SHORT PAPER

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A facile and chemoselective cleavage of trityl ethers by indium tribromide[†]

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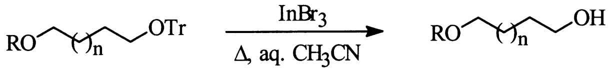
Trityl ethers are chemoselectively deprotected to the corresponding alcohols in high yields by a catalytic amount of indium tribromide in aqueous acetonitrile. The method is compatible with various functional groups such as acetonides, acetates, benzoates, olefins, carbamates, esters and ethers present in the substrate.

Keywords: trityl ethers, indium tribromide, chemoselective cleavage

Trityl ethers are widely used protecting groups for primary alcohols in carbohydrates.[1] Among various hydroxyl protective groups, trityl ethers are the most versatile[2] due to their ease of formation/removal and also to their stability towards a variety of reaction conditions. Several procedures are reported for their removal under strongly protic[3,4] or Lewis acid conditions.[5-7] Further, a few methods[8] are reported for the selective cleavage of trityl ethers under mild conditions. However, many of these procedures often involve strongly acidic conditions,[4] incompatibility with other acid sensitive groups,[4c] unsatisfactory yields, stoichiometric amount of catalysts,[7c] corrosive, hazardous reagents[3a] and necessity of anhydrous conditions. These limitations prompted us to disclose a new procedure for selective removal of trityl ethers over a wide range of functional groups present in the molecule. Recently indium trihalides have emerged as a powerful Lewis acids[9] imparting high regio- and chemoselectivity in various chemical transformations due to their exceptional stability, reactivity and recoverability from water. Since indium trihalides have unique catalytic properties in water, the use of indium tribromide for selective removal of trityl group in aqueous media is of great interest.

In this report we describe a novel and catalytic method for detritylation using indium tribromide in aqueous acetonitrile. The cleavage was effected by a catalytic amount of indium tribromide in refluxing aqueous acetonitrile with high chemoselectivity (Scheme 1).



Scheme 1

The procedure is highly selective to deprotect trityl ethers leaving other functional groups intact. Trityl ethers are deprotected in high yields (80–95%) within 0.5–2.5 h of reaction time. Further, the cleavage also proceeded smoothly with a catalytic amount of $InCl_3$ (5% w/w of ether) in refluxing aqueous acetonitrile. The deprotection was clean, high yielding and completed in a short reaction time. The cleavage occured in the presence of 5 mol % $InBr_3$ in refluxing acetonitrile : water (1:1) without affecting other functional groups. The deprotection of trityl ethers also proceeded smoothly in water alone at 60°C in the presence of either 5% indium trichloride or indium tribromide. There are many advantages in the use of indium trihalides for detritylation which avoids the use of strongly acidic or oxidising conditions. The method does not require anhydrous solvents or stringent reaction conditions. Further trityl ethers are selectively deprotected without the cleavage of glycosidic bonds or the hydrolysis of isopropylidene groups which are normally observed under strongly acidic conditions. Another advantage of the use of $InBr_3$ for this cleavage is that the reaction conditions are compatible with other hydroxyl protecting groups such as acetonides, acetates, benzoates, benzyl (Bn), methyl, allyl, *p*-methoxy benzyl (PMB) and *t*-butyldiphenylsilyl ethers (TBDPS). Other acid sensitive protecting groups such as *t*-butoxycarbonyl (BOC), and benzoyloxycarbonyl (CBz) are also unaffected by indium tribromide. Trityl ethers are chemoselectively deprotected in the presence of a wide range of functional groups such as olefins, esters, carbamates and ethers. The catalyst was recovered from the aqueous layer during work-up and recycled in subsequent reactions. Several examples illustrating this novel and rapid procedure for the removal of trityl group are summarised in Table 1.

In summary, $InBr_3$ is found to be a superior Lewis acid for the selective cleavage of trityl ethers in the presence of various functional groups. In addition to its simplicity and mild reaction conditions, this procedure has the ability to tolerate a wide variety of functional groups.

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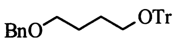
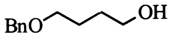
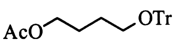
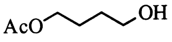
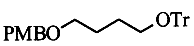
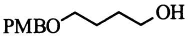
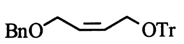
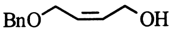
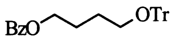
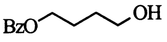
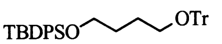
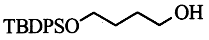
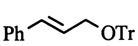
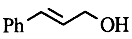
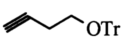
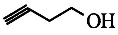
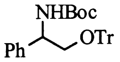
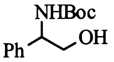
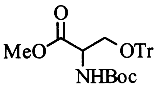
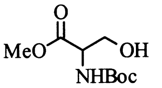
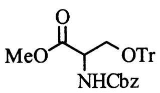
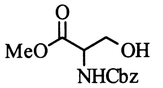
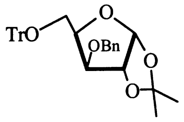
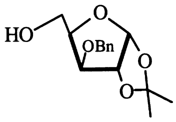
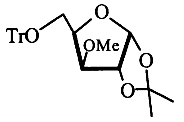
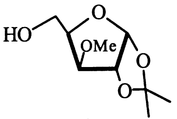
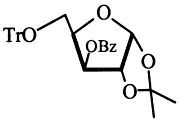
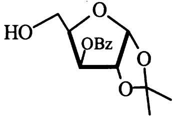
[†] This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

Table 1 $InCl_3$ catalysed detritylation of ethers in aqueous media

Entry	Ether **(1)**	Alcohol[a] **(2)**	Reaction time/h	Yield[b]/ %
(a)			2.5	90
(b)			1.5	85
(c)			2.0	92
(d)			3.0	95
(e)			2.5	90
(f)			1.5	87
(g)			2.5	90
(h)			2.0	93
(i)			3.0	84
(j)			3.0	81
(k)			3.5	89
(l)			2.5	90
(m)			2.0	92
(n)			3.0	95

[a] All the products were characterised by 1H NMR, IR and mass spectra.

[b] Isolated and unoptimised yields using 5mol% $InCl_3$.

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10 *General procedure:* A mixture of trityl ether (5 mmol) and $InCl_3$ or $InBr_3$ (0. 25 mmol) in acetonitrile: water (1:1, 10 ml) was stirred under reflux for an appropriate time (Table 1). After completion of the reaction as indicated by TLC, the reaction mixture was diluted with water (10 ml) and extracted twice with ethyl acetate (2 x 15 ml). The combined organic layers were dried over anhydrous Na_2SO_4, concentrated *in vacuo* and purified by column chromatography on silica gel (Merck, 100–200 mesh, ethyl acetate – hexane, 2:8) to give pure alcohol. Spectral data for compound **1a:** 1H NMR ($CDCl_3$) : δ 2.05 (m, 4H), 3.30 (t, 2H, *J* = 6.8 Hz), 3.70 (t, 2H, *J* = 6.8 Hz), 4.50 (s, 2H), 7.25–7.35 (m, 15H), 7.45-7.55 (m, 5H). **2a:** 1H NMR ($CDCl_3$) : δ 1.75 (m, 4H), 3.05 (brs, OH), 3.55 (t, 3H, *J* = 6.8 Hz), 3.65 (t, 3H, *J* = 6.8 Hz), 4.50 (s, 2H), 7.35–7.45 (m, 5H). **1b:** 1H NMR ($CDCl_3$) : δ 1.95 (m, 4H), 2.05 (s, 3H), 3.20 (t, 2H, *J* = 7.0 Hz), 4.25 (t, 2H, *J* = 7.0 Hz), 7.25–7.35 (m, 10H), 7.45-7.55 (m, 5H). **2b:** 1H NMR ($CDCl_3$) : δ 1.80 (m, 4H), 2.05 (s, 3H), 3.05 (brs, OH), 3.30 (t, 2H, *J* = 7.0 Hz), 4.25 (t, 2H, *J* = 7.0 Hz).