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DIISOPROPYLETHYLAMINE : AN EFFECTIVE CATALYST FOR THE INTRODUCTION OF THE t-BUTYLDIMETHYLSILYL GROUP

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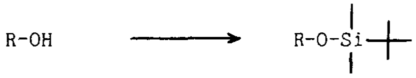
ABSTRACT: The rapid reaction of t-butyldimethylchlorosilane with alcohols catalysed by diisopropylethylamine at room temperature gave high isolated yields of the t-butyldimethylsilyl ethers.

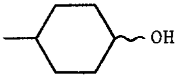
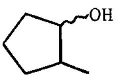
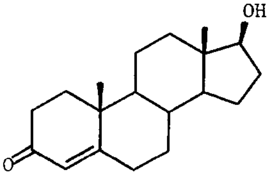
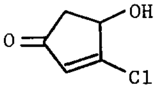
The t-butyldimethylsilyl (TBDMS) group has become firmly established as a protecting group[1,2,3] for alcohols. Since its introduction by Corey and Venkateswarlu[1] the more common method for the formation of TBDMS ethers has relied on the direct reaction of t-butyldimethylchlorosilane (TBDMCS) with alcohols catalysed by the base imidazole,[1] and more recently[2] Et_3N/4-dimethylaminopyridine, LiS, HMPT, Na_2CO_3, $AgNO_3$/pyridine, Et_3N. The more reactive silylating agents[3] TBDMS perchlorate and TBDMS triflate are most efficient, but these reagents are especially sensitive to moisture. Acid catalysed methods[4] employing TBDMS allylsilane, enol ethers, and ketene acetals have also been reported.



$$R\text{-}OH \longrightarrow R\text{-}O\text{-}\overset{|}{\underset{|}{Si}}\text{-}C(CH_3)_3$$

We now report a very effective catalysis of the reaction of TBDMCS with alcohols by diisopropylethylamine (DIPEA). A number of representative examples is presented in the table with high yields being obtained for the 1° and 2° alcohols. Excellent results were obtained for the hindered alcohol 5, while the substrate 7[2c] which reacts with imidazole, was derivatised cleanly in the presence of DIPEA. Even the 3° alcohol 6 reacts under the new conditions, albeit slowly. Of particular note is the faster rate of reaction in DMF which results in an exothermic process at room temperature with 1° alcohols, (entry 2). Such a rapid reaction has not previously been reported for TBDMCS. We observed[2c] that the reaction also proceeds in DMF without added base, although not to completion. Under these conditions reaction may involve the 'onium' complex,[6] $Me_2N\text{-}\overset{+}{C}\text{-}O\text{-}\overset{|}{\underset{|}{Si}}\text{-}C(CH_3)_3$.

In conclusion the rapid rate of reaction, choice of solvent (CH_2Cl_2 or DMF), the poor nucleophilicity, and volatility of the base used in the present procedure will undoubtedly extend the scope for a simple preparation of TBDMS ethers.

	Substrate	Solvent (TBDMCS eq)[a]	Time (T °C) hr	TBDMS ether Isolated Yield
1	$CH_3(CH_2)_8CH_2$-OH	CH_2Cl_2	1 (r.t.)	93%
2	$PhCH_2CH_2OH$	CH_2Cl_2 DMF 2	1 (r.t.) 10 min (r.t.)	92% 98%
3		CH_2Cl_2	4 (r.t.)	84%
4		CH_2Cl_2	4 (r.t.)	88%
5		CH_2Cl_2 (2.1)	6 (50°C)	86%
		DMF (2.1)	1.5 (r.t.)	100%
6	linalool	neat (2.4)	40 (100°C)	53%
7		CH_2Cl_2 (3.0)	16 (80°C)	75%
		DMF (3.0)	6 (r.t.)	90%

[a] Typically TBDMCS (1.2 eq) and DIPEA (1.5 eq) was used[5]

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5. Reactions in CH_2Cl_2 were worked up by chromatography and in DMF as follows: water (10-20 eq) was added and the mixture left 10 mins to hydrolyse TBDMCS. Ether was added and the mixture was stirred with sodium bicarbonate solution for 15 min, dried, and volatile material (including the base) was evaporated (0.1 mm) to leave the pure TBDMS ether. All new compounds gave satisfactory ^1H-nmr, mass spectral, and HRMS data.
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