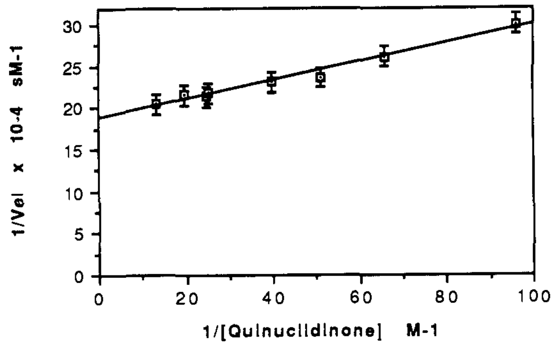

Figure 1. Lineweaver-Burk plot of the enolization of quinuclidinone **3** catalyzed by 0.0025 M **1b** at 20 °C.

Table I. Deuteration of Quinuclidinone **3** in $CDCl_3/D_2O$ at 20 °C[a]

catalyst	$k_{obsd} \times 10^5$, s^{-1}	approx half-life
none	0.3	64 h
6	0.4	49 h
7	0.5	36 h
8	2.4	8 h
5	2.0	10 h
1b	17.0	66 min

[a] In all cases, initial quinuclidinone concentration is 0.025 M and catalyst concentration is 0.0025 M.

It underscores the importance of effective complexation in bringing recognition and catalytic functionality together to create a microenvironment for catalysis.

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Electrostatic Contributions to Solvation Energies: Comparison of Free Energy Perturbation and Continuum Calculations

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Recently, considerable progress has been made in the application of free energy perturbation techniques to the calculation of solvation energies and solvation energy differences.[1-3] These methods can be used to artificially create a solute molecule in the solvent by varying one or more perturbation parameters such as atomic radius and charge. Cavity and van der Waals terms can be separated from electrostatic terms by first "growing in" the cavity and then "growing in" the charge.[3] The electrostatic term can then be compared directly to the predictions of continuum calculations in which the solute is treated in atomic detail but the solute is treated as a dielectric continuum.[4] In this communication we compare electrostatic contributions to the solvation free energies of polar solutes in water using both methods.[5] Our results suggest that the continuum and microscopic treatments of water provide very similar descriptions of solute-solvent interaction free energies.

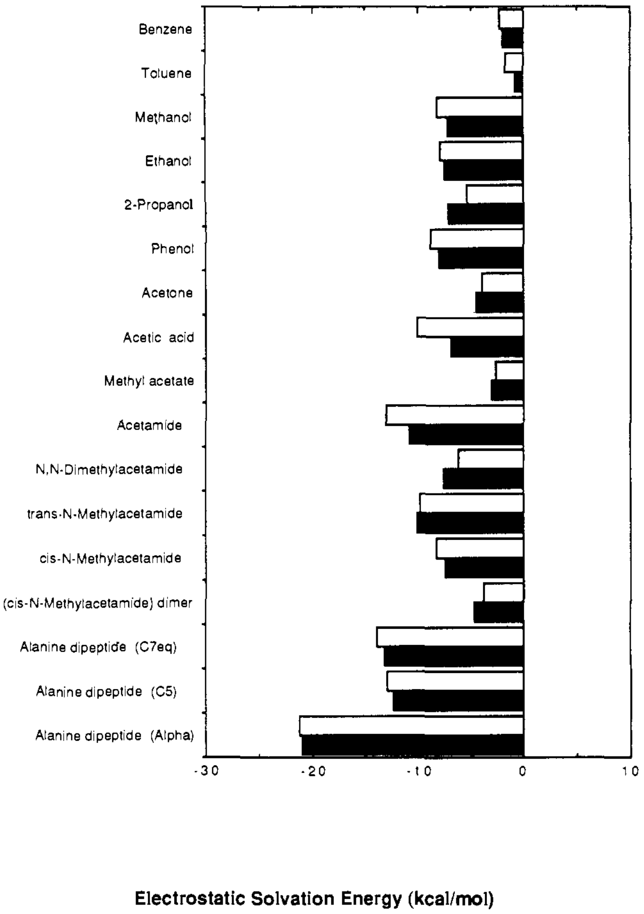

Figure 1. Comparison of electrostatic solvation free energies obtained from free energy perturbation (unfilled bars) and the continuum electrostatic method with no solute polarizability ($\epsilon = 1$, solid bars).

The continuum calculations are based on the finite difference Poisson-Boltzmann (FDPB) method and were carried out with the Delphi program.[6] The solute/solvent system is mapped onto a three-dimensional lattice by assigning a value of the charge, dielectric constant, and ionic strength to each lattice point. The solute molecule is treated as a region of space defined by its solvent-accessible surface. Charges are placed at atomic nuclei as in any conventional force field. The volume enclosed by the solute is assigned a uniform dielectric constant (ϵ). The molecular dielectric constant is normally taken as 2 to account for electronic polarizability.[7] However, in order to be consistent with the free energy calculation which ignores electronic polarizability in the solute, calculationss were carried out with the molecular dielectric constant set to 1. The solvent is assigned a dielectric constant of 80. The atomic radii used to define the solute cavity are set equal to van der Waals radii given by $(2)^{-5/6}\ \sigma$ where σ is the Lennard Jones diameter defined in the OPLS force field.[8] Atomic charges are also taken from the OPLS force field.

The free energy perturbation (FEP) calculations were carried out by using the BOSS Version 2.0 program[9] kindly provided by Professor William Jorgenson. The solute molecules are placed in a 20-Å box containing ~512 TIP4P[10] water molecules. The perturbation consisted of electrically charging and discharging

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Table I. Comparison of Electrostatic Solvation Free Energies Obtained from Free Energy Perturbation (FEP) and Continuum Electrostatic (FDPB) Methods

solute[a]	$-\Delta G_{sol}$, kcal/mol	
	FEP	FDPB ($\epsilon = 1$)
methanol	7.1 ± 0.3	8.09
ethanol	7.4 ± 0.2	7.84
2-propanol	7.1 ± 0.3	5.37
acetone	4.5 ± 0.2	3.89
methyl acetate	3.1 ± 0.2	2.61
acetic acid	6.8 ± 0.3	10.06
N,*N*-dimethylacetamide	7.5 ± 0.5	6.19
acetamide	10.8 ± 0.5	12.95
(*Z*)-*N*-methylacetamide	10.1 ± 0.5	9.77
(*E*)-*N*-methylacetamide	7.4 ± 0.6	6.19
(*E*)-*N*-methylacetamide dimer	4.6 ± 0.2	3.77
alanine dipeptide (C7eq)	13.1 ± 0.4	13.85
alanine dipeptide (C5)	12.3 ± 0.5	12.87
alanine dipeptide (αR)	20.9 ± 0.7	21.09
benzene	1.9 ± 0.3	2.19
toluene	0.7 ± 0.2	1.69
phenol	8.0 ± 0.7	8.79
ammonium ion	103.9 ± 0.7[b]	95.19
acetate ion	91.3 ± 1.4[b]	77.59
ammonium acetate	47.7 ± 0.9	40.5

[a] Geometries obtained by energy minimization using OPLS/AMBER in vacuo. [b] Value includes a −19.3 kcal/mol correction for the 8.5-Å solvent cutoff employed (Jorgensen, W. L.; Blake, J. F.; Buckner, J. K. *Chem. Phys.* **1989**, *129*, 193.

each solute over eight equal stages. TIP4P water is reported to have a dielectric constant of ~50[11] while we used the experimental value of about 80 in the FDPB calculations. Using a dielectric constant of 50 results in only minor changes in the FDPB energies. The FEP simulations followed a standard protocol in which 600 000 configurations were used for equilibration and then 10 blocks of 100 000 configurations were averaged to give the free energy change for each stage. The energies reported are the averages of the charging and discharging free energies. The error limits correspond to the root mean square of the standard deviations of the energy fluctuations of each stage.

The results are summarized in Table I and Figure 1. It is evident that, overall, there is excellent agreement between the FEP calculations and the FDPB calculations. Whether this should be viewed as confirming the continuum treatment or the TIP4P model is to some extent a matter of one's perspective. In any case, the success of the Born model of ion solvation,[12] which has been explained in part by a recent FEP study,[13] is extended here to the more general case of polyatomic solutes with complex charge distributions. It should be pointed out that the FDPB calculations produce solvation free energies for the ammonium and acetate ions which are closer to the experimental values than those obtained from the free energy simulations (only the sum of the experimental values can be reliably determined experimentally; for ammonium and acetate the value is ~15 kcal/mol[14]). The tendency of current water models to overestimate the solvation free energies of ions is well-known and appears due, at least in part, to the neglect of electronic polarization.[13,15]

The agreement between the two sets of calculations which ignore electronic polarizability suggests that there are now available two very different methods which yield a consistent picture of the electrostatic component of solute–solvent interactions. The FDPB calculations are extremely fast (about 10 s on a Convex C2 computer) but at the sacrifice of information as to the organization of solvent molecules around the solute. The FEP calculations require 3–4 orders of magnitude more computer time but can provide a detailed description of solvent structure when that is of interest. Finally, it should be pointed out that no attempt has been made to optimize parameters for the FDPB calculations. The OPLS parameters were used so as to facilitate comparison with the FEP calculations and might ultimately have to be modified in future attempts to reproduce experimental solvation energies.[16]

Supplementary Material Available: Nonbonded parameters and partial charge sets for the molecules listed in Table I (10 pages). Ordering information is given on any current masthead page.

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Group 4 Metal Dicarbollide Chemistry. Synthesis, Structure, and Reactivity of Electrophilic Alkyl Complexes $(Cp^*)(C_2B_9H_{11})M(R)$ (M = Hf, Zr)

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Fourteen-electron, d^0 bent-metallocene alkyl complexes of general type $(C_5R_5)_2M(R)^{n+}$ exhibit a rich insertion, olefin polymerization, and C–H activation chemistry which is highly sensitive to the structural and electronic properties of the $(C_5R_5)_2M$ fragment.[1-4] Known complexes of this type include *neutral* group 3[1] and lanthanide[2] complexes $(C_5R_5)_2M(R)$ and *cationic* group 4[3] and actinide[4] species $(C_5R_5)_2M(R)^+$. Here we describe a new class of *neutral, d^0, group 4 metal* bent-metallocene complexes of general form $(Cp^*)(C_2B_9H_{11})M(R)$ (M = Zr, Hf). The formal replacement of a uninegative $C_5R_5^-$ ligand of $(C_5R_5)_2M(R)^+$ by the isolobal, dinegative dicarbollide ligand $(C_2B_9H_{11}^{2-})$[5] reduces the overall charge by 1 unit but leaves the gross structural and metal frontier orbital properties unchanged, thus allowing preparation of electrophilic metal alkyl complexes with new metal/charge combinations.

Hawthorne has developed the coordination chemistry of $C_2B_9H_{11}^{2-}$, which is electronically and sterically comparable to Cp^{*-}.[5] The parent acid $C_2B_9H_{13}$ contains two acidic hydrogens which can cleave M–C bonds of electrophilic metals.[3b,5d] The reaction of equimolar amounts of $C_2B_9H_{13}$[6] and $Cp^*M(Me)_3$ (M

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