the top intensity shifting gradually to higher wavelengths. Finally, a new band developes at about 660 nm. In the light of literature data,[2a,8] this can be assigned to the MnO_4^{3-} ion. To our knowledge this is the first clear-cut case where the transient appearance of a manganate(V) intermediate has been demonstrated in a permanganate oxidation.

The changes in relative intensity of the two bands in Figure 2 are due to the increasing concentration of the soluble manganese(IV) species, which does not absorb above ca. 540 nm but has a gradually increasing absorptivity below that wavelength.[4]

The slower phase can be rationalized in terms of the following reactions:

$$2MnO_4^{2-} \rightarrow MnO_4^- + MnO_4^{3-} \qquad (6)$$

$$2MnO_4^{3-} \rightarrow MnO_4^{2-} + Mn^{IV}_{sol} \qquad (7)$$

The MnO_4^- formed in (6) is rapidly reduced by sulfite to MnO_4^{2-}, eq 3–5; therefore, permanganate ion is not detectable during the slow phase. MnO_4^{2-} is consumed via disproportionation only, reaction 6.

Work is in progress on the kinetics of the title reaction.

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Registry No. SO_3^{2-}, 14265-45-3; MnO_4^-, 14333-13-2; MnO_4^{3-}, 14333-15-4; MnO_4^{2-}, 14333-14-3.

Evaluation of Reaction Free Energy Surfaces in Aqueous Solution: An Integral Equation Approach

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The effects of a solvent medium on chemical reactions can be very large. When a reaction occurs in a solution, one must consider not only the potential energy for the reaction species but also the free energy due to solvent rearrangement. As a result changes in the reaction rate of up to 20 orders of magnitude are well-known.[1] In this communication, we present a test of a computationally feasible method to calculate such solvent effects for polar systems. It is based on the use of our extended RISM integral equation approach[2] to calculate solvation structure and a charging approach[3] to obtain free energy differences. The integral equation approach used is based on the RISM integral equation generalized for continuous potentials, developed by Chandler and co-workers.[4,5] This element is in common with the further development by Kojima and Arakawa[6] and with the numerical studies by Johnson and Hazoume.[7] Our development for polar systems[2] is distinguished from these earlier studies in that the screening of the Coulomic interactions among charged sites in polar molecules is handled analytically at the outset in close analogy to the Debye–Huckel summation in ionic solutions. This provides substantial simplification from both the analytical and computational viewpoints. The test case is the free energy surface for the S_N2 exchange reaction of chloride with methyl chloride ($Cl^- + CH_3Cl$). Using the interaction site potentials calculated by Chandrasekhar et al.,[8] we are able to compare our results with their elegant Monte Carlo results along a reaction coordinate for collinear approach. The reaction coordinate here is defined as[8] $r_C = r_{CCl'} - r_{CCl}$ where Cl′ is the leaving group.

The reactant species for this calculation are conveniently viewed as a *single* polyatomic molecule with bond distances and interaction potentials with the solvent that are a function of the reaction coordinate. The S_N2 reaction free energy surface in solution is then equivalent to the calculation of the intramolecular potential of mean force or cavity distribution function[9,10] for the polyatomic at infinite dilution in a molecular solvent.

In order to calculate the (multipoint) potential of mean force or equivalent free energy, the pairwise additive site–site interaction potential of the solute–solvent system is expressed as a function of a coupling parameter λ.[3] That is, the total potential energy U is given by

$$U(\lambda) = \lambda\sum_{\mu\nu} u_{\mu\nu} + \sum_{\nu\nu'} \mathrm{u}_{\nu\nu'} \qquad (1)$$

where index μ refers to the atomic interaction sites on the "solute" molecule and ν to sites on the solvent molecules. The sums include all distinct intermolecular site–site pairs. The free energy of the system can be expressed as an integral over the coupling parameter as

$$A = A_0 + \int_0^1 \mathrm{d}\lambda \, \mathrm{d}A(\lambda)/\mathrm{d}\lambda \qquad (2)$$

where A_0 is a reference free energy (noninteracting solute).

With use of the relation of the free energy to the partition function, $-\beta A = \ln Q$, to take the free energy derivative (β is the inverse of the product of Boltzmann's constant and the temperature), the free energy can be expressed as

$$A - A_0 = \int_0^1 \mathrm{d}\lambda \int \mathrm{d}r \sum_{\mu\nu} u_{\mu\nu} \frac{e^{-\beta U(\lambda)}}{Q} \qquad (3)$$

where $A - A_0$ is the free energy to add the solute molecule, and the spatial integration over r extends over all solvent coordinates. Equation 3 can be expressed exactly in terms of the solute–solvent radial site–site distribution functions[10] $g_{\mu\nu}(r)$ as

$$A - A_0 = 4\pi\rho \int_0^1 \mathrm{d}\lambda \sum_{\mu\nu} \int_0^\infty \mathrm{d}r \, r^2 u_{\mu\nu}(r) g_{\mu\nu}^{\lambda}(r) \qquad (4)$$

where ρ is the solvent density and $g^\lambda(r)$ refers to the distribution functions for the system with the interaction potential $U(\lambda)$. The relevant potential of mean force is then given by the difference

$$W(r_C) = A\{r_C\} - A\{r_C = \infty\} + U_0(r_C) \qquad (5)$$

where $A\{r_C\}$ is the charging free energy of the solute molecule with the intramolecular bond distances and solute–solvent interaction potentials defined by the reaction coordinate r_C[8] and $U_0(r_C)$ is the gas-phase intramolecular potential.

The solute–solvent correlation functions were calculated by using the extended RISM equation for infinitely dilute solutions.[2] The solvent was described here using the TIPS water potential;[11] the water pair distribution functions obtained by this procedure

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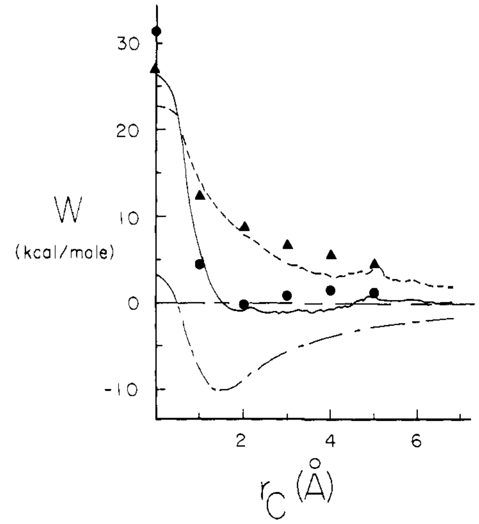

Figure 1. Comparison of extended RISM and simulation[4] for reaction free energy surface (eq 5) at 25 °C. Gas-phase potential (- - -); solvent contribution, MC (- - -), RISM (▲); total free energy, simulation (—), RISM (●).

are qualitatively reliable.[12] The Lennard-Jones and charge parameters as a function of the reaction coordinate from Chandrasekhar et al. were used for the chlorine sites. The CH_3 moiety was simplified here as a single "atomic" site with Lennard-Jones parameters from TIPS methanol[13] and total charge equal to that in the all atom CH_3 representation.[8] As in previous calculations, a necessary repulsive term was added to the H-O and H-Cl potentials to avoid catastrophic overlap of the corresponding site charges in the calculations. An equally spaced λ grid of $\Delta\lambda = 0.1$ was found adequate for the calculation of the relative quantity in eq 5.

Our values calculated at representative points, along with the gas-phase potential and Monte Carlo results, are shown in Figure 1, at 25 °C. It is clear that the new results follow the Monte Carlo simulation rather well and manifest a dramatic solvent effect on the reaction surface. The RISM theory yields a barrier height of 31 kcal/mol, slightly larger than the Monte Carlo and apparent experimental results of 26.3 and 26.6 kcal/mol, respectively. Also in accord with the Monte Carlo results, the ion-dipole potential minimum is substantially flattened by the solvent, with the potential becoming slightly repulsive further along the reaction coordinate.

The present comparative calculation has several sources for discrepancy. The approximate RISM theory successfully describes the short-range liquid structure, but the theory improperly describes the long-range order of polar liquids.[2,14] However, the largest part of this long-range error should be constant throughout the reaction, since the reaction system has a fixed net charge, and this part will cancel in the calculation of the potential of mean force. Also, we treat the methyl species as a single site while the Monte Carlo methyl potential included the hydrogens explicitly. Since most of the free energy changes are due to the transfer of charge from one chlorine to the other, this latter effect should be small. Further, in the Monte Carlo calculation, the TIP4P water potential was used,[15] while we use the simpler three-site TIPS form.

The charging method presented here presently requires only a small fraction of the computational time of the Monte Carlo simulation.[8] Further, the charging free energies do not invoke any pair additivity assumptions regarding the multipoint solute potential of mean force[9] and have been shown to allow reasonably accurate calculation of free energy differences. These results encourage further application of the method to various chemical reactions as well as to conformational equilibria.

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Registry No. Cl^-, 16887-00-6; CH_3Cl, 74-87-3.

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Claisen Rearrangement of 6-Alkenyl-2-methylenetetrahydropyrans. A New Approach to Annulated 4-Cyclooctenones and a Stereospecific Synthesis of Precapnelladiene

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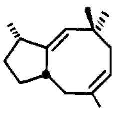
In recent years, several bicyclic marine natural products have been discovered that incorporate uncommon fused eight-membered rings in their structure. Precapnelladiene (**1**),[1] dactylol (**2**),[2] the closely related poitediol,[3] and neolemanyl acetate (**3**),[4] are exemplary of this family of sesquiterpenes. Hydrocarbon **1**, the presumed precursor to the tricyclic capnellenes and capnellenols, likely serves as a key biosynthetic intermediate in the soft coral *Capnella imbricata*.



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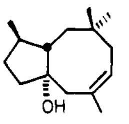

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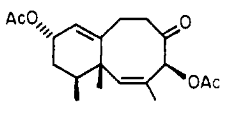

3

As part of a larger program directed toward the synthesis of mesocyclic[5] systems of this type,[6] we have investigated the feasibility of applying aliphatic Claisen rearrangement strategy[7] to the construction of these unusual molecular frameworks. The earlier studies by Büchi (**4** → **5**),[8] Danishefsky (**6** → **7**),[9] and Rhoads (**8** → **9**)[10] hold some relevance to the present report.[11]

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