Estimation of Li^+, K^+ and Ca^{2+} Complexation with [12]crown-4, [15]crown-5 and [18]crown-6 Using a Na^+ ISE in Dioxane-Water, Part IV*

Cation Equilibrium Constants of Macrocyclic Ethers with Ion Selective Electrodes

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Abstract. The (1:1) Na^+ equilibrium constants, K_{e1}, of macrocyclic ethers of [12]crown-4, [12]crown-5 and [18]crown-6 were determined with a Na^+ ISE in the presence of a second cation e.g. Li^+, K^+ and Ca^{2+} in dioxane/water (50/50). We estimated the (1:1) equilibrium constants, K_{e2} of the macrocyclic ethers with Li^+, K^+ and Ca^{2+} by this way. The binding selectivity of a macrocyclic ether between two cations was estimated in the same binary solvent mixture where the water hydration role is diminished. Results showed clearly the effect of macrocyclic size and cation radii in a solution.

Key words: macrocyclic ethers; equilibrium constants; Li^+, K^+, Na^+, Ca^{2+}; potentiometry; ISE electrode.

Macrocyclic ethers have received great attention since they were first characterized for their ability to bind alkali and alkaline earth cations. Such behaviors depend on several factors like number and type of donor atoms, macrocyclic size, cation radii as well as a diamond lattice structure or the conformational ability. Such artificial receptors are also influenced by the polar solvents due to dipole-solvent interactions [1, 2]. They have been attractive, in particular, for the ion transfer process through the various membranes.

The ion binding of the macrocyclic receptors has the prime importance for chemical and biological processes where the organization of the binding sites around the substrate controls the binding ability and selectivity [1, 5]. Solvation plays the major role in molecular and cationic recognition influencing the stability of molecular conformation. The structure and conformation of such molecules are essential to rule out their ionophoric properties, however, the complex formation and ion transport phenomena in solution are still not completely understood. Some laboratories have reported the ionophore role of a variety of such molecules using different ion selective electrodes in water or in non aqueous solutions [3–9].

We have studied design and synthesis of crown ether type macrocyclic molecules as well as their cationic recognition in solutions with spectroscopic and electrochemical methods [10–15]. We previously reported the binding of such molecules to Na^+ and K^+ using ion selective electrodes in water and in water-dioxane solutions [12–15]. The crown ether oxygen dipoles hydrated in water are partly liberated in the presence of dioxane in water (50/50). This is also more suitable for the junction potential balance of the electrodes due to at least 50% water in such a mixture since water free solvents are not so practical for the analytical work.

Continuing our work on estimation of the cation binding in dioxane-water solutions we now utilized the Na^+ ISE in the presence of two cations and a receptor. The equilibrium constants, K_{e1}, of Na^+ ion with the macrocyclic ethers of [18]crown-6, [15]crown-5, [12]crown-4 were estimated with an Na^+

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ISE in dioxane-water mixtures in the presence of a second cation. However, we used an analytical formula to determine the amount of the second complexed cation in dioxane-water (50/50) using the Na^+ ISE. The 1:1 equilibrium constants of Li^+, K^+ and Ca^{2+} cations were estimated with the Na^+ ISE in the presence of a macrocyclic ligand and Na^+ with Eqs. (1–5). The complexation selectivity of crown ethers between the two cations in a solution was, therefore, reported using an ISE.

The binding between the receptors in the equilibrium of the cations responding to a single sensor is examined in a solution. Actually, such measurements could be important for biological processes e.g. the estimation of Na^+/K^+ ion balance due to their prime roles. Gokel et al. have reported the Ca^{2+}/Na^+ selectivity of some crown ethers in methanol with a Na^+ ISE [6]. Perfect cation sensors have been established so far as reported by Simon et al. [7–9].

The 1:1 complexation stoichiometry, (n/m) of equilibrium was determined using a Na^+ ISE in the presence of identical amounts of cation and macrocyclic ligand, $[A_0^+] = [L_0]$. Quite reliable results studied with the linear regression method were obtained measuring the experimental mole fraction of complexed Na^+, P_1, which depend on the initial cation concentration, $[L_0]$, in the equation, $1/\{K_{e1}[L_0]^{m+n-1}\} = (1-P_1)^2/P_1$ for $m = n = 1$, Eqs. (1, 3) [5, 6]. However, the crown ether equilibrium constants, K_{e2}, of Li^+, K^+ and Ca^{2+} ions were estimated in the presence of Na^+ using Eqs. (4, 5) [10–16].

Experimental

The chemicals and crown ethers from FLUKA were used without further purification. Dioxane from MERCK was distilled over metallic sodium. The salts of NaCl, KCl, LiCl and CaCl$_2$ were dried and then dissolved in dioxane/water (50/50, v/v). The Na$^+$

ISE, a combined glass electrode from ORION model ROSE, No 86-11 was used in a thermostated and stirred cell in dioxane/water solution. Potentiometric mV measurements of $[A_1^+]$ concentrations were carried out in the presence of, $[L_0]$, $[A_{01}^+]$ and $[A_{02}^+]$ for K_{e1} and K_{e2} estimations with a millivolt meter from ORION model 920A.

The calibrations of the ISE with NaCl were also done in the presence of a second cation at 25°C, see Fig. 1. The mV measurements of complex solutions of cations in the presence of crown ethers gave the uncomplexed Na$^+$ using calibration curves, Fig. 1. The K_{e1} was estimated using Eq. (3) where mole fraction, $P_1 = [A_1^+L]/([A_1^+] + [A_1^+L])$, of 1:1 stoichiometry of complexed cation depends on initial cation concentration, $[L_0]$ which is experimentally equivalent to initial crown concentration (see Table 1) [10–16]. The equilibrium constant of second cation, K_{e2}, was obtained from Eqs. (4 and 5).

Results and Discussion

Considering the macrocyclic ether in the complexation equilibrium of Na^+ and a second cation we determined the concentration of free Na^+ in the solution using a Na^+ ISE, Eqs. (1, 2). The Na^+ and cations are involved in the following equilibrium of equations, Eqs. (1–5).

K_{e1} is 1:1 stoichiometry of crown ether/Na^+ equilibrium constant and K_{e2} is 1:1 equilibrium constant of crown ether/second cation, Li^+, K^+ and Ca^{2+}. $[A_1^+]$ and $[A_2^+]$ are the concentrations of the free Na^+ and free second cation in solution, respectively. $[L]$ is the concentration of free crown ether equivalent to cation concentrations for 1:1 ratio. The following relationships are considered to estimate the 1:1 equilibrium constants of cations with the same macrocyclic ligand (crown ether) in solution [10–16].

$$K_{e1}[A_1^+][L] = [A_1^+L] \qquad (1)$$

$$K_{e2}[A_2^+][L] = [A_2^+L] \qquad (2)$$

$$1/(K_{e1}[L_0]) = (1 - P_1)^2/P_1 \qquad (3)$$

$$[A_2^+L] = [A_1^+] - ([A_1^+L]/K_{e1}[A_1^+]) \qquad (4)$$

$$K_{e2} = [A_2^+L]/([A_{02}^+] - [A_2^+L])^2 \qquad (5)$$

**Table 1.** The ISE data for K_{e1} of NaCl/KCl/[15]crown-5 at 25 °C in dioxane/water using Eq. (3)

Ion conc.[a]	mV[b]	mV[c]	Invers.conc	P_1[d]	$(1-P_1)^2/P_1$[e]	$(1-P_1)^2/P_1$[f]
0.197	−039.75	−037.84	5.07	0.0856	9.76	9.43
0.104	−053.45	−051.56	9.64	0.0805	10.51	10.34
0.048	−069.57	−068.02	20.86	0.0700	12.34	12.58
0.025	−082.88	−081.67	39.55	0.0551	16.19	16.32
0.013	−096.95	−096.10	77.79	0.0391	23.64	23.95
0.006	−112.40	−111.90	163.15	0.0232	41.19	41.00

[a] Na$^+$ concentrations equivalent to crown concentrations; [b] Free cation potentials; [c] Complexed cation potentials; [d] Mole fraction of complexed cation; [e] Measured data; [f] Least squares data.

Table 2. The bicationic equilibrium constants of crowns at 25 °C using the Na+ ISE in dioxane/water[a]

Cations	[12]crown-4				[15]crown-5				[18]crown-6			
	$\ln K_{e1}$	$-\Delta G^c$	$\ln K_{e2}$	$-\Delta G^c$	$\ln K_{e1}$	$-\Delta G^c$	$\ln K_{e2}$	$-\Delta G^c$	$\ln K_{e1}$	$-\Delta G^c$	$\ln K_{e2}$	$-\Delta G^c$
Na+ [b]	1.17	2.89	–	–	3.50	8.63	–	–	4.67	11.53	–	–
Na+/K+	0.89	2.19	1.76	4.34	3.69	9.19	1.34	3.30	1.61	3.98	4.88	12.03
Na+/Li+	0.67	1.65	0.34	0.84	3.04	7.50	−1.09	−2.68	4.38	10.80	−0.65	−1.59
Na+/Ca2+	1.33	3.29	2.08	5.13	3.28	8.02	−0.19	−0.47	3.80	9.36	1.44	3.55

[a] See Table 1 for data of equilibrium constants; [b] No second cation available; [c] In kJ/mol.
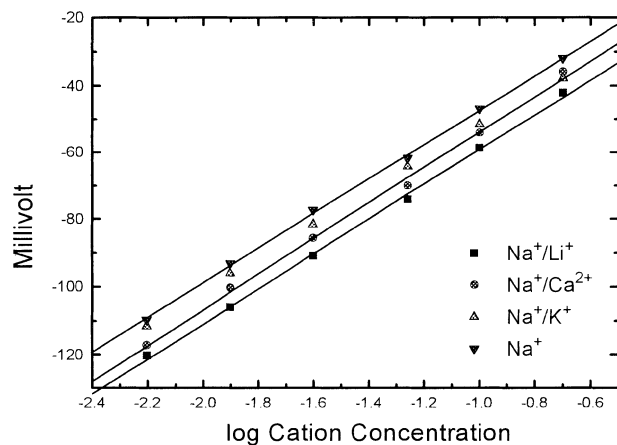
Fig. 1. The calibration of Na+ and Na+/Li+, Na+/K+ and Na+/Ca2+ with Na+ ion selective electrode
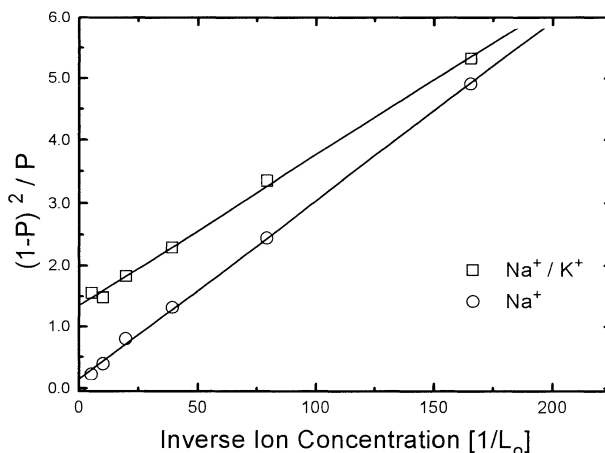
Fig. 2. The Plot of $(1-P)^2/P$ *versus* inverse ion concentration of [15] crown-5/Na+ and [15]crown-5/Na+/K+ complex solutions to estimate 1:1 stoichiometry association constants K_{e1}, see Tables 1, 2

Since $K_{e1}[A_1^+]/[A_1^+L] = K_{e2}[A_2^+]/[A_2^+L]$ and $[L] = [L_0] - [A_1^+L] - [A_2^+L]$ the complexed second cation equilibrium, Eq. (4), could be considered where crown concentration is equivalent to initial Na+ and second cation concentrations, $[L_0] = [A_{01}^+] = [A_{02}^+]$. K_{e1} estimation in the presence of a second cation using Eq. (3) is shown in Table 1. Therefore, the equilibrium constant, K_{e2}, given by unified Eqs. (4, 5) was estimated using the common method [3–6] (see Tables 2, 3).

The selectivity of a neutral ligand is a quite important factor for the analytical estimations. Some authors have reported interesting results on the binding roles of macrocyclic ethers used as ISE electrodes [7–9]. We have been also currently studying such molecules for cation complexing in a dioxane/water (50/50) binary solvent. In such a medium the conductance role of water is involved for a proper liquid junction potential and almost no ion pairing takes place due to experimental concentration limits [14, 15]. The Na+ ISE used is not responded by the second cation as it was examined by calibration measurements (Fig. 1). We reported the thermodynamic equilibrium constants, $\ln K_{e1}$ and $\ln K_{e2}$ in Table 2 and their selectivities from the ratio of constants, K_{e1}/K_{e2} in Table 3.

The importance of such measurements is due to the fact that the different sensors respond in different solvents in different ways. Also to design a sensor sensitive to most of the cations is too difficult [7–9]. Accordingly, the results of ion binding with the method presented are also reliable to represent cation radii and crown ether size relationships even in a semi-polar solution [1]. The best ion binding effect shown by [18]crown-6 for Na+/K+ is the selectivity of 4/100 which is probably due to not only the sensor role but also the effect of the solvent mixture. The Na+/K+ selectivity is naturally favouring the Na+ for [15]crown-5. [12]crown-4 is the least favoured ligand in all cation competition measurements. However, Ca2+ as a biologically important cation, displayed a not very promising role under our experimental conditions [1, 7–9].

Table 3. The cation selectivities of crown ethers in dioxane/water estimated with Na$^+$ ISE at 25 °C

Crowns	K_{e1}/K_{e2}[a]	$K_{e1}Na^+$	$K_{e2}Li^+$	K_{e1}/K_{e2}[b]	$K_{e1}Na^+$	$K_{e2}K^+$	K_{e1}/K_{e2}[c]	$K_{e1}Na^+$	$K_{e2}Ca^{2+}$
[12]crown-4	1.38	1.95	1.41	0.42	2.43	5.82	0.48	3.79	7.97
[15]crown-5	61.46	20.89	0.34	1.71	39.96	23.39	32.40	26.57	0.82
[18]crown-6	153.13	79.63	0.52	0.04	5.01	131.45	10.55	44.53	4.22

[a] Na$^+$/Li$^+$ equilibrium constant ratio; [b] Na$^+$/K$^+$ constant ratio; [c] Na$^+$/Ca^{2+} constant ratio.

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