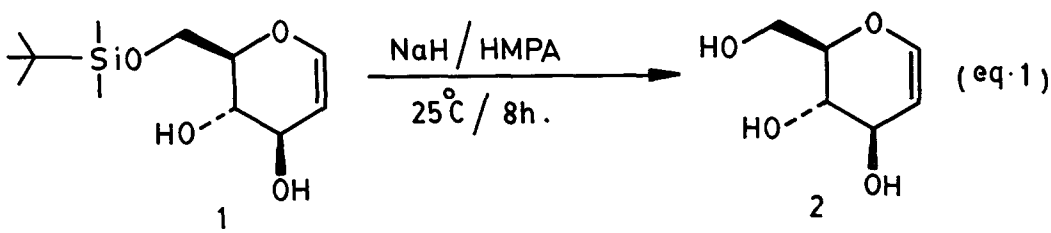
Tetrahedron Letters,Vol.29,No.47,pp 6161-6162,1988 0040-4039/88 $3.00 + .00
Printed in Great Britain Pergamon Press plc

REDUCTIVE CLEAVAGE OF t-BUTYLDIMETHYLSILYL ETHERS WITH SODIUM HYDRIDE

Mohammed Saleh Shekhani,* Khalid Mohammed Khan, and Khalid Mahmood
HEJ Research Institute of Chemistry, University of Karachi, Karachi-32, Pakistan.

Abstract:- t-Butyldimethylsilyl ethers are cleaved with sodium hydride in hexamethylphosphoric triamide (HMPA) or N,N'-dimethylpropyleneurea (DMPU).

Since the introduction of t-butyldimethylsilyl (TBDMS) group[1,2] in organic synthesis, it has become one of the most useful protective groups.[3] TBDMS ethers are usually cleaved with fluoride ion, aqueous acid, boron trifluoride etherate, N-bromosuccinimide or with lithium or trityl tetrafluoroborates.[4] In certain cases some problems may be encountered during the cleavage of TBDMS ethers.[1] They are in general stable to bases and to reducing agents. In connection with a synthetic study, when we treated 6-O-TBDMS derivative **1** of D-glucal with NaH (4 equiv.) in hexamethylphosphoric triamide (HMPA), we isolated D-glucal **2** in 99% yield as the only product (eq. 1), which to the best of our knowledge is the first example of the reductive cleavage of this type. This led us to a detailed study of the behaviour of TBDMS ethers towards this reagent. We discovered that NaH in HMPA cleaves TBDMS ethers in excellent yield (table 1).



1 2

In a typical experiment, to a well stirred suspension of NaH in HMPA, under argon, was added dropwise a solution of the silyl ether in HMPA (in cases where the silyl ether is not soluble in HMPA a saturated solution in THF can be added), and the mixture was allowed to stir at 25°C. In general 2 equiv. of NaH were used per equiv. of the silyl ether (additional NaH was used to account for the free hydroxyl groups wherever necessary). The reaction takes much longer time with 1 equiv. of NaH. Upon completion of the reaction (TLC analysis, 8 to 12h.), the reaction was quenched by either wet ether, or water, filtered through Celite, and the filtrate was subjected to the aqueous workup to afford pure deprotected alcohol (table 1). In cases of entries (10 to 13) the HMPA was stripped under high vacuum and the residue was chromatographed on silica gel column. Many of these reactions (entries 1,2,4,6, and 11), were repeated by replacing HMPA with the noncarcinogenic N,N'-dimethylpropyleneurea (DMPU).[5] In the case of t-butyldiphenylsilyl derivative[6] (entry 13) the reaction was complete within 5 min. at 0°C.

Table-1: Cleavage of TBDMS ethers with NaH in HMPA or DMPU at room temperature.

No.	Substrate	Time	Product	% Yield (isolated)
1.	O-TBDMS-Stigmasterol	9h	Stigmasterol	96%
2.	$CH_3(CH_2)_{17}OTBDMS$	10h	Stearyl alcohol	97%
3.	OTBDMS-Cholesterol	10h	Cholesterol	91%
4.	$PhCH_2OTBDMS$	8h	Benzyl alcohol	96%
5.	$CH_3(CH_2)_7OTBDMS$	8h	1-Octanol	89%
6.	$CH_3(CH_2)_5\ CH(CH_3)OTBDMS$	10h	2-Octanol	92%
7.	$TBDMSO(CH_2)_4OTBDMS$	12h	1,4-Butanediol	70%
8.	$CH_3CH(OTBDMS)(CH_2)_2OTBDMS$	10h	1,3-Butanediol	69%
9.	O-TBDMS-Furfuryl alcohol	8h	Furfuryl alcohol	93%
10.	3,6-di-O-TBDMS-D-Glucal	8h	D-Glucal	90%
11.	6-O-TBDMS-D-Glucal	8h	D-Glucal	90%
12.	Methyl 2-deoxy-6-O-TBDMS--α-D-glucopyranoside	8h	Methyl 2-deoxy--α-D-glucopyranoside	90%
13.	Methyl 2-deoxy-6-OTBDPS--α-D-glucopyranoside[a]	5min	Methyl 2-deoxy--α-D-glucopyranoside	90%

[a] TBDPS = t-Bu$(Ph)_2$Si-

Acknowledgement: This work was supported by Pakistan Science Foundation's grant No. S-KU/CHEM (185).

References and Notes

1. For a review see: Lalonde, M; Chan, T. H. Synthesis, **1985**, 817.
2. (a) Stork, G.; Hudrlik, P. F. J. Am. Chem. Soc., **1968**, 90, 4462. (b) Corey, E. J.; Varma, R. K. J. Am. Chem. Soc., **1971**, 93, 7319.
3. Greene, T. W. 'Protective Groups in Organic Synthesis', John Wiley & Sons, New York, **1981**.
4. For methods of cleavage of TBDMS ethers see: (a) Corey, E. J.; Venkateswarlu, A. J. Am. Chem. Soc., **1972**, 94, 619. (b) Torisowa, Y.; Shibasaki, M.; Ikegami, S. Tetrahedron Lett., **1979**, 20, 1865. (c) Newton, R. E.; Reynold, D.P.; Finch, M. A. W.; Kelley, D. R.; Roberts, S. M. Tetrahedron Lett., **1978**, 19, 3981. (d) Kelley, D. R.; Roberts, S. M. Synth. Commun., **1979**, 9, 295. (e) Corey, E. J.; Ponder, J. W.; Ulrich, P. Tetrahedron Lett., **1980**, 21, 137 (f) Metcalf, B. M.; Burkhart, J. P.; Hund, K. Tetrahedron Lett., **1980**, 21, 35. (g) Ganem, B.; Small Jr., V. R. J. Org. Chem., **1974**, 39, 3728. (h) Batten, R. J.; Dixon, A. J.; Taylor, R. J. K. Synthesis, **1980**, 234.
5. Mukhopadhyay, T.; Seebach, D. Helv. Chim. Acta., **1982**, 65, 385.
6. Methyl 2-deoxy-α-D-glucopyranoside was prepared as described: Corey, E. J.; Weigel, L. O.; Chamberlin. A. R.; Lipshutz. B. J. Am. Chem. Soc., **1980**, 102, 1439.

(Received in UK 4 October 1988)