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Indium tribromide/[bmim]PF_6: a novel and recyclable catalytic system for the deprotection of 1,1-diacetates

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A mild and highly efficient method has been developed for the deprotection of 1,1-diacetates using a catalytic amount of indium tribromide immobilised in 1-butyl-3-methylimidazolium hexafluorophosphate as an ionic liquid. This affords the corresponding the parent aldehydes in excellent yields. The recovered ionic liquid containing catalyst has been recycled in three subsequent runs.

Keywords: 1,1-diacetates, aldehydes, deprotection, indium tribromide, ionic liquid

Organic solvents are a major source of waste, and their efficient control can produce a substantial improvement in the environmental impact of a process. Consequently there has been considerable recent research into replacing the use of volatile organic solvent with clean solvents as the reaction media.[1] In this respect, room temperature ionic liquids (RTILs), mainly consisting of 1,3-dialkylimidazolium cations have attracted increasing interest as alternative environmentally benign reaction media.[2] These solvents are nonflammable, have a high thermal stability, tuneable polarity, immiscibility with a number of organic solvent, negligible vapour pressure and recyclability. A variety of chemical reactions from alkylation and polymerisation to biocatalysis and electroplation have already been carried out in these solvent.[3] Because of the distinct advantages of ionic liquids, they can make an important contribution to green chemistry.

The protection–deprotection of aldehydes functionalities is useful in synthetic organic chemistry, and a plethora of reagents and methods have been developed to this end. In recent years, 1,1-diacetates have been introduced as a suitable protection group for this purpose[4] because of their stability in neutral and basic medium and ease of preparation.[5] In addition, they can be converted into other useful functional groups by reaction with appropriate nucleophiles[6] and used as carbonyl surrogates for asymmetric synthesis.[7] The synthesis of optically active aldehydes by lipase-catalysed resolution of the corresponding acylals has been reported.[8] However, the final stages of chemical manipulation require their cleavage so as to regenerated the parent aldehydes. Therefore, considerable interest has been focused on mild, selective methods used for the conversion of 1,1-diacetates to the corresponding aldehydes. A variety of reagents have been developed for this transformation. These include hydrochloric acid,[9] sulfuric acid,[10] montmorillonite clays,[11] expansive graphite,[12] zeolite,[13] boron triiodide-*N,N*-diethylaniline complex,[14] ceric ammonium nitrate (CAN) coated on silica gel,[15] neutral alumina under microwave irradiation,[16] $CeCl_3{\cdot}7H_2O/NaI$,[17] CBr_4,[18] $[NO^+{\cdot}crown{\cdot}H(NO_3)_2^-]$,[19] $AlCl_3$,[20] zirconium (IV) chloride[5f] and $BiCl_3$,[21] layered zirconium sulfophenyl phosphonate,[22] $Sc(OTf)_3$,[23] base-catalysed cleavage by sodium hydroxide or potassium carbonate in aqueous THF[24] and potassium phenoxides.[25] However, most of these methods require a high catalyst loading, have a long reaction time and involve the use of volatile organic solvents such as CH_2Cl_2, CH_3CN, benzene in high temperature reaction conditions or large amounts of solid supports, which eventually result in generation of a large amount of toxic waste. With increasing environmental concerns, it is imperative that novel environmentally benign solvents and reagents be developed. One example of such an environmentally friendly, mild method for deprotection of 1,1-diacetates using β-cyclodextrin in aqueous medium has also been reported.[26]

Recently, indium compounds have become attractive candidates for use as regents in organic synthesis because most indium compounds are relatively non-toxic, readily available at low cost and water-tolerant.[27] Indium tribromide has been found to be an effective catalyst in promoting various organic transformations.[28] In view of the emerging importance of ionic liquid as novel reaction media, we report a mild and highly efficient method for the deprotection of 1, 1-diacetates using a catalytic amount of indium tribromide in ionic liquid.

As shown in Table 1, treatment of phenylmethanediol diacetate (**1b**) in [bmim]PF_6 ionic liquid in the presence of 10 mol% $InBr_3$ at room temperature afforded benzaldehyde in 96% yield. Under similar reaction conditions, various 1,1-diacetates underwent deprotection smoothly to give the corresponding aldehydes (**2**) in excellent yield. The reactions were mild and no side products or decomposition of products were observed. In the absence of the catalyst, the reaction did not yield any product even after a long reaction time. Lower catalyst loading could be used with only a marginal drop in reaction rate (**1a**). In addition, the 2-furanylmethanediol diacetate (**1k**) also gave good yield. It should be mentioned that delicate electronic effects were observed, that is, aryl 1,1-diacetates with electron-rich groups (**1b**–**1g**) reacted rapidly, which substitution of electron-withdrawing groups (**1h**–**1j**) on the benzene ring decreased the reactivity, requiring longer reaction times. Only a trace of products were obtained from (*m*-nitrophenyl) methanediol diacetate (**1o**) and (*p*-nitrophenyl)methanediol diacetate (**1p**). These substrates have a strong electron-withdrawing groups. However, the deprotection of **1o** and **1p** could be achieved for more than 10 h at 70 °C in excellent yields. Therefore, this method could be applied to chemoselective deprotection of aryl 1, 1-diacetates because of difference of their electronic effects.

Various functional groups are tolerated under the present reaction conditions. Acid sensitive or oxidisable groups such as methoxy, benzyloxy, methylenedioxy, nitro, chloro and double bonds survive under such conditions. The phenolic acetate function (**1m** and **1n**) remains unaffected under these reaction conditions. The present procedure is a selective deprotection of aryl aldehydes diacetates to aryl aldehydes in the presence of the phenolic acetate. Acetals such as 1,1-ethylenedioxy-1-phenylmethane (**q**) and 1,1-dimethoxy1-phenylmethane (**r**) could be converted to their corresponding carbonyl compounds under these conditions.

$$\underset{\mathbf{1}}{RCH(OAc)_2} \xrightarrow[\text{[bmim]PF}_6]{10\%\ InBr_3} \underset{\mathbf{2}}{RCHO}$$

Scheme 1

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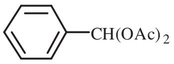
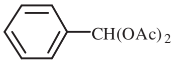
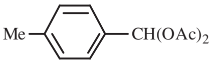
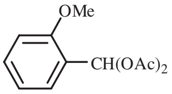
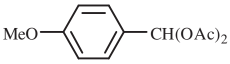
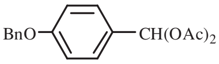
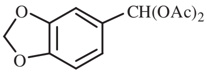
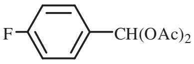
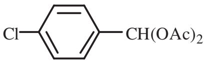
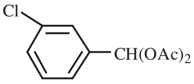
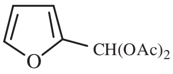
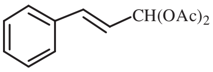
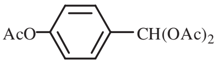
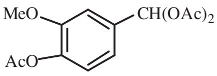
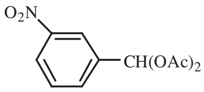
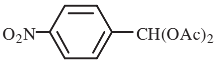
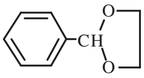
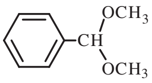
Table 1 The deprotection of 1,1-diacetates using $InBr_3$/[bmim]PF_6

Entry	Substrate	Time/min	Yield/%[a]	M.p. (T/°C)[b.p.(T/°C)/Torr	
				Found	Reported[29]
a		40	95[b]	60–62/10	178/760
b		20	96		
c		18	94	84–85/10	200/760
d		18	95	36–37	37–38
e		15	96	116–118/10	249.5/760
f		16	92	74–75	72–74
g		15	95	36–37	37
h		25	97	63–65/10	181.5/760
i		50	96	47–48	47.5
j		45	95	92–95/10	213–214/760
k		25	90	48–51/10	161.7/760
l		60	92	118–120/10	248
m		25	94	134–135/10	265/760[30]
n		20	93	76–78	
o		10 h	95[c]	57–58	58
p		12 h	96[c]	105–106	106
q		1 h	93		
r		1 h	94		

[a]Isolated yield after purification. [b]5 mol% $InBr_3$ was used. [c]70 °C.

The reuseability of this $InBr_3$/[bmim]PF_6 system was studied in the deprotection of phenylmethanediol diacetate (**1b**). The product could be simple separated from [bmim]PF_6 by diethyl ether extraction and $InBr_3$ was still left in the [bmim]PF_6, so that the recovery and reuse of $InBr_3$/[bmim]PF_6 was very convenient. The products obtained were of the same purity and yield as in the first run after the reuse of $InBr_3$/[bmim]PF_6 system for three times.

In summary, we describe a simple and efficient catalytic procedure for the deprotection of 1,1-diacetates using a catalytic amount of $InBr_3$ immobilised in [bmim]PF_6 ionic liquid at ambient temperature. The easy work-up procedures combined with ease of recovery and reuse of this novel catalytic system make the method amenable for scale-up operation.

Experimental

Boiling points and melting points are uncorrected. ^1H NMR spectra were recorded on a BRUKER AC-P-200 spectrometer, using $CDCl_3$ as solvent and TMS as internal standard. IR spectra were obtained on a FTS-135 spectrometer. 1,1-diacetates were prepared according to the procedure reported in literature.[31]

General procedure for the deprotection of 1,1-diacetate (**1**): A mixture of 1,1-diacetate (**1**, 1 mmol) and $InBr_3$ (36 mg, 10 mol%) in 1-butyl-3-methylimidazolium hexafluorophosphate (2 ml) was stirred at room temperature. After completion of reaction (monitored by TLC), the product was extracted with diethyl ether (3 × 10 ml). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and the solvent was evaporated under reduced pressure. The product was purified by column chromatography on silica gel to afford pure aldehyde **2**. The remaining ionic liquid was further washed with ether and recycled for subsequent reactions. The products were characterised by their melting points or boiling points, IR, ^1HNMR spectra and by comparison with their literature data.

Vanillin acetate (**2n**): IR (KBr): 830, 862, 1126, 1155, 1279, 1427, 1507, 1600, 1690, 1757, 2753, 2846, 2967, 3017 cm^{-1}. δ_H: 2.35 (s, 3H), 3.91 (s, 3H), 7.21–7.24 (m, 1H), 7.46–7.50 (m, 2H), 9.95 (s, 1H).

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