The Existence of Second-Row Anomeric Interactions. Conformational Analysis of 2-Substituted 5-Methyl-5-aza-1,3-dithiacyclohexanes

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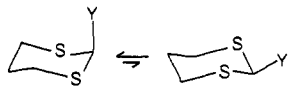
Abstract: The conformational analysis of several 2-substituted 5-methyl-5-aza-1,3-dithiacyclohexanes made the evaluation of S–C–Y anomeric interactions possible, where Y = SCH_3, SC_6H_5, COC_6H_5, $CO_2CH_2CH_3$, and $CO_2C_6H_5$. The relative order of the effects as a function of substituent is similar to that previously encountered in the corresponding 2-substituted 1,3-dithianes; however, the effects are smaller in magnitude in the title compounds, and we attribute this to the decreased ring dipole, which leads to a diminished influence of dipole–dipole interactions on these equilibria. Nevertheless, the observed anomeric effects are significant and can be explained in terms of endo and exo hyperconjugative interactions, which indicate that second-row elements are able to participate in anomeric interactions. Plots of ln K versus $1/T$ are linear, permitting evaluation of the enthalpic and entropic contributions to the S–C–Y anomeric effect. For the S–C–S segment, the effect is of enthalpic origin and overcomes unfavorable steric and entropic components in the axial conformer. For the compounds incorporating S–C–C(O) segments, the entropy term is mainly responsible for the axial predominance; the measured $\Delta H° \sim 0$ for these derivatives still reflects a significant enthalpic anomeric effect owing to the countervailing steric effects in the axial conformers.

Recently, several research groups have determined the conformational equilibria of 2-substituted 1,3-dithianes in which the effective participation of second-row heteroatoms in the anomeric effect is apparent.[1-4] Particularly pertinent to the present article is the finding of significant anomeric effects (axial preferences) in those systems containing the methylthio, phenylthio, carbomethoxy, benzoyl, and carboxy groups[2] (eq 1).



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The relative paucity of studies aimed at an understanding of S–C–Y anomeric segments prompted us to evaluate the conformational behavior of the related 2-substituted 5-methyl-5-aza-1,3-dithiacyclohexanes (**1–5**; Scheme I) in which the effect of the ring nitrogen could not be anticipated. In carrying out this study, special attention was given to the relative importance of the endo and exo anomeric effects[5] and to the precise contribution of the enthalpic and entropic components to the equilibria.[6,7]

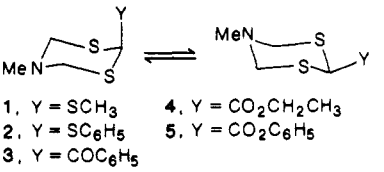
We provide herein systematic evidence for the existence of second-row anomeric interactions.

Results and Discussion

A. Preparation of the 2-Substituted Dithiazines. The parent 5-methyl-5-aza-1,3-dithiacyclohexane was prepared by reaction of formaldehyde, methylamine, and hydrogen sulfide, according to the published procedure.[8] The desired derivatives **1–5** were then obtained by the slow addition of the 2-lithio salt of the dithiazine[9] to the appropriate electrophile (Scheme II).

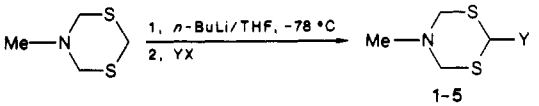
B. Determination of the Conformational Equilibria. The low-temperature ^1H and ^{13}C NMR spectra of mobile dithiazines **1–5** gave rise to two sets of signals, which correspond to the axial and equatorial conformers that result from ring interconversion, the barriers for nitrogen inversion being substantially lower.[10] Consideration of the γ-gauche effect[11] in the ^{13}C NMR spectra permitted assignment of the respective signals to the axial and equatorial conformers. Specifically, C-4,6 in the axial conformers is shielded (~5 ppm) relative to that in the equatorial conformers. Once the major and minor isomers had been assigned, the signals in the corresponding low-temperature ^1H NMR spectra were assigned. The assignment of the signals to the axial and equatorial isomers could also be made on the basis of the long-range W

Scheme I



1, Y = SCH_3 4, Y = $CO_2CH_2CH_3$
2, Y = SC_6H_5 5, Y = $CO_2C_6H_5$
3, Y = COC_6H_5

Scheme II



1-5

1, YX = CH_3SSCH_3 4, YX = $(EtO)_2CO$
2, YX = $C_6H_5SSC_6H_5$ 5, YX = $(C_6H_5O)_2CO$
3, YX = C_6H_5COOEt

Table III. Low-Temperature Conformational Equilibria of 2-Substituted 5-Methyl-5-aza-1,3-dithiacyclohexanes (Scheme I)

substituent	solvent	temp, K	$1/K$	$\Delta G°$, kcal/mol
SCH_3	THF-d_8	171	1.39 ± 0.04	0.11 ± 0.02
SC_6H_5	$C_6D_5CD_3$	186	3.06 ± 0.02	0.41 ± 0.01
SC_6H_5	THF-d_8	171	3.50 ± 0.19	0.43 ± 0.02
SC_6H_5	$CD_2Cl_2/CFCl_3$ (15:85)	186	4.88 ± 0.13	0.59 ± 0.01
SC_6H_5	CD_2Cl_2	186	3.78 ± 0.06	0.49 ± 0.01
SC_6H_5	CD_3COCD_3	186	1.88 ± 0.03	0.23 ± 0.01
SC_6H_5	CD_3OD	186	2.27 ± 0.02	0.30 ± 0.01
COC_6H_5	$C_6D_5CD_3$	186	4.50 ± 0.09	0.56 ± 0.01
COC_6H_5	THF-d_8	171	2.19 ± 0.05	0.27 ± 0.01
COC_6H_5	CD_2Cl_2	186	1.46 ± 0.01	0.14 ± 0.01
COC_6H_5	CD_3COCD_3	186	0.59 ± 0.01	−0.20 ± 0.01
$CO_2CH_2CH_3$	$C_6D_5CD_3$	186	6.10 ± 0.14	0.67 ± 0.01
$CO_2CH_2CH_3$	THF-d_8	171	6.70 ± 0.21	0.65 ± 0.01
$CO_2CH_2CH_3$	CD_2Cl_2	186	2.17 ± 0.07	0.29 ± 0.01
$CO_2CH_2CH_3$	CD_3COCD_3	186	1.79 ± 0.01	0.21 ± 0.01
$CO_2CH_2CH_3$	CD_3OD	186	3.36 ± 0.03	0.45 ± 0.01
$CO_2C_6H_5$	$C_6D_5CD_3$	186	11.17 ± 0.29	0.89 ± 0.01
$CO_2C_6H_5$	THF-d_8	171	8.07 ± 0.07	0.71 ± 0.01
$CO_2C_6H_5$	CD_2Cl_2	186	4.51 ± 0.02	0.56 ± 0.01
$CO_2C_6H_5$	CD_3COCD_3	186	2.76 ± 0.02	0.38 ± 0.01
$CO_2C_6H_5$	CD_3OD	186	5.60 ± 0.08	0.64 ± 0.01

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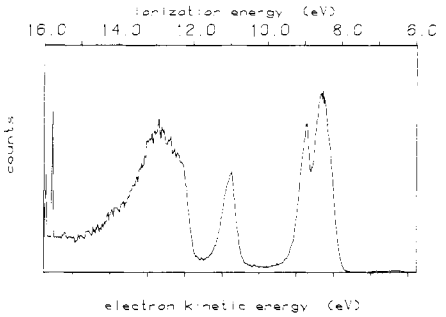


Figure 1. Photoelectron spectrum of 5-methyl-5-aza-1,3-dithiacyclohexane.

Table IV. Comparison of the Conformational Free-Energy Differences in 2-Substituted 1,3,5-Dithiazines (This Work), 1,3-Dithianes,[2] 1,3,5-Trithianes,[17] and Cyclohexanes[18]

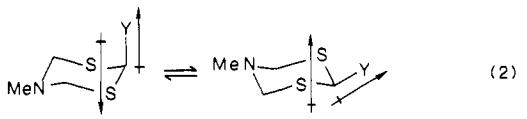
substituent	$\Delta G°_{dithiazine}$ (CD_2Cl_2,[a] 186 K)	$\Delta G°_{dithiane}$ (CD_2Cl_2, 173 K)	$\Delta G°_{trithiane}$ ($CDCl_3$–CS_2, 190 K)	$\Delta G°_{cyclohexane}$ (ambient temp)
SCH_3	0.11	0.64	0.47	−1.0[b]
SC_6H_5	0.49	0.92	0.79	ca. −1.1[c]
COC_6H_5	0.14	1.16		ca. −1.3[d]
$CO_2CH_2CH_3$	0.29	0.83[e]	0.54[e,f]	−1.27[e]
$CO_2C_6H_5$	0.56			

[a] Except for Y = SCH_3, which was measured in THF-d_8, at 171 K. [b] Reference 19. [c] Estimated as ca. 0.1 kcal/mol greater than that for SCH_3: ref 20. [d] Assuming a conformational energy close to that of COCl: see ref 18. [e] Corresponds to CO_2CH_3. [f] In CD_3COCD_3–$CDCl_3$ (3:1).

coupling contant (ca. 2 Hz) observed for H-2e/H-4,6e.[12,13] Tables I and II (supplementary material) list the chemical shifts of **1–5** at various temperatures and in different solvents.

Integration of the peak areas for each of the conformers in the spectra recorded well below the coalescence temperature afforded the equilibrium constants, K,[14] and the conformational free-energy differences, $\Delta G° = -RT \ln K$, which are summarized in Table III. Axial preferences are observed for all substituents, in all solvents (with one single exception: **3**, Y = COC_6H_5, in CD_3C-OCD_3; see discussion below).

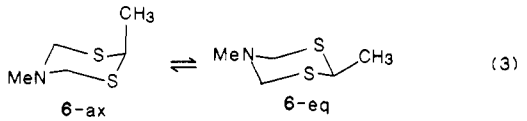
There is a general tendency for a diminished axial preference in the more polar solvents, and this result confirms the importance of dipole–dipole interactions in these systems:[2,15] electrostatic dipole–dipole repulsion disfavors the equatorial conformer, while dipole–dipole attraction favors the axial conformer[16] (Eq 2).



(2)

C. Relative Magnitude of the Anomeric Effect in 1–5. Table IV summarizes the conformational free-energy differences observed for **1–5** in solvent CD_2Cl_2. For comparison purposes, Table IV includes also the $\Delta G°$ values for the 2-substituted 1,3-dithiane analogues in CD_2Cl_2.[2] In addition, some related values in 1,3,5-trithianes[17] and cyclohexanes[18] are incorporated in Table IV.

Of immediate interest in relation to the goals of this work is the comparison of the $\Delta G°$ values in the dithiazines versus the dithianes: the magnitude of the anomeric effect is significantly smaller in the former. That this is not due to increased steric repulsion between an axial substituent at C(2) and the methylene groups at C(4,6) was deduced after determination of the conformational equilibrium of 2,5-dimethyl-5-aza-1,3-dithiacyclohexane (**6**; eq 3): the conformational free-energy difference ($\Delta G°$

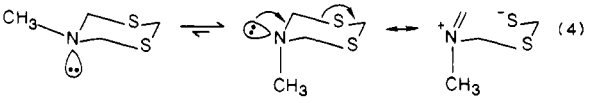


(3)

$= -1.98 \pm 0.05$ kcal/mol) is of similar magnitude to that reported for 2-methyl-1,3-dithiane: $\Delta G°_{342K} = -1.77 \pm 0.01$ kcal/mol.[12,21] This is in agreement with what could be expected from the structural data of the 1,3,5-dithiazine and 1,3-dithiane rings reported by Katritzky et al.[22]

Because the diminished axial preference of electronegative substituents at C(2) in 1,3,5-trithianes relative to 1,3-dithianes has been explained by Ōki and co-workers[17] in terms of a lower lying HOFO (highest occupied fragment orbital), which is less capable of participating in stabilizing $n_S \rightarrow \sigma^*_{C-Y}$ hyperconjugation,[23] it was decided to compare the photoelectron spectrum of the parent 5-methyl-5-aza-1,3-dithiacyclohexane (Figure 1)[24] with that of 1,3-dithiane.[25] Most significant is the similarity in the lowest ionization potential: 8.55 and 8.54 eV, respectively. This result indicates that the smaller anomeric effect found in the 5-aza analogues (this work) as compared with the 2-substituted 1,3-dithianes[2] is not due to a lower lying HOFO in the former, leading to decreased $n_S \rightarrow \sigma^*_{C-Y}$ interactions.

It is also of interest that the PE spectrum of the dithiazine does not show any splitting of bands, which could have been expected if the lone pair orbital at nitrogen was to interact with those on sulfur.[26] This constitutes additional evidence that the methyl group at nitrogen adopts an axial orientation in order to avoid the repulsion between lone pairs of electrons[13] and possibly to allow for favorable $n_N \rightarrow \sigma^*_{C-S}$ orbital interactions[2,6,27,28] (eq 4).



(4)

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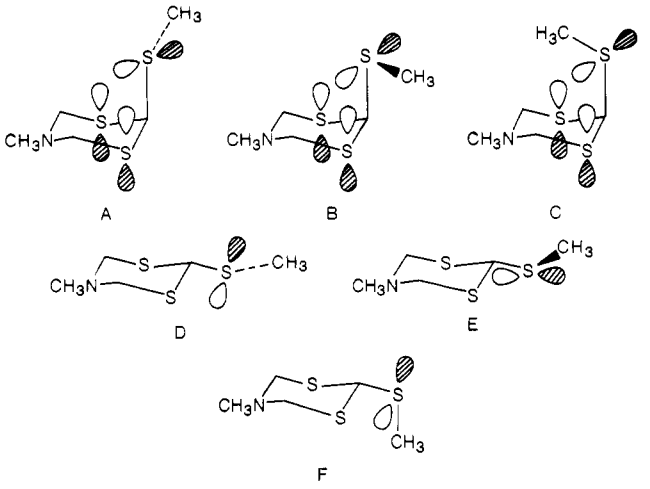
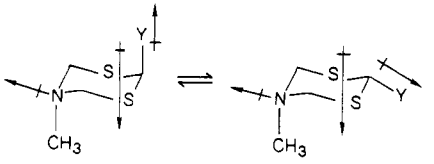
Scheme III



The axial disposition of the *N*-alkyl group in the dithiazine causes some cancellation of the ring dipole encountered in the 1,3-dithiane ring. In this way, the dipole moment, $\mu = 2.09$ D, determined by Havinga and Kalff[29] for the latter drops to $\mu = 1.47$ in 5-methyl-5-aza-1,3-dithiacyclohexane.[13] It is very likely that the smaller anomeric effects observed in this system are the consequence of a less important dipole–dipole component stabilizing the axial conformers (eq 5).


(5)

In spite of the difficulties associated with the quantitative determination of anomeric effects,[15,30,31] comparison of $\Delta G°_{\text{dithiazine}}$ versus $\Delta G°_{\text{cyclohexane}}$ (Table IV) suggests a relative order in the magnitude of the observed anomeric effects as follows: $CO_2C_6H_5 > CO_2CH_2CH_3 > COC_6H_5$ and $SC_6H_5 > SCH_3$. Because the group dipoles associated with these two series of substituents are expected to be fairly similar,[32] this trend, which is also observed in the 1,3-dithiane analogues,[2] is adequately explained in terms of endo and exo hyperconjugative interactions.[5]

Indeed, the antiperiplanar orientation of the p-type lone-pair orbital on the endocyclic sulfurs and the axial C(2)–SCH_3 bond allows for a significant endo anomeric interaction in conformations A and B (Scheme III; conformer C is disfavored on steric grounds). Axial **1** is also stabilized by exo anomeric interactions in A and B (Scheme III). However, exo anomeric interactions also stabilize the equatorial conformers D–F (Scheme III), and a relatively weak axial preference is therefore observed.

Substitution of the methyl group for a phenyl group in **2** ($SCH_3 \rightarrow SC_6H_5$) leads to an increased axial preference because the endo–anomeric effect is stronger in axial **2** (lower energy of the σ^*_{C-S} orbital; greater stabilization through the $n_S \rightarrow \sigma^*_{C-S}$ interaction[33]), but the exo anomeric interactions are less important (lower energy of the donor n_S orbital).

In **3–5**, the endo–anomeric effect results from $n_S \rightarrow \sigma^*_{C-C(O)}$ interactions, whereas torsion about the exocyclic C–C(O) bond can now turn on $\pi_{CO} \rightarrow \sigma^*_{C-S}$ interactions associated with an exo anomeric effect. We note, however, that $\pi_{CO} \rightarrow \sigma^*_{CX}$ interactions have been shown not to be dominant in controlling the conformational preferences of 2-substituted cyclohexanones containing oxygen[34] and selenium[35] substituents probably because of the low energy of the π_{CO} orbital.[36] The interactions in our systems are formally analogous. One can focus, therefore, on the unique endo anomeric interaction in the axial conformations.

D. Enthalpic Anomeric Effect. Recently, Booth et al.[6] have stressed that in studies of the anomeric effect it is the $\Delta H°$ values

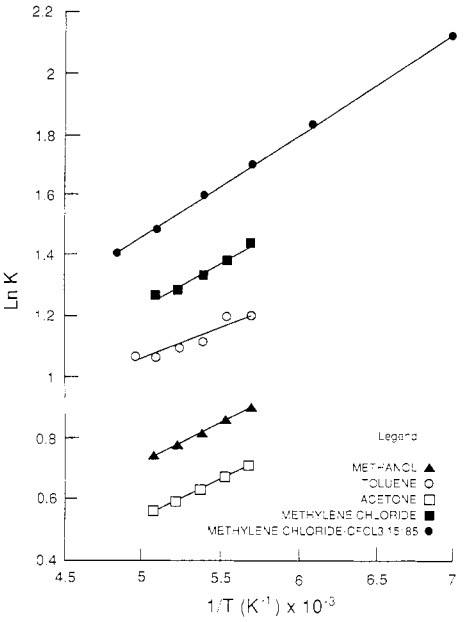


Figure 2. ln *K* as a function of $1/T$ for 5-methyl-2-(thiophenyl)-5-aza-1,3-dithiacyclohexane (**2**).

Table VII. Thermodynamic Parameters for **2–5** (Scheme I)

compd	solvent	$\Delta H°$ (error),[a] kcal/mol	$\Delta S°$ (error),[b] cal/(mol·K)
2	$C_6D_5CD_3$	+0.44 (0.21)	+0.09 (1.10)
2	$CD_2Cl_2/CFCl_3$ (15:85)	+0.70 (0.03)	+0.56 (0.19)
2	CD_2Cl_2	+0.59 (0.19)	+0.51 (0.99)
2	CD_3COCD_3	+0.50 (0.04)	+1.40 (0.22)
2	CD_3OD	+0.54 (0.06)	+1.29 (0.34)
3	$C_6D_6CD_3$	+0.10 (0.08)	−2.46 (0.42)
3	CD_2Cl_2	−0.01 (0.04)	−0.80 (0.23)
3	CD_3COCD_3	−0.25 (0.05)	−2.04 (0.24)
4	$C_6D_5CD_3$	−0.35 (0.10)	−5.46 (0.55)
4	CD_2Cl_2	−0.03 (0.04)	−1.70 (0.23)
4	CD_3COCD_3	−0.04 (0.11)	−1.38 (0.57)
4	CD_3OD	+0.27 (0.15)	−0.95 (0.79)
5	$C_6D_5CD_3$	−0.06 (0.21)	−4.99 (1.18)
5	CD_2Cl_2	−0.17 (0.16)	−3.90 (0.85)
5	CD_3COCD_3	−0.05 (0.12)	−2.24 (0.62)
5	CD_3OD	+0.29 (0.18)	−1.87 (0.93)

[a] Positive values indicate that the axial conformer is favored enthalpically. [b] Positive values indicate that the equatorial conformer is favored entropically.

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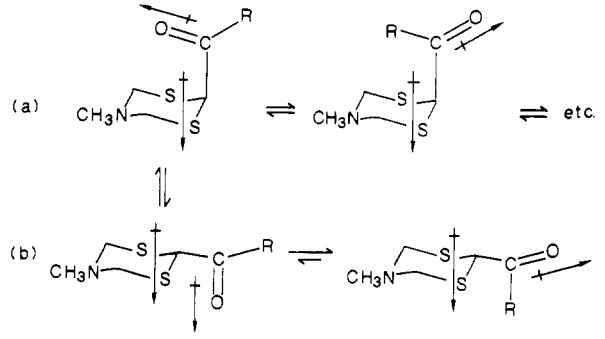
Scheme IV



that correlate with the steric, polar, and stereoelectronic interactions of interest. We therefore deemed it necessary to evaluate the enthalpic and entropic contributions to the anomeric interactions involved in our S–C–Y system. This rigorous study is particularly important in view of the fact that the existence of significant anomeric effects in X–C–Y segments containing second-row and lower row elements has been questioned on theoretical grounds.[37]

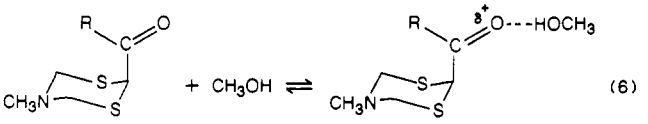
The equilibrium data for **2–5**-ax and **2–5**-eq were derived by direct integration of the signal pairs in the temperature range 176–202 K (solvents CD_2Cl_2, CD_3COCD_3, $C_6D_5CD_3$, and CD_3OD); compound **2** was also analyzed in the temperature range 144–207 K in solvent $CD_2Cl_2/CFCl_3$ 15:85). The mean values (Tables V and VI; supplementary material) were obtained, when possible, from several integrations (five minimum) of the various pairs of peaks of each spectrum, and the standard deviations of the mean values are the errors in K (Table V). (In some cases, however, partial overlap of signals with solvent peaks did not permit accurate integration of all the sets of signals.) Plots of $\ln K$ versus $1/T$ (Figure 2 is a representative example with **2**) are linear, and the thermodynamic parameters derived from these plots by use of a weighted nonlinear least-squares program[7] are listed in Table VII. The errors are calculated based on the error in K and the error in the temperature T (±2 K) and are reported at the 95% confidence level.

The thermodynamic data obtained for the **2**-ax ⇌ **2**-eq equilibrium shows definitively that the axial preference of the thiophenyl group is of enthalpic origin; the enthalpy term dominates over the entropy contribution, which actually favors **2**-eq, especially in the more polar solvents (Table VII). The enthalpy terms responsible for the anomeric effect (axial preference) in **2** are fairly unaffected by the polarity of the solvent so that a dipole–dipole mechanism does not seem responsible for the effect; rather, stereoelectronic interactions (see Section C) could account for the results.

These sizable $\Delta H°$ terms (0.4–0.7 kcal/mol) must of course overcome the steric hindrance present in **2**-ax so that the magnitude of the anomeric effect in this system may well exceed 1.0 kcal/mol. This observation, together with other published work,[2,17,41] provides experimental evidence in support of a significant anomeric interaction in S–C–S segments and argues against the suggestion of Schleyer et al.[37] that such stabilizing interactions should be negligibly small.

In contrast to **2**, the thermodynamic data for the carbonyl derivatives **3–5** show that the $\Delta H°$ term in most solvents is close to zero. Of course, $\Delta H° \sim 0$ in these systems may still be indicative of a significant anomeric effect owing to the countervailing steric effect. Inspection of Table VII shows that the axial predominance of **3–5** is controlled by the entropy difference, the axial conformers being of higher entropy. A likely explanation for this phenomenon can be advanced in terms of the local dipole–dipole interactions present in the axial and equatorial conformers. (A significant solvent effect is found in the equilibria of **3–5**; the anomeric effect decreases as the polarity of the solvent increases.) For axial **3–5**, the C=O dipole should always be aligned antiparallel to the ring dipole, independently of rotation around the C(2)–C(O) bond (Scheme IVa), and all rotamers would then be favorable on electrostatic grounds. In equatorial **3–5**, however, a lower energy rotamer would only be obtained when the C=O bond dipole is pointing away from the ring dipole; this would restrict the rotational freedom of the equatorial conformer (Scheme IVb). Supporting evidence for this explanation comes from the observation that this entropy effect is more important in the less polar solvents, where the electrostatic interaction is more demanding (Table VII).

Interestingly, $\Delta H°$ is positive for **4** and **5** *in methanol* but negative in all other solvents. A plausible interpretation of this effect is as follows: hydrogen bonding by the hydroxylic solvent methanol to the carbonyl group makes the endo anomeric effect more effective, by lowering the energy of the $\sigma^*_{C-C(O)}$ orbital (eq 6).



(6)

These results, together with the previous results,[1-4,7,17,41] leave little doubt that second-row anomeric interactions exist.

Experimental Section

General Information. Melting points, determined with an electrothermal apparatus, are uncorrected. ^1H NMR (400.13-MHz) and ^{13}C NMR (100.6-MHz) spectra were recorded on a Bruker WM-400 NMR spectrometer. Some ^1H NMR (89.9-MHz) and ^{13}C NMR (22.49-MHz) spectra were recorded on a JEOL FX-90Q instrument. Chemical shifts are given in parts per million downfield from TMS. The probe thermocouple was used for temperature measurement, after calibration. Temperatures are believed to be accurate to within ±2 K. Deuteriated solvents were purchased from Merck Sharpe & Dohme Isotopes or Aldrich. Trichlorofluoromethane was purchased from Matheson.

Flask, stirring bars, and hypodermic needles used for the generation of organometallic compounds were dried for ca. 12 h at 120 °C and allowed to cool in a desiccator over anhydrous calcium sulfate. Anhydrous solvents (ethers) were obtained by distillation from benzophenone ketyl.[38] The BuLi employed was titrated according to the method of Juaristi et al.[39]

Microanalyses were performed by M. K. Yang of the Microanalytical Laboratory of Simon Fraser University.

5-Methyl-5-aza-1,3-dithiacyclohexane. Methylamine (15.3 mL of a 40% aqueous solution, 0.2 mol), formaldehyde (120 mL of a 37% aqueous solution, 1.48 mol), and 100 mL of water were mixed in a 2-L round-bottom flask and stirred at 0 °C for 15 min. A solution of sodium hydrogen sulfide (28 g, 0.5 mol) in 300 mL of water was then added dropwise, and the resulting reaction mixture was stirred at 0–5 °C for 24 h. The solid materials were filtered and washed with water until the filtrate was neutral, then dissolved in chloroform, dried over anhydrous sodium sulfate, concentrated, and recrystallized from hot hexane to afford 20.25 g (75% yield) of white crystals with mp 63–65 °C (lit.[8] mp 64–65 °C).

Anal. Calcd for $C_4H_9NS_2$: C, 35.52; H, 6.71; N, 10.36. Found: C, 35.59; H, 6.64; N, 10.19.

2-Substituted 5-Methyl-5-aza-1,3-dithiacyclohexanes. General Procedure. 5-Methyl-5-aza-1,3-dithiacyclohexane (freshly sublimed, 0.54 g, 4 mmol) was placed in a 50-mL flask provided with rubber septa and under nitrogen. Tetrahydrofuran (THF, ca. 20 mL) was added via cannula, and the flask was immersed in a dry ice/acetone bath (ca. −78 °C) before the addition of 2.67 mL (4.2 mmol) of *n*-BuLi 1.45 M in hexane. The reaction mixture was then stirred at −78 °C for 60 min and transferred under positive pressure of nitrogen to another flask containing the electrophile in THF, at −78 °C. The mixture was stirred at −78 °C

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for 1 h and at ambient temperature for an additional hour before it was quenched with saturated aqueous ammonium chloride. The aqueous layer was extracted with ether and worked up in the usual way.

2-(Methylthio)-5-methyl-5-aza-1,3-dithiacyclohexane (1). The general procedure was followed, with 2 equiv of dimethyl disulfide as the electrophile. The product (clear oil, slightly yellow) was purified by flash chromatography[40] [hexane/ethyl acetate (9:1)] followed by distillation at reduced pressure; bp 105 °C/1.5 mmHg; yield 39%. ^1H and ^{13}C NMR spectra are in Tables I and II, respectively (supplementary material).

Anal. Calcd for $C_5H_{11}NS_3$: C, 33.12; H, 6.11; N, 7.72. Found: C, 33.30; H, 6.09; N, 7.73.

2-(Phenylthio)-5-methyl-5-aza-1,3-dithiacyclohexane (2). The general procedure was followed, with 2 equiv of diphenyl disulfide as the electrophile. The product was purified by flash chromatography[40] [hexane/ethyl acetate (70:30)] and recrystallized from methanol/acetone (70:30). The pure product (white crystals with mp 75–77 °C) was obtained in 50% yield. ^1H and ^{13}C NMR spectra are in Tables I and II, respectively (supplementary material).

Anal. Calcd for $C_{10}H_{13}NS_3$: C, 49.34; H, 5.38; N, 5.75. Found: C, 49.28; H, 5.33; N, 5.93.

2-Benzoyl-5-methyl-5-aza-1,3-dithiacyclohexane (3). The general procedure was carried out with 10 equiv of ethyl benzoate as the electrophile. The unreacted ethyl benzoate was removed by distillation (58 °C/1 mmHg), and the desired product was purified by flash chromatography[40] [hexane/ethyl acetate (30:70)] and subsequent recrystallization from hexane/chloroform (9:1) to afford **3** as white crystals, mp 109–111 °C, in 48% yield. ^1H and ^{13}C NMR spectra are in Tables I and II, respectively (supplementary material).

Anal. Calcd for $C_{11}H_{12}NOS_2$: C, 55.20; H, 5.47; N, 5.85. Found: C, 55.44; H, 5.31; N, 5.99.

2-Carboethoxy-5-methyl-5-aza-1,3-dithiacyclohexane (4). The general procedure was carried out with 10 equiv of diethyl carbonate. Excess carbonate was removed by distillation (50 °C/5 mmHg), and the desired product was purified by flash chromatography[40] [hexane/ethyl acetate (80:20)] and distillation in a Kugelrohr apparatus, bp 93 °C/0.2 mmHg, to afford pure **4** as a colorless oil in 30% yield. ^1H and ^{13}C NMR spectra are in Tables I and II, respectively (supplementary material).

Anal. Calcd for $C_7H_{13}NO_2S_2$: C, 40.56; H, 6.32; N, 6.76. Found: C, 40.57; H, 6.32; N, 6.77.

2-Carbophenoxy-5-methyl-5-aza-1,3-dithiacyclohexane (5). The general procedure was followed with 10 equiv of diphenyl carbonate. The product was purified by flash chromatography[40] (pure methylene chloride) followed by crystallization from hot petroleum ether and sublimation at 80 °C/0.1 mmHg. Pure **5** was obtained in 35% yield as white crystals, mp 84–85 °C. ^1H and ^{13}C NMR spectra are in Tables I and II, respectively (supplementary material).

Anal. Calcd for $C_{11}H_{13}NO_2S_2$: C, 51.74; H, 5.13; N, 5.48. Found: C, 51.93; H, 5.15; N, 5.44.

2,5-Dimethyl-5-aza-1,3-dithiacyclohexane (6). The general procedure was followed with 2 equiv of methyl iodide as the electrophile. The product was purified by flash chromatography[40] (pure CH_2Cl_2 eluent) and distillation (bp 70 °C/0.1 mmHg) to afford pure **6** as a colorless oil, in 83% yield. ^1H NMR (400 MHz, CD_2Cl_2) δ 1.43 (d, J = 6.9 Hz, 3 H), 2.53 (s, 3 H), 4.08 (d, J = 12.8 Hz, 2 H), 4.25 (q, J = 6.9 Hz, 1 H) 4.68 (d, J = 12.8 Hz, 2 H).

Anal. Calcd for $C_5H_{11}NS_2$: C, 40.23; H, 7.43; N, 9.38. Found: C, 40.51; H, 7.56; N, 9.46.

Acknowledgment. We are indebted to Dr. A. Flores-Parra for a generous gift of 5-methyl-5-aza-1,3-dithiacyclohexane, and for her advice on its preparation. We thank Prof. R. S. Glass for the PE spectrum and G. Uribe for recording the Jeol ^1H and ^{13}C NMR spectra. We are also grateful to the Natural Sciences and Engineering Research Council of Canada for financial support in the form of an operating grant (to B.M.P.) and an International Collaborative Research Grant (to E.J. and B.M.P.) and to the Consejo Nacional de Ciencia y Tecnología de México for a scholarship to E.A.G.

Supplementary Material Available: Tables I and II listing the ambient and low-temperature ^1H and ^{13}C NMR signal assignments in **1–5** and Tables V and VI listing the equilibrium data for the conformational equilibria of **2–5** (8 pages). Ordering information is given on any current masthead page.

Oxidations by Methyl(trifluoromethyl)dioxirane. 2.[1] Oxyfunctionalization of Saturated Hydrocarbons†

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Abstract: The reaction of methyl(trifluoromethyl)dioxirane (**1b**), a novel dioxirane species, with two open-chain, four cyclic, and five polycyclic saturated hydrocarbons and two aralkyl hydrocarbons in CH_2Cl_2/1,1,1-trifluoropropanone has been studied; under mild conditions (−22 to 0 °C), it gives alcohols and/or ketones (deriving from further oxidation of secondary alcohols) in high yields and within very short reaction times. Primary C–H bonds are not appreciably oxidized and high regioselectivities were determined for attack at tertiary over secondary C–H bonds, with the exception of norbornane, which showed opposite regioselectivity. The reaction is also highly stereoselective, since hydroxylations of *cis*- and *trans*-decalin and of *cis*- and *trans*-1,2-dimethylcyclohexane were found to be in each case stereospecific with retention. From kinetic data, E_a = 14.3 kcal mol^{-1} and log A = 9.9 were estimated for cyclohexane oxidation. Relative rates change in the order cyclohexane (0.78) < norbornane (1) < bicyclo[2.2.2]octane (9.2) < adamantane (146); *cis*-1,2-dimethylcyclohexane was observed to be 7-fold more reactive than its trans isomer, demonstrating remarkable discrimination for equatorial vs axial C–H attack (also noticed in the case of *cis*- and *trans*-decalin). The relative rate of oxidation of cumene vs ethylbenzene was found to be ca. 3.1 (after statistical correction), i.e., in sharp excess over values usually recorded in classical radical H-atom abstraction from benzylic position. Rate constants determined for the reactions of cumene and of ethylbenzene show the title dioxirane (**1b**) is more reactive than dimethyldioxirane (**1a**) by factors of ca. 600 and over 700, respectively. The whole of the observations is better accommodated by an "oxenoid" mechanism, involving concerted O-atom insertion by dioxirane into C–H bonds of hydrocarbons.

During the past 15 years, the achievement of selective conversions of alkanes into oxygenated compounds has continued to pose a challenge to the community of chemists.[2-4] Along with the older methods,[5] some more recent studies have regarded alkane oxidations by peroxy acids,[4-6] peroxides,[7] hydroxy radicals,[8] *N*-oxides,[9] ozone,[10,11] hydrogen peroxide, and ozone in superacids.[12] Homogeneous catalysis by transition-metal ions[3i] has been em-

† Dedicated to the memory of Professor Angelo Mangini (University of Bologna, Italy), deceased in August 1988.

(1) For paper 1, see: Troisi, L.; Cassidei, L.; Lopez, L.; Mello, R.; Curci, R. *Tetrahedron Lett.* **1989**, *30*, 257.

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