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The small-scale preparation and NMR characterization of isotopically enriched organotin compounds

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Synthetic methods for the small-scale laboratory preparation of isotopically enriched dibutyltin dichloride, dibutyltin di-iodide, tributyltin chloride, tributyltin iodide, diphenyltin dichloride, triphenyltin chloride and triphenyltin iodide have been successfully established. Organotin iodides were prepared from redistribution reactions between tin(IV) iodide and the corresponding tetraorganotin, with the exception of dibutyltin di-iodide, which was prepared directly from the reaction between tin metal and iodobutane. The development of novel procedures for the dealkylation/dearylation of tetraorganotins by acid hydrolysis produced superior yields of tributyltin chloride and diphenyltin dichloride in comparison with redistribution reactions. Organotin iodide redistribution reaction products were converted to their chloride analogues via the fluoride salts using an aqueous ethanolic solution of potassium fluoride. The insolubility of organotin fluoride salts was exploited to isolate and purify the isotopically enriched compounds, and to prevent losses during the purification procedure.

The nuclear magnetic resonance (NMR) spectroscopic study of 'natural abundance' and isotopically enriched organotin compounds gave proton (^{1}H) and carbon-13 (^{13}C) spectra for butyltins, $Bu_{4-n}SnX_n$, and phenyltins, $Ph_{4-n}SnX_n$ (X = I, Cl), allowing the assignment of ^{1}H and ^{13}C chemical shifts, and ^{119}Sn–^{13}C and ^{117}Sn–^{13}C coupling constants. The ^{13}C NMR spectroscopic analysis of ^{117}Sn-enriched organotin compounds has allowed the assignment of certain resonances and tin–carbon coupling constants which were previously unobservable. The spectral patterns show that $\delta(^{1}H)$ and $\delta(^{13}C)$ values are sensitive to structural changes, and that ^{13}C shielding decreases with an increase in the electronegativity of the substituent. The tin–carbon coupling constants are also sensitive to structural changes, and for alkyl and aryl compounds the couplings decrease in the order $^{1}J > {}^{3}J > {}^{2}J > {}^{4}J$. The ^{13}C chemical shift values and the magnitude of tin–carbon coupling constants are shown to be solvent-dependent. The ^{13}C spectra of the isotopically enriched compounds show that the degree of isotopic enrichment and the nature of the isotope used (magnetic or non-magnetic) are reflected in the spectral pattern obtained. Copyright © 2000 John Wiley & Sons, Ltd.

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INTRODUCTION

During a recent study to develop high-accuracy analytical methods for measurement of organotin compounds in environmental matrices by isotope dilution analysis, isotopically enriched organotin compounds were required as internal standards. Chemical measurement procedures based on isotope dilution mass spectrometry (ID–MS) offer the possibility of very accurate results, with clear levels of uncertainty, and traceability to the SI unit for amount of substance, the mole.[1–4] When used for organotin compounds enriched in low-abundance naturally occurring isotopes, such as ^{116}Sn or ^{117}Sn, on-line ID–MS can provide a method for the accurate determination of organotin compounds of

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environmental concern. This is because ID analysis overcomes a number of sample matrix effects which can affect conventional instrument calibration. In spite of the substantial benefits on offer, ID analysis remains an under-exploited method of analysis, primarily because of the lack of suitable enriched internal-calibration standards. With this in mind, we undertook a series of experiments to assess the possibility of producing isotopically enriched organotin compounds under standard laboratory conditions.

The high cost of the enriched starting material for synthesis of isotopically enriched organotin compounds necessitates the use of only small quantities. Synthetic methods for the manufacture of organotins are readily available,[5,6] but application of these methods on a small scale (<1 g) revealed several difficulties. The use of air- and moisture-sensitive compounds, and the difficulties of accurate measurement and transfer of reactive starting materials, pose a major problem when used on a small scale; many methods involve the use of starting materials (e.g. Bu_3SnOMe,[7] Na-Sn-Zn,[8] Ph_3SnH[9]) which cannot be obtained in an isotopically enriched form without loss of expensive enriched material; and methods of separation such as fractional distillation are not viable on a small scale, because of the chemical proximity of reaction product mixtures, which results in significant loss of labelled compounds. Other problems encountered include unwanted reactions resulting from catalysis by decomposition products, and the difficulty of separation of organotins from equilibrium mixtures of reaction products.

Synthetic routes for the successful small-scale preparation of isotopically labelled organotins therefore require, wherever possible, the use of reasonably stable reagents, along with maintenance of acceptable reaction yields, ease of product isolation and generic preparation apparatus. The current work has developed such methods for the small-scale preparation of isotopically labelled butyl- and phenyl-substituted organotins, with characterization of products by NMR spectroscopy.

EXPERIMENTAL

Reagents for synthesis

Isotopically enriched ^{116}Sn (granulated) and ^{117}Sn (foil 0.3 mm thick) were obtained from AEA Technology plc (Isotope Section, 220 Harwell, Didcot OX11 0RA, Oxfordshire, UK). All other starting materials and reagents were supplied by Aldrich Chemical Company Ltd (The Old Brickyard, New Road, Gillingham, Dorset SP8 4XT, UK) unless otherwise stated. Merck pre-coated (0.2 mm) silica gel 60 F_{254} self-indicating thin-layer chromatography plates were supplied by BDH Chemicals Ltd, (Merck Ltd, Hunter Boulevard, Magna Park, Lutterworth, Leics. LE17 4XN, UK) together with the corresponding 'silica gel 60' (230–400 mesh) for larger-scale column separations.

^{116}Sn-labelled tin (IV) iodide

The isotopic composition of the ^{116}Sn used was reported to be: ^{112}Sn, <0.02%; ^{114}Sn, <0.01%; ^{115}Sn, 0.04%; ^{116}Sn, 98.0%; ^{117}Sn, 0.68%; ^{118}Sn, 0.70%; ^{119}Sn, 0.09%; ^{120}Sn, 0.31%; ^{122}Sn, 0.04%; ^{124}Sn, 0.14% AEA Technology plc, Isotope Section, 220 Harwell, Didcot, Oxon OX11 0RA, UK.

A mixture of 0.5014 g (4.3 mmol) of ^{116}Sn and 2.0 g iodine (7.85 mmol) was introduced into a 50 ml round-bottomed flask containing glacial acetic acid (10 ml) and acetic anhydride (10 ml). A small crystal of potassium iodide was added as a catalyst. The flask was attached to a condenser and heated gently until a vigorous reaction was initiated. The mixture was gently held at reflux for 0.5 h. The reaction mixture was allowed to cool until orange crystals of tin(IV) iodide began to precipitate. The orange crystalline product was filtered quickly using a small Büchner pump and recrystallized from chloroform. Sufficient hot chloroform was added to dissolve the solid, and the solution was filtered again to remove undissolved tin. The solution was concentrated under vacuum until a faint orange precipitate appeared, and allowed to cool. The resulting orange crystals were filtered and dried in a vacuum desiccator. The yield of $^{116}SnI_4$ was 2.247 g (83%), m.p. 143 °C (lit.[10] 143 °C).

^{117}Sn-labelled tin(IV) iodide

^{117}Sn-enriched tin(IV) iodide was prepared similarly to the ^{116}Sn-labelled compound described above but using 1.464 g (12.5 mmol) of ^{117}Sn. The isotopic composition of the ^{117}Sn used was reported[10] to be: ^{112}Sn, <0.03%; ^{114}Sn, <0.01%; ^{115}Sn, <0.05%; ^{116}Sn, 7.6 ± 0.1%; ^{117}Sn, 92.1 ± 0.2%; ^{118}Sn, 0.2 ± 0.1%; ^{119}Sn, 0.1 ± 0.1%; ^{120}Sn, <0.04%; ^{122}Sn, <0.01%; ^{124}Sn, <0.01%. The yield

of recrystallized $^{117}SnI_4$ was 5.142 g (73%), m.p. 143 °C (lit.[10] 143 °C).

^{116}Sn-labelled tetrabutyltin

A solution of *n*-bromobutane (0.896 g, 6.54 mmol) was prepared in diethyl ether (20 ml). This solution was introduced dropwise, with stirring, into a 100-ml round-bottomed flask containing a slight excess of magnesium (0.17 g, 7 mmol) in diethyl ether (10 ml), under a nitrogen atmosphere. After the addition was complete, the mixture was warmed to reflux and stirred for 15 min to form the Grignard reagent. ^{116}Sn-labelled tin(IV) iodide (1.02 g, 1.63 mmol) was dissolved in diethyl ether (30 ml) and added dropwise to the Grignard reagent. The reaction was left to be stirred for 2 h and became very pale orange as the remaining tin(IV) iodide was consumed. Any unreacted Grignard reagent was carefully hydrolysed with water (10 ml) and unreacted magnesium was removed by filtration. The products were treated with a minimum volume (5 ml) of a 20% (w/v) solution of potassium fluoride in 60% aqueous ethanol, according to the procedure described by Prince,[11] to remove any organotin halides as insoluble fluoride salts. The fluoride salts were collected by filtration and the organic fraction was separated from the aqueous fraction. The aqueous fraction was extracted with diethyl ether (2×10 ml). The combined organic fractions were dried ($MgSO_4$), and the solvent was removed under vacuum to yield 0.488 g (86%) of ^{116}Sn-labelled tetrabutyltin as a colourless oil, b.p. 142–145 °C (10 mmHg) [lit.[12] 147–149 °C (12 mmHg)]. For the NMR results, see Table 1.

^{117}Sn-labelled tetrabutyltin

n-Butylmagnesium bromide was prepared as described above but using *n*-bromobutane (1.918 g, 14 mmol) and magnesium (0.384 g, 16 mmol). The reaction between the Grignard reagent and ^{117}Sn-labelled tin(IV) iodide (1.714 g, 2.7 mmol) produced 0.792 g ^{117}Sn-labelled tetrabutyltin as a colourless oil (83%). For the NMR results, see Table 1.

^{116}Sn-labelled tributyltin iodide (redistribution reaction)

^{116}Sn-labelled tin(IV) iodide (0.2055 g, 0.329 mmol) was added to ^{116}Sn-labelled tetrabutyltin (0.34 g, 0.985 mmol) in a 50-ml round-bottomed flask. The mixture was heated to 220 °C under a nitrogen atmosphere and the resulting melt was stirred for 3 h. The reaction products were dissolved in hexane (3×15 ml) and the insoluble products were removed by filtration. The hexane was removed under vacuum to leave a straw-coloured oil. NMR spectroscopic analysis showed this oil consisted of ~70% tributyltin, iodide ~20% tetrabutyltin and ~10% mono- and di-butyltin products. Chromatographic separation of products (silica gel/heptane) yielded 0.178 g of tributyltin iodide (33%). For the NMR results, see Table 1.

^{117}Sn-labelled tributyltin chloride (acid hydrolysis)

Concentrated hydrochloric acid (conc. HCl) (1 g, 13.9 mmol, specific gravity 1.18) was added dropwise to ^{117}Sn-labelled tetrabutyltin (0.5055 g, 1.46 mmol) in a 10 ml round-bottomed flask. The reagents were protected from light (amber glassware) and moisture and stirred at room temperature under a nitrogen atmosphere for 72 h. The reaction products were extracted with diethyl ether (30×20 ml). The combined ether extracts were dried ($MgSO_4$) and the ether was removed under vacuum. NMR spectroscopic analysis showed the resulting oil to be a mixture of tributyltin chloride (90%) and unreacted tetrabutyltin (10%).

^{117}Sn-labelled tributyltin chloride was purified from the fluoride salt according to the following general procedure described by Prince:[11] tributyltin chloride was treated with a minimum volume (5 ml) of a 20% (w/v) solution of potassium fluoride in 60% aqueous ethanol, and separated from tetrabutyltin as the insoluble fluoride salt. The fluoride was isolated by filtration, washed with a minimum of dry diethyl ether and dried in a vacuum oven at 40 °C for 1 h to yield tributyltin fluoride as a fine white crystalline powder. The fluoride was treated with concentrated hydrochloric acid (2 ml) and extracted with diethyl ether (3×15 ml). The combined ether extracts were dried ($MgSO_4$), and the ether was removed under vacuum to yield 0.331 g (70%) of tributyltin chloride as a colourless oil, b.p. 140–142 °C (5 mmHg) [lit.:[13] 130–132 °C (4 mmHg)]. For the NMR results, see Table 1.

^{117}Sn-labelled dibutyltin dichloride

^{117}Sn-labelled dibutyltin diiodide was prepared according to the procedure described by Oakes and Hutton.[14] *n*-Butyl iodide (1.789 g, 9.72 mmol) was mixed with *n*-butanol (0.085 g, 1.15 mmol) and added to ^{117}Sn foil (0.5171 g, 4.42 mmol) and

Table 1 NMR spectroscopic analysis of butyltins (Bu_nSnX_{4-n})

Compound		C1			C2			C3			C4		
		^{13}C peak	^{117}Sn–^{13}C satellites	^{119}Sn–^{13}C satellites	^{13}C peak	^{117}Sn–^{13}C satellites	^{119}Sn–^{13}C satellites	^{13}C peak	^{117}Sn–^{13}C satellites	^{119}Sn–^{13}C satellites	^{13}C peak	^{117}Sn–^{13}C satellites	^{119}Sn–^{13}C satellites
Bu_4Sn	(ppm)	8.8	6.37, 10.97	11.04, 6.47	29.3	29.2, 29.5[a]		27.5	27.1, 28.8[a]		13.7	No data[d]	
	Area (%)	95	3.9, 4.0	4.8, 4.2	71.3	7.2, 8.0		79.1	6.9, 6.6		100		
	J^{13}C–Sn (Hz)	—	(−) 299[b]	(−) 312.5	—	19.5		—	52.5		—		
$Bu_4{}^{116}Sn$	(ppm)	8.8	—	—	29.3	—	—	27.4	—	—	13.7	—	—
	Area (%)	100	—	—	98	—	—	81	—	—	95	—	—
	J^{13}C–Sn (Hz)	—	—	—	—	—	—	—	—	—	—	—	—
$Bu_4{}^{117}Sn$	(ppm)	8.8	6.6, 11	—	29.3	29.5, 29.2	—	27.4	27.1, 27.8	—	13.7	No data[d]	
	Area (%)	8.62	73.7, 72.1	—	14.18	56.8, 74.9	—	9.87	61, 73.9	—	100		
	J^{13}C–Sn (Hz)	—	(−) 299.1	—	—	19.5	—	—	50	—	—		
Bu_3SnCl	(ppm)	17.4	15, 19.8	14.9 , 19.9	27.7	27.5, 27.9[a]		26.7	26.2, 27.1[a]		13.4	No data[d]	
	Area (%)	100	3.5, 4.6	4.0, 4.4	72.8	9.6, 9.2		98.1	5.4, 5.6		90.9		
	J^{13}C–Sn (Hz)	—	(−) 322.3	(−) 338.1	—	23.1		—	63.5		—		
$Bu_3{}^{117}SnCl$	(ppm)	17.5	15.1, 19.86	—	27.8	27.64, 27.96	—	26.8	26.35, 27.26	—	13.55	13.53, 13.57	—
	Area (%)	15.8	80, 85.8	—	17.1	90.6, 93.9	—	14.1	91.8, 92.3	—	No data[c]	100, 99	—
	J^{13}C–Sn (Hz)	—	(−) 322.2	—	—	22	—	—	62.3	—	—	2.5	—
Bu_3SnI	(ppm)	16.44	14.2, 18.6	14.1, 18.7	29.25	28.95, 29.3[a]		26.77	26.16, 27.15[a]		13.65	No data[d]	
	Area (%)	98.1	4.1, 4.3	4.5, 4.8	90	7.9, 8.9		83	5.0, 5.2		100		
	J^{13}C–Sn (Hz)	—	(−) 301.46[b]	(−) 315.1	—	23.35		—	63.69			—	
$Bu_3{}^{116}SnI$	(ppm)	16.44	—	—	29.28	—	—	26.80	—	—	13.68	—	—
	Area (%)	100	—	—	89.2	—	—	94.9	—	—	89.7	—	—
	J^{13}C–Sn (Hz)	—	—	—	—	—	—	—	—	—	—	—	—
Bu_2SnCl_2	(ppm)	26.54	23.6, 29.51	23.45, 29.6	26.81	26.54, 27.06[a]		26.24	25.64, 26.8[a]		13.44	No data[d]	
	Area (%)	95.1	4.5, 5.1	5.0, 2.9	99	8.0, no data[b]		90.6	No data[c], 8.0		100		
	J^{13}C–Sn (Hz)	—	(−) 401.7	(−) 419.8	—	34.2		—	80.6		—		
$Bu_2{}^{117}SnCl_2$	(ppm)	26.53	23.56, 29.47	—	26.83	26.6, 27.06	—	26.26	25.66, 26.83	—	13.44	13.43, 13.46	—
	Area (%)	15.8	79.3, 84.4	—	No data[c]	71.1, 83.2	—	11.05	65, 71.9	—	No data	90.5, 100	—
	J^{13}C–Sn (Hz)	—	(−) 401.6	—	—	31.7	—	—	79.4	—	—	2.5	—
Bu_2SnI_2	(ppm)	16.37	14.12, 18.5	14.08, 18.6	29.06	28.71, 29.29[a]		26.54	26.02, 27.23[a]		13.53	No data[d]	
	Area (%)	92.1	3.5, 4.2	4.8, 4.5	89	3.8, 4.0		84	5.0, 5.2		100		
	J^{13}C–Sn (Hz)	—	(−) 300.3	(−) 313.8	—	24		—	64.7		—		
$BuSnCl_3$	(ppm)	33.17	28.61, 37.74	28.39, 37.95	26.72	26.27, 27.17[a]		25.55	24.71, 26.42[a]		13.26	No data	
	Area (%)	92.3	5.2, 4.7	4.9, 5.0	85	4.5, 4.3		88.2	3.9, 5.0		100		
	J^{13}C–Sn (Hz)	—	(−) 620.1	(−) 649.4	—	61.1		—	116.0		—		

[a] ^{117}Sn–^{13}C and ^{119}Sn–^{13}C satellites have merged.
[b] Negative values assigned to ^1J (Sn–C).
[c] No data: superimposed signals.
[d] No data: Sn-^{13}C satellites have merged with ^{13}C peak.

lithium (0.0026 g, 0.38 mmol) in a 100 ml round-bottomed flask under a nitrogen atmosphere. The foil was cut as finely as possible using a stainless steel scalpel on a ceramic plate to obtain a maximum surface area for reaction. The mixture was heated under reflux at 165 °C for 8 h. In a change to the reported procedure which used fractional distillation to obtain dibutyltin dichloride, the reaction products were dissolved in pentane (100 ml) and filtered to remove any unreacted tin. The pentane was removed under vacuum to leave an orange oil. NMR spectroscopic analysis of this oil showed that dibutyltin diiodide was the principal product; for the results see Table 1.

The resulting oil was treated with 5 ml of potassium fluoride in aqueous ethanol to obtain the difluoride salt, which was immediately precipitated as a yellow solid and was collected by filtration. The yellow solid was dried over P_2O_5 at 55 °C for 2 h becoming white as free iodine, a by-product of the reaction, was liberated. Dibutyltin dichloride was obtained from the fluoride salt by the general procedure described earlier, and the resulting white solid was recrystallized twice from petroleum ether (b.p. 60–80 °C) to yield 0.711 g (53%) of dibutyltin dichloride as white crystalline platelets, m.p. 40–41 °C (lit.:[15] 39–41 °C).

^{117}Sn-labelled tetraphenyltin

A solution of bromobenzene (3.14 g, 20 mmol) in diethyl ether (20 ml) was added dropwise with stirring to a slight excess of magnesium (0.55 g, 26 mmol) in diethyl ether (10 ml) under a nitrogen atmosphere. After the addition was complete, the mixture was warmed to reflux and stirred for 15 min to prepare the Grignard reagent. The solution developed a steely grey coloration and became dark brown as the reaction proceeded. The solution was allowed to cool to room temperature, and ^{117}Sn-labelled tin(IV) iodide (2.5 g, 3.98 mmol) dissolved in ether (30 ml) was added dropwise to the reaction mixture. The tin(IV) iodide was consumed with the formation of a fine white precipitate, and an additional 2 h period of reflux was continued.

The white precipitate was collected by filtration after the Grignard reagent had been hydrolysed with water (10 ml). The solid was dissolved in dichloromethane (50 ml) and filtered to remove unreacted magnesium and other insoluble impurities. The dichloromethane was removed under vacuum to leave a white solid, which was recrystallized twice from ethanol to yield 1.427 g (84%) of white crystalline tetraphenyltin, n.p. 224–226 °C (lit.:[16] 225.7 °C). For the NMR results, see Table 2.

^{117}Sn-labelled triphenyltin chloride (redistribution reaction)

^{117}Sn-labelled tin(IV) iodide (0.1566 g, 0.25 mmol) was added to ^{117}Sn-labelled tetraphenyltin (0.32033 g, 0.752 mmol) in a 50-ml round-bottomed flask. The mixture was heated to 220 °C under a nitrogen atmosphere and the resulting melt was stirred for 3 h. The reaction products were dissolved in ethanol and a yellow/brown precipitate (0.22 g) was collected by filtration. The ethanol extract was dried and triphenyltin chloride was prepared from the fluoride salt as described for tributyltin chloride, above. The resulting white solid was recrystallized twice from ethanol to yield 0.054 g (11%) of triphenyltin chloride as white crystalline platelets, m.p. 104–105.5 °C (lit.:[15] 106 °C). For the NMR results, see Table 2.

^{117}Sn-labelled diphenyltin dichloride (acid hydrolysis)

^{117}Sn-labelled diphenyltin dichloride was prepared from ^{117}Sn-labelled tetraphenyltin (0.4 g, 1.17 mmol) and HCl (1 g, 13.9 mmol, specific gravity 1.18) as described above for tributyltin chloride. The product was recrystallized from petroleum ether (b.p. 60–80 °C) to yield 0.322 g (63%) of diphenyltin dichloride as white prisms. For the NMR results, see Table 2.

Concentrated hydrochloric acid (1 g, 13.9 mmol, specific gravity 1.18) was added dropwise to ^{117}Sn-labelled tetraphenyltin (0.4 g, 1.17 mmol) in a 10-ml round-bottomed flask. The reagents were protected from light and moisture under a nitrogen atmosphere and stirred at room temperature for 48 h. The reaction products were extracted with diethyl ether (3×20 ml). The combined ether fractions were dried ($MgSO_4$) and the ether was removed under vacuum. Diphenyltin dichloride was prepared from the difluoride salt as described and recrystallized from petroleum ether (b.p. 60–80 °C) to yield 0.322 g (63%) of diphenyltin dichloride as white prisms, m.p. 40–42 °C (lit.:[6] 42 °C). For the NMR data, see Table 2.

Instrumentation

A JEOL EX270 MHz NMR spectrometer was used to obtain ^{1}H spectra at 270 MHz, and ^{13}C spectra at

Table 2 NMR spectroscopic analysis of phenyltins (Ph_nSnCl_{4-n})

Compound		C1			C2, C6			C3, C5			C4		
		^{13}C peak	^{117}Sn–^{13}C satellites	^{119}Sn–^{13}C satellites	^{13}C peak	^{117}Sn–^{13}C satellites	^{119}Sn–^{13}C satellites	^{13}C peak	^{117}Sn–^{13}C satellites	^{119}Sn–^{13}C satellites	^{13}C peak	^{117}Sn–^{13}C satellites	^{119}Sn–^{13}C satellites
Ph_4Sn	(ppm)	137.93	—[a]	—[a]	137.23	137.1, 137.6[c]		128.63	128.3, 129.1[c]		129.13	129.1, 129.3[c]	
	Area (%)	12.72	—[a]	—[a]	100	8.5, 6.8		92.8	9.16, 9.0		46.37	4.0, 4.0	
	$J^{13}C$–Sn (Hz)	—	—[a]	—[a]	—	37.4		—	51.4		—	12.5	
$Ph_4{}^{117}Sn$	(ppm)	137.95	141.65, 134.2	—	137.23	136.96, 137.5	—	128.63	128.27, 129	—	129.13	129, 129.2	—
	Area (%)	2	10.9, 7.6	—	12.1	57.5, 63.2	—	11.9	65.7, 48.7	—	8.27	38, 29.3	—
	$J^{13}C$–Sn (Hz)	—	(−) 506.6[b]	—	—	36.6	—	—	47.1	—	—	11	—
Ph_3SnCl	(ppm)	137.25	—[a]	—[a]	136.08	135.72, 136.44[c]		129.23	128.64, 129.6[c]		130.46	130.35, 130.55[c]	
	Area (%)	13.8	—[a]	—[a]	98.62	8.6, 8.1		100	7.6, 7.7		53.4	7.6, 6.0	
	$J^{13}C$–Sn (Hz)	—	—[a]	—[a]	—	49		—	64.7		—	13.5	
$Ph_3{}^{117}SnCl$	(ppm)	—[a]	132.9, 141.56	—	136.1	135.7, 136.44	—	129.11	128.66, 129.56	—	130.44	130.35, 130.55	—
	Area (%)	—[a]	12.3, 10.5	—	12.9	60.9, 68.7	—	16.6	73.8, 78.4	—	9.1	47.6, 42	—
	$J^{13}C$–Sn (Hz)	—	(−) 588.4	—	—	48.9	—	—	61	—	—	13.5	—
Ph_2SnCl_2	(ppm)	136.86	—[a]	—[a]	135.0	134.54, 135.47[c]		129.69	129.1, 130.31[c]		131.81	131.68, 131.93[c]	
	Area (%)	12.6	—[a]	—[a]	89.4	6.8, 8.4		100	5.8, 7.0		67.1	6.0, 6.8	
	$J^{13}C$–Sn (Hz)	—	—[a]	—[a]	—	63.4		—	84.2		—	17.1	
$Ph_2{}^{117}SnCl_2$	(ppm)	136.86	131.32, 142.4	—	134.97	134.52, 135.42	—	129.67	129.06, 130.28	—	131.79	131.66, 131.91	—
	Area (%)	1.6	11.5, 8.6	—	15.5	75.7, 98	—	17.3	100, 92.7	—	10.2	53.9, 53	—
	$J^{13}C$–Sn (Hz)	—	(−) 753.1	—	—	61.1	—	—	83.1	—	—	17.1	—
$PhSnCl_3$	(ppm)	135.96	—[a]	—[a]	133.94	133.39, 134.52[c]		130.37	129.49, 130.71	130.08, 131.3	133.19	133.01, 133.39[c]	
	Area (%)	12.3	—[a]	—[a]	85	8.6, 9.0		100	7.1, 7.0	9.2, 8.1	49.4	6.5, 7.1	
	$J^{13}C$–Sn (Hz)	—	—[a]	—[a]	—	76.9		—	120.9	125.7	—	25.6	

[a] Intensity of quaternary carbon peak/satellite is too low to be observed.
[b] Negative values assigned to ^1J (Sn–C).
[c] ^{117}Sn–^{13}C and ^{119}Sn–^{13}C satellites have merged.

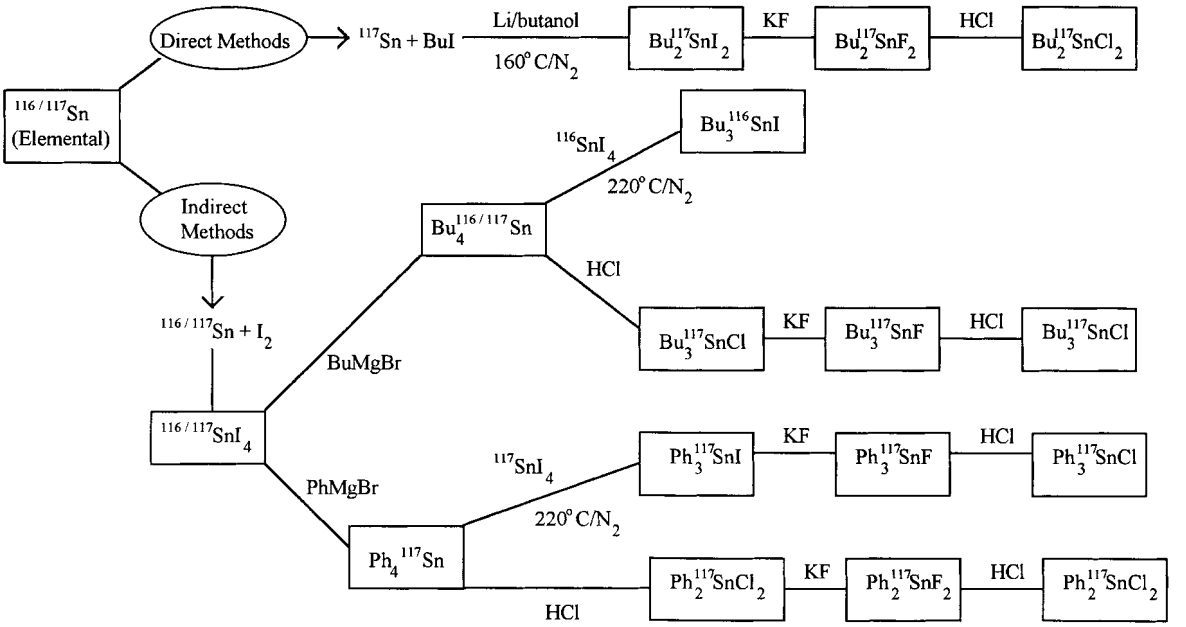

Figure 1 Methods used for the small-scale preparation of isotopically enriched organotin compounds.

67.8 MHz. Samples were prepared in deuterated chloroform ($CDCl_3$) or deuterated methanol (CD_3OD) in 5-ml NMR tubes. For ^1H spectra, samples were externally referenced to the tetramethylsilane (TMS) singlet at 0 ppm. For ^{13}C spectra, samples were referenced to the ^{13}C triplet at 77.0 ppm in $CDCl_3$, and the ^{13}C multiplet at 49.8 ppm in CD_3OD.

RESULTS AND DISCUSSION

Synthetic considerations

The reactions used to prepare isotopically enriched organotin compounds were selected from available literature methods according to the following criteria.

(a) Elemental tin must be used as a starting material.
(b) The use of volatile air-, light- and moisture-sensitive materials (e.g. $SnCl_4$) should be avoided wherever possible.
(c) Purification procedures involving wasteful separation methods (e.g. vacuum distillation) should be avoided.

The synthetic procedures developed for the preparation of isotopically enriched organotins are outlined in Fig. 1.

Direct synthetic procedures

Direct methods were used wherever possible to minimize the number of reactions and purification procedures required to prepare the organotin compounds. Direct methods for the synthesis of phenyltin halides from tin metal were unavailable except for a single method described by Nad and Kocheshkov.[17] This procedure was not attempted because of the problems associated with the small-scale separation of organotin products from the phenylmercury reagent. Methods described by Sisido *et al.* for the direct synthesis of di- and tributyltin halides using alkyl halide, iodine and an organic base[18] were used in an attempt to synthesize the corresponding phenyltin halides, but were unsuccessful. Cognate procedures for the preparation of di- and tri-phenyl halides were also developed from the direct synthesis of di- and tribenzyltin halides,[19,20] but confirmed that monosubstituted phenylhalides (PhX; X = Cl, Br, I) did not react with tin in boiling toluene, water or butanol. In the absence of a temperature-controlled autoclave and high-speed stirrer, the direct synthesis of di- and tri-butyltin halides using the above methods[20] were also unsuccessful.

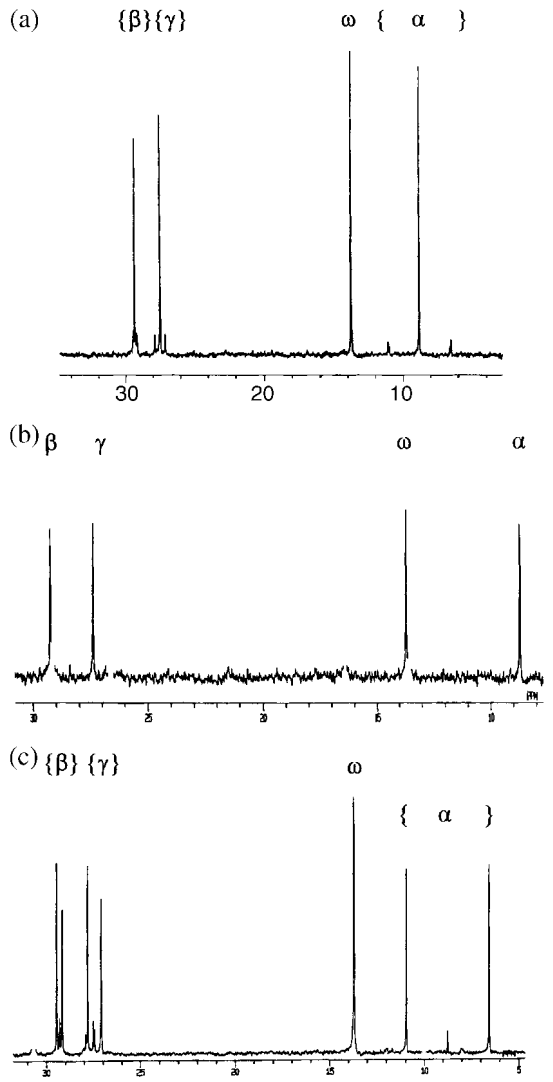

Figure 2 Comparison of the ^{13}C NMR spectra of (a) 'natural abundance' tetrabutyltin, (b) ^{116}Sn isotopically enriched tetrabutyltin and (c) ^{117}Sn isotopically enriched tetrabutyltin. Carbon signals are denoted by Greek symbols; braces show the extent of the Sn–^{13}C satellites associated with each carbon atom.

Dibutyltin di-iodide was prepared directly from tin metal using the procedure described by Oakes and Hutton[14] (Fig. 1). The use of finely cut, powdered or granulated tin was essential to ensure that the tin metal was consumed during the reaction. The procedure was modified to obtain dibutyltin dichloride (DBT) from the fluoride salt after treatment with potassium fluoride in aqueous ethanol. It was found that dibutyltin difluoride was appreciably soluble in aqueous ethanol and a minimum of reagent was used in order to prevent losses. During the conversion of the dried fluoride salt to the dichloride using concentrated HCl, the fluoride was dispersed in solution to ensure complete reaction, and to prevent a waxy coating of dichloride from inhibiting further reaction between the dibutyltin difluoride and HCl.

Indirect synthetic procedures

Tributyltin chloride (TBT), tributyltin iodide (TBTI), triphenyltin chloride (TPT) and diphenyltin dichloride (DPT) were all prepared using indirect methods by which three or more reaction procedures were used to produce each compound (Fig. 1).

The first stage of the indirect synthetic route requires the preparation of tin(IV) halide. Tin(IV) chloride is generally the preferred starting material for the synthesis of tetraorganotins[21–23] and organotin halides.[24–27] However, this highly reactive compound is volatile and very air/moisture-sensitive, and was not suitable for small-scale synthetic procedures. Tin(IV) iodide, although moisture-sensitive, is a moderately air-stable orange solid and was used as the starting material for the second stage of indirect synthesis; the Grignard preparation of tetraorganotin compounds. Tetrabutyltin and tetraphenyltin were prepared from tin(IV) iodide and the corresponding Grignard reagent (RMgBr) using the general method described by Marr *et al.*[12]

For the third stage of the indirect route, organotin halides were prepared from symmetrical tetraorganotin starting materials either by redistribution reactions between tin(IV) iodide and tetraorganotins, or dealkylation/dearylation reactions between concentrated hydochloric acid and tetraorganotins.

The final stage of preparation involves the conversion of organotin iodides to organotin chlorides (redistribution reaction products only), and further purification of organotin chlorides. In each case, the respective compounds were converted to their insoluble fluoride salts, isolated by filtration, washed with solvent, dried and converted back to the chloride using concentrated HCl (Fig. 1).

Redistribution reactions for the preparation of organotin halides produced reaction mixtures which were often difficult to separate and characterized by the presence of tarry residues and inorganic decomposition products; alternative methods of preparation were investigated to resolve this problem. During a series of experiments to monitor the stability of organotins in a range of

solvents, it was noticed that tetraphenyltin, tetrabutyltin and triphenyltin chloride all decomposed in the presence of concentrated hydrochloric acid. NMR spectroscopic analysis of products showed that reactions [1]–[3] had occurred.

$$Ph_4Sn + HCl \rightarrow Ph_3SnCl + PhH \quad [1]$$

$$Ph_3SnCl + HCl \rightarrow Ph_2SnCl_2 + PhH \quad [2]$$

$$Bu_4Sn + HCl \rightarrow Bu_3SnCl + BuH \quad [3]$$

An investigation of the methods available for the synthesis of organotin halides from tetraorganotins revealed two methods for the synthesis of phenyltin halides using hydrochloric acid.[28,29] These methods involve the use of concentrated HCl as a reagent in chloroform,[28] and dry HCl gas administered into a refluxing benzene solution (adapted from Kipping's experiment[30,31]). Levchuck *et al.* describe methods for the preparation of methyltin halides using HP.[32] Significantly, no methods for the preparation of butyltin halides using hydrogen halides were found. The reaction between tetraphenyltin and an excess of concentrated HCl proceeded via the trisubstituted compound to completion, producing a virtually quantitative yield of diphenyltin dichloride. However, the reaction between tetrabutyltin and an excess of concentrated HCl only produced tributyltin chloride as the sole product of the reaction. This was confirmed by the unsuccessful attempt to prepare dibutyltin dichloride from tributyltin chloride using an excess of concentrated HCl under the same conditions.

The development of these novel methods allowed the production of superior yields in comparison with the redistribution reactions between tin(IV) iodide and tetraorganotins, and the organotin chlorides were easily isolated from the reaction products by conversion to their insoluble fluoride salts. The above methods were used to prepare ^{117}Sn-labelled diphenyltin dichloride and ^{117}Sn-labelled tributyltin chloride. Redistribution reactions were used for the preparation of ^{116}Sn-labelled tributyltin iodide and ^{117}Sn-labelled triphenyltin iodide.

Interpretation of NMR spectra

The ^{13}C chemical shifts of *n*-tetrabutyltin, *n*-tributyltin chloride, *n*-dibutyltin dichloride and *n*-butyltin trichloride were obtained using $CDCl_3$ as solvent during the present study. These compounds have previously been assigned in CCl_4,[33–35] and the values obtained are very similar. The chemical shift differences observed are consistent with observations made by Barbieri and Tadder,[36] who found that spectral parameters are strongly dependent on the electron donor strength of the solvent used.

Comparatively few NMR studies have been made for aryltin compounds because these compounds have low solubilities and generally give rise to complicated spectra. The proton spectra of $Ph_{4-n}SnCl_n$ ($n = 1$–4) in CCl_4 have been determined by Maire and Hemmert.[37] The carbon spectra of tetraphenyltin and diphenyltin dichloride in $CDCl_2$ have been determined by McFarlane *et al.*[38] and Mitchell[34] respectively.

The spectral patterns for butyltins, $Bu_{4-n}SnCl_n$, and phenyltins, $Ph_{4-n}SnCl_n$, show that $\delta(^{13}C)$ values are sensitive to structural changes. Chemical shift values for these organotin halides (Tables 1 and 2) show that as the organic substituents are replaced by electronegative chlorine atoms, the tin atom becomes progressively more deshielded, resulting in the observed deshielding of the ^{13}C resonances. This is consistent with the work of Mitchell,[34] who has shown that ^{13}C shielding in organotin halides generally decreases with an increase in the electronegativity of substituents.

The tin–carbon coupling constants are also sensitive to structural changes, and for alkyl and aryl compounds, the couplings have been shown to decrease in the order $^1J > {}^3J > {}^2J > {}^4J$.[39] Tables 1 and 2 show that the coupling values obtained from organotin compounds in the present study are consistent with these values. The negative values observed for ^1J(Sn–C) coupling constants arise from the negative gyromagnetic ratios (γ) of ^{117}Sn ($\gamma = -9.5301$) and ^{119}Sn ($\gamma = -9.9708$).[39]

Figure 2 shows that the degree of isotopic enrichment and the nature of the isotope used are reflected in the spectral pattern obtained. This is exemplified by the Sn–C satellite chemical shift and peak intensity values given in Tables 1 and 2. The 'natural abundance' spectra (Figure 2a) show that Sn–C satellites flank the large ^{13}C peaks of α, β and γ carbons. These arise from the spin–spin coupling between ^{117}Sn and ^{119}Sn, with ^{13}C nuclei. Coupling to the α-carbon is large enough to allow observation of the individual ^{117}Sn and ^{119}Sn satellites, but these components generally merge into single satellite peaks at β and γ carbons. The coupling between the ω carbon and the magnetic isotopes of tin cannot be observed in butyltins since the satellites have merged with the carbon peak.

Figure 2(b) shows that the ^{13}C signals from spectra of organotins enriched with ^{116}Sn have no

satellites because ^{116}Sn is not a magnetic nucleus, and does not interact with ^{13}C atoms.

The spectra of organotins enriched with ^{117}Sn (Figure 2c) show almost complete coupling to ^{13}C, with a residual uncoupled ^{13}C peak between the two large ^{117}Sn–^{13}C satellites. The ^{13}C analysis of ^{117}Sn-enriched organotins has also allowed hitherto unobservable couplings to the ω-butyl carbon (Table 1) and the quaternary *ipso* phenyl carbon (Table 2) to be assigned. The ^{1}H, ^{13}C and $J(^{117,119}\text{Sn}–^{13}\text{C})$ values obtained in the present study are in general aggreement with previous literature values, and the small deviations observed arise from solvent effects.

CONCLUSIONS

Synthetic methods for the small-scale laboratory synthesis of isotopically enriched tin(IV) iodide, tetrabutyltin, tetraphenyltin, dibutyltin dichloride, tributyltin chloride, diphenyltin dichloride and triphenyltin chloride are described. These compounds have been characterized by ^{1}H and ^{13}C NMR spectroscopy.

The effect of solvent and substituent effects on chemical shift and tin–carbon coupling constant values are discussed, and the differences between the spectral patterns of organotins containing different concentrations of tin isotopes are described. The spectroscopic analysis of ^{117}Sn-enriched organotins has allowed the assignment of certain resonances and tin–carbon coupling constants which were previously unobservable using ^{13}C NMR spectroscopy.

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