Stereoelectronic Interpretation for the Anomalous ^1H NMR Chemical Shifts and One-Bond C–H Coupling Constants (Perlin Effects) in 1,3-Dioxanes, 1,3-Oxathianes, and 1,3-Dithianes. Spectroscopic and Theoretical Observations

Eusebio Juaristi,[*,1] **Gabriel Cuevas,**[2] **and Alberto Vela**[3]

Contribution from the Departamento de Química, Centro de Investigación y de Estudios Avanzados del Instituto Politécnico Nacional, Apdo. Postal 14-740, 07000 México D.F., and Departamento de Química, División de Ciencias Básicas e Ingeniería, Universidad Autónoma Metropolitana Iztapalapa, Apdo. Postal 55534, 09340 México, D.F., Mexico

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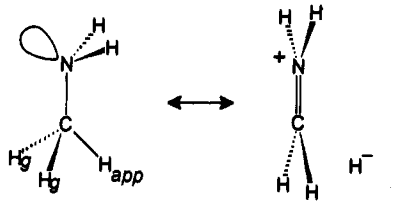
Abstract: The reverse Perlin effects observed for all C–H one bond coupling constants in 1,3-dithianes, i.e., $^1J_{C-H_{ax}} > {^1J_{C-H_{eq}}}$, seem to support the existence of a dominant $\sigma_{C-S} \rightarrow \sigma^*_{C-H_{eq}}$ stereoelectronic interaction, which leads to a weakening of the equatorial C–H bonds in these heterocycles. Further analysis of the $^1J_{C-H}$ patterns in 1,3-dioxanes and 1,3-oxathianes confirm the apparent manifestation of $n_O \rightarrow \sigma^*_{C-H_{ax}}$ as well as the novel β-oxygen effect involving $n_{O/C-H_{eq}}$ orbital interactions in a W array, as proposed very recently in the literature. Furthermore, the above mentioned stereoelectronic interactions may be at least partly responsible for the anomalous chemical shift behavior at C(2) in 1,3-dithianes and at C(5) in 1,3-dioxanes. Theoretical support for the proposed stereoelectronic orbital interactions was gained from *ab initio* Hartree–Fock 6-31G** and Kohn–Sham /LSD + BP + NLSCF/ DZVP2 calculations on the heterocycles of interest.

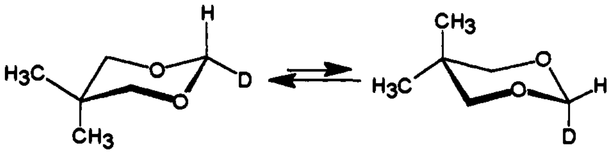
Introduction

In 1957 F. Bohlmann made the important observation that C–H bonds antiperiplanar (app) to a vicinal nitrogen lone pair in conformationally defined amines present characteristic infrared stretching frequencies ("Bohlmann bands").[4] Indeed, model studies with methylamine indicate that the C–H_{app} bond is longer and weaker than the C–H_{gauche} bonds,[5] and these observations have been interpreted as the result of $n_N \rightarrow \sigma^*_{C-H_{app}}$ hyperconjugation (A ↔ A′) (in the language employed by Cieplak[6]).

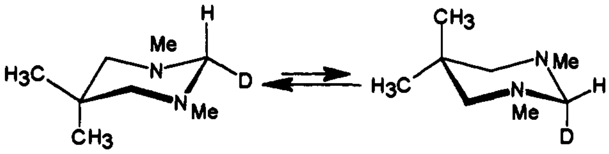


A A′

More recently, gas-phase Fourier transform IR spectra and solution ^1H NMR measurements showed that deuterium prefers the equatorial over the axial position in 5,5-dimethyl-2-*D*-1,3-dioxane (eq 1) and 2-*D*-*N*,*N*′,5,5-tetramethylhexahydro-1,3-pyrimidine (eq 2).[7]



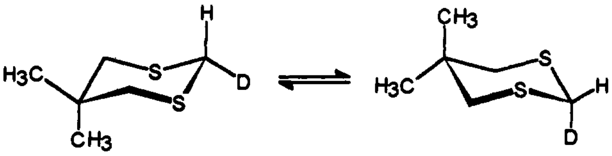
(1)



(2)

These data were interpreted by Anet and Kopelevich as confirming the importance of $n_O \rightarrow \sigma^*_{C-H(D)}$ and $n_N \rightarrow \sigma^*_{C-H(D)}$ hyperconjugative interactions in the above heterocycles (the heavier isotope prefers to occupy the stronger equatorial site, as evidenced by the larger stretching-force constant for the equatorial C–H(D) bond).[7]

In marked contrast, the isotope effect for the conformational equilibrium in 2-*D*-5,5-dimethyl-1,3-dithiane was found to be essentially zero ($K = 1$, $\Delta G° = 0$; eq 3), while only a single C–D stretching band was observed in the infrared spectrum.[7b] This finding indicated to the authors that the stretching force constants for the axial and equatorial bonds at C(2) are virtually the same; i.e., that the lone pairs on sulfur (n_S) are not involved in $n_S \rightarrow \sigma^*_{C-H(D)}$ negative hyperconjugation [7b] (double bond–no bond resonance in the language of Altona, *et al.*[8]).



(3)

In this regard, it has been observed that the magnitude of the one bond ^{13}C–^1H coupling constants for an axial C–H bond

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(1) Instituto Politécnico Nacional.

(2) Extracted from the Doctoral thesis of G.C., CINVESTAV-IPN: Mexico, 1993.

(3) Universidad Autónoma Metropolitana.

(4) Bohlmann, F. *Angew. Chem.* **1957**. *69*. 641. Bohlmann, F. *Chem. Ber.* **1958**. *91*, 2157.

(5) (a) Hehre, W. J.; Radom, L.; Schleyer, P.v.R.; Pople, J. A. *Ab Initio Molecular Orbital Theory;* Wiley: New York, 1986. (b) Krueger, P. J.; Jan, J.: Wieser, H. J. *Mol. Struct.* **1970**, *5*, 375. (c) Bernardi, F.; Schlegel, H. B.; Wolfe, S. *J. Mol. Struct.* **1976**, *35*, 149. (d) McKean, D. C. *Chem. Soc. Rev.* **1978**, *7*, 399.

(6) Cieplak, A. S. *J. Am. Chem. Soc.* **1981**, *103*, 4540. Cieplak, A. S.; Tait, B. D.; Johnson, C. R. *J. Am. Chem. Soc.* **1989**, *111*, 8447.

(7) (a) Anet, F. A. L.; Kopelevich, M. *J. Am. Chem. Soc.* **1986**, *108*, 2109. (b) Anet, F.A.L; Kopelevich, M. *J. Chem. Soc., Chem. Commun.* **1987**, 595.

(8) Romers, C.; Altona, C.; Buys, H. R.; Havinga, E. *Topics Stereochem.* **1969**, *4*, 39.

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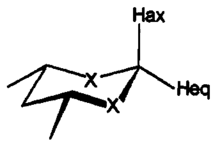
Chart 1



1. X = O

2. X = S

adjacent to oxygen or nitrogen in a six-membered ring is smaller by a significant amount (8–10 Hz) than $^2J_{C-H}$ for an equatorial C–H bond; i.e., $^3J_{C-H_{eq}} > {}^1J_{C-H_{ax}}$.[9,10] This finding has been interpreted in terms of an $n_X \rightarrow \sigma^*_{C-H_{app}}$ interaction between a pair of nonbonded electrons on oxygen or nitrogen and the axial (antiperiplanar) adjacent C–H bond; that is, double bond–no bond resonance weakens the C–H_{ax} bond and attenuates the Fermi contribution to the one bond $^{13}C-^1H$ coupling constant.[11–14]

In contrast with the situation in *cis*-4,6-dimethyl-1,3-dioxane (**1**, Chart 1) where $^1J_{C(2)-H_{ax}} = 157.4$ Hz $< {}^4J_{C(2)-H_{eq}} = 167.5$,[10a] Bailey *et al.*[15] pointed out in 1988 that the dithiane analogue **2** (Chart 1) exhibits an opposite behavior: $^1J_{C(2)-H_{ax}} = 154.1$ Hz $> {}^1J_{C(2)-H_{eq}} = 144.9$ Hz.

This reversal of the relative magnitudes of the coupling constants at C(2) in dioxanes and dithianes was explained by Wolfe *et al.*[13,16] as originating from a reversal in C–H bond lengths as a result of dominant $\sigma_{C-S} \rightarrow \sigma^*_{C-H_{eq}}$ or $\sigma_{C-H_{eq}} \rightarrow \sigma^*_{C-S}$ (rather than $n_S \rightarrow \sigma^*_{C-H_{ax}}$) interactions in **2**.

In this context, it is important to note that in 1976 Eliel and co-workers[17] brought attention to the fact that, contrary to the normal situation in which axial protons in a cyclohexane resonate upfield of the corresponding equatorial ones, in 1,3-dithiane H(2ax) is downfield from H(2eq). Furthermore, in 1,3-dioxane the "anomaly" was found at C(5), where H(5ax) is downfield from H(5eq). It was concluded[17] that these reversals cannot be ascribed solely to the anisotropy of the vicinal C–X (X = O or S) bonds.

The present study was undertaken in order (1) to examine the generality of the reversal of the "Perlin effect" [12,13] in diastereotopic methylene protons adjacent to sulfur, (2) to test the validity of Wolfe's stereoelectronic interpretation,[13,16] and (3) to explore the possibility that stereoelectronic interactions could similarly account for the anomalous ^1H NMR chemical shifts observed at C(2) in 1,3-dithiane and at C(5) in 1,3-dioxane.[17,18]

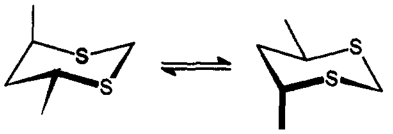
Results and Discussion

A. 1,3-Dithiane and Derivatives. All equatorial C–H bonds in 1,3-dithiane (**3**) are antiperiplanar (app) to C–S bonds in the ring.[19] Thus, should the proposal[13,16] be correct that $\sigma_{C-S} \rightarrow \sigma^*_{C-H_{app}}$ (or $\sigma_{C-H_{eq}} \rightarrow \sigma^*_{C-S_{app}}$) stereoelectronic interactions dominate over $n_S \rightarrow \sigma^*_{C-H_{ax}}$ at the C(2) in 1,3-dithiane, then one would expect a reversal of the usual relative magnitudes for *all* C–H one-bond couplings in 1,3-dithiane.

The values of the $^1J_{C-H}$ coupling constants were determined from the proton-coupled ^{13}C NMR spectra, and the assignments were achieved by the analysis of the satellite bands in the high resolution (270 MHz) ^1H NMR spectra. The $^1J_{C-H}$ obtained in 1,3-dithianes **2–5** are given in Table 1.

A1. *cis*-4,6-Dimethyl-1,3-dithiane (2). The proton-coupled ^{13}C NMR spectrum of this anancomeric[20] derivative shows, as reported by Bailey and collaborators,[15] $^1J_{C-H}$ couplings for C(2) of 154.2 and 144.3 Hz. Examination of the ^{13}C satellites in the ^1H NMR spectrum of **2** [δ H(2ax) = 4.10 ppm; δ H(2eq) = 3.56 ppm] confirms the previous conclusion[15] that the axial H(2) proton presents the larger $^1J_{C-H}$. Similarly, the $^1J_{C-H}$ couplings for C(5) are 129.5 and 124.6 Hz, and their unequivocal assignment [via the examination of the satellites at δ H(5eq) = 2.10 ppm, and δ H(5ax) = 1.33 ppm] indicates that here also the axial H(5) proton has the larger $^1J_{C-H}$: 129.5 Hz for C(5)-Hax *versus* 124.6 Hz for C(5)-H_{eq}. Finally, C(4,6)-H_{ax} is worth 138.8 Hz.

A2. *trans*-4,6-Dimethyl-1,3-dithiane (4). As expected, this conformationally heterogeneous heterocycle (eq 4) presents NMR spectra showing *average* ^1J[C(2)–H] = 149.8 Hz and ^1J[C(5)–H] = 127.8 Hz. More interestingly, the observed ^1J[C(4,6)–H] = 134.4 Hz allows estimation of the missing ^1J[C(4,6)–H_{eq}] = 130.0 Hz.[21] Comparison with ^1J[C(4,6)–H_{ax} = 138.8 Hz (see section A1 above) shows a *reverse* correlation of ^1J's relative to the situation in cyclohexane[22] or in nitrogen or oxygen heterocycles as noted in the Introduction.



(4)

A3. 2-*tert*-Butyl-1,3-dithiane (5). The above results indicate a reversal of the relative magnitudes of the $^{13}C-^1H$ one-bond coupling constants for *all* C–H bonds in 1,3-dithiane. Further supporting evidence was provided by the examination of anancomeric 2-*tert*-butyl-1,3-dithiane. The combined data extracted from the proton-coupled ^{13}C and from high-resolution ^1H NMR spectra (which permitted the measurement of the satellite bands) afforded the assignments shown in Chart 2. It is clear that $^1J_{C-H_{ax}} > {}^7J_{C-H_{eq}}$ both at C(4,6) and at C(5), contrary to the normal trend.[23]

A4. 1,3-Dithiane (3). The available information suggesting that the incorporation of substituents in a six-membered ring distorts to some extent its original structure[25] prompted the study of the parent 1,3-dithiane. Whereas the ambient temperature spectra show average chemical shifts and $^1J_{C-H}$ coupling constants (Table 1), at −90 °C ring inversion of unsubstituted **3** is sufficiently slow as to allow for the observation and measurement of the individual chemical shifts and coupling constants for the axial and equatorial C–H bonds.

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(9) Perlin, A. S.; Casu, B. *Tetrahedron Lett*, **1969**, 2921.

(10) (a) Bock, K.; Wiebe, L. *Acta Chem. Scand.* **1973**, *27*, 2676. See, also: (b) Rao, V.S. *Can. J. Chem.* **1982**, *60*, 1067. (c) Hansen, P. E. *Prog. Nucl. Magn. Reson. Spec.* **1981**, *14*, 175.

(11) David, S. In *Anomeric Effect: Origin and Consequences*; Szarek, W. A., Horton, D., Eds.; American Chemical Society Symposium Series: Washington, DC, 1979. See, also: Fraser, R. R.; Bresse, M. *Can. J. Chem.* **1983**, *61*, 576.

(12) It has been recently proposed that stereoelectronic effects upon one-bond C–H coupling constants be termed "Perlin effects".[13]

(13) Wolfe, S.; Pinto, B. M.; Varma, V.; Leung, R. Y. N. *Can. J. Chem.* **1990**, *68*, 1051.

(14) Very recently, spectroscopic evidence for hyperconjugation in the neutral ground state has been obtained from one-bond carbon–carbon coupling constants: Lambert, J. B.; Singer, R. A. *J. Am. Chem Soc.* **1992**, *114*, 10246.

(15) Bailey, W. F.; Rivera, A. D.; Rossi, K. *Tetrahedron Lett.* **1988**, *29*. 5621.

(16) Wolfe, S.; Kim, C.-K. *Can. J. Chem.* **1991**, *69*, 1408.

(17) Eliel, E. L.; Rao, V. S.; Vierhapper, F. W.; Juaristi, G. Z. *Tetrahedron Lett.* **1975**, 4339.

(18) For preliminary reports of this work, see: (a) Juaristi, E.; Cuevas, G. *Tetrahedron Lett.* **1992**, *33*, 1847. (b) Juaristi, E.; Cuevas G.; Flores-Vela, A. *Tetrahedron Lett.* **1992**, *33*, 6927.

(19) It should be noted, however, that the C(2)–H_{eq} and C(4,6)–H_{eq} bonds are *anti* to the S–C bond, whereas the C(5)–H_{eq} bond is *anti* to the C–S bond; i.e., the bond dipoles are oriented in opposite directions.

(20) Anteunis, M. J. O. In *Conformational Analysis, Scope and Present Limitations;* Chiurdoglu, G., Ed.; Academic Press: New York, 1971; p 32. See, also: Juaristi, E. *Introduction to Stereochemistry and Conformational Analysis;* Wiley: New York, 1991, Chapter 3.

(21) Each C(4,6)–H bond spends 50% of the time in the axial orientation and 50% equatorial.

(22) Chertkov, V. A.; Sergeyev, N. M. *J. Am. Chem. Soc.* **1977**, *99*, 6750.

(23) The term "reverse Perlin effect" was introduced recently in describing such unusual spectroscopic behavior.[18,24] Nevertheless, it is probably appropriate to stress that this term refers to an empirical observation rather than to the underlying fundamental of the effect.

(24) (a) Anderson, J. E.; Bloodworth, A. J.; Cai,J.; Davies, A. G.; Tallant, N. A. *J. Chem. Soc.. Chem Commun.* **1992**, 1689. (b) Anderson, J. E., Bloodworth, A. J.; Cai, J.; Davies, A. G.; Schiesser, C. H. *J. Chem. Soc., Perkin Trans. 2* **1993**, 601.

(25) This seems to be so particularly with bulky groups such as the *tert*-butyl group: Wolfe, S.; Campbell, J. R. J. *Chem. Soc.. Chem. Commun.* **1967**, 872.

Table 1. One-Bond ^{13}C–^{1}H Coupling Constants in 1,3-Dithianes **2–5**[a,b]

compd	C(2)–H$_{ax}$	C(2)–H$_{eq}$	C(4,6)–H$_{ax}$	C(4,6)–H$_{eq}$	C(5)–H$_{ax}$	C(5)–H$_{eq}$
2	154.2	144.3	138.8	(130.0)[c]	129.5	124.6
3 (25 °C)[d]	149.9	149.9	137.4	137.4	128.9	128.9
3 (–90 °C)[d]	154.2	146.2	137.3	132.9	130.2	127.4
4	149.8	149.8	134.4	134.4	128.7	128.7
5	151.5		141.6	134.9	132.0	124.5

[a] In Hz. [b] In CDCl$_3$, except where otherwise stated. [c] Estimated, see text. [d] In CD$_2$Cl$_2$.

Chart 2

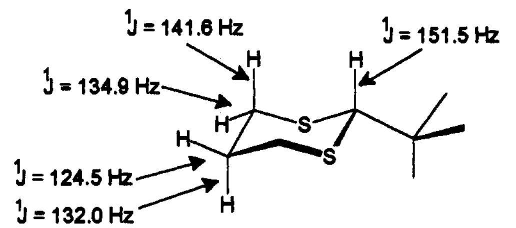
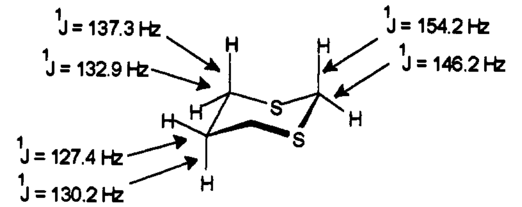
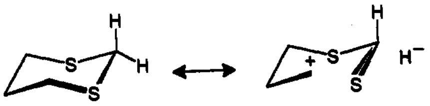


Chart 3[a]



[a] ^1J values in Hz. At –90 °C, in methylene chloride-d_2.

The data collected in Chart 3 (solvent CD$_2$Cl$_2$) confirm the anomalous order in the relative magnitudes of the C–H coupling constants at *all* carbons in 1,3-dithiane; that is, any structural deformation caused by the *tert*-butyl group in **5** is not drastic enough to alter the coupling pattern, which is in line with expectation if hyperconjugative interactions between the equatorial C–H σ-orbitals and the antiperiplanar σ C–S orbitals provoke a weakening of the equatorial C–H bonds in 1,3-dithiane, which is, as suggested by Wolfe *et al.*[13,16] manifested in the smaller values for $^1J_{\text{C–H}_{\text{eq}}}$.[26,27] Furthermore, the orbital interaction depicted as $\sigma_{\text{C–S}} \rightarrow \sigma^*_{\text{C–H}_{\text{eq}}}$ could help explain the "anomalous" chemical shift behavior for H(2) as discussed in the Introduction, since such hyperconjugation in **3** could account for upfield shifting of H(2eq) and downfield displacement for H(2ax).

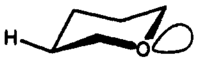


B. 1,3-Dioxane and Derivatives. In order to complement the pioneering studies that have demonstrated the sizable difference in the magnitude of $^1J_{\text{C–H}}$ for the C(2)–H$_{ax}$ and C(2)–H$_{eq}$ bonds of both *cis*-4,6-dimethyl-1,3-dioxane (**1**) and the analogous 1,3-dithiane (**2**),[15] we carried out the measurement of $^1J_{\text{C–H}}$ for all carbons in a series of 1,3-dioxanes, including **1**, and the unsubstituted parent 1,3-dioxane **6** as well as derivatives **7–9** (Table 2).

B1. *cis*- and *trans*-4,6-Dimethyl-1,3-dioxane (1 and 7). In agreement with previous reports,[10a,15] ^1J for the C(2)–H$_{ax}$ bond in **1** is smaller by 10.1 Hz than ^1J for the C(2)–H$_{eq}$ bond ("normal" Perlin effect). This phenomenon can be rationalized in terms of a dominant $n_{\text{O}} \rightarrow \sigma^*_{\text{C–H}_{\text{ax}}}$ interaction between a lone electron pair on oxygen and the axial (app) C–H bond on the adjacent C(2) carbon. (See the Introduction.)

By constrast, an attenuation of the normal Perlin effect ($^1J_{\text{C–H}_{\text{ax}}} < {}^1J_{\text{C–H}_{\text{eq}}}$) is found for the methylenic C–H bonds at C(5): $^1J_{\text{C(5)–H}_{\text{ax}}} = 126.7$ Hz $\approx {}^1J_{\text{C(5)–H}_{\text{eq}}} = 128.7$ Hz (Bock and Wiebe[10a] observed $^1J_{\text{C(5)–H}_{\text{ax}}} = {}^1J_{\text{C(5)–H}_{\text{eq}}} = 127.5$ Hz).

A plausible explanation for this phenomenon is found in the recent reports by Anderson *et al.*[24] who have suggested that a stereoelectronic interaction between a pseudoequatorial nonbonding electron pair on a β-oxygen and the equatorial C–H bond as depicted in **B** might weaken this bond.[28]



B

Finally, the value ^1J[C(4,6)–H$_{ax}$] = 137.1 Hz measured in **1** is to be compared with the estimated ^1J[C(4,6)–H$_{eq}$] = 154.9, obtained by extrapolation of ^1J[C(4,6)–H] = 146.8 Hz in mobile **7** where these hydrogens spend half the time in the axial and equatorial orientations. Thus, a normal and quite large Perlin effect is observed for these C(4,6)–H bonds adjacent to oxygen.

B2. 1,3-Dioxane (6). Because of the rapid ring inversion of this heterocycle at ambient temperature, average $^1J_{\text{C–H}}$ couplings are observed for both the axial and equatorial bonds at C(2), C(4,6), and C(5) (Table 2). Their relative magnitude, 163.0, 143.8, and 128.9 Hz, respectively, is in line with the decreasing inductive effect by two, one, and zero α oxygens at these positions.

On the other hand, the stereoelectronic interactions may be examined at temperatures below coalescence. The observed values (Table 2) confirm (1) a normal Perlin effect at C(2), $^1J_{\text{C–H}_{\text{ax}}} < {}^1J_{\text{C–H}_{\text{eq}}}$, and (2) the balance of the normal and reverse Perlin effects at C(5), $^1J_{\text{C–H}_{\text{ax}}} = {}^1J_{\text{C–H}_{\text{eq}}}$.

As discussed above, this latter observation may be ascribed to a compensation of the normal Perlin effect[9–11,22] leading to some weakening of the axial C–H bond, with the β W$_n$ oxygen effects[24] which may weaken the equatorial C–H bond. Furthermore, should this β effect result in some electronic transfer to H(5eq), it could explain at least in part the anomalous chemical shift behavior found at C(5) in 1,3-dioxane.[17] (See the Introduction.)

On the other hand, however, the normal Perlin effect observed at C(4,6) in unsubstituted dioxane **6** is much smaller than that observed in dimethylated **1** and **7** (Δ^1J = 1.4 *vs* 17.8 Hz, respectively) indicating that the structural and electronic influence exerted by alkyl substituents in this system can be quite significant.

B3. 2-*tert*-Butyl- and 2-Phenyl-1,3-dioxane (8 and 9). Quite similar data were obtained from the NMR spectra of these anancomeric derivatives (Table 2). A medium-size normal Perlin effect, $^1J_{\text{C–H}_{\text{eq}}} - {}^1J_{\text{C–H}_{\text{ax}}} = 5.5$ Hz, was observed at C(4,6), in line with the manifestation of only one $n_{\text{O}} \rightarrow \sigma^*_{\text{C–H}}$ hyperconjugation

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(26) The Fermi contact term makes the principal contribution to coupling between directly bonded nuclei; Kowalewski, J. *Prog. Nucl. Magn. Reson. Spectrosc.* **1977**, *11*, 1.

(27) For additional pertinent experimental observations in 1,3-dithiane, which may be ascribed to this stereoelectronic effect, see ref 7, and also: Juaristi, E.; Valenzuela, B. A.; Valle, L.; McPhail, A. T. *J. Org. Chem.* **1984**, *49*, 3026. Caserio, M. C.; Shih, P.; Fisher, C. L. *J. Org. Chem.* **1991**, *56*, 5517. Very recently, Merlic *et al.* established that the deuterium in 2,2-dimethyl-1,3-dithiane-5-*d* and -1,3-oxathiane-5-*d* prefers the axial position: Merlic, C. A.; Anet, F. A. L.; Kopelevich, M.; Freedberg, D. I. *Abstracts of Papers*, 207th ACS National Meeting; American Chemical Society: Washington, DC, March 13–17, 1994; ORGN-109.

(28) The term "homoanomeric" has been used by Anderson *et al.*[24] to describe this phenomenon. Nevertheless, the anomeric effect[29] is a conformational effect with stereoelectronic interactions accounting only in part for its origin. The present rationalization[24] of the β-oxygen effect upon $^1J_{\text{C–H}_{\text{eq}}}$ invokes, of course, the involvement of a stereoelectronic interaction. It would be important to demonstrate manifestations of this W-design stereoelectronic interaction in conformational equilibria.[30]

Table 2. One-Bond $^{13}C-^{1}H$ Coupling Constants in 1,3-Dioxanes **1** and **6–9**[a,b]

compd	C(2)–H_{ax}	C(2)–H_{eq}	C(4,6)–H_{ax}	C(4,6)–H_{eq}	C(5)–H_{ax}	C(5)–H_{eq}
1	157.5	167.4	137.1	(154.9)	126.7	128.7
6 (25 °C)[d]	163.0	163.0	143.8	143.8	128.9	128.9
6 (−90 °C)[d]	158.6	167.5	143.6	145.0	128.9	128.9
7	163.0	163.0	146.8	146.8	127.8	127.8
8	157.6		139.9	145.4	128.3	128.3
9	160.9		140.0	145.0	128.9	128.9

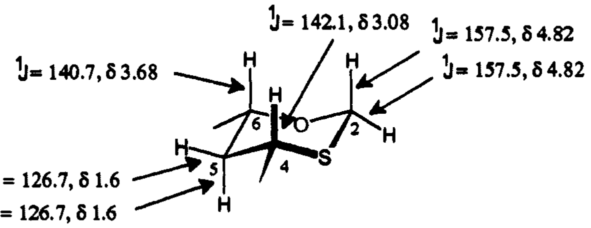
[a] In Hz. [b] In $CDCl_3$, except where otherwise indicated. [c] Estimated, see text. [d] In CD_2Cl_2.

Table 3. One-Bond $^{13}C-^{1}H$ Coupling Constants in 1,3-Oxathianes **10–14**[a,b]

compd	C(2)–H_{ax}	C(2)–H_{eq}	C(4)–H_{ax}	C(4)–H_{eq}	C(5)–H_{ax}	C(5)–H_{eq}	C(6)–H_{ax}	C(6)–H_{eq}
10 (−90°)[d]	157.5	157.5	142.7	142.7	126.9	129	139	154.4
11	157.5	157.5	142.1	(138.8)[c]	126.7	126.7	140.7	(145.2)[c]
12	156.4	156.4	138.9	138.9	125.0	125.0	139.9	139.9
13	156.0		136.2	140.6	128.8	125.7	138.1	146.2
14	156.5	156.5			124.5	124.5	142.7	

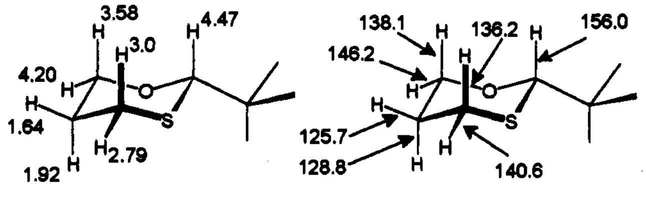
[a] In Hz. [b] In $CDCl_3$, except where otherwise stated. [c] Estimated, see text. [d] In CD_2Cl_2.

Chart 4[a]



[a] $^{1}J_{C-H}$ coupling constants in Hz. Chemical shifts in ppm.

Chart 5



¹H chemical shifts (ppm)

$^{1}J_{C-H}$ coupling constants (Hz)

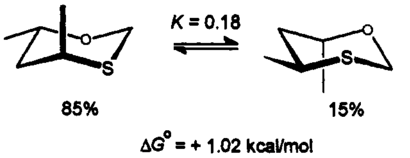
interaction. On the other hand, the complete similarity between the axial and equatorial C–H one-bond couplings at C(5) for **8** and **9** (see Table 2) is in line with the rationalization (see section B1) that the normal Perlin effect is compensated by the influence of two β Wn oxygen effects.

C. 1,3-Oxathiane and Derivatives. This section describes our observations in 1,3-oxathiane **10** and derivatives **11–14**, a series which could provide relevant information concerning the relative magnitude of stereoelectronic interactions involving oxygen *vis a vis* sulfur. The data of interest are summarized in Table 3.

C1. *cis*- and *trans*-4,6-Dimethyl-1,3-oxathiane (11 and 12). Proton-coupled ^{13}C and high-resolution ^{1}H NMR spectra of **11** provided the data indicated in Chart 4. Most interesting, similar coupling constants $^{1}J_{C-H_{ax}} \approx {}^{1}J_{C-H_{eq}}$ are observed at C(2) and C(5), suggesting a balance of the effect(s) responsible for a normal Perlin effect ($^{1}J_{C-H_{ax}} < {}^{1}J_{C-H_{eq}}$) as found for C–H bonds in cyclohexane[22] or adjacent to oxygen,[9–11] but a reverse trend (i.e., $^{1}J_{C-H_{eq}} < {}^{1}J_{C-H_{ax}}$) when the C–$H_{eq}$ is antiperiplanar to C–S bonds. (See section A and the Introduction.)

Also important is the observation of similar chemical shifts for the axial and equatorial protons at C(2) and C(5), contrary to the normal situation in which δ(ax) < δ(eq). We shall return to this point below.

The conformational behavior of *trans*-4,5-dimethyl-1,3-dioxane (**12**) was studied by Gelan and Anteunis,[32] who determined a preference for the conformer with the methyl group at C(6) occupying the equatorial orientation; $K = 0.18$, $\Delta G°_{298K} = +1.02$ kcal/mol (eq 5). From the corresponding 85:15 ratio at 25 °C, extrapolation from the $^{1}J_{C(4,6)-H}$ values in **11** and **12** allows for the estimation of $^{1}J_{C(4)-H_{eq}} = 138.3$ Hz and $^{1}J_{C(6)-H_{eq}} = 145.2$ Hz. Comparison with the corresponding couplings in the axial C(4)–H and C(6)–H bonds, 142.1 and 140.7 H, respectively, leads to the conclusion that C(4), adjacent to sulfur, presents a reverse Perlin effect, while C(6), adjacent to oxygen, shows a normal Perlin effect.

 (5)

C2. 2-*tert*-Butyl-1,3-oxathiane (13). Proton-coupled ^{13}C and high-resolution ^{1}H NMR spectra of **13** permitted also the unequivocal assignments presented in Chart 5. For the methylene C(4)–H bonds adjacent to sulfur $^{1}J_{C-H_{ax}} < {}^{1}J_{C-H_{eq}}$ (normal Perlin effect), in contrast with the observations made in 1,3-dithianes (see section A). Nevertheless, at C(5) $^{1}J_{C-H_{ax}} \approx {}^{1}J_{C-H_{eq}}$ (near balance of Perlin effects), and for the methylene adjacent to oxygen $^{1}J_{C-H_{ax}} < {}^{1}J_{C-H_{eq}}$ (normal Perlin effect).

Similarly, $^{1}J_{C(2)-H_{ax}} = {}^{1}J_{C(2)-H_{eq}} = 156.5$ Hz and $^{1}J_{C(5)-H_{ax}} = {}^{1}J_{C(5)-H_{eq}} = 124.5$ Hz in 4,4,6-trimethyl-1,3-oxathiane (**14**).

On the other hand, anomalous chemical shift behavior ($\delta H_{ax} > \delta H_{eq}$) is observed for the methylene protons at C(4) and C(5). By contrast, the protons at C(6) (adjacent to oxygen) exhibit the normal $H_{ax} < \delta H_{eq}$.

C3. Low-temperature NMR Spectra of 1,3-Oxathiane (10). At −90 °C, ring inversion of the unsubstituted heterocycle is slowed sufficiently so that individual chemical shifts and coupling constants for the axial and equatorial C–H bonds could be measured. As indicated in section A4, measurement of the parent oxathiane is important in view of previous observations that the *tert*-butyl group may distort the six-membered ring,[28] so that

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(29) (a) Kirby, A. J. *The Anomeric Effect and Related Stereoelectronic Effects at Oxygen;* Springer-Verlag: Berlin, 1983. (b) Juaristi, E.; Cuevas, G. *Recent Studies of the Anomeric Effect.* Tetrahedron Report No. 315, *Tetrahedron* **1992**, *48*, 5019. (c) *The Anomeric Effect and Associated Stereoelectronic Effects*; Thatcher, G. R. J., Ed.; ACS Symposium Series 539; American Chemical Society: Washington, DC, 1993. (d) Graczyk, P. P.; Mikolajczyk, M. *Topics Stereochem.* **1994**, *21*, 159.

(30) Interestingly enough, Eliel wrote in 1976:[31] "...one might expect that the anomeric effect, which produces an axial preference for electronegative substituents at C-2, would cause an equatorial preference for such substituents at C-5 because of the relative reversal of the ring dipole at C-5 compared to C-2...This argument is subject to question, however, since other factors besides dipole repulsion contribute to the anomeric effect..."

(31) Kaloustian, M. K.; Dennis, N.; Mager, S.; Evans, S. A.; Alcudia, F.; Eliel, E. L. *J. Am. Chem. Soc.* **1976**, *98*, 956.

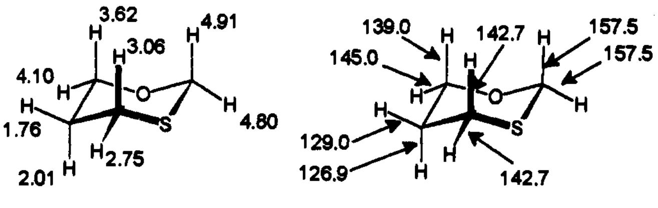
(32) Gelan, J.; Anteunis, M. *Bull. Soc. Chim. Belg.* **1968**, *77*, 423; 1970, *79*, 313.

Table 4. One-Bond $^{13}C-^{1}H$ Coupling Constants in 2-Phenyl-1,3-dioxane (**9**) and Several 5-Substituted Derivatives (**15–18**)[a,b]

compd	C(2)–H_{ax}	C(4,6)–ax	C(4,6)–H_{eq}	ΔJ(4,6)	C(5)–H_{ax}	C(5)–H_{eq}	ΔJ(5)
9	160.9	140.0	145.0	5	128.9	128.9	0
cis-**15**	160.8	138.3	150.4	12.1		154.4	
trans-**15**	160.8	142.1	152.0	9.9	141.0		13.4
cis-**16**	160.9	138.3	144.3	6.0		147.6	
trans-**16**	159.7	137.7	151.0	13.3	139.9		7.7
cis-**17**	159.7	138.3	152.6	14.3		147.6	
trans-**17**	165.3	142.7	150.4	7.7	153.1		5.5
cis-**18**	160.9	138.8	154.3	15.5		149.9	
trans-**18**	163.1	*c*	*c*	*c*		*c*	

[a] In Hz. [b] All in $CDCl_3$. [c] Unable to measure with confidence, due to overlap with other signals.

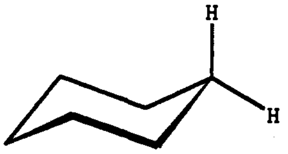
Chart 6



^1H chemical shifts (ppm)

$^1J_{C-H}$ coupling constants (Hz)

Table 5. Bond Lengths (Å), Bond Angles and Dihedral Angles (deg), and Energies (in Hartrees and in eV) Calculated for Cyclohexane, with Various Basis Sets



	RHF/STO-3G	RHF/6-31G	RHF/6-31G**
C–C	1.543 97	1.535 27	1.531 71
C–H_{eq}	1.088 12	1.085 84	1.087 04
C–H_{ax}	1.088 38	1.088 26	1.089 52
C–C–C	111.2	111.4	111.4
H–C–H	107.4	106.7	106.6
C–C–C–C	55.4	54.9	54.8
H_{eq}–C–C–C	177.1	177.3	177.4
H_{ax}–C–C–C	65.3	65.8	68.9
$E_{nuclear}$	254.879 488 63	255.877 583 00	256.239 037 42
E_{total}	–213.482 671 65	–234.111 019 32	–234.226 253 75
E_{HOMO} (eV)	–0.384 02	–0.419 87	–0.423 07
E_{LUMO} (eV)	0.585 61	0.225 46	0.226 77

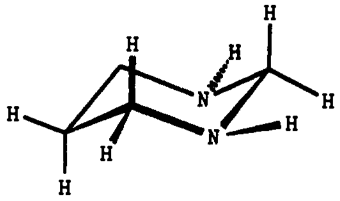
some of the NMR data extracted from **13** may not be representative of those in the parent compound.

The data presented in Chart 6 (in CD_2Cl_2 solution) confirm the anomalous chemical shifts for the equatorial and axial hydrogens at C(2), C(4), and C(5); that is, $\delta H_{ax} > \delta H_{eq}$. Interestingly, the same carbons are associated with a balance or near balance of Perlin effects ($^1J_{C-H_{ax}} \approx {}^1J_{C-H_{eq}}$) to their bonded hydrogens. However, normal chemical shifts and Perlin effects are found at C(6).

Comparison of C–H_{ax} versus C–H_{eq} ^1J coupling constants in the parent 1,3-oxathiane with those in **10–12** shows minor, but apparently significant, trend differences at C(4) and C(5). This result seems to indicate that substituent groups might provoke structural changes that lead to tangible variations in coupling patterns in this heterocycle.

Three pieces of information seem to be essential for the understanding of the unusual Perlin effects and proton chemical shifts reported above: (1) the observation made by Eliel *et al.*[17] that diamagnetic bond anisotropies alone[33] do *not* fully account for the anomalous shifts at C(2) in 1,3-dithiane, (2) the proposals made by Wolfe *et al.*[13,16] and Anderson *et al.*[24] that stereoelectronic orbital interactions weaken the equatorial C–H bonds and are responsible for the reverse Perlin effects observed at C(2) in 1,3-dithiane and at C(5) in 1,3-dioxane, and, (3) the finding[18] that *all* equatorial bonds in 1,3-dithiane, which are antiperiplanar to C–S bonds do indeed exhibit smaller $^1J_{C-H_{eq}}$ coupling constants.

Table 6. Bond Lengths (Å), Bond Angles and Dihedral Angles (deg), and Energies (in Hartrees and in eV) Calculated for Hexahydro-1,3-pyrimidine



	RHF/STO-3G	RHF/6-31G	RHF/6-31G**
C_2–N	1.486 78	1.449 17	1.446 16
$C_{4,6}$–N	1.487 94	1.455 37	1.452 32
$C_{4,6}$–C_5	1.542 85	1.529 58	1.526 02
C_2–H_{eq}	1.093 45	1.080 38	1.084 08
C_2–H_{ax}	1.103 58	1.113 10	1.102 78
$C_{4,6}$–H_{eq}	1.090 52	1.082 30	1.084 88
$C_{4,6}$–H_{ax}	1.095 97	1.095 14	1.096 31
C_5–H_{eq}	1.087 93	1.085 64	1.086 75
C_5–H_{ax}	1.086 85	1.082 36	1.084 73
N–H	1.033 82	0.995 52	0.999 51
N–C–N	108.9	109.2	109.2
C–N–C	110.1	115.4	112.4
C–C–C	110.0	110.2	109.9
H–C_2–H	107.9	107.8	107.7
H–$C_{4,6}$–H	107.8	107.4	107.3
H–C_5–H	108.5	108.6	108.4
C–N–C–C	59.8	56.1	58.4
N–C–C–C	56.0	54.3	54.6
H_{eq}–C_2–N–C	178.6	174.1	179.4
H_{ax}–C_2–N–C	59.96	67.4	62.2
$E_{nuclear}$	259.618 504 70	262.635 209 04	263.850 108 52
E_{total}	–262.939 813 81	–266.046 072 30	–266.186 526 28
E_{HOMO} (eV)	–0.2937 3	–0.3336 9	–0.3511 4
E_{LUMO} (eV)	0.5589 0	0.2232 7	0.2233 0

We consider it plausible that the anomalous chemical shifts for the axial and equatorial protons at C(2), C(4), and C(5) in 1,3-oxathiane are the result of relevant contributions by the $\sigma_{C-S} \rightarrow \sigma^*_{C-H}$ two-electron–two-orbital interactions. The β_O $W_N \rightarrow$ C(5)–H_{eq} stereoelectronic interaction proposed by Anderson *et al.*,[24] which is so clearly manifested in 1,3-dioxanes (see section B) could be relevant here. These stereoelectronic effects cause an upfield shift for the antiperiplanar equatorial hydrogens as well as a concomitant decrease on the C–H_{eq} coupling constants, which in 1,3-oxathiane is nearly balanced by the normal Perlin effect. On the "oxygen part" of the molecule, however, the well accepted $n_O \rightarrow \sigma^*_{C-H_{ax}}$ interaction appears to be dominant.

D. Concerning the Relative Magnitude of the Orbital Interactions under Consideration. Examination of the observed $^1J_{C-H}$ coupling constants in cyclohexane ($^1J_{C-H_{ax}}$ = 122 Hz; $^1J_{C-H_{eq}}$ =

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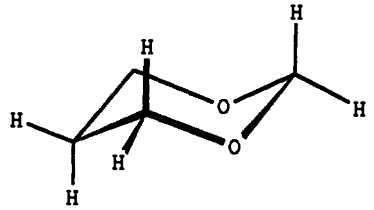
(33) Cf.: Khan, S. A.; Lambert, J. B.; Hernández, O.; Carey, F. A. *J. Am. Chem. Soc.* **1975**, *97*, 1468.

Table 7. Bond Lengths (Å), Bond Angles and Dihedral Angles (deg), and Energies (in Hartrees and in eV) Calculated for 1,3-Dioxane, with Various Basis Sets

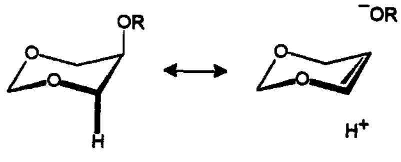


	RHF/STO-3G	RHF/6-31G	RHF/6-31G**
C_2–O	1.433 09	1.415 19	1.384 61
$C_{4,6}$–O	1.439 22	1.439 20	1.404 66
$C_{4,6}$–C_5	1.547 66	1.526 59	1.524 12
C_2–H_{eq}	1.098 16	1.071 67	1.078 69
C_2–H_{ax}	1.105 35	1.087 02	1.093 37
$C_{4,6}$–H_{eq}	1.092 88	1.077 05	1.081 73
$C_{4,6}$–H_{ax}	1.097 21	1.087 37	1.091 45
C_5–H_{eq}	1.087 16	1.084 88	1.086 73
C_5–H_{ax}	1.087 05	1.082 78	1.085 28
O–C–O	113.2	111.7	112.5
C–O–C	109.0	114.6	112.8
C–C–C	108.7	109.5	108.6
H–C_2–H	108.8	111.1	109.9
H–$C_{4,6}$–H	108.0	108.8	108.0
H–C_5–H	108.5	108.6	108.4
C–O–C–C	57.0	55.0	56.0
O–C–C–C	52.0	53.1	51.8
H_{eq}–C_2–O–C	178.8	172.9	177.6
H_{ax}–C_2–O–C	60.6	66.3	62.9
$E_{nuclear}$	261.897 956 16	263.641 199 93	267.326 591 75
E_{total}	−301.994 718 98	−305.691 006 37	−305.846 562 07
E_{HOMO} (eV)	−0.333 220 18	−0.422 767 16	−0.420 669 98
E_{LUMO} (eV)	0.531 166 11	0.227 462 26	0.234 875 11

126 Hz),[22] 1,3-dithiane (section A4), and 1,3-dioxane (section B2) suggests the following heteroatom effects upon the magnitude of one-bond C-H coupling being affected: α-oxygen = +21 Hz; β-oxygen = +3.5 Hz; n_O = −2.5 Hz; app C–O ≈ 0; Wn_O = −2 Hz; α-sulfur = +16 Hz; β-sulfur = +6 Hz, $n_S \approx 0$; and app C–S = −7.5 Hz, where α and β terms presumably arise only from inductive effects, n_X refers to the app orientation of one lone electron pair at X, and Wn_O is the influence of a pseudoequatorial β oxygen electron pair in a W arrangement.

Nevertheless, the above effects must certainly depend on the exact dihedral angle between the n-orbital on the heteroatom or C-X bond and the C-H orbital being examined. Indeed, substantial deviations from additivity are found when the above empirical increment values are applied to predict the values for the C-H one-bond coupling constants at C(4) and C(5) in the "mixed" heterocycle, 1,3-oxathiane. These deviations probably result from geometrical deformations in this system relative to the "pure" 1,3-dioxane and 1,3-dithiane.

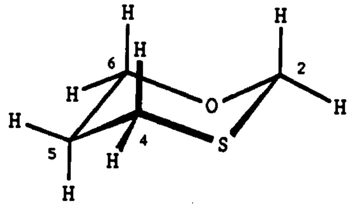
E. 2,5-Disubstituted 1,3-Dioxanes. Recently, spectroscopic, thermodynamic, and theoretical analysis of several 2,5-disubstituted-1,3-dioxanes supported a hyperconjugative $\sigma_{C(4,6)-H_{ax}} \rightarrow \sigma^*_{C-OR}$ interaction as responsible for the attractive *gauche* effect operative in this system (eq 6).[34]



(6)

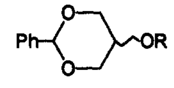
On the other hand, the accumulated $^1J_{C-H}$ data in 1,3-dioxanes (see section B) supports the importance of $n_O \rightarrow \sigma^*_{C(4,6)-H_{ax}}$ hyperconjugative orbital interactions, which apparently result in a weakening of the axial C-H bonds at C(4,6) (eq 7). It was then considered of interest

Table 8. Bond Lengths (Å), Bond Angles and Dihedral Angles (deg), and Energies (in Hartrees and in eV) Calculated for 1,3-Oxathiane, with Various Basis Sets

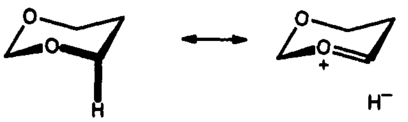


	RHF/STO-3G	RHF/6-31G	RHF/6-31G**
C_2–O	1.436 47	1.409 52	1.385 67
C_2–S	1.807 92	1.879 02	1.816 70
C_4–S	1.803 16	1.883 84	1.818 81
C_4–C_5	1.545 04	1.527 18	1.528 34
C_5–C_6	1.551 04	1.525 11	1.525 04
C_6–O	1.438 23	1.435 93	1.403 24
C_2–H_{eq}	1.092 90	1.073 61	1.079 96
C_2–H_{ax}	1.097 84	1.081 47	1.087 50
C_4–H_{eq}	1.087 16	1.078 99	1.082 66
C_4–H_{ax}	1.089 69	1.081 79	1.085 64
C_5–H_{eq}	1.088 35	1.086 89	1.087 97
C_5–H_{ax}	1.087 81	1.082 83	1.084 91
C_6–H_{eq}	1.093 29	1.077 49	1.081 95
C_6–H_{ax}	1.097 0	1.087 55	1.091 33
S–C–O	114.2	112.1	113.1
C–S–C	95.9	96.1	96.5
C–O–C	110.1	116.6	114.5
C–C–C	111.7	112.7	112.2
H–C_2–H	107.6	110.6	109.0
H–C_4–H	107.2	108.5	107.6
H–C_5–H	107.9	107.6	107.9
H–C_6–H	107.8	108.6	107.9
C–S–C–C	51.8	50.0	50.1
C–O–C–C	−64.5	−65.5	−65.1
C–S–C–O	−58.7	−51.6	−54.5
S–C–C–C	−57.1	−59.2	−57.0
O–C–C–C	60.1	61.4	60.0
$E_{nuclear}$	315.925 649 45	313.352 632 43	318.684 681 09
E_{total}	−621.332 211 47	−628.349 272 58	−628.500 105 95
E_{HOMO} (eV)	−0.253 74	−0.347 18	−0.340 97
E_{LUMO} (eV)	0.437 62	0.181 91	0.189 58

Chart 7



15, R = H
16, R = Me
17, R = Ac
18, R = SO_2Me



(7)

to examine the NMR spectroscopic behavior in a series of 2-phenyl-5-substituted-1,3-dioxanes (*cis*- and *trans*-**15**–**18**, Chart 7), with particular attention to one-bond $^1J_{C-H}$ coupling constants at C(4,6) and C(5). The results are given in Table 4, which includes for comparison purposes the corresponding data for the parent 2-phenyl-1,3-dioxane. Although we are unable at this time to explain in its totality the values reported in Table 4, we

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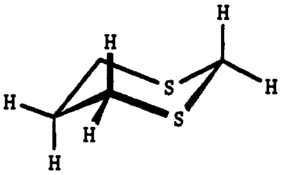
(34) (a) Juaristi, E.; Antúnez, S. *Tetrahedron* **1992**, *48*, 5941. (b) The *gauche* effect was first recognized by Wolfe [Wolfe, S.; Rauk, A.; Tel, L. M.; Csizmadia, I. G. *J. Chem. Soc (B)* **1971**, 136. Wolfe, S. *Acc. Chem. Res.* **1972**, *5*, 102] but discussed in terms of dominant nuclear–electron attraction. (c) For a review on the attractive and repulsive *gauche* effects, see: Juaristi, E. *J. Chem. Educ.* **1979**, *56*, 438.

Table 9. Bond Length (Å), Bond Angles and Dihedral Angles (deg), and Energies (in Hartrees and in eV) Calculated for 1,3-Dithiane, in Various Hartree–Fock and Kohn–Sham Levels of Theory



	RHF/STO-3G	RHF/6-31G	RHF/6-31G*	RH/6-31G**	KS/LDF + BP + NLSCF/DZVP	KS/LDF + BP + NLSCF/DZVP2
C_2–S	1.804 30	1.863 40	1.810 17	1.809 74	1.834 36	1.835 57
$C_{4,6}$–S	1.803 24	1.880 58	1.817 08	1.816 82	1.841 73	1.842 02
$C_{4,6}$–C_5	1.548 14	1.526 42	1.529 03	1.568 62	1.537 53	1.539 65
C_2–H_{eq}	1.086 98	1.076 27	1.080 96	1.081 31	1.101 39	1.100 31
C_2–H_{ax}	1.090 43	1.077 36	1.082 35	1.082 87	1.103 89	1.103 86
$C_{4,6}$–H_{eq}	1.087 40	1.079 68	1.082 91	1.083 22	1.103 33	1.101 39
$C_{4,6}$–H_{ax}	1.089 64	1.081 81	1.085 28	1.085 73	1.106 70	1.105 83
C_5–H_{eq}	1.089 33	1.088 07	1.088 06	1.088 38	1.107 68	1.107 16
C_5–H_{ax}	1.088 49	1.082 79	1.083 99	1.084 44	1.104 77	1.104 17
S–C–S	115.9	114.7	115.2	115.2	115.6	115.8
C–S–C	97.7	99.1	99.3	99.4	98.5	98.5
C–C–C	113.2	114.2	113.7	113.7	114.0	113.6
H–C_2–H	106.7	109.3	107.9	107.9	108.6	108.7
H–$C_{4,6}$–H	107.0	108.2	107.2	107.3	107.7	107.8
H–C_5–H	107.4	107.2	107.5	107.6	107.8	107.8
C–S–C–C	58.4	58.0	57.7	57.6	57.8	57.9
S–C–C–C	64.8	67.7	65.3	65.3	65.0	66.3
H_{eq}–C_2–S–C	178.5	175.7	177.5	177.4	177.6	177.8
H_{ax}–C_2–S–C	63.1	66.0	65.7	65.8	65.1	64.8
$E_{nuclear}$	377.920 938 2	370.417 133 95	377.623 167 12	377.669 523 86	373.091 808 60	372.951 172 96
E_{total}	−940.673 797 21	−951.014 406 49	−951.150 219 93	−951.162 668 75	−953.569 011 08	−953.773 461 45
E_{HOMO} (eV)	−0.238 091 82	−0.337 506 37	−0.330 287 049	−0.330 287 03	−5.285 45	−5.265 55
E_{LUMO} (eV)	0.419 179 48	0.157 435 69	0.167 056 679	0.167 056 68	−0.722 28	−0.698 69

would like to draw attention to the trends which apparently give evidence for the participation of stereoelectronic interactions involving the C(5)–OR bond (σ orbital): (1) The value for $^1J_{C(4,6)-H_{ax}}$ in all four *cis* distereomers studied is an essentially constant 138.3 Hz, which seems smaller by ca. 5 Hz than expected on purely inductive grounds; i.e., ^1J in parent **9** + β-oxygen = 140.0 + 3.5 = 143.5 Hz (calculated). By contrast, $^1J_{C(4,6)-H_{ax}}$ in *trans*-**15** and -**17** is closer to the calculated value. This observation may be in line with expectation if for *cis*-**15**–**18** the orbital stereoelectronic interaction depicted in eq 6 weakens the C(4,6)–H_{ax} bonds and leads to a decrease in the magnitude of ^1J. (2) The difference in magnitude $|^1J_{C(4,6)-H_{ax}} - {}^1J_{C(4,6)-H_{eq}}|$ is substantially larger in *cis*-**15**–**18** [$\Delta J(4,6)$ = 12.0 Hz on average], relative to that found in *trans*-**15**–**17** [$\Delta J(4,6)$ = 10 Hz in average] or in C(5)-unsubstituted **9**, where $\Delta J(4,6)$ = 5.0 Hz. (3) Whereas $|^1J_{C(5)-H_{ax}} - {}^1J_{C(5)-H_{eq}}| = 0$ in the reference compound **9**, $\Delta J(5)$ = 8.9 Hz (in average) for **15**–**17**. This difference seems to be mostly due to the higher values in $^1J_{C(5)-H_{eq}}$ observed in *cis*-**15**–**18**, which may be in accord with the canonical structure depicted on the right side of eq 6 [increased sp^2 character at C(5)].

It is clear that many more compounds should be studied before definitive trends and interpretations can be deduced. Nevertheless, it is probably safe to foresee a promising future for the use of one-bond ^{13}C–^{1}H coupling constants as probes in the study of stereoelectronic effects in organic chemistry.

F. *Ab initio* Study of the Stereoelectronic Effects Involved in 1,3-Dithianes, 1,3-Dioxanes, and 1,3-Oxathianes. Very recently, Wolfe *et al.*[13,16] reported the results of *ab initio* 6-31G* calculations on 22 fragment molecules X-CH$_2$-Y and X-CH(CH$_3$)-Y modeling the tetrahydropyran, tetrahydrothiopyran, 1,3-dioxane, and 1,3-dithiane systems. The computed C-H bond lengths, C-H stretching force constants, and atomic charges on carbon and on hydrogen provide good support for the implication that larger C-H bonds present lower one-bond C-H coupling constants, while shorter bonds are associated with larger $^1J_{C-H}$ values. Furthermore, these calculations[13,16] did exhibit longer C–H_{ax} bonds α to oxygen, but longer C–H_{eq} bonds α to sulfur, in good fitting with the experimental spectroscopic ($^1J_{C-H}$ measurements[15]) observations.

Nevertheless, specific requirements of the actual cyclic structures (from which the experimental data were taken) could alter to some degree the magnitude of the stereoelectronic interactions of interest as well as the predicted structural and physical manifestations. We would like to report herein the results of *ab initio* (STO-3G, 6-31G and 6-31G**) calculations carried out on the complete six-membered rings: cyclohexane, 1,3-diazane, 1,3-dioxane, 1,3-oxathiane, and 1,3-dithiane. For the last molecule, further examination at a different level of computation [Kohn/Sham (KS)/local spin density (LSD) with the exchange functional of Becke and the correlation energy functional of Perdew (BP) plus nonlocal spin density corrections (NLSD) in a self-consistent field with high-quality double-ζ split-valence plus polarization basis set (DZVP2)] was also performed. These *ab initio* calculations were carried out in a Cray-YMP4/32 supercomputer.

Figure 1 summarizes the relevant C-H bond lengths (Å) in the 6-31G** optimized structures and (in parentheses) the available experimental values of $^1J_{C-H}$ which were taken from the appropriate entry of Tables 1–3. Full details of the calculated structures are given in Tables 5–9.

F1. Cyclohexane. In the 4-31G calculations of Wiberg *et al.*[35] the axial and equatorial C-H bond lengths of cyclohexane are 1.088 and 1.086 Å, respectively (Figure 1a and Table 5). Our values also predict that the axial C-H bond of cyclohexane is longer (and thus weaker) than the equatorial C-H bond: C–H_{ax} = 1.090 Å and C–H_{eq} = 1.087 Å. These values are also in good agreement with those reported by Wolfe *et al.*[13] for *gauche* butane, in which the bond lengths are 1.088 Å ("axial") and 1.087 ("equatorial"). In the Cieplak language,[6] the longer and weaker

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[35] Wiberg, K. B.; Walters, V. A.; Dailey, W. P. *J. Am. Chem. Soc.* **1985**, *107*, 4860.

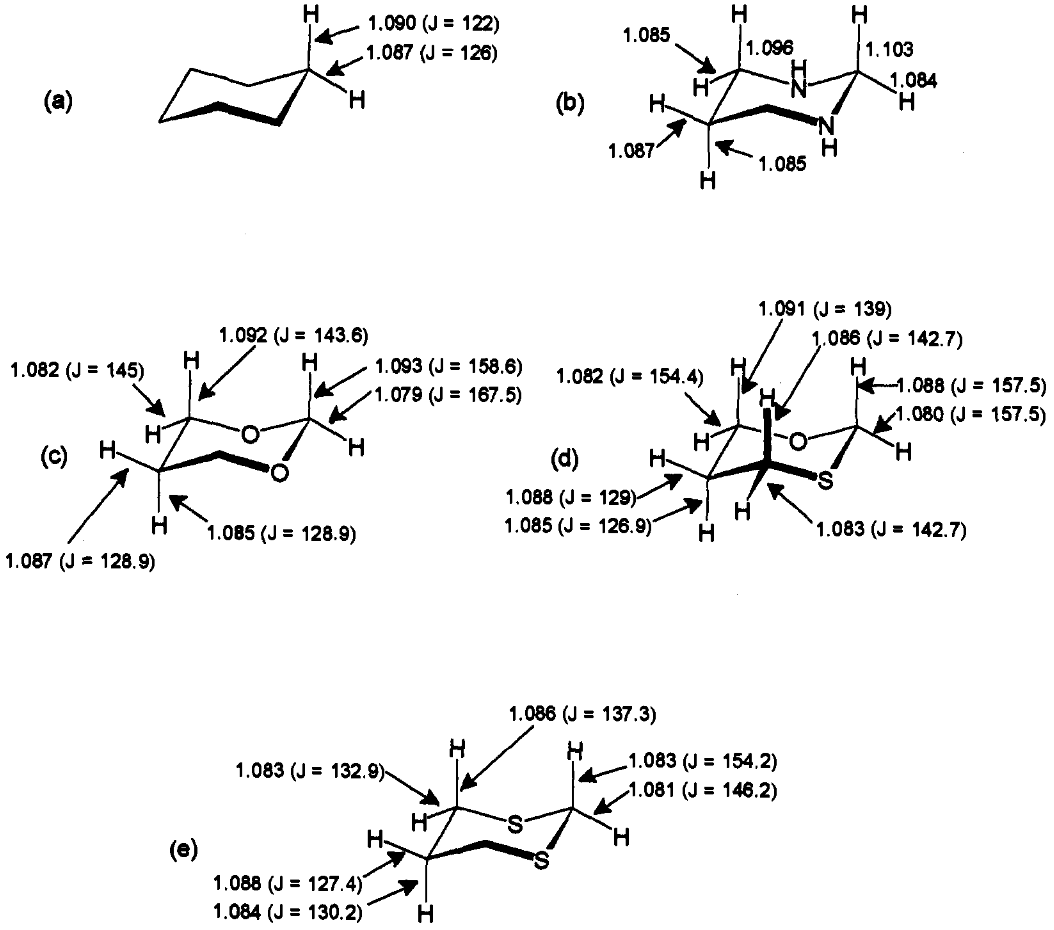

Figure 1.

axial C–H bonds are the result of $\sigma_{C-H} \rightarrow \sigma^*_{C-H}$ hyperconjugation between antiperiplanar CH bonds.[36]

F2. Hexahydro-1,3-pyrimidine. Our 6-31G** optimized structure (Figure 1b and Table 6) seems to support very well Anet and Kopelevich's $n_N \rightarrow \sigma^*_{C-H_{app}}$ hyperconjugative interpretation as already discussed in the Introduction.[7,37] In particular the axial C–H bonds adjacent to nitrogen (which are at least partly app to a lone pair at nitrogen) are markedly longer than the corresponding equatorial ones. Indeed, C(2)–H_{ax} = 1.103 Å *vs* C(2)–H_{eq} = 1.084 Å, and C(4,6)–H_{ax} = 1.096 Å *vs* C(4,6)–H_{eq} = 1.085 Å. By contrast C(5)–H_{eq} = 1.087 Å is predicted to be slightly longer than C(5)–H_{ax}; i.e., a reverse Perlin effect in predicted. It will be interesting to verify experimentally this result and, if so, to establish whether dominant $\sigma_{C-N} \rightarrow \sigma^*_{C-H_{eq}}$ or perhaps β_N W_n hyperconjugative interactions may be responsible for this behavior.

F3. 1,3-Dioxane. The theoretical results for this oxygen-containing heterocycle (Figure 1c and Table 7) are in good agreement with the experimental observations (see section B). Indeed, the axial C–H bonds adjacent to oxygen are longer (and weaker) than the corresponding equatorial C–H bonds. This trend is of course in line with the observed $^1J_{C-H_{ax}} < {}^1J_{C-H_{eq}}$ at C(2) and at C(4,6). On the other hand, the calculated bond lengths for the axial and equatorial C–H bonds at C(5) are very similar (1.087 and 1.085 Å respectively), which fits the similar $^1J_{C-H}$ couplings at this position ($^1J_{C(5)-H_{ax}} = {}^1J_{C(5)-H_{eq}}$ = 128.9 Hz). Our results are in almost perfect agreement with those reported very recently for 1,3-dioxane by Anderson *et al.*[24b]

F4. 1,3-Oxathiane. On the "oxygen part" part of this molecule, the calculations (Figure 1d and Table 8) reflect once more the effect of $n_O \rightarrow \sigma^*_{C-H_{ax}}$ interactions. Indeed, C(6)–H_{ax} is estimated to be substantially longer (1.091 Å) than C(6)–H_{eq} (1.082 Å), and this is in agreement with the observed difference in one-bond ^{13}C–^1H coupling constants: 139 and 145.4 Hz for the axial and equatorial bonds, respectively. By the same token, the calculated bond length for C(2)–H_{ax} (1.088 Å) is longer than that calculated for C(2)–H_{eq} (1.080 Å). In this case, however, the experimentally observed coupling constants ($^1J_{C(2)-H_{ax}} = {}^1J_{C-H_{eq}}$ = 157.5 Hz) do not fit the predicted order.

With respect to C(4) and C(5), calculation afforded fairly similar bond lengths for the axial and equatorial C–H bonds, in agreement with the spectroscopic measurements. Thus, the theoretical estimates apparently reproduce the stereoelectronic effect which is responsible for the weakening of the equatorial C(4)–H_{eq} and C(5)–H_{eq} and nearly balances the competing stereoelectronic effects accountable for the normal Perlin effect (see next section).

F5. 1,3-Dithiane. The C–H bond lengths estimated at the 6-31G** level are given in Figure 1e and Table 9. Nearly equal bond lengths (Δr = 0.002–0.004 Å) are found for each pair of diastereotopic, geminal C–H bonds at C(2), C(4,6), and C(5). This is in marked contrast with the "normal" situation in which the axial C–H bonds are substantially longer (by ca. 0.01 Å) than the equatorial C–H bonds (see Figures 1a–c). It seems reasonable to conclude that these *ab initio* calculations are able to exhibit the manifestation of the $\sigma_{C-S} \rightarrow \sigma^*_{C-H_{eq}}$ stereoelectronic interaction which produces a lengthening and weakening of the equatorial C–H bonds at all carbons in 1,3-dithiane.[13,15,16,18]

Nevertheless, our predicted bond lengths in the complete heterocycle (1,3-dithiane) are not in total agreement with those obtained by Wolfe *et al.*[13,16] in methylenedithiol, $CH_2(SH)_2$. These authors also found a near equivalence between the "axial" and "equatorial" C–H bonds, but observed a slightly longer C–H_{eq}

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(36) For a slightly different explanation of this effect, based on PMO theory, see ref 13.

(37) See, also: Forsyth, D. A.; Hanley, J. A. *J. Am. Chem. Soc.* **1987**, *109*, 7930.

(by 0.002 Å) relative to C–H$_{ax}$. We therefore reexamined our calculations on 1,3-dithiane at higher levels of theory (see Table 9), in particular those based in the theory of density functionals (Kohn–Sham framework[38ab]) and including electronic correlation and polarization in the heavy atoms (DZVP) or in all atoms (DZVP2). The estimated bond lengths for each pair of diastereotopic, axial and equatorial C–H bonds remained almost equal (see Table 9), but for C(2) and C(4,6) the axial bonds remained *ca.* 0.003 Å longer than their equatorial counterparts. On the other hand, Table 9 shows considerable variation of the heavy atom bond lengths. Nevertheless, benchmark studies by Delley[38c] and Pople *et al.*[38d] have shown good agreement between structures obtained from density functional theoretical methods and experimental data. In this regard, one referee has recommended caution in comparing charges on different atoms. Indeed, the charges which different techniques produce vary considerably depending on the method used.[38e] Accordingly, we restrict ourselves to the comparison of relative charge values, rather than using the absolute calculated values.

G. Conclusions. The measured one-bond ^{13}C–^{1}H coupling constants for both unsubstituted and substituted 1,3-dioxane, 1,3-dithiane, and 1,3-oxathiane support the participation of several two-orbital–two-electron stereoelectronic interactions in these heterocycles. In addition to the well-established $n_O \rightarrow \sigma^*_{C-H_{ax}}$ hyperconjugation mechanism, the spectroscopic observations suggest that Wolfe's $\sigma_{C-S} \rightarrow \sigma^*_{C-H_{eq}}$[13,16] and Anderson's β $n_O \rightarrow \sigma^*_{C-H_{eq}}$ W-design interaction[24] could indeed account for the experimentally observed reversal of Perlin effects at all carbons in 1,3-dithiane and at some positions in 1,3-dioxane and 1,3-oxathiane. Furthermore, it is suggested that the above mentioned stereoelectronic interactions are responsible, at least in part, for the anomalous chemical shift patterns encountered by Eliel *et al.* at C(2) in 1,3-dithiane and at C(5) in 1,3-dioxane.[17] Finally, some "additivity" of stereoelectronic (anomeric, *gauche*) effects may be reflected in larger than usual Perlin effects ($\Delta J_{ax/eq}$ > 10–15 Hz), as evidenced in several 5-substituted-1,3-dioxanes. *Ab initio* (HF-6-31G** and KS/LSD+BP+NLSCF/DZVP2) calculations seem to reproduce the structural manifestation of the proposed stereoelectronic interactions.

Experimental Section

^{1}H and ^{13}C NMR spectra were recorded on a Jeol GSX270 spectrometer operated in pulsed Fourier transform mode and locked on solvent deuterium.

Ab initio calculations were performed using the Cadpac 5.0 system of programs[39] (Hartree–Fock approximation) or the Dgauss 1.1 package[40] (density functionals) with exchange and local correlation according to Vosko *et al.*[41] and with nonlocal effects included in self-consisted fashion with Becke's and Perdew's parametrization method.[43] These calculations were carried out in a Cray-YMP4/432 supercomputer.

All compounds studied in this work have been previously reported as detailed below.

***cis*-4,6-Dimethyl-1,3-dioxane (1)** was prepared according to the procedure described by Pihlaja and Luoma,[43] bp 128 °C (lit.[43] bp 126.6 °C).

***cis*- and *trans*-4,6-Dimethyl-1,3-dithiane (2 and 4).** *meso*- and/or *d,l*-Pentanediol ditosylate[44] was converted into the corresponding dithiol using the polysulfide/LiAlH$_4$ method[45] and then condensed with dimethoxymethane following the general procedure described by Eliel *et al.*[46] *Cis* isomer (2) had a melting point of 80–82 °C (lit. mp[44b] 81–82.5 °C). *Trans* isomer (4) was obtained as a viscous oil.

1,3-Dithiane (3) was purchased from Aldrich Chemical Co.

2-*tert*-Butyl-1,3-dithiane (5) was prepared according to the procedure of Seebach,[47] mp 36 °C (lit.[47] mp 35.5–36.5 °C).

1,3-Dioxane (6) was prepared following the general procedure of Pihlaja,[43] bp 105–106 °C (lit.[43] bp 105 °C).

***trans*-4,6-Dimethyl-1,3-Dioxane (7)** was prepared according to the Pihlaja procedure,[43] bp 137–140 °C (lit.[43] bp 137–137.2 °C).

2-*tert*-Butyl-1,3-dioxane (8) was prepared as described by Eliel and Knoeber,[48] bp 149–150 °C (lit.[48] 147–149 °C).

2-Phenyl-1,3-dioxane (9) was prepared according to the procedure of Eliel and Knoeber,[48] mp 48–49 °C (lit.[48] mp 48–49 °C).

1,3-Oxathiane (10) was prepared as described by Carlson and Helquist,[49] bp 96–100 °C/100 mm (lit.[49] bp 96–100 °C/100 mm).

***cis*-4,6-Dimethyl-1,3-oxathiane (11)** was prepared according to the procedure of Gelan and Anteunis,[32,50] bp 50 °C/6 mm (lit.[50] bp 80 °C/50 mm).

***trans*-4,6-Dimethyl-1,3-oxathiane (12)** was prepared following the procedure of Gelan and Anteunis:[32,50] bp 55 °C/6 mm (lit.[50] bp 85 °C/50 mm).

2-*tert*-Butyl-1,3-oxathiane (13) was prepared according to the general procedure of Pihlaja and Pasanen:[50,51] bp 35 °C/0.1 mm (lit.[50] 100 °C/22 mm).

4,4,6-Trimethyl-1,3-oxathiane (14) was prepared according to the procedure described by Koskimies:[50] bp 95 °C/50 mm (lit.[50] bp 95 °C/50 mm).

***cis*- and *trans*-2-Phenyl-5-X-substituted-1,3-dioxanes** (*cis*- and *trans*-**15–18**) were prepared as recently described.[34a,52]

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(38) (a) *Density Functional Methods in Chemistry;* Labanowski, J. W., Andzelm, J. W., Eds.; Springer-Verlag: New York, 1991. (b) Parr, R. G.; Yang, W. *Density Functional Theory of Atoms and Molecules*; Oxford University Press: Oxford, 1989. (c) Delley, B. *J. Chem. Phys.* **1991**, *94*, 7245. (d) Gill, P. M. W.; Johnson, B. G.; Pople, J. A.; Frisch, M. J. *Int. J. Quantum Chem. Symp.* **1992**, *26*, 319. (e) Cf.: Cioslowski, J. *J. Am. Chem. Soc.* **1989**, *111*, 8333.

(39) Amos, R. D. *CADPAC5: The Cambridge Analytical Derivatives Package Issue 5*; Department of Chemistry, University of Cambridge, Cambridge, 1992. A suite of quantum chemistry programs developed by Amos, R. D., with contributions from Alberts, I. L.; Andrew, J. S.; Colwell, S. M.; Handy, N. C.; Jayatilaka, D.; Knowles, P. J.; Kobayashi, R.; Koga, N.; Laidig, K. E.; Maslen, P.E.; Murray, C. W.; Rice, J. E.; Sanz, J.; Simandiras, E. D.; Stone, A. J.; Su, M.D.

(40) Cf.: Andzelm, J.; Wimmer, E. *J. Chem. Phys.* **1992**, *96*, 1280. Andzelm, J. In *Density Functional Methods in Chemistry;* Labanowski, J., Ed.; Springer: New York, 1991; p 155.

(41) Vosko, S. J.; Wilk, L.; Nusair, M. *Can. J. Chem.* **1980**, *58*, 1200.

(42) Becke, A. D. *Can J. Phys.* **1988**, *88*, 1052. Becke, A. D. *Phys. Rev. A.* **1988**, *38*, 3098. Perdew, J. P. *Phys. Rev. Lett.* **1985**, *55*, 1665.

(43) Pihlaja, K.; Luoma, S. *Acta. Chem. Scand.* **1968**, *22*, 2410.

(44) (a) Eliel E. L.; Hutchins, R. O. *J. Am. Chem. Soc.* **1969**, *91*, 2703. (b) Eliel, E. L.; Hartmann, A. A.; Abatjoglou, A. G. *J. Am. Chem. Soc.* **1974**, *96*, 1807.

(45) Eliel, E. L.; Rao, V. S.; Smith, S.; Hutchins, R. O. *J. Org. Chem.* **1975**, *40*, 524.

(46) Eliel, E. L.; Rao, V. S.; Ridell, F. G.; *J. Am. Chem. Soc.* **1976**, *98*, 3583.

(47) Seebach, D. *Synthesis* **1969**, *1*, 17.

(48) Eliel, E. L.; Knoeber, M. C. *J. Am. Chem. Soc.* **1968**, *90*, 3444.

(49) Carlson, R. M.; Helquist, P. M. *J. Org. Chem.* **1968**, *33*, 2596.

(50) Koskimies, J. K. Doctoral Thesis; University of North Carolina at Chapel Hill, 1976.

(51) (a) Pihlaja, K.; Pasanen, P. *Acta. Chem. Scand.* **1970**, *24*, 2257. (b) Pasanen, P.; Pihlaja, K. *Acta. Chem. Scand.* **1971**, *25*, 1908.

(52) For X = OAc, see: Baggett, N.; Brimacombe, J. S.; Foster, A. B.; Stacey, M.; Whiffen, D. H. *J. Chem. Soc.* **1960**, 2574.