Accounting for Polarization Cost When Using Fixed Charge Force Fields. I. Method for Computing Energy

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Although it is not currently standard practice, the cost to change the electronic polarization from one appropriate for the gas phase to that implied by the charge model should be considered when deriving force fields based on fits to certain types of experimental data and for using force fields to compute observables that involve changes in molecular polarization. We present mathematical expressions and a method to estimate this polarization cost implied by a fixed charge model force field, where the fixed charge model can be any combination of point charges, higher-order multipoles, or even distributed charge densities, as long as they do not change in response to environment. These expressions illuminate the relationship between polarization costs associated with fixed charge models, self-polarization energies of polarizable models, and quantum chemical based approaches that use continuum representations of the solvent, such as the self-consistent reaction field and polarizable continuum models. The technique takes account of the tensorial nature of the polarizabilities and includes quadrupole as well as dipole polarization. The consistency of this approach to one that estimates polarization cost using an implicit solvent quantum chemistry method (PCM) is demonstrated.

1. Introduction

Hydrogen bonding among water molecules in the liquid phase of water orients their dipole moments in a coherent fashion to produce strong local electric fields. These electric fields can induce dipole moments in solvated molecules, including the water itself. Fixed charge force field models for hydrated solutes typically use charges that are designed to represent some degree of polarization to represent more accurately the nature of the solute−water interaction in the liquid phase. For example, in most of the popular fixed charge models for water molecules designed to reproduce liquid properties, the dipole moment is enhanced relative to the experimental gas phase dipole moment of 1.85 D (to 2.35 D in TIP3P[1] and 2.27 D in SPC,[2] for example).

One issue regarding polarization is when and how the energetics of polarization should be taken into account in determining force field parameters and in using the resulting force fields to compute properties related to changes of environment such as vapor pressure, solvation free energies, enthalpies of vaporization, and even ligand−protein binding free energies if the ligand's electrostatic environment changes upon binding to a protein. In the development of fixed charge water models, for example, a common objective is to optimize force field parameters to reproduce experimental heats of vaporization and density at one temperature or over a range of temperatures. The heat of vaporization is the change in enthalpy upon taking a bulk liquid to the gas phase. However, in a real system, in the gas phase the molecules would not be polarized as they are in the liquid, so one could consider the vaporization process to be performed in two (nonphysical) steps (see Figure 1), the first one of taking the fixed charge (polarized) molecules from the liquid to the gas phase and the second one of taking the polarized gas phase molecules to an unpolarized state. It is the energetics
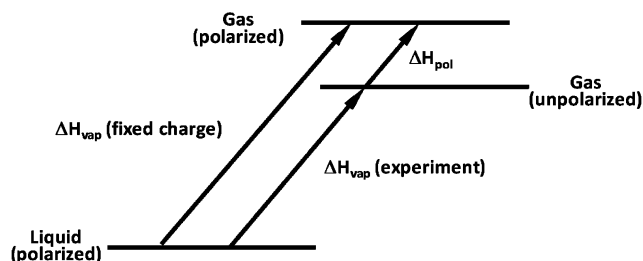

Figure 1. Diagram showing the role polarization cost plays in comparing experimental heats of vaporization with ones computed using fixed charge force fields.

of this second step and its effect on the comparison of computed and experimental results that we are concerned with here.

Taking water as an example, the common fixed charge models for water differ in whether the enthalpy change they fit to experimental data includes only the first of these two steps or both of them, usually with some approximation for the enthalpy of polarization. Since the enthalpy to vaporize strongly polarized molecules is larger than that to vaporize weakly polarized ones, when the energetics of polarization are neglected one can fit the experimental heat of vaporization data with a model that has smaller dipole moments and, generally, weaker intermolecular interactions. The SPC/E model[3] for water, developed as a variant of the SPC model, was the first to take polarization cost into account. SPC/E has a dipole moment of 2.35 D, compared with 2.27 D for SPC. Similarly, TIP4P-Ew,[4] also developed taking polarization energetics into account, has a dipole moment of 2.32 D, compared with 2.18 D for TIP4P,[1] which did not. More recently, the TIP4P/2005 model[5] for water has been reported. This model was developed also taking polarization costs into account, and the resulting dipole moment is 2.305 D. The neglect of polarization has effects on parameters other than the charge model, and the resulting thermodynamic and kinetic properties are affected as well. Consideration of polarization produces a more accurate model for the hydrogen

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bond interaction strength between water molecules in the liquid, and this results in a more accurate self-diffusion coefficient. At 25 °C, the diffusion coefficient reported for SPC water is 4.2 (10^{-9} m²/s) compared with 2.8 reported[6] for SPC/E; and that reported for TIP4P is 3.5 compared with 1.99 (±0.04)[7] and 2.4 (±0.06)[4] reported for TIP4P-Ew and 2.08 reported[5] for TIP4P/2005. These are to be compared with experimental values[8,9] of 2.23 and 2.299. (None of these water models were developed by fitting to experimental diffusion coefficients.)

One of the primary goals of polarizable force field efforts is to obtain a model that can adjust the degree of polarization in a way that depends on environment and to represent more correctly the energetics of the process. However, for fixed charge force fields, polarization needs to be handled in a more approximate, or indirect, fashion. One simple approximation for the polarization cost, used in the parametrization of SPC/E, TIP4P-Ew, and TIP4P/2005, is given by

$$\Delta E_{pol} = \frac{(\Delta|\boldsymbol{\mu}|)^2}{2\bar{\alpha}} \qquad (1)$$

where $\Delta|\boldsymbol{\mu}| = |\boldsymbol{\mu}_l| - |\boldsymbol{\mu}_g|$ is the change in the magnitude of the electric dipole moments between the liquid and gas phases, and $\bar{\alpha}$ is one-third the trace of the dipole–dipole polarizability tensor. This expression is useful for approximating the polarization cost when the dipole moments of the molecule in the gas and liquid phases are known and the polarizability is available. In the context of fixed charge force field development, or when computing properties using fixed charge models where polarization cost needs to be taken into account, one uses the charge model to compute the dipole moment in the liquid phase. In general, when using this kind of expression, it is not obvious how to extend it to treat situations where the tensorial nature of the polarizability needs to be taken into account nor how to estimate polarization energy associated with a change in the quadrupole (or higher) moment.

Although they are still rather computationally expensive, polarizable force fields are beginning to show promise for use in classical molecular simulations.[10–15] These generally use site-based polarizable centers, treated with isotropic polarizabilities or a Drude oscillator approach. With any approach, however, sites polarize to a degree that depends on the local electric field, $\boldsymbol{\mu} = \alpha\mathbf{E}$, where $\boldsymbol{\mu}$ is the induced dipole vector; $\mathbf{E}$ is the electric field; and α is the polarizability, treated here as a scalar (i.e., isotropic). As the polarizable centers polarize, energy is lowered through the interaction of the induced dipole and the field by an amount given by $W_{int} = -\boldsymbol{\mu} \cdot \mathbf{E}$. This lowering of energy is balanced by a positive polarization cost, sometimes called the self-polarization energy, until the total electrostatic energy is stationary with respect to the degree of polarization of all of the polarizable sites. The polarization cost for each site is $W_{pol} = \boldsymbol{\mu} \cdot \boldsymbol{\mu}/2\alpha$, and the time or ensemble average of such a quantity is a measure of the polarization cost for this kind of interaction model. However, although it might be useful as a guide, such a quantity is probably not useful to estimate the polarization cost associated with any particular fixed charge model.

Another useful approximation for the polarization cost can be obtained from quantum chemical approaches that generate electronic wave functions and energies for a molecule inside a cavity that is surrounded by a continuum dielectric. The cavity has a vacuum dielectric, and the continuum represents surrounding solvent. Essentially, the electric field of a solute molecule that is embedded in the cavity induces a polarization in the surrounding dielectric, which, in turn, interacts with the

molecule's electron density. There are many of these techniques, with varying degrees of sophistication, that have been described in a comprehensive review.[16] One early implementation was the Self Consistent Reaction Field (SCRF) approach, based on an Onsager model with a spherical cavity.[17–20] In these models, the charge density of the solute molecule is represented with a multipole expansion that interacts with the continuum representation of the solvent outside of the idealized cavity. Variations include modifications from a spherical cavity to one more representative of the shape of the molecule, a more detailed and accurate representation of the charge density of the solute (e.g., treating it in a continuous manner rather that as a discrete set of point multipoles), and representation of the (reaction) field at the solute that is generated by the polarized solvent as emanating from a surface charge density on the surface of the solvent cavity. These constitute a set of models collectively known as Polarizable Continuum Models (PCMs),[16,21–23] of which there are implementations in many of the available quantum chemistry software packages, e.g., GAMESS/US.[24] Variations on these models abound and include treatments where the solvent is treated as a conductor, the so-called c-PCM approaches, rather than as an insulator,[25–28] which results in a different surface charge induced on the surface of the cavity and proper accounting for the part of the solute's charge density that extends into the continuum solvent.[29–34] Also available are quantum chemistry implementations of the Conductor-like Screening Model (COSMO) that represent the continuum solvent as a conductor that interacts with a representation of the solute that is a set of point multipoles determined by the solute charge density.[35–37]

Regardless of the details, in essentially all of these formulations, there is an energy E that is a functional of the electronic wave function (in the context of Hartree–Fock Self-Consistent Field (HF-SCF) or multiconfiguration self-consistent field (MCSCF) theories) or electron density (in the context of density functional theory (DFT)), generically represented by ρ. This functional includes contributions from the electronic kinetic energy and the electron–electron and electron–nuclear electrostatic potential energy. To this functional is added the nuclear repulsion energy V_{NN}. In the absence of a solvent (gas phase), HF-SCF or DFT methods, for example, are employed to obtain the molecule's gas phase electron density, ρ_g, and corresponding energy, $E[\rho_g] + V_{NN}$, for a particular molecular structure. To represent the solvent, a functional, $E_{int}[\rho]$, is added to describe the interaction between the electron density and the surrounding dielectric continuum as well as the energy to produce the polarization in the continuum. Using HF-SCF or DFT methods, an electron density, ρ_l, and corresponding energy, $E[\rho_l] + V_{NN} + E_{int}[\rho_l]$ are obtained representing a solvated system. $E[\rho_l] + V_{NN}$ represents the *internal* energy of the molecule having been polarized by its environment but without consideration for the cost of polarizing the continuum nor the interaction between this polarized continuum and the molecule. Note that ρ_g is optimal for $E + V_{NN}$ and that ρ_l is optimal for $E + V_{NN} + E_{int}$. Therefore, $E[\rho_l] > E[\rho_g]$. For these quantum chemistry based approaches, the polarization cost is

$$E_{pol} = E[\rho_l] - E[\rho_g] \qquad (2)$$

At this point, some discussion of terminology is warranted. We note that this contribution to the energy has been discussed and referred to by a variety of different names. In his classic book, Boettcher[38] referred to this simply as "polarization energy", as did Sprik and co-workers,[39] reporting on the

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development and implementation of a polarizable force field. However, other workers use the term "polarization energy" to mean something very different. For example, Giesen[40] and co-workers in their work on implicit solvation models use this term to refer to the sum of the solute−solvent interaction energy (a negative quantity) and the cost of restructuring the *solvent*. Stone[42] refers to the polarization cost as the change in "internal energy" due to an external field. Other sources[41] have called this an electronic "distortion energy" or a "deformation" energy. The paper[3] that reported the SPC/E water model called this contribution the "Missing Term in Effective Pair Potentials" and referred to it not as a polarization energy but as "the positive self-energy representing the energy it costs to distort a molecule to its polarized state". The community of polarizable force field developers use a variety of names for this contribution, including the "self-energy"[15] or self-polarization energy. Several approaches exist for partitioning quantum chemical interaction energies, and many report something like a "polarization cost" in some form or another. Notable examples include Morokuma analysis,[43] as well as recent methods based on localized wave functions,[44] an example of which has been recently explored[45] in the context of QM/MM calculations. These schemes report polarization energies but often include in them the interaction energy between the solute and solvent as well as one or both of the changes in energy of the solvent and solute.

In this paper, we describe a mathematical expression and methodology that is useful for estimating the polarization cost of a general molecule given a particular fixed charge model used in a force field description of that molecule. Here, *fixed* means that the charge model does not respond explicitly to its environment. Most charge models in use today consist of fixed point charges located at nuclear sites. However, our procedure can be used to compute polarization energies for more general fixed charge models. These might consist of point charges and/or higher-order point multipoles, such as point dipoles, either on nuclear sites or at "off-atom" sites defined with respect to the atomic sites (e.g., "lone pair" or bond midpoint sites). The charge model could even be of a distributed nature such as one meant to describe a frozen charge density, consisting, for example, of a set of Gaussian functions centered at sites in the molecule. We demonstrate the relationship between this approach and those implied by eqs 1 and 2. In particular, our approach is more general than the one that produced eq 1, which is shown to apply in specific special cases. Our approach can be used in the development of improved fixed charge force fields when one wants to develop parameters using certain types of experimental data and for producing improved approximations for certain observables computed using fixed charge force fields that involve changes in molecular polarization.

2. Polarization Cost Expressions

Consider a charge distribution $\rho^0(r)$ that in the absence of any external electrostatic potential has a net charge q^0, a net dipole moment vector $\boldsymbol{\mu}^0 = (\mu_x^0, \mu_y^0, \mu_z^0)$ and a net quadrupole moment tensor $\boldsymbol{\Theta}^0$, with Cartesian components $\alpha = x$, y, or z, given by the following

$$
\begin{aligned}
q^0 &= \int d^3r \rho^0(r) \\
\mu_\alpha^0 &= \int d^3r\, r_\alpha \rho^0(r) \\
\Theta_{\alpha\beta}^0 &= \frac{1}{2} \int d^3r (3r_\alpha r_\beta - r^2 \delta_{\alpha\beta}) \rho^0(r)
\end{aligned}
$$

We represent by W^0 the energy to assemble this charge distribution in the absence of any external potential and consider the change in the energy upon placing this system in such a field. This field will effect some change in the charge distribution, resulting in different multipoles. The leading terms in the multipole expansion[38] for the energy are the following

$$
\begin{aligned}
W &= W^0 + W_{\text{pol}}(V) + qV + \boldsymbol{\mu} \cdot \nabla V + \frac{1}{3}\boldsymbol{\Theta} : \nabla\nabla V + \dots \\
&= W^0 + W_{\text{pol}}(V) + qV + \sum_{\alpha=x,y,z} \mu_\alpha \nabla_\alpha V \\
&\quad + \frac{1}{3} \sum_{(\alpha,\beta)=x,y,z} \Theta_{\alpha\beta} \nabla_\alpha \nabla_\beta V + \dots \\
&= W^0 + W_{\text{pol}}(V) + qV + \mu_\alpha V_\alpha + \frac{1}{3}\Theta_{\alpha\beta} V_{\alpha\beta} + \dots
\end{aligned}
$$
(3)

Here, q, $\boldsymbol{\mu}$, and $\boldsymbol{\Theta}$ are the resulting net charge, dipole moment, and quadrupole moment of the charge distribution *after* being affected by the external field, and W_{pol} is the polarization cost, the energy expended by the external field to produce the new charge distribution. V is the electrostatic potential of the external field. The final line simply introduces the use of Einstein notation for this relationship, where one is to sum over indices that are repeated, and also that $V_\alpha = \nabla_\alpha V$ and $V_{\alpha\beta} = \nabla_\alpha \nabla_\beta V$. The net charge is always origin-independent, and the dipole moment is origin-independent if the net charge is zero; however, in general, the multipole moments are origin-dependent. The potential, V, the potential gradient, ∇V, and the potential Hessian (negative of the electric field gradient), $\nabla\nabla V$, components are to be measured at the same origin and with the same axes as are used for the multipole expansion. In principle, keeping a sufficient number of terms in this expansion produces an origin-independent energy. We think of W_{pol} as the energy to distort the charge distribution, and once that charge distribution is obtained, the last three terms are the leading terms for the energy of placing this distribution into the field. Note that $W_{\text{pol}} > 0$.

The polarization cost W_{pol} is related to the polarizabilities of the molecule. Using similar notation, and borrowing heavily from Stone,[42] one can also relate the energy of the system in the presence of the external potential to the *zero* field multipoles and polarizabilities as in the following

$$
\begin{aligned}
W &= W^0 + q^0 V + \mu_\alpha^0 V_\alpha + \frac{1}{3}\Theta_{\alpha\beta}^0 V_{\alpha\beta} + \dots \\
&\quad - \frac{1}{2}\alpha_{\alpha\beta} V_\alpha V_\beta - \frac{1}{3}A_{\alpha,\beta\gamma} V_\alpha V_{\beta\gamma} - \frac{1}{6}C_{\alpha\beta,\gamma\delta} V_{\alpha\beta} V_{\gamma\delta} + \dots
\end{aligned}
$$
(4)

These are the leading terms in a long expansion where only those terms are shown that are either linear or quadratic in the potential, potential gradient, or potential Hessian. Here, the dipole−dipole polarizability tensor, $\boldsymbol{\alpha}$, the dipole−quadrupole polarizability, $\mathbf{A}$, and the quadrupole−quadrupole polarizability, $\mathbf{C}$, have been introduced. In this expression, the cost, W_{pol}, of polarizing the charge distribution is included in the terms dependent on the polarizabilities. From this, one can also derive expressions for the resulting (permanent and field-induced) multipoles.

$$\mu_\alpha \equiv \frac{\partial W}{\partial V_\alpha} = \mu_\alpha^0 - \alpha_{\alpha\beta}V_\beta - \frac{1}{3}A_{\alpha,\beta\gamma}V_{\beta\gamma} + \dots$$

$$\Theta_{\alpha\beta} \equiv 3\frac{\partial W}{\partial V_{\alpha\beta}} = \Theta_{\alpha\beta}^0 - A_{\gamma,\alpha\beta}V_\gamma - C_{\alpha\beta,\gamma\delta}V_{\gamma\delta} + \dots$$

$$(5)$$

These can be rearranged slightly to produce expressions for the *induced* dipole and quadrupole as follows

$$\mu_\alpha - \mu_\alpha^0 = -\alpha_{\alpha\beta}V_\beta - \frac{1}{3}A_{\alpha,\beta\gamma}V_{\beta\gamma} + \dots$$
$$\Theta_{\alpha\beta} - \Theta_{\alpha\beta}^0 = -A_{\gamma,\alpha\beta}V_\gamma - C_{\alpha\beta,\gamma\delta}V_{\gamma\delta} + \dots$$

$$(6)$$

One can equate the two expressions above for W (eqs 3 and 4) and derive an expression for W_{pol} in terms of the polarizabilities to obtain the following

$$W_{pol} = -(\mu_\alpha - \mu_\alpha^0)V_\alpha - \frac{1}{3}(\Theta_{\alpha\beta} - \Theta_{\alpha\beta}^0)V_{\alpha\beta} + \dots$$
$$- \frac{1}{2}\alpha_{\alpha\beta}V_\alpha V_\beta - \frac{1}{3}A_{\alpha,\beta\gamma}V_\alpha V_{\beta\gamma} - \frac{1}{6}C_{\alpha\beta,\gamma\delta}V_{\alpha\beta}V_{\gamma\delta} + \dots$$

Here we have also used the fact that $q = q^0$ since the externally applied potential does not change the net charge. Note that in parentheses are expressions for the *induced* dipole and quadrupole, and we can express these in terms of the polarizabilities using eq 6. Doing so provides the following expression for W_{pol}

$$W_{pol} = \left(\alpha_{\alpha\beta}V_\beta + \frac{1}{3}A_{\alpha,\beta\gamma}V_{\beta\gamma}\right)V_\alpha + \frac{1}{3}(A_{\gamma,\alpha\beta}V_\gamma + C_{\alpha\beta,\gamma\delta}V_{\gamma\delta})V_{\alpha\beta} + \dots$$
$$- \frac{1}{2}\alpha_{\alpha\beta}V_\alpha V_\beta - \frac{1}{3}A_{\alpha,\beta\gamma}V_\alpha V_{\beta\gamma} - \frac{1}{6}C_{\alpha\beta,\gamma\delta}V_{\alpha\beta}V_{\gamma\delta} + \dots$$
$$= \frac{1}{2}\alpha_{\alpha\beta}V_\alpha V_\beta + \frac{1}{3}A_{\alpha,\beta\gamma}V_\alpha V_{\beta\gamma} + \frac{1}{6}C_{\alpha\beta,\gamma\delta}V_{\alpha\beta}V_{\gamma\delta} + \dots$$

$$(7)$$

This is a key result, the other being eq 6 for the induced dipole and quadrupole moments expressed in terms of the polarizabilities, potential gradients, and potential Hessians.

If one truncates the expansions in eqs 6 and 7 to include only up to the quadrupole terms, one can compute the polarization cost associated with any particular charge model. This is done in two steps. In the first step, one begins by using quantum chemistry methods to compute, or experiments to measure, the gas phase dipole moment vector, $\boldsymbol{\mu}^0$, and the gas phase quadrupole moment tensor, $\boldsymbol{\Theta}^0$, for the molecule of interest. The polarized liquid phase moments, $\boldsymbol{\mu}$ and $\boldsymbol{\Theta}$, are those obtained using the charge model of the force field, applied to, say, the equilibrium structure of the molecule. The induced dipole and quadrupole moments are the differences between the liquid and gas phase values. By using, again, either quantum chemistry or experiment, one next obtains the dipole−dipole ($\boldsymbol{\alpha}$), the dipole−quadrupole ($\mathbf{A}$), and the quadrupole−quadrupole ($\mathbf{C}$) polarizability tensors. With the induced moments and polarizabilities in hand, one can view the leading terms in eq 6 as a set of linear equations and solve for the unknown potential gradients and Hessians.

$$\begin{pmatrix} 3(\boldsymbol{\mu} - \boldsymbol{\mu}^0) \\ \boldsymbol{\Theta} - \boldsymbol{\Theta}^0 \end{pmatrix} = -\begin{pmatrix} 3\boldsymbol{\alpha} & \mathbf{A} \\ \mathbf{A}^t & \mathbf{C} \end{pmatrix}\begin{pmatrix} \nabla V \\ \nabla\nabla V \end{pmatrix}$$

These, then, are the gradient and Hessian of an externally applied potential that would induce the moments implied by the force field. This potential is analogous to the reaction field produced by the solvent in response to a solute as described in implicit models of solvation (provided the induced moments are representative of the particular solvent). In the second step, one uses these potential gradients and Hessians along with the polarizabilities in eq 7 to obtain the polarization cost.

In actual practice, if one wishes to include terms beyond the dipole−dipole polarizability, one cannot directly implement the first step in this procedure exactly as described above. There are linear dependencies in eq 6 because of the high degree of symmetry and traceless nature of many of the *Cartesian* tensors involved. So, although there appear to be twelve equations and unknowns in the Cartesian form of the equations, there are only eight independent quantities. The situation is resolved simply by employing *spherical* tensor forms for the equations in this section, and these are described in detail in Appendix A.

2.1. Simplified Polarization Cost Expressions. In some limiting situations, the method described above results in simpler expressions, some of which are commonly used to estimate the polarization cost, and it is instructive to explore these cases. If the effect on the energy of including the dipole−quadrupole and quadrupole−quadrupole terms can be neglected, only the dipole−dipole term remains. This can happen for a couple of reasons. First, the external potential produced on the molecule by the surrounding solvent could have no quadrupole-inducing nature, e.g., a potential with a vanishing Hessian. Alternatively, there could be a large quadrupole-inducing effect, but if the associated dipole−quadrupole and quadrupole−quadrupole polarizabilities ($\mathbf{A}$ and $\mathbf{C}$) are large, there is very little energy cost for the quadrupole polarization and, therefore, a possibly negligible contribution to the total polarization cost.

At any rate, if the quadrupole-related terms can be neglected, one is left with the following from eq 6

$$\mu_\alpha - \mu_\alpha^0 = -\alpha_{\alpha\beta}V_\beta$$

If the induced dipole moment vectors and dipole−dipole polarizability components are known, these equations can be interpreted as a system of three linear equations in the three unknown potential gradients. In matrix form, one has the following

$$\begin{pmatrix} \mu_x - \mu_x^0 \\ \mu_y - \mu_y^0 \\ \mu_z - \mu_z^0 \end{pmatrix} = -\begin{pmatrix} \alpha_{xx} & \alpha_{xy} & \alpha_{xz} \\ \alpha_{yx} & \alpha_{yy} & \alpha_{yz} \\ \alpha_{zx} & \alpha_{zy} & \alpha_{zz} \end{pmatrix}\begin{pmatrix} V_x \\ V_y \\ V_z \end{pmatrix}$$

Since the electric field is the negative of the gradient of the potential, $\mathbf{E} = -\nabla V$, this is just the tensor form of the familiar equation $\boldsymbol{\mu}^{induced} = \boldsymbol{\alpha}\mathbf{E}$. The polarizability tensor can be inverted to produce $\boldsymbol{\alpha}^{-1}$, and if one multiplies both sides of the equation by this, the result is $\nabla V = -(\boldsymbol{\alpha}^{-1})(\boldsymbol{\mu} - \boldsymbol{\mu}^0)$. If the quadrupole-related terms can be neglected in eq 7, the expression for the polarization cost simplifies to the following

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$$
\begin{aligned}
W_{\text{pol}} &= \frac{1}{2}\alpha_{\alpha\beta}V_\alpha V_\beta \\
&= \frac{1}{2}(\nabla V)^{\text{t}}\alpha(\nabla V) \\
&= \frac{1}{2}(\boldsymbol{\mu}-\boldsymbol{\mu}^0)^{\text{t}}(\alpha^{-1})^{\text{t}}\alpha(\alpha^{-1})(\boldsymbol{\mu}-\boldsymbol{\mu}^0) \\
&= \frac{1}{2}(\boldsymbol{\mu}-\boldsymbol{\mu}^0)^{\text{t}}(\alpha^{-1})^{\text{t}}(\boldsymbol{\mu}-\boldsymbol{\mu}^0)
\end{aligned}
\tag{8}
$$

Here, the superscript t represents the transpose operation, and the expression for the potential gradient in terms of the induced dipole moment has been used.

Equation 8 is the first of three simpler expressions for the polarization cost to be derived in this section. It takes appropriate account of the tensorial nature of the polarizability and the vector nature of the induced dipole moment. This expression is general in the sense that it makes no assumptions about the nature of the dipole polarizability nor the direction of the induced polarization.

We consider next a further simplification where the polarizability can be considered to be isotropic. This results when the three eigenvalues of the tensor are degenerate and appears at first to be a rather unusual situation. However, for many molecules, including water, this is a very good approximation. This is not to say that such a molecule is equally likely to polarize in any direction. In general, the molecule will orient in the direction where its permanent dipole moment aligns with the gradient of the potential, so the polarization induced by the potential is more likely to be aligned with the permanent dipole moment even if the polarizability is isotropic.

A polarizability tensor can be diagonalized by an orthogonal transformation, $\mathbf{d} = \mathbf{R}\alpha\mathbf{R}^{\text{t}}$. Here, $\mathbf{R}$ is a three-by-three matrix that can transform (rotate) a vector from a representation relative to the lab frame to one relative to the frame in which the polarizability tensor is diagonal. Note that since $\mathbf{R}$ is a rotation matrix $\mathbf{R}^{\text{t}} = \mathbf{R}^{-1}$. The matrix $\mathbf{d}$ is a diagonal matrix of eigenvalues of α. Since $\alpha = \mathbf{R}^{\text{t}}\mathbf{d}\mathbf{R}$, we can invert both sides to obtain $\alpha^{-1} = (\mathbf{R}^{\text{t}}\mathbf{d}\mathbf{R})^{-1} = \mathbf{R}^{\text{t}}\mathbf{d}^{-1}\mathbf{R}$. Here $\mathbf{d}^{-1}$ is just a matrix with the inverses of the eigenvalues of α on the diagonal. Using this expression for α^{-1} in the expression above for the polarization cost, one obtains

$$
W_{\text{pol}} = \frac{1}{2}(\boldsymbol{\mu}-\boldsymbol{\mu}^0)^{\text{t}}\mathbf{R}^{\text{t}}\mathbf{d}^{-1}\mathbf{R}(\boldsymbol{\mu}-\boldsymbol{\mu}^0)
$$

If the three eigenvalues are equal, or replaced by their average, $\bar\alpha = \text{tr}(\alpha)/3$, then $\mathbf{d}^{-1} = (\bar\alpha)^{-1}\mathbf{I}$ is just a scalar times the identity matrix, and

$$
\begin{aligned}
W_{\text{pol}} &= \frac{1}{2}(\boldsymbol{\mu}-\boldsymbol{\mu}^0)^{\text{t}}\mathbf{R}^{\text{t}}\mathbf{I}\mathbf{R}(\boldsymbol{\mu}-\boldsymbol{\mu}^0)/\bar\alpha \\
&= \frac{|\boldsymbol{\mu}-\boldsymbol{\mu}^0|^2}{2\bar\alpha}
\end{aligned}
\tag{9}
$$

Equation 9 is the second simplified expression for the polarization cost, appropriate when there is no contribution from quadrupole polarization and when the dipole−dipole polarizability tensor is isotropic or can be approximated as such.

A final simplification can be made by assuming that the induced dipole moment vector $\boldsymbol{\mu} - \boldsymbol{\mu}^0$ is parallel to the permanent dipole moment, $\boldsymbol{\mu}^0$. This is likely to be the case especially if the polarizability is isotropic because the

permanent dipole will align with the potential gradient, which will then cause polarization in the same direction as the permanent dipole. In this case, $|\boldsymbol{\mu} - \boldsymbol{\mu}^0|^2 = (|\boldsymbol{\mu}| - |\boldsymbol{\mu}^0|)^2 = (\Delta|\boldsymbol{\mu}|)^2$, and

$$
W_{\text{pol}}^{|D|} = \frac{(\Delta|\boldsymbol{\mu}|)^2}{2\bar\alpha}
\tag{10}
$$

This final simplified expression was used to determine the polarization cost in the development, for example, of SPC/E and TIP4P-Ew, and it uses only dipole moment magnitudes and the isotropic polarizability, $\bar\alpha$.

This expression is also the polarization cost, or self-polarization energy, evaluated during the use of polarizable force fields, and so we see that the above formulation produces polarization costs for fixed charge force fields that are consistent in meaning with these as well as with those of the polarizable continuum or implicit solvent approaches.

3. Comparison with Polarization Cost from a Polarizable Continuum Model

As described in the Introduction, a common way to compute polarization costs uses quantum chemistry methods to obtain electron densities appropriate for a solvated molecule where the solvent is represented by a continuum dielectric. These models for the liquid phase system exhibit polarization, and this is generally apparent from enhanced dipole and/or quadrupole moments relative to those from a vacuum phase calculation. Using these types of methods, one can obtain a polarization cost by taking the difference between the converged vacuum phase energy and an energy calculated using the liquid phase converged wave function or density but evaluated with the gas phase Hamiltonian, i.e., without any interaction with the solvent, as described by eq 2. In this section, we investigate whether these polarization costs are consistent with those produced using our method.

Polarization costs were evaluated for ten molecules using a polarizable continuum approach for comparison with those produced using the formulation described in Section 2, which employs dipole moments and quadrupole moments in the gas and liquid phases along with gas phase polarizabilities. First, each of the ten molecules was structurally optimized (for the gas phase) using B3LYP density functional theory[46] with a cc-pV(T+d)Z basis set.[47−50] The gas phase energy, electron density, and resulting dipole and quadrupole moments and the Cartesian polarizabilities (dipole−dipole, α, dipole−quadrupole, $\mathbf{A}$, and quadrupole−quadrupole, $\mathbf{C}$) were also computed. These properties were computed relative to a reference frame coincident with the center of nuclear charge. The multipole moments were obtained from the charge density, and the polarizabilities were computed by finite difference of energies and multipole moments each with different directions of small finite perturbing electrostatic potentials (0.001 au) or potential gradients (0.001 au). Next, for the liquid phase, the electron density and resulting dipole and quadrupole moments were obtained using the same

TABLE 1: Polarization Costs (kcal/mol) and Gas and Liquid Phase Dipole (Debye) and Quadrupole (Debye-Angstrom) Moments for Ten Molecules[a]

molecule	E_{pol}^{PCM}	$|\mu_g|$	$|\mu_l|$	$|\Theta_g|$	$|\Theta_l|$	$W_{pol}^{|D|}$	W_{pol}^{dd}	W_{pol}^{dq}	W_{pol}^{qq}	W_{pol}^{D+Q}
benzene	0.27	0	0	7.42	8.43	0	0	0	0.26	0.26
butane	0.01	0.10	0.12	0.46	0.56	0	0	0	0	0
1,4-dicyanobenzene	2.10	0.00	0.00	41.05	50.72	0	0	0	1.78	1.78
ethanol	0.57	1.60	2.03	5.38	5.92	0.29	0.46	−0.18	0.25	0.53
methylethylsulfide	0.52	1.57	2.22	4.46	5.35	0.36	0.38	−0.00	0.06	0.44
nitrobenzene	1.00	4.53	5.86	6.08	6.54	1.07	0.98	−0.20	0.13	0.91
nitromethane	1.02	3.49	4.24	4.64	5.31	0.97	0.95	−0.04	0.08	0.99
N-methylacetamide	2.07	3.84	5.19	5.45	6.34	1.88	1.84	−0.03	0.10	1.91
paracresol	0.75	1.34	1.87	11.23	13.28	0.16	0.23	−0.05	0.42	0.61
water	0.70	1.92	2.24	2.63	2.79	0.68	0.57	0.09	0.03	0.69

[a] The multipole moments were computed for the gas phase using B3LYP and for the liquid phase using B3LYP with a c-PCM model for aqueous solvent. Also shown are the polarization costs computed using c-PCM polarized electron densities with the vacuum phase Hamiltonian, E_{pol}^{PCM} (eq 2), and using a simple approximation, $W_{pol}^{|D|}$ (eq 10), that estimates them from changes in the magnitude of the dipole moments and the dipole polarizabilities. Columns 7−9 show the polarization costs computed using the procedure described in this work, resolved by contributions as in eq 7, and $W_{pol}^{D+Q} = W_{pol}^{dd} + W_{pol}^{dq} + W_{pol}^{qq}$.

molecular structure, level of theory, and basis set as for the gas phase, but the presence of water was modeled by a conducting continuum model (c-PCM) method,[25,27] using standard atomic radii.[51] (Only electrostatics were included in the PCM calculations.) These multipole moments and polarizabilities were used to produce the polarization costs listed in columns 6−10 of Table 1.

The electron density from the c-PCM method was also used to evaluate a gas phase energy, i.e., with a Hamiltonian that did not include any interaction with solvent. The difference between this energy and the true gas phase energy (from the gas phase electron density) represents the polarization cost implied by the c-PCM model (eq 2) and is reported in column 1 of Table 1. The GAMESS/US Quantum Chemistry package[24] was used for all of the quantum chemistry calculations.

The magnitudes of the dipole and quadrupole are reported where the quadrupole magnitude is evaluated as

$$|\Theta|^2 = \sum_m |Q_{2m}|^2 = Q_{20}^2 + Q_{21c}^2 + Q_{21s}^2 + Q_{22c}^2 + Q_{22s}^2$$
$$= \Theta_{zz}^2 + \frac{4}{3}(\Theta_{xy}^2 + \Theta_{xz}^2 + \Theta_{yz}^2) + \frac{1}{3}(\Theta_{xx} - \Theta_{yy})^2$$

The first point apparent from the results in Table 1 is the increase in dipole and quadrupole magnitudes in going from the gas phase to the solvated phase induced by the high dielectric medium. For molecules such as nitrobenzene and *N*-methylacetamide (NMA) the dipoles increase by as much as 1.3 D, and on a percentage basis, one of the quadrupole magnitudes increases by 24% (1,4-dicyanobenzene). On examination of the last four columns of the table, one can see that for some molecules the contributions from the quadrupole terms to the polarization cost as defined by eq 7 can be considerable. This is most apparent for benzene (0.26 kcal/mol), paracresol (0.37), and dicyanobenzene (1.78), where the quadrupole terms are actually larger than the dipole terms.

The polarization costs produced from energy differences using liquid and gas phase electron densities (E_{pol}^{PCM}, using eq 2) provide the standard against which we wish to assess our method. These

exhibit a wide range of values from essentially zero for butane to over 2 kcal/mol for *N*-methylacetamide (NMA) and 1,4-dicyanobenzene. In principle, the two methods should produce consistent results for the polarization cost provided enough terms are used in the multipole moment energy expansion, eq 7. Comparing the polarization costs computed using the three polarizabilities ($W_{pol}^{D+Q} = W_{pol}^{dd} + W_{pol}^{dq} + W_{pol}^{qq}$, last column) with those computed from energy differences (E_{pol}^{PCM}, first column), one can see that the method reproduces the polarization cost to within 0.1 kcal/mol, except for NMA and paracresol, where the error is only slightly larger, 0.16 and 0.14, respectively, and for dicyanobenzene where the error is 0.32. Presumably, these cases require consideration of higher-order multipole moments for an adequate description of the change in the electron density effected by the solvent. Clearly, for dicyanobenzene, where the dipole moment is identically zero by symmetry, and where the quadrupole polarization energy (1.78 kcal/mol) is so large, it is very likely that the neglected higher-order terms will also contribute significantly to the overall polarization cost.

Also listed in Table 1 is $W_{pol}^{|D|}$, the polarization cost computed using eq 10, which is based only on differences of dipole moment magnitudes and the trace of the dipole−dipole polarizability tensor, α. Except for ethanol, this expression does a reasonable job at approximating W_{pol}^{dd}, the contribution from the dipole−dipole polarizability. However, considering the difference between this column and the first, in particular for benzene, paracresol, and dicyanobenzene, quadrupolar effects can be important, and general use of this simple approximation for molecules with larger quadrupole moments (in this case gas phase magnitudes of 7 D-Å and larger) is not to be recommended. It is surprising how well this simple approximation appears to perform for water, giving 0.68 kcal/mol of the total 0.70 kcal/mol polarization cost. This is especially fortunate since this approximation is what was used for the development of the fixed charge water models that take polarization into account. However, the agreement is somewhat fortuitous since the simple formula actually overestimates the dipole polarization by about 20% to accidently cover for a comparable amount of neglected quadrupole polarization.

We should note that the multipoles and the polarizabilities are origin-dependent. However, as more terms are added, the series converges to an origin-independent result. As an example,

polarization cost components were computed for acetamide at the SCF level using a small basis set and two different choices for the location of the origin: the center of mass and the center of nuclear charge. Admittedly, these are not very different for acetamide, but the dipole—dipole, dipole—quadrupole, and quadrupole—quadrupole contributions and the total polarization cost (all in kcal/mol) were 1.958, −0.121, 0.165, and 2.002 for an origin located at the center of mass and 1.905, −0.066, 0.164, and 2.002 for an origin located at the center of charge.

4. Conclusion and Discussion

We have presented a method for the computation of the polarization cost inherent in the charge model of a force field. The method is based on gas phase polarizabilities and on the difference in the multipole moments from the gas phase (unpolarized) description of the molecule and a solvated (polarized) description of the molecule as given by the charge model of a force field. The gas phase polarizabilities and multipole moments can be computed using quantum chemistry methods.

We have shown that polarization costs computed this way are entirely consistent with those computed using energies from gas phase and implicit solvent quantum methods (e.g., PCM) in the sense that in those methods the molecule polarizes in response to a reaction field that it induces in the solvent, and the energetics of this response can then be accurately described using a series expansion based on this field and on the gas phase polarizabilities. In other words, the cost to polarize the molecule to some particular final state of polarization can be equivalently determined in either of two ways. The first way is from constructing some external field that causes that degree of polarization and then computing the cost to distort the electron density to that extent by taking the differences in the energies obtained using the unpolarized and polarized electron densities. The second way, our approach, is to use that field (and its gradients) in a series expansion that involves the gas phase polarizabilites to get the energy. Provided enough terms are kept, these approaches give the same result. We have also shown that the polarization costs we compute have the same meaning as the self-polarization energies obtained during the use of polarizable force fields.

Since our method of evaluating polarization cost requires only multipole moments evaluated using the charge model of the force field at various structures to define the polarized state, it is appropriate to use, not only for nuclear site-based point charge models but also for more complex ones that might also have "off site" point charges, point multipoles or even distributed but frozen charge densities such as from a set of Gaussian functions at various sites in the molecule.

We have shown the relationship between our approach and other simpler but commonly used methods for approximating polarization cost. In particular, our method can account for higher-order effects, such as quadrupole polarization. For some molecules, such as those with aromatic groups, quadrupole polarization can contribute more to the polarization cost than the dipole polarization, and for molecules such as 1,4-dicyanobenzene where there is no dipole polarization, this effect can be large.

In summary, the polarization cost should be considered, not just for water but for all molecules, before comparing computed and experimental values of certain properties, such as enthalpies and free energies of vaporization or solvation where the process involves large changes in the nature of the molecular environment. The method for computing the polarization contribution to free energies and enthalpies is the subject of the companion paper (DOI 10.1021/jp911701h).

Appendix A: Real Spherical Tensor Formulation

If one wishes to compute polarization costs using terms beyond the dipole—dipole polarizability, one must use a formulation based on real spherical tensors instead of Cartesian tensors to avoid numerical singularities. Expressions from Stone's work,[42] included here for convenience, for the real spherical tensor components of the multipole moments written in terms of the Cartesian multipole moment components are as follows

$$
\begin{aligned}
Q_{00} &= q \\
Q_{10} &= \mu_z \\
Q_{11c} &= \mu_x \\
Q_{11s} &= \mu_y \\
Q_{20} &= \Theta_{zz} \\
Q_{21c} &= \frac{2}{\sqrt{3}}\Theta_{xz} \\
Q_{21s} &= \frac{2}{\sqrt{3}}\Theta_{yz} \\
Q_{22c} &= \frac{1}{\sqrt{3}}(\Theta_{xx} - \Theta_{yy}) \\
Q_{22s} &= \frac{2}{\sqrt{3}}\Theta_{xy}
\end{aligned}
$$

Expressions for the real spherical tensor components for the potential, its gradient, and Hessian in terms of the Cartesian components are as follows

$$
\begin{aligned}
V_{00} &= V \\
V_{10} &= V_z \\
V_{11c} &= V_x \\
V_{11s} &= V_y \\
V_{20} &= \frac{1}{6}(2V_{zz} - V_{xx} - V_{yy}) \\
V_{21c} &= \frac{1}{\sqrt{3}}V_{xz} \\
V_{21s} &= \frac{1}{\sqrt{3}}V_{yz} \\
V_{22c} &= \frac{1}{2\sqrt{3}}(V_{xx} - V_{yy}) \\
V_{22s} &= \frac{1}{\sqrt{3}}V_{xy}
\end{aligned}
$$

The expressions for the real spherical tensor components for the dipole—dipole polarizability in terms of the Cartesian components are as follows

$$\alpha_{10,10} = \alpha_{zz}$$
$$\alpha_{10,11c} = \alpha_{zx}$$
$$\alpha_{10,11s} = \alpha_{zy}$$
$$\alpha_{11c,11c} = \alpha_{xx}$$
$$\alpha_{11c,11s} = \alpha_{xy}$$
$$\alpha_{11s,11s} = \alpha_{yy}$$

The dipole−dipole polarizability tensor is symmetric in both Cartesian and spherical tensor form, so $\alpha_{xy} = \alpha_{yx}$ and $\alpha_{11c,\,10} = \alpha_{10,\,11c}$.

The expressions for the real spherical tensor components for the dipole−quadrupole polarizability in terms of the Cartesian components are as follows

$$\alpha_{10,20} = A_{z,zz}$$
$$\alpha_{10,21c} = \frac{2}{\sqrt{3}}A_{z,xz}$$
$$\alpha_{10,21s} = \frac{2}{\sqrt{3}}A_{z,yz}$$
$$\alpha_{10,22c} = \frac{1}{\sqrt{3}}(A_{z,xx} - A_{z,yy})$$
$$\alpha_{10,22s} = \frac{2}{\sqrt{3}}A_{z,xy}$$
$$\alpha_{11c,20} = A_{x,zz}$$
$$\alpha_{11c,21c} = \frac{2}{\sqrt{3}}A_{x,xz}$$
$$\alpha_{11c,21s} = \frac{2}{\sqrt{3}}A_{x,yz}$$
$$\alpha_{11c,22c} = \frac{1}{\sqrt{3}}(A_{x,xx} - A_{x,yy})$$
$$\alpha_{11c,22s} = \frac{2}{\sqrt{3}}A_{x,xy}$$
$$\alpha_{11s,20} = A_{y,zz}$$
$$\alpha_{11s,21c} = \frac{2}{\sqrt{3}}A_{y,xz}$$
$$\alpha_{11s,21s} = \frac{2}{\sqrt{3}}A_{y,yz}$$
$$\alpha_{11s,22c} = \frac{1}{\sqrt{3}}(A_{y,xx} - A_{y,yy})$$
$$\alpha_{11s,22s} = \frac{2}{\sqrt{3}}A_{y,xy}$$

The Cartesian components for the dipole−quadrupole polarizability have symmetry as well, such that $A_{x,xy} = A_{x,yx}$, for example. Also, due to the nature of the expressions in which this polarizability is used, A has a *traceless* aspect in that $A_{x,xx} + A_{x,yy} + A_{x,zz} = 0$. Therefore, there are not 27 (3 × 9) independent Cartesian components, but only 15 (3 × 5). The 15 spherical tensor components above are truly independent. It should be noted, however, that in the energy expressions that use the spherical tensor form there is a need for both $\alpha_{10,20}$ and $\alpha_{20,10}$, for example, and these are equal by symmetry.

Here are the expressions for the real spherical tensor components for the quadrupole−quadrupole polarizability in terms of the Cartesian components

$$\alpha_{20,20} = 3C_{zz,zz}$$
$$\alpha_{20,21c} = 2\sqrt{3}C_{zz,xz}$$
$$\alpha_{20,21s} = 2\sqrt{3}C_{zz,yz}$$
$$\alpha_{20,22c} = \sqrt{3}(C_{zz,xx} - C_{zz,yy})$$
$$\alpha_{20,22s} = 2\sqrt{3}C_{zz,xy}$$
$$\alpha_{21c,20} = 2\sqrt{3}C_{xz,zz}$$
$$\alpha_{21c,21c} = 4C_{xz,xz}$$
$$\alpha_{21c,21s} = 4C_{xz,yz}$$
$$\alpha_{21c,22c} = 2(C_{xz,xx} - C_{xz,yy})$$
$$\alpha_{21c,22s} = 4C_{xz,xy}$$
$$\alpha_{21s,20} = 2\sqrt{3}C_{yz,zz}$$
$$\alpha_{21s,21c} = 4C_{yz,xz}$$
$$\alpha_{21s,21s} = 4C_{yz,yz}$$
$$\alpha_{21s,22c} = 2(C_{yz,xx} - C_{yz,yy})$$
$$\alpha_{21s,22s} = 4C_{yz,xy}$$
$$\alpha_{22c,20} = \sqrt{3}(C_{xx,zz} - C_{yy,zz})$$
$$\alpha_{22c,21c} = 2(C_{xx,xz} - C_{yy,xz})$$
$$\alpha_{22c,21s} = 2(C_{xx,yz} - C_{yy,yz})$$
$$\alpha_{22c,22c} = C_{xx,xx} - 2C_{xx,yy} + C_{yy,yy}$$
$$\alpha_{22c,22s} = 2(C_{xx,xy} - C_{yy,xy})$$
$$\alpha_{22s,20} = 2\sqrt{3}C_{xy,zz}$$
$$\alpha_{22s,21c} = 4C_{xy,xz}$$
$$\alpha_{22s,21s} = 4C_{xy,yz}$$
$$\alpha_{22s,22c} = 2(C_{xy,xx} - C_{xy,yy})$$
$$\alpha_{22s,22s} = 4C_{xy,xy}$$

Note that there is also considerable symmetry in the Cartesian components for the quadrupole−quadrupole polarizability such that, for example, $C_{xz,xy} = C_{xz,yx} = C_{zx,xy} = C_{zx,yx}$ and $C_{xz,xy} = C_{xy,xz}$, as well as a traceless nature such that $C_{xy,xx} + C_{xy,yy} + C_{xy,zz} = 0$. Consequently, there are not 81 (9 × 9) independent components, only 15 (5 × 6/2). The expressions above for the 25 spherical tensor components are also symmetric in that $\alpha_{20,21c} = \alpha_{21c,20}$, for example, as can be seen by exploiting the symmetry in the Cartesian components, resulting in 15 independent components.

Using these relationships, the energy of a charge distribution in an external potential expressed in terms of the multipoles resulting from the field using both Cartesian and spherical tensors becomes the following

$$W = W^0 + W_{pol}(V) + qV + \mu_\alpha V_\alpha + \frac{1}{3}\Theta_{\alpha\beta}V_{\alpha\beta} + \dots$$
$$= W^0 + W_{pol}(V) + Q_{lk}V_{lk} + \dots$$

These are the counterparts to eq 3. In the first expression, the summations are over Cartesian indices, e.g., $\alpha = (x, y, z)$; and in the second, the summations are over spherical tensor indices, with $l = (0, 1, \dots)$ and for each value of l, over the $2l + 1$ values of $\kappa = (0, 1c, 1s, 2c, 2s,\dots, lc, ls)$. Similar expressions[42] for the energy in terms of the *zero* field multipoles and polarizabilities are the following

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$$W = W^0 + q^0 V + \mu_\alpha^0 V_\alpha + \frac{1}{3}\Theta_{\alpha\beta}^0 V_{\alpha\beta} + \ldots$$
$$- \frac{1}{2}\alpha_{\alpha\beta}V_\alpha V_\beta - \frac{1}{3}A_{\alpha,\beta\gamma}V_\alpha V_{\beta\gamma} - \frac{1}{6}C_{\alpha\beta,\gamma\delta}V_{\alpha\beta}V_{\gamma\delta} + \ldots$$
$$= W^0 + Q_{lk}^0 V_{lk} - \frac{1}{2}\alpha_{lk,l'\kappa'}V_{lk}V_{l'\kappa'} + \ldots$$

These are the counterparts to eq 4. By differentiating the second expression with respect to the various spherical tensor potential components V_{lk} one can obtain expressions for the spherical tensor multipole moments for the charge distribution that include the effect of the external potential.

$$Q_{lk} = \frac{\partial W}{\partial V_{lk}} = Q_{lk}^0 - \alpha_{lk,l'\kappa'}V_{l'\kappa'} + \ldots$$
$$Q_{lk} - Q_{lk}^0 = -\alpha_{lk,l'\kappa'}V_{l'\kappa'} + \ldots$$

These are the counterparts to eqs 5 and 6. The second expression relates the *induced* spherical multipole to the external field and the polarizabilities.

If we have induced multipole moments and polarizabilities in spherical tensor form, the equations above constitute a set of linear equations in the unknown potential gradients and Hessians. Considering only induced multipoles that are linear in field gradients and Hessians, the equations can be represented in matrix notation as follows

$$\begin{pmatrix} Q_{1\kappa} - Q_{1\kappa}^0 \\ Q_{2\kappa} - Q_{2\kappa}^0 \end{pmatrix} = -\begin{pmatrix} \alpha_{1\kappa,1\kappa'} & \alpha_{1\kappa,2\kappa'} \\ \alpha_{2\kappa,1\kappa'} & \alpha_{2\kappa,2\kappa'} \end{pmatrix}\begin{pmatrix} V_{1\kappa} \\ V_{2\kappa} \end{pmatrix}$$

The left side of this equation is a column vector consisting of eight known components: the three components of $Q_{1\kappa} - Q_{1\kappa}^0$ and the five components of $Q_{2\kappa} - Q_{2\kappa}^0$. The column vector on the right side consists, similarly, of eight unknown components: three for $V_{1\kappa}$ and five for $V_{2\kappa}$. The matrix of polarizabilities consists of four blocks, with the upper left being the three-by-three matrix of dipole−dipole polarizabilities, the lower right being the five-by-five matrix of quadrupole−quadrupole polarizabilities, and the off-diagonal blocks being the three-by-five and five-by-three matrix of dipole−quadrupole polarizabilities. Note that the off diagonal blocks are transposes of each other, and the matrix is symmetric. Recall that the Cartesian tensor form of this set of equations has a 12-by-12 block of polarizabilities with linear dependencies that result in a singular matrix. Since no such dependencies exist in the spherical tensor form, these equations can be readily solved. If one chooses to neglect quadrupole contributions and use only dipole−dipole polarizabilities in the analysis, the use of real spherical tensors is not required, and one is also free to use Cartesian tensors.

Supporting Information Available: Documents containing optimized molecular structures, multipole moments and polarizabilities for the molecules studied in this paper. This material is available free of charge via the Internet at http://pubs.acs.org.

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