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An efficient method for the trimethylsilylation of tertiary alcohols

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Abstract. Tertiary acetylenic alcohols have been transformed into the *O*-trimethylsilyl derivatives with trimethylsilyl chloride and triethylamine, using catalytic amounts of dimethyl sulfoxide, hexamethylphosphoric triamide, imidazole, or 1,5-diazabicyclo[5.4.0]undec-5-ene. Saturated tertiary alcohols can be trimethylsilylated in the same way.

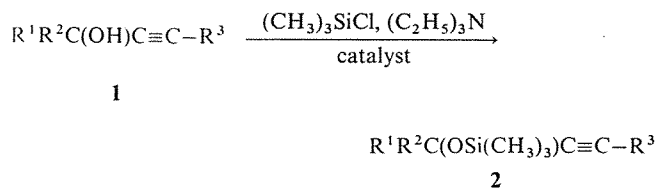
Silylation of alcohol functions has been widely used in synthesis for protection^{1,2,3} and for analysis in gas-liquid chromatography and mass-spectrometry⁴. Sterically hindered alcohols are not or only partly transformed into their *O*-trialkylsilyl derivatives in the usual way, that is employing trialkylsilyl halides and a basic reagent, *e.g.* triethylamine. The best reagent in those cases is *N*-(trimethylsilyl)imidazole^{5,6,7}. A disadvantage, however, is that a large excess of this reagent is necessary.

For some synthetic problems we needed *inter alia* the trimethylsilyl derivatives of tertiary acetylenic alcohols. As these compounds could not be trimethylsilylated in the usual way ((CH₃)₃SiCl + (C₂H₅)₃N), we looked for variants. The solution of the problem appeared to be surprisingly simple: addition of catalytic (5–15 mol %) amounts of dimethyl sulfoxide (DMSO), hexamethylphosphoric triamide (HMPT), imidazole or 1,5-diazabicyclo[5.4.0]undec-5-ene (DBU) to the mixture of the tertiary alcohol, triethylamine, trimethylsilyl chloride and ethyl ether caused an immediate reaction. This combination of reagents gave also good results in the case of saturated tertiary alcohols, *e.g.* C₄H₉(CH₃)₂C–OH and C₄H₉–(C₂H₅)(CH₃)C–OH, though with DMSO and HMPT the silylation was much faster than with the amine catalysts mentioned. The marked acceleration of the trimethylsilylation by DMSO, HMPT or the two amines suggests primary formation of onium complexes (CH₃)₂S⁺–O–Si(CH₃)₃Cl[–], [(CH₃)₂N]₃P⁺–O–Si(CH₃)₃Cl[–] and similar complexes between the amines and (CH₃)₃SiCl. It can be imagined that attack of the OH groups in the tertiary alcohols on silicon in these complexes is very easy, since electrically neutral leaving groups are expelled.

General procedure

To a mixture of dry triethylamine (0.15 mol), the tertiary alcohol (0.10 mol), and DMSO, HMPT, DBU or imidazole (0.01–0.02 mol) and dry ether (200 ml) was added with stirring trimethylsilyl chloride (0.10 mol) in 10 minutes. The temperature of the mixture rose, but was kept around 40°C by occasional cooling. After one

hour (in the case of the saturated tertiary alcohols and DBU as catalyst the reaction times were at least 4 hours) the reaction mixture was poured into ice water (200 ml). After washing the ethereal solution with water it was dried over MgSO₄ and then concentrated *in vacuo*. In the case of the volatile HC≡CC(CH₃)₂OSi(CH₃)₃ the distillation procedure was carried out at normal pressure, using an efficient distillation column.



The saturated trimethylsilyl ethers were also obtained in excellent yields.

Physical constants:

C₄H₉C(CH₃)₂–OSi(CH₃)₃ b.p. 63°/25 mm, *n*_D²⁰ 1.4094
C₄H₉C(C₂H₅)(CH₃)–OSi(CH₃)₃ b.p. 74°/25 mm, *n*_D²⁰ 1.4174

Product ^a 2			B.p. in °C/ p in mm Hg	<i>n</i> _D ²⁰
R ¹	R ²	R ³		
CH ₃	CH ₃	CH ₂ OCH ₃	90/20	1.4300
C ₂ H ₅	C ₂ H ₅	CH ₂ OCH ₃	60/0.02	—
CH ₃	CH ₃	CH ₂ OC(CH ₃) ₂ C ₄ H ₉	47/0.5	1.4320
CH ₃	CH ₃	CH ₂ OC ₆ H ₅ ^b	106/0.5	1.4899
CH ₃	CH ₃	CH ₂ SCH ₃	94/30	1.4669
Ph	CH ₃	CH ₂ OCH ₃	85/0.01	1.4937
Ph	CH ₃	CH ₂ Cl	110/1	1.5109
CH ₃	CH ₃	H	116/760	1.4050
–(CH ₂) ₅ –		H	78/20	1.4487

^a Purity according to ¹H NMR and GLC > 96%; the structure of the products 2 appeared also from further conversions with alkyllithium, resulting in 1,4-elimination of H and OSi(CH₃)₃ (to be published).

Yields (not optimised) were higher than 80% after distillation, irrespective of which catalyst was used.

^b The mass spectrum showed the expected parent peak *m/e* = 262; 189(M⁺ – (CH₃)₃Si), 168(M⁺ – OPh), 75(HO⁺ = SiMe₂) and 73(Me₃Si⁺).

Acknowledgement

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