



Use of indium hydride (Cl_2InH) for chemoselective reduction of the carbon–carbon double bond in conjugated alkenes

Brindaban C. Ranu* and Sampak Samanta

Department of Organic Chemistry, Indian Association for the Cultivation of Science, Jadavpur, Calcutta 700 032, India

Received 2 July 2002; revised 2 August 2002; accepted 9 August 2002

Abstract—Indium hydride (Cl_2InH) generated in situ from a combination of a catalytic amount of indium(III) chloride and sodium borohydride selectively reduces the carbon–carbon double bond in conjugated alkenes such as α,α -dicyano olefins, α,β -unsaturated nitriles, cyano esters, cyanophosphonate, diesters and ketones. © 2002 Elsevier Science Ltd. All rights reserved.

The use of indium metal in organic synthesis has received considerable attention in recent times because of its great potential in a variety of organic transformations.¹ One of the latest developments in indium-mediated reactions is selective reductions.² These reactions are speculated to go through single electron transfer (SET) process. Although metallic indium has been successfully used for the reduction of various functionalities such as aromatic nitro groups,^{2a} quinolines,^{2b} azides,^{2c} *vic*-aryl dibromides,^{2d} terminal alkynes^{2e} and conjugated olefins,^{2f} among others,² two major drawbacks of these processes are the use of a stoichiometric amount or more of the costly indium and its limited applicability to specific types of substrate. Recently, indium hydride (Cl_2InH) generated in situ from the combination of sodium borohydride and a catalytic amount of indium trichloride has been demonstrated to be a benign alternative to tributyltin hydride in the dehalogenation of alkyl halides and radical cyclizations.³ As a part of our interest in indium-mediated reductions,^{2d–f} we initiated an investigation to find applications for this simple reagent and we have discovered that the system $\text{InCl}_3\text{--NaBH}_4$ shows much improved activity towards reduction of carbon–carbon double bonds in conjugated alkenes compared to metallic indium^{2f} and our results are presented here (Scheme 1).

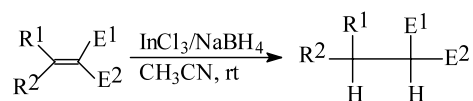
The experimental procedure is very simple.⁴ The conjugated alkene was stirred with a solution of a catalytic

amount (10–15 mol%) of indium(III) chloride and sodium borohydride in acetonitrile at room temperature for the period of time required to complete the reduction (TLC). The usual work-up and purification produced the corresponding reduction product.

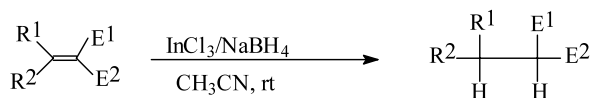
Several structurally diverse conjugated alkenes undergo selective reduction of their carbon–carbon double bond using this procedure to provide the corresponding saturated products. The alkenes include α,α -dicyano olefins, α,β -unsaturated nitriles, cyanoesters, a cyanophosphonate, dicarboxylic esters and β -aryl aromatic ketones. The results are summarized in Table 1. As is evident from the results, the conjugated monoester (entry 17) remains inert, whereas the diester (entry 16) is reduced easily. Apparently, this reagent system, $\text{InCl}_3\text{--NaBH}_4$ is quite different from metallic indium in its course of reduction as conjugated cyanoesters, diesters, nitriles which are reduced readily by this procedure do not undergo reduction by indium metal.^{2f} More significantly, the reduction of chalcone which was found to be problematic using indium metal^{2f,g} was successful using this reagent system (entry 18). In addition, reductions using this procedure are faster and proceed at room temperature unlike using indium metal, which requires a temperature of 90°C for a longer period.^{2f} To ascertain the role of indium(III) chloride a few reactions were carried out with the conjugated nitrile (listed in entry 7), cyanoester (entry 10), dicyano-olefin (entry 1)




Keywords: indium chloride; sodium borohydride; reduction; conjugated alkene; C=C bond.

* Corresponding author. Fax: 91-33-4732805; e-mail: ocbcr@mahendra.iacs.res.in



Scheme 1.

Table 1. The reduction of C=C bond in conjugated alkenes by $\text{InCl}_3/\text{NaBH}_4$ 

Entry	Alkene				Time (h)	Yield (%) ^a
	R ¹	R ²	E ¹	E ²		
1	Ph	H	CN	CN	3	85
2	<i>p</i> -(Cl)-C ₆ H ₄	H	CN	CN	3	83
3	Ph	Me	CN	CN	3.5	79
4	<i>p</i> -(Me)-C ₆ H ₄	Me	CN	CN	4	79
5	<i>c</i> <i>y</i> -C ₆ H ₁₀		CN	CN	3.5	83
6	Me ₂ CH	Me	CN	CN	4	81
7	Ph	H	CN	H	12	69
8	<i>p</i> -(Me)-C ₆ H ₄	H	CN	H	12	57
9	H	CN	H		5	84
10	Ph	H	CN	CO ₂ Et	3	88
11	Ph	Me	CN	CO ₂ Et	4.5	82 (55:45) ^b
12		H	CN	CO ₂ Et	5	78
13	Me ₂ CH	Me	CN	CO ₂ Et	5	85 (60:40) ^b
14	<i>c</i> <i>y</i> -C ₆ H ₁₀		CN	CO ₂ Et	4.5	84
15	<i>c</i> <i>y</i> -C ₈ H ₁₄		CN	CO ₂ Et	4.5	81
16	Ph	H	CO ₂ Et	CO ₂ Et	6	87
17	Ph	H	CO ₂ Et	H	18	No reaction
18	Ph	H	H	COPh	0.5	96
19		H	H	COPh	0.75	88

^a Yields refer to those of pure isolated products characterized by spectral data (IR, ¹H, ¹³C NMR).

^b The figure in parenthesis denotes the diastereomeric ratio of the product.

and chalcone (entry 18) under identical reaction conditions without the indium(III) chloride, and no reduction was observed in each case. Thus, it may be assumed that the reductions are effected by Cl_2InH , generated in situ from NaBH_4 and InCl_3 through a radical process.³

In general, reductions using this procedure are clean, high-yielding and quite fast. The reaction conditions are mild enough (room temperature) to tolerate a sensitive furan ring (entry 12). This reagent system is also highly chemoselective reducing only the C=C bond without any effect on other reducible functionality.

In conclusion, the indium hydride, Cl_2InH generated in situ from a combination of sodium borohydride and a catalytic amount of indium(III) chloride provides a highly chemoselective reduction of the carbon–carbon double bonds in a wide range of activated conjugated alkenes. Certainly, this reagent offers significant improvements with regard to convenience, cost, mildness and efficiency over the similar reduction by indium

metal which was reported earlier^{2f} and leaves great promise for other application of the indium hydride.

Acknowledgements

We are pleased to acknowledge financial support from the CSIR, New Delhi [Grant No. 01(1739)/02] for this investigation. S.S. is also thankful to CSIR for his fellowship.

References

- (a) Cintas, P. *Synlett* **1995**, 1087; (b) Li, C.-J. *Tetrahedron* **1996**, 52, 5643; (c) Li, C.-J.; Chan, T. H. *Tetrahedron* **1999**, 55, 11149; (d) Chauhan, K. K.; Frost, C. G. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3015; (e) Ranu, B. C. *Eur. J. Org. Chem.* **2000**, 2343.
- (a) Moody, C.-J.; Pitts, M. R. *Synlett* **1998**, 1028; (b) Moody, C. J.; Pitts, M. R. *Synlett* **1998**, 1029; (c) Reddy,

- G. V.; Rao, G. V.; Iyengar, D. S. *Tetrahedron Lett.* **1999**, 40, 3937; (d) Ranu, B. C.; Guchhait, S. K.; Sarkar, A. *Chem. Commun.* **1998**, 2113; (e) Ranu, B. C.; Dutta, J.; Guchhait, S. K. *J. Org. Chem.* **2001**, 66, 5624; (f) Ranu, B. C.; Dutta, J.; Guchhait, S. K. *Org. Lett.* **2001**, 3, 2603; (g) Pitts, M. R.; Harrison, J. R.; Moody, C. J. *J. Chem. Soc., Perkin Trans. 1* **2001**, 955; (h) Ranu, B. C.; Dutta, P.; Sarkar, A. *J. Chem. Soc., Perkin Trans. 1* **1999**, 1139; (i) Ranu, B. C.; Samanta, S.; Guchhait, S. K. *J. Org. Chem.* **2001**, 66, 4102; (j) Khan, F. A.; Dash, J.; Sahu, N.; Gupta, S. *Org. Lett.* **2002**, 4, 1015.
- Inoue, K.; Sawada, A.; Shibata, I.; Baba, A. *J. Am. Chem. Soc.* **2002**, 124, 906.
 - General experimental procedure. Representative one for the reduction of 1,1-dicyano-2-phenyl ethylene (entry 1).

To a stirred solution of anhydrous indium(III) chloride (30 mg, 0.135 mmol, Aldrich) and sodium borohydride (56 mg, 1.5 mmol, Aldrich) in dry acetonitrile (3 mL) was added a solution of 1,1-dicyano-2-phenyl ethylene (154 mg, 1 mmol) in acetonitrile (1 mL) at room temperature (28–30°C) under nitrogen. The reaction mixture was stirred for another 3 h as monitored by TLC and quenched with water (0.5 mL). The reaction mixture was extracted with ether (3×10 mL) and ether extract was washed with brine, dried (Na₂SO₄) and evaporated to leave the crude product which was purified by column chromatography over silica gel (hexane–ether, 70:30) to provide the corresponding alkane (131 mg, 85%) as a white solid, mp 87–88°C whose spectral data are in good agreement with those reported earlier.^{2f}