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New Application of Crown Ether. VII.[1] Synthesis and Complexation Behavior of Bis(crown ether)s Consisting of a Benzocrown Unit and a Monoazacrown Unit

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Synopsis. New bis(crown ether)s **3** consisting of a benzocrown unit and a monoazacrown unit connected by an oxyethylene linkage were synthesized. Their complexation behavior proved to be analogous to that of lariat monoazacrown ethers rather than that of bis(benzocrown ether)s.

In our previous paper,[1] it was shown that the selectivity of bis(benzocrown ether)s in the complexation with alkali metal cations could be changed by varied combinations of two benzocrown units(ring size; 15, 18, 21), and the behavior was understood by the formation of an intramolecular sandwich complex. The results led us to investigate the complexation characteristics of a new type of bis(crown ether)s consisting of a benzocrown unit and a monoazacrown unit connected by an oxyethylene linkage. This paper describes their synthesis and relative contribution of the linking group and another crown unit in the complexation with alkali metal cations.

Experimental

Material. Benzocrown ethers, 4′-hydroxybenzocrown ethers **5**, monoazacrown ethers, *N*-[2-[2-(tosyloxy)ethoxy]-ethyl]substituted monoazacrown ethers **4** were prepared according to the published methods.[1-3] The guaranteed reagent of alkali metal chlorides, alkali metal hydroxide and picric acid were used without further purification except for drying.

Synthesis of Bis(crown ether)s 3. The tosylate **4** (3 mmol) in dioxane (15 cm^3) was added dropwise to a mixture of 4′-hydroxybenzocrown ether **5** (3 mmol) and sodium hydroxide (10 mmol) in DMSO–dioxane (9:1, 15 cm^3) under nitrogen over a period of 1 h at 80 °C, and then the solution was refluxed for 20 h. After cooling, the mixture was filtered and the filtrate was concentrated under reduced pressure. The residual oily product was chromatographed over an alumina column ($CHCl_3$ eluent) and then purified by a medium pressure liquid chromatography (Silica-gel/MeOH–$CHCl_3$, 2:98(v/v)). The lariat ethers **2** were prepared by a similar method and purified by Kugelrohr distillation.

2a: Colorless liquid, bp. 150—160 °C/1.3Pa Yield 30%. ^1H NMR($CDCl_3$) δ=2.6—3.0 (6H,t), 3.5—4.2 (22H, m), 6.8—7.4 (5H, m). Found: C, 62.25; H, 8.66; N, 3.42%, M^+, 383. Calcd for $C_{20}H_{33}NO_6$: C, 62.64; H, 8.67; N, 3.56%; Mol. wt, 383.

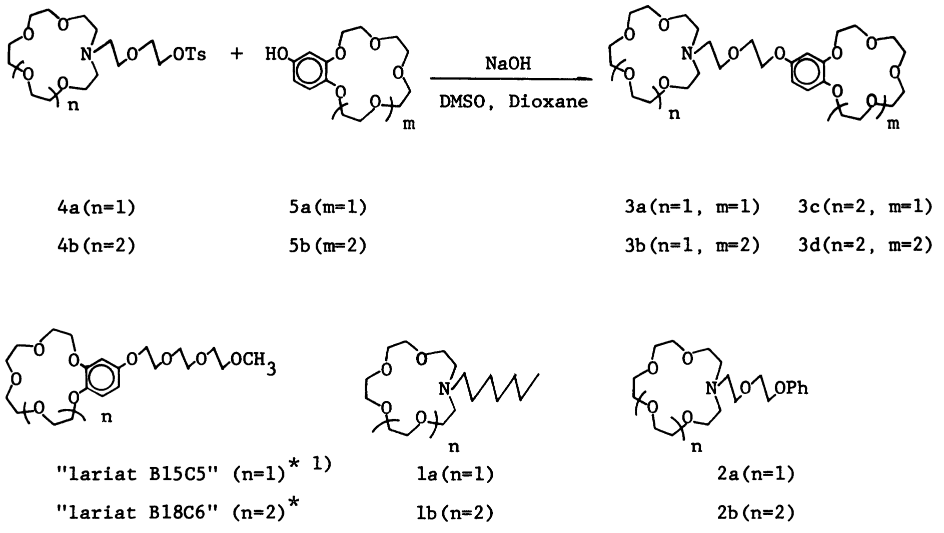
2b: Colorless liquid, bp. 135—139 °C/0.40Pa. Yield 30%. ^1H NMR ($CDCl_3$), δ=2.6—3.0 (6H, t), 3.5—4.2 (26H, m), 6.8—7.4 (5H, m). Found: C, 61.57; H, 8.75; N, 3.28%; M^+, 427. Calcd for $C_{22}H_{37}NO_7$: C, 61.80; H, 8.72; N, 3.27%; Mol.wt. 427. IR for **2a** and **2b** (neat): 2930, 2870, 1600, 1490, 1450, 1350, 1240, 1120 cm^{-1}.

3a: Yield 17%. ^1H NMR ($CDCl_3$) δ=2.6—3.0 (6H, t), 3.5—4.2 (38H, m), 6.3—6.9 (3H, m). Found: C, 58.42; H, 8.32; N, 2.47%; M^+, 573. Calcd for $C_{28}H_{47}NO_{11}$: C, 58.62; H, 8.26; N, 2.44%; Mol.wt. 573.

3b: Yield 22%. Found: C, 58.09; H, 8.30; N, 2.12%; M^+, 617.

3c: Yield 29%. ^1H NMR for **3b** and **3c** ($CDCl_3$) δ=2.6—3.0 (6H, t), 3.5—4.2 (42H, m), 6.3—6.9 (3H, m). Found: C, 58.00; H, 8.31; N, 2.32%; M^+. 617. Calcd for $C_{30}H_{51}NO_{12}$ (**3b** and **3c**): C, 58.30; H, 8.32; N, 2.26%, Mol.wt. 617.

3d: Yield 37%. ^1H NMR ($CDCl_3$) δ=2.6—3.0 (6H, t), 3.5—4.2 (46H, m), 6.3—6.9 (3H, m). Found: C, 57.34; H, 8.24; N,



* B15C5, benzo-15-crown-5; B18C6, benzo-18-crown-6.

Scheme 1.

2.06%; M^+, 661. Calcd for $C_{32}H_{55}NO_{13}$: C, 58.02; H, 8.34; N, 2.12%; Mol.wt. 661. **3a—d**: Pale yellow viscous liquid, IR (neat): 2930, 2870, 1600, 1510, 1460, 1360, 1220, 1120 cm^{-1}.

Solvent Extraction. The extraction experiment was carried out in a CH_2Cl_2–H_2O system at 25 °C, according to the Pedersen's procedure.[4] Extraction equilibria were measured under the same conditions, and four measurements were carried out at varied ligand concentrations in one system. The constants are defined as:

$$\mathrm{M^+_{aq}} + \mathrm{A^-_{aq}} + \mathrm{Cr_{org}} \overset{K_e}{\rightleftharpoons} \mathrm{MCrA_{org}}, \tag{1}$$

$$\mathrm{MCrA_{org}} \overset{K_d}{\rightleftharpoons} \mathrm{MCr^+_{org}} + \mathrm{A^-_{org}}, \tag{2}$$

$$\mathrm{Cr_{org}} \overset{P_e}{\rightleftharpoons} \mathrm{Cr_{aq}}, \tag{3}$$

$$K_e = [\mathrm{MCrA}]_{\mathrm{org}}/[\mathrm{M^+}]_{\mathrm{aq}}[\mathrm{A^-}]_{\mathrm{aq}}[\mathrm{Cr}]_{\mathrm{org}}, \tag{4}$$

$$K_d = ([\mathrm{MCr^+}]_{\mathrm{org}}[\mathrm{A^-}]_{\mathrm{org}})/[\mathrm{MCrA}]_{\mathrm{org}}, \tag{5}$$

$$P_e = [\mathrm{Cr}]_{\mathrm{aq}}/[\mathrm{Cr}]_{\mathrm{org}}. \tag{6}$$

From Eqs. 4—6 we can get:[5]

$$K_e = \frac{(1+P_e)(2[\mathrm{A}]+K_d-(K_d{}^2+4K_d[\mathrm{A}])^{1/2})}{2\mathrm{f}([\mathrm{M}]_0-[\mathrm{A}])([\mathrm{A}]_0-[\mathrm{A}])([\mathrm{Cr}]_0-[\mathrm{A}])} \tag{7}$$

where f is the single-ion activity coefficient of alkali metal cation in aqueous phase, [A] is the total concentration of the picrate anion in organic phase and $[\mathrm{M}]_0$, $[\mathrm{A}]_0$, and $[\mathrm{Cr}]_0$ is the initial concentration of the cation, picrate anion and crown unit, respectively. Equation 8 is used for intermolecular sandwich complex, while Eq. 9 for intramolecular one.[6]

$$K_e = \frac{(1+P_e)^2(2[\mathrm{A}]+K_d-(K_d{}^2+4K_d[\mathrm{A}])^{1/2})}{2\mathrm{f}([\mathrm{M}]_0-[\mathrm{A}])([\mathrm{A}]_0-[\mathrm{A}])([\mathrm{Cr}]_0-2[\mathrm{A}])^2} \tag{8}$$

$$K_e = \frac{(1+P_e)(2[\mathrm{A}]+K_d-(K_d{}^2+4K_d[\mathrm{A}])^{1/2})}{2\mathrm{f}([\mathrm{M}]_0-[\mathrm{A}])([\mathrm{A}]_0-[\mathrm{A}])([\mathrm{Cr}]_0-2[\mathrm{A}])} \tag{9}$$

P_e can be obtained from the extraction in the absence of picrates. K_e was evaluated by a regression analysis with varied K_d to minimize the deviation among the calculated values for the measurements over the range of the concentration of crown unit (8.9×10^{-6}—1.4×10^{-3} mol dm^{-3}).

Stability Constants. The complex stability constants were determined on a mixture of ligand (0.30—0.60 mmol dm^{-3}) and MCl (0.4—2.0 mmol dm^{-3}) in 90% (w/w) aqueous MeOH at 25 °C. Emf was measured with the ion selective electrode (Na^+-ISE(TOA NA-15B) for Na^+ and monovalent cation electrode (Corning cat. No. 476220) for K^+, Cs^+ against a Ag/AgCl reference electrode by use of an Orion Research Model 701A digital "Ionalyzer." The details of the method of the measurement and calculation were described by H. K. Frensdorff[7a] and G. W. Gokel, et al.[7b] The results are shown in Table 3. The following equations were used in the calculation, Eqs. 10 and 11 for monocrown ethers and 12—16 for bis(crown ether)s.[1]

$$\mathrm{M^+} + \mathrm{Cr} \overset{K_{m1}}{\rightleftharpoons} \mathrm{M^+Cr}$$

$$K_{m1} = K_{\mathrm{obsd1}} = [\mathrm{M^+Cr}]/([\mathrm{M^+}][\mathrm{Cr}]) \tag{10}$$

$$\mathrm{M^+Cr} + \mathrm{Cr} \overset{K_{m2}}{\rightleftharpoons} \mathrm{CrM^+Cr}$$

$$K_{m2} = K_{\mathrm{obsd2}} = [\mathrm{CrM^+Cr}]/([\mathrm{M^+Cr}][\mathrm{Cr}]) \tag{11}$$

$$\overline{\mathrm{Cr\;Cr'}} + \mathrm{M^+} \overset{K_{b1}}{\rightleftharpoons} \overline{\mathrm{Cr\;Cr'}}\mathrm{M^+}$$

$$K_{b1} = [\overline{\mathrm{Cr\;Cr'}}\mathrm{M^+}]/([\overline{\mathrm{Cr\;Cr'}}][\mathrm{M^+}]) \tag{12}$$

$$\overline{\mathrm{Cr\;Cr'}}\mathrm{M^+} \overset{K_{b2}}{\rightleftharpoons} \overline{\mathrm{CrM^+Cr'}}$$

$$K_{b2} = [\overline{\mathrm{CrM^+Cr'}}]/[\overline{\mathrm{Cr\;Cr'}}\mathrm{M^+}] \tag{13}$$

$$\overline{\mathrm{Cr\;Cr'}}\mathrm{M^+} + \mathrm{M^+} \overset{K'_{b1}}{\rightleftharpoons} \mathrm{M^+}\overline{\mathrm{Cr\;Cr'}}\mathrm{M^+}$$

$$K'_{b1} = [\mathrm{M^+}\overline{\mathrm{Cr\;Cr'}}\mathrm{M^+}]/([\overline{\mathrm{Cr\;Cr'}}\mathrm{M^+}][\mathrm{M^+}]) \tag{14}$$

$$K_{\mathrm{obsd1}} = K_{b1}(1+K_{b2}) \tag{15}$$

$$K_{\mathrm{obsd2}} = K'_{b1}/(1+K_{b2}) \tag{16}$$

Results and Discussion

Presence of the lariat group markedly increased the extractability of monoazacrown ethers **2—3**, as described by M. Okahara, et al.[3,8] and the effect is in marked contrast to that of the similar group in benzocrown ethers as shown in Table 1.[1] The monoazacrown ethers bearing a lariat group showed a similar extractability with small cations. Li^+ and Na^+. For K^+, Rb^+, and Cs^+ the extraction behavior of the four bis(crown ether)s **3a—d** seems to be divided into two groups depending on the azacrown unit involved; i.e., **3a** and **3b** of lower extractability and **3c** and **3d** of higher one, which may be compared with **2a** and **2b**, respectively. The comparison between **2a** and **3a** (or between **2b** and **3c**) shows that the introduction of a terminal B15C5 group in place of a phenyl group does not exert any marked increase in the extractability, and the values in the parentheses obtained with the same concentration of the azacrown unit may be explained by a concomitant increase in concentration of B15C5 group. Considerable enhancement of the extractability of **3b** over **3a** and of **3d** over **3c** could be understood by the larger complexability of B18C6 than B15C5. It should be emphasized that none of these bis(crown

Table 1. Extraction of Alkali Metal Cations[a)]

Crown Ether	Extracted Picrate Salts /%				
	Li^+	Na^+	K^+	Rb^+	Cs^+
1a	1.4	20.8	4.2	1.6	3.2
1b	4.0	17.0	79.0	53.5	25.9
2a	14.0	52.8	42.5	21.6	15.7
2b	10.0	58.4	95.9	90.0	65.4
3a	14.6	47.3	36.4	20.0	14.1
		(62.8)	(51.2)	(29.2)	(20.0)
3b	13.0	50.4	55.0	35.3	22.6
		(66.0)	(69.6)	(49.0)	(37.8)
3c	19.2	47.7	88.9	77.8	47.5
		(62.2)	(96.4)	(89.3)	(66.1)
3d	10.9	50.2	94.3	85.0	59.2

a) CH_2Cl_2=H_2O=10 cm^3, Aqueous Phase: [Picric Acid]=7.0×10^{-5} mol dm^{-3}, [Metal Hydroxide]=0.01 mol dm^{-3}; Organic Phase: [Crown Unit]=3.5×10^{-4} mol dm^{-3}. The values in parentheses are for [Crown Unit]=7.0×10^{-4} mol dm^{-3}.
The data for benzocrown ethers with Na^+, K^+, Rb^+, and C^+s are;[1] B15C5: 2.6%, 14.2%, 11.2%, 7.7%; B18C6: 3.3%, 54.1%, 27.2%, 15.8%; lariat B15C5: 2.9%, 9.9%, 4.7%, 1.5%; lariat B18C6: 4.1%, 55.2%, 30.2%, 18.8%.

Table 2. Equilibrium Constants for Extraction of Alkali Metal Picrates[a,b,c)]

Crown Ether	Na^+		K^+		Rb^+		Cs^+	
	K_e	K_d	K_e	K_d	K_e	K_d	K_e	K_d
2a	3.8×10^{5}	3.0×10^{-6}	2.0×10^{5}	7.3×10^{-6}	7.4×10^{4}	3.4×10^{-6}	1.2×10^{4}	4.9×10^{-5}
2b	2.2×10^{5}	4.6×10^{-5}	1.1×10^{12}	1.6×10^{-5} d)	3.4×10^{6}	1.0×10^{-6}	3.2×10^{5}	4.1×10^{-5}
3a	2.7×10^{5}	6.0×10^{-6}	1.7×10^{5}	4.5×10^{-6}	4.0×10^{4}	1.2×10^{-5}	1.8×10^{4}	1.8×10^{-5}
3d	4.4×10^{5}	1.2×10^{-6}	1.8×10^{11}	2.4×10^{-5} d)	1.5×10^{6}	1.0×10^{-6}	4.9×10^{5}	6.0×10^{-6}

a) The Conditions are the same as Table 1. [Crown Unit]$=9.0\times10^{-6}$—7.0×10^{-4} mol dm^{-3}. K_e/dm^2 mol^{-2} and K_d/dm^{-1} mol were calculated with Eq. 7 unless noted otherwise. b) **2a**: $P_e=0.17$; **2b**: $P_e=0.11$; **3a**: $P_e=0.25$; **3d**: $P_e=0.33$. Mean activity coefficient for 0.01 mol dm^{-3}-cation $f=0.889$. c) Standard deviations were less than 10% except for **3d**-K^+(34%). d) K_e/dm^3 mol^{-3} and K_d/dm^{-1} mol were calculated with Eq. 8.

Table 3. Complexation Stability Constants in 90% Aqueous MeOH (w/w)

Crown Ether	Na^+		K^+		Cs^+	
	log $K_{obsd\,1}$	log $K_{obsd\,2}$	log $K_{obsd\,1}$	log $K_{obsd\,2}$	log $K_{obsd\,1}$	log $K_{obsd\,2}$
1a	2.76±0.04	*	2.29±0.03	*	2.71±0.01	*
1b	2.98±0.12	*	4.17±0.01	3.21±0.21	3.53±0.08	*
2a	3.43±0.03	*	3.64±0.03	3.34±0.10	3.15±0.09	*
2b	3.48±0.01	*	4.78±0.06	3.96±0.26	3.82±0.01	*
3a	3.10±0.01	*	3.16±0.01	*	3.23±0.05	*
3d	2.93±0.05	2.93±0.04	4.66±0.01	2.85±0.02	3.21±0.01	3.06±0.01

* No regression analysis was done for $K_{obsd\,2}$, since the standard deviation of $K_{obsd\,1}$ was less than 10%.

ether)s **3a—d** shows any marked increase in extractability for cations larger than their hole size as is known in bis(benzo-15-crown-5)-K^+ or bis(benzo-18-crown-6)-Cs^+ system. These considerations lead us to the reasoning that the complexation behavior of the present bis(crown ether)s is principally governed by the effect of the lariat group and the benzocrown unit plays a minor role. The extraction equilibrium constants (Table 2) are almost consistent in tendency with the results in Table 1. The similarity in K_e of **2a** and **3a**, and of **2b** and **3d** again supports the absence of any extra effect of another crown unit in **3a—d** since the formation of the intramolecular sandwich complex is known to give rise to a definitive enhancement in K_e for bis(benzocrown ether)s.[1,9)] In the cases of **2b**-K^+ and **3d**-K^+ the calculation with Eq. 7 or Eq. 9 gave larger deviation (>60%), while the recalculation with Eq. 8 gave a good result. The result suggests that the bis(crown ether) **3d**, as well as the lariat ether **2b**, can form an intermolecular sandwich complex in some cases.

Although the stability constants in a homogeneous system are not always parallel with the results from a two-phase equilibrium we can still get the following information from Table 3. The monoazacrown ether **1b** and the lariat ethers **2a**, **2b** can form 2:1 complex with K^+. If the bis(crown ether) **3a** or **3d** forms an intramolecular sandwich complex there must be an increase in K_{obsd1} due to the contribution of K_{b2} in Eq. 15, but **3a** and **3d** show K_{obsd1} comparable with the lariat ether **2a** and **2b**, respectively. The appearance of K_{obsd2} in **3d** means that there exists the complex in which both crown units hold two cations independently (Eq. 14).

The unique behavior of the bis(crown ether)s **3** should come from their special structures. For lariat ethers, e.g. *N*-(methoxyethyl)monoaza-18-crown-6, the X-ray analysis showed that the ring donor atoms take a chair conformation. A cation larger than the hole size is disposed above the ring plane, and the lariat group in the side arm is not cradling the cation between it and the macroring but rather is pushing the cation out.[10)] This fact may explain why the lariat ether **2b** and the bis(crown ether)s **3c**, **3d** can hold K^+ as an intermolecular sandwich complex in the solvent extraction.

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References

1) Part VI. in this series: K. Kikukawa, G-X. He, A. Abe, T. Goto, R. Arata, T. Ikeda, F. Wada, and T. Matsuda, submitted to *J. Chem. Soc., Perkin Trans. 2.*

2) M. Bourgoin, K. H. Wong, J. Y. Hui, and J. Smid, *J. Am. Chem. Soc.*, **97**, 3462 (1975); T. Ikeda, A. Abe, K. Kikukawa, and T. Matsuda, *Chem. Lett.*, **1983**, 369; K. Kimura, T. Maeda, H. Tamura, and T. Shono, *J. Electroanal. Chem.*, **95**, 91 (1979).

3) A. Masuyama, Y. Nakatsuji, I. Ikeda, and M. Okahara, *Tetrahedron Lett.*, **1981**, 4665.

4) C. J. Pedersen, *Fed. Pro., Fed. Am. Soc. Exp. Biol.*, **27**, 1305 (1968).

5) H. K. Frensdorff, *J. Am. Chem. Soc.*, **93**, 4686 (1971); S. Kopolow, T. E. Hogen Esch, and J. Smid, *Macromolecules*, **6**, 133 (1973).

6) T. Maeda, K. Kimura, and T. Shono, *Bull. Chem. Soc. Jpn.*, **55**, 3506 (1982).

7) a) H. K. Frensdorff, *J. Am. Chem. Soc.*, **93**, 600 (1971); b) G. W. Gokel, D. M. Goli, C. Minganti, and L. Echegoyen, ibid., **105**, 6786 (1983).

8) R. A. Schultz, D. M. Dishong, and G. W. Gokel, *J. Am. Chem. Soc.*, **104**, 625 (1982).

9) K. H. Wong, and H. L. NG, *J. Coord. Chem.*, **11**, 49 (1981).

10) F. R. Fronczek, V. J. Gatto, R. A. Schultz. S. J. Jungk, W. J. Colucci, R. D. Gandour, and G. W. Gokel, *J. Am. Chem. Soc.*, **105**, 6717 (1983).