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Polymer-supported distannanes: a new and efficient synthesis of highly effective reagents for iodine atom transfer cyclisations

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Abstract—Polymeric distannanes were synthesised by the cross-linking of polystyrene bound tin hydride functionalities using a palladium mediated dehydrogenative coupling. The polymers were characterised by spectroscopic methods (IR and ^{13}C, ^{119}Sn NMR) and elemental analysis and were successfully applied to two iodine atom transfer cyclisations, performing as well as solution based hexaalkylditin reagents and significantly better than previously reported polymer-supported ditin reagents.

Free radical reactions are an important tool in organic synthesis and are routinely used in the preparation of even the most complex target molecules.[1] 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. Ditin reagents have also been a popular source of stannyl radicals since homolytic cleavage of tin–tin bonds takes place under mild conditions.[2] Ditin reagents have been widely used, in particular, for atom transfer cyclisations[3] where premature termination of the radical chain by a hydrogen atom donor is to be avoided. However, the toxicity and difficulty of removing organotin compounds from final products does limit the use of this methodology. There have been several approaches to developing alternative reagents for radical reactions,[4] or modified tin reagents, which can be more easily removed at the end of the reaction.[5] Of these, polymer-supported tin reagents[6] offer several advantages as they can be easily removed by filtration as well as having the potential to be easily recycled for further use. 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 preparation of a polymer-supported distannane **1** by reaction of a dialkyl tin chloride, linked to a macroporous polystyrene resin, with a soluble reactive metal (e.g., lithium naphthalenide).[7] However, utilisation of this resin in atom transfer cyclisations led to significant amounts of reduced products as well as the desired cyclised product (vide infra), presumably either as a consequence of trapping of the radical intermediates by hydrogen atoms from the polymer backbone,[8] or because of tin hydride impurities in the polymer-supported distannane reagent.[9] We now describe an experimentally much simpler method for the efficient preparation of polymer-supported distannanes, on standard polystyrene resin (1% DVB), which have been characterised by elemental analysis and gel phase/MAS NMR (^{119}Sn, ^{13}C and ^{1}H) and which give excellent results in atom transfer cyclisations, with little, or no, reduced byproducts.

We have previously described the use of tin chlorides **3** and **4** as polymer-supported reagents for the catalytic Stille reaction.[10] Reduction of dimethyltin chloride resin **4** with $LiAlH_4$[11] gave the corresponding tin hydride resin **6** (Scheme 1) in quantitative yield as determined by elemental analysis, gel-phase ^{13}C and ^{119}Sn NMR.[12] Addition of catalytic ($Pd(PPh_3)_4$) (5 mol %) to resin **6**, pre-swollen in tetrahydrofuran, resulted in immediate evolution of H_2 gas.[13] The IR spectrum of the resulting resin **8** showed the total disappearance of the IR stretch for Sn–H (~1800 cm^{-1}). Magic angle spinning (MAS) ^{119}Sn NMR of resin **8** 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 **8** was

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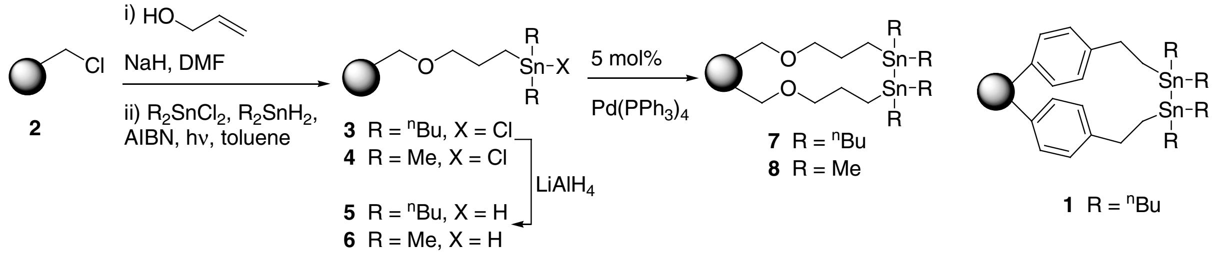
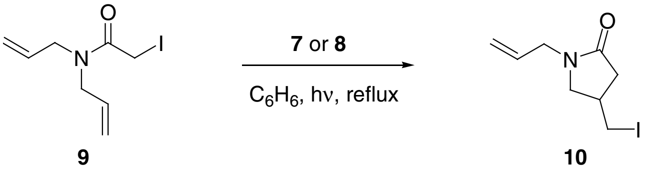


Scheme 1.

much broader than that for **6** 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 **8** and **6** and comparison with the spectra for the separate resins confirmed the ^{119}Sn peak assignments and indicated that conversion of the tin hydride to the ditin was essentially quantitative using this palladium catalysed dehydrogenation methodology. An identical sequence of reactions was used to convert dibutyltin chloride resin **3** to ditin resin **7**. However, after reduction with $LiAlH_4$, ^{119}Sn NMR analysis of **5** showed two signals at similar shifts [−80.3 ppm (broad) and −86.2 ppm (sharp)] revealing a spontaneous partial dehydrogenation[14] to the ditin polymer **7**, which was completed by treatment with catalytic ($Pd(PPh_3)_4$) (5 mol%).

Both resins **7** and **8** were used in two atom transfer reactions of iodides **9** and **11**. 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 using 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 **9** (Scheme 2) was carried out with 10 mol% of ditin reagent and very high yields of cyclised product **10** were obtained with no reduced byproducts being detected (Table 1). 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**.



Scheme 2.

Table 1. Yields from cyclisation of iodide **9** (Scheme 2)

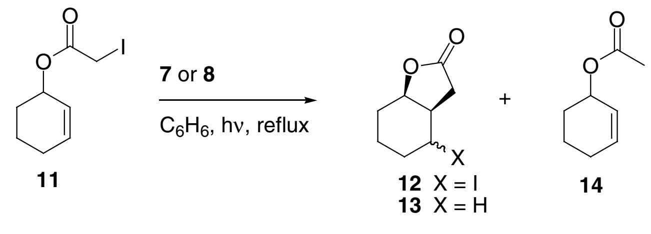
Entry	Ditin reagent	Ditin reagent (equiv)	Time (h)	Yields[a] (%)	
				9	10
1	**7**	0.1	1	24	76 (67)
2	**7**	0.1	4	0	98 (90)
3	**8**	0.1	1	0	99 (93)

[a] Yields determined by GC. Isolated yields are in parentheses.

The more demanding cyclisation of iodoester **11** (Scheme 3) was studied in greater detail. Good yields of the cyclised product **12** were again obtained using 10 mol% of ditin reagent but the reaction time required was ~16 h for completion (Table 2, entries 1–6). Again the sterically more accessible ditin polymer **8** appeared to perform somewhat better than **7**. The cyclisation could also be carried out using lower amounts of polymer-supported ditin (5 mol% and even 2 mol%) but yields of the cyclised product were reduced even after prolonged reaction (Table 2, entries 7–10).

The results are significantly better than those described previously by Neumann and co-workers,[7] who reported, for example, that cyclisation of the same substrate **11**, using macroporous ditin resin **1**, led to mixtures of reduced starting material **14** and cyclised products **12** and **13** (Table 1, entries 17 and 18). The significantly better performance of **7** and **8** 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[15] (<5–34 ppm) for the various samples tested. In cases where residual tin was detected (up to 34 ppm) this is likely to be a consequence of mechanical, rather than chemical, degradation of the resin on stirring.



Scheme 3.

Table 2. Yields from cyclisation of iodide **11** (Scheme 3)

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

[c] Recycled resin (treated with $LiAlH_4$, then Pd(0)) from previous reaction.

[d] Published results, see Ref. 7.

The polymer-supported distannane can also be recycled for further use (Table 2, entries 11–16). Resin **8** was recovered from an initial iodine-transfer cyclisation of **11** (Table 2, entry 6). The resin was dried under vacuum and then reused for the same reaction giving a 25% yield (GC) of **12** after 16 h (Table 2, 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 **12** after 16 h (Table 2, entry 16).

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12. Polymer **5** (obtained as a mixture of the desired tin hydride polymer **5** and cross-linked distannane polymer **7**): IR (ATR): $\nu_{max} = 1803\,cm^{-1}$ (Sn–H); ^{119}Sn NMR (gel phase in C_6D_6; 112 MHz): $\delta = -80.3$ (small, br), −86.2 ppm; Microanalysis: Sn: 12.5% (1.06 mmol/g); Cl < 0.1%. Polymer **6**: IR (ATR): $\nu_{max} = 1822\,cm^{-1}$ (Sn–H); ^{13}C NMR (gel phase in C_6D_6, 75.5 MHz): δ 73.1 (br), 45.6 (br), 26.8, 5.3,

-12.9 ppm; ^{119}Sn MAS NMR (C_6D_6; 112 MHz): δ -98.22 ppm; Microanalysis: Sn = 14.8% (1.25 mmol/g); Cl < 0.1%. Polymer **7**: ^{13}C NMR (gel phase in C_6D_6, 75.5 MHz): δ 72 (br), 30 (br), 27 (br), 13, 10 ppm (poorly resolved spectrum); ^{119}Sn NMR (gel phase in C_6D_6; 112 MHz): $\delta = -80.3$ (br) ppm; Microanalysis: Sn = 14.5% (1.23 mmol/g). Polymer **8**: ^{13}C NMR (gel phase in C_6D_6, 75.5 MHz): δ 73 (br), 45.3, 28.1, 7.2, -7.3 ppm; ^{119}Sn MAS NMR (C_6D_6; 112 MHz): $\delta = -99.57$ ppm; Microanalysis: Sn = 14.8% (1.25 mmol/g).

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