Organotin-mediated Synthesis of Macrocyclic Polyesters: Mechanism and Selectivity in the Reaction of Dioxastannolanes with Diacyl Dichlorides[1]

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The reaction of 2,2-di-n-butyl-1,3,2-dioxastannolane with diacyl dichlorides for the synthesis of macrocyclic tetraesters has been investigated to gain an insight into its mechanistic pathway and to ascertain the occurrence of genuine template effects. Experimental results show unambiguously that the reaction is a clean cyclo-oligomerization involving a fast transesterification equilibrium that affords a thermodynamic distribution of oligomeric esters. No evidence to support a structural or 'covalent' template effect by tin was found. Instead, dioxastannolane is not only the reagent, but also behaves as an efficient transesterification catalyst that equilibrates the macrocyclic ester mixture. In this context, the reaction can hardly be considered selective.

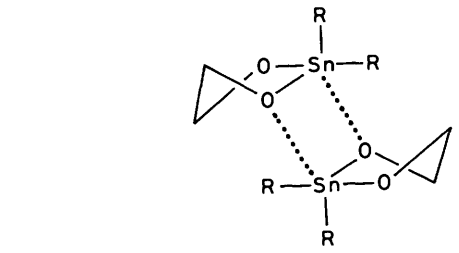
One of the most interesting applications of tin in organic chemistry is the reaction of cyclic dioxastannanes with diacyl dichlorides or dicarboxylic anhydrides, shown by Shanzer and co-workers to be a valuable tool for the synthesis of macrocyclic tetraesters.[2] The reaction can be conveniently employed, for example, to provide compounds structurally related to the macrotetrolide nactines, a class of ion-carrier antibiotics.[2]

Some particular merits have been claimed for this reaction:[2,3] (*a*) it is a one-pot reaction and gives selectively the macrocyclic tetraester; (*b*) it tolerates a wide range of structural variations in chain length, side-chain substituents, and number and type of heteroatoms in the chain; and (c) with substituted reagents, it exhibits a marked regio- and stereo-selectivity. These features have been ascribed to the association phenomena occurring with stannoxane reagents in solution.[4] For example, it has been proposed that dioxastannolane exerts a template effect in the formation of macrocyclic tetraesters through the formation of a rigid dimeric structure (**1**), on which 'insertion' of two dichloride fragments occurs.[3a,d] Moreover, with substituted substrates, the definite stereochemistry of the dimer has been assessed to determine the stereo- and regio-chemistry of the products.[5]

Tin-template effects have often been invoked to explain synthetic results with tin–oxygen reagents: the latter have also been called 'covalent templates,'[2,3,5,6] but, although there is no doubt that association is involved in their behaviour, clear evidence for a genuine template effect and a mechanistic description of the role played by tin are still lacking.

Earlier studies[1,7] on the structure of dioxastannolanes in the same reaction medium have demonstrated that these compounds are involved in a complex pattern of association equilibria, featuring fast scrambling of monomeric dioxastannolane units among dimers and higher aggregates. Thus, the distribution and the stereo- and regio-chemistry of products can not be directly correlated with that of reagents, and a rigid structure for dioxastannolane dimers is not an appropriate model for the understanding of the reaction mechanism.

The present paper reports on the basic mechanistic features of the reaction between 2,2-dibutyl-1,3,2-dioxastannolane and diacyl dichlorides and on the actual role of tin in this context.



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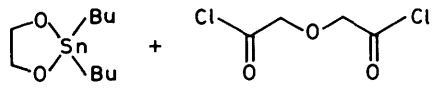

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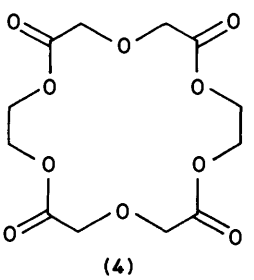


(4)

+ Bu_2SnCl_2 (5) (i)

Results

The reaction of 2,2-dibutyl-1,3,2-dioxastannolane (**2**) with oxybis(acetyl chloride) (**3**) has been selected as a reference reaction, in view of its possible application to the synthesis of polyester macrocyclic multidentate ligands [reaction (i)]. In the reference procedure, the reaction was run by mixing at 0 °C concentrated solutions of the reactants in chloroform (1 mmol per ml of $CHCl_3$ ≅ 0.85M), *i.e.* under conditions where polymerization is expected to predominate over cyclization in the absence of a specific effect, such as a template effect. Complete reaction and homogeneous solution were achieved immediately after mixing.

Products.—Apart from dibutyltin dichloride (**5**), only ester products were detected, and these appeared as a range of oligomers [t.l.c. and ^1H n.m.r.; see Figure 1(A)]. The absence

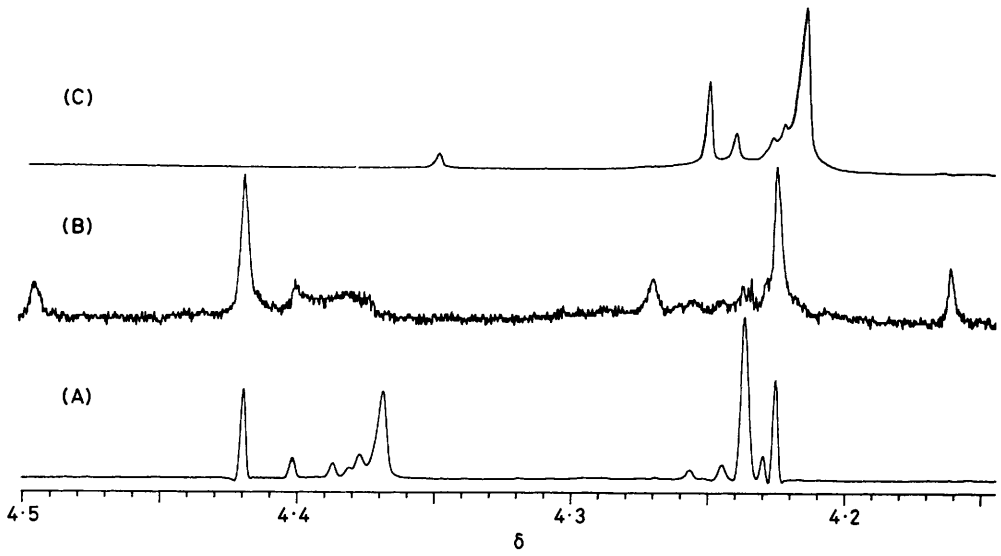


Figure 1. ^{1}H N.m.r. spectra (300 MHz) of oligomeric ester mixtures (*cf.* Table 1): (A) reaction (i) under the reference conditions; (B) reaction (i) at 0.015M concn. of reactants (δ values corrected for dilution); yields 12% (n = 1); 43% (n = 2); 45% ($n \geqslant 3$); (C) reaction (ii) under the reference conditions; only the methylene ester region of the spectrum is shown.

Table 1. Distribution of cyclic oligomers (**4′**) and (**7**) with corresponding chemical shift values from ^{1}H n.m.r. spectra[a]

	(4′)		(7)[b]
n	CH_2OCO δ (%)	$COCH_2O$ δ (%)	CH_2OCO δ (%)
1	4.496 (0)[c]	4.162 (0)[c]	4.347 (3)
2	4.419 (23)	4.225 (24)	4.249 (23)
3	4.401 (6)	4.230 (6)	4.239 (11)
4	4.387 (5)	4.245 (4)	4.225 } (63)
5	4.377 } (66)	4.256 (3)	4.221
⩾6	4.369	4.236 (63)	4.213

[a] Data obtained at 300 MHz from a run in $CDCl_3$ under the same conditions as the reference reaction (i). [b] Distribution assigned in analogy to (**4′**). [c] Values obtained at 0.015M and corrected for dilution [Figure 1(B)].

Table 2. Yields of isolated tetraester (**4**) from runs under various reaction conditions[a]

Entry	Concn. (M)[b]	Solvent	T/°C (t/min)	Yield (%)[c]
1	0.015	C_6H_6	80 (60)	38
2	0.015	$CHCl_3$	61 (140)	37
3	0.30	C_6H_6	80 (30)	16
4[d]	0.03	$CHCl_3$	61 (60)	31

[a] See procedure for the reference reaction (i). [b] Molar concentration of reactants after mixing. [c] Yield of (**4**) after crystallization from acetonitrile. [d] Obtained by influxing (during 30 min) solutions of the reagents (50 ml) into 100 ml of refluxing chloroform.

of coupled signals for the CH_2OCO moiety in the ^{1}H n.m.r. spectrum revealed that no open-chain polyesters were present and that the products were macrocyclic oligomers (**4′**) of the expected tetraester; thus the reaction appears to be a clean cyclo-oligomerization. Product distribution and chemical shift values for (**4′**) are reported in Table 1. Signals were unambiguously assigned for the first three oligomers (n = 1, 2, or 3) by characterization of the corresponding macrocyclic

Table 3. Analytical yields[a] of the tetraester (**4**) obtained under various reaction conditions[b]

Entry	Concn. (M)[c]	Mixing temp. (°C)	Reaction temp. (°C)	Yield (%)[d]
1	0.01	20	61	45
2	0.04	20	61	48
3	0.04	61	61	46
4	0.05	5	20	54
5	0.10	20	20	45
6	0.38	5	20	32
7	0.46	5	20	34
8[e]	0.46	5	20	32
9[f]	0.28	5	20	34

[a] Obtained by ^{1}H n.m.r. at 90 MHz. [b] See procedure for the reference reaction (i). [c] Molar concentration of reactants after mixing. [d] Integration of signals at 90 MHz is less accurate, owing to partial overlapping of lines. [e] Run in the presence of 1 equiv. of (**5**). [f] Run in the presence of 2 equiv. of (**5**).

products; the cyclic monomer was characterized from a run in dilute solution [0.015M; Figure 1(B)]. For higher oligomers, signals were assigned by assuming regular variations of chemical shift with n, as in the case of the first three compounds; a consistent pattern was exhibited by the R_F values in t.l.c. Since chemical shift differences decrease with increasing n, it is likely that signals indicated in Table 1 as $n \geqslant 6$ comprise all those of higher oligomers, even though high abundance and chemical shift inversion for the upfield signal are unexpected. The overall quantitative yield of ester products isolated showed the absence of by-products, and the ^{1}H n.m.r. spectrum of the isolated mixture showed that no significant variation of distribution occurred during work-up. Thus, although the reaction is not as selective as described, it unexpectedly displays exclusive formation of cyclic products and a particular distribution of oligomers.*

* For example, the reaction with 2,2-dibutyl-1,3,2-dithiastannolane, the sulphur analogue of (**2**), gave a completely different picture: extensive precipitation of insoluble polymeric materials (85% of the expected products) occurred.

Conditions.—The reaction was also run under different conditions (temperature, concentration, solvent, and procedure), but yields of isolated tetraester (**4**) were not greatly affected (Table 2). The influence of reaction conditions on the formation of the tetraester (**4**) was better investigated by ^{1}H n.m.r.: the results (Table 3, entries 1—7) confirm those inferred from isolated product yields. With dilute solutions, reaction times at room temperature became increasingly longer: in the slowest case a few hours were required to reach completion. However, the reaction rate increased on refluxing the solution, with little or no effect on product distribution.

Entries 8 and 9 in Table 3 show that addition of dibutyltin dichloride (**5**) (produced in the course of the reaction) to the dioxastannolane does not affect yields to a significant extent.

Figure 1(B) shows that a drastic decrease in concentration (0.015M) affects the amount of cyclic monomer and of higher oligomers to a larger extent than that of the dimer (n = 1, 12%; n = 2, 43%; $n \geqslant 3$, 45%).

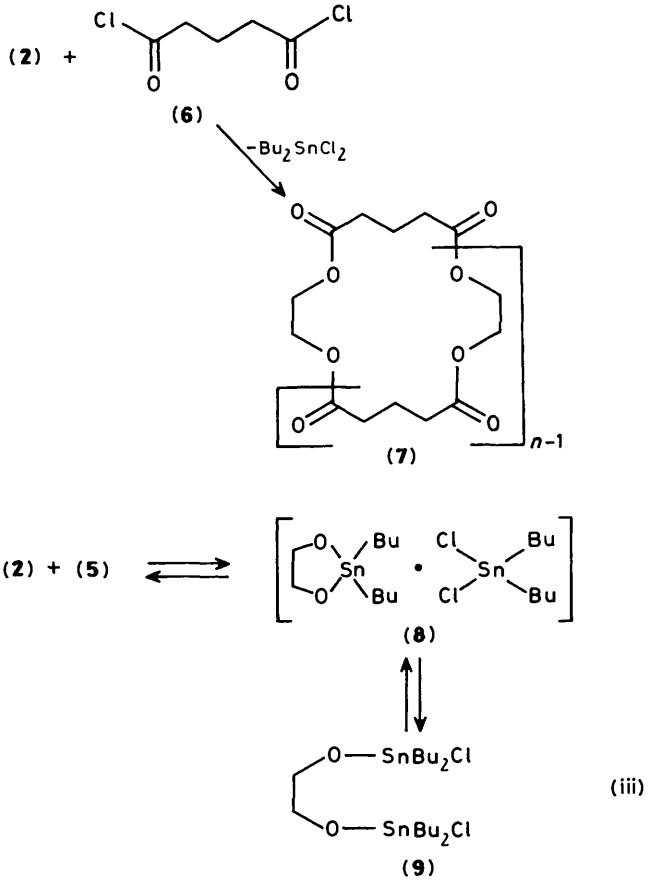
Reagents.—Treatment of (**2**) with glutaryl dichloride (**6**) affords macrocycles (**7**) of the same ring size, with the ether oxygen replaced by CH_2 [reaction (ii)]. Data in Table 1 and Figure 1(C) exhibit a close analogy to the results obtained for (**4′**): except for the monomer (3%), the distribution of products is similar, *i.e.* the oxygen atom in the acidic fragment does not appear to play a crucial role in the process.

Intermediates.—It has been suggested [3b,d,8] that the reaction proceeds in two separate steps. (*a*) On addition of the diacyl dichloride to the dioxastannolane, the first 50% of the reagent would produce quantitatively a stannylated intermediate. (*b*) This would then react with the remaining dichloride to complete ring-closure to the tetraester. This mechanism has been proposed in the light of the following experimental evidence. (i) On hydrolysis of the mixture from step (*a*), no cyclic products could be isolated. (ii) On addition of a different diacyl dichloride in step (*b*), mixed macrocyclic tetraesters were obtained. This aspect deserves more careful study.

Step (a). The ^{1}H n.m.r. spectrum of a mixture of (**2**) and (**3**) in a 1:0.5 molar ratio is shown in Figure 2(B); the corresponding spectrum for a 1:1 molar ratio is given in Figure 2(A) for direct comparison. The key observation is the complete absence of stannylated intermediates. Spectra are merely superpositions of the final distribution of esters and the residual dioxastannolane, in 1:1 ratio. ^{13}C N.m.r. spectra gave the same result.

The broad signal in Figure 2(B) at δ 3.73 corresponding to the dioxastannolane is actually due to interaction between (**2**) and (**5**). The latter has been reported to participate in Schlenk-type equilibria with stannoxanes, affording mixed oxygen–halogen species:[9] in the case of the dioxastannolane (**2**), compound (**9**) is produced [reaction (iii)]. The nature and the structure of the products of reaction (iii) are still unclear, but the existence of a fast equilibrium is proved by the dependence of chemical shifts and linewidths of the single set of signals on the mole fractions of reagents (observed in ^{1}H, ^{13}C, and ^{119}Sn n.m.r. spectra). This result has been independently checked with solutions of (**2**) + (**5**) in various ratios at the same concentration. Since (**5**) is produced virtually from the beginning of the process, all species in equilibrium (iii) [hereafter abbreviated (**8**)] [but not compound (**2**)] should be considered as reacting species. It has been shown (Table 3), however, that neither reactivity nor product distribution is affected by addition of various amounts of (**5**). Thus dibutyltin dichloride interacts strongly with (**2**), but its role in the overall reaction is still obscure.

To check the results observed for step (*a*), the reaction was run by adding increasing amounts of the dichloride (**3**) to the solution of (**2**), in molar ratios ranging from 0.4 to 1.1 (Figure 3): complete formation of products was observed at room temperature immediately after each addition, with concomitant variation of the (**4′**):(**8**) ratio, but with the final oligomeric distribution.



In conclusion, no evidence was found to support the accumulation of detectable intermediates; instead, the overall reaction is fast and leads to the same final product mixture, irrespective of reagent ratio and of addition of (**5**).

Step (b). When the addition of 0.5 equiv. of (**3**) was followed by the addition of 0.5 equiv. of glutaryl chloride (**6**), the ^{1}H n.m.r. spectrum of the resulting mixture, although providing no analytical data because of signal overlap, showed the presence of mixed macrocyclic products. Chromatographic separation afforded the mixed tetraester (**10**) as the main isolated product (12%), in sharp contrast with the experimental evidence obtained for step (*a*).

To understand the origin of the mixed derivatives, 1 equiv. of benzoyl chloride (BzCl) was added after 0.5 equiv. of (**3**). Separation of the mixture gave esters (**11**) as main products in the indicated yields, together with traces of cyclic compounds. The recovery of isolated products was 95%. Unequivocally, extensive ring-opening occurred during the reaction with benzoyl chloride. This might explain the failures in attempts to isolate cyclic products by hydrolysis after step (*a*).

The extent of product reorganization during step (*b*) was conveniently detected by ^{1}H n.m.r., after quenching the reaction with 1 equiv. of chloro(trimethyl)silane (Me_3SiCl). This reagent presents some useful advantages over BzCl: (i) it is more reactive toward the dioxastannolane; (ii) it induces an upfield shift of signals; and (iii) the final silylated compounds produced are stable in the reaction medium.[10] The resulting spectrum [Figure 2(C)] exhibits the product distribution of Scheme 1. Similar results were obtained when the reaction was quenched with

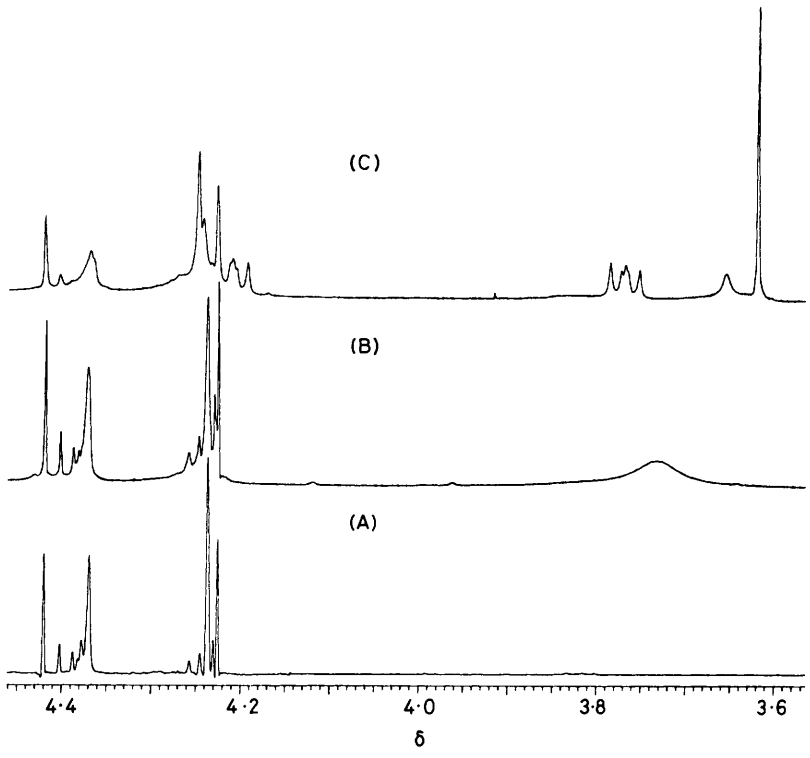


Figure 2. ^{1}H N.m.r. spectra (300 MHz) of product mixtures from reaction (i) under the reference conditions: (A) for (**2**) + (**3**) in 1:1 molar ratio (*cf.* Table 1); (B) for (**2**) + (**3**) in 1:0.5 molar ratio; (C) for (**2**) + (**3**) + Me_3SiCl in 1:0.5:1 molar ratio (*cf.* Scheme 1); the small amount of (**8**) at δ 3.654 beside the main signal for (**13**) at δ 3.619 is due to an accidental deficiency of Me_3SiCl [(**13**) 22%; (**8**) 15%]

chloro(dimethyl)phenylsilane ($PhMe_2SiCl$). Both cases show that, with respect to BzCl, quenching with the more reactive chlorosilanes causes less extensive reorganization of products.

Equilibration.—It was essential to check the stability of the polyester mixture to equilibration under the actual reaction conditions. The final solution was therefore refluxed for 2.5 h, but no significant variation was observed in its ^{1}H n.m.r. spectrum. The same result was obtained after several hours at room temperature after the addition of 1 equiv. of (**2**). Refluxing the latter mixture for 7 h merely produced slight decomposition, probably hydrolytic, but unchanged oligomeric distribution.

The next step, a check on the stability to equilibration of the pure tetraester (**4**), could not be carried out under the same conditions, because of its low solubility in the medium when isolated from the mixture.* Thus, a dilute solution of pure (**4**) ($< 10^{-2}$M), stable in the solvent in the presence of (**5**) for 7 days, to which a large excess of preformed (**8**) had been added, was observed to regenerate slowly the usual distribution of oligomers, with a half-life of the order of 20 h at room temperature. In view of the slow equilibration due to low concentration, these results provide clear evidence that the final mixture is not a kinetic, but an equilibrium distribution of oligomers.

As independent support, to the solution of products from reaction (i) was added 1 equiv. of dibutyltin dimethoxide (**14**), the open-chain analogue of (**2**) and the reaction was followed at room temperature [reaction (iv)]. The ^{1}H n.m.r. spectra showed the quantitative formation of dimethyl oxydiacetate (**15**), with an apparent half-life time of *ca.* 20 min. Furthermore, on treating the resulting mixture with 1 equiv. of Me_3SiCl, clean quenching was obtained, with almost quantitative formation of (**13**) and only traces of (**4'**), *i.e.* with nearly complete lack of product reorganization [reaction (iv)].

It is concluded that the reaction with dibutyltin dimethoxide [reaction (iv), first step] is an equilibrium, completely shifted towards products, which is much slower than quenching. On comparing yields from the second step of reaction (iv) with those of Scheme 1, it appears that equilibration of macrocyclic glycolates is much faster than that of the corresponding open-chain analogues.

Discussion

The present results show unambiguously that the reaction of 2,2-dibutyl-1,3,2-dioxastannolane with diacyl dichlorides is dominated by a transesterification equilibrium, and that the polyester products are under thermodynamic control. A thermodynamic template effect requires that the templating agent is selectively bound to one or more macrocyclic products in the final mixture, but in the present case tin is present exclusively as dibutyltin dichloride. On the other hand, a kinetic template effect can not be invoked because the product distribution is thermodynamic. Thus, it is evident that, whatever the actual mechanism and whatever template definition might be chosen, a structural or covalent template effect in the sense of a rigid framework on which insertion of diacyl dichloride fragments occurs, is lacking.† Moreover, evidence for selective

* This effect is probably due to the solvating ability towards the tetraester of higher oligomers, which are soluble in the medium.

† It must be emphasized that product structure and distribution are not determined by the kinetically controlled 'insertion' reaction of the dichloride on the dioxastannolane, as assumed in the mechanism based on the covalent template model, but by thermodynamic reorganization *via* a transesterification equilibrium.

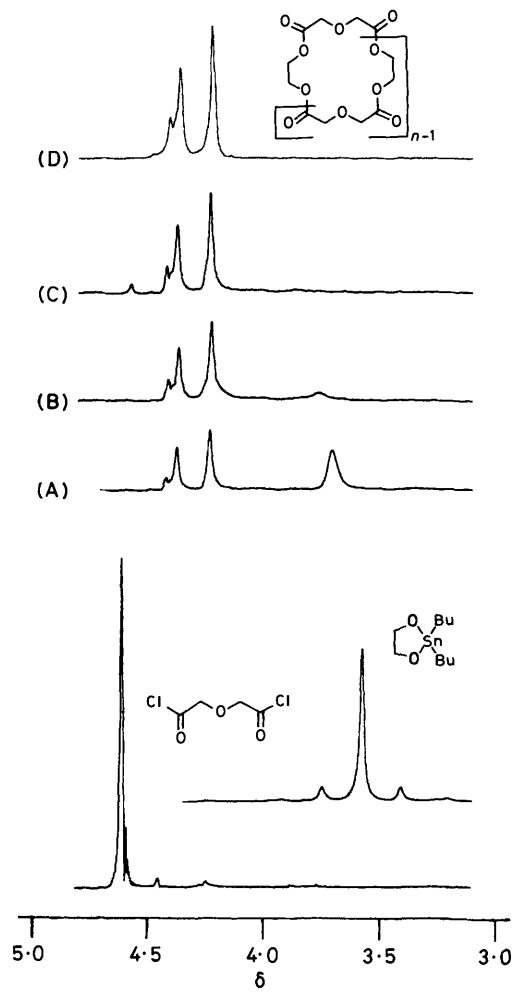
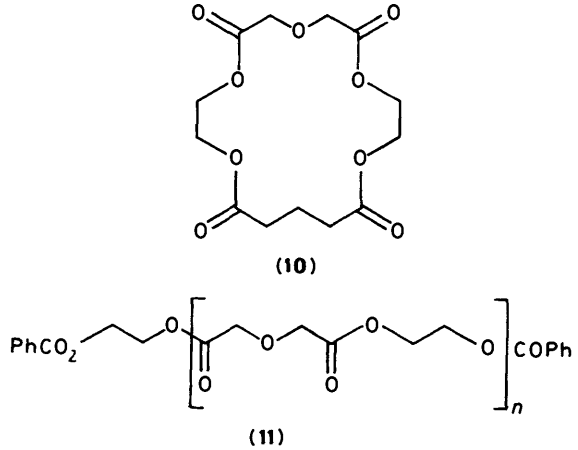


Figure 3. ^{1}H N.m.r. spectra (90 MHz) of product mixtures from reaction (i) under the reference conditions for various reactant ratios, obtained immediately after mixing at room temperature (reagent spectra are shown at the bottom of the Figure): (**2**):(**3**) ratios: (A) 1:0.4; (B) 1:0.8; (C) 1:1.1; (D) 1:1.1, after 2.5 h at 61 °C



(**10**)

(**11**)

n = 0 26%
n = 1 47%
n = 2 16%

interaction of tin with products or transition states has not been found.

A detailed description of the mechanism is not feasible with the present data; on the other hand, in the context of an equilibrium reaction, the actual mechanism appears to be irrelevant with regard to product regiochemistry, stereochemistry, and distribution. However, some conclusions can be reached.

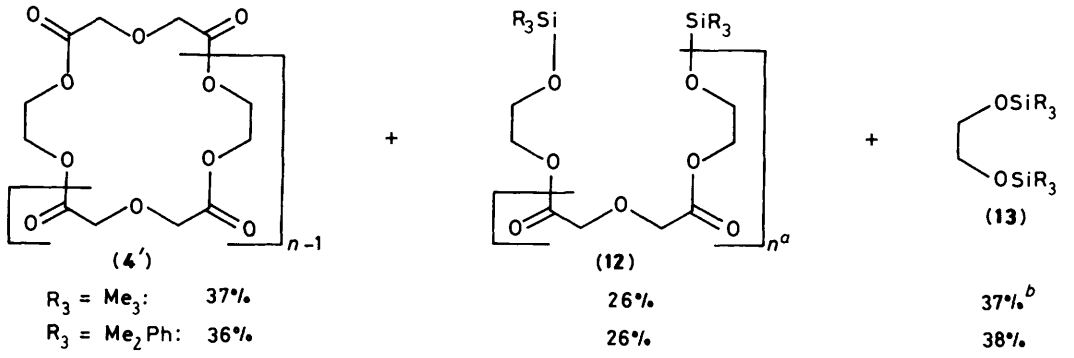
Reaction Scheme and Stoicheiometry.—It is well known that dioxastannolanes give selective monoesterification with acyl chlorides.[11] Indeed, in the reaction of (**2**) with monofunctional acid chlorides, complete disappearance of 1 equiv. of the latter accompanied an almost quantitative formation of β-(chlorostannoxy) ester as the first observable intermediate,[10] which slowly equilibrated to a mixture of diester and the starting dioxastannolane. If we assume the same functional group reactivity, the formation of an analogous intermediate can be postulated for the addition of 0.5 equiv. of a bifunctional acid chloride [Scheme 3(B), (**16**)]. However, such an intermediate could not be observed because of the very fast production of macrocyclic polyesters. Indeed, the final products were always observed immediately after mixing for any reagent ratio. A reaction scheme can thus be postulated which, at variance with that for monofunctional chlorides, involves *fast* equilibration of the intermediates to products [Scheme 3(B)].* In the transesterification equilibrium a series of oligomers with basic unit $OCH_2CH_2OCOCH_2OCH_2CO$ can thus be formed, generating the observed ester population.

In the reaction pathway of Scheme 3(B), dioxastannolane is consumed to produce (**16**) and regenerated in the last step. Thus, not only is (**2**) the reagent, but it also plays a catalytic role, taking part in the reaction with a coefficient greater than stoicheiometric [Scheme 3(A)].

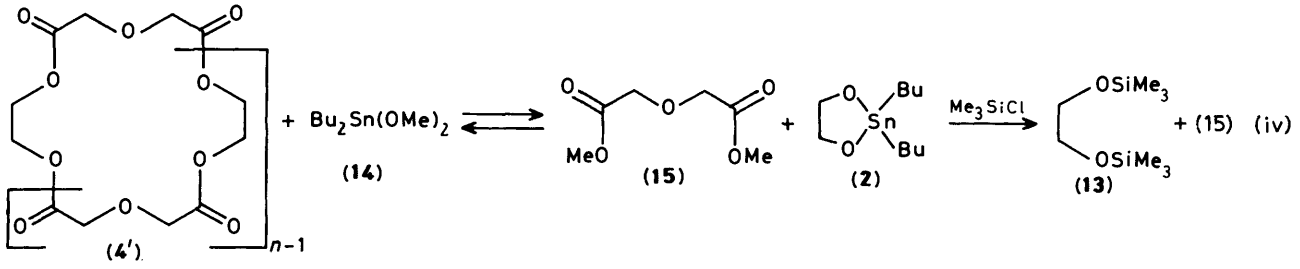
Equilibrium Position.—The transesterification equilibrium (**16**) $\rightleftharpoons$ (**4′**) (Scheme 4) is completely shifted towards the formation of cyclic polyesters and dioxastannolane. It seems likely that this might be due essentially to the stability of the five-membered-ring dioxastannolane, which is probably increased by its strong tendency to form aggregates. Thus a chelate effect of ethylene glycol on tin, *i.e.* the well known advantage of bidentate over monodentate ligands,[12] seems to be the driving force of the equilibrium: this would explain the exclusive formation of cyclic products. Support for this conclusion is provided by the quantitative formation of the dioxastannolane (**2**) from the macrocyclic products, on treatment with the open-chain analogue (**14**) (Scheme 4): the former is produced whenever possible, despite the concurrent destruction of cyclic esters.

Equilibrium Rates.—A fundamental difference from the reaction with monofunctional acid chlorides is the very fast disappearance of the intermediate (**16**): while the intermediate of the monoester reaction survives for several hours at room temperature,[10] under the same conditions the corresponding intermediates from the bifunctional compounds could not be observed. Since the difference between the two systems appears to be the formation of cyclic *vs.* open-chain products, this rate enhancement might be in some way related to 'intramolecularity'. However, if we consider the reaction of monofunctional esters as the appropriate model for the intermolecular counterpart of the macrocyclic ester ring-closure, and refer to

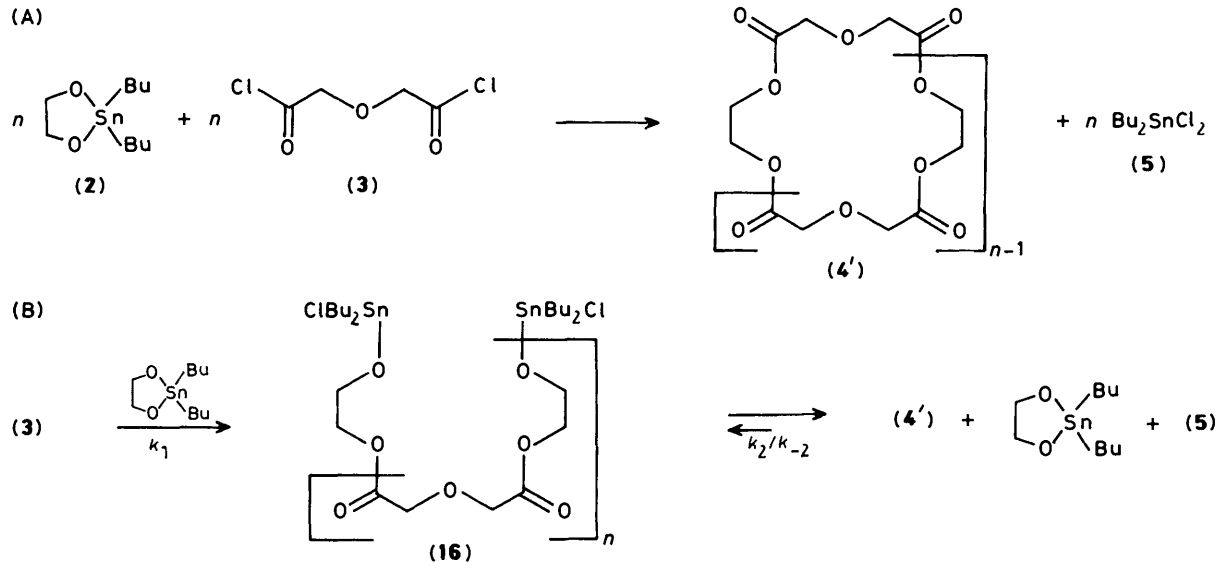
* It is possible that fast equilibration might also occur in the first stage, during the reaction with the diacyl dichloride, but under the present conditions this would be too fast to be detectable. However, reaction products would always be affected by subsequent transesterification equilibria.



Scheme 1. [a] for $n \neq 0$. [b] Partially stannylated owing to deficiency of chlorosilane



Scheme 2. Run in the presence of a stoicheiometric amount of (5)



Scheme 3. Stoicheiometry (A) and reaction pathway (B) for the reaction of oxybis(acetyl chloride) with the dioxastannolane

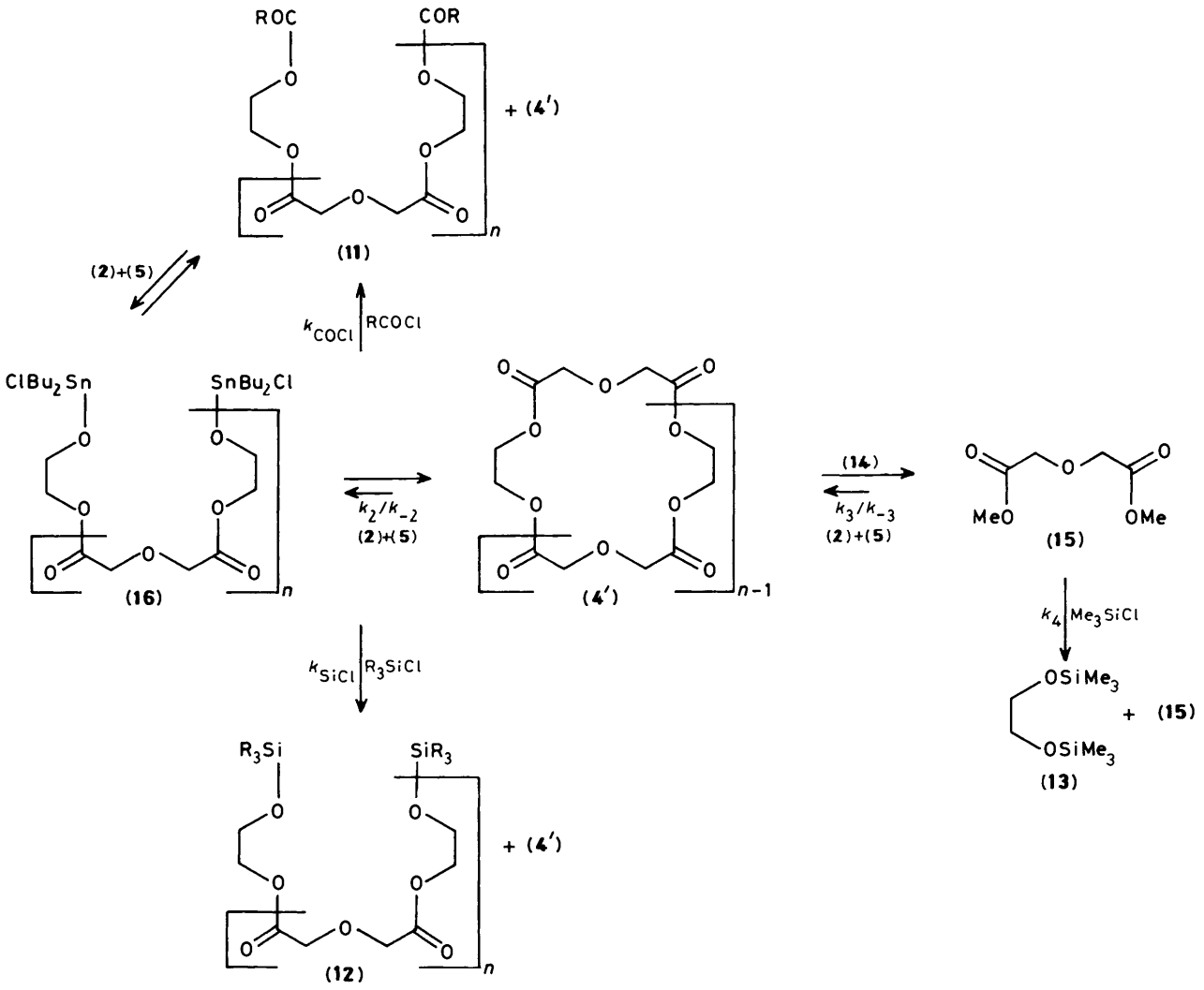
the Effective Molarity parameter EM = k_{intra}/k_{inter} to describe the tendency towards cyclization,[13] the present system appears to be characterized by values of EM $\gg$ 1M, in contrast with available evidence showing that values not greater than 0.1M are to be expected for the large size of the rings formed.[14]

The occurrence of such an effect is also suggested by the rate of ring-opening caused by (**14**) under the same conditions; this exhibits a half-life of *ca.* 20 min, *i.e.* much less than for ring-closure (Scheme 4, k_3/k_{-3}).

The possibility that the backward reaction (**4'**) ⟶ (**16**) might be slow was unambiguously ruled out by the appropriate quenching experiments, showing that with the same quenching reagent, k_{-2} is comparable with k_{Me_3SiCl} and k_{PhMe_2SiCl}, while k_4 is much larger than k_{-3}, *i.e.* both the forward and the reverse reactions are fast in comparison with the corresponding open-chain counterparts. In this context, from Scheme 4 it appears that RCOCl it is not a convenient quencher, because the resulting esters can take part in transesterification equilibria.

It is concluded that there is evidence of an effect, as yet unspecified but apparently related to intramolecularity, which gives rise to a conspicuous rate enhancement of the macrocycle-forming equilibrium, despite the fact that large rings are produced.

Oligomer Distribution.—From the foregoing description, the distribution of macrocyclic oligomers is expected to be under thermodynamic control. Thus, is the formation of the tetraester (**4**) to be considered truly selective? In the absence of a statistical



Scheme 4.

treatment for this system, distribution is unpredictable, but it may not be anomalous, *i.e.* it may not be necessary to invoke specific effects to explain the abundance of (**4**). On the other hand, it is possible that the 'intramolecularity' effects pointed out may favour the formation of some specific oligomers in the equilibrium distribution.

Conclusion.—2,2-Dibutyl-1,3,2-dioxastannolane has been proved to be an efficient transesterification catalyst in the formation of macrocyclic polyesters from diacyl dichlorides. Such a species plays the essentially double role of reagent and catalyst, equilibrating the product mixture while being consumed; at complete reaction, the resulting mixture is thus kinetically and thermodynamically stable and its oligomer distribution is defined by thermodynamic factors.

Experimental

Instruments and Techniques.—I.r. spectra were obtained for KBr pellets with a Perkin-Elmer 283 spectrophotometer. N.m.r. spectra were obtained with Perkin-Elmer R32 and Varian EM 390, FT 80A, and VXR 300 instruments. Chemical shift values (δ) are given in p.p.m. from Me_4Si, with $CHCl_3$ (δ 7.24) for ^1H and $CDCl_3$ (δ 76.9) for ^{13}C as internal secondary references. ^{13}C Spectra were recorded under broadband proton noise decoupling. Mass spectra were obtained with Varian MAT 111 and MAT 112 instruments operating at 70 and 20 eV. G.l.c.–mass spectrometric analyses were performed with an HP 5790A gas chromatograph, equipped with a mass-selective detector (HP 5970A), and Alltech capillary column (15 m × 0.25 mm i.d.), coated with RSL 150 (OV 101). Microanalyses were obtained with a Perkin-Elmer 240 C Elemental Analyzer. Column chromatography (silica gel; 230—400 mesh) and analytical and preparative t.l.c. were performed on silica gel 60 (Merck).

Samples for the ^1H n.m.r. investigation of the intermediates were prepared by adding dropwise (with a syringe through a septum cap) at 0—5 °C the appropriate volume of an acid chloride or chlorosilane solution (1 mmol per ml of $CDCl_3$) to the solution of the stannyl derivative (1 mmol per ml of $CDCl_3$) under nitrogen in a 5 mm n.m.r. tube. An analogous procedure was followed for ^{13}C n.m.r. spectra, using 10 mm n.m.r. tubes. The ^1H Fourier transform spectra were acquired with low pulse width (< 30°) and with pulse delays of 10 s.

Materials.—Chloroform (Carlo Erba RPE) was purified by washing with several portions of distilled water in a separatory funnel and left overnight over anhydrous $CaCl_2$. The solvent

was then filtered and kept in the dark over molecular sieves and Ag foil. The treated chloroform was free from ethanol and water and could be stored for several weeks without appreciable decomposition. Benzene (Carlo Erba RPE, >99.5%) and dibutyltin dichloride (Aldrich, m.p. 39—41 °C, b.p. 135 °C at 10 mmHg) were used without further purification. Chloro-(trimethyl)silane (Carlo Erba RPE, b.p. 57 °C), chloro-(dimethyl)phenylsilane (Fluka purum, *ca.* 98%, b.p. 194—198 °C), glutaryl dichloride (Fluka purum, b.p. 95—100 °C at 10 mmHg), and benzoyl chloride (Fluka purum, >98%, b.p. 70—74 °C at 11 mmHg) were purified by fractional distillation. Oxybis(acetyl chloride) (**3**) is a known compound and was prepared following a described procedure[15] in 90% yield; b.p. 61—64 °C at 0.5—1 mmHg. 2,2-Dibutyl-1,3,2-dioxastannolane (**2**) has been already described.[7a] Dibutyltin dimethoxide (**14**) is a known compound and was prepared by the described procedure[16] in 67% yield; b.p. 128—131 °C at 0.2 mbar; δ_H 3.40 (3 H, s, MeO), 1.0—1.8 (6 H, m, $[CH_2]_3$), and 0.8 (3 H, br t, Me).

Reaction (i).—*Reference procedure.* A solution of oxybis-(acetyl chloride) (513 mg, 3 mmol) in $CHCl_3$ (3 ml) was added dropwise with a syringe through a septum cap to a solution of 2,2-dibutyl-1,3,2-dioxastannolane (879 mg, 3 mmol) in $CHCl_3$ (3 ml) cooled with ice and stirred under nitrogen, at a rate such as to maintain the temperature at 5—7 °C. The solution was then allowed to warm to room temperature and poured into light petroleum (100 ml) with stirring, until the precipitation of a white gummy solid was complete. The mother liquor was decanted and the solid was washed with portions of light petroleum and dried under vacuum. The solid (510 mg) collected contained the ester product mixture (**4′**) in quantitative yield, together with small amounts of residual dibutyltin dichloride and dibutyltin oxide from adventitious hydrolysis; no ester products were detected in the mother liquors, which contained exclusively dibutyltin dichloride. The tetraester (**4**) could be recovered from the crude residue by crystallization from acetonitrile in which all other oligomers are more soluble.

Macrocyclic Polyesters (**4′**).—The crude mixture of oligomeric esters (t.l.c. in EtOAc, R_F 0.72, 0.60, 0.46, 0.33, 0.24, 0.16, 0.10, and 0.0), was chromatographed on silica gel (30 g) with pure EtOAc. From the collected fractions, a mixture (58 mg, 12%) of the two oligomers with the highest R_F values was recovered [(**4′**; n = 2 or 3)]: of these, the first (n = 2) slowly crystallizes from EtOAc at room temperature.

(*a*) 1,4,7,10,13,16-*Hexaoxacyclo-octadecane*-2,6,11,15-*tetraone* (**4′**; n = 2) had m.p. 186—186.5 °C; t.l.c. (EtOAc) R_F 0.72; ^{1}H n.m.r. see Table 1; ^{13}C δ 169.27 (CO), 67.71 (CH_2OCO), and 62.03 (OCH_2CO); *m/z* 320 (M^+), 246, 218, 204, 161 ($M/2$ + 1), 144, 101, 86 (100%), 73, 58, 44, and 42 (Found: C, 45.0; H, 5.05, $C_{12}H_{16}O_{10}$ requires C, 45.0; H, 5.0%); $\nu_{max.}$ 1 730 and 1 750 cm^{-1} (CO).

(*b*) 1,4,7,10,13,16,19,22,25-Nonaoxacycloheptacosane-2,6,-11,15,20,24-hexaone (**4′**; n = 3) showed t.l.c. (EtOAc) R_F 0.60; ^{1}H n.m.r. see Table 1; ^{13}C δ 169.35 (CO), 67.80 (CH_2OCO), and 62.29 (OCH_2CO); *m/z* 480 (M^+), 406, 364, 246, and 161 (100%).

(*c*) 1,4,7-Trioxacyclononane-2,6-dione (**4′**; n = 1) was obtained by adding oxybis(acetyl chloride) (26 mg, 0.15 mmol) in $CHCl_3$ (10 ml) dropwise to 2,2-dibutyl-1,3,2-dioxastannolane (45 mg, 0.15 mmol) in $CHCl_3$ (10 ml) following the general procedure with work-up after 4 days at room temperature; g.l.c. t_R 5.02 min (head pressure 6.0 lb in^{-2}; program: temp. 1 50 °C, time 1 2 min, rate 10 deg min^{-1}, temp. 2 280 °C); *m/z* (no M^+), 131, 116, 102, 89, 72, 61, 44, and 42 (100%); ^{1}H n.m.r. see Table 1.

(*d*) 1,7,10,16-Tetraoxacyclo-octadecane-2,6,11,15-tetraone (**7**; n = 2) had m.p. 138—138.5 °C; t.l.c. (PhH–EtOAc 2:1) R_F 0.46; ^{1}H δ 4.25 (4 H, s, CH_2O), 2.36 (4 H, t, CH_2CO), and 1.91 (2H, quint, CH_2CH_2CO); *m/z* 316 (M^+) and 159 (100%) [lit.,[3b] m.p. 144 °C; ^{1}H δ 4.25 (s), 2.40 (t), and 2.0 (quint.); *m/z* 316, 159 (100%), and 158].

(*e*) 1,7,10,13,16-Pentaoxacyclo-octadecane-2,6,11,15-tetraone (**10**) was prepared according to the reference procedure by adding oxybis(acetyl chloride) (342 mg, 2 mmol) in $CHCl_3$ (2 ml) and glutaryl dichloride (338 mg, 2 mmol) in $CHCl_3$ (2 ml) subsequently to the solution of (**2**) (1.172 g, 4 mmol) in $CHCl_3$ (4 ml). Work-up gave crude ester products (650 mg), appearing on t.l.c. (pure EtOAc, PhH–EtOAc 1:1 and 2:1) as a complex mixture of oligomers. Column chromatography on silica gel (35 g; PhH–EtOAc 2:1) gave (**7**; n = 2) (4 mg), together with (**10**) (75 mg, 12%) and (**4′**; n = 2) (5 mg). The product (**10**) had m.p. 109—110 °C; t.l.c. R_F 0.67 (EtOAc), 0.38 (PhH–EtOAc 1:1), and 0.34 (PhH–EtOAc 2:1); ^{1}H δ 4.22 (4 H, s, OCH_2CO), 4.34 (8 H, m, CH_2O), 2.36 (4 H, br t, CH_2CO), and 1.8—2.1 (2 H, quint, CH_2CH_2CO); *m/z* 318 (M^+), 260, 245 (100%), 216, 205, 160 ($M/2$ + 1), 145, and 116.

Compounds (**11**).—In accord with the reference procedure, oxybis(acetyl chloride) (342 mg, 2 mmol) in $CHCl_3$ (2 ml) and benzoyl chloride (584 mg, 4.15 mmol) in $CHCl_3$ (2 ml) were added subsequently to the solution of 2,2-dibutyl-1,3,2-dioxastannolane (1.172 g, 4 mmol) in $CHCl_3$ (4 ml). The final solution was concentrated to give products (2.1 g), from which the majority of dibutyltin dichloride was separated by distillation under vacuum. The residue was subjected to preparative t.l.c. (PhH–EtOAc 3:1) to obtain (**11**; n = 0) (138 mg, 26%), (**11**; n = 1) (403 mg 47%), and (**11**, n = 2) (127 mg, 16%) besides fractions containing open-chain benzoylated oligomers and cyclic oligomers. The recovery of ester products was 95%. The product (**11**; n = 0) had m.p. 69—70 °C; t.l.c. (PhH–EtOAc 3:1) R_F 0.89; ^{1}H δ 7.3—8.2 (5 H, m, Ph) and 4.68 (2 H, s, CH_2O); *m/z* 270 (M^+), 227, 148, 105 (100%), 77, and 51. Compound (**11**; n = 1) was a viscous oil; t.l.c. (PhH–EtOAc 3:1) R_F 0.57; ^{1}H δ 7.3—8.2 (5 H, m, Ph), 4.48 (4 H, s, CH_2OCOPh + CH_2OCOR), and 4.25 (2 H, s, OCH_2CO); *m/z* 430 (M^+), 308, 149 (100%), 105, 77, and 51. Compound (**11**; n = 2) was a viscous oil; t.l.c. (PhH–EtOAc 3:1) R_F 0.26; ^{1}H δ for $PhCO_2[CH_2]_A[CH_2]_B$-$OCO[CH_2]_CO[CH_2]_DCO_2[CH_2]_E$ 7.3—8.2 (5 H, m, Ph), 4.48 (4 H, s, A + B), 4.23 (2 H, s, C), 4.21 (2 H, s, D), and 4.31 (2 H, s, E); *m/z* (no M^+), 468, 348, 308, 189, 149 (100%), 105, and 77.

Reaction (iv).—Dibutyltin dimethoxide (885 mg, 3 mmol) in $CHCl_3$ (3 ml) was added dropwise with a syringe through a septum cap to the solution obtained from reaction (i), with stirring and cooling in ice. A sample of the resulting mixture was placed in a 5 mm n.m.r. tube and the reaction progress was followed by ^{1}H n.m.r. at room temperature. After complete formation of dimethyl oxydiacetate (**15**), chloro(trimethyl)silane (720 mg, 6.6 mmol) in $CHCl_3$ (3 ml) was added dropwise to the stirred solution, under nitrogen, with cooling in ice. The mixture was allowed to warm to room temperature; a ^{1}H n.m.r. spectrum then revealed quantitative formation of dimethyl oxydiacetate (**15**) and bis-*o*-trimethylsilylethanediol (**13**), together with traces of (**4′**) and $MeOSiMe_3$. Compound (**15**) was identified by ^{1}H n.m.r. and g.l.c.–mass spectrometry, by comparison with a pure sample prepared independently from oxybis(acetyl chloride) (**3**) and methanol, with entrainment of the evolved HCl with a stream of nitrogen. Dimethyl oxydiacetate (**15**) had g.l.c. [conditions as for (**4′**; n = 1)] t_R 4.6 min; ^{1}H δ 4.20 (2 H, s, CH_2) and 3.70 (3 H, s, Me); *m/z* (no M^+), 130, 103, 74, 59, 45 (100%), 43, and 42.

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Note added in proof: The formation of the stannylated intermediate (**16**), which could only be postulated, and its subsequent equilibration to the final oligomer mixture, have been observed by running the reaction in dilute solution (initial concentration 0.04M) and in the presence of a ten-fold excess of (**2**). Under these conditions, the reaction was slow enough so that it could be monitored by ^{1}H n.m.r. and, immediately after mixing, exhibited only small amounts of (**4**), besides the intermediate (**16**), with no evidence of the final oligomer distribution. Furthermore, quenching the 1:0.5 mixture of (**2**) + (**3**) at low concentration (initial concentration 0.028M) with Me_3SiCl before equilibration could take place to a large extent, led to only a limited amount (12%) of (**13**) being detected in the mixture, confirming that the observed dioxastannolane is not the unchanged starting material, but is regenerated in the reaction course.

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