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# The Influence of Structural Effects on the Complexing Ability of Crown Ethers. III. Rubidium Complexes Formed by the Ligands of the 18C6 Type

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A combined AM1 and molecular mechanics study of the complexation of the rubidium cation by nine substituted crown ethers, **L**, containing 18 atoms of macroring is presented. The role of microsolvation was incorporated into the models by studying the complexes surrounded by six methanol molecules. The substituent effect is related to the interaction energy, $E_{int}$, which was computed for the clusters $\mathbf{L}Rb^+(CH_3OH)_6$ in their lowest energy conformations. This is demonstrated by the linear correlation found by plotting $\log K_s$ *vs.* $E_{int}$, where $K_s$ stands for stability constant of a complex. The appropriate $K_s$ values were calculated on the basis of cyclic voltammetric measurements.

**Key words:** crown ethers, rubidium complexes, molecular modeling, stability constants

It is well known that the cation – coronand interaction in polar media depends on the properties of the ligand and the reacting ion. Cavity size, on account of the hole-size relationship, is generally regarded as the prime parameter for selectivity. Other important parameters are the number of donor atoms, possible variations in macrocyclic ring conformation and the solvation energies of the species participating in complexation equilibria [1]. The effect of ligand structure is often discussed in terms of complementarity and reorganization [2–4]. This approach is easily understood; the hole-size concept states that when the diameter of the cation and the hole of crown are of the same size, the latter is selective for the former. Unfortunately, this picture does not generally hold: coordination of a metal ion often changes the ligand conformation. Such a ligand structural reorganization is a two-step process: one which occurs prior to the binding and the other which occurs during the binding. Each step can be quantified by molecular mechanics (MM) calculations. Thus, MM formalism affords the informations, which assess the influence of structural factors on complex stability [5,6].

The major part of MM results was focused on the conformational analysis and the prediction of the structure of selected complexes [7–9]. A much smaller but very important group of studies yielded quantitative relationships between ligand structure and complex stability. From our point of view, good linear correlations for a series of potassium complexes of hexadentate coronands [10] as well as potassium, rubidium and cesium complexes with bidentate ether donors [11] are especially interesting. In both cases correlations were based on the differences in the strain energy of the free ligand and that of the metal ion complex.

A different treatment was proposed to analyse the relationship between complex stability and molecular characteristics for 4-X-benzo-15-crown-5 – $Na^+$ systems, where X = $-NH_2$, $-CH_3$, –H, –CHO, –Br, –COOH and $-NO_2$ [12]. The experimental stability constants ($\log K_s$) determined in acetone solutions correlate linearly with the average charge of the aromatic oxygen atoms from the AM1 computations on the uncomplexed ligands. Moreover, a clear linearity was obtained between $\log K_s$ and the binding energy from *ab initio* calculations. The last one was defined by

$$\Delta E = E_{compl} - (E_{ligand} - E_{ion}) \quad (1)$$

where $E_{compl}$, $E_{ligand}$ and $E_{ion}$ are the total energies of the complex, the free (uncomplexed) ligand and the sodium ion, respectively [12].

Solvation effects have not been treated [10–12]. Meanwhile, the crucial role of solvation is well known; it has been shown, for example, that the selectivity of 18-crown-6 for $K^+$ over $Li^+$ depends on the introduction of hydration effects [13]. The importance of the variation of ion – solvent contribution to the binding energy in different solvents was also established [14]. Therefore, taking into account the microsolvation of the complexed cation, we have proposed to correlate $\log K_s$ with the interaction energy, $E_{int}$, calculated by MM procedures for the clusters $LM^+(solv)_n$. Considering the series of ligands, **L**, with the macroring of 18C6 type and various substituents in methanol solutions, we found a satisfactory colinearity between $E_{int}$ and $\log K_s$ for potassium [15] and cesium complexes [16]. The focus of the present work are analogous clusters containing rubidium ions.

## EXPERIMENTAL AND COMPUTATIONAL PROCEDURES

Crown ethers **I–IX** (Table 1) were purchased or synthesized as reported previously [15]. Methanol for UV spectroscopy was used as obtained from Fluka. Rubidium perchlorate (Aldrich) was dried over $P_2O_5$ at 80°C. Tetraethylammonium perchlorate (TEAP) from Merck was purified by recrystallization from triply distilled water and vacuum drying. Cyclic voltammetric curves were recorded in a three-electrode arrangement with a PAR 273A potentiostat controlled by an IBM PC computer and a software M270 from PAR. A static mercury electrode (model 303A PAR) and a Pt counter electrode; the AgCl/Ag couple in 0.05 M solution of tetraethylammonium chloride in methanol was used as a reference electrode. All the solutions were deaerated before measurements with pure argon. Experiments were carried out at 25±1°C. All remaining experimental details were previously reported [15].

The conformations of all the complexes were generated and optimized by the HyperChem 5.11 program [17]. AMBER force field was used with the representation of potential energy [18]. A standard set of HyperChem AMBER method was applied and supplemented by the most recent AMBER program [19]. In order to mimic the microsolvation of the complexed cation, four (similarly as in the case of cesium complexes [16]) and six methanol molecules were disposed around the macrocyclic system. Different arrangements of the $CH_3OH$ molecules were examined. Placement on both sides of the macrocyclic nucleus was done manually, since molecular dynamics was unable to move the solvent molecules from one side onto another side without dissociation of the system. Thus, molecular dynamics was applied for rearrangement of solvent molecules on a single side only. Computations of atomic charges, appropriate to the coronates were performed using the AM1 procedure [20] included in the HyperChem package. The polarization effect of rubidium cation was included by the quantum-classical mode of semiempirical calculations. For this purpose, a crown ether molecule, together with the solvent molecules, were subjected to the AM1 procedure, whereas the $Rb^+$ ion was treated classically as a point charge with the constant +1 charge. Such a treatment resulted from the lack of parametrization for this cation, both in semiempirical and appropriate basis set of *ab-initio* methods. Coronand and point charge, treated as a perturbation of the wave function, were subjected for the AM1 single point calculation of charges. The resulting values were subsequently used in the MM optimization of structure, and then the whole system was returned to AM1. The procedure was carried out until self-consistency of the atomic charges and the structure of the system was reached. It should be emphasized that polarization effects of the cation were found to be crucial for a satisfactory correlation of the resulting interaction energies with the experimental data. Note also that for **VIII** and **IX** all possible stereoisomers were considered with the use of charge/structure optimization procedures and only the structures with the lowest energy were selected for further computations.

## RESULTS AND DISCUSSION

The stability constants of the complexes formed by the rubidium cation with crown ethers **I–IX** in methanol were reported [21,22]. However, significant differences are observed between the data obtained in various laboratories. As example, this is evident with the complex of 18-crown-6 for which the values of $\log K_s = 5.32$ [23] and 5.73 [24] were reported. Next, for the complex of benzo-18-crown-6 one can find the values of 4.48 [25] and 5.1 [26]. Moreover, two complexes with the cation to the ligand ratio of 1:1 and 2:1, respectively, were described [27]. Therefore, taking into account the fact that such discrepancies are not exceptional, we have decided to remeasure the complexation equilibria under the unequivocally defined conditions. To this purpose cyclic voltammetric measurements were applied.

The rubidium ions (0.5 mM) when studied in 0.05 M solutions of TEAP in methanol were found to undergo reversible one electron reduction to the metal amalgam (*cf.* also [28]). Thus, the $(E_{pa} - E_{pc})/2$ values may be assumed as approximately equal to the formal potential, E°, for the redox system

$$Rb^{+}_{solv} + e = Rb(Hg) \tag{2}$$

The addition of each ligand, belonging to the series **L**, shifts E° in a negative direction, while the reversibility of the electrode process is preserved. Thus, the variation of the potential with the ligand concentration ($c_L$) can be used to calculate the stability constant. For 1:1 complexation the observed potential shift is given by Lingane equation

$$\Delta E = E' - E° = (RT/F)\ln(c_L) + (RT/F)\ln(I_{compl} - I_{solv}) \tag{3}$$

where E′ denotes the potential determined at a given $c_L$ value, whereas the ratio of limiting currents corresponds to the change of the diffusion coefficients of rubidium ions due to complexation. (2) was derived assuming that $c_L$ is much larger than the concentration of the $Rb^+$ cations, so in the most part of our experiments the concentration range of the ligand was of about 5–70 mM. As a result, we have found that the ΔE values are linearly related to $\log c_L$ and $\Delta\Delta E/\Delta\log c_L = 60\pm4$ mV/$\log c_L$ unit for all the ligands under study; therefore, only 1:1 complexes were indeed identified. The $\log K_s$ values are collected in Table 1. It should be pointed out that i) their reproducibility was found to be ±0.1 log unit, and ii) our value for 18-crown-6 – $Rb^+$ system is comparable with those obtained earlier by polarographic measurements ($\log K_s = 5.47$ [29] and 5.43 [30] in solutions containing 0.1 M $Me_4NI$ and $Et_4NI$, respectively).

**Table 1.** Experimental stability constants, $K_s$, and calculated interaction energies (in kcal $mol^{-1}$)[a] for the rubidium coronates with four and six methanol molecules.

| No. | Ligand | $\log K_s$ | $-(E_{int})_{4solv}$ | $-(E_{int})_{6solv}$ |
|---|---|---|---|---|
| **I** | 18-crown-6 (18C6) | $5.2_1$ | 44.69 | 45.57 |
| **II** | benzo-18C6 | $4.5_0$ | 41.09 | 44.33 |
| **III** | dibenzo-18C6 | $4.1_9$ | 41.02 | 43.03 |
| **IV** | *cis-syn-cis* dicyclohexyl-18C6 | $5.2_5$ | 43.08 | 45.71 |
| **V** | *cis-anti-cis* dicyclohexyl-18C6 | $5.0_0$ | 44.48 | 45.27 |
| **VI** | phenyl-18C6 | $4.8_0$ | 43.31 | 44.98 |
| **VII** | cyclohexyl-18C6 | $4.9_8$ | 44.38 | 45.38 |
| **VIII** | 8,15-dimethyl-benzo-18C6 | $4.8_0$ | 42.06 | 44.93 |
| **IX** | 8,11,15-trimethyl-benzo-18C6 | $4.1_5$ | 41.86 | 42.91 |

[a] 1 kcal = 4.184 kJ.

Initial MM calculations were performed on gas phase systems. The results demonstrated that the rubidium ions are too large to fit in the cavity of the crown; for example in the 18-crown-6-$Rb^+$ the cation is placed about 1 Å out of the mean plane of the ring. Approximately the same conformations were observed in the X-ray structure of **I**-$Rb^+$ [31] and **III**-$Rb^+$ [32] and were reported previously by MM studies of these complexes [33,34]. Such structures were used as starting geometry for minimization of the complexes solvated. It appeared that the structural changes resulting from the added methanol were small in comparison with those described for the gaseous systems.

In our simple model four $CH_3OH$ molecules were added to the crown ether-$Rb^+$ systems, similarly as in cesium complexes [16]. Moreover, earlier in the 18-crown-6-$Rb^+$ complex it was observed that the addition of four molecules of water was sufficient to recover the qualitative agreement with aqueous phase binding enthalpies [13,35]. First we examined the conformation, in which the methanol molecules are distributed between the top and bottom sides of the macrocyclic unit [35]. However, the lowest energy conformations appeared to be those, in which the methanols are positioned on opposite sides: three on the top and one on the bottom side of the crown, although the energy difference is small (only about 1 kcal $mol^{-1}$). For such conformations we calculated the corresponding interaction energies, $(E_{int})_{4solv}$, which are collected in the fourth column of Table 1. Recall that the interaction energy is defined as the difference of the total energy of the solvated complex in its lowest energy conformation and the energy of the same system with the cation removed. Then, the resulting values were correlated with the experimental stability constants, given in Table 1. Comparison of $\log K_s$ with $(E_{\mathrm{int}})_{4solv}$ showed that these quantities are colinear to a great extent (correlation coefficient $r = 0.850$). A significant improvement of the correlation was obtained when the clusters $\mathbf{L}Rb^+(CH_3OH)_6$ were considered. Now the minimum energy could be found with five methanols positioned on the same side of the macrocyclic ring as the cation, whereas the sixth one occupies an opposite side (Fig. 1). Arrangements with other solvent molecules distributions appeared to be unfa-

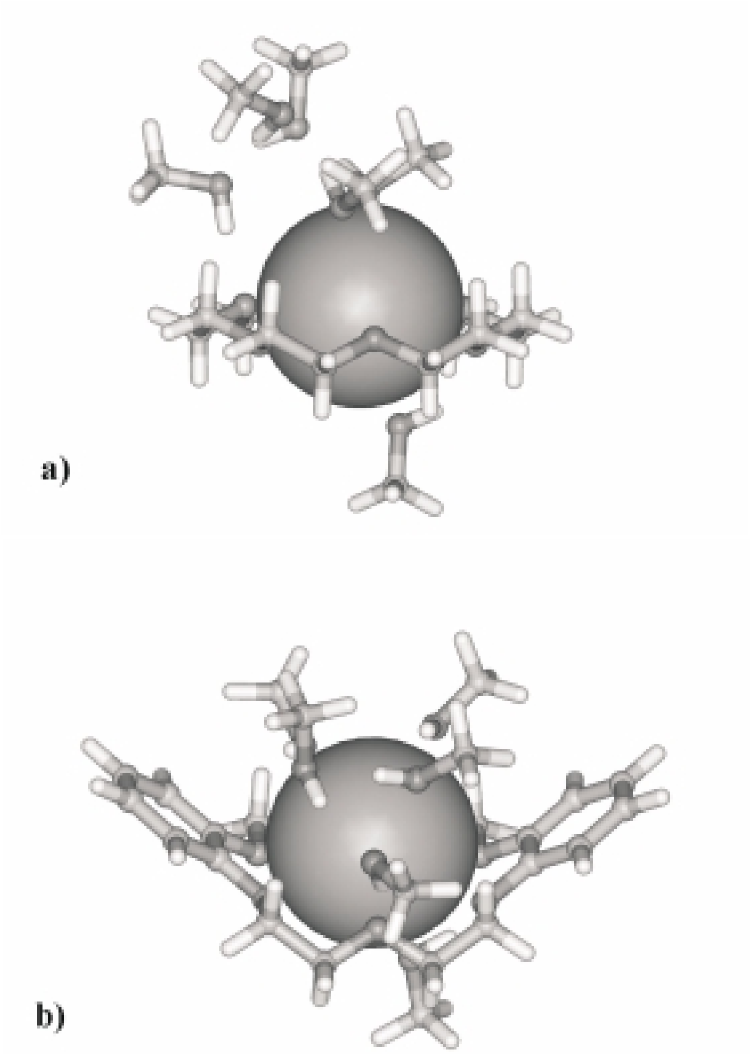

**Figure 1.** A view of the charge/structure optimized clusters of 18-crown-6 **(a)** and dibenzo-18-crown-6 **(b)** with rubidium cation and six microsolvating methanol molecules. Radius of $Rb^+$ was set as the van der Waals radius.

vourable from the energetical point of view; *e.g.* the configurations with 3:3 distribution were higher in energy by several kcal $mol^{-1}$. It should be noted here that the 5:1 arrangement built by six methanol molecules leads to the conformations being the global minimum structures for all the complexes reported in the present communication. These structures show a maximal hydrogen bond network. Forming of such bonds is highly preferable from the energetical point of view. As can be seen from Fig.1, the methanol molecules form hydrogen bonds not only between themselves, but some of these are sufficiently close to the crown, thus they can form hydrogen bonds with the oxygen atoms of the ring.

Having established the global minimum conformations, we have calculated the corresponding interaction energies. The resulting values, named $(E_{int})_{\mathbf{6solv}}$, are listed in the last column of Table 1. Figure 2 reveals a strong relationship between $(E_{int})_{6solv}$ and $\log K_s$.

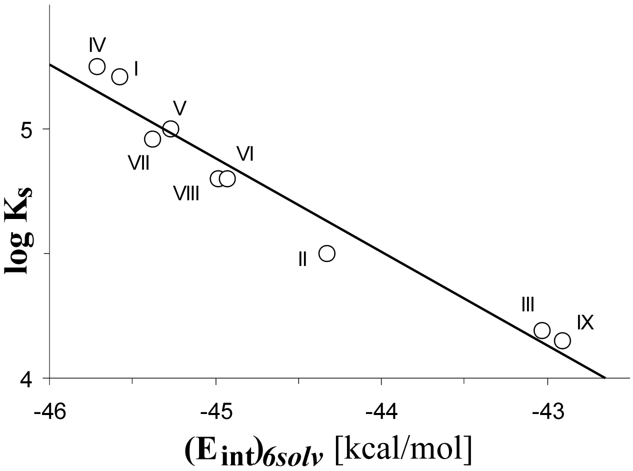

**Figure 2.** A plot of the $\log K_s$ values for rubidium coronates *vs.* interaction energies, $(E_{int})_{6solv}$.

Least-squares analysis leads to the following correlation equation

$$\log K_s = (-0.38\pm0.07)(E_{int})_{6solv} - (12.05\pm3.25) \qquad (4)$$

which holds with r = 0.977, a mean square standard deviation in $\log K_s$ of s = 0.08 and the Fisher test of F = 149.7 for all the nine complexes under study; errors of regression coefficients are calculated on the basis of Student's distribution with a confidency level of 0.95. Thus, the above-mentioned correlation is statistically significant with a probability of at least 99%.

Finally, one may conclude that correlation (4) gives a further support to the concept that the complexing ability of crown ethers with a given number of donor atoms is strongly influenced by the structural requirements of the macrocycle. This correlation also demonstrates the utility of the interaction energy approach for predicting the