

Molecular Design of Crown Ethers. 22. Synthesis of Benzocrown Ether Derivatives and Their Solvent Extraction with Univalent/Bivalent Metal Picrates[†]

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Three novel benzocrown ether derivatives have been synthesized and their cation binding behavior with uni- and bi-valent metal ions was evaluated by the solvent extraction of aqueous metal picrates. The obtained results indicate that the size-fit of crown ether and metal cation, and electron effect of the side arm attached to benzocrown ethers affect their cation binding ability and selectivity.

Keywords benzocrown ether, metal ion, solvent extraction, extractability

Introduction

Crown ethers containing hydrophobic exteriors are lipophilic hosts, which can include cations, especially alkali and alkaline earth metal ions, into their cavities via an ion-dipole interaction.²⁻⁵ In general, oxygen crown ethers are effective for the extraction of alkali and alkaline earth metal cations but not transition metal cations. Conversely, their nitrogen analogs are effective for transition metal ions but not alkali metal cations.^{6,7} As a valid method, the solvent extraction was extensively used to evaluate the cation binding abilities of crown ethers.^{1a,8-11} Uncommon complex stoichiometry, substitution effect, ring size effect, sandwiching complexation of a series of crown ethers by solvent extraction experiments have also been reported.⁹⁻¹¹ In the present study, we synthesized three novel benzocrown ether derivatives (Chart 1) and investigated their cation binding behavior with uni- and bi-valent metal ions. The

obtained results, when compared with the relevant data for compounds **1—3** and **5—7**, will promote further understanding of the complexation behavior of the benzocrown ether derivatives with alkali metal ions, alkaline earth metal ions, transition metal ions and heavy metal ions.

Experimental

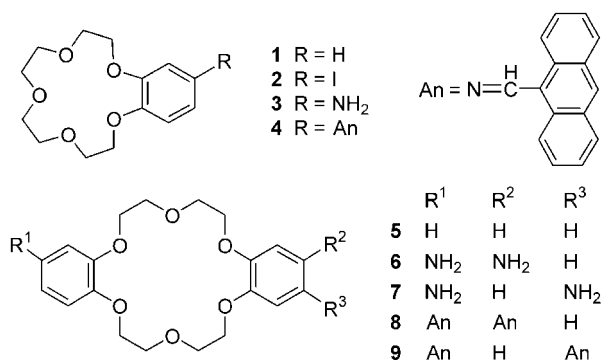
General procedure

Melting points, measured with an XT-4 apparatus, are uncorrected. ¹H NMR spectra were recorded at 300 MHz in CDCl₃ solution on a Varian Mercury VX300 instrument, using tetramethylsilane as an internal reference. Infrared and ultraviolet spectra were recorded on Bio-Rad FTS 135 and Shimadzu UV-2401/PC instruments, respectively. Elemental analyses were performed on a Perkin-Elmer 2400C instrument. Mass spectra were obtained on a VG ZAB-HS instrument.

Materials

Starting materials were commercially available unless noted otherwise. The commercially available reagents were used without further purification. Benzo-15-crown-5 (**1**),² 4'-iodo-benzo-15-crown-5 (**2**), 4'-nitro-benzo-15-crown-5, 4'-amino-benzo-15-crown-5 (**3**),¹² dibenzo-18-crown-6 (**5**)² and 2,14-dinitro-6,7,9,10,17,18,20,21-octahydro-5,8,11,16,19,22-hexaoxadibenzo[*b,k*]cyclooctadecene; 2,13-dinitro-6,7,9,10,17,18,20,21-octahydro-5,8,11,16,19,22-hexaoxadibenzo[*b,k*]cyclooctadecene; 2,14-diamino-6,7,9,10,17,18,20,21-octahydro-5,8,11,16,19,22-hexaoxadibenzo[*b,k*]cyclooctadecene (**6**);

Chart 1



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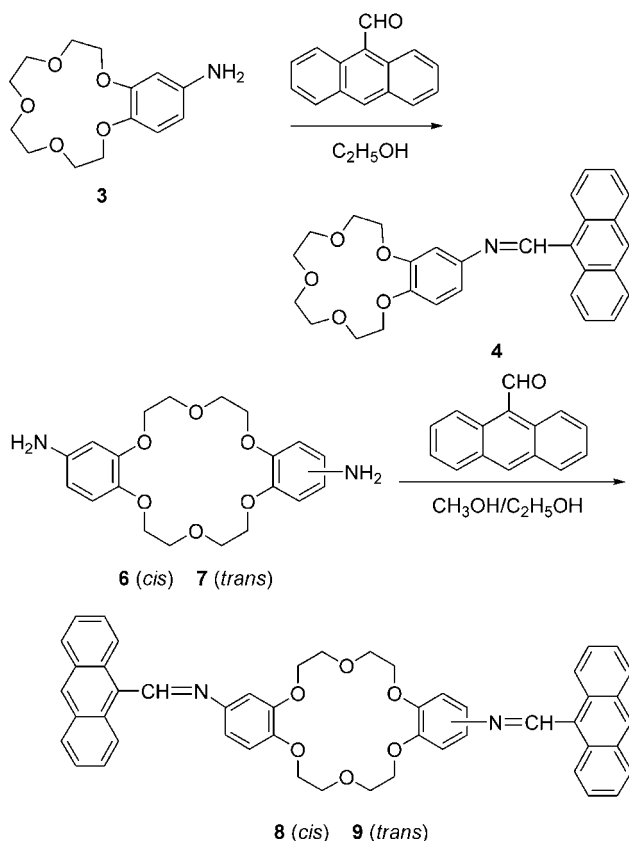
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2,13-diamino-6,7,9,10,17,18,20,21-octahydro-5,8,11,16,19,22-hexaoxadibenzo[*b,k*]cyclooctadecene (**7**)¹³ were prepared according to the reported procedures.

Synthesis

The synthetic routes of compounds **4**, **8** and **9** are shown in Scheme 1.

Scheme 1



Synthesis of 4 Benzocrown ether derivative **4** was prepared by the following procedure: 0.57 g (2 mmol) of **3** was dissolved in 40 mL of ethanol at room temperature, 0.42 g (2 mmol) of 9-anthracenecarboxaldehyde was added to the solution under stirring. Then the mixture, saffron yellow, was refluxed with stirring for 12 h under nitrogen protection. After being cooled down to room temperature, the solution was stirred for another 2 h, and then the precipitates were filtered and recrystallized twice in ethanol to give 0.75 g of product. Yield 79%, m.p. 146.0—147.5 °C; ¹H NMR (CDCl₃, 300 MHz) δ: 9.69 (s, 1H, An H-10), 8.71 (d, *J*=4 Hz, 2H, An H-4, H-5), 8.56 (s, 1H, ArN=CH) 8.06 (d, *J*=8 Hz, 2H, An H-1, H-8), 7.49—7.60 (m, 4H, An H-2, H-3, H-6, H-7), 7.00—7.07 (m, 3H, ArH), 4.21—4.26 (m, 4H, 2×ArOCH₂), 3.95—3.98 (m, 4H, 2×OCH₂), 3.78 (t, *J*₁₂=1 Hz, 8H, OCH₂CH₂O); IR (KBr) ν_{\max} : 1624 (C=NH) cm⁻¹; UV-vis (CH₃CN) λ_{\max}/nm ($\epsilon/\text{mol}^{-1} \cdot \text{L} \cdot \text{cm}^{-1}$): 216.4 (34600), 229.60 (37550), 257.0 (88900), 400.0 (13050); MS (FAB) *m/z*: 472.2 [(*M*+1)⁺, 100]. Anal. calcd for C₂₉H₂₉O₅N: C 73.87, H 6.20, N 2.97; found C 73.64, H 6.31, N 2.99.

Synthesis of 8 Benzocrown ether derivative **8**

was prepared similarly as above for **4** to give 0.75 g (yield 75%) of product from **6** and 9-anthracenecarboxaldehyde: m.p. 178.0—180.0 °C; ¹H NMR (CDCl₃, 300 MHz) δ: 9.70 (s, 2H, An H-10), 8.72 (d, *J*=10 Hz, 4H, An H-4, H-5), 8.55 (s, 2H, ArN=CH), 8.05 (d, *J*=8 Hz, 4H, An H-1, H-8), 7.51—7.58 (m, 8H, An H-2, H-3, H-6, H-7), 7.02—7.08 (m, 6H, ArH), 4.30 (m, 8H, 2×ArOCH₂), 4.11 (t, *J*₁₂=4 Hz, 8H, CH₂OCH₂); IR (KBr) ν_{\max} : 1623 (C=NH) cm⁻¹; MS (FAB) *m/z*: 767.5 (*M*+1)⁺. Anal. calcd for C₅₀H₄₂O₆N: C 78.31, H 5.52, N 3.65; found C 78.02, H 5.66, N 3.68.

Synthesis of 9 Benzocrown ether derivative **9** was prepared similarly as above for **4** to give 0.75 g (yield 81%) of product from **7** and 9-anthracenecarboxaldehyde: m.p. 206.0—208.0 °C; ¹H NMR (CDCl₃, 300 MHz) δ: 9.70 (s, 2H, An H-10), 8.73 (d, 4H, *J*=10 Hz, An H-4, H-5), 8.56 (s, 2H, ArN=CH), 8.06 (d, *J*=8 Hz, 4H, An H-1, H-8), 7.51—7.59 (m, 8H, An H-2, H-3, H-6, H-7), 7.02—7.09 (m, 6H, ArH), 4.27—4.31 (m, 8H, 2×OCH₂), 4.11 (t, *J*₁₂=4 Hz, 8H, CH₂OCH₂). IR (KBr) ν_{\max} : 1622 (C=NH) cm⁻¹; MS (FAB) *m/z*: 767.5 (*M*+1)⁺. Anal. calcd for C₅₀H₄₂O₆N: C 78.31, H 5.52, N 3.65; found C 78.38, H 5.65, N 3.68.

Solvent extraction

The general procedures employed were similar to those described in previous papers.⁹⁻¹⁴ The solvents, CH₂Cl₂ and H₂O, were saturated with each other prior to use in order to prevent volume changes of both phases during extraction. Equal volumes (5 mL) of a CH₂Cl₂ solution of the respective crown ether (0.3 mmol/L) and an aqueous solution of each metal picrate (0.03 mmol/L) were introduced into a stoppered Erlenmeyer flask, and the mixture was shaken for 15 min in a Taiyo M100L incubator thermostated at (25.0±0.1) °C. The equilibrated mixture was then allowed to stand for at least 2 h at that temperature in order to complete phase separation. The concentration of metal picrates in the aqueous phase was determined through measuring the absorbance at *ca.* 354 nm by UV-vis spectroscopy.

Results and discussion

The compound **4** was synthesized in 79% yield by reaction of 4'-amino-15-crown-5 (**3**) with 9-anthracenecarboxaldehyde in ethanol solution. Considering the difficulty in the separation of the *cis-trans* isomers **8** and **9**, we firstly prepared dinitro- dibenzo-18-crown-6 mixture, and then separated them to get *cis-trans* isomers, respectively, through their difference in solubility in chloroform and benzene. After 5% Pd-C catalyst was chosen to give perfect pure products **6** and **7** in high yields, two *cis-trans* isomers **8** and **9** were synthesized in 75% and 81% yields by reaction of **6** or **7** with 9-anthracenecarboxaldehyde in methanol-ethanol solution, respectively.

In the solvent extraction experiment, uni- and bi-valent metal cations were extracted by crown ether from a water phase into an organic phase (methylene

dichloride). The extractability of ammonium cation (NH_4^+) and univalent metal ions (alkali metal cations, Li^+ , Na^+ , K^+ , Rb^+ , Cs^+ , and heavy metal ions, Ag^+ , Tl^+) by crown ethers is listed in Table 1, and that of bivalent metal ions (alkaline earth metal cations, Mg^{2+} , Ca^{2+} , Sr^{2+} , Ba^{2+} , transition metal cations, Co^{2+} , Ni^{2+} , Cu^{2+} , Zn^{2+} , and heavy metal ion, Pb^{2+}) is listed in Table 2.

Table 1 Solvent extraction of aqueous univalent metal picrates with benzo-15-crown-5, single-armed 15-crown-5, dibenzo-18-crown-6 and double-armed dibenzo-18-crown-6^a

Ligand	Extractability ^b /%							
	NH_4^+	Li^+	Na^+	K^+	Rb^+	Cs^+	Ag^+	Tl^+
1	0.44	0.55	1.23	1.13	1.56	1.80	0.67	1.86
2	0.22	1.66	1.49	0.45	0.22	0.67	0.67	0.67
3	0.66	0.55	0.98	1.81	2.00	1.80	1.79	2.79
4	0.44	0.55	1.23	1.81	1.11	<0.1	0.22	0.70
5	0.22	1.10	0.98	1.13	0.67	1.12	0.22	2.33
6	4.37	6.91	9.34	9.05	4.67	7.42	3.81	7.91
7	3.06	3.87	7.37	9.28	3.78	3.82	5.83	8.60
8	0.22	1.10	0.74	0.91	0.89	1.80	2.24	<0.1
9	1.75	1.38	2.46	3.39	2.00	1.57	3.14	3.49

^a Temperature (25.0 ± 0.1) °C; aqueous phase (5 mL), [picrate]=0.03 mmol/L; organic phase (CH_2Cl_2 , 5 mL), [Ligand]=0.3 mmol/L. ^b Defined as percent of picrate extracted into the organic phase. Average of two or three independent runs; error < 0.2.

Table 2 Solvent extraction of aqueous bivalent metal picrates with benzo-15-crown-5, single-armed 15-crown-5, dibenzo-18-crown-6 and double-armed dibenzo-18-crown-6^a

Ligand	Extractability ^b /%								
	Mg^{2+}	Ca^{2+}	Sr^{2+}	Ba^{2+}	Co^{2+}	Ni^{2+}	Cu^{2+}	Zn^{2+}	Pb^{2+}
1	0.48	0.30	0.73	0.48	0.41	0.37	0.36	0.24	0.53
2	0.12	0.30	0.21	0.12	0.10	<0.1	0.09	<0.1	0.11
3	0.60	0.91	0.73	0.24	0.30	<0.1	0.45	0.36	0.63
4	<0.1	0.30	0.31	<0.1	<0.1	<0.1	0.18	<0.1	0.11
5	0.48	0.91	0.10	<0.1	0.20	1.23	<0.1	<0.1	0.32
6	2.63	4.86	1.78	3.26	1.73	1.47	3.41	5.13	3.47
7	3.23	9.10	3.87	1.81	2.44	0.98	4.31	5.13	5.99
8	0.24	0.91	0.52	<0.1	0.41	<0.1	0.81	<0.1	1.16
9	1.32	1.37	1.57	0.97	1.22	0.98	2.06	1.43	2.31

^a Temperature (25.0 ± 0.1) °C; aqueous phase (5 mL), [picrate]=0.03 mmol/L; organic phase (CH_2Cl_2 , 5 mL), [Ligand]=0.3 mmol/L. ^b Defined as percent of picrate extracted into the organic phase. Average of two or three independent runs; error < 0.2.

As can be seen from Table 1, all of the crown ethers give relative higher extractabilities to Na^+ , K^+ and Tl^+ because of their size-fit. In the series of crown-5 compounds, **3** and **4** reversed the selectivity of Na^+/K^+ to give higher binding ability toward K^+ than Na^+ as compared with parent crown ether **1**, which is attributed to the introduction of electron-donating substituent groups. On the other hand, *cis* isomer **8** gives the high-

est heavy metal cation Ag^+/Tl^+ selectivity up to 22 while low selectivity is found in the case of *trans* isomer **9**. Interestingly, *trans* isomer **9** gives higher extractabilities to univalent cations, except for Cs^+ , than *cis* isomer **8**. These results indicate that electron effect of the side arm attached to benzocrown ether alters not only the cation binding ability, but also cation selectivity.

In the solvent extraction of bivalent metal picrates, crown ethers **1**–**9** generally show low extractability as expected. Modified single armed 15-crown-5 **4** shows hardly any extraction effect, indicating very weak complexation between **4** and bivalent cations. For transition metal cations, the crown-6 compounds give the same extractability trend: $\text{Cu}^{2+} \approx \text{Zn}^{2+} > \text{Co}^{2+} > \text{Ni}^{2+}$. Similar to the case of univalent cations, *trans* isomer **9** gives relative higher extractabilities to bivalent cations than *cis* isomer **8**. It is noteworthy that *cis* isomer **8** gives ca. 4 times $\text{Ca}^{2+}/\text{Mg}^{2+}$ selectivity and **7** gives ca. 4 times $\text{Ca}^{2+}/\text{Ba}^{2+}$ selectivity.

In conclusion, possessing electron-donating amido group, benzocrown ethers **3**, **6** and **7** give the highest extractability but the lowest selectivity toward both uni- and bi-valent cations than other systems. On the other hand, although novel benzocrown ether derivatives **4**, **8** and **9** give the moderate extractability, they show enhanced distinct cation selectivity.

References

- (a) Part 20: Zhang, H.-Y.; Yang, Y.-W.; Liu, Y. *Chem. J. Chin. Univ.* **2000**, 21, 1858 (in Chinese).
(b) Part 21: Liu, Y.; Zhang, H.-Y.; Bai, X.-P.; Wada, T.; Inoue, Y. *J. Org. Chem.* **2000**, 65, 7105.
- (a) Pedersen, C. J. *J. Am. Chem. Soc.* **1967**, 89, 7017.
(b) Pedersen, C. J. *J. Am. Chem. Soc.* **1970**, 92, 4684.
- Takeda, Y. In *The Solvent Extraction of Metal Ions by Crown Compounds, Host-Guest Complex Chemistry III, Topics in Current Chemistry*, Eds.: Vögtle, F.; Weber, E., Springer-Verlag, Berlin, **1984**, pp. 1–38.
- Ma, S.-L.; Zhu, W.-X.; Dong, S.-J.; Guo, Q.-L.; She, Y.-B. *Chin. J. Chem.* **2003**, 21, 1178.
- Liu, S.-H.; Wu, X.-Y.; Wu, C.-T. *Acta Chim. Sinica* **1999**, 57, 1167 (in Chinese).
- Izatt, R. M.; Bruening, R. L.; Tarbet, B. J.; Griffin, L. D.; Bruening, M. L.; Krakowiak, K. E.; Bradshaw, J. S. *Pure Appl. Chem.* **1990**, 62, 1115.
- (a) Kato, M.; Ito, T. *Inorg. Chem.* **1985**, 24, 504.
(b) Kato, M.; Ito, T. *Inorg. Chem.* **1985**, 24, 509.
- Zhao, M.; Ford, W. T. *J. Incl. Phenom.* **1994**, 17, 53.
- Inoue, Y.; Liu, Y.; Tong, L.-H.; Tai, A.; Hakushi, T. *J. Chem. Soc., Chem. Commun.* **1989**, 1556.
- Inoue, Y.; Wada, D.; Liu, Y.; Ouchi, M.; Tai, A.; Hakushi, T. *J. Org. Chem.* **1989**, 54, 5268.
- Liu, Y.; Zhang, H.-Y. *Chin. J. Chem.* **2000**, 18, 66.
- Ungaro, R.; Haj, B. E.; Smid, J. *J. Am. Chem. Soc.* **1976**, 98, 5198.
- Pannell, K. H.; Yee, W.; Lewandos, G. S.; Hambrick, D. C. *J. Am. Chem. Soc.* **1977**, 99, 1457.