

Effects of Many-Body Interactions on the Preferential Solvation of Mg^{2+} in Aqueous Ammonia Solution: A Born–Oppenheimer ab Initio QM/MM Dynamics Study

Anan Tongraar,^{*,†} Kritsana Sagarik,[†] and Bernd Michael Rode[‡]

School of Chemistry, Institute of Science, Suranaree University of Technology, Nakhon Ratchasima 30000, Thailand, and Department of Theoretical Chemistry, Institute of General, Inorganic and Theoretical Chemistry, University of Innsbruck, Innrain 52a, A-6020 Innsbruck, Austria

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A combined ab initio quantum mechanical/molecular mechanical (QM/MM) molecular dynamics simulation has been performed to describe the solvation shell structure of Mg^{2+} in 18.4% aqueous ammonia solution. The most relevant region, the solvation sphere of Mg^{2+} in which the many-body effects are expected to play an important role, is treated by Born–Oppenheimer ab initio quantum mechanics using LANL2DZ basis sets, while the rest of the system is described on the basis of pairwise additive interactions. The results show a significant role of nonadditive contributions on the geometrical arrangement as well as on the coordination number of the solvated ion. An octahedral arrangement with five water and one ammonia ligand within the first solvation shell of Mg^{2+} is observed, in contrast to a polyhedral structure with six water and three ammonia molecules obtained by classical pair potential simulation. The observed differences in coordination numbers and in the preference for ligands are discussed on the basis of detailed simulation results.

1. Introduction

A comprehensive understanding of the structural properties of ions in electrolyte solutions has been a fundamental subject of experimental and theoretical studies due to their well-known relevance for many processes in solution chemistry, biochemistry, and pharmacology.^{1–7} Experimental techniques, such as neutron and X-ray diffraction, can provide a direct probe of solvation structures of ions,^{2,8–11} but—besides requiring considerable laboratory resources—they do not always lead to unambiguous results. Consequently, theoretical investigations by means of computer simulations (Monte Carlo or molecular dynamics), have become an alternative way to elucidate such structures in detail,^{2,12–16} in particular for interpretation in terms of microspecies where experimental observations reach their limitations.^{11,17,18}

During the past decades, most of the simulation works had applied potential functions for describing inter- and intramolecular interactions of each interacting atoms or molecules in the system. The potential functions employed in the simulations are usually constructed from either experimental data or ab initio quantum mechanics calculations, and mostly pairwise additivity of interactions has been assumed. The neglect of nonadditive terms (3, 4, ..., N -body) was partly necessary due to technical difficulties as well as the lack of sufficient computer capacity for deriving such many-body potentials. Although the approximation of pairwise additivity can yield reasonable results for the energetic data as well as the structural and dynamical properties of many condensed-phase systems, the importance of nonadditive contributions for the accurate description of the intermolecular interactions is well documented.^{19–23} With increasing computer speed, the inclusion of higher order, at least

three-body terms, became possible and turned out to be an essential improvement.^{22–25} Nevertheless, the reliability of the 3-body corrected potentials is not always granted and their construction usually requires some additional adjustments to obtain a good fit of the potential functions.^{24,25} In addition, the construction of higher order correction functions is hardly feasible for large molecular systems due to their complicated orientation dependence.

In general, ab initio quantum mechanical methods can be used for a correct treatment of multiple intermolecular interactions. However, the performance of ab initio calculations for a condensed-phase system consisting of a large number of molecules is still beyond the current computational feasibility. As a consequence, an alternative way is to apply the so-called combined quantum mechanical and molecular mechanical (QM/MM) methods.^{26,27} In recent years, several hybrid QM/MM models have been proposed and successfully applied to various condensed-phase systems.^{28–36} A “Born–Oppenheimer ab initio QM/MM dynamics” technique has been lately proposed and employed for studying structural and dynamical properties of various ions in solutions.^{37–42} This technique treats the active-site region, e.g., the solvation shell around ion, quantum mechanically, while the environment consisting of solvent molecules is described by molecular mechanical potentials. By this scheme, the complicated many-body contributions within the solvation sphere of the ion can be reliably included.

For ions in aqueous ammonia solution, Born–Oppenheimer ab initio QM/MM molecular dynamics simulations have been successfully applied to Li^+ and Na^+ .^{43,44} The high-accuracy QM/MM molecular dynamics simulations have predicted the lower coordination numbers of 4⁴³ (consisting of 3 water and 1 ammonia molecule) and 5.5⁴⁴ (contained 3.7 water and 1.8 ammonia molecules) for Li^+ and Na^+ , respectively, compared to the corresponding values of 6⁴³ (with 3 water and 3 ammonia molecules) and 7.1⁴⁴ (with 4.9 water and 2.2 ammonia mol-

* Corresponding author. Fax: 0066-44-224185. E-mail: anan@ccs.sut.ac.th.

[†] Suranaree University of Technology.

[‡] University of Innsbruck.

TABLE 1: Optimized Parameters of the Analytical Pair Potentials for the Interaction of Water and Ammonia with Mg²⁺ (interaction energies in kcal mol⁻¹ and distances in Å)

pair	A (kcal mol ⁻¹ Å ⁶)	B (kcal mol ⁻¹ Å ⁷)	C (kcal mol ⁻¹)	D (Å ⁻¹)
Mg–O	-12668.132	12088.985	74147.214	3.3615041
Mg–H	-5736.4832	5292.2384	18898.224	3.0376410

pair	A (kcal mol ⁻¹ Å ⁵)	B (kcal mol ⁻¹ Å ⁶)	C (kcal mol ⁻¹)	D (Å ⁻¹)
Mg–N	-5667.7431	2523.4922	101069.71	3.4047506
Mg–H	-3053.1944	2831.8170	5323.4123	2.3155955

ecules) resulting from classical pair potential simulations. The observed discrepancies have been considered due to the important role of nonadditive contributions for a proper description of the structural properties of ions in solutions, even for single-charged ions for which nonadditivity had been expected to be small.

In the present work, a Born–Oppenheimer ab initio QM/MM molecular dynamics simulation was applied to Mg²⁺ in 18.4% aqueous ammonia solution. For Mg²⁺–water and Mg²⁺–ammonia systems, the effects of nonadditivity have been studied. It was found that the assumption of pairwise additive approximation for an octahedral complex, the experimentally observed structure, led to energetic errors of 36%⁴⁵ and 30%,⁴⁶ respectively. As a result, the uncorrected pair potentials employed in the simulations for these two systems yielded coordination numbers of 8 to 10 which are much higher than of experimental values, while the results obtained from QM/MM molecular dynamics simulations confirmed the octahedral arrangement.^{47,48} For the first solvation shell structure of Mg²⁺ in aqueous ammonia solution, an earlier pair potential Monte Carlo simulation had predicted the coordination number of 7 (consisting of 4 water and 3 ammonia molecules).⁴⁹ According to the composition of the solution, which contained one magnesium ion, 37 ammonia, and 164 water molecules, the statistical average distribution of ligands around the Mg²⁺ is approximately 4.4:1 for water and ammonia, respectively. In the early MC simulation, the preference for ammonia molecules (with the water-to-ammonia ratio of 4:3) was in contrast to the chemical concept of “hard” and “soft” ions and ligands,^{50–53} in which the “hard” Mg²⁺ should preferably bind to the “harder” water over the “softer” ammonia ligand. These results have hinted, therefore, once more to a failure of the pairwise additive approximation. Since the effects of nonadditivity are usually related to the strength of binding between ion and ligand, these effects could be expected to play an even more important role for Mg²⁺ than for Li⁺ and Na⁺ in aqueous ammonia solution.

2. Methods

On the basis of the QM/MM method, the interactions within the QM region (the first solvation sphere of Mg²⁺) are treated by Born–Oppenheimer ab initio Hartree–Fock quantum mechanical calculations using LANL2DZ basis sets,^{54,55} while the interactions within the MM region and between QM and MM regions are described by classical pair potentials. The forces at the transition between QM and MM regions are smoothed using a switching function.⁵⁶ The LANL2DZ basis sets were selected as a compromise between the quality of simulation results and the requirement of CPU time.^{40,45,46}

Flexible models, which describe inter- and intramolecular interactions, were employed for water^{57,58} and ammonia.⁵⁹ The pair potential function for water–ammonia interactions was adopted from Tanabe et al.⁶⁰ The pair potential functions for

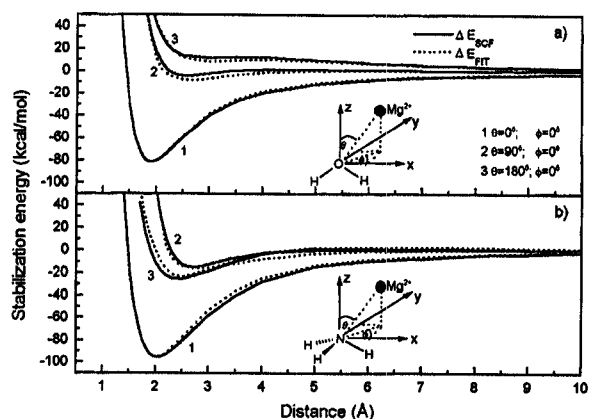


Figure 1. Comparison of the stabilization energies obtained from the SCF calculations and those from the fitted analytical function. (a) Mg²⁺–H₂O and (b) Mg²⁺–NH₃.

Mg²⁺–H₂O and Mg²⁺–NH₃ interactions were newly constructed in the present work using 6-311++G(3df,2p) basis sets.^{61,62} The 936 and 760 Hartree–Fock interaction energy points for various Mg²⁺–H₂O and Mg²⁺–NH₃ configurations obtained from Gaussian94⁶³ calculations were fitted to the analytical forms of

$$\Delta E_{\text{Mg}^{2+}\text{-H}_2\text{O}} = \sum_{i=1}^3 \left(\frac{A_{ic}}{r_{ic}^6} + \frac{B_{ic}}{r_{ic}^7} + C_{ic} \exp(-D_{ic}r_{ic}) + \frac{q_i q_c}{r_{ic}} \right) \quad (1)$$

and

$$\Delta E_{\text{Mg}^{2+}\text{-NH}_3} = \sum_{i=1}^4 \left(\frac{A_{ic}}{r_{ic}^5} + \frac{B_{ic}}{r_{ic}^6} + C_{ic} \exp(-D_{ic}r_{ic}) + \frac{q_i q_c}{r_{ic}} \right) \quad (2)$$

where *A*, *B*, *C*, and *D* are the fitting parameters (see Table 1), *r_{ic}* denotes the distances between Mg²⁺ and the *i*th atom of either water or ammonia and *q* are the atomic net charges. The charges on Mg²⁺, O and H of water, and N and H of ammonia were set to 2.0, -0.6598, 0.3299, -0.8022, and 0.2674, respectively. The comparison of the energies obtained from the SCF calculations, Δ*E*_{SCF}, and from the fit, Δ*E*_{FIT}, using the parameters given in Table 1 for some orientations is shown in Figure 1. The Mg²⁺–H₂O and Mg²⁺–NH₃ functions exhibit the global minima of -81.2 and -95.0 kcal mol⁻¹ at the Mg²⁺–O and Mg²⁺–N distances of 1.90 and 2.01 Å, with Mg²⁺ placed in the optimal position for interaction with the dipole moment of water and ammonia, respectively.

A molecular dynamics simulation with classical pairwise additive approximation was performed first, then the combined QM/MM molecular dynamics simulation using the equilibrium configuration obtained from the classical simulation was started. In practice, the sphere including the first solvation shell of the ion resulting from the pair potential simulation is usually selected as the QM region. For some considerable systems, in particular for strong ion–ligand interactions, the second solvation shell may have to be taken into account. However, when considering the Mg–(N + O) radial distribution function (RDF) obtained by the pair potential simulation (see Figure 2), the second Mg–(N + O) peak is less pronounced with a minimum around 5.5 Å. There are about 3 ammonia and between 22 and 29 water molecules within this region. Since the most expensive computational part in the QM/MM simulation is the ab initio quantum mechanical force calculations for each simulation step, determined by the selected QM size, a QM region with the

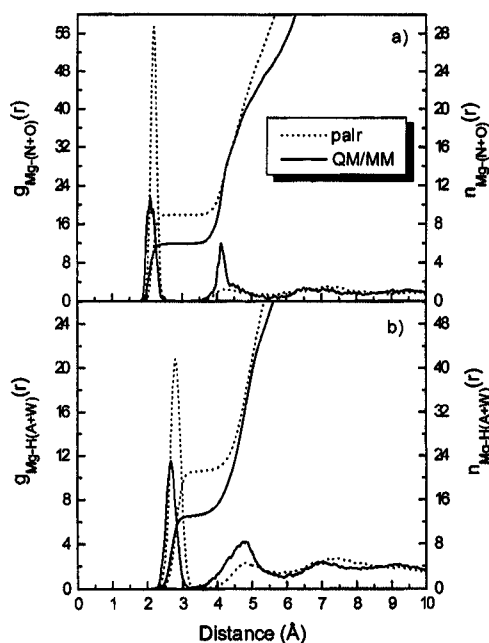


Figure 2. (a) $\text{Mg}-(\text{N} + \text{O})$ and (b) $\text{Mg}-\text{H}(\text{A} + \text{W})$ radial distribution functions and their corresponding integration numbers.

diameter of 11 Å seemed to be too time-consuming. Thus, some restrictions were to be made: The acceptable time for running each QM/MM step was estimated to be about 6–8 min, given the efficiency of the DEC Alpha XP1000 workstation at Suranaree University of Technology. This fixed CPU time for each simulation step allowed for a system containing about 3 ammonia and between 11 and 15 water molecules. This condition led to a QM region with a diameter of around 8.6 Å, being employed in the QM/MM simulation. This QM region includes the complete first solvation shell and some parts of the second solvation shell of Mg^{2+} . Since the nonadditive contributions usually play an essential role only at short ion-ligand distances, this QM size can be expected to be large enough to ensure that the quantum mechanical forces beyond the QM region would smoothly converge to pair potential forces.⁴⁶

Both pair potential and QM/MM simulations were performed in a canonical ensemble at 293 K, with a time step size of 0.2 fs. This canonical ensemble has been realized by coupling to an external temperature bath. The basic cube, with a length of 18.56 Å, contained one Mg^{2+} , 37 ammonia, and 163 water molecules, assuming the experimental density of 18.4% aqueous ammonia solution at the given temperature (0.9357 g cm^{-3}). The reaction-field procedure⁶⁴ was employed for the treatment of long-range interactions. The classical pair potential simulation started from an equilibrium configuration obtained from a previous simulation for Na^+ in aqueous ammonia solution.⁴⁴ The system was equilibrated for 60000 steps, and the simulation was continued for another 80000 steps for collecting configurations every 10th step. The QM/MM simulation started with a reequilibration for 20000 steps, followed by another 30000 steps to collect configurations every 5th step. The 6 ps interval of our QM/MM simulation can be considered long enough since it has been shown that even 2 ps interval of simulation can be sufficient for the investigation of both structural and dynamical properties of solutions.^{38–40,42} A switching function⁵⁶ was applied within an interval of 0.2 Å (i.e., between 4.3 and 4.5 Å) for smoothing the force transition at the boundary between QM and MM region.

TABLE 2: Comparison of Solvation Parameters for Mg^{2+} in 18.4% Aqueous Ammonia Solution, Obtained from Pair Potential and QM/MM Simulations ($r_{\text{max}1}$, $r_{\text{max}2}$, $r_{\text{min}1}$, and $r_{\text{min}2}$ denote the first maximum, the second maximum, the first minimum, and the second minimum of the radial distribution functions in Å, and $n_{\text{min}1}$ and $n_{\text{min}2}$ are the average numbers of ligands obtained by integration up to $r_{\text{min}1}$ and $r_{\text{min}2}$, respectively.)

	$r_{\text{max}1}$	$r_{\text{min}1}$	$n_{\text{min}1}$	$r_{\text{max}2}$	$r_{\text{min}2}$	$n_{\text{min}2}$	method	ref
$\text{Mg}-\text{O}$	2.21	2.57	6.0	4.17	5.57	24.4	pair potential MD	this work
	2.16	2.79	5.0	4.07	4.96	15.3	QM/MM MD	this work
$\text{Mg}-\text{H}(\text{W})$	2.05	3.00	4.0	4.30	4.75	9.0	pair potential MC	49
	2.80	3.33	12.1	4.80	6.40	61.9	pair potential MD	this work
$\text{Mg}-\text{H}(\text{W})$	2.64	3.22	10.0	4.63	5.82	38.2	QM/MM MD	this work
	2.70	3.75	8.1	4.90	5.40	34.0	pair potential MC	49
$\text{Mg}-\text{N}$	2.19	2.56	3.0	-	-	-	pair potential MD	this work
	2.16	2.47	1.0	4.13	5.12	5.7	QM/MM MD	this work
$\text{Mg}-\text{H}(\text{A})$	2.15	2.65	2.8	4.25	4.65	5.0	pair potential MC	49
	2.82	3.36	9.0	-	-	-	pair potential MD	this work
$\text{Mg}-\text{H}(\text{A})$	2.66	3.17	3.0	4.76	5.91	17.7	QM/MM MD	this work
	2.70	3.25	8.5	4.80	5.70	18.0	pair potential MC	49

3. Results and Discussion

Structural properties of the solvated Mg^{2+} are characterized by total RDFs of $\text{Mg}-(\text{N} + \text{O})$ and $\text{Mg}-\text{H}$ (from both water and ammonia molecules) as well as their corresponding integration numbers. The total RDFs obtained from both classical pair potential and combined QM/MM simulations are presented in Figure 2. A comparison of the structural parameters from this work with the data from an earlier MC simulation is summarized in Table 2. The pair potential simulation gives a sharp first $\text{Mg}-(\text{N} + \text{O})$ peak at 2.20 Å and the first solvation shell is well separated from the second one, leading to a coordination number of 9. In the QM/MM simulation, a broader less pronounced first peak is observed at 2.10 Å. The first solvation shell is also clearly separated from the second one, giving a coordination number of 6. The shape of the first peak in the QM/MM simulations indicates a higher flexibility of the solvate, compared to the results obtained by pair potential simulation. The second $\text{Mg}-(\text{N} + \text{O})$ peak in the pair potential simulation is less pronounced with the maximum at around 4.17 Å, yielding about 20 ligands included in this shell. In contrast for the QM/MM simulation, the second peak is well defined, with the maximum at around 4.11 Å, consisting of about 17 ligands. The $\text{Mg}-\text{H}_2\text{O}$ and $\text{Mg}-\text{NH}_3$ RDFs and their corresponding integration numbers are separately plotted in Figures 3 and 4, respectively. In the $\text{Mg}-\text{H}_2\text{O}$ RDFs, the first $\text{Mg}-\text{O}$ and $\text{Mg}-\text{H}$ peaks in QM/MM simulation have their maxima at shorter distances of 2.16 and 2.66 Å, compared to the corresponding values of 2.21 and 2.82 Å of the pair potential simulation, corresponding to 5 and 6 water molecules, respectively. In the QM/MM simulation, a smaller second solvation shell radius of Mg^{2+} is recognized, as can be seen from the distribution of water molecules within this shell. In the $\text{Mg}-\text{NH}_3$ RDFs, the pair potential simulation produces a very sharp first $\text{Mg}-\text{N}$ peak centered at 2.19 Å, giving a coordination number of 3, while the second peak has disappeared. In the QM/MM simulation, a less pronounced first $\text{Mg}-\text{N}$ peak is located at 2.16 Å, corresponding to a coordination number of only 1. The second peak is well recognized with the maximum around 4.13 Å, indicating a participation of both water and ammonia molecules in the second solvation shell of Mg^{2+} .

Figure 5 shows the probability distributions of the solvation numbers of Mg^{2+} , calculated up to second minimum of the $\text{Mg}-(\text{N} + \text{O})$ RDFs. In the pair potential simulation, about 26–32 ligands, which belong to about 23–30 water and about 3–4 ammonia molecules, are located within the solvation sphere. A

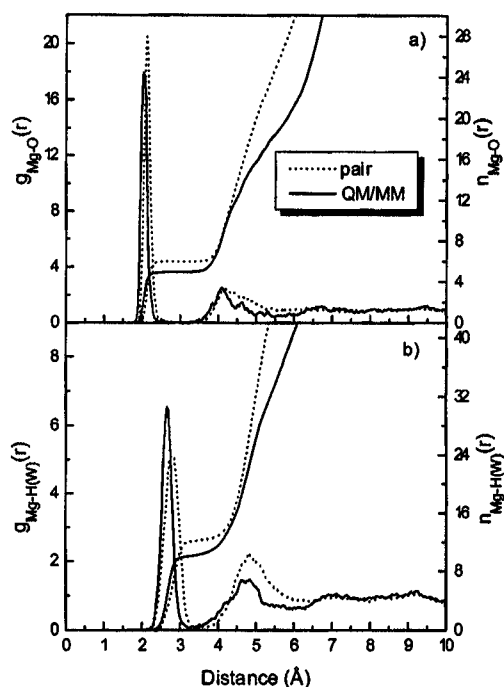


Figure 3. (a) Mg–O and (b) Mg–H(W) radial distribution functions and their corresponding integration numbers.

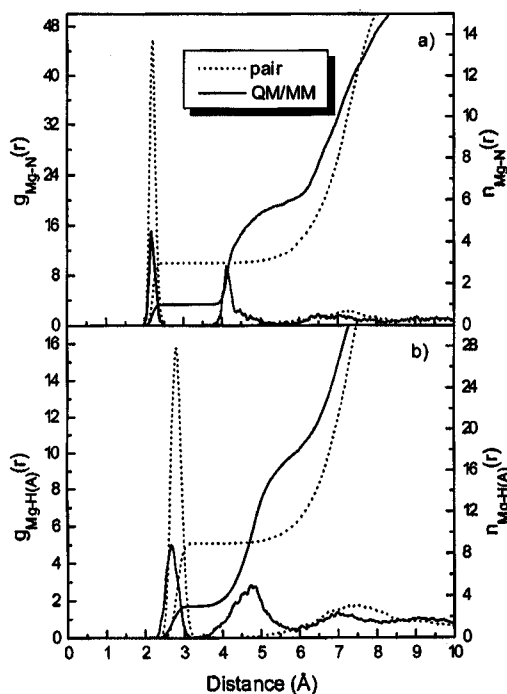


Figure 4. (a) Mg–N and (b) Mg–H(A) radial distribution functions and their corresponding integration numbers.

lower solvation number of 21–25 is observed in the QM/MM simulation, corresponding to about 14–20 water and about 5–7 ammonia molecules. The distributions of coordination numbers within the first and the second solvation shell of Mg^{2+} are plotted separately in Figure 6. In the pair potential simulation, the first solvation shell prefers a coordination number of 9, including 6 water and 3 ammonia molecules. The second solvation shell favors a coordination number of 20 (followed by 19, 18, 21, 22, 17, 23, 16, and 24 in decreasing amounts), being only water molecules. In the QM/MM simulation, a sole coordination number of 6, consisting of 5 water and 1 ammonia molecule, is observed. The second solvation shell of Mg^{2+}

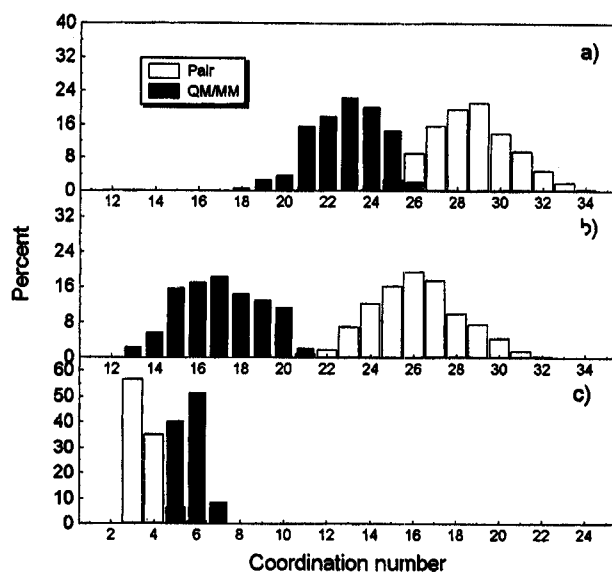


Figure 5. Coordination number distributions, calculated up to the second minimum of the Mg^{2+} –ligand RDFs: (a) Mg^{2+} –($\text{H}_2\text{O} + \text{NH}_3$), (b) Mg^{2+} – H_2O , and (c) Mg^{2+} – NH_3 .

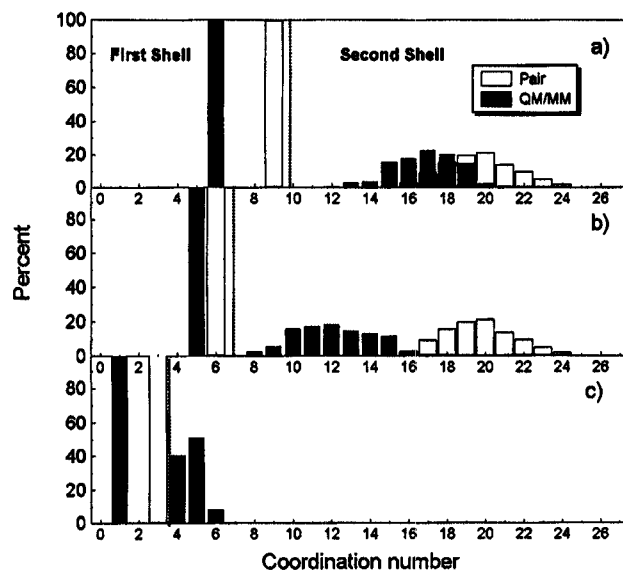


Figure 6. Coordination number distributions, calculated within the first and the second solvation shell of the Mg^{2+} : (a) Mg^{2+} –($\text{H}_2\text{O} + \text{NH}_3$), (b) Mg^{2+} – H_2O , and (c) Mg^{2+} – NH_3 .

prefers a coordination number of 17 (in addition to 18, 16, 15, 19, 14, 13, and 20 in smaller amounts), which belong to the favorable amounts of 12 (followed by 11, 10, 13, 14, 15 in comparable amounts and 9, 8, and 16 in small amounts) water and 5 (in addition to 4 and 6 in decreasing amounts) ammonia molecules.

To compare with the statistical average distribution of ligands around Mg^{2+} (of 4.4:1 for water and ammonia, respectively), the QM/MM simulation depicts a water-to-ammonia ratio of 5:1, which is clearly in good agreement with the qualitative water preferential expectations. In contrast for the pair potential simulation, the corresponding ratio of 2:1 reflects a preference for ammonia ligands. A similar trend is also found in an earlier MC simulation, in which the corresponding ratio was even 4:3.⁴⁹ These contradictory predictions are obviously due to the neglect of many-body contributions.

Figure 7 presents the O–Mg–O, N–Mg–N, and O–Mg–N angular distributions, calculated up to first minimum of the

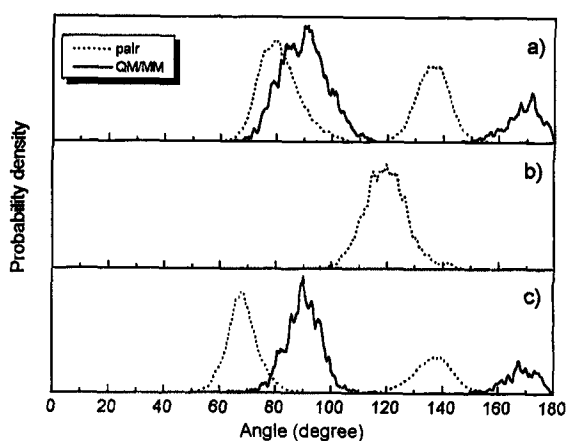


Figure 7. Distributions of (a) O–Mg–O; (b) N–Mg–N, and (c) O–Mg–N angles, calculated up to the first minimum of Mg–(N + O) RDFs.

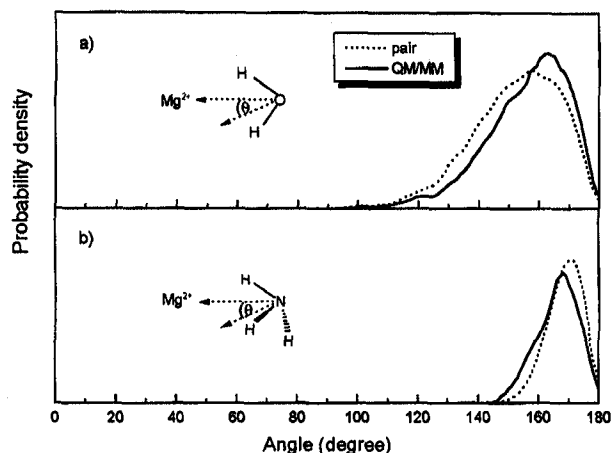


Figure 8. Distributions of θ within the first solvation shell of Mg^{2+} . (a) water, and (b) ammonia.

Mg–(N + O) RDFs. In the pair potential simulation, the solvation shell structure of Mg^{2+} is predicted approximately polyhedral by the two O–Mg–O peaks between 60 and 100° and between 120 and 150° and a single N–Mg–N peak between 100 and 140°. This structure can be classified into D_{3h} point group⁶⁵ in which the 3 ammonia molecules are arranged in the nonnearest-neighbor pattern. The QM/MM simulation clearly indicates an octahedral arrangement by a pronounced peak between 80 and 100° and a small peak between 160 and 180°. To know the influence of many-body contributions on the preferential orientations of ligands around the solvation sphere of Mg^{2+} , the angle θ , defined by the $\text{Mg}\cdots\text{O}$ axis and the dipole vector of ligands, has been used to characterize these effects. The dipole-oriented arrangements of water and ammonia molecules within the first and second solvation shell of the ion are given in Figures 8 and 9, respectively. Both pair potential and QM/MM simulations indicate that the ammonia molecules stick more rigidly to the dipole-oriented arrangement than that of water molecules. This can be ascribed to the higher binding energy of Mg^{2+} to NH_3 than to H_2O , when Mg^{2+} is located near the global minimum of the corresponding interaction energy surfaces. In the first solvation shell of Mg^{2+} , the QM/MM simulation reveals a somewhat more rigid dipole-oriented arrangement of water molecules than the pair potential simulation, whereas a slightly higher flexibility is found for the ammonia molecule's orientation. In the second solvation shell of Mg^{2+} , the QM/MM simulation predicts a stronger dipole-oriented orientation of both water and ammonia molecules than

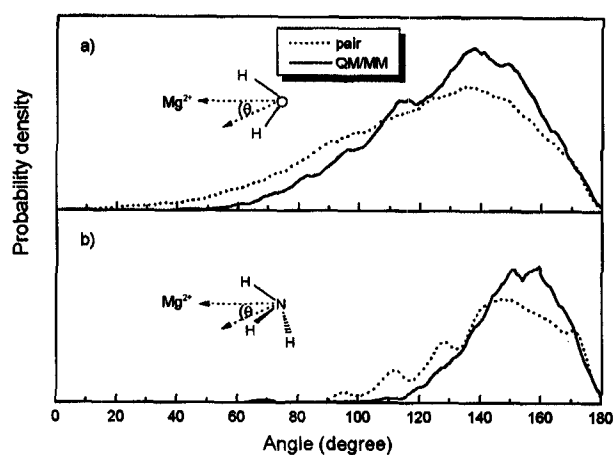


Figure 9. Distributions of θ within the second solvation shell of Mg^{2+} . (a) water and (b) ammonia.

the pair potential simulation. The results indicate a remarkable influence of Mg^{2+} on the determination of ligand arrangements beyond the first solvation shell. When the effects of many-body and electrostatic interactions are longer range than we expected, a further improvement of the simulation results can be achieved by extending the size of QM region.

Since the molecular mechanical potentials usually use fixed partial charges for each atom in the system, they cannot account for the polarization effects. For strong ion–ligand interaction systems, changes in charge distributions within the molecules can easily occur during the molecular movements due to their strong electrostatic interactions. This leads to further considerations on the importance of the different polarizability of water and ammonia molecules for the preferential water solvation. By the QM/MM method, the polarization effects, at least within the first solvation shell of Mg^{2+} , are automatically included in the quantum mechanical calculations. To estimate the different polarizability of water and ammonia molecules resulting from the ab initio simulation technique, the average Mulliken charges on O, N, H(H_2O), and H(NH_3) atoms that belong to solvent molecules inside the QM region resulting during the QM/MM simulation were compared to the fixed charges used in the pair potential for the Coulombic interactions. From the QM/MM simulation, we found that both water and ammonia molecules inside the QM part are strongly polarized by Mg^{2+} , yielding atomic charges within the molecules increased by about 40% and 28% for water and ammonia (i.e., N and O atoms are more negative and H atoms are more positive), respectively. This observation confirms well the importance of QM treatment for describing the solvation shell structure of Mg^{2+} properly.

4. Conclusion

Classical pairwise additive potentials—which lack suitable parametrization—are obviously insufficient for a correct treatment of Mg^{2+} in 18.4% aqueous ammonia solution. For such a binary solvent system, the complexity of Mg^{2+} –ligand as well as ligand–ligand interactions results in substantial nonadditive contributions, which can be corrected using the Born–Oppenheimer ab initio QM/MM dynamics method. This technique has predicted an octahedral arrangement with 5 water and 1 ammonia molecule in the first solvation shell of Mg^{2+} , and hence also gives a ligand preference in agreement with expectations according to qualitative concepts of Lewis acid–base interactions. Since experimental data is not available to our knowledge for such a system under investigation, we believe that the present QM/MM result can provide a more reliable

description of the solvated Mg^{2+} . The results of this work—in line with numerous previous investigations—demonstrate that inclusion of higher-order interaction terms is essential for the correct description of solvated ions of all kind.

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