Selective Removal of the Methyldiphenylsilyl Protecting Group Using Azide Ion

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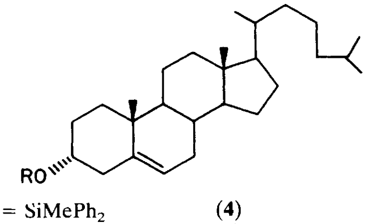
Sodium azide in dimethylformamide effects the cleavage of the methyldiphenylsilyl ether bond under conditions whereby t-butyldimethylsilyl ethers and t-butyldiphenylsilyl ethers are stable.

The use of trialkylsilyl- and alkyldiarylsilyl-moieties as protecting groups for primary and secondary alcohols is well-established.[1] Alkoxyalkylsilyl- and alkoxyarylsilyl-groups have also been recommended[2] but have not gained the same popularity. Of the plethora of silyl protecting groups now available, the t-butyldimethylsilyl[3] and methyldiphenylsilyl[4] entities are amongst the most widely used, not least because the corresponding silyl chlorides are commercially available and relatively cheap. We describe a method for the cleavage of the methyldiphenylsilyloxy bond in the presence of a t-butyldimethylsilyl ether which should prove to be useful in synthesis.

Decan-1-ol was converted into the silyl ethers (**1**)—(**3**). Treatment of compound (**1**) with one molar equivalent of sodium azide in dimethylformamide (DMF) at 40 °C for two days gave decanol (93%) after work-up and filtration of the crude product through silica gel. The related compounds (**2**)

$C_9H_{19}CH_2OR$



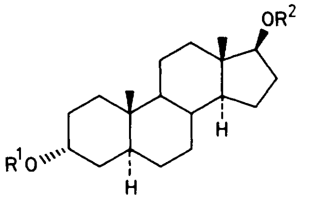
(**1**) R = $\mathrm{SiMePh_2}$ (**4**)
(**2**) R = $\mathrm{SiBu^tPh_2}$ (**5**)
(**3**) R = $\mathrm{SiBu^tMe_2}$ (**6**)

and (**3**) were recovered in practically quantitative yield after three weeks under the same reaction conditions. Similarly the cholesterol derivatives (**4**)—(**6**) were prepared using the standard methods. The methyldiphenylsilyl ether (**4**) was converted into cholesterol in quantitative yield on treatment with sodium azide (1 equiv.) in DMF at 60 °C for 48 h. The compounds (**2**), (**3**), (**5**), and (**6**) were perfectly stable under these conditions.

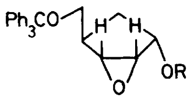
The rate of the desilylation reaction is enhanced by the addition of ammonium chloride while selectivity is retained. For example the bis-silylated compounds (**7**) and (**8**) were prepared from androsterone. Compound (**7**) was treated with azide ion (excess) in DMF containing ammonium chloride (1 equiv.) at 60 °C for 6 h to furnish the alcohol (**9**) (81%) as the only detectable steroid. In a complementary fashion compound (**8**) afforded mono-ol (**10**) (88%) under similar reaction conditions.

Obviously this method of selective deprotection cannot be used when the substrate molecule has a highly nucleofugic group. However we did find that the cyclopentane derivative (**11**) was cleanly converted into the alcohol (**12**) (80%) using azide ion together with ammonium chloride in DMF at 40 °C. The azido diols which would result from the opening of the oxirane ring have been prepared by another method and were not formed in the above reaction.

It is noteworthy that the methyldiphenylsilyloxy- and t-butyldimethylsilyloxy-bonds are cleaved at different rates using one of the standard deprotection methods, namely tetrabutylammonium fluoride. The latter silyl group is less easily cleaved. However *both* protecting groups are lost after treatment with excess of fluoride ion at room temperature over a few minutes. Similarly both protecting groups are removed by acid treatment (*e.g.* acetic acid/water/tetrahydrofuran);† hence we believe it is distinctly advantageous to use the ability of azide ion to clearly distinguish the two groups.



(**7**) $R^1 = SiMePh_2$; $R^2 = SiBu^tMe_2$
(**8**) $R^1 = SiBu^tMe_2$; $R^2 = SiMePh_2$
(**9**) $R^1 = H$; $R^2 = SiBu^tMe_2$
(**10**) $R^1 = SiBu^tMe_2$; $R^2 = H$



(**11**) $R = SiMePh_2$
(**12**) $R = H$

We believe that it will prove to be useful to employ two different, readily available silyl protecting groups to mask hydroxy groups that have to be unveiled at different stages in a synthetic scheme: recourse to less satisfactory units such as the tetrahydropyranyl system could then be circumvented.

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References

1 T. W. Greene, 'Protective Groups in Organic Sythesis,' Wiley-Interscience, New York, 1981; E. Colvin, 'Silicon in Organic Synthesis,' Butterworths, London, 1981; E. J. Corey, H. Cho, C. Rücker, and D. H. Hua, *Tetrahedron Lett.*, 1981, **22**, 3455; H. Wetter and K. Oertle, *ibid.*, 1985, **26**, 5515; M. Lalonde and T. H. Chan, *Synthesis*, 1985, 817.

2 G. G. Furin, O. A. Vyazankin, B. A. Gostevsky, and N. S. Vyazankin, *Tetrahedron*, 1988, **44**, 2675; Y. Guindon, R. Fortin, C. Yoakin, and J. W. Gillard, *Tetrahedron Lett.*, 1984, **25**, 4717.

3 E. J. Corey and A. Venkateswarlu, *J. Am. Chem. Soc.*, 1972, **94**, 6190; T. Hanamoto, T. Hayama, T. Katsaki, and M. Yamaguchi, *Tetrahedron Lett.*, 1987, **28**, 6329.

4 S. E. Denmark, R. P. Hammer, E. J. Weber, and K. L. Habermas, *J. Org. Chem.*, 1987, **52**, 165.

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† Denmark *et al.* indicate that a diphenylmethylsilyl group protecting a primary alcohol unit is removed using acetic acid/water/tetrahydrofuran (3 : 1 : 1) over 10 mins. The same conditions are often used to remove a t-butyldimethylsilyl protecting group using slightly longer reaction times.