CHEMISTRY LETTERS, pp. 1137 - 1140, 1984.

DOUBLE-ARMED 16-CROWN-5.
MARKED AND SPECIFIC ENHANCEMENT IN CATION BINDING ABILITIES

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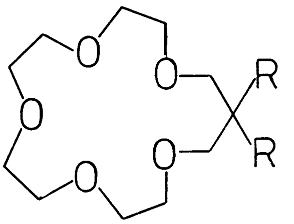
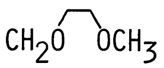
16-Crown-5 derivatives with double oxyethylene side-arms of various chain lengths were synthesized and their cation-binding abilities were assessed. In addition to the general enhancement in extractabilities for most cations, peak extractabilities were observed for the size-fitted cations, i.e. Na^+ and Ag^+, at a specific length of the side-arm.

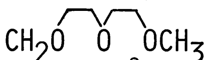
Recently Gokel et al. have synthesized new functionalized crown ethers with an additional binding site, so-called "lariat ethers".1) These lariat ethers have been reported to show higher cation-binding abilities than the corresponding parent crown ethers especially when the side-arm is bound to the parent crown ether through a nitrogen pivot.2) More recently Weber has reported the syntheses of some 16-crown-5 derivatives with double side-arms,3) but no attempt has been made to evaluate their cation-binding abilities. We have shown4) that 16-crown-5 exhibits exceptionally high selectivities for Na^+ and Ag^+, which are attributed to the most favorable cavity size and donor-atom orientation for complexation with these cations.

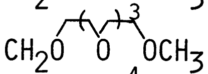


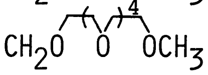
1: $R = CH_3$

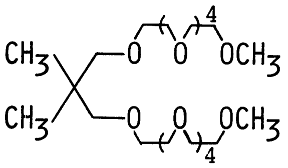
2: $R = CH_2OCH_3$

3: R = 
$CH_2O(CH_2CH_2O)CH_3$

4: R = 
$CH_2O(CH_2CH_2O)_2CH_3$

5: R = 
$CH_2O(CH_2CH_2O)_3CH_3$

6: R = 
$CH_2O(CH_2CH_2O)_4CH_3$



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We wish now to report the marked and specific enhancement in cation-binding ability exhibitted by double-armed 16-crown-5 derivatives which were designed to further raise the cation selectivity as well as the binding ability.

Double-armed 16-crown-5 derivatives, **2**, **3**, **4**, **5**, and **6**, were prepared by reactions of 15,15-bis(hydroxymethyl)-16-crown-54a) with the corresponding oligoethylene glycol monomethyl ether tosylates in the presence of NaOH as a base in tetrahydrofuran in 73-78% yields. The acyclic ligand **7** was prepared from 2,2-

dimethyl-1,3-propanediol and pentaethylene glycol monomethyl ether tosylate in the presence of NaOH in tetrahydrofuran in 79% yield. All products gave satisfactory spectral and analytical data.

The cation-binding ability of double-armed 16-crown-5 derivatives, **2**, **3**, **4**, **5**, and **6**, was assessed by solvent extraction of aqueous solutions of alkali, alkaline earth, and heavy metal picrates (3 x 10^{-3}M) at 25 °C with dichloromethane solutions of the crown ethers (3 x 10^{-3}M). For comparison purpose, the cation-binding abilities of dimethyl-16-crown-5 **1** and the side-arm mimic **7** were also assessed. In Figures 1a and 1b are plotted the % extractabilities for **1-6** with mono- and divalent cations as a function of number (n) of oxygens in a side arm.

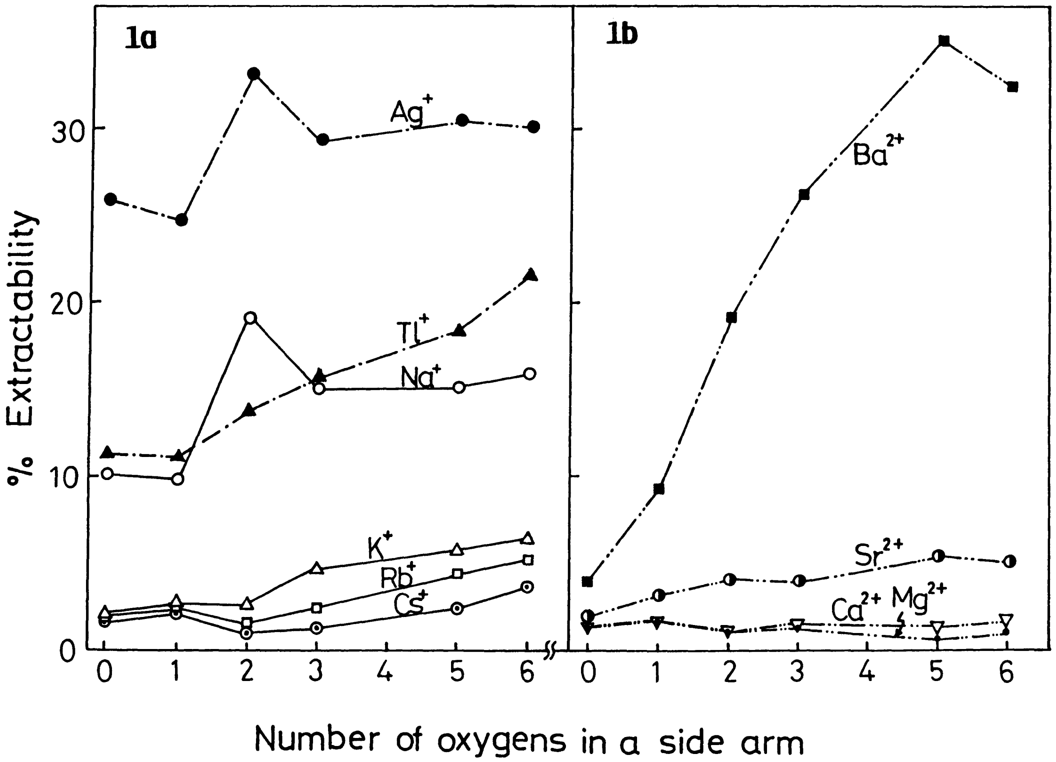

Fig. 1. Extraction of alkali, alkaline earth, and heavy metal picrates with double-armed 16-crown-5 derivatives **1** - **6**.

In general, the extractability increases gradually with extending the oxyethylene side arms. However, the changing pattern of extractability with n differs substantially depending on the cation extracted, and may be classified into three categories: 1) an optimum extractability is obtained at n = 2, 2) extractability increases gradually with increasing n, and 3) extractability does not change even in the presence of the additional binding sites.

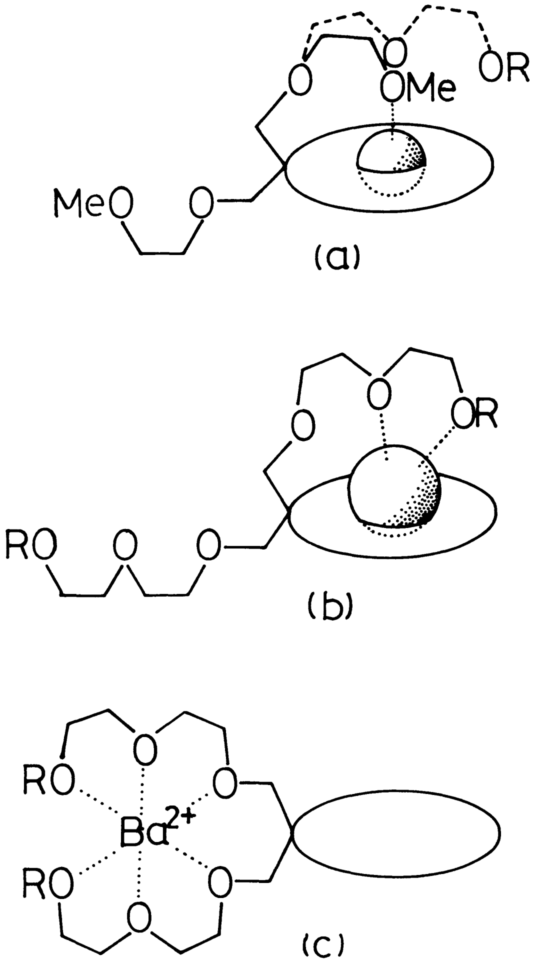

Fig. 2. Schematic drawings of the interaction between metal ion (ball) and crown ether (tray) with double side-arms.

Na$^+$ (cation diameter 2.04 Å)[5] and Ag$^+$ (2.30 Å)[5] fall in the case 1. According to the size-fit concept, these cations are best accomodated into the cavity (1.8 Å)[4] of the 16-crown-5 derivatives and the five oxygen atoms are directed inside, which makes 1:1 complex formation with Na$^+$ and Ag$^+$ most favorable. The fact that the crown ether **3** with two oxygens in a side-arm gives the maximum extractabilities for Na$^+$ and Ag$^+$ indicates that the second oxygen atom in the side-arm is placed at the most favorable position to coordinate with the cation accomodated in the crown ether cavity (Figure 2a). The dumping at n = 3 and the subsequent steady extractabilities at $n \geqq 3$ may be attributable to the steric hindrance of the extra oxyethylene units which do not contribute to raise the extractability (Fig. 2a, dashed line). Case 2 may include K$^+$, Rb$^+$, Cs$^+$, and Sr^{2+} which are too large to fit in the cavity (1.8 Å) of 16-crown-5 derivatives, and lie above the crown ether cavity just like a ball on a tray. In this situation, oxygens in the side-arm would stabilize the less-stable 1:1 crown ether-cation complex by wrapping the cation (Fig. 2b), which results in the gradual increase of extractability with increasing n. The drastic increase of extractability observed with Tl$^+$, and Ba^{2+} may rather be explained by the involvement of side-arms as a complexing agent (Fig. 2c), since even the side-arm mimic **7** does exhibit usually high extractabilities only for Tl$^+$ and Ba^{2+}, which amount to halves of the extractabilities shown by the crown ether **6** (Table 1).

Finally, with Mg^{2+} and Ca^{2+}, the extractabilities of 16-crown-5 derivatives both with and without oxyethylene side-arms were very low, and any improvement was not observed by introducing side-arms. We have reported[4c,d] that the effect of hydration of metal ions becomes the dominant factor controlling the extraction of Mg^{2+} and Ca^{2+} picrates by crown ethers. The present results indicate that the additional binding sites introduced to the crown ether are not satisfactory to raise the cation-binding ability in the case that the effect of hydration of metal ions domitates the extraction behavior.

Table 1. Extraction of metal picrates with a double-armed 16-crown-5 **6** and its side-arm mimic **7** a)

	Extractability/ %b)									
Ligand	Na^+	K^+	Rb^+	Cs^+	Ag^+	Tl^+	Mg^{2+}	Ca^{2+}	Sr^{2+}	Ba^{2+}
6	16	6	5	4	30	22	1	2	5	33
7	0	1	1	1	1	12	0	0	1	17

a) Temperature 25.0 ± 0.1 °C; aqueous phase (10 mL): [picrate] = 3×10^{-3} M; organic phase (CH_2Cl_2, 10mL): [ligand] = 3×10^{-3}M. b) % Picrate extracted into the organic phase.

Thus, 16-crown-5 derivatives with double side-arms show the enhanced extractabilities with most cations examined, which may be attributable to the cooperative effect of the additional binding sites with a crown ether ring. It should also be noted that the peak extractabilities are seen with the size-fitted cations, i.e. Na^+ and Ag^+, and as a consequence the Na^+/K^+ and Ag^+/Tl^+ selectivities are significantly enhanced for the crown ether **3**. Examination with a C-P-K molecular model reveals that only one side-arm appears to have access to the cation in the crown cavity, so that there seems to be no significance of double side-arms in such a crown ether molecule. This prompts the authors to synthesize 16-crown-5 derivatives with a single side-arm, which is currently undertaken.

Partial support of this work by a grant from the Hyogo Foundation for the Promotion of Science and Technology is gratefully acknowledged.

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(Received April 20, 1984)