USING COMPUTATIONAL METHODS TO PREDICT NMR SPECTRAL DATA FOR POLYETHER COMPOUNDS

Krysten Scott Adams

A Thesis Submitted to the
University of North Carolina at Wilmington in Partial Fulfillment
Of the Requirements for the Degree of
Master of Science

Department of Chemistry

University of North Carolina at Wilmington

2005

Approved by

Advisory Committee

Pamela J. Seaton

Jeffrey L. C. Wright

Ned H. Martin
Chair

Accepted by

Dean, Graduate School

TABLE OF CONTENTS

ABSTRACT

Naturally occurring polyether ring compounds have been studied extensively over the past several years because of their importance as biologically active hemolytic and neurotoxic substances produced by various marine phytoplankton species. These substances contain varying numbers of ether rings of varying sizes. This research was performed to predict NMR spectra, including chemical shifts and coupling constants, of such polyether ring compounds. A literature search was performed to determine the frequency of ring size occurrence within the known toxins and each structure was broken down into three-ring segments. Models of each of these three-ring substructures were built in *Spartan* and a conformer search was done followed by a semi-empirical energy minimization on the lower energy conformers. Once the most energetically favorable conformers of each compound were determined, they were submitted to the North Carolina Supercomputing Center to perform a *Hartree-Fock* single point energy calculation, as well as a calculation of isotropic shielding values using the GIAO (Gauge including atomic orbital) method. From these values, chemical shifts were calculated. Energy values were used to determine the distribution among the various conformers by using a Boltzmann function. With this distribution data a prediction of chemical shifts for each ring structure was developed as the weighted average of the chemical shifts computed for each contributing conformer. Proton-proton coupling constants were also calculated using dihedral angles measured from the several minimum energy conformers and applying a modified Karplus equation to each one. Again, application of the Boltzmann function gave a weighted average coupling constant. These numbers were

used to produce a library of NMR spectral data, which should be useful for determining the structures of novel polyether toxins.

ACKNOWLEDGMENTS

I would like to think my advisor Dr. Ned H. Martin for all of his advice and guidance throughout this research. His ability to keep on track and keep hope even when things looked bleak was a real help. I would also like to thank my committee members, Dr. Pamela Seaton and Dr. Jeffrey Wright. I would also like to thank Dr. Andrea Bourdelais for her help with this research. I would like to thank the Department of Chemistry. I would also like to thank the North Carolina Supercomputing Center and the Microelectronics Center of North Carolina for the use of the computing facilities.

Thanks to the Inorganic group at UNCW for taking me under your wing and not letting me sit alone in front of a computer screen for hours on end.

I would like to thank my husband Mike for his constant love and support throughout this research and his ability to put up with me when times got tough. I would also like to thank my parents for their unconditional love and support and for listening to me talk about things that they don't understand and don't really care about.

LIST OF TABLES

LIST OF FIGURES

Figure

Page

INTRODUCTION

Polyether ring compounds are of great importance in organic chemistry and in biochemistry. There have been many studies of polyether ring compounds over the past several years [1-5]. This is primarily due to their importance as biologically active hemolytic and neurotoxic substances produced by various marine phytoplankton species, particularly dinoflagellates. Dinoflagellates are microscopic organisms that represent a high percentage of the ocean's plankton. They are single celled organisms that have characteristics of animals such as locomotion and food ingestion, and of plants, such as the ability to photosynthesize. These organisms live mostly near the surface of the ocean where sunlight can reach, but they have also been known to inhabit deeper environments. Dinoflagellates and phytoplankton in general are of particular importance to scientists because of their contribution to the food chain. They are commonly thought of as the lowest link in the chain upon which all other marine animals depend.

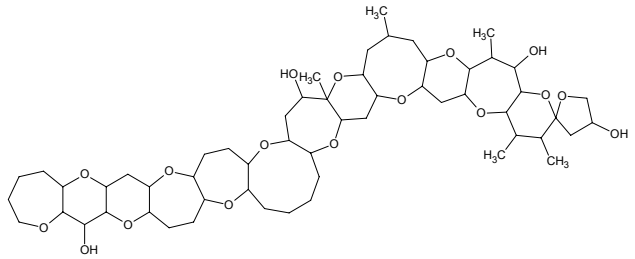
A small percentage of these phytoplankton produce toxins that can affect human health though the consumption of contaminated fish and shellfish. Over the past thirty years the incidence of these intoxications has increased and novel toxic polyethers are discovered continually. There are 60,000 reported intoxications caused by dinoflagellates per year which accounts for 20% of all disease caused by food consumption [6]. Not only do these toxins cause sickness in humans, but they also may lead to mass die-offs of fish and other animals dependent on fish for survival.

A dinoflagellate that has been of particular interest to scientists within the past few decades is *Karenia brevis*, formerly *Gymnodinium breve*. This organism

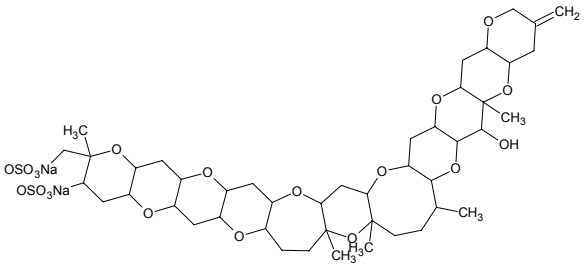
causes an environmental phenomenon known as red tide in the Gulf of Mexico. *Karenia brevis* has reddish-brown pigments. When conditions are right, the population of *Karenia brevis* explodes causing a bloom. This bloom causes the coastal waters to take on a red color, thus the term "red tide". This organism produces several neurotoxic substances known as brevetoxins.

Brevetoxins are lipid soluble polyethers with a molecular weight of around 900 g/mol. Three main brevetoxins are produced by *Karenia brevis*. They are PbTx-1, PbTx-2, and PbTx-3[7]. While brevetoxins are produced continuously by the organism, when there is a surge in the population, the brevetoxin levels become very high. Shellfish ingest this dinoflagellate leading to a buildup of brevetoxin in the tissues. While this does not seem to adversely affect the shellfish, it is very harmful to humans if they consume the contaminated shellfish, leading to a syndrome called neurotoxic shellfish poisoning (NSP). Symptoms of NSP in humans include nausea, tingling and numbness of the perioral area, loss of motor control, and severe muscular ache. Brevetoxins have also been shown to cause embryo toxicity and developmental abnormalities in fish. Morphological abnormalities have also been observed in fish such as lateral curvature of the spinal column, herniation of the brain, and malpositioned eyes [8].

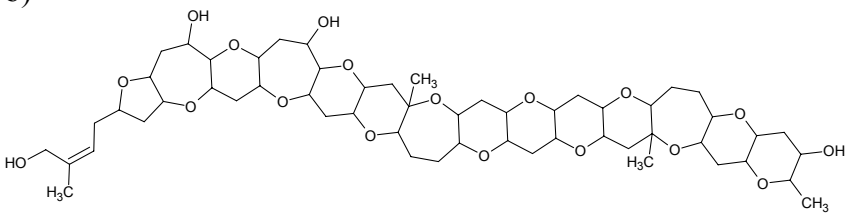
There are several toxins that are produced by dinoflagellates that cause illness. They are all polyether compounds that have a ladder frame structure (Figure 1). The main difference among these toxins is the size of the polyether rings. For example, Brevetoxin-PbTx1 (Figure 2) has three six-member rings at one terminal end, while ciguatoxin (Figure 2) has a seven-membered ring connected to two six-membered rings at



a)

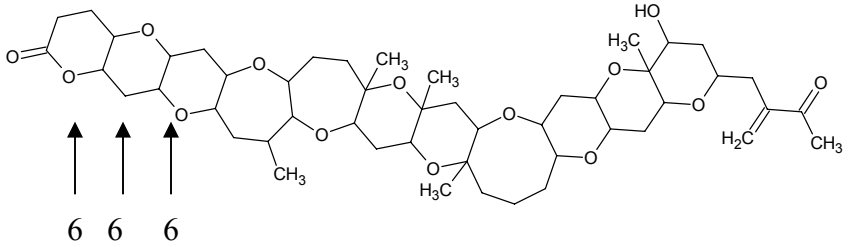


b)

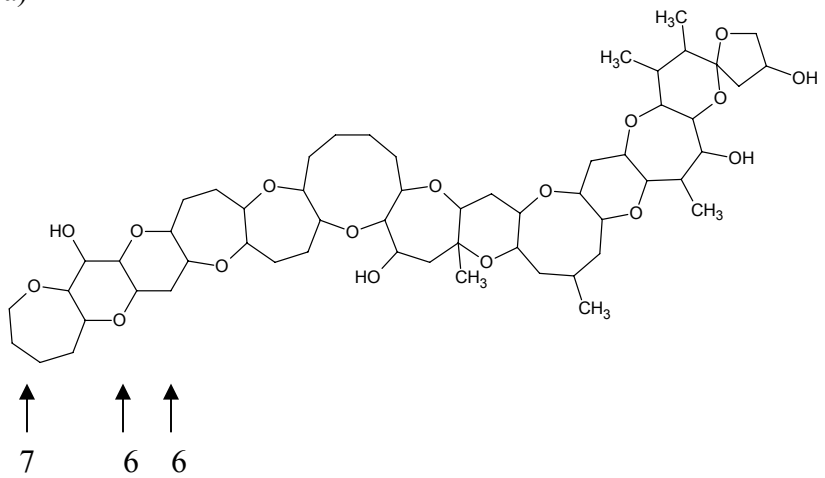


c)

Figure 1. Various naturally occurring polyether toxins a) Ciguatoxin b) Yessotoxin c) Gymnocin A



a)



b)

Figure 2. a) Brevetoxin PbTx-1 with three 6-membered rings at terminal end
b) Ciguatoxin with a 7-membered ring and two 6-membered rings at a terminal end

one terminal end. The size and structure of these polyether ring compounds appears to be crucial to their biological or toxic properties.

The various polyether toxins generally function the same way in humans. Brevetoxin as an example binds with very high affinity to the voltage dependent sodium channel in humans. The sodium ion channel is one of the major participants in the propagation of nerve impulses. There are two voltage sensitive gates on this channel. The activation gate lies on the plasma membrane of a nerve cell on the outside of the cell. This gate remains closed when resting. It responds to depolarization by opening to allow the flow of sodium ions into the cell. The inactivation gate lies on the plasma membrane of a nerve cell on the inside of the cell. It closes after depolarization to stop the flow of sodium ions [9]. The backbone of the polyether is inserted between the trasmembrane domains of the sodium channel. It then interacts with the voltage sensor and the inactivation gate on the intracellular side. When this binding occurs, the voltage sensitivity is altered. While the sodium channel should remain closed the majority of the time, the presence of brevetoxin causes it to be open continuously. This leads to an uncontrolled sodium influx which can enhance the depolarization of nerve cells causing the concentration of sodium ions to be very high in the cell. The nerve cells will then continuously synapse with each other. This is what causes neurotoxic poisoning [10].

Because the size and structure of these compounds are intimately involved with their biological activity [10], it is necessary to be able to determine the structure of novel polyether toxins as they are discovered. The primary way to identify new polyether structures is through NMR (nuclear magnetic resonance) spectroscopy, and hence a

library of NMR spectral data would aid considerably in the identification of new polyethers.

One way to develop such a spectral library efficiently is to use NMR data calculated using high level theory based on quantum mechanics. Calculating NMR data using quantum mechanical computational methods relies directly on the accurate calculation of the energy. This is because the computed NMR shift is a mathematical second derivative of the energy function. To calculate the energy with reasonable accuracy, *ab initio* theory was used, meaning "from first principles". This theory is based on approximate solutions to the Schrödinger equation. Specifically, the Hartree-Fock method was used. This method employs a simplification of the Schrödinger equation (Figure 3) that considers each electron to experience the effects of all the other electrons combined [11]. Another approximation used is the Born-Oppenheimer approximation, which states that electrons act independently of the nucleus. This allows the Schrödinger equation to be simplified by removing the kinetic energy of the nucleus from the equation (Figure 4). The third approximation is the LCAO (linear combination of atomic orbitals) approximation which states that molecular orbitals can be constructed as linear combinations of atom-centered orbitals [11]. In order to obtain the optimum results, the energy value that is calculated should be as close as possible to the Hartree-Fock limit. This approaches the "true" value of the energy, but is always somewhat higher than the "true" value. This is because Hartree-Fock theory ignores individual electron-electron interactions, so called electron correlation. [11]. As variables used in the calculations are optimized, such as using larger basis sets or improving the wavefunction used in the

$$\hat{H}\Psi = E\Psi$$

a)

$\hat{H}$ = Hamiltonion operator

Kinetic energy of nuclei

Kinetic energy of electrons

$$\hat{H} = -\frac{h^2}{8\pi^2}\sum_{A}\frac{1}{M_A}\nabla_A^2 - \frac{h^2}{8\pi^2 m}\sum_{a}\nabla_a^2 - e^2\sum_{A}^{nuclei}\sum_{a}^{electrons}\frac{Z_A}{r_{Aa}}$$

$$+ e^2\sum_{A}^{nuclei}\sum_{B>}\frac{Z_A Z_B}{r_{AB}} + e^2\sum_{a}^{electrons}\sum_{b>}\frac{1}{r_{ab}}$$

b)

Figure 3. a) Schrödinger equation showing b) Hamiltonian operator.

$$\hat{H} = \cancel{-\frac{h^2}{8\pi^2}\sum_{A}^{\text{nuclei}}\frac{1}{M_A}\nabla_A^2} - \frac{h^2}{8\pi^2 m}\sum_{a}^{\text{electrons}}\nabla_a^2 - e^2\sum_{A}^{\text{nuclei}}\sum_{a}^{\text{electrons}}\frac{Z_A}{r_{Aa}}$$

$$+ \cancel{e^2\sum_{A}^{\text{nuclei}}\sum_{B>A}\frac{Z_A Z_B}{r_{AB}}} + e^2\sum_{a}^{\text{electrons}}\sum_{b>a}\frac{1}{r_{ab}}$$

Figure 4. Simplified Hamiltonian operator without kinetic energy of nucleus

calculation, the calculated energy value approaches the Hartree-Fock limit asymptotically without going below it (Figure 5). In other words, in order to get the energy value that is closest to the "true" value, basis sets must be very large. Ideally such basis sets should be infinite [12-14], but this is a practical impossibility for calculating the energy values of large molecules.

A basis set is a combination of mathematical functions used to represent atomic orbitals. They have a simple mathematical form used to represent the radial distribution of electron density. Slater-type orbitals model experimental electron distributions well, but their form does not allow easy mathematical manipulation. The basis set used in these calculations was a moderate-sized Gaussian-type basis set designated 6-31G(d), developed by Pople et al. [15]. Gaussian-type basis sets approximate Slater-type orbitals by combining various proportions of several Gaussian distribution functions of different sizes. Each character has a meaning in a Gaussian-type basis set. In this example, there are six primitive Gaussian functions used for inner core (subvalence) electrons. There are three Gaussian functions used for small (contracted) valence orbitals. There is one Gaussian function used for large (extended) valence orbitals. The G stands for Gaussian and (d) adds a d orbital to heavy (i.e., other than hydrogen or helium) atoms [16]. Within the *Gaussian 03* software suite there is a subfunction that uses a calculation method called GIAO (gauge including atomic orbitals) [17] to calculate isotropic NMR shielding values, from which computed chemical shifts may be derived. Because of the computational simplifications of this subfunction, an infinite basis set is not necessary [17].

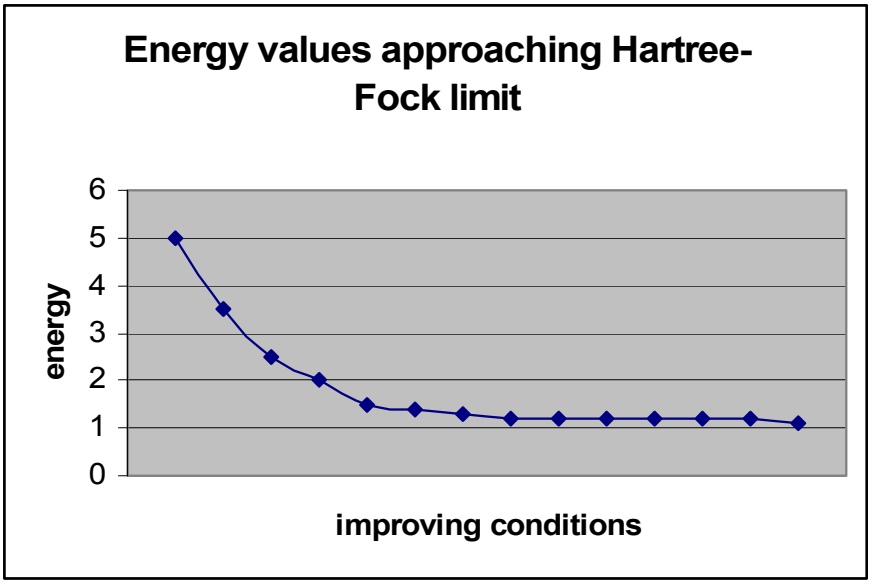


Figure 5. Energy values approaching Hartree-Fock limit. As conditions for calculations improve, the energy value asymptotically approaches the "true" value, in this case 0.

NMR spectroscopy assesses the difference between systems in the presence and absence of an external magnetic field. Therefore there are two very important terms that contribute to the net shielding. The paramagnetic term describes a secondary magnetic field produced by the electrons which acts with the applied field, and the diamagnetic term which describes a secondary magnetic field produced by the electrons that act against the applied field. It is due to these two opposing terms that GIAO is necessary. An origin is selected by the calculating program; this is typically the nucleus. However, choosing the nucleus as the origin causes the origin to change throughout the calculation because there are many nuclei present. Changing the origin causes the paramagnetic and diamagnetic terms to change. While they should theoretically be equal but opposite, often they are not. In order to avoid this, one would like to select an origin that would minimize the paramagnetic term. GIAO does this by using field dependent atomic orbitals as the origins. Each atomic orbital has its own local gauge origin placed at its center. Due to this, the task of assigning the origin is eliminated [12-14]. This allows the energy to approach the Hartree-Fock limit without using an infinite basis set.

EXPERIMENTAL PROCEDURE

A search of literature was first performed for naturally occurring polyether compounds. This search resulted in many articles dealing with natural polyether containing marine toxins [1-8]. Twelve polyether compounds were investigated. The structures of the toxins were then broken up into three-ring segments (Figures 6 and 7), in order to make these large structures easier to study and to perform calculations. The frequencies of occurrence of these three ring structures were then counted throughout the literature surveyed (Figure 8). The 6-6-6 ring system occurred the most frequently followed by the 6-6-7 ring system. In the literature surveyed, some of these ring systems such as the 9-8-8 ring system appeared only once, indicating that they rarely occur. Only those ring systems occurring more than once in the literature surveyed were used for calculations.

Models of these three-ring systems were then built in a molecular modeling computer program called *Spartan* [18]. Once built, a search of conformers was performed. Those conformers that were within 3 kcal/mol of the lowest energy conformer were then submitted for an energy minimization using the semi-empirical method, PM3.

These PM3-optimized structures were then submitted to the North Carolina Supercomputing Center (NCSC) for a single point energy calculation using the Hartree-Fock method with a 6-31G(d) basis set within *Gaussian 03* [19]. Also requested in this calculation were the isotropic shielding values. These are the values of shielding by the electrons when exposed to a magnetic field. A coupling constant calculation was also

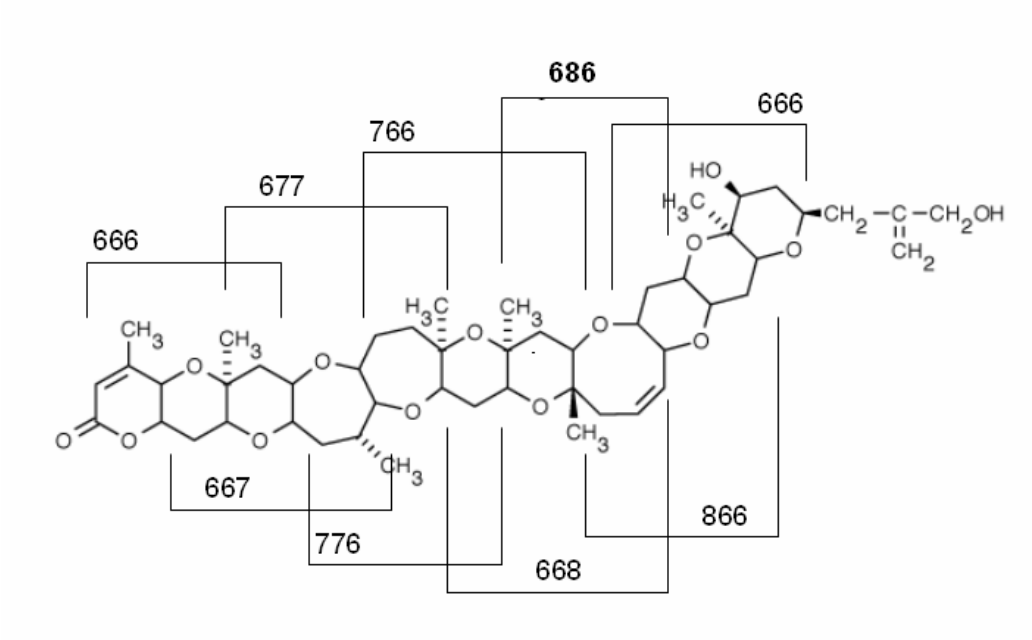


Figure 6. Brevetoxin showing three-ring segments.

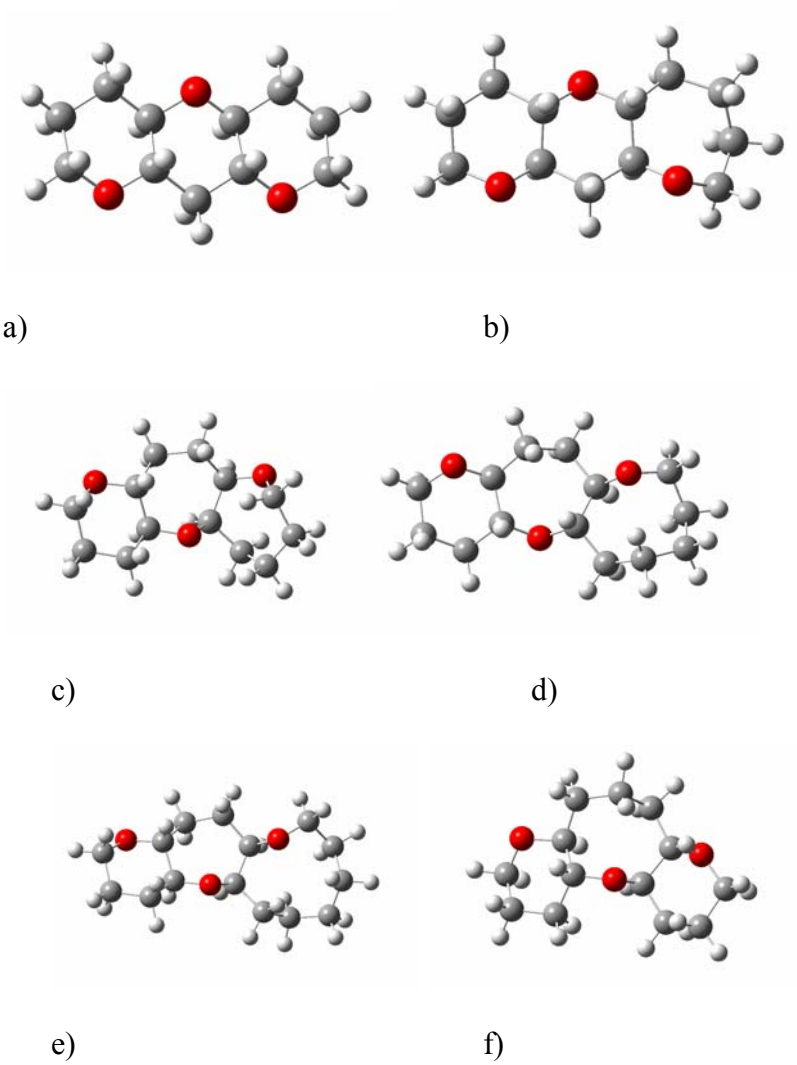


Figure 7. Various 3-ring subsystems a) 6-6-6 b) 6-6-7 c) 6-7-7 d) 6-7-8 e) 6-7-9 f) 6-8-6

6-6-6 (24 occurrences)	6-6-7 (19)
6-7-6 (10)	6-8-6 (6)
8-6-6 (7)	7-7-6 (3)
8-6-7 (7)	6-7-9 (4)
7-9-8 (2)	

(1 each): 6-7-8, 7-6-7, 7-7-9, 7-8-9, 7-9-6, 7-9-7,

8-8-6, 9-6-6, 9-8-8

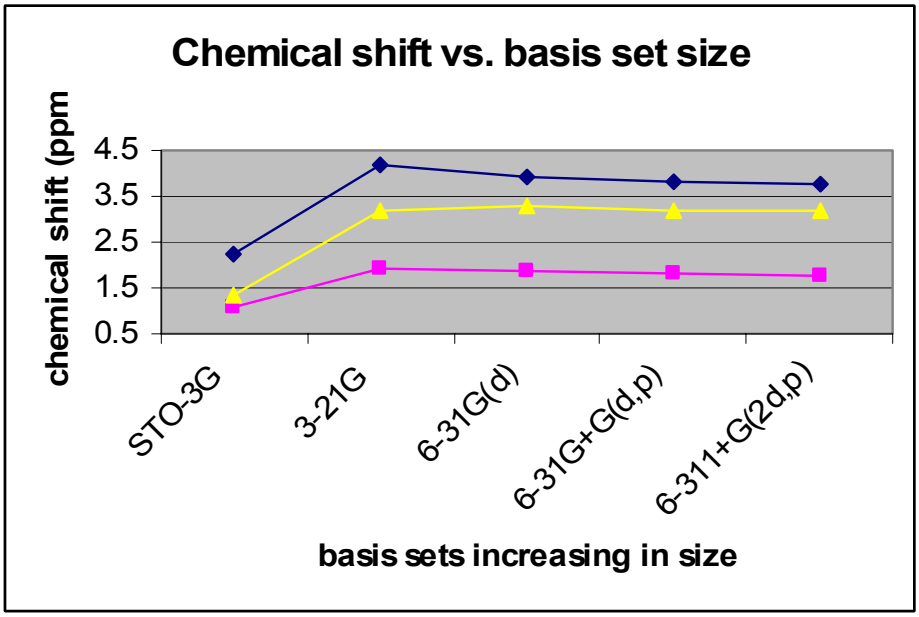
Figure 8. Frequencies of 3-ring systems.

requested. When the data came back for this particular calculation, it was noted that the coupling constant values were not close to the expected values for coupling constants. An example of this can be seen in the calculation of propene. In propene, the trans-coupling constant for the alkene hydrogen is expected to be 16.81. [20]. A model of propene was built and optimized using the Hartree-Fock method with a 6-31G(d) basis set, the same basis set used in the other calculations. A coupling constant calculation was then requested. The results of this showed the value of the trans-coupling constant between the alkene hydrogens to be -38.8 Hz. This value is very different from the expected value. James Hess at Gaussian, Inc. was then contacted to try to remedy this problem. He submitted the propene structure, with the same starting geometry optimized at 6-31G(d) for a coupling constant calculation, but this time he used the density functional theory with the B3LYP functional [21] and the aug-cc.pvtz basis set [22] for the NMR calculation. This is a very large basis set. His data showed a trans-coupling constant of 13.5 Hz between the alkene hydrogens. He performed one more calculation, this time optimizing the geometry using the B3LYP functional and the aug-cc.pvtz basis set and then requesting a coupling constant calculation. This time he obtained 16 Hz. as the trans-coupling constant for the hydrogens. This showed that the use of a very large basis and perhaps a more refined geometry were needed to provide accurate coupling constants. Had a very large basis set been used, the values would probably have been closer to the expected values. However, using a large basis set would have required a lot of computational time. This is due to the fact that the cpu time required for Hartree-Fock calculations is proportional to n^3-n^4, where n is the number of basis functions. Because NCSC was just about to shut down indefinitely, this was a practical impossibility.

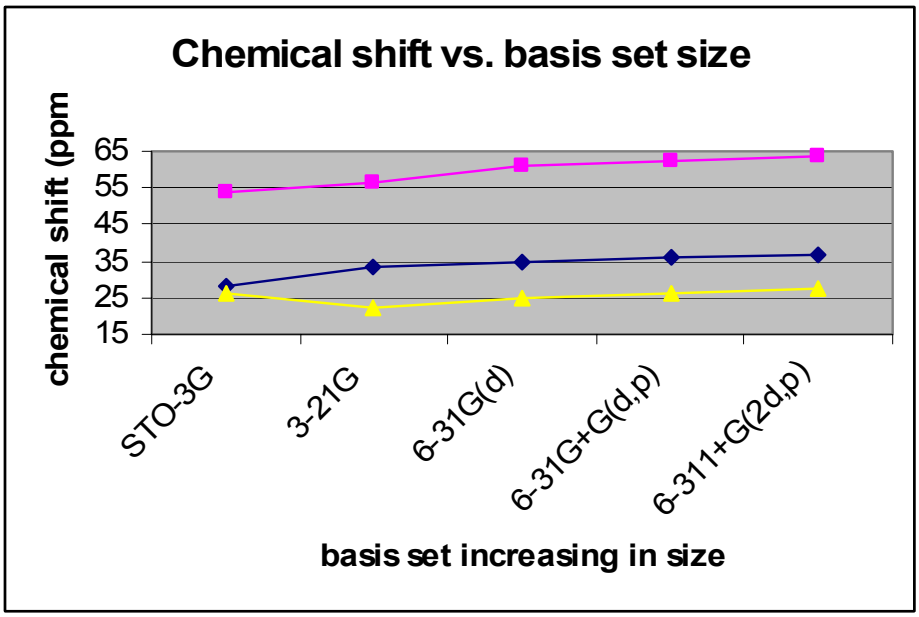
The relationship between the computed chemical shift and the size of the basis set for a carbon atom in the 6-6-6 ring system and for a hydrogen atom in the 6-6-6 ring system can be seen in Figure 9. Note that there is a dramatic change in chemical shift between the smallest basis set (STO-3G) and the next smallest (3-21G), but that the calculated chemical shift seems to level off as the basis set size is increased. It can be seen in Figure 10 how the cpu time required for a given NMR shielding calculation varies as the basis set size increases. The cpu time increases dramatically as the basis set size is increased from 6-31G(d) to 6-31G(d,p) and then even more dramatically as it is increased to 6-31++G(2d,p). We selected 6-31G(d) as the best compromise between chemical shift value and cpu time efficiency.

The *Gaussian 03* program calculates NMR isotropic shielding values. From these values the chemical shifts can be calculated. To do this, the isotropic shielding value of a standard must be known. In this case, TMS was used. The shielding value of each atom in the structure was subtracted from the shielding value of TMS, computed using the same basis set. This gives a chemical shift with TMS as a standard. An example of this for the subsystem 6-6-6 can be seen in Table 1.

The coupling constants were then calculated using a modified Karplus equation, which estimates a vicinal coupling constant as a function of the dihedral angle between vicinal hydrogens. This was done by opening the chemical structure data file from NCSC in a program called *GaussView* [23]. In this program, the dihedral angles of hydrogens can be measured. Using a modified Karplus equation, these dihedral angles can be used to calculate the coupling constant (J) of each set of atoms. There were several variations of the original Karplus equations found in literature. The problem with



a)



b)

Figure 9. Chemical shifts of a) hydrogen and b) carbon versus increasing basis set size.

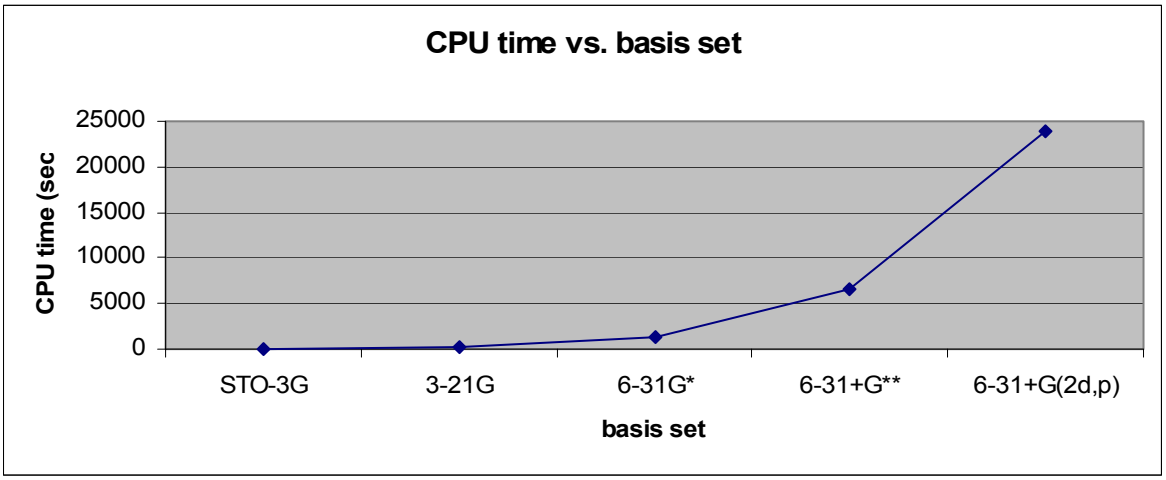


Figure 10. Graph of CPU time vs. basis set

Table 1. Calculation of chemical shifts of 6-6-6 ring system using isotropic shielding values and shielding values of TMS.

#	atom	Isotropic value of atom	Isotropic value of TMS	Chemical shift of atom
3	C	177.2	151.2	26.0
4	C	132.6	151.2	70.5
5	C	173.2	151.2	30.0
6	C	133.3	151.2	69.8
7	C	140.9	151.2	62.2
17	C	166.8	151.2	36.3
21	C	133.3	151.2	69.8
24	C	132.6	151.2	70.5
29	C	140.9	151.2	62.2
30	C	173.2	151.2	30.0
32	C	177.2	151.2	26.0
1	H	30.8	29.2	1.5
2	H	29.0	29.2	3.4
8	H	31.0	29.2	1.3
9	H	29.7	29.2	2.6
10	H	31.3	29.2	1.0
11	H	29.9	29.2	2.5
12	H	29.6	29.2	2.7
14	H	31.5	29.2	0.9
15	H	31.0	29.2	1.3
16	H	30.8	29.2	1.5
18	H	29.0	29.2	3.4
19	H	31.1	29.2	1.2
20	H	30.5	29.2	1.8
23	H	29.9	29.2	2.5
25	H	29.7	29.2	2.6
26	H	31.3	29.2	1.0
27	H	31.5	29.2	0.9
31	H	29.6	29.2	2.7

the original Karplus equation [24] was that the coupling constant of atoms when their dihedral angle was near 180° is computed to be less than the experimentally observed value. The several different modified Karplus equations correct this error in different ways. The modified Karplus equation that was used in this work for calculating coupling constants is the following:

$$J = 7.13 - 1.16\cos\theta + 6.44\cos 2\theta \text{ [25]}$$

An example of this calculation used for the subsystem 6-6-6 can be seen in Table 2.

The various conformers of the several structures had differing NMR data because the atoms are in different three-dimensional locations. Molecules exist as an ensemble of conformations, composed of a weighted average of the conformations according to their molecular energies. When a calculation is done on a particular molecule, the molecule is in one conformation of possibly many. In order to determine what the NMR data of the structure as a whole is, a mathematical distribution of conformers was needed. To determine this a Boltzmann function was used. Using the energy that was calculated from the single point Hartree-Fock energy calculation a Boltzmann factor was calculated using the following equation:

$$P = e^{-\Delta H/RT}$$

P in this equation is the Boltzmann factor. ΔH is the energy given by the single point energy calculation in kcal/mol. T is the absolute temperature. 300 K was used for these calculations because it is commonly used in NMR spectroscopy.

Table 2. Coupling constant calculation for ring system 6-6-6 using dihedral angles.

hydrogens	dihedral angle	radians	2*radians	J value
12-18				12.4
8-18	-53.9	-0.94	-1.88	4.5
14-18	63.9	1.12	2.23	2.7
8-12	-172.7	-3.01	-6.02	14.5
12-14	-54.9	-0.95	-1.91	4.3
8-14				12.4
8-16	53.5	0.93	1.86	4.6
8-10	170.3	2.97	5.94	14.3
14-16	-64.1	-1.11	-2.23	2.6
10-14	52.7	0.92	1.84	4.7
10-16				12.4
9-10	-172.3	-3.00	-6.01	14.5
9-16	-55.9	-0.97	-1.95	4.1
9-11	-179.1	-3.12	-6.25	14.7
11-19	172.1	3.00	6.00	14.5
11-20	56.3	0.98	1.96	4.0
19-20				12.4
19-23	-172.1	-3.00	-6.00	14.5
20-23	-56.3	-0.98	-1.96	4.0
23-25	179.1	3.12	6.25	14.7
1-25	55.9	0.97	1.95	4.1
25-26	172.3	3.00	6.01	14.5
1-26				12.4
1-27	64.1	1.11	2.23	2.6
1-15	-53.5	-0.93	-1.86	4.6
26-27	-52.7	-0.92	-1.84	4.7
15-26	-170.3	-2.97	-5.94	14.3
15-27				12.4
27-31	54.9	0.95	1.91	4.3
2-27	-63.9	-1.11	-2.23	2.7
15-31	172.7	3.01	6.02	14.5
2-15	53.9	0.94	1.88	4.5
2-31				12.4

Using each of these Boltzmann factors, a mathematical distribution (percent composition) of the conformers was calculated using the following equation:

$$P_1 = e^{-\Delta H/RT}$$
$$P_2 = e^{-\Delta H/RT}$$
$$P_3 = e^{-\Delta H/RT}$$

$$P = P^*/Q$$

In this equation, P is the distribution of the conformer of interest (its mole fraction in the ensemble). P* is the Boltzmann factor of the conformer of interest, and Q is the sum of P1, P_2, and P_3 (the Boltzmann factors of the various conformers. This calculation was performed for each conformer of each compound (Table 3).

Using the distribution of each conformer as well as the chemical shifts value of each hydrogen and carbon, the weighted averages of hydrogen and carbon chemical shifts were then calculated using the following equation:

Weighted average H_1 = (chemical shift H_1 of conformer 1) (conformer distribution of conformer 1) + (chemical shift H_1 of conformer 2) (conformer distribution of conformer 2) + etc…..

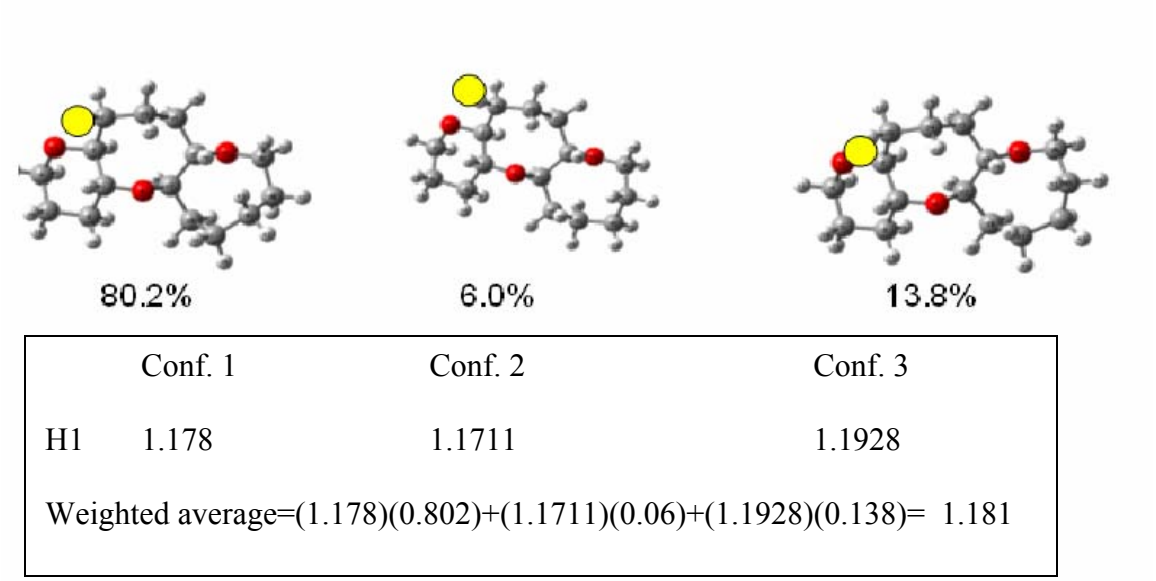
An example of this calculation can be seen in Figure 11. The same kind of equation was used to determine the weighted average of the coupling constants.

Table 3. The distributions of each conformer calculated using a Boltzmann function.

compound	E (hartrees)	ΔE (kcal/mol)	P	total of P's	%
6-6-6_1	-651.6063025	0.0	1.000	1.0000	100.0
6-6-7_1	-690.6329931	0.0	1.000	1.0305	97.0
6-6-7_2	-690.6281251	3.1	0.006	1.0305	0.5
6-6-7_3	-690.6294496	2.2	0.025	1.0305	2.4
6-7-6_1	-690.6304741	0.0	1.000	1.0000	100.0
6-7-7_1	-729.6573703	0.5	0.419	1.4190	29.6
6-7-7_2	-729.6581959	0.0	1.000	1.4190	70.5
6-7-8_1	-768.684293	0.0	1.000	2.1221	47.1
6-7-8_2	-768.6817122	1.6	0.066	2.1221	3.1
6-7-8_3	-768.6841788	0.1	0.887	2.1221	41.8
6-7-8_4	-768.6822057	1.3	0.111	2.1221	5.2
6-7-8_5	-768.6812035	1.9	0.039	2.1221	1.8
6-7-8_6	-768.6803354	2.5	0.016	2.1221	0.7
6-7-8_7	-768.67902	3.3	0.004	2.1221	0.2
6-7-9_1	-807.7118465	0.4	0.518	2.4718	20.9
6-7-9_2	-807.7108809	1.0	0.187	2.4730	7.6
6-7-9_3	-807.712472	0.0	1.000	2.4730	40.4
6-7-9_4	-807.7102401	1.4	0.095	2.4730	3.9
6-7-9_5	-807.7097619	1.7	0.058	2.4730	2.3
6-7-9_6	-807.7092766	2.0	0.035	2.4730	1.4
6-7-9_7	-807.710719	1.1	0.158	2.4730	6.4
6-7-9_8	-807.70849	2.5	0.015	2.4730	0.6
6-7-9_9	-807.7063857	3.8	0.002	2.4730	0.1
6-7-9_10	-807.7099873	1.6	0.073	2.4730	3.0
6-7-9_11	-807.708076	2.8	0.010	2.4730	0.4
6-7-9_12	-807.7078599	2.9	0.008	2.4730	0.3
6-7-9_13	-807.710944	1.0	0.200	2.4730	8.1
6-7-9_14	-807.7099616	1.6	0.071	2.4730	2.9
6-7-9_15	-807.7064763	3.8	0.002	2.4730	0.1
6-7-9_16	-807.7080632	2.8	0.010	2.4730	0.4
6-7-9_17	-807.7091617	2.1	0.031	2.4730	1.2
6-8-6_1	-729.6578678	0.0	1.000	1.0000	100.0
6-8-8_1	-807.7109519	0.0	1.000	1.2466	80.2
6-8-8_2	-807.7084854	1.5	0.075	1.2466	6.0
6-8-8_3	-807.7092799	1.0	0.172	1.2466	13.8
7-6-7_1	-729.6595947	0.0	1.000	1.0152	98.5
7-6-7_2	-729.6549482	2.9	0.008	1.0153	0.7
7-6-7_3	-729.6549733	2.9	0.008	1.0153	0.8
7-6-8_1	-768.6833841	0.7	0.309	1.9531	15.8
7-6-8_2	-768.6839615	0.3	0.568	1.9539	29.1
7-6-8_3	-768.684499	0.0	1.000	1.9539	51.2
7-6-8_4	-768.6797587	3.0	0.007	1.9539	0.3
7-6-8_5	-768.6798009	2.9	0.007	1.9539	0.4
7-6-8_6	-768.6818563	1.7	0.062	1.9539	3.2
7-7-9_1	-846.7400265	0.0	1.000	1.8594	53.8
7-7-9_2	-846.7377814	1.4	0.094	1.8599	5.1
7-7-9_3	-846.7390788	0.6	0.369	1.8599	19.8
7-7-9_4	-846.7385313	0.9	0.207	1.8599	11.1
7-7-9_5	-846.737059	1.9	0.044	1.8599	2.4
7-7-9_6	-846.7353689	2.9	0.007	1.8599	0.4
7-7-9_7	-846.7354178	2.9	0.008	1.8599	0.4

Table 3 cont.

7-7-9_8	-846.7380679	1.2	0.127	1.8599	6.8
7-7-9_9	-846.733067	4.4	0.001	1.8599	0.0
7-7-9_10	-846.7341544	3.7	0.002	1.8599	0.1
8-6-6_1	-729.6541772	1.0	0.194	1.2957	15.0
8-6-6_2	-729.6535159	1.4	0.097	1.2957	7.5
8-6-6_3	-729.6557345	0.0	1.000	1.2957	77.2
8-6-6_4	-729.6506665	3.2	0.005	1.2957	0.4



	Conf. 1	Conf. 2	Conf. 3
H1	1.178	1.1711	1.1928

Weighted average=(1.178)(0.802)+(1.1711)(0.06)+(1.1928)(0.138)= 1.181

Figure 11. The weighted average of chemical shift for hydrogen number 1 highlighted yellow in the figure for the 6-6-8 ring system

RESULTS AND DISCUSSION

After a weighted average of chemical shifts and coupling constants was calculated for each 3 ring subsystem (Tables 4,5, Appendix A,B), several corrections had to be made to each of the chemical shift values. The calculations were performed using a moderate size basis set (6-31G(d)) for computational efficiency. Because of this, the values of the chemical shifts that were obtained were not as close as desired to the literature values. In performing NMR calculations, the calculated chemical shift is not as accurate as a difference in chemical shifts. Because of the difference in electron configuration between the polyethers and tetramethylsilane (TMS), the standard used for NMR chemical shifts, a similar molecule to the ones calculated was needed that would reduce the effect of electron configuration differences and enable us to get good chemical shift values using a moderate size basis set. To correct this problem cyclohexane was used as a secondary standard to adjust calculations. A model of cyclohexane was built and its geometry was optimized using HF/6-31G(d) using *Spartan* molecular modeling software. The optimized structure was submitted to NCSC for computing isotropic shielding values using *Gaussian 03*. From these values and the isotropic shielding values of TMS, the chemical shifts were calculated. These values were then compared to the literature values of the chemical shifts of cyclohexane. From this comparison, correction factors were derived and applied to all computed carbon and hydrogen chemical shifts. A correction of 4.3 ppm was added to all carbon shifts. A correction of 0.6 ppm was added to all equatorial hydrogens in six-membered rings. A correction of 0.2 ppm was added to all axial hydrogens in six-membered rings.

Table 4. Weighted average of chemical shifts for 6-6-6 ring system

6-6-6 - 1 conformer

#	atom	conf. 1 (100%)	wt. ave
3	C	26.0	26.0
4	C	70.5	70.5
5	C	30.0	30.0
6	C	69.8	69.8
7	C	62.2	62.2
17	C	36.3	36.3
21	C	69.8	69.8
24	C	70.5	70.5
29	C	62.2	62.2
30	C	30.0	30.0
32	C	26.0	26.0
1	H	1.5	1.5
2	H	3.4	3.4
8	H	1.3	1.3
9	H	2.6	2.6
10	H	1.0	1.0
11	H	2.5	2.5
12	H	2.7	2.7
14	H	0.9	0.9
15	H	1.3	1.3
16	H	1.5	1.5
18	H	3.4	3.4
19	H	1.2	1.2
20	H	1.8	1.8
23	H	2.5	2.5
25	H	2.6	2.6
26	H	1.0	1.0
27	H	0.9	0.9
31	H	2.7	2.7

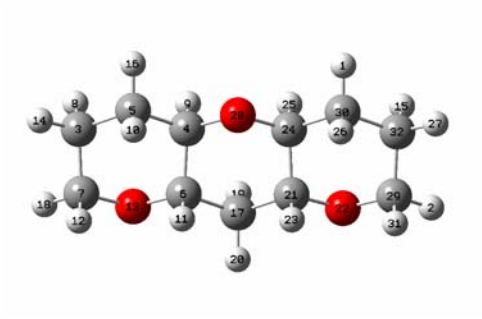
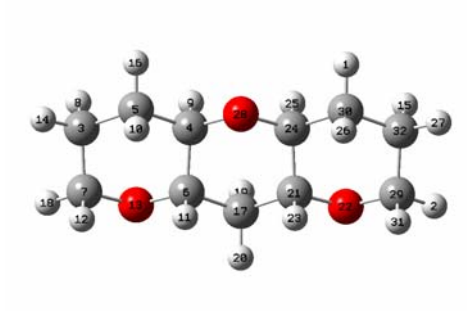


Table 5. Weighted average of coupling constants for 6-6-6 ring system

6-6-6 - 1 conformer

H's	conf. 1 (100%)	wt. ave
12-18	12.4	12.4
8-18	2.6	2.6
14-18	1.2	1.2
8-12	9.1	9.1
12-14	2.4	2.4
8-14	12.4	12.4
8-16	2.6	2.6
8-10	9.0	9.0
14-16	1.2	1.2
10-14	2.7	2.7
10-16	12.4	12.4
9-10	9.1	9.1
9-16	2.3	2.3
9-11	9.2	9.2
11-19	9.0	9.0
11-20	2.2	2.2
19-20	12.4	12.4
19-23	9.0	9.0
20-23	2.2	2.2
23-25	9.2	9.2
1-25	2.3	2.3
25-26	9.1	9.1
1-26	12.4	12.4
1-27	1.2	1.2
1-15	2.6	2.6
26-27	2.7	2.7
15-26	9.0	9.0
15-27	12.4	12.4
27-31	2.4	2.4
2-27	1.2	1.2
15-31	9.1	9.1
2-15	2.6	2.6
2-31	12.4	12.4



A correction of 0.4 ppm (the mean of 0.6 and 0.2) was added to all other hydrogens that are neither axial nor equatorial, such as those in a seven-membered ring.

The other correction that was made was due to the fact that in nature, these compounds are not simply the three-ring subsystems that were used for calculation purposes. These three-ring systems are most commonly in the middle of these compounds rather than at the end, and therefore have attachments to other carbons and oxygens (Figure 12). As can be seen in Figure 12, the terminal six-membered ring of the 6-6-7 subsystem has attachments to both carbon and oxygen as does the seven-membered ring. These attachments cause the chemical shift values to move upfield for the atoms bearing these attachments. It was noted in the literature [11] that an attachment of a carbon to another carbon adds 9 ppm to a carbon chemical shift. Attachment of an oxygen to a carbon adds 50 ppm. A hydrogen whose carbon is attached to another carbon adds 0.2 ppm to the hydrogen spectrum. A hydrogen whose carbon is attached to an oxygen adds 2.3 ppm to the hydrogen spectrum. These corrections were done as a first approximation. More correction factors should be added for more accurate results, such as the beta connection to an oxygen. An example of these corrections being made to the 6-6-6 system can be seen in Table 31.

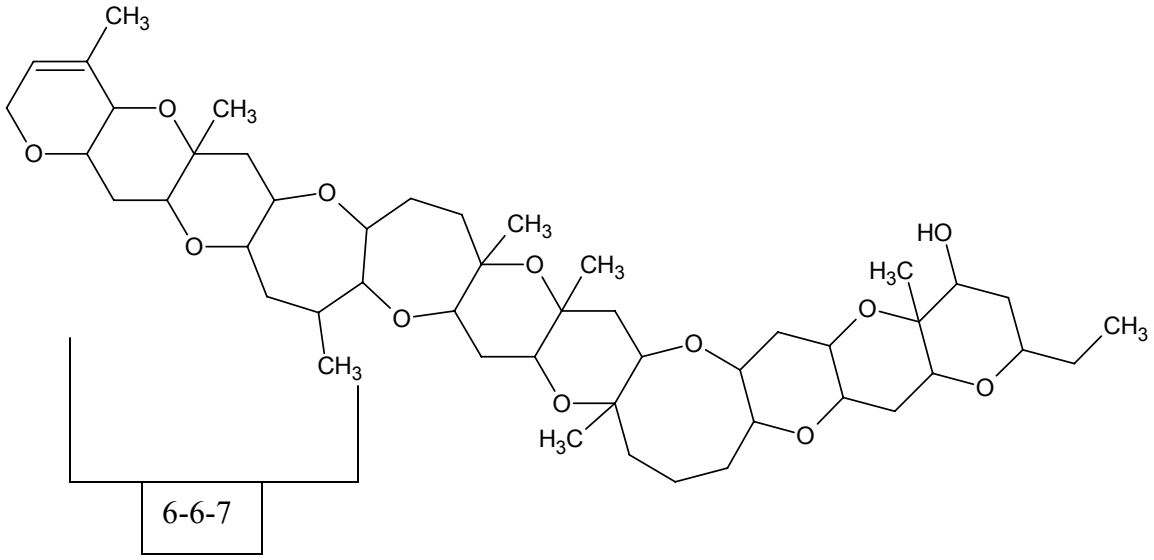


Figure 12. A 6-6-7 subsystem in brevetoxin-2. The terminal 6-membered ring has attachments to both a carbon and an oxygen, as does the terminal 7-membered ring.

Table 6. Corrections based on the cyclohexane derived correction and corrections due to attachment to carbon and oxygen performed on the 6-6-6 ring system.

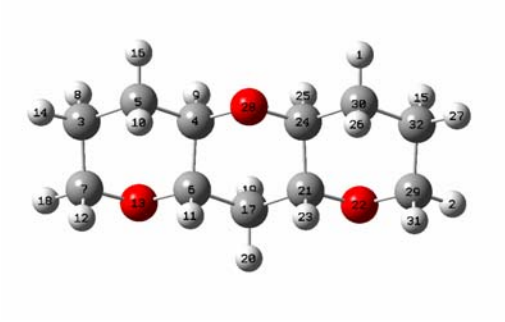
6-6-6 - 1 conformer

#	atom	conf. 1 (100%)	wt. ave	corrected
3	C	26.0	26.0	80.3
4	C	70.5	70.5	74.8
5	C	30.0	30.0	34.3
6	C	69.8	69.8	74.1
7	C	62.2	62.2	75.5
17	C	36.3	36.3	40.6
21	C	69.8	69.8	74.1
24	C	70.5	70.5	74.8
29	C	62.2	62.2	75.5
30	C	30.0	30.0	34.3
32	C	26.0	26.0	80.3
1	H	1.5	1.5	2.1
2	H	3.4	3.4	4.2
8	H	1.3	1.3	3.8
9	H	2.6	2.6	2.8
10	H	1.0	1.0	1.2
11	H	2.5	2.5	2.7
12	H	2.7	2.7	3.1
14	H	0.9	0.9	3.8
15	H	1.3	1.3	3.8
16	H	1.5	1.5	2.1
18	H	3.4	3.4	4.2
19	H	1.2	1.2	1.4
20	H	1.8	1.8	2.4
23	H	2.5	2.5	2.7
25	H	2.6	2.6	2.8
26	H	1.0	1.0	1.2
27	H	0.9	0.9	3.8
31	H	2.7	2.7	3.1

CONCLUSIONS

ACD/Labs CNMR Predictor and Database and HNMR Predictor and Database are programs that predict NMR spectra [26]. In these programs, a model of the structure is built and from that model the program will produce an NMR spectrum. This is done by use of a database within the *ACD/Labs* program. Each atom in the built structure is compared to the database and a chemical shift is produced. To determine the usefulness of the computed chemical shift data produced from quantum calculations in this work, it was compared to the predictions of the *ACD/Labs* software as well as to literature NMR values of chemical shifts [1-5,18]. The purpose of this comparison was to see if the chemical shift values calculated in this work were better than the chemical shift values calculated by *ACD/Labs*. In order to do this the three-ring subsystems were built in *ACD/Labs* software and an NMR spectrum was calculated. The chemical shifts given by *ACD/Labs* software were then corrected for attachments to carbon and oxygen in the same way that the structures in this work were. A difference was then taken between *ACD/Labs*'s predicted shift and the literature shift. The mean of average deviation (MOAD) was then taken between the chemical shifts predicted by *ACD/Labs* software and the literature value. This is the mean of the absolute values of each difference. A difference between the literature values and the calculated values done in this work were also taken. The MOAD between these values was then calculated. These MOAD differences between *ACD/Labs* and the literature values, and between the calculated values in this work and the literature values, were then compared. These comparisons can be seen in Tables 7-13.

Table 7. Comparison of ACD Labs and calculated chemical shifts versus literature values of chemical shifts for the 6-6-6 ring system.

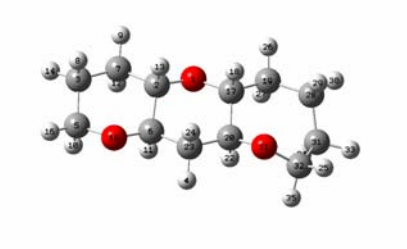


6-6-6

#	atom	Gymnocin A ($CDCl_3$) exp	corrected ACD Shift	difference exp-ACD	corrected calc shift	difference exp-calc.
3	C	77.4	70.8	6.6	80.3	-2.9
4	C	75.9	78.1	-2.2	74.8	1.1
5	C	35.1	29.6	5.5	34.3	0.8
6	C	76.9	75.0	1.9	74.1	2.8
7	C	76.7	76.9	-0.2	75.5	1.2
17	C	35.1	35.1	0.0	40.6	-5.5
21	C	75.9	75.0	0.9	74.1	1.8
24	C	76.7	78.1	-1.4	74.8	1.9
29	C	79.6	76.9	2.7	75.5	4.1
30	C	37.4	29.6	7.8	34.3	3.1
32	C	70.1	70.8	-0.7	80.3	-10.2
			MOAD	**2.7**	**MOAD**	**3.2**
1	H	2.1	1.5	0.6	2.1	0.0
2	H	n/a**	4.1	n/a	4.2	n/a
8	H	3.0	4.1	-1.2	3.8	-0.8
9	H	3.0	3.6	-0.6	2.8	0.2
10	H	1.4	1.5	-0.1	1.2	0.2
11	H	3.0	3.8	-0.8	2.7	0.3
12	H	3.0	4.1	-1.1	3.1	-0.1
14	H	n/a**	4.1	n/a	3.8	n/a
15	H	3.5	4.1	-0.6	3.8	-0.3
16	H	2.3	1.5	0.7	2.1	0.1
18	H	n/a**	3.6	n/a	4.2	n/a
19	H	1.4	1.8	-0.5	1.4	-0.1
20	H	2.2	2.2	0.1	2.4	-0.2
23	H	2.9	3.8	-0.9	2.7	0.2
25	H	3.0	3.6	-0.6	2.8	0.1
26	H	1.4	1.5	-0.1	1.2	0.1
27	H	n/a**	4.1	n/a	3.8	n/a
31	H	3.2	3.6	-0.4	3.1	0.1
			MOAD	**0.6**	**MOAD**	**0.3**

** rest of molecule

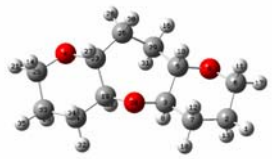
Table 8. Comparison of ACD Labs and calculated chemical shifts versus literature values of chemical shifts for the 6-6-7 ring system.



#	atom	Gymnocin A ($CDCl_3$) exp	corrected ACD SHIFT	difference exp-ACD	corrected calc. shift	difference Exp-Calculated
2	C	75.9	78.1	-2.2	73.8	2.1
3	C	76.9	70.8	6.1	80.3	-3.4
5	C	75.9	76.9	-1.0	75.3	0.6
6	C	76.7	75.0	1.7	73.6	3.1
7	C	35.1	29.6	5.5	34.2	0.9
17	C	79.6	75.6	4.1	77.8	1.8
19	C	29.4	28.6	0.8	40.7	-11.3
20	C	70.1	72.4	-2.3	72.7	-2.6
23	C	37.4	35.7	1.7	42.2	-4.8
28	C	25.1	22.9	2.2	25.2	-0.1
31	C	83.5	81.3	2.2	84.1	-0.6
32	C	80.3	78.2	2.1	74.8	5.5
			MOAD	**2.7**	**MOAD**	**2.8**
4	H	2.1	1.8	0.4	2.4	-0.3
8	H	3.0	4.1	-1.1	3.8	-0.8
9	H	2.2	1.5	0.7	2.1	0.1
11	H	3.0	3.8	-0.9	2.6	0.4
12	H	1.4	1.5	-0.2	1.2	0.2
13	H	2.9	3.6	-0.7	2.8	0.2
14	H	n/a**	4.1	n/a	3.8	n/a
16	H	n/a**	4.1	n/a	4.1	n/a
18	H	3.2	3.6	-0.4	3.0	0.2
22	H	3.5	3.8	-0.4	2.8	0.7
24	H	1.4	2.1	-0.7	1.5	-0.1
25	H	n/a**	3.9	n/a	3.8	n/a
26	H	2.1	2.0	0.1	2.1	-0.1
27	H	1.6	2.0	-0.4	1.4	0.3
29	H	1.8	1.4	0.4	1.6	0.2
30	H	1.7	1.5	0.2	1.5	0.2
33	H	n/a**	3.7	n/a	3.8	n/a
34	H	3.1	3.8	-0.7	3.9	0.8
35	H	1.2	4.4	-3.2	3.6	2.4
			MOAD	**0.8**	**MOAD**	**0.6**

** rest of molecule

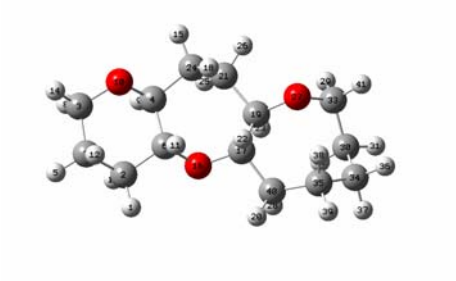
Table 9. Comparison of ACD Labs and calculated chemical shifts versus literature values of chemical shifts for the 6-7-6 ring system.



#	atom	Gymnocin A ($CDCl_3$) exp	corrected ACD SHIFT	Diff exp-ACD	corrected calc.shifts	difference exp-calc.
2	C	76.7	76	0.7	80.6	-3.9
3	C	70.1	81.9	-11.8	79.3	-9.2
5	C	79.6	84.1	-4.5	81.5	-1.9
6	C	75.9	76.9	-1.0	75.6	0.3
7	C	37.4	31.4	6.0	35.8	1.6
19	C	n/a	76.7	n/a	75.5	n/a
23	C	83.5	77.5	6.0	77.6	5.9
24	C	44.6	29.7	14.9	36.5	8.1
25	C	77.1	76.3	0.8	75.7	1.4
26	C	25.1	28.9	-3.8	35.9	-10.8
29	C	29.4	28.4	1.0	35.5	-6.1
33	C	76.5	71.3	5.2	80.6	-4.1
			MOAD	**5.1**	**MOAD**	**4.8**
1	H	n/a**	4.1	n/a	3.7	n/a
8	H	3.5	3.59	-0.1	2.9	0.6
10	H	3.2	3.52	-0.3	2.5	0.7
11	H	2.9	3.6	-0.7	3.0	-0.1
12	H	1.4	1.48	-0.1	1.3	0.1
13	H	3.0	4.1	-1.2	3.8	-0.8
14	H	2.9	3.6	-0.7	3.0	-0.1
15	H	3.0	4.1	-1.1	3.7	-0.7
16	H	1.6	1.58	0.0	1.8	-0.2
17	H	n/a**	4.1	n/a	4.1	n/a
18	H	2.1	1.48	0.7	2.2	0.0
21	H	n/a**	4.1	n/a	4.1	n/a
22	H	3.5	3.59	0.0	3.0	0.5
27	H	3.1	3.52	-0.4	2.9	0.2
28	H	1.8	1.58	0.2	2.1	-0.3
30	H	1.7	1.84	-0.2	1.9	-0.2
31	H	2.1	1.84	0.2	1.9	0.1
32	H	2.0	1.48	0.5	2.1	-0.2
34	H	1.4	1.48	0.0	1.3	0.2
35	H	n/a**	4.1	n/a	3.7	n/a
			MOAD	**0.6**	**MOAD**	**0.4**

** rest of molecule

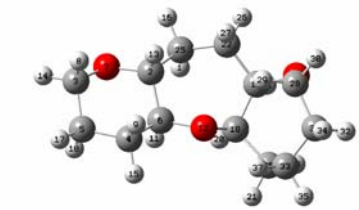
Table 10. Comparison of ACD Labs and calculated chemical shifts versus literature values of chemical shifts for the 6-7-8 ring system.



#	atom	CTx-3 (C5D5N) exp	corrected ACD SHIFT	difference exp-ACD	corrected calc shift	difference exp-calc.
1	H	1.8	1.5	0.4	1.9	-0.1
5	H	n/a**	4.1	n/a	4.5	n/a
8	H	3.4	3.6	-0.2	2.9	0.5
9	H	4.1	3.5	0.6	2.7	1.4
11	H	3.4	3.6	-0.2	2.2	1.2
12	H	3.3	4.1	-0.8	3.7	-0.4
13	H	2.6	1.5	1.1	2.2	0.4
14	H	n/a**	4.1	n/a	3.3	n/a
15	H	5.9	1.6	4.3	1.9	4.0
18	H	5.9	1.8	4.0	2.0	3.9
20	H	2.9	2.0	0.9	2.5	0.3
22	H	3.4	3.8	-0.4	3.2	0.2
23	H	4.1	3.8	0.3	2.5	1.6
25	H	5.9	1.6	4.3	1.8	4.2
26	H	5.9	1.9	4.0	1.8	4.1
28	H	2.3	2.0	0.4	2.2	0.1
29	H	3.6	4.3	-0.7	2.8	0.7
31	H	n/a**	3.6	n/a	3.4	n/a
32	H	3.6	3.6	0.0	4.1	-0.5
36	H	6.0	1.6	4.4	1.4	4.6
37	H	6.0	1.6	4.4	1.4	4.6
38	H	5.9	1.6	4.3	1.8	4.1
39	H	5.9	1.6	4.3	2.5	3.4
41	H	n/a**	4.3	n/a	3.1	n/a
			MOAD	**1.8**	**MOAD**	**1.8**

** rest of molecule

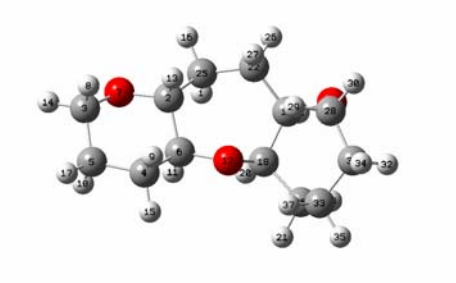
Table 11. Comparison of ACD Labs and calculated chemical shifts versus literature values of chemical shifts for the 6-7-7 ring system.



#	atom	PbTx-3 (MeOH) exp	corrected ACD SHIFT	difference exp-ACD	corrected calc shift	difference exp-calc.
2	C	87.2	80.8	6.4	78.6	8.6
3	C	81	76.6	4.4	75.3	5.7
4	C	46.6	30.6	16.1	36.3	10.3
5	C	76.1	73.7	2.4	80.5	-4.4
6	C	85.5	79.3	6.2	76.0	9.5
18	C	85.4	72.5	12.9	80.4	5.0
19	C	89.8	74.5	15.3	79.8	10.0
22	C	35.2	29.3	6.0	32.9	2.3
25	C	37.4	28.7	8.8	37.0	0.4
28	C	90.2	78.2	12.0	75.6	14.6
31	C	80.2	81.3	-1.1	85.7	-5.5
33	C	34.2	22.9	11.3	30.6	3.6
36	C	31.2	29.2	2.0	35.7	-4.5
			MOAD	**8.1**	**MOAD**	**6.5**
1	H	1.6	1.5	0.1	1.4	-1.3
8	H	3.2	3.6	-0.4	3.1	-3.5
9	H	1.5	1.5	0.0	1.3	-1.3
10	H	n/a*	4.1		3.7	
11	H	3.3	3.6	-0.3	2.6	-2.9
13	H	3.2	3.5	-0.3	2.8	-3.1
14	H	n/a**	4.1		4.1	
15	H	2.1	1.5	0.6	2.1	-1.5
16	H	1.8	1.6	0.2	2.0	-1.8
17	H	n/a**	4.1		3.7	
26	H	n/a*	1.6		1.8	
27	H	n/a	1.9		1.8	
29	H	3.2	4.0	-0.8	3.8	-4.6
30	H	n/a**	4.5		3.2	
32	H	n/a**	3.7		3.6	
34	H	n/a*	3.8		3.9	
35	H	2.0	1.4	0.6	1.3	-0.6
37	H	2.2	1.5	0.6	1.8	-1.1
38	H	1.7	2.0	-0.4	1.7	-2.1
			MOAD	**0.3**	**MOAD**	**0.3**

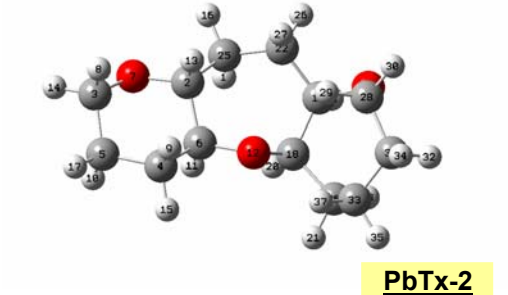
* indicates carbon connection
** rest of molecule

Table 12. Comparison of ACD Labs and calculated chemical shifts versus literature values of chemical shifts for the 6-7-7 ring system.



#	atom	PbTx-1 (MeOH) exp	corrected ACD SHIFT	difference exp-ACD	corrected calc shift	difference exp-calc.
2	C	87.2	80.8	6.4	78.6	8.6
3	C	81.9	76.6	5.3	75.3	6.6
4	C	46.5	30.6	16.0	36.3	10.2
5	C	76.1	73.7	2.4	80.5	-4.4
6	C	85.5	79.3	6.2	76.0	9.5
18	C	85.4	72.5	12.9	80.4	5.0
19	C	86.8	74.5	12.3	79.8	7.0
22	C	35.2	29.3	6.0	32.9	2.3
25	C	37.4	28.7	8.8	37.0	0.4
28	C	90.2	78.2	12.0	75.6	14.6
31	C	80.2	81.3	-1.1	85.7	-5.5
33	C	30.2	22.9	7.3	30.6	-0.4
36	C	31.2	29.2	2.0	35.7	-4.5
			MOAD	**7.6**	**MOAD**	**6.1**

Table 13. Comparison of ACD Labs and calculated chemical shifts versus literature values of chemical shifts for the 6-7-7 ring system.

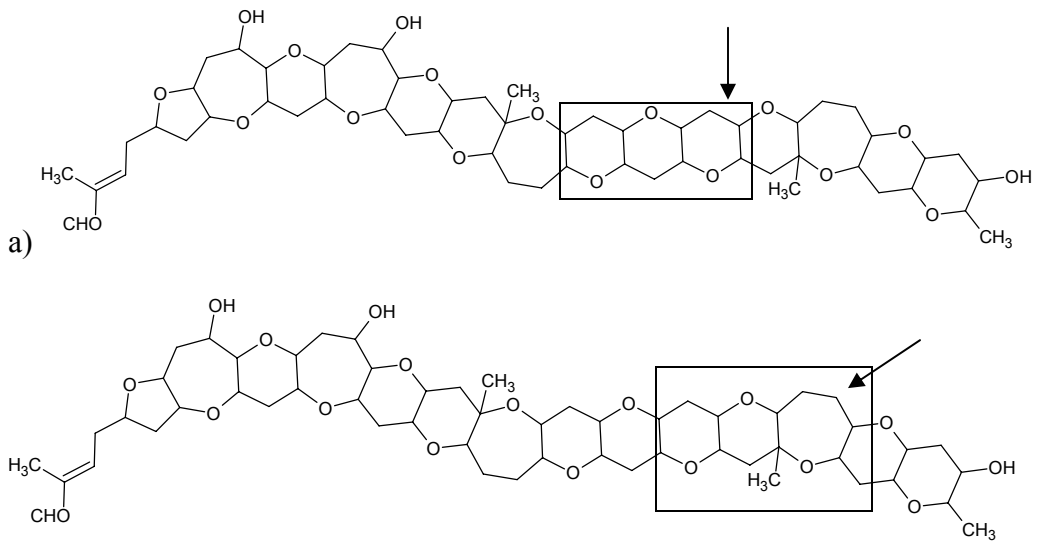


#	atom	PbTx-2 (MeOH) exp	corrected ACD SHIFT	difference exp-ACD	corrected calc shift	difference exp-calc.
2	C	84.5	80.8	3.7	78.6	5.9
3	C	78.2	76.6	1.6	75.3	2.9
4	C	43.5	30.6	13.0	36.3	7.2
5	C	74.4	73.7	0.7	80.5	-6.1
6	C	82.7	79.3	3.4	76.0	6.7
18	C	83.4	72.5	10.9	80.4	3.0
19	C	86.9	74.5	12.4	79.8	7.1
22	C	32.2	29.3	3.0	32.9	-0.7
25	C	34.2	28.7	5.6	37.0	-2.8
28	C	87.1	78.2	8.9	75.6	11.5
31	C	78.1	81.3	-3.2	85.7	-7.6
33	C	36.9	22.9	14.0	30.6	6.3
36	C	28.2	29.2	-1.0	35.7	-7.5
			MOAD	**6.2**	**MOAD**	**5.8**
1	H	1.5	1.5	0.0	1.4	0.1
8	H	3.2	3.6	-0.4	3.1	0.1
9	H	1.4	1.5	-0.1	1.3	0.1
10	H	n/a*	4.1		3.7	
11	H	3.4	3.6	-0.2	2.6	0.8
13	H	3.1	3.5	-0.4	2.8	0.3
14	H	n/a**	4.1		4.1	
15	H	2.0	1.5	0.6	2.1	-0.1
16	H	1.7	1.6	0.1	2.0	-0.3
20	H	3.6	3.8	-0.2	3.4	0.1
21	H	2.0	2.0	0.0	1.9	0.1
24	H	3.5	3.7	-0.2	3.5	0.0
26	H	1.9	1.6	0.3	1.8	0.1
27	H	1.9	1.9	0.0	1.8	0.1
29	H	3.1	4.0	-0.9	3.8	-0.7
30	H	n/a**	4.5		3.2	
32	H	n/a**	3.7		3.6	
34	H	n/a*	3.8		3.9	
35	H	1.6	1.4	0.2	1.3	0.3
37	H	1.7	1.5	0.2	1.8	-0.1
38	H	1.5	2.0	-0.6	1.7	-0.2
			MOAD	**0.4**	**MOAD**	**0.2**

* indicates carbon connection
** rest of molecule

In comparing the 6-6-6 ring system to the literature values reported for Gymnocin A in $CDCl_3$ (Table 7) it is apparent that the computed values of carbon shifts have a larger MOAD than the *ACD/Labs* predicted values. This means that *ACD/Labs* software predicted numbers closer to the literature values than our calculations. One explanation for this could be seen in carbon number 32. This carbon has a literature value shift of 70.1 ppm while the calculated value of this shift using *Gaussian 03* was 80.3 ppm, a difference of 10.2 ppm. This difference contributed a lot to the MOAD. This outlier lies on the terminal six-membered ring at the position seen in Figure 13. The reason for this chemical shift being so different from the expected value is unknown. The geometry of this molecule was checked and no problems were found. Again, a larger basis set may have prevented this problem, but this was not practical due to cpu time restrictions. The hydrogen shifts calculated by *Gaussian 03* were closer to the literature values than *ACD/Labs* software predicted. The MOAD of the calculated values for this system is 0.3 ppm while the MOAD for the ACD predicted values is 0.6 ppm.

The 6-6-7 ring system was also compared to Gymnocin A in $CDCl_3$ (Table 8). These results again show that for the carbon chemical shifts, *ACD/Labs* was closer to the literature results than the calculated values. This could be due to another outlier. Carbon number 19 has a literature chemical shift of 29.4 ppm while the calculated chemical shift is 40.7 ppm. This is a difference of 11.3 ppm. This contributed to the MOAD making it higher than that of *ACD/Labs*. Carbon 19 is on the seven-membered ring of this system in the position seen in Figure 13. The geometry of this structure was checked and no problems were found. Again the reason for this outlier is unknown. The hydrogen chemical shifts were again better than those predicted by *ACD/Labs* software for this ring



a)

b)

Figure 13. Positions of outliers seen in the carbon chemical shifts data for a) the 6-6-6 ring system and b) the 6-6-7 ring system

subsystem. The MOAD for the calculated values is 0.6 ppm while the MOAD of ACD's predicted values is 0.8 ppm.

The 6-7-6 ring system was also compared to Gymnocin A in $CDCl_3$ (Table 9). These results show that the calculated values were better than those predicted by *ACD/Labs*. For the carbon chemical shifts, the MOAD from *ACD/Lab*'s values is 5.1 ppm while the MOAD from the calculated values was only 4.8 ppm. For the hydrogen chemical shifts the MOAD from *ACD/Lab*'s values is 0.6 ppm. The MOAD from the calculated values is only 0.4 ppm.

The 6-7-8 ring system was compared with a ciguatoxin, CTx-3 in C_5D_5N (Table 10). There was no carbon chemical shift data in the literature for this particular toxin. The hydrogen data for this particular ring system shows that the calculated values are identical to the values predicted by *ACD/Labs*. The MOAD for both was 1.8 ppm.

The 6-7-7 ring system was compared to three different brevetoxins, PbTx-3, PbTx-1, and PbTx-2. In the comparison to PbTx-3 (Table 11) it is seen that the calculated values for the carbon chemical shifts are closer to the literature value than *ACD/Lab's* predicted values. The MOAD of the calculated values from the carbon shifts is 6.5 ppm while the MOAD from *ACD/Lab's* predicted shifts is 8.1 ppm. For the hydrogen chemical shifts, the MOAD for the calculated values is the same as the MOAD for *ACD/Lab's* predicted values. They are both 0.3 ppm.

For the comparison to PbTx-1 (Table 12), again the carbon chemical shift data shows that the calculated values are closer to the literature values than *ACD/Lab's* predicted values. The MOAD from the calculated values is 6.1 ppm while the MOAD

from *ACD/Lab's* values is 7.6 ppm. There was no hydrogen chemical shift data for PbTx-1 in the literature.

For the comparison to PbTx-2 (Table 13), both the carbon and the hydrogen data show that the calculated values are closer to the literature values. The MOAD in the carbon spectrum from the calculated values is 5.8 ppm while the MOAD from *ACD/Lab's* predicted values is 6.2 ppm. The MOAD in the hydrogen specrum from the calculated values is 0.2 ppm while the MOAD from the *ACD/Lab* values is 0.4 ppm.

There was no coupling constant information found in the literature surveyed, so the coupling constant calculations could not be compared to known values. They were however compared to the *ACD/Labs* values with good results. These results can be seen in Table 14,Appendix C.

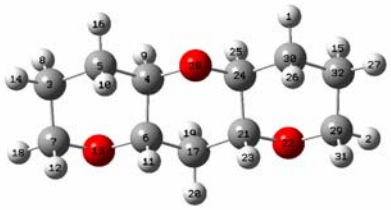
As can be seen from this data, the NMR values calculated in this research are very close to the actual literature values with certain exceptions. Because of this, this data can be used to aid in structural elucidation of new or unknown trans-fused polyether ring compounds. An example of how this research can be used is described below.

A novel compound was isolated and purified at the Center for Marine Science in Wilmington, NC. This compound is a ladder frame polyether similar to a brevetoxin, but it is not a brevetoxin. It has a molecular formula of $C_{39}H_{62}O_{11}$ and has a molecular weight of 706 amu. This compound actually competes with brevetoxin for the binding site on sodium channels but does not result in the toxic effects observed for brevetoxin. Several NMR experiments have been performed on this compound including ^{1}H NMR, ^{13}C NMR, COSY, TOCSY, HMQC, and HMBC. The structure has been almost totally determined. One problem that has been encountered however, is the placement of two

Table 14. Calculated coupling constants compared to *ACD/Labs* values for 6-6-6 ring system

666 - 1 conformer

Hydrogens	wt. ave	ACD J	Diff wt. ave - ACD
12-18	12.4	12.0	0.4
8-18	2.6	3.1	-0.6
14-18	1.2	1.7	-0.5
8-12	9.1	12.8	-3.7
12-14	2.4	3.0	-0.6
8-14	12.4	12.9	-0.5
8-16	2.6	3.2	-0.6
8-10	9.0	12.6	-3.7
14-16	1.2	1.7	-0.5
10-14	2.7	3.3	-0.6
10-16	12.4	12.9	-0.5
9-10	9.1	12.8	-3.7
9-16	2.3	2.8	-0.6
9-11	9.2	13.0	-3.8
11-19	9.0	12.8	-3.7
11-20	2.2	2.8	-0.6
19-20	12.4	12.5	-0.1
19-23	9.0	12.8	-3.7
20-23	2.2	2.8	-0.6
23-25	9.2	13.0	-3.8
1-25	2.3	2.8	-0.6
25-26	9.1	12.8	-3.7
1-26	12.4	12.9	-0.5
1-27	1.2	1.7	-0.5
1-15	2.6	3.2	-0.6
26-27	2.7	3.3	-0.6
15-26	9.0	12.6	-3.7
15-27	12.4	12.9	-0.5
27-31	2.4	3.0	-0.6
2-27	1.2	1.7	-0.5
15-31	9.1	12.8	-3.7
2-15	2.6	3.1	-0.6
2-31	12.4	12.0	0.4
			MOAD = 1.5



hydroxyl groups on the left had side of the molecule (Figure 14). Their exact placement is not known, nor is it known whether they are adjacent to each other or separated by one carbon. In order to aid in the determination of the structure, the data from the 6-7-7 ring system was used because the left side of the unknown compound consists of two seven-membered rings. The carbon chemical shift data of the 6-7-7 ring system was placed into a spreadsheet and corrections were made for each of the placements of the hydroxyl groups. This data was then compared to the actual carbon NMR data. The goal of this project was to determine the position of the hydroxyl groups. The results of this can be seen in Table 15. As can be seen in this table, the first column, labeled "calculated" is the calculated carbon chemical shift for the 6-7-7 ring system. The next column labeled "corrected" shows the carbon chemical shifts with corrections for attachments to carbon and oxygen as the structure shows. The next column labeled "in order" is simply those corrected chemical shifts in numerical order making comparison to the actual NMR spectral data easier. The next column labeled "spectra" shows the actual NMR carbon chemical shifts. This shows a best fit model. Each of the actual carbon shifts was placed next to the closest corrected chemical shift to see how well the actual data fit into the calculated spectrum. Note that these are not NMR assignments. The next column labeled "diff" shows the difference between the calculated chemical shift and the actual chemical shift. Using this model, the conformational option that had the smallest difference in these numbers should be the correct conformer according to this data. To quantify this, a total of the differences was taken as well as an MOAD. As can be seen in the table, structure option number two had the smallest total difference as well as the

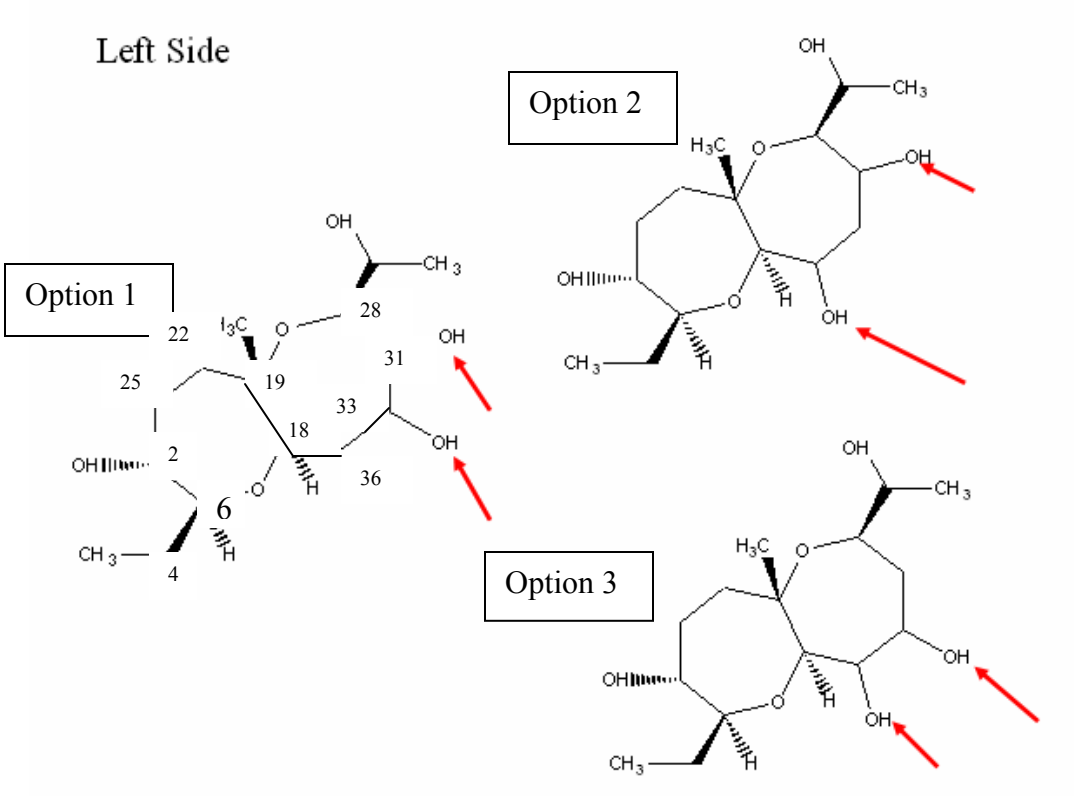


Figure 14. Left side of unknown compound. Hydroxyl groups could be at any one of these positions.

Table 15. Table of calculated carbon chemical shift data versus actual carbon NMR data for three different hydroxyl placement options.

Option 1					
#	Calculated	Corrected	in order	Spectra	difference
2	76.9	76.9	29.4	28.8	0.6
4	32.0	41.0	29.8	29.6	0.2
6	76.3	76.3	31.3	30.5	0.8
18	76.7	76.7	41.0	36.0	5.0
19	73.5	82.5	68.0	70.1	2.1
22	29.4	29.4	73.0	73.8	0.8
25	29.8	29.8	76.3	75.5	0.8
28	59.0	68.0	76.7	78.1	1.4
31	30.0	80.0	76.9	78.5	1.6
33	23.0	73.0	80.0	83.5	3.5
36	31.3	31.3	82.5	86.0	3.5
					sum: 20.3
					average: 1.8

Option 2					
#	Calculated	Corrected	in order	Spectra	difference
2	76.9	76.9	23.0	28.8	5.8
4	32.0	41.0	29.4	29.6	0.2
6	76.3	76.3	29.8	30.5	0.7
18	76.7	76.7	41.0	36	5.0
19	73.5	82.5	68.0	70.1	2.1
22	29.4	29.4	76.3	73.8	2.5
25	29.8	29.8	76.7	75.5	1.2
28	59.0	68.0	76.9	78.1	1.2
31	30.0	80.0	80.0	78.5	1.5
33	23.0	23.0	81.3	82.0	0.7
36	31.3	81.3	82.5	83.5	1.0
					sum: 21.9
					average: 2.0

Option 3					
#	Calculated	Corrected	in order	Spectra	difference
2	76.9	76.9	29.4	28.8	0.6
4	32.0	41.0	29.8	29.6	0.2
6	76.3	76.3	30.0	30.5	0.5
18	76.7	76.7	41.0	36	5.0
19	73.5	82.5	68.0	70.1	2.1
22	29.4	29.4	73.0	73.8	0.8
25	29.8	29.8	76.3	75.5	0.8
28	59.0	68.0	76.7	78.1	1.4
31	30.0	30.0	76.9	78.5	1.6
33	23.0	73.0	81.3	82.0	0.7
36	31.3	81.3	82.5	83.5	1.0
					sum: 14.7
					average: 1.3

smallest MOAD. Therefore according to this research, the left side of the compound has the hydroxyl groups placed in the positions seen in partial structure option three.

The chemical shift data calculated in this thesis research show better results than are seen in *ACD/Labs* and could be very useful in aiding the identification of unknown transfused polyethers. This is illustrated by analysis of the data of an unknown polyether, and using this data to determine the placement of the hydroxyl groups in the ring structure. Using a library of calculated chemical shifts could help to determine the size of the rings in these polyether ring compounds, as well as the placement of oxygens or other side groups attached to the rings.

REFERENCES

[1] M. Satake, M. Shoji, Y. Oshima, H. Naoki, T. Fujita, T. Yasumoto, Tetrahedron Letters. 43 (2002) 5829-5832

[2] M. Satake, M. Fukue, A Legrand, P. Cruchet, T. Yasumoto, Tetrahedron Letters. 39 (1998) 1197-1198

[3] R. Crouch, G. Martin, R. Dickey, D. Baden, R. Gawley, K. Rein, E. Mazzola, Tetrahedron Letters. 51 (1995) 8409-8422

[4] K. Murata, M. Satake, H. Naoki, H. Kaspar, T. Yasumoto, Tetrahedron Letter. 54 (1998) 735-742

[5] H. Ishida, A. Nozawa, K. Totoribe, N. Nuramatsu, H. Nakaya, K. Tsuji, K. Yamaguchi, T. Yasumoto, H. Kaspar, N. Berkett, T. Kosuje, Tetrahedron Letters. 36 (1995) 725-728

[7] Groves, Hart, The Ocean World Encyclopedia, McGraw-Hill, New York (1980)

[8] B. Halstead, Poisonous and Venomous Marine Animals of the World, Darwin Press, Princeton (1988)

[9] Campbell, Biology, 4th edition, Benjamin/Cummings Publishing, Riverside, CA (1977)

[10] R. Gawley, K. Rein, G. Jeglitsch, D. Adams, E. Theodorakis, J. Tiebes, KC Nicolaou, D. Baden, Chemistry and Biology. 2 (1995) 533-541

[11] C. Cramer, Essentials of Computational Chemistry, Wiley, West Sussex, England (2002)

[12] D. Chesnut, Reviews in Computational Chemistry. 8 (1996) 2-26

[13] A. C. Dios, Journal of Progress in Nuclear Magnetic Spectroscopy. 29 (1996) 237-243

[14] T. Helgaker, M. Jaszuiski, K. Ruud, Chemistry Reviews. 99 (1999) 293-352

[15] W.J. Hehre, L. Radom, P. Schleyer, J.A. Pople, Ab Initio Molecular Orbital Theory. Wiley, New York (1986)

[16] D.B. Chesnut, C.K. Foley, Chemical Physical Letters. Vol. 118, No. 3 (1985) 316-321

[17] R. Ditchfield, Molecular Physics. Vol. 27, No. 4 (1974) 789-807

[18] *Spartan*, version 5.0, Wavefunction, Inc. Irvine, CA (1997)

[19] M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery, Jr., T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez, and J. A. Pople, *Gaussian 03*, Revision B.01, Gaussian, Inc., Pittsburgh PA (2003)

[20] R. Silverstein, G. Bassler, T. Morril, Spectrometric Identification of Organic Compounds 5th edition. Wiley, New York (1991) 218

[21] J. Foresman, A. Frisch, Exploring Chemistry with Electronic Structure Methods 2nd edition. Gaussian, Inc, Pittsburgh (1993) 118-120

[22] A. Frisch, M. Frisch, G. Trucks. Gaussian 03 User's Reference. Gaussian, Inc. Pittsburgh (1994) 26

[23] *Gaussview 03*, Gaussian, Inc, Wallingford, CT (2003)

[24] D. Pavia, G. Lampman, G. Kriz, Introduction to Spectroscopy 3rd edition. Harcourt, Orlando (2001) 225

[25] C. Haasnoot, F. de Leeuw, C. Altona, Tetrahedron Letters. 36 (1980) 2783-2792

[26] *ACD/Labs*, version 4.5, Advanced Chemistry Developments, Toronto, ON (2001)

Appendix A. Weighted average of chemical shifts

6-7-6 - 1 conformer

#	atom	conf. 1 (100%)	wt. ave
2	C	26.3	26.3
3	C	75.0	75.0
5	C	77.2	77.2
6	C	62.3	62.3
7	C	31.5	31.5
19	C	71.2	71.2
23	C	73.3	73.3
24	C	32.2	32.2
25	C	62.4	62.4
26	C	31.6	31.6
29	C	31.2	31.2
33	C	26.3	26.3
1	H	0.8	0.8
8	H	2.7	2.7
10	H	2.3	2.3
11	H	2.6	2.6
12	H	1.1	1.1
13	H	1.3	1.3
14	H	2.6	2.6
15	H	1.2	1.2
16	H	1.4	1.4
17	H	3.3	3.3
18	H	1.6	1.6
21	H	3.3	3.3
22	H	2.8	2.8
27	H	2.7	2.7
28	H	1.7	1.7
30	H	1.5	1.5
31	H	1.5	1.5
32	H	1.5	1.5
34	H	1.1	1.1
35	H	0.8	0.8

6-7-7 - 2
conformers

#	atom	conf. 1 (29.6%)	conf. 2 (70.5%)	wt. ave
2	C	76.9	73.1	74.3
3	C	62.3	61.8	62.0
4	C	32.0	32.0	32.0
5	C	26.3	26.1	26.2
6	C	76.3	69.7	71.7
18	C	76.7	75.8	76.1
19	C	73.5	76.2	75.5
22	C	29.4	28.2	28.6
25	C	29.8	33.8	32.7
28	C	59.0	63.6	62.3
31	C	32.0	31.1	31.4
33	C	23.0	27.6	26.3
36	C	31.3	31.4	31.4
1	H	0.9	1.1	1.0
8	H	2.7	2.7	2.7
9	H	1.1	1.1	1.1
10	H	1.2	1.1	1.2
11	H	2.4	2.4	2.4
13	H	2.5	2.6	2.6
14	H	3.3	3.3	3.3
15	H	1.6	1.5	1.5
16	H	1.5	1.7	1.6
17	H	0.9	0.8	0.8
20	H	3.0	3.1	3.0
21	H	1.5	1.5	1.5
24	H	3.1	3.1	3.1
26	H	1.7	1.3	1.4
27	H	1.2	1.4	1.4
29	H	3.0	3.3	3.2
30	H	3.0	2.5	2.6
32	H	1.3	0.8	0.9
34	H	0.9	1.3	1.2
35	H	1.0	0.8	0.9
37	H	1.5	1.3	1.4
38	H	1.2	1.3	1.3

6-7-8 - 7 conformers

#	atom	conf. 1 (47.1%)	conf. 2 (3.1%)	conf. 3 (41.8%)	conf. 4 (5.2%)	conf. 5 (1.8%)	conf. 6 (0.7%)	conf. 7 (0.2%)	wt. ave
2	C	31.9	31.4	32.1	31.5	32.0	32.3	32.0	31.9
3	C	62.3	61.9	62.3	61.9	62.6	62.3	62.3	62.2
4	C	77.6	72.0	76.7	72.0	73.6	76.5	77.6	76.6
6	C	75.8	73.6	76.8	73.6	70.2	77.1	76.5	75.8
7	C	26.4	26.3	26.4	26.3	26.3	26.4	26.4	26.4
17	C	76.7	72.3	78.6	72.8	77.9	77.9	74.9	77.1
19	C	71.1	76.8	79.5	69.1	82.5	77.3	80.3	74.9
21	C	33.1	31.3	32.1	29.7	31.5	32.5	33.4	32.4
24	C	29.9	31.2	29.4	31.3	29.7	29.5	30.0	29.8
30	C	24.2	29.9	34.4	30.4	33.5	24.0	30.0	29.1
33	C	63.2	68.3	67.4	63.3	68.0	63.3	65.0	65.2
34	C	26.6	25.2	28.5	28.2	29.5	19.4	21.9	27.4
35	C	23.3	24.4	27.0	25.3	25.9	26.6	26.1	25.0
40	C	32.8	28.3	40.5	34.8	40.0	36.7	35.9	36.1
1	H	1.6	1.6	0.8	1.6	1.5	1.5	1.5	1.3
5	H	0.8	0.8	2.6	0.8	0.8	0.8	0.8	1.6
8	H	2.6	2.6	2.4	2.6	2.6	2.7	2.6	2.5
9	H	2.3	2.4	2.6	2.4	2.7	2.4	2.3	2.5
11	H	2.6	2.6	1.2	2.6	2.8	2.6	2.7	2.0
12	H	1.2	1.2	1.1	1.2	1.2	1.2	1.3	1.2
13	H	1.0	1.1	3.3	1.1	1.0	1.1	1.0	2.0
14	H	3.3	3.3	1.4	3.3	3.3	3.3	3.3	2.5
15	H	1.4	1.6	1.6	1.6	1.2	1.4	1.4	1.5
18	H	1.6	1.3	1.6	1.4	1.5	1.6	1.5	1.6
20	H	1.6	1.6	2.9	1.4	1.7	1.6	1.7	2.1
22	H	2.8	3.0	2.8	2.9	2.9	2.9	3.0	2.8
23	H	2.9	2.7	1.0	2.7	2.5	2.6	2.8	2.1
25	H	1.2	1.6	1.4	1.7	1.3	1.1	1.3	1.4
26	H	1.6	1.2	1.1	1.2	1.7	1.4	1.8	1.4
28	H	1.1	1.2	2.7	1.4	1.2	1.4	1.4	1.8
29	H	2.9	2.6	1.3	2.9	2.8	2.8	2.7	2.2
31	H	0.5	1.3	0.7	0.9	1.4	0.8	1.5	0.7
32	H	1.5	0.8	1.4	1.3	0.7	1.1	0.6	1.4
36	H	1.1	1.3	0.8	0.9	1.5	1.3	1.5	1.0
37	H	1.0	1.1	1.0	1.2	0.8	1.1	0.9	1.0
38	H	1.4	0.8	1.5	1.2	1.2	1.3	1.4	1.4
39	H	1.2	1.6	3.3	1.2	1.4	1.1	1.0	2.1
41	H	3.1	3.4	1.5	3.1	3.4	3.0	3.4	2.5

6-7-9 - 18 conformers

#	atom	conf. 1 (20.9%)	conf. 2 (7.6%)	conf. 3 (40.4%)	conf. 4 (3.9%)	conf. 5 (2.3%)	conf. 6 (1.4%)	conf. 7 (6.4%)	conf. 8 (0.6%)	wt. ave
2	C	31.9	32.1	32.2	32.1	32.0	32.1	32.3	32.1	32.1
3	C	77.3	73.4	73.1	73.3	76.5	74.0	74.2	72.3	74.5
4	C	62.4	61.7	61.7	61.7	62.3	61.7	62.5	61.1	62.0
6	C	26.5	26.2	26.1	26.1	26.5	26.2	26.4	26.2	26.3
7	C	75.7	67.7	68.3	67.9	76.2	65.9	70.7	68.3	71.0
14	C	29.3	34.3	34.2	34.0	29.3	34.0	27.3	30.3	32.0
20	C	30.0	29.0	29.8	28.2	28.1	27.2	26.6	29.4	29.5
22	C	70.0	77.0	77.7	74.7	69.9	77.1	67.0	72.9	75.2
26	C	79.5	70.0	78.5	76.2	81.1	67.7	80.0	75.4	78.0
30	C	24.4	31.5	27.0	30.1	23.0	29.4	24.5	27.3	27.2
33	C	63.0	68.4	68.0	64.2	62.0	69.8	61.9	65.0	66.1
34	C	20.1	31.1	30.2	30.5	27.6	28.9	20.0	29.8	26.3
37	C	28.1	26.4	27.3	28.6	30.3	30.5	28.5	24.7	27.7
38	C	19.4	26.0	27.9	29.9	19.2	22.9	19.0	26.4	24.4
41	C	28.5	32.8	35.2	35.4	37.0	34.4	28.4	33.6	32.2
1	H	1.6	1.5	1.5	1.5	1.5	1.5	1.5	1.6	1.5
8	H	2.5	2.6	2.6	2.6	2.5	2.6	2.8	3.3	2.6
9	H	2.7	2.6	2.6	2.6	2.7	2.6	2.6	2.6	2.6
11	H	1.2	1.2	1.1	1.1	1.2	1.2	1.1	1.2	1.2
12	H	2.4	2.5	2.4	2.4	2.3	2.6	2.6	2.7	2.4
13	H	1.1	1.1	1.1	1.0	1.1	1.1	1.1	1.3	1.1
15	H	3.3	3.3	3.3	3.3	3.3	3.3	3.2	3.3	3.3
16	H	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8
17	H	1.3	1.2	1.4	1.4	1.6	1.3	1.4	1.0	1.3
18	H	1.4	1.6	1.6	1.6	1.5	1.6	2.2	2.0	1.6
19	H	0.9	1.0	1.0	1.1	0.9	1.1	1.3	1.2	1.0
21	H	1.8	1.3	1.3	1.2	1.7	1.4	1.2	0.9	1.4
23	H	1.3	1.6	1.5	1.5	1.3	1.5	1.4	1.5	1.5
25	H	2.7	2.8	2.7	2.9	2.8	2.9	2.7	2.5	2.7
27	H	2.6	3.4	3.2	3.2	2.8	3.3	2.6	2.7	3.0
28	H	1.8	1.4	1.4	1.3	1.5	1.5	1.6	1.7	1.5
29	H	2.7	2.8	2.9	2.8	2.9	2.4	2.8	2.9	2.8
31	H	0.7	0.8	0.6	1.4	0.4	1.3	0.7	0.5	0.8
32	H	1.0	1.0	1.0	0.9	1.4	0.8	1.1	1.3	1.0
35	H	1.5	0.8	1.0	1.2	1.0	1.4	1.5	1.3	1.3
36	H	1.1	1.3	1.0	0.8	1.0	0.8	1.1	1.1	1.0
39	H	1.0	1.3	1.5	1.3	1.6	1.1	1.1	2.3	1.3
40	H	0.9	0.7	1.2	1.3	1.4	1.1	0.9	0.8	1.0
42	H	1.1	1.6	1.5	1.7	1.2	2.0	1.1	1.7	1.4
43	H	0.5	1.1	0.7	0.5	0.4	0.7	0.5	0.8	0.6
44	H	3.0	3.2	3.3	3.1	3.2	3.5	3.1	3.4	3.2

conf. 9 (0.1%)	conf. 10 (3.0%)	conf. 11 (0.4%)	conf. 12 (0.3%)	conf. 13 (8.1%)	conf. 14 (2.9%)	conf. 15 (0.1%)	conf. 16 (0.4%)	conf. 17 (1.2%)	wt. ave
32.1	32.0	32.0	32.2	32.1	32.0	32.2	32.4	32.4	32.1
73.6	73.1	76.8	72.3	76.0	76.8	72.3	73.5	74.0	74.5
61.7	61.8	62.3	61.1	62.2	62.3	61.2	62.0	62.3	62.0
26.2	26.1	26.4	26.1	26.5	26.5	26.1	26.3	26.4	26.3
67.0	69.1	76.3	68.1	76.3	76.1	67.6	70.1	70.9	71.0
34.1	33.9	29.7	30.2	29.8	29.5	30.0	28.5	28.0	32.0
28.0	28.4	27.0	29.3	30.2	31.2	28.3	28.7	29.6	29.5
75.3	75.9	75.2	77.7	80.0	80.6	72.9	74.6	78.0	75.2
66.8	77.3	77.7	75.1	81.0	77.0	74.7	76.3	77.2	78.0
26.6	28.8	29.2	31.5	30.2	30.0	28.9	28.8	31.2	27.2
62.6	61.7	58.0	67.0	67.1	71.8	66.1	66.6	70.9	66.1
25.2	20.7	20.7	23.5	21.1	28.6	29.8	29.7	28.1	26.3
21.1	28.5	29.0	32.2	27.5	27.6	33.1	32.6	25.0	27.7
22.5	26.4	20.8	19.3	21.7	21.6	22.4	22.6	27.9	24.4
32.0	27.8	26.5	33.8	29.3	28.4	37.8	37.2	28.5	32.2
1.5	1.5	1.6	1.6	1.5	1.6	1.6	1.5	1.5	1.5
2.6	2.6	2.5	3.3	2.5	2.5	3.3	3.0	2.9	2.6
2.6	2.6	2.7	2.6	2.7	2.7	2.6	2.6	2.6	2.6
1.1	1.1	1.2	1.1	1.2	1.2	1.1	1.1	1.2	1.2
2.5	2.3	2.3	2.7	2.3	2.4	2.7	2.7	2.6	2.4
1.1	1.1	1.1	1.3	1.1	1.2	1.2	1.1	1.1	1.1
3.3	3.3	3.3	3.2	3.3	3.3	3.2	3.2	3.2	3.3
0.8	0.8	0.9	0.7	0.8	0.8	0.8	0.7	0.8	0.8
1.4	1.3	1.2	0.6	1.3	0.8	0.6	0.7	1.1	1.3
1.6	1.7	1.5	2.0	1.5	1.4	2.1	2.3	2.2	1.6
1.1	1.0	0.9	1.2	0.8	0.9	1.2	1.3	1.3	1.0
1.3	1.3	1.5	0.9	1.7	1.7	0.9	1.1	1.2	1.4
1.5	1.5	1.4	1.4	1.5	1.4	1.4	1.2	1.4	1.5
3.0	3.1	3.1	2.6	2.7	2.6	2.5	2.5	2.5	2.7
3.5	3.1	2.9	2.5	2.8	2.7	2.6	2.6	2.7	3.0
1.3	1.5	1.6	1.8	1.8	1.5	1.9	1.9	1.5	1.5
2.7	2.6	3.0	2.6	2.6	2.4	2.8	2.7	2.7	2.8
1.6	1.5	0.7	1.3	1.5	1.3	0.8	0.7	1.4	0.8
1.0	0.7	1.4	0.9	0.7	0.9	1.2	1.2	0.7	1.0
1.1	1.9	0.8	1.2	1.9	1.3	1.1	1.1	1.5	1.3
1.0	0.8	1.9	0.8	0.8	0.9	1.4	1.4	0.7	1.0
1.2	1.1	1.0	1.0	1.1	1.0	1.3	1.3	1.8	1.3
0.9	0.9	1.1	1.0	1.0	1.0	0.7	0.7	1.1	1.0
1.7	1.5	1.5	2.2	1.2	2.1	1.9	1.9	1.7	1.4
0.9	0.7	1.1	1.0	0.5	1.2	1.2	1.2	0.7	0.6
3.1	3.1	2.9	3.4	3.4	3.5	3.2	3.2	3.5	3.2

6-8-6 - 1 conformer

atom	#	conf. 1 (100%)	wt. ave
2	C	68.6	68.6
3	C	29.1	29.1
4	C	62.0	62.0
5	C	26.5	26.5
7	C	69.6	69.6
18	C	33.6	33.6
19	C	74.4	74.4
21	C	31.5	31.5
22	C	66.0	66.0
24	C	20.4	20.4
28	C	34.3	34.3
31	C	26.5	26.5
36	C	62.1	62.1
1	H	1.2	1.2
8	H	1.1	1.1
9	H	2.6	2.6
10	H	1.2	1.2
12	H	3.1	3.1
13	H	2.9	2.9
14	H	1.4	1.4
15	H	3.3	3.3
16	H	0.8	0.8
17	H	1.5	1.5
20	H	2.5	2.5
25	H	1.0	1.0
26	H	1.6	1.6
27	H	1.4	1.4
29	H	1.2	1.2
30	H	2.7	2.7
32	H	1.4	1.4
33	H	1.1	1.1
34	H	1.2	1.2
35	H	0.8	0.8
37	H	2.6	2.6
38	H	3.3	3.3

6-8-8 - 3 conformers

#	atom	conf. 1 (80.2%)	conf. 2 (6%)	conf. 3 (13.8%)	wt. ave
2	C	68.4	68.6	68.5	68.4
3	C	28.8	29.7	29.6	28.9
4	C	62.1	62.0	62.1	62.1
5	C	26.4	26.6	26.6	26.5
7	C	69.7	69.9	69.8	69.7
18	C	34.1	30.8	38.0	34.5
19	C	73.3	76.0	69.0	72.9
21	C	33.0	33.4	31.1	32.8
22	C	69.9	69.1	69.2	69.7
24	C	20.5	21.1	21.1	20.6
28	C	34.4	34.0	34.0	34.3
31	C	22.7	22.2	25.2	23.0
35	C	27.0	26.0	28.8	27.2
36	C	63.9	67.5	61.6	63.8
38	C	24.4	28.6	30.4	25.4
1	H	1.2	1.2	1.2	1.2
8	H	1.2	1.1	1.1	1.1
9	H	2.6	2.6	2.6	2.6
10	H	1.2	1.2	1.2	1.2
12	H	3.0	3.1	3.0	3.0
13	H	2.9	2.9	2.9	2.9
14	H	1.4	1.4	1.4	1.4
15	H	3.3	3.3	3.3	3.3
16	H	0.8	0.8	0.8	0.8
17	H	1.5	1.5	1.5	1.5
20	H	2.7	2.7	2.6	2.7
25	H	1.1	1.0	1.0	1.1
26	H	1.5	1.5	1.6	1.5
27	H	1.4	1.3	1.3	1.4
29	H	1.1	1.2	1.2	1.1
30	H	2.7	2.9	2.9	2.8
32	H	1.4	1.5	1.3	1.4
33	H	1.2	1.0	1.3	1.2
34	H	1.0	1.6	1.1	1.1
37	H	3.1	3.4	3.0	3.1
39	H	1.5	0.9	1.2	1.4
40	H	2.9	2.7	3.0	2.9
41	H	1.5	0.8	1.4	1.4
42	H	1.1	1.4	0.8	1.1
43	H	1.0	1.1	1.3	1.1
44	H	0.5	1.4	0.9	0.6

7-6-7 - 3 conformers

#	atoms	conf. 1 (98.5%)	conf. 2 (0.7%)	conf. 3 (0.8%)	wt. ave
2	C	68.1	72.9	68.3	68.2
3	C	68.1	68.3	73.0	68.2
5	C	72.5	72.7	71.9	72.5
6	C	72.5	72.0	72.7	72.5
7	C	39.7	39.3	39.2	39.7
16	C	36.7	36.6	32.7	36.6
17	C	61.4	61.5	61.4	61.4
18	C	61.4	61.4	61.5	61.4
21	C	29.9	29.6	29.8	29.9
23	C	20.8	22.0	20.7	20.8
26	C	36.7	32.8	36.6	36.6
31	C	29.9	29.9	29.7	29.9
35	C	20.8	20.7	22.0	20.8
4	H	1.7	1.8	1.8	1.7
8	H	2.5	2.5	2.5	2.5
9	H	0.9	0.9	1.3	0.9
10	H	2.7	2.7	2.6	2.7
11	H	2.7	2.7	2.7	2.7
12	H	1.3	1.3	1.3	1.3
13	H	2.5	2.4	2.6	2.5
19	H	3.0	2.7	3.0	3.0
20	H	3.2	3.3	3.2	3.2
22	H	1.2	1.4	1.2	1.2
24	H	1.2	1.1	1.2	1.2
25	H	1.2	1.3	1.2	1.2
27	H	1.1	1.1	1.1	1.1
28	H	1.7	1.6	1.7	1.7
29	H	1.7	1.7	1.6	1.7
30	H	0.9	1.3	0.9	0.9
32	H	3.2	3.2	3.3	3.2
33	H	3.0	3.0	2.7	3.0
34	H	1.2	1.2	1.1	1.2
36	H	1.2	1.1	1.4	1.2
37	H	1.2	1.2	1.3	1.2
38	H	1.1	1.1	1.1	1.1

7-6-8 - 6 conformers

#	atom	conf. 1 (15.8%)	conf. 2 (29.1%)	conf. 3 (51.2%)	conf. 4 (0.3%)	conf. 5 (0.4%)	conf. 6 (3.2%)	wt. ave
2	C	68.4	68.2	76.8	74.5	76.9	69.8	72.7
3	C	73.7	68.5	68.6	73.7	74.0	68.9	69.4
5	C	72.3	72.8	73.4	72.4	72.4	73.7	73.0
6	C	73.7	67.3	76.4	72.9	76.5	73.6	73.2
7	C	39.5	36.8	40.3	39.5	40.0	38.1	39.1
17	C	61.7	61.5	61.4	61.6	61.8	61.4	61.5
18	C	29.7	29.7	29.8	29.7	29.7	29.7	29.7
22	C	22.1	20.7	20.8	22.0	22.0	20.8	21.0
26	C	32.8	36.6	36.5	32.8	32.8	36.3	35.9
28	C	64.0	59.1	69.6	63.7	69.6	54.7	65.2
30	C	24.6	31.8	32.5	29.8	32.5	30.4	31.0
33	C	26.9	25.2	32.6	21.8	32.8	26.5	29.3
37	C	22.3	23.9	24.8	26.3	24.8	26.5	24.2
40	C	30.5	34.2	36.0	33.0	36.0	36.9	34.6
4	H	1.8	1.7	1.8	1.9	1.9	1.7	1.7
8	H	2.5	2.5	2.5	2.5	2.5	2.6	2.5
9	H	1.1	1.1	1.0	1.3	1.0	1.2	1.1
10	H	2.7	2.6	2.7	2.6	2.6	2.6	2.7
11	H	2.6	2.9	2.6	2.7	2.6	2.6	2.7
12	H	1.3	1.3	1.3	1.3	1.3	1.3	1.3
13	H	2.6	2.9	2.5	2.5	2.5	2.9	2.6
16	H	1.3	0.9	0.9	1.3	1.3	0.9	1.0
19	H	3.3	3.2	3.1	3.3	3.3	3.2	3.2
20	H	2.7	3.0	3.0	2.7	2.7	3.0	3.0
21	H	1.1	1.2	1.2	1.1	1.1	1.2	1.2
23	H	1.4	1.1	1.1	1.4	1.4	1.1	1.2
24	H	1.3	1.2	1.1	1.2	1.2	1.1	1.2
25	H	1.1	1.1	1.1	1.1	1.1	1.1	1.1
27	H	1.6	1.7	1.7	1.6	1.6	1.7	1.7
29	H	3.2	2.8	3.6	3.4	3.6	2.6	3.3
31	H	2.9	3.1	2.7	2.9	2.8	3.0	2.9
32	H	0.6	0.7	1.4	1.5	1.4	0.5	1.0
34	H	1.5	1.3	0.8	0.6	0.8	1.4	1.1
35	H	1.1	1.3	0.8	0.9	0.9	1.4	1.0
36	H	1.1	0.8	1.4	1.5	1.4	1.2	1.2
38	H	1.2	1.6	1.5	1.0	1.5	1.4	1.5
39	H	1.5	1.2	1.0	1.3	1.0	0.7	1.2
41	H	1.6	1.5	1.8	1.6	1.8	1.6	1.7

7-7-9 - 9 conformers

#	atom	conf. 1 (53.8%)	conf. 2 (5.1%)	conf. 3 (19.8%)	conf. 4 (11.1%)	conf. 5 (2.4%)	wt. ave
1	C	33.4	33.5	33.4	33.4	33.5	33.4
2	C	68.0	68.0	68.0	68.0	68.0	67.9
6	C	23.4	23.4	23.4	23.3	23.3	23.3
11	C	32.8	32.3	32.9	32.0	33.1	32.7
12	C	73.8	73.6	73.5	73.6	73.7	73.6
17	C	76.2	76.0	76.1	75.9	76.1	76.0
20	C	69.1	68.5	72.2	68.3	69.6	69.6
21	C	69.5	78.2	77.5	82.9	82.1	73.6
23	C	29.3	39.9	33.4	34.6	31.6	31.9
26	C	28.2	29.7	30.4	30.1	30.5	29.1
29	C	27.8	27.6	28.1	27.4	28.2	27.8
32	C	18.2	23.4	30.9	20.7	22.6	22.1
36	C	28.3	31.9	24.5	31.4	27.8	27.8
40	C	20.3	29.5	26.9	24.3	28.6	23.2
43	C	24.4	28.8	31.0	31.6	30.0	27.0
46	C	63.2	67.4	69.4	69.4	73.1	65.6
3	H	2.5	2.5	2.5	2.5	2.5	2.5
5	H	3.6	3.6	3.6	3.6	3.6	3.6
7	H	0.9	0.9	0.9	0.9	0.9	0.9
8	H	1.3	1.4	1.4	1.4	1.4	1.4
9	H	0.7	0.7	0.7	0.7	0.7	0.7
10	H	1.2	1.2	1.2	1.2	1.2	1.2
13	H	1.3	1.4	1.3	1.4	1.4	1.3
14	H	1.6	1.6	1.6	1.6	1.6	1.6
15	H	3.0	3.0	3.0	3.0	2.9	3.0
18	H	1.4	1.3	1.3	1.3	1.4	1.4
19	H	2.8	2.8	2.7	2.8	2.7	2.8
22	H	3.2	3.2	3.1	3.2	3.1	3.2
24	H	2.7	2.6	2.7	2.6	2.6	2.7
27	H	1.2	1.2	1.3	1.3	1.3	1.3
28	H	1.7	1.8	1.8	1.8	1.8	1.7
30	H	1.0	1.0	1.0	1.0	1.0	1.0
31	H	2.8	2.7	2.9	2.5	2.7	2.8
33	H	1.2	1.1	1.5	1.0	1.2	1.3
34	H	1.3	1.7	1.3	1.5	1.2	1.3
35	H	1.1	1.3	1.2	1.6	1.6	1.2
37	H	1.2	1.1	1.0	1.0	1.0	1.1
38	H	0.9	0.8	1.1	1.0	1.0	0.9
39	H	0.9	1.2	1.6	0.9	1.0	1.2
41	H	1.1	1.4	0.7	1.0	1.1	1.0
42	H	1.3	1.0	1.4	1.2	1.3	1.3
44	H	1.2	1.4	0.7	0.8	0.9	1.1
45	H	0.7	0.7	1.4	1.2	1.3	0.9
47	H	3.0	3.1	3.4	3.4	3.6	3.2

conf. 6 (0.4%)	conf. 7 (0.4%)	conf. 8 (6.8%)	conf. 9 (0.1%)	wt. ave
33.4	33.4	33.5	33.4	33.4
68.0	68.0	67.9	68.0	67.9
23.4	23.4	23.4	23.4	23.3
33.0	33.1	32.1	32.5	32.7
73.7	74.0	73.5	73.7	73.6
76.3	76.4	76.0	76.0	76.0
69.9	69.0	70.7	68.4	69.6
69.0	70.1	75.0	75.0	73.6
39.2	28.4	37.5	34.0	31.9
27.0	27.9	30.4	29.0	29.1
28.1	27.9	27.7	27.5	27.8
18.9	25.2	29.1	24.5	22.1
30.8	30.3	24.8	34.7	27.8
27.7	20.1	27.8	30.0	23.2
22.9	31.7	27.1	35.5	27.0
61.8	60.8	65.0	68.5	65.6
2.5	2.5	2.5	2.5	2.5
3.6	3.6	3.6	3.6	3.6
0.9	0.9	0.9	0.9	0.9
1.4	1.4	1.4	1.4	1.4
0.6	0.7	0.7	0.7	0.7
1.2	1.2	1.2	1.2	1.2
1.3	1.4	1.4	1.3	1.3
1.6	1.7	1.6	1.6	1.6
3.0	3.0	3.0	3.0	3.0
1.4	1.5	1.3	1.4	1.4
2.7	2.8	2.7	2.8	2.8
3.4	3.3	3.2	3.2	3.2
3.0	2.8	2.6	2.7	2.7
1.3	1.3	1.3	1.3	1.3
1.6	1.5	1.9	1.7	1.7
0.9	1.0	1.1	1.0	1.0
3.0	3.0	2.9	2.7	2.8
1.5	0.9	1.5	1.4	1.3
1.2	1.8	1.4	1.4	1.3
1.1	0.8	1.2	1.2	1.2
1.0	1.5	1.1	1.2	1.1
1.3	0.9	0.7	1.4	0.9
1.4	1.5	2.0	0.8	1.2
1.0	1.2	1.1	0.8	1.0
1.0	1.1	1.2	1.5	1.3
1.7	1.3	1.5	1.0	1.1
0.5	1.0	0.5	1.3	0.9
3.2	3.1	3.3	3.3	3.2

8-6-6 - 4 conformers

#	atom	conf. 1 (15.0%)	conf. 2 (7.5%)	conf. 3 (77.2%)	conf. 4 (0.4%)	wt. ave
2	C	64.5	57.9	63.2	63.8	63.1
4	C	31.8	29.9	30.6	28.2	30.8
6	C	24.7	26.8	24.0	25.8	24.3
11	C	24.3	26.7	31.4	23.8	30.0
14	C	27.3	32.9	31.0	28.3	30.6
17	C	65.2	70.6	70.2	67.0	69.6
18	C	69.7	67.3	69.5	69.9	69.4
21	C	33.6	34.2	34.7	35.1	34.5
25	C	70.0	69.3	69.1	69.7	69.3
28	C	63.9	64.3	63.8	63.1	63.9
31	C	62.2	62.1	62.1	62.2	62.2
33	C	26.1	26.0	26.0	26.1	26.0
36	C	30.1	30.1	30.1	29.9	30.1
1	H	2.7	2.6	2.8	3.0	2.8
3	H	3.4	3.2	3.3	3.5	3.3
7	H	1.4	1.5	1.1	0.8	1.2
8	H	0.7	0.6	1.0	1.3	0.9
9	H	1.3	1.3	1.3	1.4	1.3
10	H	0.9	1.1	1.1	1.2	1.1
12	H	1.6	1.5	1.4	2.2	1.4
13	H	1.3	0.7	1.0	0.9	1.0
15	H	1.7	1.6	1.7	1.7	1.7
16	H	1.2	1.4	1.3	1.3	1.3
20	H	3.5	3.3	3.4	3.8	3.4
22	H	3.0	3.1	2.8	3.0	2.9
23	H	1.0	0.9	1.0	1.0	1.0
24	H	1.4	1.4	1.3	1.4	1.3
26	H	1.8	1.8	1.7	1.7	1.7
29	H	2.4	2.4	2.4	2.4	2.4
30	H	2.8	2.6	2.5	2.7	2.6
32	H	3.3	3.3	3.3	3.3	3.3
34	H	2.7	2.7	2.7	2.7	2.7
35	H	1.3	1.3	1.3	1.3	1.3
37	H	0.9	0.9	0.9	0.9	0.9
38	H	1.4	1.4	1.4	1.4	1.4

Appendix B. Weighted average of coupling constants

6-6-7- 3 conformers

hydrogens	conf. 1 (97%)	conf. 2 (0.5)	conf. 3 (2.4%)	wt. ave
10-16	12.4	12.4	12.4	12.4
8-10	14.5	14.5	14.5	14.5
10-14	4.2	4.2	4.3	4.2
8-16	4.4	4.4	4.5	4.4
14-16	2.7	2.7	2.7	2.7
8-14	12.4	12.4	12.4	12.4
8-9	4.5	4.5	4.6	4.5
8-12	14.4	14.3	14.3	14.4
9-14	2.7	2.7	2.6	2.7
12-14	4.7	4.7	4.7	4.7
9-12	12.4	12.4	12.4	12.4
9-13	4.3	4.3	4.1	4.3
12-13	14.4	14.4	14.5	14.4
11-13	14.7	14.7	14.7	14.7
11-24	14.5	14.5	14.5	14.5
4-11	3.8	3.9	4.0	3.8
4-24	12.4	12.4	12.4	12.4
4-22	4.6	4.4	3.7	4.6
22-24	14.2	14.2	14.6	14.2
18-22	14.6	14.6	14.7	14.6
18-26	4.7	0.9	11.7	4.7
18-27	14.0	14.0	1.4	14.0
26-27	12.4	12.4	12.4	12.4
26-29	2.1	7.4	2.0	2.1
26-30	5.6	1.3	14.7	5.6
27-30	2.4	7.6	1.7	2.4
29-30	12.4	12.4	12.4	12.4
29-33	0.9	8.6	1.6	0.9
30-33	8.0	11.1	14.5	8.0
29-34	13.8	0.8	6.5	13.8
30-34	1.0	8.7	1.6	1.0
33-34	12.4	12.4	12.4	12.4
33-35	0.7	13.3	14.5	0.7
25-33	8.6	0.8	4.2	8.6
35-34	9.0	0.8	4.0	9.0
25-34	11.0	8.2	3.3	11.0
25-35	12.4	12.4	12.4	12.4
27-29	14.7	11.9	6.3	14.7

6-7-6- 1 conformer

hydrogens	conf. 1 (100%)	wt. ave
22-32	3.8	3.8
22-34	14.6	14.6
32-34	12.4	12.4
32-35	2.7	2.7
15-32	4.5	4.5
34-35	4.7	4.7
15-34	14.3	14.3
15-35	12.4	12.4
14-15	14.5	14.5
15-21	4.5	4.5
14-35	4.3	4.3
21-35	2.6	2.6
14-21	12.4	12.4
22-27	14.6	14.6
27-28	1.4	1.4
27-30	11.8	11.8
28-30	12.4	12.4
16-28	6.5	6.5
16-30	1.9	1.9
28-31	1.7	1.7
30-31	14.7	14.7
16-31	12.4	12.4
10-16	1.3	1.3
10-31	14.4	14.4
8-10	14.7	14.7
8-12	14.5	14.5
8-18	3.9	3.9
12-18	12.4	12.4
1-12	4.7	4.7
12-13	14.3	14.3
1-18	2.7	2.7
13-18	4.5	4.5
1-13	12.4	12.4
1-11	4.2	4.2
1-17	2.7	2.7
11-13	14.5	14.5
13-17	4.4	4.4
11-17	12.4	12.4

6-7-7- 2 conformers

hydrogens	conf. 1 (29.6%)	conf. 2 (70.5%)	wt. ave
8-14	12.4	12.4	12.4
8-10	14.5	14.6	14.6
8-17	4.3	3.9	4.0
10-14	4.6	4.0	4.2
14-17	2.6	3.0	2.9
10-17	12.4	12.4	12.4
9-10	14.3	14.4	14.4
10-15	4.6	4.3	4.4
9-17	4.8	4.7	4.7
15-17	2.7	2.8	2.8
9-15	12.4	12.4	12.4
9-11	14.6	14.2	14.3
11-15	4.4	4.7	4.6
11-13	14.6	14.6	14.6
1-13	14.7	13.9	14.1
13-16	2.0	4.9	4.0
1-16	12.4	12.4	12.4
1-26	1.0	2.0	1.7
1-27	14.2	14.7	14.6
16-26	8.0	6.2	6.7
16-27	1.1	1.9	1.7
26-27	12.4	12.4	12.4
24-26	6.7	0.8	2.5
24-27	12.6	13.6	13.3
20-24	8.6	10.1	9.6
20-21	6.4	13.8	11.6
20-38	1.7	0.9	1.1
21-38	12.4	12.4	12.4
21-35	5.1	14.7	11.9
21-37	2.6	2.1	2.3
35-38	2.7	2.0	2.2
37-38	14.7	5.9	8.5
35-37	12.4	12.4	12.4
32-35	4.8	5.0	5.0
32-37	14.0	2.7	6.1
34-35	2.6	14.1	10.7
34-37	5.2	4.8	4.9
32-34	12.4	12.4	12.4
30-32	2.0	2.1	2.1
29-32	14.6	5.1	7.9
30-34	5.5	14.6	11.9
29-34	1.9	2.3	2.2
29-30	12.4	12.4	12.4

6-7-8- 7 conformers

hydrogens	conf. 1 (47.1%)	conf. 2 (3.1%)	conf. 3 (41.8%)	conf. 4 (5.2%)	conf. 5 (1.8%)	conf. 6 (0.7%)	conf. 7 (0.2%)	wt. ave
8-14	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4
5-8	4.4	3.7	4.3	3.8	4.6	4.4	4.4	4.3
8-12	14.5	14.7	14.5	14.7	14.4	14.5	14.5	14.5
5-14	2.6	3.0	2.6	3.0	2.5	2.6	2.6	2.6
12-14	4.6	3.9	4.6	3.9	4.8	4.6	4.6	4.5
5-12	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4
1-5	2.6	2.8	2.7	2.8	2.6	2.7	2.6	2.7
5-13	4.8	4.7	4.7	4.7	4.8	4.8	4.8	4.7
1-12	4.6	4.3	4.5	4.3	4.7	4.6	4.6	4.5
12-13	14.3	14.4	14.3	14.4	14.3	14.3	14.3	14.3
1-13	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4
1-11	3.8	4.7	3.7	4.7	3.6	3.7	3.7	3.8
11-13	14.6	14.2	14.6	14.2	14.6	14.6	14.6	14.5
9-11	14.6	14.6	14.6	14.6	14.5	14.6	14.6	14.6
9-15	1.7	1.0	2.1	1.0	10.2	2.2	1.8	2.0
9-18	14.6	14.1	14.7	14.1	0.7	14.7	14.6	14.3
15-18	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4
15-25	1.3	8.3	0.9	8.2	1.1	0.8	1.0	1.7
15-26	7.5	1.1	8.3	1.1	14.2	8.5	8.0	7.4
18-25	14.3	10.9	13.8	11.1	7.7	13.6	14.1	13.7
18-26	1.2	8.3	0.9	8.2	1.2	0.8	1.0	1.6
25-26	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4
23-25	10.5	6.7	7.7	6.8	2.4	6.9	9.9	8.9
23-26	0.7	12.5	1.1	12.4	14.7	1.4	0.7	2.1
22-23	14.4	11.3	11.9	11.5	13.6	11.4	14.3	13.0
20-22	2.3	2.5	2.8	4.2	3.7	0.7	1.0	2.6
22-28	14.7	5.4	14.7	3.5	14.4	13.0	11.3	13.8
20-28	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4
20-38	0.9	4.6	1.1	4.4	0.9	5.8	7.1	1.3
20-39	11.1	14.1	7.9	13.3	8.5	2.4	1.5	9.8
28-38	11.4	3.3	14.3	9.3	14.0	13.1	12.0	12.3
28-39	0.9	4.5	1.1	0.7	1.0	6.0	7.4	1.1
38-39	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4
36-38	6.6	5.8	1.1	1.4	1.4	6.8	3.4	3.9
36-39	1.9	2.3	11.4	14.5	11.7	12.5	14.5	6.8
37-38	12.8	13.3	10.6	7.2	9.8	1.7	4.4	11.4
37-39	6.4	5.8	1.2	1.4	1.5	6.8	3.4	3.8
36-37	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4
31-36	4.4	0.7	1.3	0.8	1.6	1.9	3.8	2.7
31-37	3.4	12.4	14.4	8.8	14.6	12.0	4.0	8.8
32-36	14.2	10.1	7.1	13.6	6.4	9.0	14.5	10.9
32-37	4.4	0.7	1.4	0.8	1.8	1.9	3.6	2.8
31-32	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4
31-41	4.1	3.5	4.5	5.7	5.0	6.8	7.3	4.4
29-31	3.1	14.7	14.4	1.9	14.2	1.3	12.5	8.3
32-41	14.4	4.0	3.0	13.5	2.6	12.7	1.3	9.0
29-32	4.5	3.3	4.2	6.2	4.7	7.4	7.1	4.5
29-41	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4

6-7-9- 17 conformers

hydrogens	conf. 1 (20.9%)	conf. 2 (7.6%)	conf. 3 (40.4%)	conf. 4 (3.9%)	conf. 5 (2.3%)	conf. 6 (1.4%)	conf. 7 (6.4%)	conf. 8 (0.6%)	wt. ave
9-15	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4
9-11	14.5	14.7	14.7	14.7	14.5	14.7	14.5	14.7	13.3
9-16	4.4	3.8	3.8	3.8	4.4	3.7	4.4	3.2	5.3
11-15	4.6	4.0	4.0	4.0	4.6	3.9	4.6	3.4	4.0
15-16	2.6	3.0	3.0	3.0	2.6	3.1	2.5	3.4	3.1
11-16	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4
11-13	14.3	14.4	14.4	14.4	14.3	14.4	4.6	4.1	12.1
13-16	4.8	4.6	4.6	4.6	4.8	4.6	14.3	14.4	5.4
1-11	4.6	4.3	4.3	4.3	4.6	4.2	2.6	2.9	5.5
1-16	2.6	2.8	2.8	2.8	2.6	2.9	4.8	4.7	3.2
1-13	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4
1-12	3.7	4.8	4.8	4.8	3.8	5.0	3.8	5.9	4.4
12-13	14.6	14.1	14.2	14.2	14.6	14.0	14.6	13.4	14.3
8-12	14.6	14.6	14.6	14.6	14.6	14.6	14.5	13.9	14.6
8-18	1.9	5.3	5.2	5.2	2.2	5.3	11.1	9.1	4.6
8-19	14.6	13.6	13.7	13.6	14.7	13.6	0.9	9.9	13.0
18-19	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4
18-21	8.1	5.5	5.7	5.6	8.5	4.9	14.5	12.0	7.3
18-23	1.1	2.3	2.2	2.2	0.9	2.8	1.5	7.5	1.8
19-21	0.9	2.5	2.4	2.4	0.8	3.1	1.4	7.1	1.9
19-23	14.1	14.7	14.7	14.7	13.8	14.7	7.0	1.5	13.7
21-23	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4
21-25	8.0	0.7	0.7	0.7	5.9	0.7	2.8	1.5	3.1
23-25	11.4	12.8	12.9	13.0	13.2	12.5	4.8	6.9	12.0
25-27	7.2	8.2	8.9	8.6	9.3	5.9	5.6	2.2	8.2
27-28	14.7	14.7	12.2	14.0	13.7	14.1	14.5	8.8	13.0
17-27	2.7	2.7	0.7	0.9	5.0	4.1	3.4	0.9	1.9
17-28	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4
17-42	12.1	13.2	8.5	11.1	11.5	14.6	12.2	13.5	10.4
17-43	5.2	5.8	0.9	0.9	1.2	2.8	4.9	5.4	3.3
28-42	5.2	5.7	0.9	0.9	1.1	2.6	4.8	5.1	3.3
28-43	5.0	2.5	14.1	11.7	10.8	5.6	5.4	2.9	9.1
42-43	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4
39-42	4.2	1.5	1.1	4.5	4.8	2.9	4.5	3.0	2.9
39-43	14.2	11.9	10.9	5.8	5.3	5.3	14.1	14.6	11.5
40-42	3.4	9.9	11.4	12.3	12.3	14.7	3.2	5.2	8.2
40-43	4.5	1.6	1.1	4.2	4.8	2.6	4.8	2.9	3.0
39-40	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4
35-39	5.3	2.1	4.1	0.8	4.8	5.2	5.1	2.9	4.1
35-40	13.7	14.7	3.8	8.8	3.2	2.8	13.9	5.3	8.9
36-39	2.7	6.0	14.4	13.6	14.1	13.7	2.9	14.7	9.3
36-40	5.1	2.2	3.9	0.8	4.4	5.2	4.9	2.6	3.9
35-36	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4
31-35	2.9	0.8	4.2	6.9	5.3	0.7	3.1	4.3	3.5

hydrogens	conf. 1 (20.9%)	conf. 2 (7.6%)	conf. 3 (40.4%)	conf. 4 (3.9%)	conf. 5 (2.3%)	conf. 6 (1.4%)	conf. 7 (6.4%)	conf. 8 (0.6%)	wt. ave
31-36	12.4	8.8	3.5	13.5	2.5	12.3	12.4	3.5	7.4
32-35	7.2	13.6	14.4	2.1	13.7	10.1	7.1	14.2	11.4
32-36	3.1	0.8	4.1	6.0	5.4	0.7	3.2	4.2	3.5
31-32	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4
29-31	2.4	4.7	5.5	14.3	4.8	14.6	2.5	4.2	6.2
29-32	5.4	2.9	2.2	1.4	2.8	1.8	5.4	3.4	3.6
31-44	4.9	2.7	2.0	1.7	2.5	1.9	4.8	3.0	3.4
32-44	14.0	14.7	14.7	6.0	14.7	5.7	14.0	14.7	12.2
29-44	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4

.

hydrogens	conf. 9 (0.1%)	conf. 10 (3.0%)	conf. 11 (0.4%)	conf. 12 (0.3%)	conf. 13 (8.1%)	conf. 14 (2.9%)	conf. 15 (0.1%)	conf. 16 (0.4%)	conf. 17 (1.2%)	wt. ave
9-15	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4
9-11	14.7	14.7	14.5	14.7	4.3	4.4	3.3	4.0	4.3	13.3
9-16	3.8	3.8	4.3	3.3	14.5	14.5	14.7	14.6	14.5	5.3
11-15	3.9	3.9	4.6	3.4	2.6	2.6	3.4	2.9	2.6	4.0
15-16	3.0	3.0	2.6	3.4	4.5	4.6	3.4	4.1	4.5	3.1
11-16	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4
11-13	4.2	4.2	4.6	4.1	4.5	4.6	4.1	4.3	4.5	12.1
13-16	12.7	12.7	14.3	14.4	2.7	2.6	2.9	2.8	2.7	5.4
1-11	2.8	2.8	2.7	2.9	14.3	14.3	14.4	14.4	14.3	5.5
1-16	4.6	4.6	4.8	4.7	4.8	4.8	4.7	4.7	4.8	3.2
1-13	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4
1-12	4.9	4.9	3.8	5.9	3.8	3.7	5.8	4.3	3.9	4.4
12-13	14.1	14.1	14.6	13.5	14.6	14.6	13.5	14.4	14.5	14.3
8-12	12.7	14.6	14.6	13.9	14.7	14.6	14.0	14.7	14.6	14.6
8-18	5.3	5.3	2.0	9.4	2.4	2.1	10.3	12.4	11.8	4.6
8-19	13.6	13.6	14.7	9.6	14.7	14.7	8.5	2.8	1.4	13.0
18-19	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4
18-21	5.3	5.3	8.2	12.2	8.5	8.5	13.0	14.7	14.7	7.3
18-23	2.5	2.5	1.0	7.2	0.9	0.9	6.2	3.0	2.0	1.8
19-21	2.7	2.7	0.9	6.8	0.8	0.8	5.9	2.7	1.8	1.9
19-23	14.7	14.7	14.0	1.7	13.8	13.9	2.2	5.1	6.3	13.7
21-23	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4
21-25	0.7	0.8	5.8	1.5	5.1	6.5	1.6	2.0	2.5	3.1
23-25	12.7	12.7	13.3	6.9	13.7	12.7	6.8	5.9	5.2	12.0
25-27	7.5	9.9	8.9	2.3	10.3	8.8	3.0	3.8	4.6	8.2
27-28	14.4	11.9	8.5	4.4	14.4	5.4	5.8	5.7	10.0	13.0
17-27	3.6	0.8	1.0	3.3	3.5	2.5	2.2	2.4	0.7	1.9
17-28	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4
17-42	13.5	12.4	6.2	7.2	11.7	2.0	6.1	5.6	14.5	10.4
17-43	5.3	4.8	4.0	3.2	6.1	8.9	4.1	4.5	3.6	3.3
28-42	5.2	4.9	4.2	3.2	6.2	8.7	4.1	4.5	3.3	3.3
28-43	2.9	5.5	12.3	12.4	4.2	10.4	12.4	12.3	4.6	9.1
42-43	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4
39-42	7.0	4.5	5.0	3.5	5.2	5.0	0.7	0.7	3.2	2.9
39-43	11.4	13.9	3.2	4.4	13.6	3.0	9.5	9.2	14.6	11.5
40-42	3.3	3.2	13.9	14.6	2.7	13.9	13.2	13.4	4.7	8.2
40-43	7.2	4.9	4.6	3.3	5.5	4.7	0.7	0.7	3.2	3.0
39-40	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4
35-39	4.6	4.6	4.3	3.2	2.9	5.5	2.8	3.1	2.4	4.1
35-40	13.9	14.1	3.4	4.5	14.7	2.4	14.7	14.6	12.3	8.9
36-39	3.2	3.4	14.2	14.6	5.1	13.5	5.1	4.7	8.1	9.3
36-40	4.9	4.4	4.5	3.3	2.8	5.7	2.8	3.1	2.6	3.9
35-36	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4

hydrogens	conf. 9 (0.1%)	conf. 10 (3.0%)	conf. 11 (0.4%)	conf. 12 (0.3%)	conf. 13 (8.1%)	conf. 14 (2.9%)	conf. 15 (0.1%)	conf. 16 (0.4%)	conf. 17 (1.2%)	wt. ave
32-35	0.7	14.7	5.6	11.2	14.2	8.4	10.7	10.8	4.8	11.4
32-36	9.3	2.4	2.5	1.0	4.1	0.9	1.1	1.1	3.0	3.5
31-32	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4
29-31	13.0	12.5	1.3	14.7	12.8	13.2	4.1	4.1	14.6	6.2
29-32	0.7	7.2	7.3	3.3	6.8	0.7	3.4	3.3	2.0	3.6
31-44	0.8	7.7	6.8	3.5	7.2	0.8	3.0	3.0	2.2	3.4
32-44	8.5	1.1	12.8	3.8	1.3	8.3	14.7	14.7	5.2	12.2
29-44	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4	12.4

6-8-6- 1 conformer

hydrogens	conf. 1 (100%)	wt. ave
9-15	12.41	12.41
9-10	14.65	14.65
9-16	3.83	3.83
15-16	3.00	3.00
10-15	4.02	4.02
10-16	12.41	12.41
8-10	14.29	14.29
10-14	4.52	4.52
8-16	4.92	4.92
14-16	2.63	2.63
8-14	12.41	12.41
8-12	14.49	14.49
12-14	4.08	4.08
12-13	14.73	14.73
1-13	14.22	14.22
13-17	4.13	4.13
1-17	12.41	12.41
1-27	5.84	5.84
1-29	2.29	2.29
17-27	13.20	13.20
17-29	5.95	5.95
25-27	11.26	11.26
26-27	0.97	0.97
25-29	0.94	0.94
26-29	11.18	11.18
25-26	12.41	12.41
20-25	14.60	14.60
20-26	3.12	3.12
20-30	14.73	14.73
30-32	4.05	4.05
30-33	14.48	14.48
32-33	12.41	12.41
32-34	4.38	4.38
32-35	2.75	2.75
33-34	14.38	14.38
33-35	4.69	4.69
34-35	12.41	12.41
34-37	14.60	14.60
34-38	4.24	4.24
35-37	4.03	4.03
35-38	2.81	2.81
37-38	12.41	12.41

6-8-8- 3 conformers

hydrogens	conf. 1 (80.2%)	conf. 2 (6%)	conf. 3 (13.8%)	wt. ave
9-15	12.4	12.4	12.4	12.4
9-10	14.6	14.6	14.6	14.6
9-16	2.8	3.8	3.8	3.0
10-15	4.0	4.0	4.0	4.0
15-16	3.0	3.0	3.0	3.0
10-16	12.4	12.4	12.4	12.4
8-10	14.3	14.3	14.3	14.3
8-16	4.9	4.8	4.8	4.9
10-14	4.5	4.5	4.5	4.5
14-16	2.6	2.7	2.7	2.7
8-14	12.4	12.4	12.4	12.4
8-12	14.5	14.5	14.5	14.5
12-14	4.0	3.9	4.0	4.0
12-13	14.7	14.7	14.7	14.7
13-17	4.1	4.3	4.3	4.2
1-13	14.2	14.1	14.1	14.2
1-17	12.4	12.4	12.4	12.4
1-27	5.9	5.9	5.9	5.9
1-29	2.3	2.3	2.3	2.3
17-27	13.2	13.1	13.1	13.2
17-29	6.0	6.0	6.1	6.0
27-29	12.4	12.4	12.4	12.4
25-27	11.3	11.2	11.3	11.3
25-29	0.9	1.0	3.3	1.3
26-27	1.0	1.0	0.9	1.0
26-29	11.2	11.2	11.1	11.2
25-26	12.4	12.4	12.4	12.4
20-25	14.6	14.7	14.7	14.6
20-26	3.0	2.3	2.2	2.9
20-30	14.7	14.3	14.3	14.6
30-32	2.9	4.9	6.9	3.6
30-33	14.6	3.0	1.5	12.1
32-33	12.4	12.4	12.4	12.4
32-34	11.2	14.6	12.8	11.6
32-39	1.0	3.1	0.7	1.1
33-34	0.9	3.1	0.7	1.0
33-39	11.4	4.8	9.8	10.8
34-39	12.4	12.4	12.4	12.4
34-42	1.8	1.1	14.1	3.5
34-43	6.4	8.3	1.0	5.8
39-42	6.6	8.1	1.0	5.9
39-43	12.8	11.1	8.1	12.1
42-43	12.4	12.4	12.4	12.4
41-42	14.3	9.7	14.1	14.0
41-43	4.2	0.7	1.0	3.5
42-44	4.2	0.7	1.0	3.5
43-44	3.5	12.9	8.2	4.7
41-44	12.4	12.4	12.4	12.4

40-41	4.6	2.9	6.9	4.8
40-44	3.1	14.7	1.6	3.6
37-41	14.4	4.4	13.0	13.6
37-44	4.1	3.1	6.3	4.3
37-40	12.4	12.4	12.4	12.4

7-6-7- 3 conformers

hydrogens	conf. 1 (98.5%)	conf. 2 (0.7%)	conf. 3 (0.8%)	wt. ave
19-20	12.4	12.4	12.4	12.4
19-22	0.7	13.3	0.7	0.8
19-24	9.2	0.8	9.2	9.1
20-22	8.8	0.9	8.8	8.7
20-24	10.8	8.1	10.8	10.8
22-24	12.4	12.4	12.4	12.4
22-25	0.9	8.7	0.9	1.0
22-27	8.0	10.8	8.0	8.0
24-25	13.8	0.8	13.9	13.8
24-27	1.0	9.0	1.0	1.0
25-27	12.4	12.4	12.4	12.4
25-30	14.7	12.2	14.7	14.7
25-28	7.8	7.1	7.8	7.8
27-30	2.4	7.3	10.4	2.5
27-28	5.6	1.5	5.6	5.6
28-30	12.4	12.4	12.4	12.4
11-28	5.0	1.7	5.0	5.0
11-30	13.8	14.1	13.8	13.8
11-13	14.7	14.7	14.7	14.7
4-13	4.3	4.1	4.4	4.3
12-13	14.2	14.3	14.2	14.2
4-12	12.4	12.4	12.4	12.4
4-8	4.3	4.4	4.1	4.3
8-12	14.2	14.2	14.3	14.2
8-10	14.7	14.7	14.7	14.7
10-29	5.0	5.0	0.9	4.9
9-10	13.8	13.8	14.1	13.8
9-29	12.4	12.4	12.4	12.4
9-37	14.7	14.7	4.4	14.6
9-38	2.4	2.4	7.3	2.5
29-37	2.1	2.1	7.1	2.1
29-38	5.6	5.6	1.5	5.6
37-38	12.4	12.4	12.4	12.4
34-37	13.8	13.9	0.8	13.7
34-38	1.0	1.0	9.0	1.1
36-37	0.9	0.9	8.7	1.0
36-38	8.0	7.9	10.8	8.0
34-36	12.4	12.4	12.4	12.4
32-34	10.8	10.8	8.1	10.8
32-36	8.8	8.8	0.9	8.7
33-34	9.2	9.2	0.8	9.1
33-36	0.7	0.7	13.3	0.8
32-33	12.4	12.4	12.4	12.4

7-6-8- 6 conformers

hydrogens	conf. 1 (15.8%)	conf. 2 (29.1%)	conf. 3 (51.2%)	conf. 4 (0.3%)	conf. 5 (0.4%)	conf. 6 (3.2%)	wt. ave
19-20	12.4	12.4	12.4	12.4	12.4	12.4	12.4
19-21	8.1	10.8	11.0	8.1	8.2	11.0	10.5
19-23	0.8	8.8	8.6	0.9	0.8	8.6	7.4
20-21	0.8	9.2	9.1	0.8	0.8	9.1	7.7
20-23	13.3	0.7	0.7	13.3	13.3	0.7	2.8
21-23	12.4	12.4	12.4	12.4	12.4	12.4	12.4
21-24	0.8	13.8	13.9	0.8	0.8	13.9	11.7
21-25	8.8	1.0	1.0	8.8	8.7	1.0	2.3
23-24	8.5	0.9	0.9	8.5	8.4	0.9	2.2
23-25	11.0	8.0	8.0	11.0	11.1	8.0	8.5
24-25	12.4	12.4	12.4	12.4	12.4	12.4	12.4
16-24	12.0	14.7	14.7	12.0	4.7	14.7	14.2
16-25	7.5	2.4	2.4	7.5	7.6	2.4	3.3
24-27	7.3	2.1	2.1	7.3	7.4	2.1	3.0
25-27	1.4	5.6	5.6	1.4	1.3	5.6	4.9
16-27	12.4	12.4	12.4	12.4	12.4	12.4	12.4
10-16	14.0	13.8	13.9	14.1	14.0	14.0	13.9
10-27	0.9	4.9	4.8	0.9	0.9	4.7	4.2
8-10	14.6	14.6	14.6	14.6	14.6	14.6	14.6
4-8	4.3	4.7	4.6	4.3	4.3	4.8	4.6
8-12	14.3	14.0	14.2	14.3	14.3	14.0	14.2
4-12	12.4	12.4	12.4	12.4	12.4	12.4	12.4
4-13	3.8	3.8	3.5	3.8	3.6	3.2	3.6
12-13	14.5	14.5	14.6	14.5	14.5	14.7	14.5
11-13	14.7	14.7	14.7	14.7	14.7	14.5	14.7
9-11	14.6	14.2	14.5	12.6	14.5	13.8	14.4
11-41	3.2	4.2	1.3	0.7	1.3	0.8	2.4
9-41	12.4	12.4	12.4	12.4	12.4	12.4	12.4
9-38	0.9	5.9	1.2	7.0	1.2	1.4	2.6
9-39	11.5	2.3	10.3	12.4	10.4	14.5	8.3
38-41	11.1	13.1	11.6	1.8	11.6	7.2	11.8
39-41	0.9	6.0	1.4	6.6	1.3	1.4	2.7
38-39	12.4	12.4	12.4	12.4	12.4	12.4	12.4
35-38	6.4	0.9	0.9	3.6	0.9	0.7	1.8
35-39	12.9	10.9	14.0	4.2	14.0	12.8	12.8
36-38	1.9	11.3	8.2	14.5	8.2	9.7	8.2
36-39	6.5	0.9	1.0	3.6	1.0	0.7	1.8
35-36	12.4	12.4	12.4	12.4	12.4	12.4	12.4
32-35	3.6	4.3	14.6	4.3	14.6	14.0	9.8
34-35	4.1	3.2	3.8	3.2	3.8	4.9	3.7
32-36	4.1	3.5	3.5	3.4	3.5	4.7	3.7
34-36	14.3	14.6	3.8	14.6	3.9	2.9	8.6
32-34	12.4	12.4	12.4	12.4	12.4	12.4	12.4
31-32	3.2	4.2	14.1	12.4	14.1	1.1	9.1
31-34	4.4	3.1	1.3	7.3	1.3	7.6	2.5
29-32	4.0	3.0	1.3	7.4	1.4	7.2	2.4
29-34	14.4	14.7	6.7	1.1	6.7	12.5	10.4
29-31	12.4	12.4	12.4	12.4	12.4	12.4	12.4

H's	conf 1 (53.8%)	conf 2 (5.1%)	conf 3 (19.8%)	conf 4 (11.1%)	conf 5 (2.4%)	conf 6 (0.4%)	conf 7 (0.4%)	conf 8 (6.8%)	conf 9 (0.1%)	wt. ave
3-5	12.41	12.41	12.41	12.41	12.41	12.41	12.41	12.41	12.41	12.40
3-7	4.58	4.55	4.55	4.53	4.58	4.58	4.60	4.50	4.57	4.55
3-8	14.26	14.27	14.28	14.28	14.26	14.26	14.25	14.29	14.27	14.26
5-7	2.79	2.82	2.82	2.82	2.78	2.79	2.78	2.84	2.80	2.80
5-8	4.73	4.69	4.68	4.68	4.73	4.73	4.73	4.67	4.69	4.70
7-8	12.41	12.41	12.41	12.41	12.41	12.41	12.41	12.41	12.41	12.40
7-9	2.34	2.31	2.33	2.31	2.33	2.33	2.35	2.32	2.34	2.33
7-10	5.25	5.31	5.29	5.30	5.28	5.29	5.26	5.29	5.27	5.27
8-9	14.71	14.71	14.71	14.71	14.53	14.71	14.72	14.71	14.71	14.69
8-10	2.38	2.34	2.35	2.33	2.36	2.36	2.37	2.34	2.36	2.36
9-10	12.41	12.41	12.41	12.41	12.41	12.41	12.41	12.41	12.41	12.40
9-13	14.05	14.10	14.09	14.11	2.14	14.05	14.03	14.13	14.07	13.78
9-14	0.92	0.88	0.94	0.95	0.93	0.92	0.91	0.96	0.93	0.93
10-13	1.12	1.16	1.15	1.17	1.13	1.11	1.10	1.19	1.14	1.14
10-14	7.93	7.85	7.89	7.83	7.92	7.96	7.96	7.81	7.91	7.89
13-14	12.41	12.41	12.41	12.41	12.41	12.41	12.41	12.41	12.41	12.40
13-15	12.94	12.86	12.90	12.86	12.88	12.92	12.97	12.87	12.94	12.90
14-15	6.30	6.39	6.35	6.41	6.36	6.31	6.25	6.39	6.30	6.33
15-19	8.74	8.76	8.80	8.78	8.66	8.69	8.74	8.84	8.79	8.75
18-19	6.45	6.61	6.39	6.69	6.34	6.27	6.31	6.62	6.57	6.47
19-30	1.67	1.58	1.69	1.53	1.73	1.78	1.76	1.57	1.59	1.65
18-30	12.41	12.41	12.41	12.41	12.41	12.41	12.41	12.41	12.41	12.40
18-27	5.41	5.28	5.37	5.24	5.34	5.42	5.43	5.28	5.37	5.36
18-28	2.57	2.75	2.67	2.82	2.59	2.56	2.51	2.83	2.63	2.64
27-30	2.40	2.49	2.42	2.52	2.45	2.39	2.37	2.49	2.41	2.43
28-30	14.73	14.72	14.73	14.71	14.73	14.73	14.73	14.71	14.73	14.71
24-27	4.14	4.72	4.27	4.98	3.78	3.46	3.80	5.05	4.67	4.34
24-28	14.24	13.88	14.13	13.71	14.39	14.53	14.41	13.64	13.95	14.09
22-24	14.06	14.56	14.09	14.66	13.73	13.33	13.54	14.62	14.47	14.17
22-23	3.13	14.61	12.05	14.73	14.22	1.02	5.38	14.09	3.79	7.78
22-34	4.59	1.45	0.78	2.06	1.05	8.09	2.65	0.81	3.83	3.05
33-34	12.41	12.41	12.41	12.41	12.41	12.41	12.41	12.41	12.41	12.40
33-35	12.26	5.12	14.72	6.03	2.08	11.06	3.42	14.58	12.27	11.55
33-37	4.76	5.00	2.54	4.19	8.86	0.94	4.39	3.11	2.43	4.23
34-35	4.88	5.23	2.31	4.38	8.71	0.92	4.60	2.77	2.43	4.25
34-37	5.22	12.13	5.76	12.34	10.44	11.30	14.06	5.37	8.15	6.66
35-37	12.41	12.41	12.41	12.41	12.41	12.41	12.41	12.41	12.41	12.40
35-38	3.25	13.60	3.90	14.30	14.11	12.11	13.84	3.09	7.56	5.46
3539	4.42	0.79	4.02	4.18	4.64	5.30	4.71	5.22	1.23	4.18
37-38	4.68	0.74	3.90	3.95	4.30	5.41	4.99	5.00	1.27	4.25
37-39	14.10	8.95	14.33	3.75	3.37	4.73	3.14	13.57	14.40	12.35
38-39	12.41	12.41	12.41	12.41	12.41	12.41	12.41	12.41	12.41	12.40
38-41	4.93	3.36	2.28	3.24	5.57	4.28	3.47	2.30	0.75	3.96
38-42	13.85	14.57	12.21	4.52	2.52	3.40	6.71	5.77	9.16	11.62
39-41	2.82	4.39	8.53	14.62	13.57	14.13	12.41	14.72	13.52	6.50
39-42	5.15	3.40	2.16	3.23	5.36	4.60	3.68	2.55	0.72	4.06

41-42	12.41	12.41	12.41	12.41	12.41	12.41	12.41	12.41	12.41	12.40
41-44	3.29	1.01	3.30	0.76	0.77	5.51	0.73	5.73	0.94	2.99
41-45	12.40	11.05	14.69	11.50	13.35	2.50	10.49	2.26	10.94	11.95
42-44	7.06	10.99	4.45	10.65	9.00	13.62	12.10	13.35	11.18	7.66
42-45	3.09	0.92	2.91	0.87	0.69	5.37	0.72	5.90	1.08	2.83
44-45	12.41	12.41	12.41	12.41	12.41	12.41	12.41	12.41	12.41	12.40
44-47	14.03	14.69	4.91	3.96	8.06	14.72	11.95	14.70	5.87	11.01
31-44	5.38	3.47	2.19	3.06	0.80	3.05	8.03	3.44	1.73	4.14
45-47	4.83	3.16	2.41	3.35	0.85	2.73	7.48	2.90	1.99	3.87
31-45	2.47	3.98	14.65	14.71	13.37	4.60	1.09	4.20	14.57	6.71
31-47	12.41	12.41	12.41	12.41	12.41	12.41	12.41	12.41	12.41	12.40
27-28	12.41	12.41	12.41	12.41	12.41	12.41	12.41	12.41	12.41	12.40

8-6-6- 4 conformers

hydrogens	conf. 1 (15.0%)	conf. 2 (7.5%)	conf. 3 (77.2%)	conf. 4 (0.4%)	wt. ave
1-3	12.41	12.41	12.41	12.41	12.42
1-7	14.68	12.46	0.99	1.89	3.91
1-8	3.27	7.28	8.31	6.74	7.48
3-7	3.50	7.67	7.76	5.93	7.11
3-8	3.85	1.09	11.69	13.01	9.74
7-8	12.41	12.41	12.41	12.41	12.42
7-9	3.11	5.21	0.77	6.49	1.48
7-10	14.66	2.66	10.58	1.87	10.57
8-9	4.35	13.88	11.89	12.56	10.92
8-10	3.32	5.02	0.74	6.78	1.47
9-10	12.41	12.41	12.41	12.41	12.42
9-12	0.88	0.66	2.56	4.82	2.18
9-13	11.03	12.86	14.73	3.28	14.00
10-12	11.25	9.72	5.27	13.92	6.54
10-13	0.96	0.67	2.59	4.59	2.21
12-13	12.41	12.41	12.41	12.41	12.42
12-15	6.17	1.21	2.92	4.90	3.29
12-16	12.81	7.72	4.95	13.70	6.38
13-15	2.11	14.32	14.69	3.24	12.74
13-16	6.41	1.14	2.85	4.94	3.27
15-16	12.41	12.41	12.41	12.41	12.42
15-20	14.41	13.47	10.86	13.55	11.61
16-20	3.75	0.73	0.98	5.30	1.39
20-22	5.21	6.23	6.56	6.54	6.34
22-24	14.58	14.27	14.17	14.41	14.25
22-26	3.63	4.36	4.58	4.06	4.42
24-26	12.41	12.41	12.41	12.41	12.42
24-29	14.54	14.47	14.47	14.57	14.50
26-29	3.75	3.85	3.82	3.57	3.82
29-30	14.70	14.73	14.73	14.73	14.74
23-30	14.54	14.45	14.44	14.49	14.47
30-38	3.94	4.18	4.22	4.07	4.18
23-38	12.41	12.41	12.41	12.41	12.42
23-37	4.72	4.71	4.72	4.74	4.73
23-35	14.33	14.34	14.34	14.33	14.36
35-38	4.60	4.54	4.53	4.57	4.54
37-38	2.64	2.67	2.67	2.64	2.66
35-37	12.41	12.41	12.41	12.41	12.42
32-37	4.57	4.45	4.42	4.49	4.45
34-37	2.62	2.70	2.71	2.67	2.70
34-35	14.48	14.53	14.54	14.51	14.54
34-37	4.35	4.22	4.22	4.28	4.24
32-34	12.41	12.41	12.41	12.41	12.42

Appendix C. Calculated coupling constants compared to *ACD/Labs* values

Hydrogens	wt. ave	ACD J	Difference wt. ave - ACD
10-16	12.4	12.0	0.4
8-10	14.5	12.8	1.7
10-14	4.2	2.9	1.3
8-16	4.4	3.1	1.3
14-16	2.7	1.8	0.9
8-14	12.4	12.9	-0.5
8-9	4.5	3.2	1.4
8-12	14.4	12.6	1.7
9-14	2.7	1.7	0.9
12-14	4.7	3.3	1.4
9-12	12.4	12.9	-0.5
9-13	4.3	3.0	1.3
12-13	14.4	12.7	1.7
11-13	14.7	13.0	1.7
11-24	14.5	12.8	1.7
4-11	3.8	2.6	1.2
4-24	12.4	12.5	-0.1
4-22	4.6	3.2	1.4
22-24	14.2	12.5	1.7
18-22	14.6	12.8	1.7
18-26	4.7	3.3	1.4
18-27	14.0	12.3	1.7
26-27	12.4	14.6	-2.2
26-29	2.1	1.3	0.8
26-30	5.6	4.0	1.6
27-30	2.4	1.6	0.9
29-30	12.4	13.8	-1.4
29-33	0.9	0.3	0.6
30-33	8.0	5.7	2.2
29-34	13.8	12.2	1.7
30-34	1.0	0.4	0.6
33-34	12.4	13.9	-1.5
33-35	0.7	0.1	0.6
25-33	8.6	6.2	2.4
35-34	9.0	6.5	2.5
25-34	11.0	9.4	1.6
25-35	12.4	12.6	-0.2
27-29	14.7	13.0	1.7
			MOAD= 1.3

676- 1 conformer

hydrogens	wt. ave	ACD J	Diff
22-32	3.8	2.6	1.2
22-34	14.6	12.8	1.7
32-34	12.4	12.9	-0.5
32-35	2.7	1.8	0.9
15-32	4.5	3.1	1.4
34-35	4.7	3.3	1.4
15-34	14.3	12.6	1.7
15-35	12.4	12.9	-0.5
14-15	14.5	12.8	1.7
15-21	4.5	3.2	1.4
14-35	4.3	3.0	1.3
21-35	2.6	1.7	0.9
14-21	12.4	12.0	0.4
22-27	14.6	12.9	1.7
27-28	1.4	0.5	0.9
27-30	11.8	8.5	3.2
28-30	12.4	14.6	-2.2
16-28	6.5	4.6	1.9
16-30	1.9	1.1	0.8
28-31	1.7	1.0	0.7
30-31	14.7	12.9	1.7
16-31	12.4	14.6	-2.2
10-16	1.3	0.7	0.7
10-31	14.4	12.7	1.7
8-10	14.7	13.0	1.7
8-12	14.5	12.8	1.7
8-18	3.9	2.7	1.2
12-18	12.4	12.9	-0.5
1-12	4.7	3.3	1.4
12-13	14.3	12.6	1.7
1-18	2.7	1.8	0.9
13-18	4.5	3.2	1.4
1-13	12.4	12.9	-0.5
1-11	4.2	2.9	1.3
1-17	2.7	1.8	0.9
11-13	14.5	12.8	1.7
13-17	4.4	3.1	1.3
11-17	12.4	12.0	0.4

MOAD = 1.3

677- 2 conformers

Hydrogens	wt. ave	ACD	Diff
8-14	12.4	12	0.4
8-10	14.6	3.02	11.6
8-17	4.0	12.77	-8.8
10-14	4.2	1.69	2.5
14-17	2.9	3.19	-0.3
10-17	12.4	12.9	-0.5
9-10	14.4	3.34	11.0
10-15	4.4	1.73	2.6
9-17	4.7	12.61	-7.9
15-17	2.8	3.19	-0.4
9-15	12.4	12.9	-0.5
9-11	14.3	12.85	1.5
11-15	4.6	2.6	2.0
11-13	14.6	12.92	1.7
1-13	14.1	1.18	12.9
13-16	4.0	12.94	-8.9
1-16	12.4	14.6	-2.2
1-26	1.7	5.76	-4.0
1-27	14.6	0.49	14.1
16-26	6.7	0.36	6.4
16-27	1.7	12.45	-10.8
26-27	12.4	14.6	-2.2
24-26	2.5	4.78	-2.2
24-27	13.3	10.92	2.4
20-24	9.6	6.19	3.5
20-21	11.6	4.6	7.0
20-38	1.1	0.94	0.2
21-38	12.4	14.6	-2.2
21-35	11.9	3.56	8.3
21-37	2.3	1.71	0.6
35-38	2.2	1.73	0.5
37-38	8.5	13	-4.5
35-37	12.4	13.8	-1.4
32-35	5.0	3.39	1.6
32-37	6.1	12.31	-6.3
34-35	10.7	1.17	9.6
34-37	4.9	3.65	1.2
32-34	12.4	13.93	-1.5
30-32	2.1	1.24	0.8
29-32	7.9	12.84	-5.0
30-34	11.9	3.89	8.1
29-34	2.2	1.14	1.1
29-30	12.4	12.6	-0.2

MOAD = 4.2

Hydrogens	wt. ave	ACD	diff
8-14	12.4	12.0	0.4
5-8	4.3	3.0	1.3
8-12	14.5	12.8	1.7
5-14	2.6	1.7	0.9
12-14	4.5	3.2	1.3
5-12	12.4	12.9	-0.5
1-5	2.7	1.7	0.9
5-13	4.7	3.3	1.4
1-12	4.5	3.2	1.3
12-13	14.3	12.6	1.7
1-13	12.4	12.9	-0.5
1-11	3.8	2.6	1.2
11-13	14.5	12.9	1.7
9-11	14.6	12.9	1.7
9-15	2.0	1.0	1.0
9-18	14.3	12.9	1.5
15-18	12.4	14.6	-2.2
15-25	1.7	0.6	1.1
15-26	7.4	5.4	2.0
18-25	13.7	12.6	1.1
18-26	1.6	0.5	1.1
25-26	12.4	14.6	-2.2
23-25	8.9	7.6	1.2
23-26	2.1	0.0	2.1
22-23	13.0	12.6	0.4
20-22	2.6	1.4	1.2
22-28	13.8	13.0	0.8
20-28	12.4	14.6	-2.2
20-38	1.3	0.1	1.2
20-39	9.8	8.0	1.8
28-38	12.3	9.8	2.5
38-39	12.4	13.8	-1.4
36-38	3.9	4.7	-0.8
36-39	6.8	1.1	5.7
37-38	11.4	11.2	0.3
37-39	3.8	4.6	-0.7
36-37	12.4	13.8	-1.4
31-36	2.7	3.1	-0.3
31-37	8.8	2.3	6.5
32-36	10.9	12.5	-1.6
32-37	2.8	3.1	-0.3
31-32	12.4	2.8	9.6
31-41	4.4	2.8	1.5
29-31	8.3	2.1	6.2

32-41	9.0	12.7	-3.7
29-32	4.5	3.2	1.3
29-41	12.4	12.6	-0.2

MOAD=1.8

679 - 18 conformers

hydrogens	wt. ave	ACD	diff
9-15	12.4	12.0	0.4
9-11	13.3	13.9	-0.6
9-16	5.3	2.6	2.7
11-15	4.0	2.8	1.2
15-16	3.1	2.0	1.1
11-16	12.4	12.9	-0.5
11-13	12.1	12.7	-0.6
13-16	5.4	3.2	2.2
1-11	5.5	3.0	2.5
1-16	3.2	12.9	-9.7
1-13	12.4	12.9	-0.5
1-12	4.4	3.3	1.0
12-13	14.3	12.4	2.0
8-12	14.6	12.9	1.7
8-18	4.6	3.7	1.0
8-19	13.0	12.0	1.0
18-19	12.4	14.6	-2.2
18-21	7.3	4.1	3.2
18-23	1.8	1.4	0.5
19-21	1.9	1.5	0.4
19-23	13.7	13.0	0.7
21-23	12.4	14.6	-2.2
21-25	3.1	0.1	3.0
23-25	12.0	11.3	0.7
25-27	8.2	6.4	1.8
27-28	13.0	10.6	2.5
17-27	1.9	1.4	0.5
17-28	12.4	14.6	-2.2
17-42	10.4	6.2	4.2
17-43	3.3	0.3	3.1
28-42	3.3	0.3	3.0
28-43	9.1	12.4	-3.3
42-43	12.4	13.8	-1.4
39-42	2.9	0.3	2.6
39-43	11.5	9.3	2.2
40-42	8.2	8.3	-0.1
40-43	3.0	0.3	2.7
39-40	12.4	13.8	-1.4
35-39	4.1	2.8	1.3
35-40	8.9	2.6	6.2
36-39	9.3	12.7	-3.4
36-40	3.9	2.7	1.3
35-36	12.4	13.8	-1.4

31-35	3.5	2.9	0.6
31-36	7.4	2.4	5.0
32-35	11.4	12.6	-1.2
32-36	3.5	2.8	0.6
31-32	12.4	13.9	-1.5
29-31	6.2	3.9	2.3
29-32	3.6	1.4	2.2
31-44	3.4	1.3	2.2
32-44	12.2	12.9	-0.7
29-44	12.4	12.6	-0.2
			MOAD=1.9

686- 1
conformer

hydrogens	wt. ave	ACD	diff
9-15	12.41	12.0	0.4
9-10	14.65	12.9	1.7
9-16	3.83	2.6	1.2
15-16	3.00	2.0	1.0
10-15	4.02	2.8	1.2
10-16	12.41	12.9	-0.5
8-10	14.29	12.6	1.7
10-14	4.52	3.2	1.4
8-16	4.92	3.5	1.5
14-16	2.63	1.7	0.9
8-14	12.41	12.9	-0.5
8-12	14.49	12.8	1.7
12-14	4.08	2.8	1.3
12-13	14.73	13.0	1.7
1-13	14.22	12.5	1.7
13-17	4.13	2.9	1.3
1-17	12.41	14.6	-2.2
1-27	5.84	4.2	1.7
1-29	2.29	1.4	0.9
17-27	13.20	11.5	1.7
17-29	5.95	4.2	1.7
25-27	11.26	9.7	1.6
26-27	0.97	0.2	0.8
25-29	0.94	0.1	0.8
26-29	11.18	8.1	3.1
25-26	12.41	14.6	-2.2
20-25	14.60	12.9	1.7
20-26	3.12	2.1	1.0
20-30	14.73	13.0	1.7
30-32	4.05	2.8	1.2
30-33	14.48	12.8	1.7
32-33	12.41	12.9	-0.5
32-34	4.38	3.1	1.3
32-35	2.75	1.8	1.0
33-34	14.38	12.7	1.7
33-35	4.69	3.3	1.4
34-35	12.41	12.9	-0.5
34-37	14.60	12.9	1.7
34-38	4.24	3.0	1.3
35-37	4.03	2.8	1.2
35-38	2.81	1.9	1.0
37-38	12.41	12.0	0.4

MOAD = 1.3

688- 3 conformers

hydrogens	wt. ave	ACD	diff
9-15	12.4	12	0.4
9-10	14.6	12.92	1.7
9-16	3.0	2.62	0.4
10-15	4.0	2.77	1.2
15-16	3.0	2.01	1.0
10-16	12.4	12.9	-0.5
8-10	14.3	12.57	1.7
8-16	4.9	3.43	1.4
10-14	4.5	3.16	1.4
14-16	2.7	1.72	0.9
8-14	12.4	12.9	-0.5
8-12	14.5	12.79	1.7
12-14	4.0	2.78	1.2
12-13	14.7	13	1.7
13-17	4.2	2.85	1.3
1-13	14.2	12.52	1.7
1-17	12.4	14.6	-2.2
1-27	5.9	4.18	1.7
1-29	2.3	1.42	0.8
17-27	13.2	11.52	1.7
17-29	6.0	4.25	1.7
27-29	12.4	13.8	-1.4
25-27	11.3	9.68	1.6
25-29	1.3	0.13	1.1
26-27	1.0	0.17	0.8
26-29	11.2	8.13	3.1
25-26	12.4	14.6	-2.2
20-25	14.6	12.87	1.8
20-26	2.9	2.03	0.9
20-30	14.6	13	1.6
30-32	3.6	1.92	1.7
30-33	12.1	12.91	-0.8
32-33	12.4	8.11	4.3
32-34	11.6	8.11	3.5
32-39	1.1	0.15	0.9
33-34	1.0	0.11	0.9
33-39	10.8	9.8	1.0
34-39	12.4	13.8	-1.4
34-42	3.5	1.07	2.4
34-43	5.8	4.58	1.2
39-42	5.9	4.7	1.2
39-43	12.1	11.18	0.9
42-43	12.4	13.8	-1.4
41-42	14.0	12.6	1.4

41-43	3.5	2.88	0.6
42-44	3.5	2.9	0.6
43-44	4.7	2.4	2.3
41-44	12.4	13.93	-1.5
40-41	4.8	3.19	1.6
40-44	3.6	2.04	1.5
37-41	13.6	12.67	0.9
37-44	4.3	2.84	1.5
37-40	12.4	12.6	-0.2
			MOAD = 1.4

767- 3
conformers

hydrogens	wt. ave	ACD	diff
19-20	12.4	12.6	-0.2
19-22	0.8	0.12	0.7
19-24	9.1	6.63	2.5
20-22	8.7	6.31	2.4
20-24	10.8	9.24	1.6
22-24	12.4	13.93	-1.5
22-25	1.0	0.29	0.7
22-27	8.0	5.74	2.3
24-25	13.8	12.14	1.6
24-27	1.0	0.37	0.7
25-27	12.4	13.8	-1.4
25-30	14.7	12.99	1.7
25-28	7.8	1.27	6.5
27-30	2.5	1.55	1.0
27-28	5.6	3.98	1.6
28-30	12.4	14.6	-2.2
11-28	5.0	3.5	1.5
11-30	13.8	12.1	1.7
11-13	14.7	12.93	1.7
4-13	4.3	2.99	1.3
12-13	14.2	12.54	1.7
4-12	12.4	12.5	-0.1
4-8	4.3	2.99	1.3
8-12	14.2	12.54	1.7
8-10	14.7	12.93	1.7
10-29	4.9	3.5	1.4
9-10	13.8	12.1	1.7
9-29	12.4	14.6	-2.2
9-37	14.6	12.99	1.6
9-38	2.5	1.56	0.9
29-37	2.1	1.27	0.8
29-38	5.6	3.98	1.6
37-38	12.4	13.8	-1.4
34-37	13.7	12.14	1.6
34-38	1.1	0.37	0.7
36-37	1.0	0.29	0.7
36-38	8.0	5.74	2.3
34-36	12.4	13.93	-1.5
32-34	10.8	9.24	1.6
32-36	8.7	6.31	2.4
33-34	9.1	6.63	2.5
33-36	0.8	0.12	0.7
32-33	12.4	12.6	-0.2

MOAD = 1.6

768- 6 conformers

hydrogens	wt. ave	ACD	diff
19-20	12.4	12.6	-0.2
19-21	10.5	0.14	10.3
19-23	7.4	6.53	0.8
20-21	7.7	6.21	1.5
20-23	2.8	9.38	-6.6
21-23	12.4	13.93	-1.5
21-24	11.7	5.74	6.0
21-25	2.3	0.3	2.0
23-24	2.2	0.37	1.8
23-25	8.5	12.15	-3.7
24-25	12.4	13.8	-1.4
16-24	14.2	1.56	12.7
16-25	3.3	12.99	-9.7
24-27	3.0	3.94	-1.0
25-27	4.9	1.3	3.6
16-27	12.4	14.6	-2.2
10-16	13.9	12.23	1.7
10-27	4.2	3.35	0.8
8-10	14.6	12.85	1.8
4-8	4.6	3.19	1.4
8-12	14.2	12.47	1.7
4-12	12.4	12.5	-0.1
4-13	3.6	2.39	1.2
12-13	14.5	12.85	1.7
11-13	14.7	12.92	1.8
9-11	14.4	12.73	1.6
11-41	2.4	0.62	1.8
9-41	12.4	14.6	-2.2
9-38	2.6	0.36	2.2
9-39	8.3	8.78	-0.5
38-41	11.8	8.42	3.4
39-41	2.7	0.42	2.3
38-39	12.4	13.8	-1.4
35-38	1.8	0.31	1.5
35-39	12.8	12.26	0.6
36-38	8.2	5.91	2.3
36-39	1.8	0.35	1.5
35-36	12.4	13.8	-1.4
32-35	9.8	2.63	7.1
34-35	3.7	12.83	-9.1
32-36	3.7	2.63	1.0
34-36	8.6	2.41	6.2

32-34	12.4	13.93	-1.5
31-32	9.1	4.8	4.3
31-34	2.5	0.68	1.8
29-32	2.4	12.6	-10.2
29-34	10.4	12.43	-2.0
29-31	12.4	12.6	-0.2
			MOAD = 3.0

hydrogens	wt. ave	ACD	diff
3-5	12.40	12.6	-0.2
3-7	4.55	3.2	1.4
3-8	14.26	12.6	1.7
5-7	2.80	1.8	1.0
5-8	4.70	3.3	1.4
7-8	12.40	13.9	-1.5
7-9	2.33	1.4	0.9
7-10	5.27	1.5	3.8
8-9	14.69	13.0	1.7
8-10	2.36	1.5	0.8
9-10	12.40	13.8	-1.4
9-13	13.78	12.4	1.4
9-14	0.93	0.3	0.6
10-13	1.14	0.5	0.6
10-14	7.89	5.7	2.2
13-14	12.40	14.6	-2.2
13-15	12.90	11.3	1.6
14-15	6.33	4.5	1.8
15-19	8.75	6.3	2.5
18-19	6.47	4.6	1.9
19-30	1.65	1.0	0.7
18-30	12.40	14.6	-2.2
18-27	5.36	3.8	1.5
18-28	2.64	1.7	1.0
27-30	2.43	1.5	0.9
28-30	14.71	13.0	1.7
24-27	4.34	2.9	1.5
24-28	14.09	12.5	1.6
22-24	14.17	12.4	1.8
22-23	7.78	2.1	5.7
22-34	3.05	3.2	-0.2
33-34	12.40	14.6	-2.2
33-35	11.55	8.9	2.7
33-37	4.23	3.5	0.7
34-35	4.25	3.6	0.6
34-37	6.66	3.9	2.7
35-37	12.40	13.8	-1.4
35-38	5.46	2.2	3.3
3539	4.18	3.1	1.1
37-38	4.25	3.3	1.0
37-39	12.35	12.4	0.0

38-39	12.40	13.8	-1.4
38-41	3.96	3.5	0.5
38-42	11.62	12.2	-0.5
39-41	6.50	1.9	4.6
39-42	4.06	3.6	0.4
41-42	12.40	13.8	-1.4
41-44	2.99	2.2	0.8
41-45	11.95	9.0	3.0
42-44	7.66	5.7	2.0
42-45	2.83	2.0	0.9
44-45	12.40	13.9	-1.5
44-47	11.01	12.3	-1.3
31-44	4.14	3.8	0.3
45-47	3.87	3.4	0.5
31-45	6.71	1.6	5.1
31-47	12.40	12.6	-0.2
27-28	12.40	14.6	-2.2
			MOAD = 1.6

866- 4
conformers

hydrogens	wt. ave	ACD	diff
1-3	12.42	12.6	-0.2
1-7	3.91	6.0	-2.1
1-8	7.48	0.4	7.1
3-7	7.11	10.1	-3.0
3-8	9.74	5.6	4.2
7-8	12.42	13.9	-1.5
7-9	1.48	0.0	1.5
7-10	10.57	10.3	0.3
8-9	10.92	7.7	3.3
8-10	1.47	0.0	1.4
9-10	12.42	13.8	-1.4
9-12	2.18	1.7	0.5
9-13	14.00	3.7	10.3
10-12	6.54	13.0	-6.5
10-13	2.21	1.7	0.6
12-13	12.42	13.8	-1.4
12-15	3.29	13.0	-9.7
12-16	6.38	1.9	4.5
13-15	12.74	1.9	10.8
13-16	3.27	3.5	-0.2
15-16	12.42	14.6	-2.2
15-20	11.61	9.3	2.3
16-20	1.39	0.2	1.2
20-22	6.34	4.7	1.7
22-24	14.25	12.5	1.8
22-26	4.42	3.2	1.2
24-26	12.42	12.5	-0.1
24-29	14.50	12.8	1.7
26-29	3.82	2.6	1.2
29-30	14.74	13.0	1.7
23-30	14.47	12.7	1.7
30-38	4.18	2.9	1.2
23-38	12.42	12.9	-0.5
23-37	4.73	3.3	1.4
23-35	14.36	12.6	1.7
35-38	4.54	3.2	1.4
37-38	2.66	1.7	0.9
35-37	12.42	12.9	-0.5
32-37	4.45	2.9	1.5
34-37	2.70	2.9	-0.2
34-35	14.54	3.1	11.5
34-37	4.24	1.8	2.5

32-34	12.42	12.0	0.4
			MOAD = 2.6