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Effect of the Folding of Methylene Units in the Conformational Preferences of Small Diesters

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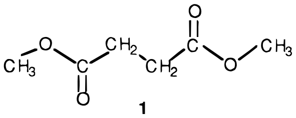
The conformational preferences of dimethyl succinate and ethylene glycol diacetate have been explored in the gas phase using ab initio quantum mechanical calculations at the HF/6-31G(d) and MP2/6-31G(d) levels. Furthermore, the effects of both aqueous and carbon tetrachloride solvents have been estimated using the self-consistent reaction-field model developed by Miertus, Scrocco, and Tomasi and adapted to semiempirical methods by Orozco and Luque. The results have been interpreted in terms of the so-called "folding of methylene units", which is the tendency of the methylene units to adopt a *gauche* conformations when a short aliphatic segment is placed between two carbonyls. For dimethyl succinate the lowest energy conformation corresponds to the TTGTT as expected from our previous studies on the folding of methylene units. On the other hand, for ethylene glycol diacetate the global minimum is the TGG$\bar{\text{S}}$T conformation, which is stabilized by the simultaneous combination of two stereoelectronic effects: (i) the folding of methylene units and (ii) the *gauche* oxygen effects.

Introduction

During the past few years we have reported a set of experimental[1−4] and theoretical[1,3−7] studies about the so-called "folding of methylene units". This consists in the tendency of the methylene units to adopt a *gauche* conformation when the aliphatic segment is placed between two carbonyl groups. Recently published studies based on X-ray crystallography and quantum mechanical calculations on small diamide compounds [RNHCO-$(CH_2)_n$CONHR, with $n = 2$, 3, and 4] concluded that the central methylene units do not keep a *trans* conformation but tends to fold into a *gauche* one.[1,2,5] These results were very important for organic and macromolecular chemistry since the methylene segments are usually considered in *all-trans* conformation in the solid state.

We extended our findings of the folding of methylene units to the asparagine and glutamine residues in peptides and proteins.[3,7] It was found that for the χ_1 and χ_2 side chain dihedral angles, in which methylene units are comprised between the backbone and side chain carbonyl groups, the *gauche* is the most populated conformation. More recently, we investigated the conformational properties of a set of small diketones [CH_3-$CO(CH_2)_nCOCH_3$, with $n = 2$, 3, and 4]. The results showed a strong parallelism with those found for diamides, giving a detailed picture of the folding of methylene units in ketones. Furthermore, the study of the conformational preferences of a compound with only one keto group revealed that the presence of the second carbonyl group plays a crucial role in the folding of methylene units.

We now investigate the existence of the folding of methylene units in diesters. More especifically, quantum mechanical calculations in gas phase, aqueous solution, and CCl_4 solution were performed on dimethyl succinate (**1**) and ethylene glycol diacetate (**2**), which contain two methylene units like the most simple diamide and diketone previously studied. A comparison of the effects of the amide, keto, and ester groups on the folding of methylene units has been performed along the work.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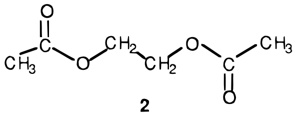
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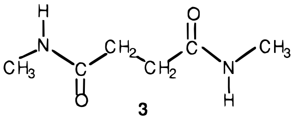
Structural Background

Three compounds closely related with **1** and **2** have been investigated in our previous works. These are *N,N′*-dimethylsuccinamide[2,5] (**3**), 2,5-hexanedione[6] (**4**), and *N*-(2-(acetylamino)ethylene)acetamide[4] (**5**).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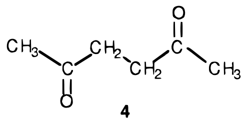
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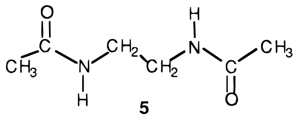
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***N,N′*-Dimethylsuccinamide.** The conformational preferences of the succinamide moiety were recently investigated in *N,N′*-succinylbis(*N*-propylglycinamide) using X-ray crystallography.[2] In this compound the succinamide unit present a TTGTT conformation. Ab initio quantum mechanical studies on **3** indicated that such folded conformation is favored with respect to the expected *all-trans* one by about 0.5−1 kcal/mol, depending on the computational level.[5]

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2,5-Hexanedione. Two different minima were found and characterized for **4** after a conformational search at the HF/6-31G(d) level.[6] These are the TGT and TTT. The latter was destabilized with respect to the former by 0.8 and 1.5 kcal/mol at the HF/6-31G(d) and MP2/6-31G(d) levels, respectively.

***N*-(2-(Acetylamino)ethylene)acetamide.** This compound was recently investigated by X-ray crystallography and quantum mechanical calculations.[4] Note that in **5** the two methylene units are separated from the carbonyl groups by the nitrogen atoms of the amide bonds. Therefore, the folding of methylene units should not be expected in this case. In the solid state a TST$\bar{S}$T conformation was found, which is similar to that characteristic of the γ-form of nylons. A complete exploration of the conformational space permits to characterize six different minima at the HF/6-31G(d) level. One such minima corresponds to the conformation determined by X-ray diffraction, although it is unfavored with respect to the global minimum by 3.0 kcal/mol. Inspection to the different minima revealed that the folding of methylene units requires dicarbonylic segments rather than diamine segments.

Methods

Gas-Phase Calculations. A complete exploration of the conformational space was performed in order to characterize the minimum energy structures of **1** and **2**. Since each of the three backbone dihedral angles are expected to have three minima, 27 different minima may be anticipated for the potential energy hypersurfaces of such compounds. However due to both the achiral nature and the chemical symmetry of the two compounds, the number of different minima can be reduced to 18. All of these structures were taken as starting points in HF/6-31G(d) geometry optimizations.[8] Frequency analyses were performed to verify the nature of minimum state of the stationary points located during geometry optimizations, as well as to obtain zero point energies (ZPE) and thermal corrections to the energy. Møller−Plesset perturbation treatment[9] at the MP2/6-31G(d) level was used to compute electron correlation energy.

Solvent-Phase Calculations. The free energies of solvation (ΔG_{solv}) were determined using a semiempirical AM1 adapted version[10−12] of the SCRF developed by Miertus, Scrocco, and Tomasi (MST/AM1).[13,14] According to this method, the ΔG_{solv} was determined as the addition of electrostatic and steric contributions (eq 1). The steric component was computed as the sum of the cavitation and van der Waals terms.

$$\Delta G_{\mathrm{solv}} = \Delta G_{\mathrm{elec}} + \Delta G_{\mathrm{cav}} + \Delta G_{\mathrm{vdW}} \tag{1}$$

The cavitation term was determined using Pierotti's scaled particle theory,[15] while the van der Waals term (eq 2) was evaluated by means of a linear relation with the molecular surface area:[10−12]

$$\Delta G_{\mathrm{vdW}} = \sum_i \xi_i S_i \tag{2}$$

where S_i is the portion of the molecular surface area belonging to atom i and ξ_i is the hardness of atom i.

Table 1. Selected Dihedral Angles[a] (deg) and Relative Energies (kcal/mol) of Dimethyl Succinate (1) Minimum Energy Conformations[b]

	I	II	III	IV	V	VI
C−O−C(=O)−C	−179.7	180.0	−179.9	−179.4	179.2	176.6
O−C(=O)−C−C	−169.4	−179.9	−179.2	−175.6	18.6	70.9
C(=O)−C−C−C(=O)	68.5	180.0	62.1	−178.8	58.4	61.9
C−C−C(=O)−O	−169.4	−179.9	25.2	59.4	18.7	70.5
C−C(=O)−O−C	−179.8	180.0	−179.7	179.4	179.2	176.6
ΔE(HF/6-31G(d))	0.0	0.7	1.7	2.1	3.1	3.6
ΔE(HF/6-31G(d))[c]	0.0	0.6	1.7	2.2	3.1	3.9
ΔE(MP2/6-31G(d))	0.0	1.6	1.2	2.4	2.0	2.7
ΔE(MP2/6-31G(d))[c]	0.0	1.5	1.2	2.5	2.0	3.0

[a] From ab initio HF/6-31G(d) geometry optimizations. [b] Conformers which are >3 kcal/mol greater in energy than the most stable form are not included in the table. [c] Zero-point energy and thermal corrections computed at the HF/6-31G(d) level are included.

The electrostatic interaction between the solute and the solvent was computed using the MST-SCRF approach, in which the solvent is represented as a continuous dielectric, which reacts against the solute charge distribution generating a reaction field. The effect of the solvent reaction field on the solute is introduced as a perturbation operator (V_{R}) in the solute hamiltonian (eq 3).

$$(H_0 + V_{\mathrm{R}})\Psi = E\Psi \tag{3}$$

The perturbation operator is computed in terms of a set of point charges located at the solute/solvent interface, *i.e.* the solute cavity. Such imaginary charges were determined by solving the Laplace equation at the solute/solvent interface. The electrostatic potential of the solute was computed at the AM1 level using the *ortho* method.[16]

In all cases the solute/solvent interface was determined using a molecular shape algorithm.[10−12] Standard van der Waals radii (C = 1.5 Å; N = 1.5 Å; O = 1.4 Å; H = 1.2 Å; H(bound to polar atoms) = 0.8 Å) were used. Scaling factors of 1.2 and 1.8 were used for water and CCl_4, respectively. Since the change of the molecular geometry upon solvation has a negligible effect on the thermodynamic parameters, only gas-phase-optimized geometries were used.[17,18] Previous studies indicated that the root mean square deviations between experimental and MST/AM1 ΔG_{solv} are l.0 and 0.40 kcal/mol for aqueous[13] and CCl_4[12] solutions, respectively. The conformational free energy differences in solution were estimated by adding $\Delta\Delta G_{\mathrm{solv}}$ to the relative energies in the gas phase.

Gas-phase calculations were performed with Gaussian-94[19] computer program. Solvation calculations were performed with an adapted version of MOPAC93 Revision 2 program,[20] which permits MST calculations with H_2O and CCl_4 solvents. All the calculations were run on a IBM-SP2 at the Centre de Supercomputacio de Catalunya (CESCA).

Results and Discussion

Folding of Methylene Units in the Gas Phase. The results from the HF/6-31G(d) geometry optimizations on the potential energy surfaces of **1** and **2** are displayed in Tables 1 and 2, respectively. Relative energies esti-

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Table 2. Selected Dihedral Angles[a] (deg) and Relative Energies (kcal/mol) of Ethylene Glycol Diacetate (2) Minimum Energy Conformations[b]

	I	II	III	IV	V	VI	VII	VIII
C−C(=O)−O−C	−174.2	179.3	179.1	179.9	179.2	−179.3	177.6	−176.1
C(=O)−O−C−C	79.7	80.0	−178.5	−179.9	−179.0	−179.2	84.2	92.5
O−C−C−O	64.5	58.2	68.4	179.9	64.2	175.5	180.0	−81.6
C−C−O−C(=O)	−95.8	80.1	−178.4	180.0	82.4	85.6	−84.2	92.5
C−O−C(=O)−C	179.5	179.4	179.2	179.9	179.3	178.3	−177.8	−176.2
Δ*E*(HF/6-31G(d))	0.0	0.4	0.4	0.5	0.8	0.8	1.1	1.1
Δ*E*(HF/6-31G(d))c	0.0	0.4	0.3	0.4	0.7	0.8	1.1	1.0
Δ*E*(MP2/6-31G(d))	0.0	1.3	2.4	3.1	2.2	2.9	0.9	2.4
Δ*E*(MP2/6-31G(d))	0.0	1.3	2.2	3.0	2.2	2.9	0.8	2.4

[a] From ab initio HF/6-31G(d) geometry optimizations. [b] Conformers which are >3 kcal/mol greater in energy than the most stable form are not included in the table. [c] Zero-point energy and thermal corrections computed at the HF/6-31G(d) level are included.

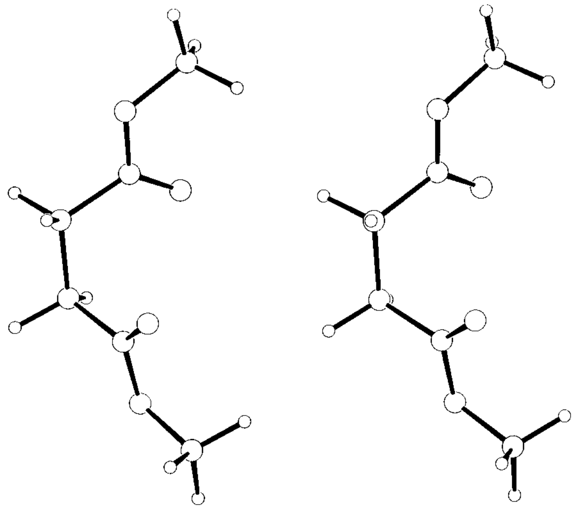

Figure 1. Stereopairs showing the lowest energy minimum (TTGTT conformation) of dimethyl succinate.

mated at the HF/6-31G(d) and MP2/6-31G(d) levels on such geometries are also included in Tables 1 and 2.

The exploration of the potential energy hypersurfaces of **1** and **2** provided eight and nine minima, respectively, which were characterized as such using frequency analyses. Equivalent and isoenergetic structures to the minima listed in Tables 1 and 2 were found by changing the sign of the three central backbone dihedral angles, as it should be expected from the chemical and molecular symmetry of the two compounds (data not shown). For instance, TTGTT and TTG̅TT are equivalent and isoenergetic minima. The potential energy hypersurfaces of the diesters **1** and **2** seem to be flatter than those of the related diamide **3** and diketone **4**. Thus, only two different minima were characterized for both **3** and **4**. On the other hand, six different minima were found for the diamide **5**, indicating this compound also presents a complex conformational behavior.

For **1**, the lowest energy minimum corresponds to the TTGTT conformation (Figure 1), as expected from our previous findings on the folding of methylene units. Thus, the carbonyl groups induce a *gauche* conformation for the bond defined by the first and second carbon atoms next to the carbonyl groups. The *all-trans* conformation is destabilized by 0.6 kcal/mol with respect to the lowest energy on at the HF/6-31G(d) level. However, single-point calculations at the MP2/6-31G(d) increase such relative energy to 1.5 kcal/mol. These results are almost identical to those found for **4**. Regarding to the diamide **3**, the *all-trans* conformation was about 0.5 kcal/mol less favored than the TTGTT. This low-energy value was attributed to the fact that the TTGTT is not a real minimum on the potential energy surface of **3**, the real minimum in the gas phase being TTGS̅T conformation. Such a minimum is stabilized by an intramolecular seven-membered hydrogen-bonded system and is 2.90 kcal/mol favored with respect to the *all-trans*. However, X-ray crystallography has demonstrated that in the solid state the optimal conformation is the TTGTT, which forms an infinite network of intermolecular hydrogen bonds. The relative energies of the other six minima found in the potential energy hypersurface of **1** range from 1.2 to 3.7 kcal/mol. The effects of the electron correlation on energies are similar to those previously observed in diamides and diketones.

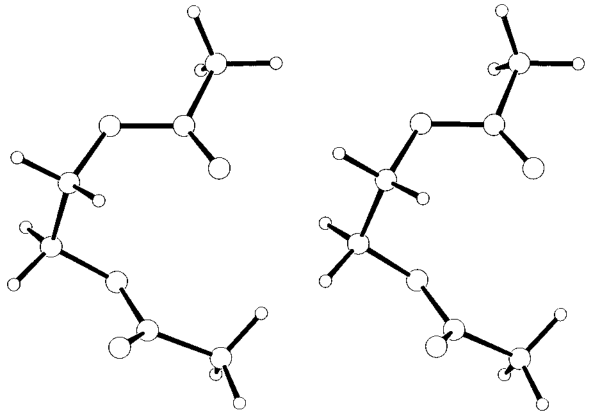

Figure 2. Stereopairs showing the lowest energy minimum (TGGS̅T conformation) of ethylene glycol diacetate.

A first inspection of the results of Table 2 suggests that **2** has a conformational behavior different from that of **1**. Thus, the lowest energy conformation corresponds to the TGGS̅T structure (Figure 2), although the C−C−O−C(=O) backbone dihedral angle is in the frontier between the *skew* conformation and the expected *gauche* one. Note that two different effects are combined in **2**: (i) the folding of methylene units, which is induced by the carbonyl group of the ester bonds on the C(=O)−O−C−C and C−C−O−C(=O) dihedral angles; and (ii) the *gauche* oxygen effect, which tends to favor a *gauche* conformation with respect to *cis* and *trans* ones on the O−C−C−O sequence.[21−23] As a result, a *gauche* conformation should be ideally expected for the three central dihedral angles of the lowest energy conformation. The small distortions with respect to such ideal conformation should be at-

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tributed to two different effects: (i) the simultaneous combination of two stereoelectronic effects in a very small size compound and (ii) the presence of the alkoxy oxygen between the carbonyl group and the methylene units. Thus, previous experimental and computational studies on **5** indicated that the stabilization of the folded conformations decreases when the carbonyl groups and the methylene units are separated by other group.[4] The distortions are more evident in the C−C−O−C(=O) dihedral angle, which is slightly deviated, *i.e.* by 6°, toward a *skew* conformation. However, note that the second minimum energy conformation corresponds to the expected TGGGT structure. Furthermore, it is also largely stabilized with respect to the *all-trans* conformation.

The electron correlation effects play an important role in the relative energies for the minimum energy conformations of **2**. Thus, relative energies range from 0.0 to 2.3 kcal/mol at the HF level, whereas at the MP2 level they vary from 0.0 to 3.4 kcal/mol. The calculations displayed for **1** as well as those reported for diamides and diketones indicated that the folding of methylene units is qualitatively described at the HF level, but correlated wave functions are needed in order to have a quantitative estimation of such structural pattern. A similar effect was observed by other authors for the *gauche* oxygen effect.[23,24] Therefore, the combination of the two features provides an important role to the electron correlation effects.

The *all-trans* conformation is unfavored with respect to the global minimum by 0.4 and 3.0 kcal/mol at the HF/6-31G(d) and MP2/6-31G(d) levels, respectively. Thus, electron correlation effects introduce a destabilization of 2.6 kcal/mol. A comparison with the results of Table 1 permits us to discern between the influences of electron correlation on both the folding of methylene units and the *gauche* oxygen effect. For **1**, the change from HF to MP2 introduces a variation in the relative energy between the TTGTT and TTTTT conformers of 0.9 kcal/mol, which would be associated with the stabilizing effect of two carbonyl groups. Therefore, for the *all-trans* conformation of **2** the electron correlation effects would be approximately divided in two different contributions: (i) 0.9 kcal/mol associated with the folding of two methylene units and (ii) 1.7 kcal/mol associated with the *gauche* oxygen effect.

The results presented up to here seems to be interesting for the structural modeling of polymers. Thus, they support both the reported TTGTT conformation of the succinate units[25] and the kink conformations postulated for the ethylene glycol moieties in polyesters [GT$\bar{G}$ in poly(ethylene adipate)[26] and poly(ethylene suberate);[26] TGT in poly(ethylene succinate)[25]].

Aqueous-Phase Calculations. Solvation free energies (ΔG_{solv}) in aqueous solution for **1** and **2** are reported in Tables 3 and 4, respectively, where both the electrostatic and steric [cavitation + van der Waals] contributions are included. For both **1** and **2** the electrostatic term is the leading contribution to ΔG_{solv} ranging from −9.4 to −10.4 and from −9.2 to −10.9 kcal/mol, respectively, whereas in the steric term the largest variation is 0.3 kcal/mol. Note that ΔG_{solv} values range from −5.7 to −6.7 and from −5.8 to −7.2 kcal/mol for **1** and **2**, respectively. Thus, diesters display a slightly more hydrophilic character than the diketone **4** ($\Delta G_{solv} \approx -5$ kcal/mol), but a much more hydrophobic character than the diamide 3 ($\Delta G_{solv} \approx -14$ kcal/mol).

Table 3. Electrostatic and Steric [Cavitation + van der Waals] Contributions to the Free Energy of Solvatation (kcal/mol) of Dimethyl Succinate (1) in Aqueous Solution[a]

	I	II	III	IV	V	VI
ΔG_{elec}	−10.0	−9.4	−10.4	−9.7	−10.4	−9.9
ΔG_{ster}	3.8	3.7	3.7	3.8	3.7	3.7
ΔG_{solv}	−6.2	−5.7	−6.7	−5.9	−6.7	−6.2
$\Delta\Delta G_{solv}$	0.5	1.0	0.0	0.8	0.0	0.5
$\Delta\Delta G_{conf}$	0.0	2.0	0.7	2.8	1.5	3.0

[a] Conformational free energy differences ($\Delta\Delta G_{conf}$) were computed by adding $\Delta\Delta G_{solv}$ to the best estimates of relative energies in the gas phase.

Table 4. Electrostatic and Steric [Cavitation + van der Waals] Contributions to the Free Energy of Solvatation (kcal/mol) of Ethylene Glycol Diacetate (1) in Aqueous Solution[a]

	I	II	III	IV	V	VI	VII	VIII
ΔG_{elec}	−9.4	−9.9	−10.9	−10.0	−10.7	−10.0	−9.7	−9.2
ΔG_{ster}	3.5	3.6	3.7	3.7	3.6	3.7	3.6	3.4
ΔG_{solv}	−5.9	−6.3	−7.2	−6.3	−7.1	−6.3	−6.1	−5.8
$\Delta\Delta G_{solv}$	1.3	0.9	0.0	0.9	0.1	0.9	1.1	1.4
$\Delta\Delta G_{conf}$	0.0	0.9	0.9	2.6	1.0	2.5	0.6	2.5

[a] Conformational free energy differences ($\Delta\Delta G_{conf}$) were computed by adding $\Delta\Delta G_{solv}$ to the best estimates of relative energies in the gas phase.

The effect of a polar solvent like water is very important on the potential energy hypersurfaces of diesters. Thus, the largest values of $\Delta\Delta G_{solv}$ are 1.0 and 1.4 kcal/mol for **1** and **2** respectively. Free conformational energies (ΔG_{conf}) were obtained by the classical thermodynamical scheme. This is adding the $\Delta\Delta G_{solv}$ values to the best estimation of the gas-phase relative energies. Results are included in Tables 3 and 4.

The effects of the aqueous solvent on the folding of methylene units are different for each diester. For **1**, water stabilizes the TTGTT conformation with respect to the *all-trans* one by 0.5 kal/mol. This must be attributed to that the former has a larger dipole moment than the latter (1.34 and 0.01 Debyes for the TTGTT and *all-trans*, respectively), and therefore it provides a better electrostatic interaction with the bulk solvent. For **2** the effect is the contrary; water stabilizes the *all-trans* conformation with respect to the lowest energy one by 0.4 kcal/mol. This feature must be also explained in terms of solute−solvent electrostatic interactions (Table 4), even taken into account that the dipole moment of the *all-trans* conformation is much more smaller than that of the global minimum (0.01 and 3.28 Debyes for the *all-trans* and the TGG$\bar{S}$T, respectively). In this case, the polar oxygen atoms are very hidden in the TGG$\bar{S}$T conformation due to folding in three consecutive dihedral angles (see Figure 2). On the contrary, in the *all-trans* conformation they are accessible to the solvent, providing strong electrostatic interactions with the solvent.

Organic-Phase Calculations. Tables 5 and 6 display the results obatined in carbon tetrachloride solution for **1** and **2**, respectively. For the two compounds the ranges of variation of both the electrostatic and steric terms are very small. The largest value of $\Delta\Delta G_{solv}$ for **1** is 0.3 kcal/mol, which indicates that the organic solvent does not have any influence in its potential energy surface. Indeed, the energy difference between the

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Table 5. Electrostatic and Steric [Cavitation + van der Waals] Contributions to the Free Energy of Solvatation (kcal/mol) of Dimethyl Succinate (1) in Carbon Tetrachloride Solution[a]

	I	II	III	IV	V	VI
ΔG_{elec}	−1.0	−0.8	−1.0	−0.9	−1.1	−0.9
ΔG_{ster}	−6.7	−6.9	−6.6	−7.0	−6.5	−6.8
ΔG_{solv}	−7.7	−7.7	−7.6	−7.9	−7.6	−7.7
$\Delta\Delta G_{\text{solv}}$	0.2	0.2	0.3	0.0	0.3	0.2
$\Delta\Delta G_{\text{conf}}$	0.0	1.5	1.3	2.3	2.1	3.0

[a] Conformational free energy differences ($\Delta\Delta G_{\text{conf}}$) were computed by adding $\Delta\Delta G$solv to the best estimates of relative energies in the gas phase.

Table 6. Electrostatic and Steric [Cavitation + van der Waals] Contributions to the Free Energy of Solvatation (kcal/mol) of Ethylene Glycol Diacetate (1) in Tetrachloride Solution[a]

	I	II	III	IV	V	VI	VII	VIII
ΔG_{elec}	−0.9	−0.9	−1.0	−1.0	−1.0	−1.0	−1.0	−0.8
ΔG_{ster}	−6.6	−7.1	−7.2	7.2	−7.2	−7.1	−7.0	−7.0
ΔG_{solv}	−7.5	−8.0	−8.2	−8.2	−8.2	−8.1	−8.0	−8.1
$\Delta\Delta G_{\text{solv}}$	0.7	0.2	0.0	0.0	0.0	0.1	0.2	0.1
$\Delta\Delta G_{\text{conf}}$	0.0	0.8	1.5	2.3	1.5	2.3	0.3	2.8

[a] Conformational free energy differences ($\Delta\Delta G_{\text{conf}}$) were computed by adding $\Delta\Delta G_{\text{solv}}$ to the best estimates of relative energies in the gas phase.

TTGTT conformation and the *all-trans* one is the same in both the gas phase and carbon tetrachloride solution.

On the other hand, for **2** the largest value of $\Delta\Delta G_{\text{solv}}$ is 1.0 kcal/mol, and the $\Delta\Delta G_{\text{conf}}$ between the global minimum and the *all-trans* conformation is 2.3 kcal/mol. Note that the *all-trans* conformation is stabilized with respect to the TGG$\bar{\text{S}}$T one by 0.7 kcal/mol when the molecule is taken from the gas phase to carbon tetrachloride solution. This must be explained in terms of the van der Waals interactions between the solute and the solvent. Thus, the molecular surface area accessible to the solvent is larger in the *all-trans* conformation than in the folded one.

Conclusions

The results indicate that the tendency of the methylene units to fold in a *gauche* conformation is present in diesters. Furthermore, the folding of the methylene units in dicarbonylic compounds seems to be almost independent of the chemical nature of the carbonyl group. Thus, similar results have been found for **1** and the related diamide and diketone. On the other hand, a *gauche* oxygen effect has been found for the central O−C−C−O sequence of **2**. This stereoelectronic effect is combined with the folding of methylene units induced by the carbonyl goups. As a result the TGG$\bar{\text{S}}$T conformation has the lowest energy conformation for **2**. Solvents do not display any remarkable effect in the conformational preferences of **1** and **2**, indicating that polarizable environment do not have any stabilizing effect on the folding of methylene units.

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Supporting Information Available: Complete computational results of the dimethyl succinate and ethylene glycol diacetate (10 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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