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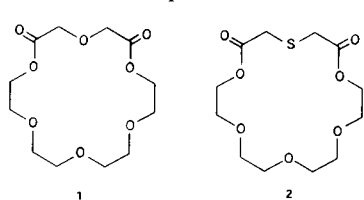
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Two new series of macrocyclic polyether-diester ligands (**4-15**) containing a pyridine subcyclic unit have been prepared by treating various oligoethylene glycols and sulfur-containing oligoethylene glycols with 2,6- and 3,5-pyridine dicarbonyl chlorides. The compounds prepared from 2,6-pyridine dicarbonyl chloride were: 3,6,9,12-tetraoxa-18-azabicyclo[12.3.1]octadeca-1(18), 14,16-triene-2,13-dione (**4**); 3,6,9,12,15-pentaoxa-21-azabicyclo[15.3.1]heneicosa-1(21),17,19-triene-2,16-dione (**5**); 3,6,12,15-tetraoxa-9-thia-21-azabicyclo[15.3.1]heneicosa-1(21),17,19-triene-2,16-dione (**6**); 3,9,15-trioxa-6,12-dithia-21-azabicyclo[15.3.1]heneicosa-1(21),17,19-triene-2,16-dione (**7**); 3,6,9,12,15,18-hexaoxa-24-azabicyclo[18.3.1]tetracos-1(24),20,22-triene-2,19-dione (**8**); 3,6,9,12,15,18,21-heptaoxa-27-azabicyclo[21.3.1]heptacos-1(27),23,25-triene-2,22-dione (**9**); and the corresponding analogues from 3,5-pyridine dicarbonyl chloride (**10-15**). The solid potassium thiocyanate complex of compound **5** was also prepared.

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The synthesis and unique cation complexing properties of the macrocyclic polyethers, first reported by Pedersen (**2**) have been the object of intensive research (3-7). The majority of work has concerned macrocyclic polyethers, the so-called crown compounds, although many aza (**8**) and thia crown compounds have been studied (6,9-13).

We have recently reported the synthesis and unique cation complexing characteristics of macrocyclic polyether-diester **1-3** and **5** (14,15). The complexing properties of these compounds in methanol have been shown to



be both similar and different to those of corresponding crown polyethers. Compound **1** complexed with the alkali and alkaline earth metal cations much the same as 18-crown-6 (same structure as **1** except without the two carbonyl oxygens) but with diminished stability (14). Compound **2** showed no heat of reaction with Na^+ , K^+ , or Ba^{2+} but did complex strongly with Ag^+ (15). These results are similar to those for the thia crown compounds which have two or more sulfur atoms (13).

Compound **3** exhibited a cation selectivity pattern similar to that for valinomycin, a natural macrocyclic antibiotic, in that $\text{K}^+ > \text{Ba}^{2+}$ (14). This result demonstrates the possibility of designing synthetic macrocyclic compounds containing oxygen donor atoms which have cation selective properties similar to the natural antibiotics. Such molecules can then be used to investigate biological cation transport and selectivity processes (14).

Compound **5** (Chart I) has been found to complex with Na^+ , K^+ , Ba^{2+} , and Ag^+ in methanol with a log K of 4.3

to 4.9 (15). Frensch and Vogtle also found that compound **5** complexed strongly with K^+ in methanol (16). That the pyridine nitrogen is responsible for the high cation complexing ability of compound **5** is shown by the fact that neither compound **11**, where the pyridine nitrogen is outside the polyether cavity, nor the benzene analogue (17) which has no nitrogen, formed complexes with any cation in methanol as shown by the lack of heat of reaction (18). In this paper, we report the synthesis of these new macrocyclic polyether-diester compounds which contain a pyridine subcyclic unit (Chart I). A more complete analysis of the cation complexing ability of these compounds will be reported later (18).

We have previously reported the synthesis of a wide variety of macrocyclic polyether-diester compounds containing the following diacid moieties: oxalic (19), malonic (20-22), succinic (21-23), glutaric (21,22), adipic (22), maleic (23), diglycolic (14,24), thiodiglycolic (15,24), phthalic (17,22), isophthalic (17), terephthalic (17), and 1,8-naphthoic (17). Others have reported a variety of macrocyclic diesters (25,26) but only a few have been prepared from the oligoethylene glycols. Frensch and Vogtle have prepared compound **5** and three somewhat similar compounds with pyridine and benzene subcyclic units (16).

Results and Discussion.

Compounds **4-15** (Chart I) were prepared from the appropriate pyridine dicarbonyl chloride and oligoethylene glycol. The dichloride and the glycol each in benzene were simultaneously dripped into a large volume of stirring

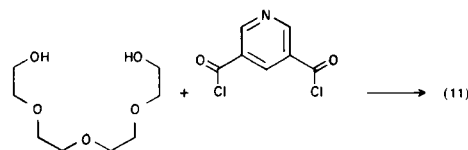
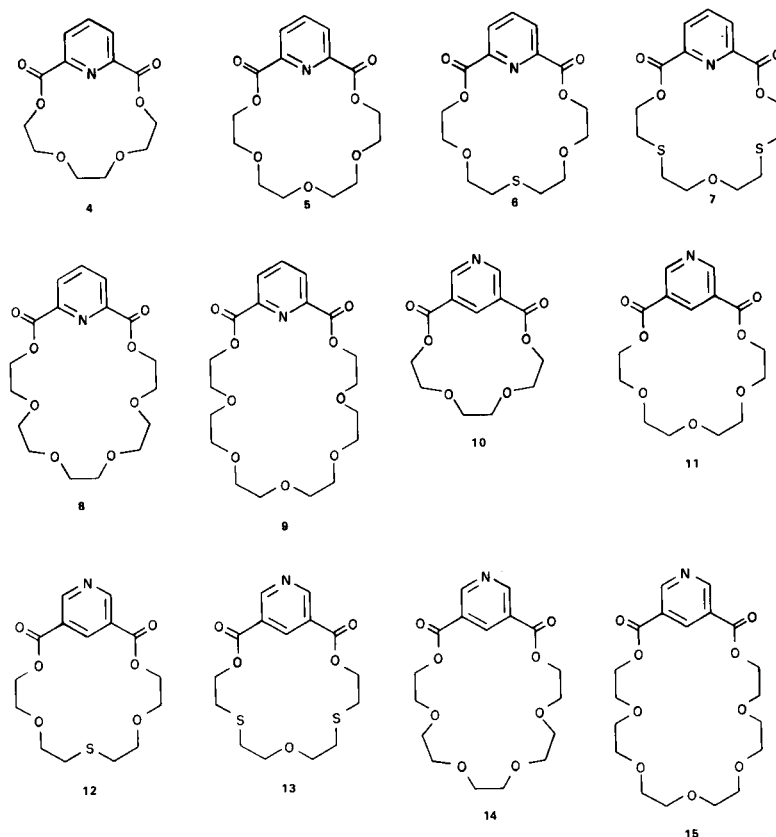


Chart I



benzene. Compound **11**, for example, was prepared from tetraethylene glycol and 3,5-pyridine dicarbonyl chloride.

Yields of the 2,6-pyridine compounds (**4-9**) varied from 4 to 28.5% with the exception of compound **5** which was isolated in a 78% yield. This remarkable yield has been duplicated by Frensch and Vogtle (16) as well as other workers (27). Even though no cations were present during the course of this preparation, we believe the high yield is due to a template effect. Two molecules of hydrogen chloride are liberated in each reaction. One hydrogen chloride molecule could protonate the pyridine nitrogen and the resulting ion could act as a template for ring closure. No complexed proton was observed as the product was isolated after the benzene solvent was removed under vacuum. This process would remove all hydrogen chloride from the mixture.

The yields of the 3,5-pyridine compounds (**10-15**) were below 10% except for compound **11**. The yield for compound **11** (32.7%) was comparable to other macrocyclic polyether-diester compounds (24). The lower yields for the other compounds of this series are probably due to the difficulty in working with 3,5-pyridine dicarbonyl chloride which readily polymerizes (28). We stored the acid chloride in the freezer compartment and freshly sublimed a sample for each preparation.

The structures proposed for the macrocyclic compounds are consistent with data derived from ir and nmr spectra, combustion analyses and molecular-weight determinations. The ir of all compounds exhibited carbonyl bands at 1720-1730 cm^{-1} as expected for the esters of the pyridine dicarboxylic acids (29). Compounds **8** and **9** exhibited two carbonyl bands in the ir at 1720 and 1705 or 1700 cm^{-1} . This indicates that one of the carbonyl oxygens is in a different plane as was found for compound **1** (24). Molecular models of compounds **4-7** and **10-13** have a ridged structure due to the constraints of the pyridine ring.

The nmr spectra of the aromatic portion for all compounds except **10** exhibited the expected peaks at 7.91-8.43 δ for the 2,6-pyridine compounds (**4-9**) and 8.94 \pm 0.03 δ (t, 1H) and 9.43 \pm 0.03 (d, 2H) for compounds **11-15** (30). The nmr spectrum for compound **10** exhibited a downfield shift for the single proton which faces into the polyether cavity. This same downfield shift for the hydrogen in the cavity was observed for the corresponding benzene compound prepared from isophthaloyl chloride and triethylene glycol (17). A CPK molecular model of this compound shows extreme crowding due to the hydrogen atom pointing into the cavity. The typical polyether-diester nmr peaks appeared at 4.50 \pm 0.13 δ (COOCH_2) for all compounds, 3.87 \pm 0.08 ($\text{COOCH}_2\text{CH}_2\text{O}$) for all compounds except **7** and **13**, 3.75 \pm 0.10 (ether OCH_2)

Table I

Comparison of Physical Properties of Various Macrocyclic Compounds with an Aromatic Subcyclic Group

Compounds	Entry		Yield %	M.p. (b.p.)	Remarks
15 Member Rings					
	1	X = CH; Y = N; Z = O (4)	9.6	139-140	a
	2	X = N; Y = CH; Z = O (10)	1	137-137.5	a
	3	X, Y = CH; Z = O	2	138-140	b
	4	X = CNO ₂ ; Y = CH; Z = O	2.6	161-163	b
18 Member Rings					
	5	A, B = O; X = CH; Y = N; Z = O (5)	70-78	86.5-87.5	a,c
	6	A, B = O; X = N; Y = CH; Z = O (11)	32.7	112-113	a
	7	A, B = O; X = CH; Y = N; Z = H ₂	29	40-41	d
	8	A, B = O; X, Y = CH; Z = O	33	95.5-96.5	b
	9	A, B = O; X = CNO ₂ ; Y = CH; Z = O	17	157-158	b
	10	A = O; B = S; X = CH; Y = N; Z = O (6)	10.7	96-97.5	a
	11	A = O; B = S; X = N; Y = CH; Z = O (12)	9.3	108-109	a
	12	A = O; B = S; X, Y = CH; Z = O	21	oil	b
	13	A = O; B = S; X = CNO ₂ ; Y = CH; Z = O	1.5	oil	b
	14	A = S; B = O; X = CH; Y = N; Z = O (7)	4.2	127-129	a
15	A = S; B = O; X = N; Y = CH; Z = O (13)	8.3	103-104	a	
21 Member Rings					
	16	X = CH; Y = N; Z = O (8)	24.7	143-144.5	a
	17	X = N; Y = CH; Z = O (14)	6.9	54.5-55.5	a
	18	X, Y = CH; Z = O	28	103.5-104.5	b
	19	X = CNO ₂ ; Y = CH; Z = O	30	104-105	b
24 Membered Rings					
	20	X = CH; Y = N; Z = O (9)	28.5	110-111	a
	21	X = N; Y = CH; Z = O (15)	7.5	50-51	a
	22	X, Y = CH; Z = O	31	106.5-108.5	b
	23	X = CNO ₂ ; Y = CH; Z = O	6	90-92	b

Remarks. (a) This work. (b) Reference 17. (c) Reference 16. (d) Reference 31.

for all compounds, 3.08 ± 0.01 (COOCH₂CH₂S) for compounds **7** and **13**, and 2.94 ± 0.05 (sulfide SCH₂) for compounds **6**, **7**, **12**, and **13** (17,24). As with the comparable macrocyclic polyether-diester compounds prepared from isophthaloyl chloride (17), those compounds derived

from penta- and hexaethylene glycols (**8**, **9**, **14**, and **15**) exhibited two nmr singlets for the ether methylene hydrogens.

All compounds (with the exception of **10**) were submitted for combustion analysis only after a satisfactory

molecular weight had been determined by osmometry (average error was 2.6% of calculated). This technique was used to ensure that quoted yields are based on monomer formation and to check the purity of samples submitted for analyses.

Compound **10** was analyzed *via* mass spectrometry using the chemical ionization technique. The base peak of the spectrum (mass 282, $M + 1$) is the so called quasi-molecular ion.

A comparison of physical properties for various macrocyclic polyether-diester compounds containing an aromatic subcyclic unit is given in Table I. One non-ester compound (entry 7) is also listed. A number of macrocyclic polyethers containing a benzene ring (X and $Y = CH$ and $Z = H_2$) have been prepared in yields of 2-67%. No physical properties were given for those compounds although each was distilled (32). It is apparent that the polyethers have a lower melting point than the diesters (compare entries 5 and 7). This was also observed for the crown compounds versus the 2,6-diketo crown compounds (24). The polyether-diester compounds derived from isophthaloyl and 2,6-pyridine dicarbonyl chloride, which one might expect to be similar, have similar physical properties. Thus, **4**, **5**, and **9** have about the same melting points as the comparable benzene compounds (entries 1, 5, 20 versus entries 3, 8, and 22). Compound **8** is an exception in that its melting point differs from the corresponding benzene derivative (compare entries 16 and 18). The compounds which have the nitrogen outside the polyether cavity generally have much different melting points than those which have the nitrogen atom as part of the cavity (entries 1, 5, 10, 14, 16, and 20 versus entries 2, 6, 11, 15, 17, and 21).

Compound **5** formed a stable potassium thiocyanate complex. Neither compound **11** nor the corresponding benzene compound (17) formed stable complexes with any metal cations. Cation complex formation was not attempted for the other compounds.

The preliminary data for cation-ligand interactions for compound **5** using a calorimetric titration in methanol have been published (15) and are mentioned in the introduction. More complete data will be reported in the future (18).

EXPERIMENTAL

All infrared (ir) spectra were obtained on a Perkin-Elmer Model 457 spectrophotometer. The proton nuclear magnetic resonance (nmr) spectra were obtained on a Varian EM-390 spectrometer in deuteriochloroform using tetramethylsilane as an internal standard. Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tennessee, or by Eisenhower Laboratories, Holly Hill, Florida. The molecular weight determinations were by osmometry on a Hitachi Perkin-Elmer 115 Molecular Weight Apparatus. Melting points were determined on a Thomas-Hoover capillary type melting point apparatus and are uncorrected. Reagent grade solvents were used without further purification.

Materials.

Starting materials were either purchased: triethylene glycol (Baker), tetraethylene glycol (Aldrich), pentaethylene glycol (Columbia), 2,6-pyridine dicarbonyl chloride (Aldrich); or prepared in our laboratory: 1,4,10,13-tetraoxa-7-thiatridecane (24), 1,7,13-trioxa-4,10-dithiatridecane (24), hexaethylene glycol (33), and 3,5-pyridine dicarbonyl chloride.

3,5-Pyridine dicarbonyl chloride was prepared by the method similar to that of Meyer and Tropsch (28). 3,5-Pyridine dicarboxylic acid (Aldrich, 50 g., 0.30 mole) was mixed with an excess of thionyl chloride and refluxed 24 hours. The thionyl chloride was then removed under reduced pressure. Dry benzene was added and the mixture refluxed 24 hours. The volume of the benzene solution was reduced to 100 ml. and hexane was added to precipitate the acid chloride. The product was collected on a glass frit, washed with cold hexane, dried in a vacuum desiccator and stored in the freezer compartment. The acid chloride was sublimed at 100° at 1 mm for each reaction. The yield from combined sublimations was 45.4 g. (74.2%).

General Procedure for Synthesis.

The appropriate glycol and diacid chloride, each dissolved in 200 ml. of benzene unless otherwise specified, were simultaneously dripped into 1 l. of rapidly stirring benzene at 50°, or at reflux for compounds **10-15** (this was done in an effort to drive off most of the hydrogen chloride gas formed). The mixture was allowed to stir at 50° for at least two days during which time hydrogen chloride gas was evolved. After the reaction was complete, the benzene was removed under reduced pressure. The crude product was purified either by continuous extraction with hot hexane (34) or by repeated extraction with boiling hexane (35). Specific details are given for each compound.

3,6,9,12-Tetraoxa-18-azabicyclo[12.3.1]octadeca-1(18),14,16-triene-2,13-dione (**4**).

2,6-Pyridine dicarbonyl chloride (20.4 g., 0.10 mole) and triethylene glycol (15.02 g., 0.10 mole) were used. A 50/50 mixture of THF/benzene was used to dissolve each of the reactants. Continuous extraction (34) of the reaction mixture with hot hexane gave a white powder (2.70 g., 9.6%). An analytical sample was prepared by sublimation, m.p. 139-140°; ir (potassium bromide): 1730 cm^{-1} ; nmr: δ 3.91 (m, 4H, $\text{COOCH}_2\text{CH}_2\text{O}$), 4.02 (s, 4H, $\text{OCH}_2\text{CH}_2\text{O}$), 4.47 (m, 4H, COOCH_2), and 7.91-8.31 (m, 3H, aromatic H).

Anal. Calcd. for $\text{C}_{13}\text{H}_{15}\text{NO}_6$: C, 55.51; H, 5.38; mol. wt. 281.27. Found: C, 55.27; H, 5.52; mol. wt. 283.

3,6,9,12,15-Pentaoxa-21-azabicyclo[15.3.1]heneicosa-1(21),17,19-triene-2,16-dione (**5**).

2,6-Pyridine dicarbonyl chloride (20.4 g., 0.10 mole) and tetraethylene glycol (19.4 g., 0.10 mole) were used. Continuous extraction (34) of the reaction mixture with hot hexane gave 25.41 g. (78%) of a white crystalline product. An analytical sample was prepared by sublimation, m.p. 86.5-87.5°; ir (potassium bromide): 1730 cm^{-1} ; nmr: δ 3.80 (s, 8H, $\text{OCH}_2\text{CH}_2\text{O}$), 3.91 (m, 4H, $\text{COOCH}_2\text{CH}_2\text{O}$), 4.57 (m, 4H, COOCH_2), and 7.91-8.38 (m, 3H, aromatic H).

Anal. Calcd. for $\text{C}_{15}\text{H}_{19}\text{NO}_7$: C, 55.38; H, 5.89; N, 4.31; mol. wt. 325.32. Found: C, 55.46; H, 5.96; N, 4.47; mol. wt. 329.

The potassium thiocyanate complex of **5** was prepared by dissolving 1.0 g. (0.0031 mole) of **5** and 0.30 g. (0.0031 mole) of potassium thiocyanate in 25 ml. of hot, anhydrous methanol. Some of the methanol was allowed to evaporate as the complex crystallized. The complex was recrystallized from methanol/

chloroform to give colorless needles, m.p. 197-198.5°; ir (potassium bromide): 2060, 1725, 1715 cm^{-1} ; nmr: δ 3.80 (s, 8H, $\text{OCH}_2\text{CH}_2\text{O}$), 3.90 (m, 4H, $\text{COOCH}_2\text{CH}_2\text{O}$), 4.76 (m, 4H, COOCH_2), and 8.10-8.60 (m, 3H, aromatic H).

Anal. Calcd. for $\text{C}_{15}\text{H}_{19}\text{NO}_7\cdot\text{KSCN}$: C, 45.49; H, 4.53; N, 6.63. Found: C, 45.30; H, 4.34; N, 6.42.

3,6,12,15-Tetraoxa-9-thia-21-azabicyclo[15.3.1]heneicosa-1(21),17,19-triene-2,16-dione (**6**).

2,6-Pyridine dicarbonyl chloride (20.4 g., 0.10 mole) and 1,4,10,13-tetraoxa-7-thiatridecane (21.0 g., 0.10 mole) were used. A 30/70 mixture of THF/benzene was used to dissolve each of the reactants. Continuous extraction (34) of the reaction mixture with hot hexane gave 3.65 g. (10.7%) of the desired product. Recrystallization from hexane gave white crystals, m.p. 96-97.5°; ir (potassium bromide): 1715 cm^{-1} ; nmr: δ 2.89 (t, 4H, $\text{SCH}_2\text{CH}_2\text{O}$), 3.89 (m, 8H, $\text{COOCH}_2\text{CH}_2\text{OCH}_2$), 4.59 (m, 4H, COOCH_2), and 7.97-8.43 (m, 3H, aromatic H).

Anal. Calcd. for $\text{C}_{15}\text{H}_{19}\text{NO}_6\text{S}$: C, 52.78; H, 5.61; N, 4.10; mol. wt. 341.39. Found: C, 52.69; H, 5.56; N, 4.04; mol. wt. 355.

3,9,15-Trioxa-6,12-dithia-21-azabicyclo[15.3.1]heneicosa-1(21),17,19-triene-2,16-dione (**7**).

2,6-Pyridine dicarbonyl chloride (21.0 g., 0.103 mole) and 1,7,13-trioxa-4,10-dithiatridecane (23.26 g., 0.103 mole) were used. A 50/50 mixture of THF/benzene was used to dissolve each of the reactants. Continuous extraction (34) of the reaction mixture with hot hexane gave white needles. Recrystallization yielded 1.56 g. (4.2%) of the desired product, m.p. 127-129°; ir (potassium bromide): 1720, 1710 cm^{-1} ; nmr: δ 2.99 (t, 4H, $J = 7$ Hz, $\text{COOCH}_2\text{CH}_2\text{SCH}_2$), 3.09 (t, 4H, $J = 6$ Hz, $\text{COOCH}_2\text{CH}_2\text{S}$), 3.74 (t, 4H, $J = 7$ Hz, $\text{OCH}_2\text{CH}_2\text{S}$), 4.62 (t, 4H, $J = 6$ Hz, COOCH_2) and 7.94-8.40 (m, 3H, aromatic H).

Anal. Calcd. for $\text{C}_{15}\text{H}_{19}\text{NO}_5\text{S}_2$: C, 50.40; H, 5.36; N, 3.92; mol. wt. 357.45. Found: C, 50.25; H, 5.37; N, 3.80; mol. wt. 367.

3,6,9,12,15,18-Hexaoxa-24-azabicyclo[18.3.1]tetracos-1(24),20,22-triene-2,19-dione (**8**).

2,6-Pyridine dicarbonyl chloride (20.4 g., 0.10 mole) and pentaethylene glycol (23.8 g., 0.10 mole) were used. Continuous extraction (34) of the reaction mixture with hot hexane gave 9.14 g. (24.7%) of white powder. An analytical sample was prepared by recrystallization of a small portion of extracted product, m.p. 143-144.5°; ir (potassium bromide): 1720, 1705 cm^{-1} ; nmr: δ 3.70 and 3.78 (both s, 12H, $\text{OCH}_2\text{CH}_2\text{O}$), 3.93 (m, 4H, $\text{COOCH}_2\text{CH}_2\text{O}$), 4.61 (m, 4H, COOCH_2) and 7.94-8.41 (m, 3H, aromatic H).

Anal. Calcd. for $\text{C}_{17}\text{H}_{23}\text{NO}_8$: C, 55.28; H, 6.28; N, 3.79; mol. wt. 369.38. Found: C, 55.02; H, 6.27; N, 3.59; mol. wt. 397.

3,6,9,12,15,18,21-Heptaoxa-27-azabicyclo[21.3.1]heptacos-1(27),23,25-triene-2,22-dione (**9**).

2,6-Pyridine dicarbonyl chloride (20.4 g., 0.10 mole) and hexaethylene glycol (28.23 g., 0.10 mole) were used. A 50/50 mixture of THF/benzene was used to dissolve each of the reactants. Continuous extraction (34) of the reaction mixture with hot hexane gave 11.8 g. (28.5%) of the desired product. An analytical sample was prepared by recrystallization from chloroform/hexane, m.p. 110-111°; ir (potassium bromide): 1720, 1700 cm^{-1} ; nmr: δ 3.60 and 3.76 (both s, 16H, $\text{OCH}_2\text{CH}_2\text{O}$), 3.93 (m, 4H, $\text{COOCH}_2\text{CH}_2\text{O}$), 4.60 (m, 4H, COOCH_2), and 7.97-8.41 (m, 3H, aromatic H).

Anal. Calcd. for $\text{C}_{19}\text{H}_{27}\text{NO}_9$: C, 55.20; H, 6.58; N, 3.39; mol. wt. 413.43. Found: C, 54.96; H, 6.66; N, 3.31; mol. wt. 436.

3,6,9,12-Tetraoxa-16-azabicyclo[12.3.1]octadeca-1(18),14,16-triene-2,13-dione (**10**).

Freshly sublimed 3,5-pyridine dicarbonyl chloride (12.32 g., 0.0604 mole) and triethylene glycol (9.07 g., 0.0604 mole) were used. The normal extraction method (35) did not give a detectable amount of the desired product. The crude reaction mixture was depolymerized (36) at 275°/0.8 mm using 0.20 g. magnesium chloride hexahydrate. A small amount of yellow viscous oil was obtained by this procedure. This oil was then extracted with boiling hexane; cooling the decanted solution gave 0.028 g. (<1%) of the desired product. Recrystallization from methanol gave white needles, m.p. 137-137.5°; ir (potassium bromide): 1730 cm^{-1} ; nmr: δ 3.80 (m, 8H, $\text{COOCH}_2\text{CH}_2\text{OCH}_2$), 4.47 (m, 4H, COOCH_2), 9.31 (s, 2H, aromatic $\text{H}_{2,6}$), and 9.39 (s, 1H, aromatic H_4); ms: m/e 282 ($M + 1$, base).

Anal. Calcd. for $\text{C}_{13}\text{H}_{15}\text{NO}_6$: C, 55.51; H, 5.38; N, 4.98. Found: C, 55.48; H, 5.34; N, 4.94.

3,6,9,12,15-Pentaoxa-19-azabicyclo[15.3.1]heneicosa-1(21),17,19-triene-2,16-dione (**11**).

Freshly sublimed 3,5-pyridine dicarbonyl chloride (6.32 g., 0.031 mole) and tetraethylene glycol (6.02 g., 0.031 mole) were used. The crude reaction mixture was repeatedly extracted (35) with boiling hexane. Upon cooling, 3.30 g. (32.7%) of the white, crystalline product was collected. An analytical sample was prepared by recrystallization from methanol, white needles, m.p. 112-113°; ir (potassium bromide): 1720 cm^{-1} ; nmr: δ 3.72 (s, 8H, $\text{OCH}_2\text{CH}_2\text{O}$), 3.79 (m, 4H, $\text{COOCH}_2\text{CH}_2\text{O}$), 4.50 (m, 4H, COOCH_2), 8.91 (t, 1H, $J = 2$ Hz, aromatic H_4), and 9.36 (d, 2H, $J = 2$ Hz, aromatic $\text{H}_{2,6}$).

Anal. Calcd. for $\text{C}_{15}\text{H}_{19}\text{NO}_7$: C, 55.38; H, 5.89; mol. wt. 325.32. Found: C, 55.51; H, 5.97; mol. wt. 332.

Attempts were made to form the sodium thiocyanate and potassium thiocyanate complexes of **11** by the method employed in forming the potassium thiocyanate complex of **5**. In each case the macrocyclic diester was recovered and analyzed. No complexation of the salt was observed, i.e., no band was found in the ir spectrum characteristic of thiocyanate.

3,6,12,15-Tetraoxa-9-thia-19-azabicyclo[15.3.1]heneicosa-1(21),17,19-triene-2,16-dione (**12**).

Freshly sublimed 3,5-pyridine dicarbonyl chloride (7.84 g., 0.0384 mole) and 1,4,10,13-tetraoxa-7-thiatridecane (8.08 g., 0.0384 mole) were used. The crude reaction mixture was repeatedly extracted (35) with boiling hexane. Upon cooling, 1.22 g. (9.3%) of the solid, white product was collected. Recrystallization of the white powder from methanol gave colorless needles, m.p. 108-109°; ir (potassium bromide): 1720 cm^{-1} ; nmr: δ 2.93 (t, 4H, SCH_2), 3.84 (m, 8H, $\text{COOCH}_2\text{CH}_2\text{OCH}_2$), 4.57 (m, 4H, COOCH_2), 8.97 (t, 1H, $J = 2$ Hz, aromatic H_4), and 9.46 (d, 2H, $J = 2$ Hz, aromatic $\text{H}_{2,6}$).

Anal. Calcd. for $\text{C}_{15}\text{H}_{19}\text{NO}_6\text{S}$: C, 52.78; H, 5.61; mol. wt. 341.39. Found: C, 52.94; H, 5.64; mol. wt. 351.

3,9,15-Trioxa-6,12-dithia-19-azabicyclo[15.3.1]heneicosa-1(21),17,19-triene-2,16-dione (**13**).

Freshly sublimed 3,5-pyridine dicarbonyl chloride (6.23 g., 0.031 mole) and 1,7,13-trioxa-4,10-dithiatridecane (6.79 g., 0.030 mole) were used. The glycol was dissolved in a 30/70 mixture of THF/benzene. The crude reaction mixture was repeatedly extracted (35) with boiling hexane. Upon cooling, 0.89 g. (8.3%) of a white crystalline product was collected. An analytical sample

was prepared by sublimation, m.p. 103-104°; ir (potassium bromide): 1725 cm⁻¹; nmr: δ 2.91 (t, 4H, J = 6.5 Hz, OCH₂CH₂S), 3.07 (t, 4H, J = 5.5 Hz, COOCH₂CH₂S), 3.74 (t, 4H, J = 6.5 Hz, OCH₂CH₂S), 4.62 (t, 4H, J = 5.5 Hz, COOCH₂), 8.89 (t, 1H, J = 2 Hz, aromatic H₄), and 9.47 (d, 2H, J = 2 Hz, aromatic H_{2,6}).

Anal. Calcd. for C₁₅H₁₉NO₅S₂: C, 50.40; H, 5.36; N, 3.92; mol. wt. 357.45. Found: C, 50.50; H, 5.46; N, 3.90; mol. wt. 361.

3,6,9,12,15,18-Hexaoxa-22-azabicyclo[18.3.1]tetracos-1(24),20,22-triene-2,19-dione (14).

Freshly sublimed 3,5-pyridine dicarbonyl chloride (7.38 g., 0.036 mole) and pentaethylene glycol (8.62 g., 0.036 mole) were used. The crude reaction mixture was repeatedly extracted (35) with boiling hexane. Upon cooling 0.92 g. (6.9%) of a waxy solid was collected. Recrystallization of the product from absolute ethanol to obtain an analytical sample gave colorless prisms, m.p. 54.5-55.5°; ir (potassium bromide): 1720 cm⁻¹; nmr: δ 3.65 and 3.71 (both s, 12H, OCH₂CH₂O), 3.84 (m, 4H, COOCH₂CH₂O), 4.57 (m, 4H, COOCH₂), 8.91 (t, 1H, J = 2 Hz, aromatic H₄), and 9.44 (s, 2H, aromatic H_{2,6}).

Anal. Calcd. for C₁₇H₂₃NO₈: C, 55.28; H, 6.28; mol. wt. 369.38. Found: C, 55.19; H, 6.39; mol. wt. 367.

3,6,9,12,15,18,21-Heptaoxa-25-azabicyclo[21.3.1]heptacos-1(27),23,25-triene-2,22-dione (15).

Freshly sublimed 3,5-pyridine dicarbonyl chloride (5.30 g., 0.026 mole) and hexaethylene glycol (7.33 g., 0.026 mole) were used. The crude reaction mixture was repeatedly extracted (35) with boiling hexane. Upon cooling, 0.81 g. (7.5%) of a white powder was collected. An analytical sample was prepared by recrystallization from hexane, colorless needles, m.p. 50-51°; ir (potassium bromide): 1720 cm⁻¹; nmr: δ 3.63 and 3.73 (both s, 16H, OCH₂CH₂O), 3.89 (m, 4H, COOCH₂CH₂O), 4.61 (m, 4H, COOCH₂), 8.91 (t, 1H, J = 2 Hz, aromatic H₄), and 9.46 (s, 2H, aromatic H_{2,6}).

Anal. Calcd. for C₁₉H₂₇NO₉: C, 55.20; H, 6.58; mol. wt. 413.43. Found: C, 54.95; H, 6.62; mol. wt. 415.

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