Sonochemical, Aerobic Conversion of Alkyl Halides into Alcohols Promoted by Trialkyltin Halide/$NaBH_3CN$ Catalytic System

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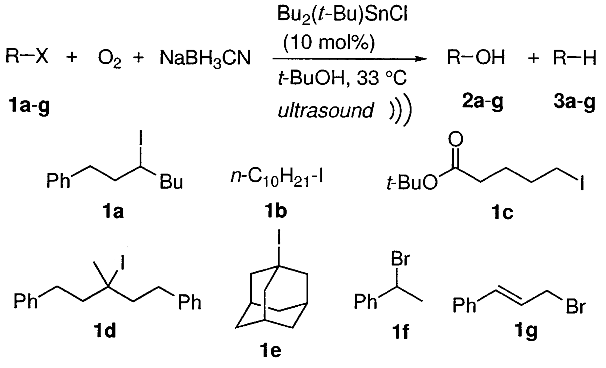
(Received April 14, 1997; CL970273)

Under sonochemical conditions, various alkyl halides were converted into the corresponding alcohols in high yields through an aerobic radical reaction promoted by trialkyltin halide/$NaBH_3CN$ catalytic system.

Earlier we reported the Bu_3SnH-mediated reaction that aerobically converts an alkyl halides into the corresponding alcohols.[1,2] In this reaction, reductive cleavage of a carbon–halogen bond by a tin hydride reagent forms a carbon radical, which is then trapped by molecular oxygen to produce the corresponding alcohol. Here we report an improved procedure, which makes use of catalytic amount of Bu_2(*t*-Bu)SnCl (10 mol%) and stoichiometric $NaBH_3CN$ under ultrasound irradiation[3,4] (Scheme 1). The procedure is applicable to primary, secondary, and tertiary alkyl iodides as well as benzylic and allylic bromides, most of them being transformed to the corresponding alcohols in nearly quantitative yields.



Scheme 1.

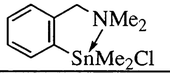
We first examined various metal hydrides as a stoichiometric reducing agent in the presence of a catalytic amount of Bu_3SnCl[5] for the aerobic conversion under ultrasound irradiation. Table 1 summarizes results of the reaction of secondary iodide **1a** in the presence of 10 mol% of Bu_3SnCl and 1-2 mol equiv of metal hydride in *t*-BuOH at 33 °C. The reaction was quenched after 5-6 hs and the yields of alcohol **2a** and simple reduction product **3a** were analyzed by GLC. It can be seen from entries 1-4 in Table 1 that the ratio of **2a**:**3a** increases from 14 : 86 to 98 : 2 with decreasing reducing ability of borohydride reagents while the conversion of halide **1a** became lower in this order. Among these stoichiometric reducing agents, we chose $NaBH_3CN$ as a reagent for further studies considering both the rate of reaction and the selectivity. The compatibility of this reagent with a wide range of functional groups is also beneficial for applications to complex molecules.

Table 1. Sonochemical, Aerobic Conversion of **1a** to **2a** in the Presence of Bu_3SnCl (10 mol%) and Various Stoichiometric Reducing Agents (1 equiv)[a]

entry	reducing agent	time, h	ROH (**2**) yield[b]/%	RH (**3**) yield[b]/%	ratio[b] of **2**:**3**
1	Me_4NBH_4	6	7	42	14:86
2	$NaBH_4$	6	41	6	87:13
3	$NaBH_3CN$	6	23	1	96:4
4	$NaBH_3(OAc)$	5	12	0.3	98:2

[a] Reaction in *t*-BuOH at 33 °C. [b] Determined by GLC analysis.

Table 2. Sonochemical, Aerobic Conversion of **1a** to **2a** in the Presence of Various Organotin Reagents (10 mol%) and $NaBH_3CN$ (1 equiv)[a]

entry	organotin reagent	time, h	ROH (**2**) yield[b]/%	RH (**3**) yield[b]/%	ratio[b] of **2**:**3**
1	Bu_3SnCl	6	23	1	96:4
2	$Bu_2(^tBu)SnCl$	6	64	3	96:4
3	Ph_3SnCl	6	76	21	78:22
4	Bu_2SnCl_2	6	45	10	82:18
5	$Bu_2SnCl(OAc)$	6	48	7	87:13
6		6	0	3	0:100

[a] Reaction in *t*-BuOH at 33 °C. [b] Determined by GLC analysis.

Next, various tin reagents were examined in the presence of $NaBH_3CN$ (Table 2). Compared with Bu_3SnCl, bulkier Bu_2(*t*-Bu)SnCl[6] increased the rate of the conversion of alkyl iodide **1a** while the selectivity of **2a**:**3a** being kept to a very high level (96 : 4) (entries 1,2, Table 2). As shown in entry 3 in Table 2, the reaction with Ph_3SnCl was faster than that with Bu_2(*t*-Bu)SnCl, but the selectivity to alcohol was rather low (78 : 22). Bu_2SnCl_2 and $Bu_2SnCl(OAc)$ are not as efficient as Bu_2(*t*-Bu)SnCl in both the activity and the selectivity (entries 4,5). The reaction with the pentacoordinated tin chloride[7] produced only reduction product **3a** in very low yield (entry 6, Table 2).

Having realized that the combination of Bu_2(*t*-Bu)SnCl and $NaBH_3CN$ is an efficient catalyst system, we carried out the optimization of reaction conditions in more details with this catalytic system and found that the use of 3 equiv of $NaBH_3CN$ causes smoother conversion and that the formation of the reduction product **3** is suppressed by bubbling the air through the irradiated mixture of Bu_2(*t*-Bu)SnCl and $NaBH_3CN$ in *t*-BuOH for 1 h before addition of alkyl halide **1**. Under these optimized conditions,[8] secondary iodide **1a** was transformed to alcohol **2a** in 100% isolated yield (entry 1, Table 3). Results with various alkyl halides including primary (**1b**,**c**) and tertiary alkyl iodides (**1d**,**e**), and an allylic (**1f**) and benzylic bromides (**1g**) are summarized in Table 3. All substrates except for allylic bromide **1g** were transformed to the corresponding alcohols in excellent yields within reasonable reaction period with occasional formation of a minute amount of reduction product **3**. In the case of acyclic *tert*-alkyl iodide **1d**, the formation of small amounts of olefins was observed (entry 3, Table 3), but this was naturally not

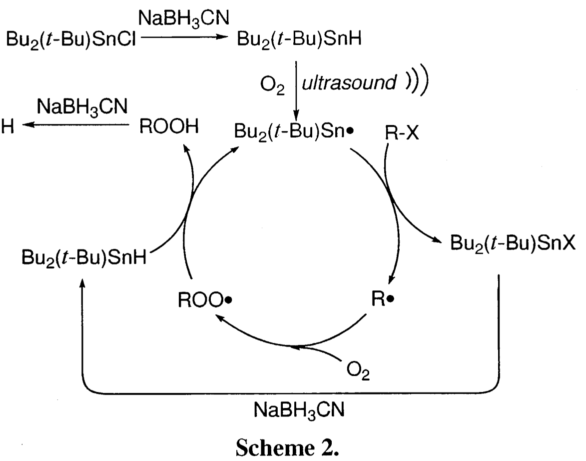
Table 3. Sonochemical, Aerobic Conversion of **1** to **2** in the Presence of Bu_2(*t*-Bu)SnCl (10 mol%) and $NaBH_3CN$ (3 equiv)[a]

entry	R-X (**1**)	time, h	ROH (**2**) isolated yield/%	RH (**3**) yield[b]/%
1	**1a**	13	100	0
2	**1b**	20	98	2
3	**1c**	16	95	5
4	**1d**	22	90[c]	0
5	**1e**	18	100	0
6	**1f**	20	96	3
7	**1g**	16	67[d]	25

[a] Reaction in *t*-BuOH at 33 °C. Air was bubled into the irradiated mixture of Bu_2(*t*-Bu)SnCl and $NaBH_3CN$ in *t*-BuOH for 1 h before an addition of **1**. [b] Determined by GLC analysis. [c] Small amount of olefins were observed in the crude mixture. [d] Obtained as a mixture of $PhCH{=}CHCH_2OH$ (60%) and $PhCH(OH)CH{=}CH_2$ (7%). Starting material was recovered in 7% yield.

the case for the reaction of cyclic substrate adamantyl iodide (**1e**) (entry 4, Table 3). The reaction of cinnamyl bromide (**1g**) gave both cinnamyl alcohol and 1-phenyl-2-propenol in a ratio of 90 : 10 together with reduction product β-methylstyrene (**3g**, 25%). Formation of the reduction product may be due to the ionic reduction of the bromide with $NaBH_3CN$ in this particular case.

A plausible reaction mechanism is shown in Scheme 2. Without ultrasound irradiation, no reaction takes place at ca 30 °C. Although the reaction proceeds at higher temperature (above 50 °C in the presence of AIBN) without irradiation, the formation of notable amounts of reduced product **3** can not be avoided. Clearly, the ultrasound irradiation plays important roles both in radical initiation with molecular oxygen and in the formation of Bu_2(*t*-Bu)SnH from Bu_2(*t*-Bu)SnX (X = halogen) and $NaBH_3CN$ (note that $NaBH_3CN$ is only partly dissolved in *t*-BuOH).



Scheme 2.

Finally we would like to note that while Bu_3Sn-, Me_3Sn- and Ph_3Sn-based reagents have been used in various types of reactions including radical reaction as well as transition metal-catalyzed reactions,[9] the corresponding Bu_2(*t*-Bu)Sn-based reagents have rarely been applied to organic synthesis despite of their easy availability.[6,10]

References and Notes

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8 Experimental procedure: Into a slurry mixture of $NaBH_3CN$ (94.3 mg, 1.50 mmol), Bu_2(*t*-Bu)SnCl (13.8 mL, 0.05 mmol) and *t*-BuOH (1.55 mL) in a flask equipped with a $CaCl_2$-drying tube was bubbled dry air through a Teflon tube (0.8-mm I.D) at a rate of 20 mL/min. The flask was immersed in a water bath, and the mixture was irradiated with ultrasound [with a 20 KHz, 200 W ultrasound generator equipped with a tapered titanium horn (3 mm ID tip); operated at 25% of the full power; internal temperature 33 °C]. After 1 h, 3-iodo-1-phenylheptane (**1a**) (114.7 mL, 0.5 mmol) was added to the solution. The irradiation and bubbling of air were continued for 13 hs. The mixture was poured into water (15 mL) and extracted with ether (15 mL × 4). Combined organic layer was dried over $MgSO_4$, concentrated under reduced pressure, and purified by flash chromatography (silica gel, 20% EtOAc in hexane) to afford 96.2 mg (100%) of pure **2a**.

9 M. Pereyre, J.-P. Quintard, and A. Rahm, Tin in Organic Synthesis, Butterworth & Co. Ltd (1987).

10 For the use of Bu_2(*t*-Bu)SnH, see: E. Nakamura, K. Sato, and Y. Imanishi, *Synlett*, **1995**, 525.