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Simulation of an S_N1 Reaction in Supercritical Water

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Recently supercritical fluids have been subjected to intense study to understand their solvent properties.[1,2] These fluids are important as solvents for chemical reactions, including those for treatment of organic wastes[3] and reactions that normally require costly and/or toxic solvents.[4] Many of the properties of these fluids have been determined, but several questions about the molecular basis of these properties remain. It is well-known that solvation is often a determining factor in the products of chemical reactions.[5] Since, above the critical temperature, the fluid density, and therefore dielectric constant, can be varied enormously and continuously by small changes in pressure at constant temperature, the solvent environment of solutes can be changed, so that the chemistry is similar to that in ambient water, polar organic solvents, or the gas phase. For reactions involving charge separation, this variation of conditions will be particularly dramatic. In this work, we consider a model S_N1 reaction to investigate the effect of supercritical water density on the competition between ionic and radical pathways for a reaction in which ions are the conventional intermediates.

In ambient solution, the solvent stabilization of ions can be a substantial fraction of a chemical bond. In the gas phase, ionic products are not thermodynamically stable and hence radicals form when neutral chemical bonds break. It is clear that in sufficiently low-density supercritical water, the solvent stabilization of ions will also be negligible. The threshold bulk density at which ions are stabilized when bonds break has not been studied directly. Several researchers[6−8] have indicated that a crossover between ionic and radical reaction pathways exists in supercritical water and correlated their experimental observations with the ionic product and dielectric constant of the solvent. It is therefore qualitatively clear that changes in density in supercritical water solvents can reduce the efficacy of one reaction pathway, but increase that of another. This should be correlated with solvent properties, but it is likely that the nature of the solute also has a role in dictating this threshold density, since local solvent density can be greater than the bulk if solute−solvent interactions are substantial.[9,10]

The reaction barrier in the gas phase is determined solely by interactions within the reactants. In the condensed phase, the interactions among the reactants and solvent molecules help to determine the chemistry of the system. The free energy change along the reaction coordinate, or potential of mean force (PMF), which is the condensed phase analogue of the gas-phase adiabatic free energy surface, can be obtained from computer simulation by using free energy perturbation.[11]

The dissociation stage of an S_N1 reaction is the rate-limiting step and has been the subject of thorough experimental[12] and theoretical[13] work. Keirstead et al.[14] have used an empirical valence bond[15,16] approach to treat this problem in ambient water. The method describes the solute electronic state (degree of ionic character) as a linear combination of diabatic states: an ionic state, with full charge separation, and a covalent state, with a bonding interaction and no charge separation. The weight of each form in the most stable state (adiabatic ground state) is determined by diagonalizing the model Hamiltonian, *including* the energetics of solvation. In the work described here, we adopt this form for the adiabatic Hamiltonian (eq 1) and use it to determine the free energy surface of the *tert*-butyl chloride system in supercritical aqueous solution. The form is

$$H_{\mathrm{ad}} = K_{\mathrm{w}} + K_{\mathrm{s}} + V_{\mathrm{w}} + {}^{1}/_{2}(V_{\mathrm{s}}^{\mathrm{ion}} + V_{\mathrm{s}}^{\mathrm{cov}}) + {}^{1}/_{2}(V_{\mathrm{int}}^{\mathrm{ion}} + V_{\mathrm{int}}^{\mathrm{cov}}) - {}^{1}/_{2}\{[(V_{\mathrm{s}}^{\mathrm{ion}} - V_{\mathrm{s}}^{\mathrm{cov}}) + (V_{\mathrm{int}}^{\mathrm{ion}} + V_{\mathrm{int}}^{\mathrm{cov}})]^2 + 4V_{\mathrm{el}}^2\}^{1/2} \quad (1)$$

Here *K* and *V* are the kinetic and potential energies, respectively; the subscripts refer to water, solute, and water−solute intermolecular interaction energies, the superscripts to the pure ionic and covalent states, and V_{el} is the electronic coupling parameter, which is independent of solvent effects. The model used by Keirstead et al.[14] has been substantially revised,[17] including use of a nonpolar covalent state and exponentially varying electronic coupling. See Supporting Information for a complete description of the solute model. The well-studied[18] SPC/E potential[19] was used to model water. Simulations were performed at 673 K and solvent densities of 0.29, 0.087, and 0.0435 g cm^{-3}, and ambient water for comparison. Dielectric constants for SPC/E water at these conditions are 5.44, 2.06, 1.5, and 89.0, respectively,[20] and the ionic products are 8.6×10^{-16}, 4.2×10^{-24}, 2.6×10^{-28}, and 10^{-14}.[21]

The reaction coordinate was defined as the distance r_{A} between the central carbon atom of the *tert*-butyl group and the chlorine atom. Solvation effects were treated by using statistical mechanical perturbation theory[11] to calculate the change in Helmholtz free energy, *A*, in the solution at each step along the reaction coordinate. The change $\delta A(r_{\mathrm{A}} + \delta r_{\mathrm{A}})$ was obtained from the ensemble average at fixed r_{A}, when the system was perturbed from r_{A} by a step δr_{A} via the exact expression[11]

$$\delta A(r_{\mathrm{A}}) = -k_{\mathrm{B}}T \ln\langle \exp[-(U_{\mathrm{sol}}(r + \delta r_{\mathrm{A}}) - U_{\mathrm{sol}}(r_{\mathrm{A}}))/k_{\mathrm{B}}T]\rangle_{r_{\mathrm{A}}} \quad (2)$$

where U_{sol} is the sum of the ground-state water−solute and solute intramolecular potential energies and the brackets indicate a thermal average over solvent configurations.

Molecular dynamics (MD) simulations were performed at intervals of 0.25 Å along the reaction coordinate. At each distance

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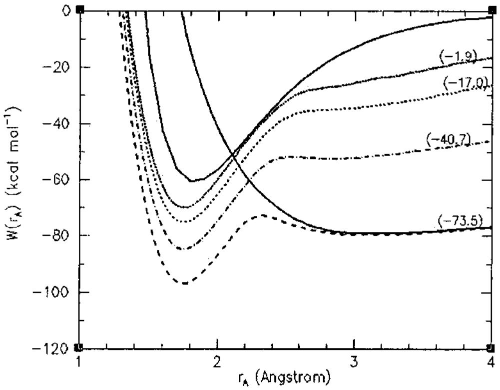

Figure 1. Free energy surfaces for *tert*-butyl chloride in supercritical (673 K) water: 0.29 g cm^{-3} (- — -), 0.087 g cm^{-3} (•••), 0.0435 g cm^{-3} (···), and ambient water (- - -). The asymptotic limits are shown in brackets. Solid lines are ambient diabatic ionic and covalent states.

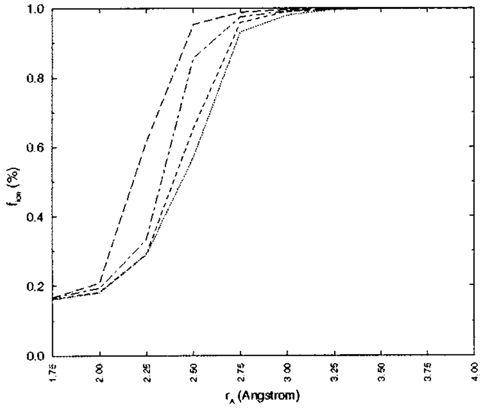

Figure 2. Fraction f_{ion} of ionic character as a function of separation of the *tert*-butyl and chlorine groups. For key see Figure 1.

r_A, 20 ps of MD was performed after equilibration during which the average required in eq 2 was evaluated for $\delta r_A = \pm 0.125$ Å. In all cases the MD time step was 2 fs. Cubic periodic boundary conditions were applied, using the Ewald sum to treat long-range forces. The PMF was calculated as

$$W(r_A) = \sum_{r=\infty}^{r_A} \delta A(r) \tag{3}$$

We set the relative free energies via

$$W(|r_A| = \infty) = \begin{cases} 0;\ \text{neutral radicals} \\ E_{\text{ion}} + E_{\text{aff}} + \Delta A_{\text{solv}};\ \text{ions} \end{cases} \tag{4}$$

where E_{ion} and E_{aff} are the ionization energy of *tert*-butyl and the electron affinity of chlorine, respectively; ΔA_{solv}, the solvation free energy of the isolated ions, was taken from the literature[20] for the chloride ion except at the lowest density. We use the Born model at this lowest density and for the *tert*-butyl ion; ion stability may be underestimated due to neglect of local density augmentation in this case.

Figure 1 shows the adiabatic ground-state free energy surfaces as a function of reaction coordinate for the four densities considered. In ambient water, the *t*-BuCl molecule ($r_A = 1.8$ Å) exists as a partially ionic (~20%) state while the separated *t*-Bu and Cl entities exist as a 100% ionic state (Figure 2). At intermediate distances, the ionic character, f_{ion}, varies between these limits in a manner determined both by the intrinsic electronic properties of the solute and by solvent stabilization (see eq 1). The barrier separating bonded and dissociated species is associated with the covalent/ionic curve crossing and the transition from predominantly covalent to ionic character, as indicated in Figure 1. For ambient water, there is an energy barrier of 23 kcal mol^{-1}, similar to that calculated by Hartsough et al.[22] and in good agreement with the 19.5 ± 0.5 kcal mol^{-1} estimated by Abraham.[12] The key features of this free energy surface—the positions of the global minimum (1.8 Å), transition state (2.3 Å), local minimum for the contact ion pair (3.0 Å) and depth of this minimum (8.5 kcal mol^{-1})—are in good agreement with results in the literature.[12,14,22]

The surfaces for supercritical conditions (Figure 1) show desolvation of the dipolar molecular solute ($r_A \sim 1.8$ Å) and products ($r \rightarrow \infty$) with decreasing solvent density. The polarity of the reactant and products does not vary significantly with solvent density (Figure 2). Due to the greater polarity of the ion pair, the overall free energy of separation ($W(r_A{=}\infty) - W(r_A{=}1.8$ Å)) increases with decreasing density, but not as much as expected based on bulk dielectric constant, since local density augmentation enhances ion solvation.[9] Notably, even at the lowest density considered here (~0.04 g cm^{-3}), the ion pair product is more stable than radicals by 2 kcal mol^{-1}, although this is only slightly larger than $k_BT = 1.4$ kcal mol^{-1} (673 K).

The free energy surfaces also show that the local minimum for the contact ion pair diminishes in depth and moves to smaller separations with decreasing solvent density. The ionic state becomes less stable with decreasing solvent density, moving the position of the covalent−ionic curve crossing to greater separation. This in turn shifts the position of the transition state and increases the barrier height until the local minimum for the contact ion pair disappears (Figure 1).

Relative destabilization of ionic products with decreasing solvent density leads to an increase of the dissociation barrier, from 23 (ambient) to 35 kcal mol^{-1} (0.29 g cm^{-3}, 673 K), which continues to grow with decreasing solvent density. For the two lowest density cases studied, the contact ion pair is no longer a locally stable intermediate, although an inflection occurs at a separation corresponding to the transition state at higher densities. The mechanistic view relevant to ambient and higher density supercritical water is no longer valid at lower densities where there is no intermediate free energy barrier.

It is important to note that although the local minimum for the contact ion pair is removed at the lower densities, the system remains ionic in nature. This can be seen in Figure 2. The reactant molecule is predominantly covalent at all solvent densities. As the separation distance is increased, the ionic character increases rapidly over a range of about 0.5 Å. This increase becomes less rapid with decreasing solvent density. By 3 Å, the *tert*-butyl and chloride units are almost completely ionic for all solvent densities considered here. Nevertheless, in the gas phase, the transition to an ionic state would not occur.

As noted earlier, local density augmentation is expected to stabilize the ionic products more effectively than would be expected from the bulk dielectric constant. By extrapolation of the results in Figure 1, a crossover from ionic to radical products would occur at ~0.03 g cm^{-3} ($\epsilon = 1.34$ for SPC/E water). However, using the Born model this crossover would occur at ~0.08 g cm^{-3} ($\epsilon = 1.97$). Local density enhancement around the solute species is not accounted for in the simple Born model approach. Based on the free energy gap between the asymptotic diabatic states, covalent products are significant (~20%) at the density 0.0435 g cm^{-3}, but at 0.087 g cm^{-3} covalent products are insignificant (~10^{-4}%). Thus, not only does the change in dielectric constant have direct mechanistic impact, results suggest that the highly compressible nature of supercritical water will lead to significant shifts in the thermodynamic state where such mechanistic change occurs. These shifts may be better captured by correlating with similar chemical phenomena,[6] rather than with bulk dielectric constant.[8]

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