

Development and Testing of a
Protocol for Computational Prediction of
 ^1H and ^{13}C NMR Chemical Shifts

and

Thermochemistry and Reaction Analysis
of Benzyne Formation and Trapping

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Abstract

Elucidating structures of novel compounds and investigation of new reactions are two tasks that experimental organic chemists address on a frequent basis. The pursuit of these objectives can be rigorous and time-consuming. Of the methods employed in elucidating the structure of novel compounds, nuclear magnetic resonance (NMR) is by far the most widely applied. Investigation into new reactions may require any number of techniques to understand the reaction scope, kinetics, optimal conditions, mechanisms, etc. In both cases, the use of computational methods is well-suited to augment the experimentalist's data to guide and understand the system being investigated.

A protocol for facilitating computational prediction of NMR chemical shifts was developed. Application to a set of natural products previously evaluated against computed NMR shifts, showed improved accuracy, through analysis of the corrected mean-absolute error (CMAE). The protocol was further employed successfully to aid in analysis of experimental spectra for compounds synthesized by collaborators where multiple diastereomers were possible. Graphing templates were also created to allow for rapid inspection of possible structures without more in-depth statistical analysis.

Thermodynamic and mechanistic analysis on the formation and reaction of benzyne was also performed. Thermodynamic restrictions on the ring-size of fused benzynocycloalkanes were investigated. Additionally, analysis of the energetics and transition state geometries for small-molecule trapping (both intra and intermolecular) of benzyne are discussed.

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ACRONYMS

AO	atomic orbital
BSSE	basis set superposition error
CMAE	corrected mean-absolute error
CPCM	conductor-like polarizable continuum model
CSA	chemical shift anisotropy
CSGT	continuous set of gauge transformations
DFT	density functional theory
GIAO	gauge-independent atomic orbital
DDDA	hexadehydro-Diels-Alder
HF	Hartree-Fock
IEFPCM	integral equation-formalism polarizable continuum model
IGAIM	individual gauges for atoms in molecules
IRC	intrinsic reaction coordinate
MAE	mean-absolute error
MC/MM	Monte-Carlo/multiple minimum
<i>m</i> -CPBA	<i>meta</i> -chloroperoxybenzoic acid
MM	molecular mechanics
MPLC	medium-pressure liquid chromatography
NHC	N-heterocyclic carbene
NMR	nuclear magnetic resonance
NOE	nuclear Overhauser effect
PES	potential energy surface
QST	quadratic synchronous transit
ROTEP	ring opening transesterification polymerization
SCF	self-consistent field
STQN	synchronous transit-guided quasi-Newton
TFA	trifluoroacetic acid
TMS	tetramethylsilane
TS	transition state
UFF	universal force field

1. INTRODUCTION

1.1 Background of Computational Chemistry

Computational chemistry combines theoretical chemistry developments from as far back as the early 20th century^{1,2} with computing resources to calculate theoretical parameters for a variety of chemical systems. These chemical systems can be exactly described by analytically solving the time-independent Schrödinger equation, Eq. (1.1). However, the analytic solution to this equation is limited to only one-electron systems.

$$E\Psi = \hat{H}\Psi \quad (1.1)$$

Because solving the Schrödinger equation for a system of more than one electron is not analytically possible, Hartree developed an approach shortly after Schrödinger's publication in 1926,² known as self-consistent field (SCF) theory.³ The SCF approach to solving many-electron systems formally places each electron into its own one-electron potential. The eigenfunction of the Schrödinger equation, Ψ , is then described as a product of these one-electron wave functions, known as the Hartree product, Ψ_{HP} (Equation 1.2a & 1.2b).

$$\Psi_{HP} = \prod_{i=1}^n \psi_i(r_i) \quad (1.2a)$$

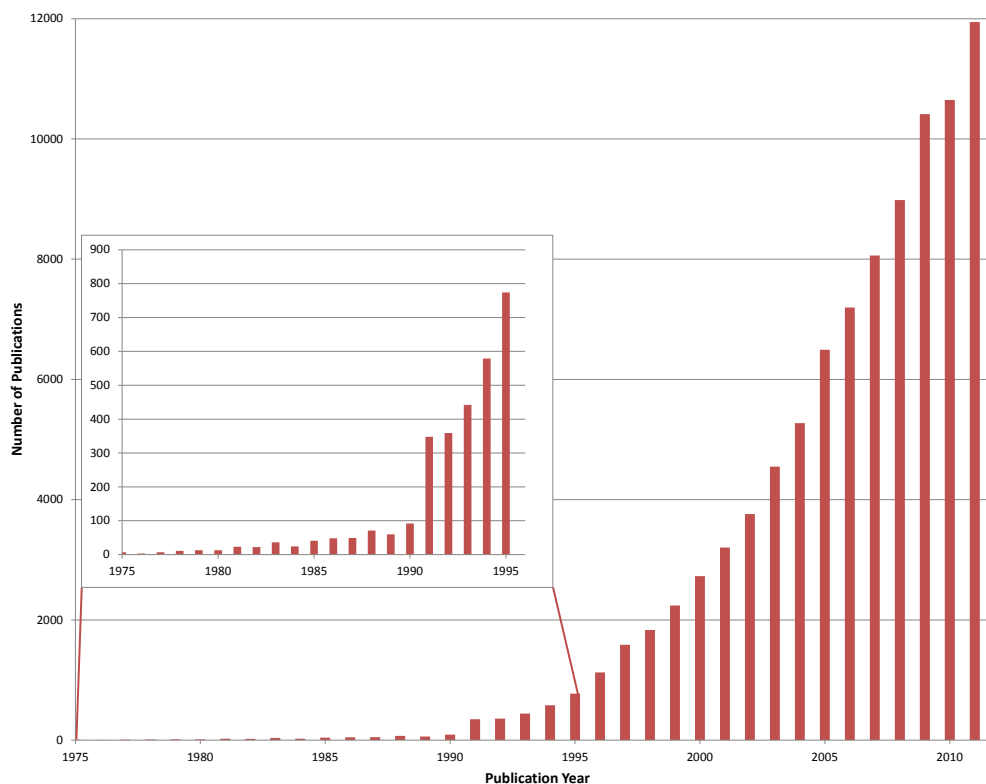
$$\Psi(x_1, x_2, \dots, x_n) = \chi_1(x_1), \chi_2(x_2), \dots, \chi_n(x_n) \quad (1.2b)$$

The SCF approach constructs an initial guess of the one-electron wave functions, ψ_i , for each occupied atomic orbital (AO). The solution of the one-electron Schrödinger equation, Eq. (1.3), for each wave function generates a new set of wave functions. The process is iteratively executed until a stop criterion is met, for example when the predicted change in electronic energy is below a specified threshold value.

$$h_i\psi_i = \varepsilon\psi_i \quad (1.3)$$

The initial work by Hartree used a representation of the wave function that was not antisymmetric, Eq. (1.2b). Soon after Hartree's work, Fock expanded the theory to account for the antisymmetric requirement of the wave functions through the use of a Slater determinant,⁴ giving rise to the Hartree-Fock (HF) method.⁵

The use of HF theory saw increased usage as computing technology began developing in the 1950s. However, for most systems, the cost of evaluating the exchange energy was too expensive given the computing resources available. In the early 1960s, work by Hohenberg and Kohn⁶ as well as Kohn and Sham,⁷ addressed the issue of evaluating the many-body wave function by instead describing the system as a collection of non-interacting electrons in an effective potential described by the ground-state electron density of the system, now referred to as density functional theory (DFT). By 1990, the number of papers citing DFT in their title or abstract began to dramatically rise, and continues to do so (Fig. 1.1). Since the initial development, DFT has been expanded to incorporate calculations for a wide variety of chemical parameters, two of particular interest are computation of NMR chemical shift values and computation of various thermodynamic quantities.

Fig. 1.1 Number of Publications Listing DFT as a Topic

Graph compiled from data provided from a search of “dft” or “density functional theory” as a topic keyword on the Web of Knowledge database

1.2 Theory of Computing NMR Chemical Shifts

A chemical shift, as observed experimentally, is the result of a two-part calculation. First, the magnetic shielding, σ , of a nucleus is proportional to the second derivative of energy relative to the external magnetic field and the internal magnetic moment of the nucleus under observation. The chemical shift is the observed difference in magnetic shielding values for the observed nucleus in the molecule relative to the same nucleus in a reference compound, commonly tetramethylsilane (TMS). Additionally, the chemical shift experienced

by a nucleus is dependent upon the orientation of the nucleus with respect to the external magnetic field, an effect termed chemical shift anisotropy (CSA). In a solution state NMR experiment, this orientation effect is averaged by the rapid tumbling of the molecules.

In the computation of chemical shifts, the applied external magnetic field is represented as a vector, which requires an origin. Selecting the position of the magnetic field is an interesting problem, since we know the chemical shift is influenced by the position and orientation of the nucleus relative to the external field (via the CSA effect). Three main methods, continuous set of gauge transformations (CSGT),⁸⁻¹⁰ gauge-independent atomic orbital (GIAO),¹⁰⁻¹⁴ and individual gauges for atoms in molecules (IGAIM)^{8,9} present various solutions to the problem of choosing the origin of the magnetic field. Regardless of the method selected, a NMR calculation provides a magnetic shielding tensor for each nucleus in the molecule. The tensor is a 3x3 matrix, describing the magnitude and direction of σ , for each combination of the three axis directions (x, y and z):

$$\begin{bmatrix} \sigma_{xx} & \sigma_{xy} & \sigma_{xz} \\ \sigma_{yx} & \sigma_{yy} & \sigma_{yz} \\ \sigma_{zx} & \sigma_{zy} & \sigma_{zz} \end{bmatrix} \quad (1.4)$$

The tensor can be reduced to a coordinate frame where the off-diagonal components are removed, resulting in a principal axis system, containing three diagonal elements (σ_{xx} , σ_{yy} and σ_{zz}), and three eigenvectors (which describe the orientation of the principal axes). The isotropic shielding, σ_{iso} , is the average of these three diagonal elements. This value is translated to a chemical shift, δ , by subtracting the isotropic shielding of the same nucleus in the reference molecule (computed in the same manner) from the isotropic shielding of the nucleus under investigation.

1.3 Calculation of Thermodynamic Quantities by DFT

In evaluating the feasibility of unknown reactions, calculating accurate thermodynamic parameters is critical. Specifically, accurate calculation of the Gibb’s free energy change, ΔG , and activation energy ΔG^\ddagger provide insight into a reaction. The incorporation of electron correlation effects in DFT allow for the computation of these thermodynamic quantities.¹⁵ However, because the functionals describing exchange interaction and electron correlation is only known for a free-electron gas (through the Thomas-Fermi model^{16,17}), DFT functionals have been developed with a wide variety of solutions to describing the exchange and correlation functionals. The choice of DFT functional is crucial to obtaining meaningful data, and comparisons of DFT functional performances have been published for various systems.^{18–20} The M06 suite of functionals²¹ has shown a broad applicability in calculation of various reaction thermodynamics for a range of chemical systems, thus the M06-2X functional was applied for all thermodynamic calculations in this work unless otherwise specified. The 6-31+G(d,p) Pople-type basis set was applied for all optimization and thermodynamic calculations unless indicated otherwise.

Energy calculations using an electronic structure approach such as DFT do not implicitly include any temperature or pressure effects, that is, the quantities generated are only valid at $T = 0$ K and $p = 0$ atm. One component of the thermodynamic calculation is the electronic energy. The electronic energy is the calculated energy required to strip all electrons from the atoms, and separate all atoms and electrons from each other infinitely far apart. To include bulk effects based upon temperature, solvation and entropy, the theory of the Born-Oppenheimer approximation²² is utilized. The Born-Oppenheimer approximation states that the response of electrons to external perturbation is significantly more rapid than that of a nucleus, such that the electron reorganization upon movement of a nucleus can be viewed as nearly instantaneous. This approximation can be applied to incorporate temperature effects by evaluating the total energy as a function of nuclear position on the

Born-Oppenheimer potential energy surface (PES). The resulting Born-Oppenheimer PES can be used to extract vibrational modes that can be used with the results of the DFT calculation to describe thermodynamic quantities at finite temperatures and pressures. In practice, a standard temperature of 298.150 K and pressure of 1.000 00 atm are used for the calculation unless otherwise specified. From the incorporation of temperature and pressure, thermal free energy (G) can be derived from the calculated enthalpy (H) and entropy (S) terms. The combined value, sum of electronic and thermal free energies, in solution represents the Gibb's free energy of a system. This value is used for all free energy calculations without further correction.

1.4 Methods for Locating a Transition State

A transition state (also referred to as a saddle point) is any point along a PES that has a second derivative of energy with respect to the reaction coordinate that is negative, but all second derivatives in another direction are positive. A transition state is uniquely identifiable as having one and only one negative (imaginary) frequency. Transition states are typically more difficult to locate than minima on the PES, but modern computational software packages (e.g. Gaussian 09²³) have provided algorithms to aid in their location.

The synchronous transit-guided quasi-Newton (STQN)^{24,25} and Bernaly²⁶ are two algorithms embedded into the Gaussian 09²³ software package that are commonly utilized when searching for a transition state. For the STQN algorithm, there are two further options, originating from the quadratic synchronous transit (QST) approach, QST2 and QST3. For QST2, a starting geometry and final geometry are provided, and the algorithm searches for a saddle point along the path connecting those two points. The QST3 method is almost identical except that an initial guess at the transition state is provided along with the starting and final geometries. The Bernaly algorithm is the default optimization algorithm Gaussian utilizes when performing standard geometry optimizations, and the method in

which further optimization steps are chosen is altered in order to locate a transition state.

Once a saddle point has been located, there is no guarantee that it is actually a transition state for the reaction under study. It is common to analyze the imaginary frequency to see if the molecular vibration corresponds to the desired reaction. A more thorough method to validating a given transition state is to carry out an intrinsic reaction coordinate (IRC) analysis. Starting at the previously located transition state, this analysis tracks the molecule down the PES in both the forward and backward direction. It continues until it reaches the maximum number of steps set during the calculation, or when it reaches a minimum. A successful IRC analysis provides a plot of the energy for each step along the PES back to the reactant and toward the product. Using this method, a located transition state can be confirmed for the pathway if the IRC leads to the expected minima along the reaction coordinate (i.e., presumed reactant and product).

1.5 Solvation Modeling

An unmodified DFT calculation operates on the system without the presence of a solvent (i.e., in the gas phase). In the condensed phase, solvents can play a significant role, influencing both conformational preference²⁷ and reaction thermodynamics²⁸ through interaction with the solute molecules. Calculations in the condensed phase must then appropriately model or account for these interactions either explicitly or implicitly.

Explicit modeling of these effects can be achieved by including individual solvent molecules in the calculations. Calculations involving explicit modeling of solvent add substantial complexity to the calculations by requiring additional interactions in the system.

Alternatively, models for defining the effect of the solvent on the solute implicitly, without the need for defining individual solvent molecules, have also been developed. Implicit

models benefit from greater simplicity in both computational complexity (or cost) and implementation into a calculation for the user. Implicit models, also known as continuum solvation models, define the solvent by a continuous medium and places the solute inside this environment. The goal of implicit modeling is to accurately reflect electrostatic interactions, dispersion effects, and cavitation changes that the solvent exerts on the solute. The molecular cavity used is described by a series of interlocking van der Waals-spheres centered on each atom of the solute. The radius of the spheres used is controlled by the protocol selected for the computation.

2. DEVELOPING A PROTOCOL FOR FACILE COMPUTATION OF NMR CHEMICAL SHIFTS

2.1 Introduction

The interrogation of organic reaction mixtures and structure elucidation by NMR spectroscopy is employed on a routine basis by experimental organic chemists. For even modestly complex molecules, multiple types of NMR experiments are often required to fully elucidate a molecule's structure. The first commercial NMR instrument, the HR-30 by Varian, was produced in 1952.²⁹ Today, there is still continued interest in developing more refined NMR experimental procedures aimed at structure elucidation.^{30,31} Computation of these NMR chemical shift values can augment the current need for more advanced NMR experimentation.

2.2 The Process of Calculating NMR Chemical Shifts

Calculating NMR chemical shifts at the most basic level involves a single calculation as implemented in the Gaussian 09²³ software utilizing the keyword `NMR`. The default method, GIAO,¹⁰⁻¹⁴ calculates the magnetic shielding tensors of the individual atoms. Magnetic shielding tensors of a shift reference (such as TMS) scale the values to the more understandable δ scale.

This analysis yields chemical shifts values for each atom in the geometry specified in the program. However, since most molecular vibrations are of short duration on the NMR timescale, the above method does not take into account the various conformations that a molecule may sample during the course of an experimental NMR acquisition. Incorporation

rating chemical shift values of multiple conformers can improve the matching between the computed and experimental chemical shifts.

Incorporating multiple conformers into the chemical shift calculation is a twofold process. The first step is to generate a set of conformers using a Monte-Carlo/multiple minimum (MC/MM) search. This expands the conformational space sampled, providing a more accurate representation of the conformers observed experimentally. After generating the set of conformers, individual DFT geometry optimization calculations and frequency analysis of each conformer is followed by calculation of each conformers NMR spectra. The thermodynamic analysis provides relative energies of the conformers, which can be used to Boltzmann weight the calculated NMR shifts, yielding a single set of averaged chemical shifts for the structure.

2.2.1 Specific Implementation for Calculating NMR Chemical Shifts

To generate the initial set of conformers, a MC/MM conformational search was carried out with Macromodel (v9.8)³² as implemented in Maestro (Schrödinger Software, v9.1.207).³³ For each structure, the search utilized one of three force fields (AMBER94, OPLS_2005, or MMFFs). A molecular mechanics (MM) current energy calculation was done utilizing each of the three force fields. Whichever force field utilized the least number of medium- and low-quality parameters for the energy calculation was picked for the conformational search. The conformational search was conducted using MC/MM torsional sampling, keeping all structures that fall within a 5.02 kcal/mol window.

After the conformational search, each conformer is exported to a Gaussian input format using a Python script developed by group member, Mr. Patrick Willoughby (writeg09-inputs-default.py, A-1.1). Two files, one for running the geometry optimization/thermochemistry calculation and one for the NMR calculation are generated from the script.

Geometry optimization is performed using the M06-2X²¹ functional with the 6-31+g(d,p) Pople-type basis set. After optimization, frequency analysis is executed which includes a calculation of thermochemical values for the system, including the Gibb's Free Energy. Using the final geometry from the optimization, the NMR calculation is performed using the B3LYP³⁴⁻³⁷ functional and the 6-311+g(2d,p) Pople-type basis set. Both the optimization and NMR calculation are performed using the integral equation-formalism polarizable continuum model (IEFPCM) solvation model,³⁸⁻⁴⁰ and typically in chloroform unless it is otherwise noted. The radii of Bondi⁴¹ is used to calculate the molecular cavity accessible by the solvent (see section 1.5, page 8).

After calculating the NMR properties for each conformer, the script (`nmr-data_compilation.py`, A-2.1) performs a Boltzmann weighting of the conformers using the data from the thermochemistry calculation. The chemical shifts for each conformer are scaled according to the Boltzmann contribution calculated for that conformer. The combined sum of these scaled shifts results in the average chemical shifts used to compare against experimental data.

2.3 Examining Optimization Protocols

Gaussian 09 calculates thermochemical information from the final optimized structure. The standard optimization/thermochemical calculation protocol employed utilizes the `opt` keyword without any modification, followed by a frequency analysis (using the `freq` keyword). The geometry used for the frequency calculation must be a stationary point (in this case a minimum) in order to obtain meaningful thermochemical data. As part of the frequency calculation, an analytic Hessian matrix indicates if the input geometry is a stationary point (by finding that the 2nd derivative of the PES is 0). Occasionally, the final geometry from optimization is not a stationary point as determined by the analytic calculation of the Hessian matrix. This occurs when the optimization utilizes an approximate Hessian matrix, while the frequency calculation uses an analytically calculated Hessian. The thermochemical

information in this situation is not reliable.

We investigated a series of more rigorous optimization procedures, which more reliably would ensure a minimum structure is obtained. The more rigorous the optimization options, the longer the calculation takes. The large majority of structures we investigated were tractable enough to allow for the most rigorous optimization to complete within a reasonable time limit. Assessment of these protocols is based upon their computational speed and reliability in finding a minimum structure.

Table 2.1 Optimization Procedures and Effect on Calculation Time

Entry #	Optimization Protocol	Relative Calculation Time
1	opt, freq	1.00
2	opt, opt=calcall	9.03
3	opt=calcf, opt=calcf, freq	8.20
4	opt=calcf, opt=calcall	4.63

The default optimization (entry **1**) is clearly the fastest method for optimization and thermochemical calculation. However, as stated earlier, the optimization may not always result in a geometry that is determined to be a stationary point during frequency analysis, this results in inaccurate thermochemical results. Entry **2** utilizes an initial optimization (with an approximate Hessian matrix) followed by an optimization with the `calcall` option. The `calcall` option instructs Gaussian to calculate a new analytic Hessian matrix for each optimization step, and then executes the frequency calculation after finding the stationary point. Utilizing this option prevents the conflict where the final optimization geometry is determined to not be a stationary point after the analytic Hessian matrix is calculated, since the Hessian matrix is calculated at each optimization step. However, this benefit

comes at a significant computational cost. The cost can be especially high if numerous optimization steps are required for the second optimization, when the Hessian matrix must be calculated for each step. This occurs when the input geometry is greatly displaced from the final geometry. The computational cost of this method could be decreased by reducing the disparity between the final geometry of the first optimization and the finished optimized geometry. In entry **2**, this disparity is reduced by performing an initial optimization using the computationally inexpensive `opt` protocol before the more expensive `opt=calcall`.

The protocol utilized for entries **3** and **4** uses the `calcfc` option. This option requests that an analytic Hessian matrix be calculated for the starting geometry to guide the optimization, but not every step as with the `calcall` option. Starting with the analytic Hessian matrix will hopefully result in a final geometry that is closer to the geometry achieved from the `calcall` optimization. The first attempt, entry **3**, tried a two-step optimization with one `calcfc` optimization followed by a second `calcfc` optimization. A subsequent frequency calculation on the final geometry provides the thermodynamic information. While a slight speed increase was obtained, the improvement was not satisfactory. Another protocol (entry **4**) was tested, which combined the reliability of the `calcall` option and the decreased computational cost of using the `calcfc` option to start the optimization. This combination gave reliable thermochemical results (by ensuring a minimum stationary point was always obtained) with a modest increase in computational cost. For future computational NMR work, the protocol in entry **4** is used for all geometry optimizations unless a particular conformer failed to optimize within the allowed time limits. In those cases, alternative multi-step optimizations are employed to achieve full convergence prior to computing the NMR. The default script (A-1.1) was updated to include a second output command in the Gaussian input file for the `calcall` section of the protocol (`write-g09-inputs-calcFCcalcall.py`, A-1.2).

2.4 Methods of Analysis

The main way to evaluate the computed data is through statistical analysis compared to an experimental spectrum. However, we have also developed a graphical comparison template for the OriginPro software program for plotting the shift values of the spectra.

2.4.1 Statistical Analysis Methods

Statistical analysis methods are the primary resource used to evaluate the fit of computed chemical shifts against an experimental spectrum. At least a partial assignment of the experimental spectrum is necessary in order to carry out this analysis. Correlation coefficients (r), mean-absolute error (MAE), and CMAE are the three statistical parameters utilized for comparison. Overall performance of the computational predication is assessed through calculation of combined ^1H and ^{13}C values of these parameters, Eq. (2.1).⁴²

$$\text{MAE}_{comb} = \sqrt{\text{MAE}_C \times \text{MAE}_H} \quad (2.1a)$$

$$\text{CMAE}_{comb} = \sqrt{\text{CMAE}_C \times \text{CMAE}_H} \quad (2.1b)$$

$$r_{comb} = 1 - \sqrt{(1 - r_C) \times (1 - r_H)} \quad (2.1c)$$

The CMAE is a MAE analysis after applying a linear correction to the computed values. The CMAE analysis usually increase the difference between the CMAE value of the correct computed/experimental pair and an incorrect computer/experimental pairing, improving the possibility of identifying the structure corresponding to the experimental data. In all cases, comparing the experimental spectrum with the correct structure’s computed spectrum is defined as a “matched” comparison, while any computed spectrum for an incorrect structure is defined as a “mismatched” comparison.

The calculation of the MAE (or CMAE) involves pairing each computed shift with the

corresponding assigned experimental value. The definition for computing the MAE is:

$$\text{MAE} = \frac{1}{n} \sum_{i=1}^n |\delta_{\text{comp},i} - \delta_{\text{exp},i}| = \frac{1}{n} \sum_{i=1}^n |e_i| \quad (2.2)$$

Where n is the number of chemical shift values, $\delta_{\text{comp},i}$ is the computed value of the i th chemical shift, and $\delta_{\text{exp},i}$ is the experimental value of the i th chemical shift. The value $\delta_{\text{comp},i} - \delta_{\text{exp},i}$ can also be thought of as the error in the computed shift calculation of the i th value, or e_i . The CMAE, a derivation from this expression, is computed with the following equations:

$$\delta_{\text{corr},i} = \frac{\delta_{\text{comp},i} - a}{b} \quad (2.3a)$$

$$\text{CMAE} = \frac{1}{n} \sum_{i=1}^n |\delta_{\text{corr},i} - \delta_{\text{exp},i}| = \frac{1}{n} \sum_{i=1}^n |e_{\text{corr},i}| \quad (2.3b)$$

For the CMAE analysis, a linear regression analysis of the computed and experimental shifts gives the constants a and b which are used in Eq. (2.3a) to calculate the corrected shifts, $\delta_{\text{corr},i}$. The corrected shifts are then applied in a similar manner as the MAE to Eq. (2.3b), where now the value $e_{\text{corr},i}$ represents the error in the corrected shift for the i th value. In both cases, MAE and CMAE, a small value of e_i or $e_{\text{corr},i}$ (typically ≤ 0.05 and ≤ 2 ppm for ^1H and ^{13}C NMR respectively) for a computed structure corresponding to the correct structure and larger values for computed shifts that have an incorrect structure compared to the experimental structure. The correlation coefficient can have a value from -1 to 1, with a value of 1 indicating an exact match between the computed and experimental shifts.

As an example to the analysis performed, the first step is to assemble a table (i.e. Table 2.2). This example will utilize the analysis of *cis*-carvomenthone (**201a**, Fig. 2.1). The table is set up so the corresponding shifts from the computed structure are matched up with the assigned shifts of the experimental spectrum. After plotting the two data sets, a linear regression analysis provides the values for the corrected shifts, Eq. (2.3a). The original computed shifts, when compared against the experimental values provides

the “Error” column, and the MAE, while the new corrected shifts compared against the experimental values provide the “Corrected Error” column, and the CMAE.

Fig. 2.1 Structure and Numbering of *cis*-carvomenthone (**201a**)

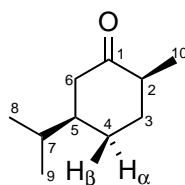


Table 2.2 Example MAE and CMAE Analysis of *cis*-Carvomenthone (**201a**)

Position	Comp. ^1H	Exp. ^1H	Error	Corrected Shifts	Corrected Error
2	2.47	2.45	-0.02	2.39	0.06
3 α	1.87	1.87	0.00	1.83	0.04
3 β	1.70	1.68	-0.02	1.68	0.00
4 α	1.69	1.68	-0.01	1.67	0.01
4 β	1.88	1.68	-0.20	1.84	-0.16
5	1.61	1.68	0.07	1.59	0.09
6 α	2.36	2.33	-0.03	2.28	0.05
6 β	2.51	2.33	-0.18	2.42	-0.09
7	1.45	1.49	0.04	1.44	0.05
8 Me	0.90	0.91	0.01	0.94	-0.03
9 Me	0.88	0.89	0.01	0.92	-0.03
10 Me	1.06	1.10	0.04	1.08	0.02
(Corrected) Mean Absolute Errors:			0.05		0.05

In this example, we see that since the quality of the computed data is so high (an average absolute error across all ^1H shifts of equal to or less than 0.05 ppm), there is little room for the CMAE to improve the results. Shown in a separate table are the extra columns for comparing the computed *trans*-carvomenthone (**201b**) with the *cis*-carvomenthone experimental data (a mismatched comparison, Table 2.3). In this case, the MAE starts at

Table 2.3 Example Mismatched MAE and CMAE Analysis of Carvomenthone (**201**)

Position	Comp. 201b ^1H	Exp. 201a ^1H	Error	Corrected Shifts	Corrected Error
2	2.48	2.45	-0.03	2.38	0.07
3 α	1.29	1.87	-0.44	1.39	0.48
3 β	2.12	1.68	0.58	2.08	-0.40
4 α	1.87	1.68	0.13	1.87	-0.19
4 β	1.55	1.68	-0.19	1.60	0.08
5	1.55	1.68	0.13	1.60	0.08
6 α	2.33	2.33	0.09	2.25	0.08
6 β	2.24	2.33	0.00	2.18	0.15
7	1.51	1.49	-0.02	1.57	-0.08
8 Me	0.91	0.91	0.00	1.06	-0.15
9 Me	0.89	0.89	0.00	1.05	-0.16
10 Me	0.92	1.10	0.18	1.07	0.03
(Corrected) Mean Absolute Errors:			0.15		0.16

0.15 ppm, and after the CMAE correction, increases to 0.16 ppm. The difference between in the CMAE for match and mismatched increases by 320%. This increase in disparity between the two proposed structures demonstrates the utility of the CMAE analysis even for small, relatively well-defined organic molecules. Additionally, this type of analysis is useful even if only partial assignment of the experimental spectrum is possible. For this example, the chemical shifts of position 3 β , 4 α , 4 β , 5, 6 α , 6 β were unable to be unambiguously assigned. If we repeat the analysis, including a new linear regression analysis with only the remaining shifts, a larger separation between matched and mismatched errors is observed for both MAE and CMAE (Table 2.4). An analogous process can be carried out with ^{13}C data.

Table 2.4 Summarized MAE and CMAE Results for *cis*-Carvomenthone Before and After Removal of Uncertain Shifts

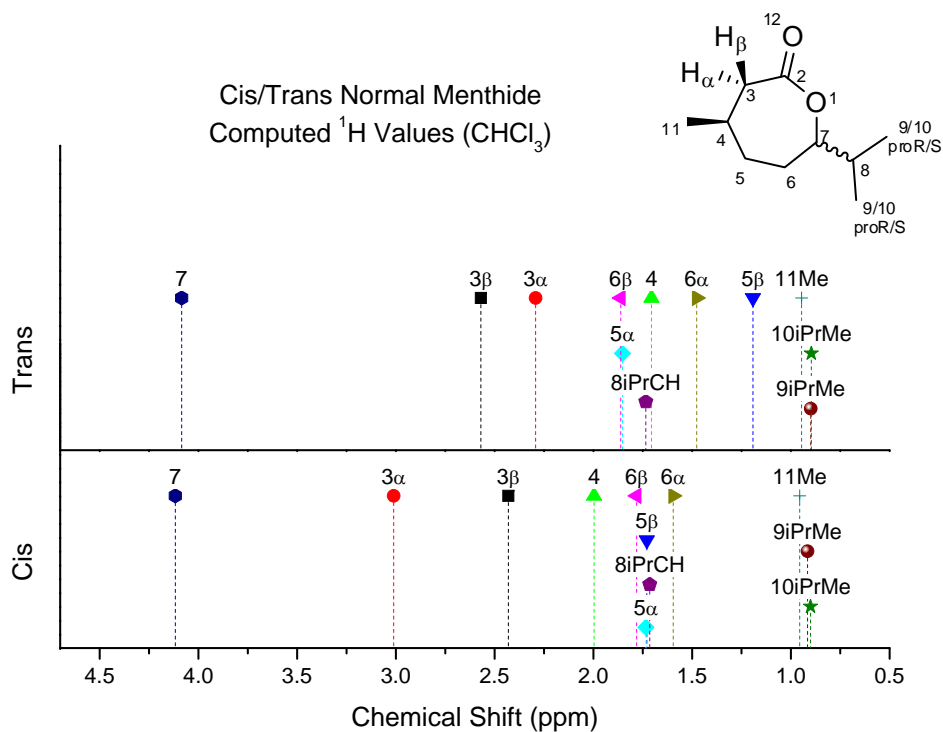
		Matched	Mismatched
Full Set of Shifts	MAE	0.05	0.15
	CMAE	0.05	0.16
Partial Set of Shifts	MAE	0.02	0.14
	CMAE	0.02	0.16

2.4.2 Qualitative Graphical Analysis

Statistical analysis is valuable for quantitative assessment of the fit for a computed data set to an experimental spectrum. However, it is limited to meaningful application only when some reasonable amount of assignment or correlation between the computed and experimental shifts can be made. It can also be time consuming to correlate the shifts to the experimental values, perform linear regression analysis, and recompute errors (for CMAE) to arrive at a result. We needed a way to quickly dismiss stereoisomers, that due to the distribution of chemical shifts on the spectrum, cannot be possible structures of the experimental spectrum under analysis. These two factors prompted the design of a graphing template that could quickly aid in comparison of possible structures and their NMR spectra.

Using the data analysis software OriginPro from OriginLab[®], we have developed two graph templates (one being Fig. 2.2) which provide a stacked comparison of two data sets (any mixture of computed and experimental sets can be combined).

Fig. 2.2 Example of a Stacked Graphical Comparison



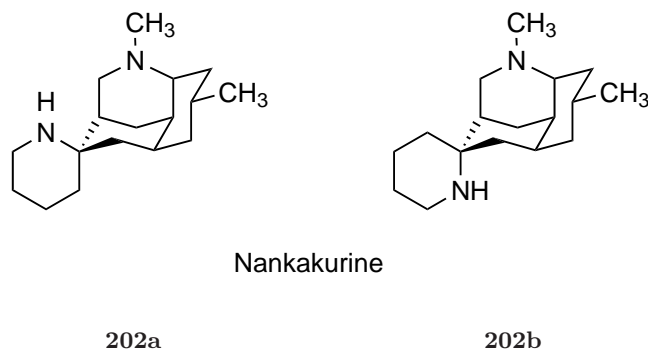
This template is useful in analyzing an experimental NMR spectrum when considering one or more diastereomers. Regions of the computed NMR spectra where shifts are present in only one of the diastereomers can be used as a guide for examining the experimental spectrum. In Fig. 2.2, only the *trans* diastereomer shows a shift in the ~ 1.25 ppm region. Recall that the average error in computed ^1H chemical shifts for a “matched” comparison is often less than 0.1 ppm, so even the fine differences in chemical shift in the 1.25 ppm region can be used to guide the interpretation. Utilizing the template with an experimental spectrum showing a shift at ~ 1.25 ppm would quickly lead to a determination that the compound is likely the *trans* diastereomer. The graphical comparison can aid in comparing the rest of the peaks, or a formal statistical analysis could be performed with any peaks that have been

assigned. In this example, the relatively simple comparison is only between two possible diastereomers. To address the complexity of quickly scanning multiple diastereomers, we also developed a similar graphing template to allow plotting of up to four diastereomers.

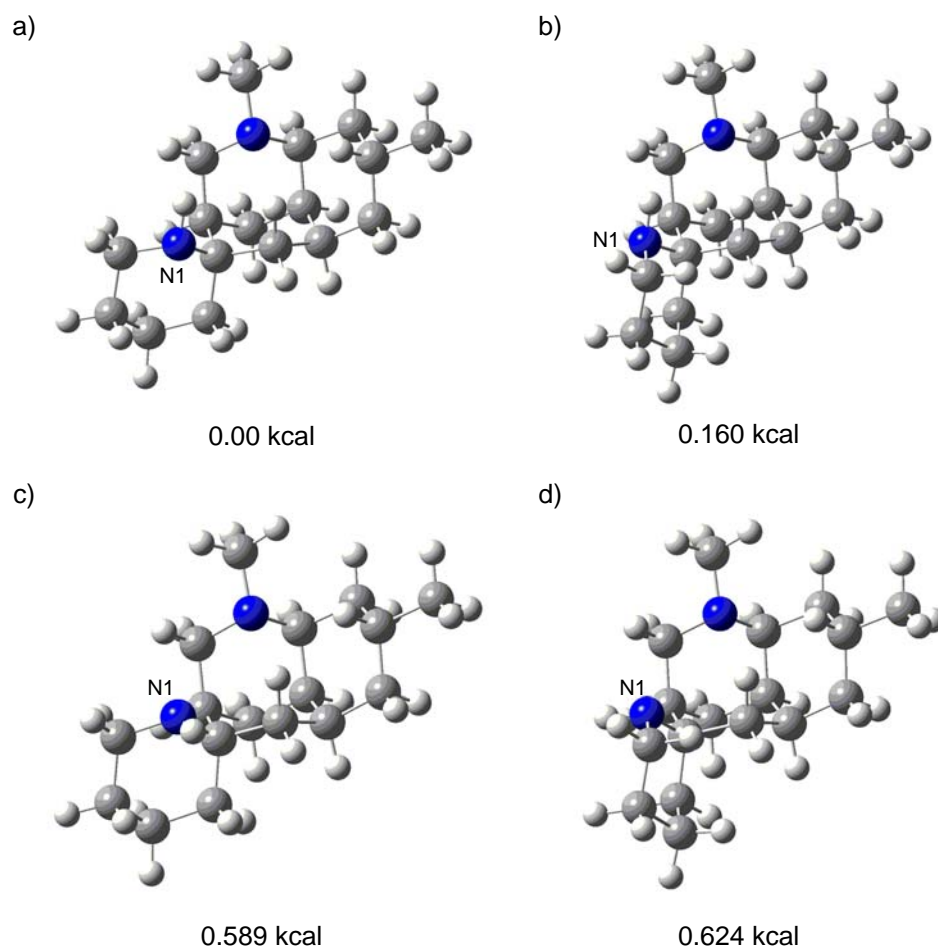
2.5 Comparison of our Protocol with a Previously Computed Natural Product

We began testing our protocol on a natural product, nankakurine (**202**, Fig. 2.3), which was previously calculated by Goodman and coworkers.⁴³ Nankakurine was chosen for the complex magnetic environment with through-space shielding, but was also simplified through a rigid molecular structure reducing conformational flexibility. Two diastereomers, the revised diastereomer (**202a**) and the originally proposed diastereomer (**202b**), were compared. The epimeric center is indicated by a “*”.

Fig. 2.3 Nankakurine Natural Product Used to Test NMR Computation



For the **202** system, we found restricted conformational flexibility, observing only four conformers for each epimer. However, within those four conformers, the **202** structures show some significant conformational changes. There are four total conformers, in two distinct sets (representing each chair flip of the molecule). Within each set of chair-flip conformers, we observe a second conformer resulting from the nitrogen atom inversion at N1 (Fig. 2.4).

Fig. 2.4 Conformers of Nankakurine

Conformer pairs a/c and b/d are related by nitrogen inversion

Conformer pairs a/b and c/d are related by chair-chair flips

Performing the statistical analysis on the system of **202** diastereomers, we found that the CMAE values were very closely matched for both the correct and incorrect diastereomer. From analysis of this system, we learned that due to the small structural change resulting from the diastereomeric pair, and the almost analogous conformational space sampled,

the majority of the shifts calculated were relatively well isolated from the change in diastereomer. In as, both diastereomers sampled the exact same four types of conformers (chair-chair flip, and nitrogen inversion), as well as most of the protons are in roughly the same environment, regardless of diastereomer analyzed. This results in CMAE values that are both very low (0.054 and 0.072, respectively). However, we were encouraged by the results in that, comparing the accuracy of our computed set (r , MAE and CMAE), to those of Goodman,⁴³ we observe a 37.9% decrease in the CMAE (Table 2.5).

Table 2.5 Comparison of Our Protocol and Goodman’s on Computed Nankakurine Shifts

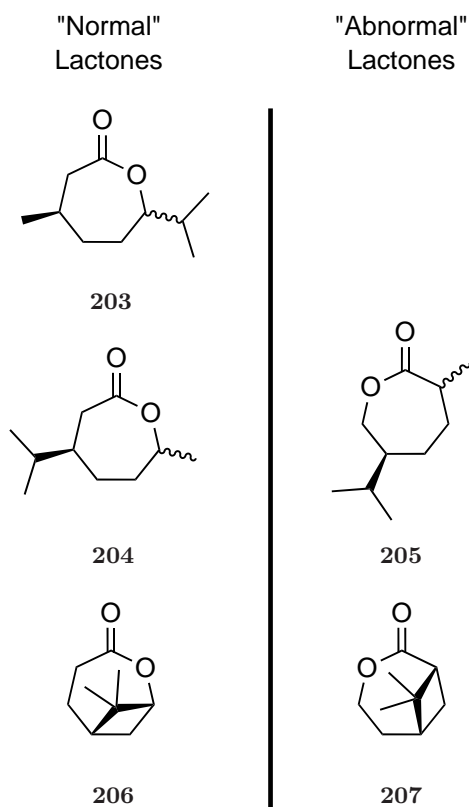
		Matched		Mismatched	
		Our Data	Goodman Data	Our Data	Goodman Data
¹ H	r	0.9894	0.9508	0.9828	0.8570
	MAE	0.104	0.108	0.130	0.177
	CMAE	0.054	0.087	0.072	0.151
¹³ C	r	0.9946	0.9865	0.9924	0.9804
	MAE	4.108	1.505	4.026	1.622
	CMAE	1.009	1.179	3.400	1.417
Combined Parameters	r_{comb}	0.9924	0.9869	0.9885	0.9730
	MAE _{comb}	0.653	0.403	0.724	0.536
	CMAE _{comb}	0.233	0.322	0.494	0.461

Having verified the accuracy of our protocol to compute structures of moderate complexity, and compare them to previous calculations, we attempted to extend our protocol to calculations relevant to work within our group and collaborations. A central goal to these investigations is to demonstrate the straightforward application of our protocol and

accompanying scripts to enhance analysis of the experimental NMR spectra.

2.6 Evaluating Stereoisomers of Bioderived Lactones

Lactones are a useful substrate in ring opening transesterification polymerization (ROTEP) reactions,⁴⁴ a growing field in the area of polymer synthesis. As polymers are used in wide variety of daily products, there is a large incentive to use substrates that are derived from renewable sources. In the Hoyer group, Drs. Aman Kulshretha and Susanna Emond investigated the synthesis of bio-derived lactones, Fig. 2.5.

Fig. 2.5 Set of Bio-derived Lactones Synthesized

¹"Normal" lactones are defined as containing the oxygen on the more substituted side of the carbonyl

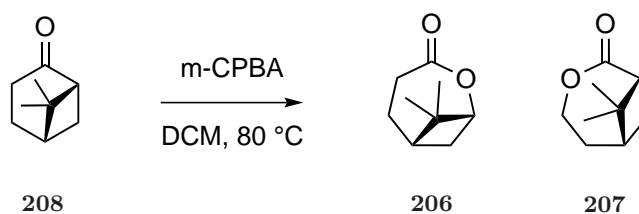
²"Abnormal" lactones contain the oxygen on the less substituted side of the carbonyl.

The configuration of the stereocenters in the lactone influences the properties and type of polymer synthesized.⁴⁵ Previous work involving these lactones utilized low field-strength NMR analysis, resulting in both overlapping resonances as well as an incomplete assignment of all chemical shifts. We aimed to fully characterize the NMR spectra of these compounds with the aid of computationally predicted NMR chemical shifts.

2.6.1 Lactones Derived from β -pinene: A Small Molecule Test Case

The lactones, **206** and **207** derived from the parent molecule β -pinene, were ideal candidates to test our protocol on. There is limited conformational space to sample the molecule over as the constrained [4.1.1]bicyclic skeleton limits the flexibility of the molecule. We could also examine through-space shielding effects as one of the methyl groups will be placed almost directly above the lactone ring. In order to compare the computationally predicted chemical shifts against experimental data, Dr. Kulshretha prepared **206** and **207** through Baeyer-Villiger oxidation of nopinone (**208**, Scheme 2.1). The oxidation generates both the normal and abnormal lactones as a mixture.

Scheme 2.1 Synthesis of Normal and Abnormal β -pinene Lactones from Nopinone



The comparison of computed shifts for a matched and mismatched structure is not necessary here, as the chemical shift differences for each molecule are easily distinguished by experimental NMR. Specifically, **207** contains two proton resonances next to the lactone oxygen, while **206** only contains one proton resonance. However, we could still examine the accuracy of the computed shifts for each structure (Table 2.6). Additionally, the computed shifts (and the geometries from their calculation) would prove to be a valuable aid in completing a full assignment of the experimental NMR spectra.

Table 2.6 Statistical Matching Parameters of Computed Shifts of β -Pinene Lactones

		206	207
^1H	r	0.9956	0.9980
	MAE	0.088	0.080
	CMAE	0.073	0.063
^{13}C	r	0.9996	0.9997
	MAE	4.064	4.474
	CMAE	1.128	0.914
Combined Parameters	r_{comb}	0.9986	0.9993
	MAE_{comb}	0.598	0.598
	CMAE_{comb}	0.287	0.239

We observed that the computed shifts match extremely well for both the normal and abnormal lactones. For the ^1H predicted shifts, the CMAE values of 0.088 and 0.080 indicate a high degree of agreement between the computationally predicted shifts and the experimental values. Through the course of this project, we observed that the lowest ^1H CMAE values achieved are in the range of 0.05 to 0.1 ppm. Linear scaling of the shifts can also have a significant impact on the computed error, as evidenced by the decrease in error between the MAE and CMAE. The large decrease, especially for the ^{13}C comparison indicates the protocol contains a systematic error in the computation of the chemical shifts (a similar effect was observed for nankakurine, **202**, page 20).

Analysis of these lactones presented the opportunity to examine other NMR shift effects, such as the through-space shielding effects experienced by the methyl group (and proton) positioned directly over (and under) the lactone ring. The computed and experimental

values are summarized in Table 2.7. The maximum absolute error for any single proton after linear correction was 0.15 and 0.11 ppm for the normal and abnormal lactones. While the minimum absolute error was only 0.01 ppm for both lactones. We can see that especially for the methyl groups, the predicted shifts are in excellent agreement with the experimental values. In these bridged systems, we define the *syn* position of the bridge to be pointing towards the ring system, while the *anti* position is defined as pointing away from the ring system (see 3D model, Fig. 2.6, page 28). It appears that the *syn* protons were less well predicted than the *anti* protons, while the methyl groups are predicted accurately to nearly the same extent.

Table 2.7 Accuracy of ^1H Computation for Bridging Methyl and Methylenes

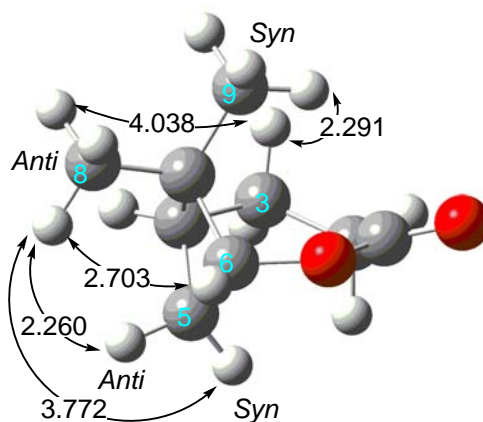
		Normal Lactone, 206			Abnormal Lactone, 207		
		Comp.	Exp.	Exp-Comp	Comp.	Exp.	Exp-Comp
Methyl	Syn	0.88	0.89	0.01	1.08	1.04	-0.04
	Anti	1.28	1.30	0.08	1.39	1.38	-0.01
Methylene	Syn	2.22	2.11	-0.11	2.39	2.30	-0.09
	Anti	2.59	2.65	0.06	2.42	2.45	0.03

During assignment of the experimental NMR spectra, we found great utility in using the optimized geometries determined for the NMR calculations. Guided by the Karplus equation,⁴⁶⁻⁴⁸ we could use the computed geometries to inspect dihedral angles of specific coupling interactions and verify the observed coupling constant was consistent with the geometry.

The computed geometries also allowed us to interrogate interatomic distances. In order to confirm the *syn/anti* orientation of the bridging methyl groups and the methylene (-

CH₂-) hydrogens, a nuclear Overhauser effect (NOE) experiment can provide information about the proximity of neighboring protons to the selected proton. The signal enhancement observed can be correlated to interatomic distance with high accuracy for protons less than 4.0 Å apart.⁴⁹ We used the computed geometries to guide our NOE experiment by selecting protons with interatomic distances well-suited for observation by an NOE experiment (Fig. 2.6). The *syn* position is defined as facing towards the ring, while the *anti* position is defined as facing away from the ring.

Fig. 2.6 Selected Interatomic Distances of Protons in β -Pinene Normal Lactone



¹All distances reported are in Å.

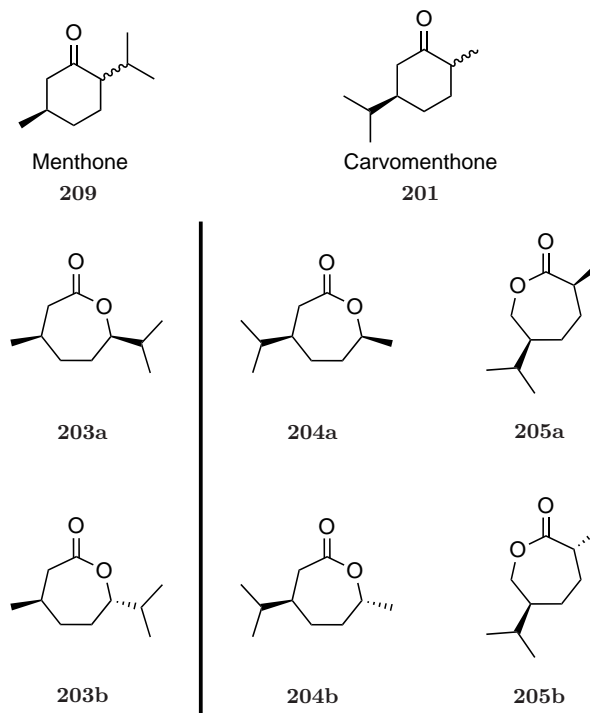
²Selected carbon numbering is given in cyan.

According to the computed interatomic distances, we planned that irradiating the “axial” proton on C3 should provide an NOE enhancement to the proton signal of the *syn* methyl group, C9, but little to no signal for the *anti* methyl group, C8. We were then guided by the large difference in interatomic distance between the *anti* methyl group, C8 and the two bridgehead methylene protons on C5. Irradiating the *anti* methyl group should provide a large enhancement for the *anti* proton on C5, and minor if any enhancement for the *syn* proton on C5. Through this two-step approach, we could confirm the *syn/anti* assign-

ment of both methyl groups on the bridgehead carbon, C7, and the methylene bridgehead protons on C5.

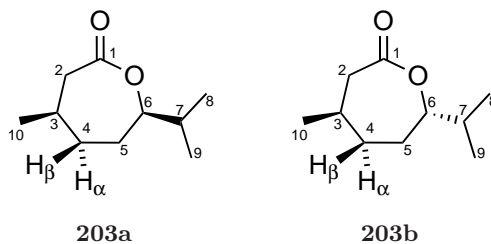
2.6.2 Lactones From Menthone and Carvone: Pairs of Diastereomers

We continued our computational prediction of chemical shifts by extending the method to analyzing pairs of diastereomers in a series of bio-derived lactones (Fig. 2.7). These lactones have no thorough NMR characterization present in reported literature. The lactones are derived from the corresponding parent compounds, menthone (**209**) and carvomenthone (**201**), which are synthesized by Dr. Emond as separate diastereomers. Evaluation of these compounds as diastereomers seems unnecessary at first. However, because there is no thorough NMR characterization available in the literature, simple comparison to determine the configuration was not possible. The accurate determination of the configurations in these substrates is critical for understanding the resulting properties of polymers derived from their use (see page 24).

Fig. 2.7 Lactones Derived from Menthone and Carvomenthone

Statistical Comparison of the Normal *cis/trans*-Menthide

The menthide lactones are the first to be examined. This data set proved to be especially troublesome, as all attempts to fully optimize the conformers of the normal *cis*-menthide proved to be unsuccessful, failing to locate a minimum stationary point. The comparison for this set will then be for only the experimental *cis* and *trans* compared against the computed *trans* chemical shifts (Fig. 2.8).

Fig. 2.8 Diastereomers and Numbering Scheme of Normal Menthlide

For this series, Dr. Emond was able to conclusively assign all the ^{13}C resonances. In the ^1H data, there were some overlapping peaks that could not be resolved. Discussion will relate only to the findings for the *trans* diastereomer since computed data for the *cis* diastereomer is not available.

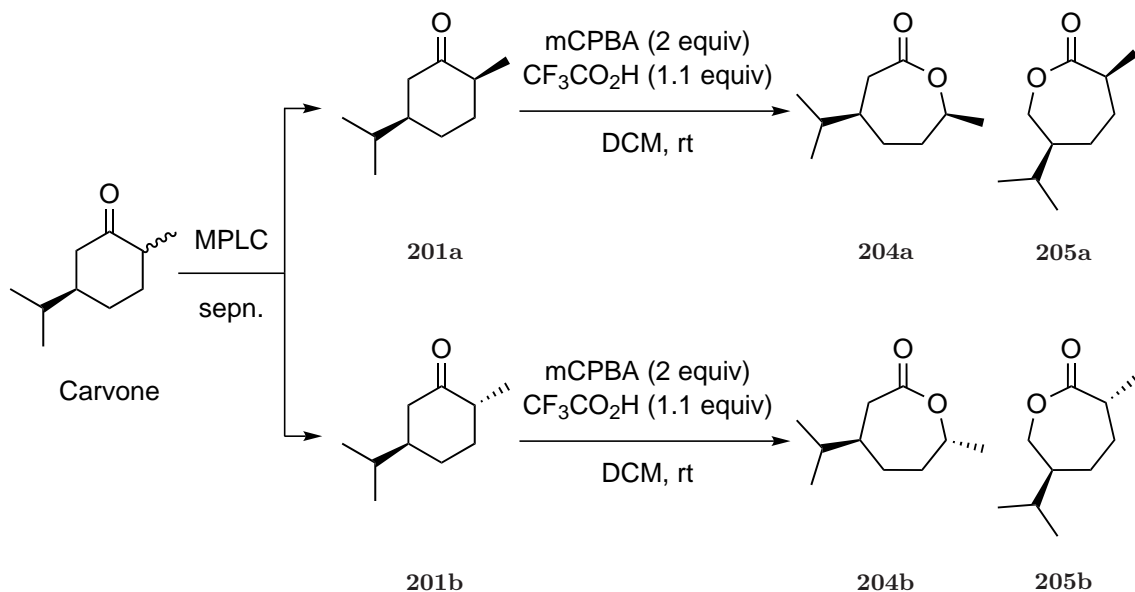
In the *trans* diastereomer, the $\text{H}3\beta$, $\text{H}5$, and $\text{H}7$ resonances were all overlapped in the range of 1.85 ppm. This overlap did compare well with the computed results obtained, as both $\text{H}5$ and $\text{H}7$ were computed to be at 1.75 and 1.78 ppm respectively. The computed value of $\text{H}3\beta$ was computed to be 1.91 ppm, however the overlapping region was broad so distinction between these peaks was difficult. The largest error between the computed and experimental value was for $\text{H}6\alpha$, at 0.12 ppm. Throughout the course of this project, it was observed that protons residing near heteroatoms, and π systems are typically the least reliable in terms of accurate computation. However, the overall CMAE for the computed *trans* against the experimental *trans* values was only 0.05 ppm. This is contrasted with the CMAE for the experimental *cis* against the computed *trans* which was at 0.20 ppm. Recall that typically, values for a matched strongly matched comparison is below 0.1 ppm.

Due to the larger spectral width of the ^{13}C NMR, Errors in the ^{13}C NMR, when comparing computed and experimental data tend to be larger, due to the larger spectral width in a ^{13}C NMR experiment. Additionally, accurate computation of shifts near or part of a

π systems is a common difficulty encountered throughout this project. In the case of computing ^{13}C shifts, the unscaled computed shift for C1 in the *trans* compound is 185.51 ppm, while the experimental value is assigned at 174.80 ppm. For this protocol employed, these π system shifts are consistently over-predicted. In this menthine series, the other peaks that were difficult to predict were those of the methine carbons, specifically, C3 and C7. These both had corrected errors of over 2.0 ppm, while the majority of corrected errors are well below 1.0 ppm. The C8 methyl group also shows a large error of 2.67 ppm, which is likely due to the proximity to the lactone portion, influencing the chemical shift. The observed chemical shift for the two methyl groups are 18.10 and 16.80 ppm with C8 being more downfield.

Analysis of Carvomenthides from Carvomenthone

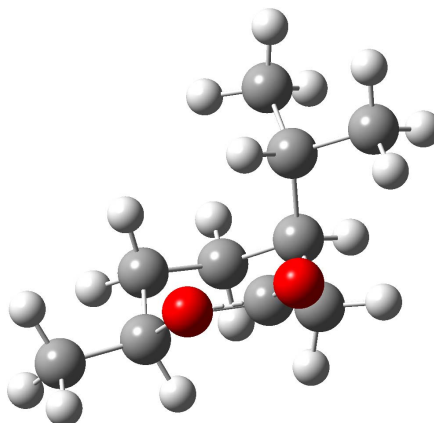
Dr. Emond used both the mixture and the pure substrates, separated by medium-pressure liquid chromatography (MPLC), in the preparation of the carvomenthides (**204a** – **205b**, Scheme 2.2). Treatment of the lactone with *meta*-chloroperoxybenzoic acid (*m*-CPBA) and trifluoroacetic acid (TFA) provides the Baeyer-Villager oxidation products (**204a** – **205b**).

Scheme 2.2 Synthesis of Carvomenthides from Carvone

Computation of the chemical shift for the complete set of lactones was also completed during this time. Before statistical analysis of the lactones could take place, spectral assignment of at least some key resonances were needed. In this instance, the use of the graphical output (Fig. 2.2) for the computed shifts proved a useful tool for Dr. Emond to quickly distinguish relevant peaks in the complex NMR spectra.

Additional data computed during the calculation of the chemical shifts also proved quite valuable. In particular, the thermodynamic computation and Boltzmann weighting of the conformers had an occasion to provide useful insight into the dominant conformer in a population. In particular, during the analysis of the normal carvomenthides, the *cis* diastereomer (**204a**) showed a conformational preference for a chair-like conformation where the isopropyl group occupied an axial position (Fig. 2.9).

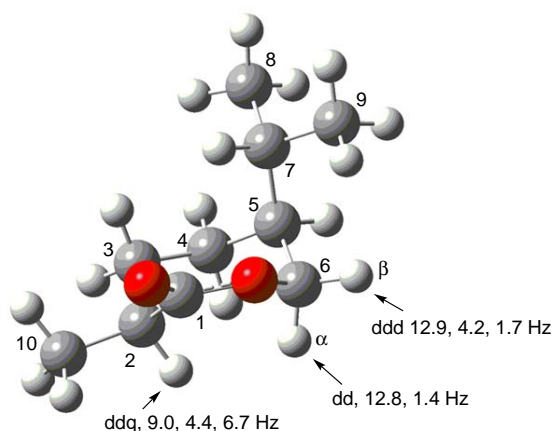
Fig. 2.9 Lowest Energy Conformer of Normal *cis*-Carvomenthide (**204a**)



This conformer of **204a** was the predominant conformer predicted. The relative energy of the next lowest energy conformer was 1.49 kcal higher than this conformer, and was the chair-chair flip conformer. Visualizing this “non-intuitive” conformer, guided evaluation of coupling constants. In particular, Dr. Emond was guided to assess a long-range W-coupling interaction only present due to the axial orientation of the isopropyl group.

A similar effect was also observed for the lowest energy conformer of the abnormal *cis*-carvomenthide (**205a**) diastereomer. In this diastereomer, the isopropyl group was also found to occupy an axial position as the dominant conformer. In this case, the difference in relative energy for the next lowest energy conformer was even greater, at 2.08 kcal higher than the conformer with the isopropyl group axial. Again, Dr. Emond was able to utilize the conformational data generated even before thorough analysis of the computed shifts was complete. The conformational predication confirmed the experimental NMR findings (Fig. 2.10).

Fig. 2.10 Conformational Preference and Supported NMR Assignments of Abnormal *cis*-Carvomenthide (**205a**)



The experimental spectrum revealed only a single large coupling for H2, and also a single large coupling for both H6 β and H6 α . The lowest energy conformer by 2.08 kcal (Fig. 2.10), with the isopropyl group axial, is the only way to satisfy the requirements of the observed coupling constants. If a conformer of a chair-chair flip were the dominant conformer, then H6 β would have a large two large coupling constants. One geminal, and one vicinal to the now axial proton on C5.

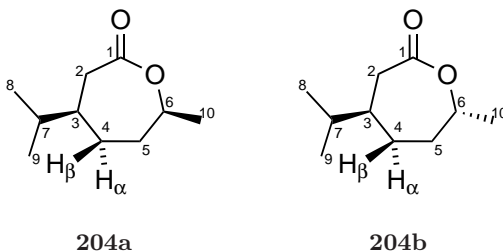
Once Dr. Emond had completed her NMR assignments, the data was passed to me to perform the statistical comparison of the computed and experimentally measured chemical shifts for the three sets of lactones (**203**, **204**, **205**).

Statistical Comparison of Normal *cis/trans*-Carvomenthide

Both sets of computed chemical shifts were obtained for the normal carvomenthides (**204**). Additionally, the experimental spectra for these compounds were more resolved and separated than those of the normal menthilde series. The analysis will include comparison of

both diastereomers (Fig. 2.11) compared against both sets of computed chemical shift data.

Fig. 2.11 Diastereomers and Numbering Scheme for Normal Carvomenthide



For this pair of diastereomers, Dr. Emond was able to assign with great certainty the *trans* diastereomer. The *cis* diastereomer proved more difficult as mentioned earlier, it adopts an unusual conformational orientation with the isopropyl group in the axial position. This locked conformation did facilitate observation of some long range-coupling within the molecule to aid in the assignment.

In a similar situation as before, we observe that the computed shifts for the atoms next to the carbonyl group ($H_{3\alpha/\beta}$) typically suffer the greatest in accuracy. Surprisingly, the *cis* diastereomer has fairly accurate computation of those values. After scaling the shifts, the errors drop to -0.05 and 0.00 ppm. However, the scaling for the *cis* diastereomer was assisted slightly as some peaks were not assignable, so could not be included. This reduces the number of data points to fit the linear regression line to, which reduces complexity and the chance of outliers skewing the fitting results. In the *trans* diastereomer, which is fully assigned, the $H_{3\alpha/\beta}$ errors are more in line with the typical expectation of 0.11 and -0.12 ppm.

The effect of switching from *cis* to *trans* has a large effect on the 4β proton shift. In the *trans* diastereomer, the shift is predicted to be 1.53 ppm, while in the *cis* diastereomer, it is 2.04 ppm. The CMAE values are summarized, highlighting how distinct the two sets

of computed shifts are (Table 2.8).

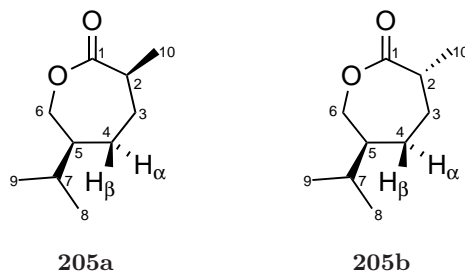
Table 2.8 Calculated CMAE Values for Normal Carvomenthide (**204**)

		Experimental			
		204a		204b	
		Matched	Mismatched	Matched	Mismatched
Computed	¹ H	0.04	0.13	0.05	0.19
	¹³ C	1.16	2.79	1.26	1.21

Solely relying on the computed ¹³C shifts for the assignment of the *trans* diastereomer may have lead to the wrong answer. However, on the scale of ¹³C errors, a difference of only 0.05 ppm would be considered inconclusive. Looking to the provided ¹H comparison would then give a clear indicator that the correct assignment is in fact to the *trans* diastereomer, based on a CMAE of 0.05 ppm for the matched *trans* configuration, compared to 0.19 ppm for the *cis* configuration.

Statistical Analysis of Abnormal *cis/trans*-Carvomenthide

Analysis of the abnormal *cis/trans*-carvomenthide is the last pair of diastereomers analyzed using our NMR computation protocol. It is also the only set that has a fully assigned experimental spectrum, so a complete analysis of the shifts is possible. The abnormal carvomenthide diastereomers (Fig. 2.12) were found to be one of the more straight-forward pairs to analyze. With only minor guidance from the computed shifts, Dr. Emond was able to assign the *trans* diastereomers shifts fully.

Fig. 2.12 Diastereomers and Numbering Scheme for Abnormal Carvomenthide

The optimization process showed that, unsurprisingly, the *trans* diastereomer prefers a conformer where both the isopropyl and methyl group are equatorial. However, initial evaluation of the experimental NMR was not as clear cut as the DFT calculated geometries. Through collaborative work, H2 was found to have a unique shift and a large (i.e., 10.9 Hz) coupling constant which indicated an axial orientation. This led to the conclusion that the experimental NMR and computed geometry were in agreement.

The experimental NMR data for the *cis* diastereomer was more problematic. With the guidance of 3D models from the NMR computation, we could probe the various coupling constants and orientations of the molecule. We were fortunate that there was only one conformer present in any significant quantity. This allowed for use of the computed geometry to aid in the coupling constant analysis.

The simple coupling constant analysis may have damaged the quality of the computed NMR data, by facilitating full assignment of the experimental spectrum. In looking at the CMAE value for the *cis* diastereomer, the matched and mismatched values are 0.11 and 0.10 ppm respectively. When a full set of computed and experimental shifts can be matched up, the impact of outliers can negatively impact the assignment. In this case, the computed shift for both H3 β and H4 β in the *cis* diastereomer show corrected errors of 0.40 and -0.51 ppm. Removing these two outliers from the analysis results in a CMAE decrease

to 0.04 ppm. We are confident in our assignment of the experimental spectra, so in this case, these values are not erroneous and should be included in the analysis. However, utilizing shifts with uncertain assignment can be troublesome for this very reason. The matching for the *trans* isomer is very good, with a CMAE value of only 0.05 ppm, compared to the other ^1H CMAE values (Table 2.9).

Table 2.9 Calculated CMAE Values for Abnormal Carvomenthide (**205**)

Computed		Experimental			
		205a		205b	
		Matched	Mismatched	Matched	Mismatched
^1H	0.11	0.10	0.14	0.05	
^{13}C	1.70	2.51	1.72	1.33	

2.7 Concluding Remarks

The computation of NMR chemical shifts is not only manageable and straight-forward, but the utility of such data is invaluable for the assessment of complex NMR spectra. In this chapter, the ability of a rapid and reliable NMR computation protocol was compared first against another method for distinguishing between diastereomers. The protocol was then tested against a previously unknown set of compounds, which prior to their assignment had little to no experimental data available in the literature. We also gained further understanding of the conformational and stereochemical properties of these lactones for use in the development new biorenewable polymers.

Further, the utility of non-chemical shift related data generated in the process was shown to be crucial answering various questions that arose. The thermodynamic preferences, and visualization of the conformational space sampled both provide clues and information that are helpful in completing an NMR chemical assignment of a complex product.

3. EXAMINING THERMODYNAMICS OF BENZYNE

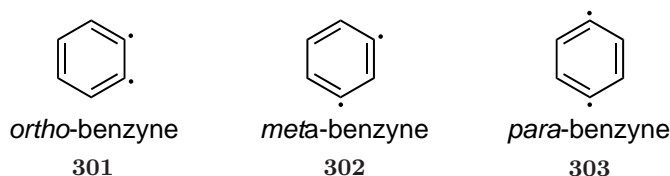
FORMATION AND REACTION

3.1 Introduction to Benzyne: Structure, Formation and Reactivity

3.1.1 The Structure of Benzyne

The aryne class of compounds are a set of neutral, reactive organic intermediates, formally derived from a parent arene by abstraction of two hydrogens. These reactive intermediates were first described in 1902 by Stoermer and Kahlert, when they described the existence of the aryne derived from β -elimination of 3-bromobenzofuran.⁵⁰ The simplest aryne however is benzyne (**301**), derived from the parent arene, benzene (**302**), and while the first aryne was described in 1902, it wasn't until 1927 that the presence of benzyne was used to rationalize a reaction outcome.⁵¹ There are three possible isomers of benzyne, named according to the relative position of the two unpaired electrons to each other (Fig. 3.1). Henceforth "benzyne" will refer to the *ortho*- isomer (**301**).

Fig. 3.1 Isomers of Benzyne

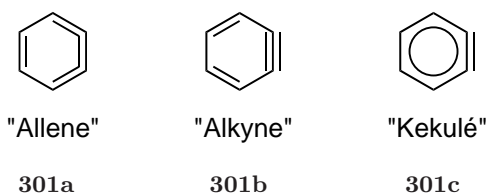


The *ortho*- isomer of benzyne (**301**), also referred to as 1,2-didehydrobenzene is frequently utilized in organic synthesis as a reactive intermediate. The *para*- isomer (**304**) is ubiquitous in biological pathways, and is a key intermediate in the Bergman cyclization.⁵²

The *meta*-benzyne (**303**) isomer's existence and structure is still under active investigation, utilizing work in mass spectrometry,⁵³ scanning tunneling microscopy⁵⁴ and computational chemistry.⁵⁵

There are multiple ways of representing the structure of benzyne (Fig. 3.2). Some representations include the "allene" form (**301a**), the "alkyne" form (**301b**), and the kekulé form (**301c**). These forms are especially pertinent to research conducted in our lab towards the synthesis of **301** (discussed in 3.1.3), where **301a** best represents the initial structure after initial formation, and **301b** & **301c** best represent the reactivity observed for **301**.

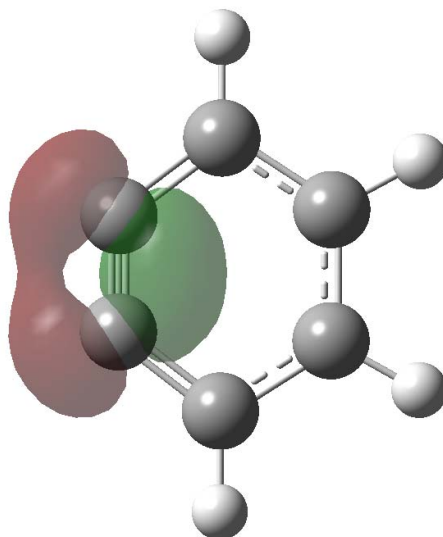
Fig. 3.2 Various Representations of Benzyne



3.1.2 Reactivity of Benzyne

Looking at representations **301b** and **301c** we see that benzyne can be considered as a benzene ring containing a triple bond. The reactivity of benzyne arises from the strain placed on the six-membered ring by the inclusion of a triple bond. Considering that the optimum orientation for the *p* orbitals forming a triple bond is achieved when the two orbitals are aligned parallel to each other with a dihedral angle of 0°, a large distortion is observed for the triple bond of benzyne. In benzyne, the *p* orbitals involved in the triple bond are pointed away from each other, resulting in diminished electron density between the two carbon atoms (Fig. 3.3).

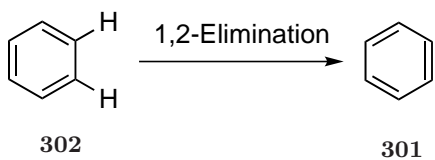
Fig. 3.3 Overlap of the p Orbitals in Benzyne's Triple Bond



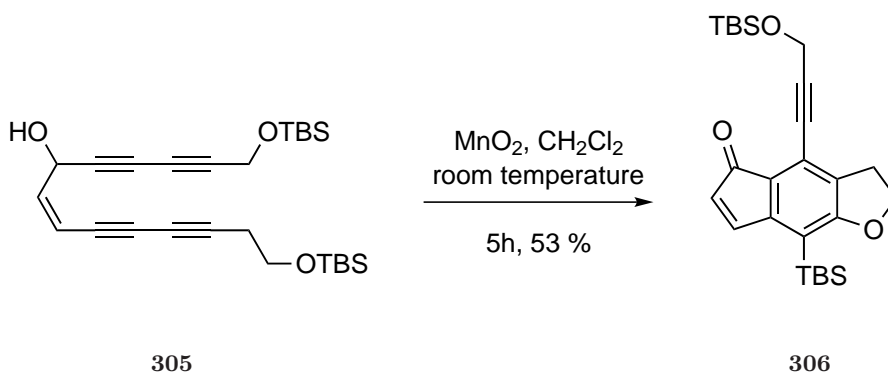
Orbitals generated from NBO⁵⁶ analysis and visualized with an isovalue of 0.08

3.1.3 Synthesis of Benzyne

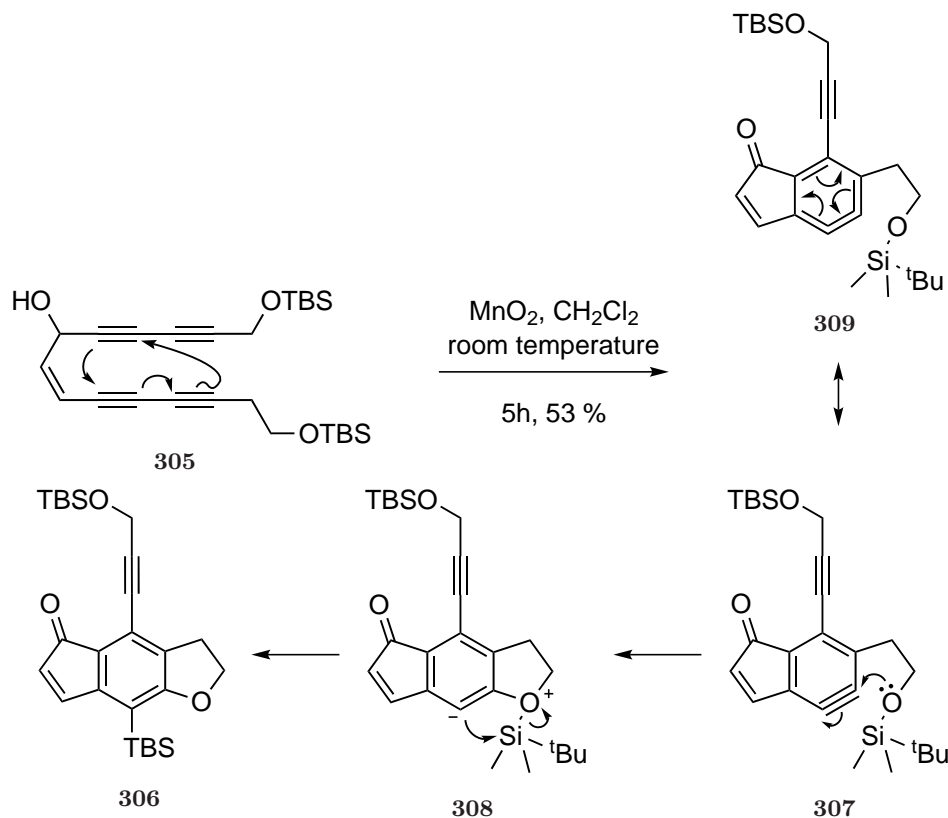
Formally, the generation of **301** is a 1,2-elimination from **302**, and in the most basic version, this elimination is simply an abstraction of two hydrogens (Scheme 3.1). However, this pathway is not synthetically feasible. Various methodologies have been developed for the generation of benzyne, most often pairing the elimination of one substituent with a second stable leaving group to facilitate the elimination, or through extrusion of highly-stable gases. These methods have been reviewed previously.⁵⁷

Scheme 3.1 1,2-Elimination of an Arene to form an Aryne

In addition to the previous methodology for generation of benzyne, Dr. Beeraiah Baire observed cyclization of a linear tetrayne precursor **305** to a tricyclic benzenoid product **306** (Scheme 3.2).

Scheme 3.2 Cyclization of a Linear Tetrayne to Benzenoid **306**

We proposed that this product arises by a [4 + 2] cycloaddition, or hexadehydro-Diels-Alder (HDDA) reaction, of **305** to give a benzyne intermediate **307**. This reactive benzyne intermediate then undergoes intramolecular trapping by the silyl ether through a net 1,3-migration (proceeding through zwitterion **308**) of the silyl group from the ether oxygen to the distal benzyne carbon, yielding the final benzenoid **306** (Scheme 3.3).

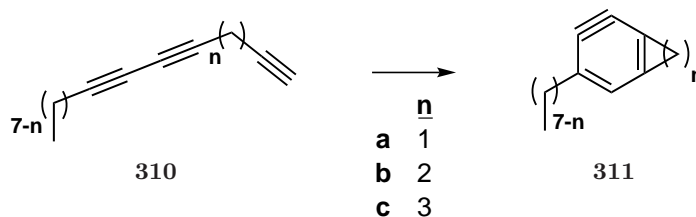
Scheme 3.3 Mechanism of Benzenoid Formation from Linear Tetrayne

In this mechanism, we see that from the initial [4 + 2] cycloaddition of **305**, we arrive at a resonance form of benzyne, **309**, analogous to that of **301a** described earlier. The available scope of this reaction has been extensively tested and further work on this reaction is pursued by members in the group. While pursuing synthetic work to broaden our understanding of the scope for this transformation, we turned our attention towards gaining insight into the thermodynamics of this transformation and the subsequent reactions. These calculations utilized the conductor-like polarizable continuum model (CPCM) solvation model^{58,59} with universal force field (UFF)⁶⁰ radii in chloroform solvation unless otherwise specified.

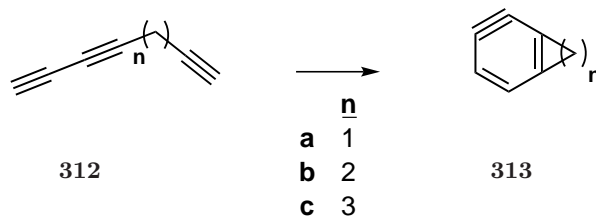
3.2 Ring-Size Restrictions on Fused Benzynocycloalkane Formation

During the initial investigation of this reaction, it was observed that a combination of electronic and steric effects in the starting triyne influenced the temperature required, rate and efficiency of the transformation in Scheme 3.2. An additional variable was the atom-length of the tether that connected the alkyne and diyne pieces together. The transformation of a pure hydrocarbon triyne into benzyne (**310** to **311**, Scheme 3.4) has only been achieved under very high temperature and low pressure (600 °C and 10^{-2} torr) by Johnson and coworkers.^{61,62} Still, this most basic model system was an ideal choice for modeling this reaction of **310**, and used to study the effect tether length had on the thermodynamics of forming the benzyne intermediate.

Scheme 3.4 Model to Examine Thermodynamics of Benzynocycloalkane Formation



We predicted that with decreasing ring size, the increased strain would eventually result in an unfavorable ($\Delta G > 0$) reaction. The added hydrocarbon “tail” was added to allow for direct comparison of thermodynamic results (Table 3.1) between different ring sizes, by either removing or adding carbons to the “tail” as the ring size changed. The addition of the “tail” was shown to have no effect on the overall trend or calculated ΔG values by calculation of the analogous reaction (Scheme 3.5) for triynes containing no “tail” (ΔG w/o tail).

Scheme 3.5 Analogous Model Benzynocycloalkane Formation without Extra “Tail”

The difference in measured ΔG values is likely due to the large flexibility in the “tail” portion. The large flexible portion causes the PES to have a wide and shallow minimum, which adds variable amount of error to the calculation. However, the two model reactions show agreement in the overall trend and approximate magnitude in differences between the various ring sizes.

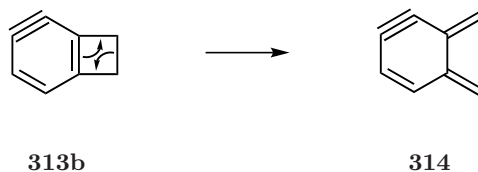
Table 3.1 Calculated ΔG Values for Benzynocycloalkane Formation from **310** and **312**

Entry #	ΔG	Rel. ΔG	ΔG w/o “Tail”
	kcal/mol	kcal/mol	kcal/mol
a	20.85	0.00	19.23
b	-9.37	-35.29	-12.61
c	-35.14	-62.24	-38.14

In the three tether lengths examined, only the tether corresponding to formation of the benzynocyclopropane **311a** showed a free energy corresponding to an unfavorable reaction. Surprisingly, even the formation of the four-membered benzynocyclobutane **311b** showed an overall free energy change corresponding to -9.37 kcal/mol, and was over 35 kcal/mol lower in energy than that of **311a**. Having previously observed formation of a five-membered ring (**306**), it was expected that this would show a favorable free energy.

A second isomer of the fused cyclobutane **313b** exists, namely the ring-opened diene (**314**). The thermodynamic impact of maintaining the fused bicyclic system was investigated by computing the change in free energy from **313b** to **314** (Scheme 3.6).

Scheme 3.6 Ring-Opening of Benzynocyclobutane to a Diene

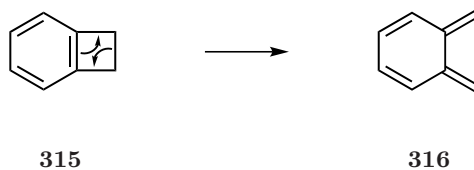


By undergoing the ring-opening, the strain from the four-membered ring is relieved. However, a computed change in free energy of 9.95 kcal/mol indicates that the resulting ring-opened diene is less stable than the fused bicyclic system. As a comparison, the calculated ΔG for the analogous reaction with the extra “tail” extension calculated to be 9.22 kcal/mol. Opening the cyclobutane ring results in loss of strong aromatic character to one of at least non-aromatic properties. The measurement of the bond length alternation (Δ_R), defined as the difference between the longest and shortest bond in the ring, provides an indication of aromatic character.⁶³ Molecules that are aromatic in nature will have a small Δ_R , while anti-aromatic molecules will have a high Δ_R . The calculated Δ_R for **314** is almost twice that of **313b** (the full list of bond lengths is given in Table 3.2). Additionally, when the cyclobutane undergoes ring-opening, the two methylenes are allowed to twist to avoid steric buttressing between the vinyl hydrogens. This results in a dihedral angle between the two exocyclic carbons of 22.190°, while the cyclobutane ring in **313b** is locked at a dihedral of 0.000°.

Table 3.2 Bond Lengths for **311b** and **314**

	313b	314
	(Å)	(Å)
	1.38514	1.44533
	1.25211	1.22375
	1.38619	1.44174
	1.41704	1.35777
	1.39630	1.48308
	1.40226	1.52673
Δ_R	0.16493	0.30298
St. Dev.	0.06046	0.10824

To confirm the alkyne in benzyne was not exerting an unknown effect, the analysis was carried out on the analogous benzene system, going from benzocyclobutane (**315**) to the ring-opened diene (**316**, Scheme 3.7). For this transformation, a free energy difference of 14.68 kcal/mol was calculated, demonstrating an even greater thermodynamic preference to the cyclobutane isomer instead of the ring-opened isomer.

Scheme 3.7 Ring-Opening of Benzocyclobutane to the Diene **316**

Evaluating the bond length alternation demonstrates an even more dramatic shift away from aromatic character, with the difference coming to almost a ten-fold increase in Δ_R

values (Table 3.3). The similarity between the calculated Δ_R values for the unopened benzyne **313b** and the ring-opened benzene **316** serve to provide gauge, indicating the strain placed on the aromatic character of the system by the inclusion of the triple bond in the benzyne ring. The similar distortion effect from steric buttressing is also observed, with the dihedral angle of the exocyclic methylenes in **316** measuring at 22.173°.

Table 3.3 Bond Lengths for **315** and **316**

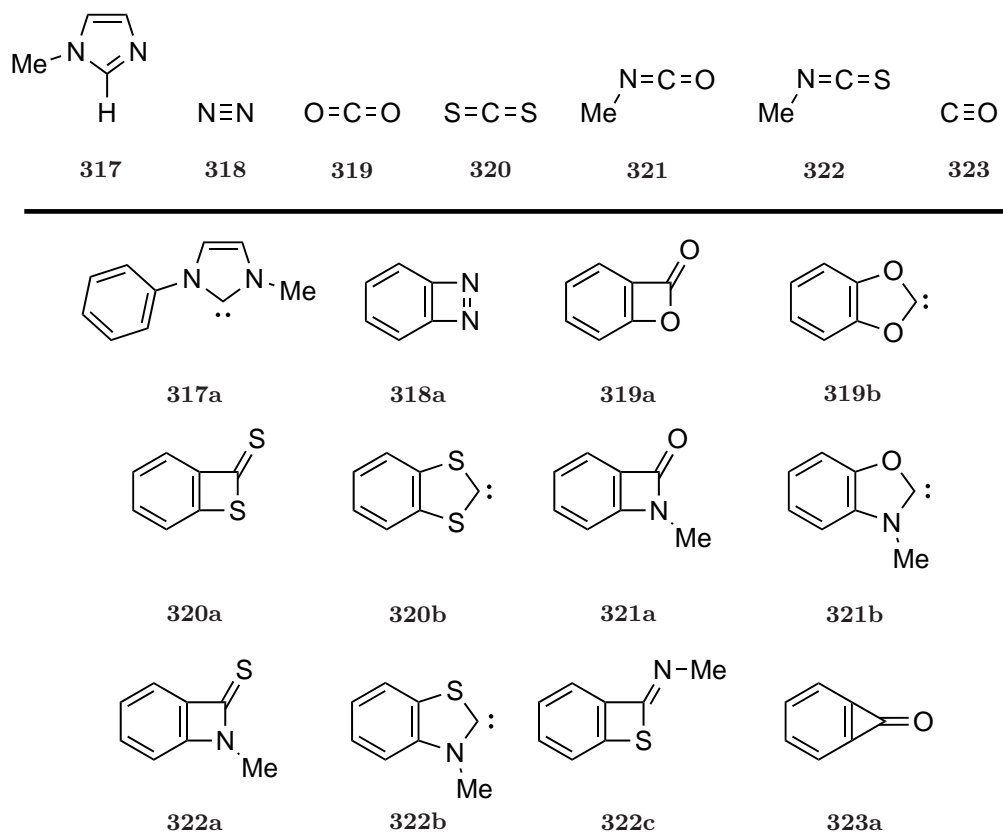
	315	316
	(Å)	(Å)
	1.38675	1.46638
	1.39284	1.49209
	1.38675	1.46638
	1.40323	1.34759
	1.40106	1.45872
	1.40323	1.34759
Δ_R	0.01648	0.14450
St. Dev.	0.00788	0.06467

3.3 Thermodynamics and Transition States of Small Molecule Intermolecular Trapping

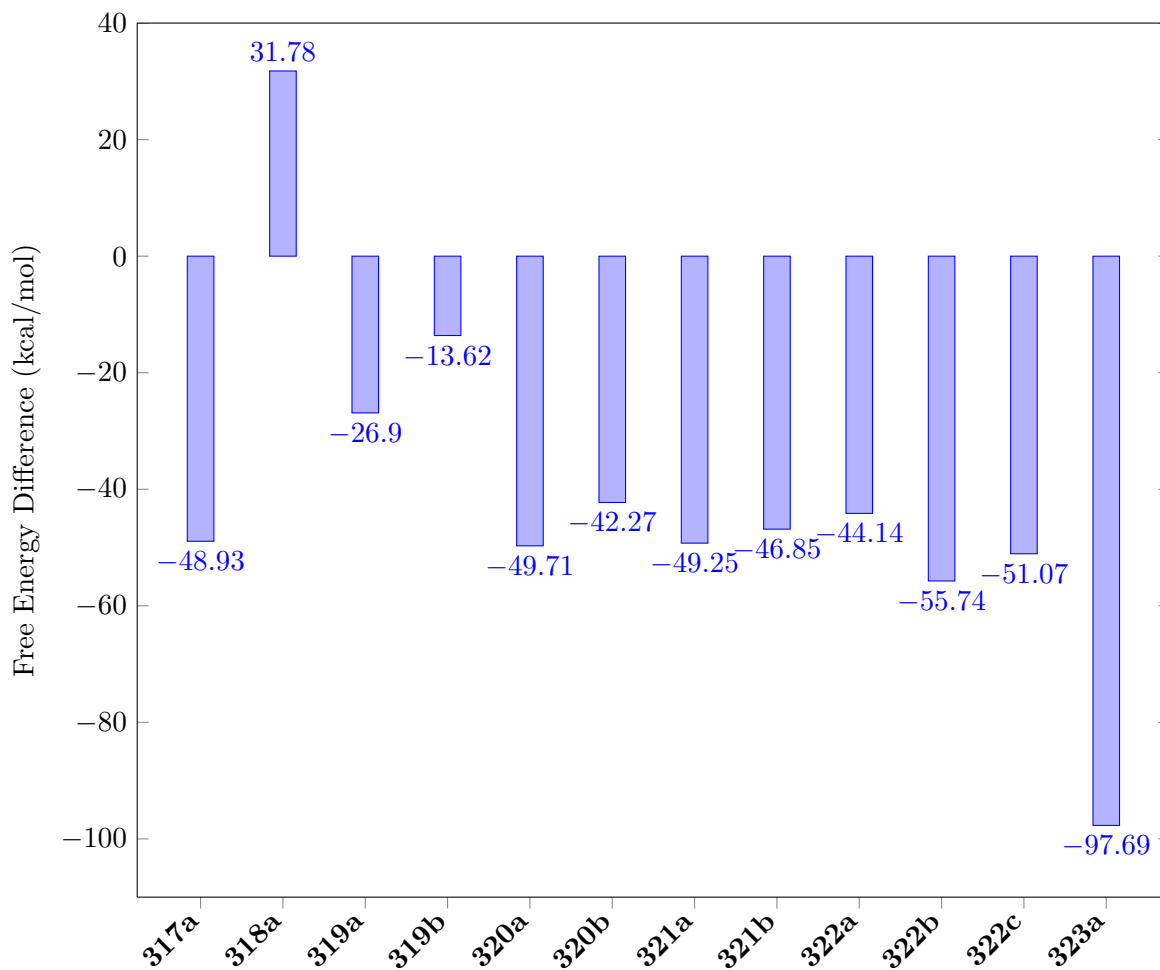
Part of the aryne class of compounds, benzyne is classified as being highly reactive, a fact further evidenced by the available literature on reactions of benzyne.^{64,65} These methods are usually aim at achieving further synthetic goals. An area under represented is reactions of benzyne with small molecule traps to generate further, possibly moderately reactive compounds. To evaluate this area, the thermodynamic reactivity of benzyne was evaluated

with a selection of seven small molecule traps, which give rise to a total of twelve distinct products (Fig. 3.4)

Fig. 3.4 Small Molecule Traps and Corresponding Products with Benzyne



Demonstrating the highly reactive nature of benzyne, all of the small molecule trapping products, except for that from N_2 (**318a**) were calculated to be lower in free energy than that of the starting materials. There is some precedent for highly stable molecules like CO_2 to undergo addition reactions with benzyne when part of a multi-component reaction.⁶⁶ Free energies in solution were calculated for all products, and the overall free energy change was calculated as the difference between the product and the two independent starting materials (Fig. 3.5).

Fig. 3.5 Calculated Free Energy Difference of Trapping Products

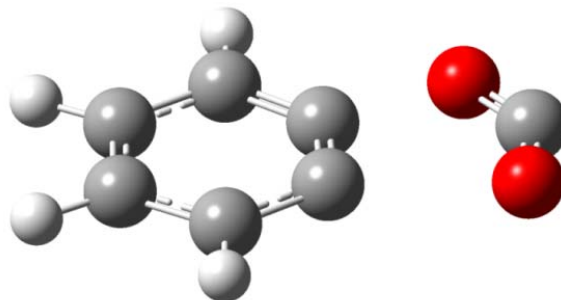
These results indicate that for every small molecule trap, generation of a carbene from benzyne is a favorable reaction pathway, including CO_2 . Unexpectedly, the trapping of carbon monoxide to give benzocyclopropanone (**323a**) has the largest difference in free energy. This could be understood by considering the combination of two relatively high energy species into an stable aromatic compound. A limited number of these systems were tracked further in attempts to locate transition states.

3.3.1 Transition State and Analysis of Benzodioxole Carbene Formation

The formation of the benzodioxole carbene **319b** is computed to have a favorable free energy difference of -13.62 kcal/mol in chloroform. The computed geometry of the transition state (TS) leading to **319b** shows it is completely planar and C_{2v} symmetric. While the reaction may be energetically favorable in terms of absolute product and reactant free energies, the reaction could have a prohibitively high barrier to activation, which required locating a transition state for this transformation.

Initial attempts to locate the transition state by either QST2 or QST3 proved to be unsuccessful. The subsequent TS transition state search utilized the approximate geometry from the failed QST2 calculation as a starting point. Utilizing this method, a transition state was located (Fig. 3.6), containing a single imaginary frequency of -552.72 cm^{-1}

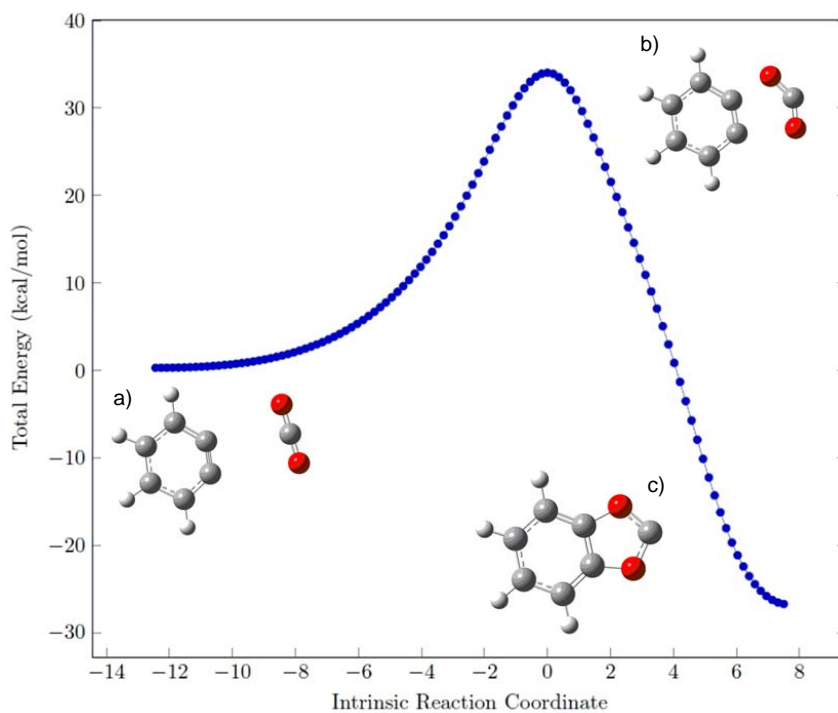
Fig. 3.6 Transition State Leading to Formation of **319b**



The imaginary frequency corresponds to a molecular vibration that indicated the possibility of an asynchronous ring closing to **319b**. In order to verify that this process is concerted and asynchronous, an IRC analysis was performed starting from the obtained transition state geometry. The IRC analysis proceeded very smoothly, to show in the reverse direction the CO_2 slowly moving away from the benzyne ring to separate starting substrates, and in the forward direction to closing first one C–O bond, and then the next.

The absence of any second local minimum prior to formation of the carbene found in the IRC analysis provides further support for the postulated concerted and asynchronous transition state. A fine grained step-by-step snapshot of the reaction PES and the molecular rearrangement leading to the transition state, and on to product was achieved by obtaining up to 100 points along the reaction coordinate in each direction. The resulting energy diagram provides thorough detail and molecular geometries for each point along the coordinate (Fig. 3.7).

Fig. 3.7 Intrinsic Reaction Coordinate Plot for the Formation of **319b**



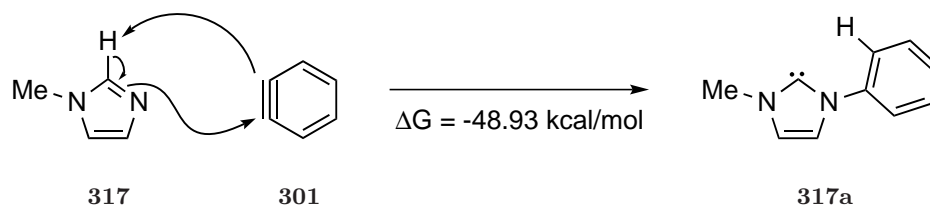
- a) Starting geometry
- b) Transition state geometry
- c) Final geometry

With confirmation that the transition state connects the reactants to the products assignment of the transition state to this transformation can be made with much greater certainty. From the IRC, the activation energy for the reaction is also easily assessed, which is calculated to be at 34.03 kcal/mol.

3.3.2 Generation of N-heterocyclic Carbenes by Benzyne Trapping

N-heterocyclic carbene (NHC) are a class of persistent carbene that are exceptionally stable, some even thermodynamically stable when kept dry and free of oxygen. Their robust nature has found them used as ligands in transition metal catalysis.^{67,68} The initial screening of small molecule traps found that the generation of an NHC by trapping with benzyne is a favorable process with a difference in free energy of -48.93 kcal/mol (Scheme 3.8). Moreover the tethered NHC **317a**, could also be accessed by generating the benzyne through the triyne cyclization (Scheme 3.2, page 43) providing rapid access to functionalized benzenoid NHCs.

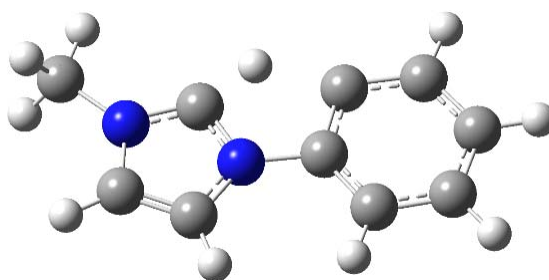
Scheme 3.8 Generation of NHC Through Hydrogen Abstraction By Benzyne



It was unknown at the time whether the mechanism for this reaction would be step-wise or concerted. Early attempts at finding a transition state were successful utilizing the QST2 and QST3 algorithms. The transition state located had one imaginary frequency at -1542.04 cm^{-1} . This molecular vibration of the transition state (Fig. 3.8) appeared to be isolated to only a proton transfer between the imidazole carbon and the benzyne carbon. The transition state for the proton transfer is completely planar with respect to the four non-hydrogen atoms comprising the 5-membered ring in the transition state. However, after

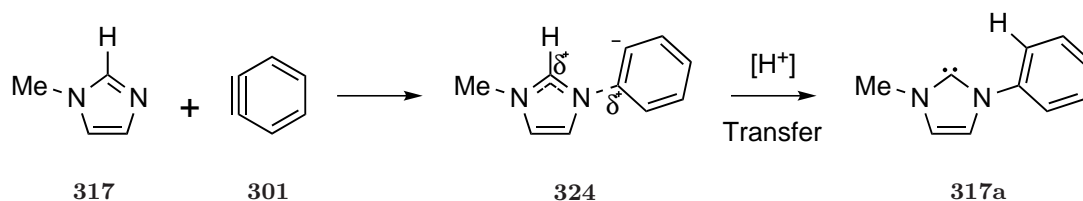
proton transfer, there is a relaxation of the geometry and **317a** twists to a dihedral angle of 34.3° .

Fig. 3.8 Transition State For Proton Transfer From Zwitterionic Intermediate to Benzyne



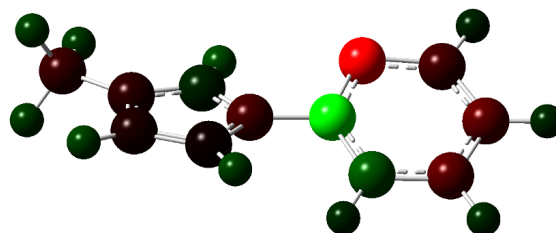
In order to then reoptimize the structure back to the starting material, the transition state was perturbed slightly to bias it towards dissociation. An unexpected result produced a new minimum that was not the separated products, but instead an intermediate structure **324**. The resulting minimum appeared to be a geometry just before the proton transfer step, providing indication of a step-wise mechanism (Scheme 3.9).

Scheme 3.9 NHC Generation By Benzyne Through Zwitterionic Intermediate



Examining the Mulliken charges revealed a zwitterionic species with a highly negative (-2.324) charge on one benzyne carbon, and a very positive (1.671) charge on the other carbon, considering that almost all other atoms had Mulliken charges between -0.3 and 0.3 (Fig. 3.9).

Fig. 3.9 Zwitterionic Intermediate on to NHC Formation, Prior to Proton Transfer



¹Red indicates negative charge, while green indicates positive charge

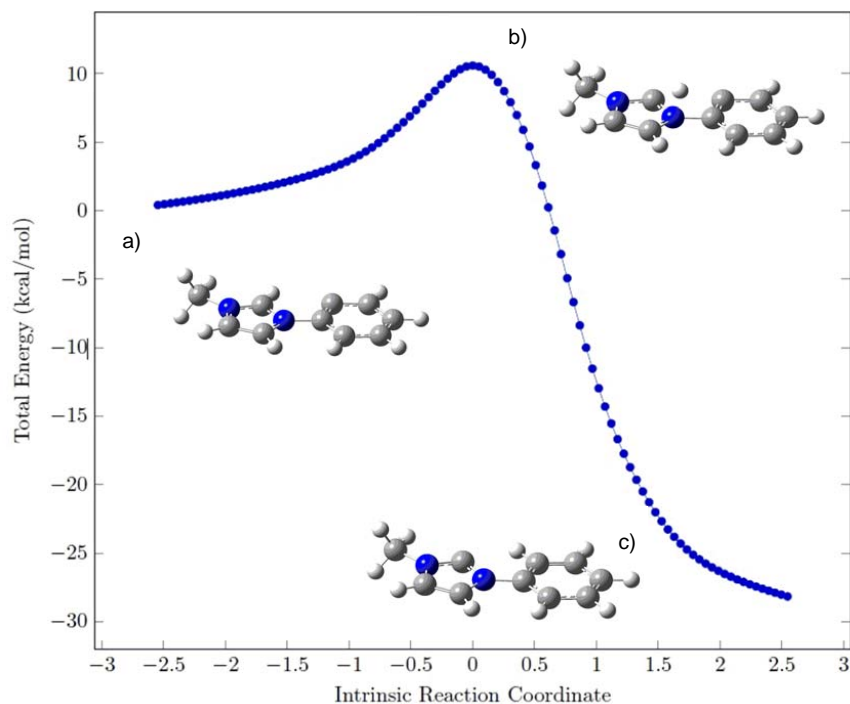
²The benzyne carbons have Mulliken charges of -2.324 and 1.671

The nitrogen tethered to the benzyne ring also has a partial negative charge. This could indicate the mechanism proceeds through initial nucleophilic attack by nitrogen on benzyne, followed by a large amount of the triple bond electron density being placed onto the distal benzyne carbon. This benzyne carbon is now electron rich enough to undergo hydrogen-atom abstraction of the C–H bond of the imidazole portion, generating the NHC. Like NHC **317a**, this intermediate also shows a torqued central four-atom unit with a dihedral measuring 25.0°.

Finding that the mechanism for the NHC generation proceeds step-wise meant that there should be a first transition state for the initial nucleophilic attack on benzyne. However, all attempts to locate a transition state for this process were unsuccessful. In some cases, the interaction of two approaching species towards each other can suffer from basis set superposition error (BSSE). At some intermediate distance, the overlap of the individual species basis sets will lead to an artificial lowering of the overall energy. This may lead to incorrect or failed optimizations as the predicted energies do not lead to the correct optimization choices by the algorithm. To correct for this energy discrepancy, a calculation known as the counterpoise calculation^{69,70} can separate these interactions to determine the

error introduced by BSSE. Still, in the case of the first transition state, and even attempting to find an imidazole/benzyne pre-complex, the counterpoise calculation indicated no lower energy pre-complex or possible lead to a first transition state.

Turning back to the zwitterionic intermediate **324** and the proton transfer transition state, the goal became to verify the connection between the intermediate **324** and NHC **317a**. Similar to the previously checked transition state, an IRC calculation was the best way to verify the relationship between the three species. Of particular interest was the dihedral distortion observed for both **324** and **317a**, but not in the transition state. The IRC calculation proved to be very helpful and also opened some further questions (Fig. 3.10). In the IRC analysis, both the forward and reverse searches led to geometries that remained planar. In examining the energy plot, it appears that the energies are approaching a plateau, not showing any indication of further distortion as seen in **324** and **317a**. We were not able to establish if there is a further barrier to distorting to the final geometries.

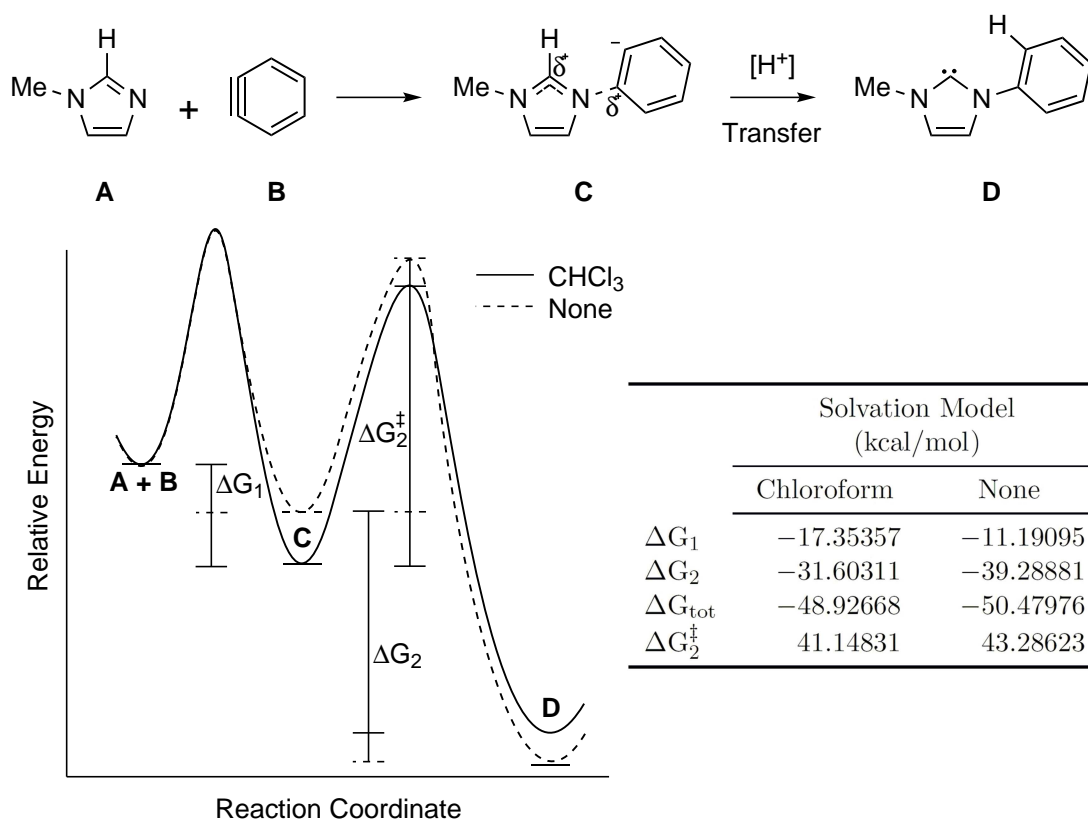
Fig. 3.10 Intrinsic Reaction Coordinate Plot for Proton Transfer Step of NHC Formation

- a) Starting geometry
- b) Transition state geometry
- c) Final geometry

While the first transition state remained elusive, the role solvent played was also briefly investigated. The role of solvent would likely be most critical for the zwitterionic intermediate as well as the subsequent proton transfer step. The optimized solvent geometries were reoptimized without using a continuum solvent model (gas phase) to observe what effect lack of solvent would have on the stability of these species. When looking at the gas phase energies, it follows the expectation that invoking charged species in the gas phase results in a destabilizing effect. It is clear that the first step, ending at the zwitterionic intermediate is much less favorable in the gas phase. However, the overall reaction to the neutral carbene

is found to be more favorable (Fig. 3.11).

Fig. 3.11 Free Energy Diagram of NHC Formation By Benzyne Trapping of N-Methyl Imidazole



3.4 Concluding Remarks

The highly reactive nature of benzyne results in diverse patterns of reactivity. This same diverse reactivity results in a difficulty storing, handling and preparing benzyne in a simple way. The new methodology (the HDDA reaction), and further reactions of benzyne were investigated computationally to better understand the basics of this reactive intermediate. In this chapter, the effect of ring-size in a fused bicyclic ring system was explored with respect to the free energy of the cyclization reaction to make benzyne. Further understanding was

gained by the study of the effect substituents had on the relative aromatic/anti-aromatic character of the resulting benzyne, through analysis of ring-opening free energy calculations.

Further computational studies were conducted on the reactivity of benzyne itself. The highly reactive nature of benzyne led to unexpected reactions with highly stable molecules such as CO₂ that were predicted to lead to energetically favorable products that included carbenes and 4-membered fused ring systems. Two of these systems, the benzodioxole carbene and the NHC produced by a reaction with benzyne were further explored. Transition states were identified for each system and verified as valid transition states utilizing intrinsic reaction coordinate (IRC) analysis, which connected the computed transition states with the reactants and products. Utilizing the compiled data for the generation of the NHC, a free energy diagram describing the reaction in both chloroform and the gas phase was presented. The computation of favorable reaction thermodynamics for these systems has led to further investigation, and we are now looking to test the feasibility of these reactions experimentally.

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SCRIPTS AND UTILITIES

A-1 Maestro Scripts

A-1.1 write-g09-inputs-default.py

write-g09-inputs-default.py

```
#####
#####
#
# By Patrick H. Willoughby, August 2011
#
# This python script is intended to be run from the Maestro
# Command Input Area.
#
# While in the command input area enter:
# pythonimport "title of this script"
#
# If you can't see the command input area then open Maestro,
# select Maestro and check the box to the left of
# "Command Input Area"
#
#####
#####

from schrodinger import maestro
from schrodinger import structure
from schrodinger import project
import os
from math import exp as exp

#####
##### BEGIN main program loop #####

def main ():
# Dictionary holding column names for project table properties depending on the
# force field being used
columns = {'mm2' : ['r_mmod_Potential_Energy-MM2*', '
r_mmod_Relative_Potential_Energy-MM2*'], 'mm3': ['r_mmod_Potential_Energy-MM3*
*', 'r_mmod_Relative_Potential_Energy-MM3*'],
'amber': ['r_mmod_Potential_Energy-AMBER*', 'r_mmod_Relative_Potential_Energy-
AMBER*'], 'opls': ['r_mmod_Potential_Energy-OPLSA*', '
r_mmod_Relative_Potential_Energy-OPLSA*'],
'amber94': ['r_mmod_Potential_Energy-AMBER94', 'r_mmod_Relative_Potential_Energy-
AMBER94'], 'mmff': ['r_mmod_Potential_Energy-MMFF94', '
r_mmod_Relative_Potential_Energy-MMFF94'],
'mmffs': ['r_mmod_Potential_Energy-MMFF94s', 'r_mmod_Relative_Potential_Energy-
MMFF94s'], 'opls2001': ['r_mmod_Potential_Energy-OPLS-AA', '
r_mmod_Relative_Potential_Energy-OPLS-AA'],
'opls2005': ['r_mmod_Potential_Energy-OPLS-2005', '
r_mmod_Relative_Potential_Energy-OPLS-2005']}

# Start by selecting all entries in the project table, and making sure the first
# entry is in the workspace
maestro.command("entryselectall")
```

```

maestro.command("eplayergotofirst")

# Grab the entire project table
pt = maestro.project_table_get()

currentforcefield = ''
for forcefield in columns.keys():
    if not pt[1][columns[forcefield][0]] == None :
        currentforcefield = forcefield
        break

# Create a directory to store the input files.
os.popen( "mkdir " + str( pt[1]['s_m_title']+'-gaussian_files' ) )

# Create a dictionary with keys being each conformer name and a list of the
# absolute and relative MM energies for the conformer.
energies = {}

# Make a loop to operate on every conformation in the project table.
# This loop operates on one conformation.
conf_num = 1
for row in pt.selected_rows:
    structure = maestro.workspace_get()

# Open the output file for writing
outputfile = open( row['s_m_title'] + "-opt_freq-conf-" + str(conf_num) + ".
com", 'w' )
nmr_outputfile = open( row['s_m_title'] + "-nmr-conf-" + str(conf_num) + '.
com', 'w' )

# Add the conformer energy to the dictionary of energies
energies[ str( row['s_m_title'] + row['s_m_entry_id'] ) ] = [ row[columns[
currentforcefield][0]], row[columns[currentforcefield][1]] ]

# Write the Gaussian stuff that goes into every input deck.

print >> outputfile, gaussian_input( "link", str( pt[1]['s_m_title'] ), str(
conf_num ) )
print >> nmr_outputfile, gaussian_nmr_input( "link", str( pt[1]['s_m_title'] )
, str( conf_num ) )
print >> outputfile, gaussian_input( "route" )
print >> nmr_outputfile, gaussian_nmr_input( "route" )
print >> outputfile, gaussian_input( "title", str( pt[1]['s_m_title'] ), str(
conf_num ) )
print >> nmr_outputfile, gaussian_nmr_input( "title", str( pt[1]['s_m_title'
]), str( conf_num ) )
print >> outputfile, gaussian_input( "molecule" )
print >> nmr_outputfile, gaussian_nmr_input( "molecule" )
print >> nmr_outputfile, gaussian_nmr_input( "readline" )
print >> nmr_outputfile, gaussian_nmr_input( "end" )

# This loop operates on one atom.

for atom in structure.atom:
    outputstring = "%2s %10.6f %10.6f %10.6f" % (atom.element, atom.x, atom.y
, atom.z)
    print >> outputfile, outputstring

print >> outputfile, gaussian_input( "readline" )
print >> outputfile, gaussian_input("end")

```

```

# Close the opened output file.

    outputfile.flush()
    outputfile.close()
    nmr_outputfile.flush()
    nmr_outputfile.close()
    maestro.command("eplayerstepeahead")
    conf_num += 1

# Write the collected energy data for each conformer to a CSV file

    # Sum the exponential relative energies to create the denominator term

    denominator = 0
    for key in energies:
        denominator = denominator + exp( -( energies[key][1] * 1000 ) / ( 8.314472 *
            298.15 ) )

    energiesfile = open( str( pt[1]['s_m_title'] ) + '_MM_energies.csv', 'w' )
    energiesfile.write( 'Conformer,MM Energy,Relative MM Energy,Boltzman Weight\n\n'
        )

    for key in energies:
        temp = exp( -( energies[key][1] * 1000 ) / ( 8.314472 * 298.15 ) ) /
            denominator
        energiesfile.write( str( key ) + ',' + str( energies[key][0] ) + ',' + str(
            energies[key][1] ) + ',' + str( temp ) + '\n' )

    energiesfile.flush()
    energiesfile.close()

# Archive and compress the input files in the folder for easy transfer over sftp
os.popen( "sleep 2; tar cjf " + str( pt[1]['s_m_title'] ) + ".tar.bz2 " + str( pt
    [1]['s_m_title'] + '*conf*.com' ) )

# Move the created input files "-gaussian_files" directory.
os.popen( "mv " + str( pt[1]['s_m_title'] + '*conf* ' ) + str( pt[1]['s_m_title'
    ] + '-gaussian_files' ) )

##### END main program loop #####
#####

# define extra functions

def convert_mmat_symbol(mmat):
#   mmat2Number = {1:'C',2:'C',3:'C',15:'O',16:'O',24:'N',25:'N',26:'N',41:'H',42:'H
    ',43:'H',49:'S',56:'F',57:'Cl',58:'Br',59:'I'}
#   symbol = mmat2Number[mmat]
#   return symbol
    return {1:'C',2:'C',3:'C',15:'O',16:'O',24:'N',25:'N',26:'N',41:'H',42:'H',43:'H'
        ,49:'S',56:'F',57:'Cl',58:'Br',59:'I'}[mmat]

def gaussian_input(which_section,candidate_filename="X", conformer_number="Y"):
# Current acceptable values for which_section are
# link, route, title, molecule, and end

    ENDLINE = "\n"
    LINK1 = "%mem=16gb\n"
    LINK2 = "%nproc=8\n"
    LINK3 = "%chk=%s \n" % (candidate_filename + '-conf-' + conformer_number + ".
        chk")

```

```

LINK4      = "\nradii=bondi"
ROUTE1    = "# m062x/6-31+G(d,p) opt=(verytight,calcfc) integral(ultrafinegrid)
           scrf=(iefpcm,read,solvent=chloroform)"
TITLE1    = "Candidate Structure: %s, Conformer: %s geometry optimization and
           frequency calculation with chloroform solvation" % (candidate_filename,
           conformer_number)
MOL1      = "0 1"
CARTHEAD  = "          X          Y          Z\n"

LINKZERO  = LINK1 + LINK2 + LINK3
ROUTE    = ROUTE1 + ENDLINE
TITLE    = TITLE1 + ENDLINE
MOLECULE = MOL1
READLINE = LINK4 + ENDLINE
END      = ENDLINE

if (which_section == "link"): return LINKZERO
if (which_section == "route"): return ROUTE
if (which_section == "title"): return TITLE
if (which_section == "molecule"): return MOLECULE
if (which_section == "readline"): return READLINE
if (which_section == "end"): return END

return "There is a problem generating the gaussian file."

def gaussian_nmr_input(which_section, candidate_filename="X", conformer_number="Y"):
    ENDLINE = "\n"
    LINK1   = "%mem=16gb\n"
    LINK2   = "%nproc=8\n"
    LINK3   = "%chk=%s \n" % (candidate_filename + '-conf-' + conformer_number + '
    .chk')
    LINK4   = "radii=bondi\n"
    ROUTE1  = "# b3lyp/6-311+G(2d,p) nmr guess=read geom=check integral(
           ultrafinegrid) scrf=(iefpcm,read,solvent=chloroform)"
    TITLE1  = "Candidate Structure: %s, Conformer: %s, NMR calculation with
           chloroform solvation" % (candidate_filename, conformer_number)
    MOL1    = "0 1"
    CARTHEAD = "          X          Y          Z\n"

    LINKZERO = LINK1 + LINK2 + LINK3
    ROUTE    = ROUTE1 + ENDLINE
    TITLE    = TITLE1 + ENDLINE
    MOLECULE = MOL1 + ENDLINE
    READLINE = LINK4 + ENDLINE
    END      = ENDLINE

    if (which_section == "link"): return LINKZERO
    if (which_section == "route"): return ROUTE
    if (which_section == "title"): return TITLE
    if (which_section == "molecule"): return MOLECULE
    if (which_section == "readline"): return READLINE
    if (which_section == "end"): return END

    return "There is a problem generating the gaussian file."

#####
#####
# Run the program
main()

```

A-1.2 write-g09-inputs-calcFCcalcall.py

write-g09-inputs-calcFCcalcall.py

```
#####
#####
#
# By Daniel J. Marell, January 2012
#
# This is a revised program of the parent
# write-g09-inputs-default.py
# Written by Patrick H. Willoughby, August 2011
#
# This modified version produces a Gaussian 09 input file
# to run a 2-part optimization, a calcFC opt then a calcall opt
#
# This python script is intended to be run from the Maestro
# Command Input Area.
#
# While in the command input area enter:
# pythonimport "title of this script"
#
# If you can't see the command input area then open Maestro,
# select Maestro and check the box to the left of
# "Command Input Area"
#
#####
#####

from schrodinger import maestro
from schrodinger import structure
from schrodinger import project
import os
from math import exp as exp

#####
##### BEGIN main program loop #####

def main ():
# Dictionary holding column names for project table properties depending on the
# force field being used
columns = {'mm2' : ['r_mmod_Potential_Energy-MM2*', '
r_mmod_Relative_Potential_Energy-MM2*'], 'mm3' : ['r_mmod_Potential_Energy-MM3*
*', 'r_mmod_Relative_Potential_Energy-MM3*'],
'amber' : ['r_mmod_Potential_Energy-AMBER*', 'r_mmod_Relative_Potential_Energy-
AMBER*'], 'opls' : ['r_mmod_Potential_Energy-OPLSA*', '
r_mmod_Relative_Potential_Energy-OPLSA*'],
'amber94' : ['r_mmod_Potential_Energy-AMBER94', 'r_mmod_Relative_Potential_Energy-
AMBER94'], 'mmff' : ['r_mmod_Potential_Energy-MMFF94', '
r_mmod_Relative_Potential_Energy-MMFF94'],
'mmffs' : ['r_mmod_Potential_Energy-MMFF94s', 'r_mmod_Relative_Potential_Energy-
MMFF94s'], 'opls2001' : ['r_mmod_Potential_Energy-OPLS-AA', '
r_mmod_Relative_Potential_Energy-OPLS-AA'],
'opls2005' : ['r_mmod_Potential_Energy-OPLS-2005', '
r_mmod_Relative_Potential_Energy-OPLS-2005']]

# Start by selecting all entries in the project table, and making sure the first
# entry is in the workspace
maestro.command("entryselectall")
maestro.command("eplayergotofirst")
```



```

# Grab the entire project table
pt = maestro.project_table_get()

currentforcefield = ''
for forcefield in columns.keys():
    if not pt[1][columns[forcefield][0]] == None :
        currentforcefield = forcefield
        break

# Create a directory to store the input files.
os.popen( "mkdir " + str( pt[1]['s_m_title']+'-gaussian_files' ) )

# Create a dictionary with keys being each conformer name and a list of the
# absolute and relative MM energies for the conformer.
energies = {}

# Make a loop to operate on every conformation in the project table.
# This loop operates on one conformation.
conf_num = 1
for row in pt.selected_rows:
    structure = maestro.workspace_get()

# Open the output file for writing
outputfile = open( row['s_m_title'] + "-opt_freq-conf-" + str(conf_num) + ".com", 'w' )
nmr_outputfile = open( row['s_m_title'] + "-nmr-conf-" + str(conf_num) + '.com', 'w' )

# Add the conformer energy to the dictionary of energies
energies[ str( row['s_m_title'] + row['s_m_entry_id'] ) ] =[ row[columns[
currentforcefield][0]], row[columns[currentforcefield][1]] ]

# Write the Gaussian stuff that goes into every input deck.

print >> outputfile, gaussian_input( "link", str( pt[1]['s_m_title']), str(
conf_num ))
print >> nmr_outputfile, gaussian_nmr_input( "link", str( pt[1]['s_m_title'])
, str( conf_num ) )
print >> outputfile, gaussian_input( "route" )
print >> nmr_outputfile, gaussian_nmr_input( "route" )
print >> outputfile, gaussian_input( "title", str( pt[1]['s_m_title']), str(
conf_num ))
print >> nmr_outputfile, gaussian_nmr_input( "title", str( pt[1]['s_m_title'
]), str( conf_num ))
print >> outputfile, gaussian_input( "molecule" )
print >> nmr_outputfile, gaussian_nmr_input( "molecule" )
print >> nmr_outputfile, gaussian_nmr_input( "readline" )
print >> nmr_outputfile, gaussian_nmr_input( "end" )

# This loop operates on one atom.

for atom in structure.atom:
    outputstring = "%2s %10.6f %10.6f %10.6f" % (atom.element, atom.x, atom.y
, atom.z)
    print >> outputfile, outputstring

print >> outputfile, gaussian_input( "readline" )
print >> outputfile, gaussian_input("end")

```

```

    print >> outputfile, gaussian_input( "link2", str( pt[1]['s_m_title']), str(
        conf_num ))
    print >> outputfile, gaussian_input( "route2" )
    print >> outputfile, gaussian_input( "title2", str( pt[1]['s_m_title']), str
        ( conf_num ))
    print >> outputfile, gaussian_input( "molecule2" )
    print >> outputfile, gaussian_input( "end" )

# Close the opened output file.

    outputfile.flush()
    outputfile.close()
    nmr_outputfile.flush()
    nmr_outputfile.close()
    maestro.command("eplayerstepeahead")
    conf_num += 1

# Write the collected energy data for each conformer to a CSV file

    # Sum the exponential relative energies to create the denominator term

    denominator = 0
    for key in energies:
        denominator = denominator + exp( -( energies[key][1] * 1000 ) / ( 8.314472 *
            298.15 ) )

    energiesfile = open( str( pt[1]['s_m_title'] ) + '_MM_energies.csv', 'w' )
    energiesfile.write( 'Conformer,MM Energy,Relative MM Energy,Boltzman Weight\n\n'
        )

    for key in energies:
        temp = exp( -( energies[key][1] * 1000 ) / ( 8.314472 * 298.15 ) ) /
            denominator
        energiesfile.write( str( key ) + ',' + str( energies[key][0] ) + ',' + str(
            energies[key][1] ) + ',' + str( temp ) + '\n' )

    energiesfile.flush()
    energiesfile.close()

# Archive and compress the input files in the folder for easy transfer over sftp
    os.popen( "sleep 2; tar cjf " + str( pt[1]['s_m_title'] ) + ".tar.bz2 " + str( pt
        [1]['s_m_title'] + '*conf*.com' ) )

# Move the created input files "-gaussian_files" directory.
    os.popen( "mv " + str( pt[1]['s_m_title'] + '*conf* ' ) + str( pt[1]['s_m_title'
        ] + '-gaussian_files' ) )

##### END main program loop #####
#####

# define extra functions

def convert_mmat_symbol(mmat):
#   mmat2Number = {1:'C',2:'C',3:'C',15:'O',16:'O',24:'N',25:'N',26:'N',41:'H',42:'H
#   ',43:'H',49:'S',56:'F',57:'Cl',58:'Br',59:'I'}
#   symbol = mmat2Number[mmat]
#   return symbol
    return {1:'C',2:'C',3:'C',15:'O',16:'O',24:'N',25:'N',26:'N',41:'H',42:'H',43:'H'
        ,49:'S',56:'F',57:'Cl',58:'Br',59:'I'}[mmat]

def gaussian_input(which_section,candidate_filename="X", conformer_number="Y"):
# Current acceptable values for which_section are

```

```

# link, route, title, molecule, and end

ENDLINE = "\n"
LINK1 = "%mem=16gb\n"
LINK2 = "%nproc=8\n"
LINK3 = "%chk=%s \n" % (candidate_filename + '-conf-' + conformer_number + ".chk")
LINK4 = "\nradii=bondi"
ROUTE1 = "# m062x/6-31+G(d,p) opt=(verytight,calcf) integral(ultrafinegrid) scrf=(iefpcm,read,solvent=chloroform)"
TITLE1 = "Candidate Structure: %s, Conformer: %s geometry optimization and frequency calculation with chloroform solvation" % (candidate_filename, conformer_number)
MOL1 = "0 1"
CARTHEAD = " X Y Z\n"

LINK2_1 = "--Link1--\n"
LINK2_2 = "%chk=%s" % (candidate_filename + '-conf-' + conformer_number + ".chk")
ROUTE2 = "# m062x/6-31+G(d,p) opt=(verytight,calcall) integral(ultrafinegrid) scrf=check geom=checkpoint"
TITLE2 = "Candidate Structure: %s, Conformer: %s geometry optimization and frequency calculation with chloroform solvation" % (candidate_filename, conformer_number)
MOL2 = "0 1"

LINKZERO = LINK1 + LINK2 + LINK3
ROUTE = ROUTE1 + ENDLINE
TITLE = TITLE1 + ENDLINE
MOLECULE = MOL1
READLINE = LINK4 + ENDLINE
END = ENDLINE

LINK2 = LINK2_1 + LINK2_2
ROUTE2 = ROUTE2 + ENDLINE
TITLE2 = TITLE2 + ENDLINE
MOLECULE2 = MOL2

if (which_section == "link"): return LINKZERO
if (which_section == "route"): return ROUTE
if (which_section == "title"): return TITLE
if (which_section == "molecule"): return MOLECULE
if (which_section == "readline"): return READLINE
if (which_section == "end"): return END

if (which_section == "link2"): return LINK2
if (which_section == "route2"): return ROUTE2
if (which_section == "title2"): return TITLE2
if (which_section == "molecule2"): return MOLECULE2

return "There is a problem generating the gaussian file."

def gaussian_nmr_input(which_section, candidate_filename="X", conformer_number="Y"):
ENDLINE = "\n"
LINK1 = "%mem=16gb\n"
LINK2 = "%nproc=8\n"
LINK3 = "%chk=%s \n" % (candidate_filename + '-conf-' + conformer_number + '.chk')

```

```

LINK4      = "radii=bondi\n"
ROUTE1     = "# b3lyp/6-311+G(2d,p) nmr guess=read geom=check integral(
             ultrafinegrid) scrf=(iefpcm,read,solvent=chloroform)"
TITLE1     = "Candidate Structure: %s, Conformer: %s, NMR calculation with
             chloroform solvation" % (candidate_filename,conformer_number)
MOL1       = "0 1"
CARTHEAD   = "          X          Y          Z\n"

LINKZERO   = LINK1 + LINK2 + LINK3
ROUTE      = ROUTE1 + ENDLINE
TITLE      = TITLE1 + ENDLINE
MOLECULE   = MOL1 + ENDLINE
READLINE   = LINK4 + ENDLINE
END        = ENDLINE

if (which_section == "link"): return LINKZERO
if (which_section == "route"): return ROUTE
if (which_section == "title"): return TITLE
if (which_section == "molecule"): return MOLECULE
if (which_section == "readline"): return READLINE
if (which_section == "end"): return END

return "There is a problem generating the gaussian file."

#####
#####
# Run the program
main()

```

A-2 NMR Scripts

A-2.1 nmr-data_compilation.py

nmr-data_compilation.py

```
#####  
#  
#           nmr-data_compilation.py           #  
#  
#           Copyright Patrick H. Willoughby September 2011           #  
#  
#           Does Boltzmann-analysis and searches for imaginary           #  
#           frequencies, and compiles the NMR shielding tensors           #  
#           then prints the data into several .csv files for           #  
#           viewing in a spreadsheet application           #  
#  
#####  
  
import sys  
import re  
import math  
  
HARTREE_TO_KCAL = 627.509391  
TEMPERATURE = 298.0  
GAS_CONSTANT = 0.001986  
  
PROTON_SHIFT_TMS = input("""Enter the computed NMR shield tensor for the protons in  
TMS:  
""")  
CARBON_SHIFT_TMS = input("""Enter the computed NMR shield tensor for the protons in  
TMS:  
""")  
OUTPUT_PREFIX = raw_input("""Enter the name of the candidate structure:  
""") + "-nmr_data_compilation"  
  
#Below are the index values for the master data structure.  
NAME = 0; CONF_NUM = 1; ENERGY = 2; KCAL_E = 3; REL_E = 4; BOLTZMANN_FACTOR = 5;  
MOL_X = 6; CARBON_CS = 7; PROTON_CS = 8; IMAG_FREQUENCIES = 9  
  
#Below are the index values for the proton and carbon chemical shift data  
substructures.  
ATOM_NUMBER = 0 ; ISOTROPIC_VALUE = 1; REF_SHIFT = 2; WEIGHTED_SHIFT = 3;  
  
def main():  
    lofc_freq = read_gaussian_freq_outfiles()  
    lofc_nmr = read_gaussian_nmr_outfiles()  
    locs = prepare_list_of_chemical_shifts(lofc_nmr)  
    lofe = get_list_of_free_energies(lofc_freq)  
    lofe = boltzmann_analysis(lofe)  
    lofe = report_chemical_shifts(lofc_nmr, lofe)  
    summed_proton_shifts = final_proton_chemical_shifts(lofe)  
    summed_carbon_shifts = final_carbon_chemical_shifts(lofe)  
    lofe = count_imaginary_freq(lofc_freq, lofe)  
    write_final_shift_csv(summed_proton_shifts, summed_carbon_shifts)  
    write_master_csv(lofe)  
  
def boltzmann_analysis(lofe):  
    lofe = kcal_convert(lofe)  
    minE = find_minimum_E(lofe)
```

```

lofe = calc_rel_E(lofe, minE)
lofe = calc_boltzmann_weights(lofe)
denom = calc_boltzmann_denominator(lofe)
lofe = calc_mol_fraction(lofe, denom)

return lofe

def report_chemical_shifts(lofc_nmr, lofe):
    get_chemical_shifts(lofc_nmr, lofe)
    ref_chemical_shift(lofe)
    boltzmann_chemical_shifts(lofe)

return lofe

def write_master_csv(lofe):

    masterpwriter = open(OUTPUT_PREFIX+"-master_proton.csv",'w')
    mastercwriter = open(OUTPUT_PREFIX+"-master_carbon.csv",'w')

    print>> masterpwriter, "filename, energy (a.u.), energy (kcal), rel energy (kcal)
    , boltzmann factor, eq mole fraction, imaginary freqs"
    for conformation in lofe:
        print >> masterpwriter, conformation[NAME],",", conformation[ENERGY],",",
        conformation[KCAL_E],",", conformation[REL_E],",", conformation[
        BOLTZMANN_FACTOR],",", conformation[MOL_X],",", conformation[
        IMAG_FREQUENCIES]
    print>>masterpwriter, " "
    for conformation in lofe:
        print >> masterpwriter, "conformation",",", conformation[NAME],",", "mole
        fraction",",", conformation[MOL_X]
        print >> masterpwriter, "Atom Number, Isotropic Value, Shift of Ref, Ref
        Chemical Shift, Avg Chemical Shift"
        for proton in conformation[PROTON_CS]:
            print >> masterpwriter, proton[ATOM_NUMBER],",", proton[ISOTROPIC_VALUE],
            ",", PROTON_SHIFT_TMS ,",", proton[REF_SHIFT],",", proton[
            WEIGHTED_SHIFT]
        print >> masterpwriter, " "

    print>> mastercwriter, "filename, energy (a.u.), energy (kcal), rel energy (kcal)
    , boltzmann factor, eq mole fraction"
    for conformation in lofe:
        print >> mastercwriter, conformation[NAME],",", conformation[ENERGY],",",
        conformation[KCAL_E],",", conformation[REL_E],",", conformation[
        BOLTZMANN_FACTOR],",", conformation[MOL_X]
    print>>mastercwriter, " "
    for conformation in lofe:
        print >> mastercwriter, "conformation",",", conformation[NAME],",", "mole
        fraction",",", conformation[MOL_X]
        print >> mastercwriter, "Atom Number, Isotropic Value, Shift of Ref, Ref
        Chemical Shift, Avg Chemical Shift"
        for carbon in conformation[CARBON_CS]:
            print >> mastercwriter, carbon[ATOM_NUMBER],",", carbon[ISOTROPIC_VALUE],
            ",", CARBON_SHIFT_TMS ,",", carbon[REF_SHIFT],",", carbon[
            WEIGHTED_SHIFT]
        print >> mastercwriter, " "

def write_final_shift_csv(summed_proton_shifts, summed_carbon_shifts):
    ATOM_NUMBER = 0; SHIFT = 1
    pwriter = open(OUTPUT_PREFIX+"-avg_proton.csv",'w')
    cwriter = open(OUTPUT_PREFIX+"-avg_carbon.csv",'w')

```

```

print >> pwriter, "ATOM NUMBER, CHEMICAL SHIFT"
for item in summed_proton_shifts:
    print >> pwriter, item[ATOM_NUMBER],",",item[SHIFT]

print >> cwriter, "ATOM NUMBER, CHEMICAL SHIFT"
for item in summed_carbon_shifts:
    print >> cwriter, item[ATOM_NUMBER],",",item[SHIFT]

return 0

def final_proton_chemical_shifts(lofe):
    ATOM_NUMBER = 0; SHIFT = 1
    final_proton_cshift = []

    for proton in lofe[0][PROTON_CS]:
        final_proton_cshift.append([proton[ATOM_NUMBER],proton[WEIGHTED_SHIFT]])

    for conformation in lofe[1:]:
        counter = 0
        for proton in conformation[PROTON_CS]:
            final_proton_cshift[counter][SHIFT] += proton[WEIGHTED_SHIFT]
            counter += 1

    return final_proton_cshift

def final_carbon_chemical_shifts(lofe):
    ATOM_NUMBER = 0; SHIFT = 1
    final_carbon_cshift = []

    for carbon in lofe[0][CARBON_CS]:
        final_carbon_cshift.append([carbon[ATOM_NUMBER],carbon[WEIGHTED_SHIFT]])

    for conformation in lofe[1:]:
        counter = 0
        for carbon in conformation[CARBON_CS]:
            final_carbon_cshift[counter][SHIFT] += carbon[WEIGHTED_SHIFT]
            counter += 1

    return final_carbon_cshift

def kcal_convert(lofe):
    NAME = 0; CONF_NUM = 1; ENERGY = 2
    for entry in lofe:
        entry.append(entry[ENERGY] * HARTREE_TO_KCAL)

    return lofe

def find_minimum_E(lofe):
    minE = 0
    for entry in lofe: #This finds the minimum energy
        if entry[KCAL_E] < minE:
            minE = entry[KCAL_E]

    return minE

def calc_rel_E(lofe, minE):
    for entry in lofe:
        entry.append(entry[KCAL_E] - minE)

    return lofe

```

```

def calc_boltzmann_weights(lofe):
    for entry in lofe:
        entry.append(math.exp( (-1 * entry[REL_E]) / (TEMPERATURE * GAS_CONSTANT)))

    return lofe

def calc_boltzmann_denomenator(lofe):
    Boltzmann_denomenator = 0
    for entry in lofe:
        Boltzmann_denomenator = Boltzmann_denomenator + entry[BOLTZMANN_FACTOR]

    return Boltzmann_denomenator

def calc_mol_fraction(lofe, Boltzmann_denomenator):
    for entry in lofe:
        entry.append(entry[BOLTZMANN_FACTOR]/Boltzmann_denomenator)

    return lofe

def ref_chemical_shift(lofe):
    for conformation in lofe:
        for proton in conformation[PROTON_CS]:
            proton.append(abs(PROTON_SHIFT_TMS - float(proton[ISOTROPIC_VALUE])))
        for carbon in conformation[CARBON_CS]:
            carbon.append(abs(CARBON_SHIFT_TMS - float(carbon[ISOTROPIC_VALUE])))

    return lofe

def boltzmann_chemical_shifts(lofe):
    for conformation in lofe:
        for proton in conformation[PROTON_CS]:
            proton.append(proton[REF_SHIFT] * conformation[MOL_X])
        for carbon in conformation[CARBON_CS]:
            carbon.append(carbon[REF_SHIFT] * conformation[MOL_X])

    return lofe

def get_chemical_shifts(lofc_nmr, lofe):
    ATOM_NUMBER = 0; ATOM_SYMBOL = 1; ISOTROPIC_VALUE = 4
    counter = 0
    for file in lofc_nmr:
        proton_chemicalshift_table = []
        carbon_chemicalshift_table = []
        for line in file[2]:
            if "Isotropic" in line:
                linesplit = line.split()
                if linesplit[ATOM_SYMBOL] == "C":
                    carbon_chemicalshift_table.append([linesplit[ATOM_NUMBER],
                                                         linesplit[ISOTROPIC_VALUE]])
                if linesplit[ATOM_SYMBOL] == "H":
                    proton_chemicalshift_table.append([linesplit[ATOM_NUMBER],
                                                         linesplit[ISOTROPIC_VALUE]])
            lofe[counter].append(carbon_chemicalshift_table)
            lofe[counter].append(proton_chemicalshift_table)
            counter += 1
    return lofe

def prepare_list_of_chemical_shifts(lofc_nmr):
    list_of_chemical_shifts = []
    for file in lofc_nmr:
        list_of_chemical_shifts.append([file[0], file[1]])

```



```

return list_of_chemical_shifts

def count_imaginary_freq(lofc_freq, lofe):
    LINE_POS_OF_FREQUENCY_A = 2; LINE_POS_OF_FREQUENCY_B = 3; LINE_POS_OF_FREQUENCY_C
    = 4;
    counter = 0
    for file in lofc_freq:
        IMAG_FREQUENCIES = 0
        for line in file[2]:
            if "Frequencies -- " in line:
                freq_linesplit = line.split()
                if float(freq_linesplit[LINE_POS_OF_FREQUENCY_A]) < 0:
                    IMAG_FREQUENCIES = IMAG_FREQUENCIES + 1
                if float(freq_linesplit[LINE_POS_OF_FREQUENCY_B]) < 0:
                    IMAG_FREQUENCIES = IMAG_FREQUENCIES + 1
                if float(freq_linesplit[LINE_POS_OF_FREQUENCY_C]) < 0:
                    IMAG_FREQUENCIES = IMAG_FREQUENCIES + 1

        lofe[counter].append(IMAG_FREQUENCIES)
        counter += 1

    return lofe

def get_list_of_free_energies(lofc_freq):
    LINE_POS_OF_FREE_ENERGY = 7
    list_of_free_energies = []
    for file in lofc_freq:
        for line in file[2]:
            if "Free Energies=" in line:
                free_linesplit = line.split()
                free_energy = float(free_linesplit[LINE_POS_OF_FREE_ENERGY])
                list_of_free_energies.append([file[0], file[1], free_energy])
    return list_of_free_energies

def get_conf_number(filename):
    split_filename = re.findall(r'\w+', filename)
    rev_filename = split_filename[::-1]
    conf_number = rev_filename[1]
    split_conf_number = re.findall('[0-9]*', conf_number)
    return split_conf_number[0]

def read_gaussian_nmr_outfiles():
    list_of_nmr_outfiles = []
    list_of_files = sys.argv[1:]
    for file in list_of_files:
        if file.find('nmr-') != -1:
            list_of_nmr_outfiles.append([file, int(get_conf_number(file)), open(file, "r"
            ).readlines()]])

    return list_of_nmr_outfiles

def read_gaussian_freq_outfiles():
    list_of_freq_outfiles = []
    list_of_files = sys.argv[1:]
    for file in list_of_files:
        if file.find('freq-') != -1:
            list_of_freq_outfiles.append([file, int(get_conf_number(file)), open(file, "
            r").readlines()]])

    return list_of_freq_outfiles

```

```
if __name__ == "__main__":
    main()
print """
The script successfully performed the Boltzmann weighting,
compiled the results of the NMR computation, and assembled
these data in the following .csv files:

%s-master_proton.csv

%s-avg_proton.csv

%s-master_carbon.csv

%s-avg_carbon.csv
""" % (OUTPUT_PREFIX, OUTPUT_PREFIX, OUTPUT_PREFIX, OUTPUT_PREFIX)
```

SUPPORTING INFORMATION

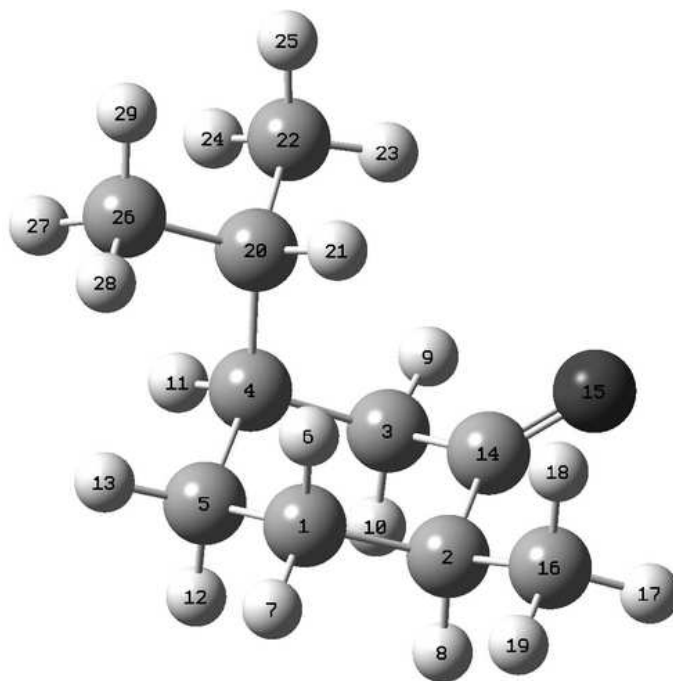
S-I Calculated Geometries, Energies and NMR Shielding Tensors for Compounds with Computed NMR Shifts

S-I.1	<i>cis</i> -Carvomenthone (201a)	81
S-I.2	<i>trans</i> -Carvomenthone (201b)	97
S-I.3	Nankakurine – Revised Diastereomer(202a)	111
S-I.4	Nankakurine – Originally Proposed Diastereomer (202b)	120
S-I.5	Normal <i>trans</i> -Menthide (203b)	129
S-I.6	Normal <i>cis</i> -Carvomenthide (204a)	135
S-I.7	Normal <i>trans</i> -Carvomenthide (204b)	147
S-I.8	Abnormal <i>cis</i> -Carvomenthide (205a)	153
S-I.9	Abnormal <i>trans</i> -Carvomenthide (205b)	167
S-I.10	Normal Lactone of β -Pinene (206)	175
S-I.11	Abnormal Lactone of β -Pinene (207)	177

All geometries extracted are in the standard (x,y,z) coordinate system. Energies reported (in hartrees) indicate the level of theory they are obtained at. Energies reported include: 1) energies from optimizations (SCF Energy), 2) energies from NMR calculations (SCF Energy from NMR), 3) Gibb’s free energy (Sum of Electronic and Thermal Free Energies)

S-I.1 *cis*-Carvomenthone (201a)

Fig. S1 201a – Conformer 1



SCF Energy - E(RM062X) -466.957 997 808
 SCF Energy from NMR - E(RB3LYP) -467.291 748 885
 Sum of Electronic and Thermal Free Energies -466.729 834 000

Table S1 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **201a** – Conformer 1

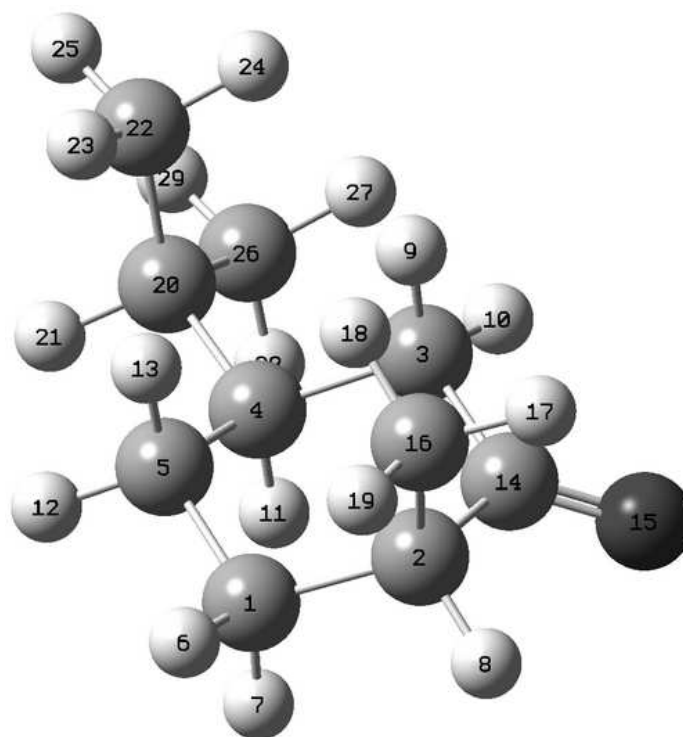
Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	-0.947 279	-1.520 474	-0.078 644	146.8990	36.7086
2	C	-1.929 336	-0.349 551	0.140 883	131.7715	51.8361
3	C	-0.009 795	0.951 482	1.240 809	133.3244	50.2832
4	C	0.981 364	-0.180 309	0.887 180	131.1437	52.4639
5	C	0.206 542	-1.507 481	0.925 378	150.8655	32.7421
6	H	-0.558 595	-1.467 469	-1.104 474	30.3115	1.5534
7	H	-1.506 878	-2.459 165	-0.004 839	29.9441	1.9208
8	H	-2.386 502	-0.496 909	1.132 360	29.3401	2.5248

Continued on next page

Table S1 – continued from previous page

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
9	H	0.455 963	1.938 412	1.250 219	29.2453	2.6196
10	H	-0.421 000	0.756 911	2.239 580	29.2676	2.5973
11	H	1.756 700	-0.206 501	1.666 171	30.2016	1.6633
12	H	-0.198 261	-1.643 411	1.937 060	30.0152	1.8497
13	H	0.875 732	-2.353 144	0.742 262	29.7904	2.0745
14	C	-1.158 504	0.955 909	0.256 239	-46.6537	230.2613
15	O	-1.436 235	1.940 260	-0.408 895	—	—
16	C	-3.016 347	-0.296 113	-0.923 351	167.1928	16.4148
17	H	-3.726 141	0.511 314	-0.728 917	30.5584	1.3065
18	H	-2.576 264	-0.124 870	-1.910 794	31.0415	0.8234
19	H	-3.562 432	-1.243 466	-0.948 868	31.2574	0.6075
20	C	1.696 244	0.083 370	-0.457 179	150.5958	33.0118
21	H	0.935 249	0.243 733	-1.235 681	30.5290	1.3359
22	C	2.560 603	1.346 770	-0.389 124	160.9833	22.6243
23	H	1.968 764	2.247 522	-0.208 676	30.3877	1.4772
24	H	3.303 203	1.257 385	0.413 548	31.4642	0.4007
25	H	3.099 708	1.490 272	-1.330 442	31.0125	0.8524
26	C	2.560 127	-1.108 166	-0.880 626	161.7347	21.8729
27	H	3.264 694	-1.373 171	-0.082 076	31.3929	0.4720
28	H	1.961 874	-1.993 797	-1.111 927	30.5926	1.2723
29	H	3.142 353	-0.858 344	-1.772 744	31.0731	0.7918

Fig. S2 201a – Conformer 2



SCF Energy - E(RM062X) -466.956 332 496
SCF Energy from NMR - E(RB3LYP) -467.292 225 553
Sum of Electronic and Thermal Free Energies -466.729 305 000

Table S2 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for 201a – Conformer 2

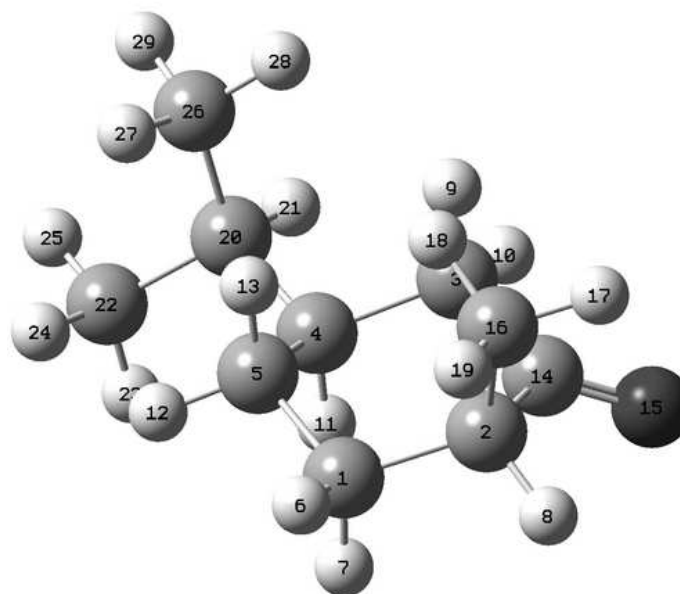
Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	1.424 114	-1.143 683	-1.120 536	146.4062	37.2014
2	C	2.195 203	-0.176 827	-0.202 202	131.1068	52.5008
3	C	-0.073 020	0.877 348	0.435 844	141.7922	41.8154
4	C	-0.789 636	-0.070 617	-0.546 520	131.3300	52.2776
5	C	-0.011 499	-1.386 942	-0.648 099	153.2530	30.3546
6	H	1.976 538	-2.088 242	-1.180 966	30.0260	1.8389
7	H	1.396 110	-0.724 037	-2.134 023	29.9765	1.8884
8	H	3.116 761	0.146 486	-0.696 650	29.4200	2.4449

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Table S2 – continued from previous page

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
9	H	-0.086 538	0.432 163	1.440 704	29.4323	2.4326
10	H	-0.549 288	1.859 116	0.492 529	29.7829	2.0820
11	H	-0.756 334	0.402 956	-1.540 534	30.1614	1.7035
12	H	-0.519 913	-2.059 022	-1.349 380	30.5611	1.3038
13	H	-0.004 452	-1.892 692	0.325 649	29.8378	2.0271
14	C	1.375 868	1.076 467	0.049 014	-50.3354	233.9430
15	O	1.867 534	2.189 700	-0.045 680	—	—
16	C	2.568 401	-0.822 919	1.142 887	163.4942	20.1134
17	H	3.109 829	-0.116 017	1.777 945	30.8288	1.0361
18	H	1.687 232	-1.168 500	1.690 878	30.3607	1.5042
19	H	3.214 300	-1.687 326	0.963 115	30.8579	1.0070
20	C	-2.280 997	-0.275 531	-0.211 384	144.9660	38.6416
21	H	-2.654 392	-0.999 607	-0.949 876	30.1496	1.7153
22	C	-2.522 330	-0.864 209	1.181 564	167.2746	16.3330
23	H	-1.975 811	-1.799 060	1.337 487	30.6863	1.1786
24	H	-2.224 859	-0.158 417	1.965 298	31.2912	0.5737
25	H	-3.587 474	-1.074 633	1.320 137	31.0366	0.8283
26	C	-3.085 333	1.015 784	-0.384 231	160.6166	22.9910
27	H	-2.819 419	1.754 639	0.379 635	30.9689	0.8960
28	H	-2.910 146	1.465 692	-1.367 139	31.0495	0.8154
29	H	-4.157 045	0.815 684	-0.287 405	30.8726	0.9923

Fig. S3 201a – Conformer 3



SCF Energy - E(RM062X) -466.956 327 984
SCF Energy from NMR - E(RB3LYP) -467.292 250 850
Sum of Electronic and Thermal Free Energies -466.728 725 000

Table S3 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for 201a – Conformer 3

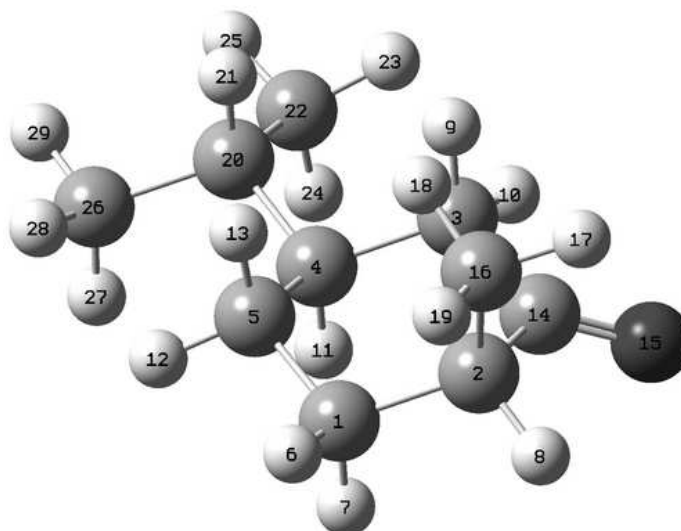
Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	1.069 944	-1.380 230	-0.930 407	146.3687	37.2389
2	C	2.125 406	-0.490 498	-0.246 712	131.0681	52.5395
3	C	0.220 363	1.140 003	0.352 450	134.2092	49.3984
4	C	-0.783 981	0.247 741	-0.403 220	131.3784	52.2292
5	C	-0.327 588	-1.213 486	-0.326 712	160.9567	22.6509
6	H	1.395 792	-2.424 589	-0.865 453	30.0197	1.8452
7	H	1.026 282	-1.124 240	-1.996 525	30.0774	1.7875
8	H	3.038 053	-0.468 779	-0.850 797	29.4176	2.4473
9	H	0.214 840	0.872 421	1.418 417	29.0464	2.8185
10	H	-0.036 369	2.199 709	0.267 211	29.9743	1.8906
11	H	-0.748 035	0.548 670	-1.462 202	30.1926	1.6723

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Table S3 – continued from previous page

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
12	H	-1.030 843	-1.860 373	-0.862 238	30.3425	1.5224
13	H	-0.326 212	-1.544 730	0.719 734	30.2536	1.6113
14	C	1.630 234	0.941 682	-0.156 379	-49.9573	233.5649
15	O	2.339 985	1.884 480	-0.468 537	—	—
16	C	2.487 328	-0.994 010	1.160 979	163.4995	20.1081
17	H	3.231 466	-0.343 186	1.628 721	30.8287	1.0362
18	H	1.613 116	-1.040 207	1.816 542	30.3684	1.4965
19	H	2.908 495	-2.000 986	1.088 700	30.8721	0.9928
20	C	-2.229 594	0.492 866	0.075 604	144.8184	38.7892
21	H	-2.369 091	1.583 363	0.087 169	30.3860	1.4789
22	C	-3.250 557	-0.090 559	-0.905 106	160.2374	23.3702
23	H	-3.082 747	0.281 337	-1.921 187	30.9751	0.8898
24	H	-3.196 289	-1.184 464	-0.929 533	30.8364	1.0285
25	H	-4.268 169	0.181 460	-0.607 387	30.8193	1.0456
26	C	-2.499 704	-0.029 417	1.489 735	166.9560	16.6516
27	H	-2.470 474	-1.124 255	1.515 284	31.2187	0.6462
28	H	-1.775 475	0.347 408	2.218 895	30.7412	1.1237
29	H	-3.495 328	0.281 051	1.821 547	31.0377	0.8272

Fig. S4 201a – Conformer 4

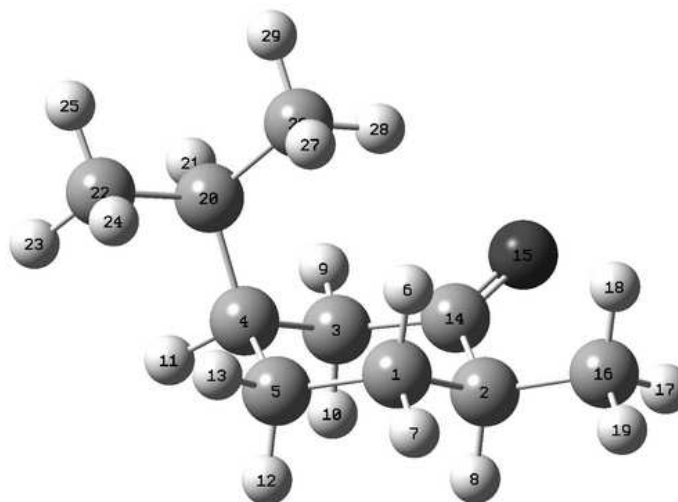


SCF Energy - E(RM062X) -466.956 274 003
 SCF Energy from NMR - E(RB3LYP) -467.292 236 672
 Sum of Electronic and Thermal Free Energies -466.728 989 000

Table S4 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **201a** – Conformer 4

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	1.257 157	-1.439 734	-0.777 704	146.8870	36.7206
2	C	2.209 321	-0.378 327	-0.201 676	131.7479	51.8597
3	C	0.120 221	1.057 961	0.291 344	135.6344	47.9732
4	C	-0.805 184	-0.039 694	-0.274 288	129.5862	54.0214
5	C	-0.131 557	-1.411 259	-0.135 308	154.9697	28.6379
6	H	1.713 282	-2.428 749	-0.655 619	30.0183	1.8466
7	H	1.148 405	-1.270 140	-1.856 584	30.0554	1.8095
8	H	3.103 464	-0.301 973	-0.828 549	29.4490	2.4159
9	H	0.169 582	0.942 022	1.385 379	29.6147	2.2502
10	H	-0.251 988	2.061 785	0.078 847	29.3970	2.4679
11	H	-0.948 082	0.160 971	-1.349 209	30.6499	1.2150
12	H	-0.747 276	-2.179 817	-0.610 782	29.9870	1.8779
13	H	-0.068 506	-1.673 550	0.930 511	30.3729	1.4920
14	C	1.536 195	0.978 577	-0.236 443	-49.6073	233.2149
15	O	2.114 866	1.968 633	-0.655 364	—	—
16	C	2.649 535	-0.702 209	1.235 671	163.7384	19.8692
17	H	3.323 556	0.068 892	1.619 239	30.8280	1.0369
18	H	1.798 463	-0.781 985	1.917 790	30.3665	1.4984
19	H	3.180 424	-1.658 678	1.245 600	30.8746	0.9903
20	C	-2.194 285	0.007 543	0.393 422	142.4909	41.1167
21	H	-2.045 641	-0.189 701	1.466 683	30.5450	1.3199
22	C	-2.855 160	1.382 292	0.245 401	161.0610	22.5466
23	H	-2.304 365	2.170 485	0.764 483	30.5420	1.3229
24	H	-2.927 302	1.658 532	-0.814 035	31.4003	0.4646
25	H	-3.869 272	1.363 248	0.656 050	31.0358	0.8291
26	C	-3.129 835	-1.068 547	-0.167 565	160.5330	23.0746
27	H	-3.214 795	-0.969 715	-1.257 059	31.3359	0.5290
28	H	-2.784 799	-2.080 814	0.056 125	30.3947	1.4702
29	H	-4.132 526	-0.959 482	0.256 922	30.9868	0.8781

Fig. S5 201a – Conformer 5



SCF Energy - E(RM062X) -466.953 841 772
SCF Energy from NMR - E(RB3LYP) -467.288 664 184
Sum of Electronic and Thermal Free Energies -466.725 996 000

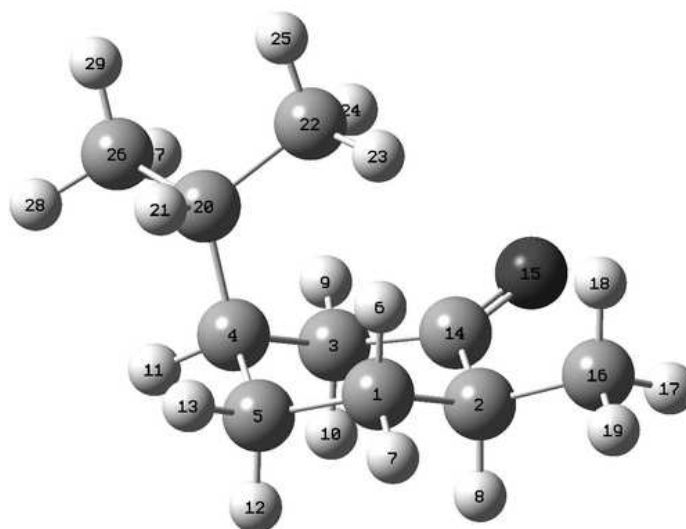
Table S5 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **201a** – Conformer 5

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	-0.723 626	1.481 195	0.312 356	143.6563	39.9513
2	C	-1.853 099	0.555 267	-0.177 218	132.7238	50.8838
3	C	-0.068 415	-0.894 230	-1.311 024	129.8990	53.7086
4	C	1.066 540	0.085 768	-0.934 668	133.1814	50.4262
5	C	0.487 175	1.479 217	-0.626 049	155.6621	27.9455
6	H	-0.441 136	1.177 411	1.325 561	30.2359	1.6290
7	H	-1.122 863	2.498 598	0.392 162	29.9357	1.9292
8	H	-2.162 861	0.915 704	-1.170 989	29.2985	2.5664
9	H	0.290 138	-1.927 290	-1.345 508	29.6379	2.2270
10	H	-0.431 646	-0.631 045	-2.314 564	29.0318	2.8331
11	H	1.683 558	0.194 494	-1.836 311	29.6307	2.2342
12	H	0.175 243	1.931 584	-1.577 090	30.0050	1.8599
13	H	1.270 993	2.128 627	-0.221 362	29.7931	2.0718
14	C	-1.283 307	-0.830 677	-0.412 327	-48.1059	231.7135

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Table S5 – continued from previous page

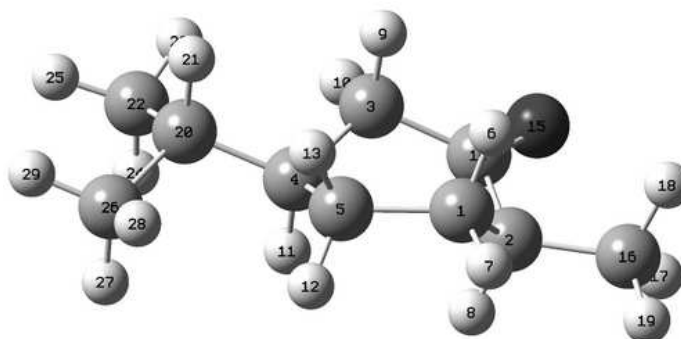
Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
15	O	-1.784 797	-1.834 815	0.066 813	—	—
16	C	-3.048 455	0.547 241	0.765 011	167.0990	16.5086
17	H	-3.850 558	-0.091 825	0.388 249	30.5350	1.3299
18	H	-2.755 449	0.171 612	1.750 532	31.0387	0.8262
19	H	-3.437 599	1.562 354	0.884 983	31.2517	0.6132
20	C	2.024 800	-0.506 818	0.124 036	141.5152	42.0924
21	H	2.310 503	-1.492 337	-0.271 166	30.0877	1.7772
22	C	3.306 644	0.322 102	0.242 734	159.2106	24.3970
23	H	3.769 661	0.485 502	-0.736 194	31.0290	0.8359
24	H	3.106 267	1.301 048	0.692 038	30.8343	1.0306
25	H	4.034 200	-0.188 302	0.881 828	30.8093	1.0556
26	C	1.423 304	-0.734 409	1.514 618	162.3639	21.2437
27	H	1.274 317	0.214 378	2.040 351	31.3093	0.5556
28	H	0.466 322	-1.264 430	1.478 720	30.8850	0.9799
29	H	2.109 931	-1.335 490	2.119 438	31.0346	0.8303

Fig. S6 201a – Conformer 6

SCF Energy - E(RM062X) -466.954 233 138
SCF Energy from NMR - E(RB3LYP) -467.287 425 809
Sum of Electronic and Thermal Free Energies -466.725 564 000

Table S6 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **201a** – Conformer 6

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	-1.067 873	1.457 736	0.511 627	146.2731	37.3345
2	C	-1.891 108	0.340 785	-0.156 833	132.2590	51.3486
3	C	0.265 807	-0.433 855	-1.348 492	137.4884	46.1192
4	C	1.075 398	0.687 927	-0.667 613	135.0751	48.5325
5	C	0.143 409	1.861 077	-0.327 740	145.3729	38.2347
6	H	-0.753 718	1.132 192	1.510 298	30.0260	1.8389
7	H	-1.723 165	2.322 689	0.663 303	29.8992	1.9657
8	H	-2.285 593	0.759 210	-1.097 985	29.4018	2.4631
9	H	0.857 699	-1.340 018	-1.507 943	29.3388	2.5261
10	H	-0.059 201	-0.073 909	-2.335 040	29.4490	2.4159
11	H	1.785 924	1.062 091	-1.415 662	29.7914	2.0735
12	H	-0.216 171	2.300 123	-1.268 615	29.7328	2.1321
13	H	0.714 327	2.641 922	0.187 347	30.0611	1.8038
14	C	-1.002 871	-0.808 677	-0.608 696	-47.6969	231.3045
15	O	-1.323 086	-1.973 671	-0.441 114	—	—
16	C	-3.048 757	-0.130 780	0.713 098	166.8276	16.7800
17	H	-3.662 022	-0.872 808	0.197 442	30.3557	1.5092
18	H	-2.671 211	-0.588 551	1.633 552	31.0766	0.7883
19	H	-3.681 525	0.718 535	0.986 118	31.2293	0.6356
20	C	1.933 665	0.188 338	0.524 814	143.0595	40.5481
21	H	2.125 348	1.061 544	1.164 765	30.1494	1.7155
22	C	1.285 503	-0.899 753	1.390 880	159.0823	24.5253
23	H	0.297 993	-0.623 384	1.770 601	31.1669	0.6980
24	H	1.176 069	-1.833 818	0.829 042	31.1894	0.6755
25	H	1.922 748	-1.108 988	2.255 882	31.0184	0.8465
26	C	3.285 571	-0.325 835	0.017 964	157.5125	26.0951
27	H	3.141 625	-1.163 610	-0.675 406	30.8893	0.9756
28	H	3.837 860	0.458 438	-0.509 075	30.9713	0.8936
29	H	3.905 242	-0.684 065	0.846 238	31.0509	0.8140

Fig. S7 201a – Conformer 7

SCF Energy - E(RM062X) -466.953 710 188
 SCF Energy from NMR - E(RB3LYP) -467.289 314 281
 Sum of Electronic and Thermal Free Energies -466.727 282 000

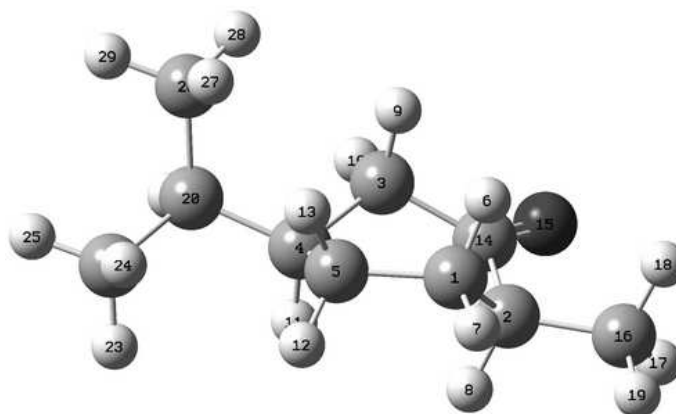
Table S7 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **201a** – Conformer 7

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	1.231 528	-1.460 191	0.482 700	152.1221	31.4855
2	C	1.945 435	-0.422 925	-0.395 703	136.2583	47.3493
3	C	0.000 966	1.035 835	0.455 611	136.6020	47.0056
4	C	-0.864 015	-0.083 460	-0.135 294	140.2733	43.3343
5	C	-0.293 029	-1.462 853	0.268 207	152.1140	31.4936
6	H	1.468 885	-1.237 905	1.531 263	30.4238	1.4411
7	H	1.643 741	-2.453 257	0.278 058	30.0601	1.8048
8	H	1.605 707	-0.562 609	-1.435 029	29.4187	2.4462
9	H	-0.000 145	0.964 298	1.554 808	29.8059	2.0590
10	H	-0.360 889	2.034 540	0.201 201	29.2667	2.5982
11	H	-0.811 900	0.006 980	-1.231 930	30.4572	1.4077
12	H	-0.551 669	-2.194 403	-0.504 176	29.6975	2.1674
13	H	-0.783 950	-1.797 004	1.191 237	30.5104	1.3545
14	C	1.449 598	0.952 364	0.014 336	-48.5747	232.1823
15	O	2.170 062	1.936 077	0.017 219	—	—
16	C	3.464 204	-0.529 627	-0.344 579	167.6816	15.9260
17	H	3.937 226	0.231 549	-0.968 269	30.2190	1.6459
18	H	3.821 485	-0.394 560	0.681 770	31.3312	0.5337

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Table S7 – continued from previous page

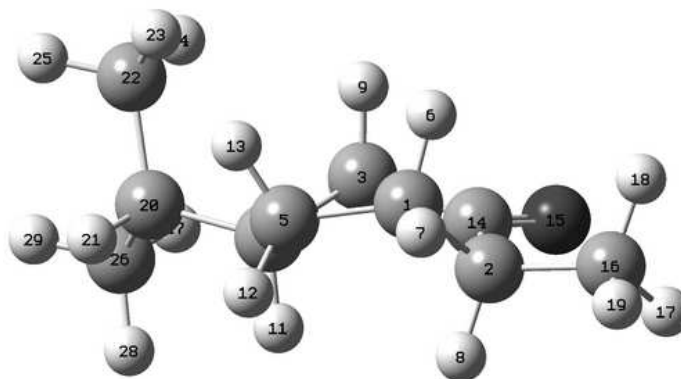
Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
19	H	3.783 313	-1.515 870	-0.692 517	31.1850	0.6799
20	C	-2.349 512	0.049 374	0.248 985	142.0973	41.5103
21	H	-2.411 492	-0.031 855	1.345 481	30.6751	1.1898
22	C	-2.943 002	1.397 516	-0.170 554	160.7544	22.8532
23	H	-2.489 049	2.238 963	0.358 648	30.5190	1.3459
24	H	-2.804 210	1.556 987	-1.247 201	31.4079	0.4570
25	H	-4.017 851	1.420 290	0.034 290	31.0065	0.8584
26	C	-3.176 994	-1.084 498	-0.365 112	161.1760	22.4316
27	H	-3.092 711	-1.064 026	-1.459 062	31.3815	0.4834
28	H	-2.853 370	-2.069 683	-0.019 143	30.4460	1.4189
29	H	-4.234 704	-0.970 259	-0.108 763	30.9909	0.8740

Fig. S8 201a – Conformer 8

SCF Energy - E(RM062X) -466.953 455 609
SCF Energy from NMR - E(RB3LYP) -467.288 701 398
Sum of Electronic and Thermal Free Energies -466.726 233 000

Table S8 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **201a** – Conformer 8

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	1.026 231	-1.371 230	0.653 581	152.2754	31.3322
2	C	1.931 206	-0.540 525	-0.267 892	136.4702	47.1374
3	C	0.054 994	1.170 622	0.130 361	134.7346	48.8730
4	C	-0.833 922	0.045 376	-0.410 587	143.3979	40.2097
5	C	-0.458 634	-1.300 292	0.248 415	160.8053	22.8023
6	H	1.157 574	-1.003 469	1.679 549	30.4432	1.4217
7	H	1.368 450	-2.410 895	0.653 931	30.0427	1.8222
8	H	1.719 255	-0.831 207	-1.310 043	29.4053	2.4596
9	H	-0.031 396	1.229 844	1.225 656	29.4193	2.4456
10	H	-0.223 296	2.151 300	-0.268 622	29.8239	2.0410
11	H	-0.615 693	-0.041 399	-1.485 086	29.7943	2.0706
12	H	-0.688 055	-2.111 551	-0.450 754	30.1663	1.6986
13	H	-1.077 809	-1.471 524	1.136 411	30.2896	1.5753
14	C	1.518 404	0.920 257	-0.166 373	-49.3697	232.9773
15	O	2.313 179	1.835 611	-0.297 058	—	—
16	C	3.416 960	-0.736 481	0.010 471	167.6090	15.9986
17	H	4.028 174	-0.120 987	-0.652 377	30.1524	1.7125
18	H	3.651 392	-0.457 024	1.043 166	31.3491	0.5158
19	H	3.691 615	-1.785 175	-0.131 895	31.1662	0.6987
20	C	-2.334 098	0.388 794	-0.313 981	146.7238	36.8838
21	H	-2.486 715	1.279 009	-0.940 821	30.1533	1.7116
22	C	-3.192 510	-0.740 259	-0.890 005	161.1179	22.4897
23	H	-2.855 379	-1.024 139	-1.893 011	30.9803	0.8846
24	H	-3.147 864	-1.630 947	-0.253 178	30.9616	0.9033
25	H	-4.240 591	-0.432 706	-0.957 184	30.8745	0.9904
26	C	-2.793 215	0.743 132	1.103 157	168.4562	15.1514
27	H	-2.625 792	-0.086 223	1.799 520	31.1438	0.7211
28	H	-2.275 879	1.624 682	1.493 130	30.9977	0.8672
29	H	-3.865 916	0.961 156	1.105 185	31.2097	0.6552

Fig. S9 201a – Conformer 9

SCF Energy - E(RM062X) -466.953 313 023
 SCF Energy from NMR - E(RB3LYP) -467.288 955 672
 Sum of Electronic and Thermal Free Energies -466.726 162 000

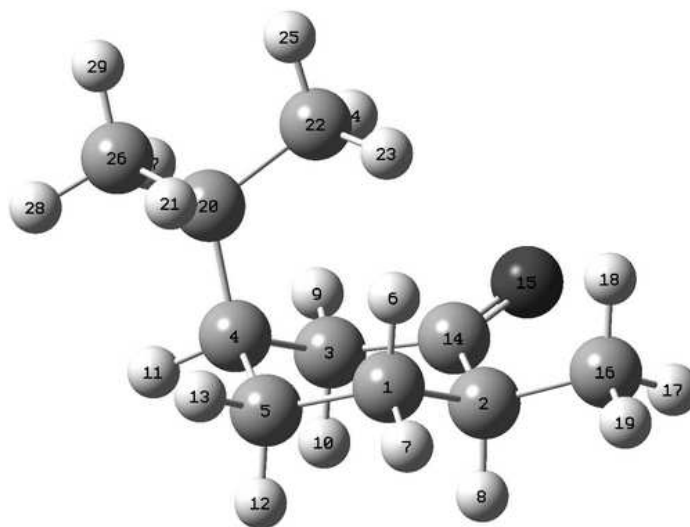
Table S9 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **201a** – Conformer 9

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	1.296 870	-1.510 475	0.187 298	151.9584	31.6492
2	C	1.991 984	-0.271 688	-0.395 861	136.2841	47.3235
3	C	-0.168 981	0.832 015	0.463 525	141.5454	42.0622
4	C	-0.839 728	-0.216 678	-0.432 209	142.6075	41.0001
5	C	-0.185 688	-1.599 011	-0.218 790	153.9736	29.6340
6	H	1.389 239	-1.468 696	1.280 514	30.3781	1.4868
7	H	1.832 733	-2.409 735	-0.132 427	30.0514	1.8135
8	H	1.808 301	-0.255 989	-1.482 787	29.4050	2.4599
9	H	-0.229 302	0.521 082	1.517 471	29.7422	2.1227
10	H	-0.633 628	1.819 505	0.392 016	29.6622	2.2027
11	H	-0.649 057	0.084 075	-1.472 429	29.9127	1.9522
12	H	-0.285 494	-2.173 632	-1.146 571	30.0357	1.8292
13	H	-0.734 624	-2.154 040	0.550 476	30.1956	1.6693
14	C	1.305 179	0.973 667	0.145 185	-49.3624	232.9700
15	O	1.902 761	2.020 157	0.330 240	—	—
16	C	3.495 456	-0.250 773	-0.145 160	167.4931	16.1145
17	H	3.955 018	0.645 972	-0.565 367	30.1527	1.7122

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Table S9 – continued from previous page

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
18	H	3.702 797	-0.265 259	0.930 119	31.3445	0.5204
19	H	3.964 204	-1.129 368	-0.596 765	31.1711	0.6938
20	C	-2.372 610	-0.273 128	-0.270 023	147.0947	36.5129
21	H	-2.701 149	-1.183 705	-0.792 342	30.2888	1.5761
22	C	-2.816 579	-0.380 738	1.191 744	166.8357	16.7719
23	H	-2.303 388	-1.187 693	1.724 664	30.7613	1.1036
24	H	-2.621 456	0.555 433	1.727 021	31.4373	0.4276
25	H	-3.892 106	-0.574 407	1.248 266	31.0640	0.8009
26	C	-3.058 171	0.919 574	-0.941 384	160.4789	23.1287
27	H	-2.773 345	1.861 354	-0.458 677	30.9336	0.9313
28	H	-2.790 336	0.986 918	-2.000 722	31.0167	0.8482
29	H	-4.146 886	0.830 339	-0.870 327	30.8848	0.9801

Fig. S10 201a – Conformer 10

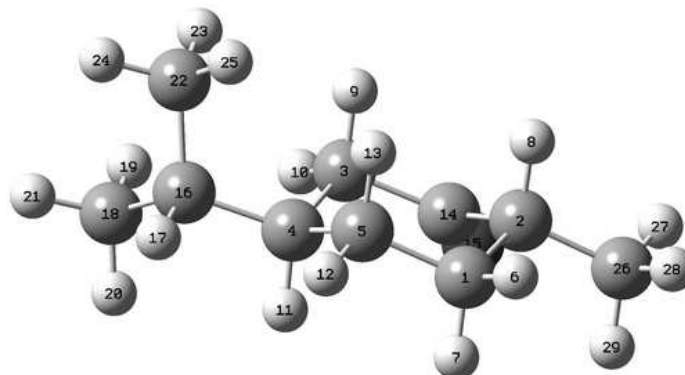
SCF Energy - E(RM062X) -466.954 233 138
SCF Energy from NMR - E(RB3LYP) -467.287 425 809
Sum of Electronic and Thermal Free Energies -466.725 564 000

Table S10 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **201a** – Conformer 10

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	-1.067 873	1.457 736	0.511 627	146.2731	37.3345
2	C	-1.891 108	0.340 785	-0.156 833	132.2590	51.3486
3	C	0.265 807	-0.433 855	-1.348 492	137.4884	46.1192
4	C	1.075 398	0.687 927	-0.667 613	135.0751	48.5325
5	C	0.143 409	1.861 077	-0.327 741	145.3729	38.2347
6	H	-0.753 717	1.132 192	1.510 298	30.0260	1.8389
7	H	-1.723 164	2.322 689	0.663 303	29.8992	1.9657
8	H	-2.285 593	0.759 210	-1.097 984	29.4018	2.4631
9	H	0.857 699	-1.340 018	-1.507 943	29.3388	2.5261
10	H	-0.059 201	-0.073 909	-2.335 040	29.4490	2.4159
11	H	1.785 924	1.062 090	-1.415 662	29.7914	2.0735
12	H	-0.216 171	2.300 123	-1.268 615	29.7328	2.1321
13	H	0.714 327	2.641 922	0.187 347	30.0611	1.8038
14	C	-1.002 871	-0.808 677	-0.608 696	-47.6969	231.3045
15	O	-1.323 086	-1.973 671	-0.441 114	—	—
16	C	-3.048 757	-0.130 780	0.713 098	166.8276	16.7800
17	H	-3.662 022	-0.872 807	0.197 442	30.3557	1.5092
18	H	-2.671 211	-0.588 550	1.633 553	31.0766	0.7883
19	H	-3.681 525	0.718 535	0.986 118	31.2293	0.6356
20	C	1.933 665	0.188 338	0.524 814	143.0595	40.5481
21	H	2.125 347	1.061 544	1.164 765	30.1494	1.7155
22	C	1.285 503	-0.899 753	1.390 880	159.0823	24.5253
23	H	0.297 993	-0.623 385	1.770 601	31.1669	0.6980
24	H	1.176 069	-1.833 818	0.829 042	31.1894	0.6755
25	H	1.922 748	-1.108 988	2.255 882	31.0184	0.8465
26	C	3.285 571	-0.325 835	0.017 964	157.5125	26.0951
27	H	3.141 625	-1.163 610	-0.675 406	30.8893	0.9756
28	H	3.837 861	0.458 438	-0.509 074	30.9713	0.8936
29	H	3.905 242	-0.684 065	0.846 238	31.0509	0.8140

S-I.2 *trans*-Carvomenthone (201b)

Fig. S11 201b – Conformer 1



SCF Energy - E(RM062X) -466.958 742 037
 SCF Energy from NMR - E(RB3LYP) -467.294 925 758
 Sum of Electronic and Thermal Free Energies -466.731 688 000

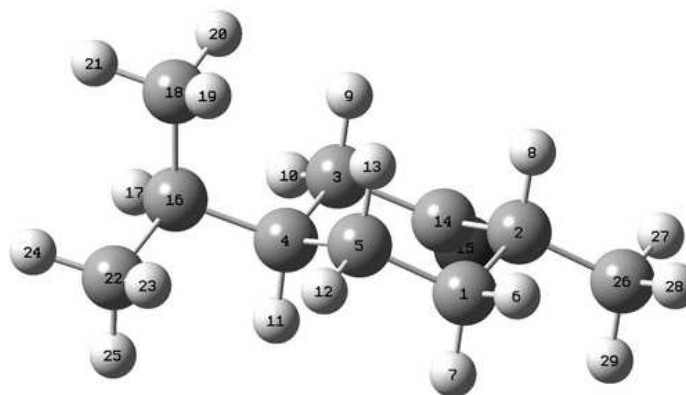
Table S11 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **201b** – Conformer 1

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	1.349 734	-1.413 211	-0.543 057	142.5474	41.0602
2	C	2.040 902	-0.366 200	0.353 530	132.3439	51.2637
3	C	-0.202 526	0.872 719	0.484 908	137.6391	45.9685
4	C	-0.852 544	-0.176 471	-0.440 836	130.1289	53.4787
5	C	-0.147 725	-1.524 219	-0.254 736	147.0047	36.6029
6	H	1.844 495	-2.379 401	-0.397 047	29.7406	2.1243
7	H	1.503 029	-1.130 495	-1.593 787	30.5210	1.3439
8	H	1.907 593	-0.692 481	1.396 784	29.3767	2.4882
9	H	-0.350 857	0.571 287	1.531 060	29.6724	2.1925
10	H	-0.627 216	1.869 712	0.344 799	29.6302	2.2347
11	H	-0.667 394	0.145 127	-1.477 897	30.1341	1.7308
12	H	-0.601 710	-2.270 210	-0.917 536	30.2779	1.5870
13	H	-0.289 232	-1.879 104	0.775 149	30.0001	1.8648
14	C	1.287 467	0.947 001	0.237 120	-47.3047	230.9123
15	O	1.840 402	1.992 941	-0.059 911	—	—

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Table S11 – continued from previous page

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
16	C	-2.383 485	-0.265 760	-0.277 992	145.0583	38.5493
17	H	-2.705 632	-1.083 645	-0.938 594	30.1447	1.7202
18	C	-3.080 296	1.011 890	-0.753 540	160.4320	23.1756
19	H	-2.861 100	1.854 724	-0.088 947	30.9653	0.8996
20	H	-2.762 585	1.285 739	-1.765 042	31.0323	0.8326
21	H	-4.166 293	0.875 662	-0.762 902	30.8652	0.9997
22	C	-2.830 505	-0.611 796	1.145 078	167.1825	16.4251
23	H	-2.593 110	0.200 542	1.841 176	31.3204	0.5445
24	H	-3.914 911	-0.757 832	1.172 168	31.0485	0.8164
25	H	-2.361 957	-1.528 073	1.516 258	30.6946	1.1703
26	C	3.523 708	-0.219 352	0.043 327	167.1575	16.4501
27	H	3.996 633	0.516 084	0.698 454	30.5762	1.2887
28	H	4.030 661	-1.179 838	0.172 283	31.2203	0.6446
29	H	3.667 986	0.111 077	-0.989 921	31.0515	0.8134

Fig. S12 201b – Conformer 2

SCF Energy - E(RM062X) -466.958 696 298

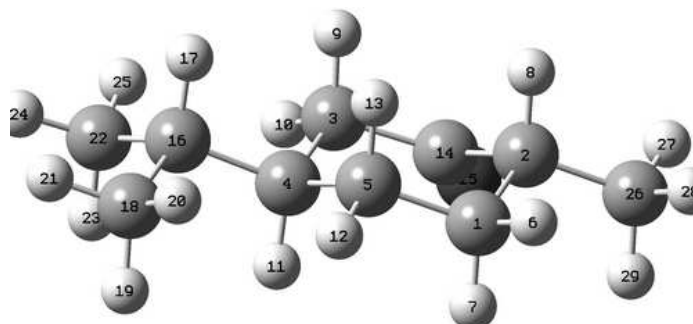
SCF Energy from NMR - E(RB3LYP) -467.294 939 888

Sum of Electronic and Thermal Free Energies -466.731 445 000

Table S12 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **201b** – Conformer 2

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	1.070 206	-1.510 199	-0.134 644	142.5389	41.0687
2	C	1.997 068	-0.418 154	0.436 980	132.1375	51.4701
3	C	0.036 630	1.221 656	0.230 094	130.0821	53.5255
4	C	-0.852 496	0.110 557	-0.364 412	130.2084	53.3992
5	C	-0.402 716	-1.248 204	0.183 326	154.8504	28.7572
6	H	1.384 564	-2.479 379	0.267 310	29.7329	2.1320
7	H	1.210 687	-1.554 635	-1.223 583	30.6179	1.2470
8	H	1.865 119	-0.420 859	1.530 250	29.4019	2.4630
9	H	-0.105 113	1.258 617	1.318 840	29.2819	2.5830
10	H	-0.214 049	2.201 045	-0.186 892	29.8123	2.0526
11	H	-0.672 771	0.103 336	-1.451 068	30.1546	1.7103
12	H	-1.017 424	-2.051 149	-0.237 542	30.0668	1.7981
13	H	-0.543 798	-1.270 183	1.272 717	30.4201	1.4448
14	C	1.498 036	0.937 477	-0.031 359	-46.7583	230.3659
15	O	2.218 612	1.737 916	-0.604 289	—	—
16	C	-2.351 547	0.417 422	-0.170 198	144.9460	38.6616
17	H	-2.498 593	1.453 127	-0.508 295	30.3529	1.5120
18	C	-2.809 641	0.331 468	1.288 628	167.0181	16.5895
19	H	-2.767 913	-0.700 864	1.653 008	31.2315	0.6334
20	H	-2.201 353	0.952 110	1.953 900	30.7517	1.1132
21	H	-3.846 770	0.669 691	1.376 963	31.0545	0.8104
22	C	-3.224 698	-0.481 773	-1.049 769	160.1269	23.4807
23	H	-3.165 888	-1.527 580	-0.728 767	30.8518	1.0131
24	H	-4.274 235	-0.177 359	-0.987 272	30.8107	1.0542
25	H	-2.917 659	-0.430 032	-2.099 544	30.9745	0.8904
26	C	3.460 388	-0.655 633	0.091 781	167.2123	16.3953
27	H	4.102 648	0.115 324	0.524 326	30.5790	1.2859
28	H	3.781 431	-1.630 218	0.470 336	31.2195	0.6454
29	H	3.604 838	-0.642 021	-0.992 936	31.0394	0.8255

Fig. S13 201b – Conformer 3



SCF Energy - E(RM062X) -466.958 737 191
SCF Energy from NMR - E(RB3LYP) -467.294 947 024
Sum of Electronic and Thermal Free Energies -466.731 747 000

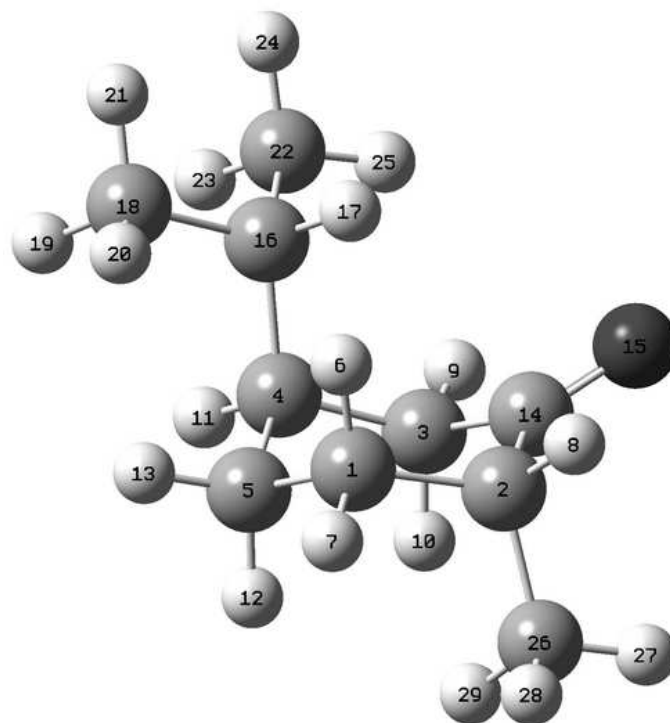
Table S13 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **201b** – Conformer 3

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	1.232 523	-1.494 193	-0.246 662	142.8533	40.7543
2	C	2.083 401	-0.377 359	0.386 546	132.7970	50.8106
3	C	-0.036 886	1.069 566	0.412 465	131.3684	52.2392
4	C	-0.883 714	-0.082 298	-0.170 358	128.3371	55.2705
5	C	-0.233 654	-1.427 035	0.180 032	148.1897	35.4179
6	H	1.665 067	-2.463 206	0.024 951	29.7647	2.1002
7	H	1.302 037	-1.409 600	-1.340 280	30.5873	1.2776
8	H	2.006 435	-0.487 268	1.479 421	29.3753	2.4896
9	H	-0.116 741	1.037 331	1.509 789	29.8346	2.0303
10	H	-0.383 385	2.046 494	0.070 811	29.2541	2.6108
11	H	-0.882 767	0.021 983	-1.267 995	30.6002	1.2647
12	H	-0.779 078	-2.244 486	-0.299 773	29.6883	2.1766
13	H	-0.307 915	-1.584 812	1.266 777	30.5451	1.3198
14	C	1.427 517	0.947 662	0.054 081	-46.5522	230.1598
15	O	2.030 720	1.858 353	-0.489 192	—	—
16	C	-2.348 666	0.007 270	0.302 207	142.3173	41.2903
17	H	-2.344 577	-0.109 192	1.397 228	30.5551	1.3098
18	C	-3.204 916	-1.113 275	-0.297 112	160.4951	23.1125
19	H	-3.151 036	-1.089 296	-1.392 772	31.3425	0.5224

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Table S13 – continued from previous page

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
20	H	-2.889 960	-2.104 745	0.036 981	30.4074	1.4575
21	H	-4.253 411	-0.985 147	-0.011 252	30.9865	0.8784
22	C	-2.978 352	1.363 219	-0.033 757	160.8729	22.7347
23	H	-2.901 430	1.563 552	-1.109 771	31.3836	0.4813
24	H	-4.039 755	1.366 047	0.232 364	31.0355	0.8294
25	H	-2.502 304	2.189 558	0.499 734	30.5662	1.2987
26	C	3.542 766	-0.435 851	-0.041 170	167.3265	16.2811
27	H	4.124 549	0.366 729	0.418 494	30.5794	1.2855
28	H	3.980 265	-1.395 461	0.248 448	31.2165	0.6484
29	H	3.628 134	-0.331 549	-1.127 257	31.0653	0.7996

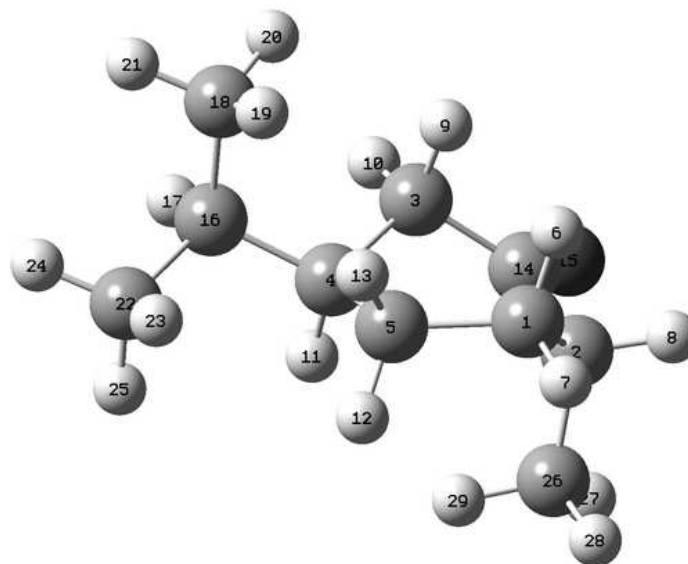
Fig. S14 201b – Conformer 4

SCF Energy - E(RM062X) -466.955 461 680
SCF Energy from NMR - E(RB3LYP) -467.289 083 772
Sum of Electronic and Thermal Free Energies -466.727 051 000

Table S14 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **201b** – Conformer 4

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	-0.893 936	-1.436 626	-0.634 939	150.9879	32.6197
2	C	-1.844 048	-0.221 613	-0.612 828	130.9046	52.7030
3	C	-0.222 521	0.916 524	1.041 548	137.2696	46.3380
4	C	0.782 858	-0.239 846	0.850 592	131.9194	51.6882
5	C	-0.023 445	-1.528 884	0.622 084	156.7503	26.8573
6	H	-0.249 535	-1.372 788	-1.519 681	29.7687	2.0962
7	H	-1.493 482	-2.346 859	-0.749 928	30.3031	1.5618
8	H	-2.222 428	-0.026 281	-1.621 403	29.4258	2.4391
9	H	0.258 047	1.879 261	1.223 737	29.4282	2.4367
10	H	-0.858 010	0.690 165	1.907 887	29.0433	2.8216
11	H	1.354 894	-0.348 459	1.783 123	30.2662	1.5987
12	H	-0.655 841	-1.702 335	1.501 912	29.8465	2.0184
13	H	0.642 106	-2.393 980	0.549 722	30.0462	1.8187
14	C	-1.120 840	1.039 450	-0.169 574	-49.7469	233.3545
15	O	-1.277 319	2.101 026	-0.751 786	—	—
16	C	1.799 238	0.066 858	-0.272 269	150.4728	33.1348
17	H	1.245 258	0.316 575	-1.189 957	30.4278	1.4371
18	C	2.691 747	-1.140 869	-0.571 881	161.5309	22.0767
19	H	3.183 015	-1.489 893	0.345 256	31.3818	0.4831
20	H	2.130 079	-1.978 646	-0.994 454	30.5764	1.2885
21	H	3.472 809	-0.869 076	-1.288 354	31.0464	0.8185
22	C	2.672 577	1.274 964	0.082 679	161.0573	22.5503
23	H	3.205 725	1.095 561	1.024 580	31.4690	0.3959
24	H	3.419 577	1.446 905	-0.698 171	31.0027	0.8622
25	H	2.091 144	2.194 147	0.189 179	30.4076	1.4573
26	C	-3.048 210	-0.454 066	0.317 492	162.6137	20.9939
27	H	-3.694 107	0.427 927	0.351 633	30.8504	1.0145
28	H	-3.637 069	-1.296 307	-0.056 773	30.8007	1.0642
29	H	-2.734 152	-0.689 472	1.338 556	30.2932	1.5717

Fig. S15 201b – Conformer 5



SCF Energy - E(RM062X) -466.952 104 799
SCF Energy from NMR - E(RB3LYP) -467.286 751 340
Sum of Electronic and Thermal Free Energies -466.724 302 000

Table S15 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for 201b – Conformer 5

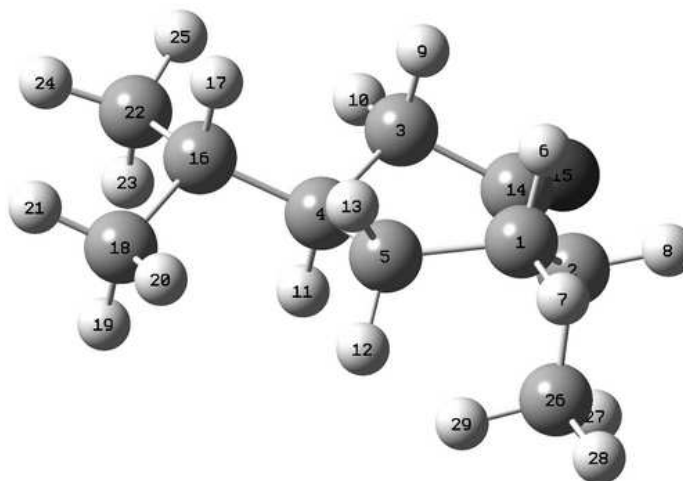
Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	1.001 648	-1.096 008	1.243 359	154.2702	29.3374
2	C	2.083 027	-0.413 510	0.399 669	134.7689	48.8387
3	C	0.146 973	1.259 034	0.105 407	134.0390	49.5686
4	C	-0.671 436	0.040 361	-0.353 862	144.2059	39.4017
5	C	-0.348 908	-1.202 406	0.511 370	164.0290	19.5786
6	H	0.869 394	-0.524 229	2.169 387	29.9579	1.9070
7	H	1.345 983	-2.091 958	1.541 747	30.1704	1.6945
8	H	2.986 509	-0.264 267	1.002 937	29.5251	2.3398
9	H	-0.052 047	1.472 110	1.165 343	29.1997	2.6652
10	H	-0.097 212	2.157 601	-0.468 831	29.9413	1.9236
11	H	-0.352 227	-0.176 055	-1.383 479	29.8132	2.0517
12	H	-0.360 577	-2.093 123	-0.126 034	30.1972	1.6677

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Table S15 – continued from previous page

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
13	H	-1.133 316	-1.355 143	1.260 899	30.3219	1.5430
14	C	1.624 187	0.974 553	-0.025 983	-51.0793	234.6869
15	O	2.412 173	1.794 228	-0.468 338	—	—
16	C	-2.177 979	0.358 464	-0.445 608	146.0257	37.5819
17	H	-2.277 280	1.169 985	-1.180 437	30.1780	1.6869
18	C	-2.779 958	0.855 013	0.871 284	168.7446	14.8630
19	H	-2.672 212	0.110 808	1.668 441	31.1118	0.7531
20	H	-2.313 879	1.785 303	1.209 206	30.9726	0.8923
21	H	-3.850 051	1.047 661	0.745 269	31.1952	0.6697
22	C	-2.957 744	-0.847 601	-0.975 688	161.1378	22.4698
23	H	-2.954 666	-1.668 394	-0.249 732	30.9353	0.9296
24	H	-4.001 016	-0.578 742	-1.167 890	30.8847	0.9802
25	H	-2.524 054	-1.220 658	-1.909 938	31.0009	0.8640
26	C	2.474 229	-1.229 574	-0.843 139	163.4837	20.1239
27	H	3.246 481	-0.710 779	-1.416 244	30.5298	1.3351
28	H	2.863 452	-2.204 431	-0.535 265	30.8673	0.9976
29	H	1.615 096	-1.399 482	-1.499 520	30.6629	1.2020

Fig. S16 201b – Conformer 6

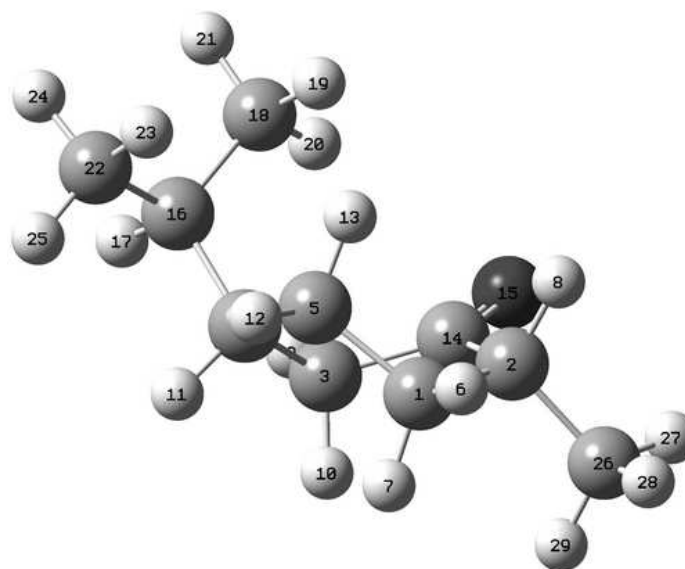


SCF Energy - E(RM062X) -466.952 169 912
 SCF Energy from NMR - E(RB3LYP) -467.287 082 314
 Sum of Electronic and Thermal Free Energies -466.724 397 000

Table S16 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **201b** – Conformer 6

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	-1.281 844	-1.347 021	-0.966 600	154.4547	29.1529
2	C	-2.166 654	-0.389 752	-0.165 233	134.9143	48.6933
3	C	-0.089 338	1.102 828	-0.526 719	136.1630	47.4446
4	C	0.717 031	-0.064 906	0.067 223	141.1892	42.4184
5	C	0.154 447	-1.425 126	-0.420 991	155.4493	28.1583
6	H	-1.258 777	-1.008 776	-2.009 148	29.8891	1.9758
7	H	-1.733 181	-2.344 875	-0.974 780	30.1995	1.6654
8	H	-3.149 157	-0.297 224	-0.642 706	29.5214	2.3435
9	H	-0.011 737	1.083 719	-1.624 844	29.6049	2.2600
10	H	0.268 290	2.076 249	-0.186 453	29.4009	2.4640
11	H	0.601 366	-0.008 040	1.160 884	30.4916	1.3733
12	H	0.202 728	-2.150 572	0.397 968	29.7417	2.1232
13	H	0.801 037	-1.817 189	-1.215 591	30.4955	1.3694
14	C	-1.556 198	1.001 789	-0.169 212	-50.4127	234.0203
15	O	-2.217 947	1.984 915	0.121 133	—	—
16	C	2.226 988	0.052 763	-0.216 918	141.0417	42.5659
17	H	2.362 915	-0.047 610	-1.305 060	30.6114	1.2535
18	C	2.992 924	-1.080 307	0.473 679	160.9051	22.7025
19	H	2.862 740	-1.013 585	1.561 131	31.4021	0.4628
20	H	2.652 626	-2.068 556	0.152 851	30.4258	1.4391
21	H	4.063 706	-1.008 050	0.259 920	30.9624	0.9025
22	C	2.807 171	1.400 362	0.221 331	160.9586	22.6490
23	H	2.575 492	1.591 273	1.276 712	31.4209	0.4440
24	H	3.896 324	1.397 912	0.113 600	31.0140	0.8509
25	H	2.419 041	2.234 890	-0.367 908	30.5501	1.3148
26	C	-2.384 597	-0.849 217	1.285 775	163.9955	19.6121
27	H	-3.031 426	-0.147 461	1.817 874	30.6152	1.2497
28	H	-2.859 321	-1.834 819	1.291 653	30.8804	0.9845
29	H	-1.438 678	-0.925 087	1.830 813	30.6634	1.2015

Fig. S17 201b – Conformer 7



SCF Energy - E(RM062X) -466.953 089 581
 SCF Energy from NMR - E(RB3LYP) -467.287 211 393
 Sum of Electronic and Thermal Free Energies -466.725 333 000

Table S17 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **201b** – Conformer 7

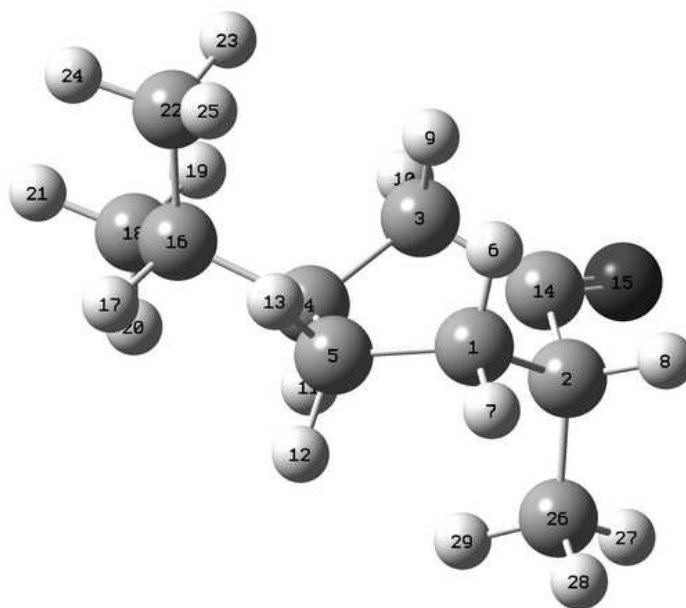
Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	-1.129 636	-1.619 720	-0.174 225	149.3055	34.3021
2	C	-1.877 989	-0.322 140	-0.499 184	131.5022	52.1054
3	C	-0.167 395	0.573 630	1.194 317	135.8610	47.7466
4	C	0.923 180	-0.430 129	0.735 022	138.7858	44.8218
5	C	0.376 707	-1.406 641	-0.328 933	158.3843	25.2233
6	H	-1.484 353	-2.415 219	-0.837 657	30.0669	1.7980
7	H	-1.361 541	-1.938 230	0.851 893	30.2923	1.5726
8	H	-1.849 365	-0.154 469	-1.584 306	29.8052	2.0597
9	H	0.265 789	1.505 446	1.567 833	29.9035	1.9614
10	H	-0.741 728	0.121 207	2.014 888	28.9461	2.9188
11	H	1.190 827	-1.026 021	1.617 147	29.4852	2.3797
12	H	0.914 005	-2.357 659	-0.265 170	30.2028	1.6621

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Table S17 – continued from previous page

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
13	H	0.561 346	-1.010 554	-1.336 935	30.7291	1.1358
14	C	-1.185 827	0.881 500	0.125 254	-52.5217	236.1293
15	O	-1.483 861	2.019 762	-0.197 923	—	—
16	C	2.209 138	0.297 666	0.291 049	143.1862	40.4214
17	H	2.571 006	0.845 810	1.172 702	30.1527	1.7122
18	C	1.972 417	1.324 836	-0.819 942	167.6185	15.9891
19	H	1.596 420	0.850 588	-1.733 577	31.3888	0.4761
20	H	1.254 972	2.094 704	-0.520 315	30.8847	0.9802
21	H	2.911 932	1.825 427	-1.074 838	31.2995	0.5654
22	C	3.295 211	-0.700 273	-0.116 871	161.2287	22.3789
23	H	3.023 975	-1.218 744	-1.043 383	31.0341	0.8308
24	H	4.245 477	-0.186 094	-0.290 981	30.9639	0.9010
25	H	3.453 846	-1.456 310	0.660 115	30.9799	0.8850
26	C	-3.342 451	-0.354 006	-0.044 323	162.6955	20.9121
27	H	-3.862 593	0.562 514	-0.332 076	30.4972	1.3677
28	H	-3.855 338	-1.206 400	-0.499 164	30.7767	1.0882
29	H	-3.403 920	-0.462 428	1.044 237	31.1107	0.7542

Fig. S18 201b – Conformer 8

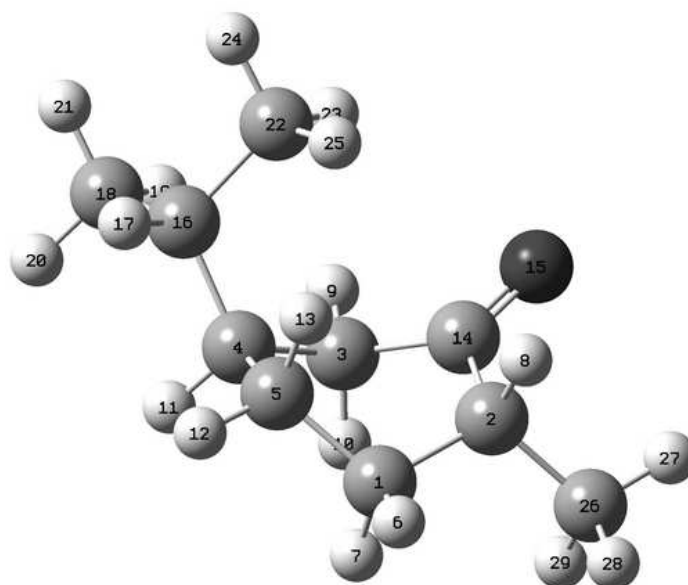


SCF Energy - E(RM062X) -466.951 917 684
 SCF Energy from NMR - E(RB3LYP) -467.286 782 118
 Sum of Electronic and Thermal Free Energies -466.724 125 000

Table S18 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **201b** – Conformer 8

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	-1.291 417	-1.510 044	-0.613 975	153.8449	29.7627
2	C	-2.149 708	-0.298 511	-0.236 785	134.8801	48.7275
3	C	0.125 379	0.851 543	-0.619 722	141.1419	42.4657
4	C	0.678 394	-0.174 537	0.386 027	143.5242	40.0834
5	C	0.029 829	-1.564 391	0.171 892	157.3139	26.2937
6	H	-1.074 726	-1.464 346	-1.687 762	29.8641	2.0008
7	H	-1.864 780	-2.429 050	-0.452 220	30.2009	1.6640
8	H	-3.023 848	-0.240 849	-0.896 429	29.5304	2.3345
9	H	0.307 781	0.505 174	-1.647 144	29.5079	2.3570
10	H	0.583 502	1.837 990	-0.512 343	29.7804	2.0845
11	H	0.391 774	0.181 857	1.385 458	29.9327	1.9322
12	H	-0.132 448	-2.028 770	1.150 895	29.9425	1.9224
13	H	0.726 213	-2.219 363	-0.363 751	30.3404	1.5245
14	C	-1.369 494	0.990 937	-0.452 892	-51.2074	234.8150
15	O	-1.930 105	2.074 510	-0.467 289	—	—
16	C	2.219 551	-0.254 708	0.381 074	146.1775	37.4301
17	H	2.477 902	-1.137 847	0.983 533	30.2554	1.6095
18	C	2.858 231	0.964 733	1.049 804	160.7440	22.8636
19	H	2.641 671	1.881 754	0.490 515	30.9447	0.9202
20	H	2.488 420	1.095 808	2.071 805	31.0246	0.8403
21	H	3.946 596	0.855 479	1.092 866	30.8944	0.9705
22	C	2.797 817	-0.453 552	-1.022 558	167.0340	16.5736
23	H	2.681 697	0.455 899	-1.622 846	31.4110	0.4539
24	H	3.867 573	-0.676 658	-0.965 901	31.0225	0.8424
25	H	2.311 797	-1.275 848	-1.558 383	30.7336	1.1313
26	C	-2.654 397	-0.354 425	1.214 215	163.6904	19.9172
27	H	-3.270 686	0.518 860	1.440 776	30.5317	1.3332
28	H	-3.257 982	-1.255 141	1.359 385	30.8787	0.9862
29	H	-1.824 712	-0.383 300	1.927 377	30.6481	1.2168

Fig. S19 201b – Conformer 9



SCF Energy - E(RM062X) -466.952 950 502
SCF Energy from NMR - E(RB3LYP) -467.287 345 108
Sum of Electronic and Thermal Free Energies -466.725 286 000

Table S19 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **201b** – Conformer 9

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	-1.450 621	1.543 053	0.114 296	149.1717	34.4359
2	C	-1.963 109	0.122 886	0.376 269	131.5161	52.0915
3	C	0.107 375	-0.414 220	-1.053 371	142.2883	41.3193
4	C	0.910 903	0.769 779	-0.453 568	138.4010	45.2066
5	C	0.031 416	1.634 243	0.475 991	151.6810	31.9266
6	H	-2.043 167	2.253 562	0.699 907	30.0912	1.7737
7	H	-1.598 998	1.804 539	-0.942 842	30.2391	1.6258
8	H	-2.025 973	-0.038 549	1.461 280	29.7778	2.0871
9	H	0.747 077	-1.248 584	-1.350 658	29.7025	2.1624
10	H	-0.413 908	-0.063 293	-1.955 085	29.3186	2.5463
11	H	1.215 128	1.399 894	-1.298 737	29.6260	2.2389

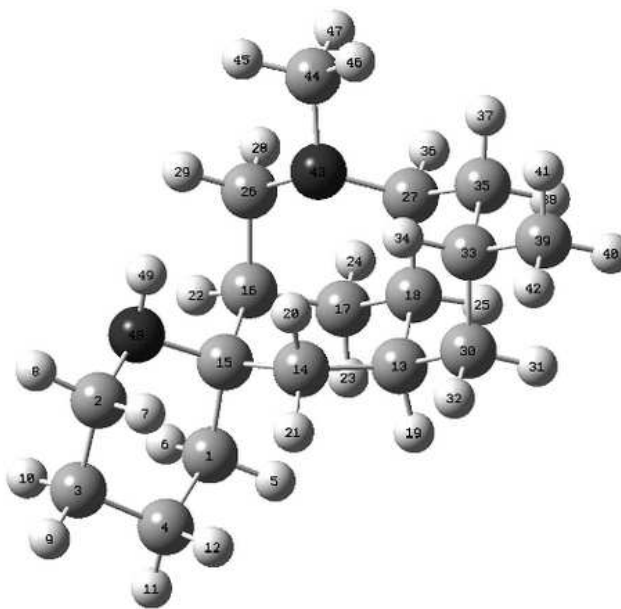
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Table S19 – continued from previous page

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
12	H	0.384 074	2.669 942	0.442 743	30.0154	1.8495
13	H	0.148 737	1.298 657	1.515 542	30.6355	1.2294
14	C	-0.981 774	-0.920 918	-0.140 656	-52.8652	236.4728
15	O	-1.112 918	-2.101 546	0.138 016	—	—
16	C	2.203 822	0.314 344	0.256 096	144.5982	39.0094
17	H	2.575 265	1.191 479	0.806 260	30.3175	1.5474
18	C	3.285 520	-0.096 329	-0.745 381	160.5258	23.0818
19	H	2.971 629	-0.967 947	-1.331 146	30.8959	0.9690
20	H	3.509 535	0.717 676	-1.442 464	31.0671	0.7978
21	H	4.211 167	-0.366 068	-0.227 051	30.9428	0.9221
22	C	1.961 883	-0.812 202	1.265 292	166.0253	17.5823
23	H	1.677 139	-1.739 273	0.755 121	31.3412	0.5237
24	H	2.873 788	-1.014 094	1.835 558	31.2173	0.6476
25	H	1.169 330	-0.568 978	1.980 962	31.0916	0.7733
26	C	-3.343 962	-0.132 138	-0.239 599	162.8704	20.7372
27	H	-3.700 865	-1.135 863	0.001 854	30.4652	1.3997
28	H	-4.063 388	0.598 078	0.142 007	30.7982	1.0667
29	H	-3.301 946	-0.029 791	-1.329 591	31.1301	0.7348

S-I.3 Nankakurine – Revised Diastereomer(202a)

Fig. S20 202a – Conformer 1



SCF Energy - E(RM062X) -775.099 413 763
 SCF Energy from NMR - E(RB3LYP) -775.608 465 248
 Sum of Electronic and Thermal Free Energies -774.683 062 000

Table S20 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **202a** – Conformer 1

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	2.645 924	-0.284 964	1.121 739	145.6803	38.1985
2	C	3.061 887	-0.314 747	-1.738 533	138.1991	45.6797
3	C	4.192 868	-0.744 373	-0.813 030	152.3163	31.5625
4	C	3.609 622	-1.293 585	0.487 818	158.2814	25.5974
5	H	2.179 934	-0.733 573	2.004 648	29.7536	2.1014
6	H	3.222 428	0.584 598	1.466 674	30.9379	0.9171
7	H	2.482 083	-1.204 262	-2.037 409	28.7647	3.0903
8	H	3.460 033	0.135 058	-2.653 243	29.1953	2.6597

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Table S20 – continued from previous page

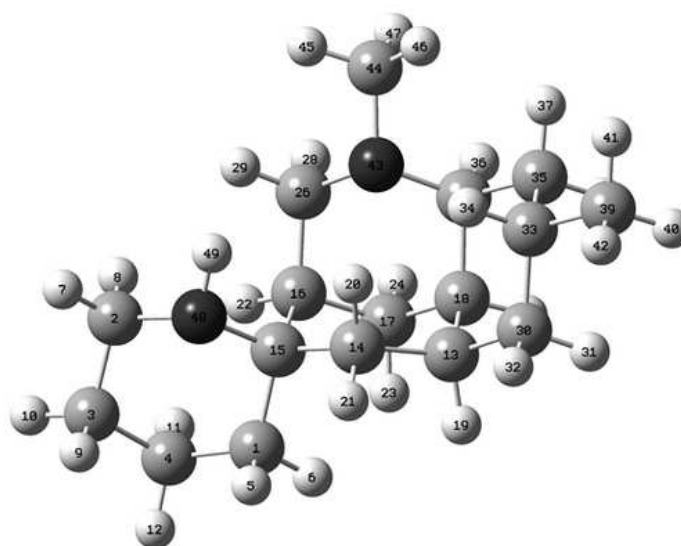
Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
9	H	4.817 200	-1.495 056	-1.309 066	30.3061	1.5489
10	H	4.826 006	0.126 259	-0.596 497	30.5419	1.3131
11	H	4.407 002	-1.530 092	1.200 573	30.3571	1.4979
12	H	3.088 045	-2.236 207	0.278 539	30.2190	1.6360
13	C	-0.540 580	-1.145 592	0.929 915	143.9137	39.9651
14	C	0.528 585	-0.902 319	-0.152 946	143.2553	40.6235
15	C	1.550 392	0.221 805	0.156 845	124.5810	59.2978
16	C	0.851 532	1.450 518	0.800 680	133.6760	50.2028
17	C	0.027 293	1.042 491	2.023 216	147.7008	36.1780
18	C	-1.109 706	0.152 585	1.532 850	140.8497	43.0291
19	H	-0.057 217	-1.683 382	1.759 072	30.1175	1.7375
20	H	0.034 879	-0.650 236	-1.095 222	30.0622	1.7928
21	H	1.056 471	-1.849 267	-0.318 437	29.5661	2.2889
22	H	1.648 183	2.146 325	1.095 154	30.7693	1.0857
23	H	0.631 687	0.517 402	2.770 335	29.9253	1.9297
24	H	-0.375 923	1.941 621	2.506 378	30.4385	1.4165
25	H	-1.749 305	-0.127 780	2.381 335	30.3971	1.4579
26	C	-0.086 446	2.231 626	-0.127 235	121.2219	62.6569
27	C	-2.015 491	0.916 314	0.549 213	113.5813	70.2975
28	H	-0.424 133	3.132 366	0.426 930	29.8436	2.0114
29	H	0.446 378	2.597 638	-1.011 354	28.8531	3.0019
30	C	-1.676 245	-2.030 980	0.395 150	138.2550	45.6238
31	H	-2.274 539	-2.393 781	1.244 793	30.6875	1.1675
32	H	-1.256 990	-2.917 557	-0.100 028	30.3609	1.4941
33	C	-2.623 346	-1.297 773	-0.565 200	156.7968	27.0820
34	H	-2.066 223	-1.014 811	-1.468 623	29.9263	1.9287
35	C	-3.143 840	-0.016 140	0.093 255	140.5753	43.3035
36	H	-2.466 640	1.767 252	1.104 586	29.9266	1.9284
37	H	-3.843 967	0.497 571	-0.574 314	29.7727	2.0823
38	H	-3.719 835	-0.292 135	0.988 647	31.0288	0.8262
39	C	-3.780 339	-2.203 913	-0.982 867	159.2459	24.6329
40	H	-4.373 272	-2.494 855	-0.106 965	31.3512	0.5038
41	H	-4.447 095	-1.695 357	-1.687 373	30.8820	0.9730
42	H	-3.413 599	-3.118 855	-1.460 210	30.8992	0.9558
43	N	-1.242 229	1.456 093	-0.582 487	—	—
44	C	-2.064 595	2.286 645	-1.451 361	138.6569	45.2219
45	H	-1.433 234	2.735 618	-2.223 064	29.7894	2.0656
46	H	-2.833 329	1.693 382	-1.950 341	29.0105	2.8445

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Table S20 – continued from previous page

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
47	H	-2.559 918	3.103 363	-0.892 348	30.5140	1.3410
48	N	2.230 050	0.694 822	-1.070 475	—	—
49	H	1.515 066	0.996 756	-1.729 488	30.5467	1.3083

Fig. S21 202a – Conformer 2



SCF Energy - E(RM062X) -775.100 103 338
 SCF Energy from NMR - E(RB3LYP) -775.608 650 973
 Sum of Electronic and Thermal Free Energies -774.683 317 000

Table S21 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **202a** – Conformer 2

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	2.436 785	-1.463 642	0.335 760	143.8831	39.9957
2	C	3.347 842	0.815 163	-1.194 158	138.6495	45.2293
3	C	4.362 162	-0.199 298	-0.671 990	152.0445	31.8343
4	C	3.834 867	-0.889 967	0.588 171	158.7253	25.1535

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Table S21 – continued from previous page

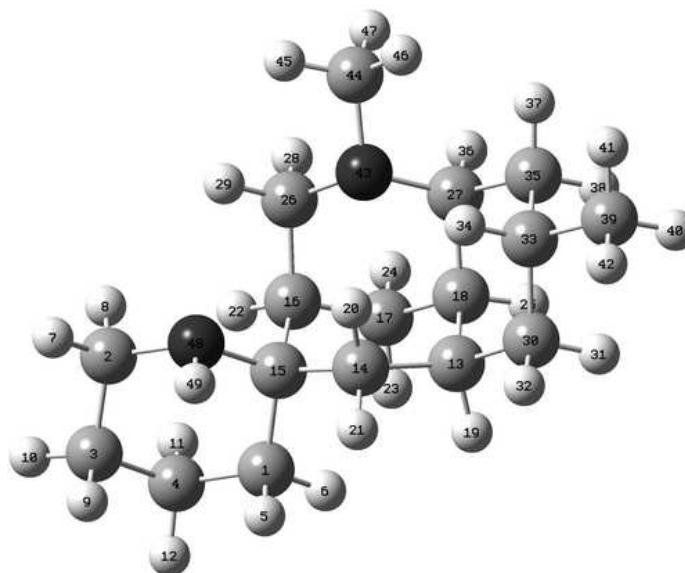
Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
5	H	2.517 451	-2.253 240	-0.423 130	30.8939	0.9611
6	H	2.044 026	-1.934 560	1.242 063	29.5917	2.2633
7	H	3.683 857	1.233 490	-2.147 971	29.2891	2.5659
8	H	3.271 957	1.653 911	-0.481 210	28.8450	3.0100
9	H	4.537 151	-0.952 804	-1.451 113	30.4388	1.4162
10	H	5.316 786	0.299 237	-0.473 118	30.2837	1.5713
11	H	3.811 408	-0.173 291	1.418 671	30.2860	1.5690
12	H	4.512 905	-1.695 019	0.891 609	30.4443	1.4107
13	C	-0.864 170	-1.474 087	0.429 833	144.3132	39.5656
14	C	0.145 710	-1.118 514	-0.675 380	132.8788	51.0000
15	C	1.437 946	-0.418 854	-0.207 682	124.0051	59.8737
16	C	1.127 296	0.657 679	0.879 662	148.9117	34.9671
17	C	0.309 197	0.064 695	2.029 323	147.3410	36.5378
18	C	-1.044 757	-0.348 908	1.466 351	140.9032	42.9756
19	H	-0.470 152	-2.341 556	0.979 800	29.9665	1.8885
20	H	-0.342 920	-0.462 403	-1.400 072	29.8296	2.0254
21	H	0.426 551	-2.036 459	-1.209 457	30.8017	1.0533
22	H	2.074 429	1.040 107	1.275 229	29.4513	2.4037
23	H	0.811 355	-0.791 728	2.491 734	30.0990	1.7560
24	H	0.178 137	0.823 974	2.811 333	30.3396	1.5154
25	H	-1.676 775	-0.739 991	2.275 884	30.3868	1.4682
26	C	0.359 565	1.878 373	0.362 737	121.6389	62.2399
27	C	-1.790 029	0.870 640	0.893 145	113.6116	70.2672
28	H	0.300 690	2.613 168	1.192 882	29.7802	2.0748
29	H	0.906 819	2.370 584	-0.449 834	28.8777	2.9773
30	C	-2.221 500	-1.870 588	-0.170 288	138.2905	45.5883
31	H	-2.830 663	-2.346 919	0.612 902	30.7196	1.1354
32	H	-2.076 641	-2.619 907	-0.960 513	30.4272	1.4278
33	C	-3.016 025	-0.679 061	-0.723 592	156.6151	27.2637
34	H	-2.469 807	-0.251 985	-1.575 498	29.9699	1.8851
35	C	-3.146 721	0.406 198	0.349 938	140.3431	43.5357
36	H	-1.972 091	1.574 576	1.734 304	29.9450	1.9100
37	H	-3.736 733	1.247 452	-0.029 365	29.7731	2.0819
38	H	-3.712 071	-0.007 465	1.197 858	31.0292	0.8258
39	C	-4.391 312	-1.126 565	-1.215 975	159.1578	24.7210
40	H	-4.976 257	-1.545 227	-0.387 746	31.3432	0.5118
41	H	-4.954 493	-0.286 009	-1.635 239	30.8937	0.9613
42	H	-4.302 700	-1.897 286	-1.989 063	30.9209	0.9341

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Table S21 – continued from previous page

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
43	N	-0.983 787	1.562 025	-0.127 741	—	—
44	C	-1.626 866	2.785 172	-0.587 218	138.5632	45.3156
45	H	-0.954 743	3.308 664	-1.272 801	29.7621	2.0929
46	H	-2.550 916	2.565 779	-1.125 750	29.0003	2.8547
47	H	-1.863 629	3.466 958	0.251 882	30.4825	1.3725
48	N	2.059 430	0.152 112	-1.422 053	—	—
49	H	1.407 621	0.808 380	-1.847 538	30.3482	1.5068

Fig. S22 202a – Conformer 3



SCF Energy - E(RM062X) -775.098 714 564

SCF Energy from NMR - E(RB3LYP) -775.607 445 851

Sum of Electronic and Thermal Free Energies -774.682 378 000

Table S22 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **202a** – Conformer 3

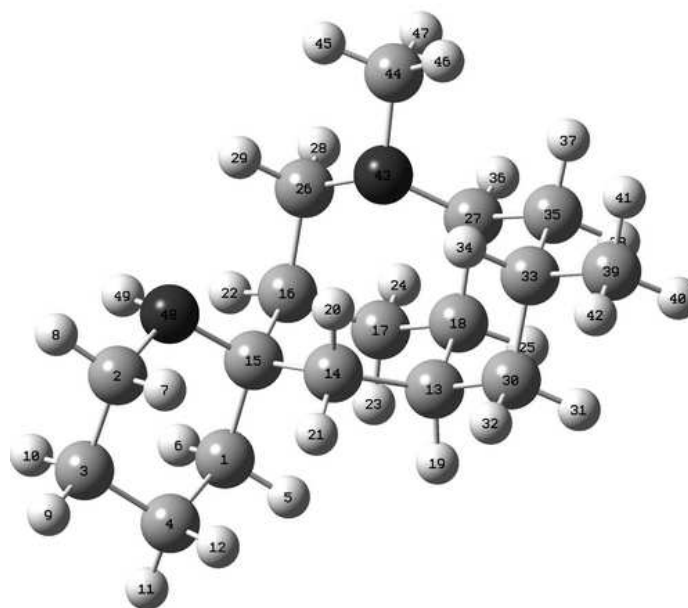
Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	2.427 184	-1.439 529	0.369 460	142.0715	41.8073
2	C	3.370 652	0.790 557	-1.204 556	137.7926	46.0862
3	C	4.371 559	-0.221 778	-0.641 539	150.1807	33.6981
4	C	3.824 501	-0.870 158	0.631 618	158.7501	25.1287
5	H	2.516 824	-2.238 460	-0.380 719	30.9575	0.8975
6	H	2.023 430	-1.906 295	1.273 903	29.4687	2.3863
7	H	3.720 345	1.178 797	-2.166 587	29.2229	2.6321
8	H	3.293 613	1.649 953	-0.526 064	29.0328	2.8222
9	H	4.544 823	-1.002 011	-1.396 021	30.5804	1.2746
10	H	5.333 295	0.268 517	-0.452 127	30.3446	1.5104
11	H	3.792 695	-0.129 119	1.440 557	30.1670	1.6880
12	H	4.491 690	-1.670 628	0.969 605	30.3860	1.4690
13	C	-0.851 891	-1.458 922	0.444 775	144.6802	39.1986
14	C	0.151 260	-1.106 597	-0.668 113	133.6128	50.2660
15	C	1.437 561	-0.395 052	-0.203 977	124.4472	59.4316
16	C	1.119 814	0.697 552	0.856 042	147.7643	36.1145
17	C	0.311 741	0.116 320	2.018 544	147.8452	36.0336
18	C	-1.039 753	-0.321 532	1.467 543	140.7315	43.1473
19	H	-0.448 311	-2.315 334	1.005 031	29.9749	1.8801
20	H	-0.334 944	-0.459 733	-1.400 461	29.6419	2.2131
21	H	0.436 094	-2.032 649	-1.188 767	30.8838	0.9712
22	H	2.064 019	1.096 587	1.243 054	29.6003	2.2547
23	H	0.823 948	-0.724 154	2.498 494	30.1023	1.7527
24	H	0.174 037	0.890 853	2.783 988	30.4089	1.4461
25	H	-1.663 301	-0.709 113	2.285 325	30.3693	1.4857
26	C	0.338 942	1.899 501	0.318 253	121.4644	62.4144
27	C	-1.800 683	0.882 239	0.881 445	113.8601	70.0187
28	H	0.279 383	2.651 226	1.133 653	29.9027	1.9523
29	H	0.878 847	2.363 745	-0.512 419	28.6473	3.2077
30	C	-2.207 538	-1.876 363	-0.144 305	138.2342	45.6446
31	H	-2.808 355	-2.348 473	0.647 929	30.7155	1.1395
32	H	-2.058 564	-2.634 801	-0.925 063	30.4309	1.4241
33	C	-3.016 763	-0.700 584	-0.709 382	156.5783	27.3005
34	H	-2.477 570	-0.277 835	-1.567 842	29.9480	1.9070
35	C	-3.155 148	0.396 139	0.351 480	140.2151	43.6637
36	H	-1.986 223	1.596 004	1.713 958	29.9365	1.9185

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Table S22 – continued from previous page

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
37	H	-3.756 062	1.226 105	-0.035 622	29.7704	2.0846
38	H	-3.712 135	-0.013 190	1.207 044	31.0306	0.8244
39	C	-4.388 742	-1.169 456	-1.190 947	159.1629	24.7159
40	H	-4.966 565	-1.582 741	-0.355 006	31.3432	0.5118
41	H	-4.962 285	-0.340 970	-1.620 054	30.8928	0.9622
42	H	-4.294 481	-1.950 028	-1.953 457	30.9258	0.9292
43	N	-1.006 415	1.563 446	-0.153 307	—	—
44	C	-1.661 752	2.770 464	-0.635 090	138.7943	45.0845
45	H	-0.997 600	3.283 907	-1.335 819	29.7841	2.0709
46	H	-2.587 035	2.532 496	-1.163 851	29.0189	2.8361
47	H	-1.899 934	3.469 423	0.189 801	30.5144	1.3406
48	N	2.022 770	0.242 895	-1.407 698	—	—
49	H	2.080 179	-0.473 257	-2.132 935	31.3822	0.4728

Fig. S23 202a – Conformer 4



SCF Energy - E(RM062X) -775.098 524 888
 SCF Energy from NMR - E(RB3LYP) -775.607 656 183
 Sum of Electronic and Thermal Free Energies -774.682 323 000

Table S23 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **202a** – Conformer 4

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	2.619 772	-0.312 170	1.125 398	144.1494	39.7294
2	C	3.094 781	-0.288 116	-1.730 957	137.4027	46.4761
3	C	4.199 376	-0.763 551	-0.787 745	150.4350	33.4438
4	C	3.580 236	-1.324 774	0.491 240	158.1751	25.7037
5	H	2.142 258	-0.767 199	1.999 422	29.6409	2.2141
6	H	3.202 961	0.546 794	1.489 599	31.0189	0.8361
7	H	2.502 112	-1.147 967	-2.067 897	29.0270	2.8280
8	H	3.521 587	0.174 974	-2.626 402	29.1156	2.7394
9	H	4.824 211	-1.515 067	-1.283 792	30.3854	1.4696
10	H	4.846 027	0.090 086	-0.539 916	30.6898	1.1652
11	H	4.359 030	-1.588 966	1.214 945	30.2962	1.5588
12	H	3.046 524	-2.254 525	0.255 529	30.0791	1.7759
13	C	-0.528 484	-1.145 721	0.896 736	144.5278	39.3510
14	C	0.523 258	-0.882 027	-0.198 207	144.7889	39.0899
15	C	1.548 052	0.222 355	0.140 632	124.2952	59.5836
16	C	0.845 532	1.449 996	0.779 978	133.7418	50.1370
17	C	0.033 002	1.039 822	2.009 478	147.9836	35.8952
18	C	-1.099 546	0.140 739	1.524 822	140.7997	43.0791
19	H	-0.030 909	-1.691 997	1.711 849	30.1130	1.7420
20	H	0.022 967	-0.592 862	-1.124 423	29.9063	1.9487
21	H	1.042 112	-1.828 140	-0.394 768	29.8387	2.0163
22	H	1.638 267	2.153 407	1.074 025	30.7665	1.0885
23	H	0.645 317	0.523 851	2.755 949	29.9376	1.9174
24	H	-0.377 012	1.936 983	2.490 615	30.4735	1.3815
25	H	-1.724 531	-0.155 812	2.378 677	30.3872	1.4678
26	C	-0.099 648	2.224 425	-0.146 676	121.6807	62.1981
27	C	-2.024 366	0.908 504	0.562 669	113.8320	70.0468
28	H	-0.421 530	3.135 691	0.400 595	29.9942	1.8608
29	H	0.427 602	2.557 730	-1.044 953	28.4934	3.3616
30	C	-1.665 799	-2.032 102	0.367 156	138.0600	45.8188
31	H	-2.248 223	-2.410 287	1.221 129	30.6902	1.1648
32	H	-1.247 419	-2.909 094	-0.145 505	30.3441	1.5109
33	C	-2.633 216	-1.294 721	-0.569 227	156.6910	27.1878
34	H	-2.091 475	-0.995 439	-1.476 690	29.8979	1.9571
35	C	-3.153 963	-0.026 158	0.113 978	140.3689	43.5099
36	H	-2.471 654	1.751 769	1.133 253	29.9293	1.9257

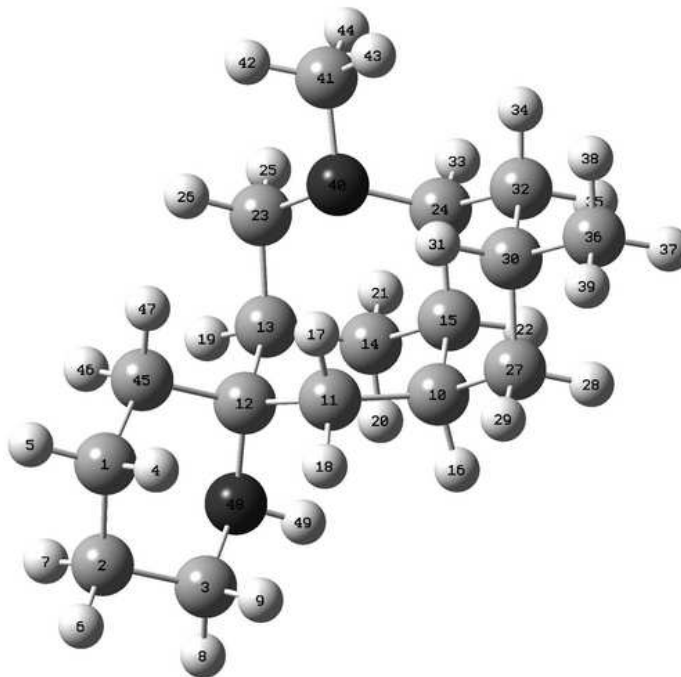
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Table S23 – continued from previous page

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
37	H	-3.868 227	0.490 493	-0.536 161	29.7739	2.0811
38	H	-3.713 750	-0.317 988	1.014 678	31.0399	0.8151
39	C	-3.789 067	-2.204 949	-0.981 067	159.2330	24.6458
40	H	-4.366 570	-2.511 893	-0.100 281	31.3527	0.5023
41	H	-4.470 337	-1.692 837	-1.668 944	30.8863	0.9687
42	H	-3.422 449	-3.110 711	-1.475 723	30.8963	0.9587
43	N	-1.270 914	1.457 147	-0.575 806	—	—
44	C	-2.105 087	2.295 691	-1.424 227	138.8344	45.0444
45	H	-1.486 553	2.743 927	-2.206 653	29.8152	2.0398
46	H	-2.887 815	1.709 864	-1.910 243	29.0309	2.8241
47	H	-2.584 119	3.113 690	-0.852 303	30.5616	1.2934
48	N	2.184 409	0.685 204	-1.114 859	—	—
49	H	2.728 131	1.521 614	-0.894 848	31.4332	0.4218

S-I.4 Nankakurine – Originally Proposed Diastereomer (202b)

Fig. S24 202b – Conformer 1



SCF Energy - E(RM062X) -775.099 320 833

SCF Energy from NMR - E(RB3LYP) -775.608 400 202

Sum of Electronic and Thermal Free Energies -774.683 058 000

Table S24 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **202b** – Conformer 1

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	3.223 133	-0.352 241	-1.729 853	158.6616	25.2172
2	C	4.221 783	-0.797 804	-0.662 242	152.0739	31.8049
3	C	3.474 683	-1.271 521	0.578 532	138.3552	45.5236
4	H	2.648 936	-1.221 314	-2.077 232	30.3233	1.5317
5	H	3.745 763	0.051 009	-2.603 809	30.3651	1.4899
6	H	4.864 703	-1.601 314	-1.036 975	30.2914	1.5636
7	H	4.868 256	0.047 173	-0.390 360	30.5565	1.2985

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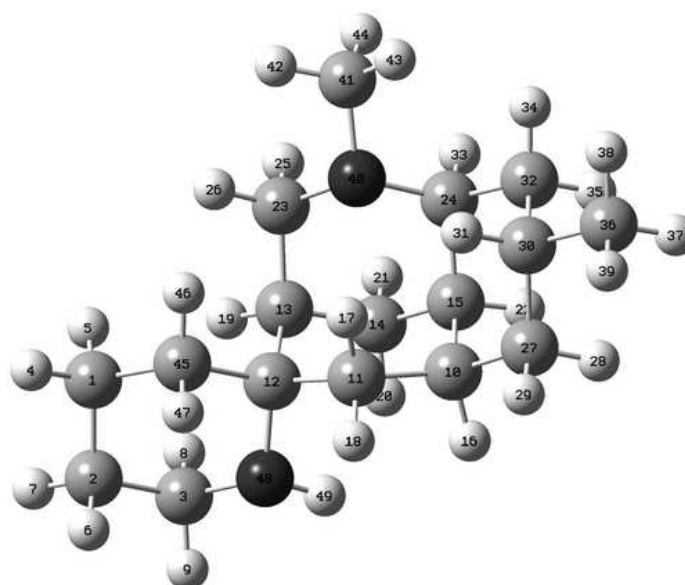
Table S24 – continued from previous page

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
8	H	4.177 121	-1.514 718	1.381 848	29.1765	2.6785
9	H	2.929 932	-2.198 988	0.335 254	28.7866	3.0684
10	C	-0.511 629	-1.154 535	0.875 633	145.6992	38.1796
11	C	0.524 006	-0.863 308	-0.226 068	149.0196	34.8592
12	C	1.547 980	0.246 739	0.114 225	124.3013	59.5775
13	C	0.844 653	1.456 789	0.786 871	133.6557	50.2231
14	C	0.040 286	1.019 210	2.013 626	148.7503	35.1285
15	C	-1.088 765	0.120 247	1.521 802	141.2419	42.6369
16	H	0.000 317	-1.705 122	1.680 121	30.0884	1.7666
17	H	0.002 526	-0.570 496	-1.139 964	30.0334	1.8216
18	H	1.052 838	-1.797 085	-0.450 886	29.6615	2.1935
19	H	1.640 733	2.151 158	1.085 262	30.7133	1.1417
20	H	0.656 301	0.496 639	2.754 402	30.0714	1.7836
21	H	-0.370 659	1.905 071	2.514 499	30.4872	1.3678
22	H	-1.710 005	-0.190 083	2.373 440	30.4056	1.4494
23	C	-0.114 235	2.242 550	-0.114 683	121.0340	62.8448
24	C	-2.021 340	0.894 434	0.571 542	113.6533	70.2255
25	H	-0.447 384	3.133 094	0.458 349	29.8615	1.9935
26	H	0.401 935	2.617 825	-1.004 053	28.7956	3.0594
27	C	-1.646 612	-2.044 440	0.347 844	138.0381	45.8407
28	H	-2.222 647	-2.431 150	1.202 340	30.6854	1.1696
29	H	-1.226 944	-2.915 635	-0.173 522	30.3528	1.5022
30	C	-2.622 082	-1.304 523	-0.578 647	156.6115	27.2673
31	H	-2.086 766	-0.997 809	-1.487 482	29.9332	1.9218
32	C	-3.145 740	-0.042 342	0.114 317	140.5781	43.3007
33	H	-2.473 526	1.726 019	1.154 790	29.9079	1.9471
34	H	-3.862 543	0.476 260	-0.531 413	29.7713	2.0837
35	H	-3.703 902	-0.343 105	1.013 044	31.0387	0.8163
36	C	-3.776 299	-2.216 866	-0.990 653	159.2443	24.6345
37	H	-4.348 352	-2.531 430	-0.109 046	31.3476	0.5074
38	H	-4.462 829	-1.703 325	-1.672 182	30.8858	0.9692
39	H	-3.408 290	-3.118 075	-1.492 497	30.8960	0.9590
40	N	-1.275 524	1.469 375	-0.560 960	—	—
41	C	-2.121 019	2.315 066	-1.391 757	138.7108	45.1680
42	H	-1.509 095	2.784 680	-2.166 914	29.8076	2.0474
43	H	-2.898 022	1.729 542	-1.887 063	29.0256	2.8294
44	H	-2.607 450	3.116 575	-0.803 447	30.5241	1.3309
45	C	2.274 349	0.706 781	-1.161 786	141.3799	42.4989

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Table S24 – continued from previous page

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
46	H	2.852 466	1.610 648	-0.920 098	30.7110	1.1440
47	H	1.531 854	0.986 084	-1.916 715	30.1047	1.7503
48	N	2.590 390	-0.208 919	1.071 891	—	—
49	H	2.141 759	-0.540 735	1.921 581	30.0988	1.7562

Fig. S25 202b – Conformer 2

SCF Energy - E(RM062X) -775.099 688 816

SCF Energy from NMR - E(RB3LYP) -775.608 371 720

Sum of Electronic and Thermal Free Energies -774.683 128 000

Table S25 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **202b** – Conformer 2

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	3.531 665	0.766 649	-1.180 100	159.0466	24.8322
2	C	4.394 708	-0.316 223	-0.525 883	151.9852	31.8936

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Table S25 – continued from previous page

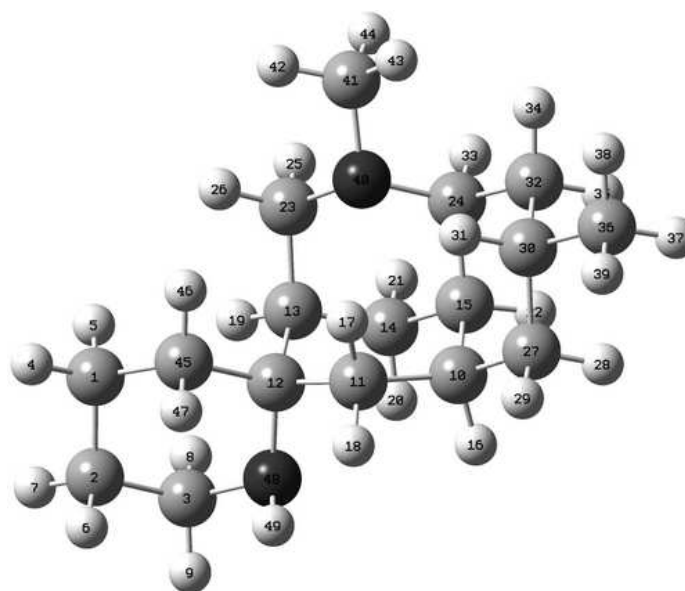
Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
3	C	3.684 367	-0.918 502	0.683 817	138.8082	45.0706
4	H	4.004 743	1.124 078	-2.101 055	30.4442	1.4108
5	H	3.454 497	1.632 651	-0.509 271	30.2724	1.5826
6	H	4.583 326	-1.114 612	-1.255 650	30.4541	1.4009
7	H	5.365 218	0.089 469	-0.220 962	30.2830	1.5720
8	H	3.639 838	-0.169 107	1.491 582	28.8817	2.9733
9	H	4.252 251	-1.770 140	1.071 252	29.2713	2.5837
10	C	-0.832 467	-1.459 664	0.417 153	145.3608	38.5180
11	C	0.153 707	-1.087 619	-0.705 010	134.2315	49.6473
12	C	1.441 804	-0.375 375	-0.251 442	124.4487	59.4301
13	C	1.122 902	0.717 779	0.816 271	149.7566	34.1222
14	C	0.343 087	0.114 577	1.986 347	149.1169	34.7619
15	C	-1.013 729	-0.333 452	1.453 769	141.1181	42.7607
16	H	-0.416 482	-2.320 086	0.963 184	30.0188	1.8362
17	H	-0.352 732	-0.436 848	-1.420 967	29.5619	2.2931
18	H	0.448 603	-2.000 792	-1.239 409	30.8957	0.9593
19	H	2.068 992	1.127 900	1.185 012	29.4449	2.4101
20	H	0.876 392	-0.726 683	2.445 099	30.0314	1.8236
21	H	0.211 856	0.873 393	2.768 307	30.4649	1.3901
22	H	-1.620 240	-0.733 593	2.278 238	30.3717	1.4833
23	C	0.316 291	1.918 490	0.310 252	120.0618	63.8170
24	C	-1.797 476	0.867 473	0.890 932	113.6276	70.2512
25	H	0.254 693	2.650 605	1.143 000	29.7171	2.1379
26	H	0.835 735	2.423 150	-0.511 226	29.0101	2.8449
27	C	-2.192 134	-1.883 896	-0.157 916	138.3172	45.5616
28	H	-2.777 719	-2.371 620	0.636 232	30.7248	1.1302
29	H	-2.045 579	-2.631 220	-0.949 706	30.4401	1.4149
30	C	-3.020 633	-0.709 765	-0.697 910	156.6639	27.2149
31	H	-2.497 559	-0.270 628	-1.558 195	29.9607	1.8943
32	C	-3.154 913	0.371 854	0.378 508	140.3694	43.5094
33	H	-1.976 158	1.571 526	1.732 740	29.9408	1.9142
34	H	-3.771 994	1.199 350	0.012 234	29.7752	2.0798
35	H	-3.692 072	-0.054 745	1.238 254	31.0275	0.8275
36	C	-4.394 271	-1.185 999	-1.167 227	159.2025	24.6763
37	H	-4.956 597	-1.616 384	-0.329 399	31.3380	0.5170
38	H	-4.981 610	-0.357 414	-1.577 095	30.8941	0.9609
39	H	-4.302 599	-1.954 991	-1.941 683	30.9266	0.9284
40	N	-1.029 322	1.570 941	-0.150 773	—	—

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Table S25 – continued from previous page

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
41	C	-1.708 547	2.777 733	-0.601 080	138.6087	45.2701
42	H	-1.062 999	3.312 141	-1.303 547	29.8061	2.0489
43	H	-2.639 107	2.535 939	-1.118 439	29.0182	2.8368
44	H	-1.941 839	3.458 454	0.239 965	30.4929	1.3621
45	C	2.137 092	0.216 282	-1.488 934	144.1875	39.6913
46	H	1.500 508	0.986 255	-1.937 524	30.0859	1.7691
47	H	2.227 808	-0.591 452	-2.228 618	30.7675	1.0875
48	N	2.360 227	-1.408 745	0.286 970	—	—
49	H	1.925 770	-1.882 006	1.074 990	29.8572	1.9978

Fig. S26 202b – Conformer 3



SCF Energy - E(RM062X) -775.099 602 704
 SCF Energy from NMR - E(RB3LYP) -775.608 116 205
 Sum of Electronic and Thermal Free Energies -774.683 137 000

Table S26 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **202b** – Conformer 3

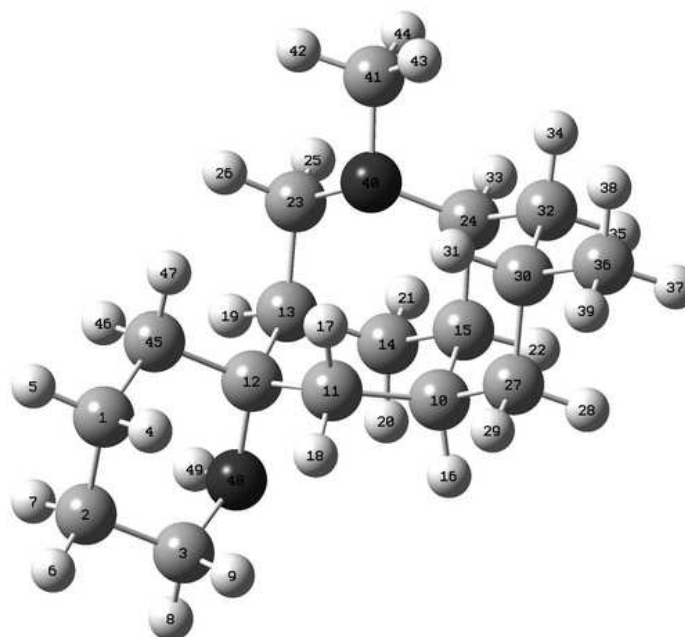
Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	3.507 383	0.777 493	-1.183 669	158.9692	24.9096
2	C	4.385 056	-0.304 968	-0.550 286	150.4503	33.4285
3	C	3.697 207	-0.914 038	0.674 278	137.8756	46.0032
4	H	3.963 113	1.145 038	-2.109 480	30.3779	1.4771
5	H	3.433 350	1.638 660	-0.505 862	30.1303	1.7247
6	H	4.560 008	-1.099 879	-1.288 862	30.5988	1.2562
7	H	5.364 043	0.097 867	-0.266 496	30.3524	1.5026
8	H	3.667 767	-0.177 418	1.486 214	29.0332	2.8218
9	H	4.271 922	-1.767 248	1.048 782	29.2337	2.6213
10	C	-0.845 231	-1.461 062	0.449 458	145.4845	38.3943
11	C	0.157 353	-1.112 165	-0.664 089	133.6556	50.2232
12	C	1.436 826	-0.377 046	-0.219 640	123.8876	59.9912
13	C	1.118 824	0.714 224	0.842 286	148.0034	35.8754
14	C	0.327 781	0.118 870	2.008 003	149.0256	34.8532
15	C	-1.028 858	-0.319 802	1.467 961	140.6460	43.2328
16	H	-0.438 867	-2.313 762	1.011 540	29.8440	2.0110
17	H	-0.339 408	-0.490 801	-1.412 181	29.6609	2.1941
18	H	0.459 128	-2.040 338	-1.172 408	31.0361	0.8189
19	H	2.064 698	1.120 587	1.216 486	29.6004	2.2546
20	H	0.858 001	-0.729 484	2.451 430	29.6345	2.2205
21	H	0.196 987	0.880 351	2.787 745	30.5657	1.2893
22	H	-1.646 829	-0.705 030	2.291 229	30.3698	1.4852
23	C	0.324 931	1.914 671	0.318 916	120.3498	63.5290
24	C	-1.798 467	0.878 864	0.881 713	113.5418	70.3370
25	H	0.251 781	2.650 300	1.147 309	29.7482	2.1068
26	H	0.856 977	2.415 093	-0.496 936	28.9973	2.8577
27	C	-2.200 745	-1.881 960	-0.137 608	138.4283	45.4505
28	H	-2.799 320	-2.356 379	0.654 983	30.7429	1.1121
29	H	-2.050 800	-2.639 854	-0.918 921	30.4581	1.3969
30	C	-3.015 131	-0.708 986	-0.701 141	156.6745	27.2043
31	H	-2.479 287	-0.283 661	-1.560 603	29.9685	1.8865
32	C	-3.153 651	0.386 359	0.360 730	140.3227	43.5561
33	H	-1.981 472	1.595 551	1.711 917	29.9547	1.9003
34	H	-3.761 618	1.213 379	-0.021 650	29.7777	2.0773
35	H	-3.702 603	-0.026 608	1.219 694	31.0307	0.8243
36	C	-4.386 819	-1.181 100	-1.180 203	159.1507	24.7281

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Table S26 – continued from previous page

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
37	H	-4.961 342	-1.597 590	-0.343 607	31.3390	0.5160
38	H	-4.963 889	-0.353 460	-1.606 285	30.8975	0.9575
39	H	-4.292 188	-1.959 956	-1.944 410	30.9299	0.9251
40	N	-1.013 408	1.564 002	-0.160 071	—	—
41	C	-1.682 292	2.765 551	-0.639 077	138.5913	45.2875
42	H	-1.024 199	3.287 859	-1.339 057	29.8033	2.0517
43	H	-2.605 140	2.518 188	-1.167 556	29.0198	2.8352
44	H	-1.927 327	3.459 331	0.187 841	30.4933	1.3617
45	C	2.114 230	0.214 479	-1.472 702	142.5925	41.2863
46	H	1.467 984	0.972 429	-1.929 489	29.9582	1.8968
47	H	2.207 947	-0.600 168	-2.206 593	30.8610	0.9940
48	N	2.328 832	-1.383 572	0.413 732	—	—
49	H	2.392 233	-2.172 312	-0.229 992	31.6829	0.1721

Fig. S27 202b – Conformer 4



SCF Energy - E(RM062X) -775.099 299 709
 SCF Energy from NMR - E(RB3LYP) -775.608 223 098
 Sum of Electronic and Thermal Free Energies -774.683 162 000

Table S27 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **202b** – Conformer 4

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	3.189 954	-0.403 037	-1.739 592	158.6029	25.2759
2	C	4.211 311	-0.807 192	-0.677 235	150.3382	33.5406
3	C	3.490 576	-1.256 488	0.594 110	137.6573	46.2215
4	H	2.615 892	-1.286 502	-2.049 746	30.1708	1.6842
5	H	3.692 684	-0.023 445	-2.635 665	30.2864	1.5686
6	H	4.863 230	-1.609 432	-1.041 508	30.3816	1.4734
7	H	4.850 955	0.054 970	-0.441 249	30.7012	1.1538
8	H	4.209 060	-1.459 877	1.394 594	29.1494	2.7056
9	H	2.963 192	-2.198 221	0.399 139	28.9244	2.9306
10	C	-0.530 552	-1.152 428	0.906 816	145.6340	38.2448
11	C	0.520 381	-0.894 855	-0.188 259	146.7334	37.1454
12	C	1.539 219	0.225 434	0.116 322	124.0282	59.8506
13	C	0.849 060	1.446 413	0.781 894	133.3025	50.5763
14	C	0.045 452	1.026 201	2.013 235	148.7728	35.1060
15	C	-1.095 639	0.139 045	1.528 336	140.6666	43.2122
16	H	-0.032 746	-1.695 003	1.723 385	29.9794	1.8756
17	H	0.013 862	-0.638 463	-1.121 127	30.1244	1.7306
18	H	1.052 803	-1.835 212	-0.373 417	29.8212	2.0338
19	H	1.650 101	2.141 413	1.074 141	30.8306	1.0244
20	H	0.669 873	0.489 701	2.733 435	29.5702	2.2848
21	H	-0.353 010	1.918 794	2.512 729	30.6264	1.2286
22	H	-1.724 956	-0.150 933	2.381 453	30.3911	1.4639
23	C	-0.096 716	2.235 871	-0.128 564	120.7847	63.0941
24	C	-2.015 130	0.910 143	0.562 845	113.5966	70.2822
25	H	-0.428 911	3.131 633	0.436 802	29.8304	2.0246
26	H	0.425 856	2.602 257	-1.017 749	28.8062	3.0488
27	C	-1.671 265	-2.035 026	0.378 778	138.1100	45.7688
28	H	-2.258 207	-2.406 508	1.232 663	30.7048	1.1502
29	H	-1.257 325	-2.916 756	-0.129 627	30.3701	1.4849
30	C	-2.632 180	-1.295 756	-0.563 276	156.7578	27.1210
31	H	-2.087 334	-1.004 218	-1.471 505	29.9415	1.9135
32	C	-3.147 036	-0.020 598	0.112 114	140.5183	43.3605
33	H	-2.461 411	1.754 717	1.131 891	29.9234	1.9316
34	H	-3.856 347	0.497 084	-0.542 632	29.7739	2.0811
35	H	-3.711 654	-0.305 423	1.012 022	31.0348	0.8202
36	C	-3.792 886	-2.200 451	-0.973 817	159.1941	24.6847

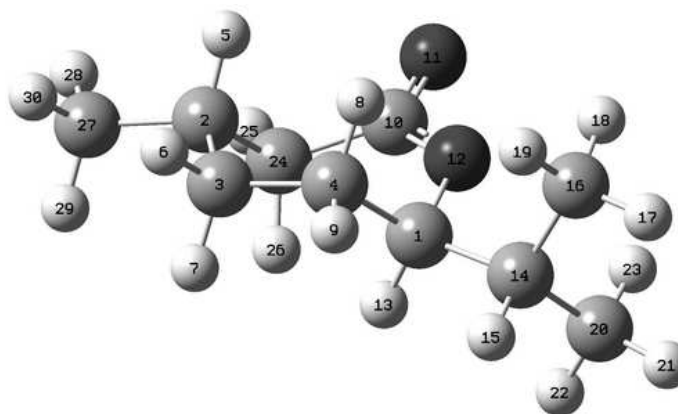
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Table S27 – continued from previous page

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
37	H	-4.374 305	-2.499 531	-0.092 928	31.3508	0.5042
38	H	-4.469 353	-1.687 398	-1.665 739	30.8891	0.9659
39	H	-3.430 778	-3.110 889	-1.463 185	30.9023	0.9527
40	N	-1.257 946	1.462 738	-0.573 842	—	—
41	C	-2.092 541	2.300 724	-1.423 360	138.6620	45.2168
42	H	-1.472 085	2.756 212	-2.200 171	29.8089	2.0461
43	H	-2.868 536	1.712 053	-1.916 494	29.0193	2.8357
44	H	-2.579 700	3.112 773	-0.850 317	30.5188	1.3362
45	C	2.243 799	0.665 373	-1.184 395	139.8079	44.0709
46	H	2.824 485	1.575 750	-0.969 046	30.7938	1.0612
47	H	1.493 847	0.930 164	-1.938 444	29.9998	1.8552
48	N	2.527 461	-0.274 078	1.109 185	—	—
49	H	3.059 363	0.529 424	1.445 185	31.7205	0.1345

S-I.5 Normal *trans*-Menthide (203b)

Fig. S28 203b – Conformer 1



SCF Energy - E(RM062X) -542.169 990 504
 SCF Energy from NMR - E(RB3LYP) -542.553 134 970
 Sum of Electronic and Thermal Free Energies -541.937 504 000

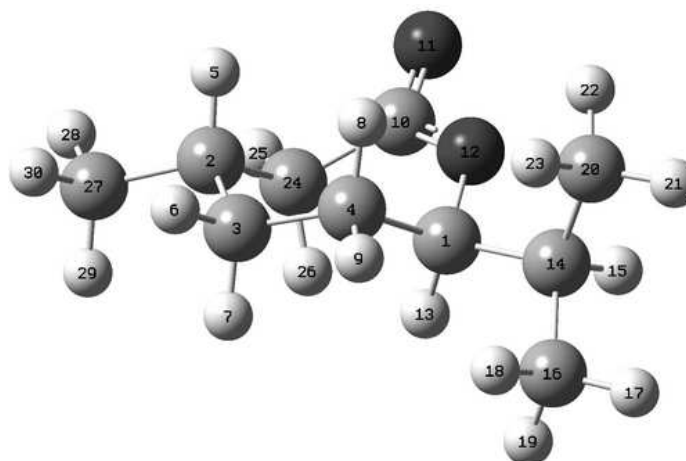
Table S28 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **203b** – Conformer 1

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	-0.857 662	-0.409 469	0.349 807	94.9056	88.7020
2	C	2.245 895	-0.377 236	-0.204 793	146.4929	37.1147
3	C	1.381 435	-1.619 213	0.027 254	140.7721	42.8355
4	C	-0.079 989	-1.487 457	-0.401 047	145.1562	38.4514
5	H	2.257 574	-0.153 014	-1.280 775	30.1207	1.7442
6	H	1.833 479	-2.462 325	-0.507 661	29.9770	1.8879
7	H	1.419 337	-1.870 212	1.097 757	30.5819	1.2830
8	H	-0.146 784	-1.278 651	-1.475 889	30.1355	1.7294
9	H	-0.584 640	-2.445 722	-0.231 107	30.1413	1.7236
10	C	0.543 647	1.525 568	-0.169 542	-2.2084	185.8160
11	O	0.638 831	2.613 479	-0.702 544	—	—
12	O	-0.634 142	0.892 917	-0.242 703	—	—
13	H	-0.530 494	-0.367 329	1.397 622	27.5596	4.3053
14	C	-2.374 984	-0.619 072	0.337 307	143.0604	40.5472
15	H	-2.536 059	-1.582 316	0.839 873	30.2113	1.6536

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Table S28 – continued from previous page

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
16	C	-2.941 794	-0.706 420	-1.081 500	168.5560	15.0516
17	H	-4.026 128	-0.846 035	-1.042 713	31.1850	0.6799
18	H	-2.738 992	0.217 624	-1.632 136	30.8946	0.9703
19	H	-2.515 762	-1.543 014	-1.642 677	30.7411	1.1238
20	C	-3.083 543	0.469 715	1.144 366	161.5150	22.0926
21	H	-4.151 756	0.248 719	1.225 914	30.9190	0.9459
22	H	-2.672 226	0.545 929	2.156 598	30.9769	0.8880
23	H	-2.973 471	1.442 792	0.656 367	30.6763	1.1886
24	C	1.702 198	0.862 802	0.537 509	137.1302	46.4774
25	H	2.479 379	1.626 342	0.603 021	29.5338	2.3311
26	H	1.416 391	0.583 570	1.559 011	29.2478	2.6171
27	C	3.681 586	-0.643 546	0.249 331	157.2322	26.3754
28	H	4.331 558	0.207 277	0.026 063	30.7399	1.1250
29	H	3.711 896	-0.821 004	1.330 900	31.0827	0.7822
30	H	4.088 461	-1.527 840	-0.250 343	30.8001	1.0648

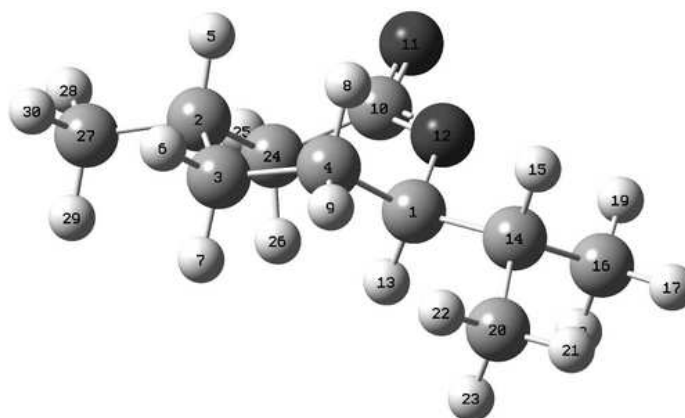
Fig. S29 203b – Conformer 2

SCF Energy - E(RM062X) -542.169 535 189
SCF Energy from NMR - E(RB3LYP) -542.552 804 001
Sum of Electronic and Thermal Free Energies -541.937 459 000

Table S29 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **203b** – Conformer 2

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	0.912 188	-0.061 797	-0.327 385	94.1342	89.4734
2	C	-2.131 115	-0.600 844	0.318 150	146.4012	37.2064
3	C	-1.005 620	-1.638 471	0.322 171	140.7964	42.8112
4	C	0.383 146	-1.097 326	0.661 880	152.0900	31.5176
5	H	-2.208 921	-0.163 231	1.323 355	30.1210	1.7439
6	H	-1.263 758	-2.427 953	1.037 274	29.9534	1.9115
7	H	-0.970 553	-2.112 397	-0.670 166	30.6839	1.1810
8	H	0.387 609	-0.649 688	1.663 526	30.4668	1.3981
9	H	1.085 307	-1.937 640	0.688 250	30.0265	1.8384
10	C	-0.896 596	1.578 934	-0.168 467	-1.7396	185.3472
11	O	-1.239 999	2.704 436	0.134 805	—	—
12	O	0.393 953	1.255 228	-0.013 802	—	—
13	H	0.599 998	-0.317 206	-1.348 802	27.6042	4.2607
14	C	2.436 134	0.103 970	-0.324 505	144.4800	39.1276
15	H	2.634 885	0.984 455	-0.948 679	29.8770	1.9879
16	C	3.120 669	-1.099 328	-0.974 840	162.9034	20.7042
17	H	4.194 553	-0.913 015	-1.065 693	30.7923	1.0726
18	H	2.994 604	-2.006 518	-0.374 247	31.1739	0.6910
19	H	2.724 585	-1.294 227	-1.976 839	30.9414	0.9235
20	C	2.992 732	0.370 088	1.075 088	167.5501	16.0575
21	H	4.056 979	0.616 006	1.014 613	31.0858	0.7791
22	H	2.475 673	1.204 588	1.557 071	30.5366	1.3283
23	H	2.891 890	-0.515 124	1.712 769	31.2633	0.6016
24	C	-1.869 538	0.544 627	-0.683 086	137.1137	46.4939
25	H	-2.796 532	1.087 884	-0.875 273	29.5191	2.3458
26	H	-1.518 416	0.129 611	-1.635 900	29.2486	2.6163
27	C	-3.462 795	-1.271 282	-0.021 568	157.2482	26.3594
28	H	-4.291 335	-0.559 975	0.039 408	30.7420	1.1229
29	H	-3.436 064	-1.677 141	-1.039 735	31.0846	0.7803
30	H	-3.667 366	-2.097 161	0.666 424	30.7994	1.0655

Fig. S30 203b – Conformer 3



SCF Energy - E(RM062X) -542.168 628 918
 SCF Energy from NMR - E(RB3LYP) -542.552 439 622
 Sum of Electronic and Thermal Free Energies -541.937 340 000

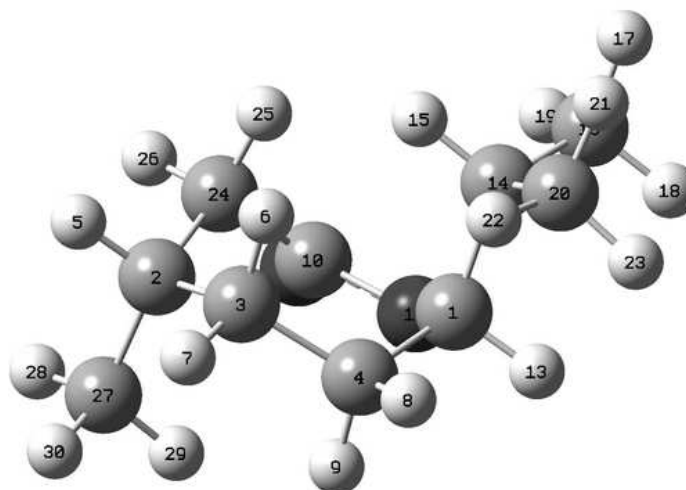
Table S30 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **203b** – Conformer 3

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	-0.919 386	-0.224 788	0.017 890	91.8084	91.7992
2	C	2.227 146	-0.493 680	-0.160 400	146.5522	37.0554
3	C	1.213 257	-1.638 636	-0.223 456	140.7742	42.8334
4	C	-0.160 514	-1.276 542	-0.788 993	147.3639	36.2437
5	H	2.408 496	-0.127 801	-1.180 893	30.1030	1.7619
6	H	1.641 222	-2.448 502	-0.825 322	29.9760	1.8889
7	H	1.083 126	-2.038 757	0.793 167	30.6243	1.2406
8	H	-0.072 922	-0.905 656	-1.818 372	30.4555	1.4094
9	H	-0.761 728	-2.188 517	-0.832 854	29.6701	2.1948
10	C	0.743 543	1.571 859	-0.051 946	-1.7224	185.3300
11	O	1.023 186	2.697 939	-0.413 321	—	—
12	O	-0.470 841	1.099 578	-0.360 664	—	—
13	H	-0.741 064	-0.355 337	1.095 608	28.0945	3.7704
14	C	-2.434 500	-0.229 269	-0.216 889	144.6951	38.9125
15	H	-2.599 242	-0.181 926	-1.302 631	30.1780	1.6869
16	C	-3.098 073	0.984 122	0.439 856	162.0719	21.5357

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Table S30 – continued from previous page

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
17	H	-4.181 971	0.940 724	0.298 557	31.0121	0.8528
18	H	-2.900 019	0.985 800	1.519 044	31.3781	0.4868
19	H	-2.732 381	1.924 006	0.023 525	30.1759	1.6890
20	C	-3.064 276	-1.513 895	0.330 511	162.1505	21.4571
21	H	-4.148 616	-1.481 806	0.192 682	30.8441	1.0208
22	H	-2.696 234	-2.416 858	-0.161 839	30.7016	1.1633
23	H	-2.868 027	-1.605 871	1.405 569	31.3125	0.5524
24	C	1.719 895	0.690 796	0.689 521	137.3621	46.2455
25	H	2.554 339	1.340 706	0.958 774	29.5363	2.3286
26	H	1.271 456	0.314 742	1.617 048	29.2578	2.6071
27	C	3.551 378	-0.995 882	0.416 001	157.3501	26.2575
28	H	4.312 639	-0.210 707	0.402 047	30.7383	1.1266
29	H	3.415 485	-1.320 798	1.454 319	31.0892	0.7757
30	H	3.925 853	-1.848 088	-0.159 117	30.8033	1.0616

Fig. S31 203b – Conformer 4

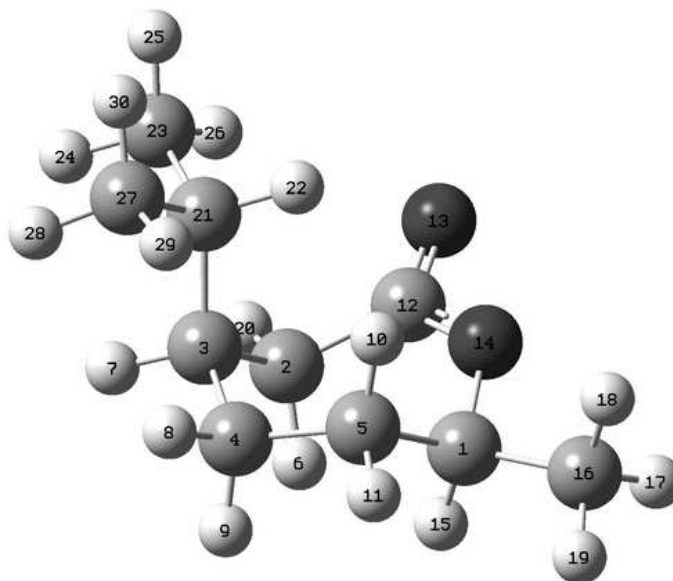
SCF Energy - E(RM062X) -542.165 252 005
SCF Energy from NMR - E(RB3LYP) -542.545 413 963
Sum of Electronic and Thermal Free Energies -541.932 246 000

Table S31 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **203b** – Conformer 4

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	0.914 812	-0.107 380	-0.807 131	92.4804	91.1272
2	C	-1.790 772	-0.906 698	0.726 880	150.2969	33.3107
3	C	-0.657 947	-1.849 009	0.303 046	150.2422	33.3654
4	C	0.120 140	-1.405 495	-0.935 389	155.7061	27.9015
5	H	-2.228 730	-1.331 565	1.638 190	29.8767	1.9882
6	H	0.033 459	-1.977 971	1.146 135	29.7748	2.0901
7	H	-1.089 295	-2.837 122	0.103 890	30.2842	1.5807
8	H	0.831 546	-2.191 170	-1.210 409	29.9755	1.8894
9	H	-0.553 263	-1.296 555	-1.792 985	29.7094	2.1555
10	C	-0.916 408	1.395 728	-0.027 461	-1.6231	185.2307
11	O	-1.498 475	2.443 718	-0.229 524	—	—
12	O	0.059 675	1.064 481	-0.884 947	—	—
13	H	1.497 840	0.006 078	-1.728 375	28.0662	3.7987
14	C	1.916 637	-0.023 462	0.352 758	149.9747	33.6329
15	H	1.399 149	-0.162 025	1.307 604	29.3594	2.5055
16	C	2.607 986	1.341 342	0.369 413	162.4368	21.1708
17	H	3.348 511	1.379 827	1.173 502	30.9903	0.8746
18	H	3.127 064	1.517 541	-0.580 189	31.1966	0.6683
19	H	1.896 591	2.157 566	0.519 540	30.4991	1.3658
20	C	2.946 422	-1.149 547	0.219 027	162.2537	21.3539
21	H	3.720 923	-1.040 074	0.983 316	30.8883	0.9766
22	H	2.493 774	-2.137 853	0.339 033	30.7528	1.1121
23	H	3.434 568	-1.112 360	-0.762 339	31.3458	0.5191
24	C	-1.288 917	0.491 994	1.130 641	135.4092	48.1984
25	H	-0.440 489	0.410 019	1.816 587	28.8990	2.9659
26	H	-2.083 654	1.025 636	1.655 533	29.2401	2.6248
27	C	-2.902 925	-0.808 473	-0.320 327	164.9915	18.6161
28	H	-3.731 821	-0.199 204	0.052 846	30.7889	1.0760
29	H	-2.550 275	-0.347 797	-1.249 714	30.7105	1.1544
30	H	-3.289 654	-1.802 560	-0.565 148	31.0496	0.8153

S-I.6 Normal *cis*-Carvomenthide (204a)

Fig. S32 204a – Conformer 1



SCF Energy - E(RM062X) -542.169 260 511
 SCF Energy from NMR - E(RB3LYP) -542.548 839 790
 Sum of Electronic and Thermal Free Energies -541.935 530 000

Table S32 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **204a** – Conformer 1

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	-2.055 131	-0.327 730	0.109 051	100.9720	82.6356
2	C	0.274 970	0.914 930	1.266 550	140.5636	43.0440
3	C	0.999 288	-0.399 149	0.885 769	138.1549	45.4527
4	C	0.028 421	-1.586 084	0.926 571	147.1657	36.4419
5	C	-1.119 496	-1.518 524	-0.080 958	148.3533	35.2543
6	H	-0.425 689	0.722 447	2.087 010	28.9935	2.8714
7	H	1.742 705	-0.571 535	1.677 420	30.5060	1.3589
8	H	0.581 600	-2.518 929	0.782 370	29.7326	2.1323
9	H	-0.401 237	-1.638 689	1.935 873	30.2907	1.5742
10	H	-0.748 484	-1.500 506	-1.114 152	30.1042	1.7607

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Table S32 – continued from previous page

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
11	H	-1.724 899	-2.426 303	0.019 996	30.2878	1.5771
12	C	-0.462 949	1.541 626	0.105 097	-1.3645	184.9721
13	O	-0.140 604	2.606 945	-0.381 136	—	—
14	O	-1.497 656	0.890 467	-0.447 697	—	—
15	H	-2.241 423	-0.157 444	1.176 915	27.3433	4.5216
16	C	-3.376 194	-0.511 273	-0.615 990	159.1524	24.4552
17	H	-3.996 541	0.382 031	-0.515 055	30.4933	1.3716
18	H	-3.198 050	-0.697 917	-1.679 397	30.5235	1.3414
19	H	-3.914 132	-1.364 067	-0.195 075	30.8182	1.0467
20	H	0.985 283	1.667 899	1.608 816	29.0190	2.8459
21	C	1.782 507	-0.266 740	-0.438 210	149.4261	34.1815
22	H	1.078 730	0.013 209	-1.236 606	30.3061	1.5588
23	C	2.843 946	0.834 080	-0.339 291	160.4138	23.1938
24	H	3.545 914	0.611 062	0.474 020	31.4098	0.4551
25	H	3.416 469	0.896 542	-1.269 553	30.9610	0.9039
26	H	2.403 477	1.817 255	-0.155 002	30.1582	1.7067
27	C	2.441 843	-1.588 626	-0.840 795	161.2666	22.3410
28	H	3.071 316	-1.968 142	-0.025 952	31.3759	0.4890
29	H	1.707 934	-2.359 965	-1.090 401	30.5995	1.2654
30	H	3.079 881	-1.441 302	-1.717 324	31.0051	0.8598

Fig. S33 204a – Conformer 2

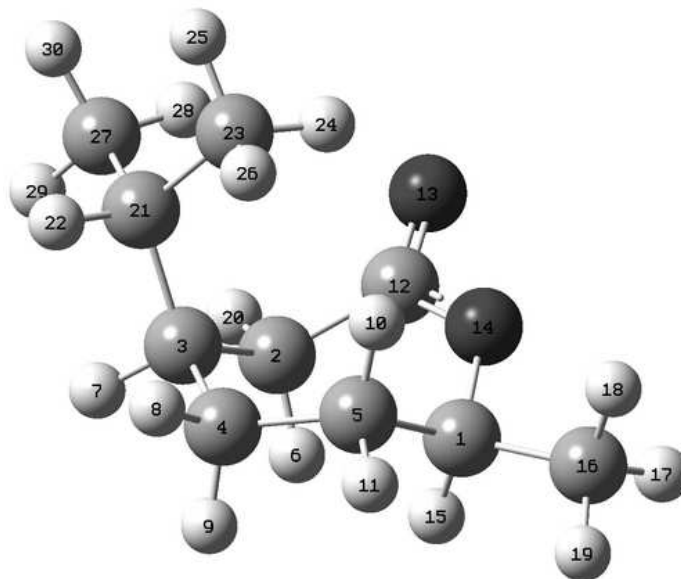


SCF Energy - E(RM062X) -542.164 392 485
 SCF Energy from NMR - E(RB3LYP) -542.544 841 222
 Sum of Electronic and Thermal Free Energies -541.930 683 000

Table S33 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **204a** – Conformer 2

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	1.982 353	-0.542 589	-0.188 145	102.0054	81.6022
2	C	-0.174 012	0.930 545	-1.333 792	139.6398	43.9678
3	C	-1.105 414	-0.230 149	-0.920 861	140.4514	43.1562
4	C	-0.344 999	-1.551 893	-0.708 200	152.6906	30.9170
5	C	0.898 408	-1.545 676	0.191 589	144.3578	39.2498
6	H	0.489 669	0.597 069	-2.139 331	28.7803	3.0846
7	H	-1.726 249	-0.393 582	-1.811 362	30.0766	1.7883
8	H	-1.043 553	-2.309 211	-0.332 673	29.8129	2.0520
9	H	-0.024 045	-1.902 271	-1.698 104	30.1893	1.6756
10	H	0.650 742	-1.377 116	1.244 140	29.9035	1.9614
11	H	1.348 197	-2.543 741	0.135 067	30.2169	1.6480
12	C	0.652 507	1.509 875	-0.212 054	-2.8714	186.4790
13	O	0.446 095	2.610 506	0.258 970	—	—
14	O	1.657 213	0.784 306	0.300 854	—	—
15	H	2.101 461	-0.488 433	-1.277 171	27.2050	4.6599
16	C	3.318 341	-0.872 959	0.452 254	159.3255	24.2821
17	H	4.053 109	-0.096 152	0.229 263	30.4674	1.3975
18	H	3.205 938	-0.950 210	1.537 960	30.5375	1.3274
19	H	3.686 460	-1.827 354	0.068 278	30.8330	1.0319
20	H	-0.776 010	1.757 238	-1.715 083	29.4151	2.4498
21	C	-2.096 838	0.170 373	0.199 231	145.7069	37.9007
22	H	-2.345 479	1.227 802	0.031 323	29.8498	2.0151
23	C	-3.394 980	-0.633 799	0.073 836	158.3263	25.2813
24	H	-3.204 696	-1.706 131	0.200 211	30.8003	1.0646
25	H	-4.112 128	-0.333 080	0.844 018	30.9180	0.9469
26	H	-3.863 074	-0.485 246	-0.904 419	31.0493	0.8156
27	C	-1.560 150	0.042 047	1.629 202	161.4196	22.1880
28	H	-1.421 963	-1.011 724	1.896 712	31.2378	0.6271
29	H	-0.610 919	0.562 359	1.783 792	30.5920	1.2729
30	H	-2.285 213	0.466 635	2.330 423	30.9932	0.8717

Fig. S34 204a – Conformer 3



SCF Energy - E(RM062X) -542.164 222 687
SCF Energy from NMR - E(RB3LYP) -542.544 090 829
Sum of Electronic and Thermal Free Energies -541.930 083 000

Table S34 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for 204a – Conformer 3

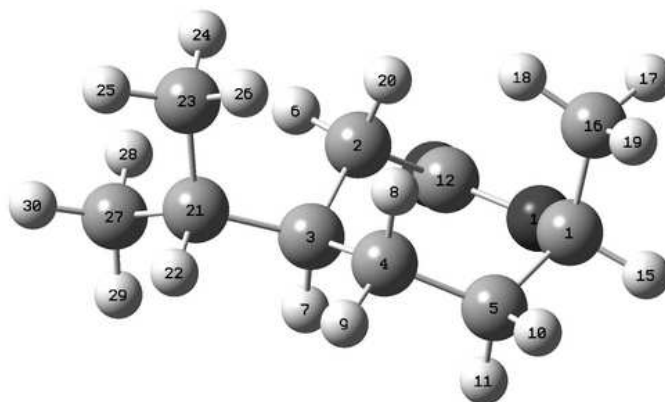
Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	2.065 495	-0.121 331	-0.202 303	102.2069	81.4007
2	C	-0.467 219	0.620 451	-1.298 259	146.5638	37.0438
3	C	-0.988 637	-0.771 408	-0.873 821	140.2793	43.3283
4	C	0.146 897	-1.790 310	-0.673 764	145.9931	37.6145
5	C	1.338 912	-1.396 715	0.208 185	144.5956	39.0120
6	H	0.246 294	0.488 103	-2.119 980	29.0608	2.8041
7	H	-1.535 932	-1.119 023	-1.760 469	29.9164	1.9485
8	H	-0.286 270	-2.721 010	-0.286 340	29.9812	1.8837
9	H	0.550 018	-2.029 882	-1.666 773	29.8931	1.9718
10	H	1.063 309	-1.287 999	1.261 658	29.7847	2.0802
11	H	2.067 040	-2.214 618	0.160 045	30.1471	1.7178

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Table S34 – continued from previous page

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
12	C	0.186 492	1.445 595	-0.215 483	-3.5721	187.1797
13	O	-0.307 042	2.463 898	0.227 175	—	—
14	O	1.367 578	1.053 747	0.283 483	—	—
15	H	2.142 257	-0.048 443	-1.294 019	27.2424	4.6225
16	C	3.450 963	-0.028 524	0.411 328	159.3275	24.2801
17	H	3.915 539	0.929 439	0.167 459	30.4690	1.3959
18	H	3.386 746	-0.122 113	1.499 681	30.5238	1.3411
19	H	4.080 345	-0.834 452	0.026 267	30.8186	1.0463
20	H	-1.290 249	1.227 953	-1.676 417	29.1566	2.7083
21	C	-2.049 203	-0.756 598	0.252 496	143.0121	40.5955
22	H	-2.513 896	-1.752 290	0.212 781	30.0133	1.8516
23	C	-1.510 636	-0.581 375	1.677 034	163.3878	20.2198
24	H	-0.922 228	0.334 764	1.792 934	30.8878	0.9771
25	H	-2.350 073	-0.517 299	2.377 101	31.1389	0.7260
26	H	-0.893 093	-1.429 316	1.983 828	30.6868	1.1781
27	C	-3.148 255	0.272 253	-0.030 568	159.8772	23.7304
28	H	-2.780 503	1.293 300	0.117 615	30.3791	1.4858
29	H	-3.519 701	0.188 457	-1.058 228	30.9461	0.9188
30	H	-3.992 741	0.121 041	0.648 514	30.8754	0.9895

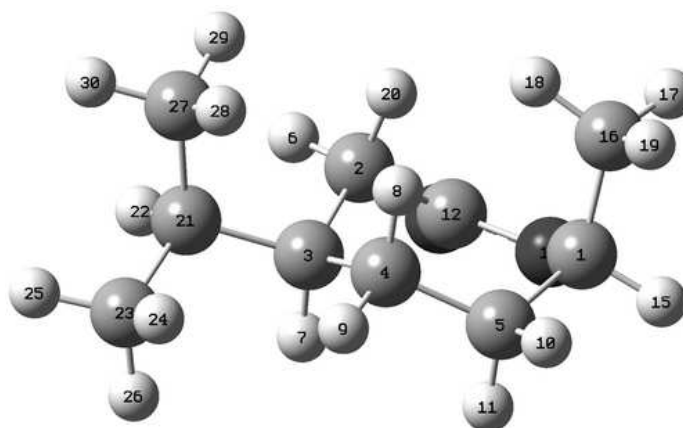
Fig. S35 204a – Conformer 4



SCF Energy - E(RM062X) -542.163 494 264
 SCF Energy from NMR - E(RB3LYP) -542.546 004 235
 Sum of Electronic and Thermal Free Energies -541.931 402 000

Table S35 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **204a** – Conformer 4

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	2.304665	-0.569330	-0.218367	102.7965	80.8111
2	C	-0.257854	0.743061	0.571561	142.3522	41.2554
3	C	-0.876035	-0.174422	-0.502740	136.9666	46.6410
4	C	-0.100464	-1.487454	-0.636863	149.0473	34.5603
5	C	1.334701	-1.315590	-1.131097	145.8154	37.7922
6	H	-0.967133	1.517757	0.867365	29.3512	2.5137
7	H	-0.818127	0.347861	-1.469802	30.3811	1.4838
8	H	-0.102196	-2.019655	0.323244	29.7538	2.1111
9	H	-0.628351	-2.132656	-1.348991	30.4171	1.4478
10	H	1.774942	-2.305891	-1.296124	29.9429	1.9220
11	H	1.332613	-0.807271	-2.103339	29.8063	2.0586
12	C	0.967485	1.504579	0.117892	-2.6991	186.3067
13	O	0.970483	2.717931	0.039768	—	—
14	O	2.095533	0.867830	-0.225609	—	—
15	H	3.289554	-0.631067	-0.687861	27.2731	4.5918
16	C	2.440424	-1.117993	1.195287	165.1893	18.4183
17	H	3.161514	-0.519756	1.757433	30.4186	1.4463
18	H	1.499641	-1.141968	1.746721	29.9445	1.9204
19	H	2.816891	-2.143456	1.135384	30.8712	0.9937
20	H	-0.019302	0.162302	1.467967	29.4581	2.4068
21	C	-2.375834	-0.427716	-0.225926	143.2827	40.3249
22	H	-2.683950	-1.204181	-0.940001	30.2027	1.6622
23	C	-2.646994	-0.955235	1.186238	167.2360	16.3716
24	H	-2.424851	-0.191469	1.940175	31.4317	0.4332
25	H	-3.702909	-1.222110	1.292358	31.0930	0.7719
26	H	-2.053420	-1.845117	1.417133	30.7917	1.0732
27	C	-3.229939	0.811477	-0.504833	160.4172	23.1904
28	H	-3.007016	1.622546	0.197051	30.8619	1.0030
29	H	-3.064066	1.187301	-1.519443	30.9776	0.8873
30	H	-4.292889	0.572471	-0.399448	30.8954	0.9695

Fig. S36 204a – Conformer 5

SCF Energy - E(RM062X) -542.163 420 262
 SCF Energy from NMR - E(RB3LYP) -542.545 837 090
 Sum of Electronic and Thermal Free Energies -541.931 194 000

Table S36 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **204a** – Conformer 5

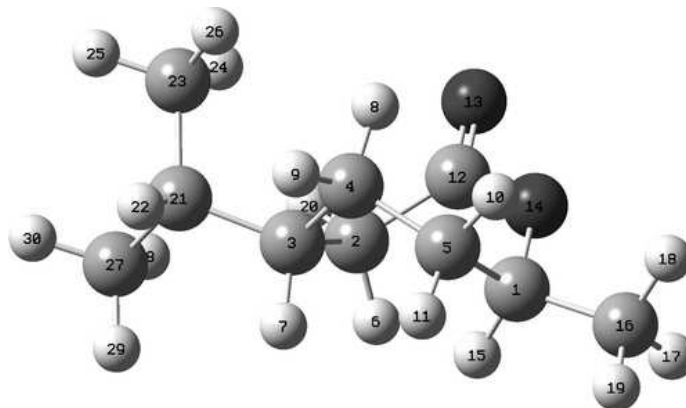
Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	2.097 508	-0.984 012	-0.215 801	102.6984	80.9092
2	C	0.037 371	1.040 575	0.537 683	133.7876	49.8200
3	C	-0.889 425	0.199 083	-0.362 946	137.1544	46.4532
4	C	-0.492 663	-1.279 081	-0.350 343	158.4283	25.1793
5	C	0.885 650	-1.549 602	-0.952 112	145.9129	37.6947
6	H	-0.432 700	2.001 874	0.757 659	29.4802	2.3847
7	H	-0.781 744	0.568 586	-1.394 203	30.3071	1.5578
8	H	-0.533 103	-1.663 539	0.677 099	30.2321	1.6328
9	H	-1.223 345	-1.855 995	-0.926 674	30.2157	1.6492
10	H	1.044 105	-2.633 025	-1.005 002	29.9352	1.9297
11	H	0.917 043	-1.177 033	-1.983 538	29.9266	1.9383
12	C	1.371 394	1.394 628	-0.080 404	-2.4276	186.0352
13	O	1.680 037	2.547 455	-0.313 063	—	—
14	O	2.261 154	0.446 622	-0.405 469	—	—
15	H	2.983 203	-1.358 104	-0.735 385	27.2675	4.5974
16	C	2.227 941	-1.381 588	1.248 057	165.1819	18.4257

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Table S36 – continued from previous page

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
17	H	3.134 174	-0.942 757	1.672 302	30.4170	1.4479
18	H	1.375 289	-1.081 249	1.858 555	29.9568	1.9081
19	H	2.312 510	-2.470 756	1.306 753	30.8919	0.9730
20	H	0.202 277	0.532 513	1.492 815	28.9616	2.9033
21	C	-2.363 603	0.441 482	0.033 956	142.8225	40.7851
22	H	-2.514 111	1.528 656	-0.018 825	30.1584	1.7065
23	C	-3.337 559	-0.200 875	-0.957 114	160.2623	23.3453
24	H	-3.340 293	-1.292 365	-0.868 315	30.9244	0.9405
25	H	-4.357 504	0.145 137	-0.762 904	30.7830	1.0819
26	H	-3.082 597	0.057 240	-1.990 554	30.9724	0.8925
27	C	-2.685 739	-0.005 297	1.462 926	167.6379	15.9697
28	H	-2.590 750	-1.091 754	1.567 020	31.2474	0.6175
29	H	-2.030 531	0.467 769	2.201 290	30.9162	0.9487
30	H	-3.716 690	0.260 301	1.716 756	31.0947	0.7702

Fig. S37 204a – Conformer 6

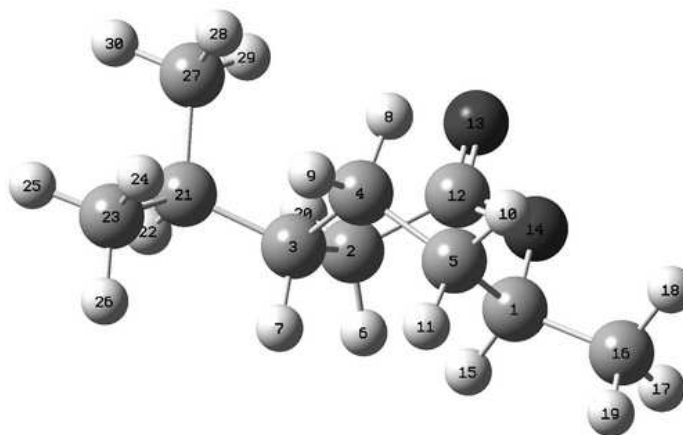


SCF Energy - E(RM062X) -542.165 745 134
 SCF Energy from NMR - E(RB3LYP) -542.546 978 417
 Sum of Electronic and Thermal Free Energies -541.933 151 000

Table S37 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **204a** – Conformer 6

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	-2.076 727	-0.484 595	0.349 955	104.8322	78.7754
2	C	0.414 186	0.713 125	0.856 392	146.0696	37.5380
3	C	0.856 309	-0.657 455	0.255 316	141.1340	42.4736
4	C	0.025 982	-1.053 576	-0.974 369	149.2078	34.3998
5	C	-1.410 196	-1.453 078	-0.622 844	144.0410	39.5666
6	H	0.045 036	0.584 389	1.879 461	29.0562	2.8087
7	H	0.683 855	-1.426 080	1.021 939	30.0904	1.7745
8	H	0.010 122	-0.227 174	-1.695 985	30.2841	1.5808
9	H	0.514 873	-1.891 861	-1.483 423	30.4706	1.3943
10	H	-2.014 278	-1.516 304	-1.535 314	30.1433	1.7216
11	H	-1.420 261	-2.444 351	-0.153 737	30.2020	1.6629
12	C	-0.651 302	1.453 884	0.074 538	-1.9229	185.5305
13	O	-0.481 268	2.561 097	-0.393 432	—	—
14	O	-1.853 939	0.876 228	-0.088 783	—	—
15	H	-1.643 812	-0.597 625	1.349 990	27.2339	4.6310
16	C	-3.579 255	-0.665 136	0.430 696	161.3390	22.2686
17	H	-4.016 174	0.028 395	1.152 792	30.3899	1.4750
18	H	-4.031 674	-0.488 545	-0.549 228	30.6809	1.1840
19	H	-3.808 428	-1.687 869	0.741 961	30.7178	1.1471
20	H	1.253 191	1.407 187	0.912 357	29.4091	2.4558
21	C	2.369 194	-0.681 702	-0.051 964	142.6631	40.9445
22	H	2.579 414	-1.693 468	-0.426 423	30.2030	1.6619
23	C	2.773 125	0.312 626	-1.143 807	168.1073	15.5003
24	H	2.537 210	1.343 263	-0.854 277	31.0951	0.7698
25	H	3.851 564	0.259 431	-1.322 697	31.2341	0.6308
26	H	2.266 704	0.105 906	-2.090 996	30.8868	0.9781
27	C	3.209 281	-0.479 394	1.211 326	160.8121	22.7955
28	H	3.100 985	0.535 145	1.610 475	30.9600	0.9049
29	H	2.919 063	-1.185 598	1.996 762	31.0789	0.7860
30	H	4.270 688	-0.631 636	0.992 629	30.9205	0.9444

Fig. S38 204a – Conformer 7



SCF Energy - E(RM062X) -542.165 698 992
SCF Energy from NMR - E(RB3LYP) -542.546 816 347
Sum of Electronic and Thermal Free Energies -541.932 836 000

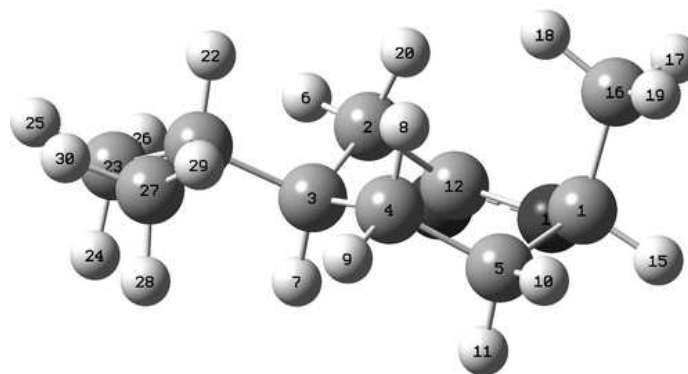
Table S38 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **204a** – Conformer 7

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	-2.004 242	-0.675 639	0.257 835	104.7445	78.8631
2	C	0.169 525	0.929 209	1.017 768	138.3358	45.2718
3	C	0.905 585	-0.348 918	0.506 771	140.9627	42.6449
4	C	0.305 845	-0.881 024	-0.803 472	157.8956	25.7120
5	C	-1.073 835	-1.517 340	-0.610 268	144.1054	39.5022
6	H	-0.287 657	0.742 112	1.995 425	28.5826	3.2823
7	H	0.776 696	-1.131 719	1.267 268	30.1568	1.7081
8	H	0.235 291	-0.065 231	-1.534 204	30.6877	1.1772
9	H	0.975 202	-1.625 486	-1.245 574	30.2602	1.6047
10	H	-1.546 986	-1.684 349	-1.584 896	30.1350	1.7299
11	H	-0.970 869	-2.494 985	-0.123 896	30.3256	1.5393
12	C	-0.909 160	1.478 673	0.106 912	-1.4856	185.0932
13	O	-0.878 612	2.600 136	-0.357 050	—	—
14	O	-1.967 516	0.702 502	-0.182 550	—	—
15	H	-1.677 010	-0.710 096	1.302 604	27.2441	4.6208
16	C	-3.452 943	-1.111 894	0.171 597	161.3388	22.2688

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Table S38 – continued from previous page

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
17	H	-4.082 382	-0.501 670	0.823 313	30.3986	1.4663
18	H	-3.812 671	-1.019 301	-0.857 053	30.6848	1.1801
19	H	-3.538 322	-2.157 893	0.478 386	30.7193	1.1456
20	H	0.876 259	1.750 069	1.151 868	29.5222	2.3427
21	C	2.422 119	-0.072 283	0.402 958	142.4021	41.2055
22	H	2.708 726	0.426 064	1.339 842	30.2754	1.5895
23	C	3.236 549	-1.364 436	0.310 256	161.0799	22.5277
24	H	3.039 825	-1.897 763	-0.625 891	30.9176	0.9473
25	H	4.307 701	-1.141 361	0.340 039	30.8613	1.0036
26	H	3.007 341	-2.039 141	1.141 759	31.0334	0.8315
27	C	2.764 357	0.866 706	-0.757 023	167.0320	16.5756
28	H	2.603 092	0.369 802	-1.719 924	31.3165	0.5484
29	H	2.155 654	1.777 468	-0.742 790	30.6446	1.2203
30	H	3.816 337	1.164 045	-0.709 490	31.1165	0.7484

Fig. S39 204a – Conformer 8

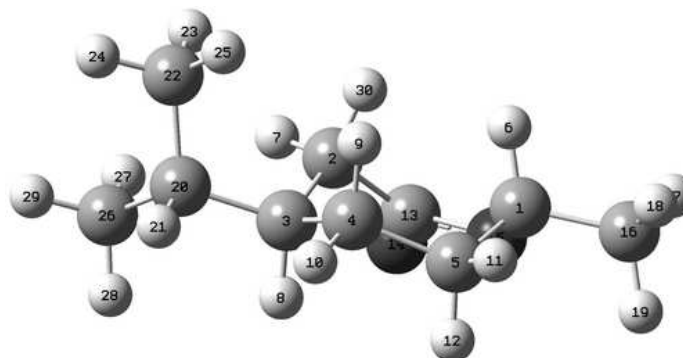
SCF Energy - E(RM062X) -542.161 921 458
SCF Energy from NMR - E(RB3LYP) -542.544 682 644
Sum of Electronic and Thermal Free Energies -541.929 255 000

Table S39 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **204a** – Conformer 8

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	2.262 643	-0.769 533	-0.237 074	103.0430	80.5646
2	C	-0.034 810	0.897 345	0.636 696	136.8196	46.7880
3	C	-0.908 528	-0.066 762	-0.194 215	135.6202	47.9874
4	C	-0.269 343	-1.456 473	-0.254 281	151.1870	32.4206
5	C	1.105 158	-1.490 097	-0.923 057	145.7829	37.8247
6	H	-0.608 151	1.776 676	0.929 153	29.0907	2.7742
7	H	-0.983 219	0.320 127	-1.223 416	30.8443	1.0206
8	H	-0.212 744	-1.872 302	0.762 333	30.3216	1.5433
9	H	-0.915 364	-2.127 195	-0.827 217	29.9557	1.9092
10	H	1.418 778	-2.535 905	-1.021 707	29.9107	1.9542
11	H	1.023 912	-1.092 333	-1.942 555	29.8988	1.9661
12	C	1.176 570	1.457 249	-0.074 764	-1.5131	185.1207
13	O	1.259 030	2.635 920	-0.361 533	—	—
14	O	2.208 890	0.671 250	-0.407 881	—	—
15	H	3.161 967	-1.006 816	-0.810 957	27.2734	4.5915
16	C	2.531 328	-1.166 669	1.208 094	165.3263	18.2813
17	H	3.380 507	-0.599 314	1.596 439	30.4101	1.4548
18	H	1.677 394	-1.015 430	1.869 550	29.9268	1.9381
19	H	2.787 663	-2.229 959	1.233 455	30.8808	0.9841
20	H	0.276 352	0.393 113	1.557 078	29.4249	2.4400
21	C	-2.338 957	-0.080 454	0.398 811	144.4375	39.1701
22	H	-2.239 223	-0.167 917	1.491 809	30.7329	1.1320
23	C	-3.081 850	1.221 548	0.077 076	159.9284	23.6792
24	H	-3.258 701	1.290 453	-1.002 865	31.3435	0.5214
25	H	-4.054 628	1.241 627	0.577 572	30.9108	0.9541
26	H	-2.533 254	2.116 235	0.382 373	30.4032	1.4617
27	C	-3.182 250	-1.260 403	-0.094 585	161.3709	22.2367
28	H	-3.207 569	-1.284 067	-1.191 222	31.3235	0.5414
29	H	-2.804 552	-2.222 713	0.259 293	30.5854	1.2795
30	H	-4.212 283	-1.156 157	0.260 005	30.9741	0.8908

S-I.7 Normal *trans*-Carvomenthide (204b)

Fig. S40 204b – Conformer 1



SCF Energy - E(RM062X) -542.168 496 435
 SCF Energy from NMR - E(RB3LYP) -542.551 625 328
 Sum of Electronic and Thermal Free Energies -541.936 203 000

Table S40 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **204b** – Conformer 1

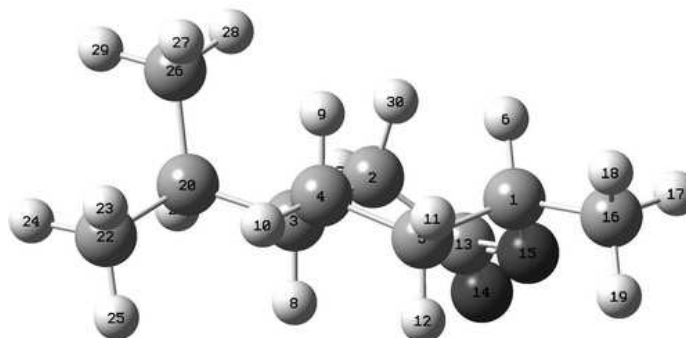
Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	2.122 385	-0.523 656	0.292 566	101.7056	81.9020
2	C	-0.425 554	0.745 873	0.633 425	145.2387	38.3689
3	C	-0.943 615	-0.258 234	-0.422 757	137.1790	46.4286
4	C	-0.138 409	-1.560 578	-0.394 293	143.4141	40.1935
5	C	1.353 278	-1.402 395	-0.690 473	142.9742	40.6334
6	H	1.776 910	-0.697 302	1.319 277	27.3507	4.5142
7	H	-1.181 238	1.499 912	0.858 411	29.4730	2.3919
8	H	-0.812 019	0.197 746	-1.415 613	30.3403	1.5246
9	H	-0.250 092	-2.031 528	0.591 928	30.1035	1.7614
10	H	-0.568 719	-2.254 968	-1.125 348	30.2510	1.6139
11	H	1.817 720	-2.394 598	-0.675 621	30.0032	1.8617
12	H	1.509 702	-0.993 560	-1.697 368	30.2589	1.6060
13	C	0.775 824	1.517 104	0.145 834	-3.1892	186.7968
14	O	0.726 076	2.696 780	-0.140 374	—	—
15	O	1.946 429	0.883 315	-0.012 145	—	—
16	C	3.621 340	-0.749 593	0.213 851	159.1872	24.4204

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Table S40 – continued from previous page

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
17	H	4.149 303	-0.056 668	0.872 750	30.4775	1.3874
18	H	3.857 157	-1.772 977	0.515 305	30.8251	1.0398
19	H	3.970 709	-0.595 802	-0.811 680	30.5357	1.3292
20	C	-2.456 972	-0.522 955	-0.255 163	143.6497	39.9579
21	H	-2.693 970	-1.352 553	-0.936 017	30.2383	1.6266
22	C	-2.839 234	-0.955 721	1.163 350	167.4817	16.1259
23	H	-2.675 671	-0.142 490	1.879 701	31.4642	0.4007
24	H	-3.900 810	-1.218 255	1.203 598	31.1362	0.7287
25	H	-2.268 048	-1.826 222	1.499 531	30.8266	1.0383
26	C	-3.297 378	0.679 814	-0.690 433	160.6420	22.9656
27	H	-3.133 358	1.543 491	-0.036 671	30.8250	1.0399
28	H	-3.056 646	0.981 686	-1.714 645	30.9807	0.8842
29	H	-4.363 451	0.435 604	-0.647 972	30.9113	0.9536
30	H	-0.187 503	0.219 767	1.565 142	29.4934	2.3715

Fig. S41 204b – Conformer 2

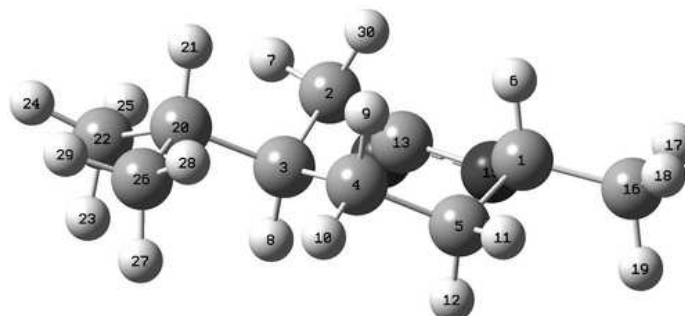


SCF Energy - E(RM062X) -542.168 389 401
 SCF Energy from NMR - E(RB3LYP) -542.551 370 060
 Sum of Electronic and Thermal Free Energies -541.936 133 000

Table S41 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **204b** – Conformer 2

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	1.998 079	-0.722 052	0.357 293	101.5874	82.0202
2	C	-0.195 151	1.110 832	0.549 906	137.0237	46.5839
3	C	-0.976 258	0.098 184	-0.319 902	137.6292	45.9784
4	C	-0.469 111	-1.330 665	-0.104 202	152.4833	31.1243
5	C	1.003 606	-1.544 146	-0.458 021	143.3184	40.2892
6	H	1.683 140	-0.662 854	1.406 484	27.3668	4.4981
7	H	-0.769 640	2.032 988	0.661 422	29.6138	2.2511
8	H	-0.807 403	0.363 141	-1.374 770	30.2423	1.6226
9	H	-0.620 172	-1.610 825	0.947 442	30.5332	1.3317
10	H	-1.067 697	-2.023 411	-0.704 596	30.0668	1.7981
11	H	1.247 941	-2.600 806	-0.302 652	30.0001	1.8648
12	H	1.183 775	-1.329 682	-1.519 645	30.3680	1.4969
13	C	1.114 875	1.520 402	-0.076 082	-2.9691	186.5767
14	O	1.304 079	2.627 901	-0.538 345	—	—
15	O	2.112 153	0.628 334	-0.159 060	—	—
16	C	3.406 409	-1.283 495	0.281 151	159.1620	24.4456
17	H	4.108 158	-0.631 920	0.806 605	30.4905	1.3744
18	H	3.433 958	-2.274 829	0.739 885	30.8289	1.0360
19	H	3.720 618	-1.370 204	-0.763 450	30.5354	1.3295
20	C	-2.494 101	0.252 142	-0.072 167	142.6093	40.9983
21	H	-2.726 526	1.304 180	-0.288 286	30.1224	1.7425
22	C	-3.321 262	-0.604 972	-1.033 551	160.4254	23.1822
23	H	-3.242 068	-1.669 801	-0.790 363	30.9554	0.9095
24	H	-4.379 108	-0.332 134	-0.968 907	30.7994	1.0655
25	H	-2.997 214	-0.466 528	-2.070 628	30.9799	0.8850
26	C	-2.903 383	-0.026 048	1.377 018	167.7908	15.8168
27	H	-2.736 217	-1.075 884	1.641 412	31.2656	0.5993
28	H	-2.352 922	0.597 765	2.088 335	30.9611	0.9038
29	H	-3.969 764	0.180 233	1.511 503	31.1100	0.7549
30	H	-0.020 939	0.699 603	1.550 799	29.0086	2.8563

Fig. S42 204b – Conformer 3



SCF Energy - E(RM062X) -542.167 141 614
 SCF Energy from NMR - E(RB3LYP) -542.550 372 752
 Sum of Electronic and Thermal Free Energies -541.934 520 000

Table S42 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **204b** – Conformer 3

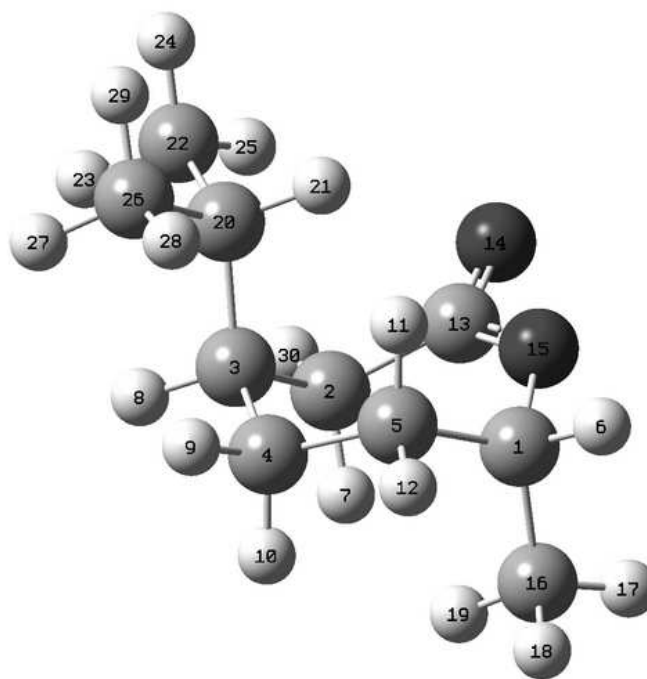
Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	2.142 659	-0.593 717	0.306 707	102.0999	81.5077
2	C	-0.233 064	0.934 500	0.723 419	139.9874	43.6202
3	C	-0.980 613	-0.131 631	-0.113 250	135.8838	47.7238
4	C	-0.273 106	-1.486 530	-0.007 856	145.1380	38.4696
5	C	1.187 150	-1.498 698	-0.465 275	142.9449	40.6627
6	H	1.909 499	-0.605 721	1.378 225	27.3167	4.5482
7	H	-0.882 124	1.781 284	0.944 934	29.2391	2.6258
8	H	-0.973 480	0.181 015	-1.169 819	30.8168	1.0481
9	H	-0.327 117	-1.829 254	1.036 847	30.6413	1.2236
10	H	-0.810 690	-2.224 839	-0.609 141	29.8122	2.0527
11	H	1.564 238	-2.523 517	-0.374 550	29.9891	1.8758
12	H	1.259 718	-1.228 915	-1.527 276	30.3423	1.5226
13	C	0.957 915	1.522 265	0.007 463	-1.9837	185.5913
14	O	0.959 281	2.649 377	-0.446 034	—	—
15	O	2.057 761	0.775 703	-0.162 081	—	—
16	C	3.595 022	-0.982 815	0.098 514	159.2483	24.3593
17	H	4.257 943	-0.270 173	0.594 255	30.4899	1.3750
18	H	3.773 796	-1.978 063	0.512 381	30.8293	1.0356
19	H	3.830 610	-0.998 744	-0.969 954	30.5446	1.3203

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Table S42 – continued from previous page

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
20	C	-2.459 420	-0.185 276	0.340 108	144.1613	39.4463
21	H	-2.463 596	-0.198 704	1.441 045	30.7460	1.1189
22	C	-3.225 535	1.052 929	-0.139 235	160.1732	23.4344
23	H	-3.305 758	1.038 801	-1.232 672	31.3456	0.5193
24	H	-4.239 741	1.059 680	0.271 307	30.9135	0.9514
25	H	-2.744 795	1.992 165	0.146 292	30.3754	1.4895
26	C	-3.192 414	-1.437 179	-0.151 863	161.6617	21.9459
27	H	-3.107 496	-1.529 217	-1.241 865	31.3640	0.5009
28	H	-2.805 946	-2.354 097	0.299 641	30.6177	1.2472
29	H	-4.256 330	-1.366 990	0.094 556	30.9847	0.8802
30	H	0.073 374	0.491 564	1.678 327	29.4210	2.4439

Fig. S43 204b – Conformer 4



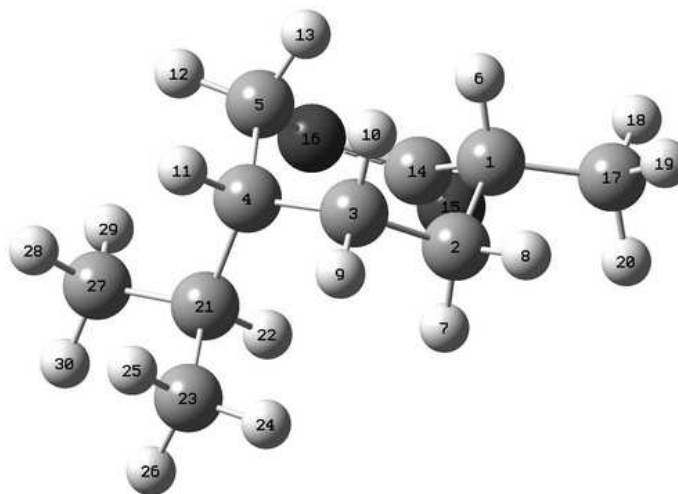
SCF Energy - E(RM062X) -542.164 337 332
 SCF Energy from NMR - E(RB3LYP) -542.543 500 218
 Sum of Electronic and Thermal Free Energies -541.931 298 000

Table S43 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **204b** – Conformer 4

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	-2.009 190	-0.507 958	-0.635 952	102.5076	81.1000
2	C	-0.024 602	0.843 067	1.158 642	137.7345	45.8731
3	C	0.829 936	-0.407 395	0.864 811	137.9671	45.6405
4	C	-0.057 485	-1.641 904	0.659 809	153.7936	29.8140
5	C	-0.935 129	-1.592 801	-0.589 961	151.7196	31.8880
6	H	-2.570 417	-0.661 064	-1.561 172	27.2750	4.5899
7	H	-0.820 817	0.588 516	1.863 814	29.0455	2.8194
8	H	1.417 032	-0.586 423	1.777 380	30.5580	1.3069
9	H	0.569 927	-2.537 120	0.609 228	29.8975	1.9674
10	H	-0.688 251	-1.768 924	1.548 677	29.9325	1.9324
11	H	-0.314 924	-1.491 848	-1.488 541	29.6320	2.2329
12	H	-1.467 458	-2.546 205	-0.688 292	30.2696	1.5953
13	C	-0.628 615	1.493 703	-0.068 829	-1.3381	184.9457
14	O	-0.352 444	2.633 497	-0.388 685	—	—
15	O	-1.474 311	0.823 443	-0.865 926	—	—
16	C	-3.012 019	-0.522 735	0.509 967	165.1863	18.4213
17	H	-3.750 945	0.269 078	0.365 539	30.4303	1.4346
18	H	-3.532 484	-1.484 877	0.504 438	30.9047	0.9602
19	H	-2.555 061	-0.397 994	1.492 613	29.8777	1.9872
20	C	1.843 874	-0.157 825	-0.272 653	150.3335	33.2741
21	H	1.291 186	0.123 705	-1.181 789	30.2457	1.6192
22	C	2.786 667	0.999 291	0.075 400	160.4932	23.1144
23	H	3.317 873	0.788 565	1.012 111	31.4008	0.4641
24	H	3.534 234	1.130 746	-0.712 585	30.9769	0.8880
25	H	2.254 329	1.947 425	0.187 416	30.2175	1.6474
26	C	2.659 654	-1.414 557	-0.587 710	161.2276	22.3800
27	H	3.150 092	-1.789 952	0.319 331	31.3554	0.5095
28	H	2.043 446	-2.219 941	-0.997 298	30.5684	1.2965
29	H	3.438 963	-1.186 495	-1.320 968	30.9845	0.8804
30	H	0.578 766	1.621 978	1.625 840	28.9064	2.9585

S-I.8 Abnormal *cis*-Carvomenthide (205a)

Fig. S44 205a – Conformer 1



SCF Energy - E(RM062X) -542.164 619 571
 SCF Energy from NMR - E(RB3LYP) -542.544 017 109
 Sum of Electronic and Thermal Free Energies -541.931 279 000

Table S44 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **205a** – Conformer 1

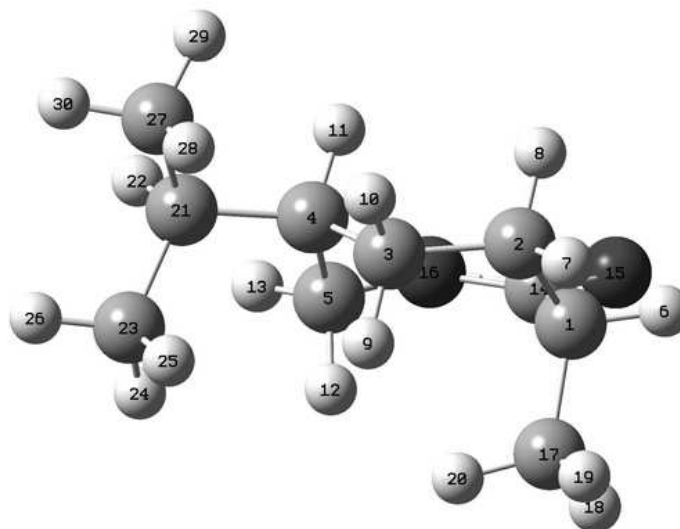
Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	-1.905 425	0.417 034	0.236 772	140.1980	43.4096
2	C	-0.890 383	1.506 432	-0.177 001	151.8476	31.7600
3	C	0.321 235	1.629 499	0.747 149	147.6298	35.9778
4	C	1.194 004	0.370 113	0.838 145	133.6748	49.9328
5	C	0.404 488	-0.797 930	1.434 280	110.2317	73.3759
6	H	-1.993 616	0.426 040	1.331 499	29.0793	2.7856
7	H	-0.580 174	1.333 593	-1.215 862	30.2808	1.5841
8	H	-1.427 824	2.460 731	-0.172 089	30.4274	1.4375
9	H	0.929 717	2.482 300	0.431 896	29.7080	2.1569
10	H	-0.038 809	1.867 716	1.757 006	30.2667	1.5982
11	H	1.990 609	0.582 628	1.567 864	30.6219	1.2430
12	H	1.074 294	-1.561 679	1.829 852	27.3954	4.4695

Continued on next page

Table S44 – continued from previous page

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
13	H	-0.243 814	-0.461 462	2.250 346	27.4509	4.4140
14	C	-1.424 755	-0.965 415	-0.174 454	-5.7268	189.3344
15	O	-1.946 793	-1.613 170	-1.057 677	—	—
16	O	-0.373 442	-1.513 700	0.457 366	—	—
17	C	-3.277 696	0.687 231	-0.375 648	162.9619	20.6457
18	H	-3.992 487	-0.097 297	-0.117 966	30.6775	1.1874
19	H	-3.657 605	1.643 853	-0.007 652	31.0531	0.8118
20	H	-3.207 234	0.736 379	-1.465 744	30.6055	1.2594
21	C	1.886 624	-0.017 271	-0.485 751	153.5849	30.0227
22	H	1.114 266	-0.261 880	-1.227 566	30.1582	1.7067
23	C	2.720 634	1.141 663	-1.038 411	161.3452	22.2624
24	H	2.103 499	1.996 734	-1.327 610	30.5953	1.2696
25	H	3.447 958	1.483 580	-0.291 313	31.3681	0.4968
26	H	3.275 526	0.819 590	-1.924 701	30.9699	0.8950
27	C	2.766 695	-1.258 342	-0.307 666	161.1646	22.4430
28	H	3.508 802	-1.092 817	0.483 602	31.3011	0.5638
29	H	2.179 284	-2.143 769	-0.050 104	30.3313	1.5336
30	H	3.306 957	-1.477 359	-1.233 455	30.9122	0.9527

Fig. S45 205a – Conformer 2

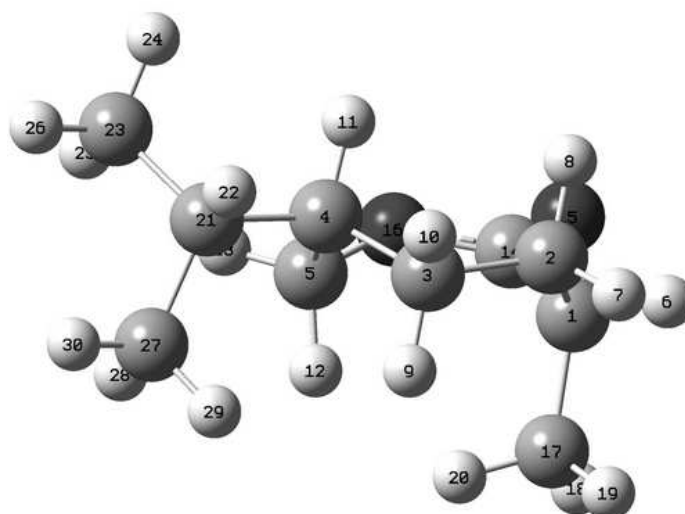


SCF Energy - E(RM062X) -542.158 664 695
 SCF Energy from NMR - E(RB3LYP) -542.540 917 545
 Sum of Electronic and Thermal Free Energies -541.926 295 000

Table S45 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **205a** – Conformer 2

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	2.007 276	0.832 462	-0.109 601	134.3871	49.2205
2	C	0.833 531	1.421 723	-0.911 356	149.6918	33.9158
3	C	-0.574 726	1.179 021	-0.369 364	158.7669	24.8407
4	C	-0.991 588	-0.293 534	-0.377 466	132.6224	50.9852
5	C	-0.122 159	-1.129 858	0.558 146	104.0576	79.5500
6	H	2.921 158	1.201 870	-0.582 661	28.8329	3.0320
7	H	1.008 333	2.502 648	-0.960 171	30.1060	1.7589
8	H	0.891 661	1.050 174	-1.942 425	30.0651	1.7998
9	H	-0.654 692	1.578 982	0.649 874	30.2057	1.6592
10	H	-1.270 151	1.758 620	-0.985 263	30.2066	1.6583
11	H	-0.837 635	-0.692 102	-1.391 845	30.2510	1.6139
12	H	0.038 398	-0.633 310	1.519 052	27.2697	4.5952
13	H	-0.602 522	-2.091 202	0.754 590	27.8750	3.9899
14	C	2.163 873	-0.675 201	-0.246 891	-4.7326	188.3402
15	O	3.215 176	-1.170 763	-0.602 140	—	—
16	O	1.149 035	-1.516 990	0.003 060	—	—
17	C	2.058 627	1.291 359	1.356 402	167.5349	16.0727
18	H	2.963 600	0.917 468	1.842 258	30.4906	1.3743
19	H	2.085 201	2.384 898	1.379 761	30.8884	0.9765
20	H	1.197 916	0.969 079	1.944 575	30.1811	1.6838
21	C	-2.482 533	-0.516 515	-0.032 119	145.3002	38.3074
22	H	-2.650 298	-1.600 243	-0.104 299	30.0352	1.8297
23	C	-2.844 352	-0.083 680	1.392 878	166.5511	17.0565
24	H	-2.238 098	-0.594 586	2.147 844	31.1062	0.7587
25	H	-2.712 627	0.996 052	1.522 514	31.1589	0.7060
26	H	-3.893 842	-0.314 485	1.600 666	31.1043	0.7606
27	C	-3.412 697	0.155 816	-1.044 372	160.1220	23.4856
28	H	-3.402 686	1.245 425	-0.936 366	30.8976	0.9673
29	H	-3.125 695	-0.088 076	-2.072 785	30.9724	0.8925
30	H	-4.443 210	-0.178 746	-0.890 219	30.8078	1.0571

Fig. S46 205a – Conformer 3



SCF Energy - E(RM062X) -542.158 493 639
SCF Energy from NMR - E(RB3LYP) -542.540 986 250
Sum of Electronic and Thermal Free Energies -541.926 197 000

Table S46 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for 205a – Conformer 3

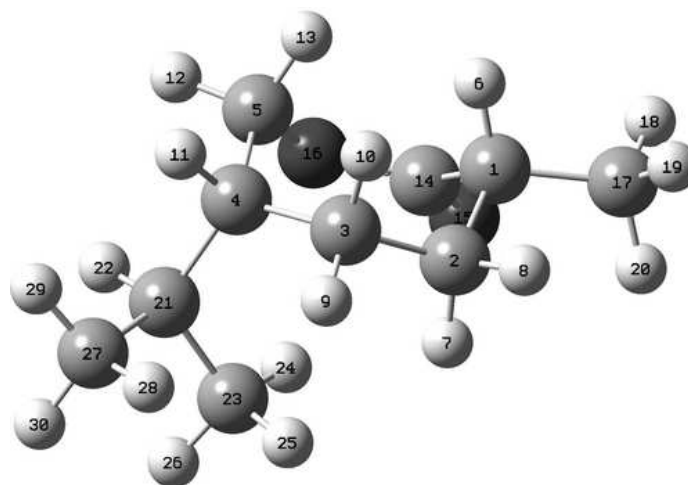
Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	2.136 246	0.603 034	-0.192 058	134.4397	49.1679
2	C	1.143 321	1.204 678	-1.201 740	149.4707	34.1369
3	C	-0.311 870	1.332 213	-0.754 916	149.2368	34.3708
4	C	-1.005 716	-0.007 720	-0.498 085	132.5612	51.0464
5	C	-0.365 318	-0.760 700	0.665 076	110.1393	73.4683
6	H	3.128 089	0.692 559	-0.643 180	28.8437	3.0212
7	H	1.523 495	2.202 576	-1.448 649	30.1301	1.7348
8	H	1.186 764	0.616 884	-2.127 523	29.9523	1.9126
9	H	-0.371 078	1.958 190	0.145 275	29.7587	2.1062
10	H	-0.861 566	1.866 774	-1.538 743	30.4212	1.4437
11	H	-0.882 218	-0.636 274	-1.392 985	30.3138	1.5511
12	H	-0.162 336	-0.098 616	1.511 257	27.5405	4.3244
13	H	-1.021 482	-1.558 006	1.017 362	27.7181	4.1468

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Table S46 – continued from previous page

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
14	C	2.003 653	-0.902 390	-0.010 179	-4.9593	188.5669
15	O	2.954 491	-1.642 696	-0.168 348	—	—
16	O	0.835 749	-1.476 209	0.317 734	—	—
17	C	2.198 420	1.350 515	1.149 402	167.5304	16.0772
18	H	2.987 258	0.934 987	1.781 800	30.4868	1.3781
19	H	2.435 590	2.400 469	0.953 180	30.8753	0.9896
20	H	1.262 468	1.322 484	1.709 649	30.1818	1.6831
21	C	-2.525 711	0.171 575	-0.271 525	144.0643	39.5433
22	H	-2.865 312	0.863 491	-1.054 067	30.2265	1.6384
23	C	-3.296 955	-1.138 062	-0.456 399	160.4714	23.1362
24	H	-3.088 008	-1.586 718	-1.432 632	30.8514	1.0135
25	H	-3.041 803	-1.872 438	0.315 549	30.7919	1.0730
26	H	-4.374 278	-0.956 830	-0.388 645	30.8558	1.0091
27	C	-2.860 587	0.801 284	1.085 647	166.3115	17.2961
28	H	-2.612 189	0.121 447	1.908 947	31.5108	0.3541
29	H	-2.325 738	1.742 039	1.247 608	30.6856	1.1793
30	H	-3.932 485	1.011 661	1.149 377	31.0708	0.7941

Fig. S47 205a – Conformer 4

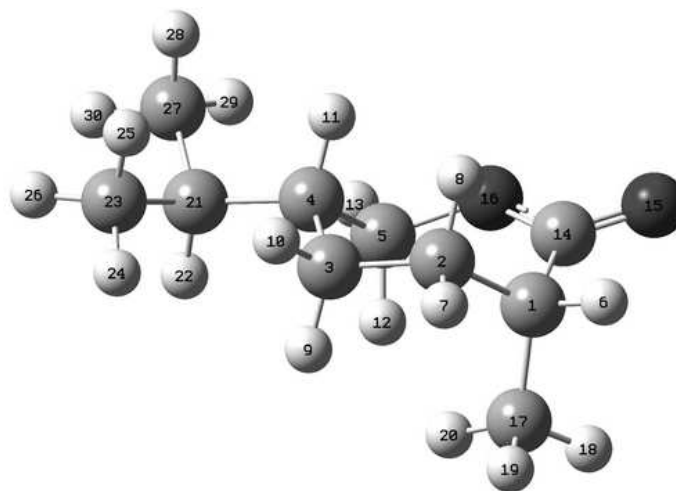


SCF Energy - E(RM062X) -542.160 145 896
 SCF Energy from NMR - E(RB3LYP) -542.540 171 877
 Sum of Electronic and Thermal Free Energies -541.926 339 000

Table S47 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **205a** – Conformer 4

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	-1.838 755	0.594 849	0.237 352	141.6817	41.9259
2	C	-0.716 745	1.424 264	-0.425 186	148.1818	35.4258
3	C	0.574 349	1.561 566	0.392 079	152.6104	30.9972
4	C	1.278 150	0.276 983	0.867 935	137.0764	46.5312
5	C	0.328 881	-0.695 029	1.559 402	105.7452	77.8624
6	H	-1.841 737	0.801 869	1.314 814	28.9269	2.9380
7	H	-0.527 501	1.017 602	-1.423 910	30.1757	1.6892
8	H	-1.115 348	2.433 408	-0.577 991	30.3544	1.5105
9	H	1.285 701	2.169 555	-0.179 464	29.7708	2.0941
10	H	0.326 606	2.146 790	1.287 505	30.1590	1.7059
11	H	1.942 344	0.592 695	1.686 102	30.3298	1.5351
12	H	0.903 432	-1.471 657	2.067 537	27.6466	4.2183
13	H	-0.288 885	-0.184 505	2.305 929	27.1633	4.7016
14	C	-1.558 047	-0.882 346	0.030 169	-5.5380	189.1456
15	O	-2.205 985	-1.586 467	-0.716 012	—	—
16	O	-0.513 265	-1.441 310	0.661 842	—	—
17	C	-3.204 221	0.952 162	-0.343 452	163.5024	20.1052
18	H	-3.992 832	0.322 451	0.074 549	30.6798	1.1851
19	H	-3.433 184	1.997 336	-0.119 801	31.0708	0.7941
20	H	-3.205 126	0.819 733	-1.428 965	30.6682	1.1967
21	C	2.199 428	-0.417 366	-0.165 472	145.0504	38.5572
22	H	2.405 884	-1.422 710	0.228 718	29.8416	2.0233
23	C	1.606 770	-0.583 023	-1.568 875	160.6382	22.9694
24	H	0.643 259	-1.099 334	-1.563 200	30.6157	1.2492
25	H	1.479 352	0.391 489	-2.053 794	31.1155	0.7494
26	H	2.294 245	-1.167 267	-2.188 795	30.9474	0.9175
27	C	3.537 149	0.323 341	-0.267 148	157.9734	25.6342
28	H	3.389 428	1.348 046	-0.628 108	30.7753	1.0896
29	H	4.040 769	0.375 118	0.703 351	31.0013	0.8636
30	H	4.205 825	-0.180 821	-0.971 949	30.9211	0.9438

Fig. S48 205a – Conformer 5



SCF Energy - E(RM062X) -542.157 349 822
SCF Energy from NMR - E(RB3LYP) -542.539 920 978
Sum of Electronic and Thermal Free Energies -541.924 665 000

Table S48 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for 205a – Conformer 5

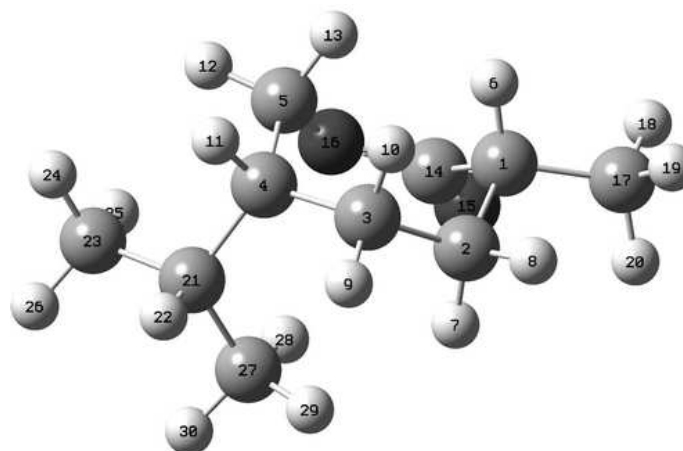
Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	2.117 892	0.726 086	-0.150 466	134.7655	48.8421
2	C	0.965 842	1.408 661	-0.906 978	149.8664	33.7412
3	C	-0.431 846	1.348 122	-0.290 271	151.4980	32.1096
4	C	-1.026 639	-0.059 883	-0.209 530	131.7684	51.8392
5	C	-0.166 347	-0.962 016	0.673 727	107.0765	76.5311
6	H	3.035 398	0.984 277	-0.686 287	28.8467	3.0182
7	H	1.250 062	2.462 138	-1.011 050	30.1094	1.7555
8	H	0.924 667	0.997 808	-1.924 013	30.0217	1.8432
9	H	-0.425 687	1.794 495	0.715 110	30.3757	1.4892
10	H	-1.078 379	1.980 975	-0.904 697	29.9963	1.8686
11	H	-1.043 213	-0.493 887	-1.221 928	30.6613	1.2036
12	H	0.120 357	-0.440 625	1.591 945	27.6167	4.2482
13	H	-0.715 647	-1.857 812	0.962 614	27.7094	4.1555
14	C	2.105 445	-0.791 458	-0.252 700	-5.0930	188.7006
15	O	3.082 060	-1.409 746	-0.627 342	—	—

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Table S48 – continued from previous page

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
16	O	1.005 732	-1.503 406	0.037 733	—	—
17	C	2.305 513	1.220 578	1.292 628	167.4136	16.1940
18	H	3.182 128	0.751 185	1.746 788	30.4686	1.3963
19	H	2.469 999	2.302 046	1.271 702	30.8657	0.9992
20	H	1.444 279	1.030 591	1.934 937	30.1812	1.6837
21	C	-2.474 442	-0.086 040	0.343 919	149.2472	34.3604
22	H	-2.410 773	-0.010 969	1.441 058	30.7956	1.0693
23	C	-3.333 222	1.080 571	-0.152 502	161.7564	21.8512
24	H	-2.978 140	2.047 134	0.212 925	30.6307	1.2342
25	H	-3.344 378	1.111 455	-1.248 988	31.2964	0.5685
26	H	-4.365 320	0.953 393	0.188 292	30.9871	0.8778
27	C	-3.174 967	-1.402 138	-0.015 046	159.9687	23.6389
28	H	-3.333 354	-1.453 703	-1.098 614	31.2739	0.5910
29	H	-2.603 951	-2.286 569	0.280 068	30.4918	1.3731
30	H	-4.153 757	-1.461 619	0.470 325	30.8856	0.9793

Fig. S49 205a – Conformer 6

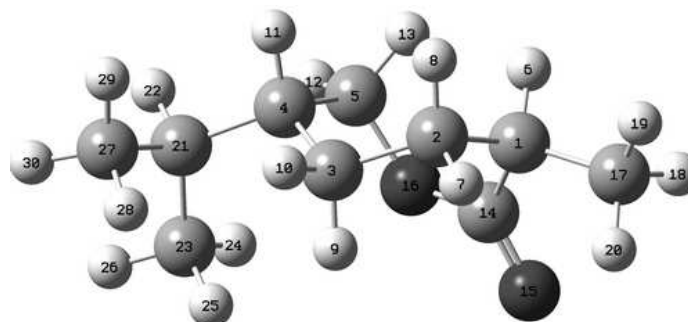


SCF Energy - E(RM062X) -542.160 100 797
 SCF Energy from NMR - E(RB3LYP) -542.539 573 001
 Sum of Electronic and Thermal Free Energies -541.925 874 000

Table S49 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **205a** – Conformer 6

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	1.900 491	0.340 272	-0.295 821	141.7129	41.8947
2	C	1.053 930	1.396 176	0.448 510	148.0961	35.5115
3	C	-0.218 808	1.857 168	-0.274 344	146.3933	37.2143
4	C	-1.243 104	0.792 515	-0.707 941	138.0291	45.5785
5	C	-0.598 545	-0.360 232	-1.470 559	111.8138	71.7938
6	H	1.887 197	0.565 783	-1.369 523	28.8870	2.9779
7	H	0.841 477	1.018 490	1.453 779	30.0411	1.8238
8	H	1.690 597	2.277 708	0.583 168	30.2986	1.5663
9	H	-0.728 637	2.599 194	0.352 841	29.9539	1.9110
10	H	0.103 095	2.389 155	-1.179 441	29.8678	1.9971
11	H	-1.862 584	1.276 923	-1.477 802	30.2170	1.6479
12	H	-1.360 193	-0.966 653	-1.961 525	27.3492	4.5157
13	H	0.075 925	0.017 679	-2.245 847	27.3294	4.5355
14	C	1.286 883	-1.031 489	-0.081 194	-5.3216	188.9292
15	O	1.795 455	-1.889 549	0.609 908	—	—
16	O	0.097 772	-1.307 226	-0.640 005	—	—
17	C	3.345 420	0.348 238	0.195 913	163.4816	20.1260
18	H	3.931 660	-0.443 607	-0.275 680	30.6731	1.1918
19	H	3.804 075	1.312 589	-0.037 715	31.0653	0.7996
20	H	3.382 743	0.198 036	1.278 455	30.6765	1.1884
21	C	-2.245 434	0.364 327	0.392 175	144.5890	39.0186
22	H	-2.849 342	1.261 852	0.588 033	30.0042	1.8607
23	C	-3.194 806	-0.726 728	-0.110 967	160.3968	23.2108
24	H	-3.621 571	-0.472 141	-1.087 735	30.8990	0.9659
25	H	-2.674 297	-1.686 650	-0.203 794	30.6469	1.2180
26	H	-4.020 229	-0.865 182	0.593 642	30.7920	1.0729
27	C	-1.631 625	-0.051 583	1.733 908	161.9697	21.6379
28	H	-0.943 860	-0.896 105	1.624 233	30.9017	0.9632
29	H	-1.098 616	0.775 448	2.210 279	30.5531	1.3118
30	H	-2.429 678	-0.360 303	2.417 317	31.0465	0.8184

Fig. S50 205a – Conformer 7



SCF Energy - E(RM062X) -542.160 414 157
SCF Energy from NMR - E(RB3LYP) -542.540 979 083
Sum of Electronic and Thermal Free Energies -541.927 954 000

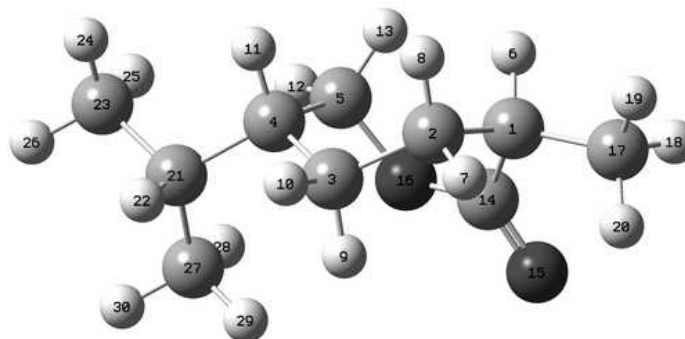
Table S50 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for 205a – Conformer 7

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	-2.042 015	0.503 283	0.336 448	143.0289	40.5787
2	C	-1.030 875	1.586 086	-0.137 160	149.6777	33.9299
3	C	0.370 966	1.091 689	-0.510 465	159.9780	23.6296
4	C	1.153 847	0.461 222	0.647 229	134.9334	48.6742
5	C	0.315 220	-0.605 646	1.363 920	108.3262	75.2814
6	H	-2.066 106	0.492 907	1.431 389	28.7579	3.1070
7	H	-1.461 118	2.067 990	-1.021 766	30.5200	1.3449
8	H	-0.958 327	2.356 915	0.638 559	30.0018	1.8631
9	H	0.289 023	0.374 202	-1.337 158	30.5828	1.2821
10	H	0.936 941	1.942 825	-0.900 562	30.3287	1.5362
11	H	1.335 222	1.250 489	1.391 862	30.1598	1.7051
12	H	0.956 993	-1.337 703	1.859 456	27.8188	4.0461
13	H	-0.332 114	-0.162 808	2.124 065	27.1659	4.6990
14	C	-1.600 445	-0.884 333	-0.094 982	-3.9626	187.5702
15	O	-2.195 561	-1.567 854	-0.900 623	—	—
16	O	-0.480 149	-1.389 834	0.455 112	—	—
17	C	-3.450 955	0.801 070	-0.166 335	163.6585	19.9491
18	H	-4.174 707	0.080 028	0.220 979	30.7556	1.1093
19	H	-3.747 987	1.802 679	0.157 491	30.9206	0.9443

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Table S50 – continued from previous page

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
20	H	-3.483 254	0.765 339	-1.258 474	30.7045	1.1604
21	C	2.537 263	-0.086 483	0.231 861	143.9978	39.6098
22	H	3.018 766	-0.417 982	1.163 289	30.1116	1.7533
23	C	2.458 628	-1.298 455	-0.701 303	165.7822	17.8254
24	H	1.872 716	-2.113 635	-0.267 234	30.5944	1.2705
25	H	2.002 837	-1.033 080	-1.661 159	31.0978	0.7671
26	H	3.465 101	-1.676 585	-0.907 244	31.0899	0.7750
27	C	3.421 204	1.003 725	-0.378 540	160.7841	22.8235
28	H	3.065 868	1.290 842	-1.374 026	31.0252	0.8397
29	H	3.439 850	1.902 104	0.248 504	31.0277	0.8372
30	H	4.448 950	0.644 036	-0.487 916	30.8579	1.0070

Fig. S51 205a – Conformer 8

SCF Energy - E(RM062X) -542.160 579 831
 SCF Energy from NMR - E(RB3LYP) -542.541 311 139
 Sum of Electronic and Thermal Free Energies -541.927 588 000

Table S51 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **205a** – Conformer 8

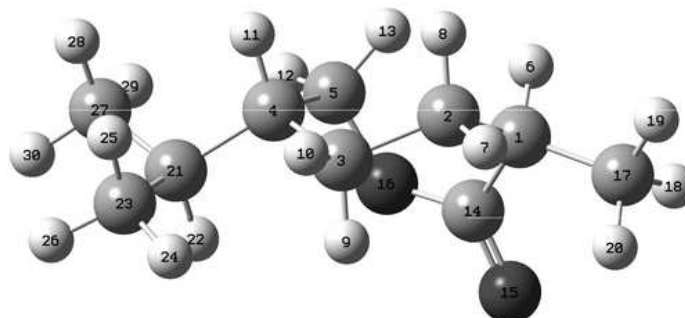
Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	2.064 214	-0.452 806	0.392 273	142.9824	40.6252
2	C	1.262 458	-1.541 598	-0.377 261	149.4797	34.1279

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Table S51 – continued from previous page

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
3	C	-0.119 500	-1.125 899	-0.890 694	151.3412	32.2664
4	C	-1.133 270	-0.763 363	0.200 616	134.7055	48.9021
5	C	-0.531 916	0.232 515	1.200 016	115.1821	68.4255
6	H	1.945 568	-0.618 244	1.468 523	28.7425	3.1224
7	H	1.864 870	-1.839 909	-1.242 053	30.5327	1.3322
8	H	1.170 762	-2.425 816	0.263 754	29.9010	1.9639
9	H	-0.004 968	-0.280 778	-1.581 882	30.2593	1.6056
10	H	-0.532 936	-1.948 334	-1.484 124	30.4517	1.4132
11	H	-1.341 812	-1.677 753	0.775 208	30.2751	1.5898
12	H	-1.306 057	0.807 172	1.711 958	27.6317	4.2332
13	H	0.057 264	-0.278 000	1.964 850	27.4432	4.4217
14	C	1.516 660	0.936 222	0.110 576	-4.1323	187.7399
15	O	2.126 904	1.798 767	-0.484 509	—	—
16	O	0.280 142	1.231 546	0.554 575	—	—
17	C	3.551 971	-0.520 436	0.062 971	163.6116	19.9960
18	H	4.125 630	0.196 832	0.654 712	30.7636	1.1013
19	H	3.925 587	-1.526 402	0.274 587	30.9211	0.9438
20	H	3.719 543	-0.302 588	-0.995 131	30.6906	1.1743
21	C	-2.472 931	-0.285 057	-0.401 675	145.9759	37.6317
22	H	-2.703 429	-0.975 536	-1.225 335	30.3384	1.5265
23	C	-3.611 484	-0.385 996	0.616 709	159.8148	23.7928
24	H	-3.715 026	-1.407 022	0.998 158	31.0576	0.8073
25	H	-3.440 801	0.279 417	1.471 154	30.9294	0.9355
26	H	-4.563 096	-0.093 940	0.161 726	30.8786	0.9863
27	C	-2.404 550	1.131 827	-0.980 319	164.8734	18.7342
28	H	-2.238 389	1.871 356	-0.188 986	31.1805	0.6844
29	H	-1.600 039	1.244 183	-1.712 586	30.6662	1.1987
30	H	-3.348 951	1.380 404	-1.474 330	31.0891	0.7758

Fig. S52 205a – Conformer 9



SCF Energy - E(RM062X) -542.160 224 026
SCF Energy from NMR - E(RB3LYP) -542.541 035 379
Sum of Electronic and Thermal Free Energies -541.927 132 000

Table S52 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for 205a – Conformer 9

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	2.128 294	0.256 322	-0.507 482	142.6059	41.0017
2	C	1.152 568	1.471 649	-0.517 757	150.5802	33.0274
3	C	-0.194 850	1.266 256	0.183 877	151.7950	31.8126
4	C	-1.146 074	0.297 407	-0.536 315	132.7391	50.8685
5	C	-0.358 694	-0.919 297	-1.023 929	112.8632	70.7444
6	H	2.193 161	-0.159 504	-1.520 204	28.7397	3.1252
7	H	1.664 815	2.302 295	-0.021 820	30.5386	1.3263
8	H	0.980 508	1.784 252	-1.554 267	29.9378	1.9271
9	H	-0.021 398	0.908 831	1.209 304	30.7199	1.1450
10	H	-0.682 055	2.240 174	0.282 456	30.0584	1.8065
11	H	-1.531 027	0.799 704	-1.438 177	30.8003	1.0646
12	H	-1.009 262	-1.743 133	-1.315 952	27.4732	4.3917
13	H	0.267 276	-0.669 018	-1.883 914	27.3822	4.4827
14	C	1.620 601	-0.879 009	0.367 716	-4.2805	187.8881
15	O	2.213 759	-1.307 432	1.334 297	—	—
16	O	0.454 228	-1.462 704	0.033 045	—	—
17	C	3.531 593	0.668 856	-0.073 753	163.0175	20.5901
18	H	4.228 123	-0.171 330	-0.118 388	30.7117	1.1532
19	H	3.896 041	1.462 500	-0.731 954	30.9278	0.9371

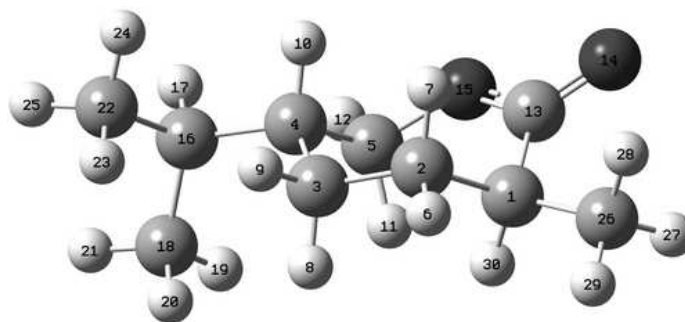
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Table S52 – continued from previous page

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
20	H	3.518 433	1.047 796	0.951 942	30.7134	1.1515
21	C	-2.354 037	-0.105 331	0.336 133	148.0367	35.5709
22	H	-1.981 707	-0.783 931	1.117 615	30.2267	1.6382
23	C	-2.996 421	1.106 136	1.019 457	161.7042	21.9034
24	H	-2.325 446	1.585 660	1.736 284	30.6104	1.2545
25	H	-3.290 402	1.854 770	0.272 559	31.4391	0.4258
26	H	-3.898 007	0.801 109	1.559 341	31.0196	0.8453
27	C	-3.421 959	-0.837 489	-0.483 166	160.4196	23.1880
28	H	-3.820 195	-0.174 509	-1.261 110	31.4341	0.4308
29	H	-3.043 268	-1.739 988	-0.969 982	30.4262	1.4387
30	H	-4.255 618	-1.137 581	0.158 851	30.8920	0.9729

S-I.9 Abnormal *trans*-Carvomenthene (205b)

Fig. S53 205b – Conformer 1



SCF Energy - E(RM062X) -542.163 734 082
 SCF Energy from NMR - E(RB3LYP) -542.545 617 507
 Sum of Electronic and Thermal Free Energies -541.930 878 000

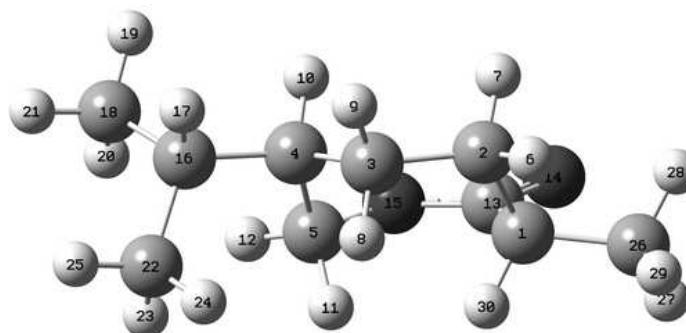
Table S53 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for 205b – Conformer 1

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	1.870 093	0.581 393	0.447 566	140.8188	42.7888
2	C	0.891 314	1.447 605	-0.377 237	146.6269	36.9807
3	C	-0.590 631	1.225 840	-0.071 370	152.5309	31.0767
4	C	-1.098 159	-0.188 717	-0.365 630	134.0328	49.5748
5	C	-0.334 062	-1.243 723	0.434 604	104.6113	78.9963
6	H	1.133 998	2.494 660	-0.166 617	30.1422	1.7227
7	H	1.088 310	1.292 226	-1.446 303	30.4352	1.4297
8	H	-0.764 601	1.458 772	0.988 272	30.4120	1.4529
9	H	-1.170 204	1.949 539	-0.653 621	30.0205	1.8444
10	H	-0.911 470	-0.410 300	-1.427 195	30.2542	1.6107
11	H	-0.164 904	-0.932 839	1.471 351	27.4679	4.3970
12	H	-0.890 394	-2.183 635	0.450 009	27.8288	4.0361
13	C	1.990 360	-0.801 103	-0.168 664	-5.4704	189.0780
14	O	3.004 039	-1.210 825	-0.694 578	—	—
15	O	0.919 757	-1.612 177	-0.168 718	—	—
16	C	-2.617 692	-0.358 004	-0.135 336	145.4479	38.1597
17	H	-2.853 712	-1.388 569	-0.435 923	30.0203	1.8446
18	C	-3.030 938	-0.197 930	1.331 871	166.7126	16.8950

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Table S53 – continued from previous page

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
19	H	-2.500 347	-0.893 589	1.989 963	31.1263	0.7386
20	H	-2.841 803	0.820 389	1.688 081	31.1665	0.6984
21	H	-4.102 588	-0.390 739	1.442 476	31.1076	0.7573
22	C	-3.440 450	0.576 533	-1.024 833	160.2474	23.3602
23	H	-3.358 321	1.617 520	-0.694 932	30.9418	0.9231
24	H	-3.114 143	0.522 721	-2.068 990	30.9874	0.8775
25	H	-4.499 064	0.302 102	-0.984 218	30.8259	1.0390
26	C	3.247 561	1.233 337	0.534 225	163.2771	20.3305
27	H	3.956 339	0.599 538	1.071 331	30.6658	1.1991
28	H	3.648 455	1.416 942	-0.466 635	30.6675	1.1974
29	H	3.164 689	2.189 968	1.056 477	31.0500	0.8149
30	H	1.465 012	0.467 928	1.461 665	29.0759	2.7890

Fig. S54 205b – Conformer 2

SCF Energy - E(RM062X) -542.163 578 052
 SCF Energy from NMR - E(RB3LYP) -542.545 705 624
 Sum of Electronic and Thermal Free Energies -541.930 800 000

Table S54 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **205b** – Conformer 2

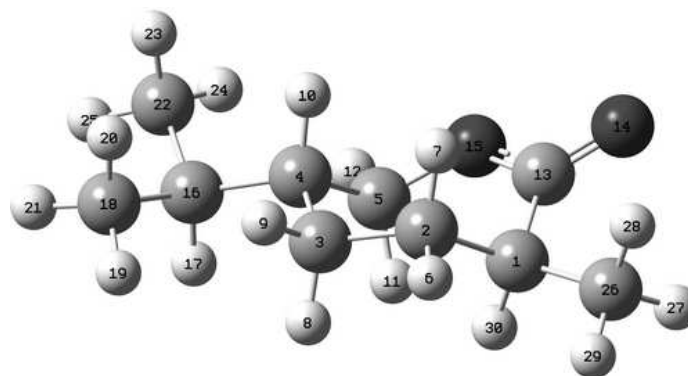
Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	-1.952 121	-0.545 803	0.327 558	141.0895	42.5181

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Table S54 – continued from previous page

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
2	C	-1.154 167	-1.341 606	-0.730 250	146.3249	37.2827
3	C	0.347 411	-1.446 257	-0.464 149	143.4994	40.1082
4	C	1.095 638	-0.110 421	-0.437 402	133.9752	49.6324
5	C	0.541 045	0.830 569	0.631 619	110.5671	73.0405
6	H	-1.572 856	-2.353 409	-0.755 311	30.1590	1.7059
7	H	-1.337 414	-0.904 657	-1.720 849	30.3356	1.5293
8	H	0.495 106	-1.961 065	0.495 304	30.0025	1.8624
9	H	0.795 505	-2.083 546	-1.235 384	30.2230	1.6419
10	H	0.943 683	0.389 828	-1.405 342	30.3370	1.5279
11	H	0.332 787	0.302 444	1.568 864	27.7421	4.1228
12	H	1.246 053	1.634 557	0.848 315	27.6678	4.1971
13	C	-1.831 024	0.943 802	0.058 987	-5.6819	189.2895
14	O	-2.760 200	1.632 446	-0.307 862	—	—
15	O	-0.635 596	1.539 167	0.200 817	—	—
16	C	2.618 179	-0.318 906	-0.260 515	144.9722	38.6354
17	H	2.890 141	-1.149 323	-0.926 125	30.2761	1.5888
18	C	3.418 985	0.906 857	-0.707 357	160.6349	22.9727
19	H	3.186 973	1.175 531	-1.742 601	30.8613	1.0036
20	H	3.208 781	1.777 767	-0.076 616	30.7630	1.1019
21	H	4.492 857	0.706 470	-0.639 308	30.8723	0.9926
22	C	3.008 048	-0.717 675	1.167 871	166.4409	17.1667
23	H	2.837 228	0.107 650	1.868 989	31.5241	0.3408
24	H	2.447 365	-1.587 386	1.523 541	30.7125	1.1524
25	H	4.072 634	-0.966 571	1.211 972	31.0985	0.7664
26	C	-3.422 624	-0.954 693	0.334 624	163.3525	20.2551
27	H	-4.000 107	-0.357 322	1.043 509	30.6765	1.1884
28	H	-3.862 488	-0.821 126	-0.657 740	30.6629	1.2020
29	H	-3.505 610	-2.008 431	0.612 959	31.0461	0.8188
30	H	-1.520 494	-0.749 512	1.316 272	29.0682	2.7967

Fig. S55 205b – Conformer 3



SCF Energy - E(RM062X) -542.162 592 398
SCF Energy from NMR - E(RB3LYP) -542.544 760 534
Sum of Electronic and Thermal Free Energies -541.929 880 000

Table S55 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for 205b – Conformer 3

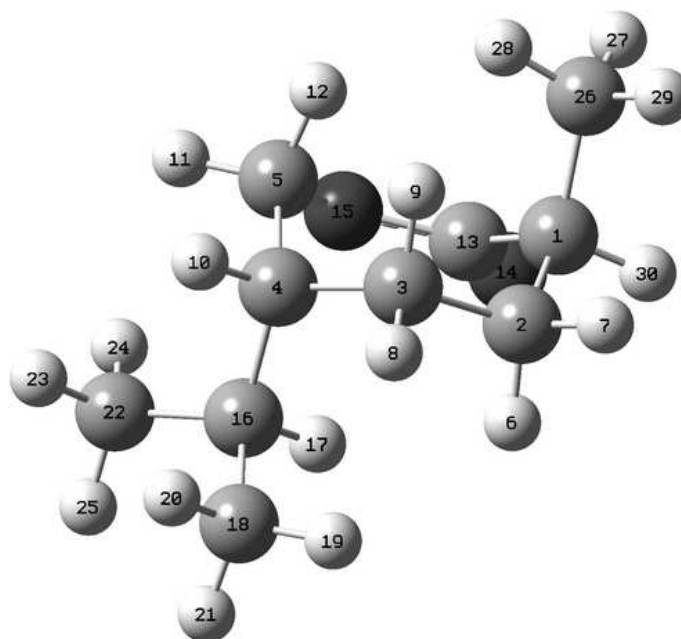
Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	1.985 793	0.557 603	0.375 962	141.3243	42.2833
2	C	1.018 010	1.419 012	-0.465 273	146.4985	37.1091
3	C	-0.452 193	1.372 112	-0.046 332	144.9448	38.6628
4	C	-1.117 943	-0.004 020	-0.145 563	133.0241	50.5835
5	C	-0.362 102	-1.037 516	0.691 438	107.4091	76.1985
6	H	1.361 237	2.456 151	-0.386 595	30.1504	1.7145
7	H	1.119 083	1.140 133	-1.522 695	30.4042	1.4607
8	H	-0.540 337	1.730 761	0.990 884	30.6028	1.2621
9	H	-0.996 337	2.085 182	-0.672 138	29.7922	2.0727
10	H	-1.085 150	-0.338 488	-1.194 376	30.7116	1.1533
11	H	-0.082 886	-0.620 127	1.666 113	27.7905	4.0744
12	H	-0.974 952	-1.920 161	0.872 302	27.6207	4.2442
13	C	1.940 367	-0.881 310	-0.103 038	-5.6122	189.2198
14	O	2.874 126	-1.436 035	-0.643 278	—	—
15	O	0.799 976	-1.576 827	0.037 347	—	—
16	C	-2.600 091	0.005 227	0.305 723	149.0898	34.5178
17	H	-2.610 140	-0.015 176	1.407 036	30.8063	1.0586

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Table S55 – continued from previous page

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
18	C	-3.360 023	1.256 310	-0.144 237	161.8707	21.7369
19	H	-2.981 736	2.167 756	0.324 768	30.6568	1.2081
20	H	-3.291 947	1.376 910	-1.232 428	31.3266	0.5383
21	H	-4.418 841	1.161 680	0.115 535	31.0002	0.8647
22	C	-3.339 825	-1.233 958	-0.212 277	160.1452	23.4624
23	H	-3.421 313	-1.187 290	-1.304 549	31.2808	0.5841
24	H	-2.838 902	-2.171 219	0.044 150	30.4493	1.4156
25	H	-4.353 133	-1.275 886	0.198 353	30.8966	0.9683
26	C	3.414 273	1.088 501	0.294 330	163.3999	20.2077
27	H	4.108 996	0.450 871	0.845 173	30.6630	1.2019
28	H	3.747 777	1.132 519	-0.746 297	30.6788	1.1861
29	H	3.452 114	2.096 597	0.715 166	31.0569	0.8080
30	H	1.656 054	0.580 923	1.422 640	29.0244	2.8405

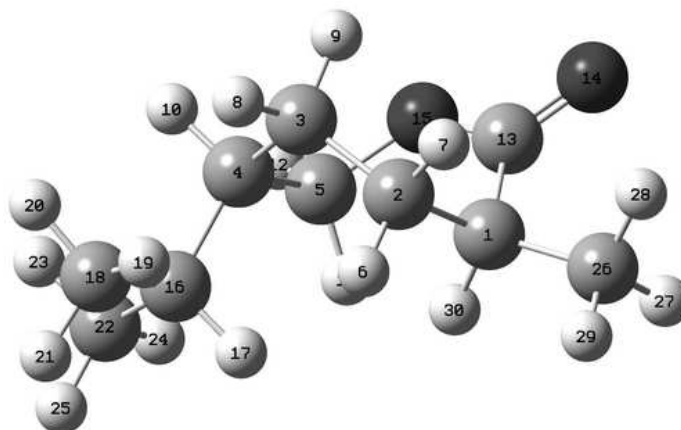
Fig. S56 205b – Conformer 4



SCF Energy - E(RM062X) -542.159 715 149
 SCF Energy from NMR - E(RB3LYP) -542.539 307 334
 Sum of Electronic and Thermal Free Energies -541.925 785 000

Table S56 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **205b** – Conformer 4

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	-1.888 046	0.463 261	-0.511 212	133.8130	49.7946
2	C	-0.757 967	1.481 899	-0.749 386	155.5131	28.0945
3	C	0.214 277	1.704 729	0.407 860	153.7684	29.8392
4	C	1.014 910	0.458 344	0.809 598	132.9585	50.6491
5	C	0.105 177	-0.600 259	1.431 443	109.9798	73.6278
6	H	-0.206 353	1.191 046	-1.651 556	29.8354	2.0295
7	H	-1.248 428	2.433 484	-0.984 472	30.4831	1.3818
8	H	0.900 718	2.513 084	0.137 347	29.9133	1.9516
9	H	-0.336 048	2.060 846	1.287 896	29.9852	1.8797
10	H	1.692 930	0.758 971	1.623 616	30.5793	1.2856
11	H	0.688 089	-1.318 718	2.008 508	27.4733	4.3916
12	H	-0.624 096	-0.146 119	2.107 030	27.2643	4.6006
13	C	-1.441 033	-0.992 536	-0.450 729	-5.1760	188.7836
14	O	-1.881 855	-1.817 229	-1.227 216	—	—
15	O	-0.573 695	-1.434 732	0.474 034	—	—
16	C	1.895 302	-0.122 137	-0.317 004	154.2387	29.3689
17	H	1.243 572	-0.473 353	-1.128 602	30.0807	1.7842
18	C	2.833 726	0.942 106	-0.892 009	161.4703	22.1373
19	H	2.289 692	1.751 312	-1.387 255	30.5520	1.3129
20	H	3.447 953	1.382 678	-0.096 611	31.3355	0.5294
21	H	3.507 736	0.495 712	-1.629 248	30.9435	0.9214
22	C	2.703 879	-1.325 949	0.176 062	161.3073	22.3003
23	H	3.314 579	-1.049 615	1.044 811	31.3139	0.5510
24	H	2.060 248	-2.163 227	0.459 398	30.3926	1.4723
25	H	3.378 281	-1.678 645	-0.609 877	30.9119	0.9530
26	C	-2.811 272	0.824 248	0.663 651	167.7184	15.8892
27	H	-3.635 399	0.109 658	0.736 921	30.5199	1.3450
28	H	-2.300 030	0.854 381	1.627 005	30.0764	1.7885
29	H	-3.235 207	1.816 420	0.482 666	30.9199	0.9450
30	H	-2.507 554	0.475 525	-1.411 758	28.8305	3.0344

Fig. S57 205b – Conformer 5

SCF Energy - E(RM062X) -542.161 614 596
 SCF Energy from NMR - E(RB3LYP) -542.541 053 565
 Sum of Electronic and Thermal Free Energies -541.927 499 000

Table S57 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for 205b – Conformer 5

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	1.502 087	0.611 453	0.581 018	142.7210	40.8866
2	C	0.640 311	1.414 413	-0.423 796	152.1622	31.4454
3	C	-0.254 505	0.555 170	-1.320 885	156.4561	27.1515
4	C	-1.150 224	-0.444 753	-0.576 611	136.7659	46.8417
5	C	-0.322 374	-1.487 084	0.210 596	108.0889	75.5187
6	H	0.041 708	2.133 775	0.146 783	29.9730	1.8919
7	H	1.317 437	1.996 023	-1.059 952	30.7309	1.1340
8	H	-0.881 217	1.207 532	-1.935 474	30.0931	1.7718
9	H	0.373 582	-0.001 120	-2.026 112	30.3121	1.5528
10	H	-1.721 472	-0.984 162	-1.345 471	30.2502	1.6147
11	H	-0.293 775	-1.246 981	1.278 386	27.7940	4.0709
12	H	-0.751 655	-2.484 106	0.109 536	27.4436	4.4213
13	C	1.948 176	-0.683 618	-0.072 910	-4.5023	188.1099
14	O	3.075 700	-0.889 774	-0.468 327	—	—
15	O	1.026 403	-1.648 148	-0.264 033	—	—
16	C	-2.177 252	0.214 106	0.366 985	147.3377	36.2699

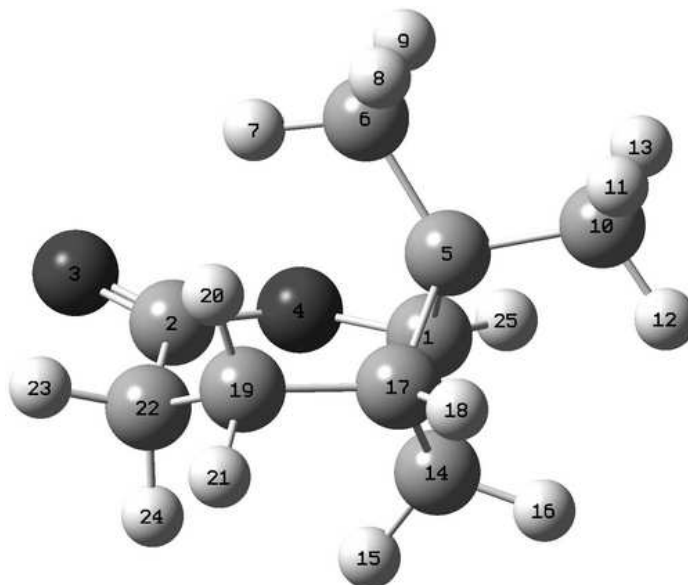
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Table S57 – continued from previous page

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
17	H	-1.624 517	0.683 089	1.196 191	30.2352	1.6297
18	C	-2.996 358	1.298 238	-0.336 598	160.9672	22.6404
19	H	-2.384 163	2.153 831	-0.634 565	30.5141	1.3508
20	H	-3.475 378	0.892 627	-1.236 310	31.3057	0.5592
21	H	-3.785 441	1.667 253	0.325 793	30.9707	0.8942
22	C	-3.119 351	-0.840 493	0.959 362	161.1783	22.4293
23	H	-3.681 172	-1.335 428	0.157 828	31.3871	0.4778
24	H	-2.585 007	-1.612 418	1.521 492	30.8091	1.0558
25	H	-3.840 607	-0.375 721	1.638 296	30.9065	0.9584
26	C	2.698 005	1.422 774	1.066 107	164.8698	18.7378
27	H	3.274 857	0.874 575	1.815 057	30.7622	1.1027
28	H	3.361 522	1.662 479	0.231 510	30.7043	1.1606
29	H	2.347 590	2.357 872	1.512 244	30.9646	0.9003
30	H	0.879 796	0.353 011	1.444 041	28.8748	2.9901

S-I.10 Normal Lactone of β -Pinene (206)

Fig. S58 206 – Conformer 1



SCF Energy - E(RM062X) -501.635 899 100
 SCF Energy from NMR - E(RB3LYP) -501.975 408 400
 Sum of Electronic and Thermal Free Energies -501.450 490 000

Table S58 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **206** – Conformer 1

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	-0.496 124	-0.504 913	-1.081 236	95.0974	88.5102
2	C	1.788 127	-0.396 856	-0.136 537	-2.5374	186.1450
3	O	2.790 865	-1.042 224	0.093 129	—	—
4	O	0.849 500	-0.978 317	-0.905 720	—	—
5	C	-1.272 166	-0.314 349	0.246 733	135.0936	48.5140
6	C	-0.819 271	-1.116 860	1.458 847	163.3260	20.2816
7	H	0.244 906	-1.012 551	1.686 374	30.8750	0.9899
8	H	-1.377 132	-0.795 292	2.345 238	31.1767	0.6882
9	H	-1.018 803	-2.181 480	1.298 483	31.1015	0.7634
10	C	-2.766 945	-0.538 718	0.013 080	154.7181	28.8895

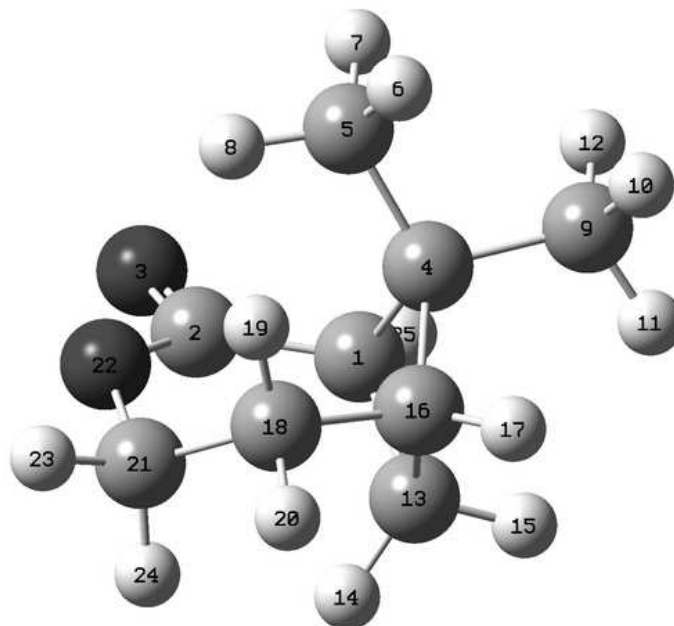
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Table S58 – continued from previous page

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
11	H	-3.334 684	-0.202 034	0.886 681	30.7964	1.0685
12	H	-3.135 027	0.010 159	-0.858 991	30.3526	1.5123
13	H	-2.974 386	-1.602 830	-0.141 956	30.7759	1.0890
14	C	-0.657 250	1.000 486	-1.360 635	155.4110	28.1966
15	H	0.184 164	1.517 625	-1.826 136	29.6821	2.1828
16	H	-1.548 068	1.179 417	-1.964 973	29.2984	2.5665
17	C	-0.911 611	1.204 279	0.155 756	138.2349	45.3727
18	H	-1.727 461	1.882 399	0.427 964	29.7029	2.1620
19	C	0.358 244	1.584 108	0.914 107	156.4086	27.1990
20	H	0.272 429	1.262 211	1.957 403	29.8890	1.9759
21	H	0.451 605	2.674 739	0.933 372	30.0725	1.7924
22	C	1.667 878	1.050 420	0.311 001	144.5429	39.0647
23	H	2.486 187	1.197 637	1.017 279	29.1063	2.7586
24	H	1.922 250	1.634 877	-0.580 960	28.8373	3.0276
25	H	-0.914 188	-1.206 124	-1.805 746	27.5547	4.3102

S-I.11 Abnormal Lactone of β -Pinene (207)

Fig. S59 207 – Conformer 1



SCF Energy - E(RM062X) -501.634 249 141
 SCF Energy from NMR - E(RB3LYP) -501.973 754 661
 Sum of Electronic and Thermal Free Energies -501.448 041 000

Table S59 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for 207 – Conformer 1

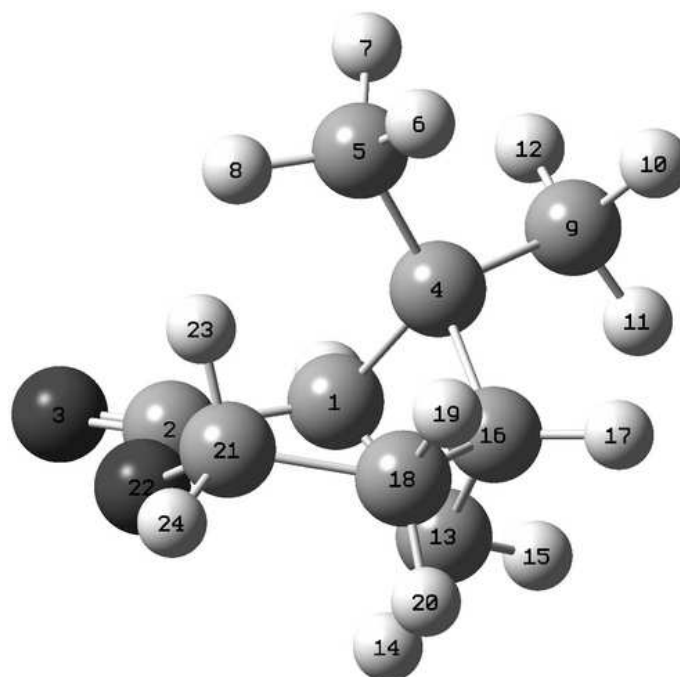
Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	-0.221 474	-0.743 948	-0.832 199	125.6433	57.9643
2	C	1.121 626	-1.077 428	-0.229 616	-1.6233	185.2309
3	O	1.515 809	-2.224 881	-0.161 389	—	—
4	C	-1.197 509	-0.151 801	0.248 351	137.6390	45.9686
5	C	-0.963 053	-0.501 796	1.712 993	161.4246	22.1830
6	H	-1.616 750	0.105 944	2.349 030	31.1786	0.6863
7	H	-1.207 787	-1.555 048	1.887 448	31.0260	0.8389
8	H	0.067 568	-0.338 892	2.036 879	30.4130	1.4519
9	C	-2.644 295	-0.483 637	-0.119 002	153.6197	29.9879

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Table S59 – continued from previous page

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
10	H	-3.327 339	0.096 546	0.511 075	30.8395	1.0254
11	H	-2.871 865	-0.253 614	-1.163 694	30.0830	1.7819
12	H	-2.844 953	-1.547 002	0.047 417	30.7275	1.1374
13	C	-0.367 332	0.593 557	-1.600 395	161.6493	21.9583
14	H	0.500 771	0.989 021	-2.129 518	29.5067	2.3582
15	H	-1.190 187	0.516 776	-2.311 695	29.4810	2.3839
16	C	-0.799 969	1.263 711	-0.274 050	138.1865	45.4211
17	H	-1.629 536	1.977 010	-0.328 554	29.7054	2.1595
18	C	0.381 900	1.896 242	0.465 169	151.6682	31.9394
19	H	0.201 319	1.889 868	1.545 296	29.3414	2.5235
20	H	0.468 628	2.948 382	0.168 461	30.1174	1.7475
21	C	1.743 199	1.286 406	0.153 913	113.1358	70.4718
22	O	1.877 878	-0.135 170	0.365 187	—	—
23	H	2.496 457	1.710 084	0.818 854	27.6139	4.2510
24	H	2.047 227	1.502 159	-0.872 941	27.0235	4.8414
25	H	-0.561 607	-1.648 655	-1.339 428	28.9960	2.8689

Fig. S60 207 – Conformer 2



SCF Energy - E(RM062X) -501.626 888 110
 SCF Energy from NMR - E(RB3LYP) -501.967 201 057
 Sum of Electronic and Thermal Free Energies -501.441 868 000

Table S60 Cartesian Coordinates, Isotropic Shielding Tensors and Scaled NMR Shifts for **207** – Conformer 2

Center #	Atom Type	Cartesian Coordinates			NMR Shielding Tensor	Scaled NMR Shifts
		X	Y	Z		
1	C	-0.147 254	-0.997 579	-0.550 244	123.6353	59.9723
2	C	1.282 459	-0.982 149	-0.067 140	-6.1618	189.7694
3	O	1.919 221	-2.003 805	0.088 049	—	—
4	C	-1.187 994	-0.194 094	0.294 482	138.8110	44.7966
5	C	-1.007 619	-0.106 376	1.812 176	157.2783	26.3293
6	H	-1.385 801	0.850 762	2.189 376	30.5464	1.3185
7	H	-1.573 544	-0.903 654	2.304 005	30.7893	1.0756
8	H	0.030 363	-0.214 237	2.133 601	30.6301	1.2348
9	C	-2.596 533	-0.722 257	0.003 887	150.8277	32.7799
10	H	-3.336 518	-0.063 513	0.472 054	30.6540	1.2109
11	H	-2.813 317	-0.765 092	-1.067 203	30.2082	1.6567
12	H	-2.720 547	-1.726 937	0.420 586	30.8059	1.0590
13	C	-0.357 440	0.034 355	-1.688 248	150.3092	33.2984
14	H	0.534 214	0.343 615	-2.239 772	30.2567	1.6082
15	H	-1.117 065	-0.302 667	-2.394 184	29.3695	2.4954
16	C	-0.898 746	1.029 290	-0.633 852	136.6651	46.9425
17	H	-1.791 219	1.593 936	-0.925 981	29.6819	2.1830
18	C	0.184 456	2.010 738	-0.194 041	148.2542	35.3534
19	H	-0.238 031	2.764 441	0.481 178	29.7772	2.0877
20	H	0.526 502	2.544 730	-1.088 003	29.5372	2.3277
21	C	1.388 243	1.431 579	0.546 541	110.5938	73.0138
22	O	1.946 635	0.187 883	0.067 953	—	—
23	H	1.169 954	1.302 992	1.607 088	27.0351	4.8298
24	H	2.227 562	2.123 308	0.468 558	27.4667	4.3982
25	H	-0.396 838	-2.041 356	-0.750 681	28.8261	3.0388

S-II Calculated and Experimental NMR Chemical Shifts

S-II.1	Carvomenthones (201)	181
S-II.2	Nankakurines (202)	182
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All calculated shifts were obtained using the methods described in 2.2.1. Statistical analysis was executed according to the method and equations described in 2.4.1. Any experimental shifts that were assigned as a range of shifts are given in **bold**. For any analysis of these shifts, the average value of the range was used. Any shifts assignments that were incomplete were matched with the closest computed chemical shift in the corresponding structure, and are provided in *italics*. If there was more than one distinct set of unknown shifts, a superscript *italics*^a will be applied. Assigned shifts in *italics* and within the same superscript group can be switched with other shifts within *italics* and part of the same superscript group (e.g., shifts in *italics*^a can be switched with other shifts in *italics*^a, but not with those in *italics*^b).

S-II.1 Carvomenthones (201)

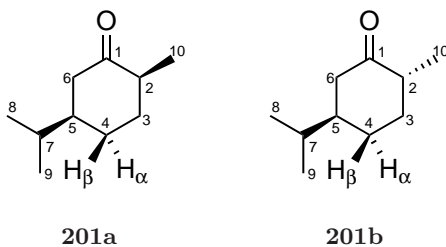


Table S61 Calculated and Experimental ^1H Shifts (in ppm) for carvomenthones **201**

Position	Computed		Experimental	
	201a	201b	201a	201b
2	2.47	2.48	2.45	2.33
3 α	1.87	1.29	1.87	1.30
3 β	1.70	2.12	1.60–1.75	2.10
4 α	1.69	1.87	1.60–1.75	1.86
4 β	1.88	1.55	1.60–1.75	1.44
5	1.61	1.55	1.60–1.75	1.51–1.61
6 α	2.36	2.33	2.28–2.38	2.40
6 β	2.51	2.24	2.28–2.38	2.06
7	1.45	1.51	1.49	1.51–1.61
8 Me	0.90	0.91	0.91	0.90
9 Me	0.88	0.89	0.89	0.89
10 Me	1.06	0.92	1.10	1.01

Table S62 Calculated and Experimental ^{13}C Shifts (in ppm) for carvomenthones **201**

Position	Computed		Experimental	
	201a	201b	201a	201b
1	232.16	230.49	215.30	213.70
2	51.87	51.15	44.40	45.00
3	36.69	40.92	31.50	35.20
4	30.08	33.99	25.00	29.00
5	52.15	54.11	44.90	46.70
6	47.62	50.36	43.10	45.50
7	36.85	39.59	30.70	32.90
8	21.22	21.36	20.14	19.70
9	21.37	20.72	20.07	19.40
10	18.30	16.39	16.00	14.50

S-II.2 Nankakurines (202)

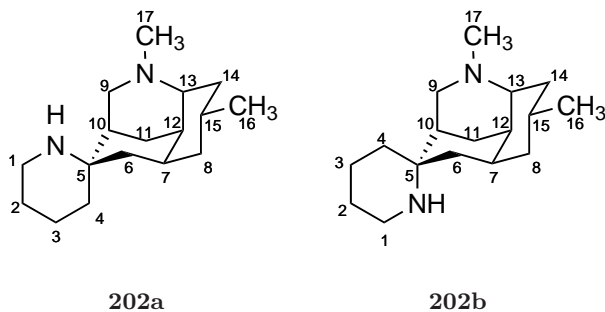


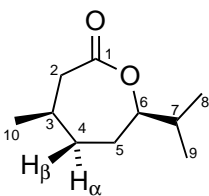
Table S63 Calculated and Experimental⁴³ ¹H Shifts (in ppm) for nankakurines **202**

Position	Computed		Experimental	
	202a	202b	202a	202b
1 R	2.73	2.75	2.82 ^a	2.66 ^a
1 S	2.79	2.76	2.82 ^a	2.76 ^a
2 R	1.40	1.34	1.58 ^b	1.16 ^a
2 S	1.38	1.38	1.53 ^b	1.28 ^a
3 R	1.50	1.49	1.57	1.66–1.75^a
3 S	1.52	1.55	1.57	1.66–1.75^a
4 R	1.44	1.38	1.66	1.66–1.75^a
4 S	1.62	1.43	1.66	1.54–1.43^a
6 R	1.93	1.97	2.29 ^c	2.58 ^a
6 S	1.52	1.45	1.64 ^c	1.66–1.75^a
7	1.78	1.83	1.85	1.82–1.95^a
8 R	1.42	1.41	1.49 ^d	1.43–1.54^a
8 S	1.11	1.10	1.20 ^d	1.16 ^a
9 R	3.03	2.91	3.00 ^e	2.87 ^a
9 S	1.96	2.02	2.14 ^e	1.82–1.95^a
10	1.75	1.67	1.81	1.43–1.54^a
11 R	1.79	1.99	1.83 ^f	2.39 ^a
11 S	1.41	1.28	1.53 ^f	1.15 ^a
12	1.43	1.43	1.53	1.43–1.54^a
13	1.88	1.88	2.03	1.66–1.75^a
14 R	0.78	0.78	0.89 ^g	0.82 ^a
14 S	2.04	2.04	2.02 ^g	1.82–1.95^a
15	1.87	1.86	1.95	2.21 ^a
16 Me	0.76	0.76	0.85	0.79 ^b
17 Me	2.05	2.04	2.12	1.93 ^b

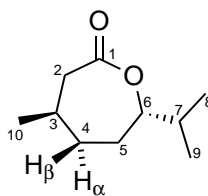
Table S64 Calculated and Experimental⁴³ ¹³C Shifts (in ppm) for nankakurines **202**

Position	Computed		Experimental	
	202a	202b	202a	202b
1	45.42	45.46	41.00	—
2	32.00	32.44	26.30	—
3	25.11	24.80	20.90	<i>22.60^a</i>
4	39.42	41.64	34.60	—
5	59.34	59.46	56.10	<i>56.50^a</i>
6	45.77	42.83	40.00	—
7	39.35	38.08	34.50	—
8	45.39	45.40	41.90	—
9	62.13	63.07	58.50	<i>56.10^a</i>
10	41.70	42.37	37.40	—
11	36.01	34.71	32.50	—
12	42.78	42.72	36.90	—
13	69.96	70.02	65.10	<i>63.30^a</i>
14	43.23	43.18	40.00	—
15	26.95	26.95	22.00	<i>23.00^a</i>
16	24.43	24.43	23.00	<i>22.90^a</i>
17	44.96	44.98	43.40	—

S-II.3 Normal Menthides (203)



203a



203b

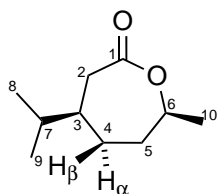
Table S65 Calculated and Experimental ^1H Shifts (in ppm) for normal menthides **203**

Position	Computed		Experimental	
	203a	203b	203a	203b
2 α	—	2.34	2.54	2.47
2 β	—	2.61	2.89	2.54
3	—	1.75	2.18	1.85
4 α	—	1.90	1.69–1.80	1.95
4 β	—	1.24	1.69–1.80	1.29
5 α	—	1.52	1.69–1.80	1.60
5 β	—	1.91	1.69–1.80	1.85
6	—	4.13	4.02	4.05
7	—	1.78	1.87	1.85
8 Me	—	0.94	0.98	0.98
9 Me	—	0.94	0.98	0.97
10 Me	—	0.99	1.05	1.04

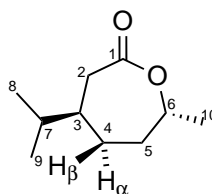
Table S66 Calculated and Experimental ^{13}C Shifts (in ppm) for normal menthides **203**

Position	Computed		Experimental	
	203a	203b	203a	203b
1	—	185.51	174.50	174.80
2	—	46.42	40.80	42.30
3	—	37.12	26.70	<i>30.20^a</i>
4	—	42.82	<i>34.30^a</i>	37.20
5	—	35.42	<i>26.74^a</i>	30.70
6	—	89.91	84.90	84.50
7	—	39.56	33.30	<i>33.10^a</i>
8	—	18.94	17.30	18.10
9	—	19.85	17.70	16.80
10	—	26.32	18.50	23.70

S-II.4 Normal Carvomenthides (204)



204a



204b

Table S67 Calculated and Experimental ^1H Shifts (in ppm) for normal carvomenthides **204**

Position	Computed		Experimental	
	204a	204b	204a	204b
2 α	2.88	2.35	2.80	2.42–2.51
2 β	2.79	2.59	2.76	2.42–2.51
3	1.41	1.53	1.51–1.57	1.57
4 α	1.56	1.73	1.98	1.82
4 β	2.04	1.53	1.58–1.65	1.47
5 α	1.59	1.55	1.66–1.80	1.65
5 β	1.76	1.87	1.66–1.80	1.91
6	4.54	4.51	4.44	4.42
7	1.57	1.64	1.58–1.62	1.69
8 Me	1.00	0.85	1.02	0.87
9 Me	0.87	0.86	0.90	0.90
10 Me	1.26	1.25	1.35	1.35

Table S68 Calculated and Experimental ^{13}C Shifts (in ppm) for normal carvomenthides **204**

Position	Computed		Experimental	
	204a	204b	204a	204b
1	185.05	186.60	174.20	175.60
2	42.81	42.44	38.30	38.00
3	45.12	46.33	38.70	40.20
4	35.63	36.02	30.00	31.10
5	35.84	40.46	32.00	35.70
6	82.14	81.92	76.30	76.50
7	35.15	40.36	28.90	33.40
8	22.56	19.85	20.60	18.60
9	22.05	19.72	20.30	18.40
10	24.07	24.41	22.20	22.40

S-II.5 Abnormal Carvomenthides (205)

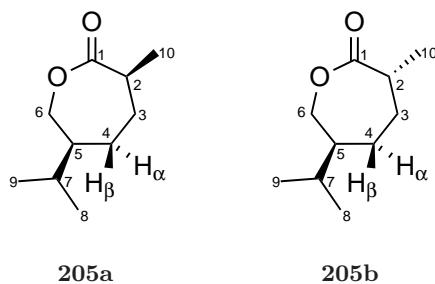


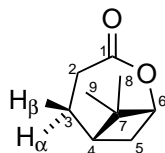
Table S69 Calculated and Experimental ^1H Shifts (in ppm) for abnormal carvomenthides 205

Position	Computed		Experimental	
	205a	205b	205a	205b
2	2.81	2.80	2.75	2.72
3 α	1.47	1.47	1.52–1.69	1.48–1.60
3 β	1.57	1.72	2.01	1.78
4 α	1.60	1.79	1.52–1.69	1.84–1.88
4 β	2.11	1.59	1.52–1.69	1.48–1.60
5	1.27	1.51	1.42	1.48–1.60
6 α	4.42	4.14	4.30	4.0
6 β	4.45	4.23	4.36	4.07
7	1.71	1.62	1.73	1.68
8 Me	0.89	0.88	0.91	0.91
9 Me	1.01	0.87	1.01	0.90
10 Me	1.09	1.07	1.20	1.20

Table S70 Calculated and Experimental ^{13}C Shifts (in ppm) for abnormal carvomenthides **205**

Position	Computed		Experimental	
	205a	205b	205a	205b
1	189.23	189.17	178.10	178.10
2	43.30	42.59	37.60	37.10
3	31.93	37.04	30.50	31.90
4	35.44	35.79	28.10	<i>31.08^a</i>
5	49.87	49.72	43.60	44.60
6	73.36	76.14	69.60	71.60
7	30.64	37.76	25.60	<i>31.12^a</i>
8	22.15	20.14	<i>20.75^a</i>	19.40
9	22.39	20.88	<i>20.82^a</i>	19.20
10	20.57	20.25	18.60	18.40

S-II.6 Normal Lactone of β -Pinene (206)



206

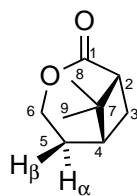
Table S71 Calculated and Experimental ^1H Shifts (in ppm) for normal lactone of β -pinene **206**

Position	Computed	Experimental
2 α	3.03	2.93
2 β	2.76	2.83
3 α	1.79	1.95
3 β	1.98	1.87
4	2.16	2.28
5 <i>anti</i>	2.57	2.65
5 <i>syn</i>	2.18	2.11
6	4.31	4.33
8 Me	1.22	1.30
9 Me	0.81	0.89

Table S72 Calculated and Experimental ^{13}C Shifts (in ppm) for normal lactone of β -pinene **206**

Position	Computed	Experimental
1	186.15	174.90
2	39.06	33.90
3	27.20	27.20
4	45.37	40.90
5	28.20	26.30
6	88.51	83.90
7	48.51	43.00
8	28.89	27.20
9	20.28	18.30

S-II.7 Abnormal Lactone of β -Pinene (207)



207

Table S73 Calculated and Experimental ^1H Shifts (in ppm) for abnormal lactone of β -pinene **207**

Position	Computed	Experimental
2	2.87	2.94
3 <i>anti</i>	2.38	2.45
3 <i>syn</i>	2.36	2.30
4	2.16	2.26
5 α	1.75	1.86
5 β	2.52	2.46
6 α	4.84	4.69
6 β	4.25	4.32
8	1.31	1.38
9	0.99	1.04

Table S74 Calculated and Experimental ^{13}C Shifts (in ppm) for abnormal lactone of β -pinene **207**

Position	Computed	Experimental
1	185.24	174.50
2	57.97	53.10
3	21.97	19.70
4	45.42	40.80
5	31.94	27.40
6	70.48	66.10
7	45.97	40.30
8	29.99	28.40
9	22.19	20.60

S-III Calculated Geometries and Free Energies for Benzyne, Related Compounds and Reactions

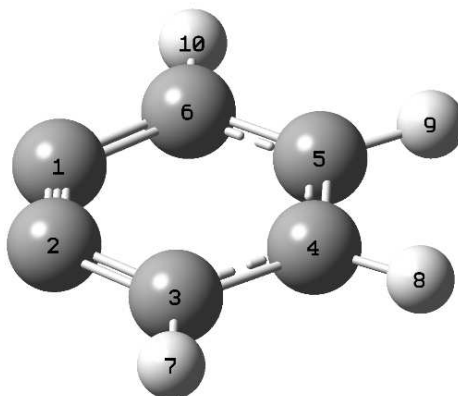
S-III.1	Benzyne (301)	193
S-III.2	1,4,6-tridecatriyne (310a)	196
S-III.3	1,5,7-tridecatriyne (310b)	198
S-III.4	1,6,8-tridecatriyne (310c)	200
S-III.5	3-hexylbenzylcyclopropane (311a)	202
S-III.6	3-pentylbenzylcyclobutane (311b)	204
S-III.7	3-butylbenzylcyclopentane (311c)	206
S-III.8	1,3,6-heptatriyne (312a)	207
S-III.9	1,3,7-octatriyne (312b)	208
S-III.10	1,3,8-nonatriyne (312c)	209
S-III.11	Benzylcyclopropane (313a)	210
S-III.12	Benzylcyclobutane (313b)	211
S-III.13	Benzylcyclopentane (313c)	212
S-III.14	Benzylcyclobutane Ring Opened Diene (314)	213
S-III.15	Benzocyclobutane (315)	214
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S-III.17	N-Methylimidazole (317)	216
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S-III.25	Benzodioxole Carbene (319b)	231
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S-III.27	Carbon Disulfide (320)	234
S-III.28	Benzodithioate (320a)	235
S-III.29	Benzodithiolane Carbene (320b)	236
S-III.30	Methyl Isocyanate (321)	237
S-III.31	Benzo- β -Lactam (321a)	238
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S-III.33	Methyl Isothiocyanate (322)	240
S-III.34	Benzo- β -Thiolactam (322a)	241
S-III.35	Benzothiazole Carbene (322b)	242
S-III.36	Benzo- β -Thioimide (322c)	243
S-III.37	Carbon Monoxide (323)	245
S-III.38	Benzocyclopropanone (323a)	246

All geometries extracted are in the standard (x,y,z) coordinate system. Energies reported (in hartrees) indicate the level of theory they are obtained at. Energies reported include: 1) energies from optimizations (SCF Energy), 2) Gibb's free energy (Sum of Electronic and Thermal Free Energies). Entries corresponding to transition states will also report calculated imaginary frequencies.

S-III.1 Benzyne (**301**)

Fig. S61 Optimized Geometry of **301** - Solvation in CHCl_3



SCF Energy - E(RM062X) -230.822 458 591
 Sum of Electronic and Thermal Free Energies - E(RM062X) -230.773 291 000

Table S75 Cartesian Coordinates, Electronic and Free Energies of Optimized Geometry of **301** - Solvation in CHCl_3

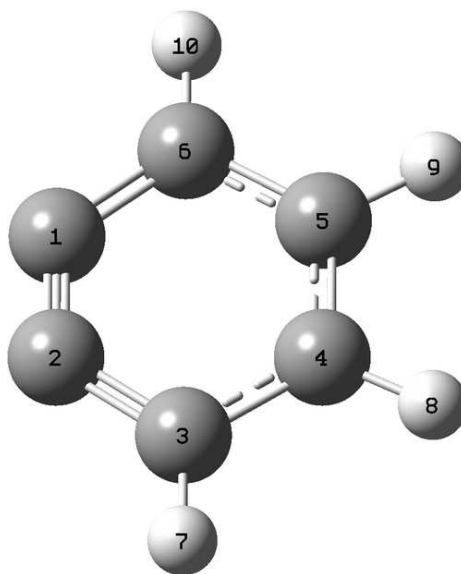
Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
1	C	0.000 000	0.623 314	-1.232 873
2	C	0.000 000	-0.623 314	-1.232 873

Continued on next page

Table S75 – continued from previous page

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
3	C	0.000 000	-1.465 161	-0.132 318
4	C	0.000 000	-0.703 794	1.053 181
5	C	0.000 000	0.703 794	1.053 181
6	C	0.000 000	1.465 161	-0.132 318
7	H	0.000 000	-2.548 206	-0.133 237
8	H	0.000 000	-1.226 935	2.005 298
9	H	0.000 000	1.226 935	2.005 298
10	H	0.000 000	2.548 206	-0.133 237

Fig. S62 Optimized Geometry of **301** - No Solvation



SCF Energy - E(RM062X) -230.819 701 209

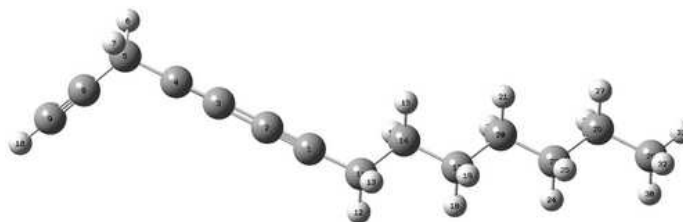
Sum of Electronic and Thermal Free Energies - E(RM062X) -230.770 387 000

Table S76 Cartesian Coordinates, Electronic and Free Energies of Optimized Geometry of **301** - No Solvation

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
1	C	0.000 000	0.623 079	-1.233 101
2	C	0.000 000	-0.623 079	-1.233 101
3	C	0.000 000	-1.462 378	-0.132 632
4	C	0.000 000	-0.703 335	1.053 729
5	C	0.000 000	0.703 335	1.053 729
6	C	0.000 000	1.462 378	-0.132 632
7	H	0.000 000	-2.545 664	-0.133 965
8	H	0.000 000	-1.226 371	2.005 995
9	H	0.000 000	1.226 371	2.005 995
10	H	0.000 000	2.545 664	-0.133 965

S-III.2 1,4,6-tridecatriyne (310a)

Fig. S63 Optimized Geometry of 310a



SCF Energy - E(RM062X) -543.924 641 779
 Sum of Electronic and Thermal Free Energies - E(RM062X) -543.692 501 000

Table S77 Cartesian Coordinates, Electronic and Free Energies of Optimized Geometry of 310a

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
1	C	-1.229 515	0.857 913	-0.293 878
2	C	-2.362 185	0.426 353	-0.350 933
3	C	-3.653 626	-0.057 675	-0.414 545
4	C	-4.786 887	-0.482 165	-0.471 014
5	C	-6.159 269	-0.998 933	-0.541 807
6	H	-6.147 466	-2.083 484	-0.386 498
7	H	-6.560 026	-0.829 705	-1.547 390
8	C	-7.046 392	-0.372 859	0.449 692
9	C	-7.777 186	0.138 664	1.261 891
10	H	-8.423 131	0.592 936	1.981 746
11	C	0.148 023	1.344 477	-0.222 202
12	H	0.246 872	1.999 723	0.651 401
13	H	0.353 295	1.962 009	-1.104 679
14	C	1.175 954	0.205 176	-0.135 064
15	H	1.067 712	-0.443 037	-1.012 550
16	H	0.955 877	-0.409 570	0.745 543
17	C	2.605 140	0.735 952	-0.054 008
18	H	2.700 966	1.389 961	0.823 643
19	H	2.811 799	1.361 244	-0.933 487
20	C	3.646 171	-0.378 688	0.030 011
21	H	3.550 625	-1.031 077	-0.849 007

Continued on next page

Table S77 – continued from previous page

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
22	H	3.435 523	-1.006 299	0.907 035
23	C	5.078 472	0.144 967	0.116 678
24	H	5.174 292	0.797 016	0.996 348
25	H	5.289 054	0.774 370	-0.759 508
26	C	6.122 445	-0.967 431	0.199 391
27	H	6.025 685	-1.617 422	-0.679 739
28	H	5.910 106	-1.595 532	1.074 120
29	C	7.549 358	-0.429 498	0.286 738
30	H	7.673 532	0.201 656	1.173 084
31	H	8.282 063	-1.239 275	0.345 663
32	H	7.790 193	0.178 959	-0.591 423

S-III.3 1,5,7-tridecatriyne (310b)

Fig. S64 Optimized Geometry of 310b



SCF Energy - E(RM062X) -543.930 984 550
 Sum of Electronic and Thermal Free Energies - E(RM062X) -543.700 572 000

Table S78 Cartesian Coordinates, Electronic and Free Energies of Optimized Geometry of 310b

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
1	C	-0.182 046	0.875 654	-0.045 783
2	C	0.963 664	0.475 628	-0.064 278
3	C	2.269 138	0.026 157	-0.084 877
4	C	3.413 848	-0.375 152	-0.103 900
5	C	4.804 302	-0.828 449	-0.120 361
6	H	5.023 594	-1.302 017	-1.082 568
7	H	4.950 384	-1.588 303	0.653 936
8	C	5.785 189	0.340 531	0.113 795
9	H	5.565 833	0.813 853	1.075 578
10	H	5.640 238	1.099 328	-0.661 073
11	C	7.176 735	-0.116 990	0.098 234
12	C	8.318 608	-0.510 923	0.082 555
13	H	9.329 954	-0.855 404	0.069 412
14	C	-1.574 852	1.322 733	-0.022 589
15	H	-1.732 971	1.946 896	0.864 979
16	H	-1.758 128	1.962 007	-0.894 410
17	C	-2.572 678	0.153 730	-0.018 186
18	H	-2.376 311	-0.481 760	0.853 303
19	H	-2.404 891	-0.464 052	-0.908 176
20	C	-4.018 986	0.641 832	0.010 409
21	H	-4.202 896	1.286 693	-0.859 986
22	H	-4.174 408	1.266 924	0.900 543

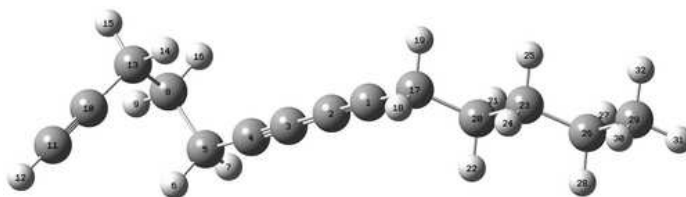
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Table S78 – continued from previous page

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
23	C	-5.029 778	-0.503 231	0.013 982
24	H	-4.843 224	-1.150 012	0.882 657
25	H	-4.874 557	-1.127 911	-0.876 723
26	C	-6.479 980	-0.023 310	0.045 955
27	H	-6.664 055	0.623 570	-0.821 412
28	H	-6.632 812	0.600 330	0.936 088
29	C	-7.480 310	-1.177 551	0.048 493
30	H	-7.329 268	-1.821 291	0.921 469
31	H	-8.512 010	-0.815 584	0.072 298
32	H	-7.361 587	-1.797 209	-0.846 604

S-III.4 1,6,8-tridecatriyne (310c)

Fig. S65 Optimized Geometry of 310c



SCF Energy - E(RM062X) -543.933 321 924
 Sum of Electronic and Thermal Free Energies - E(RM062X) -543.702 443 000

Table S79 Cartesian Coordinates, Electronic and Free Energies of Optimized Geometry of 310c

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
1	C	-1.032 978	0.412 340	0.212 160
2	C	0.087 092	-0.010 388	0.012 001
3	C	1.364 537	-0.484 040	-0.213 936
4	C	2.485 641	-0.902 615	-0.417 134
5	C	3.847 806	-1.396 228	-0.631 039
6	H	4.286 547	-0.869 713	-1.486 748
7	H	3.805 576	-2.457 705	-0.895 958
8	C	4.743 055	-1.209 068	0.603 704
9	H	5.729 599	-1.626 070	0.380 055
10	C	5.480 336	1.090 711	-0.031 360
11	C	5.967 872	1.753 617	-0.916 895
12	H	6.397 532	2.346 437	-1.694 975
13	C	4.889 591	0.260 667	1.024 128
14	H	3.906 994	0.667 542	1.289 393
15	H	5.513 962	0.323 840	1.920 770
16	H	4.326 792	-1.770 895	1.445 088
17	C	-2.396 248	0.893 719	0.437 212
18	H	-2.518 330	1.862 269	-0.062 203
19	H	-2.538 008	1.072 372	1.509 796
20	C	-3.464 660	-0.087 934	-0.069 544
21	H	-3.333 992	-1.052 152	0.435 651
22	H	-3.309 727	-0.264 860	-1.140 382

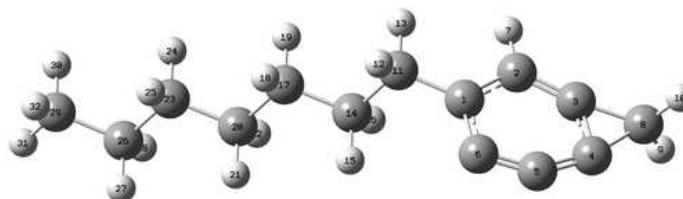
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Table S79 – continued from previous page

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
23	C	-4.877 819	0.437 140	0.170 704
24	H	-4.996 549	1.407 195	-0.331 726
25	H	-5.020 483	0.622 591	1.244 400
26	C	-5.959 100	-0.522 442	-0.323 474
27	H	-5.838 196	-1.490 352	0.179 232
28	H	-5.812 839	-0.708 107	-1.395 085
29	C	-7.369 524	0.011 257	-0.081 037
30	H	-7.518 362	0.965 642	-0.596 963
31	H	-8.130 216	-0.687 374	-0.440 279
32	H	-7.543 913	0.178 925	0.986 989

S-III.5 3-hexylbenzylcyclopropane (**311a**)

Fig. S66 Optimized Geometry of **311a**



SCF Energy - E(RM062X) -543.893 715 183
 Sum of Electronic and Thermal Free Energies - E(RM062X) -543.659 271 000

Table S80 Cartesian Coordinates, Electronic and Free Energies of Optimized Geometry of **311a**

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
1	C	2.135 207	-0.073 403	-0.586 437
2	C	3.015 876	-1.042 834	0.007 263
3	C	4.243 412	-0.621 489	0.449 578
4	C	4.759 600	0.682 507	0.387 975
5	C	3.791 941	1.376 029	-0.181 855
6	C	2.615 622	1.249 529	-0.662 930
7	H	2.689 618	-2.074 159	0.087 346
8	C	5.610 326	-0.390 668	0.976 901
9	H	5.767 140	-0.377 475	2.054 737
10	H	6.467 386	-0.733 091	0.398 151
11	C	0.761 714	-0.483 747	-1.049 554
12	H	0.597 626	-0.099 218	-2.063 084
13	H	0.697 280	-1.576 976	-1.100 115
14	C	-0.340 983	0.050 967	-0.127 124
15	H	-0.253 627	1.143 584	-0.069 135
16	H	-0.176 760	-0.332 721	0.888 833
17	C	-1.741 401	-0.331 283	-0.600 827
18	H	-1.896 982	0.053 485	-1.618 381
19	H	-1.817 978	-1.425 579	-0.667 479
20	C	-2.845 597	0.196 851	0.313 199
21	H	-2.767 860	1.290 983	0.380 284
22	H	-2.688 969	-0.187 931	1.330 694

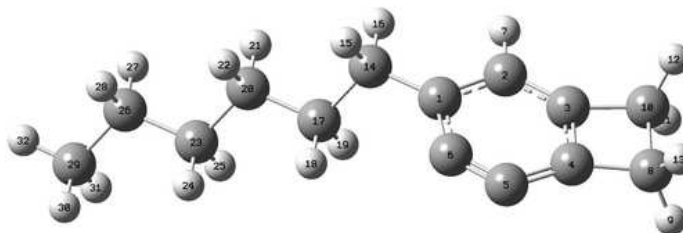
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Table S80 – continued from previous page

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
23	C	-4.248 429	-0.181 185	-0.158 258
24	H	-4.326 372	-1.275 574	-0.226 342
25	H	-4.405 811	0.203 771	-1.175 772
26	C	-5.354 390	0.345 469	0.754 827
27	H	-5.275 264	1.438 179	0.821 853
28	H	-5.195 799	-0.039 450	1.770 473
29	C	-6.750 838	-0.040 297	0.270 853
30	H	-6.858 746	-1.129 088	0.222 384
31	H	-7.528 742	0.345 121	0.936 054
32	H	-6.938 497	0.357 459	-0.732 160

S-III.6 3-pentylbenzycyclobutane (311b)

Fig. S67 Optimized Geometry of 311b



SCF Energy - E(RM062X) -543.953 179 216
 Sum of Electronic and Thermal Free Energies - E(RM062X) -543.715 512 000

Table S81 Cartesian Coordinates, Electronic and Free Energies of Optimized Geometry of 311b

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
1	C	1.061 720	-0.280 774	-0.543 813
2	C	2.097 167	-1.072 995	0.018 114
3	C	3.356 547	-0.520 047	0.264 036
4	C	3.695 499	0.811 356	-0.006 926
5	C	2.643 233	1.531 205	-0.549 684
6	C	1.522 997	1.016 096	-0.763 694
7	H	1.877 604	-2.112 746	0.247 050
8	C	5.116 311	0.683 365	0.488 642
9	H	5.362 175	1.283 461	1.367 978
10	C	4.750 888	-0.817 598	0.800 593
11	H	4.792 981	-1.077 491	1.861 011
12	H	5.323 215	-1.547 394	0.222 982
13	H	5.891 456	0.813 981	-0.270 259
14	C	-0.319 983	-0.798 960	-0.826 653
15	H	-0.506 924	-0.757 018	-1.907 338
16	H	-0.373 552	-1.853 328	-0.533 718
17	C	-1.408 297	-0.000 873	-0.100 822
18	H	-1.330 826	1.055 155	-0.392 177
19	H	-1.224 074	-0.041 798	0.980 679
20	C	-2.813 759	-0.514 370	-0.404 455
21	H	-2.884 174	-1.573 123	-0.118 441

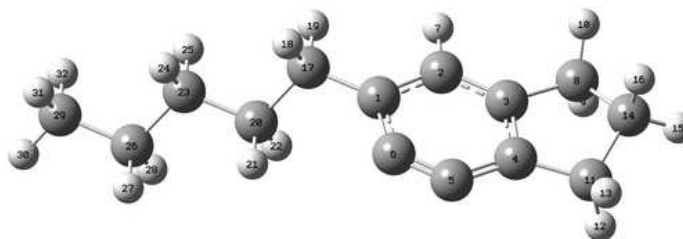
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Table S81 – continued from previous page

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
22	H	-2.988 334	-0.473 154	-1.488 692
23	C	-3.906 035	0.275 860	0.313 516
24	H	-3.834 617	1.335 110	0.029 123
25	H	-3.731 684	0.234 091	1.397 899
26	C	-5.314 585	-0.232 577	0.010 541
27	H	-5.383 673	-1.290 760	0.293 904
28	H	-5.487 038	-0.189 807	-1.072 597
29	C	-6.396 366	0.565 659	0.735 506
30	H	-6.360 876	1.621 178	0.445 732
31	H	-6.256 740	0.513 711	1.820 486
32	H	-7.396 936	0.187 842	0.506 971

S-III.7 3-butylbenzyncyclopentane (**311c**)

Fig. S68 Optimized Geometry of **311c**



SCF Energy - E(RM062X) -230.822 458 591

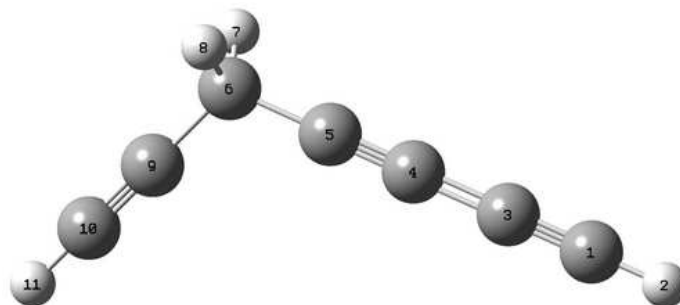
Sum of Electronic and Thermal Free Energies - E(RM062X) -230.773 291 000

Table S82 Cartesian Coordinates, Electronic and Free Energies of Optimized Geometry of **311c**

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
1	C	0.000 000	0.623 314	-1.232 873
2	C	0.000 000	-0.623 314	-1.232 873
3	C	0.000 000	-1.465 161	-0.132 318
4	C	0.000 000	-0.703 794	1.053 181
5	C	0.000 000	0.703 794	1.053 181
6	C	0.000 000	1.465 161	-0.132 318
7	H	0.000 000	-2.548 206	-0.133 237
8	H	0.000 000	-1.226 935	2.005 298
9	H	0.000 000	1.226 935	2.005 298
10	H	0.000 000	2.548 206	-0.133 237

S-III.8 1,3,6-heptatriyne (312a)

Fig. S69 Optimized Geometry of 312a



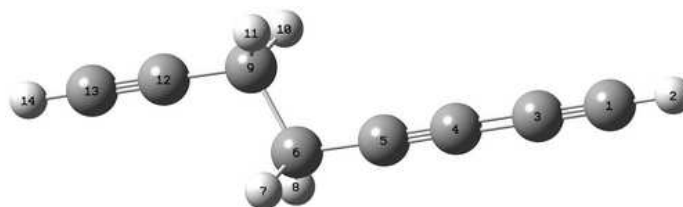
SCF Energy - E(RM062X) -268.845 259 196
 Sum of Electronic and Thermal Free Energies - E(RM062X) -268.798 457 000

Table S83 Cartesian Coordinates, Electronic and Free Energies of Optimized Geometry of 312a

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
1	C	-3.635 567	0.505 120	0.000 001
2	H	-4.660 573	0.808 234	0.000 002
3	C	-2.475 197	0.162 182	0.000 000
4	C	-1.151 080	-0.229 330	-0.000 001
5	C	0.009 556	-0.573 817	-0.000 001
6	C	1.414 913	-0.996 431	0.000 000
7	H	1.603 322	-1.622 304	-0.879 292
8	H	1.603 320	-1.622 303	0.879 294
9	C	2.341 992	0.144 291	0.000 001
10	C	3.107 177	1.076 665	0.000 000
11	H	3.783 169	1.904 296	-0.000 003

S-III.9 1,3,7-octatriyne (312b)

Fig. S70 Optimized Geometry of 312b



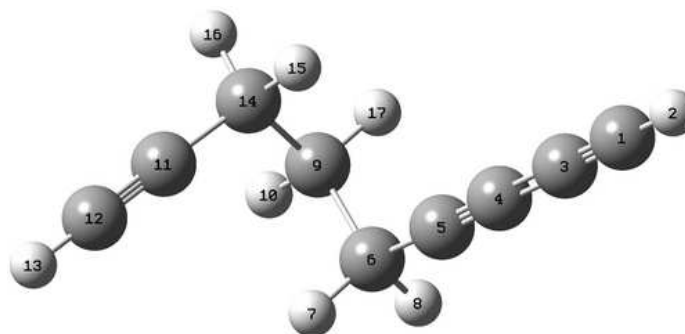
SCF Energy - E(RM062X) -308.147 424 806
 Sum of Electronic and Thermal Free Energies - E(RM062X) -308.073 908 000

Table S84 Cartesian Coordinates, Electronic and Free Energies of Optimized Geometry of 312b

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
1	C	-4.418 652	-0.323 144	0.000 000
2	H	-5.465 585	-0.538 161	0.000 001
3	C	-3.232 918	-0.080 389	0.000 000
4	C	-1.880 667	0.198 568	0.000 000
5	C	-0.694 680	0.450 350	0.000 000
6	C	0.741 498	0.722 152	0.000 000
7	H	0.998 260	1.318 580	0.881 086
8	H	0.998 259	1.318 580	-0.881 085
9	C	1.565 541	-0.583 538	0.000 000
10	H	1.306 908	-1.178 604	-0.880 928
11	H	1.306 907	-1.178 603	0.880 929
12	C	3.003 766	-0.305 986	0.000 000
13	C	4.186 402	-0.060 380	0.000 000
14	H	5.233 514	0.152 425	0.000 000

S-III.10 1,3,8-nonatriyne (312c)

Fig. S71 Optimized Geometry of 312c



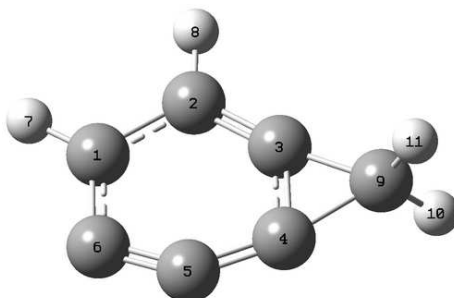
SCF Energy - E(RM062X) -347.445 489 151
 Sum of Electronic and Thermal Free Energies - E(RM062X) -347.345 295 000

Table S85 Cartesian Coordinates, Electronic and Free Energies of Optimized Geometry of 312c

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
1	C	4.183 101	-0.843 006	0.267 024
2	H	5.138 271	-1.269 963	0.484 938
3	C	3.100 826	-0.360 157	0.020 093
4	C	1.866 915	0.191 260	-0.262 483
5	C	0.785 015	0.677 932	-0.516 240
6	C	-0.529 772	1.260 383	-0.788 042
7	H	-1.028 586	0.662 065	-1.559 391
8	H	-0.394 241	2.266 059	-1.198 671
9	C	-1.413 549	1.327 817	0.467 428
10	H	-2.360 807	1.801 680	0.193 706
11	C	-2.368 939	-0.957 705	0.155 490
12	C	-2.928 570	-1.685 840	-0.630 506
13	H	-3.422 936	-2.336 026	-1.319 255
14	C	-1.687 706	-0.050 858	1.085 773
15	H	-0.743 328	-0.508 347	1.402 484
16	H	-2.301 060	0.067 966	1.984 320
17	H	-0.931 244	1.957 615	1.220 647

S-III.11 Benzyne cyclopropane (**313a**)

Fig. S72 Optimized Geometry of **313a**



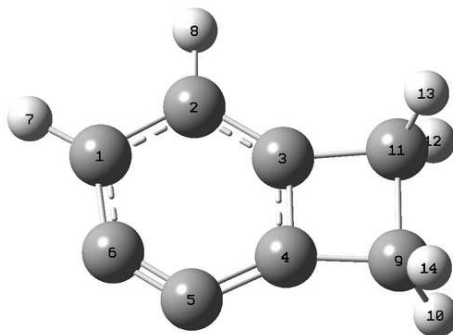
SCF Energy - E(RM062X) -268.819 210 858
 Sum of Electronic and Thermal Free Energies - E(RM062X) -268.767 808 000

Table S86 Cartesian Coordinates, Electronic and Free Energies of Optimized Geometry of **313a**

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
1	C	1.698 241	0.430 919	0.000 000
2	C	0.521 208	1.249 447	0.000 000
3	C	-0.693 195	0.613 350	0.000 000
4	C	-0.913 011	-0.774 334	0.000 000
5	C	0.297 290	-1.297 776	0.000 000
6	C	1.531 136	-0.962 086	0.000 000
7	H	2.668 279	0.920 313	0.000 000
8	H	0.620 954	2.328 666	0.000 000
9	C	-2.096 546	0.132 100	0.000 000
10	H	-2.679 984	0.200 655	0.917 020
11	H	-2.679 985	0.200 655	-0.917 019

S-III.12 Benzynocyclobutane (313b)

Fig. S73 Optimized Geometry of 313b



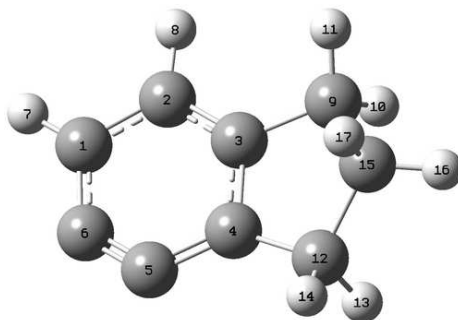
SCF Energy - E(RM062X) -308.174 513 332
 Sum of Electronic and Thermal Free Energies - E(RM062X) -308.094 006 000

Table S87 Cartesian Coordinates, Electronic and Free Energies of Optimized Geometry of 313b

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
1	C	2.115 075	0.415 749	-0.000 001
2	C	0.955 283	1.229 928	0.000 000
3	C	-0.305 804	0.630 496	0.000 000
4	C	-0.515 012	-0.756 068	0.000 000
5	C	0.661 192	-1.487 612	0.000 000
6	C	1.782 229	-0.929 884	0.000 000
7	H	3.112 262	0.838 103	0.000 000
8	H	1.077 320	2.308 887	0.000 000
9	C	-2.021 536	-0.654 708	0.000 000
10	H	-2.516 286	-1.045 391	0.892 265
11	C	-1.803 924	0.905 841	0.000 000
12	H	-2.181 013	1.410 671	0.892 423
13	H	-2.181 014	1.410 674	-0.892 420
14	H	-2.516 286	-1.045 391	-0.892 266

S-III.13 Benzynocyclopentane (**313c**)

Fig. S74 Optimized Geometry of **313c**



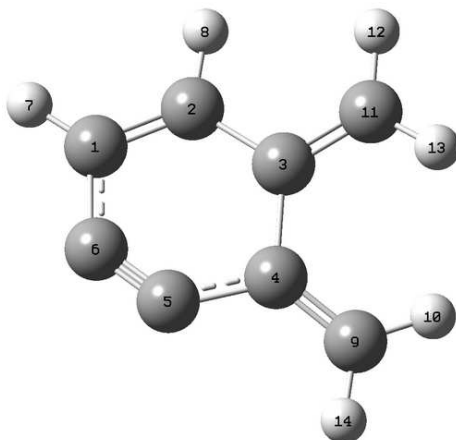
SCF Energy - E(RM062X) -347.515 496 421
 Sum of Electronic and Thermal Free Energies - E(RM062X) -347.406 068 000

Table S88 Cartesian Coordinates, Electronic and Free Energies of Optimized Geometry of **313c**

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
1	C	2.446 877	0.428 511	-0.055 702
2	C	1.264 196	1.197 070	0.002 938
3	C	-0.007 228	0.605 202	0.051 243
4	C	-0.199 158	-0.795 994	0.047 858
5	C	1.015 954	-1.453 953	0.001 771
6	C	2.145 790	-0.925 091	-0.050 742
7	H	3.430 434	0.879 335	-0.103 285
8	H	1.349 763	2.280 745	0.002 775
9	C	-1.359 927	1.282 080	0.143 651
10	H	-1.542 466	1.600 561	1.177 790
11	H	-1.437 001	2.168 585	-0.491 176
12	C	-1.656 175	-1.161 146	0.123 612
13	H	-1.911 822	-1.453 935	1.149 813
14	H	-1.921 022	-1.993 653	-0.532 363
15	C	-2.344 553	0.164 936	-0.270 209
16	H	-3.329 291	0.280 370	0.187 095
17	H	-2.473 249	0.188 301	-1.357 179

S-III.14 Benzynocyclobutane Ring Opened Diene (**314**)

Fig. S75 Optimized Geometry of **314**



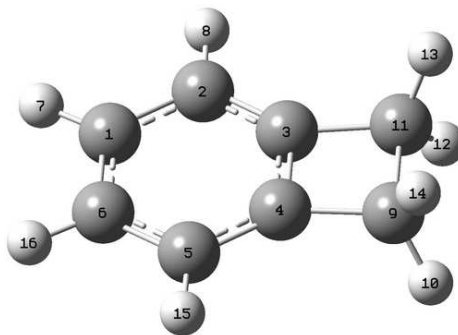
SCF Energy - E(RM062X) -308.155 566 918
 Sum of Electronic and Thermal Free Energies - E(RM062X) -308.078 148 000

Table S89 Cartesian Coordinates, Electronic and Free Energies of Optimized Geometry of **314**

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
1	C	2.096 751	0.056 044	0.088 124
2	C	1.141 650	1.017 539	0.170 882
3	C	-0.311 481	0.773 003	0.003 175
4	C	-0.844 053	-0.657 688	-0.016 969
5	C	0.296 790	-1.521 514	-0.220 101
6	C	1.481 732	-1.229 833	-0.128 433
7	H	3.156 430	0.248 749	0.190 655
8	H	1.439 278	2.050 394	0.332 940
9	C	-2.119 686	-1.009 290	0.201 240
10	H	-2.872 475	-0.274 043	0.462 803
11	C	-1.133 679	1.821 021	-0.191 491
12	H	-0.760 640	2.839 261	-0.152 596
13	H	-2.187 945	1.687 358	-0.409 223
14	H	-2.422 791	-2.047 409	0.136 858

S-III.15 Benzocyclobutane (315)

Fig. S76 Optimized Geometry of 315



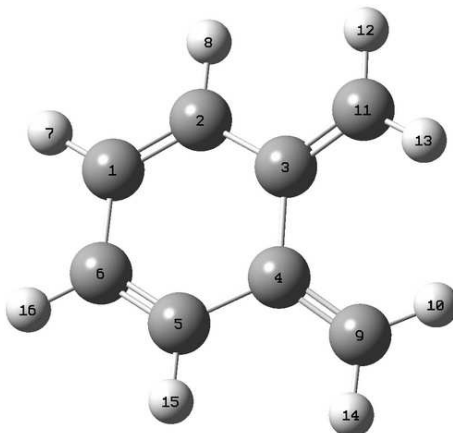
SCF Energy - E(RM062X) -309.506 467 462
 Sum of Electronic and Thermal Free Energies - E(RM062X) -309.400 165 000

Table S90 Cartesian Coordinates, Electronic and Free Energies of Optimized Geometry of 315

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
1	C	0.000 001	0.700 530	-1.910 890
2	C	0.000 001	1.438 902	-0.717 628
3	C	0.000 000	0.696 419	0.453 609
4	C	0.000 000	-0.696 419	0.453 609
5	C	-0.000 001	-1.438 902	-0.717 628
6	C	-0.000 001	-0.700 530	-1.910 890
7	H	0.000 001	1.224 386	-2.862 243
8	H	0.000 002	2.524 808	-0.733 291
9	C	0.000 001	-0.786 842	1.970 076
10	H	0.890 609	-1.241 092	2.412 264
11	C	-0.000 001	0.786 842	1.970 076
12	H	0.890 605	1.241 095	2.412 266
13	H	-0.890 609	1.241 092	2.412 264
14	H	-0.890 605	-1.241 095	2.412 266
15	H	-0.000 002	-2.524 808	-0.733 291
16	H	-0.000 001	-1.224 386	-2.862 243

S-III.16 Benzocyclobutane Ring Opened Diene (316)

Fig. S77 Optimized Geometry of 316



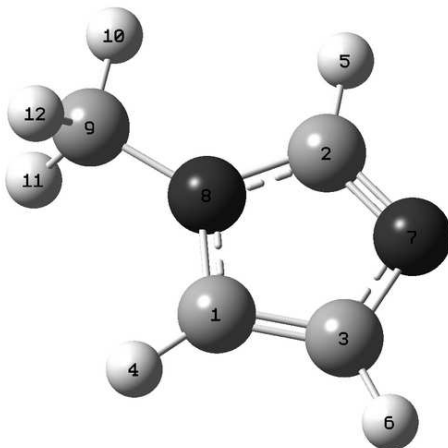
SCF Energy - E(RM062X) -309.479 988 793
 Sum of Electronic and Thermal Free Energies - E(RM062X) -309.376 765 000

Table S91 Cartesian Coordinates, Electronic and Free Energies of Optimized Geometry of 316

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
1	C	-0.126 135	0.718 371	1.831 334
2	C	-0.201 838	1.404 636	0.674 050
3	C	-0.007 742	0.746 006	-0.621 634
4	C	0.007 742	-0.746 006	-0.621 634
5	C	0.201 838	-1.404 636	0.674 050
6	C	0.126 135	-0.718 371	1.831 334
7	H	-0.233 243	1.231 825	2.781 643
8	H	-0.353 285	2.480 755	0.672 423
9	C	-0.201 838	-1.482 865	-1.730 190
10	H	-0.443 766	-1.031 578	-2.686 574
11	C	0.201 838	1.482 865	-1.730 190
12	H	0.152 136	2.566 680	-1.688 851
13	H	0.443 766	1.031 578	-2.686 574
14	H	-0.152 136	-2.566 680	-1.688 851
15	H	0.353 285	-2.480 755	0.672 423
16	H	0.233 243	-1.231 825	2.781 643

S-III.17 N-Methylimidazole (317)

Fig. S78 Optimized Geometry of 317 - Solvation in CHCl₃

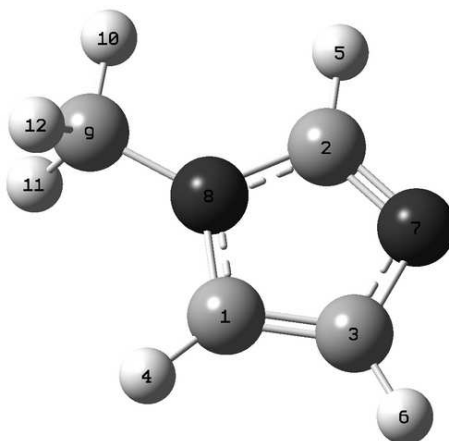


SCF Energy - E(RM062X) -265.435 857 255
 Sum of Electronic and Thermal Free Energies - E(RM062X) -265.364 371 000

Table S92 Cartesian Coordinates, Electronic and Free Energies of Optimized Geometry of 317 - Solvation in CHCl₃

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
1	C	0.224 619	1.109 775	0.000 000
2	C	0.192 413	-1.083 011	0.000 000
3	C	1.501 503	0.605 449	0.000 000
4	H	-0.161 817	2.117 691	0.000 000
5	H	-0.217 622	-2.083 930	0.000 000
6	H	2.432 494	1.153 566	0.000 000
7	N	1.471 781	-0.768 311	0.000 000
8	N	-0.605 092	0.015 716	0.000 000
9	C	-2.058 978	0.033 147	0.000 000
10	H	-2.419 200	-0.995 544	-0.000 005
11	H	-2.429 007	0.542 105	0.891 668
12	H	-2.429 008	0.542 115	-0.891 662

Fig. S79 Optimized Geometry of **317** - No Solvation



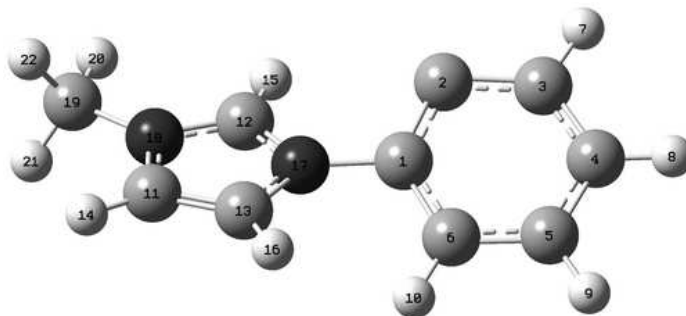
SCF Energy - E(RM062X) -265.427 540 637
Sum of Electronic and Thermal Free Energies - E(RM062X) -265.356 167 000

Table S93 Cartesian Coordinates, Electronic and Free Energies of Optimized Geometry of **317** - No Solvation

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
1	C	0.223 174	1.111 161	0.000 000
2	C	0.197 646	-1.081 789	0.000 000
3	C	1.498 968	0.604 915	0.000 000
4	H	-0.162 387	2.119 382	0.000 000
5	H	-0.209 066	-2.084 374	0.000 000
6	H	2.430 561	1.151 339	0.000 000
7	N	1.471 625	-0.766 216	0.000 000
8	N	-0.607 523	0.016 488	0.000 000
9	C	-2.056 960	0.030 548	0.000 000
10	H	-2.416 102	-0.999 397	0.000 000
11	H	-2.434 343	0.536 068	0.891 892
12	H	-2.434 343	0.536 069	-0.891 892

S-III.18 Benzene N-heterocyclic Carbene Zwitterionic Intermediate (324)

Fig. S80 Optimized Geometry of **324** - Solvation in CHCl_3



SCF Energy - E(RM062X) -496.309 928 520
 Sum of Electronic and Thermal Free Energies - E(RM062X) -496.165 269 000

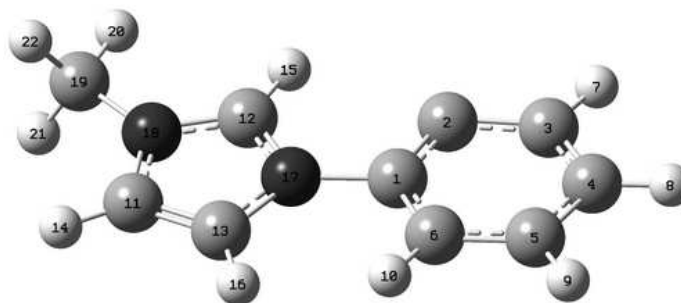
Table S94 Cartesian Coordinates, Electronic and Free Energies of Optimized Geometry of **324** - Solvation in CHCl_3

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
1	C	0.929 853	0.006 260	-0.026 673
2	C	1.360 312	-1.297 020	-0.284 782
3	C	2.771 300	-1.390 502	-0.233 526
4	C	3.628 544	-0.314 124	0.022 470
5	C	3.101 435	0.953 388	0.283 249
6	C	1.719 410	1.121 681	0.271 215
7	H	3.242 106	-2.359 085	-0.412 470
8	H	4.706 911	-0.458 957	0.028 115
9	H	3.750 884	1.794 437	0.505 578
10	H	1.287 479	2.090 906	0.509 738
11	C	-2.524 424	1.129 718	-0.264 030
12	C	-1.414 018	-0.722 316	0.176 270
13	C	-1.191 474	1.403 970	-0.332 180
14	H	-3.387 622	1.755 638	-0.424 625
15	H	-1.158 390	-1.744 267	0.407 479
16	H	-0.678 135	2.317 546	-0.581 754
17	N	-0.518 153	0.234 502	-0.052 888

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Table S94 – continued from previous page

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
18	N	-2.639 899	-0.204 997	0.055 344
19	C	-3.892 547	-0.933 552	0.238 263
20	H	-3.658 611	-1.974 080	0.456 137
21	H	-4.447 272	-0.499 349	1.069 939
22	H	-4.481 324	-0.874 341	-0.676 990

Fig. S81 Optimized Geometry of **324** - No Solvation

SCF Energy - E(RM062X) -496.287 575 003
Sum of Electronic and Thermal Free Energies - E(RM062X) -496.144 388 000

Table S95 Cartesian Coordinates, Electronic and Free Energies of Optimized Geometry of **324** - No Solvation

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
1	C	-0.939 113	0.041 756	-0.001 986
2	C	-1.305 663	-1.297 729	-0.069 466
3	C	-2.711 128	-1.441 370	-0.063 646
4	C	-3.609 219	-0.372 082	-0.004 734
5	C	-3.138 252	0.942 295	0.070 230
6	C	-1.765 351	1.165 402	0.077 220
7	H	-3.137 521	-2.444 437	-0.110 147
8	H	-4.681 874	-0.554 657	-0.011 764
9	H	-3.826 545	1.779 704	0.128 290
10	H	-1.386 250	2.182 500	0.153 319

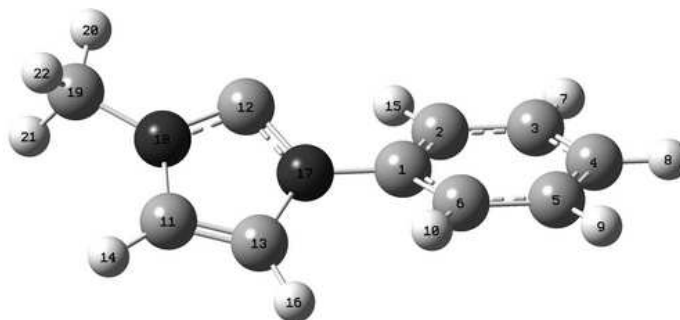
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Table S95 – continued from previous page

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
11	C	2.547 299	1.157 215	-0.071 984
12	C	1.389 117	-0.716 990	0.050 875
13	C	1.218 901	1.466 023	-0.086 536
14	H	3.423 315	1.784 531	-0.119 494
15	H	1.058 253	-1.747 982	0.100 565
16	H	0.730 509	2.422 708	-0.157 586
17	N	0.519 484	0.284 380	-0.008 206
18	N	2.631 791	-0.215 303	0.013 910
19	C	3.859 840	-0.996 748	0.060 275
20	H	3.595 823	-2.052 104	0.114 953
21	H	4.446 376	-0.817 614	-0.842 108
22	H	4.440 412	-0.722 833	0.942 548

S-III.19 Benzene N-heterocyclic Carbene (**317a**)

Fig. S82 Optimized Geometry of **317a** - Solvation in CHCl₃



SCF Energy - E(RM062X)

-496.360 959 591

Sum of Electronic and Thermal Free Energies - E(RM062X) -496.215 632 000

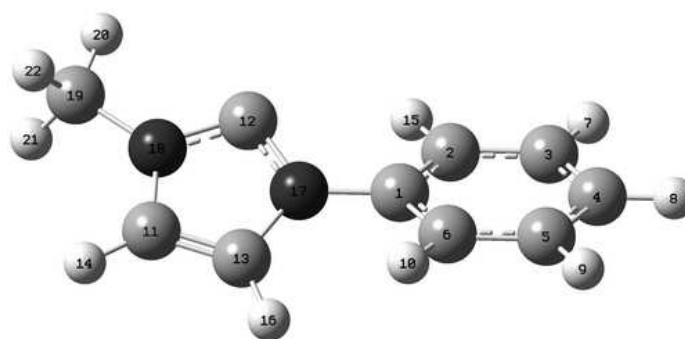
Table S96 Cartesian Coordinates, Electronic and Free Energies of Optimized Geometry of **317a** - Solvation in CHCl₃

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
1	C	-0.848 126	0.033 551	-0.018 733
2	C	-1.429 708	-1.200 421	-0.314 559
3	C	-2.814 494	-1.336 477	-0.263 561
4	C	-3.622 084	-0.247 533	0.067 711
5	C	-3.033 160	0.981 817	0.358 869
6	C	-1.646 919	1.125 114	0.324 502
7	H	-3.263 912	-2.297 089	-0.494 234
8	H	-4.701 043	-0.357 370	0.099 802
9	H	-3.650 263	1.833 275	0.627 140
10	H	-1.190 030	2.075 023	0.582 815
11	C	2.541 059	1.081 457	-0.354 625
12	C	1.440 445	-0.825 299	0.279 330
13	C	1.217 203	1.343 610	-0.453 990
14	H	3.401 346	1.697 708	-0.566 549
15	H	-0.791 376	-2.035 027	-0.580 675
16	H	0.696 088	2.226 453	-0.788 674
17	N	0.567 250	0.176 003	-0.067 570
18	N	2.644 290	-0.228 662	0.089 037
19	C	3.916 915	-0.888 363	0.336 551

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Table S96 – continued from previous page

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
20	H	3.707 034	-1.903 979	0.667 712
21	H	4.511 539	-0.917 239	-0.579 191
22	H	4.473 054	-0.357 880	1.112 614

Fig. S83 Optimized Geometry of **317a** - No Solvation

SCF Energy - E(RM062X) -496.352 403 018
 Sum of Electronic and Thermal Free Energies - E(RM062X) -496.206 999 000

Table S97 Cartesian Coordinates, Electronic and Free Energies of Optimized Geometry of **317a** - No Solvation

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
1	C	-0.846 305	0.040 984	-0.015 348
2	C	-1.414 006	-1.208 244	-0.270 722
3	C	-2.796 850	-1.353 012	-0.230 787
4	C	-3.618 559	-0.261 407	0.051 884
5	C	-3.043 578	0.980 587	0.308 779
6	C	-1.658 711	1.134 510	0.284 293
7	H	-3.235 241	-2.325 899	-0.429 568
8	H	-4.696 852	-0.379 823	0.075 896
9	H	-3.670 705	1.834 762	0.543 670
10	H	-1.214 684	2.095 582	0.522 477
11	C	2.543 247	1.102 477	-0.302 257

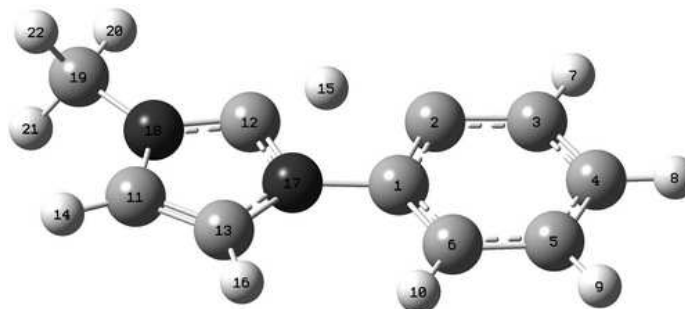
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Table S97 – continued from previous page

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
12	C	1.436 322	-0.833 471	0.236 570
13	C	1.220 477	1.371 836	-0.388 166
14	H	3.403 587	1.727 933	-0.485 196
15	H	-0.759 629	-2.044 201	-0.488 412
16	H	0.704 608	2.270 853	-0.684 612
17	N	0.567 656	0.189 200	-0.058 047
18	N	2.641 649	-0.228 751	0.075 696
19	C	3.904 385	-0.912 076	0.289 878
20	H	3.676 333	-1.940 169	0.566 769
21	H	4.502 766	-0.902 883	-0.624 967
22	H	4.466 154	-0.432 393	1.095 657

S-III.20 Proton Transfer Transition State for Benzene N-heterocyclic Carbene (from **324** to **317a**)

Fig. S84 Optimized Geometry of Transition State to **317a** - Solvation in CHCl_3



SCF Energy - E(RM062X) -496.291 120 686
 Sum of Electronic and Thermal Free Energies - E(RM062X) -496.150 058 000
 Imaginary Frequency (cm^{-1}) -1542.040

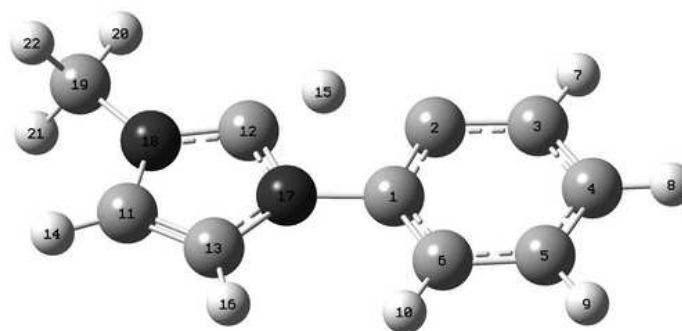
Table S98 Cartesian Coordinates, Electronic and Free Energies for Optimized Geometry of Transition State to **317a** - Solvation in CHCl_3

Center #	Atomic #	Cartesian Coordinates		
		X	Y	Z
1	C	0.688 182	-0.610 905	0.000 000
2	C	-0.213 475	-1.680 277	0.000 000
3	C	0.403 965	-2.937 693	0.000 000
4	C	1.800 201	-3.091 742	0.000 000
5	C	2.633 815	-1.973 882	0.000 000
6	C	2.073 278	-0.692 367	0.000 000
7	H	-0.204 701	-3.841 766	0.000 000
8	H	2.238 860	-4.086 600	0.000 000
9	H	3.713 061	-2.090 923	0.000 000
10	H	2.708 222	0.189 938	0.000 000
11	C	-0.709 313	2.741 563	0.000 000
12	C	-1.337 708	0.599 249	0.000 000
13	C	0.422 898	1.981 909	0.000 000
14	H	-0.842 600	3.812 426	0.000 000
15	H	-1.474 084	-0.675 844	0.000 000
16	H	1.460 905	2.272 893	0.000 000
17	N	0.000 000	0.673 924	0.000 000

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Table S98 – continued from previous page

Center #	Atomic #	Cartesian Coordinates		
		X	Y	Z
18	N	-1.781 666	1.864 107	0.000 000
19	C	-3.184 336	2.262 664	0.000 000
20	H	-3.792 215	1.359 766	0.000 000
21	H	-3.400 413	2.851 391	0.892 444
22	H	-3.400 413	2.851 391	-0.892 444

Fig. S85 Optimized Geometry of Transition State to **317a** - No Solvation

SCF Energy - E(RM062X) -496.278 936 384
Sum of Electronic and Thermal Free Energies - E(RM062X) -496.138 018 000
Imaginary Frequency (cm⁻¹) -1261.020

Table S99 Cartesian Coordinates, Electronic and Free Energies for Optimized Geometry of Transition State to **317a** - No Solvation

Center #	Atomic #	Cartesian Coordinates		
		X	Y	Z
1	C	0.685 856	-0.624 414	0.000 000
2	C	-0.220 426	-1.683 952	0.000 000
3	C	0.401 700	-2.939 941	0.000 000
4	C	1.795 584	-3.092 316	0.000 000
5	C	2.632 475	-1.976 069	0.000 000
6	C	2.071 544	-0.697 337	0.000 000
7	H	-0.207 520	-3.843 151	0.000 000
8	H	2.234 634	-4.087 151	0.000 000

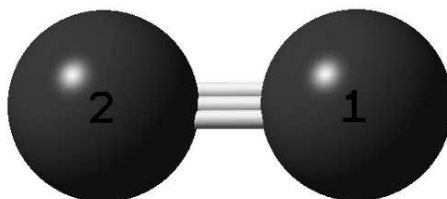
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Table S99 – continued from previous page

Center #	Atomic #	Cartesian Coordinates		
		X	Y	Z
9	H	3.711 471	-2.094 541	0.000 000
10	H	2.706 472	0.186 049	0.000 000
11	C	-0.701 844	2.745 435	0.000 000
12	C	-1.333 289	0.606 320	0.000 000
13	C	0.425 022	1.976 215	0.000 000
14	H	-0.827 780	3.817 233	0.000 000
15	H	-1.521 149	-0.622 569	0.000 000
16	H	1.465 099	2.258 936	0.000 000
17	N	0.000 000	0.671 969	0.000 000
18	N	-1.777 866	1.873 350	0.000 000
19	C	-3.178 354	2.268 331	0.000 000
20	H	-3.784 079	1.363 420	0.000 000
21	H	-3.400 840	2.855 453	0.893 006
22	H	-3.400 840	2.855 453	-0.893 006

S-III.21 Dinitrogen (318)

Fig. S86 Optimized Geometry of 318



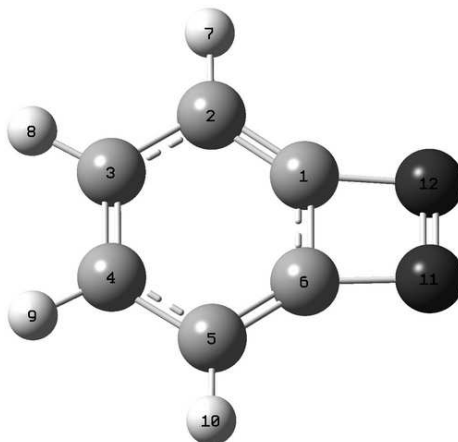
SCF Energy - E(RM062X) -109.492 343 554
Sum of Electronic and Thermal Free Energies - E(RM062X) -109.504 987 000

Table S100 Cartesian Coordinates, Electronic and Free Energies of Optimized Geometry of 318

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
1	N	0.000 000	0.000 000	0.549 101
2	N	0.000 000	0.000 000	-0.549 101

S-III.22 1,2-diazabenzene (318a)

Fig. S87 Optimized Geometry of 318a



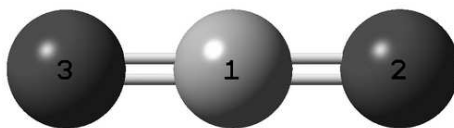
SCF Energy - E(RM062X) -340.285 665 586
 Sum of Electronic and Thermal Free Energies - E(RM062X) -340.227 628 000

Table S101 Cartesian Coordinates, Electronic and Free Energies of Optimized Geometry of 318a

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
1	C	-0.538 256	0.697 781	0.000 000
2	C	0.578 712	1.466 780	0.000 000
3	C	1.785 735	0.691 048	0.000 000
4	C	1.785 735	-0.691 048	0.000 000
5	C	0.578 712	-1.466 780	0.000 000
6	C	-0.538 256	-0.697 781	0.000 000
7	H	0.593 769	2.550 131	0.000 000
8	H	2.736 209	1.214 239	0.000 000
9	H	2.736 209	-1.214 239	0.000 000
10	H	0.593 769	-2.550 131	0.000 000
11	N	-2.041 018	-0.629 207	0.000 000
12	N	-2.041 018	0.629 207	0.000 000

S-III.23 Carbon Dioxide (319)

Fig. S88 Optimized Geometry of 319



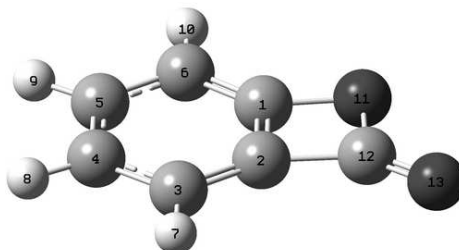
SCF Energy - E(RM062X) -188.518 377 441
Sum of Electronic and Thermal Free Energies - E(RM062X) -188.527 950 000

Table S102 Cartesian Coordinates, Electronic and Free Energies of Optimized Geometry of 319

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
1	C	0.000 000	0.000 000	0.000 000
2	O	0.000 000	0.000 000	-1.162 713
3	O	0.000 000	0.000 000	1.162 713

S-III.24 Benzo- β -Lactone (319a)

Fig. S89 Optimized Geometry of 319a



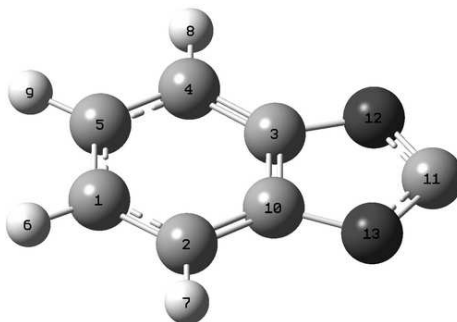
SCF Energy - E(RM062X) -419.406 256 654
 Sum of Electronic and Thermal Free Energies - E(RM062X) -419.344 114 000

Table S103 Cartesian Coordinates, Electronic and Free Energies of Optimized Geometry of 319a

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
1	C	0.022 367	-0.799 842	0.000 000
2	C	0.273 813	0.561 944	0.000 001
3	C	-0.728 881	1.507 713	0.000 000
4	C	-2.030 343	0.971 703	0.000 000
5	C	-2.259 997	-0.408 255	0.000 000
6	C	-1.224 178	-1.368 309	0.000 000
7	H	-0.549 140	2.576 386	0.000 001
8	H	-2.881 072	1.643 866	-0.000 001
9	H	-3.286 559	-0.760 871	0.000 000
10	H	-1.417 467	-2.433 408	0.000 001
11	O	1.368 623	-1.215 933	0.000 000
12	C	1.720 288	0.169 751	0.000 000
13	O	2.818 354	0.611 658	0.000 000

S-III.25 Benzodioxole Carbene (319b)

Fig. S90 Optimized Geometry of 319b



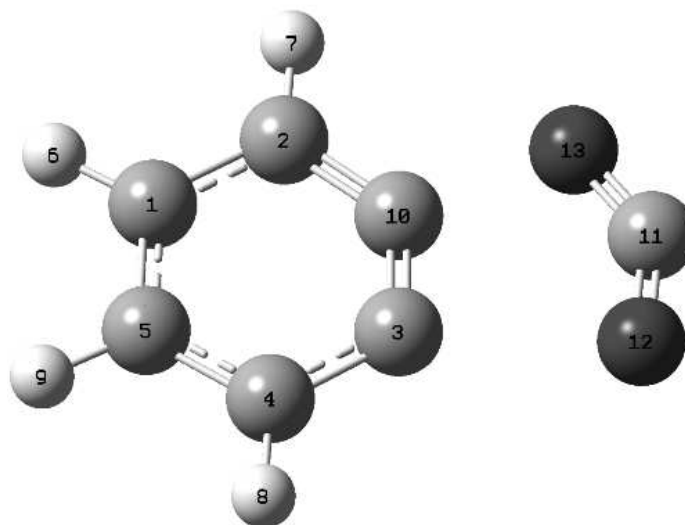
SCF Energy - E(RM062X) -419.385 969 514
 Sum of Electronic and Thermal Free Energies - E(RM062X) -419.322 951 000

Table S104 Cartesian Coordinates, Electronic and Free Energies of Optimized Geometry of 319b

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
1	C	0.000 000	-2.071 961	0.702 053
2	C	0.000 000	-0.886 748	1.440 547
3	C	0.000 000	0.273 725	-0.687 588
4	C	0.000 000	-0.886 748	-1.440 547
5	C	0.000 000	-2.071 961	-0.702 053
6	H	0.000 000	-3.019 932	1.229 011
7	H	0.000 000	-0.873 834	2.523 681
8	H	0.000 000	-0.873 834	-2.523 681
9	H	0.000 000	-3.019 932	-1.229 011
10	C	0.000 000	0.273 725	0.687 588
11	C	0.000 000	2.400 636	0.000 000
12	O	0.000 000	1.600 220	-1.075 147
13	O	0.000 000	1.600 220	1.075 147

S-III.26 Transition State Leading to **319b**

Fig. S91 Optimized Geometry of Transition State to **319b**



SCF Energy - E(RM062X) -419.289 219 651
 Sum of Electronic and Thermal Free Energies - E(RM062X) -419.232 380 000
 Imaginary Frequency (cm^{-1}) -552.720

Table S105 Cartesian Coordinates, Electronic and Free Energies for Optimized Geometry of Transition State to **319b**

Center #	Atomic #	Cartesian Coordinates		
		X	Y	Z
1	C	-2.296 944	0.323 485	0.000 000
2	C	-1.195 734	1.190 946	0.000 000
3	C	0.205 064	-0.774 939	0.000 000
4	C	-0.861 537	-1.666 891	0.000 000
5	C	-2.132 634	-1.071 378	0.000 000
6	H	-3.298 083	0.742 603	0.000 000
7	H	-1.295 238	2.270 414	0.000 000
8	H	-0.751 275	-2.746 517	0.000 000
9	H	-3.013 895	-1.706 287	0.000 000
10	C	0.000 000	0.503 317	0.000 000
11	C	2.378 737	0.593 488	0.000 000

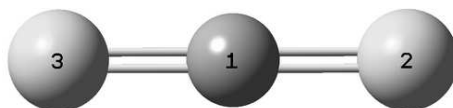
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Table S105 – continued from previous page

Center #	Atomic #	Cartesian Coordinates		
		X	Y	Z
12	O	2.471 120	-0.582 064	0.000 000
13	O	1.500 978	1.438 516	0.000 000

S-III.27 Carbon Disulfide (320)

Fig. S92 Optimized Geometry of **320**



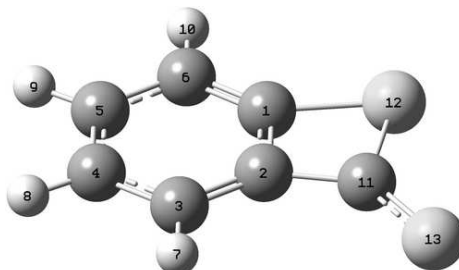
SCF Energy - E(RM062X) -834.396 762 689
Sum of Electronic and Thermal Free Energies - E(RM062X) -834.412 762 000

Table S106 Cartesian Coordinates, Electronic and Free Energies of Optimized Geometry of **320**

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
1	C	0.000 000	0.000 000	0.000 000
2	S	0.000 000	0.000 000	1.554 779
3	S	0.000 000	0.000 000	-1.554 779

S-III.28 Benzodithioate (320a)

Fig. S93 Optimized Geometry of 320a



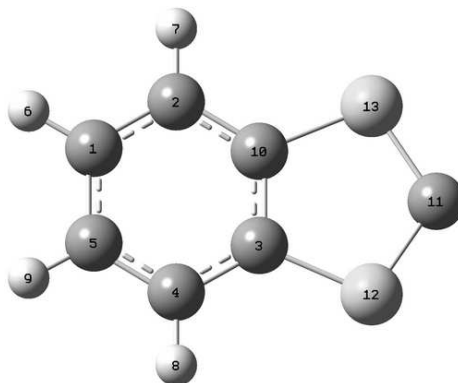
SCF Energy - E(RM062X) -1065.320 508 020
 Sum of Electronic and Thermal Free Energies - E(RM062X) -1065.265 277 000

Table S107 Cartesian Coordinates, Electronic and Free Energies of Optimized Geometry of 320a

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
1	C	-0.689 113	0.837 012	0.000 000
2	C	-0.163 692	-0.459 559	0.000 000
3	C	-0.968 954	-1.584 244	0.000 000
4	C	-2.352 931	-1.348 832	0.000 000
5	C	-2.866 911	-0.049 840	0.000 000
6	C	-2.040 104	1.092 614	0.000 000
7	H	-0.558 996	-2.588 846	0.000 000
8	H	-3.038 708	-2.188 974	0.000 001
9	H	-3.943 806	0.087 335	0.000 000
10	H	-2.458 647	2.092 239	-0.000 001
11	C	1.267 130	-0.102 946	0.000 000
12	S	0.901 673	1.682 848	0.000 000
13	S	2.653 803	-0.914 535	0.000 000

S-III.29 Benzodithiolane Carbene (320b)

Fig. S94 Optimized Geometry of 320b



SCF Energy - E(RM062X)

-1065.309 447 010

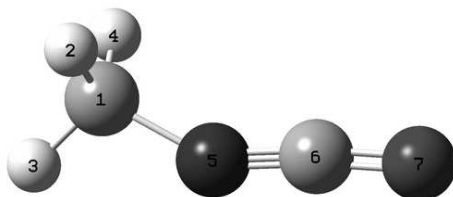
Sum of Electronic and Thermal Free Energies - E(RM062X)-1065.253 422 000

Table S108 Cartesian Coordinates, Electronic and Free Energies of Optimized Geometry of 320b

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
1	C	0.000 000	0.702 157	-2.588 904
2	C	0.000 000	1.412 000	-1.396 803
3	C	0.000 000	-0.698 296	-0.192 555
4	C	0.000 000	-1.412 000	-1.396 803
5	C	0.000 000	-0.702 157	-2.588 904
6	H	0.000 000	1.239 218	-3.531 468
7	H	0.000 000	2.497 113	-1.395 111
8	H	0.000 000	-2.497 113	-1.395 111
9	H	0.000 000	-1.239 218	-3.531 468
10	C	0.000 000	0.698 296	-0.192 555
11	C	0.000 000	0.000 000	2.366 671
12	S	0.000 000	-1.396 242	1.431 008
13	S	0.000 000	1.396 242	1.431 008

S-III.30 Methyl Isocyanate (321)

Fig. S95 Optimized Geometry of **321**



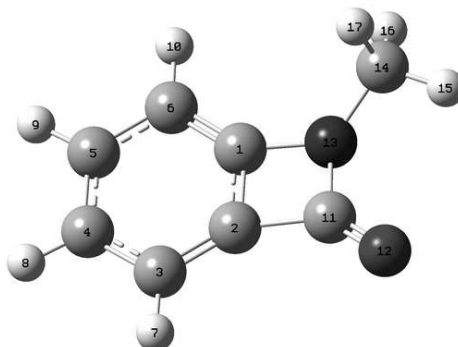
SCF Energy - E(RM062X) -207.909 942 935
Sum of Electronic and Thermal Free Energies - E(RM062X) -207.886 645 000

Table S109 Cartesian Coordinates, Electronic and Free Energies of Optimized Geometry of **321**

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
1	C	1.778 247	0.126 710	0.000 000
2	H	1.984 737	0.722 196	-0.891 280
3	H	2.423 699	-0.750 729	-0.000 003
4	H	1.984 738	0.722 190	0.891 283
5	N	0.407 586	-0.301 774	0.000 000
6	C	-0.751 295	-0.038 288	0.000 000
7	O	-1.925 999	0.111 028	0.000 000

S-III.31 Benzo- β -Lactam (**321a**)

Fig. S96 Optimized Geometry of **321a**



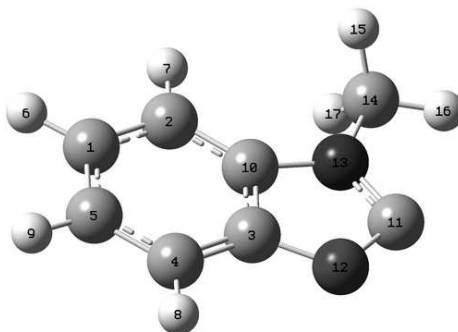
SCF Energy - E(RM062X) -438.838 054 345
 Sum of Electronic and Thermal Free Energies - E(RM062X) -438.738 428 000

Table S110 Cartesian Coordinates, Electronic and Free Energies of Optimized Geometry of **321a**

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
1	C	-0.074 646	0.585 757	-0.130 961
2	C	-0.235 494	-0.804 284	-0.057 836
3	C	-1.462 847	-1.405 939	0.050 828
4	C	-2.565 256	-0.518 795	0.093 225
5	C	-2.390 713	0.861 267	0.040 138
6	C	-1.118 030	1.474 531	-0.071 499
7	H	-1.598 233	-2.479 907	0.115 840
8	H	-3.568 390	-0.921 791	0.180 062
9	H	-3.268 457	1.498 731	0.085 635
10	H	-1.004 130	2.551 582	-0.105 302
11	C	1.284 839	-0.884 577	-0.088 177
12	O	2.157 678	-1.696 452	0.050 919
13	N	1.348 176	0.518 654	-0.284 861
14	C	2.367 007	1.419 439	0.215 410
15	H	3.333 400	0.924 392	0.107 398
16	H	2.374 736	2.337 090	-0.374 965
17	H	2.203 260	1.666 556	1.271 246

S-III.32 Benzoxazole Carbene (321b)

Fig. S97 Optimized Geometry of 321b



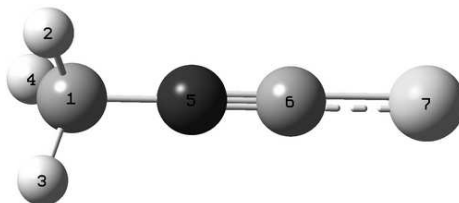
SCF Energy - E(RM062X) -438.837 254 576
 Sum of Electronic and Thermal Free Energies - E(RM062X) -438.734 597 000

Table S111 Cartesian Coordinates, Electronic and Free Energies of Optimized Geometry of 321b

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
1	C	1.983 719	1.307 387	0.000 000
2	C	0.603 040	1.505 348	0.000 000
3	C	0.378 275	-0.909 786	0.000 000
4	C	1.746 327	-1.126 275	0.000 000
5	C	2.543 529	0.019 360	0.000 000
6	H	2.641 773	2.169 718	0.000 000
7	H	0.169 878	2.499 709	0.000 000
8	H	2.166 532	-2.125 228	0.000 000
9	H	3.622 925	-0.087 960	0.000 000
10	C	-0.183 835	0.357 920	0.000 000
11	C	-1.856 461	-1.186 803	0.000 000
12	O	-0.646 457	-1.821 741	0.000 000
13	N	-1.561 595	0.127 197	0.000 000
14	C	-2.559 167	1.183 833	0.000 000
15	H	-2.444 472	1.803 033	-0.892 268
16	H	-3.541 910	0.715 343	-0.000 002
17	H	-2.444 474	1.803 030	0.892 271

S-III.33 Methyl Isothiocyanate (322)

Fig. S98 Optimized Geometry of **322**



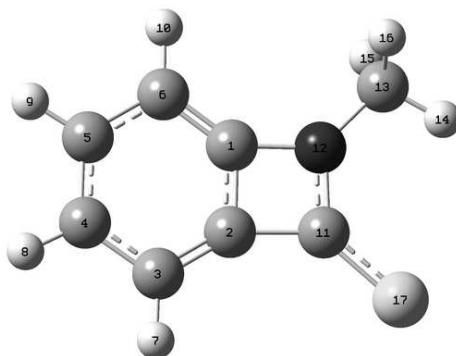
SCF Energy - E(RM062X) -530.859 949 538
Sum of Electronic and Thermal Free Energies - E(RM062X) -530.838 987 000

Table S112 Cartesian Coordinates, Electronic and Free Energies of Optimized Geometry of **322**

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
1	C	2.410 227	0.000 000	-0.000 501
2	H	2.772 848	-0.891 142	-0.515 483
3	H	2.774 671	-0.000 084	1.028 073
4	H	2.772 848	0.891 226	-0.515 337
5	N	0.990 385	0.000 000	0.001 018
6	C	-0.179 835	0.000 000	0.000 358
7	S	-1.789 714	0.000 000	-0.000 220

S-III.34 Benzo- β -Thiolactam (**322a**)

Fig. S99 Optimized Geometry of **322a**



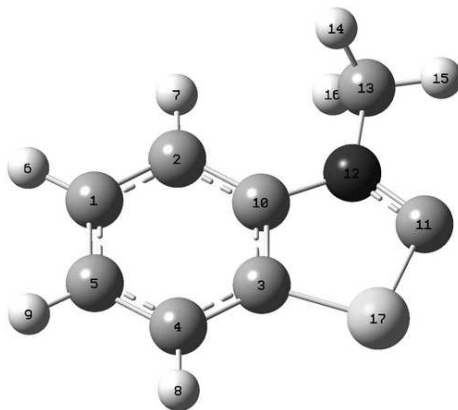
SCF Energy - E(RM062X) -761.779 387 634
 Sum of Electronic and Thermal Free Energies - E(RM062X) -761.682 616 000

Table S113 Cartesian Coordinates, Electronic and Free Energies of Optimized Geometry of **322a**

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
1	C	0.578 434	0.717 828	-0.000 001
2	C	0.355 211	-0.669 518	-0.000 001
3	C	1.371 978	-1.579 520	0.000 000
4	C	2.679 678	-1.017 010	0.000 001
5	C	2.882 992	0.354 824	0.000 001
6	C	1.814 366	1.297 683	0.000 000
7	H	1.216 519	-2.652 891	0.000 000
8	H	3.538 965	-1.678 755	0.000 001
9	H	3.900 813	0.732 223	0.000 001
10	H	1.993 687	2.366 062	0.000 000
11	C	-1.130 835	-0.354 753	-0.000 001
12	N	-0.830 424	0.986 626	-0.000 002
13	C	-1.642 631	2.174 460	0.000 001
14	H	-2.687 461	1.859 467	-0.000 002
15	H	-1.445 136	2.774 535	0.892 642
16	H	-1.445 132	2.774 543	-0.892 633
17	S	-2.544 653	-1.164 096	0.000 000

S-III.35 Benzothiazole Carbene (**322b**)

Fig. S100 Optimized Geometry of **322b**



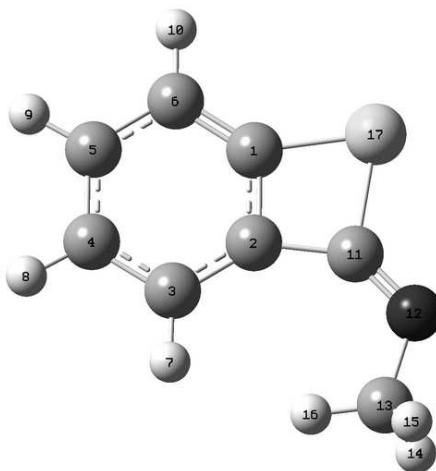
SCF Energy - E(RM062X) -761.800 304 962
 Sum of Electronic and Thermal Free Energies - E(RM062X) -761.701 104 000

Table S114 Cartesian Coordinates, Electronic and Free Energies of Optimized Geometry of **322b**

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
1	C	-2.330 956	1.119 284	0.000 000
2	C	-0.998 953	1.515 854	0.000 001
3	C	-0.367 187	-0.836 758	-0.000 001
4	C	-1.706 755	-1.229 808	-0.000 002
5	C	-2.682 667	-0.239 660	-0.000 002
6	H	-3.110 389	1.873 793	0.000 000
7	H	-0.730 180	2.566 639	0.000 002
8	H	-1.976 730	-2.280 481	-0.000 003
9	H	-3.730 302	-0.521 493	-0.000 002
10	C	-0.021 825	0.517 171	0.000 001
11	C	2.158 048	-0.395 415	0.000 000
12	N	1.373 979	0.688 155	0.000 001
13	C	1.938 425	2.037 175	0.000 002
14	H	1.611 625	2.576 084	0.892 584
15	H	3.021 607	1.942 225	0.000 002
16	H	1.611 626	2.576 085	-0.892 580
17	S	1.109 758	-1.779 812	-0.000 001

S-III.36 Benzo- β -Thioimidate (**322c**)

Fig. S101 Optimized Geometry of **322c**



SCF Energy - E(RM062X)

-761.789 676 998

Sum of Electronic and Thermal Free Energies - E(RM062X) -761.693 669 000

Table S115 Cartesian Coordinates, Electronic and Free Energies of Optimized Geometry of **322c**

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
1	C	0.787 105	0.816 728	0.000 000
2	C	0.061 376	-0.381 634	0.000 000
3	C	0.701 390	-1.612 152	0.000 000
4	C	2.104 594	-1.590 759	0.000 000
5	C	2.813 913	-0.387 725	0.000 000
6	C	2.166 007	0.858 953	0.000 000
7	H	0.167 671	-2.555 747	0.000 000
8	H	2.649 749	-2.528 514	0.000 001
9	H	3.899 155	-0.415 614	0.000 000
10	H	2.726 673	1.786 685	0.000 000
11	C	-1.299 325	0.240 500	0.000 000
12	N	-2.509 692	-0.075 831	0.000 000
13	C	-2.871 393	-1.486 349	0.000 000
14	H	-3.486 380	-1.685 217	0.881 119

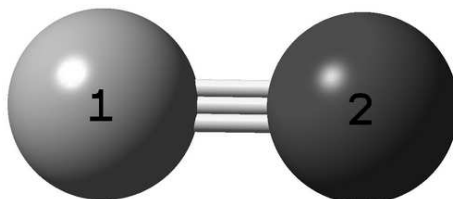
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Table S115 – continued from previous page

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
15	H	-3.486 384	-1.685 215	-0.881 117
16	H	-2.013 461	-2.164 931	-0.000 003
17	S	-0.604 449	1.939 625	0.000 000

S-III.37 Carbon Monoxide (323)

Fig. S102 Optimized Geometry of **323**



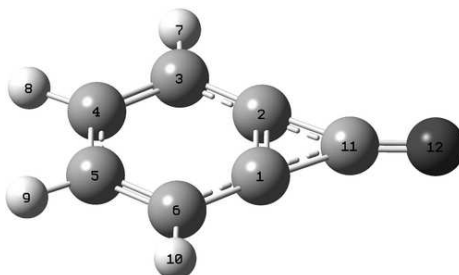
SCF Energy - E(RM062X) -113.277 589 723
Sum of Electronic and Thermal Free Energies - E(RM062X) -113.291 541 000

Table S116 Cartesian Coordinates, Electronic and Free Energies of Optimized Geometry of **323**

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
1	C	0.000 000	0.000 000	-0.646 214
2	O	0.000 000	0.000 000	0.484 660

S-III.38 Benzocyclopropanone (**323a**)

Fig. S103 Optimized Geometry of **323a**



SCF Energy - E(RM062X) -344.159 577 518
 Sum of Electronic and Thermal Free Energies - E(RM062X) -344.102 041 000

Table S117 Cartesian Coordinates, Electronic and Free Energies of Optimized Geometry of **323a**

Center #	Atom Type	Cartesian Coordinates		
		X	Y	Z
1	C	0.000 000	0.440 326	0.691 810
2	C	0.000 000	0.440 326	-0.691 810
3	C	0.000 000	-0.729 337	-1.467 461
4	C	0.000 000	-1.890 234	-0.713 364
5	C	0.000 000	-1.890 234	0.713 364
6	C	0.000 000	-0.729 337	1.467 461
7	H	0.000 000	-0.742 448	-2.550 957
8	H	0.000 000	-2.851 472	-1.217 981
9	H	0.000 000	-2.851 472	1.217 981
10	H	0.000 000	-0.742 448	2.550 957
11	C	0.000 000	1.690 785	0.000 000
12	O	0.000 000	2.899 261	0.000 000

