Synthesis of nitro and amino derivatives of benzothiacrown ethers

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The condensation reaction of 1,2-bis(2-haloethoxy)-4-nitrobenzenes with acyclic α, ω -(oxa)alkanedithiols in the presence of alkali metal carbonates produced a series of nitrobenzodithiacrown ethers with macrocycles of different size. The structures of three ethers were established by X-ray diffraction. A new method was developed for the synthesis of nitrobenzomonothia-15-crown-5 ether. Nitro derivatives of benzodithiacrown ethers were tested as reagents for extraction of palladium(II), platinum(IV), and rhodium(III) from hydrochloric acid solutions. Extraction of Pd^{II} salts was found to be highly selective compared to that of Pt^{IV} and Rh^{III} salts. Benzodithia-15-crown-5 ether is the most efficient extractant for palladium(II). Reduction of nitrobenzothiacrown ethers with hydrazine hydrate in the presence of a platinum catalyst afforded their amino derivatives.

Key words: 1,2-bis(2-haloethoxy)-4-nitrobenzenes, α,ω -(oxa)alkanedithiols, condensation, nitrobenzothiacrown ethers, X-ray diffraction study, reduction, aminobenzothiacrown ethers, extraction, palladium.

Thiacrown ethers are among the most promising macrocyclic sulfides.^{1,2} Sulfur-containing macroheterocycles have attracted interest because these compounds can form stable complexes with transition and heavy metal ions.^{3,4} These compounds can be used as selective extractants, materials for ion-selective electrodes, reagents for modifications of chromatographic sorbents, *etc.* The development of procedures for the synthesis of important functionalized derivatives of thiacrown ethers is of great importance for the extension of the possibilities of the practical use of these compounds.

In the present study, we developed convenient procedures for the synthesis of nitro and amino derivatives of benzothiacrown ethers with macrocycles of different size and different combinations of O and S atoms. The condensation reactions of 1,2-bis(2-haloethoxy)-4-nitrobenzenes **1a,b** with terminal (oxa)alkanedithiols **2a**-**d** in the presence of alkali metal carbonates (M_2CO_3) in aqueous ethanol produced nitrobenzodithiacrown ethers **3a**-**d** in 48-89% yields (Scheme 1). To suppress side reactions,

Scheme 1 M₂CO FtOH-H_C HS 1a,b 2a- O_2N 3a-d 1: X = Cl (a), I (b) 2, 3 М 2, 3 Μ п n 2 0 Cs Na а С b Li d 3 Κ 1

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condensation was performed under high-dilution conditions.

We chose alkali metal carbonates for the synthesis of compounds 3a-d based on the data, which we have obtained earlier⁵ in studying the influence of the metal cation on the efficiency of condensation of 3,4-bis(2-haloethoxy)benzaldehydes with dithiols 2a-d in the synthesis of formyl derivatives of benzodithiacrown compounds.

Apparently, the reactions of dihalides **1a**,**b** with dithiols **2a**—d start with deprotonation of dithiol under the action of bases in an aqueous ethanolic solution giving rise to the thiolate anion or its ion pair (Scheme 2). The nucleophilic substitution at one of the terminal saturated carbon atoms of dihalide affords podand 4. Subsequent deprotonation of the thiol group and cyclization of the resulting ion pair consisting of the hydrated metal ion and the anion of podand 4 give compounds 3a-d. The hydrated cation can form additional coordination bonds involving the oxygen atoms of dihalide and dithiol through partial dehydration. Apparently, this preorganization of the intermediate provides the basis for the template effect of the metal ion facilitating the loss of the halide ion as a result of the intramolecular nucleophilic substitution.

Since we succeeded in synthesizing the formyl derivative of benzodithia-12-crown-4 ether only starting from diiodide **1b**, and the yields of formylbenzodithia-15(18,21)-crown-5(6,7) ethers were virtually independent of the nature of the halide ion in 3,4-bis(2-haloethoxy)benzaldehydes,⁵ we used diiodide **1b** in the synthesis of compound **3a**, whereas other nitrobenzodithiacrown ethers **3b**—**d** were prepared starting from dichloride **1a**. Compounds **3a,c,d** were synthesized for the first time. Compound **3b** has been prepared earlier⁶ by condensation of diiodide **1b** with dithiol **2b** in the presence of Na₂CO₃ in 58% yield. The conditions proposed in the present study allowed the synthesis of crown ether **3b** from dichloride **1a** in substantially higher yield (89%), one reaction step being eliminated.

High yields achieved in the presence of Li_2CO_3 (in the synthesis of 15-membered macrocycle **3b**), Na_2CO_3 (in the synthesis of 18-membered macrocycle **3c**), or K_2CO_3 (in the synthesis of 21-membered macrocycle **3d**) are most likely attributed to the best correspondence between the size of the metal cation, which is partially (in the case of Na^+ or K^+) or completely (in the case of Li^+) hydrated in an aqueous alcoholic solution, and the size of the cavity of the intermediate in the cyclization step giving dithiacrown ether. The good yield of 12-membered macrocycle **3a** achieved in the reaction with the use of Cs_2CO_3 is apparently due to the specific template effect of the Cs^+ ion. This effect has been observed in the synthesis of sulfur-containing crown compounds with macrocycles of different size.^{7,8}

A procedure for the synthesis of the nitro derivative of benzomonothia-15-crown-5 ether **3e** by condensation of 1,2-bis[2-(tosyloxy)ethoxy]-4-nitrobenzene with bis(2-hydroxyethyl)sulfide in the presence of Bu^tONa in *tert*-butyl alcohol was documented.⁹ We developed a new



n = 0—3

Q⁺ is an alkali metal cation with different degrees of hydration



approach to the synthesis of compound 3e from available 4-nitropyrocatechol (5) and 2-(2-chloroethoxy)ethanol (6) (Scheme 3). The reaction of compounds 5 and 6 in the presence of a base produced dithiol 7. A small amount of nitrophenol 8, which was produced via alkylation of 4-nitropyrocatechol (5) at the hydroxy group located in the *para* position with respect to the nitro group, was isolated along with the dithiol. Two different nitrophenols can theoretically be formed as a result of alkylation at one of two hydroxy groups of pyrocatechol 5. The fact that the reaction produced nitrophenol 8 was confirmed by NOE experiments. Thus, the 2D spectrum shows an intense cross-peak between the methylene protons of the CH₂OAr group and the proton of the benzene ring in the *meta* position with respect to the nitro group. Based on these data, the mechanism of formation of diol 7 can be suggested. Apparently, deprotonation of 4-nitropyrocatechol (5) with a base initially occurs at the more acidic hydroxy group in the *para* position with respect to the electron-withdrawing nitro group to give the phenolate ion. The nucleophilic substitution of the chlorine atom in 2-(2-chloroethoxy)ethanol (6) with this ion affords nitrophenol 8. The next step involves deprotonation of the second hydroxy group in the benzene ring of compounds 8 under the action of the base followed by alkylation of the resulting phenolate with an excess of compound 6 to give diol 7. The treatment of diol 7 with thionyl chloride in the presence of pyridine affords dichloride 9, and the reaction of the latter with sodium sulfide produces benzomonothiacrown ether 3e in substantially higher yield (64% in the absence of a base and 73% in the presence of Na_2CO_3) compared to that obtained according to the procedure described earlier⁹ (18%).

Reduction of nitrobenzothiacrown ethers 3a-e with hydrazine hydrate in the presence of platinum on carbon afforded amino derivatives 10a-e in high yields (Scheme 4).



It should be noted that this reaction imposes stringent requirements on the purity of the starting nitro compounds. In the case of chromatographically pure nitrobenzothiacrown ethers, which were not recrystallized, a larger amount of the catalyst was required for complete reduction due, probably, to partial poisoning of its active surface by traces of dithiols used in the synthesis of nitro compounds or traces of by-products containing the mercapto group.

Compounds **3a–e** were reduced by analogy with the known procedure⁹ for the synthesis of aminobenzomonothia-15-crown-5 ether (**10e**) using the platinum catalyst instead of the palladium catalyst. The platinum catalyst proved to be much more efficient in the synthesis of amino derivatives **10a–e**. For example, an attempt to reduce compound **3c** in the presence of the Pd/C catalyst (10%) led to an increase in the reaction time to 70 h, whereas the reaction was completed in 7 h in the presence of a smaller amount of the Pt/C catalyst (10%). The difference in the reduction rate can also be associated with higher resistance of the platinum catalyst to poisoning of

Table 1. Physicochemical characteristics, yields, and elemental analysis data for compounds 3a-e, 7-9, and 10a-e

Com- po-	$R_{\rm f}^{\ a}$	M.p./°C (solvent)	Yield (%)	Found Calculated (%)		- (%)	Molecular formula
und				С	Н	N	-
3a	0.73	159—161 (AcOEt)	48	<u>47.95</u> 47.82	<u>5.31</u> 5.02	<u>4.58</u> 4.65	$C_{12}H_{15}NO_4S_2$
3b	0.51	129—131 ^b (EtOH)	89	_	—	_	$C_{14}H_{19}NO_5S_2$
3c	0.39	128—129 (hexane)	67	$\frac{48.75}{48.78}$	<u>6.12</u> 6.01	<u>3.54</u> 3.56	$C_{16}H_{23}NO_6S_2$. .0.25H ₂ O
3d	0.61	69–71 (hexane)	58	<u>49.77</u> 49.87	<u>6.52</u> 6.28	<u>3.17</u> 3.23	$C_{18}H_{27}NO_7S_2$
3e	0.49	105—107 ^c (pentane)	73	—	_	_	C ₁₄ H ₁₉ NO ₆ S
7 d	0.34	Oil	28	—	—	—	$C_{14}H_{21}NO_8$
8 d	0.49	115—117 (hexane)	3	_	-	_	C ₁₀ H ₁₃ NO ₆
9 d	0.63	Oil	93	—	—	—	C ₁₄ H ₁₉ Cl ₂ NO ₆
10a	0.42	119–121 (EtOH)	88	<u>53.22</u> 53.11	<u>6.17</u> 6.31	<u>4.99</u> 5.16	$C_{12}H_{17}NO_2S_2$
10b	0.37	87—89 (EtOH)	95	<u>52.52</u> 52.55	<u>6.54</u> 6.77	<u>4.17</u> 4.38	C ₁₄ H ₂₁ NO ₃ S ₂ · •0.25H ₂ O
10c	0.35	80—82 (EtOH)	83	<u>52.58</u> 52.79	<u>7.25</u> 7.06	<u>3.65</u> 3.85	C ₁₆ H ₂₅ NO ₄ S ₂ · •0.25H ₂ O
10d ^e	0.30	Oil	90	—	—	—	$C_{18}H_{29}NO_5S_2$
10e	0.26	131—133 ^f (EtOH)	95	—	-	_	$C_{14}H_{21}NO_4S$

^{*a*} In benzene—AcOEt, 10:1 (**3a**–c), benzene—AcOEt, 1:1 (**3d**), benzene—AcOEt, 5:1 (**3e**), benzene—EtOH, 5:1 (**7–9**), and benzene—EtOH, 10:1 (**10a–e**), systems.

^b Cf. lit. data⁶: m.p. 125–126 °C.

^c Cf. lit. data⁹: m.p. 104–105 °C.

^d The high-resolution mass spectrum is given in the Experimental section.

^e The high-resolution mass spectrum, found: $m/z 403.1488 [M]^+$.

 $C_{18}H_{29}NO_5S_2$. Calculated: M = 403.1487.

^{*f*}*Cf*. lit. data⁹: m.p. 132–134 °C.

its active surface with traces of dithiol **2c** used in the synthesis of nitro derivative **3c**.

The structures of the resulting compounds were established by ¹H and ¹³C NMR and IR spectroscopy and were confirmed by mass spectrometry and elemental analysis (Tables 1-3).

The three-dimensional structures of nitrobenzodithiacrown ethers **3a,c,d** were studied by X-ray diffraction. Their crystal structures are shown in Figs 1–3. Selected bond lengths and bond angles are given in Table 4. In the structure of **3a**, the crown macrocycle is disordered over two orientations of the C(10)–C(11) chain between the S(1) and S(2) atoms (the atomic numbering scheme used in Figs 1–3 differs from the IUPAC nomenclature). This disorder, as well as high mosaicity of the crystals, resulted in a decrease in the accuracy of the X-ray diffraction data for **3a,c**. In spite of this, a comparison of molecules **3a,c,d**



Fig. 1. Crystal structure of nitrobenzodithiacrown ether **3a**. Here and in Figs 2 and 3, the displacement ellipsoids are drawn at the 50% probability level.



Fig. 2. Crystal structure of nitrobenzodithiacrown ether 3c.

Com- pound	IR (KBr), v/cm ⁻¹	¹ H NMR (CDCl ₃), δ (<i>J</i> /Hz)	$MS, m/z (I_{\rm rel} (\%))^*$
3a	1515 (NO ₂)	2.99 (m, 4 H, 2 CH ₂ S); 3.06 (s, 4 H, 2 CH ₂ S); 4.43 (m, 4 H, 2 CH ₂ OAr); 6.85 (d, 1 H, H(14), $J = 9.0$); 7.69 (d, 1 H, H(11), $J = 2.3$); 7.93 (dd, 1 H, H(13), $J = 9.0$, $J = 2.3$)	301 [M] ⁺ (61), 241 (60), 181 (100), 166 (60), 92 (85), 87 (79), 79 (65), 64 (72), 61 (75), 51 (61)
3c	1513 (NO ₂)	2.96 (t, 2 H, CH ₂ S, $J = 6.6$); 2.99 (t, 2 H, CH ₂ S, $J = 6.9$); 3.15 (t, 2 H, CH ₂ S, $J = 6.4$); 3.18 (t, 2 H, CH ₂ S, $J = 6.6$); 3.62 (s, 4 H, 2 CH ₂ O); 3.74 (t, 2 H, CH ₂ O, $J = 6.6$); 3.75 (t, 2 H, CH ₂ O, $J = 6.9$); 4.27 (m, 4 H, 2 CH ₂ OAr); 6.87 (d, 1 H, H(20), $J = 9.0$); 7.71 (d, 1 H, H(17), $J = 2.5$); 7.91 (dd, 1 H, H(19), $J = 9.0$, $J = 2.5$)	389 [M] ⁺ (11), 181 (67), 148 (83), 105 (81), 89 (77), 87 (100), 79 (55), 61 (95), 60 (100), 59 (92), 58 (99)
3d	1513 (NO ₂)	2.949 (t, 2 H, CH ₂ S, $J = 6.4$); 2.954 (t, 2 H, CH ₂ S, $J = 6.3$); 3.06, 3.07 (both t, 2 H each, 2 CH ₂ S, $J = 6.2$); 3.67 (s, 8 H, 4 CH ₂ O); 3.78 (t, 2 H, CH ₂ O, $J = 6.4$); 3.79 (t, 2 H, CH ₂ O, J = 6.3); 4.27, 4.29 (both t, 2 H each, 2 CH ₂ OAr, $J = 6.2$); 6.90 (d, 1 H, H(23), $J = 9.2$); 7.74 (d, 1 H, H(20), $J = 2.6$); 7.91 (dd, 1 H, H(22), $J = 9.2$, $J = 2.6$)	433 [M] ⁺ (10), 193 (61), 151 (64), 105 (86), 89 (91), 87 (100), 86 (64), 73 (58), 71 (72), 61 (95), 60 (88)
7	3370 (OH); 1515 (NO ₂)	2.66 (br.s, 2 H, 2 OH); 3.70, 3.77, 3.96 (all m, 4 H each, 6 CH ₂ O); 4.26 (m, 4 H, 2 C <u>H</u> ₂ OAr); 6.93 (d, 1 H, H(6), J = 9.0); 7.78 (d, 1 H, H(3), $J = 2.8$); 7.91 (dd, 1 H, H(5), $J = 9.0$, $J = 2.8$)	331 [M] ⁺ (75), 182 (60), 181 (73), 166 (47), 165 (40), 155 (45), 89 (100), 87 (49), 79 (42), 73 (37)
8	3404, 3111 (OH); 1512 (NO ₂)	3.72, 3.84, 3.93 (all m, 2 H each, 3 CH_2O); 4.27 (m, 2 H, CH_2OAr); 6.89 (d, 1 H, H(3), $J = 9.5$); 7.77 (dd, 1 H, H(4), $J = 9.5$, $J = 2.6$); 7.78 (d, 1 H, H(6), $J = 2.6$)	243 [M] ⁺ (22), 181 (42), 89 (100), 79 (32), 69 (33), 57 (32), 55 (24), 53 (52), 52 (49), 51 (38)
9	1515 (NO ₂)	3.669, 3.672 (both t, 2 H each, 2 CH ₂ O, $J = 5.9$); 3.87 (t, 4 H, 2 CH ₂ Cl, $J = 5.9$); 3.95 (m, 4 H, 2 CH ₂ O); 4.27 (m, 4 H, 2 CH ₂ OAr); 6.96 (d, 1 H, H(6), $J = 9.1$); 7.81 (d, 1 H, H(3), J = 2.7); 7.91 (dd, 1 H, H(5), $J = 9.1$, $J = 2.7$)	371 (2 ³⁷ Cl) [M] ⁺ (2), 369 (³⁵ Cl, ³⁷ Cl) [M] ⁺ (33), 367 (2 ³⁵ Cl) [M] ⁺ (46), 182 (24), 181 (45), 109 (49), 107 (94), 89 (82), 79 (21), 65 (58), 63 (100)
10a	3448, 3362 (NH ₂)	2.89, 2.94 (both m, 2 H each, 2 CH_2S); 3.07 (m, 4 H, 2 CH_2S); 3.49 (br.s, 2 H, NH ₂); 4.30 (m, 4 H, 2 CH_2OAr); 6.24 (dd, 1 H, H(13), $J = 8.2$, $J = 2.7$); 6.25 (br.s, 1 H, H(11)); 6.67 (d, 1 H, H(14), $J = 8.2$)	271 [M] ⁺ (89), 183 (78), 151 (84), 99 (53), 95 (100), 92 (53), 87 (39), 67 (27), 60 (38), 58 (85)
10b	3419, 3345 (NH ₂)	2.89 (t, 2 H, CH ₂ S, $J = 6.1$); 2.96 (t, 2 H, CH ₂ S, $J = 6.6$); 3.04 (t, 2 H, CH ₂ S, $J = 6.1$); 3.06 (t, 2 H, CH ₂ S, $J = 5.5$); 3.79 (t, 2 H, CH ₂ O, $J = 6.1$); 3.80 (t, 2 H, CH ₂ O, $J = 6.6$); 4.15 (t, 2 H, CH ₂ OAr, $J = 6.1$); 4.20 (t, 4 H, CH ₂ OAr, J = 5.5); 6.24 (dd, 1 H, H(16), $J = 8.5$, $J = 2.6$); 6.30 (d, 1 H, H(14), $J = 2.6$); 6.74 (d, 1 H, H(17), $J = 8.5$)	315 [M] ⁺ (34), 272 (57), 151 (100), 149 (21), 107 (18), 93 (20), 92 (93), 79 (18), 70 (24), 61 (31)
10c	3425, 3387 (NH ₂)	2.92, 2.93 (both t, 2 H each, 2 CH ₂ S, $J = 6.4$); 3.04, 3.11 (both t, 2 H each, 2 CH ₂ S, $J = 6.6$); 3.48 (br.s, 2 H, NH ₂); 3.63 (s, 4 H, 2 CH ₂ O); 3.73, 3.75 (both t, 2 H each, 2 CH ₂ O, J = 6.4); 4.11, 4.14 (both t, 2 H each, 2 CH ₂ OAr, $J = 6.6$); 6.22 (dd, 1 H, H(19), $J = 8.5$, $J = 2.4$); 6.29 (d, 1 H, H(17), J = 2.4); 6.70 (d, 1 H, H(20), $J = 8.5$)	359 [M] ⁺ (8), 152 (26), 151 (100), 103 (23), 95 (46), 89 (34), 87 (50), 67 (29), 61 (62), 60 (66), 59 (52)
10d	3422, 3352 (NH ₂)	2.88 (t, 2 H, CH ₂ S, $J = 6.6$); 2.91 (t, 2 H, CH ₂ S, $J = 6.4$); 2.97 (t, 2 H, CH ₂ S, $J = 6.6$); 3.01 (t, 2 H, CH ₂ S, $J = 6.5$); 3.657, 3.664 (both s, 4 H each, 4 CH ₂ O); 3.75 (t, 2 H, CH ₂ O, J = 6.6); 3.77 (t, 2 H, CH ₂ O, $J = 6.4$); 4.11 (t, 2 H, CH ₂ OAr, J = 6.6); 4.15 (t, 2 H, CH ₂ OAr, $J = 6.5$); 6.23 (dd, 1 H, H(22), $J = 8.2$, $J = 2.6$); 6.30 (d, 1 H, H(20), $J = 2.6$); 6.74 (d, 1 H, H(23), $J = 8.2$)	403 [M] ⁺ (24), 191 (22), 151 (100), 95 (36), 89 (47), 87 (51), 86 (25), 71 (32), 61 (48), 60 (43)

Table 2. IR, ¹H NMR, and mass spectra of compounds 3a,c,d, 7–9, and 10a–d

* The molecular ion peak and ten most intense peaks are given. The ionization energies were 60 (7 and 10d) and 70 eV (other compounds).

Table 3. ¹³C NMR spectra of compounds 3c, 7–9, and 10d

Com-	¹³ C NMR, δ				
pound					
3c	29.79 (2 SCH ₂ CH ₂ OAr); 30.70 (2 CH ₂ S); 69.47				
	(2 CH ₂ O); 69.90, 69.98 (both <u>C</u> H ₂ OAr); 71.46, 71.60				
	(both CH ₂ O); 106.80 (C(17)); 111.31 (C(20)); 117.66				
	(C(19)); 140.58 (C(18)); 147.41 (C(16a)); 153.49				
	(C(20a))				
7	61.41 (2 CH ₂ OH); 68.66 (3 CH ₂ O); 68.74, 72.74,				
	72.77 (all CH ₂ O); 107.77, 111.03 (C(3), C(6));				
	117.95 (C(5)); 141.41 (C(4)); 147.91 (C(2));				
	153.70 (C(1))				
8	61.58 (CH ₂ O); 68.96, 69.03 (<u>C</u> H ₂ OAr, <u>C</u> H ₂ CH ₂ OAr);				
	72.63 (CH ₂ O); 111.07 (C(6)); 111.95 (C(3)); 116.39				
	(C(4)); 142.63 (C(5)); 146.82 (C(1)); 151.34 (C(2))				
9	42.70, 42.76 (both CH ₂ Cl); 68.95, 69.07, 69.36, 69.46				
	(2 <u>C</u> H ₂ OAr, 2 <u>C</u> H ₂ CH ₂ OAr); 71.60, 71.64				
	(both CH ₂ O); 108.77, 111.79 (C(3), C(6)); 118.07				
	(C(5)); 141.50 (C(4)); 148.30 (C(2)); 154.22 (C(1))				
10d	31.20, 31.35 (both SCH ₂ CH ₂ OAr); 31.91, 32.12				
	(both CH_2S); 69.39 (\underline{CH}_2OAr); 70.29, 70.31 (both				
	CH ₂ O); 70.76 (<u>C</u> H ₂ OAr); 70.98, 71.04 (both CH ₂ O);				
	71.42 (2 CH ₂ O); 102.22 (C(20)); 107.05 (C(22));				
	116.58 (C(23)); 141.11 (C(23a)); 141.38 (C(19a));				

Note. The spectra of compounds 7-9 and 10d were recorded in CDCl₃; of compound 3c, in DMSO-d₆.

149.63 (C(21))

based on the main geometric parameters revealed their common features.

All compounds are characterized by a distortion of the bond angles at the C(2) and C(7) atoms, which are shared by two cyclic systems, exocyclic with respect to the benzene ring. This distortion is typical of benzocrown systems. 10,11 The O(1)-C(2)-C(3) and O(2)-C(7)-C(6)



Fig. 3. Crystal structure of nitrobenzodithiacrown ether 3d.

Table 4. Selected bond lengths (*d*) and bond angles (ω) in the structures of **3a**,**c**,**d**

Parameter	3a	3c	3d
Bond		d/Å	
O(1) - C(1)	1.398(12)	1.455(8)	1.447(2)
O(1) - C(2)	1.394(11)	1.373(8)	1.371(2)
O(2)-C(7)	1.323(11)	1.347(11)	1.360(2)
O(2) - C(8)	1.460(11)	1.446(10)	1.450(2)
O(1)O(2)	2.49	2.58	2.61
Angle		ω/deg	
C(1) - O(1) - C(2)	119.6(8)	116.8(6)	117.3(2)
C(7) - O(2) - C(8)	120.8(7)	118.0(7)	116.9(2)
C(11) - O(3) - C(12)	_	114.6(7)	113.2(2)
C(13) - O(4) - C(14)	_	110.3(7)	112.5(2)
C(15) - O(5) - C(16)	—	_	112.4(2)
O(1) - C(2) - C(3)	125.3(9)	126.6(8)	124.3(2)
O(1) - C(2) - C(7)	114.5(8)	113.3(7)	115.9(2)
O(2) - C(7) - C(2)	113.3(8)	116.5(6)	115.6(2)
O(2)-C(7)-C(6)	125.9(9)	123.3(8)	124.2(2)

bond angles in molecules **3a,c,d** are increased, on the average, to $124.9(6)^{\circ}$, whereas the O(1)–C(2)–C(7) and O(2)-C(7)-C(2) bond angles are decreased, on the average, to $114.9(6)^{\circ}$. Such distortions lead to a decrease in the distance between the O(1) and O(2) atoms to 2.49–2.61 Å, which is smaller than the sum of the van der Waals radii (~2.8 Å). This is mainly associated with the conjugation of the lone electron pairs of the O(1)and O(2) atoms located on the p orbitals with the benzene ring.^{10,11} This conjugation is evidenced by the predominantly sp^2 -hybridized state of the O(1) and O(2) atoms, resulting in the substantially shorter $O(1)/O(2)-C_{Ar}$ distances compared to the $O(1)/O(2)-C_{Alk}$ distances (aver., 1.361(8) and 1.443(8) Å, respectively) and the larger bond angles at the O(1) and O(2) atoms compared to the bond angles at the other O atoms (aver., 118.2(5) and $112.6(4)^{\circ}$, respectively). This conjugation is favored by the conformations of the C(1)-O(1)-C(2)-C(3) and C(8) - O(2) - C(7) - C(6) fragments characterized by the rather small torsion angles $(0.8-14.2^{\circ})$. It should be noted that the shortest O(1)...O(2) distance and the largest deviations of the CAlk-O-CAr-CAr torsion angles from the values ideal for conjugation (0 or 180°) were found in compound 3a. This undoubtedly reflects the conformational strain of the 12-membered macroheterocycle.

In all compounds, both sulfur atoms are located outside the macrocyclic cavity, which is characteristic of the single-crystal structures of benzothiacrown ethers.^{11,12} In macrocycles with this geometry, the orbitals of the lone electron pairs on the sulfur atoms should point away from the center of the macrocycle. Taking also into account that the distance between the S(1) and S(2) atoms in compounds **3c** and **3d** is rather large (7.64 and 8.01 Å, respectively), it can be concluded that the conformations of the dithiacrown macrocycles observed in the crystals are unfavorable for the formation of inclusion complexes with metal ions. The data on the efficient extraction of Pd^{II} salts with compounds **3a,c,d** presented below suggest that their dithiacrown systems are rather flexible in solution due to which these systems can relatively easily adopt conformations favorable for the complex formation. This assumption agrees well with the fact that the macrocycle in the crystal structure of **3a** exists in two different conformations.

The nitro derivatives of benzodithiacrown ethers 3a-dwere tested as reagents for extraction of palladium(II), platinum(IV), and rhodium(III) salts from hydrochloric acid solutions. Solutions of K₂[PdCl₄], K₂[PtCl₆], and Na₃[RhCl₆] at the concentration $C_{\rm M} = 2 \cdot 10^{-3} \text{ mol } L^{-1}$ in HCl ($C_A = 0.7 \text{ mol } L^{-1}$) were used as models. The extraction was carried out with the use of solutions of compounds 3a-d in dichloromethane at the concentration $C_{\rm F} = 2 \cdot 10^{-3} \text{ mol } \text{L}^{-1}$. We chose dichloromethane because of high solubility of the compounds under study in this organic solvent and the fast phase separation after extraction. The use of carbon tetrachloride, benzene, or toluene as the solvent resulted in the formation of phases of difficultly separable emulsions in the course of mixing. The data on the extraction of Pd^{II}, Pt^{IV}, and Rh^{III} salts under the above-described conditions are presented in Table 5. As can be seen from these data, benzodithiacrown ethers are rather efficient extractants for palladium(II), which could be expected because PdII, being a soft acid (in accord with Pearson's hard-soft acid-base principle), forms stable complexes with S- and S,N-containing molecules. Because of this, the compounds under study proved to be inefficient for extraction of platinum(IV) and rhodium(III) belonging to hard acids. In addition, it should be taken into account that highly charged rhodium(III) complexes are difficult to extract because of their high hydrophilicity. Among the nitro derivatives of benzodi-

Table 5. Distribution coefficients (D_M) for extraction of palladium(II), platinum(IV), and rhodium(III) salts $(C_M = 2 \cdot 10^{-3} \text{ mol } L^{-1})$ from an HCl solution $(C_A = 0.7 \text{ mol } L^{-1})$ with solutions of extractants **3a-d** $(C_E = 2 \cdot 10^{-3} \text{ mol } L^{-1})$ in dichloromethane

Com-		D_{M}^{*}	
pound	Pd ^{II}	Pt ^{IV}	Rh ^{III}
3 a	0.46	0.045	0.030
3b	22.4	0.037	0.025
3c	0.79	0.050	0.033
3d	4.89	0.043	0.028

 $*D_{\rm M} = (0.002 - C_{\rm aq}^{\rm eq})/C_{\rm aq}^{\rm eq}$, where $C_{\rm aq}^{\rm eq}$ is the equilibrium concentration of metals in the aqueous phase after extraction.

thiacrown ethers under examination, compound **3b** containing the 15-membered macrocycle is characterized by the largest distribution coefficient in the extraction of palladium(II). This is apparently due to the correspondence between the sizes of the complex ion and the macrocyclic ligand. However, the unambiguous conclusion can be drawn only after the synthesis of individual palladium complexes with the compounds in question.

To summarize, we developed new convenient and efficient procedures for the synthesis of nitro and amino derivatives of benzothiacrown ethers with macrocycles of different size and different combinations of heteroatoms O and S. In the crystalline state, the sulfur atoms of the dithiacrown fragment were demonstrated to be oriented unfavorable for the simultaneous coordination of the metal ion. However, the flexible macroheterocyclic fragment can undergo a structural rearrangement in solution, thus providing good binding of Pd^{II} salts. This was demonstrated by experiments on extraction. High selectivity of extraction of Pd^{II} salts compared to that of Pt^{IV} and Rh^{III} salts was found.

Experimental

The ¹H and ¹³C NMR spectra were recorded on a Bruker DRX500 spectrometer (500.13 and 125.76 MHz, respectively) in CDCl₃ or DMSO-d₆ using the solvent as the internal standard ($\delta_{\rm H}$ 7.27 and 2.50; $\delta_{\rm C}$ 77.00 and 39.43, respectively). The chemical shifts and spin-spin coupling constants were measured with an accuracy of 0.01 ppm and 0.1 Hz, respectively. Two-dimensional homonuclear ¹H—¹H COSY and heteronuclear ¹H—¹³C COSY (HSQC and HMBC) spectra were used for the assignment of the proton and carbon signals. The mass spectra were obtained on Varian MAT 311A and Finnigan MAT-212 instruments. The high-resolution mass spectra were measured on a Finnigan MAT-212 instrument (perfluorokerosene as the standard) using a direct inlet system (the ionization energy was 60 or 70 eV). The IR spectra were recorded on Shimadzu IR-435 and Bruker IFS-113v spectrophotometers in films or KBr pellets.

The course of the reactions was monitored by TLC on DC-Alufolien Kieselgel 60 F_{254} plates (Merck). Column chromatography was performed with the use of silica gel (Kieselgel 60, 0.063–0.100 mm, Merck).

Elemental analyses were carried out in the Laboratory of Microanalysis of the A. N. Nesmeyanov Institute of Organoelement Compounds of the Russian Academy of Sciences and in the Center of Collaborative Research of the M. V. Lomonosov Moscow State Academy of Fine Chemical Technology.

The melting points were measured on a MEL-Temp II instrument in capillaries.

Dithiols $2\mathbf{a}-\mathbf{c}$ were commercial products (Aldrich). 3,6,9-Trioxa-1,11-undecanedithiol (2d), 1,2-bis(2-chloroethoxy)-4-nitrobenzene (1a), and 1,2-bis(2-iodoethoxy)-4nitrobenzene (1b) were prepared according to procedures described earlier.^{6,13}

12-Nitro-2,3,5,6,8,9-hexahydro-1,10,4,7-benzodioxadithiacyclododecene (3a). A solution of diiodide 1b (3.33 g, 7.2 mmol) and 1,2-ethanedithiol (2a) (0.66 mL, 7.9 mmol) in ethanol (450 mL) was added dropwise with stirring and refluxing to a 1 : 1 aqueous-ethanolic solution (360 mL) of Cs_2CO_3 (11.74 g, 36 mmol) under argon. The reaction mixture was refluxed for 20 h and concentrated *in vacuo*. Water (200 mL) was added to the residue, and the mixture was extracted with chloroform. The extracts were concentrated *in vacuo*, and the residue was purified by silica gel column chromatography using benzene as the eluent. The yield was 1.04 g (48%).

Nitrobenzodithiacrown ethers 3b-d (general procedure). A solution of dichloride 1a (2.02 g, 7.2 mmol) and dithiol 2b-d (7.9 mmol) in ethanol (300 mL) was added dropwise with stirring and refluxing to a 1 : 1 aqueous-ethanolic solution (360 mL) of M_2CO_3 (M = Li, Na, or K) (36 mmol) under argon. The reaction mixture was refluxed for 48 h (for compounds 3b,c) or 77 h (for compound 3d) and concentrated *in vacuo*. Water (200 mL) was added to the residue, and the mixture was extracted with chloroform. The extracts were concentrated *in vacuo*, and the residue was purified by silica gel column chromatography using benzene and benzene—AcOEt (5 : 1) for **3b**, benzene—AcOEt (10 : 1) for **3c**, and benzene—AcOEt (5 : 1) and then benzene—AcOEt (1 : 1) for **3d** as the eluents. The yields, physicochemical parameters, and spectroscopic characteristics of compounds **3b**—**d** are given in Tables 1—3.

1,2-Bis[2-(2-hydroxyethoxy]-4-nitrobenzene (7) and **2-[2-(2-hydroxyethoxy]-5-nitrophenol (8).** A solution of 2-(2-chloroethoxy)ethanol (6) (5.1 mL, 48.3 mmol) in *n*-butanol (15 mL) was added dropwise with stirring to a boiling solution of 4-nitropyrocatechol (5) (2.50 g, 16.1 mmol) and NaOH (2.07 g, 51.8 mmol) in *n*-butanol (50 mL) under argon. The reaction mixture was refluxed for 60 h and then concentrated *in vacuo*. Water was added to the residue, and the mixture was extracted with chloroform. The extracts were concentrated *in vacuo*, and the residue was purified by silica gel column chromatography using AcOEt as the eluent. Compounds **7** and **8** were obtained in yields of 1.37 g (28%) and 0.10 g (3%), respectively. The high-resolution mass spectrum of compound **7**, found: m/z 331.1268 [M]⁺. C₁₄H₂₁NO₈. Calculated:

Table 6. Crystallographic parameters and the X-ray diffraction data collection and refinement statistics for compounds **3a,c,d**

Parameter	3a	3c	3d
Molecular formula	C ₁₂ H ₁₅ NO ₄ S ₂	C ₁₆ H ₂₃ NO ₆ S ₂	C ₁₈ H ₂₇ NO ₇ S ₂
Μ	301.37	389.47	433.53
Crystal system	Monoclinic	Orthorhombic	Orthorhombic
Space group	$P2_1/c$	$P2_{1}2_{1}2_{1}$	Pbca
$a/\text{\AA}$	15.0682(12)	4.7106(3)	8.1101(2)
b/Å	10.4511(8)	12.8364(9)	18.5248(5)
c/Å	8.6043(6)	30.351(2)	27.3007(8)
β/deg	97.526(4)	90	90
$V/Å^3$	1343.33(18)	1835.3(2)	4101.60(19)
Z	4	4	8
$d_{\rm calc}/{\rm g~cm^{-3}}$	1.490	1.410	1.404
F(000)	632	824	1840
$\mu(Mo-K_{\alpha})/mm^{-1}$	0.405	0.322	0.299
Crystal dimensions/mm	0.46×0.12×0.08	$0.40 \times 0.08 \times 0.06$	0.36×0.36×0.16
Scan mode/θ-scanning range/deg	ω/2.38—29.00	ω/1.72—28.99	ω/1.49—29.00
Ranges	$-16 \le h \le 20$.	$-6 \le h \le 5$.	$-10 \le h \le 9$.
of reflection	$-13 \le k \le 14$,	$-17 \le k \le 15$,	$-25 \le k \le 24$,
indices	$-11 \le l \le 11$	$-35 \le l \le 41$	$-37 \le l \le 32$
Number of measured reflections	7845	12533	21988
Number of independent	3414	4819	5281
reflections (R_{int})	(0.1221)	(0.1141)	(0.0593)
Number of reflections with $I > 2\sigma(I)$	1805	3188	3876
Number of refinement variables	189	226	361
R Factors based on	$R_1 = 0.1681$,	$R_1 = 0.1277,$	$R_1 = 0.0494,$
reflections with $I > 2\sigma(I)$	$wR_2 = 0.3190$	$wR_2 = 0.2846$	$wR_2 = 0.0867$
<i>R</i> Factors based on	$R_1 = 0.2587$,	$R_1 = 0.1765,$	$R_1 = 0.0779$,
all reflections	$wR_2 = 0.3509$	$wR_2 = 0.3069$	$wR_2 = 0.0932$
Goodness-of-fit on F^2	1.095	1.097	1.055
Residual electron density (min/max)/e Å ⁻³	-0.645/0.836	-0.606/1.295	-0.278/0.379

M = 331.1267. The high-resolution mass spectrum of compound **8**, found: m/z 243.0742 [M]⁺. C₁₀H₁₃NO₆. Calculated: M = 243.07428.

1,2-Bis[2-(2-chloroethoxy)ethoxy]-4-nitrobenzene (9). A solution of SOCl₂ (10.8 mL, 148 mmol) in chloroform (10 mL) was added dropwise to a solution of compound **7** (2.4 g, 7.25 mmol) and pyridine (1.2 mL, 14.9 mmol) in chloroform (10 mL) precooled to 0 °C. The reaction mixture was refluxed for 25 h and then cooled. A 5% HCl solution was added with stirring. The organic layer was separated, and the aqueous layer was extracted with chloroform. The organic phases were combined and concentrated *in vacuo*, and the residue was purified by silica gel column chromatography using a 5 : 1 benzene—AcOEt mixture as the eluent. The yield was 2.5 g (93%). The high-resolution mass spectrum, found: m/z 367.0589 [M]⁺. C₁₄H₁₉Cl₂NO₆. Calculated: M = 367.0589 (³⁵Cl).

15-Nitro-2,3,5,6,8,9,11,12-octahydro-1,4,10,13,7-benzotetraoxathiacyclopentadecene (3e). A solution of dichloride 9 (0.21 g, 0.57 mmol) in ethanol (20 mL) was added dropwise with stirring and refluxing to a 1 : 1 aqueous-ethanolic solution (40 mL) of $Na_2S \cdot 9H_2O$ (0.75 g, 3.1 mmol) and Na_2CO_3 (0.08 g, 0.74 mmol) under argon. The reaction mixture was refluxed for 15 h, cooled, and concentrated *in vacuo*. Water was added to the residue, and the mixture was extracted with chloroform. The extracts were concentrated, and the residue was purified by silica gel column chromatography using a 5 : 1 benzene—AcOEt mixture as the eluent. The yield was 0.14 g (73%).

Aminobenzothiacrown ethers 10a-e (general procedure). A solution of N₂H₄·H₂O (0.47 mL, 9.7 mmol) in ethanol (10 mL) was added dropwise with stirring and refluxing to a solution of nitro compound 3a-e (0.3 mmol) and the Pt/C (10%) catalyst (13 mg) in ethanol (40 mL) under argon. The reaction mixture was refluxed for 3-8 h until the starting nitro compound was completely consumed (TLC monitoring), and the catalyst was filtered off. The filtrate was concentrated *in vacuo* to dryness, water was added to the residue, and the mixture was extracted with chloroform. The extracts were concentrated *in vacuo*. The purity of the reaction products was confirmed by ¹H NMR spectroscopy. The yields, physicochemical parameters, and spectroscopic characteristics of compounds 10a-e are given in Tables 1-3.

X-ray diffraction study. Single crystals of compounds 3a,c,d suitable for X-ray diffraction were grown by slow evaporation of solutions in a hexane-CH₂Cl₂ mixture. Single crystals of dithiacrown ethers coated with perfluorinated oil were mounted on a Bruker SMART-CCD diffractometer under a flow of cooled nitrogen (T = 120 K). The experimental X-ray diffraction data sets were collected from the single crystals using the ω -scanning technique and Mo-K α radiation ($\lambda = 0.71073$ Å). The X-ray reflections were processed using the Bruker SAINT software.¹⁴ The structures of **3a,c,d** were solved by direct methods and refined by the full-matrix least-squares method based on F^2 with anisotropic displacement parameters for all nonhydrogen atoms. The hydrogen atoms were placed geometrically and refined using a riding model (for **3a,c**) or isotropically (for **3d**). All calculations were performed with the use of the SHELXTL-Plus program package.¹⁵ Crystallographic parameters and the X-ray diffraction data collection and refinement statistics are given in Table 6.

The structures of 3a,c are characterized by rather high R factors because of considerable mosaicity of the crystals

and their weak reflection ability (the I/σ ratio was 3.9 and 3.2, respectively). High mosaicity of the crystals made it impossible to choose the parameters for the correct integration of experimental reflections using the SAINT program. In these experiments, a large number of residual electron density peaks were found in the region of the crown fragment, which is apparently indicative of a certain disorder of the macrocycle manifested in the existence of a series of similar conformations. However, we failed to extract these minor disorder components. High flexibility of the macrocycles resulting in their disorder in the crystals is, apparently, responsible for strong mosaicity of the crystals.

The atomic coordinates and other experimental data were deposited with the Cambridge Structural Database* (CSD refcodes 615202 (**3a**), 615203 (**3c**), and 615204 (**3d**)).

Extraction was carried out in calibration tubes with ground stoppers at room temperature. The volumetric ratio of the aqueous phase to the organic phases was 1 : 1. The stirring time was 10 min. The aqueous phases were analyzed after extraction by the spectrophotometric method described earlier.¹⁶

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