Solvent Effects on Molecular Geometries and Isomerization Processes: A Study of Push-Pull Ethylenes in Solution

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Received August 31, 1992

Abstract: A detailed study of enamines substituted ($H_2NC(H)$=$C(H)R$) by an electron acceptor group (R = NO_2, CN, CHO) in solution has been performed by using the self-consistent reaction field (SCRF) approach. The solvent effects on the *E-Z* equilibrium as well as on the barriers to internal rotation are in agreement with the known experimental data. Consideration of the electronic wave function allows a detailed analysis of the solvent effects. The polarization of the solute under the influence of the solvent as well as the modifications of its geometry are far from being negligible. Preliminary attempts to estimate electron correlation effects have also been evaluated, and they appear less important than the former effects.

Introduction

Solvent effects on the physico-chemical properties and on chemical reactivity of organic molecules have long been known and rationalized on the basis of both empirical and theoretical models.[1] The state of the art for theoretical treatment of the solute–solvent interactions may be divided into two main approaches.[2] The first uses methods based on statistical mechanics[3] and leads to quite accurate values of thermodynamic properties in the liquid state, but has the disadvantage of describing the molecular systems in a somewhat simplified way, neglecting in particular the details of the electronic structure. In the second approach, the analysis of solvent effects on the nuclear and electronic structure of the solute's molecule is performed through the use of a continuum model[4-7] in which the average solute–solvent interactions are explicitly considered in the solute's Hamiltonian. This essentially consists of the description of the solvent as a polarizable and dielectric continuum surrounding a cavity in which the solute is placed.[8] The contributions to the free energy of solvation arising from this model, i.e., electrostatic + induction,[4-7,9-11] dispersion,[12-15] and cavitation,[16] can then be computed using previously proposed formulas. Although, in principle, the shape of the cavity should be better defined by a isodensity surface[17] or some simplification of it, as cavities expressed in terms of intersecting spheres centered on the solute atoms, in some cases, it can be approximated by a constant coordinate cavity (spherical,[4] spheroidal,[18] ellipsoidal[19]) which leads to analytical expressions for the electrostatic interaction developed as a multipolar series. Moreover, this kind of cavity is well adapted to the development of an efficient algorithm to perform geometry optimization in solution. However, although geometry optimizations are easily performed in the case of spherical cavities, only recently has an optimization method for an ellipsoidal cavity been proposed.[20] It is worth mentioning that Tomasi et al.[21] have also proposed an optimization numerical procedure based on their earlier cavity model.[6,9] Likewise, Cramer and Truhlar have recently developed a new parametrization technique to include aqueous solvation effects in the framework of the AM1 and PM3 semiempirical methods, where optimization of solute's geometry can be performed.[22]

Owing to the fact that the solute–solvent interactions are in general much smaller than the intramolecular forces, one expects that the solute's geometry does not undergo important changes in going from the gas phase to solution. However, geometry optimization in solution is required, when properties need to be computed at equilibrium, as, for instance, in the calculation of vibrational frequencies. In addition, in the case of polar molecules, for which there are some geometrical parameters with relative small force constants (such as torsional angles), whose variations can cause substantial changes of the permanent electric moments, important solvent effects can appear on these parameters.

The properties of any chemical process in solution are usually described by means of free energy variations. They can be split in one term describing the change of the intrinsic free energy and

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another which accounts for the differential free energy of solvation corresponding to the chemical species involved in the process. In order to compare the results of theoretical calculations for a given process with experimental data, it is then necessary to compute both contributions. The free energy of solvation can be obtained using the cavity model, as has already been mentioned. The intrinsic free energy variation has often been approximated as the difference between the total molecular energies obtained in quantum chemical computation, although it cannot always be justified as correct, in particular when entropy changes due to the symmetry modifications are possible. The possibility of dealing with optimized geometries allows computation of vibrational frequencies to derive all the contributions needed to get the intrinsic free energy of a molecule in solution.

Our aim in this work is to examine in detail the geometrical changes of the solute induced by its interactions with the solvent, as well as the modifications on the chemical energies of selected isomerization processes which result from electronic and nuclear polarization. Likewise, electron correlation effects may, in some cases, modify strongly the results of SCF computations on solvated molecules,[23] and will be investigated. For this purpose, we have chosen three simple push–pull ethylenes derived from vinylamine by substituting an electron-withdrawing group for a hydrogen on the β-carbon. These ethylenes presents E–Z isomerization according to the equilibrium:

$$R = NO_2 \quad (1)$$
$$CHO \quad (2)$$
$$CN \quad (3)$$
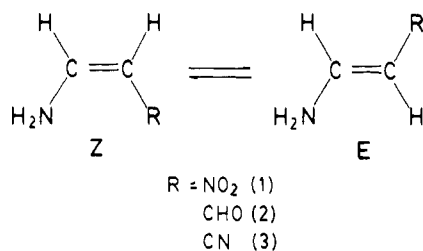
These types of molecules are quite polar, and the properties concerning the configurational equilibria are strongly dependent on the solvent. Thus, the cis–trans population ratio changes with the polarity of the solvent.[24-26] The rotational barrier around the C=C double bond, which is typically lower than that for simple ethylenes, presents a strong effect of solvent polarity[27,28] leading to a decrease of the barrier, having been used as a significant support for a zwitterionic transition state. In the case of enamines containing primary or secondary amino groups, an alternative mechanism via the rotation of the deprotonated enamine has been shown to occur.[29] The barrier for rotation around the C–NR_1R_2 bond has, in general, an opposite solvent effect increasing with the polarity solvent. This framework allows us a thorough analysis of the geometrical changes induced by the solvent on a set of representative organic compounds in several structures (planar isomers and transition states), as well as the examination of the influence of the geometry optimization on the energetics of the isomerization.

Interest in these compounds, which has been strongly stimulated during the last few years,[30] is not only related to their particular low barriers, but also to their chemical properties. In particular,

nitroenamines are useful intermediates in synthetic organic chemistry,[31-33] and some derivatives play important roles in biological processes.[34,35]

Although an increasing number of theoretical works have appeared on push–pull ethylenes, aimed at examining electron distributions on the ground and transition states,[34,36] only a few theoretical works have included the solvent effects. Olsson and Sandström in a pioneer work[37] estimated the rotational barrier of some 6,6-dihetero-substituted fulvenes in solution by using the CNDO/2 method and a spherical cavity model of solvation, considering only the dipolar term. The results indicated a considerable discrepancy with experiment, which was attributed to the failure of this semiempirical model to describe rotational barriers correctly. More recently, we have shown that the use of the AM1 method and a more involved cavity model gives a more accurate description of the intrinsic barrier, as well as of the solvation contribution, leading to a semiquantitative agreement with experiment.[38] Furthermore, a comparative study of the continuum and discrete models for the solvation of the Z and E isomers of **1** in methanol was carried out[38b] in order to consider explicitly the intermolecular hydrogen bonding. Results showed the convergence of both methods when in the supermolecule approach a large enough number of solvent molecules to account for direct interactions are considered. This convergence indicates that the solute–solvent hydrogen bonds are, to a large extent, electrostatic. In fact, the mixed continuum–discrete approach performed in this previous work[38b] did not give any change in the description of solvation of **1**, relative to the other models. Nevertheless, the computations concerning the cavity model were carried out at a perturbational level, so that in a further study[39] we undertook the analysis of the modifications of the electronic structures of compounds **1–3** induced by the solvent, by including the solute–continuum interaction term in the Hamiltonian. These calculations were carried out at the HF level (3–21+G basis sets). Wiberg et al.[40] have presented a theoretical study about the solvent effects on some conformational and molecular properties, at the HF and SCF–CI levels using the spherical cavity model and a reaction field derived from the dipole moment only. Geometry optimizations were carried out at the HF level. One of the molecules examined by these authors was the 2-nitroethenamine (**1**), for which rotational barriers somewhat higher than experimental results and than our earlier estimations[38,39] were obtained. This difference could be justified by the use of a spherical cavity and to a larger extent to the neglect of higher multipole moments, which are important in these kinds of structures.

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Method of Computation

Computations have been carried out at the 6-31+G level[41] and using the GAUSSIAN 90 program.[42] The use of diffuse orbitals in the basis set is important since it is required to correctly describe the electronic density of anions or systems in which there is a substantial charge transfer, as the zwitterions studied here.

The average effect of the solvent on the electronic and nuclear structure of the solute's molecule has been taken into account by using a cavity model in which the liquid is represented by a polarizable continuum characterized by a macroscopic quantity such as the dielectric permittivity ϵ. The solute is placed in a cavity created in this medium. Its charge distribution polarizes the continuum which in turn creates an inhomogeneous electric field inside the cavity. The free energy for the corresponding electrostatic interaction is easily obtained if the electrostatic potential is expanded in a spherical multipole moment series and leads to:

$$\Delta F = -^1/_2 R_l^m M_l^m \tag{1}$$

Here, R_l^m is a component of the so-called "reaction field" and it derives from the multipole moments through the equation:

$$R_l^m = f_{ll''}^{mm'} M_{l'}^{m'} \tag{2}$$

Repeated indices stand for a sum over all their possible values: l from 0 to ∞ and m from $-l$ to $+l$. In practice a good convergence is obtained for $l \le 6$. The factors $f_{ll''}^{mm'}$ depend only on the dielectric properties of the medium and on the cavity shape, and can be computed analytically in the case of a constant coordinate cavity shape such as the sphere or the ellipsoid.[19]

The perturbation of the solute's electronic distribution by the solvent can be taken into account by means of the self-consistent reaction field (SCRF).[11] It uses a Fock operator which is modified to account for the electrostatic interaction, and a whole SCF computation is performed so that the electronic distribution is optimized in order to minimize the total energy of the molecule plus the free energy of solvation. We call this quantity the SCRF energy in contrast to the usual SCF energy. One is then able to define a free energy of solvation ΔF_{sol} as the difference between the SCF energy for the fully optimized structure in a vacuum and the SCRF energy for a fully optimized structure in the solvent. This quantity can be further analyzed in an electrostatic term ΔF_{sol}^{el} which is the solvation free energy computed by using in (1) the geometry and the multipole moments of the unperturbed molecule, and an induced term ΔF_{sol}^{ind} which represents the variation of this quantity when the geometry and the wave function are optimized in the presence of the solvent.

The definition of the cavity shape is a crucial point in this model. We have previously proposed to use the isodensity surface enclosing a volume equal to the experimental molecular volume (i.e., the partial molar volume divided by Avogadro's number). This surface has the remarkable property of enclosing the largest molecular electronic density for a given enclosed volume and appears as the best physical definition of the cavity shape. In practice, this surface is not far from the surface defined by the van der Waals spheres (with somewhat increased radii) and may be, as a first approximation, estimated from it. However, we have shown in a previous work[39] that, for the systems studied here, the isodensity surface may be fitted reasonably well by an ellipsoid which presents the great advantage of leading to very efficient algorithms to compute the solvation energy[19] and its
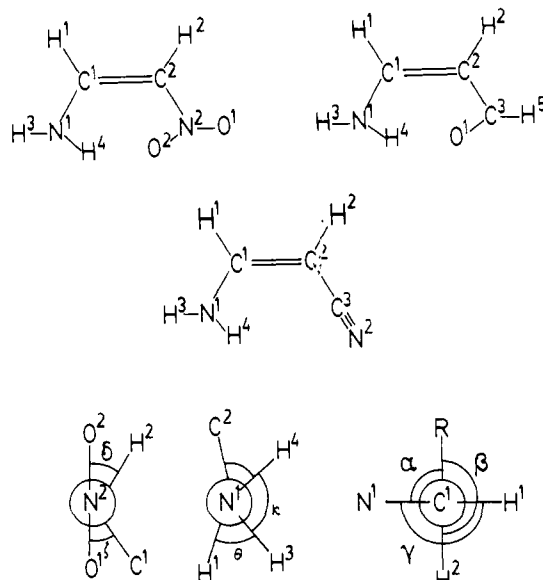

Figure 1. Atomic numbering and dihedral angles definition.

derivatives with respect to the atomic coordinates.[20] This last possibility opens the door to the computation of reactive paths in solution, as the isomerization processes studied in this work. It also allows the computation of harmonic force constants which are needed to define the transition states and to compute the free energy of the species. In practice, the ellipsoidal cavity is defined by the three semi-axes and the three Euler angles which define the orientation of axes in the reference frame, this information being obtained from the van der Waals solid, that is, the solid of uniform density whose surface is that of van der Waals. The cavity volume is also deduced from the van der Waals volume by means of an empirical linear relationship.[20] To deal with this volume, the semi-axes are multiplied by the corresponding proportionality factor.

The potential energy surfaces were inspected by the linear synchronous transit method[43] and the transition states located on the surfaces by using Schlegel's algorithm.[44]

Results and Discussion

The structures studied in this work were fully optimized for each dielectric constant, including the derivation with respect to the reaction field factor. This means that the size and shape of the cavity were modified during the optimization procedure. With respect to the initial cavity corresponding to the structure in gas phase, the changes in the cavity volume are small. Thus, the greatest variation of volume was found for the $TS_{C=C}$ of 1, where the cavity volume changed from 135.0 Å³ ($\epsilon = 1.0$) to 135.5 Å³ ($\epsilon = 38.8$). According to this, the semi-axes of the ellipsoid changed typically in 0.1 Å. For a given compound, the cavity volume changes very slightly from one to another structure, in all cases less than 1%.[45] The transition structures were directly located on the energy surfaces, testing their nature by means of calculations of the force constant matrix, where only one negative value was found. Figure 1 gives the definition for the dihedral angles and the numbering system hereafter employed. For compound 2, each Z, E configurational isomer has two conformers, due to the s-cis and s-trans arrangement of the carbonyl group relative to the double bond. In both, the Z and E isomers, the most stable conformation corresponds to s-cis,[36d,39] this confor-

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(45) Cavity volumes at $\epsilon = 38.8$ in Å³: compound 1, 134.1 (Z and E), 135.5 ($TS_{C=C}$), 135.0 (TS_{C-N}); anion of 1, 131.6 (Z and E), 132.2 ($TS_{C=C}$); compound 2, 127.3 (Z and E), 128.1 ($TS_{C=C}$), 128.3 (TS_{C-N}); anion of 2, 124.0 (Z and E), 124.6 ($TS_{C=C}$); compound 3, 124.7 (Z and E), 125.5 (TS_{C-C} and TS_{C-N}); anion of 3, 121.4 (Z and E).

Table I. Average Change, $\bar{\Delta}$, for Each Type of Geometrical Parameter[a] When Going from the Gas Phase to the Continuum

molecule	structure	distances		bond angles		dihedral angles	
		$\epsilon = 2.0$	$\epsilon = 38.8$	$\epsilon = 2.0$	$\epsilon = 38.8$	$\epsilon = 2.0$	$\epsilon = 38.8$
1	Z	0.004	0.013	0.2	0.7		
	E	0.004	0.016	0.3	0.9		
	TS$_{C=C}$	0.006	0.017	1.5	4.5	2.1	4.8
	TS$_{C1-N1}$	0.001	0.002	0.2	0.8	0.3	7.8
anion **1**	Z	0.003	0.011	0.3	0.8		
	E	0.006	0.016	0.3	1.1		
	TS$_{C=C}$	0.004	0.011	0.7	2.3	1.1	4.5
2	Z	0.002	0.006	0.2	0.5		
	E	0.003	0.009	0.2	0.5		
	TS$_{C=C}$	0.003	0.012	1.4	3.8	1.2	2.6
	TS$_{C1-N1}$	0.001	0.002	0.2	0.5	0.1	0.4
anion **2**	Z	0.002	0.005	0.1	0.4		
	E	0.002	0.005	0.3	0.7		
	TS$_{C=C}$	0.003	0.010	0.5	1.4	0.5	1.2
3	Z	0.001	0.005	0.2	0.7		
	E	0.002	0.005	0.1	0.3		
	TS$_{C=C}$	0.004	0.001	0.8	2.2	1.6	6.3
	TS$_{C1-N1}$	0.001	0.003	1.0	1.6	17.0	18.7
anion **3**	Z	0.001	0.004	0.2	0.6		
	E	0.001	0.003	0.6	1.6		
	TS$_{C=C}$	0.003		0.6		0.5	

[a] Distances in Å and angles in deg.

Table II. Dipole Moments (Debyes)

molecule	structure	gas phase	$\epsilon = 2.0$	$\epsilon = 38.8$
1	Z	7.32	8.30	10.48
	E	8.16	9.29	11.91
	TS$_{C=C}$	11.49	13.47	17.50
	TS$_{C1-N1}$	3.88	4.32	5.06
2	Z	4.06	4.58	5.58
	E	5.50	6.26	7.71
	TS$_{C=C}$	7.82	9.52	13.08
	TS$_{C1-N1}$	2.76	3.02	3.45
3	Z	5.73	6.46	7.77
	E	6.81	7.61	8.95
	TS$_{C=C}$	10.91	11.61	14.23
	TS$_{C1-N1}$	3.40	6.12	7.59

mation only having been considered for this study. The anions studied correspond to the N-deprotonation of the hydrogen in anti with respect to the C=C double bond (H[3] in Figure 1), since this leads to the most stable conformational form.

Geometrical Structure. Analysis of the molecular structure of these systems in the gas phase, examination of their changes with respect to simple ethylenes, and their relative changes when passing from the planar isomers to the transition structures have been done elsewhere.[39] In Table I the average change when passing from the gas phase to the continuum, $\bar{\Delta}$, for each type of geometrical parameters (g_i), i.e., distances, bond angles, and dihedral angles, are collected. It is defined as

$$\bar{\Delta} = \frac{1}{n}\sum_{i=1}^{n}|\Delta_i| = \frac{1}{n}\sum_{i=1}^{n}|g_i(\epsilon) - g_i(\text{vacuum})| \qquad (3)$$

As expected, the higher values of $\bar{\Delta}$ appear for $\epsilon = 38.8$, where the average change for distances is 0.003–0.017 Å, for bond angle 0.3–4.5°, and for dihedral angles 0.4–6.3°. In this last set of parameters there are two abnormally high values for the transition structures of rotation around the Cl–N1 bond for **1** and **3**, which will be commented on later. For a given compound, $\bar{\Delta}$ increases in the sequence TS$_{C-N}$ < Z < E < TS$_{C=C}$. This order reflects the different polar character of each structure, as visible in Table II, if one assumes that the dipole moment can be taken as a primary index of the polar character. Comparing the different sets of geometrical parameters, it can be seen that angles, in particular the dihedral ones, are more affected by solvent effects than the distances. As indicated in the Introduction, this is a result of the fact that force constants for angular deformations are, in general, smaller than those of bond stretchings, and as a

consequence the former can be modified by the solute–solvent interactions easier than the latter.

The value of $\bar{\Delta}$ gives a global idea of the structural change undergone by a molecule under perturbation of the reaction field. The next step may be to examine the distribution of these changes among the different internal coordinates. In Table III, the individual changes, Δ, for structures of **1** have been collected. As can be observed the changes are not distributed in a smilar way among the different coordinates, but rather concentrated in some of them, namely, for distances, the C=C double bond, the carbon atom of the substituent group bonds, and the distances of the nitro group.
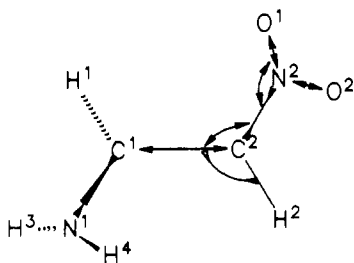
Figure 2 gives a schematic idea of the main changes for TS$_{C=C}$. There is a lengthening of the C1–C2 bond, and a shortening of the C1–N1 and C2–N2 bonds. This is in agreement with the expected increase in the weight of the more polar resonance form in polar solvents.[27]
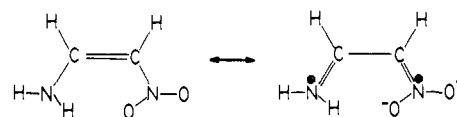
The main change in the dihedral angles is observed for α in TS$_{C=C}$. It is the angle between the RC=C and the C=C—N-(amino) planes (Figure 1). The solvent induces an important decrease of α when going from the gas phase (89.3°) to $\epsilon = 38.8$ (78.3°). This distorsion can be fully understood if one takes into account the multipole moments of increasing order whose contributions to the solvation energy increases for a nonperpendicular arrangement. This can be demonstrated by carrying out a computation in which the solute—solvent interaction is limited to the dipolar term. One notices a smaller variation of α which remains closer to a right angle ($\alpha = 85.0°$). The results of Wiberg et al.[40] show the same trend of solvent effects on the transition structure of **1**, reducing the angle α, although the final value in solution is close to 90° since the basis set used by these authors gives a TS in the gas phase of 101.2°, and only the dipolar term is considered. The dihedral angle denoted by β, which is the angle between the two planes containing the C=C bond and a substituent of C$_2$, respectively, also undergoes interesting variations. The breakdown of the π bond between the ethylenic carbons in the transition structure implies a strong polarization of the charge which gives some carbanionic character to C2, this

Table III. Changes Induced by Solvent, $\Delta(\epsilon) = g_i(\epsilon) - g_i(\text{vacuum})$, on Geometrical Parameters, g_i, of the Structures of $\mathbf{1}$[a]

g_i	Z $\epsilon = 2$	Z $\epsilon = 38.8$	E $\epsilon = 2$	E $\epsilon = 38.8$	TS$_{C=C}$ $\epsilon = 2$	TS$_{C=C}$ $\epsilon = 38.8$	TS$_{Cl-N1}$ $\epsilon = 2$	TS$_{Cl-N1}$ $\epsilon = 38.8$
C^1H^1	0.000	−0.001	0.000	−0.002	0.000	0.002	0.000	0.000
C^1C^2	0.006	0.023	0.007	0.026	0.003	0.006	0.001	0.001
C^2H^2	0.000	0.000	−0.001	−0.001	0.002	0.005	0.000	0.000
C^1N^1	−0.006	−0.020	−0.008	−0.027	−0.005	−0.010	−0.001	−0.003
N^1H^3	0.001	0.003	0.001	0.003	0.001	0.002	0.001	−0.001
N^1H^4	0.000	0.000	0.001	0.003	0.002	0.008	0.001	0.002
C^2N^2	−0.010	−0.037	−0.012	−0.043	−0.015	−0.034	−0.002	−0.001
N^2O^1	0.003	0.013	0.004	0.019	0.003	0.019	0.000	−0.003
N^2O^2	0.006	0.024	0.006	0.022	0.023	0.063	0.003	0.007
$C^2C^1H^1$	−0.1	−0.2	0.2	0.6	−0.8	−2.8	−0.4	−0.6
$C^1C^2H^2$	−0.4	−1.5	−0.5	−2.0	−2.0	−6.2	−0.2	0.0
$C^2C^1N^1$	0.0	−0.4	−0.2	−0.8	0.2	1.0	0.2	0.8
$C^1N^1H^3$	0.0	0.1	0.0	0.0	−0.3	−1.2	0.2	1.3
$C^1N^1H^4$	0.4	1.0	0.2	0.7	1.6	5.0	0.2	1.8
$C^1C^2N^2$	0.1	0.4	0.3	1.1	3.7	10.9	0.2	−0.6
$C^2N^2O^1$	0.4	1.2	0.5	1.5	2.2	5.9	0.4	0.5
$C^2N^2O^2$	0.3	0.8	0.3	1.1	−1.1	−2.7	0.1	0.6
α					−1.3	−11.0	0.0	−2.4
β					4.5	8.3	0.0	−3.1
γ					−0.2	−2.5	0.0	−2.2
δ					−3.0	−6.0	0.0	25.3
ζ					−1.3	−5.3	0.0	29.7
η					−1.1	−3.1	0.7	−1.2
θ					2.0	3.0	−0.6	−7.1
κ					3.1	5.7	0.2	6.1

[a] Distances in Å and angles in deg.

Figure 2. Geometrical changes induced by the solvent effects on the transition structure for rotation around the $C^1=C^2$ bond of compound **1**.

being reflected in a partial pyramidalization ($\beta = 168.8°$, in vacuo). In solution, the electronic polarization of the solvent induces a charge transfer from C2 toward the nitro group, thus reducing the carbanionic character (atomic net charges borne by C2 are −0.300, −0.289, and −0.225e in vacuo, for $\epsilon = 2.0$ and $\epsilon = 38.8$, respectively) and decreasing its pyramidalization degree (β increases from 168.8° in vacuo to more than 177° in a polar solvent).

It is worth noticing that the geometrical changes when passing from the planar to the transition structure in vacuo undergo the same kind of deformation as those observed by the solvent effects. Therefore, since it is generally recognized that the push–pull effect increases when going from the ground to the twisted state, we can conclude that the solvent effects increase the push–pull character of these systems.

As can be deduced from Table II, the transition structure for rotation around the C1–N1 bond exhibits the smallest charge separation; therefore, this structure is characterized by the smallest value of $\bar{\Delta}$. However, in TS$_{C1-N1}$ two significant geometrical changes are found in the nitro derivative for dihedral angles δ and ζ, which correspond (see Figure 2) to the dihedral angles of the nitro group plane with the N_2C_2H plane and the $N_2C_2C_1$ plane, respectively. This is a fair example of the great sensitivity of internal coordinates with small force constants to the presence of the molecular environment.

The main structural changes for compounds **2** and **3** are summarized in Tables IV (distances) and V (angles). This behavior is similar to that examined for **1**. The most noticeable

difference appears for the transition structures of **3**. Concerning TS$_{C=C}$, there is a strong decrease in the pyramidalization degree of C2 (β increases from 152.7° to 169.4° when going from vacuum to $\epsilon = 38.8$). This can be understood by the polarization of the electronic distribution which favors the localization of the negative charge on the CN group, thus reducing the carbanionic character of C2. It is worth noticing that CN is the less efficient electron-withdrawing group; therefore, C2 shows the greatest pyramidalization in a vacuum.

The most important geometrical change of Table I ($\bar{\Delta}$) was observed for the dihedral angles of TS$_{C1-N1}$ of **3**. In Figure 3 the structures corresponding to vacuum and $\epsilon = 38.8$ have been drawn. In the first case, the pyramidalization of the amino group corresponds to a s-cis orientation with respect to the double bond, as observed in the case of compounds **1** and **2**. Nevertheless, in solution the pyramidalized amino group adopts a s-trans orientation for **3**. In fact, these two structures represents the two minima corresponding to the inversion of a substituted amine. In most of the TS$_{C1-N1}$ the preferred orientation is the s-cis, because of two facts. (a) For compounds **1** and **2**, O2 of the nitro group and O1 of the formyl group interact favorably with the hydrogen atoms of the amino group if they are placed in s-cis. (b) The s-trans orientation implies a repulsive interaction between the lone pair of the aminic nitrogen located on the molecular plane and the acceptor group.

Indeed, for **1** and **2**, the s-trans arrangement is not a stationary point on the potential surface. Nevertheless, for **3**, the linear disposition of the acceptor group reduces the electronic repulsion between the substituent, on the one hand, and, on the other hand, the stabilizing interactions are smaller in the s-cis arrangement. Thus, for **3** both arrangements are transition structures on the surface, the s-cis being slightly more stable than the s-trans in vacuo. However, the latter has a polar character ($\mu = 5.11$ D) higher than the s-cis ($\mu = 3.40$ D), and in solution the solute–solvent interactions are able to invert the stability order. Moreover, in a highly polar medium, s-cis is no longer a transition structure on the surface.
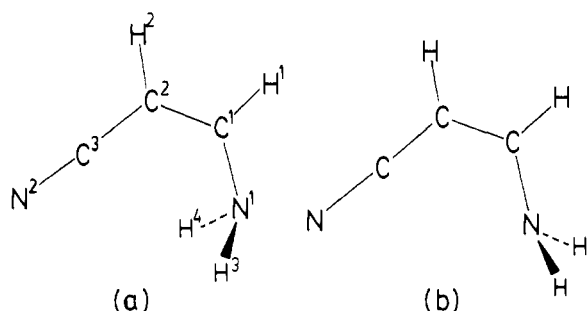
Energetics of the Isomerization in Solution. The free energy solvation, ΔF_{sol}, is defined as explained in the methodology section. The results are collected in Table VI. For the neutral forms of a given compound, the sequence of stabilization by the solvent

Table IV. Changes Induced by Solvent, Δ, on Some Distances (Å) of the Anion of **1** and the Structures of **2** and **3**[a]

molecule	structure	ε	C¹C²	C¹N¹	C²N² C²C³	N²O¹ C³O¹ C³N²	N²O²
anion **1**	*Z*	2.0	0.003	−0.001	−0.008	0.007	0.008
		38.8	0.012	−0.003	−0.022	0.022	0.026
	E	2.0	0.006	−0.004	−0.012	0.010	0.011
		38.8	0.018	−0.011	−0.030	0.032	0.035
	TS$_{C=C}$	2.0	0.001	−0.001	−0.009	0.010	0.012
		38.8	0.004	−0.001	−0.020	0.028	0.031
2	*Z*	2.0	0.003	−0.003	−0.004	0.004	
		38.8	0.011	−0.010	−0.013	0.014	
	E	2.0	0.005	−0.006	−0.006	0.006	
		38.8	0.015	−0.017	−0.019	0.019	
	TS$_{C=C}$	2.0	0.004	−0.003	−0.009	0.010	
		38.8	0.014	−0.006	−0.027	0.041	
anion **2**	*Z*	2.0	−0.002	0.003	0.000	0.003	
		38.8	−0.005	0.009	0.000	0.009	
	E	2.0	0.000	0.000	−0.002	0.005	
		38.8	0.000	0.001	−0.005	0.017	
	TS$_{C=C}$	2.0	0.002	0.000	−0.006	0.011	
		38.8	0.007	0.002	−0.019	0.038	
3	*Z*	2.0	0.003	−0.004	−0.002	0.001	
		38.8	0.011	−0.012	−0.006	0.004	
	E	2.0	0.004	−0.005	−0.002	0.001	
		38.8	0.011	−0.014	−0.006	0.004	
	TS$_{C=C}$	2.0	0.008	−0.004	−0.008	0.004	
		38.8	0.023	−0.008	−0.026	0.014	
anion **3**	*Z*	2.0	0.001	0.001	−0.003	0.001	
		38.8	0.003	0.006	−0.006	0.002	
	E	2.0	−0.001	0.001	−0.001	0.000	
		38.8	−0.005	0.006	0.000	0.000	
	TS$_{C=C}$	2.0	0.006	−0.001	−0.004	0.002	

[a] For atomic numbering see Figure 1.

Table V. Changes Induced by Solvent, Δ, on Some Bond and Dihedral Angles (deg) of the Transition Structures of Rotation around the C=C Bond, TS$_{C=C}$.

molecule	ε	C¹C²N² C¹C²C³	C¹C²H²	C²C³O¹	α	β	ζ
anion **1**	2.0	1.2	−0.9		−2.3	2.2	−2.3
	38.8	4.1	−3.0		−12.8	4.6	−6.8
2	2.0	4.1	−1.7	2.0	−0.3	2.8	
	38.8	10.9	−4.3	4.6	−1.3	5.2	
anion **2**	2.0	0.8	−0.3	0.0	−0.5	0.9	
	38.8	3.5	−1.1	0.0	−1.7	2.2	
3	2.0	0.5	0.6		−1.9	4.4	
	38.8	0.6	2.5		−7.3	16.7	
anion **3**	2.0	−1.0	0.7		0.1	−0.2	

Figure 3. Transition structures for rotation around the C¹–N¹ bond in a vacuum (a) and in solution (ε = 38.8) (b) of compound **3**.

is TS$_{C=C}$ ≫ *E* > *Z* > TS$_{C1-N1}$, the differences increasing when passing from ε = 2.0 to 38.8. The only exception is for TS$_{C1-N1}$ of **3**, but we already mentioned that in this case there is a significant change in the geometrical structure which increases the polar character of this structure. However, there is no a direct parallelism between ΔF_{sol} and the dipole moment variations for the structures of **3**. This again emphasizes the important role played by the higher multipole moments, which in general are for the transition structures higher than for the planar isomers, as shown in Table VII. This remark, together with the fact that in a nonspherical cavity the reaction field factors are tensorial

Table VI. Free Energy of Solvation, ΔF_{sol} (kal/mol)[a]

molecule	structure	ΔF_{sol} ε = 2.0	ΔF_{sol} ε = 38.8	ΔF_{sol} − Born term ε = 2.0	ΔF_{sol} − Born term ε = 38.8
1	*Z*	−4.48	−12.27		
	E	−5.46	−14.70		
	TS$_{C=C}$	−13.95	−41.44		
	TS$_{C1-N1}$	−3.49	−9.40		
anion of **1**	*Z*	−29.62	−61.55	−4.25	−12.25
	E	−30.36	−64.20	−5.18	−15.19
	TS$_{C=C}$	−32.71	−71.78	−7.02	−21.78
2	*Z*	−3.09	−8.41		
	E	−4.23	−11.54		
	TS$_{C=C}$	−11.02	−33.88		
	TS$_{C1-N1}$	−2.74	−7.51		
anion of **2**	*Z*	−30.76	−63.88	−4.7	−13.12
	E	−30.65	−63.90	−4.9	−13.70
	TS$_{C=C}$	−32.59	−71.28	−6.3	−20.09
3	*Z*	−3.82	−10.20		
	E	−4.25	−11.00		
	TS$_{C=C}$	−11.10	−31.25		
	TS$_{C1-N1}$	−3.92	−11.34		
anion of **3**	*Z*	−31.98	−67.04	−5.98	−16.39
	E	−29.18	−60.04	−3.45	−9.87
	TS$_{C=C}$	−33.50	−7.39		

[a] (ΔF_{sol} − Born term) represents the difference between the free energy of solvation of the anions and the contributions to that term of the charge term.

Table VII. Contributions of the Multipole Moments to the Total Energy (kcal/mol) of **3** in a continuum of ε = 38.8.

<R_lM_l>	*Z*	*E*	TS$_{C=C}$	TS$_{C-N}$
l = 1	−8.69	−9.20	−28.50	−9.15
l = 2	−2.88	−3.05	−7.88	−2.86
Σl_i(*i* = 3–6)	−1.67	−1.70	−8.38	−3.19

quantities, indicates that it is very difficult to make even qualitative guesses from the consideration of the dipole moment alone.

For the anions, as expected, ΔF_{sol} is much larger than for neutral molecules due to the Born term (see Table VI). Nevertheless, since the volume is similar for all the structures of a given compound, the differences in the solvation energy mainly come

Table VIII. Electrostatic, ΔF_{sol}^{elec}, and Induction, ΔF_{sol}^{ind}, Contributions to the Solvation Free Energy[a]

molecule	structure	ΔF_{sol}^{elec}	ΔF_{sol}^{ind}(g.vac)	ΔF_{sol}^{ind}(g.sol)
1	Z	−9.11	−2.14	−3.16
	E	−11.07	−2.31	−3.63
	TS$_{C=C}$	−27.71	−7.65	−13.73
2	Z	−6.83	−1.18	−1.58
	E	−9.12	−1.81	−2.42
	TS$_{C=C}$	−23.06	−5.97	−10.82
3	Z	−8.07	−1.87	−2.13
	E	−8.88	−1.89	−2.12
	TS$_{C=C}$	−22.66	−9.87	−11.32

[a] ΔF_{sol}^{ind}(g.vac) is the contribution when the calculation in solution is carried out at the vacuum geometry, whereas ΔF_{sol}^{ind}(g.sol) is the contribution when optimization geometry within the cavity is performed.

Table IX. Relative Energies (kcal/mol) for Isomerization Processes in the Gas Phase and Solution

molecule	structure	gas phase	$\epsilon = 2.0$	$\epsilon = 38.8$
1	Z	0.00	0.00	0.00
	E	3.65	2.67	1.12
	TS$_{C=C}$	43.96	34.48	14.68
	TS$_{C1−N1}$	22.04	23.04	24.81
anion of **1**	Z	0.00	0.00	1.79
	E	0.76	0.02	0.00
	TS$_{C=C}$	13.96	10.87	5.62
2	Z	0.00	0.00	0.00
	E	4.23	3.09	1.10
	TS$_{C=C}$	47.23	39.31	21.76
	TS$_{C1−N1}$	20.86	21.21	21.76
anion of **2**	Z	0.28	0.17	0.30
	E	0.00	0.00	0.00
	TS$_{C=C}$	15.73	13.79	8.36
3	Z	0.00	0.00	0.00
	E	1.67	1.25	0.88
	TS$_{C=C}$	56.53	49.24	35.48
	TS$_{C1−N1}$	13.58	13.48	12.45
anion of **3**	Z	5.38	2.58	0.00
	E	0.00	0.00	1.61
	TS$_{C=C}$	28.53	24.20	

Table X. Experimental Data for **1** and Some Push-Pull Ethylenes Related to **1-3**

molecule	solvent	ΔG_{a1}	ref
$O_2NC(H)=C(H)NH_2$	CHCl$_3$ ($\epsilon = 4.9$)	>1.5	24, 25
	CH$_3$OH ($\epsilon = 32.70$)	0.65	24, 25
	(CH$_3$)$_2$SO ($\epsilon = 46.68$)	0.24	24, 25
EtOC(H)=C(H)NH$_2$	CS$_2$ ($\epsilon = 2.63$)	1.8	26
MeOC(H)=C(H)NH(CH$_3$)	PCE ($\epsilon = 3.60$)	0.9	26
	PCE + pyridine	0.6	26
	H$_2$O ($\epsilon = 78.39$)	−1.3	26
		$\Delta G^{\ddagger}_{C=C}$	
$O_2NC(H)=C(H)NH_2$	(CH$_3$)$_2$NCHO ($\epsilon = 36.7$)	21.29	24, 25
$O_2N(H)=C(H)NH(CH_3)$	o-Cl$_2$C$_6$H$_4$ ($\epsilon = 9.9$)	21.10	24, 25
	(CH$_3$)$_2$NCHO ($\epsilon = 36.7$)	19.2	24, 25
		$\Delta G^{\ddagger}_{C1N1}$	
$O_2NC(H)=C(H)N(CH_3)_2$	CH$_2$Cl$_2$ ($\epsilon = 9.08$)	16.5	25, 48
HOCC(H)=C(H)N(CH$_3$)$_2$	CCl$_4$ ($\epsilon = 2.2$)	14.6	49
	CHCl$_3$ ($\epsilon = 4.9$)	15.8	49
	CH$_3$OH ($\epsilon = 32.70$)	16.5	49
NCC(H)=C(H)N(CH$_3$)$_2$	CCl$_4$ ($\epsilon = 2.2$)	12.9	50

are smaller than in simple ethylenic compounds (62–65 kcal/mol),[47] as expected for push–pull ethylenes.[27] The sequence of the barriers, **1** < **2** < **3**, is consistent with the electron-withdrawing character of group R, which is known to be, NO$_2$ > CHO > CN.[27] This trend is also observed for the anions, although the barriers are smaller than for the thermal mechanism.[36b] The barrier to internal rotation around the C1–N1 bond undergoes variations which follow the opposite sequence: **1** > **2** > **3**. This again is perfectly consistent with the intramolecular charge transfer which weakens the C=C bond and strengthens the C1–N1 and C2–R bonds. Concerning the isomers, for neutral molecules, Z isomer is the preferred form, in particular for **1** and **2**, where an intramolecular hydrogen bond stabilizes this arrangement. Deprotonation of the amino group favors the E isomer with respect to the Z, as a consequence of the smaller increasing of the electron repulsion for the more opened structure E.

A summary of the experimental information about the isomerization for the compounds studied or some derivatives of them has been collected in Table X. The theoretical results in solution agree fairly well with these data. Thus, the C=C barriers strongly lower with the increase in the polar character of the solvent. On the contrary, the C1–N1 barriers increase when going from the apolar to the polar solvent,[25,48,49] except for **3**. However, as has previously been pointed out, for this case an additional term, that of the conformational change of the amino group, is involved. Unfortunately, there is no experimental information about the solvent effects on this barrier, but Hobson and Reeves[50] have found that, for the N,N-dimethyl derivative of **3** in CCl$_4$, $\Delta S^{\ddagger}$ is close to zero for this rotation process; they have interpreted this as indirect evidence of the peculiar behavior of this compound in solution, compared to other push–pull ethylenes. Changes predicted in the population ratio of isomers also agree with experimental information for **1** and some derivatives of **2**, where the E:Z ratio increases with the solvent polarity.

Beyond this qualitative comparison, it is convenient to examine the shortcomings of the scheme employed in order to bear in mind the factors lacking for a more ambitious quantitative comparison with experiment in solution. First of all, the free energy of solvation does not reduce to the free energy of interaction obtained in the scheme presented in this work. On one hand, within the continuum model two important terms are missing:

from the dipolar and multipolar terms. The inclusion of the negative charge in the system causes noticeable changes in the solvation contributions. Thus, the zwitterionic character of the transition structures for rotation around the double bond is strongly reduced for anions. For the planar geometries the difference between the E and Z isomers is also reduced, and even inversed for compound **3**.

In order to analyze the influence of the modifications of the electronic wave function and of the molecular geometry under the influence of the solvent, we give in Table VIII the electrostatic and the induced contributions to the free energy of solvation, ΔF_{sol}^{el} and ΔF_{sol}^{ind}, respectively, defined as explained in the methodology section, for the vacuum geometry (g.vac) and for the optimized geometry in solution (g.sol). One first notices that, at fixed geometry, the induced contribution is more than 15% of the electrostatic one, and that the geometry relaxation further increases the interaction in a total which amounts, in some cases, to 30% of the free energy of solvation. These remarks justify a posteriori the care taken to perform SCRF computations on solvated molecules and to optimize the geometry in the cavity. Cramer and Truhlar have recently reached the same conclusion from their semiempirical solvation model.[22a,46]

Let us now examine the influence of the solute–solvent interaction on the isomerization processes. Table IX shows the relative energy of the four structures considered for each compound. In all cases, zero level was assigned to the most stable planar isomer.

The gas-phase results give the typical characteristic known for these compounds. Rotational barriers around the C=C bond

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the dispersion and the cavitation terms. Nonetheless, in the chemical processes, such as isomerizations considered here, the free energy changes due to these contributions can be considered as constant for all the structures involved, leading us to assume that only slight modifications of the chemical energies will appear by the explicit consideration of these two contributions.[13,51] On the other hand, the use of an ellipsoidal cavity, and, in any case, of a rather crude model of the solvent, strongly limits the quantitative character of the results. Thus, the simulation of solvent by a continuum precludes the explicit consideration of short-range solute–solvent interactions, in particular the intermolecular hydrogen bonding when the push–pull ethylenes are dissolved in good hydrogen-bond acceptor or donor solvents. However, as indicated in the Introduction for previous results obtained with the supermolecule approach,[38b] the relatively good agreement of the present results with experiment reveals that the continuum approach is able to account for the main part of the hydrogen bonds, since it has largely an electrostatic origin.

Bearing in mind these limitations, some additional points on the numerical values deserve our attention. Experimental data for compound **1** suggest that the C1—N1 and C=C barriers in a polar solvent should change their relative order, the barrier for rotation around the C1—N1 bond becoming higher than that of C=C bond. This is in agreement with the theoretical prediction for $\epsilon = 38.8$ (Table IX). Likewise, it is clear from this table that the results obtained on the free molecule cannot be used to interpret the experimental data in solution. Finally one must remember that the experimental rotational barriers around the C1–N1 bond have been obtained with doubly substituted amino groups, whereas our computations deal with primary amino compounds in which the Z isomer may be stabilized by an intramolecular hydrogen bond. Since the energy of this isomer is taken as the origin to define the height of the barrier, our results appear as upper limits of the barriers given in Table X.

Contrary to previous results,[39] the optimization of molecular structure in solution has shown for compound **3** the possibility of substantial changes in the geometry of the TS$_{C1-N1}$, leading to further polar distribution which allows a relative stabilization with respect to the planar isomer in solution and, as a consequence, the decrease of the rotational barrier around the C1–N1 bond with the increase of the solvent polarity.

Concerning the prediction of isomer population, it is clear that solvent effects should be included in the calculations, since gas-phase estimations would predict the existence of only the Z isomer, whereas in polar solvents the displacement of the equilibrium toward the E form allows the existence of both isomers.

The rotational barrier around the C=C double bond for the enamine anion decreases also with the polarity of the solvent, although the effect is less pronounced than for the thermal mechanism. However, since the intrinsic rotation for the anionic mechanism is smaller than for the thermal one, the anion barriers remain lower. According to this mechanism

$$AH_Z \rightleftharpoons A_Z^- + H^+ \qquad (a)$$

$$A_Z^- \rightleftharpoons A_E^- \qquad (b)$$

$$A_E^- + H^+ \rightleftharpoons AH_E \qquad (c)$$
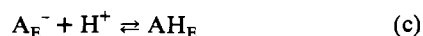
the first step is the deprotonation of the amino group. The experimental enthalpy variation of this process for **1** in N,N-dimethylformamide is 16.8 kcal/mol,[24,25] and for the enaminone derived from **2** (MeC(O)C(H)=C(H)NH(Me)) 15.0–19.3 kcal/mol, depending on the solvent.[26] Therefore, it may be concluded that the rate-determining step of the anionic mechanism is (a). According to the values for rotation via the thermal mechanism, one should conclude that, in solvents with basic properties (which have usually a dielectric permittivity, $\epsilon > 20$), the specific rate

Table XI. Eigenvalue of the Transition Vectors for Rotation around the C=C and the C1—N1 Bonds

structure	molecule	gas phase	$\epsilon = 2.0$	$\epsilon = 38.8$
TS$_{C=C}$	1	0.182 12	0.114 24	0.025 23
	2	0.228 46	0.169 41	0.046 64
	3	0.436 70	0.315 77	0.159 58
TS$_{C1-N1}$	1	0.071 55	0.077 14	0.084 58
	2	0.069 34	0.072 10	0.081 74
	3	0.056 22	0.041 94	0.037 41

constants should be interpreted as the sum of the rate constants of the two parallel mechanisms for rotation around the C=C bond, as was suggested by Kozerski et al.[26]

Finally the changes induced by the solvent on the topology of the potential surface in the critical points for rotation may be examined. Table XI gives the negative eigenvalue associated with the transition vector for the two processes studied, C=C and C1—N1 rotations, in the gas phase and in solution. As is seen, the curvature for rotation around C=C bond increases in the sequence **1 < 2 < 3**, whereas the opposite is observed for the C1-N1 rotation. For a given compound, the curvature diminishes with the increase of the dielectric permittivity for the C=C rotation, whereas the curvature increases for the rotations of C1—N1, except for compound **3** which again exhibits a different behavior. In fact, the processes studied involve a transition vector whose main component is the torsional angle of a fragment of the molecule with respect to the other fragment. This means that the main modifications of the potential energy surface along the reaction path come from the variation of the solute–solvent energy of interaction with this angle. This makes the interpretation of the solvent effect rather easy.

Until now, the chemical energy presented has been obtained as the difference between the SCF molecular energies of two structures:

$$\Delta E_{12}(\epsilon) = E_1^{HF} - E_2^{HF} \qquad (4)$$

If one considers $\epsilon = 1.0$, i.e, gas phase, the energies calculated from ab initio calculations have the *status* of internal energies or free energies at 0 K. However, when a condensed phase is considered, as mentioned in the Methodology section, SCF energy includes a free energy contribution due to the solute–solvent interactions, in such a way that the previous ΔE_{12} can be decomposed as follows:

$$\Delta E_{1,2}(\epsilon) = [E_1^{HF} - E_2^{HF}] + [\Delta F_{1,sol}(\epsilon) - \Delta F_{2,sol}(\epsilon)] \qquad (5)$$

Thus, this result contains a combination of an internal and a free energy. Usually, solvent effects described by a continuum model on equilibria or reactive processes have been estimated in this way.[10,19,39,40,52,53] The meaning given to ΔE_{12} is to emphasize the role of the solvent in the energetic of the process, so that the difference with experiments are usually within reasonable limits.[54] Given that we are dealing with well-located stationary points of the solute in solution, we have carried out calculations of the vibrational frequencies in order to get the free energy at 25 °C by means of expression:

$$G^{298}(\epsilon) = E^{HF}(\epsilon = 1) + ZPE(\epsilon) + \Delta H(0 \rightarrow 298 \text{ K}) -$$
$$298 S^{298}(\epsilon) + \Delta F_{sol}(\epsilon)$$
$$= G_0^{298}(\epsilon) + \Delta F_{sol}(\epsilon) \qquad (6)$$

where the zero-point energy (ZPE), the thermal corrections ($\Delta H(0 \rightarrow 298$ K)), and the entropy (S^{298}) have been added to the SCF molecular energy of the solute in order to get the intrinsic

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Table XII. Relative Free Energies (kcal/mol) for Isomerization Processes in the Gas Phase and Solution

molecule	structure	gas phase	$\epsilon = 2.0$	$\epsilon = 38.8$
1	Z	0.00	0.00	0.00
	E	2.26	1.30	−0.38
	$TS_{C=C}$	40.95	32.18	13.63
	TS_{C1-N1}	18.55	19.35	20.97
2	Z	0.00	0.00	0.00
	E	2.67	1.60	−0.33
	$TS_{C=C}$	44.16	36.84	20.37
	TS_{C1-N1}	17.34	17.68	17.97
3	Z	0.00	0.00	0.00
	E	1.16	0.85	0.75
	$TS_{C=C}$	53.42	46.60	33.56
	TS_{C1-N1}	10.99	11.10	10.77

Gibbs free energy of the solute $(G_0^{298}(\epsilon))$. In this equation, we have assumed that $\Delta F_{sol} = \Delta G_{sol}$. This seems to be quite reasonable because this term refers to a charge process in solution. Moreover, since we are interested in the energy difference between two species, the quantity of interest is:

$$\Delta G_{12}^{298}(\epsilon) = [G_{1,0}^{298}(\epsilon) - G_{2,0}^{298}(\epsilon)] + [\Delta F_{1,sol}(\epsilon) - \Delta F_{2,sol}(\epsilon)]$$
$$(7)$$

It is to be expected that $\Delta G_{sol} - \Delta F_{sol}$ remains quite constant among the species of a same chemical family of compounds.

Table XII includes the relative free energies for the neutral compounds of **1–3**. A comparison of these results with those of Table IX indicates that the same trend given by ΔE_{12} is found where ΔG_{12} is used. Owing to the changes in the thermal corrections and the entropy of the solute with ϵ, the variations of ΔG with the polarity of the solvent are slightly smaller. Thus, the change of ΔG for $TS_{C=C}$ when passing from gas phase to $\epsilon = 38.8$ is −27.3 and −23.8 kcal/mol for **1** and **2**, respectively, whereas those of ΔE are −29.3 and −25.5 kcal/mol. Nevertheless, the factor which induces the main change from ΔE to ΔG is the intrinsic free energy in gas phase, which implies a reduction of the barriers of 3–4 kcal/mol and the energy gap between isomers of 0.5–1.5 kcal/mol. Since these two factors have opposite direction, the final relative energies supplied by ΔE and ΔG do not differ by more than 1–4 kcal/mol. Therefore, although the change from internal to free energy of a solute in solution involves, in general, some tens of kcal/mol and is significant for accurate estimation of individual solvation energy, as we have recently shown using the same technique,[55] it does not play an important role in the case of the energetics of isomerism, mainly due to the rough constancy of the correction between the different geometries of a same molecule.

In recent years there has been an increasing interest in the inclusion of the solvation effects into correlated wave functions.[40,56,57] As a preliminary attempt to consider the electron correlation effects into our model, we have performed some calculations, in a similar way to Wiberg et al.,[40] for compound

1. The energy differences for the Z–E isomers in vacuum and in continuum with $\epsilon = 38.8$ are respectively 4.40 and 2.41 kcal/mol, whereas for the C=C barrier the results including CISD are 43.41 and 11.74 kcal/mol. Comparing these results with those in Table IX, it can be seen that the correlation effects are rather small on the chemical energies of these isomerization processes in solution.

Concluding Remarks

In this work an application of the cavity model to describe the solvent effects on chemical process of isomerization have been presented, including the relaxation of the solute's molecular geometry in solution. Computational efficiency of the method allowing the consideration of the multipole moments up to an advanced element of the series and the use of an ellipsoidal cavity offers the possibility of including the solvent effects in a routine manner with extremely low computational cost.

Nuclear relaxation is, in general, much less important than electronic relaxation, although, as shown for some transition structures involving delicate compromise of the torsional angles, nuclear relaxation may become decisive to change the trends of the solvent effect. From the energetic point of view, nuclear relaxation increases the solvation contribution of all the solutes, the magnitude of this enhancement generally being proportional to ΔF_{sol}, and, as a result, increasing the discriminating role of the solvent between different solutes.

The reasonable picture of the isomerism of push–pull enamines in solution, given by the use of the continuum model, indicates that solute–solvent long-range interactions are the main contribution to the differential solvation energy of the species involved in the isomerization process. Consideration of free energy instead of internal energy to calculate the energies of chemical interest in solution does not introduce important modifications in the theoretical results, the error being typically a few kilocalories/mole.

Preliminary results indicate CI contributions to be relatively unimportant in the solvent effects on the isomerization process of these push–pull ethylenes. In our opinion, the necessity of considering correlated wave functions in solvent effect simulations is the same as for the studies on isolated molecules and can be limited to the systems which cannot be well described at the SCF level.[23] For the time being, one can already use a many-body Perturbation scheme,[58] but a MCSCF[59,56] approach has also been proposed, and works allowing a more complete treatment of correlation effects in solvated molecules are in progress and will help to get a deeper insight in the subject.

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