

Facile Procedure for Acetalization Using Diols, Alkoxysilane and a Catalytic Amount of Trimethylsilyl Trifluoromethanesulfonate

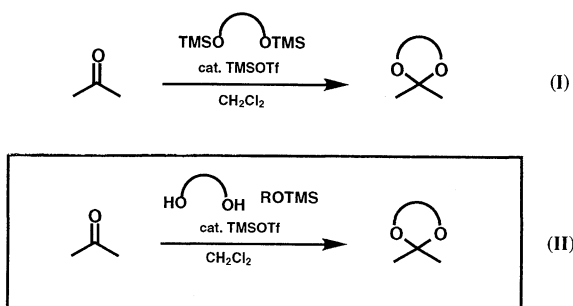
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In the presence of *sec*- or *tert*-alkoxysilane and a catalytic amount of trimethylsilyl trifluoromethanesulfonate (TMSOTf), carbonyl compounds react with various diols to give acetals in high yields.

The acetal group is not only the most widely used protective group for carbonyl compounds¹ but also an efficient chiral auxiliary group for enantioselective synthesis.² Acetalization using alkoxysilane and TMSOTf as a catalyst (eq. I) has been reported by Noyori et al.³ Noyori's method is useful for the synthesis of acetals, especially under mild conditions, but trimethylsilylated diols must be prepared. This report describes a convenient procedure for acetalization of carbonyl compounds using a diol, a *sec*- or *tert*-alkoxysilane and a catalytic amount of TMSOTf without the need to prepare the silylated diols. (eq. II)



The reaction of the ketone **1a** with ethylene glycol and an alkoxysilane⁴ (isopropoxytrimethylsilane, *sec*-phenethyloxytrimethylsilane or *tert*-butoxytrimethylsilane) in the presence of a catalytic amount of TMSOTf proceeded smoothly at -20 °C to give the corresponding acetal in high yield. (Table 1)

The results of the acetalization of carbonyl compounds with various diols are summarized in Table 2. Notably, acetalization

Table 1.

Entry	RO-TMS	Isolated yield / %
1	3a	98
2	3b	96
3	3c	97

using chiral diols has been achieved (entry 1,2,4,5,7) and 2-cyclohexenone as typical α,β -unsaturated ketone is acetalized

Table 2.

Entry	Ketone	Diol	RO-TMS	Acetal ^a	Yield / % ^b
1	1a	2b	3a		99
2	1a	2b	3b		98
3	1a	2c	3b		92
4	1a	2d	3a		89
5	1a	2e	3a		85
6	1b	2a	3a		88
7	1c	2b	3b		96
8	1d	2a	3a		84 ^c

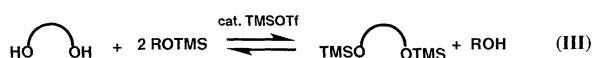
^a Acetals were identified by ¹HNMR, ¹³CNMR, and MS.

^b Isolated yield. ^c GLC yield.

without double-bond migration (entry 8).⁵

A typical procedure is as follows: to a mixture of the ketone **1a** (117 mg, 0.672 mmol), the diol **2a** (50 mg, 0.862 mmol) and isopropoxytrimethylsilane (355 mg, 2.68 mmol) in dry dichloromethane was added TMSOTf (1.7 mg, 0.007 mmol, 1 mol%) at -20 °C under argon atmosphere. The reaction mixture was stirred at the same temperature for 3 h, quenched by addition of pyridine and the solvent was evaporated under reduced pressure. The residue was purified by silica-gel chromatography to afford acetal **4a** (144 mg, 0.659 mmol, 98 %).

When diol **2a** was treated with isopropoxytrimethylsilane in the presence of a catalytic amount of TMSOTf in dichloromethane at -20 °C, disilylated diol was shown to be formed by GLC analysis. (eq. III) This observation suggest that the alkoxyisilane of the diol was generated in situ and reacted with the carbonyl compound in the presence of a catalytic amount of TMSOTf to afford the acetal.



References and Notes

- 1 T. W. Greene, "Protective Group in Organic Synthesis," John Wiley & Sons, New York (1981); H. J. E. Loewenthal, "Protective Groups in Organic Chemistry," ed by J. F. W. McOmie, Plenum Press, London (1973), Chap9.
- 2 For review, see: A. Alexakis and P. Mangeney, *Tetrahedron: Asymmetry*, **1**, 477 (1990); J. K. Whitesell, *Chem. Rev.*, **89**, 1581 (1989); For recent example, see: Y. Kondo, J. R. Green, and J. Ho, *J. Org. Chem.*, **56**, 7199 (1991); C. Giordano and L. Coppi, *J. Org. Chem.*, **57**, 2765 (1992); J. Aube, J. A. Heppert, M. L. Milligan, M. J. Smith, and P. Zenk, *J. Org. Chem.*, **57**, 3563 (1992); T. L. Underiner and L. A. Paquette, *J. Org. Chem.*, **57**, 5438 (1992); H. Fujioka, T. Yamanaka, N. Matsunaga, M. Fuji, and Y. Kita, *Synlett*, **1992**, 35; T. Fujisawa, Y. Ukaji, T. Noro, K. Date, and M. Shimizu, *Tetrahedron*, **48**, 5629 (1992); P. Maglioli, O. D. Lucchi, G. Deigog, and G. Valle, *Tetrahedron: Asymmetry*, **3**, 365 (1992); P. A. Rose, S. R. Abrams, and A. C. Shaw, *Tetrahedron: Asymmetry*, **3**, 443 (1992); S. Tang and R. M. Kennedy, *Tetrahedron Lett.*, **33**, 7823 (1992); E. J. Corey and L. I. Wu, *J. Am. Chem. Soc.*, **115**, 9327 (1993); T. Sugimura, S. Goto, K. Koguro, T. Futagawa, S. Misaki, Y. Morimoto, N. Yasuoka, and A. Tai, *Tetrahedron Lett.*, **34**, 505 (1993); J. P. Konopelski and R. A. Kasar, *Tetrahedron Lett.*, **34**, 4587 (1993); B. Chitkul, Y. Pinyopronpanich, C. Thebtaranonth, Y. Thebtaranonth, and W. C. Taylor, *Tetrahedron Lett.*, **35**, 1099 (1994); K. Tomooka, T. Igarashi, and T. Nakai, *Tetrahedron Lett.*, **35**, 1913 (1994); K. Kato, H. Suemune, and K. Sakai, *Tetrahedron Lett.*, **35**, 3103 (1994).
- 3 T. Tsunoda, M. Suzuki, and R. Noyori, *Tetrahedron Lett.*, **21**, 1357 (1980).
- 4 Alkoxyisilanes were prepared by silylating the corresponding alcohols with chlorotrimethylsilane and Et₃N.
- 5 Acetal with double-bond migration was not detected by GLC analysis.