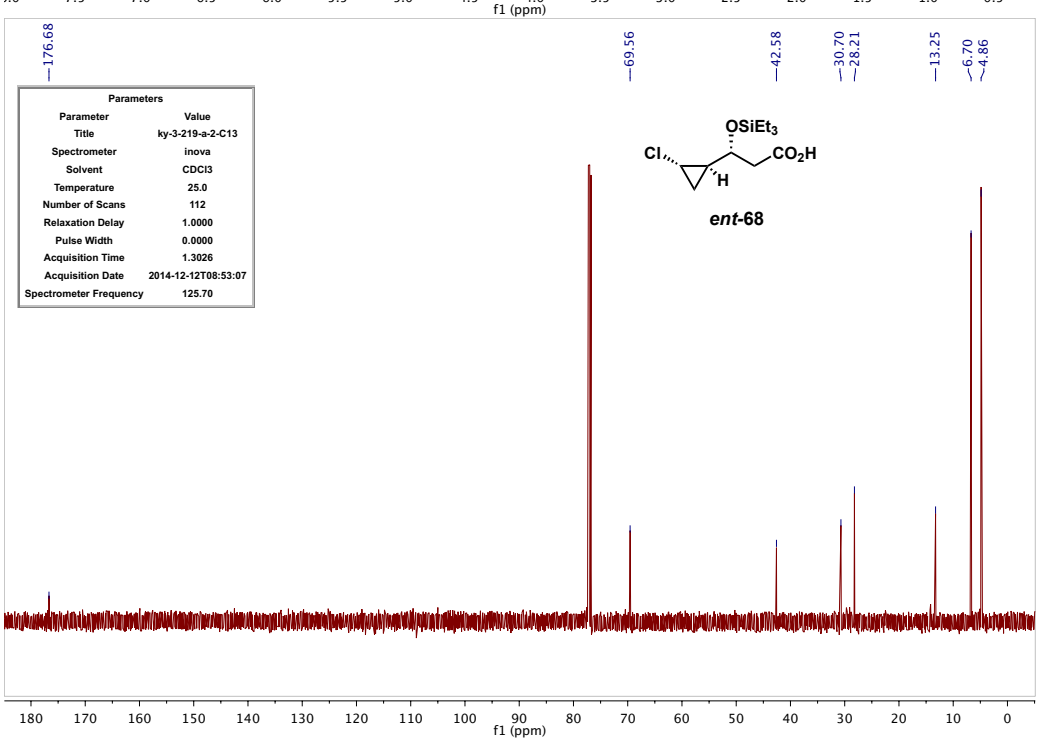

Parameters
Parameter Value
Title ky-3-203-a-1
Spectrometer vnmrs
Solvent cdcl3
Temperature 26.0
Number of Scans 8
Relaxation Delay 8.0000
Pulse Width 0.0000
Acquisition Time 2.5001
Acquisition Date 2014-11-24T22:29:42
Spectrometer Frequency 399.78
OH
Cl
CO2Bu-t
H
S10
1.00
0.82
0.88
2.04
9.09
1.05
1.95
f1 (ppm)

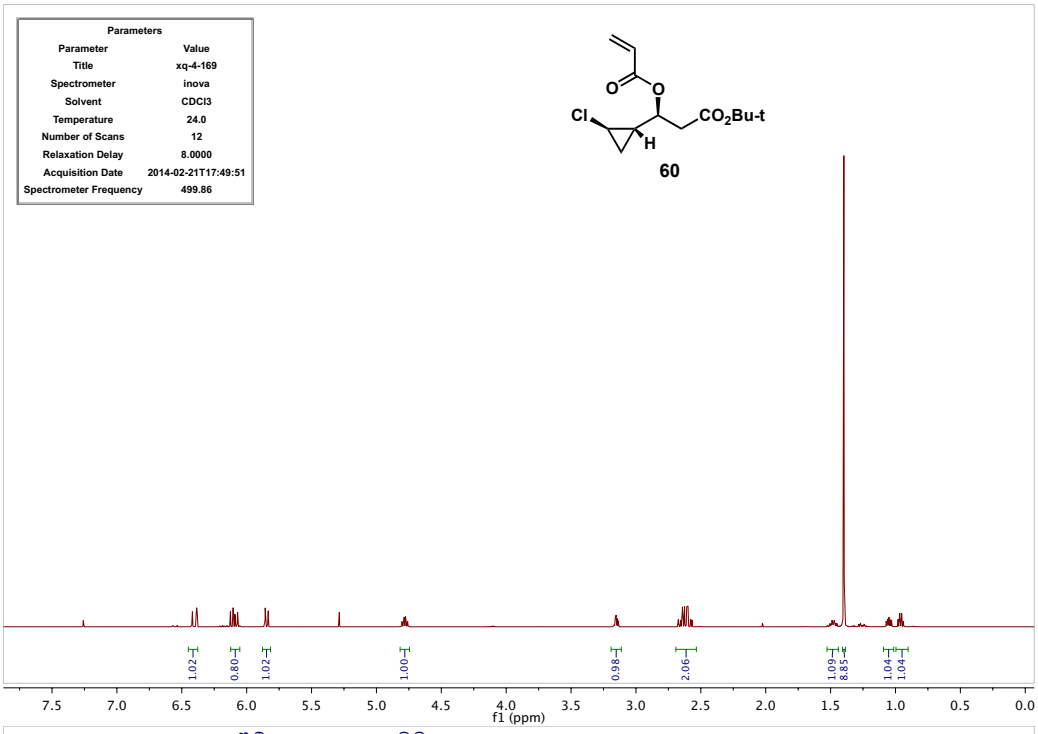

171.86
81.54
68.39
41.71
30.07
30.06
28.05
28.03
27.32
13.01
Parameters
Parameter Value
Title ky-3-203-a-7-C13
Spectrometer inova
Solvent CDCl3
Temperature 25.0
Number of Scans 692
Relaxation Delay 1.0000
Acquisition Date 2015-03-14T15:19:44
Spectrometer Frequency 125.70
OH
Cl
CO2Bu-t
H
S10
f1 (ppm)

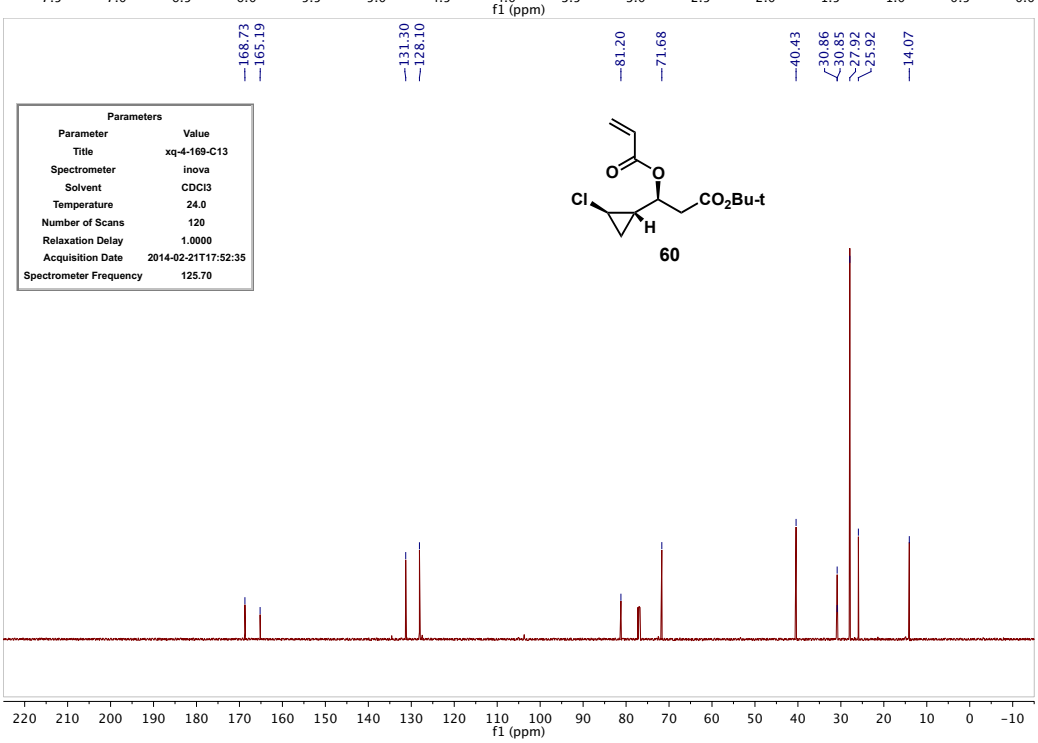

Parameters
Parameter Value
Title ky-3-218-hplc-major-2
Spectrometer inova
Solvent CDCl3
Temperature 25.0
Number of Scans 8
Relaxation Delay 8.0000
Pulse Width 0.0000
Acquisition Time 2.5001
Acquisition Date 2014-12-09T09:21:14
Spectrometer Frequency 499.86
OSiEt3
Cl
CO2H
H
23
1.14
1.00
2.03
1.01
10.25
5.98
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

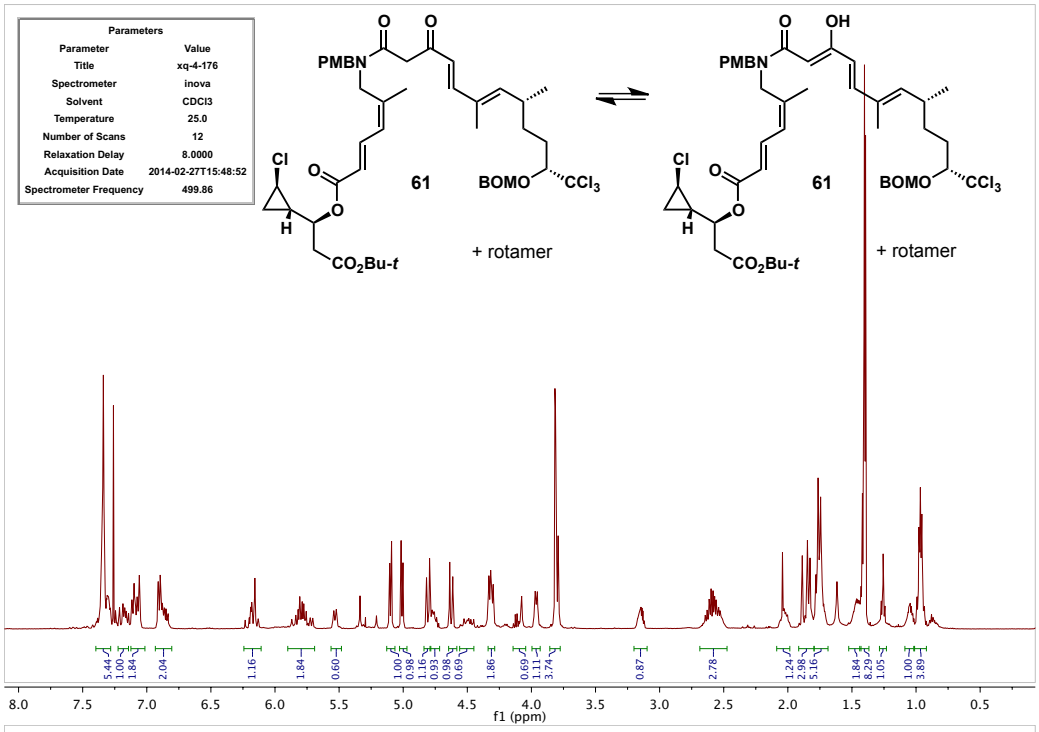

176.77
69.55
42.60
30.69
28.21
13.25
6.77
6.70
4.86
Parameters
Parameter Value
Title ky-3-218-hplc-major-C13
Spectrometer inova
Solvent CDCl3
Temperature 25.0
Number of Scans 164
Relaxation Delay 1.0000
Pulse Width 0.0000
Acquisition Time 1.3026
Acquisition Date 2014-12-08T19:54:08
Spectrometer Frequency 125.70
OSiEt3
Cl
CO2H
H
23
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

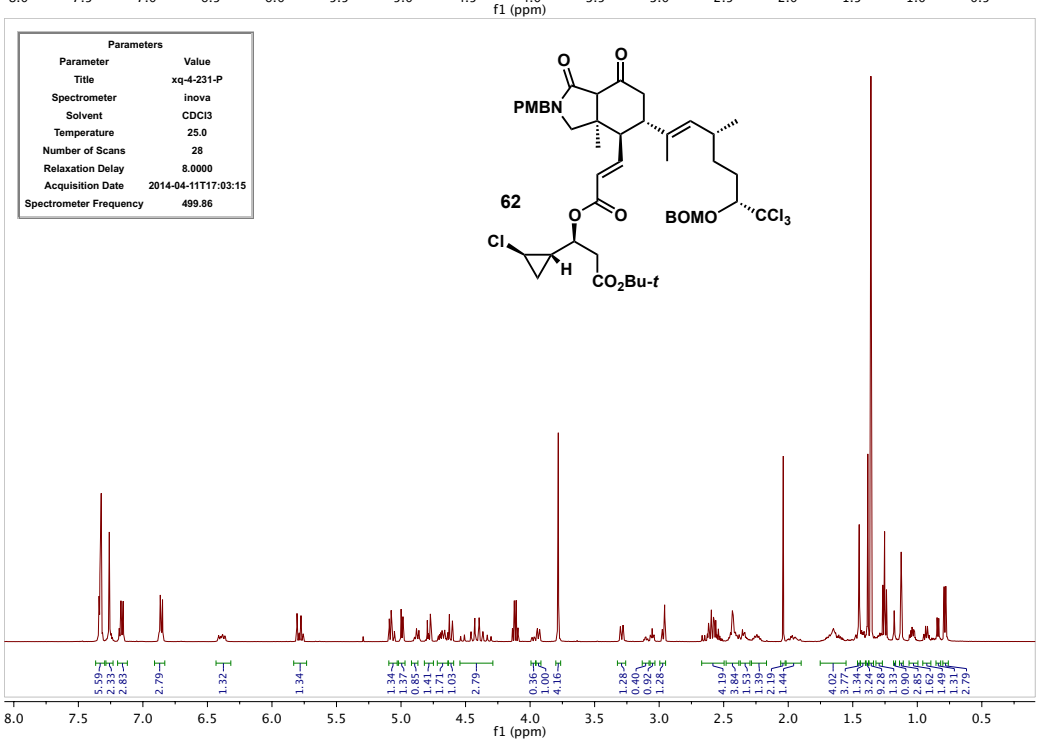

Parameters
Parameter Value
Title ky-3-219-a-2
Spectrometer inova
Solvent CDCl3
Temperature 25.0
Number of Scans 8
Relaxation Delay 8.0000
Pulse Width 0.0000
Acquisition Time 2.5001
Acquisition Date 2014-12-12T08:41:18
Spectrometer Frequency 499.86
OSiEt3
Cl
CO2H
H
ent-68
1.00
0.89
2.00
0.96
10.22
6.25
f1 (ppm)

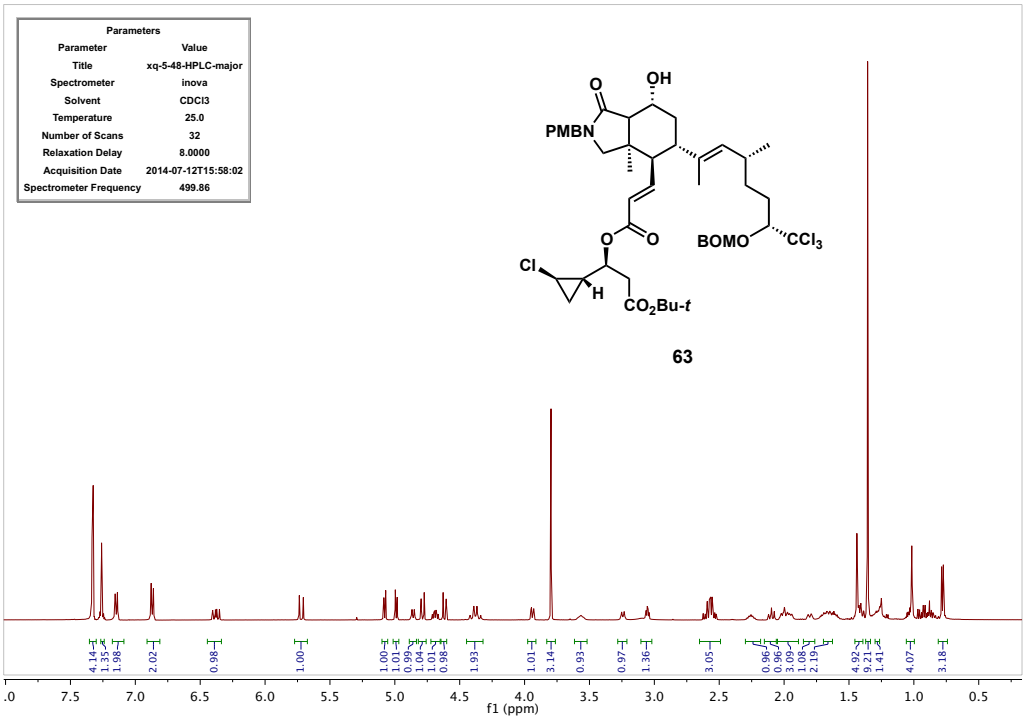

176.68
69.56
42.58
30.70
28.21
13.25
6.70
4.86
Parameters
Parameter Value
Title ky-3-219-a-2-C13
Spectrometer inova
Solvent CDCl3
Temperature 25.0
Number of Scans 112
Relaxation Delay 1.0000
Pulse Width 0.0000
Acquisition Time 1.3026
Acquisition Date 2014-12-12T08:53:07
Spectrometer Frequency 125.70
OSiEt3
Cl
CO2H
H
ent-68
f1 (ppm)

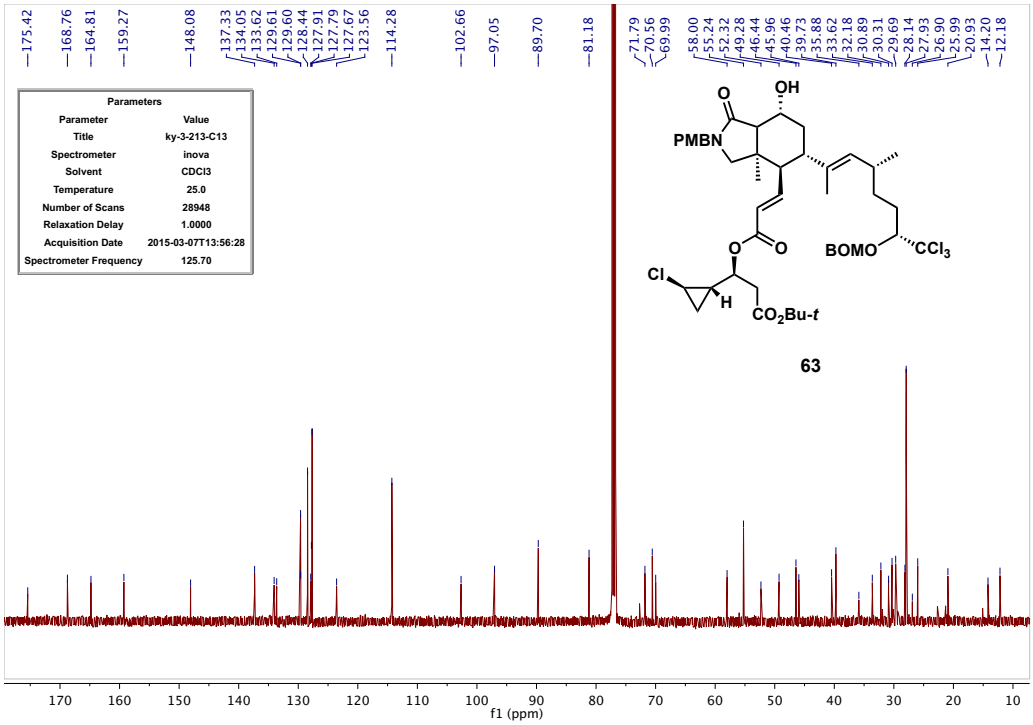

Parameters
Parameter Value
Title xq-4-169
Spectrometer inova
Solvent CDCl3
Temperature 24.0
Number of Scans 12
Relaxation Delay 8.0000
Acquisition Date 2014-02-21T17:49:51
Spectrometer Frequency 499.86
Cl
O
O
CO2Bu-t
H
60
1.02
0.80
1.02
1.00
0.98
2.06
1.09
8.85
1.04
1.04
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

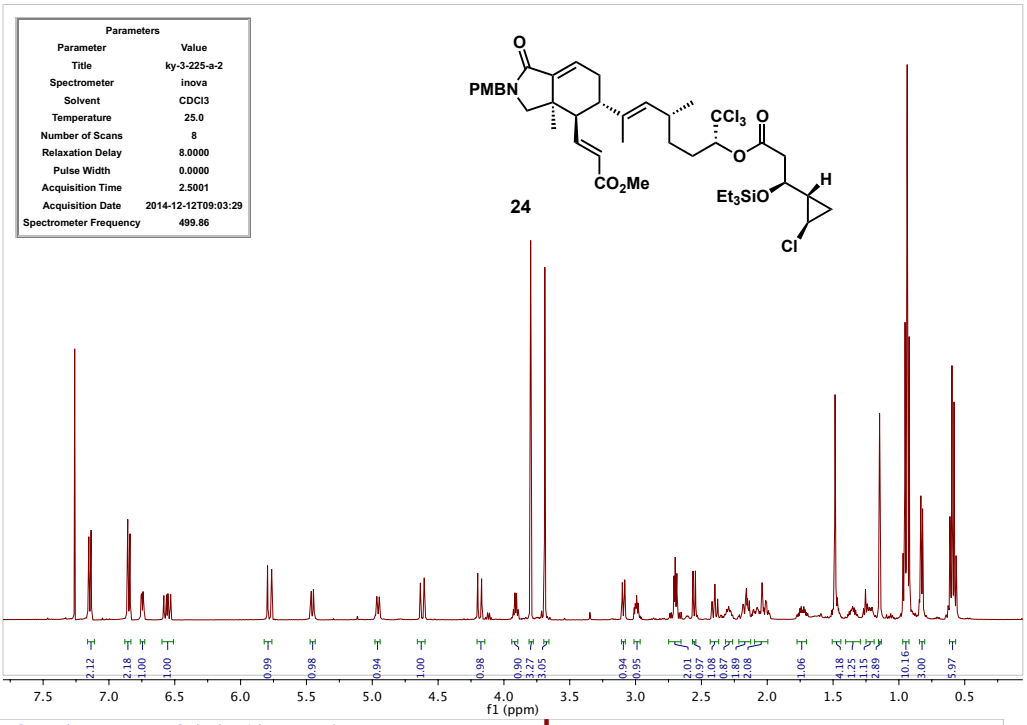

168.73
165.19
131.30
128.10
81.20
71.68
40.43
30.86
30.85
27.92
25.92
14.07
Parameters
Parameter Value
Title xq-4-169-C13
Spectrometer inova
Solvent CDCl3
Temperature 24.0
Number of Scans 120
Relaxation Delay 1.0000
Acquisition Date 2014-02-21T17:52:35
Spectrometer Frequency 125.70
Cl
O
O
CO2Bu-t
H
60
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

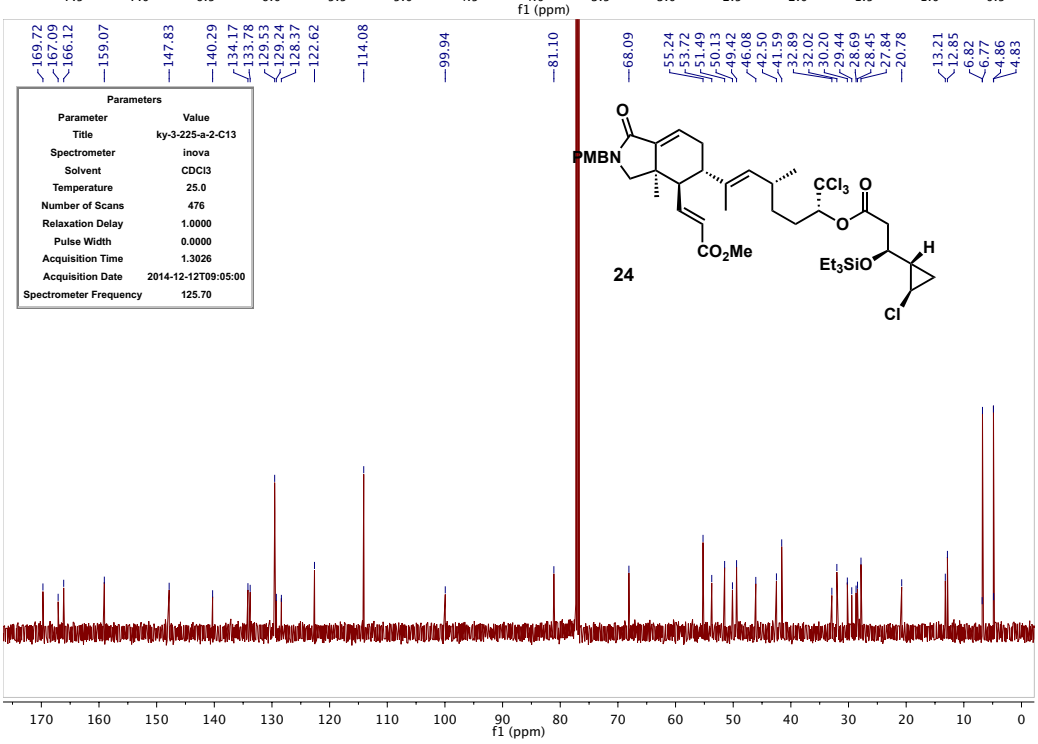

Parameters
Parameter Value
Title xq-4-176
Spectrometer inova
Solvent CDCl3
Temperature 25.0
Number of Scans 12
Relaxation Delay 8.0000
Acquisition Date 2014-02-27T15:48:52
Spectrometer Frequency 499.86
PMBN
61
BOMO
CCl3
Cl
H
CO2Bu-t
+ rotamer
OH
f1 (ppm)

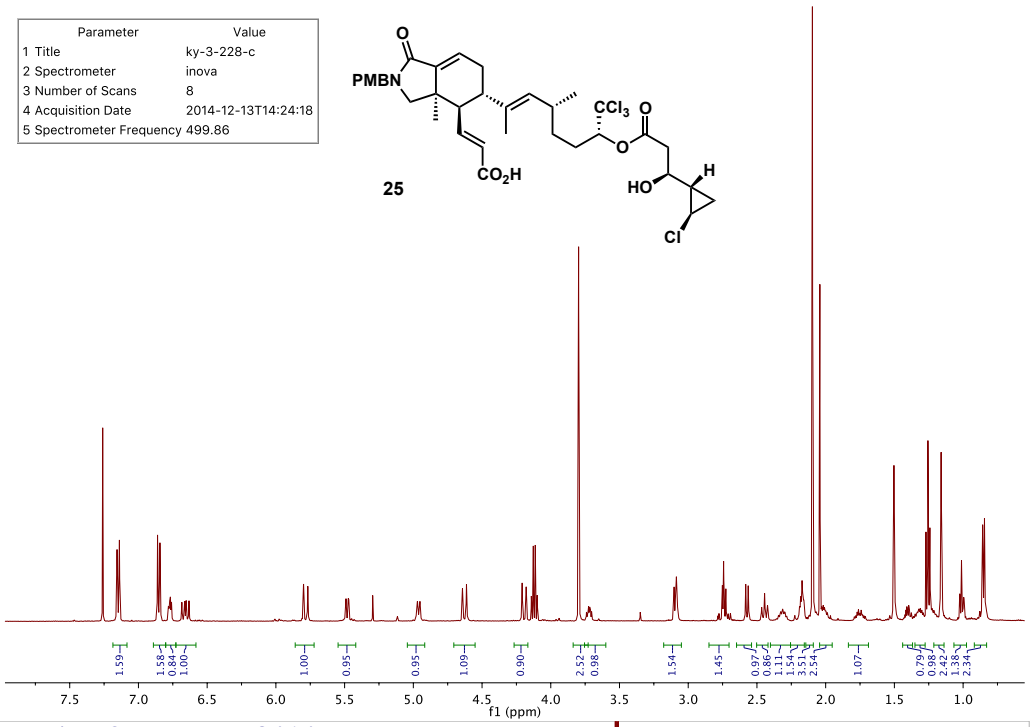

Parameters
Parameter Value
Title xq-4-231-P
Spectrometer inova
Solvent CDCl3
Temperature 25.0
Number of Scans 28
Relaxation Delay 8.0000
Acquisition Date 2014-04-11T17:03:15
Spectrometer Frequency 499.86
PMBN
62
BOMO
CCl3
Cl
H
CO2Bu-t
f1 (ppm)

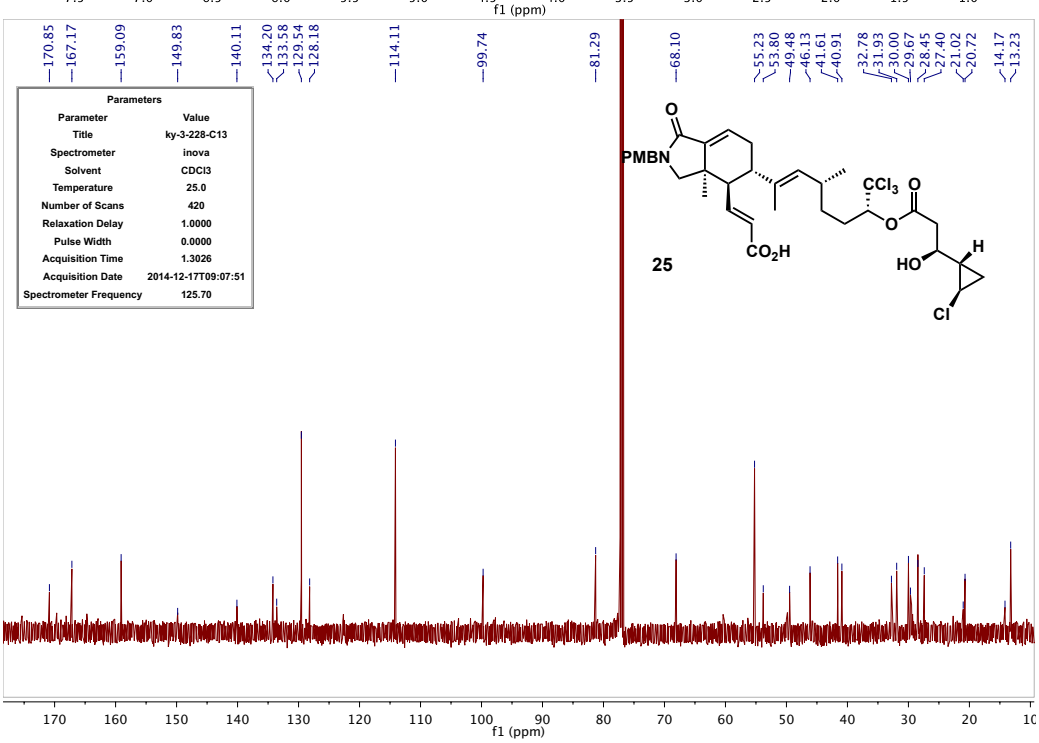

Parameters
Parameter Value
Title xq-5-48-HPLC-major
Spectrometer inova
Solvent CDCl3
Temperature 25.0
Number of Scans 32
Relaxation Delay 8.0000
Acquisition Date 2014-07-12T15:58:02
Spectrometer Frequency 499.86
OH
O
PMBN
O
O
BOMO
CCl3
Cl
H
CO2Bu-t
63
f1 (ppm)

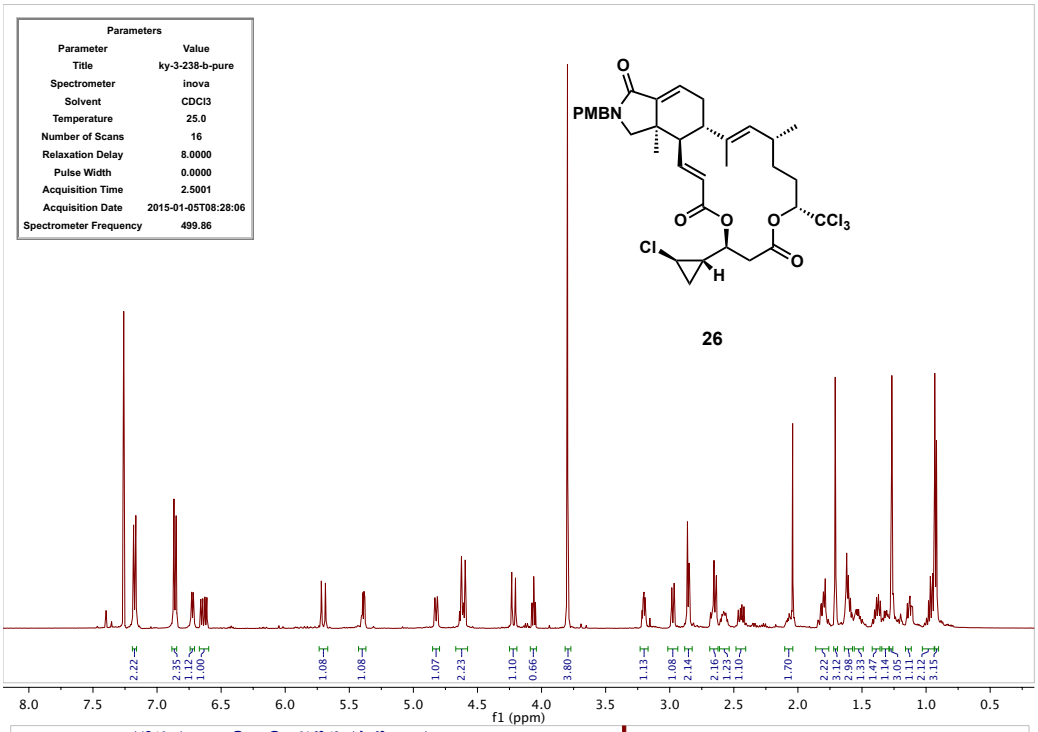

175.42
168.76
164.81
159.27
148.08
137.33
134.05
133.62
129.61
129.60
128.44
127.91
127.79
127.67
123.56
114.28
102.66
97.05
89.70
81.18
71.79
70.56
69.99
58.00
55.24
52.32
49.28
46.44
45.96
40.46
39.73
35.88
33.62
32.18
30.89
30.31
29.69
28.14
27.93
26.90
25.99
20.93
14.20
12.18
Parameters
Parameter Value
Title ky-3-213-C13
Spectrometer inova
Solvent CDCl3
Temperature 25.0
Number of Scans 28948
Relaxation Delay 1.0000
Acquisition Date 2015-03-07T13:56:28
Spectrometer Frequency 125.70
OH
O
PMBN
O
O
BOMO
CCl3
Cl
H
CO2Bu-t
63
f1 (ppm)

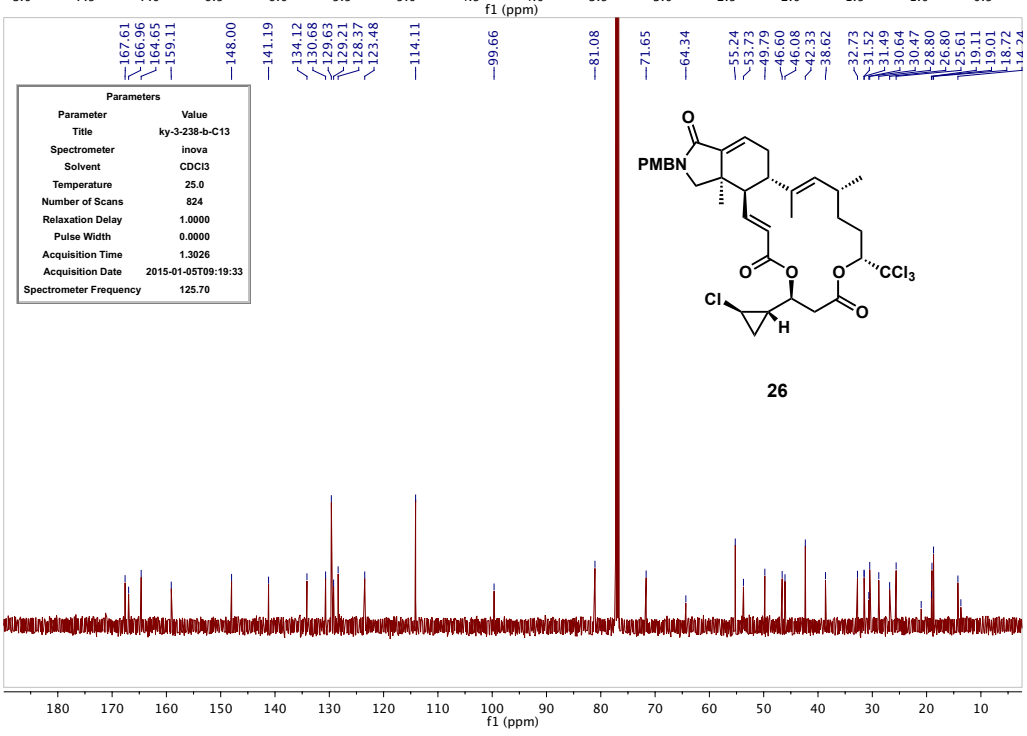

Parameters
Parameter Value
Title ky-3-225-a-2
Spectrometer inova
Solvent CDCl3
Temperature 25.0
Number of Scans 8
Relaxation Delay 8.0000
Pulse Width 0.0000
Acquisition Time 2.5001
Acquisition Date 2014-12-12T09:03:29
Spectrometer Frequency 499.86
PMBN
CCl3
CO2Me
Et3SiO
H
Cl
24
f1 (ppm)

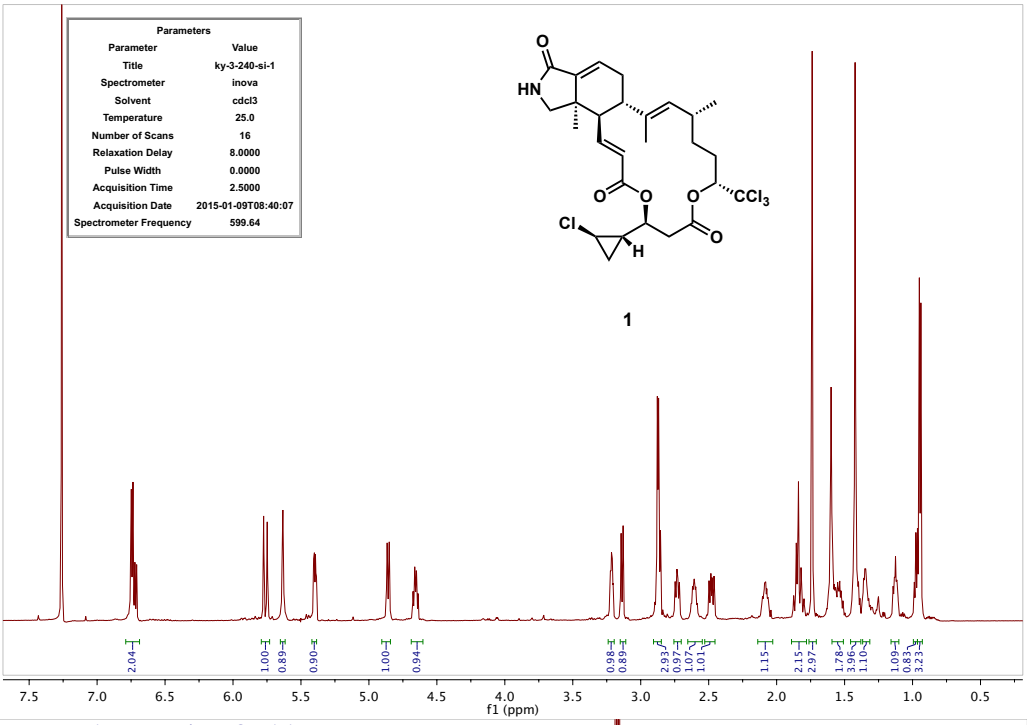

169.72
167.09
166.12
159.07
147.83
140.29
134.17
133.78
129.53
129.24
128.37
122.62
114.08
99.94
81.10
68.09
55.24
53.72
51.49
50.13
49.42
46.08
42.50
41.59
32.89
32.02
30.20
29.44
28.69
28.45
27.84
20.78
13.21
12.85
6.82
6.77
4.86
4.83
Parameters
Parameter Value
Title ky-3-225-a-2-C13
Spectrometer inova
Solvent CDCl3
Temperature 25.0
Number of Scans 476
Relaxation Delay 1.0000
Pulse Width 0.0000
Acquisition Time 1.3026
Acquisition Date 2014-12-12T09:05:00
Spectrometer Frequency 125.70
PMBN
CCl3
CO2Me
Et3SiO
H
Cl
24
f1 (ppm)

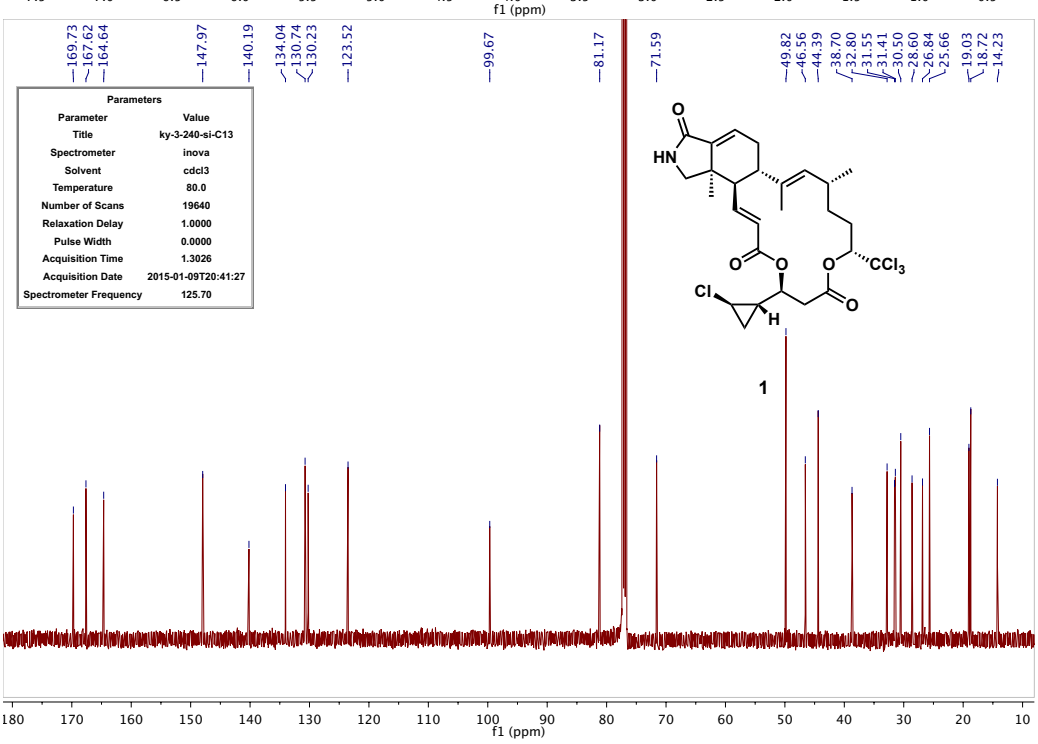

Parameter Value
1 Title ky-3-228-c
2 Spectrometer inova
3 Number of Scans 8
4 Acquisition Date 2014-12-13T14:24:18
5 Spectrometer Frequency 499.86
PMBN
CCl3
CO2H
HO
Cl
25
f1 (ppm)

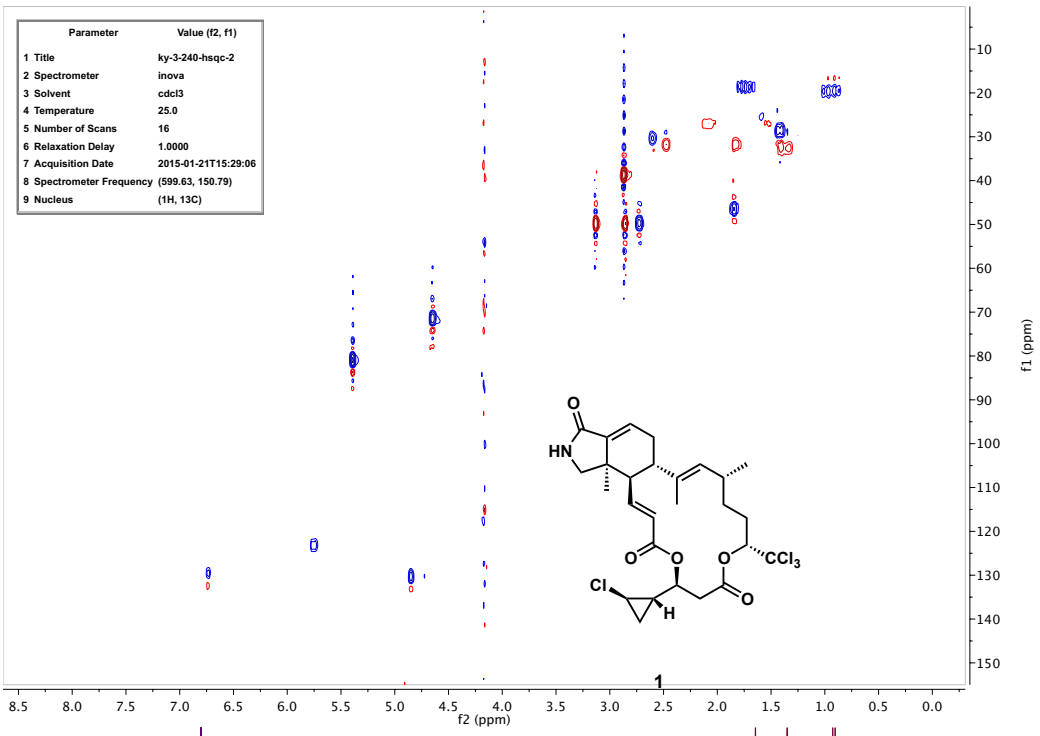

Parameters
Parameter Value
Title ky-3-228-C13
Spectrometer inova
Solvent CDCl3
Temperature 25.0
Number of Scans 420
Relaxation Delay 1.0000
Pulse Width 0.0000
Acquisition Time 1.3026
Acquisition Date 2014-12-17T09:07:51
Spectrometer Frequency 125.70
PMBN
CCl3
CO2H
HO
Cl
25
f1 (ppm)

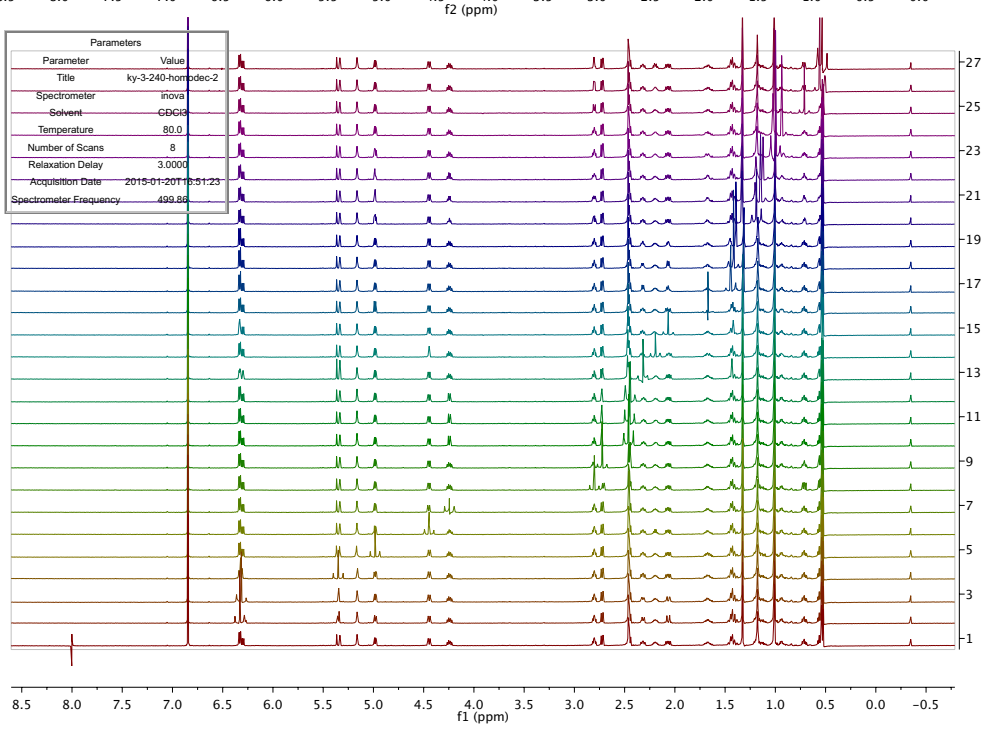

Parameters
Parameter Value
Title ky-3-238-b-pure
Spectrometer inova
Solvent CDCl3
Temperature 25.0
Number of Scans 16
Relaxation Delay 8.0000
Pulse Width 0.0000
Acquisition Time 2.5001
Acquisition Date 2015-01-05T08:28:06
Spectrometer Frequency 499.86
PMBN
O
O
O
O
O
CCl3
Cl
H
O
26
f1 (ppm)

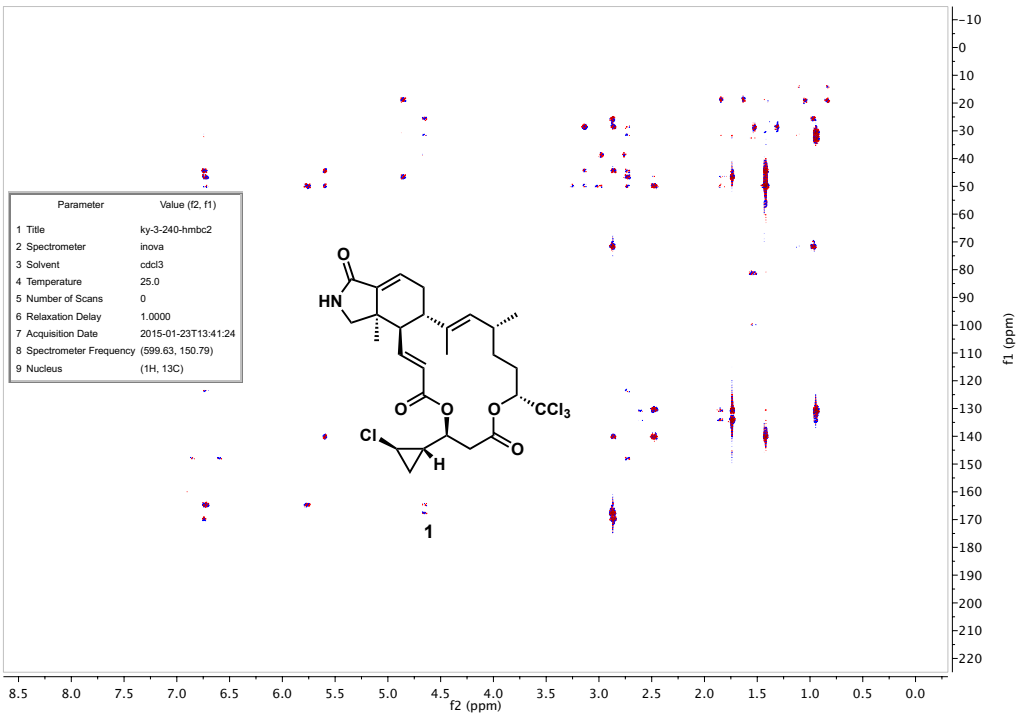

167.61
166.96
164.65
159.11
148.00
141.19
134.12
130.68
129.63
129.21
128.37
123.48
114.11
99.66
81.08
71.65
64.34
55.24
53.73
49.79
46.60
46.08
42.33
38.62
32.73
31.52
31.49
30.64
30.47
28.80
26.80
25.61
19.11
19.01
18.72
14.24
Parameters
Parameter Value
Title ky-3-238-b-C13
Spectrometer inova
Solvent CDCl3
Temperature 25.0
Number of Scans 824
Relaxation Delay 1.0000
Pulse Width 0.0000
Acquisition Time 1.3026
Acquisition Date 2015-01-05T09:19:33
Spectrometer Frequency 125.70
PMBN
O
O
O
O
O
CCl3
Cl
H
O
26
f1 (ppm)

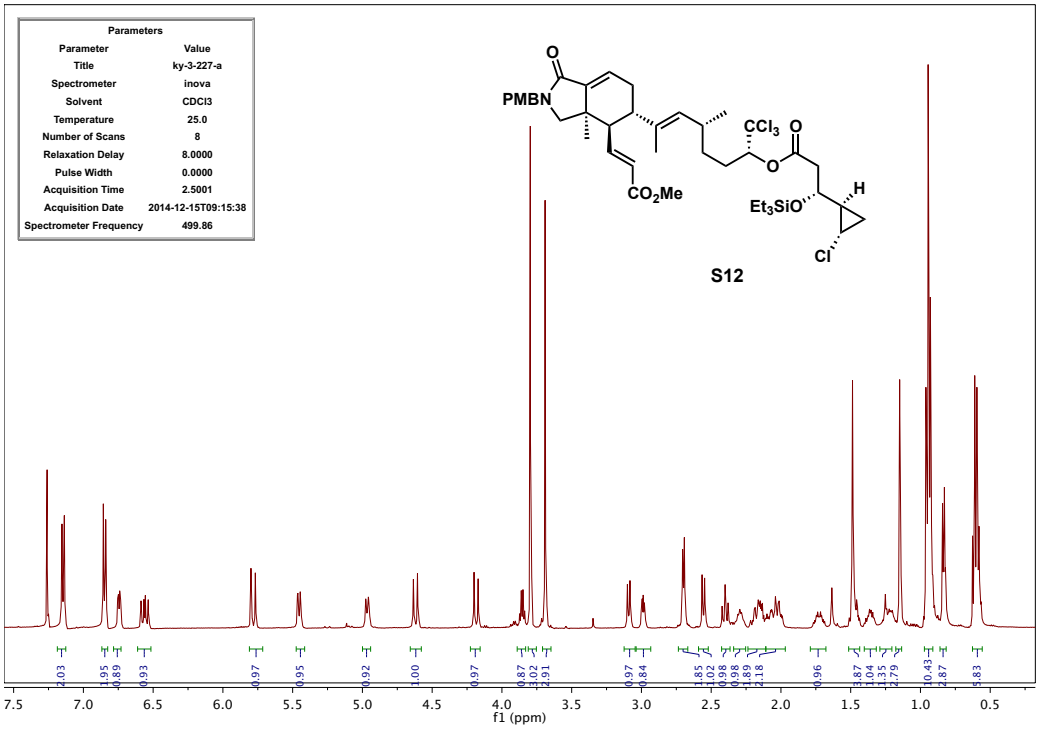

Parameters
Parameter Value
Title ky-3-240-si-1
Spectrometer inova
Solvent cdcl3
Temperature 25.0
Number of Scans 16
Relaxation Delay 8.0000
Pulse Width 0.0000
Acquisition Time 2.5000
Acquisition Date 2015-01-09T08:40:07
Spectrometer Frequency 599.64
HN
O
O
O
O
O
CCl3
Cl
H
O
1
2.04
1.00
0.89
0.90
1.00
0.94
0.98
0.89
2.93
0.97
1.07
1.01
1.15
2.15
2.97
1.78
3.96
1.10
1.09
0.83
3.23
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

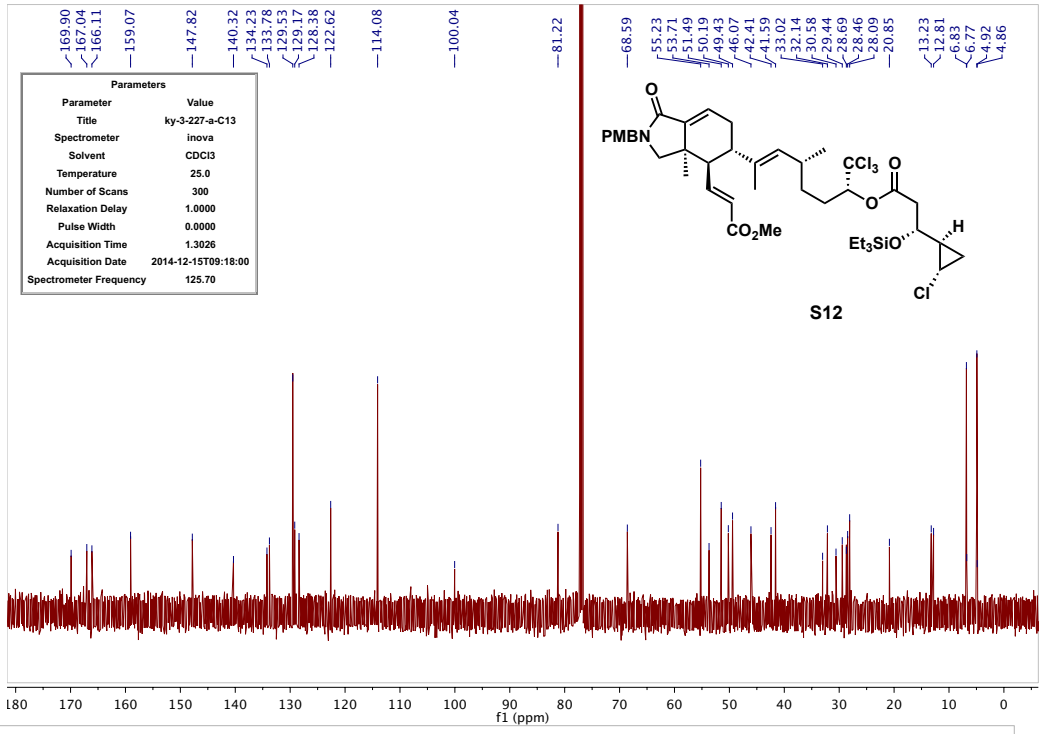

169.73
167.62
164.64
147.97
140.19
134.04
130.74
130.23
123.52
99.67
81.17
71.59
49.82
46.56
44.39
38.70
32.80
31.55
31.41
30.50
28.60
26.84
25.66
19.03
18.72
14.23
Parameters
Parameter Value
Title ky-3-240-si-C13
Spectrometer inova
Solvent cdcl3
Temperature 80.0
Number of Scans 19640
Relaxation Delay 1.0000
Pulse Width 0.0000
Acquisition Time 1.3026
Acquisition Date 2015-01-09T20:41:27
Spectrometer Frequency 125.70
HN
O
O
O
O
O
CCl3
Cl
H
O
1
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

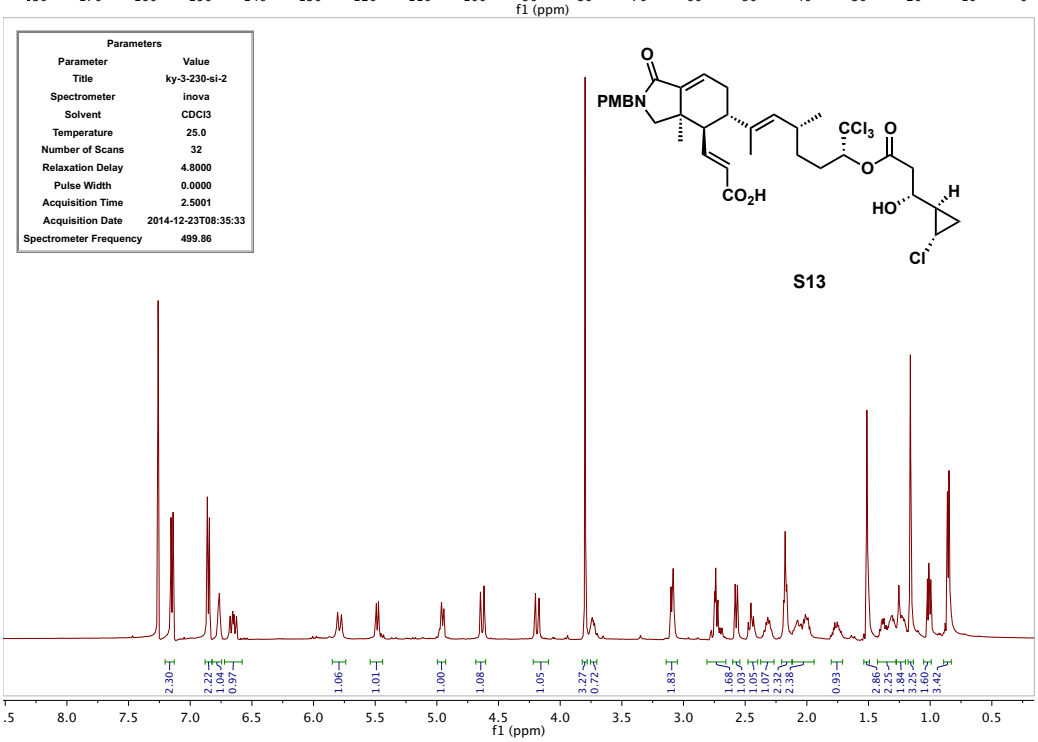

Parameter Value (f2, f1)
1 Title ky-3-240-hsqc-2
2 Spectrometer inova
3 Solvent cdcl3
4 Temperature 25.0
5 Number of Scans 16
6 Relaxation Delay 1.0000
7 Acquisition Date 2015-01-21T15:29:06
8 Spectrometer Frequency (599.63, 150.79)
9 Nucleus (1H, 13C)
HN
O
O
O
O
CCl3
Cl
H
O
1
f2 (ppm)
f1 (ppm)

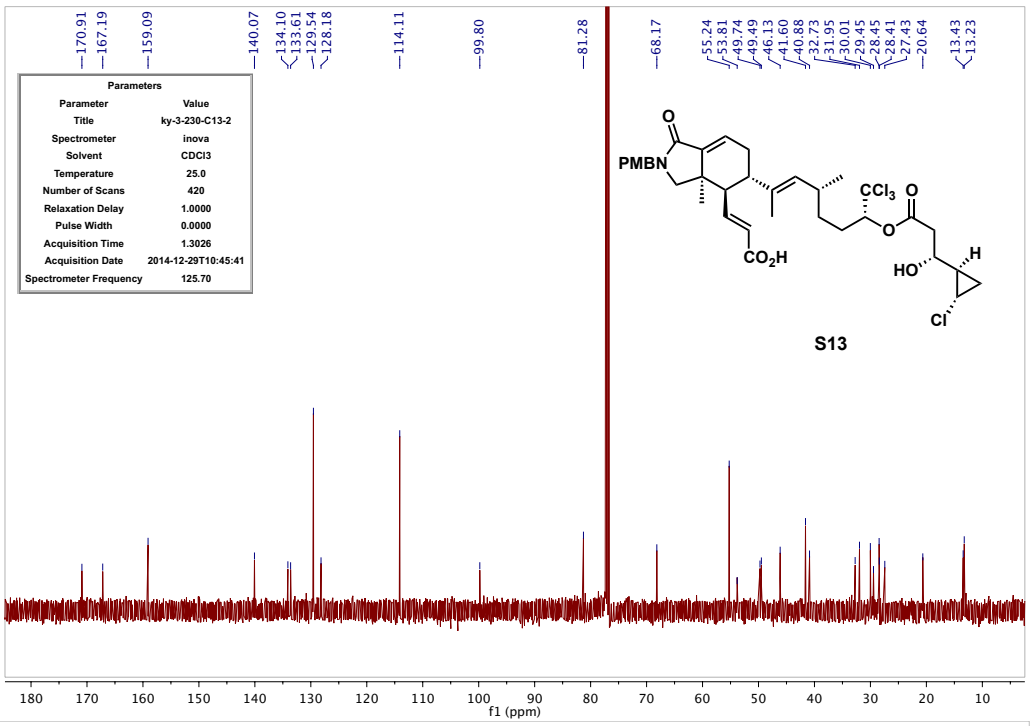

Parameters
Parameter Value
Title ky-3-240-homodec-2
Spectrometer inova
Solvent CDCl3
Temperature 80.0
Number of Scans 8
Relaxation Delay 3.0000
Acquisition Date 2015-01-20T13:51:23
Spectrometer Frequency 499.86
f1 (ppm)

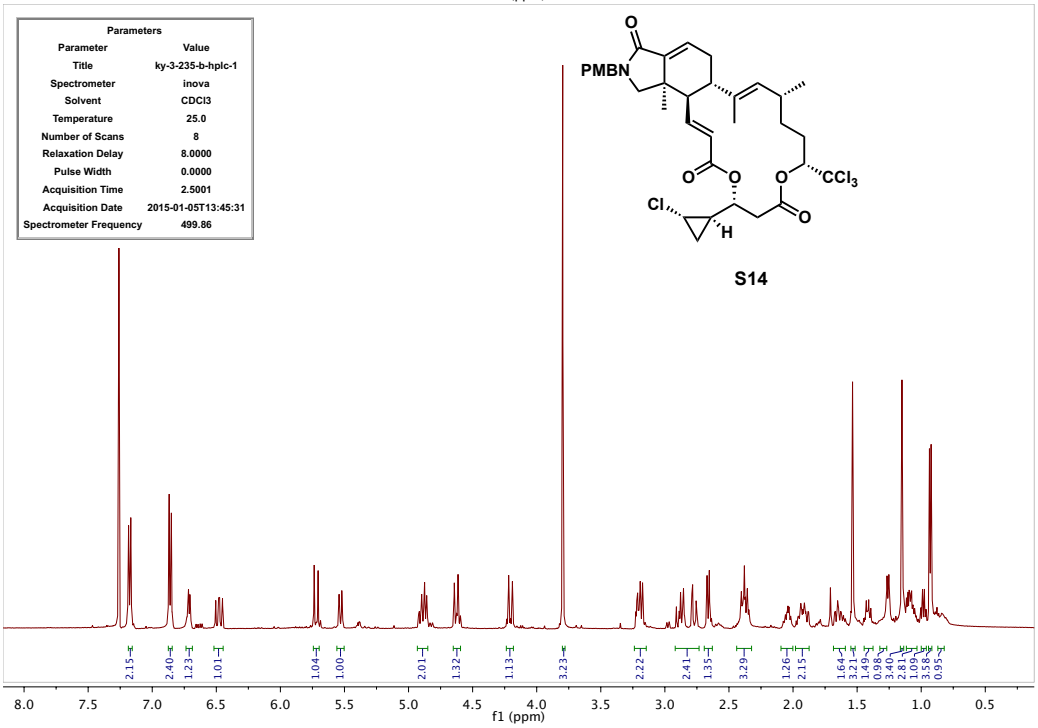

Parameter Value (f2, f1)
1 Title ky-3-240-hmbc2
2 Spectrometer inova
3 Solvent cdcl3
4 Temperature 25.0
5 Number of Scans 0
6 Relaxation Delay 1.0000
7 Acquisition Date 2015-01-23T13:41:24
8 Spectrometer Frequency (599.63, 150.79)
9 Nucleus (1H, 13C)
HN
O
O
O
O
CCl3
Cl
H
O
1
f2 (ppm)
f1 (ppm)

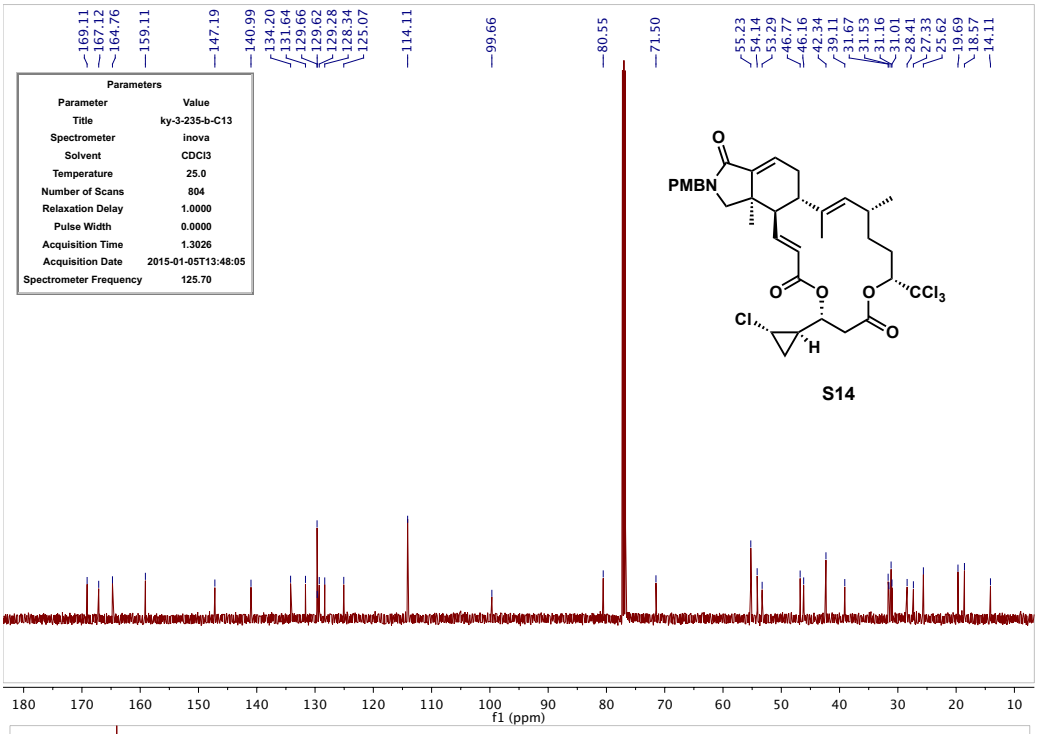

Parameters
Parameter Value
Title ky-3-227-a
Spectrometer inova
Solvent CDCl3
Temperature 25.0
Number of Scans 8
Relaxation Delay 8.0000
Pulse Width 0.0000
Acquisition Time 2.5001
Acquisition Date 2014-12-15T09:15:38
Spectrometer Frequency 499.86
PMBN
O
CCl3
O
O
CO2Me
Et3SiO
H
Cl
S12
f1 (ppm)


169.90
167.04
166.11
159.07
147.82
140.32
134.23
133.78
129.53
129.17
128.38
122.62
114.08
100.04
81.22
68.59
55.23
53.71
51.49
50.19
49.43
46.07
42.41
41.59
33.02
32.14
30.58
29.44
28.69
28.46
28.09
20.85
13.23
12.81
6.83
6.77
4.92
4.86
Parameters
Parameter Value
Title ky-3-227-a-C13
Spectrometer inova
Solvent CDCl3
Temperature 25.0
Number of Scans 300
Relaxation Delay 1.0000
Pulse Width 0.0000
Acquisition Time 1.3026
Acquisition Date 2014-12-15T09:18:00
Spectrometer Frequency 125.70
PMBN
CCl3
CO2Me
Et3SiO
H
Cl
S12
f1 (ppm)

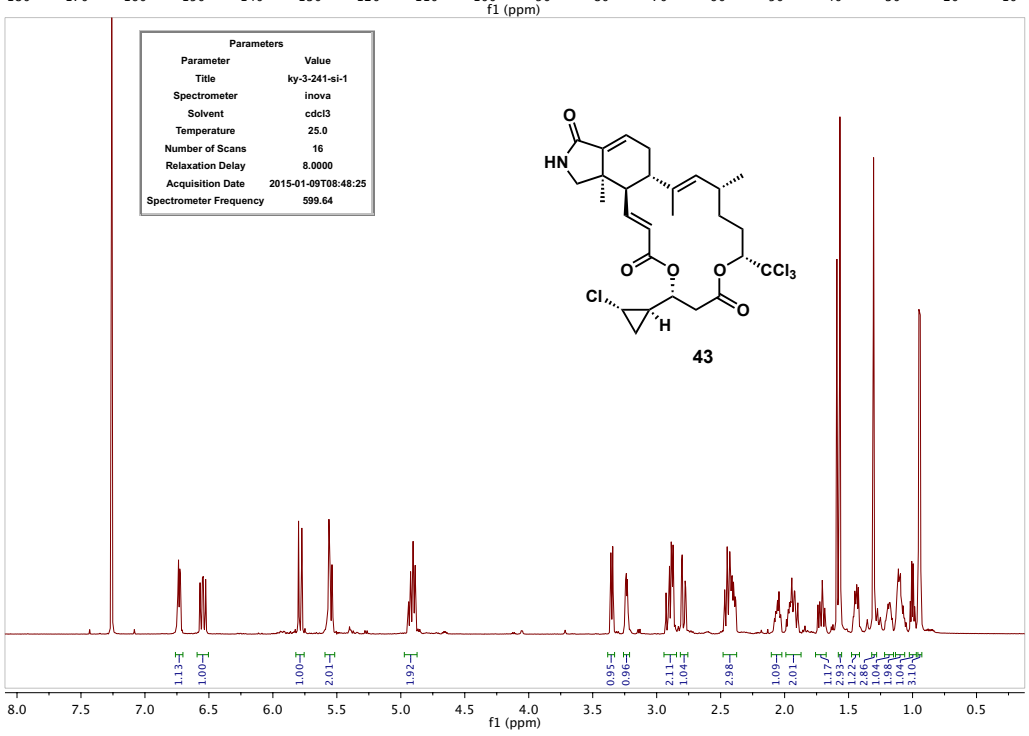

Parameters
Parameter Value
Title ky-3-230-si-2
Spectrometer inova
Solvent CDCl3
Temperature 25.0
Number of Scans 32
Relaxation Delay 4.8000
Pulse Width 0.0000
Acquisition Time 2.5001
Acquisition Date 2014-12-23T08:35:33
Spectrometer Frequency 499.86
PMBN
CCl3
CO2H
HO
H
Cl
S13
2.30
2.22
1.04
0.97
1.06
1.01
1.00
1.08
1.05
3.27
0.72
1.83
1.68
1.03
1.05
1.07
2.23
2.38
0.93
2.86
2.25
1.84
3.25
1.60
3.42
f1 (ppm)


170.91
167.19
159.09
140.07
134.10
133.61
129.54
128.18
114.11
99.80
81.28
68.17
55.24
53.81
49.74
49.49
46.13
41.60
40.88
32.73
31.95
30.01
29.45
28.45
28.41
27.43
20.64
13.43
13.23
Parameters
Parameter Value
Title ky-3-230-C13-2
Spectrometer inova
Solvent CDCl3
Temperature 25.0
Number of Scans 420
Relaxation Delay 1.0000
Pulse Width 0.0000
Acquisition Time 1.3026
Acquisition Date 2014-12-29T10:45:41
Spectrometer Frequency 125.70
PMBN
CCl3
CO2H
HO
Cl
S13
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

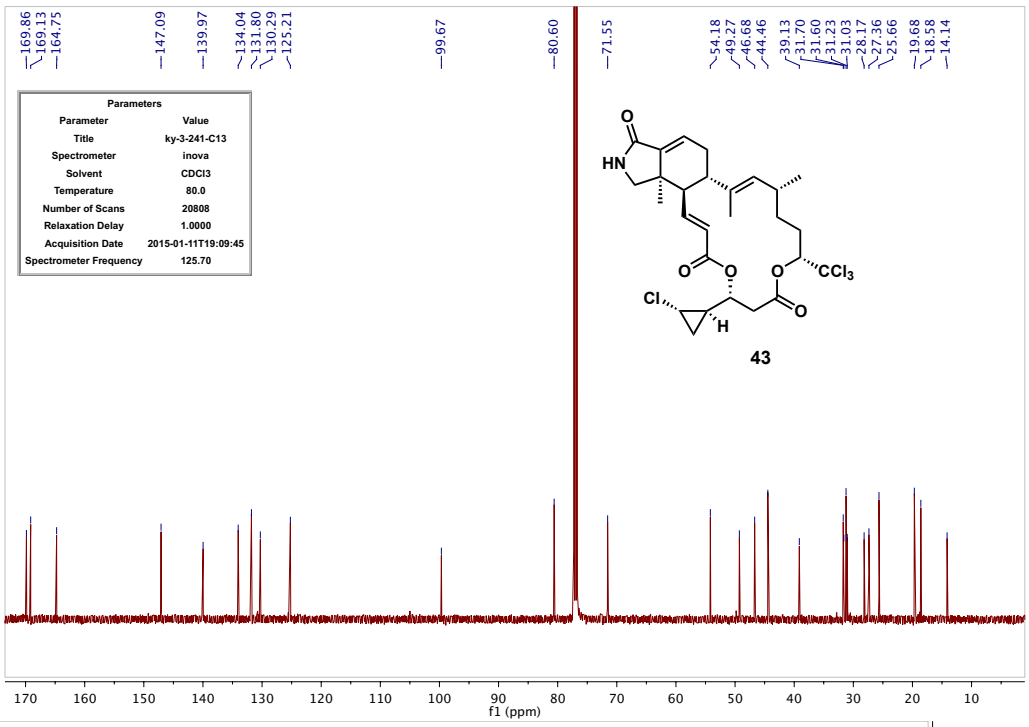

Parameters
Parameter Value
Title ky-3-235-b-hplc-1
Spectrometer inova
Solvent CDCl3
Temperature 25.0
Number of Scans 8
Relaxation Delay 8.0000
Pulse Width 0.0000
Acquisition Time 2.5001
Acquisition Date 2015-01-05T13:45:31
Spectrometer Frequency 499.86
PMBN
CCl3
Cl
H
S14
2.15 2.40 1.23 1.01 1.04 1.00 2.01 1.32 1.13 3.23 2.22 2.41 1.35 3.29 1.26 2.15 1.64 3.21 1.49 0.98 3.46 2.81 1.09 3.58 0.95
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

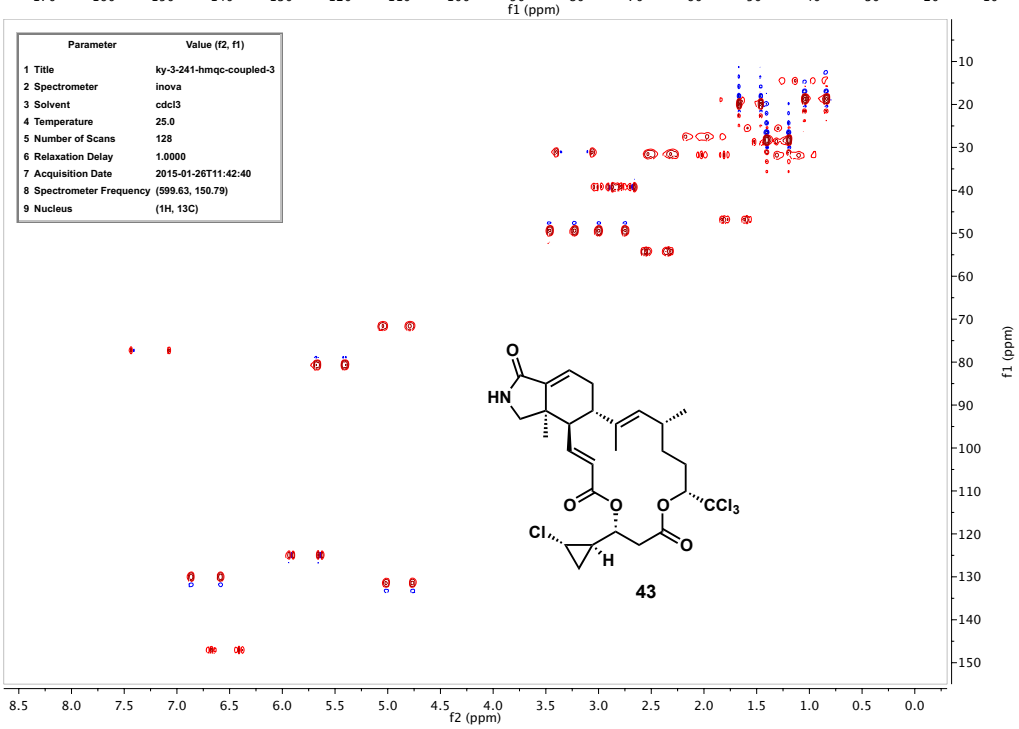

169.11
167.12
164.76
159.11
147.19
140.99
134.20
131.64
129.66
129.62
129.28
128.34
125.07
114.11
99.66
80.55
71.50
55.23
54.14
53.29
46.77
46.16
42.34
39.11
31.67
31.53
31.16
31.01
28.41
27.33
25.62
19.69
18.57
14.11
Parameters
Parameter Value
Title ky-3-235-b-C13
Spectrometer inova
Solvent CDCl3
Temperature 25.0
Number of Scans 804
Relaxation Delay 1.0000
Pulse Width 0.0000
Acquisition Time 1.3026
Acquisition Date 2015-01-05T13:48:05
Spectrometer Frequency 125.70
PMBN
O
O
O
O
CCl3
Cl
H
O
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

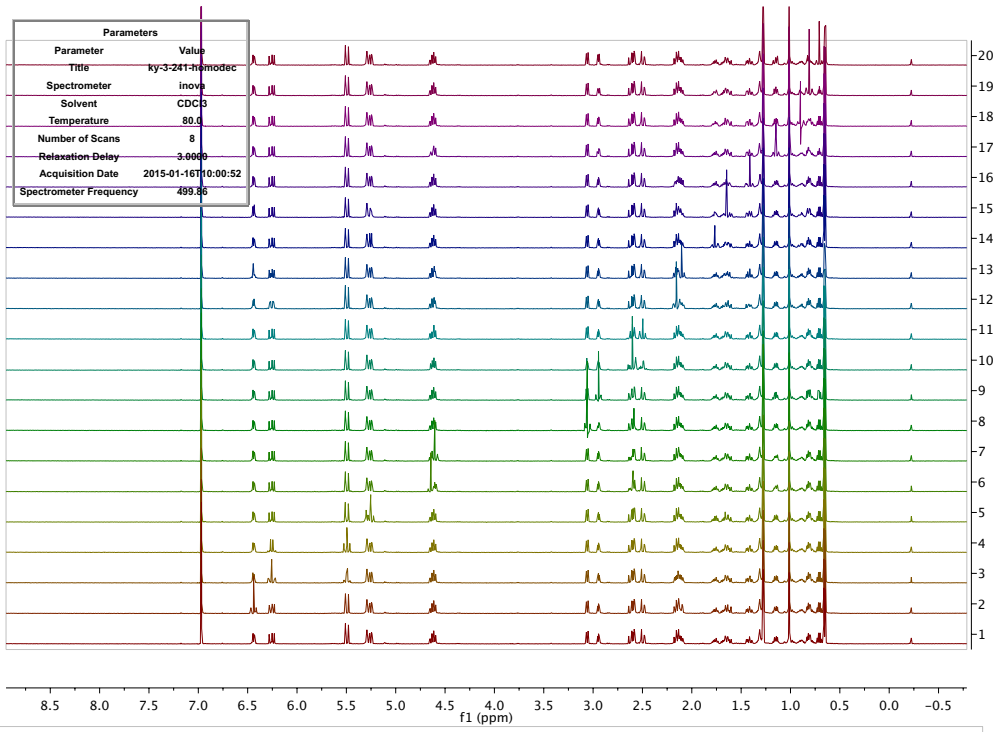
S14

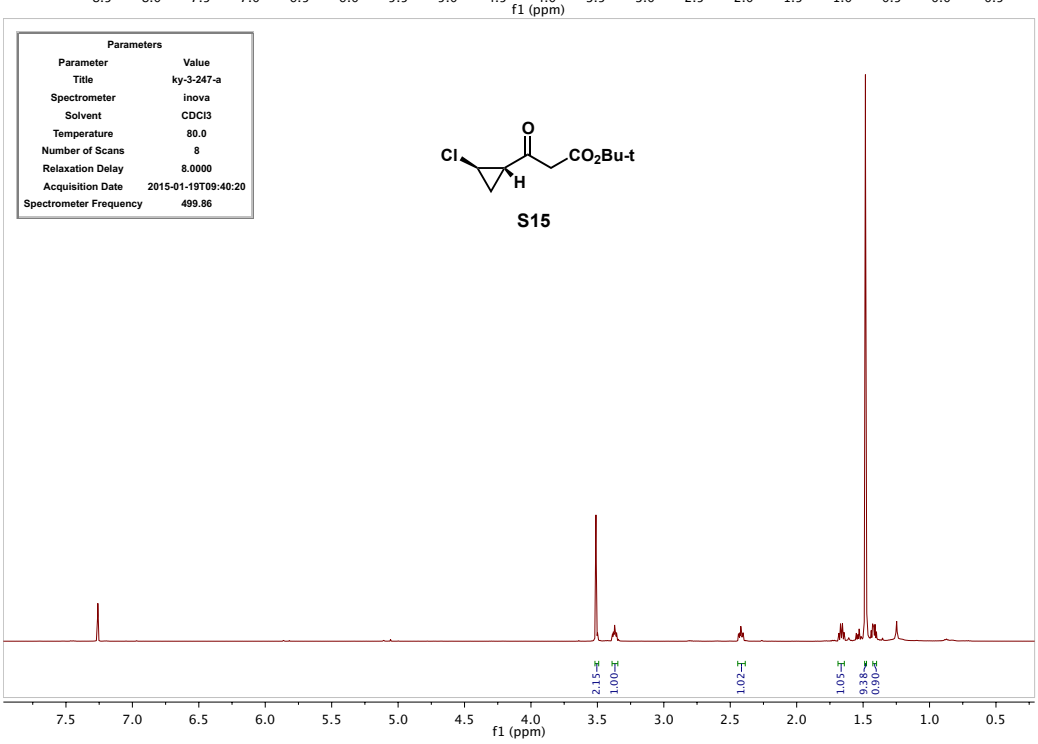

Parameters
Parameter Value
Title ky-3-241-si-1
Spectrometer inova
Solvent cdcl3
Temperature 25.0
Number of Scans 16
Relaxation Delay 8.0000
Acquisition Date 2015-01-09T08:48:25
Spectrometer Frequency 599.64
HN
O
O
O
O
CCl3
Cl
H
O
1.13
1.00
1.00
2.01
1.92
0.95
0.96
2.11
1.04
2.98
1.09
2.01
1.17
2.93
1.22
2.86
1.04
1.98
1.04
3.10
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

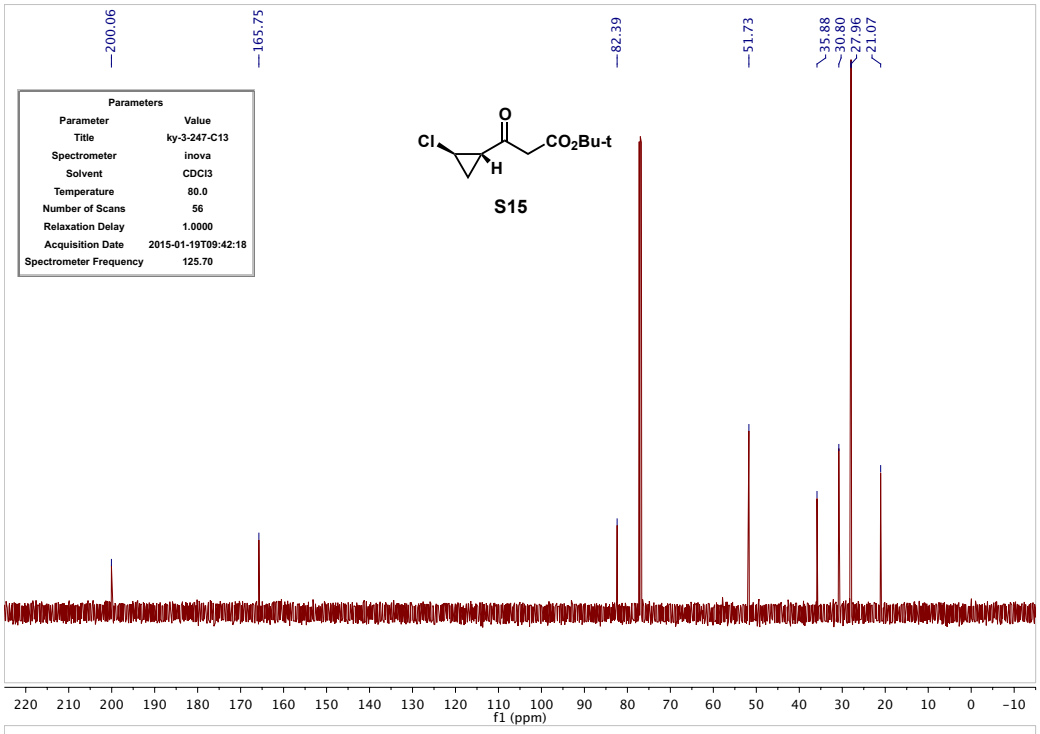
43

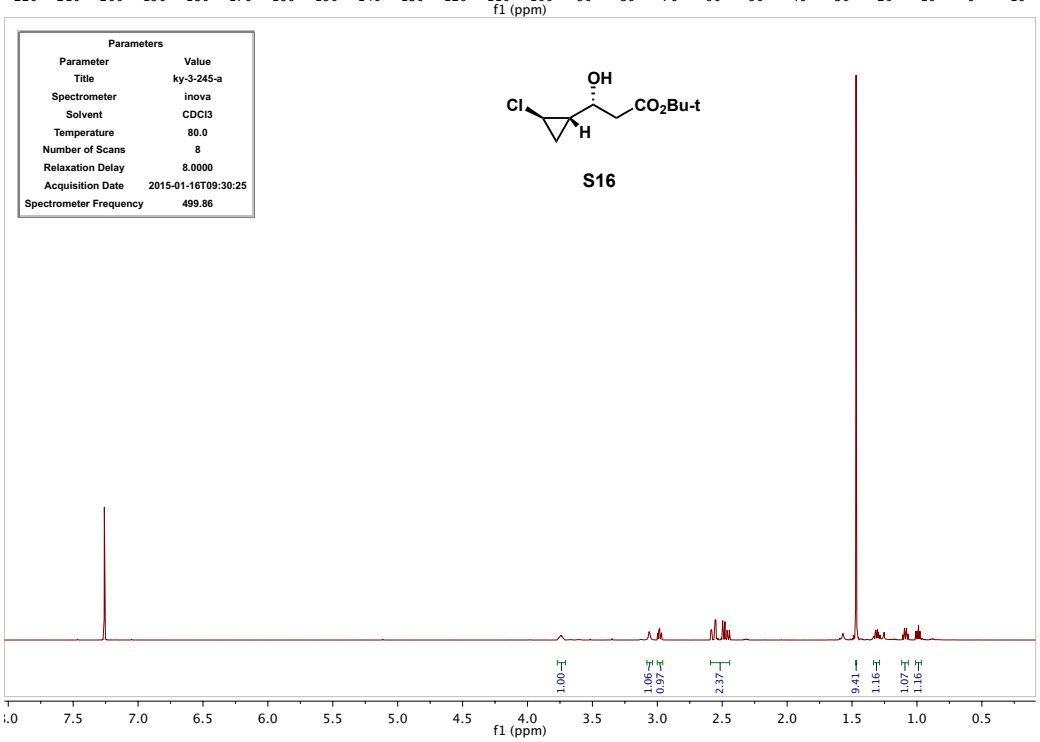

169.86
169.13
164.75
147.09
139.97
134.04
131.80
130.29
125.21
99.67
80.60
71.55
54.18
49.27
46.68
44.46
39.13
31.70
31.60
31.23
31.03
28.17
27.36
25.66
19.68
18.58
14.14
Parameters
Parameter Value
Title ky-3-241-C13
Spectrometer inova
Solvent CDCl3
Temperature 80.0
Number of Scans 20808
Relaxation Delay 1.0000
Acquisition Date 2015-01-11T19:09:45
Spectrometer Frequency 125.70
HN
O
O
O
O
CCl3
Cl
H
O
43
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

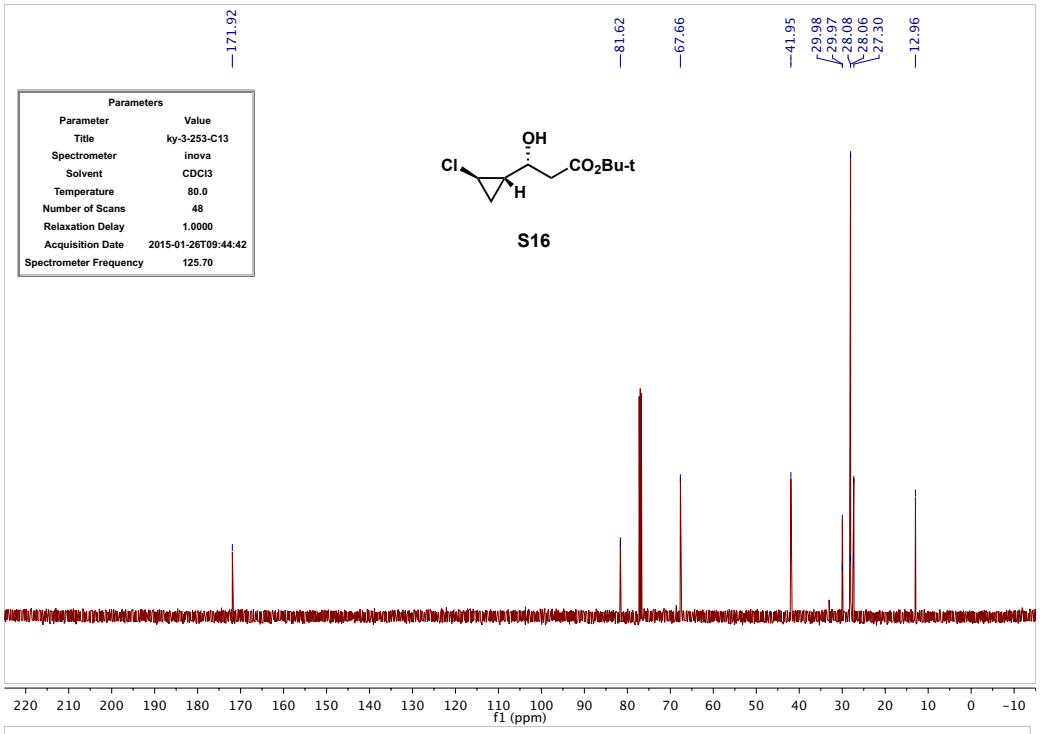

Parameter Value (f2, f1)
1 Title ky-3-241-hmqc-coupled-3
2 Spectrometer inova
3 Solvent cdcl3
4 Temperature 25.0
5 Number of Scans 128
6 Relaxation Delay 1.0000
7 Acquisition Date 2015-01-26T11:42:40
8 Spectrometer Frequency (599.63, 150.79)
9 Nucleus (1H, 13C)
HN
O
O
O
O
CCl3
Cl
H
O
43
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f2 (ppm)
10 20 30 40 50 60 70 80 90 100 110 120 130 140 150
f1 (ppm)

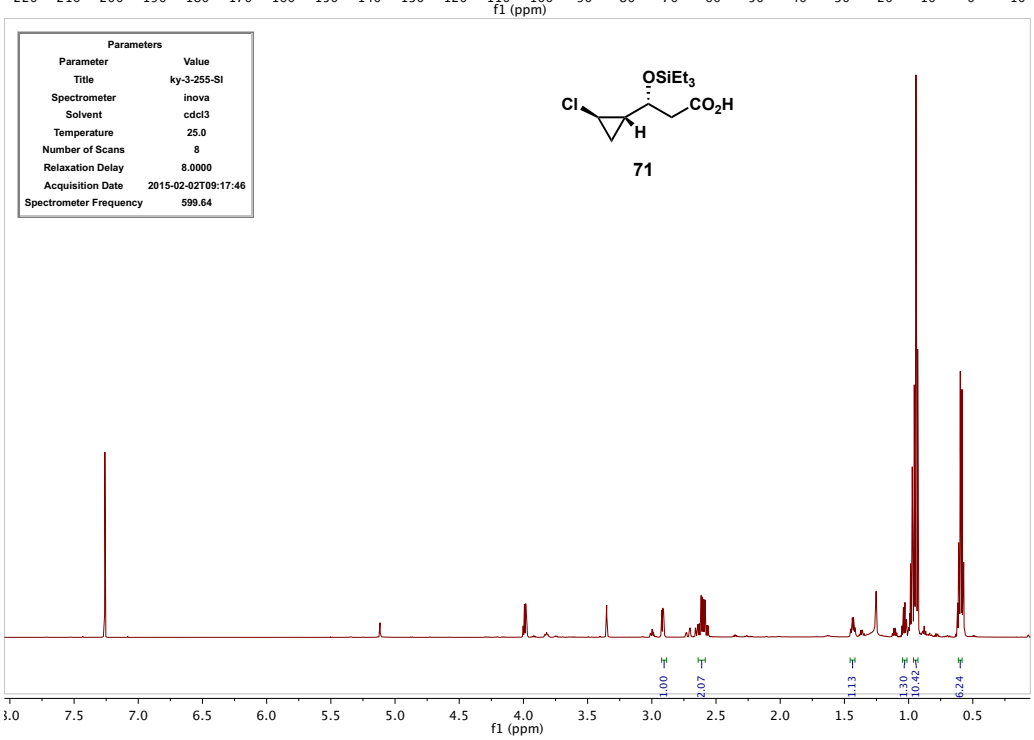

Parameters
Parameter Value
Title ky-3-241-homodec
Spectrometer inova
Solvent CDCl3
Temperature 80.0
Number of Scans 8
Relaxation Delay 3.0000
Acquisition Date 2015-01-16T10:00:52
Spectrometer Frequency 499.86
f1 (ppm)

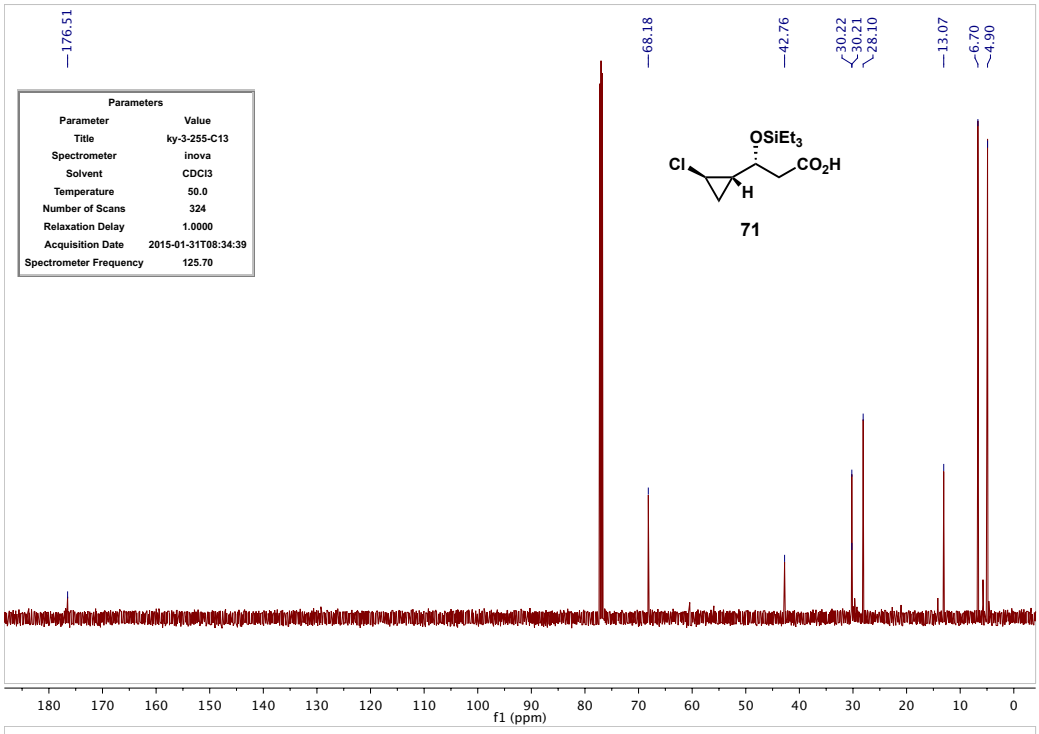

Parameters
Parameter Value
Title ky-3-247-a
Spectrometer inova
Solvent CDCl3
Temperature 80.0
Number of Scans 8
Relaxation Delay 8.0000
Acquisition Date 2015-01-19T09:40:20
Spectrometer Frequency 499.86
Cl
O
CO2Bu-t
H
S15
2.15
1.00
1.02
1.05
9.38
0.90
f1 (ppm)

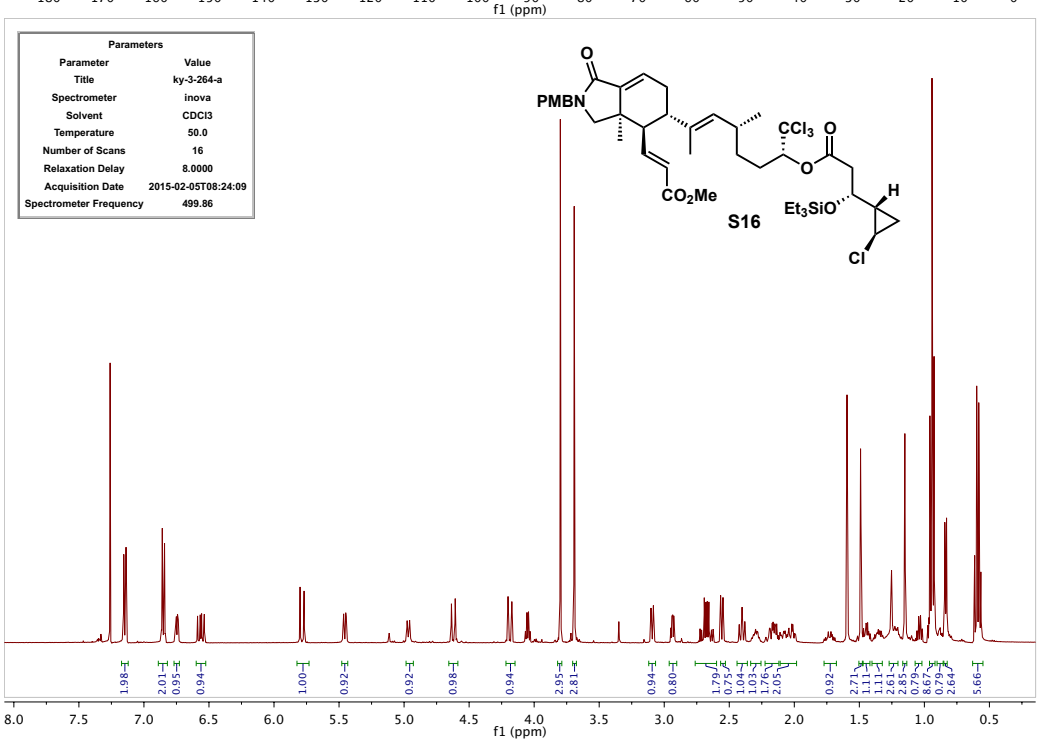

200.06
165.75
82.39
51.73
35.88
30.80
27.96
21.07
Parameters
Parameter Value
Title ky-3-247-C13
Spectrometer inova
Solvent CDCl3
Temperature 80.0
Number of Scans 56
Relaxation Delay 1.0000
Acquisition Date 2015-01-19T09:42:18
Spectrometer Frequency 125.70
Cl
O
CO2Bu-t
H
S15
f1 (ppm)

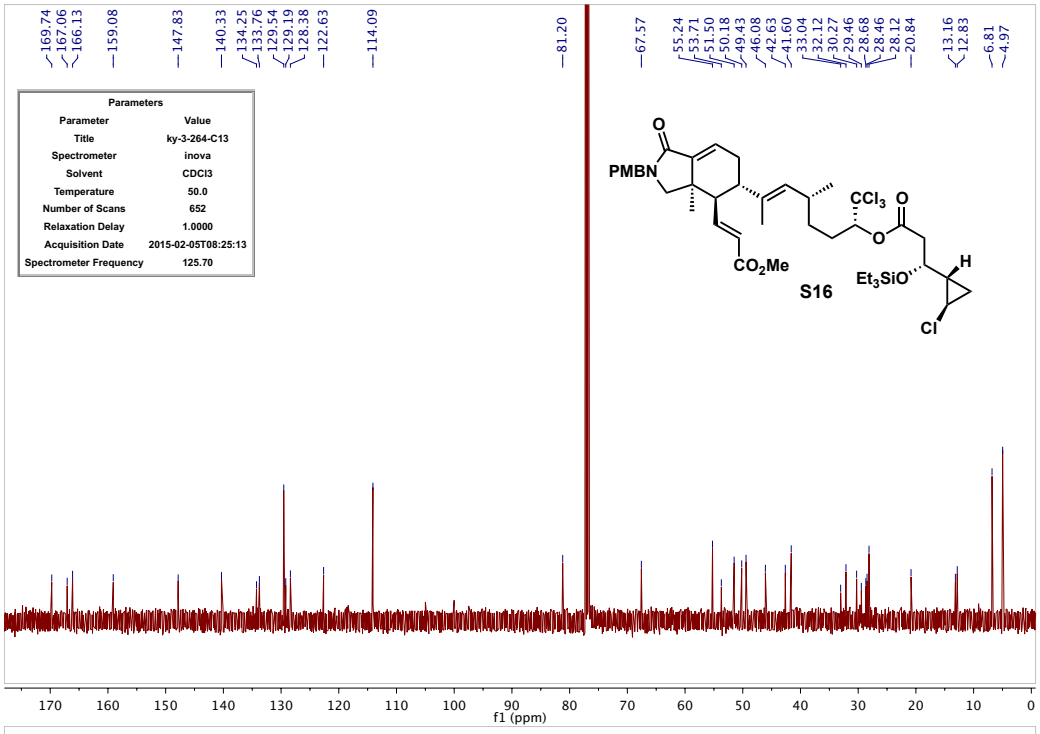

Parameters
Parameter Value
Title ky-3-245-a
Spectrometer inova
Solvent CDCl3
Temperature 80.0
Number of Scans 8
Relaxation Delay 8.0000
Acquisition Date 2015-01-16T09:30:25
Spectrometer Frequency 499.86
OH
Cl
CO2Bu-t
H
S16
1.00
1.06
0.97
2.37
9.41
1.16
1.07
1.16
f1 (ppm)

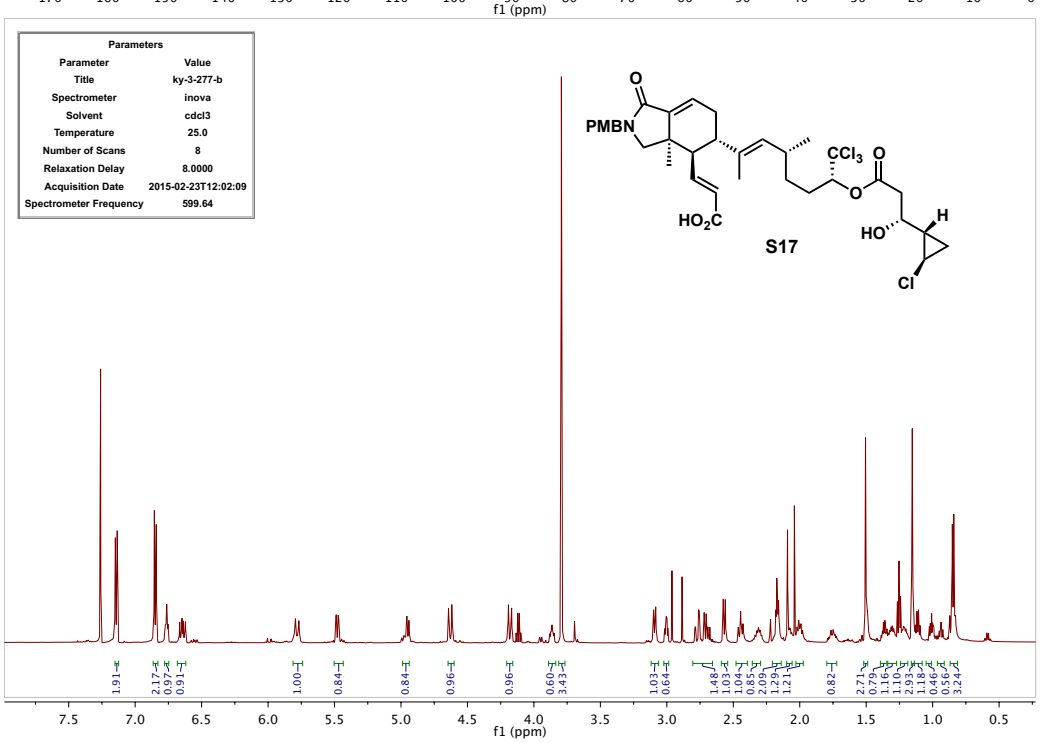

171.92
81.62
67.66
41.95
29.98
29.97
28.08
28.06
27.30
12.96
Parameters
Parameter Value
Title ky-3-253-C13
Spectrometer inova
Solvent CDCl3
Temperature 80.0
Number of Scans 48
Relaxation Delay 1.0000
Acquisition Date 2015-01-26T09:44:42
Spectrometer Frequency 125.70
OH
Cl
CO2Bu-t
H
S16
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

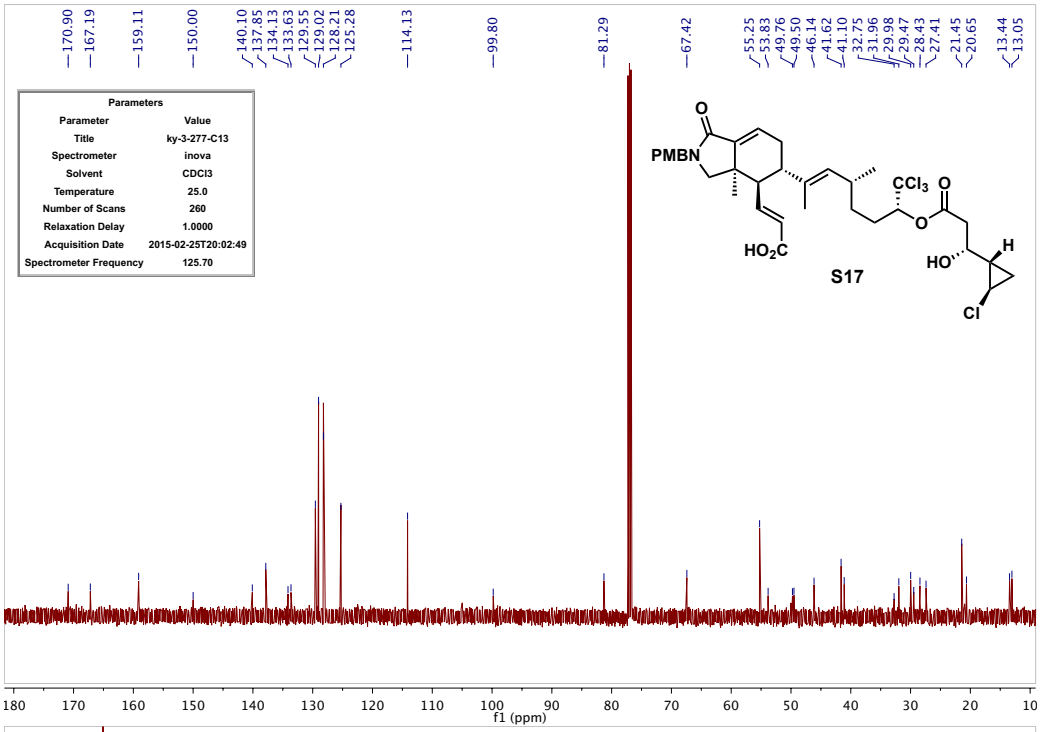

Parameters
Parameter Value
Title ky-3-255-SI
Spectrometer inova
Solvent cdcl3
Temperature 25.0
Number of Scans 8
Relaxation Delay 8.0000
Acquisition Date 2015-02-02T09:17:46
Spectrometer Frequency 599.64
OSiEt3
Cl
CO2H
H
71
1.00
2.07
1.13
1.30
10.42
6.24
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

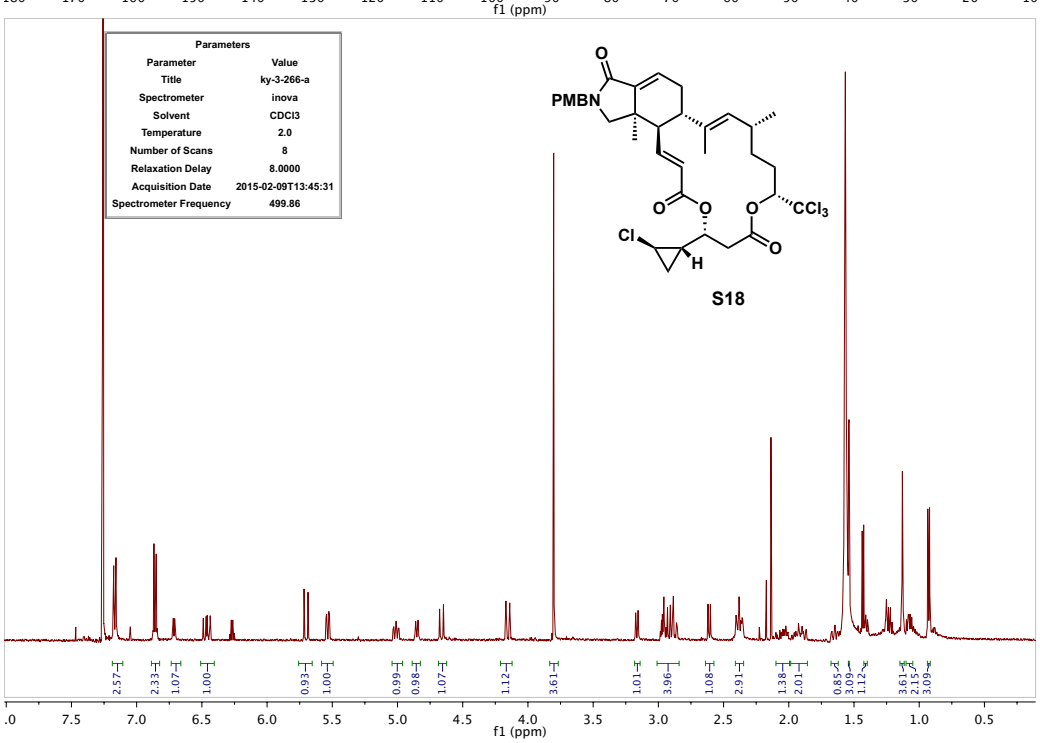

176.51
68.18
42.76
30.22
30.21
28.10
13.07
6.70
4.90
Parameters
Parameter Value
Title ky-3-255-C13
Spectrometer inova
Solvent CDCl3
Temperature 50.0
Number of Scans 324
Relaxation Delay 1.0000
Acquisition Date 2015-01-31T08:34:39
Spectrometer Frequency 125.70
OSiEt3
Cl
CO2H
H
71
f1 (ppm)

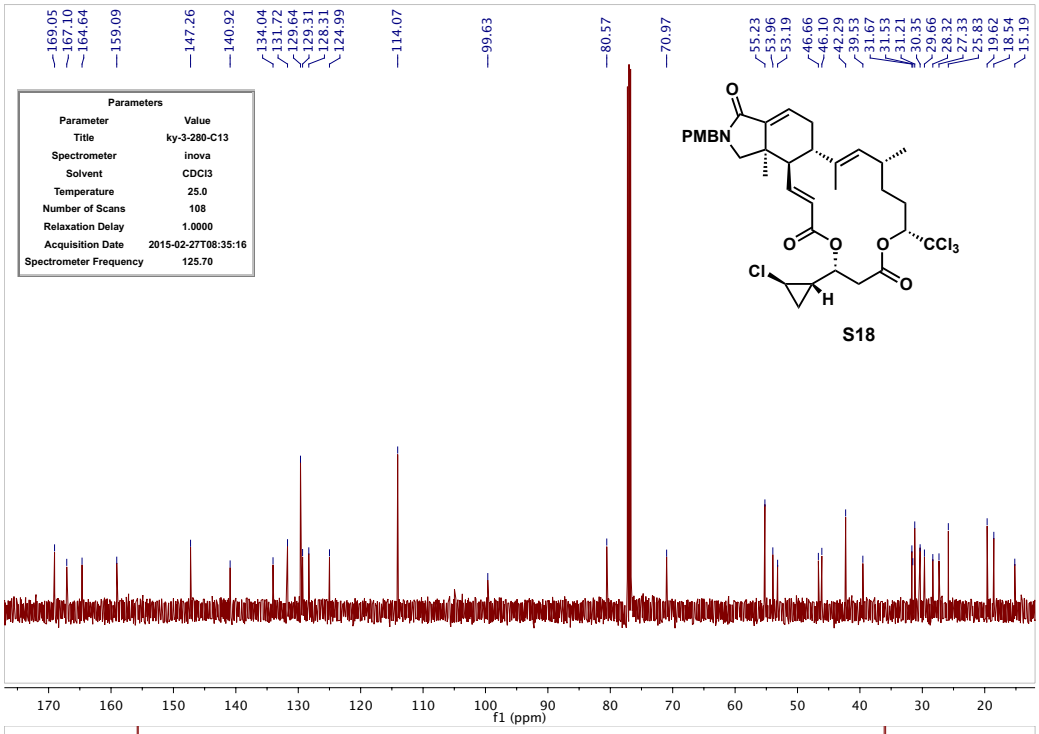

Parameters
Parameter Value
Title ky-3-264-a
Spectrometer inova
Solvent CDCl3
Temperature 50.0
Number of Scans 16
Relaxation Delay 8.0000
Acquisition Date 2015-02-05T08:24:09
Spectrometer Frequency 499.86
PMBN
CCl3
CO2Me
Et3SiO
H
Cl
S16
f1 (ppm)

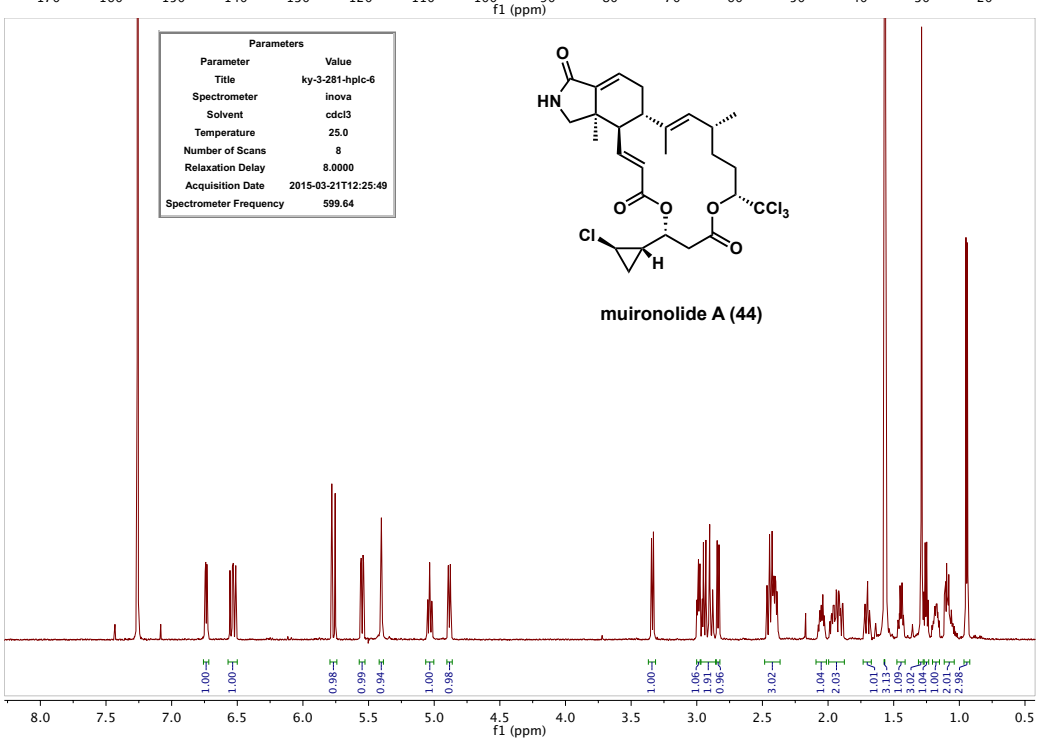

169.74
167.06
166.13
159.08
147.83
140.33
134.25
133.76
129.54
129.19
128.38
122.63
114.09
81.20
67.57
55.24
53.71
51.50
50.18
49.43
46.08
42.63
41.60
33.04
32.12
30.27
29.46
28.68
28.46
28.12
20.84
13.16
12.83
6.81
4.97
Parameters
Parameter Value
Title ky-3-264-C13
Spectrometer inova
Solvent CDCl3
Temperature 50.0
Number of Scans 652
Relaxation Delay 1.0000
Acquisition Date 2015-02-05T08:25:13
Spectrometer Frequency 125.70
PMBN
CCl3
CO2Me
Et3SiO
S16
Cl
f1 (ppm)

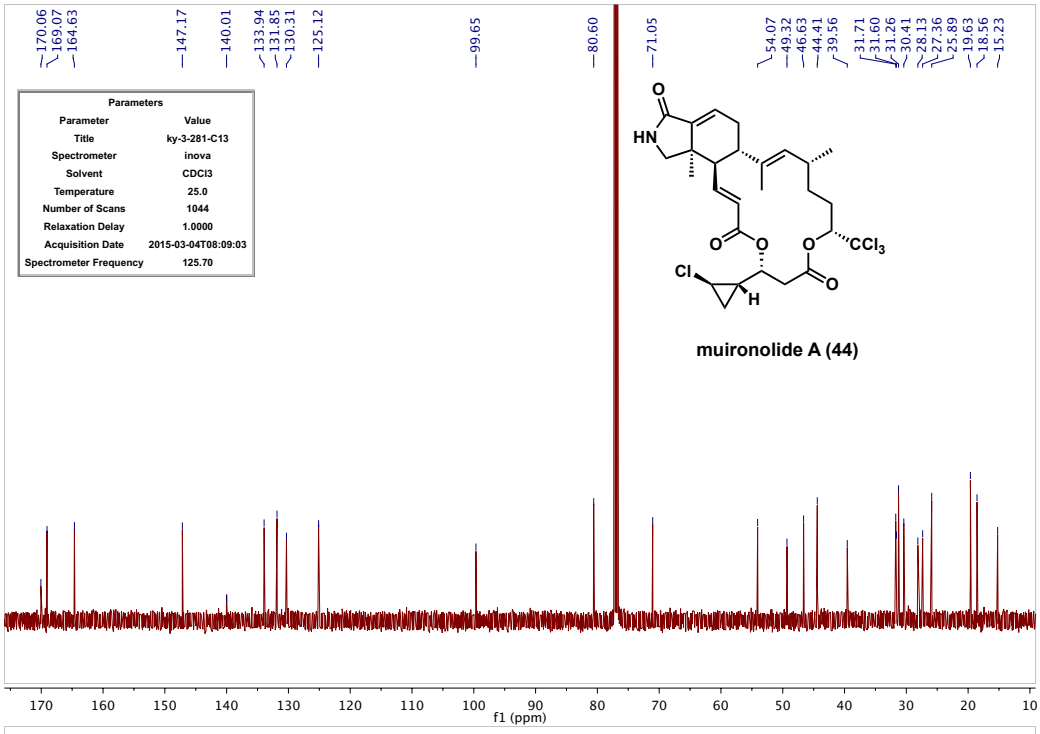

Parameters
Parameter Value
Title ky-3-277-b
Spectrometer inova
Solvent cdcl3
Temperature 25.0
Number of Scans 8
Relaxation Delay 8.0000
Acquisition Date 2015-02-23T12:02:09
Spectrometer Frequency 599.64
PMBN
CCl3
HO2C
HO
S17
Cl
1.91
2.17
0.97
0.91
1.00
0.84
0.84
0.96
0.96
0.60
3.43
1.03
0.64
1.48
1.03
1.04
0.85
2.09
1.29
1.21
0.82
2.71
0.79
1.16
1.16
2.93
1.18
0.46
0.56
3.24
f1 (ppm)

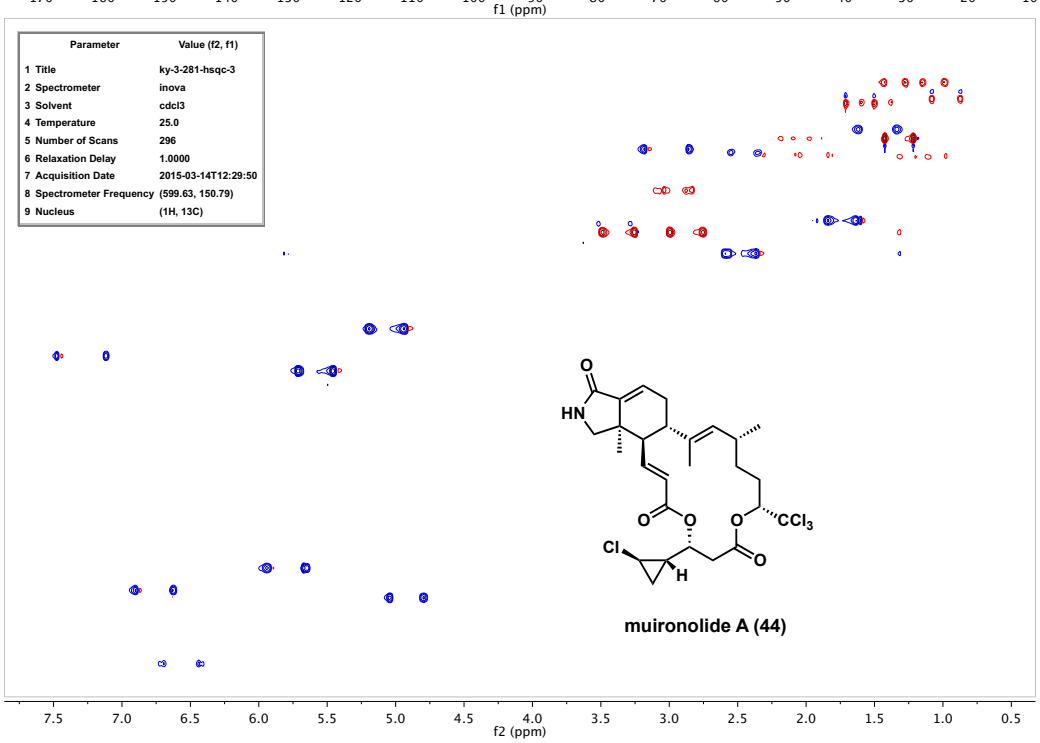

170.90
167.19
159.11
150.00
140.10
137.85
134.13
133.63
129.55
129.02
128.21
125.28
114.13
99.80
81.29
67.42
55.25
53.83
49.76
49.50
46.14
41.62
41.10
32.75
31.96
29.98
29.47
28.43
27.41
21.45
20.65
13.44
13.05
Parameters
Parameter Value
Title ky-3-277-C13
Spectrometer inova
Solvent CDCl3
Temperature 25.0
Number of Scans 260
Relaxation Delay 1.0000
Acquisition Date 2015-02-25T20:02:49
Spectrometer Frequency 125.70
PMBN
CCl3
HO2C
HO
Cl
S17
f1 (ppm)

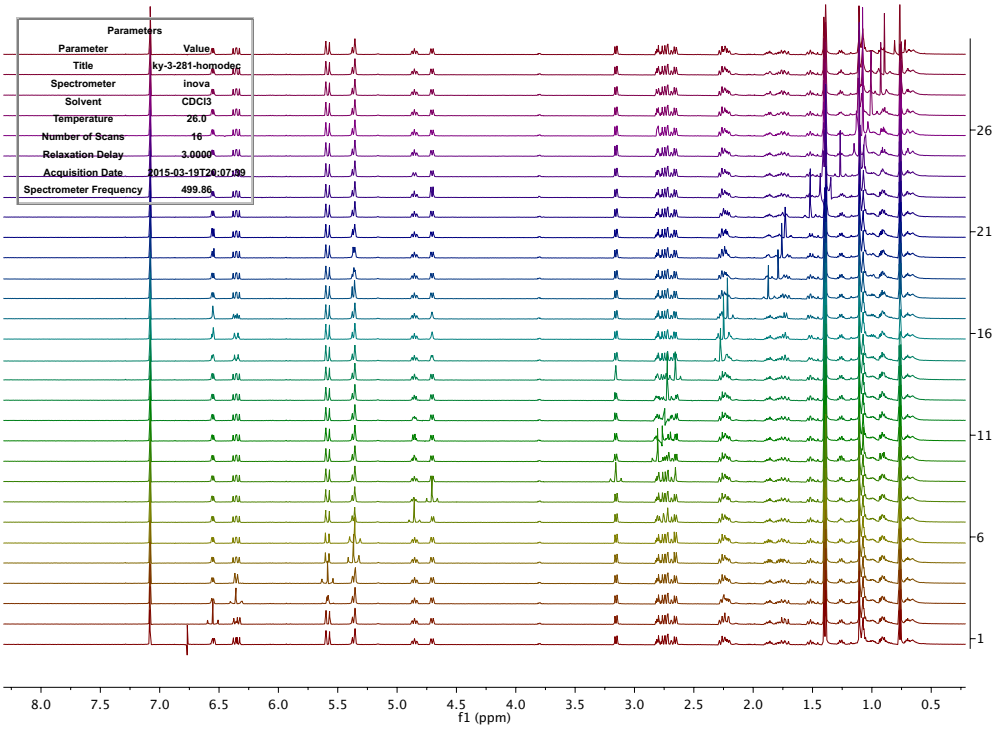

Parameters
Parameter Value
Title ky-3-266-a
Spectrometer inova
Solvent CDCl3
Temperature 2.0
Number of Scans 8
Relaxation Delay 8.0000
Acquisition Date 2015-02-09T13:45:31
Spectrometer Frequency 499.86
PMBN
CCl3
Cl
H
S18
2.57
2.33
1.07
1.00
0.93
1.00
0.99
0.98
1.07
1.12
3.61
1.01
3.96
1.08
2.91
1.38
2.01
0.85
3.09
1.12
3.61
2.15
3.09
f1 (ppm)

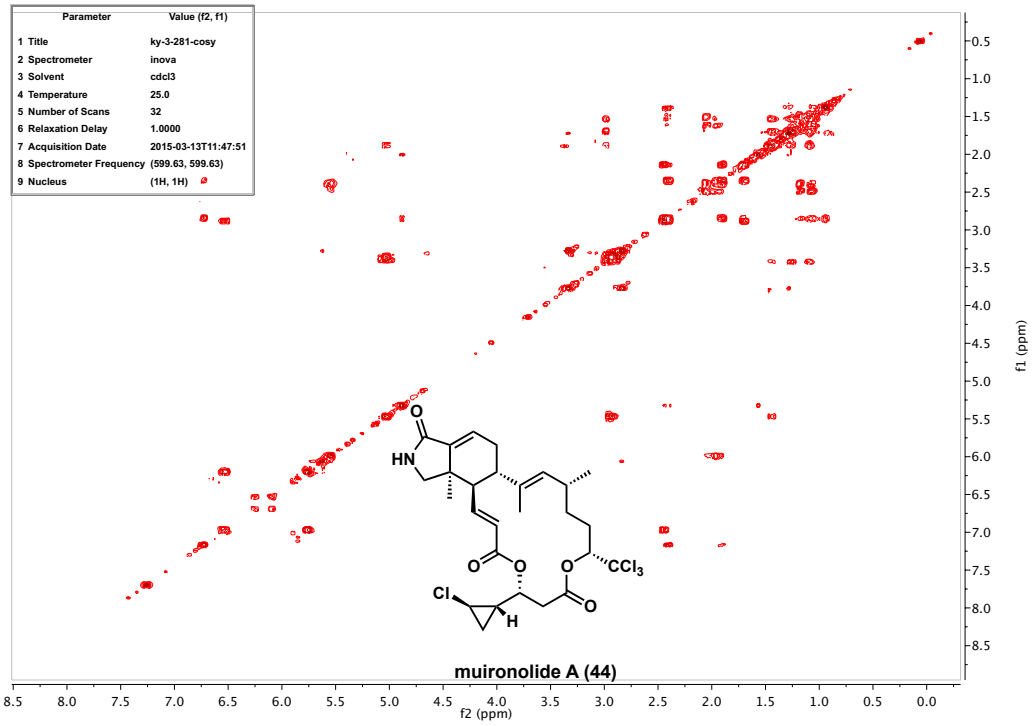

169.05
167.10
164.64
159.09
147.26
140.92
134.04
131.72
129.64
129.31
128.31
124.99
114.07
99.63
80.57
70.97
55.23
53.96
53.19
46.66
46.10
42.29
39.53
31.67
31.53
31.21
30.35
29.66
28.32
27.33
25.83
19.62
18.54
15.19
Parameters
Parameter Value
Title ky-3-280-C13
Spectrometer inova
Solvent CDCl3
Temperature 25.0
Number of Scans 108
Relaxation Delay 1.0000
Acquisition Date 2015-02-27T08:35:16
Spectrometer Frequency 125.70
PMBN
O
O
O
O
CCl3
Cl
H
O
S18
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)


Parameters
Parameter Value
Title ky-3-281-hplc-6
Spectrometer inova
Solvent cdcl3
Temperature 25.0
Number of Scans 8
Relaxation Delay 8.0000
Acquisition Date 2015-03-21T12:25:49
Spectrometer Frequency 599.64
HN
O
O
O
O
CCl3
Cl
H
O
muironolide A (44)
1.00
1.00
0.98
0.99
0.94
1.00
0.98
1.00
1.06
1.91
0.96
3.02
1.04
2.03
1.01
3.13
1.09
3.02
1.04
1.00
2.01
2.98
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

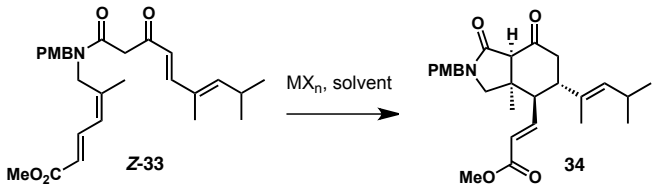

170.06
169.07
164.63
147.17
140.01
133.94
131.85
130.31
125.12
99.65
80.60
71.05
54.07
49.32
46.63
44.41
39.56
31.71
31.60
31.26
30.41
28.13
27.36
25.89
19.63
18.56
15.23
Parameters
Parameter Value
Title ky-3-281-C13
Spectrometer inova
Solvent CDCl3
Temperature 25.0
Number of Scans 1044
Relaxation Delay 1.0000
Acquisition Date 2015-03-04T08:09:03
Spectrometer Frequency 125.70
muironolide A (44)
f1 (ppm)


Parameter Value (f2, f1)
1 Title ky-3-281-hsqc-3
2 Spectrometer inova
3 Solvent cdcl3
4 Temperature 25.0
5 Number of Scans 296
6 Relaxation Delay 1.0000
7 Acquisition Date 2015-03-14T12:29:50
8 Spectrometer Frequency (599.63, 150.79)
9 Nucleus (1H, 13C)
muironolide A (44)
f2 (ppm)


Parameters
Parameter Value
Title ky-3-281-homodec
Spectrometer inova
Solvent CDCl3
Temperature 26.0
Number of Scans 16
Relaxation Delay 3.0000
Acquisition Date 2015-03-19T20:07:39
Spectrometer Frequency 499.86
26
21
16
11
6
1
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)


Parameter Value (f2, f1)
1 Title ky-3-281-cosy
2 Spectrometer inova
3 Solvent cdcl3
4 Temperature 25.0
5 Number of Scans 32
6 Relaxation Delay 1.0000
7 Acquisition Date 2015-03-13T11:47:51
8 Spectrometer Frequency (599.63, 599.63)
9 Nucleus (1H, 1H)
0.5 1.0 1.5 2.0 2.5 3.0 3.5 4.0 4.5 5.0 5.5 6.0 6.5 7.0 7.5 8.0 8.5
f1 (ppm)
HN
O
O
O
O
O
CCl3
Cl
H
O
muironolide A (44)
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f2 (ppm)

General Procedure for the Metal Catalyzed IMDA Reaction in Table 1.



(E)-methyl 3-((3aR,4R,5S,7aR)-2-(4-methoxybenzyl)-3a-methyl-5-((E)-4-methylpent -2-en-2-yl)-1,7-dioxooctahydro-1H-isoindol-4-yl)acrylate (34). The β-keto amide ***Z*-33** was prepared according to a described synthetic procedure. A metal salt in Table 1 (10 mol%) was added to a solution of ***Z*-33** (17.6 μmol, 1.0 equiv) in solvent (0.6 mL). Et_3N (2.0 equiv) was added to the reaction mixture and was heated for a duration specified in Table 1. The crude mixture was quenched with ethyl acetate (2 mL) and water (3 mL). The layers were separated and the aqueous layer was extracted with ethyl acetate (3x1 mL). The combined organic layers were washed with brine, dried with sodium sulfate, and concentrated in vacuo. The crude oil was purified by column chromatography (silica, 80% ethyl acetate – hexanes) to give isoindolinone **34**. ^1H NMR (500 MHz, $CDCl_3$); δ (ppm): 7.15 (t, J = 7.9 Hz, 2H), 6.84 (d, J = 8.5 Hz, 2H), 6.64 (dd, J = 15.3, 11.0 Hz, 1H), 5.62 (d, J = 15.3 Hz, 1H), 4.70 (t, J = 12.6 Hz, 1H), 4.53 (d, J = 14.4 Hz, 1H), 4.28 (d, J = 14.4 Hz, 1H), 4.19 – 4.11 (m, 2H), 3.77 (s, 3H), 3.22 (d, J = 10.2 Hz, 1H), 3.03 (s, 1H), 2.86 (d, J = 10.2 Hz, 1H), 2.55 – 2.48 (m, 2H), 2.46 – 2.30 (m, 3H), 1.46 (s, 3H), 1.24 (t, J = 7.1 Hz, 3H), 1.04 (s, 3H), 0.86 (d, J = 6.6 Hz, 3H), 0.78 (d, J = 6.6 Hz, 3H).

General Procedure for the Asymmetric IMDA Reaction in Figure 7.

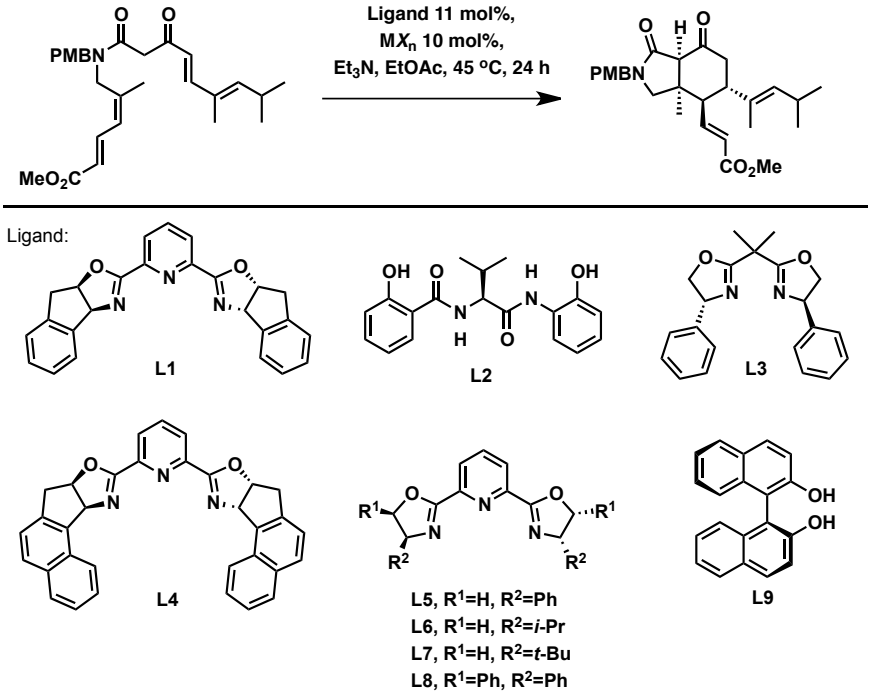


Table A: Ligand screening for IMDA reaction

entry	ligand	conv., %	dr	ee
1	L1	79%	>30:1	40%
2	L2	65%	8:1	17%
3	L3	87%	>30:1	0%
4	L4	85%	>30:1	0%
5	L5	86%	30:1	4%
6	L6	87%	30:1	20%
7	L7	86%	30:1	1%

8	L8	87%	30:1	0%
9	L9	83%	>30:1	8%

(E)-methyl 3-((3aR,4R,5S,7aR)-2-(4-methoxybenzyl)-3a-methyl-5-((E)-4-methylpent -2-en-2-yl)-1,7-dioxooctahydro-1H-isoindol-4-yl)acrylate (34).[82] The β-keto amide ***Z*-33** was prepared according to a described synthetic procedure. $La(OTf)_3$ (10 mol%) was added to a solution of ligand in Table A (11 mol%) in ethyl acetate (0.2 mL) and stirred for 30 min at 23 °C. The preformed catalyst and Et_3N (2.0 equiv) was added to 5 (17.6 μmol, 1.0 equiv) in ethyl acetate (0.4 mL) and was heated to 45 °C for 24 h. The crude mixture was quenched with ethyl acetate (2 mL) and water (3 mL). The layers were separated and the aqueous layer was extracted with ethyl acetate (3 x 1 mL). The combined organic layers were washed with brine, dried with sodium sulfate, and concentrated in vacuo. The crude oil was purified by column chromatography (silica, 80% ethyl acetate – hexanes) to give isoindoledione **34**. ^{1}H NMR (500 MHz, $CDCl_3$); δ (ppm): 7.15 (t, J = 7.9 Hz, 2H), 6.84 (d, J = 8.5 Hz, 2H), 6.64 (dd, J = 15.3, 11.0 Hz, 1H), 5.62 (d, J = 15.3 Hz, 1H), 4.70 (t, J = 12.6 Hz, 1H), 4.53 (d, J = 14.4 Hz, 1H), 4.28 (d, J = 14.4 Hz, 1H), 4.19 – 4.11 (m, 2H), 3.77 (s, 3H), 3.22 (d, J = 10.2 Hz, 1H), 3.03 (s, 1H), 2.86 (d, J = 10.2 Hz, 1H), 2.55 – 2.48 (m, 2H), 2.46 – 2.30 (m, 3H), 1.46 (s, 3H), 1.24 (t, J = 7.1 Hz, 3H), 1.04 (s, 3H), 0.86 (d, J = 6.6 Hz, 3H), 0.78 (d, J = 6.6 Hz, 3H).

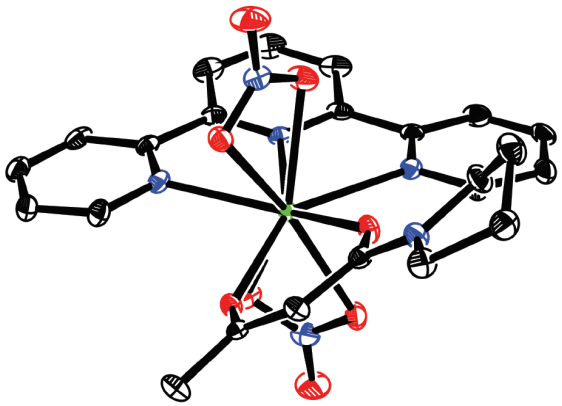
General Procedure for the synthesis of $Ln(terpy)(NO_3)_3(H_2O)_n$. $Ln(NO_3)_3(H_2O)_n$ (Ln = Dy, Sm, Eu) (0.2 mmol, 1.0 equiv) was added to a solution of 2,2':6',2"-terpyridine (0.2 mmol, 1.0 equiv) in ethanol (4.0 mL) at 23 °C for 1 h to

form a white suspension. The suspension was filtered and washed with ethanol (3 x 4 mL) and dried in vacuo to give Ln(terpy)$(NO_3)_3(H_2O)_n$. This material was used without further purification of characterization.

General Procedure for the synthesis of Ln(terpy)$(NO_3)_2$(pyracac) or Ln(terpy)$(NO_3)_2$(dbacac). 1-(Pyrrolidin-1-yl)butane-1,3-dione (0.3 mmol, 3.0 eqiv) or N,N-dibenzyl-3-oxobutanamide (0.3 mmol, 3.0 equiv) was added to a solution of Ln(terpy)$(NO_3)_2(H_2O)_n$ (Ln = Dy, Sm, Eu) (0.1 mmol, 1.0 equiv) in MeCN-EtOH (1:1, 0.8 mL) at 23 °C followed by Et_3N (0.2 mmol, 2.0 equiv). The mixture was stirred for 1 h at 23 °C. The stir bar was removed and the solution was allowed to slowly evaporate at 23 °C for about 36 h to form colorless crystals suitable for X-ray crystallography.

X-ray Data Collection, structure solution and Refinement

The crystal was mounted on a glass fiber and transferred to a Bruker Kappa APEX II CCD diffractometer. The APEX2 software program was used to determine the unit cell parameters and data collection. The data were collected at 100K using Oxford Cryostream Plus system. The raw frame data were processed using APEX2 program. The absorption correction was applied using program SADABS. Subsequent calculations were carried out using SHELXTL program.



ORTEP drawing of Dy(terpy)$(NO_3)_2$(pyacac) with 50% probability ellipsoids and H atoms and solvent have been omitted for clarity.

X-ray Crystallographic Data for Dy(terpy)$(NO_3)_2$(pyacac).

Identification code	ky2108_0m	
Empirical formula	C26 H26 Dy N7 O7	
Formula weight	711.04	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1/n$	
Unit cell dimensions	a = 9.1631(3) Å	a= 90°.
	b = 27.7638(10) Å	b= 93.537(2)°.
	c = 10.7721(4) Å	g = 90°.
Volume	2735.23(17) $Å^3$	
Z	4	

Density (calculated)	1.727 Mg/m^3
Absorption coefficient	2.790 mm^{-1}
F(000)	1412
Crystal size	0.300 x 0.200 x 0.050 mm^3
Theta range for data collection	1.467 to 28.282°.
Index ranges	-10<=h<=12, -37<=k<=37, -14<=l<=12
Reflections collected	27116
Independent reflections	6786 [R(int) = 0.0453]
Completeness to theta = 25.242°	100.0 %
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6786 / 0 / 372
Goodness-of-fit on F^2	1.047
Final R indices [I>2sigma(I)]	R1 = 0.0292, wR2 = 0.0547
R indices (all data)	R1 = 0.0426, wR2 = 0.0578
Extinction coefficient	n/a
Largest diff. peak and hole	0.528 and -1.384 e.$Å^{-3}$

Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for Dy(terpy)$(NO_3)_2$(pyacac). U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	10776(3)	1654(1)	10211(3)	21(1)

C(2)	12075(3)	1885(1)	10532(3)	24(1)
C(3)	12141(3)	2375(1)	10402(3)	24(1)
C(4)	10913(3)	2622(1)	9945(3)	22(1)
C(5)	9634(3)	2369(1)	9648(3)	16(1)
C(6)	8249(3)	2614(1)	9211(3)	17(1)
C(7)	8120(4)	3114(1)	9212(3)	23(1)
C(8)	6785(4)	3320(1)	8861(3)	26(1)
C(9)	5625(4)	3025(1)	8506(3)	23(1)
C(10)	5812(3)	2529(1)	8489(3)	16(1)
C(11)	4613(3)	2196(1)	8092(3)	15(1)
C(12)	3306(3)	2358(1)	7519(3)	20(1)
C(13)	2249(3)	2026(1)	7143(3)	23(1)
C(14)	2506(3)	1544(1)	7337(3)	22(1)
C(15)	3823(3)	1407(1)	7930(3)	20(1)
C(16)	5652(3)	-89(1)	7922(3)	20(1)
C(17)	6553(3)	271(1)	8679(3)	14(1)
C(18)	7359(3)	116(1)	9722(3)	16(1)
C(19)	8312(3)	418(1)	10473(3)	15(1)
C(20)	8953(3)	-254(1)	11963(3)	20(1)
C(21)	10062(3)	-251(1)	13081(3)	24(1)
C(22)	10051(4)	264(1)	13535(3)	26(1)
C(23)	9933(3)	552(1)	12339(3)	21(1)
C(24)	4603(4)	654(1)	5164(3)	28(1)

C(25)	6149(4)	674(1)	4962(4)	36(1)
Dy(1)	7294(1)	1413(1)	9064(1)	11(1)
N(1)	9562(3)	1887(1)	9779(2)	17(1)
N(2)	7117(3)	2325(1)	8852(2)	14(1)
N(3)	4863(3)	1725(1)	8308(2)	16(1)
N(4)	9018(3)	244(1)	11499(2)	17(1)
N(5)	8510(3)	1443(1)	6647(2)	21(1)
N(6)	5871(3)	1431(1)	11404(2)	20(1)
N(7)	3382(4)	630(1)	5314(3)	41(1)
O(1)	6518(2)	706(1)	8246(2)	15(1)
O(2)	8552(2)	862(1)	10215(2)	17(1)
O(3)	7218(2)	1583(1)	6790(2)	22(1)
O(4)	9233(2)	1302(1)	7612(2)	26(1)
O(5)	9035(3)	1445(1)	5619(2)	34(1)
O(6)	5463(2)	1136(1)	10565(2)	19(1)
O(7)	6837(2)	1738(1)	11121(2)	24(1)
O(8)	5372(3)	1427(1)	12434(2)	35(1)

Bond lengths [Å] and angles [°] for Dy(terpy)$(NO_3)_2$(pyacac).

C(1)-N(1)	1.345(4)
C(1)-C(2)	1.378(4)
C(1)-H(1)	0.9500

C(2)-C(3)	1.369(5)
C(2)-H(2)	0.9500
C(3)-C(4)	1.381(5)
C(3)-H(3)	0.9500
C(4)-C(5)	1.386(4)
C(4)-H(4)	0.9500
C(5)-N(1)	1.348(4)
C(5)-C(6)	1.490(4)
C(6)-N(2)	1.349(4)
C(6)-C(7)	1.393(4)
C(7)-C(8)	1.381(5)
C(7)-H(7)	0.9500
C(8)-C(9)	1.376(5)
C(8)-H(8)	0.9500
C(9)-C(10)	1.388(4)
C(9)-H(9)	0.9500
C(10)-N(2)	1.359(4)
C(10)-C(11)	1.479(4)
C(11)-N(3)	1.348(4)
C(11)-C(12)	1.387(4)
C(12)-C(13)	1.381(5)
C(12)-H(12)	0.9500
C(13)-C(14)	1.372(5)

C(13)-H(13)	0.9500
C(14)-C(15)	1.383(4)
C(14)-H(14)	0.9500
C(15)-N(3)	1.344(4)
C(15)-H(15)	0.9500
C(16)-C(17)	1.503(4)
C(16)-H(16A)	0.9800
C(16)-H(16B)	0.9800
C(16)-H(16C)	0.9800
C(17)-O(1)	1.294(3)
C(17)-C(18)	1.375(4)
C(18)-C(19)	1.427(4)
C(18)-H(18)	0.9500
C(19)-O(2)	1.286(3)
C(19)-N(4)	1.335(4)
C(20)-N(4)	1.473(4)
C(20)-C(21)	1.527(4)
C(20)-H(20A)	0.9900
C(20)-H(20B)	0.9900
C(21)-C(22)	1.512(5)
C(21)-H(21A)	0.9900
C(21)-H(21B)	0.9900
C(22)-C(23)	1.515(4)

C(22)-H(22A)	0.9900
C(22)-H(22B)	0.9900
C(23)-N(4)	1.469(4)
C(23)-H(23A)	0.9900
C(23)-H(23B)	0.9900
C(24)-N(7)	1.142(5)
C(24)-C(25)	1.448(5)
C(25)-H(25A)	0.9800
C(25)-H(25B)	0.9800
C(25)-H(25C)	0.9800
Dy(1)-O(2)	2.2428(19)
Dy(1)-O(1)	2.2500(19)
Dy(1)-O(7)	2.452(2)
Dy(1)-O(4)	2.458(2)
Dy(1)-N(3)	2.479(2)
Dy(1)-O(3)	2.491(2)
Dy(1)-O(6)	2.521(2)
Dy(1)-N(1)	2.539(2)
Dy(1)-N(2)	2.546(2)
Dy(1)-N(5)	2.896(2)
Dy(1)-N(6)	2.909(2)
N(5)-O(5)	1.234(3)
N(5)-O(4)	1.261(3)

N(5)-O(3)	1.264(3)
N(6)-O(8)	1.226(3)
N(6)-O(6)	1.260(3)
N(6)-O(7)	1.279(3)

N(1)-C(1)-C(2)	123.0(3)
N(1)-C(1)-H(1)	118.5
C(2)-C(1)-H(1)	118.5
C(3)-C(2)-C(1)	118.7(3)
C(3)-C(2)-H(2)	120.6
C(1)-C(2)-H(2)	120.6
C(2)-C(3)-C(4)	119.2(3)
C(2)-C(3)-H(3)	120.4
C(4)-C(3)-H(3)	120.4
C(3)-C(4)-C(5)	119.4(3)
C(3)-C(4)-H(4)	120.3
C(5)-C(4)-H(4)	120.3
N(1)-C(5)-C(4)	121.6(3)
N(1)-C(5)-C(6)	116.1(3)
C(4)-C(5)-C(6)	122.3(3)
N(2)-C(6)-C(7)	121.9(3)
N(2)-C(6)-C(5)	116.4(3)
C(7)-C(6)-C(5)	121.7(3)

C(8)-C(7)-C(6)	119.1(3)
C(8)-C(7)-H(7)	120.5
C(6)-C(7)-H(7)	120.5
C(9)-C(8)-C(7)	119.0(3)
C(9)-C(8)-H(8)	120.5
C(7)-C(8)-H(8)	120.5
C(8)-C(9)-C(10)	119.9(3)
C(8)-C(9)-H(9)	120.0
C(10)-C(9)-H(9)	120.0
N(2)-C(10)-C(9)	121.2(3)
N(2)-C(10)-C(11)	116.6(3)
C(9)-C(10)-C(11)	122.2(3)
N(3)-C(11)-C(12)	121.6(3)
N(3)-C(11)-C(10)	116.2(3)
C(12)-C(11)-C(10)	122.2(3)
C(13)-C(12)-C(11)	119.0(3)
C(13)-C(12)-H(12)	120.5
C(11)-C(12)-H(12)	120.5
C(14)-C(13)-C(12)	119.8(3)
C(14)-C(13)-H(13)	120.1
C(12)-C(13)-H(13)	120.1
C(13)-C(14)-C(15)	118.4(3)
C(13)-C(14)-H(14)	120.8

C(15)-C(14)-H(14)	120.8
N(3)-C(15)-C(14)	122.8(3)
N(3)-C(15)-H(15)	118.6
C(14)-C(15)-H(15)	118.6
C(17)-C(16)-H(16A)	109.5
C(17)-C(16)-H(16B)	109.5
H(16A)-C(16)-H(16B)	109.5
C(17)-C(16)-H(16C)	109.5
H(16A)-C(16)-H(16C)	109.5
H(16B)-C(16)-H(16C)	109.5
O(1)-C(17)-C(18)	126.0(3)
O(1)-C(17)-C(16)	115.1(3)
C(18)-C(17)-C(16)	119.0(3)
C(17)-C(18)-C(19)	123.9(3)
C(17)-C(18)-H(18)	118.0
C(19)-C(18)-H(18)	118.0
O(2)-C(19)-N(4)	116.4(3)
O(2)-C(19)-C(18)	123.3(3)
N(4)-C(19)-C(18)	120.3(3)
N(4)-C(20)-C(21)	103.0(2)
N(4)-C(20)-H(20A)	111.2
C(21)-C(20)-H(20A)	111.2
N(4)-C(20)-H(20B)	111.2

C(21)-C(20)-H(20B) 111.2

H(20A)-C(20)-H(20B)109.1

C(22)-C(21)-C(20) 104.0(3)

C(22)-C(21)-H(21A) 111.0

C(20)-C(21)-H(21A) 111.0

C(22)-C(21)-H(21B) 111.0

C(20)-C(21)-H(21B) 111.0

H(21A)-C(21)-H(21B)109.0

C(21)-C(22)-C(23) 103.1(3)

C(21)-C(22)-H(22A) 111.2

C(23)-C(22)-H(22A) 111.2

C(21)-C(22)-H(22B) 111.2

C(23)-C(22)-H(22B) 111.2

H(22A)-C(22)-H(22B)109.1

N(4)-C(23)-C(22) 103.0(3)

N(4)-C(23)-H(23A) 111.2

C(22)-C(23)-H(23A) 111.2

N(4)-C(23)-H(23B) 111.2

C(22)-C(23)-H(23B) 111.2

H(23A)-C(23)-H(23B)109.1

N(7)-C(24)-C(25) 178.8(4)

C(24)-C(25)-H(25A) 109.5

C(24)-C(25)-H(25B) 109.5

H(25A)-C(25)-H(25B)109.5

C(24)-C(25)-H(25C) 109.5

H(25A)-C(25)-H(25C)109.5

H(25B)-C(25)-H(25C)109.5

O(2)-Dy(1)-O(1) 76.14(7)

O(2)-Dy(1)-O(7) 82.05(7)

O(1)-Dy(1)-O(7) 127.41(7)

O(2)-Dy(1)-O(4) 84.20(7)

O(1)-Dy(1)-O(4) 82.20(7)

O(7)-Dy(1)-O(4) 142.34(7)

O(2)-Dy(1)-N(3) 147.16(7)

O(1)-Dy(1)-N(3) 85.43(8)

O(7)-Dy(1)-N(3) 88.20(8)

O(4)-Dy(1)-N(3) 120.32(7)

O(2)-Dy(1)-O(3) 130.91(7)

O(1)-Dy(1)-O(3) 77.94(7)

O(7)-Dy(1)-O(3) 145.39(7)

O(4)-Dy(1)-O(3) 51.35(7)

N(3)-Dy(1)-O(3) 68.97(7)

O(2)-Dy(1)-O(6) 77.12(7)

O(1)-Dy(1)-O(6) 77.17(7)

O(7)-Dy(1)-O(6) 51.34(7)

O(4)-Dy(1)-O(6) 154.89(8)

N(3)-Dy(1)-O(6)	72.37(7)
O(3)-Dy(1)-O(6)	135.15(7)
O(2)-Dy(1)-N(1)	78.60(8)
O(1)-Dy(1)-N(1)	143.51(7)
O(7)-Dy(1)-N(1)	73.59(7)
O(4)-Dy(1)-N(1)	69.37(7)
N(3)-Dy(1)-N(1)	128.37(8)
O(3)-Dy(1)-N(1)	99.95(8)
O(6)-Dy(1)-N(1)	121.90(7)
O(2)-Dy(1)-N(2)	139.05(7)
O(1)-Dy(1)-N(2)	144.70(7)
O(7)-Dy(1)-N(2)	72.66(7)
O(4)-Dy(1)-N(2)	96.45(8)
N(3)-Dy(1)-N(2)	64.71(8)
O(3)-Dy(1)-N(2)	74.09(7)
O(6)-Dy(1)-N(2)	108.66(7)
N(1)-Dy(1)-N(2)	63.79(8)
O(2)-Dy(1)-N(5)	107.67(8)
O(1)-Dy(1)-N(5)	78.63(7)
O(7)-Dy(1)-N(5)	153.96(7)
O(4)-Dy(1)-N(5)	25.59(7)
N(3)-Dy(1)-N(5)	94.73(8)
O(3)-Dy(1)-N(5)	25.77(7)

O(6)-Dy(1)-N(5)	153.33(7)
N(1)-Dy(1)-N(5)	84.52(7)
N(2)-Dy(1)-N(5)	85.21(7)
O(2)-Dy(1)-N(6)	77.01(7)
O(1)-Dy(1)-N(6)	101.92(7)
O(7)-Dy(1)-N(6)	25.85(7)
O(4)-Dy(1)-N(6)	159.04(7)
N(3)-Dy(1)-N(6)	80.61(7)
O(3)-Dy(1)-N(6)	149.53(7)
O(6)-Dy(1)-N(6)	25.57(7)
N(1)-Dy(1)-N(6)	97.52(8)
N(2)-Dy(1)-N(6)	91.79(7)
N(5)-Dy(1)-N(6)	175.22(7)
C(1)-N(1)-C(5)	118.0(3)
C(1)-N(1)-Dy(1)	119.9(2)
C(5)-N(1)-Dy(1)	121.83(19)
C(6)-N(2)-C(10)	118.8(3)
C(6)-N(2)-Dy(1)	121.47(19)
C(10)-N(2)-Dy(1)	119.41(18)
C(15)-N(3)-C(11)	118.4(3)
C(15)-N(3)-Dy(1)	118.5(2)
C(11)-N(3)-Dy(1)	122.38(19)
C(19)-N(4)-C(23)	121.9(2)

C(19)-N(4)-C(20)	126.4(3)
C(23)-N(4)-C(20)	111.7(2)
O(5)-N(5)-O(4)	121.8(3)
O(5)-N(5)-O(3)	121.9(3)
O(4)-N(5)-O(3)	116.3(2)
O(5)-N(5)-Dy(1)	178.6(2)
O(4)-N(5)-Dy(1)	57.39(13)
O(3)-N(5)-Dy(1)	58.90(14)
O(8)-N(6)-O(6)	122.2(3)
O(8)-N(6)-O(7)	121.6(3)
O(6)-N(6)-O(7)	116.2(2)
O(8)-N(6)-Dy(1)	175.0(2)
O(6)-N(6)-Dy(1)	59.75(13)
O(7)-N(6)-Dy(1)	56.71(13)
C(17)-O(1)-Dy(1)	132.30(18)
C(19)-O(2)-Dy(1)	133.19(18)
N(5)-O(3)-Dy(1)	95.34(16)
N(5)-O(4)-Dy(1)	97.02(16)
N(6)-O(6)-Dy(1)	94.68(15)
N(6)-O(7)-Dy(1)	97.44(16)

Anisotropic displacement parameters ($Å^2 x\ 10^3$) for $Dy(terpy)(NO_3)_2(pyacac)$. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2\ a^{*2}U^{11} +$

... + 2 h k a* b* U^{12}]

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	17(2)	24(2)	22(2)	-2(1)	-1(1)	0(1)
C(2)	14(2)	38(2)	19(2)	-6(2)	2(1)	-4(2)
C(3)	18(2)	32(2)	22(2)	-14(2)	4(1)	-11(2)
C(4)	24(2)	19(2)	25(2)	-7(1)	7(1)	-7(1)
C(5)	17(2)	20(2)	12(1)	-4(1)	6(1)	-4(1)
C(6)	22(2)	17(2)	12(1)	-3(1)	7(1)	-4(1)
C(7)	34(2)	16(2)	21(2)	-1(1)	10(1)	-6(1)
C(8)	38(2)	12(2)	28(2)	2(1)	8(2)	2(2)
C(9)	30(2)	16(2)	23(2)	6(1)	5(1)	7(1)
C(10)	20(2)	18(2)	12(1)	1(1)	7(1)	-1(1)
C(11)	16(2)	17(2)	12(1)	3(1)	4(1)	4(1)
C(12)	21(2)	26(2)	14(2)	4(1)	5(1)	12(1)
C(13)	17(2)	39(2)	15(2)	1(1)	1(1)	9(2)
C(14)	14(2)	31(2)	23(2)	-3(1)	0(1)	0(1)
C(15)	14(1)	20(2)	25(2)	1(1)	3(1)	-1(1)
C(16)	28(2)	16(2)	15(2)	0(1)	-4(1)	-4(1)
C(17)	12(1)	17(2)	14(1)	-3(1)	4(1)	2(1)
C(18)	20(2)	11(1)	15(2)	2(1)	0(1)	-2(1)
C(19)	15(1)	17(2)	14(1)	2(1)	3(1)	2(1)

C(20)	24(2)	18(2)	18(2)	6(1)	-1(1)	4(1)
C(21)	24(2)	29(2)	18(2)	4(1)	0(1)	6(2)
C(22)	27(2)	32(2)	18(2)	3(1)	-4(1)	0(2)
C(23)	23(2)	24(2)	16(2)	0(1)	-6(1)	1(1)
C(24)	41(2)	20(2)	21(2)	-6(1)	-11(2)	4(2)
C(25)	41(2)	29(2)	36(2)	-6(2)	-3(2)	-4(2)
Dy(1)	10(1)	11(1)	12(1)	0(1)	0(1)	0(1)
N(1)	14(1)	18(1)	18(1)	-3(1)	2(1)	-1(1)
N(2)	17(1)	14(1)	12(1)	0(1)	3(1)	2(1)
N(3)	14(1)	18(1)	17(1)	2(1)	4(1)	1(1)
N(4)	20(1)	15(1)	17(1)	2(1)	-4(1)	2(1)
N(5)	25(1)	19(1)	21(1)	-2(1)	8(1)	-8(1)
N(6)	21(1)	19(1)	20(1)	0(1)	4(1)	2(1)
N(7)	43(2)	41(2)	38(2)	-12(2)	-6(2)	6(2)
O(1)	16(1)	13(1)	15(1)	2(1)	-3(1)	0(1)
O(2)	17(1)	15(1)	18(1)	4(1)	-4(1)	-2(1)
O(3)	26(1)	22(1)	17(1)	5(1)	5(1)	8(1)
O(4)	14(1)	48(2)	16(1)	-4(1)	0(1)	-2(1)
O(5)	38(1)	49(2)	18(1)	-2(1)	14(1)	-6(1)
O(6)	19(1)	20(1)	17(1)	-1(1)	1(1)	-3(1)
O(7)	29(1)	20(1)	23(1)	-4(1)	7(1)	-9(1)
O(8)	43(2)	42(2)	21(1)	-5(1)	16(1)	-5(1)

Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3) for $Dy(terpy)(NO_3)_2(pyacac)$.

	x	y	z	U(eq)
H(1)	10735	1314	10298	25
H(2)	12908	1708	10839	28
H(3)	13021	2544	10623	29
H(4)	10945	2961	9836	27
H(7)	8938	3310	9450	28
H(8)	6670	3660	8866	31
H(9)	4698	3161	8272	27
H(12)	3141	2693	7387	24
H(13)	1347	2130	6750	28
H(14)	1797	1310	7072	27
H(15)	3999	1074	8076	24
H(16A)	4675	44	7723	30
H(16B)	5570	-387	8401	30
H(16C)	6125	-158	7150	30
H(18)	7275	-212	9957	19
H(20A)	9234	-487	11325	24
H(20B)	7961	-333	12217	24
H(21A)	9764	-476	13733	29

H(21B)	11045	-344	12832	29
H(22A)	10964	342	14035	31
H(22B)	9205	324	14041	31
H(23A)	9462	868	12464	26
H(23B)	10907	605	12013	26
H(25A)	6431	386	4509	53
H(25B)	6710	689	5766	53
H(25C)	6353	962	4475	53

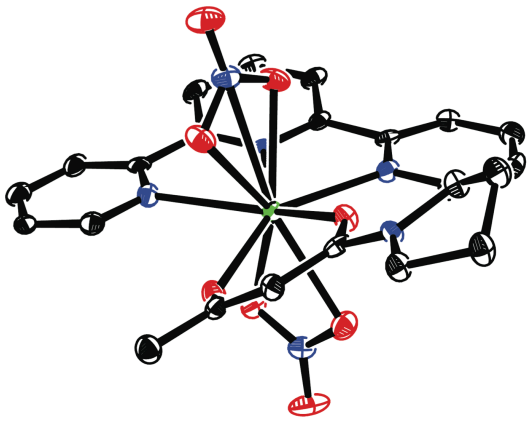
Torsion angles [°] for Dy(terpy)$(NO_3)_2$(pyacac).

N(1)-C(1)-C(2)-C(3)	-0.3(5)
C(1)-C(2)-C(3)-C(4)	-0.5(5)
C(2)-C(3)-C(4)-C(5)	1.0(5)
C(3)-C(4)-C(5)-N(1)	-0.8(4)
C(3)-C(4)-C(5)-C(6)	176.9(3)
N(1)-C(5)-C(6)-N(2)	-7.6(4)
C(4)-C(5)-C(6)-N(2)	174.5(3)
N(1)-C(5)-C(6)-C(7)	170.5(3)
C(4)-C(5)-C(6)-C(7)	-7.4(4)
N(2)-C(6)-C(7)-C(8)	1.5(4)
C(5)-C(6)-C(7)-C(8)	-176.5(3)
C(6)-C(7)-C(8)-C(9)	-0.8(5)

C(7)-C(8)-C(9)-C(10)	-0.8(5)
C(8)-C(9)-C(10)-N(2)	1.8(4)
C(8)-C(9)-C(10)-C(11)	-178.8(3)
N(2)-C(10)-C(11)-N(3)	9.8(4)
C(9)-C(10)-C(11)-N(3)	-169.6(3)
N(2)-C(10)-C(11)-C(12)	-169.6(2)
C(9)-C(10)-C(11)-C(12)	10.9(4)
N(3)-C(11)-C(12)-C(13)	-1.2(4)
C(10)-C(11)-C(12)-C(13)	178.3(3)
C(11)-C(12)-C(13)-C(14)	-0.1(4)
C(12)-C(13)-C(14)-C(15)	1.1(4)
C(13)-C(14)-C(15)-N(3)	-0.8(5)
O(1)-C(17)-C(18)-C(19)	-1.4(5)
C(16)-C(17)-C(18)-C(19)	176.6(3)
C(17)-C(18)-C(19)-O(2)	-2.8(5)
C(17)-C(18)-C(19)-N(4)	177.6(3)
N(4)-C(20)-C(21)-C(22)	28.4(3)
C(20)-C(21)-C(22)-C(23)	-39.2(3)
C(21)-C(22)-C(23)-N(4)	34.2(3)
C(2)-C(1)-N(1)-C(5)	0.5(4)
C(2)-C(1)-N(1)-Dy(1)	175.3(2)
C(4)-C(5)-N(1)-C(1)	0.1(4)
C(6)-C(5)-N(1)-C(1)	-177.8(2)

C(4)-C(5)-N(1)-Dy(1)	-174.6(2)
C(6)-C(5)-N(1)-Dy(1)	7.5(3)
C(7)-C(6)-N(2)-C(10)	-0.5(4)
C(5)-C(6)-N(2)-C(10)	177.6(2)
C(7)-C(6)-N(2)-Dy(1)	-173.7(2)
C(5)-C(6)-N(2)-Dy(1)	4.4(3)
C(9)-C(10)-N(2)-C(6)	-1.2(4)
C(11)-C(10)-N(2)-C(6)	179.4(2)
C(9)-C(10)-N(2)-Dy(1)	172.2(2)
C(11)-C(10)-N(2)-Dy(1)	-7.3(3)
C(14)-C(15)-N(3)-C(11)	-0.4(4)
C(14)-C(15)-N(3)-Dy(1)	-170.9(2)
C(12)-C(11)-N(3)-C(15)	1.4(4)
C(10)-C(11)-N(3)-C(15)	-178.1(2)
C(12)-C(11)-N(3)-Dy(1)	171.5(2)
C(10)-C(11)-N(3)-Dy(1)	-8.0(3)
O(2)-C(19)-N(4)-C(23)	4.5(4)
C(18)-C(19)-N(4)-C(23)	-175.9(3)
O(2)-C(19)-N(4)-C(20)	-178.1(3)
C(18)-C(19)-N(4)-C(20)	1.4(4)
C(22)-C(23)-N(4)-C(19)	160.8(3)
C(22)-C(23)-N(4)-C(20)	-17.0(3)
C(21)-C(20)-N(4)-C(19)	175.3(3)

C(21)-C(20)-N(4)-C(23)	-7.1(3)
C(18)-C(17)-O(1)-Dy(1)	-13.4(4)
C(16)-C(17)-O(1)-Dy(1)	168.58(18)
N(4)-C(19)-O(2)-Dy(1)	-158.05(19)
C(18)-C(19)-O(2)-Dy(1)	22.4(4)
O(5)-N(5)-O(3)-Dy(1)	178.6(2)
O(4)-N(5)-O(3)-Dy(1)	-1.4(3)
O(5)-N(5)-O(4)-Dy(1)	-178.6(2)
O(3)-N(5)-O(4)-Dy(1)	1.4(3)
O(8)-N(6)-O(6)-Dy(1)	-174.6(3)
O(7)-N(6)-O(6)-Dy(1)	5.5(2)
O(8)-N(6)-O(7)-Dy(1)	174.4(2)
O(6)-N(6)-O(7)-Dy(1)	-5.7(3)



ORTEP drawing of Sm(terpy)$(NO_3)_2$(pyacac) with 50% probability ellipsoids and H atoms and solvent have been omitted for clarity.

X-ray Crystallographic Data for Sm(terpy)$(NO_3)_2$(pyacac).

Identification code	ky03042014_0m	
Empirical formula	C31 H36 N7 O10 Sm	
Formula weight	817.02	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1/n$	
Unit cell dimensions	a = 9.7347(2) Å	a= 90°.
	b = 11.5779(3) Å	
	b=92.4370(10)°.	
	c = 29.1920(6) Å	g = 90°.
Volume	3287.18(13) $Å^3$	
Z	4	
Density (calculated)	1.651 Mg/m^3	
Absorption coefficient	1.855 mm^{-1}	
F(000)	1652	
Crystal size	0.15 x 0.1 x 0.1 mm^3	
Theta range for data collection	1.396 to 28.289°.	
Index ranges	-11<=h<=12, -15<=k<=10, -38<=l<=38	
Reflections collected	22466	
Independent reflections	8135 [R(int) = 0.0295]	
Completeness to theta = 25.242°	99.8 %	
Absorption correction	Semi-empirical from equivalents	

Max. and min. transmission	0.7457 and 0.6450
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	8135 / 0 / 444
Goodness-of-fit on F^2	1.064
Final R indices [I>2sigma(I)]	R1 = 0.0319, wR2 = 0.0618
R indices (all data)	R1 = 0.0425, wR2 = 0.0648
Extinction coefficient	n/a
Largest diff. peak and hole	1.161 and -1.511 e.$Å^{-3}$

Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for $Sm(terpy)(NO_3)_2(pyacac)$. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	2047(3)	318(3)	296(1)	30(1)
C(2)	3542(3)	244(3)	466(1)	27(1)
C(3)	4583(3)	1088(3)	1169(1)	23(1)
C(4)	4418(3)	1549(3)	1654(1)	26(1)
C(5)	5349(3)	868(3)	1984(1)	24(1)
C(6)	4865(4)	-321(4)	2102(1)	43(1)
C(7)	2073(3)	558(3)	1109(1)	28(1)
C(8)	1269(4)	-37(3)	715(1)	34(1)
C(9)	5740(3)	6644(2)	1481(1)	14(1)

C(10)	6359(3)	8235(3)	968(1)	19(1)
C(11)	7721(3)	8874(3)	923(1)	22(1)
C(12)	8324(3)	8901(3)	1416(1)	23(1)
C(13)	7951(3)	7726(3)	1605(1)	21(1)
C(14)	6101(3)	5889(3)	1855(1)	15(1)
C(15)	5387(3)	4929(2)	1967(1)	16(1)
C(16)	5907(3)	4198(3)	2364(1)	22(1)
C(18)	-197(3)	5845(2)	548(1)	12(1)
C(19)	-1587(3)	5976(3)	415(1)	16(1)
C(20)	-2563(3)	5369(3)	648(1)	19(1)
C(21)	-2145(3)	4655(3)	1003(1)	18(1)
C(22)	-748(3)	4564(2)	1124(1)	15(1)
C(23)	-227(3)	3777(3)	1494(1)	17(1)
C(24)	1583(3)	3249(3)	1987(1)	21(1)
C(25)	832(3)	2360(3)	2172(1)	25(1)
C(26)	-494(3)	2178(3)	2004(1)	27(1)
C(27)	-1036(3)	2894(3)	1662(1)	23(1)
C(28)	885(2)	6428(2)	289(1)	12(1)
C(29)	3205(3)	6792(3)	226(1)	16(1)
C(30)	2984(3)	7440(3)	-166(1)	17(1)
C(31)	1647(3)	7575(3)	-336(1)	17(1)
C(32)	585(3)	7060(2)	-108(1)	16(1)
N(1)	3482(3)	606(2)	950(1)	22(1)

N(2)	6615(2)	7476(2)	1366(1)	16(1)
N(6)	1800(2)	7318(2)	1764(1)	22(1)
N(7)	3588(2)	3588(2)	561(1)	16(1)
N(4)	208(2)	5172(2)	904(1)	12(1)
N(3)	1085(2)	3942(2)	1649(1)	17(1)
N(5)	2197(2)	6290(2)	456(1)	12(1)
O(1)	5706(2)	1173(2)	998(1)	28(1)
O(2)	6408(2)	1255(2)	2139(1)	40(1)
O(3)	4612(2)	6561(2)	1239(1)	16(1)
O(4)	4269(2)	4539(2)	1757(1)	21(1)
O(5)	1620(2)	7293(2)	1333(1)	22(1)
O(6)	2477(2)	3477(2)	778(1)	20(1)
O(7)	4363(2)	4416(2)	684(1)	21(1)
O(8)	3850(2)	2936(2)	249(1)	21(1)
O(9)	2172(2)	6375(2)	1958(1)	29(1)
O(10)	1638(2)	8207(2)	1984(1)	35(1)
Sm(1)	2725(1)	5329(1)	1238(1)	13(1)

Bond lengths [Å] and angles [°] for Sm(terpy)$(NO_3)_2$(pyacac).

C(1)-C(2)	1.520(4)
C(1)-C(8)	1.521(5)
C(1)-H(3)	0.9900

C(1)-H(1)	0.9900
C(2)-N(1)	1.477(4)
C(2)-H(12)	0.9900
C(2)-H(13)	0.9900
C(3)-O(1)	1.225(4)
C(3)-N(1)	1.347(4)
C(3)-C(4)	1.528(4)
C(4)-C(5)	1.515(4)
C(4)-H(6)	0.9900
C(4)-H(7)	0.9900
C(5)-O(2)	1.195(4)
C(5)-C(6)	1.499(5)
C(6)-H(2)	0.9800
C(6)-H(5)	0.9800
C(6)-H(4)	0.9800
C(7)-N(1)	1.468(4)
C(7)-C(8)	1.529(5)
C(7)-H(8)	0.9900
C(7)-H(9)	0.9900
C(8)-H(11)	0.9900
C(8)-H(10)	0.9900
C(9)-O(3)	1.283(3)
C(9)-N(2)	1.337(4)

C(9)-C(14)	1.432(4)
C(10)-N(2)	1.471(3)
C(10)-C(11)	1.529(4)
C(10)-H(21)	0.9900
C(10)-H(20)	0.9900
C(11)-C(12)	1.533(4)
C(11)-H(19)	0.9900
C(11)-H(18)	0.9900
C(12)-C(13)	1.517(4)
C(12)-H(16)	0.9900
C(12)-H(17)	0.9900
C(13)-N(2)	1.478(3)
C(13)-H(14)	0.9900
C(13)-H(15)	0.9900
C(14)-C(15)	1.358(4)
C(14)-H(25)	0.9500
C(15)-O(4)	1.307(3)
C(15)-C(16)	1.505(4)
C(16)-H(23)	0.9800
C(16)-H(22)	0.9800
C(16)-H(24)	0.9800
C(18)-N(4)	1.346(3)
C(18)-C(19)	1.399(3)

C(18)-C(28)	1.484(4)
C(19)-C(20)	1.383(4)
C(19)-H(32)	0.9500
C(20)-C(21)	1.375(4)
C(20)-H(31)	0.9500
C(21)-C(22)	1.394(4)
C(21)-H(30)	0.9500
C(22)-N(4)	1.349(3)
C(22)-C(23)	1.486(4)
C(23)-N(3)	1.351(3)
C(23)-C(27)	1.392(4)
C(24)-N(3)	1.346(4)
C(24)-C(25)	1.384(4)
C(24)-H(29)	0.9500
C(25)-C(26)	1.378(4)
C(25)-H(28)	0.9500
C(26)-C(27)	1.384(4)
C(26)-H(26)	0.9500
C(27)-H(27)	0.9500
C(28)-N(5)	1.356(3)
C(28)-C(32)	1.391(4)
C(29)-N(5)	1.344(3)
C(29)-C(30)	1.378(4)

C(29)-H(36)	0.9500
C(30)-C(31)	1.382(4)
C(30)-H(33)	0.9500
C(31)-C(32)	1.388(4)
C(31)-H(34)	0.9500
C(32)-H(35)	0.9500
N(6)-O(10)	1.226(3)
N(6)-O(5)	1.263(3)
N(6)-O(9)	1.274(3)
N(6)-Sm(1)	2.931(3)
N(7)-O(8)	1.219(3)
N(7)-O(7)	1.263(3)
N(7)-O(6)	1.282(3)
N(7)-Sm(1)	2.969(2)
N(4)-Sm(1)	2.605(2)
N(3)-Sm(1)	2.595(2)
N(5)-Sm(1)	2.571(2)
O(3)-Sm(1)	2.3256(19)
O(4)-Sm(1)	2.2795(18)
O(5)-Sm(1)	2.536(2)
O(6)-Sm(1)	2.536(2)
O(7)-Sm(1)	2.548(2)
O(9)-Sm(1)	2.504(2)

C(2)-C(1)-C(8)	103.0(3)
C(2)-C(1)-H(3)	111.2
C(8)-C(1)-H(3)	111.2
C(2)-C(1)-H(1)	111.2
C(8)-C(1)-H(1)	111.2
H(3)-C(1)-H(1)	109.1
N(1)-C(2)-C(1)	102.7(3)
N(1)-C(2)-H(12)	111.2
C(1)-C(2)-H(12)	111.2
N(1)-C(2)-H(13)	111.2
C(1)-C(2)-H(13)	111.2
H(12)-C(2)-H(13)	109.1
O(1)-C(3)-N(1)	123.1(3)
O(1)-C(3)-C(4)	118.7(3)
N(1)-C(3)-C(4)	118.2(3)
C(5)-C(4)-C(3)	108.9(3)
C(5)-C(4)-H(6)	109.9
C(3)-C(4)-H(6)	109.9
C(5)-C(4)-H(7)	109.9
C(3)-C(4)-H(7)	109.9
H(6)-C(4)-H(7)	108.3
O(2)-C(5)-C(6)	122.2(3)
O(2)-C(5)-C(4)	121.9(3)

C(6)-C(5)-C(4)	116.0(3)
C(5)-C(6)-H(2)	109.5
C(5)-C(6)-H(5)	109.5
H(2)-C(6)-H(5)	109.5
C(5)-C(6)-H(4)	109.5
H(2)-C(6)-H(4)	109.5
H(5)-C(6)-H(4)	109.5
N(1)-C(7)-C(8)	103.5(3)
N(1)-C(7)-H(8)	111.1
C(8)-C(7)-H(8)	111.1
N(1)-C(7)-H(9)	111.1
C(8)-C(7)-H(9)	111.1
H(8)-C(7)-H(9)	109.0
C(1)-C(8)-C(7)	103.1(3)
C(1)-C(8)-H(11)	111.1
C(7)-C(8)-H(11)	111.1
C(1)-C(8)-H(10)	111.1
C(7)-C(8)-H(10)	111.1
H(11)-C(8)-H(10)	109.1
O(3)-C(9)-N(2)	117.1(2)
O(3)-C(9)-C(14)	123.4(3)
N(2)-C(9)-C(14)	119.5(2)
N(2)-C(10)-C(11)	103.8(2)

N(2)-C(10)-H(21)	111.0
C(11)-C(10)-H(21)	111.0
N(2)-C(10)-H(20)	111.0
C(11)-C(10)-H(20)	111.0
H(21)-C(10)-H(20)	109.0
C(10)-C(11)-C(12)	103.2(2)
C(10)-C(11)-H(19)	111.1
C(12)-C(11)-H(19)	111.1
C(10)-C(11)-H(18)	111.1
C(12)-C(11)-H(18)	111.1
H(19)-C(11)-H(18)	109.1
C(13)-C(12)-C(11)	103.6(2)
C(13)-C(12)-H(16)	111.0
C(11)-C(12)-H(16)	111.0
C(13)-C(12)-H(17)	111.0
C(11)-C(12)-H(17)	111.0
H(16)-C(12)-H(17)	109.0
N(2)-C(13)-C(12)	103.0(2)
N(2)-C(13)-H(14)	111.2
C(12)-C(13)-H(14)	111.2
N(2)-C(13)-H(15)	111.2
C(12)-C(13)-H(15)	111.2
H(14)-C(13)-H(15)	109.1

C(15)-C(14)-C(9)	124.9(2)
C(15)-C(14)-H(25)	117.6
C(9)-C(14)-H(25)	117.6
O(4)-C(15)-C(14)	126.4(2)
O(4)-C(15)-C(16)	114.4(2)
C(14)-C(15)-C(16)	119.1(2)
C(15)-C(16)-H(23)	109.5
C(15)-C(16)-H(22)	109.5
H(23)-C(16)-H(22)	109.5
C(15)-C(16)-H(24)	109.5
H(23)-C(16)-H(24)	109.5
H(22)-C(16)-H(24)	109.5
N(4)-C(18)-C(19)	121.7(2)
N(4)-C(18)-C(28)	117.7(2)
C(19)-C(18)-C(28)	120.6(2)
C(20)-C(19)-C(18)	119.0(3)
C(20)-C(19)-H(32)	120.5
C(18)-C(19)-H(32)	120.5
C(21)-C(20)-C(19)	119.3(2)
C(21)-C(20)-H(31)	120.4
C(19)-C(20)-H(31)	120.4
C(20)-C(21)-C(22)	119.3(3)
C(20)-C(21)-H(30)	120.3

C(22)-C(21)-H(30)	120.3
N(4)-C(22)-C(21)	121.7(3)
N(4)-C(22)-C(23)	116.4(2)
C(21)-C(22)-C(23)	121.9(3)
N(3)-C(23)-C(27)	121.8(3)
N(3)-C(23)-C(22)	116.5(2)
C(27)-C(23)-C(22)	121.7(2)
N(3)-C(24)-C(25)	123.3(3)
N(3)-C(24)-H(29)	118.3
C(25)-C(24)-H(29)	118.3
C(26)-C(25)-C(24)	118.5(3)
C(26)-C(25)-H(28)	120.7
C(24)-C(25)-H(28)	120.7
C(25)-C(26)-C(27)	119.2(3)
C(25)-C(26)-H(26)	120.4
C(27)-C(26)-H(26)	120.4
C(26)-C(27)-C(23)	119.3(3)
C(26)-C(27)-H(27)	120.3
C(23)-C(27)-H(27)	120.3
N(5)-C(28)-C(32)	121.5(2)
N(5)-C(28)-C(18)	116.2(2)
C(32)-C(28)-C(18)	122.3(2)
N(5)-C(29)-C(30)	124.0(2)

N(5)-C(29)-H(36)	118.0
C(30)-C(29)-H(36)	118.0
C(29)-C(30)-C(31)	118.1(3)
C(29)-C(30)-H(33)	120.9
C(31)-C(30)-H(33)	120.9
C(30)-C(31)-C(32)	119.2(3)
C(30)-C(31)-H(34)	120.4
C(32)-C(31)-H(34)	120.4
C(31)-C(32)-C(28)	119.5(2)
C(31)-C(32)-H(35)	120.3
C(28)-C(32)-H(35)	120.3
C(3)-N(1)-C(7)	126.9(3)
C(3)-N(1)-C(2)	120.6(3)
C(7)-N(1)-C(2)	111.6(2)
C(9)-N(2)-C(10)	122.6(2)
C(9)-N(2)-C(13)	125.5(2)
C(10)-N(2)-C(13)	111.8(2)
O(10)-N(6)-O(5)	121.6(3)
O(10)-N(6)-O(9)	121.8(2)
O(5)-N(6)-O(9)	116.6(2)
O(10)-N(6)-Sm(1)	169.3(2)
O(5)-N(6)-Sm(1)	59.53(14)
O(9)-N(6)-Sm(1)	58.12(14)

O(8)-N(7)-O(7)	122.8(2)
O(8)-N(7)-O(6)	121.0(2)
O(7)-N(7)-O(6)	116.2(2)
O(8)-N(7)-Sm(1)	173.01(17)
O(7)-N(7)-Sm(1)	58.50(13)
O(6)-N(7)-Sm(1)	58.07(13)
C(18)-N(4)-C(22)	118.9(2)
C(18)-N(4)-Sm(1)	119.26(17)
C(22)-N(4)-Sm(1)	121.05(16)
C(24)-N(3)-C(23)	117.9(3)
C(24)-N(3)-Sm(1)	119.95(18)
C(23)-N(3)-Sm(1)	121.58(18)
C(29)-N(5)-C(28)	117.7(2)
C(29)-N(5)-Sm(1)	120.51(16)
C(28)-N(5)-Sm(1)	121.29(17)
C(9)-O(3)-Sm(1)	134.76(18)
C(15)-O(4)-Sm(1)	133.32(18)
N(6)-O(5)-Sm(1)	95.05(16)
N(7)-O(6)-Sm(1)	96.51(15)
N(7)-O(7)-Sm(1)	96.49(15)
N(6)-O(9)-Sm(1)	96.28(15)
O(4)-Sm(1)-O(3)	75.33(7)
O(4)-Sm(1)-O(9)	78.21(8)

O(3)-Sm(1)-O(9)	84.26(7)
O(4)-Sm(1)-O(5)	123.90(7)
O(3)-Sm(1)-O(5)	77.80(7)
O(9)-Sm(1)-O(5)	50.71(7)
O(4)-Sm(1)-O(6)	93.32(7)
O(3)-Sm(1)-O(6)	125.23(6)
O(9)-Sm(1)-O(6)	146.55(7)
O(5)-Sm(1)-O(6)	141.70(6)
O(4)-Sm(1)-O(7)	80.91(7)
O(3)-Sm(1)-O(7)	74.92(6)
O(9)-Sm(1)-O(7)	153.61(7)
O(5)-Sm(1)-O(7)	136.19(7)
O(6)-Sm(1)-O(7)	50.31(6)
O(4)-Sm(1)-N(5)	149.86(7)
O(3)-Sm(1)-N(5)	82.19(6)
O(9)-Sm(1)-N(5)	119.58(7)
O(5)-Sm(1)-N(5)	68.88(7)
O(6)-Sm(1)-N(5)	83.38(7)
O(7)-Sm(1)-N(5)	73.96(7)
O(4)-Sm(1)-N(3)	81.10(7)
O(3)-Sm(1)-N(3)	151.68(7)
O(9)-Sm(1)-N(3)	75.66(7)
O(5)-Sm(1)-N(3)	103.41(7)

O(6)-Sm(1)-N(3)	71.05(7)
O(7)-Sm(1)-N(3)	116.79(7)
N(5)-Sm(1)-N(3)	125.09(7)
O(4)-Sm(1)-N(4)	143.47(7)
O(3)-Sm(1)-N(4)	140.72(7)
O(9)-Sm(1)-N(4)	96.60(7)
O(5)-Sm(1)-N(4)	72.95(7)
O(6)-Sm(1)-N(4)	71.09(7)
O(7)-Sm(1)-N(4)	109.77(6)
N(5)-Sm(1)-N(4)	63.18(7)
N(3)-Sm(1)-N(4)	62.75(7)
O(4)-Sm(1)-N(6)	100.11(7)
O(3)-Sm(1)-N(6)	77.16(7)
O(9)-Sm(1)-N(6)	25.60(7)
O(5)-Sm(1)-N(6)	25.42(6)
O(6)-Sm(1)-N(6)	156.53(6)
O(7)-Sm(1)-N(6)	150.82(7)
N(5)-Sm(1)-N(6)	94.07(7)
N(3)-Sm(1)-N(6)	91.99(7)
N(4)-Sm(1)-N(6)	86.88(7)
O(4)-Sm(1)-N(7)	88.43(7)
O(3)-Sm(1)-N(7)	99.89(7)
O(9)-Sm(1)-N(7)	164.60(7)

O(5)-Sm(1)-N(7)	144.60(6)
O(6)-Sm(1)-N(7)	25.41(6)
O(7)-Sm(1)-N(7)	25.00(6)
N(5)-Sm(1)-N(7)	75.79(7)
N(3)-Sm(1)-N(7)	94.87(7)
N(4)-Sm(1)-N(7)	89.54(6)
N(6)-Sm(1)-N(7)	169.79(7)

Anisotropic displacement parameters ($Å^2 x\ 10^3$) for $Sm(terpy)(NO_3)_2(pyacac)$. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	41(2)	20(2)	30(2)	1(1)	-8(1)	3(2)
C(2)	34(2)	20(2)	28(2)	-2(1)	-1(1)	6(1)
C(3)	25(2)	16(2)	28(2)	5(1)	-1(1)	5(1)
C(4)	23(2)	26(2)	29(2)	-2(1)	-1(1)	4(1)
C(5)	22(1)	26(2)	24(2)	-2(1)	1(1)	0(1)
C(6)	43(2)	46(2)	41(2)	15(2)	-1(2)	-10(2)
C(7)	20(2)	33(2)	32(2)	7(1)	0(1)	-3(1)
C(8)	30(2)	29(2)	41(2)	10(2)	-8(1)	-8(1)
C(9)	14(1)	12(1)	16(1)	-6(1)	-2(1)	1(1)

C(10)20(1)	15(2)	22(1)	2(1)	-5(1)	-2(1)
C(11)19(1)	20(2)	26(2)	1(1)	-1(1)	-6(1)
C(12)20(1)	24(2)	25(2)	0(1)	-3(1)	-7(1)
C(13)19(1)	23(2)	20(1)	0(1)	-7(1)	-3(1)
C(14)11(1)	22(2)	12(1)	-2(1)	-1(1)	0(1)
C(15)14(1)	18(2)	15(1)	0(1)	-1(1)	4(1)
C(16)21(1)	25(2)	19(1)	5(1)	-6(1)	-3(1)
C(18)11(1)	12(1)	13(1)	-5(1)	0(1)	0(1)
C(19)12(1)	15(2)	20(1)	-1(1)	-1(1)	2(1)
C(20)10(1)	20(2)	26(1)	-6(1)	-1(1)	1(1)
C(21)13(1)	21(2)	21(1)	-8(1)	4(1)	-3(1)
C(22)16(1)	14(1)	16(1)	-5(1)	1(1)	-2(1)
C(23)17(1)	18(2)	15(1)	-2(1)	4(1)	-2(1)
C(24)18(1)	28(2)	18(1)	1(1)	0(1)	1(1)
C(25)27(2)	30(2)	18(1)	7(1)	3(1)	-1(1)
C(26)29(2)	31(2)	23(2)	5(1)	5(1)	-7(1)
C(27)19(1)	29(2)	22(1)	2(1)	1(1)	-4(1)
C(28)10(1)	11(1)	14(1)	-4(1)	-1(1)	1(1)
C(29)12(1)	20(2)	17(1)	-3(1)	-1(1)	0(1)
C(30)17(1)	18(2)	16(1)	-2(1)	2(1)	-2(1)
C(31)21(1)	14(2)	15(1)	1(1)	-1(1)	2(1)
C(32)12(1)	17(2)	19(1)	-2(1)	-4(1)	4(1)
N(1) 23(1)	20(1)	24(1)	1(1)	1(1)	0(1)

N(2) 14(1)	17(1)	15(1)	-1(1)	-5(1)	-1(1)
N(6) 16(1)	26(2)	24(1)	-9(1)	0(1)	3(1)
N(7) 10(1)	20(1)	16(1)	2(1)	-4(1)	2(1)
N(4) 11(1)	13(1)	14(1)	-3(1)	0(1)	1(1)
N(3) 18(1)	19(1)	13(1)	-1(1)	1(1)	1(1)
N(5) 10(1)	14(1)	13(1)	-1(1)	-1(1)	0(1)
O(1) 22(1)	32(1)	30(1)	7(1)	4(1)	3(1)
O(2) 27(1)	35(2)	57(2)	1(1)	-13(1)	-1(1)
O(3) 14(1)	15(1)	18(1)	0(1)	-6(1)	0(1)
O(4) 19(1)	19(1)	25(1)	6(1)	-8(1)	-5(1)
O(5) 24(1)	26(1)	18(1)	-5(1)	-4(1)	6(1)
O(6) 14(1)	19(1)	26(1)	-4(1)	4(1)	-5(1)
O(7) 12(1)	17(1)	35(1)	-5(1)	4(1)	-4(1)
O(8) 18(1)	24(1)	20(1)	-6(1)	0(1)	7(1)
O(9) 41(1)	27(1)	18(1)	-3(1)	-1(1)	0(1)
O(10)37(1)	36(2)	32(1)	-20(1)	-2(1)	8(1)
Sm(1)11(1)	15(1)	12(1)	0(1)	-3(1)	0(1)

Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for $Sm(terpy)(NO_3)_2(pyacac)$.

	x	y	z	U(eq)

H(3)	1855	-217	37	37
H(1)	1803	1114	199	37
H(12)	3897	-554	441	33
H(13)	4128	771	292	33
H(6)	4666	2378	1668	31
H(7)	3450	1468	1740	31
H(2)	5562	-702	2302	65
H(5)	4716	-771	1820	65
H(4)	4002	-266	2261	65
H(8)	1711	1343	1163	34
H(9)	2032	104	1396	34
H(11)	1274	-887	754	40
H(10)	305	237	691	40
H(21)	5602	8782	1022	23
H(20)	6124	7779	689	23
H(19)	7568	9665	803	26
H(18)	8334	8453	718	26
H(16)	9334	9008	1422	28
H(17)	7909	9529	1594	28
H(14)	8647	7139	1532	25
H(15)	7860	7756	1941	25
H(25)	6899	6074	2039	18

H(23)	5199	4147	2592	33
H(22)	6739	4548	2504	33
H(24)	6121	3421	2254	33
H(32)	-1856	6474	169	19
H(31)	-3511	5445	563	23
H(30)	-2801	4228	1166	22
H(29)	2495	3375	2105	26
H(28)	1222	1887	2409	30
H(26)	-1030	1568	2121	33
H(27)	-1951	2785	1543	28
H(36)	4125	6694	341	20
H(33)	3730	7784	-315	20
H(34)	1457	8016	-606	20
H(35)	-338	7137	-222	19

Torsion angles [°] for Sm(terpy)$(NO_3)_2$(pyacac).

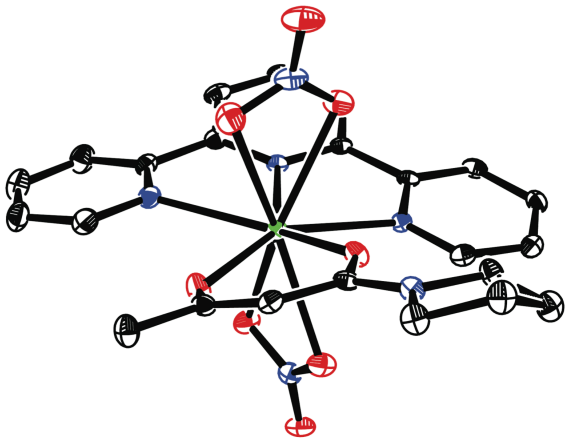
C(8)-C(1)-C(2)-N(1)	-34.7(3)
O(1)-C(3)-C(4)-C(5)	-63.1(4)
N(1)-C(3)-C(4)-C(5)	116.8(3)
C(3)-C(4)-C(5)-O(2)	103.5(4)
C(3)-C(4)-C(5)-C(6)	-76.1(4)
C(2)-C(1)-C(8)-C(7)	40.3(3)

N(1)-C(7)-C(8)-C(1)	-29.8(3)
N(2)-C(10)-C(11)-C(12)	-28.5(3)
C(10)-C(11)-C(12)-C(13)	38.5(3)
C(11)-C(12)-C(13)-N(2)	-33.0(3)
O(3)-C(9)-C(14)-C(15)	7.9(4)
N(2)-C(9)-C(14)-C(15)	-171.2(3)
C(9)-C(14)-C(15)-O(4)	-0.2(5)
C(9)-C(14)-C(15)-C(16)	178.5(3)
N(4)-C(18)-C(19)-C(20)	-2.1(4)
C(28)-C(18)-C(19)-C(20)	176.5(2)
C(18)-C(19)-C(20)-C(21)	0.1(4)
C(19)-C(20)-C(21)-C(22)	0.4(4)
C(20)-C(21)-C(22)-N(4)	1.0(4)
C(20)-C(21)-C(22)-C(23)	-177.9(3)
N(4)-C(22)-C(23)-N(3)	15.3(4)
C(21)-C(22)-C(23)-N(3)	-165.8(3)
N(4)-C(22)-C(23)-C(27)	-162.9(3)
C(21)-C(22)-C(23)-C(27)	16.0(4)
N(3)-C(24)-C(25)-C(26)	-0.3(5)
C(24)-C(25)-C(26)-C(27)	-0.9(5)
C(25)-C(26)-C(27)-C(23)	0.5(5)
N(3)-C(23)-C(27)-C(26)	1.2(5)
C(22)-C(23)-C(27)-C(26)	179.3(3)

N(4)-C(18)-C(28)-N(5)	-4.2(4)
C(19)-C(18)-C(28)-N(5)	177.2(2)
N(4)-C(18)-C(28)-C(32)	174.3(2)
C(19)-C(18)-C(28)-C(32)	-4.3(4)
N(5)-C(29)-C(30)-C(31)	-0.5(4)
C(29)-C(30)-C(31)-C(32)	0.0(4)
C(30)-C(31)-C(32)-C(28)	0.7(4)
N(5)-C(28)-C(32)-C(31)	-0.9(4)
C(18)-C(28)-C(32)-C(31)	-179.4(3)
O(1)-C(3)-N(1)-C(7)	-174.2(3)
C(4)-C(3)-N(1)-C(7)	5.9(5)
O(1)-C(3)-N(1)-C(2)	-5.7(5)
C(4)-C(3)-N(1)-C(2)	174.3(3)
C(8)-C(7)-N(1)-C(3)	177.7(3)
C(8)-C(7)-N(1)-C(2)	8.4(3)
C(1)-C(2)-N(1)-C(3)	-153.6(3)
C(1)-C(2)-N(1)-C(7)	16.5(3)
O(3)-C(9)-N(2)-C(10)	-3.3(4)
C(14)-C(9)-N(2)-C(10)	175.8(3)
O(3)-C(9)-N(2)-C(13)	178.9(3)
C(14)-C(9)-N(2)-C(13)	-1.9(4)
C(11)-C(10)-N(2)-C(9)	-169.9(2)
C(11)-C(10)-N(2)-C(13)	8.2(3)

C(12)-C(13)-N(2)-C(9)	-166.3(3)
C(12)-C(13)-N(2)-C(10)	15.7(3)
C(19)-C(18)-N(4)-C(22)	3.5(4)
C(28)-C(18)-N(4)-C(22)	-175.1(2)
C(19)-C(18)-N(4)-Sm(1)	-166.6(2)
C(28)-C(18)-N(4)-Sm(1)	14.8(3)
C(21)-C(22)-N(4)-C(18)	-3.0(4)
C(23)-C(22)-N(4)-C(18)	176.0(2)
C(21)-C(22)-N(4)-Sm(1)	167.0(2)
C(23)-C(22)-N(4)-Sm(1)	-14.1(3)
C(25)-C(24)-N(3)-C(23)	1.9(4)
C(25)-C(24)-N(3)-Sm(1)	-169.2(2)
C(27)-C(23)-N(3)-C(24)	-2.3(4)
C(22)-C(23)-N(3)-C(24)	179.5(2)
C(27)-C(23)-N(3)-Sm(1)	168.7(2)
C(22)-C(23)-N(3)-Sm(1)	-9.5(3)
C(30)-C(29)-N(5)-C(28)	0.3(4)
C(30)-C(29)-N(5)-Sm(1)	-172.1(2)
C(32)-C(28)-N(5)-C(29)	0.4(4)
C(18)-C(28)-N(5)-C(29)	179.0(2)
C(32)-C(28)-N(5)-Sm(1)	172.74(19)
C(18)-C(28)-N(5)-Sm(1)	-8.7(3)
N(2)-C(9)-O(3)-Sm(1)	178.27(17)

C(14)-C(9)-O(3)-Sm(1)	-0.8(4)
C(14)-C(15)-O(4)-Sm(1)	-14.8(4)
C(16)-C(15)-O(4)-Sm(1)	166.48(19)
O(10)-N(6)-O(5)-Sm(1)	167.6(2)
O(9)-N(6)-O(5)-Sm(1)	-11.7(2)
O(8)-N(7)-O(6)-Sm(1)	-171.9(2)
O(7)-N(7)-O(6)-Sm(1)	6.9(2)
O(8)-N(7)-O(7)-Sm(1)	171.9(2)
O(6)-N(7)-O(7)-Sm(1)	-6.9(2)
O(10)-N(6)-O(9)-Sm(1)	-167.4(2)
O(5)-N(6)-O(9)-Sm(1)	11.9(2)



ORTEP drawing of Eu(terpy)$(NO_3)_2$(pyacac) with 50% probability ellipsoids and H atoms and solvent have been omitted for clarity.

X-ray Crystallographic Data for Eu(terpy)$(NO_3)_2$(pyacac).

Identification code	ky_2_227_n_0m	
Empirical formula	C23 H23 Eu N6 O8	
Formula weight	663.43	
Temperature	107(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 9.452(3) Å	a= 87.037(7)°.
	b = 9.782(3) Å	b= 74.201(7)°.
	c = 13.752(4) Å	g = 87.784(7)°.
Volume	1221.4(6) $Å^3$	
Z	2	
Density (calculated)	1.804 Mg/m^3	
Absorption coefficient	2.629 mm^{-1}	
F(000)	660	
Crystal size	0.100 x 0.050 x 0.050 mm^3	
Theta range for data collection	2.085 to 26.552°.	
Index ranges	-11<=h<=11, -12<=k<=12, -11<=l<=17	
Reflections collected	8252	
Independent reflections	5028 [R(int) = 0.0415]	
Completeness to theta = 25.242°	99.4 %	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5028 / 0 / 344	

Goodness-of-fit on F^2	1.020
Final R indices [I>2sigma(I)]	R1 = 0.0483, wR2 = 0.1078
R indices (all data)	R1 = 0.0700, wR2 = 0.1179
Extinction coefficient	n/a
Largest diff. peak and hole	2.135 and -1.831 e.$Å^{-3}$

Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for Eu(terpy)$(NO_3)_2$(pyacac). U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	5869(8)	1717(7)	6521(5)	24(2)
C(2)	7384(8)	1771(7)	6114(5)	22(2)
C(3)	7972(8)	3004(7)	5715(5)	24(2)
C(4)	7060(7)	4139(6)	5759(5)	18(1)
C(5)	5559(7)	4023(6)	6210(5)	16(1)
C(6)	4542(7)	5231(6)	6338(5)	16(1)
C(7)	5064(8)	6570(6)	6128(5)	21(1)
C(8)	4080(8)	7659(7)	6244(5)	22(2)
C(9)	2616(8)	7414(7)	6564(5)	23(2)
C(10)	2137(7)	6069(7)	6769(5)	18(1)
C(11)	545(7)	5752(7)	7125(5)	18(1)

C(12)	-556(8)	6722(7)	7089(5)	23(2)
C(13)	-2001(8)	6361(8)	7455(5)	27(2)
C(14)	-2348(7)	5050(8)	7840(5)	23(2)
C(15)	-1190(7)	4146(7)	7828(5)	22(2)
C(16)	-1796(7)	-182(7)	8503(6)	25(2)
C(17)	-175(7)	130(6)	8234(5)	17(1)
C(18)	743(7)	-695(7)	8654(5)	19(1)
C(19)	2280(7)	-480(6)	8493(5)	18(1)
C(20)	4612(7)	-1211(7)	8867(6)	22(2)
C(21)	4927(8)	-2359(7)	9571(5)	24(2)
C(22)	3964(7)	-3494(7)	9423(6)	25(2)
C(23)	2548(7)	-2753(7)	9373(5)	21(2)
Eu(1)	2181(1)	2554(1)	7350(1)	14(1)
N(1)	4964(6)	2809(5)	6594(4)	18(1)
N(2)	3088(6)	5005(5)	6662(4)	15(1)
N(3)	217(6)	4462(6)	7478(4)	18(1)
N(4)	1847(6)	3430(6)	9389(4)	22(1)
N(5)	2199(6)	1713(6)	5305(4)	20(1)
N(6)	3062(6)	-1413(5)	8895(4)	17(1)
O(1)	2953(5)	560(4)	8032(3)	19(1)
O(2)	207(5)	1197(5)	7619(4)	22(1)
O(3)	2976(5)	3701(5)	8664(3)	25(1)
O(4)	882(5)	2730(5)	9165(4)	25(1)

O(5)	1683(6)	3811(6)	10242(4)	34(1)
O(6)	2890(5)	988(5)	5840(4)	27(1)
O(7)	2086(7)	1352(5)	4500(4)	37(1)
O(8)	1658(5)	2851(4)	5665(3)	20(1)

Bond lengths [Å] and angles [°] for Eu(terpy)$(NO_3)_2$(pyacac).

C(1)-N(1)	1.333(8)
C(1)-C(2)	1.390(10)
C(1)-H(1)	0.9500
C(2)-C(3)	1.372(10)
C(2)-H(2)	0.9500
C(3)-C(4)	1.373(10)
C(3)-H(3)	0.9500
C(4)-C(5)	1.392(9)
C(4)-H(4)	0.9500
C(5)-N(1)	1.353(8)
C(5)-C(6)	1.481(9)
C(6)-N(2)	1.347(8)
C(6)-C(7)	1.406(9)
C(7)-C(8)	1.373(9)
C(7)-H(7)	0.9500
C(8)-C(9)	1.360(10)

C(8)-H(8)	0.9500
C(9)-C(10)	1.397(9)
C(9)-H(9)	0.9500
C(10)-N(2)	1.336(8)
C(10)-C(11)	1.489(9)
C(11)-N(3)	1.345(8)
C(11)-C(12)	1.390(9)
C(12)-C(13)	1.374(10)
C(12)-H(12)	0.9500
C(13)-C(14)	1.378(10)
C(13)-H(13)	0.9500
C(14)-C(15)	1.378(10)
C(14)-H(14)	0.9500
C(15)-N(3)	1.328(9)
C(15)-H(15)	0.9500
C(16)-C(17)	1.514(9)
C(16)-H(16A)	0.9800
C(16)-H(16B)	0.9800
C(16)-H(16C)	0.9800
C(17)-O(2)	1.306(8)
C(17)-C(18)	1.382(9)
C(18)-C(19)	1.431(9)
C(18)-H(18)	0.9500

C(19)-O(1)	1.267(7)
C(19)-N(6)	1.343(8)
C(20)-N(6)	1.475(8)
C(20)-C(21)	1.519(9)
C(20)-H(20A)	0.9900
C(20)-H(20B)	0.9900
C(21)-C(22)	1.518(9)
C(21)-H(21A)	0.9900
C(21)-H(21B)	0.9900
C(22)-C(23)	1.514(9)
C(22)-H(22A)	0.9900
C(22)-H(22B)	0.9900
C(23)-N(6)	1.474(8)
C(23)-H(23A)	0.9900
C(23)-H(23B)	0.9900
Eu(1)-O(2)	2.268(4)
Eu(1)-O(1)	2.300(4)
Eu(1)-O(3)	2.471(5)
Eu(1)-O(4)	2.474(5)
Eu(1)-O(8)	2.498(5)
Eu(1)-N(3)	2.559(5)
Eu(1)-N(1)	2.569(6)
Eu(1)-O(6)	2.569(5)

Eu(1)-N(2)	2.620(5)
Eu(1)-N(4)	2.906(6)
Eu(1)-N(5)	2.966(6)
N(4)-O(5)	1.216(8)
N(4)-O(4)	1.272(7)
N(4)-O(3)	1.273(7)
N(5)-O(7)	1.212(7)
N(5)-O(8)	1.273(7)
N(5)-O(6)	1.282(7)
N(1)-C(1)-C(2)	123.7(6)
N(1)-C(1)-H(1)	118.2
C(2)-C(1)-H(1)	118.2
C(3)-C(2)-C(1)	118.2(6)
C(3)-C(2)-H(2)	120.9
C(1)-C(2)-H(2)	120.9
C(2)-C(3)-C(4)	119.3(6)
C(2)-C(3)-H(3)	120.4
C(4)-C(3)-H(3)	120.4
C(3)-C(4)-C(5)	119.6(6)
C(3)-C(4)-H(4)	120.2
C(5)-C(4)-H(4)	120.2
N(1)-C(5)-C(4)	121.6(6)
N(1)-C(5)-C(6)	116.5(6)

C(4)-C(5)-C(6)	121.8(6)
N(2)-C(6)-C(7)	120.7(6)
N(2)-C(6)-C(5)	117.7(5)
C(7)-C(6)-C(5)	121.5(6)
C(8)-C(7)-C(6)	119.6(7)
C(8)-C(7)-H(7)	120.2
C(6)-C(7)-H(7)	120.2
C(9)-C(8)-C(7)	119.0(6)
C(9)-C(8)-H(8)	120.5
C(7)-C(8)-H(8)	120.5
C(8)-C(9)-C(10)	119.9(6)
C(8)-C(9)-H(9)	120.1
C(10)-C(9)-H(9)	120.1
N(2)-C(10)-C(9)	121.5(6)
N(2)-C(10)-C(11)	116.7(6)
C(9)-C(10)-C(11)	121.8(6)
N(3)-C(11)-C(12)	121.1(6)
N(3)-C(11)-C(10)	116.5(6)
C(12)-C(11)-C(10)	122.4(6)
C(13)-C(12)-C(11)	119.0(7)
C(13)-C(12)-H(12)	120.5
C(11)-C(12)-H(12)	120.5
C(12)-C(13)-C(14)	120.3(7)

C(12)-C(13)-H(13) 119.9

C(14)-C(13)-H(13) 119.9

C(15)-C(14)-C(13) 116.9(7)

C(15)-C(14)-H(14) 121.6

C(13)-C(14)-H(14) 121.6

N(3)-C(15)-C(14) 124.3(7)

N(3)-C(15)-H(15) 117.9

C(14)-C(15)-H(15) 117.9

C(17)-C(16)-H(16A) 109.5

C(17)-C(16)-H(16B) 109.5

H(16A)-C(16)-H(16B) 109.5

C(17)-C(16)-H(16C) 109.5

H(16A)-C(16)-H(16C) 109.5

H(16B)-C(16)-H(16C) 109.5

O(2)-C(17)-C(18) 126.4(6)

O(2)-C(17)-C(16) 114.8(6)

C(18)-C(17)-C(16) 118.8(6)

C(17)-C(18)-C(19) 124.4(6)

C(17)-C(18)-H(18) 117.8

C(19)-C(18)-H(18) 117.8

O(1)-C(19)-N(6) 117.1(6)

O(1)-C(19)-C(18) 124.7(6)

N(6)-C(19)-C(18) 118.1(6)

N(6)-C(20)-C(21) 103.2(5)

N(6)-C(20)-H(20A) 111.1

C(21)-C(20)-H(20A) 111.1

N(6)-C(20)-H(20B) 111.1

C(21)-C(20)-H(20B) 111.1

H(20A)-C(20)-H(20B) 109.1

C(22)-C(21)-C(20) 102.7(5)

C(22)-C(21)-H(21A) 111.2

C(20)-C(21)-H(21A) 111.2

C(22)-C(21)-H(21B) 111.2

C(20)-C(21)-H(21B) 111.2

H(21A)-C(21)-H(21B) 109.1

C(23)-C(22)-C(21) 103.8(5)

C(23)-C(22)-H(22A) 111.0

C(21)-C(22)-H(22A) 111.0

C(23)-C(22)-H(22B) 111.0

C(21)-C(22)-H(22B) 111.0

H(22A)-C(22)-H(22B) 109.0

N(6)-C(23)-C(22) 102.7(5)

N(6)-C(23)-H(23A) 111.2

C(22)-C(23)-H(23A) 111.2

N(6)-C(23)-H(23B) 111.2

C(22)-C(23)-H(23B) 111.2

H(23A)-C(23)-H(23B)109.1

O(2)-Eu(1)-O(1) 77.00(16)

O(2)-Eu(1)-O(3) 125.94(16)

O(1)-Eu(1)-O(3) 85.46(16)

O(2)-Eu(1)-O(4) 74.76(16)

O(1)-Eu(1)-O(4) 78.42(16)

O(3)-Eu(1)-O(4) 51.59(15)

O(2)-Eu(1)-O(8) 80.08(16)

O(1)-Eu(1)-O(8) 126.19(15)

O(3)-Eu(1)-O(8) 145.22(15)

O(4)-Eu(1)-O(8) 139.29(15)

O(2)-Eu(1)-N(3) 82.50(17)

O(1)-Eu(1)-N(3) 148.25(17)

O(3)-Eu(1)-N(3) 87.28(17)

O(4)-Eu(1)-N(3) 72.91(17)

O(8)-Eu(1)-N(3) 72.50(16)

O(2)-Eu(1)-N(1) 147.38(17)

O(1)-Eu(1)-N(1) 81.74(16)

O(3)-Eu(1)-N(1) 75.92(17)

O(4)-Eu(1)-N(1) 124.70(16)

O(8)-Eu(1)-N(1) 93.21(16)

N(3)-Eu(1)-N(1) 126.11(17)

O(2)-Eu(1)-O(6) 76.84(17)

O(1)-Eu(1)-O(6)	76.98(16)
O(3)-Eu(1)-O(6)	147.32(16)
O(4)-Eu(1)-O(6)	145.82(16)
O(8)-Eu(1)-O(6)	50.51(15)
N(3)-Eu(1)-O(6)	121.58(16)
N(1)-Eu(1)-O(6)	74.44(17)
O(2)-Eu(1)-N(2)	141.83(16)
O(1)-Eu(1)-N(2)	141.17(16)
O(3)-Eu(1)-N(2)	70.79(16)
O(4)-Eu(1)-N(2)	107.13(16)
O(8)-Eu(1)-N(2)	74.81(15)
N(3)-Eu(1)-N(2)	62.86(17)
N(1)-Eu(1)-N(2)	63.25(16)
O(6)-Eu(1)-N(2)	106.93(16)
O(2)-Eu(1)-N(4)	100.39(17)
O(1)-Eu(1)-N(4)	81.32(16)
O(3)-Eu(1)-N(4)	25.80(15)
O(4)-Eu(1)-N(4)	25.79(15)
O(8)-Eu(1)-N(4)	151.04(16)
N(3)-Eu(1)-N(4)	78.83(17)
N(1)-Eu(1)-N(4)	100.52(17)
O(6)-Eu(1)-N(4)	158.20(16)
N(2)-Eu(1)-N(4)	88.72(16)

O(2)-Eu(1)-N(5)	75.49(16)
O(1)-Eu(1)-N(5)	101.45(16)
O(3)-Eu(1)-N(5)	158.57(15)
O(4)-Eu(1)-N(5)	149.45(15)
O(8)-Eu(1)-N(5)	25.12(14)
N(3)-Eu(1)-N(5)	96.49(17)
N(1)-Eu(1)-N(5)	84.95(17)
O(6)-Eu(1)-N(5)	25.50(15)
N(2)-Eu(1)-N(5)	92.13(15)
N(4)-Eu(1)-N(5)	174.23(16)
C(1)-N(1)-C(5)	117.5(6)
C(1)-N(1)-Eu(1)	120.3(4)
C(5)-N(1)-Eu(1)	122.0(4)
C(10)-N(2)-C(6)	119.4(5)
C(10)-N(2)-Eu(1)	120.4(4)
C(6)-N(2)-Eu(1)	119.5(4)
C(15)-N(3)-C(11)	118.4(6)
C(15)-N(3)-Eu(1)	118.8(4)
C(11)-N(3)-Eu(1)	122.5(4)
O(5)-N(4)-O(4)	121.6(6)
O(5)-N(4)-O(3)	122.9(6)
O(4)-N(4)-O(3)	115.4(5)
O(5)-N(4)-Eu(1)	178.7(5)

O(4)-N(4)-Eu(1)	57.8(3)
O(3)-N(4)-Eu(1)	57.6(3)
O(7)-N(5)-O(8)	122.0(6)
O(7)-N(5)-O(6)	122.3(6)
O(8)-N(5)-O(6)	115.7(5)
O(7)-N(5)-Eu(1)	174.7(5)
O(8)-N(5)-Eu(1)	56.4(3)
O(6)-N(5)-Eu(1)	59.6(3)
C(19)-N(6)-C(23)	126.3(5)
C(19)-N(6)-C(20)	122.2(5)
C(23)-N(6)-C(20)	111.5(5)
C(19)-O(1)-Eu(1)	132.9(4)
C(17)-O(2)-Eu(1)	130.5(4)
N(4)-O(3)-Eu(1)	96.6(4)
N(4)-O(4)-Eu(1)	96.4(4)
N(5)-O(6)-Eu(1)	94.9(4)
N(5)-O(8)-Eu(1)	98.5(4)

Anisotropic displacement parameters ($Å^2 x\ 10^3$) for Eu(terpy)$(NO_3)_2$(pyacac). The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2\ a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}

C(1)	31(4)	17(3)	24(4)	3(3)	-8(3)	6(3)
C(2)	26(4)	18(3)	20(4)	-3(3)	-4(3)	9(3)
C(3)	19(3)	35(4)	19(4)	-5(3)	-2(3)	-3(3)
C(4)	23(3)	16(3)	16(3)	3(3)	-7(3)	-3(3)
C(5)	25(3)	14(3)	11(3)	-4(2)	-6(3)	-2(3)
C(6)	22(3)	16(3)	10(3)	-3(2)	-5(3)	3(3)
C(7)	33(4)	13(3)	17(3)	-2(3)	-10(3)	4(3)
C(8)	34(4)	15(3)	17(3)	-2(3)	-8(3)	-2(3)
C(9)	34(4)	15(3)	22(4)	-5(3)	-12(3)	11(3)
C(10)	20(3)	23(3)	10(3)	-2(3)	-2(3)	9(3)
C(11)	26(4)	22(3)	12(3)	-7(3)	-12(3)	4(3)
C(12)	28(4)	28(4)	16(3)	-8(3)	-10(3)	10(3)
C(13)	33(4)	31(4)	23(4)	-11(3)	-17(3)	14(3)
C(14)	17(3)	41(4)	13(3)	-14(3)	-5(3)	2(3)
C(15)	24(4)	28(4)	15(3)	-4(3)	-8(3)	4(3)
C(16)	21(4)	22(4)	31(4)	0(3)	-7(3)	-1(3)
C(17)	18(3)	14(3)	18(3)	-3(3)	-3(3)	1(2)
C(18)	14(3)	25(4)	13(3)	0(3)	2(3)	-3(3)
C(19)	28(4)	10(3)	14(3)	-2(3)	-2(3)	0(3)
C(20)	19(3)	25(4)	24(4)	0(3)	-6(3)	0(3)
C(21)	24(4)	24(4)	25(4)	4(3)	-10(3)	2(3)
C(22)	20(4)	17(3)	36(4)	6(3)	-8(3)	0(3)

C(23)	22(3)	16(3)	24(4)	5(3)	-8(3)	1(3)
Eu(1)	16(1)	14(1)	14(1)	2(1)	-6(1)	0(1)
N(1)	24(3)	14(3)	18(3)	0(2)	-9(2)	4(2)
N(2)	24(3)	12(3)	14(3)	-3(2)	-11(2)	4(2)
N(3)	19(3)	24(3)	12(3)	0(2)	-7(2)	5(2)
N(4)	31(3)	21(3)	16(3)	2(2)	-11(3)	-1(3)
N(5)	26(3)	16(3)	17(3)	4(2)	-7(3)	-6(2)
N(6)	15(3)	15(3)	22(3)	1(2)	-8(2)	-1(2)
O(1)	20(2)	16(2)	21(2)	6(2)	-8(2)	-1(2)
O(2)	18(2)	20(2)	27(3)	4(2)	-6(2)	-1(2)
O(3)	26(3)	36(3)	14(2)	1(2)	-6(2)	-12(2)
O(4)	23(3)	34(3)	19(3)	5(2)	-8(2)	-7(2)
O(5)	47(3)	41(3)	14(3)	-3(2)	-8(2)	-8(3)
O(6)	32(3)	22(3)	26(3)	-3(2)	-8(2)	6(2)
O(7)	69(4)	23(3)	29(3)	-5(2)	-27(3)	-3(3)
O(8)	27(3)	16(2)	19(2)	2(2)	-9(2)	4(2)

Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for Eu(terpy)$(NO_3)_2$(pyacac).

	x	y	z	U(eq)
H(1)	5456	853	6762	29

H(2)	7994	976	6111	26
H(3)	8999	3071	5412	29
H(4)	7451	4999	5482	22
H(7)	6091	6720	5908	25
H(8)	4417	8569	6103	26
H(9)	1920	8155	6648	28
H(12)	-313	7621	6815	28
H(13)	-2764	7017	7442	33
H(14)	-3340	4783	8102	28
H(15)	-1412	3237	8087	26
H(16A)	-2366	557	8898	37
H(16B)	-1969	-1048	8903	37
H(16C)	-2101	-258	7882	37
H(18)	325	-1455	9079	23
H(20A)	4739	-303	9114	27
H(20B)	5263	-1292	8173	27
H(21A)	5980	-2644	9375	29
H(21B)	4648	-2082	10282	29
H(22A)	4422	-3964	8789	30
H(22B)	3787	-4177	9998	30
H(23A)	2041	-3241	8957	25
H(23B)	1873	-2649	10057	25

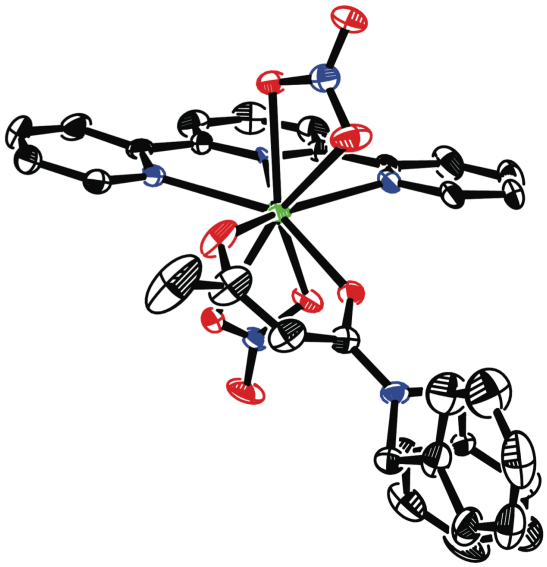
Torsion angles [°] for Eu(terpy)$(NO_3)_2$(pyacac).

N(1)-C(1)-C(2)-C(3)	-3.5(11)
C(1)-C(2)-C(3)-C(4)	1.9(10)
C(2)-C(3)-C(4)-C(5)	0.4(10)
C(3)-C(4)-C(5)-N(1)	-1.3(10)
C(3)-C(4)-C(5)-C(6)	175.9(6)
N(1)-C(5)-C(6)-N(2)	-11.1(8)
C(4)-C(5)-C(6)-N(2)	171.6(6)
N(1)-C(5)-C(6)-C(7)	169.1(6)
C(4)-C(5)-C(6)-C(7)	-8.2(10)
N(2)-C(6)-C(7)-C(8)	-0.7(10)
C(5)-C(6)-C(7)-C(8)	179.1(6)
C(6)-C(7)-C(8)-C(9)	0.2(10)
C(7)-C(8)-C(9)-C(10)	0.0(10)
C(8)-C(9)-C(10)-N(2)	0.3(10)
C(8)-C(9)-C(10)-C(11)	179.7(6)
N(2)-C(10)-C(11)-N(3)	11.5(8)
C(9)-C(10)-C(11)-N(3)	-167.9(6)
N(2)-C(10)-C(11)-C(12)	-167.7(6)
C(9)-C(10)-C(11)-C(12)	12.9(10)
N(3)-C(11)-C(12)-C(13)	2.4(10)
C(10)-C(11)-C(12)-C(13)	-178.5(6)

C(11)-C(12)-C(13)-C(14)	-0.8(10)
C(12)-C(13)-C(14)-C(15)	-0.6(10)
C(13)-C(14)-C(15)-N(3)	0.5(10)
O(2)-C(17)-C(18)-C(19)	1.5(11)
C(16)-C(17)-C(18)-C(19)	-177.5(6)
C(17)-C(18)-C(19)-O(1)	7.4(11)
C(17)-C(18)-C(19)-N(6)	-175.7(6)
N(6)-C(20)-C(21)-C(22)	32.3(7)
C(20)-C(21)-C(22)-C(23)	-40.7(7)
C(21)-C(22)-C(23)-N(6)	32.5(7)
C(2)-C(1)-N(1)-C(5)	2.7(10)
C(2)-C(1)-N(1)-Eu(1)	179.4(5)
C(4)-C(5)-N(1)-C(1)	-0.2(9)
C(6)-C(5)-N(1)-C(1)	-177.5(6)
C(4)-C(5)-N(1)-Eu(1)	-176.9(5)
C(6)-C(5)-N(1)-Eu(1)	5.8(7)
C(9)-C(10)-N(2)-C(6)	-0.8(9)
C(11)-C(10)-N(2)-C(6)	179.8(6)
C(9)-C(10)-N(2)-Eu(1)	169.2(5)
C(11)-C(10)-N(2)-Eu(1)	-10.2(7)
C(7)-C(6)-N(2)-C(10)	1.0(9)
C(5)-C(6)-N(2)-C(10)	-178.8(6)
C(7)-C(6)-N(2)-Eu(1)	-169.1(5)

C(5)-C(6)-N(2)-Eu(1)	11.1(7)
C(14)-C(15)-N(3)-C(11)	1.1(10)
C(14)-C(15)-N(3)-Eu(1)	-173.4(5)
C(12)-C(11)-N(3)-C(15)	-2.5(9)
C(10)-C(11)-N(3)-C(15)	178.3(6)
C(12)-C(11)-N(3)-Eu(1)	171.7(5)
C(10)-C(11)-N(3)-Eu(1)	-7.5(7)
O(1)-C(19)-N(6)-C(23)	-173.7(6)
C(18)-C(19)-N(6)-C(23)	9.2(10)
O(1)-C(19)-N(6)-C(20)	4.0(9)
C(18)-C(19)-N(6)-C(20)	-173.2(6)
C(22)-C(23)-N(6)-C(19)	165.5(6)
C(22)-C(23)-N(6)-C(20)	-12.4(8)
C(21)-C(20)-N(6)-C(19)	169.4(6)
C(21)-C(20)-N(6)-C(23)	-12.6(7)
N(6)-C(19)-O(1)-Eu(1)	-172.7(4)
C(18)-C(19)-O(1)-Eu(1)	4.3(10)
C(18)-C(17)-O(2)-Eu(1)	-21.4(10)
C(16)-C(17)-O(2)-Eu(1)	157.6(4)
O(5)-N(4)-O(3)-Eu(1)	-178.7(6)
O(4)-N(4)-O(3)-Eu(1)	1.0(6)
O(5)-N(4)-O(4)-Eu(1)	178.7(5)
O(3)-N(4)-O(4)-Eu(1)	-1.0(6)

O(7)-N(5)-O(6)-Eu(1)	-174.3(5)
O(8)-N(5)-O(6)-Eu(1)	6.9(5)
O(7)-N(5)-O(8)-Eu(1)	174.0(5)
O(6)-N(5)-O(8)-Eu(1)	-7.1(5)



ORTEP drawing of Dy(terpy)$(NO_3)_2$(dbacac) with 50% probability ellipsoids and H atoms and solvent have been omitted for clarity.

X-ray Crystallographic Data for Dy(terpy)$(NO_3)_2$(dbacac).

Identification code	ky_2_154_0m	
Empirical formula	C35 H33 Dy N6 O8.50	
Formula weight	836.17	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1/n$	
Unit cell dimensions	a = 19.2296(9) Å	a= 90°.

	b = 9.2999(4) Å b= 112.085(2)°.
	c = 21.3594(9) Å g = 90°.
Volume	3539.5(3) $Å^3$
Z	4
Density (calculated)	1.569 Mg/m^3
Absorption coefficient	2.172 mm^{-1}
F(000)	1676
Crystal size	0.250 x 0.100 x 0.050 mm^3
Theta range for data collection	1.217 to 32.428°.
Index ranges	-22<=h<=29, -14<=k<=9, -32<=l<=32
Reflections collected	34853
Independent reflections	12568 [R(int) = 0.0468]
Completeness to theta = 25.242°	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7464 and 0.5470
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	12568 / 10 / 454
Goodness-of-fit on F^2	1.193
Final R indices [I>2sigma(I)]	R1 = 0.0686, wR2 = 0.1227
R indices (all data)	R1 = 0.1224, wR2 = 0.1361
Extinction coefficient	n/a
Largest diff. peak and hole	2.270 and -1.180 $e.Å^{-3}$

Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for Dy(terpy)$(NO_3)_2$(dbacac). U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	7335(3)	-746(6)	3784(3)	29(1)
C(2)	7297(4)	-1913(7)	3360(3)	37(2)
C(3)	7744(4)	-1880(7)	2990(3)	40(2)
C(4)	8213(4)	-710(7)	3046(3)	34(1)
C(5)	8221(3)	399(6)	3474(2)	24(1)
C(6)	8694(3)	1704(6)	3541(2)	22(1)
C(7)	9230(3)	1774(7)	3246(3)	31(1)
C(8)	9639(4)	3023(8)	3315(3)	39(2)
C(9)	9519(3)	4154(7)	3673(3)	32(1)
C(10)	8985(3)	4017(6)	3966(2)	22(1)
C(11)	8827(3)	5210(6)	4355(3)	23(1)
C(12)	9222(4)	6488(7)	4478(4)	39(2)
C(13)	9045(4)	7551(8)	4853(4)	50(2)
C(14)	8479(4)	7301(6)	5078(3)	42(2)
C(15)	8104(4)	6023(6)	4930(3)	33(1)
C(16)	7503(3)	2805(6)	6012(3)	23(1)
C(17)	6963(3)	1685(7)	5852(3)	34(1)

C(18)	6698(4)	942(9)	5251(3)	43(2)
C(19)	6097(5)	-156(13)	5135(5)	88(4)
C(20)	7647(3)	2813(6)	7223(3)	29(1)
C(21)	7026(4)	3541(7)	7387(3)	35(1)
C(22)	6386(4)	4060(9)	6887(4)	49(2)
C(23)	5801(5)	4647(10)	7038(5)	63(2)
C(24)	7098(5)	3645(7)	8052(3)	45(2)
C(25)	6486(6)	4263(8)	8194(4)	54(2)
C(26)	5864(6)	4726(9)	7684(5)	61(2)
C(27)	8182(3)	4758(6)	6761(3)	25(1)
C(28)	8989(3)	4568(6)	7219(3)	26(1)
C(29)	9424(3)	3496(7)	7097(3)	31(1)
C(30)	10164(4)	3312(8)	7524(4)	49(2)
C(31)	10483(5)	4224(10)	8072(5)	68(3)
C(32)	10067(5)	5322(9)	8176(4)	71(3)
C(33)	9322(5)	5496(8)	7754(3)	47(2)
C(34)	5351(15)	5290(30)	4883(15)	130(10)
C(35)	4779(16)	6030(30)	5095(16)	127(10)
C(36)	5170(20)	7030(50)	5660(20)	280(30)
C(37)	5970(20)	6690(50)	5813(18)	208(18)
Dy(1)	7772(1)	2522(1)	4589(1)	20(1)
N(1)	7778(2)	405(5)	3840(2)	22(1)
N(2)	8590(2)	2801(4)	3907(2)	16(1)

N(3)	8271(3)	4981(5)	4581(2)	26(1)
N(4)	7755(3)	3415(5)	6633(2)	24(1)
N(5)	9175(3)	1398(5)	5572(2)	24(1)
N(6)	6543(3)	4121(5)	3626(2)	27(1)
O(1)	9753(3)	926(5)	5991(2)	42(1)
O(2)	8583(3)	645(4)	5320(2)	32(1)
O(3)	9121(2)	2693(4)	5368(2)	28(1)
O(4)	6685(2)	4209(6)	4255(2)	41(1)
O(5)	6922(2)	3186(5)	3449(2)	26(1)
O(6)	6075(2)	4896(5)	3220(2)	33(1)
O(7)	7746(2)	3305(4)	5582(2)	22(1)
O(8)	6929(2)	1096(5)	4762(2)	38(1)
O(9)	6072(14)	5890(30)	5271(15)	197(11)

Bond lengths [Å] and angles [°] for Dy(terpy)$(NO_3)_2$(dbacac).

C(1)-N(1)	1.345(7)
C(1)-C(2)	1.397(9)
C(1)-H(1)	0.9500
C(2)-C(3)	1.370(10)
C(2)-H(2)	0.9500
C(3)-C(4)	1.389(9)
C(3)-H(3)	0.9500

C(4)-C(5)	1.375(8)
C(4)-H(4)	0.9500
C(5)-N(1)	1.356(7)
C(5)-C(6)	1.491(8)
C(6)-N(2)	1.345(6)
C(6)-C(7)	1.397(8)
C(7)-C(8)	1.380(9)
C(7)-H(7)	0.9500
C(8)-C(9)	1.369(9)
C(8)-H(8)	0.9500
C(9)-C(10)	1.395(8)
C(9)-H(9)	0.9500
C(10)-N(2)	1.342(6)
C(10)-C(11)	1.485(8)
C(11)-N(3)	1.345(7)
C(11)-C(12)	1.382(8)
C(12)-C(13)	1.392(10)
C(12)-H(12)	0.9500
C(13)-C(14)	1.367(11)
C(13)-H(13)	0.9500
C(14)-C(15)	1.364(9)
C(14)-H(14)	0.9500
C(15)-N(3)	1.333(7)

C(15)-H(15)	0.9500
C(16)-O(7)	1.265(6)
C(16)-N(4)	1.355(6)
C(16)-C(17)	1.419(8)
C(17)-C(18)	1.375(9)
C(17)-H(17)	0.9500
C(18)-O(8)	1.288(7)
C(18)-C(19)	1.492(10)
C(19)-H(19A)	0.9800
C(19)-H(19B)	0.9800
C(19)-H(19C)	0.9800
C(20)-N(4)	1.462(7)
C(20)-C(21)	1.524(9)
C(20)-H(20A)	0.9900
C(20)-H(20B)	0.9900
C(21)-C(24)	1.377(8)
C(21)-C(22)	1.378(10)
C(22)-C(23)	1.392(10)
C(22)-H(22)	0.9500
C(23)-C(26)	1.343(12)
C(23)-H(23)	0.9500
C(24)-C(25)	1.442(11)
C(24)-H(24)	0.9500

C(25)-C(26)	1.349(12)
C(25)-H(25)	0.9500
C(26)-H(26)	0.9500
C(27)-N(4)	1.463(7)
C(27)-C(28)	1.502(8)
C(27)-H(27A)	0.9900
C(27)-H(27B)	0.9900
C(28)-C(33)	1.382(8)
C(28)-C(29)	1.387(8)
C(29)-C(30)	1.383(9)
C(29)-H(29)	0.9500
C(30)-C(31)	1.387(12)
C(30)-H(30)	0.9500
C(31)-C(32)	1.367(13)
C(31)-H(31)	0.9500
C(32)-C(33)	1.386(11)
C(32)-H(32)	0.9500
C(33)-H(33)	0.9500
C(34)-C(35)#1	1.25(4)
C(34)-O(9)	1.435(10)
C(34)-C(35)	1.506(10)
C(34)-C(34)#1	1.69(6)
C(35)-C(34)#1	1.25(4)

C(35)-C(36)	1.487(10)
C(36)-C(37)	1.495(10)
C(37)-O(9)	1.449(10)
Dy(1)-O(8)	2.229(4)
Dy(1)-O(7)	2.260(3)
Dy(1)-O(5)	2.447(4)
Dy(1)-O(2)	2.467(4)
Dy(1)-N(3)	2.482(5)
Dy(1)-O(4)	2.492(4)
Dy(1)-O(3)	2.506(4)
Dy(1)-N(2)	2.528(4)
Dy(1)-N(1)	2.540(4)
Dy(1)-N(6)	2.893(5)
Dy(1)-N(5)	2.920(5)
N(5)-O(1)	1.216(6)
N(5)-O(2)	1.271(6)
N(5)-O(3)	1.273(6)
N(6)-O(6)	1.223(6)
N(6)-O(4)	1.267(6)
N(6)-O(5)	1.280(6)
N(1)-C(1)-C(2)	123.6(6)
N(1)-C(1)-H(1)	118.2
C(2)-C(1)-H(1)	118.2

C(3)-C(2)-C(1)	117.7(6)
C(3)-C(2)-H(2)	121.2
C(1)-C(2)-H(2)	121.2
C(2)-C(3)-C(4)	119.8(6)
C(2)-C(3)-H(3)	120.1
C(4)-C(3)-H(3)	120.1
C(5)-C(4)-C(3)	119.2(6)
C(5)-C(4)-H(4)	120.4
C(3)-C(4)-H(4)	120.4
N(1)-C(5)-C(4)	122.3(6)
N(1)-C(5)-C(6)	115.7(5)
C(4)-C(5)-C(6)	121.9(5)
N(2)-C(6)-C(7)	121.5(5)
N(2)-C(6)-C(5)	117.1(5)
C(7)-C(6)-C(5)	121.4(5)
C(8)-C(7)-C(6)	118.6(6)
C(8)-C(7)-H(7)	120.7
C(6)-C(7)-H(7)	120.7
C(9)-C(8)-C(7)	119.9(6)
C(9)-C(8)-H(8)	120.1
C(7)-C(8)-H(8)	120.1
C(8)-C(9)-C(10)	119.1(6)
C(8)-C(9)-H(9)	120.4

C(10)-C(9)-H(9)	120.4
N(2)-C(10)-C(9)	121.4(5)
N(2)-C(10)-C(11)	117.0(5)
C(9)-C(10)-C(11)	121.6(5)
N(3)-C(11)-C(12)	121.5(6)
N(3)-C(11)-C(10)	116.2(5)
C(12)-C(11)-C(10)	122.3(5)
C(11)-C(12)-C(13)	119.0(7)
C(11)-C(12)-H(12)	120.5
C(13)-C(12)-H(12)	120.5
C(14)-C(13)-C(12)	118.7(7)
C(14)-C(13)-H(13)	120.6
C(12)-C(13)-H(13)	120.6
C(15)-C(14)-C(13)	119.2(7)
C(15)-C(14)-H(14)	120.4
C(13)-C(14)-H(14)	120.4
N(3)-C(15)-C(14)	123.1(7)
N(3)-C(15)-H(15)	118.4
C(14)-C(15)-H(15)	118.4
O(7)-C(16)-N(4)	117.6(5)
O(7)-C(16)-C(17)	122.2(5)
N(4)-C(16)-C(17)	120.2(5)
C(18)-C(17)-C(16)	125.0(5)

C(18)-C(17)-H(17) 117.5

C(16)-C(17)-H(17) 117.5

O(8)-C(18)-C(17) 125.6(6)

O(8)-C(18)-C(19) 115.0(6)

C(17)-C(18)-C(19) 119.4(6)

C(18)-C(19)-H(19A) 109.5

C(18)-C(19)-H(19B) 109.5

H(19A)-C(19)-H(19B) 109.5

C(18)-C(19)-H(19C) 109.5

H(19A)-C(19)-H(19C) 109.5

H(19B)-C(19)-H(19C) 109.5

N(4)-C(20)-C(21) 113.9(5)

N(4)-C(20)-H(20A) 108.8

C(21)-C(20)-H(20A) 108.8

N(4)-C(20)-H(20B) 108.8

C(21)-C(20)-H(20B) 108.8

H(20A)-C(20)-H(20B) 107.7

C(24)-C(21)-C(22) 119.3(7)

C(24)-C(21)-C(20) 119.0(7)

C(22)-C(21)-C(20) 121.7(5)

C(21)-C(22)-C(23) 121.4(7)

C(21)-C(22)-H(22) 119.3

C(23)-C(22)-H(22) 119.3

C(26)-C(23)-C(22) 119.5(9)

C(26)-C(23)-H(23) 120.3

C(22)-C(23)-H(23) 120.3

C(21)-C(24)-C(25) 118.1(8)

C(21)-C(24)-H(24) 121.0

C(25)-C(24)-H(24) 121.0

C(26)-C(25)-C(24) 120.3(7)

C(26)-C(25)-H(25) 119.8

C(24)-C(25)-H(25) 119.8

C(23)-C(26)-C(25) 121.4(8)

C(23)-C(26)-H(26) 119.3

C(25)-C(26)-H(26) 119.3

N(4)-C(27)-C(28) 113.1(5)

N(4)-C(27)-H(27A) 109.0

C(28)-C(27)-H(27A) 109.0

N(4)-C(27)-H(27B) 109.0

C(28)-C(27)-H(27B) 109.0

H(27A)-C(27)-H(27B)107.8

C(33)-C(28)-C(29) 118.7(6)

C(33)-C(28)-C(27) 120.5(6)

C(29)-C(28)-C(27) 120.7(5)

C(30)-C(29)-C(28) 120.6(6)

C(30)-C(29)-H(29) 119.7

C(28)-C(29)-H(29) 119.7

C(29)-C(30)-C(31) 120.0(8)

C(29)-C(30)-H(30) 120.0

C(31)-C(30)-H(30) 120.0

C(32)-C(31)-C(30) 119.6(7)

C(32)-C(31)-H(31) 120.2

C(30)-C(31)-H(31) 120.2

C(31)-C(32)-C(33) 120.5(8)

C(31)-C(32)-H(32) 119.8

C(33)-C(32)-H(32) 119.8

C(28)-C(33)-C(32) 120.5(8)

C(28)-C(33)-H(33) 119.7

C(32)-C(33)-H(33) 119.7

C(35)#1-C(34)-O(9) 122(3)

C(35)#1-C(34)-C(35) 105(3)

O(9)-C(34)-C(35) 108(2)

C(35)#1-C(34)-C(34)#159(2)

O(9)-C(34)-C(34)#1 131(3)

C(35)-C(34)-C(34)#1 45.7(18)

C(34)#1-C(35)-C(36) 129(4)

C(34)#1-C(35)-C(34) 75(3)

C(36)-C(35)-C(34) 109(3)

C(35)-C(36)-C(37) 102(3)

O(9)-C(37)-C(36)	112(3)
O(8)-Dy(1)-O(7)	76.28(14)
O(8)-Dy(1)-O(5)	93.45(15)
O(7)-Dy(1)-O(5)	127.64(13)
O(8)-Dy(1)-O(2)	78.50(17)
O(7)-Dy(1)-O(2)	82.32(14)
O(5)-Dy(1)-O(2)	146.58(13)
O(8)-Dy(1)-N(3)	148.87(17)
O(7)-Dy(1)-N(3)	81.62(14)
O(5)-Dy(1)-N(3)	82.88(14)
O(2)-Dy(1)-N(3)	120.12(15)
O(8)-Dy(1)-O(4)	80.74(18)
O(7)-Dy(1)-O(4)	75.81(13)
O(5)-Dy(1)-O(4)	51.83(13)
O(2)-Dy(1)-O(4)	152.80(15)
N(3)-Dy(1)-O(4)	72.70(16)
O(8)-Dy(1)-O(3)	124.31(15)
O(7)-Dy(1)-O(3)	74.89(13)
O(5)-Dy(1)-O(3)	141.40(13)
O(2)-Dy(1)-O(3)	51.26(13)
N(3)-Dy(1)-O(3)	68.87(14)
O(4)-Dy(1)-O(3)	134.23(15)
O(8)-Dy(1)-N(2)	143.64(14)

O(7)-Dy(1)-N(2)	138.18(13)
O(5)-Dy(1)-N(2)	74.23(13)
O(2)-Dy(1)-N(2)	93.08(14)
N(3)-Dy(1)-N(2)	64.88(14)
O(4)-Dy(1)-N(2)	113.99(13)
O(3)-Dy(1)-N(2)	70.22(13)
O(8)-Dy(1)-N(1)	79.57(15)
O(7)-Dy(1)-N(1)	147.96(14)
O(5)-Dy(1)-N(1)	74.24(13)
O(2)-Dy(1)-N(1)	72.42(13)
N(3)-Dy(1)-N(1)	128.06(14)
O(4)-Dy(1)-N(1)	120.62(14)
O(3)-Dy(1)-N(1)	102.59(14)
N(2)-Dy(1)-N(1)	64.23(13)
O(8)-Dy(1)-N(6)	88.48(16)
O(7)-Dy(1)-N(6)	101.63(13)
O(5)-Dy(1)-N(6)	26.07(13)
O(2)-Dy(1)-N(6)	165.17(14)
N(3)-Dy(1)-N(6)	74.69(14)
O(4)-Dy(1)-N(6)	25.88(13)
O(3)-Dy(1)-N(6)	143.53(13)
N(2)-Dy(1)-N(6)	93.26(13)
N(1)-Dy(1)-N(6)	98.45(14)

O(8)-Dy(1)-N(5)	101.57(16)
O(7)-Dy(1)-N(5)	77.33(13)
O(5)-Dy(1)-N(5)	153.73(12)
O(2)-Dy(1)-N(5)	25.56(13)
N(3)-Dy(1)-N(5)	94.57(15)
O(4)-Dy(1)-N(5)	151.64(13)
O(3)-Dy(1)-N(5)	25.70(12)
N(2)-Dy(1)-N(5)	81.00(12)
N(1)-Dy(1)-N(5)	87.32(13)
N(6)-Dy(1)-N(5)	169.22(13)
C(1)-N(1)-C(5)	117.4(5)
C(1)-N(1)-Dy(1)	121.4(4)
C(5)-N(1)-Dy(1)	121.3(4)
C(10)-N(2)-C(6)	119.4(4)
C(10)-N(2)-Dy(1)	119.1(3)
C(6)-N(2)-Dy(1)	121.2(3)
C(15)-N(3)-C(11)	118.4(5)
C(15)-N(3)-Dy(1)	119.4(4)
C(11)-N(3)-Dy(1)	120.6(4)
C(16)-N(4)-C(20)	124.7(5)
C(16)-N(4)-C(27)	120.6(4)
C(20)-N(4)-C(27)	114.7(4)
O(1)-N(5)-O(2)	122.6(5)

O(1)-N(5)-O(3)	121.9(5)
O(2)-N(5)-O(3)	115.5(4)
O(1)-N(5)-Dy(1)	178.8(4)
O(2)-N(5)-Dy(1)	56.9(2)
O(3)-N(5)-Dy(1)	58.7(2)
O(6)-N(6)-O(4)	121.5(5)
O(6)-N(6)-O(5)	122.6(5)
O(4)-N(6)-O(5)	115.9(5)
O(6)-N(6)-Dy(1)	173.7(4)
O(4)-N(6)-Dy(1)	59.1(3)
O(5)-N(6)-Dy(1)	57.1(2)
N(5)-O(2)-Dy(1)	97.6(3)
N(5)-O(3)-Dy(1)	95.6(3)
N(6)-O(4)-Dy(1)	95.0(3)
N(6)-O(5)-Dy(1)	96.8(3)
C(16)-O(7)-Dy(1)	134.9(3)
C(18)-O(8)-Dy(1)	134.0(4)
C(34)-O(9)-C(37)	106(2)

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,-y+1,-z+1

Anisotropic displacement parameters ($Å^2 x\ 10^3$) for $Dy(terpy)(NO_3)_2(dbacac)$. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2\ a^{*2}U^{11} +$

... + 2 h k a* b* U^{12}]

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	33(3)	26(3)	22(2)	3(2)	3(2)	-3(2)
C(2)	41(4)	25(3)	30(3)	-1(3)	-1(3)	-10(3)
C(3)	51(4)	31(3)	29(3)	-14(3)	7(3)	-4(3)
C(4)	40(4)	41(4)	20(2)	-6(2)	10(2)	5(3)
C(5)	25(3)	27(3)	15(2)	0(2)	2(2)	6(2)
C(6)	24(3)	21(3)	19(2)	0(2)	6(2)	4(2)
C(7)	28(3)	40(4)	25(3)	-1(3)	12(2)	10(3)
C(8)	27(3)	57(4)	41(3)	7(3)	21(3)	2(3)
C(9)	31(3)	34(3)	35(3)	8(3)	16(3)	-6(3)
C(10)	18(2)	25(3)	19(2)	4(2)	4(2)	-3(2)
C(11)	22(3)	20(3)	22(2)	6(2)	1(2)	3(2)
C(12)	26(3)	29(3)	54(4)	4(3)	8(3)	-4(3)
C(13)	47(4)	22(3)	59(4)	-2(4)	-6(3)	-2(4)
C(14)	73(5)	11(3)	33(3)	-1(2)	10(3)	4(3)
C(15)	56(4)	19(3)	26(3)	6(2)	17(3)	11(3)
C(16)	18(2)	32(4)	21(2)	2(2)	9(2)	6(2)
C(17)	31(3)	48(4)	28(3)	-2(3)	18(3)	-10(3)
C(18)	31(3)	68(5)	37(3)	-12(3)	19(3)	-20(3)
C(19)	83(7)	133(10)	68(6)	-45(6)	50(5)	-80(7)

C(20)	38(3)	27(3)	22(2)	3(2)	13(2)	0(2)
C(21)	53(4)	30(3)	32(3)	-6(3)	28(3)	-13(3)
C(22)	47(4)	59(5)	51(4)	0(4)	28(4)	10(4)
C(23)	56(5)	71(6)	70(6)	-4(5)	33(5)	15(5)
C(24)	78(5)	31(4)	38(3)	-7(3)	36(4)	-17(4)
C(25)	109(7)	30(4)	52(4)	-10(3)	64(5)	-21(4)
C(26)	80(6)	37(4)	94(7)	-10(5)	63(6)	-8(4)
C(27)	36(3)	23(3)	21(2)	3(2)	16(2)	6(2)
C(28)	34(3)	23(3)	18(2)	1(2)	8(2)	-3(2)
C(29)	27(3)	29(3)	35(3)	5(3)	10(3)	6(2)
C(30)	34(4)	38(4)	70(5)	20(4)	12(4)	3(3)
C(31)	41(5)	58(6)	75(6)	25(5)	-13(4)	-2(4)
C(32)	73(6)	42(5)	53(5)	-2(4)	-26(4)	-7(4)
C(33)	60(5)	42(4)	31(3)	-5(3)	9(3)	-3(4)
Dy(1)	20(1)	25(1)	16(1)	0(1)	8(1)	0(1)
N(1)	24(2)	20(2)	16(2)	2(2)	3(2)	-2(2)
N(2)	20(2)	10(2)	17(2)	2(1)	4(2)	2(1)
N(3)	39(3)	17(2)	21(2)	3(2)	12(2)	6(2)
N(4)	27(2)	29(3)	17(2)	3(2)	10(2)	5(2)
N(5)	31(3)	23(2)	21(2)	6(2)	12(2)	9(2)
N(6)	25(2)	30(3)	25(2)	2(2)	9(2)	-3(2)
O(1)	41(3)	43(3)	36(2)	20(2)	8(2)	23(2)
O(2)	47(3)	15(2)	24(2)	3(2)	2(2)	-3(2)

O(3)	23(2)	25(2)	32(2)	11(2)	6(2)	0(2)
O(4)	39(3)	62(3)	23(2)	4(2)	12(2)	20(2)
O(5)	26(2)	32(2)	19(2)	2(2)	7(2)	6(2)
O(6)	27(2)	36(2)	31(2)	11(2)	5(2)	9(2)
O(7)	27(2)	23(2)	19(2)	1(2)	11(2)	1(2)
O(8)	32(2)	57(3)	30(2)	-16(2)	18(2)	-21(2)

Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for Dy(terpy)$(NO_3)_2$(dbacac).

	x	y	z	U(eq)
H(1)	7031	-766	4047	35
H(2)	6972	-2702	3330	44
H(3)	7734	-2655	2697	48
H(4)	8524	-676	2790	41
H(7)	9310	978	3003	37
H(8)	10003	3098	3115	47
H(9)	9797	5020	3721	39
H(12)	9608	6638	4309	46
H(13)	9313	8434	4950	60
H(14)	8348	8008	5336	50
H(15)	7704	5869	5082	40

H(17)	6769	1429	6185	41
H(19A)	5662	97	4730	132
H(19B)	5949	-186	5527	132
H(19C)	6286	-1102	5073	132
H(20A)	8124	2896	7619	34
H(20B)	7528	1777	7142	34
H(22)	6343	4015	6429	59
H(23)	5362	4988	6686	75
H(24)	7539	3318	8407	54
H(25)	6520	4345	8648	65
H(26)	5462	5117	7786	73
H(27A)	7944	5460	6968	30
H(27B)	8160	5161	6325	30
H(29)	9211	2884	6717	37
H(30)	10454	2560	7443	59
H(31)	10988	4086	8372	82
H(32)	10290	5970	8541	85
H(33)	9037	6260	7833	56

Torsion angles [°] for Dy(terpy)$(NO_3)_2$(dbacac).

N(1)-C(1)-C(2)-C(3)	0.8(9)
C(1)-C(2)-C(3)-C(4)	-0.1(10)

C(2)-C(3)-C(4)-C(5)	0.2(10)
C(3)-C(4)-C(5)-N(1)	-1.0(9)
C(3)-C(4)-C(5)-C(6)	-178.1(5)
N(1)-C(5)-C(6)-N(2)	-5.5(7)
C(4)-C(5)-C(6)-N(2)	171.8(5)
N(1)-C(5)-C(6)-C(7)	173.4(5)
C(4)-C(5)-C(6)-C(7)	-9.3(8)
N(2)-C(6)-C(7)-C(8)	-2.4(8)
C(5)-C(6)-C(7)-C(8)	178.7(5)
C(6)-C(7)-C(8)-C(9)	0.6(9)
C(7)-C(8)-C(9)-C(10)	0.4(9)
C(8)-C(9)-C(10)-N(2)	0.4(9)
C(8)-C(9)-C(10)-C(11)	-179.6(5)
N(2)-C(10)-C(11)-N(3)	-3.6(7)
C(9)-C(10)-C(11)-N(3)	176.4(5)
N(2)-C(10)-C(11)-C(12)	176.8(5)
C(9)-C(10)-C(11)-C(12)	-3.3(8)
N(3)-C(11)-C(12)-C(13)	0.9(9)
C(10)-C(11)-C(12)-C(13)	-179.4(5)
C(11)-C(12)-C(13)-C(14)	-0.9(10)
C(12)-C(13)-C(14)-C(15)	-0.1(10)
C(13)-C(14)-C(15)-N(3)	1.2(10)
O(7)-C(16)-C(17)-C(18)	6.1(10)

N(4)-C(16)-C(17)-C(18)	-176.4(6)
C(16)-C(17)-C(18)-O(8)	4.0(13)
C(16)-C(17)-C(18)-C(19)	-176.5(8)
N(4)-C(20)-C(21)-C(24)	-147.3(6)
N(4)-C(20)-C(21)-C(22)	34.6(9)
C(24)-C(21)-C(22)-C(23)	-2.0(12)
C(20)-C(21)-C(22)-C(23)	176.1(7)
C(21)-C(22)-C(23)-C(26)	0.8(14)
C(22)-C(21)-C(24)-C(25)	1.6(10)
C(20)-C(21)-C(24)-C(25)	-176.5(6)
C(21)-C(24)-C(25)-C(26)	-0.2(10)
C(22)-C(23)-C(26)-C(25)	0.7(14)
C(24)-C(25)-C(26)-C(23)	-1.0(12)
N(4)-C(27)-C(28)-C(33)	-133.0(6)
N(4)-C(27)-C(28)-C(29)	49.6(7)
C(33)-C(28)-C(29)-C(30)	3.4(9)
C(27)-C(28)-C(29)-C(30)	-179.1(6)
C(28)-C(29)-C(30)-C(31)	-1.5(10)
C(29)-C(30)-C(31)-C(32)	-1.5(13)
C(30)-C(31)-C(32)-C(33)	2.4(14)
C(29)-C(28)-C(33)-C(32)	-2.5(11)
C(27)-C(28)-C(33)-C(32)	-180.0(7)
C(31)-C(32)-C(33)-C(28)	-0.4(13)

C(35)#1-C(34)-C(35)-C(34)#1	0.001(5)
O(9)-C(34)-C(35)-C(34)#1	-131(4)
C(35)#1-C(34)-C(35)-C(36)	127(4)
O(9)-C(34)-C(35)-C(36)	-4(5)
C(34)#1-C(34)-C(35)-C(36)	126(4)
C(34)#1-C(35)-C(36)-C(37)	80(6)
C(34)-C(35)-C(36)-C(37)	-7(6)
C(35)-C(36)-C(37)-O(9)	16(6)
C(2)-C(1)-N(1)-C(5)	-1.6(8)
C(2)-C(1)-N(1)-Dy(1)	177.5(4)
C(4)-C(5)-N(1)-C(1)	1.7(8)
C(6)-C(5)-N(1)-C(1)	179.0(5)
C(4)-C(5)-N(1)-Dy(1)	-177.4(4)
C(6)-C(5)-N(1)-Dy(1)	-0.1(6)
C(9)-C(10)-N(2)-C(6)	-2.1(7)
C(11)-C(10)-N(2)-C(6)	177.8(4)
C(9)-C(10)-N(2)-Dy(1)	171.4(4)
C(11)-C(10)-N(2)-Dy(1)	-8.6(6)
C(7)-C(6)-N(2)-C(10)	3.2(7)
C(5)-C(6)-N(2)-C(10)	-177.9(4)
C(7)-C(6)-N(2)-Dy(1)	-170.3(4)
C(5)-C(6)-N(2)-Dy(1)	8.7(6)
C(14)-C(15)-N(3)-C(11)	-1.2(8)

C(14)-C(15)-N(3)-Dy(1)	164.9(5)
C(12)-C(11)-N(3)-C(15)	0.1(8)
C(10)-C(11)-N(3)-C(15)	-179.5(5)
C(12)-C(11)-N(3)-Dy(1)	-165.8(4)
C(10)-C(11)-N(3)-Dy(1)	14.5(6)
O(7)-C(16)-N(4)-C(20)	-167.9(5)
C(17)-C(16)-N(4)-C(20)	14.5(8)
O(7)-C(16)-N(4)-C(27)	10.8(7)
C(17)-C(16)-N(4)-C(27)	-166.8(5)
C(21)-C(20)-N(4)-C(16)	-102.2(6)
C(21)-C(20)-N(4)-C(27)	79.1(6)
C(28)-C(27)-N(4)-C(16)	-111.5(5)
C(28)-C(27)-N(4)-C(20)	67.3(6)
O(1)-N(5)-O(2)-Dy(1)	178.7(4)
O(3)-N(5)-O(2)-Dy(1)	-0.2(5)
O(1)-N(5)-O(3)-Dy(1)	-178.7(4)
O(2)-N(5)-O(3)-Dy(1)	0.2(4)
O(6)-N(6)-O(4)-Dy(1)	-172.6(5)
O(5)-N(6)-O(4)-Dy(1)	6.8(5)
O(6)-N(6)-O(5)-Dy(1)	172.5(5)
O(4)-N(6)-O(5)-Dy(1)	-7.0(5)
N(4)-C(16)-O(7)-Dy(1)	163.5(3)
C(17)-C(16)-O(7)-Dy(1)	-19.0(8)

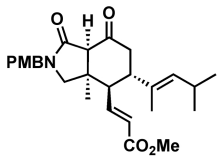
C(17)-C(18)-O(8)-Dy(1)	-1.8(12)
C(19)-C(18)-O(8)-Dy(1)	178.7(6)
C(35)#1-C(34)-O(9)-C(37)	-107(4)
C(35)-C(34)-O(9)-C(37)	14(4)
C(34)#1-C(34)-O(9)-C(37)	-32(5)
C(36)-C(37)-O(9)-C(34)	-19(5)

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,-y+1,-z+1

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Project1\XQ\xq-3-158-DA1.lcd



6
racemic

xq-3-158-DA
1mg/ml
10ul
5% i-PrOH in Hex
1.0ml/min
AD-H analytical
1mg/ml
10 uL injection
210nm

Acquired by	: Admin
Sample Name	: xq-3-158-DA
Sample ID	: xq-3-158-DA
Vail #	:
Injection Volume	: 10 uL
Data File Name	: xq-3-158-DA1.lcd
Method File Name	: ATH-OD-J-analytical-hplc.lcm
Batch File Name	:
Report File Name	: Default.lcr
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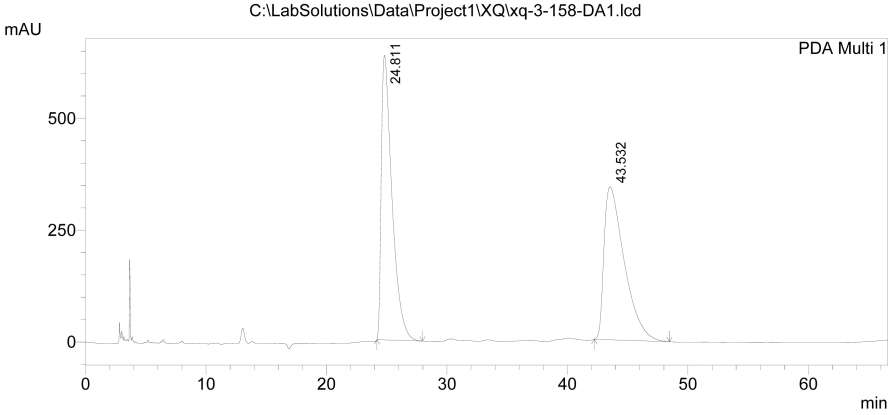


1 PDA Multi 1/210nm 4nm

PeakTable

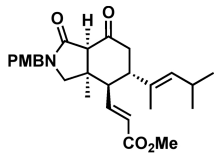
PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	24.811	39341091	636385	49.622	65.045
2	43.532	39940274	341985	50.378	34.955
Total		79281365	978370	100.000	100.000

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Project1\XQ\xq-3-89-4-DA-1.lcd

5% iPrOH/Hex
1 ml/min
AD-H analytical
10 ul injection
4mg/ml
210 nm



6
entry 1: L1

Acquired by	: Admin
Sample Name	: xq-3-89-4-DA
Sample ID	: xq-3-89-4-DA
Vail #	:
Injection Volume	: 10 uL
Data File Name	: xq-3-89-4-DA-1.lcd
Method File Name	: ces-OD-H-analytical.lcm
Batch File Name	:
Report File Name	: Default.lcr
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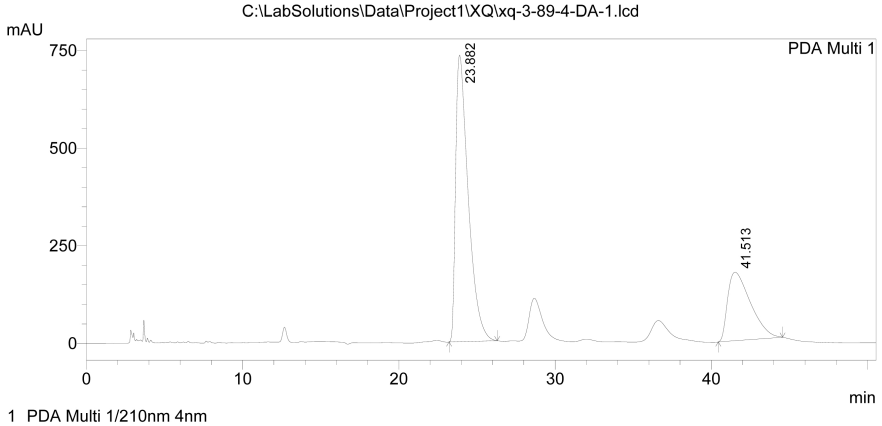


1 PDA Multi 1/210nm 4nm

PeakTable

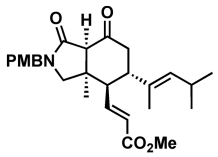
PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	23.882	41141618	733864	69.800	80.708
2	41.513	17800592	175423	30.200	19.292
Total		58942210	909287	100.000	100.000

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Project1\XQ\xq-3-114-1-DA.lcd

Acquired by	: Admin
Sample Name	: xq-3-114-1-DA
Sample ID	: xq-3-114-1-DA
Vail #	:
Injection Volume	: 10 uL
Data File Name	: xq-3-114-1-DA.lcd
Method File Name	: ces-OD-H-analytical.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 5/13/2013 11:54:54 AM
Data Processed	: 5/13/2013 5:08:54 PM



6

entry 2: L2

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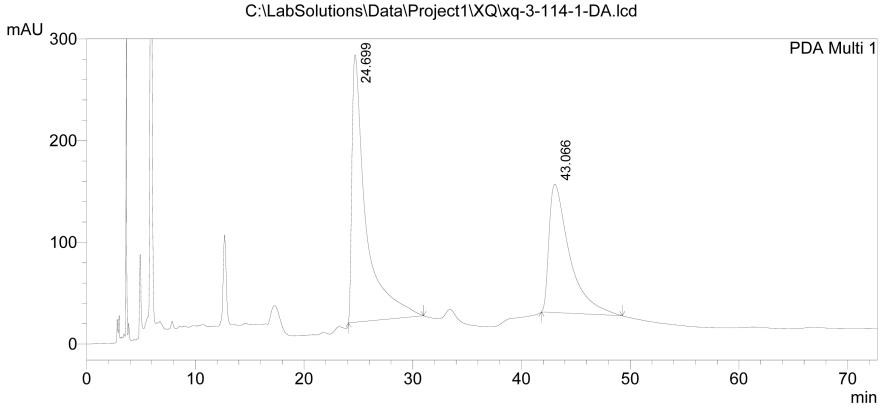


1 PDA Multi 1/210nm 4nm

PeakTable

PDA Ch1 210nm 4nm

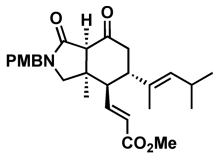
Peak#	Ret. Time	Area	Height	Area %	Height %
1	24.699	23575805	262910	58.691	67.545
2	43.066	16593283	126327	41.309	32.455
Total		40169087	389237	100.000	100.000

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Project1\XQ\xq-3-117-4-DA.lcd

5% i-PrOH in Hex
1 ml/min
AD-H analytical
4mg/ml
10 uL injection
210nm

Acquired by	: Admin
Sample Name	: xq-3-117-4-DA
Sample ID	: xq-3-117-4-DA
Vail #	:
Injection Volume	: 15 uL
Data File Name	: xq-3-117-4-DA.lcd
Method File Name	: ces-OD-H-analytical.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 5/16/2013 5:14:17 PM
Data Processed	: 1/10/2015 3:15:20 PM



6
entry 3: L3

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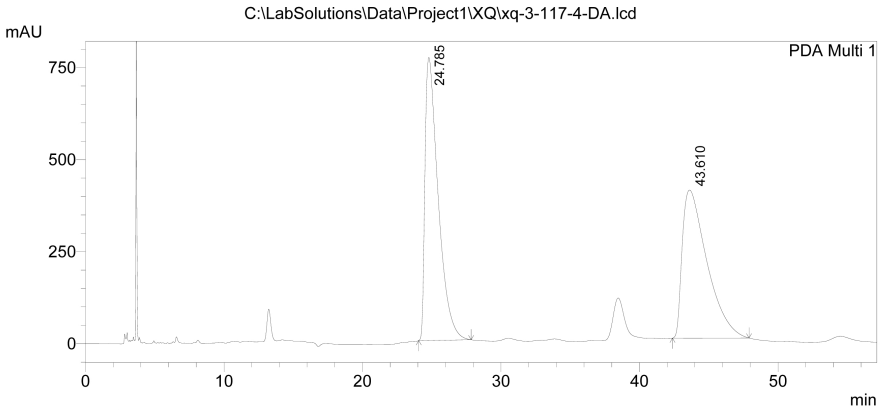


1 PDA Multi 1/210nm 4nm

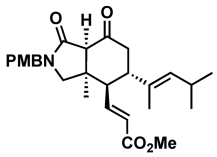
PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	24.785	50874894	768478	50.509	65.637
2	43.610	49849787	402315	49.491	34.363
Total		100724681	1170794	100.000	100.000

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Project1\XQ\xq-3-154-DA1.lcd



6

entry 4: L4

xq-3-154-DA
1mg/ml
10ul
5% i-PrOH in Hex
1.0ml/min
AD-H analytical
1mg/ml
10 uL injection
210nm

Acquired by	: Admin
Sample Name	: xq-3-154-DA
Sample ID	: xq-3-154-DA
Vail #	:
Injection Volume	: 10 uL
Data File Name	: xq-3-154-DA1.lcd
Method File Name	: ATH-OD-J-analytical-hplc.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 6/24/2013 12:32:03 PM
Data Processed	: 6/26/2013 4:58:01 PM

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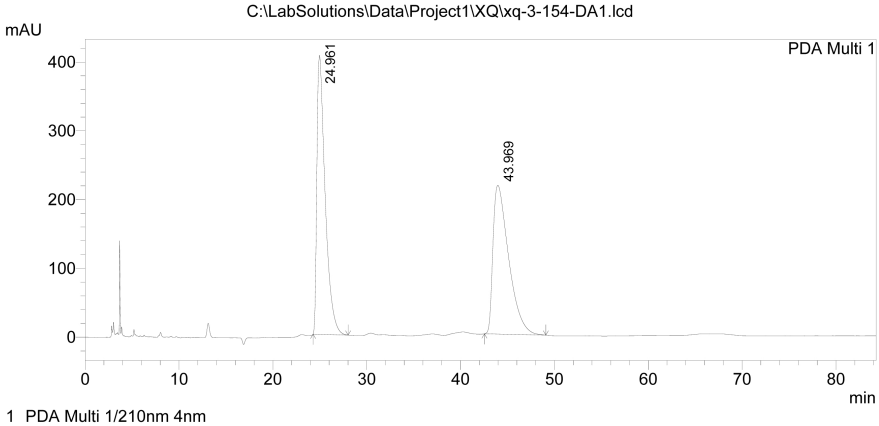


1 PDA Multi 1/210nm 4nm

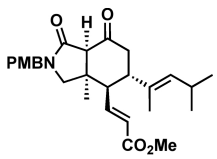
PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	24.961	24874323	405611	49.743	65.200
2	43.969	25131571	216492	50.257	34.800
Total		50005894	622103	100.000	100.000

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Project1\XQ\xq-3-117-2-DA.lcd



6
entry 5: L5

5% i-PrOH in Hex
1 ml/min
AD-H analytical
4mg/ml
10 uL injection
210nm

Acquired by	: Admin
Sample Name	: xq-3-117-2-DA
Sample ID	: xq-3-117-2-DA
Vail #	:
Injection Volume	: 15 uL
Data File Name	: xq-3-117-2-DA.lcd
Method File Name	: ces-OD-H-analytical.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 5/16/2013 3:16:55 PM
Data Processed	: 5/16/2013 5:14:29 PM

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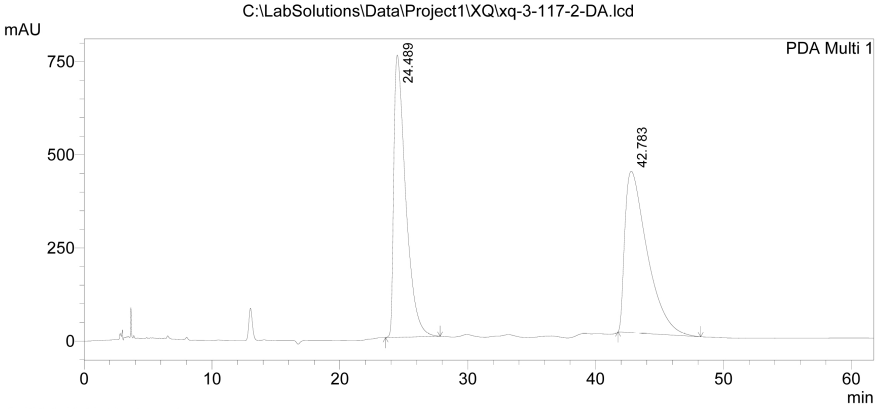

1 PDA Multi 1/210nm 4nm

PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	24.489	49006998	757791	48.212	63.618
2	42.783	52642805	433368	51.788	36.382
Total		101649803	1191159	100.000	100.000

==== Shimadzu LCsolution Analysis Report ====

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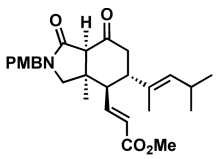

6

entry 6: L6

5% i-PrOH in Hex
1 ml/min
AD-H analytical
4mg/ml
10 uL injection
210nm

Acquired by	: Admin
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Sample ID	: xq-3-117-1-DA
Vail #	:
Injection Volume	: 15 uL
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Method File Name	: ces-OD-H-analytical.lcm
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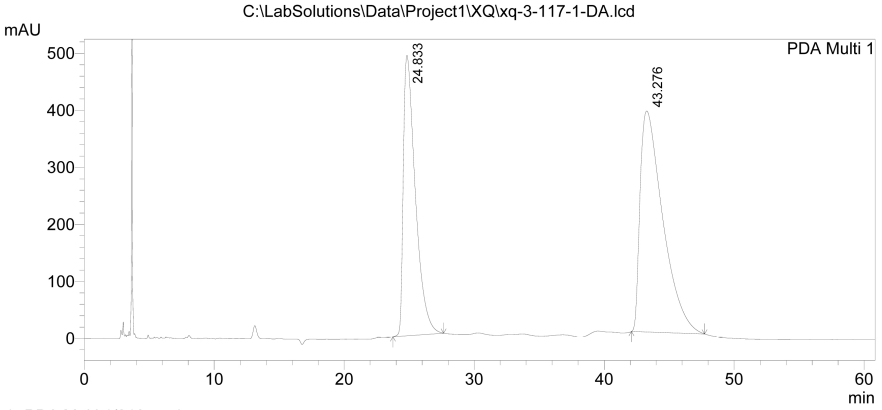

1 PDA Multi 1/210nm 4nm

PeakTable

PDA Ch1 210nm 4nm

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1	24.833	31638227	491757	40.174	55.927
2	43.276	47115323	387520	59.826	44.073
Total		78753550	879277	100.000	100.000

==== Shimadzu LCsolution Analysis Report ====

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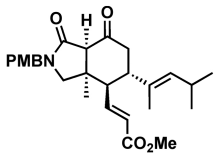

6

entry 7: L7

5% i-PrOH in Hex
1 ml/min
AD-H analytical
4mg/ml
10 uL injection
210nm

Acquired by	: Admin
Sample Name	: xq-3-117-3-DA
Sample ID	: xq-3-117-3-DA
Vail #	:
Injection Volume	: 15 uL
Data File Name	: xq-3-117-3-DA.lcd
Method File Name	: ces-OD-H-analytical.lcm
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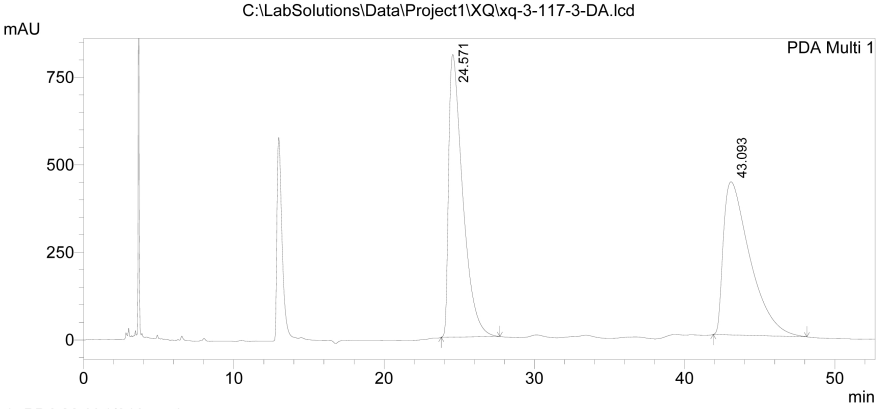

1 PDA Multi 1/210nm 4nm

PeakTable

PDA Ch1 210nm 4nm

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1	24.571	52568496	807299	49.409	64.862
2	43.093	53825775	437340	50.591	35.138
Total		106394271	1244639	100.000	100.000

==== Shimadzu LCsolution Analysis Report ====

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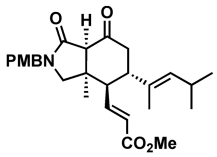

6

entry 8: L8

5% i-PrOH in Hex
1 ml/min
AD-H analytical
4mg/ml
15 uL injection
210nm

Acquired by	: Admin
Sample Name	: xq-3-124-DA
Sample ID	: xq-3-124-DA
Vail #	:
Injection Volume	: 15 uL
Data File Name	: xq-3-124-DA1.lcd
Method File Name	: ces-OD-H-analytical.lcm
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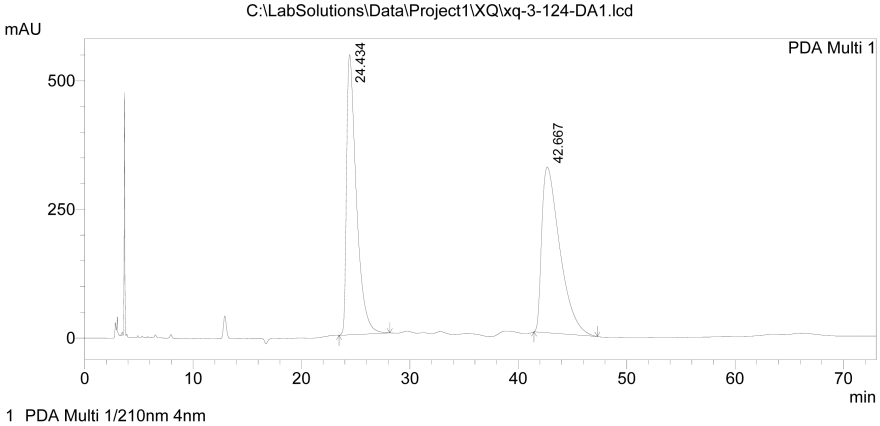

1 PDA Multi 1/210nm 4nm

PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	24.434	34276785	544506	47.818	62.839
2	42.667	37405011	322001	52.182	37.161
Total		71681797	866507	100.000	100.000

==== Shimadzu LCsolution Analysis Report ====

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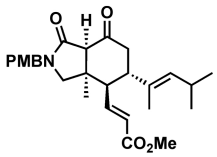

6
entry 9: L9

5% i-PrOH in Hex
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AD-H analytical
4mg/ml
10 uL injection
210nm

Acquired by	: Admin
Sample Name	: xq-3-114-3-DA
Sample ID	: xq-3-114-3-DA
Vail #	:
Injection Volume	: 15 uL
Data File Name	: xq-3-114-3-DA.lcd
Method File Name	: ces-OD-H-analytical.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 5/13/2013 2:26:27 PM
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<Chromatogram>

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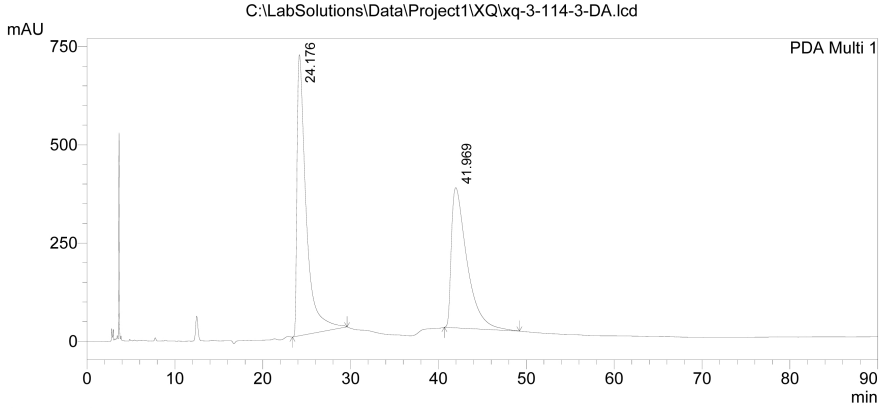
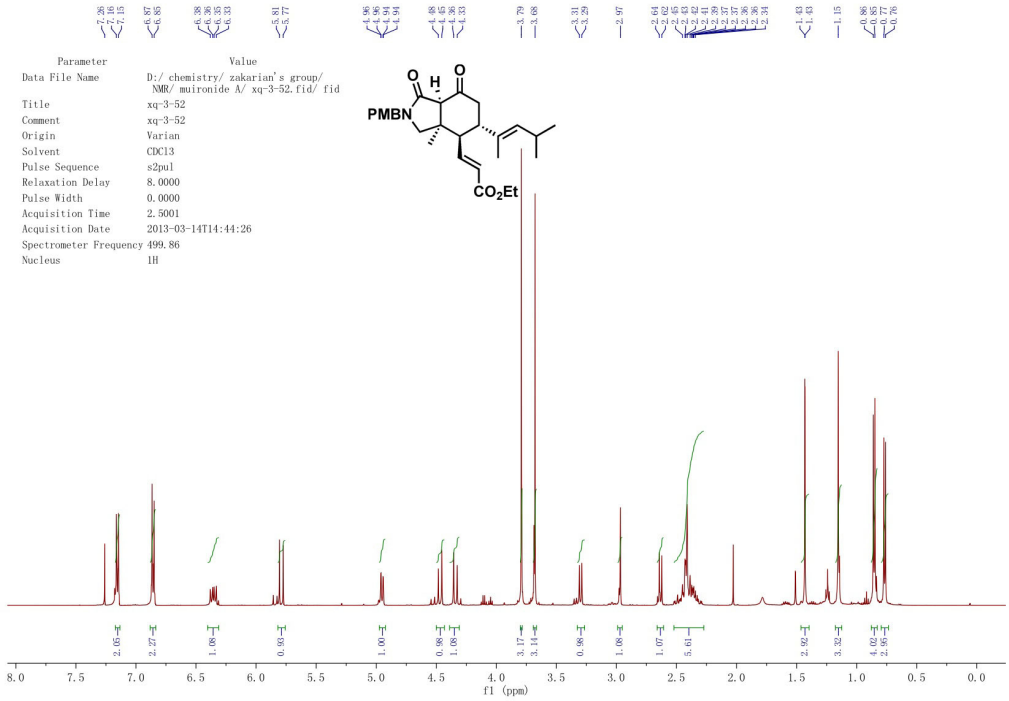


1 PDA Multi 1/210nm 4nm

PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	24.176	51908615	715264	54.167	66.725
2	41.969	43921931	356699	45.833	33.275
Total		95830546	1071963	100.000	100.000


7.26 7.18 7.15 6.87 6.85 6.38 6.36 6.35 6.33 5.81 5.77 4.96 4.95 4.94 4.94 4.48 4.45 4.36 4.33 3.79 3.68 3.31 3.29 2.97 2.64 2.62 2.45 2.43 2.42 2.41 2.39 2.37 2.36 2.36 2.34 1.43 1.43 1.15 0.86 0.85 0.77 0.76
Parameter Value
Data File Name D:/ chemistry/ zakarian's group/ NMR/ muironide A/ xq-3-52.fid/ fid
Title xq-3-52
Comment xq-3-52
Origin Varian
Solvent CDCl3
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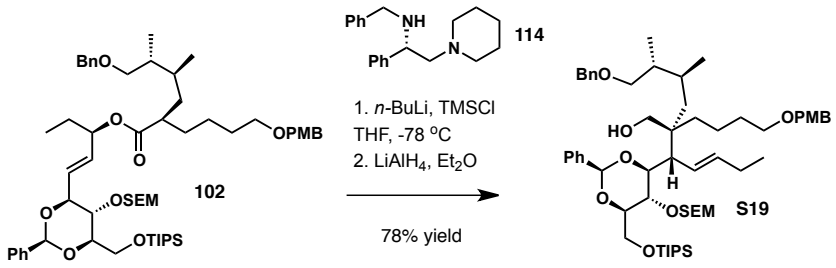
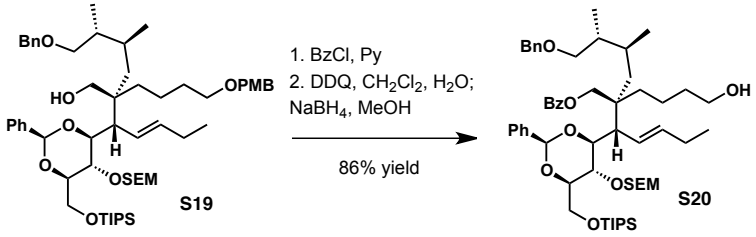
Relaxation Delay 8.0000
Pulse Width 0.0000
Acquisition Time 2.5001
Acquisition Date 2013-03-14T14:44:26
Spectrometer Frequency 499.86
Nucleus 1H
O
H
O
PMBN
CO2Et
2.05 2.27 1.08 0.93 1.00 0.98 1.08 3.17 3.14 0.98 1.08 1.07 5.61 2.92 3.32 4.02 2.95
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)



Alcohol (S19). *n*-Butyllithium (2.37 M in hexanes, 15.5 mL, 36.8 mL) was added to a solution of **114** (11.06 g, 37.6 mmol) in dry THF (41 mL) at −78 °C and the solution was stirred for 30 min. A solution of **102** (7.4o g, 7.35 mmol) in dry THF (20 mL total with rinses) was added dropwise. After 1 h, chlorotrimethylsilane (4.7 mL, 36.8 mmol), freshly distilled from CaH_2, was added dropwise. The reaction mixture was stirred at −78 °C for 20 min, at 0 °C for 20 min, then warmed to 23 °C and stirred for 12 h. The solution was quenched with water and diluted with ethyl acetate (3x100 mL), and the combined organic layers were washed with 1 M aqueous HCl (2x50 mL). The aqueous layer was brought to pH>9 using NaOH and extracted with ethyl acetate (3x100 mL) to recover the chiral amine. The organic layer was dried with sodium sulfate and concentrated. The crude oil was submitted to the next step without further purification.

The crude residue was dissolved in dry ether (258 ml) and lithium aluminum hydride (2.89 g, 72.4 mmol) was added carefully at 0 °C. The reaction mixture was warmed to 23 °C and stirred for 18 h. The mixture was then heated at reflux for 1 h, then cooled to 23 °C, and then to 0 °C. An additional 100 mL of ether was added. Water (2.9 ml) was added carefully with vigorous stirring. After 5 min, 3 M aqueous NaOH (2.9 ml) was added. After an additional 5 min, water (8.7 ml) was added and the mixture was allowed to stir at 23 °C for 1 h. The white precipitate was filtered off, and washed with dichloromethane. The filtrate was concentrated and the residue was purified by column

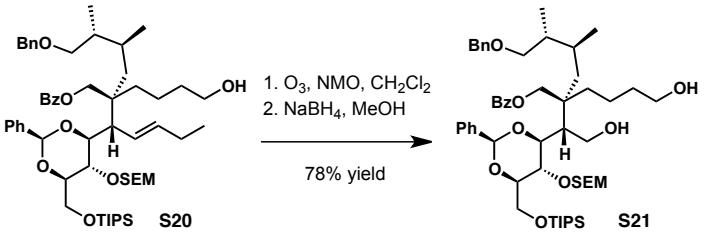
chromatography (silica, 20% ethyl acetate – hexanes) afforded **S19** (9.98 g, 10.03 mmol, 78%). ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 7.44 (dd, *J* = 6.5, 3.2 Hz, 2H), 7.31 (dd, *J* = 4.6, 2.2 Hz, 8H), 7.24 – 7.20 (m, 2H), 6.87 – 6.82 (m, 2H), 5.56 – 5.52 (m, 2H), 5.47 (s, 1H), 4.82 – 4.75 (m, 2H), 4.50 – 4.43 (m, 3H), 4.37 (s, 2H), 4.15 – 4.09 (m, 3H), 4.06 (dd, *J* = 11.6, 1.7 Hz, 1H), 3.78 (s, 5H), 3.71 – 3.55 (m, 5H), 3.49 – 3.36 (m, 4H), 3.35 – 3.27 (m, 2H), 3.24 – 3.19 (m, 1H), 2.05 (d, *J* = 7.6 Hz, 4H), 1.30 – 1.25 (m, 4H), 1.00 – 0.92 (m, 7H), 0.91 – 0.83 (m, 3H), 0.78 (dd, *J* = 6.9, 2.6 Hz, 6H), 0.51 (d, *J* = 5.7 Hz, 2H), 0.43 – 0.36 (m, 2H).



Alcohol (**S20)**. Benzoyl chloride (2.5 mL, 21.5 mmol) was added to a solution **S19** (9.99 g, 10.07 mmol) in pyridine (26.3 mL) and the mixture was heated at 80 °C for 1 h. The solution was cooled to 23 °C, quenched with methanol (2.2 mL, 52.6 mmol) and stirred for 10 min. The mixture was diluted with dichloromethane (500 mL). The organic layer was washed with 1 M HCl (2x200 mL), water, saturated aqueous sodium bicarbonate, dried with sodium sulfate, and concentrated. The crude ester was submitted to the next step without further purification.

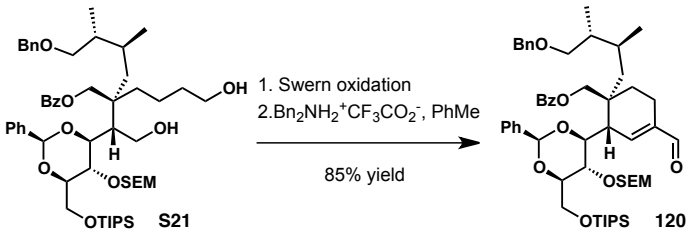
The residue was dissolved in dichloromethane (160 mL) and water (6.4 mL), followed by addition of 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (2.77 g, 12.18 mmol), and the mixture was stirred vigorously for 1.5 h at 23 °C. The reaction mixture was diluted with dichloromethane and washed with a 1:1 mixture of saturated aqueous sodium bicarbonate and saturated aqueous sodium thiosulfate. The aqueous layer was extracted

with dichloromethane, and the combined organic layers were dried with sodium sulfate, and concentrated. To help improve separation between the desired alcohol and *p*-methoxybenzaldehyde, the crude alcohol was then was dissolved in MeOH (288 mL), followed by addition of sodium borohydride (1.94 g, 51.4 mmol), at 0 °C. The solution was stirred for 10 min and then quenched with water. The solution was diluted with ethyl acetate, and washed with water. The aqueous layers were then extracted with ethyl acetate (2x300mL). The combined organic layers were washed with brine, dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica, 20% ethyl acetate – hexanes) to afford **S20** (8.44 g, 8.66 mmol, 88%). ^{1}H NMR (600 MHz, $CDCl_3$); δ (ppm): 8.06 – 8.02 (m, 2H), 7.46 – 7.42 (m, 2H), 7.42 – 7.38 (m, 2H), 7.29 – 7.27 (m, 3H), 7.31 (dt, *J* = 6.7, 1.4 Hz, 3H), 5.59 (dd, *J* = 15.4, 10.5 Hz, 1H), 5.44 (s, 1H), 4.61 (s, 2H), 4.46 (q, *J* = 12.1 Hz, 2H), 4.36 (d, *J* = 11.6 Hz, 1H), 4.24 (d, *J* = 11.7 Hz, 1H), 4.05 (dd, *J* = 11.4, 1.4 Hz, 1H), 3.96 (td, *J* = 8.1, 4.3 Hz, 1H), 3.61 (ddd, *J* = 10.8, 9.5, 8.0 Hz, 3H), 3.46 (q, *J* = 5.7 Hz, 2H), 3.42 – 3.36 (m, 1H), 3.31 – 3.20 (m, 2H), 2.62 – 2.56 (m, 1H), 1.53 – 1.34 (m, 7H), 1.12 – 1.02 (m, 19H), 0.98 (t, *J* = 7.5 Hz, 3H), 0.89 – 0.83 (m, 2H), 0.76 (d, *J* = 6.9 Hz, 3H), 0.72 (d, *J* = 6.8 Hz, 3H).



Diol (S21). Ozone was bubbled through a solution of **S20** (7.4 g, 7.58 mmol), *N*-methylmorpholine-*N*-oxide (3.55 g, 30.34 mmol), in dichloromethane (161 mL) at -78 °C. The progress of the reaction was monitored by TLC. After the starting material was consumed, the solution was purged with O_2 and argon. A saturated aqueous solution of

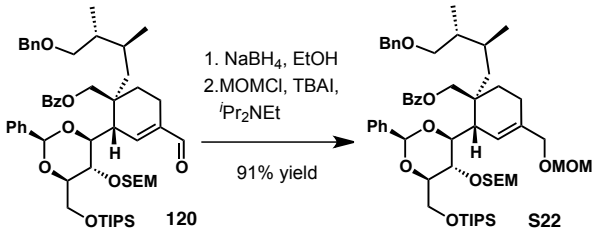
ammonium chloride was added at 23 °C. Dilute with dichloromethane and water. The aqueous layer was extracted with dichloromethane (4x110 mL). The combined organic layers were dried with sodium sulfate and concentrated. The crude residue was dissolved in ethanol (108 mL), cooled to -10 °C, and sodium borohydride (0.287 g, 7.58 mmol) was added. Additional sodium borohydride was added after 30 min and 1 h 30 min (1 equiv for each addition). After 2 h the solution was diluted with dichloromethane and quenched carefully with saturated aqueous solution of ammonium chloride. The aqueous layer was extracted with dichloromethane (5x100 ml). The combined organic layers were dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica, 75% ethyl acetate − hexanes) to give **S21** (5.61 g, 5.91 mmol, 78%). H NMR (500 MHz, $CDCl_3$); δ (ppm): 8.08 – 7.98 (m, 2H), 7.54 (ddt, *J* = 8.7, 7.3, 1.3 Hz, 1H), 7.46 – 7.36 (m, 3H), 7.35 – 7.30 (m, 3H), 5.44 (s, 1H), 4.92 – 4.79 (m, 2H), 4.58 – 4.40 (m, 3H), 4.07 – 3.97 (m, 3H), 3.93 (h, *J* = 6.6 Hz, 1H), 3.66 – 3.56 (m, 2H), 3.49 (s, 1H), 3.32 – 3.19 (m, 2H), 1.87 – 1.34 (m, 10H), 1.12 – 1.00 (m, 13H), 0.97 – 0.84 (m, 2H), 0.76 (d, *J* = 7.0 Hz, 3H), 0.68 (d, *J* = 6.8 Hz, 2H).



Aldehyde (120). Dimethylsulfoxide (4.4 mL, 61.80 mmol) was added to a solution of oxalyl chloride (2.61 mL, 30.90 mmol) in dichloromethane (137 mL) at -78 °C. After 20 min, a solution of **S21** (11.76 g, 12.36 mmol) in dichloromethane (137 ml total with rinses) was added dropwise, and the mixture was stirred for 25 min. Triethylamine (12.9 mL, 92.70 mmol) was added dropwise. After stirring at -78 °C for 10 min, the mixture

was brought to 0 °C and stirred for 20 min. The reaction was quenched with 1 M aqueous HCl (200 mL). The aqueous layer was extracted with ethyl acetate (3x100 mL). The combined organic layers were washed with water and saturated aqueous sodium bicarbonate, dried with sodium sulfate, and concentrated to give the crude dialdehyde, which was used without further purification.

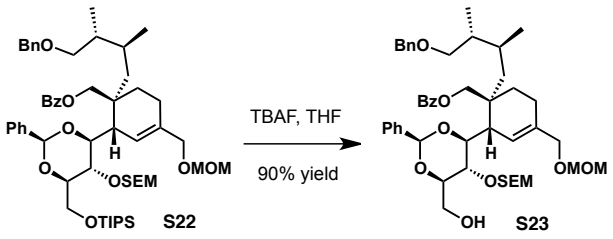
The crude dialdehyde was dissolved in dry toluene (773 mL) and dibenzylammonium trifluoroacetate (11.31 g, 36.33 mmol) was added. The mixture was stirred at 23 °C for 12 h, then heated at 36 °C for 8 h, and then finally cooled to 23 °C and stirred for an additional 8 h. The solution was directly applied on a silica column (silica, 15% ethyl acetate – hexanes) to afford **120** (9.77 g, 10.51 mmol, 85%). 1H NMR (500 MHz, $CDCl_3$); δ (ppm): 9.49 (s, 1H), 8.07 – 7.98 (m, 2H), 7.56 – 7.50 (m, 1H), 7.41 – 7.36 (m, 3H), 7.35 – 7.21 (m, 2H), 7.16 (dd, *J* = 14.3, 7.3 Hz, 6H), 6.89 (dd, *J* = 3.4, 1.7 Hz, 1H), 5.46 (s, 1H), 4.87 – 4.74 (m, 2H), 4.48 – 4.38 (m, 2H), 4.38 – 4.31 (m, 2H), 4.12 – 4.02 (m, 2H), 4.02 – 3.93 (m, 2H), 3.67 – 3.58 (m, 1H), 3.59 – 3.50 (m, 2H), 3.25 (ddd, *J* = 42.2, 9.4, 6.9 Hz, 3H), 2.25 (dd, *J* = 16.0, 10.5 Hz, 2H), 1.99 (dd, *J* = 7.5, 4.1 Hz, 1H), 1.93 (dt, *J* = 12.7, 6.1 Hz, 1H), 1.88 – 1.74 (m, 3H), 1.15 – 0.97 (m, 18H), 0.91 – 0.81 (m, 3H), 0.77 (dd, *J* = 10.0, 6.9 Hz, 4H).



MOM Ether (S22). Sodium borohydride (1.67 g, 42.04 mmol) was added to a solution of **120** (9.77 g, 10.51 mmol) in ethanol (188 mL) at -70 °C. The mixture was allowed to warm to 0 °C while stirring over 1.5 h, at which point it was diluted with

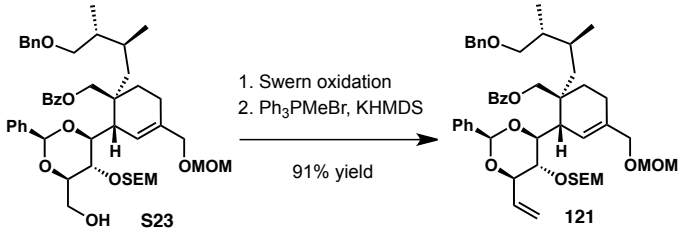
dichloromethane and quenched carefully with a saturated aqueous solution of ammonium chloride. The aqueous layer was extracted with dichloromethane (3x100 mL). The combined organic layers were dried with sodium sulfate, and concentrated to give the crude alcohol, which was used without further purification.

The residue was dissolved in dichloromethane (58 ml), and di-isopropylethylamine (55.1 mL, 316.42 mmol), chloromethyl methyl ether (8.0 mL, 105.12 mmol), and tetra-*n*-butylammonium iodide (0.368 g, 0.998 mmol) were added at 0 °C. The reaction mixture was stirred for 14 h at 23 °C. The reaction mixture was diluted with dichloromethane (400 mL). The organic layer was washed with 1 M aqueous HCl (2x200 mL), water, saturated aqueous sodium bicarbonate, dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica, 20% ethyl acetate – hexanes) to give **S22** (9.09 g, 9.56 mmol, 91%). ^{1}H NMR (500 MHz, $CDCl_3$); δ (ppm): 8.03 (dd, *J* = 8.3, 1.4 Hz, 2H), 7.52 (ddt, *J* = 8.7, 7.3, 1.4 Hz, 1H), 7.45 – 7.34 (m, 4H), 7.33 – 7.26 (m, 6H), 5.44 (s, 1H), 4.82 – 4.73 (m, 2H), 4.65 – 4.56 (m, 2H), 4.48 – 4.38 (m, 2H), 4.36 – 4.30 (m, 2H), 4.06 (d, *J* = 2.7 Hz, 2H), 3.98 – 3.94 (m, 2H), 3.93 – 3.81 (m, 2H), 3.63 – 3.50 (m, 3H), 3.35 (s, 3H), 3.33 – 3.28 (m, 1H), 2.87 (s, 1H), 2.87 (s, 1H), 1.99 (d, *J* = 7.1 Hz, 2H), 1.96 – 1.89 (m, 2H), 1.85 – 1.75 (m, 2H), 1.63 (dd, *J* = 14.3, 6.2 Hz, 1H), 1.14 – 1.00 (m, 18H), 0.94 – 0.85 (m, 3H), 0.80 (d, *J* = 6.9 Hz, 3H), 0.76 (d, *J* = 6.8 Hz, 3H).



Alcohol (S23). Tetra-*n*-butylammonium fluoride (1.0 M in THF, 13.5 mL, 13.47

mmol) was added to a solution of **S22** (8.76 g, 8.98 mmol) in THF (160 mL) at 23 °C. After 1 h and 10 min the reaction was quenched with a saturated aqueous solution of ammonium chloride. The aqueous layer was extracted with ethyl acetate (3x200 mL). The combined organic layers were washed with brine, dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica, 20% ethyl acetate – hexanes then 60% ethyl acetate – hexanes) to give **S23** (7.12 g, 8.14 mmol, 96%). ^{1}H NMR (600 MHz, $CDCl_3$); δ (ppm): 8.07 – 7.94 (m, 2H), 7.53 (td, *J* = 7.3, 1.4 Hz, 1H), 7.47 – 7.35 (m, 3H), 7.35 – 7.28 (m, 5H), 5.75 (d, *J* = 3.7 Hz, 1H), 5.46 (s, 1H), 4.77 (d, *J* = 6.7 Hz, 1H), 4.67 (d, *J* = 6.7 Hz, 1H), 4.61 (d, *J* = 1.0 Hz, 2H), 4.52 – 4.40 (m, 2H), 4.34 (d, *J* = 1.9 Hz, 2H), 3.97 – 3.86 (m, 4H), 3.82 (t, *J* = 9.1 Hz, 1H), 3.75 – 3.61 (m, 2H), 3.54 – 3.44 (m, 1H), 3.38 – 3.29 (m, 3H), 3.25 (dd, *J* = 9.3, 6.6 Hz, 1H), 2.83 (s, 1H), 2.57 (t, *J* = 7.1 Hz, 1H), 2.04 (s, 3H), 1.94 – 1.75 (m, 3H), 1.61 (dd, *J* = 14.3, 6.7 Hz, 1H), 0.98 – 0.87 (m, 2H), 0.83 (d, *J* = 6.9 Hz, 2H), 0.79 (d, *J* = 6.8 Hz, 2H).

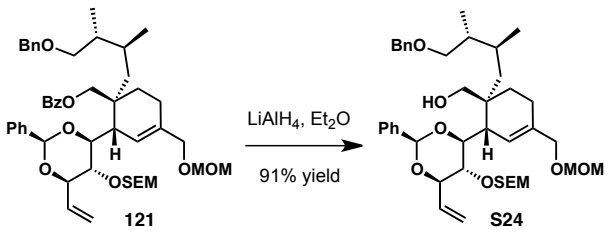


Alkene (121). Dimethylsulfoxide (1.5 mL, 20.86 mmol) was added to a solution of oxalyl chloride (0.9 mL, 10.43 mmol) in dichloromethane (98 mL) at -78 °C. After 20 min, a solution of **S23** (7.12 g, 8.69 mmol) in dichloromethane (49 mL total with rinses) was then added dropwise, and the mixture was stirred for 25 min.

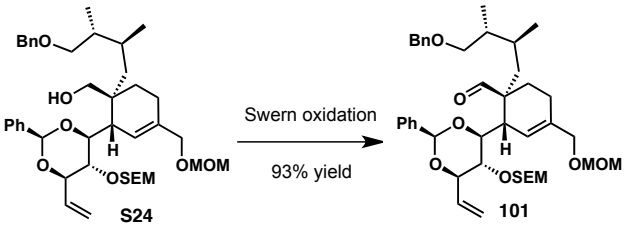
Triethylamine (4.4 mL, 31.29 mmol) was added at -78 °C and after 10 min the mixture was brought to 0 °C and stirred for 20 min. The reaction was quenched with 1 M aqueous HCl (100 mL). The aqueous layer was extracted with ethyl acetate (3x150 mL).

The combined organic layers were washed with water and saturated aqueous sodium bicarbonate, dried with sodium sulfate, and concentrated to give the crude aldehyde, which was used without further purification.

Potassium bis(trimethylsilyl)amide (0.5 M in toluene, 34.8 ml, 17.38 mmol) was added to a mixture of methyltriphenylphosphonium bromide (8.07 g, 22.60 mmol) in toluene (87 mL) at 0 °C. After 45 min, a solution of the crude aldehyde dissolved in toluene (51 mL total with rinses) was added dropwise. After 30 min the solution was allowed to warm to 23 °C and stirred for 1 h. Quench with a saturated aqueous solution of ammonium chloride. The aqueous layer was extracted with ethyl acetate (3x150 mL). The combined organic layers were washed with brine, dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica, 20% ethyl acetate – hexanes) to give **121** (6.49 g, 7.91 mmol, 91%). ^{1}H NMR (600 MHz, $CDCl_3$); δ (ppm): 8.05 – 8.01 (m, 1H), 7.55 – 7.50 (m, 1H), 7.46 – 7.42 (m, 1H), 7.41 – 7.37 (m, 1H), 7.34 – 7.28 (m, 4H), 6.08 (ddd, *J* = 17.1, 10.5, 6.5 Hz, 1H), 5.74 (d, *J* = 2.6 Hz, 1H), 5.55 – 5.41 (m, 2H), 5.28 (dt, *J* = 10.6, 1.1 Hz, 1H), 4.72 (d, *J* = 6.5 Hz, 1H), 4.67 (d, *J* = 6.4 Hz, 1H), 4.64 – 4.56 (m, 2H), 4.50 – 4.41 (m, 1H), 4.40 – 4.32 (m, 1H), 4.11 – 4.04 (m, 1H), 3.95 (s, 1H), 3.87 (dd, *J* = 9.2, 4.1 Hz, 1H), 3.65 – 3.47 (m, 2H), 3.38 – 3.29 (m, 3H), 3.24 (dd, *J* = 9.3, 6.6 Hz, 1H), 2.86 (s, 1H), 1.92 (dt, *J* = 13.3, 6.5 Hz, 1H), 1.88 – 1.81 (m, 1H), 1.78 (dt, *J* = 13.1, 6.4 Hz, 1H), 1.63 (dd, *J* = 14.4, 6.7 Hz, 1H), 0.93 – 0.85 (m, 2H), 0.82 (d, *J* = 6.9 Hz, 2H), 0.77 (d, *J* = 6.8 Hz, 2H).

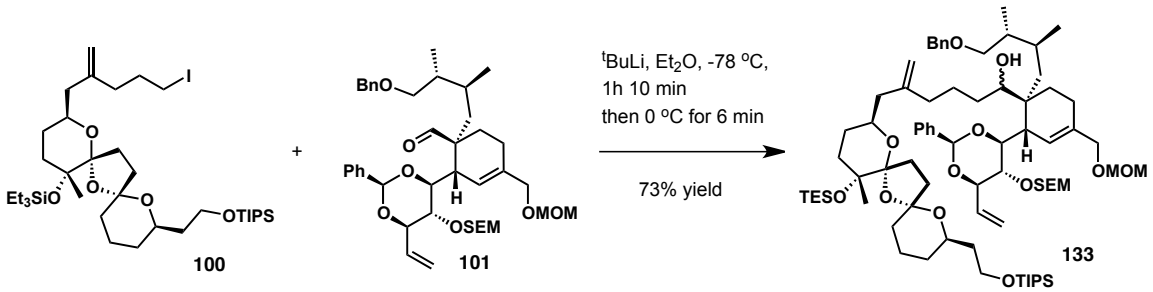


Alcohol (S24). Lithium aluminum hydride (1.84 g, 48.56 mmol) was carefully added to a solution of **121** (6.49 g, 7.96 mmol) in dry ether (185 mL) at -78 °C. The reaction mixture stirred for 1 h and additional lithium aluminum hydride (0.91 g, 23.88 mmol) was added. At 2 h the solution was placed in a 0 °C ice bath. After 10 min, an additional 1000 mL of ether was added. Water (2.75 mL) was added dropwise with vigorous stirring. After 5 min, 3 M aqueous NaOH (2.75 mL) was added. After an additional 5 min, water (8.25 mL) was added and the mixture was allowed to stir at 23 °C for 2 h. The white precipitate was filtered off, washed with dichloromethane, concentrated, and the residue was purified by column chromatography (silica, 30% ethyl acetate – hexanes) to give **S24** (6.26 g, 7.24 mmol, 91%). ^{1}H NMR (600 MHz, $CDCl_3$); δ (ppm): 7.47 (dd, *J* = 7.4, 2.3 Hz, 2H), 7.41 – 7.35 (m, 3H), 7.32 (tdd, *J* = 11.2, 10.5, 5.7, 2.0 Hz, 6H), 6.07 (ddd, *J* = 17.1, 10.5, 6.6 Hz, 1H), 5.71 (d, *J* = 2.6 Hz, 1H), 5.53 (s, 1H), 5.49 (ddd, *J* = 18.0, 3.3, 1.9 Hz, 1H), 5.33 – 5.30 (m, 1H), 4.74 (s, 2H), 4.70 (d, *J* = 6.0 Hz, 2H), 4.63 – 4.56 (m, 2H), 4.46 (q, *J* = 12.1 Hz, 2H), 4.14 – 4.06 (m, 1H), 3.94 (s, 2H), 3.84 (dd, *J* = 9.1, 4.9 Hz, 1H), 3.67 (dd, *J* = 11.3, 6.4 Hz, 1H), 3.65 – 3.57 (m, 2H), 3.47 (dd, *J* = 11.3, 6.7 Hz, 1H), 3.37 – 3.30 (m, 3H), 3.24 (dd, *J* = 9.3, 6.6 Hz, 1H), 2.83 (s, 1H), 2.22 (t, *J* = 6.5 Hz, 1H), 1.98 (s, 2H), 1.85 – 1.79 (m, 1H), 1.79 – 1.67 (m, 3H), 1.61 (t, *J* = 6.0 Hz, 1H), 1.47 (dd, *J* = 14.3, 7.3 Hz, 1H), 0.98 – 0.85 (m, 2H), 0.85 – 0.75 (m, 6H).



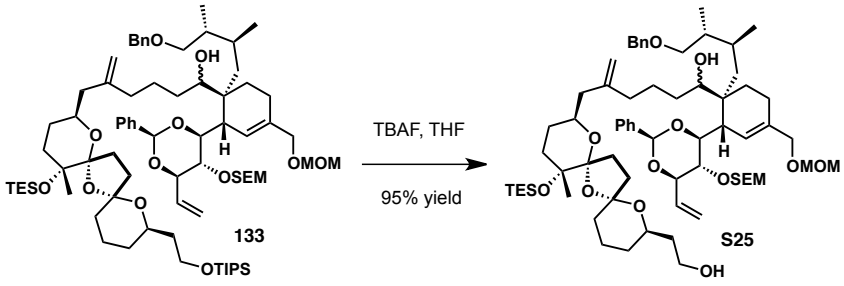
Aldehyde (101). Dimethylsulfoxide (1.23 mL, 17.24 mmol) was added to a solution of oxalyl chloride (0.73 ml, 8.62 mmol) in dichloromethane (81 ml) at -78 °C. After 20

min, a solution of **S24** (5.11 g, 7.18 mmol) in dichloromethane (41 ml total with rinses) was added dropwise, and the mixture was stirred for 25 min. Triethylamine (3.61 ml, 25.87 mmol) was added at -78 °C and, after 10 min the mixture was brought to 0 °C and stirred for 20 min. The reaction was quenched with 1 M aqueous HCl (100 mL). The aqueous layer was extracted with ethyl acetate (3x100 mL). The combined organic layers were washed with water and saturated aqueous sodium bicarbonate, dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica, 20% ethyl acetate – hexanes) to give aldehyde **101** (5.2 g, 6.68 mmol, 93%). 1H NMR (600 MHz, $CDCl_3$); δ (ppm): 9.56 (s, 1H), 7.50 – 7.40 (m, 1H), 7.38 – 7.27 (m, 4H), 6.01 (ddd, *J* = 17.2, 10.5, 6.8 Hz, 1H), 5.91 (s, 1H), 5.51 – 5.42 (m, 1H), 5.30 (ddd, *J* = 10.4, 1.7, 0.9 Hz, 1H), 5.30 (ddd, *J* = 10.4, 1.7, 0.9 Hz, 1H), 4.66 (d, *J* = 6.4 Hz, 1H), 4.63 – 4.55 (m, 1H), 4.53 – 4.40 (m, 2H), 4.12 – 4.02 (m, 1H), 3.93 (s, 1H), 3.68 – 3.55 (m, 2H), 3.43 (t, *J* = 8.8 Hz, 1H), 3.35 (s, 2H), 3.26 (dd, *J* = 9.3, 6.4 Hz, 1H), 2.96 (d, *J* = 8.7 Hz, 1H), 2.13 – 1.98 (m, 2H), 1.98 – 1.89 (m, 1H), 1.84 (d, *J* = 22.0 Hz, 1H), 1.80 – 1.70 (m, 2H), 1.01 – 0.85 (m, 2H), 0.84 (d, *J* = 6.9 Hz, 2H), 0.65 (d, *J* = 6.5 Hz, 2H), 0.01 (s, 6H).



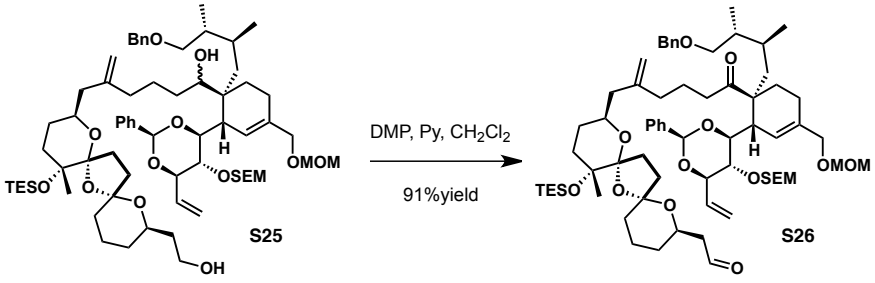
Alcohol (133). A solution of iodide **100** (3.28 g, 4.28 mmol) in ether (16 mL) was added dropwise to freshly titrated *t*-BuLi (1.66 M in pentane, 5.20 mL, 8.58 mmol) in ether (30 mL) at -78 °C and stirred for 1 h 10 min. A solution of aldehyde **101** (3.04 g, 4.28 mmol) in ether (16 mL) was added to the reaction mixture dropwise and stirred at -

78 °C. After 1 h, the reaction mixture was placed in a 0 °C bath and continued to stir for and additional 6 min. The reaction was quenched with saturated aqueous ammonium chloride and diluted with dichloromethane. The aqueous layer was extracted with dichloromethane (4x150 mL). The combined organic layers were washed with a saturated aqueous solution of sodium bicarbonate, dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica, 15% ethyl acetate – hexanes) to afford **133** (4.18 g, 3.12 mmol, 73%). ^{1}H NMR (600 MHz, $CDCl_3$); δ (ppm): 7.51 – 7.44 (m, 1H), 7.38 – 7.28 (m, 4H), 6.11 (ddt, *J* = 17.1, 10.6, 6.5 Hz, 1H), 5.79 – 5.67 (m, 1H), 5.54 – 5.44 (m, 1H), 5.32 – 5.25 (m, 1H), 4.85 (d, *J* = 12.1 Hz, 1H), 4.79 – 4.69 (m, 1H), 4.67 (dd, *J* = 6.5, 2.9 Hz, 1H), 4.64 – 4.58 (m, 1H), 4.51 – 4.41 (m, 1H), 4.01 (dq, *J* = 30.1, 7.1, 6.6 Hz, 1H), 3.87 – 3.78 (m, 1H), 3.67 – 3.57 (m, 1H), 3.57 – 3.47 (m, 1H), 3.41 – 3.33 (m, 2H), 3.32 (s, 1H), 3.27 – 3.19 (m, 1H), 2.88 (s, 1H), 2.75 (d, J = 9.8 Hz, 1H), 2.27 – 2.13 (m, 2H), 2.13 – 1.94 (m, 4H), 1.83 – 1.70 (m, 3H), 1.64 (dt, *J* = 14.0, 8.0 Hz, 2H), 1.49 – 1.31 (m, 3H), 1.31 – 1.20 (m, 2H), 1.11 – 1.00 (m, 9H), 1.00 – 0.88 (m, 6H), 0.80 (ddd, *J* = 18.2, 9.5, 6.9 Hz, 3H), 0.56 (q, *J* = 7.9 Hz, 3H), 0.01 (d, *J* = 6.1 Hz, 6H).



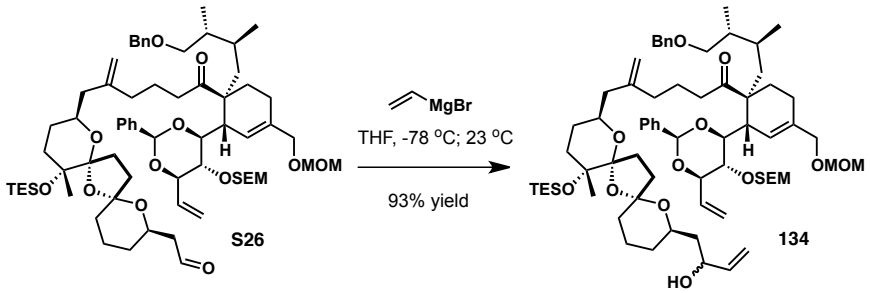
Diol (S25). Tetra-*n*-butylammonium fluoride (1.0 M in THF, 8.41 mL, 8.41 mmol) was added to a solution of **133** (5.4 g, 4.00 mmol) in THF (57 mL) at 23 °C. After 1 h 30 min, a saturated aqueous solution of ammonium chloride was added. The aqueous layer

was extracted with ethyl acetate (4x200 mL). The combined organic layers were washed with brine, dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica, 30% ethyl acetate – hexanes) to give the desired product **S25** (4.03 g, 3.80 mmol, 95%). ^{1}H NMR (600 MHz, $CDCl_3$); δ (ppm): 7.50 – 7.43 (m, 1H), 7.38 – 7.28 (m, 4H), 6.10 (dddd, *J* = 17.0, 10.6, 6.4, 4.7 Hz, 1H), 5.81 – 5.67 (m, 1H), 5.58 – 5.42 (m, 1H), 5.36 – 5.25 (m, 1H), 4.82 – 4.70 (m, 2H), 4.66 (dd, *J* = 9.6, 6.5 Hz, 1H), 4.63 – 4.56 (m, 1H), 4.50 – 4.41 (m, 1H), 4.10 – 3.99 (m, 2H), 3.93 (s, 2H), 3.71 – 3.59 (m, 2H), 3.59 – 3.47 (m, 2H), 3.35 (d, *J* = 3.0 Hz, 2H), 3.29 (dd, *J* = 9.2, 7.4 Hz, 1H), 3.23 (td, *J* = 8.9, 6.9 Hz, 1H), 2.89 (s, 1H), 2.36 (ddd, *J* = 28.2, 14.1, 4.9 Hz, 1H), 2.28 – 2.11 (m, 2H), 2.07 (dd, *J* = 14.1, 7.6 Hz, 2H), 2.01 – 1.92 (m, 3H), 1.92 – 1.85 (m, 2H), 1.84 – 1.71 (m, 4H), 1.71 – 1.55 (m, 5H), 1.54 – 1.41 (m, 2H), 1.38 – 1.25 (m, 4H), 1.00 – 0.88 (m, 7H), 0.85 – 0.70 (m, 4H), 0.56 (q, *J* = 7.9 Hz, 4H), 0.00 (d, *J* = 1.0 Hz, 6H).



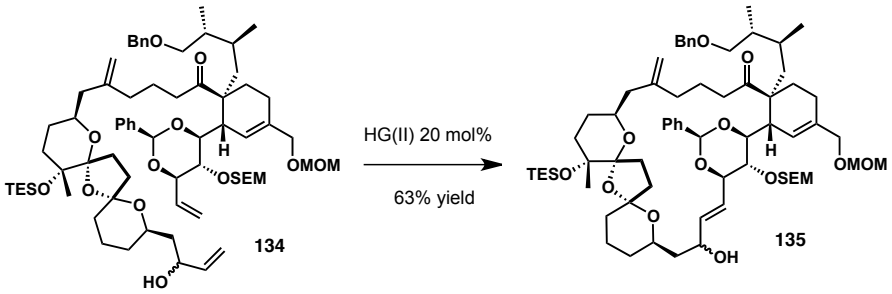
Keto Aldehyde (S26). Dess-Martin periodinane (7.76 g, 18.29 mmol) was added to a solution of **S25** (4.85 g, 4.57 mmol) and pyridine (4.44 mL, 54.87 mmol) in dichloromethane (46 mL) at 23 °C. At 1 h, Dess-Martin periodinane (2.42 g, 2.28 mmol) was added to the reaction mixture and the reaction continued to stir for an additional 1 h. The reaction was quenched with a 1:1 mixture of saturated aqueous sodium bicarbonate – saturated aqueous sodium thiosulfate and dilute with dichloromethane. The aqueous layer

was extracted with dichloromethane (3x200 mL). The combined organic layers was washed with water, 1M HCl (100 mL), water, a saturated aqueous solution of sodium bicarbonate, dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica, 20% ethyl acetate – hexanes) to give **S26** (4.39 g, 4.15 mmol, 91%). ^{1}H NMR (600 MHz, $CDCl_3$); δ (ppm): 9.71 (t, *J* = 2.4 Hz, 1H), 7.50 – 7.41 (m, 1H), 7.31 (td, *J* = 7.9, 6.0 Hz, 4H), 6.15 (ddd, *J* = 17.0, 10.5, 6.2 Hz, 1H), 5.77 (d, *J* = 4.6 Hz, 1H), 5.48 (s, 1H), 5.34 – 5.23 (m, 2H), 4.78 (d, *J* = 1.8 Hz, 1H), 4.72 – 4.62 (m, 2H), 4.55 (d, *J* = 2.5 Hz, 1H), 4.43 (s, 1H), 4.38 (ddt, *J* = 13.2, 7.6, 4.2 Hz, 1H), 4.11 – 4.03 (m, 1H), 3.88 (s, 1H), 3.80 (dd, *J* = 9.3, 3.9 Hz, 1H), 3.65 (td, *J* = 9.6, 7.2 Hz, 1H), 3.53 (td, *J* = 9.6, 7.3 Hz, 1H), 3.44 (t, *J* = 9.0 Hz, 1H), 3.32 (s, 2H), 3.20 (dd, *J* = 9.3, 6.7 Hz, 1H), 3.06 (s, 1H), 2.59 – 2.30 (m, 3H), 2.23 – 2.04 (m, 3H), 2.03 – 1.84 (m, 4H), 1.83 – 1.69 (m, 4H), 1.64 (d, *J* = 10.1 Hz, 2H), 1.62 – 1.40 (m, 6H), 1.28 (s, 4H), 0.93 (q, *J* = 7.5, 7.0 Hz, 7H), 0.80 (d, *J* = 6.8 Hz, 2H), 0.65 (d, *J* = 5.7 Hz, 2H), 0.56 (q, *J* = 7.9 Hz, 4H), 0.02 (s, 6H).



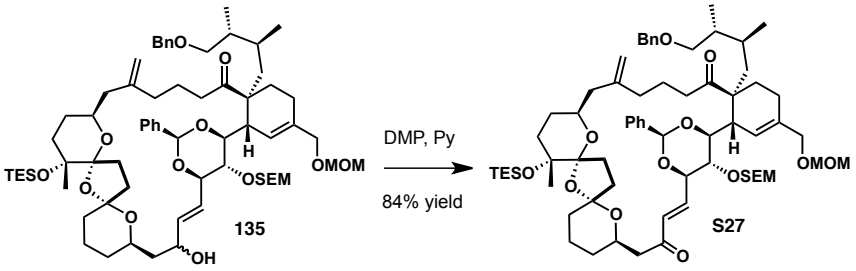
Allylic Alcohol (134). Vinylmagnesium bromide (0.77 M in THF, 27.0 mL, 20.77 mmol) was added to a solution of **S26** (4.39 g, 4.15 mmol) in THF (32 mL) at -78 °C. After 5 min, the solution was placed in a -30 °C dry ice - acetone bath and was warmed to - 20 °C over 1 h 25 min. The reaction mixture was quenched with a saturated aqueous solution of ammonium chloride and diluted with dichloromethane. The aqueous layer was

extracted with dichloromethane (4x100 mL). The combined organic layers were washed with a saturated aqueous solution of sodium bicarbonate, dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica, 20% ethyl acetate – hexanes) to give the desired product **134** (4.20 g, 3.86 mmol, 93%). ^{1}H NMR (600 MHz, $CDCl_3$); δ (ppm): 7.47 – 7.42 (m, 1H), 7.31 (td, *J* = 8.0, 6.0 Hz, 4H), 6.15 (dddd, *J* = 17.0, 10.6, 6.2, 1.5 Hz, 1H), 5.92 – 5.79 (m, 1H), 5.77 (d, *J* = 4.4 Hz, 1H), 5.53 – 5.45 (m, 1H), 5.34 – 5.26 (m, 1H), 5.20 (ddt, *J* = 17.2, 5.2, 1.7 Hz, 1H), 4.99 (ddt, *J* = 10.5, 6.0, 1.6 Hz, 1H), 4.75 – 4.70 (m, 1H), 4.70 – 4.62 (m, 1H), 4.55 (dd, *J* = 2.3, 1.1 Hz, 1H), 4.43 (s, 1H), 4.15 (d, *J* = 10.4 Hz, 1H), 4.12 – 3.99 (m, 2H), 3.88 (d, *J* = 8.1 Hz, 1H), 3.79 – 3.71 (m, 5H), 3.65 (td, *J* = 9.6, 7.2 Hz, 1H), 3.53 (td, *J* = 9.5, 7.0 Hz, 1H), 3.44 (td, *J* = 9.0, 1.9 Hz, 1H), 3.39 – 3.27 (m, 3H), 3.20 (dd, *J* = 9.3, 6.8 Hz, 1H), 3.10 – 3.00 (m, 1H), 2.56 – 2.28 (m, 1H), 2.27 – 2.06 (m, 1H), 2.27 – 2.03 (m, 3H), 2.02 – 1.89 (m, 3H), 1.89 – 1.68 (m, 10H), 1.56 (m, 7H), 1.37 – 1.22 (m, 3H), 1.02 – 0.87 (m, 6H), 0.86 – 0.75 (m, 2H), 0.70 – 0.61 (m, 2H), 0.56 (qd, *J* = 7.9, 1.3 Hz, 3H), 0.11 – 0.04 (m, 6H).



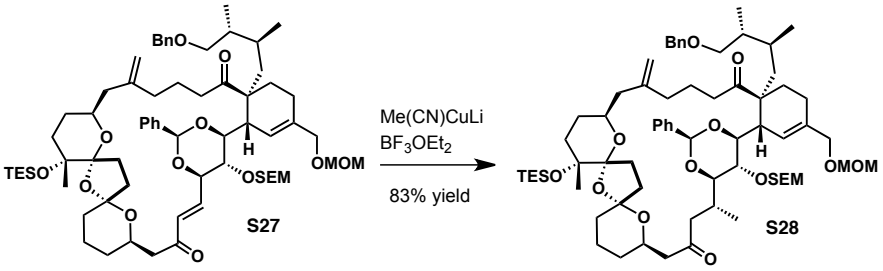
Macrocycle (135). Hoveyda-Grubbs catalyst, 2nd generation (0.166 g, 0.264 mmol) was added to a solution of **134** (3.21 g, 0.2.64 mmol) in degassed dichloromethane (528 mL). The reaction was then refluxed at 44 °C for 21 h. After cooling to 23 °C, the reaction mixture was concentrated on a rotary evaporator. The residue was purified by

column chromatography (silica, 10% ethyl acetate – dichloromethane) to give desired macrocycle **135** (2.00 g, 1.66 mmol, 63%). ^{1}H NMR (600 MHz, $CDCl_3$); δ (ppm): 7.54 – 7.49 (m, 1H), 7.39 – 7.28 (m, 5H), 6.08 – 5.87 (m, 2H), 5.72 (d, *J* = 4.7 Hz, 1H), 4.91 (s, 1H), 4.82 – 4.76 (m, 1H), 4.76 – 4.66 (m, 2H), 4.61 – 4.54 (m, 2H), 4.49 (d, *J* = 6.7 Hz, 1H), 4.40 (d, *J* = 9.2 Hz, 2H), 4.24 – 4.14 (m, 1H), 4.02 – 3.94 (m, 1H), 3.92 – 3.85 (m, 2H), 3.92 – 3.85 (m, 2H), 3.33 (d, *J* = 1.2 Hz, 2H), 3.27 (dd, *J* = 9.0, 6.5 Hz, 1H), 3.12 (ddd, *J* = 13.4, 9.2, 7.0 Hz, 1H), 3.08 – 2.98 (m, 1H), 2.42 (s, 1H), 2.27 – 2.07 (m, 4H), 2.07 – 1.87 (m, 4H), 1.87 – 1.74 (m, 3H), 1.74 – 1.56 (m, 7H), 1.47 (qd, *J* = 13.4, 12.7, 4.6 Hz, 2H), 1.40 – 1.30 (m, 2H), 1.27 (d, *J* = 4.2 Hz, 3H), 0.94 (td, *J* = 7.9, 2.6 Hz, 8H), 0.70 (dd, *J* = 10.0, 6.7 Hz, 2H), 0.64 (dd, *J* = 17.7, 6.1 Hz, 2H), 0.56 (qd, *J* = 7.9, 3.8 Hz, 4H), 0.02 (s, 6H).



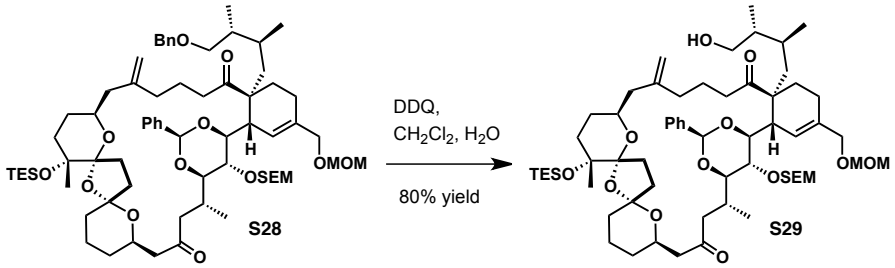
Enone (S27). Dess-Martin periodinane (2.14 g, 5.05 mmol) was added to a solution of **135** (2.0 g, 1.68 mmol) and pyridine (1.3 mL, 15.15 mmol) in dichloromethane (84 mL) at 23 °C. After 2 h 30 min, the mixture was diluted with dichloromethane and a 1:1 mixture of saturated aqueous sodium bicarbonate – saturated aqueous sodium thiosulfate was added to the reaction flask. The aqueous layer was extracted with dichloromethane (3x100 mL). The combined organic layers were washed with water, 1M HCl (100 mL), water, a saturated aqueous solution of sodium bicarbonate, dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica, 20% ethyl

acetate – hexanes) to give the desired product **S27** (1.67 g, 1.41 mmol, 84%). ^{1}H NMR (600 MHz, $CDCl_3$); δ (ppm): 7.51 – 7.41 (m, 2H), 7.40 – 7.27 (m, 6H), 6.97 (dd, *J* = 16.0, 4.4 Hz, 1H), 6.48 (dd, *J* = 16.1, 1.8 Hz, 1H), 5.85 (s, 1H), 4.99 – 4.91 (m, 1H), 4.74 (dd, *J* = 29.8, 7.1 Hz, 4H), 4.59 (d, *J* = 1.4 Hz, 2H), 4.41 (s, 3H), 3.90 (s, 2H), 3.84 (s, 1H), 3.73 – 3.60 (m, 2H), 3.35 (s, 3H), 3.28 (dd, *J* = 9.3, 6.7 Hz, 1H), 3.13 (dd, *J* = 9.3, 7.0 Hz, 1H), 2.96 (s, 1H), 2.86 (dd, *J* = 15.6, 4.0 Hz, 1H), 2.70 (dd, *J* = 15.7, 9.1 Hz, 1H), 2.41 (s, 1H), 2.29 (ddd, *J* = 16.7, 9.5, 6.0 Hz, 1H), 2.21 – 2.08 (m, 4H), 2.05 (td, *J* = 12.0, 8.3 Hz, 2H), 2.00 – 1.86 (m, 5H), 1.86 – 1.77 (m, 2H), 1.77 – 1.68 (m, 4H), 1.54 – 1.46 (m, 2H), 1.41 (td, *J* = 13.0, 4.2 Hz, 1H), 1.24 (s, 3H), 1.22 – 1.13 (m, 1H), 0.94 (t, *J* = 7.9 Hz, 10H), 0.70 (dd, *J* = 12.8, 6.4 Hz, 5H), 0.56 (q, *J* = 7.9 Hz, 6H), 0.03 (s, 6H).



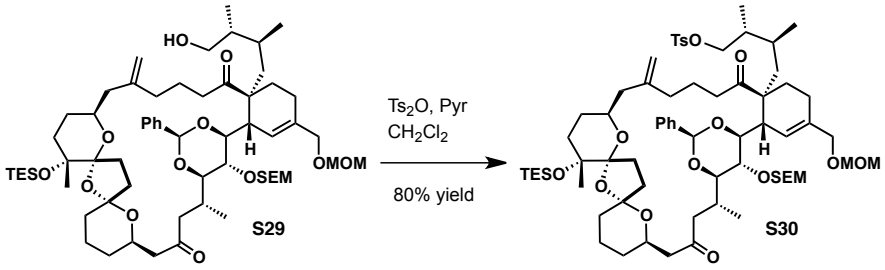
Diketone (S28). Methyl lithium (1.55 M in ether, 6.18 mL, 9.57 mmol) was added to copper cyanide (0.883 g, 9.85 mmol) in THF (12 mL) at -20 °C. The solution was then placed in a 0 °C ice bath and stirred for 10 min. The clear solution was cooled to -78 °C and freshly distilled boron trifluoride diethyl etherate (1.15 mL, 9.29 mmol) was added dropwise to the reaction mixture. After 5 min, a solution of **S27** (1.67 g, 1.41 mmol) in THF (15 mL total with rinses) was added dropwise to the yellow solution and the mixture was stirred at -78 °C. After 1 h 45 min, a 9:1 mixture of saturated aqueous ammonium chloride: ammonia was added to the solution at -78 °C. The ice bath was removed and the solution was stirred vigorously for 1 h at 23 °C. The solution was diluted with ethyl

acetate. The aqueous layer was extracted with ethyl acetate (3x100 mL). The combined organic layers were washed with a 9:1 mixture of saturated aqueous ammonium chloride: ammonia (100 mL), brine, dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica, 25% ethyl acetate - hexanes) to give **S28** (1.40 g, 1.17 mmol, 83%). ^{1}H NMR (600 MHz, $CDCl_3$); δ (ppm): 7.42 – 7.36 (m, 2H), 7.36 – 7.27 (m, 6H), 5.81 (s, 1H), 5.44 (s, 1H), 4.98 (s, 1H), 4.77 – 4.65 (m, 3H), 4.63 – 4.53 (m, 2H), 4.42 (s, 2H), 4.27 (s, 1H), 4.02 (s, 1H), 3.93 (s, 2H), 3.71 – 3.52 (m, 4H), 3.48 (d, *J* = 7.5 Hz, 1H), 3.41 – 3.25 (m, 5H), 3.25 – 3.14 (m, 2H), 2.70 (dd, *J* = 18.1, 3.5 Hz, 1H), 2.64 – 2.52 (m, 3H), 2.51 – 2.39 (m, 2H), 2.27 (ddt, *J* = 17.3, 12.7, 6.0 Hz, 1H), 2.19 – 2.09 (m, 4H), 2.08 – 1.69 (m, 15H), 1.54 (d, *J* = 0.6 Hz, 7H), 1.42 – 1.25 (m, 7H), 1.12 (d, *J* = 6.8 Hz, 3H), 1.00 – 0.89 (m, 11H), 0.81 (dd, *J* = 10.9, 6.5 Hz, 3H), 0.73 (d, *J* = 6.9 Hz, 2H), 0.56 (q, *J* = 7.9 Hz, 6H), 0.02 (d, *J* = 9.5 Hz, 6H).



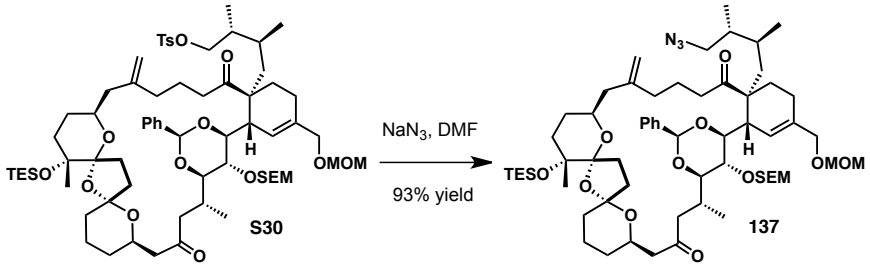
Alcohol (S29). 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (1.97 g, 8.73 mmol), was added to a solution of diketone **S28** (2.1 g, 1.74 mmol) in dichloromethane (87 mL) and water (9 mL) at 23 °C and stirred vigorously for 1.5 h. The reaction mixture was diluted with dichloromethane and quenched with a 1:1 mixture of saturated aqueous sodium bicarbonate and saturated aqueous sodium thiosulfate. The aqueous layer was extracted with dichloromethane (3x100 mL). The combined organic layers were dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica,

40% ethyl acetate – hexanes) to deliver **S29** (0.640 g, 0.574 mmol, 33%) and recovered starting material (**S28**) (1.36 g, 1.11 mmol, 64%). The recovered starting material (**S28**) was re-submitted to the reaction conditions described above (the reaction time for additional reactions was increased to 2 h). Four recycles of the recovered starting material (**S28**) were performed. The total amount of product isolated from the 5 reactions was 1.55 g, 1.39 mmol, 80%. ^{1}H NMR (600 MHz, $CDCl_3$); δ (ppm): 7.42 – 7.27 (m, 3H), 5.82 (s, 1H), 5.45 (s, 1H), 4.99 (s, 1H), 4.77 – 4.66 (m, 2H), 4.60 (q, *J* = 6.5 Hz, 2H), 3.94 (s, 1H), 3.69 – 3.53 (m, 3H), 3.36 (s, 3H), 3.23 (d, *J* = 8.7 Hz, 1H), 2.70 (dd, *J* = 18.0, 3.6 Hz, 1H), 2.58 (ddd, *J* = 19.7, 11.9, 5.0 Hz, 2H), 2.52 – 2.37 (m, 2H), 2.22 – 2.07 (m, 3H), 2.01 – 1.90 (m, 2H), 1.87 (td, *J* = 15.8, 15.3, 4.2 Hz, 1H), 1.85 – 1.66 (m, 5H), 1.45 – 1.28 (m, 4H), 1.12 (d, *J* = 6.8 Hz, 2H), 0.97 – 0.86 (m, 8H), 0.82 (d, *J* = 6.2 Hz, 2H), 0.71 (d, *J* = 6.9 Hz, 2H), 0.56 (q, *J* = 7.9 Hz, 4H), 0.03 (s, 6H).



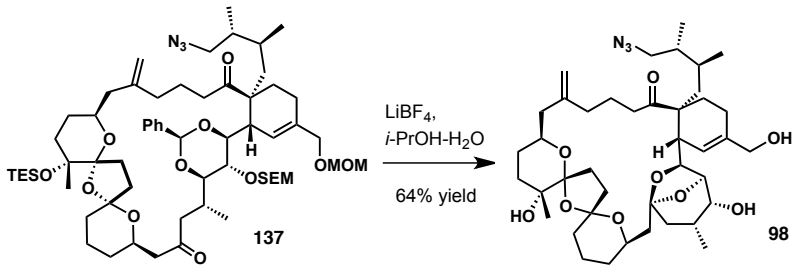
Tosylate (S30). *p*-Toluenesulfonic anhydride (1.1 g, 3.31 mmol) was added to a solution of pyridine (2.90 mL, 33.37 mmol) and alcohol **S29** (1.50 g, 1.34 mmol) in dichloromethane (80 mL) at 23 °C for 20 min. The reaction mixture was diluted with dichloromethane and water. The aqueous layer was extracted with dichloromethane (4x100 mL). The combined organic layers were washed with 1 M HCl (100 mL), water, and a saturated aqueous solution of sodium bicarbonate, dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica, 20% ethyl

acetate – hexanes) to deliver **S30** (1.49, 1.18 mmol, 88%). ^{1}H NMR (500 MHz, $CDCl_3$); δ (ppm): 7.80 – 7.69 (m, 3H), 7.40 – 7.30 (m, 9H), 5.80 (s, 1H), 5.41 (s, 1H), 4.98 (s, 1H), 4.71 (d, *J* = 16.1 Hz, 4H), 4.64 – 4.55 (m, 2H), 4.27 (s, 1H), 3.93 (s, 2H), 3.77 (ddd, *J* = 29.7, 9.5, 7.0 Hz, 2H), 3.71 – 3.51 (m, 5H), 3.36 (s, 4H), 3.20 (d, *J* = 9.0 Hz, 1H), 2.70 (dd, *J* = 18.1, 3.5 Hz, 1H), 2.65 – 2.51 (m, 3H), 2.51 – 2.39 (m, 7H), 2.22 – 2.09 (m, 3H), 2.09 – 1.95 (m, 5H), 1.96 – 1.84 (m, 2H), 1.84 – 1.65 (m, 5H), 1.55 (s, 9H), 1.35 – 1.22 (m, 8H), 1.12 (d, *J* = 6.8 Hz, 3H), 0.94 (t, *J* = 7.9 Hz, 17H), 0.75 (dd, *J* = 22.5, 6.5 Hz, 3H), 0.68 (d, *J* = 6.8 Hz, 3H), 0.57 (q, *J* = 7.9 Hz, 9H), 0.11 (s, 6H).



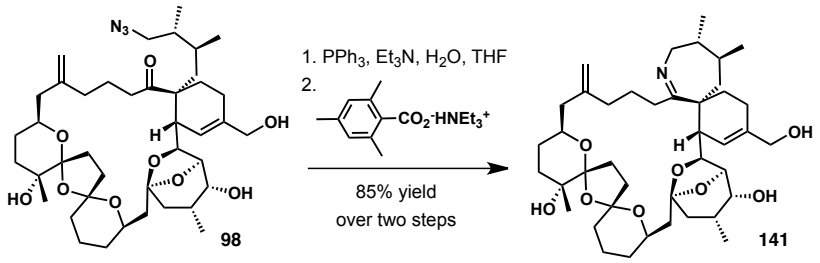
Azide (137). Sodium azide (4.71 g, 72.39 mmol) was added to a solution of **S30** (1.49 g, 1.17 mmol) in DMF (90 mL) and the reaction mixture was heated at 80 °C. After 1 h, the solution was cooled to 23 °C and diluted with water. The aqueous layer was extracted with ethyl acetate (5x75 mL). The combined organic phases were dried with sodium sulfate, concentrated, and dried under vacuum. The residue was purified by column chromatography (15% ethyl acetate - hexanes) to give the desired product **137** (1.21 g, 1.09 mmol, 93%). ^{1}H NMR (500 MHz, $CDCl_3$); δ (ppm): 7.42 – 7.28 (m, 3H), 5.81 (s, 1H), 5.45 (s, 1H), 4.98 (s, 1H), 4.79 – 4.66 (m, 2H), 4.60 (q, *J* = 6.4 Hz, 2H), 4.27 (q, *J* = 5.1 Hz, 1H), 4.02 (ddt, *J* = 11.6, 8.3, 4.3 Hz, 1H), 3.70 – 3.54 (m, 3H), 3.36 (s, 2H), 3.23 (d, *J* = 9.0 Hz, 1H), 3.09 (dd, *J* = 12.1, 7.1 Hz, 1H), 3.01 – 2.90 (m, 1H), 2.76 – 2.67 (m, 1H), 2.65 – 2.51 (m, 2H), 2.50 – 2.40 (m, 2H), 2.21 – 1.91 (m, 7H), 1.91 – 1.68 (m, 6H),

1.56 (s, 16H), 1.44 – 1.28 (m, 3H), 1.28 – 1.23 (m, 3H), 1.12 (d, J = 6.8 Hz, 2H), 0.94 (t, J = 7.9 Hz, 7H), 0.82 (d, J = 6.5 Hz, 2H), 0.74 (d, J = 6.8 Hz, 2H), 0.56 (q, J = 7.9 Hz, 4H), 0.03 (s, 6H).



Azido Triol (98). A 0.328 M solution of lithium tetrafluoroborate in 4% aq. isopropanol is prepared by dissolving lithium tetrafluoroborate (13.0 g, 139.0 mmol), in isopropanol (406 mL) and water (17.7 mL). Azide **137** (1.37 g, 1.21 mmol) is dissolved in a 4% aq. isopropanol – lithium tetrafluoroborate solution (0.328 M, 370 mL, 121 mmol) under argon and the mixture is heated at 90 °C in a sealed vessel. After 3 h, the solution was cooled to 23 °C, and carefully quenched with a saturated aqueous solution of sodium bicarbonate. The reaction mixture is diluted with ethyl acetate and additional water. The aqueous layer is extracted with ethyl acetate (5x250 mL). The combined organic layers were dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica, 60% then 100% ethyl acetate - hexanes) to give the desired product **98** (0.359 g, 0.484 mmol, 40%) and partially ketalized and partially deprotected intermediates. These intermediates were re-submitted to the reaction conditions listed above (3 recycles of the intermediates were performed). A total of 0.571 g, 0.770 mmol, 64% of azido triol **98** was isolated from the 4 reactions. ^{1}H NMR (600 MHz, $CDCl_3$); δ (ppm): 5.26 – 5.15 (m, 1H), 4.79 (d, J = 27.0 Hz, 2H), 4.35 (dd, J = 4.4, 1.9 Hz, 1H), 4.14 – 3.98 (m, 3H), 3.91 (dd, J = 11.6, 4.4 Hz, 1H), 3.57 (s, 1H), 3.17 (dd,

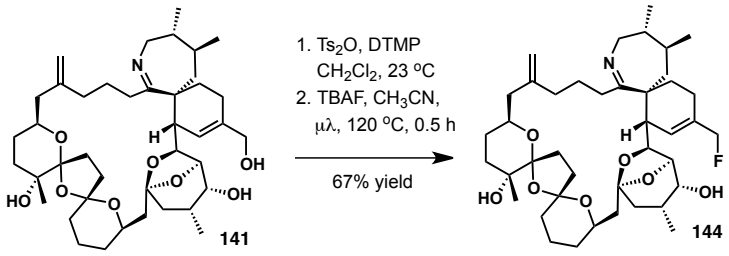
J = 7.2, 5.4 Hz, 2H), 2.90 (d, *J* = 11.7 Hz, 1H), 2.58 – 2.31 (m, 3H), 2.28 (dd, *J* = 12.6, 4.0 Hz, 1H), 2.22 – 1.47 (m, 28H), 1.42 – 1.17 (m, 8H), 0.97 (d, *J* = 6.8 Hz, 3H), 0.89 (d, *J* = 6.9 Hz, 3H), 0.79 (d, *J* = 6.9 Hz, 3H)



PnTX-OH (141). Triphenylphosphine (9.0 mg, 33.7 μmol) was added to a solution of azido triol **98** (10.0 mg, 13.5 μmol) in THF−H_2O (3:1, 4.5 mL). The reaction vessel was capped and heated at 55 °C for 36 h. After cooling, the reaction mixture was concentrated under reduced pressure. The crude material was dissolved in 5 mL of distilled toluene and concentrated and this was repeated three times. The crude residue was used immediately to the next step without further purification.

The crude residue was dissolved in 14 mL of a mixture prepared by dissolving 2,4,6-trimethylbenzoic acid (91.0 mg, 0.553 mmol) and triethylamine (77.0 μL, 0.553 mmol) in 19 mL of freshly distilled toluene. The solution was heated at 85 °C for 60 h. After cooling, the solution was directly applied on a silica column (silica, 70% ethyl acetate – hexanes, 1% triethylamine) to afford PnTX-OH **141** (8.0 mg, 11.5 μmol, 85%). ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 5.14 (s, 1H), 4.76 (d, *J* = 6.2 Hz, 2H), 4.46 (dd, *J* = 5.0, 2.0 Hz, 1H), 4.13 – 3.95 (m, 6H), 3.85 (dd, *J* = 11.6, 4.9 Hz, 2H), 3.78 (dd, *J* = 11.1, 4.8 Hz, 1H), 3.72 (dd, *J* = 4.2, 2.1 Hz, 1H), 3.61 (dd, *J* = 11.3, 1.4 Hz, 1H), 3.29 – 3.25 (m, 2H), 3.01 – 2.93 (m, 1H), 2.41 – 1.51 (m, 30H), 1.49 – 1.41 (m, 4H), 1.23 (s, 3H), 1.17 (d, *J* =

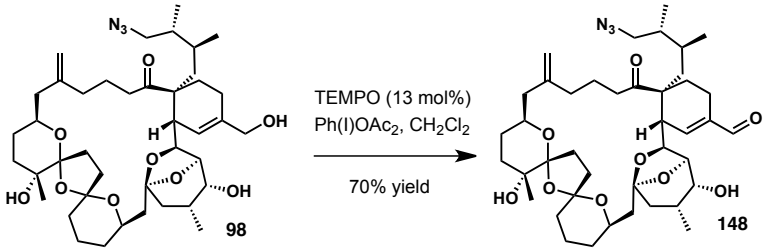
6.7 Hz, 3H), 1.02 (d, *J* = 6.7 Hz, 3H), 0.92 (d, *J* = 6.6 Hz, 3H). MS-ESI (*m*/z): $[M+H]^+$ calcd for $C_{41}H_{64}NO_8$, 698.46; found, 698.51.



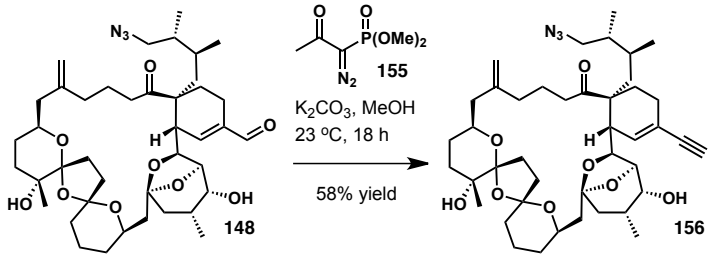
PnTX-Fluorine (144). *p*-Toluenesulfonic anhydride (19.0 mg, 57.4 μmol) was added to a solution of PnTX-OH **141** (4.0 mg, 5.74 μmol) in CH_2Cl_2 (600 μL) at 23 °C . The reaction mixture was stirred at 23 °C for 12 h. The resulting mixture was concentrated under reduced pressure and used immediately to the next step without further purification.

Tetrabutylammonium fluoride (1M in THF, 58.0 μL, 57.4 μmol) was added to a solution of crude tosylate dissolved in freshly distilled acetonitrile (600 μL) in a microwave vial and capped. The reaction mixture was heated by microwave irradiation at 120 °C for 30 min. The mixture was diluted with ethyl acetate (4 mL) and water (4 mL). The aqueous later was extracted with ethyl acetate (3x5 mL). The combined organic layers were washed with brine, dried over sodium sulfate, concentrated and the residue was purified by column chromatography (silica, 50% ethyl acetate – hexanes) to give fluoride **144** (2.27 mg, 3.85 μmol, 67%). ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 5.22 (s, 1H), 4.79 – 4.72 (m, 3H), 4.67 (s, 1H), 4.45 (d, *J* = 5.1 Hz, 2H), 4.15 – 4.01 (m, 3H), 3.87 (dd, *J* = 11.5, 5.0 Hz, 2H), 3.78 (d, *J* = 11.3 Hz, 2H), 3.69 (d, *J* = 11.0 Hz, 1H), 3.67 – 3.58 (m, 3H), 3.34 – 3.25 (m, 2H), 2.96 (t, *J* = 14.4 Hz, 2H), 2.54 – 1.82 (m, 26H), 1.80 – 1.61 (m, 12H), 1.51 – 1.40 (m, 5H), 1.24 (s, 3H), 1.18 (d, *J* = 6.7 Hz, 3H), 1.03 (d, *J* =

6.7 Hz, 3H), 0.93 (d, J = 6.6 Hz, 3H). ^{19}F NMR (564 MHz, $CDCl_3$) δ (ppm): -214.69 (s, 1F) MS-ESI (m/z): $[M+H]^+$ calcd for $C_{41}H_{63}FNO_7$, 700.45; found, 700.42.

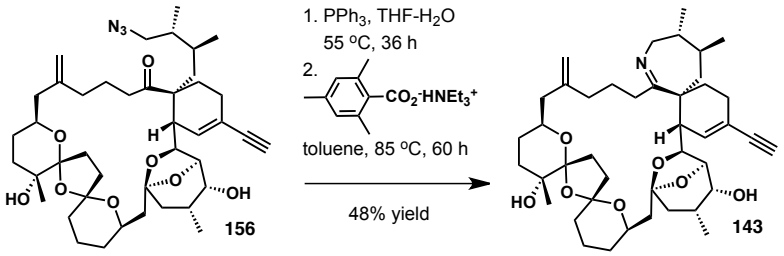


Azido aldehyde (148). To a solution of azido triol **98** (33.0 mg, 44.5 μmol) in dichloromethane (4.5 mL) was added a solution of 2,2,6,6-tetramethylpiperidine-1-oxyl (1.0 mg, 6.4 μmol) and iodobenzene diacetate (0.112 g, 0.347 mmol) in dichloromethane (3.0 mL). The solution was allowed to stir at 23 °C for 2 h and 15 min. The solution was directly applied on a silica column (silica, 60% ethyl acetate – hexanes) to afford aldehyde **148** (23.0 mg, 31.4 μmol, 70%). ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 9.43 (s, 1H), 6.26 (d, J = 2.0 Hz, 1H), 4.80 (d, J = 29.5 Hz, 2H), 4.12 – 3.99 (m, 4H), 3.58 (s, 1H), 3.16 (d, J = 7.3 Hz, 2H), 3.10 (d, J = 11.4 Hz, 1H), 2.60 – 2.42 (m, 4H), 2.27 (dd, J = 13.0, 4.0 Hz, 2H), 2.23 – 2.06 (m, 6H), 2.00 – 1.47 (m, 22H), 1.40 (dd, J = 14.2, 11.7 Hz, 2H), 1.28 – 1.23 (m, 6H), 1.00 (d, J = 6.8 Hz, 4H), 0.85 (d, J = 6.9 Hz, 3H), 0.79 (d, J = 7.0 Hz, 3H). MS-ESI (m/z): $[M+Na]^+$ calcd for $C_{41}H_{61}N_3NaO_9$, 762.43; found, 762.35.



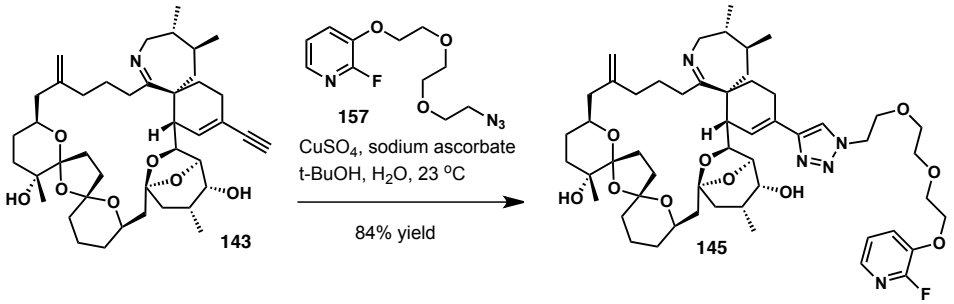
Azido alkyne (156). Potassium carbonate (21.5 mg, 0.155 mmol) was added to a solution of Ohira-Bestman reagent **155** (30.0 mg, 0.155 mmol) and aldehyde **148** (23.0 mg, 31.8

μmol) in dry methanol (6.9 mL) at room temperature and the reaction mixture was stirred for 18 h. The resulting solution was diluted with dichloromethane and quenched with saturated aqueous ammonium chloride. The layers were separated and the aqueous layer was extracted with dichloromethane (3x10 mL), dried over sodium sulfate and concentrated. The residue was purified by column chromatography (silica, 60% ethyl acetate – hexanes) to give alkyne **156** (13 mg, 18.4 μmol, 58%). ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 5.68 (d, *J* = 2.1 Hz, 1H), 4.89 – 4.72 (m, 2H), 4.33 (dd, *J* = 4.3, 2.0 Hz, 1H), 4.12 – 4.00 (m, 2H), 3.91 (dd, *J* = 11.5, 4.4 Hz, 1H), 3.62 – 3.50 (m, 1H), 3.19 (d, *J* = 7.1 Hz, 2H), 2.91 (s, 1H), 2.58 – 2.41 (m, 2H), 2.34 – 2.06 (m, 7H), 2.01 – 1.64 (m, 18H), 1.41 – 1.30 (m, 3H), 1.28 – 1.22 (m, 5H), 0.98 (d, *J* = 6.8 Hz, 3H), 0.91 (d, *J* = 6.8 Hz, 2H), 0.79 (d, *J* = 6.8 Hz, 3H). MS-ESI (m/z): $[M+Na]^+$ calcd for $C_{42}H_{61}N_3NaO_8$, 758.44; found, 758.41.



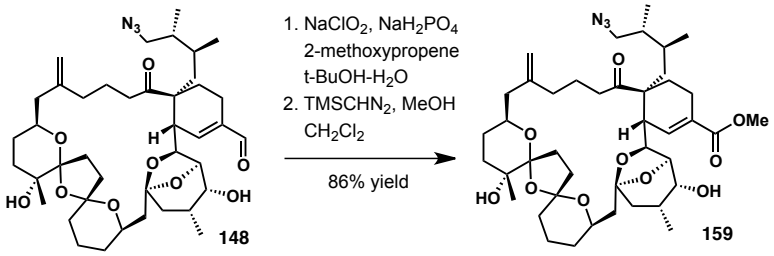
PnTX-yne (143). Triphenylphosphine (11.8 mg, 45.2 μmol) was added to a solution of azido alkyne **156** (13.3 mg, 18.1 μmol) in THF−H_2O (3:1, 6.0 mL). The reaction vessel was capped and heated at 55 °C for 36 h. After cooling, the reaction mixture was concentrated under reduced pressure. The crude material was dissolved in 5 mL of distilled toluene and concentrated and this was repeated three times. The crude residue was used immediately to the next step without further purification.

The crude residue was dissolved in 13.5 mL of a mixture prepared by dissolving 2,4,6-trimethylbenzoic acid (0.132 g, 0.804 mmol) and triethylamine (112 μL, 0.804 mmol) in 20 mL of freshly distilled toluene. The solution was heated at 85 °C for 60 h. After cooling, the solution was directly applied on a silica column (silica, 70% ethyl acetate – hexanes, 1% triethylamine) to afford PnTX-yne **143** (6.0 mg, 8.70 μmol, 48%). ^{1}H NMR (600 MHz, CD_3OD) δ (ppm): 5.64 (s, 1H), 4.75 (d, *J* = 15.6 Hz, 2H), 4.44 (dd, *J* = 4.9, 1.9 Hz, 1H), 4.17 – 4.09 (m, 2H), 3.86 (ddd, *J* = 14.5, 11.3, 4.8 Hz, 2H), 3.69 (dd, *J* = 4.4, 1.9 Hz, 1H), 3.52 (dd, *J* = 11.5, 1.4 Hz, 1H), 3.39 (d, *J* = 11.7 Hz, 1H), 3.08 (dd, *J* = 11.9, 3.5 Hz, 1H), 2.64 (q, *J* = 7.2 Hz, 3H), 2.45 – 1.70 (m, 18H), 1.66 – 1.33 (m, 12H), 1.21 (d, *J* = 6.7 Hz, 4H), 1.08 (t, *J* = 7.2 Hz, 5H), 1.01 (d, *J* = 6.7 Hz, 3H), 0.97 (dd, *J* = 6.6, 3.4 Hz, 3H). MS-ESI (*m*/z): $[M+H]^+$ calcd for $C_{42}H_{62}NO_7$, 692.44; found, 692.41.



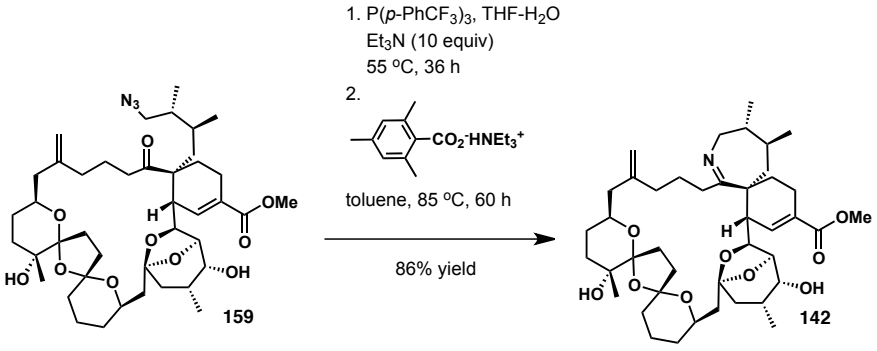
PnTX-2-fluoropyridine (145). Azide **157** was prepared according to a described synthetic procedure. Alkyne **143** (3.0 mg, 4.34 μmol) was dissolved in 300 μL of a mixture prepared by dissolving azide **157** (90 mg, 0.318 mmol), sodium ascorbate (23.0 mg, 0.116 mmol) and copper (II) sulfate (9.0 mg, 58.0 μmol) in *tert*-butanol−water (4:1, 30 mL) at 23 °C. The reaction mixture was stirred at 23 °C for 12 h. The resulting solution was diluted with ethyl acetate and water. The layers were separated and the aqueous layer was extracted with ethyl acetate (3x10 mL), dried over sodium sulfate and

concentrated. The residue was purified by column chromatography (silica, 1% methanol – ethyl acetate, 2% triethylamine) to give triazole **145** (3.46 mg, 3.60 μmol, 84%). ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 7.76 (dq, *J* = 2.8, 1.4 Hz, 1H), 7.61 – 7.59 (s, 1H), 7.31 (d, *J* = 9.2 Hz, 1H), 7.10 (dd, *J* = 7.9, 4.9 Hz, 1H), 5.96 (s, 1H), 4.77 (d, *J* = 6.1 Hz, 2H), 4.59 (dd, *J* = 5.1, 1.9 Hz, 1H), 4.52 (t, *J* = 5.1 Hz, 2H), 4.19 (s, 2H), 4.11 (d, *J* = 7.1 Hz, 2H), 3.93 (dd, *J* = 11.6, 4.9 Hz, 1H), 3.88 (t, *J* = 5.1 Hz, 2H), 3.81 (d, *J* = 13.0 Hz, 2H), 3.70 (dd, *J* = 5.9, 3.1 Hz, 2H), 3.63 (dd, *J* = 8.5, 3.9 Hz, 3H), 3.42 (d, *J* = 11.6 Hz, 1H), 3.08 – 2.97 (m, 1H), 2.46 – 2.25 (m, 6H), 2.26 – 2.10 (m, 7H), 2.11 – 1.94 (m, 6H), 1.88 (ddt, *J* = 19.6, 14.0, 6.7 Hz, 5H), 1.79 – 1.58 (m, 26H), 1.56 – 1.46 (m, 6H), 1.23 (s, 3H), 1.18 (d, *J* = 6.7 Hz, 3H), 1.15 – 1.12 (m, 1H), 1.03 (d, *J* = 6.7 Hz, 3H), 0.91 (d, *J* = 6.6 Hz, 3H). MS-ESI (*m*/z): $[M+H]^+$ calcd for $C_{53}H_{77}FN_5O_{10}$, 962.57; found, 962.68.



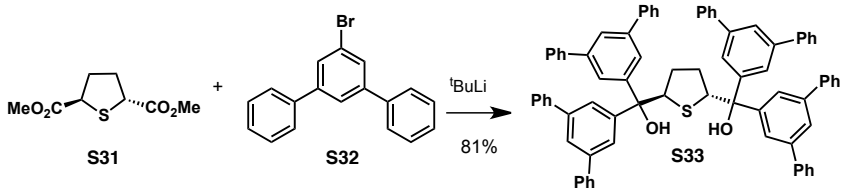
Azido methyl ester (159). Sodium chlorite (12.0 mg, 0.135 mmol) was added to a solution of aldehyde **148** (10.0 mg, 13.5 μmol), sodium phosphate dibasic (18.0 mg, 0.150 mmol) and 2-methoxypropene (0.54 mL, 5.66 mmol) in *tert*-butanol−water (4:1, 2.2 mL) at 0 °C. This solution was stirred at 0 °C for 10 min and warmed to 23 °C for 50 min. The reaction mixture was diluted with ethyl acetate and water. The layers were separated and the aqueous layer was extracted with ethyl acetate (4x10 mL), dried over sodium sulfate and concentrated. The crude residue was used immediately to the next step without further purification.

Trimethylsilyldiazomethane (1.13 M in hexane, 0.170 mL, 0.195 mmol) was added dropwise to a solution of the crude residue in a mixture of dichloromethane (2.3 mL) and methanol (0.6 mL) at 23 °C and stirred for 10 min. The mixture was concentrated under reduced pressure and the residue was purified by column chromatography (silica, 50% ethyl acetate – hexanes) to afford methyl ester **159** (8.5 mg, 11.6 μmol, 86%). ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 6.44 (q, *J* = 1.9 Hz, 1H), 4.86 – 4.74 (m, 2H), 4.43 (dd, *J* = 4.4, 2.0 Hz, 1H), 4.10 (s, 1H), 3.96 (dd, *J* = 11.7, 4.4 Hz, 1H), 3.75 (s, 3H), 3.58 (s, 1H), 3.18 (d, *J* = 7.3 Hz, 2H), 2.97 (d, *J* = 11.6 Hz, 1H), 2.51 (dq, *J* = 14.2, 7.1 Hz, 3H), 2.32 – 2.16 (m, 4H), 2.15 – 1.96 (m, 8H), 1.95 – 1.81 (m, 8H), 1.75 – 1.65 (m, 7H), 1.46 – 1.35 (m, 3H), 1.26 (s, 4H), 0.99 (d, *J* = 6.8 Hz, 3H), 0.87 (d, *J* = 6.9 Hz, 3H), 0.80 (d, *J* = 6.9 Hz, 3H). MS-ESI (*m*/z): $[M+Na]^+$ calcd for $C_{42}H_{63}N_3NaO_{10}$, 792.44; found, 792.49.



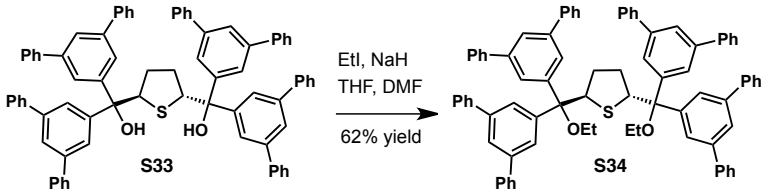
PnTX methyl ester (142). Tris(4-(trifluoromethyl)phenyl)phosphine (25.0 mg, 52.9 μmol) was added to a solution of azido methyl ester **159** (16.0 mg, 21.1 μmol) in THF−H_2O (3:1, 7.0 mL). The reaction vessel was capped and heated at 55 °C for 36 h. After cooling, the reaction mixture was concentrated under reduced pressure. The crude material was dissolved in 5 mL of distilled toluene and concentrated and this was repeated three times. The crude residue was used immediately to the next step without further purification.

The crude residue was dissolved in 17 mL of a mixture prepared by dissolving 2,4,6-trimethylbenzoic acid (0.142 g, 0.868 mmol) and triethylamine (121 μL, 0.868 mmol) in 22 mL of freshly distilled toluene. The solution was heated at 85 °C for 60 h. After cooling, the solution was directly applied on a silica column (silica, 70% ethyl acetate – hexanes, 1% triethylamine) to afford PnTX methyl ester **142** (13.2 mg, 18.1 μmol, 86%). ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 6.39 (s, 1H), 4.77 (d, *J* = 10.2 Hz, 2H), 4.54 (dd, *J* = 5.1, 2.0 Hz, 1H), 4.13 – 4.07 (m, 1H), 3.91 (dd, *J* = 11.4, 4.9 Hz, 1H), 3.75 (s, 4H), 3.63 (d, *J* = 11.0 Hz, 1H), 3.33 (d, *J* = 15.3 Hz, 1H), 2.44 – 2.30 (m, 4H), 2.10 – 2.19 (m, 7H), 2.08 – 1.91 (m, 5H), 1.91 – 1.84 (m, 4H), 1.77 – 1.60 (m, 12H), 1.51 (q, *J* = 14.9, 13.8 Hz, 3H), 1.24 (d, *J* = 11.0 Hz, 4H), 1.18 (d, *J* = 6.7 Hz, 3H), 1.04 (d, *J* = 6.7 Hz, 3H), 0.92 (d, *J* = 6.6 Hz, 3H). MS-ESI (*m*/z): $[M+H]^+$ calcd for $C_{42}H_{64}NO_9$, 726.46; found, 726.46.

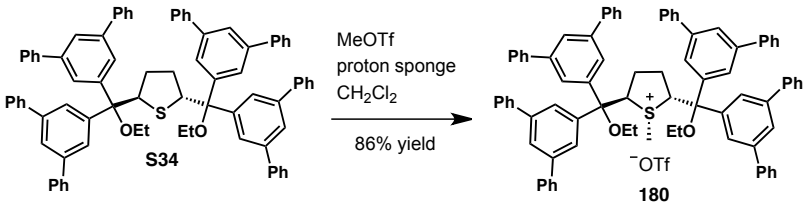


Alcohol (S33). *t*-BuLi (1.7 M solution in pentane, 2.85 mL, 4.85 mmol) was added dropwise to a solution of 3,5-diphenyl-1-bromobenzene (1.01 g, 4.85 mmol) in THF (40 mL) at -20 °C. After 20 minutes a solution of **S31** (0.165 g, 0.808 mmol), prepared from (2*R*,5*S*)-diethyl 2,5-dibromohexanedioate,[83] in THF (10 mL) was added dropwise. The resulting solution was maintained at -20 °C for 1 h and then allowed to warm up to 23 °C and stirred for 16 h. The solution was quenched with saturated aqueous ammonium chloride and extracted with Et2O (4x50 mL). The combined organic extracts were dried over $MgSO_4$, evaporated under reduced pressure, and the crude product purified by

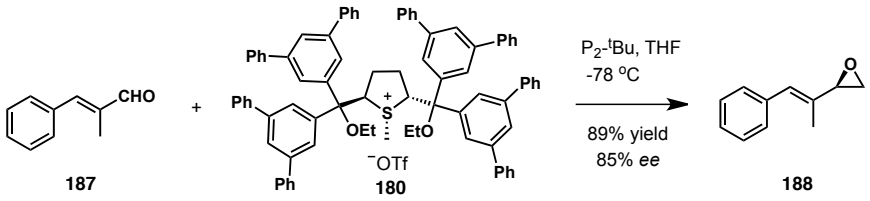
column chromatography (silica, 50% CH_2Cl_2 − hexane) affording alcohol **S33** (0.691 g, 0.654 mmol, 81%). ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 7.83 (d, *J* = 24.1 Hz, 2H), 7.82 (d, *J* = 1.7 Hz, 2H), 7.74 (d, *J* = 1.7 Hz, 3H), 7.76 (d, *J* = 30.0 Hz, 2H), 7.65 – 7.57 (m, 13H), 7.42 (ddd, *J* = 7.8, 6.9, 3.5 Hz, 11H), 7.37 – 7.31 (m, 6H), 4.98 (s, 2H), 3.74 (s, 2H), 2.17 – 2.07 (m, 2H), 1.81 (dd, *J* = 7.9, 5.0 Hz, 2H).



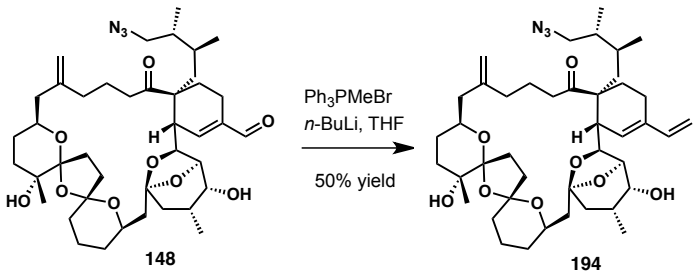
Ether (S34). NaH (60% in mineral oil, 0.100 g, 3.50 mmol) was added to a solution of **S33** (0.420 g, 0.584 mmol) in THF (5.8 mL) and DMF (1.5 mL) at 0 °C. After 10 min iodoethane (0.60 mL, 11.68 mmol) was added dropwise and the resulting solution was allowed to warm to 23 °C and stirred for 12 h. The reaction mixture was diluted with CH_2Cl_2 (50 mL) and water (100 mL). The organic phase was separated and the aqueous layer was extracted with CH_2Cl_2 (3x50 mL). The combined organic extracts were dried over sodium sulfate and then evaporated under reduced pressure. The crude material was purified by column chromatography (silica, 30% CH_2Cl_2 − hexane) affording **S34** (0.405 g, 0.362 mmol, 62%). ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 7.74 (s, 6H), 7.71 (t, *J* = 1.6 Hz, 2H), 7.65 (d, *J* = 1.6 Hz, 4H), 7.61 – 7.56 (m, 17H), 7.38 (td, *J* = 7.2, 6.4, 1.2 Hz, 9H), 7.36 – 7.28 (m, 17H), 4.35 (s, 2H), 3.36 (p, *J* = 7.2 Hz, 2H), 3.13 (p, *J* = 7.1 Hz, 2H), 1.85 (s, 2H), 1.39 (s, 2H), 1.09 (t, *J* = 6.9 Hz, 6H).



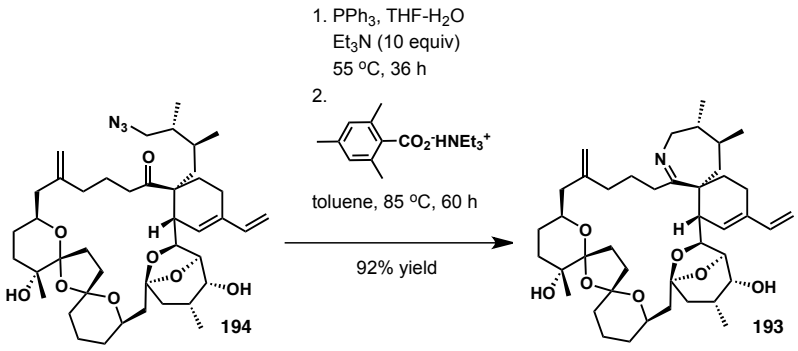
Ylide (180). Methyl triflate (27.0 μL, 0.242 mmol) was added to a solution **S34** (90.0 mg, 80.9 μmol) and proton sponge (35.0 mg, 80.9 μmol) in CH_2Cl_2 (1.0 mL) at 23 °C. The resulting solution was stirred at 23 °C for 12 h. The resulting reaction mixture was concentrated and directly purified by column chromatography (30% ethyl acetate – hexanes) to afford **180** (89.0 mg, 69.6 μmol, 86%). ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 7.82 (s, 1H), 7.77 (t, *J* = 1.5 Hz, 1H), 7.71 (s, 2H), 7.66 – 7.55 (m, 7H), 7.55 – 7.48 (m, 5H), 7.47 – 7.31 (m, 24H), 7.31 – 7.21 (m, 30H), 6.92 (dd, *J* = 7.4, 1.2 Hz, 1H), 5.94 (t, *J* = 8.6 Hz, 1H), 3.64 (s, 1H), 3.25 (dd, *J* = 10.3, 6.0 Hz, 2H), 3.11 (t, *J* = 8.1 Hz, 2H), 3.02 (s, 3H), 2.79 (s, 3H), 2.62 (d, *J* = 13.9 Hz, 1H), 2.26 (s, 2H), 1.17 (q, *J* = 7.2 Hz, 6H).



Epoxide (188). Phosphazene base P_2-*t*Bu (2M in THF, 34.0 μL, 68.4 μmol) was added to a solution of aldehyde **187** (10.0 mg, 68.4 μmol) and ylide **180** (88.0 mg, 68.4 μmol) in THF (3.4 mL) at -78 °C. After stirring for 1 h at -78 °C, the reaction mixture was allowed to warm to 23 °C. The resulting solution was diluted with CH_2Cl_2 (5 mL) and water (5 mL). The two phases were separated and the aqueous layer was extracted with CH_2Cl_2 (3x10 mL). The combined organic layers were dried with sodium sulfate, evaporated and purified by column chromatography (silica, 100% hexane, 3% triethyl amine) to afford **188** (9.8 mg, 60.9 μmol, 89%, 85% *ee*). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.37 – 7.31 (m, 2H), 7.31 – 7.26 (m, 2H), 7.27 – 7.21 (m, 2H), 6.70 – 6.62 (m, 1H), 3.50 (ddd, *J* = 4.2, 2.7, 0.7 Hz, 1H), 2.95 (dd, *J* = 5.2, 4.2 Hz, 1H), 2.82 (dd, *J* = 5.2, 2.7 Hz, 1H), 1.74 (s, 3H).

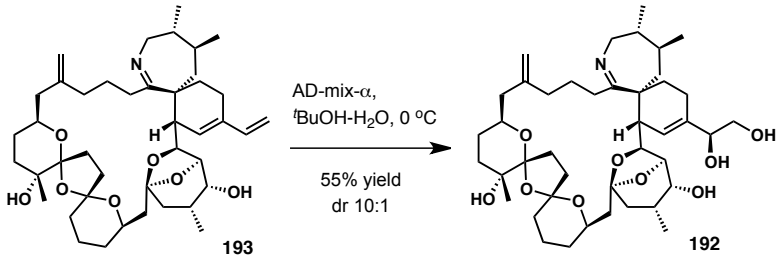


Alkene (194). *n*-BuLi (2.13 M in hexane, 434 μL, 0.924 mmol) was added to a mixture of methyltriphenylphosphonium bromide (0.417 g, 1.17 mmol) in THF (18 mL) at -78 °C. After 45 min, a solution of aldehyde **148** (36.0 mg, 48.7 μmol) dissolved in THF (6.4 mL total with rinses) was added dropwise. After 30 min the solution was allowed to warm to -10 °C and stirred for 20 min. Quench with a saturated aqueous solution of ammonium chloride. The aqueous layer was extracted with ethyl acetate (3x20 mL). The combined organic layers were washed with brine, dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica, 60% ethyl acetate – hexanes) to give **194** (17.0 mg, 24.4 μmol, 50%). ^{1}H NMR (600 MHz, $CDCl_3$); δ (ppm): 6.28 (dd, *J* = 17.5, 10.6 Hz, 1H), 5.25 – 5.09 (m, 2H), 5.04 (d, *J* = 10.8 Hz, 1H), 4.80 (d, *J* = 25.3 Hz, 2H), 4.35 (t, *J* = 2.9 Hz, 1H), 4.20 – 4.01 (m, 2H), 3.93 (dd, *J* = 11.5, 4.4 Hz, 1H), 3.58 (d, *J* = 9.2 Hz, 1H), 3.17 (d, *J* = 7.4 Hz, 2H), 2.99 (d, *J* = 11.5 Hz, 1H), 2.54 (dt, *J* = 15.9, 7.6 Hz, 1H), 2.44 (ddd, *J* = 17.6, 7.8, 4.4 Hz, 1H), 2.39 – 2.26 (m, 3H), 2.25 – 1.61 (m, 33H), 1.43 – 1.28 (m, 6H), 1.24 – 1.14 (m, 4H), 0.98 (d, *J* = 6.8 Hz, 3H), 0.87 (d, *J* = 6.9 Hz, 3H), 0.79 (d, *J* = 6.9 Hz, 3H).



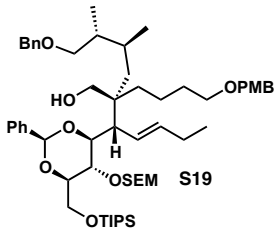
PnTX G (193). Triphenylphosphine (16.0 mg, 59.3 μmol) was added to a solution of **194** (17.5 mg, 23.7 μmol), triethylamine (33 μL, 0.237 mmol) in THF−H_2O (3:1, 8.0 mL). The reaction vessel was capped and heated at 55 °C for 36 h. After cooling, the reaction mixture was concentrated under reduced pressure. The crude material was dissolved in 5 mL of distilled toluene and concentrated and this was repeated three times. The crude residue was used immediately to the next step without further purification.

The crude residue was dissolved in 19 mL of a mixture prepared by dissolving 2,4,6-trimethylbenzoic acid (0.160 g, 0.972 mmol) and triethylamine (136.0 μL, 0.972 mmol) in 25 mL of freshly distilled toluene. The solution was heated at 85 °C for 60 h. After cooling, the solution was directly applied on a silica column (silica, 60% ethyl acetate – hexanes) to afford PnTX G **193** (15.9 mg, 21.8 μmol, 92%). ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 6.28 (dd, *J* = 17.5, 10.7 Hz, 1H), 5.21 – 5.11 (m, 2H), 5.04 (d, *J* = 10.7 Hz, 1H), 4.80 – 4.67 (m, 2H), 4.47 (dd, *J* = 5.0, 2.0 Hz, 1H), 4.15 – 4.00 (m, 2H), 3.87 (dd, *J* = 11.5, 4.9 Hz, 1H), 3.83 – 3.76 (m, 1H), 3.72 (s, 1H), 3.62 (dd, *J* = 11.2, 1.5 Hz, 1H), 3.37 (d, *J* = 11.5 Hz, 1H), 3.05 – 2.90 (m, 1H), 2.41 – 2.11 (m, 8H), 2.11 – 1.99 (m, 2H), 1.98 – 1.82 (m, 4H), 1.82 – 1.56 (m, 10H), 1.56 – 1.33 (m, 4H), 1.23 (s, 3H), 1.17 (d, *J* = 6.7 Hz, 3H), 1.03 (d, *J* = 6.7 Hz, 3H), 0.92 (d, *J* = 6.6 Hz, 3H).



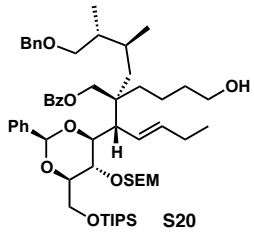
Tetraol (192). AD-mix-α (32.0 mg, 2 mol%) was added to a solution of **193** (8.0 mg, 11.5 μmol) in *tert*-butanol (0.6 mL) and water (0.6 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 5 h. The reaction mixture was quenched with aqueous solution of sodium sulfite (5 mL) and stirred at 23 °C for 30 min. The resulting solution was diluted with ethyl acetate and the two layers were separated. The aqueous layer was extracted with ethyl acetate (3x5 mL) and the combined organic layers were dried with sodium sulfate and concentrated. The crude residue was purified by column chromatrography (silica, 60% ethyl acetate – hexanes) to afford tetraol **192** (15.9 mg, 21.8 μmol, 92%). ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 5.24 (d, *J* = 7.8 Hz, 1H), 5.11 (s, 1H), 4.76 (d, *J* = 8.2 Hz, 2H), 4.47 (d, *J* = 5.1 Hz, 1H), 4.29 (hept, *J* = 6.9 Hz, 2H), 4.16 – 4.00 (m, 3H), 3.90 – 3.83 (m, 2H), 3.76 (s, 1H), 3.68 (d, *J* = 17.0 Hz, 1H), 3.61 (d, *J* = 11.1 Hz, 1H), 3.53 (ddd, *J* = 18.0, 11.0, 7.7 Hz, 1H), 3.45 – 3.38 (m, 1H), 3.35 (s, 1H), 3.29 (d, *J* = 10.6 Hz, 1H), 2.96 (t, *J* = 14.2 Hz, 1H), 2.32 (d, *J* = 14.4 Hz, 2H), 2.28 – 2.09 (m, 2H), 2.03 (dd, *J* = 15.1, 4.8 Hz, 1H), 1.96 – 1.90 (m, 1H), 1.89 – 1.81 (m, 3H), 1.76 – 1.55 (m, 20H), 1.47 (dd, *J* = 13.9, 12.0 Hz, 1H), 1.23 (s, 3H), 1.17 (d, *J* = 6.7 Hz, 3H), 1.03 (dd, *J* = 6.8, 2.1 Hz, 3H), 0.95 – 0.91 (m, 2H), 0.91 – 0.82 (m, 6H).

Parameter	Value
1 Title	ky-4-2-a
2 Spectrometer	inova
3 Number of Scans	8
4 Acquisition Date	2015-04-16T11:19:31
5 Spectrometer Frequency	499.86



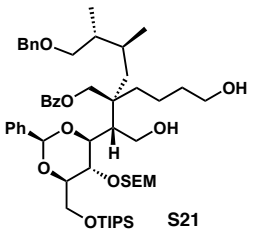
S19

Parameter	Value
1 Title	ky-4-17-a
2 Spectrometer	inova
3 Number of Scans	8
4 Acquisition Date	2015-05-03T13:29:48
5 Spectrometer Frequency	599.64

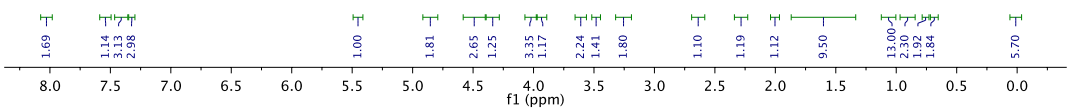


S20

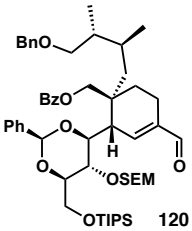
Parameter	Value
1 Title	ky-4-35-d
2 Spectrometer	inova
3 Number of Scans	16
4 Acquisition Date	2015-05-15T08:48:57
5 Spectrometer Frequency	499.86



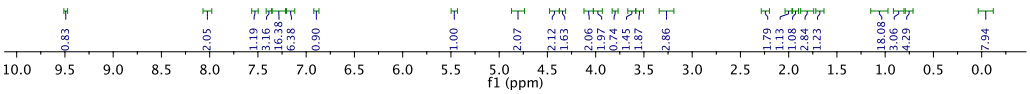
S21



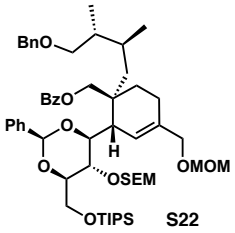
Parameter	Value
1 Title	ky-4-37-2-crude
2 Spectrometer	inova
3 Number of Scans	8
4 Acquisition Date	2015-05-29T12:00:52
5 Spectrometer Frequency	599.64



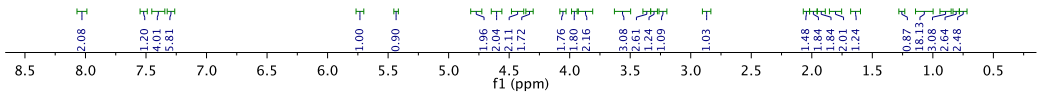
120



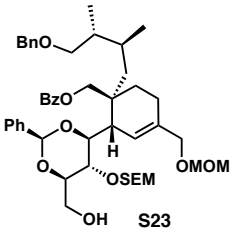
Parameter	Value
1 Title	ky-4-38-a
2 Spectrometer	inova
3 Number of Scans	8
4 Acquisition Date	2015-06-01T09:27:18
5 Spectrometer Frequency	599.64



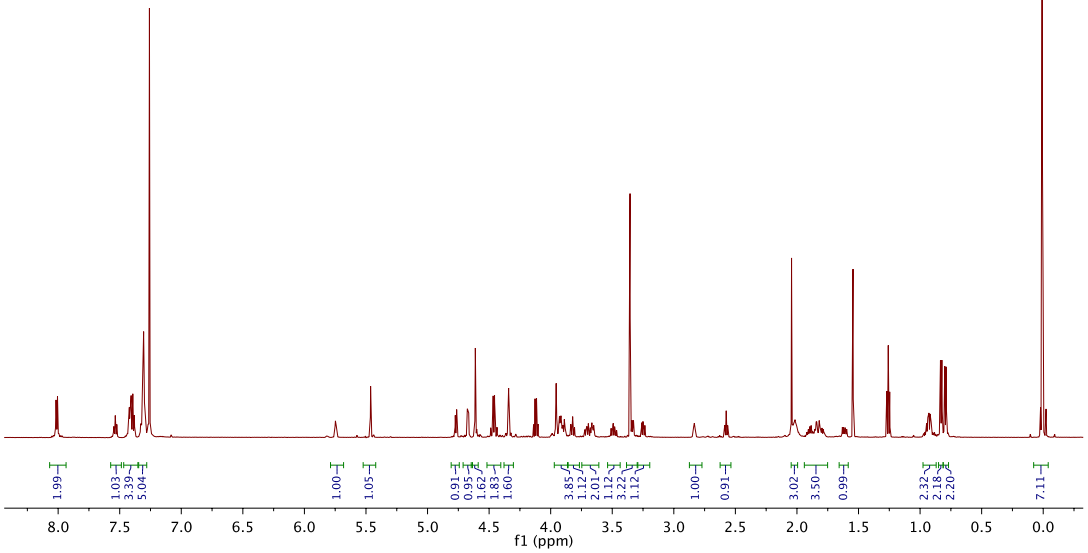
S22



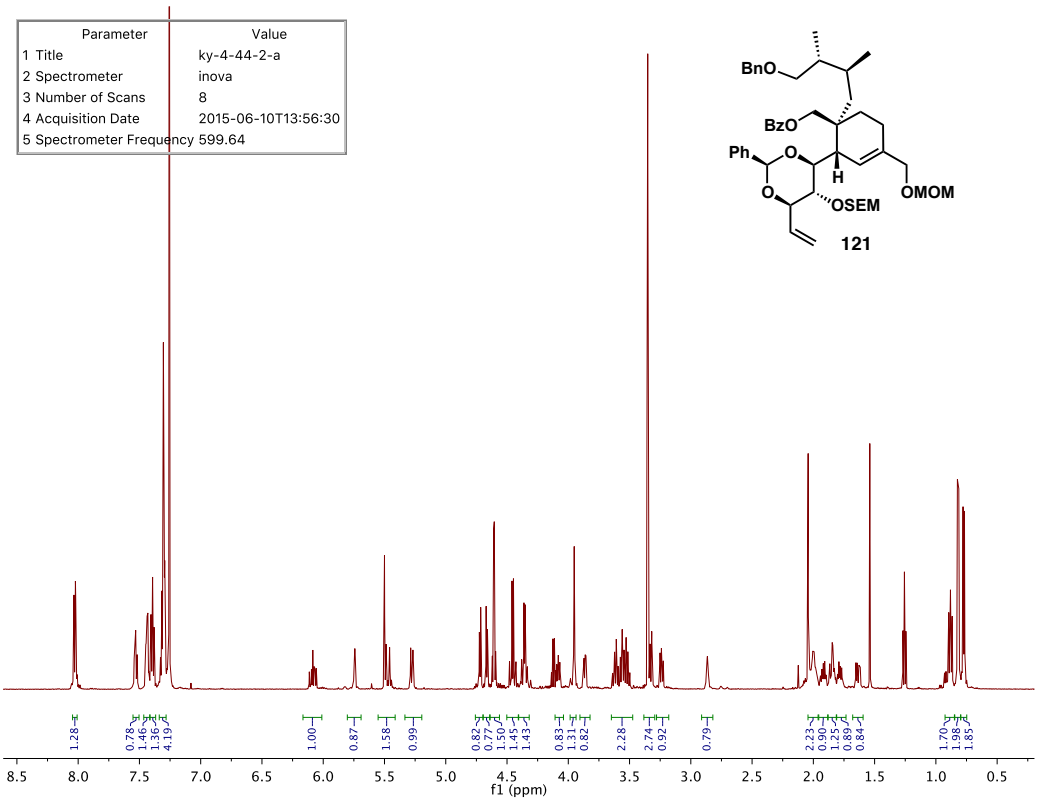
Parameter	Value
1 Title	ky-4-43-a-2
2 Spectrometer	inova
3 Number of Scans	8
4 Acquisition Date	2015-06-09T13:13:21
5 Spectrometer Frequency	599.64



S23

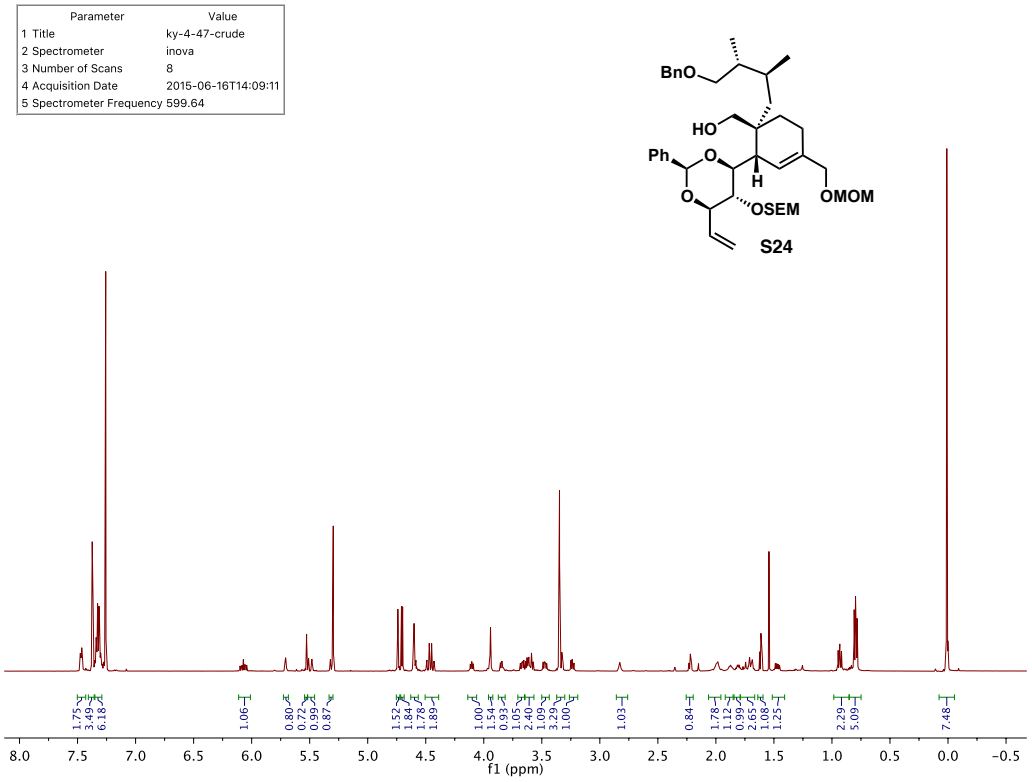


Parameter	Value
1 Title	ky-4-44-2-a
2 Spectrometer	inova
3 Number of Scans	8
4 Acquisition Date	2015-06-10T13:56:30
5 Spectrometer Frequency	599.64



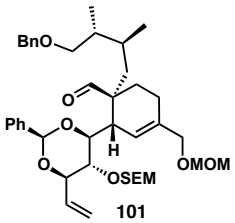
121

Parameter	Value
1 Title	ky-4-47-crude
2 Spectrometer	inova
3 Number of Scans	8
4 Acquisition Date	2015-06-16T14:09:11
5 Spectrometer Frequency	599.64



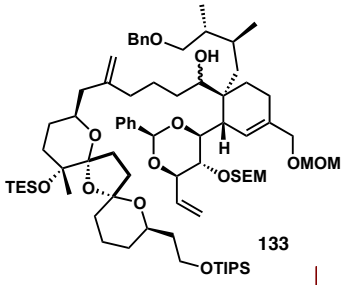
S24

Parameter	Value
1 Title	ky-4-50-a
2 Spectrometer	inova
3 Number of Scans	8
4 Acquisition Date	2015-06-22T09:25:41
5 Spectrometer Frequency	499.86



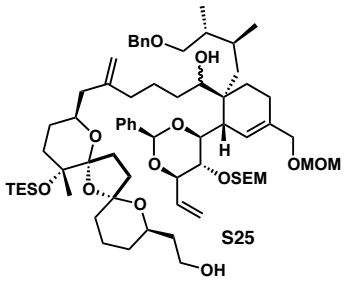
101

Parameter	Value
1 Title	ky-4-66-b
2 Spectrometer	inova
3 Number of Scans	8
4 Acquisition Date	2015-07-07T10:59:58
5 Spectrometer Frequency	599.64



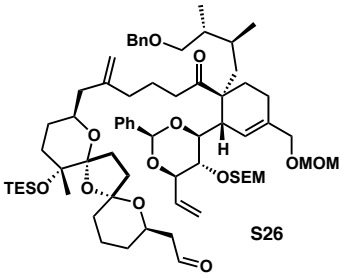
133

Parameter	Value
1 Title	ky-4-84-b
2 Spectrometer	inova
3 Number of Scans	8
4 Acquisition Date	2015-07-21T09:21:10
5 Spectrometer Frequency	599.64



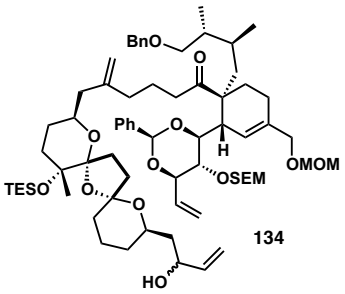
S25

Parameter	Value
1 Title	ky-4-88-a
2 Spectrometer	inova
3 Number of Scans	8
4 Acquisition Date	2015-07-28T12:50:46
5 Spectrometer Frequency	599.64



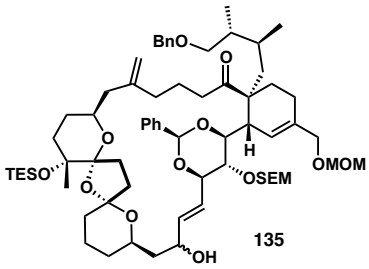
S26

Parameter	Value
1 Title	ky-4-96-crude
2 Spectrometer	inova
3 Number of Scans	8
4 Acquisition Date	2015-08-03T13:28:37
5 Spectrometer Frequency	599.64



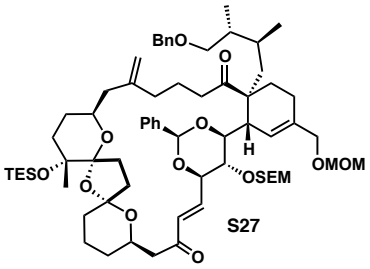
134

Parameter	Value
1 Title	ky-4-98-b
2 Spectrometer	inova
3 Number of Scans	8
4 Acquisition Date	2015-08-06T14:48:37
5 Spectrometer Frequency	599.64



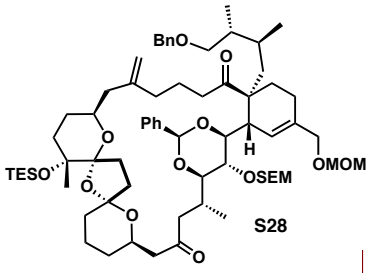
135

Parameter	Value
1 Title	ky-4-114-a
2 Spectrometer	inova
3 Number of Scans	8
4 Acquisition Date	2015-08-28T16:40:05
5 Spectrometer Frequency	599.64



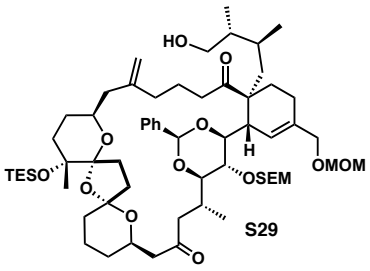
S27

Parameter	Value
1 Title	ky-4-117-a
2 Spectrometer	inova
3 Number of Scans	8
4 Acquisition Date	2015-08-22T18:43:49
5 Spectrometer Frequency	599.64

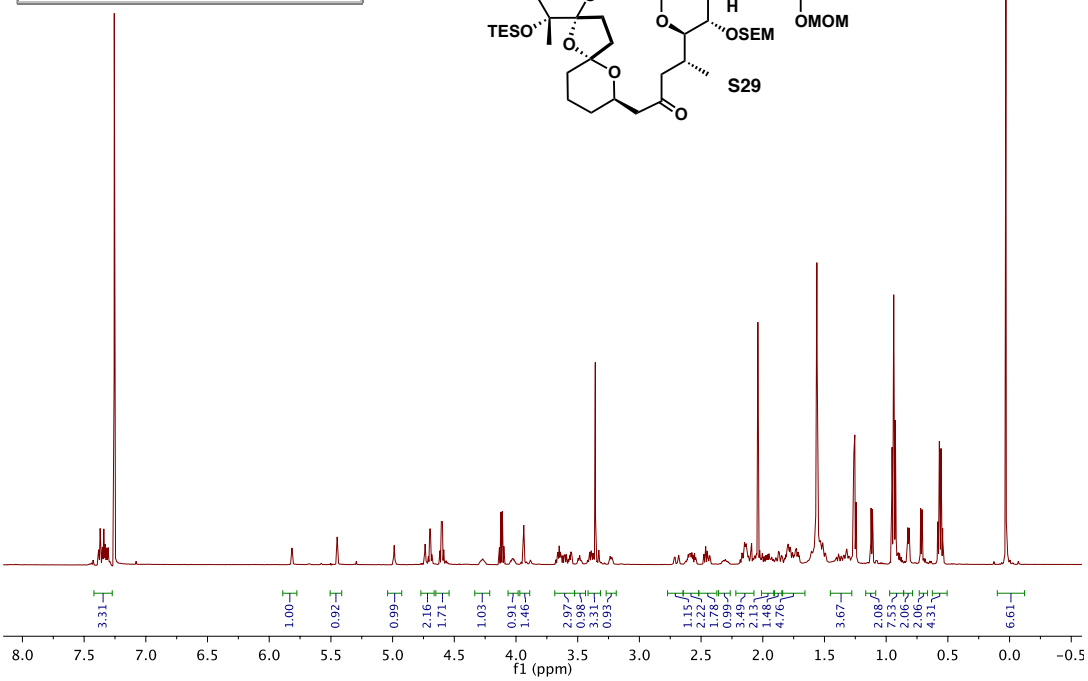


S28

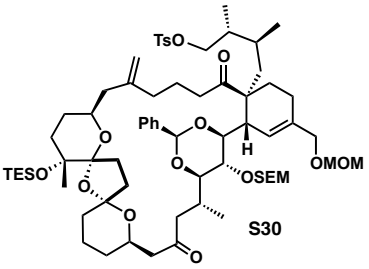
Parameter	Value
1 Title	ky-4-125-b
2 Spectrometer	inova
3 Number of Scans	8
4 Acquisition Date	2015-09-02T08:48:11
5 Spectrometer Frequency	599.64



S29

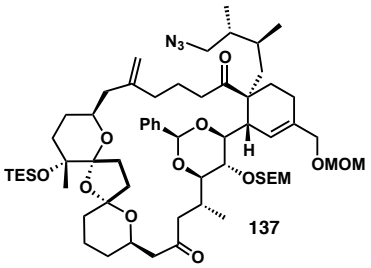


Parameter	Value
1 Title	ky-4-133-a
2 Spectrometer	inova
3 Number of Scans	8
4 Acquisition Date	2015-09-09T09:05:25
5 Spectrometer Frequency	499.86



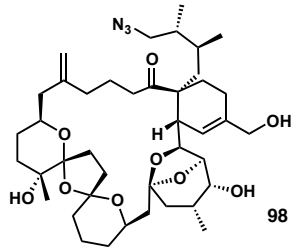
S30

Parameter	Value
1 Title	ky-4-139-a
2 Spectrometer	inova
3 Number of Scans	8
4 Acquisition Date	2015-09-12T10:48:32
5 Spectrometer Frequency	599.64



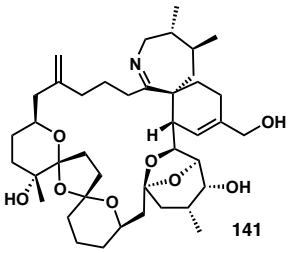
137

Parameter	Value
1 Title	ky-4-142-b-2
2 Spectrometer	inova
3 Number of Scans	8
4 Acquisition Date	2015-09-15T09:11:28
5 Spectrometer Frequency	599.64



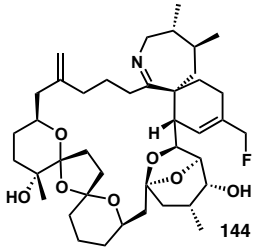
98

Parameter	Value
1 Title	ky-5-61-a-b-c
2 Spectrometer	inova
3 Number of Scans	40
4 Acquisition Date	2016-02-24T09:01:02
5 Spectrometer Frequency	599.64

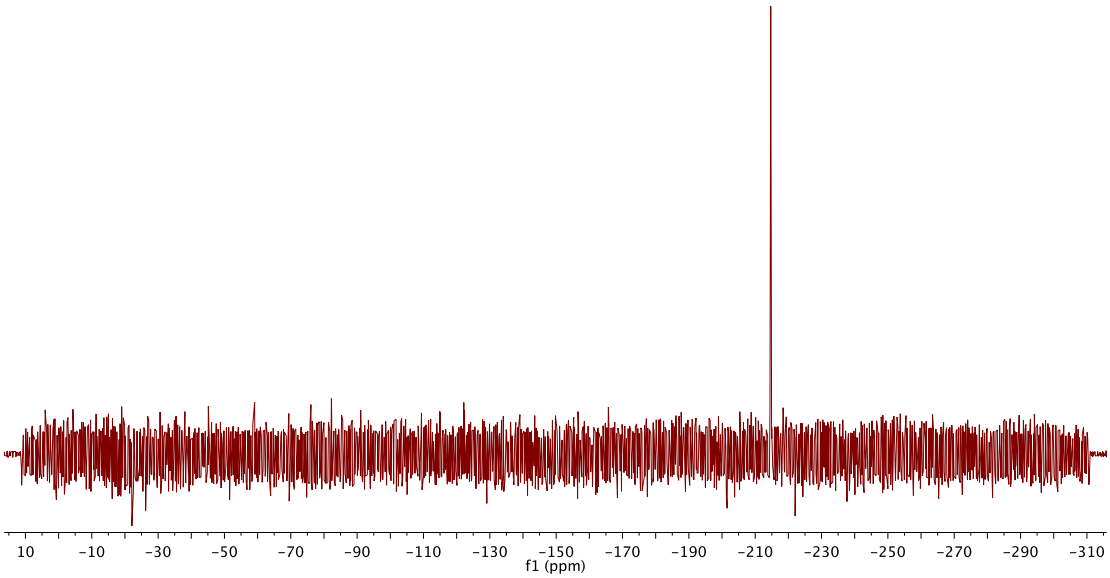


141

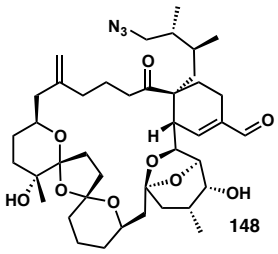
Parameter	Value
1 Title	ky-5-159-a-F19
2 Spectrometer	vnmrs
3 Number of Scans	24
4 Acquisition Date	2016-05-27T15:44:47
5 Spectrometer Frequency	376.11



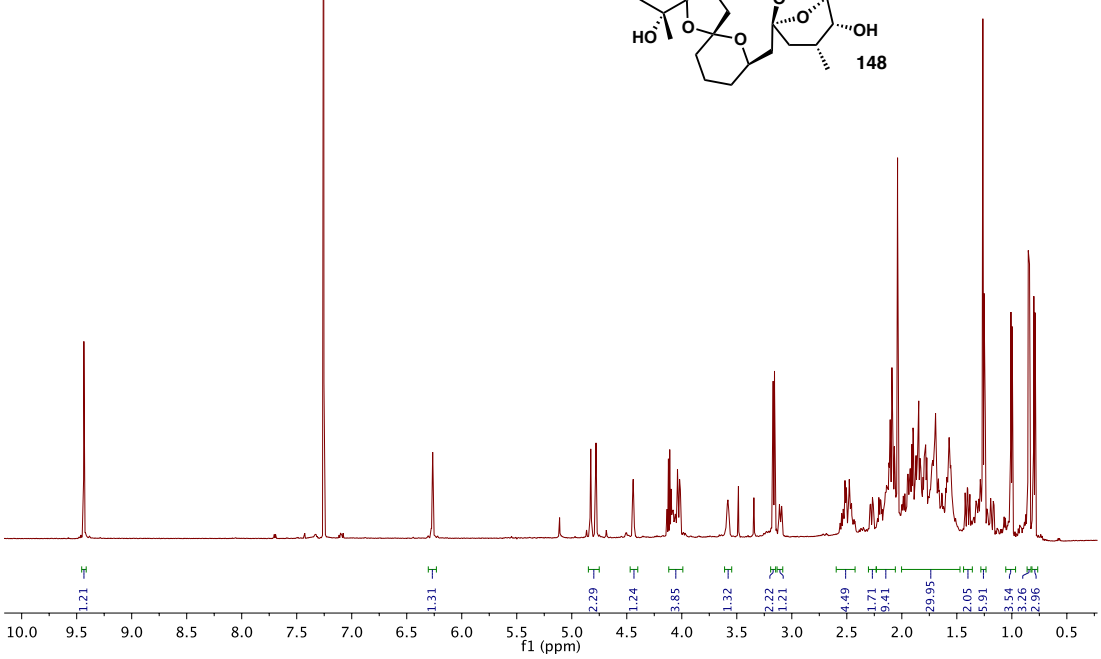
144



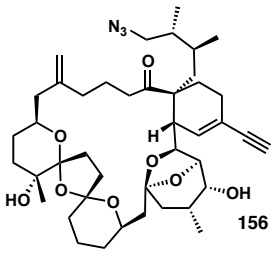
Parameter	Value
1 Title	ky-6-49-a
2 Spectrometer	inova
3 Number of Scans	12
4 Acquisition Date	2017-01-10T11:57:46
5 Spectrometer Frequency	599.64



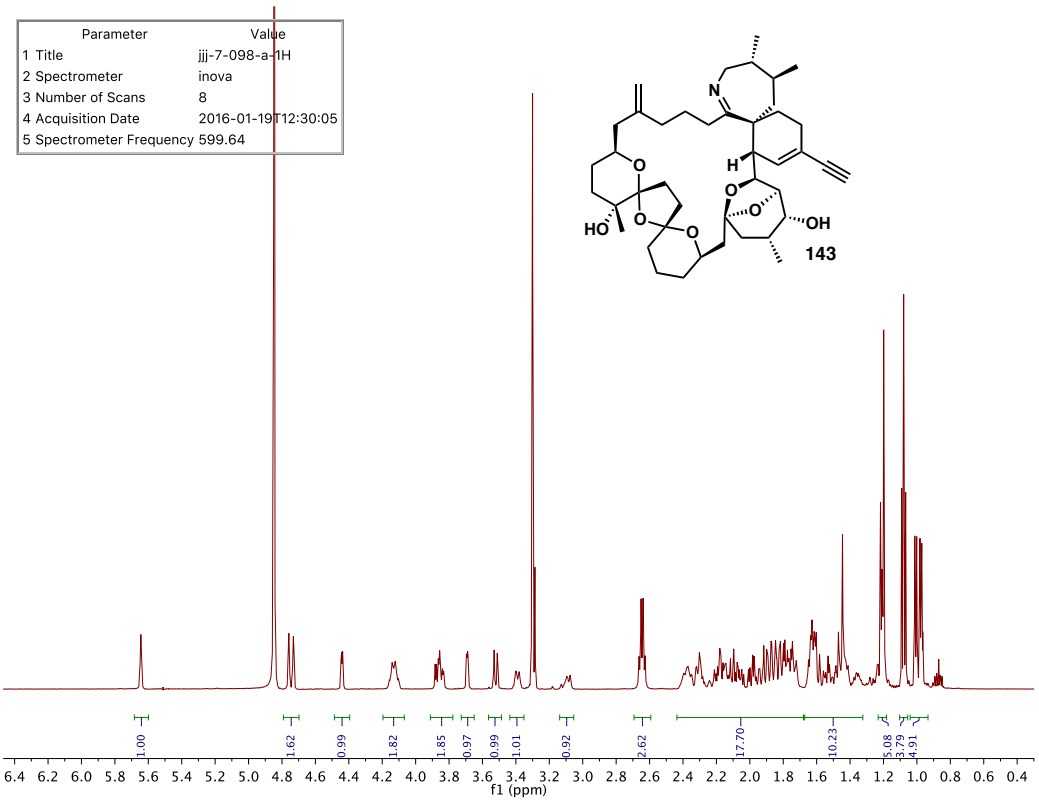
148

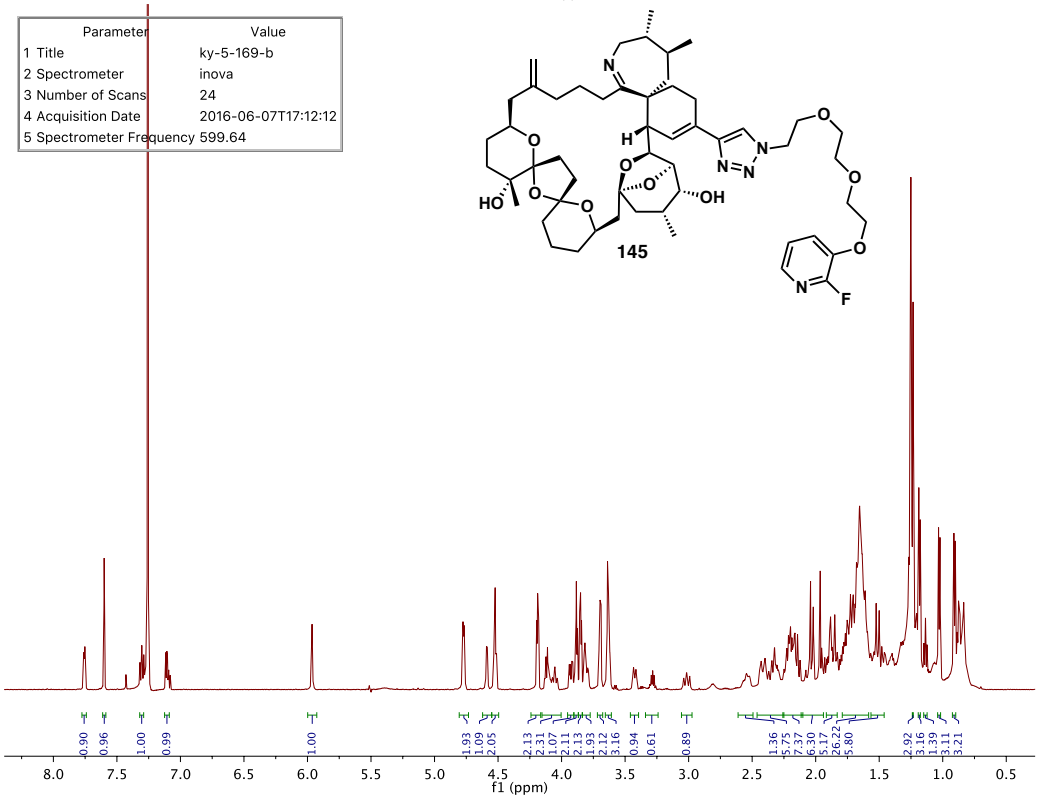


Parameter	Value
1 Title	jjj-7-095-a
2 Spectrometer	inova
3 Number of Scans	8
4 Acquisition Date	2016-01-12T10:57:21
5 Spectrometer Frequency	499.86



156


Parameter Value
1 Title jjj-7-098-a-1H
2 Spectrometer inova
3 Number of Scans 8
4 Acquisition Date 2016-01-19T12:30:05
5 Spectrometer Frequency 599.64
143
f1 (ppm)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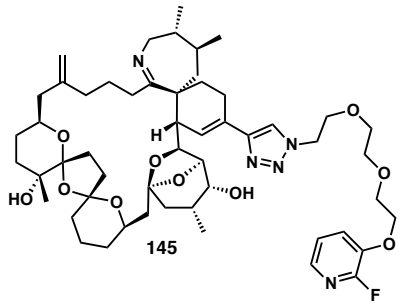
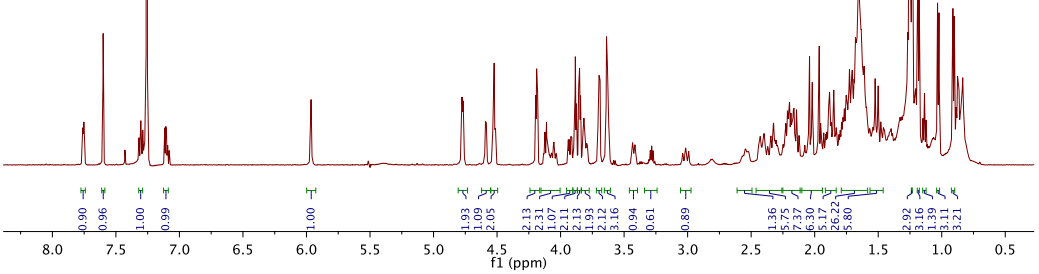
1 Title ky-5-169-b
2 Spectrometer inova
3 Number of Scans 24
4 Acquisition Date 2016-06-07T17:12:12
5 Spectrometer Frequency 599.64
145
f1 (ppm)

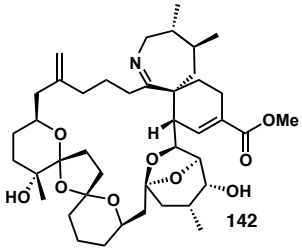
Parameter	Value
1 Title	ky-5-169-b
2 Spectrometer	inova
3 Number of Scans	24
4 Acquisition Date	2016-06-07T17:12:12
5 Spectrometer Frequency	599.64



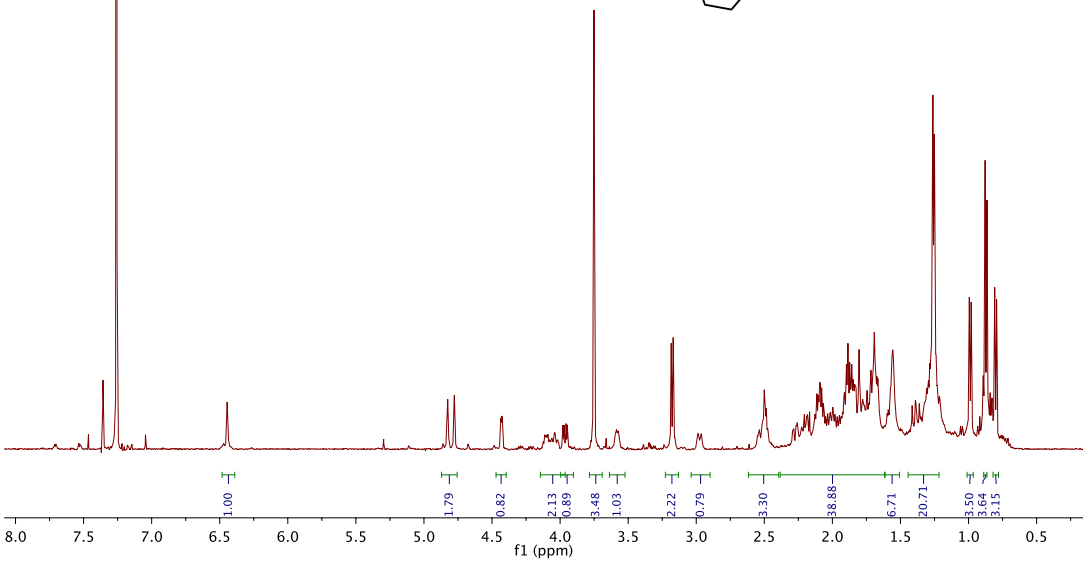
145



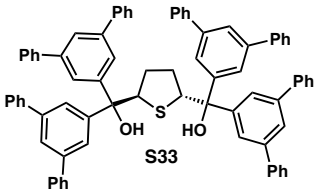
Parameter	Value
1 Title	ky-5-33-a-2
2 Spectrometer	inova
3 Number of Scans	36
4 Acquisition Date	2016-02-08T12:03:40
5 Spectrometer Frequency	499.86



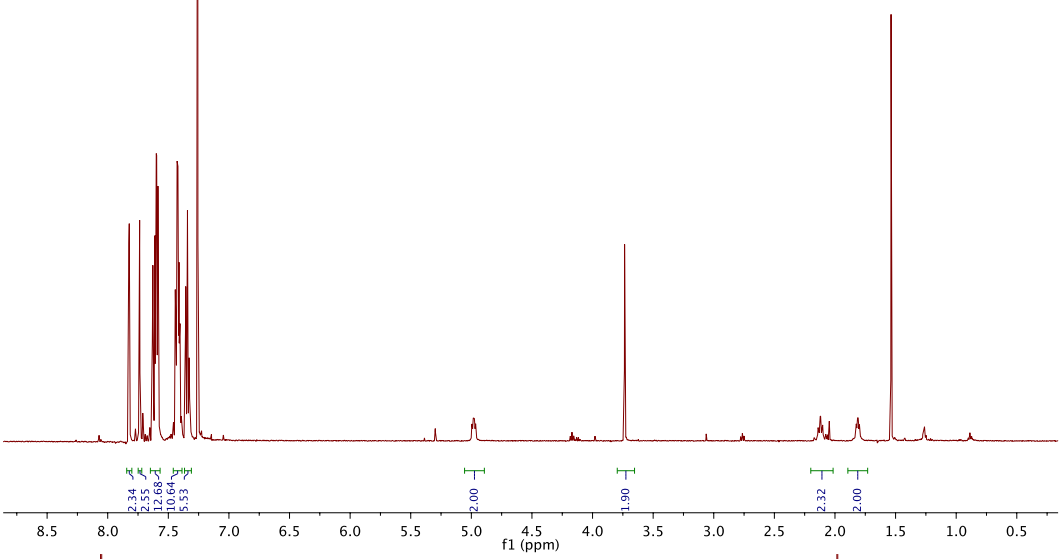
142



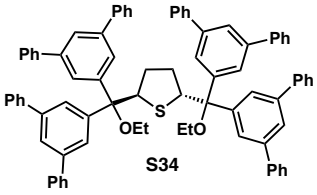
Parameter	Value
1 Title	ky-5-15-b
2 Spectrometer	inova
3 Number of Scans	8
4 Acquisition Date	2016-01-24T12:22:37
5 Spectrometer Frequency	499.86



S33

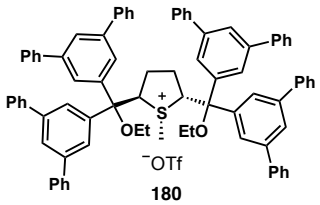


Parameter	Value
1 Title	ky-5-26-A
2 Spectrometer	inova
3 Number of Scans	88
4 Acquisition Date	2016-01-30T15:08:25
5 Spectrometer Frequency	599.64



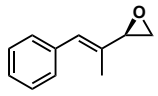
S34

Parameter	Value
1 Title	ky-5-30-b
2 Spectrometer	inova
3 Number of Scans	28
4 Acquisition Date	2016-02-02T16:40:30
5 Spectrometer Frequency	599.64

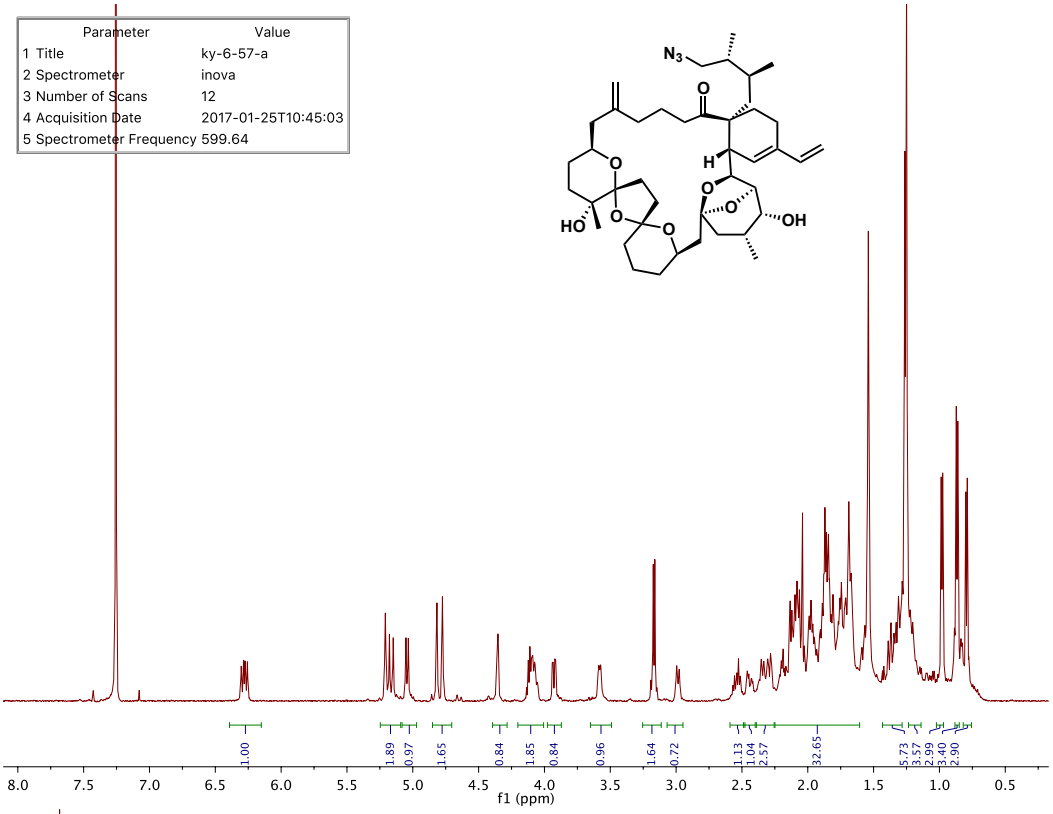


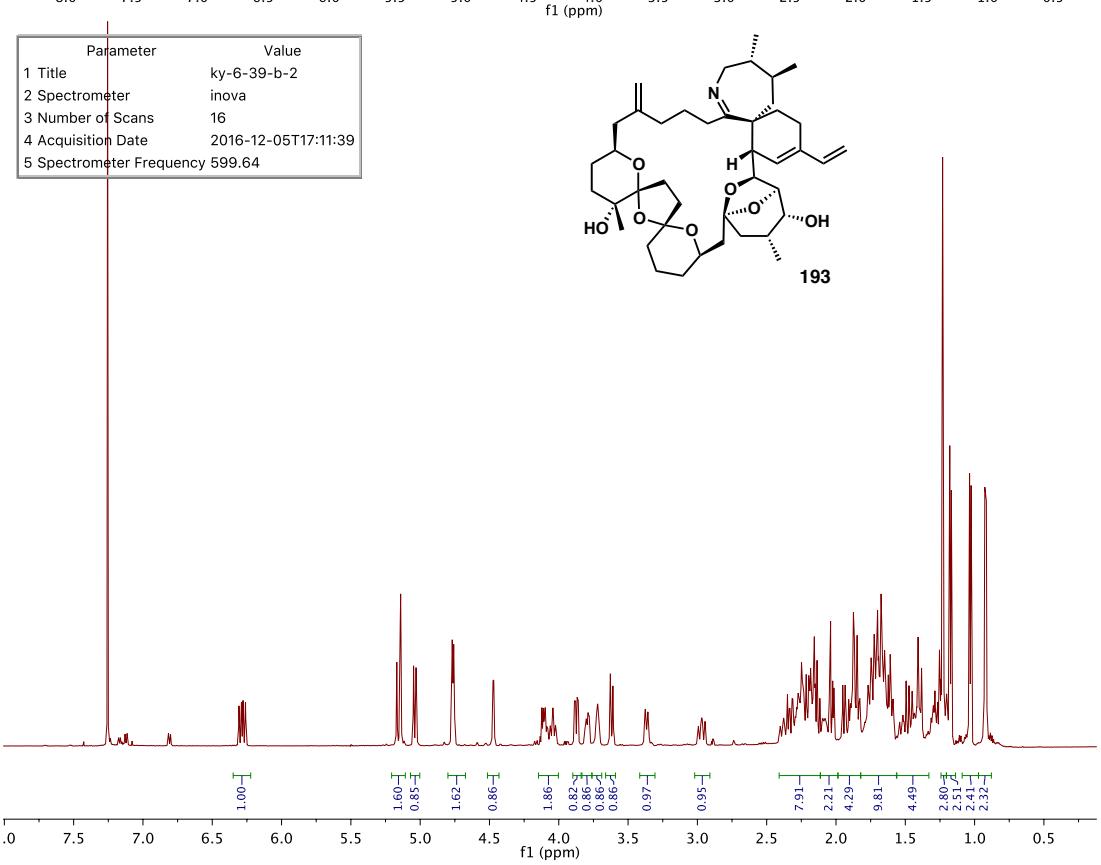
180

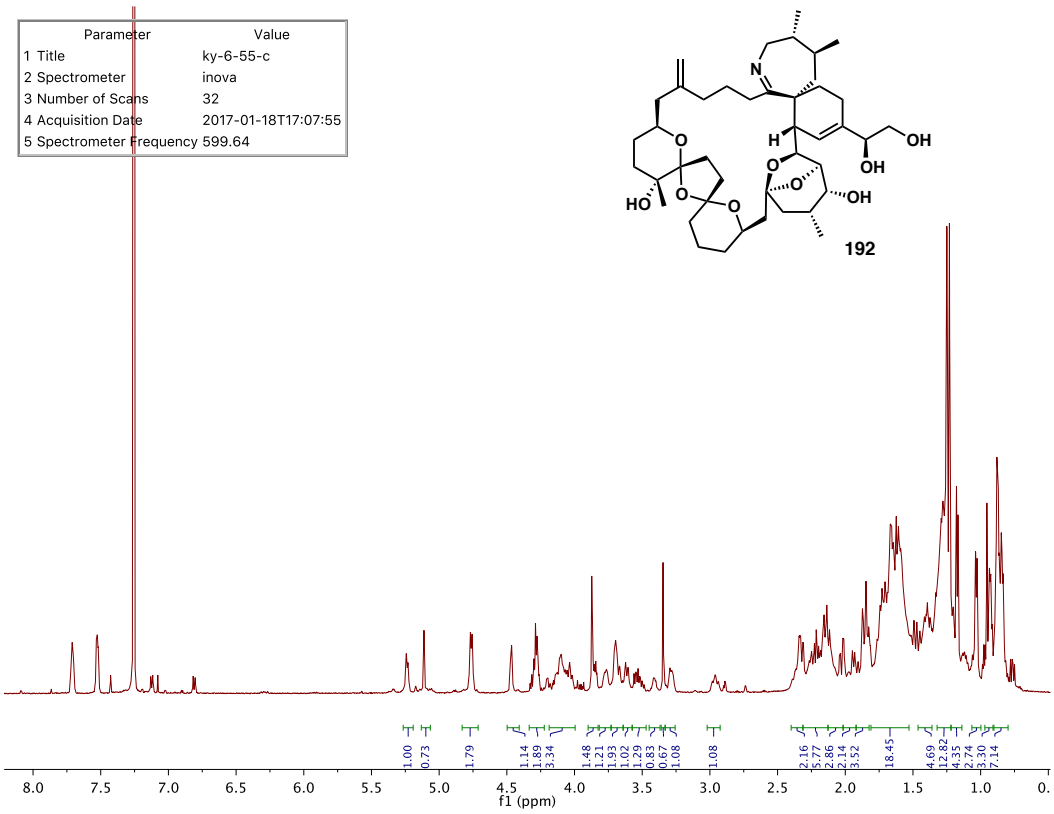
Parameter	Value
1 Title	ky-5-57-a
2 Spectrometer	inova
3 Number of Scans	24
4 Acquisition Date	2016-02-19T13:58:42
5 Spectrometer Frequency	499.86



188


Parameter Value
1 Title ky-6-57-a
2 Spectrometer inova
3 Number of Scans 12
4 Acquisition Date 2017-01-25T10:45:03
5 Spectrometer Frequency 599.64
N3
O
H
O
HO
O
O
O
OH
1.00
1.89
0.97
1.65
0.84
1.85
0.84
0.96
1.64
0.72
1.13
1.04
2.57
32.65
5.73
3.57
2.99
3.40
2.90
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


Parameter Value
1 Title ky-6-39-b-2
2 Spectrometer inova
3 Number of Scans 16
4 Acquisition Date 2016-12-05T17:11:39
5 Spectrometer Frequency 599.64
N
O
H
O
HO
O
O
O
OH
193
1.00
1.60
0.85
1.62
0.86
1.86
0.82
0.86
0.86
0.86
0.97
0.95
7.91
2.21
4.29
9.81
4.49
2.80
2.51
2.41
2.32
.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


Parameter Value
1 Title ky-6-55-c
2 Spectrometer inova
3 Number of Scans 32
4 Acquisition Date 2017-01-18T17:07:55
5 Spectrometer Frequency 599.64
N
H
OH
OH
O
O
O
O
O
O
HO
OH
192
1.00 0.73 1.79 1.14 1.89 3.34 1.48 1.21 1.93 1.02 1.29 0.83 0.67 1.08 1.08 2.16 5.77 2.86 2.14 3.52 18.45 4.69 12.82 4.35 2.74 3.10 7.14
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.
f1 (ppm)

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