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Ionic Hydrogen-Bond Networks and Ion Solvation. 1. An Efficient Monte Carlo/Quantum Mechanical Method for Structural Search and Energy Computations: Ammonium/Water

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Hydrogen-bond networks about solvated ions can form many alternative structures, requiring extensive conformational searches with accurate but affordable energy computation. For this purpose we are combining Monte Carlo searches with a computationally efficient density-functional-based tight-binding (DFTB+) method. The approach is tested for the stepwise hydration energies of the ammonium ion in $NH_4^+(H_2O)_n$ clusters ($n = 1-8$), for which experimental data are available. For each cluster size n, we perform Monte Carlo searches, where for each conformation we calculate the minimized energy using the DFTB+ method (and, for comparison, using MM3 or OPLS-AA force field). The Monte Carlo/DFTB+ search identifies the lowest energy structure that can be reoptimized with other quantum mechanical methods (here with HF, B3LYP, B3PW91, MP2, DFT, and CBS-Q, CBS-QB3, and CBS-APNO methods). Calculated geometries and charge densities for the clusters are also presented. The results show that the binding energies calculated by the DFTB+ method reproduce the values measured experimentally and predicted by highly correlated, but significantly more computationally intensive, ab initio quantum chemical methods. The encouraging results suggest that the Monte Carlo/DFTB+ approach is a computationally efficient quantum chemical method for relatively large solvated systems, as demonstrated here for cluster ions.

Introduction

The solvation of ions is fundamental to many natural and industrial processes, such as acid/base equilibrium, catalysis, electrolytes, and chemistry in ionizing astrochemical environments. Ion−solvent interactions involve strong ionic hydrogen bond networks, as reviewed recently.[1−3] In biology, ion solvation is important in enzyme activity, protein and RNA and DNA folding, and membrane transport.[3−5] These functions involve ionic sites, such as protonated amine functions, that are partially or fully solvated. Understanding of $N^+-H\cdots$water ionic hydrogen bonding, a subclass of cation−solvent interaction, will help us to understand the functions of protonated basic amino acid residues, such as His, Lys, Arg, N-terminal amine; protonated amino terminals of zwitterions at active sites of proteins and amino sugars; and the ammonium ion itself as a biological reservoir of ammonia.[6]

Fundamental understanding of ion solvation requires addressing the following questions:

What is the nature of the bonding between the ion and the nearest solvent molecules (orbital interactions, electrostatic, resonance charge-transfer, covalent contributions, as well as energy and geometry of the inner solvent shell)?

What is the relation between clusters amenable to computation and experiment and the structures of the outer solvent shells in bulk solvation?

How far does the effect of the ion extend into the solvent, and how many solvent molecules are required for convergence to macroscopic solvation? In other words, how many solvation shells need to be added, and how should they be modeled, explicitly or implicitly?

For organic ions, what is the relation between solvation of charged headgroups and of the hydrophobic substituents?

How can one extrapolate from clusters to obtain single-ion solvation energies, and how do these results compare with experimental values?

What are the contributions of various physical factors (dielectric, cavity, hydrogen bonding, as well as “hydrophilic” and “hydrophobic” terms) to the solvation of ions with diverse structures?

How does solvation in clusters and bulk solvent relate to solvation in membranes/surfaces/interfaces?

What is the relation among the solvation of cations, anions, ion pairs, and zwitterions?

In the present series of papers, we shall combine advanced computational methods and available experimental data to address these questions in the solvation of organic and biological ions. In this paper, the first in the series, we present an efficient computational procedure for performing conformational searches combined with energy calculations for ammonium−water cluster ions containing one to eight H_2O molecules, to model ion−solvent interactions in the inner solvent shells near the ammonium ion. In following papers, we shall extend this approach to larger clusters and more complex cations, anions, and ion pairs.

Fundamental properties of ammonium−water hydrogen bonds can be addressed by combining experiments using mass spectrometry and state-of-the-art quantum chemical methodolo-

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gies to study protonated $BH^+(H_2O)_n$ clusters (B = NH_3 and alkylamines).[7-10] The properties of these clusters provide significant insights into intimate ion–solvent interactions in the inner shells and allow a systematic stepwise approach toward macroscopic solvation.[1]

Experimentally, the stepwise hydration energies of ammonium have been measured with a series of equilibriums (eq 1).[10-13]

$$NH_4^+(H_2O)_{n-1} + H_2O \rightarrow NH_4^+(H_2O)_n \qquad (1)$$

The stepwise hydration energies (i.e., minus reaction enthalpies $-\Delta H_s$) for the first seven molecules of water to ammonium are shown in Table 1. The stepwise hydration energies decrease from 84.5 ± 1.5 kJ/mol for the first H_2O molecule (two recent data sets) until they approach and then undershoot the limiting value at infinity, 44 kJ/mol, which is the macroscopic bulk enthalpy of water.[14]

The fact that the stepwise hydration enthalpies for $n = 6$ and 7 (38 and 35 kJ/mol as listed in Table 1) undershoot the macroscopic limit (and then reach it again at large n) suggests that the binding energies may oscillate about the limiting value with further increasing n, as observed in measurements on the stepwise solvation of proton.[15] Some structural information for the observable clusters $NH_4^+(H_2O)_n$ ($n = 2-6$) has been proposed on the basis of vibrational predissociation spectroscopy.[16,17] In particular, hydrogen-bonded single and double rings have been suggested for clusters containing three to six cluster water molecules.[16]

Theoretical calculations provide a useful complementary tool to study the geometries and energetics of ionic hydrogen bonds.[2,17-19] Calculations can provide fine details of potential energy surfaces, and at the same time, they can expand the experimental data to larger clusters and more isomers. For example, the structure, vibration, and dynamics of ammonium in aqueous solution have been studied extensively with classical[20] and ab initio[17,21-23] (with a small cluster model $n \leq 5$) molecular simulations, to compute bulk solvation energies and to rationalize the fast rotation[21] of ammonium within strongly binding water cages. Ab initio calculations have been applied to identify structures and assign the corresponding vibrational spectroscopic data of the small clusters ($n \leq 6$) in experiment.[17df] In addition, simple electrostatic models have shown that NH_4^+ appears isotropic to the solvent beyond about 3.5 Å (1 Å = 0.1 nm), making such rotation possible.[24]

Theoretical Approaches to Solvation and Hydrogen Bonding. Stepwise hydration can be calculated on the basis of the reaction energy of eq 1:

$$\Delta E = E_{NH_4^+(H_2O)_n} - E_{NH_4^+(H_2O)_{n-1}} - E_{H_2O} \qquad (2)$$

Experiments show that for cluster sizes n up to 5 H_2O molecules the stepwise hydration energy ($-\Delta E$) decreases with n until it approaches the macroscopic water condensation enthalpy of 44 kJ/mol, and then it fluctuates around this value for $n > 5$. In principle, this might allow extrapolating from clusters to full bulk solvation energies to find single-ion solvation energies in truly single-ion systems.[1]

Reliable and accurate quantum chemical calculations on larger clusters may help assess the validity of this approach and explain its thermochemical and electronic structure basis. However, a full quantum chemical treatment of $NH_4^+(H_2O)_n$ clusters using conventional ab initio electronic structure methods is limited to a relatively small number of H_2O molecules, because the complexity and the large number of local minima in the potential energy surface significantly increases with n.[17]

Classical molecular dynamics simulations (CMD), based on molecular mechanics (MM) force fields, constitute one of the most computationally efficient methods to study large ion/solvent assemblies. In general, MM force fields treating the different interatomic interactions in a molecular system are expressed as a sum of functions describing bond stretches, chemical angle changes, rotations about chemical bonds (torsions), electrostatic and nonbonded interactions, as well as hydrogen-bonding and even coupling/cross terms. Most force fields use either fixed charges or bond dipoles to compute the electrostatic interaction components, while others include empirical terms that consider polarizable atomic charges and multipole electrostatics.[25-28] In addition, some MM approaches include an extra term comprising a Lennard-Jones structural formulation in order to explicitly treat hydrogen bonds. It has been found that TIP[29] and SPC[30] MM water models with parameters treating the mixed electrostatics–hydrogen bond interactions perform reasonably well in protein simulations. Despite their success, MM force fields based on fixed-charge models do not account for important quantum effects such as polarization and resonant charge transfer that sometimes can dominate the dynamics and thermochemistry of water-solute interactions. More recently, force fields including charge polarization have been developed.[31] The most popular approaches in this area have been the use of a fluctuating charge model with the CHARMm (abbreviation of *c*hemistry at *Har*vard *m*acromolecular *m*echanics) force field and the OPLS/PFF force field based on polarizable dipoles by Brooks and collaborators.[32] As pointed out by Friesner,[33] despite initial encouraging results obtained in the simulation of 22 small proteins and also on 2 ns CMD simulation of the bovine pancreatic trypsin inhibitor (BPTI), further work leading to a systematic improvement and validation of these methods is necessary. In this work, we use the OPLS-AA[20] and MM3[28] models in our simulations for NH_4^+–water clusters.

In principle, conventional electronic structure calculations based on highly correlated ab initio methodologies provide a systematic approach that can accurately treat quantum effects, such as charge-transfer, polarization, charge density fluctuations, and dispersion forces, important in the proper description of solvent–solute interactions.[34] However, the use of these methodologies is limited by the complexity of the potential energy surfaces of relatively large systems. Despite major advances in the development of efficient computational algorithms and the advent of powerful hardware, state-of-the-art quantum chemical calculations can only be used to compute single-point energy calculations of molecules of up to 100 atoms, and their use to probe molecular conformations and the dynamics of molecules in solution is hampered by their prohibitive computational cost. Thus, in the case of $NH_4^+(H_2O)_n$ clusters, performing a comprehensive conformational search with ab initio calculations already becomes impractical for $n > 4$, even with very computationally efficient density functional theory methods (DFT).[17]

Recently, a more efficient parametric Hamiltonian quantum mechanical method based on density functional theory has been developed. The self-consistent charge density functional theory based tight binding (SCC-DFTB) method, developed by Frauenheim and co-workers, belongs to the class of semiempirical methods that is related to a second-order expansion of the DFT total energy, E, with respect to charge density variation:[35]

$$E = \sum_{i}^{\mathrm{occ}} \langle \varphi_i | \hat{\mathrm{H}}^0 | \varphi_i \rangle + \frac{1}{2} \sum_{A,B} \gamma_{AB} \Delta q_A \Delta q_B + E_{\mathrm{rep}} \qquad (3)$$

In eq 3, the first term corresponds to the sum-over-states of a one-electron Kohn−Sham-type Hamiltonian parametrized from a well-known reference electron density, the second term depends on the Coulomb-correlation-exchange kernel representing a second-order correction due to charge density fluctuations from a reference value, and E_{rep} contains corrections for double-counting in the sum-over-states and the ion−ion repulsion (fitted with a polynomial or spline function). With proper treatment on the eigenvalue solver, computational complexity can scale linearly with the size of the system as in the DFTB+ program,[36] making it feasible to conduct conformational searches of relatively large systems such as ammonium−water clusters with $n > 4$.

In this work, we assess the performance of DFTB+ as well as the MM force fields OPLS-AA and MM3 in the conformational search of $NH_4^+(H_2O)_n$ ($n = 1-8$) to generate global minimum energy structures that are used in the calculation of stepwise hydration energies with these models and conventional ab initio quantum chemical methodologies. These results are compared directly with the experimental values available in the literature.[11−13]

Computational Methods

The computational procedure for searching the lowest energy of the $NH_4^+(H_2O)_n$ clusters includes the following steps:

(1) For each cluster n, a starting geometry is selected by adding one more water molecule to the previous cluster ($n - 1$) (starting with the unsolvated NH_4^+ ion).

(2) Using a Monte Carlo move, a new conformation is formed.

(3) The minimized energy of the new conformation is calculated by the tight-binding method (or, alternatively, with either MM3 or OPLS-AA force fields).

(4) The cluster energy in step 3 is compared with the cluster energy from the previous cycle for the same cluster size n. If the new energy is lower, this energy and the corresponding geometry are saved, and the previous value is discarded; the Monte Carlo move is kept when Metropolis sampling accepts the current energy.

(5) Steps 2−4 are repeated until the lowest energy (within ±0.1 kJ/mol) for a given n appears 10 times. This energy (may belong to the same or different structures) is used as the global minimum energy, and the structure corresponding to this energy from the last computation cycle is considered as the global lowest energy structure for cluster size n. Note that different runs of the procedure may give different lowest energies and

TABLE 1: Stepwise Hydration Energies (in kJ/mol) for $NH_4^+(H_2O)_n$ Clusters ($n = 1-8$) Computed at the AM1, PM3, PM6, OM1, OM2, OM3, HF/aug-cc-pVTZ, PBE/aug-cc-pVTZ, B3LYP/aug-cc-pVTZ, B3PW91/aug-cc-pVTZ, MP2/aug-cc-pVDZ, CBS-QB3, CBS-Q, and CBS-APNO Levels of Theory Using the Lowest Energy Structures Obtained with the Monte Carlo Search Procedure Proposed in This Work Combined the DFTB+ Quantum Chemistry Method[a]

	$n = 1$	$n = 2$	$n = 3$	$n = 4$	$n = 5$	$n = 6$	$n = 7$	$n = 8$
expl[b]	86.2[e] 83.3[d] 72.4[c]	72.8[e] 61.5[c] 57.3[d]	57.3[e] 56.1[c] 51.0[d]	51.0[c] 45.2[d]	44.4[d] 41.0[c]	38.0[d]	35.0[d]	−
AM1	64.0	59.5	45.4	51.4	28.4	38.5 (46.5)	30.9 (34.7)	43.7
PM3	56.4	50.7	45.0	39.5	40.8	39.7 (29.1)	42.5 (29.5)	36.8
PM6	64.2	56.7	51.5	46.0	40.7	39.8 (39.0)	43.3 (44.3)	26.9
OM1	76.0	60.8	54.9	27.6	56.0	28.2 (33.0)	35.4 (25.0)	17.3
OM2	82.9	69.9	60.0	36.0	60.8	44.8 (38.1)	45.1 (46.7)	51.2
OM3	95.7	73.6	59.4	48.5	44.6	42.4 (47.8)	53.9 (54.3)	96.2
DFTB+	83.4	68.4	59.1	50.1	38.0	35.6 (32.1)	33.3 (32.7)	36.6
HF	76.4	64.5	55.4	47.6	41.2	40.6 (34.1)	36.3 (32.9)	36.0
PBE	89.7	71.6	59.6	50.1	53.8	51.5 (44.8)	48.4 (51.5)	62.7
B3LYP	85.9	69.6	58.3	49.2	49.5	47.5 (40.7)	44.8 (44.3)	52.0
B3PW91	84.6	67.6	56.0	46.8	44.6	42.6 (38.9)	42.5 (41.0)	48.7
MP2	86.6	72.6	62.6	54.3	56.9	55.3 (43.7)	47.5 (47.5)	61.5
CBS-QB3	80.2	65.6	55.5	47.7	44.8	42.2 (33.1)	33.8 (42.7)	51.1
CBS-Q	79.2	65.1	55.4	47.4	47.5	46.2 (34.6)	39.0 (44.3)	47.5
CBS-APNO	80.7	68.2	52.7	46.8	−	−	−	−

[a] Values in parentheses were computed after reoptimization of the OPLS-AA lowest energy structures. [b] Experimental enthalpies and G2/G3 results ($n = 1-3$, not listed) are of a similar accuracy as those from the CBSs methods. These CBS and G2/G3 methods are free of BSSE effect,[51−53] which is also neglectable for HF, DFT, and MP calculations with the fairly large basis set used in the cases.[54] [c] Reference 11. [d] Reference 12. [e] Reference 13.

structures. The more runs, the larger the probability to identify the actual global minimum energy.

(6) Using the last structure from step 5, the optimized geometry and energy are recomputed with various quantum mechanical methods.

(7) Steps 1−6 are repeated for the next cluster size.

The following sections explain details in the above procedure.

(a) Conformational Searches. Basin-hopping (Monte Carlo plus minimization) was used for the conformational search of the $NH_4^+(H_2O)_n$ clusters in this work.[37] At each Monte Carlo step, a randomly selected molecule (water or ammonium) was subjected to random translational and rotational moves.[38] A three-dimensional uniformly distributed random unit vector (v_x, v_y, v_z) for the translational move and a four-dimensional Hamiltonian quaternion (q_0, q_1, q_2, q_3) for the orientational move were generated with the Marsaglia algorithm.[39] The Hamiltonian quaternion approach has successfully been employed for computing CCl_4 spherical potentials.[40] The detailed relationship between the rotation Eulerian angles (ϕ, θ, φ) and the quaternion and the consequent rotational matrix **R** have been reported in the literature.[39]

The molecular system was placed inside a cubic box with a length approximately equal to 1.0−2.0 nm (depending on the cluster size), avoiding vaporization/dissociation in the simulations. The maximum Cartesian displacements for each move were constrained to obtain acceptance probabilities of about 40% for new configurations. After each Monte Carlo move, an energy minimization with either the force field or tight-binding approach is conducted, and the final structure is accepted or rejected according to the Metropolis sampling at 300 K.[41] In the case of the MM3 and OPLS-AA force fields, a local version of the TINKER molecular modeling software (version 4.2) was used to perform the conformational search.[42−44] The TINKER Monte Carlo module was modified in order to treat molecular clusters. An rms gradient stopping criterion was set to 0.04 kJ mol^{-1} $Å^{-1}$ for the energy minimization.

In the case of the tight-binding energy minimization, the DFTB+ software package (version 1.01) was used to optimize the structures produced by the Monte Carlo conformational search.[35] A python script was implemented for interfacing a locally developed Monte Carlo routine to the DFTB+ program. The tight-binding parameters were set as follows: stopping criterion for the SCC (self-consistent-charge) was set to 1.0×10^{-6} (in *e*), the tolerance for the maximum difference in any charge between two SCC cycles, while the maximum number of SCC cycles was set to 1000. The default configuration for the Broyden charge mixing method was adopted. In addition, s and p Slater atomic orbitals for nitrogen and oxygen and only s type for hydrogen were accounted, by using mio−0−1 (as-is) of the Slater−Koster parameters.[45] We note that dispersion constants from this reference have been tested for biological system.[46]

Lowest energy configurations corresponding to $NH_4^+(H_2O)_n$ ($n = 1-8$) clusters were obtained by this procedure. Specifically, for each cluster size *n*, the Monte Carlo procedure was applied until the conformation with the lowest energy (within an energy variation of ±0.1 kJ/mol) was obtained 10 times, and this was then selected as the operational global minimum energy conformation of the cluster.

(b) Quantum Chemistry Calculations. The global structures obtained from the Monte Carlo procedure described above were reoptimized using a variety of quantum chemical methodologies including the semiempirical methods AM1[47] and PM3/PM6[48] and OMx,[49] Hartree−Fock (HF), the gradient corrected exchange-correlation DFT functional PBE,[50] second-order Møller−Plesset perturbation theory[51] (MP2), the complete basis set model (CBS) proposed by Petersson and collaborators,[52] as well as the Gaussian-2[53a] (G2) and Gaussian-3[53b] (G3) methods. In the case of the HF, PBE, and MP2, Dunning's augmented triple-ζ correlation consistent basis sets[54] aug-cc-pVTZ were used (herein HF/aug-cc-pVTZ, PBE/aug-cc-pVTZ, and MP2/aug-cc-pVTZ, respectively). All calculations were carried out with the Gaussian 03[55] (version D.01) suite of programs. In addition, atomic charges were computed by performing natural bond orbital (NBO) analysis[56] in the case of the HF and PBE[49] wave functions. In the case of the DFTB+ calculations, the charges were obtained via Mulliken analysis. We note that the CBSs and G2/G3 results include thermal corrections (RT, ∼2.4 kJ/mol) at 298 K.

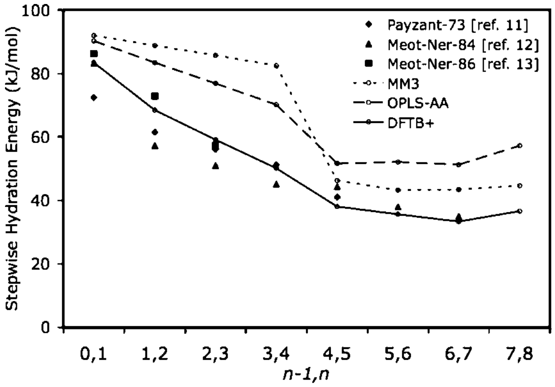

Figure 1. The stepwise hydration energies (lines), calculated with MM3 (dotted), OPLS-AA (dashed), and DFTB (solid), compared with the experimental enthalpies (points: Payzant-73,[11] diamond; Meot-Ner-84,[12] triangle; Meot-Ner-86,[13] square).

Results and Discussion

(a) Stepwise Hydration Energies from MM and DFTB+ Calculations and Comparison with Experimental Values. Figure 1 depicts the stepwise hydration energies for $NH_4^+(H_2O)_n$ as a function of the cluster size *n*, computed at 0 K using the global minima obtained by the search procedure described above using the MM3 and OPLS-AA force fields and the tight binding DFTB+ quantum chemistry model. The corresponding experimental data obtained from three sources in the NIST Cluster Ion database[57] are also plotted in Figure 1 for comparison.

As observed in Figure 1, the DFTB+ results agree remarkably well with experiment. The calculated stepwise hydration energies are within the range of experimental values, within 2 kJ/mol of the latest experimental series for $n = 1-3$, and within less than 5 kJ/mol of all the average experimental values. Experimental uncertainties are estimated as about ±6 kJ/mol on the basis of these measurements. The DFTB+ binding energies show a similar mean absolute deviation of 6.4 kJ/mol versus the high-level CBS calculations in Table 1.

Note that the first hydration shell includes four H_2O molecules that bind directly to the N−H hydrogens. The fifth H_2O molecule must lie in the second shell, bonded to the first shell by a water−water hydrogen bond(s). In a clustering series, such hydration shell filling by the *n*th ligand molecule can lead to a significant drop in the stepwise hydration energy. In this case the decrease in the hydration energy of the *n* to the $n + 1$ solvent molecule is significantly larger than that of the preceding decrease in the hydration energy of the $n - 1$ to *n* solvent molecule.[13] In the present work, the stepwise hydration energy decrease computed with the DFTB+ between $n = 4$ and 5 was found to be 12 kJ/mol, slightly larger than the decrease of 9 kJ/mol in going from $n = 3$ to 4 (see Figure 1). This may indicate a very small hydration-shell-filling effect at $n = 4$.

The shell-filling effects may not be observed when the binding energies are already converging to the limiting bulk value of about $\Delta H_{\text{vap,water}} = 44$ kJ/mol within the calculation uncertainty (≈6 kJ/mol). This is likely the case in the present system, where $\Delta H_{3,4}$ and $\Delta H_{4,5}$ are both near this value and the binding energy cannot decrease much below this macroscopic limit. In this case, the inner-shell binding energy of water to the ion at step n is similar to the outer-shell water−water bonding energy at step $n + 1$.

The DFTB+ predictions are in good agreement with experimental results, which show no significant shell-filling effects for the $NH_4^+(H_2O)_n$ series within the experimental uncertainty (≈6 kJ/mol).[13] In 1973, Payzant and co-workers reported the energy gap of 10 kJ/mol for $n = 4-5$, close to the average change of 7 kJ/mol for $n = 1-4$; in 1984, Meot-Ner measured the $NH_4^+(H_2O)_n$ system up to $n = 7$ with mass spectroscopy and obtained a negligible gap of 1 kJ/mol from $n = 4-5$ (Figure 1 and Table 1).

In contrast to the DFTB+ calculations and the experimental results, the stepwise hydration energies computed with the force fields MM3 and OPLS-AA show an abrupt drop beween $n = 4$ and 5. As observed in Figure 1, the MM3 and OPLS-AA force field simulations group the stepwise hydration energies into an inner hydration shell of water ($n = 1-4$) and an outer shell ($n = 5-8$). The predicted stepwise hydration energy gaps between the two groups are 36 kJ/mol (MM3) and 18 kJ/mol (OPLS-AA). In addition, the stepwise hydration energies computed with the MM3 and OPLS-AA force fields are found to decrease much more slowly for the first four H_2O molecules than the experimental values, decreasing by a factor of 3.4−3.8% (MM3) and 7.5−8.7% (OPLS-AA) for each additional H_2O molecule. It appears therefore that these force-field models do not reproduce well the hydration behavior of the experimental trends. This supports the need for efficient computational procedures based on quantum mechanical calculations such as the ones proposed in this work.

(b) Quantum Chemical Calculations of Stepwise Hydration Energies. In addition to the DFTB+ calculations, we also calculated the stepwise hydration energies for $NH_4^+(H_2O)_n$ ($n = 1-8$) by different semiempirical and ab initio levels of theory and listed them in Table 1. The semiempirical and ab initio hydration energies were computed after reoptimization of the low-energy structures obtained by the Monte Carlo/DFTB+ search described above. The experimental hydration energies are also listed for comparison. For $n = 6$ and 7, the lowest energy structures obtained with OPLS-AA were also reoptimized with the different quantum chemistry methods, and the resulting hydration energies are listed in parentheses.

The results listed in Table 1 show that the tight-binding results closely reproduce the high-level quantum mechanical calculations. For the cases of $n \leq 7$, the DFTB+ approach, as well as the ab initio methods HF, CBS-QB3, CBS-Q, and CBS-APNO predict hydration energies with a relatively small deviation (within ±3 kJ/mol) with respect to the average experimental results. The hydration energies computed at the PBE/aug-cc-pVTZ and MP2/aug-cc-pVDZ levels of theory are closer to or above the highest experimental values, likely overestimating the binding energy. The calculated results with the three-parameter hybrid DFT functionals, B3LYP/aug-cc-pVTZ and B3PW91/aug-cc-pVTZ, are close to the experimental and DFTB+ results for $n = 1-3$ and on the average between the HF and PBE results. The results in Table 1 also indicate that the PW91 exchange-correlation functional predicts smaller stepwise hydration energies, closer to the mean values in experiment. In addition, the semiempirical methods used in this study predict significantly lower hydration energy values than the ones obtained with first-principles calculations for $n = 1-7$, with the exception of PM6, which predicts hydration energies closer to experiment and the ones obtained with correlated ab initio methods. The trend, however, is less clear in the case of the large cluster ($n = 8$), with the semiempirical methods predicting quite different binding energies, raising questions about their ability to systematically describe the ion−water interactions in larger clusters.

For the isomers of $n = 6$, all quantum mechanical methods, with the exception of AM1 and OM1/3, suggest that the DFTB structure is more stable than the OPLS-AA structure. For $n = 7$, the PM3, OM1, HF/aug-cc-pVTZ, B3LYP/aug-cc-pVTZ, and B3PW91/aug-cc-pVTZ calculations favor the DFTB structure, while others favor the OPLS-AA structure.

With the exception of HF, all quantum chemical methods predict an oscillation in the hydration energy when going from $n = 6$ to 8, with a decrease from $n = 6$ to 7 and an increase from $n = 7$ to 8 (Table 1). This oscillation may indicate that the binding energy of these clusters is the result of a delicate balance between the number of hydrogen bonds (attractions) and the steric effects (repulsions).

(c) Computational Advantages of the Tight-Binding Method. Computational efficiency is the most important advantage of the tight-binding method over more accurate correlated ab initio quantum chemical methodologies. For example, for $n = 8$, a DFTB+ single energy calculation takes less than 10 s using one CPU (2.8 GHz Opteron) of the Biowulf cluster at NIH, Bethesda, MD, while a similar calculation using the highly correlated CBS-QB3 method requires ≈144 000 s of CPU time on the same hardware, a factor of 14 400! Considering the greater computational demand involved in the corresponding gradient calculations, it is clear that the use of ab initio methods such as CBS-QB3 (or even more efficient methods such as DFT) for conducting Monte Carlo conformational searches and molecular dynamics simulations of $NH_4^+(H_2O)_n$ clusters is computationally prohibitive. In addition, despite the fact that the computational efficiency of conventional semiempirical methods such as AM1 and PM3/PM6 is comparable to DFTB, the results obtained in this work seem to indicate that these methods tend to underestimate the binding energies of the clusters. In principle, it may be possible to reparameterize these efficient Hamiltonians to improve their accuracy and reliability, but this is beyond the present study.

(d) Structures of Solvated Ammonium Ion Clusters. Figure 2 shows minimum energy structures for $n = 4-8$ computed with the Monte Carlo conformational search using the MM3 and OPLS-AA force fields and the DFTB+ quantum chemistry model. The corresponding structures for $n = 1-3$ (not shown) can be obtained by removing water molecules from the $n = 4$ cluster.

For $n > 4$, the cluster structures predicted by the MM3 force field are significantly different from the ones obtained with OPLS-AA and DFTB+. In the MM3 structures, ammonium is found to coordinate to more than four molecules of water for $n = 5-8$ (sometimes as many as 7 as in the case of $n = 7$), in contrast to the structures predicted by OPLS-AA and DFTB+. These additional water molecules coordinated to the ammonium ion in the MM3 structures exhibit unusual N···O distances

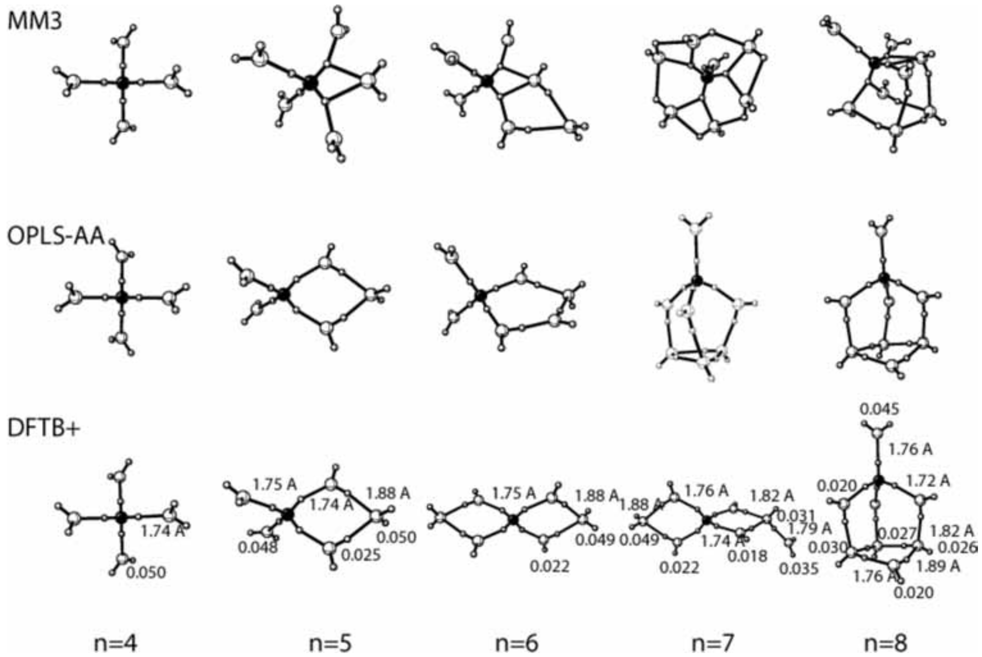

Figure 2. The clusters $NH_4^+(H_2O)_n$, $n = 4-8$, obtained from the Monte Carlo conformational search, with the MM3, OPLS-AA, and DFTB+ methods. (Nitrogen, filled black circles; oxygen, large open circles; hydrogen, small open circles. Lines are added where atom−atom distances are less than sums of the two corresponding van der Waals radii. The total DFTB+ charges on the water molecules and the hydrogen bond distances are marked.)

(<2.6 Å), even shorter than the ionic hydrogen bonding N···O distances (≈2.7 Å).

With the exception of the cases where $n = 6$ and 7, the OPLS-AA and DFTB+ methods yield similar geometries, with DFTB+ predicting slightly longer (by ≈0.1 Å) hydrogen bonds.

In addition, the prediction of four-membered (heavy atom) ring structures in clusters with $n = 5-8$ by OPLS-AA and DFTB+ is in excellent agreement with infrared spectroscopic experiments.[58] As can be observed in Figure 2, while OPLS-AA predicts the formation of 3-D network structures for $n \geq 7$, the DFTB+ calculations predict the formation of these network structures in clusters with $n \geq 8$. Three-dimensional cage structures have been identified previously in protonated water clusters.[15,37]

In the case of $n = 6$, reoptimization of the OPLS-AA structure with DFTB+ does not lead to significant changes in the original OPLS-AA structure, which was found to lie approximately 3.5 kJ/mol above the bicyclic structure identified by the DFTB+ search as the global minimum. Similar results were obtained with ab initio CBS-QB3 calculations. In the case of $n = 7$, reoptimization of the OPLS-AA structure at the DFTB+ level of theory leads to a 3-D network structure very similar to the original OPLS-AA structure, which is only 0.6 kJ/mol less stable than the tight-binding global minimum. Calculations at the CBS-QB3 level indicate that the 3-D cage structure is actually lower in energy than the bicyclic structure by 8.9 kJ/mol. These results suggest that the formation of 3-D cage structures in $NH_4^+(H_2O)_n$ clusters starts at $n \geq 7$ and that the combination of computationally efficient methodologies based on the OPLS-AA force field and efficient quantum chemistry methodologies such as DFTB+ provide a reliable and efficient computational tool to probe the potential energy surfaces of these clusters.

(e) Charge Densities. Figure 3 depicts a plot of the charges on NH_4^+ and on the H_2O molecules in $NH_4^+(H_2O)_n$ clusters as a function of n computed with DFTB+ (using the Hückel approach), as well as with HF and PBE (using the natural bond orbital approach). The results show that despite the difference in the actual values, the DFTB, HF, and PBE charges follow essentially the same trend: the net electron density transfer from the H_2O molecules to the NH_4^+ ion increases steadily from zero at $n = 0$ until it reaches a value of ≈0.20 *e* for $n \geq 4$. As seen in the inset in Figure 3, in the case of $n > 4$, the electron deficiency on the water molecules placed in the second cluster shell seems to be significant, suggesting an important net electron density transfer from outer shells in these types of clusters. In view of the structures in Figure 2, the electron density transfer from water molecules forming ring structures that are directly hydrogen-bonded to ammonium is smaller than the corresponding electron density transfer from the H_2O molecules either external to the rings or forming water rings that are not directly hydrogen-bonded to the ammonium ion. Thus, larger positive charges seem to accumulate in outer water

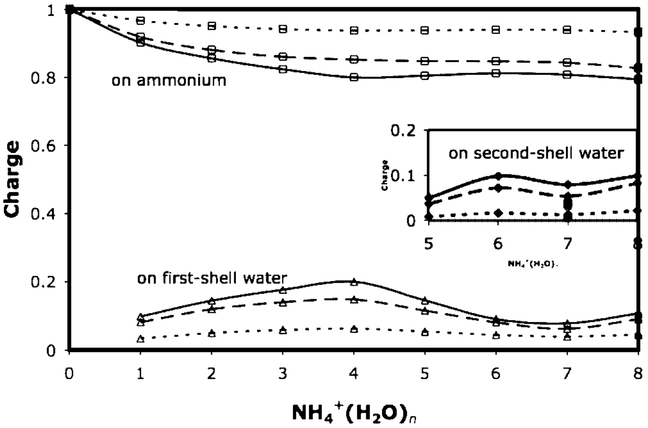

Figure 3. Calculated charges in $NH_4^+(H_2O)_n$ clusters as a function of the total number of water molecules in the clusters, using DFTB (solid), PBE (dashed), and HF (dotted) calculations. Charges remaining on the NH_4^+ core ion are shown on the top plots (squares). The total charge on the H_2O molecules directly attached to the ammonium ion in clusters $n = 1-8$ are shown in the plots starting from $n = 1$ (triangles). Charges on the second water shell (for $n = 5-8$, diamonds) are shown in the insert (charges on the third shell are marked as open circles).

shells located further from the ammonium ion, minimizing Coulombic repulsions.

Conclusions

In this work, we present a computationally efficient procedure to identify low-energy isomers in solvated systems. The method applied Monte Carlo conformational searches using tight-binding calculations and allows extending conformational searches to an ion (NH_4^+) solvated by up to eight water molecules. This approach reproduced well both the experimental and highly correlated ab initio quantum chemistry results for the stepwise hydration energies of these clusters. It also identified ring and cage structures observed in other analogous systems. In contrast, computationally efficient models such as the MM3 force field that use fixed point charges and bond dipoles fail to reproduce the stepwise hydration energies of ammonium−water ionic hydrogen-bonded systems. The ability of the quantum chemical methods including tight-binding theory to properly describe the charge density fluctuations is particularly critical in the study of ionic hydrogen bonds in systems of moderate size, since large electronic density changes can occur with various conformations.[59,60] Consequently, it is not surprising that MM3 fails in predicting the stepwise hydration energies of the $NH_4^+(H_2O)_n$ clusters.

The reasonably good agreement between the DFTB stepwise hydration energies and the experimental data and quantum chemical results by accurate but more computational intensive methodologies such as CBSs and G2/G3 is encouraging and suggests that this method can explore the potential energy surfaces of larger clusters.

Contrary to the tight-binding results, the PBE and MP2 calculations overestimate the binding energies of the ionic hydrogen bonds. Similar overestimation of the binding energies occurred with other DFT exchange-correlation functionals such as the three-parameter hybrid B3LYP and B3PW91. It is rather surprising that the DFT-based tight-binding method performs better than DFT. It is quite possible that this might be the result of a systematic cancelation of errors. Although encouraging, more work is needed for a systematic validation of DFTB in treating other ionic systems.

In summary, the calculated DFTB binding energies for the $NH_4^+(H_2O)_n$ clusters ($n = 1-8$), found by Monte Carlo/DFTB+ conformational searches, are in good agreement with experiment. The calculated low-energy structures and their charge densities vary considerably with cluster size and show migration of the positive charge from the ammonium ion to outer sites, in agreement with electrostatic arguments.

The results obtained in this work are encouraging and suggest that the possibility of using the computationally efficient DFTB approach for simulating relatively large ion/solvent systems.[61] Currently, we are applying such tight-binding studies to hydrated clusters containing hundreds to thousands of water molecules.

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