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G2(MP2) Characterization of Conformational Preferences in 2-Substituted Ethanols (XCH_2CH_2OH) and Related Systems

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The preferred conformation of species of the general form $XCH_2{-}CH_2Y$ can be gauche (X = Y = F or X = F, Y = Me) or trans (X = F, Y = Cl or Br, and [X, Y] = [Cl, Br]). If either or both of X or Y = OH, then new degrees of freedom open, and the possibility of H ···X interaction complicates the picture. We present G2MP2 calculations on the series, which represent the preferences faithfully. NBO analyses of DFT densities help us to understand the patterns of conformational preferences. We address the question of whether hydrogen bonding as generally understood plays a central role in establishing preferences in the alcohols and diols. A consistent account of conformational preferences can be founded on simple notions of electrostatic attraction.

Introduction

The gauche effect is now part of the standard vocabulary of conformational analysis.[1] The term embraces the preference of 1,2-difluoroethane for the gauche form,[2] which is shared by a few other molecules including propyl fluoride,[3] chloride,[4] and alcohol.[5] It is also implicated in the preference for antiperiplanar orientations of lone-pair-bearing substituents observed in sugars and is often discussed with the related anomeric effect.[6] The hyperconjugation or local orbital mixing models[7] offer an explanation of the preferences by reference to the enhanced mixing and stabilization achieved when the best sigma donor bond or lone pair is anti (trans) to the best acceptor antibond. In the haloethanol and ethane diols, in which gauche conformations are prominent, interactions commonly called internal hydrogen bonding play an important role as well.

Thorough investigations have shown that large basis sets and some correlation correction are required for trustworthy estimates of the relative energies of the conformations in these systems.[8] Experimental investigations typically reveal relative free energies (from abundance studies) or enthalpy values (from temperature-dependent observations of vibrational spectra) rather than internal energies.[9,10] The very accurate extrapolated methods such as G2[11] and its variants and extensions or the complete basis set (CBS[12]) family of schemes that permit estimates of enthalpy and free-energy changes accompanying conformational change would seem to be well suited to these comparisons. We present results of G2MP2[13] calculations on the internal and Gibbs energies of conformers in the series listed in Table 1. For certain of these systems, we also found optimized B3LYP/6-311G** structures and conducted NBO analyses of the DFT charge densities. This permits a discussion of the nature of bonding and delocalization in the favored conformations.

TABLE 1: Species Reported

X→ Y↓	F	methyl	O anion	OH	Cl	Br
F	**	**				
O anion	**	**				
OH	**	**		**		
Cl	**	**	**	**	**	
Br	**	**	**	**	**	**

Methods

We used Spartan 2002 for Windows,[14] which provides a powerful builder, to generate initial structures for all conformations. Spartan 2002 permits RHF, DFT, and MP2 geometry optimizations for sets of conformers, in extended basis sets, and can generate families of conformers. We used Gaussian 98W[15] for all G2MP2 calculations. The G2MP2 scheme generates optimum structures in MP2/6-31G* and uses these structures, single-point MP2 and QCISD(T) calculations in extended basis sets, and empirical terms to estimate the energy. Thermal corrections are derived from these structures and scaled RHF/6-31G* frequencies to estimate thermodynamic functions. (There may be appreciable errors in such estimates for systems with very low frequency modes.) In a training set, G2MP2 achieved "chemical accuracy" or about 1.5 kcal/mol[16] in atomization energies. Differences in energy between conformations may be better than this owing to cancellation of errors in such closely comparable systems.

Plan

We address the following questions: Does G2MP2 provide a convincing representation of the gauche effect in 1,2-difluoroethane and 1-fluoropropane, for which the gauche preference is experimentally established? According to G2MP2, what are the conformational preferences for other 1,2-dihalogenated ethanes and 1-halo propanes? What is the impact of the substitution of OH for halogen in these systems? What is the role of hyperconjugation in the conformational preferences in these systems? Is there a preferable alternative explanation for conformational preferences that does not appeal to hyperconjugation or hydrogen bonding?

1,2-Disubstituted Ethanes

Table 2 summarize the energies reported in the course of G2MP2 calculations. The geometric structures (optimized in MP2/6-31G*) are collected in the Supporting Information.

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TABLE 2: Relative Energy for Gauche and Anti 1,2-Dihaloethanes[a]

species	rel *E*298 (gauche) kcal/mol	*G*298 (gauche) kcal/mol
1,2-difluoroethane	−0.80	−0.73 (−1.14)
1-chloro-2-fluoroethane	+0.46	+0.54 (+0.13)
1-bromo-2-fluoroethane	+1.35	+0.92 (+0.51)
1,2-difluoroethane	+1.11	+0.77 (0.36)
1-chloro-2-bromoethane	+1.40	+1.50 (+1.09)
1,2-dibromoethane	+1.88	+2.01 (+1.61)
1-fluoropropane	−0.18	−0.07 (−0.48)
1-chloropropane	+0.15	−0.05 (−0.46)
1-bromopropane	+0.02	+0.15 (−0.26)

[a] Relative internal and Gibbs free-energy values are in kcal/mol. There appears (in parentheses) an explicit correction to the relative free energy for symmetry numbers ω. A negative relative energy favors the gauche conformer.

In accord with many other calculations, we found that the 1,2-difluoroethane's experimentally established preference for the gauche orientation is captured at the QCISD(T)/6-311G**//MP2/6-31G* level of theory, but a much more realistic estimate near 0.7 kcal/mol is obtained in the G2MP2 values of internal energy and free energy. The 1-halopropanes show such a slight conformational energy preference that the statistical correction to the free energy is decisive. Substituting 1,2-difluoroethane with even a single heavier halogen removes the gauche preference, and the trans (anti) structure is favored more and more decisively as one descends the periodic table. The dibromo system prefers the trans form by 1.5 kcal/mol (the difference in free energy with symmetry number correction). These results are all in accord with the equivalent calculations of Yamada and Bozzielli,[17] who treated the 1,2-difluoroethane, and Wiberg, et al.,[18] who treated fluoro and chloro systems.

Rablen et al.[19] have examined the role of hyperconjugation in establishing the gauche preference in a variety of substituted ethanes. These investigators verified that hyperconjugation was indeed at work in these systems and established a ranking of the effectiveness of donation, CH > CC > CCl > CF. The influence of hyperconjugation can be masked or overruled by electrostatic influences, which may be expected to be reflected in the dihedral angles in the gauche conformations.

Weinhold's natural bond analysis attempts to represent the charge distribution as a collection of chemically meaningful entities—cores, two-center bonds, and lone pairs − extracting these one- and two-center functions from portions of the density matrix. For a calculation such as HF or DFT, which defines a density from a single determinant of orbitals, the analysis also derives energies for local orbitals from the Fock matrix. The NBO analysis also defines values of the second-order perturbation theory stabilization arising from pairwise mixing of these orbitals with antibonding counterparts to the orbitals and one-center "Rydberg" levels. In particular, delocalization of the type appealed to by qualitative MO theory is made specific and quantitative. Selected values from the NBO analysis of B3LYP/6-311G** densities for the gauche and trans dihaloethanes are gathered in Table 3.

An inspection of the NBO report shows that lone pairs and local two-center bond orbitals mix with Rydberg levels and antibonding orbitals with amplitude primarily on neighboring atoms. This represents the major portion of delocalization. There are, however, important effects of more far-flung delocalization. Bond orbitals mix effectively with antibonding orbitals oriented antiperiplanar; this is the source of hyperconjugative stereoelectronic effects

The gauche arrangement would be favored by hyperconjugation. Consider the trans dichloroethane. The most significant second-order perturbation theory stabilization results from mixing with CCl bonds with CCl antibonds, 4.14 kcal/mol. CH−CH* mixing yields 2.59 kcal/mol; there are twice as many interactions of this kind than of type CCl−CCl*. Among the lone-pair interactions, we see more extensive stabilization at the neighboring carbon with the CC* antibond than with the CH* antibond. There is lesser but significant mixing of the lone pairs with the remote CCl* antibond. How does this picture change as we rotate into the gauche conformation? Symmetry descends from C_{2h} to C_2. Where once (CCl, CCl*) and (CH, CH*) were antiperiplanar pairs, now CH is antiperiplanar with CCl*, and CCl is antiperiplanar with CH*. (A CH bond is also antiperiplanar to a CH*.) Now an effective donor is antiperiplanar with an effective acceptor, and we expect enhanced stabilization according to the perturbative picture. Relatively numerous and large interactions favor the gauche conformation. As we shift to the bromo system, interactions grow stronger in general and favor the gauche conformation more strongly. The gauche conformation is most weakly favored by hyperconjugation for the fluoro system, oddly the only system for which gauche is the observed form. This is consistent with earlier observations that hyperconjugation though significant for both difluoro- and dichloroethanes is not the sole determinant of conformational preference. Electrostatic and steric interactions, favoring the trans arrangement, must play their roles.

In preparation for the study of 2-haloethanols, we extend the series of 1-X, 2-Y-ethanes to the methyl- and halo-substituted ethoxide anions (Table 4). None of the 2-halo ethoxides shows any preference for the gauche conformation. The balance tips further toward the trans chain as we increase the size of the halogen. Methyl substitution shifts the balance back to the gauche conformer of propane-1-oxide.

2-Substituted Ethanols

When X or Y becomes the hydroxyl group −OH, new degrees of freedom must be considered. For XCH_2CH_2OH, we may anticipate trans or gauche torsions for the heavy-atom chain XCCO and also trans or gauche torsions for the CCOH chain. Names for the conformations are tT, tG, gG, g*G, and gT, with the capital letters referring to the heavy-atom chain. Species gG and g*G differ in the sense of the rotation around the CO bond; gG permits the closest approach of the hydroxyl hydrogen to halogen X.

Our G2MP2 results are summarized in Tables 5 and 6. Gaussian free energies must be corrected for symmetry number contributions to the entropy of the form $-RT\ \ln(\omega)$. All conformers have a symmetry number of $\omega = 2$ except tT, for which $\omega = 1$. The tT free energy has thus been shifted upward by 0.411 kcal/mol relative to that of the other species.

We can divide the conformations into two sets, G and T; within set G, the form Gg that brings the H atom close to the X substituent is distinct from Gt and Gg*. The most stable form is always Gg except for propanol (X = methyl.) Propanol shows only very small differences in conformational energies. For all other species, the T set is less stable than the Gg form, and there is little energy difference between Tt and Tg. The remaining Gt and Gg* forms are the least stable, with the Gg* form less stable than Gt.

Buemi[20] has investigated the conformational equilibria for XCH_2CH_2OH systems with X = F, Cl, Br, and I. His MP2 calculations are generally consistent with our results. For heavier atoms Br and I, Buemi used the LANL1DZ basis and pseudopotential, so comparisons must be made with care.

TABLE 3: NBO Analysis for 1,2-Dihaloethanes[a]

(a) trans Dichloroethane

entity	energy (hartrees)	important admixtures: entity and (stabilization in kcal/mol)
CCl bonds	−0.668	CCl* (4.14 × 1)
CC bond	−0.698	
CH bond	−0.555	CH* (2.59 × 2)
Cl σ lone pairs	−0.914	
Cl π lone pairs	−0.328, −0.334	CH* (3.42); CC* (3.67) and CCl (1.83)

(b) gauche Dichloroethane

entity	energy (hartrees)	important admixtures: entity and (stabilization in kcal/mol)
CCl bonds	−0.671	CH* (1.85 × 2)
CC bond	−0.698	
CH bond	−0.554, −0.554	CCl* (5.96 × 2); CH* (2.61 × 1)
Cl σ lone pairs	−0.907	
Cl π lone pairs	−0.321, −0.328	CH* (4.03 and 2.77); CC* (4.32) and CCl

(c) trans Dibromoethane

entity	energy (hartrees)	important admixtures: entity and (stabilization in kcal/mole)
CBr bonds	−0.598	CBr* (5.38 × 1)
CC bond	−0.707	
CH bond	−0.555	CH* (2.78 × 2)
Br σ lone pairs	−0.943	
Br π lone pairs	−0.301, −0.312	CH* (2.49); CC* (2.73) and CBr (1.79)

(d) gauche Dibromoethane

entity	energy (hartrees)	important admixtures: entity and (stabilization)
CBr bonds	−0.605	CH* (2.32 × 2)
CC bond	−0.703	
CH bond	−0.552, −0.553	CBr* (6.33 × 2); CH* (2.73 × 1)
Br σ lone pairs	−0.938	
Br π lone pairs	−0.295, −0.305	CH* (2.84 and 2.22); CC* (3.42)

(e) trans Difluoroethane

entity	energy (hartrees)	important admixtures: entity and (stabilization)
CF bonds	−0.925	CF* (1.48)
CC bond	−0.656	
CH bond	−0.540	CH* (2.11 × 2), CF* (0.59)
F σ lone pairs	−1.039	
F π lone pairs	−0.400, −0.404	CH* (2.49); CC* (2.73) and CF* (1.39)

(f) gauche Difluoroethane

entity	energy (hartrees)	important admixtures: entity and (stabilization)
CF bonds	−0.925	CH* (0.81)
CC bond	−0.666	
CH bond	−0.539, 0.541	CF* (4.51 and 1.48); CH* (2.17)
F σ lone pairs	−1.031	
F π lone pairs	−0.393, −0.398	CH* (2.79 and 0.67); CC* (6.10) and CF* (<0.5)

[a] Table 3 extracts some details from an NBO analysis of B3LYP/6-311G** densities, including assigned energies for bonds and lone pairs, and the estimate of stabilization arising from the mixing of remote entities. The energies are in hartrees, and the stabilization is in kcal/mol. Where there are several identical stabilization terms, the number of such terms is indicated as a multiplier.

TABLE 4: Relative Energies of Gauche and Anti 2-Haloethoxides[a]

species	rel *E*298 (gauche) kcal/mol	*G*298 (gauche) kcal/mol
2-fluoroethoxide	+2.20	+2.18 (+1.77)
2-chloroethoxide	+4.04	+3.66 (+3.25)
2-bromoethoxide	+4.93	+5.02 (+4.61)
propyl-1-oxide	+0.93	−0.71 (−1.12)

[a] The free-energy values in parentheses are corrected for symmetry numbers ω. A negative relative energy favors the gauche conformer.

TABLE 5: Relative Energies for 2-X-Ethanols[a]

(a) G2MP2 Conformer Free Energies

form	gG	tT	gT	tG	g*G
X = F	0	2.039	1.810	1.532	2.000
X = Cl	0	1.721	1.318	1.868	2.337
X = Br	0	1.483	1.003	1.793	2.263
X = methyl	0.181	0.439	0.050	0	0.205

(b) Buemi's Relative MP2 Energies, kcal/mol

form	gG	tT	gT	tG	g*G
X = F	0	2.58	2.59	2.98	3.26
X = Cl	0	1.71	1.51	2.48	2.60
X = Br	0	0.98	1.01	2.39	2.77
X = I	0	0.68	0.36	1.94	2.39

(c) Experimental Enthalpy Differences

form	gG	tT	gT	tG	g*G
X = F	0	362	433	not observed, low population at equilibrium	
X = Cl	0	604	411		
X = Br	0	411	315		

(d) MP2 Estimates of Energy Differences, cm^{-1}

form	gG	tT	gT	tG	g*G
X = F	0	939(788)	954(897)	1074(828)	1191(1061)
X = Cl	0	604	541	897	917
X = Br	0	875(557)	758(525)	1142	1193

[a] Relative free energies are in kcal/mol. Table values in section a include the statistical correction $-R\ \ln(\omega)$; the symmetry number = 1 for tT and 2 for all other forms. Other Tables, referring to electronic energies (sections b and d) or experimentally deduced enthalpies (section c) do not include the statistical correction. (Section b): Note that MP2/6-31G* is used for F and Cl; LANL1DZ is used for Br and I. (Section c): Values as reported by Durig et al. in cm^{-1}; 1000 cm^{-1} = 2.86 kcal/mol. (Section d): Values in parentheses for Br used the 6-311+G** basis set, and those for F used 6-311++G** basis sets. Other values refer to 6-31G** basis sets; 1000 cm^{-1} = 2.86 kcal/mol.

Experimental and computational investigations have been reported for fluoroethanol,[21] chloroethanol,[22] and bromoethanol[23] by Durig and co-workers. Experimental estimates of the enthalpy differences between conformers present in mixtures are quoted in Table 5, section c. Our G2MP2 estimates are in general agreement with the reports that Gg is the stable species, with Gg* and Gt′ less stable than intermediate forms Tt and Tg. MP2 calculations in extended basis sets conducted by Durig and co-workers[21] are summarized in Table 5, section d. In making comparisons among values in Table 5, take note of the 0.41 kcal/mol free-energy penalty for the tT species because all other species have a symmetry number of 2 whereas its symmetry number is 1.

The (free-) energy differences between gG and g*G or tG provide a guess at the contribution of −OH···X interactions to stabilization. Structurally, these differ primarily in the removal of the H from the interaction with the neighboring halogen X. G2MP2 free energies place all the interaction energies in the neighborhood of 2−3 kcal/mol. As intermediate results from

TABLE 6: Energies, Free-Energy Comparisons, and Structural Parameters of 1,2-Ethanediol[a]

(a) G2MP2 Values of Energies

species	$G298$	$E0$	rel $E0$	rel DFT	QCISD	$E298$
1 = gGt	−229.921062	−229.893774	0	0	−229.761786	−229.888641
2 = gGg	−229.920367	−229.893136	0.4	0.1	−229.761857	−229.888065
3 = gGg*	−229.920077	−229.892718	0.7	1.7	−229.759453	−229.887278
5 = tTg	−229.917600	−229.890024	1.6	3.0	−229.756849	−229.884623
6 = gTg*	−229.917548	−229.890023	1.6	2.6	−229.757509	−229.884667
9 = gGg	−229.917248	−229.889574	2.6	2.7	−229.756783	−229.883922
10 = gGt	−229.916481	−229.888771	3.1	3.7	−229.754992	−229.883371
8 = tGt	−229.916789	−229.889567	2.6	3.6	−229.755122	−229.884026
7 = gTg	−229.916656	−229.889774	2.5	2.7	−229.757081	−229.884403
4 = tTt	−229.917224	−229.890216	2.2	3.1	−229.756674	−229.884748

(b) Free-Energy Comparisons and G2MP2 Structural Parameters

species	G2MP2 relative G	with $R \ln(\omega)$ term	relative G value[27]	OH···O distance	O···O distance	OH···O angle
1 = gGt	0	0	0	2.2409	2.7428	110.8
2 = gGg	0.44	0.44	0.42	2.2258	2.7792	114.8
3 = gGg*	0.62	1.03	0.84	2.5858	2.7984	92.3
5 = tTg	2.17	2.17	2.22	3.9246	3.6351	
6 = gTg*	2.20	2.61	2.64	3.9610	3.6928	
9 = gGg	2.39	2.80	2.87	2.7110	2.7925	84.6
10 = gGt	2.87	2.87	3.03	2.8752	2.8752	*
8 = tGt	2.68	3.09	3.43	3.6303	2.8729	*
7 = gTg	2.76	3.17	3.21	3.6926	3.6926	
4 = tTt	2.41	3.23	3.36	4.2886	3.5831	

[a] (Section a): Relative energies are in kcal/mol, while all other values are in hartrees. (Section b): Relative energies are in kcal/mol; distances are in angstroms, and angles are in degrees. OH···O angles for species xGy with OH pointed away from the interaction zone are not reported.

the G2MP2 calculations, we recover QCISD(T)/6-311G**//MP2/6-31G* estimates of the gG−(t or g*)G internal-energy gaps. These average 2.83, 2.57, and 2.64 kcal/mol for F, Cl, and Br, respectively.

It is a bit surprising that estimates of this kind are not very different for the halogens, although their electronegativity, size, and thus local charge density are quite varied. The question of why the Gg conformer is as strongly preferred to Gg* in $BrCH_2CH_2OH$ as in FCH_2CH_2OH occurred in the electronic structure modeling class project of coauthors P.C. and K.D., which was simply to evaluate the dipoles and moments of inertia of the conformations of bromoethanol for use in studies in their laboratory. This report contains an extension of their studies, which addressed the possibility of hydrogen bonding, hyperconjugation, and electrostatic effects.

Structures and details of the G2MP2 energies of the 2-haloethanols and 1-propanol are presented in the Supporting Information tables. Propanol is distinct from the 2-haloethonaols in ways that show the interaction OH···methyl to be repulsive. Trans-to-gauche torsion of the heavy-atom chain has essentially no effect on bond angles, whereas the twist of the OH into the zone of interaction with methyl is resisted (+71°), the CCO angle is opened, and the OH bond is very slightly shortened.

Consider the haloethanol sequences Tt → Gt → Gg and Tt → Gt → Gg*. The COH angle is almost unchanged in the first step as the skeleton is twisted. If the OH is shifted into the interaction zone, then the angle COH decreases by 2.2° for F, 1.2° for Cl, and 1.6° for Br. The gauche twist in the opposite sense leaves the angle changed by less than 0.2°. The CCOH torsion follows the sequence 180 → 180 → [−60, +60], approximately. More precisely, the second angle is near 170° for all halogens. The bromoethanol leaves the final torsions at ±61°, and in the chloroethanol, we find ±63°. The corresponding torsion angles in the fluoroethanol are −64°and +54°, showing that there is a unique −OH···F− attraction that is not present in the heavier halogens. It seems not to be a coincidence that we expect H bonding only for F and not for Cl or Br. We will return to this question after reviewing the G2MP2 results for ethane-1,2-diol.

Other geometric parameters for 2-substituted ethanols are found in the Supplemental Information. In the most stable Gg conformer, the COH angle is slightly compressed, as is the FCC angle, compared with the Gt or Gg* conformers. The OH bond and FC distances are very slightly extended in Gg. In the chloro and bromo species, the COH and XCC compression is less marked—it is about half that of the fluoro system. The OH and CX bond extensions hardly change.

PM3 calculations also select the gG conformation for all haloethanols, but PM3 fails to describe the higher-energy conformations; in some cases, no minimum-energy structure is found.

1,2-Ethanediols

The natural conclusion in the series is $HOCH_2CH_2OH$. A third torsional degree of freedom comes into play so that structures require three labels referring to torsions HOCC, OCCO, and CCOH, for example, tTt. There are 10 symmetry-distinct forms among the $3^3 = 27$ possible assignments of torsion angles. Experimental data is available for the most stable gGt structure[24] and hints that gGg is present in mixtures.[25] The first computational team to investigate the entire set of 10 distinguishable conformers[26] showed that nonlocal gradient-corrected DFT calculations and MP2 and MP4 calculations were in general agreement both in structure and energy ranking. Their DFT relative energies are included in Table 6, section a, in which G2MP2 estimates of internal energies and thermodynamic functions are presented. We calculate a correlation coefficient of 0.92 between our relative $E0$ values and DFT values.

Symmetry terms become important in free-energy comparisons, as Cramer and Truhlar[27] made clear. Once we add proper corrections to the G2MP2 results, we reproduce their reported

TABLE 7: NBO Analysis for XCH_2CH_2OH[a]

(a) 2-Fluoroethanol gG

entity	energy of bonds and lone pairs	energy of antibonds	important admixtures: entity and (stabilization)
CF bond	−0.90980	0.21023	CH* (1.04)
OH bond	−0.70934	0.42564	CC* (<0.5), CH* (1.85)
CO bond	−0.82370	0.29395	CH* (0.95)
CC bond	−0.64936	0.36661	
CH (F site)	−0.53202, −0.53631	0.38457, 0.37906	CH* (2.32), CO* (0.76 and 3.75);
CH (OH site)	−0.51711, −0.51892	0.38385, 0.39053	CF* (1.01 and 4.45), CH* (2.40)
F σ lone pair	−1.03837		
F π lone pairs	−0.3956, −0.39755		CH* (6.07 and 2.68), CC*(4.53), C′H* (0.76)
O σ lone pair	−0.60791		
O π lone pair	−0.30056		CC* (1.16 and 5.78)

(b) 2-fluoroethanol g*G

entity	energy (hartrees) bonds, lone pairs	energy (hartrees) antibonds	important admixtures: entity and (stabilization)
CF bond	−0.90964	0.23387	CH* (0.87)
OH bond	−0.71418	0.42188	CC* (2.50), CH* (0.67)
CO bond	−0.82206	0.28773	CH (0.94)
CC bond	−0.64973	0.37234	OH* (1.44)
CH (F site)	−0.52598, −0.52266	0.38299, 0.39105	CH (2.24), CO* (1.22 and 3.67)
CH (OH site)	−0.51783, −0.51956	0.37733, 0.38486	CH* (2.22), CF* (1.49 and 4.55)
F σ lone pair	−1.03837	−1.03837	
F π lone pairs	−0.39561 −0.39755	−0.39561 −0.39755	CH* (5.69 and 4.47), CC* (6.00) C’H* (0.71)
O σ lone pair	−0.60791	−0.60791	
O π lone pair	−0.30056	−0.30056	CC* (0.96)

[a] The energies of NBO entities are reported in hartrees. The stabilizations are in kcal/mol. Interactions of “geminal” entities (sharing a common atom) and those less than 0.5 kcal/mol are not reported.

order of conformer stability with a single exception. The mean absolute deviation between our G2MP2 results and the Cramer–Truhlar reported MP2-based free energies is about 0.1 kcal/mol.

The three most stable conformers, all lying within a range of less than a kilocalorie/mole, all have gauche heavy-atom skeletons with O•••O distances in the range of 2.74 to 2.80 Å and OH bonds pointing into the interaction zone. The OH•••O angles for these species range between 85 and 115°. The set of all xGy structures have O•••O distances between 2.74 and 2.87 Å and include O•••H distances ranging from 2.24 to 3.63 Å. The longer distances are for systems in which the OH bond points out of the interaction zone. The energy difference of about 3 kcal/mol between the two types of structures may be a reasonable estimate of the strength of the interaction.

Question of Hydrogen Bonding

We have seen marked effects on conformational preference in $HOCH_2CH_2X$ arising from the special properties of the X•••HO interactions. One is tempted to call these X•••HO interactions hydrogen bonding, especially for X = F or OH. As context for the discussion of the interactions in 2-haloethanol and ethane-1,2-diol, we consider the complex of methanol with methyl fluoride and the methanol dimer. These resemble the 2-haloethanols and ethane-1,2-diol, but the OH•••OH and OH•••F approaches are not constrained by the short heavy-atom chain as in the substituted ethanes. We characterized the complexes by B3LYP/6-311G** optimization and NBO analysis of the DFT charge distribution. The reliability of density functional methods in the study of weak interactions has been judiciously reviewed.[28] On the basis of remarks in the review, we made no counterpoise corrections in any of our estimates of binding energies in the methanol–methyl fluoride complex or the methanol dimer. The methanol dimer is bound by about 9 kcal/mol compared with the system with the oxygens constrained to be separated by 20 Å. In the complex, the O•••O distance is about 2.80 Å, and the H•••O distance is about 1.88 Å. The O•••HO angle is about 160°, which departs from the ideal arrangement of 180°. We suggest that this may be a side effect of a very soft O•••HO deformation mode and the unsymmetric arrangement of the methyl groups. The methanol–methyl fluoride complex is bound by about 6 kcal/mol. The F•••O distance is 2.84 Å, the F•••H distance is 1.98 Å, and the OH•••F angle is about 150°. It is not surprising that the more weakly bound complex departs more severely from the ideal geometry than does the more strongly bound complex.

Hydrogen bonding of the form OH•••Z, with Z = OH or F, is expected to extend the participating OH bond and make the participating H more positive. In the complex of methyl fluoride and methanol, the expectations are fulfilled; upon complexation, the OH bond increases from 0.961 to 0.964 Å. The positive charge assigned by NBO analysis to the OH hydrogen increases from 0.441 to 0.455 electrons. In the methanol dimer, the OH bond extension is modest, from 0.966 to 0.968, and the NBO charge on H increases markedly from 0.441 to 0.473 electrons.

NBO analysis of the B3LYP/6-311G** density shows that as the conformation of 2-fluoroethanol changes from g*G to gG (moving the OH hydrogen toward the F) the NBO charge on the OH hydrogen increases only by 0.001 electron. In the process, the OH bond distances increase by 0.0028 Å in 2-fluoroethanol.

The NBO analysis of the B3LYP Fock matrix for the complex of methanol and methyl fluoride shows significant mixing from a F lone pair into the OH σ antibond, contributing a stabilization of 4.15 kcal/mol. This is entirely consistent with our understanding of hydrogen bonding. If we find some analogous mixing and stabilization in 2-haloethanols, we would be assured that hydrogen bonding as commonly understood would account for the preference of the Gg conformation. However, NBO output does not include the mixing of any F lone pair with the

OH antibond. (Table 7 shows a sample of the NBO report.) This means that such terms contribute less than 0.5 kcal/mol, the threshold for inclusion in the report. If one assumes that hydrogen bonding is an essentially a consequence of perturbative mixing, then we cannot claim that hydrogen bonding is at work in these systems. The OH···X angles in the most stable gG conformers of 2-haloethanols are much more acute (e.g., approximately 110° for the fluoro system) than the near-150° that the methanol−methyl fluoride complex favors. One may well consider any possible hydrogen bonding to be weakened as a consequence, relative to the complexes of molecules free to assume an optimum orientation.

There are other differences as well in the mixing patterns as the OH is rotated out of the zone of interaction and as bonds and lone pairs assume antiperiplanar orientation with various neighboring antibonds. We do not pursue the study of these details here.

Electrostatic Picture of Conformational Preferences

The conformational preferences in the 2-haloethanols can be considered to result from the simple electrostatic attraction of the positive hydrogen with the halogen. Figure 1 in which electrostatic potential is represented on an isodensity surface for each 2-halothanol makes this qualitatively clear. If electrostatic attractions of point charges at the halogen with those of the OH hydrogens tell the tale, then the most stable conformation should be predictable by molecular mechanics. This is the case. According to MMFF the Gg conformation is the most stable for the chloro and bromo systems by about 1.4 kcal/mol over tT, and the fluoro system's preference is greater, about 2.4 kcal/mol. This may be attributed to a fortunate alignment of the bond dipole for OH antiparallel with the bond dipole of CF. The CBr and CCl bond dipoles are smaller that the CF bond dipole and, according to NBO atomic charges, are perhaps even reversed in direction for CBr. The ranking of higher-energy structures is not reliable, but the range of energies of the set of conformations is realistic.

A very similar story plays out for ethane-1,2-diol. In the estimate of the stabilization of conformers of the diol, we found the −OH···O interaction to be about 3 kcal/mol. This is substantially less than the estimate of the binding energy in the methanol dimer, about 9 kcal/mol according to our B3LYP/6-311G** calculations. The dimer displays a minor OH bond extension from 0.966 to 0.969 Å and an increase in the NBO-assigned positive charge on the H from 0.4414 to 0.4737 electrons. The ethane-1,2-diol shows a similar OH bond extension from 0.961 to 0.964 Å and a smaller increase in charge on H from 0.4513 to 0.4664 electrons.

NBO analysis of the methanol dimer's B3LYP/6-311G** density reveals that O lone pairs mix with OH* and produce stabilizations of 2.71 and 6.16 kcal/mol. Once again, if we find similar mixing in the ethane-1,2-diols, we can attribute the stabilization to hydrogen bonding. NBO analysis of B3LYP/6-311G* densities for tTt, tGt, and tGg shows no such mixing except for the latter, the most stable of the conformer set and one in which the O···H distance is the shortest. That mixing, however, contributes a stabilization of only 0.67 kcal/mol, to be compared with the conformational energy differences of about 2.5 kcal/mol.

As we found in the 2-haloethanols, one need not appeal to hydrogen bonding of the type recognized in the methanol dimer to account for the conformational preferences in ethane-1,2-diol. The NBO analysis shows only minor perturbative mixing and stabilization compared with that found in the methanol dimer, and simple electrostatic stabilization of the negative oxygen in close proximity to the positive hydrogen suffices to explain the relative stabilities. This is made clear in Figure 1 in which the electrostatic potential is represented on the isodensity surface for these molecules.

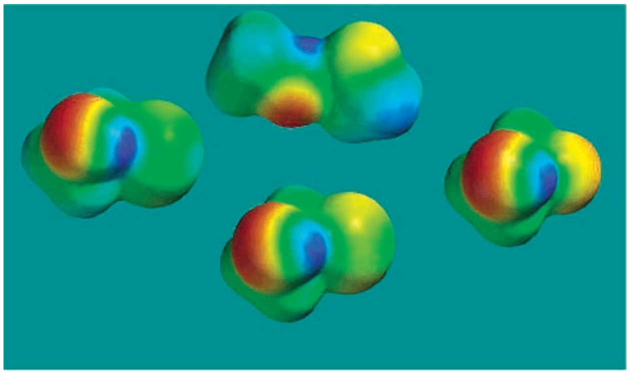

Figure 1. Electrostatic potential mapped onto the density isosurfaces for 2-haloethanols and the methanol−methylfluoride complex. Top center: methanol−methyl fluoride complex; left: 2-bromoethanol; right: 2-fluoroethanol; bottom center: 2-chloroethanol. Potential is color-coded according to the spectrum, with blue being most positive and red being most negative. In the Gg conformers of the 2-haloethanols, the OH is visible as a form with prominent red (O) and blue (H) coloring. The halogen immediately to the right of the OH zone ranges from predominantly green (a modestly negative potential) for Br to very yellow (a more strongly negative potential) for F; Cl is intermediate in potential and coloring. Alternating positive and negative zones suggest electrostatic stabilization. The separation of zones of opposite potential (which would be necessary to form the Gg* conformer from the Gg conformer) requires work. This picture makes plausible the idea that the Gg−Gg* energy differences are comparable for all halogens. The methanol−methyl fluoride complex can align atoms O−H···F more effectively so that the H-bonding region in which zones of differently signed potential are juxtaposed is not clearly visible. We can, however, see that the methyl groups (blue) lie far from one another.

As already observed for the 2-haloethanols, the most stable conformers of ethane-1,2-diol enjoy a favorable arrangement of point charges and a stabilizing antiparallel alignment of the OH and CO bond dipoles. If simple electrostatics again tells the tale, then molecular mechanics would capture the conformational preferences. An instant calculation shows that MM2 does in fact identify the three most stable conformers in the order established by much more demanding methods. As already observed,[25] this modest but surprising success cannot be matched by semiempirical methods.

The conformational preferences have been attributed to an improvement in the orbital overlap match between radical fragments in the gauche orientation as opposed to those in the trans orientation.[29] This seems to be a simple and appealing qualitative representation of what might be a subtle balance of many influences. If it is the significant effect, then it should be prominent in the results of the NBO analysis of local orbital mixing. Our results suggest that the mixing model provides at best a refinement of the simple electrostatic description, especially for the OH-substituted species.

Conclusions

We can now respond to the questions posed in the Introduction. The subtle choice of low-energy conformations in the 1,2-dihalosubstituted ethanes is apparently well described by G2MP2 calculations. The method captures the experimentally established preferences for gauche conformations in difluoroethane and in 1-fluoro and chloropropanes as well as in propan-1-ol. Systems with other halogens prefer a trans heavy-atom skeleton. If the substituents include hydroxyl, then G2MP2 confirms a marked preference for a gauche conformation of the heavy-atom chain and the placement of the hydroxyl so as to interact with the neighboring substituent.

NBO analysis of B3LYP densities shows the importance of $\sigma-\sigma^*$ mixing (hyperconjugation) in these systems. Such mixing is only one of several significant influences and may be masked by steric or electrostatic effects.

The gauche–gauche conformations that bring OH into proximity with halogen or OH are convincingly represented by G2MP2 as the preferred conformations in 2-haloethanols and ethane-1,2-diol. Although it may be tempting to ascribe this to hydrogen bonding, NBO analysis shows no significant $\sigma-\sigma^*$ mixing in the substituted ethanes. Such mixing is by contrast prominent in the complexes of methanol with fluoromethane or methanol, in which hydrogen bonding seems to be evident. Modeling methods with no recognition of mixing but that incorporate electrostatic attraction and a steric requirement—MMFF mechanics—do predict the most stable conformations in all of these OH-substituted systems.

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Supporting Information Available: Details of the energies evaluated in G2MP2 and geometric parameters for all species. This material is available free of charge via the Internet at http://pubs.acs.org.

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