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Tetrahedron Letters 44 (2003) 8819–8821

TETRAHEDRON
LETTERS

SbCl₅-wet acetonitrile: a new system for chemoselective *O*-desilylation

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Received 8 August 2003; revised 17 September 2003; accepted 23 September 2003

Abstract—A new efficient method for deprotection of TBDMS derivatives of phenols, primary alcohols, carboxylic acids and secondary amines, consisting of SbCl₅ and MeCN with 0.1% water (w/v), is reported. It effects *inter alia* desilylation of a CH₂OTBDMS group in the presence of a ketal function.

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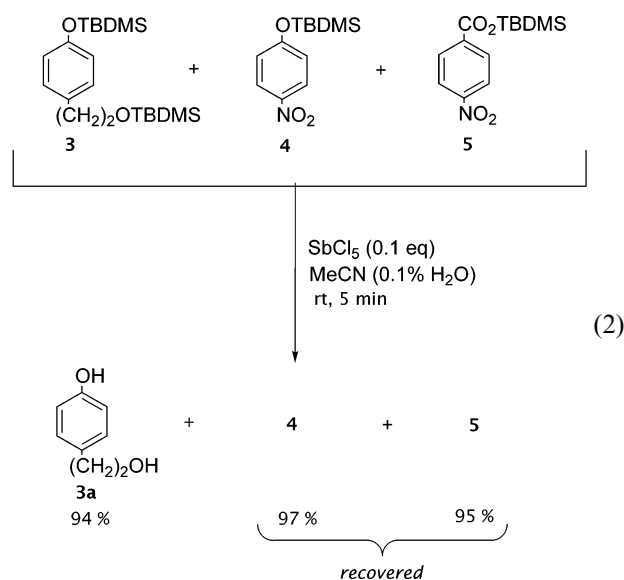
The application of silyl groups as protecting groups for O, N, S, etc., in synthesis is well known.¹ Since its introduction to organic chemistry by Corey,² one such group namely, the *t*-butyldimethylsilyl group (TBDMS) has occupied a privileged position. Its popularity, especially with respect to *O*-protection, is undoubtedly due to its enhanced stability in basic and mildly acidic conditions, compared with other common silicon-based analogues, and the mildness of conditions under which it can be removed. In connection with our current studies on the synthesis of heterocyclic compounds, an attempted desilylation of substance **1**, and other structurally related compounds,³ with a variety of F⁻ ion sources in THF led to intractable mixtures. However, a solution of **1** in wet acetonitrile, 0.1% water (w/v), on treatment with a sub-stoichiometric quantity of SbCl₅ (0.1 equiv.) cleanly afforded the nitron **1a** in good yield (Eq. (1)).



This observation led us to examine the scope of this reaction for the deprotection of other silylated compounds.⁴ Our results (Table 1) show that the same

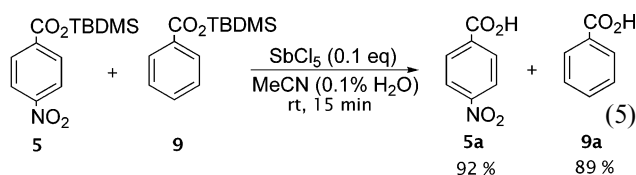
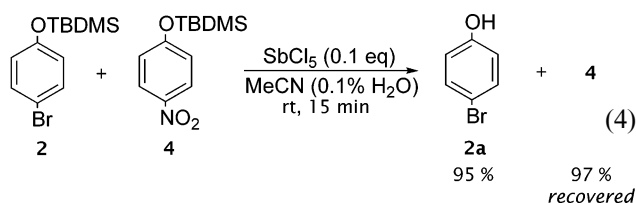
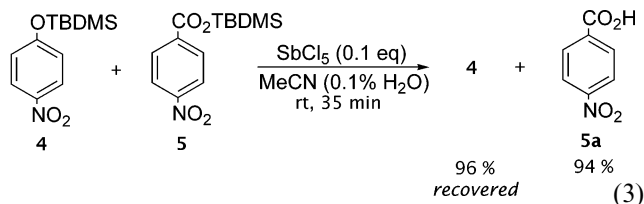
system brings about an efficient deprotection of TBDMS derivatives of phenols, primary alcohols, carboxylic acids, and primary and secondary amines in good to excellent yields.⁵

The different rates of desilylation observed (Table 1; entries 1, 2, 3 and 4) prompted us to examine the existence if any, of substrate selectivity in a mixture consisting of different silyl ethers. With this end in view, an equimolar mixture (0.06 M) of **3**, **4** and **5** in wet acetonitrile (0.1% H₂O) was exposed, in a competitive reaction, to the action of SbCl₅ (0.1 equiv.) at rt and the following results were obtained (Eq. (2)).



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Thus, whilst no discrimination was observed in the cleavage between the phenolic and the alcoholic TBDMS groups in **3** (Eq. (2)), high chemoselectivity was noted for the *p*-nitro silyl ester **5** in the presence of the *p*-nitro silyl ether **4** (Eq. (3)). A similar rate difference noted for the TBDMS derivatives of *p*-bromo and *p*-nitro phenols, **2** and **4** respectively, was again reflected in the preferential conversion of **2** into **2a** (Eq. (4)). However, no such selectivity was observed between the silyl ester of benzoic acid **9** and its *p*-nitro derivative **5** (Eq. (5)).

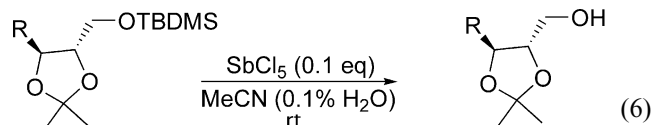


In experiments involving substances **10**, **11** and **12**, all of which contained both ketal and *O*-TBDMS groups, it is the latter that are selectively deprotected to provide the corresponding primary alcohols **10a**, **11a** and **12a** in excellent yields⁶ (Eq. (6) and (7)).

Table 1. Silyl compounds deprotected by $\text{SbCl}_5/\text{MeCN}$ (0.1% H_2O) at rt

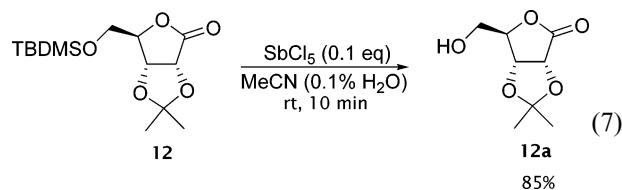
Entry	Silyl compound $p\text{-R}^1\text{-C}_6\text{H}_4\text{-R}^2$	Product $p\text{-R}^1\text{-C}_6\text{H}_4\text{-R}^2$	Time	Yield (%)
1	2 $\text{R}^1 = \text{OTBDMS}$ $\text{R}^2 = \text{Br}$	2a $\text{R}^1 = \text{OH}$ $\text{R}^2 = \text{Br}$	15 min	93
2	3 $\text{R}^1 = \text{OTBDMS}$ $\text{R}^2 = (\text{CH}_2)_2\text{OTBDMS}$	3a $\text{R}^1 = \text{OH}$ $\text{R}^2 = (\text{CH}_2)_2\text{OH}$	10 min	92
3	4 $\text{R}^1 = \text{OTBDMS}$ $\text{R}^2 = \text{NO}_2$	4a $\text{R}^1 = \text{OH}$ $\text{R}^2 = \text{NO}_2$	31 h	94
4	5 $\text{R}^1 = \text{CO}_2\text{TBDMS}$ $\text{R}^2 = \text{NO}_2$	5a $\text{R}^1 = \text{CO}_2\text{H}$ $\text{R}^2 = \text{NO}_2$	40 min	85
5	6 $\text{R}^1 = \text{NHTBDMS}$ $\text{R}^2 = \text{CH}_3$	6a $\text{R}^1 = \text{NH}_2\text{ac}$ $\text{R}^2 = \text{CH}_3$	5 min	62 ^a
6	7 $\text{R}^1 = \text{CH}_2\text{NHTBDMS}$ $\text{R}^2 = \text{H}$	7a $\text{R}^1 = \text{CH}_2\text{NH}_2$ $\text{R}^2 = \text{H}$	5 min	72 ^a
7	8 $(\text{CH}_2)_5\text{NTBDMS}$	8a $(\text{CH}_2)_5\text{NH}$	5 min	75 ^a

^a Estimated by ¹H NMR.

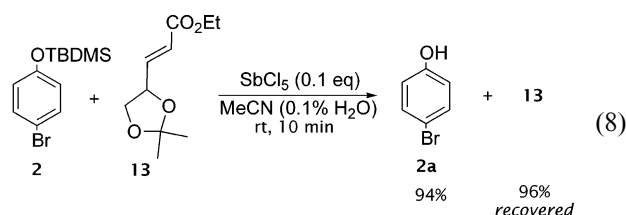


10: R = H
11: R = CH_2OTBDMS

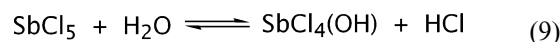
10a: R = H; 96%; 10 min
11a: R = CH_2OH ; 84%; 15 min



A similar selectivity in favour of desilylation was also observed in a competition experiment involving the ketal-ester **13** and the phenolic OTBDMS ether **2** as shown in Eq. (8).



In principle these reactions could be yet another example⁷ of a simple protic acid catalysed process (i.e. HCl generated in situ from SbCl_5 and the water present in MeCN) (Eq. (9)).



That water is clearly implicated in these reactions is supported by the observation that they became progressively slower as the water content in the acetonitrile was reduced by successive distillations from CaH_2 and P_2O_5 . In spite of similar readings by a pH meter⁸ for both a solution of SbCl_5 (6×10^{-3} M) in MeCN containing 0.1% water and a 0.265 M solution of HCl in the same solvent system, the OTBDMS cleavage in **10** with *aq.* HCl occurred non-selectively (Eq. (6)). A similar result was observed for the competition process shown in Eq. (2). Instead only glycerol, in the former, and a mixture of varying proportions of **3a**, **4a** and **5a**, in the latter, were obtained. On the basis of these observations the following mechanism involving an Sb(V) intermediate of type **14** for the *O*-desilylation⁹ of **10** is suggested (the precise number of OH groups attached to Sb(V) remains undetermined) (Scheme 1).

In conclusion, SbCl_5 in sub-stoichiometric quantity, in moist acetonitrile, is introduced as an efficient and mild system for the deprotection of TBDMS derivatives of amines, phenols, primary alcohols and aryl carboxylic acids in good to excellent yields. High selectivity for OTBDMS cleavage is noted in the presence of a ketal group. A similar discrimination was observed for aryl

