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SHORT COMMUNICATION

Desilylation of t-Butyldimethylsilyl Ethers of Hydroxyquinones

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Desilylation of a series of hydrolytically stable hydroxyquinone t-butyldimethylsilyl ethers was achieved in high yields by the use of potassium fluoride in the presence of catalytic amounts of aqueous 48% hydrobromic acid (HBr), or basic aluminium oxide (Al_2O_3), and tetra-n-butylammonium fluoride (Bu_4NF) as cleaving agents. © 1998 John Wiley & Sons, Ltd.

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INTRODUCTION

Protection of functional groups of hydroxyquinones against destructive conditions during multistage syntheses of several quinonoid compounds, such as the anthracyclines, the well-known antibiotics with anticancer activity, is a common procedure.[1] However, the trialkylsilyl group,[2] though a widely used protecting group, has quite a limited use in the protection of hydroxyquinones, i.e. in the regiospecific protection of juglone (5-hydroxy-1,4-naphthoquinone) by Me_2SiCN_2.[3] Deprotection of the cyanosilylated derivative is achieved by methanol or silverfluoride in tetrahydrofuran (THF).[3]

We have recently reported on the synthesis of the hydrolytically stable t-butyldimethylsilyl (TBDMS) ethers of ten biologically important hydroxyquinones **1a–10a** (Table 1) by protection of all their hydroxyl groups.[4,5] The simplicity and efficacy of the new silylation method prompted us to study desilylation of the new compounds, on which we report now. Two powerful desilylating agents, potassium fluoride (KF)[6,7] and tetra-n-butylammonium fluoride (TBAF)[8] were employed in three different desilylating procedures (A, B for KF and C for TBAF) which have been used for the first time in the desilylation of hydroxyquinone silylethers.

RESULTS AND DISCUSSION

(Fluoride-based reagents are the best choice for cleaving silyl ethers.[2] In addition, KF and TBAF can selectively cleave phenolic silyl ethers[6,7] (which form the majority of compounds **1–10**) in the presence of alcoholic silyl ethers, whereas TBAF in excess leads to effective deprotection of both types of silyl ethers.[8,9]

Hydroxyquinone TBDMS ethers **1–10** were cleaved to the corresponding hydroxyquinones **1a–10a** in high to quantitative yields. Table 2 presents the reaction conditions and yields determined for each hydroxyquinone silyl ether in each desilylation procedure.

Aqueous 48% HBr[6] (method A) and basic Al_2O_3[7] (method B) were used to enhance reactivity of KF,[6] which resulted in the effective desilylation of the phenolic hydroxyquinone silyl ethers **1–6**. Compound **7** was not cleaved by KF even after prolonged stirring, probably due to the high steric hindrance of the two adjacent TBDMS groups.

TBAF was used in carefully controlled conditions for the cleavage of phenolic silyl ethers **1–7**, and in 100% excess for the cleavage of the alcoholic ethers 8 and 9; this resulted in the conversion of all but **2**, to the free hydroxyquinones in high yields. Compound **2** failed to be cleaved even after prolonged stirring at elevated temperatures ($\leq$60°C). Therefore a two-step process was applied to the desilylation of **10**, consisting of

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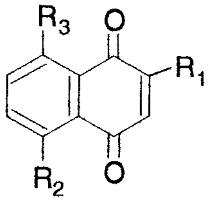
Table 1 Structures of the hydroxyquinones **1a–10a** and their silyl ethers **1–10**[a]



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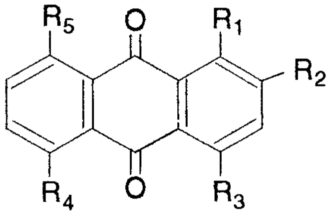

II

Compound	Type	R$_1$	R$_2$	R$_3$	R$_4$	R$_5$
1	I	H	OSiMe$_2$tBu	H		
1a	I	H	OH	H		
2	I	H	OSiMe$_2$tBu	OSiMe$_2$tBu		
2a	I	H	OH	OH		
3	I	OSiMe$_2$tBu	H	H	H	H
3a	II	OH	H	H	H	H
4	II	OSiMe$_2$tBu	H	OSiMe$_2$tBu	H	H
4a	II	OH	H	OH	H	H
5	II	OSiMe$_2$tBu	H	H	OSiMe$_2$tBu	H
5a	II	OH	H	H	OH	H
6	II	OSiMe$_2$tBu	H	H	H	OSiMe$_2$tBu
6a	II	OH	H	H	H	OH
7	II	OSiMe$_2$tBu	OSiMe$_2$tBu	H	H	H
7a	II	OH	OH	H	H	H
8	I	OSiMe$_2$tBu	H	H		
8a	I	OH	H	H		
9	II	H	CH$_2$(OSiMe$_2$tBu)	H	H	H
9a	II	H	CH$_2$(OH)	H	H	H
10	I	CH(OSiMe$_2$tBu)CH$_2$CH=C(CH$_3$)$_2$	OSiMe$_2$tBu	OSiMe$_2$tBu		
10a	I	CH(OH)CH$_2$CH=C(CH$_3$)$_2$	OH	OH		

[a] From Refs. 4, 5.

treatment with KF/HBr or KF/Al$_2$O$_3$ in the first step followed by treatment with a 100% excess of TBAF.

All hydroxyquinones obtained were identified by TLC analysis and their IR spectra and melting points were in agreement with the published one.[1,10]

EXPERIMENTAL

Analytical TLC was performed on precoated Merck sheets. Melting points were determined in a heated oil bath. Infrared spectra were recorded on a Jasco IR-Report-100 spectrometer.

The hydroxyquinones employed were purchased from Fluka Chemical Co. and were of analytical reagent grade. The silylating agent, N-methyl-N-(tert-butyldimethylsilyl)-2,2,2-trifluoroacetamide (MTBSTFA) containing 1% TBDMSCl, was also obtained from Fluka Chemical Co., and was normally stored in the cold and dark under N$_2$. All solvents were freshly dried by distillation over anhydrous Na$_2$SO$_4$.

The hydroxyquinone TBDMS ethers **1–10** were prepared from the corresponding hydroxyquinones **1a–10a** according to the procedure published by the authors previously.[4,5]

Desilylation procedures A,[6,] B[7] and C[8] were applied as initially reported.

Method A

A mixture of silyl ether (**1–7**), anhydrous KF and aqueous 48% HBr in DMF was stirred under

Table 2 Conditions for desilylation of hydroxyquinone TBDMS ethers by methods A, B and C

	Method A					Method B				Method C			
Silyl ether	T(°C)	t(h)	KF/silyl ether (mol)	HBr/silyl ether (mol)	yield (%)	>T(°C)	t(h)	KF/silyl ether (mol)	yield (%)	T(°C)	t (min)	TBAF/ silyl ether mol/mol	yield (%)
1	r.t[a]	0.5	2	0.4	87	r.t.	2.5	3	90	r.t.	0.25	1	97
2	r.t.	0.5	4	0.8	89	r.t.	1.5	6	93	60	48	2	—
3	r.t.	0.5	2	0.4	89	r.t.	1.5	3	96	r.t.	0.25	1	99
4	r.t.	0.5	4	0.8	89	r.t.	1.5	6	95	r.t.	0.25	2	99
5	r.t.	0.5	4	0.8	89	r.t.	1.5	6	96	r.t.	0.25	2	98
6	r.t.	0.5	4	0.8	88	r.t.	1.5	6	97	r.t.	0.25	2	99
7	r.t.	48	4	0.8	—	r.t.	48	6	—	r.t.	0.25	2	99
8	—	—	—	—	—	—	—	—	—	r.t.	0.25	2	96
9	—	—	—	—	—	—	—	—	—	r.t.	0.25	2	97
10	r.t.	0.5	4	0.8	75[b]	r.t.	1.5	6	85[b]	r.t.	0.25	2	75–85

[a] r.t., room temperature.

[b] Refers to the total yield of **10a** by the successive use of methods A (or B) and C.

nitrogen at room temperature (Table 2) and the crude product was treated with aqueous hydrochloric acid (HCl), extracted with chloroform ($CHCl_3$), washed and dried.[6]

Method B

A mixture of silyl ether (**1–7**), 3 M in acetonitrile (CH_3CN) and KF (37% w/w) – basic Al_2O_3 was stirred at room temperature (Table 2).[7] The crude product was washed with 15*n* ml methanol (MeOH), diluted with 15*n* ml water, extracted with 3 × 20*n* ml $CHCl_3$ (where *n* is the number of TBDMS groups of the silyl ether) and the combined extracts were dried over anhydrous sodium sulphate (Na_2SO_4).

Method C

A mixture of silyl ether (**1–10**) and 1 M TBAF in THF was stirred at room temperature (Table 2).[8]After 15 min an excess of aqueous NH_4Cl was added and the mixture was extracted with $CHCl_3$ and dried over anhydrous Na_2SO_4.

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