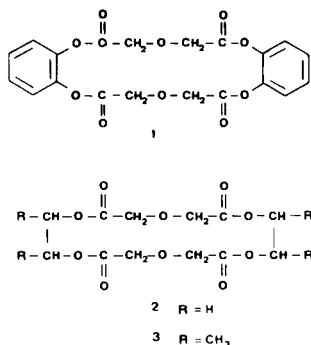


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A new series of macrocycles containing the diglycolyl moiety have been prepared. The compounds prepared were: 7,9,18,20-tetrahydridibenzo[*b,k*][1,4,7,10,13,16]hexaoxacyclooctadecin-6,10,17,21-tetraone (**1**), 1,4,7,10,13,16-hexaoxacyclooctadecane-2,6,11,15-tetraone (**2**), 8,7,17,18-tetramethyl-1,4,7,10,13,16-hexaoxacyclooctadecane-2,6,11,15-tetraone (**3**) and 2,5,8,15,18,21-hexaoxatricyclo[20,4,0,0^{9,14}]hexacosan-3,7,16,20-tetraone (**4**). The compound **4** has been isolated in the four diastereoisomers: *trans-syn-trans* **4a**, *trans-anti-trans* **4b**, *cis-syn-cis* **4c** and *cis-anti-cis* **4d**.

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The chemistry of polyether-ester macrocycles has been extensively studied during these last years. Recently a variety of macrocyclic di- and tetraesters and other analogous compounds have been reported [1-3]. The most commonly adopted methods for the preparation of these macrocycles have been reviewed by Bradshaw and co-workers [1]. Moreover, the complexing characteristics of some of these compounds with metal cations have also been previously reported to behave in almost the same manner as those of the corresponding crown polyethers [4-7]. We have previously reported a convenient method for the preparation of macrocyclic tetraesters by action of various diacyl chlorides with 1,3,2-dioxastibolanes, benzodioxastiboles, dioxastannolanes and benzodioxastannoles [8,9] and studied their electron impact mass spectrometric behaviour [10,11]. We have now found that this cleavage method of the O-M-O (M = Sn, Sb) bond could be applied successfully to the preparation of a new series of macrocyclic polyether-tetraesters containing the diglycolyl moiety and 1,2-cyclohexanediol *trans* and *cis*, ethylene glycol, 2,3-butandiol and catechol subcyclic units (Scheme).



Scheme

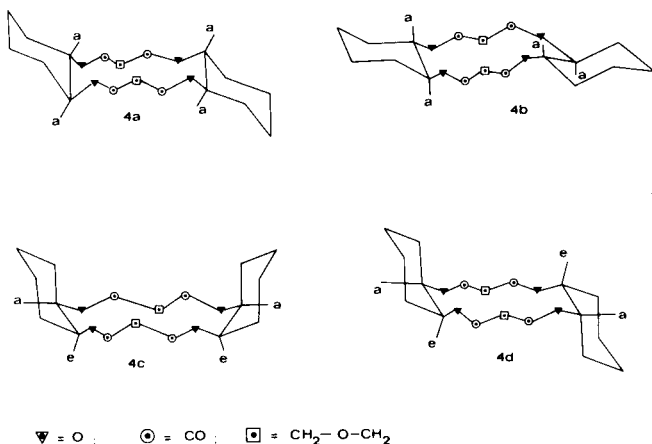
Compound **1** was prepared by treating 2,2-dibutyl-1,3,2-benzodioxastannole or 2-chloro-1,3,2-benzodioxastibole

with diglycolyl chloride in benzene solution. Yields were generally good. The structure proposed for macrocycle **1** is consistent with data derived from ir, ¹H-nmr and ms spectra and elemental analyses. The carbonyl band appeared at 1780 cm⁻¹ as expected for the ester groups in the ir spectra. The nmr spectra of compounds **1** exhibited peaks at δ 7.20 for the aromatic portion and at δ 4.48 for the CO-CH₂-O group.

By the same procedure, we prepared the macrocyclic compounds **2** and **3** containing ethylene glycol and 2,3-butandiol as subcyclic units respectively. Also for these compounds the structures were determined by analytical and spectroscopic data. The carbonyl bands in the ir spectra occurred at 1740-1750 cm⁻¹ for the ester groups. The nmr spectra of these compounds exhibited peaks at δ 4.06 (CO-CH₂-O-) and at δ 4.30 and 5.01 (CH₂-O and CH-O) as previously reported for the macrocyclic compounds derived from diglycolyl chloride [12].

Moreover, some observations can be made on the preparation of macrocycles containing the cyclohexanediol isomers as subunits. Among the several crown ethers synthesized, but containing the cyclohexyl group as a subunit, dicyclohexyl-18-crown-6 was widely investigated in the past years. It was prepared by catalytic hydrogenation [13] of dibenzo-18-crown-6, and two of the five possible isomers were isolated and structurally identified by X-ray diffraction as the *cis-syn-cis* and *cis-anti-cis* isomers respectively [14]. Recently Stoddart and co-workers have synthesized stereospecifically the *trans-syn-trans* and *trans-anti-trans* isomers of dicyclohexyl-18-crown-6 from the diastereoisomeric (±) and *meso*-2,2-methylene dioxacyclohexanols and diethylenglycol ditosylate or from the condensation reaction between the *trans*-cyclohexanediol-1,2- and the same ditosylate [15]. In the former case, a mixture of macrocyclic isomers was obtained in four steps, while in the latter, the preparation of dimeric isomers was accompanied by a one step formation of monomeric macrocyclic

compounds. Using our method, a mixture of two isomer macrocyclic tetraesters was obtained from each diastereoisomer of dioxacyclostannolane or stibolane (see Figure).



Figure

These compounds were separated by fractional crystallization from ethyl acetate and then recrystallized, or by chromatography on silica gel using an ethyl acetate-benzene mixture. All the isomers were isolated as a white solid and have different melting points. For these compounds the structure **4** was assigned by analytical and spectroscopic data.

In the four isomers the carbonyl bands appeared at 1740-1760 cm^{-1} in the ir spectra. The nmr spectra were very interesting in that the two isomers obtained from the *trans* derivative exhibited peaks for the CH-O-CO group at δ 4.78 due to the compound at mp 276-278° and δ 4.87 due to the compound at mp 188-190°. The same group appeared at δ 5.14 for each compound at mp 265-268° and 148-151° obtained from the *cis* derivative. The O-CH₂-CO groups exhibited peaks at δ 4.08 and at δ 4.12 in the isomers obtained by *trans* derivative and at δ 4.18 by *cis* derivative. All the mass spectra of **2-4** showed molecular ions and a characteristic peak at $(M/2 + 1)^+$. A study on the cation complexation properties, on the exact attribution of structure to each isomer **4** and a spectroscopic mass investigation on the mechanistic aspects of the fragmentation of the compounds **1-4** will be reported in a future work.

EXPERIMENTAL

Melting points were determined using an electrothermal capillary melting point apparatus and are uncorrected. The ir spectra were recorded on a Perkin-Elmer 157 G spectrophotometer. The nmr spectra were determined on a Varian EM 360L spectrometer; chemical shifts were measured in ppm (δ) using tetramethylsilane as an internal reference. The mass spectra were run on a VG ZAB-2F instrument operating at 70 eV (200 μA). Microanalyses for CHN were carried out on a Carlo Erba model 1106 Elemental Analyzer.

Starting Materials.

The following compounds were prepared as previously described: 2-chloro-1,3,2-benzodioxastibole [16], 2-chloro-4,5-dimethyl-1,3,2-dioxastibolane [17], *trans*-2-chloro-1,3,2-dioxacyclohexanestibolane [9], *cis*-2-chloro-1,3,2-dioxacyclohexanestibolane [9], 2,2-di-*n*-butyl-1,3,2-benzodioxastannole [18], 2,2-di-*n*-butyl-1,3,2-dioxastannolane [19], *meso*-2,2-di-*n*-butyl-4,5-dimethyl-1,3,2-dioxastannolane [19], *trans*-2,2-di-*n*-butyl-1,3,2-dioxacyclohexanestannolane [20] and *cis*-2,2-di-*n*-butyl-1,3,2-dioxacyclohexanestannolane [20]. Diglycolyl dichlorides were prepared following literature procedure [12].

General Synthesis.

The macrocyclic compounds were prepared by dropping the diglycolyl chlorides dissolved in 5 ml of benzene to a rapidly stirred solution of stibolic or stannolic compounds in 20 ml of benzene at reflux. The resulting mixture was stirred under reflux for a further night. The benzene solvent was then removed under vacuum and the crude product was purified by column chromatography on silica gel using a mixture of benzene-ethyl acetate (5:1) as eluent. Using this general procedure, the following compounds were prepared and specific details are given for each compound. 7,9,18,20-Tetrahydrodibenzo[*b,h*][1,4,7,10,13,16]hexaoxacyclooctadecine-6,10,17,21-tetraone (**1**).

The 2-chloro-1,3,2-benzodioxastibole or 2,2-dibutyl-1,3,2-benzodioxastannole (0.01 moles) and diglycolyl chloride (0.01 moles) were reacted. The crude product was purified by chromatography to give **1**, yield 18%, mp 208-209°; ir (potassium bromide): 2920, 1780, 1600, 1500, 1460, 1440, 1420, 1370, 1300, 1240, 1150, 1130, 1050, 980, 950, 910, 850, 780, 760, 720 cm^{-1} ; ¹H nmr (deuteriochloroform): δ 7.20 (s, 8H, arom) and 4.48 ppm (s, 8H, O-CH₂-CO); ms: m/e 388 (M-CO).

Anal. Calcd. for C₂₀H₁₆O₁₀: C, 57.69; H, 3.87. Found: C, 57.63; H, 3.86.

1,4,7,10,13,16-Hexaoxacyclooctadecane-2,6,11,15-tetraone (**2**).

The 2-chloro-1,3,2-dioxastibolane or 2,2-dibutyl-1,3,2-dioxastannolane (0.01 mole) and diglycolyl chloride (0.01 mole) were used. The crude product was purified by chromatography to give **2**, yield 20%, mp 185-187°; ir (potassium bromide): 2920, 1750, 1730, 1460, 1430, 1410, 1380, 1330, 1310, 1280, 1240, 1220, 1150, 1070, 1050, 1030, 990, 950, 920, 850, 730 cm^{-1} ; ¹H nmr (deuteriochloroform): δ 4.33 (s, 8H, CH₂-O-CO) and 4.10 ppm (s, O-CH₂-CH₂); ms: m/e 320.

Anal. Calcd. for C₁₂H₁₆O₁₀: C, 45.00; H, 5.04. Found: C, 44.85; H, 5.02.

2,3,11,12-Tetramethyl-1,4,7,10,13,16-hexaoxacyclooctadecane-2,6,11,15-tetraone (**3**).

The 2-chloro-4,5-dimethyl-1,3,2-dioxastibolane or 2,2-dibutyl-4,5-dimethyl-1,3,2-dioxastannolane (0.01 mole) and diglycolyl chlorides (0.01 mole) were used. The crude product was purified by chromatography to give **3**, yield 24%, mp 128-130°; ir (potassium bromide): 2920, 1750, 1730, 1460, 1420, 1380, 1360, 1310, 1270, 1260, 1210, 1150, 1130, 1080, 1030, 980, 950, 860, 840, 720 cm^{-1} ; ¹H nmr (deuteriochloroform): δ 5.01 (m, 4H, CH₃-CH-OCO), 4.16 (s, 8H, O-CH₂-CO) and 1.21 ppm (d, 12H, CH₃-CH-O); ms: m/e 376.

Anal. Calcd. for C₁₆H₂₄O₁₀: C, 51.06; H, 6.43. Found: C, 51.02; H, 6.45.

trans-2,5,8,15,18,21-Hexaoxatricyclo[20,4,0,0^{9,14}]hexacosan-3,7,16,20-tetraone (**4a, 4b**).

The *trans*-2-chloro-1,3,2-dioxacyclohexanestibolane or *trans*-2,2-dibutyl-1,3,2-dioxacyclohexanestannolane (8.6 mmoles) and diglycolyl chloride (8.6 mmoles) in 20 ml of benzene were used. The benzene was removed under reduced pressure. The crude product was then treated with ethyl acetate to give a white powder, yield 14%, mp 276-278°; ir (potassium bromide): 2960, 1750, 1460, 1430, 1380, 1360, 1300, 1260, 1210, 1150, 1120, 1060, 1030, 1000, 980, 960, 910, 850, 770 cm^{-1} ; ¹H nmr (deuteriochloroform): δ 4.80 (m, 4H, -CH-O), 4.08 (s, 8H, CO-CH₂-O) and 2.10-1.06 ppm (m, 16H, CH₂-CH); ms: m/e 428.

Anal. Calcd. for C₂₀H₂₈O₁₀: C, 56.07; H, 6.59. Found: C, 56.05; H, 6.61.

The mother liquors from ethyl acetate were concentrated under

vacuum to afford a viscous product which was subject to column chromatography on silica gel with ethyl acetate-benzene (1:5) as eluent to give a white powder, yield 8%, mp 188-190°; ir (potassium bromide): 2940, 2860, 1760, 1450, 1380, 1320, 1280, 1250, 1220, 1140, 1050, 1020, 920, 900, 850, 760 cm^{-1} ; nmr (deuteriochloroform): δ 4.87 (m, 4H, CH-O), 4.12 (s, 8H, CO-CH₂-O) and 2.10-1.12 ppm (m, 16H, CH₂); ms: m/e 428.

Anal. Calcd. for C₂₀H₂₈O₁₀: C, 56.07; H, 6.59. Found: C, 56.08; H, 6.61.

cis-2,5,15,18,21-Hexaoxatricyclo[20,4,0,0^{9,14}]hexacosan-3,7,16,20-tetraone (**4c**, **4d**).

The *cis*-2-chloro-1,3,2-dioxacyclohexanastibolane or *cis*-2,2-dibutyl-1,3,2-dioxacyclohexanastannolane (5.7 mmoles) and diglycolyl chloride (5.7 mmoles) in 20 ml of benzene were used. During the course of the reaction a white powder was formed which was filtered to give a yield of 24%, mp 265-268°; ir (potassium bromide): 2940, 2860, 1740, 1430, 1400, 1380, 1350, 1310, 1270, 1200, 1140, 1030, 1000, 970, 930, 890, 850, 820 cm^{-1} ; ¹H nmr (deuteriochloroform): δ 5.15 (m, 4H, CH-O), 4.18 (s, 8H, CO-CH₂-O) and 2.10-1.26 ppm (m, 16H, -CH₂); ms: m/e 428.

Anal. Calcd. for C₂₀H₂₈O₁₀: C, 56.07; H, 6.59. Found: C, 55.98; H, 5.57.

The filtrate, after evaporation of benzene, was purified by column chromatography on silica gel with ethyl acetate-benzene (1:5) as eluent to give a white powder, yield 10%, mp 148-151°; ir (potassium bromide): 2940, 2860, 1740, 1450, 1420, 1400, 1380, 1350, 1310, 1270, 1260, 1200, 1140, 1040, 1030, 1000, 970, 930, 890, 850, 820, 730 cm^{-1} ; ¹H nmr (deuteriochloroform): δ 5.14 (m, 4H, CH-O), 4.18 (s, 8H, CO-CH₂-O) and 2.22-1.03 ppm (m, 16H, CH₂); ms: m/e 428.

Anal. Calcd. for C₂₀H₂₈O₁₀: C, 56.07; H, 6.59. Found: C, 55.93; H, 6.60.

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