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Catalytic Asymmetric Aldol Reaction of Silyl Enol Ethers with Aldehydes by the Use of Chiral Diamine Coordinated Tin(II) Triflate

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Highly enantioselective aldol reaction of silyl enol ethers with aldehydes is performed by the use of a catalytic amount of chiral diamine coordinated tin(II) triflate according to a slow addition procedure.

Recently we have reported on the highly diastereo- and enantioselective aldol reaction of silyl enol ethers of thioesters[1)] or esters[2)] with aldehydes in the presence of a novel promoter system, combined use of chiral diamine coordinated tin(II) triflate and tributyltin fluoride or dibutyltindiacetate. According to these reactions, optically active aldols are easily prepared starting from both achiral aldehydes and silyl enol ethers, however, stoichiometric use of chiral source still remained as a problem in terms of practical use. In this communication, we would like to describe an efficient catalytic asymmetric aldol reaction (that requires only a catalytic amount of chiral source) by using chiral diamine coordinated tin(II) triflate as a catalyst.

In the previous paper, we have reported that a chiral promoter system consisted of chiral diamine coordinated tin(II) triflate and dibutyltindiacetate, is quite effective for the aldol reaction of silyl enol ethers of thioesters with aldehydes.[3)] In the course of our investigations to characterize this promoter system and to clarify the mechanism of this reaction, effect of the amount of dibutyltindiacetate was examined by taking the reaction of silyl enol ether of S-ethyl propanethioate with benzaldehyde as a model. The results are summarized in Table 1. When a half equivalent of dibutyltindiacetate was used, the product was isolated as OH form 5 and the diastereo- and enantioselectivities slightly lowered compared with those of the stoichiometric use. Further, when the above reaction was carried out by the use of a quarter equivalent of dibutyltindiacetate, a mixture of trimethylsilyl ether 4 and OH form 5 were produced with lower selectivities. More remarkable is the result shown in entry 4; in the presence of 30 mol% of tin(II) triflate, 36 mol% of chiral diamine and 7.5 mol% of dibutyltindiacetate, this aldol reaction smoothly proceeded to afford trimethylsilyl ether 4 in 69% yield with good selectivities as a main product along with OH form 5 in 19% yield with high selectivities.

These results indicate a possibility that the metal exchange from tin to silicon on the produced aldol 6 took place along with a regeneration of chiral

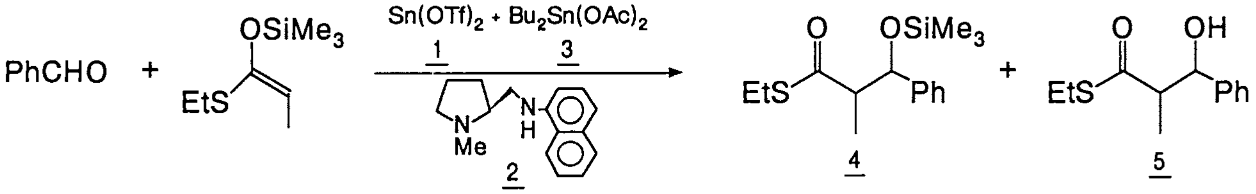
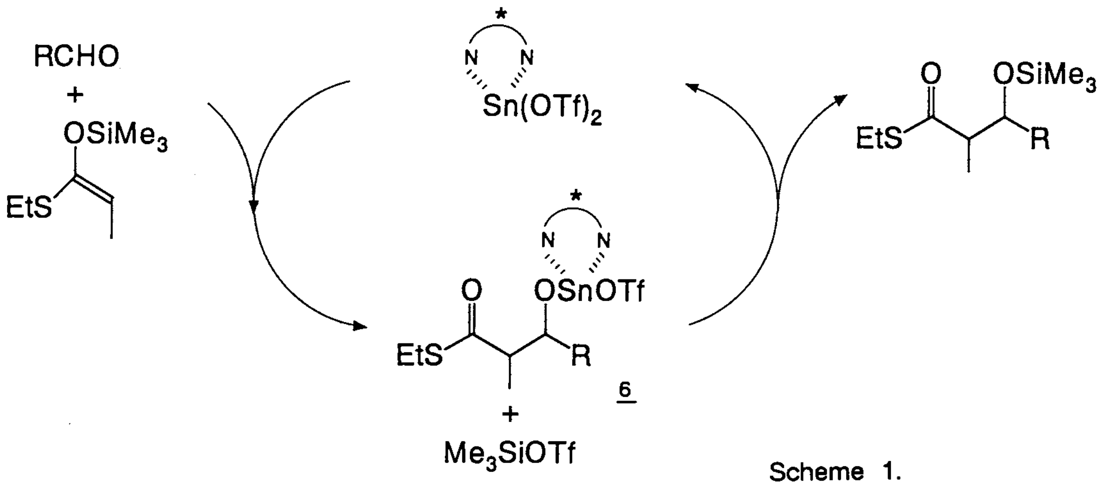


Table 1. Effect of the amount of $^{n}Bu_2Sn(OAc)_2$

Entry	Equiv. 1	2	3	Yield/%(syn/anti, ee/%[a]) 4	5
1	1.0	1.2	1.1	0	85 (100/0, >98)
2	1.0	1.2	0.5	0	83 (95/5, 93)
3	1.0	1.2	0.25	39 (83/17, 77)	48 (88/12, 87)
4	0.3	0.36	0.075	69 (75/25, 67)	19 (92/8, 84)

a) Optical purity given is that of the syn diastereomer.

diamine coordinated tin(II) triflate when less than a half equivalent of dibutyltindiacetate was used. Based on this consideration, we supposed that a catalytic cycle shown in the following Scheme 1 would be completed. A metal exchange reaction of 6 with trimethylsilyl triflate (TMSOTf) is considered as a key step and if this step is slow, undesirable achiral TMSOTf promoted aldol reaction proceeds at the same time to result in lowering the selectivities. So, in order to keep TMSOTf in low concentration as possible during the reaction, we tried the slow addition of the substrates to the solution of the catalyst; namely a dichloromethane solution of a silyl enol ether and an aldehyde was added slowly over 9 h to a dichloromethane solution of the catalyst. The results are shown in Table 2. As expected, aldols were obtained in good yields with excellent ees and high diastereoselectivities.



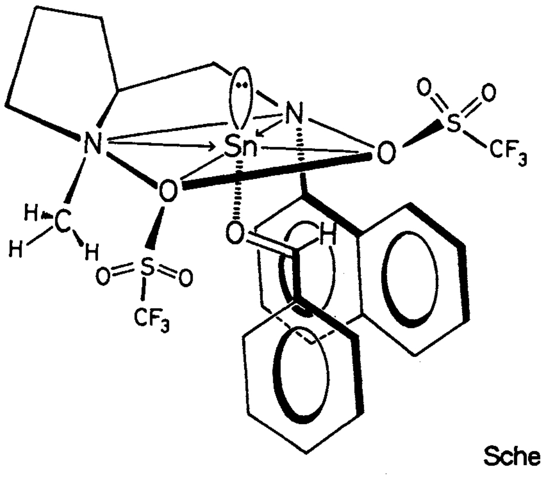
Scheme 1.

Table 2. Catalytic asymmetric aldol reaction by using a slow addition procedure

R	Cat./mol%	Yield/%	syn/anti	ee/%
Ph	20	86	93/7	91
$CH_3(CH_2)_6$	20	76	100/0	>98
$c\text{-}C_6H_{11}$	30	64	>99/1	92
p-Cl Ph	20	80	93/7	93

A typical experimental procedure is described for the reaction of silyl enol ether of S-ethyl propanethioate with an aldehyde; to a vigorously stirred suspension of tin(II) triflate(0.08 mmol, 20 mol%)[4)] in dichloromethane(1 ml) was added (S)-1-methyl-2-[(N-1-naphthylamino)methyl]-pyrrolidine(0.088 mmol) in dichloromethane(1 ml). The mixture was cooled to -78 °C, then a mixture of silyl enol ether of S-ethyl propanethioate(0.4 mmol) and an aldehyde(0.4 mmol) in dichloromethane(1.5 ml) was slowly added to this solution over 9 h. The mixture was further stirred for 15 h, then quenched with saturated aqueous sodium hydrogen carbonate. After usual work up, the aldol was isolated as the corresponding trimethylsilyl ether.

The assumed transition state of this asymmetric aldol reaction is shown in Scheme 2. In the chiral diamine coordinated tin(II) triflate having the rigid bicycle structure, its conformation is highly controlled by mutual interaction between pyrrolidyl, naphthylamino and trifluoromethanesulfonyl groups, and re face of an approaching aldehyde is almost completely shielded.



Scheme 2.

Thus, the catalytic asymmetric aldol reaction[5)] was performed in more than 90% ee with high diastereoselectivities by the use of a catalytic amount of chiral diamine coordinated tin(II) triflate.[6)] While, perfect stereochemical control (syn/anti=100/0, syn aldol=>98% ee) was already shown by combined use of a stoichiometric amount of three components, tin(II) triflate, chiral diamine and tributyltin fluoride or dibutyltindiacetate.[1b,3)] Therefore, further studies are now in progress to clarify whether this nearly 10% difference is ascribed to the discrimination ability of the catalyst or to the incompleteness of the catalytic cycle, as well as to determine the structure of the three components complex.

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References

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3) T. Mukaiyama, H. Uchiro, and S. Kobayashi, Chem. Lett., 1989, 1757.

4) In the case of catalytic use, tin(II) triflate of high quality should be employed. If the selectivities are lower than reported, tin(II) triflate must be rewashed with ether and sufficiently dried in vacuo.

5) Reetz et al. reported aldol reaction of ketene silyl acetal derived from methyl isobutylate with isobutylaldehyde by the use of chiral titanium and aluminium catalysts, however, yields and ees were low to moderate; M. T. Reetz, S-H Kyung, C. Bolm, and T. Zierke, Chem. Ind., 1986, 824. Ito et al. reported the asymmetric aldol-type reaction of α-isocyanocarboxylates, carboxamides and phosphonates with aldehydes by the use of the gold(I) complex coordinated with an optically active ferrocenylphosphine ligand as a catalyst; Y Ito, M. Sawamura, H. Hamashima, T. Emura, and T. Hayashi, Tetrahedron Lett., 30, 4681 (1989), and references cited therein. See also, G. A. Slough, R. G. Bergman, and C. H. Heathcock, J. Am. Chem. Soc., 111, 938 (1989).

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