Lawrence Berkeley National Laboratory

Recent Work

Title

Binding Modes and Dynamics of Distamycin A with Several A-T-rich Oligomers by Two-dimensional NMR

Permalink

<https://escholarship.org/uc/item/31k1h6cp>

Author

Pelton, J.G.

Publication Date

1990

Lawrence Berkeley Laboratory

UNIVERSITY OF CALIFORNIA

CHEMICAL BIODYNAMICS DIVISION

Binding Modes and Dynamics of Distamycin A with Several A-T-rich Oligomers by Two-dimensional NMR

J.G. Pelton
(Ph.D. Thesis)

January 1990

Prepared for the U.S. Department of Energy under Contract Number DE-AC03-76SF00098.

1 LOAN COPY 1
1 CIRCULATES 1
1 FOR 2 WEEKS 1

Bldg. 500 Library

LBL-28620

COPY 2

DISCLAIMER

This document was prepared as an account of work sponsored by the United States Government. While this document is believed to contain correct information, neither the United States Government nor any agency thereof, nor the Regents of the University of California, nor any of their employees, makes any warranty, express or implied, or assumes any legal responsibility for the accuracy, completeness, or usefulness of any information, apparatus, product, or process disclosed, or represents that its use would not infringe privately owned rights. Reference herein to any specific commercial product, process, or service by its trade name, trademark, manufacturer, or otherwise, does not necessarily constitute or imply its endorsement, recommendation, or favoring by the United States Government or any agency thereof, or the Regents of the University of California. The views and opinions of authors expressed herein do not necessarily state or reflect those of the United States Government or any agency thereof or the Regents of the University of California.

**Binding Modes and Dynamics of Distamycin A with Several A-T-rich
Oligomers by Two-dimensional NMR**

by

Jeffrey Grant Pelton

Ph.D Thesis

January, 1990

Chemical Biodynamics Division

Lawrence Berkeley Laboratory

University of California

Berkeley, CA 94720

This work was supported by the Director, Office of Energy Research, Office of General
Life Sciences, Structural Biology Division of the U.S. Department of Energy under
Contract No. DE-AC03-76SF00098

Binding Modes and Dynamics of Distamycin A with Several A-T-rich Oligomers by Two-Dimensional NMR

by

Jeffrey Grant Pelton

Abstract

Nuclear Overhauser effect spectroscopy has been used to identify the binding modes and to probe the dynamics of distamycin A in complexes with d(CGCGAATTCGCG)₂, d(CGCAAATTGGC):d(GCCAATTTGCG), and d(CGCAAATTTGCG)₂. Distamycin A binds to the minor-groove of the AATT segment of the d(CGCGAATTCGCG)₂ duplex. The binding site is characterized by drug-DNA van der Waals contacts, three-center hydrogen bonds, and stacking of sugar O4' atoms over each of the drug pyrrole rings. At low drug:DNA ratios (0.5), distamycin A binds in both orientations within the five central A-T base pairs of the d(CGCAAATTGGC):d(GCCAATTTGCG) undecamer and has a preference (2.2:1) for binding with the formyl end directed toward the 5' side of the A-rich strand. The NOE data are consistent with models in which the drug slides between AAAT and AATT sites in the preferred binding orientation, and between AATT and ATTT sites in the less favored orientation. At high drug:DNA ratios a 2:1 complex is observed in which both drugs bind in the central AAATT segment. The drugs are in close contact with the DNA and one another. Distamycin A binds in one-drug and symmetric two-drug binding modes with d(CGCAAATTTGCG)₂. For the 2:1 complex the NOE data, as well as observed linewidth changes of the DNA resonances as a function of temperature, were consistent with a model in which each drug slides in fast exchange between AATT and ATTT sites. Molecular modeling of the 2:1 complexes shows that the minor groove must expand relative to the respective 1:1 complexes in order to accommodate both

drugs, indicating that the phosphate backbone can be distorted in response to ligand binding. Energy refinement suggests that electrostatic interactions, intermolecular hydrogen bonds, and stacking interactions contribute to stabilization of these complexes.

This dissertation is dedicated to my parents
for their support these twenty-some years.

I would sleep

.....but thou must dance.

Thomas Mann

Acknowledgements

Many have contributed to this work in terms of both science and my emotional well being. First and foremost is Dave Wemmer. His influence can be seen from the first to last page of the text. His patience when things were tough and his excitement when things were interesting made graduate study very enjoyable. His time and effort are most appreciated. Professors Tinoco, Hearst, Sauer, and Kim need also be mentioned for providing excellent role models whether they were always aware of it or not.

Dave and Rachel Klevit (University of Washington) laid the foundation for this work. Rachel was very kind in providing me with a sample of the distamycin A - A₂T₂ complex and in providing data on distamycin A binding with A₃T₂. David Koh also played no small part by synthesizing the A₃T₂ and A₃T₃ DNA sequences and providing Chinese wisdom. John Hubbard of the Hearst group and Bill Ross of the Tinoco group also provided help with the AMBER program.

Certainly one is influenced by those around him. The critical reader will see the mark of various people in the following pages. Joe (Ann) Pease and David O'brien were constant friends and influences as were Beth Snowden, Debbie Kallick, and Vasant Kumar. In the middle and later stages Eric Peterson was always a willing listener when things were or were not going well (Hey! Lets go to Roma's). Milan and Jody Tomic provided friendship and a friend, traces of which can be especially seen in the latter chapters (Lets go to the Improv I). In addition, the rest of the Wemmer group made many contributions. Rick Storrs and Kalle Gehring were always on alert at group meetings. Also, Patty Fagan, Kay Lee, Mark Kubinec, Marty Pagel, Fred Damberger, and Brian Volkman, the newer students, brought with them great and varied personalities which made the last year at Berkeley much easier.

Finally, to the reader I want to say two things. The first can be attributed to my father who always told me that "it isn't the big leap, but what you do every day that gets things done". The second can be attributed, I believe, to General D. Eisenhower who observed that the people who got ahead were those who did the work at hand.

Table of Contents

Acknowledgements	iv
Table of Contents	vi
List of tables	ix
List of figures	x

Chapter 1

Introduction

1.1 Introduction	1
1.2 Distamycin A	2
1.3 Deoxyribonucleic acid structure	5
1.4 Nuclear magnetic resonance spectroscopy	8
1.5 NMR and biomolecules	24
1.6 Model building	25

Chapter 2

Structural Modeling of the Distamycin A - d(CGCGAATTCGCG)₂

Complex Using 2D NMR and Molecular Mechanics

2.1 Introduction	29
2.2 Materials and Methods	30
2.3 Structural analysis, NOESY experiments	34
2.4 Quantitative distance measurements, SKEWSY experiments	42
2.5 AMBER structures	49
2.6 Distamycin A - A ₂ T ₂ discussion	55
2.7 Distamycin A - A ₂ T ₂ conclusions	60

Chapter 3

Structure and Dynamics of Distamycin A with

d(CGCAAATTGGC):d(GCCAATTTGCG) at low Drug:DNA Ratios

3.1 Introduction	62
3.2 Materials and Methods	62
3.3 A ₃ T ₂ duplex	63
3.4 Titration of the A ₃ T ₂ duplex with distamycin A	63
3.5 Drug proton assignments	66
3.6 A ₃ T ₂ with one-half equivalent of distamycin A	68
3.7 Dynamics	72
3.8 Discussion	75

Chapter 4

Structural Characterization of the 2:1 Distamycin A -

d(CGCAAATTGGC):d(GCCAATTTGCG) Complex by 2D NMR

4.1 Introduction	84
4.2 Materials and Methods	84
4.3 DNA and drug proton assignments	85
4.4 Intermolecular contacts	89
4.5 Discussion	91

Chapter 5

Binding Modes and Dynamics of Distamycin A with d(CGCAAATTTGCG)₂

Determined by 2D NMR

5.1 Introduction	100
5.2 Materials and Methods	100
5.3 Titration of the A ₃ T ₃ duplex with distamycin A	101
5.4 Assignment of resonances in the 2:1 A ₃ T ₃ complex	107

5.5 Intermolecular contacts	113
5.6 Distamycin A binding modes in a crystallization buffer	114
5.7 Discussion	115
5.8 Conclusions	129

Chapter 6

Summary

Summary and Conclusions	130
-------------------------------	-----

Appendices

Appendix A. SKEWSY methodology	133
Appendix B. Distamycin A - A ₂ T ₂ coordinates	135
Appendix C. Free A ₃ T ₂ duplex assignments	184
Appendix D. A ₃ T ₂ adenine C2H assignments	185
Appendix E. Distamycin A - A ₃ T ₂ coordinates	187
Appendix F. Distamycin A - A ₃ T ₃ spectra	204
Appendix G. Distamycin A - A ₃ T ₃ coordinates	206

List of Tables

1 - 1	NOESY pulse and receiver phase cycling	22
2 - 1	Atom types and point charges for distamycin A	32
2 - 2	Intensity and relaxation matrices for two and three-spin systems	40
2 - 3	Intensity and relaxation matrices for the A6 and A18 spin systems	41
2 - 4	Calculated distances and constraints for the distamycin A - A ₂ T ₂ complexes	48
3 - 1	¹ H chemical shift assignments of the free A ₃ T ₂ duplex and both one-drug complexes	64
3 - 2	Distamycin A - A ₃ T ₂ intermolecular contacts at one-half equivalent of added drug	71
4 - 1	DNA and drug proton assignments of the 2:1 distamycin A - A ₃ T ₂ complex	90
4 - 2	Intermolecular NOEs in the 2:1 distamycin A - A ₃ T ₂ complex	92
5 - 1	Chemical shift assignments of free and bound forms of the A ₃ T ₃ duplex	104
5 - 2	Intermolecular drug-DNA and drug-drug NOEs	117
5 - 3	Distamycin A - A ₃ T ₃ hydrogen bonds	127
E - 1	Distance constraints for the 2:1 distamycin A - A ₃ T ₂ complexes	187
G - 1	Distance constraints for the 2:1 distamycin A - A ₃ T ₃ complexes	206

List of Figures

1 - 1 Schematic of distamycin A	3
1 - 2 Schematic of the nucleotide unit	6
1 - 3 Polymer of DNA	7
1 - 4 Watson-Crick base pairing scheme	9
1 - 5 Schematic of ideal B-form DNA	10
1 - 6 Schematic of DNA helical parameters	11
1 - 7 Exchange of a ligand on a macromolecule	18
1 - 8 NMR spectra of a proton attached to an exchanging ligand	19
1 - 9 Pulse sequence and vector picture of the NOESY experiment	21
1-10 NMR spectrum of the non-exchangeable protons of distamycin A	27
1-11 NMR spectrum of the non-exchangeable protons of the A ₃ T ₂ duplex	28
2 - 1 NOESY spectrum of the distamycin A - A ₂ T ₂ complex	35
2 - 2 Experimental and simulated NOE buildup curves	38
2 - 3 SKEWSY and NOESY NMR pulse sequences	43
2 - 4 Model for three-spin system	44
2 - 5 Stereodrawing of the distamycin A - A ₂ T ₂ complex	51
2 - 6 Hydrogen bond scheme for the distamycin A - A ₂ T ₂ complex	52
3 - 1 Titration of the A ₃ T ₂ duplex with distamycin A	65
3 - 2 NOE difference spectra of the A ₃ T ₂ duplex with three- quarters of an equivalent of distamycin A	67
3 - 3 NOESY spectrum of the A ₃ T ₂ duplex with one-half equivalent of distamycin A	69
3 - 4 NOESY spectrum of the A ₃ T ₂ duplex with 1.3 equivalents of distamycin A	74

3 - 5 Models for distamycin A binding sites on the A ₃ T ₂ duplex	7 8
4 - 1 NOESY spectrum of the A ₃ T ₂ duplex with 2.0 equivalents of distamycin A	8 6
4 - 2 Schematic of distamycin A binding sites on the A ₃ T ₂ duplex	9 4
4 - 3 Stereodrawing of the 2:1 distamycin A - A ₃ T ₂ complex	9 6
5 -1 Proton spectra of the A ₃ T ₃ duplex with increasing levels of distamycin A	1 0 2
5 - 2 NOESY spectrum of the A ₃ T ₃ duplex with one-half equivalent of distamycin A	1 0 6
5 - 3 NOESY spectrum of the A ₃ T ₃ duplex with 2.0 equivalents of distamycin A	1 0 8
5 - 4 Spectra of the A ₃ T ₃ duplex with 2.0 equivalents of distamycin A at various temperatures	1 1 1
5 - 5 Expansion of the C2'H/C2"H region of a NOESY spectrum of the 2:1 distamycin A - A ₃ T ₃ complex	1 1 2
5 - 6 Proton spectra of the 2:1 distamycin A - A ₃ T ₃ complex in crystallization buffer	1 1 6
5 - 7 Schematic of models for the binding of distamycin A to the A ₃ T ₃ duplex	1 1 9
5 - 8 Sliding model for the binding of distamycin A to the A ₃ T ₃ duplex	1 2 1
5 -9 Stereodrawings of 2:1 distamycin A - A ₃ T ₃ complexes C1 and C2	1 2 5
C - 1 NOESY spectrum of the free A ₃ T ₂ complex	1 8 4
D - 1 NOE difference spectra of the A ₃ T ₂ imino protons	1 8 6
F - 1 NOESY spectrum of the free A ₃ T ₃ duplex	2 0 4
F - 2 NOE difference spectra of the 2:1 distamycin A - A ₃ T ₃ complex	2 0 5

Chapter 1

Introduction

Distamycin A, a DNA minor-groove binding antibiotic, has been studied since the early 1960's as an agent directed against DNA-containing viruses, and the inhibition of protein synthesis (DiMarco *et al.*, 1963). As early as 1970 the drug was shown to act as a deoxyribonucleic acid (DNA) "template poison" specifically inhibiting the initiation of RNA synthesis (Puschendorf *et al.*, 1971). However, only recently have models of distamycin A - DNA complexes been put forth (Patel, 1982; Schultz & Dervan, 1984; Kopka *et al.*, 1985a-c; Patel & Shapiro, 1985). In order to test and extend these models, the interaction of distamycin A with several DNA oligomers was studied at the molecular level using two-dimensional nuclear magnetic resonance (2D NMR) techniques. The specific goals of the present work were to further define the sequence specificity and forces responsible for binding of the drug. Given an understanding of the principles involved one should then be able to design new drugs, sequence specific probes, and affinity cleaving molecules that recognize specific DNA sequences. In the course of this work it also became clear that one could use distamycin A as a probe of DNA structure and flexibility and that the ensuing results would shed light on both the relatively recent crystal structures of several DNA oligomers (Drew *et al.*, 1981; Nelson *et al.*, 1987; Coll *et al.*, 1987; Yoon *et al.*, 1988) and the sequence specific recognition of DNA by proteins, a process which is, as yet, incompletely understood.

After a brief introduction to the molecules and techniques used, structural investigations on a distamycin A - d(CGCGAATTCGCG)₂ (A₂T₂) complex, which are an extension of a previous NMR study (Klevit *et al.*, 1986) will be presented (Chapter 2). Here the main structural features of the distamycin A - DNA complex, the general characteristics of which are observed in the later studies, are described in

detail. Next, structural and dynamic aspects of the distamycin A - d(CGCAAATTGGC):d(GCCAATTTGCG) (A₃T₂) system at low drug:DNA ratios (<1.5) are presented (Chapter 3). In the course of this work, it became apparent that two drugs could bind simultaneously in the minor groove of the undecamer. Structural aspects of this 2:1 complex are described in detail in chapter 4. Finally, a 2:1 distamycin A - d(CGCAAATTTGCG)₂ (A₃T₃) complex is described and the results are compared with those obtained in a recent X-ray crystallographic investigation of the same system (Coll *et al.*, 1987)(Chapter 5).

1.2 Distamycin A

Distamycin A (Figure 1-1) and netropsin¹ are examples of non-intercalating antibiotics that bind preferentially to the minor groove of A-T- and I-C-rich B-form DNA sequences (Krey *et al.*, 1973) [for reviews see Hahn (1975) and Zimmer (1986)]. The complexes formed between these drugs and various DNA oligomers have been used as model systems for the investigation of sequence-specific recognition of DNA and have thus been the subject of much study. In particular, structural investigations of distamycin A-DNA complexes have aimed at understanding the possible binding modes, sequence specificity, and forces responsible for drug binding, while kinetic investigations have aimed at understanding how the drug exchanges between the possible binding modes.

Preferred sequences for the binding of distamycin A have been identified by affinity cleaving studies (Schultz & Dervan, 1984). This work showed that distamycin A covers five base pairs, that it binds preferentially to 5'-AAATT-3' in two orientations to a degree dependent on flanking sequences, and that in general, the drug prefers sites with consecutive adenine residues. Hydroxyl-radical footprinting

¹contains only two N-methylpyrrolicarboxamide units, and a guanidinoacetyl group replaces the formamide group of distamycin A

Figure 1-1. Schematic of distamycin A. The drug consists of three N-methyl pyrrolicarboxamide units capped by a formyl group and a propylamidine group. The numbering scheme used in this work is shown.

studies have confirmed these results (Portugal & Waring, 1987). Calorimetric studies (Breslauer *et al.*, 1987) also indicate that distamycin A has a high affinity for the polymers poly d(A):poly d(T) and poly d(A-T). NMR studies (Klevit *et al.*, 1986) of distamycin A with d(CGCGAATTCGCG)₂ indicated that the minimal binding site consists of just four A-T base pairs. Subsequent calorimetric studies (Breslauer *et al.*, 1987) have shown that distamycin A binds tightly to the four-base site 5'-AATT-3' within the sequence d(GCGAATTCGC)₂, with a binding constant of $2.7 \times 10^8 \text{ M}^{-1}$. This is in striking contrast to the binding constant of $2 \times 10^5 \text{ M}^{-1}$ reported for the 5'-TATA-3' site within the sequence d(GGTATACC)₂ (Fish *et al.*, 1988), obtained by quantitative analysis of footprinting data, showing that the drug displays a high degree of A-T sequence specificity. Sequence specificity is also evidenced in the crystallographic study of distamycin A with d(CGCAAATTTGCG)₂ (Coll *et al.* 1987), where it was found that the drug bound to a 5'-ATTT-3' sequence, although other sites with four base pairs were available. The A-T sequence specificity of distamycin A is still not well understood. Similar results have been obtained from footprinting (Ward *et al.*, 1988; Fish *et al.*, 1988), calorimetric (Marky *et al.*, 1983), crystallographic (Kopka *et al.*, 1985 a-c; Coll *et al.*, 1989), and NMR (Patel, 1982; Patel & Shapiro, 1985; Sarma *et al.*, 1985; Pardi *et al.*, 1983) studies of netropsin-DNA complexes and also Hoechst 33258- (Pjura *et al.*, 1987; Teng *et al.*, 1988; Carrondo *et al.*, 1989) DNA complexes. Analysis of these data indicates that van der Waals forces, hydrogen bonds, and both hydrophobic effects (Zimmer *et al.*, 1972) and electrostatic interactions (Lavery *et al.*, 1986; Zakrzewska *et al.*, 1987) contribute to the stability of the complexes and the sequence specificity of these drugs.

In addition to the emerging structural picture, drugs of this general class have been shown to undergo several dynamical processes. For instance, NMR studies of

distamycin A with the A₂T₂ duplex have shown that the drug off-rate was approximately 4 s⁻¹ and that the "flip-rate" between the two symmetry related 5'-AATT-3' binding sites was approximately 2 s⁻¹ (Klevit *et al.*, 1986). The minor-groove binding drugs netropsin (Patel & Shapiro, 1985, 1986), a netropsin analogue² (Lee *et al.*, 1988), 4S (+) and 4R (-) - anthelvencin A (Lee *et al.*, 1989), and a bis-(quaternary ammonium) heterocycle SN6999 (Leupin *et al.*, 1986) have also been shown to exchange between two symmetrically related binding sites on their respective DNA sequences, indicating that such a process is a common feature of these minor-groove binding antibiotics and must be considered when analyzing data obtained on these and similar systems.

1.3 Deoxyribonucleic Acid Structure

Deoxyribonucleic acids (DNA) are polymers made from nucleotide building blocks [see Saenger (1984) for a comprehensive review]. The nucleotide consists of a D-2'-deoxyribose sugar moiety that is phosphorylated at the 5' position and has either a purine or pyrimidine base connected by a β -glycosidic C1'-N bond at the 1' position. The conformation of the nucleotide can be described by six backbone torsion angles, five endocyclic torsion angles, and the angle χ which describes the orientation of the base relative to the sugar (Figure 1-2). Note that both the endocyclic torsion angle ν_3 and the exocyclic backbone torsion angle δ refer to the same conformation about the C3'-C4' bond and are therefore not independent.

The nucleotide units are condensed into a polymer by formation of 3',5' phosphodiester bonds (Figure 1-3). The two strands are then wound about one another to form either right-handed (A- and B-form)(Chandrasekaran & Arnott, 1989) or left-handed (Z-form) helices (Wang *et al.*, 1979). In the double helix the two purine bases, adenine (A) and guanine (G), pair with the pyrimidine bases

² second pyrrole ring of netropsin replaced with an imidazole ring

Figure 1-2. Schematic of the nucleotide unit. It consists of a phosphorylated D-2'-deoxyribose sugar and either a purine or pyrimidine base. Torsion angles used to describe the conformation of the nucleotide are shown.

Figure 1-3. Polymer of DNA made of nucleotide units. Schematic representations of the four bases, adenine (A), guanine (G), thymine (T), and cytosine (C) are shown in relation to the sugar-phosphate backbone. Black dots denote hydrogen atoms.

thymine (T) and cytosine (C), respectively (Watson & Crick, 1954) (Figure 1-4). A model of B-form DNA (Chandrasekaran & Arnott, 1989), the focus of this work, is presented in Figure 1-5. Moreover, although each nucleotide of the polymer is determined by the set of angles described above, a summary of such does not lead to a clear visual picture of a DNA molecule. For this reason more intuitive parameters have been developed. These parameters have recently been standardized (Dickerson *et al.*, 1989). Several of the more important ones are shown in Figure 1-6. Distinguishing characteristics of ideal B-form DNA are the helical twist of 10 base pairs per turn, the sugar conformation which is C2' - endo (δ , -144°), a low propeller twist (4°), and an axial rise of 0.33 nm. Also, of particular importance to the later studies is the presence of a wide (1.17 nm) major groove and a relatively narrow (0.57 nm) minor groove (Saenger, 1984). Data derived from single-crystal X-ray studies show that there are significant variations in the conformation of each nucleotide in the sequence d(CGCGAATTCGCG)₂, although average values are generally near those of ideal B-DNA (Drew *et al.*, 1981).

1.4 Nuclear Magnetic Resonance Spectroscopy

Basics

Many nuclei have non-zero ground-state spin angular momentum which gives rise to a nuclear magnetic moment:

$$\mu = (\gamma h/2\pi) \mathbf{I} \quad (1-1)$$

where γ is the magnetogyric ratio ($\text{radians} \cdot \text{s}^{-1} \cdot \text{gauss}^{-1}$), h is Plank's constant ($\text{J}\cdot\text{s}$), and $\mathbf{I}$ denotes the spin angular momentum (Abragam, 1961). The interaction of this nuclear magnetic moment with an external magnetic field lifts the degeneracy of the nuclear spin states. If the external field is applied in the z direction (H_{Oz}), the energy of each state takes the form (Slichter, 1978a):

T : A

G : C

Figure 1-4. Schematic of the Watson-Crick base pairing scheme for A-T and G-C base pairs.

Figure 1-5. Schematic of an ideal B-form DNA model of the sequence $d(\text{CGCGAATTCGCG})_2$ derived from fiber diffraction studies (Chandrasekaran & Arnott, 1989). The major and minor grooves are indicated.

Figure 1-6. Coordinate system and definition of several parameters used to describe the conformation of base pairs in the DNA double-helix. I and II denote bases of strands one and two, respectively.

$$E = -(\gamma h/2\pi)H_{Oz}m_z \quad (1-2)$$

where m_z corresponds to a particular eigenvalue of I_z , the z-component of the spin angular momentum. For protons, m_z can take values of +1/2 or -1/2, and thus, the transition energy is given as:

$$\Delta E = (\gamma h/2\pi)H_{Oz} \quad (1-3)$$

In addition to the static field, local fields, such as those due to induced electron currents, contribute to the actual field felt by a particular nucleus. These local fields vary with chemical environment and give rise to a dispersion in transition frequencies. This effect is described by replacing the magnetic field H by the quantity $(1 - \sigma)H$, where σ is chemical shielding tensor. In solution isotropic tumbling of the molecule reduces the chemical shift tensor to a scalar quantity (Emsley *et al.*, 1965a).

The spins are in contact with a thermal reservoir known as the lattice, and therefore the populations of the spins in the various states are governed by the Boltzmann distribution. The net magnetization induced by a static field applied in the z direction is given by:

$$M_O = N(\gamma h/2\pi)[I(I+1)]H_{Oz}/3kT \quad (1-4)$$

where N is the number of spins, I is the spin angular momentum quantum number, k is the Boltzmann constant (J/K), and T is the temperature of the system in degrees Kelvin (Abragam, 1961). After placement in a magnetic field, the spins attain this equilibrium magnetization with a first-order time constant T_1 (Emsley *et al.*, 1965b).

The NMR spectra described in the following chapters were acquired in the pulse Fourier- transform mode [for comprehensive reviews see Farrar & Becker, 1971;

Chandrakumar & Subramanian, 1987; Ernst *et al.*, 1987). Here, one or more radiofrequency (*rf*) pulses is applied to the sample, after which the resultant voltage induced in a coil placed around the sample is measured as a function of time. This response or free-induction-decay (FID) is then Fourier-transformed with respect to time converting the signal from the time domain into the frequency domain, i.e., the conventional NMR spectrum.

The time evolution of a spin system can be described quantum mechanically with density matrix formalism (Chandrakumar & Subramanian, 1987). The time dependence of the density matrix ($\rho(t)$) is given by :

$$\rho(t) = e^{-iHt} \rho(0) e^{iHt} \quad (1-5)$$

where $\rho(0)$ is the density matrix at an initial time, and H is the Hamiltonian appropriate for the system during the time t . The density matrix contains all of the available statistical information about an ensemble of spins. The expectation value $\langle O(t) \rangle$ of a measurable property of the ensemble is then given as :

$$\langle O(t) \rangle = \text{Tr} (\rho(t) O) \quad (1-6)$$

where O is a matrix representation of the observable of interest (Sakurai, 1985).

Dipolar Coupling

The magnetic moment of one spin can couple with that of another spin through dipole-dipole coupling. The secular portion of the Hamiltonian that describes this interaction for like spins is given by:

$$H = \frac{1}{4} \left(\frac{\gamma h}{2\pi} \right)^2 \sum_{i \neq j} \frac{(1-3\cos^2\theta_{ij})(3I_{iz}I_{jz} - I_i \cdot I_j)}{r_{ij}^3} \quad (1-7)$$

where r_{ij} is the internuclear vector and θ_{ij} is the angle between the internuclear vector and the magnetic field (Slichter, 1978b). Direct effects due to dipolar

coupling are not observed in NMR spectra of liquid samples because the term $(1 - 3\cos^2\theta_{ij})$ averages to zero in the course of molecular tumbling. However, the coupling does provide a mechanism for spin-relaxation. For a particular spin i , the dynamics of this relaxation process can be described by the following master equation (Kalk & Berendsen, 1976):

$$\frac{dM_{zi}}{dt} = -R_{1i}(M_{zi} - M_{0i}) - \sum_{i \neq j} R_{tij}(M_{zi} - M_{zj}) \quad (1-8)$$

where M_{z0} and M_{zi} are the equilibrium and actual magnetization components of spin i , M_{zj} is the actual magnetization component of spin j , and where R_{1i} and R_{tij} correspond to rate constants for spin-lattice and cross-relaxation, respectively. It is the second term of [1-8] that describes transfer of magnetization between pairs of spins and gives rise to the nuclear Overhauser effect (NOE). Assuming that the molecules undergo isotropic tumbling, and that all internuclear vectors can be described with one correlation time τ_c with independent fluctuations, the spin-lattice (R_{1i}) and cross-relaxation (R_{tij}) rates are given by:

$$R_{1i} = \frac{3}{10} \left(\frac{\gamma^2 h}{2\pi} \right)^2 \sum_j \frac{1}{r_{ij}^6} \left[\frac{\tau_c}{1 + (\omega\tau_c)^2} + \frac{4\tau_c}{1 + (2\omega\tau_c)^2} \right] \quad (1-9)$$

$$R_{tij} = \left(\frac{\gamma^2 h}{2\pi} \right)^2 \frac{1}{r_{ij}^6} \left[\tau_c - \frac{6\tau_c}{1 + (2\omega\tau_c)^2} \right]$$

where ω is the transition frequency (Kalk & Berendsen, 1976). The correlation time for the DNA duplexes described in the next chapters (eleven and twelve base pairs) is on the order of 6 ns, and with an 11.7 T magnet, the transition frequency is 500 MHz.

In the spin-diffusion limit ($\omega\tau_c \gg 1$), which is the case for the duplexes studied in this work ($\omega\tau_c \approx 19$), the spin-lattice and cross-relaxation rates reduce to (Macura & Ernst, 1980):

$$R_{1i} = 0 \quad (1-10)$$

$$R_{tij} = \frac{1}{10} \left(\frac{\gamma^2 h}{2\pi} \right)^2 \sum_j \frac{\tau_c}{r_{ij}^6}$$

and for two spins, [1-8] simplifies to:

$$\frac{dM_{zi}}{dt} = - R_{tij} (M_{zi} - M_{zj}) \quad (1-11)$$

Equation 1-11 describes the response of the net magnetization associated with spin i as a function of the population difference of spins i and j . If the system is perturbed from equilibrium, say by a selective inversion of M_{zj} , then at short times, the change in the magnetization of spin i is governed by the following equation:

$$\Delta M_{zi} = - R_{tij} (M_{0i} + M_{0j}) \Delta t \quad (1-12)$$

where M_{0i} and M_{0j} represent the magnetization of spins i and j at equilibrium. Thus, the rate of change of the magnetization of spin i with respect to time is proportional to the cross-relaxation rate R_{tij} , which is a function of the inverse sixth-power of the distance between the pair of spins [1-10]. By taking ratios of cross-relaxation rates obtained at short times, the distance between a pair of spins i and j can be determined if the distance and cross-relaxation rate between another pair of spins k and l are known [1-13], provided the equilibrium magnetization for both spins is the same (Macura & Ernst, 1980).

$$r_{ij} = \left[\frac{R_{tkl}}{R_{tij}} \right]^{\frac{1}{6}} r_{kl} \quad (1-13)$$

Here R_{tij} and R_{tkl} are the cross-relaxation rates and r_{ij} and r_{kl} are the internuclear distances of the i - j and k - l spin pairs, respectively. For the DNA duplexes described herein, NOEs and therefore distances can be determined for proton pairs that are less than 0.5 nm apart. However, [1-13] must be used with caution since second-order exchange processes (spin diffusion) can result in the transfer of magnetization first from i to j and then from j to l (three-spin system) leading to systematic errors in the measured distances.

Chemical Exchange

As just described, magnetization can be transferred between spins through the nuclear Overhauser effect. Magnetization can also be transferred between different environments through chemical exchange processes. Such is the case when a ligand can bind to two different sites on a macromolecule (Figure 1-7). It can be shown in the case of two-site exchange, that the line-width and resonance frequency of a particular spin are a function of both the lifetime (τ) and the difference in chemical shift ($\omega_a - \omega_b$) of the spin in the two sites (Carrington & McLachlan, 1967). The results are summarized schematically in Figure 1-8 for the case in which the two sites are equally populated. As can be seen in this figure, in the slow-exchange limit ($\Delta\omega\tau \gg 1$), two distinct lines appear in the spectrum. As the exchange rate is increased, each line broadens until they coalesce ($\Delta\omega\tau \approx 1$, intermediate exchange). Further increases in the rate of exchange ($\Delta\omega\tau \ll 1$, fast exchange) result in the narrowing of the single peak, which resonates at the population-weighted average of the chemical shifts corresponding to the two sites.

Double-resonance methods can be used to measure exchange rates in the slow-exchange limit (rate-constants of approximately 0.1 to 100 s⁻¹) (Forsen & Hoffman, 1963). The z-component of the magnetization of a spin that exchanges between two sites A and B can be expressed as follows:

$$\frac{dM_{za}}{dt} = \frac{(M_{0a} - M_{za})}{T_{1a}} - k_a M_{za} + k_b M_{zb} \quad (1-14)$$

where M_{za} and M_0 are the current and equilibrium values of the z-component of magnetization at site A, M_{zb} is the z-component of the magnetization at site B, T_{1a} is the spin-lattice time constant for the spin in site A, and k_a and k_b are rate constants

for exchange from and to site A, respectively. If the resonance at site B is saturated with a strong r_f pulse ($M_{bz}=0$) and if $k_a \gg 1/T_{1a}$, [1-14] reduces to:

$$\frac{dM_{za}}{dt} = -k_a M_{za} \quad (1-15)$$

in analogy with [1-12]. Thus, in the short-time limit, monitoring the change in the intensity of peak A as a function of time allows for determination of the rate constant k_a .

Nuclear Overhauser Effect / Exchange Spectroscopy

The nuclear Overhauser effect spectroscopy (NOESY) experiment (Jeener *et al.*, 1979) is the two-dimensional analogue of the one-dimensional NOE and chemical exchange experiments just described. The pulse sequence is shown in Figure 1-9. Aside from an explanation of several artifacts that can appear in the spectrum and that can be removed by cycling the pulse and receiver phases (Table 1-1, discussed below), a density matrix treatment of the evolution of the spins during the pulse sequence is essentially identical to the classical vector representation. Because the vector representation provides a more intuitive picture of the experiment, it will be used in the following discussion.

Figure 1-7. Exchange of a ligand (dark grey) between two sites, A and B, on a macromolecule (light grey) with forward and reverse rate constants k_a and k_b , respectively. A proton attached to the ligand assumes resonance frequencies ω_a and ω_b in sites A and B, respectively.

Figure 1-8. NMR spectra of a proton attached to the ligand of figure 1-7 for various values of $\Delta\omega\tau_c$. (A) Slow exchange, (B) intermediate exchange, and (C) fast exchange.

As shown in Figure 1-9, the first 90°_x pulse rotates the magnetization that is initially at equilibrium along the $+z$ axis to the $-y$ axis. Each spin then rotates in the x - y plane at a characteristic frequency during the delay t_1 and is thereby frequency labeled. At the end of the t_1 time period, the second 90°_x pulse rotates the $\pm y$ components of the magnetization to the $\pm z$ axes. During the subsequent mixing period (τ_m), magnetization is transferred between spins by the nuclear Overhauser effect [1-8], or between environments (chemical shifts) by chemical exchange processes [1-14]. The third 90°_x pulse then rotates the magnetization back to the x - y plane where the signal is detected during the time period t_2 . After an appropriate delay to allow the spins to re-equilibrate, the delay t_1 is incremented and the pulse sequence is repeated.

A density matrix treatment of the pulse sequence [1-5] indicates that unwanted peaks will appear in the NOESY spectrum due to zero-, single-, and double-quantum coherences. To suppress peaks due to single-quantum coherences (and artifacts due to quadrature detection), the phase of each pulse and the receiver are cycled as summarized in Table 1-1. To suppress artifacts due to observable magnetization resulting from zero- and double-quantum coherences, a frequency off-set is added by incrementing the mixing time slightly with each t_1 value, and the magnetization is made to "grow in" with a $\sin(\omega t_2)$ dependence through application of a 180° refocusing pulse near the midpoint of the mixing period (Macura *et al.*, 1981). The final data set consists of a signal that is a function of the time periods t_1 and t_2 ($S(t_1, t_2)$). Fourier transformation of this signal first with respect to t_2 and then t_1 results in a two-dimensional spectrum. Peaks along the diagonal reflect the normal one-dimensional spectrum, while cross peaks indicate that magnetization has been transferred either between spins which are close enough to relax one another

A. Nuclear Overhauser Effect / Exchange Spectroscopy (NOESY)

Figure 1-9. Pulse sequence (A) and vector model (B) of the nuclear Overhauser effect spectroscopy experiment.

Table 1-1. NOESY Pulse and Receive Phase Cycling.

α	β	γ	δ^a
x	x	x	x
- x	x	x	- x
x	x	- x	- x
- x	x	- x	x
y	y	y	y
- y	y	y	- y
y	y	- y	- y
- y	y	- y	y
- x	- x	- x	- x
x	- x	- x	x
- x	- x	x	x
x	- x	x	- x
- y	- y	- y	- y
y	- y	- y	y
- y	- y	y	y
y	- y	y	- y

^aPhase of receiver.

(less than 0.5 nm apart), or between environments (chemical exchange) during the mixing period.

It has been shown that the intensity of a particular peak (a_{kl}) in the spectrum is given by:

$$a_{kl}(\tau_m) = \left[e^{-\mathbf{L}\tau_m} \right]_{kl} M_{l0} \quad (1-16)$$

where $\mathbf{L}$ is the sum of kinetic ($\mathbf{K}$) and relaxation ($\mathbf{R}$) matrices, and M_{l0} is the equilibrium bulk magnetization associated with the l spins (Macura & Ernst 1980). The kinetic matrix contains rate constants for chemical exchange, while the relaxation matrix contains rate constants associated with spin-lattice and cross relaxation³. Inversion of [1-16] gives the rate-constant matrix $\mathbf{L}$ in terms of the the matrix of cross peak intensities ($\mathbf{a}(\tau_m)$), the mixing time (τ_m), and the equilibrium magnetization of each spin ($\mathbf{M}_0$) as follows (Olejniczak *et al.*, 1986; Perrin & Gipe, 1984):

$$\mathbf{L} = - \left(\frac{1}{\tau_m} \right) \ln \left[\mathbf{a}(\tau_m) \mathbf{M}_0^{-1} \right] \quad (1-17)$$

This is more easily calculated by the following equation (Bremer *et al.*, 1984; Perrin & Gipe, 1984):

$$\mathbf{L} = - \left(\frac{1}{\tau_m} \right) \mathbf{X} [\ln(\mathbf{E})] \mathbf{X}^{-1} \quad (1-18)$$

where $\mathbf{X}$ and $\mathbf{E}$ are the eigenvectors and the eigenvalues of the matrix $[\mathbf{a}(\tau_m) \mathbf{M}_0^{-1}]$, respectively. In principle, measurement of the cross and diagonal peaks in a NOESY spectrum, combined with the intensities of the diagonal peaks at equilibrium allows for calculation of the rate-constant matrix $\mathbf{L}$. If only dipolar relaxation processes occur, $\mathbf{L}$ reduces to the relaxation matrix $\mathbf{R}$ and, since the off-diagonal elements of $\mathbf{R}$ correspond to cross-relaxation rates between pairs of spins, it is possible to

³ For two spins i and j , the diagonal elements of $\mathbf{R}$ are equal to the sum of R_{1j} and R_{tjj} , while the off-diagonal elements correspond to R_{tij} (see [1-8]).

calculate distances between these spins as described [1-13]. Similarly, if only chemical exchange processes are present, L reduces to the kinetic matrix K , and back calculation yields rate constants for exchange.

In practice it is usually not possible to calculate the matrix L because of severe overlap of the diagonal peaks. In this case, the intensities of the cross peaks, which reflect the amount of magnetization that has been transferred (ΔM), can be measured in NOESY experiments acquired with short mixing times, and a first-order two-spin analysis can be used to obtain proton-proton distances and exchange rate-constants ([1-12] and [1-15]).

1.5 NMR and Molecules

Distamycin A and DNA are comprised of two classes of protons. One class, that consists of drug amide and amidinium protons and DNA amino and imino protons, exchange rapidly with solvent and must therefore be observed in H_2O . Conversely, the drug aromatic and aliphatic resonances and the DNA aromatic and sugar resonances do not exchange rapidly with solvent and can therefore be observed in D_2O which significantly reduces the dynamic range needed for observation of the resonances. One-dimensional spectra of the non-exchangeable resonances of distamycin A and the A_3T_2 duplex are shown in Figures 1-10 and 1-11, respectively.

One NOESY spectrum contains sufficient information to assign the majority of DNA resonances of a right-handed helix (Hare *et al.*, 1983; Feigon *et al.*, 1983; Scheek *et al.*, 1984). The procedure relies on the fact that the aromatic proton of each base (pyrimidine H6 or purine H8) is close to and gives an NOE to the C1'H and C2'H/C2''H protons of its own sugar and the sugar of its 5' neighbor. By correlating the intra- and inter-residue cross peaks, the aromatic, C1'H, and C2'H/C2''H protons can be assigned to a particular residue in the sequence. Given these assignments, NOEs from

both C1'H and C2'H/C2"H to C3'H, C4'H, and C5'H/C5"H allows for the assignment of the remaining sugar resonances provided that they are well resolved in the spectrum.

The adenine C2H and both G and T imino protons are generally too distant from the other aromatic and sugar protons to give significant NOEs and cannot, therefore, be assigned by sequential methods. However, for sequences that contain three or more consecutive adenine residues it is sometimes possible to assign the C2H protons through observation of weak NOEs to both the C1'H of the 3' neighboring residue and the 3' neighbor of the complementary base (Patel *et al.*, 1986; Weiss *et al.*, 1984; Behling *et al.*, 1986; Kintanar *et al.*, 1987).

For sequences that do not contain consecutive adenine residues, the adenine C2H and DNA imino protons can be assigned by one-dimensional NOE experiments (Chou *et al.*, 1983) where each imino proton (12-16 ppm) is irradiated in turn. By this method the thymine imino protons can be identified by sharp NOEs to the A C2H protons, and the guanine imino protons can be identified by the appearance of relatively broad NOEs to amino protons. After the imino protons are assigned as belonging to either A-T or G-C base pairs, analysis of sequential imino-imino NOEs allows for the sequential assignment of each imino proton and consequently each adenine C2H proton to a specific base pair in the sequence.

1.6 Model Building

Models of distamycin A - DNA complexes consistent with distances derived from NOESY data were generated with the Assisted Model Building and Energy Refinement (AMBER) molecular mechanics package. The objective of this algorithm is to minimize the potential function:

$$E_{\text{tot}} = \sum_{\text{Bonds}} K_r(R - R_0)^2 + \sum_{\text{Angles}} K_\theta(\theta - \theta_0)^2 + \sum_{\substack{\text{Dihedral} \\ \text{Angles}}} \frac{V_n}{2} [1 + \cos(\phi - \gamma)]$$

(1-19)

$$+ \sum_{i \neq j} \left[\frac{A_{ij}}{r_{ij}^{12}} - \frac{B_{ij}}{r_{ij}^6} \right] + \sum_{i \neq j} \frac{q_i q_j}{\epsilon r_{ij}} + \sum_{i \neq j} \left[\frac{C_{ij}}{r_{ij}^{12}} - \frac{D_{ij}}{r_{ij}^{10}} \right]$$

van der Waals Electrostatic Hydrogen Bonds

See Weiner *et al.* (1984) for a description of the parameters used in [1-19] relevant to nucleic acids. NMR constraints were included by addition of a harmonic potential function similar to that used for bonds (see chapter 2).

Figure 1-10. ^1H NMR spectrum of the nonexchangeable protons of distamycin A. General chemical shifts of the various resonances are denoted at the top of the spectrum.

Figure 1-11. ^1H NMR spectrum of the nonexchangeable protons of the A_3T_2 duplex. Chemical shifts of the various resonances are outlined at the top of the spectrum.

Chapter 2

Structural Modeling of the Distamycin A - d(CGCGAATTCGCG)₂ Complex Using 2D NMR and Molecular Mechanics

2.1 Introduction

Recently the NMR resonance assignments, kinetics, and a qualitative structure of the distamycin A-d(CGCGAATTCGCG)₂ complex were reported (Klevit *et al.*, 1986). I have quantified the structure of this complex by further application of 2D-NMR techniques and molecular mechanics calculations in order to evaluate the forces responsible for the tight binding of the drug ($K_b \approx 10^8$) at the molecular level⁴.

To obtain as accurate constraints as possible for the modeling studies, I began quantitative interpretation of NOESY spectra (Jeener *et al.*, 1979) [1-13]. However, these spectra were complicated by the fact that both relatively short and long drug-DNA contacts occur. Extension of the mixing time to increase the intensities of the long-distance contacts resulted in significant spin diffusion (second-order NOEs) in the short range contacts. Spin diffusion was included in the analysis by using both SKEWSY⁵ (Bremer *et al.*, 1984) and NOESY experiments, which taken together provided upper bounds for many DNA-DNA and drug-DNA proton distances. These constraints were added to a modified AMBER (Weiner *et al.*, 1984) molecular mechanics potential function to generate a structure of the complex. Structural analysis revealed, in addition to van der Waals contacts between drug CH and adenine C2H protons and three-

⁴ The remaining text of Chapter 2 is reprinted with permission from *Biochemistry*. Copyright 1988 American Chemical Society.

⁵ Skewed Exchange Spectroscopy

center drug-DNA hydrogen bonds, that DNA O4' atoms which line the walls of the minor groove sandwich each of the three drug pyrrole rings. These stacking interactions may contribute to the stability of the complex.

2.2 Materials and Methods

NMR spectroscopy

NMR samples were prepared as described previously (Klevit *et al.*, 1986). The sample was dissolved in buffer consisting of 10 mM sodium phosphate and 10 mM sodium chloride. NMR spectra were obtained on a GN-500 spectrometer. SKEWSY and NOESY experiments were obtained in phase sensitive mode using TPPI (Drobny *et al.*, 1979). NOESY experiments were obtained at 50, 100, 150, 200, 250, and 500 ms mixing times. A SKEWSY experiment was obtained in which both delay periods were 500 ms. This value was chosen to insure that sufficient relaxation occurred during τ_s (see Figure 2-3) to differentiate the SKEWSY and NOESY peak volumes. All experiments were conducted at 13.5°C to limit chemical exchange of the drug between equivalent sites on the DNA (Klevit *et al.*, 1986). For each t_1 64 scans were signal averaged taking 1024 complex points with a recycle time of 2.1 seconds. 512 t_1 s were recorded per experiment. A spectral width of 5000 Hz resulted in a digital resolution of 4.9Hz/point. The residual HDO resonance was saturated during both the recycle and mixing times. The data were transferred to tape and processed with FTNMR software (Hare Research) on Vaxstation II or Vax 11/785 computers. In t_2 the data were apodized with a sinebell window function phase shifted 60° and skewed toward the beginning of the FID, prior to Fourier transformation. In t_1 the data were zero filled to 2048 complex points and apodized as in t_2 prior to the second Fourier transformation. Peak volumes were measured using FTNMR.

Background peak volumes defined in regions with no signal were subtracted before distance calculations were performed.

Molecular mechanics calculations

The initial DNA coordinates were taken from the crystal structure of d(CGCGAATTCGCG)₂ (Fratini *et al.*, 1982). The initial distamycin A structure was created using the crystal structure of netropsin (Berman *et al.*, 1979) and standard angles and distances. Protons were added with inhouse software. Energy refinements were performed with a modified version of the AMBER molecular mechanics package. NMR constraints were included by adding the following term to the normal potential function:

$$E_{\text{nmr}} = K_{\text{nmr}}(R-R_0)^2 \quad \text{if} \quad R \geq R_0 \quad (2-1)$$

$$E_{\text{nmr}} = 0.0 \quad \text{if} \quad R < R_0$$

R_0 is the upper bound on a given proton-proton distance and K_{nmr} is an adjustable force constant. Point charges for distamycin A were determined from MNDO (Dewar & Theil, 1977) calculations. The AMBER data base consists of an array of atom types to which force-field parameters are assigned. For example, an sp^2 hybridized carbon atom in a six membered ring has a particular van der Waals radius and Lennard-Jones parameters associated with it. Atom types (denoted with two-letter symbols) and point charges used for the distamycin A refinement are presented in Table 2-1. All-atom force field parameters for the nucleic acid were taken from those described previously (Weiner *et al.*, 1986). Most distamycin A force field parameters were taken from the united-atom model of netropsin (Caldwell & Kollman, 1986) except that Lennard-Jones parameters for the carbon atoms were taken from the all-atom model (Weiner *et al.*, 1986). An angle potential for CW-CM-HC (AMBER atom types, see Table 2-1) of 35.0 kcal/mole/deg²

Table 2-1. Atom Types and Point Charges
for Distamycin A.

<u>Atom</u>	<u>Atom</u> <u>Type</u>	<u>Point</u> <u>Charge</u>	<u>Atom</u>	<u>Atom</u> <u>Type</u>	<u>Point</u> <u>Charge</u>
O1	O	-0.20	N4	NA	-0.21
C1	C	0.35	C12	CT	0.22
HF	HC	0.03	C12H	HC	0.01
N1	N	-0.32	C10	CW	-0.07
HN1/3/5	H	0.18	C14	CM	0.03
C2	CM	-0.15	C17	CW	0.02
C3	CM	-0.07	H17	HC	0.14
H3/9/15	HC	0.09	N6	NA	-0.20
C5	CW	-0.01	C18	CT	0.19
H5	HC	0.12	C18H	HC	0.01
N2	NA	-0.17	C16	CW	-0.12
C6	CT	0.21	C19	C	0.43
C6H	HC	0.01	O4	O	-0.31
C4	CW	-0.13	N7	N	-0.40
C7/13	C	0.44	HN7	H	0.17
O2/3	O	-0.37	C20	CT	0.17
N3/N5	N	-0.34	C20H	HC	0.02
C8	CM	0.00	C21	CT	-0.04
C9/15	CM	-0.08	C21H	HC	0.07
C11	CW	0.02	C22	CA	0.39
H11	HC	0.11	N8/9	N2	-0.28
NH8/9	H3	0.25			

and 109.5° and specific torsional parameters for C-CW-CM-HC of 6.59 kcal/mol and 180° and for HC-CW-NA-CT of 1.71 kcal/mol and 180° were added to the standard database. These parameters were estimated from values reported for CM-CM-HC, C-CM-CM-HC, and HC-CM-CM-CT respectively (Weiner *et al.*, 1986). All degrees of freedom were refined. A 1.2 nm nonbonded and 0.4 nm hydrogen bond cutoff were employed. Solvent effects were accounted for through the use of a distance dependent dielectric constant.

Distamycin A and the DNA were separately refined to an rms energy gradient of 0.1 (kcal/mol)/Å. The energy refined drug was then interactively docked into the minor groove of the DNA using a PS300 Evans and Sutherland graphics terminal. The adenine C2H to drug H3 contacts indicated by NOESY experiments were used as a guide in the docking procedure. The initial complex was refined with an NMR force constant, K_{nmr} , of 10,000 (kcal/mol)/Å² to an rms energy gradient of 0.1 (kcal/mol)/Å. Two structures were then further refined employing NMR force constants of 10,000 and 0.59 (kcal/mol)/Å² to an rms energy gradient of 0.05 (kcal/mol)/Å. The dependence of the final AMBER structure on starting coordinates was investigated by refining a complex derived from idealized B-form coordinates (Chandrasekaran and Arnott, 1989) using an NMR force constant of 10,000 (kcal/mol)/Å² to an rms energy gradient of 0.05 (kcal/mol)/Å.

Buildup curves

Buildup curves were evaluated by numerical integration of the following differential equations:

$$\frac{dM_{zi}}{dt} = -\rho_i(M_{zi} - M_{0i}) - \sum_{j \neq i} \sigma_{ij}(M_{zj} - M_{0j})$$

$$\rho_i = \frac{3}{10} \left(\frac{\gamma^2 h}{2\pi} \right)^2 \sum_j \frac{1}{r_{ij}^6} \left[\tau_c + \frac{3\tau_c}{1 + (\omega\tau_c)^2} + \frac{6\tau_c}{1 + 4(\omega\tau_c)^2} \right] \quad (2-2)$$

$$\sigma_{ij} = \frac{1}{10} \left(\frac{\gamma^2 h}{2\pi} \right)^2 \frac{1}{r_{ij}^6} \left[\frac{6\tau_c}{1 + 4(\omega\tau_c)^2} - \tau_c \right]$$

These expressions are a rearrangement of [1-8] and [1-9] which simplify the calculation (Kalk & Berendsen, 1976). Isotropic rotation and one correlation time for all proton pairs were assumed.

2.3 Structural analysis. NOESY experiments.

Klevit *et al.* reported several abnormalities in the NOESY spectrum of the complex at 27°C (Klevit *et al.*, 1986). Specifically, the C8H to C1'H resonances of residues G16⁶ and A18 were missing from the sequential connectivity pattern of strand 2. These peaks appear in spectra (Figure 2-1) taken at 13.5°C indicating these residues do not undergo large structural changes.

My data also suggest that the previously reported (Klevit *et al.*, 1986) C1'H assignments of T7 and T19 should be reversed. The degeneracy of the T7 and T19 C6H resonances along with the complexity of the NOESY spectrum and weak cross peak intensities make it difficult to assign these C1'H protons to their respective bases using the sequential connectivity patterns. There were no cross peaks between the originally assigned T19 C1'H and T20 C6H protons in NOESY spectra taken at 200, 250, and 500 ms. There were also no cross peaks between T7 C1'H and T8 C6H at 200 and 250 ms, and only a weak cross peak between these resonances at 500 ms. In contrast, all of these spectra contain cross peaks from the originally assigned T7 C1'H and T20 C6H protons. They also contain cross

⁶ The numbering scheme for the DNA duplex is for the asymmetric dodecamer, i.e., strand 1, residues 1-12, and strand 2, 13-24.

Figure 2-1. NOESY spectrum of the distamycin A-A₂T₂ complex. Aromatic to C1'H region of a symmetrized NOESY spectrum taken at 13.5°C with a mixing time of 500 ms. Aromatic C6H resonances of cytosine and thymine, and C8H resonances of adenine and guanine and C2H resonances of adenine (shown explicitly) are along the vertical axis. Numbers denote the positions of the C1'H resonances along the horizontal axis. T7 and T19 C1'H assignments are reversed with respect to those reported previously (Klevit *et al.*, 1986). Short dashed lines show sequential connectivities between T7 C1'H and T8 C6H and between T19 C1'H and T20 C6H. Solid lines connect resonances A6 C2H, H3-2, T7 C1'H, and T19 C1'H, which comprise one spin system. Long dashed lines connect resonances A18 C2H, H3-3, T8 C1'H, and T19 C1'H, which comprise a second spin system. Reprinted with permission from *Biochemistry*. Copyright 1988, American Chemical Society.

peaks between T19 C1'H and T8 C6H, although at 500 ms this peak is weak. Therefore, I believe that T7 C1'H should be assigned to 5.60 ppm and T19 C1'H should be assigned to 5.37 ppm. This change does not alter the assigned binding orientation of the drug or the other assignments, but would introduce errors during quantitative refinement.

To obtain as accurate constraints as possible for the subsequent molecular mechanics calculations, I attempted to analyze NOESY spectra quantitatively. For a simple two-spin system, in the short mixing time limit (linear regime), the rate of magnetization transfer is proportional to the inverse sixth-power of the distance between the spins [1-10, 1-11]. To observe the long distance NOEs, the NOESY mixing time was increased. However, this resulted in spin diffusion for the short range contacts which severely complicated the analysis. Experimental buildup curves between cytosine C5H and C6H protons and adenine C2H and drug H3 protons are presented in Figure 2-2a. The approximately linear NOE buildup for the cytosine protons suggest they comprise a two-spin system at short mixing times. However, the nonlinear buildup of the drug to DNA resonances requires a more careful analysis. Klevit *et al.* (1986) reported cross peaks in the NOESY spectrum between A6 C2H and both T7 and T19 C1'H and between A18 C2H and both T8 and T19 C1'H (with corrected assignments as discussed above). From the NOESY spectrum presented in Figure 2-1, these peaks can be seen to be components of two coupled four-spin systems between A6 C2H, H3-2, T7 C1'H, and T19 C1'H, and between A18 C2H, H3-3, T8 C1'H, and T19 C1'H. Thus, a normal analysis cannot be used to determine distances between these protons.

Figure 2-2. Experimental and simulated NOE buildup curves. Experimental points are denoted (□) C11 H5-H6, (▲) H3-3-A18 C2H, (●) H3-2-A6 C2H, and (■) H3-1-A5 C2H. (a) Experimental NOE buildup curves for the distamycin A-DNA complex. Data were taken from NOESY experiments with mixing times of 50, 100, and 150 ms. (b) Simulated NOE buildup curves for the distamycin A-DNA complex. Simulated data are represented by solid lines. DNA adenine C2H-drug H3 buildup curves were simulated by using a four-spin approximation with distances within 0.05 nm of structure H_D. C11 C5H-C6H data were simulated by using a four-spin approximation including C5H, C6H, and CH₂' protons of the same residue and the CH₂" proton of the 5' neighbor. Distances were taken from idealized B-form coordinates. A correlation time of 6 ns and a spectrometer frequency of 500 MHz were used in all simulations. Adenine C2H-drug H3 experimental points were scaled by 2.1 relative to the C11 data (see text). Reprinted with permission from *Biochemistry*. Copyright 1988, the American Chemical Society.

**Table 2-2. Intensity and Relaxation Matrices for
the Two and Three-Spin Systems of Figure 2-4.**

Intensity Matrix a Relaxation Matrix R
Two Spin System

1)	0.32	0.17		2.6	-1.2
2)	0.17	0.32		<u>-1.2</u>	2.6

Three Spin System

1)	0.27	0.15	0.06		3.0	-1.2
2)	0.15	0.32	0.02		<u>-1.2</u>	2.6
3)	0.06	0.02	0.41			

**Table 2-3. Intensity and Relaxation Matrices for
the A6 and A18 Spin Systems**

	<u>Intensity Matrix a</u>				<u>Relaxation Matrix R</u>			
A6 C2H	0.36	0.26	0.15	0.09	2.9	-1.9	-0.65	-0.32
H3-2	0.26	0.34	0.08	0.08	-1.9	3.0	-0.16	-0.27
T19 C1'H	0.15	0.08	0.55	-	-0.65	-0.16	1.29	0.06
T7 C1'H	0.09	0.08	-	0.62	-0.32	-0.27	0.06	0.99
A18 C2H	0.15	0.37	0.21	0.14	2.8	-1.3	-0.77	-0.46
H3-3	0.37	0.38	0.12	0.07	-1.3	2.0	-0.48	-0.21
T19 C1'H	0.21	0.12	0.46	-	-0.77	-0.48	1.7	0.09
T8 C1'H	0.14	0.07	-	0.69	-0.46	-0.21	0.09	0.78

2.4 Quantitative distance measurements: SKEWSY experiments

The NOESY spectrum, or intensity matrix a , can be related to the relaxation matrix R , whose off-diagonal elements are proportional to the inverse sixth power of the distance between two spins, by the following equation (Macura & Ernst, 1980) [1-16]:

$$a \propto e^{-R\tau_m} \quad (2-3)$$

where τ_m is the NOESY mixing time. In theory, one NOESY experiment or intensity matrix a , combined with a knowledge of the intensities of the peaks at equilibrium (M_0) is sufficient for calculation of R [1-17, 1-18]. By taking ratios of cross relaxation rates (off diagonal elements of R), and provided that the distance between one pair of protons is known (distance marker), the distance between the other pairs can be calculated even in the presence of spin diffusion. In practice, however, a cannot usually be determined due to poor resolution of the diagonal peaks. To circumvent this problem, Bremer *et al.* introduced the SKEWSY experiment (Bremer *et al.*, 1984). It contains an initial 180° pulse and delay period τ_s prior to the normal NOESY sequence (Figure 2-3). As described by Bremer *et al.*, this sequence transfers diagonal peak information into the cross peaks. Thus, SKEWSY and NOESY spectra together contain sufficient information to calculate a (appendix A), and by back calculation R [1-18], and the distances of interest.

The advantage of the SKEWSY/NOESY method is that small sets of spins that are involved in spin diffusion can be treated as isolated systems. Spins that are coupled to these sets of spins, but that are not part of spin diffusion pathways in the set do not affect the calculation of cross-relaxation rates, and hence distances. For example, consider the spin system presented in Figure 2-4. Spin 1 is dipolar-coupled to both 2 and 3, but spins 2 and 3 are spatially distant and are

Figure 2-3. SKEWSY (top) and NOESY (bottom) NMR pulse sequences. The SKEWSY delay periods τ_s and τ_m have the same value as the NOESY mixing time τ_m . Reprinted with permission from *Biochemistry*. Copyright 1988, the American Chemical Society.

Figure 2-4. Model three-spin system. Model spin system used to determine the effect of spin 3 on the distance calculation between spins 1 and 2. Reprinted with permission from *Biochemistry*. Copyright 1988, the American Chemical Society.

weakly coupled. Buildup curves were used to determine the intensity matrices for both the isolated two-spin (1 & 2) and three-spin systems (data taken at 500 ms). The relaxation matrix for the two-spin system was then calculated directly from the two-spin intensities, and an approximate two-spin relaxation matrix was calculated for the three-spin system by using intensities from only spins 1 and 2. The results are presented in Table 2-2. Comparison of the relaxation matrices reveals that the diagonal element of spin 1 has increased in the approximate case, reflecting an apparent increase in spin-lattice relaxation, but that the cross-relaxation rate between spins 1 and 2 (underlined), which contains the distance information, has not been affected. Thus, for determining the distance between spins 1 and 2, introduction of the third spin into the calculations is unnecessary. Its presence is manifested only in a greater rate of spin-lattice relaxation of spin 1.

To simplify the analysis, A6 C2H, H3-2, T7 C1'H, and T19 C1'H, and A18 C2H, H3-3, T8 C1'H, and T19 C1'H, were treated as separate four-spin groups. The interaction of any member of the set with other protons was neglected for the reasons discussed above. The cross peak intensities among members of each set along with the drug diagonal peaks of H3-2 and H3-3 were measured from the NOESY (Figure 2-1) and SKEWSY (not shown) spectra taken with a mixing time of 500 ms. These data were used in the procedure developed by Bremer *et al.* to calculate an intensity matrix **a**, and from it, the relaxation matrix **R** (see appendix A). The results are presented in Table 2-3. Notice that the cross peak intensities between T7 C1'H and T19 C1'H, and between T8 C1'H and T19 C1'H were set to zero. NOESY spectra taken at 200 and 250 ms show no cross peaks between either of these proton pairs. At 500 ms, however, a weak signal occurs between T7 C1'H and T19 C1'H. This peak is probably due to exchange between

the two possible binding orientations of the drug rather than NOE. Since the intensity matrix elements of these spin pairs were set to zero, the relaxation rates, 0.06/sec, and 0.09 s^{-1} for T7-T19 and T8-T19 respectively, reflect the uncertainty in the data.

The magnitude of the off-diagonal elements of R for both H3-2 - A6 C2H and H3-3 -A18 C2H reveals that these pairs are strongly coupled and hence spatially close. It can also be seen that T19 C1'H is more strongly coupled to A6 C2H than T7 C1'H, but that the T7 sugar is more strongly coupled to the drug H3-2 proton. In addition, T19 C1'H is more strongly coupled to both A18 C2H and H3-3 than is T8 C1'H.

Conversion of cross-relaxation rates to distances still requires a known distance reference ([1-13]), such as that between cytosine C5H and C6H (2.45Å) (Patel *et al.*, 1987). However, at a 500 ms mixing time, the two-spin approximation is not valid due to spin diffusion from these protons to the CH2' and CH2'' protons. This could not be corrected by the SKEWSY/NOESY method due to insufficient resolution of these cross peaks in the spectrum. However, application of the two-spin approximation to the 50 ms NOESY data, (represented by the buildup curve, Figure 2-2a), does allow for the calculation of upper bounds on the C5H-C6H and A C2H-H3 distances. The upper bounds for A6 C2H-H3-2 and A18 C2H-H3-3 were then used, along with the relaxation matrices, to derive upper bounds between protons in the coupled spin systems. To account for experimental errors (integration, chemical exchange), 0.02 nm was added to distances derived from the relaxation matrices that were less than 0.3 nm and 0.03 nm was added to distances greater than 0.3 nm. In addition, a 0.5 nm upper bound was used for drug-DNA contacts determined from 1D NOEs

reported previously (Klevit *et al.*, 1986). A summary of the distance constraints is presented in Table 2-4.

Attempts were made to estimate the uncertainties associated with the distance constraints by simulating the buildup curves of Figure 2-2a. The simulated curves fit the experimental points reasonably, although there were significant deviations at longer mixing times. Possibilities for the poor fit at long mixing times include spin diffusion or other relaxation processes not modeled in the simulations. Another factor complicating the analysis is the use of a short relaxation delay (2.1 s), combined with different T_1 values for the C11 and adenine C2H protons that resulted in partial saturation and differential scaling of their buildup curves. A NOESY experiment obtained with a recycle delay of 10.2 s and a mixing time of 100 ms revealed that each of the A C2H - H3 NOEs should be scaled by a factor of 2.1 relative to the C11 C5H - C6H distance marker in shorter recycle delay data sets. This distortion has been considered in the subsequent analysis.

Figure 2-2b presents simulated buildup curves for the C11 C5H - C6H and three A C2H - H3 proton pairs along with the experimental points vertically scaled by 2.1 relative to the C11 pair to account for differential saturation. The fit of the simulated and experimental data are good at 50 ms. However, at longer mixing times there are deviations that suggest differential saturation combines with other relaxation phenomena (spin diffusion) to contribute to the behavior of the NOE buildup curves. Taking a conservative approach, the A C2H - H3 distances obtained from the 50 ms NOESY data and those derived from them in the SKEWSY/NOESY analysis were used only as upper bound constraints in the subsequent AMBER calculations. Because of the uncertainties in the data, no attempt was made to either estimate lower bounds or include such terms in the AMBER potential function. The differential saturation phenomena I have observed

Table 2-4. Calculated distances and constraints for the distamycin A-
d(CGCGAATTCGCG)₂ structures.

Atom Pair	Structure	H _D Å	W _D Å	H _I Å	Deviation H _D vs H _I Å	Constraint ^a Ro Å
A5 C2H	H3-1	2.2	2.2	2.2	0.0	2.7 ^b
A5 C2H	A6 C1'H	4.6	4.7	4.9	0.3	-
H3-1	A6 C1'H	2.8	2.8	3.0	0.2	4.2 ^b
A6 C2H	H3-2	2.6	2.4	2.6	0.0	2.7 ^b
A6 C2H	T7 C1'H	3.2	3.0	3.9	0.7	3.9
A6 C2H	T19 C1'H	3.5	5.0	3.5	0.0	3.5
H3-2	T7 C1'H	2.5	2.5	3.5	1.0	4.0
H3-2	T19 C1'H	4.2	4.8	3.7	-0.5	4.3
A18 C2H	H3-3	2.3	2.3	2.2	-0.1	2.6 ^b
A18 C2H	T19 C1'H	3.0	3.2	2.8	-0.2	3.0
A18 C2H	T8 C1'H	3.4	4.0	3.4	0.0	3.4
H3-3	T19 C1'H	2.5	2.8	2.5	0.0	3.3
H3-3	T8 C1'H	2.4	2.7	2.5	0.1	3.8
HN-1	A5 C2H	2.8	2.8	2.7	-0.1	5.0
HN-2	A5 C2H	3.5	3.5	3.7	0.2	5.0
	A6 C2H	4.0	3.4	3.9	-0.1	5.0
HN-3	A6 C2H	3.5	3.7	3.4	-0.1	5.0
	A18 C2H	4.4	4.2	3.8	-0.6	5.0
C21HA	A17 C2H	2.3	2.3	2.3	0.0	5.0
C21HB	C9 C1'H	2.6	2.4	3.2	0.6	5.0

^a Constraint distances are the sum of the upper bound calculated from the relaxation matrix and an additional 0.2Å if the upper bound was less than 3.0Å or 0.3Å if the upper bound was greater than 3.0Å.

^b Upper bound derived from 50ms NOESY data. Uncertainty added to only the H3-1 - A6 C1'H pair.

stress the importance of making T_1 measurements and adjusting the recycle delay accordingly when trying to quantify distance information.

2.5 Amber structures

In the following discussion, I denote the refined uncomplexed DNA structure starting from crystal coordinates as F , the highly constrained complex [K_{nmr} of 10,000 (kcal/mol)/ $\text{\AA}^2$] as H_D , the weakly constrained complex [K_{nmr} of 0.59 (kcal/mol)/ $\text{\AA}^2$] as W_D , and the highly constrained complex starting from idealized B-form coordinates as H_I (coordinates are listed in appendix B). Table 2-4 presents calculated distances for H_D , W_D , and H_I , along with deviations of H_D from H_I , and the NMR constraints. The data show that H_D satisfied all of the constraints. Three distances, those between A6 C2H and T19 C1'H, between A18 C2H and T19 C1'H, and between A18 C2H and T8 C1'H, however, were at their respective constraint values. These proton pairs, along with the H3-2 - T19 C1'H pair, violated their respective upper-bound constraints when the NMR force constant was reduced. A possible reason will be discussed below. The data also show that H_I satisfied all of the constraints. Three distances, those between A6 C2H and T7 C1'H, between A6 C2H and T19 C1'H, and between A18 C2H and T8 C1'H, were at their respective upper bounds.

The binding energy of distamycin A to $d(\text{CGCGAATTCGCG})_2$ was 106.3 kcal/mol (H_D) and increased to 129.1 kcal/mol (W_D) upon reduction of K_{nmr} . The difference in binding energy is the sum of bond (-1.2 kcal/mol change between W_D and H_D), angle (-1.4), dihedral (5.0), van der Waals (7.6), electrostatic (14.4), hydrogen bond (0.01), and constraint energies (-1.6). Although several constraints were violated and the binding energy increased, an rms difference between coordinates in the two structures of 0.028 nm indicates that they are very similar. The difference in total energy of H_D from H_I was

+16.6 kcal/mol, and an rms deviation between H_D and H_I including the drug and AATT base pairs was 0.10 nm. The rms deviation between drug molecules alone was 0.06 nm. Further discussion will focus on the general structural characteristics of H_D, W_D, and H_I; differences will be noted where appropriate.

Distamycin A fits snugly into the AATT minor-groove binding site with each of the three pyrrole rings approximately parallel to the walls of the groove (Figure 2-5). The amidinium group (charge +1) is also positioned in the center of the minor groove at the point of minimum electrostatic potential energy (Lavery *et al.*, 1982). In addition, the data for H_D and W_D in Table 2-4 show that the A5,A6, and A18 C2H protons are in van der Waals contact with the H3-1, H3-2, and H3-3 drug pyrrole protons respectively, although the A6 C2H to H3-2 distance is somewhat longer than the other two.

If the hydrogen-bond distance (N-N or N-O) is defined as 0.30 nm, only one hydrogen bond, that between A5 N3 and HN-1, occurs in this structure. Longer hydrogen bonds exist between HN-3 and T20 O2 (0.32 nm), HN-5 and T7 O2 (0.4 nm), HN-7 and T8 O2 (0.44 nm), HN-7 and A18 N3 (0.34 nm), and the drug O4' and G4 amino group (0.43 nm) in structure H_D. Two additional long hydrogen bonds between HN-3 and A6 N3 (0.44 nm), and HN-5 and T19 O2 (0.36 nm) were observed when the NMR constraints were relaxed (W_D). The hydrogen-bond pattern in H_I is similar to that in H_D, although the HN-7 - A18 N3 hydrogen bond is 0.04 nm longer in H_I, while the drug O4' - G4 amino group and the HN-7 - T8 O2 hydrogen bonds are 0.05 and 0.06 nm shorter, respectively. The drug-DNA hydrogen-bonding scheme is presented in Figure 2-6. Note that in H_D HN-7 and in W_D HN-3 and HN-5 are potentially involved in three-center hydrogen bonds with adenine N3 and thymine O2 atoms (Jeffrey & Maluszynska, 1982). Longer than normal three-center hydrogen bonds have

Figure 2-5. Stereodrawing of the distamycin A - d(CGCGAATTCGCG)₂ complex. Structure of the drug-DNA complex obtained with an NMR force constant of 10,000 kcal/mol/Å² (structure H_D). Reprinted with permission from *Biochemistry*. Copyright 1988, the American Chemical Society.

Figure 2-6. Hydrogen-bonding scheme for the distamycin A-A₂T₂ complex. Solid lines denote hydrogen bonds in the highly constrained structure H_D. Dashed lines denote the additional hydrogen bonds that formed when the NMR constraints were relaxed (W_D). Reprinted with permission from *Biochemistry*. Copyright 1988, the American Chemical Society.

been reported in crystal structures of drug-DNA complexes (Kopka *et al.*, 1985c; Pjura *et al.*, 1987; Coll *et al.*, 1987) and will be discussed further below.

The NOESY sequential connectivity patterns and the AMBER calculations suggest that only minor changes in DNA structure occurred due to drug binding. For example, the helical repeat of F, H_D, and W_D were all 9.8 residues/turn, while the helical repeat of H_I was 10.0 residues/turn based on local helical twist angles. These data agree with the crystal structure of the dodecamer (Dickerson & Drew, 1981) and also molecular mechanics calculations (Kollman *et al.*, 1982). Although there were local deviations, these values are identical with those found in the respective starting structures. RMS deviations between H_D and W_D and the initially refined DNA helix (F) were both 0.05 nm. Although changes in DNA structure were small, there are several points worth noting. van der Waals contacts between A5 C2H and H3-1 and between A6 C2H and H3-2 caused an increase in roll angle (Dickerson *et al.*, 1989) (Figure 1-6)(change relative to F of 10° H_D, 6° W_D) at the A5-A6 step. In fact H3-1 is positioned slightly under A5 C2H while H3-2 is positioned slightly above A6 C2H. Thus, the first two pyrrole rings can be seen to wedge themselves against and between these residues. The constraints on T19 C1'H caused a repositioning of T19 closer to A18 which resulted in an increased buckle (defined as the angle between the bases after the propeller twist has been set to zero, Figure 1-6) of the T19-A6 pair (change relative to F of 4° H_D, 0.5° W_D). Similarly, the constraints on T7 C1'H caused a repositioning of the T7 base closer to A6 which resulted in an increased buckle of T7 and A18 (a change relative to F of 20° H_D, 16° W_D). Finally, the constraints on T8 C1'H caused an increase in the buckle (change relative to F of 14° H_D, 6° W_D) of the T8-A17 pair. In H_I, the T19 base was

moved closer to T20 rather than A18, which caused an increase in the buckle of the A6-T19 base pair of 7° relative to H_D , while the buckle of the T7-A18 and T8 -A17 base pairs was reduced by 6° and 18° , respectively, relative to H_D .

Inspection of minor-groove widths revealed that the minor groove of the free DNA increased 0.14 - 0.24 nm relative to the starting structure upon energy refinement (Fratini *et al.*, 1982). It then decreased 0.05 - 0.2 nm to an average value of 1.12 nm upon refinement of the complex. In the crystal structure of the free DNA, the groove is so narrow at points that it must widen to accommodate the drug. The groove widths of the symmetry-related sequences are quite different from one another in the crystal, so it is difficult to know which to compare with. The minor-groove width of H_I decreased from 1.18 nm for the classical B-form DNA to an average of 1.13 nm. In addition, the minor-groove width of a complex between distamycin A and idealized B-form coordinates refined without NMR constraints decreased to an average value of 1.12 nm.

Further structural analysis revealed that pyrrole rings 1 and 2 are nearly parallel to one another (dihedral angle between rings 1 and 2, $-3^\circ H_D$, and $-9^\circ W_D$, $-1^\circ H_I$), while ring 3 is rotated significantly (dihedral angle between rings 2 and 3, $43^\circ H_D$ and $52^\circ W_D$, $36^\circ H_I$) to conform to the groove of the helix. In addition, the O4' atoms which lie along the walls of the minor groove were found to stack within 0.35 to 0.42 nm over the center of each of the three pyrrole rings. Specifically, the O4' atoms of pairs A6-C21, T7-T20, and T8-T19 stack over rings 1, 2, and 3, respectively. Reduction of the NMR force constant caused an increase of 0.03 nm in the T8 O4' - pyrrole-3 -T19 O4' distance. The other two distances were not significantly affected. The possible significance of this will be discussed below. This type of stacking interaction has also been observed in crystal structures of nucleosides and nucleotides (Bugg *et al.*, 1971), Z-DNA

(Wang *et al.*, 1979), and both netropsin (Kopka *et al.*, 1985c) and Hoechst 33258 (Teng *et al.*, 1988) with d(CGCGAATTCGCG)₂.

2.6 Distamycin A - A₂T₂ discussion

Analysis of spin diffusion in strongly coupled spin systems has been the subject of extensive study (Kalk & Berendsen, 1976; *et al.*, 1981; Keepers and James, 1984; Olejniczak *et al.*, 1986). I believe that the SKEWSY/NOESY method (Bremer *et al.*, 1984) is excellent for analyzing small groups of strongly coupled spins because only those spins that are involved in spin diffusion within the set need to be included in the analysis. I have shown that other spins which are coupled to only one member of the system can be neglected without error. In contrast, accurate methods of accounting for spin diffusion that employ the measurement of the actual magnetization transferred (as opposed to rates of transfer) must include all spins in the system which interact, not just those involved in spin diffusion among themselves.

One of the problems associated with molecular mechanics calculations is in finding the global energy minimum. The incorporation of distance constraints into the potential function should reduce this problem while adding experimental data specific to this system into the calculation. An important test of these calculations is to determine whether two different starting structures can be refined to the same final structure. In this regard I have refined complexes from both crystal coordinates (Fratini *et al.*, 1982) (H_D) and idealized B-form coordinates (Chandrasekaran & Arnott, 1989) (H_I) of d(CGCGAATTCGCG)₂. Structures H_D and H_I are similar in many respects as evidenced by an rms fit of the drug and central AATT region of 0.10 nm, by an rms fit of the drugs alone of 0.06 nm, and by small deviations in the constrained distances as shown in Table 2-4. The data also show that global structural characteristics such as drug

conformation, hydrogen bonding, and van der Waals contacts are similar. There were, however, local structural differences between H_D and H_I. Most notable was the positioning of T19 under A6 in H_D and above A6 in H_I. In addition, although there were local variations, the average helical repeat of each structure was the same as that of the starting structure, indicating that the AMBER potential function does not move the DNA significantly unless many NMR constraints are applied. Finally, the formamide and propylamidinium portions of the drug are oriented slightly differently, giving hydrogen-bond lengths between DNA and drug O4' and HN-7 atoms that were slightly different in H_D and H_I. Thus, on the local level, the calculations show that there are small structural perturbations, but they are not defined with very high precision. As new NMR techniques that provide larger numbers of more accurate constraints are developed in conjunction with more accurate molecular mechanics potential functions, our ability to observe finer changes in the solution structure of DNA will improve.

The pyrrole rings in the structure are aligned to an 5'- AAT -3' sequence with rings 1, 2, and 3 close to A5, A6, and A18 respectively. This binding site is different from that found in the crystal structure of distamycin A with d(CGCAAATTTGCG)₂ (Coll *et al.*, 1987) in which the three pyrrole rings are aligned to a 5'- ATT -3' sequence, although an 5'- AAT -3' site is available to the drug. Occupation of different binding sites may in part account for the differences in the dihedral angles of the drug in the two structures [1 and 2; Coll *et al.* (1987) 15°, H_D 4°; 2 and 3, Coll *et al.* (1987) 11°, H_D 46°]. It is interesting to note in structures H_D, W_D, and H_I that the A6 C2H-H3-2 distance is somewhat longer than the other two A C2H-H3 pairs, indicating a bowing out of the drug to better accommodate the helical twist of the DNA.

The NOESY sequential connectivity assignments and the AMBER calculations support the conclusion that only small structural perturbations of the DNA occur upon drug binding. The same conclusion has come from NMR (Patel & Shapiro, 1986) and crystallographic studies (Kopka *et al.*, 1985a) of netropsin and from crystallographic studies of Hoechst 33258 (Pjura *et al.*, 1987).

Analysis of H_D and W_D revealed potential three-center hydrogen bonds between drug amide and A N3 and T O2 atoms similar to those of the distamycin A-d(CGCAAATTTGCG)₂ (Coll *et al.*, 1987), and both netropsin (Kopka *et al.*, 1985a)(Wang *et al.* 1989), and Hoechst 33258-DNA (Pjura *et al.*, 1987; Teng *et al.* 1988) crystal structures. As pointed out by Kopka *et al.* (1985a), these are the same hydrogen bonds that occur in the spine of hydration of the free DNA sequence (Drew & Dickerson, 1981). A characteristic feature of all of these structures is the presence of at least several abnormally long hydrogen bonds between drug and DNA minor-groove atoms. In H_D , W_D , and H_I , most of the hydrogen bonds between amide and A N3 and T O2 atoms are too long to be considered normal (0.3 nm), with four of seven being longer than 0.33 nm. In the crystal structure of distamycin A with d(CGCAAATTTGCG)₂ (Coll *et al.* 1987) the distances between drug amide N3 and potential hydrogen-bonding sites T7 and T19 O2 were 0.39 and 0.44 nm, respectively. It was suggested that this was due to a different periodicity of the drug pyrrole-amides and the DNA. In fact, five of six hydrogen bonds between drug amide and DNA T O2 and A N3 atoms were greater than 0.30 nm, with two longer than 0.33 nm. In the netropsin complex four of six amide-DNA hydrogen bonds were 0.33 nm or longer (Kopka *et al.*, 1985c), and in the recently reported crystal structure of Hoechst 33258 and d(CGCGAATTCGCG)₂ (Pjura *et al.*, 1987), in which the benzimidazole NH groups form three-center hydrogen bonds with A N3 and T O2 atoms, three of four are

longer than 0.33 nm. Long hydrogen bonds thus seem to be a common motif for these minor-groove binders. I agree with Kopka *et al.* (1985c) that the hydrogen-bond energy is mostly electrostatic in character, and in the hydrophobic environment of the minor groove the interactions may not be dissipated with distance as quickly, thus providing stabilization in spite of their length.

The calculations suggest that the width of the minor groove in the complex is narrowed relative to that of "fiber" B-DNA. Energy refinement of the d(CGCGAATTCGCG)₂ crystal structure (Fratini *et al.*, 1982) without drug resulted in an expansion of the minor groove. Subsequent refinement with distamycin A reduced it again to an average of 1.12 nm, compared to the idealized B-form minor-groove width of 1.18 nm. I determined, however, that the compaction of the groove is due to the AMBER potential function rather than the NMR constraints since the minor groove was narrowed to the same degree in a complex refined without NMR distance constraints. Narrow minor grooves have been seen in other structures' A-T-rich sequences. For example, the minor groove of distamycin A with d(CGCAAATTTGCG)₂ (Coll *et al.*, 1987) was reported to be narrow. Whether the drug occupies an already narrow groove, as seen in the (A₆)-containing sequence characterized recently (Nelson *et al.*, 1987), or whether drug binding narrows the minor groove will require further analysis. In this regard, the crystal structure of d(CGCGAATTCGCG)₂ (Fratini *et al.*, 1982) and of its complex with netropsin (Kopka *et al.*, 1985c) show that the drug actually widens the already narrow minor groove from 0.05 to 0.20 nm, with an average value identical with that of structure H_D. A similar expansion is seen in the complex of this sequence with Hoechst 33258 (Pjura *et al.*, 1987).

These structures and recent work on the distamycin A-d(CGCAAATTTGCG)₂ complex (Coll *et al.*, 1987), the netropsin-d(CGCGAATTCGCG)₂ complex (Kopka *et al.*, 1985b), the netropsin-d(GGAATTCC)₂ complex (Patel & Shapiro, 1985), the Hoechst 33258 (a N-methylpiperazine derivative)-d(CGCGAATTCGCG)₂ complex (Pjura *et al.*, 1987), and the SN6999 (a bis(quarternary ammonium) heterocycle)-d(GCATTAAATGC)₂ complex (Leupin *et al.*, 1986) suggest that these minor-groove-binding drugs are in van der Waals contact with the DNA atoms along the minor groove. Specifically, I note that the O4' atoms stack over the center of each of the three pyrrole rings. Specific van der Waals interactions between netropsin and DNA O4' atoms have also been noted (Kopka *et al.*, 1985c). This type of interaction, a heteroatom stacking over an aromatic ring, has also been found in crystal structures of nucleosides and nucleotides and has been suggested as a stabilizing force in the binding of aromatic molecules to nucleic acids (Bugg *et al.*, 1971) and also Z-DNA (Wang *et al.*, 1979). It provides an additional explanation for the fact that increasing numbers of N-methylpyrrole rings increase the stability of the complex, although hydrophobic effects and hydrogen bonding probably also play a role. (Zimmer *et al.*, 1975).

A possible explanation for the distance constraint violations of T8 and T19 (WD) may be found in the fact that the T8 O4'-pyrrole 3-T19 O4' distance is 0.03 nm shorter in the highly constrained structure than in the weakly constrained structure. Thus, the NMR data effectively increase the stacking between the T8 and T19 O4' atoms and pyrrole ring 3. This suggests that the interaction is important but is simply not well modeled by the AMBER potential function, thus causing violations when the constraints were relaxed.

Another possibility is that the drug undergoes small conformational fluctuations within the minor groove during the mixing time. A measured NOE

would then be a distance-weighted (inverse sixth power) average that could cause a proton-proton distance to appear shorter than the actual "average" distance. Since only 4 of the possible 19 constraints were violated, this possibility seems less likely.

2.7 Distamycin A - A₂T₂ conclusions

The SKEWSY/NOESY method can be used to accurately determine distances among a set of dipolar-coupled spins. Spins that interact with only one member of the set can be neglected without error. The effect of a neglected spin is to increase the apparent spin-lattice relaxation of the spin to which it is coupled.

The distamycin A-d(CGCGAATTCGCG)₂ complex is characterized by van der Waals contacts between adenine C2H and drug H3 protons, potential three-center hydrogen bonds between adenine N3 and thymine O2 atoms that protrude from the minor groove, and stacking of DNA O4' atoms over each of the three pyrrole rings. The first two rings of the drug are approximately parallel, while the third ring is turned to conform to the rotation of the helix. No large structural changes were observed for the DNA.

There have been a number of suggestions for the high stability of distamycin A-DNA complexes. These include electrostatic forces, hydrogen bonding, and hydrophobic effects. The importance of electrostatic forces is still uncertain, but it is certainly not the only factor since 6 M urea and 0.1 M NaCl do not dissociate the complex (Hahn, 1975). In addition, theoretical calculations suggest that hydrogen-bond formation is not required for the binding of netropsin and presumably also distamycin A to the minor groove (Zakrzewska *et al.*, 1983). The present data suggest that the dipole-induced dipole interactions of the sugar O4' atoms and the three N-methylpyrrole rings contribute to the stability of the complex and provide a molecular basis for the fact that binding is

enhanced by the addition of N-methylpyrrole rings.

Chapter 3

Structure and Dynamics of Distamycin A with d(CGCAAATTGGC):d(GCCAATTTGCG) at Low Drug:DNA Ratios

3.1 Introduction

To investigate the interaction of distamycin A with a sequence that contains more than a minimal four A-T base binding site, and as a first step toward understanding the previously observed A-T sequence specificity, I have investigated the interaction of distamycin A with d(CGCAAATTGGC):d(GCCAATTTGCG)⁷ (A₃T₂) also using 2D NMR. In the course of my investigation I observed a new 2:1 distamycin A - A₃T₂ complex in which two drugs bound simultaneously in the minor groove of the A-T segment of this undecamer (Chapter 4). In this chapter I discuss the interaction of distamycin A with the A₃T₂ duplex at low and intermediate drug:DNA ratios. Nuclear Overhauser effect spectroscopy (NOESY)(Jeener *et al.*, 1979) was used to obtain intermolecular drug-DNA contacts and to monitor exchange of the drug among the various complexes.

3.2 Materials and Methods

Distamycin A was purchased from Sigma and used without further purification. Drug concentrations were determined optically at 303 nm using an extinction coefficient of 34,000 M⁻¹cm⁻¹. Due to its instability in aqueous solution, fresh samples were prepared for each titration. The DNA strands d(CGCAAATTGGC) and d(GCCAATTTGCG) were synthesized and purified as described (Chapter 4). Absorbances were determined at 80°C with extinction coefficients (Warshaw & Cantor, 1970) of 1.04 x10⁵ and 1.01x10⁵ M⁻¹cm⁻¹ for the A-rich and T-rich strands, respectively. The DNA was dissolved in buffer consisting of 10 mM sodium

⁷ Numbering scheme for the undecamer is strand 1, d(CGCAAATTGGC), residues 1 through 11, and strand 2, d(GCCAATTTGCG), residues 12-22.

phosphate (pH 7.0) and 10 mM sodium chloride. Duplex concentrations used in various experiments ranged from 1-2 mM.

NOESY spectra were acquired on a GN-500 spectrometer (General Electric Instruments) at drug:DNA ratios of 0.5:1 with mixing times of 50 ms (35°C) and 150 ms (20°, 35°C), and 1.3:1 with a mixing time of 300 ms (35°C). For each t_1 , 64 scans were signal-averaged taking 1024 complex points, with a recycle time of 2.2 s; 512 t_1 s were recorded per experiment. Spectra were processed as described (Chapter 1). A spectral width of 5000 Hz resulted in a digital resolution of 4.9 Hz/point. Spectra of exchangeable protons were acquired with a $1-\bar{3}-3-\bar{1}$ pulse (Hore, 1983) to suppress the solvent resonance. One-dimensional NOE difference spectra were acquired by interleaving on- and off-resonance saturated spectra.

3.3 A₃T₂ duplex

The aromatic (purine H8 and pyrimidine H6), C1'H, and adenine C2H resonances of the free duplex were assigned using a combination of NOESY (Appendix C) and one-dimensional nuclear Overhauser effect difference spectra (1D NOEs) of the imino protons using standard methods (Chapter 1). The assignments are summarized in Table 3-1.

3.4 Titration of the A₃T₂ duplex with distamycin A

Spectra of the the A₃T₂ duplex acquired with increasing amounts of distamycin A are presented in Figure 3-1. After an initial addition of drug, resonances corresponding to the free duplex diminish in intensity, as evidenced by the adenine C2H protons, while new resonances appear throughout the spectrum. In particular, two sets of three resonances (intensity ratio 2.2:1) appear in the chemical shift range characteristic of the drug H3 protons (6.3 - 6.7 ppm) suggesting that the drug binds in two sites (major and minor) within the minor groove of the A₃T₂ duplex.

Table 3-1. A₃T₂ and drug assignments.

Proton	No drug	one-half equivalent	Proton	No drug	one-half equivalent
C1 H6	7.59		C13 H6	7.43	
C1 C1'H	5.70		C13 C1'H	6.01	
G2 H8	7.93		C14 H6	7.46	
G2 C1'H	5.86		C14 C1'H	5.20	
C3 H8	7.32		A15 C2H	7.23	7.25m
C3 C1'H	5.36				7.35M
A4 C2H	7.20	7.23m ^a 7.31M	A15 H8	8.26	
A4 H8	8.20		A15 C1'H	5.95	
A4 C1'H	5.83		A16 C2H	7.60	8.07m 7.96M
A5 C2H	7.07	7.27 m 7.44 M	A16 H8	8.21	
A5 H8	8.12		A16 C1'H	6.19	
A5 C1'H	5.92		T17 H6	7.13	
			T17 C1'H	5.90	
A6 C2H	7.57	8.08 m 8.12 M	T18 H6	7.43	
A6 H8	8.09		T18 C1'H	6.13	
A6 C1'H	6.12		T19 H6	7.28	
T7 H6	7.09		T19 C1'H	5.89	
T7 C1'H	5.89		G20 H8	7.91	
T8 H6	7.21		G20 C1'H	5.78	
T8 C1'H	5.78		C21 H8	7.34	
G9 H8	7.84		C21 C1'H	5.75	
G9 C1'H	5.55		G22 H8	7.91	
G10 H8	7.72		G22 C1'H	6.12	
G10 C1'H	5.93		H3-1		6.47m 6.35M
C11 H6	7.25		H3-2		6.61m 6.68M
C11 C1'H	5.88		H3-3		6.41m 6.49M
G12 H6	7.90				
G12 C1'H	5.90				

^aM-major drug form, m-minor drug form.

Figure 3-1. Expansions of the aromatic and C1'H regions of NMR spectra acquired at several points in a titration of the A₃T₂ duplex with distamycin A (35°C). Numbers denote the number of equivalents of distamycin A added. Plus signs denote positions of the adenine C2H resonances of the free duplex (bottom). Asterisks indicate the positions of the three major-form one-drug H3 resonances (0.5 equivalents) and the two two-drug H3-2 resonances (2.0 equivalents).

These resonances continue to grow in intensity as the drug:DNA ratio is increased. In addition, at three-quarters of an equivalent of added drug, and more clearly after one equivalent has been added, new peaks corresponding to the two-drug complex (Chapter 4) appear at 6.2 ppm (drug H3-2) and near 8.5 ppm (adenine H8s). These two-drug resonances grow in intensity while those between 6.3 and 6.7 ppm decrease when distamycin A is added above stoichiometric ratios. After two equivalents have been added, the six original peaks are completely gone and the spectrum contains resonances corresponding to only one form of the A₃T₂ duplex (two-drug mode)(Chapter 4). Additions of distamycin A in excess of two equivalents result in the appearance of free drug H3 and H5 pyrrole resonances at 6.49 and 6.58 ppm, respectively, indicating that the drug binding sites have become saturated.

3.5 Drug proton assignments

H3 proton assignments of the drug in the major binding orientation were determined through intramolecular 1D NOEs from the drug amide protons (Klevit *et al.*, 1986). The downfield region of an NMR spectrum of the A₃T₂ duplex acquired with three-quarters of an equivalent of distamycin A and NOE difference spectra used to assign these protons are presented in Figure 3-2. Integration of the amide peaks (A-D) revealed that the intensity of peak B is 2.2 times that of peak A, similar to the intensity ratio observed between the two sets of three peaks that appear between 6.3 and 6.7 ppm, that the intensity of B plus A is equal to that of C, and that the intensity of C is one-sixth that of D. Since there are four amide and four amidinium protons per drug, these data indicate that peaks B and A must correspond to amide protons in major and minor binding forms, respectively, that peak C must contain a major and a minor form amide resonance, and that D must contain the remaining protons.

Figure 3-2. Amide and aromatic region of a spectrum of the A₃T₂ duplex acquired in H₂O with three-quarters of an equivalent of distamycin A (A), and representative NOE difference spectra (B-D). The letter M denotes resonances of the preferred binding orientation. Weak amide resonances at 8.89, 9.82, 9.95, and 10.02 ppm are due to the 2:1 complex (Chapter 4).

Irradiation of peak A (Figure 3-2B) resulted in NOEs to two sharp resonances near 8.1 ppm which can be assigned to the drug formyl protons and magnetization transfer to peak B. Similarly, irradiation of peak B (Figure 3-2C) resulted in NOEs to the formyl protons, a major form H3 resonance at 6.35 ppm, and magnetization transfer to peak A. Since HN-1 is the only amide proton close to both the formyl and pyrrole H3-1 protons, peaks B and A must correspond to HN-1 resonances in the major and minor binding sites, respectively, and the resonance at 6.35 ppm must belong to H3-1 in the major binding orientation (designated H3-1M). Magnetization transfer between A and B indicates in addition, that the drug exchanges between the two binding sites at a measurable rate.

Irradiation of peak C (Figure 3-2D) resulted in NOEs to H3-1M and a resonance at 6.68 ppm. Since HN-3 is the only amide proton that is close to both H3-1 and another H3 proton (H3-2), peak C must contain the major and minor form HN-3 resonances, and the resonance at 6.68 ppm must correspond to H3-2M. Finally, irradiation of D resulted in NOEs to H3-2M, a minor-form H3 resonance at 6.61 ppm, and a major form resonance at 6.49 ppm. By elimination, peak D must contain the HN-5 and HN-7 resonances, and since both are close to H3-3, the major form resonance at 6.49 ppm must correspond to H3-3M. NOEs to the minor form H3 protons were weak, which prevented their assignment by 1D methods. Assignment of these resonances by 2D methods will be described presently.

3.6 A₃T₂ with one-half equivalent of distamycin A

The observed magnetization transfer between amide peaks A and B suggested that exchange of the drug between binding sites could be helpful in verifying assignments. A NOESY/exchange spectrum of the A₃T₂ duplex was acquired with one-half equivalent of distamycin A (Figure 3-3). Cross peaks in this spectrum can be divided into several classes: 1) those arising from exchange of the drug between

Figure 3-3. Aromatic and C1'H regions of a NOESY/exchange spectrum of the A₃T₂ duplex with one-half equivalent of added distamycin A (mixing time 150 ms, 35°C). Adenine C2H resonances of the free duplex and drug H3 assignments of the major binding orientation are denoted along the diagonal. Exchange cross peaks correlating free and major-form bound C2H resonances are denoted by the letter M. Arrows indicate the positions of the free A6 and A16 C2H resonances and are directed toward exchange-transferred NOEs with the drug H3 protons (dashed box). Intermolecular H3- C2H NOEs are outlined by the solid box.

binding sites, *ii*) those arising from NOE, and *iii*) those arising from a combination of exchange and NOE.

Cross peaks due to exchange were used to assign the minor form H3 and bound adenine C2H resonances. In figure 3-3 exchange cross peaks correlate each major form H3 resonance with a minor form H3 resonance. These cross peaks arise when, during the mixing period, the drug exchanges between major and minor binding sites, and allow for the direct assignment of the minor form H3 resonances given the major form H3 assignments. Cross peaks due to exchange also correlate each adenine C2H resonance of the free A₃T₂ duplex with two new downfield-shifted resonances. For example, A5 C2HF (free duplex) (7.07 ppm) is connected by cross peaks with resonances at 7.27 and 7.44 ppm. These cross peaks arise when a drug dissociates from one undecamer and binds to one of two sites on another oligomer that was initially free of drug. Hence, the exchange cross peaks correlate each free adenine C2H resonance with the chemical shift that proton assumes upon drug binding in the major and minor sites, allowing for assignment of the bound A C2H protons. I was unable to assign the remaining resonances of the two one-drug complexes because of the relatively low effective concentrations of these species at low drug:DNA ratios (0.5), and because of complications due to exchange of the drug between one-drug and two-drug complexes at higher drug:DNA ratios (1.0, see below). The one-drug DNA C2H and drug H3 chemical shift are presented in Table 3-1.

The second class of cross peaks, those due to NOE, were used to identify contacts between adenine C2H and both the major and minor form drug H3 protons. In Figure 3-3 NOE cross peaks correlate each major form H3 resonance with two A C2H resonances (Table 3-2). One set, those between H3-1 and A5 C2H, between H3-2 and A6 C2H, and between H3-3 and A16 C2H are approximately three times as

Table 3-2. Distamycin A - DNA NOEs
observed with one-half equivalent of added drug

Drug proton	DNA proton
H3-1 M ^a	A4 M, A5 M
H3-2 M	A5 M, A6 M
H3-3 M	A6 M, A16 M
H3-1 m ^b	A6 m /A16 m ^c , A15 m
H3-2 m	A6 m / A16 m
H3-3 m	A5 m, A6 m / A16 m

^aM denotes major binding form.

^bm denotes minor binding form.

^cDegenerate chemical shifts.

intense as those between H3-1, -2, -3 and A4, A5, and A6 C2H, respectively. NOE cross peaks also correlate the minor form H3-1 and H3-2 protons (designated H3-1m and H3-2m) with A6 and/or A16 C2H (degenerate chemical shifts) and H3-3m with both A5 and A6/A16 C2H. In addition, a weak NOE is observed between H3-1m and A15 C2H. Although weak, this cross peak was also observed in a NOESY/exchange spectrum acquired at 20°C (not shown) indicating that it does arise from an intermolecular contact.

The third class of cross peaks, exchange-transferred NOEs, arise from a combination of exchange and NOE, and provide further evidence of specific contacts between the minor form H3 and A6/A16 resonances. For example, the cross peak between H3-3m and A6 C2HF arises when magnetization is transferred through NOE from H3-3m to A6 C2Hm, after which the drug dissociates leaving A6 C2H at the chemical shift characteristic of A6 C2HF. Thus, the presence of an exchange-transferred NOE between H3-3m and A6 C2HF indicates that H3-3m was close to A6 C2H at some point during the mixing period and that the H3-3m - A6/A16 C2H NOE is due, at least in part, to a H3-3m - A6 C2Hm contact. Exchange-transferred NOEs are also seen between A16 C2HF and H3-3M and between A6 C2HF and both H3-2M and H3-2m indicating that these protons were in close contact during a portion of the mixing period.

3.7 Dynamics

In addition to information on bound resonance assignments and intermolecular contacts, the NOESY/exchange spectrum obtained with one-half equivalent of distamycin A (Figure 3-3) contains information on the rate of exchange of the drug between binding sites. Since the binding constant of distamycin A for A-T -rich sequences is large (Breslauer *et al.*, 1987), the off-rate is significantly smaller than the on-rate, and therefore, in the short mixing time limit, the exchange cross

peak to diagonal peak ratio is essentially a measure of the fraction of molecules that have dissociated from a particular binding site during the mixing period. Rate constants of 2.4 ± 1.5 and $3.3 \pm 1.5 \text{ s}^{-1}$ (35°C, 10 mM sodium phosphate, 10 mM sodium chloride) for dissociation of the drug from the major and minor binding forms, respectively, were obtained from a NOESY/exchange spectrum of the A₃T₂ duplex acquired with one-half equivalent of distamycin A (mixing time 50 ms, not shown). A more accurate determination would require an analysis of the cross peak intensities as a function of time in order to include T₁ and cross-relaxation processes, which was not attempted.

Exchange cross peaks correlating the major and minor form drug H3 resonances (Figure 3-3) can either arise from exchange of the drug between binding sites on the same oligomer, or by dissociation and subsequent reassociation of the drug in the opposite orientation on a second DNA molecule. If these peaks arise mainly from the first process, exchange peaks correlating the chemical shifts of the major and minor form adenine C2H resonances should also be observed. These peaks are not observed in the spectrum, however, and I therefore conclude that the H3-H3 cross peaks are due mainly to exchange of the drug between DNA molecules. Rate constants based on these cross peaks are similar to those obtained above supporting this conclusion.

When more than one equivalent of distamycin A is added to the A₃T₂ duplex, an equilibrium exists between the two one-drug and the two-drug binding modes (Figure 3-1). To investigate exchange of the drug between these modes, I obtained a NOESY/exchange spectrum of the A₃T₂ duplex with approximately 1.3 equivalents of distamycin A (Figure 3-4). In this spectrum exchange cross peaks correlate each one-drug H3 resonance with two new upfield-shifted peaks that correspond to H3 protons of the two-drug complex (Chapter 4). Analysis of these cross peaks allowed specific assignment of the two-drug H3 protons given the one-drug H3 assignments

Figure 3-4. Expansion of the drug H3 region of a NOESY/exchange spectrum of the A₃T₂ duplex with 1.3 equivalents of distamycin A (300 ms mixing time, 35°C). The shifts of the major (M) and minor (m) form H3 protons are indicated along the diagonal. D1 and D2 refer to drugs 1 and 2 of the two-drug complex (Chapter 4).

(Table 3-1). Several exchange processes appear to contribute to the intensities of these peaks and I was therefore unable to obtain off-rates from these data (see below). Off-rates for the two drugs from the 2:1 complex were equal to within 25% and were measured to be $1.0 \pm 0.5 \text{ s}^{-1}$ (35°) based on NOESY/exchange spectra acquired with excess (3.0 equivalents) distamycin A.

3.8 Discussion

Spectra of the A₃T₂ duplex with less than stoichiometric amounts of distamycin A reveal that the drug binds to two sites within the minor groove of the undecamer with the major form populated approximately 2.2 times that of the minor form. At higher ratios, but still below one equivalent, a new two-drug binding mode is observed that becomes the only species present after addition of two equivalents of distamycin A. Since the two-drug complex appears at substoichiometric drug:DNA ratios, the second drug must bind with an affinity similar to that of the first drug. Integration of the H3 resonances of Figure 3-1 indicate that the two-drug to major form one-drug equilibrium constant ratio is 0.2. Although no evidence has been found for a 2:1 distamycin A:A₂T₂ complex, the two-drug to one-drug equilibrium constant ratio for distamycin A with A₃T₃ was found to be 1.7, and thus, it appears that it is easier to form the two-drug complex with longer stretches of A-T base pairs. Whether distamycin A binds preferentially in the 2:1 mode with sequences such as poly(dA):poly(dT) and poly [d(A-T)]:poly [d(A-T)], that contain longer stretches of A-T base pairs remains to be determined.

The intermolecular H3 - C2H contacts derived from the NOESY/exchange spectrum with one-half equivalent of distamycin A allows for characterization of the one-drug binding sites. As can be seen in Table 3-2, each major form H3 proton shows NOEs to two adenine C2H protons of adjacent base pairs, with one set of three NOEs approximately three times as intense as the other set. These data are consistent with

two models for drug binding. In the first model (Figure 3-5A) the drug is oriented so that each pyrrole ring lies between two A-T base pairs with each H3 proton close to two adenine C2H protons. For example, in Figure 3-5A the second pyrrole ring is placed between residues A5 and A6 so H3-2 is close to A5 and A6 C2H. In order to account for the observed differences in the NOE cross peak intensities, the drug must be positioned so H3-1, -2, and -3 are closer to A5, A6 and A16 C2H than A4, A5 and A6 C2H, respectively. In the second model (Figure 3-5B), distamycin A occupies either A⁴A⁵A⁶T or the adjacent A⁵A⁶TT binding site with the drug positioned so that each H3 proton is close to one C2H proton. It is further assumed that the drug exchanges between these binding sites at a rate that is fast compared to the NMR time scale so that each H3 proton "appears" close to two C2H protons. For example, in this model H3-2 is close to and should give an NOE to A5 and A6 C2H when the drug occupies the A⁴A⁵A⁶T and A⁵A⁶TT binding sites, respectively. In order to explain the intensities of the NOE cross peaks, distamycin A must have a slightly greater affinity for the A⁵A⁶TT site than the A⁴A⁵A⁶T site.

Although both models account for the observed major form NOEs, the second model (model B) is consistent with previous NMR and X-ray crystallographic investigations of both distamycin A- and netropsin-DNA complexes. The model B binding sites are similar to those found in an NMR study of the distamycin A - A₂T₂ complex (Klevit *et al.*, 1986; Chapter 1) where the drug is oriented in a four-base site with each H3 proton close to one C2H proton. Moreover, calorimetric studies have shown that distamycin A has a high affinity ($K_b \approx 10^8$) for the 5'- AATT -3' (d(CGCGAATTCGCG)₂) site (Breslauer *et al.*, 1987), which is similar to one of the two major form sites of model B. In addition, crystallographic studies of distamycin A with the A₃T₃ duplex have shown that the drug binds to a 5'- ATTT -3' site with each H3 proton in close contact with an adenine C2H proton, even though the binding

Figure 3-5. Models considered for the binding of distamycin A within the minor groove of the A₃T₂ duplex in both major (preferred) (A-B) and minor (C-D) orientations. Arrows denote H3-C2H NOEs.

region contained more than four A-T base pairs (Coll *et al.*, 1987). H3-C2H close contacts have also been noted in X-ray (Kopka *et al.*, 1985a-c; Coll *et al.*, 1989) and NMR studies (Patel, 1982; Patel and Shapiro, 1985, 1986; Sarma *et al.*, 1985) of netropsin:DNA complexes. Furthermore, sliding of distamycin A along the minor groove between adjacent binding sites has been proposed for the 2:1 distamycin A:A₃T₃ complex (Chapter 5). In that study preferential broadening of the adenine H8 and C1'H resonances of the duplex at reduced temperature as well as the NOE data (H3 - C2H, H3 - C1'H NOEs) were consistent with a model in which each drug of the two-drug complex was capable of sliding in fast exchange between adjacent AATT and ATTT sites. Sliding models have also been considered to explain NOE data obtained in several other drug-DNA complexes (Lee *et al.*, 1989; Wang *et al.*, 1989). Thus, based on these observations, I favor model B to explain the major-form NOE data.

For the minor binding form, as can be seen in Table 3-2, H3-1 and H3-3 are each close to at least two C2H protons, while H3-2 gives a strong NOE to A6/A16 C2H. In addition, the exchange-transferred NOE between H3-3m and A6 C2HF suggests that the H3-3m - A6/16 C2H NOE is due to a H3-3m - A6 C2Hm contact. Exactly as for the major form data, two analogous models are consistent with this set of data. In the first model (Figure 3-5C), the drug pyrrole rings are placed between A-T base pairs so each H3 proton is close to two C2H protons, while in the second model (Figure 3-5D) the drug is assumed to slide in fast exchange between A¹⁵A¹⁶TT and A¹⁶TTT binding sites. Furthermore, to account for the approximately equal intensities of the H3-C2H NOEs, in the second model the drug is assumed to have an equal preference for both sites. Again, based on the NMR and X-ray crystallographic data presented above, I favor the sliding model (Figure 3-5D) to account for these NOE data.

Structures of distamycin A bound to the major form AATT (Figure 3-5B) and minor form ATTT (Figure 3-5D) sites were created using a combination of

interactive docking and energy refinement with the Assisted Model Building and Energy Refinement (AMBER) (Weiner *et al.*, 1984) molecular mechanics program which was modified to include semiquantitative H3 - C2H distance constraints (Chapter 1). In addition to electrostatic interactions, the complexes appear to be stabilized by potential three-center hydrogen bonds (Taylor *et al.*, 1984) between the drug amide protons and both A N3 and T O2 atoms, and by stacking interactions between each of the drug pyrrole rings and the DNA sugar O4' atoms on each side of the groove. Similar observations have been noted in other distamycin A-(Coll *et al.*, 1987; see also Chapter 1), netropsin-(Kopka *et al.*, 1985a-c; Coll *et al.*, 1989), and Hoechst 33258-DNA (Pjura *et al.*, 1987; Teng *et al.*, 1988; Carrondo *et al.*, 1989) complexes, and also Z-DNA (Wang *et al.*, 1979).

The available data indicate that the minimal one-drug binding site consists of four A-T base pairs (Breslauer *et al.*, 1987; Klevit *et al.*, 1986; Chapter 1) and that the minimal two-drug site consists of five A-T base pairs (Chapter 4). When only one drug is bound to the five-base AAATT site, the data presented herein are consistent with a model in which distamycin A is able to slide between two adjacent four-base sites. In contrast, only a single one-drug binding site (ATTT) was found in a crystallographic study of distamycin A with d(CGCAAATTTGCG)₂, although other sites with four A-T base pairs were available. Moreover, in a recent NMR study of distamycin A with A₃T₃ (Chapter 5), at low drug:DNA ratios (0.5) only one set of three H3 resonances was observed. These resonances may correspond to drug binding to one site as observed in the crystal structure, or they may be averages resulting from the fact that the drug can slide between several sites at a rate that is fast compared to the NMR time scale. The present results support the latter interpretation.

Regardless of whether distamycin A binds to only one site or slides between two sites, the titration and NOE data reveal that the drug prefers binding with the formyl end directed toward the 5' side of the A-rich strand by a factor of 2.2. A similar orientational preference was observed for the binding of a distamycin A - EDTA-Fe(II) affinity cleaving molecule to a GAAATTG site (Schultz and Dervan, 1984) suggesting that the attached EDTA-Fe(II) moiety does not greatly perturb the drug binding equilibrium.

Assuming that the sliding model is correct and that the H3-C2H cross peak intensities correlate with extent of occupancy, the data indicate that distamycin A prefers the sequence AAATTG (major site) to CAATT (minor site) by a factor of approximately three, although they contain the same central base pairs. This specificity could be due to differences in hydrogen bonding of the drug with the terminal base pairs. Another possibility is that the Watson and Crick strands are structurally inequivalent with the result that the AAATTG site is preferred to the CAATT site. In this regard, relatively strong NOEs appear in NOESY spectra of the free duplex (Appendix C) between each adenine C2H proton and the C1'H of both its 3' neighbor and the 3' neighbor of the complementary residue. NOEs of this type have been observed with other A-rich sequences and, as noted previously (Patel *et al.*, 1986; Weiss *et al.*, 1984; Behling *et al.*, 1986; Kintanar *et al.*, 1987; Celda *et al.*, 1989), are indicative of deviations from ideal B-form DNA. Ongoing structural studies of these sequences (Kintanar *et al.*, 1987; Celda *et al.*, 1988) should shed light on this possibility.

NOESY/exchange spectra acquired at low and intermediate drug:DNA ratios indicate that distamycin A undergoes several dynamical processes (Figures 3-3 and 3-4). Drug off-rates of 2.4 ± 1.5 and 3.3 ± 1.5 s⁻¹ (35°C) from the major and minor one-drug binding modes, respectively, are similar to the off-rate of 4 s⁻¹ (27°C)

measured for distamycin A with A₂T₂ (Klevit *et al.*, 1986). Furthermore, in the two one-drug A₃T₂ complexes as well as the two-drug A₃T₃ complex (Chapter 5), the data are consistent with models in which distamycin A slides between adjacent binding sites within the minor groove at a rate that is fast on the NMR time scale. In contrast, although the rate of "flip-flop" exchange⁸ of distamycin A with the symmetry related AATT sites of the A₂T₂ duplex was comparable to the off-rate (4 s⁻¹, 27°C)(Klevit *et al.*, 1986), in the present study flip-flop exchange between major and minor binding forms was too slow to be measured. Moreover, the rate of exchange (dissociation / "flip-flop") of distamycin A and netropsin with A₂T₂ are similar (Patel *et al.*, 1985), and although the mechanism of exchange was not examined, the rate of exchange (dissociation and/or "flip-flop") of several other minor-groove binding antibiotics between symmetry related binding sites is considerably faster (Lee *et al.*, 1988; Lee *et al.*, 1989; Leupin *et al.*, 1986; Wang *et al.*, 1989).

Comparison of the two one-drug complexes and the 2:1 complex shows that distamycin A binds with the formyl group directed toward the 5' end of the A-rich strand in both the major one-drug and D1 (drug 1 of the two-drug complex, Chapter 4; Figure 4-2) two-drug binding sites and binds with the formyl group directed toward the 5' end of the T-rich strand in the minor one-drug and D2 two-drug binding sites. Assuming that the primary exchange process at intermediate drug:DNA ratios (1.3) is dissociation of a drug from the two-drug complex (Figure 3-4), analysis of these structures shows that dissociation of drug 2 should result in a set of D1 H3 - H3M cross peaks while dissociation of drug 1 should result in a set of D2 H3 - H3m cross peaks. These are observed in Figure 3-4. However, cross peaks are also observed between H3M and the D2 H3 resonances and between H3m and the D1

⁸ Exchange of the drug between binding sites while associated with the same oligomer.

H3 resonances indicating that other exchange processes, such as exchange of the drug from a one-drug to two-drug complex also contribute to the intensities of these peaks. Hence, I was unable to obtain off-rates for the drugs from the 2:1 complex from these data. Two-drug distamycin A off-rates were determined from NOESY/exchange spectra with excess drug to be nearly equal (within 25%) and were measured to be $1.0 \pm 0.5 \text{ s}^{-1}$ at 35°C. These rates are a factor of five greater than those for the two drugs from the 2:1 distamycin A - A₃T₃ complex (0.2 s^{-1}) (Chapter 5). Further kinetic and thermodynamic measurements are needed to relate these differences as well as those of the other drugs to the structures of the respective complexes.

Chapter 4

Structural Characterization of a 2:1 Distamycin A- d(CGCAAATTGGC):d(GCCAATTTGCG) Complex by 2D NMR

4.1 Introduction

In this chapter I further examine the binding of distamycin A to d(CGCAAATTGGC):d(GCCAATTTGCG), henceforth called the A₃T₂ duplex, using NMR spectroscopy. As stated previously, my major motivation was to examine which binding sites were occupied in solution when a sequence with more than the minimal four A-T base pairs was available. Titration of the DNA with distamycin A showed that at low drug:DNA ratios, at least two different binding sites were occupied (Chapter 3). At higher amounts of added drug, but still below a 1:1 ratio, a new binding mode was evident, which became the only form present at a drug:DNA ratio of 2:1. It is the structure of this 2:1 complex derived from NOESY experiments which will be described in this chapter.

4.2 Materials and Methods

Distamycin A was purchased from Sigma and used without further purification. Drug concentrations were calculated with an extinction coefficient of 34,000 M⁻¹cm⁻¹ at 303 nm. Due to the instability of the drug in aqueous solutions, fresh samples were prepared for each titration.

The deoxynucleotides d(CGCAAATTGGC) and d(GCCAATTTGCG) were synthesized using the phosphite triester method (Letsinger & Lunsford, 1976; Matteucci & Caruthers, 1981) using phosphoramidite reagents (American Bionetics) on an Applied Biosystems 381A synthesizer. After deprotection by heating overnight at

60°C in 15 M NH₄OH, the dimethoxytrityl (DMT) containing oligomers were purified by reverse-phase C18 chromatography on an IBM LC/9533 ternary-gradient chromatograph using a triethylammonium acetate - acetonitrile solvent system. The dimethoxytrityl groups were cleaved in 80% (v/v) acetic acid, then the strands were mixed, annealed, and applied to a hydroxylapatite column (BioRad DNA-grade) to remove excess single strands. The duplex was then dialyzed against 5 mM sodium phosphate (pH 7.0) and 5 mM sodium chloride. The final sample buffer contained 10 mM sodium phosphate, 10 mM sodium chloride, 1 mM EDTA, and 0.5 mM 2,2,3,3-tetradeutero-3-(trimethylsilyl)-propionic acid (TSP) as an internal reference. Absorbances were determined at 80°C. Double-strand DNA concentrations for samples used in various experiments ranged from 2-4 mM. The purity of the oligomer was greater than 90% based on the results of polyacrylamide gel electrophoresis.

NMR samples were prepared by drying in a Speed Vac concentrator (Savant) and dissolving in 99.96% ²H₂O (ICN Biochemicals). To observe exchangeable protons the sample was redissolved in 400 µl of a 90:10 (v/v) H₂O/²H₂O solution.

NOESY spectra were acquired on a GN-500 spectrometer (General Electric Instruments) and were processed as described previously (Chapter 2). One-dimensional NOE difference spectra of exchangeable protons were acquired by interleaving on- and off-resonance saturated spectra. A $1-\bar{3}-3-\bar{1}$ pulse (Hore, 1983) was used to suppress the solvent resonance.

4.3 DNA and drug proton assignments

Expansions of the aromatic to upfield (1.0 ppm) and aromatic to C1'H regions of a NOESY spectrum of the A₃T₂ duplex taken with two equivalents of added drug are shown in Figure 4-1. In the aromatic to C1'H region, cross peaks correlating each DNA aromatic proton (pyrimidine H6 or purine H8) with a C1'H on the same base,

Figure 4-1. Expansion of the aromatic to upfield and aromatic to C1'H regions of a NOESY spectrum of the 2:1 distamycin A - A₃T₂ complex (20°C, mixing time 150 ms). The sequential connectivities of the A-rich and T-rich strands are denoted by solid and broken lines, respectively. Intraresidue aromatic to C1'H cross peaks are indicated with numbers. Drug proton and DNA C2H proton positions are explicitly labeled.

and with a C1'H proton on the 5' neighboring base were found for both DNA strands, allowing for the assignment of these protons by sequential methods (Hare *et al.*, 1983; Scheek *et al.*, 1984). These connectivities were confirmed by assignment of the C2'H and C2''H protons. A review of the intensities of these cross peaks did not suggest any striking conformational changes in the A₃T₂ duplex. A more detailed conformational picture would require an analysis of the time dependence of the NOESY cross peaks, which was not attempted in this study. Additional peaks in this region arise from intermolecular contacts (discussed below).

Cross peaks in the aromatic to C1'H region of the NOESY spectrum were also used to assign several adenine C2H resonances. In general, for A-rich sequences, NOEs are observed from the C2H of an adenine residue to the C1'H of its 3' neighbor, and to the 3' neighbor of the complementary base (Chapter 1). These are clearly seen in NOESY spectra of the A₃T₂ duplex alone (Appendix C). Since A6 and T19 are the 3' neighbor, and the 3' neighbor of the complementary base of A5 respectively, the resonance at 7.71 ppm, with cross peaks to A6 and T19 C1'H must belong to A5 C2H. Another pair of cross peaks connect the resonance at 8.13 ppm with T8 and T17 C1'H, which must therefore belong to A16 C2H. Finally, cross peaks correlate a resonance at 8.07 ppm with T7 C1'H and A5 C2H and must belong to A6 C2H. These assignments were confirmed, and in addition, the A4 and A15 C2H assignments were determined by systematic one-dimensional NOE experiments of the DNA imino protons (Appendix D). The DNA aromatic and C1'H proton assignments are summarized in Table 1.

The origin of the drug H3 pyrrole resonances in the 2:1 complex were determined by first assigning these resonances after addition of a stoichiometric amount of distamycin A. At this point in the titration, two sets of drug resonances appeared (ratio 2.2/1) between 6.3 and 6.7 ppm corresponding to the binding of distamycin A in one of two orientations (Chapter 3). The drug H3 proton assignments

associated with the major binding form were determined through one-dimensional NOEs of the drug amide protons as described (Chapter 3). The drug H3 proton assignments associated with the minor binding form were then obtained by analysis of chemical exchange cross peaks observed in a NOESY spectrum taken with 0.5 equivalents of added distamycin A (Figure 3-3). These cross peaks occur due to exchange of the drug between the major and minor binding sites, allowing for the direct transfer of the major form assignments to the minor form. These major and minor form assignments were then transferred to the 2:1 complex in a similar manner, by analysis of chemical exchange cross peaks observed between the 1:1 and 2:1 complexes in a NOESY spectrum acquired with 1.3 equivalents of added drug (Figure 3-4). The drug proton assignments are summarized in Table 4-1.

4.4 Intermolecular contacts

In addition to the intramolecular NOEs used in assignment of DNA resonances, the NOESY spectrum contains many intermolecular (drug-DNA) NOEs, indicating close proximity of specific drug-DNA proton pairs. In Figure 4-1 it can be seen that each H3 proton gives a strong NOE to a C1'H proton. Specifically, the chemical shift degenerate H3-1 protons of the two drugs, which will hereafter be referred to as D1 and D2, give NOEs to A6 and T17 C1'H, while the D1 and D2 H3-2 protons give NOEs to T7 and T18 C1'H, respectively, and the D1 and D2 H3-3 protons give NOEs to T8 and T19 C1'H, respectively. Cross peaks also correlate each drug H3 proton with an adenine C2H proton. Specifically, cross peaks correlate the D1 and D2 H3-1 protons with A5 and A16 C2H, the H3-2 drug protons with A6 C2H, and the D1 and D2 H3-3 protons with A16 and A5 C2H, respectively. An NOE is observed between H3-1 and A6 C2H, but is weaker than the other H3-1 - C2H cross peaks by a factor of three, and may contain contributions from the H3-1 protons of both drugs. Intermolecular

Table 4-1. DNA and drug assignments in the 2:1 distamycin A - A₃T₂ complex.

DNA Assignments (ppm)					
Residue	Aromatic*	C1'H	Residue	Aromatic*	C1'H
C1	7.61	5.74	G12	7.95	6.00
G12	7.97	5.84	C13	7.51	6.06
C3	7.33	5.80	C14	7.46	5.83
A4	8.48	5.44	A15	8.53	5.65
A5	8.28	5.74	A16	8.44	6.08
A6	8.17	5.28	T17	7.24	5.33
T7	7.06	5.45	T18	7.30	5.58
T8	7.23	5.19	T19	7.30	5.27
G9	7.67	5.60	G20	7.76	5.78
G10	7.71	5.89	C21	7.33	5.65
C11	7.44	6.20	G22	7.94	6.15
Drug assignments					
HF	D1	7.92	D2	7.99	
H3-1		6.00		6.00	
H3-2		6.35		6.33	
H3-3		6.14		6.22	
CH ₂		1.12		1.12	
		2.14		2.20	

* purine H8 or pyrimidine H6 proton

NOEs are also observed between two sharp resonances at 7.92 and 7.99 ppm, which can be assigned to the D1 and D2 formyl protons, and A5 and A16 C1'H respectively.

In the aromatic to upfield region of the NOESY spectrum (Figure 4-1), it can be seen that NOEs connect the D1 and D2 formyl protons with a resonance at 1.12 ppm and with resonances at 2.14 and 2.20 ppm (not shown), respectively. Examination of the upfield region of the NOESY spectrum revealed the presence of strong NOEs between the resonance at 1.12 ppm and the resonances at 2.14 and 2.20 ppm. Furthermore, the resonance at 1.12 ppm is J coupled to these resonances and to a pair near 3.5 ppm. This pattern is indicative of the D1 and D2 propylamidinium protons. Thus, the peak at 1.12 ppm contains two C20 methylene resonances, one from each drug, while the peaks at 2.14 and 2.20 ppm correspond to the other C20 protons of D1 and D2, respectively. The cross peaks in the aromatic to upfield region therefore represent intermolecular drug-drug contacts between the formyl and methylene groups. NOEs are also observed between the C20 protons and both A4 and A15 C2H, which are degenerate in chemical shift. A summary of the drug-DNA and drug-drug contacts is given in Table 4-2.

4.5 Discussion

In titrations of the A₃T₂ duplex with distamycin A, resonances associated with the new 2:1 binding mode are observed before a stoichiometry of 1:1 is reached (Chapter 3) accounting for approximately 10% of the total at three-quarters of an equivalent of added drug. This indicates that the drug binding affinity in the 2:1 mode is almost as high as in the 1:1 modes. Furthermore, I have studied the binding of distamycin A to an oligonucleotide containing the sequence 5'- AAATTT -3', and find a very similar 2:1 binding mode (Chapter 5). However, in this case, the 2:1 complex becomes populated at lower amounts of added drug (below one-half equivalent), indicating an affinity that is essentially the same as in the 1:1 mode.

Table 4-2. Intermolecular NOEs observed in the 2:1 complex.

Drug proton	DNA proton correlated with D1	DNA proton correlated with D2
NOEs observed between drug and DNA protons		
HF	A5 C1'H	A16 C1'H
H3 - 1	A5 C2H	A16 C2H
	A6 C1'H	T17 C1'H
H3 - 2	A6 C2H	A6 C2H
	T7 C1'H	T18 C1'H
H3 - 3	A16 C2H	A5 C2H
	T8 C1'H	T19 C1'H
CH ₂	A15 C2H	A4 C2H
NOEs observed between drug protons		
	HF D1	CH ₂ D2
	HF D2	CH ₂ D1

The precise drug binding sites can be inferred from the intermolecular drug-DNA NOEs. For D1, the H3-1, 2, and 3 pyrrole protons give strong NOEs (and are therefore close) to A5, A6, and A16 C2H and A6, T7, and T8 C1'H protons, respectively. Hence, the D1 pyrrole rings span the A5-A6-T7 sequence, oriented so the formyl proton is near the 5' side of the A-rich strand. NOEs between D1 HF and A5 C1'H, and between D1 CH₂ and A15 C2H confirm this binding orientation. Similarly the H3-1, 2, and 3 pyrrole protons of D2 are close to A16, A6, and A5 C2H and T17, T18, and T19 C1'H, respectively. This indicates that the D2 pyrrole rings span the A5-A6-T7 sequence in a manner similar to D1, but with the drug oriented so the formyl proton is near the 5' side of the T-rich strand. NOEs between D2 HF and A16 C1'H, and between D2 CH₂ and A4 C2H confirm the binding orientation of D2. Furthermore, the observed inter-drug HF-CH₂ NOEs confirm the positions of D1 and D2 relative to one another. Together, these data indicate that there is a two-drug minor-groove binding site in the central portion of this undecamer, with D1 in close contact with the sequence 5'- AATT -3' of the A-rich strand, and with D2 in close contact with the sequence 5'- ATTT -3' of the T-rich strand, as indicated in Figure 4-2 (coordinates are listed in Appendix E).

The NMR data also indicate that the sequence and orientational specificity in the 2:1 mode is very high. At low drug:DNA ratios, where 1:1 complexes dominate, there is evidence that the drug binds to all four possible binding sites comprised of four successive A-T base pairs (Chapter 3). However, I observe only one form of the 2:1 complex. It seems reasonable that the antiparallel orientation of the drugs is favored because it reduces charge-charge repulsion between the positively-charged propylamidinium groups. Moreover, of the two possible antiparallel complexes (differing by exchange of the drugs across the minor groove), only one is observed, indicating that the drugs are able to "read the walls" of the minor groove in

Figure 4-2. Schematic of the distamycin A binding sites on the A₃T₂ duplex. Intermolecular contacts are represented by lines.

considerable detail. The exact mechanism by which this is accomplished is not yet clear.

Qualitative modeling was carried out with the Assisted Model Building and Energy Refinement (AMBER) molecular mechanics package as described previously for a 1:1 complex (Chapter 1). For the present calculations the D1 and D2 H3 to C1'H and adenine C2H proton distances were used as constraints. The resulting structure is presented in Figure 4-3. In previous studies of distamycin A- and netropsin-DNA complexes, electrostatic interactions, hydrogen bonds, and van der Waals forces have been put forth to account for the large binding energy associated with these drugs. In this model, the charged end of each distamycin A molecule is located deep in the minor groove where the electrostatic potential is large (Lavery *et al.*, 1982), thus contributing favorably to the free energy of complex formation. Hydrogen bonds between the drug amide and A N3 and T O2 atoms also stabilize the complex. For D1 hydrogen bonds are observed between HN-1 and A5 N3, HN-3 and A6 N3, HN-5 and T7 O2, and between HN-7 and T8 O2. Analogous hydrogen bonds are observed for D2. Previous studies of 1:1 distamycin A- and netropsin-DNA complexes (Chapter 1; Coll *et al.*, 1987; Kopka *et al.*, 1985a-c) have shown that three-center (Taylor *et al.*, 1984) hydrogen bonds form between the drug amide and A N3 and T O2 atoms on opposite strands of the duplex. Formation of such hydrogen bonds in the 2:1 complex is impossible since the drugs are pushed to the sides of the groove.

Molecular modeling also suggests that the distamycin A molecules are staggered with respect to one another so that the drug pyrrole rings of one drug stack with the amide linkages of the opposing drug on one side, and with DNA sugar O1' atoms on the other side. Staggering also explains the absence of NOEs between H3 protons on opposite drugs. Previous studies of minor-groove binding molecules have shown that they are in complete van der Waals contact with the floor and walls of the minor

Figure 4-3. Stereodrawing of the distamycin A - A₃T₂ complex obtained by energy refinement using semiquantitative distance constraints derived from NOESY spectra.

groove. In particular, stacking interactions were noted between the DNA sugar O1' atoms and the drug aromatic rings (Chapter 1; Kopka *et al.*, 1985a-c; Teng *et al.*, 1988) analogous to those that stabilize Z-DNA (Wang *et al.*, 1979). These interactions are also present in the 2:1 complex, although altered in detail due to the different positions of the drugs. Thus, in addition to electrostatic forces and hydrogen bond formation, drug-DNA and drug-drug stacking interactions appear to contribute to the stability of the complex.

Recent crystallographic studies have shown the minor groove of A-T -rich sequences to be narrow when compared with ideal B-form DNA (Coll *et al.*, 1987; Fratini *et al.*, 1982; Nelson *et al.*, 1987). For example, the minor-groove width of the A-rich region of d(CGCGAATTCGCG)₂ ranged from 0.32 to 0.40 nm (closest phosphate distance less 0.58 nm)(Fratini *et al.*, 1982), compared to the ideal B-form value of 0.60 nm (Chandrasekaran and Arnott, 1989). If the thickness of each drug is taken as 0.34 nm, binding two drugs must expand the minor groove to at least 0.68 nm, a value significantly larger than found in the crystal structures of these A-rich sequences. In addition, an analog of distamycin A with fluoromethylene groups linking pyrrole rings has been observed to bind in the minor groove (Wang *et al.*, 1987), although the detailed structure of this complex is not yet known and the affinity is relatively low. The width of these groups is similar to the stacked distamycin As. Minor groove widening has also been observed as the result of drug binding to G-C sequences. In an NMR study of the 2:1 actinomycin D-d(ATGCGCAT)₂ complex, it was shown that the pentapeptide lactone ring associated with the benzenoid portion of each drug bind simultaneously in the minor groove of the G-rich region of the octomer with concomitant minor groove widening (Scott *et al.*, 1988). Also, in a recent NMR study of the G-C specific drug chromomycin (Gao *et al.*, 1989), it was shown that the drug binds as a dimer to the sequence d(TTGGCCAA)₂.

and that sugar ring D of one drug and the chromomycinone unit of the other overlap and expand the minor groove. Taken together these data show that the phosphate backbone of DNA is flexible and that the major- and minor-groove widths of both A-T and G-C -rich regions can be altered to accommodate binding of other molecules. Helix distortions have also been observed in several protein-DNA complexes (Otwinowski *et al.*, 1988; Anderson *et al.*, 1987; McClarin *et al.*, 1986). Whether this flexibility is sequence dependent, and relates to binding specificity, remains to be determined. In any case, for the 2:1 mode, it is clear that the intrinsic width (shape) of the minor groove is not a factor in determining such specificity .

The identification of this complex by NMR may have implications for other types of measurements on this class of drug as well. For instance, a considerable amount of work has been reported using footprinting and affinity cleaving methods. (Schultz & Dervan,,1984; Schultz & Dervan, 1983; Taylor *et al.*, 1984) Since most of this work was performed at very low drug concentrations relative to the number of DNA binding sites, no problems should arise from 2:1 binding. However, some DNase I footprinting work has been conducted at sufficiently high drug:DNA ratios that the 2:1 binding mode could be important (Fish *et al.*, 1988). Moreover, in a recent study of the minor-groove binding drugs 4S (+) and 4R (-) anthelvencin A, a binding site size of four base pairs was obtained by footprinting methods, but a binding site size of only two base pairs was obtained by optical titration under saturating conditions, (Lee *et al.*, 1989) suggesting that these molecules form a type of 2:1 complex. Since these molecules are charged at both ends, it would seem that formation of a complex similar to that seen here would be destabilized by intermolecular charge-charge repulsion, although formation of a highly staggered complex might be investigated. Data obtained by other methods which utilize high drug:DNA ratios (such as calorimetry) are most likely to be affected. From the limited information now

available, it is easier to form the 2:1 complex with larger A-rich sequences (AATT << AAATT < AAATTT) (see chapters 3 and 5). Whether distamycin A binding to polymers such as $d(A)_n \cdot d(T)_n$ and $d(AT)_n$ occurs preferentially in the 2:1 mode is, as yet, unclear.

The structure of this complex, including both the sequence and orientational specificity, also suggests a new strategy for the design of new drugs and probes. In fact, it may be possible to combine recognition of one strand of the DNA with specific interactions between two drug molecules (or another part of the same drug molecule), to create a sequence-specific recognition complex. Interactions that stabilize the present 2:1 mode, and which should be used as a guide in the design of such drugs, include drug-drug and drug-DNA stacking, hydrogen bonding, and electrostatic forces.

Chapter 5

Binding Modes of Distamycin A with d(CGCAAATTTGCG)₂ Determined by 2D NMR⁹

5.1 Introduction

Recently, an X-ray crystallographic study of distamycin A with the symmetric d(CGCAAATTTGCG)₂ dodecamer revealed that the drug bound to only one four base-pair site, namely 5'-ATTT-3', although other sites with four base pairs were available (Coll *et al.*, 1987). I expected, based on my previous studies of distamycin A with d(CGCGAATTCGCG)₂ (Chapter 2) and d(CGCAAATTGGC):d(GCCAATTTGCG) (A₃T₂ duplex) (Chapters 3 and 4), that the sequence d(CGCAAATTTGCG)₂ (A₃T₃ duplex), would contain several good one-drug distamycin A binding sites, and might also contain a two-drug site analogous to that seen for the A₃T₂ duplex, in contrast to the crystallographic result. I therefore undertook an investigation of this system using nuclear Overhauser effect spectroscopy (NOESY) (Jenner *et al.*, 1979) in order to determine the binding modes present, and to probe the dynamics of drug exchange between these modes in solution.

5.2 Materials and Methods

The self-complementary oligomer d(CGCAAATTTGCG) was synthesized and purified as described (Chapter 4). The extinction coefficient for the sequence was calculated (Warshaw & Cantor, 1970) to be $1.125 \times 10^5 \text{ M}^{-1} \text{ cm}^{-1}$. Absorbances were determined at 80°C. Double-strand DNA concentrations used in the various experiments ranged from 1-4 mM, in buffer consisting of 10 mM sodium phosphate (pH 7.0) and 10 mM sodium chloride.

⁹ The text of this chapter is reprinted with permission from the *Journal of the American Chemical Society*. Copyright 1989, American Chemical Society.

NOESY spectra were acquired on a GN-500 spectrometer (General Electric Instruments) at drug:DNA ratios of 0.5:1 (30°C), and 2:1 (20°C, 50°C), and were processed as described (Chapter 1). All NOESY experiments were performed with a 150 ms mixing period. For each t_1 , 64 scans were signal averaged, taking 1024 complex points, with a recycle time of 2.2 s; 400 to 512 t_1 s were recorded per experiment. A spectral width of 5000 Hz resulted in a digital resolution of 4.9 Hz/point. One-dimensional NOE difference spectra of exchangeable protons were acquired by interleaving on- and off-resonance saturated spectra. A $1-\bar{3}-3-\bar{1}$ pulse sequence (Hore, 1983) was used to suppress the solvent resonance.

Results

5.3 Titration of the A₃T₃ duplex with distamycin A

Spectra obtained at several points in a titration of the A₃T₃ duplex with distamycin A are presented in Figure 5-1. After the initial addition of drug, the spectra are quite complex due to the appearance of many new resonances, as well as the broadening and the reduced intensity of resonances belonging to the free duplex. In particular, six new resonances appear between 6.0 and 6.7 ppm, characteristic of the drug H3 pyrrole protons, while the A4, A5 and A6 C2H resonances of the free duplex which resonate at 7.11, 7.00, 7.53 ppm¹⁰ (appendix F, see figure F-1), respectively (Table 5-1), become significantly broader and reduced in intensity. Upon further drug additions, the upfield set of H3 pyrrole resonances at 6.02, 6.20, and 6.34 ppm, and also several peaks near 8.3 ppm grow in intensity, while the other set of H3 resonances at 6.44, 6.50 and 6.67 ppm begin to diminish. This trend continues until the downfield set of H3 resonances essentially disappear (1.5 equivalents), and growth of the upfield set of H3 resonances stops (2.0 equivalents). At this point, DNA resonances corresponding to only one strand of the A₃T₃ duplex are

¹⁰ Numbering scheme for the symmetric A₃T₃ duplex is 5' to 3', residues 1-12. Resonances of the free duplex were assigned by standard methods (Chapter 1).

Figure 5-1. (top) Schematic of distamycin A. It consists of a formyl group followed by three N-methylpyrrole carboxamide units, and a propylamidine group. (bottom) Aromatic and C1'H regions of NMR spectra acquired at several points in a titration of d(CGCAAATTTGCG)₂ with distamycin A (35°C). The three upfield H3 pyrrole proton chemical shifts (two-drug mode) are indicated by the right most asterisks. The three downfield pyrrole H3 protons (one-drug mode) are indicated by the left most asterisks. Plus signs denote the chemical shifts of the three adenine C2H resonances of the uncomplexed dodecamer. Reprinted with permission from the *Journal of the American Chemical Society*. Copyright 1989, American Chemical Society.

Table 5-1. Chemical Shift Assignments of the A₃T₃ Duplex (ppm)

DNA Proton	Free Duplex	Two-Drug Complex	Difference
C1 H6	7.61	7.60	-0.01
C1 C1'H	5.71	5.73	0.02
G2 H8	7.93	7.96	0.03
G2 C1'H	5.84	5.86	0.02
C3 H6	7.31	7.35	0.04
C3 C1'H	5.31	5.63	0.32
A4 H8	8.21	8.38	0.17
A4 C1'H	5.75	5.70	-0.05
A4 C2H	7.11	7.40	0.29
A5 H8	8.11	8.34	0.23
A5 C1'H	5.88	5.66	-0.22
A5 C2H	7.00	7.61	0.61
A6 H8	8.10	8.30	0.20
A6 C1'H	6.12	5.73	-0.39
A6 C2H	7.53	8.10	0.57
T7 H6	7.12	7.16	0.04
T7 C1'H	5.90	5.40	-0.50
T8 H6	7.43	7.32	-0.11
T8 C1'H	6.11	5.54	-0.57
T9 H6	7.28	7.27	-0.01
T9 C1'H	5.85	5.39	-0.46
G10 H8	7.91	7.81	-0.10
G10 C1'H	5.78	5.79	0.01
C11 H6	7.36	7.34	-0.02
C11 C1'H	5.73	5.69	-0.04
G12 H8	7.94	7.93	-0.01
G12 C1'H	6.12	6.13	0.01

observed, suggesting the formation of a symmetric 2:1 drug:DNA complex. Upon further additions of distamycin A resonances from free drug H3 and H5 pyrrole protons appear at 6.58 and 6.49 ppm, respectively, indicating that the drug binding sites become saturated.

The initial appearance and then disappearance of the downfield set of H3 resonances, combined with the appearance of a set of upfield H3 resonances, which then grew in intensity until two equivalents of drug had been added, suggest that it is possible for distamycin A to bind in both one-drug and symmetric two-drug modes. From the intensities of the H3 resonances associated with both of these modes, it was found that the binding constant for binding of the second drug was larger than the binding constant for binding of the first drug by a factor of approximately 1.7. To investigate whether I could detect exchange of the drug between these binding modes, I acquired a NOESY spectrum of the duplex at a relatively low drug:DNA ratio (0.5 equivalents) where both binding modes were populated (Figure 5-2). In this spectrum cross peaks correlate the upfield and downfield sets of H3 resonances. These cross peaks are due to exchange, and arise when a drug initially in one binding mode has transferred to the other mode during the mixing time. From the intensities of the exchange cross peaks and the diagonal peaks associated with the two-drug mode, the drug off-rate from the 2:1 complex is calculated to be $0.2 \pm 0.1 \text{ s}^{-1}$ at 30°C. A more accurate determination would require an analysis of the time dependence of the cross and diagonal peak intensities in order to account for both longitudinal and cross relaxation effects (Jeener *et al.*, 1979), which was not attempted.

For the one-drug binding mode, the fact that only one set of H3 resonances is seen suggests that distamycin A either binds to only one site, as observed in the crystal structure of the drug with the A₃T₃ duplex (Coll *et al.*, 1987), or that the drug is in fast exchange among several binding sites. In the latter case the drug H3

Figure 5-2. Expansion of a NOESY/exchange spectrum of the A₃T₃ duplex acquired after addition of one-half equivalent of distamycin A (30°C, 150 ms). The downfield and upfield sets of H3 resonances correspond to the one-drug and two-drug binding modes, respectively. The cross peaks arise from chemical exchange of the drug between binding modes. Reprinted with permission from the *Journal of the American Chemical Society*. Copyright 1989, American Chemical Society.

protons would resonate at population-weighted average chemical shifts. The behavior seen in the 2:1 mode (see below) suggests that such dynamic averaging may well occur (see also section 3.7). At low drug concentrations, where the one-drug mode is significantly populated, a complex mixture of species is present in solution precluding a structural characterization of the 1:1 binding site(s). At high drug concentrations, however, the 2:1 complex is the primary species present, facilitating assignment and structural characterization of this complex, which will be discussed presently

5.4 Assignment of resonances in the 2:1 A₃T₃ complex

Expansions of the aromatic to upfield (1.0 ppm) and aromatic to C1'H regions of a NOESY spectrum of the 2:1 complex are presented in Figure 5-3. This spectrum contains both intramolecular NOEs used to assign DNA resonances, and intermolecular NOEs used to identify drug-DNA contact points. The DNA aromatic and C1'H protons can be assigned from NOESY spectra by observation of sequential NOEs between an aromatic proton and both its own C1'H, and the C1'H of its 5' neighbor as described (Chapter 1). For the A₃T₃ duplex with two equivalents of added drug, sequential connectivities can be traced from C1 to C3, and from T7 to G12. However, the aromatic to C1'H cross peaks associated with A4, A5, and A6 are either missing or are ambiguous. Analysis of the aromatic to C2'H/C2''H/CH₃ region of this spectrum revealed cross peaks between C3 C2'H/C2''H and A4 H8, and between A6 H8 and T7 CH₃, which were used to identify the A4 and A6 H8 chemical shifts. Given these assignments, it was clear from the aromatic to C2'H/C2''H NOEs associated with the three adenine residues that A5 H8 resonates at 8.34 ppm.

One-dimensional spectra of the A₃T₃ duplex with two equivalents of drug were collected at various temperatures (Figure 5-4). As the temperature is reduced from 55 to 5°C, there is a general broadening of the peaks, with several, including

Figure 5-3. Expansions of the aromatic to upfield and aromatic to C1'H regions of a NOESY spectrum of the 2:1 distamycin A-d(CGCAAATTTGCG)₂ complex (20°C, 150 ms). Sequential connectivities are denoted by solid lines. Intra-residue aromatic to C1'H cross peaks are indicated with numbers. Drug proton and DNA C2H proton chemical shifts are explicitly labeled. Dashed lines denote cytosine C5H to aromatic proton connectivities. Peaks labeled with an X, which were also observed in NOESY spectra of the free duplex (Appendix F, see figure F-1), result from oligonucleotide impurities, and represent less than 10% of the total DNA concentration. Reprinted with permission from the *Journal of the American Chemical Society*. Copyright 1989, American Chemical Society.

both the aromatic and C1'H resonances of A4, A5 and A6, broadening more than the other aromatic and C1'H peaks. This differential line broadening is indicative of an exchange process (Chapter 1) that is at an intermediate rate on the NMR time scale, whereby the linewidth of a particular resonance is dependent on the chemical shift difference of the proton in its various binding sites and the rate of exchange (Chapter 1).

I reasoned that the adenine aromatic to C1'H cross peaks in the NOESY spectrum acquired at 20°C (Figure 5-3) were weak because of exchange broadening, and therefore acquired a NOESY spectrum of the 2:1 complex at 50°C, where these resonances were better resolved. In this spectrum all of the aromatic to C1'H cross peaks were weak, and in particular, the inter-residue C3 C1'H to A4 H8, and intra-residue A6 H8 to C1'H cross peaks were not visible. However, the sequential connectivities could be traced unambiguously in the aromatic to C2'H/C2''H region (Figure 5-5), confirming the A4, A5, and A6 H8 assignments. Given the C2'H/C2''H assignments, it was then possible, using aromatic - C2'H/C2''H - C1'H cross peaks, to assign each of the adenine C1'H peaks. The fact that resonances corresponding to only one strand of the duplex were observed after the addition of two equivalents of drug indicates that the DNA in the complex is symmetric, showing that the drugs must bind in a symmetric fashion. Moreover, a review of the intensities of the observed intra- and inter-residue DNA cross peaks in both NOESY spectra did not suggest any striking conformational changes to the A₃T₃ duplex upon drug binding. A more quantitative analysis was not attempted because of complications due to exchange of the drug between binding sites (see below) during the NOESY mixing period.

The adenine C2H resonances were assigned using both the NOESY spectrum of Figure 5-3, and sequential 1D NOEs of the DNA imino protons (Appendix F, figure F-2). The DNA aromatic and C1'H assignments of the A₃T₃ duplex alone and with two

Figure 5-4. Spectra of the 2:1 distamycin A - A₃T₃ complex obtained at various temperatures. Numbers denote the temperature at which each spectrum was acquired in degrees Celsius. Asterisks denote the general chemical shifts of the DNA adenine H8 (8.3 ppm) and C1'H (5.7 ppm) resonances. Clear differential broadening of the aromatic and sugar protons in the A-T -rich segment is evident at low temperature. Reprinted with permission from the *Journal of the American Chemical Society*. Copyright 1989, American Chemical Society.

Figure 5-5. Expansion of the aromatic to C2'H/C2''H/CH₃ region of a symmetrized NOESY spectrum of the A₃T₃ duplex with 2.0 equivalents of distamycin A (50°C, 150 ms). Aromatic to C2'H sequential connectivities are indicated by solid lines. Intraresidue aromatic to C2'H NOEs are indicated by residue name and number. Aromatic methyl proton chemical shifts are labeled explicitly. Reprinted with permission from the *Journal of the American Chemical Society*. Copyright 1989, American Chemical Society.

equivalents of drug are summarized in Table 5-1, together with the change in chemical shift upon complex formation. Drug H3 resonances were assigned by observation of NOEs to these protons from drug amides (8-11ppm) as described (Chapter 3). The presence of two drugs in the minor groove complicated assignment of the drug aromatic protons, since both intra- and intermolecular NOEs between amide and H3 protons are possible. For this reason, I was initially unable to specifically assign H3-2 and H3-3 to either 6.20 or 6.34 ppm, although H3-1 was unambiguous at 6.02 ppm. However, when the intermolecular contacts below were examined, it became clear that H3-2 must resonate at 6.34 ppm and H3-3 must resonate at 6.20 ppm to be consistent with all of the observed NOEs. In addition, my study of the 2:1 distamycin A - A₃T₂ complex (Chapters 3 and 4) showed that the nonequivalent H3-3 protons were found to resonate downfield of the H3-1 protons and upfield of the H3-2 protons, consistent with the assignments here.

5.5 Intermolecular Contacts

The NOESY spectrum of the 2:1 complex (Figure 5-3) contains many intermolecular drug:DNA NOEs, in addition to the intramolecular ones, that can be used to identify contact points between these molecules. In particular, NOEs are observed between A5 C2H and both H3-1 and H3-3 (with the assignments as above), and between A6 C2H and each of the H3 protons. If the H3-2 and H3-3 assignments were reversed, then an NOE would be expected between H3-1 or H3-3 and A4 C2H, but no such NOE is seen, confirming the assignments. Intermolecular NOEs are also observed in this spectrum between both A4 and A5 C2H and a pair of resonances at 1.19 and 2.18 ppm, which must be the geminal C20 protons of the drug in this complex, as in the A₃T₂ complex (Chapter 4).

Strong NOEs are also observed in Figure 5-3 between the drug H3 and DNA C1'H protons. Specifically, NOEs are observed between H3-1 and either T7 or T9 C1'H

(too close to be resolved), and both H3-2 and H3-3 show NOEs to T8 and either T7 or T9 C1'H. There are also NOEs between the drug formyl proton and both A5 and A6 C1'H, although at the temperature at which this spectrum was acquired these peaks are poorly resolved, and consequently, the NOEs between these proton pairs are broad. At 50°C, where these peaks are better resolved, the NOESY spectrum revealed distinct cross peaks between the formyl proton and these C1'H protons, confirming the presence of both contacts.

Finally, cross peaks are observed in Figure 5-3 from the drug formyl proton to resonances at 1.19 and 2.18 ppm, and from each of the drug H3 protons to the other two, with the H3-1 to H3-2 cross peak significantly less intense than the others. All of these NOEs represent intermolecular drug-drug contacts, since the distances between these protons on a single drug are larger than 0.5 nm. The drug-drug and drug-DNA contact points are summarized in Table 5-2.

5.6 Distamycin A binding modes in crystallization buffer

It was apparent that the NMR results were not consistent with the X-ray crystal structure of distamycin A with the A₃T₃ duplex derived under different solvent conditions (Coll *et al.*, 1987). In order to determine the effect of the crystallization buffer on the distamycin A binding modes, I acquired spectra of the A₃T₃ duplex in the crystallization buffer (20 mM sodium cacodylate (pH 6.5), 8 mM MgCl₂, 1 mM spermine, 10% (v/v) 2-methyl-2,4-pentanediol, 1 mM DNA, 1.1 mM distamycin A) and also in phosphate buffer (pH 7.0), using identical drug and DNA concentrations (Figure 5-6). The A₃T₃ duplex resonances in the crystallization buffer are broad because of an increase in viscosity associated with addition of the alcohol. Comparison of the two spectra clearly shows, however, that the 2:1 complex, as evidenced by the H3 resonances at 6.02, 6.20, and 6.34 ppm, is the primary species present under both buffer conditions.

5.7 Discussion

Spectra obtained at intermediate points in the titration of the A₃T₃ duplex with distamycin A indicate that both one-drug and two-drug binding modes occur with this sequence. Moreover, as indicated by the binding-constant ratio (2:1/1:1) of approximately 1.7, binding of the second drug is slightly more favorable than binding of the first drug. This is to be compared to distamycin A binding with the A₃T₂ duplex (Chapters 3 and 4), where the ratio of equilibrium constants (2:1/1:1) is 0.2. Thus, addition of another A-T base pair (A₃T₃ vs A₃T₂) facilitates formation of the 2:1 complex relative to the one-drug complex.

The off-rate for each drug of the 2:1 complex was determined to be $0.2 \pm 0.1 \text{ s}^{-1}$ at 30°C, which is a factor of five slower than for the drug in the 2:1 complex with the A₃T₂ duplex ($1.0 \pm 0.5 \text{ s}^{-1}$, 35°C) (Chapter 3). This reflects the fact that there are fundamental differences in the binding of distamycin A between these sequences. The kinetic parameters listed here, as well as those obtained from a thermodynamic analysis of the 2:1 binding mode, should provide needed insight into these differences.

Several models for the binding of two distamycin A molecules in the minor groove of the A₃T₃ duplex were considered in an attempt to explain both the drug-DNA and drug-drug NOEs. In order to be consistent with the data, the model must account for the fact that A5 and A6 C2H are close to two and all three drug H3 protons, respectively, and that both H3-2 and H3-3 are close to at least two C1'H protons. In model A (Figure 5-7A), two drugs were placed symmetrically in the minor groove with each pyrrole ring positioned between two base pairs so that each drug H3 proton is close to two C1'H protons. As can be seen in the figure, this model accounts for the five observed drug H3 to DNA C1'H NOEs. An NOE is also expected between H3-1 and A6 C1'H, but it is not observed experimentally. The absence of this cross peak could be due to exchange broadening, since other NOEs expected to A6 C1'H, such as the A6 H8 to C1'H NOE, were also missing. A comparison of predicted

Figure 5-6. Spectra of the aromatic and C1'H resonances of the 2:1 distamycin A - A₃T₃ complex (1.1 mM distamycin A, 1.0 mM A₃T₃ duplex, 35°C); (top) in 10 mM sodium phosphate (pH 7.0) and 10 mM sodium chloride, and (bottom) in 20 mM sodium cacodylate (pH 6.5), 8 mM magnesium chloride, 1 mM spermine, and 10% (v/v) 2-methyl-2,4-pentanediol (crystallization buffer). The lower spectrum was acquired with a $1-\bar{3}-3-\bar{1}$ pulse to suppress the aliphatic alcohol resonances. Lines correlate the three upfield (two-drug) and the three downfield (one-drug) H₃ resonances. Reprinted with permission from the *Journal of the American Chemical Society*. Copyright 1989, American Chemical Society.

Table 5-2. Intermolecular Drug-DNA and Drug-Drug Contacts

Drug Proton	DNA and Drug Protons
FH	A5 C1'H, A6 C1'H
H3 - 1	A5 C2H, A6 C2H,T7 and/or T9 C1'H H3-2, H3-3
H3 - 2	A6 C2H, T7 and/or T9 C1'H, T8 C1'H H3-1, H3-3
H3 - 3	A5 C2H, A6 C2H, T7 and/or T9 C1'H, T8 C1'H H3-1, H3-2
C20 CH ₂	A5 C2H, A4 C2H, FH

and experimentally observed drug H3 to DNA A C2H NOEs showed that this model is inconsistent with the observed NOEs between A5 C2H and H3-1 and between A6 C2H and H3-3, which have intensities that indicating distances between these proton pairs of less than 0.28 and 0.35 nm, respectively¹¹. A structure of model A was generated by interactively docking distamycin A into the minor groove of the A₃T₃ duplex. In this structure, the distance between each of these proton pairs (A5 C2H - H3-1, 0.54 nm; A6 C2H - H3-3, 0.43 nm) is too long to account for the intensities of the observed cross peaks. Furthermore, this model does not account for the observed drug-drug C20 CH₂ to FH NOEs which are less than 0.35 nm apart experimentally, but are 1.1 nm apart in this model.

In model B (Figure 5-7B), the drugs were again arranged symmetrically in the minor groove with each pyrrole ring positioned between two base pairs to satisfy the drug H3 to adenine C2H NOEs. This model was rejected because it failed to explain the observed drug H3 to DNA C1'H NOEs. Specifically, NOEs are observed between H3-1 and either T7 or T9 C1'H, and between H3-2 and T8 C1'H (all distances less than 0.3 nm), while in models generated by interactive docking, these distances (H3-1 - T7 C1'H, 0.56 nm; H3-1 - T9 C1'H, 0.58 nm; H3-2 - T8 C1'H, 0.44 nm) are too long to account for the intensities of the observed cross peaks.

Because models A and B failed to explain the observed NOEs, I considered a third model in which each drug was able to occupy either a 5'- AATT -3' or a 5'- ATTT -3' site, related by shifting the drug on the DNA sequence by one base pair. In this model, each of the drug pyrrole rings was positioned opposite a DNA base ring, which, depending on the site occupied, places the H3 protons adjacent to either of two A C2H and C1'H protons. This mode of binding, with the drug pyrrole rings in close contact with the DNA base pairs, has been observed in both 1:1 complexes of distamycin A

¹¹Distance upper limit based on comparison of drug-DNA cross peak intensities with cytosine C5H-C6H cross peak intensities (distance 0.245 nm).

Figure 5-7. Schematic of models A and B considered in the binding of distamycin A to the A₃T₃ duplex. Circles represent drug pyrrole rings and arrows indicate expected NOEs from the H3 protons. In model A, the drugs are oriented so that each of the drug H3 protons is close to two C1'H protons consistent with the observed H3-C1'H NOEs. In model B, the drugs are oriented so that each H3 proton is close to two adenine C2H protons consistent with the observed H3-C2H NOEs. Reprinted with permission from the *Journal of the American Chemical Society*. Copyright 1989, American Chemical Society.

(Chapters 2 and 3; Coll *et al.*, 1987) and netropsin (Patel, 1982, Kopka *et al.*, 1985a-c; Patel & Shapiro, 1986; Coll *et al.*, 1989) with A-T rich sequences, and in the 2:1 complex of distamycin A with d(CGCAAATTGGC):d(GCCAATTTGCG) (Chapter 4). It is necessary to assume, in order to account for the fact that only one set of drug and DNA resonances is observed, that the drug slides between the two sites at a rate that is near the fast exchange limit. Such a sliding model accounts for the observed temperature dependent linewidth of the aromatic and C1'H resonances (Figure 5-4). Together, these assumptions lead to three different drug configurations within the A₃T₃ duplex denoted C1, C2, and C3 (Figure 5-8).

The close contacts predicted in the three structures C1, C2, and C3 account for all of the observed intermolecular NOEs. In C1, in which both drugs bind to AATT sites, the close contacts predicted between A5 C2H and H3-1, and between A6 C2H and both H3-2 and H3-3, account for three of the five observed H3 - C2H NOEs. Similarly, the close contacts predicted between T7 C1'H and H3-2, and between T8 C1'H and H3-3 account for two of the five observed C1'H - H3 cross peaks. An NOE is also predicted between A6 C1'H and H3-1 which is not seen in the NOESY spectrum. As noted previously however, the A6 C1'H resonance is broad at 20°C, and the expected cross peak may be missing due to exchange broadening. NOEs observed between the drug formyl proton and A5 C1'H, between the drug C20 methylene protons and A5 C2H, and between the H3-2 and H3-3 protons of opposing drugs are also consistent with this mode of binding .

In C2, in which both drugs occupy ATTT binding sites, the close contacts predicted between A5 C2H and H3-3, and between A6 C2H and both H3-1 and H3-2 (also occurring in C1), account for the other H3 - C2H NOEs observed in Figure 5-3. Similarly, the close contacts expected between T7 C1'H and H3-1, between T8 C1'H and H3-2, and between T9 C1'H and H3-3, account for the remaining C1'H-H3 NOEs.

Figure 5-8. Schematic of the sliding model comprised of structures C1, C2, and C3. Circles represent drug pyrrole rings and attached H3 protons. NOEs are observed between each H3 proton (circle) and the adenine base to which it is adjacent, on either strand. NOEs from the DNA C1'H to drug FH and H3 protons are indicated by arrows. Reprinted with permission from the *Journal of the American Chemical Society*. Copyright 1989, American Chemical Society.

Furthermore, NOEs between the drug formyl proton and A6 C1'H, between the drug C20 methylene protons and A4 C2H, and between the drug H3-1 and H3-2 protons of opposing drugs are consistent with this mode of binding.

Finally, in C3, in which one drug occupies a 5'- AATT - 3' site, and the other drug occupies a 5'- ATTT -3' site, the drug-drug NOEs expected between the formyl and C20 methylene protons of opposing drugs, as seen in the previous 2:1 complex (Chapter 4), and between the H3-1 and H3-3 protons are observed experimentally.

The analysis above shows that the three structures C1, C2, and C3, when taken together, are consistent with the observed stoichiometry, all of the observed NOEs, and the temperature-dependent exchange behavior. This interpretation is strengthened by my observation of a non-exchanging 2:1 complex with the A₃T₂ duplex (Chapter 4). Thus, I conclude that two types of binding sites: 5'- AATT -3' and 5'- ATTT -3' are occupied within the A₃T₃ sequence, and that the complex is symmetric on the average due to rapid exchange of each drug between these two sites. In all of the binding sites, the formyl end of the drug is directed toward the 5' end of the strand with which it is in contact. Thus, the two positively-charged propylamidinium groups are directed toward opposite ends of the helix, which minimizes any possible interaction between them, and positions them to interact favorably with the DNA phosphates (Lavery *et al.*, 1982). Sliding models have also been considered in the study of other minor-groove binding antibiotics (Lee *et al.*, 1988; Wang *et al.*, 1989).

As mentioned previously, the three H3 - H3 NOEs, each of which corresponds to a different model (Figure 5-8), differ in intensity. Since the intensity of a NOE cross peak is a function of both the time two protons are near one another, and also the distance by which they are separated, these differences may reflect differences in the detailed interactions between the drug molecules in the three complexes, or they may

reflect differences in the populations of the three complexes in solution. In the latter case, which I favor, C2 (H3-1 - H3-2 NOE) would be populated approximately twice that of C3 (H3-1 - H3-3 NOE), while C3 would be populated approximately twice that of C1 (H3-2 - H3-3 NOE).

Based on the model for distamycin A binding to the A₃T₃ duplex described here, as well as the very similar model for distamycin A binding to the the A₃T₂ duplex (Chapter 4), I conclude that the sequence and orientational specificity of drug binding in the 2:1 mode is high. For the A₃T₂ duplex, one drug binds to an 5'- AATT -3' site, while the other drug is in close contact with the sequence 5'- ATTT -3' of the complementary strand. The addition of a 6th A-T base pair in A₃T₃ effectively creates two adjacent binding sites, both AATT and ATTT, on each strand of the helix. The pyrrole rings of the two drugs can all be adjacent to one another as in C3, or they can be staggered, with only two of the three rings in close contact, as in C1 and C2. Moreover, I did not see any evidence for drug binding in the opposite orientation with the two positively-charged propylamidinium groups in close contact. Furthermore, of the two possible antiparallel complexes (related by interchange of the drugs across the minor groove) only one is observed, indicating that the drugs are able to "read" the walls of the groove in considerable structural detail.

Models of C1 and C2 (Figure 5-9) were generated with a modified version of the AMBER (Weiner *et al.*, 1984) molecular mechanics program using semi-quantitative intermolecular drug - drug and drug - DNA distance constraints derived from NOEs between these protons (Appendix G). The energy-minimized structures show hydrogen bonds between the drug amide protons and both the adenine N3 and thymine O2 atoms on the strand with which the drug is associated (Table 5-3). Three-center hydrogen bonds seen in other drug-DNA complexes (Chapter 2; Coll *et al.*, 1987; Kopka *et al.*, 1985a-c; Pjura *et al.*, 1987; Teng *et al.*, 1988) are not

possible in the 2:1 complex, because each drug is pushed against one wall of the minor groove.

Analysis of the energy-minimized structures also suggests that stacking interactions are important in stabilizing each complex. In C1, on one side the three pyrrole rings stack with A6, T7, and T8 sugar oxygen atoms respectively. On the other side pyrrole ring one stacks with the positively-charged amidinium group, while pyrrole rings two and three stack over the N7 and N5 amide groups of the opposing drug respectively. For C2 and C3 the stacking interactions are similar to C1 and to those observed in the 2:1 distamycin A-A₃T₂ complex (Chapter 4). Interactions between sugar oxygen atoms and aromatic rings have also been observed in 1:1 distamycin A- (Chapter 2; Coll *et al.*, 1987), netropsin- (Kopka *et al.*, 1985a-c), and Hoechst 33258-DNA complexes (Pjura *et al.*, 1987; Teng *et al.*, 1988), as well as intramolecularly in Z-DNA (Wang *et al.*, 1979).

These findings are quite different from those found in the single-crystal X-ray study of Coll *et al.* (1987) with the same drug and DNA oligomer. They observe a single 1:1 binding mode for distamycin A with this duplex at a 1.1:1 drug:DNA ratio. NMR spectra of the A₃T₃ duplex with distamycin A added to this level, obtained in both phosphate buffer and in the buffer used in the X-ray study (Figure 5-6), revealed that the 2:1 complex was the primary species present. Thus, observation of only the 1:1 complex in the crystalline state appears to be due to selection by crystal packing forces, rather it being the dominant form in the solution. In this regard, all of the A-T rich oligomers so far crystallized with, and without drug, have narrow minor grooves (Coll *et al.*, 1987; Kopka *et al.*, 1985; Coll *et al.*, 1989; Pjura *et al.*, 1987; Teng *et al.*, 1988; Fratini *et al.*, 1982; Nelson *et al.*, 1987; Yoon *et al.*, 1988). For instance, the minor-groove width of the A-T region of d(CGCGAATTCGCG)₂ (Fratini *et al.*, 1982) ranged from 0.32 to 0.40 nm (closest

Figure 5-9. Stereodrawings of structures C1 (A) and C2 (B) obtained by energy refinement using semiquantitative distance constraints derived from NOESY spectra (see text). Reprinted with permission from the *Journal of the American Chemical Society*. Copyright 1989, American Chemical Society.

Figure 5-9 (continued). Stereodrawings of structures C1 (A) and C2 (B) obtained by energy refinement using semiquantitative distance constraints derived from NOESY spectra (see text).

Table 5-3. Drug-DNA Hydrogen Bonds

Drug amide Proton	DNA proton Structure C1	DNA proton Structure C2
HN-1	A5 N3	A6 N3
HN-3	A6 N3	T7 O2
HN-5	T7 O2	T8 O2
HN-7	T8 O2	T9 O2

phosphate distance less two phosphate radii), while the minor groove width of the A₃T₃ duplex with one bound drug was near 0.40 nm. If the van der Waals thickness of each drug is taken to be 0.34 nm, then the minor-groove width of the A₃T₃ duplex must expand at least 0.28 nm compared to the A₃T₃ duplex with one bound drug in order to accommodate both molecules. The fact that the 2:1 complex with the expanded minor groove was not crystallized, although it was present in the buffer, supports the notion of Wang and coworkers (Coll *et al.*, 1989) that a relatively narrow minor groove is, in fact, necessary for the crystallization of these oligomers in the P2₁2₁2₁ space group.

It is interesting to note that the 2:1 complex forms more easily relative to the one-drug complex when a G-C base pair (A₃T₂G) is replaced with an A-T base pair (A₃T₃). This may be due to differences in the details of the stacking interactions in C1 and C2 relative to C3 and the 2:1 A₃T₂ complex (Chapter 4). Another possibility is that the flanking G-C base pairs behave differently than A-T base pairs with regard to allowable backbone conformational changes, hindering formation of the 2:1 complex in A₃T₂. Helix distortions have also been noted in several protein-DNA complexes (Otwinowski *et al.*, 1988; Anderson *et al.*, 1987; Mc Clarin *et al.*, 1986). The degree to which A-T and G-C base pairs alter the flexibility of the phosphate backbone, and whether it is a factor in sequence-specific protein recognition remains to be determined.

The sequence and orientational specificity seen in the 2:1 distamycin A-DNA complexes have implications for the design of new drugs and sequence specific probes. As discussed previously (Chapter 4), it may be possible to design molecules that, instead of interacting with both strands of the DNA, interact with one strand of the duplex and another drug molecule (or another part of the same drug) in a sequence specific manner. Interactions that stabilize the present 2:1 complex, and which

should be considered in the design of such molecules includes drug-drug and drug-DNA stacking, hydrogen bonding, and electrostatic forces.

5.8 Conclusions

Both 1:1 and 2:1 binding modes have been observed for the binding of distamycin A with the sequence d(CGCAAATTTGCG)₂, in contrast to the crystallographic result of Coll *et al.* (1987) in which only a one-drug binding mode was evident. The data obtained on the 2:1 complex are consistent with a model in which each drug slides between 5'- AATT -3', and 5'- ATTT -3' binding sites associated with each strand of the duplex at a rate that is fast on the NMR time scale. Modeling of the 2:1 complexes indicates that electrostatic interactions, hydrogen bonds, and both drug-drug and drug-DNA stacking interactions are important in stabilizing the complex. Furthermore, binding two distamycin A molecules must expand the minor groove relative to what is observed in the X-ray study of the 1:1 distamycin A-A₃T₃ complex (Coll *et al.*, 1987). These findings, in conjunction with those on actinomycin D (Scott *et al.*, 1988) and chromomycin (Gao *et al.*, 1989) which expand the minor groove of G-C regions, and P1-F₄S-P1 (Wang *et al.*, 1989) which expands the minor groove of A-T -rich regions, suggest that the phosphate backbone of both A-T and G-C regions can be distorted to accommodate ligands. Whether the flexibility seen here is strongly sequence dependent, and is important in sequence-specific recognition by proteins remains to be determined. It also remains to be seen whether the characteristics of the 2:1 complex can be exploited in the design of new sequence-specific recognition complexes.

Chapter 6

Summary and Conclusions

In the preceding chapters, the binding of distamycin A to d(CGCGAATTCGCG)₂ (A₂T₂), d(CGCAAATTGGC):d(GCCAATTTGCG) (A₃T₂), and d(CGCAAATTTGCG)₂ (A₃T₃) have been described. For A₂T₂, and for A₃T₂ at low drug:DNA ratios (0.5 equivalents), distamycin A binds in the minor groove of the A-T segment of each oligomer in a one-drug mode. For A₂T₂ there is a single one-drug binding site (AATT) which is characterized by close H3 - C2H contacts, potential three-center hydrogen bonds between the drug amide and DNA adenine N3 and thymine O2 atoms, and by stacking of sugar O4' atoms of A6-C21, T7-T20, and T8-T19, over drug pyrrole rings 1, 2, and 3, respectively. With the addition of another A-T base pair (A₃T₂), distamycin A binds in two orientations within the AAATT segment and has a 2.2:1 preference for binding with the drug formyl group directed toward the 5' side of the A-rich strand. In the preferred orientation, the NOE data are consistent with a model in which distamycin A slides in fast exchange between adjacent AAAT and AATT binding sites. Similarly, the pattern of NOEs associated with the less favored orientation are consistent with the drug sliding between adjacent AATT and ATTT sites, again in fast exchange. Off-rates for the drug from the high and low affinity sites were measured to be 2.4 ± 1.5 and $3.3 \pm 1.5 \text{ s}^{-1}$, respectively. Molecular mechanics calculations suggest that electrostatic interactions, hydrogen bonds, and van der Waals contacts similar to those seen for the A₂T₂ complex, contribute to the stability of this complex.

With the addition of yet another A-T base pair (A₃T₃), one set of three H3 pyrrole resonances is observed at low drug:DNA ratios. These resonances may result from drug binding in only one site, or they may be averages resulting from rapid

exchange of the drug between several binding sites. The results obtained with A₃T₂ support the latter interpretation.

At higher drug:DNA ratios, but still below one equivalent, two drugs bind simultaneously in the minor-groove of the A₃T₂ and A₃T₃ duplexes. For the A₃T₂ duplex, one drug binds with the formyl end close to the second adenine base of the A-rich strand, while the other drug binds with the formyl end close to the second adenine base of the complementary strand. For the symmetric A₃T₃ duplex, NOEs from drug pyrrole H3 to DNA C1'H and adenine C2H protons, as well as observed linewidth changes of the DNA protons as a function of temperature were consistent with a model in which each drug of the 2:1 complex slides in fast exchange between AATT and ATTT binding sites. Off-rates for the drugs from the 2:1 complexes were 1.0 ± 0.5 and $0.2 \pm 0.1 \text{ s}^{-1}$ (35°C) for the A₃T₂ and A₃T₃ duplexes, respectively.

Formation of the 2:1 distamycin A - A₃T₃ complex is in striking contrast to that obtained with X-ray methods, where only one one-drug distamycin A binding site (ATTT) was observed with the same sequence (Coll *et al.*, 1987). Formation of 2:1 complexes may have implications for other studies as well. For example the 2:1 binding mode may also be of consequence in calorimetric (Breslauer *et al.*, 1987) and other physical studies conducted at high drug:DNA ratios.

The above results indicate that the minimal one-drug binding site consists of four A-T base pairs and that the minimal two-drug site consists of five A-T base pairs. Although there was no evidence for a 2:1 distamycin A-A₂T₂ complex, the two-drug to one-drug equilibrium constant ratios for distamycin A with A₃T₂ and A₃T₃ were measured to be 0.2 and 1.7, respectively, and thus, it appears that it is easier to form the 2:1 complex with longer stretches of A-T base pairs.

Molecular modeling of the 2:1 complexes indicates that the minor groove must expand 0.2 to 0.3 nm relative to that observed in single-crystal studies of A-T -rich

oligomers and 1:1 distamycin A-, and netropsin-DNA complexes, which indicates that the phosphate backbone can be distorted in response to ligand binding. The degree to which A-T and G-C base pairs alter the flexibility of the phosphate backbone, and whether it is a factor in sequence-specific protein recognition remains to be determined. Moreover, formation of the 2:1 A₃T₂ and A₃T₃ complexes, including both the orientational and sequence specificity, suggests a new strategy for the design of new drugs and probes. In fact, it may be possible to combine recognition of one strand of the DNA with specific interactions between two drug molecules to create a sequence-specific recognition complex. Interactions that stabilize the 2:1 complexes, and which should be used as a guide in the design of such drugs, include drug-drug and drug DNA stacking, hydrogen bonding, and electrostatic interactions.

Appendix A

SKEWSY Methodology

The relaxation matrix **R** can be calculated from a knowledge of the NOESY cross and diagonal peak volumes at a given mixing time ($a_{ij}(\tau_m)$), and the equilibrium diagonal peak volumes ($a_{ij}(\tau_m=0)$). The off-diagonal elements of **R** correspond to cross-relaxation rates between spin pairs and are a function of the inverse sixth-power of the distance between the spins. As described in Chapter 1, the distance between one pair of spins *i* and *j* can be determined if the distance and cross-relaxation rate between another pair of spins *k* and *l* is known, by taking ratios of these rate constants [1-13]. Since cross-relaxation rates are used to calculate distances, the method does not suffer from complications due to second-order exchange processes (spin diffusion) unlike the method of determining distances using cross peak volumes and the short-time approximation [1-12].

In general it is not possible to measure the diagonal peak volumes in a NOESY spectrum due to poor resolution of these peaks, and therefore, it is not usually possible to back calculate the relaxation matrix. The SKEWSY experiment has the effect of "transferring" information about the diagonal peak intensities into the cross peaks. Hence, a combination of SKEWSY and NOESY cross peak intensities contain sufficient information to calculate the intensity matrix **a** and the relaxation matrix **R**.

A theoretical analysis of the SKEWSY experiment shows that the intensities of the cross and diagonal peaks are given by¹²:

$$S_{ij} = -a_{ij} + 2a_{ij} \sum_{k=1}^N a_{jk} \quad (A-1)$$

where the a_{ij} denote the elements of the matrix $\exp[-R\tau_m]$ as in the NOESY experiment [1-16]. Given the cross peaks intensities in both SKEWSY and NOESY

¹² In the derivation of equation A-1, Bremer *et al.* (1984) implicitly assumed that the equilibrium magnetization of each spin is the same.

experiments, linear equations can be written in terms of the mixing coefficients a_{ij} , and the matrix $\mathbf{a}$ can be calculated. The relaxation matrix can then be calculated from the intensity matrix $\mathbf{a}$, and distances can be calculated by taking ratios of cross-relaxation rates. The procedure for generating linear equations in terms of the a_{ij} is presented below for a two-spin system.

For a two-spin system, the following SKEWSY (S_{ij}) and NOESY (M_{ij}) peak intensities, which are expressed in terms of mixing coefficients a_{ij} , must be measured:

$$S_{12} = -a_{12} + 2a_{12}(a_{21} + a_{22}) \quad (\text{A-2a})$$

$$S_{21} = -a_{21} + 2a_{21}(a_{11} + a_{12}) \quad (\text{A-2b})$$

$$S_{11} = -a_{11} + 2a_{11}(a_{11} + a_{12}) \quad (\text{A-2c})$$

$$M_{12} = M_{21} = a_{12} = a_{21} \quad (\text{A-2d})$$

Equations A-2a, A-2b, and A-2c can be rearranged as follows:

$$S_{12} = a_{12}(2a_{12} + 2a_{22} - 1) \quad (\text{A-3a})$$

$$S_{21} = a_{21}(2a_{21} + 2a_{11} - 1) \quad (\text{A-3b})$$

$$S_{11} = a_{11}(2a_{11} + 2a_{12} - 1) \quad (\text{A-3c})$$

Using equations A-3a, A-3b, and A-3c, three linear equations can be created in terms of a_{11} , a_{22} and a_{12} [A-4], which can be solved for the intensity matrix $\mathbf{a}$. Note that a_{12} is equivalent to a_{21} .

$$\begin{pmatrix} 0 & 2 & 2 \\ 2 & 0 & 2 \\ -1 & 0 & S_{11}/S_{21} \end{pmatrix} \begin{pmatrix} a_{11} \\ a_{22} \\ a_{12} \end{pmatrix} = \begin{pmatrix} S_{12}/M_{12} + 1 \\ S_{21}/M_{21} + 1 \\ 0 \end{pmatrix} \quad (\text{A-4})$$

As can be seen in [A-4], only one diagonal peak, S_{11} , need be measured.

Appendix B

Distamycin A - A₂T₂ coordinates

Coordinates of the 1:1 distamycin A - A₂T₂ structures H_D, W_D, and H_I are summarized in the following pages. Structures H_D and W_D were generated starting from X-ray coordinates (Fratini *et al.*, 1982) with NMR constraints (K_{nmr}) of 10,000 (kcal/mol)/Å², and 0.59 (kcal/mol)/Å², respectively. Structure H_I was generated starting from ideal B-form coordinates (Chandrasekaran & Arnott, 1989) using an NMR force constant of 10,000 (kcal/mol)/Å². In this calculation 1.2 nm nonbonded and 0.4 nm hydrogen bond cutoffs were used along with a distance-dependent dielectric function.

Coordinates for Hp d(CGCGAATTCGCG)₂ with Distamycin A

$$K_{\text{NMR}} = 10,000 \text{ kcal} \cdot \text{mol}^{-1} \cdot \text{\AA}^{-2}$$

ATOM	1	H	HB	1	-19.360	4.890	-21.295
ATOM	2	O5'	CYT	2	-19.228	4.188	-21.936
ATOM	3	C5'	CYT	2	-18.513	3.141	-21.315
ATOM	4	H5A'	CYT	2	-19.089	2.760	-20.471
ATOM	5	H5B'	CYT	2	-18.368	2.341	-22.042
ATOM	6	C4'	CYT	2	-17.151	3.645	-20.830
ATOM	7	H4'	CYT	2	-16.610	4.081	-21.672
ATOM	8	O1'	CYT	2	-17.338	4.632	-19.827
ATOM	9	C1'	CYT	2	-16.388	4.410	-18.804
ATOM	10	H1'	CYT	2	-15.423	4.789	-19.144
ATOM	11	N1	CYT	2	-16.862	5.045	-17.544
ATOM	12	C6	CYT	2	-18.123	4.789	-17.069
ATOM	13	H6	CYT	2	-18.728	4.037	-17.552
ATOM	14	C5	CYT	2	-18.646	5.486	-16.033
ATOM	15	H5	CYT	2	-19.645	5.261	-15.691
ATOM	16	C4	CYT	2	-17.828	6.513	-15.467
ATOM	17	N4	CYT	2	-18.338	7.331	-14.553
ATOM	18	HN4A	CYT	2	-17.796	8.140	-14.267
ATOM	19	HN4B	CYT	2	-19.265	7.181	-14.196
ATOM	20	N3	CYT	2	-16.602	6.772	-15.931
ATOM	21	C2	CYT	2	-16.077	6.026	-16.943
ATOM	22	O2	CYT	2	-14.931	6.263	-17.318
ATOM	23	C3'	CYT	2	-16.318	2.515	-20.206
ATOM	24	H3'	CYT	2	-16.781	1.540	-20.369
ATOM	25	C2'	CYT	2	-16.313	2.889	-18.726
ATOM	26	H2A'	CYT	2	-15.418	2.545	-18.212
ATOM	27	H2B'	CYT	2	-17.198	2.465	-18.253
ATOM	28	O3'	CYT	2	-15.021	2.547	-20.771
ATOM	29	P	POM	3	-13.928	1.400	-20.470
ATOM	30	OA	POM	3	-14.615	0.277	-19.794
ATOM	31	OB	POM	3	-13.170	1.158	-21.717
ATOM	32	O5'	GUA	4	-12.954	2.115	-19.407
ATOM	33	C5'	GUA	4	-12.025	3.096	-19.830
ATOM	34	H5A'	GUA	4	-11.339	2.660	-20.558
ATOM	35	H5B'	GUA	4	-12.558	3.924	-20.299
ATOM	36	C4'	GUA	4	-11.203	3.636	-18.654
ATOM	37	H4'	GUA	4	-10.498	4.371	-19.046
ATOM	38	O1'	GUA	4	-12.056	4.287	-17.726
ATOM	39	C1'	GUA	4	-11.668	3.917	-16.418
ATOM	40	H1'	GUA	4	-10.851	4.560	-16.088
ATOM	41	N9	GUA	4	-12.851	4.034	-15.532
ATOM	42	C8	GUA	4	-14.040	3.359	-15.635
ATOM	43	H8	GUA	4	-14.186	2.530	-16.308
ATOM	44	N7	GUA	4	-14.993	3.822	-14.876
ATOM	45	C5	GUA	4	-14.388	4.879	-14.201
ATOM	46	C6	GUA	4	-14.934	5.804	-13.263
ATOM	47	O6	GUA	4	-16.085	5.862	-12.838

ATOM	48	N1	GUA	4	-14.011	6.744	-12.831
ATOM	49	H1	GUA	4	-14.365	7.480	-12.218
ATOM	50	C2	GUA	4	-12.692	6.755	-13.208
ATOM	51	N2	GUA	4	-11.903	7.685	-12.683
ATOM	52	HN2A	GUA	4	-12.263	8.370	-12.028
ATOM	53	HN2B	GUA	4	-10.932	7.698	-12.949
ATOM	54	N3	GUA	4	-12.167	5.897	-14.092
ATOM	55	C4	GUA	4	-13.069	4.995	-14.568
ATOM	56	C3'	GUA	4	-10.428	2.539	-17.908
ATOM	57	H3'	GUA	4	-10.485	1.583	-18.433
ATOM	58	C2'	GUA	4	-11.164	2.484	-16.570
ATOM	59	H2A'	GUA	4	-10.521	2.178	-15.748
ATOM	60	H2B'	GUA	4	-11.995	1.787	-16.674
ATOM	61	O3'	GUA	4	-9.076	2.951	-17.788
ATOM	62	P	POM	5	-7.927	1.998	-17.174
ATOM	63	OA	POM	5	-8.396	0.596	-17.219
ATOM	64	OB	POM	5	-6.639	2.369	-17.801
ATOM	65	O5'	CYT	6	-7.897	2.477	-15.642
ATOM	66	C5'	CYT	6	-7.326	3.723	-15.292
ATOM	67	H5A'	CYT	6	-6.237	3.654	-15.315
ATOM	68	H5B'	CYT	6	-7.648	4.486	-16.003
ATOM	69	C4'	CYT	6	-7.796	4.156	-13.902
ATOM	70	H4'	CYT	6	-7.471	5.182	-13.720
ATOM	71	O1'	CYT	6	-9.206	4.113	-13.830
ATOM	72	C1'	CYT	6	-9.544	4.161	-12.461
ATOM	73	H1'	CYT	6	-9.533	5.212	-12.169
ATOM	74	N1	CYT	6	-10.862	3.515	-12.233
ATOM	75	C6	CYT	6	-11.183	2.346	-12.867
ATOM	76	H6	CYT	6	-10.429	1.846	-13.458
ATOM	77	C5	CYT	6	-12.422	1.812	-12.772
ATOM	78	H5	CYT	6	-12.643	0.891	-13.289
ATOM	79	C4	CYT	6	-13.373	2.522	-11.972
ATOM	80	N4	CYT	6	-14.621	2.079	-11.894
ATOM	81	HN4A	CYT	6	-15.291	2.606	-11.347
ATOM	82	HN4B	CYT	6	-14.910	1.268	-12.413
ATOM	83	N3	CYT	6	-13.057	3.653	-11.331
ATOM	84	C2	CYT	6	-11.790	4.147	-11.413
ATOM	85	O2	CYT	6	-11.499	5.151	-10.768
ATOM	86	C3'	CYT	6	-7.292	3.276	-12.756
ATOM	87	H3'	CYT	6	-7.231	2.236	-13.081
ATOM	88	C2'	CYT	6	-8.419	3.431	-11.731
ATOM	89	H2A'	CYT	6	-8.116	4.044	-10.886
ATOM	90	H2B'	CYT	6	-8.722	2.441	-11.388
ATOM	91	O3'	CYT	6	-6.034	3.745	-12.301
ATOM	92	P	POM	7	-5.265	3.092	-11.039
ATOM	93	OA	POM	7	-5.671	1.675	-10.915
ATOM	94	OB	POM	7	-3.832	3.445	-11.139
ATOM	95	O5'	GUA	8	-5.890	3.907	-9.800
ATOM	96	C5'	GUA	8	-5.699	5.305	-9.690
ATOM	97	H5A'	GUA	8	-4.645	5.519	-9.506
ATOM	98	H5B'	GUA	8	-5.995	5.788	-10.622
ATOM	99	C4'	GUA	8	-6.548	5.901	-8.561
ATOM	100	H4'	GUA	8	-6.415	6.984	-8.586

ATOM	101	O1'	GUA	8	-7.921	5.600	-8.778
ATOM	102	C1'	GUA	8	-8.456	5.008	-7.607
ATOM	103	H1'	GUA	8	-8.850	5.793	-6.960
ATOM	104	N9	GUA	8	-9.511	4.029	-7.965
ATOM	105	C8	GUA	8	-9.368	2.848	-8.649
ATOM	106	H8	GUA	8	-8.411	2.466	-8.972
ATOM	107	N7	GUA	8	-10.488	2.228	-8.896
ATOM	108	C5	GUA	8	-11.451	3.047	-8.317
ATOM	109	C6	GUA	8	-12.866	2.883	-8.238
ATOM	110	O6	GUA	8	-13.544	1.957	-8.675
ATOM	111	N1	GUA	8	-13.489	3.910	-7.547
ATOM	112	H1	GUA	8	-14.492	3.792	-7.399
ATOM	113	C2	GUA	8	-12.828	4.982	-7.002
ATOM	114	N2	GUA	8	-13.543	5.882	-6.334
ATOM	115	HN2A	GUA	8	-14.547	5.783	-6.224
ATOM	116	HN2B	GUA	8	-13.055	6.669	-5.938
ATOM	117	N3	GUA	8	-11.501	5.142	-7.059
ATOM	118	C4	GUA	8	-10.866	4.147	-7.736
ATOM	119	C3'	GUA	8	-6.156	5.375	-7.174
ATOM	120	H3'	GUA	8	-5.166	4.916	-7.174
ATOM	121	C2'	GUA	8	-7.259	4.353	-6.923
ATOM	122	H2A'	GUA	8	-7.428	4.167	-5.866
ATOM	123	H2B'	GUA	8	-6.979	3.425	-7.418
ATOM	124	O3'	GUA	8	-6.196	6.468	-6.273
ATOM	125	P	POM	9	-5.780	6.340	-4.722
ATOM	126	OA	POM	9	-5.313	4.962	-4.457
ATOM	127	OB	POM	9	-4.921	7.493	-4.374
ATOM	128	O5'	ADE	10	-7.203	6.533	-4.001
ATOM	129	C5'	ADE	10	-7.876	7.775	-4.065
ATOM	130	H5A'	ADE	10	-7.257	8.554	-3.617
ATOM	131	H5B'	ADE	10	-8.062	8.033	-5.108
ATOM	132	C4'	ADE	10	-9.221	7.726	-3.331
ATOM	133	H4'	ADE	10	-9.704	8.695	-3.464
ATOM	134	O1'	ADE	10	-10.036	6.713	-3.900
ATOM	135	C1'	ADE	10	-10.344	5.756	-2.904
ATOM	136	H1'	ADE	10	-11.318	6.006	-2.479
ATOM	137	N9	ADE	10	-10.378	4.409	-3.515
ATOM	138	C8	ADE	10	-9.332	3.632	-3.952
ATOM	139	H8	ADE	10	-8.297	3.882	-3.770
ATOM	140	N7	ADE	10	-9.690	2.576	-4.632
ATOM	141	C5	ADE	10	-11.076	2.654	-4.634
ATOM	142	C6	ADE	10	-12.079	1.851	-5.201
ATOM	143	N6	ADE	10	-11.826	0.769	-5.936
ATOM	144	HN6A	ADE	10	-12.586	0.213	-6.318
ATOM	145	HN6B	ADE	10	-10.864	0.532	-6.129
ATOM	146	N1	ADE	10	-13.358	2.196	-5.011
ATOM	147	C2	ADE	10	-13.642	3.276	-4.297
ATOM	148	H2	ADE	10	-14.689	3.500	-4.191
ATOM	149	N3	ADE	10	-12.804	4.115	-3.704
ATOM	150	C4	ADE	10	-11.510	3.748	-3.927
ATOM	151	C3'	ADE	10	-9.077	7.424	-1.834
ATOM	152	H3'	ADE	10	-8.093	7.707	-1.455
ATOM	153	C2'	ADE	10	-9.294	5.915	-1.809

ATOM	154	H2A'	ADE	10	-9.636	5.559	-0.840
ATOM	155	H2B'	ADE	10	-8.359	5.422	-2.069
ATOM	156	O3'	ADE	10	-10.099	8.130	-1.150
ATOM	157	P	POM	11	-10.224	8.129	0.456
ATOM	158	OA	POM	11	-9.041	7.452	1.029
ATOM	159	OB	POM	11	-10.582	9.495	0.895
ATOM	160	O5'	ADE	12	-11.501	7.178	0.678
ATOM	161	C5'	ADE	12	-12.807	7.654	0.425
ATOM	162	H5A'	ADE	12	-13.015	8.515	1.062
ATOM	163	H5B'	ADE	12	-12.886	7.963	-0.619
ATOM	164	C4'	ADE	12	-13.858	6.575	0.705
ATOM	165	H4'	ADE	12	-14.839	7.009	0.505
ATOM	166	O1'	ADE	12	-13.651	5.468	-0.161
ATOM	167	C1'	ADE	12	-13.535	4.306	0.640
ATOM	168	H1'	ADE	12	-14.529	3.893	0.814
ATOM	169	N9	ADE	12	-12.697	3.302	-0.040
ATOM	170	C8	ADE	12	-11.331	3.232	-0.166
ATOM	171	H8	ADE	12	-10.657	3.912	0.333
ATOM	172	N7	ADE	12	-10.914	2.276	-0.952
ATOM	173	C5	ADE	12	-12.093	1.664	-1.362
ATOM	174	C6	ADE	12	-12.375	0.587	-2.217
ATOM	175	N6	ADE	12	-11.425	-0.100	-2.850
ATOM	176	HN6A	ADE	12	-11.668	-0.861	-3.477
ATOM	177	HN6B	ADE	12	-10.465	0.186	-2.725
ATOM	178	N1	ADE	12	-13.655	0.247	-2.422
ATOM	179	C2	ADE	12	-14.619	0.908	-1.788
ATOM	180	H2	ADE	12	-15.628	0.535	-1.888
ATOM	181	N3	ADE	12	-14.485	1.931	-0.961
ATOM	182	C4	ADE	12	-13.182	2.273	-0.801
ATOM	183	C3'	ADE	12	-13.814	6.046	2.147
ATOM	184	H3'	ADE	12	-13.349	6.753	2.836
ATOM	185	C2'	ADE	12	-12.987	4.774	1.977
ATOM	186	H2A'	ADE	12	-13.137	4.043	2.770
ATOM	187	H2B'	ADE	12	-11.933	5.040	1.912
ATOM	188	O3'	ADE	12	-15.153	5.780	2.532
ATOM	189	P	POM	13	-15.537	5.127	3.953
ATOM	190	OA	POM	13	-14.341	5.155	4.823
ATOM	191	OB	POM	13	-16.802	5.742	4.411
ATOM	192	O5'	THY	14	-15.826	3.600	3.528
ATOM	193	C5'	THY	14	-17.085	3.235	2.992
ATOM	194	H5A'	THY	14	-17.858	3.419	3.739
ATOM	195	H5B'	THY	14	-17.301	3.838	2.111
ATOM	196	C4'	THY	14	-17.138	1.753	2.606
ATOM	197	H4'	THY	14	-18.147	1.539	2.268
ATOM	198	O1'	THY	14	-16.249	1.428	1.550
ATOM	199	C1'	THY	14	-15.855	0.069	1.669
ATOM	200	H1'	THY	14	-16.227	-0.567	0.849
ATOM	201	N1	THY	14	-14.372	0.016	1.681
ATOM	202	C6	THY	14	-13.610	0.792	2.522
ATOM	203	H6	THY	14	-14.102	1.525	3.144
ATOM	204	C5	THY	14	-12.258	0.651	2.577
ATOM	205	C7	THY	14	-11.441	1.521	3.513
ATOM	206	H7A	THY	14	-12.078	2.073	4.205

ATOM	207	H7B	THY	14	-10.759	0.891	4.086
ATOM	208	H7C	THY	14	-10.855	2.229	2.925
ATOM	209	C4	THY	14	-11.587	-0.350	1.760
ATOM	210	O4	THY	14	-10.403	-0.670	1.816
ATOM	211	N3	THY	14	-12.412	-0.975	0.857
ATOM	212	H3	THY	14	-12.096	-1.812	0.380
ATOM	213	C2	THY	14	-13.769	-0.818	0.756
ATOM	214	O2	THY	14	-14.380	-1.393	-0.136
ATOM	215	C3'	THY	14	-16.855	0.802	3.762
ATOM	216	H3'	THY	14	-16.021	1.162	4.364
ATOM	217	C2'	THY	14	-16.462	-0.447	2.977
ATOM	218	H2A'	THY	14	-17.354	-1.026	2.740
ATOM	219	H2B'	THY	14	-15.762	-1.057	3.538
ATOM	220	O3'	THY	14	-18.033	0.650	4.536
ATOM	221	P	POM	15	-18.074	-0.208	5.898
ATOM	222	OA	POM	15	-16.751	-0.126	6.555
ATOM	223	OB	POM	15	-19.297	0.161	6.643
ATOM	224	O5'	THY	16	-18.254	-1.708	5.366
ATOM	225	C5'	THY	16	-19.387	-2.094	4.618
ATOM	226	H5A'	THY	16	-20.291	-1.995	5.219
ATOM	227	H5B'	THY	16	-19.480	-1.455	3.740
ATOM	228	C4'	THY	16	-19.225	-3.544	4.150
ATOM	229	H4'	THY	16	-20.027	-3.762	3.444
ATOM	230	O1'	THY	16	-17.962	-3.690	3.508
ATOM	231	C1'	THY	16	-17.218	-4.708	4.158
ATOM	232	H1'	THY	16	-17.420	-5.650	3.647
ATOM	233	N1	THY	16	-15.765	-4.358	4.159
ATOM	234	C6	THY	16	-15.316	-3.258	4.856
ATOM	235	H6	THY	16	-16.014	-2.666	5.424
ATOM	236	C5	THY	16	-14.020	-2.860	4.822
ATOM	237	C7	THY	16	-13.574	-1.637	5.602
ATOM	238	H7A	THY	16	-14.423	-1.106	6.039
ATOM	239	H7B	THY	16	-12.898	-1.945	6.399
ATOM	240	H7C	THY	16	-13.044	-0.956	4.936
ATOM	241	C4	THY	16	-13.049	-3.592	4.040
ATOM	242	O4	THY	16	-11.862	-3.296	3.931
ATOM	243	N3	THY	16	-13.559	-4.691	3.386
ATOM	244	H3	THY	16	-12.868	-5.255	2.899
ATOM	245	C2	THY	16	-14.878	-5.114	3.389
ATOM	246	O2	THY	16	-15.203	-6.102	2.734
ATOM	247	C3'	THY	16	-19.291	-4.539	5.316
ATOM	248	H3'	THY	16	-19.772	-4.107	6.195
ATOM	249	C2'	THY	16	-17.813	-4.812	5.565
ATOM	250	H2A'	THY	16	-17.647	-5.781	6.023
ATOM	251	H2B'	THY	16	-17.450	-4.041	6.240
ATOM	252	O3'	THY	16	-20.010	-5.679	4.885
ATOM	253	P	POM	17	-20.282	-6.952	5.836
ATOM	254	OA	POM	17	-19.909	-6.602	7.225
ATOM	255	OB	POM	17	-21.637	-7.467	5.542
ATOM	256	O5'	CYT	18	-19.202	-7.997	5.266
ATOM	257	C5'	CYT	18	-19.316	-8.473	3.939
ATOM	258	H5A'	CYT	18	-20.248	-9.028	3.824
ATOM	259	H5B'	CYT	18	-19.327	-7.625	3.254

ATOM	260	C4'	CYT	18	-18.144	-9.380	3.559
ATOM	261	H4'	CYT	18	-18.282	-9.668	2.518
ATOM	262	O1'	CYT	18	-16.924	-8.672	3.680
ATOM	263	C1'	CYT	18	-15.951	-9.505	4.283
ATOM	264	H1'	CYT	18	-15.454	-10.087	3.508
ATOM	265	N1	CYT	18	-15.024	-8.626	5.049
ATOM	266	C6	CYT	18	-15.541	-7.672	5.882
ATOM	267	H6	CYT	18	-16.599	-7.693	6.097
ATOM	268	C5	CYT	18	-14.768	-6.701	6.418
ATOM	269	H5	CYT	18	-15.218	-5.964	7.067
ATOM	270	C4	CYT	18	-13.380	-6.724	6.084
ATOM	271	N4	CYT	18	-12.600	-5.735	6.503
ATOM	272	HN4A	CYT	18	-11.615	-5.757	6.273
ATOM	273	HN4B	CYT	18	-12.967	-5.017	7.104
ATOM	274	N3	CYT	18	-12.850	-7.683	5.313
ATOM	275	C2	CYT	18	-13.652	-8.666	4.805
ATOM	276	O2	CYT	18	-13.134	-9.575	4.163
ATOM	277	C3'	CYT	18	-18.060	-10.648	4.413
ATOM	278	H3'	CYT	18	-18.910	-10.712	5.094
ATOM	279	C2'	CYT	18	-16.750	-10.455	5.176
ATOM	280	H2A'	CYT	18	-16.223	-11.395	5.329
ATOM	281	H2B'	CYT	18	-16.984	-9.993	6.134
ATOM	282	O3'	CYT	18	-18.021	-11.758	3.533
ATOM	283	P	POM	19	-18.406	-13.249	4.000
ATOM	284	OA	POM	19	-19.448	-13.169	5.047
ATOM	285	OB	POM	19	-18.650	-14.051	2.780
ATOM	286	O5'	GUA	20	-17.045	-13.760	4.677
ATOM	287	C5'	GUA	20	-16.010	-14.313	3.889
ATOM	288	H5A'	GUA	20	-16.327	-15.284	3.507
ATOM	289	H5B'	GUA	20	-15.785	-13.656	3.048
ATOM	290	C4'	GUA	20	-14.739	-14.490	4.721
ATOM	291	H4'	GUA	20	-14.011	-15.036	4.123
ATOM	292	O1'	GUA	20	-14.197	-13.213	5.035
ATOM	293	C1'	GUA	20	-13.746	-13.278	6.369
ATOM	294	H1'	GUA	20	-12.816	-13.845	6.394
ATOM	295	N9	GUA	20	-13.516	-11.933	6.945
ATOM	296	C8	GUA	20	-14.412	-11.068	7.522
ATOM	297	H8	GUA	20	-15.460	-11.293	7.647
ATOM	298	N7	GUA	20	-13.893	-9.938	7.911
ATOM	299	C5	GUA	20	-12.547	-10.060	7.580
ATOM	300	C6	GUA	20	-11.463	-9.148	7.757
ATOM	301	O6	GUA	20	-11.485	-8.032	8.270
ATOM	302	N1	GUA	20	-10.263	-9.637	7.268
ATOM	303	H1	GUA	20	-9.458	-9.019	7.375
ATOM	304	C2	GUA	20	-10.109	-10.883	6.709
ATOM	305	N2	GUA	20	-8.889	-11.257	6.346
ATOM	306	HN2A	GUA	20	-8.110	-10.614	6.381
ATOM	307	HN2B	GUA	20	-8.724	-12.230	6.122
ATOM	308	N3	GUA	20	-11.110	-11.754	6.556
ATOM	309	C4	GUA	20	-12.306	-11.278	6.994
ATOM	310	C3'	GUA	20	-15.000	-15.218	6.054
ATOM	311	H3'	GUA	20	-15.990	-15.674	6.115
ATOM	312	C2'	GUA	20	-14.850	-14.078	7.056

ATOM	313	H2A'	GUA	20	-14.574	-14.427	8.050
ATOM	314	H2B'	GUA	20	-15.783	-13.516	7.085
ATOM	315	O3'	GUA	20	-13.993	-16.165	6.352
ATOM	316	P	POM	21	-13.978	-17.637	5.699
ATOM	317	OA	POM	21	-14.375	-18.604	6.746
ATOM	318	OB	POM	21	-14.695	-17.603	4.406
ATOM	319	O5'	CYT	22	-12.406	-17.816	5.412
ATOM	320	C5'	CYT	22	-11.829	-17.418	4.181
ATOM	321	H5A'	CYT	22	-11.851	-18.258	3.486
ATOM	322	H5B'	CYT	22	-12.380	-16.588	3.739
ATOM	323	C4'	CYT	22	-10.389	-16.944	4.396
ATOM	324	H4'	CYT	22	-9.964	-16.684	3.425
ATOM	325	O1'	CYT	22	-10.427	-15.781	5.210
ATOM	326	C1'	CYT	22	-9.503	-15.916	6.268
ATOM	327	H1'	CYT	22	-8.540	-15.544	5.916
ATOM	328	N1	CYT	22	-10.017	-15.182	7.462
ATOM	329	C6	CYT	22	-11.228	-15.516	8.012
ATOM	330	H6	CYT	22	-11.769	-16.368	7.630
ATOM	331	C5	CYT	22	-11.782	-14.785	9.006
ATOM	332	H5	CYT	22	-12.733	-15.092	9.413
ATOM	333	C4	CYT	22	-11.057	-13.638	9.450
ATOM	334	N4	CYT	22	-11.586	-12.849	10.378
ATOM	335	HN4A	CYT	22	-11.114	-11.990	10.634
ATOM	336	HN4B	CYT	22	-12.477	-13.075	10.785
ATOM	337	N3	CYT	22	-9.860	-13.320	8.947
ATOM	338	C2	CYT	22	-9.323	-14.071	7.940
ATOM	339	O2	CYT	22	-8.235	-13.736	7.473
ATOM	340	C3'	CYT	22	-9.504	-17.995	5.083
ATOM	341	H3'	CYT	22	-9.991	-18.972	5.096
ATOM	342	C2'	CYT	22	-9.365	-17.422	6.491
ATOM	343	H2A'	CYT	22	-8.408	-17.670	6.936
ATOM	344	H2B'	CYT	22	-10.173	-17.825	7.100
ATOM	345	O3'	CYT	22	-8.261	-18.080	4.402
ATOM	346	P	POM	23	-7.142	-19.184	4.776
ATOM	347	OA	POM	23	-7.784	-20.293	5.514
ATOM	348	OB	POM	23	-6.340	-19.471	3.567
ATOM	349	O5'	GUA	24	-6.203	-18.387	5.807
ATOM	350	C5'	GUA	24	-5.374	-17.334	5.360
ATOM	351	H5A'	GUA	24	-4.616	-17.724	4.680
ATOM	352	H5B'	GUA	24	-5.973	-16.589	4.834
ATOM	353	C4'	GUA	24	-4.691	-16.663	6.554
ATOM	354	H4'	GUA	24	-4.050	-15.862	6.185
ATOM	355	O1'	GUA	24	-5.692	-16.122	7.402
ATOM	356	C1'	GUA	24	-5.444	-16.551	8.724
ATOM	357	H1'	GUA	24	-4.742	-15.856	9.187
ATOM	358	N9	GUA	24	-6.709	-16.584	9.493
ATOM	359	C8	GUA	24	-7.707	-17.528	9.490
ATOM	360	H8	GUA	24	-7.652	-18.454	8.937
ATOM	361	N7	GUA	24	-8.747	-17.211	10.208
ATOM	362	C5	GUA	24	-8.415	-15.971	10.742
ATOM	363	C6	GUA	24	-9.147	-15.118	11.619
ATOM	364	O6	GUA	24	-10.275	-15.291	12.075
ATOM	365	N1	GUA	24	-8.445	-13.975	11.964

ATOM	366	H1	GUA	24	-8.939	-13.333	12.583
ATOM	367	C2	GUA	24	-7.187	-13.672	11.502
ATOM	368	N2	GUA	24	-6.602	-12.562	11.939
ATOM	369	HN2A	GUA	24	-7.097	-11.911	12.534
ATOM	370	HN2B	GUA	24	-5.698	-12.314	11.567
ATOM	371	N3	GUA	24	-6.493	-14.460	10.676
ATOM	372	C4	GUA	24	-7.164	-15.589	10.326
ATOM	373	C3'	GUA	24	-3.866	-17.657	7.385
ATOM	374	H3'	GUA	24	-3.649	-18.578	6.842
ATOM	375	C2'	GUA	24	-4.761	-17.911	8.591
ATOM	376	H2A'	GUA	24	-4.198	-18.189	9.482
ATOM	377	H2B'	GUA	24	-5.474	-18.691	8.328
ATOM	378	O3'	GUA	24	-2.657	-17.061	7.810
ATOM	379	H	HE	25	-2.861	-16.244	8.270
ATOM	380	H	HB	26	-9.674	-9.402	19.158
ATOM	381	O5'	CYT	27	-9.388	-8.530	19.442
ATOM	382	C5'	CYT	27	-8.012	-8.393	19.154
ATOM	383	H5A'	CYT	27	-7.673	-7.410	19.482
ATOM	384	H5B'	CYT	27	-7.455	-9.158	19.695
ATOM	385	C4'	CYT	27	-7.757	-8.545	17.652
ATOM	386	H4'	CYT	27	-6.685	-8.467	17.475
ATOM	387	O1'	CYT	27	-8.174	-9.825	17.203
ATOM	388	C1'	CYT	27	-8.672	-9.647	15.893
ATOM	389	H1'	CYT	27	-7.823	-9.465	15.232
ATOM	390	N1	CYT	27	-9.494	-10.810	15.470
ATOM	391	C6	CYT	27	-10.462	-11.321	16.295
ATOM	392	H6	CYT	27	-10.635	-10.856	17.256
ATOM	393	C5	CYT	27	-11.198	-12.399	15.937
ATOM	394	H5	CYT	27	-11.952	-12.776	16.612
ATOM	395	C4	CYT	27	-10.910	-12.984	14.663
ATOM	396	N4	CYT	27	-11.577	-14.059	14.259
ATOM	397	HN4A	CYT	27	-11.301	-14.490	13.383
ATOM	398	HN4B	CYT	27	-12.299	-14.467	14.828
ATOM	399	N3	CYT	27	-9.948	-12.507	13.871
ATOM	400	C2	CYT	27	-9.230	-11.412	14.243
ATOM	401	O2	CYT	27	-8.344	-11.004	13.498
ATOM	402	C3'	CYT	27	-8.517	-7.503	16.809
ATOM	403	H3'	CYT	27	-9.046	-6.758	17.408
ATOM	404	C2'	CYT	27	-9.493	-8.368	16.019
ATOM	405	H2A'	CYT	27	-9.740	-7.938	15.048
ATOM	406	H2B'	CYT	27	-10.394	-8.530	16.609
ATOM	407	O3'	CYT	27	-7.667	-6.883	15.872
ATOM	408	P	POM	28	-6.648	-5.717	16.295
ATOM	409	OA	POM	28	-7.312	-4.418	16.062
ATOM	410	OB	POM	28	-6.087	-6.039	17.627
ATOM	411	O5'	GUA	29	-5.514	-5.939	15.182
ATOM	412	C5'	GUA	29	-4.489	-6.898	15.359
ATOM	413	H5A'	GUA	29	-3.672	-6.437	15.916
ATOM	414	H5B'	GUA	29	-4.855	-7.758	15.921
ATOM	415	C4'	GUA	29	-3.973	-7.408	14.007
ATOM	416	H4'	GUA	29	-3.071	-7.995	14.189
ATOM	417	O1'	GUA	29	-4.958	-8.251	13.424
ATOM	418	C1'	GUA	29	-5.249	-7.801	12.113

ATOM	419	H1'	GUA	29	-4.594	-8.314	11.408
ATOM	420	N9	GUA	29	-6.679	-8.074	11.819
ATOM	421	C8	GUA	29	-7.780	-7.529	12.431
ATOM	422	H8	GUA	29	-7.719	-6.731	13.155
ATOM	423	N7	GUA	29	-8.915	-8.064	12.077
ATOM	424	C5	GUA	29	-8.545	-9.055	11.174
ATOM	425	C6	GUA	29	-9.339	-10.044	10.520
ATOM	426	O6	GUA	29	-10.552	-10.225	10.602
ATOM	427	N1	GUA	29	-8.591	-10.908	9.738
ATOM	428	H1	GUA	29	-9.090	-11.692	9.319
ATOM	429	C2	GUA	29	-7.236	-10.806	9.560
ATOM	430	N2	GUA	29	-6.652	-11.690	8.756
ATOM	431	HN2A	GUA	29	-7.194	-12.413	8.291
ATOM	432	HN2B	GUA	29	-5.658	-11.636	8.613
ATOM	433	N3	GUA	29	-6.472	-9.901	10.186
ATOM	434	C4	GUA	29	-7.181	-9.063	10.995
ATOM	435	C3'	GUA	29	-3.666	-6.276	13.018
ATOM	436	H3'	GUA	29	-3.558	-5.317	13.527
ATOM	437	C2'	GUA	29	-4.904	-6.312	12.124
ATOM	438	H2A'	GUA	29	-4.709	-5.911	11.134
ATOM	439	H2B'	GUA	29	-5.689	-5.730	12.605
ATOM	440	O3'	GUA	29	-2.472	-6.595	12.324
ATOM	441	P	POM	30	-1.776	-5.569	11.292
ATOM	442	OA	POM	30	-2.427	-4.248	11.422
ATOM	443	OB	POM	30	-0.309	-5.690	11.442
ATOM	444	O5'	CYT	31	-2.198	-6.209	9.880
ATOM	445	C5'	CYT	31	-1.483	-7.311	9.355
ATOM	446	H5A'	CYT	31	-0.521	-6.976	8.966
ATOM	447	H5B'	CYT	31	-1.310	-8.044	10.145
ATOM	448	C4'	CYT	31	-2.279	-8.001	8.246
ATOM	449	H4'	CYT	31	-1.746	-8.900	7.934
ATOM	450	O1'	CYT	31	-3.556	-8.382	8.727
ATOM	451	C1'	CYT	31	-4.431	-8.512	7.620
ATOM	452	H1'	CYT	31	-4.594	-9.579	7.461
ATOM	453	N1	CYT	31	-5.711	-7.798	7.869
ATOM	454	C6	CYT	31	-5.755	-6.645	8.606
ATOM	455	H6	CYT	31	-4.829	-6.174	8.900
ATOM	456	C5	CYT	31	-6.936	-6.096	8.976
ATOM	457	H5	CYT	31	-6.936	-5.190	9.564
ATOM	458	C4	CYT	31	-8.127	-6.768	8.553
ATOM	459	N4	CYT	31	-9.312	-6.338	8.968
ATOM	460	HN4A	CYT	31	-10.143	-6.834	8.668
ATOM	461	HN4B	CYT	31	-9.384	-5.552	9.591
ATOM	462	N3	CYT	31	-8.087	-7.863	7.786
ATOM	463	C2	CYT	31	-6.885	-8.366	7.391
ATOM	464	O2	CYT	31	-6.860	-9.325	6.626
ATOM	465	C3'	CYT	31	-2.537	-7.141	7.010
ATOM	466	H3'	CYT	31	-2.862	-6.141	7.303
ATOM	467	C2'	CYT	31	-3.695	-7.933	6.417
ATOM	468	H2A'	CYT	31	-3.309	-8.765	5.832
ATOM	469	H2B'	CYT	31	-4.327	-7.304	5.797
ATOM	470	O3'	CYT	31	-1.413	-7.106	6.148
ATOM	471	P	POM	32	-1.412	-6.247	4.779

ATOM	472	OA	POM	32	-2.063	-4.946	5.039
ATOM	473	OB	POM	32	-0.045	-6.288	4.213
ATOM	474	O5'	GUA	33	-2.373	-7.095	3.807
ATOM	475	C5'	GUA	33	-2.000	-8.383	3.357
ATOM	476	H5A'	GUA	33	-1.147	-8.310	2.681
ATOM	477	H5B'	GUA	33	-1.706	-8.996	4.209
ATOM	478	C4'	GUA	33	-3.170	-9.080	2.648
ATOM	479	H4'	GUA	33	-2.909	-10.135	2.545
ATOM	480	O1'	GUA	33	-4.357	-8.961	3.428
ATOM	481	C1'	GUA	33	-5.367	-8.350	2.641
ATOM	482	H1'	GUA	33	-5.940	-9.132	2.140
ATOM	483	N9	GUA	33	-6.260	-7.502	3.469
ATOM	484	C8	GUA	33	-5.984	-6.289	4.052
ATOM	485	H8	GUA	33	-5.029	-5.791	3.965
ATOM	486	N7	GUA	33	-6.968	-5.789	4.746
ATOM	487	C5	GUA	33	-7.982	-6.729	4.607
ATOM	488	C6	GUA	33	-9.316	-6.722	5.115
ATOM	489	O6	GUA	33	-9.853	-5.864	5.811
ATOM	490	N1	GUA	33	-10.051	-7.826	4.713
ATOM	491	H1	GUA	33	-11.037	-7.829	4.978
ATOM	492	C2	GUA	33	-9.542	-8.854	3.959
ATOM	493	N2	GUA	33	-10.344	-9.869	3.661
ATOM	494	HN2A	GUA	33	-11.329	-9.867	3.907
ATOM	495	HN2B	GUA	33	-9.952	-10.638	3.145
ATOM	496	N3	GUA	33	-8.295	-8.871	3.475
ATOM	497	C4	GUA	33	-7.562	-7.781	3.829
ATOM	498	C3'	GUA	33	-3.463	-8.499	1.260
ATOM	499	H3'	GUA	33	-2.602	-7.979	0.837
ATOM	500	C2'	GUA	33	-4.609	-7.550	1.584
ATOM	501	H2A'	GUA	33	-5.215	-7.308	0.716
ATOM	502	H2B'	GUA	33	-4.187	-6.637	2.001
ATOM	503	O3'	GUA	33	-3.856	-9.576	0.427
ATOM	504	P	POM	34	-4.155	-9.408	-1.146
ATOM	505	OA	POM	34	-4.030	-7.980	-1.512
ATOM	506	OB	POM	34	-3.377	-10.431	-1.879
ATOM	507	O5'	ADE	35	-5.710	-9.806	-1.212
ATOM	508	C5'	ADE	35	-6.128	-11.134	-0.958
ATOM	509	H5A'	ADE	35	-5.683	-11.808	-1.691
ATOM	510	H5B'	ADE	35	-5.795	-11.433	0.038
ATOM	511	C4'	ADE	35	-7.655	-11.270	-1.016
ATOM	512	H4'	ADE	35	-7.906	-12.299	-0.753
ATOM	513	O1'	ADE	35	-8.245	-10.386	-0.075
ATOM	514	C1'	ADE	35	-9.052	-9.448	-0.767
ATOM	515	H1'	ADE	35	-10.084	-9.800	-0.745
ATOM	516	N9	ADE	35	-8.941	-8.125	-0.116
ATOM	517	C8	ADE	35	-7.878	-7.256	-0.099
ATOM	518	H8	ADE	35	-6.981	-7.422	-0.675
ATOM	519	N7	ADE	35	-8.038	-6.218	0.680
ATOM	520	C5	ADE	35	-9.309	-6.412	1.206
ATOM	521	C6	ADE	35	-10.096	-5.676	2.106
ATOM	522	N6	ADE	35	-9.660	-4.566	2.696
ATOM	523	HN6A	ADE	35	-10.276	-4.063	3.325
ATOM	524	HN6B	ADE	35	-8.703	-4.279	2.551

ATOM	525	N1	ADE	35	-11.329	-6.112	2.401
ATOM	526	C2	ADE	35	-11.748	-7.251	1.866
ATOM	527	H2	ADE	35	-12.733	-7.558	2.172
ATOM	528	N3	ADE	35	-11.110	-8.043	1.016
ATOM	529	C4	ADE	35	-9.875	-7.560	0.717
ATOM	530	C3'	ADE	35	-8.241	-10.936	-2.393
ATOM	531	H3'	ADE	35	-7.518	-11.102	-3.193
ATOM	532	C2'	ADE	35	-8.582	-9.461	-2.219
ATOM	533	H2A'	ADE	35	-9.345	-9.132	-2.918
ATOM	534	H2B'	ADE	35	-7.682	-8.865	-2.361
ATOM	535	O3'	ADE	35	-9.396	-11.736	-2.584
ATOM	536	P	POM	36	-10.257	-11.704	-3.948
ATOM	537	OA	POM	36	-9.483	-10.970	-4.974
ATOM	538	OB	POM	36	-10.726	-13.079	-4.228
ATOM	539	O5'	ADE	37	-11.529	-10.804	-3.540
ATOM	540	C5'	ADE	37	-12.565	-11.336	-2.732
ATOM	541	H5A'	ADE	37	-12.989	-12.219	-3.214
ATOM	542	H5B'	ADE	37	-12.161	-11.627	-1.762
ATOM	543	C4'	ADE	37	-13.689	-10.314	-2.525
ATOM	544	H4'	ADE	37	-14.476	-10.781	-1.931
ATOM	545	O1'	ADE	37	-13.188	-9.193	-1.814
ATOM	546	C1'	ADE	37	-13.724	-8.013	-2.372
ATOM	547	H1'	ADE	37	-14.714	-7.810	-1.961
ATOM	548	N9	ADE	37	-12.758	-6.925	-2.096
ATOM	549	C8	ADE	37	-11.425	-6.936	-2.419
ATOM	550	H8	ADE	37	-10.989	-7.700	-3.041
ATOM	551	N7	ADE	37	-10.725	-5.967	-1.902
ATOM	552	C5	ADE	37	-11.674	-5.253	-1.186
ATOM	553	C6	ADE	37	-11.566	-4.121	-0.370
ATOM	554	N6	ADE	37	-10.400	-3.518	-0.132
ATOM	555	HN6A	ADE	37	-10.316	-2.777	0.552
ATOM	556	HN6B	ADE	37	-9.575	-3.933	-0.545
ATOM	557	N1	ADE	37	-12.670	-3.620	0.192
ATOM	558	C2	ADE	37	-13.846	-4.204	-0.036
ATOM	559	H2	ADE	37	-14.710	-3.690	0.406
ATOM	560	N3	ADE	37	-14.076	-5.296	-0.766
ATOM	561	C4	ADE	37	-12.929	-5.797	-1.313
ATOM	562	C3'	ADE	37	-14.281	-9.807	-3.848
ATOM	563	H3'	ADE	37	-13.884	-10.357	-4.702
ATOM	564	C2'	ADE	37	-13.810	-8.355	-3.859
ATOM	565	H2A'	ADE	37	-14.486	-7.711	-4.409
ATOM	566	H2B'	ADE	37	-12.825	-8.334	-4.324
ATOM	567	O3'	ADE	37	-15.694	-9.930	-3.812
ATOM	568	P	POM	38	-16.632	-9.538	-5.067
ATOM	569	OA	POM	38	-15.777	-9.363	-6.263
ATOM	570	OB	POM	38	-17.773	-10.479	-5.110
ATOM	571	O5'	THY	39	-17.179	-8.092	-4.627
ATOM	572	C5'	THY	39	-18.136	-7.978	-3.590
ATOM	573	H5A'	THY	39	-19.114	-8.307	-3.942
ATOM	574	H5B'	THY	39	-17.831	-8.606	-2.754
ATOM	575	C4'	THY	39	-18.222	-6.538	-3.079
ATOM	576	H4'	THY	39	-18.848	-6.512	-2.188
ATOM	577	O1'	THY	39	-16.931	-6.064	-2.745

ATOM	578	C1'	THY	39	-16.975	-4.652	-2.735
ATOM	579	H1'	THY	39	-17.056	-4.326	-1.699
ATOM	580	N1	THY	39	-15.767	-4.049	-3.350
ATOM	581	C6	THY	39	-14.948	-4.757	-4.196
ATOM	582	H6	THY	39	-15.274	-5.730	-4.525
ATOM	583	C5	THY	39	-13.765	-4.249	-4.630
ATOM	584	C7	THY	39	-12.866	-5.070	-5.536
ATOM	585	H7A	THY	39	-13.410	-5.896	-5.996
ATOM	586	H7B	THY	39	-12.467	-4.429	-6.324
ATOM	587	H7C	THY	39	-12.033	-5.466	-4.955
ATOM	588	C4	THY	39	-13.338	-2.927	-4.208
ATOM	589	O4	THY	39	-12.253	-2.399	-4.442
ATOM	590	N3	THY	39	-14.279	-2.244	-3.476
ATOM	591	H3	THY	39	-14.044	-1.308	-3.171
ATOM	592	C2	THY	39	-15.482	-2.733	-3.019
ATOM	593	O2	THY	39	-16.251	-2.015	-2.387
ATOM	594	C3'	THY	39	-18.785	-5.535	-4.083
ATOM	595	H3'	THY	39	-18.354	-5.716	-5.070
ATOM	596	C2'	THY	39	-18.239	-4.245	-3.486
ATOM	597	H2A'	THY	39	-18.943	-3.838	-2.761
ATOM	598	H2B'	THY	39	-18.048	-3.515	-4.266
ATOM	599	O3'	THY	39	-20.204	-5.534	-4.101
ATOM	600	P	POM	40	-21.047	-4.689	-5.191
ATOM	601	OA	POM	40	-20.437	-4.910	-6.521
ATOM	602	OB	POM	40	-22.482	-4.984	-4.986
ATOM	603	O5'	THY	41	-20.799	-3.148	-4.797
ATOM	604	C5'	THY	41	-21.374	-2.570	-3.638
ATOM	605	H5A'	THY	41	-22.458	-2.503	-3.744
ATOM	606	H5B'	THY	41	-21.145	-3.183	-2.765
ATOM	607	C4'	THY	41	-20.783	-1.170	-3.427
ATOM	608	H4'	THY	41	-21.033	-0.814	-2.426
ATOM	609	O1'	THY	41	-19.373	-1.249	-3.536
ATOM	610	C1'	THY	41	-18.887	-0.019	-4.021
ATOM	611	H1'	THY	41	-18.732	0.644	-3.169
ATOM	612	N1	THY	41	-17.649	-0.231	-4.810
ATOM	613	C6	THY	41	-17.551	-1.282	-5.691
ATOM	614	H6	THY	41	-18.417	-1.915	-5.834
ATOM	615	C5	THY	41	-16.405	-1.532	-6.376
ATOM	616	C7	THY	41	-16.329	-2.709	-7.331
ATOM	617	H7A	THY	41	-16.006	-2.356	-8.311
ATOM	618	H7B	THY	41	-15.599	-3.428	-6.959
ATOM	619	H7C	THY	41	-17.295	-3.207	-7.433
ATOM	620	C4	THY	41	-15.243	-0.682	-6.194
ATOM	621	O4	THY	41	-14.137	-0.844	-6.706
ATOM	622	N3	THY	41	-15.455	0.389	-5.359
ATOM	623	H3	THY	41	-14.685	1.037	-5.247
ATOM	624	C2	THY	41	-16.609	0.678	-4.669
ATOM	625	O2	THY	41	-16.687	1.704	-3.997
ATOM	626	C3'	THY	41	-21.275	-0.144	-4.459
ATOM	627	H3'	THY	41	-21.732	-0.653	-5.310
ATOM	628	C2'	THY	41	-19.987	0.548	-4.907
ATOM	629	H2A'	THY	41	-20.016	1.622	-4.764
ATOM	630	H2B'	THY	41	-19.820	0.313	-5.958

ATOM	631	O3'	THY	41	-22.205	0.746	-3.859
ATOM	632	P	POM	42	-22.924	1.943	-4.677
ATOM	633	OA	POM	42	-22.956	1.588	-6.112
ATOM	634	OB	POM	42	-24.178	2.293	-3.975
ATOM	635	O5'	CYT	43	-21.896	3.170	-4.496
ATOM	636	C5'	CYT	43	-21.580	3.656	-3.207
ATOM	637	H5A'	CYT	43	-22.462	4.110	-2.752
ATOM	638	H5B'	CYT	43	-21.255	2.825	-2.579
ATOM	639	C4'	CYT	43	-20.440	4.678	-3.257
ATOM	640	H4'	CYT	43	-20.179	4.922	-2.230
ATOM	641	O1'	CYT	43	-19.310	4.123	-3.912
ATOM	642	C1'	CYT	43	-18.906	4.994	-4.952
ATOM	643	H1'	CYT	43	-18.215	5.718	-4.534
ATOM	644	N1	CYT	43	-18.275	4.197	-6.040
ATOM	645	C6	CYT	43	-18.994	3.234	-6.698
ATOM	646	H6	CYT	43	-20.059	3.156	-6.531
ATOM	647	C5	CYT	43	-18.395	2.344	-7.521
ATOM	648	H5	CYT	43	-18.999	1.599	-8.017
ATOM	649	C4	CYT	43	-16.981	2.460	-7.686
ATOM	650	N4	CYT	43	-16.337	1.555	-8.413
ATOM	651	HN4A	CYT	43	-15.335	1.640	-8.528
ATOM	652	HN4B	CYT	43	-16.848	0.844	-8.907
ATOM	653	N3	CYT	43	-16.271	3.415	-7.073
ATOM	654	C2	CYT	43	-16.897	4.299	-6.244
ATOM	655	O2	CYT	43	-16.224	5.171	-5.693
ATOM	656	C3'	CYT	43	-20.797	5.982	-3.971
ATOM	657	H3'	CYT	43	-21.879	6.115	-4.030
ATOM	658	C2'	CYT	43	-20.154	5.783	-5.341
ATOM	659	H2A'	CYT	43	-19.916	6.736	-5.809
ATOM	660	H2B'	CYT	43	-20.831	5.203	-5.967
ATOM	661	O3'	CYT	43	-20.160	7.019	-3.241
ATOM	662	P	POM	44	-20.678	8.543	-3.282
ATOM	663	OA	POM	44	-22.119	8.558	-3.610
ATOM	664	OB	POM	44	-20.185	9.199	-2.052
ATOM	665	O5'	GUA	45	-19.858	9.129	-4.527
ATOM	666	C5'	GUA	45	-18.684	9.888	-4.320
ATOM	667	H5A'	GUA	45	-18.947	10.865	-3.912
ATOM	668	H5B'	GUA	45	-18.024	9.379	-3.618
ATOM	669	C4'	GUA	45	-17.933	10.068	-5.638
ATOM	670	H4'	GUA	45	-17.037	10.656	-5.445
ATOM	671	O1'	GUA	45	-17.544	8.795	-6.141
ATOM	672	C1'	GUA	45	-17.742	8.851	-7.536
ATOM	673	H1'	GUA	45	-16.946	9.457	-7.968
ATOM	674	N9	GUA	45	-17.732	7.517	-8.177
ATOM	675	C8	GUA	45	-18.778	6.665	-8.426
ATOM	676	H8	GUA	45	-19.797	6.864	-8.132
ATOM	677	N7	GUA	45	-18.444	5.581	-9.066
ATOM	678	C5	GUA	45	-17.076	5.727	-9.274
ATOM	679	C6	GUA	45	-16.147	4.875	-9.940
ATOM	680	O6	GUA	45	-16.370	3.791	-10.473
ATOM	681	N1	GUA	45	-14.858	5.384	-9.949
ATOM	682	H1	GUA	45	-14.160	4.803	-10.413
ATOM	683	C2	GUA	45	-14.504	6.592	-9.400

ATOM	684	N2	GUA	45	-13.239	6.984	-9.506
ATOM	685	HN2A	GUA	45	-12.543	6.398	-9.951
ATOM	686	HN2B	GUA	45	-12.980	7.893	-9.156
ATOM	687	N3	GUA	45	-15.362	7.395	-8.761
ATOM	688	C4	GUA	45	-16.631	6.907	-8.732
ATOM	689	C3'	GUA	45	-18.802	10.750	-6.713
ATOM	690	H3'	GUA	45	-19.731	11.167	-6.321
ATOM	691	C2'	GUA	45	-19.072	9.589	-7.661
ATOM	692	H2A'	GUA	45	-19.292	9.920	-8.674
ATOM	693	H2B'	GUA	45	-19.893	8.995	-7.258
ATOM	694	O3'	GUA	45	-18.080	11.720	-7.445
ATOM	695	P	POM	46	-17.795	13.194	-6.865
ATOM	696	OA	POM	46	-18.635	14.150	-7.618
ATOM	697	OB	POM	46	-17.854	13.148	-5.389
ATOM	698	O5'	CYT	47	-16.263	13.393	-7.316
ATOM	699	C5'	CYT	47	-15.191	13.107	-6.437
ATOM	700	H5A'	CYT	47	-15.025	13.965	-5.784
ATOM	701	H5B'	CYT	47	-15.418	12.238	-5.819
ATOM	702	C4'	CYT	47	-13.917	12.789	-7.226
ATOM	703	H4'	CYT	47	-13.104	12.640	-6.514
ATOM	704	O1'	CYT	47	-14.130	11.583	-7.943
ATOM	705	C1'	CYT	47	-13.820	11.777	-9.308
ATOM	706	H1'	CYT	47	-12.771	11.516	-9.448
ATOM	707	N1	CYT	47	-14.748	10.940	-10.126
ATOM	708	C6	CYT	47	-16.103	11.138	-10.053
ATOM	709	H6	CYT	47	-16.492	11.971	-9.490
ATOM	710	C5	CYT	47	-16.976	10.290	-10.642
ATOM	711	H5	CYT	47	-18.033	10.494	-10.567
ATOM	712	C4	CYT	47	-16.426	9.170	-11.331
ATOM	713	N4	CYT	47	-17.244	8.236	-11.805
ATOM	714	HN4A	CYT	47	-16.860	7.405	-12.237
ATOM	715	HN4B	CYT	47	-18.239	8.339	-11.700
ATOM	716	N3	CYT	47	-15.107	8.983	-11.449
ATOM	717	C2	CYT	47	-14.246	9.859	-10.852
ATOM	718	O2	CYT	47	-13.037	9.665	-10.965
ATOM	719	C3'	CYT	47	-13.537	13.894	-8.222
ATOM	720	H3'	CYT	47	-14.089	14.810	-8.009
ATOM	721	C2'	CYT	47	-13.960	13.281	-9.556
ATOM	722	H2A'	CYT	47	-13.328	13.611	-10.375
ATOM	723	H2B'	CYT	47	-14.991	13.575	-9.747
ATOM	724	O3'	CYT	47	-12.139	14.132	-8.146
ATOM	725	P	POM	48	-11.448	15.422	-8.831
ATOM	726	OA	POM	48	-12.431	16.526	-8.878
ATOM	727	OB	POM	48	-10.130	15.640	-8.195
ATOM	728	O5'	GUA	49	-11.189	14.922	-10.335
ATOM	729	C5'	GUA	49	-10.057	14.138	-10.649
ATOM	730	H5A'	GUA	49	-9.167	14.768	-10.639
ATOM	731	H5B'	GUA	49	-9.938	13.340	-9.913
ATOM	732	C4'	GUA	49	-10.220	13.499	-12.030
ATOM	733	H4'	GUA	49	-9.314	12.945	-12.279
ATOM	734	O1'	GUA	49	-11.312	12.604	-12.043
ATOM	735	C1'	GUA	49	-11.605	12.334	-13.397
ATOM	736	H1'	GUA	49	-10.985	11.496	-13.720

ATOM	737	N9	GUA	49	-13.040	12.009	-13.537
ATOM	738	C8	GUA	49	-14.122	12.693	-13.045
ATOM	739	H8	GUA	49	-14.035	13.628	-12.514
ATOM	740	N7	GUA	49	-15.268	12.117	-13.275
ATOM	741	C5	GUA	49	-14.925	10.974	-13.991
ATOM	742	C6	GUA	49	-15.746	9.938	-14.527
ATOM	743	O6	GUA	49	-16.965	9.810	-14.438
ATOM	744	N1	GUA	49	-15.018	8.988	-15.223
ATOM	745	H1	GUA	49	-15.554	8.200	-15.582
ATOM	746	C2	GUA	49	-13.656	9.016	-15.383
ATOM	747	N2	GUA	49	-13.093	8.047	-16.096
ATOM	748	HN2A	GUA	49	-13.653	7.327	-16.540
ATOM	749	HN2B	GUA	49	-12.088	8.003	-16.145
ATOM	750	N3	GUA	49	-12.872	9.966	-14.865
ATOM	751	C4	GUA	49	-13.566	10.911	-14.176
ATOM	752	C3'	GUA	49	-10.538	14.486	-13.152
ATOM	753	H3'	GUA	49	-11.252	15.239	-12.818
ATOM	754	C2'	GUA	49	-11.207	13.586	-14.191
ATOM	755	H2A'	GUA	49	-10.500	13.306	-14.973
ATOM	756	H2B'	GUA	49	-12.066	14.092	-14.633
ATOM	757	O3'	GUA	49	-9.376	15.098	-13.671
ATOM	758	H	HE	50	-8.771	14.411	-13.961
ATOM	759	O1	DIS	51	-11.867	-12.832	1.644
ATOM	760	C1	DIS	51	-11.486	-11.732	1.248
ATOM	761	HF	DIS	51	-10.424	-11.590	1.118
ATOM	762	N1	DIS	51	-12.287	-10.677	1.042
ATOM	763	HN1	DIS	51	-11.815	-9.808	0.814
ATOM	764	C2	DIS	51	-13.698	-10.522	1.124
ATOM	765	C3	DIS	51	-14.505	-9.393	0.889
ATOM	766	H3	DIS	51	-14.174	-8.377	0.752
ATOM	767	C5	DIS	51	-14.497	-11.639	0.996
ATOM	768	H5	DIS	51	-14.185	-12.671	0.990
ATOM	769	N2	DIS	51	-15.790	-11.224	0.781
ATOM	770	C6	DIS	51	-16.951	-12.121	0.516
ATOM	771	HM1	DIS	51	-17.170	-12.252	-0.544
ATOM	772	HM2	DIS	51	-16.830	-13.138	0.888
ATOM	773	HM3	DIS	51	-17.897	-11.790	0.943
ATOM	774	C4	DIS	51	-15.792	-9.845	0.686
ATOM	775	C7	DIS	51	-16.945	-8.968	0.291
ATOM	776	O2	DIS	51	-17.859	-9.462	-0.366
ATOM	777	N3	DIS	51	-16.952	-7.695	0.724
ATOM	778	HN3	DIS	51	-16.150	-7.381	1.257
ATOM	779	C8	DIS	51	-17.952	-6.700	0.545
ATOM	780	C9	DIS	51	-17.950	-5.295	0.661
ATOM	781	H9	DIS	51	-17.084	-4.666	0.804
ATOM	782	C11	DIS	51	-19.263	-7.118	0.511
ATOM	783	H11	DIS	51	-19.628	-8.134	0.539
ATOM	784	N4	DIS	51	-20.067	-6.010	0.440
ATOM	785	C12	DIS	51	-21.552	-6.035	0.350
ATOM	786	HM4	DIS	51	-22.061	-5.678	1.246
ATOM	787	HM5	DIS	51	-21.964	-5.434	-0.462
ATOM	788	HM6	DIS	51	-21.975	-7.026	0.184
ATOM	789	C10	DIS	51	-19.267	-4.885	0.520

ATOM	790	C13	DIS	51	-19.762	-3.462	0.547
ATOM	791	O3	DIS	51	-20.955	-3.272	0.778
ATOM	792	N5	DIS	51	-18.923	-2.466	0.219
ATOM	793	HN5	DIS	51	-17.997	-2.729	-0.085
ATOM	794	C14	DIS	51	-19.193	-1.067	0.146
ATOM	795	C15	DIS	51	-18.543	0.019	-0.476
ATOM	796	H15	DIS	51	-17.696	-0.043	-1.140
ATOM	797	C17	DIS	51	-20.159	-0.554	0.985
ATOM	798	H17	DIS	51	-20.779	-1.095	1.682
ATOM	799	N6	DIS	51	-20.219	0.802	0.797
ATOM	800	C18	DIS	51	-21.141	1.726	1.514
ATOM	801	HM7	DIS	51	-21.860	2.230	0.868
ATOM	802	HM8	DIS	51	-21.759	1.246	2.273
ATOM	803	HM9	DIS	51	-20.643	2.532	2.053
ATOM	804	C16	DIS	51	-19.214	1.166	-0.078
ATOM	805	C19	DIS	51	-18.887	2.582	-0.481
ATOM	806	O4	DIS	51	-19.770	3.428	-0.365
ATOM	807	N7	DIS	51	-17.616	2.922	-0.733
ATOM	808	HN7	DIS	51	-16.893	2.214	-0.676
ATOM	809	C20	DIS	51	-17.186	4.310	-0.876
ATOM	810	HC1	DIS	51	-18.036	4.992	-0.883
ATOM	811	HC2	DIS	51	-16.551	4.577	-0.033
ATOM	812	C21	DIS	51	-16.400	4.507	-2.173
ATOM	813	HC3	DIS	51	-15.472	3.950	-2.084
ATOM	814	HC4	DIS	51	-16.965	4.084	-3.000
ATOM	815	C22	DIS	51	-16.071	5.951	-2.505
ATOM	816	N8	DIS	51	-14.802	6.302	-2.769
ATOM	817	HNC	DIS	51	-14.558	7.251	-3.005
ATOM	818	HND	DIS	51	-14.062	5.612	-2.698
ATOM	819	N9	DIS	51	-17.050	6.871	-2.573
ATOM	820	HNA	DIS	51	-16.850	7.825	-2.833
ATOM	821	HNB	DIS	51	-18.021	6.608	-2.440

Coordinates for W_D d(CGCGAATTCGCG)₂ with Distamycin A

$$K_{NMR} = 0.59 \text{ kcal} \cdot \text{mol}^{-1} \cdot \text{\AA}^{-2}$$

ATOM	1	H	HB	1	-19.441	4.508	-21.320
ATOM	2	O5'	CYT	2	-19.220	3.838	-21.971
ATOM	3	C5'	CYT	2	-18.452	2.835	-21.341
ATOM	4	H5A'	CYT	2	-19.036	2.381	-20.540
ATOM	5	H5B'	CYT	2	-18.202	2.072	-22.080
ATOM	6	C4'	CYT	2	-17.164	3.435	-20.772
ATOM	7	H4'	CYT	2	-16.627	3.953	-21.569
ATOM	8	O1'	CYT	2	-17.465	4.364	-19.745
ATOM	9	C1'	CYT	2	-16.409	4.312	-18.808
ATOM	10	H1'	CYT	2	-15.538	4.802	-19.247
ATOM	11	N1	CYT	2	-16.841	4.924	-17.523
ATOM	12	C6	CYT	2	-18.053	4.599	-16.968
ATOM	13	H6	CYT	2	-18.637	3.804	-17.408
ATOM	14	C5	CYT	2	-18.552	5.276	-15.908
ATOM	15	H5	CYT	2	-19.513	4.998	-15.503
ATOM	16	C4	CYT	2	-17.762	6.356	-15.402
ATOM	17	N4	CYT	2	-18.265	7.166	-14.477
ATOM	18	HN4A	CYT	2	-17.751	8.008	-14.239
ATOM	19	HN4B	CYT	2	-19.160	6.974	-14.064
ATOM	20	N3	CYT	2	-16.576	6.667	-15.931
ATOM	21	C2	CYT	2	-16.070	5.940	-16.965
ATOM	22	O2	CYT	2	-14.955	6.221	-17.395
ATOM	23	C3'	CYT	2	-16.252	2.363	-20.152
ATOM	24	H3'	CYT	2	-16.710	1.374	-20.212
ATOM	25	C2'	CYT	2	-16.133	2.818	-18.697
ATOM	26	H2A'	CYT	2	-15.151	2.619	-18.274
ATOM	27	H2B'	CYT	2	-16.900	2.318	-18.106
ATOM	28	O3'	CYT	2	-15.010	2.381	-20.831
ATOM	29	P	POM	3	-13.866	1.278	-20.553
ATOM	30	OA	POM	3	-14.503	0.113	-19.901
ATOM	31	OB	POM	3	-13.101	1.096	-21.805
ATOM	32	O5'	GUA	4	-12.920	2.013	-19.477
ATOM	33	C5'	GUA	4	-12.043	3.049	-19.878
ATOM	34	H5A'	GUA	4	-11.325	2.659	-20.602
ATOM	35	H5B'	GUA	4	-12.614	3.851	-20.347
ATOM	36	C4'	GUA	4	-11.269	3.624	-18.686
ATOM	37	H4'	GUA	4	-10.598	4.398	-19.062
ATOM	38	O1'	GUA	4	-12.162	4.226	-17.763
ATOM	39	C1'	GUA	4	-11.705	3.947	-16.456
ATOM	40	H1'	GUA	4	-10.906	4.642	-16.192
ATOM	41	N9	GUA	4	-12.852	4.050	-15.523
ATOM	42	C8	GUA	4	-14.031	3.350	-15.572
ATOM	43	H8	GUA	4	-14.186	2.511	-16.231
ATOM	44	N7	GUA	4	-14.963	3.804	-14.783
ATOM	45	C5	GUA	4	-14.352	4.875	-14.138
ATOM	46	C6	GUA	4	-14.877	5.796	-13.183
ATOM	47	O6	GUA	4	-16.013	5.839	-12.717
ATOM	48	N1	GUA	4	-13.953	6.749	-12.787
ATOM	49	H1	GUA	4	-14.297	7.484	-12.167
ATOM	50	C2	GUA	4	-12.648	6.777	-13.208

ATOM	51	N2	GUA	4	-11.855	7.719	-12.710
ATOM	52	HN2A	GUA	4	-12.203	8.397	-12.040
ATOM	53	HN2B	GUA	4	-10.896	7.751	-13.014
ATOM	54	N3	GUA	4	-12.143	5.925	-14.109
ATOM	55	C4	GUA	4	-13.048	5.010	-14.552
ATOM	56	C3'	GUA	4	-10.446	2.567	-17.932
ATOM	57	H3'	GUA	4	-10.496	1.595	-18.425
ATOM	58	C2'	GUA	4	-11.140	2.534	-16.569
ATOM	59	H2A'	GUA	4	-10.460	2.292	-15.757
ATOM	60	H2B'	GUA	4	-11.943	1.799	-16.618
ATOM	61	O3'	GUA	4	-9.101	3.016	-17.862
ATOM	62	P	POM	5	-7.908	2.104	-17.268
ATOM	63	OA	POM	5	-8.324	0.685	-17.316
ATOM	64	OB	POM	5	-6.644	2.527	-17.909
ATOM	65	O5'	CYT	6	-7.873	2.572	-15.732
ATOM	66	C5'	CYT	6	-7.347	3.838	-15.380
ATOM	67	H5A'	CYT	6	-6.257	3.814	-15.422
ATOM	68	H5B'	CYT	6	-7.712	4.592	-16.079
ATOM	69	C4'	CYT	6	-7.810	4.241	-13.979
ATOM	70	H4'	CYT	6	-7.526	5.279	-13.797
ATOM	71	O1'	CYT	6	-9.216	4.140	-13.881
ATOM	72	C1'	CYT	6	-9.525	4.171	-12.506
ATOM	73	H1'	CYT	6	-9.513	5.220	-12.204
ATOM	74	N1	CYT	6	-10.833	3.515	-12.252
ATOM	75	C6	CYT	6	-11.164	2.349	-12.889
ATOM	76	H6	CYT	6	-10.423	1.860	-13.506
ATOM	77	C5	CYT	6	-12.396	1.805	-12.763
ATOM	78	H5	CYT	6	-12.625	0.887	-13.284
ATOM	79	C4	CYT	6	-13.328	2.497	-11.926
ATOM	80	N4	CYT	6	-14.567	2.040	-11.809
ATOM	81	HN4A	CYT	6	-15.220	2.551	-11.228
ATOM	82	HN4B	CYT	6	-14.866	1.229	-12.323
ATOM	83	N3	CYT	6	-13.000	3.622	-11.281
ATOM	84	C2	CYT	6	-11.741	4.130	-11.398
ATOM	85	O2	CYT	6	-11.441	5.131	-10.755
ATOM	86	C3'	CYT	6	-7.247	3.379	-12.845
ATOM	87	H3'	CYT	6	-7.118	2.351	-13.187
ATOM	88	C2'	CYT	6	-8.377	3.441	-11.811
ATOM	89	H2A'	CYT	6	-8.093	4.013	-10.931
ATOM	90	H2B'	CYT	6	-8.650	2.425	-11.527
ATOM	91	O3'	CYT	6	-6.021	3.922	-12.383
ATOM	92	P	POM	7	-5.188	3.274	-11.160
ATOM	93	OA	POM	7	-5.498	1.830	-11.086
ATOM	94	OB	POM	7	-3.782	3.723	-11.271
ATOM	95	O5'	GUA	8	-5.837	3.996	-9.876
ATOM	96	C5'	GUA	8	-5.695	5.391	-9.685
ATOM	97	H5A'	GUA	8	-4.652	5.629	-9.471
ATOM	98	H5B'	GUA	8	-5.992	5.913	-10.595
ATOM	99	C4'	GUA	8	-6.584	5.898	-8.543
ATOM	100	H4'	GUA	8	-6.503	6.986	-8.521
ATOM	101	O1'	GUA	8	-7.937	5.538	-8.795
ATOM	102	C1'	GUA	8	-8.445	4.875	-7.652
ATOM	103	H1'	GUA	8	-8.847	5.619	-6.963

ATOM	104	N9	GUA	8	-9.491	3.896	-8.027
ATOM	105	C8	GUA	8	-9.356	2.724	-8.728
ATOM	106	H8	GUA	8	-8.404	2.357	-9.083
ATOM	107	N7	GUA	8	-10.477	2.092	-8.940
ATOM	108	C5	GUA	8	-11.430	2.893	-8.320
ATOM	109	C6	GUA	8	-12.840	2.716	-8.188
ATOM	110	O6	GUA	8	-13.531	1.790	-8.605
ATOM	111	N1	GUA	8	-13.443	3.736	-7.468
ATOM	112	H1	GUA	8	-14.441	3.617	-7.294
ATOM	113	C2	GUA	8	-12.775	4.826	-6.967
ATOM	114	N2	GUA	8	-13.468	5.740	-6.298
ATOM	115	HN2A	GUA	8	-14.463	5.638	-6.143
ATOM	116	HN2B	GUA	8	-12.973	6.545	-5.948
ATOM	117	N3	GUA	8	-11.456	4.997	-7.073
ATOM	118	C4	GUA	8	-10.838	4.000	-7.761
ATOM	119	C3'	GUA	8	-6.198	5.336	-7.166
ATOM	120	H3'	GUA	8	-5.171	4.967	-7.144
ATOM	121	C2'	GUA	8	-7.225	4.221	-7.012
ATOM	122	H2A'	GUA	8	-7.391	3.931	-5.977
ATOM	123	H2B'	GUA	8	-6.891	3.358	-7.587
ATOM	124	O3'	GUA	8	-6.386	6.373	-6.217
ATOM	125	P	POM	9	-5.947	6.242	-4.672
ATOM	126	OA	POM	9	-5.560	4.842	-4.394
ATOM	127	OB	POM	9	-5.013	7.345	-4.358
ATOM	128	O5'	ADE	10	-7.341	6.526	-3.920
ATOM	129	C5'	ADE	10	-7.937	7.808	-3.958
ATOM	130	H5A'	ADE	10	-7.273	8.537	-3.491
ATOM	131	H5B'	ADE	10	-8.101	8.101	-4.997
ATOM	132	C4'	ADE	10	-9.288	7.824	-3.231
ATOM	133	H4'	ADE	10	-9.710	8.823	-3.344
ATOM	134	O1'	ADE	10	-10.163	6.874	-3.824
ATOM	135	C1'	ADE	10	-10.511	5.895	-2.862
ATOM	136	H1'	ADE	10	-11.486	6.156	-2.447
ATOM	137	N9	ADE	10	-10.553	4.561	-3.503
ATOM	138	C8	ADE	10	-9.514	3.842	-4.042
ATOM	139	H8	ADE	10	-8.483	4.154	-3.965
ATOM	140	N7	ADE	10	-9.874	2.752	-4.664
ATOM	141	C5	ADE	10	-11.255	2.749	-4.521
ATOM	142	C6	ADE	10	-12.256	1.876	-4.975
ATOM	143	N6	ADE	10	-11.984	0.801	-5.710
ATOM	144	HN6A	ADE	10	-12.731	0.190	-6.021
ATOM	145	HN6B	ADE	10	-11.024	0.622	-5.965
ATOM	146	N1	ADE	10	-13.536	2.148	-4.681
ATOM	147	C2	ADE	10	-13.813	3.237	-3.977
ATOM	148	H2	ADE	10	-14.857	3.400	-3.768
ATOM	149	N3	ADE	10	-12.973	4.137	-3.478
ATOM	150	C4	ADE	10	-11.683	3.836	-3.802
ATOM	151	C3'	ADE	10	-9.172	7.483	-1.740
ATOM	152	H3'	ADE	10	-8.175	7.701	-1.353
ATOM	153	C2'	ADE	10	-9.474	5.989	-1.746
ATOM	154	H2A'	ADE	10	-9.853	5.637	-0.790
ATOM	155	H2B'	ADE	10	-8.563	5.448	-1.997
ATOM	156	O3'	ADE	10	-10.154	8.227	-1.038

ATOM	157	P	POM	11	-10.279	8.191	0.568
ATOM	158	OA	POM	11	-9.092	7.506	1.124
ATOM	159	OB	POM	11	-10.635	9.548	1.036
ATOM	160	O5'	ADE	12	-11.555	7.232	0.779
ATOM	161	C5'	ADE	12	-12.863	7.710	0.527
ATOM	162	H5A'	ADE	12	-13.061	8.582	1.153
ATOM	163	H5B'	ADE	12	-12.949	8.002	-0.520
ATOM	164	C4'	ADE	12	-13.917	6.641	0.838
ATOM	165	H4'	ADE	12	-14.900	7.083	0.669
ATOM	166	O1'	ADE	12	-13.747	5.531	-0.033
ATOM	167	C1'	ADE	12	-13.696	4.353	0.749
ATOM	168	H1'	ADE	12	-14.709	3.987	0.916
ATOM	169	N9	ADE	12	-12.886	3.326	0.058
ATOM	170	C8	ADE	12	-11.521	3.260	-0.080
ATOM	171	H8	ADE	12	-10.847	3.970	0.374
ATOM	172	N7	ADE	12	-11.098	2.260	-0.803
ATOM	173	C5	ADE	12	-12.271	1.617	-1.172
ATOM	174	C6	ADE	12	-12.528	0.480	-1.955
ATOM	175	N6	ADE	12	-11.558	-0.224	-2.534
ATOM	176	HN6A	ADE	12	-11.777	-1.006	-3.143
ATOM	177	HN6B	ADE	12	-10.604	0.072	-2.390
ATOM	178	N1	ADE	12	-13.799	0.111	-2.158
ATOM	179	C2	ADE	12	-14.776	0.827	-1.614
ATOM	180	H2	ADE	12	-15.777	0.480	-1.810
ATOM	181	N3	ADE	12	-14.672	1.908	-0.853
ATOM	182	C4	ADE	12	-13.370	2.260	-0.665
ATOM	183	C3'	ADE	12	-13.830	6.128	2.283
ATOM	184	H3'	ADE	12	-13.262	6.806	2.922
ATOM	185	C2'	ADE	12	-13.116	4.793	2.088
ATOM	186	H2A'	ADE	12	-13.311	4.084	2.891
ATOM	187	H2B'	ADE	12	-12.047	4.990	2.018
ATOM	188	O3'	ADE	12	-15.149	5.976	2.778
ATOM	189	P	POM	13	-15.456	5.510	4.292
ATOM	190	OA	POM	13	-14.193	5.537	5.062
ATOM	191	OB	POM	13	-16.637	6.257	4.776
ATOM	192	O5'	THY	14	-15.878	3.977	4.060
ATOM	193	C5'	THY	14	-17.160	3.657	3.556
ATOM	194	H5A'	THY	14	-17.913	3.810	4.331
ATOM	195	H5B'	THY	14	-17.392	4.301	2.707
ATOM	196	C4'	THY	14	-17.206	2.205	3.076
ATOM	197	H4'	THY	14	-18.160	2.026	2.588
ATOM	198	O1'	THY	14	-16.168	1.957	2.147
ATOM	199	C1'	THY	14	-16.025	0.554	2.048
ATOM	200	H1'	THY	14	-16.625	0.210	1.207
ATOM	201	N1	THY	14	-14.609	0.158	1.867
ATOM	202	C6	THY	14	-13.581	0.877	2.429
ATOM	203	H6	THY	14	-13.826	1.746	3.024
ATOM	204	C5	THY	14	-12.285	0.507	2.261
ATOM	205	C7	THY	14	-11.172	1.309	2.908
ATOM	206	H7A	THY	14	-11.556	2.174	3.450
ATOM	207	H7B	THY	14	-10.633	0.665	3.604
ATOM	208	H7C	THY	14	-10.479	1.646	2.137
ATOM	209	C4	THY	14	-11.952	-0.672	1.479

ATOM	210	O4	THY	14	-10.824	-1.086	1.220
ATOM	211	N3	THY	14	-13.044	-1.354	0.999
ATOM	212	H3	THY	14	-12.884	-2.239	0.533
ATOM	213	C2	THY	14	-14.365	-1.023	1.181
ATOM	214	O2	THY	14	-15.253	-1.757	0.759
ATOM	215	C3'	THY	14	-17.029	1.157	4.172
ATOM	216	H3'	THY	14	-16.226	1.466	4.844
ATOM	217	C2'	THY	14	-16.586	-0.040	3.337
ATOM	218	H2A'	THY	14	-17.432	-0.680	3.083
ATOM	219	H2B'	THY	14	-15.840	-0.606	3.885
ATOM	220	O3'	THY	14	-18.235	0.902	4.871
ATOM	221	P	POM	15	-18.297	-0.114	6.128
ATOM	222	OA	POM	15	-17.013	-0.036	6.859
ATOM	223	OB	POM	15	-19.570	0.120	6.844
ATOM	224	O5'	THY	16	-18.373	-1.575	5.456
ATOM	225	C5'	THY	16	-19.478	-1.968	4.669
ATOM	226	H5A'	THY	16	-20.394	-1.942	5.261
ATOM	227	H5B'	THY	16	-19.583	-1.271	3.840
ATOM	228	C4'	THY	16	-19.272	-3.381	4.103
ATOM	229	H4'	THY	16	-20.068	-3.573	3.381
ATOM	230	O1'	THY	16	-18.009	-3.459	3.451
ATOM	231	C1'	THY	16	-17.269	-4.538	3.999
ATOM	232	H1'	THY	16	-17.500	-5.440	3.432
ATOM	233	N1	THY	16	-15.813	-4.212	3.991
ATOM	234	C6	THY	16	-15.356	-3.111	4.678
ATOM	235	H6	THY	16	-16.061	-2.516	5.238
ATOM	236	C5	THY	16	-14.054	-2.737	4.655
ATOM	237	C7	THY	16	-13.594	-1.524	5.442
ATOM	238	H7A	THY	16	-14.436	-0.979	5.877
ATOM	239	H7B	THY	16	-12.933	-1.849	6.246
ATOM	240	H7C	THY	16	-13.040	-0.853	4.786
ATOM	241	C4	THY	16	-13.086	-3.499	3.894
ATOM	242	O4	THY	16	-11.893	-3.223	3.790
ATOM	243	N3	THY	16	-13.604	-4.603	3.253
ATOM	244	H3	THY	16	-12.921	-5.179	2.766
ATOM	245	C2	THY	16	-14.931	-4.999	3.246
ATOM	246	O2	THY	16	-15.271	-5.993	2.607
ATOM	247	C3'	THY	16	-19.311	-4.462	5.192
ATOM	248	H3'	THY	16	-19.800	-4.103	6.100
ATOM	249	C2'	THY	16	-17.827	-4.719	5.412
ATOM	250	H2A'	THY	16	-17.643	-5.708	5.817
ATOM	251	H2B'	THY	16	-17.458	-3.970	6.109
ATOM	252	O3'	THY	16	-19.990	-5.598	4.684
ATOM	253	P	POM	17	-20.303	-6.898	5.588
ATOM	254	OA	POM	17	-20.001	-6.577	7.000
ATOM	255	OB	POM	17	-21.646	-7.399	5.219
ATOM	256	O5'	CYT	18	-19.206	-7.955	5.068
ATOM	257	C5'	CYT	18	-19.313	-8.514	3.772
ATOM	258	H5A'	CYT	18	-20.238	-9.087	3.691
ATOM	259	H5B'	CYT	18	-19.334	-7.708	3.038
ATOM	260	C4'	CYT	18	-18.130	-9.432	3.452
ATOM	261	H4'	CYT	18	-18.250	-9.768	2.424
ATOM	262	O1'	CYT	18	-16.921	-8.704	3.551

ATOM	263	C1'	CYT	18	-15.939	-9.503	4.182
ATOM	264	H1'	CYT	18	-15.433	-10.102	3.426
ATOM	265	N1	CYT	18	-15.030	-8.588	4.923
ATOM	266	C6	CYT	18	-15.564	-7.618	5.727
ATOM	267	H6	CYT	18	-16.625	-7.640	5.926
ATOM	268	C5	CYT	18	-14.803	-6.633	6.255
ATOM	269	H5	CYT	18	-15.266	-5.886	6.882
ATOM	270	C4	CYT	18	-13.410	-6.660	5.944
ATOM	271	N4	CYT	18	-12.638	-5.666	6.366
ATOM	272	HN4A	CYT	18	-11.648	-5.696	6.159
ATOM	273	HN4B	CYT	18	-13.015	-4.942	6.953
ATOM	274	N3	CYT	18	-12.866	-7.629	5.196
ATOM	275	C2	CYT	18	-13.656	-8.625	4.694
ATOM	276	O2	CYT	18	-13.128	-9.540	4.069
ATOM	277	C3'	CYT	18	-18.037	-10.661	4.367
ATOM	278	H3'	CYT	18	-18.881	-10.687	5.057
ATOM	279	C2'	CYT	18	-16.721	-10.433	5.110
ATOM	280	H2A'	CYT	18	-16.181	-11.362	5.284
ATOM	281	H2B'	CYT	18	-16.951	-9.947	6.058
ATOM	282	O3'	CYT	18	-18.001	-11.824	3.556
ATOM	283	P	POM	19	-18.339	-13.293	4.132
ATOM	284	OA	POM	19	-19.334	-13.159	5.218
ATOM	285	OB	POM	19	-18.632	-14.167	2.974
ATOM	286	O5'	GUA	20	-16.947	-13.765	4.780
ATOM	287	C5'	GUA	20	-15.954	-14.393	3.991
ATOM	288	H5A'	GUA	20	-16.306	-15.380	3.685
ATOM	289	H5B'	GUA	20	-15.753	-13.796	3.100
ATOM	290	C4'	GUA	20	-14.651	-14.549	4.780
ATOM	291	H4'	GUA	20	-13.946	-15.107	4.166
ATOM	292	O1'	GUA	20	-14.105	-13.263	5.045
ATOM	293	C1'	GUA	20	-13.624	-13.282	6.369
ATOM	294	H1'	GUA	20	-12.681	-13.829	6.390
ATOM	295	N9	GUA	20	-13.415	-11.916	6.902
ATOM	296	C8	GUA	20	-14.327	-11.041	7.435
ATOM	297	H8	GUA	20	-15.373	-11.273	7.556
ATOM	298	N7	GUA	20	-13.825	-9.891	7.788
ATOM	299	C5	GUA	20	-12.473	-10.010	7.476
ATOM	300	C6	GUA	20	-11.400	-9.082	7.635
ATOM	301	O6	GUA	20	-11.437	-7.951	8.116
ATOM	302	N1	GUA	20	-10.190	-9.575	7.173
ATOM	303	H1	GUA	20	-9.390	-8.950	7.279
ATOM	304	C2	GUA	20	-10.020	-10.833	6.651
ATOM	305	N2	GUA	20	-8.795	-11.200	6.295
ATOM	306	HN2A	GUA	20	-8.026	-10.544	6.308
ATOM	307	HN2B	GUA	20	-8.614	-12.177	6.102
ATOM	308	N3	GUA	20	-11.010	-11.722	6.521
ATOM	309	C4	GUA	20	-12.213	-11.245	6.936
ATOM	310	C3'	GUA	20	-14.852	-15.251	6.137
ATOM	311	H3'	GUA	20	-15.831	-15.723	6.241
ATOM	312	C2'	GUA	20	-14.691	-14.086	7.108
ATOM	313	H2A'	GUA	20	-14.376	-14.407	8.099
ATOM	314	H2B'	GUA	20	-15.634	-13.540	7.156
ATOM	315	O3'	GUA	20	-13.814	-16.169	6.423

ATOM	316	P	POM	21	-13.795	-17.663	5.822
ATOM	317	OA	POM	21	-14.141	-18.597	6.916
ATOM	318	OB	POM	21	-14.557	-17.686	4.556
ATOM	319	O5'	CYT	22	-12.230	-17.835	5.485
ATOM	320	C5'	CYT	22	-11.702	-17.464	4.224
ATOM	321	H5A'	CYT	22	-11.729	-18.326	3.556
ATOM	322	H5B'	CYT	22	-12.287	-16.660	3.778
ATOM	323	C4'	CYT	22	-10.266	-16.952	4.371
ATOM	324	H4'	CYT	22	-9.897	-16.687	3.379
ATOM	325	O1'	CYT	22	-10.298	-15.783	5.176
ATOM	326	C1'	CYT	22	-9.330	-15.885	6.199
ATOM	327	H1'	CYT	22	-8.396	-15.474	5.812
ATOM	328	N1	CYT	22	-9.831	-15.172	7.410
ATOM	329	C6	CYT	22	-11.015	-15.547	7.994
ATOM	330	H6	CYT	22	-11.534	-16.420	7.631
ATOM	331	C5	CYT	22	-11.568	-14.832	9.000
ATOM	332	H5	CYT	22	-12.498	-15.171	9.432
ATOM	333	C4	CYT	22	-10.875	-13.657	9.418
ATOM	334	N4	CYT	22	-11.395	-12.893	10.371
ATOM	335	HN4A	CYT	22	-10.949	-12.015	10.609
ATOM	336	HN4B	CYT	22	-12.259	-13.154	10.813
ATOM	337	N3	CYT	22	-9.700	-13.304	8.888
ATOM	338	C2	CYT	22	-9.163	-14.038	7.869
ATOM	339	O2	CYT	22	-8.097	-13.668	7.377
ATOM	340	C3'	CYT	22	-9.316	-17.970	5.019
ATOM	341	H3'	CYT	22	-9.773	-18.960	5.060
ATOM	342	C2'	CYT	22	-9.125	-17.385	6.417
ATOM	343	H2A'	CYT	22	-8.138	-17.592	6.816
ATOM	344	H2B'	CYT	22	-9.886	-17.813	7.067
ATOM	345	O3'	CYT	22	-8.109	-18.018	4.272
ATOM	346	P	POM	23	-6.951	-19.106	4.564
ATOM	347	OA	POM	23	-7.554	-20.293	5.206
ATOM	348	OB	POM	23	-6.136	-19.265	3.339
ATOM	349	O5'	GUA	24	-6.044	-18.359	5.658
ATOM	350	C5'	GUA	24	-5.257	-17.241	5.300
ATOM	351	H5A'	GUA	24	-4.449	-17.556	4.638
ATOM	352	H5B'	GUA	24	-5.871	-16.501	4.783
ATOM	353	C4'	GUA	24	-4.671	-16.599	6.559
ATOM	354	H4'	GUA	24	-4.041	-15.759	6.264
ATOM	355	O1'	GUA	24	-5.737	-16.130	7.370
ATOM	356	C1'	GUA	24	-5.486	-16.529	8.700
ATOM	357	H1'	GUA	24	-4.795	-15.816	9.152
ATOM	358	N9	GUA	24	-6.746	-16.575	9.476
ATOM	359	C8	GUA	24	-7.734	-17.530	9.484
ATOM	360	H8	GUA	24	-7.681	-18.448	8.919
ATOM	361	N7	GUA	24	-8.758	-17.233	10.233
ATOM	362	C5	GUA	24	-8.428	-15.995	10.772
ATOM	363	C6	GUA	24	-9.149	-15.156	11.673
ATOM	364	O6	GUA	24	-10.260	-15.350	12.162
ATOM	365	N1	GUA	24	-8.462	-13.996	11.993
ATOM	366	H1	GUA	24	-8.959	-13.349	12.606
ATOM	367	C2	GUA	24	-7.221	-13.672	11.497
ATOM	368	N2	GUA	24	-6.640	-12.555	11.919

ATOM	369	HN2A	GUA	24	-7.124	-11.914	12.533
ATOM	370	HN2B	GUA	24	-5.747	-12.298	11.529
ATOM	371	N3	GUA	24	-6.535	-14.451	10.657
ATOM	372	C4	GUA	24	-7.195	-15.591	10.324
ATOM	373	C3'	GUA	24	-3.859	-17.599	7.395
ATOM	374	H3'	GUA	24	-3.620	-18.511	6.847
ATOM	375	C2'	GUA	24	-4.780	-17.878	8.576
ATOM	376	H2A'	GUA	24	-4.238	-18.155	9.480
ATOM	377	H2B'	GUA	24	-5.479	-18.663	8.287
ATOM	378	O3'	GUA	24	-2.665	-17.001	7.860
ATOM	379	H	HE	25	-2.886	-16.191	8.326
ATOM	380	H	HB	26	-9.987	-9.185	19.021
ATOM	381	O5'	CYT	27	-9.675	-8.323	19.305
ATOM	382	C5'	CYT	27	-8.282	-8.253	19.083
ATOM	383	H5A'	CYT	27	-7.914	-7.281	19.413
ATOM	384	H5B'	CYT	27	-7.788	-9.033	19.663
ATOM	385	C4'	CYT	27	-7.961	-8.443	17.599
ATOM	386	H4'	CYT	27	-6.878	-8.415	17.473
ATOM	387	O1'	CYT	27	-8.413	-9.710	17.146
ATOM	388	C1'	CYT	27	-8.820	-9.532	15.806
ATOM	389	H1'	CYT	27	-7.926	-9.391	15.197
ATOM	390	N1	CYT	27	-9.656	-10.672	15.347
ATOM	391	C6	CYT	27	-10.713	-11.113	16.100
ATOM	392	H6	CYT	27	-10.953	-10.603	17.021
ATOM	393	C5	CYT	27	-11.452	-12.182	15.720
ATOM	394	H5	CYT	27	-12.277	-12.504	16.339
ATOM	395	C4	CYT	27	-11.070	-12.835	14.506
ATOM	396	N4	CYT	27	-11.731	-13.911	14.095
ATOM	397	HN4A	CYT	27	-11.379	-14.408	13.284
ATOM	398	HN4B	CYT	27	-12.512	-14.270	14.617
ATOM	399	N3	CYT	27	-10.024	-12.425	13.784
ATOM	400	C2	CYT	27	-9.308	-11.334	14.172
ATOM	401	O2	CYT	27	-8.350	-10.981	13.490
ATOM	402	C3'	CYT	27	-8.630	-7.382	16.703
ATOM	403	H3'	CYT	27	-9.163	-6.610	17.262
ATOM	404	C2'	CYT	27	-9.592	-8.219	15.866
ATOM	405	H2A'	CYT	27	-9.763	-7.793	14.876
ATOM	406	H2B'	CYT	27	-10.533	-8.333	16.403
ATOM	407	O3'	CYT	27	-7.700	-6.808	15.813
ATOM	408	P	POM	28	-6.674	-5.666	16.284
ATOM	409	OA	POM	28	-7.316	-4.354	16.062
ATOM	410	OB	POM	28	-6.152	-6.023	17.622
ATOM	411	O5'	GUA	29	-5.515	-5.880	15.195
ATOM	412	C5'	GUA	29	-4.498	-6.846	15.382
ATOM	413	H5A'	GUA	29	-3.688	-6.390	15.952
ATOM	414	H5B'	GUA	29	-4.877	-7.705	15.939
ATOM	415	C4'	GUA	29	-3.965	-7.356	14.037
ATOM	416	H4'	GUA	29	-3.062	-7.938	14.230
ATOM	417	O1'	GUA	29	-4.939	-8.205	13.445
ATOM	418	C1'	GUA	29	-5.216	-7.760	12.130
ATOM	419	H1'	GUA	29	-4.545	-8.266	11.435
ATOM	420	N9	GUA	29	-6.637	-8.048	11.811
ATOM	421	C8	GUA	29	-7.755	-7.513	12.402

ATOM	422	H8	GUA	29	-7.714	-6.717	13.129
ATOM	423	N7	GUA	29	-8.878	-8.055	12.023
ATOM	424	C5	GUA	29	-8.483	-9.038	11.122
ATOM	425	C6	GUA	29	-9.257	-10.026	10.442
ATOM	426	O6	GUA	29	-10.470	-10.218	10.499
ATOM	427	N1	GUA	29	-8.487	-10.875	9.667
ATOM	428	H1	GUA	29	-8.971	-11.661	9.234
ATOM	429	C2	GUA	29	-7.129	-10.770	9.524
ATOM	430	N2	GUA	29	-6.523	-11.649	8.731
ATOM	431	HN2A	GUA	29	-7.053	-12.369	8.248
ATOM	432	HN2B	GUA	29	-5.525	-11.593	8.613
ATOM	433	N3	GUA	29	-6.383	-9.867	10.176
ATOM	434	C4	GUA	29	-7.116	-9.037	10.973
ATOM	435	C3'	GUA	29	-3.653	-6.227	13.045
ATOM	436	H3'	GUA	29	-3.547	-5.266	13.551
ATOM	437	C2'	GUA	29	-4.888	-6.268	12.147
ATOM	438	H2A'	GUA	29	-4.693	-5.859	11.160
ATOM	439	H2B'	GUA	29	-5.680	-5.696	12.628
ATOM	440	O3'	GUA	29	-2.458	-6.548	12.353
ATOM	441	P	POM	30	-1.763	-5.528	11.313
ATOM	442	OA	POM	30	-2.424	-4.210	11.427
ATOM	443	OB	POM	30	-0.296	-5.637	11.474
ATOM	444	O5'	CYT	31	-2.169	-6.181	9.901
ATOM	445	C5'	CYT	31	-1.437	-7.276	9.384
ATOM	446	H5A'	CYT	31	-0.477	-6.930	8.998
ATOM	447	H5B'	CYT	31	-1.258	-8.002	10.180
ATOM	448	C4'	CYT	31	-2.218	-7.985	8.276
ATOM	449	H4'	CYT	31	-1.679	-8.887	7.985
ATOM	450	O1'	CYT	31	-3.498	-8.364	8.751
ATOM	451	C1'	CYT	31	-4.368	-8.502	7.641
ATOM	452	H1'	CYT	31	-4.542	-9.569	7.499
ATOM	453	N1	CYT	31	-5.644	-7.773	7.865
ATOM	454	C6	CYT	31	-5.695	-6.632	8.620
ATOM	455	H6	CYT	31	-4.772	-6.174	8.943
ATOM	456	C5	CYT	31	-6.881	-6.078	8.969
ATOM	457	H5	CYT	31	-6.887	-5.182	9.572
ATOM	458	C4	CYT	31	-8.067	-6.731	8.504
ATOM	459	N4	CYT	31	-9.258	-6.297	8.895
ATOM	460	HN4A	CYT	31	-10.086	-6.778	8.562
ATOM	461	HN4B	CYT	31	-9.339	-5.523	9.531
ATOM	462	N3	CYT	31	-8.017	-7.813	7.720
ATOM	463	C2	CYT	31	-6.810	-8.320	7.347
ATOM	464	O2	CYT	31	-6.772	-9.266	6.566
ATOM	465	C3'	CYT	31	-2.466	-7.149	7.021
ATOM	466	H3'	CYT	31	-2.790	-6.143	7.291
ATOM	467	C2'	CYT	31	-3.619	-7.952	6.433
ATOM	468	H2A'	CYT	31	-3.228	-8.798	5.871
ATOM	469	H2B'	CYT	31	-4.244	-7.338	5.791
ATOM	470	O3'	CYT	31	-1.338	-7.136	6.161
ATOM	471	P	POM	32	-1.324	-6.295	4.781
ATOM	472	OA	POM	32	-1.940	-4.974	5.031
ATOM	473	OB	POM	32	0.038	-6.376	4.209
ATOM	474	O5'	GUA	33	-2.312	-7.124	3.817

ATOM	475	C5'	GUA	33	-1.966	-8.418	3.358
ATOM	476	H5A'	GUA	33	-1.122	-8.358	2.671
ATOM	477	H5B'	GUA	33	-1.670	-9.036	4.206
ATOM	478	C4'	GUA	33	-3.158	-9.095	2.666
ATOM	479	H4'	GUA	33	-2.918	-10.155	2.566
ATOM	480	O1'	GUA	33	-4.332	-8.950	3.459
ATOM	481	C1'	GUA	33	-5.346	-8.354	2.668
ATOM	482	H1'	GUA	33	-5.915	-9.144	2.175
ATOM	483	N9	GUA	33	-6.243	-7.500	3.483
ATOM	484	C8	GUA	33	-5.964	-6.300	4.087
ATOM	485	H8	GUA	33	-4.997	-5.820	4.035
ATOM	486	N7	GUA	33	-6.962	-5.786	4.751
ATOM	487	C5	GUA	33	-7.990	-6.705	4.565
ATOM	488	C6	GUA	33	-9.338	-6.684	5.030
ATOM	489	O6	GUA	33	-9.884	-5.826	5.718
ATOM	490	N1	GUA	33	-10.074	-7.778	4.599
ATOM	491	H1	GUA	33	-11.064	-7.777	4.848
ATOM	492	C2	GUA	33	-9.554	-8.810	3.858
ATOM	493	N2	GUA	33	-10.349	-9.824	3.542
ATOM	494	HN2A	GUA	33	-11.337	-9.825	3.777
ATOM	495	HN2B	GUA	33	-9.947	-10.593	3.034
ATOM	496	N3	GUA	33	-8.294	-8.839	3.412
ATOM	497	C4	GUA	33	-7.561	-7.759	3.795
ATOM	498	C3'	GUA	33	-3.461	-8.520	1.276
ATOM	499	H3'	GUA	33	-2.599	-8.013	0.838
ATOM	500	C2'	GUA	33	-4.595	-7.558	1.605
ATOM	501	H2A'	GUA	33	-5.211	-7.312	0.744
ATOM	502	H2B'	GUA	33	-4.164	-6.648	2.021
ATOM	503	O3'	GUA	33	-3.880	-9.598	0.457
ATOM	504	P	POM	34	-4.188	-9.442	-1.116
ATOM	505	OA	POM	34	-4.078	-8.015	-1.491
ATOM	506	OB	POM	34	-3.401	-10.460	-1.846
ATOM	507	O5'	ADE	35	-5.740	-9.855	-1.179
ATOM	508	C5'	ADE	35	-6.149	-11.182	-0.903
ATOM	509	H5A'	ADE	35	-5.675	-11.867	-1.608
ATOM	510	H5B'	ADE	35	-5.839	-11.451	0.107
ATOM	511	C4'	ADE	35	-7.673	-11.342	-1.003
ATOM	512	H4'	ADE	35	-7.916	-12.370	-0.732
ATOM	513	O1'	ADE	35	-8.305	-10.453	-0.093
ATOM	514	C1'	ADE	35	-9.092	-9.525	-0.819
ATOM	515	H1'	ADE	35	-10.126	-9.871	-0.811
ATOM	516	N9	ADE	35	-8.986	-8.188	-0.191
ATOM	517	C8	ADE	35	-7.904	-7.342	-0.147
ATOM	518	H8	ADE	35	-6.986	-7.539	-0.680
ATOM	519	N7	ADE	35	-8.073	-6.282	0.599
ATOM	520	C5	ADE	35	-9.367	-6.437	1.080
ATOM	521	C6	ADE	35	-10.170	-5.665	1.937
ATOM	522	N6	ADE	35	-9.734	-4.542	2.501
ATOM	523	HN6A	ADE	35	-10.354	-4.013	3.105
ATOM	524	HN6B	ADE	35	-8.781	-4.254	2.338
ATOM	525	N1	ADE	35	-11.413	-6.080	2.220
ATOM	526	C2	ADE	35	-11.834	-7.226	1.699
ATOM	527	H2	ADE	35	-12.830	-7.514	1.987

ATOM	528	N3	ADE	35	-11.187	-8.040	0.874
ATOM	529	C4	ADE	35	-9.937	-7.586	0.599
ATOM	530	C3'	ADE	35	-8.217	-11.039	-2.404
ATOM	531	H3'	ADE	35	-7.459	-11.200	-3.172
ATOM	532	C2'	ADE	35	-8.596	-9.570	-2.263
ATOM	533	H2A'	ADE	35	-9.357	-9.281	-2.982
ATOM	534	H2B'	ADE	35	-7.708	-8.957	-2.406
ATOM	535	O3'	ADE	35	-9.348	-11.864	-2.638
ATOM	536	P	POM	36	-10.103	-11.911	-4.065
ATOM	537	OA	POM	36	-9.286	-11.173	-5.054
ATOM	538	OB	POM	36	-10.495	-13.311	-4.335
ATOM	539	O5'	ADE	37	-11.438	-11.057	-3.789
ATOM	540	C5'	ADE	37	-12.518	-11.612	-3.060
ATOM	541	H5A'	ADE	37	-12.924	-12.473	-3.592
ATOM	542	H5B'	ADE	37	-12.167	-11.936	-2.078
ATOM	543	C4'	ADE	37	-13.626	-10.572	-2.867
ATOM	544	H4'	ADE	37	-14.439	-11.027	-2.297
ATOM	545	O1'	ADE	37	-13.095	-9.490	-2.121
ATOM	546	C1'	ADE	37	-13.580	-8.292	-2.679
ATOM	547	H1'	ADE	37	-14.589	-8.099	-2.311
ATOM	548	N9	ADE	37	-12.652	-7.192	-2.342
ATOM	549	C8	ADE	37	-11.335	-7.055	-2.704
ATOM	550	H8	ADE	37	-10.841	-7.741	-3.371
ATOM	551	N7	ADE	37	-10.733	-6.017	-2.192
ATOM	552	C5	ADE	37	-11.732	-5.420	-1.435
ATOM	553	C6	ADE	37	-11.756	-4.271	-0.630
ATOM	554	N6	ADE	37	-10.682	-3.506	-0.437
ATOM	555	HN6A	ADE	37	-10.708	-2.707	0.188
ATOM	556	HN6B	ADE	37	-9.818	-3.791	-0.877
ATOM	557	N1	ADE	37	-12.900	-3.932	-0.022
ATOM	558	C2	ADE	37	-13.972	-4.700	-0.183
ATOM	559	H2	ADE	37	-14.868	-4.367	0.319
ATOM	560	N3	ADE	37	-14.080	-5.806	-0.906
ATOM	561	C4	ADE	37	-12.907	-6.123	-1.515
ATOM	562	C3'	ADE	37	-14.176	-10.011	-4.191
ATOM	563	H3'	ADE	37	-13.806	-10.573	-5.051
ATOM	564	C2'	ADE	37	-13.624	-8.587	-4.175
ATOM	565	H2A'	ADE	37	-14.245	-7.884	-4.723
ATOM	566	H2B'	ADE	37	-12.623	-8.613	-4.604
ATOM	567	O3'	ADE	37	-15.595	-10.040	-4.169
ATOM	568	P	POM	38	-16.496	-9.549	-5.418
ATOM	569	OA	POM	38	-15.606	-9.273	-6.567
ATOM	570	OB	POM	38	-17.627	-10.491	-5.574
ATOM	571	O5'	THY	39	-17.071	-8.145	-4.882
ATOM	572	C5'	THY	39	-18.125	-8.120	-3.936
ATOM	573	H5A'	THY	39	-19.064	-8.394	-4.418
ATOM	574	H5B'	THY	39	-17.912	-8.842	-3.147
ATOM	575	C4'	THY	39	-18.261	-6.741	-3.284
ATOM	576	H4'	THY	39	-18.959	-6.817	-2.450
ATOM	577	O1'	THY	39	-17.007	-6.307	-2.789
ATOM	578	C1'	THY	39	-17.043	-4.896	-2.668
ATOM	579	H1'	THY	39	-17.103	-4.647	-1.614
ATOM	580	N1	THY	39	-15.835	-4.245	-3.231

ATOM	581	C6	THY	39	-14.997	-4.894	-4.108
ATOM	582	H6	THY	39	-15.295	-5.859	-4.490
ATOM	583	C5	THY	39	-13.815	-4.344	-4.490
ATOM	584	C7	THY	39	-12.909	-5.075	-5.464
ATOM	585	H7A	THY	39	-13.411	-5.932	-5.915
ATOM	586	H7B	THY	39	-12.611	-4.387	-6.256
ATOM	587	H7C	THY	39	-12.014	-5.412	-4.942
ATOM	588	C4	THY	39	-13.405	-3.050	-3.976
ATOM	589	O4	THY	39	-12.324	-2.498	-4.171
ATOM	590	N3	THY	39	-14.348	-2.429	-3.192
ATOM	591	H3	THY	39	-14.133	-1.500	-2.848
ATOM	592	C2	THY	39	-15.556	-2.957	-2.794
ATOM	593	O2	THY	39	-16.325	-2.294	-2.103
ATOM	594	C3'	THY	39	-18.744	-5.622	-4.207
ATOM	595	H3'	THY	39	-18.194	-5.659	-5.149
ATOM	596	C2'	THY	39	-18.314	-4.426	-3.368
ATOM	597	H2A'	THY	39	-19.065	-4.224	-2.605
ATOM	598	H2B'	THY	39	-18.161	-3.539	-3.974
ATOM	599	O3'	THY	39	-20.149	-5.634	-4.395
ATOM	600	P	POM	40	-20.872	-4.681	-5.482
ATOM	601	OA	POM	40	-20.088	-4.730	-6.736
ATOM	602	OB	POM	40	-22.312	-5.022	-5.504
ATOM	603	O5'	THY	41	-20.730	-3.188	-4.896
ATOM	604	C5'	THY	41	-21.444	-2.765	-3.749
ATOM	605	H5A'	THY	41	-22.518	-2.848	-3.920
ATOM	606	H5B'	THY	41	-21.180	-3.392	-2.898
ATOM	607	C4'	THY	41	-21.090	-1.308	-3.422
ATOM	608	H4'	THY	41	-21.511	-1.063	-2.446
ATOM	609	O1'	THY	41	-19.674	-1.171	-3.368
ATOM	610	C1'	THY	41	-19.289	-0.047	-4.136
ATOM	611	H1'	THY	41	-19.331	0.833	-3.493
ATOM	612	N1	THY	41	-17.942	-0.269	-4.733
ATOM	613	C6	THY	41	-17.710	-1.378	-5.513
ATOM	614	H6	THY	41	-18.521	-2.069	-5.690
ATOM	615	C5	THY	41	-16.495	-1.628	-6.061
ATOM	616	C7	THY	41	-16.297	-2.850	-6.938
ATOM	617	H7A	THY	41	-16.267	-2.538	-7.982
ATOM	618	H7B	THY	41	-15.352	-3.332	-6.691
ATOM	619	H7C	THY	41	-17.107	-3.572	-6.806
ATOM	620	C4	THY	41	-15.389	-0.718	-5.839
ATOM	621	O4	THY	41	-14.250	-0.859	-6.274
ATOM	622	N3	THY	41	-15.700	0.377	-5.065
ATOM	623	H3	THY	41	-14.949	1.044	-4.911
ATOM	624	C2	THY	41	-16.928	0.658	-4.499
ATOM	625	O2	THY	41	-17.074	1.688	-3.845
ATOM	626	C3'	THY	41	-21.633	-0.320	-4.470
ATOM	627	H3'	THY	41	-22.350	-0.796	-5.141
ATOM	628	C2'	THY	41	-20.363	0.073	-5.214
ATOM	629	H2A'	THY	41	-20.415	1.072	-5.630
ATOM	630	H2B'	THY	41	-20.218	-0.646	-6.019
ATOM	631	O3'	THY	41	-22.245	0.777	-3.811
ATOM	632	P	POM	42	-22.940	2.002	-4.606
ATOM	633	OA	POM	42	-23.022	1.663	-6.044

ATOM	634	OB	POM	42	-24.160	2.403	-3.871
ATOM	635	O5'	CYT	43	-21.844	3.166	-4.431
ATOM	636	C5'	CYT	43	-21.564	3.677	-3.143
ATOM	637	H5A'	CYT	43	-22.425	4.227	-2.761
ATOM	638	H5B'	CYT	43	-21.356	2.846	-2.468
ATOM	639	C4'	CYT	43	-20.330	4.582	-3.141
ATOM	640	H4'	CYT	43	-20.059	4.726	-2.098
ATOM	641	O1'	CYT	43	-19.256	3.952	-3.818
ATOM	642	C1'	CYT	43	-18.745	4.849	-4.786
ATOM	643	H1'	CYT	43	-18.003	5.480	-4.300
ATOM	644	N1	CYT	43	-18.165	4.075	-5.914
ATOM	645	C6	CYT	43	-18.927	3.156	-6.585
ATOM	646	H6	CYT	43	-19.994	3.134	-6.414
ATOM	647	C5	CYT	43	-18.369	2.257	-7.428
ATOM	648	H5	CYT	43	-19.004	1.544	-7.933
ATOM	649	C4	CYT	43	-16.952	2.321	-7.600
ATOM	650	N4	CYT	43	-16.337	1.400	-8.333
ATOM	651	HN4A	CYT	43	-15.333	1.462	-8.453
ATOM	652	HN4B	CYT	43	-16.868	0.703	-8.826
ATOM	653	N3	CYT	43	-16.205	3.243	-6.981
ATOM	654	C2	CYT	43	-16.792	4.137	-6.136
ATOM	655	O2	CYT	43	-16.088	4.984	-5.587
ATOM	656	C3'	CYT	43	-20.522	5.965	-3.771
ATOM	657	H3'	CYT	43	-21.569	6.270	-3.792
ATOM	658	C2'	CYT	43	-19.916	5.759	-5.155
ATOM	659	H2A'	CYT	43	-19.588	6.698	-5.596
ATOM	660	H2B'	CYT	43	-20.640	5.255	-5.795
ATOM	661	O3'	CYT	43	-19.710	6.829	-2.996
ATOM	662	P	POM	44	-19.948	8.411	-2.883
ATOM	663	OA	POM	44	-21.399	8.686	-2.853
ATOM	664	OB	POM	44	-19.076	8.834	-1.763
ATOM	665	O5'	GUA	45	-19.320	8.980	-4.247
ATOM	666	C5'	GUA	45	-18.266	9.924	-4.218
ATOM	667	H5A'	GUA	45	-18.629	10.878	-3.831
ATOM	668	H5B'	GUA	45	-17.461	9.566	-3.575
ATOM	669	C4'	GUA	45	-17.674	10.121	-5.613
ATOM	670	H4'	GUA	45	-16.792	10.750	-5.520
ATOM	671	O1'	GUA	45	-17.276	8.860	-6.133
ATOM	672	C1'	GUA	45	-17.613	8.876	-7.500
ATOM	673	H1'	GUA	45	-16.885	9.497	-8.019
ATOM	674	N9	GUA	45	-17.607	7.525	-8.101
ATOM	675	C8	GUA	45	-18.646	6.648	-8.288
ATOM	676	H8	GUA	45	-19.660	6.844	-7.973
ATOM	677	N7	GUA	45	-18.311	5.544	-8.894
ATOM	678	C5	GUA	45	-16.951	5.702	-9.141
ATOM	679	C6	GUA	45	-16.026	4.839	-9.797
ATOM	680	O6	GUA	45	-16.246	3.738	-10.293
ATOM	681	N1	GUA	45	-14.743	5.363	-9.848
ATOM	682	H1	GUA	45	-14.051	4.779	-10.318
ATOM	683	C2	GUA	45	-14.394	6.596	-9.353
ATOM	684	N2	GUA	45	-13.138	7.002	-9.503
ATOM	685	HN2A	GUA	45	-12.440	6.405	-9.927
ATOM	686	HN2B	GUA	45	-12.892	7.938	-9.218

ATOM	687	N3	GUA	45	-15.252	7.413	-8.734
ATOM	688	C4	GUA	45	-16.511	6.908	-8.657
ATOM	689	C3'	GUA	45	-18.667	10.749	-6.609
ATOM	690	H3'	GUA	45	-19.572	11.132	-6.134
ATOM	691	C2'	GUA	45	-18.975	9.564	-7.516
ATOM	692	H2A'	GUA	45	-19.291	9.870	-8.513
ATOM	693	H2B'	GUA	45	-19.735	8.948	-7.034
ATOM	694	O3'	GUA	45	-18.061	11.739	-7.421
ATOM	695	P	POM	46	-17.739	13.222	-6.877
ATOM	696	OA	POM	46	-18.591	14.172	-7.624
ATOM	697	OB	POM	46	-17.764	13.203	-5.399
ATOM	698	O5'	CYT	47	-16.217	13.407	-7.370
ATOM	699	C5'	CYT	47	-15.123	13.224	-6.490
ATOM	700	H5A'	CYT	47	-14.972	14.133	-5.908
ATOM	701	H5B'	CYT	47	-15.311	12.400	-5.803
ATOM	702	C4'	CYT	47	-13.849	12.880	-7.271
ATOM	703	H4'	CYT	47	-13.039	12.747	-6.553
ATOM	704	O1'	CYT	47	-14.062	11.657	-7.960
ATOM	705	C1'	CYT	47	-13.758	11.820	-9.331
ATOM	706	H1'	CYT	47	-12.709	11.556	-9.469
ATOM	707	N1	CYT	47	-14.687	10.967	-10.130
ATOM	708	C6	CYT	47	-16.043	11.165	-10.056
ATOM	709	H6	CYT	47	-16.431	12.004	-9.502
ATOM	710	C5	CYT	47	-16.918	10.310	-10.630
ATOM	711	H5	CYT	47	-17.976	10.508	-10.543
ATOM	712	C4	CYT	47	-16.370	9.182	-11.309
ATOM	713	N4	CYT	47	-17.188	8.244	-11.772
ATOM	714	HN4A	CYT	47	-16.803	7.403	-12.184
ATOM	715	HN4B	CYT	47	-18.182	8.355	-11.677
ATOM	716	N3	CYT	47	-15.051	8.990	-11.422
ATOM	717	C2	CYT	47	-14.188	9.871	-10.835
ATOM	718	O2	CYT	47	-12.979	9.664	-10.937
ATOM	719	C3'	CYT	47	-13.456	13.955	-8.293
ATOM	720	H3'	CYT	47	-13.990	14.887	-8.098
ATOM	721	C2'	CYT	47	-13.898	13.319	-9.610
ATOM	722	H2A'	CYT	47	-13.276	13.633	-10.443
ATOM	723	H2B'	CYT	47	-14.931	13.610	-9.792
ATOM	724	O3'	CYT	47	-12.053	14.164	-8.228
ATOM	725	P	POM	48	-11.329	15.412	-8.956
ATOM	726	OA	POM	48	-12.288	16.534	-9.049
ATOM	727	OB	POM	48	-10.011	15.623	-8.320
ATOM	728	O5'	GUA	49	-11.074	14.850	-10.439
ATOM	729	C5'	GUA	49	-9.987	13.987	-10.705
ATOM	730	H5A'	GUA	49	-9.057	14.557	-10.692
ATOM	731	H5B'	GUA	49	-9.936	13.205	-9.946
ATOM	732	C4'	GUA	49	-10.167	13.321	-12.071
ATOM	733	H4'	GUA	49	-9.311	12.674	-12.271
ATOM	734	O1'	GUA	49	-11.336	12.532	-12.087
ATOM	735	C1'	GUA	49	-11.619	12.261	-13.442
ATOM	736	H1'	GUA	49	-10.991	11.428	-13.762
ATOM	737	N9	GUA	49	-13.052	11.932	-13.593
ATOM	738	C8	GUA	49	-14.137	12.605	-13.092
ATOM	739	H8	GUA	49	-14.055	13.538	-12.556

ATOM	740	N7	GUA	49	-15.279	12.021	-13.319
ATOM	741	C5	GUA	49	-14.931	10.885	-14.042
ATOM	742	C6	GUA	49	-15.745	9.842	-14.573
ATOM	743	O6	GUA	49	-16.961	9.696	-14.471
ATOM	744	N1	GUA	49	-15.014	8.907	-15.284
ATOM	745	H1	GUA	49	-15.545	8.115	-15.641
ATOM	746	C2	GUA	49	-13.654	8.948	-15.457
ATOM	747	N2	GUA	49	-13.090	7.990	-16.184
ATOM	748	HN2A	GUA	49	-13.650	7.272	-16.631
ATOM	749	HN2B	GUA	49	-12.085	7.952	-16.240
ATOM	750	N3	GUA	49	-12.874	9.901	-14.937
ATOM	751	C4	GUA	49	-13.572	10.835	-14.237
ATOM	752	C3'	GUA	49	-10.344	14.302	-13.233
ATOM	753	H3'	GUA	49	-10.878	15.197	-12.914
ATOM	754	C2'	GUA	49	-11.217	13.521	-14.218
ATOM	755	H2A'	GUA	49	-10.664	13.243	-15.115
ATOM	756	H2B'	GUA	49	-12.086	14.122	-14.488
ATOM	757	O3'	GUA	49	-9.106	14.653	-13.815
ATOM	758	H	HE	50	-8.661	13.851	-14.099
ATOM	759	O1	DIS	51	-12.064	-12.764	1.614
ATOM	760	C1	DIS	51	-11.646	-11.695	1.174
ATOM	761	HF	DIS	51	-10.578	-11.590	1.054
ATOM	762	N1	DIS	51	-12.411	-10.630	0.901
ATOM	763	HN1	DIS	51	-11.909	-9.787	0.642
ATOM	764	C2	DIS	51	-13.818	-10.423	0.959
ATOM	765	C3	DIS	51	-14.591	-9.284	0.668
ATOM	766	H3	DIS	51	-14.232	-8.287	0.470
ATOM	767	C5	DIS	51	-14.654	-11.518	0.919
ATOM	768	H5	DIS	51	-14.378	-12.559	0.982
ATOM	769	N2	DIS	51	-15.937	-11.073	0.709
ATOM	770	C6	DIS	51	-17.130	-11.950	0.533
ATOM	771	HM1	DIS	51	-17.342	-12.198	-0.507
ATOM	772	HM2	DIS	51	-17.049	-12.919	1.025
ATOM	773	HM3	DIS	51	-18.068	-11.541	0.904
ATOM	774	C4	DIS	51	-15.900	-9.700	0.544
ATOM	775	C7	DIS	51	-17.040	-8.804	0.149
ATOM	776	O2	DIS	51	-17.923	-9.271	-0.567
ATOM	777	N3	DIS	51	-17.072	-7.555	0.648
ATOM	778	HN3	DIS	51	-16.283	-7.265	1.215
ATOM	779	C8	DIS	51	-18.068	-6.550	0.481
ATOM	780	C9	DIS	51	-18.081	-5.152	0.664
ATOM	781	H9	DIS	51	-17.236	-4.522	0.905
ATOM	782	C11	DIS	51	-19.371	-6.962	0.308
ATOM	783	H11	DIS	51	-19.736	-7.975	0.250
ATOM	784	N4	DIS	51	-20.164	-5.849	0.206
ATOM	785	C12	DIS	51	-21.633	-5.861	-0.028
ATOM	786	HM4	DIS	51	-22.226	-5.543	0.830
ATOM	787	HM5	DIS	51	-21.965	-5.221	-0.846
ATOM	788	HM6	DIS	51	-22.039	-6.841	-0.280
ATOM	789	C10	DIS	51	-19.375	-4.731	0.399
ATOM	790	C13	DIS	51	-19.866	-3.308	0.425
ATOM	791	O3	DIS	51	-21.063	-3.117	0.643
ATOM	792	N5	DIS	51	-19.021	-2.304	0.137

ATOM	793	HN5	DIS	51	-18.090	-2.549	-0.173
ATOM	794	C14	DIS	51	-19.293	-0.905	0.165
ATOM	795	C15	DIS	51	-18.688	0.226	-0.421
ATOM	796	H15	DIS	51	-17.947	0.219	-1.205
ATOM	797	C17	DIS	51	-20.153	-0.461	1.145
ATOM	798	H17	DIS	51	-20.723	-1.065	1.834
ATOM	799	N6	DIS	51	-20.181	0.908	1.114
ATOM	800	C18	DIS	51	-21.023	1.768	1.993
ATOM	801	HM7	DIS	51	-21.835	2.276	1.470
ATOM	802	HM8	DIS	51	-21.522	1.231	2.800
ATOM	803	HM9	DIS	51	-20.487	2.567	2.503
ATOM	804	C16	DIS	51	-19.263	1.340	0.176
ATOM	805	C19	DIS	51	-18.964	2.782	-0.142
ATOM	806	O4	DIS	51	-19.835	3.617	0.095
ATOM	807	N7	DIS	51	-17.716	3.140	-0.474
ATOM	808	HN7	DIS	51	-16.994	2.433	-0.544
ATOM	809	C20	DIS	51	-17.316	4.539	-0.596
ATOM	810	HC1	DIS	51	-18.187	5.183	-0.709
ATOM	811	HC2	DIS	51	-16.785	4.841	0.307
ATOM	812	C21	DIS	51	-16.410	4.739	-1.813
ATOM	813	HC3	DIS	51	-15.491	4.189	-1.630
ATOM	814	HC4	DIS	51	-16.893	4.297	-2.682
ATOM	815	C22	DIS	51	-16.041	6.179	-2.131
ATOM	816	N8	DIS	51	-14.818	6.458	-2.608
ATOM	817	HNC	DIS	51	-14.545	7.403	-2.831
ATOM	818	HND	DIS	51	-14.129	5.720	-2.681
ATOM	819	N9	DIS	51	-16.922	7.179	-1.962
ATOM	820	HNA	DIS	51	-16.692	8.137	-2.178
ATOM	821	HNB	DIS	51	-17.885	7.023	-1.680

Coordinates for H_I, idealized d(CGCGAATTCGCG)₂ with
 Distamcyin A, K_{NMR} = 10,000 kcal·mol⁻¹·Å⁻²

ATOM	1	H	HB	1	-0.118	9.810	1.829
ATOM	2	O5'	CYT	2	0.272	9.077	1.346
ATOM	3	C5'	CYT	2	1.363	8.579	2.091
ATOM	4	H5A'	CYT	2	2.102	9.370	2.221
ATOM	5	H5B'	CYT	2	1.006	8.262	3.071
ATOM	6	C4'	CYT	2	2.012	7.389	1.380
ATOM	7	H4'	CYT	2	2.806	6.997	2.019
ATOM	8	O1'	CYT	2	1.082	6.345	1.166
ATOM	9	C1'	CYT	2	1.622	5.544	0.136
ATOM	10	H1'	CYT	2	2.460	4.985	0.556
ATOM	11	N1	CYT	2	0.575	4.665	-0.449
ATOM	12	C6	CYT	2	-0.684	5.146	-0.701
ATOM	13	H6	CYT	2	-0.884	6.198	-0.552
ATOM	14	C5	CYT	2	-1.684	4.330	-1.108
ATOM	15	H5	CYT	2	-2.665	4.742	-1.292
ATOM	16	C4	CYT	2	-1.368	2.942	-1.254
ATOM	17	N4	CYT	2	-2.332	2.070	-1.526
ATOM	18	HN4A	CYT	2	-2.109	1.080	-1.514
ATOM	19	HN4B	CYT	2	-3.268	2.380	-1.722
ATOM	20	N3	CYT	2	-0.140	2.471	-1.019
ATOM	21	C2	CYT	2	0.862	3.319	-0.658
ATOM	22	O2	CYT	2	1.996	2.871	-0.508
ATOM	23	C3'	CYT	2	2.610	7.736	0.009
ATOM	24	H3'	CYT	2	2.190	8.668	-0.373
ATOM	25	C2'	CYT	2	2.158	6.561	-0.867
ATOM	26	H2A'	CYT	2	2.966	6.128	-1.452
ATOM	27	H2B'	CYT	2	1.366	6.906	-1.532
ATOM	28	O3'	CYT	2	4.014	7.842	0.146
ATOM	29	P	POM	3	4.967	8.306	-1.071
ATOM	30	OA	POM	3	4.161	9.124	-2.003
ATOM	31	OB	POM	3	6.210	8.856	-0.489
ATOM	32	O5'	GUA	4	5.316	6.906	-1.781
ATOM	33	C5'	GUA	4	6.134	5.956	-1.125
ATOM	34	H5A'	GUA	4	7.150	6.343	-1.043
ATOM	35	H5B'	GUA	4	5.748	5.767	-0.123
ATOM	36	C4'	GUA	4	6.161	4.625	-1.884
ATOM	37	H4'	GUA	4	6.784	3.932	-1.316
ATOM	38	O1'	GUA	4	4.857	4.070	-1.966
ATOM	39	C1'	GUA	4	4.746	3.424	-3.218
ATOM	40	H1'	GUA	4	5.255	2.459	-3.180
ATOM	41	N9	GUA	4	3.319	3.270	-3.582
ATOM	42	C8	GUA	4	2.373	4.253	-3.718
ATOM	43	H8	GUA	4	2.605	5.306	-3.656
ATOM	44	N7	GUA	4	1.161	3.812	-3.908
ATOM	45	C5	GUA	4	1.312	2.428	-3.908
ATOM	46	C6	GUA	4	0.336	1.394	-4.030
ATOM	47	O6	GUA	4	-0.875	1.515	-4.186
ATOM	48	N1	GUA	4	0.877	0.121	-3.928
ATOM	49	H1	GUA	4	0.217	-0.658	-3.923
ATOM	50	C2	GUA	4	2.220	-0.130	-3.795

ATOM	51	N2	GUA	4	2.617	-1.396	-3.738
ATOM	52	HN2A	GUA	4	1.952	-2.161	-3.761
ATOM	53	HN2B	GUA	4	3.601	-1.587	-3.636
ATOM	54	N3	GUA	4	3.146	0.828	-3.689
ATOM	55	C4	GUA	4	2.630	2.086	-3.731
ATOM	56	C3'	GUA	4	6.715	4.742	-3.313
ATOM	57	H3'	GUA	4	7.056	5.754	-3.540
ATOM	58	C2'	GUA	4	5.497	4.362	-4.156
ATOM	59	H2A'	GUA	4	5.760	3.892	-5.101
ATOM	60	H2B'	GUA	4	4.918	5.267	-4.339
ATOM	61	O3'	GUA	4	7.785	3.821	-3.433
ATOM	62	P	POM	5	8.663	3.664	-4.776
ATOM	63	OA	POM	5	8.245	4.697	-5.748
ATOM	64	OB	POM	5	10.084	3.540	-4.386
ATOM	65	O5'	CYT	6	8.153	2.234	-5.303
ATOM	66	C5'	CYT	6	8.461	1.056	-4.581
ATOM	67	H5A'	CYT	6	9.537	0.873	-4.605
ATOM	68	H5B'	CYT	6	8.146	1.170	-3.543
ATOM	69	C4'	CYT	6	7.727	-0.149	-5.173
ATOM	70	H4'	CYT	6	7.900	-1.012	-4.528
ATOM	71	O1'	CYT	6	6.336	0.111	-5.192
ATOM	72	C1'	CYT	6	5.776	-0.470	-6.351
ATOM	73	H1'	CYT	6	5.554	-1.515	-6.132
ATOM	74	N1	CYT	6	4.579	0.330	-6.735
ATOM	75	C6	CYT	6	4.668	1.696	-6.799
ATOM	76	H6	CYT	6	5.634	2.164	-6.668
ATOM	77	C5	CYT	6	3.577	2.468	-7.001
ATOM	78	H5	CYT	6	3.690	3.541	-7.043
ATOM	79	C4	CYT	6	2.326	1.793	-7.147
ATOM	80	N4	CYT	6	1.214	2.509	-7.253
ATOM	81	HN4A	CYT	6	0.324	2.036	-7.335
ATOM	82	HN4B	CYT	6	1.249	3.514	-7.220
ATOM	83	N3	CYT	6	2.223	0.461	-7.075
ATOM	84	C2	CYT	6	3.345	-0.298	-6.894
ATOM	85	O2	CYT	6	3.236	-1.521	-6.864
ATOM	86	C3'	CYT	6	8.183	-0.487	-6.599
ATOM	87	H3'	CYT	6	8.903	0.248	-6.962
ATOM	88	C2'	CYT	6	6.883	-0.404	-7.403
ATOM	89	H2A'	CYT	6	6.787	-1.215	-8.120
ATOM	90	H2B'	CYT	6	6.871	0.550	-7.929
ATOM	91	O3'	CYT	6	8.767	-1.780	-6.580
ATOM	92	P	POM	7	9.515	-2.421	-7.859
ATOM	93	OA	POM	7	9.976	-1.328	-8.743
ATOM	94	OB	POM	7	10.479	-3.431	-7.369
ATOM	95	O5'	GUA	8	8.311	-3.193	-8.587
ATOM	96	C5'	GUA	8	7.727	-4.333	-7.988
ATOM	97	H5A'	GUA	8	8.408	-5.182	-8.061
ATOM	98	H5B'	GUA	8	7.520	-4.134	-6.936
ATOM	99	C4'	GUA	8	6.401	-4.669	-8.672
ATOM	100	H4'	GUA	8	5.928	-5.489	-8.128
ATOM	101	O1'	GUA	8	5.530	-3.555	-8.612
ATOM	102	C1'	GUA	8	4.666	-3.636	-9.722
ATOM	103	H1'	GUA	8	3.889	-4.374	-9.521

ATOM	104	N9	GUA	8	4.096	-2.298	-9.997
ATOM	105	C8	GUA	8	4.764	-1.115	-10.187
ATOM	106	H8	GUA	8	5.840	-1.049	-10.238
ATOM	107	N7	GUA	8	3.991	-0.069	-10.279
ATOM	108	C5	GUA	8	2.710	-0.598	-10.165
ATOM	109	C6	GUA	8	1.440	0.052	-10.179
ATOM	110	O6	GUA	8	1.206	1.254	-10.276
ATOM	111	N1	GUA	8	0.384	-0.839	-10.079
ATOM	112	H1	GUA	8	-0.546	-0.424	-10.122
ATOM	113	C2	GUA	8	0.527	-2.195	-9.919
ATOM	114	N2	GUA	8	-0.569	-2.929	-9.782
ATOM	115	HN2A	GUA	8	-1.493	-2.536	-9.922
ATOM	116	HN2B	GUA	8	-0.471	-3.906	-9.563
ATOM	117	N3	GUA	8	1.711	-2.812	-9.871
ATOM	118	C4	GUA	8	2.762	-1.962	-10.006
ATOM	119	C3'	GUA	8	6.551	-5.069	-10.148
ATOM	120	H3'	GUA	8	7.566	-4.885	-10.505
ATOM	121	C2'	GUA	8	5.562	-4.134	-10.853
ATOM	122	H2A'	GUA	8	4.980	-4.625	-11.629
ATOM	123	H2B'	GUA	8	6.127	-3.307	-11.282
ATOM	124	O3'	GUA	8	6.232	-6.445	-10.263
ATOM	125	P	POM	9	6.336	-7.254	-11.654
ATOM	126	OA	POM	9	7.284	-6.554	-12.547
ATOM	127	OB	POM	9	6.532	-8.688	-11.344
ATOM	128	O5'	ADE	10	4.854	-7.068	-12.241
ATOM	129	C5'	ADE	10	3.743	-7.643	-11.582
ATOM	130	H5A'	ADE	10	3.808	-8.730	-11.636
ATOM	131	H5B'	ADE	10	3.735	-7.342	-10.533
ATOM	132	C4'	ADE	10	2.433	-7.180	-12.224
ATOM	133	H4'	ADE	10	1.610	-7.662	-11.693
ATOM	134	O1'	ADE	10	2.304	-5.769	-12.102
ATOM	135	C1'	ADE	10	1.922	-5.266	-13.366
ATOM	136	H1'	ADE	10	0.848	-5.407	-13.493
ATOM	137	N9	ADE	10	2.248	-3.828	-13.493
ATOM	138	C8	ADE	10	3.465	-3.228	-13.707
ATOM	139	H8	ADE	10	4.383	-3.782	-13.833
ATOM	140	N7	ADE	10	3.422	-1.923	-13.750
ATOM	141	C5	ADE	10	2.076	-1.641	-13.541
ATOM	142	C6	ADE	10	1.349	-0.441	-13.456
ATOM	143	N6	ADE	10	1.932	0.750	-13.538
ATOM	144	HN6A	ADE	10	1.377	1.585	-13.398
ATOM	145	HN6B	ADE	10	2.932	0.796	-13.665
ATOM	146	N1	ADE	10	0.022	-0.490	-13.254
ATOM	147	C2	ADE	10	-0.553	-1.677	-13.118
ATOM	148	H2	ADE	10	-1.611	-1.648	-12.929
ATOM	149	N3	ADE	10	0.012	-2.876	-13.174
ATOM	150	C4	ADE	10	1.351	-2.791	-13.391
ATOM	151	C3'	ADE	10	2.354	-7.528	-13.718
ATOM	152	H3'	ADE	10	3.073	-8.298	-14.003
ATOM	153	C2'	ADE	10	2.654	-6.171	-14.352
ATOM	154	H2A'	ADE	10	2.289	-6.089	-15.374
ATOM	155	H2B'	ADE	10	3.729	-5.997	-14.323
ATOM	156	O3'	ADE	10	1.025	-7.937	-13.988

ATOM	157	P	POM	11	0.615	-8.735	-15.324
ATOM	158	OA	POM	11	1.581	-8.406	-16.394
ATOM	159	OB	POM	11	0.348	-10.145	-14.967
ATOM	160	O5'	ADE	12	-0.776	-8.019	-15.681
ATOM	161	C5'	ADE	12	-1.907	-8.154	-14.844
ATOM	162	H5A'	ADE	12	-2.266	-9.183	-14.881
ATOM	163	H5B'	ADE	12	-1.643	-7.909	-13.814
ATOM	164	C4'	ADE	12	-3.023	-7.205	-15.296
ATOM	165	H4'	ADE	12	-3.890	-7.376	-14.656
ATOM	166	O1'	ADE	12	-2.593	-5.861	-15.135
ATOM	167	C1'	ADE	12	-2.654	-5.167	-16.369
ATOM	168	H1'	ADE	12	-3.573	-4.581	-16.412
ATOM	169	N9	ADE	12	-1.443	-4.316	-16.479
ATOM	170	C8	ADE	12	-0.148	-4.703	-16.238
ATOM	171	H8	ADE	12	0.116	-5.719	-16.001
ATOM	172	N7	ADE	12	0.734	-3.746	-16.305
ATOM	173	C5	ADE	12	-0.037	-2.637	-16.619
ATOM	174	C6	ADE	12	0.294	-1.287	-16.801
ATOM	175	N6	ADE	12	1.533	-0.825	-16.628
ATOM	176	HN6A	ADE	12	1.742	0.166	-16.695
ATOM	177	HN6B	ADE	12	2.253	-1.485	-16.366
ATOM	178	N1	ADE	12	-0.676	-0.418	-17.103
ATOM	179	C2	ADE	12	-1.926	-0.855	-17.232
ATOM	180	H2	ADE	12	-2.648	-0.096	-17.530
ATOM	181	N3	ADE	12	-2.370	-2.101	-17.077
ATOM	182	C4	ADE	12	-1.365	-2.963	-16.749
ATOM	183	C3'	ADE	12	-3.405	-7.415	-16.765
ATOM	184	H3'	ADE	12	-3.057	-8.380	-17.138
ATOM	185	C2'	ADE	12	-2.674	-6.256	-17.439
ATOM	186	H2A'	ADE	12	-3.171	-5.932	-18.346
ATOM	187	H2B'	ADE	12	-1.662	-6.585	-17.672
ATOM	188	O3'	ADE	12	-4.814	-7.343	-16.872
ATOM	189	P	POM	13	-5.597	-7.555	-18.264
ATOM	190	OA	POM	13	-4.650	-8.068	-19.279
ATOM	191	OB	POM	13	-6.852	-8.288	-17.987
ATOM	192	O5'	THY	14	-5.966	-6.040	-18.644
ATOM	193	C5'	THY	14	-6.799	-5.277	-17.791
ATOM	194	H5A'	THY	14	-7.802	-5.703	-17.765
ATOM	195	H5B'	THY	14	-6.388	-5.281	-16.781
ATOM	196	C4'	THY	14	-6.869	-3.827	-18.269
ATOM	197	H4'	THY	14	-7.442	-3.255	-17.539
ATOM	198	O1'	THY	14	-5.555	-3.299	-18.338
ATOM	199	C1'	THY	14	-5.435	-2.536	-19.518
ATOM	200	H1'	THY	14	-5.815	-1.534	-19.317
ATOM	201	N1	THY	14	-4.013	-2.549	-19.955
ATOM	202	C6	THY	14	-3.348	-3.745	-20.099
ATOM	203	H6	THY	14	-3.912	-4.659	-19.994
ATOM	204	C5	THY	14	-2.014	-3.799	-20.344
ATOM	205	C7	THY	14	-1.312	-5.136	-20.495
ATOM	206	H7A	THY	14	-0.641	-5.288	-19.649
ATOM	207	H7B	THY	14	-2.024	-5.962	-20.540
ATOM	208	H7C	THY	14	-0.721	-5.129	-21.412
ATOM	209	C4	THY	14	-1.240	-2.579	-20.454

ATOM	210	O4	THY	14	-0.022	-2.507	-20.595
ATOM	211	N3	THY	14	-1.987	-1.427	-20.377
ATOM	212	H3	THY	14	-1.467	-0.559	-20.445
ATOM	213	C2	THY	14	-3.336	-1.341	-20.096
ATOM	214	O2	THY	14	-3.862	-0.235	-19.989
ATOM	215	C3'	THY	14	-7.526	-3.685	-19.649
ATOM	216	H3'	THY	14	-7.928	-4.639	-19.994
ATOM	217	C2'	THY	14	-6.353	-3.237	-20.520
ATOM	218	H2A'	THY	14	-6.649	-2.578	-21.331
ATOM	219	H2B'	THY	14	-5.889	-4.133	-20.929
ATOM	220	O3'	THY	14	-8.561	-2.721	-19.557
ATOM	221	P	POM	15	-9.578	-2.418	-20.771
ATOM	222	OA	POM	15	-9.699	-3.633	-21.608
ATOM	223	OB	POM	15	-10.791	-1.786	-20.206
ATOM	224	O5'	THY	16	-8.773	-1.306	-21.604
ATOM	225	C5'	THY	16	-8.570	-0.019	-21.058
ATOM	226	H5A'	THY	16	-9.506	0.540	-21.067
ATOM	227	H5B'	THY	16	-8.220	-0.115	-20.030
ATOM	228	C4'	THY	16	-7.499	0.751	-21.829
ATOM	229	H4'	THY	16	-7.371	1.722	-21.352
ATOM	230	O1'	THY	16	-6.258	0.074	-21.799
ATOM	231	C1'	THY	16	-5.454	0.705	-22.770
ATOM	232	H1'	THY	16	-5.113	1.651	-22.351
ATOM	233	N1	THY	16	-4.313	-0.157	-23.173
ATOM	234	C6	THY	16	-4.488	-1.511	-23.324
ATOM	235	H6	THY	16	-5.487	-1.914	-23.238
ATOM	236	C5	THY	16	-3.442	-2.341	-23.564
ATOM	237	C7	THY	16	-3.673	-3.833	-23.714
ATOM	238	H7A	THY	16	-3.619	-4.100	-24.769
ATOM	239	H7B	THY	16	-2.895	-4.377	-23.176
ATOM	240	H7C	THY	16	-4.644	-4.128	-23.315
ATOM	241	C4	THY	16	-2.095	-1.812	-23.667
ATOM	242	O4	THY	16	-1.073	-2.479	-23.802
ATOM	243	N3	THY	16	-2.013	-0.440	-23.581
ATOM	244	H3	THY	16	-1.084	-0.042	-23.680
ATOM	245	C2	THY	16	-3.060	0.427	-23.348
ATOM	246	O2	THY	16	-2.862	1.640	-23.317
ATOM	247	C3'	THY	16	-7.811	0.989	-23.307
ATOM	248	H3'	THY	16	-8.397	0.159	-23.706
ATOM	249	C2'	THY	16	-6.409	0.981	-23.930
ATOM	250	H2A'	THY	16	-6.145	1.934	-24.380
ATOM	251	H2B'	THY	16	-6.373	0.183	-24.670
ATOM	252	O3'	THY	16	-8.503	2.217	-23.458
ATOM	253	P	POM	17	-9.013	2.751	-24.890
ATOM	254	OA	POM	17	-9.253	1.593	-25.778
ATOM	255	OB	POM	17	-10.083	3.748	-24.665
ATOM	256	O5'	CYT	18	-7.721	3.529	-25.438
ATOM	257	C5'	CYT	18	-7.218	4.668	-24.769
ATOM	258	H5A'	CYT	18	-7.962	5.465	-24.785
ATOM	259	H5B'	CYT	18	-6.993	4.416	-23.732
ATOM	260	C4'	CYT	18	-5.932	5.159	-25.442
ATOM	261	H4'	CYT	18	-5.580	6.032	-24.894
ATOM	262	O1'	CYT	18	-4.946	4.134	-25.397

ATOM	263	C1'	CYT	18	-4.517	3.865	-26.719
ATOM	264	H1'	CYT	18	-3.707	4.558	-26.947
ATOM	265	N1	CYT	18	-4.074	2.447	-26.843
ATOM	266	C6	CYT	18	-4.980	1.417	-26.858
ATOM	267	H6	CYT	18	-6.039	1.624	-26.812
ATOM	268	C5	CYT	18	-4.580	0.126	-26.893
ATOM	269	H5	CYT	18	-5.326	-0.655	-26.904
ATOM	270	C4	CYT	18	-3.173	-0.120	-26.912
ATOM	271	N4	CYT	18	-2.736	-1.374	-26.887
ATOM	272	HN4A	CYT	18	-1.740	-1.550	-26.868
ATOM	273	HN4B	CYT	18	-3.387	-2.140	-26.915
ATOM	274	N3	CYT	18	-2.280	0.874	-26.854
ATOM	275	C2	CYT	18	-2.707	2.169	-26.833
ATOM	276	O2	CYT	18	-1.865	3.068	-26.790
ATOM	277	C3'	CYT	18	-6.145	5.536	-26.914
ATOM	278	H3'	CYT	18	-7.187	5.783	-27.126
ATOM	279	C2'	CYT	18	-5.683	4.266	-27.621
ATOM	280	H2A'	CYT	18	-5.383	4.442	-28.651
ATOM	281	H2B'	CYT	18	-6.505	3.555	-27.608
ATOM	282	O3'	CYT	18	-5.294	6.629	-27.204
ATOM	283	P	POM	19	-5.420	7.475	-28.567
ATOM	284	OA	POM	19	-6.231	6.713	-29.540
ATOM	285	OB	POM	19	-5.777	8.868	-28.225
ATOM	286	O5'	GUA	20	-3.896	7.442	-29.063
ATOM	287	C5'	GUA	20	-2.909	8.227	-28.429
ATOM	288	H5A'	GUA	20	-3.167	9.284	-28.515
ATOM	289	H5B'	GUA	20	-2.852	7.964	-27.372
ATOM	290	C4'	GUA	20	-1.540	7.996	-29.077
ATOM	291	H4'	GUA	20	-0.819	8.632	-28.562
ATOM	292	O1'	GUA	20	-1.158	6.634	-28.934
ATOM	293	C1'	GUA	20	-0.974	6.058	-30.217
ATOM	294	H1'	GUA	20	0.085	6.107	-30.474
ATOM	295	N9	GUA	20	-1.453	4.656	-30.194
ATOM	296	C8	GUA	20	-2.733	4.206	-29.996
ATOM	297	H8	GUA	20	-3.577	4.872	-29.912
ATOM	298	N7	GUA	20	-2.841	2.910	-29.907
ATOM	299	C5	GUA	20	-1.533	2.458	-30.064
ATOM	300	C6	GUA	20	-1.005	1.132	-30.040
ATOM	301	O6	GUA	20	-1.610	0.082	-29.838
ATOM	302	N1	GUA	20	0.364	1.091	-30.258
ATOM	303	H1	GUA	20	0.796	0.165	-30.234
ATOM	304	C2	GUA	20	1.142	2.205	-30.465
ATOM	305	N2	GUA	20	2.446	2.036	-30.643
ATOM	306	HN2A	GUA	20	2.872	1.119	-30.576
ATOM	307	HN2B	GUA	20	3.020	2.848	-30.808
ATOM	308	N3	GUA	20	0.664	3.455	-30.458
ATOM	309	C4	GUA	20	-0.679	3.517	-30.256
ATOM	310	C3'	GUA	20	-1.542	8.324	-30.575
ATOM	311	H3'	GUA	20	-2.336	9.024	-30.842
ATOM	312	C2'	GUA	20	-1.756	6.943	-31.185
ATOM	313	H2A'	GUA	20	-1.394	6.884	-32.206
ATOM	314	H2B'	GUA	20	-2.820	6.711	-31.171
ATOM	315	O3'	GUA	20	-0.273	8.868	-30.885

ATOM	316	P	POM	21	0.102	9.426	-32.347
ATOM	317	OA	POM	21	-1.065	9.259	-33.240
ATOM	318	OB	POM	21	0.735	10.753	-32.190
ATOM	319	O5'	CYT	22	1.227	8.371	-32.790
ATOM	320	C5'	CYT	22	2.476	8.332	-32.127
ATOM	321	H5A'	CYT	22	2.990	9.287	-32.253
ATOM	322	H5B'	CYT	22	2.322	8.154	-31.062
ATOM	323	C4'	CYT	22	3.357	7.211	-32.688
ATOM	324	H4'	CYT	22	4.302	7.215	-32.142
ATOM	325	O1'	CYT	22	2.704	5.964	-32.491
ATOM	326	C1'	CYT	22	2.625	5.283	-33.728
ATOM	327	H1'	CYT	22	3.538	4.699	-33.848
ATOM	328	N1	CYT	22	1.393	4.442	-33.748
ATOM	329	C6	CYT	22	0.156	5.027	-33.677
ATOM	330	H6	CYT	22	0.079	6.103	-33.687
ATOM	331	C5	CYT	22	-0.974	4.292	-33.571
ATOM	332	H5	CYT	22	-1.929	4.794	-33.522
ATOM	333	C4	CYT	22	-0.820	2.873	-33.524
ATOM	334	N4	CYT	22	-1.891	2.116	-33.314
ATOM	335	HN4A	CYT	22	-1.787	1.114	-33.221
ATOM	336	HN4B	CYT	22	-2.791	2.542	-33.169
ATOM	337	N3	CYT	22	0.381	2.286	-33.562
ATOM	338	C2	CYT	22	1.506	3.053	-33.694
ATOM	339	O2	CYT	22	2.598	2.491	-33.750
ATOM	340	C3'	CYT	22	3.626	7.386	-34.188
ATOM	341	H3'	CYT	22	3.421	8.406	-34.516
ATOM	342	C2'	CYT	22	2.645	6.387	-34.789
ATOM	343	H2A'	CYT	22	2.976	6.033	-35.758
ATOM	344	H2B'	CYT	22	1.686	6.888	-34.900
ATOM	345	O3'	CYT	22	4.975	7.044	-34.461
ATOM	346	P	POM	23	5.651	7.290	-35.906
ATOM	347	OA	POM	23	4.649	7.895	-36.810
ATOM	348	OB	POM	23	6.958	7.951	-35.702
ATOM	349	O5'	GUA	24	5.919	5.787	-36.404
ATOM	350	C5'	GUA	24	6.973	5.025	-35.849
ATOM	351	H5A'	GUA	24	7.932	5.491	-36.077
ATOM	352	H5B'	GUA	24	6.856	4.988	-34.764
ATOM	353	C4'	GUA	24	6.955	3.589	-36.386
ATOM	354	H4'	GUA	24	7.752	3.031	-35.895
ATOM	355	O1'	GUA	24	5.700	3.013	-36.059
ATOM	356	C1'	GUA	24	5.108	2.505	-37.239
ATOM	357	H1'	GUA	24	5.436	1.472	-37.364
ATOM	358	N9	GUA	24	3.633	2.571	-37.143
ATOM	359	C8	GUA	24	2.813	3.668	-37.203
ATOM	360	H8	GUA	24	3.179	4.660	-37.414
ATOM	361	N7	GUA	24	1.551	3.408	-36.994
ATOM	362	C5	GUA	24	1.527	2.031	-36.800
ATOM	363	C6	GUA	24	0.434	1.150	-36.543
ATOM	364	O6	GUA	24	-0.753	1.433	-36.393
ATOM	365	N1	GUA	24	0.822	-0.179	-36.486
ATOM	366	H1	GUA	24	0.070	-0.846	-36.322
ATOM	367	C2	GUA	24	2.117	-0.616	-36.625
ATOM	368	N2	GUA	24	2.354	-1.921	-36.567

ATOM	369	HN2A	GUA	24	1.601	-2.585	-36.432
ATOM	370	HN2B	GUA	24	3.308	-2.241	-36.611
ATOM	371	N3	GUA	24	3.153	0.200	-36.836
ATOM	372	C4	GUA	24	2.793	1.509	-36.911
ATOM	373	C3'	GUA	24	7.121	3.463	-37.908
ATOM	374	H3'	GUA	24	7.656	2.540	-38.132
ATOM	375	C2'	GUA	24	5.685	3.328	-38.389
ATOM	376	H2A'	GUA	24	5.611	2.818	-39.349
ATOM	377	H2B'	GUA	24	5.231	4.318	-38.440
ATOM	378	O3'	GUA	24	7.779	4.552	-38.521
ATOM	379	H	HE	25	8.664	4.618	-38.155
ATOM	380	H	HB	26	-5.279	-6.465	-38.195
ATOM	381	O5'	CYT	27	-5.170	-7.414	-38.290
ATOM	382	C5'	CYT	27	-4.034	-7.656	-39.094
ATOM	383	H5A'	CYT	27	-3.907	-8.732	-39.222
ATOM	384	H5B'	CYT	27	-4.187	-7.198	-40.071
ATOM	385	C4'	CYT	27	-2.773	-7.070	-38.452
ATOM	386	H4'	CYT	27	-1.935	-7.227	-39.134
ATOM	387	O1'	CYT	27	-2.898	-5.677	-38.241
ATOM	388	C1'	CYT	27	-1.934	-5.343	-37.264
ATOM	389	H1'	CYT	27	-0.953	-5.390	-37.740
ATOM	390	N1	CYT	27	-2.219	-4.010	-36.670
ATOM	391	C6	CYT	27	-3.504	-3.628	-36.383
ATOM	392	H6	CYT	27	-4.306	-4.341	-36.511
ATOM	393	C5	CYT	27	-3.791	-2.372	-35.966
ATOM	394	H5	CYT	27	-4.815	-2.103	-35.755
ATOM	395	C4	CYT	27	-2.692	-1.462	-35.847
ATOM	396	N4	CYT	27	-2.917	-0.184	-35.566
ATOM	397	HN4A	CYT	27	-2.138	0.466	-35.599
ATOM	398	HN4B	CYT	27	-3.844	0.141	-35.350
ATOM	399	N3	CYT	27	-1.436	-1.837	-36.105
ATOM	400	C2	CYT	27	-1.167	-3.120	-36.477
ATOM	401	O2	CYT	27	0.001	-3.456	-36.651
ATOM	402	C3'	CYT	27	-2.426	-7.693	-37.092
ATOM	403	H3'	CYT	27	-3.295	-8.190	-36.660
ATOM	404	C2'	CYT	27	-2.046	-6.472	-36.246
ATOM	405	H2A'	CYT	27	-1.107	-6.597	-35.712
ATOM	406	H2B'	CYT	27	-2.850	-6.275	-35.536
ATOM	407	O3'	CYT	27	-1.366	-8.613	-37.279
ATOM	408	P	POM	28	-0.831	-9.564	-36.091
ATOM	409	OA	POM	28	-1.941	-9.780	-35.137
ATOM	410	OB	POM	28	-0.151	-10.722	-36.709
ATOM	411	O5'	GUA	29	0.281	-8.640	-35.388
ATOM	412	C5'	GUA	29	1.489	-8.339	-36.060
ATOM	413	H5A'	GUA	29	2.089	-9.245	-36.155
ATOM	414	H5B'	GUA	29	1.271	-7.955	-37.057
ATOM	415	C4'	GUA	29	2.295	-7.277	-35.306
ATOM	416	H4'	GUA	29	3.201	-7.076	-35.881
ATOM	417	O1'	GUA	29	1.562	-6.064	-35.212
ATOM	418	C1'	GUA	29	1.868	-5.475	-33.965
ATOM	419	H1'	GUA	29	2.844	-4.990	-34.018
ATOM	420	N9	GUA	29	0.805	-4.517	-33.582
ATOM	421	C8	GUA	29	-0.533	-4.765	-33.414

ATOM	422	H8	GUA	29	-0.960	-5.755	-33.473
ATOM	423	N7	GUA	29	-1.255	-3.703	-33.193
ATOM	424	C5	GUA	29	-0.326	-2.665	-33.209
ATOM	425	C6	GUA	29	-0.512	-1.258	-33.057
ATOM	426	O6	GUA	29	-1.560	-0.656	-32.842
ATOM	427	N1	GUA	29	0.663	-0.537	-33.198
ATOM	428	H1	GUA	29	0.578	0.481	-33.199
ATOM	429	C2	GUA	29	1.896	-1.112	-33.377
ATOM	430	N2	GUA	29	2.953	-0.313	-33.457
ATOM	431	HN2A	GUA	29	2.858	0.696	-33.425
ATOM	432	HN2B	GUA	29	3.860	-0.730	-33.594
ATOM	433	N3	GUA	29	2.088	-2.430	-33.497
ATOM	434	C4	GUA	29	0.938	-3.153	-33.429
ATOM	435	C3'	GUA	29	2.690	-7.701	-33.881
ATOM	436	H3'	GUA	29	2.365	-8.718	-33.652
ATOM	437	C2'	GUA	29	1.944	-6.675	-33.027
ATOM	438	H2A'	GUA	29	2.450	-6.448	-32.092
ATOM	439	H2B'	GUA	29	0.948	-7.068	-32.825
ATOM	440	O3'	GUA	29	4.099	-7.599	-33.778
ATOM	441	P	POM	30	4.911	-7.977	-32.438
ATOM	442	OA	POM	30	3.981	-8.603	-31.473
ATOM	443	OB	POM	30	6.154	-8.674	-32.833
ATOM	444	O5'	CYT	31	5.298	-6.514	-31.898
ATOM	445	C5'	CYT	31	6.212	-5.709	-32.619
ATOM	446	H5A'	CYT	31	7.201	-6.170	-32.614
ATOM	447	H5B'	CYT	31	5.876	-5.609	-33.652
ATOM	448	C4'	CYT	31	6.302	-4.308	-32.010
ATOM	449	H4'	CYT	31	6.931	-3.693	-32.656
ATOM	450	O1'	CYT	31	5.013	-3.723	-31.969
ATOM	451	C1'	CYT	31	4.911	-2.940	-30.799
ATOM	452	H1'	CYT	31	5.371	-1.971	-30.999
ATOM	453	N1	CYT	31	3.474	-2.854	-30.416
ATOM	454	C6	CYT	31	2.715	-3.993	-30.358
ATOM	455	H6	CYT	31	3.197	-4.951	-30.492
ATOM	456	C5	CYT	31	1.378	-3.944	-30.156
ATOM	457	H5	CYT	31	0.815	-4.865	-30.120
ATOM	458	C4	CYT	31	0.793	-2.649	-30.004
ATOM	459	N4	CYT	31	-0.525	-2.537	-29.898
ATOM	460	HN4A	CYT	31	-0.945	-1.620	-29.817
ATOM	461	HN4B	CYT	31	-1.108	-3.356	-29.943
ATOM	462	N3	CYT	31	1.521	-1.528	-30.072
ATOM	463	C2	CYT	31	2.873	-1.607	-30.257
ATOM	464	O2	CYT	31	3.527	-0.568	-30.292
ATOM	465	C3'	CYT	31	6.885	-4.306	-30.590
ATOM	466	H3'	CYT	31	7.095	-5.321	-30.250
ATOM	467	C2'	CYT	31	5.755	-3.684	-29.764
ATOM	468	H2A'	CYT	31	6.126	-3.013	-28.993
ATOM	469	H2B'	CYT	31	5.190	-4.494	-29.304
ATOM	470	O3'	CYT	31	8.075	-3.534	-30.608
ATOM	471	P	POM	32	9.069	-3.428	-29.341
ATOM	472	OA	POM	32	8.862	-4.606	-28.470
ATOM	473	OB	POM	32	10.424	-3.113	-29.846
ATOM	474	O5'	GUA	33	8.500	-2.129	-28.591

ATOM	475	C5'	GUA	33	8.652	-0.845	-29.166
ATOM	476	H5A'	GUA	33	9.679	-0.500	-29.043
ATOM	477	H5B'	GUA	33	8.416	-0.887	-30.231
ATOM	478	C4'	GUA	33	7.685	0.145	-28.514
ATOM	479	H4'	GUA	33	7.721	1.089	-29.061
ATOM	480	O1'	GUA	33	6.362	-0.350	-28.584
ATOM	481	C1'	GUA	33	5.618	0.344	-27.610
ATOM	482	H1'	GUA	33	5.350	1.325	-28.007
ATOM	483	N9	GUA	33	4.416	-0.436	-27.246
ATOM	484	C8	GUA	33	4.328	-1.781	-26.994
ATOM	485	H8	GUA	33	5.191	-2.429	-26.953
ATOM	486	N7	GUA	33	3.110	-2.216	-26.830
ATOM	487	C5	GUA	33	2.332	-1.070	-26.955
ATOM	488	C6	GUA	33	0.918	-0.904	-26.883
ATOM	489	O6	GUA	33	0.064	-1.771	-26.720
ATOM	490	N1	GUA	33	0.524	0.418	-27.016
ATOM	491	H1	GUA	33	-0.480	0.589	-26.954
ATOM	492	C2	GUA	33	1.391	1.462	-27.222
ATOM	493	N2	GUA	33	0.884	2.683	-27.345
ATOM	494	HN2A	GUA	33	-0.113	2.842	-27.268
ATOM	495	HN2B	GUA	33	1.513	3.424	-27.610
ATOM	496	N3	GUA	33	2.715	1.319	-27.314
ATOM	497	C4	GUA	33	3.125	0.030	-27.177
ATOM	498	C3'	GUA	33	7.977	0.422	-27.035
ATOM	499	H3'	GUA	33	8.515	-0.417	-26.590
ATOM	500	C2'	GUA	33	6.571	0.515	-26.431
ATOM	501	H2A'	GUA	33	6.379	1.472	-25.956
ATOM	502	H2B'	GUA	33	6.450	-0.294	-25.709
ATOM	503	O3'	GUA	33	8.733	1.617	-26.930
ATOM	504	P	POM	34	9.257	2.198	-25.518
ATOM	505	OA	POM	34	9.419	1.076	-24.568
ATOM	506	OB	POM	34	10.388	3.113	-25.784
ATOM	507	O5'	ADE	35	8.007	3.084	-25.035
ATOM	508	C5'	ADE	35	7.594	4.215	-25.777
ATOM	509	H5A'	ADE	35	8.370	4.981	-25.741
ATOM	510	H5B'	ADE	35	7.428	3.932	-26.818
ATOM	511	C4'	ADE	35	6.285	4.787	-25.224
ATOM	512	H4'	ADE	35	5.999	5.628	-25.858
ATOM	513	O1'	ADE	35	5.263	3.798	-25.270
ATOM	514	C1'	ADE	35	4.716	3.651	-23.973
ATOM	515	H1'	ADE	35	3.889	4.353	-23.861
ATOM	516	N9	ADE	35	4.243	2.264	-23.762
ATOM	517	C8	ADE	35	4.986	1.121	-23.584
ATOM	518	H8	ADE	35	6.065	1.121	-23.519
ATOM	519	N7	ADE	35	4.283	0.023	-23.525
ATOM	520	C5	ADE	35	2.977	0.473	-23.661
ATOM	521	C6	ADE	35	1.741	-0.192	-23.695
ATOM	522	N6	ADE	35	1.633	-1.516	-23.627
ATOM	523	HN6A	ADE	35	0.723	-1.960	-23.696
ATOM	524	HN6B	ADE	35	2.479	-2.065	-23.585
ATOM	525	N1	ADE	35	0.623	0.530	-23.851
ATOM	526	C2	ADE	35	0.723	1.845	-23.971
ATOM	527	H2	ADE	35	-0.211	2.359	-24.106

ATOM	528	N3	ADE	35	1.814	2.602	-23.954
ATOM	529	C4	ADE	35	2.934	1.838	-23.797
ATOM	530	C3'	ADE	35	6.409	5.261	-23.770
ATOM	531	H3'	ADE	35	7.443	5.474	-23.490
ATOM	532	C2'	ADE	35	5.834	4.063	-23.021
ATOM	533	H2A'	ADE	35	5.480	4.314	-22.025
ATOM	534	H2B'	ADE	35	6.603	3.295	-22.950
ATOM	535	O3'	ADE	35	5.600	6.415	-23.640
ATOM	536	P	POM	36	5.559	7.305	-22.301
ATOM	537	OA	POM	36	6.298	6.608	-21.227
ATOM	538	OB	POM	36	5.896	8.701	-22.655
ATOM	539	O5'	ADE	37	3.993	7.228	-21.960
ATOM	540	C5'	ADE	37	3.046	7.913	-22.756
ATOM	541	H5A'	ADE	37	3.241	8.985	-22.720
ATOM	542	H5B'	ADE	37	3.122	7.575	-23.790
ATOM	543	C4'	ADE	37	1.623	7.648	-22.254
ATOM	544	H4'	ADE	37	0.932	8.194	-22.898
ATOM	545	O1'	ADE	37	1.343	6.255	-22.328
ATOM	546	C1'	ADE	37	0.989	5.796	-21.035
ATOM	547	H1'	ADE	37	-0.095	5.854	-20.930
ATOM	548	N9	ADE	37	1.466	4.410	-20.842
ATOM	549	C8	ADE	37	2.757	3.949	-20.777
ATOM	550	H8	ADE	37	3.612	4.606	-20.828
ATOM	551	N7	ADE	37	2.862	2.654	-20.642
ATOM	552	C5	ADE	37	1.539	2.229	-20.615
ATOM	553	C6	ADE	37	0.938	0.962	-20.517
ATOM	554	N6	ADE	37	1.645	-0.163	-20.434
ATOM	555	HN6A	ADE	37	1.167	-1.059	-20.434
ATOM	556	HN6B	ADE	37	2.652	-0.104	-20.421
ATOM	557	N1	ADE	37	-0.399	0.875	-20.560
ATOM	558	C2	ADE	37	-1.113	1.985	-20.693
ATOM	559	H2	ADE	37	-2.182	1.848	-20.720
ATOM	560	N3	ADE	37	-0.676	3.231	-20.803
ATOM	561	C4	ADE	37	0.680	3.288	-20.748
ATOM	562	C3'	ADE	37	1.430	8.090	-20.797
ATOM	563	H3'	ADE	37	2.160	8.843	-20.496
ATOM	564	C2'	ADE	37	1.626	6.774	-20.056
ATOM	565	H2A'	ADE	37	1.148	6.764	-19.081
ATOM	566	H2B'	ADE	37	2.693	6.591	-19.938
ATOM	567	O3'	ADE	37	0.114	8.597	-20.661
ATOM	568	P	POM	38	-0.457	9.140	-19.256
ATOM	569	OA	POM	38	0.679	9.327	-18.327
ATOM	570	OB	POM	38	-1.376	10.263	-19.539
ATOM	571	O5'	THY	39	-1.320	7.874	-18.759
ATOM	572	C5'	THY	39	-2.572	7.592	-19.352
ATOM	573	H5A'	THY	39	-3.254	8.424	-19.169
ATOM	574	H5B'	THY	39	-2.446	7.471	-20.429
ATOM	575	C4'	THY	39	-3.205	6.316	-18.790
ATOM	576	H4'	THY	39	-4.173	6.201	-19.270
ATOM	577	O1'	THY	39	-2.434	5.154	-19.067
ATOM	578	C1'	THY	39	-2.674	4.192	-18.046
ATOM	579	H1'	THY	39	-3.072	3.252	-18.458
ATOM	580	N1	THY	39	-1.428	3.841	-17.324

ATOM	581	C6	THY	39	-0.272	4.580	-17.411
ATOM	582	H6	THY	39	-0.320	5.575	-17.826
ATOM	583	C5	THY	39	0.917	4.065	-17.000
ATOM	584	C7	THY	39	2.182	4.898	-17.083
ATOM	585	H7A	THY	39	2.675	4.728	-18.038
ATOM	586	H7B	THY	39	1.957	5.960	-16.969
ATOM	587	H7C	THY	39	2.863	4.603	-16.284
ATOM	588	C4	THY	39	0.990	2.703	-16.501
ATOM	589	O4	THY	39	2.012	2.042	-16.335
ATOM	590	N3	THY	39	-0.234	2.126	-16.261
ATOM	591	H3	THY	39	-0.259	1.127	-16.085
ATOM	592	C2	THY	39	-1.451	2.641	-16.633
ATOM	593	O2	THY	39	-2.490	2.044	-16.367
ATOM	594	C3'	THY	39	-3.468	6.329	-17.287
ATOM	595	H3'	THY	39	-2.585	6.666	-16.743
ATOM	596	C2'	THY	39	-3.688	4.833	-17.106
ATOM	597	H2A'	THY	39	-4.684	4.561	-17.449
ATOM	598	H2B'	THY	39	-3.560	4.529	-16.074
ATOM	599	O3'	THY	39	-4.623	7.089	-16.976
ATOM	600	P	POM	40	-5.109	7.333	-15.456
ATOM	601	OA	POM	40	-3.920	7.595	-14.616
ATOM	602	OB	POM	40	-6.225	8.305	-15.479
ATOM	603	O5'	THY	41	-5.705	5.910	-15.012
ATOM	604	C5'	THY	41	-6.819	5.334	-15.663
ATOM	605	H5A'	THY	41	-7.719	5.915	-15.456
ATOM	606	H5B'	THY	41	-6.659	5.328	-16.741
ATOM	607	C4'	THY	41	-7.000	3.886	-15.190
ATOM	608	H4'	THY	41	-7.702	3.400	-15.868
ATOM	609	O1'	THY	41	-5.752	3.201	-15.235
ATOM	610	C1'	THY	41	-5.505	2.558	-13.995
ATOM	611	H1'	THY	41	-5.896	1.542	-14.055
ATOM	612	N1	THY	41	-4.045	2.605	-13.681
ATOM	613	C6	THY	41	-3.405	3.821	-13.600
ATOM	614	H6	THY	41	-3.977	4.725	-13.733
ATOM	615	C5	THY	41	-2.069	3.924	-13.399
ATOM	616	C7	THY	41	-1.404	5.288	-13.392
ATOM	617	H7A	THY	41	-0.700	5.349	-12.562
ATOM	618	H7B	THY	41	-0.860	5.425	-14.327
ATOM	619	H7C	THY	41	-2.139	6.091	-13.298
ATOM	620	C4	THY	41	-1.257	2.737	-13.248
ATOM	621	O4	THY	41	-0.041	2.733	-13.080
ATOM	622	N3	THY	41	-1.957	1.551	-13.324
ATOM	623	H3	THY	41	-1.385	0.714	-13.245
ATOM	624	C2	THY	41	-3.315	1.416	-13.574
ATOM	625	O2	THY	41	-3.811	0.294	-13.666
ATOM	626	C3'	THY	41	-7.552	3.801	-13.763
ATOM	627	H3'	THY	41	-7.893	4.775	-13.410
ATOM	628	C2'	THY	41	-6.338	3.328	-12.968
ATOM	629	H2A'	THY	41	-6.618	2.702	-12.127
ATOM	630	H2B'	THY	41	-5.823	4.214	-12.601
ATOM	631	O3'	THY	41	-8.631	2.881	-13.759
ATOM	632	P	POM	42	-9.539	2.612	-12.454
ATOM	633	OA	POM	42	-9.434	3.781	-11.552

ATOM	634	OB	POM	42	-10.869	2.143	-12.902
ATOM	635	O5'	CYT	43	-8.767	1.377	-11.780
ATOM	636	C5'	CYT	43	-8.750	0.111	-12.412
ATOM	637	H5A'	CYT	43	-9.728	-0.365	-12.319
ATOM	638	H5B'	CYT	43	-8.514	0.233	-13.469
ATOM	639	C4'	CYT	43	-7.674	-0.782	-11.790
ATOM	640	H4'	CYT	43	-7.612	-1.714	-12.353
ATOM	641	O1'	CYT	43	-6.416	-0.141	-11.851
ATOM	642	C1'	CYT	43	-5.585	-0.782	-10.908
ATOM	643	H1'	CYT	43	-5.237	-1.712	-11.357
ATOM	644	N1	CYT	43	-4.470	0.117	-10.511
ATOM	645	C6	CYT	43	-4.693	1.452	-10.298
ATOM	646	H6	CYT	43	-5.708	1.820	-10.302
ATOM	647	C5	CYT	43	-3.671	2.312	-10.082
ATOM	648	H5	CYT	43	-3.884	3.359	-9.929
ATOM	649	C4	CYT	43	-2.352	1.759	-10.073
ATOM	650	N4	CYT	43	-1.303	2.568	-9.985
ATOM	651	HN4A	CYT	43	-0.373	2.167	-10.040
ATOM	652	HN4B	CYT	43	-1.427	3.560	-9.876
ATOM	653	N3	CYT	43	-2.135	0.448	-10.216
ATOM	654	C2	CYT	43	-3.185	-0.402	-10.403
ATOM	655	O2	CYT	43	-2.970	-1.609	-10.461
ATOM	656	C3'	CYT	43	-7.920	-1.111	-10.314
ATOM	657	H3'	CYT	43	-8.510	-0.318	-9.850
ATOM	658	C2'	CYT	43	-6.503	-1.105	-9.732
ATOM	659	H2A'	CYT	43	-6.219	-2.069	-9.316
ATOM	660	H2B'	CYT	43	-6.453	-0.329	-8.969
ATOM	661	O3'	CYT	43	-8.575	-2.363	-10.195
ATOM	662	P	POM	44	-9.104	-2.930	-8.779
ATOM	663	OA	POM	44	-9.453	-1.788	-7.905
ATOM	664	OB	POM	44	-10.108	-3.981	-9.052
ATOM	665	O5'	GUA	45	-7.799	-3.644	-8.168
ATOM	666	C5'	GUA	45	-7.265	-4.802	-8.779
ATOM	667	H5A'	GUA	45	-7.997	-5.609	-8.739
ATOM	668	H5B'	GUA	45	-7.034	-4.582	-9.820
ATOM	669	C4'	GUA	45	-5.977	-5.259	-8.087
ATOM	670	H4'	GUA	45	-5.639	-6.173	-8.578
ATOM	671	O1'	GUA	45	-4.974	-4.264	-8.233
ATOM	672	C1'	GUA	45	-4.407	-4.003	-6.964
ATOM	673	H1'	GUA	45	-3.599	-4.713	-6.777
ATOM	674	N9	GUA	45	-3.914	-2.606	-6.917
ATOM	675	C8	GUA	45	-4.648	-1.452	-7.012
ATOM	676	H8	GUA	45	-5.727	-1.444	-7.039
ATOM	677	N7	GUA	45	-3.936	-0.363	-7.080
ATOM	678	C5	GUA	45	-2.625	-0.824	-7.007
ATOM	679	C6	GUA	45	-1.395	-0.104	-7.032
ATOM	680	O6	GUA	45	-1.234	1.105	-7.171
ATOM	681	N1	GUA	45	-0.285	-0.920	-6.882
ATOM	682	H1	GUA	45	0.623	-0.454	-6.917
ATOM	683	C2	GUA	45	-0.352	-2.283	-6.724
ATOM	684	N2	GUA	45	0.787	-2.954	-6.590
ATOM	685	HN2A	GUA	45	1.685	-2.487	-6.653
ATOM	686	HN2B	GUA	45	0.745	-3.954	-6.480

ATOM	687	N3	GUA	45	-1.498	-2.974	-6.717
ATOM	688	C4	GUA	45	-2.600	-2.192	-6.873
ATOM	689	C3'	GUA	45	-6.174	-5.521	-6.587
ATOM	690	H3'	GUA	45	-7.228	-5.625	-6.322
ATOM	691	C2'	GUA	45	-5.548	-4.266	-5.986
ATOM	692	H2A'	GUA	45	-5.211	-4.419	-4.965
ATOM	693	H2B'	GUA	45	-6.288	-3.467	-6.017
ATOM	694	O3'	GUA	45	-5.456	-6.695	-6.253
ATOM	695	P	POM	46	-5.522	-7.380	-4.796
ATOM	696	OA	POM	46	-6.270	-6.496	-3.875
ATOM	697	OB	POM	46	-5.925	-8.794	-4.960
ATOM	698	O5'	CYT	47	-3.973	-7.336	-4.375
ATOM	699	C5'	CYT	47	-3.012	-8.090	-5.091
ATOM	700	H5A'	CYT	47	-3.195	-9.155	-4.947
ATOM	701	H5B'	CYT	47	-3.082	-7.862	-6.155
ATOM	702	C4'	CYT	47	-1.598	-7.742	-4.619
ATOM	703	H4'	CYT	47	-0.888	-8.305	-5.226
ATOM	704	O1'	CYT	47	-1.377	-6.353	-4.816
ATOM	705	C1'	CYT	47	-0.889	-5.775	-3.621
ATOM	706	H1'	CYT	47	0.199	-5.835	-3.646
ATOM	707	N1	CYT	47	-1.402	-4.377	-3.514
ATOM	708	C6	CYT	47	-2.751	-4.135	-3.531
ATOM	709	H6	CYT	47	-3.438	-4.968	-3.540
ATOM	710	C5	CYT	47	-3.245	-2.876	-3.555
ATOM	711	H5	CYT	47	-4.315	-2.727	-3.558
ATOM	712	C4	CYT	47	-2.299	-1.808	-3.581
ATOM	713	N4	CYT	47	-2.737	-0.564	-3.730
ATOM	714	HN4A	CYT	47	-2.074	0.195	-3.815
ATOM	715	HN4B	CYT	47	-3.720	-0.385	-3.850
ATOM	716	N3	CYT	47	-0.979	-2.026	-3.572
ATOM	717	C2	CYT	47	-0.506	-3.308	-3.514
ATOM	718	O2	CYT	47	0.709	-3.487	-3.466
ATOM	719	C3'	CYT	47	-1.379	-8.071	-3.136
ATOM	720	H3'	CYT	47	-2.190	-8.690	-2.747
ATOM	721	C2'	CYT	47	-1.383	-6.686	-2.496
ATOM	722	H2A'	CYT	47	-0.730	-6.647	-1.631
ATOM	723	H2B'	CYT	47	-2.405	-6.454	-2.199
ATOM	724	O3'	CYT	47	-0.139	-8.743	-2.987
ATOM	725	P	POM	48	0.333	-9.386	-1.583
ATOM	726	OA	POM	48	-0.829	-9.470	-0.673
ATOM	727	OB	POM	48	1.137	-10.594	-1.867
ATOM	728	O5'	GUA	49	1.324	-8.259	-1.013
ATOM	729	C5'	GUA	49	2.598	-8.065	-1.592
ATOM	730	H5A'	GUA	49	3.210	-8.956	-1.444
ATOM	731	H5B'	GUA	49	2.496	-7.879	-2.662
ATOM	732	C4'	GUA	49	3.291	-6.865	-0.943
ATOM	733	H4'	GUA	49	4.285	-6.756	-1.379
ATOM	734	O1'	GUA	49	2.527	-5.700	-1.209
ATOM	735	C1'	GUA	49	2.378	-4.981	-0.004
ATOM	736	H1'	GUA	49	3.268	-4.368	0.146
ATOM	737	N9	GUA	49	1.170	-4.128	-0.061
ATOM	738	C8	GUA	49	-0.151	-4.488	0.016
ATOM	739	H8	GUA	49	-0.481	-5.495	0.217

ATOM	740	N7	GUA	49	-0.988	-3.505	-0.168
ATOM	741	C5	GUA	49	-0.162	-2.402	-0.362
ATOM	742	C6	GUA	49	-0.487	-1.034	-0.598
ATOM	743	O6	GUA	49	-1.600	-0.528	-0.722
ATOM	744	N1	GUA	49	0.634	-0.223	-0.666
ATOM	745	H1	GUA	49	0.447	0.766	-0.820
ATOM	746	C2	GUA	49	1.926	-0.675	-0.556
ATOM	747	N2	GUA	49	2.913	0.211	-0.623
ATOM	748	HN2A	GUA	49	2.722	1.200	-0.738
ATOM	749	HN2B	GUA	49	3.862	-0.122	-0.602
ATOM	750	N3	GUA	49	2.245	-1.958	-0.362
ATOM	751	C4	GUA	49	1.159	-2.770	-0.277
ATOM	752	C3'	GUA	49	3.397	-7.011	0.582
ATOM	753	H3'	GUA	49	3.213	-8.031	0.921
ATOM	754	C2'	GUA	49	2.331	-6.048	1.088
ATOM	755	H2A'	GUA	49	2.557	-5.649	2.077
ATOM	756	H2B'	GUA	49	1.373	-6.566	1.091
ATOM	757	O3'	GUA	49	4.669	-6.587	1.031
ATOM	758	H	HE	50	4.828	-5.696	0.711
ATOM	759	O1	DIS	51	-2.018	-6.044	-10.373
ATOM	760	C1	DIS	51	-1.387	-5.562	-11.311
ATOM	761	HF	DIS	51	-0.321	-5.733	-11.333
ATOM	762	N1	DIS	51	-1.903	-4.731	-12.225
ATOM	763	HN1	DIS	51	-1.223	-4.296	-12.840
ATOM	764	C2	DIS	51	-3.229	-4.266	-12.450
ATOM	765	C3	DIS	51	-3.736	-3.379	-13.419
ATOM	766	H3	DIS	51	-3.167	-2.739	-14.075
ATOM	767	C5	DIS	51	-4.275	-5.058	-12.024
ATOM	768	H5	DIS	51	-4.218	-5.930	-11.392
ATOM	769	N2	DIS	51	-5.428	-4.612	-12.625
ATOM	770	C6	DIS	51	-6.768	-5.250	-12.505
ATOM	771	HM1	DIS	51	-7.092	-5.778	-13.402
ATOM	772	HM2	DIS	51	-6.840	-6.005	-11.721
ATOM	773	HM3	DIS	51	-7.580	-4.556	-12.287
ATOM	774	C4	DIS	51	-5.099	-3.588	-13.490
ATOM	775	C7	DIS	51	-6.015	-2.925	-14.480
ATOM	776	O2	DIS	51	-6.999	-3.551	-14.869
ATOM	777	N3	DIS	51	-5.718	-1.683	-14.898
ATOM	778	HN3	DIS	51	-4.878	-1.255	-14.524
ATOM	779	C8	DIS	51	-6.406	-0.879	-15.850
ATOM	780	C9	DIS	51	-6.028	0.227	-16.636
ATOM	781	H9	DIS	51	-5.036	0.647	-16.714
ATOM	782	C11	DIS	51	-7.775	-1.005	-15.926
ATOM	783	H11	DIS	51	-8.403	-1.690	-15.376
ATOM	784	N4	DIS	51	-8.242	-0.102	-16.844
ATOM	785	C12	DIS	51	-9.668	0.039	-17.255
ATOM	786	HM4	DIS	51	-10.153	0.942	-16.884
ATOM	787	HM5	DIS	51	-9.835	0.062	-18.331
ATOM	788	HM6	DIS	51	-10.314	-0.769	-16.911
ATOM	789	C10	DIS	51	-7.180	0.677	-17.266
ATOM	790	C13	DIS	51	-7.269	1.858	-18.196
ATOM	791	O3	DIS	51	-8.380	2.325	-18.441
ATOM	792	N5	DIS	51	-6.148	2.299	-18.787

ATOM	793	HN5	DIS	51	-5.312	1.762	-18.608
ATOM	794	C14	DIS	51	-5.974	3.355	-19.730
ATOM	795	C15	DIS	51	-4.924	3.688	-20.603
ATOM	796	H15	DIS	51	-4.008	3.136	-20.731
ATOM	797	C17	DIS	51	-6.900	4.374	-19.779
ATOM	798	H17	DIS	51	-7.795	4.480	-19.185
ATOM	799	N6	DIS	51	-6.497	5.280	-20.728
ATOM	800	C18	DIS	51	-7.239	6.514	-21.108
ATOM	801	HM7	DIS	51	-7.399	6.630	-22.179
ATOM	802	HM8	DIS	51	-8.240	6.584	-20.683
ATOM	803	HM9	DIS	51	-6.754	7.440	-20.799
ATOM	804	C16	DIS	51	-5.265	4.883	-21.214
ATOM	805	C19	DIS	51	-4.388	5.652	-22.168
ATOM	806	O4	DIS	51	-4.726	6.776	-22.534
ATOM	807	N7	DIS	51	-3.232	5.105	-22.553
ATOM	808	HN7	DIS	51	-2.972	4.191	-22.207
ATOM	809	C20	DIS	51	-2.333	5.774	-23.475
ATOM	810	HC1	DIS	51	-2.909	6.182	-24.307
ATOM	811	HC2	DIS	51	-1.815	6.586	-22.963
ATOM	812	C21	DIS	51	-1.315	4.773	-24.015
ATOM	813	HC3	DIS	51	-0.702	4.439	-23.181
ATOM	814	HC4	DIS	51	-1.867	3.918	-24.404
ATOM	815	C22	DIS	51	-0.421	5.311	-25.116
ATOM	816	N8	DIS	51	0.914	5.244	-25.000
ATOM	817	HNC	DIS	51	1.527	5.601	-25.717
ATOM	818	HND	DIS	51	1.327	4.821	-24.176
ATOM	819	N9	DIS	51	-0.972	5.824	-26.225
ATOM	820	HNA	DIS	51	-0.404	6.160	-26.990
ATOM	821	HNB	DIS	51	-1.974	5.786	-26.356

Appendix C

Free A₃T₂ Duplex Assignments

Figure C-1. Expansion of the aromatic to C1'H region of a NOESY spectrum of the A₃T₂ duplex without drug (20°C, 150 ms). Solid and dashed lines denote sequential connectivities of the A-rich and T-rich strands, respectively. Numbers denote intraresidue NOEs. Adenine C2H resonance positions are labeled explicitly.

Appendix D

A₃T₂ Adenine C₂H Assignments

The adenine C₂H resonances of residues 5, 6, and 16 (A₃T₂ duplex, 2.0 equivalents distamycin A) were assigned by analysis of the NOESY spectrum of figure 4-1. The adenine A₄ and A₁₅ C₂H resonances remain to be assigned. Figure D-1 shows an expansion of the downfield region of a spectrum of the 2:1 complex, along with representative one-dimensional NOE difference spectra. Irradiation of the A₅ and A₁₆ imino protons (previously assigned) resulted in NOEs to the A₆ imino proton as expected, and to peak B, which contains two protons. Since, in addition to A₆, A₄ and A₁₅ are the neighbors of A₅ and A₁₆ respectively, peak B must correspond to the A₄ and A₁₅ imino protons. Irradiation of peak B resulted in a sharp NOE to a single resonance at 7.50 ppm corresponding to the A₄ and A₁₅ C₂H protons. This completes the adenine C₂H resonance assignments of the A₃T₂ duplex with two equivalents of drug. The G-C imino protons were not assigned due to insufficient resolution.

Figure D-1. One-dimensional NOE difference spectra used in the assignment of the A4 and A15 imino protons. The top NMR spectrum corresponds to the downfield region obtained from the 2:1 complex in H₂O. The middle and bottom spectra were obtained by saturation of the A5 and A16 imino protons, respectively. The A5-T, A6-T, and A16-T imino proton assignments were determined through the observation of an NOE to a previously assigned C2H proton, when the corresponding imino proton was irradiated.

Appendix E

Distamycin A - A₃T₂ Coordinates

NMR constraints (Table E-1) and coordinates of the 2:1 distamycin A - A₃T₂ complex generated using the AMBER molecular mechanics program (Chapter 1) are summarized below. In this calculation, K_{NMR} was set to 300 (kcal/mol)/Å². In addition, 1.2 nm nonbonded and 0.4 nm hydrogen-bond cutoffs were used along with a distance-dependent dielectric function.

Table E-1. Distance constraints used to refine the 2:1 distamycin A - A₃T₂ complex.

Drug Proton	DNA Proton	Distance (nm)	DNA Proton	Distance (nm)
Drug 1			Drug 2	
HF	A5 C1'H	0.30	A16 C1'H	0.30
	CH ₂ (D2)	0.50	CH ₂ (D1)	0.50
H3-1	A6 C1'H	0.30	A16 C2H	0.50
	A5 C2H	0.50	T17 C1'H	0.30
H3-2	T7 C1'H	0.30	T18 C1'H	0.30
	A6 C2H	0.25	A6 C2H	0.50
H3-3	T8 C1'H	0.30	A5 C2H	0.25
	A16 C2H	0.25	T19 C1'H	0.30
CH ₂	HF (D1)	0.50	HF (D1)	0.50
	A15 C2H	0.50	A4 C2H	0.50

Coordinates for the 2:1 Distamycin A : A3T2
Complex

ATOM	1	H	HB	1	0.665	9.400	0.096
ATOM	2	O5'	CYT	2	0.305	9.218	0.967
ATOM	3	C5'	CYT	2	1.359	8.835	1.826
ATOM	4	H5A'	CYT	2	2.092	9.639	1.884
ATOM	5	H5B'	CYT	2	0.949	8.657	2.821
ATOM	6	C4'	CYT	2	2.041	7.556	1.330
ATOM	7	H4'	CYT	2	2.773	7.244	2.078
ATOM	8	O1'	CYT	2	1.104	6.506	1.185
ATOM	9	C1'	CYT	2	1.677	5.586	0.279
ATOM	10	H1'	CYT	2	2.478	5.061	0.802
ATOM	11	N1	CYT	2	0.643	4.665	-0.262
ATOM	12	C6	CYT	2	-0.608	5.124	-0.588
ATOM	13	H6	CYT	2	-0.808	6.184	-0.542
ATOM	14	C5	CYT	2	-1.601	4.275	-0.941
ATOM	15	H5	CYT	2	-2.576	4.669	-1.186
ATOM	16	C4	CYT	2	-1.287	2.879	-0.952
ATOM	17	N4	CYT	2	-2.248	1.983	-1.147
ATOM	18	HN4A	CYT	2	-2.020	0.999	-1.049
ATOM	19	HN4B	CYT	2	-3.180	2.275	-1.384
ATOM	20	N3	CYT	2	-0.062	2.431	-0.661
ATOM	21	C2	CYT	2	0.934	3.308	-0.356
ATOM	22	O2	CYT	2	2.065	2.873	-0.151
ATOM	23	C3'	CYT	2	2.756	7.710	-0.022
ATOM	24	H3'	CYT	2	2.438	8.620	-0.531
ATOM	25	C2'	CYT	2	2.285	6.476	-0.798
ATOM	26	H2A'	CYT	2	3.099	5.960	-1.301
ATOM	27	H2B'	CYT	2	1.529	6.781	-1.522
ATOM	28	O3'	CYT	2	4.154	7.723	0.202
ATOM	29	P	POM	3	5.210	8.058	-0.972
ATOM	30	OA	POM	3	4.532	8.911	-1.972
ATOM	31	OB	POM	3	6.461	8.520	-0.335
ATOM	32	O5'	GUA	4	5.482	6.615	-1.632
ATOM	33	C5'	GUA	4	6.255	5.646	-0.950
ATOM	34	H5A'	GUA	4	7.276	6.014	-0.836
ATOM	35	H5B'	GUA	4	5.833	5.470	0.040
ATOM	36	C4'	GUA	4	6.294	4.316	-1.711
ATOM	37	H4'	GUA	4	6.938	3.635	-1.152
ATOM	38	O1'	GUA	4	4.994	3.743	-1.783
ATOM	39	C1'	GUA	4	4.813	3.249	-3.096
ATOM	40	H1'	GUA	4	5.310	2.282	-3.192
ATOM	41	N9	GUA	4	3.371	3.129	-3.407
ATOM	42	C8	GUA	4	2.430	4.124	-3.465
ATOM	43	H8	GUA	4	2.675	5.173	-3.397
ATOM	44	N7	GUA	4	1.204	3.699	-3.586
ATOM	45	C5	GUA	4	1.340	2.314	-3.638
ATOM	46	C6	GUA	4	0.352	1.291	-3.740
ATOM	47	O6	GUA	4	-0.868	1.418	-3.790
ATOM	48	N1	GUA	4	0.891	0.014	-3.767
ATOM	49	H1	GUA	4	0.224	-0.758	-3.755
ATOM	50	C2	GUA	4	2.237	-0.249	-3.759

ATOM	51	N2	GUA	4	2.625	-1.518	-3.831
ATOM	52	HN2A	GUA	4	1.950	-2.274	-3.848
ATOM	53	HN2B	GUA	4	3.613	-1.714	-3.790
ATOM	54	N3	GUA	4	3.175	0.698	-3.655
ATOM	55	C4	GUA	4	2.665	1.958	-3.577
ATOM	56	C3'	GUA	4	6.825	4.452	-3.147
ATOM	57	H3'	GUA	4	7.299	5.419	-3.326
ATOM	58	C2'	GUA	4	5.539	4.280	-3.952
ATOM	59	H2A'	GUA	4	5.721	3.946	-4.969
ATOM	60	H2B'	GUA	4	5.003	5.229	-3.959
ATOM	61	O3'	GUA	4	7.742	3.394	-3.363
ATOM	62	P	POM	5	8.590	3.223	-4.725
ATOM	63	OA	POM	5	8.154	4.246	-5.699
ATOM	64	OB	POM	5	10.020	3.093	-4.370
ATOM	65	O5'	CYT	6	8.062	1.794	-5.237
ATOM	66	C5'	CYT	6	8.352	0.617	-4.508
ATOM	67	H5A'	CYT	6	9.429	0.439	-4.506
ATOM	68	H5B'	CYT	6	8.014	0.734	-3.477
ATOM	69	C4'	CYT	6	7.638	-0.598	-5.110
ATOM	70	H4'	CYT	6	7.836	-1.454	-4.463
ATOM	71	O1'	CYT	6	6.240	-0.352	-5.141
ATOM	72	C1'	CYT	6	5.765	-0.558	-6.458
ATOM	73	H1'	CYT	6	5.477	-1.607	-6.538
ATOM	74	N1	CYT	6	4.641	0.381	-6.729
ATOM	75	C6	CYT	6	4.815	1.733	-6.592
ATOM	76	H6	CYT	6	5.802	2.120	-6.389
ATOM	77	C5	CYT	6	3.775	2.594	-6.690
ATOM	78	H5	CYT	6	3.953	3.654	-6.586
ATOM	79	C4	CYT	6	2.484	2.028	-6.919
ATOM	80	N4	CYT	6	1.418	2.818	-6.933
ATOM	81	HN4A	CYT	6	0.494	2.425	-7.069
ATOM	82	HN4B	CYT	6	1.511	3.801	-6.738
ATOM	83	N3	CYT	6	2.302	0.709	-7.054
ATOM	84	C2	CYT	6	3.376	-0.132	-6.998
ATOM	85	O2	CYT	6	3.196	-1.334	-7.183
ATOM	86	C3'	CYT	6	8.099	-0.920	-6.537
ATOM	87	H3'	CYT	6	9.057	-0.448	-6.761
ATOM	88	C2'	CYT	6	6.965	-0.336	-7.376
ATOM	89	H2A'	CYT	6	6.852	-0.838	-8.335
ATOM	90	H2B'	CYT	6	7.169	0.722	-7.534
ATOM	91	O3'	CYT	6	8.194	-2.328	-6.662
ATOM	92	P	POM	7	8.811	-3.036	-7.972
ATOM	93	OA	POM	7	9.531	-2.017	-8.766
ATOM	94	OB	POM	7	9.509	-4.266	-7.543
ATOM	95	O5'	ADE	8	7.488	-3.457	-8.783
ATOM	96	C5'	ADE	8	6.745	-4.601	-8.413
ATOM	97	H5A'	ADE	8	7.369	-5.491	-8.510
ATOM	98	H5B'	ADE	8	6.416	-4.510	-7.377
ATOM	99	C4'	ADE	8	5.519	-4.763	-9.316
ATOM	100	H4'	ADE	8	5.001	-5.678	-9.027
ATOM	101	O1'	ADE	8	4.637	-3.663	-9.134
ATOM	102	C1'	ADE	8	4.261	-3.201	-10.415
ATOM	103	H1'	ADE	8	3.459	-3.839	-10.788

ATOM	104	N9	ADE	8	3.794	-1.799	-10.359
ATOM	105	C8	ADE	8	4.530	-0.638	-10.344
ATOM	106	H8	ADE	8	5.608	-0.618	-10.397
ATOM	107	N7	ADE	8	3.816	0.451	-10.258
ATOM	108	C5	ADE	8	2.511	-0.026	-10.210
ATOM	109	C6	ADE	8	1.264	0.610	-10.095
ATOM	110	N6	ADE	8	1.140	1.933	-10.024
ATOM	111	HN6A	ADE	8	0.228	2.359	-9.908
ATOM	112	HN6B	ADE	8	1.976	2.494	-10.068
ATOM	113	N1	ADE	8	0.155	-0.142	-10.051
ATOM	114	C2	ADE	8	0.271	-1.462	-10.113
ATOM	115	H2	ADE	8	-0.654	-2.015	-10.086
ATOM	116	N3	ADE	8	1.377	-2.191	-10.214
ATOM	117	C4	ADE	8	2.483	-1.395	-10.260
ATOM	118	C3'	ADE	8	5.900	-4.809	-10.807
ATOM	119	H3'	ADE	8	6.965	-4.981	-10.974
ATOM	120	C2'	ADE	8	5.498	-3.417	-11.277
ATOM	121	H2A'	ADE	8	5.289	-3.379	-12.346
ATOM	122	H2B'	ADE	8	6.293	-2.720	-11.016
ATOM	123	O3'	ADE	8	5.119	-5.761	-11.503
ATOM	124	P	POM	9	5.558	-7.309	-11.546
ATOM	125	OA	POM	9	6.816	-7.398	-12.316
ATOM	126	OB	POM	9	5.499	-7.846	-10.168
ATOM	127	O5'	ADE	10	4.387	-7.982	-12.422
ATOM	128	C5'	ADE	10	3.223	-8.542	-11.839
ATOM	129	H5A'	ADE	10	3.235	-9.617	-12.018
ATOM	130	H5B'	ADE	10	3.178	-8.372	-10.762
ATOM	131	C4'	ADE	10	1.956	-7.945	-12.458
ATOM	132	H4'	ADE	10	1.098	-8.459	-12.033
ATOM	133	O1'	ADE	10	1.850	-6.571	-12.146
ATOM	134	C1'	ADE	10	0.955	-5.987	-13.070
ATOM	135	H1'	ADE	10	-0.050	-6.041	-12.653
ATOM	136	N9	ADE	10	1.362	-4.584	-13.298
ATOM	137	C8	ADE	10	2.637	-4.103	-13.468
ATOM	138	H8	ADE	10	3.502	-4.750	-13.510
ATOM	139	N7	ADE	10	2.718	-2.803	-13.540
ATOM	140	C5	ADE	10	1.392	-2.399	-13.437
ATOM	141	C6	ADE	10	0.786	-1.133	-13.430
ATOM	142	N6	ADE	10	1.511	-0.022	-13.512
ATOM	143	HN6A	ADE	10	1.056	0.881	-13.493
ATOM	144	HN6B	ADE	10	2.511	-0.104	-13.619
ATOM	145	N1	ADE	10	-0.549	-1.042	-13.317
ATOM	146	C2	ADE	10	-1.249	-2.167	-13.217
ATOM	147	H2	ADE	10	-2.316	-2.036	-13.165
ATOM	148	N3	ADE	10	-0.805	-3.422	-13.175
ATOM	149	C4	ADE	10	0.550	-3.471	-13.298
ATOM	150	C3'	ADE	10	1.869	-8.056	-13.982
ATOM	151	H3'	ADE	10	2.862	-7.958	-14.424
ATOM	152	C2'	ADE	10	1.022	-6.833	-14.343
ATOM	153	H2A'	ADE	10	0.013	-7.123	-14.635
ATOM	154	H2B'	ADE	10	1.510	-6.298	-15.157
ATOM	155	O3'	ADE	10	1.261	-9.286	-14.339
ATOM	156	P	POM	11	1.122	-9.771	-15.874

ATOM	157	OA	POM	11	2.177	-9.116	-16.676
ATOM	158	OB	POM	11	0.998	-11.245	-15.877
ATOM	159	O5'	ADE	12	-0.294	-9.155	-16.322
ATOM	160	C5'	ADE	12	-1.502	-9.651	-15.776
ATOM	161	H5A'	ADE	12	-1.665	-10.682	-16.091
ATOM	162	H5B'	ADE	12	-1.445	-9.620	-14.687
ATOM	163	C4'	ADE	12	-2.682	-8.781	-16.217
ATOM	164	H4'	ADE	12	-3.561	-9.101	-15.660
ATOM	165	O1'	ADE	12	-2.378	-7.433	-15.900
ATOM	166	C1'	ADE	12	-2.669	-6.608	-17.005
ATOM	167	H1'	ADE	12	-3.692	-6.238	-16.921
ATOM	168	N9	ADE	12	-1.676	-5.511	-17.018
ATOM	169	C8	ADE	12	-0.311	-5.631	-17.136
ATOM	170	H8	ADE	12	0.186	-6.577	-17.296
ATOM	171	N7	ADE	12	0.343	-4.510	-17.020
ATOM	172	C5	ADE	12	-0.664	-3.581	-16.808
ATOM	173	C6	ADE	12	-0.630	-2.197	-16.601
ATOM	174	N6	ADE	12	0.529	-1.549	-16.564
ATOM	175	HN6A	ADE	12	0.550	-0.547	-16.439
ATOM	176	HN6B	ADE	12	1.375	-2.079	-16.706
ATOM	177	N1	ADE	12	-1.776	-1.529	-16.403
ATOM	178	C2	ADE	12	-2.913	-2.220	-16.415
ATOM	179	H2	ADE	12	-3.809	-1.642	-16.253
ATOM	180	N3	ADE	12	-3.087	-3.528	-16.601
ATOM	181	C4	ADE	12	-1.901	-4.169	-16.793
ATOM	182	C3'	ADE	12	-2.995	-8.874	-17.716
ATOM	183	H3'	ADE	12	-2.435	-9.687	-18.182
ATOM	184	C2'	ADE	12	-2.529	-7.515	-18.226
ATOM	185	H2A'	ADE	12	-3.127	-7.167	-19.062
ATOM	186	H2B'	ADE	12	-1.488	-7.618	-18.530
ATOM	187	O3'	ADE	12	-4.390	-9.070	-17.892
ATOM	188	P	POM	13	-5.045	-9.389	-19.335
ATOM	189	OA	POM	13	-3.969	-9.816	-20.256
ATOM	190	OB	POM	13	-6.220	-10.263	-19.121
ATOM	191	O5'	THY	14	-5.571	-7.947	-19.818
ATOM	192	C5'	THY	14	-6.726	-7.372	-19.233
ATOM	193	H5A'	THY	14	-7.621	-7.887	-19.582
ATOM	194	H5B'	THY	14	-6.663	-7.470	-18.149
ATOM	195	C4'	THY	14	-6.816	-5.879	-19.559
ATOM	196	H4'	THY	14	-7.619	-5.448	-18.966
ATOM	197	O1'	THY	14	-5.599	-5.256	-19.189
ATOM	198	C1'	THY	14	-5.435	-4.119	-19.999
ATOM	199	H1'	THY	14	-6.056	-3.314	-19.607
ATOM	200	N1	THY	14	-3.989	-3.780	-20.068
ATOM	201	C6	THY	14	-3.089	-4.743	-20.452
ATOM	202	H6	THY	14	-3.463	-5.719	-20.722
ATOM	203	C5	THY	14	-1.759	-4.498	-20.498
ATOM	204	C7	THY	14	-0.797	-5.592	-20.923
ATOM	205	H7A	THY	14	0.056	-5.607	-20.244
ATOM	206	H7B	THY	14	-1.274	-6.573	-20.912
ATOM	207	H7C	THY	14	-0.439	-5.381	-21.931
ATOM	208	C4	THY	14	-1.243	-3.188	-20.159
ATOM	209	O4	THY	14	-0.060	-2.870	-20.191

ATOM	210	N3	THY	14	-2.198	-2.273	-19.763
ATOM	211	H3	THY	14	-1.865	-1.330	-19.556
ATOM	212	C2	THY	14	-3.560	-2.515	-19.671
ATOM	213	O2	THY	14	-4.320	-1.643	-19.255
ATOM	214	C3'	THY	14	-7.095	-5.545	-21.033
ATOM	215	H3'	THY	14	-7.001	-6.437	-21.654
ATOM	216	C2'	THY	14	-5.985	-4.545	-21.359
ATOM	217	H2A'	THY	14	-6.352	-3.677	-21.893
ATOM	218	H2B'	THY	14	-5.242	-5.060	-21.963
ATOM	219	O3'	THY	14	-8.391	-4.975	-21.161
ATOM	220	P	POM	15	-9.052	-4.612	-22.595
ATOM	221	OA	POM	15	-8.462	-5.497	-23.623
ATOM	222	OB	POM	15	-10.521	-4.566	-22.420
ATOM	223	O5'	THY	16	-8.542	-3.111	-22.880
ATOM	224	C5'	THY	16	-9.004	-2.032	-22.090
ATOM	225	H5A'	THY	16	-10.035	-1.790	-22.351
ATOM	226	H5B'	THY	16	-8.970	-2.319	-21.037
ATOM	227	C4'	THY	16	-8.114	-0.795	-22.251
ATOM	228	H4'	THY	16	-8.436	-0.085	-21.496
ATOM	229	O1'	THY	16	-6.757	-1.161	-22.034
ATOM	230	C1'	THY	16	-5.983	-0.552	-23.043
ATOM	231	H1'	THY	16	-5.826	0.486	-22.754
ATOM	232	N1	THY	16	-4.688	-1.264	-23.232
ATOM	233	C6	THY	16	-4.642	-2.558	-23.696
ATOM	234	H6	THY	16	-5.564	-3.045	-23.980
ATOM	235	C5	THY	16	-3.473	-3.245	-23.782
ATOM	236	C7	THY	16	-3.459	-4.670	-24.303
ATOM	237	H7A	THY	16	-3.003	-4.674	-25.294
ATOM	238	H7B	THY	16	-2.861	-5.294	-23.638
ATOM	239	H7C	THY	16	-4.466	-5.084	-24.371
ATOM	240	C4	THY	16	-2.221	-2.621	-23.395
ATOM	241	O4	THY	16	-1.111	-3.148	-23.393
ATOM	242	N3	THY	16	-2.348	-1.322	-22.965
ATOM	243	H3	THY	16	-1.494	-0.806	-22.771
ATOM	244	C2	THY	16	-3.519	-0.610	-22.852
ATOM	245	O2	THY	16	-3.481	0.543	-22.433
ATOM	246	C3'	THY	16	-8.195	-0.084	-23.611
ATOM	247	H3'	THY	16	-9.089	-0.367	-24.171
ATOM	248	C2'	THY	16	-6.896	-0.544	-24.267
ATOM	249	H2A'	THY	16	-6.550	0.151	-25.030
ATOM	250	H2B'	THY	16	-7.044	-1.538	-24.685
ATOM	251	O3'	THY	16	-8.117	1.317	-23.391
ATOM	252	P	POM	17	-8.770	2.390	-24.396
ATOM	253	OA	POM	17	-10.237	2.360	-24.224
ATOM	254	OB	POM	17	-8.033	3.663	-24.219
ATOM	255	O5'	GUA	18	-8.422	1.788	-25.845
ATOM	256	C5'	GUA	18	-8.429	2.579	-27.018
ATOM	257	H5A'	GUA	18	-8.539	1.887	-27.851
ATOM	258	H5B'	GUA	18	-9.293	3.245	-27.027
ATOM	259	C4'	GUA	18	-7.131	3.394	-27.168
ATOM	260	H4'	GUA	18	-7.288	4.331	-26.644
ATOM	261	O1'	GUA	18	-6.040	2.655	-26.625
ATOM	262	C1'	GUA	18	-5.165	2.294	-27.674

ATOM	263	H1'	GUA	18	-4.401	3.065	-27.763
ATOM	264	N9	GUA	18	-4.478	1.025	-27.362
ATOM	265	C8	GUA	18	-4.993	-0.244	-27.309
ATOM	266	H8	GUA	18	-6.026	-0.470	-27.529
ATOM	267	N7	GUA	18	-4.131	-1.156	-26.955
ATOM	268	C5	GUA	18	-2.951	-0.442	-26.769
ATOM	269	C6	GUA	18	-1.644	-0.895	-26.423
ATOM	270	O6	GUA	18	-1.283	-2.046	-26.197
ATOM	271	N1	GUA	18	-0.717	0.133	-26.349
ATOM	272	H1	GUA	18	0.250	-0.152	-26.183
ATOM	273	C2	GUA	18	-1.018	1.458	-26.540
ATOM	274	N2	GUA	18	-0.024	2.338	-26.486
ATOM	275	HN2A	GUA	18	0.931	2.045	-26.307
ATOM	276	HN2B	GUA	18	-0.213	3.306	-26.695
ATOM	277	N3	GUA	18	-2.244	1.903	-26.844
ATOM	278	C4	GUA	18	-3.160	0.899	-26.976
ATOM	279	C3'	GUA	18	-6.783	3.624	-28.648
ATOM	280	H3'	GUA	18	-7.663	3.768	-29.276
ATOM	281	C2'	GUA	18	-6.045	2.314	-28.927
ATOM	282	H2A'	GUA	18	-5.479	2.354	-29.854
ATOM	283	H2B'	GUA	18	-6.719	1.460	-28.949
ATOM	284	O3'	GUA	18	-5.810	4.636	-28.880
ATOM	285	P	POM	19	-5.976	6.191	-28.508
ATOM	286	OA	POM	19	-7.124	6.753	-29.246
ATOM	287	OB	POM	19	-5.881	6.316	-27.033
ATOM	288	O5'	GUA	20	-4.597	6.740	-29.132
ATOM	289	C5'	GUA	20	-3.774	7.676	-28.452
ATOM	290	H5A'	GUA	20	-4.127	8.688	-28.650
ATOM	291	H5B'	GUA	20	-3.796	7.508	-27.375
ATOM	292	C4'	GUA	20	-2.306	7.528	-28.880
ATOM	293	H4'	GUA	20	-1.707	8.194	-28.257
ATOM	294	O1'	GUA	20	-1.895	6.180	-28.663
ATOM	295	C1'	GUA	20	-1.402	5.645	-29.881
ATOM	296	H1'	GUA	20	-0.324	5.805	-29.930
ATOM	297	N9	GUA	20	-1.730	4.201	-29.987
ATOM	298	C8	GUA	20	-2.960	3.641	-30.211
ATOM	299	H8	GUA	20	-3.851	4.221	-30.384
ATOM	300	N7	GUA	20	-2.972	2.340	-30.207
ATOM	301	C5	GUA	20	-1.651	2.000	-29.955
ATOM	302	C6	GUA	20	-1.061	0.716	-29.784
ATOM	303	O6	GUA	20	-1.629	-0.370	-29.728
ATOM	304	N1	GUA	20	0.311	0.772	-29.616
ATOM	305	H1	GUA	20	0.771	-0.135	-29.523
ATOM	306	C2	GUA	20	1.028	1.941	-29.537
ATOM	307	N2	GUA	20	2.345	1.851	-29.388
ATOM	308	HN2A	GUA	20	2.811	0.949	-29.390
ATOM	309	HN2B	GUA	20	2.880	2.700	-29.303
ATOM	310	N3	GUA	20	0.474	3.159	-29.632
ATOM	311	C4	GUA	20	-0.872	3.127	-29.840
ATOM	312	C3'	GUA	20	-2.062	7.868	-30.357
ATOM	313	H3'	GUA	20	-2.845	8.510	-30.765
ATOM	314	C2'	GUA	20	-2.083	6.476	-30.969
ATOM	315	H2A'	GUA	20	-1.570	6.440	-31.923

ATOM	316	H2B'	GUA	20	-3.123	6.192	-31.113
ATOM	317	O3'	GUA	20	-0.794	8.494	-30.477
ATOM	318	P	POM	21	-0.196	9.003	-31.890
ATOM	319	OA	POM	21	-1.198	8.757	-32.951
ATOM	320	OB	POM	21	0.363	10.358	-31.699
ATOM	321	O5'	CYT	22	1.023	7.977	-32.115
ATOM	322	C5'	CYT	22	2.166	8.029	-31.283
ATOM	323	H5A'	CYT	22	2.704	8.966	-31.437
ATOM	324	H5B'	CYT	22	1.848	7.984	-30.240
ATOM	325	C4'	CYT	22	3.095	6.834	-31.538
ATOM	326	H4'	CYT	22	3.874	6.842	-30.774
ATOM	327	O1'	CYT	22	2.324	5.648	-31.416
ATOM	328	C1'	CYT	22	2.525	4.842	-32.560
ATOM	329	H1'	CYT	22	3.391	4.209	-32.360
ATOM	330	N1	CYT	22	1.290	4.063	-32.851
ATOM	331	C6	CYT	22	0.114	4.706	-33.132
ATOM	332	H6	CYT	22	0.106	5.783	-33.208
ATOM	333	C5	CYT	22	-1.041	4.024	-33.311
ATOM	334	H5	CYT	22	-1.948	4.569	-33.532
ATOM	335	C4	CYT	22	-0.983	2.603	-33.179
ATOM	336	N4	CYT	22	-2.094	1.887	-33.288
ATOM	337	HN4A	CYT	22	-2.052	0.892	-33.103
ATOM	338	HN4B	CYT	22	-2.986	2.341	-33.382
ATOM	339	N3	CYT	22	0.162	1.968	-32.907
ATOM	340	C2	CYT	22	1.317	2.675	-32.748
ATOM	341	O2	CYT	22	2.361	2.065	-32.527
ATOM	342	C3'	CYT	22	3.769	6.797	-32.918
ATOM	343	H3'	CYT	22	4.775	6.388	-32.813
ATOM	344	C2'	CYT	22	2.911	5.804	-33.686
ATOM	345	H2A'	CYT	22	3.465	5.311	-34.484
ATOM	346	H2B'	CYT	22	2.051	6.335	-34.093
ATOM	347	O3'	CYT	22	3.830	8.045	-33.576
ATOM	348	H	HE	23	4.360	8.644	-33.046
ATOM	349	H	HB	24	-0.518	-9.400	-35.492
ATOM	350	O5'	GUA	25	0.033	-8.746	-35.055
ATOM	351	C5'	GUA	25	1.210	-8.572	-35.815
ATOM	352	H5A'	GUA	25	1.742	-9.522	-35.874
ATOM	353	H5B'	GUA	25	0.939	-8.256	-36.823
ATOM	354	C4'	GUA	25	2.122	-7.516	-35.181
ATOM	355	H4'	GUA	25	3.013	-7.418	-35.805
ATOM	356	O1'	GUA	25	1.449	-6.265	-35.138
ATOM	357	C1'	GUA	25	1.655	-5.705	-33.855
ATOM	358	H1'	GUA	25	2.631	-5.218	-33.826
ATOM	359	N9	GUA	25	0.575	-4.753	-33.519
ATOM	360	C8	GUA	25	-0.780	-4.967	-33.511
ATOM	361	H8	GUA	25	-1.224	-5.930	-33.716
ATOM	362	N7	GUA	25	-1.488	-3.905	-33.247
ATOM	363	C5	GUA	25	-0.534	-2.906	-33.071
ATOM	364	C6	GUA	25	-0.689	-1.509	-32.819
ATOM	365	O6	GUA	25	-1.733	-0.871	-32.713
ATOM	366	N1	GUA	25	0.523	-0.838	-32.743
ATOM	367	H1	GUA	25	0.462	0.175	-32.638
ATOM	368	C2	GUA	25	1.749	-1.444	-32.872

ATOM	369	N2	GUA	25	2.845	-0.710	-32.720
ATOM	370	HN2A	GUA	25	2.789	0.281	-32.515
ATOM	371	HN2B	GUA	25	3.740	-1.173	-32.780
ATOM	372	N3	GUA	25	1.904	-2.745	-33.124
ATOM	373	C4	GUA	25	0.730	-3.419	-33.224
ATOM	374	C3'	GUA	25	2.538	-7.870	-33.744
ATOM	375	H3'	GUA	25	2.342	-8.916	-33.502
ATOM	376	C2'	GUA	25	1.664	-6.917	-32.935
ATOM	377	H2A'	GUA	25	2.070	-6.697	-31.950
ATOM	378	H2B'	GUA	25	0.664	-7.339	-32.837
ATOM	379	O3'	GUA	25	3.917	-7.579	-33.609
ATOM	380	P	POM	26	4.741	-7.877	-32.255
ATOM	381	OA	POM	26	3.827	-8.511	-31.280
ATOM	382	OB	POM	26	6.006	-8.545	-32.628
ATOM	383	O5'	CYT	27	5.078	-6.390	-31.740
ATOM	384	C5'	CYT	27	5.978	-5.569	-32.461
ATOM	385	H5A'	CYT	27	6.953	-6.055	-32.519
ATOM	386	H5B'	CYT	27	5.600	-5.423	-33.474
ATOM	387	C4'	CYT	27	6.153	-4.194	-31.805
ATOM	388	H4'	CYT	27	6.822	-3.612	-32.441
ATOM	389	O1'	CYT	27	4.900	-3.527	-31.730
ATOM	390	C1'	CYT	27	4.698	-3.076	-30.403
ATOM	391	H1'	CYT	27	5.146	-2.086	-30.310
ATOM	392	N1	CYT	27	3.245	-3.094	-30.084
ATOM	393	C6	CYT	27	2.524	-4.250	-30.240
ATOM	394	H6	CYT	27	3.036	-5.149	-30.549
ATOM	395	C5	CYT	27	1.188	-4.286	-30.032
ATOM	396	H5	CYT	27	0.656	-5.216	-30.168
ATOM	397	C4	CYT	27	0.558	-3.058	-29.660
ATOM	398	N4	CYT	27	-0.760	-3.015	-29.524
ATOM	399	HN4A	CYT	27	-1.199	-2.119	-29.353
ATOM	400	HN4B	CYT	27	-1.324	-3.837	-29.659
ATOM	401	N3	CYT	27	1.251	-1.923	-29.526
ATOM	402	C2	CYT	27	2.599	-1.913	-29.719
ATOM	403	O2	CYT	27	3.201	-0.852	-29.577
ATOM	404	C3'	CYT	27	6.741	-4.269	-30.389
ATOM	405	H3'	CYT	27	7.209	-5.234	-30.186
ATOM	406	C2'	CYT	27	5.495	-4.049	-29.536
ATOM	407	H2A'	CYT	27	5.720	-3.648	-28.551
ATOM	408	H2B'	CYT	27	4.991	-5.008	-29.429
ATOM	409	O3'	CYT	27	7.691	-3.225	-30.266
ATOM	410	P	POM	28	8.526	-2.948	-28.915
ATOM	411	OA	POM	28	8.236	-4.021	-27.939
ATOM	412	OB	POM	28	9.924	-2.642	-29.290
ATOM	413	O5'	CYT	29	7.828	-1.593	-28.404
ATOM	414	C5'	CYT	29	7.946	-0.404	-29.162
ATOM	415	H5A'	CYT	29	8.993	-0.100	-29.211
ATOM	416	H5B'	CYT	29	7.585	-0.580	-30.176
ATOM	417	C4'	CYT	29	7.121	0.731	-28.551
ATOM	418	H4'	CYT	29	7.174	1.584	-29.229
ATOM	419	O1'	CYT	29	5.763	0.334	-28.439
ATOM	420	C1'	CYT	29	5.262	0.718	-27.172
ATOM	421	H1'	CYT	29	4.887	1.740	-27.247

ATOM	422	N1	CYT	29	4.227	-0.267	-26.747
ATOM	423	C6	CYT	29	4.515	-1.607	-26.781
ATOM	424	H6	CYT	29	5.512	-1.921	-27.054
ATOM	425	C5	CYT	29	3.580	-2.541	-26.494
ATOM	426	H5	CYT	29	3.852	-3.586	-26.531
ATOM	427	C4	CYT	29	2.276	-2.068	-26.151
ATOM	428	N4	CYT	29	1.330	-2.946	-25.842
ATOM	429	HN4A	CYT	29	0.390	-2.619	-25.649
ATOM	430	HN4B	CYT	29	1.526	-3.932	-25.843
ATOM	431	N3	CYT	29	1.980	-0.763	-26.121
ATOM	432	C2	CYT	29	2.943	0.161	-26.411
ATOM	433	O2	CYT	29	2.647	1.353	-26.358
ATOM	434	C3'	CYT	29	7.623	1.154	-27.165
ATOM	435	H3'	CYT	29	8.556	0.650	-26.904
ATOM	436	C2'	CYT	29	6.483	0.705	-26.252
ATOM	437	H2A'	CYT	29	6.353	1.357	-25.392
ATOM	438	H2B'	CYT	29	6.712	-0.304	-25.911
ATOM	439	O3'	CYT	29	7.819	2.557	-27.189
ATOM	440	P	POM	30	8.399	3.380	-25.930
ATOM	441	OA	POM	30	9.027	2.432	-24.984
ATOM	442	OB	POM	30	9.168	4.533	-26.446
ATOM	443	O5'	ADE	31	7.039	3.928	-25.279
ATOM	444	C5'	ADE	31	6.249	4.877	-25.970
ATOM	445	H5A'	ADE	31	6.782	5.827	-26.033
ATOM	446	H5B'	ADE	31	6.041	4.521	-26.980
ATOM	447	C4'	ADE	31	4.917	5.087	-25.250
ATOM	448	H4'	ADE	31	4.299	5.759	-25.849
ATOM	449	O1'	ADE	31	4.234	3.852	-25.127
ATOM	450	C1'	ADE	31	3.514	3.874	-23.915
ATOM	451	H1'	ADE	31	2.589	4.437	-24.051
ATOM	452	N9	ADE	31	3.253	2.481	-23.485
ATOM	453	C8	ADE	31	4.163	1.463	-23.329
ATOM	454	H8	ADE	31	5.229	1.619	-23.401
ATOM	455	N7	ADE	31	3.635	0.290	-23.111
ATOM	456	C5	ADE	31	2.271	0.556	-23.104
ATOM	457	C6	ADE	31	1.141	-0.265	-22.956
ATOM	458	N6	ADE	31	1.234	-1.583	-22.788
ATOM	459	HN6A	ADE	31	0.407	-2.169	-22.751
ATOM	460	HN6B	ADE	31	2.156	-1.990	-22.767
ATOM	461	N1	ADE	31	-0.077	0.295	-22.987
ATOM	462	C2	ADE	31	-0.174	1.605	-23.183
ATOM	463	H2	ADE	31	-1.176	2.003	-23.207
ATOM	464	N3	ADE	31	0.801	2.487	-23.352
ATOM	465	C4	ADE	31	2.023	1.889	-23.309
ATOM	466	C3'	ADE	31	5.091	5.677	-23.844
ATOM	467	H3'	ADE	31	6.147	5.787	-23.593
ATOM	468	C2'	ADE	31	4.434	4.620	-22.954
ATOM	469	H2A'	ADE	31	3.889	5.054	-22.119
ATOM	470	H2B'	ADE	31	5.217	3.958	-22.584
ATOM	471	O3'	ADE	31	4.440	6.936	-23.803
ATOM	472	P	POM	32	4.546	7.919	-22.530
ATOM	473	OA	POM	32	5.732	7.537	-21.731
ATOM	474	OB	POM	32	4.394	9.311	-23.008

ATOM	475	O5'	ADE	33	3.226	7.518	-21.707
ATOM	476	C5'	ADE	33	1.959	8.016	-22.092
ATOM	477	H5A'	ADE	33	1.911	9.085	-21.882
ATOM	478	H5B'	ADE	33	1.811	7.858	-23.161
ATOM	479	C4'	ADE	33	0.837	7.298	-21.337
ATOM	480	H4'	ADE	33	-0.124	7.700	-21.662
ATOM	481	O1'	ADE	33	0.857	5.908	-21.599
ATOM	482	C1'	ADE	33	0.077	5.280	-20.601
ATOM	483	H1'	ADE	33	-0.944	5.183	-20.968
ATOM	484	N9	ADE	33	0.623	3.948	-20.280
ATOM	485	C8	ADE	33	1.941	3.577	-20.194
ATOM	486	H8	ADE	33	2.753	4.275	-20.322
ATOM	487	N7	ADE	33	2.126	2.310	-19.948
ATOM	488	C5	ADE	33	0.831	1.817	-19.841
ATOM	489	C6	ADE	33	0.327	0.531	-19.599
ATOM	490	N6	ADE	33	1.151	-0.499	-19.444
ATOM	491	HN6A	ADE	33	0.786	-1.440	-19.396
ATOM	492	HN6B	ADE	33	2.143	-0.319	-19.488
ATOM	493	N1	ADE	33	-1.004	0.339	-19.555
ATOM	494	C2	ADE	33	-1.795	1.396	-19.739
ATOM	495	H2	ADE	33	-2.854	1.201	-19.683
ATOM	496	N3	ADE	33	-1.451	2.659	-19.977
ATOM	497	C4	ADE	33	-0.098	2.804	-20.025
ATOM	498	C3'	ADE	33	0.931	7.415	-19.817
ATOM	499	H3'	ADE	33	1.968	7.289	-19.501
ATOM	500	C2'	ADE	33	0.108	6.204	-19.381
ATOM	501	H2A'	ADE	33	-0.909	6.495	-19.130
ATOM	502	H2B'	ADE	33	0.585	5.737	-18.523
ATOM	503	O3'	ADE	33	0.393	8.643	-19.358
ATOM	504	P	POM	34	0.451	9.074	-17.803
ATOM	505	OA	POM	34	1.686	8.523	-17.203
ATOM	506	OB	POM	34	0.167	10.523	-17.714
ATOM	507	O5'	THY	35	-0.795	8.287	-17.162
ATOM	508	C5'	THY	35	-2.122	8.610	-17.529
ATOM	509	H5A'	THY	35	-2.378	9.614	-17.189
ATOM	510	H5B'	THY	35	-2.218	8.573	-18.615
ATOM	511	C4'	THY	35	-3.090	7.591	-16.921
ATOM	512	H4'	THY	35	-4.071	7.734	-17.375
ATOM	513	O1'	THY	35	-2.636	6.280	-17.220
ATOM	514	C1'	THY	35	-2.899	5.438	-16.118
ATOM	515	H1'	THY	35	-3.938	5.113	-16.145
ATOM	516	N1	THY	35	-1.926	4.310	-16.133
ATOM	517	C6	THY	35	-0.586	4.586	-16.266
ATOM	518	H6	THY	35	-0.273	5.620	-16.320
ATOM	519	C5	THY	35	0.341	3.602	-16.342
ATOM	520	C7	THY	35	1.816	3.946	-16.451
ATOM	521	H7A	THY	35	2.275	3.343	-17.236
ATOM	522	H7B	THY	35	1.970	5.003	-16.678
ATOM	523	H7C	THY	35	2.303	3.715	-15.504
ATOM	524	C4	THY	35	-0.060	2.212	-16.288
ATOM	525	O4	THY	35	0.705	1.258	-16.366
ATOM	526	N3	THY	35	-1.417	2.001	-16.150
ATOM	527	H3	THY	35	-1.727	1.038	-16.109

ATOM	528	C2	THY	35	-2.381	2.991	-16.056
ATOM	529	O2	THY	35	-3.557	2.674	-15.892
ATOM	530	C3'	THY	35	-3.221	7.711	-15.397
ATOM	531	H3'	THY	35	-2.615	8.528	-15.002
ATOM	532	C2'	THY	35	-2.684	6.362	-14.924
ATOM	533	H2A'	THY	35	-3.198	5.999	-14.045
ATOM	534	H2B'	THY	35	-1.626	6.493	-14.702
ATOM	535	O3'	THY	35	-4.586	7.923	-15.080
ATOM	536	P	POM	36	-5.131	8.034	-13.565
ATOM	537	OA	POM	36	-3.989	8.303	-12.664
ATOM	538	OB	POM	36	-6.308	8.929	-13.563
ATOM	539	O5'	THY	37	-5.639	6.531	-13.302
ATOM	540	C5'	THY	37	-6.664	5.983	-14.107
ATOM	541	H5A'	THY	37	-7.594	6.531	-13.950
ATOM	542	H5B'	THY	37	-6.379	6.067	-15.156
ATOM	543	C4'	THY	37	-6.886	4.501	-13.802
ATOM	544	H4'	THY	37	-7.632	4.128	-14.500
ATOM	545	O1'	THY	37	-5.666	3.795	-13.978
ATOM	546	C1'	THY	37	-5.484	2.906	-12.893
ATOM	547	H1'	THY	37	-6.017	1.980	-13.105
ATOM	548	N1	THY	37	-4.021	2.699	-12.684
ATOM	549	C6	THY	37	-3.210	3.790	-12.486
ATOM	550	H6	THY	37	-3.669	4.752	-12.317
ATOM	551	C5	THY	37	-1.860	3.697	-12.533
ATOM	552	C7	THY	37	-0.996	4.920	-12.285
ATOM	553	H7A	THY	37	-0.429	4.770	-11.366
ATOM	554	H7B	THY	37	-0.296	5.044	-13.112
ATOM	555	H7C	THY	37	-1.595	5.826	-12.184
ATOM	556	C4	THY	37	-1.221	2.427	-12.802
ATOM	557	O4	THY	37	-0.016	2.268	-12.964
ATOM	558	N3	THY	37	-2.085	1.357	-12.905
ATOM	559	H3	THY	37	-1.650	0.447	-13.055
ATOM	560	C2	THY	37	-3.469	1.424	-12.841
ATOM	561	O2	THY	37	-4.132	0.391	-12.894
ATOM	562	C3'	THY	37	-7.398	4.243	-12.384
ATOM	563	H3'	THY	37	-7.701	5.169	-11.891
ATOM	564	C2'	THY	37	-6.174	3.614	-11.727
ATOM	565	H2A'	THY	37	-6.462	2.919	-10.950
ATOM	566	H2B'	THY	37	-5.572	4.417	-11.309
ATOM	567	O3'	THY	37	-8.474	3.324	-12.452
ATOM	568	P	POM	38	-9.564	3.197	-11.273
ATOM	569	OA	POM	38	-8.914	3.554	-9.992
ATOM	570	OB	POM	38	-10.778	3.926	-11.700
ATOM	571	O5'	THY	39	-9.907	1.616	-11.257
ATOM	572	C5'	THY	39	-8.915	0.614	-11.433
ATOM	573	H5A'	THY	39	-9.411	-0.347	-11.552
ATOM	574	H5B'	THY	39	-8.373	0.820	-12.355
ATOM	575	C4'	THY	39	-7.902	0.524	-10.283
ATOM	576	H4'	THY	39	-7.751	1.506	-9.855
ATOM	577	O1'	THY	39	-6.639	0.077	-10.738
ATOM	578	C1'	THY	39	-5.908	-0.393	-9.618
ATOM	579	H1'	THY	39	-5.610	-1.417	-9.849
ATOM	580	N1	THY	39	-4.733	0.498	-9.388

ATOM	581	C6	THY	39	-4.891	1.836	-9.099
ATOM	582	H6	THY	39	-5.875	2.214	-8.872
ATOM	583	C5	THY	39	-3.847	2.702	-9.105
ATOM	584	C7	THY	39	-4.067	4.167	-8.776
ATOM	585	H7A	THY	39	-3.504	4.787	-9.475
ATOM	586	H7B	THY	39	-5.123	4.437	-8.837
ATOM	587	H7C	THY	39	-3.706	4.359	-7.765
ATOM	588	C4	THY	39	-2.512	2.239	-9.426
ATOM	589	O4	THY	39	-1.508	2.939	-9.540
ATOM	590	N3	THY	39	-2.422	0.884	-9.639
ATOM	591	H3	THY	39	-1.498	0.511	-9.828
ATOM	592	C2	THY	39	-3.456	-0.025	-9.573
ATOM	593	O2	THY	39	-3.208	-1.223	-9.650
ATOM	594	C3'	THY	39	-8.269	-0.387	-9.114
ATOM	595	H3'	THY	39	-9.026	0.086	-8.486
ATOM	596	C2'	THY	39	-6.896	-0.425	-8.443
ATOM	597	H2A'	THY	39	-6.760	-1.318	-7.842
ATOM	598	H2B'	THY	39	-6.803	0.454	-7.808
ATOM	599	O3'	THY	39	-8.689	-1.667	-9.557
ATOM	600	P	POM	40	-9.354	-2.740	-8.550
ATOM	601	OA	POM	40	-10.171	-2.012	-7.554
ATOM	602	OB	POM	40	-9.966	-3.819	-9.357
ATOM	603	O5'	GUA	41	-8.075	-3.352	-7.794
ATOM	604	C5'	GUA	41	-7.225	-4.261	-8.459
ATOM	605	H5A'	GUA	41	-7.761	-5.201	-8.597
ATOM	606	H5B'	GUA	41	-6.957	-3.857	-9.434
ATOM	607	C4'	GUA	41	-5.938	-4.524	-7.672
ATOM	608	H4'	GUA	41	-5.415	-5.349	-8.155
ATOM	609	O1'	GUA	41	-5.083	-3.391	-7.708
ATOM	610	C1'	GUA	41	-4.506	-3.257	-6.427
ATOM	611	H1'	GUA	41	-3.709	-3.994	-6.309
ATOM	612	N9	GUA	41	-3.967	-1.890	-6.250
ATOM	613	C8	GUA	41	-4.647	-0.709	-6.106
ATOM	614	H8	GUA	41	-5.711	-0.655	-5.935
ATOM	615	N7	GUA	41	-3.907	0.357	-6.230
ATOM	616	C5	GUA	41	-2.628	-0.152	-6.424
ATOM	617	C6	GUA	41	-1.388	0.519	-6.645
ATOM	618	O6	GUA	41	-1.186	1.721	-6.787
ATOM	619	N1	GUA	41	-0.312	-0.350	-6.706
ATOM	620	H1	GUA	41	0.605	0.071	-6.847
ATOM	621	C2	GUA	41	-0.411	-1.703	-6.524
ATOM	622	N2	GUA	41	0.716	-2.387	-6.386
ATOM	623	HN2A	GUA	41	1.608	-1.933	-6.533
ATOM	624	HN2B	GUA	41	0.679	-3.238	-5.840
ATOM	625	N3	GUA	41	-1.568	-2.358	-6.391
ATOM	626	C4	GUA	41	-2.644	-1.525	-6.364
ATOM	627	C3'	GUA	41	-6.177	-4.877	-6.195
ATOM	628	H3'	GUA	41	-7.225	-5.090	-5.977
ATOM	629	C2'	GUA	41	-5.666	-3.613	-5.504
ATOM	630	H2A'	GUA	41	-5.357	-3.793	-4.478
ATOM	631	H2B'	GUA	41	-6.449	-2.856	-5.542
ATOM	632	O3'	GUA	41	-5.353	-5.988	-5.898
ATOM	633	P	POM	42	-5.497	-6.859	-4.554

ATOM	634	OA	POM	42	-6.014	-6.001	-3.466
ATOM	635	OB	POM	42	-6.157	-8.141	-4.880
ATOM	636	O5'	CYT	43	-3.947	-7.137	-4.253
ATOM	637	C5'	CYT	43	-3.153	-7.894	-5.143
ATOM	638	H5A'	CYT	43	-3.420	-8.950	-5.071
ATOM	639	H5B'	CYT	43	-3.316	-7.560	-6.169
ATOM	640	C4'	CYT	43	-1.669	-7.699	-4.816
ATOM	641	H4'	CYT	43	-1.092	-8.249	-5.562
ATOM	642	O1'	CYT	43	-1.357	-6.312	-4.887
ATOM	643	C1'	CYT	43	-0.928	-5.862	-3.612
ATOM	644	H1'	CYT	43	0.162	-5.914	-3.607
ATOM	645	N1	CYT	43	-1.415	-4.470	-3.360
ATOM	646	C6	CYT	43	-2.731	-4.213	-3.068
ATOM	647	H6	CYT	43	-3.441	-5.019	-2.976
ATOM	648	C5	CYT	43	-3.187	-2.949	-2.911
ATOM	649	H5	CYT	43	-4.227	-2.794	-2.667
ATOM	650	C4	CYT	43	-2.245	-1.890	-3.073
ATOM	651	N4	CYT	43	-2.679	-0.636	-3.057
ATOM	652	HN4A	CYT	43	-2.042	0.122	-3.266
ATOM	653	HN4B	CYT	43	-3.652	-0.443	-2.890
ATOM	654	N3	CYT	43	-0.964	-2.120	-3.387
ATOM	655	C2	CYT	43	-0.531	-3.406	-3.543
ATOM	656	O2	CYT	43	0.637	-3.593	-3.889
ATOM	657	C3'	CYT	43	-1.299	-8.194	-3.414
ATOM	658	H3'	CYT	43	-1.997	-8.956	-3.063
ATOM	659	C2'	CYT	43	-1.390	-6.910	-2.597
ATOM	660	H2A'	CYT	43	-0.752	-6.952	-1.719
ATOM	661	H2B'	CYT	43	-2.423	-6.782	-2.282
ATOM	662	O3'	CYT	43	0.021	-8.711	-3.457
ATOM	663	P	POM	44	0.695	-9.445	-2.188
ATOM	664	OA	POM	44	-0.354	-9.718	-1.182
ATOM	665	OB	POM	44	1.546	-10.545	-2.690
ATOM	666	O5'	GUA	45	1.654	-8.291	-1.611
ATOM	667	C5'	GUA	45	2.903	-8.029	-2.219
ATOM	668	H5A'	GUA	45	3.556	-8.898	-2.120
ATOM	669	H5B'	GUA	45	2.753	-7.825	-3.280
ATOM	670	C4'	GUA	45	3.576	-6.810	-1.579
ATOM	671	H4'	GUA	45	4.511	-6.617	-2.107
ATOM	672	O1'	GUA	45	2.716	-5.690	-1.730
ATOM	673	C1'	GUA	45	2.703	-4.985	-0.507
ATOM	674	H1'	GUA	45	3.594	-4.357	-0.459
ATOM	675	N9	GUA	45	1.480	-4.164	-0.386
ATOM	676	C8	GUA	45	0.180	-4.571	-0.234
ATOM	677	H8	GUA	45	-0.105	-5.605	-0.131
ATOM	678	N7	GUA	45	-0.688	-3.599	-0.216
ATOM	679	C5	GUA	45	0.095	-2.456	-0.341
ATOM	680	C6	GUA	45	-0.274	-1.079	-0.359
ATOM	681	O6	GUA	45	-1.401	-0.593	-0.296
ATOM	682	N1	GUA	45	0.819	-0.234	-0.446
ATOM	683	H1	GUA	45	0.599	0.760	-0.478
ATOM	684	C2	GUA	45	2.124	-0.654	-0.517
ATOM	685	N2	GUA	45	3.078	0.268	-0.575
ATOM	686	HN2A	GUA	45	2.856	1.256	-0.526

ATOM	687	HN2B	GUA	45	4.031	-0.029	-0.707
ATOM	688	N3	GUA	45	2.482	-1.942	-0.523
ATOM	689	C4	GUA	45	1.424	-2.791	-0.432
ATOM	690	C3'	GUA	45	3.881	-6.945	-0.077
ATOM	691	H3'	GUA	45	4.862	-6.513	0.127
ATOM	692	C2'	GUA	45	2.815	-6.068	0.562
ATOM	693	H2A'	GUA	45	3.121	-5.676	1.532
ATOM	694	H2B'	GUA	45	1.887	-6.637	0.645
ATOM	695	O3'	GUA	45	3.837	-8.265	0.423
ATOM	696	H	HE	46	3.993	-8.239	1.369
ATOM	697	O1	DIS	47	-2.562	-9.194	-10.513
ATOM	698	C1	DIS	47	-1.839	-8.511	-11.236
ATOM	699	HF	DIS	47	-0.807	-8.398	-10.953
ATOM	700	N1	DIS	47	-2.280	-7.831	-12.302
ATOM	701	HN1	DIS	47	-1.616	-7.236	-12.773
ATOM	702	C2	DIS	47	-3.585	-7.764	-12.848
ATOM	703	C3	DIS	47	-4.197	-6.835	-13.707
ATOM	704	H3	DIS	47	-3.823	-5.851	-13.948
ATOM	705	C5	DIS	47	-4.289	-8.944	-12.925
ATOM	706	H5	DIS	47	-4.004	-9.895	-12.498
ATOM	707	N2	DIS	47	-5.401	-8.728	-13.700
ATOM	708	C6	DIS	47	-6.403	-9.766	-14.071
ATOM	709	HM1	DIS	47	-6.427	-10.005	-15.135
ATOM	710	HM2	DIS	47	-6.248	-10.731	-13.588
ATOM	711	HM3	DIS	47	-7.432	-9.509	-13.821
ATOM	712	C4	DIS	47	-5.350	-7.432	-14.185
ATOM	713	C7	DIS	47	-6.330	-6.794	-15.135
ATOM	714	O2	DIS	47	-7.258	-7.478	-15.563
ATOM	715	N3	DIS	47	-6.175	-5.494	-15.436
ATOM	716	HN3	DIS	47	-5.348	-5.042	-15.076
ATOM	717	C8	DIS	47	-6.974	-4.644	-16.253
ATOM	718	C9	DIS	47	-6.763	-3.355	-16.781
ATOM	719	H9	DIS	47	-5.845	-2.791	-16.741
ATOM	720	C11	DIS	47	-8.317	-4.932	-16.375
ATOM	721	H11	DIS	47	-8.845	-5.793	-15.996
ATOM	722	N4	DIS	47	-8.902	-3.940	-17.120
ATOM	723	C12	DIS	47	-10.305	-3.948	-17.620
ATOM	724	HM4	DIS	47	-10.969	-3.248	-17.115
ATOM	725	HM5	DIS	47	-10.403	-3.707	-18.678
ATOM	726	HM6	DIS	47	-10.810	-4.909	-17.523
ATOM	727	C10	DIS	47	-7.972	-2.939	-17.316
ATOM	728	C13	DIS	47	-8.246	-1.598	-17.944
ATOM	729	O3	DIS	47	-9.416	-1.227	-18.012
ATOM	730	N5	DIS	47	-7.215	-0.894	-18.439
ATOM	731	HN5	DIS	47	-6.303	-1.331	-18.391
ATOM	732	C14	DIS	47	-7.184	0.363	-19.112
ATOM	733	C15	DIS	47	-6.169	1.018	-19.830
ATOM	734	H15	DIS	47	-5.158	0.667	-19.958
ATOM	735	C17	DIS	47	-8.322	1.141	-19.189
ATOM	736	H17	DIS	47	-9.284	0.964	-18.737
ATOM	737	N6	DIS	47	-8.046	2.235	-19.971
ATOM	738	C18	DIS	47	-9.020	3.297	-20.345
ATOM	739	HM7	DIS	47	-9.190	3.393	-21.417

ATOM	740	HM8	DIS	47	-10.019	3.156	-19.931
ATOM	741	HM9	DIS	47	-8.739	4.298	-20.022
ATOM	742	C16	DIS	47	-6.724	2.169	-20.364
ATOM	743	C19	DIS	47	-5.990	3.168	-21.219
ATOM	744	O4	DIS	47	-6.530	4.225	-21.540
ATOM	745	N7	DIS	47	-4.753	2.858	-21.617
ATOM	746	HN7	DIS	47	-4.369	1.947	-21.400
ATOM	747	C20	DIS	47	-4.017	3.659	-22.573
ATOM	748	HC1	DIS	47	-2.953	3.449	-22.476
ATOM	749	HC2	DIS	47	-4.175	4.718	-22.370
ATOM	750	C21	DIS	47	-4.489	3.321	-23.990
ATOM	751	HC3	DIS	47	-3.730	2.711	-24.479
ATOM	752	HC4	DIS	47	-5.404	2.727	-23.948
ATOM	753	C22	DIS	47	-4.794	4.545	-24.822
ATOM	754	N8	DIS	47	-3.983	4.918	-25.820
ATOM	755	HNC	DIS	47	-4.383	5.602	-26.466
ATOM	756	HND	DIS	47	-3.190	4.356	-26.095
ATOM	757	N9	DIS	47	-5.952	5.195	-24.665
ATOM	758	HNA	DIS	47	-6.187	5.848	-25.417
ATOM	759	HNB	DIS	47	-6.725	4.709	-24.199
ATOM	760	O1	DIS	48	-4.287	7.595	-20.347
ATOM	761	C1	DIS	48	-3.616	6.565	-20.349
ATOM	762	HF	DIS	48	-2.722	6.571	-20.951
ATOM	763	N1	DIS	48	-3.925	5.439	-19.687
ATOM	764	HN1	DIS	48	-3.262	4.682	-19.783
ATOM	765	C2	DIS	48	-5.005	5.113	-18.815
ATOM	766	C3	DIS	48	-5.319	3.929	-18.125
ATOM	767	H3	DIS	48	-4.745	3.016	-18.137
ATOM	768	C5	DIS	48	-6.041	6.003	-18.627
ATOM	769	H5	DIS	48	-6.146	6.997	-19.028
ATOM	770	N2	DIS	48	-6.985	5.401	-17.831
ATOM	771	C6	DIS	48	-8.268	6.018	-17.395
ATOM	772	HM1	DIS	48	-8.558	5.792	-16.369
ATOM	773	HM2	DIS	48	-8.276	7.107	-17.434
ATOM	774	HM3	DIS	48	-9.132	5.722	-17.989
ATOM	775	C4	DIS	48	-6.568	4.112	-17.559
ATOM	776	C7	DIS	48	-7.371	3.047	-16.864
ATOM	777	O2	DIS	48	-8.597	3.148	-16.889
ATOM	778	N3	DIS	48	-6.711	2.040	-16.267
ATOM	779	HN3	DIS	48	-5.702	2.122	-16.275
ATOM	780	C8	DIS	48	-7.184	0.887	-15.567
ATOM	781	C9	DIS	48	-6.509	-0.188	-14.958
ATOM	782	H9	DIS	48	-5.441	-0.328	-14.920
ATOM	783	C11	DIS	48	-8.539	0.666	-15.423
ATOM	784	H11	DIS	48	-9.357	1.271	-15.776
ATOM	785	N4	DIS	48	-8.716	-0.520	-14.753
ATOM	786	C12	DIS	48	-10.030	-1.149	-14.444
ATOM	787	HM4	DIS	48	-10.269	-2.005	-15.075
ATOM	788	HM5	DIS	48	-10.130	-1.531	-13.429
ATOM	789	HM6	DIS	48	-10.886	-0.484	-14.560
ATOM	790	C10	DIS	48	-7.476	-1.022	-14.418
ATOM	791	C13	DIS	48	-7.207	-2.295	-13.658
ATOM	792	O3	DIS	48	-8.051	-3.188	-13.688

ATOM	793	N5	DIS	48	-6.054	-2.380	-12.978
ATOM	794	HN5	DIS	48	-5.475	-1.550	-13.005
ATOM	795	C14	DIS	48	-5.493	-3.432	-12.194
ATOM	796	C15	DIS	48	-4.260	-3.538	-11.534
ATOM	797	H15	DIS	48	-3.500	-2.780	-11.494
ATOM	798	C17	DIS	48	-6.193	-4.598	-11.958
ATOM	799	H17	DIS	48	-7.191	-4.848	-12.284
ATOM	800	N6	DIS	48	-5.411	-5.424	-11.181
ATOM	801	C18	DIS	48	-5.815	-6.776	-10.698
ATOM	802	HM7	DIS	48	-6.385	-6.771	-9.771
ATOM	803	HM8	DIS	48	-6.456	-7.320	-11.391
ATOM	804	HM9	DIS	48	-4.999	-7.469	-10.497
ATOM	805	C16	DIS	48	-4.198	-4.794	-10.961
ATOM	806	C19	DIS	48	-3.001	-5.312	-10.205
ATOM	807	O4	DIS	48	-3.139	-6.159	-9.326
ATOM	808	N7	DIS	48	-1.797	-4.841	-10.558
ATOM	809	HN7	DIS	48	-1.734	-4.207	-11.346
ATOM	810	C20	DIS	48	-0.549	-5.260	-9.940
ATOM	811	HC1	DIS	48	-0.457	-6.344	-9.969
ATOM	812	HC2	DIS	48	0.272	-4.825	-10.509
ATOM	813	C21	DIS	48	-0.451	-4.784	-8.488
ATOM	814	HC3	DIS	48	-0.591	-3.706	-8.478
ATOM	815	HC4	DIS	48	-1.255	-5.226	-7.898
ATOM	816	C22	DIS	48	0.880	-5.106	-7.836
ATOM	817	N8	DIS	48	2.001	-4.538	-8.302
ATOM	818	HNC	DIS	48	2.910	-4.714	-7.897
ATOM	819	HND	DIS	48	1.940	-3.875	-9.063
ATOM	820	N9	DIS	48	0.933	-5.935	-6.782
ATOM	821	HNA	DIS	48	1.810	-6.156	-6.331
ATOM	822	HNB	DIS	48	0.081	-6.338	-6.416

Appendix F

Distamycin A - A₃T₃ Spectra

Figure F-1. Expansion of the aromatic to C1'H region of a NOESY spectrum of the A₃T₃ duplex without drug (20°C, 150 ms). Solid lines indicate sequential connectivities. Dashed line denotes cytosine C5H to aromatic NOE. Numbers denote intrareidue NOEs. A6 C2H is labeled explicitly. Peaks labeled with an X are due to an oligonucleotide impurity. Reprinted with permission from the *Journal of the American Chemical Society*. Copyright 1989, American Chemical Society.

Figure F-2. Spectrum of the exchangeable and aromatic resonances of the 2:1 distamycin A - A₃T₃ complex along with representative NOE difference spectra (45°C) used to assign the DNA imino and C2H, and drug H3 resonances. DNA imino resonances are labeled A-D (12-15 ppm), and drug amide resonances are labeled E-G (8-11 ppm). Asterisks denote peaks that have been saturated. In spectrum C, the broad lump at 13.48 ppm is due to an oligonucleotide impurity. Reprinted with permission from the *Journal of the American Chemical Society*. Copyright 1989, American Chemical Society.

Appendix G

Distamycin A - A₃T₃ coordinates

NMR constraints (Table G-1) and coordinates for the two symmetric 2:1 distamycin A - A₃T₃ complexes (both drugs bound to AATT (C1) and to ATTT (C2) sites) generated using the AMBER molecular mechanics program (Chapter 1) are summarized below. In this calculation, K_{nmr} was set to 300 (kcal/mol)/Å². In addition, 1.2 nm nonbonded and 0.4 nm hydrogen-bond cutoffs were used along with a distance-dependent dielectric function.

Table G-1. Distance constraints used to refine the 2:1 distamycin A - A₃T₃ complexes (both drugs in AATT (C1) and ATTT (C2) binding sites).

Drug Proton	DNA Proton	Distance (nm)	DNA Proton	Distance (nm)
C1 complex			C2 complex	
HF	A5 C1'H	0.40	A6 C1'H	0.40
H3-1	A5 C2H	0.35	A6 C2H	0.25
	A6 C1'H	-	T7 C1'H	0.30
H3-2	A6 C2H	0.25	A6' C2H	0.25
	T7 C1'H	0.30	T8 C1'H	0.30
H3-3	A6' C2H	0.25	A5' C2H	0.30
	T8 C1'H	0.30	T9 C1'H	0.35
CH ₂ C20	A5' C2H	0.40	A4' C2H	0.50

Coordinates for the 2:1 Distamycin A - A3T3

Complex (C1) both drugs in AATT binding sites

ATOM	1	H	HB	1	-0.156	9.996	1.359
ATOM	2	O5'	CYT	2	0.238	9.228	0.939
ATOM	3	C5'	CYT	2	1.283	8.754	1.763
ATOM	4	H5A'	CYT	2	2.035	9.535	1.878
ATOM	5	H5B'	CYT	2	0.874	8.506	2.743
ATOM	6	C4'	CYT	2	1.933	7.507	1.158
ATOM	7	H4'	CYT	2	2.686	7.136	1.856
ATOM	8	O1'	CYT	2	0.985	6.477	0.961
ATOM	9	C1'	CYT	2	1.563	5.591	0.025
ATOM	10	H1'	CYT	2	2.350	5.038	0.541
ATOM	11	N1	CYT	2	0.532	4.698	-0.567
ATOM	12	C6	CYT	2	-0.710	5.176	-0.896
ATOM	13	H6	CYT	2	-0.906	6.235	-0.808
ATOM	14	C5	CYT	2	-1.700	4.348	-1.304
ATOM	15	H5	CYT	2	-2.669	4.757	-1.550
ATOM	16	C4	CYT	2	-1.391	2.952	-1.368
ATOM	17	N4	CYT	2	-2.351	2.072	-1.629
ATOM	18	HN4A	CYT	2	-2.130	1.083	-1.565
ATOM	19	HN4B	CYT	2	-3.277	2.376	-1.874
ATOM	20	N3	CYT	2	-0.174	2.486	-1.073
ATOM	21	C2	CYT	2	0.819	3.344	-0.713
ATOM	22	O2	CYT	2	1.946	2.898	-0.512
ATOM	23	C3'	CYT	2	2.601	7.753	-0.202
ATOM	24	H3'	CYT	2	2.195	8.650	-0.673
ATOM	25	C2'	CYT	2	2.199	6.513	-1.009
ATOM	26	H2A'	CYT	2	3.048	6.021	-1.477
ATOM	27	H2B'	CYT	2	1.473	6.808	-1.767
ATOM	28	O3'	CYT	2	3.999	7.875	-0.011
ATOM	29	P	POM	3	4.998	8.296	-1.207
ATOM	30	OA	POM	3	4.235	9.104	-2.183
ATOM	31	OB	POM	3	6.228	8.843	-0.597
ATOM	32	O5'	GUA	4	5.356	6.879	-1.883
ATOM	33	C5'	GUA	4	6.185	5.953	-1.207
ATOM	34	H5A'	GUA	4	7.197	6.355	-1.136
ATOM	35	H5B'	GUA	4	5.802	5.787	-0.199
ATOM	36	C4'	GUA	4	6.230	4.603	-1.931
ATOM	37	H4'	GUA	4	6.878	3.941	-1.353
ATOM	38	O1'	GUA	4	4.931	4.027	-1.980
ATOM	39	C1'	GUA	4	4.762	3.470	-3.267
ATOM	40	H1'	GUA	4	5.273	2.507	-3.313
ATOM	41	N9	GUA	4	3.327	3.316	-3.593
ATOM	42	C8	GUA	4	2.373	4.291	-3.736
ATOM	43	H8	GUA	4	2.595	5.346	-3.686
ATOM	44	N7	GUA	4	1.166	3.836	-3.926
ATOM	45	C5	GUA	4	1.331	2.453	-3.925
ATOM	46	C6	GUA	4	0.373	1.405	-4.062
ATOM	47	O6	GUA	4	-0.842	1.508	-4.204
ATOM	48	N1	GUA	4	0.938	0.139	-3.996
ATOM	49	H1	GUA	4	0.291	-0.649	-4.014

ATOM	50	C2	GUA	4	2.284	-0.093	-3.861
ATOM	51	N2	GUA	4	2.711	-1.350	-3.849
ATOM	52	HN2A	GUA	4	3.699	-1.519	-3.744
ATOM	53	HN2B	GUA	4	2.065	-2.131	-3.906
ATOM	54	N3	GUA	4	3.190	0.879	-3.725
ATOM	55	C4	GUA	4	2.652	2.127	-3.747
ATOM	56	C3'	GUA	4	6.759	4.689	-3.373
ATOM	57	H3'	GUA	4	7.217	5.655	-3.591
ATOM	58	C2'	GUA	4	5.477	4.464	-4.173
ATOM	59	H2A'	GUA	4	5.658	4.077	-5.173
ATOM	60	H2B'	GUA	4	4.932	5.406	-4.226
ATOM	61	O3'	GUA	4	7.691	3.635	-3.548
ATOM	62	P	POM	5	8.538	3.420	-4.904
ATOM	63	OA	POM	5	8.090	4.402	-5.914
ATOM	64	OB	POM	5	9.970	3.326	-4.544
ATOM	65	O5'	CYT	6	8.031	1.963	-5.362
ATOM	66	C5'	CYT	6	8.365	0.816	-4.602
ATOM	67	H5A'	CYT	6	9.447	0.676	-4.603
ATOM	68	H5B'	CYT	6	8.031	0.954	-3.573
ATOM	69	C4'	CYT	6	7.694	-0.445	-5.160
ATOM	70	H4'	CYT	6	7.947	-1.276	-4.500
ATOM	71	O1'	CYT	6	6.284	-0.270	-5.163
ATOM	72	C1'	CYT	6	5.781	-0.591	-6.446
ATOM	73	H1'	CYT	6	5.559	-1.659	-6.461
ATOM	74	N1	CYT	6	4.594	0.261	-6.738
ATOM	75	C6	CYT	6	4.694	1.626	-6.661
ATOM	76	H6	CYT	6	5.650	2.072	-6.432
ATOM	77	C5	CYT	6	3.621	2.426	-6.854
ATOM	78	H5	CYT	6	3.742	3.498	-6.791
ATOM	79	C4	CYT	6	2.374	1.783	-7.122
ATOM	80	N4	CYT	6	1.279	2.520	-7.257
ATOM	81	HN4A	CYT	6	0.392	2.058	-7.420
ATOM	82	HN4B	CYT	6	1.310	3.517	-7.130
ATOM	83	N3	CYT	6	2.260	0.452	-7.176
ATOM	84	C2	CYT	6	3.363	-0.335	-7.007
ATOM	85	O2	CYT	6	3.231	-1.554	-7.089
ATOM	86	C3'	CYT	6	8.143	-0.780	-6.590
ATOM	87	H3'	CYT	6	9.047	-0.235	-6.864
ATOM	88	C2'	CYT	6	6.938	-0.327	-7.408
ATOM	89	H2A'	CYT	6	6.839	-0.879	-8.339
ATOM	90	H2B'	CYT	6	7.057	0.734	-7.622
ATOM	91	O3'	CYT	6	8.363	-2.178	-6.676
ATOM	92	P	POM	7	8.960	-2.881	-8.001
ATOM	93	OA	POM	7	9.453	-1.829	-8.916
ATOM	94	OB	POM	7	9.866	-3.970	-7.574
ATOM	95	O5'	ADE	8	7.646	-3.542	-8.654
ATOM	96	C5'	ADE	8	7.057	-4.689	-8.070
ATOM	97	H5A'	ADE	8	7.762	-5.522	-8.106
ATOM	98	H5B'	ADE	8	6.813	-4.481	-7.027
ATOM	99	C4'	ADE	8	5.773	-5.092	-8.803
ATOM	100	H4'	ADE	8	5.352	-5.961	-8.295
ATOM	101	O1'	ADE	8	4.835	-4.029	-8.739
ATOM	102	C1'	ADE	8	4.230	-3.884	-10.007

ATOM	103	H1'	ADE	8	3.397	-4.583	-10.095
ATOM	104	N9	ADE	8	3.788	-2.481	-10.178
ATOM	105	C8	ADE	8	4.573	-1.354	-10.209
ATOM	106	H8	ADE	8	5.652	-1.392	-10.196
ATOM	107	N7	ADE	8	3.913	-0.230	-10.240
ATOM	108	C5	ADE	8	2.589	-0.650	-10.239
ATOM	109	C6	ADE	8	1.378	0.057	-10.250
ATOM	110	N6	ADE	8	1.369	1.385	-10.310
ATOM	111	HN6A	ADE	8	0.501	1.900	-10.294
ATOM	112	HN6B	ADE	8	2.258	1.860	-10.326
ATOM	113	N1	ADE	8	0.215	-0.618	-10.256
ATOM	114	C2	ADE	8	0.266	-1.948	-10.239
ATOM	115	H2	ADE	8	-0.688	-2.452	-10.247
ATOM	116	N3	ADE	8	1.337	-2.736	-10.229
ATOM	117	C4	ADE	8	2.492	-2.015	-10.216
ATOM	118	C3'	ADE	8	6.009	-5.438	-10.282
ATOM	119	H3'	ADE	8	7.074	-5.482	-10.517
ATOM	120	C2'	ADE	8	5.329	-4.271	-10.993
ATOM	121	H2A'	ADE	8	4.937	-4.546	-11.969
ATOM	122	H2B'	ADE	8	6.066	-3.476	-11.098
ATOM	123	O3'	ADE	8	5.389	-6.680	-10.570
ATOM	124	P	POM	9	5.534	-7.403	-12.006
ATOM	125	OA	POM	9	6.608	-6.730	-12.770
ATOM	126	OB	POM	9	5.592	-8.864	-11.786
ATOM	127	O5'	ADE	10	4.130	-7.047	-12.708
ATOM	128	C5'	ADE	10	2.942	-7.725	-12.339
ATOM	129	H5A'	ADE	10	3.040	-8.786	-12.573
ATOM	130	H5B'	ADE	10	2.774	-7.614	-11.267
ATOM	131	C4'	ADE	10	1.733	-7.161	-13.095
ATOM	132	H4'	ADE	10	0.848	-7.730	-12.805
ATOM	133	O1'	ADE	10	1.544	-5.796	-12.739
ATOM	134	C1'	ADE	10	1.315	-5.067	-13.926
ATOM	135	H1'	ADE	10	0.269	-5.171	-14.219
ATOM	136	N9	ADE	10	1.666	-3.640	-13.751
ATOM	137	C8	ADE	10	2.919	-3.079	-13.694
ATOM	138	H8	ADE	10	3.830	-3.655	-13.747
ATOM	139	N7	ADE	10	2.927	-1.780	-13.596
ATOM	140	C5	ADE	10	1.578	-1.459	-13.576
ATOM	141	C6	ADE	10	0.907	-0.230	-13.499
ATOM	142	N6	ADE	10	1.584	0.914	-13.443
ATOM	143	HN6A	ADE	10	2.592	0.861	-13.460
ATOM	144	HN6B	ADE	10	1.113	1.805	-13.368
ATOM	145	N1	ADE	10	-0.434	-0.213	-13.452
ATOM	146	C2	ADE	10	-1.076	-1.379	-13.504
ATOM	147	H2	ADE	10	-2.152	-1.320	-13.481
ATOM	148	N3	ADE	10	-0.571	-2.608	-13.604
ATOM	149	C4	ADE	10	0.791	-2.580	-13.637
ATOM	150	C3'	ADE	10	1.922	-7.221	-14.621
ATOM	151	H3'	ADE	10	2.756	-7.856	-14.927
ATOM	152	C2'	ADE	10	2.200	-5.763	-14.957
ATOM	153	H2A'	ADE	10	1.939	-5.512	-15.984
ATOM	154	H2B'	ADE	10	3.257	-5.575	-14.776
ATOM	155	O3'	ADE	10	0.730	-7.593	-15.281

ATOM	156	P	POM	11	0.375	-9.140	-15.547
ATOM	157	OA	POM	11	1.304	-9.650	-16.579
ATOM	158	OB	POM	11	0.262	-9.833	-14.245
ATOM	159	O5'	ADE	12	-1.087	-9.022	-16.201
ATOM	160	C5'	ADE	12	-2.253	-8.953	-15.403
ATOM	161	H5A'	ADE	12	-2.712	-9.941	-15.356
ATOM	162	H5B'	ADE	12	-2.021	-8.624	-14.388
ATOM	163	C4'	ADE	12	-3.235	-7.944	-16.003
ATOM	164	H4'	ADE	12	-4.156	-7.963	-15.420
ATOM	165	O1'	ADE	12	-2.656	-6.660	-15.889
ATOM	166	C1'	ADE	12	-3.016	-5.893	-17.011
ATOM	167	H1'	ADE	12	-4.031	-5.513	-16.905
ATOM	168	N9	ADE	12	-2.022	-4.803	-17.129
ATOM	169	C8	ADE	12	-0.659	-4.945	-17.223
ATOM	170	H8	ADE	12	-0.177	-5.907	-17.323
ATOM	171	N7	ADE	12	0.008	-3.826	-17.172
ATOM	172	C5	ADE	12	-0.988	-2.874	-17.009
ATOM	173	C6	ADE	12	-0.935	-1.483	-16.846
ATOM	174	N6	ADE	12	0.229	-0.842	-16.825
ATOM	175	HN6A	ADE	12	1.072	-1.380	-16.960
ATOM	176	HN6B	ADE	12	0.260	0.158	-16.683
ATOM	177	N1	ADE	12	-2.075	-0.793	-16.682
ATOM	178	C2	ADE	12	-3.219	-1.467	-16.669
ATOM	179	H2	ADE	12	-4.105	-0.858	-16.538
ATOM	180	N3	ADE	12	-3.412	-2.782	-16.787
ATOM	181	C4	ADE	12	-2.233	-3.446	-16.965
ATOM	182	C3'	ADE	12	-3.554	-8.167	-17.490
ATOM	183	H3'	ADE	12	-3.074	-9.072	-17.866
ATOM	184	C2'	ADE	12	-2.968	-6.912	-18.145
ATOM	185	H2A'	ADE	12	-3.537	-6.591	-19.014
ATOM	186	H2B'	ADE	12	-1.937	-7.129	-18.424
ATOM	187	O3'	ADE	12	-4.961	-8.259	-17.640
ATOM	188	P	POM	13	-5.658	-8.664	-19.039
ATOM	189	OA	POM	13	-4.632	-9.242	-19.934
ATOM	190	OB	POM	13	-6.888	-9.428	-18.737
ATOM	191	O5'	THY	14	-6.089	-7.233	-19.629
ATOM	192	C5'	THY	14	-7.174	-6.529	-19.060
ATOM	193	H5A'	THY	14	-8.114	-7.025	-19.305
ATOM	194	H5B'	THY	14	-7.062	-6.506	-17.974
ATOM	195	C4'	THY	14	-7.207	-5.083	-19.555
ATOM	196	H4'	THY	14	-7.970	-4.564	-18.980
ATOM	197	O1'	THY	14	-5.954	-4.469	-19.312
ATOM	198	C1'	THY	14	-5.783	-3.469	-20.287
ATOM	199	H1'	THY	14	-6.433	-2.624	-20.063
ATOM	200	N1	THY	14	-4.343	-3.099	-20.347
ATOM	201	C6	THY	14	-3.402	-4.073	-20.568
ATOM	202	H6	THY	14	-3.734	-5.088	-20.730
ATOM	203	C5	THY	14	-2.078	-3.794	-20.574
ATOM	204	C7	THY	14	-1.067	-4.896	-20.826
ATOM	205	H7A	THY	14	-0.207	-4.760	-20.169
ATOM	206	H7B	THY	14	-1.496	-5.882	-20.644
ATOM	207	H7C	THY	14	-0.727	-4.837	-21.861
ATOM	208	C4	THY	14	-1.612	-2.439	-20.364

ATOM	209	O4	THY	14	-0.441	-2.087	-20.412
ATOM	210	N3	THY	14	-2.602	-1.516	-20.088
ATOM	211	H3	THY	14	-2.315	-0.553	-19.929
ATOM	212	C2	THY	14	-3.958	-1.795	-20.030
ATOM	213	O2	THY	14	-4.748	-0.917	-19.698
ATOM	214	C3'	THY	14	-7.538	-4.894	-21.043
ATOM	215	H3'	THY	14	-7.655	-5.855	-21.546
ATOM	216	C2'	THY	14	-6.307	-4.140	-21.554
ATOM	217	H2A'	THY	14	-6.554	-3.412	-22.322
ATOM	218	H2B'	THY	14	-5.605	-4.873	-21.946
ATOM	219	O3'	THY	14	-8.725	-4.118	-21.133
ATOM	220	P	POM	15	-9.492	-3.849	-22.529
ATOM	221	OA	POM	15	-9.146	-4.935	-23.471
ATOM	222	OB	POM	15	-10.910	-3.565	-22.219
ATOM	223	O5'	THY	16	-8.813	-2.488	-23.054
ATOM	224	C5'	THY	16	-9.143	-1.243	-22.470
ATOM	225	H5A'	THY	16	-10.148	-0.943	-22.769
ATOM	226	H5B'	THY	16	-9.108	-1.331	-21.383
ATOM	227	C4'	THY	16	-8.134	-0.170	-22.888
ATOM	228	H4'	THY	16	-8.341	0.734	-22.324
ATOM	229	O1'	THY	16	-6.824	-0.603	-22.577
ATOM	230	C1'	THY	16	-5.947	0.148	-23.378
ATOM	231	H1'	THY	16	-5.853	1.134	-22.936
ATOM	232	N1	THY	16	-4.649	-0.566	-23.491
ATOM	233	C6	THY	16	-4.635	-1.893	-23.842
ATOM	234	H6	THY	16	-5.572	-2.370	-24.091
ATOM	235	C5	THY	16	-3.485	-2.608	-23.873
ATOM	236	C7	THY	16	-3.510	-4.074	-24.261
ATOM	237	H7A	THY	16	-3.125	-4.177	-25.276
ATOM	238	H7B	THY	16	-2.872	-4.642	-23.582
ATOM	239	H7C	THY	16	-4.521	-4.482	-24.218
ATOM	240	C4	THY	16	-2.221	-1.977	-23.554
ATOM	241	O4	THY	16	-1.138	-2.549	-23.506
ATOM	242	N3	THY	16	-2.304	-0.634	-23.250
ATOM	243	H3	THY	16	-1.438	-0.117	-23.092
ATOM	244	C2	THY	16	-3.469	0.099	-23.161
ATOM	245	O2	THY	16	-3.429	1.268	-22.793
ATOM	246	C3'	THY	16	-8.153	0.209	-24.375
ATOM	247	H3'	THY	16	-8.632	-0.586	-24.950
ATOM	248	C2'	THY	16	-6.663	0.293	-24.719
ATOM	249	H2A'	THY	16	-6.403	1.242	-25.188
ATOM	250	H2B'	THY	16	-6.430	-0.536	-25.383
ATOM	251	O3'	THY	16	-8.814	1.454	-24.552
ATOM	252	P	POM	17	-9.292	1.984	-26.005
ATOM	253	OA	POM	17	-9.445	0.820	-26.903
ATOM	254	OB	POM	17	-10.429	2.908	-25.798
ATOM	255	O5'	THY	18	-8.050	2.850	-26.553
ATOM	256	C5'	THY	18	-7.946	4.240	-26.298
ATOM	257	H5A'	THY	18	-8.771	4.775	-26.770
ATOM	258	H5B'	THY	18	-7.998	4.397	-25.219
ATOM	259	C4'	THY	18	-6.610	4.810	-26.803
ATOM	260	H4'	THY	18	-6.495	5.790	-26.347
ATOM	261	O1'	THY	18	-5.584	3.921	-26.385

ATOM	262	C1'	THY	18	-4.973	3.373	-27.537
ATOM	263	H1'	THY	18	-4.131	4.019	-27.773
ATOM	264	N1	THY	18	-4.432	2.011	-27.287
ATOM	265	C6	THY	18	-5.135	0.876	-27.611
ATOM	266	H6	THY	18	-6.143	0.954	-27.987
ATOM	267	C5	THY	18	-4.602	-0.358	-27.438
ATOM	268	C7	THY	18	-5.413	-1.590	-27.798
ATOM	269	H7A	THY	18	-5.133	-1.921	-28.798
ATOM	270	H7B	THY	18	-5.199	-2.391	-27.088
ATOM	271	H7C	THY	18	-6.483	-1.379	-27.772
ATOM	272	C4	THY	18	-3.261	-0.515	-26.913
ATOM	273	O4	THY	18	-2.702	-1.590	-26.722
ATOM	274	N3	THY	18	-2.627	0.662	-26.574
ATOM	275	H3	THY	18	-1.641	0.591	-26.321
ATOM	276	C2	THY	18	-3.160	1.928	-26.720
ATOM	277	O2	THY	18	-2.537	2.917	-26.323
ATOM	278	C3'	THY	18	-6.477	4.945	-28.330
ATOM	279	H3'	THY	18	-7.411	5.201	-28.832
ATOM	280	C2'	THY	18	-5.981	3.547	-28.681
ATOM	281	H2A'	THY	18	-5.513	3.504	-29.664
ATOM	282	H2B'	THY	18	-6.823	2.861	-28.639
ATOM	283	O3'	THY	18	-5.417	5.815	-28.701
ATOM	284	P	POM	19	-5.498	7.419	-28.662
ATOM	285	OA	POM	19	-6.544	7.873	-29.600
ATOM	286	OB	POM	19	-5.509	7.859	-27.248
ATOM	287	O5'	GUA	20	-4.045	7.750	-29.272
ATOM	288	C5'	GUA	20	-3.056	8.444	-28.530
ATOM	289	H5A'	GUA	20	-3.227	9.517	-28.613
ATOM	290	H5B'	GUA	20	-3.079	8.165	-27.478
ATOM	291	C4'	GUA	20	-1.653	8.089	-29.029
ATOM	292	H4'	GUA	20	-0.927	8.671	-28.459
ATOM	293	O1'	GUA	20	-1.425	6.705	-28.795
ATOM	294	C1'	GUA	20	-0.944	6.114	-29.989
ATOM	295	H1'	GUA	20	0.143	6.208	-30.028
ATOM	296	N9	GUA	20	-1.372	4.697	-30.035
ATOM	297	C8	GUA	20	-2.651	4.212	-29.993
ATOM	298	H8	GUA	20	-3.515	4.855	-30.037
ATOM	299	N7	GUA	20	-2.737	2.918	-29.861
ATOM	300	C5	GUA	20	-1.410	2.503	-29.847
ATOM	301	C6	GUA	20	-0.857	1.194	-29.724
ATOM	302	O6	GUA	20	-1.453	0.144	-29.497
ATOM	303	N1	GUA	20	0.521	1.175	-29.871
ATOM	304	H1	GUA	20	0.957	0.253	-29.835
ATOM	305	C2	GUA	20	1.290	2.302	-30.053
ATOM	306	N2	GUA	20	2.601	2.155	-30.205
ATOM	307	HN2A	GUA	20	3.156	2.977	-30.381
ATOM	308	HN2B	GUA	20	3.036	1.241	-30.169
ATOM	309	N3	GUA	20	0.787	3.541	-30.105
ATOM	310	C4	GUA	20	-0.567	3.578	-30.002
ATOM	311	C3'	GUA	20	-1.471	8.360	-30.527
ATOM	312	H3'	GUA	20	-2.253	9.015	-30.913
ATOM	313	C2'	GUA	20	-1.569	6.951	-31.101
ATOM	314	H2A'	GUA	20	-1.041	6.861	-32.044

ATOM	315	H2B'	GUA	20	-2.622	6.705	-31.237
ATOM	316	O3'	GUA	20	-0.193	8.937	-30.733
ATOM	317	P	POM	21	0.274	9.500	-32.171
ATOM	318	OA	POM	21	-0.890	9.483	-33.084
ATOM	319	OB	POM	21	1.022	10.757	-31.953
ATOM	320	O5'	CYT	22	1.307	8.374	-32.669
ATOM	321	C5'	CYT	22	2.602	8.274	-32.107
ATOM	322	H5A'	CYT	22	3.151	9.201	-32.278
ATOM	323	H5B'	CYT	22	2.518	8.109	-31.031
ATOM	324	C4'	CYT	22	3.388	7.110	-32.725
ATOM	325	H4'	CYT	22	4.364	7.064	-32.239
ATOM	326	O1'	CYT	22	2.683	5.899	-32.485
ATOM	327	C1'	CYT	22	2.474	5.245	-33.721
ATOM	328	H1'	CYT	22	3.357	4.643	-33.938
ATOM	329	N1	CYT	22	1.245	4.403	-33.643
ATOM	330	C6	CYT	22	-0.004	4.964	-33.697
ATOM	331	H6	CYT	22	-0.115	6.021	-33.872
ATOM	332	C5	CYT	22	-1.123	4.228	-33.513
ATOM	333	H5	CYT	22	-2.087	4.713	-33.561
ATOM	334	C4	CYT	22	-0.948	2.834	-33.265
ATOM	335	N4	CYT	22	-2.013	2.083	-33.014
ATOM	336	HN4A	CYT	22	-2.923	2.507	-32.938
ATOM	337	HN4B	CYT	22	-1.892	1.105	-32.785
ATOM	338	N3	CYT	22	0.263	2.274	-33.181
ATOM	339	C2	CYT	22	1.378	3.039	-33.378
ATOM	340	O2	CYT	22	2.480	2.495	-33.313
ATOM	341	C3'	CYT	22	3.579	7.254	-34.244
ATOM	342	H3'	CYT	22	3.483	8.292	-34.567
ATOM	343	C2'	CYT	22	2.445	6.374	-34.758
ATOM	344	H2A'	CYT	22	2.607	6.032	-35.776
ATOM	345	H2B'	CYT	22	1.540	6.973	-34.730
ATOM	346	O3'	CYT	22	4.847	6.729	-34.603
ATOM	347	P	POM	23	5.505	6.978	-36.056
ATOM	348	OA	POM	23	4.444	7.377	-37.006
ATOM	349	OB	POM	23	6.706	7.826	-35.889
ATOM	350	O5'	GUA	24	5.982	5.497	-36.457
ATOM	351	C5'	GUA	24	7.131	4.920	-35.870
ATOM	352	H5A'	GUA	24	8.023	5.464	-36.184
ATOM	353	H5B'	GUA	24	7.050	4.983	-34.784
ATOM	354	C4'	GUA	24	7.258	3.439	-36.255
ATOM	355	H4'	GUA	24	8.128	3.030	-35.740
ATOM	356	O1'	GUA	24	6.087	2.766	-35.818
ATOM	357	C1'	GUA	24	5.427	2.195	-36.933
ATOM	358	H1'	GUA	24	5.724	1.148	-36.996
ATOM	359	N9	GUA	24	3.960	2.314	-36.776
ATOM	360	C8	GUA	24	3.194	3.449	-36.748
ATOM	361	H8	GUA	24	3.611	4.432	-36.894
ATOM	362	N7	GUA	24	1.923	3.235	-36.545
ATOM	363	C5	GUA	24	1.836	1.851	-36.433
ATOM	364	C6	GUA	24	0.705	1.009	-36.213
ATOM	365	O6	GUA	24	-0.467	1.339	-36.040
ATOM	366	N1	GUA	24	1.032	-0.337	-36.221
ATOM	367	H1	GUA	24	0.250	-0.975	-36.079

ATOM	368	C2	GUA	24	2.305	-0.826	-36.394
ATOM	369	N2	GUA	24	2.483	-2.142	-36.392
ATOM	370	HN2A	GUA	24	1.702	-2.774	-36.261
ATOM	371	HN2B	GUA	24	3.420	-2.503	-36.460
ATOM	372	N3	GUA	24	3.375	-0.048	-36.580
ATOM	373	C4	GUA	24	3.076	1.279	-36.587
ATOM	374	C3'	GUA	24	7.390	3.163	-37.759
ATOM	375	H3'	GUA	24	7.963	2.245	-37.903
ATOM	376	C2'	GUA	24	5.950	2.913	-38.178
ATOM	377	H2A'	GUA	24	5.879	2.297	-39.074
ATOM	378	H2B'	GUA	24	5.446	3.867	-38.331
ATOM	379	O3'	GUA	24	7.979	4.213	-38.495
ATOM	380	H	HE	25	8.870	4.354	-38.165
ATOM	381	H	HB	26	-5.367	-6.298	-37.845
ATOM	382	O5'	CYT	27	-5.303	-7.249	-37.959
ATOM	383	C5'	CYT	27	-4.225	-7.526	-38.827
ATOM	384	H5A'	CYT	27	-4.151	-8.604	-38.976
ATOM	385	H5B'	CYT	27	-4.411	-7.047	-39.789
ATOM	386	C4'	CYT	27	-2.908	-7.003	-38.246
ATOM	387	H4'	CYT	27	-2.113	-7.191	-38.972
ATOM	388	O1'	CYT	27	-2.963	-5.606	-38.026
ATOM	389	C1'	CYT	27	-1.984	-5.321	-37.048
ATOM	390	H1'	CYT	27	-1.005	-5.414	-37.522
ATOM	391	N1	CYT	27	-2.210	-3.979	-36.447
ATOM	392	C6	CYT	27	-3.476	-3.547	-36.147
ATOM	393	H6	CYT	27	-4.308	-4.224	-36.276
ATOM	394	C5	CYT	27	-3.707	-2.286	-35.712
ATOM	395	H5	CYT	27	-4.717	-1.977	-35.488
ATOM	396	C4	CYT	27	-2.570	-1.425	-35.587
ATOM	397	N4	CYT	27	-2.736	-0.146	-35.273
ATOM	398	HN4A	CYT	27	-3.645	0.215	-35.038
ATOM	399	HN4B	CYT	27	-1.927	0.467	-35.294
ATOM	400	N3	CYT	27	-1.333	-1.848	-35.861
ATOM	401	C2	CYT	27	-1.121	-3.133	-36.259
ATOM	402	O2	CYT	27	0.030	-3.510	-36.456
ATOM	403	C3'	CYT	27	-2.522	-7.655	-36.909
ATOM	404	H3'	CYT	27	-3.369	-8.190	-36.476
ATOM	405	C2'	CYT	27	-2.157	-6.448	-36.037
ATOM	406	H2A'	CYT	27	-1.246	-6.596	-35.462
ATOM	407	H2B'	CYT	27	-2.989	-6.238	-35.365
ATOM	408	O3'	CYT	27	-1.440	-8.538	-37.138
ATOM	409	P	POM	28	-0.867	-9.517	-35.990
ATOM	410	OA	POM	28	-1.956	-9.787	-35.026
ATOM	411	OB	POM	28	-0.175	-10.641	-36.658
ATOM	412	O5'	GUA	29	0.240	-8.595	-35.275
ATOM	413	C5'	GUA	29	1.439	-8.265	-35.948
ATOM	414	H5A'	GUA	29	2.050	-9.161	-36.066
ATOM	415	H5B'	GUA	29	1.207	-7.866	-36.937
ATOM	416	C4'	GUA	29	2.237	-7.206	-35.182
ATOM	417	H4'	GUA	29	3.135	-6.985	-35.761
ATOM	418	O1'	GUA	29	1.487	-6.005	-35.064
ATOM	419	C1'	GUA	29	1.779	-5.447	-33.800
ATOM	420	H1'	GUA	29	2.755	-4.960	-33.832

ATOM	421	N9	GUA	29	0.720	-4.497	-33.389
ATOM	422	C8	GUA	29	-0.612	-4.750	-33.181
ATOM	423	H8	GUA	29	-1.043	-5.738	-33.249
ATOM	424	N7	GUA	29	-1.324	-3.694	-32.904
ATOM	425	C5	GUA	29	-0.395	-2.657	-32.923
ATOM	426	C6	GUA	29	-0.570	-1.256	-32.719
ATOM	427	O6	GUA	29	-1.606	-0.657	-32.445
ATOM	428	N1	GUA	29	0.602	-0.533	-32.879
ATOM	429	H1	GUA	29	0.519	0.484	-32.839
ATOM	430	C2	GUA	29	1.824	-1.102	-33.134
ATOM	431	N2	GUA	29	2.883	-0.306	-33.225
ATOM	432	HN2A	GUA	29	3.781	-0.721	-33.420
ATOM	433	HN2B	GUA	29	2.799	0.700	-33.120
ATOM	434	N3	GUA	29	2.006	-2.415	-33.306
ATOM	435	C4	GUA	29	0.859	-3.138	-33.210
ATOM	436	C3'	GUA	29	2.649	-7.644	-33.766
ATOM	437	H3'	GUA	29	2.379	-8.681	-33.560
ATOM	438	C2'	GUA	29	1.852	-6.672	-32.897
ATOM	439	H2A'	GUA	29	2.322	-6.466	-31.938
ATOM	440	H2B'	GUA	29	0.860	-7.096	-32.741
ATOM	441	O3'	GUA	29	4.051	-7.465	-33.653
ATOM	442	P	POM	30	4.881	-7.820	-32.317
ATOM	443	OA	POM	30	3.966	-8.426	-31.326
ATOM	444	OB	POM	30	6.117	-8.528	-32.717
ATOM	445	O5'	CYT	31	5.281	-6.348	-31.808
ATOM	446	C5'	CYT	31	6.183	-5.558	-32.559
ATOM	447	H5A'	CYT	31	7.167	-6.030	-32.574
ATOM	448	H5B'	CYT	31	5.822	-5.471	-33.585
ATOM	449	C4'	CYT	31	6.307	-4.147	-31.978
ATOM	450	H4'	CYT	31	6.932	-3.559	-32.652
ATOM	451	O1'	CYT	31	5.023	-3.546	-31.919
ATOM	452	C1'	CYT	31	4.905	-2.855	-30.692
ATOM	453	H1'	CYT	31	5.366	-1.874	-30.812
ATOM	454	N1	CYT	31	3.469	-2.794	-30.299
ATOM	455	C6	CYT	31	2.713	-3.937	-30.273
ATOM	456	H6	CYT	31	3.188	-4.883	-30.489
ATOM	457	C5	CYT	31	1.390	-3.904	-29.992
ATOM	458	H5	CYT	31	0.828	-4.826	-29.981
ATOM	459	C4	CYT	31	0.815	-2.621	-29.729
ATOM	460	N4	CYT	31	-0.489	-2.518	-29.506
ATOM	461	HN4A	CYT	31	-0.894	-1.600	-29.365
ATOM	462	HN4B	CYT	31	-1.082	-3.330	-29.539
ATOM	463	N3	CYT	31	1.538	-1.498	-29.775
ATOM	464	C2	CYT	31	2.873	-1.560	-30.049
ATOM	465	O2	CYT	31	3.515	-0.514	-30.072
ATOM	466	C3'	CYT	31	6.923	-4.121	-30.571
ATOM	467	H3'	CYT	31	7.276	-5.110	-30.274
ATOM	468	C2'	CYT	31	5.742	-3.673	-29.711
ATOM	469	H2A'	CYT	31	6.052	-3.088	-28.848
ATOM	470	H2B'	CYT	31	5.210	-4.565	-29.381
ATOM	471	O3'	CYT	31	7.995	-3.192	-30.572
ATOM	472	P	POM	32	8.973	-2.987	-29.304
ATOM	473	OA	POM	32	8.885	-4.183	-28.438

ATOM	474	OB	POM	32	10.290	-2.538	-29.808
ATOM	475	O5'	ADE	33	8.278	-1.753	-28.543
ATOM	476	C5'	ADE	33	8.354	-0.444	-29.076
ATOM	477	H5A'	ADE	33	9.361	-0.046	-28.942
ATOM	478	H5B'	ADE	33	8.124	-0.472	-30.142
ATOM	479	C4'	ADE	33	7.335	0.480	-28.401
ATOM	480	H4'	ADE	33	7.313	1.433	-28.932
ATOM	481	O1'	ADE	33	6.044	-0.093	-28.466
ATOM	482	C1'	ADE	33	5.250	0.579	-27.514
ATOM	483	H1'	ADE	33	4.893	1.513	-27.949
ATOM	484	N9	ADE	33	4.127	-0.280	-27.090
ATOM	485	C8	ADE	33	4.142	-1.638	-26.889
ATOM	486	H8	ADE	33	5.042	-2.230	-26.965
ATOM	487	N7	ADE	33	2.975	-2.156	-26.624
ATOM	488	C5	ADE	33	2.137	-1.047	-26.616
ATOM	489	C6	ADE	33	0.759	-0.909	-26.411
ATOM	490	N6	ADE	33	0.000	-1.973	-26.179
ATOM	491	HN6A	ADE	33	-1.003	-1.886	-26.100
ATOM	492	HN6B	ADE	33	0.452	-2.872	-26.122
ATOM	493	N1	ADE	33	0.202	0.315	-26.435
ATOM	494	C2	ADE	33	0.995	1.357	-26.675
ATOM	495	H2	ADE	33	0.511	2.321	-26.688
ATOM	496	N3	ADE	33	2.304	1.364	-26.902
ATOM	497	C4	ADE	33	2.825	0.108	-26.869
ATOM	498	C3'	ADE	33	7.603	0.754	-26.917
ATOM	499	H3'	ADE	33	8.111	-0.102	-26.469
ATOM	500	C2'	ADE	33	6.186	0.874	-26.347
ATOM	501	H2A'	ADE	33	5.966	1.873	-25.978
ATOM	502	H2B'	ADE	33	6.073	0.140	-25.548
ATOM	503	O3'	ADE	33	8.365	1.939	-26.762
ATOM	504	P	POM	34	8.838	2.480	-25.314
ATOM	505	OA	POM	34	8.990	1.324	-24.404
ATOM	506	OB	POM	34	9.972	3.409	-25.519
ATOM	507	O5'	ADE	35	7.573	3.344	-24.815
ATOM	508	C5'	ADE	35	7.192	4.527	-25.493
ATOM	509	H5A'	ADE	35	7.989	5.268	-25.411
ATOM	510	H5B'	ADE	35	7.030	4.305	-26.549
ATOM	511	C4'	ADE	35	5.897	5.113	-24.916
ATOM	512	H4'	ADE	35	5.643	5.998	-25.501
ATOM	513	O1'	ADE	35	4.841	4.167	-25.030
ATOM	514	C1'	ADE	35	4.197	4.042	-23.776
ATOM	515	H1'	ADE	35	3.391	4.774	-23.707
ATOM	516	N9	ADE	35	3.695	2.660	-23.603
ATOM	517	C8	ADE	35	4.440	1.507	-23.559
ATOM	518	H8	ADE	35	5.517	1.501	-23.645
ATOM	519	N7	ADE	35	3.745	0.416	-23.397
ATOM	520	C5	ADE	35	2.442	0.887	-23.320
ATOM	521	C6	ADE	35	1.221	0.228	-23.122
ATOM	522	N6	ADE	35	1.181	-1.091	-22.960
ATOM	523	HN6A	ADE	35	0.309	-1.588	-22.828
ATOM	524	HN6B	ADE	35	2.057	-1.590	-22.992
ATOM	525	N1	ADE	35	0.082	0.938	-23.108
ATOM	526	C2	ADE	35	0.163	2.256	-23.279

ATOM	527	H2	ADE	35	-0.775	2.790	-23.261
ATOM	528	N3	ADE	35	1.250	3.007	-23.453
ATOM	529	C4	ADE	35	2.384	2.249	-23.460
ATOM	530	C3'	ADE	35	6.030	5.506	-23.438
ATOM	531	H3'	ADE	35	7.075	5.550	-23.126
ATOM	532	C2'	ADE	35	5.276	4.374	-22.748
ATOM	533	H2A'	ADE	35	4.863	4.662	-21.783
ATOM	534	H2B'	ADE	35	5.972	3.546	-22.619
ATOM	535	O3'	ADE	35	5.400	6.759	-23.242
ATOM	536	P	POM	36	5.493	7.560	-21.846
ATOM	537	OA	POM	36	6.307	6.773	-20.894
ATOM	538	OB	POM	36	5.853	8.964	-22.141
ATOM	539	O5'	ADE	37	3.967	7.522	-21.345
ATOM	540	C5'	ADE	37	2.979	8.298	-21.995
ATOM	541	H5A'	ADE	37	3.243	9.355	-21.941
ATOM	542	H5B'	ADE	37	2.911	8.003	-23.043
ATOM	543	C4'	ADE	37	1.614	8.096	-21.332
ATOM	544	H4'	ADE	37	0.884	8.711	-21.858
ATOM	545	O1'	ADE	37	1.233	6.736	-21.446
ATOM	546	C1'	ADE	37	0.643	6.314	-20.235
ATOM	547	H1'	ADE	37	-0.416	6.570	-20.205
ATOM	548	N9	ADE	37	0.880	4.859	-20.107
ATOM	549	C8	ADE	37	2.104	4.237	-20.144
ATOM	550	H8	ADE	37	3.032	4.781	-20.247
ATOM	551	N7	ADE	37	2.059	2.941	-20.025
ATOM	552	C5	ADE	37	0.698	2.687	-19.937
ATOM	553	C6	ADE	37	-0.011	1.487	-19.812
ATOM	554	N6	ADE	37	0.652	0.342	-19.701
ATOM	555	HN6A	ADE	37	0.169	-0.542	-19.670
ATOM	556	HN6B	ADE	37	1.660	0.385	-19.720
ATOM	557	N1	ADE	37	-1.354	1.500	-19.810
ATOM	558	C2	ADE	37	-1.962	2.681	-19.913
ATOM	559	H2	ADE	37	-3.044	2.646	-19.910
ATOM	560	N3	ADE	37	-1.410	3.895	-20.000
ATOM	561	C4	ADE	37	-0.046	3.833	-20.015
ATOM	562	C3'	ADE	37	1.614	8.468	-19.843
ATOM	563	H3'	ADE	37	2.565	8.910	-19.540
ATOM	564	C2'	ADE	37	1.394	7.113	-19.172
ATOM	565	H2A'	ADE	37	0.838	7.192	-18.242
ATOM	566	H2B'	ADE	37	2.377	6.683	-18.981
ATOM	567	O3'	ADE	37	0.560	9.384	-19.606
ATOM	568	P	POM	38	0.311	10.066	-18.165
ATOM	569	OA	POM	38	1.472	9.789	-17.291
ATOM	570	OB	POM	38	-0.139	11.458	-18.385
ATOM	571	O5'	THY	39	-0.938	9.211	-17.631
ATOM	572	C5'	THY	39	-2.193	9.341	-18.263
ATOM	573	H5A'	THY	39	-2.600	10.337	-18.084
ATOM	574	H5B'	THY	39	-2.073	9.202	-19.339
ATOM	575	C4'	THY	39	-3.183	8.289	-17.766
ATOM	576	H4'	THY	39	-4.068	8.393	-18.386
ATOM	577	O1'	THY	39	-2.644	6.986	-17.927
ATOM	578	C1'	THY	39	-3.064	6.205	-16.829
ATOM	579	H1'	THY	39	-4.098	5.896	-16.972

ATOM	580	N1	THY	39	-2.135	5.057	-16.652
ATOM	581	C6	THY	39	-0.785	5.294	-16.553
ATOM	582	H6	THY	39	-0.440	6.317	-16.575
ATOM	583	C5	THY	39	0.111	4.284	-16.440
ATOM	584	C7	THY	39	1.596	4.585	-16.340
ATOM	585	H7A	THY	39	2.134	4.010	-17.095
ATOM	586	H7B	THY	39	1.806	5.645	-16.486
ATOM	587	H7C	THY	39	1.953	4.286	-15.354
ATOM	588	C4	THY	39	-0.337	2.907	-16.416
ATOM	589	O4	THY	39	0.395	1.931	-16.310
ATOM	590	N3	THY	39	-1.700	2.735	-16.548
ATOM	591	H3	THY	39	-2.032	1.780	-16.587
ATOM	592	C2	THY	39	-2.632	3.751	-16.695
ATOM	593	O2	THY	39	-3.818	3.471	-16.860
ATOM	594	C3'	THY	39	-3.614	8.449	-16.302
ATOM	595	H3'	THY	39	-3.205	9.360	-15.861
ATOM	596	C2'	THY	39	-3.021	7.194	-15.668
ATOM	597	H2A'	THY	39	-3.602	6.853	-14.819
ATOM	598	H2B'	THY	39	-2.000	7.418	-15.362
ATOM	599	O3'	THY	39	-5.033	8.451	-16.271
ATOM	600	P	POM	40	-5.879	8.771	-14.936
ATOM	601	OA	POM	40	-5.053	9.616	-14.047
ATOM	602	OB	POM	40	-7.221	9.231	-15.359
ATOM	603	O5'	THY	41	-6.037	7.320	-14.260
ATOM	604	C5'	THY	41	-6.976	6.394	-14.768
ATOM	605	H5A'	THY	41	-7.988	6.708	-14.508
ATOM	606	H5B'	THY	41	-6.885	6.354	-15.853
ATOM	607	C4'	THY	41	-6.716	4.986	-14.227
ATOM	608	H4'	THY	41	-7.390	4.295	-14.729
ATOM	609	O1'	THY	41	-5.381	4.595	-14.489
ATOM	610	C1'	THY	41	-5.091	3.482	-13.665
ATOM	611	H1'	THY	41	-5.278	2.585	-14.256
ATOM	612	N1	THY	41	-3.675	3.511	-13.208
ATOM	613	C6	THY	41	-3.006	4.696	-13.040
ATOM	614	H6	THY	41	-3.579	5.611	-13.023
ATOM	615	C5	THY	41	-1.657	4.728	-12.900
ATOM	616	C7	THY	41	-0.936	6.054	-12.749
ATOM	617	H7A	THY	41	-0.387	6.055	-11.807
ATOM	618	H7B	THY	41	-0.227	6.173	-13.569
ATOM	619	H7C	THY	41	-1.633	6.894	-12.756
ATOM	620	C4	THY	41	-0.883	3.499	-12.933
ATOM	621	O4	THY	41	0.342	3.424	-12.936
ATOM	622	N3	THY	41	-1.638	2.347	-12.983
ATOM	623	H3	THY	41	-1.160	1.446	-13.012
ATOM	624	C2	THY	41	-3.014	2.301	-13.040
ATOM	625	O2	THY	41	-3.597	1.233	-12.914
ATOM	626	C3'	THY	41	-6.911	4.807	-12.722
ATOM	627	H3'	THY	41	-6.467	5.645	-12.183
ATOM	628	C2'	THY	41	-6.095	3.534	-12.517
ATOM	629	H2A'	THY	41	-6.755	2.678	-12.634
ATOM	630	H2B'	THY	41	-5.626	3.526	-11.536
ATOM	631	O3'	THY	41	-8.279	4.613	-12.393
ATOM	632	P	POM	42	-8.794	4.466	-10.864

ATOM	633	OA	POM	42	-8.066	5.444	-10.028
ATOM	634	OB	POM	42	-10.274	4.472	-10.884
ATOM	635	O5'	THY	43	-8.323	2.989	-10.420
ATOM	636	C5'	THY	43	-8.949	1.842	-10.964
ATOM	637	H5A'	THY	43	-9.916	1.666	-10.492
ATOM	638	H5B'	THY	43	-9.115	2.018	-12.028
ATOM	639	C4'	THY	43	-8.054	0.600	-10.857
ATOM	640	H4'	THY	43	-8.289	0.001	-11.731
ATOM	641	O1'	THY	43	-6.687	0.963	-10.928
ATOM	642	C1'	THY	43	-5.967	0.146	-10.037
ATOM	643	H1'	THY	43	-5.835	-0.809	-10.525
ATOM	644	N1	THY	43	-4.658	0.767	-9.723
ATOM	645	C6	THY	43	-4.602	2.110	-9.448
ATOM	646	H6	THY	43	-5.528	2.644	-9.282
ATOM	647	C5	THY	43	-3.426	2.782	-9.439
ATOM	648	C7	THY	43	-3.417	4.280	-9.191
ATOM	649	H7A	THY	43	-3.286	4.465	-8.125
ATOM	650	H7B	THY	43	-4.351	4.736	-9.525
ATOM	651	H7C	THY	43	-2.591	4.742	-9.734
ATOM	652	C4	THY	43	-2.181	2.089	-9.702
ATOM	653	O4	THY	43	-1.081	2.629	-9.770
ATOM	654	N3	THY	43	-2.304	0.731	-9.933
ATOM	655	H3	THY	43	-1.441	0.214	-10.099
ATOM	656	C2	THY	43	-3.496	0.027	-9.952
ATOM	657	O2	THY	43	-3.503	-1.187	-10.175
ATOM	658	C3'	THY	43	-8.218	-0.307	-9.626
ATOM	659	H3'	THY	43	-9.123	-0.092	-9.056
ATOM	660	C2'	THY	43	-6.926	-0.033	-8.865
ATOM	661	H2A'	THY	43	-6.664	-0.881	-8.243
ATOM	662	H2B'	THY	43	-7.015	0.883	-8.281
ATOM	663	O3'	THY	43	-8.182	-1.628	-10.144
ATOM	664	P	POM	44	-8.811	-2.920	-9.429
ATOM	665	OA	POM	44	-9.907	-2.516	-8.526
ATOM	666	OB	POM	44	-9.051	-3.864	-10.545
ATOM	667	O5'	GUA	45	-7.588	-3.526	-8.574
ATOM	668	C5'	GUA	45	-7.300	-4.917	-8.626
ATOM	669	H5A'	GUA	45	-8.126	-5.489	-8.201
ATOM	670	H5B'	GUA	45	-7.183	-5.230	-9.664
ATOM	671	C4'	GUA	45	-5.986	-5.261	-7.913
ATOM	672	H4'	GUA	45	-5.602	-6.179	-8.361
ATOM	673	O1'	GUA	45	-5.022	-4.227	-8.095
ATOM	674	C1'	GUA	45	-4.391	-3.996	-6.847
ATOM	675	H1'	GUA	45	-3.602	-4.735	-6.696
ATOM	676	N9	GUA	45	-3.844	-2.619	-6.775
ATOM	677	C8	GUA	45	-4.531	-1.442	-6.632
ATOM	678	H8	GUA	45	-5.595	-1.397	-6.465
ATOM	679	N7	GUA	45	-3.798	-0.370	-6.716
ATOM	680	C5	GUA	45	-2.511	-0.870	-6.877
ATOM	681	C6	GUA	45	-1.269	-0.180	-6.993
ATOM	682	O6	GUA	45	-1.087	1.029	-7.088
ATOM	683	N1	GUA	45	-0.177	-1.032	-7.006
ATOM	684	H1	GUA	45	0.734	-0.575	-7.069
ATOM	685	C2	GUA	45	-0.271	-2.402	-6.964

ATOM	686	N2	GUA	45	0.854	-3.107	-6.983
ATOM	687	HN2A	GUA	45	0.793	-4.113	-6.965
ATOM	688	HN2B	GUA	45	1.761	-2.654	-7.030
ATOM	689	N3	GUA	45	-1.434	-3.063	-6.914
ATOM	690	C4	GUA	45	-2.519	-2.244	-6.867
ATOM	691	C3'	GUA	45	-6.157	-5.496	-6.405
ATOM	692	H3'	GUA	45	-7.202	-5.590	-6.107
ATOM	693	C2'	GUA	45	-5.512	-4.239	-5.839
ATOM	694	H2A'	GUA	45	-5.155	-4.378	-4.823
ATOM	695	H2B'	GUA	45	-6.259	-3.447	-5.869
ATOM	696	O3'	GUA	45	-5.435	-6.668	-6.077
ATOM	697	P	POM	46	-5.474	-7.346	-4.617
ATOM	698	OA	POM	46	-6.168	-6.433	-3.683
ATOM	699	OB	POM	46	-5.927	-8.746	-4.766
ATOM	700	O5'	CYT	47	-3.910	-7.345	-4.250
ATOM	701	C5'	CYT	47	-2.994	-8.125	-4.996
ATOM	702	H5A'	CYT	47	-3.164	-9.185	-4.804
ATOM	703	H5B'	CYT	47	-3.126	-7.935	-6.062
ATOM	704	C4'	CYT	47	-1.555	-7.752	-4.625
ATOM	705	H4'	CYT	47	-0.877	-8.317	-5.266
ATOM	706	O1'	CYT	47	-1.374	-6.365	-4.868
ATOM	707	C1'	CYT	47	-0.771	-5.761	-3.742
ATOM	708	H1'	CYT	47	0.310	-5.810	-3.879
ATOM	709	N1	CYT	47	-1.289	-4.368	-3.605
ATOM	710	C6	CYT	47	-2.637	-4.142	-3.505
ATOM	711	H6	CYT	47	-3.313	-4.983	-3.458
ATOM	712	C5	CYT	47	-3.147	-2.889	-3.479
ATOM	713	H5	CYT	47	-4.213	-2.752	-3.382
ATOM	714	C4	CYT	47	-2.218	-1.810	-3.570
ATOM	715	N4	CYT	47	-2.678	-0.569	-3.666
ATOM	716	HN4A	CYT	47	-3.669	-0.399	-3.707
ATOM	717	HN4B	CYT	47	-2.032	0.195	-3.812
ATOM	718	N3	CYT	47	-0.900	-2.014	-3.680
ATOM	719	C2	CYT	47	-0.408	-3.290	-3.673
ATOM	720	O2	CYT	47	0.808	-3.452	-3.729
ATOM	721	C3'	CYT	47	-1.233	-8.047	-3.154
ATOM	722	H3'	CYT	47	-2.035	-8.623	-2.689
ATOM	723	C2'	CYT	47	-1.139	-6.648	-2.552
ATOM	724	H2A'	CYT	47	-0.379	-6.599	-1.778
ATOM	725	H2B'	CYT	47	-2.113	-6.393	-2.136
ATOM	726	O3'	CYT	47	-0.010	-8.762	-3.072
ATOM	727	P	POM	48	0.522	-9.408	-1.689
ATOM	728	OA	POM	48	-0.616	-9.555	-0.756
ATOM	729	OB	POM	48	1.365	-10.579	-2.013
ATOM	730	O5'	GUA	49	1.484	-8.257	-1.112
ATOM	731	C5'	GUA	49	2.748	-8.018	-1.695
ATOM	732	H5A'	GUA	49	3.390	-8.889	-1.551
ATOM	733	H5B'	GUA	49	2.636	-7.832	-2.764
ATOM	734	C4'	GUA	49	3.402	-6.798	-1.043
ATOM	735	H4'	GUA	49	4.394	-6.659	-1.476
ATOM	736	O1'	GUA	49	2.606	-5.654	-1.310
ATOM	737	C1'	GUA	49	2.456	-4.932	-0.107
ATOM	738	H1'	GUA	49	3.343	-4.315	0.041

ATOM	739	N9	GUA	49	1.242	-4.087	-0.163
ATOM	740	C8	GUA	49	-0.078	-4.457	-0.086
ATOM	741	H8	GUA	49	-0.402	-5.467	0.109
ATOM	742	N7	GUA	49	-0.921	-3.479	-0.265
ATOM	743	C5	GUA	49	-0.103	-2.369	-0.449
ATOM	744	C6	GUA	49	-0.439	-1.000	-0.660
ATOM	745	O6	GUA	49	-1.556	-0.500	-0.768
ATOM	746	N1	GUA	49	0.676	-0.180	-0.722
ATOM	747	H1	GUA	49	0.477	0.809	-0.860
ATOM	748	C2	GUA	49	1.972	-0.623	-0.619
ATOM	749	N2	GUA	49	2.949	0.275	-0.668
ATOM	750	HN2A	GUA	49	3.903	-0.047	-0.654
ATOM	751	HN2B	GUA	49	2.748	1.265	-0.757
ATOM	752	N3	GUA	49	2.300	-1.906	-0.445
ATOM	753	C4	GUA	49	1.220	-2.728	-0.369
ATOM	754	C3'	GUA	49	3.509	-6.937	0.483
ATOM	755	H3'	GUA	49	3.354	-7.961	0.825
ATOM	756	C2'	GUA	49	2.418	-6.000	0.984
ATOM	757	H2A'	GUA	49	2.627	-5.598	1.975
ATOM	758	H2B'	GUA	49	1.470	-6.537	0.976
ATOM	759	O3'	GUA	49	4.766	-6.470	0.930
ATOM	760	H	HE	50	4.786	-6.516	1.888
ATOM	761	O1	DIS	51	-1.695	-6.168	-10.151
ATOM	762	C1	DIS	51	-1.223	-5.468	-11.044
ATOM	763	HF	DIS	51	-0.238	-5.057	-10.885
ATOM	764	N1	DIS	51	-1.869	-5.137	-12.173
ATOM	765	HN1	DIS	51	-1.367	-4.497	-12.780
ATOM	766	C2	DIS	51	-3.154	-5.492	-12.680
ATOM	767	C3	DIS	51	-3.822	-5.101	-13.848
ATOM	768	H3	DIS	51	-3.436	-4.392	-14.563
ATOM	769	C5	DIS	51	-3.938	-6.433	-12.046
ATOM	770	H5	DIS	51	-3.704	-6.995	-11.155
ATOM	771	N2	DIS	51	-5.118	-6.547	-12.746
ATOM	772	C6	DIS	51	-6.244	-7.459	-12.394
ATOM	773	HM1	DIS	51	-6.577	-8.099	-13.212
ATOM	774	HM2	DIS	51	-6.021	-8.162	-11.591
ATOM	775	HM3	DIS	51	-7.148	-6.950	-12.059
ATOM	776	C4	DIS	51	-5.079	-5.682	-13.826
ATOM	777	C7	DIS	51	-6.205	-5.393	-14.800
ATOM	778	O2	DIS	51	-7.272	-5.981	-14.639
ATOM	779	N3	DIS	51	-6.065	-4.351	-15.640
ATOM	780	HN3	DIS	51	-5.134	-3.962	-15.722
ATOM	781	C8	DIS	51	-7.000	-3.666	-16.477
ATOM	782	C9	DIS	51	-6.845	-2.535	-17.305
ATOM	783	H9	DIS	51	-5.912	-2.062	-17.559
ATOM	784	C11	DIS	51	-8.354	-3.855	-16.289
ATOM	785	H11	DIS	51	-8.842	-4.588	-15.666
ATOM	786	N4	DIS	51	-9.030	-2.938	-17.058
ATOM	787	C12	DIS	51	-10.510	-2.862	-17.210
ATOM	788	HM4	DIS	51	-10.972	-2.014	-16.706
ATOM	789	HM5	DIS	51	-10.851	-2.786	-18.243
ATOM	790	HM6	DIS	51	-11.048	-3.726	-16.819
ATOM	791	C10	DIS	51	-8.111	-2.080	-17.630

ATOM	792	C13	DIS	51	-8.424	-0.813	-18.390
ATOM	793	O3	DIS	51	-9.573	-0.381	-18.322
ATOM	794	N5	DIS	51	-7.417	-0.145	-18.983
ATOM	795	HN5	DIS	51	-6.506	-0.588	-18.971
ATOM	796	C14	DIS	51	-7.384	1.118	-19.653
ATOM	797	C15	DIS	51	-6.339	1.839	-20.268
ATOM	798	H15	DIS	51	-5.286	1.585	-20.263
ATOM	799	C17	DIS	51	-8.565	1.784	-19.910
ATOM	800	H17	DIS	51	-9.567	1.507	-19.628
ATOM	801	N6	DIS	51	-8.288	2.864	-20.709
ATOM	802	C18	DIS	51	-9.305	3.788	-21.285
ATOM	803	HM7	DIS	51	-9.331	3.802	-22.375
ATOM	804	HM8	DIS	51	-10.332	3.560	-21.000
ATOM	805	HM9	DIS	51	-9.178	4.832	-20.998
ATOM	806	C16	DIS	51	-6.932	2.878	-20.969
ATOM	807	C19	DIS	51	-6.224	3.840	-21.886
ATOM	808	O4	DIS	51	-6.822	4.854	-22.237
ATOM	809	N7	DIS	51	-5.011	3.492	-22.345
ATOM	810	HN7	DIS	51	-4.624	2.619	-22.010
ATOM	811	C20	DIS	51	-4.262	4.061	-23.464
ATOM	812	HC1	DIS	51	-3.214	4.095	-23.185
ATOM	813	HC2	DIS	51	-4.355	3.376	-24.304
ATOM	814	C21	DIS	51	-4.744	5.455	-23.874
ATOM	815	HC3	DIS	51	-5.748	5.361	-24.277
ATOM	816	HC4	DIS	51	-4.803	6.078	-22.989
ATOM	817	C22	DIS	51	-3.953	6.215	-24.917
ATOM	818	N8	DIS	51	-3.177	5.596	-25.824
ATOM	819	HNC	DIS	51	-2.729	6.128	-26.558
ATOM	820	HND	DIS	51	-3.027	4.590	-25.799
ATOM	821	N9	DIS	51	-4.215	7.522	-25.036
ATOM	822	HNA	DIS	51	-4.402	7.858	-25.983
ATOM	823	HNB	DIS	51	-4.753	7.965	-24.305
ATOM	824	O1	DIS	52	0.574	6.486	-26.429
ATOM	825	C1	DIS	52	0.893	5.679	-25.558
ATOM	826	HF	DIS	52	1.648	4.945	-25.796
ATOM	827	N1	DIS	52	0.305	5.615	-24.356
ATOM	828	HN1	DIS	52	0.605	4.839	-23.773
ATOM	829	C2	DIS	52	-0.717	6.425	-23.789
ATOM	830	C3	DIS	52	-1.545	6.237	-22.669
ATOM	831	H3	DIS	52	-1.722	5.299	-22.172
ATOM	832	C5	DIS	52	-0.700	7.774	-24.071
ATOM	833	H5	DIS	52	-0.055	8.280	-24.774
ATOM	834	N2	DIS	52	-1.630	8.392	-23.266
ATOM	835	C6	DIS	52	-1.932	9.851	-23.248
ATOM	836	HM1	DIS	52	-1.907	10.301	-22.255
ATOM	837	HM2	DIS	52	-1.244	10.462	-23.832
ATOM	838	HM3	DIS	52	-2.916	10.110	-23.640
ATOM	839	C4	DIS	52	-2.191	7.440	-22.437
ATOM	840	C7	DIS	52	-3.345	7.646	-21.489
ATOM	841	O2	DIS	52	-4.072	8.616	-21.693
ATOM	842	N3	DIS	52	-3.708	6.606	-20.720
ATOM	843	HN3	DIS	52	-3.043	5.846	-20.662
ATOM	844	C8	DIS	52	-4.896	6.348	-19.970

ATOM	845	C9	DIS	52	-5.317	5.218	-19.247
ATOM	846	H9	DIS	52	-4.798	4.274	-19.184
ATOM	847	C11	DIS	52	-5.888	7.305	-19.871
ATOM	848	H11	DIS	52	-5.890	8.306	-20.270
ATOM	849	N4	DIS	52	-6.894	6.804	-19.082
ATOM	850	C12	DIS	52	-8.119	7.540	-18.661
ATOM	851	HM4	DIS	52	-9.026	7.227	-19.179
ATOM	852	HM5	DIS	52	-8.364	7.442	-17.603
ATOM	853	HM6	DIS	52	-8.077	8.617	-18.822
ATOM	854	C10	DIS	52	-6.576	5.505	-18.748
ATOM	855	C13	DIS	52	-7.465	4.533	-18.025
ATOM	856	O3	DIS	52	-8.684	4.657	-18.137
ATOM	857	N5	DIS	52	-6.878	3.528	-17.361
ATOM	858	HN5	DIS	52	-5.864	3.529	-17.353
ATOM	859	C14	DIS	52	-7.445	2.403	-16.700
ATOM	860	C15	DIS	52	-6.858	1.238	-16.186
ATOM	861	H15	DIS	52	-5.818	0.955	-16.295
ATOM	862	C17	DIS	52	-8.762	2.436	-16.286
ATOM	863	H17	DIS	52	-9.481	3.225	-16.440
ATOM	864	N6	DIS	52	-9.017	1.291	-15.569
ATOM	865	C18	DIS	52	-10.320	0.936	-14.941
ATOM	866	HM7	DIS	52	-10.302	0.896	-13.852
ATOM	867	HM8	DIS	52	-11.133	1.628	-15.166
ATOM	868	HM9	DIS	52	-10.710	-0.036	-15.241
ATOM	869	C16	DIS	52	-7.848	0.561	-15.489
ATOM	870	C19	DIS	52	-7.612	-0.705	-14.716
ATOM	871	O4	DIS	52	-8.408	-1.081	-13.861
ATOM	872	N7	DIS	52	-6.355	-1.138	-14.741
ATOM	873	HN7	DIS	52	-5.883	-0.936	-15.608
ATOM	874	C20	DIS	52	-5.478	-0.951	-13.611
ATOM	875	HC1	DIS	52	-4.599	-0.495	-14.055
ATOM	876	HC2	DIS	52	-5.899	-0.292	-12.858
ATOM	877	C21	DIS	52	-5.022	-2.277	-13.035
ATOM	878	HC3	DIS	52	-4.853	-2.894	-13.899
ATOM	879	HC4	DIS	52	-4.065	-2.121	-12.538
ATOM	880	C22	DIS	52	-5.956	-2.976	-12.071
ATOM	881	N8	DIS	52	-5.494	-3.280	-10.848
ATOM	882	HNC	DIS	52	-6.109	-3.644	-10.135
ATOM	883	HND	DIS	52	-4.577	-2.950	-10.563
ATOM	884	N9	DIS	52	-7.220	-3.253	-12.430
ATOM	885	HNA	DIS	52	-7.891	-3.632	-11.755
ATOM	886	HNB	DIS	52	-7.591	-2.853	-13.283

Coordinates for the 2:1 Distamycin A - A3T3

Complex (C2) both drugs in ATTT Binding Sites

ATOM	1	H	HB	1	-0.147	9.911	1.478
ATOM	2	O5'	CYT	2	0.254	9.158	1.037
ATOM	3	C5'	CYT	2	1.304	8.672	1.846
ATOM	4	H5A'	CYT	2	2.048	9.458	1.983
ATOM	5	H5B'	CYT	2	0.900	8.392	2.820
ATOM	6	C4'	CYT	2	1.968	7.450	1.205
ATOM	7	H4'	CYT	2	2.727	7.070	1.892
ATOM	8	O1'	CYT	2	1.032	6.413	0.986
ATOM	9	C1'	CYT	2	1.607	5.570	0.009
ATOM	10	H1'	CYT	2	2.418	5.018	0.486
ATOM	11	N1	CYT	2	0.580	4.680	-0.594
ATOM	12	C6	CYT	2	-0.664	5.159	-0.916
ATOM	13	H6	CYT	2	-0.867	6.214	-0.805
ATOM	14	C5	CYT	2	-1.647	4.335	-1.348
ATOM	15	H5	CYT	2	-2.617	4.744	-1.589
ATOM	16	C4	CYT	2	-1.330	2.942	-1.444
ATOM	17	N4	CYT	2	-2.280	2.063	-1.738
ATOM	18	HN4A	CYT	2	-2.060	1.074	-1.673
ATOM	19	HN4B	CYT	2	-3.204	2.368	-1.992
ATOM	20	N3	CYT	2	-0.114	2.476	-1.146
ATOM	21	C2	CYT	2	0.872	3.330	-0.759
ATOM	22	O2	CYT	2	1.997	2.881	-0.552
ATOM	23	C3'	CYT	2	2.629	7.742	-0.150
ATOM	24	H3'	CYT	2	2.239	8.666	-0.580
ATOM	25	C2'	CYT	2	2.199	6.544	-1.004
ATOM	26	H2A'	CYT	2	3.027	6.080	-1.535
ATOM	27	H2B'	CYT	2	1.442	6.875	-1.714
ATOM	28	O3'	CYT	2	4.030	7.831	0.038
ATOM	29	P	POM	3	5.032	8.264	-1.149
ATOM	30	OA	POM	3	4.277	9.098	-2.110
ATOM	31	OB	POM	3	6.269	8.787	-0.530
ATOM	32	O5'	GUA	4	5.374	6.855	-1.847
ATOM	33	C5'	GUA	4	6.183	5.905	-1.183
ATOM	34	H5A'	GUA	4	7.202	6.287	-1.103
ATOM	35	H5B'	GUA	4	5.795	5.730	-0.178
ATOM	36	C4'	GUA	4	6.205	4.565	-1.926
ATOM	37	H4'	GUA	4	6.845	3.884	-1.362
ATOM	38	O1'	GUA	4	4.898	4.007	-1.981
ATOM	39	C1'	GUA	4	4.733	3.446	-3.267
ATOM	40	H1'	GUA	4	5.245	2.483	-3.311
ATOM	41	N9	GUA	4	3.299	3.291	-3.604
ATOM	42	C8	GUA	4	2.355	4.269	-3.784
ATOM	43	H8	GUA	4	2.579	5.324	-3.734
ATOM	44	N7	GUA	4	1.153	3.819	-4.016
ATOM	45	C5	GUA	4	1.310	2.435	-3.997
ATOM	46	C6	GUA	4	0.352	1.392	-4.175
ATOM	47	O6	GUA	4	-0.848	1.499	-4.408
ATOM	48	N1	GUA	4	0.899	0.125	-4.045
ATOM	49	H1	GUA	4	0.249	-0.661	-4.065

ATOM	50	C2	GUA	4	2.234	-0.116	-3.846
ATOM	51	N2	GUA	4	2.639	-1.380	-3.789
ATOM	52	HN2A	GUA	4	1.985	-2.152	-3.868
ATOM	53	HN2B	GUA	4	3.619	-1.561	-3.638
ATOM	54	N3	GUA	4	3.146	0.849	-3.699
ATOM	55	C4	GUA	4	2.621	2.103	-3.760
ATOM	56	C3'	GUA	4	6.732	4.669	-3.368
ATOM	57	H3'	GUA	4	7.181	5.641	-3.577
ATOM	58	C2'	GUA	4	5.451	4.442	-4.168
ATOM	59	H2A'	GUA	4	5.634	4.061	-5.169
ATOM	60	H2B'	GUA	4	4.907	5.386	-4.219
ATOM	61	O3'	GUA	4	7.673	3.626	-3.559
ATOM	62	P	POM	5	8.521	3.439	-4.919
ATOM	63	OA	POM	5	8.054	4.423	-5.919
ATOM	64	OB	POM	5	9.954	3.360	-4.565
ATOM	65	O5'	CYT	6	8.032	1.980	-5.388
ATOM	66	C5'	CYT	6	8.387	0.831	-4.642
ATOM	67	H5A'	CYT	6	9.468	0.692	-4.671
ATOM	68	H5B'	CYT	6	8.078	0.964	-3.604
ATOM	69	C4'	CYT	6	7.699	-0.426	-5.188
ATOM	70	H4'	CYT	6	7.958	-1.257	-4.530
ATOM	71	O1'	CYT	6	6.291	-0.240	-5.165
ATOM	72	C1'	CYT	6	5.765	-0.554	-6.441
ATOM	73	H1'	CYT	6	5.536	-1.621	-6.455
ATOM	74	N1	CYT	6	4.582	0.307	-6.715
ATOM	75	C6	CYT	6	4.699	1.671	-6.662
ATOM	76	H6	CYT	6	5.663	2.109	-6.449
ATOM	77	C5	CYT	6	3.636	2.481	-6.862
ATOM	78	H5	CYT	6	3.771	3.552	-6.821
ATOM	79	C4	CYT	6	2.381	1.849	-7.116
ATOM	80	N4	CYT	6	1.299	2.598	-7.278
ATOM	81	HN4A	CYT	6	0.405	2.150	-7.436
ATOM	82	HN4B	CYT	6	1.343	3.596	-7.154
ATOM	83	N3	CYT	6	2.246	0.519	-7.137
ATOM	84	C2	CYT	6	3.339	-0.278	-6.953
ATOM	85	O2	CYT	6	3.192	-1.498	-6.990
ATOM	86	C3'	CYT	6	8.118	-0.767	-6.625
ATOM	87	H3'	CYT	6	9.026	-0.237	-6.917
ATOM	88	C2'	CYT	6	6.907	-0.299	-7.423
ATOM	89	H2A'	CYT	6	6.782	-0.842	-8.358
ATOM	90	H2B'	CYT	6	7.036	0.762	-7.634
ATOM	91	O3'	CYT	6	8.313	-2.168	-6.709
ATOM	92	P	POM	7	8.852	-2.886	-8.048
ATOM	93	OA	POM	7	9.282	-1.846	-9.008
ATOM	94	OB	POM	7	9.792	-3.956	-7.648
ATOM	95	O5'	ADE	8	7.510	-3.573	-8.612
ATOM	96	C5'	ADE	8	6.973	-4.717	-7.976
ATOM	97	H5A'	ADE	8	7.706	-5.525	-8.002
ATOM	98	H5B'	ADE	8	6.744	-4.483	-6.935
ATOM	99	C4'	ADE	8	5.695	-5.198	-8.671
ATOM	100	H4'	ADE	8	5.341	-6.086	-8.146
ATOM	101	O1'	ADE	8	4.683	-4.206	-8.594
ATOM	102	C1'	ADE	8	4.000	-4.150	-9.829

ATOM	103	H1'	ADE	8	3.200	-4.892	-9.840
ATOM	104	N9	ADE	8	3.485	-2.775	-10.016
ATOM	105	C8	ADE	8	4.224	-1.617	-10.017
ATOM	106	H8	ADE	8	5.303	-1.615	-9.963
ATOM	107	N7	ADE	8	3.521	-0.522	-10.064
ATOM	108	C5	ADE	8	2.216	-0.994	-10.106
ATOM	109	C6	ADE	8	0.983	-0.331	-10.143
ATOM	110	N6	ADE	8	0.930	0.995	-10.120
ATOM	111	HN6A	ADE	8	0.050	1.485	-10.140
ATOM	112	HN6B	ADE	8	1.802	1.495	-10.040
ATOM	113	N1	ADE	8	-0.151	-1.046	-10.244
ATOM	114	C2	ADE	8	-0.061	-2.372	-10.266
ATOM	115	H2	ADE	8	-1.008	-2.906	-10.359
ATOM	116	N3	ADE	8	1.037	-3.126	-10.174
ATOM	117	C4	ADE	8	2.169	-2.363	-10.103
ATOM	118	C3'	ADE	8	5.923	-5.545	-10.149
ATOM	119	H3'	ADE	8	6.973	-5.432	-10.425
ATOM	120	C2'	ADE	8	5.054	-4.516	-10.870
ATOM	121	H2A'	ADE	8	4.603	-4.913	-11.776
ATOM	122	H2B'	ADE	8	5.683	-3.660	-11.112
ATOM	123	O3'	ADE	8	5.497	-6.878	-10.370
ATOM	124	P	POM	9	5.744	-7.639	-11.771
ATOM	125	OA	POM	9	6.853	-6.974	-12.489
ATOM	126	OB	POM	9	5.800	-9.092	-11.505
ATOM	127	O5'	ADE	10	4.378	-7.318	-12.552
ATOM	128	C5'	ADE	10	3.170	-7.956	-12.189
ATOM	129	H5A'	ADE	10	3.245	-9.024	-12.401
ATOM	130	H5B'	ADE	10	2.980	-7.817	-11.124
ATOM	131	C4'	ADE	10	2.000	-7.368	-12.984
ATOM	132	H4'	ADE	10	1.095	-7.918	-12.724
ATOM	133	O1'	ADE	10	1.814	-5.999	-12.639
ATOM	134	C1'	ADE	10	1.587	-5.293	-13.842
ATOM	135	H1'	ADE	10	0.552	-5.434	-14.157
ATOM	136	N9	ADE	10	1.889	-3.855	-13.689
ATOM	137	C8	ADE	10	3.123	-3.255	-13.617
ATOM	138	H8	ADE	10	4.055	-3.796	-13.663
ATOM	139	N7	ADE	10	3.088	-1.960	-13.495
ATOM	140	C5	ADE	10	1.729	-1.684	-13.497
ATOM	141	C6	ADE	10	1.022	-0.481	-13.410
ATOM	142	N6	ADE	10	1.673	0.670	-13.283
ATOM	143	HN6A	ADE	10	1.178	1.544	-13.190
ATOM	144	HN6B	ADE	10	2.681	0.636	-13.255
ATOM	145	N1	ADE	10	-0.319	-0.499	-13.405
ATOM	146	C2	ADE	10	-0.931	-1.678	-13.493
ATOM	147	H2	ADE	10	-2.010	-1.653	-13.481
ATOM	148	N3	ADE	10	-0.383	-2.887	-13.603
ATOM	149	C4	ADE	10	0.978	-2.823	-13.601
ATOM	150	C3'	ADE	10	2.254	-7.432	-14.501
ATOM	151	H3'	ADE	10	3.099	-8.066	-14.778
ATOM	152	C2'	ADE	10	2.526	-5.974	-14.834
ATOM	153	H2A'	ADE	10	2.302	-5.730	-15.872
ATOM	154	H2B'	ADE	10	3.572	-5.771	-14.611
ATOM	155	O3'	ADE	10	1.093	-7.799	-15.208

ATOM	156	P	POM	11	0.681	-9.338	-15.396
ATOM	157	OA	POM	11	1.558	-9.932	-16.428
ATOM	158	OB	POM	11	0.557	-9.972	-14.065
ATOM	159	O5'	ADE	12	-0.783	-9.138	-16.013
ATOM	160	C5'	ADE	12	-1.888	-8.809	-15.195
ATOM	161	H5A'	ADE	12	-2.485	-9.710	-15.047
ATOM	162	H5B'	ADE	12	-1.571	-8.437	-14.219
ATOM	163	C4'	ADE	12	-2.748	-7.727	-15.857
ATOM	164	H4'	ADE	12	-3.686	-7.672	-15.306
ATOM	165	O1'	ADE	12	-2.116	-6.460	-15.767
ATOM	166	C1'	ADE	12	-2.489	-5.687	-16.891
ATOM	167	H1'	ADE	12	-3.492	-5.285	-16.785
ATOM	168	N9	ADE	12	-1.474	-4.610	-17.055
ATOM	169	C8	ADE	12	-0.123	-4.787	-17.230
ATOM	170	H8	ADE	12	0.322	-5.761	-17.374
ATOM	171	N7	ADE	12	0.583	-3.691	-17.186
ATOM	172	C5	ADE	12	-0.371	-2.709	-16.956
ATOM	173	C6	ADE	12	-0.268	-1.323	-16.764
ATOM	174	N6	ADE	12	0.928	-0.744	-16.744
ATOM	175	HN6A	ADE	12	1.018	0.248	-16.589
ATOM	176	HN6B	ADE	12	1.737	-1.323	-16.911
ATOM	177	N1	ADE	12	-1.369	-0.586	-16.530
ATOM	178	C2	ADE	12	-2.538	-1.222	-16.462
ATOM	179	H2	ADE	12	-3.422	-0.608	-16.253
ATOM	180	N3	ADE	12	-2.754	-2.534	-16.594
ATOM	181	C4	ADE	12	-1.624	-3.245	-16.854
ATOM	182	C3'	ADE	12	-3.058	-7.991	-17.336
ATOM	183	H3'	ADE	12	-2.536	-8.872	-17.710
ATOM	184	C2'	ADE	12	-2.532	-6.721	-18.017
ATOM	185	H2A'	ADE	12	-3.185	-6.412	-18.827
ATOM	186	H2B'	ADE	12	-1.529	-6.926	-18.391
ATOM	187	O3'	ADE	12	-4.458	-8.177	-17.453
ATOM	188	P	POM	13	-5.160	-8.726	-18.798
ATOM	189	OA	POM	13	-4.126	-9.307	-19.682
ATOM	190	OB	POM	13	-6.339	-9.531	-18.408
ATOM	191	O5'	THY	14	-5.681	-7.363	-19.457
ATOM	192	C5'	THY	14	-6.740	-6.644	-18.856
ATOM	193	H5A'	THY	14	-7.699	-7.097	-19.108
ATOM	194	H5B'	THY	14	-6.623	-6.644	-17.771
ATOM	195	C4'	THY	14	-6.701	-5.190	-19.317
ATOM	196	H4'	THY	14	-7.409	-4.625	-18.721
ATOM	197	O1'	THY	14	-5.408	-4.659	-19.102
ATOM	198	C1'	THY	14	-5.270	-3.565	-19.971
ATOM	199	H1'	THY	14	-5.824	-2.730	-19.560
ATOM	200	N1	THY	14	-3.828	-3.265	-20.155
ATOM	201	C6	THY	14	-2.978	-4.275	-20.528
ATOM	202	H6	THY	14	-3.393	-5.252	-20.730
ATOM	203	C5	THY	14	-1.645	-4.075	-20.641
ATOM	204	C7	THY	14	-0.733	-5.222	-21.035
ATOM	205	H7A	THY	14	0.172	-5.192	-20.426
ATOM	206	H7B	THY	14	-1.220	-6.187	-20.891
ATOM	207	H7C	THY	14	-0.453	-5.111	-22.083
ATOM	208	C4	THY	14	-1.079	-2.766	-20.398

ATOM	209	O4	THY	14	0.108	-2.493	-20.516
ATOM	210	N3	THY	14	-1.985	-1.796	-20.007
ATOM	211	H3	THY	14	-1.654	-0.837	-19.884
ATOM	212	C2	THY	14	-3.345	-1.995	-19.840
ATOM	213	O2	THY	14	-4.058	-1.079	-19.440
ATOM	214	C3'	THY	14	-7.068	-4.962	-20.787
ATOM	215	H3'	THY	14	-7.030	-5.902	-21.340
ATOM	216	C2'	THY	14	-5.960	-4.015	-21.257
ATOM	217	H2A'	THY	14	-6.360	-3.157	-21.786
ATOM	218	H2B'	THY	14	-5.286	-4.572	-21.904
ATOM	219	O3'	THY	14	-8.362	-4.379	-20.841
ATOM	220	P	POM	15	-9.179	-4.185	-22.220
ATOM	221	OA	POM	15	-8.743	-5.230	-23.172
ATOM	222	OB	POM	15	-10.614	-4.049	-21.887
ATOM	223	O5'	THY	16	-8.658	-2.765	-22.765
ATOM	224	C5'	THY	16	-9.086	-1.553	-22.169
ATOM	225	H5A'	THY	16	-10.118	-1.338	-22.450
ATOM	226	H5B'	THY	16	-9.023	-1.636	-21.083
ATOM	227	C4'	THY	16	-8.173	-0.407	-22.610
ATOM	228	H4'	THY	16	-8.446	0.492	-22.066
ATOM	229	O1'	THY	16	-6.838	-0.751	-22.295
ATOM	230	C1'	THY	16	-5.991	0.001	-23.125
ATOM	231	H1'	THY	16	-5.879	0.982	-22.685
ATOM	232	N1	THY	16	-4.699	-0.714	-23.288
ATOM	233	C6	THY	16	-4.697	-2.025	-23.698
ATOM	234	H6	THY	16	-5.644	-2.496	-23.920
ATOM	235	C5	THY	16	-3.547	-2.731	-23.814
ATOM	236	C7	THY	16	-3.583	-4.180	-24.262
ATOM	237	H7A	THY	16	-3.125	-4.257	-25.249
ATOM	238	H7B	THY	16	-3.012	-4.791	-23.561
ATOM	239	H7C	THY	16	-4.604	-4.561	-24.313
ATOM	240	C4	THY	16	-2.273	-2.109	-23.522
ATOM	241	O4	THY	16	-1.186	-2.675	-23.565
ATOM	242	N3	THY	16	-2.348	-0.786	-23.136
ATOM	243	H3	THY	16	-1.467	-0.291	-22.996
ATOM	244	C2	THY	16	-3.512	-0.062	-22.960
ATOM	245	O2	THY	16	-3.468	1.086	-22.526
ATOM	246	C3'	THY	16	-8.219	-0.077	-24.107
ATOM	247	H3'	THY	16	-8.598	-0.937	-24.662
ATOM	248	C2'	THY	16	-6.745	0.155	-24.443
ATOM	249	H2A'	THY	16	-6.566	1.150	-24.846
ATOM	250	H2B'	THY	16	-6.451	-0.605	-25.160
ATOM	251	O3'	THY	16	-9.020	1.073	-24.341
ATOM	252	P	POM	17	-9.403	1.574	-25.832
ATOM	253	OA	POM	17	-9.318	0.419	-26.753
ATOM	254	OB	POM	17	-10.657	2.355	-25.745
ATOM	255	O5'	THY	18	-8.220	2.589	-26.227
ATOM	256	C5'	THY	18	-8.119	3.866	-25.626
ATOM	257	H5A'	THY	18	-8.930	4.513	-25.963
ATOM	258	H5B'	THY	18	-8.189	3.752	-24.542
ATOM	259	C4'	THY	18	-6.763	4.515	-25.936
ATOM	260	H4'	THY	18	-6.660	5.371	-25.274
ATOM	261	O1'	THY	18	-5.759	3.544	-25.684

ATOM	262	C1'	THY	18	-4.984	3.379	-26.851
ATOM	263	H1'	THY	18	-4.165	4.098	-26.786
ATOM	264	N1	THY	18	-4.473	1.984	-26.935
ATOM	265	C6	THY	18	-5.299	0.933	-27.270
ATOM	266	H6	THY	18	-6.339	1.118	-27.492
ATOM	267	C5	THY	18	-4.858	-0.350	-27.275
ATOM	268	C7	THY	18	-5.805	-1.475	-27.654
ATOM	269	H7A	THY	18	-5.641	-1.745	-28.697
ATOM	270	H7B	THY	18	-5.610	-2.346	-27.027
ATOM	271	H7C	THY	18	-6.847	-1.175	-27.521
ATOM	272	C4	THY	18	-3.492	-0.659	-26.904
ATOM	273	O4	THY	18	-2.994	-1.781	-26.847
ATOM	274	N3	THY	18	-2.741	0.435	-26.546
ATOM	275	H3	THY	18	-1.756	0.284	-26.357
ATOM	276	C2	THY	18	-3.148	1.750	-26.575
ATOM	277	O2	THY	18	-2.348	2.632	-26.270
ATOM	278	C3'	THY	18	-6.575	5.011	-27.377
ATOM	279	H3'	THY	18	-7.530	5.257	-27.843
ATOM	280	C2'	THY	18	-5.902	3.800	-28.003
ATOM	281	H2A'	THY	18	-5.368	4.045	-28.915
ATOM	282	H2B'	THY	18	-6.680	3.075	-28.226
ATOM	283	O3'	THY	18	-5.696	6.129	-27.371
ATOM	284	P	POM	19	-5.543	7.108	-28.645
ATOM	285	OA	POM	19	-6.252	6.497	-29.789
ATOM	286	OB	POM	19	-5.896	8.476	-28.206
ATOM	287	O5'	GUA	20	-3.966	7.078	-28.990
ATOM	288	C5'	GUA	20	-3.044	7.921	-28.327
ATOM	289	H5A'	GUA	20	-3.375	8.958	-28.400
ATOM	290	H5B'	GUA	20	-2.998	7.642	-27.275
ATOM	291	C4'	GUA	20	-1.633	7.835	-28.937
ATOM	292	H4'	GUA	20	-0.999	8.511	-28.361
ATOM	293	O1'	GUA	20	-1.119	6.515	-28.838
ATOM	294	C1'	GUA	20	-0.966	5.963	-30.135
ATOM	295	H1'	GUA	20	0.089	6.015	-30.410
ATOM	296	N9	GUA	20	-1.427	4.558	-30.101
ATOM	297	C8	GUA	20	-2.699	4.091	-29.905
ATOM	298	H8	GUA	20	-3.555	4.743	-29.881
ATOM	299	N7	GUA	20	-2.782	2.801	-29.738
ATOM	300	C5	GUA	20	-1.463	2.371	-29.844
ATOM	301	C6	GUA	20	-0.909	1.061	-29.737
ATOM	302	O6	GUA	20	-1.490	0.014	-29.465
ATOM	303	N1	GUA	20	0.460	1.038	-29.964
ATOM	304	H1	GUA	20	0.889	0.111	-29.961
ATOM	305	C2	GUA	20	1.214	2.154	-30.236
ATOM	306	N2	GUA	20	2.511	2.001	-30.478
ATOM	307	HN2A	GUA	20	2.935	1.081	-30.465
ATOM	308	HN2B	GUA	20	3.028	2.782	-30.850
ATOM	309	N3	GUA	20	0.718	3.396	-30.267
ATOM	310	C4	GUA	20	-0.629	3.436	-30.086
ATOM	311	C3'	GUA	20	-1.564	8.220	-30.418
ATOM	312	H3'	GUA	20	-2.338	8.939	-30.694
ATOM	313	C2'	GUA	20	-1.753	6.862	-31.086
ATOM	314	H2A'	GUA	20	-1.368	6.849	-32.101

ATOM	315	H2B'	GUA	20	-2.812	6.611	-31.103
ATOM	316	O3'	GUA	20	-0.267	8.747	-30.652
ATOM	317	P	POM	21	0.175	9.369	-32.073
ATOM	318	OA	POM	21	-0.980	9.320	-32.994
ATOM	319	OB	POM	21	0.871	10.648	-31.819
ATOM	320	O5'	CYT	22	1.258	8.294	-32.577
ATOM	321	C5'	CYT	22	2.557	8.253	-32.016
ATOM	322	H5A'	CYT	22	3.061	9.207	-32.179
ATOM	323	H5B'	CYT	22	2.479	8.076	-30.943
ATOM	324	C4'	CYT	22	3.401	7.134	-32.641
ATOM	325	H4'	CYT	22	4.368	7.120	-32.137
ATOM	326	O1'	CYT	22	2.742	5.890	-32.442
ATOM	327	C1'	CYT	22	2.549	5.274	-33.703
ATOM	328	H1'	CYT	22	3.438	4.684	-33.927
ATOM	329	N1	CYT	22	1.319	4.432	-33.668
ATOM	330	C6	CYT	22	0.074	5.005	-33.653
ATOM	331	H6	CYT	22	-0.027	6.075	-33.730
ATOM	332	C5	CYT	22	-1.047	4.262	-33.515
ATOM	333	H5	CYT	22	-2.009	4.754	-33.512
ATOM	334	C4	CYT	22	-0.878	2.851	-33.382
ATOM	335	N4	CYT	22	-1.944	2.092	-33.155
ATOM	336	HN4A	CYT	22	-1.827	1.099	-32.999
ATOM	337	HN4B	CYT	22	-2.853	2.513	-33.058
ATOM	338	N3	CYT	22	0.331	2.280	-33.353
ATOM	339	C2	CYT	22	1.448	3.052	-33.508
ATOM	340	O2	CYT	22	2.549	2.504	-33.477
ATOM	341	C3'	CYT	22	3.617	7.324	-34.151
ATOM	342	H3'	CYT	22	3.496	8.366	-34.450
ATOM	343	C2'	CYT	22	2.523	6.425	-34.714
ATOM	344	H2A'	CYT	22	2.731	6.109	-35.731
ATOM	345	H2B'	CYT	22	1.599	6.995	-34.708
ATOM	346	O3'	CYT	22	4.910	6.851	-34.492
ATOM	347	P	POM	23	5.570	7.111	-35.943
ATOM	348	OA	POM	23	4.529	7.622	-36.860
ATOM	349	OB	POM	23	6.827	7.867	-35.753
ATOM	350	O5'	GUA	24	5.942	5.619	-36.410
ATOM	351	C5'	GUA	24	7.061	4.949	-35.864
ATOM	352	H5A'	GUA	24	7.979	5.471	-36.139
ATOM	353	H5B'	GUA	24	6.978	4.944	-34.776
ATOM	354	C4'	GUA	24	7.127	3.494	-36.348
ATOM	355	H4'	GUA	24	7.971	3.011	-35.856
ATOM	356	O1'	GUA	24	5.922	2.848	-35.969
ATOM	357	C1'	GUA	24	5.280	2.342	-37.124
ATOM	358	H1'	GUA	24	5.581	1.301	-37.246
ATOM	359	N9	GUA	24	3.812	2.447	-36.977
ATOM	360	C8	GUA	24	3.033	3.574	-36.941
ATOM	361	H8	GUA	24	3.439	4.562	-37.088
ATOM	362	N7	GUA	24	1.766	3.345	-36.724
ATOM	363	C5	GUA	24	1.695	1.959	-36.618
ATOM	364	C6	GUA	24	0.577	1.102	-36.392
ATOM	365	O6	GUA	24	-0.599	1.416	-36.213
ATOM	366	N1	GUA	24	0.922	-0.241	-36.401
ATOM	367	H1	GUA	24	0.151	-0.890	-36.247

ATOM	368	C2	GUA	24	2.199	-0.712	-36.587
ATOM	369	N2	GUA	24	2.397	-2.025	-36.580
ATOM	370	HN2A	GUA	24	1.628	-2.670	-36.441
ATOM	371	HN2B	GUA	24	3.339	-2.372	-36.659
ATOM	372	N3	GUA	24	3.257	0.080	-36.782
ATOM	373	C4	GUA	24	2.940	1.402	-36.784
ATOM	374	C3'	GUA	24	7.265	3.318	-37.867
ATOM	375	H3'	GUA	24	7.816	2.398	-38.070
ATOM	376	C2'	GUA	24	5.823	3.135	-38.313
ATOM	377	H2A'	GUA	24	5.743	2.588	-39.252
ATOM	378	H2B'	GUA	24	5.345	4.111	-38.397
ATOM	379	O3'	GUA	24	7.888	4.399	-38.527
ATOM	380	H	HE	25	8.779	4.493	-38.184
ATOM	381	H	HB	26	-5.399	-6.385	-37.918
ATOM	382	O5'	CYT	27	-5.312	-7.335	-38.026
ATOM	383	C5'	CYT	27	-4.223	-7.590	-38.889
ATOM	384	H5A'	CYT	27	-4.122	-8.666	-39.031
ATOM	385	H5B'	CYT	27	-4.417	-7.121	-39.854
ATOM	386	C4'	CYT	27	-2.922	-7.032	-38.307
ATOM	387	H4'	CYT	27	-2.121	-7.201	-39.030
ATOM	388	O1'	CYT	27	-3.008	-5.637	-38.085
ATOM	389	C1'	CYT	27	-2.005	-5.329	-37.139
ATOM	390	H1'	CYT	27	-1.040	-5.402	-37.645
ATOM	391	N1	CYT	27	-2.236	-3.990	-36.535
ATOM	392	C6	CYT	27	-3.499	-3.579	-36.197
ATOM	393	H6	CYT	27	-4.322	-4.272	-36.296
ATOM	394	C5	CYT	27	-3.739	-2.319	-35.762
ATOM	395	H5	CYT	27	-4.747	-2.028	-35.508
ATOM	396	C4	CYT	27	-2.615	-1.437	-35.679
ATOM	397	N4	CYT	27	-2.796	-0.158	-35.372
ATOM	398	HN4A	CYT	27	-2.004	0.474	-35.426
ATOM	399	HN4B	CYT	27	-3.706	0.185	-35.117
ATOM	400	N3	CYT	27	-1.379	-1.840	-35.988
ATOM	401	C2	CYT	27	-1.157	-3.124	-36.382
ATOM	402	O2	CYT	27	-0.005	-3.485	-36.607
ATOM	403	C3'	CYT	27	-2.521	-7.670	-36.968
ATOM	404	H3'	CYT	27	-3.370	-8.180	-36.511
ATOM	405	C2'	CYT	27	-2.119	-6.457	-36.121
ATOM	406	H2A'	CYT	27	-1.177	-6.596	-35.595
ATOM	407	H2B'	CYT	27	-2.915	-6.251	-35.405
ATOM	408	O3'	CYT	27	-1.462	-8.578	-37.206
ATOM	409	P	POM	28	-0.883	-9.548	-36.055
ATOM	410	OA	POM	28	-1.961	-9.797	-35.074
ATOM	411	OB	POM	28	-0.208	-10.685	-36.718
ATOM	412	O5'	GUA	29	0.239	-8.625	-35.367
ATOM	413	C5'	GUA	29	1.428	-8.304	-36.062
ATOM	414	H5A'	GUA	29	2.030	-9.205	-36.188
ATOM	415	H5B'	GUA	29	1.184	-7.905	-37.048
ATOM	416	C4'	GUA	29	2.246	-7.253	-35.307
ATOM	417	H4'	GUA	29	3.149	-7.054	-35.887
ATOM	418	O1'	GUA	29	1.520	-6.036	-35.197
ATOM	419	C1'	GUA	29	1.818	-5.475	-33.935
ATOM	420	H1'	GUA	29	2.800	-5.001	-33.966

ATOM	421	N9	GUA	29	0.768	-4.509	-33.533
ATOM	422	C8	GUA	29	-0.565	-4.751	-33.315
ATOM	423	H8	GUA	29	-1.002	-5.737	-33.370
ATOM	424	N7	GUA	29	-1.269	-3.688	-33.044
ATOM	425	C5	GUA	29	-0.334	-2.657	-33.079
ATOM	426	C6	GUA	29	-0.501	-1.254	-32.877
ATOM	427	O6	GUA	29	-1.528	-0.651	-32.579
ATOM	428	N1	GUA	29	0.669	-0.536	-33.065
ATOM	429	H1	GUA	29	0.586	0.481	-33.038
ATOM	430	C2	GUA	29	1.886	-1.112	-33.326
ATOM	431	N2	GUA	29	2.944	-0.316	-33.441
ATOM	432	HN2A	GUA	29	2.859	0.691	-33.361
ATOM	433	HN2B	GUA	29	3.839	-0.735	-33.639
ATOM	434	N3	GUA	29	2.064	-2.429	-33.483
ATOM	435	C4	GUA	29	0.915	-3.148	-33.371
ATOM	436	C3'	GUA	29	2.645	-7.695	-33.889
ATOM	437	H3'	GUA	29	2.346	-8.723	-33.677
ATOM	438	C2'	GUA	29	1.869	-6.699	-33.028
ATOM	439	H2A'	GUA	29	2.346	-6.501	-32.071
ATOM	440	H2B'	GUA	29	0.870	-7.103	-32.867
ATOM	441	O3'	GUA	29	4.050	-7.557	-33.774
ATOM	442	P	POM	30	4.865	-7.923	-32.432
ATOM	443	OA	POM	30	3.936	-8.526	-31.451
ATOM	444	OB	POM	30	6.102	-8.635	-32.820
ATOM	445	O5'	CYT	31	5.264	-6.454	-31.918
ATOM	446	C5'	CYT	31	6.168	-5.664	-32.667
ATOM	447	H5A'	CYT	31	7.153	-6.133	-32.676
ATOM	448	H5B'	CYT	31	5.812	-5.576	-33.695
ATOM	449	C4'	CYT	31	6.283	-4.254	-32.084
ATOM	450	H4'	CYT	31	6.913	-3.664	-32.751
ATOM	451	O1'	CYT	31	4.997	-3.656	-32.031
ATOM	452	C1'	CYT	31	4.864	-2.984	-30.796
ATOM	453	H1'	CYT	31	5.328	-2.002	-30.894
ATOM	454	N1	CYT	31	3.423	-2.926	-30.421
ATOM	455	C6	CYT	31	2.672	-4.071	-30.390
ATOM	456	H6	CYT	31	3.156	-5.018	-30.577
ATOM	457	C5	CYT	31	1.342	-4.039	-30.139
ATOM	458	H5	CYT	31	0.784	-4.964	-30.124
ATOM	459	C4	CYT	31	0.756	-2.756	-29.909
ATOM	460	N4	CYT	31	-0.553	-2.653	-29.719
ATOM	461	HN4A	CYT	31	-0.964	-1.738	-29.582
ATOM	462	HN4B	CYT	31	-1.144	-3.466	-29.774
ATOM	463	N3	CYT	31	1.475	-1.630	-29.961
ATOM	464	C2	CYT	31	2.815	-1.692	-30.206
ATOM	465	O2	CYT	31	3.452	-0.643	-30.236
ATOM	466	C3'	CYT	31	6.887	-4.236	-30.672
ATOM	467	H3'	CYT	31	7.255	-5.221	-30.380
ATOM	468	C2'	CYT	31	5.692	-3.816	-29.818
ATOM	469	H2A'	CYT	31	5.983	-3.249	-28.937
ATOM	470	H2B'	CYT	31	5.165	-4.719	-29.515
ATOM	471	O3'	CYT	31	7.944	-3.291	-30.663
ATOM	472	P	POM	32	8.885	-3.052	-29.376
ATOM	473	OA	POM	32	8.809	-4.243	-28.503

ATOM	474	OB	POM	32	10.199	-2.565	-29.851
ATOM	475	O5'	ADE	33	8.125	-1.835	-28.652
ATOM	476	C5'	ADE	33	8.161	-0.534	-29.208
ATOM	477	H5A'	ADE	33	9.167	-0.123	-29.117
ATOM	478	H5B'	ADE	33	7.891	-0.580	-30.265
ATOM	479	C4'	ADE	33	7.165	0.389	-28.500
ATOM	480	H4'	ADE	33	7.172	1.361	-28.996
ATOM	481	O1'	ADE	33	5.853	-0.129	-28.575
ATOM	482	C1'	ADE	33	5.088	0.520	-27.581
ATOM	483	H1'	ADE	33	4.753	1.487	-27.959
ATOM	484	N9	ADE	33	3.947	-0.336	-27.194
ATOM	485	C8	ADE	33	3.958	-1.703	-27.078
ATOM	486	H8	ADE	33	4.856	-2.291	-27.192
ATOM	487	N7	ADE	33	2.792	-2.237	-26.856
ATOM	488	C5	ADE	33	1.956	-1.131	-26.772
ATOM	489	C6	ADE	33	0.578	-1.019	-26.555
ATOM	490	N6	ADE	33	-0.202	-2.089	-26.428
ATOM	491	HN6A	ADE	33	0.236	-2.996	-26.461
ATOM	492	HN6B	ADE	33	-1.208	-2.000	-26.365
ATOM	493	N1	ADE	33	0.034	0.201	-26.456
ATOM	494	C2	ADE	33	0.807	1.267	-26.606
ATOM	495	H2	ADE	33	0.285	2.216	-26.484
ATOM	496	N3	ADE	33	2.116	1.308	-26.866
ATOM	497	C4	ADE	33	2.642	0.045	-26.941
ATOM	498	C3'	ADE	33	7.461	0.594	-27.013
ATOM	499	H3'	ADE	33	7.959	-0.286	-26.599
ATOM	500	C2'	ADE	33	6.054	0.717	-26.417
ATOM	501	H2A'	ADE	33	5.869	1.691	-25.979
ATOM	502	H2B'	ADE	33	5.934	-0.066	-25.667
ATOM	503	O3'	ADE	33	8.264	1.750	-26.846
ATOM	504	P	POM	34	8.765	2.258	-25.399
ATOM	505	OA	POM	34	8.884	1.094	-24.495
ATOM	506	OB	POM	34	9.916	3.165	-25.598
ATOM	507	O5'	ADE	35	7.514	3.142	-24.915
ATOM	508	C5'	ADE	35	7.115	4.283	-25.648
ATOM	509	H5A'	ADE	35	7.896	5.043	-25.592
ATOM	510	H5B'	ADE	35	6.960	4.017	-26.694
ATOM	511	C4'	ADE	35	5.803	4.857	-25.102
ATOM	512	H4'	ADE	35	5.538	5.712	-25.726
ATOM	513	O1'	ADE	35	4.760	3.888	-25.171
ATOM	514	C1'	ADE	35	4.189	3.743	-23.880
ATOM	515	H1'	ADE	35	3.357	4.441	-23.782
ATOM	516	N9	ADE	35	3.740	2.351	-23.658
ATOM	517	C8	ADE	35	4.514	1.218	-23.572
ATOM	518	H8	ADE	35	5.593	1.234	-23.640
ATOM	519	N7	ADE	35	3.840	0.113	-23.418
ATOM	520	C5	ADE	35	2.525	0.553	-23.364
ATOM	521	C6	ADE	35	1.312	-0.128	-23.193
ATOM	522	N6	ADE	35	1.284	-1.451	-23.080
ATOM	523	HN6A	ADE	35	0.411	-1.949	-22.968
ATOM	524	HN6B	ADE	35	2.163	-1.946	-23.105
ATOM	525	N1	ADE	35	0.162	0.568	-23.171
ATOM	526	C2	ADE	35	0.223	1.887	-23.333

ATOM	527	H2	ADE	35	-0.723	2.406	-23.319
ATOM	528	N3	ADE	35	1.298	2.650	-23.515
ATOM	529	C4	ADE	35	2.442	1.912	-23.506
ATOM	530	C3'	ADE	35	5.931	5.310	-23.644
ATOM	531	H3'	ADE	35	6.971	5.464	-23.349
ATOM	532	C2'	ADE	35	5.289	4.142	-22.904
ATOM	533	H2A'	ADE	35	4.903	4.412	-21.922
ATOM	534	H2B'	ADE	35	6.037	3.357	-22.797
ATOM	535	O3'	ADE	35	5.191	6.506	-23.512
ATOM	536	P	POM	36	5.137	7.335	-22.137
ATOM	537	OA	POM	36	5.984	6.658	-21.131
ATOM	538	OB	POM	36	5.353	8.763	-22.451
ATOM	539	O5'	ADE	37	3.598	7.121	-21.727
ATOM	540	C5'	ADE	37	2.561	7.727	-22.475
ATOM	541	H5A'	ADE	37	2.792	8.781	-22.636
ATOM	542	H5B'	ADE	37	2.464	7.236	-23.444
ATOM	543	C4'	ADE	37	1.231	7.657	-21.717
ATOM	544	H4'	ADE	37	0.505	8.276	-22.248
ATOM	545	O1'	ADE	37	0.752	6.320	-21.680
ATOM	546	C1'	ADE	37	0.532	5.927	-20.337
ATOM	547	H1'	ADE	37	-0.500	6.092	-20.041
ATOM	548	N9	ADE	37	0.888	4.496	-20.210
ATOM	549	C8	ADE	37	2.153	3.966	-20.291
ATOM	550	H8	ADE	37	3.037	4.570	-20.434
ATOM	551	N7	ADE	37	2.210	2.673	-20.161
ATOM	552	C5	ADE	37	0.875	2.319	-20.025
ATOM	553	C6	ADE	37	0.267	1.070	-19.870
ATOM	554	N6	ADE	37	1.030	-0.012	-19.777
ATOM	555	HN6A	ADE	37	0.639	-0.940	-19.736
ATOM	556	HN6B	ADE	37	2.029	0.127	-19.811
ATOM	557	N1	ADE	37	-1.073	0.971	-19.843
ATOM	558	C2	ADE	37	-1.784	2.098	-19.944
ATOM	559	H2	ADE	37	-2.867	1.969	-19.917
ATOM	560	N3	ADE	37	-1.325	3.353	-20.059
ATOM	561	C4	ADE	37	0.041	3.402	-20.099
ATOM	562	C3'	ADE	37	1.398	8.160	-20.278
ATOM	563	H3'	ADE	37	2.334	8.709	-20.152
ATOM	564	C2'	ADE	37	1.404	6.854	-19.488
ATOM	565	H2A'	ADE	37	1.010	6.990	-18.486
ATOM	566	H2B'	ADE	37	2.434	6.506	-19.433
ATOM	567	O3'	ADE	37	0.313	9.006	-19.954
ATOM	568	P	POM	38	0.268	9.862	-18.586
ATOM	569	OA	POM	38	1.539	9.676	-17.852
ATOM	570	OB	POM	38	-0.215	11.225	-18.902
ATOM	571	O5'	THY	39	-0.887	9.087	-17.791
ATOM	572	C5'	THY	39	-2.218	9.140	-18.262
ATOM	573	H5A'	THY	39	-2.665	10.105	-18.021
ATOM	574	H5B'	THY	39	-2.226	9.016	-19.344
ATOM	575	C4'	THY	39	-3.045	8.005	-17.661
ATOM	576	H4'	THY	39	-3.988	7.970	-18.202
ATOM	577	O1'	THY	39	-2.372	6.769	-17.831
ATOM	578	C1'	THY	39	-2.694	5.941	-16.735
ATOM	579	H1'	THY	39	-3.696	5.536	-16.859

ATOM	580	N1	THY	39	-1.645	4.890	-16.609
ATOM	581	C6	THY	39	-0.323	5.263	-16.602
ATOM	582	H6	THY	39	-0.087	6.317	-16.617
ATOM	583	C5	THY	39	0.677	4.350	-16.590
ATOM	584	C7	THY	39	2.128	4.798	-16.579
ATOM	585	H7A	THY	39	2.669	4.298	-17.383
ATOM	586	H7B	THY	39	2.223	5.877	-16.706
ATOM	587	H7C	THY	39	2.579	4.513	-15.628
ATOM	588	C4	THY	39	0.376	2.934	-16.581
ATOM	589	O4	THY	39	1.216	2.043	-16.577
ATOM	590	N3	THY	39	-0.968	2.619	-16.597
ATOM	591	H3	THY	39	-1.214	1.631	-16.581
ATOM	592	C2	THY	39	-2.006	3.539	-16.605
ATOM	593	O2	THY	39	-3.168	3.141	-16.577
ATOM	594	C3'	THY	39	-3.353	8.174	-16.169
ATOM	595	H3'	THY	39	-2.894	9.081	-15.771
ATOM	596	C2'	THY	39	-2.717	6.922	-15.564
ATOM	597	H2A'	THY	39	-3.294	6.544	-14.728
ATOM	598	H2B'	THY	39	-1.710	7.180	-15.240
ATOM	599	O3'	THY	39	-4.764	8.214	-16.020
ATOM	600	P	POM	40	-5.488	8.533	-14.615
ATOM	601	OA	POM	40	-4.503	9.164	-13.709
ATOM	602	OB	POM	40	-6.767	9.218	-14.908
ATOM	603	O5'	THY	41	-5.820	7.062	-14.058
ATOM	604	C5'	THY	41	-6.883	6.307	-14.611
ATOM	605	H5A'	THY	41	-7.841	6.689	-14.258
ATOM	606	H5B'	THY	41	-6.849	6.384	-15.699
ATOM	607	C4'	THY	41	-6.739	4.827	-14.252
ATOM	608	H4'	THY	41	-7.470	4.255	-14.818
ATOM	609	O1'	THY	41	-5.437	4.393	-14.593
ATOM	610	C1'	THY	41	-5.156	3.221	-13.859
ATOM	611	H1'	THY	41	-5.419	2.373	-14.474
ATOM	612	N1	THY	41	-3.720	3.170	-13.501
ATOM	613	C6	THY	41	-3.068	4.323	-13.151
ATOM	614	H6	THY	41	-3.655	5.216	-12.989
ATOM	615	C5	THY	41	-1.721	4.359	-13.022
ATOM	616	C7	THY	41	-1.017	5.658	-12.680
ATOM	617	H7A	THY	41	-0.525	5.552	-11.713
ATOM	618	H7B	THY	41	-0.261	5.867	-13.438
ATOM	619	H7C	THY	41	-1.715	6.496	-12.637
ATOM	620	C4	THY	41	-0.934	3.162	-13.237
ATOM	621	O4	THY	41	0.292	3.123	-13.235
ATOM	622	N3	THY	41	-1.667	2.018	-13.482
ATOM	623	H3	THY	41	-1.170	1.130	-13.544
ATOM	624	C2	THY	41	-3.040	1.959	-13.621
ATOM	625	O2	THY	41	-3.599	0.882	-13.821
ATOM	626	C3'	THY	41	-6.926	4.494	-12.771
ATOM	627	H3'	THY	41	-6.526	5.306	-12.162
ATOM	628	C2'	THY	41	-6.056	3.247	-12.628
ATOM	629	H2A'	THY	41	-6.656	2.339	-12.623
ATOM	630	H2B'	THY	41	-5.483	3.324	-11.713
ATOM	631	O3'	THY	41	-8.285	4.223	-12.469
ATOM	632	P	POM	42	-8.796	3.963	-10.956

ATOM	633	OA	POM	42	-8.035	4.849	-10.049
ATOM	634	OB	POM	42	-10.275	4.016	-10.966
ATOM	635	O5'	THY	43	-8.364	2.445	-10.631
ATOM	636	C5'	THY	43	-8.989	1.355	-11.282
ATOM	637	H5A'	THY	43	-10.051	1.327	-11.037
ATOM	638	H5B'	THY	43	-8.881	1.483	-12.359
ATOM	639	C4'	THY	43	-8.340	0.022	-10.887
ATOM	640	H4'	THY	43	-8.754	-0.753	-11.532
ATOM	641	O1'	THY	43	-6.939	0.108	-11.099
ATOM	642	C1'	THY	43	-6.260	-0.397	-9.967
ATOM	643	H1'	THY	43	-6.138	-1.473	-10.073
ATOM	644	N1	THY	43	-4.964	0.325	-9.849
ATOM	645	C6	THY	43	-4.964	1.692	-9.700
ATOM	646	H6	THY	43	-5.902	2.207	-9.556
ATOM	647	C5	THY	43	-3.827	2.420	-9.796
ATOM	648	C7	THY	43	-3.861	3.923	-9.576
ATOM	649	H7A	THY	43	-3.480	4.137	-8.577
ATOM	650	H7B	THY	43	-4.874	4.321	-9.661
ATOM	651	H7C	THY	43	-3.223	4.420	-10.306
ATOM	652	C4	THY	43	-2.568	1.773	-10.091
ATOM	653	O4	THY	43	-1.516	2.365	-10.311
ATOM	654	N3	THY	43	-2.622	0.394	-10.157
ATOM	655	H3	THY	43	-1.745	-0.106	-10.295
ATOM	656	C2	THY	43	-3.764	-0.373	-10.009
ATOM	657	O2	THY	43	-3.676	-1.601	-10.019
ATOM	658	C3'	THY	43	-8.581	-0.376	-9.424
ATOM	659	H3'	THY	43	-9.340	0.257	-8.961
ATOM	660	C2'	THY	43	-7.210	-0.153	-8.796
ATOM	661	H2A'	THY	43	-7.030	-0.850	-7.987
ATOM	662	H2B'	THY	43	-7.171	0.867	-8.421
ATOM	663	O3'	THY	43	-8.972	-1.739	-9.373
ATOM	664	P	POM	44	-9.434	-2.460	-8.002
ATOM	665	OA	POM	44	-9.807	-1.419	-7.020
ATOM	666	OB	POM	44	-10.403	-3.522	-8.354
ATOM	667	O5'	GUA	45	-8.081	-3.174	-7.491
ATOM	668	C5'	GUA	45	-7.592	-4.310	-8.171
ATOM	669	H5A'	GUA	45	-8.326	-5.115	-8.106
ATOM	670	H5B'	GUA	45	-7.454	-4.038	-9.213
ATOM	671	C4'	GUA	45	-6.254	-4.825	-7.628
ATOM	672	H4'	GUA	45	-6.004	-5.729	-8.184
ATOM	673	O1'	GUA	45	-5.231	-3.860	-7.831
ATOM	674	C1'	GUA	45	-4.533	-3.684	-6.614
ATOM	675	H1'	GUA	45	-3.751	-4.441	-6.530
ATOM	676	N9	GUA	45	-3.948	-2.324	-6.579
ATOM	677	C8	GUA	45	-4.613	-1.127	-6.543
ATOM	678	H8	GUA	45	-5.672	-1.051	-6.364
ATOM	679	N7	GUA	45	-3.861	-0.085	-6.756
ATOM	680	C5	GUA	45	-2.589	-0.625	-6.900
ATOM	681	C6	GUA	45	-1.343	0.020	-7.149
ATOM	682	O6	GUA	45	-1.147	1.198	-7.432
ATOM	683	N1	GUA	45	-0.262	-0.840	-7.051
ATOM	684	H1	GUA	45	0.657	-0.403	-7.129
ATOM	685	C2	GUA	45	-0.375	-2.188	-6.823

ATOM	686	N2	GUA	45	0.744	-2.896	-6.715
ATOM	687	HN2A	GUA	45	1.646	-2.441	-6.792
ATOM	688	HN2B	GUA	45	0.687	-3.811	-6.296
ATOM	689	N3	GUA	45	-1.545	-2.828	-6.689
ATOM	690	C4	GUA	45	-2.618	-1.988	-6.727
ATOM	691	C3'	GUA	45	-6.295	-5.160	-6.133
ATOM	692	H3'	GUA	45	-7.315	-5.282	-5.765
ATOM	693	C2'	GUA	45	-5.598	-3.936	-5.550
ATOM	694	H2A'	GUA	45	-5.191	-4.139	-4.565
ATOM	695	H2B'	GUA	45	-6.315	-3.118	-5.501
ATOM	696	O3'	GUA	45	-5.532	-6.338	-5.934
ATOM	697	P	POM	46	-5.510	-7.131	-4.532
ATOM	698	OA	POM	46	-6.129	-6.287	-3.488
ATOM	699	OB	POM	46	-5.993	-8.508	-4.766
ATOM	700	O5'	CYT	47	-3.932	-7.188	-4.242
ATOM	701	C5'	CYT	47	-3.087	-8.019	-5.009
ATOM	702	H5A'	CYT	47	-3.332	-9.067	-4.828
ATOM	703	H5B'	CYT	47	-3.230	-7.804	-6.069
ATOM	704	C4'	CYT	47	-1.619	-7.766	-4.652
ATOM	705	H4'	CYT	47	-1.006	-8.392	-5.300
ATOM	706	O1'	CYT	47	-1.314	-6.393	-4.872
ATOM	707	C1'	CYT	47	-0.841	-5.816	-3.664
ATOM	708	H1'	CYT	47	0.247	-5.880	-3.688
ATOM	709	N1	CYT	47	-1.327	-4.407	-3.530
ATOM	710	C6	CYT	47	-2.659	-4.135	-3.339
ATOM	711	H6	CYT	47	-3.365	-4.943	-3.234
ATOM	712	C5	CYT	47	-3.125	-2.866	-3.301
ATOM	713	H5	CYT	47	-4.176	-2.692	-3.126
ATOM	714	C4	CYT	47	-2.178	-1.817	-3.485
ATOM	715	N4	CYT	47	-2.617	-0.571	-3.622
ATOM	716	HN4A	CYT	47	-1.972	0.171	-3.855
ATOM	717	HN4B	CYT	47	-3.604	-0.378	-3.584
ATOM	718	N3	CYT	47	-0.877	-2.063	-3.676
ATOM	719	C2	CYT	47	-0.426	-3.353	-3.682
ATOM	720	O2	CYT	47	0.775	-3.555	-3.857
ATOM	721	C3'	CYT	47	-1.302	-8.113	-3.193
ATOM	722	H3'	CYT	47	-2.067	-8.766	-2.769
ATOM	723	C2'	CYT	47	-1.301	-6.740	-2.534
ATOM	724	H2A'	CYT	47	-0.623	-6.711	-1.688
ATOM	725	H2B'	CYT	47	-2.315	-6.531	-2.197
ATOM	726	O3'	CYT	47	-0.031	-8.739	-3.139
ATOM	727	P	POM	48	0.533	-9.418	-1.786
ATOM	728	OA	POM	48	-0.591	-9.620	-0.847
ATOM	729	OB	POM	48	1.394	-10.559	-2.164
ATOM	730	O5'	GUA	49	1.477	-8.264	-1.185
ATOM	731	C5'	GUA	49	2.754	-8.020	-1.738
ATOM	732	H5A'	GUA	49	3.389	-8.895	-1.593
ATOM	733	H5B'	GUA	49	2.663	-7.820	-2.807
ATOM	734	C4'	GUA	49	3.401	-6.812	-1.058
ATOM	735	H4'	GUA	49	4.401	-6.673	-1.471
ATOM	736	O1'	GUA	49	2.617	-5.660	-1.321
ATOM	737	C1'	GUA	49	2.463	-4.950	-0.112
ATOM	738	H1'	GUA	49	3.356	-4.345	0.055

ATOM	739	N9	GUA	49	1.260	-4.090	-0.172
ATOM	740	C8	GUA	49	-0.063	-4.447	-0.111
ATOM	741	H8	GUA	49	-0.398	-5.454	0.077
ATOM	742	N7	GUA	49	-0.894	-3.460	-0.296
ATOM	743	C5	GUA	49	-0.063	-2.358	-0.465
ATOM	744	C6	GUA	49	-0.383	-0.984	-0.671
ATOM	745	O6	GUA	49	-1.494	-0.472	-0.782
ATOM	746	N1	GUA	49	0.741	-0.178	-0.729
ATOM	747	H1	GUA	49	0.554	0.812	-0.878
ATOM	748	C2	GUA	49	2.031	-0.632	-0.609
ATOM	749	N2	GUA	49	3.017	0.257	-0.649
ATOM	750	HN2A	GUA	49	2.824	1.247	-0.756
ATOM	751	HN2B	GUA	49	3.968	-0.072	-0.619
ATOM	752	N3	GUA	49	2.345	-1.919	-0.433
ATOM	753	C4	GUA	49	1.256	-2.730	-0.371
ATOM	754	C3'	GUA	49	3.484	-6.974	0.468
ATOM	755	H3'	GUA	49	3.311	-8.001	0.794
ATOM	756	C2'	GUA	49	2.397	-6.030	0.965
ATOM	757	H2A'	GUA	49	2.597	-5.643	1.965
ATOM	758	H2B'	GUA	49	1.444	-6.557	0.938
ATOM	759	O3'	GUA	49	4.739	-6.528	0.939
ATOM	760	H	HE	50	4.742	-6.582	1.898
ATOM	761	O1	DIS	51	-4.907	-6.054	-13.789
ATOM	762	C1	DIS	51	-4.140	-5.126	-14.033
ATOM	763	HF	DIS	51	-3.158	-5.151	-13.581
ATOM	764	N1	DIS	51	-4.433	-4.085	-14.824
ATOM	765	HN1	DIS	51	-3.674	-3.435	-14.999
ATOM	766	C2	DIS	51	-5.580	-3.758	-15.601
ATOM	767	C3	DIS	51	-5.814	-2.690	-16.478
ATOM	768	H3	DIS	51	-5.122	-1.922	-16.756
ATOM	769	C5	DIS	51	-6.753	-4.470	-15.485
ATOM	770	H5	DIS	51	-6.935	-5.333	-14.864
ATOM	771	N2	DIS	51	-7.702	-3.856	-16.274
ATOM	772	C6	DIS	51	-9.116	-4.301	-16.412
ATOM	773	HM1	DIS	51	-9.382	-4.656	-17.407
ATOM	774	HM2	DIS	51	-9.386	-5.130	-15.756
ATOM	775	HM3	DIS	51	-9.860	-3.538	-16.189
ATOM	776	C4	DIS	51	-7.121	-2.763	-16.899
ATOM	777	C7	DIS	51	-7.749	-1.751	-17.828
ATOM	778	O2	DIS	51	-8.966	-1.780	-17.999
ATOM	779	N3	DIS	51	-6.929	-0.831	-18.381
ATOM	780	HN3	DIS	51	-5.937	-0.971	-18.245
ATOM	781	C8	DIS	51	-7.185	0.313	-19.190
ATOM	782	C9	DIS	51	-6.341	1.244	-19.847
ATOM	783	H9	DIS	51	-5.258	1.188	-19.965
ATOM	784	C11	DIS	51	-8.458	0.834	-19.171
ATOM	785	H11	DIS	51	-9.323	0.443	-18.660
ATOM	786	N4	DIS	51	-8.466	1.974	-19.929
ATOM	787	C12	DIS	51	-9.678	2.793	-20.208
ATOM	788	HM4	DIS	51	-9.588	3.847	-19.947
ATOM	789	HM5	DIS	51	-9.989	2.791	-21.252
ATOM	790	HM6	DIS	51	-10.567	2.469	-19.667
ATOM	791	C10	DIS	51	-7.185	2.198	-20.404

ATOM	792	C13	DIS	51	-6.780	3.317	-21.335
ATOM	793	O3	DIS	51	-7.642	4.131	-21.662
ATOM	794	N5	DIS	51	-5.545	3.313	-21.868
ATOM	795	HN5	DIS	51	-4.937	2.548	-21.608
ATOM	796	C14	DIS	51	-4.954	4.190	-22.825
ATOM	797	C15	DIS	51	-3.728	4.156	-23.521
ATOM	798	H15	DIS	51	-3.029	3.338	-23.559
ATOM	799	C17	DIS	51	-5.454	5.471	-22.931
ATOM	800	H17	DIS	51	-6.329	5.880	-22.454
ATOM	801	N6	DIS	51	-4.631	6.193	-23.757
ATOM	802	C18	DIS	51	-4.871	7.603	-24.180
ATOM	803	HM7	DIS	51	-4.827	7.763	-25.256
ATOM	804	HM8	DIS	51	-5.849	7.992	-23.895
ATOM	805	HM9	DIS	51	-4.172	8.330	-23.767
ATOM	806	C16	DIS	51	-3.525	5.418	-24.052
ATOM	807	C19	DIS	51	-2.257	5.894	-24.713
ATOM	808	O4	DIS	51	-2.026	7.102	-24.729
ATOM	809	N7	DIS	51	-1.358	5.009	-25.170
ATOM	810	HN7	DIS	51	-1.585	4.022	-25.217
ATOM	811	C20	DIS	51	-0.140	5.514	-25.785
ATOM	812	HC1	DIS	51	-0.468	6.181	-26.546
ATOM	813	HC2	DIS	51	0.517	5.959	-25.049
ATOM	814	C21	DIS	51	0.662	4.526	-26.593
ATOM	815	HC3	DIS	51	1.145	3.894	-25.852
ATOM	816	HC4	DIS	51	-0.048	4.027	-27.252
ATOM	817	C22	DIS	51	1.762	5.078	-27.481
ATOM	818	N8	DIS	51	2.750	4.256	-27.863
ATOM	819	HNC	DIS	51	3.459	4.558	-28.514
ATOM	820	HND	DIS	51	2.751	3.293	-27.545
ATOM	821	N9	DIS	51	1.707	6.331	-27.966
ATOM	822	HNA	DIS	51	2.410	6.674	-28.603
ATOM	823	HNB	DIS	51	0.898	6.911	-27.786
ATOM	824	O1	DIS	52	-3.247	7.704	-21.346
ATOM	825	C1	DIS	52	-2.732	6.593	-21.251
ATOM	826	HF	DIS	52	-1.842	6.414	-21.832
ATOM	827	N1	DIS	52	-3.216	5.577	-20.519
ATOM	828	HN1	DIS	52	-2.638	4.742	-20.499
ATOM	829	C2	DIS	52	-4.390	5.461	-19.721
ATOM	830	C3	DIS	52	-4.884	4.407	-18.933
ATOM	831	H3	DIS	52	-4.408	3.453	-18.773
ATOM	832	C5	DIS	52	-5.366	6.431	-19.794
ATOM	833	H5	DIS	52	-5.350	7.350	-20.355
ATOM	834	N2	DIS	52	-6.410	6.050	-18.992
ATOM	835	C6	DIS	52	-7.663	6.829	-18.789
ATOM	836	HM1	DIS	52	-7.954	6.963	-17.747
ATOM	837	HM2	DIS	52	-7.628	7.845	-19.182
ATOM	838	HM3	DIS	52	-8.542	6.393	-19.264
ATOM	839	C4	DIS	52	-6.128	4.801	-18.473
ATOM	840	C7	DIS	52	-7.062	3.952	-17.657
ATOM	841	O2	DIS	52	-8.251	4.261	-17.655
ATOM	842	N3	DIS	52	-6.568	2.863	-17.039
ATOM	843	HN3	DIS	52	-5.568	2.733	-17.115
ATOM	844	C8	DIS	52	-7.222	1.838	-16.287

ATOM	845	C9	DIS	52	-6.766	0.635	-15.698
ATOM	846	H9	DIS	52	-5.754	0.217	-15.773
ATOM	847	C11	DIS	52	-8.554	2.001	-15.959
ATOM	848	H11	DIS	52	-9.218	2.814	-16.197
ATOM	849	N4	DIS	52	-8.960	0.914	-15.241
ATOM	850	C12	DIS	52	-10.348	0.676	-14.753
ATOM	851	HM4	DIS	52	-10.913	-0.035	-15.358
ATOM	852	HM5	DIS	52	-10.423	0.284	-13.739
ATOM	853	HM6	DIS	52	-10.976	1.567	-14.734
ATOM	854	C10	DIS	52	-7.871	0.093	-15.049
ATOM	855	C13	DIS	52	-7.918	-1.206	-14.304
ATOM	856	O3	DIS	52	-8.969	-1.844	-14.325
ATOM	857	N5	DIS	52	-6.862	-1.528	-13.549
ATOM	858	HN5	DIS	52	-6.080	-0.892	-13.599
ATOM	859	C14	DIS	52	-6.642	-2.632	-12.680
ATOM	860	C15	DIS	52	-5.478	-3.112	-12.059
ATOM	861	H15	DIS	52	-4.493	-2.680	-12.146
ATOM	862	C17	DIS	52	-7.668	-3.509	-12.399
ATOM	863	H17	DIS	52	-8.700	-3.453	-12.704
ATOM	864	N6	DIS	52	-7.148	-4.568	-11.700
ATOM	865	C18	DIS	52	-7.914	-5.788	-11.315
ATOM	866	HM7	DIS	52	-7.686	-6.192	-10.329
ATOM	867	HM8	DIS	52	-8.995	-5.645	-11.291
ATOM	868	HM9	DIS	52	-7.772	-6.631	-11.991
ATOM	869	C16	DIS	52	-5.809	-4.312	-11.457
ATOM	870	C19	DIS	52	-4.829	-5.233	-10.784
ATOM	871	O4	DIS	52	-5.127	-6.418	-10.643
ATOM	872	N7	DIS	52	-3.652	-4.750	-10.362
ATOM	873	HN7	DIS	52	-3.476	-3.752	-10.396
ATOM	874	C20	DIS	52	-2.792	-5.624	-9.580
ATOM	875	HC1	DIS	52	-3.254	-5.742	-8.611
ATOM	876	HC2	DIS	52	-2.658	-6.559	-10.108
ATOM	877	C21	DIS	52	-1.396	-5.096	-9.329
ATOM	878	HC3	DIS	52	-0.908	-5.003	-10.299
ATOM	879	HC4	DIS	52	-1.515	-4.148	-8.816
ATOM	880	C22	DIS	52	-0.506	-5.954	-8.453
ATOM	881	N8	DIS	52	0.782	-5.611	-8.305
ATOM	882	HNC	DIS	52	1.418	-6.165	-7.750
ATOM	883	HND	DIS	52	1.127	-4.787	-8.784
ATOM	884	N9	DIS	52	-0.992	-7.030	-7.815
ATOM	885	HNA	DIS	52	-0.415	-7.548	-7.169
ATOM	886	HNB	DIS	52	-1.972	-7.267	-7.885

References

- Abragam, A. (1961) *Principles of Nuclear Magnetism*, Chapter 1, Oxford, New York, NY.
- Anderson, J. E., Ptashne, M. & Harrison, S. C. (1987) *Nature (London)* 326, 846-852.
- Behling, R. W. & Kearns, D. R. (1986) *Biochemistry* 25, 3335-3346.
- Berman, H. M., Neidle, S., Zimmer, C., & Thrum, H. (1979) *Biochim. Biophys. Acta* 561, 124-131.
- Bremer, J., Mendez, G. L. & Moore, W. J. (1984) *J. Am. Chem. Soc.* 106, 4691-4696.
- Breslauer, K. J., Remeta, D. P., Chou, W.-Y., Ferranti, R., Curry, J., Zaunczkowski, D., Snyder, J. G. & Marky, L. A. (1987) *Proc. Natl. Acad. Sci. U.S.A.* 84, 8922-8926.
- Bugg, C. E., Thomas, J. M., Sundaralingam, M. & Rao, S. J. (1971) *Biopolymers* 10, 175-219.
- Caldwell, J. & Kollman, P. (1986) *Biopolymers* 25, 249-266.
- Carrington, A. & McLachlan, A. D. (1967) *Introduction to Magnetic Resonance*, Chapter 12, Harper & Row, New York, NY.
- Carrondo, M. A. A. F. de C. T., Coll, M., Aymami, J., Wang, A. H.-J., van der Marel, G. A., van Boom, J. H. & Rich, A. (1989) *Biochemistry* 28, 7849-7859.
- Celda, B., Widmer, H., Leupin, W., Chazin, W., Denny, W. A. & Wüthrich, K. (1989) *Biochemistry* 28, 1462-1471.
- Chandrakumar, N. & Subramanian, S. (1987) *Modern Techniques in High Resolution FT-NMR*, Springer-Verlag, New York, NY.

- Chandrasekaran, R. & Arnott, S. (1989) in *Landolt-Börnstein Numerical Data and Functional Relationships*, (Saenger, W. Ed.) Vol VII/16, pp. 30-170, Springer-Verlag, New York, NY.
- Chou, S.-H., Hare, D. R., Wemmer, D. E. & Reid, B. R. (1983) *Biochemistry* 22, 3037-3041.
- Coll, M., Frederick, C. A., Wang, A. H.-J. & Rich, A. (1987) *Proc. Natl. Acad. Sci. U.S.A.* 84, 8385-8389.
- Coll, M., Aymami, J., van der Marel, G. A., van Boom, J. H., Rich, A. & Wang, A. H.-J. (1989) *Biochemistry* 28, 310-320.
- Crick, F. H. C. & Watson, J. D. (1954) *Proc. R. Soc.* 223A, 80-96.
- Dewar, M. J. S. & Thiel, W. (1977) *J. Am. Chem. Soc.* 99, 4899-4907.
- Dickerson, R. E., Bansal, M., Calladine, C. R., Diekmann, S., Hunter, W. N., Kennard, O., Lavery, R., Nelson, H. C. M., Olson, W.K., Saenger, W., Shakked, Z., Sklenar, H., Soumpasis, D. M., Tung, C.-S., von Kitzing, E., Wang, A. H.-J. & Zhurkin, V. B. (1989) *J. Mol. Biol.* 205, 787-791.
- Dickerson, R. E. & Drew, H. R. (1981) *J. Mol. Biol.* 149, 761-786.
- Dimarco, A., Ghione, M., Migliacci, A., Morviloe, E. & Sanfilippo, A. (1963) *Giorn. Micorbiol.* 11, 87.
- Drew, H. R., Wing, R. M., Takano, T., Broka, C., Tanaka, S., Itakura, K. & Dickerson, R. E. (1981) *Proc. Natl. Acad. Sci. U.S.A.* 78, 2179-2183.
- Drobny, G., Pines, A., Sinton, S., Weitekamp, D. & Wemmer, D. E. (1979) *Faraday Div. Chem. Soc. Symp.* 13, 49.
- Emsley, J. W., Feeney, J. & Sutcliffe, L. H. (1965a) *High Resolution Nuclear Magnetic Resonance Spectroscopy*, Chapter 3, Pergamon Press, New York, NY.
- Emsley, J. W., Feeney, J. & Sutcliffe, L. H. (1965b) *High Resolution Nuclear Magnetic Resonance Spectroscopy*, Chapter 2, Pergamon Press, New York, NY.

- Ernst, R. R., Bodenhausen, G. & Wokaer, A. (1987) *Principles of NMR in One and Two Dimensions*, Oxford, New York, NY.
- Farrar, T. C. & Becker, E. D. (1971) *Pulse and Fourier Transform NMR*, Academic Press, Orlando, Florida.
- Feigon, J., Leupin, W., Denny, W. A. & Kearns, D. R. (1983) *Biochemistry* 22, 5930-5942.
- Fish, L., Lane, M. J. & Vournakis, J. N. (1988) *Biochemistry* 27, 6026-6032.
- Forsen, S. & Hoffman, R. A. (1963) *J. Chem. Phys.* 39, 2892-2901.
- Fratini, A. V., Kopka, M. L., Drew, H. R. & Dickerson, R. E. (1982) *J. Biol. Chem.* 257, 14686-14707.
- Gao, X. & Patel, D. J. (1989) *Biochemistry* 28, 751-762.
- Hahn, F. E. (1975) in *Antibiotics III: Mechanism of Action of Antimicrobial and Antitumor Agents* (Corcoran, J. W. & Hahn, F. E. Eds.) pp. 79-100, Springer-Verlag, NY.
- Hare, D. R., Wemmer, D. E., Chou, S.-H., Drobny, G. & Reid, B. R. (1983) *J. Mol. Biol.* 171, 319-336.
- Hore, P. J. (1983) *J. Magn. Reson.* 55, 283-300.
- Jeener, J., Meier, B. H. Bachmann, P. & Ernst, R. R. (1979) *J. Chem. Phys.* 71, 4546-4553.
- Jeffrey, G. A. & Maluszynska, H. (1982) *Int. J. Biol. Macromol.* 4, 173-185.
- Kalk, A. & Berendsen, H. J. C. (1976) *J. Magn. Reson.* 24, 343-366.
- Keepers, J. W. & James, T. L. (1984) *J. Magn. Reson.* 57, 404-426.
- Kintanar, A., Klevit, R. E. & Reid, B. R. (1987) *Nucleic Acids Res.* 15, 5845-5862.
- Klevit, R. E., Wemmer, D. E. & Reid, B. R. (1986) *Biochemistry* 25, 3296-3303.
- Kollman, P., Keepers, J. W. & Weiner, P. (1982) *Biopolymers* 21, 2345-2376.

- Kopka, M. L., Yoon, C., Goodsell, D., Pjura, P. & Dickerson, R. E. (1985a) *Proc. Natl. Acad. Sci. U.S.A.* **82**, 1276-1380.
- Kopka, M. L., Yoon, C., Goodsell, D., Pjura, P. & Dickerson, R. E. (1985b) *J. Mol. Biol.* **183**, 553-563.
- Kopka, M. L., Pjura, P., Yoon, C., Goodsell, D. & Dickerson, R. E. (1985c) in *Structure and Motion: Membranes, Nucleic Acids & Proteins* (Clementi, E., Corongiu, G., Sarma, M. H. & Sarma, R. H., Eds.) pp. 461-483, Adenine, Guilderland, NY.
- Krey, A. K., Allison, R. G. & Hahn, F. E. (1973) *FEBS Lett.* **29**, 58-62.
- Kumar, A., Wagner, G., Ernst, R. R. & Wüthrich, K. (1981) *J. Am. Chem. Soc.* **103**, 3654-3658.
- Lavery, R., Pullman, A. & Pullman, B. (1982) *Theor. Chem. Acta* **62**, 93-106.
- Lavery, R., Zakrzewska, K. & Pullman, B. (1986) *J. Biomol. Struct. Dyn.* **3**, 1155-1170.
- Lee, M., Chang, D.-K., Hartley, J. A., Pon, R. T., Krowicki, K. & Lown, J. W. (1988) *Biochemistry* **27**, 445-455.
- Lee, M., Shea, R. G., Hartley, S. A., Kissinger, J., Pon, R. T., Vesnaver, G., Breslauer, K. J., Dabrowick, J. C. & Lown, J. W. (1989) *J. Am. Chem. Soc.* **111**, 345-354.
- Letsinger, R. L. & Lunsford, W. B. (1976) *J. Am. Chem. Soc.* **98**, 3655-3661.
- Leupin, W., Chazin, W. J., Hyberts, S., Denny, W. A. & Wüthrich, K. (1986) *Biochemistry* **25**, 5902-5910.
- Macura, S. & Ernst R. R. (1980) *Molecular Physics* **41**, 95-117.
- Macura, S., Huang, Y., Suter, D., Ernst, R. R. (1981) *J. Magn. Reson.* **43**, 259-281.
- Marky, L. A., Blumenfeld, K. S. & Breslauer, K. J. (1983) *Nucleic Acids Res.* **11**, 2857-2870.
- Matteucci, M. D. & Caruthers, M. H. (1981) *J. Am. Chem. Soc.* **103**, 3185-3191.

- McClarín, J. A., Frederick, C. A., Wang, B.-C., Greene, P., Boyer, H. W., Grable, J. & Rosenberg, J. M. (1986) *Science* 234, 1526-1541.
- Nelson, H. C. M., Finch, J. T., Luisi, B. F., Klug, A. (1987) *Nature (London)* 330, 221-226.
- Olejniczak, E. T., Gampe Jr., R. T. & Fesik, S. W. (1986) *J. Magn. Reson.* 67, 28-41.
- Otwinowski, Z., Schevitz, R. W., Zhang, R.-G., Lawson, C. L., Joachimiak, A., Marmorstein, R. Q., Luisi, B. R. & Sigler, P. B. (1988) *Nature (London)* 335, 321-329.
- Pardi, A., Morden, D. M., Patel, D. J. & Tinoco, I. (1983) *J. Am. Chem. Soc.* 105, 1107-1113.
- Patel, D. J. (1982) *Proc. Natl. Acad. Sci. U.S.A.* 79, 6424-6428.
- Patel, D. J. & Shapiro, L. (1985) *Biochimie* 67, 887-915.
- Patel, D. J. & Shapiro, L. (1986) *J. Biol. Chem.* 261, 1230-1239.
- Patel, D. J., Shapiro, L. & Hare, D. (1987) *Annu. Rev. Biophys. Biophys. Chem.* 16, 423-454.
- Patel, D. J., Shapiro, L., Kozłowski, S. A., Gaffney, B. L. & Jones, R. A. (1986) *J. Mol. Biol.* 188, 677-692.
- Perrin, C. L. & Gipe, R. K. (1984) *J. Am. Chem. Soc.* 106, 4036-4038.
- Pjura, P. E., Grzeskowiak, K. & Dickerson, R. E. (1987) *J. Mol. Biol.* 197, 257-271.
- Portugal, J. & Waring, M. J. (1987) *Eur. J. Biochem.* 167, 281-289.
- Puschendorf, B., Petersen, E., Wolf, H., Werchau, H. & Grunicke, H. (1971) *Biochim. Biophys. Res. Commun.* 43, 617.
- Saenger, W. (1984) *Principles of Nucleic Acid Structure* (Cantor, C. ed.) Chapter 9, Springer-Verlag, New York, NY.

- Sakurai, J. J. (1985) *Modern Quantum Mechanics* (Tuan, S. F. Ed.), p. 178, Benjamin/Cummings, Menlo Park, CA.
- Sarma, M. H., Gupta, G. & Sarma, R. H. (1985) *J. Biomol. Struct. Dyn.* 2, 1085-1095.
- Scheek, R. M., Boelens, R., Russo, W., van Boom, J. H. & Kaptein, R. (1984) *Biochemistry* 23, 1271-1376.
- Schultz, P. G. & Dervan, P. B. (1984) *J. Biomol. Struct. Dyn.* 1, 1133-1147.
- Schultz, P. G. & Dervan, P. B. (1983) *J. Am. Chem. Soc.* 105, 7748-7750.
- Scott, E. V., Zon, G., Marzilli, L. G. & Wilson, W. D. (1988) *Biochemistry* 27, 7940-7951.
- Slichter, C. P. (1978a) *Principles of Magnetic Resonance*, Chapter 1, Springer-Verlag, New York, NY.
- Slichter, C. P. (1978b) *Principles of Magnetic Resonance*, Chapter 3, Springer-Verlag, New York, NY.
- Taylor, J. S., Schultz, P. G. & Dervan, P. B. (1984) *Tetrahedron* 40, 457-465.
- Taylor, R., Kennard, O. & Werner, V. W. (1984) *J. Am. Chem. Soc.* 106, 244-248.
- Teng, M.-K., Usman, N., Frederick, C. A. & Wang, A. H.-J. (1988) *Nucleic Acids Res.* 16, 2671-2690.
- Wang, A. H.-J., Cottens, S., Dervan, P. B., Yesinowski, J. P., van der Marel, G. A. & van Boom, J. H. (1989) *J. Biomolec. Struct. Dyn.* 7, 101-117.
- Wang, A. H.-J., Quigley, G. J., Kolpak, F. J., Crawford, J. L., van Boom, J. H., van der Marel, G. & Rich, A. (1979) *Nature (London)* 282, 680-686.
- Ward, B., Reh fuss, R., Goodisman, J. & Dabrowiak, J. C. (1988) *Biochemistry* 27, 1198-1205.
- Warshaw, M. & Cantor, C. (1970) *Biopolymers* 9, 1079-1103.

- Weiner, S. J., Kollman, P. A., Case, D. A., Singh, U. C., Ghio, C., Alagona, G., Profeta, S. & Weiner, P. (1984) *J. Am. Chem. Soc.* 106, 765-784.
- Weiss, M. A., Patel, D. J., Sauer, R. T. & Karplus, M. (1984) *Nucleic Acids Res.* 12, 4035-4047.
- Yoon, C., Prive, G. G., Goodsell, D. S. & Dickerson, R. E. (1988) *Proc. Natl. Acad. Sci. USA* 85, 6332-6336.
- Zakrzewska, K., Lavery, R. & Pullman, B. (1983) *Nucleic Acids Res.* 11, 8825-8839.
- Zakrzewska, K., Lavery, R. & Pullman, B. (1987) *J. Biomol. Struct. Dyn.* 4, 833-843.
- Zimmer, C. & Wahnert, U. (1986) *Prog. Biophys. Mol. Biol.* 47, 31-112.
- Zimmer, C. Luck, G., Thrum, H. & Pitra, C. (1972) *Eur. J. Biochem.* 26, 81-89.

*LAWRENCE BERKELEY LABORATORY
TECHNICAL INFORMATION DEPARTMENT
UNIVERSITY OF CALIFORNIA
BERKELEY, CALIFORNIA 94720*