New Applications of Crown Ethers. Part 6.[1] Structural Effects of Bis(benzocrown ether)s and Substituted Benzocrown Ethers on Solvent Extraction and Complexation of Alkali-metal Cations

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Bis(benzocrown ether)s consisting of benzo-15-crown-5 (B15C5), benzo-18-crown-6 (B18C6) and/or benzo-21-crown-7 (B21C7) with the following linking chains, -$(CH_2)_n$- (n = 2 and 8), -$(CH_2)_3$-O-, -O-$(CH_2)_6$-O-, and -$(O\text{-}CH_2CH_2)_n$-O- (n = 2—5), were prepared and their complexation behaviour was characterized using solvent extraction of alkali-metal picrates and complexation with alkali-metal chlorides. Bis(benzocrown ether)s were distinguished from the corresponding mono(benzocrown ether)s by their remarkable high extraction ability of a cation larger than the hole size of a crown unit, the so-called 'biscrown effect'. Bis(B15C5)s (**4a**—**h**) and bis(B18C6)s (**5a**—**h**) preferentially extracted K^+ and Cs^+, respectively. Bis(benzocrown ether)s containing the B21C7 unit (**6a**)—(**8a**) did not show this 'biscrown effect' because of the large hole size of B21C7. An unsymmetrical bis(crown ether) (**7b**) consisting of B15C5 and B18C6 selectively extracted Rb^+. The 'biscrown effect' was favourably exerted with the oligoethyleneglycol linkage rather than the hydrocarbon one. Little or no effect of lipophilic groups or donor oxygens in the side chain of mono(benzocrown ether)s was observed in the extraction of alkali-metal picrates. Stability constants were determined by the ion-selective electrode method in 90% methanol aqueous solution at 25 °C. In bis(B15C5)s with Na^+, and bis(B18C6)s with Na^+ or K^+, two crown rings in one molecule acted as two individual moieties. Bis(B15C5)s bound with K^+ to form preferentially an intramolecular 2:1 crown ether unit-K^+ complex. Both bis(B15C5)s with Cs^+ and bis(B18C6)s with Cs^+ systems also showed the 'biscrown effect'.

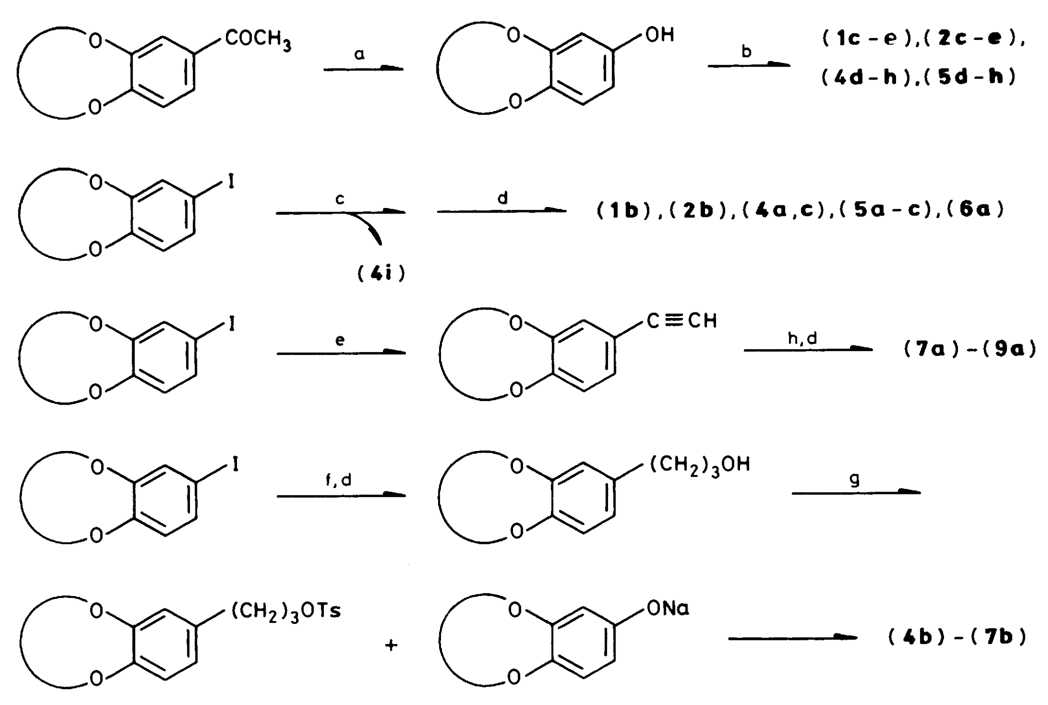
The hole size–ionic diameter relationship, *i.e.*, 'lock and key' concept in the complexation of cations by crown ethers (macrocyclic polyethers), is well documented, although the relationship is not always a critical factor.[2,3] Lariat crown ethers[4] and bis(crown ether)s[5,6] have been devised to fit the 'lock' with the 'key' (cation). Bis(crown ether)s, having two crown rings in one molecule, are well known to bind a cation larger than the hole size of the crown unit as sandwich structure, and to show remarkable enhancement of complexation and change of selectivity, the so-called 'biscrown effect'.[6] In this report, the structural effects of bis(benzocrown ether)s and substituted benzocrown ethers on the solvent extraction of alkali-metal picrates and equilibrium binding constants (stability constants) with alkali-metal chlorides are described. The solvent extraction method was mainly employed to characterize the bis(crown ether)s, since the method was expected to reflect this feature of bis(crown ether)s more sensitively.[3]

Experimental

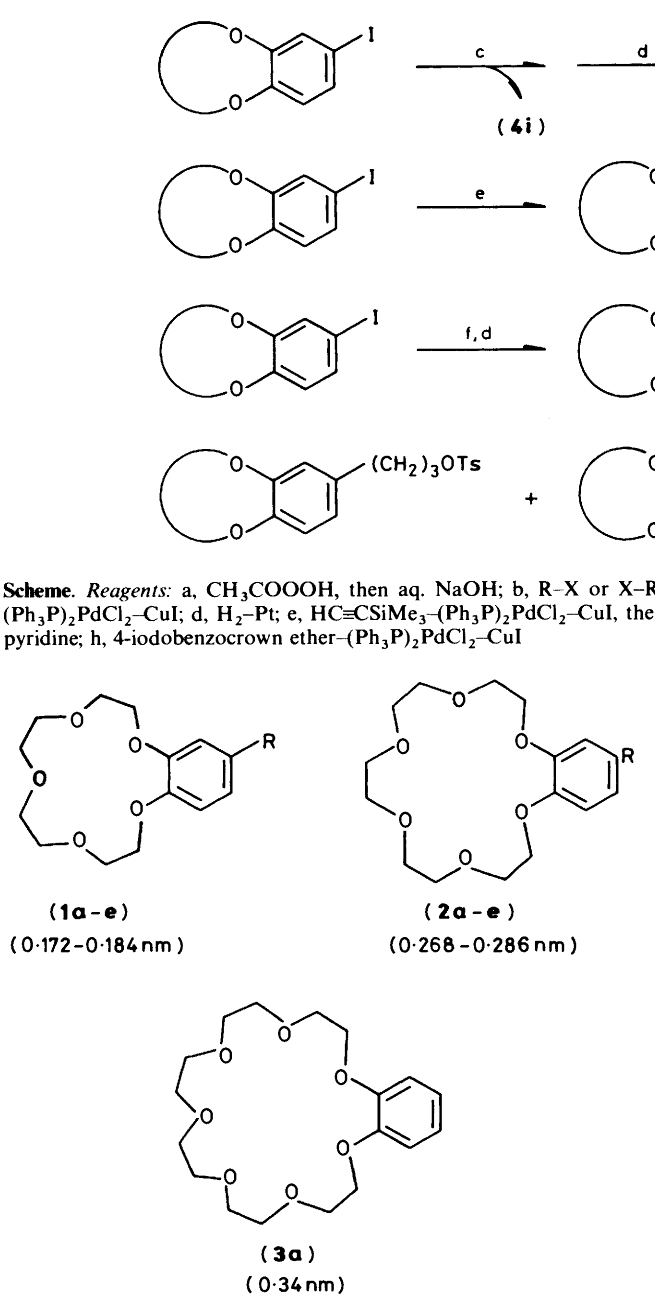
Materials.—Methylene dichloride was purified by successive washing with concentrated H_2SO_4, aqueous alkaline solution, and distilled water and dried over ($CaCl_2$). After distillation, it was saturated with distilled water before use. Methanol was distilled from sodium methoxide and diluted with distilled water to give 90% (w/w) methanol solutions. Samples of picric acid, alkali-metal chlorides, and alkali-metal hydroxides were not further purified except for drying.

Benzocrown Ether.—The substituted benzocrown ethers (**1**)—(**3**) and the bis(benzocrown ether)s (**4**)—(**9**) were prepared by the methods reported previously[5,7] as described briefly in the Scheme. The purity and structure of the crown ethers were confirmed by i.r., n.m.r., mass spectra, and elemental analysis. The following are physical data of new compounds: 4-n-octylbenzo-15-crown-5 (**1b**), oil, b.p. 145—153 °C at 0.005 Torr, *m/e* 380 (M^+), δ 0.5—2.7 (m, 17 H), 3.5—4.5 (m, 16 H), and 6.5—7.0 (m, 3 H) (Found: C, 69.3; H, 9.5. Calc. for $C_{27}H_{36}O_5$: C, 69.4; H, 9.5%); 4-n-octylbenzo-18-crown-6 (**2b**), crystals, m.p. 40.2—41.0 °C (from hexane), *m/e* 425 (M^+) (Found: C, 67.8; H, 9.7. Calc. for $C_{24}H_{40}O_6$: C, 67.9; H, 9.5%); 4-(1,4,7,10-tetraoxaundecanyl)benzo-15-crown-5 (**1e**), oil, b.p. 140—150 °C at 0.002 Torr, *m/e* 430 (M^+) (Found: C, 58.4; H, 8.0. Calc. for $C_{21}H_{34}O_9$: C, 58.6; H, 8.0%); 4-(1,4,7,10-tetraoxaundecanyl)benzo-18-crown-6 (**2e**), oil, b.p. 205—215 °C at 0.001 Torr, *m/e* 474 (M^+) (Found: C, 58.1; H, 8.3. Calc. for $C_{23}H_{38}O_{10}$: C, 58.2; H, 8.1%); 1,2-bis-(4-benzo-15-crown-5)ethane (**4a**), m.p. 106.7—108.7 °C (Found: C, 64.0; H, 7.7. Calc. for $C_{30}H_{42}O_{10}$: C, 64.0; H, 7.5%); 1,2-bis-(4-benzo-18-crown-6)ethane (**5a**), m.p. 87.6—89.4 °C (Found: C, 62.7; H, 7.8%. Calc. for $C_{34}H_{50}O_{12}$: C, 62.8; H, 7.7%); 1,2-bis-(4-benzo-21-crown-7)ethane (**6a**), m.p. 86.9—88.1 °C (Found: C, 61.65; H, 7.9. Calc. for $C_{38}H_{58}O_{14}$: C, 61.8; H, 7.9%); 1-(4-benzo-15-crown-5)-2-(4-benzo-18-crown-6)ethane (**7a**), m.p. 102.1—103.6 °C (Found: C, 63.6; H, 7.6. Calc. for $C_{32}H_{46}O_{11}$: C, 63.35; H, 7.6%); 1-(4-benzo-15-crown-5)-2-(4-benzo-21-crown-7)ethane (**8a**), m.p. 70.1—71.8 °C; 1-(4-benzo-18-crown-6)-2-(4-benzo-21-crown-7)ethane (**9a**), m.p. 75.5—77.1 °C (Found: C, 62.6; H, 7.8. Calc. for $C_{36}H_{54}O_{13}$: C, 62.2; H, 7.8%).

Solvent Extraction.—Solvent extraction was carried out with alkali-metal picrates in a methylene dichloride–water system according to Pedersen's procedure.[8] The percent of a picrate salt extracted [Ex(%)] was based on the picrate concentration ($\lambda_{max.}$ 356 nm) in the aqueous phase after equilibration under the following conditions, CH_2Cl_2 =



Scheme. *Reagents:* a, CH_3COOOH, then aq. NaOH; b, R–X or X–R–X–NaOH, X = Cl or OTs; c, HC≡CH, RC≡CH or HC≡C–R′–C≡CH–$(Ph_3P)_2PdCl_2$–CuI; d, H_2–Pt; e, $HC{\equiv}CSiMe_3$–$(Ph_3P)_2PdCl_2$–CuI, then Na_2CO_3 in aq. MeOH; f, $HC{\equiv}CCH_2OH$–$(Ph_3P)_2PdCl_2$–CuI; g, TsCl–pyridine; h, 4-iodobenzocrown ether–$(Ph_3P)_2PdCl_2$–CuI



a; R = H

b; R = n-C_8H_{17}

c; R = n-C_4H_9O

d; R = n-$C_{16}H_{33}O$

e; R = $CH_3(OCH_2CH_2)_3O$

Ionic diameter

Na^+ 0·204, K^+ 0·276, Rb^+ 0·298, Cs^+ 0·340 nm

Substituted benzocrown ethers and their hole size (in parentheses), and ionic diameter of alkali-metal cations (J. D. Lamb, R. M. Izatt, C. S. Swain, and J. J. Christensen, *J. Am. Chem. Soc.*, 1980, **102**, 475)

H_2O = 10 ml, [picric acid] = 7 × 10^{-5}M, [M(OH)] = 0.01M, [crown unit] = 3.5 × 10^{-4}M at 25.0 °C.

Extraction equilibrium constants (K_e) were measured under the same conditions except for the concentration of crown ethers (9.0 × 10^{-6}—7.0 × 10^{-4}M). The distribution constants (P_e) of the crown ethers were obtained in the absence of the picrate salts using spectrophotometric measurement of the crown ethers. The K_e were obtained by the following equations according to Frensdorff's[9] and Smid's[10] procedure. Dissociation constants (K_d) of crown ether complexes of alkali-metal picrates in organic phase were evaluated by regression analysis for fitting of 4—8 data points per system and by minimizing the deviation of K_e in the process.

Overall extraction equilibrium constant is defined as

$$M^+_{aq} + A^-_{aq} + Cr_{org} \overset{K_e}{\rightleftharpoons} MCrA_{org} \qquad (1)$$

$$MCrA_{org} \overset{K_d}{\rightleftharpoons} MCr^+_{org} + A^-_{org} \qquad (2)$$

$$Cr_{org} \overset{P_e}{\rightleftharpoons} Cr_{aq} \qquad (3)$$

For an extraction by forming a 1:1 complex only, a single relation with two unknown K_e and K_d can be written as (4). For

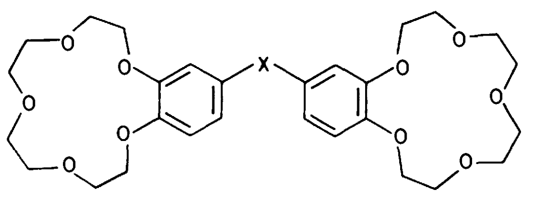
$$K_e = \frac{(1 + P_e)[2A + K_d - (K_d^2 + 4K_dA)^{\frac{1}{2}}]}{2f(M_O - A)(A_O - A)(Cr_O - A)} \qquad (4)$$

an extraction with a 2:1 (crown ether unit–cation) complex, two types of complexes, intermolecular and intramolecular, must be considered, and K_e can be represented by equations (5) and (6), respectively. f Is the single-ion activity coefficient of the cation in

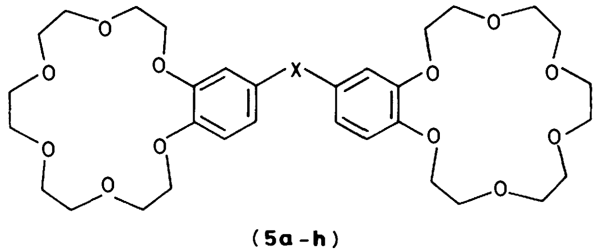
$$K_e = \frac{(1 + P_e)^2[2A + K_d - (K_d^2 + 4K_dA)^{\frac{1}{2}}]}{2f(M_O - A)(A_O - A)(Cr_O - 2A)^2} \qquad (5)$$

$$K_e = \frac{(1 + P_e)[2A + K_d - (K_d^2 + 4K_dA)^{\frac{1}{2}}]}{2f(M_O - A)(A_O - A)(Cr_O - 2A)} \qquad (6)$$

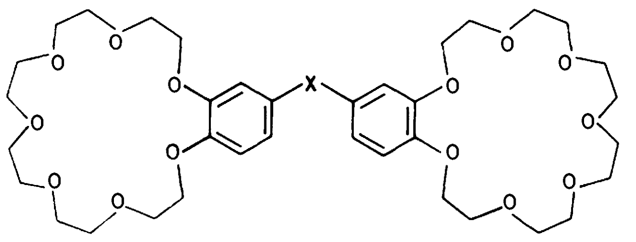
aqueous phase (f = 0.889 is used in this paper), A is the total



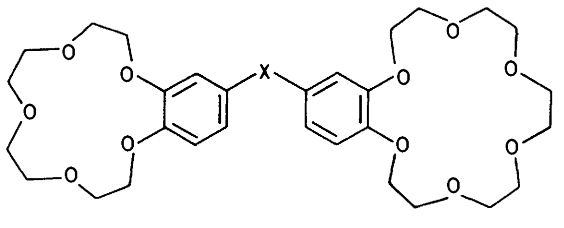
(4a-i)



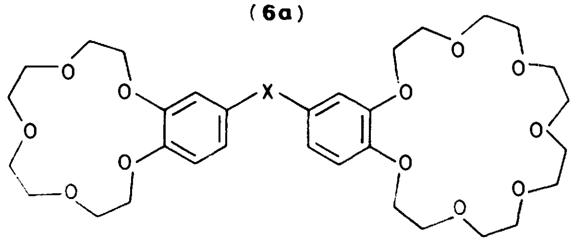
(5a-h)



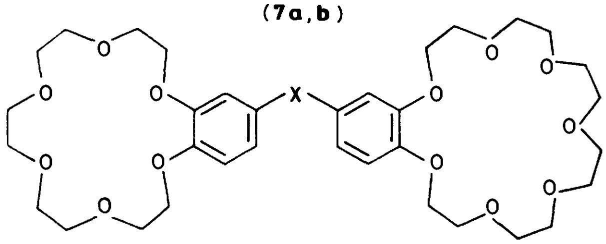
(6a)



(7a,b)



(8a)



(9a)

a; X = CH_2CH_2
b; X = $OCH_2CH_2CH_2$
c; X = $(CH_2)_8$
d; X = $O(CH_2)_6O$
e; X = $O(CH_2CH_2O)_2$
f; X = $O(CH_2CH_2O)_3$
g; X = $O(CH_2CH_2O)_4$
h; X = $O(CH_2CH_2O)_5$
i; X = C≡C

concentration of picrate anion in the organic phase and M_O, A_O, and Cr_O are initial concentrations of the cation, picrate anion, and crown ether unit, respectively.

Stability Constants.—The stability constants were determined for a mixture of 2.5 × 10^{-4}—8.0 × 10^{-4}M-crown ether unit and 4.0 × 10^{-4}—2.0 × 10^{-3}M-metal chloride in 90% (w/w) methanolic aqueous solution at 25 °C by measuring the e.m.f. for the respective electrode [Na^+-ISE(TOA NA-115B) for Na^+ and monovalent cation electrode (Corning Cat. No. 476220) for K^+ and Cs^+] against an Ag–AgCl reference electrode using an Orion Research model 701A digital 'Ionanalyzer'. 3—8 Points of varying ratios of crown ether to metal chloride were involved in one group of measurements and standard deviations were < 10%. The results from 2—5 groups of the measurements at different concentrations gave the average stability constants and standard deviations as in Table 5.

In the case of mono(crown ether)s, the stability constants for 1:1 (K_{m1}) and 2:1 (K_{m2}) crown ether–cation complexes were obtained with the same procedure reported by Frensdorff.[11] When the stability constant increased as the concentration of the crown ether increased and the deviation was larger than 10% in one group measurement, the K_{m1} and K_{m2} were calculated with regression analysis [equations (7)—(10)]. The K_{m1} and K_{m2} in Table 5 are shown as $K_{1\text{obs}}$ and $K_{2\text{obs}}$, respectively.

$$M^+ + Cr \overset{K_{\text{m1}}}{\rightleftharpoons} M^+Cr \tag{7}$$

$$M^+Cr + Cr \overset{K_{\text{m2}}}{\rightleftharpoons} CrM^+Cr \tag{8}$$

$$K_{\text{m1}} = \frac{[M^+Cr]}{[M^+][Cr]} \tag{9}$$

$$K_{\text{m2}} = \frac{[CrM^+Cr]}{[Cr][M^+Cr]} \tag{10}$$

For bis(crown ether)s, the following complexes (**10**)—(**13**) can exist in homogeneous solution as shown in equations (11)—(14), where $[\overset{\frown}{\text{Cr}\;\;\text{CrM}^+}]_{\text{total}}$ means the total concentration of 1:1 stoicheiometric crown ether–cation complexes (**10**) and (**11**). At first the stability constants were calculated with the

$$\overset{\frown}{\text{Cr}\;\;\text{Cr}} + M^+ \overset{K_{\text{b1}}}{\rightleftharpoons} \underset{\textbf{(10)}}{\overset{\frown}{\text{Cr}\;\;\text{CrM}^+}} \tag{11}$$

$$\overset{\frown}{\text{Cr}\;\;\text{CrM}^+} \overset{K_{\text{b2}}}{\rightleftharpoons} \underset{\textbf{(11)}}{\overset{\frown}{\text{CrM}^+\text{Cr}}} \tag{12}$$

$$\overset{\frown}{\text{Cr}\;\;\text{CrM}^+} + M^+ \overset{K'_{\text{b1}}}{\rightleftharpoons} \underset{\textbf{(12)}}{M^+\overset{\frown}{\text{Cr}\;\;\text{CrM}^+}} \tag{13}$$

$$\overset{\frown}{\text{Cr}\;\;\text{CrM}^+} + \overset{\frown}{\text{Cr}\;\;\text{Cr}} \overset{K'_{\text{b2}}}{\rightleftharpoons} \underset{\textbf{(13)}}{\overset{\frown}{\text{Cr}\;\;\text{CrM}^+}\overset{\frown}{\text{Cr}\;\;\text{Cr}}} \tag{14}$$

Table 1. Solvent extraction of alkali-metal picrates by substituted benzocrown ethers

Crown ether	Ex(%)^a			
	Na^+	K^+	Rb^+	Cs^+
(1a)	2.6	14.2	11.2	7.7
(1b)	3.0	11.5	4.8	1.4
(1c)	2.2	9.1	4.6	1.7
(1d)	2.2	8.4	3.8	1.3
(1e)	2.9	9.9	4.7	1.5
(2a)	3.3	54.1	27.2	15.8
(2b)	3.5	61.4	33.0	20.1
(2c)	3.8	56.7	30.0	17.6
(2d)	3.8	56.5	29.8	17.3
(2e)	4.1	55.2	30.2	18.8
(3a)	3.5	31.3	54.7	64.4

^{a} The values were based on picrate salts in the aqueous phase.

Table 2. Solvent extraction of alkali-metal picrates by bis(benzocrown ether)s

Crown ether	Ex(%)^a			
	Na^+	K^+	Rb^+	Cs^+
(4a)	6.5	53.2	46.8	22.2
(4b)	6.3	65.4	41.4	12.5
(4c)	4.9	61.8	35.1	9.8
(4d)	7.5	79.2	46.9	11.6
(4e)	9.1	86.5	61.5	18.2
(4f)	10.2	86.7	61.5	18.2
(4g)	9.4	84.5	58.6	19.0
(4h)	8.0	80.5	52.7	15.5
(4i)	1.8	19.0	4.8	1.4
(5a)	7.1	54.1	53.8	69.3
(5b)	4.9	59.0	41.0	72.4
(5c)	4.3	60.8	36.8	48.0
(5d)	5.4	61.0	45.7	71.0
(5e)	6.5	62.7	54.7	85.1
(5f)	6.0	62.5	54.6	82.5
(5g)	5.9	60.8	51.2	78.9
(5h)	6.1	60.6	51.4	77.8
(6a)	5.1	36.6	53.8	59.3

^{a} The values were based on picrate salts in the aqueous phase.

$$K_{1\mathrm{obs}} = \frac{[\overgroup{\mathrm{Cr}\quad \mathrm{Cr}}\mathrm{M}^+]_{\mathrm{total}}}{[\overgroup{\mathrm{Cr}\quad \mathrm{Cr}}][\mathrm{M}^+]} \tag{15}$$

$$K_{2\mathrm{obs}} = \frac{[\mathrm{M}^+\overgroup{\mathrm{Cr}\quad \mathrm{Cr}}\mathrm{M}^+]}{[\overgroup{\mathrm{Cr}\quad \mathrm{Cr}}\mathrm{M}^+]_{\mathrm{total}}[\mathrm{M}^+]} \tag{16}$$

assumption that a bis(crown ether) acts as a simple crown ether to form 1:1 crown ether–cation complexes (**10**) and/or (**11**). When the constants increased greatly or sometimes changed to negative with decrease of the crown ether concentration, the 2:2 crown ether unit–cation complex (**12**) was considered and the $K_{1\mathrm{obs}}$ and $K_{2\mathrm{obs}}$ values were calculated by regression analysis.

Since the intermolecular 2:1 complex (**13**) was not important in the present conditions ($[\mathrm{M}^+] > [\overgroup{\mathrm{Cr}\quad \mathrm{Cr}}]$), (**13**) was not considered in the present analysis.

Results and Discussion

Solvent Extraction.—Extraction equilibrium constants (K_e) can quantitatively characterize the solvent extraction behaviour of crown ethers. In this report, however, the percentage of picrate salt extracted [Ex(%)], rather than K_e, is mainly used for comparison of the behaviour of the various benzocrown ethers for the following reasons. (1) The structural effects of the crown ethers on Ex(%) are essentially parallel to those of K_e (compare Table 4 with Tables 1—3). (2) K_e Values are differently expressed depending on the type of the complex extracted as described in equations (4)—(6), K_e for 1:1 complexes and *intramolecular* 2:1 complexes are expressed in l^2 mol^{-2}, and those for *intermolecular* 2:1 complexes in l^3 mol^{-3}. Therefore, it is difficult to compare directly the K_e value of bis(crown ether)s with those of mono(crown ether)s.

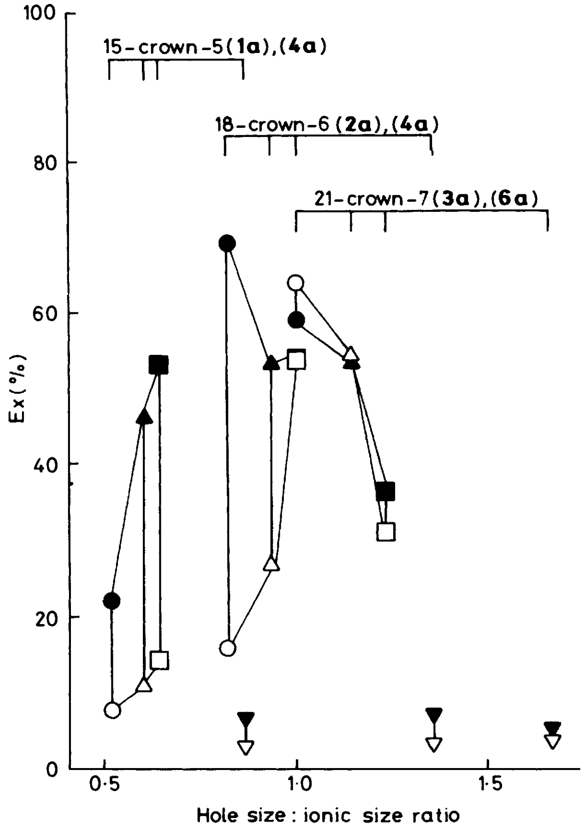


Figure 1. Effect of hole size/ionic size ratio on solvent extraction: ▽—▼, Na^+; □—■, K^+; △—▲, Rb^+; ○—●, Cs^+; ▽□△○, (**1a**),(**2a**),(**3a**); ▼■▲●, (**4a**),(**5a**),(**6a**)

The structural effects on Ex(%) are summarized in Tables 1—3. All crown ethers used in this report hardly extracted Na^+. The low extractability of Na^+ has been much discussed in terms of its high hydration energy.[2,12] The selective extraction of K^+ by (**1a**—**e**), though the extractability is still low, can be attributed to the formation of a 2:1 complex [see also K_e of (**1a**) in Table 4].[10,13,14]

The lipophilic side chain can be expected to increase the extraction ability of crown ethers. In lariat ethers, with a flexible side arm with one or more donor atoms, the extra co-ordination by the donor atom(s) increases the complexation with cations.[4] In the benzocrown ethers examined here, however, only slight or no enhancement of Ex(%) was observed by the introduction of lipophilic side chain or donor oxygen atom(s) in the side chain (Table 1). In contrast to the conventional lariat ethers, the side chain of (**1c**—**e**) and (**2c**—**e**) is rather far from the cavity to affect the complexation.

Figure 1 plots Ex(%) of simple mono(benzocrown ether)s (**1a**)—(**3a**) and bis(benzocrown ether)s (**4a**)—(**6a**) against the

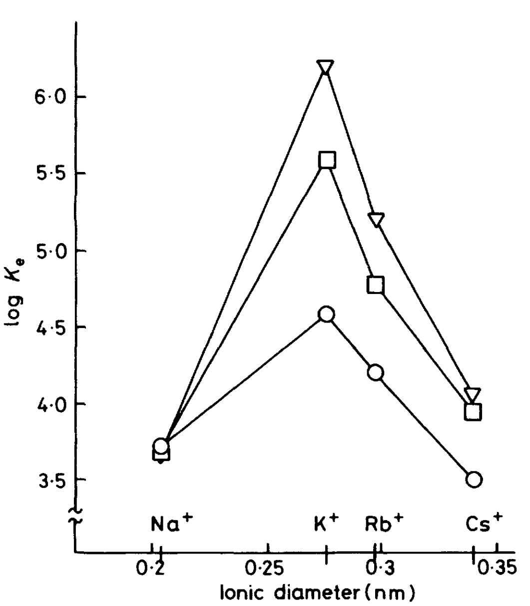


Figure 2. Extraction equilibrium constants of mono(benzo-15-crown-5) and bis(benzo-15-crown-5)s: ○, (**1a**); □, (**4c**); ▽, (**4f**)

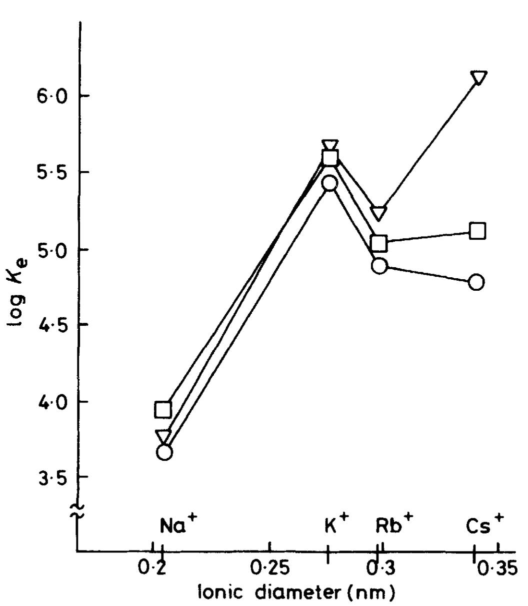


Figure 3. Extraction equilibrium constants of mono(benzo-18-crown-6) and bis(benzo-18-crown-6)s: ○, (**2a**); □, (**5c**); ▽, (**5f**)

Table 3. Solvent extraction of alkali-metal picrates by unsymmetrical bis(benzocrown ether)s

Crown ether	Ex(%)^a			
	Na$^+$	K$^+$	Rb$^+$	Cs$^+$
(**7a**)	7.8	48.0	54.0	69.2
(**7b**)	4.1	49.2	62.4	56.1
(**8a**)	7.8	59.7	48.0	43.7
(**9a**)	5.5	58.0	51.0	59.2

^{a} The values were based on picrate salts in the aqueous phase.

ratio of hole size to ionic size. Figure 3 indicates the following features of the present extraction. (1) Sodium cation is differently behaved from other alkali-metal cations. (2) Ex(%) of mono(benzocrown ether)s clearly showed a maximum at a hole size/ ionic size ratio of 1. (3) When the ratio of hole size to ionic size was <1, linking two crown ethers resulted in a remarkable enhancement of Ex(%). On the other hand, when the ratio was more than one, no effect was observed by the linking. (4) The linking of B18C6 changed the selectivity from K$^+$ to Cs$^+$.

Point (2) shows the validity of 'lock and key' concept in this extraction, *i.e.*, typical size recognition of alkali-metal cations. Points (3) and (4) are characteristics of the so-called 'biscrown effect'.[5,10,15–18] The intramolecular sandwich structure of the complexes may be responsible for the 'biscrown effect'.

The structure of the linking chain considerably affected the extraction but not decisively. The rigid straight linking chain, which prevents the formation of an intramolecular sandwich structure, is a reason for the absence of 'biscrown effect' with (**4i**). The replacement of methylene groups in the linking chain by oxygen atoms increased the extraction of the cations larger than hole size [compare (**4c**) with (**4d** and **e**), (**5c**) with (**5d** and **e**), see also Figures 2 and 3]. The principal role of the oxygen atoms is in increasing the flexibility of the linking chain to attain an intramolecular sandwich structure.[5]

In view of the 'lock and key' concept, the unsymmmetrical bis(crown ether)s consisting of two crown ethers with different hole sizes are of interest (Table 3). It is noteworthy that the Ex(%) of (**7b**) was best for Rb$^+$ due to the co-operative binding by B15C5 and B18C6 moieties. To date, the preferential extraction of Rb$^+$ has hardly been achieved by crown ethers. The same combination with a shorter linking chain, (**7a**) however, extracted Cs$^+$ best, though the extraction of Rb$^+$ was still better than K$^+$ with little resemblance to the behaviour of other symmetrical bis(benzocrown ether)s, (**4a**—**h**) and (**5a**—**h**). The large hole size of B21C7 may be responsible for the lack of characteristic features of the unsymmetrical bis(benzocrown ether)s, including the B21C7 moiety.

Extraction Equilibrium Constants (K_e).—As described in the Experimental section, three equations were used to calculate K_e corresponding to the three types of complexes, 1:1 (crown unit:cation), intermolecular 2:1, and intramolecular 2:1 complexes. The K_e values of some typical bis(benzocrown ether)s are summarized in Table 4. It is noticeable that K_e of bis(benzocrown ether)s with a cation larger than the hole size can be calculated with equation (6) to give the lowest standard deviation *i.e.*, the formation of intramolecular 2:1 complexes (values in parentheses in Table 4). As previously reported,[14] (**1a**) extracted K$^+$ and Rb$^+$ as 2:1 complexes, and K_e should be calculated by equation (5) to give the least standard deviation with reasonable K_d (the values in brackets in Table 4). Plots of K_e against ionic size are shown in Figure 2 and 3 to compare mono(benzocrown ether)s with bis(benzocrown ether)s. As mentioned before, K_e of (**1a**) cannot directly compare with those of (**4c** and **f**). Thus, K_e of (**1a**) calculated with equation (**4**) is used in Figure 2, although K_e thus obtained has more than 10% standard deviation with the unreasonable assumptions $K_d = 0$, and the dependence of K_e on the concentration of crown ether (if a reasonable K_d such as 10^{-5} is assumed, K_e shows more than 20% of standard deviation). Figures 2 and 3 show that the structural effects on K_e are essentially parallel with those of Ex(%), *i.e.*, a 'biscrown effect' is observed for K_e to K$^+$ with (**4c** and **f**), and to Cs$^+$ with (**5c** and **f**). The K_e values of (**7b**) for K$^+$ and Rb$^+$ were the same within the experimental error, although (**7b**) selectively extracted Rb$^+$.

Stability Constants.—Since the stability constant in homogeneous solution is one of the most basic complexing properties

Table 4. Extraction equilibrium constants (K_e) and dissociation constants (K_d)[a]

Crown ethers	$10^4\ K_e/10^6\ K_d$			
	Na$^+$	K$^+$	Rb$^+$	Cs$^+$
		Benzo-15-crown-5 series		
(1a)	0.50 ± 0.05/0.2[b]	[560 ± 40]/110[b]	[100 ± 10]/100	0.30 ± 0.02/0.2
(4c)	0.47 ± 0.01/6	(39 ± 3)/10	(5.8 ± 0.4)/30	0.85 ± 0.1/10
(4f)	0.43 ± 0.04/50	(160 ± 10)/40	(15 ± 1)/120	1.1 ± 0.05/90
		Benzo-18-crown-6 series		
(2a)	0.45 ± 0.04/2	27 ± 1.9/12	7.8 ± 0.15/5.6	6.0 ± 0.3/0.2
(5c)	0.87 ± 0.1/1	40 ± 1.2/5	(11 ± 0.5)/15	(13 ± 0.9)/40
(5f)	0.56 ± 0.05/10	46 ± 1.5/3	(17 ± 1.0)/40	(140 ± 20)/20
		Unsymmetrical bis(crown ether)		
(7b)	0.50 ± 0.03/4	26 ± 1.4/5	(26 ± 2.0)/40	(11 ± 0.7)/130

[a] Unless otherwise noted, K_e was calculated from equation (4) for 1:1 complexes and is expressed in $l^2\ mol^{-2}$. K_e In parentheses was obtained by calculation from equation (6) for intramolecular 2:1 complexes and is expressed in $l^2\ mol^{-2}$. K_e In brackets was calculated from equation (5) for intermolecular 2:1 complexes and is expressed in $l^3\ mol^{-3}$. [b] Published data for the same system (**1a**)–Na$^+$, $K_e = 0.522 \times 10^4$, (**1a**)–K$^+$, $K_e = 730 \times 10^4$ (ref. 13).

Table 5. Stability constants of bis(benzocrown ether)s in 90% methanolic aqueous solution[a]

Crown ether	Na$^+$		K$^+$		Cs$^+$	
	log K_{1obs}	log K_{2obs}	log K_{1obs}	log K_{2obs}	log K_{1obs}	log K_{2obs}
			Mono(crown ether)s			
15C5	2.95 ± 0.01	*b*	3.00 ± 0.08	2.24 ± 0.16	2.10 ± 0.01	*b*
18C6	3.46 ± 0.08	*b*	5.50 ± 0.01	*b*	3.49 ± 0.01	*b*
(1a)	2.68 ± 0.01	*b*	2.63 ± 0.01	2.74 ± 0.04	2.08 ± 0.09	*b*
(2a)	3.62 ± 0.02	*b*	4.75 ± 0.01	*b*	3.45 ± 0.01	*b*
			Bis(crown ether)s			
(4c)	2.90 ± 0.08	*b*	4.17 ± 0.13 (log K_{b2} 1.53)[c]	*b*	2.62 ± 0.05 (log K_{b2} 0.39)[c]	*b*
(4f)	2.78 ± 0.10	2.83 ± 0.12	4.64 ± 0.09 (log K_{b2} 2.01)[c]	*b*	2.89 ± 0.01 (log K_{b2} 0.74)[c]	*b*
(5c)	3.84 ± 0.07	3.13 ± 0.10	4.98 ± 0.09	4.14 ± 0.04	4.07 ± 0.01 (log K_{b2} 0.50)[c]	*b*
(5f)	3.49 ± 0.12	3.15 ± 0.12	5.04 ± 0.14	3.93 ± 0.08	4.20 ± 0.07 (log K_{b2} 0.67)[c]	*b*

[a] For mono(crown ether)s, $K_{1obs} = K_{m1}$ and $K_{2obs} = K_{m2}$ in equations (7) and (8). For bis(crown ether)s, $K_{1obs} = K_{b1}(1 + K_{b2})$ and $K_{2obs} = K'_{b1}/(1 + K_{b2})$ in equations (11)—(13). Published data for the same system: 15C5–Na$^+$, log K 2.97;[16] 18C6–Na$^+$, log K 3.73,[16] 3.66;[17] 18C6–K$^+$, log K 5.35;[17] (**1a**)–Na$^+$, log K 2.48.[16] [b] The standard deviation of K_{1obs} was < 10% in one group measurement, no regression analysis was done in calculating K_{2obs}. [c] Estimated log K_{b2}, see text.

for crown ethers, many methods have been employed to determine it in methanol or in aqueous methanol solution. Frensdorff measured the constants for many mono(crown ether)s by the potentiometric titration method.[11] Recently Gokel *et al.* showed that very good results can also be obtained with a simple ion-selective electrode (i.s.e.) method.[3] For bis(crown ether)s, however, only a few investigations have been made to determine the stability constant in homogeneous solution.[5] 'Biscrown effect' has been characterized in solvent extraction but the complexation behaviour of bis(crown ether)s in homogeneous solution are still unclear, because the complexation equilibria of bis(crown ether)s are more complicated than those of mono(crown ether)s. In the present study, three types of crown ether-cation complexes (**10**)—(**12**) were considered to calculate the stability constants as described in equations (11)—(13). The observed stability constants, K_{1obs} and K_{2obs}, are summarized in Table 5. The stability constant K_{b2} [equation (12)] for intramolecular 2:1 crown ether unit–cation complex (**11**) cannot be obtained directly from this experiment but we can rewrite equations (15) and (16) as:

$$K_{1obs} = \frac{[\overset{\frown}{\mathrm{Cr\quad CrM^+}}]_{total}}{[\overset{\frown}{\mathrm{Cr\quad Cr}}][\mathrm{M^+}]} = \frac{[(\mathbf{10})] + [(\mathbf{11})]}{[\overset{\frown}{\mathrm{Cr\quad Cr}}][\mathrm{M^+}]} = K_{b1}(1 + K_{b2}) \quad (17)$$

$$K_{2obs} = \frac{[\mathrm{M^+}\overset{\frown}{\mathrm{Cr\quad CrM^+}}]}{[\overset{\frown}{\mathrm{Cr\quad CrM^+}}]_{total}[\mathrm{M^+}]} = \frac{[(\mathbf{12})]}{[(\mathbf{10})][\mathrm{M^+}] + [(\mathbf{11})][\mathrm{M^+}]} = \frac{K'_{b1}}{1 + K_{b2}} \quad (18)$$

It is clear that the formation of intramolecular 2:1 crown ether unit–cation complex could cause an increase in K_{1obs} and a decrease in K_{2obs} for bis(crown ether)s. K_{b1} can be reasonably expected to be close to K_{m1} of the corresponding monomeric species. K_{b2} can be estimated with equation (17) with an assumption that K_{b1} is equal to K_{m1}, and the K_{b2} estimated are shown in parentheses of Table 5. For mono(crown ether)s, please note that the K_{1obs} and K_{2obs} are equal to K_{m1} and K_{m2} in equations (7)—(10), respectively.

The K_{1obs} values for monocrown–Na^+ systems determined in this study are in good agreement with those determined earlier by i.s.e. and calorimetric methods.[16,17] No evidence for 2:1 stoicheiometry was found in monocrown–Na^+ systems. The complexation behaviour of bis(crown ether)s with Na^+ is very close to that of their corresponding monomeric species. As shown in Table 5, the bis(crown ether)s, (**4f**) and (**5c** and **f**) can catch two Na^+ ions to form a 2:2 crown ether unit–cation complex (**12**) and show that K_{2obs} is almost equal to K_{1obs}, *i.e.*, $K_{b2} \approx 0$ and $K_{b1} \approx K'_{b1}$. These results are consistent with those from the solvent extraction experiment.[18] The two crown units of the bis(crown ether)s act as two individual moieties in complexation with Na^+ since the diameter of Na^+ is similar to or smaller than the hole size of (**1a**) or (**2a**).

The K_{2obs} ($=K_{m2}$) values for 15C5 and (**1a**)–K^+ systems showed the formation of considerable 2:1 sandwich structure complexes, whereas those for 18C6 and (**2a**)–K^+ systems were negligible as expected by the good fitness of hole size–cation diameter. The 2:1 complex of 15C5–K^+ in anhydrous methanol was determined by Christensen *et al.* by a calorimetric titration method.[19]

From a comparison of the complexation behaviour of (**1a**) with that of (**4c** or **f**), we can find a large increase in K_{1obs} and a decrease of K_{2obs}. It should be due to the formation of intramolecular 2:1 crown ether unit–cation complex (**11**). On the other hand, the larger K_{2obs} for (**5c** and **f**) suggest the 2:2 crown ether unit–cation complex (**12**) [equation (13)] just as in the (**4f**)–Na^+ system. The good fitness of the hole size of 18-crown ring system with K^+ gave a large K_{1obs} for monocrown–K^+ systems.

The 2:1 complex of the 18-crown ring system with Cs^+ does exist in certain conditions but in this study no 2:1 stoicheiometry was observed for monocrown–Cs^+ systems.[20] In bis(benzocrown ether)s–Cs^+, the relatively large K_{1obs} and small K_{2obs} show that intramolecular 2:1 crown ether unit–cation complex (**11**) must be formed But the K_{b2} value shows that (**11**) from (**5c** and **f**) with Cs^+ is not as stable as that of (**4c** and **f**) with K^+. In the extraction of Cs^+, (**5c** and **f**) clearly showed the 'biscrown effect'. However, in the complexation of Cs^+ in homogeneous solution, it was not so clear. Since the lipophilicity of the 2:1 sandwich complex is higher than that of the 1:1 complex, solvent extraction may reflect more sensitively the formation of the intramolecular sandwich structure.

In conclusion, the 'biscrown effect' can also be found in homogeneous solution although the homogeneous stability constants are not always parallel to the two-phase equilibrium constants. For the relatively inflexible crown ethers such as benzocrown ethers and bis(benzocrown ether)s, the cation diameter–hole size relationship is still very important to their complexation in homogeneous solution.

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