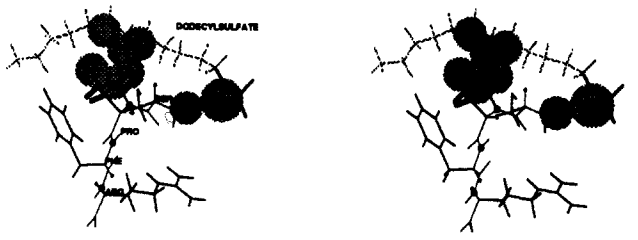

Figure 8. Relaxed stereomodel for the interaction of SerProPheArg with SDS constructed with the Mendyl program (Tripos Associates, St. Louis, MO) based on the observed changes in chemical shifts and coupling constants. (The small filled circles locate the peptide bond nitrogens.)

β-protons shift −0.20 and −0.23 ppm.[29] Thus, downfield shifts of 0.030 ppm for α-, 0.021 for β-, and 0.036 for β'-Ser between native peptide and 0.96:1 SDS:peptide are in the direction predicted from an increase in pK_a as would be expected from the presence of a nearby negatively charged group. However, since the interaction perturbs the β-protons more than would be expected from pK_a effects alone, additional factors probably are involved.

Among the other shifts produced by the SDS–peptide interaction, the largest was the H1 resonance of SDS itself (−0.046 ppm) suggesting a local perturbation such as that of a nearby positively charged group. The nature of the changes in δH1 of SDS with increasing ratios of SDS:peptide appeared complex, similar to what might be expected from interactions near a positively charged group whose pK_a was changing and whose state of protonation was affecting the peptide's conformation. SDS also rather substantially shifted β^t- and γ^t-Pro and the ring Phe resonances and decreased Pro $J_{\gamma\beta'}$ by 25%. Smaller downfield shifts were observed for α-Phe and β'-Arg. The lack of shifts in the β^c- and γ^c-Pro resonances indicated that interaction with SDS did not disrupt the unique environment for these Pro[7] (in BK) protons (neither did a change in pH from 7.4 to 8.4, Table II).

A proposed stereomolecular graphic model for the SDS–SerProPheArg complex incorporating as much of these data as possible is illustrated in Figure 8. This model assumes that the sulfate group of SDS interacts electrostatically with the α-amino group of Ser and that the middle methylene groups of SDS interact with the β^t- and γ^t-Pro protons. In this model the alkyl chain does not interact directly with the Phe ring, and, thus, the shifts observed for those protons are attributed to an indirect effect resulting from the suggested Pro-Phe ring interactions or to changes in rotomer populations as suggested by the coupling constant results.

Finally, it seems reasonable that the changes in the chemical environment of the Phe ring(s) detected by NMR also contribute significantly to the changes in CD of BK and SerProPheArg upon interaction with SDS.[13]

Acknowledgment. This work was supported in part by the National Institutes of Health Research Grant GM 28793 (J.R.C.) and HL 26284 (J.M.S.). We also thank Kansas State University Professors Joseph Paukstelis for providing time on the NMR and R. Krishnamoorthi for his assistance with the COSY experiment and acknowledge the excellent technical assistance of Robert O. Coombs and Karl Hahn (University of Colorado Medical School). This is Contribution No. 89-375-J from the Kansas Agricultural Experiment Station.

Registry No. BK, 58-82-2; [99% ^{13}C-2-Gly^6]BK, 124419-26-7; [Gly^6,*p*-fluoro-Phe^8]BK, 124419-27-8; SerProPheArg, 16875-08-4; SDS, 151-21-3.

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Oligomerization Equilibria and Dynamics of 2,2-Di-*n*-butyl-1,3,2-dioxastannolanes

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Abstract: The ^{119}Sn and ^{13}C NMR spectra of solutions of 2,2-di-*n*-butyl-1,3,2-dioxastannolane (**1**) and a number of its symmetrical derivatives in nonpolar solvents have been studied as functions of temperature and concentration. The compounds studied included (1*S*,6*S*)-8,8-di-*n*-butyl-7,9,8-dioxastannabicyclo[4.3.0]nonane (**2**), obtained from di-*n*-butyltin oxide and (*S*,*S*)-1,2-cyclohexanediol. A new method of resolution of *trans*-1,2-cyclohexanediol has been developed. Solutions of **1**, **2**, and related derivatives of disecondary diols were found to contain mixtures of oligomers that have been identified as dimers, trimers, tetramers, and pentamers. In contrast to earlier work, no evidence for the presence of monomers was obtained. The compositions of the mixtures are extremely temperature dependent; trimers and tetramers are the major constituents below −20 °C, but dimers increasingly dominate as the temperature is raised. Thermodynamic parameters for the equilibria of **1** and **2** have been measured. A derivative of a ditertiary diol, 2,2-di-*n*-butyl-4,4,5,5-tetramethyl-1,3,2-dioxastannolane, exists in nonpolar solvents predominantly as a dimer over the temperature range studied, from −60 to +80 °C. Activation parameters for a process in this dimer that causes the ^{13}C NMR signals of the pairs of nonequivalent methyl carbons to coalesce have been determined by total line shape analysis. A series of related reversible associative processes involving dimers, trimers, tetramers, pentamers, and possibly monomers and hexamers accounts for the changes observed in the NMR spectra with temperature.

2,2-Di-*n*-butyl-1,3,2-dioxastannolanes have been shown to be very useful intermediates for achieving selective reactions of diols or polyols.[1] Reactions that result in monoacylation, monoalkylation, or monooxidation of diols can be performed in high yield via an intermediate of this type, and the reaction is also often regiospecific or highly regioselective. As a result, reactions involving these intermediates and the related tri-*n*-butylstannyl ether intermediates have become part of the standard armory of methods employed when blocking groups are required for diols or polyols.[1] The source of the regioselectivity has been related to the oligomeric structures assumed by the tin-containing derivatives although the precise cause has not been clearly identified.[1] In addition, the considerable selectivity observed in the formation of macrocyclic

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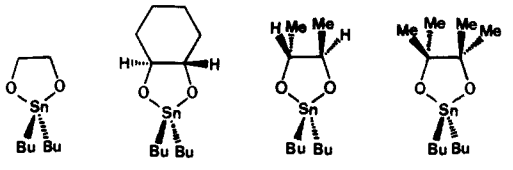
di- and tetralactones from 2,2-di-*n*-butyl-1,3,2-dioxastannolanes and diacyl dihalides has been connected with the self-association of the tin derivatives.[1,2]

In order to understand the reactivity of these widely used intermediates, it is necessary to fully define the species that are present in solution and to determine the factors that influence their equilibria. Tin-119 NMR spectroscopy has proven to be a powerful technique for obtaining information about the coordination status of tin atoms.[3] Acyclic analogues of 1,3,2-dioxastannolanes, dialkyltin dialkoxides, have been shown by means of ^{119}Sn NMR chemical shifts from spectra recorded at or above ambient temperature to exist in nonpolar solutions as rapidly equilibrating mixtures of monomeric and dimeric forms. Straight chain primary dialkoxides are thought to exist chiefly as dimers containing pentacoordinate tin with ^{119}Sn NMR chemical shifts of −125 to −165 ppm, while di-*tert*-butoxy derivatives exist as monomers containing tetracoordinate tin with shifts of 0 to −34 ppm, depending on conditions. Di-*n*-butyl- or dimethyltin diisopropoxides or other secondary or large primary dialkoxides are present in nonpolar solvents as mixtures of monomers and dimers whose compositions change to favor monomers on increasing temperature or dilution.[4]

The formation of cyclic 1,3,2-dioxastannolanes from 1,2-ethanediol derivatives favors more associated structures.[1-14] The simplest derivative, 2,2-di-*n*-butyl-1,3,2-dioxastannolane (**1**) crystallized as an infinite ribbon polymer.[5] Two 2,2-di-*n*-butyl-1,3,2-dioxastannolanes derived from carbohydrate *vic*-diols have been studied by X-ray crystallography; one exists as a dimer,[6] the other as a pentamer.[7] Earlier studies of solutions of **1** in nonpolar solvents, using NMR spectroscopy[4,8-13] and molecular weight measurements,[14] were interpreted as indicating that the dimer is the major species present.[4-14] Because the ^{119}Sn NMR spectra of solutions of 2,2-di-*n*-butyl-1,3,2-dioxastannolanes, particularly at low temperatures, contained signals with chemical shifts in the range −250 to −300 ppm, it was concluded that the mixtures in solution included species with hexacoordinate tin.[8,12] These species have to be more associated than dimers.[8,12] In addition, it was suggested that the monomer is a significant component of the mixture present for **1** at concentrations less than 0.05 M in chloroform-*d* and that the monomer–dimer equilibration rate is slow on the NMR time scale at room temperature.[8]



1 2 4 5

We have examined the ^{119}Sn and ^{13}C NMR spectra of 1,3,2-dioxastannolanes derived from a diprimary diol, from cyclic and noncyclic disecondary diols, and from a ditertiary diol at high field over a range of temperatures and concentrations. For the first time, the identities of all of the major species present have been established. We have also clarified the complex equilibria that these compounds undergo.

Experimental Section

Proton, carbon-13, and tin-119 NMR spectra were recorded on a Nicolet NT-360 NB spectrometer at 361.04, 90.79, and 134.62 MHz, respectively. A few ^{13}C NMR spectra were recorded at 125.8 MHz on a Bruker AM-500 spectrometer. The references for ^{13}C and ^{119}Sn NMR chemical shifts were internal tetramethylsilane or the central peak of chloroform-*d* (77.0 ppm) and external tetramethyltin at 23 °C, respectively. Spectrometer temperatures for ^{13}C and ^{119}Sn NMR spectra were calibrated by using the equations of van Geet against ^{1}H NMR chemical shift differences recorded through the decoupler coil for pure ethylene glycol or methanol samples in capillary tubes in the solvent of interest.[15] Carbon-13 NMR spectra were recorded in 16 K blocks over spectral ranges of 100–120 ppm with 60° pulses, 2–5-s pulse intervals and broad band ^{1}H decoupling. Tin-119 NMR spectra were normally recorded over a spectral range of 240 ppm in 16 K blocks with 90° pulses; ranges of 400–600 ppm were used to search for signals of tetracoordinate and heptacoordinate tin. Tin-119 NMR spectra were recorded with pulse intervals of 0.5–1 s, and broad band ^{1}H NMR decoupling was only applied during acquisition. Chloroform-*d* and dichlorofluoromethane were dried over phosphorus pentoxide and then distilled onto molecular sieves (4 Å) for storage.

Solutions for NMR studies of tin derivatives were prepared as follows. An equimolar mixture of the diol and di-*n*-butyltin oxide in benzene was refluxed for 12 h in an apparatus for the azeotropic removal of water. By the end of the reflux period, the reaction mixture was homogeneous. The reaction flask was attached to a vacuum line, the benzene was removed under vacuum, and the previously dried NMR solvent was distilled onto the solid 1,3,2-dioxastannolane derivative through the vacuum system. The resulting solution was poured through a sintered glass filter under vacuum into the NMR tube which was then sealed. Concentrations were estimated from the known amount of starting materials and from the solution height.

Line shape analysis of the exchange process evident in the signals of the four 4,4,5,5-methyl carbons and C-4 and C-5 of 2,2-di-*n*-butyl-4,4,5,5-tetramethyl-1,3,2-dioxastannolane (**5**) was performed by using a modification of a program for classical two-site exchange written by Binsch.[16] Only the methyl ^{13}C NMR signals could be simulated for spectra recorded in chloroform-*d* because the solvent signals obscured the quaternary carbon signals. Simulations were performed for spectra recorded at 13 different temperatures between 23 and 80 °C for a 0.23 M solution and at 11 different temperatures between 30 and 70 °C for a 0.36 M solution. Chemical shifts for the simulation were obtained by linear extrapolation of the values obtained at five temperatures between −10 and 28 °C for the 0.23 M solution and at six temperatures between −20 and 30 °C for the 0.36 M solution. The chemical shift variation with temperature was small, −0.057 Hz-deg^{-1} for the 0.23 M solution. The T_2^* values at each temperature for the exchanging signals were taken to be the same as that of the butyl methyl carbon, which is not affected by exchange. The calculated line shapes were compared with the experimental ones by superposition. Sufficient calculations were performed so that it was possible to define the range of rates that gave simulated spectra indistinguishable from the experimental spectra. Reported rates are the center of the range which gave satisfactory fits and uncertainties, half the range. The rates were used to calculate ΔG^* values which were used in a weighted (according to uncertainties) linear least-squares program to determine ΔH^* and ΔS^* values.

(*S*,*S*)-1,2-Cyclohexanediol. Tetra-*O*-acetyl-α-D-glucopyranosyl bromide (24.7 g, 60 mmol), *trans*-1,2-cyclohexanediol (7 g, 60 mmol), yellow mercuric oxide (78 g, 360 mmol), and mercuric bromide (4.87 g, 13.5 mmol) were mechanically stirred in carbon tetrachloride (600 mL) until the glycosyl halide was consumed (15 h). Iodine (60.9 g, 240 mmol) was added, and the mechanically stirred solution, maintained at 20 ± 3 °C with an ice–water bath, was irradiated for 1 h with a 500-W tungsten filament lamp. The mixture was filtered, and the filtrate was washed with sodium thiosulfate solutions (1 M, 3 × 200 mL) and with water (200 mL), dried (magnesium sulfate), and concentrated to a mixture of a major and a minor ortho ester. Column chromatography on silica gel

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Table I. ^{119}Sn NMR Chemical Shifts of Compounds **1–5**

		trimer		tetramer		pentamer		
compd	dimer	pent[a]	hex[b]	pent[a]	hex[b]	pent[a]	hex1[b]	hex2[b]
1[c]	−126.8	−126.8	−283.0	−131.4	−266.1	*d*	*d*	*d*
1[e]	−126.7	−126.7	−283.1	−131.5	−266.8	−133.6	−257.8	−260.1
1[f]	−127.3	−127.3	−283.9	−132.1	−268.1	−134.3	−259.7	−261.3
2[g]	−141.5	−142.5	−291.8	−148.7	−276.1	*d*	*d*	*d*
2[h]	−142.2	−142.2	−292.3	−148.5	−275.3	−150.2	−257.5	−270.9
3[i]	*d*	−142.0, −142.2, −142.9	−292.5,[j] −293.7	−148.1,[j] −148.6	−275.2	*d*	*d*	*d*
4[k]	−132.0	−132.0	−284.9	−138.1	−266.0	*d*	*d*	*d*
5[l]	−139.6	*d*	*d*	*d*	*d*	*d*	*d*	*d*

−142.9

[a] Signal of the pentacoordinate tin atoms. [b] Signals of hexacoordinate tin atoms. [c] On a 0.5 M solution in chloroform-*d* at −60 °C. [d] Not observed. [e] On a 0.52 M solution in chloroform-*d*/dichlorofluoromethane, 3:1 at −80 °C. [f] On a 0.072 M solution in chloroform-*d*/dichlorofluoromethane, 3:2 at −95 °C. [g] On a 0.063 M solution in chloroform-*d*/dichlorofluoromethane, 3:1 at −75 °C. [h] On a 0.43 M solution in chloroform-*d*/dichlorofluoromethane, 3:1 at −60 °C. [i] On a 0.5 M solution in chloroform-*d* at −50 °C. [j] Small peak. [k] On a 0.5 M solution in chloroform-*d* at −60 °C. [l] On a 0.23 M solution in chloroform-*d* at 20 °C.

using 2:3 ethyl acetate/hexane as eluent gave the major cyclic ortho ester, (1′*S*,2′*S*)-1′,2′-cyclohexyl-2,3,4,6-tetra-*O*-acetyl-D-glucopyranosyl ortho ester, a syrup; $[\alpha]^{23}_D$ +42° (*c* 1.09, acetone), lit.[17] +47.5°; ^{13}C NMR (20 MHz) 20.4, 20.4, 28.3, 28.9 (C-4, C-5, C-3, and C-6 cyclohexyl carbons, respectively), 23.3 (acetyl Me), 61.5 (C-6), 67.9, 69.8, 70.1, 72.3 (C-5, C-4, C-3, C-2), 80.5 (cyclohexyl C-2), 84.1 (cyclohexyl C-1), 117.1 (C-1), lit.[17] 117.1, 169.1, 169.2, 169.9, 170.6 (acetyl CO).

The (*S*,*S*)-ortho ester (4.5 g) and Amberlite IR-120 (H^+) (3 g) were stirred in 30% aqueous methanol (100 mL) at 85 °C for 3 days. The mixture was filtered, and the filtrate was concentrated. A 0.1% sodium methoxide solution (75 mL) was added and the resulting solution was stirred 48 h. The solution was neutralized with Amberlite IR-120 (H^+), activated charcoal (3 g) was added and then stirred for 30 m. The mixture was filtered, and the filtrate was concentrated. The resulting syrup was fractionated by column chromatography on silica gel (100 g) with chloroform–tetrahydrofuran 3:2 as eluent. The title compound was recrystallized from ethyl acetate and petroleum ether (30–60 °C); yield, 725 mg (62%); mp 110–111 °C; lit.[18] 113–114 °C; $[\alpha]^{23}_D$ +42.9° (*c* 0.38, water); lit.[18] +46.5°, lit.[19] +41.4°.

Results and Discussion

Compounds. 2,2-Di-*n*-butyl-1,3,2-dioxastannolane derivatives were prepared by treatment of the following diols with di-*n*-butyltin oxide with azeotropic removal of water: 1,2-ethanediol, (*S*,*S*)-1,2-cyclohexanediol, *trans*-1,2-cyclohexanediol, (*R*,*R*)-2,3-butanediol, and 2,3-dimethyl-2,3-butanediol. Resolution of *trans*-1,2-cyclohexanediol to give (*S*,*S*)-1,2-cyclohexanediol was accomplished by means of a reaction developed by Praly and Descotes.[17] The diastereomeric mixture of β-glycosides obtained when *trans*-1,2-cyclohexanediol is reacted with 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide yields two diastereomeric cyclic ortho esters when treated with iodine under irradiation.[17] One of the two ortho esters is preferred in the reaction, and it can be separated by chromatography. Hydrolysis yields (*S*,*S*)-1,2-cyclohexanediol. This method of resolution of *trans*-1,2-cyclohexanediol is more reproducible, although longer, than recrystallization of the monomenthyloxyacetyl ester.[18] The value of the optical rotation obtained here, +42.9°, was slightly smaller than the largest literature value, +46.5°.[18] There was no evidence in the spectra to be discussed later that any of the (*R*,*R*)-enantiomer was obtained.

NMR Spectroscopy. The parent compound (**1**) has been studied previously by ^{1}H, ^{13}C, and ^{119}Sn NMR spectroscopy at lower field strengths.[4,8,9,14] Chloroform-*d* had been used as the solvent of choice for studies of 1,3,2-dioxastannolanes at low temperature because of their poor solubility in most other solvents.[8,10–12] We have found that **1** and **2** are soluble in mixtures of chloroform-*d* and dichlorofluoromethane at concentrations <0.5 M at temperatures as low as −100 °C.

Considerable caution has been taken to avoid moisture during the preparation of samples of compounds **1–5**. In initial experiments, it was observed that both ^{119}Sn and ^{13}C NMR spectra of samples prepared without these precautions contained additional signals. Compound **5** was particularly sensitive in this regard. Davies and Price have reported that treatment of chloroform solutions of **1** with water gave ethylene glycol and a soluble hydrated form of dibutyltin oxide.[20]

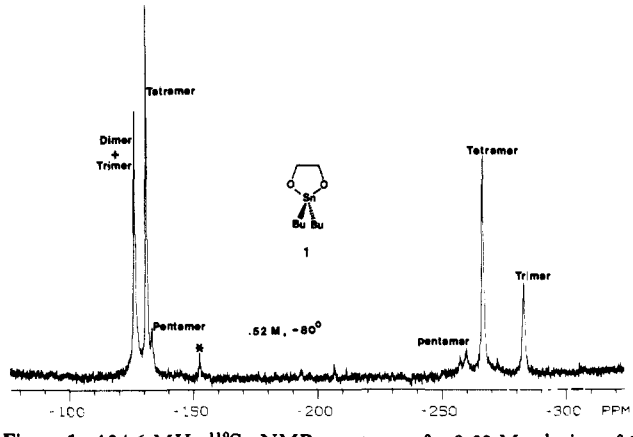

Figure 1. 134.6 MHz ^{119}Sn NMR spectrum of a 0.52 M solution of **1** in chloroform-*d*/dichlorofluoromethane, 3:1 at −80 °C.

In order to determine optimum parameters for recording ^{119}Sn NMR spectra, T_1 measurements were performed on the signals of the tin nuclei of **2** and a number of related carbohydrate derivatives over a range of temperatures. The values obtained ranged from 14 to 197 ms, but for **2** were always less than 100 ms. The details of these results will be reported elsewhere.[21] To ensure that integrations were reliable, pulse intervals were kept longer than 5 T_1, and the decoupler was gated off during the pulse delay to avoid the negative NOE effect arising from the negative magnetogyric ratio of ^{119}Sn.

2,2-Di-*n*-butyl-1,3,2-dioxastannolane (1). As previously reported,[4,8,9] the ^{119}Sn NMR spectra of solutions of **1** in chloroform-*d* at room temperature or slightly above contain a single broad signal. For a 0.5 M solution in chloroform-*d* at 55 °C, the signal is centered at about −170 ppm with a line width of about 2700 Hz. The position of the signal is quite concentration dependent; the peaks from a 0.52 M solution in chloroform-*d*/dichlorofluoromethane, 3:1 and from a 0.072 M solution in chloroform-*d*/dichlorofluoromethane, 3:2 are centered at about −165 ppm and about −137 ppm, with line widths of 2700 and 3800 Hz, respectively. As the temperature is lowered, the band broadens reaching a maximum line width between 35 and 15 °C of about

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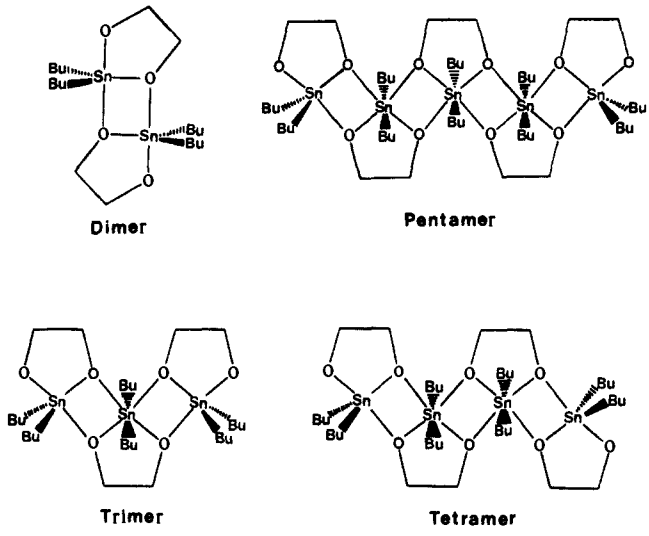

Figure 2. Structures of oligomeric species of **1**.

9000 Hz for the 0.5 M solution in chloroform-*d*. When the temperature is lowered further, it splits into two broad bands near −130 ppm and between −260 and −300 ppm. At still lower temperatures, between −30 and −50 °C, depending on concentration, the two bands each sharpen into two major peaks. No signals were observed in the region between +50 and −100 ppm, even for a 0.02 M sample at any temperature. Chemical shifts are listed in Table I. A ^{119}Sn NMR spectrum of **1** is shown in Figure 1.

Increasingly lower frequency ^{119}Sn NMR absorption is associated with increased coordination at tin;[3] shifts in the −120 to −150 ppm region for 1,3,2-dioxastannolanes have been assigned to pentacoordinate tin, while values between −250 and −300 ppm are assigned to hexacoordinate tin.[4,8-10,12] The relative intensities of the four peaks observed at low temperatures are highly concentration dependent. However, at all concentrations and in all solvents employed the intensities of the two central peaks, that is, the peaks at −131 and −266 ppm, are almost the same. The intensity of these two peaks increases dramatically relative to the intensities of the other two peaks as the concentration is increased. Thus, these two peaks must be assigned to one species.

In order to make structural assignments, it is necessary to consider the structures and symmetries of possible contributors to the equilibria (Figure 2). It will be assumed that conformational processes in the five-membered rings are fast at the temperatures at which the present spectra have been recorded, although slowing of ring inversion has been reported for 1,3,2-dithiastannolanes at temperatures below −80 °C.[22] Crude strain-energy calculations of ring-inversion barriers for the five-membered rings in chelates of metals with ethylene diamine indicated that the barrier size is highly dependent on metal–N bond length; the bond length must be >2.30 Å for the barrier-to-ring inversion to be large enough for the process to be observed by NMR.[23] The Sn–X bond lengths are about 2.44 Å in the 1,3,2-dithiastannolanes[22] but average 2.07 Å in 1,3,2-dioxastannolanes.[5-7] In addition, it is assumed that the butyl substituents adopt equatorial orientations in a trigonal-bipyramidal about pentacoordinate tin or are opposed across an octahedral tin as observed in solid-state structures[5-7] and that tricoordinate oxygen atoms are planar or invert rapidly. With these assumptions, the dimer has C_{2h} symmetry, and the two pentacoordinate tin atoms are equivalent. A trimer, with C_{2v} symmetry, has a single hexacoordinate tin atom and two equivalent pentacoordinate tin atoms. A tetramer, with C_{2h} symmetry, has two tin atoms in equivalent pentacoordinate environments and two in equivalent hexacoordinate environments. A pentamer would have the same symmetry as the trimer and hence would have two equivalent pentacoordinate tin atoms, two equivalent hexacoordinate tin atoms, and another tin in a different hexacoordinate environment.

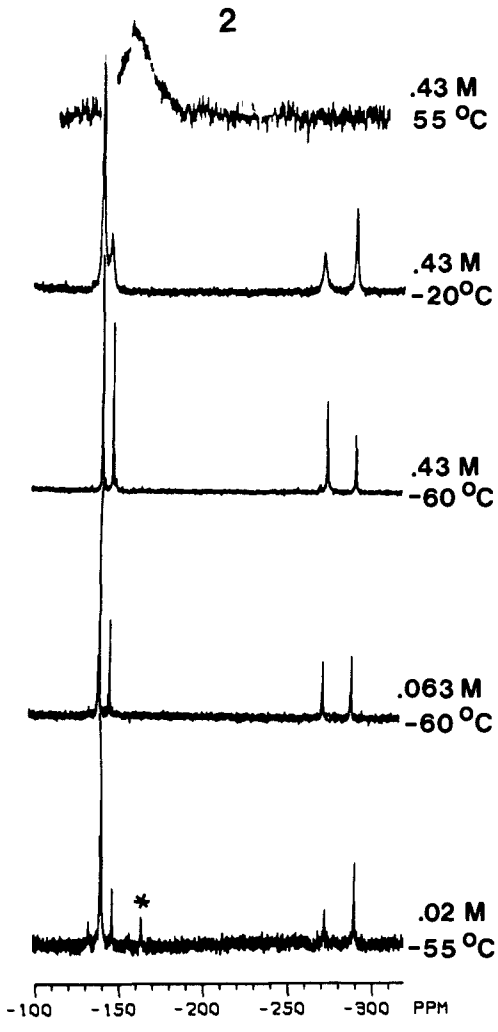

Figure 3. The effect of temperature and concentration on the ^{119}Sn NMR spectra of solutions of **2** in chloroform-*d*/dichlorofluoromethane, 3:1.

Only a tetramer can give rise to two equally intense pentacoordinate and hexacoordinate tin NMR signals. Thus, the two central equally intense signals at −131 and −266 ppm, shown to belong to one species, must be assigned to a tetramer. The other major hexacoordinate tin signal, that at −283 ppm, decreases in intensity relative to the tetramer signals as the concentration is increased. Thus, it must be assigned to a less associated species. The only possibility is a trimer. The ^{119}Sn NMR spectrum of a trimer should also contain a signal in the pentacoordinate region of the spectrum having twice the intensity of the signal at −283 ppm. The intensity of the remaining signal, at −126 ppm, was always greater than twice that of the hexacoordinate trimer signal. Hence, the chemical shift of the signal of the tin atoms in the dimer must be the same as that due to the tin atoms in pentacoordinate environments in the trimer. Figure 3 shows the effects of changing temperature and concentration on the very similar ^{119}Sn NMR spectra of **2**.

At temperatures below −60 °C, two additional low intensity signals appear in the hexacoordinate region on the high frequency side of tetramer signal with intensity ratios 1:2. At the same temperatures, an additional signal appears on the low frequency side of the pentacoordinate tetramer signal with about the same intensity as the larger of the two other new signals. These signals are assigned to the pentamer (see Figure 1).

The signals in the spectra of a 0.072 M sample in a 3:2 mixture of chloroform-*d* and dichlorofluoromethane were integrated carefully at nine temperatures between −85 °C and −45 °C. Equilibrium constants were obtained for the following equilibria:

(22) Abel, E. W.; Bhargava, S. K.; Orrell, K. G.; Sik, V. *J. Chem. Soc., Dalton Trans.* **1982**, 2073–2078.
(23) Hawkins, C. J.; Peachey, R. M.; Szoredi, C. L. *Austral. J. Chem.* **1978**, *31*, 973–981.

$$\text{two dimers} \rightleftharpoons \text{tetramer} \quad (1)$$

$$\text{three dimers} \rightleftharpoons \text{two trimers} \quad (2)$$

$$\text{four trimers} \rightleftharpoons \text{three tetramers} \quad (3)$$

$$\text{dimer} + \text{trimer} \rightleftharpoons \text{pentamer} \quad (4)$$

The equilibrium constants were used to derive enthalpy and entropy values for the equilibria. The results are shown in Table II. Each value represents an overall change in which the products have two more Sn–O bonds than the starting materials and two pentacoordinate tin atoms have become hexacoordinate. As expected, more associated species are more stable but are strongly disfavored by the entropy term. The largest change in entropy for an oligomerization equilibrium comes from the loss of translational energy levels through the reduction in the number of species.[24] Estimates of the entropy changes for each of the above equilibria in the gas phase were made by evaluation of the translational partition functions.[24] Values calculated at 210 and 300 K ranged from 40.4 to 43.2 cal (deg^{-1} mol^{-1}). Reduction of rotational energy levels on association gives the next most important contribution to the overall entropy change. The values of this factor were calculated approximately from the rotational partition functions[24] by evaluating the moments of inertia along each axis in a dimer with averaged geometry from the crystal structure determinations[5-7] that was made symmetric inside each "monomer" unit. The moments of inertia in the trimers, tetramers, and pentamers were estimated roughly by assuming that the dimer atoms were twice, three times, and four times further away from the center on average. This process gave estimates of the entropy changes for the four equilibria that ranged from 12.7 to 14.4 cal (deg^{-1} mol^{-1}), resulting in overall estimated changes of 53.1–57.6 cal (deg^{-1} mol^{-1}). The entropy changes calculated for the gas phase should provide an upper limit for those in solution. Here, the observed values in solution are approximately half the values calculated.

The accuracy of the above treatment may be tested by calculating average chemical shifts. The data in Table II was used to calculate populations of the individual species at 55 °C. The ^{119}Sn NMR chemical shifts for each species were measured at six temperatures at −55 °C and below and then linearly extrapolated to 55 °C. The average value calculated was −134 ppm, in excellent agreement with the observed value of −137 ± 5 ppm.

The large values of the entropy terms make the equilibria extremely temperature dependent (see Table III). At 200 K for the 0.072 M solution, the mole fractions of dimer, trimer, tetramer, and pentamer are 0.139, 0.517, 0.286, and 0.058, respectively; at 298 K, they are 0.760, 0.206, 0.034, and <0.001, respectively. The mole fraction of dimer present for the 0.072 M solution only becomes more than 0.5 when the temperature is greater than −20 °C and, for more concentrated samples, the proportion of dimer is smaller. This finding is in contrast to that obtained previously where virtually all authors have considered the dimer to be the most important species in solution under all conditions,[1-14] except at very low concentrations or at very low temperatures.[8,10,12] One possible cause of the underestimation of the contribution of higher oligomers is that the signals of hexacoordinate tin are approximately twice as broad as those of pentacoordinate tin, at least in spectra recorded at 134.6 Hz. In addition, the previous workers have discussed these equilibria in terms of monomers, dimers, and "polymers". As a result, they associated the mole fraction of pentacoordinate tin with the amount of dimer present, although they were aware that this assumption was not precisely correct.[8,10,12] The fact that the higher oligomers present are largely the trimer and the tetramer has major implications for the evaluation of the equilibria. For instance, a 0.85 M solution in chloroform-*d* at room temperature was roughly calculated to have a mole fraction of pentacoordinate tin of 0.65, and it was concluded that the dimer was the predominant species present.[8] The trimer has a mole fraction of pentacoordinate tin of 0.67, and, hence, at room temperature, it is probably the major species present in this solution which is more concentrated than any studied here.

The above data were determined in a solvent mixture containing chloroform-*d* and dichlorofluoromethane to obtain reliable intensities over a sufficient range of temperatures to allow definition of entropy and enthalpy values for the equilibria. Nevertheless, the relative intensities of signals in spectra of samples of similar concentrations in chloroform-*d*, and the mixed solvent were very similar as might be expected from the similarity of the structures of the two halogenated methanes. For instance, at −60 °C, the % intensities based on peak heights for the peaks at −127, −131, −266, and −283 ppm were 27, 38, 26, and 9% for a 0.5 M solution in chloroform-*d* and 24, 37, 29, and 11% for the corresponding peaks for a 0.52 M solution in chloroform-*d*/dichlorofluoromethane, 3:1. At 55 °C, the line widths for both samples were about 2700 Hz, and the average chemical shifts were −170 ± 5

Table II. Thermodynamic Parameters from the Oligomerization Equilibria of Compounds **1** and **2**[a]

compd	equilibrium	enthalpy (kcal mol^{-1})	entropy (cal mol^{-1} deg^{-1})	free energy[b] (kcal mol^{-1})
1[c]	1	−7.1 ± 1.3	−22.9 ± 6.3	−2.5 ± 0.1
	2	−8.8 ± 1.8	−27.6 ± 8.8	−3.3 ± 0.1
	3	−3.7 ± 0.7	−13.4 ± 3.6	−1.03 ± 0.03
	4	−11 ± 3.9	−49 ± 19	−1.4 ± 0.2
2[d]	1	−7.1 ± 0.8	−22.7 ± 3.8	−2.6 ± 0.1
	2	−7.9 ± 1.0	−23.5 ± 4.5	−3.2 ± 0.1
	3	−5.6 ± 0.6	−20.9 ± 2.6	−1.40 ± 0.05
2[e]	1	−9.1 ± 0.9	−31.6 ± 3.7	−2.8 ± 0.1
	2	−10.3 ± 0.8	−34.2 ± 4.3	−3.4 ± 0.2
	3	−6.2 ± 0.8	−24.1 ± 3.5	−1.4 ± 0.1
	4	−8.6 ± 1.3	−34.6 ± 5.5	−1.6 ± 0.2

[a] Uncertainties are at the 95% confidence level. [b] At 200 K. [c] For a 0.072 M solution in chloroform-*d*/dichlorofluoromethane, 3:2. [d] For a 0.063 M solution in chloroform-*d*/dichlorofluoromethane, 3:1. [e] For a 0.43 M solution in chloroform-*d*/dichlorofluoromethane, 3:1.

Table III. Calculated Mole Fractions of the Oligomers in Solutions of Compounds **1** and **2**[a]

compd	concn (M)	temp (K)	mole fraction of oligomer: dimer	trimer	tetramer	pentamer
1	0.072[b]	200	0.14	0.52	0.29	0.058
1	0.072[b]	300	0.77	0.20	0.032	0.00002
2	0.063[c]	200	0.16	0.49	0.34	*d*
2	0.063[c]	300	0.76	0.22	0.027	*d*
2	0.43[c]	200	0.059	0.36	0.43	0.15
2	0.43[c]	300	0.70	0.25	0.046	0.0015

[a] Calculated from the equilibrium constants at that temperature using an iterative procedure. [b] In chloroform-*d*/dichlorofluoromethane, 3:2. [c] In chloroform-*d*/dichlorofluoromethane, 3:1. [d] Not observed for this sample.

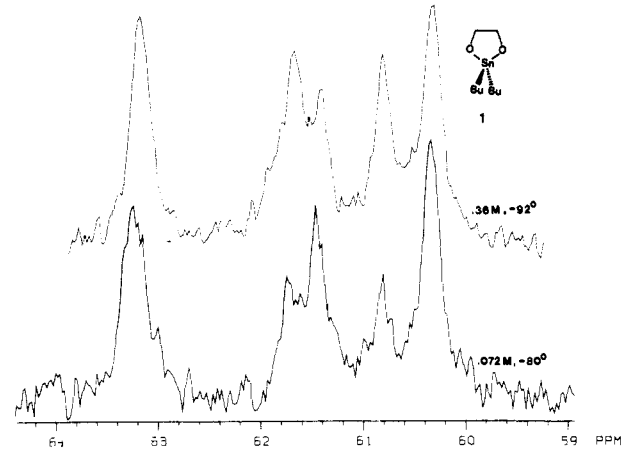

Figure 4. The effect of concentration on the signals assigned to C-4 and C-5 of the 1,3,2-dioxastannolane ring in the low-temperature 90.8 MHz ^{13}C NMR spectra of **1**.

(24) Wiberg, K. B. *Physical Organic Chemistry*; Wiley: New York, 1964; pp 210–272.

Table IV. ^{13}C NMR Chemical Shifts for 2,2-Di-*n*-butyl-1,3,2-dioxastannolane Derivatives **1–5**

compd	temp (°C)	chemical shifts[a] (ppm)						
		diol derived carbons			butyl carbons			
		C-4, C-5	cyclohexyl β-carbons or Me	cyclohexyl γ-carbons	C-α	C-β	C-γ	C-δ
1[b]	55	63.4			22.0[c]	27.5	27.4	13.6
2[d]	50	79.0[e]	34.3	25.3	22.9[c]	27.5	27.0	13.6
3[d]	50	79.0[e]	34.3	25.3	23.6[c]	27.5	27.0	13.6
4[c]	25	74.7	21.2		23.1[c]	27.5	27.0	13.6
5[f]	23	78.3[c]	26.5[c]		25.0	27.3	27.1	13.6
		75.1[c]	25.4[c]					

[a] In chloroform-*d*. [b] 0.25 M solution. [c] Signal broadened by exchange. [d] 0.5 M solution. [e] C-1 and C-6 in **2** and **3**. [f] 0.23 M solution.

ppm for the former and −168 ± 5 ppm for the latter.

The ^{13}C NMR spectra of **1** at 55 °C are simple but become complex as the temperature is lowered. High-temperature chemical shifts are listed in Table IV. The signals of two types of carbons, the OCH_2 carbons (C-4 and C-5) and the α-$SnCH_2$ carbons (C-α), show sufficiently complex behavior to be related to the conclusions drawn from the ^{119}Sn NMR spectra. At 55 °C, both are sharp singlets flanked by tin-119/117 satellites as reported earlier.[8] The signal assigned to C-4 and C-5 splits as the temperature is lowered into what becomes five separate bands at the lowest temperatures studied (see Figure 4). The mole fractions of dimer, trimer, tetramer, and pentamer present at −80 °C in a 0.072 M solution in a 3:2 mixture of chloroform-*d* and dichlorofluoromethane were 0.10, 0.49, 0.30, and 0.11, respectively; at −80 °C in a 0.52 M solution in a 3:1 mixture of chloroform-*d* and dichlorofluoromethane, they were 0.07, 0.40, 0.46, and 0.07, respectively. Analysis of the symmetries of the two major species present at low temperatures, the trimer and the tetramer, indicate that there are seven environments possible for these carbons; they can be attached to a dicoordinate oxygen (DO) atom that is attached to a single pentacoordinate (PT) atom in both species, to a tricoordinate oxygen atom (TO) attached to one PT atom and one hexacoordinate tin (HT) atom (two different environments in both the trimer and the tetramer), and to a TO atom attached to two HT atoms in the tetramer. Of the five signals shown in Figure 4, the two at extreme high and low frequencies appear to have the same intensities at both concentrations. Therefore, these two lines must result from overlap from signals of both species. The central signal has low intensity compared to its two neighbors in the spectrum from the high concentration sample but high intensity in that from the low concentration sample. Thus, the central signal is a trimer signal, while the two signals flanking the trimer signal are tetramer signals. In general, these conclusions are consistent with the structural assignments made previously.

As the temperature is lowered, the signal for C-α at 22.2 ppm splits into two signals that have chemical shifts of about 19.5 and 26.7 ppm at −60 °C. Further decrease in temperature results in each of the two signals splitting further into two signals. The initial splitting had previously been explained by suggesting that there are different environments for butyl groups in the dimer.[8,12] Since the dimer has now been shown to be a minor constituent at low temperatures, alternative explanations of the spectral changes must be developed. The most probable cause of the initial splitting is the different coordination levels at tin. In support of this conclusion, the C-α signal of **5** (vide infra), which is only present as a dimer, appears as a singlet at all temperatures. The two low-frequency signals at 19.16 and 19.42 ppm can be assigned to α-carbons attached to pentacoordinate tin (PT) on the basis of the magnitudes of their one-bond carbon–tin coupling constants ($^1J_{C,Sn}$), while the high-frequency signals are assigned to α-carbons attached to hexacoordinate tin (HT). In a 125.8 MHz spectrum of the 0.072 M solution of **1** at −84 °C, a pair of satellite peaks caused by ^{119}Sn and ^{117}Sn coupling were observed on each side of the peaks at 19.16 and 19.42 ppm with coupling constants ($^1J_{C,Sn}$) of 586 and 579 Hz, respectively. These values are similar to those measured for the two different α-carbons in the 2,2-di-*n*-butyl-1,3,2-dioxastannolane derivative of benzyl 4,6-*O*-benzylidene-β-D-galactopyranoside in chloroform-*d*, 580 and 586 and 603 and 612 Hz, for coupling to Sn-117 and Sn-119, respectively,[25] and for 2,2-di-*n*-butyl-4,4,5,5-tetramethyl-1,3,2-dioxastannolane (**5**) in chloroform-*d*, 563 and 589 Hz. Both compounds exist predominantly as one dimer in solution. In the spectra of tin IV compounds, $^1J_{Sn,C}$ values ranging from 307 to 1175 Hz have been observed.[14,26] The magnitude of $^1J_{Sn,C}$ has been related to the size of the C–Sn–C bond angle, increasing with increasing angle size.[26] C–Sn–C bond angles are larger about hexacoordinate tin than pentacoordinate tin in crystal structures containing dialkyldialkoxytin derivatives.[5-7,27] The values of 653[14] or 643 Hz[8] reported for **1** at ambient temperature are averages of values from pentacoordinate tin mainly in the dimer and the trimer and from hexacoordinate tin mainly in the trimer. Because the average value is larger than the value observed for the signals at 19.16 and 19.42 ppm at low temperature and because of their similarity to values observed in 2,2-di-*n*-butyl-1,3,2-dioxastannolanes where the tin is pentacoordinate,[25] these latter signals are assigned to α-carbons attached to pentacoordinate tin (PT). If the symmetries considered previously are valid, ^{13}C NMR spectra of the trimer should contain one signal for a C-α attached to PT and one signal for a C-α attached to hexacoordinate tin (HT) with intensity ratios of two to one; spectra of the tetramer should contain two equally intense C-α signals for carbons attached to PT and HT. The additional splitting observed when the temperature was lowered beyond −60 °C is caused by the different environments in the trimer and tetramer; in each pair, the high-frequency signal is more intense at lower concentrations and must be assigned to the trimer.

The monomer has been considered to be an important constituent in the equilibrium mixtures present in solutions of **1**[8,9] and its 4-methyl derivative,[28] particularly at low concentrations[8,28] or elevated temperatures.[9] Picard et al.[9] analyzed "dimer–monomer" equilibria at room temperature and above by considering the observed ^{119}Sn NMR chemical shifts as averages of dimer and monomer shifts. Here, the dimer chemical shift was shown to be about −127 ppm. The choice of the room-temperature chemical shift of a 0.1 M solution in chloroform-*d*/mesitylene, 1:1 of −181 ppm as the chemical shift of the dimer as well as the use of an over-simple model[9] invalidate the results. Roelens and Taddei observed an additional small signal at a slightly larger frequency than the OCH_2 signal in both the ^1H and ^{13}C NMR spectra of 0.2 M solutions of **1** at room temperature in chloroform-*d* that increased in intensity as the solutions were diluted.[8] Shanzer et al. made similar observations for chloroform-*d* solutions of 4-methyl-2,2-di-*n*-butyl-1,3,2-dioxastannolane.[28] Here, no signals were observed in the region of the ^{119}Sn NMR spectra, +50 to −100 ppm, where monomers are expected to absorb,[4] for 0.2 or 0.02 M solutions of **1** in chloroform-*d* either at room temperature or −55 °C indicating that monomers were not present. To confirm that our negative results were not caused by line broadening due to exchange or by some other unanticipated difficulty, we attempted to repeat the previous observations. We did not observe any of the extra signals in samples prepared as

(25) Grindley, T. B.; Thangarasa, R. *Can. J. Chem.* In press.
(26) (a) Mitchell, T. N. *J. Organomet. Chem.* **1973**, *59*, 189–197. (b) Lockhart, T. P.; Manders, W. F. *J. Am. Chem. Soc.* **1987**, *109*, 7015–7020. (c) Holecek, J.; Lycka, A. *Inorg. Chim. Acta* **1986**, *118*, L15–L16.
(27) Bates, P. A.; Hursthouse, M. B.; Davies, A. G.; Slater, S. *J. Organomet. Chem.* **1989**, *363*, 45–60.
(28) Shanzer, A.; Libman, J.; Gottlieb, H. E. *J. Org. Chem.* **1983**, *48*, 4612–4617.

Table V. The Effect of Water and 1,2-Ethanediol on the ^1H and ^{13}C NMR Spectra of **1**

sample	signal	chemical shifts[a] (ppm) ^1H NMR	^{13}C NMR
pure sample	$SnOCH_2$	3.625	63.170
sample + H_2O[b]	$SnOCH_2$	3.624	63.170
	new signal	3.687	64.224
sample + $(HOCH_2)_2$[b]	$SnOCH_2$	3.622	63.148
	new signal	3.695	64.194
lit.[8]	$SnOCH_2$	3.611[c]	62.89[d]
	extra signal	3.674[c]	64.06[d]

[a] 0.2 M in chloroform-*d* at 25 °C at 361.06 and 90.8 MHz for ^1H and ^{13}C NMR spectra, respectively, unless otherwise noted. [b] Much less than 1 equiv. [c] 0.2 M in chloroform-*d* at 300 MHz. [d] 0.85 M in chloroform-*d* at 20 MHz.

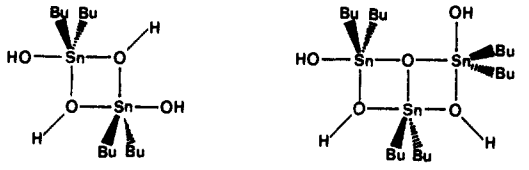

Figure 5. Possible structures for soluble hydrated forms of di-*n*-butyltin oxide. One of two dimer stereoisomers and one of the three trimer stereoisomers are illustrated.

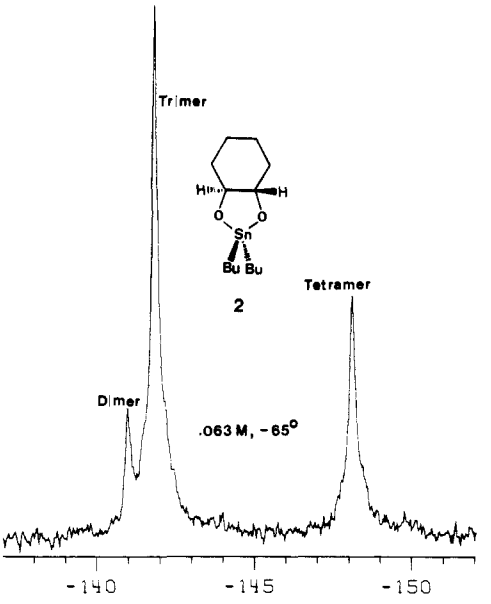

Figure 6. The part of the 134.6 MHz ^{119}Sn NMR spectrum of a solution of **2** in chloroform-*d*/dichlorofluoromethane, 3:1 that contains the signals of the pentacoordinate tin atoms.

described in the experimental or from nonsealed samples prepared as described in the Experimental Section except that the predried chloroform-*d* was transferred by syringe to the reaction product maintained in an argon atmosphere. Addition of small amounts of water or small or excess amounts of ethylene glycol produced an additional peak in the ^1H and ^{13}C NMR spectra at chemical shifts (see Table V) almost identical with those reported by Roelens and Taddei.[8] Clearly, the additional peaks observed earlier[8,28] resulted from reaction of the 1,3,2-dioxastannolanes with water in the chloroform-*d* or from the atmosphere.

Tin-119 spectra indicate that complex mixtures were obtained. The ^{119}Sn NMR spectra of the 0.2 M solutions of **1** at 55 °C with slight amounts of added water included an extra signal at −134.6 ppm, at a greater frequency and much sharper than the broad main signal which may have other signals superimposed on it. At −60 °C, the ^{119}Sn NMR spectra of this mixture closely resembled the spectra without added water, except that there were a number of additional small peaks, at −131.0, −142.5, −144.5, −152.9, −153.5, −156.0, −156.7, −253.5, and −257.5 ppm. Of these, the peaks at −131.0 and −152.9 ppm were the most intense. The spectra of a sample prepared as in the Experimental Section except that 2 extra equiv of ethylene glycol were added did not contain any new peaks, but relative intensities at −60 °C and line widths at 55 °C and at −60 °C may have been altered. The extra ethylene glycol in this sample was evident because of an extra peak at 63.87 ppm in the room temperature ^{13}C NMR spectrum, as discussed in the previous paragraph. No peaks at this chemical shift were evident in the spectra of samples prepared as in the experimental section. The fact that new peaks are present in the low-temperature ^{119}Sn NMR spectra of samples with added water but not in those with excess ethylene glycol support the suggestion of Davies and Price,[20] that soluble forms of dibutyltin oxide are produced when water is added to 1,3,2-dioxastannolanes. Most of the peaks observed were in the region of the ^{119}Sn NMR spectra where pentacoordinate tin absorbs. Therefore, these compounds probably have ladder type structures that contain two, three, or more dibutyltin oxide monomer units as illustrated in Figure 5 for a dimer and a trimer.

(1*S*,6*S*)-8,8-Di-*n*-butyl-7,9,8-dioxastannabicyclo[4.3.0]nonane (2) and Its Racemate (3). The 1,3,2-dioxastannolanes derived from *trans*-1,2-cyclohexanediol were considered to be good model compounds for the tin-derived intermediates used to achieve highly selective reactions of carbohydrate and other cyclic diols.[1] In general, the changes in the ^{119}Sn NMR spectra of **2** and **3** with temperatures were similar to those of **1**. A few minor differences were observed. The ^{119}Sn NMR chemical shifts were 8–16 ppm more negative (Table I). More importantly, as the temperature was lowered, the two central major signals, one in each of the pentacoordinate and hexacoordinate regions, sharpened at temperatures about 20 °C lower than the lowest frequency hexacoordinate tin signal. This observation provides additional confirmation that these two signals belong to one species, the tetramer. The signals in spectra of solutions of **2** were sharper than those of identical concentration samples of **1** at temperatures below −20 °C. For instance, for 0.5 M solutions at −50 °C, half-height line widths for the tetramer and trimer hexacoordinate ^{119}Sn NMR signals were 293 and 475 Hz for **1** and 75 and 67 Hz for **2**, respectively. Since the chemical shift differences are similar for **1** and **2**, this observation indicates that the rates for oligomerization equilibria are slower for the more substituted compound. Each of the four major signals in the spectrum of the racemate (**3**) was further split below −40 °C (Table I). Extra complexity is expected in the low-temperature spectra of **3** because, when the rates of equilibration of the oligomeric species are slow, solutions of **3** will contain two diastereomeric dimers, three trimers, and six tetramers. An additional difference was the observation of a small signal on the high frequency side of the pentacoordinate trimer peak in ^{119}Sn NMR spectra of **2** recorded at temperatures lower than −50 °C for samples with concentrations less than 0.15 M (see Figures 3 and 6). The relative intensity of this new signal increased with dilution, and hence it was assigned to the dimer.

Nine low-temperature spectra of a 0.063 M solution of **2** in chloroform-*d*/dichlorofluoromethane, 3:1 between −75 °C and −35 °C and ten spectra of a 0.43 M solution of **2** in the same solvent between −65 °C and −20 °C were carefully integrated. The results were used to derive thermodynamic parameters for the equilibria as previously outlined for **1** (see Table III). The parameters derived for the 0.063 M solution of **2** were almost identical with those derived from the 0.072 M solution of **1**. Evidently, the replacement of a primary center by a secondary center does not affect the equilibria much, particularly when the substituents on the secondary center are held remote from the substituents on tin by being incorporated in a ring. The equilibria are highly temperature and concentration dependent as can be seen from the calculated mole fractions at 200 and 300 K listed in Table IV.

The low-temperature ^{13}C NMR spectra are quite complex, and overlapping signals, C-1 and C-6 with chloroform-*d* and the α-CH_2 with the cyclohexyl γ-carbons or C-β or C-γ, prevent full assignments. Nevertheless, the number of signals observed for each type of carbon is close to seven, the number expected for a mixture of a trimer and a tetramer. The trimer and tetramer of **2** each

Table VI. Activation Parameters for Exchange of Methyl Groups of 5 Derived from Line Shape Analysis[a]

	0.23 M	0.36 M
$\Delta G^{\ddagger}$[b]	14.89 ± 0.05 kcal mol^{-1}	14.74 ± 0.01 kcal mol^{-1}
$\Delta H^{\ddagger}$	14.2 ± 0.5 kcal mol^{-1}	14.2 ± 0.3 kcal mol^{-1}
$\Delta S^{\ddagger}$	−2.4 ± 1.5 cal deg^{-1} mol^{-1}	−1.9 ± 1.1 cal deg^{-1} mol^{-1}

[a] Uncertainties are at the 95% confidence level. [b] At 300 K.

have C_2 symmetry; the trimer contains three equally populated diastereotopic butyl groups, while the tetramer contains four. Six separate signals can be seen for the cyclohexyl β-carbons between 33.3 and 34.0 ppm in the spectrum of the 0.43 M solution of **2** at −70 °C. In the same spectrum, four signals were observed at 20.25, 20.32, 21.71, and 22.03 ppm and were assigned to the α-CH_2 when attached to pentacoordinate tin, by analogy with the assignments made for **1**. The other three signals of the α-CH_2 must lie in the same region as the signals of the cyclohexyl γ-carbons (six lines between 24.3 and 25.1) or the C-β and C-γ signals (at least 10 lines between 27.9 and 29.0 ppm).

(4*R*,5*R*)-2,2-Di-*n*-butyl-4,5-dimethyl-1,3,2-dioxastannolane (4). The ^{119}Sn NMR spectra of **4** closely resembled those of **2**. For instance, the intensities of the four peaks (from peak heights) expressed as percentages of total intensity in the spectrum of a 0.5 M solution of **4** in chloroform-*d* at −50 °C were each within 2% of the values obtained for the corresponding peaks in the spectrum of a 0.5 M solution of **2** in chloroform-*d* at the same temperature. However, the ^{119}Sn NMR chemical shifts (Table I) were 8–10 ppm less upfield. The ^{13}C NMR spectra of the 0.5 M solution in chloroform-*d* of **4** were again complex. The singlet for C-4 and C-5 at 74.7 ppm split as the temperature was lowered into three bands each of which again split into two below −50 °C (shifts 75.07, 75.02, 74.23, 74.07, 73.34, 73.21 ppm at −65 °C). As for the comparable carbon in **2**, seven peaks should be observed if only trimers and tetramers are present. The peak at 74.07 ppm was larger than the others, consistent with the expected number of peaks.

2,2-Di-*n*-butyl-4,4,5,5-tetramethyl-1,3,2-dioxastannolane (5). The ^{119}Sn NMR spectra of **5** were very different than those observed for **1** to **4**. A single signal in the pentacoordinate tin region was observed from −60 °C to 80 °C for solutions in chloroform-*d*. Thus, it was concluded that **5** is present almost entirely as a dimer. The only change observed was that the signal broadened as the temperature was raised, changing in half-height line width from 11.8 Hz at 20 °C to 106 Hz at 80 °C. Spectra of solutions of **5** in 1,1,2,2-tetrachloroethane-d_2 were recorded at higher temperatures, but irreversible changes were observed in the spectra of samples examined above 90 °C, possibly due to disproportionation reactions as observed for related compounds.[4]

The ^{13}C NMR spectra of **5** were also comparatively simple. At 23 °C for a 0.23 M solution in chloroform-*d*, the quaternary carbons appeared as two somewhat broadened peaks at 78.3 and 75.1 ppm, while the 4,4,5,5-methyl carbons appeared as two broadened signals at 26.5 and 25.4 ppm. The four types of carbons in the two butyl groups each gave rise to a single peak. All of these observations are consistent with a dimer structure with C_{2h} symmetry. As the temperature was raised, the signals of the methyl groups coalesced at about 48 °C. The signals of the quaternary carbons broadened and disappeared under the solvent signals and presumably also coalesced. The changes in the 0.36 M solution were similar.

Line shape calculations were performed for the exchange of the methyl groups for both 0.23 and 0.36 M solutions in chloroform-*d*. Line shapes were generated for 13 temperatures between 28 and 80 °C for the 0.23 M solution and 11 temperatures between 30 and 70 °C for the 0.36 M solution by using a program for classical two-site exchange.[16] Figure 7 compares experimental and simulated spectra. The calculated rate constants[29] were used to derive kinetic parameters which are presented in Table VI.

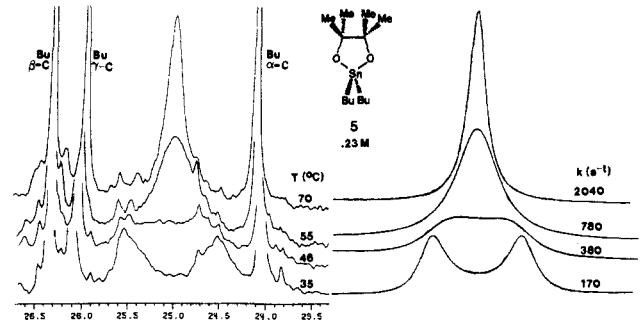

Figure 7. Simulation of exchange of 90.8 MHz ^{13}C NMR signals of the 4,4,5,5-methyl groups of **5** between diastereotopic sites in the dimer for a 0.23 M solution in chloroform-*d*. On the left are shown portions of the experimental spectra at various temperatures that include signals of three of the nonexchanging butyl carbons as well as the signals of the exchanging 4,4,5,5-methyl carbons; on the right are the simulated signals of the 4,4,5,5-methyl carbons with the rate constants shown.

A number of mechanisms can be considered for exchange of the carbons attached to dicoordinate oxygens with those attached to tricoordinate oxygens. In view of the species present in solutions of compounds **1**–**4**, the most logical pathway would involve association of dimer with trimer, assumed to be present in low concentration, to give an intermediate pentamer that dissociates to trimer plus dimer. This process would be expected to have a large negative entropy of activation, similar in magnitude to the entropies measured for the equilibria. The observation of small and slightly negative values for the entropies of activation indicate that this mechanism cannot be the sole mechanism responsible for exchange. Simple dissociation of the dimer to two monomer units would have a large positive entropy of activation and would also result in the methyl group signals coalescing as the temperature was raised. If monomers were present at a low concentration, a second associative process could occur in which a monomer and a dimer exchanged via a trimer. If both associative and dissociative mechanisms operated simultaneously, it is possible that the overall entropy of activation would be slightly negative as observed.

The cause of the broadening of the ^{119}Sn NMR signal observed as the temperature is raised to 80 °C is uncertain. On possibility is that this broadening arises from the same processes that influences the ^{13}C NMR line shapes discussed above. Both types of mechanisms, associative involving trimers and/or monomers or dissociative involving monomers, would result in exchange of tin atoms in pentacoordinate environments with tin atoms in very different environments, hexacoordinate tin for the trimer and tetracoordinate tin for the monomer. It has been shown that the amount of broadening at coalescence of an NMR signal that exchanges with the signal of a species that has a population less than 10% that of the major species is equal to the product of the population of the minor species and the chemical shift difference.[30] Hence, both types of mechanisms could cause the broadening of the ^{119}Sn NMR signal, if the species exchanging with the dimer, that is, the monomer or the trimer, were present in sufficient concentration and if the maximum temperature studied, 80 °C, was close to coalescence. The ^{119}Sn NMR signal from solutions of **5** in 1,1,2,2-tetrachloroethane-d_2 continued to broaden as the temperature was raised to 120 °C although rearrangements had occurred as measured by the ^{13}C NMR spectra of the cooled solutions. Thus, exchange with an intermediate on the pathway to rearrangement or with a very small amount of rearranged product may also cause the broadening observed in the high-temperature chloroform-*d* spectra. At this time, we cannot differentiate among the several possibilities that could influence the ^{119}Sn NMR line width above room temperature.

If a trimer was an intermediate in the exchange process, its population would increase as the temperature was lowered.

(29) A table of rate constants from the line shape analysis of the changes in the appearances of the ^{13}C NMR signals of the methyl carbons of **5** with temperature is available from the authors.

(30) (a) Anet, F. A. L.; Basus, V. J. *J. Magn. Reson.* **1978**, *32*, 339–343. (b) Okazawa, N.; Sorenson, T. S. *Can. J. Chem.* **1978**, *56*, 2737–2742.

Spectra were recorded at −60 °C for a 0.36 M solution in chloroform-*d* to search for ^{119}Sn NMR signals with chemical shifts between −250 and −310 ppm. No signals were observed under conditions where any signal having a height larger than 2% of the height of the dimer signal would have been observed.

If a monomer is involved in the exchange process, its concentration at room temperature is low. Tin-119 NMR was used to search for the monomer. The heights of any signals in the region from +50 to −80 ppm were less than 1% that of the dimer for a 0.2 M solution or less than 5% for a 0.03 M solution at 23 °C. Although it is possible that the monomer signals were too broad for observation at this temperature, searches at −20 °C were also unsuccessful. As for other oligomerization equilibria, it would be expected that the monomer–dimer equilibrium would be highly temperature dependent with the concentration of monomer increasing rapidly with temperature.

The spectra of acyclic di-*n*-butyltin dialkoxides indicate that monomers become more stable with respect to dimers as the alkoxy group becomes more branched.[4] Hence, of the 1,3,2-dioxastannolanes studied, **5** should contain the largest proportion of monomer. It has been suggested that solutions of **1** at room temperature contain the monomer to an extent observable by NMR spectroscopy and that the proportion of monomer increases with respect to dimer as the concentration decreases from 0.1 to 0.02 M and that exchange with dimer is slow at that temperature.[8] Our results indicate that the concentration of monomer present in nonpolar solvents at room temperature for **1** is negligible, probably less than 0.01%.

General Discussion. Population of Higher Oligomers. Steric effects are known to strongly influence the level of association of dialkoxydialkyltin derivatives.[1,4,12,27] It is now possible to specify the number and type of substituents required to influence the oligomerization equilibria of 2,2-di-*n*-butyl-1,3,2-dioxastannolanes. The populations of higher oligomers for *trans*-4,5-disubstituted-1,3,2-dioxastannolanes were found to be almost the same as for the unsubstituted parent compound (**1**). Supplementary ^{119}Sn NMR spectra in ref 12 indicate that monosubstitution at C-4 by methyl or phenyl groups does not affect the proportion of higher oligomers much nor does 4,4-disubstitution by methyl groups. However, solutions of the 4-methyl-4-phenyl derivative of **1** contain only a small amount of higher oligomer at low temperature.[12] The amount of higher oligomer present for 2,2-di-*n*-butyl-1,3,2-dioxastannolanes obtained from carbohydrate derived *vic*-diols ranges from negligible to substantial depending on the stereochemistry and substitution pattern of the carbohydrate diol.[25] Thus, it appears that solutions of 2,2-di-*n*-butyl-1,3,2-dioxastannolanes having mono- or disubstitution by small substituents will contain about the same amounts of trimers and higher oligomers as do those of **1**. Additional substitution, even by methyl groups, destabilizes higher oligomers significantly as observed for the 4,4,5,5-tetramethyl derivative here. 2,2-Di-*tert*-butyl-1,3,2-dioxastannolane has recently been shown to exist as a dimer both in solution and in the solid state.[27] The cause of this steric destabilization will be discussed further with the equilibria of carbohydrate derivatives where it is possible to define more precisely the nature of the steric interactions required to destabilize trimers and higher oligomers.[25]

Mechanisms of Exchange. The evidence presented in this paper is consistent with the exchange processes observed here occurring by two or more of the following related reversible associative pathways:

$$\text{monomer} + \text{monomer} \rightleftharpoons \text{dimer} \quad (5)$$

$$\text{dimer} + \text{monomer} \rightleftharpoons \text{trimer} \quad (6)$$

$$\text{dimer} + \text{dimer} \rightleftharpoons \text{tetramer} \quad (7)$$

$$\text{dimer} + \text{trimer} \rightleftharpoons \text{pentamer} \quad (8)$$

$$\text{dimer} + \text{tetramer} \rightleftharpoons \text{hexamer} \quad (9)$$

$$\text{trimer} + \text{trimer} \rightleftharpoons \text{hexamer} \quad (10)$$

The most important processes are those that involve species that are present to measurable extents, that is, processes 7 and 8. Processes 9 and 10 are necessary if dimers and tetramers are to equilibrate with trimers. Processes involving still higher oligomers may contribute to some extent. The first two processes will only become competitive with or favored over pathways 7 and 8 when higher oligomers are severely destabilized as for compound **5**. Thus, for compounds **1–4**, the most important exchange pathways are the reversible association of two dimers to a tetramer and of a dimer and a trimer to a pentamer.

Speeding up these processes causes the signals of the various types of pentacoordinate and hexacoordinate tin observed at low temperature to coalesce. The effects of changing concentration on ^{119}Sn NMR line widths support the contention that these processes occur by intermolecular pathways. At 55 °C, above the coalescence temperatures, the line widths observed for the 0.072 M solution were larger than those observed for the 0.52 or 0.50 M solutions. The line widths below coalescence for the 0.072 M solution in the −30 °C to −70 °C temperature range were always significantly narrower than those of the higher concentration samples at the same temperature as would be expected if rates at a particular temperature increased with increased concentration.

Attempted line shape analysis of the exchange of the tin signals in the eight environments of the 0.063 M solution of **2** via processes 7 and 8 using a program for multisite exchange[31] modified to apply to intermolecular exchange gave satisfactory fits for the spectra recorded at temperatures where broadening is just beginning, −20 and −25 °C, but the fits rapidly became unsatisfactory as the temperature was raised. At −20 °C, the rate constant obtained from the limited line shape calculations for two dimers ⇌ tetramer was 1200 ± 100 s^{-1}, while that for dimer + trimer ⇌ pentamer was 200 ± 50 s^{-1} yielding $\Delta G^{\ddagger}$ values of 11.2 ± 0.1 and 12.1 ± 0.1 kcal mol^{-1}, respectively. At higher temperatures, the other possible exchange processes, such as 9 and 10 and perhaps 5 and 6, also influence the line shapes, and uncertainties in several critical extrapolated parameters, particularly populations, T_2 values, and chemical shifts of the minor components, the pentamer and the dimer, made treatment of the processes that influence line shapes by means of a more complex model impossible. Because the thermodynamic parameters associated with the oligomerization equilibria include large negative entropy terms, the activation parameters for association would also have to include large negative entropies. The broader line widths observed in the ^{119}Sn NMR spectra of **1** as compared to those from spectra of **2** at the same temperature suggest that processes 7 and 8 are slowed by substitution.

Processes 7 and 8 are also evident in the broadening and coalescence of the butyl α-CH_2 ^{13}C NMR signals. It was shown earlier that the splitting of these signals occurs because the environments for the α-CH_2 carbons are different for attachment to pentacoordinate tin than for attachment to hexacoordinate tin. Roelens and Taddei had estimated the barrier to coalescence of the two groups of α-CH_2 carbons as 10–11 kcal mol^{-1} for **1**, although they ascribed the coalescence to a different process.[8] The use of the coalescence equation for this process is not quite correct, because the intensity of the group of signals due to α-CH_2 next to pentacoordinate tin is somewhat greater than the other group and also because at least two different rate processes cause this exchange. Nevertheless, the similar values obtained for **1**[8] and for **2** from the ^{119}Sn NMR spectra support the idea that they belong to the same process.

Interconversion of sites on or attached to 1,3,2-dioxastannolane rings that are homotopic in a monomer but become diastereotopic in the dimer can take place via those processes that involve monomers, that is processes 5 or 6. They can also take place via higher oligomers but only through the association of species containing odd numbers of monomer units with those containing even numbers of monomer units, namely, via process 8. For instance, several repetitions of pathway 8, in which dissociation of the pentamer unit occurs by cleavage of different Sn–O bonds

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than were formed during association, result in exchange of all of these sites. This process is consistent with the observation[8] of tin-119/117 satellites for the averaged OCH_2 signal at 55 °C because here the individual monomer units stay together during the exchange process.

A different process can be observed in the NMR spectra of 1,3,2-dioxastannolane derivatives that lack a plane or axis of symmetry relating the two substituents on tin in the monomeric structure. Luchinat and Roelens[12] examined the dynamic ^{13}C NMR spectra of the chiral and racemic 4-methyl and 4-phenyl derivatives of **1**. At room temperature, the spectra of these compounds exhibit two equally intense peaks for the α-, β-, and γ-carbons of the butyl groups. The two peaks for each carbon coalesce as the temperature is raised with $\Delta G^{\ddagger}$ of about 17 kcal mol^{-1}, considerably larger than other barriers measured for these compounds. The two butyl groups on each tin atom are diastereotopic in the monomer and thus should give anisochronous signals as long as processes that result in inverting the relationship of the butyl groups on tin to the chiral center in the same 1,3,2-dioxastannolane ring are slow. No associative process could account for the observed coalescence because, during any such process, the butyl groups maintain their relationship to the chiral center. Luchinat and Roelens have proposed a mechanism for this process that involves breaking two internal Sn–O bonds in a dimer to give a ten-membered ring intermediate that reassociates to a different dimer in which the $Sn(Bu)_2$ groups have exchanged the chiral center with which they are associated inside the two 1,3,2-dioxastannolane rings of the dimer.[12]

Conclusions

2,2-Di-*n*-butyl-1,3,2-dioxastannolanes exist in solution in nonpolar solvents as mixtures of oligomers, including dimers, trimers, tetramers, and pentamers. The amount of monomer present is below the level of detection by NMR at room temperature. The constitution of the mixture present is influenced by temperature, concentration, and the nature of the substituents on the ring. The temperature dependences of the oligomerization equilibria are particularly steep. For the parent compound (**1**), the trimer and tetramer constitute the majority of the species present below −20 °C, but the dimer dominates increasingly as the temperature is raised. Two small, 4,5-trans substituents do not influence the equilibria much, but the 4,4,5,5-tetramethyl derivative exists solely as the dimer. 1,3,2-Dioxastannolanes undergo particulary complex exchange processes through a series of related association–dissociation equilibria involving dimers, trimers, tetramers, and pentamers and possibly monomers and hexamers. The lowest barriers for compounds **1**–**4** were observed for association of two dimer molecules to a tetramer and of a dimer and a trimer to a pentamer.

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Elucidation of Motional Modes in Glycoglycerolipid Bilayers. A ^2H NMR Relaxation and Line-Shape Study†

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Abstract: In the present study, a combination of ^2H spin–lattice relaxation and line-shape analysis demonstrates that two motions are sufficient to describe the spectral and relaxation behavior of the glycolipid 1,2-di-*O*-tetradecyl-3-*O*-(β-D-glucopyranosyl)-*sn*-glycerol (β-DTGL). In the gel phase, at 25 °C, the powder and oriented-sample spectral line shapes for the glycolipid, specifically labeled at the C3-position of the glycerol backbone, are characteristic of fast-limit axially asymmetric motions. In particular, the oriented-sample spectra have powder line shapes characteristic of a system with a motionally averaged asymmetry parameter η_{eff} close or equal to unity. Moreover, the Zeeman spin–lattice relaxation times were dependent on both the polar and azimuthal angles, θ and ϕ, describing the orientation of the motional axis relative to the magnetic field direction. Inspection of the partially relaxed line shapes of powder spectra of gel-phase lipid clearly revealed the θ-dependence of the spin–lattice relaxation times. Furthermore, for oriented samples with a given θ, a ϕ-dependence of the relaxation times was also observed. This effect was most evident at the magic-angle ($\theta = 54.7°$) orientation. The nature of this ϕ-dependence puts severe constraints on the motional model and the motional rates used to simulate the gel-phase line shape and T_1 anisotropy ($T_{1Z}(\theta,\phi)$). The line-shape and relaxation features were best simulated with a 3-site jump model with relative site populations of 0.46, 0.34, and 0.20 and a correlation time of 6.7×10^{-10} s. These results indicate that a single internal motion is sufficient to describe the line shape and relaxation in the gel phase. However, a second motion, namely rotation about the long axis of the molecule as a whole, is needed to account for the observed variation in the quadrupolar echo amplitude and the spectral line shape over the temperature range of 25–60 °C. This motion does not significantly influence the line shape in the gel phase at 25 °C or the spin–lattice relaxation behavior in the gel and liquid-crystalline phases. From the line-shape study, an activation energy of about 150 kJ mol^{-1} was determined for this motion.

Glycosphingolipids constitute a class of biomolecules that can assume many biological roles.[1] Of particular importance is their capacity to function as recognition sites (cell–cell recognition,[2] immune recognition,[3] and toxin receptor[4]) and as modulators of membrane structure.[5] In addition to the structure and conformation of the oligosaccharide moiety, molecular recognition at the cell membrane surface will depend on a number of factors such as surface orientation and spatial constraint imposed by the bilayer surface, which will affect "accessibility" of the carbohydrate

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