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A NEW PREPARATION OF TRIMETHYLSILYL ETHERS[1]

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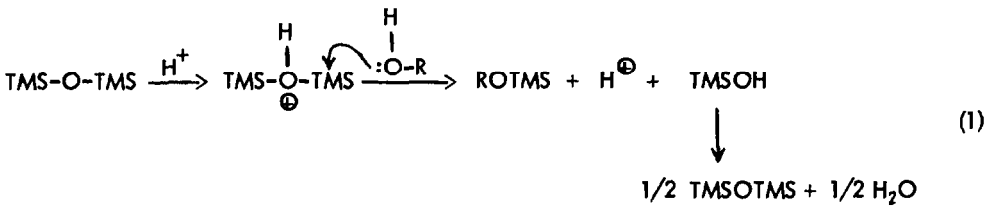
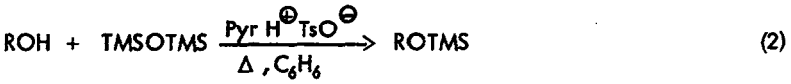
We wish to report a new method for the preparation of trimethylsilyl (TMS) ethers from alcohols under mildly acidic conditions. This compliments the most common procedure for the preparation of this popular protecting group which uses TMS chloride and a base like triethylamine.[2,3]

Our approach is based on the strategy outlined in equation 1. Thus, protonation of bistrimethylsilyl ether (BTMSE)[4] would yield a species susceptible to attack by alcohols. Despite the view that BTMSE is inert,[5] we felt that this idea is reasonable and, indeed, have found that it does work. Thus, reaction of benzyl alcohol with excess BTMSE in refluxing benzene containing a trace of p-TsOH gives the TMS ether of benzyl alcohol.[6] The reaction also works for 1-hexanol and 1-octanol but, unfortunately, fails when applied to alcohols sensitive to acid-catalyzed rearrangement. Consequently, a less acidic catalyst, pyridinium p-toluenesulfonate[7], was tried and found to be effective without causing unwanted rearrangements. In addition, a more efficient method for the removal of water is the use of a Soxhlet extractor filled with 4A molecular sieves.



(1)

The final procedure is shown in equation 2. A variety of systems have been explored (see

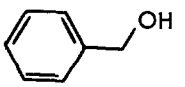
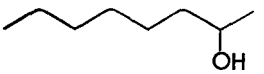
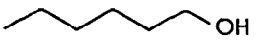
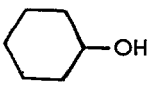
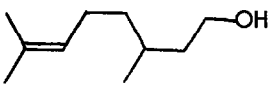
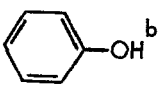
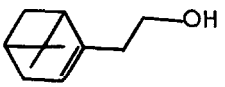


(2)

Table 1). Both primary and secondary alcohols as well as phenol give reasonable yields of pure, isolated TMS ethers.

A typical experimental procedure is as follows: 1-Hexanol (5.66 g, 55.5 mmol) was mixed with 15.0 g (168 mmol) of BTMSE, 30 ml of benzene and 0.35 g of pyridinium p-toluenesulfonate. This solution was refluxed for 4 days using a 20-cm Vigreux column and a small Soxhlet extractor. The reaction mixture was cooled to room temperature, washed with cold brine, dried over $MgSO_4$ and concentrated. Distillation gave 7.93 g (82%) of the pure TMS ether: bp 70-74° (20 mm); NMR (CCl_4) 0.1 (9H, s), 0.9 (3H, br t), 1.1-1.6 (8H, br s), 3.5 (2H, t, J = 6).

Table 1. Conversion of Alcohols into TMS Ethers[a]

ALCOHOL	% YIELD TMS ETHER (g)	ALCOHOL	% YIELD TMS ETHER (g)
	79(7.82)		80 (5.98)
	82 (7.93)		76 (6.75)
	80 (6.74)		90 (8.21)[b]
	87 (3.68)		

[a] All yields represent distilled products-pure by NMR, IR and TLC.

[b] Russian workers reported the acid-catalyzed silation of phenol with BTMSE: M. G. Vornokov and Z. I. Shabarova, J. Gen. Chem. USSR, 30, 1933 (1960).

References

1. Presented at the 30th Southeastern Regional Meeting of the American Chemical Society, Savannah, Georgia, November 8-10, 1978.
2. A. E. Pierce, "Silylation of Organic Compounds", Pierce Chemical Company, Rockford, Illinois, 1968.
3. Hexamethyldisilazane has been used in isolated examples to prepare TMS ethers with acid catalysis[2]; however, a mixture of hexamethyldisilazane, TMS chloride and pyridine works much better: H. E. Carter and R. C. Gaver, J. Lipid Res., 8, 391 (1967).
4. BTMSE is prepared in high yield from TMS chloride and excess aqueous $NaHCO_3$: bp 98-100°.
5. "Handbook of Silylation", Pierce Chemical Company, Rockford, Illinois, 1972, p. 5.
6. Continuous water removal was accomplished with a Dean-Stark trap containing 4A molecular sieves.
7. This is an effective catalyst for the preparation of tetrahydropyranyl ethers: N. Miyashita, A. Yoshikoshi and P. A. Grieco, J. Org. Chem., 42, 3772 (1977).

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