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A mild and efficient approach for the selective deprotection of benzyl and phenyl trimethylsilyl ethers in 1-butyl-3-methylimidazolium chloride

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Abstract 1-Butyl-3-methylimidazolium chloride ([*bmim*]Cl) in the absence of any catalyst mediated the selective deprotection of benzyl and phenyl trimethylsilyl (*TMS*) ethers to the corresponding alcohols and phenol in good yields at room temperature even in presence of alkyl silyl ethers. The work-up of reactions is very simple and the products do not require further purification. The ionic liquid (IL) can be recycled and reused for several runs without any significant loss of activity.

Keywords Selective deprotection; 1-Butyl-3-methylimidazolium chloride; Trimethylsilyl ethers; Alcohol.

Introduction

Trialkylsilyl-groups have been widely used as hydroxyl protecting agents in organic synthesis due to easy installation, stability to most reaction conditions, and selectivity in cleavage reactions [1–4]. Although protic acids and fluoride sources continue to be widely used for the removal of silyl protecting groups, a number of *Lewis* acids have been introduced to mediate desilylation reactions. Some recent examples from literature include: BF_3–O*Et*$_2$ [5, 6], BCl_3 [7], decaborane [8], Sc(O*Tf*)$_3$ [9], $InCl_3$ [10], $ZnBr_2$ [11], Zn(BF_4) [4, 12], Ce(O*Tf*)$_4$ [13], $CeCl_3$–$7H_2O/NaI$ [14], *TMS*O*Tf* [15], $BiOClO_4$ [16], $SbCl_5$ [17], LiCl [18], and $BiBr_3$ [19].

Other reagents, such as carboxylic acid resins [20], organotin reagents [21], I_2 [22, 23], Br_2 in methanol [24, 25], CBr_4 in methanol [26], 1-chloroethyl chloroformate in methanol [27], and *N*-iodosuccinimide [28] have also been developed to deprotect silyl ethers under mild reaction conditions.

There are also several reductive methods for deprotecting silyl ethers including catalytic transfer hydrogenation with palladium [29] and cleavage using diisobutylaluminium hydride [30] and $LiAlH_4$ [31]. Although many of these methods promote selective deprotection of bis-silyl ethers, some are strongly reducing and others are oxidizing, thereby restricting their use. Moreover, many of these methods suffer from limitations, such as harsh reaction conditions, the use of expensive reagents, and cumbersome work-up procedures. Although discrimination between two silyl ethers derived from alcohols is common, relatively few techniques have been developed to deprotect aryl silyl ethers in the presence of alkyl silyl ethers [5, 6]. Therefore, it is very important to develop a novel, neutral, and mild selective deprotection method for silyl ethers.

With ever-increasing environmental concerns, much attention has been directed toward the reduction or replacement of volatile organic compounds (VOCs) from the reaction media [32] and a variety of environmentally benign media, such as water, ionic liquids, immobilized solvents, fluorous solvents,

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$$R\text{-}OTMS \xrightarrow[\text{rt}]{[bmim]\text{Cl}} R\text{-OH}$$

R = benzyl, phenyl 90–95%

Scheme 1

and supercritical fluids have been promoted as replacements to VOCs [33]. Ionic liquids, composed entirely of ions, with a melting point below 100°C [34–36] have been emerging as promising and attractive alternatives due to their unique properties, including low volatility, high polarity, good thermal stability, capacity to dissolve various organic, inorganic, and organometallic compounds, and a fine-tuning of their miscibility with water and organic solvents by a proper choice of cation and anion. So far, ionic liquids have been used as solvents in a wide range of organic reactions [37–41].

In continuation of our studies on ionic liquids [42–44], we wish to report herein a new, mild, and highly efficient method for the selective deprotection of benzyl and phenyl trimethylsilyl ethers in [*bmim*]Cl in the absence of any catalyst at room temperature (Scheme 1).

Results and discussion

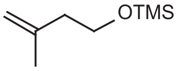
Table 1 Deprotection of 4-methoxybenzyl trimethylsilyl ether to the corresponding alcohol in various ILs and classical solvents at room temperature

Entry	Ionic liquid	Time/h	Yield/%
1	[*bmim*]Cl	0.66	95
2	[*bmim*]Br	4	80
3	[*bmim*]PF_6	24	50
4	H_2O	24	0
5	*Et*OH	24	0

In order to obtain the best solvent, we examined various ionic liquids, such as 1-butyl-3-methylimidazolium bromide ([*bmim*]Br), 1-butyl-3-methylimidazolium chloride ([*bmim*]Cl), 1-butyl-3-methylimidazolium hexafluorphosphate ([*bmim*]PF_6), and classic solvents, such as water and ethanol. Deprotection of 4-methoxybenzyl trimethylsilyl ether was selected as model reaction. The test reaction was carried out using various ionic liquids (0.20 g) followed by addition of 4-methoxybenzyl trimethylsilyl ether (0.21 g, 1 mmol). As indicated in Table 1, [*bmim*]Cl is the best suited ionic liquid for this reaction in terms of yields and easy work-up.

In order to investigate the applicability of this method we selected a variety of benzyl and phenyl silyl ethers. As can be seen in Table 2, the present method general for the cleavage of *TMS* ethers of primary and secondary benzyl alcohols (Table 2, entries 1–5 and 9–11), and phenol (Table 2, entries 12, 13). It is also noteworthy that alkyl silyl ethers

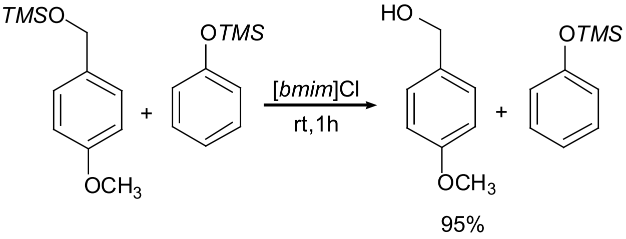
Table 2 Deprotection of benzyl and phenyl trimethylsilyl ethers to corresponding alcohols and phenols in [*bmim*]Cl at room temperature

Entry	Substrate	Product	Ref.	Time/h	Yield/%[a]
1	4-*Me*CO–*Ph*–CH_2–O*TMS*	4-*Me*CO–*Ph*–CH_2–OH	[46]	0.66	95, 95, 96, 94[b]
2	4-*Me*–*Ph*–CH_2–O*TMS*	4-*Me*–*Ph*–CH_2–OH	[46]	50	95
3	4-F–*Ph*–CH_2–O*TMS*	4-F–*Ph*–CH_2–OH	[46]	0.66	95
4	4-Br–*Ph*–CH_2–O*TMS*	4-Br–*Ph*–CH_2–OH	[47]	1	90
5	4-${}_2$ON–*Ph*–CH_2–O*TMS*	4-${}_2$ON–*Ph*–CH_2–OH	[46]	2	90
6	*Me*$(CH_2)_6$-O*TMS*	NR[c]	–	24	0
7		NR	–	24	0
8	*Cyclo*–C_6H_{11}–O*TMS*	NR	–	24	0
9	*Ph*–CH*Me*–O*TMS*	*Ph*–CH*Me*–OH	[27]	1.33	94
10	*Ph*–CH*Et*–O*TMS*	*Ph*–CH*Et*–OH	[27]	1.33	94
11	*Ph*$_2$–CH–O*TMS*	*Ph*$_2$–CH–OH	[27]	1.5	90
12	*Ph*-O*TMS*	*Ph*–OH	[27, 46]	12	95
13	4-*SMTO*–*Ph*–CH_2–O*TMS*	4-HO–*Ph*–CH_2–OH	[46]	12	92

[a] Isolated yields

[b] The same IL was used for each of the four runs

[c] No reaction



Scheme 2

(entries 6–8) are quite stable under these reaction conditions even after 24 h. Indeed, our results show that this method is a time-selective method and can cleave benzylic *TMS* ethers in the presence of *TMS*-protected phenyls by controlling the time of reaction (Scheme 2). Longer reaction times, however, led to the formation of more doubly deprotected product (Table 2, entry 13).

One of the advantages of ionic liquids is their ability to function as a recyclable reaction medium. The product is extracted into diethyl ether and from the etherical solution the pure product is isolated by solvent evaporation. The IL is reused for subsequent reactions without any decrease of reaction yields (Table 2, Entry 1).

In conclusion, a new, mild, and facile method for the selective deprotection of benzyl and phenyl silyl ethers using [*bmim*]Cl is reported. The reaction conditions allow selective deprotection of silyl-protected benzyl alcohol and phenyl derivatives in presence of alkyl silyl ethers. On the other hand, our results show that this approach is a selective method and can cleave benzylic *TMS* ethers in the presence of phenolic *TMS* by controlling the time of reaction. No by-products are formed that require complicated chromatographic purification; only extraction with *n*-hexane or diethyl ether to provide pure products. Most importantly, the [*bmim*]Cl can also be recycled and reused in further reactions without any significant loss of catalytic activity.

Experimental

The chemicals used in this work were purchased from Merck and Fluka chemical company. Melting points were taken on an Electrothermal 9100 apparatus. IR spectra were obtained on a Shimadzu IR-470 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a BRUKER DRX-300 AVANCE spectrometer at 300.13 and 75.47 MHz. NMR spectra were obtained on solutions in $CDCl_3$ using *TMS* as internal standard.

Typical procedure for deprotection of 4-methoxybenzyl-oxytrimethylsilyl ether

To 0.20 g of magnetically stirred [*bmim*]Cl (1.0 mmol) at room temperature 0.21 g 4-methoxybenzyl trimethylsilyl ether (1.0 mmol) [45] was added. The reaction progress was monitored by TLC or GC. After completion of the reaction, the product was extracted with $3 \times 5\,cm^3$ diethyl ether. Evaporation of the solvent gave 0.13 g (95%) colorless 4-methoxybenzyl alcohol with sufficient purity for most purposes. All reaction products were known and characterized by IR, ^{1}H NMR spectra, and melting point as compared with those obtained from authentic samples [27, 26, 46].

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