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MULTI-NUCLEAR (^{119}Sn, ^{13}C, ^{1}H), FOURIER-TRANSFORM, N.M.R. STUDIES OF DI- AND TRI-BUTYLSTANNYL ETHERS OF CARBOHYDRATES

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ABSTRACT

^{119}Sn-N.m.r. spectra are reported for toluene solutions of the tributylstannyl ethers of 2,3,4,6-tetra-*O*-methyl-D-glucose, 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose, methyl 2,3-di-*O*-methyl-α-D-glucopyranoside, and methyl 4,6-*O*-benzylidene-α-D-glucopyranoside, and the dibutylstannyl ether of the last sugar. In the reaction of bis(tributyltin) oxide with methyl 4,6-*O*-benzylidene-α-D-glucopyranoside in toluene, HO-3 is much more reactive than HO-2. The presence of the various tin-containing species is readily apparent from the ^{119}Sn-spectra. The importance of suppressing the nuclear Overhauser effect is demonstrated. The appearance of ^{119}Sn satellites in the ^{13}C-n.m.r. spectra demonstrates couplings of the types, $^{2}J(^{119}\text{Sn-O-}^{13}\text{C})$ and $^{3}J(^{119}\text{Sn-O-C-}^{13}\text{C})$, for the first time, and, together with the ^{13}C-chemical shifts, facilitates the determination of the site of substitution. The ^{119}Sn-chemical shifts show that different states of coordination may be recognised. However, although different sites of substitution produce separate resonances, no simple relationship between shift and position is found. ^{13}C-Chemical shifts are reported for methyl 4,6-*O*-benzylidene-α-D-glucopyranoside and its tributylstannyl ethers, and substituent effects are discussed.

INTRODUCTION

Since the pioneering work of Moffatt and his colleagues[1,2], di- and tri-butylstannyl ethers have found wide use in carbohydrate chemistry[3,4]. More recently, certain inorganic tin salts, *e.g.*, $SnCl_2$, have been utilised as catalysts for the mono-

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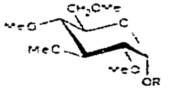
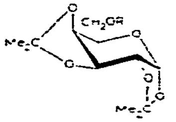
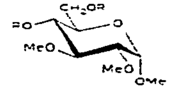
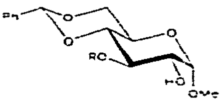
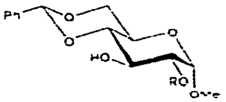
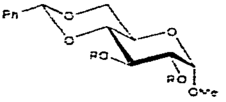
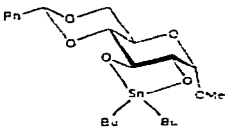
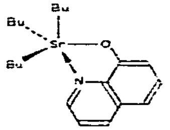
TABLE I

^{119}Sn-CHEMICAL SHIFTS[a] AND COUPLING CONSTANTS[b] FOR SOME ORGANOTIN-CARBOHYDRATE DERIVATIVES IN TOLUENE SOLUTION

Compound (R = Bu_3Sn)		*Approximate concentration* (M)	$\delta(^{119}Sn)$	$^{2}J(^{119}Sn\text{-}O\text{-}^{13}C)$	$^{3}J(^{119}Sn\text{-}O\text{-}C\text{-}^{13}C)$
	1a	0.2	99.0[c]	24	16
	1b	0.9	86.4[c]	23	13
	2	1.1	98.7	46	29[d]
	3	1.2	92.8[e] 98.6[e]	f	f
	4	0.2	101.8[g]	29	~18 (C-4) ~20 (C-2)
	5	0.05	87.3[g]	h	h
	6	0.4	77.5 (C-2)[g] 91.2 (C-3)[g]	29 (C-2) 28 (C-3)	19 (C-1) 22 (C-2) 16 (C-3) < 18 (C-4)[i]
	7	0.6	−131.6[j]	12[e,k] < 10[e,i,k]	34 (C-4)[k] 20 (C-1)[k]
$Bu_3SnOSnBu_3$	8	50% v/v	82.8[l]	f	f
	9	Neat liquid	29.0[m]	f	f
$Bu_2Sn(OMe)_2$	10	Neat liquid	−165.0[m]	f	f

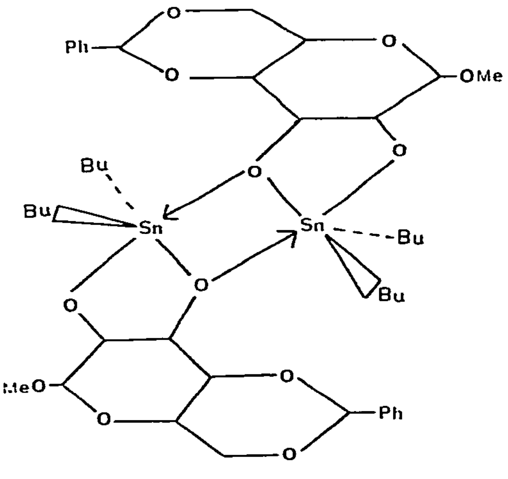
[a] In p.p.m. downfield from Me_4Sn; error in $\delta(^{119}Sn)$ is ±0.2 p.p.m. for all compounds except **9** and **10**, for which it is ±4.0 and ±2.0 p.p.m., respectively. [b] In Hz; estimated error is ±1 Hz. [c] Recorded as a mixture of two anomers. [d] A possible alternative assignment, with this as a 4-bond coupling to C-4, was considered unlikely. [e] Assignment uncertain. [f] Not recorded. [g] In a mixture of **4**, **5**, and **6**. [h] No satellites were observable, due to low concentration. [i] Not resolved. [j] Ref. 7 reports −132.0 p.p.m. converted to Me_4Sn. [k] These couplings involved two different bonding-pathways. [l] Ref. 10 reports 77.8–84.5 p.p.m. [m] From ref. 10.

of their relative concentrations. The preponderance of the β anomer contrasts with the equilibrium values (54% for α and 46% for β) determined from the ^{1}H spectrum (toluene) of the parent sugar, 2,3,4,6-tetra-*O*-methyl-D-glucose.

From the limited data available (Table I), it seems that changing the site of substitution by the tributylstannyl moiety, as in **3** and **6**, produces ^{119}Sn-shift differences which are comparable in magnitude to that observed between **1a** and **1b**. The ^{119}Sn-chemical shift for **2** is very similar to one of the values obtained for **3** (Table I). Since both compounds contain a tin substituent at C-6, this observation might indicate a relationship between the shift value and position of substitution. However, insufficient data are available to verify this possibility.

The tributyltin–carbohydrate derivatives and bis(tributyltin) oxide (**8**), showed ^{119}Sn resonances which were 70–100 p.p.m. downfield from that of tetramethyltin. This finding indicates[10] that the geometry at the tin atom in solution is tetrahedral and precludes the possibility of intramolecular coordination to tin. This argues against a previous suggestion[11] that, in a situation analogous to **6**, there was coordination between an equatorial tributylstannyl group at C-2 and the oxygen of an axial MeO-1 group.

It is well established that coordination at tin leads to significant shifts to higher fields. For example, in tributyltin 8-hydroxyquinolate (**9**), which contains[12] an intramolecularly chelated, five-coordinate tin atom, there is a shift of ~50 p.p.m. to higher field (Table I). The dibutylstannylene derivative (**7**) of methyl 4,6-*O*-benzylidene-α-D-glucopyranoside, which, in the solid state and in solution, exists as a dimer (**11**) containing five-coordinate tin, shows a ^{119}Sn resonance at −131.6 p.p.m. This shift is similar in magnitude to that (−165 p.p.m., Table I) reported for $Bu_2Sn(OMe)_2$ (**10**), which has a similar, dimeric, oxygen-bridged structure. There was no evidence[7] for the alternative structure of the dimer **11**, which involves the donation of electrons from O-2 to tin.



11

methylation of the *cis*-diol system in nucleosides[5] and carbohydrates[6] by diazomethane. There are, however, very few structural studies of these tin–carbohydrate derivatives[7–9] and it is not known for certain how tin is involved in the catalysis of the monomethylation of sugars by stannous salts, although a tin(II)–sugar intermediate has been proposed[3].

Fourier-transform (F.t.) n.m.r. spectroscopy, although used extensively to study ^{13}C nuclei, has only very recently been applied[10] to ^{119}Sn. We now report studies of a series of di- and tri-butylstannyl ethers of simple carbohydrates by this technique.

DISCUSSION

^{119}*Sn-Chemical shifts*

The ^{119}Sn-chemical shifts, δ (^{119}Sn), for the compounds studied are recorded in Table I, and a typical ^{119}Sn-spectrum, obtained for the product of the reaction between bis(tributyltin) oxide and 2,3,4,6-tetra-*O*-methyl-D-glucose in toluene, is shown in Fig. 1.

The spectrum reveals two ^{119}Sn-resonances, separated by 12.6 p.p.m., of which the more intense may be identified by inspection of the anomeric doublets in the ^{1}H spectrum, where the more intense doublet (δ 4.77, J ~6 Hz) is assigned to the β anomer (**1b**), and the less intense (δ 5.35, J ~4 Hz) to the α anomer (**1a**). The proportions of the anomeric species deduced from the ^{119}Sn peak-heights are 21% for **1a** and 79% for **1b**, values which are consistent with both the ^{1}H and ^{13}C spectra. These species are not in chemical equilibrium, as there was no temperature dependence

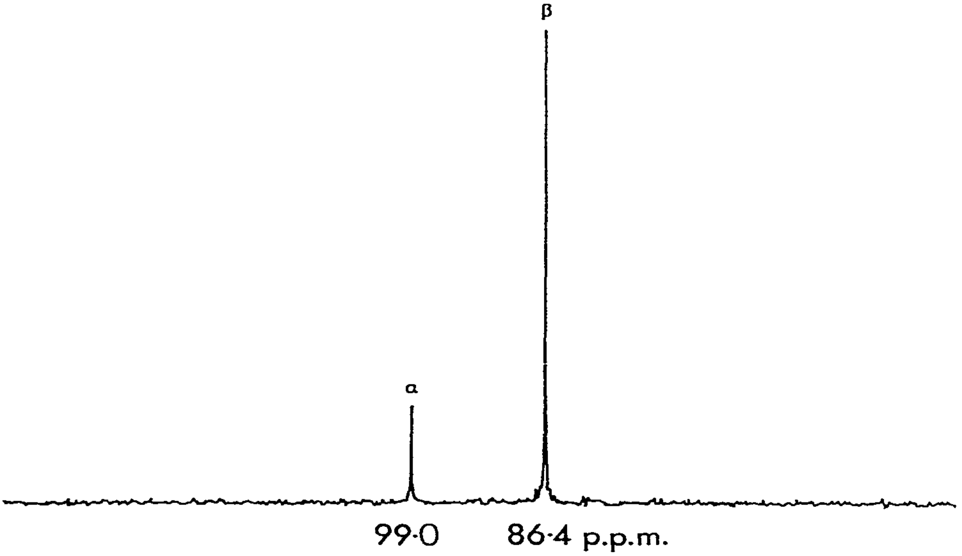


Fig. 1. ^{119}Sn-F.t.n.m.r. spectrum of the product of the reaction between bis(tributyltin) oxide and 2,3,4,6-tetra-*O*-methyl-D-glucose in toluene, at 37.08 MHz, recorded using 40 pulses.

Order of reactivity of the hydroxyl groups in methyl 4,6-O-benzylidene-α-D-glucopyranoside with bis(tributyltin) oxide (**8**)

The reaction of methyl 4,6-*O*-benzylidene-α-D-glucopyranoside with bis(tributyltin) oxide (**8**) in toluene, which had not been studied previously, follows a rather complicated pattern. After 4 h at reflux temperature, a ^{119}Sn spectrum (Fig. 2*a*) was obtained which showed five resonances. A 24-h treatment of the required stoichiometric quantities gave the 2,3-bis(tributylstannyl) ether (**6**), which showed the same two major resonances at 77.5 and 91.2 p.p.m. as before. The two peaks at 83.8 and 101.8 p.p.m. were also present, but at one-third of their previous, relative intensity. The small signal at 87.4 p.p.m. was no longer observed.

Addition of excess of sugar to the solution that gave the spectrum shown in Fig. 2*a*, followed by boiling under reflux for a further 12 h, resulted in the spectrum shown in Fig. 2*c*. Comparison with Fig. 2*a* shows that the peak at 83.8 p.p.m. has disappeared, whereas the resonances at 87.4 and 101.8 p.p.m. both increased in intensity. It thus appears that the resonance at 83.8 p.p.m. is due to unreacted **8**

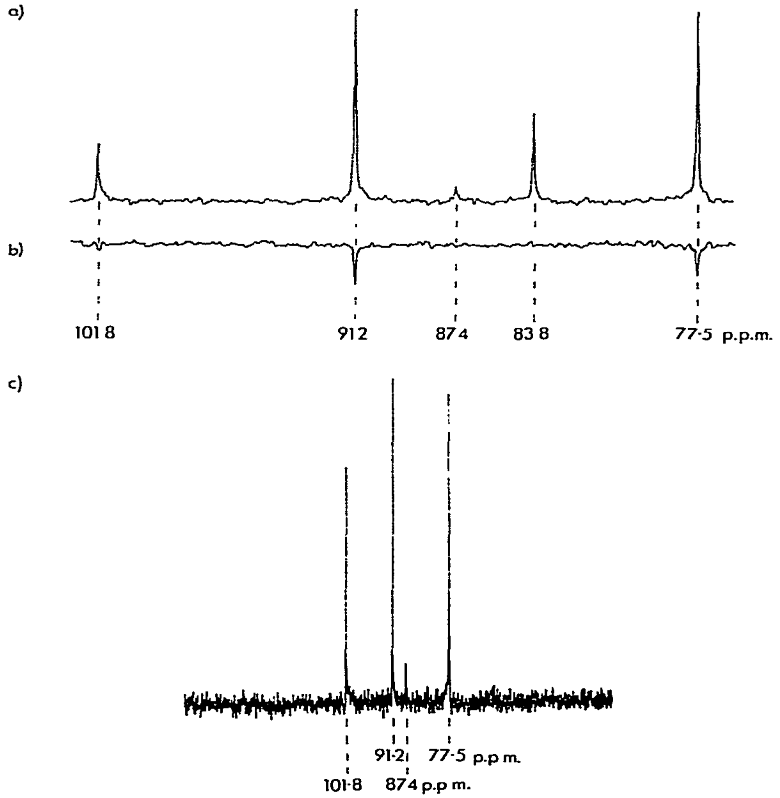


Fig. 2. ^{119}Sn-F.t.n.m.r. spectra of the products of the reaction of bis(tributyltin) oxide with methyl 4,6-*O*-benzylidene-α-D-glucopyranoside in toluene: (*a*) stoichiometric amounts boiled under reflux for 4 h; (*b*) as for (*a*), but with n.O.e; (*c*) solution (*a*) boiled for a further 12 h with excess of carbohydrate.

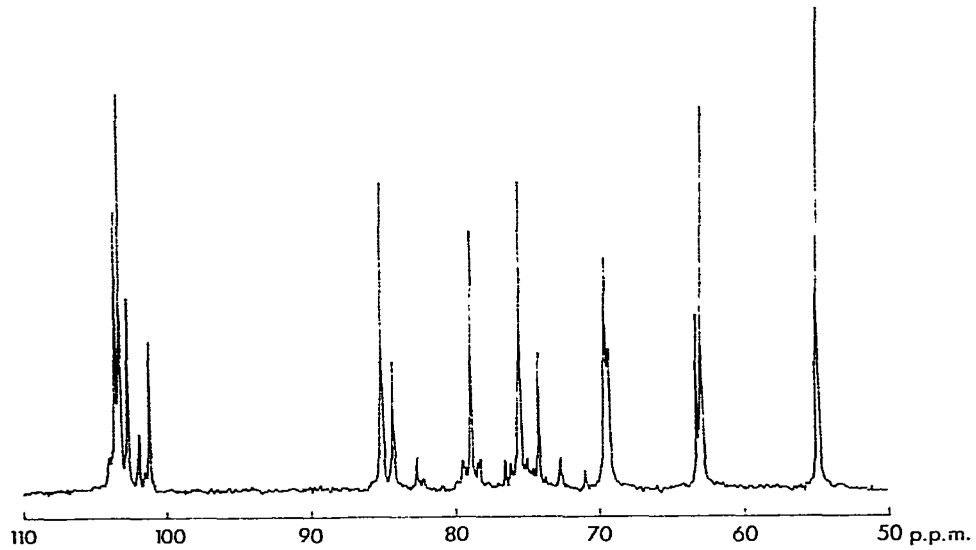


Fig. 3. ^{13}C-F.t.n.m.r. spectrum, showing the ring-carbon region, of the products of the reaction of bis(tributyltin) oxide with methyl 4,6-*O*-benzylidene-α-D-glucopyranoside in toluene (reflux, 4 h) recorded at 25.0 MHz, using 1000 pulses.

TABLE II

^{13}C-CHEMICAL SHIFTS[a] FOR SOLUTIONS OF METHYL 4,6-*O*-BENZYLIDENE-α-D-GLUCOPYRANOSIDE AND ITS TRIBUTYLSTANNYL DERIVATIVES 4–6 IN TOLUENE

Compound	*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*C-7*	*OMe*
Parent sugar	100.4	73.5	72.1	81.5	62.9	69.1	101.9	55.0
4	101.0	74.1	75.4	84.1	63.2	69.2	102.6	54.9
5	[b]	76.3	72.5	82.4	[b]	[b]	[b]	54.9[c]
6	103.0	78.8	75.4	84.9	62.9	69.4	103.4	54.9

[a] In p.p.m. (±0.1) downfield from Me_4Si, measured from the methyl resonance of toluene, taken as 21.3 p.p.m.; chemical shifts of 4, 5, and 6 were recorded for a mixture. [b] Not assignable. [c] Presumed coincident with the methoxyl resonances of 4 and 6.

(see Table I), while the resonances which increased in intensity correspond to the mono-*O*-tributylstannylated sugars. The peak at 101.8 p.p.m. was attributed to the preponderant monosubstituted derivative, the 3-tributylstannyl ether (**4**), by examination of the ^{13}C-n.m.r. spectra of the same solutions (see Fig. 3 and Table II). Similarly, the peak at 87.4 p.p.m. was assigned to the 2-substituted compound **5**, while those at 77.5 and 91.2 p.p.m. were assigned to the groups at positions 2 and 3, respectively, of the disubstituted derivative **6**.

The foregoing spectra indicate that O-3 is much more reactive to initial substitution than O-2. This inference was confirmed by a ^{13}C spectrum run after reaction for 30 min, which showed that **4** and **6** were present in comparable amounts, but that the 2-tributylstannyl ether (**5**) was very much less evident. It seems that the conversion **4**→**6** occurs almost as easily as the initial substitution to form **4**, in contrast to the slow, initial substitution at position 2. This difference in reactivity of HO-2 and HO-3 to tributylstannylation has been noted[11] for other sugars.

Effect of substituents on ^{13}C resonances

The ^{13}C spectrum of methyl 4,6-*O*-benzylidene-α-D-glucopyranoside in deuteriochloroform has been assigned previously[13] and matches the spectrum for a solution in toluene. The largest effects of tributylstannylation on the ^{13}C shifts (see Table III) are at the site of substitution: 3.3 p.p.m. for the C-3 derivative (**4**), 2.8 p.p.m. for the C-2 derivative (**5**), and 5.3 and 3.3 p.p.m. for the diether **6** at C-2 and C-3, respectively. Significant effects are observed at the carbon atom adjacent to the site of substitution, but not necessarily at both adjacent carbon atoms. For instance, the shift of 2.6 p.p.m. for the C-4 signal in **4** contrasts with that of 0.6 p.p.m. for C-2. With **5**, there is an insignificant effect (0.4 p.p.m.) for C-3, but, unfortunately, the C-1 signal was not assignable. For **6**, shifts of 2.6 and 3.4 p.p.m. were found for C-1 and C-4, respectively. The data for **6** may be rationalised in two ways. Starting with **4** and substituting at C-2, there are shifts of 2.0, 0, and 4.7 p.p.m. for C-1, C-3, and C-2, respectively. This pattern follows that for non-substituted, adjacent carbon positions and indicates a larger effect at C-2 when C-3 is tributylstannylated. An alternative approach is to start with **5** and substitute at C-3, where the shifts of 2.9 p.p.m. at C-3 and 2.5 p.p.m. at C-4 follow the original pattern. In this case, the same 2.5-p.p.m. shift is found at C-2, presumably because C-2 was already tributylstannylated.

For **7**, uncertainty in the assignment of the ^{13}C signals for C-2 and C-3 leads to two possible values for the substituent effects. However, the shift changes, with respect to the parent sugar, on dibutylstannylation are as follows: C-1, 5.0; C-2, 0.8 (6.1); C-3, 7.6 (2.3); C-4, 4.0; C-5, 2.8; C-6, 1.9; C-7, 3.9; and OMe, 1.4 p.p.m.; where the figures in parentheses denote the alternative assignment. Substituent effects for **7** are generally larger than those for **4**–**6**.

Since the dimeric structure **11** involves electron donation from O-3→Sn, it would

TABLE III

^{13}C-SUBSTITUENT EFFECTS[a] ON TRIBUTYLSTANNYLATION OF METHYL 4,6-*O*-BENZYLIDENE-α-D-GLUCOPYRANOSIDE

Compound	*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*C-7*	*OMe*
4	0.6	0.6	3.3	2.6	0.4	0.1	0.7	−0.1
5	[b]	2.8	0.4	0.9	[b]	[b]	[b]	−0.1
6	2.6	5.3	3.3	3.4	0.0	0.3	1.5	−0.1

[a] Substituent effect in p.p.m. = δ (tributylstannyl derivative) — δ (parent sugar). [b] Peak not assigned.

be expected that this might lead to a deshielding of C-3, resulting in a significant shift to low field. Thus, the 7.6-p.p.m. substituent effect is the preferred assignment for this carbon resonance. The unusually small shift (0.6 p.p.m.) observed for C-2 presumably results from an unexplained shielding factor in the dimer.

Tin–carbon coupling constants

An interesting feature of the ^{13}C spectra of these derivatives is the appearance of ^{119}Sn satellites, an example of which is shown in Fig. 4. The satellites on C-1, arising from $^{2}J(^{119}Sn\text{-}O\text{-}^{13}C)$, and on C-2, arising from $^{3}J(^{119}Sn\text{-}O\text{-}C\text{-}^{13}C)$, are clearly visible for both anomers, and the magnitude of ^{3}J is less than that of ^{2}J. These couplings thus provide a valuable aid to assignment of the ^{13}C spectra. Although, to our knowledge, no $J(^{119}Sn\text{-}O\text{-}^{13}C)$ couplings have been observed previously, Davies *et al.*[14] observed $^{3}J(^{119}Sn\text{-}O\text{-}C\text{-}^{1}H)$ couplings in tributyltin alkoxides (Bu_3SnOR) only where R is very bulky. This effect was ascribed to a low rate of exchange of the alkoxy moieties in solution between different tin sites, and a similar situation would be expected to occur in the present case, when R is a large carbohydrate residue.

The cyclic substitution in 7 presents problems in the assignment of the couplings,

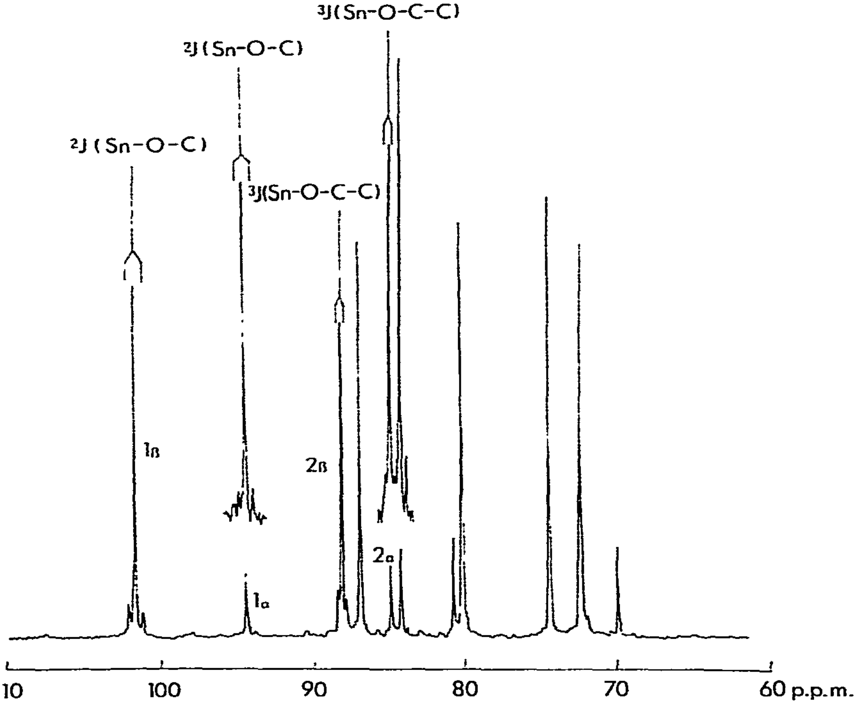


Fig. 4. ^{13}C-F.t.n.m.r. spectrum, showing the ring-carbon region, of the product of the reaction of bis(tributyltin) oxide with 2,3,4,6-tetra-*O*-methyl-D-glucose in toluene, recorded at 25.0 MHz, using 1000 pulses.

because the substituted carbon atoms each have two- and three-bond pathways to the tin atom. The contributions to the observed coupling will add algebraically[15]. The signals for **7** showing 34- and 20-Hz couplings (Table I) are assigned to C-4 and C-1, respectively, on shift arguments, but, unfortunately, similar arguments do not associate the 12-Hz coupling with C-2 or C-3 in particular. The couplings to C-2 and C-3 (12 and < 10 Hz) are low compared to normal two-bond values and, presumably, result from algebraic addition of two- and three-bond contributions that are opposite in sign. In addition, in the ^{13}C spectrum of **7**, the butyl region showed two distinct sets of one-bond Sn-C couplings, indicating the non-equivalence of the butyl groups in the dimer **11**. The couplings were the same for both butyl groups, 614 and 588 Hz for ^{119}Sn and ^{117} Sn, respectively.

SUMMARY

The benefits of the multi-nuclear approach have been demonstrated. The simple form of the ^{119}Sn spectra readily indicates the number, coordination state, and relative amounts of tin species present, although the shifts in the carbohydrate derivatives are not as yet indicative of the position of substitution. The method allowed a qualitative indication of the relative reactivity of OH groups to tributylstannylation. The site of substitution was established *via* the ^{13}C spectra, where the appearance of ^{119}Sn satellites was an essential aid to assignment.

EXPERIMENTAL

The di- and tri-butylstannyl ethers were prepared by azeotropic dehydration of dibutyltin oxide or bis(tributyltin) oxide (**8**) with the appropriate sugar in boiling toluene. Compounds **1–3** and **7** have been described elsewhere[7,8]. Compounds **4–6** were not isolated and the n.m.r. spectra of mixtures were recorded. The organotin-carbohydrates are hydrolysed fairly rapidly by adventitious moisture, and the solutions for n.m.r. measurements were therefore prepared in a glove-box under an atmosphere of dry nitrogen. Toluene was de-gassed with dry nitrogen, prior to dissolution of the organotin-carbohydrate compound.

N.m.r. spectra were recorded at 25° with JEOL FX90Q or JEOL FX100Q instruments, using 10-mm tubes and an internal deuterium lock on ~10% internal hexadeuteriobenzene. It is essential that the ^{119}Sn spectra be recorded under conditions where the nuclear Overhauser effect (n.O.e.) is suppressed. Previous studies[16] have established the importance of intramolecular dipole–dipole relaxation of tin by the alkyl protons in tribultytin chloride, leading to a significant decrease in signal intensity under conditions of proton decoupling. This arises because ^{119}Sn has a negative magnetogyric ratio (*cf.* ^{15}N, ^{29}Si). The dramatic effect of not suppressing the n.O.e. is shown in Fig. 2; there is a stronger n.O.e. on the two larger peaks, giving a negative intensity, than on the three smaller features, their intensity being decreased to zero. Further details of spin–lattice relaxation times (T_1) and n.O. effects of these compounds will be reported elsewhere.

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