Relative Gibbs Energies in Solution through Continuum Models: Effect of the Loss of Translational Degrees of Freedom in Bimolecular Reactions on Gibbs Energy Barriers

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We present here a cell model for evaluating Gibbs energy barriers corresponding to bimolecular reactions (or processes of larger molecularity) in which a loss of translational degrees of freedom takes place along the reaction coordinate. With this model, we have studied the Walden inversion processes: $X_a^- + H_3CX_b \rightarrow X_aCH_3 + X_b^-$ (X = F, Cl, Br, and I). In these processes, our model yields an increase of about 2.3−3.4 kcal/mol in Gibbs energy in solution corresponding to the loss of the translational degrees of freedom when passing from separate reactants to the TS in good agreement with experimental data. The corresponding value in the gas phase is about 6.7−7.1 kcal/mol. When the difference between these two figures is used to correct the results obtained by the standard UAHF implementation of the continuum model, the theoretical results are brought significantly closer to the experimental ones. This seems to indicate that for these reactions the parametrization used does not adequately introduce the increase in Gibbs energy corresponding to the constriction of the translational motion of the species along the reaction coordinate when passing from the gas phase to solution. Therefore, we believe that continuum models could perform much better if we released the parametrization process from the task of taking into account the constriction in translation motion in solution, which could be more adequately evaluated using the cell model proposed here, thus allowing it to focus on better reproducing all the remaining solvation effects.

Introduction

Continuum models are widely used in quantum chemical computations to take into account the effect of solvents.[1−10] In the theoretical study of chemical reactivity, calculation of the variation of the Gibbs energy along the reaction coordinate is required to evaluate the Gibbs energy barriers, the relative Gibbs energy of complexes and intermediates, and the Gibbs energy of reaction. Within the framework of continuum models, the difference in Gibbs energy in solution between two species, I and II, is usually evaluated as the difference in gas-phase Gibbs energy plus the difference in the parametrized electrostatic interaction energy between the solute and the continuum,[11] $\langle \Psi_f | \hat{H} + 1/2 \hat{V}_f | \Psi_f \rangle - \langle \Psi_0 | \hat{H} | \Psi_0 \rangle$, and the difference in nonelectrostatic terms (NET) corresponding to dispersion and short-range repulsion interaction energies between the solute and the continuum, and the cavitation energy

$$\Delta G_{sol}(II - I) = G_{gas}(II) + \left[\left\langle \Psi_f \left| \hat{H} + \frac{1}{2} \hat{V}_f \right| \Psi_f \right\rangle - \right.$$
$$\left. \langle \Psi_0 | \hat{H} | \Psi_0 \rangle + NET \right](II) - G_{gas}(I) - \left[\left\langle \Psi_f \left| \hat{H} + \frac{1}{2} \hat{V}_f \right| \Psi_f \right\rangle - \right.$$
$$\left. \langle \Psi_0 | \hat{H} | \Psi_0 \rangle + NET \right](I) \quad (1)$$

where Ψ_0 and Ψ_f are, respectively, the wave functions of solute in the gas phase and polarized by solvent, $\hat{H}$ is the Hamiltonian operator of the solute, and $\hat{V}_f$ is the operator corresponding to the electrostatic potential created by the polarized continuum in the cavity.

The parametrization of the solute−continuum interaction energy is usually based on the reproduction of the hydration Gibbs energies of a set of stable species using scaled atomic

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radii to introduce effects such as the increase in Gibbs energy associated with the constriction of the translational motion of a species when passing from gas phase to solution:[12] increasing the radii of the atoms of the system reduces in the corresponding percentage the interaction energy between the solute and the continuum, thus accounting for that above-mentioned increase in Gibbs energy. This procedure, however, presents in our opinion three main drawbacks. First, transition states are generally not taken into account in the parametrization. Second, this parametrization is usually performed by taking into consideration only one solvent, water (hydration Gibbs energies). Third, it seems difficult to include the change in Gibbs energy corresponding to the constriction of the translational motion when going from gas phase to solution by scaling a magnitude (the solute−continuum interaction) that in principle has nothing to do with it.

When two (or more) species, A and B, combine to form a complex, or a transition state (TS), A−B

$$A + B \rightarrow A-B \quad (2)$$

some of the initial translational degrees of freedom are lost and replaced by vibrational degrees of freedom of the complex system. This transformation of degrees of freedom causes an increase in the Gibbs energy of the system.[13] Using the approach in eq 1, we would get in this case

$$\Delta G_{sol} = G_{gas}(A-B) - G_{gas}(A) - G_{gas}(B) + \left[\left\langle \Psi_f \right| \hat{H} + \right.$$
$$\left. \frac{1}{2} \hat{V}_f \left| \Psi_f \right\rangle - \langle \Psi_0 | \hat{H} | \Psi_0 \rangle + NET \right](A-B) - \left[\left\langle \Psi_f \right| \hat{H} + \right.$$
$$\left. \frac{1}{2} \hat{V}_f \left| \Psi_f \right\rangle - \langle \Psi_0 | \hat{H} | \Psi_0 \rangle + NET \right](A) - \left[\left\langle \Psi_f \left| \hat{H} + \frac{1}{2} \hat{V}_f \right| \Psi_f \right\rangle - \right.$$
$$\left. \langle \Psi_0 | \hat{H} | \Psi_0 \rangle + NET \right](B) \quad (3)$$

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TABLE 1: B3LYP/6-311++G(3df,3pd)^a Electronic Energies and Gibbs Energies in Gas Phase (hartree) and Gibbs Energies of Solvation (kcal/mol) and Cavity Volumes (Å^3) in Water and Acetone Solutions Corresponding to the Structures Involved in the Reaction $X_a^- + CH_3X_b \rightarrow X_aCH_3 + X_b^-$ (X = F, Cl, Br, I)^b

			water		acetone	
	E	G_{gas}	ΔG_{solv}	v_c	ΔG_{solv}	v_c
F⁻	−99.888693	−99.902852	−105.1 (−105.1)	12.51 (12.51)		
CH₃F	−139.800284	−139.782609	−0.05 (−0.1)	73.80 (73.88)		
F⁻···CH₃F	−239.711638	−239.698505	−84.7 (−73.2)	81.67 (81.48)		
[(F···CH₃···F)⁻]‡	−239.695433	−239.680614	−67.4 (−67.9)	69.92 (69.83)		
Cl⁻	−460.303727	−460.318750	−76.0 (−76.0)	34.32 (34.32)	−65.8 (−65.8)	54.50 (54.50)
CH₃Cl	−500.159837	−500.145819	−0.3 (−0.2)	90.10 (90.13)	−0.7 (−0.7)	136.67 (136.70)
Cl⁻···CH₃Cl	−960.479259	−960.470570	−64.7 (−56.8)	119.85 (119.58)	−54.4 (−52.0)	177.90 (179.50)
[(Cl···CH₃···Cl)⁻]‡	−960.464673	−960.454985	−50.2 (−51.0)	118.53 (118.67)	−43.9 (−44.2)	175.30 (174.67)
Br⁻	−2574.238312	−2574.254488	−71.3 (−71.3)	40.82 (40.82)	−62.1 (−62.1)	64.82 (64.82)
CH₃Br	−2614.080733	−2614.067526	−0.7 (−0.4)	98.73 (98.78)	−0.9 (−0.9)	149.66 (149.73)
Br⁻···CH₃Br	−5188.333572	−5188.327862	−62.0 (−53.3)	136.20 (135.57)	−52.2 (−49.2)	200.62 (201.03)
[(Br···CH₃···Br)⁻]‡	−5188.322814	−5188.315159	−48.9 (−48.4)	135.37 (134.72)	−42.4 (−42.3)	200.13 (199.40)
I⁻	−11.487906	−11.504754	−63.8 (−63.8)	62.36 (62.36)	−55.5 (−55.5)	99.02 (99.02)
CH₃I	−51.318939	−51.308159	0.2 (−0.4)	123.64 (123.59)	−1.0 (−1.2)	187.47 (187.43)
I⁻···CH₃I	−62.819652	−62.816129	−52.9 (−48.0)	181.92 (181.72)	−46.6 (−44.9)	269.59 (270.54)
[(I···CH₃···I)⁻]‡	−62.811206	−62.805896	−42.7 (−42.8)	182.60 (181.81)	−38.4 (−38.4)	272.36 (271.49)

^{a} LANL2DZ augmented by a set of d polarization functions with exponent 0.4 and a diffuse sp shell with exponent 0.035 for I. ^{b} In parentheses are collected the values obtained from the optimized structures in water and acetone solutions.

TABLE 2: Gibbs Energies in Gas Phase, Gibbs Energies of Solvation, Gibbs Energies in Solution,^{a} Corrected Gibbs Energies, Gibbs Energies in Solution Calculated with the Correction Proposed in This Work,^{b} and Experimental Gibbs Energies in the Water and Acetone Solvents, in kcal/mol, of the Complexes and Transition Structures Involved in the Reaction $X_a^- + CH_3X_b \rightarrow X_aCH_3 + X_b^-$ (X = F, Cl, Br, I) with Respect to Reactants at the B3LYP/6-311++G(3df,3pd) (LANL2DZ augmented by a set of d Polarization Functions with Exponent 0.4 and a Diffuse sp Shell with Exponent 0.035 for I) Level of Theory^c

		water					acetone				
	ΔG_{gas}	$\Delta\Delta G_{solv}$	ΔG_{sol}	$\Delta\Delta G_{sol}$	ΔG^*_{sol}	ΔG^{exp}_{sol}	$\Delta\Delta G_{solv}$	ΔG_{sol}	$\Delta\Delta G_{sol}$	ΔG^*_{sol}	ΔG^{exp}_{sol}
F⁻···CH₃F	−8.2	20.4 (32.0)	12.2 (23.8)								
Cl⁻···CH₃Cl	−3.8	11.6 (19.4)	7.8 (15.6)				12.1 (14.5)	8.3 (10.7)			
Br⁻···CH₃Br	−3.7	10.0 (18.4)	6.3 (14.7)				10.8 (13.8)	7.1 (10.1)			
I⁻···CH₃I	−2.0	10.7 (16.2)	8.7 (14.2)				9.9 (11.8)	7.9 (9.8)			
[(F···CH₃···F)⁻]‡	3.0	37.8 (37.3)	40.8 (40.3)	−4.8 (−4.8)	36.0 (35.5)	31.8					
[(Cl···CH₃···Cl)⁻]‡	6.0	26.1 (25.2)	32.1 (31.2)	−4.4 (−4.4)	27.7 (26.8)	26.6	22.6 (22.3)	28.6 (28.3)	−4.1 (−4.1)	24.5 (24.2)	21.8
[(Br···CH₃···Br)⁻]‡	4.3	23.1 (23.3)	27.4 (27.6)	−4.3 (−4.3)	23.1 (23.3)	23.7	20.6 (20.7)	24.9 (25.0)	−4.0 (−4.0)	20.9 (21.0)	17.0
[(I···CH₃···I)⁻]‡	4.4	20.9 (21.4)	25.3 (25.8)	−4.1 (−4.1)	21.2 (21.7)	22.0	18.1 (18.3)	22.5 (22.7)	−3.8 (−3.8)	18.7 (18.9)	16.3

^{a} $\Delta G_{sol} = \Delta G_{gas} + \Delta\Delta G_{solv}$. ^{b} $\Delta G^*_{sol} = \Delta G_{sol} + \Delta\Delta G_{sol}$. ^{c} The values obtained from the optimizations in solution are shown in parentheses.

If the parametrization employed fails to properly account for the effect in solution of the transformation of translational degrees of freedom into vibrational ones, this treatment without explicit consideration of the implied degrees of freedom might amount to admitting that the Gibbs energy increase associated with the loss of translational degrees of freedom in the condensed phase is basically that in the gas phase. This, nevertheless, does not seem to be correct, because it would imply that the role played by the translational degrees of freedom when the species are confined to the cavity created by the neighboring solvent molecules is the same as when they occupy the whole container in the gas phase. However, in the gas phase, the formation of a complex implies a reduction of degrees of freedom for motion in the entire volume of the container, V, without constraints, whereas in solution, it involves a change in degrees of freedom for constrained motion within a small cavity.[14] This latter change cannot produce as large a variation in Gibbs energy as in the gas phase. Therefore, if we treat the translational degrees of freedom in solution as in the gas phase, the cost associated with their loss when two or more molecules form a complex system in solution is overestimated, and consequently, n molecular ($n > 1$) processes are kinetically overpenalized in solution by this practice. We believe that continuum models could perform much better if we released the parametrization process from the task of taking into account the constriction of the translation motion in solution, thus allowing it to focus on better reproducing all the remaining solvation effects.

We present here a model for explicitly calculating the change in Gibbs energy corresponding to the loss of translational degrees of freedom in solution along a reaction pathway when a variation in the number of molecules takes place. As an illustration of the performance of the proposed model, we also report the results obtained in the theoretical study of the Walden inversion processes

$$X_a^- + H_3CX_b \rightarrow X_aCH_3 + X_b^- \qquad (4)$$

(X = F, Cl, Br, and I) in water ($\epsilon = 78.39$) and/or acetone ($\epsilon = 20.7$) solutions. On one hand, these processes are adequate to investigate the effect produced by the loss of translational degrees of freedom and seemed good candidates for inadequate accounting for the constriction of translational motion in solution through the usual parametrization owing to the three above-mentioned drawbacks and, particularly, because of the large difference in the magnitude of the solute−continuum interaction between reactants and TS. On the other hand, the influence of solvation on the rate and the mechanism of this kind of S$_N$2 process is very important and has been investigated both experimentally[15−17] and theoretically,[18−30] thus making possible the assessment of the results obtained using eq 3 and the model proposed in the present work.

Theory and Methods

We will assume that in solution, at the pressure and the temperature considered, each of the N solute molecules is

allowed to move within an effective volume determined by the nearest-neighbor molecules of solvent and that this volume corresponds to the cavity created in the continuum models to host the solute molecule, v_c, after spending some cavitation energy, w_{cav}. Accordingly, the isothermal−isobaric partition function of the solute molecules confined within their cavities moving around the volume of the solution may be written as

$$\Delta(N,T,p)_{sol} = e^{-N(w_{int}+w_{cav})/k_BT}\left[\left(\frac{2\pi mk_BT}{h^2}\right)^{3/2} v_c e^{-pv_c/k_BT}\right]^N \Delta' \tag{5}$$

where w_{int} is the interaction energy between the solute molecule and the continuum, w_{cav} is the energy of cavitation, m is the mass of the molecule of solute, Δ' is the partition function corresponding to the nontranslational degrees of freedom of the system, and k_B and h, p and T are the Boltzmann and Planck constants, pressure and temperature, respectively.

If we take into account that

$$G = -k_BT \ln \Delta \tag{6}$$

from eq 5 the Gibbs energy variation per mole corresponding to the association of two species A and B to form a complex system A−B in solution would be

$$\Delta G^*_{sol} = G(A-B)_{sol} - G(A)_{sol} - G(B)_{sol}$$

$$= N_A[w_{int}(A-B) + w_{cav}(A-B) - w_{int}(A) - w_{cav}(A) - w_{int}(B) - w_{cav}(B)] + N_Ap[v_c(A-B) - v_c(A) - v_c(B)] +$$

$$\frac{3}{2}N_Ak_BT\ln\left(\frac{2\pi k_BT}{h^2}\right) + \frac{3}{2}N_Ak_BT\ln\left[\frac{m(A)m(B)}{m(A) + m(B)}\right] +$$

$$N_Ak_BT\ln\left[\frac{v_c(A)v_c(B)}{v_c(A-B)}\right] + k_BT\ln\left[\frac{\Delta(A)'\Delta(B)'}{\Delta(A-B)'}\right] \tag{7}$$

where N_A is the Avogadro constant and $m(A-B) = m(A) + m(B)$.

From eq 3 and employing the gas-phase isothermal−isobaric partition function

$$\Delta(N,T,p)_{gas} = \left[\left(\frac{2\pi mk_BT}{h^2}\right)^{3/2}\frac{k_BT}{p}\right]^N \Delta'' \tag{8}$$

where Δ'' is the partition function component corresponding to the nontranslational degrees of freedom of the system, we obtain

$$\Delta G_{sol} = N_Ak_BT\ln\left(\frac{k_BT}{p}\right) + \frac{3}{2}N_Ak_BT\ln\left(\frac{2\pi k_BT}{h^2}\right) +$$

$$\frac{3}{2}N_Ak_BT\ln\left(\frac{m(A)m(B)}{m(A-B)}\right) + k_BT\ln\left(\frac{\Delta(A)''\Delta(B)''}{\Delta(A-B)''}\right) +$$

$$\left[\left\langle\Psi_f\middle|\hat{H} + \frac{1}{2}\hat{V}_f\middle|\Psi_f\right\rangle - \langle\Psi_0|\hat{H}|\Psi_0\rangle + \text{NET}\right](A-B) -$$

$$\left[\left\langle\Psi_f\middle|\hat{H} + \frac{1}{2}\hat{V}_f\middle|\Psi_f\right\rangle - \langle\Psi_0|\hat{H}|\Psi_0\rangle + \text{NET}\right](A) - \left[\left\langle\Psi_f\middle|\hat{H} + \frac{1}{2}\hat{V}_f\middle|\Psi_f\right\rangle - \langle\Psi_0|\hat{H}|\Psi_0\rangle + \text{NET}\right](B) \tag{9}$$

Consequently, taking

$$\left\langle\Psi_f\middle|\hat{H} + \frac{1}{2}\hat{V}_f\middle|\Psi_f\right\rangle - \langle\Psi_0|\hat{H}|\Psi_0\rangle + \text{NET} = w_{int} + w_{cav}$$

and assuming that when A is a monatomic species

$$\frac{\Delta(A)'\Delta(B)'}{\Delta(A-B)'} \approx \frac{\Delta(A)''\Delta(B)''}{\Delta(A-B)''}$$

(this is equivalent to admit that the relation

$$\frac{q_{rot}(B)q_{vib}(B)}{q_{rot}(A-B)q_{vib}(A-B)}$$

is practically the same in the gas phase and in solution), and neglecting $N_Ap[v_c(A-B) - v_c(A) - v_c(B)]$, which is on the order of 10^{-4} kcal/mol when v_c is on the order of 10^{-30} m^3, the difference between the two Gibbs energy variations ΔG^*_{sol} and ΔG_{sol} obtained from eqs 7 and 9, respectively, is

$$\Delta\Delta G_{sol} = \Delta G^*_{sol} - \Delta G_{sol} = RT\ln\left(\frac{v_c(A)v_c(B)}{v_c(A-B)}\right) -$$

$$RT\ln\left(\frac{k_BT}{p}\right) \tag{10}$$

This expression (eq 10) would correspond then to the term to be added to eq 9, the usually employed expression for ΔG_{sol}, when the parametrization fails to take properly into account the effect of the loss of translational degrees of freedom in solution, and eq 9 evaluates this effect as in the gas phase.

Evidently, for a trimolecular process

$$A + B + C \rightarrow A-B-C \tag{11}$$
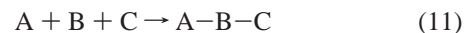
we would get

$$\Delta\Delta G_{sol} = \Delta G^*_{sol} - \Delta G_{sol} = RT\ln\left(\frac{v_c(A)v_c(B)v_c(C)}{v_c(A-B-C)}\right) -$$

$$2RT\ln\left(\frac{k_BT}{p}\right) \tag{12}$$

which yields a factor of about twice that for the bimolecular case.

Quantum chemical computations were carried out with the *Gaussian 98* series of programs[31] employing the hybrid density functional B3LYP.[32−34] Full geometry optimizations were performed in the gas phase by using the 6-311++G(3df,3pd)[35−39] (LANL2DZ augmented by a set of d polarization functions with exponent 0.4 and a diffuse sp shell with exponent 0.035 for iodine atom)[40,41] basis set, and the standard Shlegel's algorithm.[42] The nature of the stationary points was further checked, and zero-point vibrational energies (ZPVEs) were evaluated by analytical computations of harmonic vibrational frequencies at the same theory level. ΔH, ΔS, and ΔG values were calculated in the gas phase within the ideal gas, rigid rotor, and harmonic oscillator approximations.[43] A pressure of 1 atm and a temperature of 298.15 K were assumed in the calculations.

Quantum chemical computations in solution were carried out by both single point calculations on gas-phase optimized geometries and reoptimizations in the condensed phase at the B3LYP/6-311++G(3df,3pd) (LANL2DZ augmented by a set of d polarization functions with exponent 0.4 and a diffuse sp shell with exponent 0.035 for iodine atom) theory level and using a general self-consistent reaction field (SCRF) model.[2,41,44,45] In this model, the solvent is represented by a dielectric continuum characterized by its relative static dielectric permittivity, ϵ. The solute is placed in a cavity created in the continuum, the shape of which is chosen to fit as well as possible the solute molecular shape according to the solvent accessible surface. The solute charge distribution polarizes the dielectric
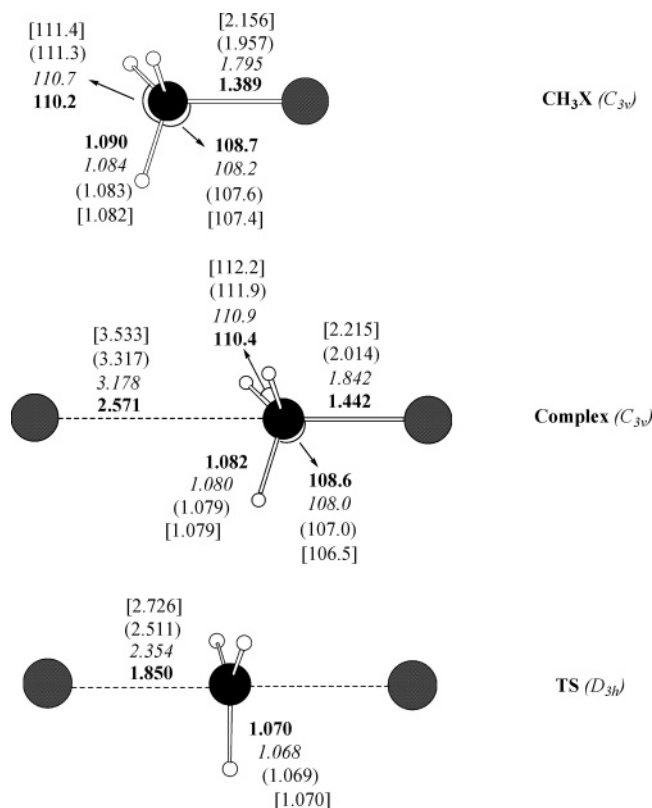
Figure 1. B3LYP/6-311++G(3df,3pd) (LANL2DZ augmented by a set of d polarization functions with exponent 0.4 and a diffuse sp shell with exponent 0.035) optimized geometries in gas phase of the most important structures located for the reaction of X_a^- with CH_3X_b (X = F (bold), Cl (italic), Br (in parentheses), I (in square brackets)). Distances are given in angstroms and bond angles in degrees.
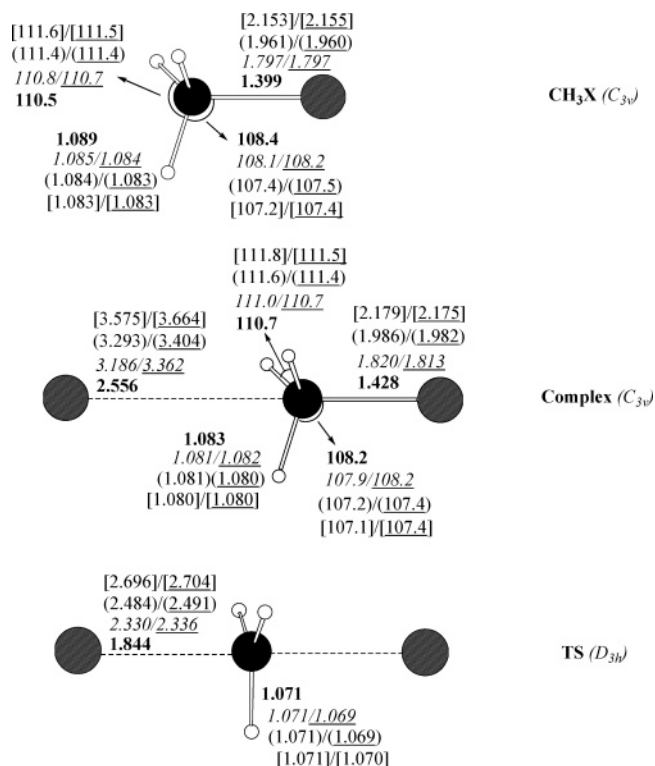
Figure 2. B3LYP/6-311++G(3df,3pd) (LANL2DZ augmented by a set of d polarization functions with exponent 0.4 and a diffuse sp shell with exponent 0.035) optimized geometries in water and in acetone (underlined values) solutions of the most important structures located for the reaction of X_a^- with CH_3X_b (X = F (bold), Cl (italic), Br (in parentheses), I (in square brackets)). Distances are given in angstroms and bond angles in degrees.
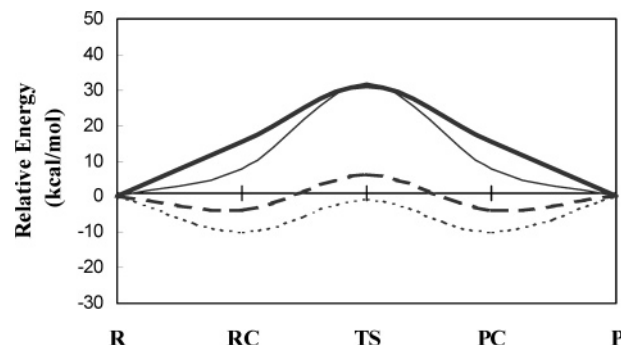
that in turn creates an electric field that modifies both the equilibrium geometry and the electronic charge of the solute. One may take into account this interaction at the SCF level by minimizing the energy of the solute plus the electrostatic free energy change corresponding to the solvation process that is given by

$$\Delta G = -\tfrac{1}{2}E_{int} \tag{13}$$

where E_{int} is the electrostatic interaction energy

$$E_{int} = \sum_\alpha V_{el}(\mathbf{r}_\alpha)Z_\alpha - \int V_{el}(\mathbf{r})\rho(\mathbf{r})\,d\mathbf{r} \tag{14}$$

In this equation, V_{el} is the electrostatic potential created by the polarized continuum in the cavity, $\mathbf{r}_\alpha$ and Z_α are the position vector and the charge of nucleus α, respectively, and $\rho(\mathbf{r})$ is the electronic density at point $\mathbf{r}$. V_{el} may be computed by following different approaches. In the model used here, the UAHF (united atom Hartree−Fock) parametrization[41] of the polarizable continuum model (PCM)[2,41,44,45] was used including both electrostatic and nonelectrostatic solute−solvent interactions. Relative permittivity values of 78.39 and 20.7 were used to simulate water and acetone, respectively, as solvents.

Results and Discussion

We investigated the Walden inversion reaction 4 for X = F, Cl, Br, and I in the gas phase and in water solution and for X = Cl, Br, and I in acetone solution. The results obtained are displayed in Tables 1 and 2 and in Figures 1−5.

Figure 3. Profiles of the relative electronic energy (ΔE, in point line), Gibbs energy in gas phase (ΔG_{gas}, in bold dashed line), and Gibbs energy in water solution from the optimized geometries both in gas phase and in condensed phase (ΔG_{sol}, in normal and thick continuous lines, respectively) for the reaction of Cl⁻ with CH_3Cl.

In all the cases studied in the present work in electronic energy, the process proceeds through an initial complex, **CR**, in which the attacking X⁻ is interacting with the CH_3X molecule along the C−X bond at a distance of 2.5−3.7 Å. This **CR** evolves through a transition state, **TS**, of D_{3h} symmetry (see Figures 1 and 2) to yield a preproduct complex, **CP**, identical with **CR**, which finally leads to the product CH_3X + X⁻. The complexes **CR** and **CP** as well as the transition state **TS** are in electronic energy more stable than the separate reactants and products. When the ZPVE and thermal corrections and the entropy are introduced, the complexes **CR** and **CP** and the transition state **TS** become destabilized with respect to reactants and products so that **TS** becomes less stable than separate reactants (e.g., see Figure 3 for the case of X = Cl).
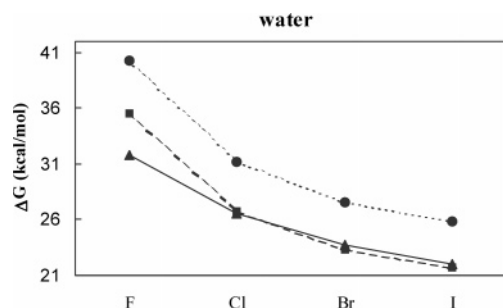
Figure 4. Comparison of the Gibbs energy barriers in water solution, ΔG_{sol} (●), ΔG_{sol}^* (■), and ΔG_{sol}^{exp} (▲), for the reaction of X_a^- with CH_3X_b, (X = F, Cl, Br, I).
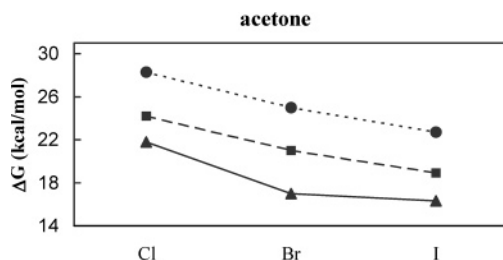

Figure 5. Comparison of the Gibbs energy barriers in acetone solution, ΔG_{sol} (●), ΔG_{sol}^* (■), and ΔG_{sol}^{exp} (▲), for the reaction of X_a^- with CH_3X_b, (X = Cl, Br, I).

When the effect of solvent is taken into account, the reactants and the products become considerably stabilized with respect to the remaining critical structures so that the complexes **CR** and **CP** disappear from the free energy profile in solution, becoming transient species, and the energy barrier corresponding to TS notably increases (see Table 1 and Figure 3).

From the values in Table 2, we clearly see that the Gibbs energy barrier for the Walden inversion reactions (eq 4) in solution is systematically overestimated by 3.3−9.0 kcal/mol when performing single point calculations and 3.8−8.5 kcal/mol when reoptimizing in water solution, and 6.2−7.9 kcal/mol when performing single point calculations and 6.4−8.0 kcal/mol when reoptimizing in acetone solution, by following the usual procedure, eq 3. On the other hand, the correction proposed in the present work for this Gibbs energy barrier in solution, eq 10, reduces its value by 4.1−4.8 kcal/mol in water and 3.8−4.1 kcal/mol in acetone solution. This factor corresponds to the difference between the Gibbs energy change owing to the loss of translational degrees of freedom in gas phase and in solution. For the reactions investigated here, the change in Gibbs energy owing to the loss of the translational degrees of freedom when passing from the separate reactants to the TS is about 6.7−7.1 kcal/mol in the gas phase, 2.3−3.1 kcal/mol in water solution, and 2.6−3.4 kcal/mol in acetone solution. These results are in good agreement with the energy of activation experimentally determined for the collision frequency Z'_{AB} in many liquids (about 3 kcal/mol).[46] It is interesting to note that in water the corrected theoretical barriers differ from the experimental values by 0.2−0.4 kcal/mol, except for X = F in which hydrogen bonding, not properly evaluated by continuum methods, is important. In the case of acetone solvent, the corrected barriers differ from the experimental ones by 2.4−4.0 kcal/mol, most likely because UAHF parametrization has been performed in water solution. Therefore, the proposed correction brings the theoretical Gibbs energy barrier in solution substantially closer to the experimental value (see Figures 4 and 5). These results seem to indicate that the parametrization

used does not adequately evaluate the effect of the constriction of the translational motion in solution along the reaction coordinate.

It is important to point out that the results predicted by our model are in reasonable agreement with those proposed by Okuno,[47] taking into account the free-volume theory.[46] This author proposed the evaluation of the thermodynamic functions in nonpolar solvents as

$$\Delta H_{liq} = \Delta H_{gas} - (1 - m)RT \qquad (15)$$

$$\Delta S_{liq} = \Delta S_{gas} - R \ln(10^{2m-2}m) \qquad (16)$$

Thus, for a bimolecular reaction, $\Delta H_{liq} = \Delta H_{gas} + RT$ and $\Delta S_{liq} = \Delta S_{gas} - R \ln(2 \cdot 10^2)$. As an illustration, using the model proposed in the present work and neglecting the relative electrostatic solute−continuum interactions, we get for X = Cl and water as the solvent $\Delta H_{sol} = \Delta H_{gas} + RT$ and $\Delta S_{sol} = \Delta S_{gas} - R \ln(1.5 \cdot 10^3$ e).

In summary, a model is proposed for explicitly evaluating the effect of the loss of translational degrees of freedom in solution on the Gibbs energy of activation in bimolecular (trimolecular) reactions. With this model, we have studied the Walden inversion processes: $X_a^- + H_3CX_b \rightarrow X_aCH_3 + X_b^-$ (X = F, Cl, Br, and I). In these processes, our model yields an increase of about 2.3−3.4 kcal/mol in Gibbs energy in solution corresponding to the loss of the translational degrees of freedom when passing from separate reactants to the TS in good agreement with experimental data. The corresponding value in gas phase is about 6.7−7.1 kcal/mol. When the difference between these two figures is used to correct the results obtained by the standard UAHF implementation of the continuum model, the theoretical results significantly approach the experimental ones. This seems to indicate that for these reactions the parametrization used is not capable of adequately introducing the increase in Gibbs energy corresponding to the constriction of the translational motion of the species along the reaction coordinate when passing from the gas phase to solution. Therefore, we believe that continuum models could perform much better if we released the parametrization process from the task of taking into account the constriction in translation motion in solution, thus allowing it to focus on better reproducing all the remaining solvation effects.

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(12) This increase is a consequence of the reduction of the volume accessible to a species when going from gas phase to solution. This decrease of volume determines an increase of the separation of the translational energy levels, thus resulting in a smaller value of the partition function.

(13) This increase is clearly seen from $\Delta G_{tr \to vib} = -k_B T \ln(Q_{vib}/Q_{tr})$ where Q_{tr} and Q_{vib} are the partition functions corresponding, respectively, to the lost translational degrees of freedom and the vibrational ones which replace them. As $Q_{tr} \gg Q_{vib}$ then $\Delta G_{tr \to vib} > 0$. See also ref 14.

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