Pergamon

Tetrahedron Letters 43 (2002) 1877–1879

TETRAHEDRON
LETTERS

An indium mediated efficient chemoselective deoxygenation of *N*-oxides and nitrones

Md Ilias, Dhiren C. Barman, Dipak Prajapati and Jagir S. Sandhu*

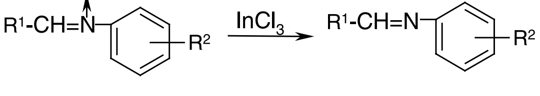
Regional Research Laboratory, Jorhat-785006, Assam, India

Received 12 November 2001; revised 11 December 2001; accepted 20 December 2001

Abstract—A simple and inexpensive procedure for the deoxygenation of *N*-oxides, such as *N*-arylnitrones, azoxybenzenes and *N*-heteroarene *N*-oxides with indium trichloride in acetonitrile at ambient pressure is described. The procedure gives high yields of deoxygenated products. © 2002 Elsevier Science Ltd. All rights reserved.

In recent years organic chemistry has witnessed the increased use of indium reagents.[1] It was found that the low reactivity of trivalent organoindium reagents can be increased by complex formation with organolithium compounds.[2] The tetraorgano-indates thus prepared are sufficiently reactive to take part in reactions at ambient temperature.[2a] Allylic indates react with imides and nitriles regioselectively at the γ-carbon to give homoallylamines.[2b] Also, indium metal[3] has been found to be an effective reducing agent and indium(III) halide complexes act[4a] as efficient Lewis acid catalysts in Mukaiyama aldol reactions, Friedel–Crafts acylations,[3] Diels–Alder reactions[4b] in water and hetero Diels–Alder cycloadditions.[4c] Our interest in indium based reagents[5] prompted us to investigate the use of indium in the chemoselective deoxygenation of *N*-oxides. The selective deoxygenation of organic *N*-oxides is a subject of considerable interest in heterocyclic synthesis and a large number of reports are available on the reduction of N–O bonds.[6] Aromatic *N*-oxides are relatively more stable than aliphatic ones. They are also resistant to deoxygenation,[7] although some undergo deoxygenation with sulfurous acid followed by the liberation of sulfuric acid.[8] Several deoxygenating agents including sodium hydrogen telluride,[6a] phosphorus,[6b] aluminium–nickel alloy,[9] titanium(0) reagents,[10] tin derivatives,[11] silanes,[12] alkali metal hydrides,[13] tetrathiomolybdate[14] and aluminium iodide[15] may be used for this purpose. However, most of these methods are deficient in some respects, such as low yields, difficult accessibility, drastic reaction conditions which effect substituents,[16] uncontrolled reduction of nitrones **1**[6b] or reductive cleavage of azoxy compounds[11] to amines rather than to the expected imines or azo compounds, respectively. Moreover, the titanium tetrachloride–$NaBH_4$ complex, used by Kano,[17] was found to reduce the aromatic ring in the substrate. Also, in a very recent finding,[18] $HCOONH_4$/10% Pd–C reduces pyridine *N*-oxides to their corresponding piperidine derivatives. We report herein, the utility of indium(III) chloride as an efficient deoxygenating agent for *N*-oxides such as nitrones, azoxybenzenes and *N*-heteroarene *N*-oxides to give the corresponding aromatic derivatives. The reaction proceeds efficiently at ambient pressure and in high yields (Scheme 1).

In a typical case, to a solution of benzaldehyde *N*-phenyl nitrone **1a** (0.40 g, 2 mmol) in dry acetonitrile (15 ml) was added anhydrous indium trichloride (0.45 g, 2 mmol) and the mixture was refluxed under a nitrogen atmosphere for 1 h (monitored by TLC). After completion of the reaction, the solvent was removed on a rotary evaporator and the residue was treated with water (50 ml). The resultant mixture was made basic (pH 8) with 25% aqueous ammonia and extracted with diethyl ether (2×30 ml), the extract dried over anhydrous Na_2SO_4 and the solvent distilled off to give the



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Scheme 1.

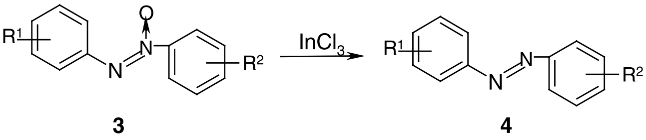
Keywords: indium trichloride; deoxygenation; azoxybenzenes; *N*-arylnitrones; *N*-oxides.

* Corresponding author. Fax: +91 0376 3370011; e-mail: drugs@csir.res.in; drrljt@csir.res.in

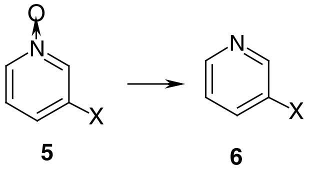
PII: S0040-4039(02)00020-5

crude product, which was purified by column chromatography (pet. ether/benzene, 4:1) to afford the imine **2a** in 95% yield. Similarly, other nitrones (entries 2–7) were reacted and the corresponding imines were isolated in high yields (Table 1), without the formation of any rearranged amides or decomposition products. The selectivity of this new method is demonstrated by several examples and the results are summarised in Table 1. A variety of nitrones, azoxybenzenes, pyridine *N*-oxides and quinoline *N*-oxides were converted efficiently to their corresponding deoxygenated derivatives. The method is general and several reducible functionalities such as methoxycarbonyl, methyl ether and cyano remain unaffected, the chloro substituents in 4-chloroquinoline 1-oxide **8b** and 3-chloropyridine 1-oxide **6a** remain unchanged, even though they are prone to dehalogenation reactions.[19] Extending the methodology to azoxybenzenes **3** gave the corresponding azobenzenes **4** as the sole products (Table 1). Similarly, the reaction of indium trichloride with quinoline and pyridine *N*-oxides, respectively, afforded the deoxygenated products **6** and **8** in high yields without the formation of any side products. It is worth mentioning here that aldonitrones rearrange to the isomeric amides by treatment with a variety of Lewis acids[20] and 2,4,4-trimethylpyrroline *N*-oxide gave decomposition products with triphenylstibine or triphenylbismuthine.[21] However, indium trichloride being a mild Lewis acid gave only the corresponding deoxygenated products in high yields without the formation of any undesirable side products. To check the efficiency of indium trichloride in this reaction we carried out the deoxygenation with a catalytic amount of indium trichloride (10 mg) under reflux conditions and found that the reaction was comparatively less effective and took 3–6 h to give 60% yields of **2a**. A further increase in the reaction time had no significant effect on the yield and resulted in a minor amount of decomposition. All the compounds obtained were characterised by spectroscopic data and finally by comparison with authentic samples (Schemes 2–4).

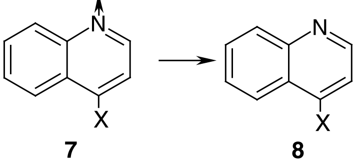
In conclusion, this new deoxygenative method using indium trichloride offers a useful alternative to the other methods available for the reduction of *N*-oxides. Its main advantages are the avoidance of strong acid media and harsh reagents, no side product formation with groups like methyl ethers and chloro substituents surviving under the reaction conditions, very mild conditions and excellent yields for a wide variety of products.



Scheme 2.



Scheme 3.



Scheme 4.

Table 1. Deoxygenation of *N*-oxides **1**, **3**, **5**, and **7** with $InCl_3$

Entry	Product[a]	R^1/X	R^2	Reaction time (h)	Yield[b] (%)
1	**2a**	C_6H_5	H	1	95
2	**2b**	4-ClC_6H_4	H	1.5	90
3	**2c**	C_6H_5	4-Cl	1	85
4	**2d**	4-OMeC_6H_4	H	1	90
5	**2e**	2-Furyl	H	1	80
6	**2f**	2-Thienyl	H	1.5	78
7	**2g**	C_6H_5CH=CH-	H	1.5	80
8	**4a**	H	H	1.5	80
9	**4b**	4-Cl	4-Cl	1	82
10	**6a**	Cl	–	1.2	75
11	**6b**	H	–	1.2	80
12	**6c**	COOMe	–	1	78
13	**6d**	CN	–	1	75
14	**8a**	H	–	1.5	80
15	**8b**	Cl	–	1.2	76

[a] Most of the products are commercially available and were identified by comparison of their TLC, IR and mass spectra with those of authentic samples.

[b] Yield of isolated products.

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