Template effect in the synthesis of formyl derivatives of benzothiacrown compounds

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The condensation of 3,4-bis(2-haloethoxy)benzaldehydes with acyclic α,ω-alkanedithiols in the presence of alkali metal carbonates in dry ethanol, DMF, MeCN and their mixtures with water gives formyl derivatives of benzothiacrown compounds in high yields. The best results are attained when the radius of the hydrated metal cation fits to the crown ether cavity. In the case of Cs^+, high yields were observed for crown ethers of any size and composition; this can be explained by a specific template effect of this cation. The influence of the nature of the leaving group in 3,4-bis(2-haloethoxy)benzaldehydes was established for reactions with dithiols containing no ether oxygen atoms.

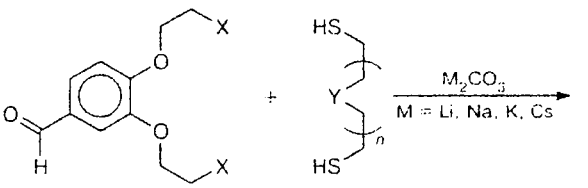
Key words: 3,4-bis(2-haloethoxy)benzaldehydes; α,ω-alkanedithiols; alkali metal carbonates; template effect; formyl derivatives of benzothiacrown compounds.

The main types of macrocyclic sulfides are thiacrown compounds, thiacryptands, and thiacyclophanes.[1,2] The rapt attention to sulfur-containing macroheterocycles is due to their capability of selective formation of strong complexes with transition and heavy metal cations.[3,4] These compounds can also be of interest as intermediates in the synthesis of polymers with thiacrown fragments, selective chromogenic and photochromic reagents for metal cations, and extractants for the separation of metal salts.

Although the first representatives of benzocrown compounds containing various combinations of sulfur and oxygen in the macrocycle were synthesized in the early 70s,[5] it was not until recently that methods for the preparation of benzothiacrown compounds having a functional group in the benzene ring were developed.[6,7] For example, 4′-formylbenzodithia-15(18)-crown-5(6) were prepared by metallation of bromo benzodithiacrown derivatives by *n*-butyllithium followed by the reaction of organolithium derivatives with DMF.

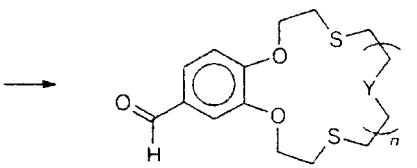
In this work aimed at developing a more convenient method for the preparation of the formyl derivatives of benzocrown compounds with different numbers of O, S, and C atoms in the macrocycle, we carried out condensation of 3,4-bis(2-haloethoxy)benzaldehydes **1a,b** with terminal dithiols **2a—e** in the presence of alkali metal carbonates (Scheme 1).

Scheme 1



1a: X = Cl
1b: X = I

2a—e



3a—e

2, 3	*n*	Y
a	0	—
b	1	O
c	2	O
d	2	S
e	3	O

The required dithiols **2a—c** are commercial chemicals. 3,6-Dithiaoctane-1,8-dithiol (**2d**), 3,6,9-trioxaundecane-1,11-dithiol (**2e**), 3,4-bis(2-chloroethoxy)benzaldehyde (**1a**), and 1,2-bis(2-chloroethoxy)benzene (**4b**) were synthesized by known procedures.[8—11] Dichloride **1a** and diiodide **1b** were prepared according to Scheme 2.

In order to avoid the formation of cyclic thioacetals in the condensation of dihalides **1a,b** with dithiols **2a—e**, aldehyde **1a** was converted into acetal **6** by the reaction with ethyl orthoformate in the presence of catalytic amounts of NH_4Cl (Scheme 3). The TLC monitoring of the reaction showed that, irrespective of the reaction

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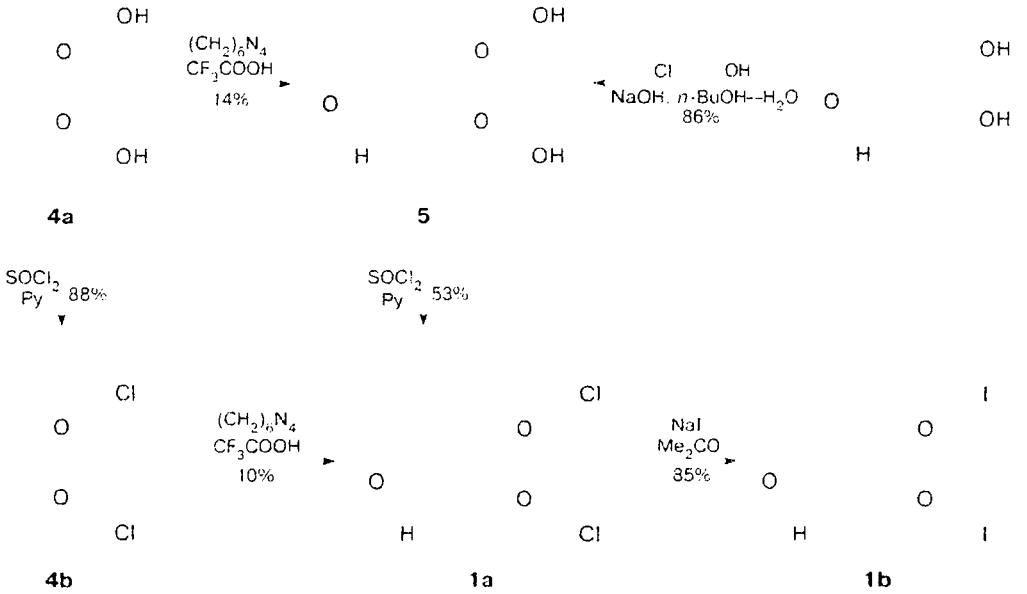
Scheme 2



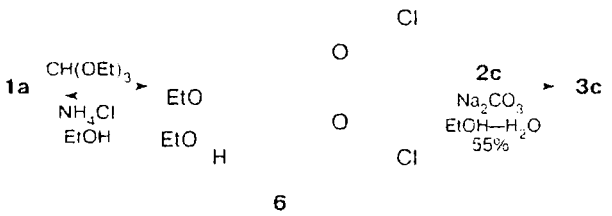
time, the reaction mixture always contains acetal **6** and aldehyde **1a**. The equilibrium cannot be shifted toward acetal because acetalization is reversible under the given conditions. Due to the difficulty of separation of dichlorides **1a** and **6**, they were introduced as a mixture into condensation with 3,6-dioxaoctane-1,8-dithiol (**2c**). This reaction gave only one product, 4′-formylbenzodithia-18-crown-6 ether (**3c**), whose yield was 55%, which was lower than the yield in a similar experiment with unprotected formyl group (Table 1). For this reason, other crown ethers **3** were prepared without protecting the formyl group.

Table 1. Synthesis of crown compounds **3a—e** by the condensation of dihalides **1a,b** with dithiols **2a—e** on treatment with M_2CO_3 in a EtOH—H_2O (1 : 1) mixture

Crown compound	Starting dihalide	M	Reaction time/h	Yield (%)*
3a	**1a**	Li	20	0
		Na	20	0
	1b	Li	50	44
		Na	50	0
		Cs	50	42
3b	**1a**	Li	18	81
		Na	18	30
		K	18	30
		Cs	18	61
	1b	Cs	18	88
3c	**1a**	Li	13	79
		Na	13	75
		K	13	41
		Cs	13	61
	1b	Li	20	81
		Cs	20	61
3d	**1a**	Na	15	0
		Cs	15	0
	1b	Li	20	62
		Na	20	33
		Cs	50	68
3e	**1a**	Li	20	58
		Na	20	67
		K	20	74
		Cs	20	53

* The yields of **3a—e** are based on the converted **1a,b**.

Scheme 3



It is known that a metal cation can efficiently assist in the reaction between two acyclic precursors giving rise to a macroheterocycle through the template effect.[12,13] The reactants are pre-organized around the metal atom in such a way as to enable the formation of 12—21-membered macroheterocycles. Their yields depend appreciably on the nature and the size of the metal cation, the nature of the counterion, the solvent, and the leaving group. Therefore, synthesis of each new type of crown compounds requires, as a rule, special selection of the reaction conditions.

No systematic study of the template effect in the formation of sulfur-containing macroheterocycles has

Table 2. Synthesis of crown compounds **3b,c** by the condensation of diiodide **1b** with dithiols **2b,c** on treatment with Cs_2CO_3 in various solvents at 80 °C for 20 h

Solvent	Yield (%)*	
	3b	**3c**
EtOH—H_2O (1 : 1)	88	61
MeCN	77	88
MeCN—H_2O (1 : 1)	86	82
DMF	50	90
DMF—H_2O (1 : 1)	95	90

* The yields of **3b,c** were calculated from the ^1H NMR spectra of the reaction mixtures.

been performed previously; this stimulated us to study this effect in relation to the influence of alkali metal cations in the synthesis of thiacrown ethers **3a—e**. As the prototype, we chose the synthesis of benzo-1,10-dithia-18-crown-6 described previously,[5] which involves condensation of 1,2-bis(2-chloroethoxy)benzene (**4b**) with 3,6-dioxaoctane-1,8-dithiol (**2c**) on treatment with Na_2CO_3 in aqueous ethanol. With optimization of the conditions of the synthesis of crown compounds **3a—e** (Scheme 1), we studied the role of the size of the alkali metal cation in M_2CO_3, the leaving group in dihalides **1a,b**, and the nature of the solvent. To suppress side processes, condensation was carried out in highly dilute solutions.

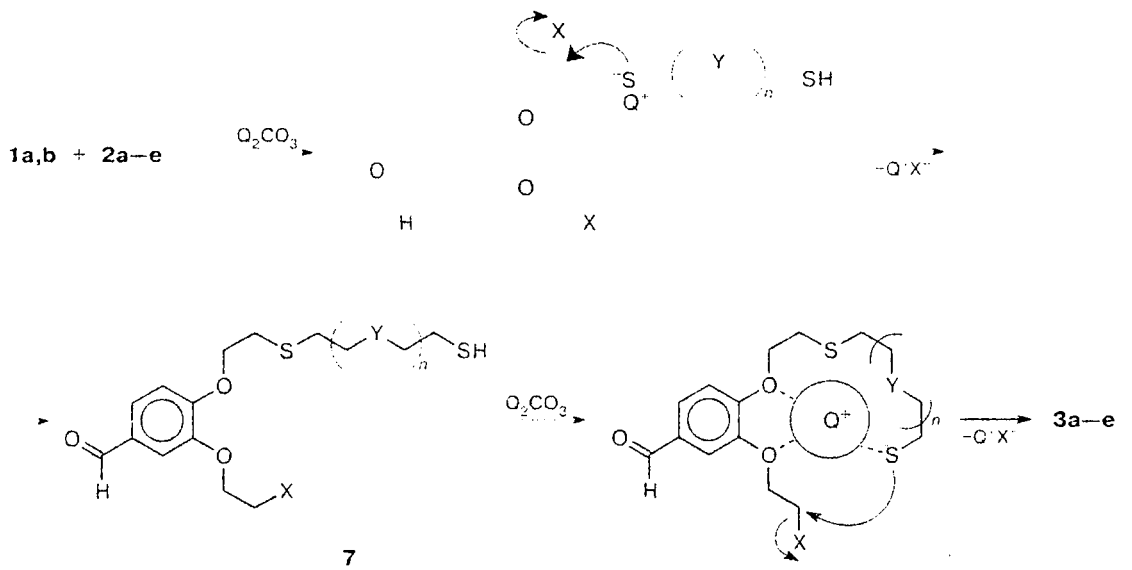
The formyl derivatives of benzocrown compounds with different numbers of sulfur, oxygen, and carbon in the macrocycle were obtained in 30—88% yields under the conditions used (see Tables 1 and 2).

The reaction of dihalide **1a,b** with dithiol **2a—e** starts, apparently, with deprotonation of dithiol on treatment with a base to give the dithiolate anion or an ion pair with this anion. The subsequent nucleophilic substitution at one of the terminal saturated carbon atoms of dihalide **1a,b** results in podand **7**, which is then deprotonated under the action of a base. Cyclization of the resulting ion pair, metal cation—podand **7** anion, affords the corresponding compound **3a—e** (Scheme 4). The hydrated metal cation can also form additional coordination bonds involving the oxygen atoms of dihalide **1a,b** and dithiol **2b,c,e** due to partial dehydration. This pre-organization of the intermediate seems to underlie the template effect of the metal ion, which facilitates the departure of the halide anion in the intramolecular nucleophilic substitution.

The replacement of the chlorine atoms in **2a** by iodine atoms, which are better leaving groups, results in a more effective reaction both in the first and second condensation steps, as indicated by the results obtained. If the dithiol contains no ether oxygen atoms (**2a,d**), the formation of macrocycle **3a,d** requires that diodide **1b** rather than dichloride **1a** be used in the reaction. However, if condensation is carried out for dithiols that do contain ether oxygen atoms (**2b,c,e**), the yields of the products virtually do not depend on the nature of the halogen atom in **1** (see Table 1). The presence of ether oxygen, much more electronegative than sulfur, in the dithiol apparently facilitates deprotonation of the mercapto group on treatment with a base; this increases the steady-state concentration of the dithiolate anion or, more precisely, the corresponding ion pair during the condensation.

When both molecules of the starting compounds contain oxygen atoms, the intermolecular interaction between the dihalide molecule and the metal cation—dithiol anion ion pair in the first step of condensa-

Scheme 4



Q^+ are alkali metal cations hydrated to different degrees.

tion can also be accomplished to a small extent *via* an intermediate in which the oxygen atoms of two fragments are involved additionally in binding to the metal cation. However, substantial competing hydration of the alkali metal cation in aqueous ethanol should also be taken into account. This shows itself, for example, as an increase in its effective (Stokes) radius,[14,15] which apparently makes this additional binding insignificant. Alkali metal cations are known to have low affinity to neutral sulfur atoms; therefore, in the case of formation of benzocrown compounds **3a,d**, which contain only two oxygen atoms, this additional binding does not appear to play an important role in the first step of condensation.

In the step of intramolecular cyclization of the resulting podand, the effect of additional binding is substantially enhanced, which leads to a more pronounced ion-selective template effect of metal cations.

It is known that Li^+ ions have no substantial influence on the synthesis of benzo-18-crown-6 ether in aqueous media;[16] in aprotic media, they even inhibit the process due to the formation of a strong complex with *ortho*-dioxyphenylene fragment of the molecule.[17] For other alkali metal cations, the rate of cyclization giving rise to crown ethers markedly increases in nonaqueous solvents, which is due to stabilization of the intermediate by the formation of coordination bonds between the metal cation and the oxygen atoms of the polyoxyethylene chain.[16,17]

It has also been suggested[18,19] that the Cs^+ ion can exhibit a specific template effect in the formation of cyclic disulfides and sulfur-containing crown compounds in DMF; this large and easily polarizable metal ion is linked both to the nucleophile and to the leaving group, and the lateral interaction between them facilitates cyclization upon the nucleophilic substitution at the carbon atom. It should be noted that not all researchers agree with this hypothesis.[20]

Analysis of the data (see Table 1) shows that of lithium, sodium, and potassium carbonates used in the synthesis of dithiacrown compounds **3b,c,e** from dichloride **1a**, the best yield of the 15-membered macrocycle **3b** was attained for Li_2CO_3, better yields of 18-membered heterocycle **3c** were obtained for lithium and sodium carbonates, and in the case of the 21-membered molecule **3e**, the highest yields were observed for sodium and potassium carbonates. This difference can be interpreted by assuming that the size of partially (for Na^+ or K^+) or completely (for Li^+) hydrated metal cation fits better to the size of the cavity in the intermediate in the step of cyclization of the dithiacrown compound. The use of Cs_2CO_3 resulted in close and unusually high yields of **3b,c,e**. Apparently, this was due to the above-described specific template effect of the Cs^+ ion, which slightly depends on the nature of the solvent because of the low susceptibility of this ion for solvation.

Indeed, the use of both anhydrous and aqueous MeCN or DMF solvents in the synthesis of crown compounds **3b,c** in the presence of Cs_2CO_3 proved almost equally efficient, although the results obtained in the presence of water were somewhat better (see Table 2), probably due to better solubility of Cs_2CO_3 under these conditions.

Attention is drawn to the unusually high yields of **3a—e**, obtained when using Li_2CO_3 (see Table 1). The lithium cation, characterized by the greatest charge density among alkali metal cations, is completely hydrated in aqueous ethanol.[14,15,21] Therefore, the efficient radius of this ion becomes even greater than that of Cs^+, which is slightly hydrated; therefore, the abnormal increase in the yield of thiacrown compounds in the case of Li^+ can be fully attributed to the template effect of the hydrated Li^+ ion, similar to the specific effect of the Cs^+ ion.

Thus, we developed a new method for the synthesis of previously unknown formyl derivatives of sulfur-containing benzocrown compounds by the condensation of 3,4-bis(2-haloethoxy)benzaldehydes with acyclic α,ω-alkanedithiols under the action of alkali metal carbonates. The influence of the nature of the leaving group on the efficiency of condensation was established, and an unusual template effect of hydrated alkali metal cations was found.

Experimental

^1H NMR spectra were recorded on a Bruker DRX-500 spectrometer in $CDCl_3$ using tetramethylsilane as the internal standard. Chemical shifts were measured with an accuracy of 0.01 ppm and spin—spin coupling constants were determined with an accuracy of 0.1 Hz. Mass spectra were run on a Varian MAT 311A instrument at an ionization energy of 70 eV with direct sample injection into the ionization area. IR spectra were measured on Shimadzu IR-435 and Bruker IFS-113v spectrophotometers in thin films or in pellets with KBr. The reactions were monitored by TLC on DC-Alufolien Kieselgel 60 F_{254} plates (Merck).

Dehydration of DMF needed for the reactions was performed by distilling the solvent from BaO *in vacuo*. Commercial anhydrous ethanol (Aldrich), MeCN (Aldrich), 1,2-bis(2-hydroxyethoxy)benzene (Aldrich), and 3,4-dihydroxybenzaldehyde (Merck) were used.

3,4-Bis(2-hydroxyethoxy)benzaldehyde (5). ***Method A.*** Urotropin (0.71 g, 5.1 mmol) was added to a solution of 1,2-bis(2-hydroxyethoxy)benzene (1.0 g, 5.1 mmol) (**4a**) in 4 mL of trifluoroacetic acid and the mixture was heated in a flow of argon for 14 h at 90 °C. Water (30 mL) was added to the cooled reaction mixture, which was then extracted with $CHCl_3$ (7 × 15 mL), the extract was concentrated *in vacuo*, and the residue was chromatographed on a column with silica gel (L 40/100, Chemapol, elution with benzene—EtOH, 20 : 1) to give 0.422 g of the initial diol **4a** and 0.090 g of product **5** (14%) (Tables 3 and 4).

Method B. A solution of 2-chloroethanol (21.7 mL, 0.33 mol) in 60 mL of *n*-BuOH was added over a period of 1 h to a boiling solution of 3,4-dihydroxybenzaldehyde (15.0 g, 0.109 mol) and NaOH (13.2 g, 0.33 mol) in a mixture of 300 mL of *n*-BuOH and 25 mL of water. The reaction mixture was refluxed for an additional 12 h, the solvent was evaporated *in vacuo*, and the residue was chromatographed on a column with silica gel (Kieselgel 60, 0.063—0.100 mm, elution with benzene—EtOH, 20 : 1) to give 20.4 g of product **5** (86%) (Tables 3 and 4).

Table 3. IR, ^{1}H NMR, mass spectra of compounds **1**, **3**[a], and **5**

Compound	IR, ν/cm^{-1}	^{1}H NMR ($CDCl_3$), δ (J/Hz)	m/z (I_{rel} (%))[b]
5	3390 (O—H) 1681 (C=O)	2.63 (br.s, 2 H, 2 OH); 4.01 (m, 4 H, 2 CH_2OH); 4.20 (m, 4 H, 2 CH_2OAr); 7.03 (d, 1 H, H-6, J = 8.2); 7.48 (s, 1 H, H-3); 7.51 (dd, 1 H, H-5, J = 8.2, J = 1.6); 9.86 (s, 1 H, CH=O)	226 (25), 182 (13), 164 (6), 163 (6), 149 (8), 139 (7), 138 (100), 137 (84), 109 (9), 81 (9), 63 (6)
1a	1687 (C=O)	3.87 (t, 2 H, CH_2Cl, J = 5.9); 3.89 (t, 2 H, CH_2Cl, J = 6.0); 4.35 (t, 2 H, CH_2O, J = 5.9); 4.38 (t, 2 H, CH_2O, J = 6.0); 7.04 (d, 1 H, H-6, J = 8.2); 7.47 (d, 1 H, H-3, J = 1.7); 7.51 (dd, 1 H, H-5, J = 8.2, J = 1.7); 9.87 (s, 1 H, CH=O)	266 (11), 264 (51), 262 (80), 200 (50), 150 (44), 149 (55), 137 (69), 109 (43), 79 (40), 65 (60), 64 (49), 63 (100), 62 (69)
1b	1685 (C=O)	3.49 (m, 4 H, 2 CH_2I); 4.36 (t, 2 H, CH_2O, J = 6.9); 4.40 (t, 2 H, CH_2O, J = 7.0); 7.01 (d, 1 H, H-6, J = 8.2); 7.45 (d, 1 H, H-3, J = 1.8); 7.50 (dd, 1 H, H-5, J = 8.2, J = 1.8); 9.87 (s, 1 H, CH=O)	446 (2), 165 (5), 164 (40), 163 (12), 155 (100), 149 (13), 79 (8), 60 (6), 57 (9), 55 (8), 51 (8)
3a	1689 (C=O)	2.98 (m, 4 H, 2 CH_2S); 3.07 (s, 4 H, 2 CH_2S); 4.42 (m, 4 H, 2 CH_2O); 6.92 (d, 1 H, H-6, J = 8.1); 7.36 (d, 1 H, H-3, J = 1.8); 7.47 (dd, 1 H, H-5, J = 8.1, J = 1.8); 9.85 (s, 1 H, CH=O)	284 (59), 224 (88), 164 (100), 163 (88), 149 (86), 92 (85), 79 (77), 61 (88), 60 (92), 59 (92), 51 (84)
3d	1682 (C=O)	2.91 (m, 6 H, 3 CH_2S); 3.10 (m, 10 H, 5 CH_2S); 4.37 (m, 4 H, 2 SH_2O); 6.98 (d, 1 H, H-6, J = 8.2); 7.42 (d, 1 H, H-3, J = 1.8); 7.47 (dd, 1 H, H-5, J = 8.2, J = 1.8); 9.86 (s, 1 H, CH=O)	404 (12), 284 (37), 256 (32), 224 (84), 165 (40), 164 (100), 163 (63), 148 (55), 121 (52), 92 (44), 87 (46)
3e	1685 (C=O)	2.95 (m, 4 H, 2 CH_2S); 3.04 (t, 2 H, CH_2S, J = 6.3); 3.06 (t, 2 H, CH_2S, J = 6.4); 3.66 (m, 8 H, 4 CH_2O); 3.78 (m, 4 H, 2 CH_2O); 4.26 (t, 2 H, CH_2O, J = 6.3); 4.28 (t, 2 H, CH_2O, J = 6.4); 6.96 (d, 1 H, H-6, J = 8.2); 7.39 (d, 1 H, H-3, J = 1.7); 7.45 (dd, 1 H, H-5, J = 8.2, J = 1.7); 9.85 (s, 1 H, CH=O)	416 (39), 193 (72), 164 (95), 163 (66), 149 (87), 105 (71), 89 (75), 87 (100), 61 (91), 60 (95), 59 (65)

[a] The spectra of compounds **3b,s** were taken from Ref. 7.
[b] Molecular ion peaks and ten most intense peaks are given.

3,4-Bis(2-chloroethoxy)benzaldehyde (1a). A solution of $SOCl_2$ (19.7 mL, 0.27 mol) in 30 mL of dry benzene was added with vigorous stirring over a period of 1 h to a boiling solution of 3,4-bis(2-hydroxyethoxy)benzaldehyde (**5**) (20.4 g, 0.09 mol) and anhydrous pyridine (21.8 mL, 0.27 mol) in 120 mL of anhydrous benzene. The reaction mixture was refluxed for 5 h and cooled, and 100 mL of 15% HCl was added. The organic layer was separated and the aqueous layer was extracted with $CHCl_3$ (2 × 50 mL). The extracts were combined, the solvent was evaporated *in vacuo*, and the residue was chromatographed on silica gel (Kieselgel 60, 0.063—0.200 mm, elution with benzene—$MeCO_2Et$, 10 : 1) to give 12.6 g of dichloride **1a** (53%) (Tables 3 and 4).

Table 4. Characteristics of compounds **1**, **3**, and **5**

Compound	m.p./°C[a]	Yield (%)	Found / Calculated (%) C	H	Molecular formula
5	99—101	14[b] 86[c]	58.13 58.40	6.19 6.24	$C_{11}H_{14}O_5$
1a	50—51	10[b] 53[d]	50.72 50.21	4.61 4.60	$C_{11}H_{12}Cl_2O_3$
1b	64—65	85	30.07 29.62	2.69 2.71	$C_{11}H_{12}I_2O_3$
3a	82—84	[e]	54.78 54.90	5.61 5.67	$C_{13}H_{16}O_3S_2$
3b	121—122[f]	[e]	—	—	$C_{15}H_{20}O_4S_2$
3c	131—132[f]	[e]	—	—	$C_{17}H_{24}O_5S_2$
3d	119—121	[e]	50.65 50.46	6.04 5.98	$C_{17}H_{24}O_5S_4$
3e	62—64	[e]	54.56 54.79	6.81 6.78	$C_{19}H_{28}O_6S_2$

[a] From heptane.
[b] Prepared by method 4 (see Experimental).
[c] Prepared from 3,4-dihydroxybenzaldehyde.
[d] Prepared from diol **5**.
[e] See Table 1.
[f] See Ref. 7.

Benzaldehyde **1a** was also prepared from 1,2-bis(2-chloroethoxy)benzene (**4b**) in 10% yield similarly to the synthesis of **5** by method *A*.

3,4-Bis(2-iodoethoxy)benzaldehyde (1b). A mixture of dichloride **1a** (5.8 g, 0.022 mol), anhydrous NaI (12.3 g, 0.082 mol), and 30 mL of anhydrous acetone was refluxed with vigorous stirring for 120 h. The precipitate was filtered off, the mother liquor was concentrated *in vacuo*, and the residue was dissolved in 50 mL of ethyl acetate and washed successively with 5% aqueous solutions of Na_2SO_3 and Na_2CO_3 and with water. The solvent was evaporated *in vacuo* and the residue was chromatographed on a column with silica gel (Kieselgel 60, 0.063—0.100 mm, elution with benzene—$MeCO_2Et$, 20 : 1) to give 8.3 g of diiodide **1b** (85%) (Tables 3 and 4).

Preparation of 4′-formylbenzo-1,10-dithia-18-crown-6 (3c)[7] with acetal protection. A mixture of dichloride **1a** (0.961 g, 3.65 mmol), triethyl orthoformate (0.86 mL, 4.6 mmol), NH_4Cl (0.011 g, 0.2 mmol), and 2 mL of anhydrous EtOH was refluxed for 3 h. The resulting solution, containing acetal **6**, was used in condensation.

Solutions of acetal **6** and 3,6-dioxaoctane-1,8-dithiol (**2c**) (0.65 mL, 4.0 mmol), each in 10 mL of EtOH, were added simultaneously over a period of 1 h to a boiling and stirred solution of $Na_2CO_3 \cdot 10H_2O$ (5.83 g, 20 mmol) in 200 mL of a 1 : 1 EtOH—H_2O mixture. The reaction mixture was refluxed for 12 h, EtOH was evaporated *in vacuo*, and the remaining

aqueous phase was extracted with a benzene—$CHCl_3$ mixture (5 × 30 mL). The extracts were concentrated *in vacuo* and the residue was chromatographed on a column with silica gel (Kieselgel 60, 0.063—0.100 mm). Elution with benzene gave 0.264 g of the initial aldehyde **1a**. Elution with a benzene—ethyl acetate mixture (20 : 1) gave 0.538 g (55 %) of aldehyde **3c**; m.p. 130—132 °C.

Preparation of crown compounds 3b,c,e (general procedure). At 75—85 °C, solutions of dihalide **1a,b** (4.24 mmol) and dithiol **2b,c,e** (4.66 mmol), each in 10 mL of a solvent, were added simultaneously with stirring over a period of 1 h to a mixture of M_2CO_3 (M = Li, Na, K, Cs) (21.2 mmol) in 200 mL of a solvent. The reaction mixture was kept at the specified temperature for 13—20 h, the solvent was evaporated, 100 mL of water was added to the residue, and the products were extracted with a benzene—$CHCl_3$ mixture (10 : 1) (5 × 30 mL). The extracts were concentrated *in vacuo* and the residue was chromatographed on a column with silica gel (Kieselgel 60, 0.063—0.100 mm); the products were eluted successively with benzene and a benzene—$MeCO_2Et$ mixture (20 : 1) for crown compounds **3b,c** or with a benzene—$MeCO_2Et$ mixture (1 : 1) for **3e**. The yields, the spectra, and the results of elemental analysis are presented in Tables 1—4.

Preparation of crown compounds 3a,d (general procedure). Solutions of diiodide **1b** (0.223 g, 0.5 mmol) and dithiol **2a,d** (0.55 mmol), each in 10 mL of EtOH, were added simultaneously with stirring over a period of 1 h to a boiling solution of Li_2CO_3, Na_2CO_3, or Cs_2CO_3 (2.5 mmol) in 200 mL of a EtOH—H_2O mixture (1 : 1). The reaction mixture was refluxed for 20—50 h, the solvent was evaporated *in vacuo*, and the residue was extracted with hot ethyl acetate (3 × 50 mL). The organic extracts were concentrated *in vacuo*, and the residue was chromatographed on a column with silica gel (Kieselgel 60, 0.063—0.100 mm); the products were eluted successively with benzene and a benzene—ethyl acetate mixture (20 : 1). The product was additionally purified by extraction with hot heptane. The yields, spectra, and the results of elemental analysis are listed in Tables 1—4.

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