Synthesis and Reductive Desulfurization of Crown Ethers Containing Thiophene Subunit[1)]

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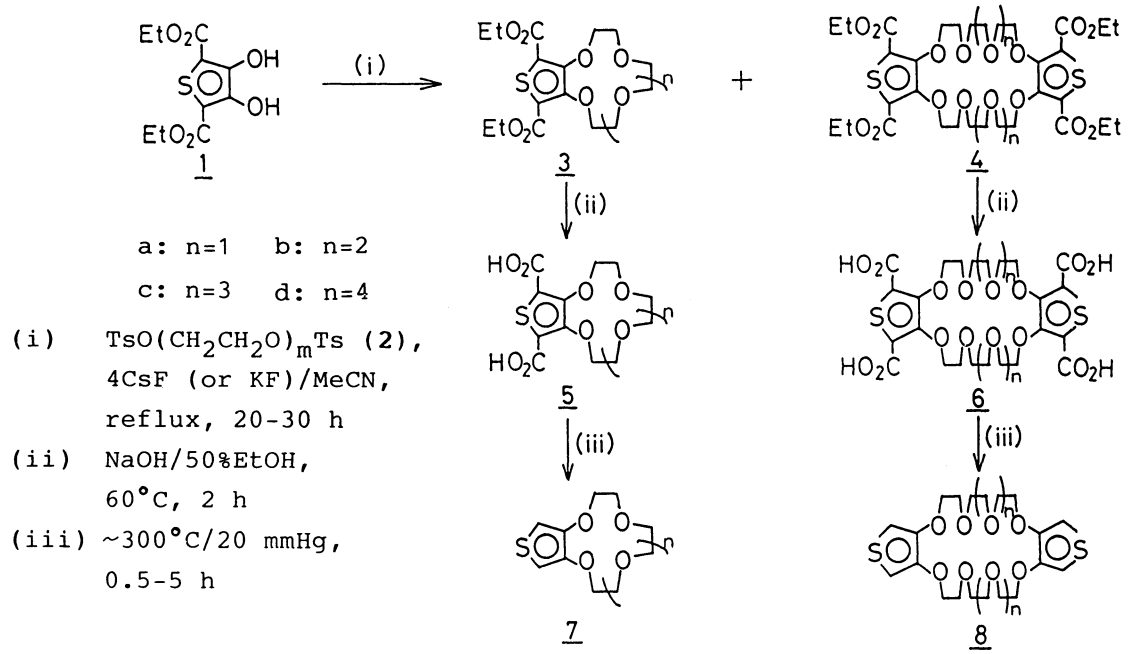
Crown ethers containing 3,4-thiophenediyl and 3,4-thiophenediylbis(methylene) subunits as a ring constituent were prepared starting from 2,5-bis(ethoxycarbonyl)-3,4-thiophenediol and 2,5-dichloro-3,4-bis(chloromethyl)thiophene, respectively. A Raney nickel desulfurization of the thiophene-containing crown ethers afforded crown ethers having two adjacent side chains, such as a methyl or ethoxycarbonylmethyl group. The extraction ability of these crown ethers towards alkali metal cations was also examined by the solvent extraction method.

In spite of much work, only a few crown ethers containing a thiophene subunit as part of the macrocyclic ring have appeared in the literature. The crown ethers so far prepared are restricted to those[2)] containing a 2,5-dimethyl-3,4-thiophenediylbis(methylene) unit, thiacrown ethers[3)] containing a 2,5-thiophenediylbis(methylene) unit, crown esters[4)] derived from 2,5-thiophenedicarboxylic acid, and azacrown ethers[5)] derived from 2,5-thiophenedicarbaldehyde. None of the thiophene analogues (thienocrown ether) of benzocrown ether, in which thiophene nucleus is directly incorporated into the crown ether ring, has been synthesized. We report here on the syntheses of crown ethers **7** and **8** (3,4-thienocrown ether) containing a 3,4-thiophenediyl subunit and those (**12**, **13**) containing a 3,4-thiophenediylbis(methylene) subunit and their extraction ability towards alkali metal cations.

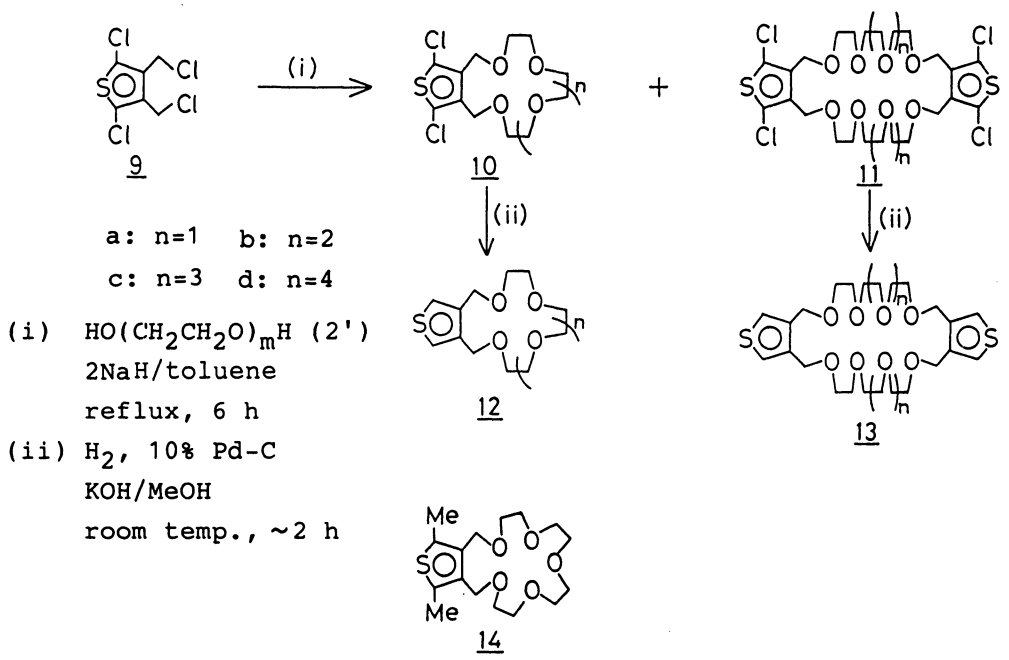
Recently, functionalized and substituted crown ethers received attention in view of the immobilization[6)] and modification of the properties of crown ethers.[7)] In this connection, we also report on the transformation of the thiophene-containing crown ethers into novel crown ethers having two adjacent methyl or ethoxycarbonylmethyl groups by a reductive desulfurization of the thiophene ring.

Results and Discussion

Synthesis. Thiophenediols, potential starting substances for the preparation of the thienocrown ethers, are unstable and easily decompose in air, although the corresponding dialkoxythiophenes are rather stable. This seems to be the principal reason for the lack of thienocrown ethers. It has been reported that 2,5-bis(ethoxycarbonyl)-3,4-thiophenediol (**1**), almost the only stable thiophenediol derivative available, reacts with 1,2-dibromoethane and bromochloromethane in the presence of a base to give 2,5-bis(ethoxycarbonyl)-



Scheme 1.



Scheme 2.

Table 1. Reaction of 2,5-Bis(ethoxycarbonyl)-3,4-thiophenediol (**1**) with Oligoethylene Glycol Ditosylates (**2**)

Reactant **2**	Base	Reaction time/h	Product	Yield/%[a]	Mp θ_m/°C
$m=3$	KF	30	**3a**	28	122—123
			4a	40	152—153
$m=4$	CsF	20	**3b**	44	66—67
			4b	2	94—95
$m=5$	CsF	25	**3c**	68	67—68
$m=6$	CsF	25	**3d**	56	41—42

a) Isolated yield based on **1** used.

3,4-ethylenedioxythiophene,[8] 2,5-bis(ethoxycarbonyl)-3,4-methylenedioxythiophene, and 6,8,14,16-tetrakis(ethoxycarbonyl)-2,4,10,12-tetraoxa-7,15-dithiatricyclo[11.3.0.0^{5,9}]hexadeca-1(16),5,8,13-tetraene,[9] respectively. The thienocrown ethers, **7** and **8**, were synthesized by the route outlined in Scheme 1. Namely, by the modification of the procedures described above, ethoxycarbonylthienocrown esters **3** (and, if any **4**) were first synthesized by the reaction of **1** and oligoethylene glycol ditosylates (**2**). The expected esters, **3** (and **4**), were obtained in relatively high yield, when **1** was reacted with **2** in refluxing MeCN for 25—30 h using CsF (KF for the synthesis of **3a**) as a base (Table 1). No satisfactory results were obtained by the use of other bases, such as NaH or EtONa, or a solvent, such as dioxane, even upon prolonged heating. Alkaline hydrolysis of **3** (or **4**) in 50% EtOH at 60 °C for 2 h gave the corresponding thienocrown acids, **5** (or **6**). It is interesting to note that the tetracarboxylic acid, **6a**, forms an adduct with four molecules of H_2O, which releases the H_2O upon heating under reduced pressure (130 °C/2 mmHg; 1 mmHg≈133.322 Pa) for 5 h. The thienocrown acids **5** (or **6**) underwent decarboxylation merely by heating at ca. 50 °C higher than their melting points under reduced pressure (20 mmHg) for 0.5—5 h to afford **7** and **8**.

The crown ethers, **12** and **13**, were synthesized as outlined in Scheme 2 in order to compare their physical properties with those of **7** and **8**. First, crown ethers **10** and/or **11**, containing a 2,5-dichloro-3,4-thiophenediylbis(methylene) unit, were prepared by the reaction of 2,5-dichloro-3,4-bis(chloromethyl)thiophene (**9**) with sodium or potassium oligoethylene glycolates according to Reinhoudt's method[2a] (Table 2). Early studies suggest that the chlorine atom(s) in chlorothiophene derivatives can be removed only with difficulty.[10] However, **10** and **11** were dechlorinated easily without any cleavage of the crown ether ring[11] by catalytic hydrogenation at room temperature in an atmospheric pressure hydrogenation apparatus; expected crown ethers **12** and **13** were obtained in good yields.

The structures of the new crown ethers were

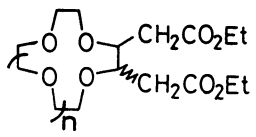
Table 2. Reaction of 2,5-Dichloro-3,4-bis(chloromethyl)thiophene (**9**) with Oligoethylene Glycols (**2'**)

Reactant **2'**	Base	Reaction time/h	Product	Yield/%[a]	Mp θ_m/°C
$m=3$	NaH	6	**10a**	6	87—88
			11a	28	98—99
$m=4$	NaH	6	**10b**	43	47—48
			11b	6	77—79
$m=5$	NaH	6	**10c**	37	45—46
			11c	8	98—100
$m=6$	*t*-BuOK	6	**10d**	38	oil[b]
			11d	2	81—83

a) Isolated yield based on **9** used. b) Bp 180 °C (bath temp)/10^{-3} mmHg.

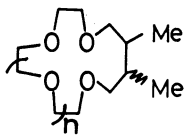
established by their elemental analyses and spectral data (MS, ^{1}H NMR, and IR).

Reductive Desulfurization. Considering the fact that thiophene ring is desulfurized by the action of Raney nickel with a complete saturation of the thiophene ring, the thiophene-containing crown ethers are potentially useful intermediates for the synthesis of crown ethers having two adjacent substituents on the macrocyclic ring. From this view, crown ethers **3**, **12**, and **13** were subjected to reductive desulfurization with Raney nickel, and found to proceed smoothly as expected. Namely, being stirred in refluxing EtOH with excess Raney nickel for 2 h, **3** yielded novel crown ethers **15** having two adjacent ethoxycarbonylmethyl groups. Similarly, novel crown ethers, **16** and **17**, having two adjacent methyl groups were obtained from **12** and **13**.



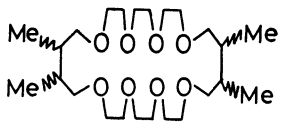
15

a: n=1
b: n=2
c: n=3
d: n=4



16

a: n=2
b: n=3
c: n=4



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An NMR spectral study suggests that the desulfurized crown ethers consist of pairs of cis and trans isomers. For example, the ^{1}H NMR spectrum (200 MHz, $CDCl_3$) of **16a** shows, together with the complex absorptions ascribable to the oxymethylene protons of the crown ring, two doublets due to methyl protons at δ 0.85 and 0.88 with the coupling constants of 6.1 and 7.2 Hz, and a multiplet at δ ca. 2 due to the adjacent methine protons. ^{13}C NMR spectrum is consistent with the assignment; two peaks for the methyl carbons at δ 13.1 and 13.8 and two peaks for the methine carbons at δ 34.3 and 35.7 together with the peaks (δ 70.2, 70.4, 70.8, 70.9, 74.5, and 74.7) due to the methylene carbons.[12]

Table 3. Extraction of Alkali Metal Picrates with Thiophene-Containing Crown Ethers[a]

Crown compd	Extractability (%)				
	Li^+	Na^+	K^+	Rb^+	Cs^+
3a	1	1	5	5	4
3b	1	4	15	8	6
3c	4	9	36	29	23
3d	5	18	55	56	52
7a	0	2	1	1	1
7b	0(2)[b]	12(25)	24(52)	14(31)	4(14)
7c	2(2)	8(21)	93(94)	83(85)	66(68)
7d	4(5)	10(17)	72(86)	93(96)	99(98)
8a	1(1)	12(39)	33(61)	48(69)	73(78)
12a	1	0	3	2	1
12b	2	11	8	6	6
12c	2	10	36	34	31
12d	4	16	51	63	68
10b	1	18	10	9	8
14[c]	2	33	24	18	10
13a	3	12	45	47	60

a) Measured by Pedersen's method[13] at 25 °C: aqueous phase: [picric acid]=7×10^{-5} M (1 M=1 mol dm^{-3}), [MNO_3]=0.1 M; organic phase (CH_2Cl_2): [crown compd]=7×10^{-4} M. H_2O:CH_2Cl_2=1:1 (v/v). b) Figures in parentheses denote the values obtained for the corresponding benzo (or dibenzo) crown ethers which were prepared according to the literatures.[14] c) Prepared according to the literature.[2a]

It should be emphasized that the present results indicate the usefulness of the incorporation of a thiophene unit for the structural modification of a crown ring.

Extraction Ability. The extraction ability of the thiophene-containing crown ethers as well as the desulfurized crown ethers towards alkali metal cations was examined by Pedersen's extraction method.[13] Tables 3 and 4 summarize the results. The thienocrown ethers, **7** and **8**, and the corresponding benzocrown

Table 4. Extraction of Alkali Metal Picrates with the Desulfurized Crown Ethers[a)]

Crown compd	Extractability (%)				
	Li^+	Na^+	K^+	Rb^+	Cs^+
15a	1	2	2	1	1
15b	4	31	13	11	6
15c	7	37	95	82	51
15d	12	21	84	87	85
18-C-6	10	31	97	96	85
16a	2	14	14	8	6
16b	5	6	75	80	75
16c	4	8	39	48	67
17	2	4	26	19	21
17-C-5[b)]	1	11	10	5	4

a) Measured under similar conditions as described in the footnote in Table 3. b) Prepared according to the literature.[15)]

ethers are similar in selectivity, but the former shows a much higher K^+/Na^+ selectivity than the latter. On the other hand, the extraction ability of the thienocrown ethers are a little lower than that of benzocrown ethers; the thiophene unit with a sulfur atom in the position opposite to the crown ring weakens the coordination interaction between the crown oxygens and the metal cations.

Crown ethers **12** and **13**, having the 3,4-thiophenediylbis(methylene) unit(s), generally exhibit a lower extractability than that of the thienocrown ethers, **7** and **8**, with the same number of oxygens. This is probably due to the less symmetry arrangement of the donor oxygen[15)] and the non-coplanarity of the thiophene ring with the crown ether ring[2b)] in the molecules. Comparisons of a series of 17-crown-5 derivatives (the parent 17-crown-5,[15)] **10b**, **12b**, **14**, and **16a**) indicate that the extractability is not affected essentially by the incorporation of the thiophene unit in the crown ring, although the selectivity for Na^+ over K^+ somewhat increases. Crown ethers **7** and **12** exhibit a similar cation selectivity with a minor difference in that **12b** shows its highest extractability for Na^+, while **7b** for K^+.

Experimental

All the melting and boiling points are uncorrected. The ^1H NMR (90 MHz, TMS as an internal reference, $CDCl_3$ solution unless otherwise noted), MS (70 eV, unless otherwise noted), and UV spectra were obtained on Hitachi R-22, Hitachi R-90H, Hitachi RMU-6M, and Hitachi 228A spectrometers, respectively. TG/DTA curves were recorded with a Seiko Denshi Kogyo TG/DTA A30 Instrument with a heating rate of 10 °C min^{-1} under N_2 stream.

2,5-Bis(ethoxycarbonyl)-3,4-thiophenediol (**1**),[9)] 2,5-dichloro-3,4-bis(chloromethyl)thiophene (**9**),[16)] and oligoethylene glycol ditosylates (**2**)[15)] were prepared as described in the literature.

General Procedure for the Syntheses of 3 and 4 by the Reaction of 2,5-Bis(ethoxycarbonyl)-3,4-thiophenediol (1) with Oligoethylene Glycol Ditosylates (2). Under an N_2 atmosphere CsF (0.06 mol; KF for the synthesis of **3a**) was added to a solution of **1** (3.9 g, 0.015 mol) in dry MeCN (250 ml); the mixture was stirred for 1 h. To the resulting yellow suspension a solution of **2** (m=4—6; 0.015 mol) in dry MeCN (100 ml) was added and the mixture was refluxed with stirring for 25—30 h. The reaction mixture was filtered while hot and the precipitate was washed with MeCN (50 ml). Treatment of the precipitate with a dilute HCl solution yielded the recovered **1**. The filtrate and the washing were combined, the solvent evaporated to dryness, and the residual mass was extracted twice with $CHCl_3$ (100 ml, 50 ml). After removing the solvent from the $CHCl_3$ extracts, the residue was chromatographed (silica gel/AcOEt–hexane (2—4:1)) giving **3b—d** and, if any, **4** which were purified by recrystallization.

The crown ethers, **3a** and **4a**, were produced by the reaction of **1** with triethylene glycol ditosylate (**2**, m=3) using KF as a base. After removing the solvent from the $CHCl_3$ extracts, the residue was treated in hot MeOH (50 ml); **4a** was separated as a precipitate. The MeOH-soluble substances, after removing the MeOH, were chromatographed (silica gel/AcOEt–hexane (2:1), repeatedly to give **3a** and another crop of **4a**.

13,15-Bis(ethoxycarbonyl)-2,5,8,11-tetraoxa-14-thiabicyclo[10.3.0]pentadeca-1(15),12-diene (3a). White crystals (MeOH); ^1H NMR δ=1.37 (t, J=7.1 Hz, 6H, $CO_2CH_2\underline{CH_3}$), 3.7—4.4 (m, 12H, CH_2CH_2O), and 4.34 (q, J=7.1 Hz, 4H, $CO_2\underline{CH_2}CH_3$); MS m/z (rel intensity) 374 (M^+, 45). Found: C, 51.25; H, 6.03%. Calcd for $C_{16}H_{22}O_8S$: C, 51.33; H, 5.92%.

13,15,28,30-Tetrakis(ethoxycarbonyl)-2,5,8,11,17,20,23,26-octaoxa-14,29-dithiatricyclo[25.3.0.0^{12,16}]triaconta-1(30),12,15,27-tetraene (4a). White prisms (MeOH–$CHCl_3$); ^1H NMR δ=1.37 (t, J=7.1 Hz, 12H, $CO_2CH_2\underline{CH_3}$), 3.6—4.4 (m, 24H, CH_2CH_2O), and 4.33 (q, J=7.1 Hz, 8H, $CO_2\underline{CH_2}CH_3$); MS m/z 748 (M^+, 1). Found: C, 51.81; H, 5.93%. Calcd for $C_{32}H_{44}O_{16}S_2$: C, 51.33; H, 5.92%.

16,18-Bis(ethoxycarbonyl)-2,5,8,11,14-pentaoxa-17-thiabicyclo[13.3.0]octadeca-1(18),15-diene (3b). White plates (MeOH); ^1H NMR δ=1.37 (t, J=7.1 Hz, 6H, $CO_2CH_2\underline{CH_3}$), 3.7—4.4 (m, 16H, CH_2CH_2O), and 4.33 (q, J=7.1 Hz, 4H, $CO_2\underline{CH_2}CH_3$); MS m/z 418 (M^+, 56). Found: C, 51.60; H, 6.38%. Calcd for $C_{18}H_{26}O_9S$: C, 51.66; H, 6.26%.

16,18,34,36-Tetrakis(ethoxycarbonyl)-2,5,8,11,14,20,23,26,29,32-decaoxa-17,35-dithiatricyclo[31.3.0.0^{15,19}]hexatriaconta-1(36),15,18,33-tetraene (4b). White crystals (AcOEt); ^1H NMR δ=1.37 (t, J=7.1 Hz, 12H, $CO_2CH_2\underline{CH_3}$), 3.6—4.4 (m, 32H, CH_2CH_2O), and 4.33 (q, J=7.1 Hz, 8H, $CO_2\underline{CH_2}CH_3$); MS m/z 836 (M^+, 3). Found: C, 51.76; H, 6.38%. Calcd for $C_{36}H_{52}O_{18}S_2$: C, 51.66; H, 6.26%.

19,21-Bis(ethoxycarbonyl)-2,5,8,11,14,17-hexaoxa-20-thiabicyclo[16.3.0]heneicosa-1(21),18-diene (3c). White needles (MeOH); ^1H NMR δ=1.37 (t, J=7.1 Hz, 6H, $CO_2CH_2\underline{CH_3}$), 3.6—4.4 (m, 20H, CH_2CH_2O), and 4.33 (q, 4H, J=7.1 Hz, $CO_2\underline{CH_2}CH_3$); MS (20 eV) m/z 462 (M^+, 100). Found: C, 51.91; H, 6.62%. Calcd for $C_{20}H_{30}O_{10}S$: C, 51.94; H, 6.54%.

22,24-Bis(ethoxycarbonyl)-2,5,8,11,14,17,20-heptaoxa-23-thiabicyclo[19.3.0]tetracosa-1(24),21-diene (3d). White prisms (petroleum ether–AcOEt); ^1H NMR δ=1.37 (t, J=7.1 Hz, 6H, $CO_2CH_2\underline{CH_3}$), 3.6—4.4 (m, 24H, $CH_2\underline{CH_2}O$), and 4.33 (q, J=7.1 Hz, 4H, $CO_2\underline{CH_2}CH_3$); MS (20 eV) m/z 506 (M^+, 72). Found: C, 52.05; H, 6.88%. Calcd for $C_{22}H_{34}O_{11}S$: C, 52.16; H, 6.77%.

General Procedure for the Hydrolysis of 3 and 4. To a

solution of **3** (0.003 mol) in EtOH (15 ml) was added 5% NaOH solution (15 ml); the mixture was stirred at 60 °C for 2 h. After cooling the reaction mixture was acidified with HCl and stirred for ca. 30 min; then most of the EtOH was distilled off. Except for **3d**, the crystalline mass separated out upon ice-cooling, which was collected by filtration. It was dissolved in a minimum amount of hot H_2O; to the hot solution a few ml of 10% HCl solution was added. The contents were cooled and the white precipitate was collected by filtration and washed with a small amount of cold H_2O to afford pure dicarboxylic acid, **5**. By this procedure **4a** yielded the tetracarboxylic acid (**6a**), as the adduct with $4H_2O$, which, in turn, converted into the free acid upon heating at 130 °C under reduced pressure (2 mmHg) for 5 h. In the case of **3d**, the mixture was extracted with $CHCl_3$ after evaporating the EtOH. The extract was washed with H_2O and dried. Evaporation of the solvent gave **5d**.

2,5,8,11-Tetraoxa-14-thiabicyclo[10.3.0]pentadeca-1(15),12-diene-13,15-dicarboxylic Acid (5a). Yield, 76%. Colorless needles; mp 263—264 °C; MS (20 eV) *m/z* 318 (M^+, 10). Found: C, 45.01; H, 4.47%. Calcd for $C_{12}H_{14}O_8S$: C, 45.28; H, 4.43%.

2,5,8,11,14-Pentaoxa-17-thiabicyclo[13.3.0]octadeca-1(18),15-diene-16,18-dicarboxylic Acid (5b). Yield, 73%. Colorless needles, mp 244—245 °C; MS (20 eV) *m/z* 362 (M^+, 10). Found: C, 46.35; H, 5.18%. Calcd for $C_{14}H_{18}O_9S$: C, 46.41; H, 5.01%.

2,5,8,11,14,17-Hexaoxa-20-thiabicyclo[16.3.0]heneicosa-1(21),18-diene-19,21-dicarboxylic Acid (5c). Yield, 67%. Colorless needles, mp 191—192 °C; MS (20 eV) *m/z* 406 (M^+, 4). Found: C, 47.07; H, 5.51%. Calcd for $C_{16}H_{22}O_{10}S$: C, 47.29; H, 5.46%.

2,5,8,11,14,17,20-Heptaoxa-23-thiabicyclo[19.3.0]tetracosa-1(24),21-diene-22,24-dicarboxylic Acid (5d). Yield, 89%. White crystals (AcOEt), mp 146—147 °C; MS (20 eV) *m/z* 450 (M^+, 1). Found: C, 47.74; H, 5.90%. Calcd for $C_{18}H_{26}O_{11}S$: C, 47.99; H, 5.82%.

Attempted recrystallization of **5d** from H_2O yielded colorless needles, mp 81—83 °C, containing H_2O in the ratio **5d**:H_2O=1:1.6 (TG and ^1H NMR), which gradually released the H_2O on being left standing at room temperature for a few days.

2,5,8,11,17,20,23,26-Octaoxa-14,29-dithiatricyclo[25.3.0.$0^{12,16}$]triaconta-1(30),12,15,27-tetraene-13,15,28,30-tetracarboxylic Acid (6a). Yield, 74%. White powder, mp 250—251.5 °C; MS (20 eV) *m/z* 546 (M^+−90, 8). Found: C, 45.46; H, 4.39%. Calcd for $C_{24}H_{28}O_{16}S_2$: C, 45.28; H, 4.43%.

6a·4H₂O: Colorless needles, mp 257—258 °C. Found: C, 40.71; H, 5.02%. Calcd for $C_{24}H_{28}O_{16}S_2$ $4H_2O$: C, 40.68; H, 5.12%. TG/DTA data were given in the text.

General Procedure for the Syntheses of 7 and 8 by the Decarboxylation of 5 and 6. Crown ether **5** or **6** (0.003 mol) was placed in a small equipment for vacuum sublimation and heated at ca. 50 °C higher than its melting point under a pressure of 20 mmHg for 0.5 (for **5a** and **6a**), 3 (for **5b**—**c**), or 5 h (for **5d**). A dark-brown color developed concomitantly with the evolution of CO_2 gas. The residual mass was chromatographed (alumina/AcOEt) to give the desired crown ether, which was purified by recrystallization.

2,5,8,11-Tetraoxa-14-thiabicyclo[10.3.0]pentadeca-1(15),12-diene (7a). Yield, 69%. Colorless crystals (petroleum ether), mp 40—41.5 °C; ^1H NMR δ=3.6—4.3 (m, 12H, CH_2CH_2O) and 6.44 (s, 2H, Th-H); MS (20 eV) *m/z* 230 (M^+, 100). Found: C, 51.99; H, 6.25%. Calcd for $C_{10}H_{14}O_4S$: C, 52.16; H, 6.13%.

2,5,8,11,14-Pentaoxa-17-thiabicyclo[13.3.0]octadeca-1(18),15-diene (7b). Yield, 58%. Colorless needles (hexane–AcOEt), mp 71—72 °C; ^1H NMR δ=3.6—4.3 (m, 16H, CH_2CH_2O) and 6.26 (s, 2H, Th-H); MS (20 eV) *m/z* 274 (M^+, 95). Found: C, 52.45; H, 6.72%. Calcd for $C_{12}H_{18}O_5S$: C, 52.54; H, 6.61%.

2,5,8,11,14,17-Hexaoxa-20-thiabicyclo[16.3.0]heneicosa-1(21),18-diene (7c). Yield, 63%. Colorless needles (hexane–AcOEt), mp 89—90 °C; ^1H NMR δ=3.6—4.3 (m, 20H, CH_2CH_2O) and 6.19 (s, 2H, Th-H); MS (20 eV) *m/z* 318 (M^+, 66). Found: C, 52.67; H, 7.11%. Calcd for $C_{14}H_{22}O_6S$: C, 52.81; H, 6.97%.

2,5,8,11,14,17,20-Heptaoxa-23-thiabicyclo[19.3.0]tetracosa-1(24),21-diene (7d). Yield, 83%. Colorless crystals (hexane–AcOEt), mp 62—63 °C; ^1H NMR δ=3.5—4.3 (m, 24H, CH_2CH_2O) and 6.20 (s, 2H, Th-H); MS (20 eV) *m/z* 362 (M^+, 57). Found: C, 52.96 H, 7.46% Calcd for $C_{16}H_{26}O_7S$: C, 53.02; H, 7.23%.

2,5,8,11,17,20,23,26-Octaoxa-14,29-dithiatricyclo[25.3.0.$0^{12,16}$]triaconta-1(30),12,15,27-tetraene (8a). Yield, 51%. Colorless needles ($CHCl_3$–AcOEt), mp 140—141 °C; ^1H NMR δ=3.6—4.3 (24H, m, CH_2CH_2O) and 6.19 (s, 4H, Th-H); MS (20 eV) *m/z* 460 (M^+, 100). Found: C, 52.00; H, 6.17%. Calcd for $C_{20}H_{28}O_8S_2$: C, 52.16; H, 6.13%.

General Procedure for the Syntheses of 10 and 11 by the Reaction of 2,5-Dichloro-3,4-bis(chloromethyl)thiophene (9) and Oligoethylene Glycolate. Under an N_2 atmosphere NaH (for **2′**, *m*=3—5) or *t*-BuOK (for **2′**, *m*=6) (0.04 mol) was added to a solution of oligoethylene glycol (**2′**; 0.02 mol) in dry toluene (120 ml); the mixture was stirred at 60°C for 1 h. The mixture was then cooled to room temperature and a solution of **9** (5.0 g, 0.02 mol) in dry toluene (50 ml) was added at once to the mixture, which was then heated to reflux for 6 h. The precipitate formed was filtered and washed with a small amount of $CHCl_3$. The filtrate and washing were combined and evaporated. The residue was dissolved in $CHCl_3$ (50 ml), washed with H_2O, and dried. After removing the solvent, the crude products were chromatographed (alumina/hexane–dioxane (4:1)) to give **10**, together with **11**, which were purified by recrystallization.

15,17-Dichloro-3,6,9,12-tetraoxa-16-thiabiscyclo[12.3.0]heptadeca-1(17),14-diene (10a). White needles (hexane); ^1H NMR δ=3.66 (s, 4H, CH_2CH_2O), 3.72 (s, 8H, CH_2CH_2O), and 4.62 (s, 4H, $ThCH_2O$); MS (20 eV) *m/z* 326 (M^+, 32) and 328 (M^++2, 27). Found: C, 44.12; H, 5.04%. Calcd for $C_{12}H_{16}Cl_2O_4S$: C, 44.05; H, 4.93%.

15,17,32,34-Tetrachloro-3,6,9,12,20,23,26,29-octaoxa-16,33-dithiatricyclo[29.3.0.$0^{14,18}$]tetratriaconta-1(34),14,17,31-tetraene (11a). White needles (hexane); ^1H NMR δ=3.66 (s, 24H, CH_2CH_2O), and 4.59 (s, 8H, $ThCH_2O$); MS (20 eV) *m/z* 652 (M^+, 17) and 654 (M^++2, 20). Found: C, 44.07; H, 4.98%. Calcd for $C_{24}H_{32}Cl_4O_8S_2$: C, 44.05; H, 4.93%.

18,20-Dichloro-3,6,9,12,15-pentaoxa-19-thiabicyclo[15.3.0]-eicosa-1(20),17-diene (10b). White crystals (hexane); ^1H NMR (C_6D_6) δ=3.36, 3.50 (s, 8H each, CH_2CH_2O), and 4.53 (s, 4H, $ThCH_2O$); MS *m/z* 370 (M^+, 22) and 372 (M^++2, 12). Found: C, 45.30; H, 5.58%. Calcd for $C_{14}H_{20}Cl_2O_5S$: C, 45.29; H, 5.43%.

18,20,38,40-Tetrachloro-3,6,9,12,15,23,26,29,32,35-decaoxa-19,39-dithiatricyclo[35.3.0.$0^{17,21}$]tetraconta-1(40),17,20,37-tetraene (11b). White prisms (hexane); ^1H NMR (C_6D_6) δ=3.49 (s, 32H, CH_2CH_2O) and 4.56 (s, 8H, $ThCH_3O$); MS (20 eV) *m/z*

740 (M^+, 6) and 742 (M^++2, 8). Found: C, 45.20; H, 5.49%. Calcd for $C_{28}H_{40}Cl_4O_{10}S_2$: C, 45.29; H, 5.43%.

21,23-Dichloro-3,6,9,12,15,18-hexaoxa-22-thiabicyclo[18.3.0]-tricosa-1(23),20-diene (10c). Colorless plates (petroleum ether); ^1H NMR (C_6D_6) δ=3.3—3.6 (m, 20H, CH_2CH_2O) and 4.61 (4H, s, $ThCH_2O$); MS (20 eV) m/z 414 (M^+, 63) and 416 (M^++2, 48). Found: C, 46.23; H, 5.92%. Calcd for $C_{16}H_{24}Cl_2O_6S$: C, 46.27; H, 5.82%.

21,23,44,46-Tetrachloro-3,6,9,12,15,18,26,29,32,35,38,41-dodecaoxa-22,45-dithiatricyclo[41.3.0.0^{20,24}]hexatetraconta-1(46),20,23,43-tetraene (11c). Colorless needles (hexane); ^1H NMR δ=3.64 (br s, 40H, CH_2CH_2O) and 4.59 (s, 8H, $ThCH_2O$); MS (20 eV) δ= 828 (M^+, 3) and 830 (M^++2, 4). Found: C, 46.35; H, 5.98%. Calcd for $C_{32}H_{48}Cl_4O_{12}S_2$: C, 46.27; H, 5.82%.

24,26-Dichloro-3,6,9,12,15,18,21-heptaoxa-25-thiabicyclo-[21.3.0]hexacosa-1(26),23-diene (10d). Colorless viscous oil; ^1H NMR (C_6D_6) δ=3.4—3.7 (m, 24H, CH_2CH_2O) and 4.60 (s, 4H, $ThCH_2O$); MS (20 eV) m/z 458 (M^+, 22) and 460 (M^++2, 16). Found: C, 46.88; H, 6.29%. Calcd for $C_{18}H_{28}Cl_2O_7S$: C, 47.06; H, 6.14%.

24,26,50,52-Tetrachloro-3,6,9,12,15,18,21,29,32,35,38,41,44,47-tetradecaoxa-25,51-dithiatricyclo[47.3.0.0^{23,27}]dopentaconta-1(52),23,26,49-tetraene (11d). White crystals (hexane); ^1H NMR δ=3.65 (br s, 48H, CH_2CH_2O) and 4.59 (s, 8H, $ThCH_2O$); MS (20 eV) m/z 916 (M^+, 1) and 918 (M^++2, 2). Found: C, 47.04; H, 6.24%. Calcd for $C_{36}H_{56}Cl_4O_{14}S_2$: C, 47.06; H, 6.14%.

General Procedure for the Preparation of 12a—d and 13 by the Catalytic Dechlorination of 10a—d and 11. The reaction was conducted at room temperature by stirring a mixture of **10** or **11** (0.005 mol), KOH (1.5 g), 10% Pd-C (0.7 g), and MeOH (100 ml) in an atmospheric pressure hydrogenation apparatus. Within 1—2 h the calculated amounts of H_2 were consumed. The catalyst was filtered off and washed with $CHCl_3$ (50 ml). The filtrate was concentrated and water added to the residue. The products were extracted with the $CHCl_3$ washing. The extract was washed with H_2O, 5% HCl solution, and then H_2O, and dried. Evaporation of the solvent gave **12a—d** or **13** as an oil.

3,6,9,12-Tetraoxa-16-thiabicyclo[12,3,0]heptadeca-1(17),14-diene (12a). Yield, 83%. Colorless viscous oil; ^1H NMR (200 MHz) δ=3.67 (s, 4H, CH_2CH_2O), 3.74 (s, 8H, CH_2CH_2O), 4.74 (s, 4H, $ThCH_2O$), and 7.24 (s, 2H, Th-H); MS (20 eV) m/z 258 (M^+, 60). Found: C, 55.24; H, 7.11%. Calcd for $C_{12}H_{18}O_4S$: C, 55.79; H, 7.02%.

3,6,9,12,15-Pentaoxa-19-thiabicyclo[15.3.0]eicosa-1(20),17-diene (12b). Yield, 88%. Colorless viscous oil, bp 160 °C (bath)/5×10^{-3} mmHg. ^1H NMR (C_6D_6) δ=3.38, 3.52 (s each, 16H, CH_2CH_2O), 4.63 (s, 4H, $ThCH_2O$), and 7.07 (s, 2H, Th-H); MS (20 eV) m/z 302 (M^+ 100). Found: C, 55.39; H, 7.49%. Calcd for $C_{14}H_{22}O_5S$: C, 55.61; H, 7.33%.

3,6,9,12,15,18-Hexaoxa-22-thiabicyclo[18.3.0]tricosa-1(23),20-diene (12c). Yield, 81%. Colorless viscous oil, bp 160 °C (bath)/10^{-3} mmHg; ^1H NMR (C_6D_6) δ=3.49, 3.52 (s each, 20H, CH_2CH_2O), 4.58 (s, 4H, $ThCH_2O$), and 7.00 (2H, s, Th-H); MS (20 eV) m/z 346 (M^+, 94). Found: C, 54.78; H, 7.71%. Calcd for $C_{16}H_{26}O_6S$: C, 55.47; H, 7.56%.

3,6,9,12,15,18,21-Heptaoxa-25-thiabicyclo[21.3.0]hexacosa-1(26),23-diene (12d). Yield, 83%. Colorless viscous oil, bp 170—190 °C (bath)/10^{-3} mmHg; ^1H NMR (C_6D_6) δ=3.4—3.7 (m, 24H, CH_2CH_2O), 4.57 (s, 4H, $ThCH_2O$), and 7.03 (s, 2H, Th-H); MS (20 eV) m/z 390 (M^+, 90). Found: C, 54.98; H, 7.96%. Calcd for $C_{18}H_{30}O_7S$: C, 55.79; H, 7.02%.

3,6,9,12,20,23,26,29-Octaoxa-16,33-dithiatricyclo[29.3.0.0^{14,18}]tetratriaconta-1(34),14,17,31-tetraene (13a). Yield, 85%. Colorless viscous oil, bp 230 °C (bath)/10^{-3} mmHg; ^1H NMR (C_6D_6) δ=3.51, 3.47 (s each, 24H, CH_2CH_2O), 4.54 (s, 8H, $ThCH_2O$), and 7.02 (s, 4H, Th-H); MS (20 eV) m/z 516 (M^+, 20). Found: C, 55.59; H, 7.11%. Calcd for $C_{24}H_{36}O_8S_2$: C, 55.79; H, 7.02%.

Reductive Desulfurization of the Thiophene-Containing Crown Ethers (3a—d, 12b—d, and 13) with Raney Nickel. W-7 Raney nickel prepared from 15 g of the alloy was added to the solution of the crown ether (0.005 mol) in EtOH (50 ml); the mixture was stirred at the reflux temperature for 2 h. The reaction mixture was filtered and the nickel was washed with EtOH (10 ml). The filtrate and the washing were combined and evaporated. The residual oil was chromatographed (silica gel/hexane–dioxane (4:1) for **16** and **17**, silica gel/AcOEt–hexane (2—4:1) for **15**) giving the desulfurized crown ether.

2,3-Bis(ethoxycarbonylmethyl)-1,4,7,10-tetraoxacyclododecane (2,3-Bis(ethoxycarbonylmethyl)-12-crown-4) (15a). Yield, 53%. Colorless oil, bp 110 °C (bath)/10^{-3} mmHg; ^1H NMR δ=1.26 (t, J=7.1 Hz, 6H, $CH_2\underline{CH_3}$), 2.40 (d, J=5.3 Hz, 2H, $\underline{CH_2}CH$), 2.55 (d, J=8.1 Hz, 2H, $\underline{CH_2}CH$), 3.66, 3.71 (br s each, 12H, CH_2CH_2O), and 4.15 (q, J=7.1 Hz, $\underline{CH_2}CH_3$, overlapped with the $CH_2\underline{CH}$ peaks, 6H); MS (50 eV) m/z 348 (M^+, 41). Found: C, 54.41; H, 8.08%. Calcd for $C_{16}H_{28}O_8$: C, 55.16; H, 8.10%.

2,3-Bis(ethoxycarbonylmethyl)-1,4,7,10,13-pentaoxacyclopentadecane (2,3-Bis(ethoxycarbonylmethyl)-15-crown-5) (15b). Yield, 51%. Colorless oil, bp 125 °C (bath)/10^{-3} mmHg; ^1H NMR δ=1.26 (t, J=7.1 Hz, 6H, $CH_2\underline{CH_3}$), 2.37 (d, J=5.1 Hz, 2H, $\underline{CH_2}CH$), 2.51 (d, J=8.1 Hz, 2H, $\underline{CH_2}CH$), and 3.55—4.3 (m, 22H, CH_2CH_2O, $CH_2\underline{CH}$, and $\underline{CH_2}CH_3$ (4.15, q, J=7.1 Hz)); MS (50 eV) m/z 392 (M^+, 30). Found: C, 54.92; H, 8.41%. Calcd for $C_{18}H_{32}O_9$: C, 55.09; H, 8.22%.

2,3-Bis(ethoxycarbonylmethyl)-1,4,7,10,13,16-hexaoxacyclooctadecane (2,3-Bis(ethoxycarbonylmethyl)-18-crown-6) (15c). Yield, 55%. Colorless oil, bp 140 °C (bath)/10^{-3} mmHg; ^1H NMR δ=1.26 (t, J=7.1 Hz, 6H, $CH_2\underline{CH_3}$), 2.49 (d, J=4.5 Hz, 2H, $\underline{CH_2}CH$), 2.55 (d, J=6.1 Hz, 2H, $\underline{CH_2}CH$), and 3.45—4.3 (m, 26H, CH_2CH_2O, $CH_2\underline{CH}$, and $\underline{CH_2}CH_3$ (4.15, q, J=7.1 Hz)); MS (50 eV) m/z 436 (M^+, 60). Found: C, 54.67; H, 8.55%. Calcd for $C_{20}H_{36}O_{10}$: C, 55.03; H, 8.31%.

2,3-Bis(ethoxycarbonylmethyl)-1,4,7,10,13,16,19-heptaoxacycloheneicosane (2,3-Bis(ethoxycarbonylmethyl)-21-crown-7) (15d). Yield, 56%. Colorless oil, bp 150 °C (bath)/10^{-3} mmHg; ^1H NMR δ=1.26 (t, J=7.1 Hz, 6H, $CH_2\underline{CH_3}$), 2.49 (d, J=3.8 Hz, 2H, $\underline{CH_2}CH$), 2.55 (d, J=5.9 Hz, 2H, $\underline{CH_2}CH$), and 3.45—4.3 (m, 30H, CH_2CH_2O, $CH_2\underline{CH}$, and $\underline{CH_2}CH_3$ (4.15, q, J=7.1 Hz)); MS (50 eV) m/z 480 (M^+, 5). Found: C, 54.14; H, 8.53%. Calcd for $C_{22}H_{40}O_{11}$: C, 54.99; H, 8.39%.

15,16-Dimethyl-1,4,7,10,13-pentaoxacycloheptadecane (16a). Yield, 49%. Colorless oil, bp 100 °C (bath)/10^{-3} mmHg; ^1H NMR (200 MHz) δ=0.85, 0.88 (d, J=6.1 Hz, 7.2 Hz each, 6H, CH_3), 1.85—2.1 (m, 2H, $\underline{CH}CH_2O$), and 3.3—3.8 (m, 20H, CH_2CH_2O); MS (20 eV) m/z 276 (M^+, 8). Found: C, 60.13; H, 10.42%. Calcd for $C_{14}H_{28}O_5$: C, 60.84; H, 10.21%.

18,19-Dimethyl-1,4,7,10,13,16-hexaoxacycloeicosane (16b). Yield, 52%. Colorless oil, bp 120 °C (bath)/10^{-3} mmHg; ^1H NMR (200 MHz) δ=0.79, 0.89 (d, J=6.7 Hz, 6.8 Hz each, 6H, CH_3), 1.85—2.15 (m, 2H, $\underline{CH}CH_2O$), and 3.25—3.8 (m, 24H, CH_2CH_2O); MS (20 eV) m/z 320 (M^+, 1). Found: C, 59.33; H, 10.21%. Calcd for $C_{16}H_{32}O_6$: C, 59.98; H, 10.07%.

21,22-Dimethyl-1,4,7,10,13,16,19-heptaoxacyclotricosane (16c).

Yield, 52%. Colorless oil, bp 140—150 °C (bath)/10^{-3} mmHg; ^{1}H NMR (200 MHz) δ=0.80, 0.90 (d, J=6.8 Hz each, 6H, CH_3), 1.8—2.15 (m, 2H, $\underline{CH}CH_2O$), and 3.2—3.9 (m, 28H, CH_2CH_2O); MS (20 eV) m/z 364 (M^+, 1). Found: C, 58.37; H, 10.05%. Calcd for $C_{18}H_{36}O_7$: C, 59.32; H, 9.96%.

12,13,26,27-Tetramethyl-1,4,7,10,15,18,21,24-octaoxacyclooctacosane (17). Yield, 43%. Colorless oil, bp 170 °C (bath)/10^{-3} mmHg; ^{1}H NMR (200 MHz) δ=0.79, 0.89 (d, J=6.7 Hz, 6.8 Hz each, 12H, CH_3), 1.8—2.15 (m, 4H, $\underline{CH}CH_2O$), and 3.25—3.8 (m, 32H, CH_2CH_2O); MS (20 eV) m/z 464 (M^+, 1). Found: C, 61.23; H, 10.96%. Calcd for $C_{24}H_{48}O_8$: C, 62.04; H, 10.41%.

Solvent Extraction. Solvent extraction was carried out according to Pedersen's method.[13] The CH_2Cl_2 solution (5 ml) containing the crown ether (7×10^{-4} mol) and the aqueous solution (5 ml) containing the metal nitrate (1×10^{-1} mol) and picric acid (7×10^{-5} mol) were mixed and shaken for 10 min at 25 °C. The solution was equilibrated. Extraction of the picrate was followed by monitoring the absorbance of the aqueous solution at 354 nm.

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