



Indium hydride: a novel radical initiator in the reduction of organic halides with tributyltin hydride

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Abstract—Dichloroindium hydride (Cl_2InH), which was generated in situ by transmetallation between tributyltin hydride and indium trichloride, acted as a novel radical initiator for the reduction of organic halides with tributyltin hydride. The reaction was revealed to proceed through a radical process under non-oxygen conditions at room temperature, and to be applicable to intramolecular radical cyclizations. © 2001 Elsevier Science Ltd. All rights reserved.

Radical reactions with tributyltin hydride (Bu_3SnH), which are initiated under mild conditions, have become a valuable method for stereoselective carbon–carbon bond formation.¹ The development of a novel radical initiator is still an important subject, though some versatile reagents such as Et_3B and Et_2Zn have been widely used at low temperature.² We wish to report here a convenient initiator, indium trichloride (InCl_3), which is stable against air and acts at user-friendly room temperature. We have recently demonstrated that dichloroindium hydride generated by transmetallation between Bu_3SnH and InCl_3 facily reduced alkyl bromides in a radical manner.³ In the context of further study on the radical reaction, InCl_3 was found to be a new type of effective initiator for the reduction of organic halides with Bu_3SnH .

The conditions for carrying out the reduction were optimized by using benzyl bromide (**1a**) with tributyltin hydride (Bu_3SnH) and indium trichloride (InCl_3) as outlined in Table 1. All treatments were done using a dry and degassed solvent in a dark room in order to avoid the influence of light and oxygen. In the absence of InCl_3 , no reduction took place (entry 3). In both cases of using a catalytic amount and an equimolar amount of InCl_3 , effective reduction proceeded at room temperature in THF to give toluene in 75 and 86% yields, respectively (entries 1 and 2). Because the addition of a radical scavenger, galvinoxyl, completely sup-

pressed the formation of toluene, a radical process is plausibly included in this reduction. The yield decreased to 35% in the reaction at 0°C , and no reduction proceeded at -78°C . Use of metal halides of other group-13 elements, such as AlCl_3 and $\text{BF}_3\cdot\text{OEt}_2$ instead of InCl_3 , was less effective (entries 4 and 5). Employment of such solvents as MeCN, CH_2Cl_2 and hexane resulted in considerably low yields (entries 6–8). We determined that the use of 0.1 equiv. of indium trichloride with 1.0 equiv. of Bu_3SnH in THF at room temperature (entry 1) was optimal, and these conditions were consequently applied to all other substrates in this study.⁴

Table 1. Effects of InCl_3 on the reduction of benzyl bromide with Bu_3SnH ^a

Entry	Catalyst (mol%)	Solvent	Yield of 2a /%
1	InCl_3 (10)	THF	75 (0) ^b
2	InCl_3 (100)	THF	86 (0) ^b
3	None	THF	0
4	AlCl_3 (10)	THF	28
5	$\text{BF}_3\cdot\text{OEt}$ (10)	THF	22
6	InCl_3 (10)	MeCN	27
7	InCl_3 (10)	CH_2Cl_2	39
8	InCl_3 (10)	Hexane	43

^a Bu_3SnH 1 mmol, **1a** 1 mmol, THF 2 mL.

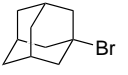

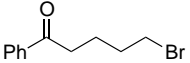
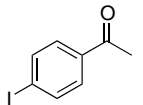
^b 1 mol% of galvinoxyl was added.

Keywords: indium and compounds; transmetallation; catalysis; radicals and radical reactions.

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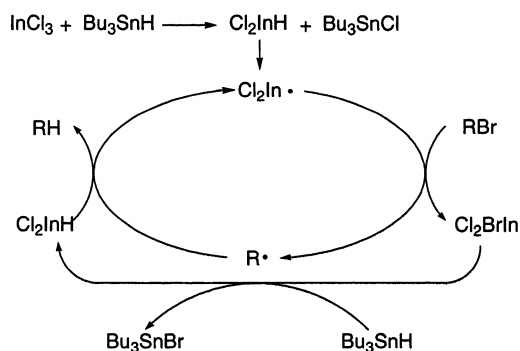
Table 2 shows the results of reduction of representative alkyl, alkenyl and aryl halides. Primary and secondary

Table 2. InCl₃-promoted reduction of various halides^a

Entry	R-X		Time/h	Yield of R-H/ %
1	1-bromododecane	1b	2.0	83
2	2-bromododecane	1c	2.0	91
3		1d	2.0	79
4	PhBr	1e	2.5	0
5		1f	2.5	12
6	PhI	1g	2.5	63
7	Ph(CH ₂) ₄ Cl	1h	2.5	0
8 ^b		1i	5.0	90
9 ^b		1j	5.0	61

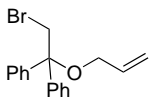
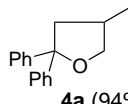
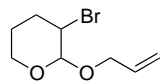
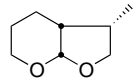
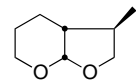
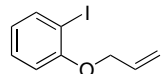
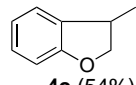
^a InCl₃ 0.1 mmol, Bu₃SnH 1 mmol, RX 1 mmol, THF 2mL, rt.

^b Bu₃SnH (3 mmol) was used.



Scheme 1. Plausible catalytic cycle.

Table 3. Radical cyclization^a

Entry	R-X	Conditions	Products (Yield/ %)
1		rt, 5 h	 4a (94%)
2		rt, 2.5 h	 4b (70%) +  4b' (7%)
3		rt, 5 h	 4c (54%)

^a InCl₃ 0.1 mmol, Bu₃SnH 1.6 mmol, RX 1 mmol, THF 2mL.

alkyl bromides, **1b** and **1c** were reduced at room temperature to the corresponding alkanes in 83 and 91% yields, respectively (entries 1 and 2). A tertiary bromide, 1-bromoadamantane (**1d**), was also reacted effectively (79% yield, entry 3). No reduction of alkyl chloride **1h** proceeded at all (entry 7). Aryl and vinyl bromides **1e** and **1f**, however, were scarcely reduced under similar conditions (entries 4 and 5). In contrast, aryl iodide **1g** was readily reduced (entry 6). Survival of the carbonyl moieties under the reduction conditions is an important aspect of this procedure, and halogenated ketones **1i** and **1j** gave the corresponding ketones in good yields (entries 8 and 9), since moderate reduction of ketones with indium hydride has been reported.³ In the case of reduction of 1-bromododecane (**1b**), the introduction of oxygen, by bubbling, completely suppressed the formation of dodecane, and the vigorous removal of oxygen, increased the yield of dodecane to 90%. Thus, this indium system needs neither heating nor oxygen, and so it is compensatory for the conventional AIBN or Et₃B system.

A plausible mechanistic pathway of the reduction is illustrated in Scheme 1. At first, transmetalation between Bu₃SnH and InCl₃ forms an indium hydride, the facile generation of which has been already confirmed.³ Next, decomposition of the hydride allows formation of an indium radical, which then reacts with organic bromide to accomplish the catalytic cycle as illustrated. In the cycle, the indium radical is regenerated, and Bu₃SnH acts as only a resource for indium hydride. Another possibility is that Bu₃SnH directly reduces organic bromides, and indium hydride acts only as a radical initiator.⁵ Although the exact radical species is unclear as yet, a catalytic amount of InCl₃ proves to act as an effective radical initiator under mild conditions.

Next, we attempted some representative cyclizations for a radical proof of this procedure (Table 3). A primary alkyl bromide such as 3-(2-bromo-1,1-diphenylethoxy)propene (**3a**) underwent cyclization to give 4-methyl-2,2-diphenyl tetrahydrofuran (**4a**) in 94% yield. The

reaction of a secondary alkyl bromide such as 2-allyloxy-3-bromo tetrahydropyran (**3b**) gave 3-methylhexahydro furo[2,3-*b*]pyran (**4b** and **4b'**) in 77% yield with high *anti*-selectivity (*anti:syn* = 10:1). 3-Methyl-2,3-dihydrobenzofuran (**4c**) was also obtained from 1-allyloxy-2-iodobenzene (**3c**) in 54% yield. In all cases, no by-products such as non-cyclized dehalogenated alkenes were detected at all.

In conclusion, InCl_3 could be employed as a novel radical initiator in the reduction with Bu_3SnH under mild conditions.

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- In a representative case, under nitrogen in a dark condition, a mixture of InCl_3 (0.1 mmol) and Bu_3SnH (1.0 mmol) in dry THF (2 mL) was stirred at -78°C for 5 min to generate dichloroindium hydride (Cl_2InH). After being warmed up to rt for 5 min, to the solution was added **1a** (1.0 mmol), and the resulting mixture was stirred for 2 h. Aqueous ammonium fluoride was added to remove tributyltin halides. After filtration, the reaction mixture was extracted with ether (2×50 mL). The combined organic layer was dried over Mg_2SO_4 and concentrated to give **2a** (86%).
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