

Indium as a reducing agent. Chemoselective reduction of α -halocarbonyl compounds and benzyl halides by indium metal in water under sonication

1 PERKIN COMMUNICATION

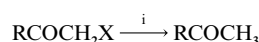
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Indium metal in water reduces α -halocarbonyl compounds and benzyl iodides to the corresponding dehalogenated products in excellent yields under sonication although simple alkyl and aryl iodides remained inert under these conditions.

In recent times, indium has emerged as one of the metals of growing interest because of its great synthetic potential.¹ However, although indium has been used extensively in carbonyl addition reactions,² its use in other domains has not been explored to a great extent.³ Remarkably, the first ionization potential of indium (5.8 eV) is much lower than that of zinc (9.4 eV) or tin (7.3 eV), and even magnesium (7.6 eV) and thus indium metal should participate readily in SET (single electron transfer) processes and therefore be a potential reducing agent. Surprisingly, reduction by indium metal is still unexplored except for a couple of recent examples.⁴ During a recent investigation into the coupling of alkyl and aryl halides by indium in dry DMF we observed a competing reduction process in the case of α -iodoketones.⁵ This prompted us to initiate a systematic investigation into the reduction by indium metal and we have discovered that indium in water reduces α -halocarbonyl compounds very efficiently (Scheme 1).



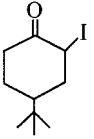
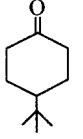
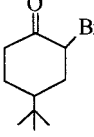
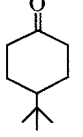
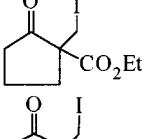
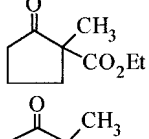
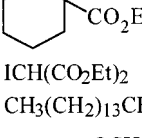
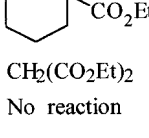
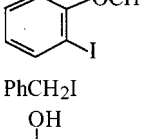
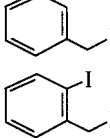
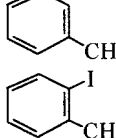
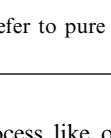
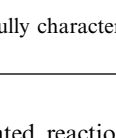
X = I, Br

Scheme 1 Reagents and conditions: (i) In, H₂O, ultrasound.

In a typical experimental procedure, a mixture of α -halocarbonyl compound and indium metal in water was sonicated in an ultrasonic cleaner for a certain period of time as required to complete the reaction. Usual workup and purification produced the corresponding dehalogenated carbonyl compound. Stirring at room temperature did not initiate the reaction even after 24 h. However, the reduction proceeded at reflux, although the reaction is rather slow and messy compared to that under sonication.

A wide range of structurally different α -iodo- and bromo-ketones and esters underwent reduction by this procedure to provide the corresponding dehalogenated carbonyl compounds. The results are reported in Table 1. The reduction of bromo compounds is slow compared to that of iodo compounds. Although alkyl- and aryl-substituted iodides (entry 12, 13) remained inert under these conditions, benzyl iodides (entry 14, 15) were reduced. Also selective reduction of a side chain-substituted iodo functionality is achieved in the presence of iodo-substitution on the aromatic ring (entry 16). The reactions are, in general, reasonably fast and high-yielding. One very important aspect of this procedure is the use of water as reaction medium which has attracted considerable interest in recent times in the context of green chemistry.⁶ It may be assumed that these reductions are also going through a

Table 1 Reduction of α -halocarbonyl compounds and benzyl halides by In/H₂O

Entry	Substrate	t/h	Product	Yield (%) ^a
1	PhCOCH ₂ I	3	PhCOCH ₃	90
2	PhCOCH ₂ Br	8	PhCOCH ₃	86
3	PhCOCH(CH ₃)I	3	PhCOCH ₂ CH ₃	87
4	PhCOCH(C ₂ H ₅)I	3.5	PhCOCH ₂ C ₂ H ₅	91
5	PhCOCH(C ₂ H ₅)Br	7.5	PhCOCH ₂ C ₂ H ₅	85
6	BrCH ₂ CO ₂ CH ₂ CH ₃	6.5	CH ₃ CO ₂ CH ₂ CH ₃	78
7		2.5		89
8		8		83
9		3.5		88
10		4.5		85
11	ICH(CO ₂ Et) ₂	6	CH ₂ (CO ₂ Et) ₂	75
12	CH ₃ (CH ₂) ₁₃ CH ₂ I	19	No reaction	
13		24	No reaction	
14	PhCH ₂ I	5	PhCH ₃	85
15		5		86
16		11		85

^a Yields refer to pure isolated products fully characterised by spectral data.

SET process like other metal-mediated reactions in aqueous media.

In conclusion, this procedure provides a very efficient and general methodology for chemoselective reduction of

α -halocarbonyl and benzyl halides and broadens the scope of indium-mediated reductions.

Experimental

α -Halocarbonyl compounds have been prepared by standard procedures.⁷ Indium metal was purchased from SRL, India, and was used without any treatment.

General procedure for reduction

A mixture of α -halocarbonyl compound or benzyl halide (1 mmol) and indium metal (1 mmol, cut into small pieces) in water (2 cm³) was sonicated in an ultrasonic cleaner for a certain period of time as required to complete the reaction (monitored by TLC). The reaction mixture was extracted with ether and the ether extract was washed with brine and dried (Na₂SO₄). Evaporation of solvent followed by purification by silica gel column chromatography produced the corresponding dehalogenated compound. Identification of the products was made on the basis of IR and ¹H NMR evidence in comparison with authentic samples.

Acknowledgements

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References

- 1 P. Cintas, *Synlett*, 1995, 1087.
- 2 C. J. Li, D. L. Chen, Y. Q. Lu, J.-X. Haberman and J. T. Mague, *J. Am. Chem. Soc.*, 1996, **118**, 4216; V. J. Bryan and T. H. Chan, *Tetrahedron Lett.*, 1996, **37**, 5341; T.-P. Loh and X. R. Li, *Tetrahedron Lett.*, 1997, **38**, 869; M. B. Isaac and L. A. Paquette, *J. Org. Chem.*, 1997, **62**, 5333; X.-H. Yi, Y. Meng and C.-J. Li, *Chem. Commun.*, 1998, 449; G. C. L. Jones and T. Russel, *Synlett*, 1998, 903; L. A. Paquette and J. L. M. Andino, *J. Org. Chem.*, 1998, **63**, 9061; P. K. Choudhury, F. Foubelo and M. Yus, *Tetrahedron Lett.*, 1998, **39**, 3581.
- 3 S. Araki, A. Imai, K. Shimizu, M. Yamada, A. Mori and Y. Butsugan, *J. Org. Chem.*, 1995, **60**, 1841; B. C. Ranu and A. Majee, *Chem. Commun.*, 1997, 1225; N. Fujiwara and Y. Yamamoto, *J. Org. Chem.*, 1997, **62**, 2318; T. P. Loh, D. S.-C. Ho, K.-C. Xu and K.-Y. Sim, *Tetrahedron Lett.*, 1997, **38**, 865; S. Araki, H. Nakano, K. Subburaj, T. Hirashita, K. Shibutani, H. Yamamura, M. Kawai and Y. Butsugan, *Tetrahedron Lett.*, 1998, **39**, 6327; B. C. Ranu, S. K. Guchhait and A. Sarkar, *Chem. Commun.*, 1998, 2113.
- 4 C. J. Moody and M. R. Pitts, *Synlett*, 1998, 1028, 1029.
- 5 B. C. Ranu, P. Dutta and A. Sarkar, *Tetrahedron Lett.*, 1998, **39**, 9557.
- 6 C.-J. Li and T.-H. Chan, *Organic Reactions in Aqueous Media*, John Wiley and Sons, New York, 1997.
- 7 S. Motohashi and M. Satomi, *Synthesis*, 1982, 1021; P. Dowd and S. C. Choi, *Tetrahedron*, 1989, **45**, 77.

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