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A Mild and Efficient Method for the Selective Cleavage of tert-Butyldimethylsilyl Ethers to Alcohols

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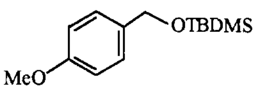
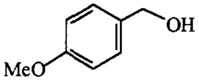
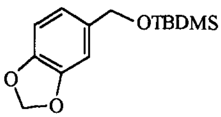
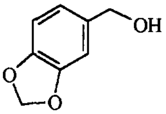
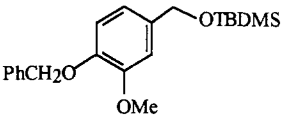
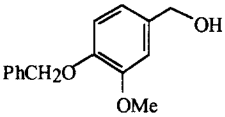
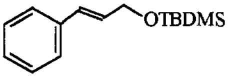
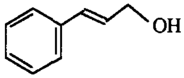
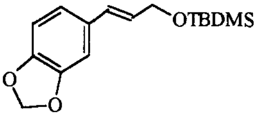
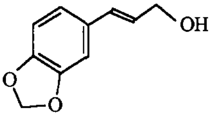
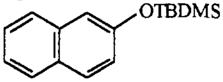
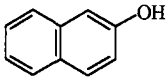
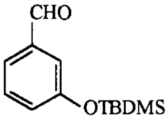
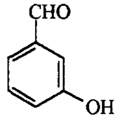
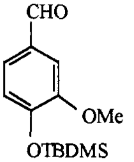
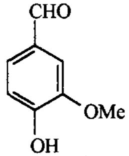
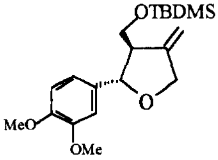
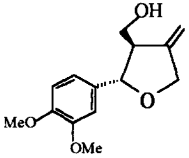
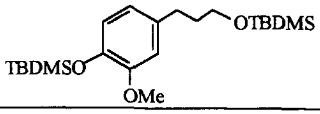
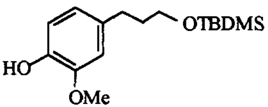
Abstract: A mild and efficient method for the selective deprotection of primary allylic and homoallylic, primary benzylic and aryl tert-butyldimethylsilyl (TBDMS) ethers has been established using a combination of H_2O and DMSO at 90°C. All other primary and secondary TBDMS ethers remained unaffected under the reaction condition. The method is very effective in deprotection of TBDMS ethers in the presence of other sensitive functional groups.

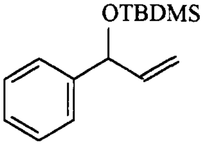
The importance of selective introduction and removal of protecting groups in organic synthesis is well established. The success of the technology largely depends on the stability of protecting groups towards different acidic or non-acidic reagents and how easily they can be inatalled and removed. The protection of alcohols as tert-butyldimethylsilyl (TBDMS) ethers has been recognised as one of the most useful methods because of its easy installation and general stability to basic and mild acidic reagents.[1] Although tetrabutylammonium fluoride[1a,2] is the most popular for cleavage of TBDMS ethers, the basic fluoride ion can affect the base-sensitive subatrares.[3] The deprotection of TBDMS ethers is also done with aqueous acids,[4] aqueous HF-CH_3CN[5] and various Lewis acids.[6] But the use of acidic reagents is undesirable for acid-sensitive substrates. There are several other methods for the deprotection of TBDMS ethers which include catalytic transfer hydrogenation using Pd,[7] reductive cleavage by DIBAL-H.[8] Recently, SiF_4,[9] DDQ[10] and ceric ammonium nitrate[11] have also been used for desilylation. But some of these reagents have strong reducing and oxidising properties and therefore, their use is limited. However, many of these methods[12] suffer from harsh conditions, expensive reagents and sometimes cumbersome extraction procedures. Although, some of the reported methods are chemoselective for deprotection of TBDMS ethers in the presence of other sensitive functional groups, very little information is available[13] in the literature about the selective desilylstion amongst different types of TBDMS ethers. We report herein a mild, efficient and highly selective method for the deprotection of primary allylic and homoallylic, primary benzylic and aryl TBDMS ethers by using a combination of H_2O and DMSO at 90°C furnishing the corresponding alcohols in good yields. All other primary TBDMS ethers and secondary TBDMS ethers remained unaffected under these reaction conditions, thus providing a mild and efficient aqueous neutral method for deprotection of TBDMS ethers without using acidic reagents or generating toxic side products.

Table 1. Deprotection of primary allylic and homoallylic, primary benzylic and aryl TBDMS ethers

Entry	R-OTBDMS	Product	Yield(%)[a]
1			81
2			84
3			83
4			85
5			80
6			79
7			87
8			86
9			81
10			82

[a] Yields refer to chromatographically pure isolated

A range of primary allylic and homoallylic, primary benzylic and aryl TBDMS ethers were prepared from the corresponding alcohols[14] using the standard procedure [TBDMS-Cl, Et_3N and 4-DMAP (cat) in CH_2Cl_2] and subjected to deprotection[15] using a combination of H_2O and DMSO at 90°C for 8 h. The results are summarises in Table 1. All the products were purified by column chromatography and the corresponding alcohols were obtained in good yields. All other primary TBDMS ethers remained unaffected. Subjecting the secondary TBDMS ethers including types **1** and **2** to our conditions gave no reactions This methodology is very effective for deprotection of TBDMS ethers in the presence of other sensitive functional groups such as tetrahydropyranyl ethers (Ar-OTHP, $ArCH_2$-OTHP remained unaffected), methoxymethyl ethers ($C_5H_{11}CH_2$-OMOM remained unaffected), methylenedioxy ethers (entry 2,5), benzyl ethers (entry 3), methyl ethers (entry 1,3,8,9,10) and aldehyde functionalities (entry 7,8). It was found that H_2O is essential for the success of the reaction. To observe any selectivity amongst aryl and benzylic TBDMS ethers, compounds **3** and **4** were subjected to deprotection separately under identical reaction conditions. It was found that benzylic TBDMS ethers deprotected selectively and the aryl one remained untouched, which is comparable with the results obtained by Lee and his co-workers[13]. Thus, the disilyl ether **3** under identical reaction conditions afforded **5** as the sole product in 86% yield. Similarly, compound **4** furnished **6** in 85% yield as the only isolable product.



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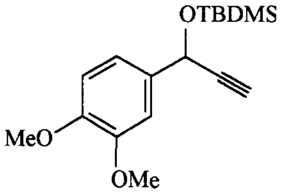

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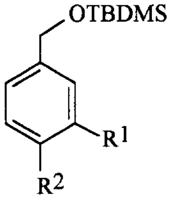
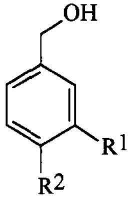


3, R^1 = OTBDMS, R^2 = H
4, R^1 = OMe, R^2 = OTBDMS



5, R^1 = OTBDMS, R^2 = H
6, R^1 = OMe, R^2 = OTBDMS

In conclusion, we have established a mild, simple and highly selective method for deprotection of primary allylic, primary benzylic, primary homoallylic and aryl TBDMS ethers using a combination of H_2O and DMSO at 90°C.

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15. General procedure for deprotection of TBDMS ethers: A mixture of the TBDMS ether (2 mmol), H_2O (2 ml) and DMSO (10 ml) was stirred at 90^0C for 8 h under N_2. The reaction mixture was allowed to cool to room temperature, diluted with H_2O (40 ml) and extracted with ether (4 x 25 ml). The organic extract was washed with H_2O (2 x 15 ml) and dried (Na_2SO_4). The solvent was removed and the residue obtained was chromatographed over silica gel using a combination of ethyl acetate - light petroleum (boiling range 60^0C to 80^0C) as eluent to afford the alcohols, which were identified by comparison (TLC, IR and ^{1}HNMR spectra) with the authentic samples.

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