

Theoretical Calculations on 1,2-Ethandiol. Gauche-Trans Equilibrium in Gas-Phase and Aqueous Solution

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Abstract: The gauche-trans equilibrium of 1,2-ethandiol was investigated in the gas phase and in aqueous solution with ab initio quantum chemical calculations and Monte Carlo simulations. MP2/6-31G**//6-31G* energy calculations and HF/6-31G* normal frequency analyses were carried out for the tGg', gGg', g'Gg' (gauche), and tTt (trans) isomers. The free energy of the most stable tGg' isomer with an intramolecular hydrogen bond is more negative by 2.8 kcal/mol than the trans form at $T = 298$ K. This coincides with the experimental finding of no trans rotamer in the gas phase. The effect of hydration on the equilibrium ratio was followed by statistical perturbation calculations using the Monte Carlo method at $T = 298$ K and $P = 1$ atm. In solution only three conformers were considered. On the basis of the gas-phase rigid-rotation potential map, two different paths were considered for the tTt to tGg' transformation and a single path for the tGg' to gGg' change. The solvation free energy for the trans rotamer is more negative by 1.2 kcal/mol than that for tGg'. Also gGg' is stabilized by about 1.0 kcal/mol upon solvation. Considering both total internal and hydration free energies, the solution contains about 97% gauche conformers. This is basically in accordance with recent NMR results. The solution structure was analyzed with use of energy pair and radial distribution functions obtained after taking 6000K configurations. Positions of the water molecules around the solutes were determined by statistical averaging of about 4500 snapshots of the solution configurations. The first hydration shell of the 1,2-ethandiol solute contains approximately six water molecules. There are, on average, four water molecules strongly hydrogen bonded to the solute in the tTt conformation. This number decreases for gauche conformers with intramolecular hydrogen bonds in solution. The water-solute hydrogen bonds are slightly bent with a favorable O...H distance of 1.8-1.9 Å. Water molecule acceptors in these bonds are more localized than those acting as proton donors.

Introduction

In theoretical studies of the mechanism of chemical processes that occur in solution, it has only recently been possible to consider explicitly the role of solvent. The use of quantum mechanical and molecular mechanical based methods limits one to consideration of gas-phase processes. It has been shown, however, that these limitations can be partially overcome by integrating the two approaches with Monte Carlo¹ or molecular dynamics² methods to yield realistic simulations of chemical processes. Several solutes, small ones and biomolecules, have been investigated in aqueous solution.^{1c} Here we report our study on a bifunctional polar molecule, 1,2-ethandiol.

1,2-Ethandiol is a simple representative of a system with "competing" H bonds.³ There is competition between intramolecular hydrogen bonding and hydrogen bonding to water due to hydration by solvent. The results for its equilibrium structure in aqueous solution may indicate general tendencies for similar systems, too.

The solute is a member of the 1,2-disubstituted ethane series for which there are a number of experimental structure determinations in the gas phase^{4,5} and ab initio calculations for the conformer energies.^{6,7} The diol conformation was investigated in the gas phase by electron diffraction,⁸ microwave,⁹ and infrared spectroscopic methods.^{10,11} These studies show that 1,2-ethandiol has a gauche O-C-C-O linkage with a possible mixture of the tGg' and gGg' conformers (Figure 1). NMR results by Chidichimo et al.¹² in the lyotropic liquid crystalline solution also find a gauche O...O arrangement. Ab initio calculations for ten conformers were carried out by Radom et al.⁶ using the 4-31G basis set and by Van Alsenoy et al.^{13a} using the 4-21G basis set and total geometry optimization. The tGg' conformer was found to be the most stable, and tTt, the most stable T form, is higher in energy by 2.0-2.6 kcal/mol. Very recently Cabral et al.^{13b} performed MP2/6-31G* and 6-31G** calculations with geometry optimization for the tGg', gGg', and tTt conformers. gGg' and

tTt are higher at the MP2/6-31G* level than tGg' by 0.2 and 3.6 kcal/mol, respectively.

If a process in solution is being considered, the contribution to the total free energy change due to solvation must also be known. As an approximation the optimal bond lengths and bond angles determined for the isolated molecule are not modified during solvation. Then the conformation of the solute will be defined by the minimum of the sum of two free energy functions: one calculated for the gas-phase molecule with different conformations and the other calculated from the free energy change following the solvation of these conformers. Such a combined

(1) (a) Valteau, J. P.; Torrie, G. M. In *Modern Theoretical Chemistry*; Berne, B. J., Ed.; Plenum Press: New York, 1977; Vol. 5. (b) Beveridge, D. L.; Jorgensen, W. L., Eds.; Computer Simulation of Chemical and Biomolecular Systems. *Ann. N.Y. Acad. Sci.* **1986**, 482. (c) Beveridge, D. L.; Di Capua, F. M. *Annu. Rev. Biophys. Chem.* **1989**, 18, 431.

(2) (a) Van Gunsteren, W. F.; Weiner, P. K., Eds. *Computer Simulation of Biomolecular Systems*; Escom: Leiden, 1989. (b) McCammon, J. A.; Harvey, S. C. *Dynamics of Proteins and Nucleic Acids*; Cambridge University Press: Cambridge, 1987.

(3) See e.g.: (a) Schuster, P.; Zundel, G.; Sandorfy, C. *The Hydrogen Bond*; North-Holland: Amsterdam, 1976; Vols. I-III. (b) Kollman, P. A. In *Modern Theoretical Chemistry*; Schaefer, H. F., III, Ed.; Plenum Press: New York, 1977; Vol. 4, Chapter 3. (c) Hobza, P.; Zahradnik, R. *Chem. Rev.* **1988**, 88, 871. (d) Beyer, A.; Karpfen, A.; Schuster, P. *Top. Current Chem.* **1984**, 120, 1. (e) Del Bene, J. E. *J. Chem. Phys.* **1987**, 86, 2110. Del Bene, J. E. *J. Phys. Chem.* **1988**, 92, 2874. Del Bene *J. Comput. Chem.* **1989**, 10, 603. (f) Alagona, G.; Ghio, C.; Cammi, R.; Tomasi, J. In *Molecules in Physics, Chemistry, and Biology*; Marunai, J., Ed.; Kluwer Academic Publishers: Dordrecht, 1988; Vol. II, p 507. (g) Kumpf, R. A.; Damewood, J. R., Jr. *J. Phys. Chem.* **1989**, 93, 4478 and references therein.

(4) Almennigen, A.; Fernholt, L.; Kveseth, K. *Acta Chem. Scand.* **1977**, 31, 297.

(5) Huang, J.; Hedberg, K. *J. Am. Chem. Soc.* **1989**, 111, 6909.

(6) Radom, L.; Lathan, W. A.; Hehre, W. J.; Pople, J. A. *J. Am. Chem. Soc.* **1973**, 95, 693.

(7) Vazquez, S.; Mosquera, R. A.; Rios, M. A.; Van Alsenoy, C. *J. Mol. Struct. (THEOCHEM)* **1989**, 188, 95.

(8) Bastiansen, O. *Acta Chem. Scand.* **1949**, 3, 415.

(9) Caminati, W.; Corbelli, G. *J. Mol. Spectrosc.* **1981**, 90, 572.

(10) Frei, H.; Ha, T.-K.; Meyer, R.; Gunthard, H. H. *Chem. Phys.* **1977**, 25, 271.

(11) Takeuchi, H.; Tasumi, M. *Chem. Phys.* **1983**, 77, 21.

(12) Chidichimo, G.; Imbardelli, D.; Longeri, M.; Saupe, A. *Mol. Phys.* **1988**, 65, 1143.

(13) (a) Van Alsenoy, C.; Van Den Enden, L.; Schafer, L. *J. Mol. Struct. (THEOCHEM)* **1984**, 108, 121. (b) Cabral, B. J. C.; Albuquerque, L. M. P. C.; Fernandes, F. M. S. *Theor. Chim. Acta* **1991**, 78, 271.

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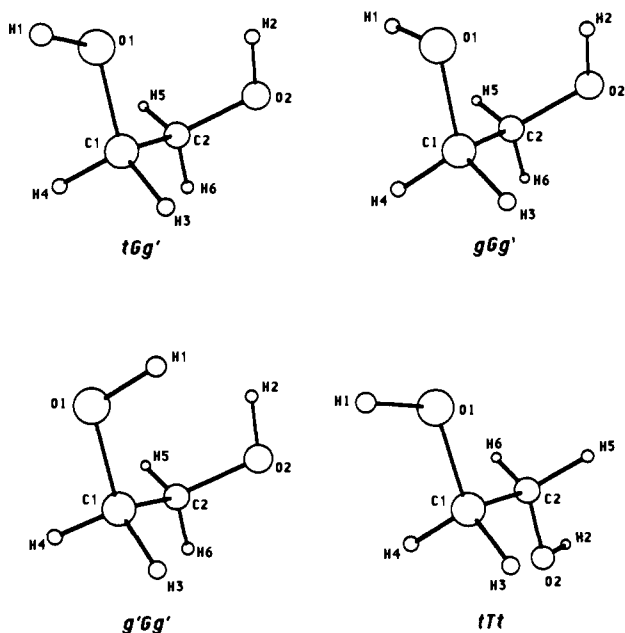


Figure 1. Schematic representation of the 1,2-ethanediol conformations considered: tGg', gGg', g'Gg', and tTt.

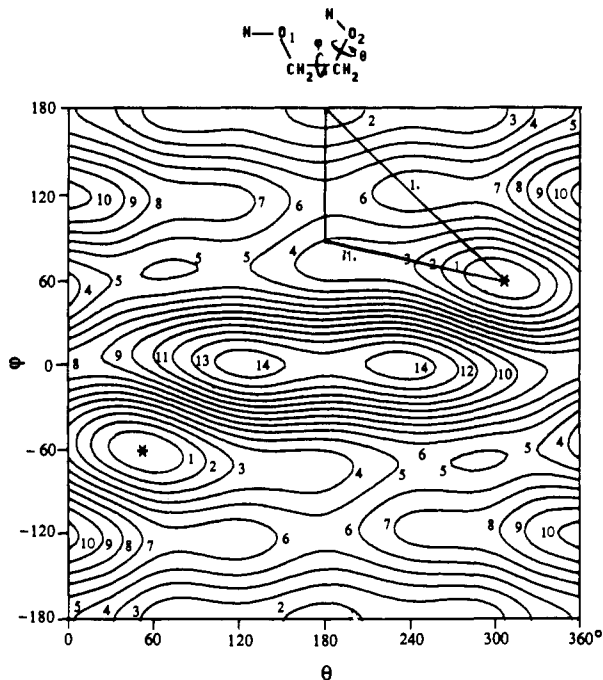


Figure 2. Potential energy hypersurface map of 1,2-ethanediol for rigid rotation about the C-C (ϕ) and C-O (θ) bonds (counterclockwise rotations are taken as positive; $H_1O_1C_1C_2$ is kept fixed at 180° ; the $\phi = \theta = 0^\circ$ conformer is displayed in the figure; the asterisk stands for the minimum energy value, taken as zero). Conformations along paths I and II were considered in calculating relative hydration free energy between tTt and tGg'. Energy in kcal/mol.

quantum chemical-statistical thermodynamic study for the 1,2-ethanediol-water system is presented in this paper. This method has been applied to calculate the total free energy difference for several chemical systems in solution.¹⁴

(14) (a) Mezei, M.; Mehrotra, P. K.; Beveridge, D. L. *J. Am. Chem. Soc.* **1985**, *107*, 2239. (b) Jorgensen, W. L.; Gao, J. *J. Am. Chem. Soc.* **1988**, *110*, 6283. (c) Cieplak, P.; Bash, P.; Singh, U. C.; Kollman, P. A. *J. Am. Chem. Soc.* **1987**, *109*, 6283. (d) Cox, J. R.; Woodcock, S.; Hillier, I. H.; Vincent, M. A. *J. Phys. Chem.* **1990**, *94*, 549. (e) Jayaram, B.; Mezei, M.; Beveridge, D. L. *J. Am. Chem. Soc.* **1988**, *110*, 1691. (f) Alagona, G.; Ghio, C.; Kollman, P. A. *J. Am. Chem. Soc.* **1985**, *107*, 2229. (g) Cieplak, P.; Kollman, P. A. *J. Am. Chem. Soc.* **1988**, *110*, 3734. (h) Grootenhuys, P. D. J.; Kollman, P. A. *J. Am. Chem. Soc.* **1989**, *111*, 2152.

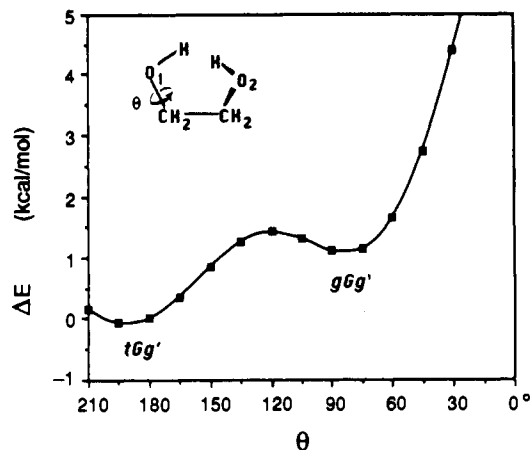


Figure 3. Potential energy profile for the rigid rotation of 1,2-ethanediol about the C_1-O_1 (θ) bond (counterclockwise rotations are taken as positive; the $\theta = 0^\circ$ cGg' conformer is displayed in the figure). Energy in kcal/mol.

Table I. Molecular Parameters for the 6-31G* Optimized Structures^a

	tGg'	gGg'	g'Gg'	tTt
C1C2	1.514	1.517	1.516	1.513
C1O1	1.408	1.409	1.405	1.403
C2O2	1.397	1.397	1.406	1.403
H1O1	0.946	0.948	0.946	0.946
H2O2	0.949	0.949	0.947	0.946
C1H3	1.087	1.082	1.087	1.087
C1H4	1.088	1.088	1.083	1.087
C2H5	1.088	1.091	1.087	1.087
C2H6	1.083	1.083	1.083	1.087
H1O1C1	110.24	109.58	108.84	109.74
H2O2C2	107.76	107.97	108.79	109.74
O1C1C2	106.72	110.56	111.17	107.24
O2C2C1	111.34	111.18	111.12	107.24
H3C1C2	109.54	109.65	109.65	109.26
H4C1C2	110.24	110.88	110.13	109.26
H5C2C1	109.13	109.55	109.74	109.26
H6C2C1	109.96	110.40	110.11	109.26
H3C1O1	110.73	106.13	110.72	111.51
H4C1O1	111.02	111.14	107.04	111.51
H5C2O2	111.06	110.83	110.70	111.51
H6C2O2	107.18	107.26	107.05	111.51
H1O1C1C2	-170.90	75.95	-81.8	180.00
O1C1C2O2	60.56	59.66	59.4	180.00
H2O2C2C1	-53.92	-46.70	-81.5	180.00

^aDistances in Å, angles in deg.

Analysis of the structure of the first hydration shell around a solute with a polar group may help in elucidating reaction mechanisms in aqueous solution¹⁵ and the structural basis of physicochemical properties such as the partition coefficient.¹⁶

Method and Calculations

Ab initio quantum chemical calculations were carried out with use of the 6-31G* basis set¹⁷ to determine the gas-phase conformational energies of 1,2-ethanediol. The UNIX version of the GAUSSIAN '86 program package,¹⁸ running on a Gould NPI computer, was used. Four different

(15) (a) Weiner, S. J.; Seibel, G. L.; Kollman, P. A. *Proc. Natl. Acad. Sci. U.S.A.* **1986**, *83*, 649. (b) Tapia, O.; Lluch, J. M.; Cardenas, R.; Andres, J. *J. Am. Chem. Soc.* **1989**, *111*, 829. (c) Tucker, S. C.; Truhlar, D. G. *J. Am. Chem. Soc.* **1990**, *112*, 3347. (d) Haydock, K.; Lim, C.; Brunger, A. T.; Karplus, M. *J. Am. Chem. Soc.* **1990**, *112*, 3826.

(16) (a) Dunn, W. J., III; Grigoras, S.; Koehler, M. G. *J. Med. Chem. Struct.-Act. Rel.* **1988**, *7*, 150.

(17) (a) Hariharan, P. C.; Pople, J. A. *Theor. Chim. Acta* **1973**, *28*, 213. (b) Hehre, W. J.; Radom, L.; Schleyer, P. v. R.; Pople, J. A. *Ab Initio Molecular Orbital Theory*; John Wiley and Sons: New York, 1986.

(18) GAUSSIAN '86: Frisch, M. J.; Binkley, J. S.; Schlegel, H. B.; Raghavachari, K.; Melius, C. F.; Martin, R. L.; Stewart, J. J. P.; Bobrowicz, F. W.; Rohlfing, C. M.; Kahn, L. R.; Defrees, D. J.; Seeger, R.; Whiteside, R. A.; Fox, D. J.; Fleuder, E. M.; Pople, J. A.; Carnegie-Mellon Quantum Chemistry Publishing Unit, Pittsburgh, PA, 1984.

Table II. Vibrational Frequencies (cm⁻¹) (6-31G* Basis Set)

	tGg'	gGg'	g'Gg'	tTt ^a		exp ^{10,11}
1	189.0	181.9	97.8	152.4	a _u	212
2	290.6	334.9	167.4	270.4	b _g	268
3	350.9	353.0	338.0	275.2	a _u	309-319
4	457.5	475.1	466.9	320.8	b _u	319-384
5	569.6	574.7	576.0	516.7	a _g	514-529
6	954.9	945.2	953.0	899.9	a _u	863-880
7	975.8	972.6	958.6	1067.2	a _g	880-1005
8	1170.5	1153.9	1151.7	1196.2	b _u	1029-1042
9	1209.5	1180.4	1170.7	1203.3	a _g	1040-1072
10	1241.5	1230.2	1233.4	1276.9	b _g	1100
11	1273.7	1306.1	1291.8	1295.3	b _u	1160-1163
12	1384.2	1350.9	1367.5	1353.8	a _u	1238-1246
13	1416.9	1503.8	1519.0	1411.8	a _g	1254-1272
14	1516.2	1512.4	1520.4	1430.5	b _g	1348-1350
15	1565.7	1568.1	1549.2	1554.0	b _u	1382-1384
16	1613.3	1589.4	1575.3	1646.1	a _g	1413-1416
17	1658.1	1652.4	1649.5	1681.0	a _g	1458-1462
18	1669.5	1663.8	1675.0	1689.4	b _u	1465-1495
19	3189.3	3155.9	3208.7	3199.3	a _g	2885
20	3198.7	3205.6	3210.5	3200.8	b _u	2891
21	3234.0	3270.2	3272.4	3222.0	b _g	2940
22	3278.3	3296.4	3276.6	3251.3	a _u	2968
23	4094.5	4086.3	4118.0	4123.7	a _g	3593-3638
24	4122.8	4101.9	4120.6	4123.8	b _u	3644-3671

^a Normal modes of vibrations are indicated for tTt with C_{2i} symmetry.

conformers of 1,2-ethanediol were investigated, namely tGg', gGg', g'Gg', and tTt, displayed in Figure 1. In order to elucidate the in vacuo barriers connecting the tTt conformer to the tGg' one, a potential energy hypersurface map (Figure 2) was calculated employing bond lengths and angles taken from Jorgensen.¹⁹ Rigid rotor approximation was applied for torsions about the C-C bond (ϕ) and about one of the C-O bonds (θ) with torsional angle changes of 30°. The position of the other hydrogen was kept trans to the C-C bond throughout (see the diagram at the top of Figure 2). The minimal energy conformer is a tGg' type with OCCO = 60° and HOCC = 307° in Figure 2. These values were used for the subsequent rigid rotation leading from tGg' to gGg' (Figure 3). The structures corresponding to local minima in Figures 2 and 3 were then fully optimized at the HF/6-31G* level. Optimized geometric parameters are given in Table I, and the calculated normal frequencies are compared with experimental values in Table II. Correlation energies for the different conformations, found important for the protonated 1,2-ethanediol by Ikuta and Nomura^{20a} and for 2-aminoethanol by Vanquickenborne et al.,^{20b} were calculated at the MP2 level.²¹ HF/6-31G* and MP2/6-31G*//6-31G* energies and zero-point corrections are given in Table III. Calculated enthalpy, entropy, and free energy differences²² at T = 298 K are also shown in that table.

By considering the internal motion as torsion or inversion with wavenumbers below 500 cm⁻¹, the calculated enthalpy and entropy may be overestimated seriously.^{17b} This question was investigated in our study at three different levels for the tTt conformer. First, all internal torsions were considered as vibrations. In the second approximation free H rotations were assumed for the HOCC torsions. In the third case these torsions were considered as hindered internal rotations.²³ The HOCC and OCCO torsions were considered as vibrations in the tGg', gGg', and g'Gg' conformers.

For a free rotation, the partition function, Q_{fr}, and the corresponding contribution to the free energy, F_{fr}, are^{22,23}

$$Q_{fr} = (1/n)(8\pi^3 I_r kT/h^2)^{1/2} \quad (1)$$

$$F_{fr} = -RT \ln Q_{fr} \quad (2)$$

where n is the symmetry number and I_r is the reduced moment of inertia

Table III. Energy Contributions (kcal/mol) Relative to the tGg' Conformer in the Gas Phase^a

	gGg'	g'Gg'	tTt
HF	0.68	1.29	2.07
MP2	0.24	1.25	3.36
ZPE	0.03 (0.03)	-0.23 (-0.25)	-0.34 (-0.38)
MP2+ZPE	0.27	1.02	3.02
Thermal Corrections (T = 298 K)			
H	-0.04 (-0.04)	0.20 (0.22)	0.21 (0.22)
-TS	0.06 (0.06)	-0.29 (-0.28)	-0.03 (-0.02) + RT ln 2
G	0.02	-0.09	0.59 (vibr) -1.03 (free rot.) -0.18 (hind. rot.)
MP2+-ZPE+G	0.29	0.93	3.61, 1.99, 2.84

^a Energies for tGg': HF = -228.925725 au, E₂ = -0.614888 au, ZPE = 0.092551 au. Values in parentheses are calculated with use of unscaled frequencies. Abbreviations vibr, free rot., and hind. rot. for G(tTt) refer to free energies obtained with different models for low-energy torsions in tTt (see text).

referring to the axis of the rotation. Other symbols have the usual meanings.

In evaluating the free energy contribution of a hindered rotation the approximation of Kilpatrick and Pitzer²⁴ was applied:

$$F = -RT(\ln Q_{class} + a/2 - a^2/24) \quad (3)$$

where

$$Q_{class} = (2\pi kT I_r/h^2)^{1/2} \int_0^{2\pi} \exp(-V(\theta)/RT) d\theta \quad (3a)$$

$$a = h\nu^*/kT \quad (3b)$$

Here ν^* is the wave number of the torsional vibration in question and V(θ) is the potential energy function of the H rotation. The V(θ) function has a periodicity of 360°, so the symmetry number is 1. The two internal motions were considered as independent hindered rotations with an average wavenumber of 244 cm⁻¹ and with a barrier of 3.5 kcal/mol obtained from Figure 2. To calculate I_r for a single asymmetric top we used the formula of Pitzer and Gwinn.²⁵ The necessary axes and values of the moments of inertia of the whole molecule were calculated from the optimized structural parameters of tTt.

(24) Kilpatrick, J. E.; Pitzer, K. S. *J. Chem. Phys.* **1949**, *17*, 1064.

(25) Pitzer, K. S.; Gwinn, W. D. *J. Chem. Phys.* **1942**, *10*, 428.

(19) Jorgensen, W. L. *J. Phys. Chem.* **1986**, *90*, 1276.

(20) (a) Ikuta, S.; Nomura, O. *Chem. Phys. Lett.* **1989**, *154*, 71. (b) Vanquickenborne, L. G.; Coussens, B.; Verlinde, C.; De Ranter, C. *J. Mol. Struct. (THEOCHEM)* **1989**, *201*, 1.

(21) (a) Moller, C.; Plesset, M. S. *Phys. Rev.* **1934**, *46*, 618. (b) Pople, J. A.; Binkley, J. S.; Seeger, R. *Int. J. Quant. Chem. Symp.* **1976**, *10*, 1.

(22) McQuarrie, D. *Statistical Mechanics*; Harper and Row: New York, 1976.

(23) (a) Pitzer, K. S. *Quantum Chemistry*; Prentice-Hall, Inc.: New York, 1953. (b) Davidson, N. *Statistical Mechanics*; McGraw-Hill: New York, 1962.

Table IV. Thermodynamic Data of Solvation and Total Free Energy Differences in Aqueous Solution

	λ^a	ΔG	ΔH	$T\Delta S$	ΔE_{SX}	ΔE_{SS}
tTt	0.000	0.0	0.0	0.0	0.0	0.0
	0.125	-0.5	-8.2	-7.7	0.6	-8.8
	0.250	-1.7	-12.2	-10.5	-2.5	-9.7
	0.375	-3.2	-2.8	0.4	-6.0	3.2
	0.500	-4.1	-0.2	3.9	-7.5	7.3
	0.625	-4.0	5.7	9.7	-8.4	14.1
	0.750	-3.9	-5.6	-1.7	-7.5	1.9
	0.875	-0.8	-8.0	-7.2	-1.2	-6.8
	1.000 ^b	1.0	-4.2	-5.2	3.1	-7.3
tGg'		0.8	-0.2	-1.0	0.4	-0.6
gGg'		-0.2	2.0	2.2	-0.7	2.7
		$\Delta G(\text{sol})$	$\Delta G(\text{gas})$	$\Delta G(\text{tot})$		
path 1						
tTt to tGg'		0.81 ± (0.45)				
tTt to tGg'		1.63 ± (0.50)				
average		1.22 ± (0.50)	-2.84	-1.62 ± (0.50)		
tGg' to gGg'		-0.95 ± (0.20)	0.29	-0.66 ± (0.20)		
tTt to gGg'				-2.28 ± (0.54)		

^aPath 1. ^bCorresponds to a tGg' geometry not fully optimized. Transformation to the total optimized tGg' structure was done in a single step. Energies in kcal/mol.

The Monte Carlo simulations were performed with the BOSS 2.0 program of Prof. Jorgensen, adapted here to run on an IBM 3081 computer. The details of calculations for N, P, T ensembles have been described by Jorgensen et al.²⁶ in previous papers. In the present simulations we used the OPLS potential function parametrized for alcohols¹⁹ and the TIP4P water model.²⁷ Preferential sampling,²⁸ proportional to $1/(R^2 + c)$, was taken with c set equal to 120. R gives the distance of the solvent molecule from the center of the C-C bond of the solute. A cut-off radius of 8.5 Å was taken for the solvent-solvent interaction and 9.75 Å for the solute-solvent interaction. The solute was placed in the center of a water box with 262 solvent molecules. Periodic boundary conditions were applied at $T = 298$ K and $P = 1$ atm. New configurations due to random translation and rotation of the solute were attempted on every 50th step. A volume change was tried after every 1000th step. Statistical averaging was done in separate runs of 100K configurations.

Statistical perturbation calculations, to estimate the relative solvation free energies of the different conformers, were based on the formula of Zwanzig²⁹ and applied according to the technique of Jorgensen and Ravimohan.³⁰ A linear coupling parameter, λ , was defined changing from 0 to 1 while transforming conformation 1 to conformation 2. Geometric parameters for the conformers were obtained from the optimized gas-phase structures of tTt, tGg', and gGg'.

In a recent paper, Straatsma and McCammon³¹ called attention to the problem of correct sampling of the configuration space for solutes with several rotation axes. Contribution to the total solvation free energy due to isomers separated by high barriers may be overlooked. In calculating the free energy change between conformers along some special path, restrictions on the solute geometry are required to maintain the desired torsional angle for the rotation with use of molecular dynamics.³² There are no such problems with Monte Carlo simulations used here. The mapping of the gas-phase potential energy surface locates transformation paths separated by single barriers. When calculating the change in solvation free energy the probability of acceptance of a new configuration of the solution is independent of the internal energy of the rigid solute.

In calculating the relative hydration free energy of tTt and tGg' to reduce the number of calculations, two paths were chosen using double-wide sampling.³⁰ The total number of configurations considered was about 200 M. Even so, the achievable accuracy of the calculated thermodynamic data is limited.

Along the first path the OCCO torsion angle changed from 180° to 60° and one of the HOCC torsions changed from 180° to 307° (see

(26) (a) Jorgensen, W. L.; Madura, J. D. *J. Am. Chem. Soc.* **1983**, *105*, 1407. (b) Jorgensen, W. L.; Swenson, C. J. *J. Am. Chem. Soc.* **1985**, *107*, 1489. (c) Jorgensen, W. L.; Gao, J. *J. Phys. Chem.* **1986**, *90*, 2174.

(27) (a) Jorgensen, W. L.; Chandrasekhar, J.; Madura, J. D.; Impey, R. W.; Klein, M. L. *J. Chem. Phys.* **1983**, *79*, 926. (b) Jorgensen, W. L.; Madura, J. D. *Mol. Phys.* **1985**, *56*, 1381.

(28) (a) Owicki, J. C.; Scheraga, H. A. *Chem. Phys. Lett.* **1977**, *47*, 600. (b) Jorgensen, W. L. *J. Phys. Chem.* **1983**, *87*, 5304.

(29) Zwanzig, R. W. *J. Chem. Phys.* **1954**, *22*, 1420.

(30) Jorgensen, W. L.; Ravimohan, C. *J. Chem. Phys.* **1985**, *83*, 3050.

(31) Straatsma, T. P.; McCammon, J. A. *J. Chem. Phys.* **1989**, *90*, 3300.

(32) Tobias, D. J.; Brooks, C. L., III *J. Chem. Phys.* **1988**, *89*, 5115.

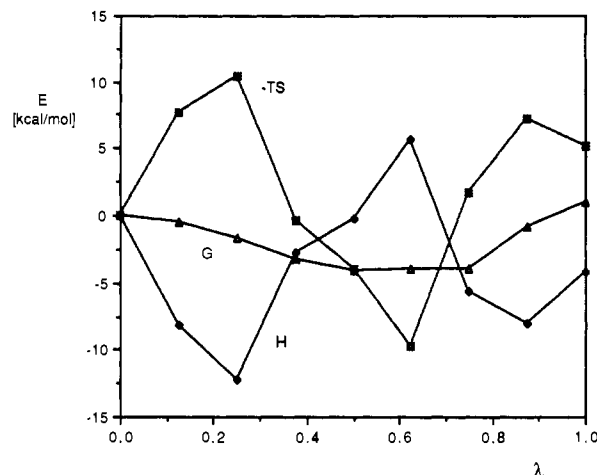
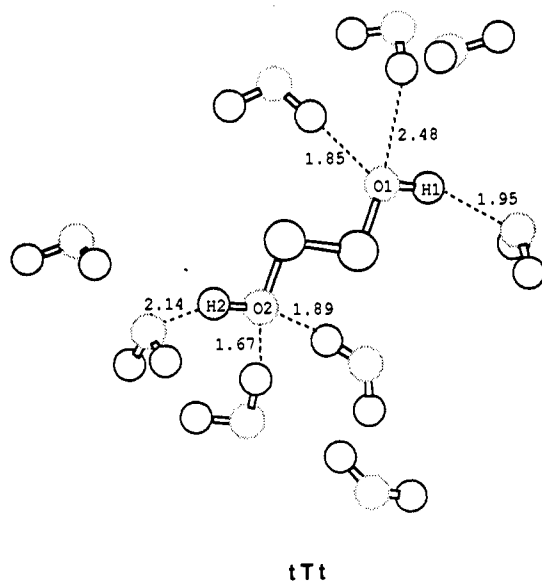
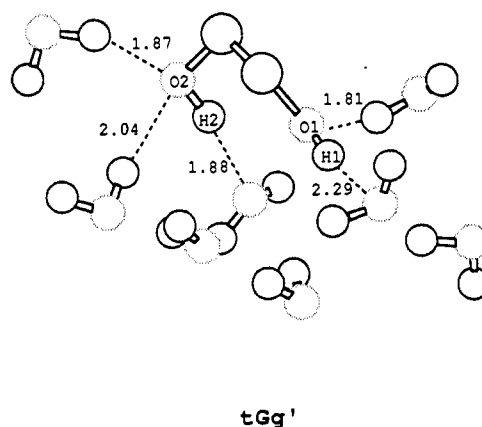
**Figure 4.** Change in the solvation thermodynamic data for 1,2-ethanediol going from the tTt to the tGg' conformer.**Figure 5.** Snapshot for the tTt conformer with water molecules satisfying criterion $O(\text{alc}) \cdots X(\text{any atom of water}) \leq 3.5$ Å.**Figure 6.** The same as Figure 5 for tGg'.

Figure 2). The other H atom was held in the trans position. Forward and backward calculations with $\Delta\lambda = 0.125$ gave rather different results for the relative free energy, ΔG , between tTt and tGg', even considering 5000K to 6000K configurations in the averaging phase. In a second series of calculations with $\Delta\lambda = 0.0625$, 2000K configurations were taken for the equilibration and 3000K for averaging. Such lengths of phases proved to be satisfactory to reach convergence for the ΔG value, number of hydrogen bonds, and the coordination number of the polar groups with water.³³ In some cases intermediate points were calculated allowing $\Delta\lambda$

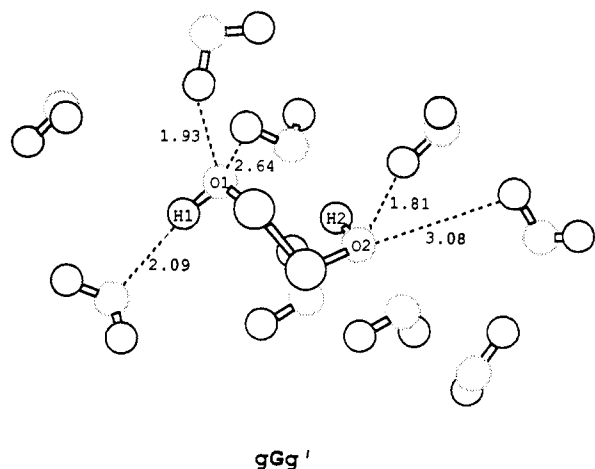


Figure 7. The same as Figure 5 for gGg' .

= 0.03–0.0325 to reach an error bar less than 0.1 kcal/mol for the given ΔG increment.

The second path was chosen to elucidate the relative importance of rotations about the C–C and C–O bonds. In its first part only the OCCO angle was changed from 180° to 84° . Then the OCCO torsion angle changed moderately, from 84° to 60° , while the HOCC angle was altered from 180° to 307° . Finally a transformation of the tGg' conformer to its geometry optimized form was carried out.

The conformation change from tGg' to gGg' was performed in five steps allowing $\Delta\lambda = 0.1$. Changes in the solvation free energy, enthalpy, and entropy values following the tTt - tGg' - gGg' transformations are shown in Figure 4 and Table IV.

The average positions of the water molecules in the first hydration shells of the alcoholic groups were determined by using a procedure based on that proposed by Marchese and Beveridge.³⁴ Snapshots (Figures 5–7) were taken at every 1000th solution configuration and collected to give approximately 4500 snapshots. In determining the average water positions the solute and the 262 water molecules were transformed in the inertia coordinate system of the solute to find a standard point of reference for comparison. Those water molecules were considered in the averaging procedure which satisfied at least one of the relations: $O(w)\cdots O(alc) < 3.5 \text{ \AA}$ or $O(w)\cdots CH_2 < 4.5 \text{ \AA}$ or $H(w)\cdots O(alc) < 2.5 \text{ \AA}$. These R values define the boundary of the first hydration shell of the solute, corresponding to the minima of the radial distribution functions in Figures 9–12. Neglecting molecules beyond this limit has minimal effect on the calculated average structure. The averages of the atomic coordinates of water oxygens, as well as hydrogens, defined centers for domains. All water molecules near the solute were investigated if their atoms belonged to any of the stated domains. A water molecule belonged to a specific oxygen and/or hydrogen domain if its atoms were closer to the center of the corresponding domain than a predefined distance limit. The coordinates of the center of the domain were recalculated by averaging over Cartesian coordinates of all atoms in the domain, considering also the one entered last. If a water molecule belonged to more domains it was considered in all of them. If the water molecule belonged to none of the existing domains, it defined a new domain center. The distance limit was set equal to 0.7 \AA for hydrogen atoms. Preliminary calculations taking distance limits of 1.5 or 1.0 \AA for the oxygen atoms gave similar results. To increase the sensitivity of the method but to avoid too many domains the distance limit of 1.0 \AA was chosen for the oxygens. Though the number and positions of domain centers are not independent of the number and order of snapshots, we found that 4500 snapshots (4500 configurations) were satisfactory to reach convergence for the coordinates of the domain centers. The centers of domains of the largest populations were within spheres with radii of about 0.2 \AA . The origins of these spheres were separated, however, at least by about 3 \AA , providing the possibility to distinguish different hydration sites around the solute atoms. To find these sites we considered centers of domains with populations not less than 40% for water oxygen or 35% for water hydrogen.

Results and Discussion

Gas Phase. Results for the gas-phase calculations are summarized in Tables I–III. HF/6-31G* optimized bond lengths and bond angles in Table I differ slightly for the four conformers. The

C–O bond lengths shorten by about 0.01 \AA upon intramolecular hydrogen bond formation in the gauche conformers. Changes in the bond angles are a few degrees at most. The optimized torsion angles are close to the ideal values for staggered conformations. Due to intramolecular hydrogen bond formation, however, they may also be considerably different from the ideal values, as was found for the HOCC torsion angles for gGg' and $g'Gg'$. Our calculated geometric parameters are consistent with those of Cabral et al.,^{17b} who performed MP2/6-31G* geometry optimization and predicted O–C and O–H bonds longer by 0.02–0.03 \AA .

HF/6-31G* normal frequencies in Table II are compared with experimental values of Frei et al.¹⁰ and Takeuchi and Tasumi.¹¹ Calculated frequencies in the most stable tGg' conformer (see below) are generally overestimated by 9–12%. Assuming a similar overestimation for the other conformers, an average scaling factor of 0.9 was applied in calculating scaled zero-point corrections. Scaled frequencies in calculating enthalpies, entropies, and free energies exert negligible effects on the relative values of interest here.

Energy values are given in Table III. The tGg' conformer was found as the most stable conformer at the Hartree-Fock level. gGg' , $g'Gg'$, and tTt are higher in energy by 0.68, 1.29, and 2.07 kcal/mol, respectively. Zero-point corrections decrease the differences by about 0.3 kcal/mol for the $g'Gg'$ and tTt conformers and leave the energy separation almost unaltered for gGg' . The second-order correlation term, relative to that of tGg' , is negative for the gGg' and $g'Gg'$ conformers and positive for tTt . As a result gGg' is higher in energy than tGg' only by 0.27 kcal/mol, in good agreement with the results of Cabral et al.^{17b} The large correlation term for tTt leads to an internal energy higher by 3.02 kcal/mol than that for tGg' .

To calculate the correct gauche–trans free energy difference in the gas phase, consideration of the correlation term proved a key problem. Del Bene has investigated several systems with an intermolecular hydrogen bond.^{3c} It was found that the third- and fourth-order correlation terms are, in those cases, of similar magnitude with opposite sign. As a result considering only the second-order term in a neutral hydrogen bonded system, the correlation correction could be predicted with a precision of about 0.1 kcal/mol. Assuming similar precision in the present case, the correlation energy change of 1.29 kcal/mol in going from tGg' to tTt indicates a marked difference.

In calculating the zero point energy terms all internal motions are considered as vibrational. At a higher temperature it may be, however, a question whether some low-frequency motions, e.g. HOCC and OCCO torsions, should be considered consistently as torsion or is it more correct to characterize these motions as internal rotations. Looking at the potential energy change due to these torsions (Figure 2) there are high barriers probably preventing even hindered rotations. The C–C rotation has a barrier of 8–9 kcal/mol; rotation of the internally bound H atom requires more than 5 kcal/mol. Even if these values are somewhat overestimated by the neglect of the geometry optimization, both show considerable barriers. The reliability of these data can be evaluated if we note that the Hartree-Fock energy difference between tTt and tGg' is 1.6 and 2.1 kcal/mol without and with geometry optimization, respectively. Thus we considered the G conformers as systems with only vibrational internal motion.

For the above reason no C–C rotation was assumed in the tTt conformer. A possibility for the H rotation was, however, investigated. The similar frequency values, 242 and 246 cm^{-1} , calculated for the HOCC torsions show that there are no significant interactions between the two motions. Thus two hydrogens exhibiting free or hindered rotations were used.

By using eqs 1 and 2 in the previous section and considering also the entropy of mixing for the tGg' optical isomers, the free energy difference of tTt and tGg' is 1.99 kcal/mol obtained by free rotation and 2.84 kcal/mol with the hindered rotation model in favor of the tGg' conformer at $T = 298 \text{ K}$.

Thus the free rotation model predicts 3–4% and the hindered rotation model about 1% of the trans conformer in the gas phase.

(33) Nagy, P. I.; Dunn, W. J., III; Nicholas, J. B. *J. Chem. Phys.* **1989**, *91*, 3707.

(34) Marchese, F. T.; Beveridge, D. L. *J. Am. Chem. Soc.* **1984**, *106*, 3713.

The equilibrium value is even smaller with the model considering only vibration. These results are in accordance with experimental findings⁸⁻¹¹ that there is no trans form in the gas phase at room temperature. Our calculations indicate such a large difference in the MP2/6-31G* energy that the tGg' conformer is preferred over tTt with use of any above model.

Solvation Thermodynamics. The main results of the solvation thermodynamics studies are summarized in Table IV and Figure 4. The changes in the thermodynamic parameters for the transformation tTt to tGg' (path I) are shown here. The free energy values were obtained from simulations with 3000K configurations and $\Delta\lambda = 0.0625$. The change to the fully optimized tGg' structure from that corresponding to the minimum energy structure in Figure 2 (structure with $\lambda = 1$ in Table IV) was done in a single step. It corresponds to a rotation of about 10° about the C-O bond for the trans hydrogen atom. The ΔH , ΔE_{SX} , and ΔE_{SS} values were obtained from calculations with 5000K to 6000K configurations. $T\Delta S$ values were calculated by the relation $T\Delta S = \Delta H - \Delta G$. The entropy term has an error similar to that of ΔH since the ΔG values are significantly more precise than ΔH 's. The error bar for ΔG is about 0.1 kcal/mol for a single step in λ . The corresponding value is about 3.4 kcal/mol for ΔH .

ΔG has a single minimum of -4.1 kcal/mol at $\lambda = 0.5$. On the contrary, the ΔH and $-T\Delta S$ terms have double minima and maxima, respectively. As a result the ΔG values are relatively small. The minimum for ΔG emerges where both ΔH and $T\Delta S$ are of moderate magnitude. This behavior of the ΔH and $-T\Delta S$ terms indicates a compensating effect during the solvation. This tendency was found along with entire path I (Figure 4) and does not seem specific to the 1,2-ethanediol system.^{33,35-37}

The relative solute-solvent interaction, ΔE_{SX} , has a similar change to ΔG with nearly coinciding minima. The minimal value for ΔE_{SX} is -8.5 kcal/mol, twice the minimal solvation free energy. Despite the considerable value for ΔE_{SX} , the solvent reorganization term, ΔE_{SS} , dominates in determining the solvation enthalpy by $\Delta H = \Delta E_{\text{SX}} + \Delta E_{\text{SS}}$. Thus the minimum-maximum character of the enthalpy function is largely defined by the ΔE_{SS} term.

Changes in the entropy term follow those for ΔE_{SS} . If the reorganization leads to a more negative enthalpy, the entropy decreases. The more ordered structure of the solvent results in a decrease in the solvent-solvent interaction energy but is also followed by a loss in the entropy. Contrary to this, a positive reorganization term entailing an increase in entropy can be explained by a less ordered structure. Data in Table IV clearly indicate the correlation between the $T\Delta S$ and ΔE_{SS} terms. It can also be seen that there is no correlation between $T\Delta S$ and ΔE_{SX} .

In calculating ΔG values two paths were considered. In path I the tGg' conformation is less favorable than the tTt conformer by 0.81 ± 0.45 kcal/mol. The path can be divided into two parts with contributions of -4.11 ± 0.32 and 4.92 ± 0.33 kcal/mol. Though the parts have reasonable relative errors, the final ΔG value of 0.81 kcal/mol has relatively large uncertainty.

Calculating ΔG along another path as well permits the determination of its final value more precisely. The overlapping ranges of the allowed ΔG intervals for the two paths can give rather well-defined values for the solvation free energy difference of tTt and tGg'. The calculated value along the second path is 1.63 ± 0.50 kcal/mol. It has contributions of -4.59 ± 0.30 and 6.22 ± 0.40 kcal/mol. Considering the ΔG values for the two paths, 0.81 ± 0.45 and 1.63 ± 0.50 kcal/mol, the average of 1.22 ± 0.50 kcal/mol was accepted in our calculation. The overlap of the two separate ΔG values defines a range of 1.13-1.26 kcal/mol embracing the mean value.

The conformations corresponding to the minima of the solvation free energy along the two paths are rather different. Since the values -4.11 and -4.59 kcal/mol are close, it means that there is a large area in the potential map with low solvation free energy.

The -4.11 kcal/mol value was obtained with values of 120° and 244° for the OCCO and HOCC torsion angles, respectively. The corresponding angles are 79° and 205° with a free energy of -4.59 kcal/mol. These results suggest that the torsion angles are allowed to vary over a wide range without a considerable increase in the solvation free energy. Holding the hydrogen atom nearly trans to the C-C bond, the OCCO moiety can reach an almost gauche conformation with largely negative solvation free energy. Allowing the H atom close to the other OH group, which is desirable for an intramolecular hydrogen bond, the solvation free energy increases steeply.

In the absence of a free energy map for the gas-phase conformation at 298 K only an approximate estimation can be given for the minima of the free energy surface in solution, considering both internal and solvation effects. The sum of the ΔHF energy along path I in Figure 2 and the corresponding solvation free energy (Table IV) gives a potential curve with double minima. The minimum corresponding to the tTt structure is higher in energy by 1-2 kcal/mol than the minimum with a OCCO rotation angle of about 90° at $\lambda = 0.75$. This value is close to that of Chidichimo et al.,¹² who found a value of 72° for this torsion angle in solution. The two minima are separated by a barrier of about 3 kcal/mol starting from the more stable, tGg'-like conformer. The top of the barrier corresponds to an eclipsed conformation with a OCCO torsional angle of 120° . The free energy surface is relatively flat around the tTt conformation. A rotation of 20 - 30° about the O-C or C-C axis requires 0.5-1.0 kcal/mol. This is approximately the energy RT at 298 K, thus small torsions of the tTt structure are expected. Similar though possibly favorable torsions are also expected for tGg'. However, in appraising the minimum at about OCCO = 90° , it must be kept in mind that these results were obtained with use of ΔHF energies without geometry optimization. In considering the free energy change going from tTt to tGg', the MP2 correlation energy is important. In fact, the sum ($\Delta HF + \Delta G_{\text{sol}}$) predicts relative tGg' free energy between 0.3 and -0.5 kcal/mol that is considerably higher than our final value of -1.62 ± 0.50 kcal/mol in Table IV. The difference is near the difference of HF and MP2 in Table III.

The transformation of the tGg' conformation to gGg' leads to a decrease in the solvation free energy by 0.95 kcal/mol. Thus hydration also stabilizes the gGg' conformer relative to tGg'. Stabilization by solvent of the tTt, tGg', and gGg' upon solvation will be discussed in the next section. The data in Table IV show that the sum of the free energy terms in the gas phase and aqueous solution is negative for the tTt to tGg' conformation change. It is on average -1.6 kcal/mol. The sum is also negative by 0.7 kcal/mol for the tGg' to gGg' transition. Thus, even if the solvation process prefers the tTt conformer as compared to tGg', the difference is not enough to compensate for the considerably higher internal free energy. The solvation free energy, however, compensates for the small energy difference between tGg' and gGg', to favor the tGg' in the gas phase. As a result, gGg' is preferred in solution by 0.7 kcal/mol. An analysis similar to that above, using the ΔHF (Figure 3) + ΔG_{sol} function, shows that a rotation of the g hydrogen atom, not involved in intramolecular hydrogen bonding, by 20 - 30° requires about 0.5 kcal/mol. So, such torsion is expected at room temperature.

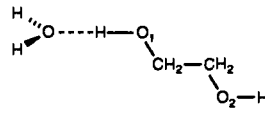
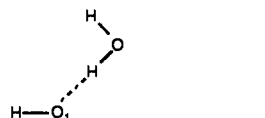
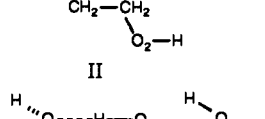
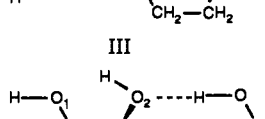
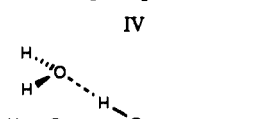
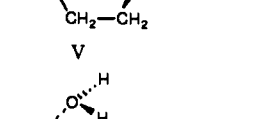
Finally, the total free energy difference between tTt and the more stable G conformer, gGg', is 2.3 kcal/mol. This free energy separation corresponds to about 97-98% of the gauche conformer in solution. This finding is in very good agreement with recent NMR results for the lyotropic liquid crystalline solution of 1,2-ethanediol, where only a gauche conformer was found.¹²

Solution Structure. The solution structure was analyzed with the aid of radial and pair interaction energy distribution functions as proved useful previously.^{26a,b,33,35,38} Results are compared with the calculated average positions of water molecules strongly bound to the solute. Snapshots of the solute in tTt, tGg', and gGg' conformations and the closest waters are shown in Figures 5-7.

The pair interaction energy distribution (Figure 8) shows a definite maxima-minima character for all three conformers. The minima are in the range of -3.50 to -2.75 kcal/mol. The latter

(35) Dunn, W. J., III; Nagy, P. I. *J. Phys. Chem.* **1990**, *94*, 2099.(36) Pearson, R. G. *J. Am. Chem. Soc.* **1986**, *108*, 6109.(37) Ben-Naim, A.; Marcus, Y. *J. Chem. Phys.* **1984**, *81*, 2016.(38) Alagona, G.; Tani, A. *J. Mol. Struct. (THEOCHEM)* **1988**, *166*, 375.

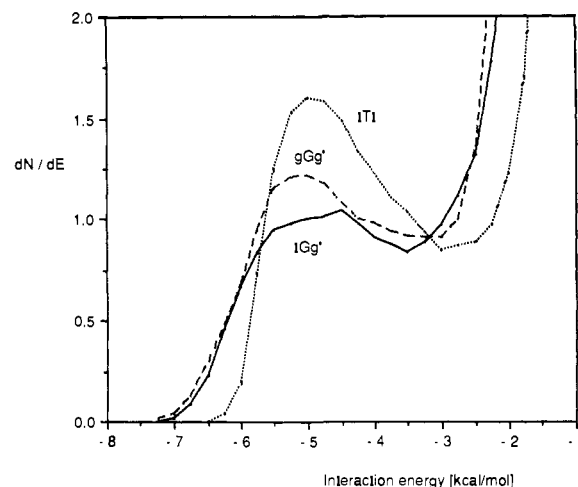
Table V. OPLS Interaction Energies for Selected Solute–Water Dimers with O...O(W) Separation of 2.75 Å^a

	E_{LJ}	E_{Coul}	E_{tot}
	1.44	-7.31	-5.87
I			
	1.33	-7.60	-6.27
II			
	1.42	-7.86	-6.44
III			
	1.29	-7.93	-6.64
IV			
	6.57	-2.55	+4.02
V	2.43	-2.31	+0.12 ^b
	1.33	-8.34	-7.01
VI			

^aEnergy values are in kcal/mol. ^bThe O...O(W) distance is 3.00 Å.

value was considered as the upper limit for the hydrogen bond energy. The most negative pair interaction energy values are different for the three curves: -6.50 kcal/mol for tTt and -7.25 kcal/mol for tGg' and gGg'. This indicates that the most favorable pair interaction energy is more negative in the gauche (G) than in the trans (T) form.

Interaction energies for selected dimers were investigated with a O...O(w) separation of 2.75 Å, the peak site for the O...O(w) radial distribution functions, and holding the water oxygen in the HOC or OCC plane (Table V). These are likely positions for

**Figure 8.** Solute-solvent pair interaction energy distribution for the tTt, gGg', and tGg' conformers of 1,2-ethanediol.

water oxygens hydrogen bonded to the solute (see Figures 5–7). The Lennard-Jones terms are nearly constant at the geometries chosen, with an exception for structure V. Holding the O₂...O(w) distance at the value of 2.75 Å in this structure, the O₁...O(w) distance is as short as 2.54 Å, nearly the shortest O...O(w) distance found in the radial distribution functions (Figure 9b). Allowing an O₂...O(w) distance of 3.00 Å, the E_{tot} term is still too high for this dimer to compete with the other structures. In structures I–IV and VI, the differences in the total energy are mainly due to the Coulomb terms. Hydration with H-acceptor water, gGg' (VI), is preferred by 0.6 kcal/mol over tGg' (III) and by 1.1 kcal/mol over tTt (I). There is a favorable charge-charge interaction in VI among O(w) and H(w), and H₂ and O₂ atoms. These stabilizing interactions in structure III, due to the larger distances, are smaller, even if the dipole moment vector of the water molecule and the bond moment vector for H₂-O₂ are nearly parallel. They are antiparallel for tTt resulting in a less negative Coulomb energy. Hydration of the solute with H-donor water molecules is favorable by 0.4 kcal/mol in tGg' (IV) over tTt (II) due also to the more preferable directionality of the remote O-H bond of the solute. Even if these structures are not geometry optimized ones and the values are only for qualitative consideration, they reflect correctly more quantitative computations. Values obtained for the total energies of the tGg' and gGg' dimers III, IV, and VI are equal or more negative than the threshold for the tTt curve in Figure 8. This supports the lower starting value for curves tGg' and gGg'.

Integration up to -2.75 kcal/mol for these curves gives the estimated number of hydrogen bonds to the solute in the given conformation (Table VI). Also the value for the conformation with minimal solvation free energy (min) along path I (see previous section) is shown here. Integration up to -0.25 kcal/mol gives

Table VI. Coordination Numbers, Hydration Sphere, and Thermodynamic Data of Aqueous Solvation^a

	coord no.					
	O1/O(W)	O2/O(W)	O1/H(W)	O2/H(W)	H1/O(W)	H2/O(W)
tGg'	3.69	2.68	0.99	1.56	0.99	0.77
gGg'	2.68	3.09	1.05	1.47	1.00	0.87
tTt	2.81	3.18	1.25	1.27	0.97	0.99
min	3.81	2.78	1.46	1.63	1.10	0.96
	$E \leq -2.75$	$E \leq -0.25$	$E \geq 1.00$	E_{SX}	$\Sigma O/O(W)$	
tGg'	3.46	49.7	0.8	-31.4	6.4	
gGg'	3.78	48.5	1.0	-32.5	5.8	
tTt	3.95	42.9	1.1	-31.8	6.0	
min	4.70	57.8	2.3	-40.2	6.6	
	H	ΔG	ΔH	ΔE_{SS}	$T\Delta S$	
tGg'	-2661.2 ± 1.9					
gGg'	-2659.0 ± 2.4	-1.0 ± 0.2	2.2 ± 3.1	3.3 ± 3.1	3.2 ± 3.1	
tTt	-2661.0 ± 2.5	-1.2 ± 0.5 ^b	0.2 ± 3.1	0.6 ± 3.1	1.4 ± 3.1	

^aX/Y is the coordination number of X by Y. E_{SX} is the solute-solvent interaction energy, ΔE_{SS} is the solvent reorganization energy. All relative values are taken in comparison with data for tGg'. ^bThe average value from Table III.

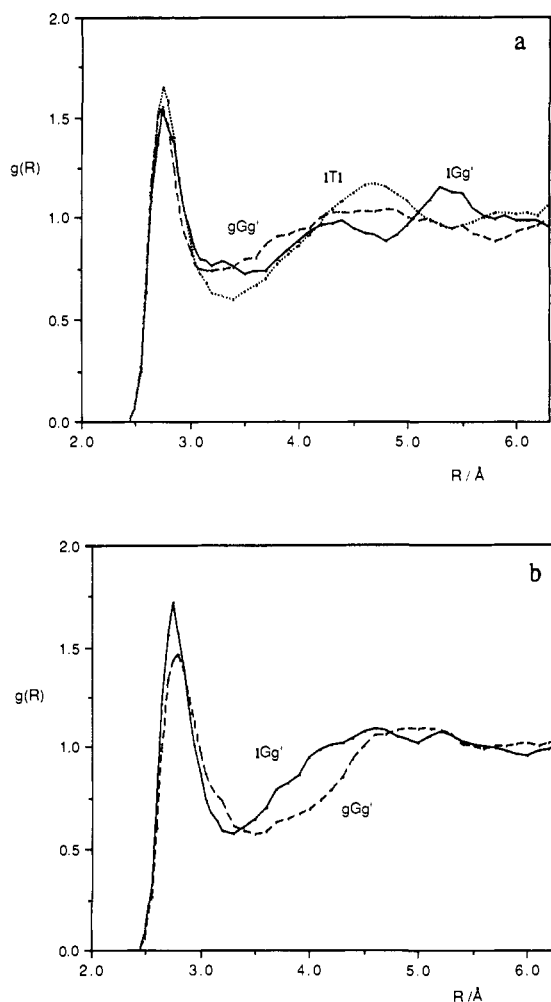


Figure 9. (a) O \cdots O(w) radial distribution functions for the diol oxygen acceptor in the intramolecular hydrogen bond: (···) tTt (average), (—) tGg', (---) gGg'. (b) O \cdots O(w) radial distribution functions for the diol oxygen donor in the intramolecular hydrogen bond: (···) tTt (average), (—) tGg', (---) gGg'.

the number of water molecules with a stabilizing effect in the solute-solvent interaction. The number of unfavorably oriented water molecules near the solute is estimated by the number of molecules with interaction energy of 1 kcal or higher.

Table VI shows increasing hydrogen bond values of 3.46, 3.78, and 3.95 for the tGg', gGg', and tTt conformers, respectively. The number of hydrogen bonds for the min conformer is higher by as much as 0.75 unit even when compared to that of tTt. It explains the marked decrease in E_{SX} , the solute-solvent interaction energy, for the min structure. Furthermore, the number of water molecules with the above stabilizing effect is 58 for min, while the lowest value, 43, was found for the tTt form which does not have a permanent dipole moment. Values of 48–50 for the G conformers are halfway between the extrema. The larger number of stabilizing water molecules in a dipole-dipole interaction with the solutes compensate in E_{SX} for the smaller number of hydrogen bonds. As a result the E_{SX} 's are similar for tTt, tGg', and gGg'. The numbers for the poor contacts are about 1 with the exception of min, where this value is 2.3. But its absence in the equilibrium mixture of conformers in solution is due to its high internal energy.

Coordination numbers given in Table VI were obtained by integrating the radial distribution functions (Figures 9–12) to their first minima. The sum of the water oxygens hydrating the hydroxy groups of 1,2-ethanediol (columns 1 and 2) is in the range 5.8–6.6 for the different conformers. The hydration spheres for the two hydroxy groups more or less overlap with the exception of the tTt form, so the upper values are overestimated. This suggests approximately 6 water molecules around the solute, about twice that found for methanol.^{26a,33}

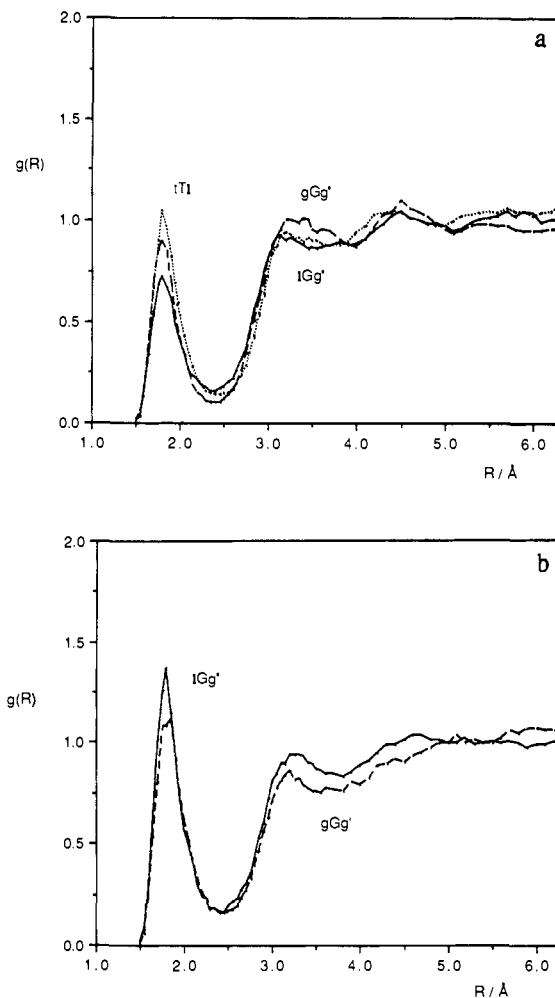


Figure 10. (a) O \cdots H(w) radial distribution functions for the diol oxygen acceptor in the intramolecular hydrogen bond. (b) O \cdots H(w) radial distribution functions for the diol oxygen donor in the intramolecular hydrogen bond. For line definition see Figure 9a.

The O1 atom, with hydrogen not participating in intramolecular hydrogen bond formation, is hydrated with 1.25 water molecules in the tTt form. A rationale of this value can be given considering random snapshots with solution structures close to the average. Figure 5 shows a normal length of 1.85 Å for the O1 \cdots H(w) hydrogen bond and a longer one with 2.48 Å. This latter bond has a partial contribution to the O1/H(w) value. The O1/H(w) value is 1.5 for the min conformer and goes to 1 for tGg' with a single water molecule bound to O1 (see Figure 6). By rotation of the H1 atom to the g position (gGg') O1/H(w) changes slightly. This is in agreement with O1 \cdots H(w) bond lengths of 1.93 and 2.64 Å to a near and a more remote water molecule in Figure 7.

All O2 atoms (the connecting H2 is intramolecularly hydrogen bonded in the G forms) are hydrated preferably by water molecules that are H-donors. The O2/H(w) values are between 1.47 and 1.63, being higher than the value of 1.27 Å for tTt. Figure 6 shows two water molecules whose hydrogens are rather close to the O2 of tGg'. The O2 atom of gGg' is hydrogen bonded also to a near water molecule and to one being located relatively far from O2 in the snapshot shown in Figure 7. On average, O2/H(w) coordination numbers are between 1 and 2. The hydration preference of O2 over O1 in G and min conformations is a consequence of the enhanced interaction energy for a structure like IV in Table V.

Hydration of the hydroxy groups by acceptor water molecules shows that H1, not involved in an intramolecular hydrogen bond, is hydrated by one water molecule in all cases. Hydration of H2 (Table VI), however, becomes restricted in going from tTt (0.99) to tGg' (0.77). Hydration in the intramolecular hydrogen region is less preferred as was shown for structure V in Table V. Even

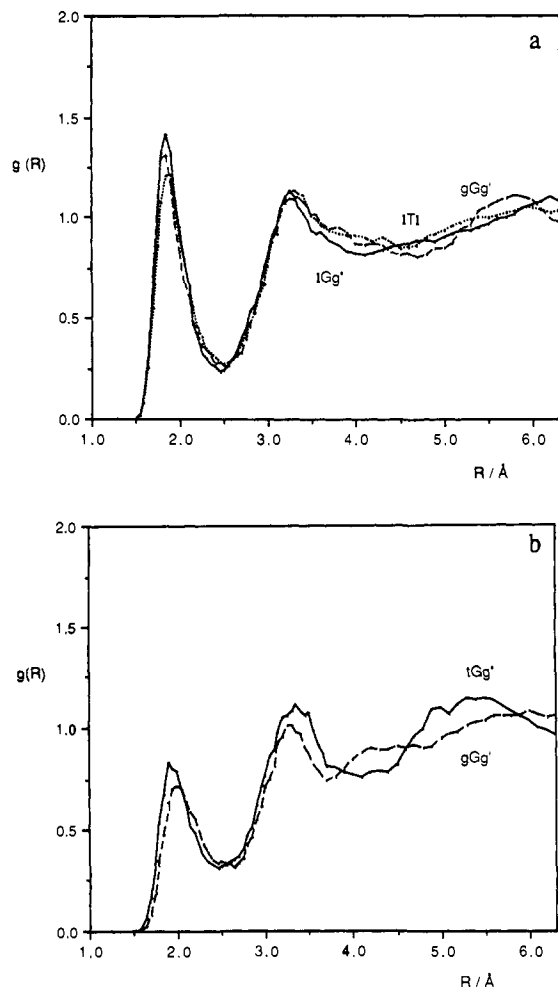


Figure 11. (a) H...O(w) radial distribution functions for hydrogen not in the intramolecular hydrogen bond. (b) H...O(w) radial distribution functions for hydrogen in the intramolecular hydrogen bond. For line definition see Figure 9.

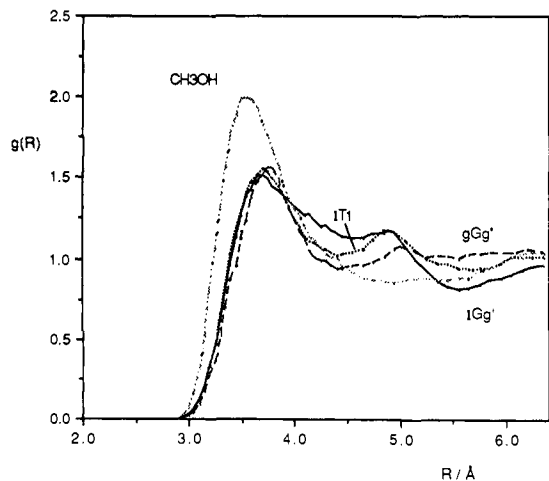


Figure 12. CH₂...O(w) radial distribution functions: (***), tTt (average), (—) tGg', (---) gGg', (---) CH₃OH.

if the geometry optimization must be very important for this dimer to estimate the correct interaction energy, the approximate value in Table V is in accord with the decreased hydration potential at this site.

Sums of the O1/H(w), O2/H(w), H1/O(w), and H2/O(w) coordination numbers give values of 4.48, 5.15, 4.31, and 4.39 for the tTt, min, tGg', and gGg' conformers, respectively. All these values are higher by 0.45–0.85 unit than the corresponding number of hydrogen bonds. This can be explained by recognizing

Table VII. Average Bond Lengths and Bond Angles for the Intermolecular Hydrogen Bonds in the Hydrated 1,2-Ethanediol^a

	tTt	tGg'	gGg'
O(W)···H1	1.87 (50%)	1.85 (61%)	1.87 (67%)
O(W)···H2	1.83 (74%)	2.02 (52%)	2.03 (47%)
H(W)···O1	1.83 (37–42%)	1.81 (47%)	1.80 (60%)
H(W)···O2	1.80 (35–38%)	1.82 (36%)	1.83 (48%)
O(W)···H1–O1	159	175	170
O(W)···H2–O2	168	156	151
O–H(W)···O1	177	169	172
O–H(W)···O2	168	174	167

^a The percent in parentheses is the fraction of snapshots with water in this position. Bond distances in Å, angles in deg. For numbering of the solute atoms see Figures 5–7.

that not all arrangements, even within the first hydration shell, correspond necessarily to a strongly negative interaction energy *with the solute*. Relatively high values for the solute–solvent pair interaction energies are obtained if water molecules are in an unfavorable orientation to the solute. These are molecules with $E_{SX} \geq 1$ kcal/mol (see Table VI). Some of these waters enhance the average coordination number in the first hydration shell, but they do not contribute to the number of water molecules with pair interaction energies within the hydrogen bond energy range. This interval was assumed here being between -7.25 and -2.75 kcal/mol for the ethanediol solute, based on curves in Figure 8.

Results obtained by averaging the positions of water molecules relative to the solute (Table VII) indicate four water molecules localized around the solute. All of these are hydrogen bonded to the tTt conformer with O···H distances of 1.8–1.9 Å. There are only three of the four waters within this interval for the G conformers. The fourth solvent molecule has an O···H separation of about 2 Å to the solute. This hydrogen bond should be weaker than the others. The O···H–O bond angles are within the range of 159–177°. There are, however, two more bent bonds with bond angles of 156° for tGg' and 151° for gGg'. These bonds are those that have a longer O···H separation. Cybulski and Scheiner³⁹ found a considerable decrease in hydrogen bond energy with increasing bent character. The longer and more bent bond explains the smaller number of hydrogen bonds with $E < -2.75$ kcal/mol for the G conformers as compared with the T conformer (Table VI).

In order to obtain an estimate of the probability of finding a water of hydration at the positions found above, the percentage of the snapshots having water in these positions was computed (Table VII). Waters as acceptors are more localized than donors. For the tTt conformer, the water molecules are localized in 50–74% at the average positions to form the O(w)···H bond. This value is only 35–42% in forming the H(w)···O bond. The calculated remarkable difference of 24% in the water localization referring to the O(w)···H bonds is attributed to the asymmetry for the coordination numbers to tTt in Table VI. For the tGg' conformer, acceptor water molecules are localized in 52–61% vs 36–47% for donor waters. Population values give overlapping ranges of 48–67% for gGg', with the value of 67% referring to an acceptor water population.

Donor water molecules with average positions close to the HOC planes are repelled by neighboring solvent molecules. Figures 5–7 show generally two donor water molecules near the solute oxygens with one more remote. A dynamic sharing of the average position results in their contributions to the number of hydrogen bonds by about 1.0–1.5 units and to the coordination number by about 2. This explains in part the corresponding values in Table VI.

Thus a model for the hydration of 1,2-ethanediol consistent with these results follows. There are 1 H-donor and 1 H-acceptor water molecules hydrogen bonded to each hydroxy group with a free hydrogen. There are, on average, 1.5 water molecules hydrating an oxygen atom connecting to an internally bonded hydrogen in the form of O···HO(w). Other water molecules, approximately

2 for tTt, gGg', and min and 3 for tGg', are bonded more loosely to the solute. They may form bridges with waters hydrogen bonded to the diol molecule. The first hydration shell of the polar groups, containing the closest, ordered group of the solvent, consists of about 6 water molecules. However, even small differences in this number may be significant.

By combining structural and thermodynamic data in Table VI some explanation may be given for the stabilization of both the gGg' and tTt conformers as compared to tGg' in aqueous solution. The E_{SX} terms are more negative by 0.4 kcal/mol for tTt and by 1.1 kcal/mol for gGg'. It is compensated by the solvent reorganization energy for tTt, resulting in a net ΔH of 0.2 kcal/mol. In the case of gGg' the reorganization term is the prevailing one and ΔH increases to 2.2 kcal/mol. In both cases the calculated entropy term is positive. Even though these numbers may not be very precise, they reflect the tendency in the structural data. We found the lower the number of waters in the first hydration shells of the polar functions the more positive the entropy term. tGg' has the largest number of waters in its hydration shells and gGg' has the fewest favoring the gGg' structure. On the other hand, the hydration for gGg' leads to an unfavorable enthalpy increase due to reorganization. tTt has fewer waters in the hydration sphere than tGg', and enthalpy effects are more favorable than for gGg'. Thus tTt has the most and tGg' has the least stabilization upon hydration.

The structural model described above is capable also of explaining several details of the radial distribution functions. The O...O(w) radial distribution functions (Figure 9a,b) have first maxima at 2.75 Å and minima between 3.2 and 3.6 Å. The radial distribution function for the tTt conformation, which is the average of the two individual O...O(w) distribution functions, has a broad, well-defined second peak (Figure 9a). It is smooth for tGg', but there is a pronounced third peak. The function for gGg' shows only a slight change after the first peak. Hydration of O2 (Figure 9b) shows unresolved band structure after the first peak.

The second band for tGg' between 4.0 and 4.5 Å (Figure 9a) is conservative for alcoholic systems^{26a,33} and is considered as a contribution from the second hydration shell. This peak for tTt is a contribution, however, due to water molecules hydrating the other diol oxygen at a distance of about 4.9 Å (see structures I and II in Table V). The characteristic third peak for tGg' between 5.3 and 5.5 Å is due to the contribution of a IV-type structure in Table V. The calculated O1...O(w) distance is ~5.4 Å. It is a dimer with largely negative interaction energy. This hydration site should not be as favorable for the gGg' conformer due to the enhanced Coulomb repulsion. Indeed, there is not a peak in this region.

The first peaks for the O...H(w) (Figure 10a,b) and H...O(w) (Figure 11a,b) radial distribution functions are at 1.80–1.85 Å. The first peak for O...O(w) is at 2.75 Å. The difference is 0.9–0.95 Å, nearly equal to the O–H bond length in water. The difference of the threshold separations, where the radial distribution functions start to increase from zero, is also 0.9–0.95 Å. These relations can be satisfied simultaneously by a linear hydrogen bond model accepted here. Table VII shows that most hydrogen bonds in this system are nearly linear.

Increased first peak values for tGg' and gGg' in Figure 10b as compared with those in Figure 10a indicate that the hydration of O2 is more preferable than that of O1 by donor water molecules in these conformations. On the contrary, H2...O(w) radial distribution functions in Figure 11b have first peak heights considerably lower than those in Figure 11a. It corresponds to reduced hydration of the H atom in the intramolecular hydrogen bond, in accordance with the low coordination number with water oxygen.

Second peaks at about 3.3 Å in Figures 10a,b and 11a,b should be conservative for systems with strongly bonded water molecules of the HX...HOH or XH...OH₂ (X = N, O) types.^{33,35,38} These peaks contain contributions from the second closest H(w) or O(w) atoms. The calculated O1...(HO)H and O1(H1...O)H(w) distances in structures I–III are in the range of 3.1–3.4 Å. Integration of the radial distribution function between 3.0 and 3.5 Å for tTt

gives about two donor water molecules around each alcoholic oxygen supporting our model with six water molecules in the first hydration shell of 1,2-ethanediol. Second peaks for the H...O(w) radial distribution functions come largely from arrangements like structure II for H1 and from structure IV with a H2...O(w) separation of 3.4 Å. This latter arrangement is favored explaining the similar height of the second peaks for the G conformers in Figure 11a,b.

O2...H(w) distances of 4.3 Å (structure II) and O1...H(w) distances of 4.50 Å (structure IV) explain the third peaks in Figure 10a,b. These sharp maxima are consequences of the hydration of a bifunctional solute.

The CH₂...O(w) radial distribution functions in Figure 12 are compared with the CH₃...O(w) functions for methanol³³ having a single hydroxyl group. The first peak sites between 3.50 and 3.75 Å roughly coincide with those for methane⁴⁰ and ethanol³⁸ considering the CH₃...O(w) radial distribution function. In ethanol the methyl group is far from the hydroxyl, thus there are only minor contributions from the first hydration sphere of the polar group. For the 1,2-ethanediol, all structures I–VI exhibit the closest CH₂...O(w) distances in the range of 3.5–3.8 Å. However, a maximum appears in the 4.8–5.1 Å interval, too. It has not been found for the solutes mentioned above. The new peak can be considered as a contribution from water molecules in the hydration sphere of the non-adjacent hydroxyl group. Structures I, III, and IV exhibit CH₂...O(w) separations of 4.8–4.9 Å, coinciding very well with the peak interval in Figure 12.

In summary, the simple structures in Table V serve as a good basis for explaining the main features of the radial distribution functions. The conclusions are coherent with our previous results for methylamine, methanol, and ethanol with a single polar functional group.

The present results can be compared with those obtained for other polyhydroxy systems. Molecular dynamics simulations of the aqueous solution of α -D-glucose were carried out by Brady⁴¹ and by Root and Stillinger⁴² for liquid glycerol. All O...O radial distribution functions have their first maxima at about 2.75 Å. The O...H radial distribution function for liquid glycerol gives the first maximum at about 2 Å. The glycerol system did not contain water molecules, thus the 1.8–2.0 Å range for the first peak of the O...H radial distribution functions and the O...O separation of about 2.7–2.8 Å may be general considering similar data for pure water,²⁷ aliphatic alcohols,¹⁹ and aqueous solutions of methanol^{26a,33} and ethanol.³⁸

All the results that are presented here have not considered polarization explicitly. Recent studies published considering polarization^{43,44} find no significant improvement compared to the TIP4P model. The model of Sprik and Klein^{43a} overestimates and the NCC potential function of Niesar et al.^{43b} underestimates the peak value of the g(O–O) function for pure liquid water. The peak of the TIP4P g(O–O) fits well to the experimental value, and g(O–H) and g(H–H) are also consistent with the experiment.⁴⁵ In this model polarization effects are considered implicitly. The parameters were calibrated to produce good experimental measurables like density and vaporization energy. Wallqvist⁴⁶ and Motakabbir and Berkowitz⁴⁷ found the polarization effects of secondary importance in predicting the water

(40) Owicki, J. C.; Scheraga, H. A. *J. Am. Chem. Soc.* **1977**, *99*, 7413.

(41) Brady, J. W. *J. Am. Chem. Soc.* **1989**, *111*, 5155.

(42) Root, L. J.; Stillinger, F. H. *J. Chem. Phys.* **1989**, *90*, 1200.

(43) (a) Sprik, M.; Klein, M. L. *J. Chem. Phys.* **1988**, *89*, 7556. (b) Niesar, U.; Corongiu, G.; Clementi, E.; Kneller, G. R.; Bhattacharya, D. K. *J. Phys. Chem.* **1990**, *94*, 7949. (c) Cieplak, P.; Kollman, P.; Lybrand, T. *J. Chem. Phys.* **1990**, *92*, 6755. (d) Wallqvist, A.; Ahlstrom, P.; Karlstrom, G. *J. Phys. Chem.* **1990**, *94*, 1649.

(44) (a) Cieplak, P.; Kollman, P. *J. Chem. Phys.* **1990**, *92*, 6761. (b) Caldwell, J.; Dang, L. X.; Kollman, P. A. *J. Am. Chem. Soc.* **1990**, *112*, 9144.

(c) Rullmann, J. A. C.; Van Duijnen, P. T. *Mol. Phys.* **1988**, *63*, 451. (d) Wang, J.; Jordan, P. C. *J. Chem. Phys.* **1990**, *93*, 2762. (e) Ramnarayan, K.; Rao, B. G.; Singh, U. C. *J. Chem. Phys.* **1990**, *92*, 7057.

(45) Soper, A. K.; Phillips, M. G. *Chem. Phys.* **1986**, *107*, 47.

(46) Wallqvist, A. *Chem. Phys. Lett.* **1990**, *165*, 437.

(47) Motakabbir, K. A.; Berkowitz, M. L. *Chem. Phys. Lett.* **1991**, *176*, 61.

structure next to a hydrophobic wall or at the liquid-vapor interface, respectively.

Acknowledging the theoretical advantages of a polarizable water model over a non-polarizable one (even though the former may be rather limiting from the computational point of view), good relative free energies have been obtained by using the TIP4P models.^{30,48} The primary aim in this paper is to point out changes in the hydration free energy and solvation shell structure upon changes in the solute conformation. In calculating individual values, the consideration of polarization may lead to significant improvement as was found for the second virial coefficient^{43b} or for ion hydration.^{44a-c}

Conclusions

MP2/6-31G**/6-31G* ab initio calculations with zero-point corrections for the tGg', gGg', g'Gg', and tTt conformers of 1,2-ethanediol show that the tGg' conformation is most stable in the gas phase. Other gauche conformers studied are less stable by 0.3–1.0 kcal/mol. The tTt conformer is higher in energy than tGg' by about 3 kcal/mol. Differences in zero-point corrections are relatively small. On the other hand, the change in the second-order correlation energy term has a substantial contribution to the relative energy of tTt. The relative free energies of the conformers at $T = 298$ K and $P = 1$ atm differ only slightly as compared to the relative MP2+ZPE energies. To obtain the reliable free energy for the tTt conformer a hindered rotation model for the HOCC torsional motion was assumed. This model results in free energy for tTt 2.8 kcal/mol higher than that for tGg'. As a consequence, the amount of the tTt conformer is

negligible in the gas-phase equilibrium mixture at 298 K and 1 atm, in accord with all available experimental results.

ΔG values for the solvation process show that the gGg' conformer is more stable in solution than tGg' by about 0.7 (± 0.2) kcal/mol. Taking an average value of 1.2 kcal/mol for the solvation free energy difference between tTt and tGg', the tTt conformer is less stable than gGg' in solution by 2.3 (± 0.5) kcal/mol. These results suggest that the solution contains rotamers with hydroxyl oxygens in the gauche position. The concentration of the trans conformer is 1–2%. Rotations by 20–30° about the C–C and O–C axis, as compared to the gas-phase optimized geometries, are allowed for the conformers in aqueous solution at 298 K. This is in excellent agreement with the NMR results of Chidichimo et al.,²⁰ who did not observe the trans conformer in the lyotropic liquid crystalline solution of 1,2-ethanediol and found a torsional angle of 72° for OCCO.

The first hydration shell of the 1,2-ethanediol solute contains approximately six water molecules. There are, on average, four water molecules strongly hydrogen bonded to the solute in the tTt conformation. This number decreases for gauche conformers with intramolecular hydrogen bonds in solution. The water-solute hydrogen bonds are slightly bent with a favorable O...H distance of 1.8–1.9 Å. Water molecule acceptors in these bonds are more localized than those acting as proton donors.

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Registry No. 1,2-Ethanediol, 107-21-1.

(48) Jorgensen, W. L.; Blake, J. F.; Buckner, J. K. *Chem. Phys.* **1989**, *129*, 193.