74143-97-8; **7e**, 71841-11-7; **7g**, 74143-98-9; **7h**, 74165-58-5; **8a**, 74143-99-0; **8b**, 66716-32-3; **8c**, 74144-00-6; **8d**, 74144-01-7; **8e**, 71841-10-6; **8f**, 74144-02-8; **8g**, 74144-03-9; **8h**, 74175-89-6; **15a**, 22946-43-6; **15b**, 21370-57-0; **15c**, 74144-04-0; **15d**, 74144-05-1; **15e**, 74144-06-2; **16**, 35998-30-2; **17a**, 74144-07-3; **18a**, 74144-08-4; **18b**, 74144-09-5; methyl 2-(methylthio)acetate, 16630-66-3; homogeranyl toluenesulfonate, 71841-08-2; geranyl bromide, 6138-90-5; *n*-pentyl bromide, 110-53-2; (*Z*)-methyl 2-(phenylthio)cinnamate, 58808-66-5.

Synthesis of Diethyl, Di-*n*-octyl, and Mono- and Dicyclohexano Macrocyclic Polyether–Diester Ligands

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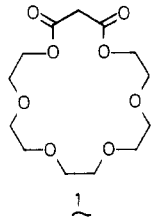
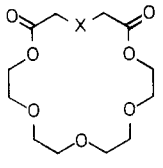
Three series of macrocyclic polyether–diester ligands have been prepared from the reaction of four diethyl-oligoethylene glycols, **24–27**, di-*n*-octyltetraethylene glycol **28**, and mono- and dicyclohexanotetraethylene glycols **29** and **30** with diglycolyl dichloride (products **6–11b**), thiadiglycolyl dichloride (products **12–17**), and 2,6-pyridinedicarbonyl chloride (products **18–23**). Compounds **11** and **17** formed trans-syn-trans and trans-anti-trans isomers, and in the case of compound **11** these isomers were isolated and characterized. The 18-membered-ring compounds **7**, **22**, and **23** formed solid potassium thiocyanate complexes.

Macrocyclic polyethers were first reported by Pedersen in 1967.[1,2] Since that time an intense interest in the synthesis and cation complexation properties of these macrocyclic compounds has developed. A number of excellent reviews have been published.[2-11]

We have recently reported the synthesis of a large number of macrocyclic polyether–diester compounds.[12-16] We have also studied the cation complexation properties of compounds **1–5**.[17-21] Compound **1** shows a cation selectivity similar to that of valinomycin ($K^+ > Ba^{2+}$) whereas compound **2a** shows much the same complexing pattern as that of 18-crown-6 ($Ba^{2+} > K^+ > Na^+$) but with diminished stability.[17] Compound **2b** shows no heat of reaction except with Ag^+ as is seen with other sulfur macrocycles.[18] Compound **4b** shows excellent complexing properties, giving heats of reaction in methanol with alkali, alkaline earth, and silver cations on the order of 4.3–4.9 log *K* units.[18] Compounds **3–5** also complex strongly with alkylammonium cations as shown by significant chemical shift changes in the ^1H NMR spectra.[16,19-21] It is interesting to note that whereas the benzylammonium cation complex of **4b** (18-membered ring) was kinetically more stable than the complex of **4d** (24-membered ring), the benzylammonium cation complex of **3c** (24-membered ring) gave the most stable complex of the furan-containing ligands.[20] Clearly, different complexing parameters are operating in these two classes of compounds.



1



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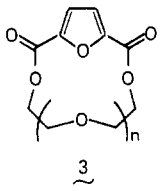
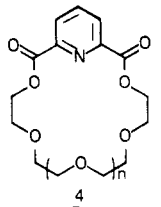
a,x = 0
b,x = S

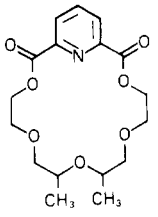


3
a,n = 3
b,n = 4
c,n = 5

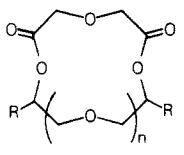
In order to study the complexing ability of the macrocyclic diester compounds more fully, we have synthesized a number of new alkyl-substituted macrocyclic polyether–diester compounds. A series of dimethyl- and tet-



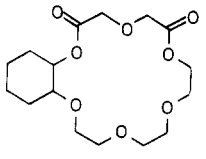
4
a,n = 0
b,n = 1
c,n = 2
d,n = 3



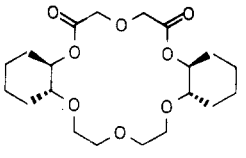
5



6 R = C_2H_5, n = 2
7 R = C_2H_5, n = 3
8 R = C_2H_5, n = 4
9 R = C_8H_{17}, n = 3



10



11a

(1) C. J. Pedersen, *J. Am. Chem. Soc.*, **89**, 7017 (1967).
(2) C. J. Pedersen in "Synthetic Multidentate Macrocyclic Compounds", R. M. Izatt and J. J. Christensen, Eds., Academic Press, New York, 1978, pp 1–53.
(3) J. M. Lehn, *Struct. Bonding (Berlin)*, **16**, 1 (1973).
(4) M. R. Truter, *Struct. Bonding (Berlin)*, **16**, 71 (1973).
(5) R. M. Izatt, D. J. Eatough, and J. J. Christensen, *Struct. Bonding (Berlin)*, **16**, 161 (1973).
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(7) J. J. Christensen, D. J. Eatough, and R. M. Izatt, *Chem. Rev.*, **74**, 351 (1974).
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(10) J. S. Bradshaw, G. E. Maas, R. M. Izatt, and J. J. Christensen, *Chem. Rev.*, **79**, 37 (1979).
(11) J. F. Stoddart, *Chem. Soc. Rev.*, **8**, 85 (1979).
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†Contribution No. 195.

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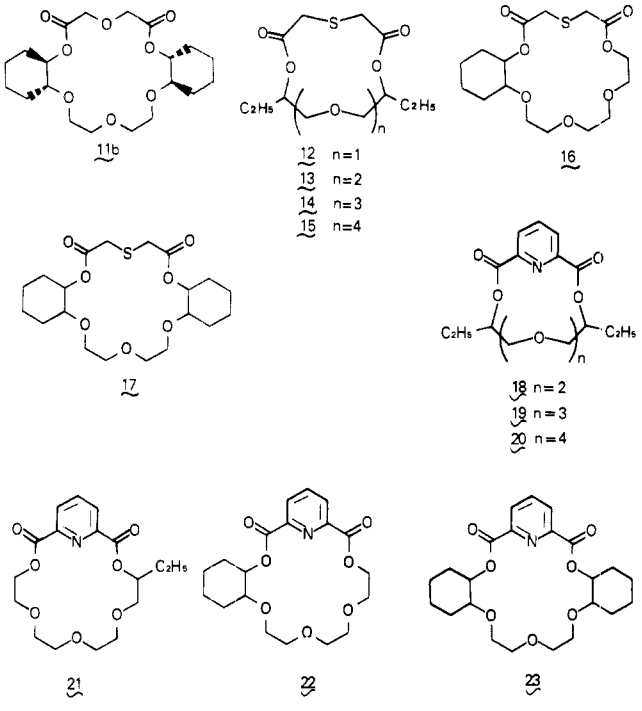
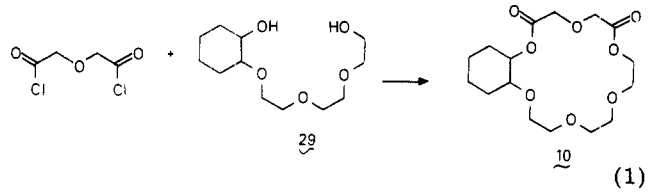
ramethyl-substituted compounds has already been reported.[16] We wish to report here the synthesis of some diethyl, di-*n*-octyl, and mono- and dicyclohexano polyether–diester macrocyclic compounds. Compounds **6–11b** were prepared from diglycolyl dichloride and the appropriate glycol, compounds **12–17** were prepared from thia-



diglycolyl dichloride and the appropriate glycol, and compounds **18–23** were prepared from 2,6-pyridinedicarbonyl chloride. Solid potassium thiocyanate complexes for compounds **7**, **21**, and **22** were also prepared.

Results and Discussion

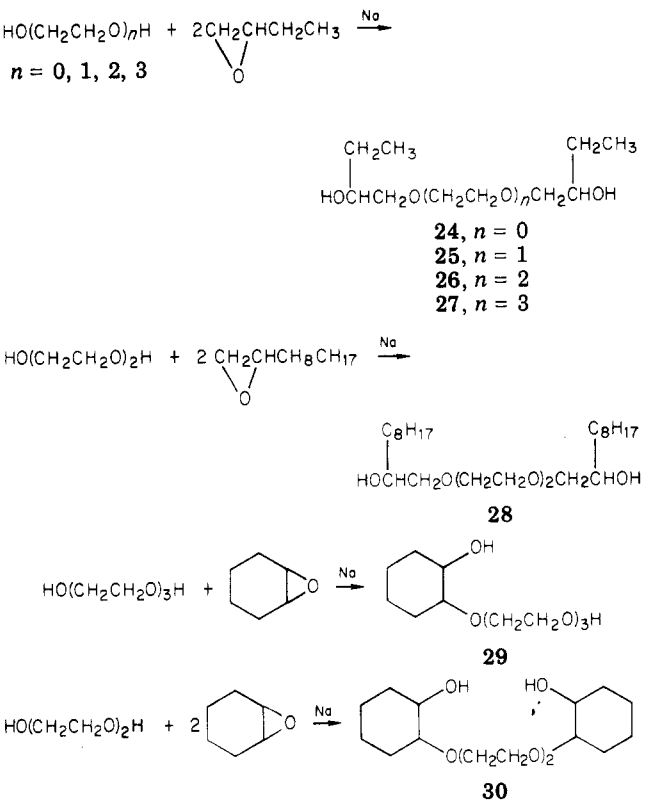
Macrocyclic compounds **6–23** were prepared by dissolving 5–15 g of the appropriate acid chloride and glycol in separate 250-mL portions of benzene and slowly and simultaneously dripping them into 1 L of warm (50 °C) stirring benzene (see eq 1). Yields were generally in the



(1)

range of 30–50% with the exception of the 12- and 15-membered-ring compounds (**12**, **6**, **13**, and **18**) and compounds **19** and **23** which gave yields of 3–13%. The low yields for compounds **19** and **23** were somewhat disappointing in light of the excellent yields usually obtained for the pyridino diester ligands.[15,21] For example, compound **4b** was prepared in an excellent yield of over 70%.[15] The dimethyl analogue of **19** was also prepared in a much diminished yield.[16] 2,6-Pyridinedicarbonyl chloride tends to decompose rapidly, and secondary glycols are less reactive so that more decomposition could take place before the acid chloride reacts with the dialkyl-substituted glycols. In several reactions, small amounts of 2,6-pyridinedicarboxylic acid were found, indicating that water was also present. In two cases (for **15** and **18**), product yields were increased by using a depolymerization catalyst[22,23] during the distillation process.

Scheme I



The glycols needed for the preparation of macrocycles **6–23** were all prepared by the base-catalyzed reaction (Na metal) of a substituted epoxide with a glycol (Scheme I). The reactions were generally clean and gave yields of 30–60%. However, some isomeric impurity can be seen in the ^{1}H NMR spectra of some of the corresponding macrocycles. These spectra indicate that small amounts of the positional isomers were formed by the opening of the epoxide in the opposite direction to form glycols **24–28** with an alkyl group on one of the second carbons. These isomers are probably present to about the same degree in glycols **24–28**, but the spectral evidence can only be observed in the case of macrocycles **18** and **20**. As mentioned above, the secondary glycols react less readily with 2,6-pyridinedicarbonyl chloride. Thus, the isomeric glycols with one primary alcohol group would react more readily and thereby increase the isomeric impurity in macrocycles **18** and **20** as was observed. Each new glycol had IR and ^{1}H NMR spectra and molecular weights consistent with the proposed structures; however, with the exception of **28**, correct elemental analyses could not be obtained. The

(14) G. E. Maas, J. S. Bradshaw, R. M. Izatt, and J. J. Christensen, *J. Org. Chem.*, **42**, 3937 (1977).
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(19) J. S. Bradshaw, G. E. Maas, R. M. Izatt, J. D. Lamb, and J. J. Christensen, *Tetrahedron Lett.*, 635 (1979).
(20) J. S. Bradshaw, S. L. Baxter, D. C. Scott, J. D. Lamb, R. M. Izatt, and J. J. Christensen, *Tetrahedron Lett.*, 3383 (1979).
(21) J. S. Bradshaw, G. E. Maas, J. D. Lamb, R. M. Izatt, and J. J. Christensen, *J. Am. Chem. Soc.*, **102**, 467 (1980).
(22) E. W. Spangel and W. H. Carruthers, *J. Am. Chem. Soc.*, **57**, 929 (1935).
(23) P. E. Fore, J. S. Bradshaw, and S. F. Nielsen, *J. Heterocycl. Chem.*, **15**, 269 (1978).

carbon percentage was low, indicative of the fact that these glycols are very hydroscopic. Correct elemental analyses were obtained on the macrocyclic compounds prepared from each of these glycols.

Macrocycle **21** was isolated from the reaction mixture during the preparation of **20** from glycol **27** and 2,6-pyridinedicarbonyl chloride. Compound **21** was formed from the monoethyltetraethylene glycol impurity in diethylpentaethylene glycol **27**. Again the amount of macrocycle byproduct **21** would be increased because the primary alcohol portion of the monosubstituted glycol is more reactive toward the acid chloride. Glycol **27** can be purified by three or four fractional distillations using the higher boiling fraction in each subsequent distillation step.

The thia and pyridino analogues of compound **9** could not be isolated. In each case, existence of the product in the reaction mixture was evidenced by the appearance of a carbonyl band in the IR and disappearance of the hydroxy band. The products could not be distilled, and all attempts at recrystalization caused the crude products to dissociate, reforming starting glycol **28**.

The structures proposed for the macrocyclic compounds are consistent with data derived from IR and ^{1}H NMR spectra, elemental analyses, and molecular weight determinations. The carbonyl bands in the IR were observed at 1710–1750 cm^{-1}, indicative of the ester functions. The ^{1}H NMR spectra were consistent with the structures (see Experimental Section) reported for these types of compounds.[14-16]

Some of the macrocycles formed complexes with potassium thiocyanate. The ^{1}H NMR spectra of these complexes were slightly different than that for the uncomplexed material. Some of the more important changes are as follows: the peak for the ethyl CH_2 hydrogen shifted from δ 1.55 to 1.72 when **7** was complexed, and the peak for the ester CH hydrogens shifted from δ 5.00 to 5.18 when **23** was complexed. Similar shifts were observed when compound **4b** was complexed with potassium or alkylammonium salts.[21]

Compound **11** separated into two fractions. Large rodlike crystals with a melting point of 180–181 °C were initially collected by a simple extraction procedure. The remainder of the extraction liquid was cooled to −20 °C, and a large amount of fine crystals separated; mp 120–180 °C. The higher melting fraction was less soluble in hexane, so that by careful fractional crystallization, the two fractions were separated. The lower melting isomer was isolated in reasonably pure form; mp 124.5–126.5 °C. The IR spectra of the two materials were quite different. The lower melting macrocycle exhibited two carbonyl bands at 1730 and 1750 cm^{-1} whereas a single carbonyl band at 1750 cm^{-1} was observed in the IR of the other isomer. The fingerprint regions of the IR spectra were also significantly different. One major difference was also observed in the ^{1}H NMR spectra. The ^{1}H NMR spectrum for the higher melting isomer has two sets of AB patterns for the four protons next to the carbonyl carbons (δ 4.21 and 4.42) whereas that for the lower melting compound gave a singlet at δ 4.30. Carbon-13 NMR spectra for the two isomers were also somewhat different. The ^{13}C NMR spectrum for the lower melting isomer exhibited four different peaks at δ 23.9, 24.1, 29.9, and 30.7 for the cyclohexane carbons while the ^{13}C NMR spectrum for the other isomer showed three different carbon peaks at δ 24.1, 30.6, and 30.7. The carbon next to the carbonyl carbon (COC) was observed at δ 69.6 for compound **11a** and at δ 67.9 for **11b**.

Stoddart and co-workers synthesized both the trans-syn-trans and the trans-anti-trans isomers of dicyclohexano-18-crown-6 and found that the trans-syn-trans isomer has a much higher melting point.[24] We believe that our dicyclohexano diester compounds are likewise the trans-syn-trans (**11a**, mp 180–181 °C) and the trans-anti-trans (**11b**, mp 124.5–126.5 °C) compounds. Starting with *trans*-1,2-cyclohexanediol, Whitham and co-workers were able to prepare only the trans-syn-trans dicyclohexano-18-crown-6 isomer, indicating that the syn isomer is more stable than the anti isomer.[25] There is evidence for two isomers for dicyclohexano thia compound **17**. In this case, the two isomers could not be completely separated so that a more complete analysis of the two isomers could not be done. Compound **23** could not be separated into isomers.

Diethyl compound **7** is also believed to be composed of syn and anti isomers. The ^{1}H NMR spectrum of the distilled reaction mixture exhibited a multiplet for the protons on the carbon next to the carbonyl carbon at δ 4.30. After about 1 month, crystals formed in the liquid. These crystals were separated and purified. The ^{1}H NMR of the solid gave two AB patterns at δ 4.21 and 4.34 which were similar to those peaks in the spectrum of **11a**. Because of the similarity of the ^{1}H NMR spectra between compound **11a** and the solid isomer of **7**, we feel that the ethyl groups in this isomer are syn to one another. Compounds **6** and **9** (but not **8**) are also believed to be syn isomers because of the sharpness of their melting points and the similarity of their ^{1}H NMR spectra in the δ 4.3 region to that of compound **11a**. Isomers could exist with all other compounds, but the ^{1}H NMR spectra for the other compounds are not definitive enough to make comparisons between the isomers. The ^{1}H NMR spectrum of the dimethyl analogue of compound **6**[16] also shows the AB patterns indicitive of the syn isomer. The other dimethyl analogues reported earlier[16] were mixtures of the syn and anti isomers.

Experimental Section

All infrared (IR) spectra were obtained on a Beckman Acculab 2 spectrophotometer. The proton nuclear magnetic resonance (^{1}H NMR) spectra were obtained on a Varian EM-390 spectrometer in deuteriochloroform with tetramethylsilane as an internal standard. The ^{13}C NMR spectra were obtained on a JEOL FX-90Q Fourier transform spectrometer in deuteriochloroform. The molecular weight determinations were done by osmometry on a Hitachi Perkin-Elmer 115 molecular weight apparatus. The elemental analyses were preformed by M-H-W Laboratories. Melting points were determined by using a Thomas-Hoover capillary-type melting point apparatus and are uncorrected.

All starting glycols and dicarbonyl chlorides were prepared in our laboratory from smaller glycols and diacids. Ethylene glycol (Aldrich), diethylene glycol (Aldrich), triethylene glycol (Aldrich), 1,2-epoxybutane (Aldrich), cyclohexene oxide (Aldrich), 1-decene (Aldrich), 2,6-pyridinedicarboxylic acid (Aldrich), diglycolic acid (Fluka), and thiodiglycolic acid (Evans) were used as purchased. Diglycolyl, thiodiglycolyl, and 2,6-pyridinedicarbonyl chlorides were prepared as reported.[14,15] The substituted glycols were prepared as follows.

5-Oxanonane-3,7-diol (24). 1,2-Butanediol (90 g, 1 mol; prepared by reacting 1,2-epoxybutane with aqueous sodium hydroxide) was placed in a three-necked flask fitted with a condenser, dropping funnel, and thermometer. A catalytic amount of sodium metal was added to the diol and allowed to dissolve as the temperature was elevated to 90 °C. 1,2-Epoxybutane (72 g, 1 mol) was then added at a rate which kept the reaction temperature at 125 °C. The reaction mixture was stirred for 16 h at room temperature and then distilled under vacuum to give 97 g (60%)

(24) I. J. Burden, A. C. Coxon, J. F. Stoddart, and C. M. Wheatley, *J. Chem. Soc., Perkin Trans. 1*, 220 (1977).
(25) R. C. Hayward, C. H. Overton, and G. H. Whitham, *J. Chem. Soc., Perkin Trans. 1*, 2413 (1976).

of clear oil: bp 148–150 °C (30 mm); IR (neat) 3400 (br), 1115 (br) cm^{-1}; ^1H NMR δ 0.80 (t, 6 H, J = 7 Hz), 1.37 (m, 4 H), 3.33 (m, 4 H), 3.55 (m, 2 H), 4.52 (s, 2 H).

Anal. Calcd for $C_8H_{18}O_3$: mol wt 162.2. Found: mol wt 175.

5,8-Dioxadodecane-3,10-diol (25). The above procedure was followed, using ethylene glycol (124 g, 2 mol) and 1,2-epoxybutane (288 g, 4 mol). The crude mixture was distilled to yielded 270 g (66%) of a clear oil: bp 130 °C (10 mm); IR (neat) 3420 (br), 1110 (br) cm^{-1}; ^1H NMR δ 0.89 (t, 6 H, J = 7 Hz), 1.40 (q, 4 H, J = 7 Hz), 3.47 (m, 8 H), 3.62 (s, 4 H).

Anal. Calcd for $C_{10}H_{22}O_4$: mol wt 206.3. Found: mol wt 209.

5,8,11-Trioxapentadecane-3,13-diol (26). The above procedure was followed with diethylene glycol (106 g, 1 mol) and 1,2-epoxybutane (142 g, 2 mol) as reactants. The reaction yielded 166 g (66%) of a clear oil: bp 198–202 °C (30 mm); IR (neat) 3450 (br), 1115 (br) cm^{-1}; ^1H NMR δ 1.03 (t, 6 H, J = 7 Hz), 1.53 (q, 4 H, J = 7 Hz), 3.49 (m, 6 H), 3.73 (s, 8 H), 4.02 (2 s, 2 H).

Anal. Calcd for $C_{12}H_{26}O_5$: mol wt 250.3. Found: mol wt 250.

5,8,11,14-Tetraoxaoctadecane-3,16-diol (27). The above procedure was used with triethylene glycol (150 g, 1.0 mol) and 1,2-epoxybutane (142 g, 2 mol) as reactants and with dimethyl sulfoxide as the solvent. The crude product was distilled three times to yield 150 g (51%) of a clear oil: bp 160–165 °C (1 mm); IR (neat) 3450 (br), 1105 (br) cm^{-1}; ^1H NMR δ 0.97 (t, 6 H, J = 7 Hz), 1.48 (q, 4 H, J = 7 Hz), 3.45 (m, 6 H), 3.66 (s, 14 H).

Anal. Calcd for $C_{14}H_{30}O_6$: mol wt 294.4. Found: mol wt 294.

11,14,17-Trioxaheptacosane-9,19-diol (28). 1,2-Epoxydecane was prepared from 1-decene by the method of Swern and coworkers using freshly prepared peracetic acid.[26] Acetic anhydride (1000 g) was mixed with 222 g of 30% H_2O_2 and kept at 40 °C for 4 h with intermittent cooling. The resulting solution contained 110 g (1.5 mol) of peracetic acid. The peracetic acid solution and 1-decene (170 g, 1.2 mol) were mixed and stirred for 24 h at 45 °C. The resulting mixture was poured into 1000 mL of water and extracted twice with 200-mL portions of ether. The combined either extracts were washed with two 100-mL portions of water and dried (anhydrous potassium carbonate), and the ether was removed under reduced pressure. The resulting odorous liquid was distilled under vacuum, giving 71 g (38%) of a clear liquid: bp 95–98 °C (30 mm); IR and ^1H NMR spectra matched those found in Satler for 1,2-epoxydecane. Diethylene glycol (24.1 g, 0.227 mol) and 1,2-epoxydecane (71 g, 0.445 mol) were reacted as reported above. The crude product was distilled under vacuum, giving a yellow oil (37 g, 39%) that crystallized in the receiver; bp 210–215 °C (1.5 mm). The solid was recrystallized from petroleum ether to give a white powder: mp 52–53.5 °C; IR (KBr) 3435 (br), 1130, 1145 (d) cm^{-1}; ^1H NMR δ 0.90 (m, 6 H), 1.29 (s, 28 H), 3.15–3.78 (m, 8 H), 3.68 (s, 8 H).

Anal. Calcd for $C_{24}H_{50}O_5$: C, 68.85; H, 12.04; mol wt 418.6. Found: C, 68.62; H, 12.10; mol wt 412.

1,2-Cyclohexano-3,6,9-trioxaundecane-1,11-diol (29). Triethylene glycol (210 g, 1.4 mol) and cyclohexane oxide (34 g, 0.35 mol) were reacted. The crude product required three careful distillations to separate the desired product from the excess triethylene glycol: 30 g (34%); bp 149–151 °C (2 mm); IR (neat) 3415 (br), 1100 (br) cm^{-1}; ^1H NMR δ 1.25–2.10 (m, 8 H), 3.16–4.0 (m, 4 H), 3.70 (s, 8 H), 4.42 (s, 2 H).

Anal. Calcd for $C_{12}H_{24}O_5$: mol wt 248.3. Found: mol wt 239.

1,2,10,11-Dicyclohexano-3,6,9-trioxaundecane-1,11-diol (30). This glycol was previously reported by Stoddart by a different synthetic route.[24] We used the above procedure with diethylene glycol (35 g, 0.33 mol), cyclohexene oxide (65 g, 0.66 mol), and dimethyl sulfoxide as the solvent. (A reaction run without dimethyl sulfoxide gave same yield.) The product was a thick pale yellow oil: 41 g (41%); bp 168–169 °C (1 mm). The ^1H NMR spectrum matched that obtained by Stoddart.[24]

Anal. Calcd for $C_{16}H_{30}O_5$: mol wt 302.3. Found: mol wt 302.

General Procedure for the Synthesis of Macrocyclic Compounds. The glycol and acid chloride in separate 250-mL portions of benzene (25 mL of tetrahydrofuran was also used with 2,6-pyridinedicarbonyl chloride) were simultaneously added to 1 L of rapidly stirring benzene at 50 °C. After hydrogen chloride had ceased to evolve, the solvent was removed under reduced pressure. The product was isolated from the crude polymer–monomer mixture by vacuum distillation or by a hot hexane extraction.[14,15] Specific details are given for each compound.

8,15-Diethyl-1,4,7,10,13-pentaoxacyclopentadecane-2,6-dione (6). Diglycolyl dichloride (8.55 g, 0.05 mol) and glycol **25** were reacted. The crude product was extracted with hot hexane and recrystallized from hexane to give 2 g (13%) of a white powder: mp 102.5–104 °C; IR (KBr) 1750 cm^{-1}; ^1H NMR δ 0.92 (t, 6 H, J = 7 Hz, CH_2CH_3), 1.57 (q, 4 H, J = 7 Hz, CH_2CH_3), 3.47 (m, 4 H, OCH_2), 3.54 (s, 4 H, OCH_2), 4.17 (AB, 2 H, J = 5.5 Hz, $COCH_2O$), 4.43 (AB, 2 H, J = 5.5 Hz, $COCH_2O$), 5.16 (m, 2 H, COOCH).

Anal. Calcd for $C_{14}H_{24}O_7$: C, 55.25; H, 7.95; mol wt 304.3. Found: C, 55.52; H, 8.15; mol wt 304.

8,18-Diethyl-1,4,7,10,13,16-hexaoxacyclooctadecane-2,6-dione (7). Diglycolyl dichloride (8.55 g, 0.05 mol) and glycol **26** were used. The crude mixture was distilled under vacuum to yield 8 g (46%) of a clear viscous liquid, bp 165–170 °C (1.5 mm). The liquid crystallized partially upon standing for 1 month. The separated crystals gave the following physical properties: mp 61.5–63 °C; IR (neat) 1750 cm^{-1}; NMR δ 0.88 (t, 6 H, J = 7 Hz, CH_2CH_3), 1.55 (m, 4 H, CH_2CH_3), 3.50 (m, 4 H, OCH_2), 3.62 (s, 8 H, OCH_2), 4.21 (AB, 2 H, J = 5 Hz, $COCH_2O$), 4.34 (AB, 2 H, J = 5 Hz, $COCH_2O$), 5.10 (m, 2 H, COOCH).

Anal. Calcd for $C_{16}H_{28}O_8$: C, 55.16; H, 8.10; mol wt 348.4. Found: C, 55.07; H, 8.28; mol wt 344.

The ^1H NMR spectrum of the liquid layer was essentially the same as that for the solid except the two AB patterns at δ 4.21 and 4.34 were not distinct, being a multiplet at δ 4.30.

Potassium Thiocyanate Complex of 7. Compound **7** (isomeric mixture; 1.0 g, 2.87×10^{-3} mol) and KSCN (0.28 g, 2.87×10^{-3} mol) were dissolved in methanol, and the solvent was evaporated to dryness. The thick viscous liquid solidified and was recrystallized twice from ethanol to give 0.4 g of a very faint pink solid: mp 137–138 °C; IR (KBr) 2050, 1735 and 1715 (d) cm^{-1}; ^1H NMR δ 0.93 (t, 6 H, J = 7 Hz, CH_3CH_2), 1.71 (q, 4 H, J = 7 Hz, CH_3CH_2), 3.74 (s, 12 H, OCH_2), 4.37 (s, 4 H, $COCH_2O$), 5.18 (m, 2 H, COOCH).

Anal. Calcd for $C_{16}H_{28}O_8$·KSCN: C, 45.82; H, 6.33. Found: C, 45.70; H, 6.10.

8,21-Diethyl-1,4,7,10,13,16,19-heptaoxacycloheneicosane-2,6-dione (8). Diglycolyl dichloride (6.84 g, 0.04 mol) and glycol **27** (11.76 g, 0.04 mol) were reacted. The crude product was distilled under vacuum to give 5.4 g (34%) of a clear, viscous liquid: bp 188–190 °C (3 mm); IR (neat) 1750 cm^{-1}; ^1H NMR δ 0.92 (t, 6 H, J = 7 Hz, CH_2CH_3), 1.60 (q, 4 H, J = 7 Hz, CH_2CH_3), 3.64 (m, 16 H, OCH_2), 4.28 (m, 4 H, $COCH_2O$), 5.10 (m, 2 H, COOCH).

Anal. Calcd for $C_{18}H_{32}O_9$: C, 55.09; H, 8.22; mol wt 392.4. Found: C, 55.26; H, 8.22; mol wt 367.

8,18-Di-*n*-octyl-1,4,7,10,13,16-hexaoxacyclooctadecane-2,6-dione (9). Diglycolyl dichloride (4.70 g, 0.0275 mol) and glycol **28** (11.5 g, 0.0275 mol) were used. The crude solidified mixture was recrystallized from hexane to yield 4.95 g (35%) of fairly large, shiny, flaky crystals: mp 68.5–69 °C; IR (KBr) 1745 cm^{-1}; ^1H NMR δ 0.90 (m, 6 H, CH_3), 1.28 (s, 28 H,), 3.53 (m, 4 H, OCH_2), 3.62 (s, 8 H, OCH_2), 4.22 (AB, 2 H, J = 5.5 Hz, $COCH_2O$), 4.46 (AB, 2 H, J = 5.5 Hz, $COCH_2O$), 5.22 (m, 2 H, COOCH).

Anal. Calcd for $C_{28}H_{52}O_8$: C, 65.08; H, 10.14; mol wt 516.7. Found: C, 65.02; H, 10.32; mol wt 501.

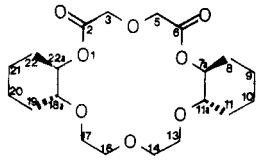
***trans*-Cyclohexano[*h*]-1,4,7,10,13,16-hexaoxacyclooctadecane-2,6-dione (10).** Diglycolyl dichloride (6.0 g, 0.035 mol) and glycol **29** (8.7 g, 0.035 mol) were reacted. The crude product was extracted with hot hexane, and the solid product was crystallized from hexane to give 4.0 g (33%) of clear shiny platelets: mp 50.5–51.5 °C; IR (KBr) 1755, 1740, 1720 (t), 1155 cm^{-1}; ^1H NMR δ 1.10–2.25 (m, 8 H), 3.6 (m, 11 H, OCH_2), 4.28 (2 s, 4 H, $COCH_2O$), 4.35 (m, 2 H, $COOCH_2$), 4.90 (m, 1 H, COOCH).

Anal. Calcd for $C_{16}H_{26}O_8$: C, 55.47; H, 7.57; mol wt 346.4. Found: C, 55.22; H, 7.52; mol wt. 341.

***trans-syn-trans*-Dicyclohexano[*h,q*]-1,4,7,10,13,16-hexaoxacyclooctadecane-2,6-dione (11a).** Diglycolyl dichloride (6.84 g, 0.04 mol) and glycol **30** (12.08 g, 0.04 mol) were reacted. The crude mixture was extracted with hot hexane. Small clear rectangular prisms were collected. When the mixture cooled, a large batch of white microcrystals separated from the filtrate to give

(26) D. Swern, G. N. Billen, and J. T. Scanlan, *J. Am. Chem. Soc.*, 68, 1504 (1946).

a total yield of 3.6 g (23%) of product (**11a** and **11b**). The larger



11a

rectangular crystals, mp 180–181 °C, were approximately half of the total amount: IR (KBr) 1750, cm^{-1}; ^1H NMR δ 1.0–2.3 (m, 16 H), 3.17 (m, 2 H, OCH_2), 3.59 (m, 8 H, OCH_2), 4.21 (AB, 2 H, J = 5.5 Hz, $COCH_2O$), 4.42 (AB, 2 H, J = 5.5 Hz, $COCH_2O$), 4.87 (m, 2 H, COOCH); ^{13}C NMR δ 24.1 (4 C, carbons 9, 10, 20, and 21), 30.5 (2 C, carbons 11 and 19), 30.7 (2 C, carbons 8 and 22), 67.7 (2 C, carbons 14 and 16), 69.6 (2 C, carbons 3 and 5), 70.8 (2 C, carbons 13 and 17), 76.6 (2 C, carbons 11a and 18a), 80.6 (2 C, carbons 7a and 22a), 169.7 (2 C, carbons 2 and 6).

Anal. Calcd for $C_{20}H_{32}O_8$: C, 59.98; H, 8.05; mol wt, 400.5. Found: C, 59.90; H, 7.96; mol wt., 391.

***trans-anti-trans*-Dicyclohexano[*h,q*]-1,4,7,10,13,16-hexaoxacyclooctadecane-1,6-dione (11b).** The small microcrystals collected during the purification of **11a** were fractionally crystallized in hexane to give a small amount of white crystalline material: mp 124.5–126.5 °C; IR (KBr) 1750, 1730 (d) cm^{-1}; ^1H NMR δ 1.0–2.3 (m, 16 H), 3.57 (m, 10 H, OCH_2), 4.30 (s, 4 H, $COCH_2O$), 4.87 (m, 2 H, COOCH); ^{13}C NMR δ 23.9 (2 C, carbons 10 and 20), 24.1 (2 C, carbons 9 and 21), 29.9 (2 C, carbons 11 and 19), 30.7 (2 C, carbons 8 and 22), 67.7 (2 C, carbons 14 and 16), 67.9 (2 C, carbons 3 and 5), 70.8 (2 C, carbons 13 and 17), 76.2 (2 C, carbons 11a and 18a), 80.3 (2 C, carbons 7a and 22a), 170.1 (2 C, carbons 2 and 6).

Anal. Calcd for $C_{20}H_{32}O_8$: C, 59.98; H, 8.05; mol wt 400.5. Found: C, 60.16; H, 8.17; mol wt 390.

8,12-Diethyl-1,7,10-trioxa-4-thiacyclododecane-2,6-dione (12). Thiadiglycolyl dichloride (11.1 g, 0.059 mol) and glycol **24** (9.59 g, 0.059 mol) were used. The crude mixture was extracted with hot hexane to give 0.85 g (6%) of a white solid: mp 96.5–97.5 °C; IR (KBr) 1745 cm^{-1}; ^1H NMR δ 0.89 (t, 6 H, J = 7 Hz, CH_3CH_2), 1.57 (q, 4 H, J = 7 Hz, CH_3CH_2), 3.32 (s, 4 H, $COCH_2S$), 3.35 (m, 2 H, OCH_2), 3.70 (2 d, 2 H, OCH_2), 5.13 (m, 2 H, COOCH).

Anal. Calcd for $C_{12}H_{20}O_5S$: C, 51.92; H, 7.38; mol wt 276.3. Found: C, 52.15; H, 7.30; mol wt 281.

8,15-Diethyl-1,7,10,13-tetraoxa-4-thiacyclopentadecane-2,6-dione (13). Thiadiglycolyl dichloride (9.35 g, 0.05 mol) and glycol **25** (10.31 g, 0.05 mol) were reacted. The crude product was extracted with hot hexane and recrystallized from hexane to give 3.2 g (20%) of a white solid: mp 121.5–122.5 °C; IR (KBr) 1740 cm^{-1}; ^1H NMR δ 0.92 (t, 6 H, J = 7 Hz, CH_3CH_2), 1.59 (q, 4 H, J = 7 Hz, CH_3CH_2), 3.3–3.7 (m, 12 H, OCH_2 and $COCH_2S$), 5.13 (m, 2 H, COOCH).

Anal. Calcd for $C_{14}H_{24}O_6S$: C, 52.48; H, 7.55; mol wt 320.4. Found: C, 52.28; H, 7.59; mol wt 324.

8,18-Diethyl-1,7,10,13,16-pentaoxa-4-thiacyclooctadecane-2,6-dione (14). Thiadiglycolyl dichloride (9.35 g, 0.05 mol) and glycol **26** (12.52 g, 0.05 mol) were reacted. The crude product was distilled under vacuum to give 6.2 g (34%) of a thick yellow oil: bp 194–195 °C (1.3 mm); IR (neat) 1730 cm^{-1}; ^1H NMR δ 0.92 (t, 6 H, J = 7 Hz, CH_3CH_2), 1.62 (m, 4 H, CH_3CH_2), 3.50 (m, 8 H, OCH_2 and $COCH_2S$), 3.60 (s, 8 H, OCH_2), 5.02 (m, 2 H, COOCH).

Anal. Calcd for $C_{16}H_{28}O_7S$: C, 52.73; H, 7.74; mol wt 364.4. Found: C, 53.00; H, 7.92; mol wt 366.

8,21-Diethyl-1,7,10,13,16,19-hexaoxa-4-thiacycloheneicosane-2,6-dione (15). Thiadiglycolyl dichloride (9.35 g, 0.05 mol) and glycol **27** (14.7 g, 0.05 mol) were used. The crude product was distilled under vacuum in the presence of $MgCl_2 \cdot 6H_2O$ to yield 10.8 g (53%) of a thick yellow liquid: bp 180–181 °C (1.5 mm); IR (neat) 1720 cm^{-1}; ^1H NMR δ 0.94 (t, 6 H, J = 7 Hz, CH_3CH_2), 1.66 (q, 4 H, J = 7 Hz, CH_3CH_2), 3.48 (m, 8 H, OCH_2 and $COCH_2S$), 3.65 (s, 12 H, OCH_2), 5.06 (m, 2 H, COOCH).

Anal. Calcd for $C_{18}H_{32}O_8S$: C, 52.92; H, 7.90; mol wt 408.5. Found: C, 52.77; H, 7.88; mol wt 398.

***trans*-Cyclohexano[*h*]-1,7,10,13,16-pentaoxa-4-thiacyclooctadecane-2,6-dione (16).** Thiadiglycolyl dichloride (5.42 g, 0.29 mol) and glycol **29** (7.29 g, 0.029 mol) were reacted. The crude material was extracted with hot hexane and distilled under vacuum to give 3.2 g (30%) of a thick clear liquid: bp 165–170 °C (1 mm); IR (neat) 1730 cm^{-1}; ^1H NMR δ 1.0–2.25 (m, 8 H), 3.3–3.7 (m, 7 H, OCH_2 and $COCH_2S$), 3.65 (s, 8 H, OCH_2), 4.33 (m, 2 H, $COOCH_2$), 4.78 (m, 1 H, COOCH).

Anal. Calcd for $C_{16}H_{26}O_7S$: C, 53.02; H, 7.23; mol wt 362.4. Found: C, 52.88; H, 7.29; mol wt 362.

***trans*-Dicyclohexano[*h,q*]-1,7,10,13,16-pentaoxa-4-thiacyclooctadecane-2,6-dione (17).** Thiadiglycolyl dichloride (7.48 g, 0.04 mol) and glycol **30** (12.08 g, 0.04 mol) were used. The crude product was distilled under vacuum to yield 4.7 g (28%) of a very thick yellow oil, bp 220 °C (1 mm). This oil crystallized upon standing overnight and was then recrystallized from ethanol to give long fine fibers: mp 120.5–121 °C; IR (KBr) 1720, 1730 (d) cm^{-1}; ^1H NMR δ 1.0–2.3 (m, 16 H), 3.38 (m, 2 H, OCH_2), 3.49 (s, 4 H, $COCH_2S$), 3.63 (m, 8 H, OCH_2), 4.82 (m, 2 H, COOCH).

Anal. Calcd for $C_{20}H_{32}O_7S$: C, 57.67; H, 7.74; mol wt 416.5. Found: C, 57.44; H, 7.72; mol wt 407.

A quantity of smaller fibers (500 mg) was also collected; mp 84–90 °C. The NMR showed two singlets at δ 3.49 (4 H). Attempts to further purify the lower melting isomer proved unsuccessful.

4,11-Diethyl-3,6,9,12-tetraoxa-18-azabicyclo[12.3.1]octadeca-1(18),14,16-triene-2,13-dione (18). 2,6-Pyridinedicarbonyl chloride (10.2 g, 0.05 mol) and glycol **25** (10.3 g, 0.05 mol) were reacted. The crude material was distilled under vacuum in the presence of $MgCl_2 \cdot 6H_2O$ to give 5.3 g (31%) of a yellow oil: bp 170–175 °C (1.5 mm); IR (neat) 1720 cm^{-1}; ^1H NMR δ 0.98 (t, 6 H, J = 7 Hz, CH_3CH_2), 1.88 (q, 4 H, J = 7 Hz, CH_3CH_2), 3.3–4.2 (m, 8 H, OCH_2), 5.03 (m, 2 H, COOCH), 7.8–8.35 (m, 3 H). Small NMR peaks appeared at δ 1.40 and 4.97, showing some isomeric impurity.

Anal. Calcd for $C_{17}H_{23}NO_6$: C, 60.52; H, 6.87; mol wt 337.4. Found: C, 60.38; H, 6.90; mol wt 330.

4,14-Diethyl-3,6,9,12,15-pentaoxa-21-azabicyclo[15.3.1]heneicosa-1(21),17,19-triene-2,16-dione (19). 2,6-Pyridinedicarbonyl chloride (10.2 g, 0.05 mol) and glycol **26** (12.5 g, 0.05 mol) were used. The crude mixture was extracted with hexane to give a small amount of white powder. This material was recrystallized from hot hexane to give 0.5 g (3%) of a white solid: mp 103.5–106.5 °C; IR (KBr) 1710 cm^{-1}; ^1H NMR δ 1.04 (t, 6 H, J = 7 Hz, CH_3CH_2), 1.89 (q, 4 H, J = 7 Hz, CH_3CH_2), 3.6–3.9 (m, 12 H, OCH_2), 5.23 (m, 2 H, COOCH), 7.9–8.4 (m, 3 H).

Anal. Calcd for $C_{19}H_{27}NO_7$: C, 59.83; H, 7.14; mol wt 381.4. Found: C, 59.86; H, 7.09; mol wt 376.

4,17-Diethyl-3,6,9,12,15,18-hexaoxa-24-azabicyclo[19.3.1]tetracosa-1(24),21,23-triene-2,19-dione (20). 2,6-Pyridinedicarbonyl chloride (9.18 g, 0.045 mol) and glycol **27** (13.23 g, 0.045 mol) were reacted. The product was distilled to give a thick yellow oil: 6.6 g (31%); bp 201 °C (1 mm). The IR of this material exhibited an alcohol band. The distilled product was then chromatographed on an 8 × 2 in. silica gel column with 2:1 ethyl ether–hexane as an eluant to remove the glycol impurities: IR (neat) 1710 cm^{-1}; ^1H NMR δ 1.03 (t, 6 H, CH_3CH_2), 1.80 (m, 4 H, CH_3CH_2), 3.3–4.0 (m, 16 H, OCH_2), 5.26 (m, 2 H, COOCH), 7.7–8.4 (m, 3 H). A small NMR peak at δ 4.50 proved to be from compound **21** as indicated below.

Anal. Calcd for $C_{21}H_{31}NO_8$: C, 59.28; H, 7.34; mol wt 425.5. Found: C, 59.08; H, 7.16; mol wt 426.

4-Ethyl-3,6,9,12,15-pentaoxa-21-azabicyclo[15.3.1]heneicosa-1(21),17,19-triene-2,16-dione (21). After it had been allowed to stand for a few weeks, crystals were observed in liquid macrocycle **20**. These crystals were isolated and recrystallized from hexane: mp 87–88.5 °C; IR (KBr) 1720 cm^{-1}; ^1H NMR δ 1.03 (t, 3 H, J = 7 Hz, CH_3CH_2), 1.88 (q, 2 H, J = 7 Hz, CH_3CH_2), 3.78 (s, 8 H, OCH_2), 3.93 (m, 4 H, OCH_2), 4.53 (m, 2 H, $COOCH_2$), 5.20 (m, 1 H, COOCH), 7.9–8.5 (m, 3 H).

Anal. Calcd for $C_{17}H_{23}NO_7$: C, 57.84; H, 6.57; mol wt 353. Found: C, 57.62; H, 6.57; mol wt 331.

***trans*-Cyclohexano[*m*]-3,6,9,12,15-pentaoxa-21-azabicyclo[15.3.1]heneicosa-1(21),17,19-triene-2,16-dione (22).** 2,6-Pyridinedicarbonyl chloride (8.16 g, 0.04 mol) and glycol **29** (9.92 g, 0.04 mol) were reacted. The crude material was extracted with hexane and recrystallized from hot hexane to give 6.4 g (42%) of a white solid: mp 95–96.5 °C; IR (KBr) 1715 cm^{-1}; ^1H NMR

δ 1.3–2.5 (m, 8 H), 3.74 (s, 8 H, OCH_2), 3.85–4.15 (m, 3 H, OCH_2), 4.40 (m, 2 H, $COOCH_2$), 4.80 (m, 1 H, COOCH), 7.8–8.4 (m, 3 H).

Anal. Calcd for $C_{19}H_{25}NO_7$: C, 60.14; H, 6.64; mol wt 379.4. Found: C, 60.08; H, 6.70; mol wt 363.

Potassium Thiocyanate Complex of 22. Compound **22** (0.475 g, 0.001 25 mol) and potassium thiocyanate (0.12 g, 0.001 25 mol) were dissolved in methanol, and the mixture was evaporated to a volume of about 5 mL. This mixture was then cooled to −20 °C. After several days clumps of clear quartzlike crystals formed; mp 174–175.5 °C; IR (KBr) 2050, 1725 cm^{-1}; ^1H NMR δ 1.2–2.70 (m, 8 H), 3.77 (s, 8 H, OCH_2), 3.86 (m, 3 H, OCH_2), 4.67 (m, 2 H, $COOCH_2$), 4.88 (m, 1 H, COOCH), 8.1–8.6 (m, 3 H).

Anal. Calcd for $C_{19}H_{25}NO_7$·KSCN: C, 50.40; H, 5.29. Found: C, 50.51; H, 5.19.

***trans*-Dicyclohexano[*d*,*m*]-3,6,9,12,15-pentaoxa-21-azabicyclo[15.3.1]heneicosa-1(21),17,19-triene-2,16-dione (23).** 2,6-Pyridinedicarbonyl chloride (9.18 g, 0.045 mol) and glycol **30** (13.6 g, 0.045 mol) were used. The crude product was extracted with hexane and recrystallized from hot hexane to give both large clear prisms and white powder: 1.03 g (6.2%); mp 137–138.5 °C; IR (KBr) 1710, 1735 cm^{-1}; ^1H NMR δ 1.2–2.4 (m, 16 H), 3.50 (m, 6 H, OCH_2), 3.80 (2 s, 4 H, OCH_2), 5.00 (m, 2 H, COOCH), 7.8–8.3 (m, 3 H).

Anal. Calcd for $C_{23}H_{31}NO_7$: C, 63.72; H, 7.21; mol wt 433.5. Found: C, 63.51; H, 7.21; mol wt 423.

Potassium Thiocyanate Complex of 23. Compound **23** (0.2 g, 4.6×10^{-4} mol) and potassium thiocyanate (0.045 g, 4.6×10^{-4} mol) were dissolved in methanol. The solvent was then evaporated to leave a pink solid. The solid was recrystallized from methanol to give a light pink crystaline solid: mp 226–227.5 °C; IR (KBr) 2050, 1725, 1715 cm^{-1}; ^1H NMR δ 1.20–2.60 (m, 16 H), 3.63 (s, 8 H, OCH_2), 3.9 (m, 2 H, OCH), 5.18 (m, 2 H, COOCH), 8.6–9.1 (m, 3 H).

Anal. Calcd for $C_{23}H_{31}NO_7$·KSCN: C, 54.32; H, 5.89. Found: C, 54.38; H, 6.78.

Attempted Synthesis of Thia and Pyridino Analogues of Compound 9. The general procedure to prepare these compounds from glycol **28** gave reaction mixtures which exhibited IR peaks at 1730 cm^{-1} and essentially no hydroxy peaks at 3400 cm^{-1}. Attempts to purify the products by recrystallization gave only starting glycol **28**. The cyclization reaction was also tried by using repurified starting materials and by using triethylamine to remove hydrochloric acid. Both these attempts resulted in the isolation of starting glycol **28**.

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Registry No. 6, 74262-06-9; **7**, 74262-07-0; **7**·KSCN complex, 74263-31-3; **8**, 74262-08-1; **9**, 74262-09-2; **10**, 74262-10-5; **11a**, 74262-11-6; **11b**, 74310-48-8; **12**, 74262-12-7; **13**, 74262-13-8; **14**, 74262-14-9; **15**, 74262-15-0; **16**, 74262-16-1; **17**, 74262-17-2; **18**, 74262-18-3; **19**, 74262-19-4; **20**, 74262-20-7; **21**, 74262-21-8; **22**, 74262-22-9; **22**·KSCN complex, 74263-33-5; **23**, 74262-23-0; **23**·KSCN complex, 74263-35-7; **24**, 74262-24-1; **25**, 74262-25-2; **26**, 74262-26-3; **27**, 74262-27-4; **28**, 74262-28-5; **29**, 74262-29-6; **30**, 74310-49-9; 1,2-butanediol, 584-03-2; 1,2-epoxybutane, 106-88-7; ethylene glycol, 107-21-1; diethylene glycol, 111-46-6; triethylene glycol, 112-27-6; 1,2-epoxydecane, 2404-44-6; 1-decene, 872-05-9; cyclohexene oxide, 286-20-4; diglycolyl dichloride, 21062-20-4; thiadiglycolyl dichloride, 7646-91-5; 2,6-pyridinedicarbonyl chloride, 3739-94-4.

Synthesis of Adamantane Derivatives. 49.[1] Substitution Reaction of 1-Adamantyl Chloride with Some Trimethylsilylated Unsaturated Compounds

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Catalytic substitution reactions at the adamantane bridgehead were studied by using α,β- and β,γ-unsaturated trimethylsilanes. Treatment of 1-adamantyl (Ad) chloride (1) with allyltrimethylsilane and its heteroanalogues, X=Y—Z—$SiMe_3$, in the presence of Lewis acid as a catalyst gave the products Ad—X—Y=Z, X=Y^+(Ad)—Z^-, and X=Y—Z—Ad, depending on the attack site of the adamantyl group on each X, Y, and Z atom. Treatment of 1 with (phenylethynyl)trimethylsilane also gave a substituted adamantane in a good yield. The substitution reactions of 1 with aryl- and heteroaryltrimethylsilanes under similar conditions occurred at a position distinct from that of acetylation, indicating that adamantylation was not influenced by an electronic effect of the trimethylsilyl group.

The synthetic study of adamantane derivatives is of considerable interest, and numerous preparative methods for them have been developed.[2] In the substitution reactions at the adamantane bridgehead, nucleophilic conditions are disfavored because of the difficulty in generating the unstable adamantyl anion[3] and since nucleophilic attack on adamantane is prohibited from the back side, dictating that drastic conditions are generally required to perform the substitution reaction.[4] Therefore, bond formation at the bridgehead of adamantane has been realized mostly under electrophilic conditions. In the past decade, the use of organosilicon compounds as reagents in organic synthesis has become a field of considerable interest.[5] Their wide applicabilities are based on the characteristic properties of the silicon atom. For instance,

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