QSPR Analysis of Solvent Effect on Selectivity of 18-Crown-6 between Nd^{3+} and Eu^{3+} Ions: a Monte Carlo Simulation Study

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We have investigated the solvent effects on $\Delta\log K_s$ (the difference of stability constant of binding) and the different free energies of binding of Nd^{3+} and Eu^{3+} ions to 18-crown-6, *i.e.*, the selectivity of Nd^{3+} and Eu^{3+} ions to 18-crown-6 using a Monte Carlo simulation of statistical perturbation theory (SPT) in diverse solvents. The stability constant ($\Delta\log K_s$) of binding of Nd^{3+} and Eu^{3+} ions to 18-crown-6, in CH_3OH was calculated in this study as -1.06 agrees well with the different experimental results of $-0.44 \sim -0.6$, respectively. We have reported here the quantitative solvent-polarity relationships (QSPR) studied on the solvent effects the relative free energies of binding of Nd^{3+} and Eu^{3+} ions to 18-crown-6. From the calculated coefficients of QSPR, we have noted that solvent polarity (E_T) and Kamlet -Taft's solvatochromic parameters (β) dominate the differences in relative solvation Gibbs free energies of Nd^{3+} and Eu^{3+} ions but basicity (Bj) dominates the negative values in differences in the stability constant ($\Delta\log K_s$) as well as the relative free energies of binding of Nd^{3+} and Eu^{3+} ions to 18-crown-6 and acidity (Aj) dominates the positive values in differences in the stability constant ($\Delta\log K_s$) as well as the relative free energies of binding of Nd^{3+} and Eu^{3+} ions to 18-crown-6.

Key Words : The difference of stability constant of binding, Monte Carlo simulation, Selectivity, Solvent Effect, Quantitative solvent-polarity relationships (QSPR)

Introduction

In the host -guest interaction, factors in the extraction selectively of any host species include the relative free energy of desolvation of the guest molecules and the free energy of organizing the host into a suitable conformation with remote substitution for binding.[1] The study of molecular recognition for host-guest interactions[1-4] has received an increasing interest, since the discovery of 18-crown-6 (1,4,7,10,13,16-hexaoxacyclooctadecane) by Perdersen in 1967.[5]

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[6-13] 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.[6-13] While solvation of singly charged metal ions has been studied extensively, significantly less information of lanthanide metal ions, *i.e.*, Eu^{3+} is known. These are important to understand complexes at molecular level in order to improve such complexes for potential application in fluoroimmuno assays,[14] optical signal amplification[15,16] and extraction from nuclear waste streams.[17] Especially the Eu^{3+} luminescence in the visible region of electromagnetic spectrum has been thoroughly investigated for application as diagnostic such as fluoroimmuno assays[14] and the luminescence property of Yb^{3+} ion emitting in the near infrared may find application in polymer-based wave-guide optical amplifiers.[15,16] Complexing agents like crown ethers and cryptands are also known to effect a dramatic change in the interaction of cations with their counterions.[18] 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 Nd^{3+} and Eu^{3+} cations stability in solution. These could be obtained from the relative free energies of Nd^{3+} and Eu^{3+} ion mutation in solution.

Several statistical mechanical procedures have evolved for computing the free energy differences. The particularly promising approaches are thermodynamic integration, umbrella sampling[19-23] and a perturbation procedure.[24-26] The ability to calculate solvation free energies of molecules accurately using perturbation procedure with the specified potential is one of the important and recent developments in computational chemistry.[26] 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.[27-29] It is known that solvent effects often play an important role in determining equilibrium constants, transition states and rates of reactions, π-facial selectivity,[30] conformations, and the other quantities of chemical, chemical physics and biochemical interest. But, few studies of solvent effects on both the relative free energies of binding of ions to 18-crown-6 and $\Delta\log K_s$ are available.

In this study, we have investigated the solvent effect on the relative stability constant of binding of Nd^{3+} and Eu^{3+} ions to

18-crown-6 and the relative free energies of binding of Nd^{3+} and Eu^{3+} ions to 18-crown-6, using Monte Carlo simulation of statistical perturbation theory (SPT). H_2O (TIP3P, TIP4P models), $CHCl_3$, CH_3CN, THF, CH_3OH, CCl_4, $MeCl_2$, MEOME, and C_3H_8 are selected as solvents.[20,25] Experimental studies of the relative free energies of binding of Nd^{3+} and Eu^{3+} ions to 18-crown-6 in methanol have been reported. But experimental data for log K_s, as well as the relative free energies of binding of Nd^{3+} and Eu^{3+} ions to 18-crown-6 in diverse solvents are not available.

We present the first calculation to computing solvent effects on the differences in log K_s (stability constant) as well the relative free energies of binding of Nd^{3+} and Eu^{3+} ions to 18-crown-6 using Monte Carlo simulation of statistical perturbation theory (SPT) in this study. We have reported here the quantitative solvent-polarity relationships (QSPR) studied on the solvent effects on the relative free energies of binding of Nd^{3+} and Eu^{3+} ions to 18-crown-6. This study provides additional interests of the solvent effect on equilibrium constants, transition states, rates of the organic reaction,[31] and the other quantities of chemical, biochemical interest and chemical-physics.

Computational Method

Monte Carlo Simulations. The procedure used here is similar to that employed in Refs. 32, 33, 34, 35 and 37. Monte Carlo simulations were carried out in the isothermal-isobaric ensemble at 25 °C and 1 atm for systems typically consisting of the ion and 18-crown-6 plus 250 solvent molecules in a cubic cell with periodic boundary conditions. First, the Monte Carlo simulations are described, including a summary of the method for computing the relative free energy changes and a brief discussion of the potential functions is given. The free energy changes were obtained *via* a series of 5 separate simulations with SPT in forward and backward directions.[32-37]

In order to study the equilibrium thermodynamics of binding, we have used Monte Carlo simulations with the thermodynamic cycle-perturbation theory and doublewide sampling.[32-37]

In the notation of this method, the relative free energy of binding between guest G and g to the host H can be expressed as $\Delta\Delta G = \Delta G_{s2} - \Delta G_{s1} = \Delta G_4 - \Delta G_3$

$$\begin{array}{lll} solvent \quad 1: & g + H \xrightarrow{\Delta G_{s1}} & g:H \\ & \Delta G_3 \downarrow & \downarrow \Delta G_4 \\ solvent \quad 1: & G + H \xrightarrow{\Delta G_{s2}} & G:H \end{array}$$

$$\Delta G_{s1} = -2.3RT \log K_{s1} \quad (1)$$

$$\Delta G_{s2} = -2.3RT \log K_{s2}\,. \quad (2)$$

Here, ΔG_s is free energies of binding of guest to host and any thermodynamic state function and log K_s is stability constant of guest to host.

From the cycle, Eq. (3) is obtained which yields Eq. (4).

$$\Delta G_{s2} - \Delta G_{s1} = \Delta G_4 - \Delta_{G3}. \quad (3)$$

$$\Delta \log K_s = \log K_{s2} - \log K_{s1} = -(\Delta G_{s2} - \Delta G_{s1})/2.3RT. \quad (4)$$

The last expression associates the difference in log K_s's with the difference in the relative free energies of binding of Nd^{3+} and Eu^{3+} ions to 18-crown-6 [35] in the one solvents.

In this study, the substitutions are H = 18-crown-6, g = Nd^{3+} and G = Eu^{3+}. ΔG_3 and ΔG_4 are available from Monte Carlo simulation in which guest is binding to host in the solvents.

Simulations were run for a coupling parameter, λ_i, which was used to smoothly transform Nd^{3+} with 18-crown-6 (λ = 0) to Eu^{3+} with 18-crown-6 (λ = 1). Simulations were run for λ_i = 0.0, 0.2, 0.4, 0.6, 0.8 and 1.0. Then for many possible features ζ of the systems including geometrical and potential function parameters, Eq. (5) can be used to represent the mutation of system 0 to 1 as λ goes from 0 to 1.[32-35]

$$\zeta(\lambda) = \zeta_0 + \lambda(\zeta_1 - \zeta_0). \quad (5)$$

In this study, each simulation entailed an equilibration period for 4×10^6 configurations starting from equilibrated boxes of solvent, followed by averaging for 2×10^7 configurations. Little drift in the averages was found during the last 1×10^7 configuration.[32-35] Metropolis and preferential sampling methods were employed in simulations, and the ranges for attempted translations and rotations of the solute and solvent molecules were adjusted to give a *ca.* 45% acceptance rate for new configurations.[32-35]

Potential Functions. The pair potential energy function of the OPLS force field is of the following form[38]:

$$E_{total} = \sum_{bonds} K_r(r - r_0)^2 + \sum_{angles} K_\theta(\theta - \theta_0)^2 + \\ + \sum_{torsions} \frac{V_n}{2}[1 \pm \cos(n\phi - \gamma)] + \sum_{non-bonded} \left[\frac{A_{ij}}{r_{ij}^{12}} + \frac{C_{ij}}{r_{ij}^{6}} - \frac{q_i q_j}{\varepsilon r_{ij}}\right] f_{ij} \quad (6)$$

f_{ij} = 0.5 if i, j are 1,4; otherwise, f_{ij} = 1.0

Where K_r, K_q, V_n, and φ are empirical parameters related to bond length, bond angle and torsion angle, respectively. The ion and molecules are represented by interaction sites located on nuclei that have associated charge, q_i and Lennard-Jones parameter σ_i and ε_i. One of the standard rules is used such that $A_{ij} = (A_{ii}A_{jj})^{1/2}$ and $C_{ij} = (C_{ii}C_{jj})^{1/2}$. Furthermore, the parameters A and C may be expressed as $A_{ii} = 4\varepsilon_i\sigma_i^{12}$ and $C_{ii} = 4\varepsilon_i\sigma_i^{6}$ where σ and ε are the Lennard-Jones radius and energy terms and i and j indices span all of the 18-crown-6, solvents and water sites. In Ref. 39, Jorgensen noted that the equation has been dominant with two-body potential functions that are parameterized to take the higher-order interaction and polarization effect into account. In Ref. 1, Kollman *et al.* also concluded that the additive force field model is adequate to describe energetics of cation comlexation with 18-crown-6.

The OPLS (optimized potential for liquid simulation) potential parameters are used for solvents and those are

Table 1. Potential parameters of ions[a]

Ion	q (e)	σ (Å)	ε (kcal /mol)
Eu^{3+}	3.0000	3.3000	0.0050
Nd^{3+}	3.0000	3.4730	0.0054

[a]Ref 40.

based on a united-atom model[32,36] but the TIP4P and TIP3P models have been used for water.[38] The 18-crown-6 is represented with the OPLS- all-atom (AA) force field.[38] The charges and Lennard-Jones parameters have been selected to yield correct thermodynamic and structural results of pure liquids.[38] The charges and Lennard-Jones parameters of ions are listed in Table 1 and are obtained by the method used in Ref. 40. In all the calculations, the bond lengths, bond angles and dihedral angles have been varied in minimization step and in simulations. The statistical uncertainties for the computed values are in ($\pm 1\sigma$) fluctuations. The intermolecular interactions were spherically truncated at 8.5, 10, 12.0 Å, depending on box-sizes of solvents and the reaction field method was used for long range correction.[32,33] For example, complex was placed center of a rectangular box of OPLS 267 MeOHs of 26.7 × 26.7 × 26.7 dimensions. The cutoff correction to the solvent-solvent energy for non-aqueous solvents is applied to only Lennard-Jones potential functions.[38]

Results and Discussion

Free Energy Differences of the Solvated Complexes. To study the solvent effect on differences in stability constant ($\Delta\log K_s$) as well as the free energy differences of binding of Nd^{3+} and Eu^{3+} ions to 18-crown-6, we have computed those in the two water models and in the other solvents.

The calculated free energy differences of binding of Nd^{3+} and Eu^{3+} ions to 18-crown-6 along with the experimental works are listed in Table 2. The reported statistical uncertainties for the computed values are ($\pm 1\sigma$) fluctuations and were obtained from separate averages over 4×10^6 to 20×10^6 configurations. The computed ordering free energy differences of binding of Nd^{3+} and Eu^{3+} ions to 18-crown-6 in several solvents is C_3H_8 > CCl_4 > $CHCl_3$ > $MeCl_2$ > MeOMe > THF > CH_3OH > CH_3CN > H_2O (TIP4P) > H_2O (TIP3P). This comes about by the change in free energy differences of binding of Nd^{3+} and Eu^{3+} ions to 18-crown-6 being less favorable in the polar and less polar or non-polar solvents than in H_2O (TIP3P). In this study, we have noted that the intermolecular interactions were depending on box-sizes of solvents and the potential cut-off, but the results truncated at 8.5, 10, 12.0 Å, depending on box-sizes of solvents are only listed in Table 2 for clarity.

The free energy difference of binding of Nd^{3+} and Eu^{3+} ions to 18-crown-6, in CH_3OH calculated in this study as -14.84 ± 0.21 agrees with the other result of -16.58 ± 0.16,[40] respectively. To describe the differences between this work and Ref. 40, potentials parameter is similar between the studies but cutoffs and numbers of solvents are different between the studies. In view of these differences, the agreement between the two works is good. Based on those results, the binding free energy difference of Nd^{3+} and Eu^{3+} ions to 18-crown-6 in the other solvents is expected to be reliable. The free energy difference of binding of Nd^{3+} and Eu^{3+} ions to 18-crown-6, in H_2O (TIP3P) is smaller than that of H_2O (TIP4P). This difference could be explained by the difference of polarity between water models.

Relative Binding Gibbs Free Energies. The relative binding Gibbs free energies of Nd^{3+} and Eu^{3+} ions to 18-crown-6 complexes can be calculated using ΔG_3 and ΔG_4 in Eq. (3) and the published data of the relative free energies[40] are also listed in Table 2. The ordering of the relative binding Gibbs free energies in several solvents is C_3H_8 > CCl_4 > $CHCl_3$ > $MeCl_2$ > CH_3CN > MeOMe > THF > CH_3OH > H_2O (TIP4P) > H_2O (TIP3P). This comes about by the change in relative binding Gibbs free energies being more favorable in H_2O (TIP3P) than in the polar and less polar or

Table 2. Relative solvation Gibbs free energies (kcal/mol) and the relative binding Gibbs free energies (kcal/mol) in diverse solvents and Born's function ($1–1/\varepsilon$) of bulk solvents

Solvent	ΔG ($Nd^{3+} \rightarrow Eu^{3+}$)[d]	Δ*G* (18-Crown-6/ Nd^{3+} → 18-Crown-6/Eu^{3+})	ΔΔ*G* of binding	1 – 1/ε
H_2O(TIP3P)	−21.6 ± 0.4	−18.9 ± 0.1	−2.7	0.987
H_2O(TIP4P)	−19.1 ± 0.4	−17.2 ± 0.2	−1.9	0.987
H_2O(TIP3P)[a]	−23.6	–	–	0.987
Exp.[b]	−19.2	–	–	0.987
CH_3CN	−10.2 ± 0.1	−15.5 ± 0.3	5.3	0.973
CH_3OH	−16.3 ± 0.1	−14.8 ± 0.2	−1.5	0.963
CH_3OH[a]	–	−16.6 ± 0.2	−0.3	0.963
Exp.[c]	–	–	−0.6 ~ −0.82	0.963
$MeCl_2$	−5.8 ± 0.1	−13.4 ± 0.2	7.6	0.888
THF	−12.4 ± 0.3	−14.5 ± 0.2	2.1	0.868
MeOMe	−11.5 ± 0.2	−14.1 ± 0.1	2.6	0.801
$CHCl_3$	−1.7 ± 0.1	−13.3 ± 0.2	11.6	0.792
CCl_4	−0.38 ± 0.02	−12.9 ± 0.2	12.5	0.552
C_3H_8	−0.06 ± 0.01	−12.7 ± 0.3	12.6	0.138

[a]Reference 42. [b]Reference 48. [c]Reference 41. [d]Reference 34 (b)

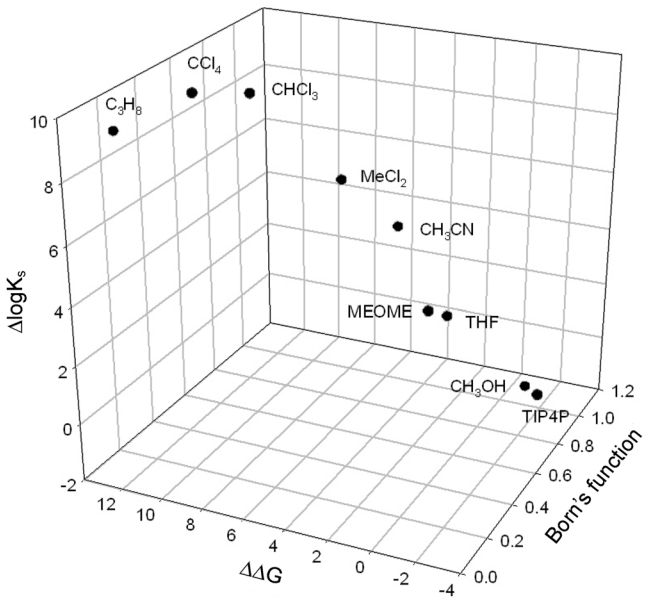

Figure 1. Plot of relative binding Gibbs free energies ($\Delta\Delta G$) of Nd^{3+} and Eu^{3+} ions to 18-crown-6 and the difference of stability constant ($\Delta\log K_s$) of binding of Nd^{3+} and Eu^{3+} ions to 18-crown-6 *vs.* Born's function of the solvent at 298 K and 1 atm.

non-polar solvents. The relative binding Gibbs free energies versus Born's function of the solvents are plotted in Figure 1. Note that the signs of the relative binding Gibbs free energies are reversed in going from H_2O (TIP3P), CH_3OH, H_2O (TIP4P), solutions to CH_3CN, THF, MeOMe, $MeCl_2$, $CHCl_3$, C_3H_8 and CCl_4 solutions. That is, 18-crown-6 binds Nd^{3+} more tightly than Eu^{3+} in H_2O (TIP3P), CH_3OH, H_2O (TIP4P), solutions, whereas 18-crown-6 favors Eu^{3+} in CH_3CN, THF, MeOMe, $MeCl_2$, $CHCl_3$, C_3H_8 and CCl_4 solutions. Similar trend has been observed in the study of alkali cation complexes of 18-crown-6 in the study of alkali cation complexes of 18-crown-6 in diverse solutions.[33(a)] Binding selectivity is often associated with the ionic radius of the cation and the size of the crown ether cavity that it will occupy, the lager mismatch between the ionic radius of the cation and the size of the crown ether cavity, the less that the cation binds favorably. Alkali and alkaline earth metal ion complexes of 18-crown-6 are enthalpy stabilized and entropy destabilized, the opposite is true of and the stability decreases along the series of lanthanide complexes is enthalpic in origin for cations up to Nd^{3+} in CH_3OH. This fact reflects the delicate balance among ligand (18-crown-6) - cation binding, solvation and ligand conformation that exits in complex systems. The complexes with the higher atomic number are generally more stable than those of the lower atomic number. Selectivity is apparently the result of delicate balance of the forces that the cation experiences as the crown ether and solvent molecules compete for the cation in solution. In this study, the cations have one positive charge and the binding cores of the hosts consist of six oxygen atoms with large partial negative charges, electrostatic interactions are also expected to play an important role in the determining the cation-biding ability of 18-crown-6 system.[33]

Table 3. Differences in the stability constant of binding of Nd^{3+} and Eu^{3+} ions to 18-crown-6

Solvent	$\log K_{s2} - \log K_{s1}$
H_2O(TIP3P)	−2.0
H_2O(TIP4P)	−1.4
CH_3CN	3.9
CH_3OH	−1.1
Exp.[a]	−0.44 ~ −0.60
$MeCl_2$	5.6
THF	1.5
MeOMe	1.9
$CHCl_3$	8.5
CCl_4	9.2
C_3H_8	9.3

Reference 41

Table 4. Structural properties of 18-Crown-6/Nd^{3+} and 18-Crown-6/Eu^{3+} ion complex in diverse solvents

Solvent	18-Crown-6/Nd^{3+} ion		18-Crown-6/Eu^{3+} ion	
	$R_{i\text{-}o}$(Å)	CN (Coordination Number)	$R_{i\text{-}o}$(Å)	CN
H_2O(TIP3P)	2.5	5.0	2.5	4.9
H_2O(TIP4P)	2.6	4.6	2.5	4.0
CH_3OH	2.5	4.0	2.5	3.6
THF	2.6	3.0	2.5	3.0
MeOMe	2.6	3.0	2.5	2.9
	$R_{i\text{-}C}$(Å)	CN	$R_{i\text{-}C}$(Å)	CN
CH_3CN	3.8	4.3	3.8	4.7
	($R_{i\text{-}CH}$) (Å)	CN	($R_{i\text{-}CH}$) (Å)	CN
$CHCl_3$	4.9	3.6	4.7	2.9
	($R_{i\text{-}Cl}$) (Å)	CN	($R_{i\text{-}Cl}$) (Å)	CN
CCl_4	3.5	0.6	3.4	0.6
	$R_{i\text{-}CH2}$(Å)	CN	$R_{i\text{-}CH2}$(Å)	CN
CH_2Cl_2	4.7	4.0	4.7	3.9
C_3H_8	4.9	2.1	4.9	2.6

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

	Nd^{3+}	Eu^{3+}
	Ion – Oxygen Distance (Å)	Ion – Oxygen Distance (Å)
This work	2.50	2.5
Veggel[a]	2.55	–
Exp.[b]	2.50	
	1st coord. Shell Distance (Å)	1st coord. Shell Distance (Å)
X-ray[b]	–	2.45
	Coordination Number	Coordination Number
This work	8.8	9.1
Veggel[a]	9.0	9.0
X-ray[b]	8-9	8.3

[a]Reference 41. [b]Reference 43.

The relative binding Gibbs free energies, in CH_3OH

Table 5. Empirical parameter of solvents polarity.[a]

	ε	E_T	β	α	π^*	DN	Aj	Bj
H_2O(TIP4P)	78.3	1	0.18	1.17	1.09	33	1	1
CH_3CN	36.6	0.46	0.31	0.19	0.75	14.1	0.37	0.86
CH_3OH	32.7	0.762	0.62	0.93	0.6	30	0.75	0.5
THF	7.6	0.207	0.55	–	0.58	20	0.17	0.67
$CHCl_3$	4.8	0.259	–	0.4	0.58	4	0.42	0.73
CCl_4	2.2	0.052	–	0	0.28	–	0.09	0.34

[a]Reference 42.

calculated in this study −1.45 kcal/mole compared well with those in ref. 40, 41, those of experimental works in CH_3OH[41] obtained by using Calorimeter, Conductance and ISE methods are $-0.6 \sim -0.82$ kcal/mol, and that of other calculation work[40] is −0.3 kcal/mol, respectively. Based on these results, the relative binding Gibbs free energies in the other solvents is also expected to be reliable.

We have reported here a new quantitative solvent-polarity relationships (QSPR) studied for the solvent effects on the relative free energies of binding of Nd^{3+} and Eu^{3+} ions to 18-crown-6. Using the following eq. (7), we calculated the coefficient of QSPR studied on the solvent effects on the relative free energies of binding of Nd^{3+} and Eu^{3+} ions to 18-crown-6 using multi-parameters regression method.[42]

$$\Delta\Delta G\ (\Delta G) = \text{m1}\ \varepsilon + \text{m2}\ E_T + \text{m3}\ \beta + \text{m4}\ \alpha + \text{m5}\ \pi^* + \text{m6 DN} + \text{m7 Aj} + \text{m8 Bj}. \quad (7)$$

Where, ε is dielectric constants, and E_T is solvent polarity. β, α and π^* are Kamlet -Taft's solvatochromic parameters. DN is donor number of solvent. Aj is solvent acity and Bj is solvent basity.[42] All of solvent polarities have been collected from the literature[31] and listed in Table 5. The calculated the coefficients of QSPR are listed in Table 6. From the coefficients of QSPR data, we have noted that E_T and β dominate the differences in relative solvation Gibbs free energies of Nd^{3+} and Eu^{3+} ions but Bj dominates the negative values in differences in the stability constant ($\Delta\log K_s$) as well as the relative free energies of binding of Nd^{3+} and Eu^{3+} ions to 18-crown-6 and Aj dominates the positive values in differences in the stability constant ($\Delta\log K_s$) as well as the relative free energies of binding of Nd^{3+} and Eu^{3+} ions to 18-crown-6.

Relative Stability Constants. According to Eq. (4), the differences in stability constant ($\Delta\log K_s$) of binding of Nd^{3+} and Eu^{3+} ions to 18-crown-6 can be calculated on the basis of relative binding Gibbs free energies. The differences in stability constant ($\Delta\log K_s$) of binding of Nd^{3+} and Eu^{3+} ions to 18-crown-6 are listed in Table 3. The signs of in stability constant ($\Delta\log K_s$) of binding of Nd^{3+} and Eu^{3+} ions to 18-crown-6 are also reversed in going from H_2O (TIP3P), CH_3OH, H_2O (TIP4P), solutions to CH_3CN, THF, MeOMe, $MeCl_2$, $CHCl_3$, C_3H_8 and CCl_4 solutions. A signs reversed of $\Delta\log K_s$ implies that 18-crown-6 binds Nd^{3+} more tightly than Eu^{3+} in H_2O (TIP3P), CH_3OH, H_2O (TIP4P) solutions, whereas 18-crown-6 favor Eu^{3+} in CH_3CN, THF, MeOMe, $MeCl_2$, $CHCl_3$, C_3H_8 and CCl_4 solutions. The relative binding Gibbs free energies of Nd^{3+} and Eu^{3+} ions to 18-crown-6 and the differences in stability constant ($\Delta\log K_s$) of binding of Nd^{3+} and Eu^{3+} ions to 18-crown-6 *vs*. Born's [*i.e.* (1 – 1/e), where e is dielectric constant of bulk solvent] function of the solvents are plotted in Figure 1.

As shown in Figure 1, relative binding Gibbs free energies of Nd^{3+} and Eu^{3+}ions to 18-crown-6 and the differences in stability constant ($\Delta\log K_s$) of binding of Nd^{3+} and Eu^{3+} ions to 18-crown-6 vs. Born's function of the solvent decreased with increasing Born's function of solvents except CH_3OH, THF and MeOMe. This trend of relative free energies of binding of Nd^{3+} and Eu^{3+} ions to 18-crown-6 and relative binding Gibbs free energies could be explained by the differences in solvation. Especially, the relative free energies of binding of Nd^{3+} and Eu^{3+} ions to 18-crown-6 in CH_3OH, THF and MeOMe could be explained by the fact that the relatively strong complex-solvent interactions exist in CH_3OH, THF and MeOMe solutions even though Born's function of CH_3OH, THF and MeOMe is small in value. The relatively strong complex-solvent interactions in CH_3OH, THF and MeOMe solutions 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.[43]

Comparing the stability constant ($\Delta\log K_s$) of binding of Nd^{3+} and Eu^{3+} ions to 18-crown-6, in CH_3OH in this study with those in ref. 41, that of CH_3OH in this study is −1.06, that of CH_3OH in ref. 41 obtained by using calorimeter, conductance and ISE methods is $-0.44 \sim -0.6$, respectively. Based on these results, the stability constant ($\Delta\log K_s$) of binding of Nd^{3+} and Eu^{3+} ion to 18-crown-6 in the other solvents is also expected to be reliable. It is necessary to note that the sign and magnitude of the calculated $\Delta\log K_s$ closely parallel the relative binding Gibbs free energies.

Structural Properties and Radial Distribution Function (rdf). The solvent-ion structure can be characterized through radial distribution functions (RDFs), g_{ai} (r), which 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 in the 18-crown-6 -ion complexes-(O, C, Cl, CH and CH_2) in the solvents obtained from RDF's are listed in Table 4. They decrease when the 18-crown-6/Nd^{3+} ion complex transforms to the 18-crown-6/Eu^{3+} ion complex in H_2O (TIP4P), THF, MEOME, $CHCl_3$ and CCl_4 solvents but they are not changed in the other solvents. The coordination numbers (CN) of solvent molecules in the first coordination shell of 18-crown-6/Nd^{3+} ion and 18-crown-6/Eu^{3+} ion complexes evaluated by integrating ion- (O, C, Cl and CH_2) solvent rdf's to their first minimum are also listed in Table 4. The number of solvent molecules in the first coordination shell around the ion decreases when 18-crown-6/Nd^{3+} ion complex transforms to the 18-crown-6/ Eu^{3+} ion complex for all solvents except CH_3CN, C_3H_8 and CCl_4. Those trends could be explained by the strengthened solvent-complex interactions when 18-crown-6/Nd^{3+} ion complex transforms to the 18-crown-6/Eu^{3+} ion complex. We couldn't compare the computed data of this study with the published work because there were no studies for structural properties when 18-crown-6/Nd^{3+} ion complex transforms to the 18-crown-6/

Eu^{3+} ion complex in the diverse solvents. Experimental data on the solute-solvent structure in Nd^{3+} and Eu^{3+} ion aqueous solutions are essentially limited to the first shell. In Table 3(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.[12,40] There is good agreement between our results and the computer simulations and experimental results.

Uncomplexed 18-crown-6 in gas phase has many conformations[44(a)] but those of apparent lowest energy (C_i) and highest symmetry (D_{3d}) are existed. The C_i form has four of sixes oxygen directed inward from the ether backbone with the other two directed outward. This conformation is observed in X-ray analysis of crystalline 18-crown-6[44(b)] and the most frequently sampled conformation in both gas- phase simulation[44(c)] and simulations of 18-crown-6 in polar solvent.[44(d)] The D_{3d} structure with each of its oxygen centers directed inward from the ether backbone, forms a nucleophilic cavity for interaction with guest molecules or ions. Proton and carbon 13 NMR[44(e)] and condensed phase simulations suggested that the D_{3d} conformation is dominant one in polar solvent.[44(d)]

The 18-crown-6 of both 18-crown-6/Cs^+ ion complex and the 18-crown-6/Rb^+ ion complex in solutions has the D_{3d} conformation with each of its oxygen centers directed inward from the ether backbone.[33(c)] But the 18-crown-6 of 18-crown-6/Nd^{3+} ion complex and the 18-crown-6/Eu^{3+} ion complex in solutions has no symmetry. We note that going from the 18-crown-6/Nd^{3+} ion complex to the 18-crown-6/Eu^{3+} ion complex, there is a gradual encapsulation of Eu^{3+} ion by 18-crown-6.

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.[45,46] Those values correspond to the number of solvent molecules that have undergone some constant critical change due to the complex, 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.[43]

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 18-crown-6/Nd^{3+} ion and 18-crown-6/Eu^{3+} ion complexes.

The rdfs of 18-crown-6/Nd^{3+} ion and 18-crown-6/Eu^{3+} ion complexes in selected solvents for clarity are plotted in Figure 2 to Figure 3. As shown in Figure 2, the positions of the first maximum of the 18-crown-6/Nd^{3+} ion complex ∠(O, CH, Cl) in the various solvents follow the ordering H_2O (TIP4P) = CH_3OH < THF < CCl_4 < $CHCl_3$. However, the positions of the first maximum of the 18-crown-6/Eu^{3+} ion complex ∠(O, CH, Cl) in the various solvents follow the different ordering H_2O (TIP4P) = CH_3OH = THF < CCl_4 < $CHCl_3$ shown in Figure 3 and the height of the first peak of g(r) are changed as 18-crown-6/Nd^{3+} ion complex transforms to the 18-crown-6/Eu^{3+} ion complex. That is due to interaction changes between the 18-crown-6/Nd^{3+} ion or 18-crown-6/Eu^{3+} ion complex molecule and solvent molecule *i.e.* the coordination number (CN) changes of solvent molecules in the first coordination shell of 18-crown-6/Nd^{3+} ion and 18-crown-6/Eu^{3+} ion complexes.

In Figure 2 and Figure 3, the second peaks are located between 4 and 8 Å in THF, CH_3OH and H_2O (TIP4P) solutions. In Figure 2, the second peaks of THF and CH_3OH have the bigger peak intensities than the other, which indi-

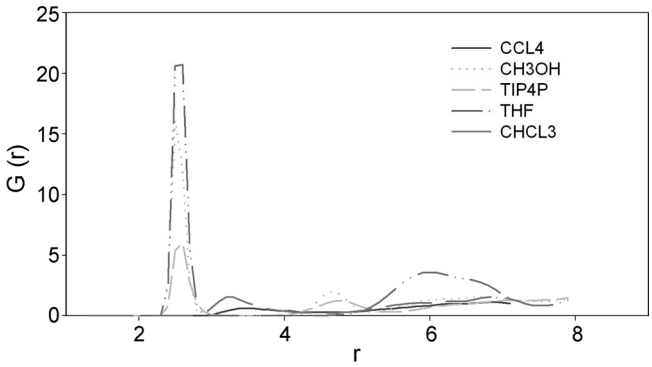

Figure 2. Radial distribution functions g(r), of 18-crown-6/Nd^{3+} ion complex in selected solvents. Distances are in angstroms throughout.

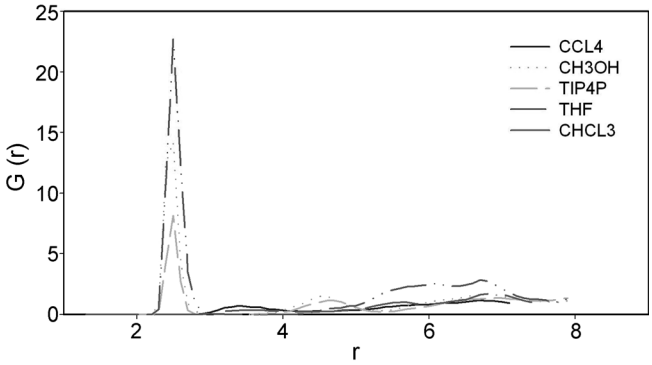

Figure 3. Radial distributions functions of 18-crown-6/Eu^{3+} ion complex in selected solvents.

Table 6. Coefficients of QSPR(quantitative solvent-polarity relationships) of $\Delta\Delta G$ = m1 ε + m2 E_T + m3 β + m4 α + m5 π^* + m6 DN + m7 Aj + m8 Bj

	m1	m2	m3	m4	m5	m6	m7	m8
ion	–0.026	–14.996	–39.498	11.101	–2.083	0.614	–12.835	–0.468
complex	–0.092	–2.007	2.324	–0.350	7.634	–0.466	8.739	–7.880

cate that 18-crown-6/Nd^{3+} ion complex in THF and CH_3OH have the clear second solvation shell. Those could be explained by the fact that the relatively stronger complex molecule-solvent molecule interactions exist in THF and CH_3OH solutions than in the others. The strong complex molecule-solvent molecule interaction in THF and CH_3OH solutions is also due to the electron pair donor properties of the solvent molecule to ion in complex, *i.e.*, Donor number (DN).[43]

In Figure 3, the second peak of THF has also the bigger peak intensities than the others, which indicate that 18-crown-6/Eu^{3+} ion complex in THF has the clear second solvation shell. Those could also be explained by the fact that the relatively stronger complex molecule-solvent molecule interactions exist in THF solutions than in the others. In both RDFs, the g(r) s of THF, CH_3OH and H_2O (TIP4P) drop to zero between the first peak and the broad second one, which indicates the absence of solvent exchange between the first and second shell in simulations. The first g(r) peaks of 18-crown-6/Nd^{3+} ion complex in $CHCl_3$ located at 3 Å, which indicate the interaction between complex and solvent, but the first g(r) peaks of 18-crown-6/Nd^{3+} ion complex in CCl_4 located at 6-8 Å which indicate no interaction between complex and solvent. The first g(r) peaks of 18-crown-6/Eu^{3+} ion complex in of $CHCl_3$ and CCl_4 g(r)s located at 6-8 Å which indicate no interaction between complex and solvent. Those simulation results maybe support the chemical concept of solubility of polar solute in non-polar solvent, which means there is no interaction between polar solute and non-polar solvent.

From those of our results, we have noted that the degree of the complex-solvents interactions is dependent on the Born's function of the solvents, the electron pair donor properties of the solvent and the differences in solvation.

Conclusion

To study the solvent effect on differences in stability constant ($\Delta\log K_s$) as well as the relative free energies of binding of Nd^{3+} and Eu^{3+} ions to 18-crown-6, we have compared differences in stability constant ($\Delta\log K_s$) as well as the relative free energies of binding of Nd^{3+} and Eu^{3+} ions to 18-crown-6 in this study with those of the experimental works, where available. There is a good agreement between the studies. From this study, we have noted that Born's function of the solvents, the electron pair donor properties of the solvent and the differences in solvation dominate the differences in the stability constant ($\Delta\log K_s$) as well as the relative free energies of binding of Nd^{3+} and Eu^{3+} ions to 18-crown-6. We have reported here the QSPR studied on the solvent effects on the relative free energies of binding of Nd^{3+} and Eu^{3+} ions to 18-crown-6. From the calculated coefficients of QSPR, we have noted that E_T and β dominate the differences in relative solvation Gibbs free energies of Nd^{3+} and Eu^{3+} ions but Bj dominates the negative values in differences in the stability constant ($\Delta\log K_s$) as well as the relative free energies of binding of Nd^{3+} and Eu^{3+} ions to 18-crown-6 and Aj dominates the positive values in differences in the stability constant ($\Delta\log K_s$) as well as the relative free energies of binding of Nd^{3+} and Eu^{3+} ions to 18-crown-6. The g(r)s of THF, CH_3OH and H_2O (TIP4P) drop to zero between the first peak and the broad second one, which indicates the absence of solvent exchange between the first and second shell in simulations. This study also provides additional information of the solvent effect on cation-π interaction, equilibrium constants, transition states, rates of the organic reaction, π-facial selectivity, conformations, and the other quantities of chemical and biochemical interest.

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