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A FACILE PROCEDURE FOR ACETALIZATION UNDER APROTIC CONDITIONS[1]

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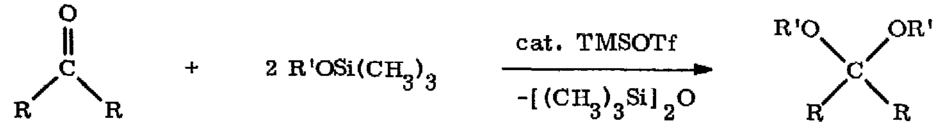
Summary: Carbonyl compounds are readily acetalized by alkoxysilanes in the presence of trimethylsilyl trifluoromethanesulfonate catalyst.

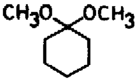
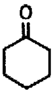
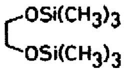
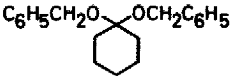
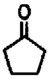
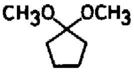
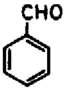
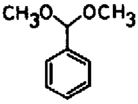
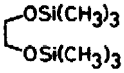
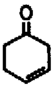
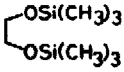
The acetal group is the most widely used protecting group for aldehydes and ketones.[2] Most practical methods for acetalization employ alcoholic media containing a Brønsted acid catalyst. Described herein is a new procedure for this operation achievable under mild, aprotic conditions.

The present method utilizes easily accessible organosilicon compounds, alkoxytrimethylsilanes and trimethylsilyl trifluoromethanesulfonate (TMSOTf) as acetalizing agent and catalyst, respectively. The reaction of carbonyl compounds and a stoichiometric amount of alkoxysilanes in dichloromethane proceeded smoothly at temperatures as low as -78 °C to give the acetals in high yields. Some examples are listed in Table I. Notably, 2-cyclohexenone, a typical α,β-unsaturated ketone, is facilely acetalized without concomitant double-bond migration (entry 6); the double bond in 3-cyclohexenone does not shift either (entry 7). Acetalization of carbonyl functions is generally a reversible process. In this particular case, the high stability of hexamethylsiloxane is the major contributing factor for shifting the equilibrium to the acetal products.



The following procedure is representative. To a stirred dichloromethane solution (1 mL) containing TMSOTf (22 mg, 0.1 mmol, 1 mol%) were successively added methoxytrimethylsilane (2.11 g, 20 mmol) and benzaldehyde (1.07 g, 10 mmol) at -78 °C under argon atmosphere. The mixture was stirred at -78 °C for an additional 3 h, quenched by addition of dry pyridine (0.2 mL) at the same temperature, poured into a saturated $NaHCO_3$ aqueous solution (15 mL), and extracted with ether (3 x 15 mL). The combined extracts were dried over a 1:1 mixture of Na_2CO_3 and Na_2SO_4 and evaporated. Bulb-to-bulb distillation of the residue gave benzaldehyde dimethyl acetal as a colorless oil (1.45 g, 94% yield, bp 125—135 °C/51 mmHg).

Table I. The TMSOTf Catalyzed Acetalization of Carbonyl Compounds with Alkoxysilanes[a]

entry	substrate	alkoxysilane	conditions temp, °C	 time, h	product (% yield[b])
1		$CH_3OSi(CH_3)_3$	-78	3	 (89)
2			-78	4	 (96)
3		$C_6H_5CH_2OSi(CH_3)_3$	-78	20	 (99)
4		$CH_3OSi(CH_3)_3$	-78	3	 (79, 90[c])
5		$CH_3OSi(CH_3)_3$	-78	3	 (94)
6			-78	20	 (92)
7			-78 then -20	3 0.2	 (99)

[a] Reaction was carried out under argon atmosphere using 1 mol % of TMSOTf in dichloromethane. All new compounds gave consistent NMR and IR characteristics and correct elemental analysis and/or mass spectral data. [b] Isolated yield. [c] Obtained by NMR analysis.

REFERENCES

1. Trialkylsilyl Triflates. VI. Part V: S. Murata, M. Suzuki, and R. Noyori, submitted for publication.
2. H. J. E. Loewnthal in "Protective Groups in Organic Chemistry", J. F. W. McOmie, Ed., Plenum Press, London and New York, 1973, Chapter 9.

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