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A facile and selective deprotection of *tert*-butyldimethylsilyl ethers of phenols using triethylamine *N*-oxide

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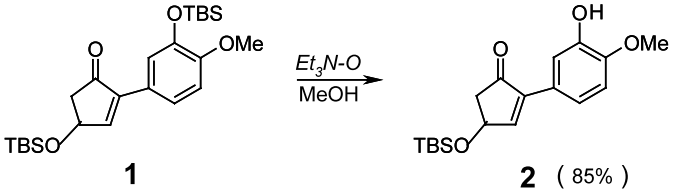
Abstract—Aryl TBS ethers can be cleaved selectively in high yields in the presence of alkyl TBS ethers by employing triethylamine *N*-oxide.

In recent years, several protection/deprotection protocols have been reported for temporarily masking hydroxyl groups because of their significance in multistep syntheses of complex synthetic targets of biological significance.[1] Amongst these, the *tert*-butyldimethylsilyl (TBS) group remains the method of choice for hydroxyl protection due to its stability and the ease by which it can be introduced and removed.[2] Furthermore, discrimination between alkyl and aryl silyl ethers facilitates deprotection of one group in the presence of the other.[3] In this regard, a number of methods exist for selective deprotection of alkyl silyl ethers while the techniques available for aryl silyl ethers are relatively few.[4] Also, it is worth mentioning that most of the methods reported for selective desilylation of aryl silyl ethers employ basic conditions. More recently, Crouch et al. reported the use of solid NaOH and a phase transfer catalyst to achieve such a similar selective desilylation under mild conditions.[5]

In conjunction with another on-going project in our laboratory, we had observed that aryl silyl ethers can be removed selectively in the presence of alkyl silyl ethers using triethylamine *N*-oxide in high yield (Scheme 1).



Scheme 1.

In our hands, the above desilylation using reported methods[3,4] led to formation of unwanted side products and failed to furnish **2** in reasonable yield. This led us to investigate the possibility of utilising Et_3N-*O* as an effective reagent for selective deprotection of aryl silyl ethers. Accordingly, we synthesised various TBS ethers and studied their cleavage with Et_3N-*O*. The results are summarised in Table 1. As can be seen in Table 1, deprotection proceeded very cleanly in high yield in all cases. However in the case of entry 10, no trace of deprotected compound was observed.

It is remarkable that side reactions do not occur during desilylation under these conditions and consistent yields were obtained despite the presence of sensitive functionality such as a chalcone, an enone or an aldehyde in some of the examples studied (entries 7, 8 and 9).

We believe that the mechanism of this selective removal involves nucleophilic attack of the *N*-oxide on the silicon with methanol acting as the proton source.

Typical experimental procedure:

To a stirred solution of the substrate **1** (0.448 g, 1 mmol) in methanol (5 ml) was added Et_3N-*O* (0.117g, 1 mmol). The reaction was monitored by TLC. After the reaction was complete, the solvent was removed under vacuum. The residue was extracted with a suitable solvent, and the organic extract was washed with water, dried and concentrated. The crude product was purified by column chromatography with ethyl acetate/hexane as eluent to afford phenol **2** as a colourless oil in 85% yield. The product obtained was identical with an authentic sample by TLC and ^{1}H NMR.

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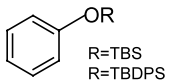
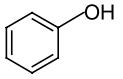
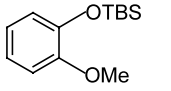
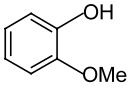
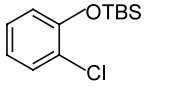
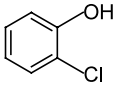
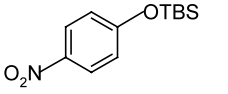
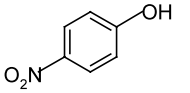
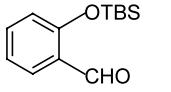
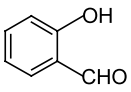
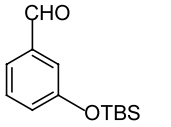
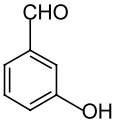
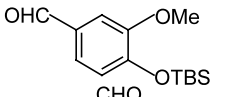
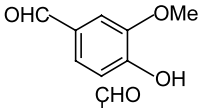
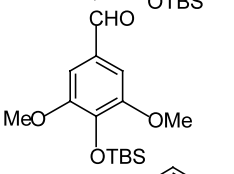
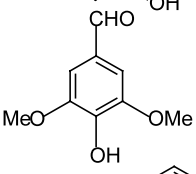
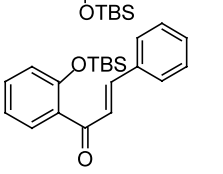
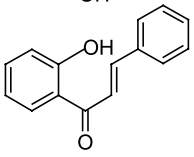
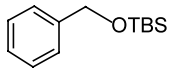
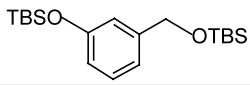
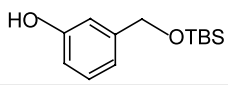
Table 1. Desilylation of aryl silyl ethers[a]

Entry	Substrate	Product	Time (h)	Yield (%)[b]
1			1	98
2			0.5	86
3			0.5	94
4			0.5	96
5			1	92
6			1	91
7			2	95
8			3	98
9			0.5	90
10		–	24	–
11			2	79

a: The reaction was carried out using 1 mmol of substrate in methanol .
b: Isolated yield.

In summary, triethylamine *N*-oxide can be used as a selective reagent for deprotection of aryl silyl ethers. The mild conditions coupled with high yields and the demonstrated applicability to functionalised molecules shows that the protocol will find wide spread use in synthesis.

References

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