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[1,1'-Bi-2-naphthalenediolato(2-)-O,O']oxotitanium. An Efficient Chiral-Catalyst for the Asymmetric Aldol Reaction of Silyl Enol Ethers with Aldehydes

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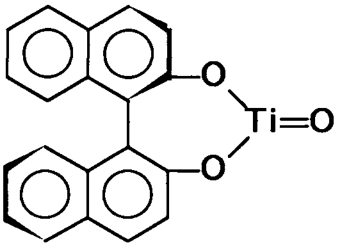
In the presence of a catalytic amount of [(R)-1,1'-bi-2-naphthalenediolato(2-)-O,O']oxotitanium, silyl enol ethers of thioesters react with aldehydes to afford the corresponding aldol adducts in high yields with good to high ees.

Asymmetric aldol reaction is one of the most powerful tools for synthesis of chiral building blocks. Though several excellent methods have already been reported, most of them require stoichiometric amounts of chiral sources.1) Recently we have reported the first practical example of catalytic asymmetric aldol reaction of silyl enol ethers with aldehydes by using chiral diamine coordinated tin(II) triflate as a catalyst.2)

In the previous papers, we have demonstrated that [1,2-benzenediolato(2-)-O,O']-oxotitanium is an efficient catalyst in the Michael reaction of ketene silyl acetals with α, β-unsaturated ketones3) and the aldol reaction of ketene silyl acetals with aldehydes.4) This titanium oxide has unprecedented and unique structure as a Lewis acid catalyst, and makes it possible to promote the synthetically valuable carbon-carbon bond forming reactions under extremely mild conditions. Our next object is to introduce a chiral source to this titanium reagent and to develop a novel chiral catalyst. In this communication, we would like to describe on enantioselective aldol reaction of silyl enol ethers of thioesters with aldehydes by using a catalytic amount of new catalyst, [(R)-1,1'-bi-2-naphthalenediolato(2-)-O,O']oxotitanium. The catalyst was shown to be the best after screening several chiral dihydroxy compounds as chiral sources.



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In the first place, the reaction of benzaldehyde with silyl enol ether of S-ethyl ethanethioate was carried out in toluene at -23 °C in the presence of a catalytic amount of [(R)-1,1'-bi-2-naphthalenediolato(2-)-O,O']oxotitanium(1) (20 mol%),5) and the corresponding aldol adduct was obtained in 61% yield with 31 %ee. Then, in order to improve the optical yield, several silyl enol ethers of thioesters were screened (see Table 1). Silyl enol ether of t-butyl ethanethioate (2) smoothly reacts with benzaldehyde at -43 °C to afford the corresponding aldol adduct in high yield (91%) with good enantioselectivity (60%ee). Further, several reaction conditions were examined to improve the enantioselectivity and the optical yield was found to be strongly dependent on solvents. When the reaction was carried out in alkyl-substituted benzene by taking the reaction of benzaldehyde with 2 as a model, good results were obtained; ethylbenzene (85% yield, 54% ee), m-xylene (92% yield, 50% ee), 1,3,5-trimethylbenzene (89% yield, 41% ee), chlorobenzene (91%yield, 16% ee). Finally the best result was obtained when toluene was employed as a solvent (91% yield, 60%ee),6) while no chiral induction was observed in dichloromethane (98% yield, 0% ee).

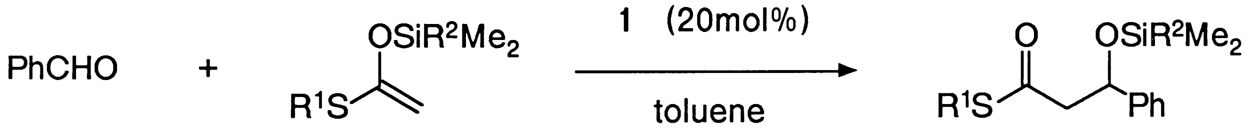

Table 1. The Effect of Silyl Enol Ethers

R^1	R^2	Temp / °C	Yield / %	ee / %
Et	Me	-23	61	31
Ph	Me	-23	38	37
^{t}Bu	Me	-23	87	44
Ph_3C	Me	-23	35	42
Et	^{t}Bu	-78	92	35
$PhCH_2$	^{t}Bu	-78	89	40
Ph_2CH	^{t}Bu	-78	60	45
^{t}Bu	^{t}Bu	-43	91	60

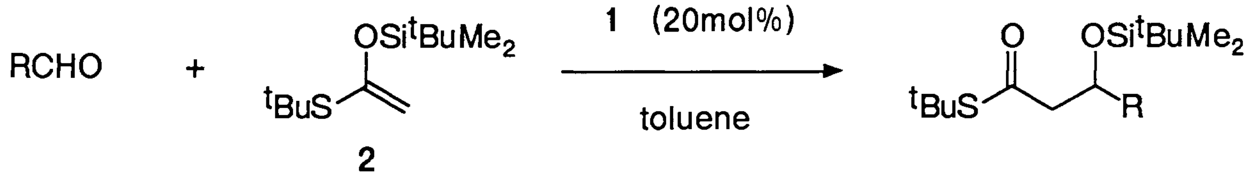

Table 2. The Asymmetric Aldol Reaction of 2 with Aldehyde

R	Temp / °C	Yield / %	ee / %
Ph	-43	91	60
p-Cl Ph	-78	91	44
α-Naphthyl	-43	97	36
β-Naphthyl	-78	98	80
(E)-PhCH=CH	-78	98	85

Then, this asymmetric aldol reaction was carried out by employing several aldehydes (see Table 2). While the reaction of α-naphthylaldehyde with 2 proceeded at -43 °C to afford the corresponding adduct in moderate selectivity (36% ee), β-naphthylaldehyde smoothly reacted with 2 at -78 °C to give the adduct in high ee (80%). Cinnamaldehyde also reacted with 2 at -78 °C to produce the corresponding aldol adduct in 85% ee.

A typical experimental procedure is described for the reaction of 2 with cinnamaldehyde; 1 (0.06 mmol) was dissolve in toluene (3 ml) and cooled to -78 °C. Then 2 (0.36 mmol) and cinnamaldehyde (0.3 mmol) in toluene (2 ml) were added and the mixture was stirred for 16 h, then quenched with phosphate buffer (pH=7). After removal of insoluble materials by filtration, the aqueous layer was extracted with dichloromethane. The combined organic layer was dried and the solvent was removed under reduced pressure. The residue was purified by thin layer chromatography (silica gel) to yield S-t-butyl 3-t-butyldimethylsiloxy-5-phenyl-4-pentenethioate (98%). The enantiomeric excess was determined to be 85% by the HPLC analysis (Daicel CHIRALCEL OD) of the corresponding alcohol derivatives.

Thus, [(R)-1,1'-bi-2-naphthalenediolato(2-)-O,O']oxotitanium is shown to be an efficient catalyst in the catalytic asymmetric aldol reaction between both achiral silyl enol ethers of thioesters and aldehydes. Further investigations to develop other asymmetric reactions by using this chiral catalyst is now in progress.

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3) T. Mukaiyama and R. Hara, *Chem. Lett.*, **1989**, 1171.

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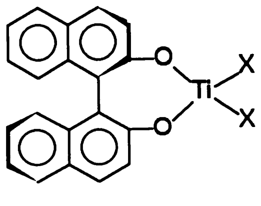
5) The catalyst **1** was prepared by mixing a stoichiometric amount of (R)-binaphthol with $({}^{i}PrO)_2Ti{=}O$ in benzene, followed by azeotropic removal of resulting 2-propanol; V. V. Lukachina, *Ukr. Khim. Zh. (Russ. Ed.)*, **53**, 382 (1987); *Chem. Abstr.*, **108**, 176209n (1987). The catalyst **1** is supposed to be monomeric by the determination of molecular weight with the freezing point depression method. $({}^{i}PrO)_2Ti{=}O$ was synthesized by the procedure similar to that described for $(EtO)_2Ti{=}O$; B. C. Bradley, R. Gaze, and W. Wardlaw, *J. Chem. Soc.*, **1955**, 721.
Reetz et al. reported the aldol, cyanation and Diels-Alder reactions proceed by the use of chiral titanium catalyst **3** to give the corresponding adducts in low to moderate yields and ees; M. T. Reetz, S-H. Kyung, C. Bolm, and T. Zierke, *Chem. Ind.*, **1986**, 824. Recently, Nakai et al. developed asymmetric glyoxylate-ene reaction with high ees by using a similar type of titanium reagents (**3** and **4**) as catalysts; K. Mikami, M. Terada, and T. Nakai, *J. Am. Chem. Soc.*, **111**, 1940 (1989).



3 : X=Cl

4 : X=Br

6) Narasaka et al. reported remarkable solvent effects of alkylated benzenes in asymmetric Diels-Alder reaction by the use of a chiral titanium dialkoxydichloride as a catalyst; K. Narasaka, M. Inoue, T. Yamada, J. Sugimori, and N. Iwasawa, *Chem. Lett.*, **1987**, 2409.

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