3670 © 1990 The Chemical Society of Japan *Bull. Chem. Soc. Jpn.*, **63**, 3670—3677 (1990) [Vol. 63, No. 12

Polytopic Cation Receptors. III.[1) Di- and Triloop Crown Hosts Having Aromatic Junctions. Synthesis, Cation Extraction, and Solid Complex Formation

Edwin Weber,* Konstantinos Skobridis, Mikio Ouchi,*,† Tadao Hakushi,† and Yoshihisa Inoue††
Institut für Organische Chemie und Biochemie der Universität Bonn,
Gerhard-Domagk-Straße 1, D-5300 Bonn-1, FR-Germany
†Department of Applied Chemistry, Faculty of Engineering, Himeji Institute of Technology,
2167 Shosha, Himeji, Hyogo 671-22
††Department of Material Science, Faculty of Science, Himeji Institute of Technology,
2167 Shosha, Himeji, Hyogo 671-22

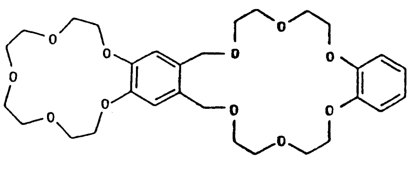
(Received May 28, 1990)

A new type of crown compound (**1**—**3**) featuring an assembly of two or three individual macrorings with different ring size, rigidity, and donor atoms and having characteristic aromatic junctions is introduced. Syntheses are described and cation binding abilities of the compounds are evaluated by solvent extraction technique and isolation of solid complexes. Due to the number of macrorings and their property, **1**—**3** are shown to be suitable hosts for the common incorporation of several cations. However, cooperativity of adjacent macrorings in complex formation depending on the used cation is also observed. The constituent bis-crown ethers **4**—**6** and monocyclic crown ethers **7**—**10** were examined as comparative compounds for solving the complexation properties of the new hosts.

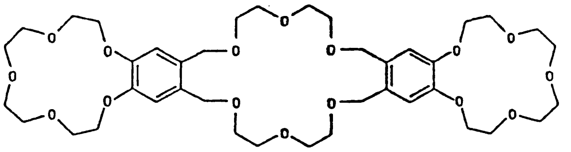
Crown ether chemistry[2) has drifted from simple macromonocyclic complexes[3) to more sophisticated structures[4) involving lariat-type complexes,[5) macro-oligocyclic cryptands,[6) rigid spherands[7) and other supramolecular systems.[8) A particular host family are the multisite crowns.[9) They make possible oligonuclear complexes with more than one and different cations in close neighborhood.[10) Due to their behavior they show promise for analytical uses and open possibilities in cooperative receptors and switching materials.[2,4,8)

A former concept for the synthesis of multisite cation receptors by which any number and type of macrocyclic binding compartment can be linked together bases on spiro junction.[1,11,12) These ligands have perpendicular orientation of the crown compartments around the spiro centers[10a) which may cause steric hindrance at complexation emanating from the spiro-substituents.[12,13) However, a coplanar orientation of crown compartments and no steric hindrance of the previous sort should be present in the heterotopic di- and tri-loop crown hosts **1**—**3** possessing aromatic junctions.

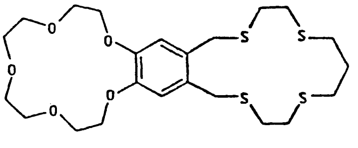
We report here the syntheses and specific cation binding properties of this new type of ligand evalu-



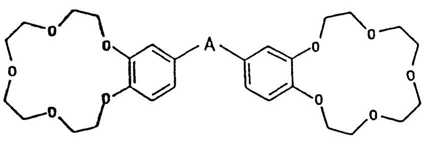
1



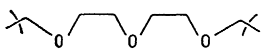
2



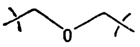
3



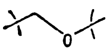
4 A=

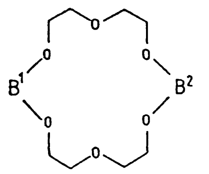


5 A=

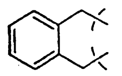


6 A=

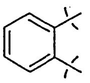




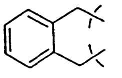
7 B¹=



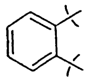
, B²=



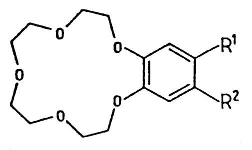
8 B¹=B²=



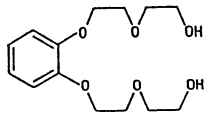
9 B¹=B²=



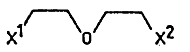
(DB18C6)



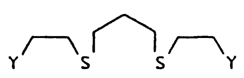
10 R^1=R^2=H (B15C5)
11 R^1=R^2=CH_2Cl
12 R^1=CHO, R^2=H
13 R^1=CH_2OH, R^2=H
14 R^1=CH_2Cl, R^2=H
15 R^1=OH, R^2=H



16



17 X^1=X^2=OH
18 X^1=OH, X^2=Cl
19 X^1=X^2=OTos



20 Y=OH
21 Y=SH

ated from picrate extraction experiments and crystalline complex formation. An additional point of this study is to compare the complexation properties of **1**—**3** with **4**—**6** or **7**—**10** which are bis-crown or constituent crown analogs of the multiloops **1**—**3**, respectively. It is expected to find out the background on polytopic and cooperative complexation behavior relating to the new crown type. Also, some of the comparative crowns (**6**, **7**, and **8**) have not been synthesized before.

Results and Discussion

Synthesis. Di- and triloop crown ethers **1** and **2** were synthesized in 65 and 54% yields, respectively, by reaction of bis(chloromethyl)-substituted benzo-15-crown-5 (**11**) with the corresponding diols **16** or **17** in the presence of NaH as a base in THF[1] under high-dilution conditions[14] and with KCl as template support.[15] Oxathia-diloop crown compound **3** was obtained in 55% yield by reaction of **11** with dithiol **21** in the presence of KOH as a base in benzene-EtOH under high-dilution conditions.[16] Bis-crown compounds **4** and **5** were prepared in 61 and 69% yields, respectively, from hydroxymethyl-substituted benzo-15-crown-5 **13** with bis-tosylate **19** or chloromethyl-substituted benzo-15-crown-5 **14** using NaH in THF. Bis-crown compound **6** was obtained in 74% yield from crown phenol **15** with **14** in the presence of CsOH as a base in DMF.[17,18] Monocyclic crown compounds **7** and **8** were synthesized in 53 and 31% yields, respectively, by reaction of bis(bromomethyl)-benzene with the corresponding diols **16** or **17** using NaH-THF and high-dilution conditions.

Intermediate **11** was prepared by chloromethylation of benzo-15-crown-5 (**10**) in 88% yield. All other intermediates were obtained according to reported procedures (see Experimental Section).

Extraction Studies. The solvent extraction technique[19] has been employed as a facile and convenient method for evaluating the complexation ability of crown ethers to cations.[20] In the present study, the solvent extraction of aqueous alkali (Na^+, K^+, Rb^+, and Cs^+), alkaline earth (Mg^{2+}, Ca^{2+}, Sr^{2+}, and Ba^{2+}), and some heavy metal (Ag^+ and Tl^+) picrates (3 mM) was performed at 25 °C with dichloromethane solution of the crown ether (3 mM per crown ether subunit). The percent extractabilities (% Ex), defined as percent picrate extracted into the organic phase, are shown in Table 1.

It is obvious[2] that the cation-binding and extraction ability is critically affected by several factors including the symmetry of the crown ether, size-fit relationship, multiplicity, and cooperative effects of neighboring binding sites, and the type of the donor atoms, which will be discussed at the proper place.

(a) Constituent Monocyclic Crowns 7—10. Previously we have reported[21] that the non-substituted

Table 1. Extraction of Metal Picrates[a]

Ligand no.	Extractability[b]/%									
	Na^+	K^+	Rb^+	Cs^+	Ag^+	Tl^+	Mg^{2+}	Ca^{2+}	Sr^{2+}	Ba^{2+}
1	2.7	6.2	4.6	3.4	6.1	18.3	0.3	0.4	14.4	32.7
2	4.9	30.4	27.3	11.5	10.2	30.7	0.5	0.7	1.8	22.4
3	1.6	4.5	2.0	0.5	41.4	6.1	0.2	0.3	0.2	0.9
4	4.9	37.9	27.5	7.8	8.9	32.7	0.4	0.5	0.9	7.7
5	5.3	35.4	30.0	10.6	8.9	40.3	0.5	0.5	1.0	6.3
6	4.2	26.1	9.1	1.7	7.6	24.9	0.5	0.4	0.6	3.7
7	0.3	2.4	2.2	1.9	1.5	14.6	0.1	0.1	6.7	30.4
8	0.2	0.9	1.2	2.2	1.9	16.6	0.1	0.1	0.3	14.2
9	0.8	23.6	15.1	7.9	4.3	30.8	1.3	0.8	4.1	82.1
10	5.3	9.0	4.4	1.7	7.0	13.4	0.7	1.3	2.1	4.4

a) Temperature 25.0±0.1 °C; aqueous phase (5 mL): [picrate]=3.0 mM; organic phase (CH_2Cl_2, 5 mL): [crown ether subunit]=3.0 mM (M=mol dm^{-3}). b) Defined as % picrate extracted into the organic phase. Average of two independent runs; error<0.5.

less symmetrical ($3m+n$)-crown-m ethers (m=5 and 6, n=1—4) in general show lower cation-binding abilities than the symmetrical $3m$-crown-m ether analogs, however they yield a significant shift in cation selectivity due to the enlarged cavity size. The dibenzo crown ethers **7**, **8**, and **9** give similar results (Table 1). That is, dibenzo-20-crown-6 (**7**) and dibenzo-22-crown-6 (**8**) show lower extractabilities in general than the more symmetrical dibenzo-18-crown-6 (**9**). The change in relative cation selectivity is observed for **8**. This crown prefers Cs^+ to the other alkali metal ions, while **7** and **9** favor K^+. It should be noted, however, that neither **8** nor symmetrical **9** but low symmetrical **7** yields the highest extractability of Sr^{2+}. This particular behavior is difficult to explain at the moment. Compared to **7**—**9**, benzo-15-crown-5 which is also listed in Table 1 shows less-selective moderate extraction.

(b) Comparative Bis-Crown Ethers 4—6. These compounds have been synthesized in order to illuminate the competition between multiplicity and cooperativity effects of neighboring crown ether rings. Wada et al.[22] have studied several bis(benzo-15-crown-5) ethers linked by a poly(oxyethylene) chain, which incorporate three to seven oxygen atoms in this segment. Thus, they dealt with compounds analogous to **4**—**6**. In their report, the effects of the chain is rather small on the cation-binding ability, while variation of the conformational energies of the bis-crown ethers in the intramolecular sandwich form would be the principal reason for the change of the extractabilities.

The present bis-crown ethers **4**, **5**, and **6** which have a short(er) bridge chain and a low number of oxygen atoms (from one to three) are rather different (Table 1). Compared with the extractabilities of simple benzo-15-crown-5 (**10**), the bis(benzo-15-crown-5) derivatives **4** and **5** show in general much higher extractabilities for cations larger than the hole size of the crown ether rings, such as K^+, Cs^+, and Tl^+. This is a clear indication of sandwich complex formation due to the cooperative effect of the terminal crown ether rings. However, there is also a noticeable dependence of the cation extractability on the length of the bridge segment in **4**—**6**. More precisely speaking, **6** which has the shortest chain length of the bis-crowns under discussion not only gave lower extractabilities compared to **4** and **5**, but yield particularly low extraction of the large cations Rb^+ and Cs^+. The data (Table 1) suggest that intramolecular sandwich complexes of **6** are only formed with K^+ but not with Rb^+, Cs^+, or Tl^+. It is also interesting to note that high extractabilities of alkaline earth picrates are neither obtained with **4** and **5** nor **6**, showing that no cooperative effect exists in this range of cations.

(c) Di- and Triloop Crown Compounds 1, 2, and 3. Taking account of the cation extraction exhibited by the bis-crown ethers **4**—**6** and by constitutional low symmetry crown analogs **6**—**10**, the cation extractabilities observed for the di- and triloop crown compounds **1**—**3** can be discussed on a sound base.

By constitution, diloop crown compound **1** is a combination of benzo-15-crown-5 (**10**) and dibenzo-20-crown-6 (**7**). If mutual interaction between the adjacent crown rings is absent, the cation extractability of **1** should be reflected by that of the individual cases of **7** and **10**. Then, % Ex values of the metal picrates for **1** are expected to be equivalent to the total of the extractabilities of **7** and **10** [(**7**+**10**)/2]. Otherwise they should markedly deviate from these calculated data.

It appears from Table 1 that this calculation is roughly true for most of the monovalent cations (except Cs^+) and the small bivalent cations (Mg^{2+}, Ca^{2+}) while the large bivalent cations (Sr^{2+}, Ba^{2+}) strongly deviate. Consequently these data support the formation of binuclear complexes in case of the monovalent cations. The high extractabilities of Sr^{2+} and Ba^{2+} compared with the values calculated from **7** and **10** suggest another interpretation. As revealed, individual **7** already has high cation ability for Sr^{2+} and Ba^{2+}. On the other hand, binding of Sr^{2+} and Ba^{2+} by **1** due to the benzo-15-crown-5 constituent is expected to be low considering the extraction of individual benzo-15-crown-5 (**10**) (Table 1). However, when the benzo-15-crown-5 ring in **1** is considered to be a bulky lipophilic group, it would make the dehydration of the Sr^{2+} and Ba^{2+} picrates easier leading to high cation extraction. In case of **1** with Cs^+ picrate, we assume formation of an intermolecular sandwich complex[10c] to a certain extent (cf. Table 1).

The triloop crown compound **2** involves the combination of two benzo-15-crown-5 (**10**) rings and one dibenzo-22-crown-6 (**8**) macrocycle. Based on the calculation mode, as above, the cation extractabilities of **2** are higher than that of the total of **10** and **8**, and even exceed diloop crown ether **1**. In particular, high extractabilities of **2** are observed for the picrates of K^+, Rb^+, Tl^+, and Ba^{2+} which suggest cooperativity of the binding sites to a great extent. A comparison between **2** and its bis-crown ether analog **4** with a diethylene glycol bridge instead of the central 22-membered ring in **2**, shows that their extractabilities largely correspond, except for Ba^{2+} picrate, which underlines the particular feature of the Ba^{2+} complex of **2**.

The present extraction data might not bear quantitative discussion, but they are indicative of the central dibenzo-22-crown-6 ring in **2** working as coordination site or bridge between the two benzo-15-crown-5 rings depending on the cation. In case of an intramolecular sandwich complex between the two benzo-15-crown-5 units, the central ring segments may not only function as shielding spacer bridges, but portion of their oxygens may also be involved in coordination to the cation, thus stabilizing the complex. Of course, this is very likely for the potential sandwich complex with Ba^{2+} picrate.

As was to be expected from the presence of a binding site with four soft S donor atoms,[2,16] the diloop crown **3** shows the highest extractability of all cations and of all studied hosts for Ag^+ (Table 1) while the extractabilities of other metal picrates are low.

Formation of Solid Complexes. To shed more light on the complexation properties of the present crown ligands, their capability to form solid complexes with inorganic salts was studied.[1] For obvious reasons they refer to different alkali and alkaline earth thiocyanates [NaSCN, KSCN, $Ba(SCN)_2$], and in case of **3** also $Co(SCN)_2$ was used. Complex formation was carried out by combining the respective crown compound with an equimolar amount of the corresponding salt(s) in acetone, chloroform-acetone or methanol as solvent.[1] A list of the isolated complexes with specification of their properties is given in Table 2.

Complexes with alkali and alkaline earth thiocyanates are colorless microcrystalline powders, except for that of **7** and **8** which came out as colorless crystals. The mixed complex of **3** with NaSCN and $Co(SCN)_2$ was isolated as a dark-green powder. In most cases, the melting points of the complexes (Table 2) were found to be significantly higher than of the free ligand (see Experimental Section). Elemental analyses (Table 2) confirm the complexes to be of different stoichiometries, 1 : 1 (ligand : salt), 1 : 2, 1 : 3, and 2 : 5, depending on the ligand species and the cation type used.

Considering the common size relationships between cation diameter and crown ring interior,[2] as well as the number of binding compartments present, the observed stoichiometries are reasonable.[1] That would mean, the benzo-15-crown-5 compartment matches Na^+, which is indicated by the NaSCN complexes of **1**—**3**, **5**, and **6**. Former studies by Reinhoudt et al.[23] on the complexation properties of *o*-bis(methylene)aromatic crowns suggest a twisted ring-contracting conformation for the *o*-xyleno-containing crown compartments in **1** and **2**. Hence the formation of bi- and trinuclear NaSCN complexes of **1** and **2**, respectively, is rational. Logically the presence of the two benzo-15-crown-5 rings in **5** and **6** accounts for the ready formation of 1 : 2 (ligand : salt) complexes with NaSCN.[24]

On the other hand, the failure of monocyclic crowns **7** and **8** to form complexes with NaSCN may be attributed to the extra methylenes introduced, since drastic decreases in cation binding ability were observed with the unsubstituted analogs, i.e. 20-crown-6 and 22-crown-6.[21] These crowns are possibly too weak for coordination of monocharged cations such as Na^+ or K^+ but yield stable 1 : 1 complexes with $Ba(SCN)_2$. Another $Ba(SCN)_2$ complex is only obtainable with **2**, yet it has an unexpected stoichiometry

Table 2. Data of Solid Complexes

Compound[a]	Yield	Mp	Analyses/%						Characteristic IR absorptions
			Found			Calcd			
		°C	C	H	N	C	H	N	KBr, cm^{-1}
$\mathbf{1}\cdot(NaSCN)_2$	83[b]	244—245	51.58	5.83	3.71	51.88	5.71	3.77	2080 (SCN), 1540, 1520 (Ar), 1260, 1140 (C-O), 955
$\mathbf{2}\cdot(NaSCN)_3\cdot H_2O$	78[c]	249—253	48.43	5.83	3.88	48.81	5.90	3.96	3600 (OH), 2080 (SCN), 1530 (Ar), 1250, 1140 (C-O), 960
$(\mathbf{2})_2\cdot[Ba(SCN)_2]_5\cdot 2H_2O$	72[c]	>240 (decomp)	37.52	4.66	4.54	37.30	4.31	4.83	3540 (OH), 2080 (SCN), 1530 (Ar), 1300, 1260, 1120, 1080 (C-O), 955
$\mathbf{3}\cdot NaSCN\cdot Co(SCN)_2$	68[d]	>115 (decomp)	39.53	4.45	5.25	39.18	4.55	5.27	2050 (SCN), 1595, 1500 (Ar), 1265, 1115, 1090 (C-O), 940
$\mathbf{5}\cdot(NaSCN)_2\cdot H_2O$	70[b]	185—187	50.64	5.73	3.73	50.65	5.84	3.69	3620 (OH), 2080 (SCN), 1525 (Ar), 1270, 1150 (C-O), 955, 830
$\mathbf{5}\cdot KSCN$	83[b]	152—154	54.92	6.35	2.12	55.15	6.27	2.08	2070 (SCN), 1520 (Ar), 1260, 1145 (C-O), 945, 865
$\mathbf{6}\cdot(NaSCN)_2\cdot 0.5H_2O$	65[b]	221—224	50.66	5.62	3.77	50.60	5.61	3.80	3500 (OH), 2070 (SCN), 1620, 1525 (Ar), 1275, 1155, 1120 (C-O), 950, 840
$\mathbf{6}\cdot KSCN\cdot H_2O$	86[b]	281—283	53.40	5.81	2.40	53.00	6.22	2.05	3600 (OH), 2075 (SCN), 1620, 1525 (Ar), 1270, 1140, (C-O), 950, 860
$\mathbf{7}\cdot(BaSCN)_2$	69[b]	244—247	45.12	4.66	4.19	44.90	4.39	4.36	2090, 2070 (SCN), 1515 (Ar), 1255, 1130 (C-O), 760
$\mathbf{8}\cdot Ba(SCN)_2$	64[b]	242—243	46.22	5.18	3.99	46.60	4.81	4.17	2080, 2070 (SCN), 1100 (C-O), 755

a) Composition examined by elemental analyses and ^1H NMR spectra. b) Solvent acetone. c) Solvent $CHCl_3$-acetone (2 : 3). d) Solvent MeOH.

(crown : salt 2 : 5) which indicates a complicated structure. Interestingly this host shows also a relatively high Ba^{2+} picrate extraction (cf. Table 1).

There is more individuality in the present ligands with reference to the coordination behavior to KSCN. Although we are aware of several 2 : 1 (ligand : salt) KSCN complexes of benzo-15-crown-5,[25,26] neither **1**, **2**, nor **3** gave crystalline complexes with KSCN. Obviously it is unfavorable for di- and triloop crowns **1**—**3** to form solid sandwich-type complexes typical of benzo-15-crown-5.[24] Not so in case of bis-crown compounds **5** and **6** which readily yield solid KSCN complexes of the expected stoichiometric ratio (1 : 1). Whether they are intra- or inter-host sandwich complexes is a problem remaining for future studies.

Due to the benzo-15-crown-5 and the tetrathiacoronand constituents, the hetero-diloop compound **3** provides binding sites for Na^+ and transition metal ions.[2] Correspondingly a mixed complex with NaSCN and $Co(SCN)_2$ (1 : 1 : 1 ligand : Na^+ : Co^{2+}) is obtained. Although not evidenced, the Co^{2+} is likely to be encircled by the thiacoronand and Na^+ by the oligoether ring.

Assumption about possible structures of the isolated complexes is further complicated by the presence of water molecules in some of the complexes, as confirmed by elemental analysis and IR (Table 2). Hydrates predominate for the complexes of high salt : ligand ratio which is explainable because of the electrostatic repulsion between adjacent cations.[1] A monohydrate was also obtained in case of the KSCN complex with **6** but not for that of **5** which indicates that the chain length of the spacer between the two benzo-15-crown-5-subunits influences complexation. Another example relating to this problem refers to bis-crown **4** which yielded no solid complex with any of the tested salts. A supposed reason for this behavior is the high flexibility of the spacer chain [oxybis-(ethyleneoxymethylene) group].

Complex formation is also evidenced in the IR spectra (Table 2). The vibration modes of the free ligand (see Experimental Section) undergo substantial shifts and splittings upon complexation, most distinct for the ν(C-O-C) absorptions of the ether bonds between 1270 and 1090 cm^{-1}. Frequency shifts were found to be in the order of 5—50 cm^{-1}. The maximum shifts are observed for the $Ba(SCN)_2$ complex of **2** and for the mixed NaSCN/$Co(SCN)_2$ complex of **3**. The marked band splitting in the ν(C-O-C) region for the $Ba(SCN)_2$ complex of **2** is attributable to the complicated structure in this complex indicating that the two macrocycles of the stoichiometric unit are probably not equivalent. Another point of interest relates to the C-N stretching frequency for SCN^- of the different complexes. Absorptions near 2060 cm^{-1} (Table 2) show evidence for the uncoordinated nature of the thiocyanate anions, while higher frequency bands near 2080 cm^{-1} are indicative of coordinated thiocyanate ions.[27] In case of the $Ba(SCN)_2$ complexes of **7** and **8**, band splitting of the νC-N absorption reflects the presence of two non-equivalent thiocyanate ions in the crystal.[28] Broad absorptions in the 3500 cm^{-1} region of the IR spectra are typical of the hydrated complexes.

Conclusions

Di- and triloop crown compounds **1**—**3** with aromatic junctions were shown to be suitable hosts for the common incorporation of several cations due to the number and specific binding compartments combined in the ligand skeleton. They can complex identical or different metal ions. In this behavior they correspond to the spiro-linked multiloop crowns formerly reported.[1,11] However, each class of multiloop hosts provide specific complexation properties as to the individual compounds.

Although there is relation, the complex formation of the di- and triloop hosts **1**—**3** is not a simple coexistence of the compartmental coordination properties allocated by the individual crown rings, but show their cooperativity in complex formation depending on the cation. The constituent bis-crown ethers **4** and **6** and monocyclic crown ethers **7**—**10**, which were examined as comparative compounds, confirm the assessment, thus allowing for multinuclear and sandwich-type complexation in case of **1**—**3**.

Usually it is risky to draw a parallel between solid cation complexes and solution complexes, and also different counter anions give rise to problems.[24,25] Nevertheless they find some close resemblance between the ability to form solid complexes with thiocyanate salts and the extractability of picrate salts in the methylene chloride–water solvent system which suggests similar complex structures in solution and in the solid state. Examples involve the ligand/cation combinations: **2**/Ba^{2+}, **5**/K^+, **6**/K^+, **7**/Ba^{2+}, or **8**/Ba^{2+}. Efforts to prepare crystals of the isolated complexes suitable for X-ray diffraction studies in order to elucidate exact studies were unsuccessful.

Experimental

General. Melting points were obtained on a Kofler apparatus (Reichert, Wien). IR spectra were recorded on a Pye-Unicam SP-1100 spectrometer. ^1H NMR spectra were taken on a Varian EM-360 (60 MHz) spectrometer; chemical shifts (δ) are expressed in ppm relative to Me_4Si (internal reference). Mass spectra were determined on an A.E.I. MS-50 instrument. Elemental analyses were performed by the Microanalytical Laboratory of the Institut für Organische Chemie und Biochemie, Universität Bonn. For column chromatography Al_2O_3 (Brockmann, grade II-III, Woelm) was used. NaH was applied as an 80% suspension in mineral oil. Tetrahydrofuran (THF) was purified by fresh distillation from $LiAlH_4$. Dimethylformamide (DMF) was fresh distilled over CaH_2. Dichloromethane for solvent extraction was purified by distillation. All other solvents were of reagent quality. 1,3-Propanedithiol, 2-chloroethanol, diethylene glycol (**17**), and 5-chloro-3-oxa-1-pentanol (**18**) were purchased from Janssen (Nettetal). 1,2-Bis(bromomethyl)benzene,[29] diethylene glycol ditosylate (**19**),[30] benzo-15-crown-5 (**10**),[31] and 4′-formyl[benzo-15-crown-5] (**12**)[32] were prepared according to the reported procedures. Dibenzo-18-crown-6 (**9**), which is commercially available (Aldrich), was a gift from Prof. M. Yamamoto of Fukuoka University.

2,2′-(1,3-Propanediyldithio)diethanethiol (21). This compound was obtained by reaction of 1,3-propanedithiol with 2-chloroethanol and subsequent conversion of the diol **20** with thiourea following the literature procedure;[35] 42% colorless oil; bp 146—148 °C/0.1 Torr (lit,[35] bp 159—161 °C/0.5 Torr) (1 Torr=133.322 Pa).

2,2′-[1,2-Phenylenebis(oxyethyleneoxy)]diethanol (16). This compound was prepared from catechol, **18**, and NaOH.[34] Unlike the literature procedure,[35] **18** was used without previous conversion into the bis-tetrahydropyranyl ether: yield 65%; colorless viscous oil; bp 185 °C/0.1 Torr (lit,[35] bp 185—187 °C/0.05 Torr).

4′,5′-Bis(chloromethyl)[benzo-15-crown-5] (11). A stirred mixture of benzo-15-crown-5 (**10**) (6.00 g, 20.1 mmol), paraformaldehyde (3.55 g, 118 mmol), and concd HCl (16 ml) was gradually heated to 50 °C within 45 min. During this time, a vigorous stream of HCl gas was passed into the mixture. Heating and passing HCl into the mixture was continued for 1.5 h. After cooling, the mixture was poured on ice and the precipitate which formed was collected, washed thoroughly with water, and dried over P_4O_{10}. Recrystallization from heptane yielded 88% colorless crystals: mp 146—148 °C; IR (KBr) 1607, 1530 (Ar), 1235, 1140 (C–O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=3.70—4.30 (16H, m, OCH_2), 4.69 (4H, s, benzyl), 6.93 (2H, s, aryl); MS *m/z* 368 (M^+). Found: C, 52.54; H, 6.27%. Calcd for $C_{16}H_{22}Cl_2O_5$: C, 52.61; H, 6.07%.

4′-(Hydroxymethyl)[benzo-15-crown-5] (13). Reduction of 4′-formyl[benzo-15-crown-5] (**12**) with $LiAlH_4$ in dry THF as described[32] yielded 74% of the title compound; colorless needles (from heptane); mp 57—59 °C (lit,[32] mp 52—54 °C).

4′-(Chloromethyl)[benzo-15-crown-5] (14). Reaction of 4′-(hydroxymethyl)[benzo-15-crown-5] (**13**) with $SOCl_2$ as described[32] yielded 69% of the title compound; colorless crystals (from petroleum ether, bp 40—46 °C); mp 65—66 °C (lit,[32] mp 65—66 °C).

4′-Hydroxy[benzo-15-crown-5] (15). Reaction of 4′-formyl-[benzo-15-crown-5] (**12**) with formic acid-H_2O_2 (30%) as described[26] yielded 54% of the title compound; colorless needles (from heptane); mp 102—104 °C (lit,[26] 102—104 °C).[36]

Di- and Triloop Crown Compounds 1 and 2 (General Procedure). 4′,5′-Bis(chloromethyl)[benzo-15-crown-5] (**11**) (7.30 g, 20.0 mmol) and 20.0 mmol of the corresponding diol (see below) in separate 250 ml-portions of dry THF were simultaneously added over a period of 8 h under N_2 to a vigorously refluxing suspension of NaH (2.40 g, 100 mmol) and KCl (1.40 g, 20 mmol) in 1 dm^3 of dry THF (high-dilution conditions;[1,14] the KCl was used to serve as a possible template ion[15]). After being boiled for additional 6 h, the mixture was allowed to cool to room temperature and was quenched with MeOH. The solvent was removed under reduced pressure, and the resulting residue was extracted with CH_2Cl_2 (3×200 ml). The combined extracts were evaporated and chromatographed on an Al_2O_3 column. First petroleum ether (bp 40—60 °C) was passed through the column to remove the mineral oil (NaH suspension). The products were eluted with $CHCl_3$ and recrystallized. Specific details are given for each compound.

1,4,7,10,13,21,24,27,34,37,40-Undecaoxa[13](1,2)[8.8](4,5)-(1,2)cyclophane (1): diol **16** (5.75 g, 20.0 mmol) was reacted to yield 65% of colorless crystals; mp 89—91 °C (from EtOH); IR (KBr) 1610, 1525 (Ar), 1260, 1145 (C–O), 950, 745 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=3.54—4.29 (32H, m, OCH_2), 4.56 (4H, s, benzyl) , 6.84 (6H, s, aryl); MS *m/z* 578 (M^+). Found: C, 62.42; H, 7.02%. Calcd for $C_{30}H_{42}O_{11}$: C, 62.27; H, 7.32%.

1,4,7,10,13,21,24,27,35,38,41,44,47,49,52,55-Hexadecaoxa-[13](1,2)[9.9](4,5)(1,2)[13](4,5)cyclophane (2): diol **17** (2.12 g, 20.0 mmol) was reacted to yield 54% of colorless crystals; mp 145—147 °C (from heptane); IR (KBr) 1535 (Ar), 1300, 1150 (C–O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=3.54—4.25 (48H, m, OCH_2), 4.55 (8H, s, benzyl), 6.84 (4H, s, aryl); MS *m/z* 796 (M^+). Found: C, 60.40; H, 7.69%. Calcd for $C_{40}H_{60}O_{16}$: C, 60.29; H, 7.59%.

1,4,7,10,13-Pentaoxa-21,24,28,31-tetrathia[13](1,2)[13](4,5)-cyclophane (3). 4′,5′-Bis(chloromethyl)[benzo-15-crown-5] (**11**) (7.30 g, 20.0 mmol) in 250 ml benzene; dithiol **21** (4.57 g, 20.0 mmol) in 250 ml of benzene and KOH (2.26 g, 40.0 mmol) in 250 ml of EtOH-H_2O (99 : 1) were placed into a three-component high-dilution-principle set-up[38] and then simultaneously added to 1 dm^3 of boiling benzene-EtOH (1 : 1) over an 8 h period under vigorous stirring.[16] The mixture was refluxed for additional 5 h and then evaporated under reduced pressure. The residue was washed thoroughly with H_2O, extracted into $CHCl_3$ and dried over $MgSO_4$. Chromatography on an Al_2O_3 column ($CHCl_3$ as eluent) and subsequent recrystallization from ethyl acetate afforded 55% colorless needles; mp 162—163 °C; IR (KBr) 1620, 1540 (Ar), 1290, 1165 (C–O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.91 (2H, m, $CH_2CH_2CH_2$), 2.50—2.92 (12H, m, SCH_2), 3.62—4.26 (20H, m, OCH_2 benzyl), 6.83 (2H, s, aryl); MS *m/z* 520 (M^+). Found: C, 52.89; H, 6.96%. Calcd for $C_{23}H_{36}O_5S_4$: C, 53.04; H, 6.97%.

Bis-crown Compounds 4 and 5 (General Procedure). To a stirred gently refluxing suspension of NaH (0.96 g, 40 mmol) in 50 ml of dry THF was added under N_2 4′-(hydroxymethyl)[benzo-15-crown-5] (**13**) (5.96 g, 20.0 mmol) in 50 ml of dry THF. After being refluxed for additional 0.5 h, diethylene glycol ditosylate (**19**) (4.14 g, 10.0 mmol; for **4**) or 4′-(chloromethyl)[benzo-15-crown-5] (**14**) (6.64 g, 20 mmol; for **5**) dissolved in 50 ml of dry THF was added. The mixture was refluxed for additional 2 h, then allowed to cool to room temperature, and quenched with MeOH. Work-up and purification as described for **1** and **2**; elution on chromatography (Al_2O_3) was effected with $CHCl_3$-MeOH (98 : 2). Specific details are given for each compound.

4,4′-[Oxybis(ethyleneoxymethylene)]bis[benzo-15-crown-5] (4): Yield 61% of a colorless oil; spectroscopic data correspond to the literature.[37]

4,4′-(Oxydimethylene)bis[benzo-15-crown-5] (5): Yield 69%, colorless crystals: mp 110—111 °C (from MeOH) (lit,[32] 107—109 °C; lit,[37] 111—112 °C); IR (KBr) 1605, 1530 (Ar), 1270, 1160 (C–O), 950 cm^{-1}.

4,4′-(Oxymethylene)bis[benzo-15-crown-5] (6). A mixture of 4′-hydroxy[benzo-15-crown-5] (**15**) (2.84 g, 10.0 mmol) and CsOH (1.65 g, 11.0 mmol) in 50 ml dry DMF was stirred at 65 °C under an atmosphere of N_2 for 30 min.[17,18] Then 4′-(chloromethyl)[benzo-15-crown-5] (**14**) (3.17 g, 10 mmol) in 50 ml of dry DMF was added at the same temperature. Heating and stirring was continued for additional 4 h. The mixture was freed from the solvent by evaporation under reduced pressure and the residue partitioned between CH_2Cl_2 and water. The organic layer was separated, washed with H_2O, dried (Na_2SO_4), and evaporated. Recrystallization from heptane yielded 74% of colorless needles; mp 115—116 °C; IR (KBr) 1615, 1525 (Ar), 1240, 1155 (C-O) cm^{-1}; ^1H NMR ($CDCl_3$) $\delta=3.60—4.30$ (32H, m, OCH_2CH_2O), 4.90 (2H, s, benzyl), 6.40—7.00 (6H, m, aryl); MS *m/z* 564 (M^+). Found: C, 61.77; H, 6.75%. Calcd for $C_{29}H_{40}O_{11}$: C, 61.69; H, 7.14%.

Crown Ethers 7 and 8. The general procedure described for **1** and **2** using 1,2-bis(bromomethyl)benzene (5.30 g, 20.0 mmol) and 20.0 mmol of diols given below was followed; elution on chromatography (Al_2O_3) was effected with $CHCl_3$-CCl_4 (2 : 1).

1,4,7,15,18,21-Hexaoxa[8.8](1,2)(1,2)cyclophane (7): diol **16** (5.72 g, 20.0 mmol) was reacted to yield 53% of colorless crystals; mp 79—80 °C (from acetone); IR (KBr) 1600, 1520 (Ar), 1260, 1140 (C-O), 750 cm^{-1}; ^1H NMR ($CDCl_3$) $\delta=3.55—4.35$ (16H, m, OCH_2CH_2O), 4.70 (4H, s, benzyl), 6.85 (4H, s, aryl), 7.30 (4H, s, aryl); MS *m/z* 388 (M^+). Found: C, 69.20; H, 7.74%. Calcd for $C_{22}H_{28}O_6$: C, 68.87; H, 7.61%.

2,5,8,17,20,23-Hexaoxa[9.9](1,2)(1,2)cyclophane (8): diol **17** (2.10 g, 20.0 mmol) was reacted to yield 31% of colorless crystals; mp 85—86 °C (from acetone); IR (KBr) 1120 (C-O), 765 cm^{-1}; ^1H NMR ($CDCl_3$) $\delta=3.65$ (16H, s, OCH_2CH_2O), 4.70 (8H, s, benzyl), 7.30 (8H, s, aryl), MS *m/z* 416 (M^+). Found: C, 68.02; H, 7.26%. Calcd for $C_{24}H_{32}O_6$: C, 67.89; H, 7.31%.

Solvent Extraction. The general procedures employed were similar to those in a previous paper.[20] Distilled CH_2Cl_2 and demineralized H_2O were saturated with each other before use in order to prevent volume changes of the phases during extraction. Equal volumes (5 ml) of a CH_2Cl_2 solution of the respective crown ether (3 mM per crown ether subunit)[22] and of an aqueous solution of the metal picrate (3.0 mM) were introduced into a stoppered Erlenmeyer flask and shaken for 10 min at 25.0±0.1 °C in a Taiyo M100L incubator. The equilibrated mixture was then allowed to stand for at least 90 min at that temperature in order to complete phase separation. The organic phase was separated by filtration (Whatman filter paper No. 1PS) The concentration of metal picrates in the organic phase was determined as reported.[20]

Preparation of Solid Complexes. General Procedure for the NaSCN, KSCN, and Ba(SCN)$_2$ Complexes of 1, 2, and 5—8. The corresponding ligand (0.25 mmol) and the calculated amount of the appropriate salt (1 equiv per individual crown ether ring) were combined under stirring in acetone or chloroform-acetone (2—3 ml). The mixture was gently refluxed for 2 h and then allowed to cool to room temperature. In those cases where the complexes did not precipitate, the crystallization was initiated by addition of ether. After storage for 12 h at 5 °C, the complexes were collected by suction filtration, washed with a few milliliters of acetone-ethyl acetate (1 : 1), and dried under vacuum (5 h, 15 Torr, 50 °C). Specific details for each complex are given in Table 2.

Mixed NaSCN-Co(SCN)$_2$ Complex of 3. Crown compound **3** (105 mg, 0.20 mmol), NaSCN (16 mg, 0.20 mmol), and $Co(SCN)_2$ (35 mg, 0.20 mmol) were combined in MeOH (2.5 ml) and gently refluxed for 2 h. The solvent was removed, the residue thoroughly digested with acetone, and dried under vacuum (5 h, 15 Torr, 50 °C) to give the complex as a dark-green powder. Properties of the complex are given in Table 2.

The work has been financially supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

References

1) Part II. E. Weber, *J. Org. Chem.*, **47**, 3478 (1982).

2) a) E. Weber in "Ullmann's Encyclopaedia of Industrial Chemistry," VCH Verlagsgesellschaft, Weinheim (1987), Vol. A8, p. 91; b) E. Weber in "Phase Transfer Catalysts: Properties and Applications," Merck-Schuchardt, Darmstadt (1987), p. 33.

3) C. J. Pedersen, *Angew. Chem.*, **100**, 1053 (1988); *Angew. Chem., Int. Ed. Eng.*, **27**, 1021 (1988).

4) a) "Host-Guest Complex Chemistry-Macrocycles," ed by F. Vögtle and E. Weber, Springer-Verlag, Berlin-Heidelberg (1985); b) "Synthesis of Macrocycles—The Design of Selective Complexing Agents (Progress in Macrocyclic Chemistry)," ed by R. M. Izatt and J. J. Christensen, Wiley, New York (1987) Vol. 3; c) "Crown Ethers and Analogs," ed by S. Patai and Z. Rappoport, Wiley, Chichester (1989).

5) G. W. Gokel and L. Echegoyen, in "Bioorganic Chemistry Frontiers," ed by H. Dugas, Springer-Verlag, Berlin-Heidelberg (1990); b) E. Weber, in Ref. 4(c), p. 305.

6) a) P. G. Potvin and J.-M. Lehn, in Ref. 4(b), p. 167; b) I. O. Sutherland, *Heterocycles*, **21**, 235 (1984).

7) a) D. J. Cram, *Angew. Chem.*, **98**, 1041 (1986); *Angew. Chem., Int. Ed. Engl.*, **25**, 1039 (1986); b) D. J. Cram, *Angew. Chem.*, **100**, 1041 (1988); *Angew. Chem., Int. Ed. Engl.*, **27**, 1009 (1988).

8) a) F. Vögtle, "Supramolekulare Chemie," Teubner, Stuttgart (1989); b) J.-M. Lehn, *Angew. Chem.*, **100**, 91 (1988); *Angew. Chem., Int. Ed. Engl.*, **27**, 89 (1988); c) J. F. Stoddart, *Ann. Rep. Progr. Chem.*, **85**, 353 (1988); d) T. J. Meade and D. H. Busch, *Prog. Inorg. Chem.*, **33**, 59 (1985).

9) G. W. Gokel and S. N. Korzeniowski, "Macrocyclic Polyether Syntheses," Springer-Verlag, Berlin-Heidelberg (1982).

10) a) M. Czugler and E. Weber, *J. Chem. Soc., Chem. Commun.*, **1981**, 472; b) K. Onan, J. Rebek, Jr., T. Costello, and L. Marshall, *J. Am. Chem. Soc.*, **105**, 6759 (1983); c) J. D. Owen, *J. Chem. Soc., Perkin Trans. 2*, **1983**, 407.

11) E. Weber, *Angew. Chem.*, **91**, 230 (1979); *Angew. Chem., Int. Ed. Engl.*, **18**, 219 (1979).

12) M. Ouchi, Y. Inoue, H. Sakamoto, A. Yamahira, M. Yoshinaga, and T. Hakushi, *J. Org. Chem.*, **487**, 3168 (1983).

13) J. Bouquant, A. Delville, J. Grandjean, and P. Laszlo, *J. Am. Chem. Soc.*, **104**, 686 (1982).

14) L. Rossa and F. Vögtle, *Top. Curr. Chem.*, **113**, 1 (1983).

15) D. H. Busch and N. A. Stephenson, *Coord. Chem. Rev.*, **100**, 119 (1990).

16) E. Weber and F. Vögtle, *Liebigs Ann. Chem.*, **1976**,

891.

17) E. Weber, H.-J. Köhler, and H. Reuter, *Chem. Ber.*, **122**, 959 (1989).

18) B. Klieser, L. Rossa, and F. Vögtle, *Kontakte (Merck)*, **1984**(1), 3.

19) Y. Takeda, *Top. Curr. Chem.*, **121**, 1 (1984).

20) M. Ouchi, Y. Inoue, K. Wada, S. Iketani, T. Hakushi, and E. Weber, *J. Org. Chem.*, **52**, 2420 (1987).

21) a) M. Ouchi, Y. Inoue, T. Kanzaki, and T. Hakushi, *J. Org. Chem.*, **49**, 1408 (1984); b) Y. Inoue, M. Ouchi, and T. Hakushi, *Bull. Chem. Soc. Jpn.*, **58**, 525 (1985).

22) F. Wada, Y. Wada, T. Goto, K. Kikukawa, and T. Matsuda, *Chem. Lett.*, **1980**, 1189.

23) D. H. Reinhoudt and F. De Jong, in "Progress in Macrocyclic Chemistry," ed by R. M. Izatt and J. J. Christensen, Wiley, New York (1979), Vol. 1, p. 157.

24) R. Hilgenfeld and W. Saenger, *Top. Curr. Chem.*, **101**, 1 (1982).

25) N. S. Poonia and A. V. Bajaj, *Chem. Rev.*, **79**, 389 (1979).

26) E. Weber and M. Czugler, *Inorg. Chim. Acta*, **61**, 33 (1982).

27) R. A. Bailey, S. L. Kozak, T. W. Michelsen, and W. N. Mills, *Coord. Chem. Rev.*, **6**, 407 (1971).

28) J.-C. G. Bünzli, D. Wessner, and H. T. T. Oauh, *Inorg. Chem. Acta*, **32**, L33 (1979).

29) W. Werner, *J. Org. Chem.*, **17**, 525 (1952).

30) J. Dale and P. O. Kristiansen, *Acta Chem. Scand.*, **26**, 1471 (1972).

31) C. J. Pedersen, *J. Am. Chem. Soc.*, **89**, 7017 (1967).

32) E. M. Hyde, B. L. Shaw, and I. Shepherd, *J. Chem. Soc., Dalton Trans.*, **1978**, 1696.

33) W. Rosen and D. H. Busch, *J. Am. Chem. Soc.*, **91**, 4694 (1969).

34) E. Weber, *Liebigs Ann. Chem.*, **1983**, 770.

35) E. P. Kyba, R. C. Helgeson, K. Madan, G. W. Gokel, T. L. Tarnowski, S. S. Moore, and D. J. Cram, *J. Am. Chem. Soc.*, **99**, 2564 (1977).

36) Cf.: Behavior in mp of a trihydrated product species which was obtained under different reaction conditions; see F. Wada, R. Arata, T. Goto, K. Kikukawa, and T. Matsuda, *Bull. Chem Soc. Jpn.*, **53**, 2061 (1980); see also F. Camps, J. Coll, and S. Ricart, *J. Heterocycl. Chem.*, **20**, 249 (1983).

37) K. H. Wong and H. L. Ng, *Tetrahedron Lett.*, **1979**, 4295.

38) F. Vögtle, *Chem.-Ztg.*, **96**, 396 (1972).