The Synthesis of Macrocyclic Polyether-diester Ligands Containing A Long-Chain Alkoxy Substituted Pyridine Subcyclic Unit

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Two new series of macrocyclic polyether-diester ligands have been prepared containing 4-pentoxy- and 4-octoxypyridine subcyclic units. The 4-alkoxy-2,6-pyridinedicarboxylic acid derivatives used as starting materials were prepared from 4-chloro-2,6-pyridinedicarbonyl chloride. The 4-octoxydiketopyridino-18-crown-6 ligand greatly facilitates the transport of silver ions across a chloroform liquid membrane.

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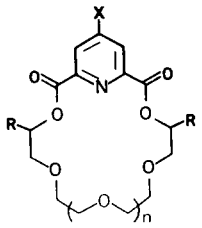
We have prepared and studied the cation complexation properites of a large number of macrocyclic polyether-diester ligands (crown diesters) (1-10). We have found that all crown diester ligands except those containing a pyridine subcyclic unit (**1-3**) form weaker complexes with metal and alkylammonium salts than do their polyether crown counter parts (11). Pyridino ligand **2** forms stable complexes (log K = 4.3-4.9) with alkali, alkaline earth,

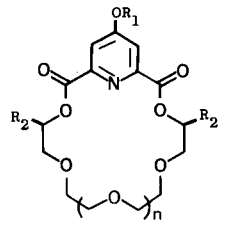


1 n=0, X=R=H
2 n=1, X=R=H
3 n=2, X=R=H
4 n=0, X=OCH_3, R=H
5 n=1, X=OCH_3, R=H
6 n=2, X=OCH_3, R=H
7 n=1, X=H, R=CH_3
8 n=1, X=OCH_3, R=CH_3
9 n=1, X=H, R=C_2H_5

silver and primary alkylammonium cations (6). Compounds **2, 5** and **7** proved to be excellent cation carriers through a chloroform liquid membrane (12). Studies of various types of carrier ligands seem to indicate that the efficiency of a carrier to transport cations may be increased by long-chain alkyl substituents (12). Also the long-chain alkyl substituents cause the carrier ligand to be more soluble in the chloroform membrane. We have reported the preparation of a number of methyl- and ethyl-substituted pyridino ligands where the small alkyl groups are attached to the polyether ring (**7-9**) (5,7). Cation transport by those compounds was the same as that for unsubstituted compound **2** (12).

We now report the preparation of two series of pyridino crown diester compounds containing long-chain alkoxy substituents on the pyridine ring. The substituents include the octoxy (compounds **10-13, 20** and **21**, Figure 1) and pentoxy groups (**14-19**). The transport of silver ions through a chloroform membrane was enhanced by compound **15** as compared with the unsubstituted macrocycle **2**.

Figure 1
Compound Structures

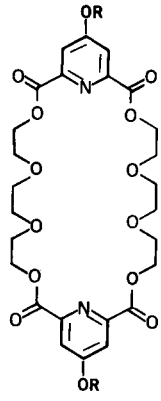


$R_1=C_8H_{17}$

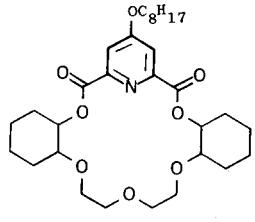
10 n=1, R_2=H
11 n=1, $R_2=CH_3$
12 n=1, $R_2=C_2H_5$
13 n=2, R_2=H

$R_1=C_5H_{11}$

14 n=0, R_2=H
15 n=1, R_2=H
16 n=1, $R_2=CH_3$
17 n=1, $R_2=C_2H_5$
18 n=2, R_2=H



19 R = C_5H_{11}
20 R = C_8H_{17}



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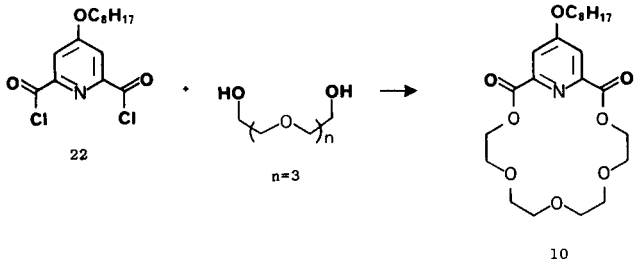
Results and Discussion.

The new macrocyclic compounds were prepared by two methods. We have previously used the reaction of diacid chlorides with the oligoethylene glycols to prepare the macrocyclic crown diester ligands (method A, Scheme I) (4). All the octoxy compounds except compound **20** were prepared using method A.

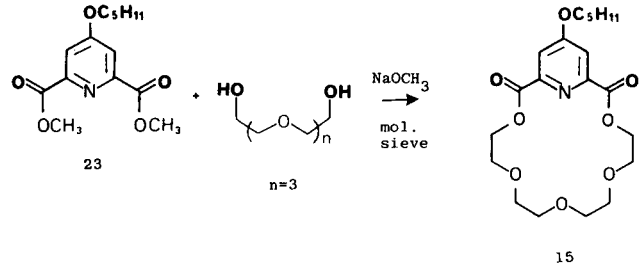
We have found that the transesterification reaction of a dimethyl diester compound with a glycol is a superior

Scheme I

Method A



Method B



method to prepare the macrocyclic crown diester ligands (method B, Scheme I) (13). The dimethyl diester and the glycol were mixed in dry benzene. The methanol by-product was removed from the reaction by molecular sieves. Methanol has also been removed by distillation in these cyclization reactions as reported by Thulin and Vötle for the preparation of macrocyclic bismalonates (14). All the pentoxy compounds (**14-19**) and compound **20** were prepared by method B. Starting 4-alkoxy-2,6-pyridinedicarboxylic acid derivatives (**22-25**) were prepared from the 4-chloro compound as was the 4-methoxy derivative (Scheme II) (6,15).

Scheme II

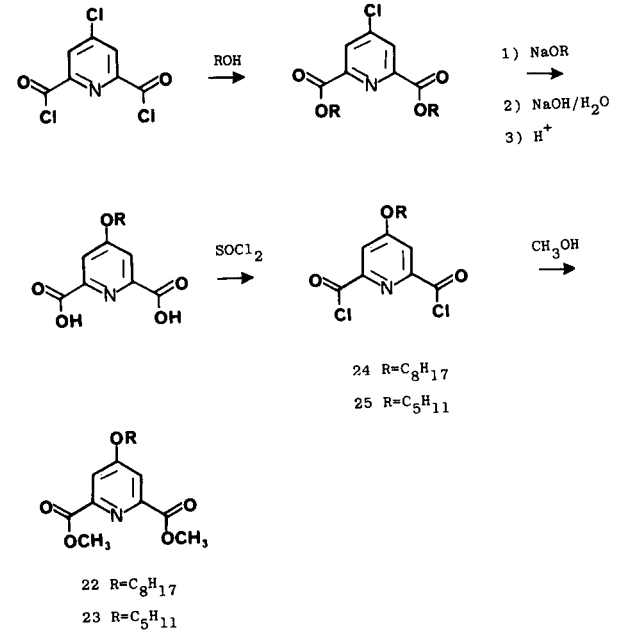


Table I

A Comparison of Physical Properties and Yields of Various Pyridino Macrocyclic Compounds

Crown-5	Synthesis	mp	Yield	Reference
1	A	139-140	9.6	a
4	A	154-154.5	1	b
14	B	99-101	6.4	c
Crown-6				
2	A	86.5-87.5	78	a
5	A	116-117	54.2	b
6	A	67-68	67	c
15	B	54.5-56.5	34	c
Crown-7				
3	A	143-144.5	24.7	a
6	A	122-123	18.5	b
13	A	26-28	19	c
18	B	oil	43	c
Dimethyl-Crown-6				
7	A	81-83	19	d
7 (S,S)	A	94	48.5	e
7 (meso)	A	102-103	38	e
8 (S,S)	A	98-99	17	e
11	A	oil	49	c
16	B	oil	68	c
Dimethyl-Crown-6				
9	A	oil	31	f
12	A	oil	34	c
17	B	oil	68	c

(a) Reference 4. (b) Reference 6. (c) This work. (d) Reference 5. (e) Reference 10. (f) Reference 7.

The structures proposed for all macrocyclic compounds are consistent with data derived from ir and nmr spectra, combustion analyses and molecular weight determinations. The nmr spectra for dimethyl and diethyl substituted compounds **11, 12, 16** and **17** showed that the positional isomers observed for compounds **7-9** (5,7) are also present in the new compounds. Two peaks were also observed for the aromatic protons in the nmr for the dimethyl and diethyl compounds indicative of the syn and anti dialkyl substituted products (7). Clear patterns were observed in the nmr spectra for all other compounds.

Table II

Cation Flux (J_M) (Moles × 10^8/sm²) from the Source Phase (a) for Ag^+-M^{n+} Mixtures using 18C6 Carriers with Varying Substituents

			Carriers (b)			
Cations (c)	18C6	DC18C6	**1**	**2**	**3**	**10**
Ag^+	507	1036	150	718	507	829
Ag^+	187	622	122	276	391	553
K^+	486	368	(d)	37	7	35
Ag^+	299	760	127	484	391	783
Cs^+	35	21	(d)	2	18	0.9
Ag^+	62	161	9	138	62	299
Tl^+	371	622	(c)	51	253	55
Ag^+	2	5	78	166	437	368
Pb^{2+}	262	507	(d)	286	37	691

(a) Fluxes across the receiving phase-chloroform phase boundary area are 0.286 times those given in the Table. Cell dimensions are given in reference 12. (b) 18C6 = 18-crown-6, DC18C6 = dicyclohexano-18-crown-6. (c) Source solution 1.0 *M* in silver nitrate for single cation determinations and 0.5 *M* in each cation for the Ag^+-M^{n+} mixtures except in the cases of Ag^+-Ba^{2+} and Ag^+-Tl^+ which were 0.15 *M* in each cation. (d) Transport rate less than the blank determination, 0.7 × 10^{-6} moles/sm², in which no carrier is present.

It is interesting to note that when diketopyridino-15-crown compounds **1** and **4** were prepared by method A (4,6) only the 1:1 adduct was isolated. Method B is an equilibrium type process. If more than one macrocyclic compound is possible, they would be more likely to form during the method B process. This was observed during the formation of pentoxy crown-5 (**14**) in that the 2:2 adduct **19** was also isolated. The corresponding octoxy crown-5 compound could not be isolated but the 2:2 adduct **20** was formed in a 14% yield.

A comparison of the physical properties and yields of various pyridino diester crown compounds is given in Table 1. The melting points of the octoxy and pentoxy substituted ligands are lower than melting points for the unsubstituted ligands. In some cases the new compounds were liquids. Product yields were not significantly different except when method B was used to prepare compound **16** and **17** where the yields were higher. We previously reported a significant decrease in product yields for the reaction of 2,6-pyridinedicarbonyl chloride with dialkyl substituted tetraethyl glycols (7). Compounds **7** and **9** were prepared in moderate yields while the analog containing *n*-octyl rather than methyl or ethyl groups could not be isolated (7). The new transesterification process (method B) gave excellent yields for the preparation of not only dimethyl and diethyl ligands **16** and **17** but also for the diphenyl analogs of compound **7** (13).

An extensive study of the transport of silver ions from Ag^+-M^{n+} binary mixtures in a water-chloroform-water liquid membrane system using pyridino ligands **1-3** and **10** as well as many other crown ligands as cation carriers has been completed (16). The pyridino ligands were superior to all other crown compounds except the dicyclohexano-18-crown-6 (DC18C6) in transporting silver ions (see Table II, complete details are reported in reference 16).

Some interesting correlations between the cation fluxes and various ligand parameters are evident from the data in Table II. Silver ion by itself is transported more effectively by the 18-crown-6 ligands (18C6, DC18C6, **2** and **10**) than the smaller 15-crown-5 (**1**) or the larger 21-crown-7 (**3**) ligands. The silver ion (radius = 1.15 Å) is too large for a 15-crown-5 ligand (cavity = 0.86-0.92 Å), too small for the 21-crown-7 (1.7 Å) but about right for the 18-crown-6 macrocycle (1.3-1.4 Å) (16). The relationship between cation radius and cavity size is also evident in the Ag^+-K^+ data. Potassium ion (radius = 1.38 Å) more closely fits the 18-crown-6 cavity than does Ag^+ so the transport of K^+ from a binary Ag^+-K^+ mixture is higher than that for Ag^+ (Table II).

Cation transport using the pyridine nitrogen substituted carriers is markedly different from that for the all oxygen 18-crown-6 ligand. The nitrogen substituted crown compound has an increased affinity of Ag^+ and a decreased affinity for alkali and alkaline earth metal cations (18). Thus, the pyridino ligands should transport Ag^+ more effectively than most other metal ions as is observed (compare data for **2** vs that for 18C6 in Table II). Only lead ion is transported more effectively than silver by **2**.

One other structural effect is shown by the data in Table II. Compound **10** transports Ag^+ at a much higher flux than does compound **2**. This result can be explained by two factors. First, the alkoxy group has an electron donating property which increases the stability of the ligand-Ag^+ complex (6). Second, the hydrophobic bulk of the octyl group decreases the carrier's solubility in water which restricts the ligand to the liquid chloroform membrane. Each of these effects is expected to enhance the transport of Ag^+.

The transport of cations by these ligands as compared

to many other crown compounds is more fully discussed in references 12 and 16.

EXPERIMENTAL

The ir spectra were obtained on a Beckman Acculab 2 spectrophotometer. The proton nmr spectra were obtained on a JEOL FX-90Q spectrometer. Elemental analyses were performed by MHW Laboratories, Phoenix, Arizona. Molecular weights were obtained by osmometry on a Hitachi Perkin-Elmer model 115 molecular weight apparatus. Melting points were determined on a Thomas-Hoover melting point apparatus and are uncorrected.

Starting Materials.

The starting unsubstituted oligoethylene glycols were purchased from Geneva Chemical Co., Orem, Utah. The substituted glycols, 4,7,10-trioxatridecane-2,12-diol (5), 5,8,11-trioxapentadecane-3,13-diol (7) and 1,2,10,11-dicyclohexano-3,6,9-trioxaundecane-1,11-diol (7), were prepared as reported. The 4-pentoxy- and 4-octoxy-2,6-pyridinedicarboxylic acid derivatives were prepared as outlined below (Scheme II).

Dimethyl 4-Pentoxy-2,6-pyridinedicarboxylate (**23**).

An excess of 1-pentanol was slowly added to 4-chloro-2,6-pyridinedicarbonyl chloride (6,15) (34.1 g, 0.145 mole) in dichloromethane. The solution was refluxed until hydrogen chloride ceased to evolve (about 1 hour), The solvents were then removed under reduced pressure and the crude dipentyl 4-chloro-2,6-pyridinedicarboxylate was added to 2.5 equivalents of sodium pentoxide in pentanol (prepared using sodium hydride). The mixture was stirred until the nmr peak for the hydrogen atoms on the 4-chloropyridine ring (δ 8.3) was replaced by the peak for the hydrogen atoms on the 4-pentoxypyridine ring (δ 7.8). Most of the pentanol was removed under reduced pressure and 8.2 g of solid potassium hydroxide in 20 ml of water was added. The aqueous pentanol mixture was refluxed for 2 hours. The cooled solution was extracted with two portions of ether to remove the excess pentanol and other organic impurities. The resulting aqueous solution was acidified with dilute hydrochloric acid to yield the 4-pentoxy-2,6-pyridinedicarboxylic acid, 27.5 g (76%) which was not further purified. The crude acid was dried and reacted with an excess of thionyl chloride catalyzed by a drop of dimethyl formamide. The excess thionyl chloride was removed under reduced pressure and the resulting 4-pentoxy-2,6-pyridinedicarbonyl chloride (**25**) was reacted carefully with dry methanol in dichloromethane. The solvents were then removed to yield solid **23** which was recrystallized from methanol, 26 g (87%), mp 72.5-73°.

Anal. Calcd. for $C_{14}H_{19}NO_5$: C, 59.77; H, 6.81; mol wt, 281.3. Found: C, 59.69; H, 6.93; mol wt, 273.1.

Dimethyl 4-Octoxy-2,6-pyridinedicarboxylate (**22**).

This compound was prepared in the same manner as reported above except that 1-octanol was used. Both the acid chloride **24**, mp 32-32.5°, and dimethyl ester **22**, mp 67.5-68° were used to form the macrocyclic compounds.

Anal. Calcd for $C_{17}H_{25}NO_5$: C, 63.13; H, 7.79; mol wt, 323.4. Found: C, 62.93; H, 7.74; mol wt, 311.4.

General Procedures for the Synthesis of Macrocyclic Compounds.

Method A.

The glycol and acid chloride each dissolved in 250 ml of benzene were added simultaneously to 1 liter of rapidly stirring benzene at 50°. After evolution of hydrogen chloride gas ceased, the solvent was removed under reduced pressure. The product was isolated by a hot hexane extraction (2,4). Specific details are given for each compound.

Method B.

The glycol and dimethyl 4-substituted-2,6-pyridinedicarboxylate were dissolved in 250 ml of dry benzene. About 20 ml of benzene was distilled from the solution to remove any traces of water. About 60 g of molecular sieves (4A) and 0.1 to 0.2 ml of 10% sodium methoxide in methanol were then added and the resulting mixture was stirred at room temperature until a tlc analysis showed that all the dimethyl ester had reacted. The solution was then filtered and the molecular sieves were washed several times with dichloromethane or hot toluene. The combined filtrate and dichloromethane or toluene washes were worked up as in method A.

19-Octoxy-3,6,9,12,15-pentaoxa-21-azabicyclo[15.3.1]heneicosa-1(21),17,19-triene-2,16-dione (**10**).

Method A was followed using 10.88 g (0.033 mole) of octoxy diacid chloride **24** and 6.4 g (0.033 mole) of tetraethylene glycol. The product was recrystallized from ethanol to give **10** as a white solid, 10.3 g (67%), mp 67-68°; ir: 1715 cm^{-1}; nmr: δ 0.9 (m, 3H, CH_3), 1.33 (m, 10H, CH_2), 1.8 (m, 2H, OCH_2CH_2), 3.85 (m, 12H, OCH_2), 4.13 (t, 2H, OCH_2 of the octoxy group), 4.52 (m, 4H, $COOCH_2$), 7.82 (s, 2H).

Anal. Calcd. for $C_{23}H_{35}NO_8$: C, 60.93; H, 7.73; mol wt, 453.5. Found: C, 60.73; H, 7.60; mol wt, 443.2.

4,14-Dimethyl-19-octoxy-3,6,9,12,15-pentaoxa-21-azabicyclo[15.3.1]heneicosa-1(21),17,19-triene-2,16-dione (**11**).

Method A was followed using 10.03 g (0.03 mole) of octoxy diacid chloride **24** and 6.71 g (0.03) of 4,7,10-trioxatridecane-2,12-diol. The product (7 g, 49%) was an oil; ir: 1715 cm^{-1}; nmr: δ 0.9 (m, 3H, CH_3), 1.2 (m, 6H, CH_3), 1.38 (m, 10H, CH_2), 1.85 (m, 2H, OCH_2CH_2), 4.82 (m, 12H, OCH_2), 4.2 (t, 2H, OCH_2 of the octoxy group), 5.3 (m, 2H, $OCHCH_3$), 7.75 and 7.80 (both s, 2H). The nmr spectrum exhibited a small peak at δ 4.9 showing isomeric impurity.

Anal. Calcd. for $C_{25}H_{39}NO_8$: C, 62.29; H, 8.10; mol wt, 481.6. Found: C, 62.22; H, 8.16; mol wt, 464.1.

4,14-Diethyl-19-octoxy-3,6,9,12,15-pentaoxa-21-azabicyclo[15.3.1]heneicosa-1(21),17,19-triene-2,16-dione (**12**).

Method A was followed using 9.6 g (0.029 mole) of octoxy diacid chloride **24** and 7.23 g (0.029 mole) of 5,8,11-trioxapentadecane-3,13-diol. The product (5 g, 34%) was an oil; ir: 1715 and 1730 (sh) cm^{-1}; nmr: δ 0.95 (m, 9H, CH_3), 1.2 (m, 4H, CH_2), 1.42 (m, 10H, CH_2), 1.85 (m, 2H, OCH_2CH_2), 3.70 (m, 12H, OCH_2), 4.18 (t, 2H, OCH_2 of the octoxy group), 5.35 (m, 2H, $OCHCH_3$), 7.75 and 7.80 (both s, 2H). The nmr spectrum exhibited a small peak at δ 4.6 showing isomeric impurity.

Anal. Calcd. for $C_{27}H_{43}NO_8$: C, 63.58; H, 8.44; mol. wt, 509.6. Found: C, 63.38; H, 8.49; mol wt, 515.5.

22-Octoxy-3,6,9,12,15,18-hexaoxa-24-azabicyclo[18.3.1]tetracosa-1(24),-20,22-triene-2,19-dione (**13**).

Method A was followed using 7.1 g (0.021 mole) of octoxy diacid chloride **24** and 5.1 g (0.021 mole) of pentaethylene glycol. The product was recrystallized from ethanol to yield **13** as a while solid, 1.94 g (19%), mp 26-28°; ir: 1720 cm^{-1}; nmr: δ 0.9 (m, 3H, CH_3), 1.35 (m, 10H, CH_2), 1.85 (m, 2H, OCH_2CH_2), 3.62 (s, 4H, OCH_2), 3.72 (m, 8H, OCH_2), 3.95 (m, 4H, $COOCH_2CH_2$), 4.15 (t, 2H, OCH_2 of the octoxy group), 4.52 (m, 4H, $COOCH_2$), 7.80 (s, 2H).

Anal. Calcd. for $C_{25}H_{39}NO_9$: C, 60.36; H, 7.85; mol wt, 497.6. Found: C, 60.61; H, 7.75; mol wt 478.5.

16-Pentoxy-3,6,9,12-tetraoxa-18-azabicyclo[12.3.1]octadeca-1(18),14,16-triene-2,13-dione (**14**) and 16,33-Dipentoxy-3,6,9,12,20,23,26,29-octoxa-35,36-diazatricyclo[28.3.1.$1^{14,18}$]hexatriconta-1(35),14(36),15,17,31,33-hexaene-2,13,19,30-tetraone (**19**).

Method B was followed using 6.0 g (0.021 mole) of pentoxy dimethylester **23** and 3.2 g (0.021 mole) of triethylene glycol. The hexane extract contained 1.9 g (24%) of white crystals of compound **19**, mp 134.5-135.5°; ir: 1715 and 1730 cm^{-1}; nmr: δ 0.9 (m, 6H, CH_3), 1.4 (m, 8H, CH_2), 1.8 (m, 4H, OCH_2CH_2), 3.9 (m, 16H, OCH_2), 4.1 (m, 4H, 4H, OCH_2 of the pentoxy group), 4.5 (m, 8H, $COOCH_2$), 7.75 (s, 4H).

Anal. Calcd. for $C_{36}H_{50}N_2O_{14}$: C, 58.86; H, 6.81; mol wt, 734.8. Found: C, 58.82; H, 6.78; mol wt, 729.66.

The hexane filtrate was evaporated to give 0.5 g (6.4%) of compound **14** which was recrystallized from ethanol, mp 99-101°; ir: 1730 and 1760 cm^{-1}; nmr δ 0.9 (m, 3H, CH_3), 1.45 (m, 4H, CH_2), 1.82 (m, 2H, OCH_2CH_2),

3.9 (m, 12H, OCH_2), 4.15 (t, 2H, OCH_2 of the pentoxy group), 7.73 (s, 2H).

Anal. Calcd. for $C_{18}H_{25}NO_7$: C, 58.86; H, 6.81. Found: C, 58.64; H, 6.78.

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

Method B was followed using 8.0 g (0.029 mole) of pentoxy dimethylester **23** and 5.52 g (0.029 mole) of tetraethylene glycol. Product **15** (4.0 g, 34%) was a white solid, mp 54.5-56.5°; ir: 1720 cm^{-1}; nmr: δ 0.95 (m, 3H, CH_3), 1.45 (m, 4H, CH_2), 1.85 (m, 2H, OCH$_2$CH_2), 3.80 (s, 8H, OCH_2), 3.90 (m, 4H, COOCH$_2$CH_2), 4.18 (t, 2H, OCH_2 of the pentoxy group), 4.55 (m, 4H, COOCH_2), 7.82 (s, 2H).

Anal. Calcd. for $C_{20}H_{29}NO_8$: C, 58.30; H, 7.05; mol wt, 411.5. Found: C, 58.21; H, 7.02; mol wt, 395.2.

4,14-Dimethyl-19-pentoxy-3,6,9,12,15-pentaoxa-21-azabicyclo[15.3.1]-heneicosa-1(21),17,19-triene-2,16-dione (**16**).

Method B was followed using 8.0 g (0.028 mole) of pentoxy dimethylester **23** and 6.3 g (0.028 mole) of 4,7,10-trioxatridecane-2,12-diol. The product was an oil, 6.0 g (68%), ir: 1710 cm^{-1} nmr: δ 0.9-1.2 (m, 9H, CH_3), 1.35 (m, 4H, CH_2), 1.8 (m, 2H, OCH$_2$CH_2), 3.75 (m, 12H, OCH_2), 4.15 (t, 2H, OCH_2 of the pentoxy group), 5.15 (m, 2H, COOCH_2). 7.75 and 7.80 (both s, 2H).

Anal. Calcd. for $C_{22}H_{33}NO_8$: C, 60.14; H, 7.52; mol wt, 439.5. Found: C, 59.52; H, 7.61; mol wt, 454.0.

4,14-Diethyl-19-pentoxy-3,6,9,12,15-pentaoxa-21-azabicyclo[15.3.1]-heneicosa-1(21),17,19-triene-2,16-dione (**17**).

Method B was followed using 5.0 g (0.018 mole) of pentoxy dimethylester **23** and 4.45 g (0.018 mole) of 5,8,11-trioxapentadecane-3,13-diol. The product was an oil, 3.6 g (43%), ir: 1710 cm^{-1}; nmr: δ 0.9-1.1 (m, 9H, CH_3), 1.45 (m, 4H, CH_2), 1.9 (m, 6H, OCH$_2$CH_2 and OCHCH_2), 3.7 (m, 12H, OCH_2), 4.15 (t, 2H, OCH$_2$ of the pentoxy group), 5.25 (m, 2H, COOC*H*), 7.75 and 7.85 (both s, 2H). The nmr spectrum exhibited a small peak at δ 4.6 showing isomeric impurity.

Anal. Calcd. for $C_{24}H_{37}NO_8$: C, 61.67; H, 7.92; mol wt, 467.4. Found: C, 61.82; H, 8.05; mol wt, 464.0.

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

Method B was followed using 5.0 g (0.018 mole) of pentoxy dimethylester **23** and 4.2 g (0.018 mole) of pentaethylene glycol. The product was an oil, 3.5 g (43%); ir: 1715 cm^{-1}; nmr: δ 0.95 (m, 3H, CH_3), 1.48 (m, 4H, CH_2), 1.85 (m, 2H, OCH$_2$CH_2), 2.78 (2s, 12H, OCH_2), 2.95 (m, 4H, COOCH$_2$CH_2), 4.20 (t, 2H, OCH_2 of the pentoxy group), 4.58 (m, 4H, COOCH_2), 7.85 (s, 2H).

Anal. Calcd. for $C_{22}H_{33}NO_9$: C, 57.97; H, 7.25; mol wt, 455.4. Found: C, 57.85; H, 7.26; mol wt, 446.8.

16,33-Dioctoxy-3,6,9,12,20,23,26,29-octoxa-35,36-diazatricyclo[28.3.1.1^{14,18}]-hexatriconta-1(35),14(36),15,17,31,33-hexaene-2,13,19,30-tetraone (**20**).

Method B was followed using 15.3 g (0.046 mole) of octoxy dimethylester **22** and 7.1 g (0.046 mole) of triethylene glycol. Product **20** was recrystallized from ethanol, 2.7 g (14%); mp 105-107°; ir: 1710 cm^{-1}; nmr: δ 0.9 (t, 6H, CH_3), 1.35 (m, 20H, CH_2), 1.85 (m, 4H, OCH$_2$CH_2), 3.80 (s, 8H, OCH_2), 3.95 (m, 8H, COOCH$_2$CH_2), 4.15 (t, 4H, OCH_2 of the octoxy group), 4.55 (m, 8H, COOCH_2), 7.73 (s, 4H).

Anal. Calcd. for $C_{42}H_{62}N_2O_{14}$: C, 61.47; H, 7.56; mol wt, 820.0. Found: C, 61.25; H, 7.60; mol wt, 835.4.

19-Oxtoxy *trans*-dicyclohexano[d,m]-3,6,9,12,15-pentaoxa-21-azabicyclo-[15.3.1]heneicosa-1(21),17,19-triene-2,16-dione (**21**).

Method A was followed using 10.0 g (0.03 mole) of octoxy diacid chloride **24** and 9.1 g (0.03 mole) of 1,2,10,11-dicyclohexano-3,6,9-trioxaundecane-1,11-diol. The product was an oil, 7 g (42%); ir: 1710 cm^{-1}; nmr: δ 0.9 (m, 3H, CH_3), 1.35 (m, 26H, CH_2), 1.8 (m, 2H, OCH$_2$CH_2), 2.1 (m, 2H, OCH$_2$C*H*), 3.5-3.8 (m, 10H, OCH_2), 4.2 (t, 2H, OCH_2 of the octoxy group), 5.0 (m, 2H, COOC*H*), 7.8 and 7.9 (both s, 1H).

Anal. Calcd. for $C_{31}H_{47}NO_8$: C, 66.23; H, 8.37; mol wt, 561.7. Found: C, 66.18; H, 8.58; mol wt, 597.4.

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