

CONDENSATION OF ENOL SILYL ETHERS WITH 2-ACETOXYTETRAHYDROFURAN
AND -TETRAHYDROPYRANS¹

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Summary: Trimethylsilyl trifluoromethanesulfonate catalyzes stereoselective condensation of enol silyl ethers and 2-acetoxytetrahydrofuran or -tetrahydropyran derivatives.

Stereoselective preparation of carbonyl compounds bearing tetrahydrofuran-2-yl or -tetrahydropyran-2-yl substituent is a subject of current interest.² We report here that the title reaction allows an easy entry to this class of compounds.

A variety of enol silyl ethers can be condensed smoothly with an equimolar amount of 2-acetoxytetrahydrofuran or a 2-acetoxytetrahydropyran derivative in the presence of a catalytic amount (1-10 mol %) of trimethylsilyl trifluoromethanesulfonate³ in dichloromethane at temperatures as low as -78 °C. Several examples are given in Table I.

The reaction of (*Z*)- or (*E*)-enol silyl ethers exhibited moderate erythro-selectivity (entries 4-6).^{4,5} When a ring-methylated tetrahydropyran derivative was employed as the substrate, the reaction proceeded stereoselectively to give solely the *cis* condensation product (entries 7 and 8).⁶ Under the present reaction conditions, starting 2-acetoxy-6-methyltetrahydropyran equilibrates readily to form the thermodynamically favored *trans* isomer which possesses the axial acetoxy group,⁷ as confirmed by ¹H NMR analysis. This stereoisomer is kinetically labile and suffers ready S_N2-type displacement with an enol silyl ether aided by the action of the silyl trifluoromethanesulfonate⁸ to afford the *cis* condensation product. These stereochemical features are consistent with the recently proposed "extended" type transition state.⁸ Alternative S_N1 mechanism via a cyclic carboxonium ion intermediate would result in a high degree of *trans* stereoselection or, at least, lead to a mixture of the *cis* and *trans* isomers, in conflict with the finding.

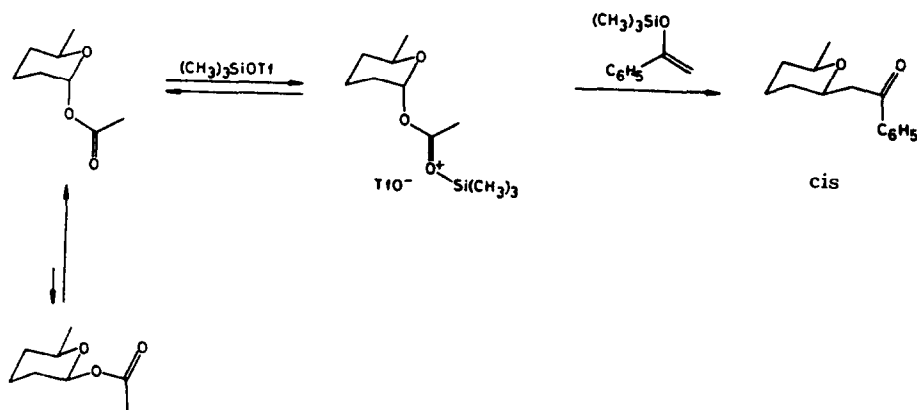


Table I. Condensation Catalyzed by Trimethylsilyl Trifluoromethanesulfonate^a

entry	enol silyl ether	acetate	cat., mol %	T, °C/ time, h	product	% yield	erythro/threo ratio
1			5	-78/4		87	
2			10	-78/4		81	
3			5	-78/10		96	
4			7	-78/10		78	70:30
5			5	-78/10		91	62:38
6			10	-78/16 ^{c,d}		79	78:22
7			10	-78/2		90	
8			10	-78/2		92	

^a A mixture of an enol silyl ether, acetate (ca. 1:1 mol ratio), and catalyst was stirred in CH_2Cl_2 . ^b E/Z = 35:65. ^c Reaction in pentane. ^d Based on consumed starting material (79%).
^e The same stereochemical outcome with the 1:1 cis/trans mixture.

REFERENCES AND NOTES

- Trialkylsilyl Triflates in Organic Synthesis. 14. Part 13: M. Suzuki, H. Takada, and R. Noyori, *J. Org. Chem.*, **47**, 902 (1982).
- For instance, R. E. Ireland, S. Thaisrivongs, N. Vanier, and C. S. Willcox, *J. Org. Chem.*, **45**, 48 (1980); R. E. Ireland, S. Thaisrivongs, and C. S. Willcox, *J. Am. Chem. Soc.*, **102**, 1155 (1980); R. E. Ireland and J.-P. Vever, *J. Org. Chem.*, **45**, 4259 (1980); R. E. Ireland and J. P. Daub, *Ibid.*, **46**, 479 (1981).
- For the synthetic utility, see R. Noyori, S. Murata, and M. Suzuki, *Tetrahedron*, **37**, 3899 (1981).
- The authentic erythro product of entry 5 was prepared as follows. Propiophenone was converted to erythro-3-hydroxy-7-methanesulfonyloxy-2-methyl-1-phenylheptan-1-one by sequential treatment with (a) LDA/THF, (b) THPO(CH_2)₄CHO/THF, (c) pyridinium p-toluenesulfonate/ CH_3OH , (d) MsCl /pyridine, and TLC separation of the threo/erythro products. This hydroxy mesylate was then cyclized to the tetrahydropyran-2-yl ketone by reaction with (e) LiAlH_4 /THF, (f) $\text{KOH}/\text{CH}_3\text{OH}$, (g) pyridinium chlorochromate/ CH_2Cl_2 . The aldehyde of entry 4 and thioester of entry 6 were derived to this ketone by reaction with phenyllithium (and chromic acid oxidation).
- For the reasonable threo/erythro nomenclature, see: footnote 8 of R. Noyori, I. Nishida, and J. Sakata, *J. Am. Chem. Soc.*, **103**, 2106 (1981).
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- S. Murata, M. Suzuki, and R. Noyori, *J. Am. Chem. Soc.*, **102**, 3248 (1980). See also ref. 5.