Pergamon

Tetrahedron Letters 40 (1999) 1985–1988

TETRAHEDRON
LETTERS

A Simple and Efficient Method for Selective Deprotection of t-Butyldimethylsilyl Ethers by Zinc Tetrafluoroborate in Water

Brindaban C. Ranu,* Umasish Jana and Adinath Majee

Department of Organic Chemistry, Indian Association for the
Cultivation of Science, Jadavpur, Calcutta - 700 032, India.

Received 20 October 1998; revised 23 December 1998; accepted 7 January 1999

Abstract: Selective deprotection of t-butyldimethylsilyl ethers has been achieved under mild conditions using an aqueous solution of zinc tetrafluoroborate. © 1999 Published by Elsevier Science Ltd. All rights reserved.

Keywords: deblocking, TBDMS ether, zinc tetrafluoroborate

The strategy of protection of a hydroxyl functionality and its subsequent deprotection at a later stage is frequently used in multistep organic synthesis. Of all the hydroxyl protecting groups,[1] the t-butyldimethylsilyl (TBDMS) ether has become the most popular and widely used means of protecting hydroxyl groups because of its ease of preparation[2] and its stability to a wide range of reaction conditions. Numerous methods are now available in the literature[3,4] for the deprotection of TBDMS ethers under a variety of conditions. One of the most effective ways for the cleavage of silyl ethers is based on the exploitation of the high affinity of silicon towards fluoride ions. Thus, a number of reagents involving one form of fluoride or another, such as tetrabutylammonium fluoride,[2] boron trifluoride etherate,[4a] hydrofluoric acid,[4b] fluorosilicic acid,[4c] ammonium fluoride,[4d] silicon fluoride,[4e] and lithium tetrafluoroborate,[4f] have been developed for the deprotection of TBDMS ethers. Among these, tetrabutylammonium fluoride (TBAF) is most frequently used. However, this reagent has some serious limitations due to the strong basicity of the 'naked' fluoride ion in THF[5] which directly affects cleavage of TBDMS ethers of the β-ketol system[2] and of phenolic compounds[6] and may promote β-elimination reactions,[7] transacylations[8] and other base-catalyzed undesired side reactions.[3a,9] In addition, the phase transfer properties of the tetrabutylammonium cation often cause difficulties in the work-up and purification of products. Although the development of acidic reagents like boron trifluoride etherate,[4a] hydrofluoric acid[4b] and fluorosilicic acids[4c] overcomes some of these difficulties, restrictions towards acid-sensitive functionalities remain. Use of relatively mild lithium tetrafluoroborate[4f] seems promising in this endeavour, but these reactions are usually long (60h). Besides, its general applicability has not been tested; only five TBDMS ethers of primary and secondary alcohols have been addressed.[4f] Again, as a reagent lithium tetrafluoroborate is not very practical being moisture-sensitive, irritant and relatively costly.[10]

PII: S0040-4039(99)00097-0

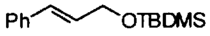
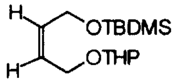
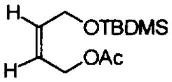
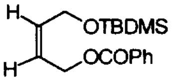
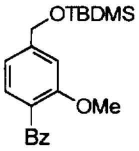
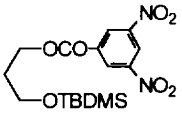
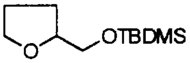
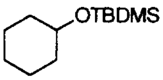
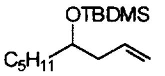
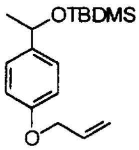
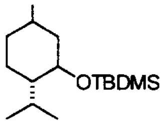
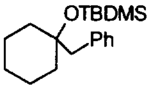
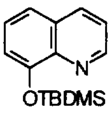
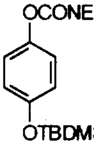
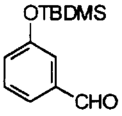
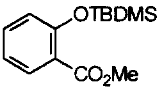
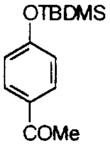
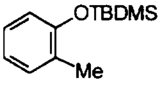
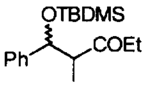
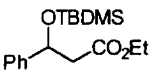
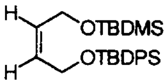
We have observed that TBDMS ethers are cleaved very efficiently by an inexpensive easily available reagent, zinc tetrafluoroborate in aqueous solution to provide the corresponding hydroxy compounds.

The experimental procedure is very simple. A suspension of the TBDMS ether (1 mmol) in an aqueous solution (40%) of zinc tetrafluoroborate (1 mmol)[11] was stirred at room temperature for the period of time required to complete the reaction (TLC). The product was isolated by extraction with ether followed by purification by using silica gel chromatography. Use of co-solvents such as THF or acetonotrile for solid and highly viscous TBDMS ethers is found to accelerate the reactions.[12]

A wide range of structurally varied TBDMS ethers were subjected to deprotection by this procedure. The results are summarized in Table 1. This procedure is found to be general being effective for the cleavage of TBDMS ethers of primary, secondary, tertiary, allylic, propargylic and homoallylic alcohols. Phenolic ethers which are usually problematic with TBAF,[6] are also deprotected without any difficulty (entries 17-22). The reactions are, in general, reasonably fast and high-yielding. The reaction conditions are mild enough not to affect the carbon-carbon double and triple bond in conjugated systems (entries 4-9). This reagent is quite compatible with sensitive functional groups such as an aldehyde (entry 19), a ketone (entry 21), a carboxylic ester (entry 20), a carbamate (entry 18) and moieties like furfuryl (entry 11) and quinoline (entry 17). Selective deprotection of TBDMS ethers in the presence of several other frequently used hydroxyl protecting groups such as tetrahydropyranyloxy (OTHP, entry 6), methoxy (entry 9), allyloxy (entry 14), benzyloxy (entry 9), 3,5-dinitrobenzyloxy (entry 10) and t-butyldiphenylsilyloxy (OTBDPS, entries 25,26) is achieved with high efficiency. Acid labile hydroxyl protecting groups like acetate (entry 7) and benzoate (entry 8) also survived the reaction conditions. Most significantly, TBDMS ethers of β-ketol systems (entries 23,24) underwent smooth cleavage to provide the corresponding alcohols in high yields without any side reaction. No β-elimination is observed during the deprotection of the TBDMS ether of 3-chloropropanol (entry 3). Thus zinc tetrafluoroborate in H_2O successfully avoids disadvantages associated with the strong basicity of tetrabutylammonium fluoride in THF. Presumably, the cleavage of TBDMS ethers by $Zn(BF_4)_2$ is rationalized as donation of F^- to Si directly from BF_4^-, leading to the formation of OBF_3^- species.

To sum up, the present procedure effected by $Zn(BF_4)_2$ in H_2O provides a very efficient method for deprotection of TBDMS ethers. The significant advantages offered by this procedure are : (a) general applicability (effective for TBDMS ethers of all types of alcohols including phenols); (b) mild conditions (room temperature, presence of no strong acid or base) compatible with a variety of sensitive functionalities like -CHO, $-CO_2Me$, $-OCONEt_2$ etc.; (c) remarkable chemoselectivity (selective deprotection in presence of acetate, benzoate and allyl, benzyl, THP, TBDPS ethers); (d) avoidance of complications associated with the basicity of 'naked' F^- as in case of TBAF (clean deprotection of β-ketol TBDMS ethers); (e) environment-friendly reaction (no involvement of toxic reagent); and (f) high yields (80-96%). Certainly, this method is a better and practical

Table 1. Deprotection of TBDMS Ethers to Corresponding Alcohols by $Zn(BF_4)_2$ in H_2O

entry	TBDMS ether	time(h)	yield (%)[a]
1	$PhCH_2OTBDMS$	10	90
2	$PhCH_2CH_2OTBDMS$	11	92
3	$ClCH_2CH_2CH_2OTBDMS$	16	85
4	$\equiv\!\!-CH_2OTBDMS$	3	82
5		12	90
6		5	89
7		6	91
8		8	92
9		5	91
10		2	95
11		5	80
12		4	93
13		10	95
14		12	85
15		10	85
16		12	87
17		13	89
18		12	92
19		4 [b]	85
20		4 [c]	85
21		24	90
22		24 [c,d]	88
23		8	92
24		6	96
25	$PhCH_2OTBDPS$	35	No reaction
26		12	90

---

[a] Yields refer to pure isolated products fully characterized by spectral data ; [b] The reaction was carried out at 50 - 60°C ; [c] The reaction was performed at reflux temperature ; [d] Four equivalents of $Zn(BF_4)_2$ were used

alternative to the existing procedures and we believe, this will find useful application particularly when selective deprotection of a TBDMS ether is required in complex molecules containing more than one hydroxy protecting moieties.

Acknowledgements : We are pleased to acknowledge the financial support from CSIR, New Delhi [Grant No. 01(1504)/98]. U.J. and A.M. are also thankful to CSIR for their fellowships.

References and Notes

1. Greene, T.W.; Wuts, P.G.M. *Protective Groups in Organic Synthesis*, 2nd ed.; Wiley : New York, 1991.
2. Corey, E.J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190.
3. (a) Lalonde, M.; Chan, T.H. *Synthesis*, **1985**, 817. (b) Dahlhoff, W.V.; Taba, K.M. *Synthesis* **1986**, 561. (c) Prakash, C.; Saleh, S.; Blair, I.A. *Tetrahedron Lett.* **1989**, *30*, 19. (d) Cort, A.D. *Synth. Commun.* **1990**, *20*, 757. (e) Bou, V.; Vilarrasa, J. *Tetrahedron Lett.* **1990**, *31*, 567. (f) Cormier, J.F. *Tetrahedron Lett.* **1991**, *32*, 187. (g) Tanemura, K.; Suzuki, T.; Horaguchi, T. *J. Chem. Soc., Perkin Trans. 1* **1992**, 2997. (h) Varma, R.S.; Lamture, J.B.; Varma, M. *Tetrahedron Lett.* **1993**, *34*, 3029. (i) Feixas, J.; Capdevila, A.; Guerrero, A. *Tetrahedron* **1994**, *50*, 8539. (j) Lee, A.S.-Y.; Yeh, H.-C.; Tsai, M.-H. *Tetrahedron Lett.* **1995**, *36*, 6891. (k) Wilson, N.S.; Keay, B.A. *J. Org. Chem.* **1996**, *61*, 2918. (l) Vaino, A.R.; Szarek, W.A.. *Chem. Commun.* **1996**, 2351. (m) Dattagupta, A.; Singh, R.; Singh, V.K. *Synlett* **1996**, 69. (n) Wilson, N.S.; Keay, B.A. *Tetrahedron Lett.* **1997**, *38*, 187. (o) Maiti, G.; Roy, S.C. *Tetrahedron Lett.* **1997**, *38*, 495. (p) Tandon, M.; Begley, T.B. *Synth. Commun.* **1997**, *27*, 2953. (q) Farras, J.; Serra, C.; Vilarrasa, J. *Tetrahedron Lett.* **1998**, *39*, 327. (r) Bartoli, G.; Bosco, M.; Marcamtoni, E.; Sambri, L.; Torregiani, E. *Synlett* **1998**, 209.
4. (a) Kelly, D.R.; Roberts, S.M.; Newton, R.F. *Synth. Commun.* **1979**, *9*, 295. (b) Collington, E.W.; Finch, H.; Smith, I.J. *Tetrahedron Lett.* **1985**, *26*, 681. (c) Shimshock, S.J.; Waltermire, R.E.; Deshong, P. *J. Am. Chem. Soc.* **1991**, *113*, 8791. (d) Zhang, W.; Robins, M.J. *Tetrahedron Lett.* **1992**, *33*, 1177. (e) Corey, E.J.; Yi, K.Y. *Tetrahedron Lett.* **1992**, *33*, 2289. (f) Metcalf, B.W.; Burkhart, J.P.; Jund, K. *Tetrahedron Lett.* **1980**, *21*, 35.
5. (a) Clark, J.H. *Chem. Rev.* **1980**, *80*, 429. (b) Hayami, J.-I.; Ono, N.; Kaji, A. *Tetrahedron Lett.* **1968**, 1385.
6. Kendall, P.M.; Johnson, J.V.; Cook, C.E. *J. Org. Chem.* **1979**, *44*, 1421.
7. Toshima, T.; Tatsuta, K.; Kinoshita, M. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 2369.
8. Franke, F.; Guthrie, R.D. *Aust. J. Chem.* **1978**, *31*, 1285.
9. Paquette, L.A.; Doherty, A.M.; Rayner, C.M. *J. Am. Chem. Soc.* **1992**, *114*, 3910.
10. *Catalog Handbook of Chemicals*, Aldrich, Milwaukee.
11. Although the reaction proceeds well with stoichiometric amount of $Zn(BF_4)_2$ (0.5 equivalent), however, use of 1 equivalent $Zn(BF_4)_2$ reduces the reaction times considerably.
12. A co-solvent like THF or acetonitrile may be used and it usually does not affect the rate of cleavage.