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Molecular Simulation of a Chemical Reaction in Supercritical Water

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Supercritical water (SCW) is receiving a great deal of attention as a solvent in a variety of processes, especially for the oxidation of organic wastes.[1] However, development of SCW technology has been hindered by a lack of knowledge about this unusual aqueous environment at the molecular level. A key issue is whether this environment is more like ambient water, a polar organic solvent, or a gas phase, for a given value of the density and temperature. While simulations of solvation in SCW have appeared recently,[2,3] here we present the first molecular simulation study of the rate of a chemical reaction in a supercritical fluid, in particular SCW. We have chosen to simulate the S_N2 substitution reaction, $Cl^- + CH_3Cl \rightleftarrows ClCH_3 + Cl^-$, since the solvent effect is large, i.e., the rate constant decreases 20 orders of magnitude from the gas phase to ambient water. It will be shown that the free energy barrier in SCW is more like the barrier in ambient water than that in a polar organic solvent, namely, dimethylformamide.

When a chemical reaction takes place in the gas phase, the free energy barrier is completely determined by the interactions among the reactants. In a condensed phase, it is also influenced by the forces exerted by the solvent. The potential of mean force (PMF) along the reaction coordinate is equivalent to the free energy surface. In this work, we compute the PMF from simulations, using the free energy perturbation method.[4]

The reaction of Cl^- and CH_3Cl has been well studied in water under ambient conditions by Monte Carlo simulation[5] and by integral equation theories.[6] The gas-phase reaction profile has been characterized with ab-initio calculations[5,6] which give the geometries, charge distributions, and energies along the reaction path. These results provide the intermolecular potential functions needed for solution-phase simulations. The form is a site–site potential with Coulombic and Lennard-Jones forces for the solute–solvent interactions. The methyl group was taken as a single site.

An asymmetric reaction coordinate is defined as $r_A = r_{CCl'} - r_{CCl^-}$, the difference between the distances from the methyl group carbon to each of the chlorine atoms. This choice of reaction coordinate reflects the symmetry of the reaction, in that $|r_A|$ ranges from infinity (reactants or products) to zero (transition-state complex). Statistical mechanical perturbation theory[4] is used in order to obtain the change in Helmholtz free energy in the solution at each step along the reaction coordinate:

$$\delta A(r_A) = -kT \ln\langle \exp[-(U_{ws}(r_A + dr_A) - U_{ws}(r_A))/kT]\rangle_{r_A} \tag{1}$$

where U_{ws} is the water–solute configurational energy and the brackets indicate averages taken for the solution at fixed r_A, when the system is perturbed from r_A to $r_A + dr_A$.

For each point along the reaction coordinate, molecular dynamics simulations were performed for about 20 ps to equilibrate the system. Then the system was perturbed by dr_A, i.e., 0.125 Å, for 15–25 ps to obtain the average in eq 1. The time step was in all cases 1 fs. The size of the simulation box was $L \times L \times 1.5L$, where $L = 28.84$ Å, and periodic boundary conditions were applied. The forces were calculated using the minimum image convention. For each value of r_A, the solutes were constrained to be collinear with the longest axis of the simulation box. The simple point charge (SPC)[7] potential was used to model water. The critical properties of the SPC model have been estimated by de Pablo et al.[8] A total of 484 water molecules were present, corresponding to a density of 0.405 g/cm^3, 1.5 times the critical density for the SPC model. The temperature was the model critical temperature (587 K). Under these reduced conditions, the experimental dielectric constant ϵ is 9.75,[9] while the calculated value for the SPC model is 14.7.[3] The calculated average pressure is 230 bar. The PMF was calculated as

$$W(r_A) = \Delta A(r_A) + \Delta U_{gas}(r_A) \tag{2}$$

where $\Delta A(r_A)$ is the change of free energy in the solution at r_A, which results from the sum of all the contributions $\delta A(r_A)$ when the solutes are brought together in small steps dr_A from infinite separation to the distance r_A. The second term, $\Delta U_{gas}(r_A)$, is the corresponding change in the gas phase. In the calculations reported we have assumed that $W(|r_A| = 8\ \text{Å}) = 0$.

Figure 1 shows the PMF as a function of the reaction coordinate for SCW, for ambient water (AW), and also for gas-phase conditions. In the gas phase,[5,6] the double-well energy surface indicates the formation of an ion–dipole complex and a symmetric transition state. In ambient water, the minimum corresponding to the ion–dipole complex disappears and the activation barrier grows to 26.3 kcal/mol according to Monte Carlo simulations.[5] This well disappears since the energy ion–dipole attraction is offset by the net weakening of the nucleophile–water hydrogen bond interaction.[10] The free energy profile obtained in SCW closely resembles that in ambient water, despite the reduction in solvent density of about 2, and in ϵ from 80 to 9.75. However, a slight minimum is present corresponding to the ion–dipole complex ($|r_A| \sim 1.5$ Å). Compared with ambient water, the hydrogen bonds between the nucleophile and water are weaker in SCW, so the desolvation does not completely compensate for the stabilization upon ion–dipole complex formation. In SCW, the activation barrier between the ion–dipole complex and the transition state is 25.3 kcal/mol, 1 kcal/mol higher than that between the reactants and the transition state. Consequently, there is an equilibrium between the reactants and the complex.

To calibrate the results against those in a polar solvent, we consider dimethylformamide ($\epsilon = 37$). The activation barrier (PMF) according to Monte Carlo simulation is 19.3 kcal/mol,[10] and the well for the ion–dipole complex is −2.7 kcal/mol. For each of these properties, SCW lies between ambient water and DMF, even though ϵ is only 9.75. Thus microscopic solvation must be important in SCW at this density.

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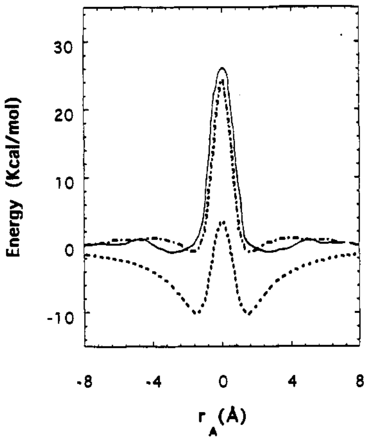

Figure 1. Calculated internal energies in the gas phase(- - -) and the potential of mean force in aqueous solution under ambient (—) and supercritical (-·-) conditions, as a function of the reaction coordinate, r_A.

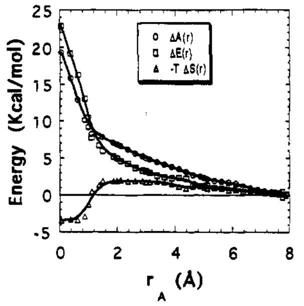

Figure 2. Calculated changes in free energy in the solution and its energetic and entropic contributions as a function of the reaction coordinate, r_A.

In order to investigate the solvent effect further, we have calculated the energetic and entropic contributions to the free energy along the reaction coordinate. The energetic contribution $\Delta E(r_A)$ was calculated by a method based on finite difference derivatives with respect to temperature,[11] for all values of r_A, except at the transition state, $r_A = 0$, where it was obtained directly from a 150-ps simulation. The entropy change, $-T\Delta S(r_A)$, is given by $\Delta A - \Delta E$.

Figure 2 shows the change in free energy and its energetic and entropic contributions as a function of the reaction coordinate. Two distinct regions are seen. For $|r_A| > 1$ the slope of ΔE versus r_A is small, and $\Delta S(r_A)$ is negative. The inflection in the curvature of $-T\Delta S$ at $r_A = 1$ is also observed at ambient conditions,[6] although ΔS remain positive at all r_A. In SCW, the formation of the ion–dipole complex is energetically favorable (because of the U_{gas} term), compensating for the entropy loss. In the second region, where $|r_A| < 1$, the energetic contribution increases rapidly and crosses the free energy curve. This is due to the weakening of the solute–solvent interactions at the transition state caused by the charge dispersal. The entropic change becomes positive, reflecting the solvent disorder resulting from less favorable solvation at the transition-state complex, compared to the reactants.

The standard deviations in the incremental free energy differences were calculated according to the method of batch means.[12] The average error of the incremental free energy differences is 0.1 kcal/mol. The maximum uncertainties for ΔE and $-T\Delta S$ are therefore of the same order as the average values of those properties, which is to be expected, given their derivative relationship to the configurational integral.[11] However, the fact that the value for ΔE for the transition state agrees reasonably with the sum of the increments strongly suggests that the curves are reliable.

To compare the results in SCW with those in a continuum solvent, we have calculated the free energy, energy, and entropy of activation with a simple implementation of the Born model[13] (at constant volume). The solute is treated as a sphere, with the Born radius for the transition-state complex takes as the sum of the radius of the chloride atom in the complex and the distance from the chloride atom to the methyl group. The reactants were described using the chloride Lennard-Jones diameter as the Born radius. Experimental values[9] were used for the dielectric constant of water, since simulated values for SPC water as a function of T and P are not available. For AW, this Born model predicts a solvent contribution of $\Delta A(r_A = 0) = 25.5$ kcal/mol, compared to the simulation estimate[10] of 22.7 kcal/mol. The model gives $-T\Delta S = -0.3$ kcal/mol and $\Delta E = 25.75$ kcal/mol for AW, in qualitative agreement with integral equation estimates.[6] In SCW, the Born model yields $\Delta A = 23.1$ kcal/mol, compared to the simulation estimate of 19.3 kcal/mol, so that both approaches exhibit the small decrease in ΔA relative to ambient water. The magnitudes of the Born predictions of ΔE (25.72 kcal/mol) and $-T\Delta S$ (–2.59 kcal/mol) in SCW are also comparable to the present simulation results of 22.8 and –3.5 kcal/mol), respectively.

According to the Born mode, the ΔA changes little as the bulk dielectric constant is decreased from 80 to 9.75. Therefore, it is possible that microheterogeneous solvation in SCW, even if it raised the local dielectric constant to 80, still may not have a large effect on ΔA. We note also that the Born model predicts that the free enegy of activation is higher in dimethylformamide (25.1 kcal/mol) than in SCW (23.1 kcal/mol), which is contrary to the simulation results (15.73 kcal/mol in DMF[10] and 19.3 kcal/mol in SCW). The molecular environment in SCW is more like ambient water than this polar organic solvent. Thus, the success of the continuum Born model at SCW conditions may be fortuitous. A detailed analysis of the structural properties from simulations under these conditions and also at other supercritical temperatures and densities will be presented[14] to demonstrate microheterogeneous distribution of the solvent.

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