JOURNAL OF PHYSICAL ORGANIC CHEMISTRY
*J. Phys. Org. Chem.* **12**, 176–186 (1999)

# Molecular orbital study of the conformational energies ($-\Delta G°$ or *A* values) of 2-alkyltetrahydro-2*H*-thiopyrans (tetrahydrothiopyrans, thiacyclohexanes, thianes)†

**Fillmore Freeman,[1]* Anna Phornvoranunt[1]‡ and Warren J. Hehre[1,2]**

[1]Department of Chemistry, University of California, Irvine, California 92697-2025, USA
[2]Wavefunction, Inc., 18401 Von Karman Avenue, Suite 370, Irvine, California 92612, USA

*Received 11 March 1998; accepted 13 May 1998*

ABSTRACT: *Ab initio* 6–31G* and MP2/6–31G*// 6–31G* methods and density functional (pBPDN**) theory were used to calculate the geometries and relative energies of the chair, boat, and twist-boat conformations of tetrahydro-2*H*-thiopyrans (tetrahydrothiopyrans, thiacyclohexanes, thianes). The chair conformation of thiacyclohexane is 5.3 and 8.0 kcal $mol^{-1}$, respectively, (1 kcal = 4.184 kJ) more stable than the twist-boat and boat structures at the MP2/6–31G*// 6-31G* level. *Ab initio* methods were used to calculate the relative energies of the rotamers in the chair conformations of 2-alkylthiacyclohexanes ($CH_3$, $C_2H_5$, *i*-$C_3H_7$, *t*-$C_4H_9$, *neo*-$C_5H_{11}$, $SiMe_3$). The MP2/6–31G*// 6–31G* conformational energies ($-\Delta G°$ or *A* values, kcal $mol^{-1}$) of the 2-alkylthiacyclohexanes (Me = 1.00; Et = 1.16; *i*-Pr = 1.02; *t*-Bu = 3.56; *neo*-Pent = 1.04; $SiMe_3$ = 2.05) are smaller than those calculated for the corresponding alkylcyclohexanes and 4-alkylthiacyclohexanes. Plots of the calculated conformational energies ($-\Delta G°$) for the 2-alkylthiacyclohexanes versus the calculated conformational energies for the corresponding alkylcyclohexanes are linear (slope = 0.680 and $r$ = 0.983 for 6–31G* and slope = 0.667 and $r$ = 0.989 for MP2/6–31G*// 6–31G*). The C(2)—S(1) bond lengths are in the range 1.827–1.840 Å and the C(6)—S(1) bond lengths are in the range 1.815–1.819 Å. With the exception of the axial 2-*t*-Bu substituent (103.0°), the C—S—C angles vary from 98.6° to 100.4°. The S(1)—C(2)—C(7) angle in the most stable axial conformer is larger that the corresponding angle in its most stable equatorial conformer. Copyright © 1999 John Wiley & Sons, Ltd.

KEYWORDS: conformational energy; 2-alkyltetrahydro-2*H*-thiopyrans; tetrahydrothiopyrans; thiacyclohexanes; thianes; molecular orbital study

## INTRODUCTION

Substituents in the chair conformation of cyclohexane[1–3] or in the 4-substituted half-chair conformation of cyclohexene (F. Freeman and W. J. Hehre, unpublished work) prefer the equatorial position. In monosubstituted cyclohexanes (**1**), the axial substituents have steric interactions with the synaxial hydrogens at C(3) and C(5) [1,3-diaxial interactions; Eqn 1]. The difference in energy between the most stable axial and equatorial conformers is designated the conformational energy ($-\Delta G°$ or *A* value). The free-energy difference between conformers is referred to as the conformational energy,[4,5] or sometimes as the *A* value.[6] For substituted cyclohexanes it is conventional to specify the value of $-\Delta G°$ for the equilibrium

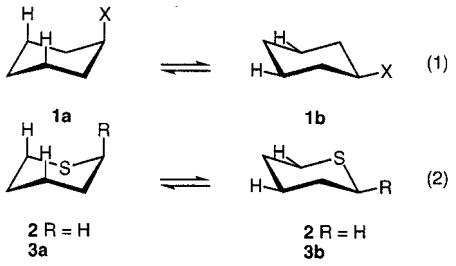
$$\text{axial} \rightleftharpoons \text{equatorial}$$

Since $-\Delta G°$ will be negative when the equatorial conformation is more stable than the axial, the value of $-\Delta G°$ is positive for substituents that favor the equatorial position.[5] The larger the conformational energy, the greater is the preference for the equatorial position. The replacement of carbon by another element in cycloalkanes or cycloalkenes[7–11] (F. Freeman, Z. M. Tsegai and W. J. Hehre, submitted; N. L. Allinger and K. H. Chen, personal communication) produces changes in several structural parameters and consequently affects the conformational characteristics of the molecules. For example, introduction of a nitrogen, an oxygen or a sulfur atom for a methylene group in cyclohexane will lead to changes in bond lengths (C—C 1.54 Å; C—N 1.47 Å; C—O 1.43 Å; C—S 1.82 Å) and in bond angles. These new elements may drastically change the non-

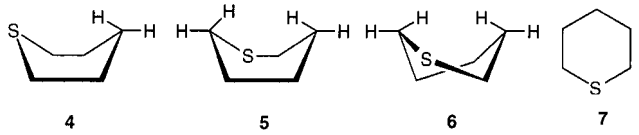
**Correspondence to:* Fillmore Freeman, Department of Chemistry, University of California, Irvine, California 92697-2025, USA.
E-mail: ffreeman@uci.edu
†Presented at the 214th American Chemical Society National Meeting, Las Vegas, Nevada, September 7–11, 1997 and the Pacific Conference on Chemistry and Spectroscopy, Irvine, California, October 21–25, 1997.
‡University of California, Irvine (UCI), 1997 Summer Undergraduate Research Fellow.
*Contract/grant sponsor:* National Science Foundation.; *Contract/grant number:* CHE-9015849; *Contract/grant number:* CHE-9311713.


CCC 0894–3230/99/030176–11 $17.50

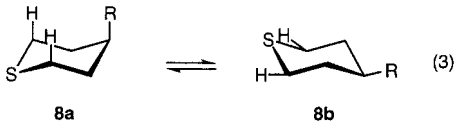
bonded interactions and conformational flexibility of the six-membered ring [Eqn 2].




The conformational properties of six-membered rings containing sulfur [**3**, Eqn 2] have been studied much less than the oxygen systems.[7–11] This study was undertaken in order to help elucidate the influences of replacing a methylene group in cyclohexane with a sulfur atom by comparing the calculated geometries (6–31G*) and single point energies (MP2/6–31G*// 6–31G*) of the conformers [chair, $C_s$ point group (**2**); boat, $C_s$ point

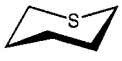



group (**4**); boat (**5**); twist-boat (skew-boat, $C_2$ point group (**6**); planar $C_{2v}$ point group (**7**)] of tetrahydro-2*H*-thiapyran (tetrahydrothiopyran, thiacyclocylohexane, thiane; **2**). The calculated 6–31G* and density functional theory (pBPDN**) results from the chair conformer **2** were compared with the structural parameters from other calculational methods and from microwave spectroscopic and x-ray diffraction data (Table 1). *Ab initio* methods were used to calculate the conformational energies ($-\Delta G°$ or *A* value; see earlier) of the rotamers of 2-alkylthiacyclohexanes [**3**, R = $CH_3$, $C_2H_5$, *i*-$C_3H_7$, *t*-$C_4H_9$, *neo*-$C_5H_{11}$, $SiMe_3$; Eqn 2] and to compare these values with those for the corresponding substituted alkylcyclohexanes (F. Freeman, Z. M. Tsegai and W. J. Hehre, unpublished work) and 4-alkylthianes [**8**; Eqn 3].[10]



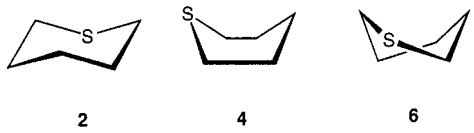

Another objective of this study was to analyze energy differences among conformers and rotamers by considering the *gauche* (synclinal) interactions and repulsive nonbonded interactions in the equatorial conformer rather than solely in terms of the 1,3-diaxial repulsive nonbonded hydrogen-hydrogen interactions in the axial conformer[10] (F. Freeman, Z. M. Tsegai and W. J. Hehre, unpublished work) [*gauche*: in A—B—C—D, ligands A and D are *gauche* if the torsion angle (ABCD) about the B—C bond is near +60° or −60°. Synclinal (*sc*): in X—A—B—Y, ligands X and Y are synclinal if the torsion angle (XABY) about the A—B bond is between +30° and +90° or between −30° and −90°[1,12]].

**Table 1.** Comparison of calculated and experimental bond lengths (Å), bond angles (°) and dihedral angles (°) for thiacyclohexane (**2**)




| Parameter | MM4[11] | pBPDN** | 6–31G* | MW[20] | ED[21] |
|---|---|---|---|---|---|
| *Bond length* | | | | | |
| C—H | 1.113 | – | – | 1.095 | 1.114 |
| $C_2$—$H_{ax}$ | – | 1.111 | 1.085 | – | – |
| $C_2$—$H_{eq}$ | – | 1.107 | 1.083 | – | – |
| $C_2$—$C_3$ | 1.531 | 1.532 | 1.528 | 1.533 | 1.528 |
| $C_3$—$C_4$ | – | 1.539 | 1.532 | 1.533 | 1.528 |
| $C_2$—$S_1$ | 1.814 | 1.836 | 1.817 | 1.832 | 1.811 |
| *Bond angle* | | | | | |
| H—C—H | 106.4 | – | – | 108.5 | 105.9 |
| H—$C_2$—H | – | 107.4 | 107.4 | – | – |
| H—$C_3$—H | – | 107.1 | 107.1 | – | – |
| $C_2$—$C_3$—$C_4$ | 112.7 | 112.9 | 112.8 | 107.9 | 112.3 |
| $C_3$—$C_4$—$C_5$ | 112.9 | 113.2 | 113.2 | 109.2 | 113.8 |
| $C_3$—$C_2$—$S_1$ | 112.8 | 97.7 | 112.9 | 114.1 | 112.7 |
| $C_2$—$S_1$—$C_6$ | 97.4 | | 98.5 | 99.2 | 97.6 |
| *Torsion angle* | | | | | |
| $C_2$—$C_3$—$C_4$—$C_5$ | – | 59.2 | 59.4 | – | 58.6 |
| $C_4$—$C_3$—$C_2$—$S_1$ | – | 60.4 | 60.0 | – | 60.8 |
| $C_5$—$C_6$—$S_1$—$C_2$ | – | 53.7 | 53.4 | – | 55.4 |

**Table 2.** Calculated energies (6–31G*) and energy differences (MP2/6–31G*/ /6–31G*)[a] of conformations of thiacyclohexane



**2** **4** **6**

| Conformation | Dipole moment (D) | Energy (hartree) | |
|---|---|---|---|
| | | 6–31G* | MP2/6–31G*/ /6–31G* |
| Chair (**2**, $C_s$) | 2.0 | −592.681604 | −593.456783 |
| Boat (**4**, $C_s$) | 2.0 | −592.668742 | −593.444105 |
| Twist-boat (**6**, $C_2$) | 2.2 | −592.673231 | −593.448390 |

[a] Energy difference = $\Delta E = E_{chair} - E_{boat} = 8.0$ kcal mol$^{-1}$; $\Delta E = E_{chair} - E_{twist\text{-}boat} = 5.3$ kcal mol$^{-1}$; $\Delta E = E_{twist\text{-}boat} - E_{boat} = 2.7$ kcal mol$^{-1}$.

## COMPUTATIONAL METHODS

The optimized geometries (6–31G*, pBPDN**) were performed with the MacSpartan Plus 1.1.6 and/or Spartan 4.1 and 5.0 computational programs and single point energy calculations (MP2/6–31G*/ /6–31G*) were performed with the Spartan 4.1 and 5.0 programs.[13–18] Frequency calculations (Supplementary Material) were computed on geometry optimized structures at the 6–31G* level with the MacSpartan Plus 1.1.6 and/or Spartan 4.1 and 5.0 programs. (MacSpartan Plus and Spartan computational programs are available from Wavefunction, Inc., 18401 Von Karman Avenue, Suite 370, Irvine, CA 92612, USA).

Conformers which contain an alkyl group directed inwards toward the ring are not included in the discussion since they are energetically unfavorable and do not contribute significantly to the population.

## RESULTS AND DISCUSSION

Thiacyclohexane (**2**) has a chair structure similar to cyclohexane (**1**), although the heterocycle is more puckered in order to accommodate the bond angles and bond lengths characteristic of sulfur. [The 6–31G*-calculated flagpole hydrogen to hydrogen distance in the boat conformation of cyclohexane (**1**) is 2.357 Å. Electron diffraction studies in the gas phase reveal a slight flattening of the chair conformation of cyclohexane. The C—C—C—C torsion angles are 55.9°, compared with 60° for the ideal chair conformation.[19]] Microwave spectroscopy (although the chair conformation of **2** was deduced from the microwave spectroscopic investigation, the rotational constants proved insufficient to specify the molecular conformation uniquely[20]), gas-phase electron diffraction studies,[21] molecular mechanics calculations[11,21,22] and molecular orbital calculations indicate that the chair conformation of **2** is the most stable form (Table 2). Frequency calculations show that the boat conformer **4** has one imaginary frequency, that the twist boat structure **6** does not have an imaginary frequency and that the planar $C_{2v}$ structure **7** has three imaginary frequencies. This suggests that the boat conformer **4** may be a transition state between the chair conformer **2** and the twist boat conformer **6** (Fig. 1). The high energy hypothetical planar form **7** would suffer from 10 eclipsing non-bonded hydrogen–hydrogen eclipsing interactions and bond angle strain.

The experimental inversion barrier for thiacyclohexane (**2**) is 9.4 kcal mol$^{-1}$ (1 kcal = 4.184 kJ). [The experimental inversion barriers for cyclohexane (10.3 kcal mol$^{-1}$), oxacyclohexane (10.3 kcal mol$^{-1}$) and azacyclohexane (10.1 kcal mol$^{-1}$) are essentially identical. As one goes down the Periodic Table (O, S, Se, Te), the barriers become lower, probably because the torsional potentials diminish.[23]] MP2/6–31G*/ /6–31G* single point energy calculations show that the chair conformer **2** (Table 2) is 8.0 and 5.3 kcal mol$^{-1}$, respectively, more stable than the boat (**4**) and twist-boat (skew-boat, **6**) structures.[21] (*R* values have been proposed

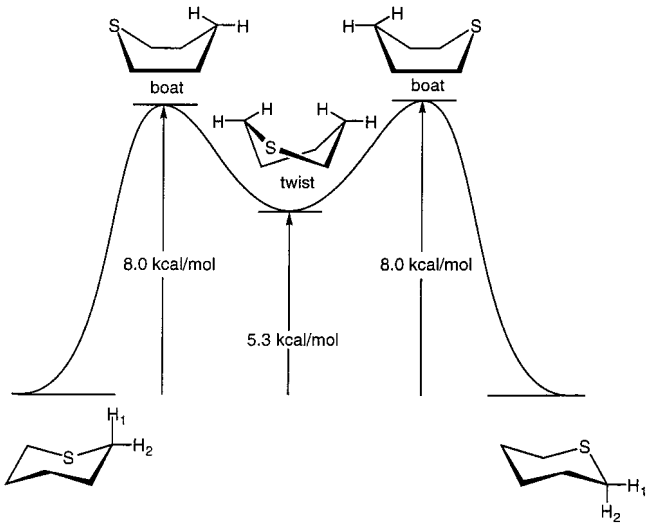


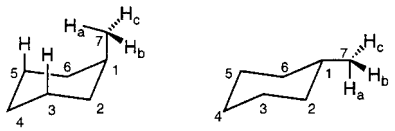

**Figure 1.** Energy diagram for ring inversion of thiacyclohexane

as a qualitative measure of the distortions of six-membered rings from the chair conformation of cyclohexane[24–26]). This suggests that the twist-boat conformer **6** is 2.7 kcal mol$^{-1}$ more stable than the boat structure **4**. Molecular mechanics calculations indicate that the twist-boat conformer **6** is 3.8[21] or 4.03[11,22] kcal mol$^{-1}$ higher in energy that the chair conformer **2**, while the chair structure (**2**) is 5.2 kcal mol$^{-1}$ more stable than the boat conformer (**4**).[21] No experimental value is available for the chair–twist-boat energy difference, but it has been estimated to be 4.02 kcal mol$^{-1}$.[11,27]

The boat conformer **4** is less stable than the chair form **2** in part because of the eclipsing interactions of the hydrogens on C(2) and C(3) and on C(5) and C(6). The 6–31G* calculated C—S—C bond angle in **4** is 97.0°, which is smaller than the value (98.5°) for thiacyclohexane (**2**). The boat conformer **3** is expected to be more stable than the boat form **5** owing to an absence of nonbonded interactions between flagpole hydrogens [the transannular strain resulting from steric crowding of the inside (flagpole) C(2) and C(5) hydrogens]. In addition, the boat conformation **5** is less stable than the boat conformer **4** owing to the eclipsing of four hydrogens. As in cyclohexane (**1**), the boat conformer (**4**) of **2** is flexible. Twisting of one of the carbon–carbon bonds relative to another leads to a twist-boat conformation (**6**), which is stabilized by removal of the transannular interaction. There is no transannular strain resulting from steric crowding of the inside (flagpole) C(2) and C(5) hydrogens in **6** since the distance between these two hydrogens is 2.655 Å, which is greater than the sum of their van der Waals radii (2 × 1.20 Å = 2.40 Å). (The van der Waals radius, which is determined from interatomic distances in crystals, is the effective size of the atomic cloud around a covalently bonded atom as perceived by another atom. The van der Waals radius is not the distance at which repulsive interactions of the electrons on two atoms outweigh the attractive forces between them.[28–34])

The 6–31G* calculated dipole moment of **2** is 2.0 D while the dielectric absorption measurement[35] and microwave spectroscopic (see earlier[20]) values are 1.71 D and 1.78 D, respectively. In the chair conformer **2**, the C(2)—C(3)—C(4)—C(5), C(6)—S(1)—C(2)—C(3) and S(1)—C(2)—C(3)—C(4) torsion angles are 59.4°, 53.4° and 60.0°, respectively. The C(6)—S(1)—C(2)—$H_{ax}$ torsion angle in **2** is 69.7°. The C(2)—C(3)—C(4), C(3)—C(4)—C(5), C(5)—C(6)—S(1) and C—S—C bond angles are 112.8°, 113.3°, 112.9° and 98.5°, respectively. The C—S—C angle in dimethyl sulfide is 98.8°.[36] The 6–31G* calculated carbon-sulfur bond length in **2** is 1.817 Å. Electron diffraction gives a carbon–sulfur bond length ($r_g$) of 1.811 Å and a C—S—C angle of 97.6° for **2** (Table 1).[21] The 6–31G* calculated C(2)—$H_{ax}$ and C(2)—$H_{eq}$ bond lengths in **2** are essentially the same (1.085 and 1.083 Å), which suggests an absence of anomeric effects.[1,7,9] [The calculational methods used here give some approximation to the equilibrium bond lengths ($r_e$), whereas the experimental values cited in the references from electron diffraction ($r_g$) and microwave ($r_s$) spectroscopic studies give vibrationally averaged values. These numbers are different physical quantities and have different numerical values. Thus, $r_e$ needs to be converted to $r_g$ and $r_s$ in order to make valid comparisons.][37]

Calculations were performed on the axial [**9a**, two *gauche* (synclinal) butane interactions] and equatorial [**9b**, zero *gauche* (synclinal) butane interactions] conformers of methylcyclohexane (**9**) (F. Freeman, Z. M. Tsegai and W. J. Hehre, submitted)[38–46] [molecular mechanics calculations give a $-\Delta G°$ value of 1.77 kcal mol$^{-1}$ for methylcyclohexane (**8, 9**)[39]] (the *gauche* interactions in cyclohexanes and thiacyclohexanes may not be comparable to those of gauche butane because the hydrogen–hydrogen interactions are minimized in the cyclic structures.[43–45]) for comparison purposes with 2-methylthiacyclohexane (**10**; see Table 3). At the 6–31G* level, the equatorial diastereomer **9b** ($C_s$ point group, energy = −273.243665 hartree, μ = 0.09 D) is more stable ($-\Delta G°$ = 2.30 kcal mol$^{-1}$) than its axial isomer **9a** ($C_s$ point group, energy = −273.239998 hartree, μ = 0.05 D). At the MP2/6–31G*/ /6–31G* level, the equatorial diastereomer **9b** ($E$ = −274.160811 hartree) is more stable ($-\Delta G°$ = 1.96 kcal mol$^{-1}$) than its axial isomer **9a** ($E$ = −274.157688 hartree).[38–44] An experimental $-\Delta G°$ value of 1.74 kcal mol$^{-1}$ has been obtained for methylcyclohexane (**9**) in $CFCl_3CDCl_3$ via low-temperature carbon-13 NMR spectroscopy.[40,41]

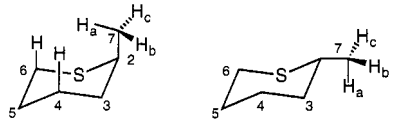



**9a** **9b**

Although steric effects are considered to be responsible for equatorial preferences in cyclohexanes, natural bond orbital analysis (NBO)[38,47] suggests that bond–antibond interactions of the exocylic C(1)—C(7) bond in methylcyclohexane with $\sigma^*_{C—C}$ and $\sigma^*_{C—H}$ bonds are mainly responsible for the equatorial preference. However, bond–antibond stereoelectronic interactions may not be the sole contributor to the equatorial preference in methylcyclohexane (**9**). At the 6–31G* level, the C(1)—C(2), C(1)—C(7) and C(1)—$H_{eq}$ bond distances in **9a** are 1.539, 1.534 and 1.088 Å, respectively. The corresponding distances in the equatorial conformer **9b** are 1.534, 1.539 and 1.091 Å, respectively. The C(1)—C(2)—C(3) and C(2)—C(3)—C(7) angles in **9a** are 113.2° and 112.5°, respectively, while the same angles in the equatorial conformer **9b** are 112.2° and 111.6°, respectively. The torsion angles C(3)—C(2)—C(1)—C(7) for **9a** and **9b** are 73.5° and 179.1°, respectively. Compared with cyclohexane, which has an $H_{ax}$—C(1)—C(2)—C(3)

**Table 3.** Comparison of calculated bond lengths (Å), bond angles (°) and dihedral angles (°) for 2-methylthiacyclohexane (10)



**10a** **10b**

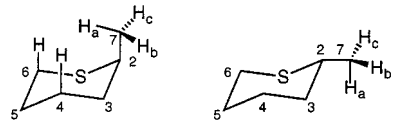
| Parameter | **10a** | | **10b** | |
|---|---|---|---|---|
| | MM4 ($r_g$)[11] | 6–31G* | MM4 ($r_g$)[11] | 6–31G* |
| *Bond length* | | | | |
| $C_2$—$H_{ax}$ | – | – | 1.114 | 1.086 |
| $C_2$—$H_{eq}$ | 1.115 | 1.085 | – | – |
| $C_6$—$H_{ax}$ | 1.111 | 1.084 | 1.112 | 1.085 |
| $C_6$—$H_{eq}$ | 1.112 | 1.083 | 1.112 | 1.083 |
| $C_2$—$C_3$ | 1.539 | 1.536 | 1.537 | 1.531 |
| $C_3$—$C_4$ | 1.527 | 1.533 | 1.526 | 1.532 |
| $C_4$—$C_5$ | 1.525 | 1.531 | 1.526 | 1.531 |
| $S_1$—$C_2$ | 1.820 | 1.830 | 1.820 | 1.830 |
| $S_1$—$C_6$ | 1.816 | 1.818 | 1.813 | 1.827 |
| *Bond angle* | | | | |
| H—$C_6$—H | 105.9 | 107.2 | 106.2 | 107.4 |
| $C_2$—$C_3$—$C_4$ | 114.7 | 114.8 | 113.0 | 113.7 |
| $S_1$—$C_2$—$C_3$ | 111.2 | 111.2 | 111.1 | 111.5 |
| $C_2$—$S_1$—$C_6$ | 99.1 | 100.3 | 97.7 | 99.4 |
| *Torsion angle* | | | | |
| $C_2$—$C_3$—$C_4$—$C_5$ | 59.0 | 59.7 | 60.0 | 60.0 |
| $S_1$—$C_2$—$C_3$—$C_4$ | 59.2 | 57.9 | 62.3 | 59.4 |
| $C_2$—$S_1$—$C_6$—$C_5$ | 54.5 | 52.8 | 55.7 | 53.6 |

torsion angle of 65.9°, the geometry of the ring in **9a** is slightly distorted since the C(3)—C(2)—C(1)—C(7) torsion angle is increased by 7.6° compared with cyclohexane.[38] This outward bending of the methyl group in **9a** helps to minimize the repulsive non-bonded hydrogen–hydrogen interactions (see earlier).[28–34]

In the axial diastereomer **9a**, the C(7)-$H_a$ distance from both C(3)-$H_{ax}$ and C(5)-$H_{ax}$ is 2.401 Å while C(7)-$H_b$ and C(7)-$H_c$ are both 2.453 Å from C(1)-$H_{eq}$. There are two *gauche* interactions in **9a** with respect to the C(3)—C(2)—C(1)—C(7) (73.5°) and C(5)—C(6)—C(1)—C(7) (73.5°) bonds.[12] In the equatorial diastereomer **9b**, the methyl group is staggered relative to the $H_{ax}$—C(1) bond, and the $H_{ax}$—C(1)—C(7)—$H_a$ torsion angle is 180°. The distances from C(1)-$H_{ax}$ to C(7)-$H_b$ and C(7)-$H_c$ are 2.481 and 2.481 Å, respectively. The equatorial conformer **9b** has an anti arrangement with respect to the C(3)—C(2)—C(1)—C(7) (179.1°) and C(5)—C(6)—C(1)—C(7) (179.1°) bonds. In this type of analysis, it is generally assumed that the repulsive *gauche* butane interactions dominate the overall energetics.[38,40–46]

The enthalpy and entropy contributions can also play important roles in determining the free energy difference between axial and equatorial conformations.[40,41,48,49]

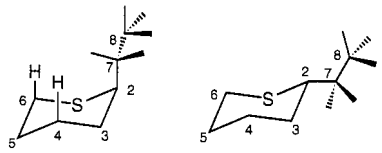
In addition, the chair conformation of cyclohexane is viewed as a structure with no strain and is compared with butane. However, the *gauche* interactions in cyclohexane may not be comparable to those of *gauche* butane because the hydrogen–hydrogen interactions are minimized in the cycloalkane.[45] A value no greater than 0.28 kcal $mol^{-1}$ per cyclohexane gauche interaction has been suggested.[43]



**10a** **10b**

Table 3 shows a comparison of calculated bond lengths, bond angles and dihedral angles for 2-methylthiacyclohexane (**10**) and Table 4 shows that the equatorial conformer **10b** is more stable than the axial conformer **10a** ($-\Delta G°$ = 1.00 kcal $mol^{-1}$). The 6–31G* calculated conformational energy for **10** is similar to the values ($-\Delta G°$ = 1.03 or 1.18 kcal $mol^{-1}$) obtained by Allinger and co-workers[11,22] using molecular mechanics, but smaller than the value of 1.42 kcal $mol^{-1}$ obtained from the respective low-temperature $^{13}C$ NMR studies of Barbarella *et al.*[50] in $CD_2Cl_2$ and of Eliel and Willer[51,52] in $CDCl_3$. The MP2/6–31G*//6–31G* calculated ($-\Delta G°$ value of 1.00 kcal $mol^{-1}$) is smaller than the

**Table 4.** Calculated energies (hartree), conformational energies ($-\Delta G°$, kcal mol$^{-1}$)[a] and dipole moments (D) of 2-alkylthiacyclohexanes

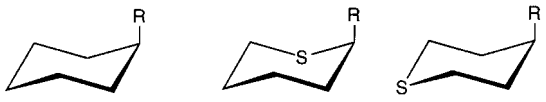


| | | 6–31G* | | | MP2/6–31G*// 6–31G* | |
|---|---|---|---|---|---|---|
| R | Compound | Energy | $-\Delta G°$ | Dipole moment | Energy | $-\Delta G°$ |
| H | **2** | −592.681604 | – | 2.0 | −593.456783 | – |
| $CH_{3ax}$ | **10a** | −631.714339 | – | 2.0 | −632.624102 | – |
| $CH_{3eq}$ | **10b** | −631.717384 | 1.91 | 2.0 | −632.626705 | 1.00 |
| $C_2H_{5ax}$ | **11a** | −670.747960 | – | 2.0 | −671.790164 | – |
| $C_2H_{5ax}$ | **11b** | −670.747190 | (0.48) | 2.0 | −671.789499 | (0.42) |
| $C_2H_{5eq}$ | **11c** | −670.750466 | 1.57 | 1.9 | −671.792007 | 1.16 |
| $C_2H_{5eq}$ | **11d** | −670.750092 | [1.34] | 1.9 | −671.791505 | [0.84] |
| $C_2H_{5eq}$ | **11e** | −670.748815 | [0.54] | 1.9 | −671.790715 | [0.35] |
| *i*-$C_3H_{7ax}$ | **12a** | −709.778975 | – | 2.0 | −710.956741 | – |
| *i*-$C_3H_{7eq}$ | **12b** | −709.781704 | 1.71 | 1.9 | −710.958375 | 1.02 |
| *i*-$C_3H_{7eq}$ | **12c** | −709.781695 | [1.71] | 1.9 | −710.958195 | [0.91] |
| *i*-$C_3H_{7eq}$ | **12d** | −709.781191 | [1.39] | 1.9 | −710.957850 | [0.70] |
| *t*-$C_4H_{9ax}$ | **13a** | −748.805254 | – | 1.9 | −750.120533 | – |
| *t*-$C_4H_{9eq}$ | **13b** | −748.811801 | 4.11 | 1.9 | −750.126213 | 3.56 |
| *neo*-$C_5H_{11ax}$ | **14a** | −787.844745 | – | 1.9 | −789.289880 | – |
| *neo*-$C_5H_{11eq}$ | **14b** | −787.847327 | 1.62 | 1.8 | −789.291532 | 1.04 |
| $SiMe_{3ax}$ | **15a** | −999.890557 | – | 1.9 | −1001.148292 | – |
| $SiMe_{3eq}$ | **15b** | −999.895280 | 2.96 | 1.8 | −1001.151559 | 2.05 |

[a] Conformational energy ($-\Delta G°$)[1–6] refers to the energy difference between the most stable axial conformer and its most stable equatorial conformer. The other values in the $-\Delta G°$ columns are the energy differences (in brackets) between the most stable axial conformer and its other equatorial conformers and the energy differences (in parentheses) between axial conformers.

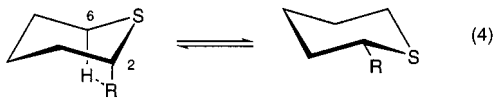
calculated values for methylcyclohexane (**9**, $-\Delta G° = 1.96$ kcal mol$^{-1}$) and 4-methylthiane (**3**, R = $CH_3$, $-\Delta G° = 1.94$ kcal mol$^{-1}$; Table 5). It is known that there is little variation in conformational energy between different heterocycles and cyclohexane at the 4-position. The smaller $-\Delta G°$ value for **10** is reasonable since the carbon–sulfur bond is longer than the carbon–carbon bond. The longer bond increases the distance between the axial methyl group and the synaxial hydrogen at C(6) in **10** [Eqn 4].

**Table 5.** Comparison of calculated (MP2/6–31G*//6–31G*) conformational energies ($-\Delta G°$, kcal mol$^{-1}$) for alkylcyclohexanes (1) (F. Freeman, Z. M. Tsegai and W. J. Hehre, submitted), 2-alkylthianes (3) and 4-alkylthianes (8)[10]



**1** **3** **8**

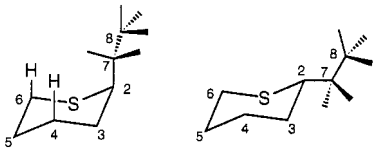
| | $-\Delta G°$ | | |
|---|---|---|---|
| R | **1** | **3** | **8** |
| $CH_3$ | 1.96 | 1.00 | 1.94 |
| $C_2H_5$ | 1.80 | 1.16 | 1.75 |
| *i*-$C_3H_7$ | 1.59 | 1.02 | 1.62 |
| *t*-$C_4H_9$ | 5.45 | 3.56 | 5.49 |
| *neo*-$C_5H_{11}$ | 1.32 | 1.04 | 1.39 |
| $SiMe_3$ | 2.69 | 2.05 | 2.76 |



**10a** **10b** (4)

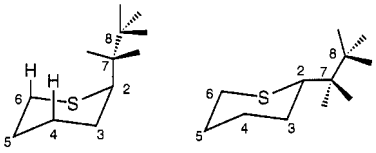
The dipole moments of **10a** and **10b** are nearly equivalent since the exocyclic carbon–carbon bonds are not polar (Table 4). In **10a**, the distances from C(7)-$H_a$ to C(4)-$H_{ax}$ and C(6)-$H_{ax}$ are 2.413 and 2.521 Å, respectively,[28–34] and C(7)-$H_b$ and C(7)-$H_c$ are 2.487 and 2.439 Å, respectively, from C(2)-$H_{eq}$. Also in **10a**, C(7)-$H_b$ is 2.496 Å from C(3)-$H_{eq}$. There are two *gauche* interactions in **10a** and its enantiomer (Table 6).[43–46] Compared with thiacyclohexane (**2**), which has $H_{ax}$—C(2)—C(3)—C(4) and $H_{ax}$—C(2)—S(1)—C(6) dihedral angles of 62.4° and 69.7°, respectively, there is an outward bending of the methyl group in **10a** by 7.9° and 8.1°, respectively. Thus, as in methylcyclohexane (**9**),

**Table 6.** Calculated torsion angles in 2-alkylthiacyclohexanes



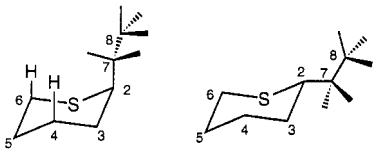
| R | | Torsion angle (°) | | | |
|---|---|---|---|---|---|
| | | $C_4$—$C_3$—$C_2$—$C_7$ | $C_6$—$S_1$—$C_2$—$C_7$ | $S_1$—$C_2$—$C_7$—$C_8$ | $C_3$—$C_2$—$C_7$—$C_8$ |
| $CH_{3ax}$ | **10a** | 70.3 | 77.8 | – | – |
| $CH_{3eq}$ | **10b** | 178.6 | 176.6 | – | – |
| $C_2H_{5ax}$ | **11a** | 70.2 | 77.5 | 66.9 | 165.8 |
| $C_2H_{5ax}$ | **11b** | 69.0 | 78.3 | 172.2 | 60.5 |
| $C_2H_{5eq}$ | **11c** | 177.7 | 176.6 | 65.4 | 171.3 |
| $C_2H_{5eq}$ | **11d** | 179.3 | 177.4 | 170.2 | 66.5 |
| $C_2H_{5eq}$ | **11e** | 174.0 | 178.8 | 66.6 | 59.3 |
| *i*-$C_3H_{7ax}$ | **12a** | 68.2 | 78.0 | 63.6 (173.9) | 46.9 (169.4) |
| *i*-$C_3H_{7eq}$ | **12b** | 172.0 | 178.0 | 61.2 (65.8) | 64.8 (168.2) |
| *i*-$C_3H_{7eq}$ | **12c** | 174.4 | 178.0 | 71.7 (162.6) | 53.9 (71.9) |
| *i*-$C_3H_{7eq}$ | **12d** | 178.7 | 177.7 | 61.3 (176.0) | 52.7 (175.5) |
| *t*-$C_4H_{9ax}$ | **13a** | 82.0 | 92.4 | 56.8 (63.8) (179.2) | 76.4 (163.0) (46.0) |
| *t*-$C_4H_{9eq}$ | **13b** | 172.3 | 176.8 | 65.0 | 60.6 |
| *neo*-$C_5H_{11ax}$ | **14a** | 68.7 | 76.1 | 95.6 | 137.9 |
| *neo*-$C_5H_{11eq}$ | **14b** | 178.2 | 176.7 | 90.2 | 137.9 |
| $SiMe_{3ax}$ | **15a** | 76.4 | 87.2 | 68.6 (51.9) (173.9) | 158.4 (81.1) (40.9) |
| $SiMe_{3eq}$ | **15b** | 175.3 | 179.8 | 174.4 (55.9) (65.6) | 59.8 (178.3) (60.2) |

**Table 7.** Calculated (6–31G*) bond angles in 2-alkylthiacyclohexanes



| R | Compound | Bond angle (°) | | | | |
|---|---|---|---|---|---|---|
| | | $C_2$—$S_1$—$C_6$ | $C_2$—$C_3$—$C_4$ | $S_1$—$C_2$—$C_3$ | $S_1$—$C_2$—$C_7$ | $C_3$—$C_2$—$C_7$ |
| H | **2** | 98.5 | 112.8 | 112.9 | – | – |
| $CH_{3ax}$ | **10a** | 100.3 | 114.8 | 111.2 | 112.6 | 113.5 |
| $CH_{3eq}$ | **10b** | 99.4 | 113.7 | 111.5 | 108.5 | 112.1 |
| $C_2H_{5ax}$ | **11a** | 100.3 | 114.8 | 110.6 | 113.6 | 113.2 |
| $C_2H_{5ax}$ | **11b** | 100.4 | 114.7 | 110.4 | 111.9 | 115.2 |
| $C_2H_{5eq}$ | **11c** | 99.4 | 113.9 | 111.0 | 109.7 | 111.5 |
| $C_2H_{5eq}$ | **11d** | 99.7 | 113.7 | 111.1 | 107.6 | 113.5 |
| $C_2H_{5eq}$ | **11e** | 98.8 | 113.1 | 111.3 | 110.2 | 113.9 |
| *i*—$C_3H_{7ax}$ | **12a** | 100.4 | 114.7 | 109.2 | 113.0 | 115.8 |
| *i*—$C_3H_{7eq}$ | **12b** | 98.6 | 113.2 | 110.7 | 111.8 | 113.4 |
| *i*—$C_3H_{7eq}$ | **12c** | 99.1 | 113.1 | 110.8 | 109.3 | 115.3 |
| *i*—$C_3H_{7eq}$ | **12d** | 100.1 | 114.1 | 110.2 | 108.8 | 113.7 |
| *t*—$C_4H_{9ax}$ | **13a** | 103.0 | 117.7 | 109.9 | 115.0 | 118.8 |
| *t*—$C_4H_{9eq}$ | **13b** | 99.2 | 113.4 | 109.7 | 111.3 | 115.3 |
| *neo*—$C_5H_{11ax}$ | **14a** | 100.2 | 114.5 | 110.1 | 113.8 | 112.9 |
| *neo*—$C_5H_{11eq}$ | **14b** | 99.6 | 113.9 | 110.6 | 109.4 | 111.8 |
| $SiMe_{3ax}$ | **15a** | 100.9 | 114.8 | 111.0 | 113.5 | 118.6 |
| $SiMe_{3eq}$ | **15b** | 99.8 | 113.6 | 111.2 | 110.4 | 113.8 |

**Table 8.** Calculated (6–31G*) bond distances (Å) of 2-alkylthiacyclohexanes

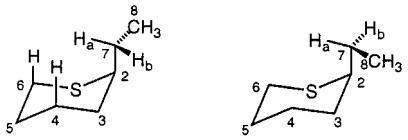


| R | Compound | $C_2$—$C_7$ | $C_2$—$C_3$ | $C_2$—$S_1$ | $C_6$—$S_1$ |
|---|---|---|---|---|---|
| H | **2** | – | 1.528 | 1.817 | 1.817 |
| $CH_{3ax}$ | **10a** | 1.531 | 1.536 | 1.830 | 1.818 |
| $CH_{3eq}$ | **10b** | 1.567 | 1.531 | 1.827 | 1.817 |
| $C_2H_{5ax}$ | **11a** | 1.537 | 1.536 | 1.832 | 1.818 |
| $C_2H_{5ax}$ | **11b** | 1.538 | 1.537 | 1.832 | 1.818 |
| $C_2H_{5eq}$ | **11c** | 1.584 | 1.532 | 1.830 | 1.816 |
| $C_2H_{5eq}$ | **11d** | 1.535 | 1.532 | 1.830 | 1.816 |
| $C_2H_{5eq}$ | **11e** | 1.536 | 1.532 | 1.831 | 1.817 |
| *i*—$C_3H_{7ax}$ | **12a** | 1.549 | 1.539 | 1.836 | 1.818 |
| *i*—$C_3H_{7eq}$ | **12b** | 1.545 | 1.533 | 1.834 | 1.816 |
| *i*—$C_3H_{7eq}$ | **12c** | 1.546 | 1.533 | 1.833 | 1.816 |
| *i*—$C_3H_{7eq}$ | **12d** | 1.547 | 1.535 | 1.836 | 1.815 |
| *t*—$C_4H_{9ax}$ | **13a** | 1.566 | 1.545 | 1.839 | 1.819 |
| *t*—$C_4H_{9eq}$ | **13b** | 1.560 | 1.537 | 1.840 | 1.815 |
| *neo*—$C_5H_{11ax}$ | **14a** | 1.547 | 1.538 | 1.834 | 1.817 |
| *neo*—$C_5H_{11eq}$ | **14b** | 1.546 | 1.533 | 1.832 | 1.816 |
| $SiMe_{3ax}$ | **15a** | 1.921 | 1.540 | 1.837 | 1.818 |
| $SiMe_{3eq}$ | **15b** | 1.919 | 1.539 | 1.826 | 1.816 |

this outward bending of the methyl group in **10a** helps to minimize the repulsive nonbonded hydrogen-hydrogen interactions.[28–34] In the equatorial conformation **10b**, there are no significant non-bonded repulsive interactions involving hydrogens (no distance between two hydrogens of less than 2.500 Å).[28–34]

The C(3)—C(2)—C(1)—C(7) torsion angle in **9a** is 73.5° and the C(4)—C(3)—C(2)—C(7) and C(6)—S(1)—C(2)—C(7) torsion angles in **10a** are 70.3° and 77.8°, respectively (Table 6). Hence the steric repulsion is minimized in **10a** by an outward bending of the methyl group away from the interior of the thiane ring. The C(2)—S(1)—C(6) bond angles in **10a** (100.3°) and **10b** (99.4°) are larger than the corresponding angle in thiacyclohexane (**2**, 98.5°; Table 6). The difference (0.90°) in axial and equatorial C(2)—S(1)—C(6) bond angles in **10** is comparable to the difference (0.97°) between the axial and equatorial C(1)—C(2)—C(3) bond angles in methylcyclohexane (**9**). However, there is a larger difference (4.1°) in axial (112.6°) and equatorial (108.5°) S(1)—C(2)—C(7) bond angles in **10** than in the axial and equatorial C(2)—C(1)—C(7) bond angles in methylcyclohexane (0.90°; Table 7). The C(2)—C(7) and C(2)—S(1) bond lengths in **10a** and **10b** are comparable (Table 8).

Table 4 shows that the three equatorial rotamers of 2-ethylthiacyclohexane [**11c** (methyl group is on sulfur side of ring), **11d** (methyl group is opposite sulfur side of ring) and **11e**] are more stable than the axial conformer **11a** ($-\Delta G° = 1.16$ kcal mol$^{-1}$). The MP2/6–31G*// 6–31G* calculated conformational energies for ethylcyclohexane and 4-ethylthiacyclohexane are 1.80 and 1.75 kcal mol$^{-1}$, respectively (Table 5).



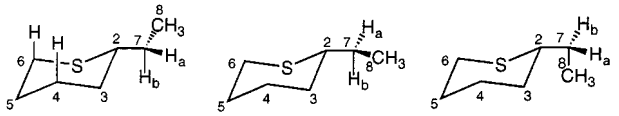
**11a** **11b**

Each rotamer (**11a, 11b**) of axial 2-ethylthiacyclohexane has three *gauche* interactions. In **11a**, the methyl group is pointed toward the sulfur side of the ring whereas in **11b** the methyl group is pointed away from the sulfur side of the ring. In rotamer **11a**, the distances from C(7)-$H_a$ to C(4)-$H_{ax}$ and to C(6)-$H_{ax}$ are 2.445 and 2.477 Å, respectively and the C(7)-$H_b$ to C(3)-$H_{eq}$ distance is 2.379 Å. The C(6)—S(1)—C(2)—C(7) angle of 77.5° in **11a** shows that the ethyl group is tilted away from the interior of the ring. In rotamer **11b**, the distances from C(7)-$H_a$ to C(4)-$H_{ax}$ and to C(6)-$H_{ax}$ are 2.404 and 2.500 Å, respectively, the C(7)-$H_b$ to C(2)-$H_{eq}$ distance is 2.435 Å and the C(8)-H to C(3)-$H_{eq}$ distance is 2.288 Å. The stronger repulsive non-bonded hydrogen–hydrogen interactions make rotamer **11b** of higher energy (0.42 kcal mol$^{-1}$) than **11a**. In particular, the C(8)-H to C(3)-$H_{eq}$ repulsive interaction in **11b** is absent in **11a** since its methyl group points toward the sulfur side of the ring.

In the three equatorial 2-ethylthiacyclohexanes there is one *gauche* interaction in **11c** and its enantiomer, one

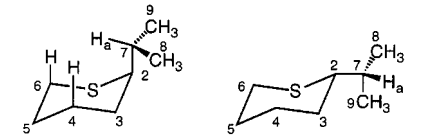
 

*gauche* interaction in **11d** and its enantiomer and two *gauche* interactions in **11e**. Coincidentally, conformer **11c** is 0.82 kcal mol$^{-1}$ (one *gauche* interaction) more stable than conformer **11e**[51,52] (in solution, the entropy and enthalpic terms must be considered[40,41]). In conformer **11c**, the C(7)-$H_b$ to C(2)-$H_{ax}$ and C(3)-$H_{eq}$ to C(7)-$H_{ax}$ distances are 2.498 and 2.388 Å, respectfully. In conformer **11d** the distances from C(2)-$H_{ax}$ to C(7)-$H_a$ and from C(3)-$H_{ax}$ to C(7)-$H_b$ are 2.495 and 2.288 Å, respectively. In **11e**, the distances from C(2)—$H_{ax}$ to C(7)-$H_a$ and from C(2)-$H_{ax}$ to C(7)-$H_b$ are 2.382 and 2.411 Å, respectively, and the C(3)-$H_{ax}$ to C(8)-H distance is 2.364 Å. Thus the greater stability of **11c** versus **11e** is due to one less *gauche* interaction and fewer repulsive non-bonded hydrogen interactions.

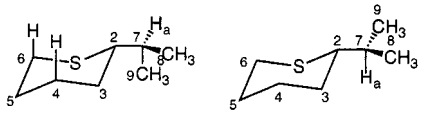


**11c** **11d** **11e**

The C(2)—S(1)—C(6) bond angles in **11a** (100.3°) and **11c** (99.4°) are the same as the respective values for **10a** and **10b** and are larger than the corresponding angle in thiacyclohexane (**2**, 98.5°; Table 7). The large difference (3.9°) in axial (**11a**, 113.6°) and equatorial (**11c**, 109.7°) or (3.4°) in axial (**11a**, 113.6°) and equatorial (**11d**, 110.2°) S(1)—C(2)—C(7) bond angles in **11** gives additional support for the increased steric repulsion in **11a** which leads to an outward bending of the ethyl group (Table 7).



**12a** **12b**



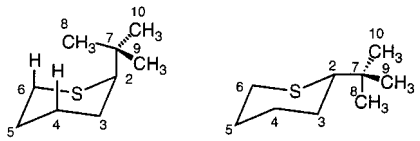
**12c** **12d**

The conformational energy of 2-isopropylthiacyclohexane (**12**) is 1.02 kcal mol$^{-1}$ (Tables 4 and 5). The axial conformer exists as the single rotamer **12a** with four *gauche* interactions, whereas there are two chiral equatorial conformers (**12b, 12c**) and an achiral rotamer **12d**. The equatorial rotamers **12b** and **12c** and their enantiomers each has three *gauche* interactions and the other rotamer **12d** has two *gauche* interactions. Conformer **12b** is 0.11 and 0.32 kcal mol$^{-1}$ more stable than equatorial conformers **12c** and **12d**, respectively. One difference between **12b** and **12c** is that one methyl group of the isopropyl group in the former points toward the sulfur side of the ring.

In the axial conformation **12a**, the distances from C(7)-$H_a$ to C(4)-$H_{ax}$ and C(6)-$H_{ax}$ are 2.493 and 2.443 Å, respectively, the distance from C(9)-H to C(3)-$H_{eq}$ is 2.220 Å and the distance from C(8)-H to C(2)-$H_{eq}$ is 2.499 Å. The C(4)—C(3)—C(2)—C(7) and C(6)—S(1)—C(2)—C(7) torsion angles are 68.2° and 78.0°, respectively (Table 6). The value of 78.0° in **12a** is consistent with the isopropyl group bending away from the interior of the ring in order to minimize non-bonded repulsive interactions. In the equatorial conformer **12b**, the C(2)-$H_{ax}$ to C(7)-H, C(2)-$H_{ax}$ to C(8)-H, C(3)-$H_{eq}$ to C(7)-H and C(3)-$H_{ax}$ to C(9)-H distances are 2.417, 2.416, 2.383 and 2.293 Å, respectively. In the equatorial conformer **12c**, the C(2)-$H_{ax}$ to C(7)-H, C(2)-$H_{ax}$ to C(8)-H, C(2)-$H_{eq}$ to C(8)-H and C(3)-$H_{ax}$ to C(9)-H distances are 2.456, 2.405, 2.308 and 2.399 Å, respectively. Although there are no non-bonded interactions between C(7)-$H_a$ and the ring hydrogens in the equatorial conformation **12d**, the distance from C(8)-H to C(3)-$H_{ax}$ is 2.174 Å.

The C(2)—S(1)—C(6) bond angles in **12a** (100.4°) and **12d** (100.1°) are similar and are larger than the corresponding angle in unsubstituted thiacyclohexane (**2**, 98.5°; Table 7), while this angle in **12c** (98.8°) is close to that in **2**. The large difference (4.2°) in axial (**12a**, 113.0°) and equatorial (**12d**, 108.8°) S(1)—C(2)—C(7) bond angles in **12** gives additional support for the increased steric repulsion in **12a** which leads to an outward bending of the isopropyl group (Table 7). A similar analysis (111.8°) between **12a** and the higher energy equatorial rotamer **12c** gives a value of 1.2°.

The axial conformer of 2-*tert*-butylthiacyclohexane (**13a**) has six *gauche* interactions and one methyl group pointing into the ring. Tables 4 and 5 show that the equatorial conformation **13b** is more stable than the axial conformer **13a** ($-\Delta G° = 3.56$ kcal mol$^{-1}$). In **13a**, the C(8)-H to C(4)-$H_{ax}$ and to C(6)-$H_{ax}$ distances are 2.161 and 2.318 Å, respectively, and the distances from C(9)-H to C(3)-$H_{ax}$ and C(10)-H to C(2)-$H_{eq}$ are 2.212 and 2.331 Å, respectively. The C(4)—C(3)—C(2)—C(7) and C(6)—S(1)—C(2)—C(7) torsion angles in **13a** are 82° and 92.4°, respectively.



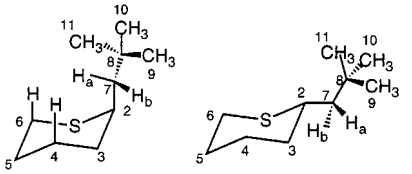
**13a** **13b**

In the equatorial conformation **13b**, the C(3)-$H_{ax}$ to C(8)-H, C(3)-$H_{ax}$ to C(9)-$H_a$, C(2)-$H_{ax}$ to C(9)-$H_b$ and C(2)-$H_{ax}$ to C(10)-H distances are 2.325, 2.141, 2.442, and 2.455 Å, respectively. The C(2)—S(1)—C(6) bond angles in **13a** (103°) and **13b** (99.2°) are larger than the corresponding angle in unsubstituted thiacyclohexane (**2**, 98.5°; Table 7). The large difference (3.7°) in axial (**13a**, 115.0°) and equatorial (**13b**, 111.3°) S(1)—C(2)—C(7)

bond angles in **13** gives additional support for the increased steric repulsion in **13a** which leads to an outward bending of the *tert*-butyl group.

The equatorial conformer (**14b**) of 2-neopentylthiacyclohexane (**14**) is more stable than its axial conformer **14a** ($-\Delta G° = 1.04$ kcal mol$^{-1}$; Tables 4 and 5). The conformational energy for **14** is similar to the values for 2-ethylthiacyclohexane (**11**, $-\Delta G° = 1.16$ kcal mol$^{-1}$) and 2-isopropylthiacyclohexane (**12**, $-\Delta G° = 1.02$ kcal mol$^{-1}$).

In the axial conformer **14a**, the distance from C(6)-$H_{ax}$ to C(7)-$H_a$ is 2.413 Å and the distance from C(4)-$H_{ax}$ to C(7)-$H_b$ is 2.531 Å. The distance from C(3)-$H_{eq}$ to C(7)-$H_b$ is 2.339 Å, and the distances from C(2)-$H_{eq}$ to C(9)-H and C(11)-H are 2.193 and 2.430 Å, respectively. In the equatorial conformer **14b**, the C(3)-$H_{ax}$ to C(7)-$H_a$ distance is 2.411 Å and the C(2)-$H_{ax}$ to C(9)-H and C(11)-H distances are 2.203 and 2.376 Å, respectively.



**14a** **14b**

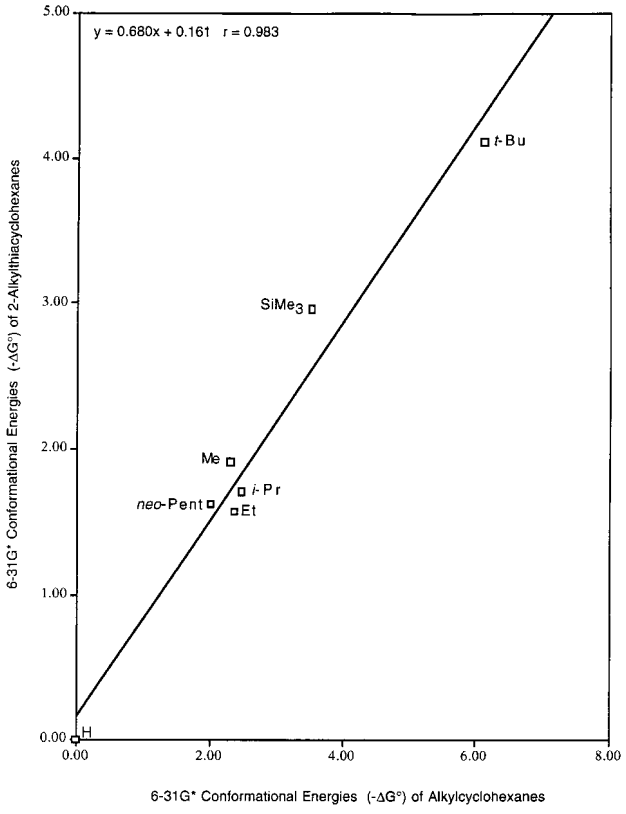



**Figure 2.** Plot of the 6–31G* conformational energies of 2-alkylthiacyclohexanes versus the conformational energies of the corresponding alkylcyclohexanes

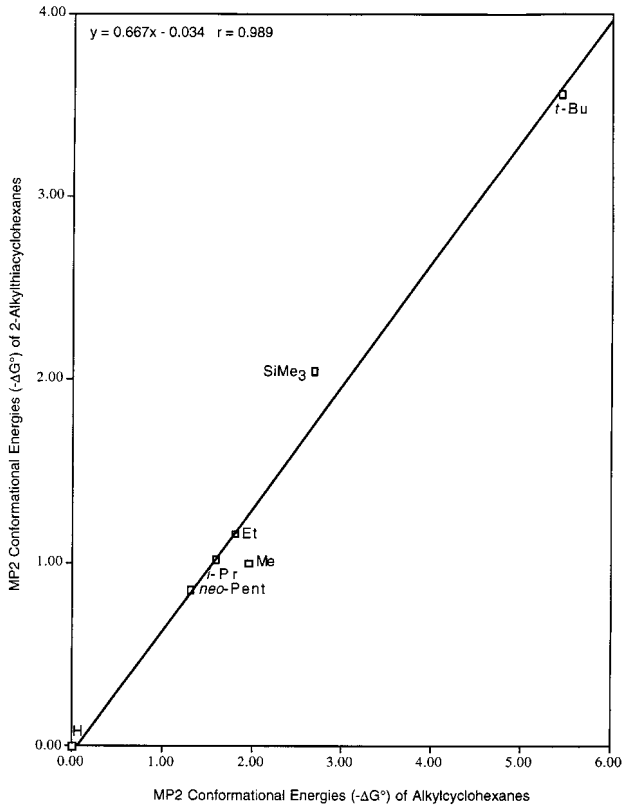
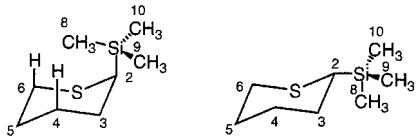



**Figure 3.** Plot of the MP2/6–31G*//6–31G* conformational energies of 2-alkylthiacylohexanes versus the conformational energies of the corresponding alkylcyclohexanes

The axial conformation of 2-(trimethylsilyl)thiacyclohexane (**15a**) has six *gauche* interactions and the equatorial conformations **15b** has four *gauche* interactions. There are no non-bonded interactions in **15b** and one such interaction (the C(6)-$H_{ax}$ to C(8)-H distance is 2.415 Å) in **15a**. The conformational energy for **15** is 2.05 kcal mol$^{-1}$, which is smaller than the value of 3.56 kcal mol$^{-1}$ for 2-*tert*-butylthiacyclohexane (**13**) owing to the longer carbon–silicon bonds (Table 8).



**15a** **15b**

## CONCLUSIONS

The conformational energies of 2-alkylthiacyclohexanes (**3**) are smaller than the conformational energies of the corresponding alkylcyclohexanes (**1**) and 4-alkylthiacyclohexanes (**8**). The $-\Delta G°$ values in **3** may be accounted for in terms of *gauche* (synclinal) interactions, repulsive non-bonded interactions, and steric effects in both the

axial and the equatorial conformer (F. Freeman, Z. M. Tsegai and W. J. Hehre, submitted).[38,40,41,43–46,48] Although 2-alkylthiacyclohexanes (**3**) show a smaller preference for the equatorial conformation than the corresponding alkylcyclohexanes (**1**), the conformational energies are influenced by similar nonbonded interactions and steric factors (Figs 2 and 3). Plots of the calculated conformational energies for the 2-alkylthiacyclohexanes (**3**) versus the calculated conformational energies for the corresponding alkylcyclohexanes (**1**) are linear [slope = 0.680 and $r = 0.983$ for 6–31G* (Fig. 2) and slope = 0.667 and $r = 0.989$ for MP2/6–31G*/ /6-31G*, Fig. 3].

The 1,3-diaxial interactions which destabilize the axial conformer are weaker in alkylthiacyclohexanes (**3**) because the carbon–sulfur bond is longer than carbon–carbon bond, which places the synaxial hydrogen and alkyl group farther apart than they would be in the corresponding alkylcyclohexanes [(**1**); Eqn 4]. The C(2)—S(1) bond lengths in (**3**) are in the range 1.827–1.840 Å and the C(6)—S(1) bond lengths are in the range 1.815—1.819 Å. With the exception of the axial *t*-Bu substituent (103.0°), the C—S—C angles vary from 98.6° to 100.4°. The S(1)—C(2)—C(7) angle in the most stable axial conformer is larger that the corresponding angle in its most stable equatorial conformer (Table 7).

## Acknowledgements

**Acknowledgment** is made to the National Science Foundation (NSF CHE-9015849 and CHE-9311713) for partial support of this work.

## REFERENCES

1. E. L. Eliel and S. H. Wilen, *Stereochemistry of Organic Compounds*, Chapt. 11. Wiley, New York (1994).
2. E. Juaristi (Ed.), *Conformational Behavior of Six-membered Rings*. VCH, New York (1995).
3. K. Gundertofte, T. Liljefors, P.-O. Norby and I. Pettersson, *J. Comput. Chem.* **17**, 429 (1996).
4. E. L. Eliel and S. H. Wilen, *Stereochemistry of Organic Compounds*, p. 695. Wiley, New York (1994).
5. F. A. Carey and R. J. Sundberg, *Advanced Organic Chemistry, Part A: Structure and Mechanisms*, p. 133. Plenum Press, New York (1993).
6. S. Winstein and N. J. Holness, *J. Am. Chem. Soc.* **77**, 5562 (1955).
7. F. Freeman, C. Lee, W. J. Hehre and H. N. Po, *J. Comput. Chem.* **18**, 1302 (1997).
8. F. Freeman, C. Lee, W. J. Hehre and H. N. Po, *J. Comput. Chem.* **19**, 1064 (1998).
9. H. N. Po, F. Freeman, C. Lee and W. J. Hehre, *J. Comput. Chem.* **14**, 1376 (1993).
10. F. Freeman, A. Phornvoranunt and W. J. Hehre, *J. Phys. Org. Chem.* **11**, 831 (1998).
11. N. L. Allinger and Y. Fan, *J. Comput. Chem.* **18**, 1827 (1997).
12. W. Klyne and V. Prelog, *Experientia* **16**, 521 (1960).
13. M. J. S. Dewar, E. G. Zoebisch, E. F. Healy and J. J. P. Stewart, *J. Am. Chem. Soc.* **107**, 3902 (1985).
14. P. C. Hariharah and J. A. Pople, *Chem. Phys. Lett.* **66**, 217 (1972).
15. M. M. Francl, W. J. Pietro, W. J. Hehre, J. S. Binkley, M. S. Gordon, D. J. DeFrees and J. A. Pople, *J. Chem. Phys.* **77**, 3654 (1982).
16. W. J. Hehre, L. Radom, P. v. R. Schleyer and J. A. Pople, *Ab Initio Molecular Orbital Theory*, pp. 38–40. Wiley, New York (1986).
17. W. J. Hehre, A. J. Shusterman and W. W. Huang, *A Laboratory Book of Computational Organic Chemistry*. Wavefunction, Irvine, CA (1996).
18. (a). W. J. Hehre and L. Lou, *A Guide to Density Functional Calculations in Spartan*. Wavefunction, Irvine, CA (1997); (b). Becke, A. D., *Phys. Rev. A.* **1988**, *38*, 3089; (c). Perdew, J. P., *Phys. Rev. B.* **1986**, *33*, 8822.
19. H. J. Geise, H. R. Buys and F. C. Mijlhoff, *J. Mol. Struct.* **9**, 447 (1971).
20. R. W. Kitchin, T. B. Malloy, Jr and R. L. Cook, *J. Mol. Spectrosc.* **57**, 179a (1975).
21. G. Schultz, A. Kucsman and I. Hargittai, *Acta. Chem. Scand. Ser. A* **42**, 332 (1988).
22. N. L. Allinger and M. J. Hickey, *J. Am. Chem. Soc.* **97**, 5167 (1975).
23. J. B. Lambert, C. E. Mixan and D. H. Johnson, *J. Am. Chem. Soc.* **95**, 4634 (1973).
24. J. B. Lambert, *J. Am. Chem. Soc.* **89**, 1836 (1967).
25. J. B. Lambert, R. G. Keske and D. K. Weary, *J. Am. Chem. Soc.* **89**, 5921 (1967).
26. D. M. Fatheree, G. L. Deeg, D. B. Matthews and J. G. Russell, *Org. Magn. Reson.* **18**, 92 (1982).
27. J. P. McCullough, H. L. Finke, W. N. Hubbard, W. D. Good, R. E. Pennington, J. F. Messerly and G. Waddington, *J. Am. Chem. Soc.* **76**, 2661 (1954).
28. A. Bondi, *J. Phys. Chem.* **68**, 441 (1964).
29. L. Pauling, Nature of the Chemical Bond, 3rd ed.; pp 260–261. Cornell University Press: Ithaca, NY, (1960).
30. D. M. Proserpio, R. Hoffmann and R. D. Levine, *J. Am. Chem. Soc.* **113**, 3217 (1991).
31. R. Chauvin, *J. Phys. Chem.* **96**, 9194 (1992).
32. M. O'Keefee and N. E. Brese, *J. Am. Chem. Soc.* **113**, 3226 (1991).
33. T. Halgren, *J. Am. Chem. Soc.* **114**, 7827 (1992).
34. N. L. Allinger, X. Zhou and J. Bergsma, *J. Mol. Struct. (Theochem)* **312**, 69 (1994).
35. C. W. N. Cumper and A. I. Vogel, *J. Chem. Soc.* 3521 (1959).
36. J. Demaison, B. T. Tan, V. Typke and H. D. Rudolph, *J. Mol. Spectrosc.* **86**, 406 (1981).
37. B. Ma, J.-H. Lii, H. F. Schaeffer, III and N. L. Allinger, *J. Am. Chem. Soc.* **100**, 8763 (1996), and references cited therein.
38. U. Salzner and P. v. R. Schleyer, *J. Org. Chem.* **59**, 2138 (1994).
39. N. L. Allinger, J. A. Hirsch, M. A. Miller, J. Tyminski and F. A. Van Catledge, *J. Am. Chem. Soc.* **90**, 1199 (1968).
40. H. Booth and J. R. Everett, *J. Chem. Soc., Chem. Commun.* 278 (1976).
41. H. Booth and J. R. Everett, *J. Chem. Soc., Perkin Trans. 2* 255 (1980).
42. D. Cremer J. S. Binkley and J. A. Pople, *J. Am. Chem. Soc.* **98**, 6863 (1976).
43. K. B. Wiberg and M. A. Murcko, *J. Am. Chem. Soc.* **110**, 8029 (1988).
44. M. A. Murcko, H. Castejon and K. B. Wiberg, *J. Phys. Chem.* **100**, 16162 (1996).
45. P. v. R. Schleyer, J. E. Williams and K. R. Blanchard, *J. Am. Chem. Soc.* **92**, 2377 (1970).
46. J. E. Anderson, in *The Chemistry of Alkanes and Cycloalkanes*, edited by S. Patai and Z. Rappoport, p. 95. Wiley, New York (1992).
47. A. E. Reed, R. B. Weinstock and F. Weinhold, *J. Phys. Chem.* **83**, 735 (1985).
48. M. E. Squillacote, *J. Chem. Soc., Chem. Commun.* 1406 (1986).
49. E. Juaristi, V. Labastida and S. Antunez, *J. Org. Chem.* **56**, 4802 (1991).
50. G. Barbarella, P. Dembech, A. Garbesi and A. Fava, *Org. Magn. Reson.* **8**, 469 (1976).
51. R. L. Willer and E. L. Eliel, *J. Am. Chem. Soc.* **99**, 1925 (1977).
52. E. L. Eliel and R. L. Willer, *J. Am. Chem. Soc.* **99**, 1936 (1977).