

Stereoselective debromination of aryl-substituted *vic*-dibromide with indium metal

Brindaban C. Ranu,*† Sankar K. Guchhait and Arunkanti Sarkar

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

Debromination of both *meso* and *dl* (*erythro* and *threo*) aryl-substituted *vic*-dibromides with indium metal in MeOH leads to *trans*-alkenes exclusively.

The protection-deprotection of olefins *via* bromination-debromination is an important process in organic synthesis. Although bromination generally proceeds smoothly and stereospecifically to give high yields of dibromides, debromination at a later stage in the synthesis often proves more difficult. This is primarily because the efficiency of this process greatly depends upon the stereoselectivity in the debromination step and compatibility of the reagent with the carbon-carbon double bond formed and other functionalities present in the substrates. Many reagents¹ including metals like Zn,^{1d} Mg^{1d} and Sm,^{1h} have been reported in the literature for this reaction, but most of them are also associated with the limitations regarding selectivity and compatibility. Thus, an efficient and selective procedure for debromination of *vic*-dibromides is needed.

In recent times there has been increasing interest in indium-mediated transformations because of certain unique properties inherent to indium.² However, although indium has been used extensively in carbonyl addition reactions,^{2,3} its potential in other domains has not been explored to any great extent.⁴ Because of the close resemblance of indium to magnesium and zinc in several respects, including first ionization potential, indium could also be a potential reducing agent. This prompted us to initiate an investigation of indium-promoted reductive debromination of *vic*-dibromides. We have observed that aryl-substituted *vic*-dibromides undergo smooth debromination to produce the corresponding (*E*)-alkenes when treated with indium metal in MeOH (Scheme 1).

The experimental procedure is very simple. A mixture of *vic*-dibromide (1 mmol) and indium metal (1 mmol, ‡ cut into small pieces) in dry MeOH (10 ml) was refluxed for a certain period of time (Table 1) until completion of the reaction (TLC). MeOH was removed and the residue was extracted with Et₂O. Evaporation of solvent followed by purification by silica gel chromatography furnished the pure alkene in high yields.

A wide range of structurally varied aryl-substituted *vic*-dibromides underwent debrominations by this procedure to provide the corresponding alkenes. The results are summarised in Table 1. Very interestingly, only *trans* olefins are obtained from all the substrates, whether they are *meso/erythro* or *dl/threo* (entries 1, 2, 4, 5, 8, 9). If debromination occurs by the usual *trans*-elimination, *meso/erythro*- or *dl/threo*-*vic*-dibromides would give *trans*- or *cis*-alkenes, respectively. It is therefore suggested that the reaction occurs *via* a common, relatively stable radical or anion intermediate which directly collapses to (*E*)-alkene. This speculation gains support from the observations that *cis*-stilbene does not undergo isomerisation to the *trans* isomer upon reflux with indium metal or oxidised

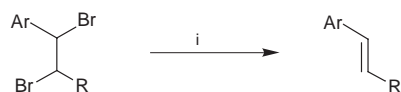
indium products§ from debromination of *erythro*-1,2-dibromo-1-phenyl-2-benzoylthane in MeOH, even after 8 h. The presence of *cis*-stilbene was also not detected upon quenching the debromination reaction of *vic*-dibromides of stilbene at an intermediate stage.

In general, the reactions are very clean and high-yielding. MeOH has been found to be the best solvent for this reaction; in pure MeCN the debromination does not proceed at all. Several sensitive functional groups, such as ketone carbonyl, carboxylic ester, hydroxy, methoxy and chloro groups on aromatic rings, remained unaffected under the present reaction conditions. No over-reduction of the produced alkene was observed with any

Table 1 Debromination of aryl-substituted *vic*-dibromides with indium metal in MeOH

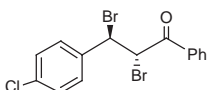
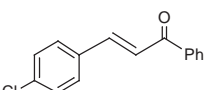
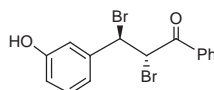
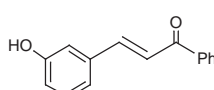
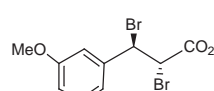
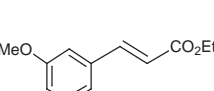

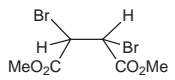
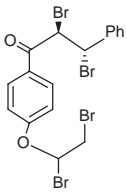
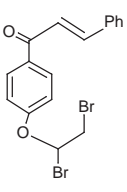
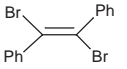
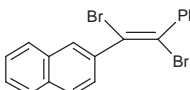
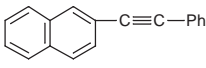
Entry	Substrate	t/h	Product	Yield (%) ^a
1		2		88
2		8		85
3		7		94
4		4 ^b		90
5		9		92
6		12 ^b		90
7		12		89
8		2		85
9		1 ^c		88
10		2 ^d		91

^a Yields refer to pure isolated products fully characterised by spectral and analytical methods. ^b The reaction was performed at room temperature (30 °C) with stirring. ^c MeOH–MeCN (1:1) was used as solvent instead of MeOH to dissolve the *vic*-dibromide. ^d MeOH–MeCN (10:1) was used. ^e 2 equiv. of indium were used.



Scheme 1 Reagents and conditions: i, In, MeOH, reflux

Table 1 (cont.) Debromination of aryl-substituted *vic*-dibromides with indium metal in MeOH

Entry	Substrate	t/h	Product	Yield (%) ^a
11		9 ^c		92
12		9 ^c		86
13		19		90
14		12	No reaction	
15		12	No reaction	
16		3.5 ^e		86
17		8.5	Ph—C≡C—Ph	88
18		7		82

^a Yields refer to pure isolated products fully characterised by spectral and analytical methods. ^b The reaction was performed at room temperature (30 °C) with stirring. ^c MeOH–MeCN (1:1) was used as solvent instead of MeOH to dissolve the *vic*-dibromide. ^d MeOH–MeCN (10:1) was used. ^e 2 equiv. of indium were used.

substrate, unlike those reactions reported using Sm^{1h} and Mg.⁵ As this reagent is inert to alkyl-substituted dibromides (entries 14, 15), selective debromination of aryl-substituted *vic*-dibromide moieties is achieved in the presence of alkyl-substituted dibromide moieties (entry 16). This procedure is also effective for the debromination of *vic*-dibromoalkenes to the corresponding alkynes (entries 17, 18).

In conclusion, the present procedure provides an efficient and general methodology for reductive debromination of aryl-substituted *vic*-dibromides to the corresponding (*E*)-alkenes; to the best of our knowledge this is the first report of indium-

promoted debromination of *vic*-dibromides.⁶ The significant improvements offered by this method over other existing debromination procedures¹ are: no overreduction of the double or triple bond formed, tolerance to several reducible functionalities, exclusive formation of (*E*)-alkenes from *cis*- as well as *trans*-dibromides, selective debromination of aryl-substituted dibromide moieties in presence of alkyl-substituted ones, and the easy availability and apparently nontoxic nature of indium metal.[¶] Thus, this reaction is endowed with considerable synthetic potential and may provide a new method for reductive debromination and conversion of a *cis*-alkene to its *trans*-isomer. Further investigations of more useful applications are in progress.

We gratefully acknowledge financial support from CSIR, New Delhi [Grant No. 01(1504)/98] for this investigation. S. K. G. and A. S. are also thankful to CSIR for their fellowships. We thank Mr A. Som for his help with this work during his tenure as a summer project student in this laboratory from IIT, Kanpur.

Notes and References

† E-mail: ocber@iacs.ernet.in

‡ Debromination also proceeds in the presence of < 1 equiv. of indium; however, the reaction is very slow, e.g. *erythro*-1,2-dibromo-1-phenyl-2-benzoylethane (entry 8) takes 9 h with 0.5 equiv of In compared to 1 h with 1 equiv under identical reaction conditions.

§ We thank one of the referees for this suggestion.

¶ Indium metal is not affected by air and moisture and thus does not require any activation before reaction. Indium can be handled easily without any special precautionary measures and is relatively inexpensive.

- (a) E. L. Allred, B. R. Beck and K.J. Voorhees, *J. Org. Chem.*, 1974, **39**, 1426; (b) D. Landini, S. Quici and F. Rolla, *Synthesis*, 1975, 397; (c) D. Savoia, E. Tagliavini, C. Trombini and A. U. Ronchi, *J. Org. Chem.*, 1982, **47**, 876; (d) E. Baciocchi, in *Chemistry of Functional Groups, Supplement D, Part 1*, ed. S. Patai and H. Rappoport, Wiley, New York, 1983; (e) S. G. Davies and S. E. Thomas, *Synthesis*, 1984, 1027; (f) K. Yanada, R. Yanada and H. Meguri, *J. Chem. Soc., Chem. Commun.*, 1990, 730; (g) J. M. Khurana and G. C. Maikap, *J. Org. Chem.*, 1991, **56**, 2582; (h) R. Yanada and N. Negoro, K. Yanada and T. Fujita, *Tetrahedron Lett.*, 1996, **37**, 9313; (i) C. Malanga, S. Mannucci and L. Lardicci, *Tetrahedron*, 1998, **54**, 1021; (j) T. S. Butcher and M. R. Detty, *J. Org. Chem.*, 1998, **63**, 177.
- P. Cintas, *Synlett*, 1995, 1087.
- 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.
- 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.
- T. Hudlicky, G. Sinai-Zingde and M. G. Natchus, *Tetrahedron Lett.*, 1987, **28**, 5287.
- For indium promoted debromination of geminal dibromides, see: S. Araki and Y. Butsugan, *J. Chem. Soc., Chem. Commun.*, 1989, 1286.

Received in Cambridge, UK, 19th August 1998; 8/06530F