A New Method for Removing the *t*-Butyldimethylsilyl Protecting Group

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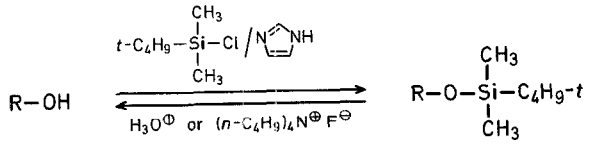
Alcohols **1** can be conveniently protected as *t*-butyldimethylsilyl (TBDMS) ethers **2** and regenerated using aqueous acid or tetrabutylammonium fluoride in aprotic solvents[2].



1 **2**

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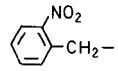
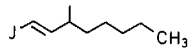
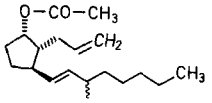
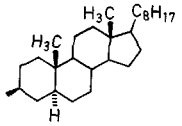
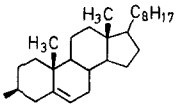
Table. Cleavage of *t*-Butyldimethylsilyl Ethers **2** with *N*-Bromosuccinimide/Dimethyl Sulphoxide[a]

Product Alcohol		Yield [%][b]	b.p./torr, or m.p.	$[\alpha]_D$[c]	Lit. b.p./torr or m.p.	Lit. $[\alpha]_D$
1a		74	71–72 °C	—	74 °C[11]	—
1b	n-C_4H_9–C≡C–CH_2–	85	82–84 °C/12	—	87 °C/15[8]	—
1c		86[d]	—[e]	—	—[7]	—
1d		73[d]	—[f]	—	—	—
1e		88	139–140 °C	+25° (*c* 1.8, $CHCl_3$)	141–143 °C[11]	+24° (*c* 1.3, $CHCl_3$)[11]
1f[g]		88	148–149 °C	−39° (*c* 5, $CHCl_3$)	148.5 °C[11]	−39.5° (*c* 2, $CHCl_3$)[11]

[a] Reaction of ether **2** with *N*-bromosuccinimide (1.1 equiv) in aqueous dimethyl sulphoxide or aqueous dimethyl sulphoxide/tetrahydrofuran for up to 17 h.

[b] Yield of isolated, purified product.

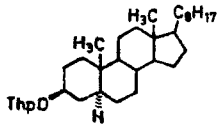
[c] $[\alpha]_D$ recorded in same solvent and under similar conditions to those reported in the literature.

[d] Purified by column chromatography (silica gel).

[e] Chromatographically and spectroscopically identical with an authentic sample prepared according to Ref. [7].

[f] The structure of the product was confirmed by proton N.M.R. and I.R. spectroscopy. M.S.: gave $m/e = 163$ (molecular ion $- C_5H_{11}$, CH_3COOH). Further proof was obtained by reconverting **2d** to **1d** using the method described in Ref. [2]. **2d** prepared in this way was identical with the original sample.

[g] The tetrahydropyranyl ether **3** (below) with similar structure was obtained unchanged after 17 h.



We have discovered that ethers **2** can be converted to the corresponding alcohols **1** in high yield using *N*-bromosuccinimide in aqueous dimethyl sulphoxide. The scope of this method can be seen from the Table.

A variety of functional groups are compatible with the deprotection procedure. Other reactions of *N*-bromosuccinimide[3], such as bromohydrin formation or oxidation, were not observed. In common with the use of aqueous acid as a means of deprotection, this new procedure is inexpensive and easy to perform. However, the aqueous acid method can only be used with acid-stable compounds and it cannot be used to selectively desilylate in the presence of a tetrahydropyranyl protecting group[2a]. In contrast the tetrahydropyranyl group is unaffected by *N*-bromosuccinimide in aqueous dimethyl sulphoxide (Table, footnote [g]).

Dimethyl sulphoxide is the solvent of choice for carrying out this reaction and 1.1 molar equivalents of *N*-bromosuccinimide are required to ensure complete deprotection. Other solvents (dichloromethane, acetone, tetrahydrofuran, methanol, for example) give mixtures of products, especially with unsaturated substrates. Side reactions were sometimes observed with Analar dimethyl sulphoxide, although these could be suppressed by the addition of a small quantity of a radical inhibitor. However, reagent grade dimethyl sulphoxide was found to be the solvent of choice.

The reaction appears to proceed by way of an ionic, rather than a radical, mechanism. Deprotection occurs efficiently in the dark and in the presence of a radical inhibitor, 4,4′-thiobis[6-*t*-butyl-3-methylphenol], but it does not take place when excess triethylamine is added to the reaction. In view of the stability of the tetrahydropyranyl group and the known ability of *N*-bromosuccinimide to act as an efficient scavenger of hydrobromic acid[4] it seems unlikely that this reaction is acid-catalysed. It is possibly the slow release of bromine that is responsible for the observed reaction[5] although more work is needed to fully elucidate the mechanism. However, despite the mechanistic uncertainties, the use of *N*-bromosuccinimide in aqueous dimethyl sulphoxide provides a useful alternative to the existing procedures for removing the *t*-butyldimethylsilyl protecting group.

***t*-Butyldimethylsilyl Ethers 2a–f and Tetrahydropyranyl Ether 3:**

With the exception of **2d**, whose preparation will be reported separately, all of the ethers were prepared from the corresponding alcohols[6] by the method of Corey and Venkateswarlu[2].

2a; yield: 90%; b.p. 138–140 °C/1.25 torr.

$C_{13}H_{21}NO_3Si$	calc.	C 58.43	H 7.87	N 5.24
(267.4)	found	58.58	7.83	5.48

2b; yield: 91%; b.p. 105–110 °C/12 torr.

M.S.: $m/e = 169.1076$ (calc. for $M^+ - C_4H_9$: 169.1044).

2c; prepared according to Ref. [7].

2e; yield: 84%; m.p. 138–140 °C.

$C_{33}H_{62}OSi$	calc.	C 78.88	H 12.35
(502.9)	found	78.63	12.55

2f; yield: 85%; m.p. 160–162 °C.

$C_{33}H_{60}OSi$	calc.	C 79.20	H 12.00
(500.9)	found	79.25	12.30

3; prepared according to Ref. [9].

Cleavage of *t*-Butyldimethylsilyl Ethers 2; General Procedure:
The ether **2** (1 g) is dissolved in laboratory grade dimethyl sulphoxide (9.5 ml) containing water (0.5 ml). With silyl ethers **2e** and **2f**, sufficient tetrahydrofuran, is then added to obtain a homogeneous solution. *N*-Bromosuccinimide (1.1 equiv) is then added and the reaction is stirred at room temperature. T.L.C. can be used to monitor the progress of the reactions but they are usually left overnight after which time (17 h) they are complete. The reaction mixture is then poured into diethyl ether (100 ml) and washed several times with brine. The organic layer is dried with magnesium sulphate and concentrated under reduced pressure to give a mixture of the product alcohol **1** and *t*-butyldimethylsilanol. The silanol can be removed under high vacuum, leaving the crude reaction product which is purified by distillation, recrystallisation, or preparative T.L.C. (in the cases of **1c** and **1d**).

t-Butyldimethylsilanol can be collected by distillation. Its physical and spectral properties are identical with those reported[10].

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[2] (a) E. J. Corey, A. Venkateswarlu, *J. Am. Chem. Soc.* **94**, 6190 (1972).
(b) R. F. Newton et al., *Tetrahedron Lett.* **1979**, 3981.

[3] See M. Fieser, L. F. Fieser, *Reagents for Organic Synthesis*, Vol. 1, John Wiley and Sons, New York, 1967, p. 78–80.

[4] P. S. Skell, J. C. Day, K. J. Shea, *J. Am. Chem. Soc.* **98**, 1195 (1976).

[5] The use of *N*-bromosuccinimide in aqueous solution to provide small concentrations of bromine has been described: H. C. Brown, Y. Yamamoto, *Synthesis* **1972**, 699. The addition of a molar equivalent of bromine to the silyl ethers usually gave a mixture of products (one of which was the expected deprotection product).

[6] Alcohols **1a**, **1e**, and **1f**, were obtained from the Aldrich Chemical Company. **1c** was prepared according to Ref. [7] and **1b** according to Ref. [8].

[7] E. J. Corey, D. J. Beames, *J. Am. Chem. Soc.* **94**, 7210 (1972).

[8] I. M. O. d'Engenieres, M. Miocque, J. A. Gautier, *Bull. Soc. Chim. Fr.* **1964**, 2477.

[9] M. Miyoshita, A. Yoshikoshi, P. A. Grieco, *J. Org. Chem.* **42**, 3772 (1977).

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