Communications to the Editor

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TRIETHYLSILYLATION OF HYDROXYL GROUPS WITH A KETENE TRIETHYLSILYL ACETAL —— 2-METHYL-1-TRIETHYLSILYLOXY-1-METHOXYPROPENE

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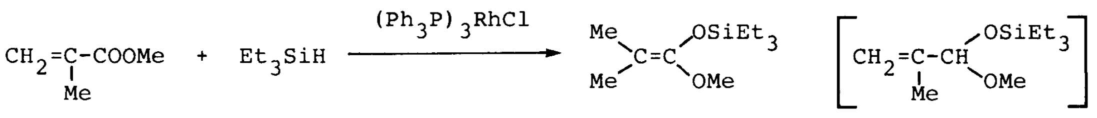
A convenient O-triethylsilylation with dimethylketene triethylsilyl methyl acetal (1), which is prepared in excellent yield by catalytic hydrosilylation of methyl metacrylate is reported. Primary alcohols react readily at room temperature. Hindered alcohols are rapidly silylated in the presence of a trace amount of trifluoromethanesulfonic acid. For phenols heating with or without solvent is required.

KEYWORDS —— protecting group; triethylsilylation; hydrosilylation; ketene silyl acetal

Among O-silylation for the protection of hydroxyl groups, use of triethylsilylation has recently been increasing,[1)] presumably taking priority over the conventional trimethylsilyl (TMS) and the tert-butyldimethylsilyl (TBDMS) groups in an intermediate sensitivity of the triethylsilyl (TES) group to hydrolysis and to attack by other nucleophiles (rough rate factors to TMS: TES, 10^{-2}; TBDMS, 10^{-4}).[2)] Reagents that have been usually employed for the triethylsilylation are TES-Cl,[1a,b,f,g)] TES-NEt_2,[1f)] TES-ClO_4,[1e)] and TES-OSO_2CF_3,[1e,d)] the latter two being suggested for the silylation of hindered alcohols. In addition, one example of the use of a ketene silyl acetal $CH_3CH{=}C(OCH_3)OSiEt_3$ was recorded by Tamura and his coworkers[3)] in their paper describing application of the trimethylsilyl counterpart for trimethylsilylation.

About a decade ago, we reported tris(triphenylphosphine)chlororhodium-catalyzed triethylhydrosilylation of some representative 2-alkenoates to yield predominantly ketene silyl acetals (1,4-addition product) except acrylate, which readily underwent alcoholysis.[4)] We have focused our attention on 1 as a triethylsilylation reagent,

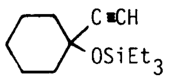
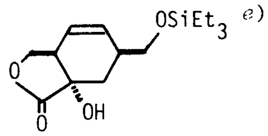
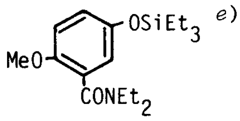
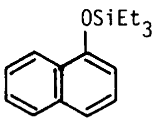


(Eq 1)

1 2

since it is readily obtainable in high yield from methyl metacrylate (Eq 1) and the only byproduct is volatile methyl isobutyrate which is readily removable. A large scale preparation of 1 follows: To a solution of methyl metacrylate (35.8 g) and triethylsilane (Shinetsu Chemicals, 50.0 g, 1.2 eq) in dry benzene (180 ml) was added tris(triphenylphosphine)chlororhodium (165 mg, 6.3 x 10^{-4} eq) and the mixture was gently refluxed for 2 h. Distillation of the reaction mixture afforded 72.5 g

Table. O-Triethylsilylation of Hydroxyl Groups [a]

Entry	Product [b]	Reaction condition [c]	bp, ^{o}C(Torr)	% Yield isolated(GLC)
1	$C_6H_5CH_2CH_2OSiEt_3$ [d]	rt(neat)/1 h	120(22)	(98)
2	n-$C_6H_{13}CH_2CH_2OSiEt_3$	rt(neat)/20 h	120-5(23)	69(92)
3	n-C_6H_{13}-CH(OSiEt$_3$)-CH_3	100^{o}C(DMF)/6 h	115-20(23)	60(88)
4	cyclo-$C_6H_{11}OSiEt_3$	85^{o}C(neat)/1.5 h rt(neat)/TFSA/0.5 h	138-40(90)	(74) (93)
5	$(C_2H_5)_2CHOSiEt_3$	rt(neat)/TFSA/20 min	105-7(90)	(98)
6	CH_3-CH(OSiEt$_3$)-$(CH_2)_5$-OSiEt$_3$ [d]	rt(neat)/TFSA/0.5 h	143-5(1.5)	85
7	$(CH_3)_2C=CH-(CH_2)_2$-C(CH_3)(OSiEt$_3$)-CH=CH_2	rt(neat)/TFSA/75 min	156-60(22)	92(98)
8		rt(neat)/TFSA/1 h	130-2(22)	85(98)
9		80^{o}C(DMF)/2 h	175-7(0.7)	95
10		reflux(MeCN)/1 h	150-3(0.04)	97
11		80^{o}C(neat)/5 h	120-5(0.8)	94

a) Excess reagent 1 (1.2-1.8 eq) was used. For the substrate not soluble in 1, a 0.5-3 fold volume of solvent was used to maintain a homogeneous reaction. The reaction was monitored by GLC and/or TLC. The product was isolated, after evaporation of low boiling volatiles, by distillation with a Kugelrohr. *b*) Structures of the products were supported by spectral data (200 MHz ^{1}H NMR and mass spectrometries). *c*) rt: room temperature; TFSA: addition of ca. 10^{-2} mol% of 2 x 10^{-2} M F_3CSO_3H in CH_2Cl_2. *d*) Satisfactory microanalyses were obtained. *e*) Preparation of the corresponding hydroxy compounds will be reported elswhere.

(94% yield) of **1** as a clear liquid, bp 90°C at 20 Torr (94% purity as determined by 200 MHz ^1H NMR spectroscopy; 1,2-addition product **2**[5] was the only impurity detected).

Representative results obtained with **1** are shown in the Table. Primary alcohols reacted exothermally on mixing the reactants at room temperature (entry 1, 2). On the other hand, tertiary alcohols such as linalool and 1-ethynylcyclohexanol did not undergo silylation under the same conditions. However, on addition of a trace amount (ca. 10^{-2} mol%) of trifluoromethanesulfonic acid (TFSA) (with or without solvent), these sterically hindered alcohols reacted smoothly (entry 7, 8).[6] This marked difference in reactivity was successfully applied for monosilylation of a primary and tertiary diol (entry 9). Secondary alcohols were apparently less reactive than primary ones (no exothermic reaction). Here again TFSA showed a beneficial effect on acceleration of the reaction (entries 4 to 6). Phenols were somewhat less reactive than secondary alcohols, requiring heating for completion of the reaction.

Thus, it is concluded that reagent **1** is highly recommended for *O*-triethylsilylation of various hydroxyl groups under mild conditions. The features superior to the existing reagents and procedures are summarized as follows. (1) Ease of preparation of the reagent **1**, in contrast to the method based on silylation of lithium enolate which is very tedious to do and not suitable for large scale preparations; (2) Product isolation procedure is simple as there is no extraneous byproduct — evaporation of any solvent used, volatile byproduct and excess reagent, followed by distillation or crystallization of the product; (3) Even sterically hindered alcohols can be silylated readily in the presence of a trace amount of TFSA, and it is no longer necessary to use activated reagents such as triethylsilyl perchlorate and trifluoromethanesulfonate in combination with amines as acid scavenger; (4) Yields are high.

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5) Formation of 1,2-addition product **2** was reported by Ojima et al.: I. Ojima, M. Kumagai, and Y. Nagai, J. Organomet. Chem., 111, 43(1976). Presence of **2** does not interfere the silylation.

6) It is reasonable to assume that $F_3CSO_3SiEt_3$ which is produced in situ is a real reacting species.

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