72 h and then hydrolyzed. Column chromatography of the organic product on silica gel (1:1 (v/v) of $CHCl_3$–hexane) provided aniline and 9-phenylfluorene: 560 mg (78%; mp 146–147 °C.

n. 9-(Methylphenylamino)fluorene (16). Heating **16** in hexane with potassium *tert*-butoxide and *n*-butyllithium caused metalation at the 9-fluorenyl carbon but led to no rearrangement, even when the reagents were heated in refluxing mesitylene.

o. Diphenyl(diphenylmethyl)amine (17). Although this compound was metalated at the benzhydrylic carbon by *n*-butyllithium with either THF or potassium *tert*-butoxide, no rearrangement ensued.

Likewise, when the expected rearrangement product of **17**, namely *N*-(triphenylmethyl)amine (**32**), was heated with *n*-butyllithium, no rearrangement to **17** was observed.

Synthesis of Authentic 6-Phenyl-1,1a,2,3,4,4a,5,6-*cis*-octahydrophenanthridine (22). A solution of 5 g (32 mmol) of 1-phenylcyclohexene in 125 mL of ether was admixed with 125 mL of a saturated aqueous solution of $NaNO_2$. The mixture was rapidly stirred at 0 °C, while dilute aqueous H_2SO_4 was added dropwise. A deep blue color developed; addition of the acid was continued until the color changed to yellow. The ether layer was separated, dried over anhydrous $MgSO_4$, and then treated with a 50 mL solution of sodium methoxide in MeOH (prepared from 1.2 g of sodium metal and 50 mL of MeOH) for 15 min. The reaction mixture was then poured into water, and then ether was added. The separated dried ether layer was evaporated and the organic residue distilled at 3 mm pressure to give 75% of 1-nitro-2-phenylcyclohexene, bp 145–150 °C.[35]

A suspension of 5.0 g of $LiAlH_4$ in 100 mL of ether was stirred at 0 °C, while a solution of 8.0 g (41.5 mmole) of 1-nitro-2-phenylcyclohexene in 50 mL of ether was introduced dropwise. The mixture was then stirred for 24 h at 25–30 °C and hydrolyzed. Acid extraction of the ether layer and basifying the extract gave 2.0 g of *cis*-1-amino-2-phenylcyclohexane. Since its ^1H NMR spectrum was indicative of high purity, it was used directly.

The foregoing amine (2.0 g) was dissolved in 20 mL of anhydrous pyridine and 2.0 mL of benzoyl chloride added dropwise. After the mixture was heated on the steam bath for 60 min, it was poured into cold water. The water suspension was extracted with ether, and the ether extract was dried and evaporated. Crystallization of the residue from petroleum ether afforded 2.2 g of *cis*-1-benzamido-2-phenylcyclohexane, mp 153–155 °C.

This benzamido derivative (1.0 g) was dissolved in 3.0 g of polyphosphoric acid, heated to 155 °C, and then admixed with 3.0 g of $POCl_3$. After the mixture was heated for 4 h at 155–160 °C, it was cooled and then quenched with an aqueous Na_2CO_3 solution. Usual acid-extraction separation yielded 500 mg of 6-phenyl-1,1a,2,3,4,4a-*cis*-hexahydrophenanthridine, mp 160–161 °C (from ethanol).

Reduction of this phenanthridine with $LiAlH_4$ in ether solution was conducted in the manner described for *cis*-1-nitro-2-phenylcyclohexene. The resulting 6-phenyl-1,1a,2,,4,4a,5,6-*cis*-octahydrophenanthridine was isolated as a colorless oil (65%) and had spectral properties identical with those exhibited by **22**, the rearrangement product from *N*-benzyl-1,1a,2,3,4,4a-*cis*-hexahydrocarbazole (**21**, section f).[35]

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Group 14† Organometallic Reagents. 4.[1] Stereodynamics of Substituted Dioxastannolanes. Carbon-13 and Tin-119 NMR Studies

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The stereodynamics of some ring-substituted dioxastannolanes have been investigated by ^{13}C and ^{119}Sn dynamic NMR spectroscopy in concentrated chloroform solution and compared with those of the unsubstituted dioxastannolane. Results show that dioxastannolanes are dynamic species, subject to complex equilibria. Substitution on the ring carbons allowed discrimination between intermolecular aggregation equilibria, which form mostly dimers along with higher oligomers, and an intramolecular process within the dimer. A mechanism is proposed for the latter process that accounts for the inversion of configuration at tin and implies an exchange of tin atoms between diol moieties. The high-energy barrier for the intramolecular process suggests that dioxastannolanes in solution have a dimeric structure with two apical and one equatorial Sn–O bonds at room temperature but become fluxional at higher temperatures. The stereochemical and reactional implications of these findings are discussed.

Introduction

Organostannoxanes are useful intermediates in organic synthesis because of their reactivity and selectivity toward electrophilic reagents.[2] These features have been ascribed to the tendency of stannoxanes, in particular dioxastannolanes, to associate to dimers and higher aggregates that can act as templates in a reaction. This effect has been proposed to account for the organotin-mediated acylation, alkylation, and oxidation of polyhydroxy compounds such

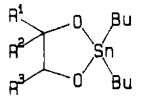
† In this paper the periodic group notation is in accord with recent actions by IUPAC and ACS nomenclature committees. A and B notation is eliminated because of wide confusion. Groups IA and IIA become groups 1 and 2. The d-transition elements comprise groups 3 through 12, and the p-block elements comprise groups 13 through 18. (Note that the former Roman number designation is preserved in the last digit of the new numbering: e.g., III → 3 and 13.)

(1) Part 3: Ricci, A.; Roelens, S.; Vannucchi, A. *J. Chem. Soc., Chem. Comm.* **1985**, 1457.

(2) For a recent review, see: David, S.; Hanessian, S. *Tetrahedron* **1985**, *41*, 643.

0022-3263/87/1952-4444$01.50/0

Chart I



	R^1	R^2	R^3
1	Me	H	H
2	Ph	H	H
3	Me	Me	H
4	Ph	Me	H
5	H	MeO_2C	MeO_2C (meso)

a = racemic form

b = pure enantiomer

as carbohydrates, which occur with high regioselectivity at a single equatorial or axial position.[2]

We have shown through dynamic NMR spectroscopy (DNMR) that 2,2-dibutyl-1,3,2-dioxastannolane in chloroform solution undergoes fast association to oligomers, among which the predominant species is a symmetrical dynamic dimer.[3] However, the nature of the dynamic process occurring in the dimer could not be ascertained unambiguously.

Substitution on the dioxastannolane framework should provide a useful probe for discriminating among the dynamic phenomena involved. Furthermore, knowledge of the structure of substituted dioxastannolanes might be helpful in understanding the nature of tin templates. For example, it might explain the high regio- and stereoselectivity in the Shanzer reaction of dioxastannolanes with dicarboxylic acid dichlorides in the synthesis of macrocyclic tetraesters,[4] which was ascribed to the presence of a specific dimer isomer.[5]

We here report on the structural features of some mono- and disubstituted 2,2-di-*n*-butyl-1,3,2-dioxastannolanes as determined by ^{13}C and ^{119}Sn DNMR and on their stereochemical and reactional implications.

Results

Mono- and disubstituted diols were azeotropically dehydrated in the presence of a stoichiometric amount of di-*n*-butyltin oxide in toluene.[6] The resulting 2,2-dibutyl-1,3,2-dioxastannolanes (dibutyl is used for di-*n*-butyl throughout the remaining text) were then subjected to NMR analysis in concentrated $CDCl_3$ solution (1 mmol/mL = 0.85 M). Chloroform is the only solvent in which dioxastannolanes are highly soluble at low temperature; therefore, our investigation covered the temperature range 213–333 K.

Monosubstituted Dioxastannolanes. Compounds **1** and **2** (Chart I) were prepared from both diols, the racemic (**a**) and the enantiomerically pure (**b**), of *S* configuration. In solution both compounds form predominantly dimers that undergo a fast exchange of monomeric units and exhibit the peculiar phenomenon of the enantiomeric self-discrimination.[6] Moreover, while the dimers of **1b** and **2b** are pure species, those from **1a** and **2a** have been shown to be a statistical 25:50:25 mixture of *RR*, *RS*(*SR*), and *SS* dimers, i.e., a 50:50 mixture of meso and racemic diastereomers.[6]

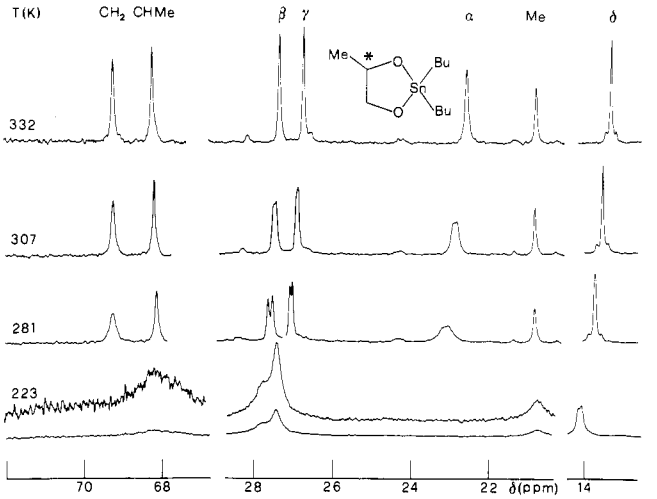


Figure 1. $^{13}C\{^1H\}$ DNMR spectra (20 MHz) of 4-methyl-2,2-dibutyl-1,3,2-dioxastannolane (enantiomerically pure compound **1b**; 0.85 M in $CDCl_3$; δ in ppm from external Me_4Si).

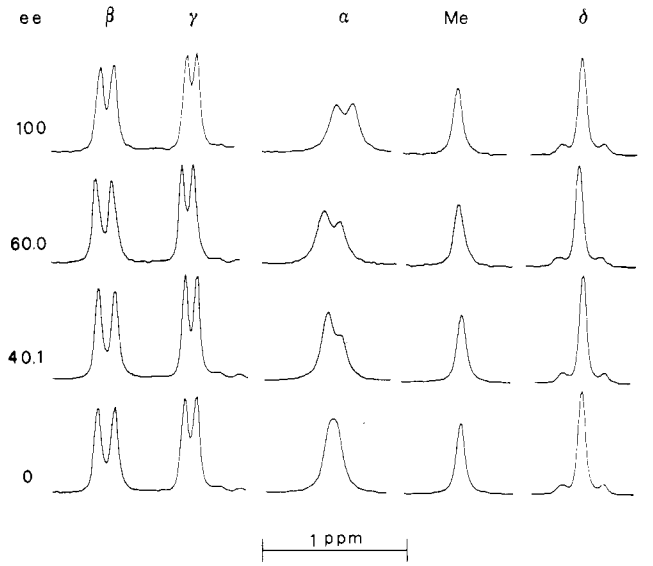


Figure 2. $^{13}C\{^1H\}$ NMR spectra (20 MHz) of the butyl region and the methyl signal of 4-methyl-2,2-dibutyl-1,3,2-dioxastannolane (**1**; 0.85 M in $CDCl_3$) vs. ee values of the parent diol.

^{13}C NMR Spectra. The room temperature ^{13}C NMR spectra of **1** and **2** show a splitting of the butyl group signals, decreasing in magnitude from the α to the δ carbon. The DNMR behavior of **1b** is shown in Figure 1: above room temperature the signals coalesce to a single line,[7] while below room temperature the narrowing superimposes on other dynamic processes, analogous to those observed in the unsubstituted dioxastannolane.[3] Similarly, **1a** and equimolar mixtures of **1a** and **1b** showed coalescence of signals above room temperature (Figure S1).[8] In the latter mixture, the α carbon signal is split into two lines of unequal intensities that coalesce at higher temperatures; on the other hand, the asymmetric carbon signal splitting is insensitive to increasing temperature. To analyze this effect in more detail, spectra of mixtures of various ee were recorded at room temperature (Figure 2). The separation of the α carbon lines and their relative intensities appear to be directly related to ee; the effect seems to depend on

(3) Roelens, S.; Taddei, M. *J. Chem. Soc., Perkin Trans. 2* **1985**, 799.
(4) Shanzer, A.; Libman, J.; Frolow, F. *Acc. Chem. Res.* **1983**, *16*, 60.
(5) Shanzer, A.; Libman, J.; Gottlieb, H. E. *J. Org. Chem.* **1983**, *48*, 4612.
(6) Luchinat, C.; Roelens, S. *J. Am. Chem. Soc.* **1986**, *108*, 4873.
(7) Coalescence of signals can only be ascribed to averaging of signals for diastereotopic butyl groups in the *dimeric* dioxastannolane; in the monomeric five-membered ring they are structurally diastereotopic and should be split at all temperatures.
(8) Figures S1 to S9 are available as supplementary material.

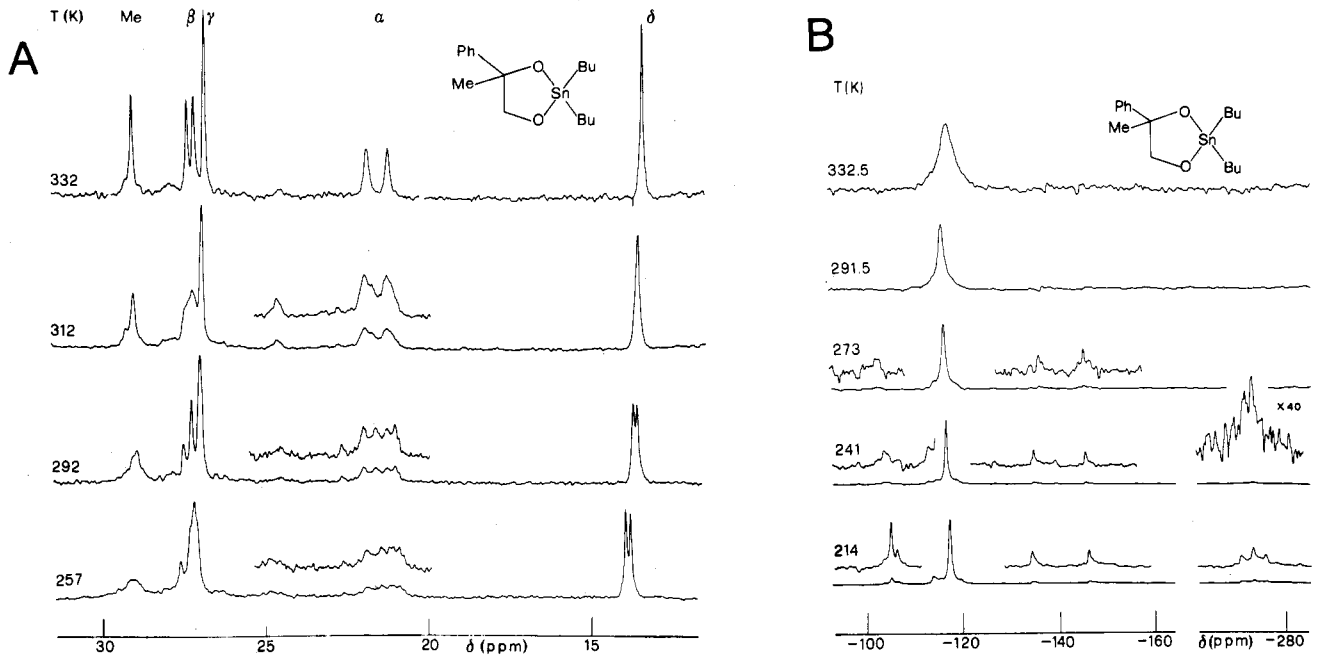


Figure 3. (A) $^{13}C\{^1H\}$ DNMR spectra (20 MHz) of the butyl region and the Me signal of 4-phenyl-4-methyl-2,2-dibutyl-1,3,2-dioxastannolane (racemic compound 4; 0.85 M in $CDCl_3$; δ in ppm from external Me_4Si). J coupling with $^{117/119}Sn$ is visible in the expanded trace. (B) $^{119}Sn\{^1H\}$ DNMR spectra (29.648 MHz) of 4-phenyl-4-methyl-2,2-dibutyl-1,3,2-dioxastannolane (racemic compound 4; 0.85 M in $CDCl_3$; δ in ppm from external Me_4Sn).

both the diastereotopism of the two groups and the enantiomeric self-discrimination in a fast-exchange regime.

The phenyl derivative **2** exhibits analogous behavior in its dependence on both temperature and ee (Figures S2–S4),[8] confirming that the phenomenon is not fortuitous and that the higher temperature processes are related to substitution on the dioxastannolane ring.

For compound **1a**, a decrease in concentration from 1.1 to 0.2 M caused an increase in line width for the α carbon from 2.6 to 5.0 Hz at 306 K, and the signal appeared as two lines approaching the coalescence point. The concentration dependence was thus taken as indicative of fast intermolecular processes among different species.

Some interesting features of the above spectral data can be pointed out. (1) In **2**, a downfield shift of the butyl signals and an upfield shift of the ring carbons and the C_{ipso} of the phenyl group is induced by decreasing temperature, particularly for the racemic **2a**; this effect is probably related to the influence of temperature on aggregation equilibrium constants and on diastereomeric composition. (2) The magnitude of splitting in **1b** is in the order $(CH_2)_\alpha \geq (CH_2)_\beta > (CH_2)_\gamma > (CH_3)_\delta$, while in **2b** the order is $(CH_2)_\alpha \gg (CH_2)_\gamma > (CH_2)_\beta \simeq (CH_3)_\delta$. (3) Even though **1b** and **2b** are single dimeric species while **1a** and **2a** are mixtures, in all four cases only a splitting into two different butyls is apparent. Thus the splitting is not averaged by the fast intermolecular exchange and is not caused by the presence of diastereomeric species. (4) The magnitudes of the splittings in the enantiomerically pure and in the racemic compounds are different, particularly for the α carbon; this signal is markedly split in the former but only barely in the latter.

^{119}Sn NMR Spectra. We used the ^{119}Sn DNMR behavior of the phenyl derivative **2a** (Figure S5)[8] for detecting processes occurring at low temperature; line broadening and splitting are analogous to those of unsubstituted dioxastannolane but show a slower exchange rate, with the appearance of several lines in the regions of pentacoordinate (downfield) and hexacoordinate (upfield) tin. The single band, broad at room temperature and narrowing with increasing temperature, suggests that the tin atoms are equivalent in the temperature range where butyl carbons are not: within the experimental uncertainty due to the large line width, the dimeric dioxastannolane exhibits two different butyls on two equal tin atoms.

The effect of diastereomeric composition is exemplified by the methyl derivatives **1a** and **1b**: room-temperature spectra revealed identical single signals at δ −165 and LW = 340 Hz, shifting to δ −157 and LW = 100 Hz at 333 K.

Disubstituted Dioxastannolanes. We studied the two *gem*-substituted compounds **3** and **4** and the *vic*-disubstituted derivative **5**.

^{13}C NMR Spectra of 3. There is no splitting of any signal in the room temperature spectrum of **3**; the low-temperature DNMR behavior shows the already described pattern (Figure S6),[8] although with a somewhat lower exchange rate. The $(CH_2)_\alpha$ signal coalesces at 257 K, a temperature higher than those observed for **2**, **1**, and the unsubstituted derivative, which appeared to coalesce at 243, 240, and 227 K, respectively.[3] Association of stannoxanes in solution is known to be strongly affected by steric hindrance,[9] and our data show that increasing substitution on dioxastannolanes slows down the rate of exchange as well. The absence of signal splitting in the high-temperature range implies that such diastereotopism occurs in unsymmetrically substituted substrates.

^{119}Sn NMR Spectra of 3. In the same range of temperature, **3** behaves like chiral compounds **1** and **2** with respect to tin (Figure S7);[8] two main lines of similar intensity are clearly resolved in the range of pentacoordinate tin, among other resonances for penta- and hexacoordinate tin. Since this pattern is shared by the unsubstituted dioxastannolane, the process does not appear to depend on chirality of the monomeric unit.

(9) For reviews on tin NMR data, see, for example: (a) Smith, P. J.; Tupciauskas, A. P. In *Annual Reports on NMR Spectroscopy*; Academic: London, 1978; Vol. 8, p 291. (b) Wrackmeyer, B. *Annual Reports on NMR Spectroscopy*; Academic: London, 1985; Vol. 16, p 73.

^{13}C NMR Spectra of 4. Compound **4** is somewhat anomalous in the series (Figure 3A). The α carbon shows four lines at room temperature that coalesce to two at 332 K; in the process, two lines decrease in intensity with respect to the other two. The δ carbon signal shows coalescence of two lines, and for the β carbon the coalescence of two signals of intensity ratio roughly 1:3 leads to two equally intense lines. The methyl signal exhibits the coalescence of two lines, with an intensity trend similar to the α carbon. Since no splitting is exhibited by any other carbon signal and exchange at room temperature is slow (Figure 3B), two or more species are present with accidentally equivalent signals.[10] As a support, a diastereomeric mixture of **4**, obtained from a 42% ee diol, exhibited the same splitting pattern as the racemic derivative, but the α carbon showed the upper field doublet (δ 21.69, 21.08) decreased in intensity with respect to the lower field one (δ 21.97, 21.27); the same occurred in the upper field line of the δ carbon, the lower field line of the methyl carbon, and the intensity ratio of the β carbon lines, which was greater than 3:1. Experiments on a more concentrated solution (1.65 M, Figure S8)[8] showed a shift of the process to lower temperature; the increase in rate with concentration points to intermolecular processes.

^{119}Sn NMR Spectra of 4. The single line for pentacoordinate tin is narrow and shows a significant broadening only above room temperature (Figure 3B). Experiments on a more concentrated solution (1.65 M) merely showed greater line widths, i.e., faster intermolecular processes. The very low intensities of other signals indicate that species other than dimers are negligible.

^{13}C NMR Spectra of 5. A dioxastannolane disubstituted on adjacent carbons could be anticipated to display DNMR processes with rates between those of monosubstituted and *gem*-disubstituted compounds. Indeed, butyl signal splitting is observed at 304 K (Figure S9),[8] giving a single line for the β carbon and approaching coalescence for the α carbon at 333 K.

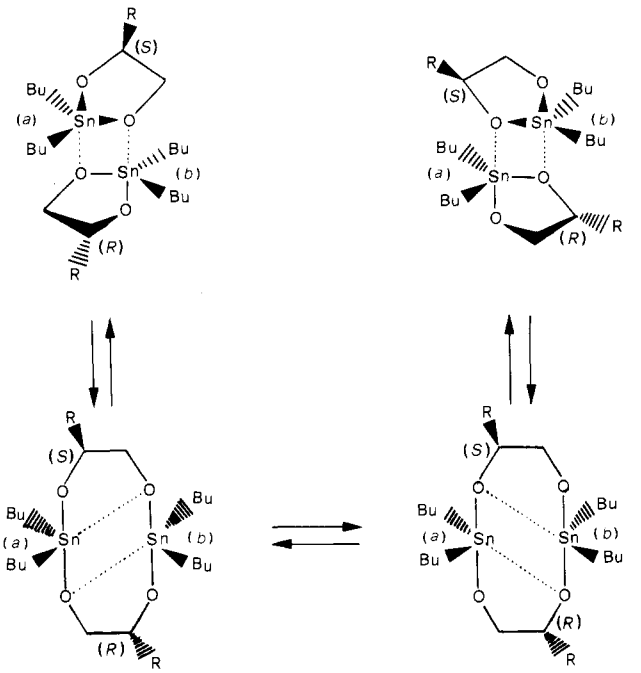
Discussion

Our results show that substituted dioxastannolanes associate in solution predominantly to dimers, as does the unsubstituted compound. Resonances for tetra-, penta-, and hexacoordinate tin in the ^{119}Sn NMR spectra are clearly discriminated,[9] and the signals for pentacoordinate tin, belonging to dimers or to chain ends of higher aggregates, appear by far the most intense. Furthermore, the low intensities of signals in the hexacoordinate tin region indicate that higher aggregates make only a small contribution to the pentacoordinate tin resonance. It is thus convenient to analyze the data assuming a dimeric structure for all systems.

The apparent simplicity of NMR spectra suggests that dynamic processes occur, averaging resonances from different isomers. The discrimination between inter- and intramolecular processes is a key point in the analysis of the structure and reactivity of these compounds; intermolecular exchange with dimers can involve monomers as well as trimers and higher homologues, while intramolecular processes involve transannular interactions with the breaking and forming of Sn–O bonds.

Although the unsubstituted monomer exchanges slowly with other aggregates on the NMR time scale,[3] the dimers of substituted compounds exchange monomer units rapidly at room temperature.[6] Scrambling of monomeric units of opposite chirality occurs in derivatives of racemic diols; thus, this process involves an intermolecular exchange and has been ascribed to the presence of higher aggregates as labile intermediates. On the other hand, there might also be a fast intramolecular exchange that is not distinguishable in unsubstituted systems. Monosubstitution turned out to be the probe for discriminating between intra- and intermolecular processes. The key result is the shape of the butyl group signals for **1** and **2**: for both the racemic and the enantiomerically pure compounds these signals are split in the temperature range where the scrambling of monomers of opposite chirality among dimers is fast. It is concluded that the fast process occurs without inversion of configuration at tin and can only be ascribed to an intermolecular exchange. On the other hand, the higher temperature process causes a coalescence of signals and is ascribed to a slow intramolecular equilibrium (Scheme I), in which a scrambling of tin atoms occurs between the two diol moieties of the dimer, causing loss of diastereotopism of the butyl groups (only the meso dimer is illustrated).[11]

Scheme I

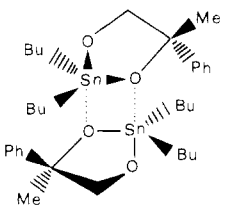


Of the two dynamic processes, only that at lower temperatures is common to all systems; the high temperature process occurs only in unsymmetrically substituted compounds and superimposes on the former. Since increasing substitution of methyl groups on the same carbon should cause a regular variation in exchange rates, the observation of diastereotopism in only the monosubstituted derivative is thus believed to depend on lack of symmetry with re-

(10) A support for this statement was found in the narrowing of the asymmetric carbon single line with increasing temperature (from 1.6 Hz at 283 K to 1.1 Hz at 332 K, with no significant variations in the solvent LW): this can occur for coalescence of nearly equal resonances, resulting in improved resolution.

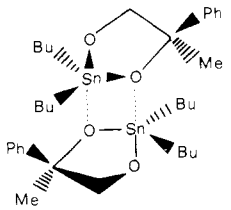
(11) In the ^{13}C NMR spectra of the phenyl derivative **2**, coupling constants $^{3}J[^{13}C–^{119/117}Sn]$ of 24 Hz with the C_{ipso} of the phenyl group are observed at all investigated temperatures. When the intramolecular equilibrium of Scheme I becomes fast, the above coupling constant should vanish. Thus, the presence of J coupling at 332 K would mean that the equilibrium is still slow for a J of 24 Hz to coalesce: indeed the line separation for the α carbon is 6 Hz for **2b**, and it is not yet at coalescence at 332 K. Alternatively, if a different mechanism is operating, it cannot admit scrambling of tin atoms within diol moieties in this range of temperature; this might be achieved, for example, by pseudorotation, but the simple spectra obtained for compound **3** would not be consistent with the expected splitting pattern for butyl groups in the apical–equatorial positions.

Chart II



6

Anti



7

Syn

spect to the plane of the molecule. Evidence for this conclusion is given by the behavior of **5**: although it is a disubstituted achiral compound like **3**, it exhibits diastereotopism of butyl groups like **1** and **2**. Molecular association can probably generate all the possible regio- and stereoisomers, but since these are exchanging rapidly even at quite low temperatures, no information about the actual isomeric composition can be obtained from NMR data.[12]

The results allow a kinetic description of the intramolecular equilibrium. In compound **1b**, T_c = 308 K for the β carbon and T_c = 296.5 K for the γ carbon; first-order rate constants were evaluated as k_{308} = 6.2 s^{-1} and $k_{296.5}$ = 2.7 s^{-1}, and both signals gave an energy barrier $\Delta G^{\ddagger}$ = 16.8 kcal/mol (70 kJ/mol). For **2b**, k_{306} = 2.2 s^{-1} was evaluated from the α carbon; the γ carbon provided T_c = 312 K, with k_{312} = 6.2 s^{-1} and a barrier value $\Delta G^{\ddagger}$ = 17.2 kcal/mol (72 kJ/mol). Compound **5** gave k_{304} = 14 s^{-1} from the α carbon, with an estimated energy barrier $\Delta G^{\ddagger} > 17.2$ kcal/mol.

In the apparently anomalous behavior of **4**, both processes are shifted to higher temperatures, and this result permitted us to study the intermolecular equilibrium. Structural assignment of the slow exchanging isomeric dimers was made by comparison of data from the racemic and the 42% ee mixtures: signals of lower intensity in the spectrum of the latter obviously belong to the meso dimer, reflecting the increased amount of pure adduct. On the other hand, the presence of one single line for pentacoordinate tin strongly supports the presence of only the trans isomer. Therefore the two species observed in the ^{13}C NMR spectrum are most likely assigned as the meso (anti) **6** and the chiral (syn) **7** (Chart II).

Although there is no marked preference for either isomer at 297 K, with increasing temperature the *anti*-**6** seems to be disfavored. The marked gap between the T_c of **3** and **4** suggests a steep increase in steric effects.

Structural and Mechanistic Considerations. The δ values for the ^{13}C NMR signals of the ring carbons and the methyl substitutent in all compounds indicate that an overall deshielding is exerted by increasing substitution, apart from the obvious electronic effects of substituents. The chemical shifts appear to be dominated by steric effects, supporting the idea that steric hindrance plays an important role in the reactivity of dioxastannolanes.

The occurrence of an intramolecular equilibrium at temperatures markedly higher than those for the intermolecular process can be explained by the need for breaking an equatorial Sn–O bond in the trigonal bipyramid for the former vs. breaking apical bonds in the latter. This behavior suggests that in solution the butyl groups preferentially occupy equatorial positions like in the solid state, as indicated by crystallographic data on pentacoordinate tin–heteroatom derivatives.[13] The low temperature splitting in lines of different intensities, observed in both the ^{13}C and the ^{119}Sn spectra, strongly supports the assignment to different aggregates and not to different butyl groups, as would be the consequence of occupying axial and equatorial positions.[14] Moreover, in the slow-exchange region such dissymmetric structures would result in more complex spectral patterns.

The overall picture is then a dimer possessing two "loose" apical and one "tight" equatorial oxygens around two pentacoordinate tin atoms. Only when the intramolecular exchange becomes fast is the dioxastannolane truly fluxional.

The lability of apical Sn–O bonds is likely to reflect an enhanced reactivity toward electrophilic reagents of one of the two oxygens in the diol; on the other hand, coordination at tin should decrease charge density on the second oxygen atom, resulting in a cooperative effect. A different reactivity is thus anticipated for the two opposite pairs of oxygens in the dimer, and this is the effect postulated in the selective tin-mediated monofunctionalization of diols.[1,2] However, it must be emphasized that the two oxygens still scramble at a rate faster than that of common organic reactions;[15] this leads to selective monofunctionalization reactions but also to unpredictable distributions of product isomers according to the Curtin–Hammett principle.[16]

Finally, for very bulky substituents as in carbohydrate derivatives, equilibria are expected to be very slow, but the actual products will depend on which nucleophilic oxygen occupies the apical position, compatible with the steric requirements of the substrate. Thus carbohydrate O-alkylations and acylations through their organotin derivatives take place selectively at a single site, but the regiochemistry is dependent on the specific substrate and solvent.[2,17]

Experimental Section

Instruments and techniques, as well as materials, general preparative procedures, and compounds **1** and **2** have been described previously.[3,6] The known[18] compound **3** as well as **4** and **5** were prepared according to the literature procedure;[3,6] satisfactory analytical data were obtained for all compounds reported. Melting points are uncorrected. ^{13}C NMR spectra were obtained under proton noise broad band decoupling; assignment of signals was done by using SEFT pulse sequences;[19] ^{119}Sn NMR spectra were recorded with proton noise decoupling under gated NOE suppression. Chemical shift values for 0.85 M solutions in $CDCl_3$ at 306 K are given in ppm from external Me_4Si (^{13}C) and Me_4Sn (^{119}Sn).

4-Methyl-2,2-dibutyl-1,3,2-dioxastannolane, Racemic Compound (1a). ^{13}C NMR: $CHCH_3$, 20.88; $CHMe$, 68.35; CH_2CHMe, 69.34; $(CH_2)_\alpha$, 23.00; $(CH_2)_\beta$, 27.58, 27.47; $(CH_2)_\gamma$, 27.00, 26.92; $(CH_3)_\delta$, 13.57. ^{119}Sn NMR: −165.

(12) The alternative explanation, which invokes the selective formation of isomeric dimers,[5] does not fit experimental evidence: fast exchange of heterochiral units is in contrast with the diastereotopism of the butyl groups. A detailed discussion on this point is available as supplementary material.

(13) Reference 2, p 644. Swisher, R. G.; Holmes, R. R. *Organometallics* **1984**, *3*, 365.

(14) A dilute (0.02 M) sample of the unsubstituted dioxastannolane at low temperature showed ^{119}Sn spectral lines of markedly different intensities in the pentacoordinate tin region (unpublished results).

(15) Preliminary kinetic experiments have shown that the unsubstituted dioxastannolane reacts with mono- and dicarboxylic acid chlorides, under the same conditions as those used in the present work, completing 50% of reaction in 5 s with acetyl chloride and glutaryl chloride and in 16 s with benzoyl chloride.

(16) For a comprehensive review, see: Seeman, J. I. *Chem. Rev.* **1983**, *83*, 83.

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(S)-4-Methyl-2,2-dibutyl-1,3,2-dioxastannolane, Enantiomerically Pure Compound (1b). ^{13}C NMR: $CHCH_3$, 20.91; $CHMe$, 68.27; CH_2CHMe, 69.33; $(CH_2)_\alpha$, 22.99, 22.87; $(CH_2)_\beta$, 27.58, 27.49; $(CH_2)_\gamma$, 27.00, 26.93; $(CH_3)_\delta$, 13.58. ^{119}Sn NMR: −165.

4-Phenyl-2,2-dibutyl-1,3,2-dioxastannolane, Racemic Compound (2a). ^{13}C NMR: Ph, C_{ipso}, 143.56; $C_{o,m}$, 128.31, 126.89; C_p, 127.64; $CHPh$, 76.02; CH_2CHPh, 69.30; $(CH_2)_\alpha$, 22.88; $(CH_2)_\beta$, 27.56; $(CH_2)_\gamma$, 27.07, 26.96; $(CH_3)_\delta$, 13.71. ^{119}Sn NMR: −153.

(S)-4-Phenyl-2,2-dibutyl-1,3,2-dioxastannolane, Enantiomerically Pure Compound (2b). ^{13}C NMR: Ph, C_{ipso}, 143.48; $C_{o,m}$, 128.32, 126.91; C_p, 127.67; $CHPh$, 75.96; CH_2CHPh, 69.43; $(CH_2)_\alpha$, 22.95, 22.63; $(CH_2)_\beta$, 27.56; $(CH_2)_\gamma$, 27.05, 26.98; $(CH_3)_\delta$, 13.71. ^{119}Sn NMR: −153.

4,4-Dimethyl-2,2-dibutyl-1,3,2-dioxastannolane (3). ^{13}C NMR: $(CH_3)_2$, 28.06; CMe_2, 70.45; CH_2CMe_2, 72.73; $(CH_2)_\alpha$, 22.72; $(CH_2)_\beta$, 27.36; $(CH_2)_\gamma$, 26.92; $(CH_3)_\delta$, 13.52. ^{119}Sn NMR: −121.

4-Phenyl-4-methyl-2,2-dibutyl-1,3,2-dioxastannolane (4). The racemic compound was prepared from a commercial diol (Janssen, >98%; mp 44–45 °C), purified by crystallization; the 42% ee sample was prepared from an enriched diol, obtained following a known procedure:[20] mp 93–95 °C. ^{13}C NMR: Ph, C_{ipso}, 149.17; $C_{o,m}$, 127.91, 125.35; C_p, 126.35; $CPhCH_3$, 29.01; $CPhMe$, 74.48; CH_2CPhMe, 71.78; $(CH_2)_\alpha$, 21.97, 21.69, 21.27, 21.08; $(CH_2)_\beta$, 27.50, 27.29; $(CH_2)_\gamma$, 26.98; $(CH_3)_\delta$, 13.61. ^{119}Sn NMR: −115.6. ^1H NMR: Ph, 7.0–7.5 (m); CH_2, 3.5 (AB, m); CH_3, 1.4 (s); Bu, 0.7–1.6 (m).

***meso*-4,5-Dicarbomethoxy-2,2-dibutyl-1,3,2-dioxastannolane (5).** The compound was prepared from *meso*-dimethyl tartrate, obtained by esterification with methanol of commercial *meso*-tartaric acid hydrate (Janssen, 99%; mp 146–148 °C): mp 195–196 °C dec. ^{13}C NMR: CO_2CH_3, 51.73; CO_2Me, 172.60; $CHCO_2Me$, 74.49; $(CH_2)_\alpha$, 26.31, 25.19; $(CH_2)_\beta$, 27.30, 27.24; $(CH_2)_\gamma$, 26.87; $(CH_3)_\delta$, 13.54. ^1H NMR: CO_2CH_3, 3.7 (s); $CHCO_2Me$, 4.55 (s); Bu, 0.8–1.8 (m).

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Registry No. **1a**, 102808-74-2; **1a** (*RR* dimer), 109905-18-2; **1a** (*RS*(*SR*) dimer), 109905-19-3; **1b**, 102916-63-2; **1b** (*SS* dimer), 109802-21-3; **2a**, 102808-75-3; **2a** (*RR* dimer), 109905-20-6; **2a** (*RS*)(*SR*) dimer), 109905-21-7; **2b**, 102916-64-3; **2b** (*SS* dimer), 109802-22-4; **3**, 109802-19-9; **3** (dimer), 109802-23-5; **4**, 109802-20-2; **4** (dimer), 109802-24-6; **5**, 89450-02-2; **5** (dimer), 109802-25-7; ^{119}Sn, 14314-35-3; 2-phenyl-1,2-propanediol, 4217-66-7; *meso*-dimethyl tartrate, 5057-96-5.

Supplementary Material Available: DNMR spectra for compounds **1–5** (Figures S1-S9) and the appendix to ref 12 (11 pages). Ordering information is given on any current masthead page.

Synthesis and Kinetic Studies of a Simple Prostacyclin Model

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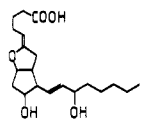
A simple prostacyclin model, (*Z*)-6,9-epoxynon-5-enoic acid, has been synthesized, and the rate of hydrolysis of the vinyl ether functional group of it and its methyl ester has been measured by monitoring UV spectral changes over the pH range 1–8 at 25.0 ± 0.1 °C and total ionic strength 0.1 M. The measurements show that (*Z*)-6,9-epoxynon-5-enoic acid is 82 times more reactive than its methyl ester at high pH when the carboxylic acid group is in an ionized form. The present results indicate that the simple model closely mimics the behavior of prostacyclin.

Introduction

Prostacyclin (1), a recently discovered prostaglandin,[1] is an extremely potent inhibitor of blood coagulation. This



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makes it a very interesting compound, but its usefulness as a therapeutic agent in the treatment of thrombosis is severely limited by its great hydrolytic lability. The half-life of prostacyclin in aqueous solution at physiological pH is only 3 min.[2] Prostacyclin, like other vinyl ethers, undergoes acid-catalyzed hydrolysis in aqueous solution.

Kinetic experiments have been carried out on prostacyclin and its methyl ester.[2,3] These measurements show that prostacyclin is 104 times more reactive than its methyl ester at high pH. The difference in reactivity decreases with increasing acid concentration and disappears at pH 1–2. The difference in reactivity at high pH indicates that the hydrolysis rate is accelerated when the carboxylic acid group is in an ionized form. It has been suggested that this acceleration might be due to electrostatic stabilization or to intramolecular general acid catalysis.[3] Solvent isotope effect measurements support the latter alternative.[3b]

In order to explore the mechanistic details of the hydrolysis of prostacyclin further, we have started an investigation of model compounds. By use of a model with a simpler structure we hope to be able to carry out the necessary structural modifications needed to elucidate

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