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Selective reduction of acid chloride with a catalytic amount of an indium compound

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Abstract

Indium hydride generated from tributyltin hydride and indium trichloride was coordinated by a phosphine to reduce acid chlorides to the corresponding aldehydes selectively. This reaction was achieved by a catalytic amount of indium trichloride. © 1999 Elsevier Science Ltd. All rights reserved.

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The low level of the ionization potential of indium metal has been successfully applied to Barbier–Grignard-type reactions and pinacol coupling.[1] Few synthetic applications of organoindium compounds, however, have been reported compared to those of aluminum or borane compounds, perhaps because of their instability. Transmetalation with stable organometallics, such as organotin compounds, is a promising route to organoindium derivatives.[2] We recently demonstrated the generation of dichloroindium hydride via transmetalation between tributyltin hydride (Bu_3SnH) and indium trichloride ($InCl_3$) which facilely promoted the reduction of carbonyl compounds and the dehalogenation of alkyl bromides.[3] No reduction of acid chlorides, however, could be promoted by the indium hydride at all, perhaps because of its lack of nucleophilicity. For the selective reduction of acyl halides to aldehydes, molecular hydrogen was generally used, for example, the Rosenmund reaction.[4] In contrast, few metal hydrides have achieved the selective reduction, except in cases assisted by exotic or expensive transition metals; however, some problematical decarbonylation from the intermediate acyl–transition metal complexes is incurred.[5]

If reduction by dichloroindium hydride is achieved and over-reduction of the produced aldehydes is suppressed, then a catalytic cycle for $InCl_3$ could be drawn as shown in Scheme 1. This is the case that we present in this paper, where the addition of a phosphine is essential for the selective transformation from acid chlorides to aldehydes.

Table 1 summarizes the effect of additives and solvents on the $InCl_3$-catalyzed reduction of benzoyl chloride (**1**) by Bu_3SnH. Without additives, no reduction proceeded at all (entry 1), even in the presence

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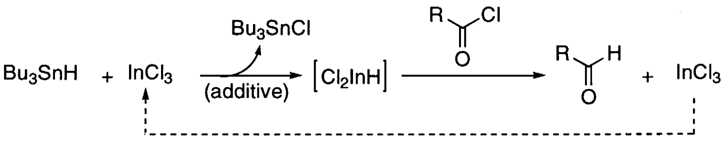


Scheme 1.

Table 1

Effect of additives and solvents[a]

$$\underset{\mathbf{1}}{\mathrm{PhCOCl}} \xrightarrow[\text{solvent}\quad -30\ ^\circ\text{C, 2 h}]{\mathrm{InCl_3}\text{ (cat.)}\quad\text{additive}\quad \mathrm{Bu_3SnH}} \underset{\mathbf{2}}{\mathrm{PhCHO}} + \underset{\mathbf{3}}{\mathrm{PhCH_2OH}}$$

Entry	Solvent	Additive (equiv)	Yield/ %	
			2	**3**
1	toluene	none	trace	trace
2[b]	toluene	none	0	10
3	toluene	MeCN (0.1)	trace	trace
4	toluene	Ph_3PO (0.1)	trace	trace
5	toluene	HMPA (0.1)	trace	trace
6	toluene	pyridine (0.1)	trace	trace
7	toluene	Ph_3P (0.1)	87	7
8	toluene	Ph_3P (0.2)	97	trace
9	toluene	Ph_3P (0.3)	82	trace
10	CH_2Cl_2	Ph_3P (0.2)	85	10
11	MeCN	Ph_3P (0.2)	85	9
12	THF	Ph_3P (0.2)	99	trace
13	toluene	$Hex^{c}{}_3P$ (0.2)	79	trace
14[b]	toluene	Ph_3P (2)	77	trace

[a] $[InCl_3]:[Bu_3SnH]:[\mathbf{1}]$ = 0.1:1:1 (in mmol) [b] 1.0 equivalent of $InCl_3$ was used.

of stoichiometric $InCl_3$ (entry 2). Additives such as acetonitrile, triphenylphosphine oxide and HMPA showed no effect, although these additives were reported as characteristic ligands to tin hydrides for promoting interesting chemoselective reductions.[6] In all these runs, benzoyl chloride was recovered mostly (entries 1–6). In contrast, triphenylphosphine was found to effect the reduction, furnishing benzaldehyde (**2**) in 87% yield along with a small degree of over-reduction to benzyl alcohol (**3**) (entry 7). This over-reduction could be suppressed by using 0.2 equimolar amounts of triphenylphosphine to increase the yield of **2** up to 97% (entry 8). A bulky phosphine such as tricyclohexylphosphine also promoted the selective reduction (entry 13).

The choice of solvent seemed unimportant, giving a high range of yield over 85% in all solvents (entries 8 and 10–12). Although among them THF gave the best yield (entry 12), we selected toluene as the most acceptable solvent for a wide range of acid chlorides, because increasing the polarity of solvents increases the reducing ability of Bu_3SnH toward aldehydes. For example, in methanol, aldehydes were facilely reduced as reported by Pereyre.[7] This may be the reason why a small amount of **3** was produced in CH_2Cl_2 or MeCN (entries 10 and 11). Of course, THF is a complementary solvent, particularly in the case of only slow reduction in toluene.

A general procedure is as follows: A mixture of $InCl_3$ (0.1 mmol) and triphenylphosphine (0.2 mmol) in 1 mL of dry toluene was stirred for 30 min at room temperature under nitrogen. After the mixture was cooled to −30°C, Bu_3SnH (1 mmol) and acid chloride (1 mmol) were subsequently added, and the resulting mixture was treated at −30°C for 2 h. After the amount of the unreacted acid chloride was monitored by GLC, to the mixture were added 20 mL of ether and 20 mL of water, and extracted by ether (20 mL×2). The organic layer was dried on anhydrous $MgSO_4$, concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel, and eluted by hexane:ethyl acetate (19:1).

Table 2 demonstrates the effective reduction of various acid chlorides to the corresponding aldehydes. Neither electron-withdrawing nor -releasing substituents on aromatic acid chlorides disturbed the facile

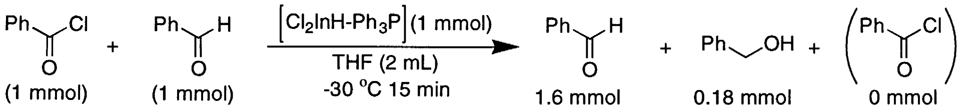
Table 2
Selective reduction of acid halides to aldehydes[a]

Entry	R	Conditions	Yield/ %	Entry	R	Conditions	Yield/ %
1	Ph	-30 °C, 2 h	97	8 [b e]	p-$NO_2C_6H_4$	-78 °C, 2 h	85
2 [c]	Ph	-30 °C, 2 h	77	9	$^nC_6H_{13}$	-30 °C, 2 h	93
3 [d]	Ph	-30 °C, 2 h	83	10 [e]	$Cl(CH_2)_5$	-30 °C, 2 h	83
4 [b e]	p-$MeOC_6H_4$	0 °C, 2 h	99	11 [e]	$CH_2=CH(CH_2)_8$	-30 °C, 2 h	92
5	p-MeC_6H_4	-30 °C, 2 h	93	12 [e]	$^nC_4H_9(C_2H_5)CH$	rt, 2 h	42 (11[f])
6	p-ClC_6H_4	-30 °C, 2 h	80	13 [e]	$^cC_6H_{11}$	rt, 2 h	62 (18[f])
7 [e]	p-CNC_6H_4	-78 °C, 4 h	91	14 [e]	^{t}Bu	rt, 2 h	39 (24[f])

[a] $[InCl_3]:[Ph_3P]:[Bu_3SnH]:RCOCl = 0.1:0.2:1:1$ (in mmol) [b] $[InCl_3]:[Ph_3P]:[Bu_3SnH]:RCOCl = 0.1:0.2:1:2$ (in mmol) [c] *p*-DNB (0.1 equiv) was added. [d] Galvinoxyl (0.1 equiv) was added. [e] THF solvent was used instead of toluene. [f] Yield of alcohols.

formation of aldehydes (entries 4–8). It is particularly notable that reducible substituents such as cyano and nitro ones tolerated the reduction conditions (entries 7 and 8). Primary aliphatic acid chlorides also gave good yields even in the cases of including terminal olefine and chloride (entries 9–11). Bulky aliphatic acid chlorides, however, gave a low range of yields (39–62%) accompanied with over-reduction to alcohols, because considerably harsh conditions were required (entries 12–14). The minimal effect of *p*-dinitrobenzene or galvinoxyl indicates that the dehalogenation proceeds via an ionic process (entries 2 and 3), although either indium hydride or tributyltin hydride has some radical characters.[3,8]

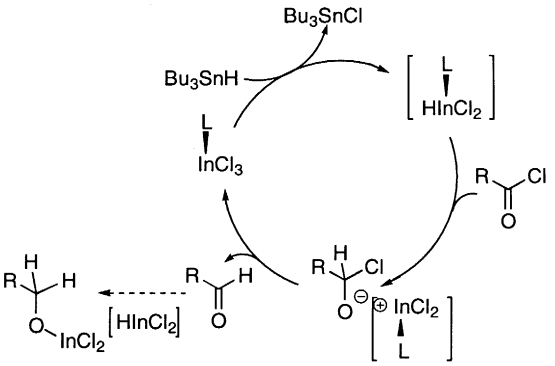
For investigation of the role of triphenylphosphine, after the generation of dichloroindium hydride was confirmed by ^{1}H NMR,[9] an equimolar amount of benzoyl chloride was added. When 2 equiv. of triphenylphosphine were added, benzaldehyde was obtained in 51% yield for 15 min at –78°C. In contrast, no reaction took place without the phosphine. The coordination of the phosphine apparently improves the reducing ability of the indium hydride. On the other hand, the reduction of benzaldehyde was considerably suppressed by the addition of triphenylphosphine from 74% (without PPh_3) to 53% yield (with PPh_3). Next, the competitive reduction between benzoyl chloride and benzaldehyde was carried out with the similarly generated indium hydride, where the coordination to indium hydride was proved to clearly promote the reduction of acid chloride over aldehyde (Scheme 2).



Scheme 2.

A plausible catalytic cycle is illustrated in Scheme 3. At first, the transmetalation between $InCl_3$ and Bu_3SnH generates a phosphine-coordinated indium hydride. Then the nucleophilic attack of the resulting hydride to an acyl carbon is allowed to produce an aldehyde accompanied with the regeneration of $InCl_3$. The coordination of the phosphine to dichloroindium hydride would play key roles in the step of the attack to the acid chloride and in inhibition of the reduction of the produced aldehyde, because the coordination plausibly increases the nucleophilicity of the hydride anion, and at the same time, decreases the acidity of the indium center. Consequently, in this catalytic cycle, the coordinated indium hydride selectively interacts with an acid chloride rather than an aldehyde. In addition, Bu_3SnH could not reduce the aldehyde under the reaction conditions.

In conclusion, we have developed a simple and efficient protocol for the transformation from acid



Scheme 3. Plausible catalytic cycle

chlorides to the corresponding aldehydes by Bu_3SnH without the assistance of a transition metal catalyst such as Pd(0).

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9. In the ^{1}H NMR study, the decreasing of Bu_3SnH (4.77 ppm) and the appearance of a broad peak at around 6.6 ppm were monitored in THF solvent, −30°C.