

Polarization Effects in Aqueous and Nonaqueous Solutions

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Abstract: Polarization effects in aqueous and nonaqueous solutions were analyzed for nine neutral and three charged organic solutes by the SM8 universal implicit solvation model and class IV partial atomic charges based on Charge Model 4M (CM4M) with the M06-2X density functional. The CM4M partial atomic charges in neutral and ionic solutes and in the corresponding clustered solutes (supersolutes), which included one solute molecule and one or two solvent molecules, were modeled in three solvents (benzene, methylene chloride, and water) and compared to those in the gas phase. The use of the supersolute approach (microsolvation) allows one to account for charge transfer from the solute to the solvent, and we find charge transfers as large as 0.06 atomic units for neutral solutes (pyridine in water) and 0.32 atomic units for ions (methoxide anion in water). Relaxation of the electronic structure of the solute in the presence of solvent increases the polarization free energy of the neutral solutes studied here, on average, by 16% in benzene, 30% in methylene chloride, and 43% in water. The increase for the ions in water averaged 43%.

1. Introduction

The polarization of molecules as they pass from the gas phase into a condensed phase gives rise to a number of chemically interesting phenomena, e.g., changes in solute electrical multipole moments,^{1–4} environmental effects on hydrogen bonds and other complexation, binding, and dissociation processes,^{5–11} solvent-induced shifts in isomeric equilibria,^{12–14} solvatochromic shifts,^{15–22} solvent effects on circular dichroism,^{23–30} and solvent effects on chemical reactivity.^{14,31–42} The accurate prediction of these phenomena poses an interesting challenge to theory. One approach to this problem is to treat both the solute and a significant number of solvent molecules explicitly using suitably high levels of electronic structure theory. However, this approach is currently not practical owing to the large size of the system that is required to converge the solvent effect and the need to sample over many degrees of solvent freedom in a thermodynamically meaningful fashion. Another approach is to replace the

explicit surrounding medium by a homogeneous continuum that is characterized by one or more bulk properties of the medium; for example, for the purpose of computing electrostatic phenomena, the continuum might be assigned the dielectric constant of the solvent.^{12–14,42–44}

A large number of methods have been developed specifically for modeling liquid-phase polarization effects.^{12–14,42–91} Many of these methods involve some sort of classical mechanical model and parametrization. One expects that a more fully quantum mechanical model based on density functional theory can be more broadly accurate,^{42,43} and in the present work, we study polarization effects by density functional theory combined with the charge model CM4M, which is presented in a previous paper⁹² in this issue of the journal. Additionally CM4M was developed to reproduce the gas-phase dipole moments of an extensive database of compounds using small to medium-sized basis sets. This allows the CM4M model to improve the accuracy of low-level quantum mechanical calculations without sacrificing the flexibility of quantum mechanical calculations and

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without introducing a significantly greater expense in computational cost.

By invoking the continuum approximation, the electronic structure problem is reduced to the size of the solute of interest. However, accurate computation of the solute polarization using continuum solvation models still poses several challenges. One important issue is that many continuum solvation models assume that the interactions of the solute and the surrounding solvent do not depend on the molecular structure of the solvent and that the dielectric response of the medium is uniform and linear at all positions outside the space that defines the solute. This assumption is particularly poor when strong, specific interactions between a solute and one or more first-shell solvent molecules are present, for example strong hydrogen bonding or π - π stacking interactions. Continuum solvation models also are problematic in cases where there is significant charge transfer between the solute and the solvent; in such an instance, the solute itself is not characterized by an integral charge. This problem is particularly acute for solutes that are themselves charged or that contain a number of charged residues, as do proteins, for instance; models incorporating charge transfer have been only rarely studied.^{93,94} Another concern is the applicability of continuum models to small charged species, e.g., metal ions, or to charged species with highly localized charges, e.g., oxyanions or transition-metal cations. For these cases, it is typically more appropriate to consider the first solvation shell of the ion as true ligands in a supermolecular complex,⁹⁵⁻⁹⁷ and this suggests that supermolecular approaches incorporating explicit solvent molecules at sites having strong, specific interactions might be a general approach for improving the performance of continuum models (including more than a small number of explicit solvent molecules, however, tends to reintroduce the problem of sampling over the range of accessible conformational space).^{42,98}

In addition to accounting for the effect of solvent molecularity and charge transfer on the polarization of the solute, there is the issue of how the solute charge distribution is represented. Modern quantum mechanical continuum models may work with the continuous charge distribution or with a truncated multipolar expansion of that distribution at one or many centers. For example, in the case of generalized Born continuum solvation models,^{12-14,42,99} a truncated monopole expansion at the nuclear centers, i.e., atomic partial charges, is used. With such methods it is critical that the charges are physically accurate—one measure of such accuracy, since atomic charges themselves are not uniquely defined, is the degree to which the charges reproduce molecular electric moments.

Representation of a solute's charge distribution as a collection of atom-centered point charges has a very long history from a qualitative, conceptual standpoint. With respect to quantitative details, models for assigning partial atomic charges may be categorized into four broad classes. Class I models involve partial atomic charges that may be derived unambiguously from experimental data, e.g., charges assigned to reproduce the dipole moment of a diatomic molecule. Class II charge models are associated with

necessarily arbitrary population analyses of a quantum mechanical wave function. Popular examples of such models include schemes based on Mulliken¹⁰⁰⁻¹⁰² and Löwdin¹⁰³⁻¹⁰⁶ population analysis and natural population analysis.¹⁰⁷ Such charge models are sensitive to the choice of basis set, and the calculated charges are somewhat arbitrary except possibly in some cases for small, well balanced basis sets. Class III charge models assign partial atomic charges to fit a computed physical observable, e.g., electric multipole moments or the electrostatic potential at particular points around a molecule. (Such fitting problems are known to be ill conditioned, so that charges for buried atoms can be unreliable.^{108,109}) Like class II charges, class III charges may show variations as a function of the molecular conformation or even the quality of the level of theory employed, although they tend to be less sensitive to basis set effects, particularly as more complete basis sets are employed. Class IV charge models are similar to class III ones in the sense that they assign partial charges in order to reproduce a physical observable, but in this case the observable is taken from experiment, not from the incomplete level of computation used for the application at hand, and the fitting involves a parametrized mapping starting from systematic class II or class III charges with mapping parameters optimized to maximize the accuracy of the charge model over a diverse training set.

The CM1,^{110,111} CM2,^{112,113} CM3,¹¹⁴⁻¹¹⁶ and CM4⁹⁸ models are all class IV charge models, with CM4 being the most recent and robust generation of mappings. Here we apply our newest CM4 parametrization, CM4M,⁹² developed for the Minnesota 2006 (M06) suite of density functionals,¹¹⁷⁻¹¹⁹ to study the polarization and charge transfer in clustered and unclustered neutral and ionic solutes using the SM8 aqueous and organic continuum solvation models.¹²⁰

We consider polarization effects in nine neutral solutes (acetic acid, benzaldehyde, chloroform, ethanol, methanethiol, methanol, nicotinamide, propionic acid, and pyridine) solvated by the three solvents, which are benzene, methylene chloride, and water. We also include three ionic solutes (acetate anion, methoxide anion, and pyridinium cation) in the set of aqueous solutes. The choice of these solutes is dictated by our intent to represent major classes of chemical compounds with various functionalities in this analysis. The set of solvents is chosen to span a range of dielectric constants¹²¹ and other solvent descriptors such as Abraham's hydrogen bond acidity and basicity parameters¹²²⁻¹²⁵ and indices¹²¹ of refraction (see Table 1). Methylene chloride (dichloromethane) is a particularly interesting case for study because of its weak hydrogen bonding and coordinative properties.¹²⁶ To study the charge transfer between a solute and solvent molecules we replace 10 of the 12 solutes by solvent-solute clusters, also called supermolecules or supersolutes. The clusters include two solvent molecules in the case of water and only one solvent molecule in the case of benzene and methylene chloride (totally 24 clusters). This approach to microsolvation is reasonable with respect to the physical nature of intramolecular interactions between the selected solutes and solvents as well as practical with respect to computational time and choice of supersolute conformation. The gas-phase charge distribution in these solutes and

Table 1. Solvent Descriptors for the Three Solvents

descriptor	C ₆ H ₆	CH ₂ Cl ₂	H ₂ O
ϵ^a	2.27	8.93	78.36
α^b	0.00	0.10	0.82
β^c	0.14	0.05	0.38
n^d	1.5011	1.4242	1.3328
γ^e	40.62	39.15	104.71
ϕ^f	1.000	0.000	0.000
ψ^g	0.000	0.667	0.000

^a Static dielectric constant¹²¹ at 298 K. ^b Abraham's hydrogen bond acidity parameter^{122–125} (which Abraham denotes as $\Sigma\alpha_2$). ^c Abraham's hydrogen bond basicity parameter^{122–125} (which Abraham denotes as $\Sigma\beta_2$). ^d Index of refraction.¹²¹ ^e $\gamma = \gamma_m / \gamma^o$, where γ_m is the macroscopic surface tension¹²¹ at a liquid–air interface at 298 K expressed in cal mol^{−1} Å^{−2}, and γ^o is 1 cal mol^{−1} Å^{−2}. ^f Aromaticity: fraction of non-hydrogenic solvent atoms that are aromatic carbon atoms. ^g Electronegative halogenicity: fraction of non-hydrogenic solvent atoms that are halogens.

clusters (36 species total) was also calculated so that it may be compared to the charge distribution in solution. Thus we performed 36 gas-phase charge distribution calculations, 16 charge distribution calculations in benzene, 16 charge distribution calculations in methylene chloride, and 22 charge distribution calculations in aqueous solution.

2. Computational Methods

The geometries of selected solutes and the corresponding solvent–solute clusters are optimized with the M06-2X density functional^{117,119} and the 6-31+G(d,p) basis set.^{127,128} The M06-2X density functional was previously recommended for applications involving main-group thermochemistry and noncovalent interactions,^{117–119} and it is especially appropriate for treating solvation in benzene because of its good ability to handle noncovalent interactions of π systems. The M06-2X/6-31+G(d,p) conformational analysis was carried out including calculation of harmonic frequencies to find the global minimum conformations in the gas phase. (Only gas-phase geometries are used in this article.) The molecular structures of the 10 solutes (out of 12) studied in this paper are shown in Figure 1. Figures 2–4 show the molecular structures of the gas-phase solute–solvent clusters for benzene, methylene chloride, and water, respectively. The Cartesian coordinates for all of the clustered solutes are given in the Supporting Information. All these calculations were carried out using *Gaussian 03*.¹²⁹

The partial atomic charges of the solutes and supersolutes in the gas phase are calculated using Charge Model 4M (CM4M)⁹² with a locally modified version¹³⁰ of the *Gaussian 03* electronic structure package.¹²⁹ CM4M, like its antecedent, CM4, is a class IV charge model that empirically maps class II charges to reproduce experimentally observable properties. As with CM4, the CM4M algorithm involves a mapping from Löwdin charges^{103–106} when the basis set used to compute the electronic structure of the solute molecule does not include diffuse functions, and it uses redistributed Löwdin charges¹³¹ when the basis set is diffuse. Also, as with its CM4 predecessor, CM4M maps the charges using an empirical scheme based upon the Mayer bond orders^{132–134} between individual atoms in the solute. The primary difference between CM4 and CM4M is that while the former was designed to be generally applicable to any level of theory for a given basis set, CM4M is designed to be especially

accurate for a small number of theoretical methods, i.e., the M06 methods. This approach is motivated by the observation that our chosen level of theory, the M06 suite of density functionals, has been shown to be significantly more accurate than any other density functional for a broad range of applications¹¹⁷ allowing CM4M to be equally broadly applicable. A complete description of CM4M is provided in ref 92.

It is known that partial atomic charges obtained from population analysis are sensitive to basis set size, and, in particular, one can obtain unphysical charges when extended basis sets are used.¹³¹ This is apparently a consequence of the fact that a large basis set on a given atom can mathematically describe electron density on neighboring atoms. For example, with a large, diffuse basis set, one can obtain a reasonably accurate electronic wave function for methane even with all of the basis functions centered only on carbon,¹³⁵ and either Mulliken or Löwdin analysis based on such a wave function would assign a partial charge of −4 to carbon and +1 to each of the hydrogen atoms. Since the CM4M model yielding class IV partial atomic charges uses class II charges from Löwdin (and, for diffuse basis sets, redistributed Löwdin) population analysis, and, since the population analysis is most meaningful for small basis sets, we employ the 6-31G(d)^{127,128} basis set for calculation of partial atomic charges in all solutes and supersolutes and in both gas and liquid phases.

The liquid-phase partial atomic charges were calculated using the universal continuum solvation model SM8¹²⁰ with a locally modified version¹³⁰ of the *Gaussian 03* electronic structure package.¹²⁹ According to SM8, the free energy of solvation is written as

$$\Delta G_s^o = \Delta E_E + \Delta E_N + G_P + G_{CDS} + \Delta G_{conc}^o \quad (1)$$

The first term in eq 1 refers to the energy of reorganization of the electronic structure of the solute (electronic relaxation) that is equal to the change in the solute's internal electronic (E) energy in moving from the gas phase to the liquid phase at the same geometry. The second term in eq 1 is the change in the solute's internal energy due to changes in the equilibrium nuclear (N) positions in the solute that accompany the solvation process (we call it geometry relaxation). The quantity of G_P is the free energy of polarization of solvent molecules by the solute. G_{CDS} is the portion of the free energy of solvation that is nominally associated with cavitation, dispersion, and solvent structure effects (CDS), and it is parametrized in terms of atomic surface tensions. The final term, ΔG_{conc}^o , of eq 1 is the free energy of liberation,¹³⁶ and it is zero in the present article because we use the same standard-state concentration for the gas phase as for solution. (It is conventional when this is done to say that the standard states are a 1 mol/L vapor and an ideal 1 mol/L solution, but actually the only issue that matters is that the concentration does not change.) Thus the SM8 model partitions the free energy of solvation into two contributions, one ($\Delta E_E + \Delta E_N + G_P$) arising from long-range bulk electrostatic effects and the other (G_{CDS}) from those electrostatic interactions between the solute and solvent molecules in the first solvation shell that are different from bulk electrostatic polarization and from other short-range effects

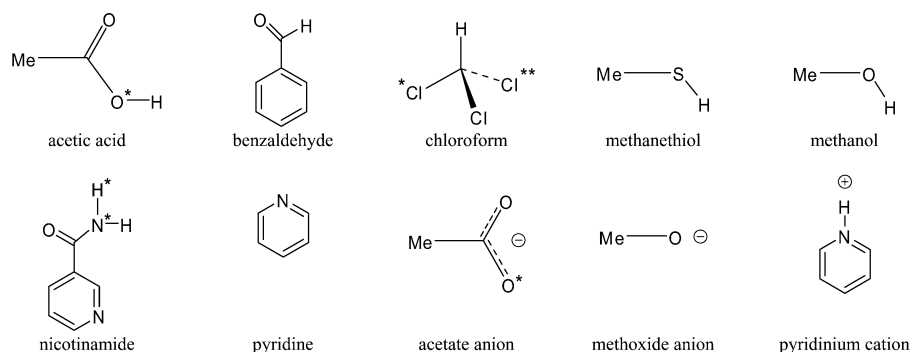


Figure 1. Molecular structures of solutes.

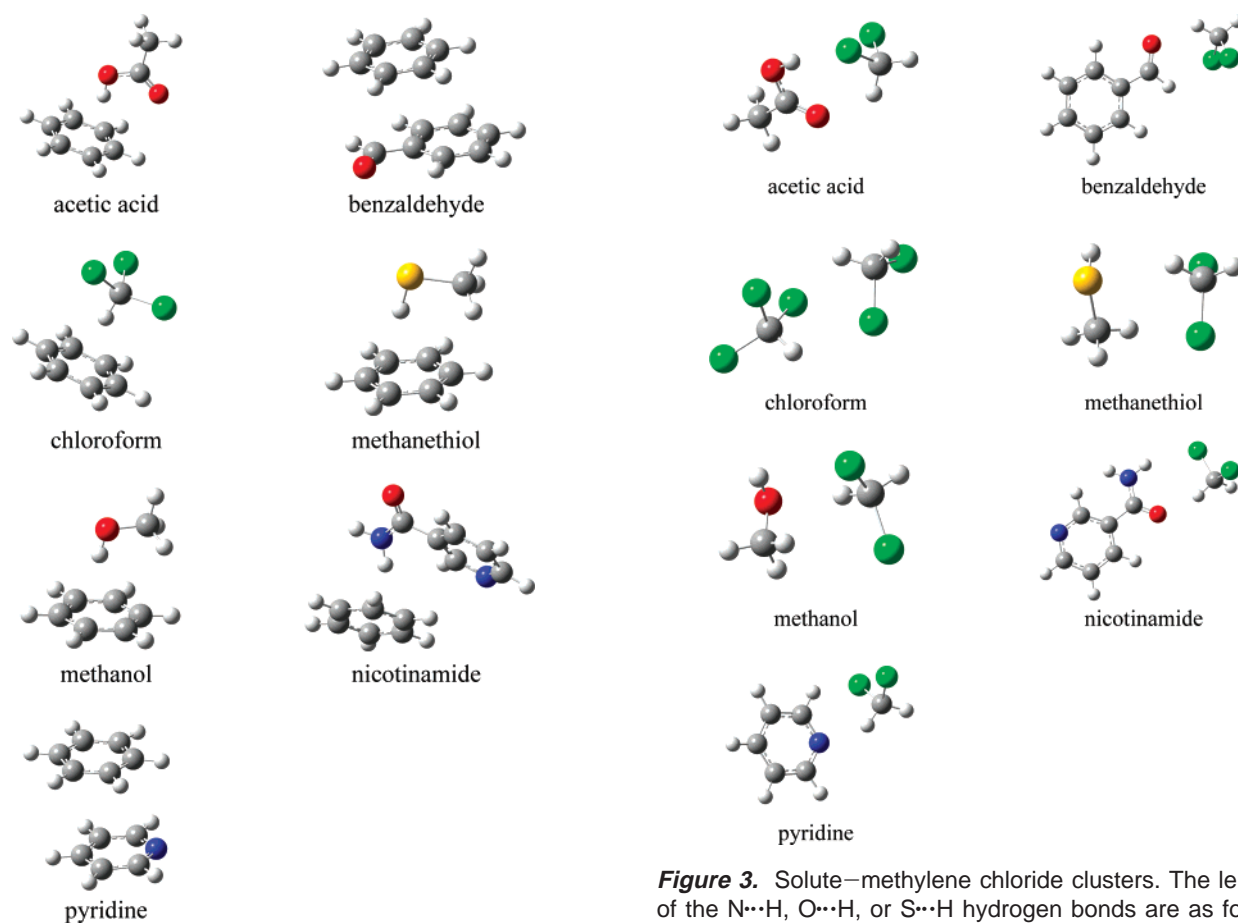


Figure 2. Solute–benzene clusters. The distances between the geometric center of the benzene ring and the geometric center of the solute ring in the benzaldehyde and pyridine clusters are 3.71 and 3.69 Å, respectively, for benzaldehyde and pyridine. The distances between the geometric center of the benzene ring and the closest hydrogen atom of the solute molecule in all other clusters are as follows (in Å): 2.25 (acetic acid), 2.19 (chloroform), 2.45 (methanethiol), 2.29 (methanol), and 2.52 (nicotinamide).

beyond bulk electrostatics. Since in the present calculation we use the supermolecule (supersolute) approach in which one or two solvent molecules are treated as part of the solute, the supersolute already partially includes part of one explicit solvent shell. Therefore, the “first solvation shell” of the SM8 model actually includes part of the second solvation shell of the original solute and most of the first solvation shell.

Because solute electronic relaxation is included in the calculation of the polarization energy but not in the calcula-

Figure 3. Solute–methylene chloride clusters. The lengths of the N···H, O···H, or S···H hydrogen bonds are as follows (in Å): 2.24 (acetic acid), 2.25 (benzaldehyde), 2.82 (methanethiol), 2.21 (methanol), 2.13 (nicotinamide), and 2.24 (pyridine). The shortest Cl···H distances for Cl in the methylene chloride and H in the solute are as follows (in Å): 2.46 (acetic acid), 3.06 (benzaldehyde), 2.83 (chloroform), 3.48 (methanethiol), 3.09 (methanol), 2.59 (nicotinamide), and 3.05 (pyridine).

tion of first-solvation-shell effects, the polarization of the solute depends on the partition of solvation effects into bulk electrostatics and first-solvation-shell effects. This partition is not unique because it depends on the choice of solute atomic radii used in the polarization calculation. These radii are part of the parametrization; however, they are not well determined by parametrizing to free energies of solvation of neutrals because the atomic surface tensions used to account for first-solvation-shell terms are very good at semiempirically making up for deficiencies in the electrostatic contributions. However the free energies of solvation of ions are very sensitive to these radii. We might hope that

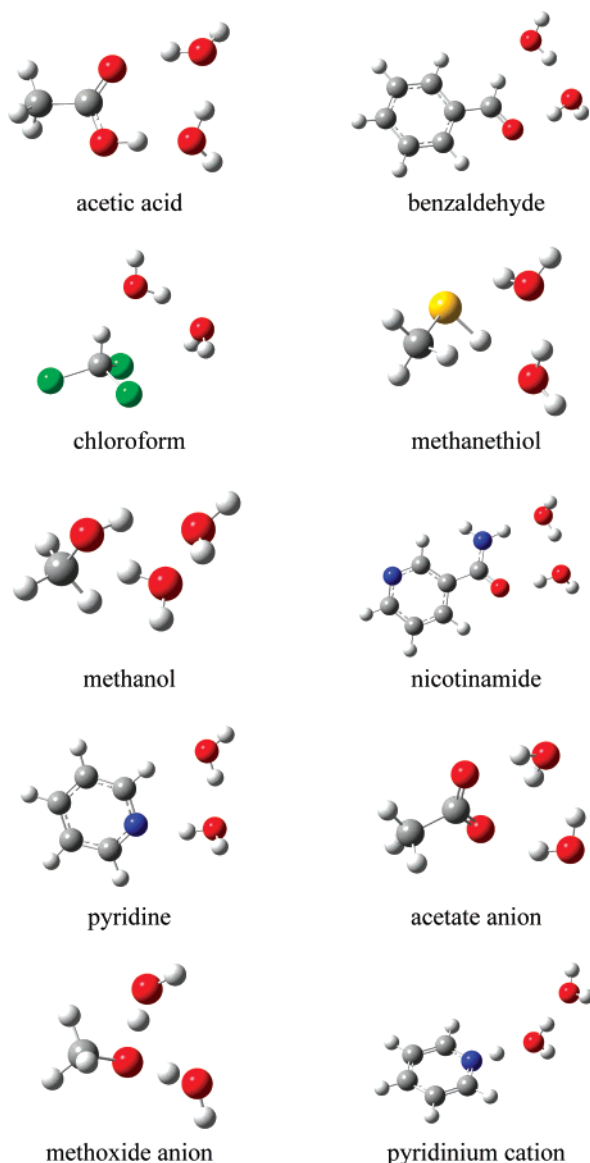


Figure 4. Solute–water clusters. The lengths of the O···H hydrogen bonds where H is the most polar hydrogen atom in the solute molecule are as follows (in Å): 1.63 (acetic acid), 2.21 (benzaldehyde), 2.02 (chloroform), 2.28 (methanethiol), 1.91 (methanol), 1.86 (nicotinamide), 2.24 (pyridine), and 1.56 (pyridinium cation). The shortest H···N, H···O, H···S, or H···Cl distances where H is an aqueous hydrogen atom are as follows (in Å): 1.81 (acetic acid), 1.84 (benzaldehyde), 2.68 (chloroform), 2.38 (methanethiol), 1.88 (methanol), 1.78 (nicotinamide), 1.82 (pyridine), 1.83–1.93 (acetate anion), and 1.47–1.49 (methoxide anion). The O–O distances between the aqueous oxygen atoms in the clusters involving two water molecules are as follows (in Å): 2.68 (acetic acid), 2.78 (benzaldehyde), 2.79 (chloroform), 2.78 (methanethiol), 2.75 (methanol), 2.70 (nicotinamide), 2.77 (pyridine), 2.95 (acetate anion), 4.22 (methoxide anion), and 2.70 (pyridinium cation) (for comparison, the equilibrium O–O distance in the isolated water dimer (H₂O)₂ calculated at the same level of theory is 2.88 Å).

the SM8 solvation model gives a reasonable partition of solvation free energy into electrostatic and other contributions (and therefore gives a reasonable estimate of solute polarization) because SM8 is based on a very large number of ionic

data in aqueous solution, and—unlike previously parametrized solvation models—it is also based on ionic solvation data in nonaqueous solvents.¹²⁰

The bulk electrostatic contribution ($\Delta E_E + \Delta E_N + G_P$) to the total solvation free energy is calculated from a self-consistent molecular orbital calculation, where the generalized Born approximation^{99,137–140} is used to compute the polarization term according to

$$G_P = \sum_k G_P(k) \quad (2)$$

where

$$G_P(k) = -\frac{1}{2} \left(1 - \frac{1}{\epsilon} \right) (q_k^2 \gamma_{kk} + q_k \sum_{k'} q_{k'} \gamma_{kk'}) \quad (3)$$

In the above equations, the summations go over atoms k in the solute. The quantity of ϵ is the dielectric constant of the solvent, q_k is the partial atomic charge of atom k , and $\gamma_{kk'}$ is a Coulomb integral involving atoms k and k' .

The self-consistently polarized partial atomic charges in solution differ from those obtained with the gas-phase electronic wave function even at the same geometry, and they depend on the nature of solvent. Polarization effects in solution can also be analyzed by comparison of atomic contributions to the polarization free energy (eqs 2 and 3) obtained in relaxed and unrelaxed calculations. The relaxed G_P terms are calculated using the liquid-phase electronic wave function optimized by solving the self-consistent reaction field equations. This is the G_P used in eq 1. The unrelaxed calculation uses charges obtained from the gas-phase electronic wave function. In other words, we neglect the electronic structure relaxation (polarization effect) upon solvation in the case called unrelaxed. Since the solute's geometry change upon solvation gives a much smaller contribution to the solvation free energy than the electronic structure relaxation does,³ we use the same gas-phase geometries in both gas-phase and liquid-phase calculations, i.e., we neglect the nuclear relaxation, which means that we assume that the ΔE_N term in eq 1 is equal to 0.

3. Results

Figure 1 shows the molecular structures of the unclustered solutes studied in the present paper. The molecular structures of the solutes clustered in benzene, methylene chloride, and water are depicted in Figures 2–4, respectively. Table 2 shows the partial atomic charges and the partial charges on selected functional groups in seven neutral solutes in the gas phase and three solvents calculated using the CM4M charge model. Table 3 shows the CM4M partial atomic and group charges of acetate anion, methoxide anion, and pyridinium cation in the gas phase and water. Atomic contributions to the polarization energies are calculated by partitioning the cross terms equally between the two atoms, as is already done in eqs 2 and 3. Group contributions are calculated by summing atomic contributions for a given group. The atomic and group contributions of bare and clustered neutral solutes in the three media are listed in Tables 4 and 5, respectively. Atomic and group contributions to the polarization energies

Table 2. Partial Atomic and Group Charges of Neutral Solutes Calculated in the Gas Phase and Solution Using the CM4M Charge Model^a

atom or group	unclustered solute				clustered solute		
	gas	C ₆ H ₆	CH ₂ Cl ₂	H ₂ O	C ₆ H ₆	CH ₂ Cl ₂	H ₂ O
Acetic Acid							
H	0.34	0.34	0.34	0.36	0.34	0.33	0.35
O	-0.42	-0.44	-0.46	-0.49	-0.44	-0.45	-0.47
O*	-0.39	-0.39	-0.39	-0.39	-0.39	-0.39	-0.41
total charge	0.00	0.00	0.00	0.00	-0.02	0.00	-0.05
CH ₃	0.08	0.09	0.10	0.11	0.08	0.10	0.10
CO	-0.03	-0.04	-0.05	-0.08	-0.05	-0.05	-0.08
COOH	-0.08	-0.09	-0.10	-0.11	-0.10	-0.10	-0.15
OH	-0.05	-0.05	-0.05	-0.03	-0.05	-0.06	-0.06
Benzaldehyde							
H	0.04	0.05	0.06	0.07	0.05	0.06	0.09
O	-0.38	-0.40	-0.42	-0.47	-0.40	-0.40	-0.42
total charge	0.00	0.00	0.00	0.00	-0.01	0.02	0.04
C ₆ H ₅	0.04	0.05	0.06	0.07	0.05	0.07	0.09
CO	-0.09	-0.10	-0.12	-0.14	-0.10	-0.10	-0.14
HCO	-0.04	-0.05	-0.06	-0.07	-0.06	-0.05	-0.05
Chloroform							
Cl	-0.07	-0.07	-0.07	-0.08	-0.08	-0.08	-0.08
Cl*	-0.07	-0.07	-0.07	-0.08	-0.08	-0.07	-0.09
Cl**	-0.07	-0.07	-0.07	-0.08	-0.08	-0.07	-0.09
H	0.13	0.13	0.14	0.15	0.13	0.14	0.16
total charge	0.00	0.00	0.00	0.00	-0.03	0.00	-0.03
CH	0.20	0.21	0.22	0.23	0.21	0.21	0.23
Methanethiol							
H	0.11	0.11	0.11	0.12	0.12	0.12	0.14
S	-0.21	-0.23	-0.24	-0.25	-0.24	-0.23	-0.25
total charge	0.00	0.00	0.00	0.00	-0.02	0.01	0.02
CH ₃	0.10	0.12	0.13	0.13	0.10	0.12	0.13
SH	-0.10	-0.12	-0.13	-0.13	-0.12	-0.11	-0.11
Methanol							
H	0.32	0.32	0.33	0.34	0.32	0.33	0.33
O	-0.48	-0.49	-0.50	-0.52	-0.49	-0.48	-0.51
total charge	0.00	0.00	0.00	0.00	-0.02	0.02	0.00
CH ₃	0.16	0.17	0.17	0.18	0.15	0.17	0.18
OH	-0.16	-0.17	-0.17	-0.18	-0.17	-0.15	-0.18
Nicotinamide							
H	0.33	0.34	0.35	0.35	0.33	0.35	0.35
H*	0.33	0.34	0.34	0.35	0.34	0.33	0.34
N	-0.42	-0.45	-0.46	-0.47	-0.45	-0.46	-0.47
N*	-0.65	-0.64	-0.64	-0.63	-0.64	-0.63	-0.62
O	-0.44	-0.47	-0.50	-0.57	-0.47	-0.48	-0.50
total charge	0.00	0.00	0.00	0.00	-0.02	0.02	0.01
C ₅ H ₄ N	0.01	0.00	0.00	0.02	0.00	0.02	0.02
CO	-0.02	-0.04	-0.06	-0.09	-0.05	-0.05	-0.08
NH ₂	0.01	0.04	0.06	0.07	0.03	0.05	0.07
Pyridine							
N	-0.42	-0.45	-0.47	-0.48	-0.45	-0.45	-0.45
total charge	0.00	0.00	0.00	0.00	0.00	0.03	0.06

^a For atomic charges, only heteroatoms and polar hydrogen atoms are shown (see Figure 1). Group charges are summed over the atoms indicated. Total charge is the sum of the partial atomic charges of the solute.

of aqueous ions are presented in Table 6. The partial atomic and group charges and the polarization energy contributions in acetic acid and methanol are compared to those in their homologous analogs, in propionic acid and ethanol, respec-

Table 3. Partial Atomic and Group Charges of Ions Calculated in the Gas Phase and Water Using the CM4M Charge Model^a

	unclustered solute		clustered solute in H ₂ O
atom or group	gas	H ₂ O	
Acetate Anion			
O	-0.60	-0.63 ^b	-0.57
O*	-0.60	-0.64 ^b	-0.57
total charge	-1.00	-1.00	-0.82
CH ₃	-0.13	-0.05	0.00
COO	-0.87	-0.95	-0.82
Methoxide Anion			
O	-0.81	-0.87	-0.70
total charge	-1.00	-1.00	-0.68
CH ₃	-0.19	-0.13	0.02
Pyridinium Cation			
H	0.37	0.39	0.37
N	-0.32	-0.31	-0.35
total charge	1.00	1.00	0.88

^a See footnote a in Table 2. ^b The lower oxygen in Figure 4 has charge -0.64, and the higher oxygen has charge -0.63.

tively, in Tables 7 and 8. Only heteroatoms and polar hydrogen atoms of these solutes are listed in Tables 2–8, whereas the data on all atoms are given in the Supporting Information. Table 9 contains solute dipole moments. All charges are in atomic units, in which the charge on a bare proton is unity.

4. Discussion

First we analyze polarization effects in unclustered solutes. Comparison of the gas-phase partial atomic charges to those in the three solvents indicates that the charges on heteroatoms typically undergo a larger change upon a solute passing from the gas phase to solution (Tables 2 and 3) than do carbon and hydrogen atoms present in the hydrocarbon parts of these solutes. For instance, the charge on O in the unclustered benzaldehyde molecule varies from -0.38 (gas) to -0.40 in benzene (5% change), -0.42 in methylene chloride (11%), and -0.47 in water (24%) in accord with the increase of dielectric constant in the series C₆H₆ → CH₂Cl₂ → H₂O.

Analysis of the molecular structures of solute–solvent clusters (Figures 2–4) indicates a physically meaningful trend that the most polar hydrogen of one molecule is bound to the center with the most negative charge in another molecule. In the case of the benzene clusters (Figure 2), a polar hydrogen atom in the molecules of acetic acid, chloroform, methanethiol, and methanol is attracted to the nucleophilic aromatic ring. The clusters of benzaldehyde and nicotinamide with benzene are additionally stabilized by π – π stacking interactions. The structure of the gas-phase water dimer is preserved in all aqueous clusters with two water molecules, except for methoxide anion (Figure 4) where the H₃C–O[−]⋯H–OH bond is likely to be stronger than the H₂O⋯H–OH bond in the isolated water dimer. Addition of one or two explicit solvent molecules to the solute allows one to include (at least to some extent) the charge-transfer effect corresponding to the redistribution of the electronic density between the solute particle and the first solvation shell; this effect is not included by fully implicit solvent models (except perhaps in an average way by parametriza-

Table 4. Atomic and Group Contributions to Polarization Energy (kcal/mol) for Unclustered Neutral Solutes^a

atom or group	C ₆ H ₆		CH ₂ Cl ₂		H ₂ O	
	unrelaxed	relaxed	unrelaxed	relaxed	unrelaxed	relaxed
Acetic Acid						
H	-0.55	-0.54	-1.15	-1.15	-2.42	-2.80
O	-0.71	-0.80	-1.45	-1.80	-3.76	-5.31
O*	0.48	0.50	0.82	0.88	0.66	0.90
total G _P	-1.44	-1.61	-2.73	-3.29	-5.74	-7.59
CH ₃	-0.44	-0.53	-0.68	-0.95	-0.70	-1.05
CO	-0.94	-1.04	-1.71	-2.07	-3.26	-4.64
COOH	-1.00	-1.08	-2.04	-2.34	-5.03	-6.54
OH	-0.06	-0.04	-0.33	-0.27	-1.77	-1.90
Benzaldehyde						
H	-0.11	-0.15	-0.17	-0.30	-0.14	-0.32
O	-0.83	-1.01	-1.63	-2.27	-3.55	-5.95
total G _P	-1.70	-2.05	-2.89	-4.04	-4.30	-7.11
C ₆ H ₅	-0.73	-0.89	-1.12	-1.58	-1.12	-1.69
CO	-0.87	-1.02	-1.60	-2.16	-3.04	-5.10
HCO	-0.97	-1.16	-1.76	-2.46	-3.18	-5.42
Chloroform						
Cl	0.03	0.03	0.05	0.06	0.03	0.04
Cl*	0.03	0.03	0.05	0.06	0.03	0.04
Cl**	0.03	0.03	0.05	0.06	0.03	0.04
H	-0.31	-0.34	-0.57	-0.71	-0.84	-1.17
total G _P	-0.30	-0.33	-0.58	-0.70	-0.94	-1.28
CH	-0.39	-0.43	-0.72	-0.87	-1.04	-1.42
Methanethiol						
H	-0.02	-0.01	-0.03	0.00	-0.04	0.00
S	-0.10	-0.13	-0.22	-0.29	-0.44	-0.62
total G _P	-0.48	-0.57	-0.79	-1.06	-1.01	-1.40
CH ₃	-0.36	-0.43	-0.55	-0.77	-0.54	-0.78
SH	-0.12	-0.14	-0.24	-0.29	-0.47	-0.62
Methanol						
H	-0.28	-0.28	-0.56	-0.58	-1.00	-1.12
O	-0.28	-0.30	-0.65	-0.72	-2.31	-2.69
total G _P	-0.84	-0.88	-1.62	-1.79	-3.58	-4.19
CH ₃	-0.28	-0.30	-0.41	-0.49	-0.28	-0.38
OH	-0.56	-0.58	-1.21	-1.30	-3.30	-3.81
Nicotinamide						
H	-2.83	-3.28	-4.26	-5.46	-3.80	-5.39
H*	-2.12	-2.39	-3.24	-3.96	-2.86	-3.68
N	-1.20	-1.44	-1.94	-2.55	-2.29	-2.65
N*	3.13	3.47	4.60	5.52	3.58	4.73
O	-0.77	-0.91	-1.69	-2.29	-4.38	-7.75
total G _P	-4.85	-5.78	-7.83	-10.53	-9.68	-14.88
C ₅ H ₄ N	-1.87	-2.24	-2.90	-3.89	-3.00	-3.95
CO	-1.15	-1.34	-2.03	-2.73	-3.59	-6.58
NH ₂	-1.83	-2.20	-2.90	-3.90	-3.09	-4.35
Pyridine						
N	-1.96	-2.44	-3.14	-4.50	-3.56	-5.19
total G _P	-2.30	-2.94	-3.58	-5.39	-3.69	-5.70

^a For atomic contributions, only heteroatoms and polar hydrogen atoms are shown (see Figure 1). Group contributions are summed over the atoms indicated. G_P is the total polarization energy of the solute.

tion). The magnitude of the charge-transfer effect depends strongly on the nature of intermolecular (specific) interactions between the solvent and the solute. For instance, the presence of hydrogen-bonding enhances this effect. Indeed, Tables 2 and 3 show that the most significant charge transfer (up to

0.06 for neutrals and up to 0.32 in ions) is observed in aqueous clusters stabilized by hydrogen bonding (Figure 4). The magnitude of the charge transfer in ions is especially impressive so that it clearly indicates the desirability of the supersolute approach in modeling solvation effects involving ions. Although the total charge of the whole cluster is an integer and is equal to the charge of the unclustered solute, the total charge of the solute in the cluster calculated by summation over all solute's atoms need not be integral because of the charge transfer between solute and solvent. Concerning the neutral solutes, there is a slight trend in the charge transfer with respect to solute's hydrogen-bonding capability (Table 2). A stronger base (for instance, pyridine) acquires more positive charge, whereas a stronger acid (for instance, acetic acid) acquires more negative charge.

It is interesting to compare the magnitudes of the charge transfer and polarization effects. For example, the charge transfer of 0.06 and 0.04 for pyridine and benzaldehyde, respectively, in water has the same size as the largest changes in charge on any of the atoms of these solutes (except O in benzaldehyde) when polarization is considered without charge transfer. For another example, the charge transfers of 0.02–0.03 for acetic acid, chloroform, and methanol in benzene are greater than or equal to the largest pure polarization changes for any of the solute atomic charges.

The difference between the total polarization energies calculated for unclustered neutral solutes using the gas-phase electronic wave function (unrelaxed G_P) and those calculated using the liquid-phase electronic wave function (relaxed G_P) varies from 0.04 kcal/mol for methanol in benzene to 5.20 kcal/mol for nicotinamide in water (Table 4). Indeed, the latter value for nicotinamide in water comprises 37% of the magnitude of the corresponding solvation free energy (−13.95 kcal/mol) calculated by the SM8 model. For comparison, the solvation free energy of methanol in benzene calculated by the SM8 model is −2.25 kcal/mol. The solvation free energies of other solutes are listed in the Supporting Information, and they can also be compared to the corresponding G_P values. The comparison of relaxed and unrelaxed G_P values shows the importance of incorporating electronic relaxation into implicit modeling of solvation effects. Electronic relaxation is most significant for solutes in water (the most polarizable medium), where, on average, it increases the polarization free energy by 43%, and it is least important for solutes in benzene, where the average increase in polarization free energy is 16% (Table 4). Tables 4–6 show that the total polarization energy is heavily dominated by the atomic contributions from solute nitrogen and oxygen heteroatoms.

The supersolute approach leads to an apparent quenching of the polarization energy of the solute because G_P in eqs 1–3 only includes the polarization due to implicit solvent, and now some solvent is explicit. For instance, the total (relaxed) G_P energy of the unclustered pyridinium cation in water is −61.60 kcal/mol, whereas the total G_P energy of the pyridinium cation in the supersolute including two water molecules calculated by summation only over the solute's atoms is −43.40 kcal/mol. Part of the reason for this difference is the charge transfer in the clustered pyridinium

Table 5. Atomic and Group Contributions to Polarization Energy (kcal/mol) for Clustered Neutral Solutes^a

atom or group	C ₆ H ₆		CH ₂ Cl ₂		H ₂ O	
	unrelaxed	relaxed	unrelaxed	relaxed	unrelaxed	relaxed
Acetic Acid						
H	0.16	0.19	0.03	0.09	0.93	1.24
O	−0.90	−1.00	−0.48	−0.58	−3.05	−3.89
O*	−0.14	−0.14	0.06	0.04	−1.66	−1.97
total <i>G_P</i> (solute)	−1.02	−1.17	−1.31	−1.60	−2.89	−3.68
total <i>G_P</i> (cluster)	−1.66	−1.88	−1.90	−2.31	−7.61	−8.96
CH ₃	−0.35	−0.43	−0.68	−0.91	−0.53	−0.76
CO	−0.70	−0.79	−0.72	−0.83	−1.64	−2.19
COOH	−0.68	−0.74	−0.63	−0.70	−2.36	−2.92
OH	0.02	0.05	0.09	0.13	−0.73	−0.73
Benzaldehyde						
H	−0.06	−0.07	−0.09	−0.09	0.08	0.17
O	−0.80	−0.96	−0.49	−0.78	−2.00	−3.06
total <i>G_P</i> (solute)	−1.36	−1.61	−1.90	−2.46	−2.63	−3.67
total <i>G_P</i> (cluster)	−1.93	−2.26	−2.41	−3.04	−8.03	−9.49
C ₆ H ₅	−0.61	−0.73	−1.17	−1.59	−1.11	−1.57
CO	−0.70	−0.82	−0.64	−0.79	−1.60	−2.27
HCO	−0.76	−0.88	−0.73	−0.87	−1.52	−2.09
Chloroform						
Cl	−0.03	−0.03	0.12	0.13	−0.12	−0.18
Cl*	−0.03	−0.03	0.07	0.07	0.08	0.09
Cl**	−0.03	−0.03	0.03	0.03	0.06	0.06
H	−0.07	−0.07	−0.35	−0.38	−0.03	0.00
total <i>G_P</i> (solute)	−0.16	−0.16	−0.25	−0.28	−0.04	−0.06
total <i>G_P</i> (cluster)	−0.77	−0.84	−1.03	−1.23	−5.06	−5.50
CH	−0.08	−0.08	−0.48	−0.51	−0.06	−0.03
Methanethiol						
H	0.11	0.12	−0.15	−0.14	0.48	0.58
S	−0.29	−0.33	0.19	0.20	−0.49	−0.62
total <i>G_P</i> (solute)	−0.39	−0.47	−0.31	−0.36	−0.10	−0.19
total <i>G_P</i> (cluster)	−1.12	−1.31	−1.02	−1.21	−5.37	−6.04
CH ₃	−0.20	−0.26	−0.35	−0.42	−0.10	−0.14
SH	−0.19	−0.21	0.04	0.06	0.00	−0.05
Methanol						
H	0.38	0.40	−1.11	−1.15	0.95	1.21
O	−1.02	−1.08	1.00	1.04	−2.12	−2.54
total <i>G_P</i> (solute)	−0.66	−0.70	−0.70	−0.72	−1.37	−1.56
total <i>G_P</i> (cluster)	−1.44	−1.58	−1.27	−1.40	−6.19	−6.87
CH ₃	−0.02	−0.03	−0.59	−0.62	−0.20	−0.23
OH	−0.64	−0.67	−0.11	−0.10	−1.17	−1.33
Nicotinamide						
H	−1.71	−1.89	−4.17	−5.12	−2.76	−3.50
H*	−1.69	−1.87	−1.62	−1.87	−0.27	−0.34
N	−1.02	−1.22	−1.46	−2.05	−2.19	−2.83
N*	2.27	2.44	3.89	4.48	1.58	1.91
O	−0.87	−1.00	−0.19	−0.26	−2.56	−3.69
total <i>G_P</i> (solute)	−3.79	−4.42	−6.00	−7.86	−6.57	−9.08
total <i>G_P</i> (cluster)	−4.19	−4.85	−6.33	−8.22	−10.57	−13.30
C ₅ H ₄ N	−1.59	−1.88	−2.96	−3.98	−3.06	−4.17
CO	−1.08	−1.22	−1.15	−1.37	−2.06	−2.99
NH ₂	−1.13	−1.32	−1.90	−2.51	−1.45	−1.92
Pyridine						
N	−1.86	−2.27	−0.95	−1.42	−1.38	−2.17
total <i>G_P</i> (solute)	−1.99	−2.48	−2.17	−3.10	−2.14	−3.37
total <i>G_P</i> (cluster)	−2.66	−3.26	−2.76	−3.77	−7.96	−9.90

^a For atomic contributions, only heteroatoms and polar hydrogen atoms are shown (see Figure 1). Group contributions are summed over the atoms indicated. *G_P* (solute) is the sum of the polarization energy contributions from each atom of the solute in the cluster. *G_P* (cluster) is the total polarization energy of the cluster (including solvent atoms of the supersolute).

Table 6. Atomic and Group Contributions to Polarization Energy (kcal/mol) for Aqueous Ions^a

atom or group	unclustered solute		clustered solute	
	unrelaxed	relaxed	unrelaxed	relaxed
Acetate Anion				
O	-45.75	-49.56	-32.50	-34.98
O*	-46.20	-49.74	-32.90	-34.59
total G_P (solute)	-75.68	-79.81	-49.37	-51.77
total G_P (cluster)			-60.55	-62.87
CH ₃	-8.44	-3.84	-3.38	-0.90
COO	-67.25	-75.97	-45.99	-50.87
Methoxide Anion				
O	-74.33	-81.61	-44.74	-47.50
total G_P (solute)	-87.97	-91.04	-44.91	-46.23
total G_P (cluster)			-68.31	-70.46
CH ₃	-13.64	-9.43	-0.17	1.28
Pyridinium Cation				
H	-24.95	-27.17	-17.75	-18.05
N	20.04	19.89	17.10	17.25
total G_P (solute)	-60.51	-61.60	-42.78	-43.40
total G_P (cluster)			-51.23	-51.71

^a See footnote a in Table 5.

cation because the total polarization energy of the whole cluster is -51.71 kcal/mol. The other reason is that a significant amount of the polarization energy of the solute is included explicitly in the supersolute calculation.

Although Table 6 shows that polarization free energies for ions are much larger than those for neutrals in Tables 4 and 5, it also shows that the percentage increases due to electronic relaxation is much smaller, averaging only 4%. In absolute energy units, though, the effect is very large, averaging 2.8 kcal/mol, whereas for neutrals the effect averages to 1.9 kcal/mol in water, 1.0 kcal/mol in methylene chloride, and 0.3 kcal/mol in benzene.

One should keep in mind that the atomic G_P contributions calculated in the present study within the generalized Born approximation (eqs 2 and 3) are not physical observables and they can have positive values, whereas the total polarization energy (which is the sum of these contributions) should always be negative because of the spontaneous nature of polarization in solution (Tables 4–8). Since the Coulomb integral involving atoms k and k' in eq 3 is a function of the distance between k and k' and the summation in eq 3 runs over all atoms of the solute molecule, the G_P contribution from any individual atom is a function of both the molecular geometry and the partial charges of all of the atoms in the molecule. Thus it is understandable that atomic polarization energies of similar atoms in different solutes can be substantially different. For instance, the atomic polarization energy of the hydroxylic oxygen atom in acetic acid is substantially different from that of the same oxygen in methanol: cf. $G_P(O) = +0.90$ kcal/mol for acetic acid in water and $G_P(O) = -2.69$ kcal/mol for methanol in water. However, the hydroxylic oxygen in acetic acid is considerably less charged. This is due in part to the effects of the carbonyl oxygen geminal to it, while the charge on the hydroxylic hydrogen remains largely unchanged. This contributes to the apparently positive contribution to the

Table 7. Partial Atomic and Group Charges for Selected Homologous Analogs^a

atom or group	gas	C ₆ H ₆	CH ₂ Cl ₂	H ₂ O
Acetic Acid				
H	0.34	0.34	0.34	0.36
O	-0.42	-0.44	-0.46	-0.49
O*	-0.39	-0.39	-0.39	-0.39
total charge	0.00	0.00	0.00	0.00
CH ₃	0.08	0.09	0.10	0.11
CO	-0.03	-0.04	-0.05	-0.08
COOH	-0.08	-0.09	-0.10	-0.11
OH	-0.05	-0.05	-0.05	-0.03
Propionic Acid				
H	0.34	0.34	0.34	0.36
O	-0.42	-0.44	-0.46	-0.49
O*	-0.39	-0.39	-0.39	-0.39
total charge	0.00	0.00	0.00	0.00
C ₂ H ₅	0.08	0.09	0.09	0.10
CH ₃	0.03	0.04	0.04	0.04
CO	-0.03	-0.04	-0.05	-0.08
COOH	-0.08	-0.09	-0.09	-0.10
OH	-0.05	-0.04	-0.04	-0.03
Methanol				
H	0.32	0.32	0.33	0.34
O	-0.48	-0.49	-0.50	-0.52
total charge	0.00	0.00	0.00	0.00
CH ₃	0.16	0.17	0.17	0.18
OH	-0.16	-0.17	-0.17	-0.18
Ethanol				
H	0.32	0.32	0.33	0.34
O	-0.48	-0.49	-0.49	-0.51
total charge	0.00	0.00	0.00	0.00
C ₂ H ₅	0.16	0.16	0.17	0.17
CH ₃	-0.01	-0.01	0.00	0.00
OH	-0.16	-0.16	-0.17	-0.17

^a See footnote a in Table 2.

polarization energy of the hydroxylic oxygen in acetic acid through the cross terms of eq 3. Additionally, the presence of the geminal carbonyl oxygen interferes with favorable polarization interactions of the hydroxylic oxygen with the surrounding solvent through simple dielectric descreening effects. As a consequence of these two physical phenomena it is unsurprising that the interactions between the hydroxylic oxygen in acetic acid and the surrounding solvent are less favorable than for the corresponding oxygen in methanol.

One might ask if the different polarization contributions discussed in the previous paragraph are unsystematic or if, in contrast, they are characteristics of functional groups. To examine this question, we carried out calculations on ethanol and propionic acid. We found that the trends in partial atomic charges and in atomic polarization energies obtained for methanol and acetic acid in different media are similar to those obtained for ethanol and propionic acid, respectively (Tables 7 and 8). Indeed, the charge on the most polar (hydroxylic) hydrogen atom remains unchanged within 0.04 atomic units in any of the four solutes placed in different media. The corresponding polarization contributions from the hydroxylic oxygen vary only a little within the same homologous series. We observe the same trends for polariza-

Table 8. Contributions to Polarization Energy (kcal/mol) for Selected Homologous Analogs^a

atom or group	C ₆ H ₆		CH ₂ Cl ₂		H ₂ O	
	unrelaxed	relaxed	unrelaxed	relaxed	unrelaxed	relaxed
Acetic Acid						
H	-0.55	-0.54	-1.15	-1.15	-2.42	-2.80
O	-0.71	-0.80	-1.45	-1.80	-3.76	-5.31
O*	0.48	0.50	0.82	0.88	0.66	0.90
total G _p	-1.44	-1.61	-2.73	-3.29	-5.74	-7.59
CH ₃	-0.44	-0.53	-0.68	-0.95	-0.70	-1.05
CO	-0.94	-1.04	-1.71	-2.07	-3.26	-4.64
COOH	-1.00	-1.08	-2.04	-2.34	-5.03	-6.54
OH	-0.06	-0.04	-0.33	-0.27	-1.77	-1.90
Propionic Acid						
H	-0.50	-0.49	-1.07	-1.08	-2.33	-2.73
O	-0.75	-0.85	-1.51	-1.86	-3.80	-5.33
O*	0.41	0.42	0.70	0.73	0.54	0.77
total G _p	-1.22	-1.34	-2.37	-2.81	-5.34	-7.02
C ₂ H ₅	-0.26	-0.31	-0.42	-0.57	-0.48	-0.68
CH ₃	-0.08	-0.10	-0.14	-0.19	-0.18	-0.26
CO	-0.86	-0.95	-1.58	-1.90	-3.08	-4.39
COOH	-0.96	-1.03	-1.95	-2.24	-4.87	-6.35
OH	-0.09	-0.08	-0.37	-0.34	-1.79	-1.96
Methanol						
H	-0.28	-0.28	-0.56	-0.58	-1.00	-1.12
O	-0.28	-0.30	-0.65	-0.72	-2.31	-2.69
total G _p	-0.84	-0.88	-1.62	-1.79	-3.58	-4.19
CH ₃	-0.28	-0.30	-0.41	-0.49	-0.28	-0.38
OH	-0.56	-0.58	-1.21	-1.30	-3.30	-3.81
Ethanol						
H	-0.20	-0.20	-0.43	-0.43	-0.79	-0.87
O	-0.32	-0.35	-0.69	-0.79	-2.24	-2.62
total G _p	-0.66	-0.70	-1.31	-1.45	-3.10	-3.62
C ₂ H ₅	-0.13	-0.15	-0.19	-0.23	-0.07	-0.12
CH ₃	-0.01	-0.02	-0.03	-0.07	-0.11	-0.17
OH	-0.53	-0.55	-1.12	-1.22	-3.03	-3.50

^a See footnote a in Table 4.**Table 9.** Dipole Moments (debye) of Unclustered Neutral Solutes in the Gas Phase and Solution^a

solute	gas (exp)	gas	C ₆ H ₆	CH ₂ Cl ₂	H ₂ O
acetic acid	1.70 ± 0.03	1.94	2.13	2.29	2.52
benzaldehyde	3.0	3.10	3.50	3.87	4.38
chloroform	1.04 ± 0.02	1.19	1.25	1.31	1.39
ethanol	1.69 ± 0.03	1.56	1.65	1.71	1.80
methanethiol	1.52 ± 0.08	1.42	1.57	1.67	1.72
methanol	1.70 ± 0.02	1.57	1.63	1.68	1.76
nicotinamide		1.94	2.12	2.30	2.75
propionic acid	1.75 ± 0.09	2.02	2.19	2.34	2.59
pyridine	2.215 ± 0.010	2.12	2.57	2.95	3.02

^a Dipole moments are calculated using the CM4M partial atomic charges in the gas phase and in solution. The corresponding experimental gas-phase values are taken from ref 121.

tion energy contributions from individual functional groups present in these compounds.

To conclude this section, we will discuss the values of dipole moments calculated for neutral solutes in three media and in the gas phase, as presented in Table 9. We note that experimental dipole moments are readily available for gas-phase molecules but not for molecules in solution, where the dipole moment is not even uniquely defined. The water

molecule is apparently the only molecule for which the effective dipole moment in the liquid phase is known from experiment.¹⁴¹ Nevertheless dipole moments in solution can be calculated using various theoretical approaches, at least for unclustered solutes or other approaches that assume no charge transfer, and analysis of the theoretical values seems to be useful for better understanding polarization effects in solution.

The increase of the magnitudes of dipole moments in solution in comparison with those in the gas phase for all of the solutes is similar to the results of previous work.³ For instance, the dipole moment of pyridine in water is 42% larger than that in the gas phase. This indicates that the change of the electronic structure of the solute upon passing from the gas phase to solution (called electronic relaxation) is significant and cannot be neglected in modeling solvation effects in various systems. Solute in water are more polar than the same solutes in methylene chloride, whereas they are more polar in methylene chloride than in benzene.

Although the present article has focused on small solutes in liquid solvents, similar polarization effects also occur for more complex situations. For example, very large polarization effects have been observed (computationally) for substrates in enzymes^{142,143} and for proteins in water.¹⁴⁴

5. Conclusions

The role of polarization effects in liquid-phase solution was studied by employing the new SM8 universal solvation model. Using SM8, the bulk electrostatic contribution to the total solvation free energy (this term contains the change in the internal energy of the solute upon solvation, the free energy of polarization of solvent molecules by the solute, and the free energy cost of polarizing the solvent) is calculated from a self-consistent molecular orbital calculation, where the generalized Born approximation is used to compute the polarization term using class IV partial atomic charges self-consistently polarized in solution.

We consider polarization effects in nine neutral solutes (acetic acid, benzaldehyde, chloroform, ethanol, methanethiol, methanol, nicotinamide, propionic acid, and pyridine) and in three solvents, namely benzene, methylene chloride, and water. We also include three ionic solutes (acetate anion, methoxide anion, and pyridinium cation) in the set of aqueous solutes. These solutes are chosen to include major organic chemical functionalities in this analysis. The results indicate the importance of electronic relaxation in solvation effects. Electronic relaxation is most significant for solutes in water (the most polarizable medium), and it is least important in benzene.

To study the charge transfer between a solute and solvent molecules we replace 10 of the 12 solutes by solvent–solute clusters, also called supermolecules or supersolutes. The clusters include two solvent molecules in the case of water and only one solvent molecule in the case of benzene and methylene chloride (totally 24 clusters). The magnitude of the charge transfer in ions is especially large, and it indicates the importance of including charge transfer in modeling solvation effects involving ions. Although there is currently considerable interest in including implicit polarization, the

present study shows that in some cases the explicit treatment of charge transfer is equally or more important. The most significant charge transfer (up to 0.06 for neutrals and up to 0.32 for ions) is observed in aqueous clusters stabilized by hydrogen bonding.

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Supporting Information Available: Complete sets of partial atomic charges and atomic contributions to polarization energy for clustered and unclustered neutral solutes in benzene, methylene chloride, and water and for clustered and unclustered aqueous ions; solvation free energy components of the SM8 model; and the Cartesian coordinates of the solutes optimized at the M06-2X/6-31+G(d,p) level of theory. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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