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Derivation of Class II Force Fields. 4. van der Waals Parameters of Alkali Metal Cations and Halide Anions

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A critical survey of previously reported van der Waals parameters for alkali metal cations and halide anions is presented. A new set of force field parameters is proposed, derived by fitting the experimental lattice constants and lattice energies of 20 ionic alkali halide crystals. These parameters are constrained to satisfy two relationships connecting the ions with the isoelectronic noble gases—the relative van der Waals radii R^* and the coefficients of the London dispersion energies C_6—using the experimentally determined noble gas van der Waals parameters. In addition to reproducing physical trends in common with atoms of isoelectronic species, the present parameters predict more accurate crystal structures and energies and, when combined with a molecular force field for water, also quite accurate gas-phase ion−water interaction energies and aqueous solution structures compared to the computed results previously reported by other authors.

I. Introduction

Many chemical and biological properties involve the binding or transport of monatomic ions.[1] For example, these ions often play a role in the catalytic functions[2] and structural integrity of proteins.[3,4] Molecular mechanics and dynamics simulations can provide a detailed understanding of the ways in which ions influence the behavior of such systems.[3,4] As such, there is a clear need for reliable force field parameters for these ionic species. In particular, for modeling the behavior of monatomic ions, parameters are needed to describe the nonbonding interactions that occur between the ions and other chemical species.

In molecular modeling applications, nonbonded interactions involving ions or charged groups in biological molecules are usually approximated by a simple model which consists of sums of pairwise isotropic van der Waals (vdW) and Coulomb interactions. It has long been recognized that in many cases such a simple model can provide only a qualitative picture of the true interactions present, since additional types of interactions, such as charge polarization, may be significant when charged systems are involved.[5,6] Nevertheless, this model is still the only approach currently practical for large-scale molecular simulations. In this paper, we present nonbond van der Waals parameters for the alkali cations and halide anions, to be used with the class II CFF force field[7−10] for simulation studies of both small and macromolecular systems. Derivation and characterization of these parameters are discussed, as well as their analysis and comparison with the prior work of others.

Several differing techniques have been used to derive the vdW parameters for monatomic ions. In many molecular mechanics and dynamics studies of ions in solution, the relevant parameters were derived either from fitting results of *ab initio* calculations of ion−solvent complexes[11−16] or by fitting Lennard-Jones van der Waals potentials to experimental binding energies of such complexes.[16,17a] Others[17b−19] have directly used solution properties such as peak positions of the radial distribution functions of solvent molecules around the ions and relative as well as absolute free energies of solvation to derive their ion van der Waals parameters. The parameters derived by Lybrand *et al.*[17] were used by Cornell *et al.* in parametrizing the AMBER molecular force field.[20]

Another approach, taken by Heinzinger *et al.*,[21a] was to assign the experimental values for the corresponding parameters of the isoelectronic noble gases to the first five alkali cations and four halide anions.[22] They later showed that this assumption worked adequately for the cations but appears to be inaccurate for the anions.[21b] For the anions they systematically adjusted the vdW potentials of noble gases toward larger radii in order to model the corresponding isoelectronic anions,[21b] employing standard ionic radii. Interestingly, calculation of the peak positions of water radial distribution functions around these ion solutes was found to give good results compared to experiment, despite the seemingly simple assumptions used in deriving the parameters.

It should be pointed out that some of these parameter sets were derived only for ion−solvent pairwise interactions,[11,13,15] rather than being intrinsic ion parameters. These pairwise values are clearly of limited utility in general molecular modeling applications. Therefore, in this article we focus on the derivation and comparison of intrinsic ion vdW parameters.

Given the extreme variation in the vdW parameters reported by various authors and the range of accuracies in the resulting simulations, it is useful to address the following questions: (1) Are the magnitudes of these different sets of parameters similar? and (2) To what extent do the values of these parameters follow expected trends deduced from basic physics? The answers should point the way to the possible need for new models and how these might be developed. Specifically, this raises the further question: (3) If van der Waals parameters are determined that properly reflect the expected physicochemical trends of the individual species in terms of radii, polarizability, *etc.*, will they result in more accurate simulations spanning a range of differing types of computed properties and also differing environments (gas, solution, *etc.*)?

From the substantial number of published simulations dealing with systems in which monatomic ions are involved, it is surprising that, to our knowledge, there has not been any comprehensive comparison or critical evaluation of the differing

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ion vdW parameters. At least in those cases where the parameters were derived to model similar physical properties, their values might be expected to be fairly similar to each other, especially since the same model (functional form) was usually used to calculate the energies of interaction.

However, there are several factors that could lead to variation among the values of the vdW coefficients obtained by differing approaches. In solution studies, one such factor may be the use of differing solvent models, as pointed out by Aqvist[18] and Marrone and Merz.[19] Similarly, molecular dynamics (MD) or Monte Carlo simulations of solutions can be significantly affected by details of the simulation procedures in addition to the choice of the vdW potential.[18,19] One way to avoid the ambiguities introduced by differing simulation models for solutions is to derive nonbond parameters from properties of crystals. Crystal structures and lattice energies are excellent probes of nonbonded interactions. For example, experimental lattice constants and lattice energies of small amide and carboxylic acid crystals were used by Hagler *et al.*[23] to derive the nonbond terms required for simulating peptide and protein molecules. In the case of alkali metal cations and halide anions, all the lattice energies and structures of the resulting simple ionic crystals have been accurately measured experimentally.[24] However, as we will discuss below, this experimental data alone does not unambiguously determine the dispersion energies, nor the R^* and ϵ parameters, for the ions even in these crystals. Nevertheless this data can be augmented by *a priori* physical considerations such as the Slater−Kirkwood approximation[25] as well as by relationships among isoelectronic species. As will be demonstrated, ion parameters can be derived which obey these basic physical properties, reflecting known trends in the periodic table, and still account for solution and crystal properties. Examination of the previously derived parameters reveals that in many cases they violate some of these basic physical principles.

While derived van der Waals parameters may be dependent on the type of measurement or simulation used to determine their values, we require that the "best" parameters should accurately model a range of systems, including gases, aqueous solutions, and crystals. It is, therefore, also interesting to examine whether the set of ion parameters we report herein, which were derived from crystal data, can do as well in predicting solution and gas-phase properties as parameters derived specifically for these environments and, conversely, whether the previous parameters which have been derived based on gas-phase and solution models[12−19,21] can produce reasonable crystal properties of ionic salts.

The remainder of this paper is organized as follows. In the next section, the calculation methodology is presented, including computation of the four types of physical properties we have examined: crystal structures and lattice energies, ion−water dimerization energies, and aqueous solution structures. We then offer a critical examination of the existing vdW parameters for alkali and halide ions, with emphasis on their consistency (or lack thereof), ability to obey expected physical trends, and the possible reasons behind any deficiencies in these properties. In the following section, we present results from calculations of crystal properties using these previously reported parameters. We then describe in detail the procedure and rationale for deriving a new set of alkali and halide ion parameters from fits to crystal data, assisted by consideration of physical trends derived from the Slater−Kirkwood equation and relationships to isoelectronic noble gases. In the subsequent section, physical properties computed using these new ion parameters are tested against experimental gas-phase and solution data for several selected cases where accurate experimental and/or *ab initio* values are available for comparison. Finally, we present our conclusions.

II. Methodology

As mentioned above, experimental data corresponding to three different phases—gas phase, aqueous solutions, and crystals—may be used to derive and evaluate the ion parameters. In this work, crystal data was used to parametrize the present set of alkali and halide ion parameters, while solution and gas-phase data were employed only for testing. Below, we describe the computational procedures. All the calculations were performed on a Silicon Graphics Indigo-XZ/R4000, using MSI molecular graphics and simulation software, Insight II and Discover.[26]

Crystal Structures and Lattice Energies. There are 20 crystals of the alkali halide salts whose structures and lattice energies have been determined experimentally.[24] These crystals all possess face-centered cubic (fcc) symmetry, with four cations and four anions in a unit cell, except for CsCl, CsBr, and CsI, which have body-centered cubic (bcc) structures and only one cation and one anion in a unit cell. Due to the high crystal symmetries, one lattice constant for each of these crystals suffices to determine the crystal structure (since all three lattice dimensions are equal and the three lattice angles are all 90°). However, in all the crystal simulations carried out in this study, crystal symmetries were not imposed (so that all degrees of freedom of the crystal unit cell and the atomic positions of the ions were relaxed). The only constraints in the simulation were periodic boundary conditions. In each of these calculations the initial, experimental structure (with small asymmetric deformations) was optimized by minimizing the total energy of the crystal (*i.e.* lattice energy) which is the sum of the energies of the Coulomb and vdW interactions among the ions. Formal charges (±1) for the cations and anions were used. A cutoff distance of 15 Å was applied to the vdW contributions, while the Ewald summation method[27] was invoked to take into account long-range charge−charge interactions. Minimizations were considered converged when the largest gradient of the energy per unit cell was less than 0.001 kcal/(mol Å).

Solvent Structure in Aqueous Solutions. The simulation system for aqueous solutions was constructed by solvating an ion with 262 water molecules in a box of dimensions 20 Å•20 Å•20 Å. MSI's consistent force field (CFF)[7−10,28] was used for the water potential. This is essentially a scaled quantum force field with vdW parameters (R^* and ϵ) and partial charges ($+0.40e$ on the hydrogen atoms) that are very similar to those used in the SPC water model proposed by Berendsen *et al.*[29] It was adjusted by fitting various forms of ice structures and their lattice energies.[30] A cutoff distance of 9.5 Å was applied for both the vdW and Coulomb interactions, and periodic boundary conditions were imposed. Prior to an MD simulation the system was relaxed, with fixed cell dimensions and a gradient tolerance of 1.0 kcal/(mol Å), to avoid any high-energy contacts. The MD simulation began with a 10 ps equilibration of the system at a constant temperature (300 K) and constant pressure (1 atm) using Berendsen *et al.*'s heat bath scheme[31] with a coupling constant of 0.1 ps for the temperature and a similar procedure for the pressure. The time step used for the simulation was 1.0 fs. The system was then maintained at 300 K and 1 atm for 30 ps. During this period, snapshots of the system at every 100th time step were taken, and the coordinates saved. The first peak positions in the water radial distribution functions around each alkali metal and halide ion were obtained from the MD simulations in order to compare with the experimental results. Test calculations with the larger cutoff distance of 14.5 Å and

TABLE 1: Comparison of Published van der Waals Parameters (R^*, ϵ)[a] for Alkali Metal Cations and Halide Anions

ion	isoelectronic rare gas	rare gas[b]	Chandrasekhar *et al.*[c,d]	Pettitt *et al.*[e]	Marrone *et al.*[f]	Aqvist[d,g]	Lybrand *et al.*[h]	Heinzinger *et al.*[i]	Rappe *et al.*[j]
				R^* (Å)					
Li^+	He	2.96	1.41	1.51		2.39		2.66 (He)	2.30
Na^+	Ne	3.09	2.13	2.50	3.40	3.74		3.06 (Ne)	2.82
K^+	Ar	3.76		3.49	4.34	5.54		3.77 (Ar)	3.64
Rb^+	Kr	4.01				6.31		4.01 (Kr)	3.94
Cs^+	Xe	4.36				7.54		4.40 (Xe)	4.34
F^-	Ne	3.09	0.98	3.01				4.49	
Cl^-	Ar	3.76	4.96	4.36			4.99	5.46	
Br^-	Kr	4.01					5.19	5.57	
I^-	Xe	4.36						6.06	
				ϵ (kcal/mol)					
Li^+	He	0.022	6.25	0.174		1.83×10^{-2}		0.036 (He)	0.05
Na^+	Ne	0.084	1.61	0.151	0.040	2.77×10^{-3}		0.086 (Ne)	0.06
K^+	Ar	0.285		0.144	0.035	3.28×10^{-4}		0.268 (Ar)	0.07
Rb^+	Kr	0.399				1.71×10^{-4}		0.383 (Kr)	0.08
Cs^+	Xe	0.561				8.06×10^{-5}		0.509 (Xe)	0.09
F^-	Ne	0.084	720.	0.697				0.0119	
Cl^-	Ar	0.285	0.117	1.09			0.107	0.0401	
Br^-	Kr	0.399					0.090	0.0645	
I^-	Xe	0.561						0.0975	

[a] R^* is the separation distance at the minimum energy, and ϵ is the corresponding well depth for the vdW interaction energy between two like ions. [b] Reference 22b. [c] Reference 14. [d] R^* and ϵ are converted from the A and B constants reported in the original paper. [e] Reference 16. [f] Reference 19. [g] Reference 18. [h] Reference 17a. [i] Reference 21. Experimental rare gas parameters, obtained by analysis of Hogervorst's data (ref 22a), were assumed for all cations. [j] Reference 34.

a longer simulation time of 60 ps showed that the above simulation protocol consistently gave satisfactorily converged results for the first peak positions of the water radial distribution functions around the ions.

Binding Energies of Ion−Water Complexes. Dzidic *et al.*[32a] and Arshadi *et al.*[32b] have determined experimental gas-phase binding energies of ion−water dimers for the alkali cations and halide anions using mass spectroscopic measurements. These data are very useful and have previously been used in the derivation as well as testing of ion vdW parameters.[14,16,17a] In the present work we used them in the validation of our ion parameters, which were derived independently. The CFF water potential[30] was used, and each ion−water dimer was fully optimized to a maximum force per atom of less than 0.001 kcal/(mol Å), starting from an initial dimer configuration based on *ab initio* molecular configurations.[11]

III. Results and Discussion

A. Evaluation of Previous vdw Parameters for Alkali Metal and Halide Ions. *Discrepancies among Previous Parameters.* The most commonly used form of the potential is the Lennard-Jones "12-6" expression, for the interaction energy between centers i and j

$$V_{ij}{}^{\mathrm{vdW}}(R_{ij}) = \frac{A_{ij}}{R_{ij}{}^{12}} - \frac{B_{ij}}{R_{ij}{}^{6}} \tag{1}$$

where R_{ij} is the internuclear distance. There is rarely enough data to determine A_{ij} and B_{ij} for each possible pair of ions i and j, so a combination rule (see below) is invoked to obtain these constants from intrinsic parameters A_i and B_i of the individual species.[33] (B_i is often denoted C_6, and represents the leading term in the dispersion energy.)

The vdW potentials have been originally reported in differing but equivalent ways. The A_i and B_i are often reported directly, but are also reported in terms of the properties R^*_i (the separation corresponding to the minimum in the vdW potential for interactions between atoms of species i), or σ_i (the separation distance at which the vdW potential is zero), and ϵ_i (the depth of the vdW potential well). The relations between these parameters for the 12-6 potential are given by

$$R^*_i = 2^{1/6}\,\sigma_i = \left(\frac{2A_i}{B_i}\right)^{1/6} \tag{2a}$$

$$\epsilon_i = \frac{B_i^{\,2}}{4A_i} \tag{2b}$$

or conversely

$$A_i = 4\epsilon_i\sigma_i^{\,12} = \epsilon_i R^*{}_i^{\,12} \tag{2c}$$

$$B_i = 4\epsilon_i\sigma_i^{\,6} = 2\epsilon_i R^*{}_i^{\,6} \tag{2d}$$

with similar expressions for other types of potentials. Here, for purposes of comparison, wherever necessary the reported parameters have been converted from A_i and B_i to the more intuitive quantities R^*_i and ϵ_i: the vdW minimum energy separation distance and well depth at that separation.

Table 1 lists the vdW parameters of alkali metal and halide ions determined by various researchers in previous studies as well as the corresponding values of the isoelectronic rare gas. The first thing we note from this table is that this set of parameters is rather sparse; only Heinzinger *et al.*[21c] gives a complete set of parameters for all the alkali metal and halide ions. Further, going across the table one can see that, when transformed into a common representation, there is a wide range of parameter values for the same ion. For example, R^* for Li^+ ranges from the value of 1.41 Å (Chandrasekhar *et al.*[14]) to the value of 2.66 Å given by Heinzinger *et al.*,[21c] and its ϵ spans the range from 0.0183 kcal/mol (Aqvist[18]) to 6.25 kcal/mol (Chandrasekhar *et al.*). Even more extreme values are the R^* = 0.98 Å and ϵ = 720 kcal/mol for F^- of Chandrasekhar *et al.* compared to the F^- values found by other workers. Overall, as may be seen from the table, there are large discrepancies among these literature values for both the alkali and halide ion parameters.

Trends in the vdW Energy ϵ. Although there is considerable variation, the R^* values in Table 1 generally increase as expected on going from lighter to heavier elements. However, in analogy to the experimental R^* and ϵ values of noble gases,[22] one expects not only R^* but also ϵ values to increase on going vertically down the rows of the periodic table of elements.

$$\begin{gathered}\epsilon(\mathrm{I}^-) > \epsilon(\mathrm{Cl}^-) > \epsilon(\mathrm{Br}^-) > \epsilon(\mathrm{F}^-) \\ \epsilon(\mathrm{Cs}^+) > \epsilon(\mathrm{Rb}^+) > \epsilon(\mathrm{K}^+) > \epsilon(\mathrm{Na}^+) > \epsilon(\mathrm{Li}^+) \end{gathered} \tag{3}$$

Interestingly, however, excluding the very unusual F^- parameters of Chandrasekhar *et al.*,[14] the ϵ parameters derived by each of the research groups for the cations or the anions *decrease* rather than increase as the ion becomes larger, except for those of Heinzinger *et al.*[21c] and Rappe *et al.*[34] The ϵ values of Rappe *et al.* for the alkali cations were assumed to increase in equal increments (0.01, from 0.05 to 0.09 kcal/mol) between the ions from Li^+ to Cs^+ (see Table 1).

Trends in Isoelectronic vdW Radius R.* There are other trends which can be deduced from consideration of physical relationships among neighboring elements in the periodic table. For example alkali metal cations, neutral noble gases, and halide anions form families of isoelectronic species (such as Na^+, Ne, and F^-). Since the nuclear charge is greater by +1 in the alkali cation than that in the isoelectronic noble gas, its electrons are expected to be more tightly bound. Consequently, as pointed out by Heinzinger *et al.*,[21] its R^* is expected to be smaller than that of the noble gas. For example $R^*(\mathrm{Na}^+)$ should be smaller than $R^*(\mathrm{Ne})$. On the other hand, F^- should have a more diffuse electron cloud than its isoelectronic noble gas, Ne, due to the lesser nuclear charge of the anion, so that $R^*(\mathrm{F}^-)$ should be larger than $R^*(\mathrm{Ne})$. In summary, relations such as the following would be expected for isoelectronic species.

$$\begin{gathered} R^*(\mathrm{F}^-) > R^*(\mathrm{Ne}) > R^*(\mathrm{Na}^+) \\ \vdots \\ R^*(\mathrm{I}^-) > R^*(\mathrm{Xe}) > R^*(\mathrm{Cs}^+) \end{gathered} \tag{4}$$

The above isoelectronic relations and the experimental R^* and ϵ values of noble gases[22] form a very useful check on the ion parameters. In fact, as noted above, Heinzinger *et al.* simply transferred experimental noble gas parameters without change to the cations and achieved considerable success in reproducing experimental aqueous solution structures of these cations but found it necessary to modify somewhat the noble gas parameters to be used for the anions.[21] From Table 1, we see that the R^* values for Na^+ and K^+ by Aqvist[18] and Marrone and Merz[19] as well as those for Rb^+ and Cs^+ by Aqvist[18] are all *larger* (instead of smaller as required by the isoelectronic relationship) than the corresponding noble gas R^* values. For example, for Na^+ Aqvist reports $R^* = 3.74$ Å and Marrone and Merz report 3.40 Å, which are both larger than the observed value for Ne of 3.09 Å. Similarly, the R^* values for F^- from Chandrasekhar *et al.*[14] (0.98 Å) and Pettitt and Rossky[16] (3.01 Å) are too small as compared to the value of 3.09 Å for Ne. Again Rappe *et al.*'s R^* parameter values reflect the correct trend.[34] Finally we note that, physically, Heinzinger *et al.*'s approximation, which assumes equality with the isoelectronic noble gases for the cations, is of course still not rigorously correct, although in test calculations good results were obtained.[21b,c]

Trends in Dispersion Coefficients. A similar trend in the coefficients of the London dispersion term in the interaction energy ($-C_6/r^6$) can also be deduced. The Slater–Kirkwood approximation[25] relates C_6 coefficients to the number of outer-shell electrons n and polarizability α by

$$C_6 = {}^3/_4\sqrt{n\alpha^3} \tag{5}$$

so that given the same number of electrons more polarizable atoms or ions must have larger C_6 coefficients. Since polarizabilities for isoelectronic species such as F^-, Ne, and Na^+ are expected to decrease in that order due to the increasing nuclear charge (verified by the polarizabilities measured experimentally[35]), the following isoelectronic relationships among the C_6 coefficients should also hold:

$$\begin{gathered} C_6(\mathrm{F}^-) > C_6(\mathrm{Ne}) > C_6(\mathrm{Na}^+) \\ \vdots \\ C_6(\mathrm{I}^-) > C_6(\mathrm{Xe}) > C_6(\mathrm{Cs}^+) \end{gathered} \tag{6}$$

Table 2 compares the C_6 coefficients for the alkali metal and halide ions, either quoted directly or calculated from the reported vdW parameters, from the same studies summarized in Table 1. Again, significant discrepancies in the C_6 values are observed. For example, C_6 for Na^+ varies from the 15.1 kcal/(mol Å^6) value reported by Aqvist[18] to 300 kcal/(mol Å^6) by Chandrasekhar *et al.*[14] Also, C_6 for Li^+ and Na^+ by Chandrasekhar *et al.* are larger, instead of smaller, than C_6 of their isoelectronic noble gases. Aqvist's C_6 values[18] for the alkali cations are extremely small, especially for the heavier ones,

TABLE 2: C_6 Coefficients of Alkali Cations and Halide Anions Reported by Various Authors (as in Table 1) Compared to the C_6 Values of the Isoelectronic Noble Gases[a]

ion	noble gases	Chandrasekhar *et al.* [b]	Pettitt *et al.*[c,d]	Marrone *et al.*[e,f]	Aqvist[g]	Lybrand *et al.*[f,h]	Heinzinger *et al.* [d,i]	Rappe *et al.*[f,j]
Li^+	30 (He)	100	4.13		6.82		25.2	14.8
Na^+	146 (Ne)	300	73.7	124	15.1		141	60.3
K^+	1611 (Ar)		520	468	18.9		1540	326
Rb^+	3318 (Kr)				21.5		3170	599
Cs^+	7707 (Xe)				29.6		7390	1200
F^-	146 (Ne)	1200	1037				195	
Cl^-	1611 (Ar)	3500	15 000			3300	2110	
Br^-	3318 (Kr)					3520	4230	
I^-	7707 (Xe)						9670	

[a] Noble gas C_6 values are either experimental results or calculated from the experimentally measured R^* and ϵ parameters. See ref 22a. Units are kcal/(mol Å^6). [b] Reference 14. [c] Reference 16. [d] Computed from the σ and ϵ values reported in the original paper. [e] Reference 19. [f] Computed from the R^* and ϵ values reported in the original paper. [g] Reference 18. [h] Reference 17a. [i] Reference 21. [j] Reference 34.

while the C_6 value of 15 000 kcal/(mol Å^6) for Cl$^-$ from Pettitt and Rossky[16] is surprisingly large.

B. Possible Origins of the Lack of Agreement in Previous vdW Parameters. In light of these discrepancies and the conflicting as well as unphysical trends observed in the literature values for the alkali metal and halide ion parameters, one must address the question: How could one apparently achieve reasonably good fits to the experimental data with these disparate parameters?

As noted above, small errors or deficiencies in simulation methodology in deriving vdW parameters may result in significantly differing parameter values. More importantly, examination of the various ways that the parameters have been derived shows that in many cases there is likely to be insufficient data to uniquely determine the parameter values with precision. An example is the very small ion−water well depth ϵ for K$^+$ (0.001 450 kcal/mol) derived by Straatsma and Berendsen in fitting *ab initio* energies of gas-phase ion−water complexes.[13,36] The problem is likely compounded by the fact that the data fitted in each case—*ab initio* quantum mechanical structures and energies of complexes with water,[11−15] experimental measurements of these quantities[16,17] or experimental first-peak positions of solvent radial distribution functions around the ions, and free energies of solvation[18,19]—are properties which are determined primarily by balanced interactions of Coulombic attractions and van der Waals repulsions; contributions from attractive London dispersions are relatively quite small. This can be inferred, for example, from the *ab initio* study of Kisternmacher *et al.*[11c] They obtained binding energies of ion−water dimers for Li$^+$, Na$^+$, K$^+$, F$^-$, and Cl$^-$ ions from *ab initio* Hartree−Fock calculations. They showed that these *ab initio* calculated binding energies agree quite well with the experimental results.[11c,32] Since the Hartree−Fock method does not include contributions from London dispersion interactions,[37] the results of Kisternmacher *et al.*[11c] are an indication of relatively small London dispersion forces in these ion−water dimers near their equilibrium structures. In addition, the fact that Aqvist[18] was able to fit experimental alkali cation solution structures and energetics with very small C_6 coefficients (see Table 2) indicates that dispersion contributions are again small in these systems.

This difficulty of determining the dispersion components of van der Waals interactions in these ion-containing systems has likely contributed to ill-determined values of the ion vdW parameters in many reported studies. Consequently, the resulting parameters can vary significantly from study to study as has been observed above. This is exacerbated by the fact that these parameters are sensitive to the solvent model and computational strategies used.[18,19] Conversely, when this is the case, the resulting parameters that are developed in one type of simulation will have limited accuracy when applied to other chemical systems or environments (*i.e.* they are not transferable) as will be shown below.

C. Crystal Calculations Using Previous vdW Parameters. As mentioned in the Introduction, we need to evaluate ion parameters based on all available experimental data, including their abilities to predict crystal properties. However, because there is always both a cation and an anion in the alkali halide ionic crystals, parameters for both cations and anions are required to be able to carry out the calculations. Thus we are limited to evaluating Heinzinger's set[21c] (which is the only complete set) and the incomplete sets of Chandrasekhar *et al.*[14] and Pettitt and Rossky[16] (see Table 1). In these computations (and the ones described in section E below) the pairwise van der Waals parameters R^*_{ij} and ϵ_{ij} were formed from the intrinsic ion parameters R^*_i, R^*_j, ϵ_i, and ϵ_j using the combination rules employed by the authors of the cited parameter sets. For our force field, the combination rules have been described in ref 33. Heinzinger's force field used Kong's rules.[38] For the others standard arithmetic and geometric mean formulas were employed:

$$R^*_{ij} = (R^*_i + R^*_j)/2 \tag{7a}$$

$$\epsilon_{ij} = (\epsilon_i \epsilon_j)^{1/2} \tag{7b}$$

The calculated lattice constants for all 20 possible alkali halide crystals are compared to the experimental constants in Table 3. This table also includes our vdW parameters derived herein, as discussed below. The corresponding lattice energies are compared in Table 4. A test calculation with Heinzinger's parameters showed that employing arithmetic and geometric mean combination rules had little effect on the computed results, increasing the root-mean-square (rms) deviation in cell constants relative to experiment by only 0.01 Å, while the rms deviation in lattice energies decreased by only 0.4 kcal/mol.

As can be seen in Table 3, the unusually small radius and extremely large well depth of F$^-$ (Table 1) used by Chandrasekhar *et al.*[14] leads to a highly distorted LiF and NaF lattice with broken symmetries (Table 3) and unrealistic lattice energies (Table 4). This demonstrates the importance of testing parameters on a wide variety of experimental data since use of these F$^-$ parameters in conjunction with a TIP4P water model[39] seemed to give quite reasonable solution results.[14] Thus, although the computed properties can be insensitive to the values of these parameters for a single system such as aqueous solutions, there can clearly be a limit on their transferability to other environments.

Results with the remaining sets of parameters are mixed: those from Pettitt and Rossky[16] (for six out of the total 20 crystals) give the smallest rms error of 0.2 Å in cell constant but the largest rms error of 36 kcal/mol in lattice energy, while parameters from Heinzinger *et al.*[21c] give the smallest rms error of 9 kcal/mol in lattice energy but the largest rms error of 0.6 Å in lattice constant.

A closer examination of Tables 3 and 4 shows that the results from Heinzinger *et al.*'s parameters[21c] consistently *overestimate* the lattice constant by about 0.6 Å while systematically *underestimating* the lattice energy by about 9 kcal/mol on average. Since the predominant contribution to the lattice energy of an ionic crystal results from Coulombic attractions between oppositely charged neighboring ions held apart by the vdW repulsions, this trend is consistent with the vdW radii of the anions, the cations, or both being systematically too large. As noted above, those authors began with noble gas values and adjusted (increased) the radii of the anions, while the radii of the cations were set equal to noble gas values. The resulting radii for the anions satisfy known trends (eq 4), while these same trends suggest that the cation radii must be too large. These observations suggest that if we begin with the noble gas values for R^*, as did these previous authors, but require that both anionic and cationic vdW radii satisfy eq 4, thus systematically decreasing the sizes of the cations, the parameters would satisfy the isoelectronic trends and also correct the systematic errors in lattice constants and energies. This then was the initial approach taken here.

D. Derivation of New vdW Parameters from Fits to Crystal Data. The total nonbond function employed in the CFF force field is a "9-6-1" potential

TABLE 3: Experimental Lattice Constants and Deviations (in Parentheses) from Experiment of Alkali Halide Crystals Calculated with the Ion van der Waals Parameters Reported by Various Authors (in Angstroms)

crystal	expt[a]	this work[b]	Chandrasekhar *et al.*[c,d]	Pettitt *et al.*[d,e]	Heinzinger *et al.*[f]
LiF	4.03	4.15(+0.12)	*g*	3.71(−0.32)	4.63(+0.60)
LiCl	5.14	5.14(+0.00)	5.57(+0.43)	5.39(+0.25)	5.81(+0.67)
LiBr	5.50	5.50(+0.00)			6.19(+0.69)
LiI	6.00	5.99(−0.01)			6.78(+0.78)
NaF	4.63	4.70(+0.07)	*g*	4.36(−0.27)	5.05(+0.42)
NaCl	5.64	5.64(+0.00)	5.25(−0.39)	5.73(+0.09)	6.15(+0.51)
NaBr	5.98	5.98(+0.00)			6.50(+0.52)
NaI	6.47	6.43(−0.04)			7.05(+0.58)
KF	5.35	5.33(−0.02)		5.20(−0.15)	5.87(+0.52)
KCl	6.29	6.29(+0.00)		6.43(+0.14)	6.91(+0.62)
KBr	6.60	6.63(+0.03)			7.22(+0.62)
KI	7.07	7.07(+0.00)			7.72(+0.65)
RbF	5.63	5.59(−0.04)			6.16(+0.53)
RbCl	6.58	6.55(−0.03)			7.19(+0.61)
RbBr	6.89	6.89(+0.00)			7.50(+0.61)
RbI	7.34	7.33(−0.01)			7.98(+0.64)
CsF	6.00	5.96(−0.04)			6.60(+0.60)
CsCl	4.12	4.13(+0.01)			4.52(+0.40)
CsBr	4.29	4.34(+0.05)			4.70(+0.41)
CsI	4.56	4.61(+0.05)			4.95(+0.39)
ave		+0.01		−0.04	+0.57
rms		0.04		0.22	0.58
max		+0.12	+0.43	−0.32	+0.78

[a] Reference 24. [b] Pairwise parameters R^*_{ij} and ϵ_{ij} from intrinsic ion values *via* the combination rules in ref 33. The experimental crystal data were used in parametrization. [c] Reference 14. [d] Pairwise parameters R^*_{ij} and ϵ_{ij} from intrinsic ion values *via* arithmetic and geometric mean combination rules, eq 7. [e] Reference 16. [f] Pairwise parameters R^*_{ij} and ϵ_{ij} from intrinsic ion parameters *via* Kong's combination rules[38]. Reference 21. [g] In the cited study, for LiF the calculated cell dimensions are 1.00, 1.64, and 25.4 Å, and cell angles are 88.8, 56.8, and 109°. For NaF, they are 1.43, 4.58, and 5.03 Å and 81.9, 95.7, and 45.3°. Thus the experimental crystal symmetry was not preserved.

$$V_{ij}\,(R_{ij}) = \epsilon_{ij}\left\{2\left(\frac{R^*_{ij}}{R_{ij}}\right)^9 - 3\left(\frac{R^*_{ij}}{R_{ij}}\right)^6\right\} + \frac{q_i q_j}{R_{ij}} \tag{8}$$

where R_{ij} is the distance between ions i and j, R^*_{ij} and ϵ_{ij} are the corresponding vdW parameters for the ij ion pair, and q_i and q_j are the ionic charges. (In this representation the dispersion constant C_6 is given by $C_6 = 3\epsilon_{ij}R^*_{ij}{}^6$). The R^*_{ij} and ϵ_{ij} are related to the parameters of the individual ions, R^*_i, R^*_j, ϵ_i, and ϵ_j by the Waldman−Hagler combination rules,[33]

$$R^*_{ij} = \left(\frac{R^*_i{}^6 + R^*_j{}^6}{2}\right)^{1/6} \tag{9a}$$

$$\epsilon_{ij} = 2(\epsilon_i\epsilon_j)^{1/2}\,\frac{R^*_i{}^3 R^*_j{}^3}{R^*_i{}^6 + R^*_j{}^6} \tag{9b}$$

The forms of the vdW potential given by eqs 1 and 8 both have the advantage that only two parameters, R^*_{ij} and ϵ_{ij}, are required to specify their forms, as compared to others such as the Huggins−Mayer potential,[40] which requires three parameters. Studies of alkanes[41] and amide crystals[23] have shown that repulsive terms of the form $(R^*_{ij}/R_{ij})^9$ provide a better fit to both gas-phase and condensed-phase experimental data than the commonly used $(R^*_{ij}/R_{ij})^{12}$ form, the latter being too repulsive. The Waldman−Hagler combination rules have been shown to fit the properties of the noble gases more accurately than other expressions, and we have found that it also provides a more accurate fit to the properties of organic crystals.[42]

TABLE 4: Experimental Lattice Energies and Deviations (in Parentheses) from Experiment for Alkali Halide Crystals Calculated with the Ion van der Waals Parameters Reported by Various Authors (in kcal/mol)

crystal	expt[a]	this work[b]	Chandrasekhar *et al.*[c,d]	Pettitt *et al.*[d,e]	Heinzinger *et al.*[f]
LiF	242	253(+11)	*g*	306(+64)	232(−10)
LiCl	199	206(+7)	202(+3)	219(+20)	186(−13)
LiBr	190	193(+3)			175(−15)
LiI	178	179(+1)			161(−17)
NaF	214	224(+10)	*g*	257(+43)	213(−1)
NaCl	183	188(+5)	218(+35)	206(+23)	176(−7)
NaBr	174	178(+4)			167(−7)
NaI	163	167(+4)			155(−8)
KF	190	199(+9)		215(+25)	185(−5)
KCl	166	170(+4)		180(+14)	158(−8)
KBr	159	161(+2)			152(−7)
KI	150	152(+2)			143(−7)
RbF	181	191(+10)			177(−4)
RbCl	159	164(+5)			153(−6)
RbBr	153	157(+4)			147(−6)
RbI	145	148(+3)			139(−6)
CsF	173	181(+8)			167(−6)
CsCl	155	154(−1)			144(−11)
CsBr	150	147(−3)			139(−11)
CsI	142	139(−3)			134(−8)
ave		+4		+32	−8
rms		6		36	9
max		+11	+35	+64	−17

[a] Reference 24. [b] Pairwise parameters R^*_{ij} and ϵ_{ij} from intrinsic ion values *via* the combination rules in ref 33. The experimental crystal data were used in parametrization. [c] Reference 14. [d] Pairwise parameters R^*_{ij} and ϵ_{ij} from intrinsic ion values *via* arithmetic and geometric mean combination rules, eq 7. [e] Reference 16. [f] Reference 21. Pairwise parameters R^*_{ij} and ϵ_{ij} from intrinsic ion parameters *via* Kong's combination rules.[38] [g] In the cited study very large lattice energies of 5176 and 2637 kcal/mol are calculated for LiF and NaF crystals. See footnote *g* of Table 3 for the corresponding crystal structures.

As discussed above, even with this relatively simple expression for the potential $V_{ij}(R_{ij})$, the available crystal data of alkali halide salts alone are not sufficient to determine both the R^* and ϵ parameters independently as required in eq 8, due to the relatively small dispersion contributions in these ionic crystals. Thus inevitably the parametrization requires additional information or constraints as provided by, for example, the isoelectronic relationships presented in eqs 3 and 4. Since the analysis discussed above indicated that systematic modification of

Heinzinger *et al.*'s R^* and ϵ parameters should yield improved results, our first step was to keep their ϵ values (Table 1), which satisfy eq 3, but adjust the R^* values to satisfy the isoelectronic relationship in eq 4 (*i.e.* $R^*(F^-) > R^*(Ne) > R^*(Na^+)$, *etc.*) with the criterion of minimizing the systematic deviations from experiment found in the crystal calculations (Tables 3 and 4). Indeed, in this way we were able to essentially account for the crystal data of these halides, with rms deviations of only 0.06 Å for lattice constants and 3 kcal/mol for lattice energies and maximum deviations of 0.17 Å and 9 kcal/mol for both, respectively. These may be compared to the rms deviations of 0.59 Å and 9 kcal/mol, with maximum deviations of 0.71 Å and 15 kcal/mol for the unmodified parameters.

However, it was found that the revised R^* values along with the unmodified ϵ parameters of Heinzinger *et al.*[21c] do not always obey the relationship dictated by the Slater−Kirkwood equation relating the dispersion coefficients of the isoelectronic anions, neutrals, and cations (eq 6). Thus further refinement using the constraints provided by eq 6 is necessary. From the Slater−Kirkwood equation (eq 5), a relation between the C_6 values of differing isoelectronic species and their polarizabilities can be obtained:

$$C_6(F^-) = \left(\frac{\alpha_{F^-}}{\alpha_{Ne}}\right)^{3/2} C_6(Ne)$$

$$C_6(Na^+) = \left(\frac{\alpha_{Na^+}}{\alpha_{Ne}}\right)^{3/2} C_6(Ne) \quad etc. \qquad (10)$$

From eq 10, C_6 coefficients for the ions can be estimated provided that C_6 values of noble gases and the polarizabilities of both the noble gases and the ions are known. Experimental values of C_6 for the noble gases have been accurately determined.[43] Accurate experimental polarizabilities of noble gases can also be found in various compilations.[34] Finally, the polarizabilities of both the alkali metal and halide ions, although less well-defined, are available from Deltour,[35] who estimated these quantities by fitting experimental indices of refraction of alkali halide salt crystals.

Given the C_6 coefficients of the ions calculated from eq 10 and the revised R^* values that satisfy eq 4, the value of ϵ for the ions can be determined from the relation between C_6 and (R^*, ϵ) (*i.e.* $C_6 = 3\epsilon R^{*6}$). However, the resulting set of (R^*,ϵ) parameters systematically underestimates the crystal lattice constants slightly (average deviation ∼ −0.1 Å) and overestimates lattice energies (average deviation ∼ +10 kcal/mol), indicating that these vdW interactions between the ions are not repulsive enough. To increase the vdW repulsive forces between the ions to provide a better fit of the crystal data, we have scaled the ϵ parameters of the cations (or equivalently the C_6 coefficients, since ϵ and C_6 are proportional to each other at a given R^*). We found that scaling factors of 2.9 for Li^+ and 1.5 for the rest of the cations are able to minimize the systematic errors in the calculated lattice constants and lattice energies of the 20 alkali halide salt crystals, while maintaining the proper relative magnitudes among isoelectronic anions, neutrals, and cations for R^*, ϵ, and C_6.

An alternative to the Slater−Kirkwood relationship (eqs 5 and 10) for obtaining the C_6 coefficients would be to calculate them from first principles such as by using density functional theory as described by Mahan[44] and Bartolotti *et al.*[45] However, we found that use of Bartolotti *et al.*'s C_6 coefficients also produces systematic errors in the calculated crystal properties (in conjunction with the R^* values determined earlier) and thus requires scaling as well. Hence the need for the scaling may be due to the fairly simple functional form of the potential (eq 8) we have employed, resulting in neglect of C_8, C_{10}, and higher order terms in the attractive potential.[46]

TABLE 5: The R^* and ϵ Parameters for the 9−6 van der Waals Potential (See Eq 8) Derived in This Work for Alkali Metal Cations and Halide Anions Compared to Experimental Values for the Isoelectronic Rare Gases

	R^* (Å)		ϵ (kcal/mol)	
ion	rare gas[a]	present work	rare gas[a]	present work
Li^+	2.96	2.40	0.022	0.017
Na^+	3.09	3.03	0.084	0.052
K^+	3.76	3.60	0.285	0.173
Rb^+	4.01	3.90	0.399	0.226
Cs^+	4.36	4.30	0.561	0.312
F^-	3.09	4.60	0.084	0.017
Cl^-	3.76	5.22	0.285	0.062
Br^-	4.01	5.47	0.399	0.083
I^-	4.36	5.77	0.561	0.123

[a] Reference 22b.

TABLE 6: Effective C_6 Coefficients Derived in This Work for the Alkali Metal and Halide Ions Compared to Experimental Noble Gas Values. Note That the Isoelectronic Relationships, C_6(Anion) > C_6(Noble Gas) > C_6(Cation), Are Satisfied

halide anions		noble gases[a]		alkali cations	
		He	30	Li^+	9.5
F^-	469	Ne	146	Na^+	120
Cl^-	3750	Ar	1611	K^+	1130
Br^-	6670	Kr	3318	Rb^+	2380
I^-	13600	Xe	7707	Cs^+	5920

[a] The noble gas C_6 values are calculated from the R^* and ϵ parameters determined by experiment. See ref 22b. Units are kcal/(mol Å^6).

The final R^* and ϵ parameters derived in this way for the halide anions and alkali metal cations are presented in Table 5, while the corresponding C_6 coefficients are given in Table 6. Results for the calculated crystal properties with these vdW parameters are listed in Tables 3 and 4 along with the experimental values and results obtained from previously reported parameters, as discussed earlier. As can be seen, the fits to the crystal data are quite good. The average, rms, and maximum deviations are, respectively, +0.01, 0.04, and +0.12 Å in lattice constants, and +4, 6, and +11 kcal/mole in lattice energies. For both properties these results are more accurate than those achieved with any of the four previous sets of vdW parameters cited, while at the same time the parameters obey fundamental trends implicit in the periodic table as well as the physics contained in the Slater−Kirkwood equation.

Obviously, the above step-by-step parametrization procedure is by no means ideal due to the lack of sufficient experimental observables needed to pin down both the R^* and ϵ parameters simultaneously. Nonetheless, the resulting values are now physically reasonable in that they obey the inequalities of eqs 3, 4, and 6. In addition, compared to previous parameters used in the literature (Table 1), they give better results for the alkali halide crystal structures and energies (Tables 3 and 4). As discussed below, they also give accurate results for solution structures and ion−water binding energies, even though the latter two properties were not involved in the fitting.

E. Comparison of Water Interaction Parameters. The values listed in Tables 1 and 2 all refer to hypothetical like-ion interactions. As discussed above, some of the parameters that have been reported by other authors were derived and tabulated for a single specific interaction, such as between the ion and water. In this case, combination rules are not required, but the

TABLE 7: Interaction Parameters of Alkali Metal Cations and Halide Anions with Water Oxygen

	R^*(Å)			
ion	CFF water[a] arithmetic mean	CFF water[a] WH comb rule[d]	SPC water[b] WH comb rule[d]	Straatsma and Berendsen[c]
Li^+	3.00	3.26	3.22	
Na^+	3.32	3.38	3.34	3.20
K^+	3.60	3.60	3.58	5.07
Rb^+	3.75	3.77	3.75	
Cs^+	3.95	4.03	4.01	
F^-	4.10	4.24	4.23	3.42
Cl^-	4.41	4.73	4.72	4.21
Br^-	4.54	4.94	4.93	4.30
I^-	4.69	5.19	5.19	

	ϵ (kcal/mol)			
ion	CFF water[e] geometric mean	CFF water[e] WH comb rule[d]	SPC water[f] WH comb rule[d]	Straatsma and Berendsen[c]
Li^+	0.068	0.037	0.029	
Na^+	0.119	0.105	0.080	0.048
K^+	0.218	0.218	0.164	1.45×10^{-3}
Rb^+	0.249	0.242	0.180	
Cs^+	0.292	0.256	0.189	
F^-	0.068	0.053	0.039	0.132
Cl^-	0.130	0.078	0.056	0.128
Br^-	0.151	0.080	0.058	0.118
I^-	0.184	0.085	0.061	

[a] CFF force field, oxygen $R^* = 3.608$ Å. [b] SPC force field, ref 29, oxygen $R^* = 3.558$ Å. [c] Reference 13. [d] Waldman−Hagler combination rules, ref 33. [e] CFF force field, oxygen $\epsilon = 0.274$ kcal/mol. [f] SPC force field, ref 29, oxygen $\epsilon = 0.155$ kcal/mol.

resulting parameters cannot be applied to any other type of system. Of course the values will then also depend on the water parameters employed.

In order to present a comparison of the values of the interaction terms corresponding to differing water models and combination rules, Table 7 lists the interaction vdW parameters between the nine alkali and halide ions and the oxygen atom of water. The values in the first three columns of data are based on the ion values derived herein and (1) the CFF water vdW potential with the arithmetic and geometric combination rules in eq 7, (2) the CFF water potential with the Waldman−Hagler combination rules[33] in eq 9, and (3) the Waldman−Hagler combination rules but with the SPC water model.[29] Finally, the last column shows the interaction parameters between five of the ions and the water oxygen atom derived by Straatsma and Berendsen[13,36] using the SPC potential for the oxygen. Not surprisingly, the interaction parameters in the first three columns are much more alike than those corresponding to the like-ion interactions. CFF and SPC values are quite close, especially for R^*. The values from the Waldman−Hagler rules weight the larger of the values of R^*_i and R^*_j more heavily than does the arithmetic mean, leading to systematically larger values of the combined R^*_{ij} and smaller values of ϵ_{ij} than those from the arithmetic−geometric mean combination rules. But in all cases the present interaction parameters also show the expected trends in R^* and ϵ with increasing atomic numbers, while the Straatsma and Berendsen values of ϵ decrease with increasing atomic numbers.

F. Test Calculations on Solution and Gas-Phase Properties. The interactions between alkali metal and halide ions and water molecules have been studied extensively, both in the gas phase and in aqueous solution. For example Dzidic *et al.*[32a] and Arshadi *et al.*[32b] have measured the ion−water dimerization energies in the gas phase for all the alkali cations and halide anions. In aqueous solution, peak positions of water radial distribution functions around the ions have also been measured by X-ray and neutron diffraction methods.[47] As mentioned above, these valuable experimental data are often used to derive ion vdW parameters. In the following, we will use them to evaluate the new alkali metal and halide ion parameters presented above.

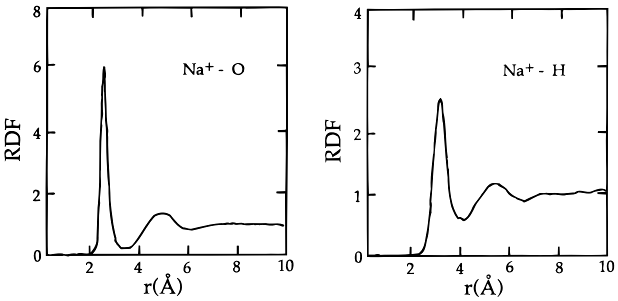

Figure 1. Radial distribution functions of Na^+−O (left) and Na^+−H (right) distances for Na^+ in water as computed with the ion parameters derived herein and the CFF force field.

TABLE 8: Calculated First-Peak Positions of Water−Ion Radial Distribution Functions Compared to Experiment

	ion−O distance (Å)		ion−H distance (Å)	
ion	expt[a]	this work	expt[b]	this work
Li^+	2.1, 1.95[b]	1.9	2.6	2.7
Na^+	2.4	2.3		3.0
K^+	2.8	2.7		3.4
Rb^+	2.9	2.9		3.6
Cs^+	3.1	3.1		3.8
F^-	2.6	2.7		1.7
Cl^-	3.2	3.2	2.2	2.2
Br^-	3.4	3.4		2.4
I^-	3.7	3.7		2.7

[a] From X-ray diffraction data in ref 47a unless otherwise noted. [b] Neutron diffraction results, refs 47b,c.

Experimental and Calculated Radial Distribution Functions in Water. The radial distribution function (rdf) around each ion was computed by analysis of the molecular dynamics simulations described in the Methodology section. For example, the Na^+−H and Na^+−O rdfs for Na^+ in liquid water are shown in Figure 1. These are very similar to other computed Na^+−water rdfs that have previously been reported.[14−16,19] Most of these are characterized by an Na^+−O distribution that reaches a first maximum of about 6 near 2.3 Å with a second maximum of about 1.5 near 5 Å and weak second minimum near 6 Å. The Na^+−H distributions reach a maximum value between 2 and 3 near 3 Å with a second maximum near 5.5 Å. The only exceptions are the two Chandrasekhar *et al.* distributions,[14] for which the Na^+−H maximum reaches 3.5 and whose Na^+−O distribution shows no second minimum. Their unusually sharp rdfs may result from their unusually large value of ϵ for Na^+ (see Table 1).

A measure of the rdfs that can be directly compared with experiment is the distances corresponding to the first maximum. These computed results are compared with the experimental values in Table 8.

As can be seen from this table, deviations are consistently no more than 0.1 Å. The calculated Li^+−oxygen first-peak position, 1.9 Å, agrees better with the neutron diffraction result of Newsome *et al.*,[47b] 1.95 Å, than with the 2.1 Å X-ray diffraction value listed by Marcus.[47a] The agreement is also within 0.1 Å for the two experimentally determined ion−hydrogen first-peak positions.

The computed rdf values previously reported are generally close to ours.[14,19] For example our value for Na^+ (2.3 Å *versus*

TABLE 9: Calculated Binding Energies ΔE (kcal/mol) of Ion−Water Dimers in the Gas Phase Compared to Experiment. Deviations from Experimental ΔH Values Are Given in Parentheses

ion	expt[a] $-\Delta H$	this work $-\Delta E$	Aqvist[b] $-\Delta E$	Lybrand *et al.*[c] $-\Delta E$	*ab initio*[d] $-\Delta E$	$-\Delta H$
Li^+	34.0	32.3(−1.7)	31.7(−2.3)		35.2	34.1(+0.1)
Na^+	24.0	24.0(+0.0)	22.8(−1.2)	23.9(−0.1)	24.0	23.3(−0.7)
K^+	17.9	18.2(+0.3)	17.8(−0.1)	17.8(−0.1)	16.6	16.2(−1.7)
Rb^+	15.9	16.2(+0.3)	16.3(+0.4)			
Cs^+	13.7	13.9(+0.2)	14.3(+0.6)			
F^-	23.3	19.8(−3.5)			23.7	22.2(−1.1)
Cl^-	13.1	13.3(+0.2)		13.0(−0.1)	11.9	11.3(−1.8)
Br^-	12.6	11.9(−0.7)				
I^-	10.2	10.4(+0.2)				

[a] Reference 32. [b] Reference 18. [c] Reference 17a. [d] Reference 11d.

the experimental value of 2.4 Å) may be compared to the value obtained with parameters optimized by liquid solution simulations: 2.55 Å by Marrone and Merz[19] (who obtained 2.45 Å using Aqvist's parameters[18]). Thus the present results indicate that the solvent (water) structures around the ions are well-predicted. This occurs despite the fact that the ion parameters were derived from crystal data and are also completely independent of the derivation of the water potential.[29,30]

Computed and Experimental Gas-Phase Interaction Energies. Table 9 shows the calculated binding energies of the ion−water complexes in the gas phase, that is, the energy, not including nuclear motions, for formation of the most stable gas-phase structure using the vdW parameters derived above. Their structures are, for example,

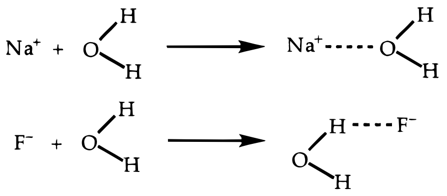

Table 9 also compares the results with experiment,[32] with *ab initio* (Hartree−Fock) calculations,[11c] and with the energies predicted with the parameters of Aqvist[18] (obtained from computed free energies of aqueous solutions) and Lybrand *et al.* [17a] (parametrized by fits to experimental and *ab initio* data for these same gas-phase complexes). The symmetries of the optimized geometries obtained with the present vdW parameters agree precisely with the *ab initio* results in each case (C_{2v} symmetry for alkali cations, C_s for F^- and Cl^-). For Br^- and I^-, structures with C_{2v} symmetry are obtained. Except for the smallest cation and anion, Li^+ and F^-, the calculated deviations of our computed energies from experiment are all 1 kcal/mol or less.

A similar, larger deviation for Li^+ was also observed in Aqvist's results[18] which are included in Table 9. Such deviations may be attributed to the larger polarization effects expected for the smaller ions, since their centers of charge can come closer to the electron distribution of the water molecule. The differences between ΔE and ΔH are expected not to be significant—on the order of 1 kcal/mol—as can be inferred from the *ab initio* calculations[11c] (see Table 9).

Thus from the test calculations reported in this section, it is clear that these vdW parameters determined for the alkali halide crystals also accurately reproduce both the radial distribution functions about the ions in liquid water and also the structures and energies of the ion−water complexes in the gas phase.

IV. Summary

We have conducted a survey of the existing van der Waals parameters for alkali metal and halide ions, motivated by the need for accurate and consistent force field parameters for these ions to be used in molecular mechanics and dynamics studies, particularly for biological systems. It was found that there are large discrepancies in the ion parameters derived by different workers and that physical trends expected from relationships to neighboring species in the periodic table, especially the isoelectronic noble gases, are often not satisfied. It was proposed that the lack of a sufficient number of experimental observables, along with the relatively small dispersion contributions to the interaction energies in the ions, are the main causes for the ill-determined ion vdW parameters that have previously been reported. To remedy this problem, constraints on the vdW radii R^* and the coefficients of the London dispersion energy C_6 were imposed in the present parametrization to ensure that the derived ion parameters obey their isoelectronic relationships with noble gases. This approach has the advantage of utilizing the accurate experimentally determined vdW parameters of noble gases to restrain the parametrization. It was also pointed out that the use of crystal data avoids the uncertainties introduced by the choice of a solvent model in parametrizations based on fitting solution data. The experimental crystal structures and lattice energies of 20 alkali halide ionic salts were fit. The resulting parameters are physically more reasonable than many of those used in the literature since they obey the expected relationships inherent in the periodic table. Furthermore, and perhaps more importantly, they reproduce the experimental data for properties of three different phases—crystal structures and energies, aqueous solution structures, and gas-phase ion−water binding energies—*even though in the present work the latter two properties were not included in the fit.* The overall accuracies with this parameter set compare favorably in each case with those employing previously reported vdW parameters.

An extension of this approach may also be applied to other ions, such as Ca^{+2}, Mg^{+2}, Fe^{+2}, and Zn^{+2}, that are also important for biomolecular simulations. Crystals of these cations are more difficult to treat accurately by the methods described herein due to the increased tendency of the charge distributions to polarize or participate in partial covalent bonding, especially in crystals containing the heavier anions. Work on these additional cations is currently being pursued in our laboratories.

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