CHEMISTRY LETTERS, pp. 297-300, 1989. © 1989 The Chemical Society of Japan

Asymmetric Aldol Reaction of Silyl Enol Ethers with Aldehydes Promoted by the Combined Use of Chiral Diamine Coordinated Tin(II) Triflate and Tributyltin Fluoride

Shū KOBAYASHI and Teruaki MUKAIYAMA
Department of Applied Chemistry, Faculty of Science,
Science University of Tokyo, Kagurazaka, Shinjuku-ku, Tokyo 162

Asymmetric aldol reaction of silyl enol ethers of thioesters with aldehydes is performed in high enantiomeric exess by the use of a new chiral promoter, a combined use of chiral diamine coordinated tin(II) triflate and tributyltin fluoride.

Aldol reaction of silyl enol ethers with aldehydes is one of the most useful methods for carbon-carbon bond formation.1) Titanium tetrachloride promoted reaction reported from this laboratory is the first example successfully employed in the cross aldol reaction,2) and after that, several promoters have been developed.1) We also found that a catalytic amount of trityl salt effectively catalyzes this reaction and that syn or anti aldol is preferentially obtained by the appropriate choice of trityl salt and the substituent on silyl group.3) Recently, due to the added importance of asymmetric synthesis, some efforts have been made on the asymmetric version of this reaction by employing the combination of either chiral silyl enol ethers (ketene silyl acetals) and prochiral aldehydes or prochiral silyl enol ethers (ketene silyl acetals) and chiral aldehydes,4) however, asymmetric aldol reaction of prochiral silyl enol ethers with prochiral aldehydes by the use of a chiral promoter has never been developed to a practical level.5) In this communication, we would like to describe on the highly enantioselective aldol reaction of silyl enol ethers of thioesters with aldehydes by the use of a new chiral promoter, a combined use of chiral diamine coordinated tin(II) triflate and tributyltin fluoride.

We have recently found that new catalyst systems, such as TMSCl-$SnCl_2$, TrCl-$SnCl_2$,6) $SnCl_4$-$ZnCl_2$,7) $SbCl_5$-$Sn(OTf)_2$,8) and $SnCl_4$-$Sn(OTf)_2$,9) etc., are effective for carbon-carbon bond forming reaction between carbonyl compounds and silyl nucleophiles. These catalysts are characterized as active cationic species, which are generated by the combination of a neutral molecule and a tin(II) compound or Lewis acids. In the course of our investigations based on this concept, we have investigated the suitable combination of these compounds in order to develop a new chiral catalyst system.

As one of chiral Lewis acids, we chose chiral diamine coordinated tin(II) triflate, successfully employed in the asymmetric allylation of aldehydes.10) When silyl enol ether of S-ethyl ethanethioate was treated with benzaldehyde in the presence of stoichiometric amounts of tin(II) triflate, (S)-1-methyl-2-[(piperidin-1-yl)methyl]-pyrrolidine, and tributyltin fluoride,[11] the aldol reaction proceeded at -78 °C to afford the corresponding adduct in 78% yield with 82% ee. The importance of the combination of chiral diamine coordinated tin(II) triflate and tributyltin fluoride is obvious from the result that no enantiomeric selection was observed by just using chiral diamine coordinated tin(II) triflate which similarly promotes the same reaction. The appropriate choice of chiral diamine improved the optical yield (Table 1).

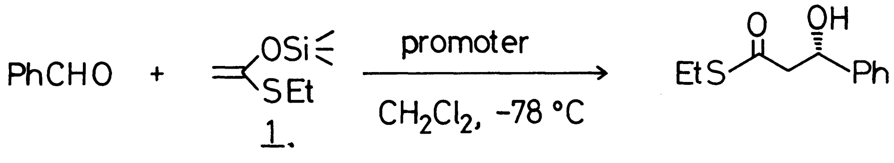
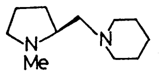


Table 1. The Reaction of Silyl Enol Ether of S-Ethyl Ethanethioate with Benzaldehyde

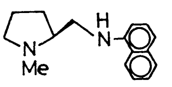
Promoter[a)]	Yield/%	ee/%
$Sn(OTf)_2$ + chiral diamine A	74	0
$Sn(OTf)_2$ + chiral diamine A + $^{n}Bu_3SnF$	78	82
$Sn(OTf)_2$ + chiral diamine B + $^{n}Bu_3SnF$	52	92
$Sn(OTf)_2$ + chiral diamine C + $^{n}Bu_3SnF$	74	78

a) Chiral diamine

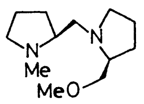
A



B



C



Several examples of this asymmetric aldol reaction are demonstrated in Table 2. In every case, aldols are obtained in high yields with high enantioselectivities.

A typical procedure is described for the reaction of silyl enol ether of S-ethyl ethanethioate(1) with benzaldehyde; to a solution of tin(II) triflate (0.4 mmol) and (S)-1-methyl-2-[(piperidin-1-yl)methyl]pyrrolidine (chiral diamine A, 0.48 mmol) in dichloromethane (1 ml) was added tributyltin fluoride (0.44 mmol) at room temperature. The mixture was stirred for 30 min and then cooled to -78 °C. After 1 in dichloromethane (0.5 ml) was added, the mixture was further stirred for 30 min. Then, benzaldehyde in dichloromethane (1 ml) was added, and the reaction mixture was stirred for 12 h, then quenched with aqueous sodium hydrogen carbonate. After the aqueous layer was extracted with dichloromethane, the organic layer was dried, and the solvent was removed under reduced pressure. The crude product was purified by thin layer chromatography (silica gel) to yield S-ethyl 3-hydroxy-3-phenyl-propanethioate (78%). The enantiomeric excess was determined to be 82% by measurement of the ^1H NMR spectrum of the corresponding acetyl derivatives using $Pr(hfc)_3$ as a chiral shift reagent.

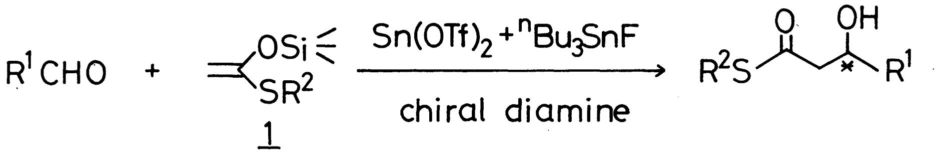
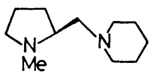


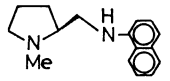
Table 2. Asymmetric Aldol Reaction of Silyl Enol Ethers with Aldehydes

Entry	R^1	R^2	Chiral diamine[a)]	Yield/%	ee/%[b)](config.)
1	Ph	Et	A	78	82 (S)
2	Ph	Et	B	52	92 (S)
3	Ph	^{t}Bu	A	73	86 (S)
4	$Ph(CH_2)_2$	Et	A	70	78
5	$Ph(CH_2)_2$	Et	B	50	81
6	$Ph(CH_2)_2$	^{t}Bu	A	71	85
7	^{i}Pr	Et	A	77	95
8	^{t}Bu	Et	A	90	>95

a) Chiral diamine A

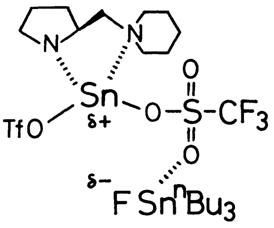


B



b) Determined by measurement of the ^{1}H-NMR spectrum of the corresponding acetyl derivatives using $Pr(hfc)_3$ as a chiral shift reagent.

At present, we assume that the active species(2) in this reaction could be shown below. The formation of the complex 2 is suggested by the observation that the mixture of tin(II) triflate, chiral diamine, and tributyltin fluoride is completely soluble in dichloromethane, while either tin(II) triflate or tributyltin fluoride is sparingly soluble under the condition.



2

Thus, the reaction would be promoted by double activations; namely, the cationic center of tin(II) triflate activates an aldehyde and, at the same time, the electronegative fluoride is able to interact with a silicon atom of a silyl enol ether to make the enol ether more reactive along with the formation of the entropically advantageous intermediate.

It should be noted that the combined use of chiral diamine coordinated tin(II) triflate and tributyltin fluoride realizes the highly enantioselective aldol reaction of both prochiral silyl enol ethers of thioesters and aldehydes.

Furthermore, the products of the present reaction, optically active β-hydroxy ester derivatives, are the important chiral building blocks, so this reaction would provide an alternative method for the preparation of these useful chiral synthetic intermediates.12)

Further investigations toward the clarification and characterization of this new chiral promoter as well as other asymmetric reactions by the use of this promoter is now in progress.

References

1) For examples, W. P. Weber, "Silicon Reagents for Organic Synthesis," Springer-Verlag, Berlin (1983).
2) T. Mukaiyama, K. Banno, and K. Narasaka, Chem. Lett., 1973, 1011.
3) T. Mukaiyama, S. Kobayashi, and M. Murakami, Chem. Lett., 1985, 447; S. Kobayashi, M. Murakami, and T. Mukaiyama, ibid., 1985, 1535.
4) C. Gennari, A. Bernardi, L. Colombo, and C. Scolastico, J. Am. Chem. Soc., 107, 5812 (1985), and references cited therein.
5) M. T, Reetz, F. Kunisch, and Heitmann, Tetrahedron Lett., 27, 4721 (1986); M. T. Reetz, S-H. Kyung, C. Bolm, and T. Zierke, Chem. Ind., 1986, 824.
6) N. Iwasawa and T. Mukaiyama, Chem. Lett., 1987, 463; T. Mukaiyama, S. Kobayashi, M. Tamura, and Y. Sagawa, ibid., 1987, 491; T. Mukaiyama, K. Wariishi, Y. Saito, M. Hayashi, and S. Kobayashi, ibid., 1988, 1011; T. Mukaiyama, H. Sugumi, H. Uchiro, and S. Kobayashi, ibid., 1988, 1291.
7) M. Hayashi, A. Inubushi, and T. Mukaiyama, Chem. Lett., 1987, 1975.
8) S. Kobayashi, M. Tamura, and T. Mukaiyama, Chem. Lett., 1988, 91.
9) T. Mukaiyama, T. Shimpuku, T. Takashima, and S. Kobayashi, submitted to Chem. Lett.
10) T. Mukaiyama, N. Minowa, T. Oriyama, and K. Narasaka, Chem. Lett., 1986, 97; N. Minowa and T. Mukaiyama, Bull. Chem. Soc. Jpn., 60, 3697 (1988); cf. T. Yura, N. Iwasawa, K. Narasaka, and T. Mukaiyama, Chem. Lett., 1988, 1025. Concerning the asymmetric aldol reaction by the use of tin(II) enolate and chiral diamine, see T. Mukaiyama, N. Iwasawa, R. W. Stevens, and T. Haga, Tetrahedron 40, 1381 (1984).
11) Commercially available from Tokyo Kasei Kogyo Co. Ltd. This reagent was used after drying in vacuo (0.1 mmHg, 100 °C, 6 h). I. Kuwajima and H. Urabe, J. Am. Chem. Soc., 104, 6831 (1982).
12) S. Masamune, T. Sato, B. Kim, and T. A. Wollmann, J. Am. Chem. Soc., 108, 8279 (1986), and references cited therein.

(Received November 24, 1988)