Synthesis of New Macrocyclic Bis-Dithiocarbonates

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Macrocyclic compounds such as crown ethers or cryptands have received considerable attention in recent years because of the ability of these compounds to complex with metal cations. Synthetic macrocyclic di- and tetra-ester compounds have been reviewed[1], but no papers concerning macrocyclic ether-thiodiesters have been published. This article describes the synthesis of the cyclic, and possibly chiral, bis-dithiocarbonates **3aa-ee** obtained by xanthation of α-diols **1a-e** and substitution with α,ω-dibromoalkanes or ethers (**2a-e**).

Compounds **3** were prepared from the appropriate α-diol **1** of the cyclic, carbocyclic, or carbohydrate series. The xanthation reaction was carried out according to the previously reported procedure[2] and the substitution reaction was performed under high dilution conditions. The crude mixture is composed of **3** and the dimer **4** which is separated by column chromatography. In the case of 2,3-butanediol (**1a**) and 1,2-cyclohexanediol (**1b**), the *trans*- and *cis*-bis-dithio-

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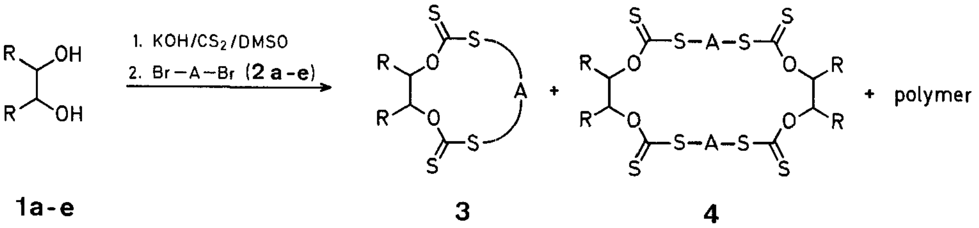
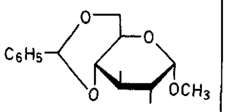
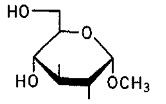


1	R	R	2	A
a	H_3C	H_3C	a	$-(CH_2)_3-$
b	$-(CH_2)_4-$		b	$-(CH_2)_4-$
c	$-(CH_2)_2-O-(CH_2)_2-$		c	$-(CH_2)_5-$
d			d	$-(CH_2)_6-$
e			e	$-(CH_2)_2-O-(CH_2)_2-$

carbonates were successively eluted and characterized by spectroscopic methods (I.R., N.M.R., and M.S.) and acidic hydrolysis.

The *cis*-bis dithiocarbonates **3** showed one I.R. band at 880 cm⁻¹ while the *trans* isomers gave a band at 850 cm⁻¹. The identification of diastereoisomers was confirmed for **3b** by the cleavage of the dithiocarbonate with sulfuric acid into *trans*- or *cis*-1,2-cyclohexanediol. The limited hydrolysis of **3de** with acetic acid leads to the deprotected sugar **3ee** which constitutes a new type of chiral crown ether.

This synthesis of chiral or achiral thio-crown ether esters has lead to a qualitative and quantitative study of their specific complexation abilities, which is now in progress.

Macrocyclic Bis-dithiocarbonates 3 and 4; General Procedure:
A mixture of the diol **1** (0.01 mol), dry dimethyl sulfoxide (50 ml), and powdered potassium hydroxide (0.025 mol) is stirred for 2–3 h at room temperature; then carbon disulfide (0.025 mol) is added dropwise over a 30 min period and stirring is continued for 4–5 h. The appropriate polymethylene (or ether-polymethylene) dibromide **2** (0.01 mol), dissolved in a mixture of benzene/dimethyl sulfoxide (3:1; ~1000 ml) is added. The resulting solution is stirred for 15 min and then maintained at room temperature for 24 h. The resulting yellow solution is poured into water (700 ml). The organic layer is separated, washed with water, and dried with sodium sulfate. After filtration, the solvent is removed under vacuum and the resulting yellow syrup is chromatographed on a silica gel column [eluent: tetrachloromethane, then tetrachloromethane/dichloromethane (1:1)] and then crystallized to give pure **3** and **4** (see Table 1). The physical properties and spectroscopic data for **3** and **4** are given in the Tables 1 and 2. A solution of **3de** (0.001 mol) in 80% acetic acid (10 ml) is heated at 70 °C, after 2 h, neutralized with sodium carbonate, and extracted with chloroform. The combined extracts are dried with sodium sulfate and reduced in volume under vacuum (1 torr). The residue is recrystallized from ethyl acetate; yield: 90%.

Table 1. Macrocyclic Bis-dithiocarbonates 3 and 4 prepared

Diol	Dibromide	Product	Yield[a] [%]	m.p. [°C][b] (solvent)	Molecular formula[c]	M.S.[d] *m/e* (M^+)
1a	**2a**	*trans*-**3aa**	14	125–126 (hexane)	$C_9H_{14}O_2S_4$ (282.4)	282
1b	**2a**	*cis*-**3ba** *trans*-**3ba**	23 (51)	125–126 (hexane) 179–180 (C_2H_5OH)	$C_{11}H_{16}O_2S_4$ (308.5)	308
1b	**2a**	**4ba**	4	180–181 (C_2H_5OH)	$C_{22}H_{32}O_4S_8$ (617.0)	617
1b	**2b**	*cis*-**3bb** *trans*-**3bb**	22 (46)	126–127 (hexane) 140–141 (C_2H_5OH)	$C_{12}H_{18}O_2S_4$ (322.5)	322
1b	**2c**	*trans*-**3bc**	20 (38)	148–149 (C_2H_5OH)	$C_{13}H_{20}O_2S_4$ (336.5)	336
1b	**2c**	**4bc**	7	109–111 (C_2H_5OH)	$C_{26}H_{40}O_4S_8$ (673.0)	—
1b	**2d**	*cis*-**3bd** *trans*-**3bd**	26 (32)	95–96 (hexane) 120–121 (hexane)	$C_{14}H_{22}O_2S_4$ (350.6)	350
1b	**2e**	*cis*-**3be** *trans*-**3be**	— (47)	160–161 (C_2H_5OH) 240–241 ($CHCl_3$)	$C_{12}H_{18}O_3S_4$ (338.5)	338
1c	**2e**	**3ce**	61	90–91 (hexane)	$C_{10}H_{16}O_4S_4$ (328.5)	328
1d	**2c**	**3de**	— (40)	190–122 (C_2H_5OAc)	$C_{20}H_{24}O_7S_4$ (504.6)	504
		3ee[e]	90	90–92 (C_2H_5OAc)	$C_{14}H_{20}O_7S_4$ (428.6)	428

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[a] For a mixture of *cis*- and *trans*-isomers. The numbers in brackets are obtained for *cis*- and *trans*-isomers from *trans*-1,2-cyclohexanediol.

[b] Melting points were determined on a Buchi apparatus (capillary method) and are uncorrected.

[c] For a mixture of *cis*- and *trans*-isomers; the microanalyses were in satisfactory agreement with the calculated values (C ±0.45, H ±0.21, S ±0.29).

[d] Mass spectra were taken with a Varian-MAT CH instrument operating at 70 eV for separated *cis*- and *trans*-isomers.

[e] Prepared by hydrolysis of **3de**.

Table 2. Spectral Data for Products **3** and **4**

Product	I.R. (KBr)[a,b] ν [cm^{-1}]	^{1}H-N.M.R. (60 MHz, $CDCl_3$)[c] δ [ppm]
trans-**3aa**	2980 (m), 2940 (m), 2920 (m), 1450 (w), 1430 (w), 1410 (m), 1380 (s), 1350 (s), 1255 (vs), 1215 (vs), 1180 (s), 1130 (m), 1060 (vs), 1040 (vs), 1020 (s), 950 (w), 850 (s), 790 (w)	5.75–5.20 (m, 2H, >CH—O); 3.64–3.00 (m, 2H, CH_2); 2.92–2.42 (m, 2H, SCH_2); 2.35 (m, 2H, SCH_2); 1.47 (d, J=6 Hz, 6H, CH_3)
cis-**3ba**	2960 (m), 2940 (m), 2880 (m), 1440 (s), 1420 (w), 1340 (m), 1310 (w), 1265 (vs), 1220 (vs), 1205 (vs), 1115 (m), 1060 (vs), 1020 (vs), 1000 (vs), 880 (m)	5.80–5.46 (m, 2H, >CH—O); 3.72–3.12 (m, 2H, CH_2); 2.98–2.18 (m, 4H, SCH_2); 2.20 [m, 8H, $(CH_2)_4$]
trans-**3ba**	2960 (m), 2940 (m), 2860 (m), 1470 (w), 1460 (w), 1440 (m), 1420 (m), 1370 (w), 1350 (s), 1325 (m), 1260 (vs), 1240 (vs), 1210 (vs), 1140 (s), 1090 (s), 1060 (vs), 1015 (s), 950 (w), 850 (m), 790 (w)	5.43–5.05 (m, 2H, >CH—O); 3.75–3.19 (m, 2H, CH_2); 2.92–2.34 (m, 4H, SCH_2); 2.25–1.05 [m, 8H, $(CH_2)_4$]
4ba	2960 (m), 2930 (m), 2860 (m), 1450 (s), 1440 (m), 1430 (w), 1420 (m), 1350 (w), 1330 (w), 1310 (w), 1260 (s), 1210 (vs), 1140 (m), 1050 (vs), 1010 (s), 960 (w), 850 (w)	6.00–5.57 (m, 4H, >CH—O); 3.30–2.87 (m, 8H, SCH_2); 2.53–1.10 [m, 16H, $(CH_2)_4$]
cis-**3bb**	2960 (s), 2860 (m), 1465 (w), 1450 (m), 1440 (s), 1420 (w), 1370 (w), 1350 (w), 1340 (w), 1310 (m), 1280 (s), 1260 (s), 1240 (s), 1220 (vs), 1135 (w), 1118 (s), 1075 (vs), 1050 (vs), 1030 (vs), 1008 (vs), 950 (m), 885 (m), 810 (w), 790 (w)	6.00–5.60 (m, 2H, >CH—O); 3.80–3.20 (m, 2H, CH_2); 2.98–2.11 (m, 4H, SCH_2); 2.10–1.40 [m, 10H, $(CH_2)_5$]
trans-**3bb**	2980 (w), 2950 (s), 2930 (s), 2860 (m), 1465 (w), 1450 (s), 1430 (s), 1410 (w), 1360 (s), 1345 (w), 1320 (w), 1280 (s), 1250 (w), 1230 (w), 1210 (vs), 1140 (s), 1090 (s), 1070 (s), 1045 (vs), 1010 (vs), 950 (w), 910 (w), 850 (m), 760 (w), 720 (w)	5.75–5.40 (m, 2H, >CH—O); 3.33–3.00 (m, 4H, SCH_2); 2.10–1.25 and 2.70–2.30 (2m, 12H, CH_2)
trans-**3bc**	2980 (m), 2940 (m), 2900 (m), 1460 (s), 1440 (w), 1410 (m), 1350 (w), 1340 (w), 1320 (w), 1280 (s), 1240 (s), 1230 (w), 1200 (vs), 1150 (w), 1135 (s), 1090 (w), 1070 (s), 1040 (vs), 950 (w), 910 (m), 860 (m), 740 (w)	6.08–5.50 (m, 2H, >CH—O); 3.20–2.75 (m, 4H, SCH_2); 2.65–1.00 (m, 14H, CH_2)
4bc	2920 (s), 2840 (s), 1450 (m), 1410 (w), 1350 (w), 1310 (w), 1200 (vs), 1140 (m), 1050 (vs), 1010 (s), 840 (w)	6.00–5.58 (m, 4H, >CH—O); 3.25–2.70 (m, 8H, SCH_2); 2.61–2.10 and 2.00–1.08 (2m, 28H, CH_2)
cis-**3bd**	2970 (m), 2940 (s), 1460 (m), 1440 (m), 1420 (m), 1370 (w), 1350 (w), 1340 (m), 1310 (m), 1290 (m), 1270 (s), 1250 (s), 1220 (vs), 1200 (vs), 1130 (w), 1120 (s), 1075 (vs), 1060 (vs), 1030 (vs), 1005 (vs), 950 (w), 930 (w), 920 (w), 880 (s), 710 (w)	6.18–5.86 (m, 2H, >CH—O); 3.13–2.73 (m, 4H, SCH_2); 2.32–1.36 (m, 16H, CH_2)
trans-**3bd**	2960 (m), 2940 (s), 2860 (m), 1450 (s), 1440 (s), 1430 (s), 1400 (w), 1350 (m), 1330 (w), 1315 (w), 1308 (w), 1290 (w), 1270 (m), 1250 (s), 1190 (vs), 1130 (s), 1060 (vs), 1040 (vs), 1010 (vs), 960 (w), 850 (w), 790 (w), 740 (m)	6.04–5.69 (m, 2H, >CH—O); 3.42–3.11 (m, 4H, SCH_2); 2.53–2.10 and 2.11–1.21 (2m, 16H, CH_2)
cis-**3be**	2970 (w), 2960 (m), 2930 (s), 2860 (m), 1480 (m), 1470 (m), 1450 (m), 1420 (w), 1385 (w), 1380 (w), 1370 (w), 1320 (w), 1300 (s), 1270 (s), 1250 (w), 1230 (vs), 1210 (s), 1150 (w), 1120 (s), 1090 (s), 1060 (vs), 1030 (s), 1010 (s), 960 (w), 940 (w), 920 (w), 880 (s), 830 (w)	6.05–5.69 (m, 2H, >CH—O); 4.10–2.70 [m, 8H, $(CH_2)_2$—O—$(CH_2)_2$]; 2.21–1.85 and 1.85–1.30 (2m, 8H, CH_2)
trans-**3be**	2980 (w), 2950 (w), 2920 (w), 2880 (m), 2850 (m), 1470 (w), 1450 (m), 1440 (w), 1390 (m), 1350 (s), 1320 (m), 1280 (s), 1245 (s), 1235 (s), 1210 (vs), 1180 (m), 1125 (vs), 1090 (w), 1070 (s), 1060 (s), 1040 (vs), 1000 (vs), 950 (w), 910 (w), 860 (m), 845 (m)	6.03–5.54 (m, 2H, >CH—O); 4.05–2.93 [m, 8H, $(CH_2)_2$—O—$(CH_2)_2$]; 1.93–1.20 (m, 8H, CH_2S)
3ce	2980 (w), 2940 (m), 2900 (m), 2860 (m), 1480 (m), 1470 (m), 1450 (m), 1440 (m), 1410 (w), 1400 (w), 1385 (w), 1360 (w), 1310 (s), 1260 (s), 1240 (s), 1220 (vs), 1130 (vs), 1120 (s), 1090 (m), 1045 (w), 1020 (w), 1000 (w), 940 (w), 880 (w), 830 (w), 800 (w), 765 (w), 740 (w)	4.90–4.68 (m, 4H, >CH—O); 4.00–3.63 (m, 8H, CH_2OCH_2); 3.28–2.93 (m, 4H, CH_2S)
3de	3060 (w), 2980 (w), 2920 (w), 2860 (m), 1460 (m), 1410 (m), 1380 (s), 1360 (m), 1340 (m), 1290 (s), 1240 (vs), 1210 (vs), 1180 (vs), 1120 (vs), 1070 (vs), 1040 (vs), 1030 (vs), 980 (vs), 930 (w), 860 (w), 760 (s), 700 (s)	7.70–7.20 (m, 5H_{arom}); 7.10–6.50 (m, H-3); 5.8 (dd, H-2); 5.65 (s, C_6H_5—C$\underline{H}$); 5.30 (d, H-1); 4.40–3.00 (m, 15H)[d]
3ee	3380 (vs), 2920 (m), 2850 (w), 1445 (w), 1370 (m), 1285 (m), 1190 (s), 1060 (vs), 900 (w)	6.80–6.40 (m, H-3, $J_{3,2}$=10.2 Hz, $J_{3,4}$=8.2 Hz); 5.70 (dd, H-2, $J_{2,3}$=10.2 Hz, $J_{2,1}$=8.4 Hz); 5.30 (d, H-1, $J_{1,2}$=8.4 Hz); 4.8 (m, OH); 4.0–3.3 (m, 15H)

[a] Recorded with a Perkin Elmer 237 spectrophotometer; w = weak, m = medium, s = strong, vs = very strong.

[b] S—CH_2, ν = 1430–1410 and 1340–1320 cm^{-1}; C=S, ν = 1316–1000 cm^{-1}; see E. Block, *Reactions of Organosulfur Compounds*, Vol. 37, Academic Press, New York, 1978, p. 296.

[c] Recorded with a Varian EM-360 spectrometer.

[d] Recorded at 80 MHz in acetone-d_6 with a Bruker WP-80 spectrometer.

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[1] J. S. Bradshaw, G. E. Maas, R. M. Izatt, J. J. Christensen, *Chem. Rev.* **79**, 37 (1979).

[2] A. Faure, B. Kryczka, G. Descotes, *Carbohydr. Res.* **24**, 127 (1979).