

New and efficient synthesis of solid-supported organotin reagents and their use in organic synthesis

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Abstract

Novel resin-bound organotin reagents have been prepared, including for the first time resin-bound dimethyl tin reagents. Mild methodology has also been developed for the very efficient synthesis of resin-bound distannanes. The resin-bound tin chloride reagents have been used in a catalytic Stille coupling cycle and the resin-bound distannanes have been used in atom transfer cyclisations and proved to be much more effective than previously described resin-bound distannanes. As expected the use of resin-bound tin reagents facilitated their easy removal at the end of the reaction, and consequently residual tin levels in the organic products were low or negligible. The resin-bound distannanes could not, however, be successfully used for the palladium catalysed stannylation of a simple aryl iodide, which would have provided a useful approach to radiolabeling of aromatic substrates. The reasons for the failure in the stannylation process is unclear but crystal structure evidence indicates that there is a hypervalent interaction between the resin-bound tin atom and an adjacent ether oxygen which may effect the reactivity of the tin intermediates in the stannylation sequence.

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1. Introduction

Organotin compounds are widely used in organic synthesis and are particularly useful in C–C bond forming reactions as both reagents and as coupling partners. However, the toxicity and difficulty of removing organotin compounds from final products does limit the use of these methodologies, particularly in an industrial context. One solution to this problem has been to use solid-supported (resin-bound) tin reagents which can be removed at the end of a reaction by simple filtration, as well as having the potential for recycling, and a number of variants have been described [1].

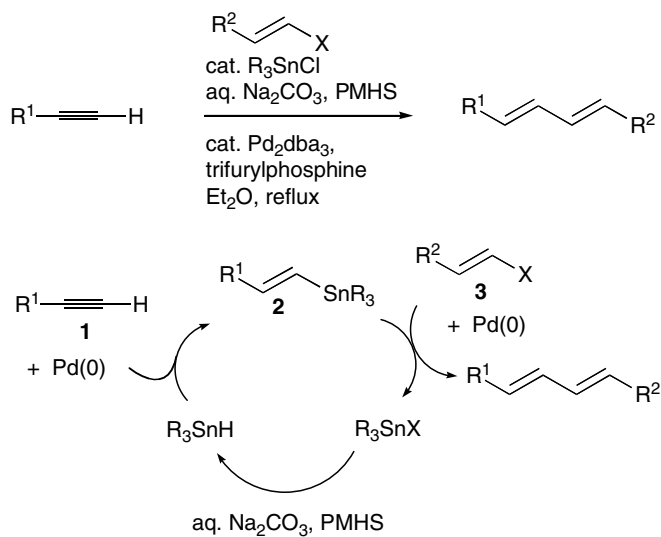
We were initially attracted to the use of resin-bound tin reagents by recent work by Maleczka et al. [2], who developed a Stille coupling protocol that involved catalytic use of trialkyltin chloride, providing a significant advantage

over the conventional Stille coupling of a vinyl stannane and organic halide, which generates stoichiometric tin byproducts [3]. Thus, in situ reduction of the trialkyltin chloride to trialkyltin hydride and hydrostannylation of an alkyne **1**, was used to generate a vinyl stannane **2**, which was coupled to an organic halide **3** using palladium catalysis. The catalytic cycle (Scheme 1) uses as little as 5 mol% of tin reagent, although trimethyltin chloride performed significantly better than tributyltin chloride. The protocol raised the possibility of using a resin-bound tin reagent for the in situ hydrostannylation of the alkyne component, and hence easy removal of all tin contaminants from the coupling reaction on completion.

In order to investigate the possibility of using resin-bound tin reagents in this way, we thus set out to prepare both tributyl and trimethyl tin chlorides and the corresponding hydrides. In the course of this work, we discovered a novel and very efficient method for the preparation of resin-bound distannanes, which we found could be used very effectively in iodine atom-transfer cyclisations. These

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resin-bound tin reagents were also investigated as potential catch-and-release reagents for the radio isotopic labeling of aromatic compounds. This paper describes in detail the results of all of these studies [4].

2. Results and discussion

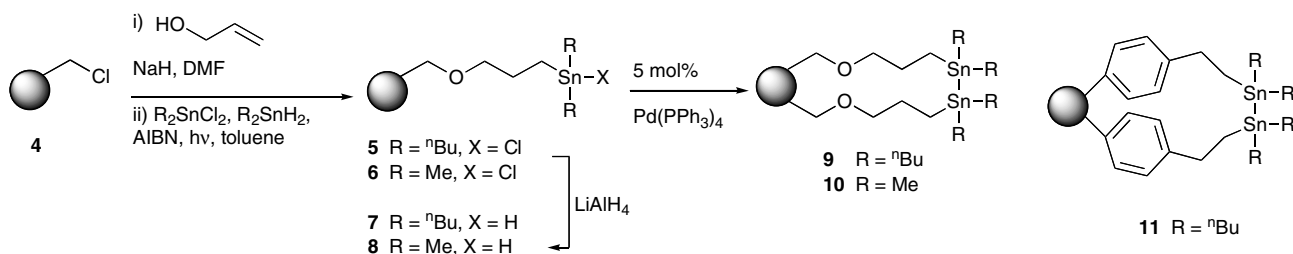
2.1. Synthesis of resin bound tin reagents

Several examples of resin-bound dibutyltin chloride and hydride reagents have been described previously [1] and have been investigated in tin hydride mediated radical reactions and stoichiometric Stille couplings, but to our knowledge the analogous resin-bound dimethyltin chloride and hydride reagents have not been described. The dialkyltin chloride resins **5** and **6** were prepared by hydrostannylation of an allyl ether, which was prepared in turn from Merrifield resin **4** (1.6 mmol/g, 1% DVB) [1f,1g,1i]. Hydrostannylation of the alkene with Bu_2SnHCl was accomplished using Neumann's procedure [1a], which involves in situ preparation of Bu_2SnHCl from a 1:1 mixture of Bu_2SnH_2 [5] and Bu_2SnCl_2 , and gave dibutyltin chloride resin **5** as a white solid.

The dimethyltin chloride resin **6** was prepared by an analogous procedure. Me_2SnH_2 was most conveniently

prepared on a small scale by reduction of Me_2SnCl_2 using Bu_3SnH , followed by distillation, according to Kuvila's method [6]. The Me_2SnH_2 , which decomposes rapidly [7], was mixed immediately with Me_2SnCl_2 to produce Me_2SnHCl , and used for the hydrostannylation of the allyl ether. The excess of Me_2SnHCl used in the synthesis of **6** decomposed during the reaction forming a grey precipitate (presumably metallic tin) which was removed by an acidic wash (1:1 1 N HCl/MeOH) to give resin **6** as a white solid. Both polymers **5** and **6** were characterized by microanalysis and by gel-phase ^{13}C and ^{119}Sn NMR. The NMR data were consistent with the literature [1c,8].

Neumann has described the preparation of a polymer-supported distannane **11** by reaction of dialkyl tin chloride, linked to a macroporous polystyrene resin, with a soluble reactive metal (e.g., lithium naphthalenide or magnesium/anthracene complex) [9]. We found this methodology unreliable when applied to resins **5** and **6**, and instead developed an alternative approach for conversion of the dialkyltin dichloride resins to the corresponding resin-bound distannanes. Thus, reduction of dimethyltin chloride resin **6** with LiAlH_4 [10] gave the corresponding tin hydride resin **8** (Scheme 2) in quantitative yield as determined by elemental analysis, gel-phase ^{13}C and ^{119}Sn NMR. Addition of catalytic ($\text{Pd}(\text{PPh}_3)_4$) (5 mol%) to resin **8**, pre-swollen in tetrahydrofuran, resulted in immediate evolution of H_2 gas [11]. The IR spectrum of the resulting resin **10** showed the total disappearance of the IR stretch for Sn–H ($\sim 1800\text{ cm}^{-1}$). Magic angle spinning (MAS) ^{119}Sn NMR of resin **10** revealed a single peak at a very similar chemical shift (-99.57 ppm relative to Me_4Sn) compared to that observed for tin hydride resin **6** (-98.22 ppm relative to Me_4Sn), but the peak for **10** was much broader than that for **8** presumably as a consequence of the more restricted mobility of the cross-linked ditin resin compared to the tin hydride resin. A spectrum (MAS ^{119}Sn NMR) of a 1:1 mixture of **10** and **8** and comparison with the spectra for the separate resins confirmed the ^{119}Sn peak assignments and indicates that conversion of the tin hydride to the ditin is essentially quantitative using this palladium catalysed dehydrogenation methodology. An identical sequence of reactions was used to convert dibutyltin chloride resin **5** to ditin resin **9**. However, after reduction with LiAlH_4 , ^{119}Sn NMR analysis of **7** showed two signals at similar shifts (-80.3 ppm (broad) and -86.2 ppm (sharp))



revealing a spontaneous partial dehydrogenation [12] to the ditin polymer **9**, which was competed by treatment with catalytic $\text{Pd}(\text{PPh}_3)_4$ (5 mol%).

2.2. Application of trialkyltin chloride resins in the catalytic Stille reaction

The resin bound tin chloride resins **5** and **6** were tested in the catalytic Stille coupling reaction protocol devised by Maleczka et al. [2]. In a typical procedure the tin chloride resin (6–100 mol%) was suspended in an aqueous $\text{Na}_2\text{CO}_3/\text{THF}$ mixture (1:20), with an alkyne **12**, palladium catalyst system (1 mol% Pd_2dba_3 , 1 mol% $\text{PdCl}_2(\text{PPh}_3)_2$ and 4 mol% tri-2-furylphosphine) and polymethylhydrosiloxane (PMHS) (1.5 equiv.). Aryl iodide or bromide **13** (1.5 equiv.) was added over 15 h by syringe pump. Using these optimised conditions, as reported by Maleczka with trimethyltin chloride, the coupling of β -bromostyrene and *o*-iodoanisole with various alkynols [13] proceeded in good yield (Table 1) despite the multiple phases in which the catalytic cycle has to take place (aqueous, organic and polymeric). Substoichiometric (30 mol%) amounts of the dimethyltin chloride resin **6** could be used satisfactorily, but lower amounts of resin (6 mol%) did give significantly reduced yields. Clearly the reducing agent PHMS is able to regenerate the polystyrene bound $\text{R}(\text{Me})_2\text{SnH}$ in contrast to its reported ineffectiveness for the regeneration of $\text{R}(\text{Bu})_2\text{SnH}$ in the polymer supported catalytic Barton–McCombie deoxygenation of secondary alcohols [1h].

After chromatographic purification the reaction products were obtained microanalytically pure and tin analysis showed low or insignificant tin content (<5–60 ppm) [14]. In comparison, using the same chromatographic purification of reactions conducted using soluble trimethyltin chloride, gave products with tin impurities >500 ppm.

The dimethyltin chloride resin **6** also gave much better results than the dibutyltin chloride resin **5** which is in good agreement with the superiority of Me_3SnCl in comparison with Bu_3SnCl in Maleczka's cycle. Maleczka reported that the catalytic cycle suffers from deactivation of the organotin hydride intermediates by oxidative coupling to give distannane species and this restricted the range of palladium catalysts that could be used successfully in the catalytic cycle. We also found that with the resin-bound tin catalysts, a dramatic decrease in yield was observed when changing to other solvents (DMF) or catalytic systems ($\text{Pd}(\text{PhCN})_2\text{Cl}_2/\text{Ph}_3\text{As}$) routinely used in Stille couplings. We had thought that the catalytic cycle might be more tolerant to various reaction conditions using polymer-supported organotin reagents since the isolation of the reactive sites by the solid support might result in the suppression of the oxidative coupling – although, of course, as we later discovered, in practice palladium mediated oxidative coupling is an effective method to prepare the resin bound distannane from the tinhydride resins **7** and **8** (vide supra) [15]. Using resins with a lower loading, and hence reduced potential for efficient oxidative coupling to give the distannane, might nonetheless prove useful in this

Table 1
Yields of Stille coupling using catalytic resin bound tin chlorides

The reaction scheme shows an alkyne **12** (with a methyl group and an R group on the triple bond) reacting with an aryl halide **13** (Ar-X) in the presence of resin **5** or **6** under specific conditions to yield an alkenyl product **14** (with a methyl group, an R group, and an Ar group on the double bond).

ArX	Alkyne	Resin	Resin equivs	Conditions	Yield of ν (%)
4-Iodoanisole	R = Ph	6	1.0	a	63
4-Iodoanisole	R = Ph	6	0.3	a	60
4-Iodoanisole	R = Ph	6	0.06	a	21
4-Iodoanisole	R = Ph	5	1.0	a	20
4-Iodoanisole	R = Ph	6	1.0	b	5
4-Iodoanisole	R = Ph	6	1.0	c	0
4-Iodoanisole	R = Me	6	0.3	a	57
4-Iodoanisole	R = Me	6	0.3	c	10
4-Iodoanisole	R = C_6H_{11}	6	0.3	a	55
β -Bromostyrene	R = Ph	6	0.3	a	50
β -Bromostyrene	R = Ph	5	1.0	a	15
β -Bromostyrene	R = Me	6	0.3	a	67
β -Bromostyrene	R = Me	6	0.3	c	7
β -Bromostyrene	R = Ph	6	0.3	a	60
Bromobenzene	R = Ph	6	0.3	a	9
Bromobenzene	R = Ph	6	1.0	a	0

Conditions: (a) 1 mol% $\text{Pd}_2\text{Cl}_2(\text{PPh}_3)_2$, 1 mol% Pd_2dba_3 , 4 mol% (2-furyl) $_3\text{P}$, 1.5 equiv. PMHS, Na_2CO_3 , $\text{H}_2\text{O}/\text{THF}$, reflux; (b) 1 mol% $\text{Pd}(\text{PhCN})_2$, Ph_3As , 1.5 equiv. PMHS, Na_2CO_3 , $\text{H}_2\text{O}/\text{THF}$, reflux; (c) 1 mol% $\text{Pd}_2\text{Cl}_2(\text{PPh}_3)_2$, 1 mol% Pd_2dba_3 , 4 mol% (2-furyl) $_3\text{P}$, 1.5 equiv. PMHS, Na_2CO_3 , $\text{H}_2\text{O}/\text{DMF}$, reflux.

context. Reaction optimisation using the less reactive Stille coupling partner bromobenzene was also unsuccessful.

2.3. Application of the resin-bound distannanes in iodine atom transfer cyclisations

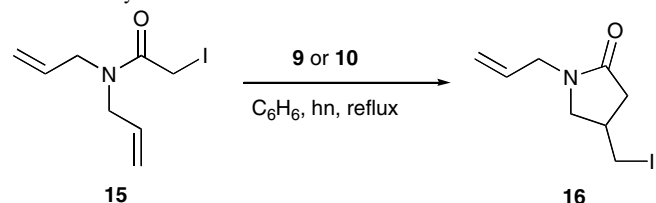
Free radical reactions are an important tool in organic synthesis and are routinely used in the preparation of even the most complex target molecules [16]. Stannyl radicals have played a central role in the development of this chemistry, and tributyltin hydride has been one of the most popular reagents for propagating radical reactions. Distannane reagents have also been a popular source of stannyl radicals since homolytic cleavage of tin–tin bonds takes place under mild conditions [17]. Distannane reagents have been widely used, in particular, for atom transfer cyclisations [18] where premature termination of the radical chain by a hydrogen atom donor is to be avoided. In order to avoid problems associated with the toxicity and difficulty of removing organotin compounds from final products there have been several approaches to developing alternative reagents for radical reactions [19], or modified tin reagents which can be more easily removed at the end of the reaction [20]. In the latter case there have been several studies on polymer-supported tin hydride reagents but surprisingly little has been reported on the preparation and utility of polymer-supported distannanes. Neumann has described the polymer-supported distannane **11**, linked to a macroporous polystyrene resin, but utilisation of this resin in atom transfer cyclisations led to significant amounts of reduced products as well as the desired cyclised product (vide infra) [9], presumably either as a consequence of trapping of the radical intermediates by hydrogen atoms from the polymer backbone [21], or because of tin hydride impurities in the polymer-supported distannane reagent [22].

Both resins **9** and **10** were used in two atom transfer reactions of iodides **15** and **17**. In a typical experiment the polymer-supported distannane was suspended in a 0.03 M solution of the iodide and the suspension heated to 80°C and irradiated by a 100-W UV Lamp. Reactions were monitored by GC and final products were purified by column chromatography to give isolated yields.

Cyclisation of diallyl amide **15** (Table 2) was carried out with 10 mol% of ditin reagent and very high yields of cyclised product **16** were obtained with no reduced byproducts being detected. The reaction was essentially complete in 1 h using the methyl substituted ditin resin **8**, but was somewhat slower using the sterically more encumbered butyl substituted ditin resin **7**.

The more demanding cyclisation of iodoester **17** was studied in greater detail. Good yields of the cyclised product **18** were again obtained using 10 mol% of ditin reagent but the reaction time required was ~16 h for completion (Table 3, entries 1–6). Again the sterically more accessible ditin polymer **10** appeared to perform somewhat better than **9**. The cyclisation could also be carried out using lower amounts of polymer-supported ditin (5 mol% and

Table 2
Yields from cyclisation of iodide **15**



Entry	Ditin reagent	Equivs. ditin reagent	Time (h)	Yields ^a (%)	
				15	16
1	7	0.1	1	24	76 (67)
2	7	0.1	4	0	98 (90)
3	8	0.1	1	0	99 (93)

^a Yields determined by GC. Isolated yields are in parenthesis.

even 2 mol%) but yields of cyclised product were reduced even after prolonged reaction (Table 3, entries 7–10).

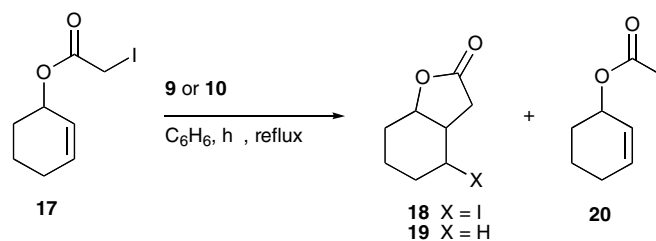
The results are significantly better than those described previously by Neumann and co-workers [9], who reported, for example, that cyclisation of the same substrate **17**, using macroporous ditin resin **11**, led to mixtures of reduced starting material **20** and cyclised products **18** and **19** (Table 3, entries 17 and 18). The significantly better performance of **9** and **10** can probably be attributed to the greater flexibility and accessibility of the polystyrene resin used here, and probably to the purity of the distannane reagent. The results are also on a par with those achieved using R_6Sn_2 reagents in solution. Clearly premature quenching of radical intermediates by hydrogen atoms abstracted from the solid support is not an issue in this system.

As anticipated the polymer-supported ditin reagent can be easily removed from the reaction by filtration and analysis of isolated products revealed very low residual tin levels [10] (<5–34 ppm) for the various samples tested. The polymer-supported distannane can also be recycled for further use (Table 3, entries 11–16). Resin **10** was recovered from an initial iodine-transfer cyclisation of **17** (Table 3, entry 6). The resin was dried under vacuum and then reused for the same reaction giving a 25% yield (GC) of **18** after 16 h (Table 3, entry 13). However, after reduction with $LiAlH_4$ and subsequent reaction with $Pd(PPh_3)_4$, the same sample of resin then gave a 79% yield (GC) of **18** after 16 h (Table 3, entry 16).

2.4. Application of resin-bound tin reagents for the preparation of isotopically labeled aromatics

The halodestannylation of arylstannanes is an efficient method for the mild and selective introduction of a halogen atom in an aromatic ring [23]. This methodology has been used to for the production of radiolabelled (iodinated and fluorinated) aromatic substrates [24] and is particularly useful since the short half-life of the fluorine and iodine isotopes precludes the storage of the radioactive compounds,

Table 3
Yields from cyclisation of iodide **17**



Entry	Ditin reagent	Equivs. ditin reagent	Time (h)	Yields ^a (%)			
				17	18	19	20
1	9	0.1	1	70	30	0	0
2	9	0.1	4	58	34	0	5
3	9	0.1	16	14	80	0	6
4	10	0.1	1	60	40	0	0
5	10	0.1	4	14	83 (78)	0	0
6	10	0.1	16	0	92 (90)	0	8
7	10	0.05	1	75	16	0	2
8	10	0.05	4	67	22	0	2
9	10	0.05	16	55	33	0	2
10		0.02	16	65	30	0	5
11	10^b	0.1	1	100	0	0	0
12	10^b	0.1	4	90	5	0	3
13	10^b	0.1	16	61	25	0	10
14	10^c	0.1	1	90	8	0	2
15	10^c	0.1	4	69	26	0	3
16	10^c	0.1	16	9	79	0	7
17	11^d	0.5	–	–	–	35	61
18	11^d	0.1	–	–	36	5	50

^a Yields determined by GC except for those in parenthesis which are isolated yields.

^b Recovered directly from previous reaction (see text).

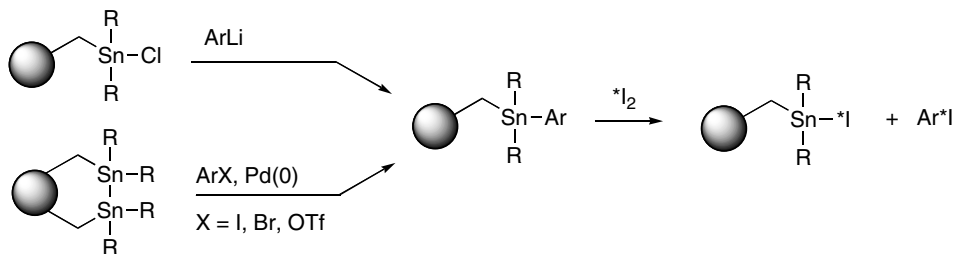
^c Recycled resin (treated with LiAlH₄, then Pd(0)) from previous reaction (see text).

^d Published results, see Ref. [9].

necessitating the rapid synthesis and purification of these compounds in situ. However, the tin by-products have to be removed due to the low tolerance of most radiopharmaceutical applications to this kind of compound. Consequently, there is interest in the development of solid-phase techniques that facilitate the synthesis and the fast purification of such radiopharmaceuticals [25]. Thus, attachment of the arylstannane precursor to an insoluble solid support followed by halodestannylation leads to release of the halogenated compound into solution while the tin byproducts remain attached to the solid support

and are easily removed by filtration. This approach has been investigated, particularly by Hunter [25], who found, for example, that resin-bound tin chlorides could be treated with aryl lithium reagents to give resin-bound aryl stannanes. Subsequent treatment with iodine gave the desired aryl iodide in good yield and easy removal of the resin-bound tin by-products (Scheme 3).

This approach is restricted, however, by the need to generate the aryl metal reagent which inevitably means that it is incompatible with some functional groups and hence with some substituted aromatics that might be of interest



Scheme 3.

as radiopharmaceuticals. An alternative approach for the formation of arylstannanes involves the relatively mild palladium mediated coupling of an aryl iodide (or bromide, triflate, etc.) with a hexaalkyldistannane [26]. The availability of resin-bound distannanes **9** and **10** prompted us to investigate the possibility of developing an analogous solid-phase based methodology and a novel catch-and-release approach to radiolabeled aryl halides (Scheme 3).

Thus, using iodoanisole as a model compound, the palladium mediated coupling of the iodoanisole with resin-bound distannanes **9** and **10** was attempted under a range of conditions (5 mol% Pd(PPh₃)₄ in refluxing dioxane, DMF, THF, toluene). However, although the complete consumption of the iodoanisole could be observed by monitoring the coupling reaction by hplc, no satisfactory analysis could be obtained for the product resin and indeed subsequent treatment of the product resin with iodine did

not lead to release of any iodoanisole. Treatment of the tin chloride resin **6** with the aryl lithium derived from iodoanisole, on the other hand, did give the desired resin-bound arylstannane which on treatment with iodine led to release of significant quantities of iodoanisole.

The failure of the resin-bound distannanes to perform as anticipated in the palladium mediated coupling with a simple aryl iodide was disappointing and somewhat perplexing. In Hunter's work [25], the resin-bound tin chlorides were prepared using rigid macroporous resins rather than the more flexible Merrifield resins used for the preparation of **9** and **10**. With this in mind we successfully prepared the corresponding distannane resins on commercial Argo-pore resin, but these were no more successful in attempted coupling with iodoanisole. It is likely that the ether linkage used in the preparation of our organotin resins influences the reactivity of the distannanes and indeed we were able

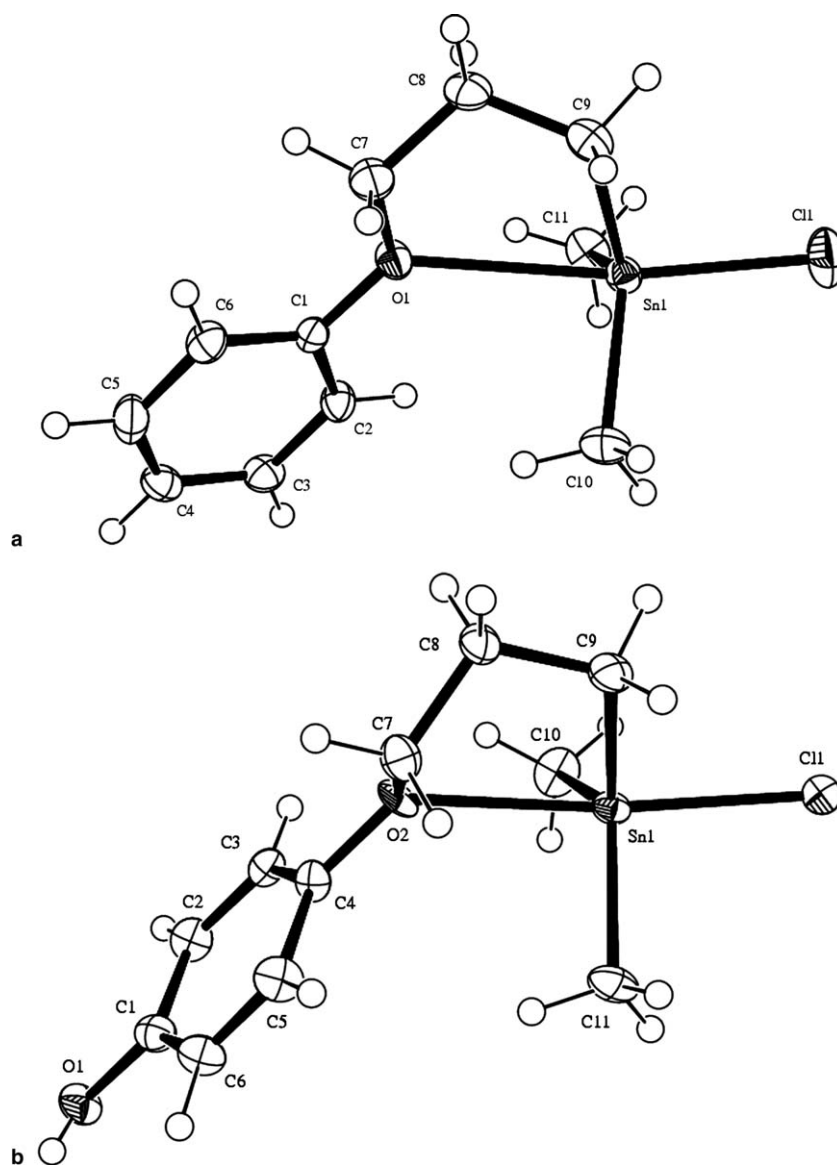
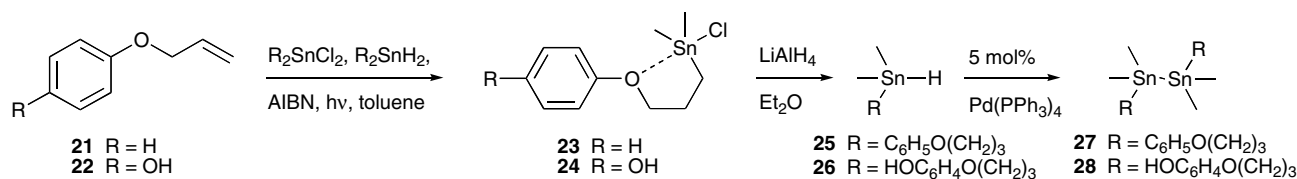


Fig. 1. Crystal structures of (a) compound **23** and (b) compound **24**.



Scheme 4.

Table 4
Bond lengths (Å) and angles (°) for compounds **23** and **24**

Bond lengths (Å) and angles (°)	23	24	
		Molecule 1	Molecule 2
Sn–O	2.773(2)	2.536(9)	2.507(7)
Sn–Cl	2.4211(18)	2.482(3)	2.498(3)
Sn–C (chain)	2.145(3)	2.162(13)	2.157(11)
Sn–C (Me1)	2.130(3)	2.127(11)	2.133(11)
Sn–C (Me2)	2.132(3)	2.109(10)	2.089(14)
Cl–Sn–O	169.07(5)	170.4(2)	170.0(2)
Cl–Sn–C (chain)	97.72(9)	95.2(4)	95.3(3)
Cl–Sn–C (Me1)	100.34(10)	97.9(4)	97.5(4)
Cl–Sn–C (Me2)	100.81(10)	95.8(4)	96.0(3)
O–Sn–C (chain)	71.40(10)	75.3(4)	75.0(4)
O–Sn–C (Me1)	84.87(11)	88.3(4)	85.5(4)
O–Sn–C (Me2)	85.44(11)	87.4(4)	90.8(4)
C (chain)–Sn–C (Me1)	120.69(15)	122.2(5)	119.3(5)
Cl (chain)–Sn–C (Me2)	116.19(14)	114.8(5)	118.2(5)
C (Me1)–Sn–C (Me2)	114.95(16)	119.3(5)	118.9(6)

to obtain crystal structures (Fig. 1) [27] of the aryloxyethyl(dimethyl)tin chlorides **23** and **24**, prepared from the corresponding allyl ethers (Scheme 4) which reveal a strong hypervalent interaction of the ether oxygen and the tin [28] in the solid state.

For compound **23** the crystal structure (Fig. 1) has one molecule in the asymmetric unit, but for **24** there are two distinct molecules in the asymmetric unit. In the crystal structure of **23** the Sn–O bond length is 2.77 Å, whereas in **24** the Sn–O bond length is shortened to 2.54 or 2.51 Å because of the electron donating effect of the *para* methoxy group. As a consequence the Sn–Cl bond is slightly longer in **24** than in **23** (see Table 4).

The tin chlorides **23** and **24** could be reduced to the corresponding tin hydrides **25** and **26** (LiAlH₄, Et₂O) and converted to the distannanes **27** and **28**, in a sequence identical to that used for the solid-phase synthesis. The soluble distannanes, **27** and **28**, however, proved to be rather unstable and decomposed on standing in CDCl₃ solution. Furthermore, attempted coupling of the distannanes to iodoanisole using 5 mol Pd(PPh₃)₄ in dioxane was not successful, although the same conditions were successfully used for the coupling of anisole using Me₆Sn₂.

3. Conclusions

Novel resin-bound organotin reagents were prepared on standard Merrified resin, including for the first time resin-

bound dimethyl tin reagents. Mild methodology was also developed for the very efficient synthesis of resin-bound distannanes. The resin-bound tin chloride reagents were successfully used in a catalytic Stille coupling cycle and the resin-bound distannanes proved to be much more effective in atom transfer cyclisations than previously described resin-bound distannanes, which had been prepared on macroporous solid supports. As expected the use of resin-bound tin reagents facilitated their easy removal at the end of the reaction (Stille coupling or atom transfer cyclisation), and consequently residual tin levels in the organic products were low or negligible. In cases where residual tin was detected this is likely to be a consequence of mechanical, rather than chemical, degradation of the resin on stirring, which could be addressed with greater attention to the stirring devices used. The resin-bound distannanes could not, however, be successfully used for the palladium catalysed stannylation of a simple aryl iodide, which would have provided a useful approach to radiolabeling of aromatic substrates. Given the success of the resin-bound reagents in the Stille coupling and atom transfer cyclisations the reasons for the failure in the stannylation process is unclear but crystal structure evidence indicates that a hypervalent interaction between the ether oxygen and the tin atom may well effect the reactivity of the tin intermediates in the stannylation sequence, and analogous solution versions of the various ether substituted tin reagents also failed to undergo the stannylation reaction under conditions which were successful using Me₆Sn₂ instead. This suggests that using an alternative linker to the ether used here might prove more successful, but an investigation of this possibility is beyond the scope of this study.

4. Experimental

All manipulations and handling were performed under an inert Ar atmosphere using standard Schlenk techniques. Dry solvents were obtained by distillation from calcium hydride. Et₂O and THF were distilled under an Ar atmosphere from a purple Na/benzophenone mixture. TLC on SiO₂ plates with UV detection (220 and 330 nm) and phosphomolybdic acid as visualising reagent. GC: column Hewlett–Packard HP5; temperature gradient of 80–250 °C at 25 °C/min. Fourier transform infrared spectra taken with a Thermo-Mattison spectrometer equipped with a SPE-CAC ATR unit. ¹H and ¹³C NMR experiments were performed on a Bruker AM300 NMR spectrometer. ¹¹⁹Sn NMR measurements were performed on a Bruker DPC400 NMR. Magic-Angle Spinning ¹¹⁹Sn NMR mea-

measurements were performed by the EPSRC solid-state NMR service at the University of Durham Industrial Research Laboratories. The ^{119}Sn chemical shifts are referenced to $\text{Sn}(\text{CH}_3)_4$. Tin analysis was carried out by digesting the sample in sulfuric acid followed by inductively coupled plasma (ICP) analysis and was performed by Medac Ltd.

4.1. Poly(4-allyloxymethyl)styrene [1f]

Allyl alcohol (6.1 mL; 70 mmol) was slowly added over 45 min to a mixture of NaH 95% (2.55 g; 106 mmol) in dry DMF (40 mL) at 0 °C. The solution was stirred for 2 h at room temperature and transferred via cannula to a suspension of Merrifield resin **4** (5 g; 1.6 mmol/g; 8 mmol) in dry DMF (20 mL). The mixture was gently stirred for 20 h at 50 °C. The excess of sodium hydride was destroyed by a slow addition of EtOH 95% at 0 °C and the polymeric material collected by filtration and washed with ethanol, water, acetone, DCM and ether (2 × 50 mL each, stirring for 10 min). After drying under vacuum at 40 °C for 2 days, a cream coloured polymer was obtained (5.1 g, 99%); ν_{max} (ATR, cm^{-1}) 1620 (C=C), 917, 1000 (–CH=CH₂); ^{13}C NMR (gel-phase in C_6D_6 , 75.5 MHz): δ 134.88, 116.91, 71.95, 70.85, 40. Microanalysis: Cl <0.1%.

4.2. Dibutyltinhydride (Bu_2SnH_2) [1d]

NaBH_4 (6 g; 160 mmol) was dissolved in 100 mL water at 0 °C and deoxygenated by bubbling Ar for 30 min. A solution of Bu_2SnCl_2 (9 g; 30 mmol) in 100 mL Et_2O was slowly added over a period of 45 min and the solution stirred for another 15 min. The organic layer was separated, washed with water (2 × 25 mL), dried over MgSO_4 and concentrated under vacuum to give Bu_2SnH_2 as a colourless oil (6 g, 85%). ν_{max} (neat, cm^{-1}) 1810 (Sn–H).

4.3. 3-(Dibutylchlorostannyl)-propyloxymethyl-polystyrene (5)

The method was adapted from a procedure described by Enholm and Schulte [1f]. To a suspension of poly(4-allyloxymethyl)styrene (2 g; 3.1 mmol), $n\text{Bu}_2\text{SnCl}_2$ (2.92 g; 9.6 mmol), AIBN (60 mg; 0.46 mmol) in dry toluene (50 mL) $n\text{Bu}_2\text{SnH}_2$ was slowly added (2.25 g; 9.5 mmol). The reaction flask was placed in a water bath to maintain the temperature below 20 °C and irradiated (220–240 V, 50 Hz, 2 A). Portions of AIBN (60 mg each) were added every 12 h. After a total reaction time of 31 h the polymeric material was collected by filtration and washed with toluene, ethanol, acetone, toluene, acetone and dichloromethane (2 × 50 mL each and stirred for 10 min before filtering). The resin was dried under vacuum at 40 °C for 2 days to give a white polymer (2.56 g, 65%). ^{13}C NMR (gel-phase in C_6D_6 , 75.5 MHz): δ 73.1(br), 71, 40, 27.8, 26.7, 26, 18.4, 15, 13.7. ^{119}Sn MAS NMR (gel-phase in C_6D_6 ; 112 MHz): δ 63.8. Microanalysis: Sn 13% (1.1 mmol/g), Cl 3.9% (1.1 mmol/g).

4.4. Dimethyltinhydride (Me_2SnH_2)

This product was obtained by modification of Kuivila's procedure [6]. A more convenient method for a large-scale synthesis is described elsewhere [29]. Me_2SnCl_2 (14 g; 64 mmol) was charged in a 250 mL two-necked flask under Ar. The flask was equipped with an addition funnel and to two consecutive traps at –78 °C via glass connections. After purging with Ar the system was evacuated with a water pump (15 mmHg). Bu_3SnH (66 mL; 245 mmol) was slowly added under stirring. The flask was heated to 60 °C and the pressure adjusted compatible with the evolution of gas. After approximately 90 min and cessation of gas evolution, the system was purged with Ar and 6 mL Me_2SnH_2 (92% yield) were obtained in the –78 °C ice trap. The necessary amount was used immediately for the next hydrostannylation step. The excess of unused dimethyltinhydride was destroyed with dilute aq HCl at –78 °C (warning: H_2 evolution).

4.5. Poly[(4-(3-dimethylchlorostannyl)-propyloxymethyl)styrene] (6)

Poly(4-allyloxymethyl)styrene (5 g; 8 mmol), Me_2SnCl_2 (4.4 g; 20 mmol) and AIBN (100 mg; 0.6×10^{-3} mmol) were suspended in 60 mL benzene. The reaction was kept at 20 °C in a circulating water bath. Me_2SnH_2 (2.1 mL; 20 mmol) was cannulated into the reaction vessel and the mixture irradiated with UV light (220–240 V, 50 Hz, 2 A) for 16 h. Another portion of AIBN (100 mg; 0.6×10^{-3} mmol) was added after 8 h. The polymeric material was collected by filtration and washed with toluene, ethanol, acetone, toluene, acetone and dichloromethane (2 × 50 mL each and shaken for 10 min before filtering). The grey polymer obtained was suspended for 2 h in a 1:1 mixture of 1 N HCl in methanol (50 mL). After washing with methanol, water, ether (2 × 50 mL each and shaken for 10 min before filtering) the resin was dried under vacuum at 40 °C for 2 days and a white polymer obtained (6.2 g, 96%). ^{13}C NMR (gel-phase in C_6D_6 , 75.5 MHz): δ 73.2, 71.1, 40, 25.9, 16.3, –0.1. ^{119}Sn MAS NMR (C_6D_6 ; 112 MHz): δ 59. Microanalysis: Sn 14.9% (1.3 mmol/g); Cl 4.81% (1.4 mmol/g).

4.6. 3-(Dibutylhydrostannyl)-propyloxymethyl-polystyrene (7) and 3-(dimehtylhydrostannyl)-propyloxymethyl-polystyrene (8)

The reduction of tin chloride resins **5** and **6** was performed according to the procedure described by Wong and co-workers [10]. A slurry of the resin **5** or **6** (3 g; **5** = 3.1 mmol, **6** = 3.9 mmol) in 45 mL anhydrous tetrahydrofuran was cooled to –55 °C under an Ar atmosphere and treated with an excess of a lithium aluminium hydride (12 mL of a 1 M solution in THF, 12 mmol). After the addition was completed the mixture was allowed to warm

to room temperature and stirring was continued for another hour. The resulting beads were collected by filtration under argon and washed rapidly with anhydrous THF and Et₂O (5 × 50 mL each and 10 min shaking before filtration) and finally evacuated in a desiccator at room temperature for 24 h to give 2.9 g **7** and 2.8 g **8**. Polymer **7**: ν_{\max} (ATR, cm⁻¹) 1803 (Sn–H). ¹³C NMR (gel-phase in C₆D₆, 75.5 MHz): δ 74 (br), 40, 30.3, 29.4, 26.7 (br), 13.3, 9.7, 7.8, 5.9. ¹¹⁹Sn NMR (gel-phase in C₆D₆; 112 MHz): δ –80.3 (small, br), –86.2. Microanalysis: Sn 12.5% (1.06 mmol/g) Cl <0.1%. Polymer **8**: ν_{\max} (ATR, cm⁻¹) 1822 (Sn–H). ¹³C NMR (gel-phase in C₆D₆, 75.5 MHz): δ 73.1 (br), 45.6 (br), 40 (br), 26.8, 5.3, –12.9. ¹¹⁹Sn MAS NMR (C₆D₆; 112 MHz): δ –98.22. Microanalysis: Sn 14.8% (1.25 mmol/g), Cl <0.1%.

4.7. Crosslinked bis-3-(methylpolystyryl)-propyloxy-tetrabutyl distannane (**9**) and crosslinked bis-3-(methylpolystyryl)-propyloxy-tetramethyl distannane (**10**)

Polymer-supported tin hydride **7** or **8** (1 g; **7** = 1.06 mmol, **8** = 1.25 mmol) was suspended in dry THF (20 mL). The suspension was deoxygenated by bubbling with Ar for 15 min. Pd(PPh₃)₄ (5 mol%) was added under a positive pressure of Ar and the suspension heavily stirred to allow dissolution of the catalyst. After evolution of gas (H₂) the mixture was very slowly stirred for 4 h. The resin was filtered and washed under Ar with dry THF (3 × 30 mL, 10 min shaking before each filtration). No weight difference was observed for either polymer **9** or **10**. Polymer **9**: ¹³C NMR (gel-phase in C₆D₆, 75.5 MHz): δ 71.5 (br), 41.6, 40 (br), 30.1 (br), 26.7 (br), 16.2, 15.4, 13.2, 9.6, 8.2, 5.3. ¹¹⁹Sn NMR (gel-phase in C₆D₆; 112 MHz): δ –82.3 (br). Microanalysis: Sn = 14.5% (1.23 mmol/g). Polymer **10**: ¹³C NMR (gel-phase in C₆D₆, 75.5 MHz): δ 73 (b), 45.3, 40 (b), 28.1, 7.2, –7.3. ¹¹⁹Sn MAS NMR (C₆D₆; 112 MHz): δ –99.57. Microanalysis: Sn 14.8% (1.25 mmol/g).

4.8. Standard procedure for catalytic Stille coupling

The procedure was adapted from that described by Maleczka. In a typical procedure the tin chloride resin **5** or **6** (6–100 mol%) was suspended in an aqueous Na₂CO₃/THF mixture (5 mL; 1:20), with an alkyne **12** (1 mmol), palladium catalyst system (1 mol% Pd₂dba₃, 1 mol% PdCl₂(PPh₃)₂ and 4 mol% tri-2-furylphosphine) and PMHS (1.5 equiv.). Aryl iodide or bromide **13** (1.5 equiv.) was added over 15 h by syringe pump. The resin was removed by filtration and washed with THF and then Et₂O (3 × 30 mL each and 10 min shaking before each filtration), the combined filtrates concentrated and the crude solid product purified by flash chromatography (hexanes/ethyl acetate, 3/1, v/v). Analytical data of isolated coupling products **14** (¹H; ¹³C; EIMS) was consistent with that reported in the literature [2].

4.9. Standard procedure for atom transfer cyclization procedure: 4-iodo-cis-hexahydro-2-coumarone (**18**)

The procedure for the radical 5-*exo* cyclization was adapted from that described by Curran and Tamine [30]. In a typical experiment the polymer-supported distannane **7** or **8** was suspended in 25 mL of a 0.03 M solution of the cyclohexen-2-en-1-yl iodoacetate **17** (or iodide **15**) in benzene and the suspension heated to 80 °C. The mixture was irradiated with a 100-W UV Lamp (Blak Ray[®], 220–240 ± 10% V, 50 Hz, 2.0 A) positioned above and to the side of the heating bath at a distance of 14 cm. Aliquots of 100 μ l were taken to monitor the reaction by TLC and GC. When an isolated yield is reported, the resin was filtered off and washed with benzene (3 × 30 mL, 10 min shaking), the combined filtrates concentrated and the crude solid product **18** purified by flash chromatography (hexanes/ethyl acetate, 3/1, v/v). Analytical data of isolated **18** (¹H; ¹³C; EIMS) was consistent with that reported in the literature [30].

Crystal structures of **23** and **24**

Compound	23	24
Empirical formula	C ₁₁ H ₁₇ ClO ₂ Sn	C ₁₁ H ₁₇ ClO ₂ Sn
Formula weight	319.39	335.39
Crystal system	Orthorhombic	Triclinic
Space group	<i>P</i> 2 ₁ 2 ₁ 2 ₁	<i>P</i> $\bar{1}$
Unit cell dimensions		
<i>a</i> (Å)	6.8719(1)	10.7920(3)
<i>b</i> (Å)	7.9780(1)	11.0704(3)
<i>c</i> (Å)	24.0387(5)	11.8391(4)
α (°)		87.995(1)
β (°)		89.886(1)
γ (°)		68.912(2)
<i>V</i> (Å ³)	1317.90(4)	1318.82(7)
<i>Z</i>	4	4
Crystal size	0.26 × 0.24 × 0.08	0.35 × 0.30 × 0.03
Shape; colour	Slab; colourless	Plate; colourless
θ Range for data collection (°)	3.06–27.47	5.12–27.49
Reflections collected	8476	6062
Independent reflections (<i>R</i> _{int})	2986 (0.0562)	2340 (0.0512)
Goodness-of-fit on <i>F</i> ²	1.039	1.177
Data/restraints/parameters	2986/0/130	2340/0/278
Final <i>R</i> indices [<i>F</i> ² > 2 σ (<i>F</i> ²)]	<i>R</i> ₁ = 0.0249, <i>wR</i> ₂ = 0.0604	<i>R</i> ₁ = 0.0249, <i>wR</i> ₂ = 0.0604
<i>R</i> indices (all data)	<i>R</i> ₁ = 0.0261, <i>wR</i> ₂ = 0.0610	<i>R</i> ₁ = 0.0249, <i>wR</i> ₂ = 0.0604

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