Table III

fitting BE	zeolite X		zeolite Y	
	k, eV/electron	ΔV, eV	k, eV/electron	ΔV, eV
N_{1s}	−41.6	−7.4	−41.6	−6.6
O_{1s}	−19.4	−3.4	−19.4	−3.7
Si_{2p}	+7.0	−2.9	+7.0	−2.4

that the N_{1s} level is sensitive to charge transfer. Vice versa, the relatively small constant k of O_{1s} and Si_{2p} will result in a small chemical shift in binding energy. Thus the fwhm of these lines is still narrow, even though each line consists of several XPS peaks with different chemical shifts.

Further information can be drawn from the intercept I of the line in Figure 5, that is

$$\Delta V = B_0 - I \tag{5}$$

Equation 5 offers a simple way to determine the Madelung energy of the zeolite lattice from experimental data, provided the binding energy of the corresponding neutral atom is known. The $N_{1s}{}^0$, $Si_{2p}{}^0$, and $O_{1s}{}^0$ energies are roughly approached by the values in Me_4NCl (402.0 eV), Si (98.5 eV), and PhOCOOPh (535.0 eV)[7] compounds, respectively. The calculated ΔV values and also the measured constant k values are listed in Table III. The X zeolites possess slightly larger ΔV values than Y zeolites, which is consistent with the fact that higher Al content in zeolites produces more negative charges on the framework. Hence the contribution from Coulombic interaction between framework and extraframework cations increases, which will result in an increase of the total Madelung energy. The Madelung energy of the potassium zeolite X was calculated theoretically using a PLUTO program.[18] The average Madelung energy calculated using this method is about −14.7 eV for cations located at site II. This value is higher than our results but still comparable. The high value obtained by the PLUTO method might be due to the ionic crystal model for the zeolite lattice employed in the calculation, since the real zeolite lattice is only partially ionic.[1]

In summary, the XPS study suggests that the framework–cation interaction in alkali-cation-exchanged zeolites is limited to a short-range scope. The probe molecules containing N atoms are sensitive indicators of charge transfer in XPS experiments. The Si_{2p} binding energy level is not a good internal reference binding energy in XPS spectra for zeolites possessing low Si/Al ratios.

Registry No. Pyrrole, 109-97-7.

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Ab Initio Molecular Orbital Conformational Analysis of Prototypical Organic Systems. 1. Ethylene Glycol and 1,2-Dimethoxyethane

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Abstract: Ab initio calculations have been used to study the changes in energy of ethylene glycol and 1,2-dimethoxyethane as a function of rotation around the central C–C bond. Geometries have been fully optimized at the 3-21G and 6-31G* levels, and single-point calculations have been carried out at higher levels (up to 6-311++G** for ethylene glycol and 6-31+G* for 1,2-dimethoxyethane), including electron correlation up to MP4(SDTQ). For ethylene glycol, the H–O–C–C angles were started in a trans orientation to prevent intramolecular hydrogen bonding. In 1,2-dimethoxyethane, the C–O–C–C dihedral angles also were started in the trans orientation. At all levels of theory, both ethylene glycol and 1,2-dimethoxyethane slightly prefer a trans O–C–C–O orientation. For both molecules, the 3-21G relative energies are quite different from those calculated at the 6-31G* level, but all larger basis sets give relative energies which agree fairly well with the 6-31G* results. Electron correlation is shown to have a significant effect on the relative energies. The highest-level calculations for both ethylene glycol and 1,2-dimethoxyethane indicate that the trans–gauche energy difference is 0.4–0.5 kcal/mol. However, these values decrease as the basis set is increased, and, in the limits of infinite basis set and complete treatment of electron correlation, the trans–gauche difference for both molecules should be somewhat lower. Vibrational frequencies have been calculated for all conformers of both ethylene glycol and 1,2-dimethoxyethane; the effect of zero-point energies and vibrational enthalpies on the trans–gauche energy difference are quite small, but there is a more significant lowering of the barrier heights. To judge the importance of intramolecular hydrogen bonding in ethylene glycol, several lower-energy gauche O–C–C–O conformers which do possess intramolecular hydrogen bonds also were located. The global minimum has one H–O–C–C angle gauche and the other H–O–C–C angle trans, in agreement with experiment. The trans–trans–gauche conformer of 1,2-dimethoxyethane, with one gauche C–O–C–C angle, also was studied and was found to be ~1.5 kcal/mol above the all-trans global minimum. For both ethylene glycol and 1,2-dimethoxyethane, the MM2 force field does a reasonable job of reproducing the trans–gauche energy differences but is in poor agreement with the ab initio syn barriers to rotation. However, the MM3 barrier heights are in much better agreement with the ab initio data. Further, most of the other conformational energy differences also are better reproduced by MM3, which in many ways appears to provide a superior treatment for these 1,2-dioxy-substituted ethane derivatives.

Introduction

Many fundamental questions in conformational analysis may be addressed by the study of 1,2-disubstituted ethanes of the form X–C–C–Y.[1] These molecules may be viewed as *structural prototypes*—the simplest structures which incorporate functional groups commonly found in larger systems. While it is usually the case that a trans orientation of the X–C–C–Y fragment is energetically preferred, there are cases in which there is no sig-

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† Vertex Pharmaceuticals.
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Table I. Calculated Conformational Energy Differences[a]

compound	basis set	calcd	expt
butane	MP3/6-31G*	0.86	0.89
2-methylbutane	MP3/6-31G*	0.81	0.75
2,3-dimethylbutane	MP3/6-31G*	0.07	0.05
acetaldehyde	MP3/6-31G*	1.03	1.17
2-methoxytetrahydropyran	6-31G*//3-21G	0.91	0.89
1,2-difluoroethane	MP3/6-311++G**	−0.76	−0.57, −0.83, −0.96
1,2-dichloroethane	MP4/6-31++G**	1.35	1.1–1.2

[a] Relative energies in kcal/mol.

nificant difference in energy between trans and gauche. Further, a few molecules of this type are actually known to prefer a gauche orientation in the gas phase. The barriers to rotation around the C–C bond also are of interest, as they can vary over a wide range.

It is important to realize that a gauche preference may result from intramolecular hydrogen bonding. Hydrogen bonding, for instance, explains the strong gauche preference seen in such molecules as 2-fluoroethanol, 2-chloroethanol, and ethylene glycol. In other cases, however, there is no possibility of such an effect, and the cause of the unusual gauche preference is less clear. Examples where hydrogen bonding is not a factor include 1,2-difluoroethane, in which the gauche form is preferred by 0.5–0.9 kcal/mol,[2,3] and 2,3-dimethylbutane, in which the trans and gauche forms are of equal energy.[4,5]

Ab initio calculations[6] represent a useful tool in the study of trans–gauche energy differences and rotational barriers. In recent studies, high-level ab initio calculations have been shown to reproduce the experimental trans–gauche energy differences in a variety of systems (Table I). In all cases, the calculated trans–gauche energy differences agree with the experimental values to within experimental error.[3,5,7–11]

Theoretical approaches allow one to calculate the energies of structures which are difficult or impossible to study experimentally. The energy differences between the global minimum conformation and these higher-energy structures, although seldom accessible through experimental methods, are nonetheless of great importance for developing a more complete understanding of intramolecular interactions. For instance, it was shown that when the possibility of intramolecular hydrogen bonding in 2-fluoroethanol was eliminated by constraining the C–C–O–H dihedral angle to be trans, there was little difference in energy between the gauche and trans F–C–C–O rotamers of 2-fluoroethanol. On the other hand, when the C–C–O–H dihedral angle in 2-chloroethanol was likewise forced to be trans, there was a preference of ∼1.0 kcal/mol for a trans Cl–C–C–O dihedral angle. In other words, there was little or no intrinsic trans preference in 2-fluoroethanol, but there was a typical trans preference in 2-chloroethanol.[11] These energies cannot be derived from experiment but provide useful information for understanding the intramolecular forces in these molecules.

As stated above, there is no generally accepted explanation for these unusual trans–gauche energy differences. However, it was first noted more than a decade ago that the substitution of more electronegative groups at the X and/or Y positions often leads to stabilization of the gauche form relative to trans.[12] Similar findings have recently been reported by Hedberg.[13] One explanation is due to Wiberg and co-workers, who have used Bader's methodology to analyze the bond paths in trans and gauche 1,2-difluoroethane.[14] They found that the gauche preference is caused by a destabilization of the trans form which results from more severely bent bonds and reduced bond overlap in the trans conformer as compared to the gauche conformer. Bond bending in 1,2-disubstituted ethanes is directly related to the electronegativity of the substituents, so this result for 1,2-difluoroethane also may shed light on other systems with electronegative substituents.

Another interesting finding from ab initio calculations on heteroatom-containing 1,2-disubstituted ethanes is that syn (0°) rotational barriers are generally larger in such compounds than in butane. This can be rationalized by the large dipole moment commonly found in the syn conformers of these systems, but the precise calculation of barrier heights is difficult even with high-level theory.[3,11]

An important class of compounds in this series is the 1,2-dioxy-substituted ethanes. Molecules in this category include ethylene glycol (EG) and 1,2-dimethoxyethane (DME). Clearly, it is of fundamental interest to determine the energy difference between the gauche and trans O–C–C–O orientations in these systems. There are also significant practical concerns, given the importance of EG in a variety of chemical processes as well as the frequent occurrence of the O–C–C–O moiety in organic compounds.[15]

In the case of EG, it is known experimentally that the central O–C–C–O dihedral prefers to adopt a gauche conformation;[16–18] calculations at various levels of theory reproduce this result.[19–23] This gauche preference, like that of the 2-haloethanols,[11] results from hydrogen bonding and thus tells us nothing directly about the *intrinsic* preferences of the O–C–C–O fragment. The more relevant datum in this context would be the O–C–C–O trans–gauche difference in EG with both H–O–C–C torsions in trans orientations. Of course, this conformation is not readily attainable experimentally. One theoretical estimate is available from Nagy and co-workers, who have been studying the gas-phase and aqueous solution-phase properties of EG.[21,22] The trans[21] and gauche[22] conformers were reported separately, but by comparing their results a trans preference of 0.91 kcal/mol may be deduced at the MP2/6-31G* level and increased to 1.00 kcal/mol after the inclusion of corrections for zero-point energy (ZPE) and vibrational enthalpy.

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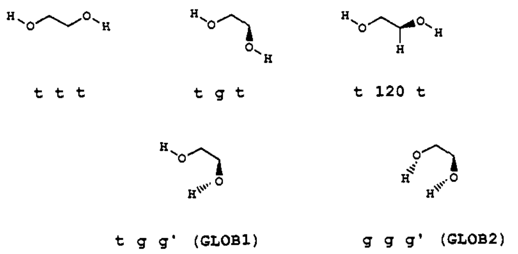

Figure 1. Conformers of ethylene glycol (EG).

For DME, the data are less clear.[24-31] As intramolecular hydrogen bonding is not possible in this case, the experimental values may be used directly. While there is some evidence that the gauche form is preferred, the exact value is uncertain and depends somewhat on phase. Solution experiments[24,29] indicate a strong gauche preference; Monte Carlo simulations are routinely able to reproduce this phenomenon.[28,30] Gas-phase experiments[25,27,29,31] suggest a much smaller gauche preference. Ab initio calculations,[26] however, show a small preference for the trans form.

Despite the ab initio calculations reported for both EG[19-23] and DME,[26] a careful study of the trans–gauche energy differences using extended basis sets and electron correlation has not been carried out. Our previous experience with heteroatom-containing systems suggests that such high-level calculations are essential in order to achieve accurate results.[3,5,7-11] To help ascertain the trans–gauche energy differences in EG and DME, as well as the rotational barriers, a series of ab initio calculations has been carried out. In this paper, larger basis sets and more complete treatment of electron correlation have been employed, and the results are compared to those of the earlier studies. To check our results against both experiment and the earlier theoretical studies, we also have located several conformers of EG which exhibit intramolecular hydrogen bonding. Finally, molecular mechanics calculations employing several popular force fields have been carried out on the same conformers of EG and DME, and the results are compared to the ab initio data and to experiment.

Calculational Details

Calculations on EG were carried out by starting the H–O–C–C dihedral angles at 180° and locating the four stationary points (two minima, two maxima) with respect to the central O–C–C–O dihedral angle. The 0° and 180° structures are constrained by symmetry. In the gauche structure, the O–C–C–O dihedral was allowed to fully relax. In the 120° transition state, a single H–C–C–O dihedral was fixed at zero, and all other internal coordinates were allowed to relax. These optimizations were carried out at the 3-21G and 6-31G* levels. Next, single-point calculations were performed including the effects of electron correlation through the third-order Møller–Plesset[32] level using the 6-31G*, 6-31+G*, and 6-311G** basis sets and through fourth-order (SDTQ) using the 6-311++G** basis set. Finally, the H–O–C–C and O–C–C–O torsion angles were rotated to allow intramolecular hydrogen bonding. Two structures, both with lower absolute energy than any of the trans O–C–C–O conformers, were located using the 6-31G* basis set. Figure 1 shows all the EG conformers studied. Frequency calculations confirmed that both of these were local minima. Single-point calculations at higher levels also were carried out on these structures. Table II summarizes the geometric data for all the EG structures, while Table III gives the energies. Vibrational frequencies are given in Table IV.

Table II. Ethylene Glycol Geometries[a]

3-21G Optimized Geometries

coord	180	gauche	120	0
r(HO)	0.9650	0.9651	0.9656	0.9666
r(CO)	1.4409	1.4415	1.4452	1.4347
r(CC)	1.5147	1.5145	1.5319	1.5524
a(HOC)	111.20	111.04	110.79	109.57
a(OCC)	105.40	106.93	107.16	109.62
t(OCCO)	180.00	78.15	120.23	0.00
t(HOCC)	180.00	200.00[b]	186.41	180.00
dipole moment (μ)	0.00	1.55	1.18	3.19

6-31G* Optimized Geometries

coord	180	gauche	120	0
r(HO)	0.9462	0.9462	0.9467	0.9465
r(CO)	1.4029	1.4005	1.4050	1.3963
r(CC)	1.5129	1.5106	1.5268	1.5451
a(HOC)	109.73	109.74	109.50	108.60
a(OCC)	107.22	108.90	108.57	0.00
t(OCCO)	180.00	71.67	120.82	0.00
t(HOCC)	180.00	193.50	182.15	180.00
dipole moment (μ)	0.00	1.72	1.23	2.75

Intramolecular Hydrogen Bonding Structures, 6-31G* Geometries

coord	GLOB1	GLOB2
r(OH1)	0.9464	0.9475
r(CO1)	1.4077	1.4089
a(COH1)	110.23	109.66
r(CC)	1.5138	1.5172
a(CCO1)	106.75	110.55
t(CCOH1)	190.66	76.56
r(CO2)	1.3972	1.3964
r(OH2)	0.9487	0.9490
t(OCCO)	60.91	58.19
a(COH2)	107.69	107.90
a(CCO2)	111.31	111.11
t(CCOH2)	−54.01	−46.41
dipole moment (μ)	2.68	2.65

[a] Bond lengths in angstroms, angles in degrees. [b] H–O–C–C torsion fixed at 200°; no stationary point could be located on the 3-21G potential surface with H–O–C–C trans.

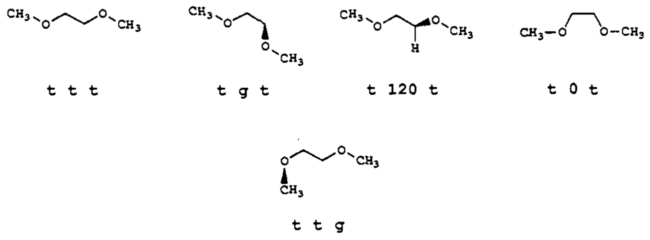

Figure 2. Conformers of 1,2-dimethoxyethane (DME).

For DME, the optimizations were carried out in the same way, again using the 3-21G and 6-31G* basis sets. In addition to the four conformers with a trans C–C–O–C dihedral, a local minimum structure with trans O–C–C–O and gauche C–C–O–C torsions was located. MP3/6-31G*//6-31G* single-point calculations were carried out on all five structures followed by single points at the MP4(SDTQ)/6-31+G*//6-31G* level. Geometries are given in Table V and energies in Table VI. Vibrational frequencies

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Table III. Ethylene Glycol Energies[a]

	180	gauche	120	0	GLOB1	GLOB2
Absolute Energies, Various Basis Sets						
3-21G	−227.65298	0.64829	0.64598	0.63164	0.65731	0.65592
6-31G*	−228.92243	0.91973	0.91585	0.90517	0.92573	0.92466
MP2	−229.53525	0.53351	0.52937	0.51847	0.54062	0.54025
MP3	−229.56025	0.55826	0.55446	0.54354	0.56510	0.56464
6-31+G*	−228.93291	0.93026	0.92679	0.91529	0.93579	0.93435
MP2	−229.55752	0.55609	0.55255	0.54002	0.56258	0.56157
MP3	−229.57997	0.57823	0.57498	0.56265	0.58454	0.58354
6-311G**	−228.99916	0.99656	0.99264	0.98182		
MP2	−229.69963	0.69809	0.69392	0.68320		
MP3	−229.72396	0.72224	0.71834	0.70788		
6-311++G**	−229.00738	0.00524	0.00136	0.99004	0.01019	0.00867
MP2	−229.71589	0.71515	0.71104	0.69943	0.72077	0.71978
MP3	−229.73802	0.73699	0.73310	0.72189	0.74244	0.74146
MP4(SDQ)	−229.73486	0.73386	0.72994	0.71875	0.73927	0.73888
MP4(SDTQ)	−229.75834	0.75759	0.75361	0.74241	0.76301	0.76212
Relative Energies, Various Basis Sets						
3-21G	0.00	2.94	4.39	13.39	−2.71	−1.84
6-31G*	0.00	1.69	4.13	10.83	−2.07	−1.40
MP2	0.00	1.09	3.69	10.53	−3.37	−3.14
MP3	0.00	1.25	3.63	10.49	−3.04	−2.75
6-31+G*	0.00	1.66	3.84	11.06	−1.81	−0.90
MP2	0.00	0.90	3.12	10.98	−3.18	−2.54
MP3	0.00	1.09	3.13	10.87	−2.87	−2.24
6-311G**	0.00	1.63	4.15	11.01		
MP2	0.00	0.97	3.58	10.31		
MP3	0.00	1.08	3.53	10.09		
6-311++G**	0.00	1.34	3.78	10.88	−1.76	−0.81
MP2	0.00	0.46	3.04	10.33	−3.06	−2.44
MP3	0.00	0.64	3.09	10.12	−2.77	−2.16
MP4(SDQ)	0.00	0.63	3.09	10.11	−2.77	−2.21
MP4(SDTQ)	0.00	0.47	2.97	10.00	−2.93	−2.37

[a] Absolute energies in hartrees, relative energies in kcal/mol.

were calculated at the 6-31G* level and are given in Table VII. Figure 2 shows the five conformers of DME.

All ab initio calculations were carried out using Gaussian86[33] and Gaussian88.[34]

Empirical forcefield calculations ("molecular mechanics") were carried out using the MM2 force field[35] as implemented in Macromodel Version 2.5 (Prof. Clark Still, Columbia University), MM3,[36] and CHARMm.[37,38]

Results

Ethylene Glycol (EG). Considering the geometries in Table II, it is clear that there is a steric repulsion between the oxygens in the gauche form. The O–C–C angles are larger in the gauche form than in the trans, and the O–C–C–O dihedral angle is larger than 60°. There is even more strain in the two eclipsed forms as measured by the significant opening of the O–C–C angles and the lengthening of the central C–C bond relative to the trans conformation.

Considering the data in Table III, it is clear that the relative energies as a function of O–C–C–O torsion angle are quite different at the 3-21G level than with any other basis set tested. The energy differences between trans and gauche and between trans and the two eclipsed forms all are much larger at the 3-21G level than with any other basis set tested. Examining the energies in Table III more carefully, we observe a gradual decrease in ΔE (trans–gauche) as the basis set is enlarged. It is not possible to state what the Hartree–Fock limit is for this problem, but a further drop of ~0.3 kcal/mol is entirely possible. This would put the trans–gauche difference at ~1 kcal/mol. Electron correlation is also seen to have a large effect on the relative energies. For instance, at the 6-31+G* level, the trans–gauche energy difference is 1.66 kcal/mol, but when electron correlation is included (MP3), the difference drops to 1.09 kcal/mol. At the 6-311++G** level, the effect is even greater: the HF trans–gauche difference is 1.34, but the MP4(SDTQ) difference is only 0.47. The post-Hartree–Fock relative energies are also basis set dependent, and in the limit of infinitely large basis sets and complete treatment of electron correlation, the trans–gauche energy difference should be somewhat lower, perhaps near 0.

We also wanted to determine the structures of EG that can form intramolecular hydrogen bonds (i.e., those which have a gauche O–C–C–O arrangement). These are the conformations seen experimentally[16-18] and the ones usually explored by theoretical methods.[19-23] We also were interested in determining the energy difference between the conformers which were able to form intramolecular hydrogen bonds and those in which the trans H–O–C–C torsions eliminated the possibility of such H-bonding. Figure 1 shows the two H-bonded conformers we considered, GLOB1 (t-G-g′) and GLOB2 (g-G-g′). Geometric data for these conformers are given in Table II and energies in Table III. As expected, GLOB1 and GLOB2 both are lower in energy than any of the conformers which cannot form intramolecular hydrogen bonds. GLOB1, with one H–O–C–C torsion trans and one gauche, is the global minimum structure, ~2.8 kcal/mol lower than the all-trans conformer. GLOB2, with both H–O–C–C torsions gauche, is ~2.2 kcal/mol below the all-trans conformer. Recent experimental[16-18] and theoretical[19-23] studies generally agree that the GLOB1 conformer, with its t-G-g′ torsion angles, is the global minimum in aqueous solution.

Vibrational frequencies, calculated at the 6-31G* level, are reported in Table IV. Zero-point energy and enthalpy corrections have only a small effect on trans–gauche relative energies but do

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Table IV. Ethylene Glycol Vibrational Frequencies, 6-31G* Basis Set

O–C–C–O Torsion = 0°, Both H–O–C–C Torsions = trans								
A1	314.1	957.7	1246.9	1346.8	1645.3	1702.3	3188.2	4115.0
A2	243.8*i*	258.1	1265.8	1408.9	3180.1			
B1	280.7	950.2	1421.0	3216.9				
B2	635.5	1201.6	1392.9	1599.7	1679.4	3164.9	4114.2	
O–C–C–O Torsion = 120°, Both H–O–C–C Torsions = trans								
A	153.0*i*	307.4	467.0	942.4	1079.3	1217.6	1386.9	1406.5
	1644.4	1671.5	3203.0	3250.5	4115.4			
B	297.4	453.0	1135.7	1227.8	1337.5	1410.6	1565.7	1679.9
	3181.7	3246.2	4115.5					
O–C–C–O Torsion = gauche, Both H–O–C–C Torsions = trans								
A	178.8	207.6	361.8	958.2	1156.2	1235.9	1376.2	1448.4
	1642.4	1666.9	3190.6	3219.0	4122.3			
B	214.7	541.1	1005.1	1204.8	1330.6	1426.1	1581.0	1664.0
	3169.1	3236.3	4121.9					
O–C–C–O Torsion = trans, both H–O–C–C Torsions = trans								
AG	517.1	1067.7	1203.9	1412.0	1646.4	1681.1	3199.3	4123.7
AU	151.9	275.9	900.0	1353.9	3251.2			
BG	271.1	1277.0	1430.5	3221.9				
BU	320.7	1197.0	1295.5	1554.2	1689.5	3200.8	4123.8	
O–C–C–O Torsion = gauche, One H–O–C–C Torsion = gauche (GLOB1)								
	188.3	291.0	350.5	458.8	569.3	955.1	976.6	
	1170.1	1208.9	1240.6	1274.8	1385.3	1416.9	1516.3	
	1564.4	1613.1	1657.8	1669.2	3190.3	3199.5	3235.1	
	3279.3	4094.3	4123.2					
O–C–C–O Torsion = gauche, Both H–O–C–C Torsions = gauche (GLOB2)								
	185.7	331.6	350.2	476.3	576.1	946.5	970.9	
	1154.0	1180.9	1231.4	1307.0	1351.4	1503.8	1512.3	
	1548.4	1589.6	1652.4	1664.3	3156.2	3205.7	3269.3	
	3296.8	4087.6	4102.5					

lower the barriers to rotation by ~0.5–0.6 kcal/mol (Table VIII). When reporting calculated rotational barriers it is important to clearly distinguish between energy and enthalpy and to indicate the temperature.[39]

A plot of relative energy as a function of O–C–C–O torsion angle is given in Figure 3. The highest-level ab initio data, obtained at the MP4(SDTQ)/6-311++G**//6-31G* level and corrected for vibrational effects, is compared to the results from MM2, MM3, and CHARMm.

1,2-Dimethoxyethane (DME). As with EG, the gauche form of DME has a larger O–C–C angle than the trans form, and the eclipsed structures have larger O–C–C angles and longer C–C bonds (Table V). The relative energies calculated at the 3-21G level are quite different than those calculated using larger basis sets (Table VI). It again appears to be the case that the trans–gauche energy difference gets smaller when electron correlation is included. Our most extensive calculations on DME, at the 6-31+G*//6-31G* level, indicate that there is a trans–gauche energy difference of ~1.4 kcal/mol at the Hartree–Fock level but only ~0.4 kcal/mol after correlation at the MP4(SDTQ) level is added. Again, there is some basis set dependence in both the HF and the post-HF relative energies, and, in the limit of infinite basis set and complete treatment of electron correlation, we expect the trans–gauche energy difference to be somewhat lower, perhaps near 0. This is in good agreement with the experimental gas-phase NMR result of 0.3 kcal/mol favoring gauche.[31]

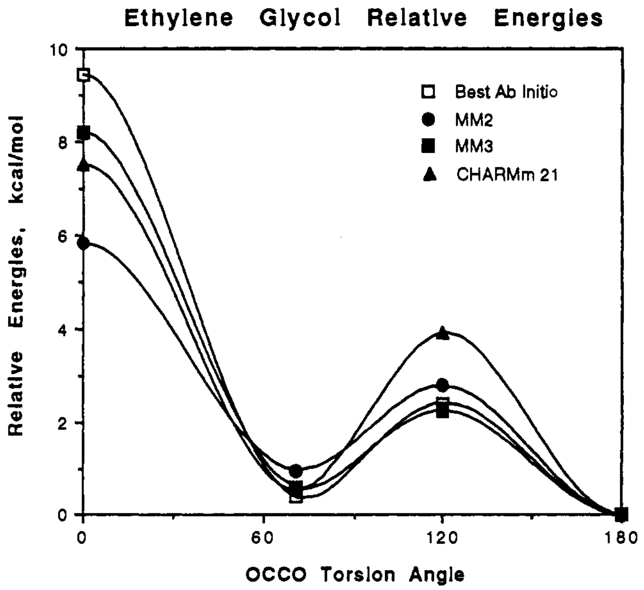

Figure 3. Ethylene glycol (EG), relative energy versus O–C–C–O torsion angle. The highest-level ab initio results, MP4(SDTQ)/6-311++G**//6-31G*, are compared with MM2, MM3, and CHARMm Version 21.[37] The H–O–C–C torsion angle are trans. Energies are in kcal/mol.

Various experimental reports[27,29] suggest that one of the low-energy conformations of DME in the gas phase adopts a gauche C–O–C–C orientation. It is known that the gauche conformation of the C–O–C–C fragment in ethers is less stable than the trans by ~1.5 kcal/mol,[8,40–42] but we wished to see whether this strong trans preference would also apply in DME. As reported in Table VI, at our highest levels this conformer is 1.44 kcal/mol above the all-trans global minimum. If this result is accurate, one might expect to see a small amount of this conformer in the gas phase (perhaps as much as 10%). This is consistent with the experimental reports.[27,29] Also, it is encouraging that the calculated C–O–C–C torsion angle, 89°, agrees well with the proposed torsion angle derived from electron diffraction work on DME[27] as well

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Table V. 1,2-Dimethoxyethane Geometric Data[a]

Conformers With Trans C–O–C–C Orientation, 3-21G Basis Set

coord	180	60	120	0
r(C1–O2)	1.4325	1.4321	1.4324	1.4328
r(O2–C3)	1.4337	1.4336	1.4376	1.4268
r(C3–C4)	1.5161	1.5156	1.5313	1.5521
a(C1–O2–C3)	114.92	114.68	114.45	113.76
a(O2–C3–C4)	105.93	107.36	107.60	110.14
t(O2–C3–C4–O5)	180.00	78.24	119.96	0.00
t(C1–O2–C3–C4)	180.00	187.82	183.85	180.00
dipole moment (μ)	0.00	1.58	1.02	2.54

Conformers With Trans C–O–C–C Orientation, 6-31G* Basis Set

coord	180	60	120	0
r(C1–O2)	1.3922	1.3911	1.3915	1.3901
r(O2–C3)	1.3947	1.3926	1.3972	1.3880
r(C3–C4)	1.5139	1.5107	1.5265	1.5444
a(C1–O2–C3)	114.29	114.17	113.98	113.51
a(O2–C3–C4)	107.70	109.31	108.99	111.37
t(O2–C3–C4–O5)	180.00	71.89	120.70	0.00
t(C1–O2–C3–C4)	180.00	184.43	181.21	180.00
dipole moment (μ)	0.00	1.53	0.95	2.06

Gauche C–O–C–C Conformer, *C*1 Symmetry, 3-21G and 6-31G* Basis Sets

internal coord	3-21G	6-31G*
r(C1–O2)	1.4327	1.3922
r(O2–C3)	1.4333	1.3943
a(C1–O2–C3)	115.04	114.44
r(C3–C4)	1.5227	1.5200
a(O2–C3–C4)	105.42	107.52
t(C1–O2–C3–C4)	181.79	181.21
r(C4–O5)	1.4358	1.3982
a(C3–C4–O5)	110.75	111.50
t(O2–C3–C4–O5)	178.96	179.44
r(O5–C6)	1.4350	1.3945
a(C4–O5–C6)	115.67	115.73
t(C3–C4–O5–C6)	85.49	89.25
dipole moment (μ)	2.29	1.78

[a] Bond lengths in Angstroms, bond and torsion angles in degrees.

as with the calculated C–O–C–C angle for methyl propyl ether.[8]

Vibrational frequencies for DME have been calculated at the 6-31G* level and are reported in Table VII. As with EG, zero-point energy and enthalpy corrections have essentially no effect on trans-gauche relative energies while barriers are lowered by ~0.5–0.6 kcal/mol (Table VIII).

A plot of relative energy as a function of O–C–C–O torsion angle in DME is given in Figure 4. The highest-level ab initio data, obtained at the MP4(SDTQ)/6-31+G*//6-31G* level and corrected for vibrational effects, is compared to the results from MM2, MM3, and CHARMm.

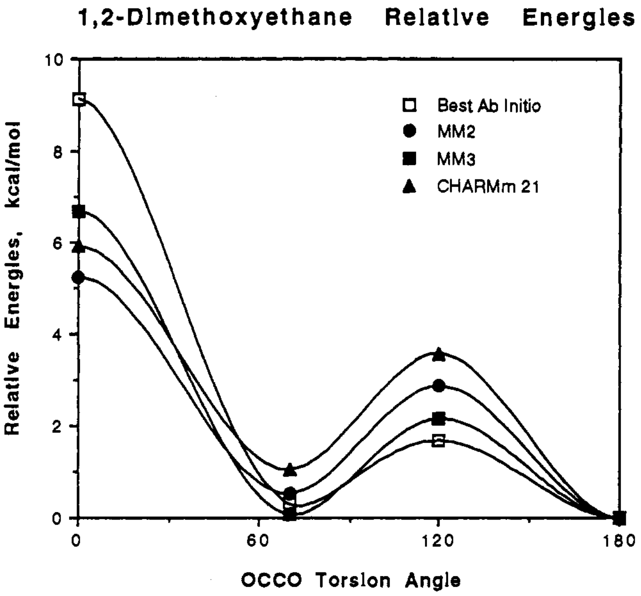

Figure 4. 1,2-Dimethoxyethane (DME) relative energy versus O–C–C–O torsion angle. The highest-level ab initio results, MP4(SDTQ)/6-31+G*//6-31G*, are compared with MM2, MM3, and CHARMm Version 21.[37] The C–O–C–C torsion angles are trans. Energies are in kcal/mol.

Force Field Calculations. We have compared the MM2,[35] MM3,[36] and CHARMm[37,38] results with those obtained by high-level ab initio calculations. These data are summarized in Table IX.

First we consider the MM2 force field. For EG, the trans-gauche energy difference calculated with MM2 is 0.97 kcal/mol, in fair agreement with the highest-level ab initio result, 0.38 kcal/mol. The gauche O–C–C–O torsion angle is 71°, in excellent agreement with the 6-31G* optimized value, 72°. For DME, the trans form is favored by 0.51 kcal/mol, in fair agreement with the experimental data and best ab initio calculations, while the O–C–C–O dihedral is 68°, again in good agreement with the experimental value, 72°. For DME, the conformer with one C–C–O–C gauche torsion was found to be 2.13 kcal/mol above the all-trans form, with a gauche angle of 78°; these are somewhat off from the ab initio values of 1.44 kcal/mol and 89°. Finally, the two hydrogen-bonding conformers of EG, GLOB1 (t-G-g′) and GLOB2 (g-G-g′), were found to be ~1.7 and ~0.6 kcal/mol more stable than the t-t-t form, only in fair agreement with the

Table VI. 1,2-Dimethoxyethane Energies, Various Basis Sets[a]

	0	gauche	120	180	gauche–COCC
		Absolute Energies			
3-21G	−305.261 86	−305.277 55	−305.275 59	−305.282 03	−305.279 63
6-31G*	−306.964 18	−306.977 96	−306.974 24	−306.980 20	−306.977 29
MP2	−307.834 50	−307.848 40	−307.844 51	−307.849 37	−307.846 96
MP3	−307.877 07	−307.890 77	−307.887 23	−307.892 13	−307.889 68
6-31G*	−306.972 40	−306.986 69	−306.983 36	−306.988 94	−306.985 86
MP2	−307.854 57	−307.869 75	−307.866 59	−307.870 38	−307.867 90
MP3	−307.895 52	−307.910 36	−307.907 45	−307.911 38	−307.908 87
MP4(SDQ)	−307.912 64	−307.927 48	−307.924 55	−307.928 35	−307.925 93
MP4(SDTQ)	−307.939 25	−307.954 07	−307.951 10	−307.954 68	−307.952 39
		Relative Energies			
3-21G	12.66	2.81	4.04	0.00	1.51
6-31G*	10.05	1.41	3.74	0.00	1.82
MP2	9.33	0.61	3.05	0.00	1.51
MP3	9.45	0.85	3.07	0.00	1.54
6-31+G*	10.38	1.41	3.50	0.00	1.93
MP2	9.92	0.40	2.38	0.00	1.56
MP3	9.95	0.64	2.47	0.00	1.58
MP4(SDQ)	9.86	0.55	2.38	0.00	1.52
MP4(SDTQ)	9.68	0.38	2.25	0.00	1.44

[a] Absolute energies in hartrees, relative energies in kcal/mol.

Table VII. 1,2-Dimethoxyethane Vibrational Frequencies, 6-31G* Basis Set

A1	172.4	386.5	993.7	1159.5	1309.1	1370.1	1599.3	1638.2
	1660.4	1699.6	3162.6	3180.5	3305.9			
A2	228.8*i*	127.4	236.0	1261.2	1307.9	1413.3	1645.5	3167.2
	3212.1							
B1	86.0	250.8	953.8	1299.4	1430.8	1645.5	3202.2	3213.0
B2	370.1	674.5	1144.9	1278.4	1379.2	1571.1	1637.2	1656.1
	1682.3	3149.5	3170.6	3305.3				
			O–C–C–O Torsion = 120°					
A	127.9*i*	89.5	232.6	347.4	402.5	939.5	1138.4	1168.8
	1290.4	1298.8	1368.2	1409.9	1604.3	1642.6	1645.1	1657.1
	1674.7	3172.0	3192.4	3221.3	3236.2	3304.0		
B	104.7	238.1	272.8	588.0	1040.8	1223.5	1285.3	1300.6
	1357.7	1409.0	1532.0	1631.7	1645.1	1655.9	1682.4	3165.1
	3177.7	3221.1	3232.2	3303.7				
			O–C–C–O Torsion = 180°					
AG	356.3	426.4	1122.2	1174.2	1297.2	1377.4	1604.4	1645.2
	1659.0	1681.5	3174.0	3190.3	3304.8			
AU	74.7	123.6	254.1	902.7	1295.6	1367.0	1645.3	3224.8
	3236.2							
BG	129.8	231.8	1268.6	1311.5	1427.7	1645.4	3207.9	3225.0
BU	159.4	543.6	1067.4	1288.0	1361.7	1507.2	1632.5	1657.7
	1688.9	3173.5	3190.4	3304.6				
			O–C–C–O Torsion = gauche					
A	80.1	133.7	247.6	294.7	390.8	950.4	1143.4	1229.5
	1296.3	1312.6	1365.0	1441.4	1601.8	1639.4	1645.6	1655.3
	1673.1	3166.7	3182.2	3205.4	3220.1	3304.6		
B	85.2	235.4	337.6	617.9	964.9	1166.7	1282.2	1296.9
	1363.2	1401.6	1551.5	1632.2	1645.6	1653.2	1673.0	3153.5
	3173.9	3218.9	3222.7	3304.3				
			O–C–C–O = Trans, C–O–C–C = gauche					
	73.6	94.6	122.2	165.6	237.0	244.0	396.4	478.8
	509.5	880.6	1046.3	1101.9	1159.3	1233.2	1289.3	1292.4
	1295.4	1321.5	1360.0	1366.7	1405.4	1450.1	1497.7	1595.6
	1632.6	1640.3	1645.5	1648.8	1657.5	1660.2	1667.6	1685.2
	3168.8	3180.6	3186.7	3204.4	3217.6	3225.1	3234.8	3287.8
	3304.2	3304.9						

Table VIII. Vibrational Corrections to Relative Energies[a]

Ethylene Glycol, MP4(SDTQ)/6-311++G**//6-31G*

item	180	gauche	120	0	GLOB1	GLOB2
ZPE	51.92	51.79	51.89	51.82	52.26	52.29
$H_{298}-H_0$	1.64	1.68	1.11	1.18	1.43	1.39
total vibrational	53.56	53.47	53.00	53.00	53.69	53.68
best ab initio result	0.00	0.47	2.97	10.00	−2.93	−2.37
corrected results	0.00	0.38	2.41	9.44	−2.80	−2.25

1,2-Dimethoxyethane, MP4(SDTQ)/6-31+G**//6-31G*

item	180	gauche	120	0	COCC gauche
ZPE	86.39	86.39	86.32	86.32	86.40
$H_{298}-H_0$	3.31	3.24	2.79	2.81	3.32
total vibrational	89.70	89.63	89.11	89.13	89.72
best ab initio result	0.00	0.38	2.25	9.68	1.44
corrected results	0.00	0.31	1.66	9.11	1.46

[a] Scaling the ab initio frequency by 0.9.

ab initio results, ~2.8 and ~2.2 kcal/mol, respectively. Significantly, the barriers to rotation in both EG and DME as calculated with MM2 are both considerably lower than those calculated with ab initio methods.

The MM3 force field gives a trans–gauche energy difference of 0.60 kcal/mol in EG, in reasonable agreement with the ab initio result of 0.38 kcal/mol, while the calculated gauche torsion angle is 77°, in fair agreement with the experimental value, 72°. For DME, the trans–gauche difference is 0.06 kcal/mol while the gauche torsion angle is 74°. The GLOB1 hydrogen-bonding conformer of EG is calculated to be 2.90 kcal/mol more stable than the all-trans t-t-t form, in near-perfect agreement with our best available ab initio results. The t-t-g conformer of DME gives a relative energy of 1.73 kcal/mol and a gauche torsion angle of 78°, in reasonable agreement with the calculated values of 1.46 kcal/mol and 89°, respectively. The barriers to rotation calculated with MM3 are 2.24 and 8.19 kcal/mol for EG, in reasonable agreement with the ab initio results, 2.41 and 9.44 kcal/mol. Likewise, the barriers in DME are calculated by MM3 to be 2.14 and 6.67 kcal/mol, in fair agreement with the ab initio barrier heights, 1.66 and 9.11 kcal/mol. While there are still differences between the ab initio and MM3 barrier heights, the agreement is much better for both DME and EG than was found with MM2.

We also have checked the macromolecular force field CHARMm;[37,38] these results are included in Table IX. Here, the gauche form of EG is found to be higher than the trans form by 0.54 kcal/mol, in good agreement with the ab initio result, 0.38 kcal/mol. Further, the gauche torsion angle is calculated to be 72°, identical with the molecular orbital value. However, for DME, the trans–gauche difference and gauche torsion angle are 1.03 kcal/mol and 66°, respectively, in less satisfactory agreement with the experimental values of ~0.3 kcal/mol favoring gauche DME and a torsion angle of 72°. The GLOB1 and GLOB2 hydrogen-bonding conformers of EG are calculated to be 4.37 and 3.27 kcal/mol, respectively, more stable than the all-trans t-t-t form. The t-t-g conformer of DME gives a relative energy and torsion angle of 1.23 kcal/mol and 81°, respectively. The barriers to rotation calculated with CHARMm are 3.90 and 7.51 kcal/mol for EG, in poor agreement with the ab initio results, 2.41 and 9.44 kcal/mol. Likewise, the barriers in DME are calculated by CHARMm to be 3.56 and 5.90 kcal/mol, also in poor agreement with the ab initio barrier heights, 1.66 and 9.11 kcal/mol.

In Figures 3 and 4, the results of the MM2, MM3, and CHARMm calculations for EG and DME are compared with the highest-level, vibrationally-corrected ab initio results.

Discussion

The trans preferences reported here for EG and DME are both small. The trends in our data suggest that larger basis sets and more complete treatment of electron correlation would further

Table IX. Comparison of MM2,[a] MM3,[b] and CHARMm[c] with ab Initio Results[d]

conf	ab initio	MM2	MM3	CHARMm
Ethylene Glycol				
t-t-t	0.00	0.00	0.00	0.00
t-g-t	0.38 (72)	0.97 (71)	0.60 (77)	0.54 (72)
t-120-t	2.41	2.78	2.24	3.90
t-0-t	9.44	5.83	8.19	7.51
t-G-g′	−2.80 (169, 61, −54)	1.67 (174, 56, −49)	−2.90 (180, 60, −51)	−4.37 (176, 58, −58)
g-G-g′	−2.25 (77, 58, −46)	−0.50 (88, 58, −48)	N/A[e]	−3.27 (83, 57, −49)
1,2-Dimethoxyethane				
t-t-t	0.00	0.00	0.00	0.00
t-g-t	0.31 (72)	0.51 (68)	0.06 (74)	1.03 (66)
t-120-t	1.66	2.86	2.14	3.56
t-0-t	9.11	5.24	6.67	5.90
t-t-g	1.46 (89)	2.13 (78)	1.73 (78)	1.23 (81)

[a] MM2 calculations performed using Macromodel Version 2.5, a program available from Dr. Clark Still of Columbia University. [b] MM3 values for GLOB1 (t-G-g′) conformer of EG was taken from ref 48. All other MM3 calculations using the 1991 parameter set were performed by Professor N. L. Allinger and Dr. Yi Fan of the University of Georgia. A constant dielectric of 1.5 was used. [c] CHARMm calculations performed with the commercial package Quanta/CHARMm. A constant dielectric of 1 was used. The charge templates method was used to assign point charges. [d] Using the ab initio relative energies from Tables III and VI. These have been corrected for vibrational effects. Dihedral angles, where applicable, are given in parentheses. [e] Not available.

lower this energy difference. Thus, in the limit of infinite basis set and complete treatment of electron correlation, the gas-phase trans–gauche energy difference for both EG and DME may well be approximately 0. It seems clear that the "normal" trans preference of ~1 kcal/mol which is found in alkanes[5] is somewhat reduced in 1,2-dioxy-substituted ethanes. In light of previous work[2,3,11–14] which clearly demonstrates a relationship between the electronegativity of the substituents and the gauche preference, it is not surprising to find a small calculated preference in these molecules as well. Of course, structural factors also may contribute to the smaller trans–gauche energy differences seen with electronegative substituents. For example, the effect might be related to the fact that molecules such as 1,2-dimethoxyethane lack the 1,6 H–H interactions which are thought to be repulsive in gauche butane.

Electron correlation also lowers the syn barrier to rotation in both EG and DME by ~0.7 kcal/mol. Clearly it is advisable to perform post-HF calculations on these kinds of systems if at all possible. It is also interesting to note that the 120° barrier in DME is quite low, ~2.2 kcal/mol before correction for vibrational effects and ~1.7 kcal/mol after correction. It is not clear why the 120° barrier in DME should be considerably lower than that for EG, while the 0° (syn) barriers are approximately the same for the two molecules.

It appears that for both EG and DME the 3-21G basis set gives much less reliable relative energies than larger basis sets which include polarization functions. The same kind of unreliable results were obtained for 1,2-dichloroethane when the very similar 4-31G basis set was used.[3] It is clearly advisable to include polarization functions at least on the non-hydrogen atoms when studying systems containing heteroatoms.

The data in Table VIII confirm that vibrational effects such as ZPE and $H_{298}-H_0$ have a negligible effect on relative energies of local minima but do lower the barriers to rotation by ~0.5 kcal/mol.

Empirical force field calculations (molecular mechanics) provide an inexpensive way to determine approximate conformational energies for organic systems.[43] For example, a number of workers have attempted to use molecular mechanics calculations in their studies of polyoxide polymers containing O–C–C–O units.[44–47] It is also true that many common organic systems contain the O–C–C–O fragment,[15] and EG and DME are prototypes of such systems. It is clearly desirable from many points of view that force field calculations on these types of molecules be as accurate as possible. The MM2[35] and MM3[36] molecular mechanics force fields are among the most widely used for small molecules, and CHARMm[37,38] is widely used for studies involving macromolecules. MM3[36] contains many improvements in its treatment of alcohols and ethers.[48] In Table IX we summarize the comparisons between the ab initio results and those obtained with the various force fields. All in all, these findings indicate that MM2 and CHARMm force fields are reasonably accurate at calculating the relative energies of the local minima for both EG and DME, although for the hydrogen-bonding conformations of EG there can be errors of 1–2 kcal/mol. On the other hand, the MM3 results are generally in better agreement both with the ab initio results and the experimental data. For example, the MM3 trans–gauche energy difference for DME is ~0, in good agreement with the most recent experimental gas-phase result, ~0.3 kcal/mol favoring the gauche form. Further, the energy difference between the t-t-t conformer of EG and the global minimum structure, which has a t-G-g′ conformation and one internal hydrogen bond, has been studied with MM3[48] and is in near-perfect agreement with our best results.[49]

Another interesting point about the data in Table IX is that the relative energies of the eclipsed syn conformations (with O–C–C–O torsions of 0°) are always higher according to the ab initio calculations than to the force fields. This difference is shown graphically in Figure 3 for EG and in Figure 4 for DME. The 298 K barrier in EG is ~9.4 kcal/mol, while the force fields give values ranging from 5.8 to 8.2 kcal/mol; in DME, while the force fields give results between 5.2 and 6.7 kcal/mol, the ab initio 298 K value is ~9.1 kcal/mol. It is important to distinguish between 0 K and room temperature barriers and to clearly specify whether energy, enthalpy, or free energy is being calculated.[39] However, it is difficult to rationalize any way in which vibrational, enthalpic, and entropic effects could account for a discrepancy of ~5 kcal/mol. In fact, the data in Table VIII indicate that vibrational corrections of ~0.6 kcal/mol are more reasonable, and these corrections have already been included in the data in Table IX. However, we note that the MM3 barriers are in much better agreement with the calculated barriers. The disagreement for

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(49) The 1992 version of the MM3 forcefield now has a direction-dependent functional form to describe hydrogen bonding. The direction-dependent function does a much better job overall of reproducing geometries, dipole moments, etc. However, this work is still in progress and it is not currently possible to calculate the "MM3(92)" relative energies for ethylene glycol. Thus, for our GLOB1 conformer of EG, we have used the original literature treatment of EG as described in reference 48. In that reference, the calculated energy difference between the t-t-t and t-G-g′ conformers of EG was 2.90 kcal/mol, in excellent agreement with all available high-level ab initio results.

the syn barrier in EG is ~1.2 kcal/mol and is ~2.4 kcal/mol for DME. This is considerably better than the errors of up to 4 kcal/mol which are seen in MM2 and CHARMm.

There are several factors that may be contributing to the remaining differences in the barrier heights calculated with the ab initio and MM3 methods. First, only minimum energy structures are used to develop the force field, and the long extrapolation to transition states is always error-prone. Second, as we have seen here and elsewhere,[3,5,7-11] transition-state structures are often stabilized, relative to ground states, by the inclusion of correlation and augmented basis sets. When these are improperly treated in the transition-state structures, the calculated barriers are simply too high. This proposition has been put forward recently to explain the ~1.0 kcal/mol discrepancy between the ab initio and MM2-calculated barrier heights in butane.[39] In fact, it is difficult to rule out the possibility that errors in the ab initio results are solely responsible for the different calculated barrier heights for EG, where the MM3 syn barrier is only ~1.2 kcal/mol lower than the ab initio barrier. Third, the molecular mechanics force field has been parameterized to reproduce experimental data, some of which has been obtained in the condensed phase (pure liquid or solution). The dipole moment of the syn barrier in EG and DME is quite large, and this conformer will be greatly stabilized in polar solvents relative to the gas phase. This effect has been seen, for example, in the 1,2-dihaloethanes, in which the population of gauche conformer increases with solvent polarity.[3,4,50] It would be instructive to analyze the Monte Carlo simulations of DME in aqueous media to see whether an estimate of the syn barrier heights may be derived and, if so, whether the barriers are significantly lowered.[28,30] To the extent that solution-phase experimental data have been used in the parameterization of a force field, we should not expect the gas-phase ab initio calculation to agree perfectly with results from that force field. Note that this is not a criticism of either approach but rather is simply a reminder that they are providing energy estimates for different reference states.

This suggests that it might be useful to reexamine all of the data used in parameterizing popular force fields for consistency. We may find that the accuracy and general utility of our force fields will improve if the "training set" used in the parameterization process is *reference-state consistent*. For example, one might imagine that only room temperature aqueous-phase solution data should be used, or 0 K gas-phase MP2/6-31G* ab initio results.[51] This aspect of force field parameterization may yet be crucial and warrants further study.

Note Added in Proof. As this manuscript went to press, we completed calculations on trans and gauche DME using even larger basis sets. At the 6-311++G**//6-31G* level, the absolute energy of the trans conformer was −307.070 54 hartrees and the relative energy of the trans conformer was found to be only 1.22 kcal/mol above the gauche form. At the MP2 level, the absolute energy of the trans form was −308.072 22 hartrees and the trans–gauche energy difference shrank to 0.21 kcal/mol. These are the smallest trans–gauche differences yet calculated at the HF and MP2 levels, respectively, supporting the hypothesis put forward here that the "limiting ab initio value" of the trans–gauche enthalpy difference in DME is approximately zero.

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Registry No. $HO(CH_2)_2OH$, 107-21-1; $MeO(CH_2)_2OMe$, 110-71-4.

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