A mild and efficient deprotection of geminal diacetates catalysed by $FeCl_3·6H_2O$ in ionic liquid

Hongying Niu, Xinying Zhang, Haiming Guo and Jianji Wang*

School of Chemical and Environmental Sciences, Henan Key Laboratory for Environmental pollution control, Henan Normal University, Xinxiang, Henan 453002, P.R. China

The selective deprotection of geminal diacetates promoted by $FeCl_3·6H_2O$ in the ionic liquid, [bmim][BF_4], can be efficiently achieved in good yield. The process is carried out under mild conditions, and the ionic liquid and the catalyst can be recycled easily.

Keywords: ionic liquid, geminal diacetate, iron(III) chloride hexahydrate

The protection and deprotection of carbonyl groups by formation and cleavage of acetals have been used in the preparation of a variety of multifunctional organic molecules.[1] Various methods have been developed for conversion of 1,1-diacetates to the corresponding aldehydes. These include acid-catalysed cleavage by sulfuric acid[2] or hydrochloric acid,[3] base-catalysed cleavage by sodium hydroxide or aqueous potassium carbonate,[4] solid phase catalysed cleavage by ceric ammonium nitrate (CAN) coated on silica gel,[5] montmorillonite K10 or KSF,[6] neutral alumina,[7] and some other methods catalysed by BI_3-N,N-diethylaniline complex,[8] potassium phenoxides[9] or CBr_4.[1d] Recently, the deprotection of geminal diacetates has also been accomplished using $InCl_3$[1a] as a catalyst. However, in spite of their potential utility, each of the above methods has some drawbacks, *e.g.* the use of a strong acid or an additional microwave oven, or environmentally hazardous solvents such as benzene, dichloromethane and acetonitrile. In addition, almost all these methods are not economic process since the catalysts and solvents cannot be recycled. Consequently, the development of more economic, environmentally friendly and efficient method is desirable.

Room temperature ionic liquids have attracted increasing interest as reaction media.[10] These liquids can solvate a wide range of organic and inorganic materials. They are highly polar yet almost non-coordinating; and they have a non-volatile nature and can be recycled. They offer an attractive alternative to conventional organic solvents. Among the ionic liquids, the air and moisture stable imidazolium ionic liquids, such as [bmim][BF_4] and [bmim][PF_6], have received particular attention since no special facilities are required. These ionic liquids have been used as environmentally benign solvents for many important reactions, *e.g.* Diels–Alder reaction,[11a] Heck reaction,[11b] hydrogenation[11c] and oxidation[11d].

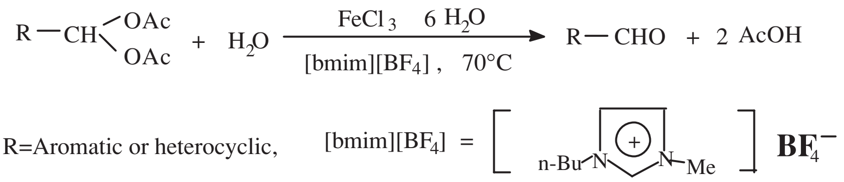
We now report the results of the first example for the efficient deprotection of geminal diacetates to the corresponding aldehydes promoted by $FeCl_3·6H_2O$ and an ionic liquid, 1-butyl-3-methylimidazolium tetrafluoroborate ([bmim][BF_4]), as the solvent.

When 1,1-diacetates (1 mmol) were heated in the ionic liquid [bmim][BF_4] (1.5 ml) in the presence of a catalytic amount (0.5 mmol) of $FeCl_3·6H_2O$ for a certain period of time as required to complete the reaction monitored by TLC or GC–MS, the corresponding aldehydes were obtained in good yield. The reaction was shown in Scheme 1 and the results were summarised in Table 1.

As shown in Table 1, a variety of diacetates can be efficiently transformed to the corresponding carbonyl compounds over 3min – 8.5h in the ionic liquid containing $FeCl_3·6H_2O$ at 70°C. The reaction is strongly affected by the substituents on the phenyl ring of the diacetates. Substrates bearing electron donating groups (entries 1–3) can be efficiently transferred to the corresponding aldehydes within 10 minutes, whereas those bearing electron withdrawing groups (entries 5–8) require a much longer reaction time (1–8.5 h). It is interesting to find that the nitro group is more electron withdrawing (entries 5–6) via the π-system than the *p*-chloro or *p*-bromo (entries 7–8) but their reaction rate is much faster. This may be caused by co-ordination between the ferric chloride and the *p*-halogen and thus increasing the halogen's electron withdrawing effect. The α,β-unsaturated diacetate (entry 9) was deprotected to 3-phenylpropenal without any decomposition. When the deacetylation of diacetates (entries 1–3) occurred, other functional groups, such as OAc and OMe (entries 1 and 2), remained unaffected. This may not be attainable using conventional methods.[2–4]

We explored various reaction conditions for this conversion and found that a ratio of 50 mol% $FeCl_3·6H_2O$ to the diacetates is sufficient to promote the reaction efficiently. In addition, it is observed that the reaction took longer time at room temperature than at 70°C. For example, 0.5h was required for the complete conversion of benzaldehyde diacetate (entry 4) to benzaldehyde at 70°C, but little product was obtained even overnight at room temperature. It should be emphasised that the catalyst immobilized in [bmim][BF_4] was recovered easily by drying the mixture at 100°C for a certain time. The solvent [bmim][BF_4] can be reused for at least four times without any detriment to the activity of the catalyst and the yield of the product.

In conclusion, an efficient and environmental friendly procedure has been found for the selective deprotection of gem-diacetates to the parent aldehydes under mild conditions by using inexpensive $FeCl_3·6H_2O$ as catalyst in [bmim][BF_4].



Scheme 1

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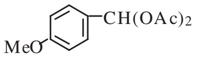
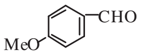
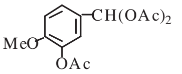
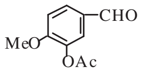
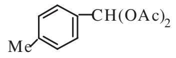
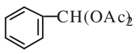
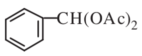
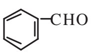
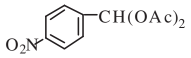
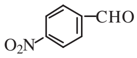
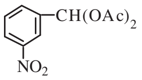
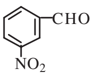
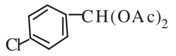
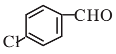
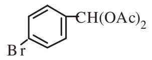
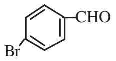
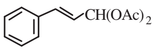
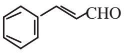
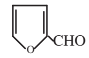
* Correspondence. E:mail: jwang@henannu.edu.cn

Table 1 Cleavage of geminal diacetates catalysed by $FeCl_3 \cdot 6H_2O$ in the ionic liquid

Entry	Substrate	Product	Reaction time	Yield%[a]
1			5min	85
2			3min	88
3			10min	83
4			0.5h	79
5			1h	91
6			1.1h	88
7			8.5h	70
8			8.5h	72
9			10min	91
10			8h	90

[a]Isolated yields

There are three major benefits in this process: (i) green and clean to environment. Both the solvent and the catalyst used in this procedure have environmentally friendly nature; (ii) an economic process. Since the catalyst is immobilised in [bmim][BF_4], after extracted with ether, both the catalyst and the solvent can be reused conveniently and efficiently in the same deprotection reaction for several times; (iii) a process of chemoselectivity. Gem-diacetates are selectively cleaved to the corresponding carbonyl compounds in the presence of other functional groups and no undesirable by-product is observed. With all the advantages mentioned above, the procedure presented in this paper provides a useful addition to the existing methods of deprotection of diacetates.

Experimental

GC–MS analyses were performed using a Hewlett-Packard 6890/5973 GC–MS instrument with HP-5 column (φ0.25mm×30m×0.25μm).

The diacetates were prepared from their corresponding carbonyl compounds according to the methods reported in literature,[12-14] They were identified by GC–MS analyses. All commercially available reagents were used without further purification.

General procedure for peprotection of 1,1-diacetates: A mixture of aldehyde diacetates (1mmol), H_2O (1mmol) and $FeCl_3 \cdot 6H_2O$ (0.5mmol) was stirred in the ionic liquid (1.5 ml) at 70°C for a period of time as required to complete the reaction. After complete conversion, as indicated by TLC or GC–MS, the reaction mixture was cooled to room temperature and extracted three times with diethyl ether or trichloromethane (3×10 ml). The combined diethyl ether or trichloromethane layers were washed with saturated $NaHCO_3$, brine and water, dried over anhydrous Na_2SO_4, and concentrated in vacuo to yield almost pure product. All the products were conformed by GC-MS analyses. The ionic liquid solution containing the catalyst was then recycled by drying at 100°C for several hours.

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