

Cation Binding Properties of Benzo-type Crown Ethers. Effect of Ring Size upon Complexation Phenomena

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Abstract

The cation-binding by a series of benzo-type crown ethers with different ring size has been performed by the solvent extraction of monovalent metal picrates (Na^+ , K^+ , Rb^+ , Cs^+ , Ag^+ , and Tl^+) between water and dichloromethane. The effect of ring size and symmetry of the crown ethers upon the cation binding ability is discussed. The results are compared with those of commercially available crown ethers (dibenzo-18-crown-6 and 18-crown-6) and it was found that the less-symmetrical benzo-crown ethers have lower cation binding ability while unique cation selectivity for thallium (I) has been observed.

1. Introduction

The chemistry of crown ethers has been developed since Pedersen's pioneering work in 1967 [1], and a number of papers and books have been published to investigate the characteristics of crown ethers. Recently, it has shifted from simple monocyclic compounds [2] to more sophisticated structures involving supramolecular systems [3]. The synthetic approach for the molecular design of crown ethers has started from benzo-type crown ethers because of the feasibility of introducing the substituents. This study has been done in many papers, however, the structures of benzo-type crown ethers are mainly symmetrical with two methylene chain between the adjacent two oxygen atoms in the crown ether skeletons, $3m$ -crown- m . The ring size of symmetrical crown ethers increases with the increase of the number of m . The alternative way of increasing the size of crown ethers is to change the number of methylene chain length between the adjacent two oxygen atoms in the ring. This crown ether has been called less-symmetrical crown ethers or crown ethers of low symmetry, $(3m+n)$ -crown- m . [4].

We have reviewed complexation by crown ethers of low symmetry and demonstrated the specific alkali metal ion selectivity of less symmetrical crown ethers. Compared with symmetrical crown ethers, crown ethers of low symmetry possessing $(3m+n)$ -crown- m skeletons showed lower cation-binding ability in general but exhibit drastically different and, in some cases, higher selectivities of specific cations.

In this context, it is our special interest to investigate the cation binding behaviors of benzo-type crown ethers of low symmetry from the standpoint of molecular symmetry and the change of ring size. In the present paper, the cation binding ability of benzo-crown ethers of low symmetry have been evaluated by solvent extraction of aqueous metal picrates. The compounds used in this study (1-3 and 5-9) are shown below with commercially available crown ethers, dibenzo-18-crown-6 (4) and 18-crown-6 (10).

2. Experimental Details

Infrared spectra were obtained on a JASCO A-100 grating spectrophotometer. Mass spectra were measured using Shimadzu GCMS-QP5000. ^1H NMR spectra were recorded on a JEOL JNM-EX 270 spectrometer in chloroform- d solution containing 1% tetramethylsilane as internal standard. UV-VIS spectra were recorded on a Hitachi U-3500 spectrophotometer. Solvent tetrahydrofuran (THF) was distilled from sodium hydride. Commercially available reagents were used in the following syntheses without further purification unless noted otherwise.

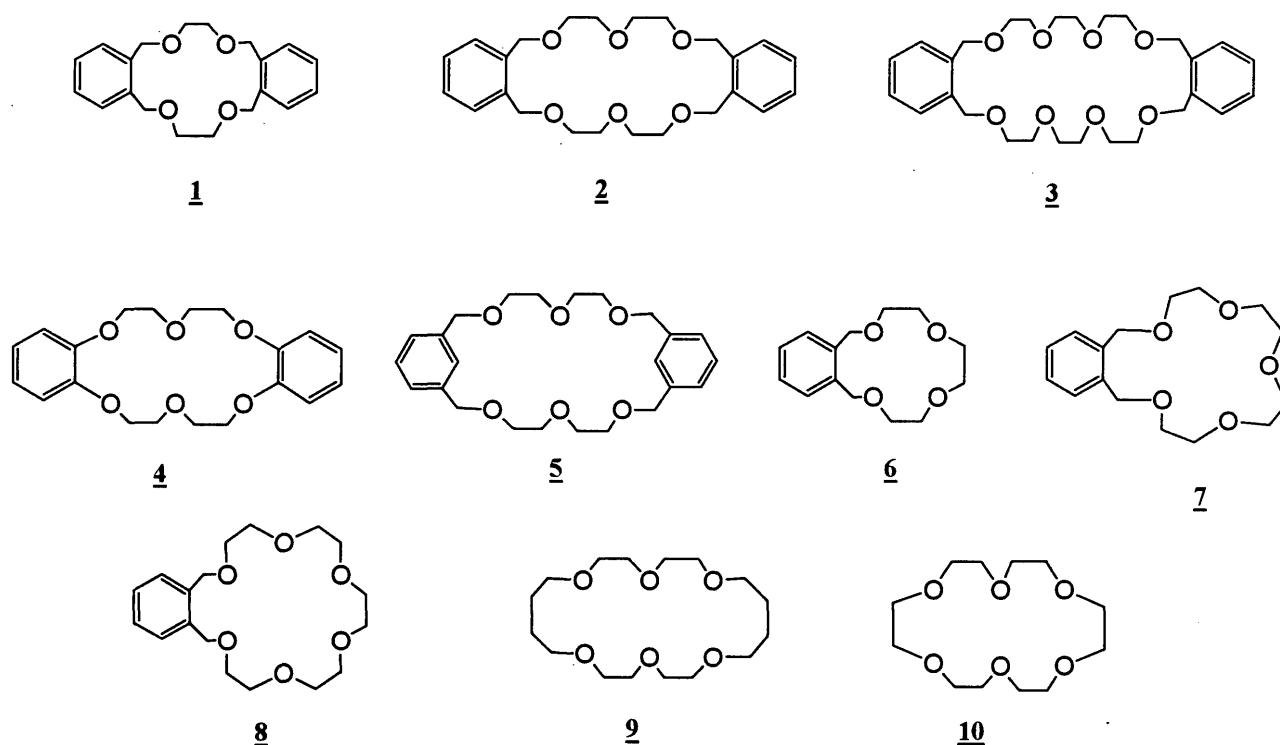
Synthesis. Dibenzo-16-Crown-4 (1), Dibenzo-22-Crown-6 (2), Dibenzo-28-Crown-6 (3), Dibenzo-24-Crown-6 (5), Benzo-20-Crown-6 (8) were synthesized from 1,2-bis(bromomethyl)benzene or 1,3-bis(bromomethyl)benzene in THF in the presence of NaH/LiOH and KCl according to the previous

reported method [6,7,8,9]. 22-Crown-6 (9) was prepared according to the reported method [10].

Benzo-14-Crown-4 (6). Sodium hydride (10.6g, 0.44mol) and THF (300mL) were introduced into a 1-L three necked flask equipped with a magnetic stirrer, reflux condenser, dropping funnel, and nitrogen inlet tube. To the stirred suspension at 66 °C was added triethylene glycol (8.9g, 0.06mol) in THF (100mL), and stirring was continued for 1 h with continuous bubbling of nitrogen. Then potassium chloride (4.8g, 0.06mol) was added. 1,2-Bis(bromomethyl) benzene (16.0g, 0.06mol) in THF(100mL) was then added dropwise to the stirred mixture over 2 h, and the stirring was continued for 3 days at 66 °C under a nitrogen atmosphere. The excess amount of NaH was eliminated by methanol. The solvent was evaporated and the residue was extracted with dichloromethane. The dichloromethane extract was dried over magnesium sulfate and the solvent was evaporated. After work-up, it was purified by column chromatography (alumina, 5% ethyl acetate in hexane) and Kugelrohr distillation to give 3.1g (21%) of the product 6: bp 142°C/0.2 Torr.; $^1\text{H NMR}$ δ 3.64-3.76 (m.12H), 4.76 (s.4H), 7.22-7.37 (m.4H); IR(neat) 2860, 1460, 1130, 1100, 750 cm^{-1} ; MS (EI), m/e 252 (M^+); Anal. Calcd for $\text{C}_{14}\text{H}_{20}\text{O}_4$: C, 66.65; H, 7.99; Found: C, 66.84, H, 7.97.

Benzo-17-Crown-5 (7) was prepared in 11% (2.8g) yield by the reaction of 1,2-bis(bromomethyl)benzene (17.5g, 0.09mol) with tetraethylene glycol (23.8g, 0.09mol) in THF in the presence of KOH (20.2g, 0.36mol) according to the procedure described above: bp 158-160°C/0.2 Torr.; $^1\text{H NMR}$ δ 3.64-3.73 (m.16H), 4.71(s.4H), 7.25-7.28 (m.2H), 7.38-7.42 (m.2H); IR(neat) 2850, 1450, 1105, 750 cm^{-1} ; MS (EI),m/e 296 (M^+); Anal. Calcd for $\text{C}_{16}\text{H}_{24}\text{O}_5$: C, 64.84; H, 8.16; Found: C, 64.54; H, 8.22.

Solvent Extraction. The general extraction procedures employed are similar to those previously presented [5]. Distilled dichloromethane and demineralized water were used. The solvents were saturated with each other before use in order to prevent volume changes of the phase during extraction. Equal volumes (10 mL) of dichloromethane solution of the respective crown ether (3.0mM) and of an aqueous solution of the corresponding metal picrate (3.0 mM) were shaken for 10 minutes at 25 °C in a Taiyo M100L incubator. The mixture was then allowed to stand for at least 2 hours at that temperature in order to complete phase separation. The organic phase was separated by filtration (Toyo filter paper No.2s). Since the picrates does not dissolve in dichloromethane, the molar extinction coefficients in 1:1 mixture of dichloromethane and acetonitrile were determined. The concentration of alkali and heavy metal metal picrate in the organic phase was determined from absorbance at 375 nm in a mixture of dichloromethane and acetonitrile.



3. Results and Discussion

Synthesis. Benzo-14-Crown-4 (**6**) was synthesized from 1,2-bis(bromomethyl)benzene and triethylene glycol in THF in the presence of NaH and KCl in 21% yield. Benzo-17-Crown-5 (**7**) was synthesized from 1,2-bis(bromomethyl)benzene and tetraethylene glycol in THF in the presence of KOH in 11% yield.

Solvent Extraction. A variety of measurement techniques for recording the cation binding ability of crown ethers have been reported. Notable among them are ion-selective electrode techniques, NMR methods, and solvent extraction techniques. In this paper, data obtained by solvent extraction of metal picrates are presented for general discussion.

The solvent extraction of metal picrates has been employed as a convenient method for evaluating cation binding ability of macrocyclic compounds. In the present study, aqueous alkali and heavy metal picrates (Na^+ , K^+ , Rb^+ , Cs^+ , Ag^+ and Tl^+) were extracted at 25°C dichloromethane solution of the crown ethers (**1-10**). The extractabilities obtained are shown in Table 1. In order to discuss the cation selectivity from a more quantitative point of view, the extraction studies have been done under a variety of conditions to determine the extraction equilibrium constants (K_{ex}). The K_{ex} values for 1:1 crown ether – metal complex (**1-8**, and **10**) are shown in Table 2.

Table 1. Solvent Extraction of Metal Picrates^{a)}

Ligand	%Extractability ^{b)}					
	Na^+	K^+	Rb^+	Cs^+	Ag^+	Tl^+
1	0.0	0.0	0.0	0.0	1.9	5.1
2	0.1	0.7	1.1	2.1	3.3	18.7
3	0.6	4.0	4.3	6.9	3.3	18.7
4	0.8	23.6	15.1	7.9	4.3	30.8
5	0.1	0.2	0.2	0.5	0.7	2.3
6	0.1	0.1	0.1	0.2	0.5	1.4
7	1.2	0.9	0.6	0.7	11.5	12.0
8	0.8	5.7	5.5	4.2	6.2	30.4
9	0.5	0.6	1.0	1.8	8.1	5.3
10	6.3	69.0	57.6	31.3	31.3	73.2

a) Temperature 25°C; aqueous(10ml):[Picrate]=3mM. Organic phase(CH_2Cl_2 , 10ml):[Ligand]=3mM.

b) Defined as percent picrate extracted into organic phase.

Table 2. Extraction Equilibrium Constants (K_{ex})^{a)}

Ligand	Log K_{ex} ^{b)}						Selectivity ^{c)}	
	Na^+	K^+	Rb^+	Cs^+	Ag^+	Tl^+	Tl^+/K^+	Tl^+/Ag^+
1	d)	1.86	d)	d)	3.44	3.75	77.6	2.0
2	2.04	2.82	2.96	3.22	3.29	4.41	38.9	16.6
3	2.84	3.67	3.73	3.97	3.58	4.58	8.1	10.0
4	2.81	4.84	4.43	4.08	3.74	5.02	1.5	19.1
5	2.10	2.38	2.38	2.63	2.91	3.39	10.2	3.0
6	2.33	2.55	2.40	2.37	2.94	3.22	7.8	1.9
7	3.15	3.01	2.88	2.90	4.31	4.29	19.1	1.0
8	2.92	3.86	3.83	3.67	3.97	5.03	14.8	11.5
10	3.89	6.20	5.17	5.17	5.09	6.71	3.2	49.9

a) CH_2Cl_2 - H_2O system at 25°C

b) Values for 1:1 crown ether-cation complexes.

c) Relative cation selectivity determined by K_{ex} .

d) Not measured.

As seen from Table 1, less-symmetrical ring-enlarged dibenzo-crown ethers (**1,2,3**, and **5**) which possess extra methylene chain adjacent to the benzene ring showed, in general, lower extractabilities compared with those of symmetrical Benzo-18-Crown-6 (**4**) and 18-Crown-6 (**10**). Dibenzo-16-Crown-4 (**1**) showed no extractabilities for alkali metal picrates while it showed low extractability for Ag^+ and Tl^+ . It should be noted that **1** showed high Tl^+ selectivities among metal cations used in this study. A more quantitative discussion was made from the K_{ex} values shown from Table 2. The degree of decrease in K_{ex} values for Tl^+ were less sensitive to the methylene chain length than those of the alkali metal ions. Thus, for the first time, higher Tl^+ selectivity with reference to alkali metal cations has been observed for ring-enlarged compounds **1**. Dibenzo-18-Crown-6 (**4**) showed the selectivity for K^+ . Ring-enlarged Dibenzo-22-Crown-6 (**2**), Dibenzo-28-Crown-8 (**3**), and Dibenzo-24-Crown-6 (**5**) showed the selectivity for Cs^+ among alkali metal cations which is explained by the size-fit concept. Unsubstituted ring-enlarged 22-Crown-6 (**9**) also showed the same results.

Ring-enlarged Benzo-14-Crown-4 (**6**), Benzo-17-Crown-5 (**7**), and Benzo-20-Crown-6 (**8**) showed lower extractabilities and no drastic change of cation selectivity seen from Table 1 and 2. This would be because of the small ring size of **6** and the effect of extra methylene chain in the crown ether ring. It can be concluded that dibenzo-crown-6 derivatives (**1-5**) are superior to monobenzo-crown ethers (**6-8**) in view of cation binding and cation selectivity.

As seen from Table 2, discussion on higher Tl^+ selectivity over K^+ and Ag^+ can be made from the data of K_{ex} values. Although the cation diameters of K^+ and Tl^+ are similar, higher Tl^+/K^+ selectivities were determined for ring-enlarged benzo-type crown ethers **1, 2, 3, 5, 6, 7, 8** compared with those of commercially available **4**, and **10**. However, there was no drastic positive change of Tl^+/Ag^+ selectivity compared with **4** and **10**. The present result also suggests the effect of benzene ring toward cation binding. This can be also explained by the high Tl^+ , and Ag^+ selectivity over alkali metal cations seen in Calixarene compounds [11, 12]. The molecular design of Tl^+ selective host molecules might be desired by the present discussion. Further investigations are now in progress toward elucidating the selectivities of ring-enlarged dibenzo-type crown ethers used in Tl^+ sensing by the method of solvent extraction and ESI Mass spectra methods [13].

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