

# Cation Binding Properties of Benzo-type Crown Ethers.3.<sup>1-2)</sup> Effect of Large Ring Size upon Complexation Phenomena of Crown-9 and Crown-10 Derivatives<sup>3)</sup>

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## Abstract

The cation-binding by two large ring-sized benzo-27-crown-9 and benzo-30-crown-10 has been evaluated by a solvent extraction of monovalent metal picrates ( $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Rb}^+$ ,  $\text{Cs}^+$ ,  $\text{Ag}^+$ , and  $\text{Tl}^+$ ) between water and dichloromethane. The effect of ring size and benzo group upon the cation binding ability is discussed. The results are compared with benzo-type crown-6-8 (benzo-18-crown-6, benzo-21-crown-7 and benzo-24-crown-8) and simple unsubstituted crown-6-8 ethers (18-crown-6, 21-crown-7 and 24-crown-8). The cation-binding ability and complex formation are discussed in view of the size of the crown ether ring and the basicity of oxygen atoms.

**Key Words:** crown ethers, solvent extraction, supramolecular chemistry

## 1. Introduction

A wide variety of functionalized crown ether compounds have been synthesized to control the complexation phenomena with cations. The original paper by Pedersen's pioneering work in 1967 [3] still gives the idea of the approach for the design of supramolecular systems. The interest in this field by our group is to explore the character of benzo-type crown ethers. We have recently reported the cation-binding abilities of less-symmetrical benzo-type crown ethers and found that dibenzo-crown-6 derivatives were superior to monobenzo-crown-ethers in view of cation binding and cation selectivity [1]. And the cation-binding ability of large ring-sized benzo-crown-7 and crown-8 ethers (1,2,5,6) has been evaluated by solvent extraction of metal picrates[4]. The results were compared with those of crown-6 derivatives (9-10). In general, large ring-sized benzo-crown-7, and crown-8 ethers have a lower cation-binding ability as the ring size increases, and a cation selectivity for large cations ( $\text{Cs}^+$  and  $\text{Tl}^+$ ). By determining the overall extraction equilibrium constants ( $K_{\text{ex}}$ ), it was found that **1** and **2** tend to form 1:1 crown ether-cation complexes under the conditions of the present experimental study. For further discussion on the ring-size and the cation-binding ability, we report in this paper the syntheses and cation-binding ability of large ring-sized mono-benzo-crown ethers, benzo-27-crown-9 (**3**) and benzo-30-crown-10 (**4**). Their syntheses are described, and their cation-binding abilities have been evaluated by solvent extraction of aqueous metal picrates. The results were compared with those of simple crown ethers 27-crown-9 (**7**), 30-crown-10 (**8**), benzo-18-crown-6 (**9**), and commercially available 18-crown-6 (**10**)

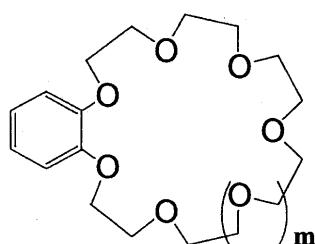
## 2. Experimental Details

Infrared spectra were obtained on a JASCO A-100 grating spectrophotometer. Mass spectra were measured using Shimadzu GCMS-QP5000.  $^1\text{H}$  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. Melting points were measured with a MEL-TEMP apparatus and are uncorrected. Solvent tetrahydrofuran (THF) was distilled from sodium hydride. Commercially available reagents were used in the following syntheses without further purification unless noted otherwise.

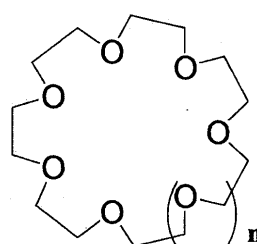
**Syntheses.** The reagents of the crown ether syntheses are prepared by the synthetic method according to the similar reported method [2].

**Synthesis.** 2,2'-[1,2-Phenylene bis(oxyethyleneoxy)]diethanol (**11**) was synthesized from catechol and ethylene glycol mono-2-chloroethyl ether in the presence of NaOH in 30% yield according to the similar reported method. [5].  $^1\text{H NMR } \delta$  3.66-3.74 (m,4H), 3.87-3.91 (t,8H), 4.13-4.17 (t,4H), 6.90 (s,4H).

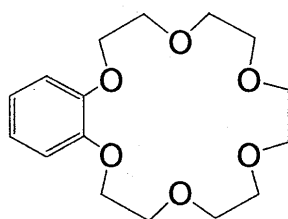
**Oligoethylene glycol ditosylates** were synthesized from the corresponding oligoethylene glycol and *p*-toluenesulfonyl chloride in THF in the presence of NaOH in 83-89% yield according to the reported method from the authors' group [6].



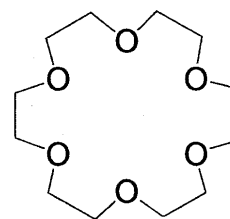
1:  $m=1$   
2:  $m=2$   
3:  $m=3$   
4:  $m=4$



5:  $n=1$   
6:  $n=2$   
7:  $n=3$   
8:  $n=4$



9



10

**Benzo-27-Crown-9 (3).** KOH (3.4g, 0.06mol) and THF (200mL) were introduced into a 2-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 2,2'-[1,2-Phenylene bis(oxyethyleneoxy)]diethanol (**11**) (1.8g, 0.006mol) in THF (200mL), and stirring was continued for 1 h with consecutive bubbling of nitrogen. Tetraethylene glycol ditosylate (3.3g, 0.0065mol) in THF(150mL) was then added dropwise to the stirred mixture over 3 h, and the stirring was continued for 2 days at 66 °C under a nitrogen atmosphere. The solvent was evaporated and the residue was extracted with chloroform. The chloroform extract was dried over magnesium sulfate and the solvent was evaporated. After work-up, it was purified by column chromatography (alumina, chloroform-hexane 2:1) to give 0.79g (28%) of the product **3** as the oily product.:  $^1\text{H NMR } \delta$  3.53-3.71 (s,28H), 4.15-4.18 (t,4H), 6.90 (s,4H); MS  $m/e$  467 ( $\text{M}^+ + \text{Na}^+$ ).

**Benzo-30-Crown-10 (4)** was synthesized from **11** (1.67g, 0.0028mol) and pentaethylene glycol ditosylate (1.88g, 0.0034mol) in THF in the presence of KOH (2.18g, 0.039mol) in 18% (0.25g) yield as the oily product according to the procedure described above.  $^1\text{H NMR } \delta$  3.53-3.71 (t,32H), 4.14-4.20 (t,4H), 6.90 (s,4H); MS  $m/e$  511 ( $\text{M}^+ + \text{Na}^+$ ).

**27-Crown-9 (7)** was synthesized from pentaethylene glycol (23.8g, 0.1mol) and pentaethylene glycol ditosylate (47.7g, 0.09mol) in THF in the presence of KOH (16.5g, 0.25mol) in 7% (2.8g) yield according to the similar procedure described above. It was purified by distillation under reduced pressure. bp 168-172°C /0.2 Torr;  $^1\text{H NMR } \delta$  3.61 (s,28H); IR (neat) 2850, 1450, 1250, 1100  $\text{cm}^{-1}$ ; MS 396 ( $\text{M}^+$ ).

**30-Crown-10 (8)** was synthesized from pentaethylene glycol (23.8g, 0.1mol) and pentaethylene glycol

ditosylate (47.7g, 0.09mol) in THF in the presence of KOH (16.5g, 0.25mol) in 8% (3.4g) yield according to the procedure described above. bp 200°C/0.3 Torr;  $^1\text{H NMR}$   $\delta$  3.67 (s, 32H); IR (neat) 2850, 1450, 1350, 1240, 1100 $\text{cm}^{-1}$ ; MS 440 ( $\text{M}^+$ ).

**Solvent Extraction.** The general extraction procedures employed are similar to those previously presented [7]. 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 90 minutes at that temperature in order to complete phase separation. The organic phase was separated by filtration (Whatman filter paper No.1PS). Since the picrates do 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 picrate in the organic phase was determined from absorbance at 375 nm in a mixture of dichloromethane and acetonitrile. The molar extinction coefficients at the absorption maximum of 375 nm for sodium, potassium, rubidium, cesium, silver, and thallium picrates are 18600, 19000, 18800, 18500, 18800, and 18900  $\text{M}^{-1}\text{cm}^{-1}$ , respectively.

## Results and Discussion

**Synthesis.** The general idea of the synthesis of mono-benzo-crown ethers has been presented in Pedersen's work [8] and the previous report [2]. In the present study, catechol was converted to **11** by reaction of catechol and ethylene glycol mono-2-chloroethyl ether in the presence of KOH in 28% yield. The compound **11** has two side chains possessing oxyethylene chains that would be the component of the crown ether ring. Thus **11** is the starting material of the synthesis of large ring mono-benzo-crown ethers. Benzo-27-crown-9 (**3**) was synthesized from **11** and tetraethylene glycol ditosylate in THF in the presence of KOH in 28% yield. Benzo-30-Crown-10 (**4**) was synthesized from **11** and pentaethylene glycol ditosylate in THF in the presence of KOH in 18% yield. No attempt was made to maximize the yields of the products.

Unsubstituted large ring-sized crown ethers, 27-crown-9 (**7**) was synthesized from pentaethylene glycol and pentaethylene glycol ditosylate in THF in the presence of KOH in 7% (2.8g) yield. Likewise, 30-crown-10 (**8**) was synthesized from pentaethylene glycol and pentaethylene glycol ditosylate in THF in the presence of KOH in 8% yield. The oily products **7** and **8** were purified by distillation under reduced pressure.

Though the general idea of the above synthetic methods has been already reported by other and our groups [5,9], the characteristic informations of the compounds have not been described in detail. As well as the reported data of crown-7 and crown-8 compounds [2], the present results would give the detailed strategic idea and direction in case of synthesizing large ring-sized macrocyclic compounds.

**Solvent Extraction.** A wide variety of measurement techniques for evaluating the characters of macrocyclic compounds have been reported. Notable among them are ion-selective electrode techniques, NMR methods, and solvent extraction. For crown ethers, solvent extraction techniques are quite popular and convenient method to evaluate cation binding ability. In the present study, aqueous some alkali and heavy metal picrates ( $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Rb}^+$ ,  $\text{Cs}^+$ ,  $\text{Ag}^+$ , and  $\text{Tl}^+$ ) were extracted at 25°C with dichloromethane solution of the crown ethers (**1-10**). The extractabilities obtained are shown in Table 1. In the present study, data obtained by this solvent extraction of metal picrates are presented for general discussion.

As seen from Table 1, large ring-sized crown-9 and crown-10 (**3,4,7,8**) possess high extractability for  $\text{K}^+$ ,  $\text{Rb}^+$  and  $\text{Tl}^+$  while crown-7 and crown-8 (**1,2,5,6**) and crown-6 derivatives (**9,10**) also possess high extractability for  $\text{K}^+$  and  $\text{Tl}^+$ . Generally it was found that large ring-sized benzo-crown ethers have lower cation binding ability as compared with those of **9** and **10**, and cation selectivity for large cation,  $\text{Tl}^+$  has been observed. This would be clearly explained by the generally accepted size-fit concept [8] and unusual high  $\text{Tl}^+$  binding ability for most crown ethers irrespective of the ring size [10]. Compared with benzo-crown ethers (**3,4**) and unsubstituted crown ethers (**7,8**) with the same ring size, the cation binding ability of benzo-crown ethers are generally lower than the corresponding unsubstituted crown ethers; e.g. the data of **3** vs. **7** and those of **4** vs. **8**. The exception is  $\text{Na}^+$  for **4**, which is the same as those for **2** discussed in the previous report [2].

As reported in the previous paper [2,4], the results are explained by the basicity of oxygen atom of the crown ether ring as this has been also already reported for small ring-sized crown-5 and 6 ethers. Basicity of oxygen atom next to the benzene ring of **3** and **4** is lower than that of **7** and **8** which causes the low binding

ability of the crown ethers for cations.

The above explanation is based on the formation of 1:1 crown ether-cation complex and the absence of any sandwich type complex between crown ether and cation.

It should be noted that the data in Table 1 provide interesting insight into the effect of benzo-type crown ether ring size upon the extractability of cations. For Na<sup>+</sup> and Ag<sup>+</sup>, the cation-binding ability is strongest with benzo-24-crown-8 (2) and other cation-binding ability (K<sup>+</sup>, Rb<sup>+</sup>, Cs<sup>+</sup>, and Tl<sup>+</sup>) of benzo-type crown ethers decreases from benzo-18-crown-6 (9) to benzo-24-crown-8 (2) and increases again with benzo-27-crown-9 (3) and benzo-30-crown-10 (4). As has already reported in the paper from other group [5], this result would suggest that crown ether ring no longer remains planar but distorts to accommodate cations which would be small to fit in the crown ether ring. To get the clear-cut evidence, the further extraction experiments to determine the extraction equilibrium constants ( $K_{ex}$ ) should be needed.

Since the size-fit concept has been mainly discussed in the case of the crown-4, 5, and 6 derivatives in the solution chemistry, more discussion on the large simple structured, ring-sized crown-7,8,9, and -10 ethers should be needed with regard to cation selectivity and complex formation of crown ether chemistry.

Table 1. Solvent Extraction of Metal Picrates<sup>a)</sup>

Ligand	%Extractability <sup>b)</sup>					
	Na <sup>+</sup>	K <sup>+</sup>	Rb <sup>+</sup>	Cs <sup>+</sup>	Ag <sup>+</sup>	Tl <sup>+</sup>
1 <sup>c)</sup>	1.7	19.7	33.1	36.4	9.0	52.8
2 <sup>c)</sup>	11.2	13.7	18.5	18.4	22.2	41.9
3	3.0	20.4	25.7	21.1	11.1	39.4
4	5.2	28.8	38.8	27.7	13.8	49.6
5 <sup>c)</sup>	3.2	24.9	43.1	52.2	22.4	63.6
6 <sup>c)</sup>	5.1	16.2	22.4	32.4	19.9	48.4
7	2.9	30.9	26.6	26.1	15.0	49.9
8	3.3	39.7	45.3	31.5	13.1	57.0
9 <sup>c)</sup>	2.9	43.0	28.6	17.0	18.2	55.0
10 <sup>c)</sup>	6.3	69.0	57.6	36.7	31.3	73.2

a) Temperature 25°C; aqueous phase (10ml): [picrate]=3mM. Organic Phase (CH<sub>2</sub>Cl<sub>2</sub>, 10ml): [Ligand]=3mM.

b) Defined as percent picrate extracted into the organic phase. Average of two independent runs.

c) Ref. 2

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