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Catalytic and supported Barton–McCombie deoxygenation of secondary alcohols: a clean reaction

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Abstract

Secondary alcohols were deoxygenated using a new version of the Barton–McCombie process involving a catalytic amount of supported tin hydride in the presence of trimethoxysilane. The products are then easily separated from the catalyst by a simple filtration avoiding pollution by toxic tin by-products. © 2000 Elsevier Science Ltd. All rights reserved.

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The deoxygenation of secondary alcohols proposed by Barton and McCombie[1] is widely used for the synthesis of bioactive compounds.[2–5] Indeed, this method allows a specific deoxygenation of polyfunctional compounds under mild reaction conditions. The substrate, usually a thionocarbonate or a xanthate, readily obtained from the secondary alcohol,[6] reacts with a tin-centered radical to give an unstable intermediate which affords, after β-elimination, an alkyl radical rapidly trapped by the tin hydride, usually tributyltin hydride. Nevertheless, the contamination by organotin compounds, well-known to be toxic and very difficult to eliminate, is the major drawback of this reaction. In order to reduce or solve this problem, Fu et al.[7] has proposed a method using the tin hydride in a catalytic amount. Previously, Neumann and Peterseim[8] had used a stoichiometric amount of a tin hydride grafted onto an unsoluble polymer.

We have decided to go one step further by using an unsoluble polymer-supported tin hydride[9,10] in a catalytic amount (Scheme 1). Such a method requires a small quantity of functionalized polymer and allows easy elimination of the supported tin by-products by simple filtration. Results already reported show a very low tin pollution level, if any, in the catalytic use of an unsoluble organotin hydride for the reduction of haloalkanes.[10,11]

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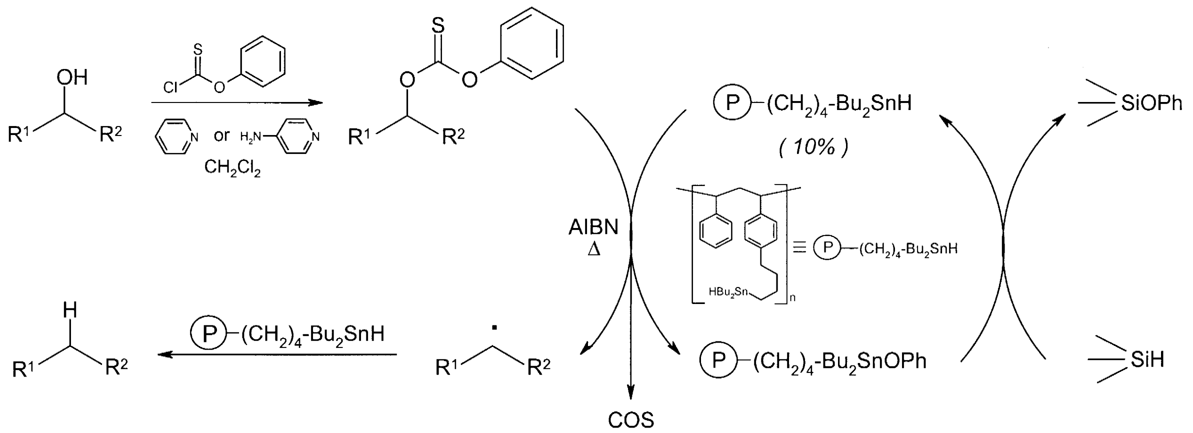

Scheme 1. Catalytic and supported variant of Barton–McCombie deoxygenation reaction

The crucial point is the regeneration of the tin hydride from the phenoxytin obtained after the deoxygenation. Indeed, the use of a reducing agent showing a specific reactivity for phenoxytin and a neutrality towards the usual organic functions is necessary in order to preserve the high selectivity of the deoxygenation method. Silanes, and particularly PMHS (polymethylhydrosiloxane), have been used in tin chemistry because of their ability to rapidly react with Sn–OR bonds[12] to give the Sn–H bonds.

Accordingly, Fu et al.[7] has shown the utility of PMHS for the formation in situ of the Sn–H bond from Sn–OPh in the presence of *n*-BuOH for deoxygenation reactions in homogeneous conditions. However, the use of PMHS in the presence of a catalytic amount of polymer-supported tin hydride (Scheme 1) gave poor results, with deoxygenation yields never exceeding 8%. We suppose that the polymeric nature of this siloxane considerably decreases its diffusion ability into the functionalized polystyrene and prevents the regeneration of the tin hydride functions. In fact, the low amount of deoxygenated product is only due to the stoichiometric reaction of the tin hydride initially present.

Thus initially, we have studied the ability of several types of less bulky hydrosil(ox)anes to regenerate Bu_3SnH from Bu_3SnOPh[13] (Fig. 1). In these homogeneous conditions, only trimethoxysilane afforded results comparable with those obtained by the use of PMHS.

Next, we used the trimethoxysilane in the Barton–McCombie deoxygenation in the presence of a small amount of supported tin hydride and the reduction went successfully (Table 1). It seems that, in contrast to PMHS, the less bulky trimethoxysilane can freely diffuse through the cavities of the polystyrene since the use of this reducing agent in the catalytic cycle allows completion of the deoxygenations after 24–36 h for three selected substrates.[14] The deoxygenation yields are comparable with those obtained in the classical stoichiometric and homogeneous version using Bu_3SnH.

Thanks to the catalytic use of a supported organotin hydride which was proved to be non-polluting,[10,11] this new variant of the Barton–McCombie deoxygenation of secondary alcohols seems especially suitable for applications in the synthesis of biologically active compounds.

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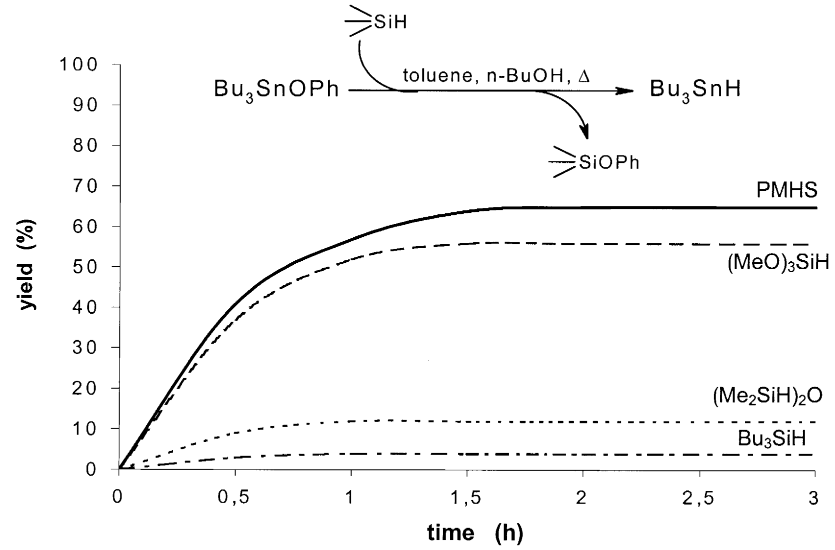
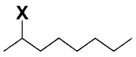
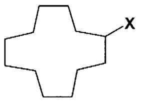
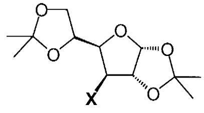


Fig. 1. Reduction of phenoxytributyltin by an hydrosil(ox)ane:Bu_3SnH formation monitored by gas chromatography. Reaction conditions: see the general procedure in Ref. 13

Table 1
Deoxygenation with a polymer-supported tin hydride/trimethoxysilane system (Fig. 1). Reaction conditions: see the general procedure in Ref. 14

Entry	Substrate	Product	Reaction time (hr)	Deoxygenation yield (%)	
				Catalytic and supported Sn-H	Stoechiometric Bu_3SnH
1 	X = OC(S)OPh	X = H	24	**70**	71[a]
2 	X = OC(S)OPh	X = H	24	**65**	68[b]
3 	X = OC(S)OPh	X = H	36	**74**	79[b]

a-reaction time : 8h / b-see ref 7.

6. *General procedure for the preparation of thionocarbonates*: Phenyl chlorothionocarbonate (1.1 equiv.) was added dropwise to a solution of the alcohol and pyridine (4 equiv.) (except entry 3: dimethylaminopyridine) in CH_2Cl_2 (50 mL). After stirring for 2 h, the reaction mixture was washed with water and extracted with ethyl acetate (3×20 mL). The organic layers were washed [(i) HCl (1 M); (ii) H_2O; (iii) saturated sodium carbonate solution; (iv) brine], dried ($MgSO_4$), and concentrated. The product was purified by chromatography (silica gel, CH_2Cl_2).
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13. *General procedure for the reduction of phenoxytributyltin under homogeneous conditions*: A mixture of phenoxytributyltin, hydrosil(ox)ane (15 equiv.), *n*-BuOH (15 equiv.) and toluene was stirred at 80°C under an argon atmosphere. Tributyltin hydride was monitored by gas chromatography (dodecane as internal reference).
14. *General procedure for the deoxygenation of thionocarbonates*: A mixture of the thionocarbonate, tin hydride polymer (1 meq.SnH/g, obtained from Amberlite XE 305[9,10] given by Rohm and Haas, 0.1 equiv.), AIBN (0.05 equiv.), trimethoxysilane (15 equiv.), *n*-BuOH (16.5 equiv.) and toluene (6 mL) was slowly stirred at 80°C under an argon atmosphere for 24 h (except entry 3: 36 h) (a new addition of AIBN (0.05 equiv.) was done every 8 h). The solution was diluted with 10 mL THF, and aqueous NaOH (1 M, 10 mL) was slowly added at room temperature. The reaction mixture was stirred for 4 h, filtered to eliminate the supported catalyst and extracted with Et_2O (3×10 mL). The organic layers were washed [(i) HCl (1 M); (ii) H_2O; (iii) brine], dried ($MgSO_4$), and concentrated. The product was purified by flash cromatography (silica gel, petroleum ether) (except entry 3: petroleum ether:Et_2O, 90:10).