Studies on the Synthesis of Heterocyclic Compounds. X. Antimony Derivatives for the Preparation of Macrocyclic Tetraesters

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Treatment of 2-chloro-1,3,2-benzodioxastibole with diacyl chlorides afforded cyclic tetraesters in yields depending on ring size. The exclusive formation of dimeric derivatives was obtained using this method. The products were characterized by analytical and spectroscopic (ir, nmr and ms) data.

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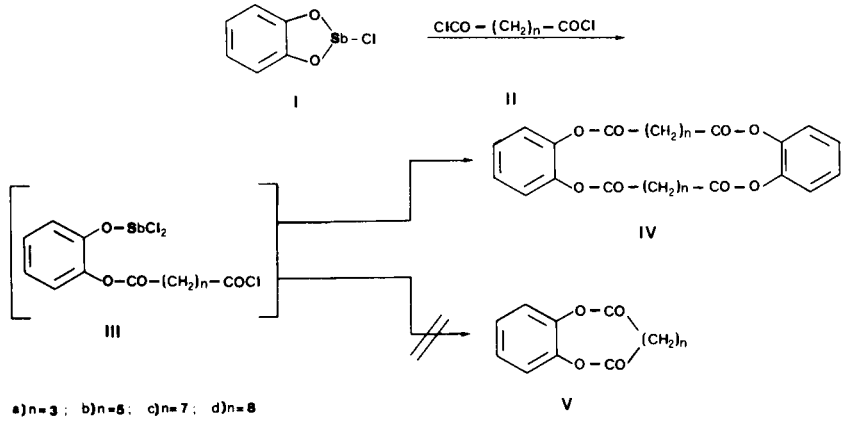
In earlier papers [1] we reported the synthesis and the structural features of five-membered heterocyclic compounds containing elements of the fifth main group. Our present research extends this work to the synthesis and characterization of a number of new macrocyclic esters of catechol. Some macrocyclic tetraesters have recently been reported [2,3]; most of them were synthesized *via* a condensation reaction of a dibasic acid with a glycol, or the salts of *o*-phthalic acid with alkyl dibromides. The yields, for the tetraesters are generally low because of the formation of mixtures of monomeric and dimeric esters, depending on the respective ring size. The specific synthesis and the structural features of macrocyclic lactones *via* the use of tin derivatives has been recently reported by Shanzer [4]. In the course of our research we have also reported a new general method for the synthesis of mono- and diesters *via* action of acyl halides on compounds containing an O-M-O (M = P, As, Sb) linkage [5]. We now report that this method using 2-chloro-1,3,2-benzodioxastibole is conveniently applicable for the preparation of macrocyclic tetraesters of catechol with 18-, 22-, 26-, 28-membered rings. The advantage in using the stibole compound is its good reactivity toward diacyl chlorides under homogeneous as well as under heterogeneous conditions. Thus, stibole I [1] is an excellent intermediate for the preparation of different macrocyclic derivatives (see Scheme) by a cleavage reaction with diacyl chlorides. The dimeric compounds IV were exclusively obtained. No 1:1 adducts V were observed.

The structure of the compounds IV have been determined by analytical and spectroscopic data. All the ir spectra of the products IV were similar. The most prominent band was due to carbonyl absorption at 1760 cm^{-1} and the =CO stretching vibrations at 1210-1220 and 1080 cm^{-1}. The nmr spectra showed three groups of signals. The aromatic proton signals appear as a symmetrical peak centered between δ 7.13 and δ 7.10, while the methylene groups adjacent to the carbonyl groups occur as a triplet centered between δ 2.56 and δ 2.46 and differed from inner methylene groups which occur as a multiplet between δ 1.93 and δ 1.13. The mass spectra of the macrocyclic tetraesters IVa-d all showed a molecular ion peak where the relative intensity decreased as the ring size increased. All of the elemental analyses are in agreement with the proposed structures.

No definite evidence concerning the presence of intermediates IIIa-d was obtained in any of the cases examined. Some by-products were isolated in increasing amounts with increasing ring size. Work is under way to explore other heterocyclic compounds containing in the elements fifth main group in the synthesis of new macrocycles.

Scheme



EXPERIMENTAL

Literature procedures were followed in the preparation of 2-chloro-1,3,2-benzodioxastibole [1], azelaoyl chloride [6] and pimeloyl chloride [6], while glutaroyl chloride and sebacoyl chloride were used as purchased. Melting points were determined using an Electrothermal melting points apparatus and are uncorrected. The ir spectra were recorded on a Perkin-Elmer 157G spectrophotometer. The nmr spectra were determined on a Varian EM360L spectrometer; chemical shifts were measured in ppm (δ) using tetramethylsilane as an internal reference. The mass spectra were run on a VGZAB-2F instrument operating at 70 eV (200 μA). Microanalyses for CHN were carried out on a Carlo Erba model 1106 Elemental Analyzer. Merck silica gel (70-230 mesh) was used for column chromatography; thin layer separation was carried out by Merck F_{254} silica gel and visualization was accomplished by uv light. All products were identified by analytical and spectroscopic data.

General Procedure for the Preparation of IVa-d.

To a rapidly stirred solution of I in dry benzene at room temperature a solution of IIa-d in dry benzene was added dropwise. The heterogeneous reaction mixture was subsequently heated under reflux until the mixture became completely homogeneous. The benzene solution was then removed using a rotary evaporator to give a residue which was purified by column chromatography on silica gel using ethyl acetate-hexane (1:4) as the eluent. Using this general procedure, the following compounds were prepared.

8,9,19,20-Tetrahydro-7*H*,18*H*-dibenzo[*b*,*k*][1,7,10,16]tetraoxacyclooctadecin-6,10,17,21-tetraone (IVa).

A mixture of I (1.5 g, 5.6 mmoles) and a glutaroyl chloride IIa (0.95 g, 5.6 mmoles) in 10 ml of dry benzene was heated for several hours. The crude product was purified by chromatography to give 500 mg of IVa, yield 43%, mp 238-240°; ir (potassium bromide): 2940, 2860, 1760, 1600, 1500, 1450, 1420, 1390, 1360, 1315, 1240, 1190, 1180, 1140, 1120, 1100, 1060, 1030, 1000, 990, 950, 940, 910, 880, 860, 840, 810, 790, 770, 740, 710 cm^{-1}; nmr (DMSO-d_6): δ 7.20 (s, 8 H, arom), 2.56 (t, 8 H, CH_2-CO) and 2.26-1.85 ppm (m, 4 H, CH_2-CH_2-CO); ms: molecular ion, m/e 412 (38%), base peak m/e 110.

Anal. Calcd. for $C_{22}H_{20}O_8$: C, 64.07; H, 4.89. Found: C, 64.10; H, 4.87.

8,9,10,11,21,22,23,24-Octahydro-7*H*,20*H*-dibenzo[*b*,*m*][1,9,12,20]tetraoxacyclodocosin-6,12,19,25-tetraone (IVb).

This compound was prepared from 3.7 mmoles of I and 3.7 mmoles of pimeloyl chloride IIb in 10 ml of dry benzene to give 320 mg of IVb, yield 36%, mp 145-147°; ir (potassium bromide): 2940, 2860, 1760, 1600, 1500, 1450, 1430, 1370, 1340, 1320, 1300, 1270, 1240, 1220, 1200, 1180, 1150, 1120, 1100, 1080, 1070, 1030, 1010, 960, 940, 920, 870, 850, 840, 770, 730 cm^{-1}; nmr (deuteriochloroform): δ 7.20 (s, 8 H, arom), 2.50 (t, 8 H, CH_2-CO) and 2.10-1.46 ppm (m, 12 H, CH_2-CH_2-CO); ms: molecular ion m/e 468 (10%), base peak m/e 125.

Anal. Calcd. for $C_{26}H_{28}O_8$: C, 66.65; H, 6.02. Found: C, 66.63; H, 6.03.

8,9,10,11,12,13,23,24,25,26,27,28-Dodecahydro-7*H*,22*H*-dibenzo[*b*,*o*][1,11,14,24]tetraoxacycloesacosin-6,14,21,29-tetraone (IVc).

This product was prepared from I (3.7 mmoles) and azeloyl chloride IIc (3.7 mmoles) in 10 ml of dry benzene to give 230 mg of IVc, yield 23%, mp 110-112°; ir (potassium bromide): 2940, 2860, 1760, 1600, 1500, 1460, 1430, 1370, 1360, 1310, 1280, 1240, 1220, 1210, 1190, 1170, 1150, 1130, 1100, 1080, 1030, 1000, 980, 950, 920, 900, 860, 830, 770, 760, 740, 720 cm^{-1}; nmr (deuteriochloroform): δ 7.13 (s, 8 H, arom), 2.41 (t, 8 H, CH_2-CO) and 1.93-1.36 ppm (m, 20 H, CH_2-CH_2-CO); ms: molecular ion, m/e 524 (6%), base peak m/e 55.

Anal. Calcd. for $C_{30}H_{36}O_8$: C, 68.68; H, 6.92. Found: C, 68.69; H, 6.92.

8,9,10,11,12,13,14,24,25,26,27,28,29,30-Tetradecahydro-7*H*,23*H*-dibenzo[*b*,*p*][1,12,15,26]tetraoxacyclooctacosin-6,15,22,31-tetraone (IVd).

This compound was prepared from I (5.6 mmoles) and sebacoyl chloride IId (5.6 mmoles) in 10 ml of dry benzene to give 190 mg of IVd, yield 18%, mp 108-110°; ir (potassium bromide): 2940, 2860, 1760, 1600, 1500, 1460, 1420, 1360, 1300, 1280, 1240, 1210, 1180, 1100, 1080, 950, 920, 830, 770 cm^{-1}; nmr (deuteriochloroform): δ 7.16 (s, 8 H, arom), 2.53 (t, 8 H, CH_2-CO), and 1.93-1.20 ppm (m, 24 H, CH_2-CH_2-CO); ms: molecular ion, m/e 552 (4%), base peak m/e 442.

Anal. Calcd. for $C_{32}H_{40}O_8$: C, 69.54; H, 7.30. Found: C, 69.51; H, 7.29.

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