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Towards Non-polluting Organotin Reagents for Synthesis

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New polymer-supported organotin reagents have been prepared. The reducing ability of a polystyrene-supported organotin hydride was evaluated by reaction with haloalkanes. The level of organotin pollution was monitored in comparison with that generated by Bu_3SnH, using ICP–MS analysis.

Keywords: polymer; organotin; hydride; reduction; pollution; ICP–MS; GC/FPD; supported reagent

INTRODUCTION

Organotin compounds have a wide range of industrial applications. They are also important tools for organic synthesis.[1,2] Easy access, stability, reactivity and selectivity have promoted them to the status of popular reagents in research laboratories. However, due to their toxicity and potential impact on the environment, they are not used in industrial synthetic processes.

Tributyltin hydride is the most frequently used organotin reagent in organic synthesis.[3] However, complete elimination of this compound or its reaction products is often difficult or incomplete, despite the use of various separation techniques.[4–7]

An attractive route towards the elimination of toxic tin residues involves the utilization of insoluble polymer-supported organotin compounds, the supported organotin residue being separated by filtration from the organic products.

Several authors have reported the synthesis and the use of organotin hydrides grafted onto various supports.[8–15] Neumann and co-workers showed that the efficiency of supported-tin hydride was similar to that of tributyltin hydride.[11–15] Furthermore, the organic products were reported to be virtually free of organotin residues.[16,17]

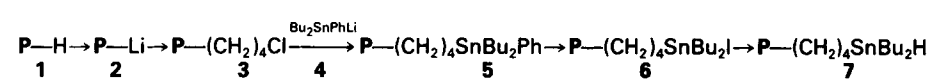
However, in the literature, no comparison between organotin pollution generated using tributyltin hydride (in homogeneous medium) and a polymer-supported tin hydride has been reported.

Results and Discussion

Recently, we proposed new methods for the synthesis of polystyrene-supported organotin hydrides[18,19] (Schemes 1 and 2). The reagents were found to contain 0.7–1.4 mmol SnH per g of polymer. The reducing efficiency was evaluated by reduction of 1-bromodecane.

We have achieved the reduction of 3-iodo-5-cholestene, a solid high-molecular-weight compound, using either tributyltin hydride or the grafted tin hydride **7**. The amounts of organotin residues were estimated by ICP–MS for total tin determination. The characterization of the organotin compounds leached after several washings of the polymer was performed by GC/FPD after aqueous ethylation.

Previously, it was important to determine the number of washings needed to recover the highest amount of organic products when polymer-supported tin hydride was used. This study was performed by monitoring the reduction of 1-bromodecane (Scheme 3), with a polymer prepared according to Scheme 1. After the filtration,



Scheme 1 Preparation of poly[4-(dibutylstannyl)butyl]styrene (**7**): first route.

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$$\underset{\mathbf{3}}{\text{P}\text{—}(CH_2)_4Cl} \xrightarrow{Bu_2SnHLi} \underset{\mathbf{8}}{\text{P}\text{—}(CH_2)_4SnBu_2H} \quad \underset{\mathbf{7}}{}$$

Scheme 2 Preparation of poly[4-(dibutylstannyl)butyl]-styrene (7): second route.

$$\underset{\mathbf{7}}{\text{P}\text{—}(CH_2)_4SnBu_2H} + BrC_{10}H_{21} \xrightarrow[THF]{AIBN} C_{10}H_{22} + \text{P}\text{—}(CH_2)_4SnBu_2Br$$

Scheme 3 Reduction of 1-bromodecane. AIBN, 2,2'-azobisisobutyronitrile.

the polymer was washed several times with tetrahydrofuran (THF). The amounts of decane recovered in each washing were determined by GC. The results are summarized in Fig. 1. No trace of decane could be detected in the fourth washing. Thus, the total amount of decane formed was recovered after one filtration and three washings. Likewise, Fig. 2 shows the amounts of free tin residue estimated by ICP–MS. The highest tin residue pollution was detected in the first filtration (after the reaction) and in the first washing. Therefore, according to Figs 1 and 2, a work-up involving more than one filtration and four washings seems to be unnecessary.

It was important to identify the organotin residues present in solution after the washings of the polymer. The origin of the organotin residues could be:

(a) the loss of organotin soluble precursors, such as Bu_2SnCl_2, used in the synthesis of $Bu_2SnPhLi$ (Scheme 4) despite several purification steps;
(b) the cleavage of Sn–C bonds in a free-radical process during the reduction of 1-bromodecane;
(c) the mechanical abrasion of the polymer beads.

The determination has been performed by GC/FPD after derivatization of tin products with $NaBEt_4$. Figure 3 shows the presence of various organotin species eluted with a retention time similar or very close to that of Bu_2SnCl_2 as Bu_2SnEt_2 (7.5 min). However, after derivatization the absence of derivatives coming from Bu_2SnPh_2 (14 min), $Bu_2SnPHCl$ as $Bu_2SnPhEt$ (11.1 min) and Bu_2SnPhH (12.8 min) should be noted. This result indicates the good stability of the grafted polymer since no large organotin species, potentially originating from by-products of the synthesis protocols (Schemes 1 and 4), are detected in the residues. Further work is being undertaken to elucidate this.

In order to compare the pollution generated by tributyltin hydride or a polymer-supported tin hydride, we have studied the reduction of 3-iodo-5-cholestene (Scheme 5). When poly[4-(dibutylstannyl)butyl]styrene **7** (1.45 mmol Sn g^{-1}, 1.0 mmol SnH g^{-1}) was used, the polymer was filtered and washed four times. The crude organic product was analyzed by GC and 5-cholestene was obtained in 60% yield.

In similar conditions (mass of iodocholestene, solvent, temperature, time), 3-iodo-5-cholestene was reduced using tributyltin hydride (1.45 mmol). After elimination of the solvent, the crude 5-cholestene was purified by crystallization (75% yield).

In each case the amount of organotin residue

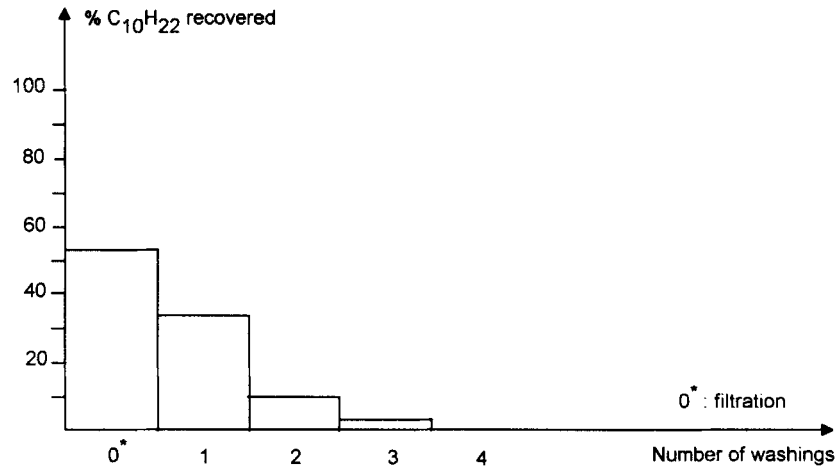


Figure 1 Reduction of 1-bromodecane: amounts of decane recovered, determined by GC analysis.

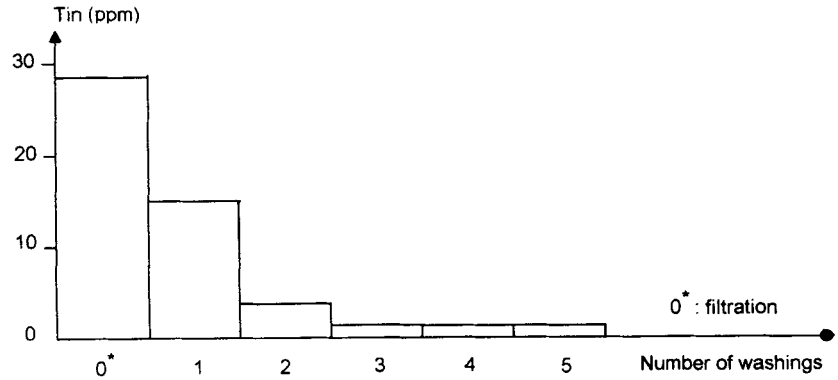


Figure 2 Reduction of 1-bromodecane: tin residue, determined by ICP–MS analysis.

was evaluated by ICP–MS; 45 ppm of organotin residue was detected for the use of 1 g of polymer (1.45 mmol Sn). To reach such a result, when tributyltin hydride was used, it was necessary to crystallize the 5-cholestene four times. It is striking that the amount of organotin residue was very high after the first crystallization. Results are summarized in Fig. 4.

Thus, we have shown that the polymer-supported tin hydride is chemically as efficient as tributyltin hydride and that it has only produced a very low level of tin pollution. Further work is in progress in order to optimize these results, to speciate the organotin residues still present and to minimize their amount.

EXPERIMENTAL

All the reactions were performed under inert atmosphere in Schlenk tubes using dry solvents. The polymers were dried *in vacuo* at 60 °C. The polymer **1** was Amberlite XE 305 (Rohm and Haas), a macroreticular polystyrene resin. Before use, the polymer was washed several times with various solvents to remove surface impurities, and dried.

The syntheses of polystyryl-lithium **2**, poly(4-chlorobutyl)styrene **3**, dibutylphenylstannyl-lithium **4**, poly[4-(dibutylstannyl)butyl]styrene (routes 1 and 2) **7**, and hydridodibutylstannyl-lithium **8** have already been described.[18,19]

For all the reactions described below, the experiments have been done using clean or new glassware in order to avoid impurities. The glasses were soaked for one week in 10% nitric acid and washed with distilled water.

Reduction of 1-bromodecane, reaction and GC analysis

A solution of 1-bromodecane **9** (3.8 mmol), decane (0.8 mmol), pentadecane (0.8 mmol) as internal reference and AIBN (0.08 mmol) in 40 ml of THF was added to 2 g (1.45 mmol Sn g^{-1}, 1.0 mmol SnH g^{-1}) of poly[4-(dibutylstannyl)-butyl]styrene **7** (prepared according to Scheme 1) suspended in 30 ml of THF. The mixture was heated at 70 °C for 6 h. After filtration, the polymer was washed six times with 20 ml of THF. The amounts of decane recovered in the filtration and in each washing were determined by GC using a capillary column (DB1, length 30 m, i.d. 0.25 mm).

Reduction of 1-bromodecane, and ICP–MS

The tin residues wee analysed by ICP–MS. Experiments were performed on a Perkin–Elmer Sciex Elan 5000 (Norwalk, USA) ICP–MS, using a free-running generator at a frequency of 40 MHz. The ICP was operated at 1000 W and standard settings were applied to the ion optics. Outer, intermediate and carrier gas flow-rates, all controlled with mass flowmeters, were 15.0, 0.85 and 0.92 l min^{-1} respectively. Nebulization was performed with a classical cross-flow nebulizer in a Ryton spray chamber. Sampler and skimmer

$$Bu_2SnCl_2 \rightarrow Bu_2SnPh_2 \rightarrow Bu_2SnPhCl \rightarrow Bu_2SnPhH \rightarrow Bu_2SnPhLi$$
4

Scheme 4 Preparation of dibutylphenylstannyl-lithium.

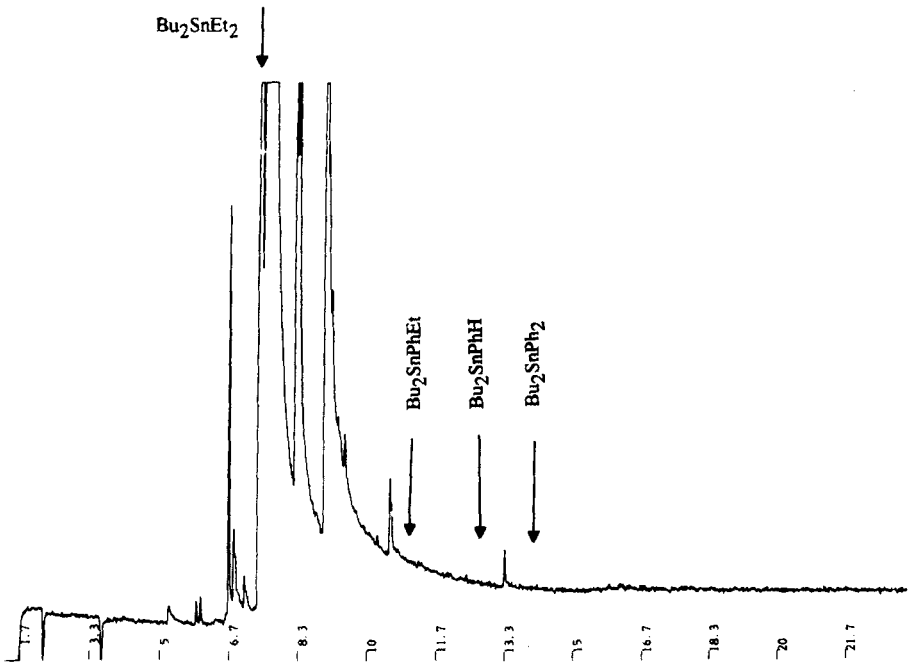


Figure 3 GC/FPD chromatogram of eluates coming from washings of the polymer after reduction of 1-bromodecane, confirming the absence of precursors of the polymer. The retention times of the tin species are obtained after ethylation of the compounds when needed for chromatographic purposes.

cones were made of nickel, with orifice diameters of 1.14 and 0.89 mm respectively.

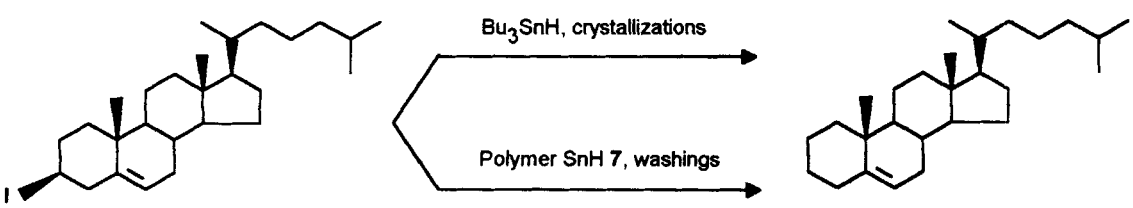
After evaporation of the solvent the samples were diluted to 1/10 000 with a 10% nitric acid solution and 2 ml of the solution was used for the analysis. The internal reference was indium.

Reduction of 1-bromodecane and GC/FPD analysis

We used a Shimadzu gas chromatograph 14 A equipped with a splitless injector, a flame photometric detector and a CP-SIL 8CB fused capillary column (length 25 m, i.d. 0.25 mm). Selectivity for tin was provided on a flame photometric detector by a 613 nm filter (band pass: 20 nm). The derivatization was a simultaneous ethylation/extraction in a solvent. Organotin compounds were derivatized in water by $NaBEt_4$ and simultaneously extracted in iso-octane. An aliquot was analysed. Retention times (after derivatization) of references were: Bu_2SnCl_2 as Bu_2SnEt_2 (7.5 min), $Bu_2SnPhCl$ as $Bu_2SnPhEt$ (11.1 min), Bu_2SnPhH (12.8 min), Bu_2SnPh_2 (14 min).

Reduction of iodocholestene

Blanks of the experiments were performed using the same procedure (purity of the materials, amounts of reagents, reaction time, temperature, etc.), either in the presence of ungrafted polymer (amberlite XE 305) or in the absence of tributyltin hydride for the reactions respectively carried out with polymer-supported tin hydride or tributyltin hydride.



Scheme 5 Reduction of 3-iodo-5-cholestene.

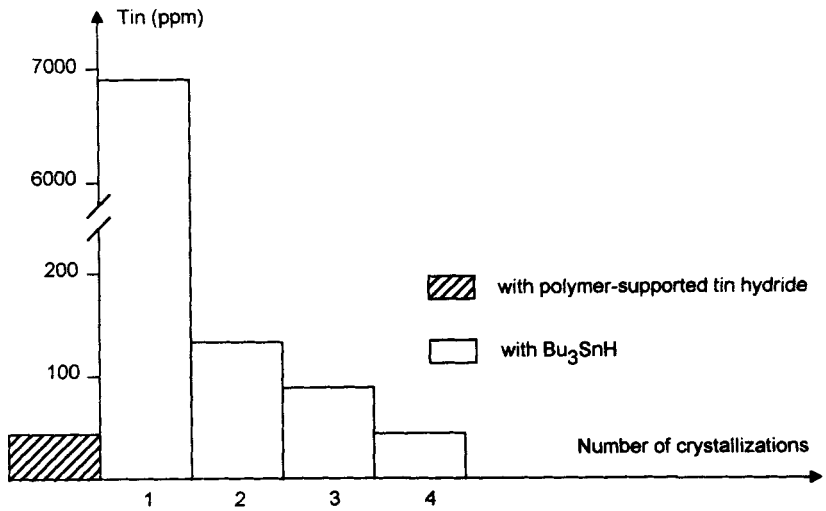


Figure 4 Reduction of 3-iodo-5-cholestene: tin residue, determined by ICP–MS analysis.

With polymer-supported tin hydride

A mixture of 3-iodo-5-cholestene (0.72 g, 1.45 mmol), 5-cholestene (0.06 g, 0.16 mmol), pentadecane (0.034 g, 0.16 mmol), AIBN (5 mol%) and poly[4-(dibutylstannyl)butyl]-styrene **7** (1 g, 1.45 mmol Sn g^{-1}, 1.0 mmol SnH g^{-1}) was suspended in 30 ml of THF. The mixture was heated for 12 h at 80 °C. The polymer was filtered and washed with THF (4 × 20 ml). All the liquid phases were gathered and the solvent was evaporated. The crude product was analysed by GC (column DB1); 5-cholestene was formed in 60% yield. The amount of tin residue was found to be 45 ppm by ICP–MS.

With Bu_3SnH

A mixture of 3-iodo-5-cholestene (0.72 g, 1.45 mmol), tributyltin hydride (0.42 g, 1.45 mmol) and AIBN (5 mol%) in 30 ml of THF was heated for 12 h at 80 °C. After elimination of the solvent, the 5-cholestene was crystallized (ether/ethanol) and was obtained in 75% yield (0.4 g, 1.1 mmol). The cholestene was crystallized three more times. The amounts of tin residue evaluated by ICP–MS were found to be 7000 ppm after one crystallization and 45 ppm after four crystallizations.

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