

Deprotection of Silyl Ethers Using 2,3-Dichloro-5,6-dicyano-*p*-benzoquinone

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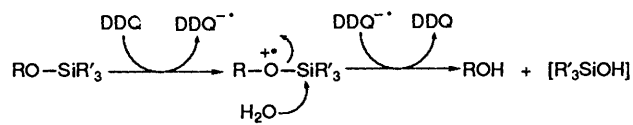
In the presence of a catalytic amount of 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ), triethylsilyl (TES) and *tert*-butyldimethylsilyl (TBDMS) ethers are readily hydrolysed to the corresponding alcohols in MeCN-H₂O (9:1) or tetrahydrofuran (THF)-H₂O (9:1). TES ethers are cleaved to alcohols more easily than TBDMS ethers. *tert*-Butyldiphenylsilyl (TBDPS) ethers are stable under these reaction conditions.

The popularity and extensive use of silyl ethers as protecting groups for alcohols¹ results from their ease of formation and removal and their stability to a wide range of reagents. Of such groups the most widely used are TES, TBDMS and TBDPS ethers²⁻⁴ and a variety of methods have been developed for their removal, *e.g.* hydrolysis using protic acids such as acetic acid. Since the strong acidity of protic acids is undesirable for acid-sensitive substrates, a less acidic reagent, fluorosilicic acid (H₂SiF₆) has been proposed.⁵ Tetrabutylammonium fluoride has also been used,⁶ but fluoride ion in an aprotic solvent is a strong base.⁷ Recently, Corey *et al.* reported the reductive cleavage of TBDMS ethers by diisobutylaluminium hydride⁸ and the use of SiF₄ as a selective desilylating reagent.⁹

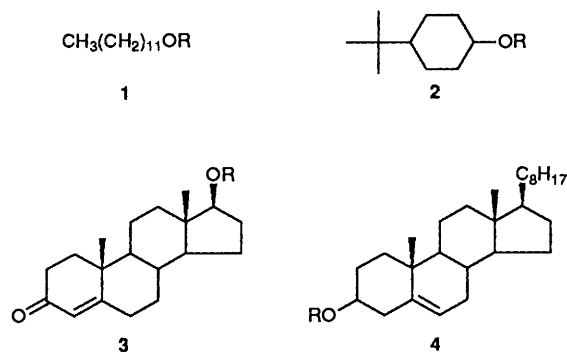
During the course of our investigations of DDQ, we reported that DDQ can catalyse the hydrolysis of acetals to aldehydes or ketones.¹⁰ Here we report a new method for the cleavage of silyl ethers using a catalytic amount of DDQ under neutral conditions.

First, we examined the hydrolysis of dodecyl TES ether in various solvents. The results are summarized in Table 1. In MeCN-H₂O (9:1) or THF-H₂O (9:1), the reaction was complete in 1 h at room temperature to give dodecyl alcohol in 93 or 97% yield, respectively. In CH₂Cl₂-H₂O (19:1), the reaction was very slow whilst in benzene-H₂O (19:1), no reaction occurred (entries 1-4). This reaction is only achieved in the presence of water, most of the dodecyl TES ether being recovered (entries 5 and 6) in its absence. Next, deprotection of various TES ethers was examined. In every case, the reaction proceeded smoothly in MeCN-H₂O or THF-H₂O within 1 h to give the corresponding alcohols in quantitative yields (entries 7-11). The reaction of the other silyl ethers, TBDMS and TBDPS ethers, was also explored. The TBDMS ethers require 3-7 h to complete the reaction (entries 12-18). The TBDMS group is less readily hydrolysed than the TES group. TBDPS ethers did not react at all under these reaction conditions (entries 19-25). The selectivity of this reaction is much the same as that described for protic acids, tetrabutylammonium fluoride, and SiF₄.

We believe that deprotection of silyl ethers with DDQ probably occurs *via* a single-electron transfer (SET) mechanism as shown in Scheme 1.¹¹



In summary, this method constitutes a new procedure for deprotection of silyl ethers under neutral conditions. Other synthetic applications of DDQ are now in progress.



a, R = SiEt₃; b, R = SiBu^tMe₂; c, R = SiBu^tPh₂; d, R = H

Table 1 Deprotection of various silyl ethers by DDQ^a

Entry	Silyl ether	Solvent	<i>t</i> /h	Yield (%) ^{b,c}
1	1a	MeCN-H ₂ O (9:1)	1	93
2		THF-H ₂ O (9:1)	1	97
3		CH ₂ Cl ₂ -H ₂ O (19:1)	7	55 (45)
4		C ₆ H ₆ -H ₂ O (19:1)	7	0 (96)
5		MeCN	1	19 (80)
6		THF	1	0 (71)
7	2a	MeCN-H ₂ O (9:1)	1	100
8		THF-H ₂ O (9:1)	1	100
9	3a	MeCN-H ₂ O (9:1)	1	88
10		THF-H ₂ O (9:1)	1	95
11 ^d	4a	THF-H ₂ O (9:1)	1	90
12	1b	MeCN-H ₂ O (9:1)	6	65 (33)
13		THF-H ₂ O (9:1)	6	86 (14)
14	2b	MeCN-H ₂ O (9:1)	3	96 (4)
15		THF-H ₂ O (9:1)	6	97 (3)
16	3b	MeCN-H ₂ O (9:1)	7	92 (4)
17		THF-H ₂ O (9:1)	7	88 (12)
18 ^d	4b	THF-H ₂ O (9:1)	7	93 (3)
19	1c	MeCN-H ₂ O (9:1)	6	0 (92)
20		THF-H ₂ O (9:1)	6	0 (96)
21	2c	MeCN-H ₂ O (9:1)	6	0 (87)
22		THF-H ₂ O (9:1)	6	0 (100)
23	3c	MeCN-H ₂ O (9:1)	6	0 (100)
24		THF-H ₂ O (9:1)	6	0 (100)
25 ^d	4c	THF-H ₂ O (9:1)	6	0 (100)

^a DDQ (0.1 mmol) in solvent (3.5 cm³) was added to a solution of the silyl ether (1.0 mmol) in solvent (3.5 cm³) under N₂ at room temp. ^b Isolated yields. ^c The figures in parentheses are the recovery of the starting materials. ^d In MeCN-H₂O (9:1), silyl ethers 4a-c were not hydrolysed at all because of their insolubility to the solvent.

Experimental

M.p.s are uncorrected. IR spectra were recorded on a Hitachi I-3000 spectrophotometer. ¹H NMR spectra were measured on

a Hitachi R-24B spectrometer using Me₄Si as the internal standard. Column chromatography was performed on Wakogel C-200 silica gel. DDQ was recrystallized from benzene–hexane.

Typical Procedure for Deprotection of Silyl Ethers.—To a solution of dodecyl TES ether **1a** (300 mg, 1.0 mmol) in MeCN–H₂O (9:1) (3.5 cm³), was added a solution of DDQ (23 mg, 0.1 mmol) in MeCN–H₂O (9:1) (3.5 cm³). After the mixture had been stirred for 1 h at room temp. under N₂ it was evaporated and the residue was chromatographed (benzene–ether = 2:1) on silica gel to give dodecyl alcohol **1d** (173 mg, 93%) as a colourless crystalline solid, m.p. 24 °C (aqueous EtOH) (lit.^{1,2} 24 °C); ν_{\max} (neat)/cm⁻¹ 3336 (OH); δ_{H} (CDCl₃) 0.92 (3 H, t, J 6, CH₃), 1.10–1.78 (20 H, br s, CH₂), 1.89 (1 H, s, OH) and 3.67 (2 H, t, J 6, CH₂).

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Paper 2/05095A

Received 23rd September 1992

Accepted 24th September 1992