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A new anisotropic force field for hydrogen bonding. III. A simple solvation model for ethane-1,2-diol

Michel Masella[1]*, Jean-Pierre Flament[2]

[1] *Laboratoire des mécanismes réactionnels, CNRS URA 1307, École polytechnique, 91128 Palaiseau cedex;*
[2] *Laboratoire de dynamique moléculaire et photonique, CNRS URA 779, Centre d'étude et de recherche lasers et applications, Université de Lille-1, Bâtiment P5, 59655 Villeneuve d'Ascq cedex, France*

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Summary — In two previous papers, we proposed a new force field for the $O(sp^3)\cdots H\text{–}O(sp^3)$ hydrogen bonds. This force-field, now called Mitra, is applied to the study of ethane-1,2-diol in gas phase and in a methoxymethane solution. In this case, the molecules of the first hydration shell are explicitly taken into account, and the rest of the solvent is considered using a dielectric continuum approach. Our results clearly show that, in solution, the intramolecular hydrogen bond of ethane-1,2-diol is broken and the dihedral O–C–C–O angle value grows from 60° to about 73° and the *trans* conformers have a more important weight in solution than in the gas phase. All these results are consistent with experiment.

modelization / hydrogen bond / ethane-1,2-diol / solvation

Résumé — Un nouveau champ de force pour la liaison hydrogène. III. Un modèle simple de solvatation pour l'éthane-1,2-diol. Dans deux précédents articles, nous avons développé un nouveau champ de force pour traiter les liaisons hydrogène du type $O(sp^3)\cdots H\text{–}O(sp^3)$. Ce champ de force, désormais appellé Mitra, a été appliqué à l'étude de l'éthane-1,2-diol dans le vide et en solution de méthoxyméthane. Dans ce dernier cas, les molécules de solvant sont explicitement prises en compte, le reste du solvant étant considéré sous la forme d'un continuum diélectrique. Les résultats obtenus montrent clairement que, en solution, il y a rupture de la liaison hydrogène intramoléculaire de l'éthane-1,2-diol, une augmentation de l'angle dièdre O–C–C–O, qui passe de 60° dans le vide à environ 73° en solution, et, enfin, une augmentation sensible du poids des conformères *trans* de l'éthane-1,2-diol. Tous ces résultats sont en accord avec les observations expérimentales.

modélisation / liaison hydrogène / éthane-1,2-diol / solvatation

Introduction

Many organic molecules capable of intramolecular hydrogen bonding are known for their unusual behavior in the gas phase and in solution, especially if they establish hydrogen bonds with solvent molecules. The most well-known are sugars, particularly glucose with the inversion of stability of its α and β isomers between gas phase and solution [1].

The ethane-1,2-diol ($HOCH_2CH_2OH$, called ethanediol in the following) has also an unusual behavior between gas phase and aqueous, alcoholic or ether-oxide solution (especially dioxane). This molecule has three different rotamers, which generate ten different conformers (fig 1). As figure 1 indicates, the *tGg'*, *gGg'* and *g'Gg'* conformers present an intramolecular hydrogen bond, which may be disrupted in the above solvents.

Numerous experimental and theoretical studies have been done on this molecule, either in the gas phase or in solution. Its possible conformations in the gas phase were explored using electronic diffraction methods (cited in [2]) and microwave [3] or infrared spectrometry [4]. These studies have pointed out that the most stable conformers are those with a *gauche* dihedral O–C–C–O angle, and presenting an intramolecular hydrogen bond. Therefore, this is probably a mixture of conformers *tGg'* and *gGg'* (cf fig 1). Ab initio calculations at different levels of theory agree with experiment [5–12]. In gas phase, *tGg'* and *gGg'* are the most stable conformers and are close in energy (the difference between both is about 0.5 kcal mol^{-1}). However, it is still impossible to predict which is the most stable.

Maleknia et al [13] used Raman spectrometry methods in aqueous solution, to show the "virtually complete absence of any intramolecular hydrogen bonds". However, the O–C–C–O dihedral angle is still *gauche*. Other studies in solution have also indicated a *gauche* behavior for the O–C–C–O angle, and an increase in the weight of the *trans* conformers. In particular, Pachler et al [14] reported a weight of $12 \pm 3\%$ for *trans* conformers in heavy water, while these forms remain unobserved in the gas phase.

In a lyotropic–nematic solution (a quaternary solution of potassium laurate, decanol, water and ethane-

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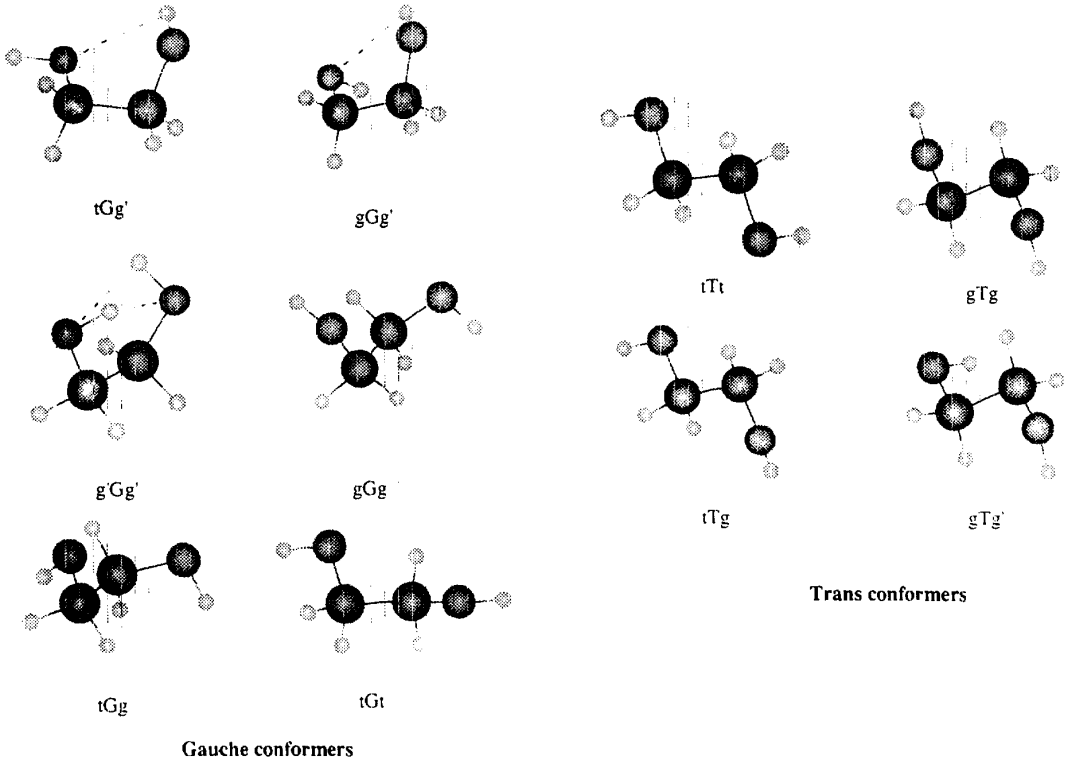

Fig 1. Ethanediol conformers, intramolecular hydrogen bonds are shown in dashed lines.

diol), the NMR results of Chidimino [15] indicated a *gauche* conformation for ethanediol, with a dihedral O–C–C–O angle value estimated at 72° (this angle is estimated in the gas phase at 57.9°, cited in [2]). This result agrees with an earlier electronic diffraction result in solution of 74° [16].

To explain these differences between the gas phase and solution, different theoretical approaches were used, approaches which may be broadly classified in three groups.

In the first group, the solvent molecules are explicitly taken into account. An ethanediol molecule is placed at the center of a box containing hundreds of solvent molecules. With this approach, Nagy et al [5, 6] studied seven ethanediol conformers (*tGg'*, *gGg'*, *g'Gg'*, *gGg*, *tGg*, *tGt* and *tTt*) in aqueous solution using Monte-Carlo simulations. They considered the OPLS [17] and TIP4P potentials [18] for ethanediol and water respectively. Intramolecular degrees of freedom were frozen during the calculations, except for the dihedral angles. Solvation energies of the seven conformers were estimated by gradually changing the dihedral O–C–C–O ethanediol angle to go from one conformer to another (fig 2).

Using the same solvent approach and molecular dynamic simulations, the ten ethanediol conformers were studied by Hooft et al [7] in aqueous solution. The authors considered the GROMOS force-field [19] for ethanediol and the SPC potential [20] for water. Only the ethanediol dihedral O–C–C–O angle was frozen during calculations.

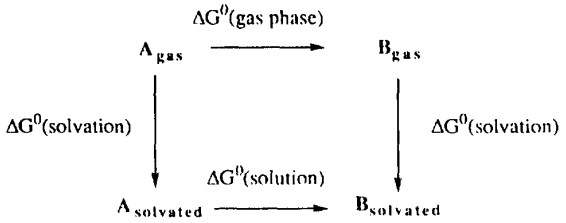

Fig 2. **A** and **B** are two ethanediol conformers; the methods presented in the *Introduction* estimate only the ΔG^0 (solvation) among ethanediol conformers.

The above methods only evaluate the solvation energy of each conformer. To evaluate their energy in solution, their gas phase energy must be added (fig 2). Nagy et al [5, 6] estimated the gas phase energies from ab initio calculations. Single energy points were made at the MP2/6-31G(d) level on HF/6-31G(d) optimized geometries. Hooft et al [7] only considered the results of the GROMOS force-field.

Nagy et al showed that 99% of the conformers in solution are *gauche*; 66.7% do not have any intramolecular hydrogen bond in solution. They correspond to *tGg* (63.7%), *tGt* (2.9%) and *gGg* (0.1%). The *tGg'* and *gGg'* weights in solution are 8.1% and 24.7% respectively. These results imply that there is an inversion of stability among the different conformers in solution. However, *tGg'* and *gGg'* still have a significant weight in solution, and, therefore, intramolecular hydrogen bonds

Table I. Energies (relative to tGg') of ethanediol conformers, in kcal mol^{-1}.

Conformer	*Semi-empirical*		*Ab initio methods*									*Empirical models*	
	AM1	*PM3*	*(a)*	*(b)*	*(c)*	*(d)*	*(e)*	*(f)*	*(g)*	*(h)*	*(i)*	*MM3(94)*	*Mitra*
tGg'	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
gGg'	−0.88	−1.39	0.23	0.20	0.02	−0.09	−0.09	−0.01	−0.19	0.42	0.50	0.98	0.39
$g'Gg'$	−0.95	−0.78	1.22	1.21	1.04	1.49	0.89	1.02	1.61	0.63	1.06	–	1.53
gGg	−0.98	−0.82	3.35	–	3.34	3.03	2.52	2.70	2.88	2.46	3.29	–	2.34
tGg	2.54	1.76	4.44	–	4.36	4.28	3.65	3.68	4.43	3.03	3.78	–	3.06
tGt	*	*	4.23	–	4.30	4.24	3.61	3.60	4.20	3.02	3.24	2.62	2.65
tTt	2.97	2.55	3.23	3.23	3.29	3.31	2.97	3.10	4.00	2.54	2.63	2.04	2.95
tTg	1.55	1.06	–	3.25	3.20	3.14	2.87	3.05	3.95	2.22	2.83	–	3.57
gTg	0.22	−0.68	–	2.99	3.09	2.93	2.59	2.70	3.60	2.23	3.09	–	3.61
gTg'	0.39	−0.43	–	–	2.81	2.67	2.38	2.59	3.72	2.80	2.86	–	4.17

* Structures not stable during optimization. Semi-empirical methods: cf [27]. Ab initio methods: (a) MP2/6-31G(d)//6-31G(d) with zero point and temperature corrections at 298 K [5, 6], (b) MP2/6-31G(d,p) [8], (c) MP4/6-31G(d), (d) MP4/6-311G(d,p), (e) NLSD/DZPV2, (f) NLSD/TZVP, (g) LSD/DZPV2 (from (c) to (g) cf [9]), (h) MP2/cc-pVTZ//HF/cc-pVDZ with zero point and temperature corrections at 298 K [27], (i) MP2/6-311+G(2d,2p)//HF/6-31G(d,p) [11]. Empirical models: MM3(94) [2].

should be observed in solution, which is not consistent with experiment.

Hooft et al [7] predicted that none of the most stable conformers would have an intramolecular hydrogen bond. However, these authors reported a 67:33 ratio in favor of *gauche* conformers, which is also not consistent with experiment.

Finally, both studies predict a more stable solvation energy for tTt than for tGg', of about 1 kcal mol^{-1}.

Another approach is to consider the solvent as a dielectric continuum, using only ab initio calculations. The solvent molecules are not explicitly taken into account; the solvent effects are introduced by adding a perturbative term to the Hamiltonian of the isolated system. This method was chosen by Alagona et al [21], who used the polarized continuum model (PMC) developed by Tomasi et al [22, 23]. Ab initio calculations were carried out at the HF/4-31G and HF/6-31G(d) levels. The perturbation introduced by the solvent is estimated on geometries optimized in vacuum. Only tGg', gGg', $g'Gg'$ and tTt were considered. The results show that $g'Gg'$, gGg' and tTt are better solvated than tGg', by 1.1, 0.6 and 0.2 kcal mol^{-1}, respectively. However, no inversion of stability in solution is expected because of the large energy difference in the gas phase between tGg' and the group composed of gGg', $g'Gg'$ and tTt (the difference between both groups is about 1.5 kcal mol^{-1}). However, the gas phase results were carried out at the SCF level, which gives results appreciably different from those of the MP2 level with a more extended basis set (table I).

The third approach is a combination of the other two by using the AM1-SM1a [24], AM1-SM2 [25], and PM3-SM3 [26] models. These models take into account the specific effects of the first solvation shell on solute molecules (in a semi-empirical way) and the influence of the rest of the solvent is taken into account using a dielectric continuum approach. Electrostatic charges of the soluted molecule are estimated with a semi-empirical method (AM1 or PM3, but the charges may be further adjusted). However, if these models try to introduce the specific influence of the first solvation shell, no solvent molecule is explicitly considered. As in previous approaches, these methods only estimate the solvation energy of the solute and their gas phase energy must be added in order to evaluate their energy in solution.

These three models were used by Cramer and Truhlar [27] to study the ten ethanediol conformers. Gas phase energies were estimated using ab initio calculations at the MP2/cc-pVTZ level on MP2/cc-VDZ optimized geometries. The geometries considered in solution were those obtained using ab initio calculations in the gas phase, or those reoptimized at the PM3-SM3 level. Whatever the model used, the results are similar for all of the models: the weight of tGg', gGg' and $g'Gg'$ decreases from 97% in the gas phase to about 80–90% in aqueous solution, while the weight of *trans* conformers increases from 2.3% in the gas phase to 5–10% in aqueous solution. These results imply that an intramolecular hydrogen bond for ethanediol should be observed in solution, which is not consistent with experiment.

None of these theoretical approaches take into account the direct interactions among ethanediol and the solvent molecules. The purpose of this article is to study such interactions. Recently, we proposed a new force-field to describe hydrogen bonds among water molecules, alcohols and ether-oxides [28, 29]. The originality of this force-field is the addition of a specific hydrogen bonding energy term (E_{tc}) to the classical exchange (E_{ex}), electrostatic (E_{elec}), polarization (E_{pol}) and intramolecular relaxation (E_{int}) terms. The E_{tc} term was introduced to more closely reproduce the ab initio results at the MP2/6-311++G(2df,2p) level for hydrogen interchange barriers in the water dimer; it stands for an anisotropic function, while more classical expressions are used for the other terms:

$$E_{ex} + E_{pol} = \sum \frac{A}{r^n} - \frac{B}{r^6}$$

$$E_{elec} = \sum \frac{qq'}{4\pi\varepsilon_0 r}$$

$$E_{\text{int}} = \sum_{\text{stretch}} k_l(l - l_0)^2 + \sum_{\text{bending}} k_\alpha(\alpha - \alpha_0)^2 + \sum_{\text{torsion}} \sum_{1,3} V_n \cos(\beta + n\beta_0)$$

$$E_{\text{tc}} = \sum f(r)g(\theta)p(\psi)$$

$$f(r) = -D_e \exp\left(-\frac{(r - r_0)^2}{\gamma_r}\right)$$

$$g(\theta) = 1 - \sum_{3,4} \alpha_n \sin^2(n\Delta\theta)$$

$$p(\psi) = 1 - \delta_4 \sin^2(4\Delta\psi)$$

Variables r, θ and ψ are given in figure 3. Because the minima of this function are close to the position of the water oxygen lone pairs (taken as sp^3 orbitals), this function is assumed to take into account the charge transfer occurring in hydrogen bonds among water molecules. Many-body interactions are not taken into account in this model (they are estimated to represent about 10–20% of the binding energy of water clusters bigger than the dimer). However, this approach gives good results for describing the minimum structures of water and alcohol clusters.

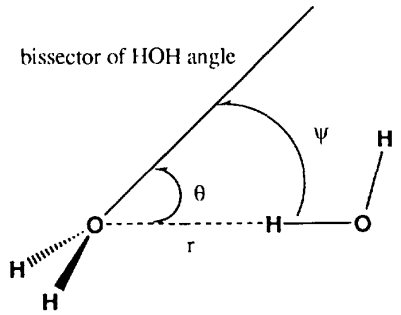

Fig 3. Definition of r, θ and ψ variables of the E_{tc} term.

The purpose here is to adapt this model (which we call Mitra) to ethanediol (by adapting some parameters in order to reproduce ab initio and experimental results in the gas phase) and, then, to study the influence of the first solvation shell molecules on ethanediol and, in particular, the competition between intra- and intermolecular hydrogen bonds. Three solvents may be considered: water, methanol and methoxymethane. Only methoxymethane is considered here, in order to facilitate the study (see below). In particular, we will focus on the study of ethanediol-methoxymethane complexes and on the insertion of solvent molecules at the intramolecular hydrogen bond of conformers tGg', gGg' and $g'Gg'$. In contrast with almost all previous theoretical approaches, none of the intramolecular degrees of freedom is frozen.

The influence of the rest of the solvent on each conformer is evaluated using a simple dielectric continuum approach. The solvent reacts in the presence of a neutral molecule of dipole moment $\vec{\mu}$, by a reaction field $\vec{R}$ [30]:

$$\vec{R} = \frac{2(\varepsilon - 1)}{(2\varepsilon + 1)} \frac{\vec{\mu}}{a_0^3} \quad (1)$$

ε is the solvent dielectric constant and a_0 the radius of a sphere surrounding the solvated molecule. The reaction field energy is given as follows:

$$E_{\text{react}} = -\vec{\mu} \cdot \vec{R} \quad (2)$$

In Mitra, the electrostatic charges q_i are located on atomic centers. Therefore, the dipole moment is given by:

$$\vec{\mu} = \sum q_i \cdot \vec{r}_i \quad (3)$$

Considering equations (1) and (3), equation (2) may be written as follows:

$$E_{\text{react}} = \frac{2(\varepsilon - 1)}{(2\varepsilon + 1)} \times \frac{1}{a_0^3} \times \sum_{i<j} q_i q_j \cdot (\vec{r}_i \cdot \vec{r}_j) \quad (4)$$

Numerous definitions exist for the radius a_0 used in equation (4), and their choice is generally arbitrary. In this paper, a_0 is the radius of the sphere which surrounds the solvated molecule in the best way, to which the half distance between the two oxygen atoms of the water dimer is added (1.5 Å). The position vectors $\vec{r}_i$ of each atom are evaluated in a orthonormal frame which origin corresponds to the center of the previous sphere (E_{react} calculated in such a way does not correspond to a ΔH^0 but to a ΔG^0).

Because of the ambiguous nature of the first solvation shell molecules in our approach (do they belong to the solvent?), the reaction field was not applied to the entire conformer–solvent molecule complexes, but only to the conformers, in their geometry perturbed by the presence of the first solvation shell molecules.

In the following sections, molecules and clusters are optimized with the SLEIPNIR program [29], until a gradient value of 10^{-3} kcal mol^{-1} Å^{-1} was reached.

Parametrization and gas phase study

In order to study the ethanediol conformers with Mitra, electrostatic charges for both molecules must be determinated, as well as some torsional parameters.

Definition of parameters

- *Electrostatic charges*

If we consider the gas phase experimental results on 2-methoxyethanol (obtained using microwave spectrometry [31]), the tGg' conformer is the most stable in the gas phase. Its dihedral O–C–C–O angle and dipole moment values were estimated at $57 \pm 3°$ and 2.36 debyes.

Electrostatic charges were assigned to reproduce the experimental dipole moment of the methoxymethanol tGg' conformer (the O–C–C–O angle is arbitrarily fixed at 57°). The charges are given in figure 4. Electrostatic charges for each type of ethanediol atoms are those of methoxyethanol (fig 4).

- *Charge transfer term E_{tc}*

Parameters of E_{tc} correspond to those for alcohol for the oxygen atoms of the H–O–C type and to those for methoxymethane for atoms of the C–O–C type [28, 29].

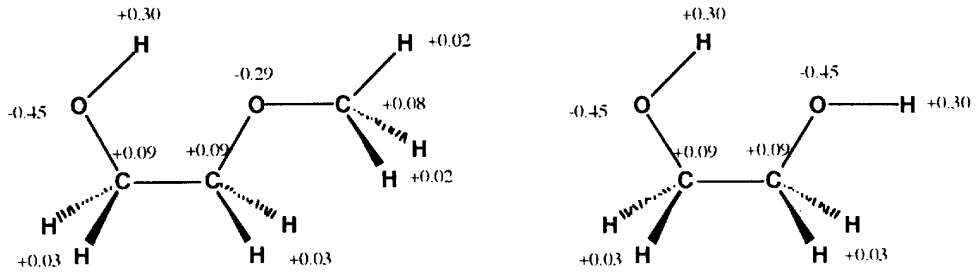

Fig 4. Electrostatic charges (in au).

• *Torsional term*

Stretching, bending and torsional parameters are those of the MM2 force-field [32], except for those corresponding to the O–C–C–O and H–O–C–C dihedral angles.

Parameters V_1, V_2 and V_3 of the O–C–C–O torsional term for ethanediol were determined to reproduce the energy of *tTt* (relative to *tGg'*). This energy was taken equal to 3 kcal mol^{-1}, which corresponds to the ab initio estimate (table I). Parameter V_3 of the H–O–C–C torsional term was estimated to make the *gGg* conformer stable during optimization (with MM2 parameters, *gGg* looses its symmetry and evolves to *gGg'*). These torsional parameters are given in table II.

Table II. Torsional parameters in kcal mol^{-1}.

	O–C–C–O	*H–O–C–C*
V_1	1.10	0.0
V_2	−2.86	0.0
V_3	−1.80	1.20

Ethanediol gas phase study

Mitra results for the ten ethanediol conformers are given in table III. In this table, the total conformer energies are decomposed in E_{tc}, E_{int} and $E_{iso\text{-}intra}$ contributions (cf *Introduction* and [27, 28]); the definition of the last term is given by equation (5):

$$E_{iso\text{-}intra} = (E_{ex} + E_{pol} + E_{elec})_{intramolecular} \quad (5)$$

Table III. Energies in kcal mol^{-1}, $E_{tot} = E_{tc} + E_{iso\text{-}intra} + E_{int}$ for the definition of $E_{iso\text{-}intra}$ see text.

Conformer	E_{tc}	$E_{iso\text{-}intra}$	E_{int}	E_{tot}
tGg'	−0.81	12.28	−2.98	8.50
gGg'	−1.60	12.89	−2.40	8.89
g'Gg'	−0.01	13.08	−3.06	10.03
gGg	0.00	13.91	−3.07	10.84
tGg	0.00	14.68	−3.12	11.56
tGt	0.00	14.12	−2.97	11.14
tTt	0.00	11.90	−0.45	11.45
tTg	0.00	12.44	−0.37	12.07
gTg	0.00	12.50	−0.40	12.11
gTg'	0.00	13.04	−0.38	12.67

In a first approximation, the E_{tc} term is assumed to describe the charge transfer occurring in hydrogen bonds (cf, *Introduction*). These phenomena are assumed to play an important role in stabilizing such bonds and are responsible for their great directionality, as the Coulson model suggests [33]. Therefore, the E_{tc} value may indicate the strength of a hydrogen bond. A large E_{tc} value corresponds to strong charge transfer while a small E_{tc} value indicates weak charge transfer. If we assume that hydrogen bonding may be characterized by the strength of the charge transfer, a zero value for E_{tc} should indicate that no hydrogen bond is established. According to this hypothesis and the results given in table III for ethanediol conformers, the large values of E_{tc} for *tGg'* and *gGg'* imply that they have an intramolecular hydrogen bond, while the zero value for the other indicates that they do not have any hydrogen bonds. We should note that the *tGg'* and *gGg'* intramolecular hydrogen bonds are weaker than intermolecular bonds. The E_{tc} for both conformers is lower than for the methanol dimer (−2.25 kcal mol^{-1} [29]). Intramolecular constraints in the two conformers prevent them from establishing an intramolecular hydrogen bond with a geometry close to the geometry of an 'ideal' bond, as was the case for the water and methanol dimers.

Energies (relative to *tGg'*) of the ten conformers are given in table I. Conformer *tGg'* is the most stable conformer, followed by *gGg'* and *g'Gg'* (+0.39 and +1.53 kcal mol^{-1}, respectively). After this first group, we find a second group composed of the remaining conformers, whose energies lie between +2.34 and +4.17 kcal mol^{-1}.

• *Comparison with other theoretical methods*

All of the theoretical results published to date for the energy (relative to *tGg'*) of ethanediol conformers are given in table I. Mitra, AM1, PM3, MM3(94) and ab initio results are compared in figure 5. In order to compare the results of the different methods more thoroughly, we have defined an energy region called the ab initio domain. This is delimited by the maximum and minimum ab initio energies (relative to *tGg'*) for each conformer (fig 5, borderlines of the domain correspond to the Min and Max profiles). As shown in figure 5, Mitra results for most of the conformers are included in the ab initio domain, except for *tGt* and *gTg'*, which are localized a little way outside (by at most about

0.5 kcal mol^{-1}). In comparison, the AM1 and PM3 results disagree with ab initio calculations for almost all of the conformers; only the *tTt* energy is included in the domain. The MM3(94) force-field gives results in better agreement with ab initio calculations. However, none of the conformers have energies included in the ab initio domain. The result for MM3(94) was expected because its parameters were derived from SCF ab initio calculations, which gives appreciably different results for the conformers than do the MP2 level, as reported by Alagona et al [21].

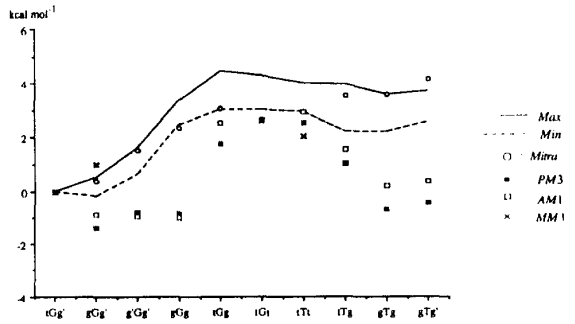

Fig 5. Comparison of ethanediol conformers energy (relative to *tGg'*) among different theoretical methods. Min and Max: their definitions are given in the text; *AM1* and *PM3*: cf [27]; *MM3*: MM3(94) force-field [2].

Even for conformer geometries, Mitra results agree with ab initio methods [5, 6]. Both kind of methods give comparable O–C–C–O dihedral angle values (table IV), except for *gGg*, for which there is a difference of about 10° between both. However, there is an uncertitude of about ±5° for the ab initio O–C–C–O dihedral angle value (table IV) and the above disagreement may not be considered as a weakness of Mitra.

Because of the agreement for the O–C–C–O dihedral angle, Mitra dipole moment values also agree with ab initio calculations (table IV).

Table IV. O–C–C–O dihedral angle value in degrees, and, in parentheses, dipole moment values in debye.

Conformer	*Mitra*	*Ab initio*	*Experiment*
tGg'	59.7° (2.46)	60.6° (2.65)	57.9° (2.28)
gGg'	57.5° (2.27)	59.7° (2.60)	(2.47)
g'Gg'	66.5° (0.38)	59.4° (0.08)	–
gGg	65.9° (1.78)	54.8° (–)	–
tGg	71.7° (3.02)	64° (–)	–
tGt	78.1° (1.65)	72.6° (–)	–
tTt	180.0° (0.0)	180.0° (0.0)	–
tTg	177.3° (2.16)	179.3° (2.32)	–
gTg	180.0° (0.0)	180.0° (0.0)	–
gTg'	180.0° (2.31)	–	–

Ab initio results at the HF/6-31G(*d*) level for dihedral angles [5, 6] and at the HF/6-31G(*d,p*) level for dipole moments [2]. Experimental values; the dihedral angle for *tGg'* is cited in [2] and dipole moments come from [3] and [34].

• *Comparison with experiment*

For Mitra, *tGg'* and *gGg'* are the most stable conformers in the gas phase. They have an intramolecular hydrogen bond and a *gauche* O–C–C–O conformation. These are consistent with gas phase experimental observations.

Methoxyethanol gas phase study

Mitra results for *tGg'*, *tGg*, *tGt* and *tTt* are given in table V, where Mitra energies (relative to *tGg'*) for the four conformers are compared to ab initio (at the HF/6-31G(*d,p*) level [2]) and MM3(94) [2] results. The *tGg'* conformer is the most stable in gas phase (as for ethanediol), and has an intramolecular hydrogen bond, stronger than that present in the ethanediol *tGg'* conformer ($E_{tc} = -1.79$ kcal mol^{-1} and -0.81 kcal mol^{-1} respectively, table III).

Table V. Energies in kcal mol^{-1}.

Conformer	*Mitra*[a]				ΔE[b]		
	E_{tc}	$E_{iso\text{-}intra}$	E_{int}	E_{tot}	*Ab initio*	*MM3*	*Mitra*
tGg'	−1.79	9.55	−2.37	5.38	0.0	0.0	0.0
tGg	0.0	1.30	−3.16	8.14	–	–	2.76
tGt	0.0	1.89	−3.11	7.79	3.54	2.14	2.41
tTt	0.0	8.36	−0.37	7.99	2.02	1.93	2.61

[a] Energy decomposition obtained by Mitra according to equation (5); [b] energy relative to *tGg'*; ab initio: results at the HF/6-31G(*d,p*) level [2]; MM3: MM3(94) results, cf, [2].

Mitra, MM3(94) [2] and ab initio (at the HF/6-31G(*d,p*) level) results for the dihedral O–C–C–O angle and dipole moment values of the four conformers are compared to experiment in table VI. As in the case of ethanediol, Mitra agrees with the experimental observations. *tGg'* is the most stable conformer in gas phase. It presents an intramolecular hydrogen bond and a *gauche* O–C–C–O conformation. The *tGg'* dihedral O–C–C–O angle value for Mitra is 54.2°, which agrees with an electronic diffraction result (at the limit of the error bar [2]): 57 ± 3°.

Conclusion of the gas phase study

As gas phase results for ethanediol and methoxyethanol indicate, the Mitra model can reproduce both ab initio and experiment results for those molecules and, therefore, it can also give a good description of intramolecular hydrogen bonding.

A simple solvation approach for ethanediol

In this section, another interpretation of the behavior of ethanediol in solution will be proposed. In particular, we will focus on the study of direct interactions among ethanediol conformers and molecules of the first solvation shell with Mitra.

Four types of solvent were considered in experimental studies: water, heavy water, decanol, and dioxane. To simplify the study, these solvents are considered

Table VI. Dihedral O–C–C–O angle value in degrees.

Conformer	*Mitra*	*Ab initio*	*MM3(94)*	*Experiment*
tGg'	54.22 (2.30)	61.40 (2.55)	62.10 (2.16)	57 ± 3 (2.36)
tGg	71.55 (2.81)	–	–	–
tGt	75.60 (1.77)	(1.64)	(1.72)	–
tTt	180.0 (0.39)	(0.33)	(0.51)	–

In parentheses, dipole moments in Debye; ab initio: results at the HF/6-31G(*d,p*) level [2]; MM3(94): MM3(94) force-field results [2]; experimental results ([2]–[31]).

hereafter as water, methanol and methoxymethane. The search of the most stable structures of complexes composed of ethanediol and solvent molecules will be more and more difficult with the nature of the three solvents. The study of ethanediol–methoxymethane complexes appears to be the easiest. The most stable complexes are a priori those where the methoxymethane oxygen points toward one of the ethanediol hydroxyl groups. To saturate all of the hydrogen bond possibilities between methoxymethane and ethanediol, one or two methoxymethane molecules must be added, in accordance with the conformer's structure (fig 6–8).

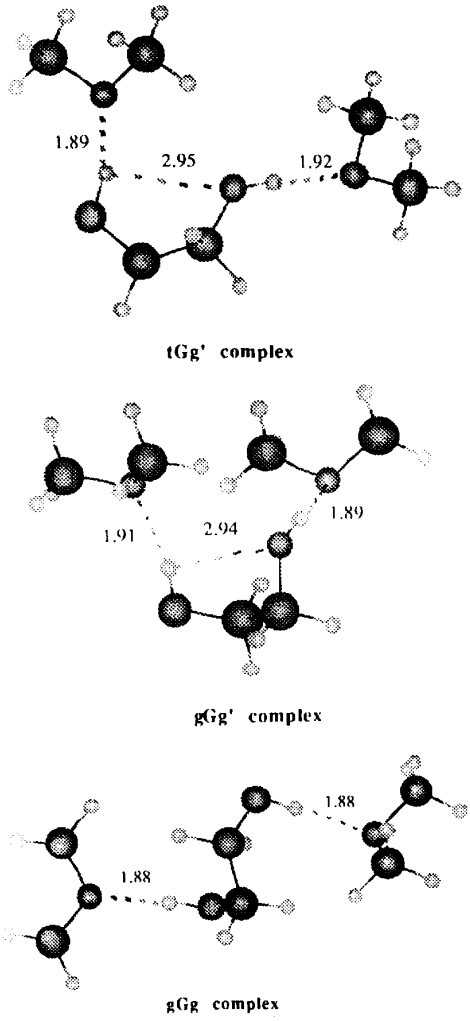

Fig 6. Ethanediol–two methoxymethane molecules complexes, optimized geometries. Interatomic distances are given in angstrom.

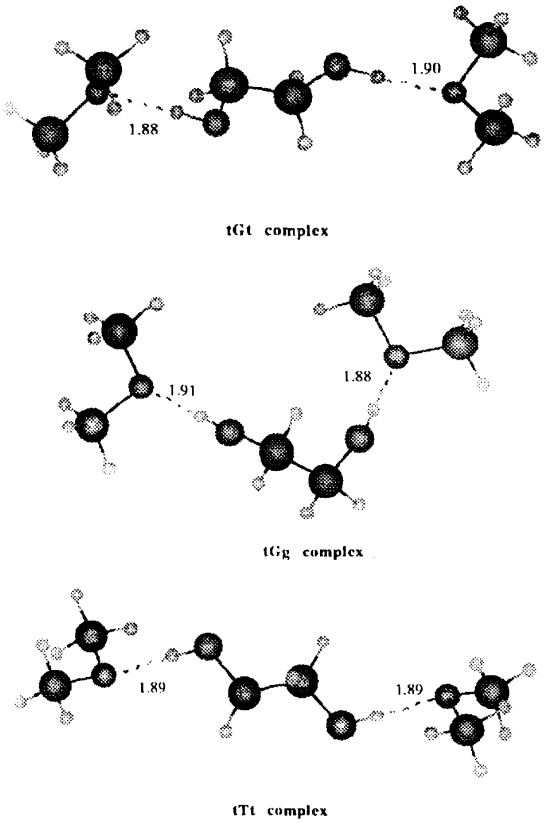

Fig 7. Ethanediol–two methoxymethane molecules complexes, optimized geometries. Interatomic distances are given in angstrom.

First, the ethanediol–methoxymethane complexes were optimized in vacuum (optimized geometries are given in fig 6–8; except for *tTg* and *gTg'*, their geometries are similar to *tTt*). The reaction field was then applied to the ethanediol conformers only (the methoxymethane molecules were ignored, cf *Introduction*), in their complexed geometry. Association and reaction field energies are given in table VII. The energy in solution of each conformer is taken as the sum of the reaction field energy and the double ethanediol–methoxymethane association energy.

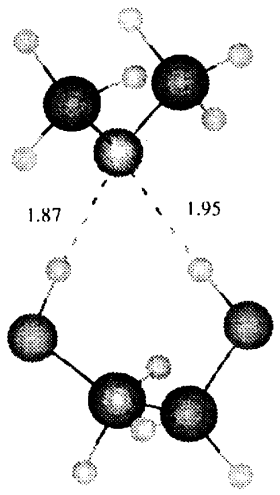

Fig 8. Ethanediol ($g'Gg'$ conformer)–one methoxymethane molecule complex.

Table VII. Energy (relative to tGg') in kcal mol^{-1}.

Conformer	ΔE_0	ΔE_1	ΔE_2	ΔE_{reac}	$\Delta E_2 + \Delta E_{reac}$
tGg'	0.0	0.00	0.00	0.00 (−0.22)	0.00
gGg'	0.39	0.13	−0.51	−0.10 (−0.32)	−0.61
$g'Gg'$	1.53	−0.62	1.82[a]	0.16[a] (−0.06)	1.98[a]
gGg	2.34	2.15	0.33	0.04 (−0.18)	0.37
tGg	3.06	3.11	1.18	−0.30 (−0.52)	0.88
tGt	2.65	2.93	1.15	0.12 (−0.10)	1.27
tTt	2.95	3.23	1.43	0.22 (0.0)	1.65
tTg	3.57	3.73	1.73	−0.03 (−0.25)	1.70
gTg	3.61	3.80	1.78	0.22 (0.0)	2.00
gTg'	4.17	3.60	1.32	−0.16 (−0.38)	1.16

ΔE_0: energy in gas phase; ΔE_1: energy of the ethanediol–one methoxymethane molecule complexes; ΔE_2: energy of ethanediol–two methoxymethane molecule complexes; ΔE_{reac}: reaction field energy, and, in parentheses, the total E_{reac} reaction field contribution; [a]: the definition of these energies for $g'Gg'$ are given in the text.

Influence of the reaction field

The stabilization due to the reaction field is weak for all of the conformers. Even for tGg, whose dipole moment is very high in gas phase (3.03 Debye, table IV), the stabilization is about −0.5 kcal mol^{-1}. This arises from the low dipole moment of methoxymethane (1.31 debyes) and from the complexes size (fig 6–8). As shown in table VII, the reaction field does not modify the stabilities of each conformer in a sensible manner. This implies that the solvation of ethanediol in a methoxymethane solution is only due to direct solute–solvent interactions.

Solvation results

In contrast to the other conformers, $g'Gg'$ may establish hydrogen bonds with only one methoxymethane molecule. Its double association energy is assumed to be the simple, to which the energy of an isolated methoxymethane molecule is added (1.65 kcal mol^{-1}). As table VII indicates, its energy in solution (relative to tGg') is quite similar to the gas phase: +1.98 and +1.53 kcal mol^{-1}, respectively.

There is an inversion of stability between tGg' and gGg' in solution. The energy difference between both decreases from +0.39 kcal mol^{-1} in the gas phase to −0.61 kcal mol^{-1} in solution (table VII). There is also a decrease of the energy difference between the tGg' and gGg' groups and the group composed of the remaining conformers:

– the gGg energy (relative to tGg') decreases from +2.34 kcal mol^{-1} in the gas phase to +0.37 kcal mol^{-1} in solution;

– for tGg and tGt, the energy difference with tGg' and gGg' is reduced by about 1 kcal mol^{-1}.

– the energy difference among *trans* conformers and tGg' and gGg' is reduced between gas phase and solution by about 2 kcal mol^{-1} and even by 3 kcal mol^{-1} for gTg' (table VII).

These results imply that the energy differences among conformers are considerably reduced in solution, as compared to the gas phase. The two conformers tGg' and gGg' have a significant weight in gas phase. In solution, six conformers are present: tGg', gGg', gGg, tGg, $\gamma Tg'$ and tGt.

The weight of each conformer in solution at 300 K has been estimated using a simple Boltzman statistic relation. The solvation energy (relative to tGg') of each conformer corresponds to the sum $\Delta E_2 + \Delta E_{reac}$ (table VII). The weight of each conformer is given by equation (6):

$$\text{weight} = \frac{\exp\left(-\dfrac{\Delta E_2 + \Delta E_{react}}{RT}\right)}{\sum_{\text{conformers}} \exp\left(-\dfrac{\Delta E_2 + \Delta E_{react}}{RT}\right)} \qquad (6)$$

In this equation, enthalpy variations are assimilated to free enthalpy variations and entropy effects are neglected. This approximation will be discussed in the *Conclusion*.

The weight of each conformer in solution (calculated with equation (6)) are given in table VIII. Our results are consistent with experiment; *gauche* conformers are still predominant in solution (they represent about 94% of the conformers) and the weight of *trans* conformers (unobserved in gas phase) increases in a sensible manner in solution, to 6% of the conformers (notably gTg' at 2.6%). However, the total weight of *trans* conformers is about twice smaller than the experimental estimate in heavy water, 12 ± 3% [14].

Experiment clearly indicates the complete absence of any intramolecular hydrogen bonds for ethanediol in solution [13]. Our results imply that tGg' and gGg' represent about 76% of the conformers in solution, and these conformers present an intramolecular hydrogen bond in the gas phase. Our approach seems to be in disagreement with experiment, but this is not the case. In solution, even if tGg' and gGg' maintain their symmetry, their intramolecular hydrogen bonds are disrupted by the insertion of a methoxymethane molecule, as results for the $O_1 \cdots H_2O_3$ distances suggest for both conformers (fig 9). These distances increase for both from about 2.10 Å in the gas phase to about 2.95 Å

Table VIII. Conformer weight in solution at 300 K.

Conformer	*gGg'*	*tGg'*	*gGg*	*tGg*	*gTg'*	*tGt*	*tTt*	*tTg*	*g'Gg'*	*gTg*
Weight	55.6%	20.0%	10.8%	4.6%	2.6%	2.4%	1.1%	1.0%	0.7%	0.6%

when a methoxymethane molecule is inserted. The intramolecular charge transfer term becomes null in solution for both conformers (table IX). This implies the complete disruption of their intramolecular hydrogen bond. Therefore, even if *tGg'* and *gGg'* have a significant weight in solution, they do not present any intramolecular hydrogen bond. Because *gGg*, *tGg* and *gTg'* do not have an intramolecular hydrogen bond in the gas phase or in solution, our results are consistent with experiment. There is a complete absence of any intramolecular hydrogen bond for ethanediol in solution.

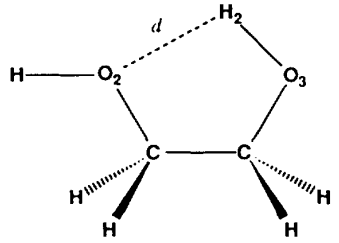

Fig 9. Definition of the *d* distance of table IX.

Table IX. Distance *d* in Å (cf fig 9).

Conformers	*tGg'*		*gGg'*	
	E_{tc}	*d*	E_{tc}	*d*
Isolated	−0.81	2.14	−1.81	2.01
Solvated	0.00	2.95	0.00	2.94

E_{tc}: intramolecular charge-transfer term for *tGg'* and *gGg'*, in kcal mol^{-1}.

For the dihedral O–C–C–O angle of ethanediol in solution, experimental results indicate a value of about 72–74° [15, 16]. In the gas phase, the most accepted value is about 60°, which corresponds to the dihedral O–C–C–O angle value of *tGg'* and *gGg'* in the gas phase (see above). Table X summarizes the dihedral O–C–C–O angle values for each conformer, in the gas phase and in solution (when each conformer is complexed by one or two methoxymethane molecules). According to this table, the dihedral angle of *tGg'*, *gGg'*, and *g'Gg'* is strongly affected by solvation. For the four conformers, the dihedral angle value grows from about 60° in gas phase to reach a value lying between 71° and 76° in solution. For the other *gauche* conformers, the dihedral O–C–C–O angle is less affected. Its value increases by 5° at most to reach a value between 70° and 78°. Therefore, the dihedral O–C–C–O angle value predicted in solution by Mitra for all of the *gauche* conformers (which are predominant in solution) lies between 70 and 78°. This result agrees with experiment (72–74°).

Even if Mitra overestimates the gas phase dihedral O–C–C–O angle value for *gGg*, *tGg* and *tGt* (as compared to ab initio results, table IV), our results cannot be considered as an artefact because these *gauche* conformers represent less than 18% of the conformers in solution (table VIII).

Table X. The dihedral O–C–C–O angle value in degrees.

Conformer	*Gas phase*	*Solution*
tGg'	59.7	72.3
gGg'	57.5	71.4
g'Gg'	66.5	75.3[a]
gGg	65.9	70.8
tGg	71.7	74.2
tGt	78.1	77.8
tTt	180.0	180.0
tTg	177.3	179.2
gTg	180.0	179.7
gTg'	180.0	179.4

Solution: value for ethanediol–two methoxymethane molecules complexes; [a] except for *g'Gg'*: value for ethanediol–one methoxymethane molecule.

The notable increase of the dihedral O–C–C–O angle value of *tGg'*, *gGg'* and *g'Gg'* appears to be a direct result of the insertion of a methoxymethane molecule (fig 6–8).

Conclusion

A simple approach is presented to study the ethanediol solvation. The solvent is taken as a hypothetical methoxymethane solution, and direct interactions between solvent molecules and ethanediol were studied in the gas phase with the Mitra model. The influence of the rest of the solvent is accounted for by using a dielectric continuum approach.

This solvation approach exhibits three important points. First, as in the case of the gas phase, *gauche* conformers are still predominant in solution (in particular, *tGg'*, *gGg'*, *gGg* and *tGg*). They represent about 94% of the conformers in solution. However, there is a large increase of the *trans* conformer weight in solution where they represent 6% of the conformers (*gTg'* represents 2.6% of the conformers in solution). Second, disruption of any intramolecular hydrogen bonds in solution, even for *tGg'* and *gGg'*. For both conformers, the intramolecular hydrogen bond is disrupted by the insertion of a solvent molecule. Third, increase of the dihedral O–C–C–O angle value in solution for all of the *gauche* conformers. For *tGg'*, *gGg'* and *g'Gg'*, this dihedral angle increases from 60° in the gas phase to 71–76° in solution. For all of the *gauche* conformers, this angle lies between 70° and 78° in solution.

These results are consistent with all of the experimental observations in solution: emergence of *trans* conformers (unobserved in gas phase), absence of any

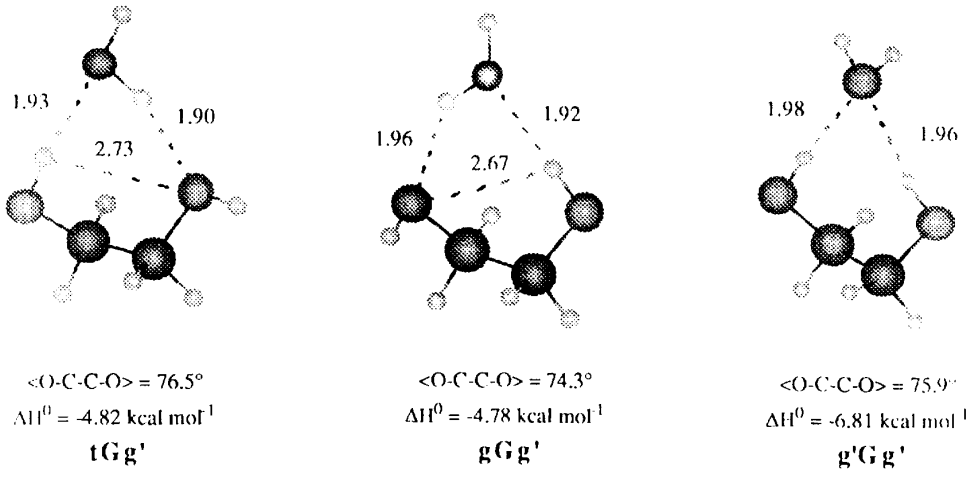

Fig 10. Ethanediol–water molecules complexes for tGg', gGg' and $g'Gg'$. The ΔH^0 given corresponds to the association energy of each complex. Interatomic distances are given in angstroms. For the three conformers, the intramolecular charge transfer term E_{tc} is null.

intramolecular hydrogen bond, and a dihedral O–C–C–O angle value estimated at 72–74°. However, two remarks should be made. First, the entropic effects are not taken into account in the solvation energy used in equation (6). The association entropy for the ethanediol–methoxymethane complexes will be more favorable for the *trans* conformers because of their less constrained structures (fig 6–8). Therefore, if entropic effects are considered, the *trans* conformer weight in solution would certainly be greater than that predicted by the present approach and in better agreement with experiment (12 ± 3% in heavy water) [14]. Second, in this solvation approach, the solvent is taken as a methoxymethane solution and most of the experimental observations were made in aqueous or alcoholic solutions. Nevertheless, by considering water or methanol as solvents instead of methoxymethane, the same tendencies are observed: insertion of a solvent molecule that disrupts the tGg' and gGg' intramolecular hydrogen bond and that is responsible for a large increase of the dihedral O–C–C–O angle value for tGg', gGg' and $g'Gg'$ (fig 10). However, these first results obtained with water and methanol have to be refined because of the large number of hydrogen bonds possible among ethanediol and such solvent molecules.

Our results in a methoxymethane solution reproduce almost all of the experimental observations of the ethanediol solvation, which no model has done to date, as far as we know. The results clearly show the great importance of insertion of solvent molecules that can disrupt intramolecular hydrogen bonds. These insertions are also responsible for sensible geometry changes for the solvated molecules (in particular, for the dihedral O–C–C–O angle of tGg', gGg' and $g'Gg'$), which exhibits the limit of solvation approaches in which internal degrees of freedom are frozen in their gas phase geometry. Our results contrast with Cramer and Truhlar's conclusion in aqueous solution [27], where the water molecules do not disrupt the ethanediol intermolecular hydrogen bonds and the conformers maintain a geometry close to that in the gas phase. We may notice here that the Cramer and Truhlar's models [24–26] do not take explicitly into account the intermolecular solvent–solute hydrogen bonds. They are considered using an energy term which takes into account many other effects (as cavitation, dispersion and entropic effects).

Our approach permits a new interpretation of the solvation processes for polyalcohols and suggests new theoretical and experimental studies. In particular, it will be interesting to apply our solvation approach to the study of the α and β glucose isomers, and to evaluate the role of the insertion of solvent molecules in the anomeric site of both isomers. However, because of the simplicity of the solvation model presented here, more accurate studies (using Monte-Carlo or molecular dynamics simulations) have to be done to confirm our conclusions, especially by considering other solvents such as water or methanol.

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