Stereoselective Cross-Aldol Reactions of Silyl Enol Ethers with Acetals Catalyzed by Iodotrimethylsilane[1)]

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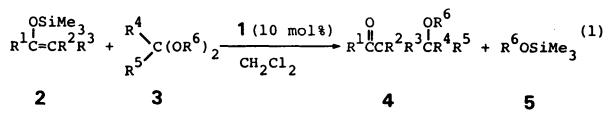
Synopsis. Iodotrimethylsilane catalyzes effectively erythroselective aldol type condensation of silyl enol ethers with acetals.

Recently, much attention has been focused on the stereoselective aldol condensations[2)] in relation to syntheses of acyclic β-hydroxy ketones as a structural unit of natural macrolide antibiotics.[3)] We have found previously that iodotrimethylsilane is an efficient catalyst for the regiospecific allylation of acetals with allylsilanes.[4)] As an extension of the work, we report here that highly nucleophilic silyl enol ethers (**2**), like allylsilanes, undergo the reaction with acetals (**3**) in the presence of a catalytic amount of iodotrimethylsilane (**1**), prepared from hexamethyldisilane and iodine at ambient temperature,[5)] to afford erythro-selective β-alkoxy ketones (**4**) in excellent yield. (Eq. 1).



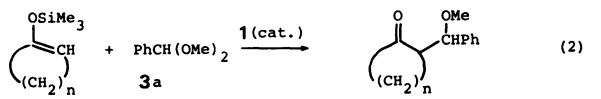
(1)

2 **3** **4** **5**

Results and Discussion

The essential feature of the reaction is rather similar to the trimethylsilyl triflate-catalyzed reaction,[6)] and the results are listed in Table 1.

In all cases, the reaction of **2** with a variety of **3** proceeds very smoothly and completes within 30 min at −78 °C.[7)] It is important to note that the reaction mixture should be hydrolyzed by a saturated hydrogen sodium carbonate solution at −78 °C. One of the important features of the present reaction is the erythro selective aldol condensation. For example, reactions of benzaldehyde dimethyl acetal (**3a**) with silyl enol ethers, **2a** and **2b**, derived from cyclopentanone and cyclohexanone, gave mixtures of erythro and threo derivatives in a ratio of 99 : 1 and 95 : 5, respectively. (Eq. 2).

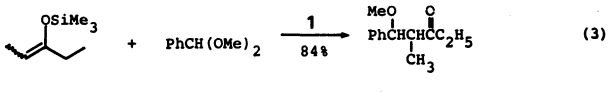


(2)

2a, n = 3 — **4a**, 87%; Erythro:Threo = 99:1

b, n = 4 — b, 89%; Erythro:Threo = 95:5

On the other hand, 3-trimethylsiloxy-2-pentene (**2c**, $E : Z = 21 : 79$), prepared by Et_3N/Me_3SiCl in DMF,[8)] gave a 57 : 43 mixture of erythro and threo derivatives. (Eq. 3).

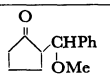
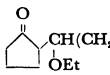
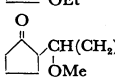
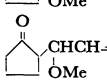
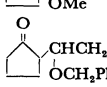
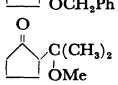
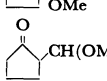
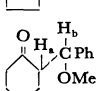
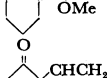
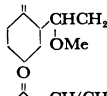
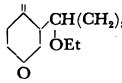
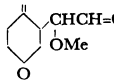
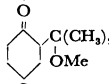
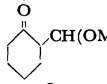
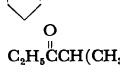
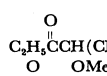
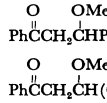
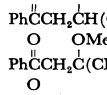
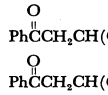
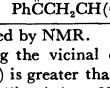


(3)

2c **3a** **4c**

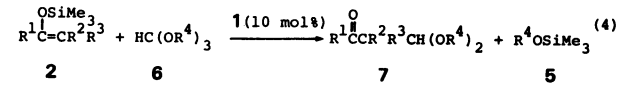
E:Z = 21:79 — Erythro:Threo = 57:43

Table 1. Reactions of silyl enol ethers (**2**) with acetals (**3**) and orthoformates (**6**) catalyzed by iodotrimethylsilane (**1**) in dichloromethane at −78 °C

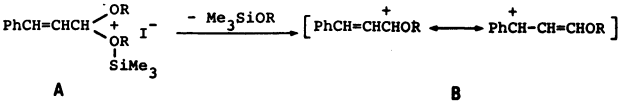
Silyl enol ether	Acetal or orthoformate	Reaction time/min	Product	Yield[a)]/% erythro[b)]/threo
 (**2a**)	$PhCHC(OMe)_2$ (**3a**)	20[c]	 (**4a**)	87 (99/ 1)
2a	$Ph(CH_2)_3CH(OEt)_2$ (**3b**)	30		90 (83/17)
2a	$CH_3(CH_2)_3CH(OMe)_2$ (**3c**)	30		70 (70/30)
2a	$PhCH=CHCH(OMe)_2$ (**3d**)	50		82 (80/20)
2a	$CH_3CH_2CH(OCH_2Ph)_2$	90		65
2a	$(CH_3)_2C(OMe)_2$ (**3e**)	50		90
2a	$CH(OMe)_3$ (**6a**)	60		81
 (**2b**)	**3a**	60	 (**4b**)	89 (95/ 5)
2b	$(CH_3)_2CHCH_2(OMe)_2$	25		70 (79/21)
2b	**3b**	30		87 (86/14)
2b	**3d**	60		92 (89/11)
2b	**3e**	60		82
2b	**6a**	60		80
(**2c**)	**3a**	55		84 (57/43)
2c	**3e**	60		86
 (**2d**)	**3a**	40		90
2d	**3c**	50		90
2d	**3e**	50		84
2d	**6a**	60		88
2d	$CH(OEt)_3$	60		87

a) Yields after isolation by TLC. b) Determined by NMR. Erythro and threo derivatives (**4**) were characterized by comparing the vicinal coupling constants (J_{ab}). Observations that J_{threo} of *e.g.* **4b** (13 Hz) is greater than $J_{erythro}$ (4 Hz) is in accordance with other erythro–threo systems.[6,10)] c) At −35 °C.

It is notable that orthoformate (**6**) reacts with **2** by catalysis of **1** to give β-keto acetal (**7**). No further reaction with the resulting β-keto acetal occurred. Apparently, the reaction of **7** with **2** is slower than the reaction of **6**.



From the mechanistic point of view, it is interesting that reactions with α,β-unsaturated acetals catalyzed by **1** proceed very selectively on the acetal carbon (see Table 1). This fact suggests strongly that a silyloxonium ion A, not a carbenium ion like B, is the most important intermediate in the reaction.



Experimental

Reactions Summarized in Table 1. The following procedure is typical. To a mixture of **2** (1.2 mmol) and **3** (or **6**) (1.0 mmol) in dry dichloromethane (2 ml) was added iodotrimethylsilane (0.02 g, 0.1 mmol) by a syringe under nitrogen at −78 °C. The reaction mixture was stirred for given conditions in Table 1 and hydrolyzed with a saturated solution of hydrogen sodium carbonate at −78 ° C.After usual work-up, the crude product was purified by preparative thin-layer chromatography on silica gel.[9]

References

1) Chemistry of Organosilicon Compounds. 179.

2) C. H. Heathcock, C. T. Buse, W. A. Kleschick, M. C. Pirrung, J. E. Shon, and J. Lampe, *J. Org. Chem.*, **45**, 1066 (1980); M. Hiramura, D. S. Garvey, L. D. Lu, and S. Masamune, *Tetrahedron Lett.*, **1979**, 3937; D. A. Evans, J. V. Nelson, E. V. gel and T. R. Taber, *J. Am. Chem. Soc.*, **103**, 3099 (1981); K. Maruoka, S. Hashimoto, and H. Nozaki, *ibid.*, **99**, 7705 (1977); T. Mukaiyama, K. Banno, K. Narasaka, *ibid.*, **96**, 7503 (1974); Y. Yamamoto, H. Yatagai, Y. Naruta, and K. Maruyama, *ibid.*, **102**, 7107 (1980), and references cited therein.

3) For review articles, see S. Masamune, *Aldrichimica Acta*, **11**, 23 (1978); P. A. Bartlett, *Tetrahedron*, **36**, 3 (1980).

4) H. Sakurai, K. Sasaki, and A. Hosomi, *Tetrahedron Lett.*, **23**, 745 (1981).

5) H. Sakurai, A. Shirahata, K. Sasaki, and A. Hosomi, *Synthesis*, **740**, (1979).

6) S. Murata, M. Suzuki, and R. Noyori, *J. Am. Chem. Soc.*, **102**, 3248 (1980).

7) Reactions can be catalyzed by a smaller amount of iodotrimethylsilane but in a slower rate.

8) E. Nakamura, K. Hashimoto, and I. Kuwajima, *Tetrahedron Lett.*, **1978**, 2079.

9) All compounds gave satisfactory spectral data and correct elemental analyses.

10) *E. g.*; T. Mukaiyama, K. Narasaka, and K. Banno, *J. Am. Chem. Soc.*, **96**, 7503 (1974); H. O. House, D. C. Crumrine, A. Y. Teranishi, and M. D. Olmstead, *ibid.*, **95**, 3310; Y. Yamamoto, H. Yatagai, and K. Maruyama, *ibid.*, **103**, 3229 (1981).