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Synthesis of Macrocyclic Compounds Using Diorganotin(IV) Dicarboxylates as Covalent Templates

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A series of new macrocyclic compounds have been prepared by treating di-*n*-butyltin(IV) dicarboxylates of diphenic acid (biphenyl-2,2′-dicarboxylic acid), thiodiacetic acid and maleic anhydride with succinyl, adipoyl and sebacoyl dichlorides. The compounds have been characterized with the help of elemental analyses and spectral data (mass, IR, ^{1}H and ^{13}C NMR).

Keywords: diorganotin(IV); covalent templates; macrocyclic; acid anhydrides

INTRODUCTION

A number of naturally occurring macrocyclic molecules exhibit different biological activities and may function as antibiotics, hormones, antitumour agents or ion carriers.[1,2] The chemistry of polyfunctional macrocycles is receiving increasing attention because they may selectively bind a range of metal ions.[3,4] Previously diacid dichlorides, cyclic anhydrides and di-isocynates have been condensed with dioxa- and dithiastannolane derivatives of diols and thiols to give macrocyclic tetralactones, thiolactones and dithiocarbamates.[5–8] A series of macrocyclic polyether tetra-esters containing the diglycolyl moiety have been prepared by the cleavage of the O–M–O (M = Sn, Sb) bond.[9] Organotin derivatives containing reactive Sn–O bonds have been used in a number of organic transformations.[10] Organotin-mediated syntheses of macrocyclic tetra-esters has been reported for the reactions of 4-phenyl- and 4-methyl-substituted dioxastannolane with glutaryl chloride.[11,12] However, macrocyclic compounds containing keto-acid anhydride ether units (Fig. 1) do not appear to have been reported earlier.

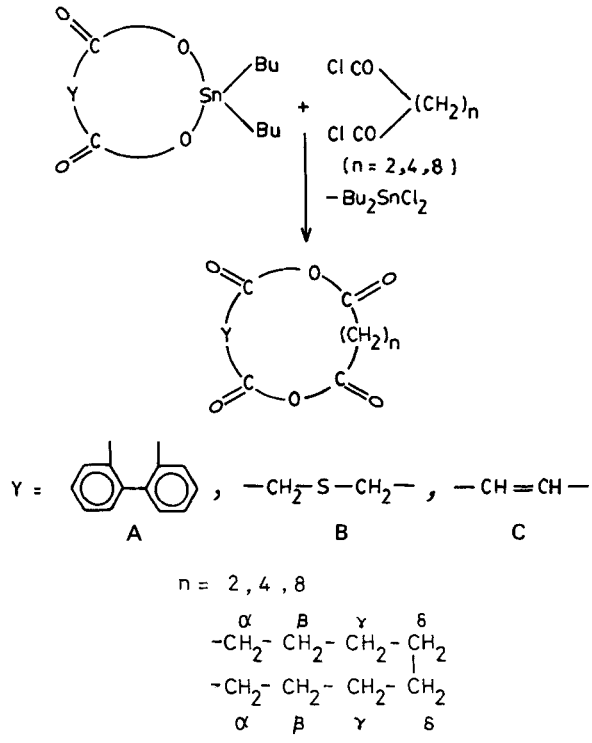

Figure 1 Structures of the macrocyclic anhydride products ($n = 2, 4, 8$).

EXPERIMENTAL

Materials and methods

Succinyl dichloride, adipoyl dichloride and sebacoyl dichloride were procured from Aldrich (USA). Thiodiacetic acid and diphenic acid (biphenyl-2,2′-dicarboxylic acid) were obtained from Merck and Fluka Chemicals, respectively. Di-n-butyltin oxide and maleic anhydride were obtained from Alpha and Sisco, respectively.

Physical measurements

Elemental analyses were carried out by the microanalytical service, R.S.I.C. Panjab University, Chandigarh, India. Infrared spectra for

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Table 1 Physical and mass spectral data (abundance, %) for macrocycles

Compound[a]		Yield	M.p.	Mass spectrum				
	n	(%)	(°C)	M^+	$(CH_2)_nCOCO_2^+$	$YCOCO_2^+$	$(CH_2)_nCO^+$	YCO^+
A	2	52	175–177	—	100 (12)	224 (20)	56 (30)	180 (100)
A	4	55	207–209	352 (5)	128 (8)	224 (19)	84 (30)	180 (100)
A	8	54	202–204	408 (4)	184 (10)	224 (22.7)	140 (30)	180 (100)
B	2	53	85–87	232 (4)	100 (11)	132 (20)	56 (100)	88 (40)
B	4	53	105–106	260 (5)	128 (10)	132 (19.7)	84 (100)	88 (35)
B	8	52	95–97	316 (3)	184 (9)	132 (18.9)	140 (100)	88 (35)
C	2	52	100–102	198 (2)	100 (10)	98 (18)	56 (100)	54 (30)
C	4	51	135–136	226 (3)	128 (12)	98 (18)	84 (100)	54 (30)
C	8	54	120–123	282 (2)	184 (9)	98 (19)	140 (100)	54 (30)

[a] All compounds are white and have a satisfactory elemental analysis. Analytical data are available from the Authors or Editor. A, B, C as in Fig. 1.

the macrocycles (**A**; $n=2,4,8$) were recorded on a Pye–Unicam spectrophotometer P 321 at 4000–200 cm^{-1} and for rest of the macrocycles (**B**, **C**; $n=2,4,8$) were recorded on an Acculab 10 IR spectrophotometer in the range 4000–250 cm^{-1}. The mass spectra were recorded on a JEOL D-300. The ^1H and ^{13}C NMR spectra were recorded on a Brucker AC 200 MHz spectrometer using TMS as an internal standard.

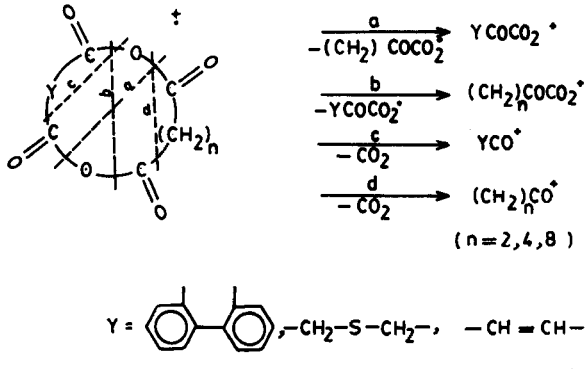

Figure 2 Mass spectral dissociation of the parent molecular ions from the macrocycles of Fig. 1.

Preparation of diorganotin(IV) dicarboxylates

Di-n-butyltin(IV) derivatives of diphenic acid, thiodiacetic acid and maleic anhydride were prepared as reported earlier.[13–15]

Preparation of macrocycles

Diacyl dichloride (0.001 mol) was added to a solution of the dibutyltin(IV) dicarboxylate (0.001 mol) in dry carbon tetrachloride (50 cm^3) under dry conditions and the mixture was refluxed (oil bath, 80 °C) for 5–6 h. After removal of the excess of solvent by distillation under reduced pressure, the reaction mixture was cooled. A solid product separated which was filtered off and the filtrate was evaporated to yield white crystals of Bu_2SnCl_2. The white solid products were washed with petroleum ether (b.p. 60–80 °C) to remove the last traces of Bu_2SnCl_2 and were then recrystallized from dry carbon tetrachloride.

RESULTS AND DISCUSSION

The reaction of cyclic diorganotin(IV) dicarboxylates with diacyl dichlorides yielded macrocyclic acid anhydride compounds as shown in Fig. 1.

Table 2 Infrared data for macrocycles

Compound[a]				
	n	ν (C=O)	ν (C—O)	ν(C—O—C)
A	2	1745s, 1785s	1290s, 1295s	1015s, 1060s
A	4	1720s, 1760s 1745s, 1780s	1260s, 1295s	1020s, 1060s
A	8	1720s, 1760s, 1780s, 1830s	1200s, 1295s	1025s, 1060s
B[b]	2	1695s, 1700s 1790s, 1865s	1295s, 1305s	1005s, 1045s
B[b]	4	1700b	1275s, 1300s	1020, 1040w
B[b]	8	1700s, 1720s 1730s	1240s, 1300s	1020s, 1045s
C	2	1720s, 1760s 1790s, 1865s	1220s, 1290s	1040s, 1070s
C	4	1700s, 1820s	1275s, 1310s	1040s, 1055m
C	8	1695s, 1710s 1815s	1235s, 1300s	1040s, 1060s

[a] A, B, C as in Fig. 1.
[b] C—S in B compounds is in the 910, 915, 925 cm^{-1} region.

The reaction may be visualized as occurring via an electrophilic attack of diacyl carbonyl at the oxygen bonded to the diorganotin(IV)[11] and subsequent expulsion of dibutyltin dichloride.[5,12,16] Characterizations of the new compounds have been carried out using data given in Tables 1–4.

Mass spectra

Mass spectral data, obtained under electron ionization conditions, show peaks due to parent molecular ions which are weak and relatively lowly abundant (Table 1). The molecular ion dissociates to give two daughter ions $(CH_2)_nCOCO_2^+$ and $YCOCO_2^+$ which lose a molecule of carbon dioxide to give more stable species such as $(CH_2)_nCO^+$ and YCO^+ which are more abundant (Fig. 2). For all compounds the fragments observed are in agreement with the structures proposed.

Infrared spectra

The IR data for all compounds have been recorded in KBr and are given in Table 2. More than two bands (due to two C=O and C–O of the two anhydride linkages O=C–O–C=O) in the spectra of the macrocyclic acid anhydrides are observed in the 1800–1700 cm^{-1} and 1310–1200 cm^{-1} regions in the solid state.[17] The presence of two ν(C–O–C) values in the 1000–1055 cm^{-1} region shows the asymmetric nature of the two anhydride linkages.[17] The absence of Sn–O and Sn–C bands in the 500–400 cm^{-1} and 600–500 cm^{-1} regions respectively, compared with the dibutyltin(IV) derivatives, confirms the formation of the new product. A band due to a C–S stretching vibration is observed in the 900 cm^{-1} region in the thiodiacetic acid compounds, which shows that the moiety Y has been retained in the macrocyclic acid anhydrides.[15]

Table 3 ^1H NMR data (δ, ppm) for macrocycles

Compound[a]			
	n	$—(CH_2)_n—$	Y protons
A	2	α 2.58 (s, 4H)	7.94–7.21 (m, 8H)
A	4	α 2.58 (t, 4H) β 2.24 (t, 4H)	7.92–7.12 (m, 8H)
A	8	α 2.26 (t, 4H) β 1.58 (s, 4H) γ, δ 1.45–1.30 (m, 8H)	7.98–7.12 (m, 8H)
B	2	α 3.03, 3.01 (s, 2H) (s, 2H)	3.37 (s, 4H)
B	4	α 2.32 (t, 4H) β 1.68 (t, 4H)	3.40 (s, 4H)
B	8	α 2.28 (t, 4H) β 1.57 (s, 4H) γ, δ 1.48–1.30 (m, 8H)	3.39 (s, 4H)
C	2	α 3.02 (s, 4H)	7.27–7.05 (d, 2H)
C	4	α 2.30 (t, 4H) β 1.66 (t, 4H)	7.52–7.41 (d, 2H)
C	8	α 2.76 (s, 4H) β 1.62 (s, 4H) γ, δ 1.43–1.30 (m, 8H)	7.48–7.40 (d, 2H)

[a] A, B, C as in Fig. 1. Methylene carbon atoms are labelled α–δ, etc., pairwise starting with the carbon following each acyl group (see Fig. 1).

Table 4 ^{13}C NMR data (δ, ppm) for macrocycles

Compound[a]				
	n	COO	$-(CH_2)_n-$	Y carbons
A	2	162.52 174.16	28.16	134.72, 142.64, 133.20, 128.66, 26.50, 130.55
A	4	168.12 174.62	23.67 33.10	30.18, 142.50, 129.85, 129.63, 29.06, 126.09
A	8	162.49 175.74	24.45 28.62 (2C) 33.73	34.72, 142.63, 133.16, 129.82, 29.37
B	2	171.35 174.13	28.01	3.31
B	4	172.44 176.62	33.65 24.20	3.84
B	8	172.13 176.64	24.85 29.04 33.86 34.14	4.14
C	2	164.34 171.28	28.48	36.65
C	4	162.50 175.93	24.35 33.79	35.75
C	8	167.35 176.53	24.70 28.89 (2) 34.00	32.74

[a] A, B, C as in Fig. 1.

NMR spectra

The ^1H and ^{13}C NMR spectra of the macrocycles have been recorded in $CDCl_3$ plus one drop of d^6-DMSO, and are listed in Tables 3 and 4.

The ^1H NMR spectra of all the macrocycles show the absence of signals due to the $SnBu_2$ groups and the presence of signals due to the methylene protons, which confirms the incorporation of the diacyl moiety and expulsion of the $SnBu_2$ groups as dibutyltin dichloride (Table 3). The Y proton signals in all the macrocyclic compounds suffer slight downfield shifts compared with the dibutyltin compounds, which may be due to the addition of two or more carbonyl groups from the diacyl dichloride. The methylene protons (α, β, γ, δ) of the diacyl moiety which have been incorporated in the macrocycles have also been identified.

In the ^{13}C NMR spectra (Table 4) the number of signals found corresponds with the magnetically non-equivalent heterotopic carbon atoms. The disappearance of butyl carbon signals and the appearance of methylene carbon signals confirms the formation of the macrocyclic compounds. The presence of two signals due to the four C=O groups shows two sets of equivalent C=O, unlike the IR data which show four different C=O groups. This may be due to the ^{13}C and the IR data being recorded in solution and in the solid state respectively. The Y-group carbon signals undergo a slight downfield shift as compared with the dibutyltin(IV) complexes. INEPT spectra of the macrocycles also confirm the presence of diacyl CH_2 groups.

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