Compressible Continuum Solvation Model for Molecular Solutes

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We have developed the first compressible continuum solvent model for calculating solvation energetics of molecular solutes. This model is shown to successfully describe the solvent effects on a chemical reaction in supercritical water (SCW), where electrostriction is known to be an important factor. In addition, it is found that compression can induce unexpected trends in the pressure dependence of the reaction path energetics.

SCW is of technological interest because novel reaction mechanisms can be achieved in this medium. Even more importantly, the thermodynamic conditions can be used to control which reaction mechanisms will be dominant in SCW.[1,2] This thermodynamic control of reactivity in SCW results from the sensitivity of the solvent's density, and thus its solvating properties, to variations in temperature (T) and pressure (P) in the compressible regime "near" the critical point. To be able to predict reactivity in SCW under varying thermodynamic conditions thus requires a detailed understanding of the solvent effects in this regime.

The primary manner in which solvents affect solute reaction rates is by altering the free energy of activation profile along the solute's reaction path, thus altering the activation barrier, $\Delta G^{\ddagger}$, which comes into the rate constant expression exponentially, *i.e.*, $k \propto \exp(-\Delta G^{\ddagger}/RT)$, where R is the ideal gas constant. In polar solvents such as water, dielectric continuum models have been shown to provide an efficient and reasonably reliable method for evaluating solvation free energies[3] and, when combined with quantum chemistry calculations of the solute energetics, solution phase free energies of activation. Continuum models are desirable because they require much less computational effort than the alternative methods of molecular dynamics or Monte Carlo simulation. In fact, continuum models are the only option for calculations near a solvent's critical point where the long time scales and long length scales associated with collective solvent motions can make converging simulations prohibitively expensive.[4,5] However, it is in just this region that all existing continuum solvation models for molecules fail because they assume an incompressible solvent, while solvents in this regime are characterized by a high compressibility.

The importance of solvent compressibility on solute reaction rates in supercritical fluids has been observed both experimentally and theoretically. In particular, the low free energy cost of solvent compression which accompanies the large isothermal compressibility is responsible (at least in part) for the large solvent "clusters" which are observed around solutes having attractive solvent–solute interactions in supercritical fluids.[6-8] Experimentally, the influence of this clustering on solvation free energies and reaction rates has been inferred from studies of spectroscopic shifts.[6,9] The influence on reactivity has also been elucidated from electrochemical experiments on the reduction of I_2 to I^-.[10] Molecular dynamics simulation of the charge transfer reaction of Cl^- with CH_3Cl in SCW shows a significant solvent density enhancement around the reacting solute.[11] The observed density enhancement is primarily an electrostriction effect, since it results to a large degree from the solvent–solute electrostatic interactions. Note that since, for this reaction, the solute charge distribution varies along the reaction coordinate—from localized on the Cl^- to delocalized over the $[Cl-CH_3-Cl]^-$ complex and back to localized on the leaving Cl^-—the degree of electrostriction also varies along the reaction path. Such electrostriction effects alter the solute's free energies of solvation along the reaction path, because the resultant higher than bulk density solvent in the vicinity of the solute has a higher dielectric constant (ϵ) than does the bulk, and thus it solvates the solute charge distribution more extensively. Incompressible continuum solvation models neglect such electrostriction effects by their very nature. The resultant failure of such incompressible models to correctly predict reaction path energetics in SCW has been demonstrated in two studies. Tucker and Gibbons found,[12] for the hydrolysis of anisole in SCW, that the incompressible continuum model predicts an activation barrier change between the states (T = 653 K, P = 23.2 MPa, ϵ = 3.8 (state 1) and T = 653 K, P = 27.3 MPa, ϵ = 10.2) (state 2) which is more than an order of magnitude larger than the experimental value.[13] In order to bring the computed activation barrier change into agreement with experiment, these authors had to assume that solvent–solute clustering causes the solute to feel an effective dielectric constant of nearly twice the bulk value. Similar results and required "corrections" were obtained by Bennett, Rossky, and Johnston for the $Cl^- + CH_3Cl$ reaction.[14] Both the *ad hoc* nature of such "effective dielectric constant" corrections and their inability to account for reaction path dependence of the solvent clustering makes such corrections unsatisfactory.

In order to accurately calculate solvation effects in supercritical fluids we have developed a compressible continuum solvation model for arbitrary charge distributions, *i.e*, molecular solutes, which can predict electrostriction effects. We note that this model may be of more general utility, as it has been postulated that electrostriction is more important under ambient conditions than previously believed.[15] The thermodynamics of electrostriction have been worked out by Frank[16] and applied to the solvation of a single point charge ion in a spherical cavity by Wood *et al.*[17,18] Extension of these ideas to the more complicated case of arbitrary charge distributions requires numerical solution. Specifically, the position dependent electrostatic potential, ϕ, depends nonlocally on the position dependent dielectric constant $\epsilon(\mathbf{r})$, which itself depends on the field dependent density $\rho[E(\mathbf{r})]$. This problem is identical to the problem of a solute with an arbitrary cavity shape in an incompressible fluid, except that the position dependent dielectric constant is no longer a constant, but varies with the field. The problem may therefore be solved with the grid-based finite

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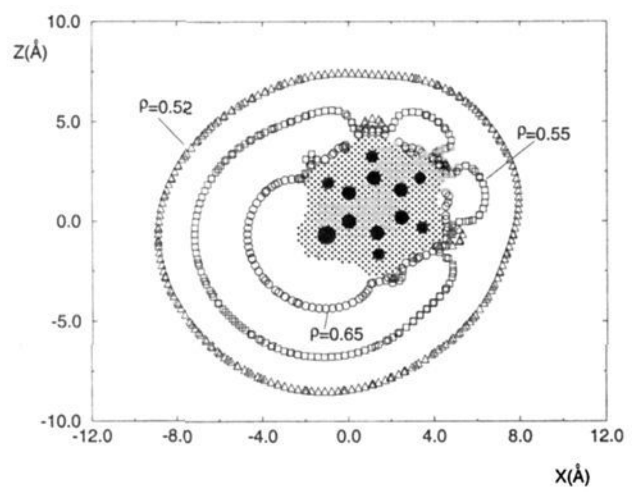

Figure 1. Density contours in the molecular plane of the phenoxy ion at state point 2.

difference algorithm proposed by Honig and co-workers for the incompressible fluid case.[19] In our model, we apply this algorithm with the following modifications for the compressible case.[20] At every iteration, the new method updates the local dielectric constant ϵ_i associated with each grid point i, in addition to updating the local electrostatic potential, ϕ_i. The updated value of the local dielectric constant is calculated from the current value of the local field E associated with the grid point as follows. The empirically determined density dependence of the dielectric constant for water, $\epsilon = \epsilon(\rho,T)$,[21] is combined with the nonlinear field dependence of the density, given in ref 16,

$$\rho(E) - \rho_{\mathrm{bulk}} = \int_0^E \frac{1}{2}\epsilon_0\rho^2\kappa_T\left(\frac{\partial\epsilon}{\partial\rho}\right)_T \mathrm{d}(E')^2 \qquad (1)$$

to yield $\epsilon(E)$. The state dependence of the calculated compression arises primarily from the state dependence of the isothermal compressibility, $\kappa_T = \rho^{-1}(\partial\rho/\partial P)_T$. The thermodynamic derivatives in eq 1 are evaluated locally from the experimentally determined equation of state for water.[21,22]

The solvation free energy in the compressible continuum model is the total electrostatic work of charging the solute in the presence of the compressible fluid, G_e, minus that of charging the solute in a vacuum. The total work G_e is found[20] in accordance with eq 6 of ref 17, generalized to allow for nonspherical E fields.

As a first test of the method,[23] we compared the compression-induced density profile of SCW around a Cl^- against that calculated from molecular dynamics simulation.[24] The continuum density profile compared very well with the simulation results over the 10 Å range for which these results are available, at both thermodynamic states considered.

The compressible continuum model has been applied to the anisole hydrolysis reaction in SCW, $PhOCH_3 + OH_2 \rightarrow PhO^- + CH_3OH_2^+$. The solute charge distribution and other relevant parameters for this reaction are taken to be the same as in the incompressible continuum study ("Delphi1" parameters),[12] although here we also use focusing.[19] The position dependent density resulting from the calculated electrostriction is shown for the phenoxy anion in Figure 1 for state point 2. The figure shows solvent density contours in the molecular plane. The electrostriction is much more pronounced around the negatively charged oxygen atom ($q = -0.8$) than around the charge-delocalized phenyl ring. At a distance of 4 Å from the oxygen atom, the density is 0.65 g/cm^3, which is 30% greater than the bulk value of $\rho = 0.50$ g/cm^3. At larger distances, where the point charge approximation to the E field becomes valid, the compression contours approach spherical. The observed compression effects are significantly more extensive for the lower density, more highly compressible state point 1. For this state the density at a distance of 4.5 Å from the oxygen is 0.6 g/cm^3, which is 2.4 times greater than the bulk value of 0.25 g/cm^3.

Using this compressible continuum model, we evaluated the electrostatic free energies of solvation along the anisole hydrolysis reaction path for the two state points (1 and 2). The electrostriction was found to noticeably affect the solvation energies. For example, the phenoxy anion at state point 2 (shown in Figure 1) is predicted to be 6.1 kcal/mol more stable when electrostriction is included than when it is not. The effect is significantly greater at the lower density state point 1, where compressibility stabilizes the molecular ion by 14.4 kcal/mol. In addition, the compression-induced stabilization ($\Delta G_c(r_c)$) is found to be strongly reaction path position (r_c) dependent with the product ions experiencing significantly more compression-induced stabilization than the neutral reactants. This compression-induced asymmetry in the solvation free energy along the reaction path decreases when the solvent compressibility, and thus all compression-induced effects, are decreased. Thus, for the less compressible, higher pressure state 2, the compression-induced asymmetry is less than for state 1. This trend opposes the pressure dependence of the asymmetry in the solvation free energy ($\Delta G_s^I(r_c)$) expected for incompressible fluids. That is, in the absence of compression, the asymmetry increases with increasing pressure, a result of the increase in the bulk dielectric constant with pressure. In the case of the anisole hydrolysis reaction, these opposing pressure effects on $\Delta G_s^I(r_c)$ and $\Delta G_c(r_c)$ roughly cancel in the total compressible solvation energy, $\Delta G_s^C(r_c) = \Delta G_s^I(r_c) + \Delta G_c(r_c)$. Thus, compression causes the reaction path asymmetry of the solvation free energy to remain roughly constant with pressure, instead of increasing, as would be expected if compression were not considered.

The pressure dependence of the asymmetry in the solvation free energies is extremely important, because it is this asymmetry which controls, at each pressure, the height and position of the free energy of activation barrier to reaction. In order to study this pressure dependence, we evaluated the free energy of activation curve $\Delta G_a(r_c)$ at each state, by combining the solvation free energies with the gas phase reaction path energetics.[12] If compression is neglected, the free energy asymmetry will cause the barrier to drop in height and move toward reactants as pressure is increased. Indeed, when compression is neglected for the anisole reaction, we find that the barrier is at products for state 1, while the barrier is at an intermediate complex (IC) for state 2. When compression is accounted for, there is very little pressure dependence to the asymmetry, and the barrier position is found to be at IC for both states. The altered pressure dependence of the solvation free energy asymmetry also affects the pressure dependence of the barrier height. The resultant change in barrier height from state point 1 to 2 is $\Delta(\Delta G^\ddagger) = -4.1$ kcal/mol when electrostriction is included. This result is in significantly better agreement with the experimental result[12,13] of $\Delta(\Delta G^\ddagger) = -1.5$ kcal/mol than is the result from the standard incompressible model,[12,20] $\Delta(\Delta G^\ddagger) = -16.1$ kcal/mol.

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