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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.

Keywords: Organotin; Distannane; Solid-phase; Stille coupling; Atom transfer

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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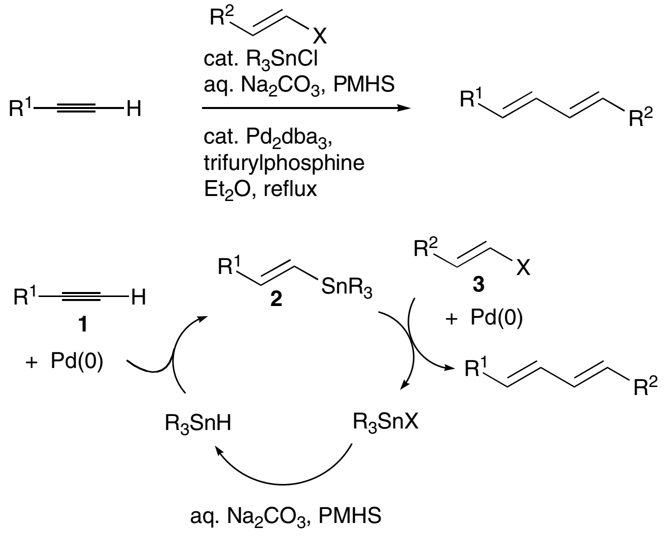


Scheme 1.

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].

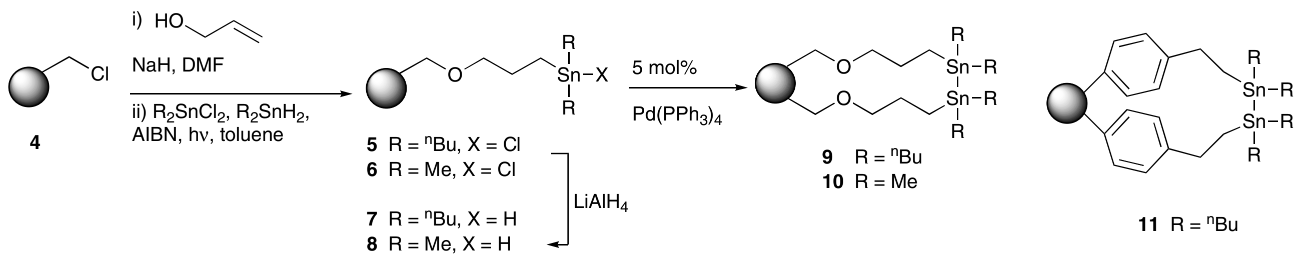
2. Results and discussion

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 ($Pd(PPh_3)_4$) (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 (~1800 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))



Scheme 2.