In Situ Generated, Polymer-supported Organotin Hydrides as Clean Reducing Agents

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Abstract: Polymer-supported organotin hydrides were generated in-situ from polymer-supported organotin halides and $NaBH_4$. Their reducing ability was monitored by reaction with 1-bromoadamantane. The residual tin pollution was estimated by ICP-MS. © 1998 Elsevier Science Ltd. All rights reserved.

Organotin compounds are important tools for organic synthesis.[1-3] Tributyltin hydride is frequently used either as a reducing agent or as a precursor of tributyltin radicals.[4-6] However, a complete elimination of this compound or its by-products from reaction mixtures is necessary since organotin compounds may cause severe damage to the environment. The separation techniques previously reported are often unsuitable.[7-10]

In order to avoid or limit the residual tin contamination, organotin hydrides anchored to an insoluble support have been prepared and used.[11-13] We have particularly developped a reagent anchored to polystyrene (Amberlite XE 305) (scheme 1) which is separated by filtration and reused without any loss of efficiency.[12-14]

P-H: Amberlite XE 305   (a): 1)BuLi/TMEDA 2)Br(CH₂)₄Cl   (b): Bu₂SnPhLi   (c): I₂   (d): NaBH₄
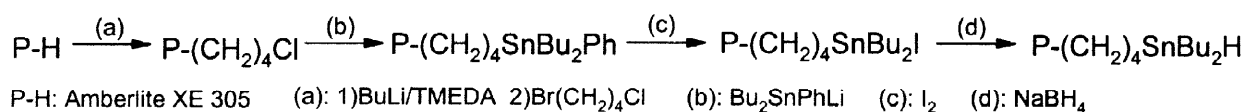
Scheme 1

However, in order to reach, if possible, the « zero » pollution level, we have chosen to use "catalytic" amounts of the polymer-supported tin hydride reagent which has been generated in situ from a polymer-supported organotin halide and sodium borohydride in excess.[15-17] (scheme 2).

In this paper, we report a comparative study concerning the reducing efficiency but also the tin pollution generated during the reduction of 1-bromoadamantane, chosen as a model, with tributyltin hydride, sodium borohydride - tributyltin halide or sodium borohydride - polymer-supported organotin halides.[18]

$$P\text{-}(CH_2)_nSnBu_2X \quad \xrightarrow[\substack{NaBH_4 \\ \\ AIBN \\ EtOH \\ 65°c}]{} \quad P\text{-}(CH_2)_nSnBu_2H$$

RH ← → RX
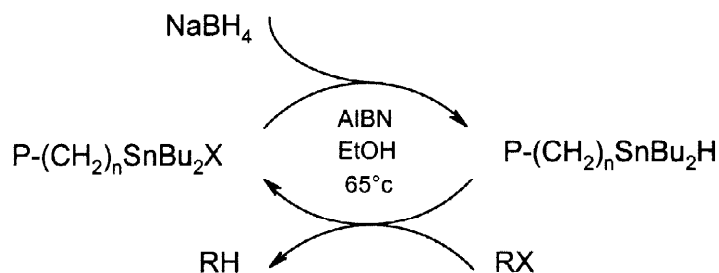
Scheme 2

To our knowledge, for this kind of reaction, it is the first report of qualitative and quantitative evaluation of the tin pollution. In addition, the influence of the length of the spacer on the polymer was analyzed using two different polymers $P(CH_2)_2SnBu_2Cl$, the polymer developped by Neumann, and $P(CH_2)_4SnBu_2I$.[19] The results are reported in Table 1.

Table 1. Reduction of 1-Bromoadamantane: Efficiency and Tin Pollution

	SnX/RX molar ratio	Yield % adamantane	Tin pollution ppm
$P(CH_2)_4SnBu_2I/NaBH_4$	0.9	97	34
	0.5	94	26
	0.2	93	blank
	0.05	75	blank
$P(CH_2)_2SnBu_2Cl/NaBH_4$	0.7	70	1975
	0.5	40	530
$Bu_3SnCl/NaBH_4$	0.5	70	$15.2\ 10^4$ [a] $9.8\ 10^4$ [b]

[a] after flash chromatography on silica column. [b] after KF treatment.

It can be observed that the $P(CH_2)_4SnBu_2I/NaBH_4$ system is the most efficient system since the yields of reduction are almost similar (over 90 %) when the amount of tin halide decreases from 0.9 to 0.2 equivalent. On the other hand, the $P(CH_2)_2SnBu_2Cl/NaBH_4$ system is less efficient; the reduction yield is only 40 % for 0.5 equivalent. This particular behaviour could be due to the shorter length of the spacer leading to a more difficult accessibility to the reactive tin moiety. A similar reduction of 1-bromoadamantane with stoichiometric amount of tributyltin hydride (yield: 98%) has shown that the polymer precursor $P(CH_2)_4SnBu_2I$ is as efficient as an homogeneous reagent.

Moreover, the organotin halide polymer can be recovered after the reduction and reused without significantly loss of its reactivity. We have only observed a very small decrease of the yield in adamantane
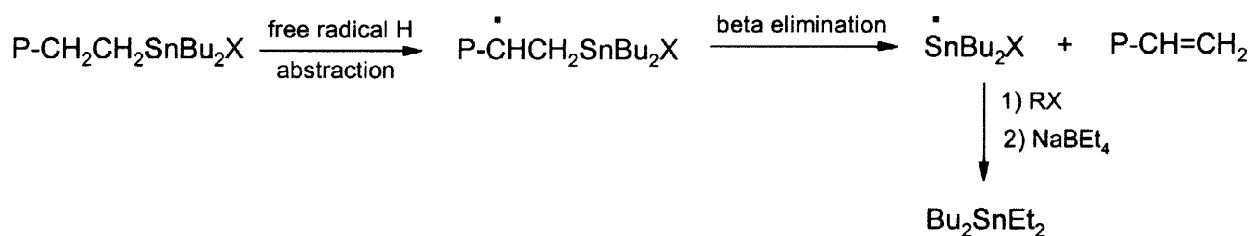
(97 % to 95 %) after five consecutive reductions; we have attributed this behaviour to the different nature of the halide (bromine versus iodine)

In these reductions, we have also quantified the residual tin pollution in the adamantane produced, using ICP-MS detection in a micellar solution (cyclohexane and sodium dodecylsulfate).[20]

With the $Bu_3SnCl-NaBH_4$ system, the pollution of adamantane was determined after one of the usual treatment of reaction mixture. Thus, crude adamantane was purified by flash chromatography (silica, petroleum ether) and the residual tin content was evaluated to $15.2 \ 10^4$ ppm. Also a treatment of the crude reaction mixture with a potassium fluoride solution[7] led to $9.8 \ 10^4$ ppm of tin.

In opposition, our results show very low pollution levels when the $P(CH_2)_4SnBu_2I/NaBH_4$ system was used, the residual tin amount decreasing with the molar ratio of tin halide to reach values identical to blank experiments.

Strikingly, the pollution generated by $P(CH_2)_2SnBu_2Cl$ was more important. This fact is probably due to the homobenzylic position of the tin atom on the spacer, leading to a degradation process in which the tin moiety is partly put in solution after hydrogen abstraction from the activated benzylic and β-stannyl position (scheme 3).

$$P\text{-}CH_2CH_2SnBu_2X \xrightarrow[\text{abstraction}]{\text{free radical H}} P\text{-}\overset{\bullet}{C}HCH_2SnBu_2X \xrightarrow{\text{beta elimination}} \overset{\bullet}{S}nBu_2X + P\text{-}CH=CH_2$$

$$\downarrow \begin{array}{l} 1)\ RX \\ 2)\ NaBEt_4 \end{array}$$

$$Bu_2SnEt_2$$

Scheme 3

In this case the determination of the residual organotin species, Bu_2SnEt_2, was performed by GC-MS and GC-FPD after derivatization by $NaBEt_4$.[20] Obviously,this process is not operative when the spacer is longer than 2. In fact the origin of the pollution is only in part the cleavage of the spacer, but also the abrasion of the beads of polymer during the magnetic stirring of the reaction. Three utilizations of the same polymer $P(CH_2)_4SnBu_2I/ NaBH_4$ (SnX/RX = 0.9) have shown that the level of the tin pollution was increased to 600 ppm of tin. The surface of the beads, examined by scanning electron microscopy, appears to be damaged.[20] To avoid this mechanical degradation, the reaction could probably be performed in a continuous system in which the organic halide solution would be pumped through an immobilized polymer.

These results clearly show that the use of a polymer-supported organotin hydride, in-situ and catalytically generated from a polymer-bound organotin halide, significantly reduces the tin pollution level while keeping a high reduction power. Compared to the traditional tributyltin hydride reagent, these compounds, specially for n = 4, can be considered as "clean" reducing reagents.

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18. General procedure for the reduction of the 1-bromoadamantane. The experiments have been performed using very clean or new glassware in order to avoid laboratory tin pollution. Under nitrogen atmosphere, in a dry Schlenk tube containing 1.0 g (0.9 mequiv. SnI) of polymer $P(CH_2)_4SnBu_2I$, 0.17g (4.5 mmoles) of sodium borohydride, 0.03g (0.18 mmole) of AIBN and 20 ml of ethanol was added a solution of 1-bromoadamantane (0.387g, 1.8 mole) and dodecane as internal standard (0.153g, 0.90 mmole) in 10 ml of ethanol. The mixture was slowly stirred at 65°C for 12 hours. After filtration the liquid phase was washed with water and extracted with pentane. The organic layer was dried and filtered (diameter of filter: 0.45 μm). The yield of adamantane was evaluated by GC analysis.
19. Materials: The polymer $P(CH_2)_4SnBu_2I$ was prepared from a macroporous polystyrene crosslinked with divinylbenzene (P-H: Amberlite XE 305 from Rohm and Haas). This synthesis was described in a previous paper.[12] The polymer contained 0.9 milliequivalent SnI per gram (% Sn : 11.12, % I : 11.43). The polymer $P(CH_2)_2SnBu_2Cl$ was prepared from Amberlite XE 305 according to the Neumann's procedure.[11] The polymer was found to contain 0.75 milliequivalent SnCl per gram (% Sn : 8.77, % Cl : 2.84).
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