

## Monte Carlo Simulation Study of Solvent Effect on Selectivity of 18-Crown-6 to between $\text{La}^{3+}$ and $\text{Nd}^{3+}$ Ion

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Received February 27, 2003

We have investigated the solvent effects on  $\Delta\log K_s$  (the difference of stability constant of binding) and the relative free energies of binding of  $\text{La}^{3+}$  to  $\text{Nd}^{3+}$  ions to 18-crown-6 by a Monte Carlo simulation of statistical perturbation theory (SPT) in diverse solvents. We compared relative binding Gibbs free energies and the differences in stability constant ( $\Delta\log K_s$ ) of binding of  $\text{La}^{3+}$  and  $\text{Nd}^{3+}$  ions to 18-crown-6 in  $\text{CH}_3\text{OH}$  in this study with the experimental. There is a good agreement between our study and the experimental. We noted that Borns function of the solvents, the electron pair donor properties of the solvent, the radii of host and guest 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  $\text{La}^{3+}$  to  $\text{Nd}^{3+}$  ions to 18-crown-6. The results of this study appear promising for providing the association properties of crown ethers with alkaline earth metals among polar solvents and the less polar or non-polar solvents.

**Key Words :** Solvent effect, Selectivity, Stability constant, Monte Carlo simulation

### Introduction

Complexing agents like crown ethers display a wide range of binding specificities and the association properties of crown ethers with alkaline cations have been mainly described in terms of similarities between cation size and the size of the inner hole of the crown ether.<sup>1</sup> The study of molecular recognition for host-guest interactions<sup>2-5</sup> has received an increasing interest, after the discovery of crown ethers by Perdersen.<sup>6</sup> Due to the large number of particles forming these systems and to the variety of different interactions established, computer simulations represent a particularly adequate theoretical tools for understanding and predicting the physicochemical properties of those solutions at the microscopical level.<sup>7-9</sup>

Interaction between cations and crown ethers in solution are widespread and the ability of the crown ether to select one cation over the other in solution is important in environmental research. Crown ethers have been proposed as separation agents for removing metal from mixed nuclear and chemical wastes.<sup>10</sup> The selectivity of 18-crown-6 (1,4,7, 10,13,16-hexaoxacyclooctadecane) depends on the way in which 6 oxygen atoms are arranged to interact with guest molecule. In the hostguest 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. In addition to the hostguest 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. It is known that solvation plays a major role in ion selectivity processes by influencing the stability and nature of hostguest complexes. Crown ether displays the ability to selectively bind specific metal cations in the presence of complex aqueous mixtures of chemically similar ions. For example, 15-crown-5 binds  $\text{Na}^+$  and 18-crown-6 binds  $\text{K}^+$  selectively, although the configuration of crown depends on the solvents in experiments.<sup>2</sup> While solvation of singly charged metal complexes ions has been studied, little information of trivalent lanthanide metal complexes is known. Lanthanide metals are important to obtain a good understanding of complexes at molecular level in order to improve such complexes for potential application in fluoroimmuno assays,<sup>11</sup> optical signal amplification<sup>12-14</sup> and extraction from nuclear waste streams.<sup>15</sup> The number of studies on complexes of trivalent lanthanide is still limited.

Several statistical mechanical procedures have evolved for computing free energy differences. Two particularly promising approaches are umbrella sampling<sup>16-20</sup> and a perturbation procedure<sup>21,22</sup> in which one ion is mutated into the other. Especially the ability to calculate solvation free energies of molecules accurately using the perturbation procedure is one of the important and recent developments in computational chemistry.<sup>23</sup> It is known that solvent effects often play an important role in determining equilibrium constants, transition states and rates of reactions,  $\pi$ -facial selectivity,<sup>24</sup> conformations, and the other quantities of chemical, chemical physics and biochemical interest.

To address those challenges and the phenomena themselves, we need the information of selectivity of 18-crown-6 to lanthanide metal cations in solution. These could be obtained from the relative free energies of binding of  $\text{La}^{3+}$  to  $\text{Nd}^{3+}$  lanthanide ion to 18-crown-6 in diverse solution. However, few studies of solvent effects on both  $\Delta\log K_s$  and

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the relative free energies of binding of  $\text{La}^{3+}$  and  $\text{Nd}^{3+}$  ions to 18-crown-6 are available. Those have promoted us to study solvent effect on both the relative free energies of binding (or selectivity) and  $\Delta\log K_s$  of  $\text{La}^{3+}$  and  $\text{Nd}^{3+}$  ions to 18-crown-6.

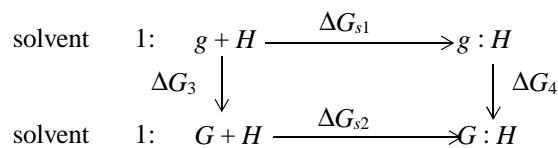
In this study, we have investigated the solvent effect on the relative stability constant of binding of  $\text{La}^{3+}$  and  $\text{Nd}^{3+}$  ions to 18-crown-6 and the relative free energies of binding of  $\text{La}^{3+}$  and  $\text{Nd}^{3+}$  ions to 18-crown-6, using Monte Carlo simulations of statistical perturbation theory (SPT).  $\text{H}_2\text{O}$  (TIP3P, TIP4P models),  $\text{CHCl}_3$ ,  $\text{CH}_3\text{CN}$ , THF,  $\text{CH}_3\text{OH}$ ,  $\text{CCl}_4$ ,  $\text{MeCl}_2$ , MEOME, and  $\text{C}_3\text{H}_8$  are selected as solvents.<sup>25</sup> Experimental and MC simulation studies of the relative free energies of binding of  $\text{La}^{3+}$  and  $\text{Nd}^{3+}$  ions to 18-crown-6 in methanol have been reported.<sup>26,27</sup> The study of experimental and calculating for  $\Delta\log K_s$ , as well as the relative free energies of binding of  $\text{La}^{3+}$  and  $\text{Nd}^{3+}$  ions to 18-crown-6 in diverse solvents, is not available. We present the first calculation to computing solvent effects on the relative free energies of binding of  $\text{La}^{3+}$  and  $\text{Nd}^{3+}$  ions to 18-crown-6 as well the differences in  $\log K_s$  (stability constant) by Monte Carlo simulation of statistical perturbation theory (SPT) in this study. This study provides additional interests of the solvent effect on rates of the organic reaction,<sup>28</sup> transition states, equilibrium constants, and the other quantities of chemical, biochemical interest and chemical-physics.

The paper is organized as followings. In section 2, we describe the computational details, *i.e.* Monte Carlo simulations and potential functions that were used. Section 3 presents the results and discussion, *i.e.* the relative free energies of binding of  $\text{La}^{3+}$  and  $\text{Nd}^{3+}$  ions to 18-crown-6 and the relative binding Gibbs free energies (*i.e.* selectivity) of  $\text{La}^{3+}$  and  $\text{Nd}^{3+}$  ions to 18-crown-6, the relative stability constants of  $\text{La}^{3+}$  and  $\text{Nd}^{3+}$  ions to 18-crown-6 and the structural properties and radial distribution function of  $\text{La}^{3+}$  and  $\text{Nd}^{3+}$  ions in 18-crown-6 complex to solvents obtained by simulations. The conclusion is summarized in section 4.

### Computational Details

**Monte Carlo Simulations.** The procedure used here is similar to that employed to study in Refs. 29-32. 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 255 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.<sup>29-32</sup>

In order to study the equilibrium thermodynamics of binding, we have used Monte Carlo simulations with the thermodynamic cycle-perturbation theory<sup>32</sup> and doublewide sampling.<sup>29-32</sup> In the notation of this method, the relative free energy of binding between guest  $G$  and  $\text{g}$  to the host  $\text{H}$  can be expressed as  $\Delta\Delta G = \Delta G_{s2} - \Delta G_{s1} = \Delta G_4 - \Delta G_3$



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

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

Here,  $\Delta G_s$  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.

The last expression associates the difference in  $\log K_s$ 's<sup>35</sup> with the difference in the relative free energies of binding of  $\text{La}^{3+}$  and  $\text{Nd}^{3+}$  ions to 18-crown-6 in the solvents.

$$\Delta G_{s2} - \Delta G_{s1} = \Delta G_4 - \Delta G_3. \quad (3)$$

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

In this study, the substitutions are  $H = 18\text{-crown-6}$ ,  $\text{g} = \text{La}^{3+}$  and  $\text{G} = \text{Nd}^{3+}$ .  $\Delta G_{s1}$  and  $\Delta G_{s2}$  are available from Monte Carlo simulation in which guest is binding to host in the solvents.

Simulations were run for a coupling parameter,  $\lambda_i$ , which was used to smoothly transform  $\text{La}^{3+}$  with 18-crown-6 ( $\lambda = 0$ ) to  $\text{Nd}^{3+}$  with 18-crown-6 ( $\lambda = 1$ ). In this context, it is convenient to define a coupling parameter  $\lambda$  that allows the smooth conversion of system 0 to 1. Then for many possible features  $\zeta$  of the systems including geometrical and potential function parameters, Eq. (5) can be used to represent the mutation of system 0 to 1 as  $\lambda$  goes from 0 to 1.<sup>29-32</sup>

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

In this study, each simulation entailed an equilibration period for  $4 \times 10^6$  configurations starting from equilibrated boxes of solvent, followed by averaging for  $2 \times 10^7$  configurations. Little drift in the averages was found during the last  $1 \times 10^7$  configuration.<sup>29,32</sup> Other details are that Metropolis and preferential sampling were employed, 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.<sup>29-32</sup>

**Potential Functions.** The pair potential energy function of the OPLS (optimized potential for liquid simulation) force field is of the following form.<sup>25</sup>

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

$f_{ij} = 0.5$  if  $i, j$  are 1,4 (*i.e.* inter- and intramolecular 1,4-interaction); otherwise,  $f_{ij} = 1.0$

Where  $K_r$ ,  $K_\theta$ ,  $V_n$ , and  $\phi$  are empirical parameters relating to bond length, bond angle and dihedral angle. The ion and

**Table 1.** OPLS parameters of  $\text{La}^{3+}$  and  $\text{Nd}^{3+}$  ions

	CHARGE	SIGMA	EPSILON
La	3.000	3.750	0.060
Nd	3.000	3.473	0.054

molecules are represented by interaction sites located on nuclei that have associated charge,  $q_i$  and Lennard-Jones parameter  $\sigma_i$  and  $\epsilon_i$ . 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  $A$  and  $C$  parameters may be expressed as  $A_{ii} = 4\epsilon_i\sigma_i^{12}$  and  $C_{ii} = 4\epsilon_i\sigma_i^6$  where  $\sigma_i$  and  $\epsilon_i$  are the Lennard-Jones radius and energy terms and  $i$  and  $j$  indices span all of the 18-crown-6, solvents and water sites. Dielectric constant ( $\epsilon$ ) is 1. In Ref. 36, 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. 2, Kollman *et al.* also concluded that the additive force field model is adequate to describe energetics of cation complexation with 18-crown-6. The OPLS potential parameters are used for solvents and those are based on a united-atom model<sup>25,29</sup> but the TIP4P and TIP3P models have been used for water.<sup>25</sup> The 18-crown-6 is represented with the OPLS-all-atom (AA) force field.<sup>25</sup> The charges and Lennard-Jones parameters have been selected to yield correct thermodynamic and structural results of pure liquids.<sup>25</sup> The OPLS parameters of ions are listed in Table 1. In all the calculations, the bond lengths, bond angles and dihedral angles have been varied in minimization step and in simulations so that 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.<sup>29-32</sup> The cutoff correction to the solvent-solvent energy for non-aqueous solvents is applied to only Lennard-Jones potential functions.<sup>25</sup>

## Results and Discussion

**Relative free energies of binding.** To study the solvent effect on the relative free energies of binding of  $\text{La}^{3+}$  and  $\text{Nd}^{3+}$  to 18-crown-6 as well as differences in stability constant ( $\Delta \log K_s$ ), we have computed those in the two water models and in the other solvents. The calculated relative free energies of binding of  $\text{La}^{3+}$  and  $\text{Nd}^{3+}$  ions to 18-crown-6 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  $4 \times 10^6$  to  $2 \times 10^7$  configurations. The computed ordering relative free energies of binding of  $\text{La}^{3+}$  and  $\text{Nd}^{3+}$  ions to 18-crown-6 in diverse solvents is  $\text{CCl}_4 > \text{C}_3\text{H}_8 > \text{CHCl}_3 > \text{MeCl}_2 > \text{MEOME} > \text{THF} > \text{CH}_3\text{CN} > \text{H}_2\text{O}$  (TIP4P)  $> \text{CH}_3\text{OH} > \text{H}_2\text{O}$  (TIP3P). This comes about by the change in relative free energies of binding of  $\text{La}^{3+}$  and  $\text{Nd}^{3+}$  ions to 18-crown-6 being more favorable in  $\text{H}_2\text{O}$  (TIP3P) than in the polar and less polar or non-polar solvents. 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

**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/ $\epsilon$ ) of bulk solvents

Solvent	$\Delta G$ ( $\text{La}^{3+} \rightarrow \text{Nd}^{3+}$ )	$\Delta G$		$\Delta\Delta G$ of binding	1-1 / $\epsilon$
		(18-Crown-6/ $\text{La}^{3+}$ $\rightarrow$ 18-Crown-6/ $\text{Nd}^{3+}$ )	18-Crown-6/ $\text{La}^{3+}$ $\rightarrow$ 18-Crown-6/ $\text{Nd}^{3+}$		
$\text{H}_2\text{O}$ (TIP3P)	$-32.24 \pm 0.12$	$-26.13 \pm 0.32$	$-6.11$	0.987	
$\text{H}_2\text{O}$ (TIP4P)	$-28.24 \pm 0.30$	$-23.97 \pm 0.44$	$-4.27$	0.987	
$\text{H}_2\text{O}$ (TIP3P) <sup>a</sup>	-32.5	-	-	0.987	
Exp. <sup>b</sup>	-32.2	-	-	0.987	
$\text{CH}_3\text{CN}$	$-16.49 \pm 0.03$	$-21.69 \pm 0.43$	5.20	0.973	
$\text{CH}_3\text{OH}$	$-26.88 \pm 0.13$	$-24.23 \pm 0.30$	-2.65	0.963	
$\text{CH}_3\text{OH}$ <sup>a</sup>	$-26.55 \pm 0.13$	$-24.54 \pm 0.47$	-2.01	0.963	
Exp. <sup>c</sup>	-	-	-1.16	0.963	
$\text{MeCl}_2$	$-6.65 \pm 0.23$	$-20.95 \pm 0.58$	14.30	0.888	
THF	$-17.18 \pm 0.14$	$-21.03 \pm 0.91$	3.85	0.868	
MEOME	$-15.86 \pm 0.19$	$-20.72 \pm 0.58$	4.86	0.801	
$\text{CHCl}_3$	$-2.61 \pm 0.06$	$-19.46 \pm 0.30$	16.85	0.792	
$\text{CCl}_4$	$-0.52 \pm 0.03$	$-18.03 \pm 0.32$	17.51	0.552	
$\text{C}_3\text{H}_8$	$-0.10 \pm 0.01$	$-18.34 \pm 0.30$	18.24	0.138	

<sup>a</sup>Ref. [26]. <sup>b</sup>Ref. [42]. <sup>c</sup>Ref. [27].

on box-sizes of solvents are only listed in Table 1 for clarity.

Comparing relative free energies of binding of  $\text{La}^{3+}$  and  $\text{Nd}^{3+}$  ions to 18-crown-6 in  $\text{CH}_3\text{OH}$  in this study with that in ref. 26, which of  $\text{CH}_3\text{OH}$  in this study is  $-24.23 \pm 0.30$  and that of  $\text{CH}_3\text{OH}$  in ref. 26 is  $-24.54 \pm 0.47$  kcal/mole, respectively. In contrast to them, the relative free energies of binding of  $\text{La}^{3+}$  and  $\text{Nd}^{3+}$  ions to 18-crown-6 in the other solvents is also expected to be reliable. The relative free energy of binding of  $\text{La}^{3+}$  and  $\text{Nd}^{3+}$  ions to 18-crown-6, in  $\text{H}_2\text{O}$  (TIP3P) is smaller than that of  $\text{H}_2\text{O}$  (TIP4P). This difference of solvation could be explained by the difference of polarity between water models.

**Relative binding Gibbs free energies.** The relative binding Gibbs free energies can be calculated using  $\Delta G_{s1}$  and  $\Delta G_{s2}$  in Eq. 3 are also listed in Table 2. The ordering of the relative binding Gibbs free energies in several solvents is  $\text{C}_3\text{H}_8 > \text{CCl}_4 > \text{CHCl}_3 > \text{MeCl}_2 > \text{CH}_3\text{CN} > \text{MEOME} > \text{THF} > \text{CH}_3\text{OH} > \text{H}_2\text{O}$  (TIP4P)  $> \text{H}_2\text{O}$  (TIP3P). This comes about by the change in relative binding Gibbs free energies being more favorable in  $\text{H}_2\text{O}$  (TIP3P) than in the polar and less polar or non-polar solvents. Note that the signs of the relative binding Gibbs free energies are reversed in going from  $\text{H}_2\text{O}$  (TIP3P),  $\text{CH}_3\text{OH}$ , and  $\text{H}_2\text{O}$  (TIP4P) solutions to  $\text{CH}_3\text{CN}$ ,  $\text{MeCl}_2$ , THF, MEOME,  $\text{CHCl}_3$ ,  $\text{C}_3\text{H}_8$  and  $\text{CCl}_4$  solutions. That is, 18-crown-6 binds  $\text{La}^{3+}$  more tightly than  $\text{Nd}^{3+}$  in  $\text{H}_2\text{O}$  (TIP3P),  $\text{CH}_3\text{OH}$ , and  $\text{H}_2\text{O}$  (TIP4P) solutions, *i.e.* the selectivity of 18-crown-6 to  $\text{La}^{3+}$  is more favorable than to  $\text{Nd}^{3+}$  in  $\text{H}_2\text{O}$  (TIP3P),  $\text{CH}_3\text{OH}$ , and  $\text{H}_2\text{O}$  (TIP4P) solutions, whereas 18-crown-6 favors  $\text{Nd}^{3+}$  in  $\text{CH}_3\text{CN}$ ,  $\text{MeCl}_2$ , THF, MEOME,  $\text{CHCl}_3$ ,  $\text{C}_3\text{H}_8$  and  $\text{CCl}_4$  solutions. Because 18-crown-6 has a cavity radius ranging between 1.3 and 1.6 Å, selectively binds  $\text{La}^{3+}$  over  $\text{Nd}^{3+}$  in  $\text{H}_2\text{O}$  (TIP3P),  $\text{CH}_3\text{OH}$ , and  $\text{H}_2\text{O}$  (TIP4P) solutions where the cationic radii are 1.04 and 1.12 Å, respectively,<sup>30</sup> whereas 18-crown-6 selectively binds  $\text{Nd}^{3+}$  in  $\text{CH}_3\text{CN}$ ,  $\text{MeCl}_2$ , THF, MEOME,  $\text{CHCl}_3$ ,  $\text{C}_3\text{H}_8$  and  $\text{CCl}_4$  solutions. It has been known<sup>26</sup> that although the lighter

lanthanides are similar in the size to  $\text{Na}^+$  and the stability constant of  $\text{La}^{3+}$  ( $\log K = 3.29$ , radius = 1.04 Å) approaches that of  $\text{Na}^+$  ( $\log K = 4.36$ , radius = 1.02 Å) in  $\text{CH}_3\text{OH}$ , entirely different thermodynamic factor are responsible for stabilities of complexes of those two cations. While alkali and alkaline earth metal ion complexes of 18-crown-6 are enthalpy stabilized and entropy destabilized, the opposite is true of lanthanide complexes and the stability decreases along the series of lanthanides is enthalpic in origin for cations up to  $\text{Nd}^{3+}$  in  $\text{CH}_3\text{OH}$ . This fact reflects the delicate balance among ligand (18-crown-6) cation binding, solvation and ligand conformation that exists in complex systems. The complexes with the higher atomic number are generally more stable than those of the lower atomic number. In this study, the cations have three positive charges 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-binding ability of 18-crown-6 system. Similar trend has been observed in the study of alkali cation complexes of 18-crown-6 and its derivatives in  $\text{H}_2\text{O}$  (TIP3P) and  $\text{CCl}_4$  solutions<sup>2</sup> and in the study of alkali cation complexes of 18-crown-6 in diverse solutions.<sup>30</sup>

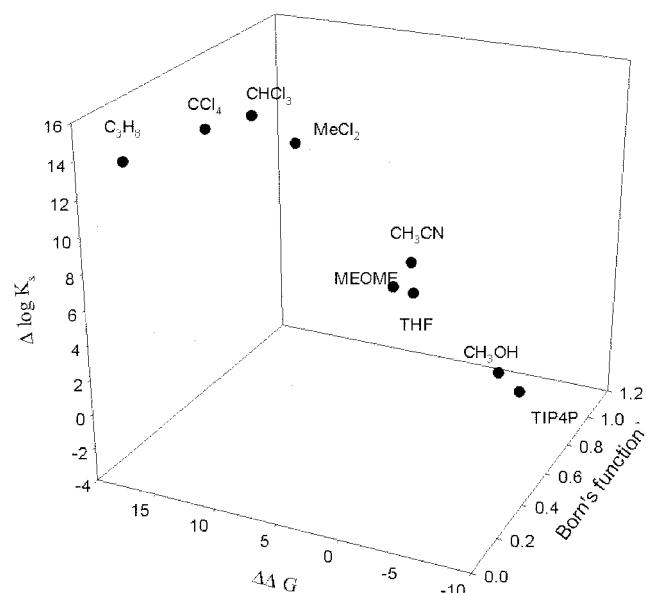
Comparing relative binding Gibbs free energies of  $\text{La}^{3+}$  and  $\text{Nd}^{3+}$  ions to 18-crown-6 in  $\text{CH}_3\text{OH}$  in this study with those in refs. 26, 27, that of  $\text{CH}_3\text{OH}$  in this study is -2.65 kcal/mole and those of  $\text{CH}_3\text{OH}$  in refs. 26, 27 are -2.01 and -1.16 kcal/mole, respectively. In contrast to them, the relative binding Gibbs free energies of  $\text{La}^{3+}$  and  $\text{Nd}^{3+}$  ions to 18-crown-6 in the other solvents are also expected to be reliable.

**Relative stability constants.** According to Eq. 4, the differences in stability constant ( $\Delta \log K_s$ ) of binding of  $\text{La}^{3+}$  and  $\text{Nd}^{3+}$  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  $\text{La}^{3+}$  and  $\text{Nd}^{3+}$  ions to 18-crown-6 are listed in Table 3. The ordering of the differences in stability constant in diverse solvents is  $\text{C}_3\text{H}_8 > \text{CCl}_4 > \text{CHCl}_3 > \text{MeCl}_2 > \text{CH}_3\text{CN} > \text{MEOME} > \text{THF} > \text{CH}_3\text{OH} > \text{H}_2\text{O}$  (TIP4P) >  $\text{H}_2\text{O}$  (TIP3P). The signs of in stability constant ( $\Delta \log K_s$ ) of binding of  $\text{La}^{3+}$  and  $\text{Nd}^{3+}$  ions to 18-crown-6 are also reversed in going from  $\text{H}_2\text{O}$  (TIP3P),  $\text{H}_2\text{O}$

**Table 3.** Differences in the stability constant of binding of  $\text{La}^{3+}$  and  $\text{Nd}^{3+}$  ions to 18-crown-6

Solvent	$\log K_{s2} - \log K_{s1}$
$\text{H}_2\text{O}$ (TIP3P)	-4.49
$\text{H}_2\text{O}$ (TIP4P)	-3.14
$\text{CH}_3\text{CN}$	3.82
$\text{CH}_3\text{OH}$	-1.95
Exp. <sup>a</sup>	-0.85
$\text{MeCl}_2$	10.50
THF	2.83
MEOME	3.57
$\text{CHCl}_3$	12.37
$\text{CCl}_4$	12.86
$\text{C}_3\text{H}_8$	13.39

<sup>a</sup>Ref. [27].



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

(TIP4P) and  $\text{CH}_3\text{OH}$  solutions to  $\text{CH}_3\text{CN}$ ,  $\text{MeCl}_2$ , MEOME, THF,  $\text{CHCl}_3$ ,  $\text{C}_3\text{H}_8$  and  $\text{CCl}_4$  solutions. A signs reversed of  $\Delta \log K_s$  also implies that 18-crown-6 binds  $\text{La}^{3+}$  more tightly than  $\text{Nd}^{3+}$  in  $\text{H}_2\text{O}$  (TIP3P),  $\text{H}_2\text{O}$  (TIP4P) and  $\text{CH}_3\text{OH}$  solutions, whereas 18-crown-6 favors  $\text{Nd}^{3+}$  in  $\text{CH}_3\text{CN}$ ,  $\text{MeCl}_2$ , THF, MEOME,  $\text{CHCl}_3$ ,  $\text{C}_3\text{H}_8$  and  $\text{CCl}_4$  solutions. The relative binding Gibbs free energies of  $\text{La}^{3+}$  and  $\text{Nd}^{3+}$  ions to 18-crown-6 and the differences in stability constant ( $\Delta \log K_s$ ) of binding of  $\text{La}^{3+}$  and  $\text{Nd}^{3+}$  ions to 18-crown-6 vs. Borns function of the solvents are plotted in Figure 1. As shown in Figure 1, relative binding Gibbs free energies of  $\text{La}^{3+}$  and  $\text{Nd}^{3+}$  ions to 18-crown-6 and the differences in stability constant ( $\Delta \log K_s$ ) of binding of  $\text{La}^{3+}$  and  $\text{Nd}^{3+}$  ions to 18-crown-6 vs. Borns function [*i.e.*  $(1-1/\epsilon)$ , where  $\epsilon$  is dielectric constant of bulk solvent] of the diverse solvents decreased with increasing Borns function of solvents except  $\text{CH}_3\text{OH}$ , THF and MEOME. This trend of relative binding Gibbs free energies of  $\text{La}^{3+}$  and  $\text{Nd}^{3+}$  ions to 18-crown-6 and the differences in stability constant ( $\Delta \log K_s$ ) of binding of  $\text{La}^{3+}$  and  $\text{Nd}^{3+}$  ions to 18-crown-6 could be explained by the differences in solvation. Especially, the relative binding Gibbs free energies of  $\text{La}^{3+}$  and  $\text{Nd}^{3+}$  ions to 18-crown-6 in  $\text{CH}_3\text{OH}$ , THF and MEOME could be explained by the fact that the relatively strong complex-solvent interactions exist in  $\text{CH}_3\text{OH}$ , THF and MEOME solutions even though Borns functions of  $\text{CH}_3\text{OH}$ , THF and MEOME are small in value. The relatively strong complex-solvent interactions in  $\text{CH}_3\text{OH}$ , THF and MEOME solutions are due to the electron pair donor properties of the solvents to ion, *i.e.*, Donor number (DN) of  $\text{CH}_3\text{OH}$ , THF and MEOME established by Gutmann.<sup>37</sup>

Comparing the difference in stability constant ( $\Delta \log K_s$ ) of binding of  $\text{La}^{3+}$  and  $\text{Nd}^{3+}$  ions to 18-crown-6 in  $\text{CH}_3\text{OH}$  in this study with that in ref. 27, that of  $\text{CH}_3\text{OH}$  in this study is -1.95 and that of  $\text{CH}_3\text{OH}$  in ref. 27 is -0.85, respectively. In

contrast to them, the difference in stability constant ( $\Delta \log K_s$ ) of binding of  $\text{La}^{3+}$  and  $\text{Nd}^{3+}$  ions 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 solvation structure can be characterized through radial distribution functions (RDFs),  $g(r)$ . The positions of the first maximum in RDFs of the ion in the 18-crown-6-ion complexes (O, Cl atoms) in the solvents are listed in Table 4. Those decrease in  $\text{H}_2\text{O}$  (TIP4P),  $\text{H}_2\text{O}$  (TIP3P),  $\text{CH}_3\text{OH}$ ,  $\text{CH}_3\text{CN}$ ,  $\text{MeCl}_2$ , THF, MEOME,  $\text{CHCl}_3$ , and when the 18-crown-6/ $\text{La}^{3+}$  ion complex transforms to the 18-crown-6/ $\text{Nd}^{3+}$  ion complex but those are equal in  $\text{CCl}_4$  and  $\text{C}_3\text{H}_8$ . The coordination numbers (CN) of solvent molecules in the first coordination shell of 18-crown-6/ $\text{La}^{3+}$  ion and 18-crown-6/ $\text{Nd}^{3+}$  ion complexes evaluated by integrating ion-(O, Cl atoms) in solvent RDFs to their first minimum are also listed in Table 3. The number of solvent molecules in the first coordination shell around the ion decreases in  $\text{H}_2\text{O}$  (TIP3P),  $\text{H}_2\text{O}$  (TIP4P),  $\text{CH}_3\text{CN}$ ,  $\text{CH}_3\text{OH}$ , THF, MEOME, and  $\text{MeCl}_2$  when 18-crown-6/ $\text{La}^{3+}$  ion complex transforms to the 18-crown-6/ $\text{Nd}^{3+}$  ion complex. Those trends could be explained by the weakened solvent complex interactions when 18-crown-6/ $\text{La}^{3+}$  ion complex transforms to the 18-crown-6/ $\text{Nd}^{3+}$  ion complex. However, the number of solvent molecules in the first coordination shell around the ion increases in  $\text{CHCl}_3$  and  $\text{CCl}_4$ . Those could be explained by the strengthened solvent complex interactions when 18-crown-6/ $\text{La}^{3+}$  ion complex transforms to the 18-crown-6/ $\text{Nd}^{3+}$  ion complex.

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.<sup>38,39</sup> 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

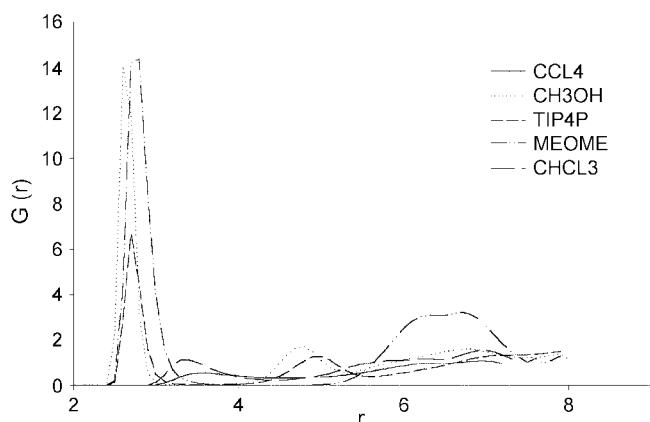
from coordination numbers based on a structural definition, like those from diffraction experiments.<sup>40</sup> Mezei and Beveridge obtained their values by integrating the ion-center of mass of water RDFs up to the minimum of the first peaks.<sup>41</sup> These values will not be significantly different if they are based on ion-oxygen RDFs. This is a straightforward definition and this has been adopted for all the calculated value for 18-crown-6/ $\text{La}^{3+}$  ion and 18-crown-6/ $\text{Nd}^{3+}$  ion complexes. We couldnt compare the data from this study with the published work because there were no studies for structural properties when 18-crown-6/ $\text{La}^{3+}$  ion complex transforms to the 18-crown-6/ $\text{Nd}^{3+}$  ion complex in the diverse solvents.

The RDFs of 18-crown-6/ $\text{La}^{3+}$  ion and 18-crown-6/ $\text{Nd}^{3+}$  ion complexes in selected solvents for clarity are plotted in Figure 2 and Figure 3. As shown in Figure 2, the ordering of smaller r-value, the positions of the first maximum of the 18-crown-6/ $\text{Nd}^{3+}$  ion complex (O, Cl atoms) in the solvents, is  $\text{CH}_3\text{OH} < \text{H}_2\text{O}$  (TIP3P) < MEOME <  $\text{CHCl}_3$  <  $\text{CCl}_4$ . But the ordering of smaller r-value, the positions of the first maximum of the 18-crown-6/ $\text{Nd}^{3+}$  ion complex (O, Cl atoms) in the solvents, is  $\text{CH}_3\text{OH} < \text{H}_2\text{O}$  (TIP3P) = MEOME <  $\text{CHCl}_3$  <  $\text{CCl}_4$  shown in Figure 3. The  $g(r)$  intensity of the first peak is changed when 18-crown-6/ $\text{La}^{3+}$  ion complex transforms to the 18-crown-6/ $\text{Nd}^{3+}$  ion complex. That is due to interaction changes between the 18-crown-6/ $\text{La}^{3+}$  ion or 18-crown-6/ $\text{Nd}^{3+}$  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/ $\text{La}^{3+}$  ion and 18-crown-6/ $\text{Nd}^{3+}$  complexes.

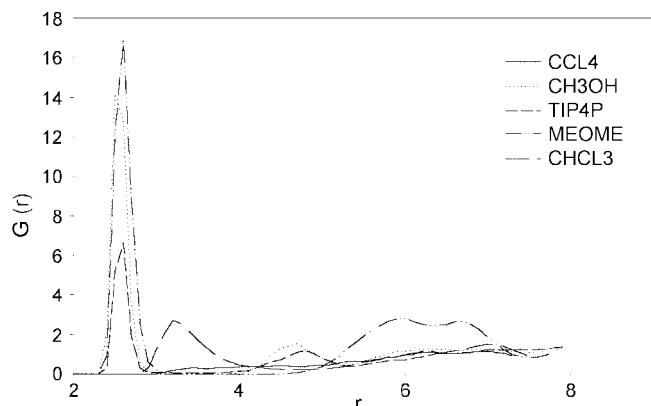
In Figure 2 and Figure 3, the second peaks are located between 4 and 8 in MEOME,  $\text{CH}_3\text{OH}$  and  $\text{H}_2\text{O}$  (TIP3P) solutions. In Figure 2, the second peaks of MEOME and  $\text{CH}_3\text{OH}$  have the bigger peak intensities than the other, which indicate that 18-crown-6/ $\text{La}^{3+}$  complexes in MEOME and  $\text{CH}_3\text{OH}$  have the clear second solvation shell. Those could be explained by the fact that the relatively stronger complex molecule-solvent molecule interactions exist in MEOME and  $\text{CH}_3\text{OH}$  solutions than in the others. The strong complex molecule-solvent molecule interaction in MEOME and  $\text{CH}_3\text{OH}$  solutions is also due to the electron pair donor properties of the solvent molecule to ion in

**Table 4.** Structural properties of 18-Crown-6/ $\text{La}^{3+}$  and 18-Crown-6/ $\text{Nd}^{3+}$  ion complex in diverse solvents

Solvent	18-Crown-6/ $\text{La}^{3+}$ ion		18-Crown-6/ $\text{Nd}^{3+}$ ion	
	$R_{i-o}$ (Å)	CN	$R_{i-o}$ (Å)	CN
$\text{H}_2\text{O}$ (TIP3P)	2.7	5.0	2.5	4.0
$\text{H}_2\text{O}$ (TIP4P)	2.7	5.1	2.6	4.1
$\text{CH}_3\text{OH}$	2.6	4.1	2.5	3.9
THF	2.7	3.8	2.6	3.0
MEOME	2.8	4.0	2.6	3.0
	$R_{i-C}$ (Å)	CN	$R_{i-C}$ (Å)	CN
$\text{CH}_3\text{CN}$	4.0	6.0	3.8	4.0
	$(R_{i-CH})$ (Å)	CN	$(R_{i-CH})$ (Å)	CN
$\text{CHCl}_3$	5.0	3.6	4.9	3.9
	$(R_{i-Cl})$ (Å)	CN	$(R_{i-Cl})$ (Å)	CN
$\text{CCl}_4$	3.6	0.6	4.1	0.7
	$R_{i-CH_2}$ (Å)	CN	$R_{i-CH_2}$ (Å)	CN
$\text{CH}_2\text{Cl}_2$	4.9	4.6	4.8	3.9
$\text{C}_3\text{H}_8$	4.8	—	4.8	1.5



**Figure 2.** Radial distribution function,  $g(r)$ , of 18-crown-6 / $\text{La}^{3+}$  ion complex in selected solvents. Distances are in angstroms throughout.



**Figure 3.** Radial distribution function of 18-crown-6/ $\text{Nd}^{3+}$  ion complex in selected solvents.

complex, *i.e.*, Donor number (DN).<sup>37</sup> In Figure 3, the second peak of MEOME has also the bigger peak intensities than the others, which indicate that 18-crown-6/ $\text{Nd}^{3+}$  ion complex in MEOME 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 MEOME solutions than in the others. From those trends of structural properties, we have noted that the degree of the complex ion-solvents interactions is dependent on the Borns function of the solvents, the electron pair donor properties of the solvent, the radii of host and guest 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  $\text{La}^{3+}$  and  $\text{Nd}^{3+}$  ions to 18-crown-6, we have calculated the differences in stability constant ( $\Delta \log K_s$ ) as well as the relative free energies of binding of  $\text{La}^{3+}$  and  $\text{Nd}^{3+}$  ions to 18-crown-6 in diverse solvents in this study. We have compared differences in stability constant ( $\Delta \log K_s$ ) as well as the relative free energies of binding of  $\text{La}^{3+}$  and  $\text{Nd}^{3+}$  ions to 18-crown-6 in this study with those of the published works. There is good agreement among the studies if we consider both methods used to obtain the stability constant ( $\Delta \log K_s$ ) of binding of  $\text{La}^{3+}$  and  $\text{Nd}^{3+}$  ions to 18-crown-6 and standard deviations. We have concluded that our results are expected to be reliable. From the results of this study, we have noted that Borns function of the solvents, the electron pair donor properties of the solvent, the radii of host and guest 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 *i.e.* selectivity of 18-crown-6 to  $\text{La}^{3+}$  and  $\text{Nd}^{3+}$  ions. The results of this study obtained by the Monte Carlo simulation of SPT appear promising for providing the association properties of crown ethers with alkaline earth metals among polar solvents and the less polar or non-polar solvents.

**Acknowledgement.** This work was supported by Korea Research Foundation Grant (KRF-2002-015-CP0156).

### References

- Michaux, G.; Reisse, J. *J. Am. Chem. Soc.* **1982**, *104*, 6895.
- Wang, J.; Kollman, P. A. *J. Am. Chem. Soc.* **1998**, *120*, 11106.
- Boehme, C.; Wipff, G. *Chem. Eur. J.* **2001**, *7*, 1398.
- Choi, H. S.; Suh, S. B.; Cho, S. J.; Kim, K. S. *Proc. Natl. Acad. Sci. USA* **1998**, *95*, 12094.
- Mazor, M. H.; McCammon, J. A.; Lybrand, T. P. *J. Am. Chem. Soc.* **1990**, *112*, 4411.
- Perdersen, C. *J. Am. Chem. Soc.* **1967**, *89*, 7017.
- Florian, J.; Warshel, A. *J. Phys. Chem. B* **1999**, *103*, 10282.
- Allen, M. P.; Tildesley, D. J. *Computer Simulation of Liquids*; Oxford University Press: Oxford, 1987.
- Simkin, B. Y.; Sheikhet I. I. *Quantum Chemical and Statistical Theory of Solution: A Comprehensive Approach*; Ellis Horwood: London, 1995.
- Schulz, W. W.; Bray, L. A. *Sep. Sci. Technol.* **1987**, *22*, 191.
- Steemers, F. J.; Verboom, W.; Reinhoudt, D. N.; van der Tol, E. B.; Verhoeven, J. W. *J. Am. Chem. Soc.* **1995**, *117*, 9408.
- oude Wolbers, M. P.; van Veggel, F. C. J. M.; Heeringa, R. H. M.; Hofstraat, J. W.; Geurts, F. A. J.; van Hummel, G. J.; Harkema, S.; Reinhoudt, D. N. *Liebigs Ann. Chem.* **1997**, 2587.
- Slooff, L. H.; Polman, A.; oude Wolbers, M. P.; van Veggel, F. C. J. M.; Reinhoudt, D. N.; Hofstraat, J. W. *J. Appl. Phys.* **1998**, *83*, 497.
- oude Wolbers, M. P.; van Veggel, F. C. J. M.; Hofstraat, J. W.; Geurts, F. A. J.; Reinhoudt, D. N. *J. Chem. Soc., Perkin Trans. 1997*, *2*, 2275.
- van Veggel, F. C. J. M.; oude Wolbers, M. P.; Reinhoudt, D. N. *J. Phys. Chem. B* **1998**, *102*, 3060.
- Valleau, J. P.; Torrie, G. M. *Statistical Mechanics, Part A*; edited by Berne, B. J., Ed.; Plenum: New York, 1977; p 169.
- Jorgensen, W. L. *J. Phys. Chem.* **1983**, *87*, 5304.
- Rebertus, D. W.; Berne, B. J.; Chandler, D. *J. Chem. Phys.* **1979**, *70*, 3395.
- Mezei, M.; Mehrotra, P. K.; Beveridge, D. L. *J. Am. Chem. Soc.* **1985**, *107*, 2239.
- Chandrasekhar, J.; Jorgensen, W. L. *J. Am. Chem. Soc.* **1985**, *107*, 2974.
- Bayly, C. I.; Kollman, P. A. *J. Am. Chem. Soc.* **1994**, *116*, 697.
- Tembe, B. L.; McCammon, J. A. *Comput. Chem.* **1984**, *8*, 281.
- Kollman, P. A. *Chem. Rev.* **1993**, *93*, 2395.
- Kim, K. S.; Tarakeshwar, P.; Lee, J. Y. *Chem. Rev.* **2000**, *100*, 4145.
- Jorgensen, W. L. *BOSS Version 4.1*; Yale University: New Haven, CT, 1999.
- van Veggel, F. C. J. M.; Reinhoudt, D. N. *Chem. Eur. J.* **1999**, *5*, 90.
- Izatt, R. M.; Bradshaw, J. S.; Nielsen, S. A.; Lamb, J. D.; Christensen, J. *J. Chem. Rev.* **1985**, *85*, 271.
- Lee, I.; Kim, C. K.; Lee, I. Y.; Kim, C. K. *J. Phys. Chem. A* **2000**, *104*, 6332.
- Kim, H. S. *Chem. Phys. Lett.* **2001**, *346*, 135.
- Kim, H. S. *Chem. Phys. Lett.* **2002**, *364*, 489.
- Kim, H. S. *Bull. Korean Chem. Soc.* **2001**, *22*, 887.
- Kim, H. S. *J. Phys. Chem. B* **2002**, *106*, 11579.
- Zwanzig, R. W. *J. Chem. Phys.* **1954**, *22*, 1420.
- Jorgensen, W. L.; Blake, J. F.; Buckner, J. K. *Chem. Phys.* **1989**, *129*, 193.
- Gorkel, G. W. *Crown Ethers and Cryptands*; The Royal Society of Chemistry: London, 1990.
- Jorgensen, W. L. Free Energy Changes in Solution in *Encyclopedia of Computational Chemistry*; Schleyer, P. v. R., Ed.; Wiley: New York, 1998; Vol. 2, p 1061.
- Christian, R. *Solvents and Solvent Effects in Organic Chemistry*, 2nd Ed.; VCH: 1988; p 20.
- Bockris, J. O'M.; Reddy, A. K. N. *Modern Electrochemistry*; Plenum Press: New York, 1970; Vol. 1, Chapter 2, p 45.
- Chung, J. J.; Kim, H. S. *Bull. Korean Chem. Soc.* **1993**, *14*, 220.
- Enderby, J. E.; Neilson, G. W. *Rep. Progr. Phys.* **1981**, *44*, 38.
- Mezei, M.; Beveridge, D. L. *J. Chem. Phys.* **1981**, *74*, 6902.
- Babu, C. S.; Lim, C. J. *Phys. Chem. B* **1999**, *103*, 7958.