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Reduction of trihalomethyl carbinols and their acetates, mesylates and tosylates by indium metal

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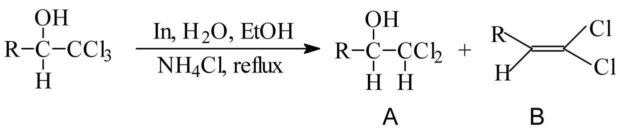
Abstract—A study of reduction of trihalomethyl carbinols and their derivatives by indium metal shows that while trichloromethyl carbinols produce a mixture of the corresponding dichloromethyl carbinol and vinylidene dichloride, the acetates, mesylates and tosylates of the trichloro- and tribromomethyl carbinols undergo clean reduction to provide the respective vinylidene dichloride only. © 2002 Elsevier Science Ltd. All rights reserved.

In recent times, indium metal has been the subject of growing interest because of its unique properties and great synthetic potential.[1] Because of the close resemblance of indium to magnesium and zinc in several respects including the first ionization potential (5.8 eV), we envisioned indium to be a potential reducing agent and initiated a systematic investigation into reduction by indium metal.[2] Interestingly, although considerable activities have been observed in indium-mediated carbonyl addition reactions during the last decade, its capability as a reducing agent has only been explored quite recently.[2,3] As part of our continuing program we have already reported the selective reduction of terminal alkynes,[2a] highly activated conjugated alkenes,[2b] α-halocarbonyl compounds,[2c] *vic*-dibromides,[2d] and *gem*-vinyl dibromides[2e] and we now disclose our results on the reduction of *gem*-trihalides in trihalomethyl carbinols and their derivatives.

The reduction of trichloromethyl carbinols by indium metal is not very clean. Upon reflux with indium in aqueous ethanolic ammonium chloride a mixture of the corresponding dichloromethyl carbinols and vinylidene dichlorides are obtained in rather low yield (30–40%) (Scheme 1). Even after prolonged periods (16–20 h) of reflux the conversion was never complete, with unreacted starting material remaining. The use of other solvents such as DMF or AcOH made the situation worse producing considerable amounts of tarry material. So, we considered the possibility of a more facile reaction by derivatization of the hydroxy functionality. Thus, the corresponding acetates, mesylates and tosylates of trichloromethyl carbinols when treated with indium in DMF resulted in the corresponding vinylidene dichlorides being obtained as single products in high yields (Scheme 2).

In a typical experimental procedure,[4] an acetate, mesylate or tosylate of the trihalomethyl carbinol (1 mmol) was heated under reflux in DMF with indium metal (1 mmol, cut into small pieces) for the period of time required to complete the reaction (TLC). The usual workup and purification by column chromatography furnished the pure product. The results are reported in Table 1.



	Yield(%)	Ratio of A/B
R = Ph,	32	72 : 28
R = p-Cl-C_6H_4	35	68 : 32
R = p-OMe-C_6H_4	40	63 : 37

Scheme 1.

Scheme 2.

Keywords: indium metal; reduction; trihalomethyl carbinols and derivatives; vinylidene dichloride.

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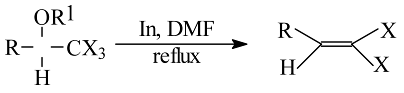
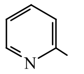
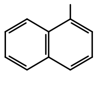
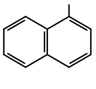
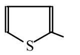
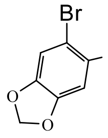
Table 1. Reduction of trihalomethyl carbinol derivatives by indium metal



Entry	R	R^1	X	Time (h)	Yield ^{a}(%)
1	Ph	Ac	Cl	5	76
2	Ph-CH=CH(t)	Ac	Cl	4.5	83
3		Ac	Cl	4	71
4	*p*-allyl-O-C_6H_4	Ac	Cl	4	73
5	*m*-MeO,*p*-BzO-C_6H_3	Ac	Cl	4	82
6	$CH_3(CH_2)_8$	Ac	Cl	6	60
7	Ph	Ms	Cl	3	93
8	Ph	Ts	Cl	3	94
9	*p*-Cl-C_6H_4	Ms	Cl	3.5	93
10	*p*-Cl-C_6H_4	Ts	Cl	3	95
11	*p*-MeO-C_6H_4	Ms	Cl	3	92
12	*p*-MeO-C_6H_4	Ts	Cl	3	92
13		Ms	Cl	3.5	92
14		Ts	Cl	3.5	93
15	*m*-MeO-C_6H_4	Ms	Cl	4	91
16	*m*,*p*-$(MeO)_2$-C_6H_3	Ms	Cl	4	83
17	*m*-Me-C_6H_4	Ms	Cl	4	90
18		Ms	Cl	3	82
19		Ms	Cl	3.5	87
20	Ph	Ms	Br	3	96
21	*p*-Cl-C_6H_4	Ms	Br	3	95
22	*p*-MeO-C_6H_4	Ms	Br	3	97

[a] Yields refer to those of pure isolated products fully characterized by spectroscopic data.

A wide range of structurally varied acetates, mesylates and tosylates of trichloro- and tribromomethyl carbinols underwent reductions by this procedure to provide the corresponding vinylidene dihalides. It was observed that reductions of mesylates and tosylates were more facile and relatively clean compared to those of acetates. Presumably, this was due to -OMs and -OTs being better leaving groups. The reduction of a non-aromatic derivatives was rather complex giving a comparatively low yield of vinylidene dichloride along with some unidentified side products (entry 6). This is not unusual for non-aromatic substrates and we obtained similar results in our earlier observations during the reduction of *vic*- and *gem*-dibromides.[2d,2e] It may be assumed that these reductions occur through a SET process and thus the intermediate radical species are more stabilized in the aryl-substituted derivatives. When 2 equiv. of indium were used, the tribromomethyl sulphonates underwent two consecutive reductions to produce the corresponding vinyl bromides as final products (entries 20–22). This is to be expected as we have observed earlier that indium reduces vinylidene dibromides to vinyl bromides.[2e] However, the trichloromethyl derivatives did not undergo any further reduction beyond vinylidene dichlorides even with 3 equiv. of indium and longer periods of reflux. These reductions are very selective not reducing Cl (entries 9, 10, 21) or Br (entry 19) functionalities attached to the aromatic rings. Moreover, double bonds (C=C) (entries 2, 4) also remained unaffected during these reductions.

In conclusion, the present procedure using indium metal provides a highly selective reduction of acetates, mesylates and tosylates of aryl-substituted trihalomethyl carbinols to the corresponding vinylidene dihalides which are useful intermediates in organic synthesis.[5] The high yield, considerably fast reaction and compatibility with other reducible functional groups make this procedure a practical alternative to existing ones.[6,7] Furthermore, this procedure also broadens the scope of reductions by indium metal.

Acknowledgements

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4. **General experimental procedure for the reduction of acetates, mesylates and tosylates of trichloro- and tribromomethyl carbinols. Representative procedure for the reduction of 2-phenyl-2-tosyloxy-1,1,1,-trichloroethane to 1,1-dichloro-2-phenylethene.** A solution of 2-phenyl-2-tosyloxy-1,1,1-trichloroethane (380 mg, 1 mmol) in DMF (2 mL) was heated under reflux at 150–160°C with indium metal (115 mg, 1 mmol, cut into small pieces) under nitrogen for 3 h (TLC). The reaction mixture was then quenched with a saturated solution of ammonium chloride and extracted with ether (3×10 mL). The ether extract was washed with brine, dried (Na_2SO_4) and evaporated to leave the crude product which was purified by column chromatography over silica gel [eluted with hexane–ether (9:1) solvent system] to furnish 1,1-dichloro-2-phenylethene as a colourless oil (163 mg, 94%). The IR, ^1H and ^{13}C NMR spectral data of this compound were found to be identical with those reported.[7] This procedure has been followed for the reduction of all the other trihalides listed in Table 1. All the products have been characterized by IR, ^1H and ^{13}C NMR spectroscopy and elemental analyses.
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