

Stereoelectronic Interactions in Cyclohexane, 1,3-Dioxane, 1,3-Oxathiane, and 1,3-Dithiane: W-Effect, $\sigma_{C-X} \leftrightarrow \sigma^*_{C-H}$ Interactions, Anomeric Effect—What Is Really Important?

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Stereoelectronic effects proposed for C–H bonds in cyclohexane, 1,3-dioxane, 1,3-oxathiane, and 1,3-dithiane were studied computationally. The balance of three effects, namely, $\sigma_{C-X} \rightarrow \sigma^*_{C-H_{eq}}$, $\sigma_{C-H_{eq}} \rightarrow \sigma^*_{C-X}$, and $n_p(X) \rightarrow \sigma^*_{C-H_{eq}}$ interactions, was necessary to explain the relative elongation of equatorial C(5)–H bonds. The role of homoanomeric $n_p \rightarrow \sigma^*_{C(5)-H_{eq}}$ interaction is especially important in dioxane. In dithiane, distortion of the ring by long C–S bonds dramatically increases overlap of $\sigma_{C(5)-H_{eq}}$ and σ^*_{C-S} orbitals and energy of the corresponding hyperconjugative interaction. Anomeric $n_p(X) \rightarrow \sigma^*_{C-H_{ax}}$ interactions with participation of axial C–H bonds dominate at C(2), C(4), and C(6). The balance of hyperconjugative interactions involving C–H_{ax} and C–H_{eq} bonds agrees well with the relative bond lengths for all C–H_{ax}/C–H_{eq} pairs in all studied compounds. At the same time, the order of one-bond spin–spin coupling constants does not correlate with the balance of stereoelectronic effects in dithiane and oxathiane displaying genuine reverse Perlin effect.

Introduction

Two-electron/two-orbital hyperconjugative¹ interactions are important for understanding of molecular properties and reactivity.^{2,3} These delocalizing interactions reflect the difference between an idealized Lewis structure and a real molecule and exhibit themselves in changes in geometry,⁴ electron density distribution, MO energies, IR spectra and bond strengths (Bohlmann effect),^{5,6} and NMR properties.⁷ The hyperconjugative effects have to be explicitly used in molecular mechanics parametrization to describe properties of covalent bonds accurately.⁸ These interactions may influence conformational equilibrium (anomeric effect,^{9,10} torsion barrier in ethane,¹¹ and other molecules¹²), modify reactivity,¹³ and

determine selectivity.¹⁴ Hyperconjugative effects are proposed to be important components of intermolecular interactions, both in ground¹⁵ and transition states.^{16,17} The importance of even weak hyperconjugative interactions increases dramatically for excited, radical, and ionic species.¹⁸

One-bond NMR spin–spin coupling constants are particularly interesting as an experimental probe for the hyperconjugative stereoelectronic effects. For example, in cyclohexane the direct ¹H–¹³C coupling constants are

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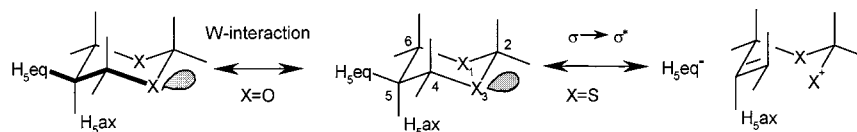


Figure 1. Stereolectronic effects proposed for C(5) in 1,3-dioxane and 1,3-dithiane.

smaller for axial hydrogens.²⁴ This phenomenon is commonly referred to as the normal Perlin effect.¹⁹ Its rationale is based on the suggestion that in cyclohexane the axial C–H bonds are longer and weaker than the equatorial bonds as the result of hyperconjugative $\sigma_{C-H} \rightarrow \sigma^*_{C-H}$ interactions with the participation of anti-periplanar C–H bonds.²⁰ The sensitivity of the direct H–C coupling constants to the subtle structural factors is widely used for stereochemical assignments, especially in carbohydrate chemistry.²¹

Substituted cyclohexanes and heterocyclohexanes are popular models in studies of stereolectronic effects.^{2,10,22} A number of recent theoretical^{6,23,24,25} and experimental^{25–29} works have found that in 1,3-heterosubstituted cyclohexanes some of the axial protons have coupling constants larger than those of the equatorial protons, which has been called the *reverse* Perlin effect. Two new types of delocalizing effects were proposed to rationalize these observations.

First, to explain the reverse Perlin effect ($^1J_{CH_{eq}} < ^1J_{CH_{ax}}$) for the C(5) atom in 1,3-dioxane and the elongation of the C(5)–H equatorial bond, Anderson, Davies et al. suggested the presence of a homoanomeric $n \rightarrow \sigma^*$ interaction between the pseudoequatorial lone electron pair on the β -oxygen and the equatorial C(5)–H bond through a W-arrangement of orbitals (the W-effect) (Figure 1).²⁶ Second, Juaristi et al.^{24,25} used the hyperconjugative interactions between the equatorial C–H σ -orbitals and the anti-periplanar C–S σ -orbitals ($\sigma_{C-S} \rightarrow$

$\sigma^*_{C-H_{eq}}$) to account for the reverse Perlin effect for all carbons except C(6) in 1,3-oxathiane and for *all* carbons in 1,3-dithiane. It was also suggested that the W-effect might be important in dithianes, whereas the $\sigma_{C-O} \rightarrow \sigma^*_{C-H_{eq}}$ interaction could be present in dioxanes.

These rationales were partially based on the earlier comprehensive study by Wolfe^{6,20b} who had proposed that (a) the $CH_{eq} \leftrightarrow C-S$ interactions resulted in lengthening of the equatorial C–H bonds and (b) for a pair of diastereotopic hydrogens in molecules of general YCH_2X type the longer C–H bond was usually associated with the lower one-bond C–H coupling constant. This statement can be considered as the new, more accurate definition of the normal Perlin effect. This definition is consistent with the assumption that Fermi contact is the main contribution to the coupling constant and that it has an inverse dependence on the distance between nuclei. Wolfe's analysis of methanedithiol implied that there was no reverse Perlin effect in dithiane. In fact, the order of the direct spin–spin coupling constants was normal: the longer bond (equatorial in this case) corresponded to the smaller constant.

However, it was found²⁵ that in dithiane longer (axial) C–H bonds at C(2) and C(4) were associated with larger coupling constants. This result was not consistent with Wolfe's proposal and indicated the genuine reverse Perlin effect. The other uncertain point in the general picture was the W-effect hypothesis. There was no experimental evidence showing that the W-geometry was really necessary.

In view of these circumstances, an independent quantitative estimation of strength and relative importance of the stereolectronic effects is necessary for understanding of the experimental data and consolidation of the different views. The issue became even more evident when recent results cast a shadow of doubt on the connection of the stereolectronic interactions with NMR parameters.³⁰

Several important questions are addressed in the present computational study. What hyperconjugative effects really do exist in 1,3-dioxane, dithiane and oxathiane? What is the relative importance of these interactions? Why do the different rules apply to the sulfur-containing heterocycles? Does the W-effect exist in dithiane, and is the $\sigma \rightarrow \sigma^*$ interaction present in dioxane? The questions are addressed using *ab initio* and DFT calculations in conjunction with the natural bond orbitals (NBO)³¹ method. The NBO method developed by Weinhold and coauthors is becoming the "state of the art" method for study of hyperconjugative interactions.³²

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Method

All structures were fully optimized at the HF/6-31G**,³³ MP2/6-31G**, and B3LYP/6-31+G** levels using the GAUSSIAN 94 package.³⁴ The 6-31G**³⁵ basis set is commonly used in computational studies on the anomeric effect.^{23,32b,36} The diffuse orbitals augmented basis set (6-31+G**) was used to take into account the relatively diffuse nature of the lone pairs. The density functional theory (B3LYP)³⁷ was applied to probe the role of electron correlation.

The NBO 4.0³⁸ program was used as interfaced to the GAUSSIAN 94 package. The NBO analysis transforms the canonical delocalized Hartree–Fock (HF) MOs into localized hybrid orbitals (NBOs). Filled NBOs describe the hypothetical, strictly localized Lewis structure. The interactions between filled and antibonding (or Rydberg) orbitals represent the deviation of the molecule from the Lewis structure and can be used as a measure of delocalizations. The energy contributions of these delocalizations were initially estimated from the second-order perturbation approach and finally calculated by deletion of the corresponding off-diagonal elements of the Fock matrix in the NBO basis.³⁹ For further details on the NBO calculations see the references.^{3,32,38}

Natural resonance theory (NRT) analysis was used as implemented in the NBO 4.0³⁸ program. Combined energy of delocalizing interactions, E_{del} , was calculated as the arithmetic sum of energies of the corresponding interactions obtained as described in the previous paragraph.

Results and Discussion

The influence of delocalizing interactions includes changes in energy, geometry, atomic charges, orbital populations, bond orders, and other properties. In principle, any of these parameters can be used for comparing these interactions. We have chosen the *combined* energy of delocalizing interactions weakening a given C–H bond as the main criterion, as will be described below.

To explain the relative elongation of equatorial C–H bonds, the stereoelectronic interactions that weaken these bonds should be compared with the corresponding interactions involving the axial C–H bonds. Therefore, we will not simply analyze the equatorial interactions in isolation but rather the *balance* of competing axial and equatorial delocalizations. NBO analysis gives the quantitative estimates of the two types of delocalizing interactions that permit such direct comparison.

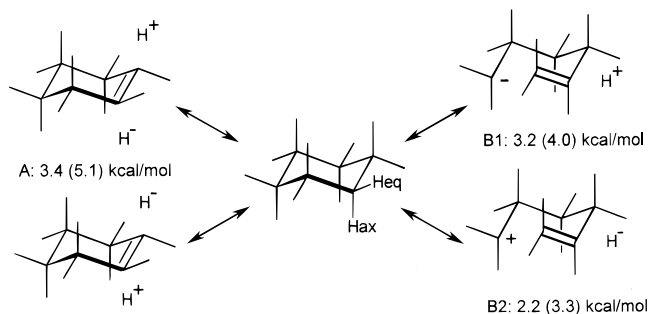


Figure 2. The main stereoelectronic interactions for cyclohexane. The energies below the structures correspond to the RHF/6-31G** data, and the numbers in brackets correspond to the B3LYP/6-31+G** data.

Cyclohexane. Stereoelectronic effects in cyclohexane are of general interest because of the ubiquity of substituted cyclohexanes in organic chemistry and also in light of the long debated issue of the comparative donor ability of C–H and C–C bonds. This question received considerable attention as one of the cornerstones of the widely discussed Cieplak model¹⁶ of nucleophilic addition to cyclohexanones.⁴⁰

At all levels of calculation NBO analysis identified three types of hyperconjugative interactions (labeled A, B1, B2) to be the most important for any C–H_{eq}/C–H_{ax} pair, as shown in Figure 2. Type A represents the two degenerate pairs of $\sigma_{\text{C–H}_{\text{ax}}} \rightarrow \sigma^*_{\text{C'–H}_{\text{ax}}}$ and $\sigma'_{\text{C'–H}_{\text{ax}}} \rightarrow \sigma_{\text{C–H}_{\text{ax}}}$ interactions present for the axial protons. Type B stands for the two pairs of delocalizations involving the equatorial C–H bonds. The delocalizations are labeled as B1 for $\sigma_{\text{C–H}_{\text{eq}}} \rightarrow \sigma^*_{\text{C–C}}$ interaction and B2 for $\sigma_{\text{C–C}} \rightarrow \sigma^*_{\text{C–H}_{\text{eq}}}$ interaction. The “charge transfer” in either direction weakens the C–H bonds, and therefore, all three interactions should be considered.⁴¹ Summation of the delocalization energies gives a higher total energy for the axial CH bonds (Table 1). Thus, the longer axial bonds and smaller $^1J_{\text{C–H}_{\text{ax}}}$ in cyclohexane agree well with the hyperconjugative description. The larger positive charge on H_{eq} is also in a good agreement with the balance of hyperconjugative interactions and indicates that the C–H bonds are better donors than the C–C bonds in cyclohexane.

Although the RHF/6-31G** is the standard level of theory for studies on hyperconjugative effects and the data seemed to correlate well with the experiment, we attempted to estimate influence of electronic correlation using density functional theory (DFT). One could expect the correlation effects to be important. Indeed, use of B3LYP gave considerably larger delocalizing energies, although their *relative* values were quite close to those from the RHF calculations.⁴²

1,3-Dioxane. The most interesting experimental finding was the reverse Perlin effect at the C(5) atom. For a

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(39) For the symmetric dioxane and dithiane molecules one can delete either one of the symmetry-related interactions at C(2) and C(5) simultaneously or both of them. The energy recalculation following the NBO deletion is a variational procedure, and thus one cannot expect the deletion energies from the two different approaches to be identical. Nevertheless, the difference was small enough to consider the interactions to be additive in the first approximation. The deletion of the individual interactions was used throughout the paper.

(40) The Cieplak's explanation of the preference for the axial addition was based on the assumption that the C–H bonds were the better electron donors and the electron-deficient reaction transition state received better electron stabilization energy than from the corresponding CC bonds during the equatorial approach.

(41) The B1-type interactions *decrease* population of the *bonding* C–H orbital, whereas the B2-type interactions *increase* population of the corresponding *antibonding* C–H orbital. Relative importance of the two interactions will be discussed below.

(42) Similar effect on the bond orders (also reflecting the delocalization strength) was found before: Glendening, E. D.; Weinhold, F. *F. J. Comp. Chem.* **1998**, *19*, 610.

Table 1. Bond Lengths, One-Bond Coupling Constants, and Total Hyperconjugative Energies for Cyclohexane^a

bond	bond length, Å		¹ J _{CH} , Hz ^b	sum of individual deletion energies (<i>E</i> _{del}), kcal/mol		natural charge at hydrogen		NRT bond order	
	RHF/6-31G**	B3LYP/6-31+G**		RHF	B3LYP	RHF	B3LYP	RHF	B3LYP
C–H _{ax}	1.0871	1.1001	122	13.5	20.4	0.215	0.231	0.9858	0.9832
C–H _{eq}	1.0895	1.0972	126	10.7	14.6	0.229	0.244	0.9876	0.9861

^a Ab initio energies in hartrees: RHF = –234.226 254 2, B3LYP = –235.902 358 8. ^b The data are from ref 25

Table 2. Optimized C–H Bond Lengths, Coupling Constants, Deletion Energies, and NRT Bond Orders for 1,3-Dioxane^a

bond	bond length, Å ^b			¹ J _{CH} , Hz ^c	sum of individual deletion energies (<i>E</i> _{del}), kcal/mol		NRT bond order	
	RHF/6-31G**	MP2/6-31G**	B3LYP/6-31+G**		RHF	B3LYP	RHF	B3LYP
C(2)–H(2) _{ax}	1.0934	1.1024	1.1070	158.6	16.4	34	0.9812	0.9763
C(2)–H(2) _{eq}	1.0787	1.0860	1.0901	167.5	16.3	21.4	0.9845	0.9829
C(4,6)–H(4,6) _{ax}	1.0914	1.0988	1.1036	143.6	17.0	26.7	0.9836	0.9798
C(4,6)–H(4,6) _{eq}	1.0817	1.0882	1.0925	145.0	10.6	16.0	0.9878	0.9866
C(5)–H(5) _{ax}	1.0852	1.0899	1.0955	128.9	13.14	18.8	0.9852	0.9829
C(5)–H(5) _{eq}	1.0867	1.0922	1.0972	128.9	13.08	20.1	0.9855	0.9807

^a Ab initio energies in hartrees: RHF = –305.846 562 1, MP2 = –306.766 702 8, B3LYP = –307.689 992 3. ^b See also refs 24 and 25. ^c The data are from ref 25.

number of alkyl- and aryl-substituted dioxanes ¹J_{C(5)–H5_{eq}} was consistently less than ¹J_{C(5)–H5_{ax}}, by an average of 6.3 Hz.²⁶ On the other hand, equal NMR couplings (¹J_{CH_{eq}} = ¹J_{CH_{ax}}) were found at C(5) for unsubstituted 1,3-dioxane.²⁵ In a good agreement with the latter observation, calculated bond lengths for the C(5)–H_{ax} and C(5)–H_{eq} bonds were very similar, with the equatorial bond about 0.002 Å longer. This is the reverse of what is observed in cyclohexane.

Anderson, Davies and co-workers²⁶ suggested that this reversal may be due to n → σ* interaction between the β-oxygen and the equatorial C(5)–H bond through a W-arrangement of orbitals. In the preliminary communication the authors also mentioned interaction of antiperiplanar σ_{O–C} and σ*_{C–H_{eq}} as an alternative rationale (Figure 1). They suggested testing the W-hypothesis with an independent experiment, but such experiment has not been performed yet.

We have found that for the C(5) the most important interactions involving the axial C–H bond are the same as for the axial C–H bonds in cyclohexane (σ_{C–H} → σ*_{C–H} interactions between antiperiplanar bonds, Table 3). The delocalization energy associated with these interactions is close to the corresponding value in cyclohexane.

However, the picture is more complex for the equatorial bond. The largest delocalizing contribution is the charge transfer from the σ_{C(5)–H_{eq}} to the antiperiplanar σ*_{C–O} bond. This interaction is greater than in cyclohexane (Figure 2), in accord with the larger electronegativity of oxygen, but for the same reason, the back transfer (σ_{C–O} → σ*_{C–H}) is decreased (Table 1). As a result, the substitution of C to O has very little influence on the total energy of the H_{eq}–C(5) ↔ C–X (X = C, O) interactions, and they are still not large enough to match the combined energy of axial interactions.

What is the additional factor increasing the length of the C(5)–H_{eq} bond? The previously suggested n_{eq} → σ*_{C–H} interaction (the W-effect) was found to be negligible: less than 0.1 kcal/mol for both levels of theory. Instead, the NBO analysis revealed the presence of a previously unconsidered homoanomeric interaction of the back lobe of the antibonding C(5)–H_{eq} orbital with the pseudoaxial oxygen lone pair. Obviously, the pseudoaxial p-like pair is a better electron donor than the sp² pseudoequatorial pair as a result of its higher energy (–0.4768 vs. –0.7674

Table 3. Summary of Main Delocalizing Interactions^a for C–H Bonds in 1,3-Dioxane^b

donor orbital	acceptor orbital	energy, kcal/mol	
		RHF/6-31G**	B3LYP/6-31+G**
σ _{C(5)–H(5)_{ax}}	σ* _{C(6)–H(6)_{ax}}	3.28	4.66
σ _{C(6)–H(6)_{ax}}	σ* _{C(5)–H(5)_{ax}}	3.29	4.76
σ _{C(5)–H(5)_{eq}}	σ* _{C(6)–O(1)}	4.23	4.50
σ _{C(6)–O(1)}	σ* _{C(5)–H(5)_{eq}}	1.63	2.86
LP(2)O(1)	σ* _{C(5)–H(5)_{eq}}	0.68	2.7
LP(1)O(1)	σ* _{C(2)–H(2)_{ax}}	2.33	5.40
LP(2)O(1)	σ* _{C(2)–H(2)_{ax}}	5.86	11.59
σ _{C(2)–H(2)_{eq}}	σ* _{C(6)–O(1)}	4.05	4.23
σ _{C(6)–O(1)}	σ* _{C(2)–H(2)_{eq}}	1.92	3.50
LP(1)O(1)	σ* _{C(2)–H(2)_{eq}}	2.18	2.95
LP(1)O(1)	σ* _{C(6)–H(6)_{eq}}	2.11	2.88
LP(1)O(1)	σ* _{C(6)–H(6)_{ax}}	2.04	4.88
LP(2)O(1)	σ* _{C(6)–H(6)_{ax}}	6.27	12.41
σ _{C(5)–H(5)_{ax}}	σ* _{C(6)–H(6)_{ax}}	3.28	4.66
σ _{C(6)–H(6)_{ax}}	σ* _{C(5)–H(5)_{ax}}	3.29	4.76
σ _{O(1)–C(2)}	σ* _{C(6)–H(6)_{eq}}	1.81	3.32
σ _{C(6)–H(6)_{eq}}	σ* _{O(1)–C(2)}	3.39	3.11
σ _{C(5)–C(4)}	σ* _{C(6)–H(6)_{eq}}	2.41	3.43
σ _{C(6)–H(6)_{eq}}	σ* _{C(5)–C(4)}	3.03	3.28

^a Energies obtained by deletion of the corresponding Fock elements followed by recalculation of the wave function. ^b Only one of each of the two symmetry-related interactions is shown.

au in the NBO basis, RHF/6-31G**). In addition, the interaction with the axial lone pair is favored as a result of a better overlap of the corresponding orbitals (Figure 3).⁴³ Although the contribution is smaller than σ_{C–H_{eq}} → σ*_{O–C} interaction, it serves to tip the balance in favor of the larger total “equatorial” delocalization.

Similar homoanomeric interactions are likely to be found in a number of six-membered heterocycles with p-donating heteroatoms, double bonds (endo- and exocyclic), and anionic fragments. Consequently, many equatorial substituents that have π-donating groups in the β-position should have a higher reactivity than the axial

(43) (a) There are two different descriptions of hybridization of the pseudoequatorial pair. Usually, it is considered to be sp²-hybridized, but sometimes, for example in ref 26 this pair is called sp³-hybridized. For many purposes either one of the descriptions can be used. However, for the case of intermolecular interactions where “the symmetry of interaction, or the energy of the nonbonding electrons is crucial, it is generally considered necessary to use” the first representation.^{10a} The NBO analysis that finds “the best hybrids” describing a Lewis structure gives sp^{1.6} hybridization for the equatorial lone pair, sp^{2.34} for the C(2)–O hybrid, and sp^{2.28} for the C(4)–O orbital (RHF/6-31G**).

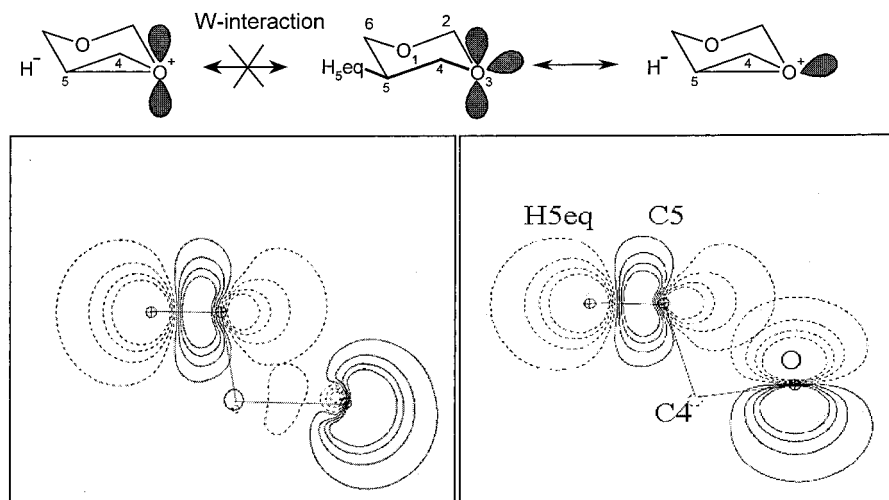


Figure 3. Two homoanomeric orbital interactions in 1,3-dioxane: (a) with the equatorial lone pair (left) and (b) with the axial lone pair (right).

Table 4. Optimized C–H Bond Lengths, Coupling Constants,^a and Total Hyperconjugative Energies for 1,3-Dithiane^b

bond	bond length, Å			¹ J _{CH} , Hz ^a	<i>E</i> _{del} , kcal/mol		NRT bond orders (B3LYP)	
	RHF/6-31G**	MP2/6-31G**	B3LYP/6-31+G**					
C(2)–H(2) _{ax}	1.0829	1.0913	1.0948	154.2	11.4	15.1	0.9856	0.9852
C(2)–H(2) _{eq}	1.0813	1.0888	1.0919	146.2	7.0	10.2	0.9892	0.9882
C(4,6)–H(4,6) _{ax}	1.0858	1.0931	1.0973	137.3	11.6	15.6	0.9856	0.9836
C(4,6)–H(4,6) _{eq}	1.0832	1.0899	1.0937	132.9	9.2	10.5	0.9877	0.9870
C(5)–H(5) _{ax}	1.0845	1.0906	1.0955	130.2	12.6	19.2	0.9861	0.9830
C(5)–H(5) _{eq}	1.0884	1.0939	1.0997	127.4	17.3	21.4	0.9809	0.9765

^a The data are from ref 25. ^b Ab initio energies in hartrees: RHF = –951.162 668 7, MP2 = –951.983 002 4, B3LYP = –953.638 783 3.



Figure 4. Winstein's "homoanomeric" interaction.

substituents. For example, Winstein⁴⁴ had shown that solvolysis of 3- β -cholesteryl tosylate (or chloride) proceeded 100 times faster than the reaction of the cyclohexyl analogue as a result of the anchimeric assistance of the double bond. In agreement with this observation, the NBO analysis of the model system (Figure 4, B3LYP/6-31G*) found 0.8 kcal/mol hyperconjugative interaction between the π -bond and σ^*_{C-X} orbital. The interaction is significant even in the ground state and should be much more important in the transition state where the electron demand is increased.⁴⁵

The agreement of the close balance of main delocalizing interactions with the similar lengths of the C(5)–H_{eq} and C(5)–H_{ax} bonds and equilibrium of normal and reverse Perlin effects is quite remarkable (Table 2). It shows that when the other factors controlling the C–H bond lengths (electronegativity, hybridization, etc.) are similar (which is generally true for YCH₂X pairs) the stereoelectronic interactions are the most important, and NBO analysis provides a good quantitative description of these interactions.

For the remaining C(2), C(4), and C(6) atoms, the $n_O \rightarrow \sigma^*_{CH_{ax}}$ (anomeric) interactions are dominant,⁴⁶ the axial bonds are longer, and normal Perlin effect is

Table 5. Main Delocalizing Interactions (*E* > 0.5 kcal/mol) for C–H Bonds in 1,3-Dithiane^a

donor orbital	acceptor orbital	energy, kcal/mol	
		RHF/6-31G**	B3LYP/6-31+G**
$\sigma_{C(5)-H(5)_{ax}}$	$\sigma^*_{C(6)-H(6)_{ax}}$	3.1	4.85
$\sigma_{C(6)-H(6)_{ax}}$	$\sigma^*_{C(5)-H(5)_{ax}}$	3.2	4.74
$\sigma_{C(5)-H(5)_{eq}}$	$\sigma^*_{C(6)-S(1)}$	5.5	6.50
$\sigma_{S(3)-C(4)}$	$\sigma^*_{C(5)-H(5)_{eq}}$	2.4	3.49
LP(2)S(1)	$\sigma^*_{C(5)-H(5)_{eq}}$	0.75	1.42
$\sigma_{S(1)-C(6)}$	$\sigma^*_{C(2)-H(2)_{eq}}$	2.01	2.9
$\sigma_{C(2)-H(2)_{eq}}$	$\sigma^*_{S(1)-C(6)}$	1.48	2.20
LP(1)S(1)	$\sigma^*_{C(2)-H(2)_{ax}}$	1.49	2.92
LP(2)S(1)	$\sigma^*_{C(2)-H(2)_{ax}}$	4.20	4.65
$\sigma_{S(1)-C(2)}$	$\sigma^*_{C(6)-H(6)_{eq}}$	1.83	1.58
$\sigma_{C(6)-H(6)_{eq}}$	$\sigma^*_{S(1)-C(2)}$	1.94	1.82
$\sigma_{C(5)-C(4)}$	$\sigma^*_{C(6)-H(6)_{eq}}$	1.88	2.94
$\sigma_{C(6)-H(6)_{eq}}$	$\sigma^*_{C(5)-C(4)}$	4.28	4.11
LP(1)S(1)	$\sigma^*_{C(6)-H(6)_{ax}}$	1.51	1.94
LP(2)S(1)	$\sigma^*_{C(6)-H(6)_{ax}}$	4.79	3.96
$\sigma_{C(5)-H(5)_{ax}}$	$\sigma^*_{C(6)-H(6)_{ax}}$	3.42	4.85
$\sigma_{C(6)-H(6)_{ax}}$	$\sigma^*_{C(5)-H(5)_{ax}}$	3.38	4.74

^a Only one of each of the two symmetry-related interactions is shown.

observed.²⁵ Magnitudes of the main interactions are summarized in Table 3 and will be discussed below in connection with the analogous interactions for dithiane.

1,3-Dithiane. 1,3-Dithianes are important and versatile synthetic intermediates.⁴⁷ At the same time they

(46) We will refer to the $n_O \rightarrow \sigma^*_{CH_{ax}}$ interactions as anomeric. Note, however, that the anomeric effect is often defined as the preference of electronegative group at anomeric carbon to occupy the axial position and the $n_O \rightarrow \sigma^*_{CX_{ax}}$ orbital interaction is only one of the factors accounting for the phenomenon. See, for example: Eliel, E. L. In *Conformational Behavior of Six-Membered Rings*; Juaristi, E. Ed.; VCH Publishers: New York, 1995.

(44) Winstein, S.; Adams, R. *J. Am. Chem. Soc.* **1948**, *70*, 838.

(45) For an interesting discussion of homoanomeric effects in cationic species, see: Sunko, D. E.; Hirs-Starcovic, S.; Pollack, S. K.; Hehre, W. J. *J. Am. Chem. Soc.* **1979**, *101*, 6163 and references therein.

Table 6. Optimized C–H Bond Lengths, Coupling Constants,^a and Total Hyperconjugative Energies for 1,3-Oxathiane^b

bond	bond length, Å			¹ J _{CH} , Hz	E _{del} , kcal/mol	extrapolated E _{del} , kcal/mol ^c	NRT bond orders (B3LYP)
	RHF/6-31G**	MP2/6-31G**	B3LYP/6-31+G**				
C(2)–H(2) _{ax}	1.0875	1.0966	1.1004	157.5	25.5	24.6	0.9816
C(2)–H(2) _{eq}	1.0800	1.0875	1.0911	157.5	15.3	15.8	0.9861
C(4)–H(4) _{ax}	1.0857	1.0929	1.0971	142.7	16.8	15.5	0.9843
C(4)–H(4) _{eq}	1.0827	1.0893	1.0931	142.7	12.8	10.5	0.9867
C(5)–H(5) _{ax}	1.0849	1.0903	1.0955	126.9	19.6	19.0	0.9825
C(5)–H(5) _{eq}	1.0880	1.0935	1.0989	129	21.9	21.5	0.9785
C(6)–H(6) _{ax}	1.0917	1.0991	1.1036	139	28.5	26.7	0.9799
C(6)–H(6) _{eq}	1.0820	1.0887	1.0928	154.4	17.5	16.0	0.9862

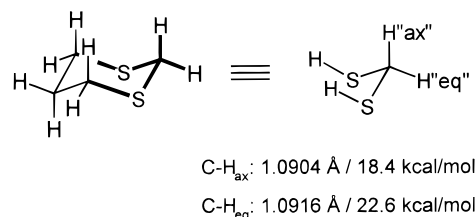
^a The data are from ref 25. ^b Ab initio energies in hartrees: HF = –628.500 105, MP2 = –629.371 426 6, B3LYP = –630.661 5457. ^c Extrapolated from the dioxane/dithiane data (B3LYP).

present a very challenging computational test of the role of hyperconjugative interactions because the order of direct coupling constants and the relative bond lengths do not agree. Bailey et al.²⁹ found ¹J_{C2–H_{eq}} to be smaller than ¹J_{C2–H_{ax}} and Juaristi et al.^{25,28a} discovered *all* C–H_{eq} one-bond couplings to be lower than the corresponding C–H_{ax} couplings. On the other hand, RHF and DFT calculations by Juaristi et al.^{25,28a} have shown that the C(2)–H and C(4,6)–H axial bonds remained ca. 0.003 Å longer than the equatorial bonds at all levels of theory used in the study. Our RHF/6-31G**, MP2/6-31G**, B3LYP/6-31G**, and B3LYP/6-31+G** calculations have also found the axial bonds to be slightly longer (Table 4).

For the C(5) atom, the experimental and theoretical data are again in good agreement, with larger delocalization energy and longer bonds being associated with smaller direct coupling constants. Interestingly, the σ^{*}_{C(4)–S} orbital was a significantly better acceptor than either the cyclohexane σ^{*}_{C–C} or the dioxane σ^{*}_{C(4)–O} orbital (vide infra). In addition, the σ_{C(4)–S} bond was a better donor than the C–C cyclohexane bond (Table 5). As the result, the two interactions for the C(5)–H_{eq} bond were large enough to explain the equatorial bond elongation. The new homoanomeric interaction (n_p → σ^{*}_{C(5)–H_{eq}}) was found as well, but it was not as important as in the dioxane case.

For C(2), C(4), and C(6) atoms, only very small differences are found in the C–H bond lengths. In agreement, Anet and Kopelevich²⁷ observed no isotope conformational effect for the 2-D-5,5-dimethyl-1,3-dithiane and concluded that the lone pairs on sulfur are not involved in negative hyperconjugation. Alternatively one may say that the hyperconjugation interactions involving the sulfur lone pairs and the axial C–H bonds are *compensated* by the delocalizing interactions (or other factors) weakening the *equatorial* bond.

The NBO analysis confirms that the negative hyperconjugation n_p(S) → σ^{*}_{C(2)–H(2)_{ax}} is considerably weaker than the analogous interaction in 1,3-dioxane and even weaker than the CH_{ax} ↔ C'H_{ax} delocalizations in cyclohexane. Nevertheless, the anomeric interaction is still the most important energetically as a result of the even weaker character of the competing equatorial interactions involving the S–C(2) and S–C(4) orbitals. The latter participate in the hyperconjugative interactions far less

**Figure 5.** B3LYP bond lengths and total hyperconjugative energies for methanedithiol.

efficiently than the C–C and C–O bonds because of the reasons described in the Discussion section. As a result, the total “axial” delocalization energy is higher than the equatorial, and the axial C–H bonds are slightly longer.

Methanedithiol. At the first glance, NBO analysis of the hyperconjugative interactions in dithiane seemed to contradict certain observations of the thorough study of delocalizing interaction in S- and O-containing molecules by Wolfe et al.⁶ This study found the equatorial C–H bonds to be longer in methanedithiol (Figure 5) and used this observation to explain the reverse Perlin effect for C(2) in dithiane.

We also found the equatorial bond to be longer. At the same time, the total *equatorial* delocalization energy was slightly larger, and the equatorial σ_{H–S} → σ^{*}_{C–H_{eq}} and σ_{C–H_{eq}} → σ^{*}_{H–S} interactions were close in strength to the axial n(S) → σ^{*}_{C–H_{ax}} interactions. Therefore, there is no controversy, and the relative order of the C–H bond lengths in methanedithiol, although different from that in dithiane, is also in agreement with the balance of hyperconjugative interactions. This example presents the additional evidence that the stereoelectronic delocalizing interactions do correlate with the C–H bond lengths, even in the presence of sulfur.

1,3-Oxathiane. One important question is the question of transferability of the results obtained on the model compounds. Is it possible to use the dioxane/dithiane delocalizing interactions for a qualitative prediction of C–H bond lengths and bond strength in other S–O containing heterocycles without doing full ab initio calculations? For this purpose we have studied the “hybrid” of dioxane and dithiane, 1,3-oxathiane.

Juaristi et al found that C(2), C(4), and C(5) in 1,3-oxathiane were associated with a balance or near balance of Perlin effects.²⁵ However, the normal Perlin effect was found at C(6). The authors suggested that the anomalous chemical shifts and Perlin effects for C(2), C(4), and C(5) resulted from the σ_{S–C} → σ^{*}_{C–H_{eq}} interactions, while on the “oxygen” part of the molecule the well-known n(O) → σ^{*}_{C–H_{ax}} interaction was dominant, resulting in the normal Perlin effect.

(47) (a) Corey, E. J.; Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1965**, *4*, 1075. (b) For a review, see: Grobel, B.-T.; Seebach, D. *Synthesis* **1977**, 357. (c) For the most recent examples, see: McHale, W. A.; Kutateladze, A. G. *J. Org. Chem.* **1998**, *63*, 9924. Reich, H. J.; Sikorsky, W. H. *J. Org. Chem.* **1999**, *64*, 14. For very efficient use of 1,3-dithianes in total synthesis, see: Smith, A. B.; Condon, S. M.; McCauley, J. A. *Acc. Chem. Res.*, **1998**, *31*, 35.

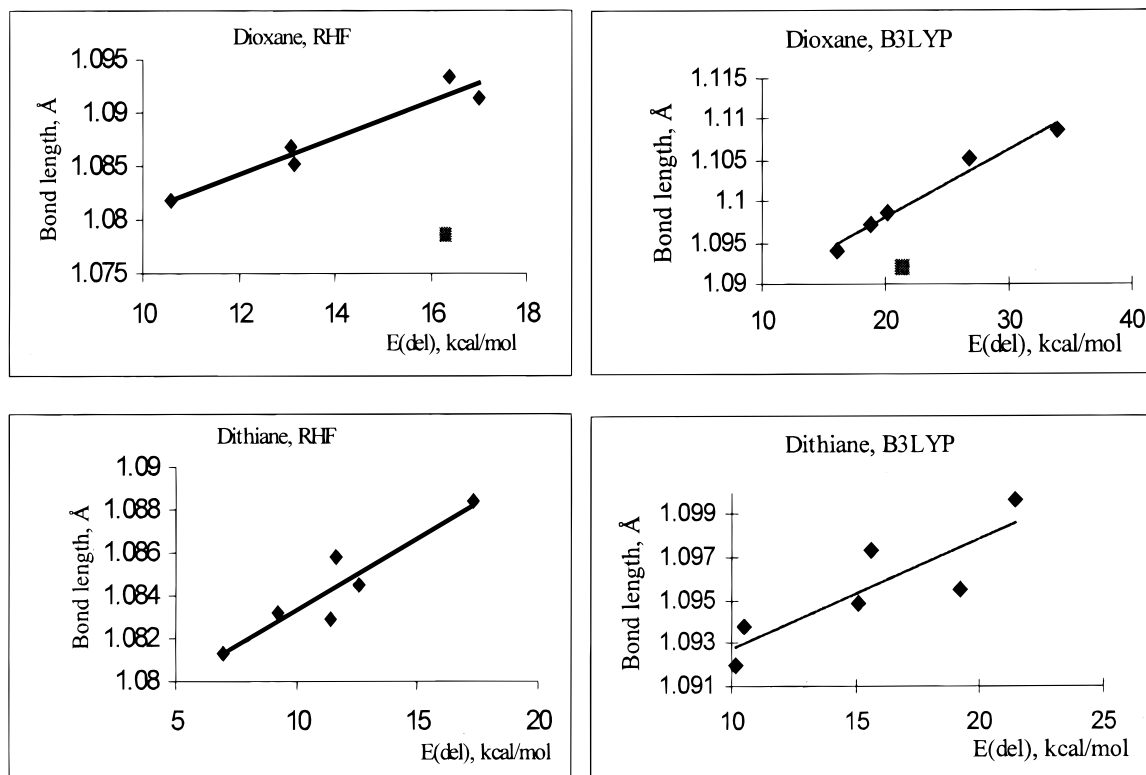


Figure 6. Bond lengths vs total delocalization energies in dioxane and dithiane (C(2)–H_{eq} in dioxane denoted as a square).

NBO analysis of 1,3-oxathiane discovered the same interactions with the similar relative importance as in dioxane and dithiane. Interestingly, simple summation of energies of the corresponding hyperconjugative effects found in dioxane and dithiane gave delocalizing energies quite close to those obtained by the rigorous quantum-mechanical calculations on oxathiane (Table 6 and Tables 12–15 in the Supplementary Information).⁴⁸

Discussion

The array of strong delocalizing interactions at C(5) is similar in all of the heterocyclohexanes ($\sigma_{C-X} \rightarrow \sigma^*_{C-H_{eq}}$, $\sigma_{C-H_{eq}} \rightarrow \sigma^*_{X-C}$, $n_p \rightarrow \sigma^*_{C-H_{eq}}$ vs $\sigma_{C-H_{ax}} \rightarrow \sigma^*_{C-H_{ax}}$ interactions), and it explains the relative elongation of the equatorial C–H bonds quite well. At all of the other carbons in dioxane, dithiane, and oxathiane, the axial bonds are found to be longer as a result of the dominant anomeric interactions. An important distinction between dioxane and dithiane, however, was that the anomeric interactions in dioxane were strong, outweighing the strong equatorial delocalizing interactions, whereas the

(48) In addition, 1,3-oxathiane provides a useful consistency check on the RHF and B3LYP methods. Although B3LYP seemed to give a slightly better qualitative description of the absolute values of the delocalizing energies looked suspiciously large for several charge transfers from the oxygen. The different strength and nature of stereoelectronic interactions in 1,3-oxathiane make it an appropriate molecule for comparison of the two methods. The data for 1,3-oxathiane had shown a discrepancy between the two levels of theory. At the B3LYP level, all interactions including oxygen were stronger than the corresponding sulfur analogues, but the relative importance was reversed for RHF. In particular, at the RHF level, sulfur shows stronger anomeric interaction than that of oxygen, which is contrary to the literature and our own results discussed above. The B3LYP data agree well with the results for dioxane and dithiane and thus seem to be more reliable in general. The absolute values of B3LYP hyperconjugative energies should still be accepted with caution because of the possible overestimation, but the relative orders of the energies describe the model systems adequately.

Table 7. Natural Population Analysis for 1,3-Dioxane and 1,3-Dithiane

atom	natural charge	
	dioxane	dithiane
C(5)	−0.5031	−0.4972
C(6)	−0.0542	−0.6162
O(1) (S(1))	−0.6608	0.2152
C(2)	0.2980	−0.7944
H(5) _{ax}	0.2355	0.2581
H(5) _{eq}	0.2290	0.2502
H(2) _{ax}	0.1529	0.2596
H(2) _{eq}	0.2086	0.2877
H(4) _{ax}	0.1831	0.2476
H(4) _{eq}	0.2214	0.2715

analogous interactions in dithiane were rather weak and became “dominant” only because the competing equatorial interactions were even weaker.

Analysis of natural charges supports the analysis based on the delocalization energies. The charges at the axial hydrogens at C2, C4 (C6) are less than the corresponding equatorial hydrogens, in agreement with the transfer of the electron density from heteroatoms to $\sigma^*_{C-H_{ax}}$ orbitals (the anomeric effect). A different order is found for the H(5)_{ax}–H(5)_{eq} pair, where the equatorial hydrogen is slightly less positive as the result of the homoanomeric interaction discussed above.

Some limitations of the hyperconjugative criterion are illustrated in Figure 6, which shows the deviation of the equatorial C(2)–H bond from the otherwise satisfactory correlation. This deviation illustrates importance of the inductive (electronegativity) effect not considered in the hyperconjugative description. The C(2)–H_{eq} bond is under the influence of two strongly electron-withdrawing neighbors (oxygens), and many properties of the C(2)–H_{eq} bond are anomalous. For example, it is the shortest of the three equatorial bonds, the bond dipole is oriented

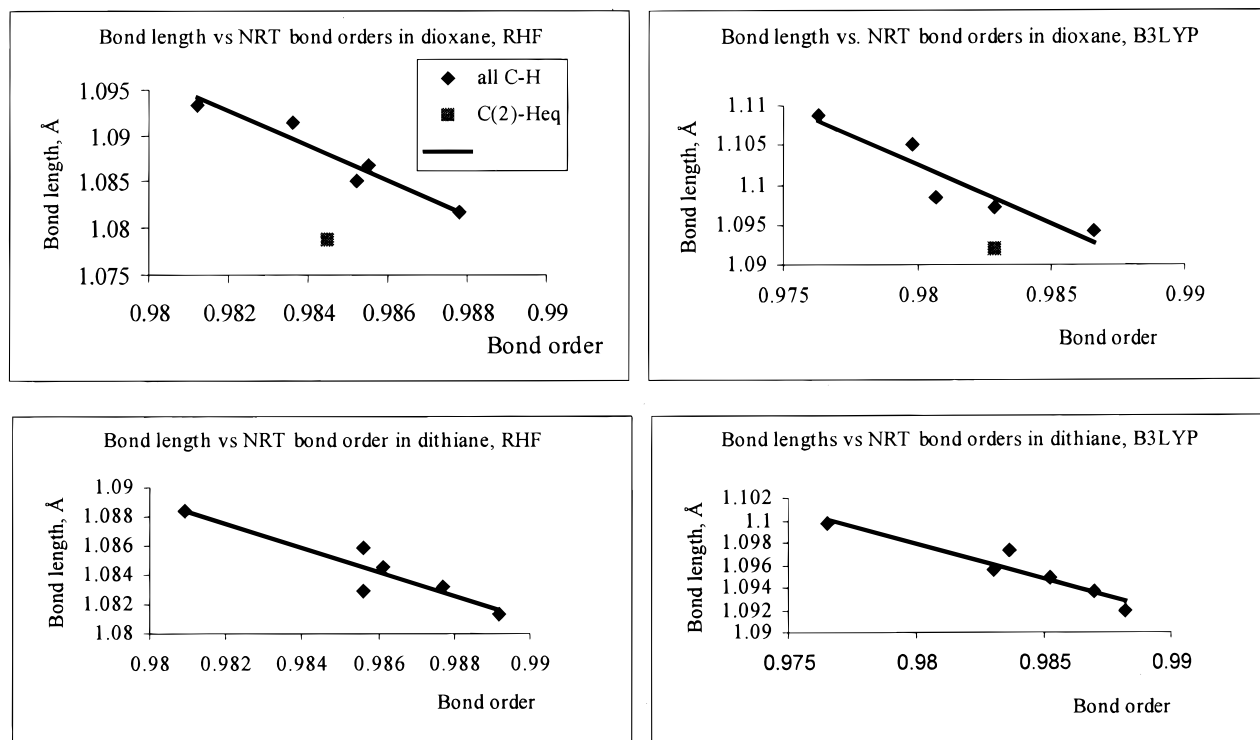


Figure 7. NRT bond orders vs bond length.

oppositely than in the other C–H bonds (Table 3), and the C(2)–H_{eq} antibond is the strongest acceptor among the C–H antibonds.

Nevertheless, for *any pair* of diastereotopic protons in *any* CH₂ group (including the dioxane –C(2)H₂– group) the effects of electronegativity are approximately the same, and the delocalization criterion is valid. Clearly, the dioxane C(2)–H_{eq} bond is an extreme example, and the electronegativity effects will be less important for N-, S-, Se-, and P-heterocycles. In fact, even in 1,3-dioxane the simple delocalization energy criterion works well for the other four C–H bonds. (*R*² for the correlation including dioxane C(5)–H and C(4)–H bonds is 0.9996 (B3LYP) or 0.9703 (RHF)).

There are no large deviations in the analogous correlation in dithiane because of the small difference in electronegativity between carbon and sulfur (Table 7). Nevertheless, the overall quality of correlation is worse as the result of the weakness of the hyperconjugative interactions and the smaller range of the bond length. As a consequence, the relative role of other factors influencing the bond length increases and the correlation between hyperconjugative interactions and bond length is eroded.

A further limitation of the simple additive approach is the assumption of equal importance of the interactions decreasing population of C–H orbitals and the interactions increasing population of the antibonding C–H orbitals. More accurate treatment can be obtained with natural resonance theory (NRT) analysis, which gives the proper weight to different delocalizing interactions (Figure 7).^{42,49}

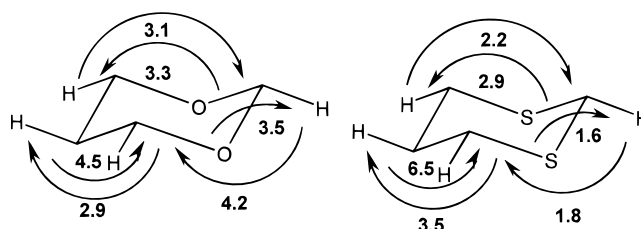


Figure 8. Summary of “equatorial” hyperconjugative interactions in dioxane and dithiane.

The relative values of equatorial hyperconjugative interactions are summarized in Figure 8. The difference between the donor ability of S–C and C–S bonds is important for stereoelectronic interpretations of selectivities of many organic reactions,^{2,50} and sulfur–carbon bonds are often considered to be electron-donating. However, the values in Figure 8 suggest that the commonly used order of the donor ability for the ground state of 1,3-dithiane and 1,3-oxathiane should be modified as follows: C–H > C–S > C–C > O–C ≈ C–O > S–C.

The relative weakness of the $\sigma_{\text{H}_{\text{eq}}-\text{C}} \rightarrow \sigma_{\text{C}-\text{S}}^*$ interactions at C(4, 6) and C(2) is interesting especially in comparison with the analogous interaction at C(5). A possible reason could be that the C(5)–H_{eq} bond is antiperiplanar to the C–S bonds whereas the C(2)–H_{eq} and C(4,6)–H_{eq} bonds are anti to the S–C bonds (Figures 10 and 11). In other words, the dithiane C–S bonds are excellent acceptors in one direction but poor acceptors in the other.

If one considers only bond polarization, then the weak acceptor properties of the S–C bonds are unexpected. The C–S bonds are polarized toward carbon, and therefore

(49) NRT: (a) General formalism: Glendening, E. D.; Weinhold, F. *J. Comp. Chem.* **1998**, *19*, 593. (b) Bond order and valency, see ref 42. (c) Chemical applications: Glendening, E. D.; Badenhop, J. K.; Weinhold, F. *J. Comp. Chem.* **1998**, *19*, 628.

(50) (a) Terasawa, T.; Okada, T. *J. Chem. Soc., Perkin Trans. 1* **1978**, 1252. (b) Kobayashi, Y. M.; Lambrecht, J.; Jochims, J. C.; Burket, U. *Chem. Ber.* **1978**, *111*, 3442. See also ref 2 and references therein.

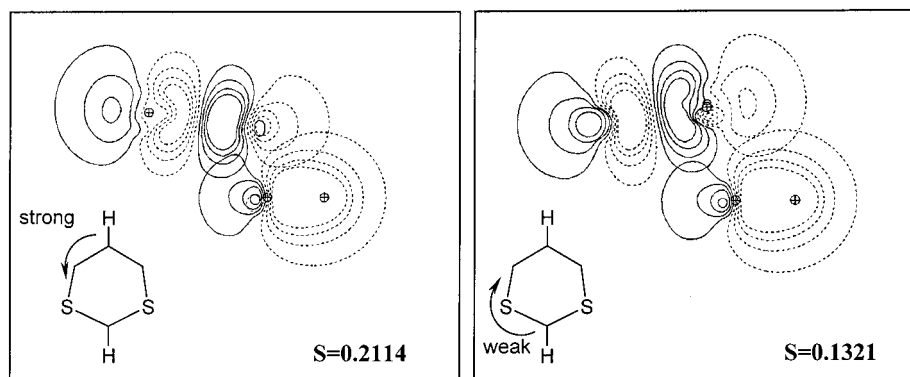


Figure 9. The $\sigma_{\text{H}_{\text{eq}}-\text{C}(5)} \rightarrow \sigma_{\text{C}(6)-\text{S}(1)}^*$ (left) and $\sigma_{\text{H}_{\text{eq}}-\text{C}(2)} \rightarrow \sigma_{\text{S}(1)-\text{C}(6)}^*$ (right) hyperconjugative interactions. The corresponding orbital overlaps in the PNBO basis are given at the right bottom corner of the schemes.

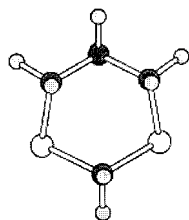


Figure 10. B3LYP/6-31+G**-optimized geometry of 1,3-dithiane. Note the ring distortion.

the corresponding antibonds are polarized in the opposite direction with the larger amplitude on sulfur. This should have made the S–C bonds better acceptors than the C–S bonds. In reality, in dithiane the situation is just the opposite, and the reason is stereoelectronic. Sulfur–carbon bonds are longer than C–C bonds, and they distort the dithiane ring (Figure 10). The $\sigma_{\text{C}(6)-\text{S}}^*$ orbital is tilted away from the C(2)–H_{eq} bond but toward the C(5)–H_{eq} bond (Figure 9), weakening the interaction with the first C–H bond and strengthening the interaction with the second C–H bond. This stereoelectronic effect is due to the cyclic structure of dithiane, and it is one of the reasons why methanedithiol is an inadequate model for dithiane.

This observation was confirmed by the analysis based on the second-order perturbation estimate of the corresponding interactions energies (Table 8), which is discussed in detail in the footnote.⁵¹

As the result, the C–H_{eq} ↔ S–C interactions in dithiane do not compensate completely for the anomeric

effect at C(2) and C(4, 6), and therefore, the stereoelectronic effects alone are not able to explain the relative order of the one-bond coupling constants in dithiane. This is the true reverse Perlin effect (satisfying both definitions discussed in the Introduction).⁵²⁵³

Conclusions

The balance of hyperconjugative interactions involving C–H_{ax} and the corresponding C–H_{eq} bonds successfully accounts for the relative bond lengths for C–H_{ax}/C–H_{eq} pairs in all of the studied compounds. The NBO analysis consolidates all experimental and theoretical data and disentangles the relative importance of the main stereoelectronic effects in heterocyclohexanes. The high transferability of the NBO hyperconjugative energies allows one to use simple, semiquantitative criteria for the prediction of the magnitude of stereoelectronic interactions in heterosubstituted cyclohexanes.

The balance of the interactions can be described either via total delocalization energy or via the NRT bond orders. These parameters correlate reasonably well with the C–H bond lengths for all compounds studied in this paper,⁵⁴ as summarized in Figure 11.

The correlation shown in Figure 11 is somewhat unexpected because of the very different dipole moments, charges, populations, and other factors characterizing C–H bonds in different compounds. This result illustrates the importance of hyperconjugative interactions in understanding molecular structure. This importance increases when the other factors such as electronegativity, etc. are similar (the situation typical for reactions involving diastereotopic and enantiotopic transition states).

(51) The energy of the interaction between a filled and unfilled orbital is proportional to the square of the corresponding Fock matrix element (or the square of the orbital overlap) and is inversely proportional to the difference between the orbital energies ($\Delta\epsilon$). For a discussion, see, for example, the ref 3. The $\Delta\epsilon$ term is always smaller for the C–S (S–C) orbitals, uniformly favoring all of the hyperconjugative interactions in dithiane comparing with the corresponding interactions in dioxane. Nevertheless, the corresponding Fock matrix element, F_{ij} (proportional to the orbital overlap) varies for the different interactions. Only for the H_{eq}–C5 ↔ C(4)–X(3) (X = O, S) interactions is the difference between dioxane and dithiane small, and this explains the larger magnitude of these interactions in dithiane. For the H_{eq}–C(2) ↔ X(3)–C(4) and H_{eq}–C(4) ↔ X(3)–C(2) interactions the orbital overlap is smaller for X = S. This is partially compensated by the favorable value of the $\Delta\epsilon$ term, and the strength of these two interactions in dioxane and dithiane is almost equal. At the same time, the orbital overlap for the H_{eq}–C(2) ↔ X(3)–C(4) and H_{eq}–C(4) ↔ X(3)–C(2) interactions is significantly smaller for dithiane, which explains the lower interaction energy. To summarize, the S–C orbitals are comparable to the corresponding O–C orbitals in donor strength, but the $\sigma^*(\text{S–C})$ orbitals are much weaker acceptors than the O–C antibonds despite the lower energy.

(52) When this work had been completed, a paper with the similar conclusion about the lack of correlation between the relative bond lengths and order of NMR constants in dithiane and oxathiane appeared: (a) Guevas, G.; Juaristi, E.; Vela, A. *J. Phys. Chem. A* **1999**, *103*, 932.

(53) Higher s-character in the axial hybrid orbital is able to explain the reverse Perlin effect at C(2), but the difference seems to be too small at C(4). s-Character in the hybrids forming the C(2)–H_{ax} and C(2)–H_{eq} bonds is 26.61% vs 25.65%, respectively. For C(4)–H bonds the difference is smaller (25.08% vs 24.97%). (a) Other contributions to spin–spin coupling (“spin–orbit” and “spin–dipole” terms) may also be important for sulfur-containing molecules. Ramsey, N. F. *Phys. Rev.* **1953**, *91*, 303. (b) For the most recent review of different approximations and correlations concerning the $^1J_{\text{C–H}}$ constants, see: Craciun, L.; Jackson, J. E. *J. Phys. Chem. A* **1998**, *102*, 3738.

(54) The most deviating data were for the C(5)–H_{eq} bonds in dithiane and oxathiane (correlation with the NRT bond orders) and for the dioxane C(2)–H_{eq} bond (both correlations). These data are denoted by squares.

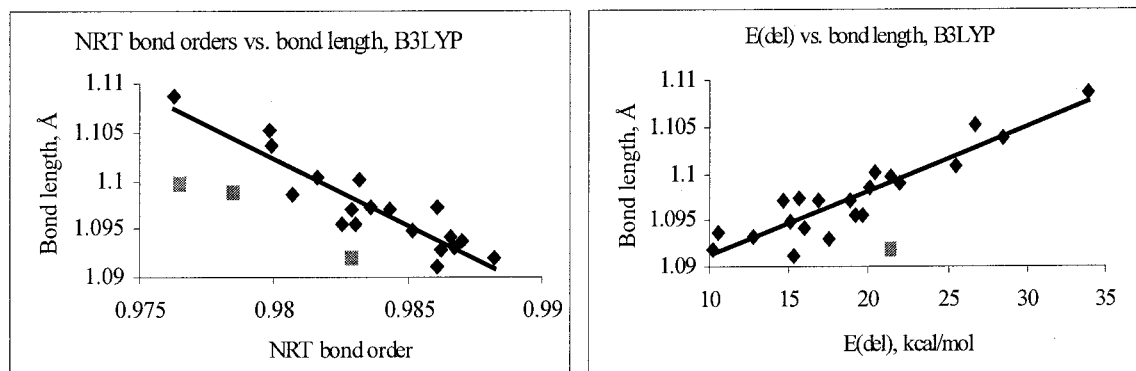


Figure 11. (a) Bond length vs NRT bond orders.⁵⁴ (b) Bond length vs combined energy of main hyperconjugative interaction in cyclohexane, 1,3-dioxane, 1,3-dithiane, and 1,3-oxathiane.

Table 8. Second-Order Perturbation Analysis of the "Equatorial" Hyperconjugative Interactions in Dithiane and Dioxane (B3LYP/6-31+G)**

donor NBO (<i>i</i>)	acceptor NBO (<i>j</i>)	$E(2)$, kcal	$E_j - E_i$, au	F_{ij} , au
C5				
$\sigma_{C(6)-S(1)}$	$\sigma^*_{C(5)-H(5)_{eq}}$	1.81	1.00	0.038
$\sigma_{C(5)-H(5)_{eq}}$	$\sigma^*_{S(3)-C(4)}$	4.47	0.65	0.048
$\sigma_{C(6)-O(1)}$	$\sigma^*_{C(5)-H(5)_{eq}}$	1.16	1.22	0.034
$\sigma_{C(5)-H(5)_{eq}}$	$\sigma^*_{C(6)-O(1)}$	3.86	0.79	0.049
C2				
$\sigma_{C(6)-S(1)}$	$\sigma^*_{C(2)-H(2)_{eq}}$	1.31	1.00	0.032
$\sigma_{C(2)-H(2)_{eq}}$	$\sigma^*_{C(6)-S(1)}$	1.17	0.69	0.025
$\sigma_{C(6)-O(1)}$	$\sigma^*_{C(2)-H(2)_{eq}}$	1.36	1.25	0.037
$\sigma_{C(2)-H(2)_{eq}}$	$\sigma^*_{C(6)-O(1)}$	3.19	0.81	0.046
C6				
$\sigma_{S(1)-C(2)}$	$\sigma^*_{C(6)-H(6)_{eq}}$	1.15	1.02	0.031
$\sigma_{C(6)-H(6)_{eq}}$	$\sigma^*_{S(1)-C(2)}$	1.33	0.67	0.027
$\sigma_{O(1)-C(2)}$	$\sigma^*_{C(6)-H(6)_{eq}}$	1.29	1.27	0.036
$\sigma_{C(6)-H(6)_{eq}}$	$\sigma^*_{O(1)-C(2)}$	2.57	0.83	0.041

For such cases, hyperconjugative stereoelectronic effects are especially significant.

The use of one-bond coupling constants as probes for stereoelectronic effects is well justified for compounds containing first row atoms where the stereoelectronic hyperconjugative interactions are strong and their balance correlates well with both the bond lengths and the NMR parameters. However, in dithiane and oxathiane the correlation between the stereoelectronic effects and the direct C–H coupling constants is less reliable. For

the sulfur-containing heterocycles, the difference in bond lengths is very small (in the range of 0.003–0.005 Å), and the relative values of the constants are defined by the interplay of other factors (in particular, *s*-character of the corresponding hybrids). As a result, the longer bond *may* correspond to the larger coupling constant, displaying genuine reverse Perlin effect.

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Supporting Information Available: The second-order perturbation estimation of main delocalizing interactions ($E_{del} > 0.5$ kcal/mol) for C–H bonds in 1,3-dioxane, 1,3-dithiane, and 1,3-oxathiane; summary of hyperconjugative interactions in 1,3-oxathiane; bond length vs total delocalization energies in 1,3-oxathiane; energies of main hyperconjugative interactions in methanedithiol; and selected properties of C–H bonds in cyclohexane, 1,3-dioxane, 1,3-dithiane, and 1,3-oxathiane. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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