Solvent Effect on Relative Gibbs Free Energy and Structural Property of Eu³⁺ to Yb³⁺ Ion Mutation: A Monte Carlo Simulation Study

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The solvent effects on the relative free energies of Eu³⁺ to Yb³⁺ ion mutation in solution have been investigated using a Monte Carlo simulation of statistical perturbation theory (SPT). Our results agree well with available data that were obtained by others. Particularly, the results of water (SPC/E) solvent are almost identical with experimental data. For the present Eu³⁺ and Yb³⁺ ions, the relative free energies of solvation *vs.* Born's function of bulk solvents decrease with increasing Born's function of bulk solvents. There is also good agreement between the calculated structural properties in this study and the published works obtained by computer simulation and experimental work.

Keywords : Solvent effect, Ion mutation, Monte carlo simulation, Relative free energy.

Introduction

The triple positive lanthanides constitute the longest series of chemically similar metal ions in the periodic table and these ions can be considered as charged sphere differing only by the progressive decrease of their ionic radii along the series. The electrostatic and steric effects mainly govern the coordination properties of those ions. The hydration of the lanthanide metal ions has been the subject of numerous studies.[1-8] Computer simulations represent particularly adequate theoretical tools for understanding and predicting the physicochemical properties of metal ions solutions at the microscopic level, which have the large number of particles forming systems and the variety of different interactions established.[1-8] While solvation of singly charged metal ions has been studied extensively, significantly less information of lanthanide metal ions, *i.e.*, Eu³⁺ and Yb³⁺ is known. These are important to understand complexes at molecular level in order to improve such complexes for potential application in fluoroimmuno assays,[9] optical signal amplification[10,11] and extraction from nuclear waste streams,[12] Especially the Eu³⁺ luminescence in the visible region of electromagnetic spectrum has been thoroughly investigated for application as diagnostic such as fluoroimmuno assays[9] and the luminescence property of Yb³⁺ ion emitting in the near infrared may find application in polymer-based wave-guide optical amplifiers.[10,11] Complexing agents like crown ethers and cryptands are also known to effect a dramatic change in the interaction of cations with their counterions.[13] The association properties of crown ethers have also been affected by lanthanide cations. To address those challenges and the phenomena themselves, we need information on the Eu³⁺ and Yb³⁺ cations stability in solution. These could be obtained from the relative free energies of Eu³⁺ to Yb³⁺ ion mutation in solution.

Several statistical mechanical procedures have evolved for computing the free energy differences. Two particularly promising approaches are umbrella sampling[14-18] and a perturbation procedure.[19-21] The ability to calculate solvation free energies of molecules accurately using perturbation procedure is one of the important and recent developments in computational chemistry.[21] The distribution of an ion binding organic solute between polar or less polar and non-polar media is an important parameter for structure-activity analyses in pharmacological research.[22-24]

It is known that solvent effects often play an important role in determining equilibrium constants, transition states and rates of reactions. The solvent effects can also affect on π-facial selectivity,[25] conformations, and other quantities of chemical and biochemical interest. But, few studies of the solvent effects on both the relative free energies of solvation and the difference in partition coefficients for lanthanide metal ions are available. This stimulated us to perform a systematic theoretical investigation.

In this study, the solvent effects on the relative free energies of solvation of Eu³⁺ to Yb³⁺ ion mutation have been studied using the Monte Carlo simulation of statistical perturbation theory (SPT). The H_2O (TIP3P, TIP4P, SPC/E models), $CHCl_3$, CH_3CN, THF, CH_3OH, CCl_4, CH_2Cl_2, MeOMe, and C_3H_8 are selected because they have the variety of the solvent properties as well as for the availability of potential function parameters.[26-27] The experimental and simulation studies of the Eu³⁺ and Yb³⁺ ions in water have been reported.[3,28] But the fundamental and theoretical studies of computing differences in the partition coefficients, and in the free energies of Eu³⁺ to Yb³⁺ ion mutation in several solvents are not available. This paper is, for the first time, studied based on fluid simulations at the atomic level for solvent effects on Eu³⁺ to Yb³⁺ ion mutation.

Computational Method

The procedure used is similar to that was employed in

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studies of the ion mutations and the organic solute mutation.[29-30] The modeled systems consisted of an ion plus 250 solvent molecules in a cubic cell with periodic boundary conditions in the isothermal-isobaric ensemble at 25 °C and 1 atm. First, the Monte Carlo simulations are described, including a summary of the method for computing the relative free energy changes, and then a brief discussion of the potential functions is given.

Monte Carlo Simulations. The free energy changes were obtained *via* a series of 5 simulations with SPT in forward and backward directions.[22,30] In Monte Carlo simulations of SPT, we used doublewide sampling.[31]

The perturbation approach[30,32] is based on

$$G_i - G_j = -k_B T \ln \langle \exp(-(H_i - H_j)/k_B T) \rangle_j. \quad (1)$$

If one considers the following thermodynamic cycle for two ions, A and B, in two solvents, log P for the ions is defined in Eqs. (2) and (3) in terms of the free energies of transfer.

From the cycle, Eq. (4) is obtained which yields Eq. (5)

solvent 1: $A \xrightarrow{\Delta G_1(AB)} B$

$\Delta G_t(A) \downarrow \qquad\qquad \downarrow \Delta G_t(B)$

solvent 2: $A \xrightarrow{\Delta G_2(AB)} B$
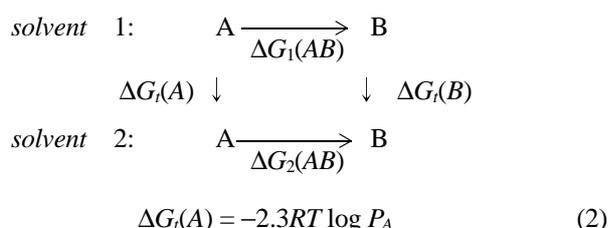
$$\Delta G_t(A) = -2.3RT \log P_A \quad (2)$$

$$\Delta G_t(B) = -2.3RT \log P_B \quad (3)$$

$$\Delta G_t(B) - \Delta G_t(A) = \Delta G_2(AB) - \Delta G_1(AB). \quad (4)$$

$$\Delta \log P = \log P_B - \log P_A = (\Delta G_1(AB) - \Delta G_2(AB))/2.3RT \quad (5)$$

The last expression in Eq. (5) associates the difference in log Ps with the difference in free energies for mutating A to B in the two solvents. That absolute log Ps could also computed by directly calculating the free energy of transfer. This would require taking the difference in absolute free energies of solvation for the ion, which could be obtained from simulations in which the ion is made to vanish in the two solvents.[31-36]

In this study, simulations were run for a coupling parameter, λ_i, which was used to smoothly transform Eu^{3+} ion ($\lambda = 0$) to Yb^{3+} ion ($\lambda = 1$). In this context, it is convenient to define a coupling parameter λ that allows the smooth conversion of system 0 to 1. Then for many possible features ζ of the systems including geometrical and potential function parameters, Eq. (6) can be used to represent the mutation of system 0 to 1 as λ goes from 0 to 1:[21]

$$\zeta(\lambda) = \zeta_0 + \lambda(\zeta_1 - \zeta_0). \quad (6)$$

Each simulation entailed an equilibration period for 4×10^6 configurations, followed by averaging for 1×10^7 configurations. Little drift in the averages was found during the last 4×10^6 configurations.[29,31] Metropolis and preferential sampling were employed, and the ranges for attempted

translations and rotations of the ions and solvent molecules were adjusted to give an approximately 45% acceptance rate for new configurations.[29,31]

Intermolecular Potential Functions. The solvent-solvent and ion-solvent interactions are assumed to be pair additive and are described in the standard Lennard-Jones plus Coulomb format.

$$\Delta E = \sum_i \sum_j (q_i q_j e^2/r_{ij} + A_{ij}/r_{ij}^{12} - C_{ij}/r_{ij}^6) \quad (7)$$

The ions and molecules are represented by interaction sites located on nuclei in the molecules that have associated partial atomic charge, q_i and Lennard-Jones radius σ_i and Lennard-Jones well depth ε_i. Furthermore, the A and C parameters may be expressed as $A_{ii} = 4\varepsilon_i \sigma_i^{12}$ and $C_{ii} = 4\varepsilon_i \sigma_i^6$ and standard combining rules are used such that $A_{ij} = (A_{ii}A_{jj})^{1/2}$ and $C_{ij} = (C_{ii}C_{jj})^{1/2}$ where i and j indices span all of the solvents and water sites. The united-atom model was used for CH_ns in the solvents: CH_ns were treated as single atoms. The SPC/E, TIP4P and TIP3P models have been used for water.[26,37,38] The charges and Lennard-Jones parameters have been selected to yield correct thermodynamic and structural results for pure solvent.[39] The OPLS potential parameter are listed in Table 1. In all the calculations, the bond lengths and bond angles have been kept fixed. The

Table 1. OPLS parameters of several solvents[a] and potential parameters of ions[b]

Solvent/Solute	Site	q (e)	σ (Å)	ε (kcal/mol)
H_2O (TIP4P)	O	0.0000	3.1536	0.1550
	H	0.5200	0.0000	0.0000
	M^c	-1.0400	0.0000	0.0000
H_2O (TIP3P)	O	-0.8340	3.1506	0.1521
	H	0.4170	0.0000	0.0000
CH_3CN	C	0.2800	3.6500	0.1500
	N	-0.4300	3.2000	0.1700
	CH_3	0.1500	3.7750	0.2070
CH_3OH	O	-0.7000	3.0700	0.1700
	H	0.4350	0.0000	0.0000
	CH_3	0.2650	3.7750	0.2070
CH_2Cl_2	CH_2	0.5000	3.8000	0.1180
	Cl	-0.2500	3.4000	0.3000
THF	O	-0.5000	3.0000	0.1700
	CH_2	0.2500	3.8000	0.1180
	CH_2	0.0000	3.9050	0.1180
MeOMe	O	-0.5000	3.0000	0.1700
	CH_3	0.2500	3.8000	0.1700
$CHCl_3$	CH	0.4200	3.8000	0.0800
	Cl	-0.1400	3.4700	0.3000
CCl_4	C	0.2480	3.8000	0.0500
	Cl	-0.0620	3.4700	0.2660
C_3H_8	CH_2	0.0000	3.9050	0.1180
	CH_3	0.0000	3.9050	0.1750
Eu	Eu^{3+}	3.0000	3.3000	0.0050
Yb	Yb^{3+}	3.0000	2.9500	0.0040

[a]Ref. 27. [b]Ref. 28. [c]M is a point on the bisector of HOH angle, 0.15 Å from the oxygen toward the hydrogen.

intermolecular interactions were spherically truncated at 8.5, 10, 12.0 Å depending on the box-sizes of the solvents and the reaction field technique activated by DIELRF parameter was used for the correction of long range interactions.[27] The cutoff correction to the solvent-solvent energy for non-aqueous solvents is applied to only Lennard-Jones potential functions.[27]

Results and Discussion

Relative free energies: To examine the solvent effect on the differences in partition coefficients, we have computed the relative free energy of Eu^{3+} to Yb^{3+} ion mutation in the three water models for comparison with the experimental and computer simulations. We have also computed those in the other solvents.

The relative free energies of Eu^{3+} to Yb^{3+} ion mutation along with the published and the experimental works are listed in Table 2. The reported statistical uncertainties for the computed values are fluctuations ($\pm 1\sigma$) and were obtained from separate averages over 4×10^6 to 1×10^7 configurations. The computed ordering of the free energies of solvation in several solvents is $C_3H_8 > CCl_4 > CHCl_3 > CH_2Cl_2 >$ THF $>$ MEOME $>$ CH_3CN $>$ CH_3OH $>$ H_2O (TIP4P) $>$ H_2O (TIP3P) H_2O (SPC/E). That is, the mutation of Eu^{3+} to Yb^{3+} ion can occur more easily in water [H_2O (SPC/E)] than in the less polar or non-polar solvents. In this study, we have noted that the results computed by the reaction field method used for the correction of long-range interactions agree more with the available data than the results obtained without the reaction field method. The relative free energies of Eu^{3+} to Yb^{3+} ion mutation computed by the reaction field method used for the correction of long-range interactions are only listed in Table 2 for clarity.

As noted in Table 2, the relative free energies of solvation *vs.* Born's function of the bulk solvents decrease with increasing Born's function. This changed trend of the relative free energies of solvation could be explained by the differ-

Table 2. Relative Gibbs Free Energies (kcal/mol) of solvation in several solvents and Born's function ($1-1/\varepsilon$) of the bulk solvents

Solvent	ΔG ($Eu^{3+} \rightarrow Yb^{3+}$)	$1-1/\varepsilon$
H_2O(SPC/E)	-49.46 ± 0.29	0.987
H_2O(TIP3P)	-46.83 ± 0.27	0.987
H_2O(TIP4P)	-42.16 ± 0.34	0.987
H_2O(TIP3P)	-46.45 ± 0.16[a]	0.987
Exp.	-50.0[b]	0.987
CH_3CN	-29.96 ± 0.45	0.973
CH_3OH	-37.74 ± 0.25	0.963
CH_2Cl_2	-11.57 ± 0.21	0.888
THF	-26.55 ± 0.12	0.868
MEOME	-29.82 ± 0.59	0.801
$CHCl_3$	-4.44 ± 0.04	0.792
CCl_4	-0.99 ± 0.04	0.552
C_3H_8	-0.11 ± 0.01	0.138[c]

[a]Ref. 28. [b]Ref. 3. [c]273 K data from *Handbook of Chem. & Phys.*, 71ˢᵗ Ed. C.R.C. Press. 1990.

ences in solvation. Especially, in CH_3OH, THF and MEOME, the relative free energies of solvation of the Eu^{3+} to Yb^{3+} ions could be explained by the fact that strong ion-solvent interactions exist in CH_3OH, THF and MEOME solutions even though Born's functions of CH_3OH, THF and MEOME are small. The strong ion-solvent interactions in CH_3OH, THF and MEOME are due to the electron pair donor properties of the solvents to ion, *i.e.*, donor number (DN) of CH_3OH, THF and MEOME established by Gutmann.[40]

In the absence of strong hydrogen bonding, the molecule with the larger dipole moment could be expected to be more favorably solvated.[41] The Eu^{3+} and Yb^{3+} in C_3H_8 provides a striking exception that points out the importance of local electrostatic interactions.[42] The computed difference in the free energies of solvation for ions in C_3H_8 is comparatively small. Clearly, the replacement of the stronger ion-solvent interactions with the weaker ion-solvent interactions is responsible for the decreasing effect.

Comparing the relative free energies of Eu^{3+} to Yb^{3+} ion mutation, in H_2O (SPC/E) in this study with those,[28,3] those of H_2O (SPC/E) and H_2O (TIP3P) are -49.45 ± 0.29 kcal/mol and -46.83 ± 0.27 kcal/mol in this study and that [28] of H_2O (TIP3P) is -46.45 kcal/mol and that of experiment [3] is -50.0 kcal/mol, respectively. We couldn't compare with the relative free energies of Eu^{3+} to Yb^{3+} ion mutation between this study and the published in the other solvents because there were no studies of the relative free energies of Eu^{3+} to Yb^{3+} ion mutation in the other solvents.

There is good agreement among three studies if considering both simulation and experimental methods used to obtain the hydration free energies and the standard deviations. In this context, we can say that the relative free energies in the other solvents are expected to be reliable as noted in Refs. [30, 43]. The trends of binding energies of [18] crown-6 linked with lanthanide cations obtained by MC are coincident with our results for the relative free energies of hydration.[28] The results without polarization effects used in this study could be reasonable as noted in Ref. [28, 29]. The relative free energy of Eu^{3+} to Yb^{3+} ion mutation, in H_2O (SPC/E) is smaller than those of H_2O (TIP3P) and H_2O (TIP4P). This difference of the relative free energies of solvation could be explained by the difference in polarity among the H_2O (SPC/E), H_2O (TIP3P) and H_2O (TIP4P) three-water models.

Partition coefficients: The calculated logarithms of the solvent/water [H_2O (SPC/E)] partition coefficients are listed in Table 3. ΔG_1 and ΔG_2 in Eq. 5 are just the difference in free energies of solvation for A and B. If solvent 1 is water [H_2O (SPC/E)] and solvent 2 is the less polar or non-polar solvent, larger values of log P imply that the change from Eu^{3+} to Yb^{3+} is more easer in H_2O (SPC/E) than the less polar or non-polar solvents. It is necessary to note that the sign and magnitude of the calculated Δlog Ps closely parallel the relative free energies of solvation.

Radial distribution function (rdf) and structural properties: The solvent-ion structure can be characterized through radial distribution functions (RDFs), g_{ai} (r), which

Table 3. Differences in the logarithms of solvents/H$_2$O (SPC/E) partition coefficients

| Solvent	log P_B–log P_A
H$_2$O(TIP3P)	1.93
H$_2$O(TIP4P)	5.36
CH$_3$CN	14.32
CH$_3$OH	8.61
CH$_2$Cl$_2$	27.82
THF	16.82
MEOME	14.47
CHCl$_3$	33.06
CCl$_4$	35.72
C$_3$H$_8$	36.24

give the probability of finding an atom of type i a distance r from an atom of type a. The positions of the first maximum of the ion-(O, N, Cl and CH$_2$) in the solvents obtained from RDF's are listed in Table 4(a). They decrease when the Eu^{3+} ion transforms to the Yb^{3+} ion in all solvents. The positions of the first maximum of the ion-(O, N, Cl and CH$_2$) in the

Table 4. Structural results of the first shell
(a) Structural properties of Eu^{3+} and Yb^{3+} ions in solutions

Solvent	Eu^{3+} ion	Yb^{3+} ion	Eu^{3+} ion	Yb^{3+} ion
	R$_{i-o}$ (Å)		Coordination Number	
H$_2$O(SPC/E)	2.6	2.5	10.0	9.0
H$_2$O(TIP3P)	2.5	2.3	9.0	8.7
H$_2$O(TIP4P)	2.5	2.4	9.0	8.7
CH$_3$OH	2.5	2.3	9.0	8.0
THF	2.5	2.4	7.0	7.0
MEOME	2.5	2.3	7.0	6.0
	R$_{i-N}$ (Å)		Coordination Number	
CH$_3$CN	2.6	2.4	9.6	8.3
	R$_{i-Cl}$ (Å)		Coordination Number	
CH$_2$Cl$_2$	2.9	2.7	2.6	3.3
CHCl$_3$	3.1	2.9	2.3	3.3
CCl$_4$	3.3	3.1	2.0	1.9
	R$_{i-CH2}$ (Å)		Coordination Number	
C$_3$H$_8$	4.7	4.5	4.6	3.6

(b) Structural properties of Eu^{3+} and Yb^{3+} ions in water

	Eu^{3+}	Yb^{3+}
	Ion – Oxygen Distance (Å)	Ion – Oxygen Distance (Å)
This work	2.5	2.30
Veggel[a]	–	2.35
Exp.[b]		2.32
	1st coord. Shell Distance (Å)	1st coord. Shell Distance (Å)
X-ray[b]	2.45	–
	Coordination Number	Coordination Number
This work	9.0	8.7
Veggel[a]	9.0	9.0
X-ray[b]	8.3	–

[a]Ref. 28. [b]Ref. 3.
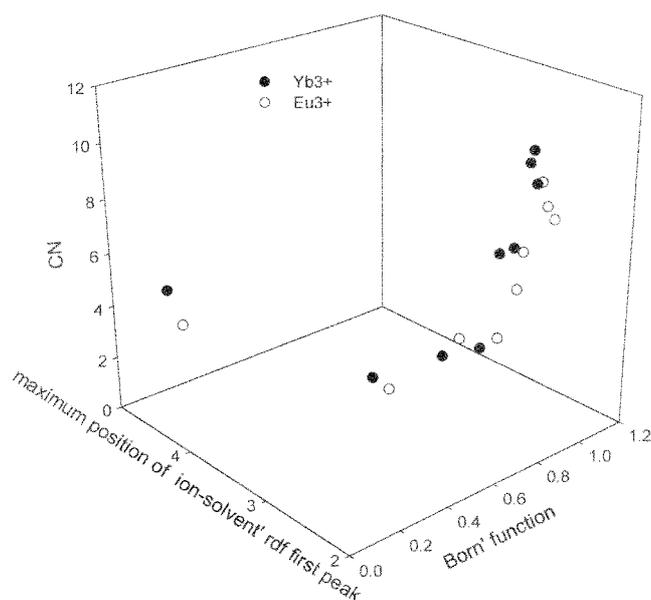
Figure 1. Plot of structural property *vs.* Born's function of bulk solvents at 298 K and 1 atm.

solvents and the number of solvent molecules in the first coordination shell *vs.* Born's function of bulk solvents are plotted in Figure 1. The coordination numbers (CN) of solvent molecules in the first coordination shell of Eu^{3+} and Yb^{3+} ions evaluated by integrating ion-(O, N, Cl and CH$_2$) solvent rdfs to their first minimum are also listed in Table 4(a). The number of solvent molecules in the first coordination shell around the ion for all solvents except THF, CHCl$_3$ and CH$_2$Cl$_2$ decreases when the Eu^{3+} ion transforms to the Yb^{3+} ion. In CHCl$_3$ and CH$_2$Cl$_2$, the number of solvent molecules in the first coordination shell of Eu^{3+} and Yb^{3+} ions increases when the Eu^{3+} ion transforms to the Yb^{3+} ion. Those trends could be also explained by the strengthened and the weakened solvent-ion interactions when the Eu^{3+} ion smoothly transforms to the Yb^{3+} ion.

Experimental data on the solute-solvent structure in Eu^{3+} and Yb^{3+} ion aqueous solutions are essentially limited to the first shell. In Table 4(b), the positions of the first maximum in ion-oxygen RDF's obtained from this study are compared with the available computer simulations and experimental results.[3,28] There is good agreement between our results and the computer simulations and experimental results. Rao and Berne have been noted that local solvation structures in aqueous ionic solutions are similar to those in relatively small cluster.[44]

The calculated coordination numbers for ions in aqueous solutions are also compared with the available the computer simulations and experimental results in Table 4(b). Both the calculated and the experimental results are sensitive to the definition of coordination number. A wide range of experimental hydration numbers is available from mobility measurements.[45] Those values correspond to the number of solvent molecules that have undergone some constant critical change due to the ion, a change that is susceptible to measurement

by a particular experimental technique. Such hydration numbers are often quite different from coordination numbers based on a structural definition, like those from diffraction experiments.[46] Mezei and Beveridge obtained their values by integrating the ion-center of mass of water rdf's up to the minimum of the first peaks.[47] These values will not be significantly different if they are based on ion-oxygen rdf's. This is a straightforward definition and this has been adopted for all the calculated value for those ions. For the present results, the coordination number is reported on the basis of integration to the minimum after the first peak in the ion-oxygen.

As shown in Table 4(b), the calculated coordination numbers from the ion-oxygen RDF's compare favorably with the computer simulations and experimental results taking into account the problems in the definition. Based on this comparison, the computed structural properties in the other solvents are also expected to be reliable.

The RDFs of Eu^{3+} and Yb^{3+} ion in selected solvents for clarity are plotted in Figure 2 to Figure 3.

As shown in Figure 2, the ordering of smaller r-value, the positions of the first maximum of the Eu^{3+} ion-(O, N, Cl) in the solvents is $THF < CH_3CN < CH_3OH < H_2O$ (SPC/E) < CCl_4. But the ordering of smaller r-value, the positions of the first maximum of the Yb^{3+} ion-(O, N, Cl) in the solvents is $CH_3OH < THF < CH_3CN < H_2O$ (SPC/E) < CCl_4 shown in Figure 3 and the g(r) intensity of the first peak is not changed
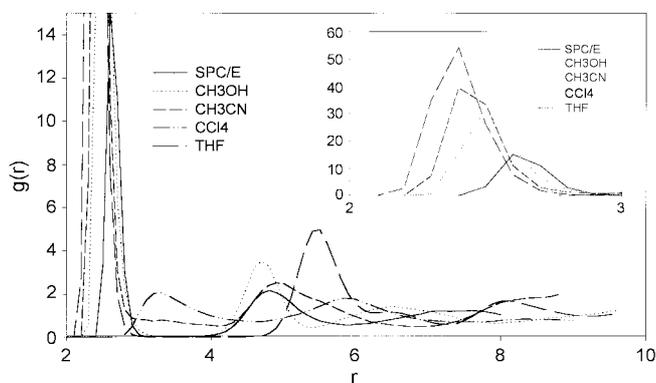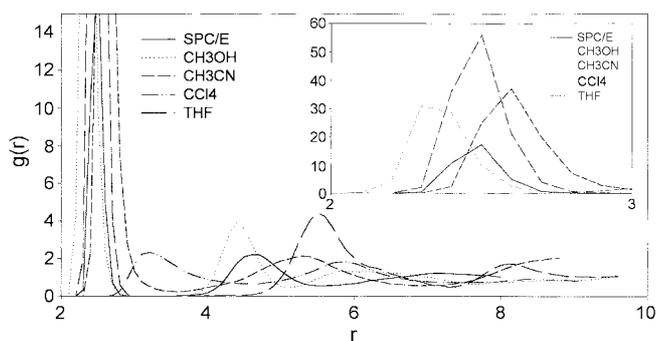
as the Eu^{3+} ion smoothly transforms to the Yb^{3+} ion. The trends of RDF pattern obtained by MC in ref. [28] are coincident with those of our hydration results. In Figure 2 and Figure 3, the second peaks are located between 4 and 6 Å. Especially, the second peaks of CH_3CN and CH_3OH have the bigger peak intensities than the others, which indicate that Eu^{3+} and Yb^{3+} ion in CH_3CN and CH_3OH have the clear second solvation shell. From those trends, we have noted that the degree of the ions - solvent interactions is dependent on the Born's function of the solvents, the electron pair donor properties of the solvent and the differences in solvation.

Conclusions

We compared the relative free energies of Eu^{3+} to Yb^{3+} ion mutation, in H_2O (SPC/E) in this study with those of the computer simulation and experimental works. There is good agreement among the three studies and it is proved that the relative free energies in the other solvents are expected to be reliable. For the Eu^{3+} to Yb^{3+} ion mutation, the relative free energies of solvation *vs.* Born's function of bulk solvents decrease with increasing Born's function. There is also good agreement between the calculated structural properties in this study and the computer simulation and experimental works. From this study, we have concluded that a Monte Carlo simulations of SPT is a good approach for estimating changes in log *P* that accompany ion mutation and the results of this study appear useful in providing both estimates of the effects of solvents changes on partitioning behavior of ion pair between polar solvent and the less polar or non-polar. For the present ions, Born's function of the solvents, the electron pair donor properties of the solvent and the differences in solvation dominate the differences in the relative free energies of solvation and partition coefficients. The results of this study appear promising for providing the association properties of crown ethers with lanthanide metals.

Figure 2. Radial distribution function of Eu^{3+} ion in selected solvents. Distances are in angstroms throughout.

Figure 3. Radial distribution function of Yb^{3+} ion in selected solvents.

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