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Computational study of the chair–chair interconversion and stereoelectronic interactions in 1,2,3-trithiacyclohexane (1,2,3-trithiane)

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ABSTRACT: *Ab initio* theory, density functional theory (DFT) and Møller–Plesset perturbation theory (MP2) with the 6–31G(d), 6–31++G(d), 6–31G(d,p), 6–31+G(d,p), 6–31++G(d,p), 6–311G(d,p) and 6–311+G(d,p) basis sets were used to study stereoelectronic hyperconjugative interactions and the mechanism of the chair–chair conformational interconversion in 1,2,3-trithiacyclohexane (1,2,3-trithiane). The relative energies, enthalpies, entropies, free energies and structural parameters of the chair, 1,4-twist and 2,5-twist conformers, a distorted 1,4-boat transition state and a 2,5-boat transition state were calculated. The HF calculated energy difference (ΔE) between the chair conformer of 1,2,3-trithiane and the distorted 1,4-boat transition state was 10.59 kcal mol^{-1} (1 kcal = 4.184 kJ). The 1,4-twist conformer and the 2,5-boat transition state are close in energy, as are the 2,5-twist conformer and the distorted 1,4-boat transition state. B3LYP/6–311+G(d,p) calculated the chair conformer of 1,2,3-trithiane to be 5.83, 10.09, and 5.96 kcal mol^{-1}, respectively, lower in energy than the 1,4-twist conformer, 2,5-twist conformer and 2,5-boat transition state. Intrinsic reaction coordinate (IRC) calculations were used to connect the transition state between the chair conformer and the 1,4-twist conformer. B3LYP/6–31+G(d,p) and B3LYP/6–311+G(d,p) calculated this transition state to be 14.25 kcal mol^{-1} higher in energy than the chair conformer. In the chair conformer, the respective C4—H and C6—H bond lengths are equal, but the C5—Heq bond is longer than the C5—Hax bond. In the 1,4-twist conformer, the C4—Hiso bond lengths are equal, the C5—Hψeq bond is longer than the C5—Hψax bond and the C6—H bond lengths are equal. In the 2,5-twist conformer, equal C—H bond lengths are found at C4 and at C5, but the C6—Hψeq bond is longer than the C6—Hψax bond. Copyright © 2003 John Wiley & Sons, Ltd.
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KEYWORDS: conformational interconversion; cyclic polysulfide (polysulfane); intrinsic reaction coordinate (IRC) calculation; stereoelectronic hyperconjugative interaction; trithiane

INTRODUCTION

Trisulfanes (trisulfides) are compounds that contain three contiguous divalent (sulfenyl) sulfur atoms. Although the chemistry of the sulfanes (sulfides) and disulfanes (disulfides) has dominated the literature, interest in the trisulfane (trisulfide) linkage has increased rapidly in the past few years (for reviews, see Refs 1 and 2). 1,2,3-Trithiacyclohexane (1,2,3-trithiane, **1**, Figs 1–4) is a stable compound and acyclic and cyclic polysulfides (polysulfanes) containing the trisulfane linkage have interesting biological activities. The trisulfane linkage is found in the fermentation-derived antitumor antibiotic calicheamicin[3,4] and two of the trisulfanes found in garlic (*Allium sativum* L.), methyl-2-propenyltrisulfane and bis(2-propenyl)trisulfane, are known to inhibit aggregation of blood platelets.[5] Among the trisulfanes isolated from marine organisms [1,2,6–9] that show bioactivity are varacin,[7] lissoclinotoxin[8] and *trans*-5-hydroxy-4-(4′-hydroxy-3′-methoxyphenyl)-4-(2″-imidazolyl)-1,2,3-trithiane (**2**, Fig. 5).[6] 1,2,3-Trithiane-5-carboxylic acid (**3**, Fig. 6) was isolated from asparagus (*A. officinalis* L.).[10] 5-(*N*,*N*-Dimethylamino)-1,2,3-trithiane (**4**, Fig. 7) is by far the most thoroughly investigated representative of the 1,2,3-trithianes because of its commercial use as an insecticide.[2] 5-Hydroxy-1,2,3-trithiane (**5**, Fig. 8)[11,12] is used in the synthesis of 1,2,3-trithian-5-yl *N*-methylcarbamate (**6**, Fig. 9).[11]

Although the structural properties and conformational interconversions of cyclohexane have been extensively studied,[13–22] comparatively little detailed work has been reported on the conformations, conformers and transition states involved in the chair–chair and twist–twist conformational interconversions of unsubstituted heterocyclohexanes in general[23–34] and triheterocyclohexanes in particular. Force field calculations are consistent with a chair conformation for 1,2,3-trithiane (**1**)[35–37] and an

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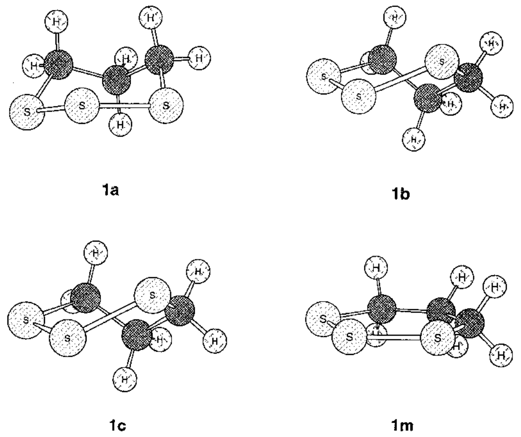
1a **1b** **1c** **1m**

Figure 1. Chair (**1a**), 1,4-twist (**1b**), 2,5-twist (**1c**) and planar (**1m**) conformations of 1,2,3-trithiane

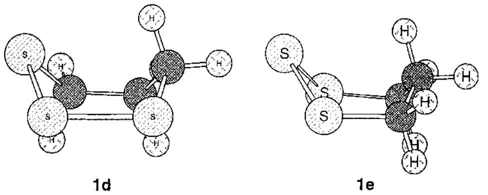
1d **1e**

Figure 2. 1,4-Boat (**1d**) and 2,5-boat (**1e**) conformations of 1,2,3-trithiane

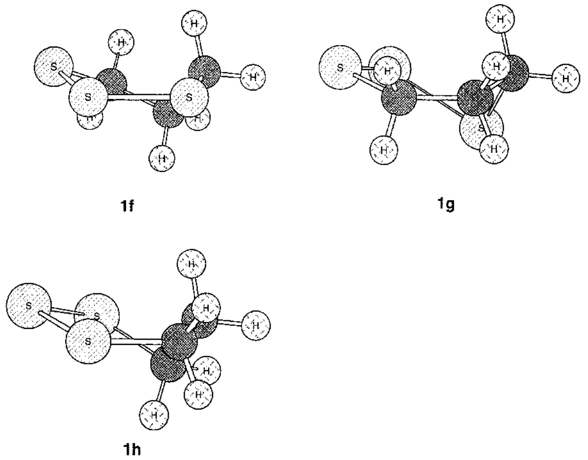
1f **1g** **1h**

Figure 3. 1,4-Half-chair (**1f** and **1g**) and 2,5-half-chair (**1h**) conformations of 1,2,3-trithiane

x-ray crystallographic study showed that 1,2,3-trithian-5-yl *N*-methylcarbamate exists in the chair conformation with the substituent in the equatorial position (**6b**).[11] The barrier to the chair–chair interconversion of 1,2,3-trithiane [**1**, $\Delta G^{\ddagger} = 13.2\,\mathrm{kcal\,mol^{-1}}$ (1 kcal = 4.184 kJ), CS_2, 265 K][38] and several 5,5-dialkyl-1,2,3-trithianes have been determined from NMR studies.[38–41]

Molecular mechanics calculations suggested that the 2,5-boat structure (**1e**) of 1,2,3-trithiane was a minimum-energy conformer.[36] In a study of the conformational interconversion of novel bicyclic spiranes (1,2,3-trithianes), it was suggested that the chair conformer

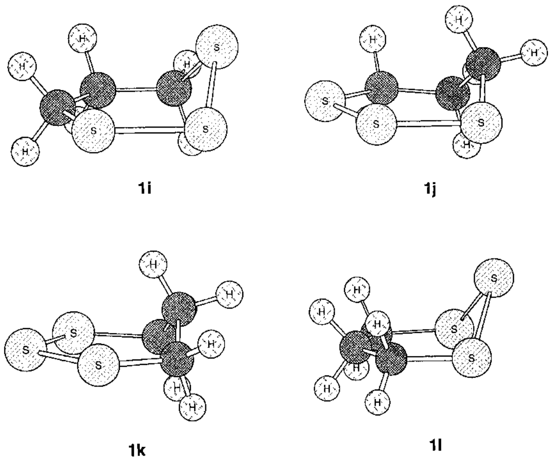
1i **1j** **1k** **1l**

Figure 4. 1,4-Sofa (**1i** and **1j**) and 2,5-sofa (**1k** and **1l**) conformations of 1,2,3-trithiane

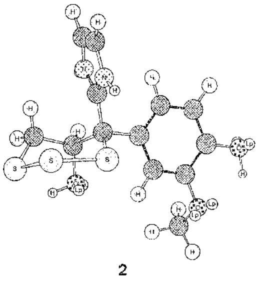
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Figure 5. Chair conformer of *trans*-5-hydroxy-4-(4′-hydroxy-3′-methoxyphenyl)-4-(2″-imidazolyl)-1,2,3-trithiane (**2**)

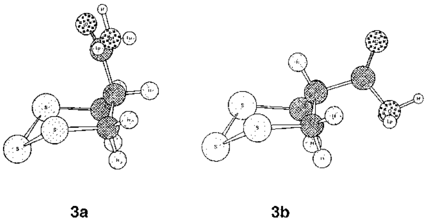
3a **3b**

Figure 6. Chair conformers of axial (**3a**) and equatorial (**3b**) 1,2,3-trithiane-5-carboxylic acid

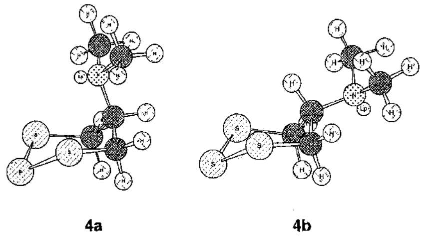
4a **4b**

Figure 7. Chair conformers of axial (**4a**) and equatorial (**4b**) 5-(*N*,*N*-dimethylamino)-1,2,3-trithiane

proceeds to the 2,5-boat form without bringing any torsional angle involving the S—S bond to 0°. It was further suggested that this boat structure pseudorotates to the inverted 2,5-boat form, which then proceeds to the inverted chair.[39] Thus, unlike cyclohexane and other

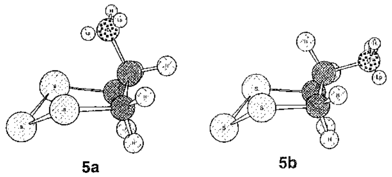

Figure 8. Chair conformers of axial (**5a**) and equatorial (**5b**) 5-hydroxy-1,2,3-trithiane

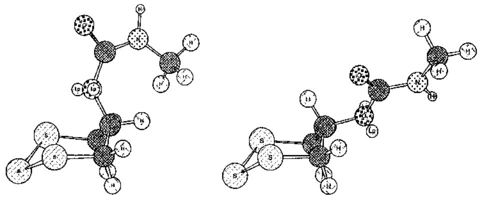

Figure 9. Chair conformers of axial (**6a**) and equatorial (**6b**) 1,2,3-trithiane-5-yl *N*-methylcarbamate

heterocyclohexanes where the boat form is a transition state between enantiomers of a twist structure, the 2,5-boat structures of 1,2,3-trithiane (**1e**) and of bicyclic spiranes (1,2,3-trithianes) have been proposed as minimum-energy conformers.[36,39]

Equilibrium geometries, reaction paths and transition states (first-order saddle points) are indispensable in the study of chemical reactions. Mapping out a reaction mechanism involves optimizing the reactants and products, finding the transition state and following the reaction path connecting them. Although calculations of equilibrium geometries for many small- and medium-sized molecules are easily done, locating the correct (desired) transition state can still be very challenging.[42–44] In addition, following the reaction path can be computationally expensive.

The understanding of stereoelectronic effects is one of the basic prerequisites for the prediction of molecular conformations and molecular reactivity, especially in systems where heteroatoms are involved. Stereoelectronic interactions involving π-bonds (conjugation) and σ-orbitals (hyperconjugation) in the ground state and transition state play significant roles in organic chemistry.[45–59] Hyperconjugation has been shown to influence chemical reactivity, conformational equilibria, conformational stability, selectivity, geometric parameters, NMR coupling constants [Perlin effect ($^1J_{\text{C–Heq}} > {}^1J_{\text{C–Hax}}$)] and torsional barriers. Alabugin and co-workers,[45,46] Anderson and co-workers,[47–49] Cai *et al.*[50] Freeman and co-workers[26–31] and Juaristi and co-workers[51–54] have used computational chemistry to investigate stereoelectronic hyperconjugative interactions in monoheterocyclohexanes and diheterocyclohexanes containing nitrogen, oxygen and/or sulfur.

In view of the importance of conformational analysis and stereoelectronic interactions in acyclic systems and heterocyclohexanes, this quantum chemical study was undertaken in order to explore the ability of *ab initio* theory, Møller–Plesset perturbation theory (MP2) and density functional theory (DFT) to calculate structural properties, relative energies, enthalpies, entropies and free energies of the respective conformers, conformations and transition states of 1,2,3-trithiane (**1**), to study the mechanisms of conformational interconversion and to investigate the stereoelectronic hyperconjugative interactions. Studies of stereoelectronic effects in carbocycles and heterocycles are useful owing to their rigid cyclic geometry, which keeps interacting orbitals in a well-defined geometry. The lone pair on sulfur and the difference in size between carbon and sulfur are seen in their contrasting conformational properties, structural properties and reactivities. For example, the C—S and S—S bond lengths are longer than the C—C bond lengths, the C—S—C bond angle is larger than the C—C—C bond angle and the S—S—S bond angle is smaller than the C—C—C bond angle.

CALCULATIONS AND COMPUTATIONAL METHODS

Calculations were carried out with the Spartan '02 Macintosh,[60] Spartan[60] and Gaussian[61–63] computational programs. Initial geometry optimizations were carried out at the HF/6–31G(d) level of theory for all structures. The level of theory and the basis set used for the calculations play an important role in determining how well the calculations reproduce the experimental data. Since 1,2,3-trithiane (**1**) has lone pair electrons, the use of diffuse functions [6–31+G(d), 6–31++G(d), 6–31+G(d,p), 6–311+G(d,p)] is recommended.[62] The MP2 and hybrid density functional calculations provide electron correlation that is often important in conformational studies.[64] Molecular structures are reported using several levels of theory, but the B3LYP/6–311+G(d,p) calculations are used in the discussion unless noted otherwise. Frequency calculations were computed at several levels of theory on the respective geometry-optimized structures at 298.15 K at 1 atm pressure. The HF, MP2 and B3LYP zero-point vibrational energies (ZPE) were scaled by 0.9135, 0.9676 and 0.9804, respectively. [65–70] The tight or very tight convergence option in Gaussian was used for structures with very small force constants (low-frequency vibrational modes).[63]

Total energies are given in hartrees [1 hartree = 1 atomic unit (au) = 627.5095 kcal mol^{-1}] and the other energies are in kcal mol^{-1}. The dipole moments are given in debye (D) and the entropies are given in entropy units (eu). To compare the calculated thermodynamic parameters between the conformers with the experimentally determined values, ΔE must be corrected for the difference in ZPE between the structures, the change in ΔH° on going from 0 to 298.15 K must be computed and ΔH° must then be converted to ΔG° using the calculated entropy difference.

Accurate geometries generally refer to bond lengths that are within about 0.01–0.02 Å of experiment and bond and dihedral angles that are within 1–2 ° of the experimentally measured value.[62,71,72]

Locating minima for functions is fairly easy, but finding transition structures (first-order saddle points) is much more difficult.[73–92] Although many different strategies have been proposed, there are no general methods which are guaranteed to work.[73–75] However, once the transition state has been found, the reaction path may be located by tracing the intrinsic reaction coordinate (IRC)[42–44] or minimum energy path (MEP), which corresponds to a steepest descent path in mass-weighted coordinates, from the transition state to the reactant and product. Although saddle points generally connect two minima on the potential energy surface (PES), these minima may not be the structures of interest (it is not always true that a saddle point must connect two minima;[62] a situation is possible where saddle points can ultimately connect to more than two minima and the IRC calculation can lead to another saddle point).[62,93–96]

RESULTS AND DISCUSSION

In addition to the chair (**1a**, C_s symmetry), 1,4-twist (**1b**, C_1 symmetry) and 2,5-twist (**1c**, C_2 symmetry) conformers (Fig. 1), structures resembling the 1,4-boat (**1d**, C_1 symmetry, Fig. 2), 2,5-boat (**1e**, C_s symmetry, Fig. 2), half-chairs (**1f**, **1g**, **1h**, Fig. 3), and sofas (**1i**, **1j**, **1k**, **1l**, Fig. 4) were considered as possible candidates for participation in the chair–chair interconversion of 1,2,3-trithiane. The hypothetical high-energy planar structure (**1m**, Fig. 1) is not expected to participate in the conformational interconversion. Frequency calculations at the HF/6–31G(d), HF/6–31+G(d,p), B3LYP/6–31+G(d,p), HF/6–311+G(d,p) and/or B3LYP/6–311+G(d,p) levels of theory verified that the chair (**1a**), 1,4-twist (**1b**) and 2,5-twist (**1c**) conformers were real and that the distorted 1,4-boat transition structure [**1d**]‡, the 2,5-boat transition structure [**1e**]‡ and transition structure [**TS-1**]‡ were transition states (Tables A and B in the Supporting Information, available at the epoc website at http://www/wiley.com/epoc). (The imaginary frequencies for the 1,4-boat transition state [**1d**]‡ and the 2,5-boat transition state [**1e**]‡ are not very large, which suggests that the desired distortions are modest.[62,63] Imaginary frequencies are typically in the range 400–2000 cm^{-1} and values $<100\ ^{-1}$ typically correspond to couplings of low-energy modes. Although the use of the tight or very tight convergence option is useful,[62] one must be wary of structures which yield only very small imaginary frequencies since this suggests a very low energy transition structure which may not correspond to the particular reaction of interest.[97]) The HF and MP2 calculations gave larger energy differences (ΔE) between the 2,5-twist conformer (**1c**) and the distorted 1,4-boat transition state [**1d**]‡ than B3LYP.

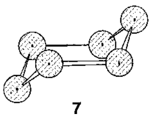

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Figure 10. Chair conformer of cyclohexasulfur (**7**)

The geometric parameters for the chair (**1a**), 1,4-twist (**1b**) and 2,5-twist (**1c**) conformers and the 1,4-boat [**1d**]‡ and 2,5-boat [**1e**]‡ transition states of 1,2,3-trithiane are given in Tables C–G in the Supporting Information. The conformation and structure of trisulfides depend on the substituents at the ends of the sulfur chain.[38,98–102] The B3LYP/6–31G(d)-calculated S—S—S—C torsional angle (τ) in the chair conformer (**1a**) was 62.4, 65.6 ° in the 1,4-twist conformer (**1b**) and 29.6 ° in the 2,5-twist conformer (**1c**). The small S—S—S—C torsional angle in **1c** leads to greater eclipsing of lone pairs of adjacent sulfurs and raises its energy relative to that of **1a** and **1b**. The torsional angle in *trans*-hydrogen trisulfide (HSSSH) is close to 86 °, which is smaller than the value for hydrogen disulfide (HSSH, 90.3 °). In dimethyltrisulfane (CH_3SSSCH_3)[98] and bis(trifluoromethyl)trisulfane (CF_3SSSCF_3),[99]the S—S—S—C torsional angles (τ) are 79 and 89 °, respectively. The respective S—S—S bond angles in **1a** (102.3 °), **1b** (101.4 °) and **1c** (103.3 °) are similar. The S—S—S bond angles in the sulfur trimer (S_3, C_{2v}), dimethyltrisulfane, bis(trifluoromethyl)trisulfane, 1,2,3-trithian-5-yl *N*-methylcarbamate (**6b**)[11] and cyclohexasulfur (S_6, D_{3d}, **7**, Fig. 10)[100–102] are 117.3, 107.3, 105.3, 101.5 and 102.6 °, respectively.

B3LYP/6–31G(d) calculated longer S—S bond lengths than HF/6–31G(d) and MP2/6–31G(d), which gave similar values. The respective MP2/6–31G(d) S—S bond lengths in the chair conformer (**1a**, 2.065 Å) and in the 2,5-twist conformer (**1c**, 2.103 Å) are equal whereas in the 1,4-twist conformer (**1b**) the S1—S2 bond length (2.082 Å) is longer than the S2—S3 bond (2.057 Å). Comparing the geometrica parameters obtained for 1,2,3-trithiane (**1**) with those of related molecules, it is seen in 1,2,3-trithian-5-yl *N*-methylcarbamate (**6b**) that the S1—S2 bond length (2.038 Å) and the S2—S3 bond length (2.041 Å) are similar,[38] that the experimental[100] and calculated[33,101,102] S—S bond lengths in cyclohexasulfur (**7**) are 2.068 and 2.064 Å, respectively. The S—S bond lengths in *cis*- and *trans*-hydrogen trisulfide (HSSSH, 2.077 Å) are longer than those in hydrogen disulfide (HSSH, 2.064 Å).[103] The electron diffraction (ED)-determined S—S bond lengths in dimethyltrisulfane and bis(trifluoromethyl)trisulfane are 2.046 and 2.040 Å, respectively, which are close to the S—S bond length in the most stable sulfur cluster (S_8, D_{4d}, 2.037 Å).[104–106]

The calculated C—H bond lengths in the chair conformer (**1a**) of 1,2,3-trithiane differ in several respects from those in the respective chair conformers of cyclohexane, tetrahydro-2*H*-thiopyran (thiacyclohexane, thiane),[30,54,103–105] 1,2-dithiacyclohexane (1,2-dithiane), 1,3-dithiacyclohexane (1,3-dithiane)[31,54] and 1,4-dithiacyclohexane (1,4-dithiane).[29] The respective S—S, C—C, S—C C4—H, and C6—H bond lengths are equal and the C5—Heq bond length is longer ($\Delta r = 0.004$ Å) than the C5—Hax bond in the chair conformer (**1a**). By analogy with 1,3-dithiane, the longer C5—Heq bond in **1a** may be attributed to a balance among many factors, including stereoelectronic interactions such as a hyperconjugative interaction between the antiperiplanar S—C σ-orbitals and the equatorial C—H σ^*-orbitals ($\sigma_{\text{S–C}} \rightarrow \sigma^*_{\text{C5–Heq}}$), a charge transfer from the $\sigma_{\text{C5–Heq}}$ bond to the antiperiplanar $\sigma^*_{\text{C–S}}$ bond and a weak homoanomeric interaction ($\text{LP}_\text{S} \rightarrow \sigma^*_{\text{C5–Heq}}$).[31,46,54]

Cuevas and Juaristi[54] observed normal Perlin effects (${}^1J_{\text{C–Heq}} > {}^1J_{\text{C–Hax}}$) in cyclohexane and at C4 in tetrahydro-2*H*-thiopyran. The normal Perlin effect involves $\sigma_{\text{C–Hax}} \rightarrow \sigma^*_{\text{C–Happ}}$ and/or $\text{n}_\text{X} \rightarrow \sigma^*_{\text{C–Happ}}$ stereoelectronic interactions which lead to weaker (longer) C—Hax bonds and smaller ${}^1J_{\text{C–Hax}}$ coupling constants relative to ${}^1J_{\text{C–Heq}}$. Reverse Perlin effects were observed for all C—H one-bond coupling constants in 1,3-dithiane[51] and at C3 in tetrahydro-2*H*-thiopyran. [54] The observed reverse Perlin effect at C3 in tetrahydro-2*H*-thiopyran is in agreement with *ab initio* theory and DFT calculations.[30,107–109]

Geometry optimization calculations on the chair conformer of tetrahydro-2*H*-thiopyran at all levels of theory used, irrespective of basis set, showed that the C3—Heq bond length was longer ($\Delta r = 0.003$ Å) than the C3—Hax bond length and that the C2—Hax ($\Delta r = 0.002$ Å) and C4—Hax ($\Delta r = 0.003$ Å) bond lengths were longer (weaker) than the respective C2—Heq and C4—Heq bond lengths.[30,54] The longer C—Hax bond lengths in the chair conformer of tetrahydro-2*H*-thiopyran may be the result of stereoelectronic hyperconjugative interactions ($\sigma_{\text{C–Hax}} \rightarrow \sigma^*_{\text{C–Hax}}$) as have been observed in the chair conformers of other heterocyclohexanes, but not in the chair conformer of 1,2,3-trithiane (**1a**). The longer C3—Heq bond (reverse Perlin effect) in tetrahydro-2*H*-thiopyran may be interpreted in terms of several stereoelectronic hyperconjugative interactions [$\sigma_{\text{S–C(2)}} \rightarrow \sigma^*_{\text{C(3)–Heq}}$, $\sigma_{\text{C(3)–Heq}} \rightarrow \sigma^*_{\text{S–C(2)}}$, $\sigma_{\text{C(3)–Heq}} \rightarrow \sigma^*_{\text{C(4)–C(5)}}$, $\sigma_{\text{C(4)–C(5)}} \rightarrow \sigma^*_{\text{C(3)–Heq}}$]. The respective calculated C—H bond lengths in the chair conformers of 1,2-dithiane and 1,4-dithiane were equal.[29] In the chair conformers of 1,3-dithiane, the C2—Hax, C4—Hax and C6—Hax ($\Delta r = 0.002$–0.004 Å) bond lengths are longer than the corresponding C—Heq bond lengths ($\sigma_{\text{C–Hax}} \rightarrow \sigma^*_{\text{C–Hax}}$) and the C5—Heq bond is longer ($\Delta r = 0.004$ Å) than the C5—Hax bond ($\sigma_{\text{S–C}} \rightarrow \sigma^*_{\text{C5–Heq}}$, $\sigma_{\text{C5–Heq}} \rightarrow \sigma^*_{\text{S–C}}$ and a weak homoanomeric interaction $\text{LP}_\text{S} \rightarrow \sigma^*_{\text{C5–Heq}}$).[31,46,47,54] The difference in the C5—Hax bond length and the C5—Heq bond length in the respective chair conformers of 1,2,3-trithiane (**1a**) and 1,3-dithiane is the same. The equal C—H bond lengths and the small bond length differences between C—Hax and C—Heq in these sulfur heterocycles are consistent with the poor ability of sulfur to participate as a donor in $\text{LP}_\text{S} \rightarrow \sigma^*_{\text{C–Hax}}$ hyperconjugation.[46,47,52–54]

In the 1,4-twist (**1b**) conformer of 1,2,3-trithiane, the C4—C5 bond length is longer than the C5—C6 bond, the C4—Hiso bond lengths are equal, the C5—Hψeq bond length is longer than the C5—Hψax bond and the C6—H bond lengths are equal. In the 2,5-twist (**1c**) conformer, the C—C bond lengths are equal, the C5—Hiso bond lengths are equal and the C4—Hψeq and C6—Hψeq bond lengths are slightly longer than the C4—Hψax and C6—Hψax bonds. In the distorted 1,4-boat transition state [**1d**]‡, the S1—S2 bond length is shorter than the S2—S3 bond, the C4—C5 bond length is shorter than the C5—C6 bond and the C—Heq bonds are longer than the C—Hax bonds. In the 2,5-boat transition state [**1e**]‡, the respective S—S, S—C, C—C, C4—H and C6—H bond lengths are equal and the C5—Heq bond length is longer than the C5—Hax bond.

The total energies and thermodynamic parameters for the conformers and transition states of 1,2,3-trithiane (**1**) are given in Tables 1–3 and their thermochemical data are given in Tables A and B in the Supporting Information. It is seen that HF calculated the respective entropy of either the twist conformer (**1b** or **1c**) to be greater than that of the chair conformer (**1a**), with the entropy of **1b** being greater than that of **1c**. MP2 calculated the entropy of **1c**

Table 1. Total energies and dipole moments (μ) for the chair (**1a**), 1,4-twist (**1b**) and 2,5-twist (**1c**) conformers of 1,2,3-trithiane

	1a		**1b**		**1c**	
Level of theory	μ (D)	Energy (hartree)	μ (D)	Energy (hartree)	μ (D)	Energy (hartree)
HF/6–31G(d)	3.65	−1309.629277	3.81	−1309.619144	3.49	−1309.613367
HF/6–31+G(d,p)	3.66	−1309.641650	3.79	−1309.631402	3.49	−1309.625611
MP2/6–31G(d)	3.39	−1310.385119	3.55	−1310.375021	3.16	−1310.369222
MP2/6–31+G(d,p)	3.60	−1310.444885	3.72	−1310.434628	3.39	−1310.428350
MP2/6–311+G(d,p)	3.51	−1310.570334	3.57	−1310.560618	3.25	−1310.556556
B3LYP/6–31G(d)	3.43	−1312.507310	3.64	−1312.498194	3.24	−1312.491373
B3LYP/6–31+G(d,p)	3.39	−1312.521278	3.57	−1312.511899	3.19	−1312.505198
B3LYP/6–311+G(d,p)	5.07	−1312.620407	5.12	−1312.611117	4.94	−1312.605584

Table 2. Thermodynamic parameters for the chair (**1a**)-to-1,4-twist (**1b**) equilibrium and the Chair (**1a**)-to-2,5-twist (**1c**) equilibrium in 1,2,3-Trithiane

Conformer	Level of theory	ΔE (kcal mol^{-1})	ΔH° (kcal mol^{-1})	ΔG°(kcal mol^{-1})
1b	HF/6–31G(d)	6.36	6.46	5.90
	HF/6–31+G(d,p)	6.43	6.53	5.99
	HF/6–311+G(d,p)	6.25	6.33	5.87
	MP2/6–31+G(d,p)	6.43	6.53	5.98
	B3LYP/6–31+G(d,p)	5.89	5.99	5.22
	B3LYP/6–311+G(d,p)	5.83	5.93	5.27
1c	HF/6–31G(d)	9.98	10.03	9.74
	HF/6–31+G(d,p)	10.07	10.11	9.82
	HF/6–311+G(d,p)	9.29	9.40	9.19
	MP2/6–31+G(d,p)	10.38	10.36	9.64
	B3LYP/6–31G(d,p)	10.00	9.41	10.50
	B3LYP/6–31+G(d,p)	10.09	9.49	10.56
	B3LYP/6–311+G(d,p)	9.31	8.78	9.89

Table 3. Relative thermodynamic parameters for the chair (**1a**), 1,4-boat transition state [**1d**]‡, 2,5-boat transition state [**1e**]‡ and transition state [**TS-1**]‡ of 1,2,3-trithiane

Structure	Level of theory	μ (D)	Total energy (hartree)	ΔE (kcal mol^{-1})	$\Delta H^{\ddagger}$ (kcal mol^{-1})	$\Delta G^{\ddagger}$ (kcal mol^{-1})
[**1d**]‡	HF/6–31G(d)	3.59	−1309.612513	10.52	10.02	10.46
	HF/6–31G(d,p)	3.60	−1309.621811	10.51	10.00	10.44
	HF/6–311+G(d,p)	3.60	−1309.624780	10.59	10.09	10.53
[**1e**]‡	HF/6–31G(d)	3.88	−1309.618761	6.60	6.14	6.80
	HF/6–31+G(d,p)	3.87	−1309.630944	6.72	6.26	6.92
	MP2/6–31+G(d,p)	3.82	−1310.433956	6.86	6.40	7.06
	B3LYP/6–31+G(d,p)	3.60	−1312.511865	5.91	5.41	6.10
	B3LYP/6–311+G(d,p)	3.55	−1312.610902	5.96	5.46	6.16
[**TS-1**]‡	HF/6–31G(d)	3.74	−1309.605252	15.08	14.83	14.63
	B3LYP/6–31G(d)	3.55	−1312.484742	14.16	13.87	13.71
	B3LYP/6–31+G(d,p)	3.49	−1312.498591	14.24	13.57	13.31
	3LYP/6–311+G(d,p)	3.43	−1312.597682	14.26	13.93	13.76

to be greater than that of **1b**, which was greater than that of **1a**. In contrast, B3LYP calculated the 2,5-twist conformer (**1c**) to have lower entropy than the 1,4-twist conformer (**1b**), which had greater entropy than the chair conformer (**1a**).

The B3LYP/6–311+G(d,p) energy differences (ΔE) between the chair conformer (**1a**) and the 1,4-twist (**1b**) and 2,5-twist (**1c**) conformers were 5.83 and 10.09 kcal mol^{-1}, respectively. The energy difference (ΔE) between **1a** and **1b** is in the range of the ΔE between the chair and twist conformers of cyclohexane (4.7–6.2 kcal mol^{-1}).[10–13,20,21] The B3LYP/6–311+G(d,p) chair-1,4-twist free energy difference ($\Delta G^{\circ}_{\text{c–t}} = 5.27$ kcal mol^{-1}) for 1,2,3-trithiane (**1**) is larger than the estimated experimental $\Delta G^{\circ}_{\text{c–t}}$ for cyclohexane (4.7–4.9 kcal mol^{-1})[10–13,20,21] and larger than the estimated experimental $\Delta G^{\circ}_{\text{c–t}}$ value of 2.9 kcal mol^{-1} for 1,3-dithiane which was obtained from substituted 1,3-dithianes.[10,31] The principal reason for the higher energy of the 2,5-twist conformer (**1b**) appears to be the deviation of its S—S—S—C torsional angle [MP2/6–31G(d), 30.3°] from a value close to 90°. This is in line with enhanced repulsive lone pair–lone pair interactions which are expected to increase the energy of the conformer.

The B3LYP/6–311+G(d,p) energy difference (ΔE) between the chair (**1a**) and the 2,5-boat transition state [**1e**]‡ was 5.96 kcal mol^{-1} and the HF/6–311+G(d,p) energy difference between the chair (**1a**) and the 1,4-boat transition state [**1d**]‡ was 10.08 kcal mol^{-1}. It has been estimated that the boat form of cyclohexane is about 5.7–7.7 kcal mol^{-1} in energy above the chair conformer.[10–13,20,21]

Attempted IRC calculations at the HF/6–31G(d), B3LYP/6–31G(d), HF/6–31+G(d), B3LYP/6–31+G(d), HF/6–31+G(d,p), B3LYP/6–31+G(d,p), HF/6–31++G(d), B3LYP/6–31++G(d), HF/6–311G(d), B3LYP/6–311G(d) and B3LYP/6–311+G(d,p) levels of theory did not alter the geometry of the 2,5-boat transition state [**1e**]‡. Although it is qualitative, the animated displacements (normal coordinates) at −54 cm^{-1} for [**1e**]‡ suggest that it is the barrier to the interconversion of the enantiomers of the 1,4-twist conformer (**1b**) of 1,2,3-trithiane.[97] Similarly, the animated displacements (normal coordinates) at −71 cm^{-1} for [**1d**]‡ suggest that it is the barrier to the interconversion of the enantiomers of the 2,5-twist conformer (**1c**). The distorted 1,4-boat transition state [**1d**]‡ is slightly less stable than the 2,5-twist conformer (**1c**). The 2,5-boat transition state [**1e**]‡

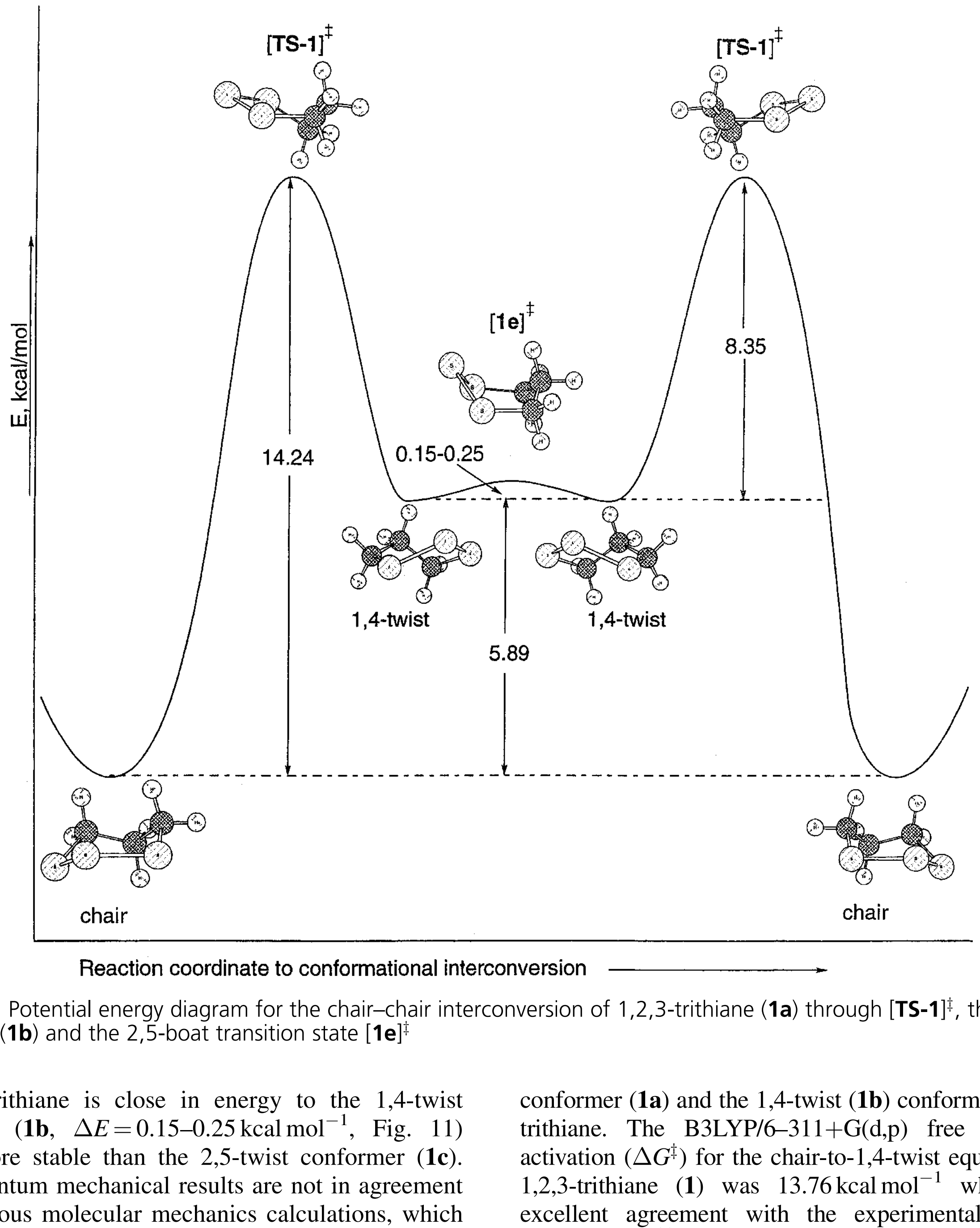
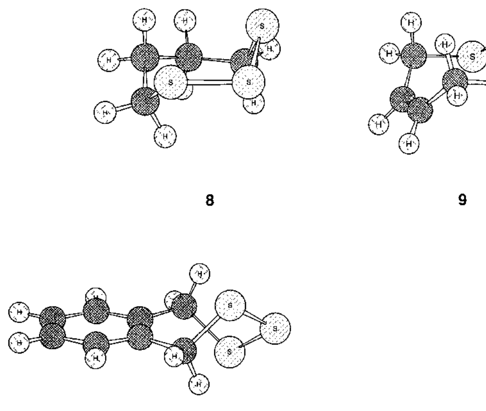


Figure 11. Potential energy diagram for the chair–chair interconversion of 1,2,3-trithiane (**1a**) through [**TS-1**]‡, the 1,4-twist conformer (**1b**) and the 2,5-boat transition state [**1e**]‡

of 1,2,3-trithiane is close in energy to the 1,4-twist conformer (**1b**, $\Delta E = 0.15$–$0.25\,\mathrm{kcal\,mol^{-1}}$, Fig. 11) and is more stable than the 2,5-twist conformer (**1c**). These quantum mechanical results are not in agreement with previous molecular mechanics calculations, which suggested that the 2,5-boat form was an energy minimum. The small energy differences among the conformers and transition states are significant contributors to the difficulty in finding pathways for the conformational interconversions in 1,2,3-trithiane (**1**).

Transition state [**TS-1**]‡ was obtained from the three half-chair structures (**1f–h**) and four sofa structures (**1i–l**) at various levels of theory. The B3LYP/6–31+G(d,p) and B3LYP/6–311+G(d,p) calculated energy difference (ΔE) between the chair conformer (**1a**) and transition state [**TS-1**]‡ was $14.25\,\mathrm{kcal\,mol^{-1}}$ (Tables 1–3). IRC calculations at the HF/6–31G(d), B3LYP/6–31G(d), B3LYP/6–31+G(d,p) and B3LYP/6–311+G(d,p) levels of theory showed that transition state [**TS-1**]‡ connected the chair conformer (**1a**) and the 1,4-twist (**1b**) conformer of 1,2,3-trithiane. The B3LYP/6–311+G(d,p) free energy of activation ($\Delta G^{\ddagger}$) for the chair-to-1,4-twist equilibrium in 1,2,3-trithiane (**1**) was $13.76\,\mathrm{kcal\,mol^{-1}}$ which is in excellent agreement with the experimental value of 13.2 kcal mol.[38] The experimentally determined barriers ($\Delta G^{\ddagger}$) to conformational interconversion in 5,5-dimethyl-1,2,3-trithiane, 5,5-diethyl-1,2,3-trithiane and 5,5-diisobutyl-1,2,3-trithiane were 15.0, 13.8 and $13.9\,\mathrm{kcal\,mol^{-1}}$, respectively.[38–41] The free energy of activation ($\Delta G^{\ddagger}$) for the conformational interconversion of 1,2,3-trithiacycloheptane (**8**), 4,5,6-trithiacycloheptene (**9**) and 1,2-dibenzo-4,5,6-trithiacycloheptene (**10**) are 6–7 (chloroethene, 143 K), 8.9 (CS_2, 183 K) and $17.4\,\mathrm{kcal\,mol^{-1}}$ (hexachlorobutadiene, 356 K), respectively (Fig. 12).[38] The experimental $\Delta G^{\ddagger}$ values for chair –chair interconversion in cyclohexane,[10–13,20,21] tetrahydro-2*H*-thiopyran (thiacyclohexane, thiane),[30,107–110] 1,2-dithiane,[111,112] 3,3,6,6-tetramethyl-1,2,4,5-tetrathiane,[113,114] 1,3-dithiane,[31,115]



8 9

10

Figure 12. HF/6–31+G(d,p) equilibrium geometry optimized conformers of 1,2,3-trithiacycloheptane (**8**), 4,5,6-trithiacyclocheptene (**9**) and 1,2-benzo-4,5,6-trithiacycloheptene (**10**)

1,4-dithiane[29,116] and cyclohexasulfur (**7**)[117] are 10.25, 9.25, 11.6, 15.9, 10.3, 9.7 and 31 kcal mol^{-1}, respectively. Hence, it is seen that increasing the number of contiguous sulfur atoms in the six-membered ring increases the barrier to conformational interconversion.

The high barriers to rotation around the O—O bond and the S—S bonds have been explained in terms of electrostatic interactions, lone pair–lone pair repulsions and in some cases pπ–dπ bonding. Accepting the ususal suggestion that lone pair–lone pair interactions are more important than lone pair–bond and bond–bond interactions, it is to be expected that the interconversion barriers in heterocyles with vicinal heteroatoms with lone pairs will be higher than that for cyclohexane and monoheterocyclohexanes.

Since conformational interconversion involves rotation (pseudorotation) about single bonds, the barrier to ring reversal is a composite of torsional parameters. Some connection, albeit not simple, between conformational interconversion barriers and rotational barriers for disulfides and trisulfides, the acyclic equivalents for the S—S and S—S—S bonds in the rings, is expected. The barrier to rotation about an S—S bond is higher than that about a C—S bond. Consequently, heterocycles with two or more vicinal heteroatoms (with lone pairs) bonded to each other have relatively high barriers to conformational interconversions. This is consistent with the increasing barrier to conformational interconversion on going from tetrahydro-2*H*-thiopyran, to 1,2-dithiane, 3,3,6,6-tetramethyl-1,2,4,5-tetrathiane and 1,2,3-trithiane (**1**, see above). Similarly, the computationally and experimentally determined barriers to conformational interconversions in tetrahydro-2*H*-pyran (10.7 kcal mol^{-1}), 1,3-dioxane (9.7 kcal mol^{-1}), 1,4-dioxane (9.7 kcal mol^{-1}), and 1,3,5-trioxane (10.9 kcal mol^{-1}) are similar to that in cyclohexane, but heterocycles containing vicinal O—O bonds (1,2-dioxane, 16.1 kcal mol^{-1}; 1,2,4,5-tetraoxane, 14.2 kcal mol^{-1}) have higher barriers.

CONCLUSIONS

Ab initio molecular orbital theory and DFT have been used to calculate the optimized geometries and relative energies of the chair, 1,4-twist and 2,5-twist conformers of 1,2,3-trithiane. Although HF and MP2 calculated slightly larger energy differences (than B3LYP) between the chair conformer and the twist conformers and between the chair conformer and the transition states, there is good overall agreement when the various methods are compared. However, there is less agreement among the methods for the calculated entropies of the conformers of 1,2,3-trithiane. Although the geometric parameters were essentially independent of the basis set used, the 6–31+G(d,p) and 6–311+G(d,p) basis sets provided relative energy data that were closer to the experimentally determined data.

Stereoelectronic hyperconjugative interactions were observed in the conformers and transition states of 1,2,3-trithiane. In the chair and 1,4-twist conformers of 1,2,3-trithiane the respective C5—Heq bond is longer than the C5—Hax bond ($\sigma_{\text{S–C}} \rightarrow \sigma^*_{\text{C5–Heq}}$ and homoanomeric interaction ($\text{LP}_\text{S} \rightarrow \sigma^*_{\text{C5–Heq}}$). In the 1,4-twist conformer, the C4—Hiso bond lengths are equal, the C5—Hψeq bond is longer than the C5—Hψax bond and the C6—H bond lengths are equal. In the 2,5-twist conformer, equal C—H bond lengths are found at C4 and at C5, but the C6—Hψeq bond is longer than the C6—Hψax bond and in the 2,5-boat conformer the C—H bonds are equal except at C5 where the C5—Hψeq bond is longer than the C5—Hψax bond.

B3LYP/6–31+G(d,p) and B3LYP/6–311+G(d,p) calculated the chair conformer of 1,2,3-trithiane to be 5.83, 10.09, and 5.98 kcal mol^{-1}, respectively, lower in energy than the 1,4-twist and 2,5-twist, conformers and the 2,5-boat transition state. The 2,5-boat transition state is close in energy to the 1,4-twist conformer and is more stable than the 2,5-twist conformer. The 1,4-boat transition state is close in energy to the 2,5-twist conformer. The HF/6-311+G(d,p) calculated energy difference (ΔE) between the chair conformer and the 1,4-boat transition state was 10.59 kcal mol^{-1}. IRC calculations were used to connect the transition state between the chair conformer and 1,4-twist conformer. The B3LYP/6–31+G(d,p) and B3LYP/6–311+G(d,p) calculated values of 13.71 and 13.79 kcal mol^{-1}, respectively, for the barrier ($\Delta G^\ddagger$) to the chair–chair conformational interconversion in 1,2,3-trithiane were in excellent agreement with the reported experimental value of 13.2 kcal mol^{-1}.

REFERENCES

1. Clennan EL, Stensaas KL. *Org. Prep. Proced. Int.* 1998; **30**: 551–600, and references cited therein.
2. Teuber L. *Sulfur Rep.* 1990; **9**: 257–349.
3. Lee MD, Dunne TS, Siegel MM, Chang CC, Morton GO, Borders DB. *J. Am. Chem. Soc.* 1987; **109**: 3464–3466.

4. Lee MD, Dunne TS, Chang CC, Ellestad GA, Siegel MM, Morton GO, McGahren WJ, Borders DB. *J. Am. Chem. Soc*. 1987; **109**: 3466–3468.
5. Freeman F, Ma X-B, Lin RI-S. *Sulfur Lett*. 1993; **15**: 253–262, and references cited therein.
6. Pearce AN, Babcock RC, Battershill CN, Lambert G, Copp BR. *J. Org. Chem*. 2002; **66**: 8257–8259.
7. Compagnone RS, Faulkner DJ, Carté BK, Chan G, Freyer A, Hemling ME, Hofmann GA, Mattern MR. *Tetrahedron* 1994; **50**: 12785–12792.
8. Litaudon M, Guyot M. *Tetrahedron Lett*. 1991; **32**: 911–914.
9. Copp BR, Blunt JW, Munro HG. *Tetrahedron Lett*. 1989; **30**: 3703–3706.
10. Kasai T, Sakamura S. *Agric. Biol. Chem*. 1982; **46**: 821–822, and references cited therein.
11. Kato A, Hashimoto Y, Otsuka I, Nakatsu K. *Chem. Lett*. 1978; 1219–1222.
12. Ichimaru M, Kato A, Hashimoto Y. *J. Nat. Prod*. 2000; **63**: 1675–1676.
13. Eliel EL, Wilen SH. *Stereochemistry of Organic Compounds*. Wiley: New York, 1994; chapt. 11, and references cited therein.
14. Juaristi E (ed.). *Conformational Behavior of Six-Membered Rings*. VCH: New York, 1995.
15. Bushweller CH. In *Conformational Behavior of Six-membered Rings*, Juaristi E (ed.). VCH: New York, 1995; chapt. 2, and references cited therein.
16. Cremer D, Szabo KJ. In *Conformational Behavior of Six-membered Rings*, Juaristi E (ed.). VCH: New York, 1995; chapt. 3 and references cited therein.
17. Pickett HM, Strauss HL. *J. Chem. Phys*. 1970; **53**: 376–388.
18. Pickett HM, Strauss HL. *J. Am. Chem. Soc*. 1970; **92**: 7281–7290.
19. Dixon DA, Komornicki A. *J. Phys. Chem*. 1990; **94**: 5630–5636.
20. Ferguson DM, Gould IR, Glauser WA, Schroeder S, Kollman PA. *J. Comput. Chem*. 1992; **13**: 525–532.
21. Leventis N, Hanna SB, Soitiriou-Leventis C. *J. Chem. Educ*. 1997; **74**: 813–814.
22. Leong MK, Mastryukov VS, Boggs JE. *J. Phys. Chem*. 1994; **98**: 6961–6966.
23. Kleinpeter E. In *Conformational Behavior of Six-membered Rings*, Juaristi E (ed.). VCH: New York, 1995; chapt. 6.
24. Lambert JB, Featherman SI. *Chem. Rev*. 1975; **75**: 611–626.
25. Chapman DM, Hester RE. *J. Phys. Chem. A* 1997; **101**: 3382–3877.
26. Freeman F, Kasner ML, Hehre WJ. *J. Phys. Chem. A* 2001; **105**: 10123–10132.
27. Freeman F, Do KU. *J. Mol. Struct*. (*Theochem*) 2002; **577**: 43–54, and references are cited therein.
28. Freeman F, Lee K. *Struct. Chem*. 2002; **13**: 149–160.
29. Freeman F, Derek E. *J. Comput. Chem*. 2003; **24**: 909–919.
30. Freeman F, Derek E. *Struct. Chem*. 2003; in press.
31. Freeman F, Le KT. *J. Phys. Chem. A* 2003; **107**: 2908–2918.
32. Feher F, Degen B, Söhngen B. *Angew. Chem*. 1968; **80**: 320.
33. Suontamo RJ, Laitinen RS, Pakkanen TA. *Acta Chem. Scand*. 1991; **45**: 687–693.
34. Arnason I, Oberhammer H. *J. Mol. Struct*. 2001; **598**: 245–250.
35. Blahous CP, Schaefer HF. *J. Phys. Chem*. 1988; 959–962.
36. Allinger NL, Hickey MJ, Kao J. *J. Am. Chem. Soc*. 1976; **98**: 2741–2745.
37. Korp JD, Bernal I, Watkins SF, Fronczek FR. *Tetrahedron Lett*. 1981; **22**: 4767–4770.
38. Kabuss S, Lüttringhaus A, Friebolin H, Mecke R. *Z. Naturforsch., Teil B* 1966; **21**: 320–324.
39. Tavernier D, Anteunis M, Becu C. *Isr. J. Chem*. 1980; **20**: 173–176.
40. Goor G, Anteunis M. *Heterocycles* 1975; **3**: 363–366.
41. Goor G, Anteunis M. *Bull. Soc. Chim. Belg*. 1975; **84**: 337–340.
42. Ayala PY, Schlegel BH. *J. Chem. Phys*. 1997; **107**: 375–384.
43. Schlegel BH. *J. Comput. Chem* 2003; **12**: 1514–1527.
44. Gonzalez C, Schlegel BH. *J. Phys. Chem*. 1990; **94**: 5523–5527.
45. Alabugin IV, Zeidan TA. *J. Am. Chem. Soc*. 2002; **124**: 3175–3185, and reference cited therein.
46. Alabugin IV. *J. Org. Chem*. 2000; **65**: 3910–3919, and references cited therein.
47. Anderson JE, Bloodworth AJ, Cai JQ, Davies AG, Tallant NA. *J. Chem. Soc., Chem. Commun*. 1992; 1689–1691.
48. Anderson JE, Bloodworth AJ, Cai JQ, Davies AG, Schiesser CH. *J. Chem. Soc., Perkin Trans. 2* 1993; 601–602.
49. Anderson JE, Bloodworth AJ, Shah A. *J. Chem. Soc., Perkin Trans. 2* 1993; 1927–1929.
50. Cai JQ, Davies AG, Schiesser CH. *J. Chem. Soc., Perkin Trans. 2* 1994; 1151–156.
51. Juaristi E, Cuevas G, Vela A. *J. Am. Chem. Soc*. 1994; **116**: 5796–5804, and references cited therein.
52. Cuevas G, Juaristi E, Vela A. *J. Mol. Struct*. (*Theochem*) 1997; **418**: 231–241.
53. Cuevas G, Juaristi E, Vela A. *J. Phys. Chem. A* 1999; **103**: 932–937, and references cited therein.
54. Cuevas G, Juaristi E. *J. Am. Chem. Soc*. 2002; **124**: 13088–13096.
55. Perrin CL. *Tetrahedron* 1995; **51**: 11901.
56. Juaristi E, Cuevas G. *The Anomeric Effect*. CRC Press: Ann Arbor, MI, 1995.
57. Thatcher G (ed.). *The Anomeric Effect and Associated Stereoelectronic Effects*. American Chemical Society Symposium Series 539. American Chemical Society: Washington, DC, 1993.
58. Kirby AJ. *Stereoelectronic Effects*. Oxford University Press: New York, 1999.
59. Deslongchamps P. *Stereoelectronic Effects in Organic Chemistry* (1st edn). Pergamon Press: Oxford, 1983.
60. *The Spartan '02 Macintosh and Spartan programs*. Wavefunction: Irvine, CA.
61. Frisch MJ, Trucks GW, Schlegel HB, Scuseria GE, Robb MA, Cheeseman JR, Zakrzewski VG, Montgomery JA, Jr, Stratmann RE, Burant JC, Dapprich S, Millam JM, Daniels AD, Kudin KN, Strain MC, Farkas O, Tomasi J, Barone V, Cossi M, Cammi R, Mennucci B, Pomelli C, Adamo C, Clifford S, Ochterski J, Petersson GA, Ayala PY, Cui Q, Morokuma K, Salvador P, Dannenberg JJ, Malick DK, Rabuck AD, Raghavachari K, Foresman JB, Cioslowski J, Ortiz JV, Baboul AG, Stefanov BB, Liu G, Liashenko A, Piskorz P, Komaromi I, Gomperts R, Martin RL, Fox DJ, Keith T, Al-Laham MA, Peng CY, Nanayakkara A, Challacombe M, Gill PMW, Johnson B, Chen W, Wong MW, Andnes JL, Gonzalez C, Head-Gordon M, Replogle ES, Pople JA. *Gaussian 98, Revision A.11*. Gaussian: Pittsburgh, PA, 2001.
62. Foresman JB, Frisch A. *Exploring Chemistry with Electronic Structure Methods* (2nd edn). Gaussian: Pittsburgh, PA, 1996.
63. Frisch A, Frisch MJ. *Gaussian 98 User's Reference* (2nd edn). Gaussian: Pittsburgh, PA, 1999.
64. Wiberg KB, Castejon H, Bailey WF, Ochterski J. *J. Org. Chem*. 2000; **65**: 1181–1187.
65. Bauschlicher CW, Jr, Partridge H. *J. Chem. Phys*. 1995; **103**: 1788–1791.
66. Rauhut G, Pulay P. *J. Phys. Chem*. 1995; **99**: 3093–3100.
67. Scott AP, Radom L. *J. Phys. Chem*. 1996; **100**: 16502–16513.
68. Wong MW. *Chem. Phys. Lett*. 1996; **256**: 391–399.
69. Jaramillo J, Scuseria GE. *Chem. Phys. Lett*. 1999; **312**: 269–276.
70. Koch W, Holthausen MC. *A Chemist's Guide to Density Functional Theory*. Wiley-VCH: Weinheim, 2000.
71. Ma B, Lii J-H, Schaefer HF, III, Allinger NL. *J. Am. Chem. Soc*. 1996; **100**: 8763, and references cited therein.
72. Hehre WJ, Radom L, Schleyer PvR, Pople JA. *Ab Initio Molecular Orbital Theory*. Wiley: New York, 1986.
73. Jensen F. *Introduction to Computational Chemistry*. Wiley: New York, 1998.
74. Cramer CJ. *Essentials of Computational Chemistry Theories and Models*. Wiley: New York, 2002.
75. Jensen F. *Introduction to Computational Chemistry*. Wiley: New York, 1998, chapt. 14.
76. Halgren TA, Lipscomb WN. *Chem. Phys. Lett*. 1977; **49**: 225–232.
77. Bell S, Crighton JS. *J. Chem. Phys*. 1984; **80**: 2464–2475.
78. Peng CY, Schlegel HB. *Isr. J. Chem*. 1994; **33**: 449–454.
79. Peng CY, Ayala PY, Schlegel HB, Frisch MJ. *J. Comput. Chem*. 1996; **17**: 49–56.
80. Dewar MJS, Healy EF, Stewart JJP. *Chem. Soc., Faraday Trans. 2* 1984; **80**: 227–233.
81. Cardenas-Laihacar C, Zerner MC. *Int. J. Quantum Chem*. 1955; **55**: 429–439.
82. Liotard DA. *Int. J. Quantum Chem*. 1992; **44**: 723–841.
83. Choi C, Elber R. *J. Chem. Phys*. 1991; **194**: 751–760.
84. Fischer T, Karplus M. *Chem. Phys. Lett*. 1992; **194**: 252–261.

85. Czerminski R, Elber R. *Int. J. Quantum Chem. Symp.* 1990; **2**: 167–186.
86. Abashkin Y, Russo N. *J. Chem. Phys.* 1994; **100**: 4477–4483.
87. Banerjee A, Adams N, Simons J, Shepard R. *J. Phys. Chem.* 1985; **89**: 52–57.
88. Helgaker T. *Chem. Phys. Lett.* 1991; **182**: 503–510.
89. Csazar P, Pulay P. *J. Mol. Struct.* 1984; **114**: 31–34.
90. Eckert F, Pulay P, Werner H-J. *J. Comput. Chem.* 1997; **18**: 1473–1483.
91. Culot P, Dive G, Nguyen VH, Ghuysen JM. *Theor. Chim. Acta* 1992; **82**: 189–205.
92. Bondensgard K, Jensen F. *J. Chem. Phys.* 1996; **104**: 8025–8031.
93. Hirsch M, Quapp W, Heidrich D. *Phys. Chem. Chem. Phys.* 1999; **1**: 5291–5299.
94. Bartsch RA, Chae YM, Ham S, Birney DM. *J. Am. Chem. Soc.* 2001; **123**: 7479–7486.
95. Caramella P, Quadrelli P, Toma L. *J. Am. Chem. Soc.* 2002; **124**: 1130–1131.
96. Reyes MB, Lobkovsky EB, Carpenter BK. *J. Am. Chem. Soc.* 2002; **124**: 641–651.
97. Hehre WJ, Shusterman AJ, Huang WW. *A Laboratory Book of Computational Chemistry.* Wavefunction: Irvine, CA, 1998.
98. Shen Q, Wells C, Hagen K. *Inorg. Chem.* 1998; **37**: 3895–3898.
99. Gaensslen M, Minkwitz R, Molzbeck W, Oberhammer H. *Inorg. Chem.* 1992; **31**: 4147–4150.
100. Steidel J, Pickardt J, Steudel R. *Z. Naturforsch. Teil B* 1978; **33**: 1554–1555.
101. Raghavachari K. *J. Chem. Phys.* 1990; **93**: 5862.
102. Freeman F, Lee EO. Unpublished.
103. Lietke M, Saleck AH, Yamada KMT, Winnewisser G, Cremer D, Kraka E, Dolgner A, Hahn J, Dobos S. *J. Phys. Chem.* 1993; **97**: 11204–11210.
104. Abraham S. *Acta Crystallogr.* 1955; **8**: 661.
105. Coppens P, Yang YW, Blessing RH, Cooper WF, Larsen FK. *J. Am. Chem. Soc.* 1977; **99**: 760–766.
106. Rettig SJ, Trotter J. *Acta Crystallogr., Sect. C* 1987; **43**: 2260–2262.
107. Freeman F, Phornvoranunt A, Hehre WJ. *J. Phys. Org. Chem.* 1998; **11**: 831–839.
108. Freeman F, Phornvoranunt A, Hehre WJ. *J. Phys. Org. Chem.* 1999; **12**: 176–186.
109. Freeman F, Hehre WJ. *J. Mol. Struct.* (*Theochem*) 2000; **529**: 225–239.
110. Lambert JB, Mixan CE, Johnson DH. *J. Am. Chem. Soc.* 1973; **95**: 4634–4639.
111. Claeson G, Androes G, Calvin M. *J. Am. Chem. Soc.* 1960; **82**: 4428–4429.
112. Claeson G, Androes G, Calvin M. *J. Am. Chem. Soc.* 1961; **83**: 4357–4361.
113. Bushweller CH, Golini J, Rao GU, O'Neil JW. *J. Am. Chem. Soc.* 1970; **92**: 3055–3058.
114. Bushweller CH, Bhat G, Letendre LJ, Brunelle JA, Bilofsky HS, Ruben H, Templeton DH, Zalkin A. *J. Am. Chem. Soc.* 1975; **97**: 66–73, and references cited therein.
115. Friebolin H, Schmid HG, Kabuss S, Faisst W. *Org. Magn. Reson.* 1969; **1**: 67–86.
116. Hunter G, Jameson RF, Shiralian M. *J. Chem. Soc., Perkin Trans. 2* 1978; 712–716.
117. Herman ZS, Weiss K. *Inorg. Chem.* 1975; **14**: 1592–1595.