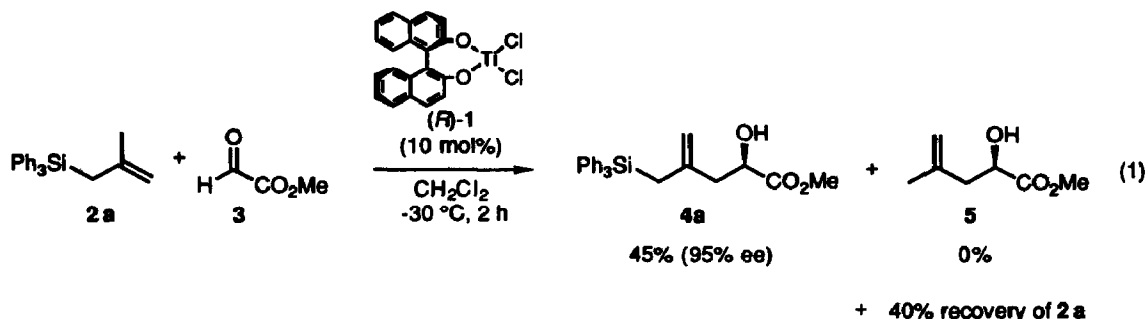# Ene Approach to Asymmetric Catalysis of the "Sakurai-Hosomi Reaction", Lewis Acid-promoted Carbonyl-Addition Reaction with Allylic Silanes

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Abstract: The chiral Lewis acid prepared from (*R*)-binaphthol and diisopropoxytitanium dichloride catalyzes the reaction of glyoxylate esters with methallylsilanes to afford mainly ene-type products rather than the products expected from the "usual" Sakurai-Hosomi reaction. The ene-type products lead eventually after protodesilylation to the "usual" products with high enantiomeric excesses.

The Lewis acid-promoted carbonyl addition reaction of allylic silanes, so-called "Sakurai-Hosomi reaction", has been well recognized as one of the most useful bond construction processes in organic synthesis.[1] Therefore, the detailed understanding of the reaction mechanisms of this carbonyl addition process and asymmetric catalysis thereof have attracted much attention.[2] In the course of studies on the asymmetric catalysis of the Sakurai-Hosomi reaction, we made the unanticipated observation that the addition products were obtained as the allylic silane, namely ene-type[3] product form by the catalysis of a chiral binaphthol-derived titanium dichloride (BINOL-TiCl$_2$, 1)[4] (eq. (1)). Herein, we now wish to report the ene approach to asymmetric catalysis of the Sakurai-Hosomi reaction.

$$Ph_3Si \diagdown \diagup + \overset{O}{\underset{H}{\diagup}} CO_2Me \xrightarrow[\substack{CH_2Cl_2 \\ -30\,°C,\ 2\ h}]{\substack{(R)\text{-}1 \\ (10\ mol\%)}} Ph_3Si \diagdown\diagup\diagdown \overset{OH}{\diagup} CO_2Me + \diagdown\diagup\diagdown \overset{OH}{\diagup} CO_2Me \quad (1)$$

2a   3   4a   5

45% (95% ee)   0%

+ 40% recovery of 2a

Surprisingly, the allylic silane 4a was obtained exclusively, in an attempted reaction of methyl glyoxylate 3 with methallyl(triphenyl)silane 2a at -30 °C in dichloromethane for 2 h, which was catalyzed by the chiral titanium dichloride (*R*)-1 (10 mol%) prepared from (*R*)-binaphthol and diisopropoxytitanium dichloride[4b,c] (eq. (1)). No "usual" Sakurai-Hosomi product 5 was obtained.

A cationic mechanism of the "usual" reaction is widely accepted to involve the β-silyl cation and hence requires the high reactivity of allylic silanes toward the electrophilic addition reaction of cationic species. According to the recent report by Mayr,[5] substituents on the silicon have a quite large effect on the reactivity of allylic silanes, which is linearly correlated with the inductive effects of

those substituents; the trimethyl group (SiMe3) activates by 1.5 orders of magnitude as compared to the triphenyl counterpart (SiPh3) in the cationic addition reaction of diarylmethyl cation to allylsilane. However, even with the methallyl(trimethyl)silane **2b**, the ene-type allylic silane **4b** was obtained as the major product (Scheme I).

Scheme I.
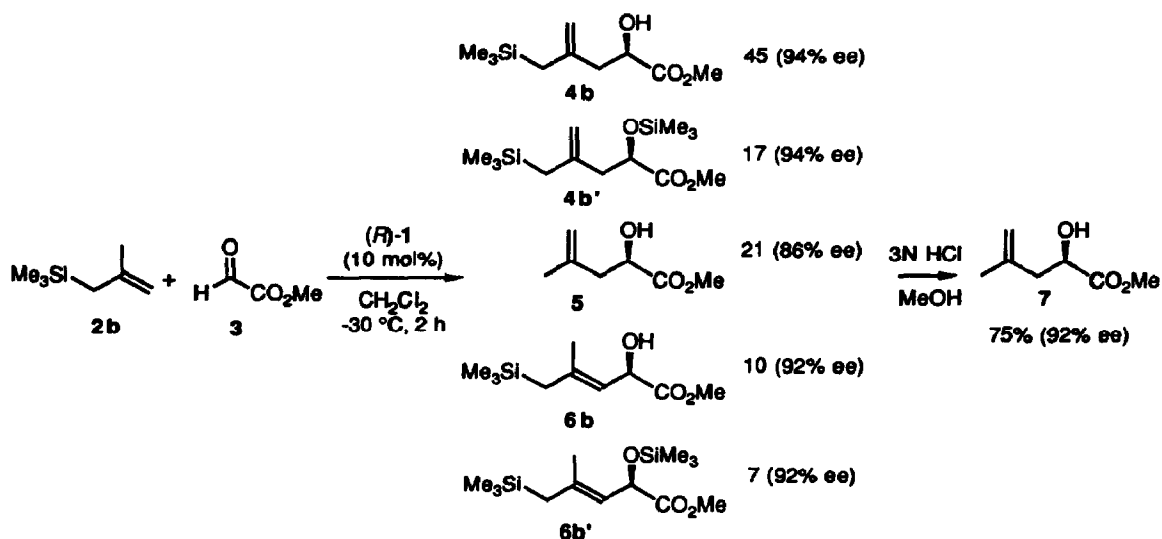
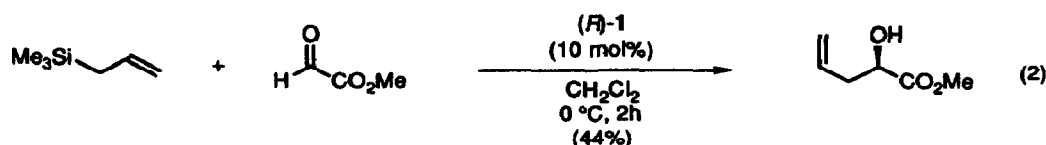Table I. The Asymmetric Sakurai-Hosomi Reaction Catalyzed by BINOL-Ti Complex (1)

entry	solvent	product ratio[a] (% ee[b])					7
		4b	**4b'**	**5**	**6b**	**6b'**	overall yield
1	CH₂Cl₂	45	: 17	: 21	: 10	: 7	75%
		(94% ee)	(94% ee)	(86% ee)	(92% ee)	(92% ee)	(92% ee)
2	toluene	42	: 19	: 18	: 12	: 9	70%
		(92% ee)	(92% ee)	(92% ee)	(92% ee)	(92% ee)	(92% ee)

[a] Determined by ¹H NMR analysis of the mixture of those products (**4b**, **4b'**, **5**, **6b**, and **6b'**). [b] Determined by ¹H NMR analysis of the (S)-(-)- and (R)-(+)-MTPA ester derivatives.

Typical experimental procedure is as follows (Scheme I). The reaction was carried out by adding the methallyl(trimethyl)silane **2b** and aldehyde **3** at -30 °C to a solution of the chiral titanium dichloride (R)-1 (10 mol%).[4b,c] The reaction proceeded smoothly within 2 h as determined by TLC monitoring. Careful hydrolytic workup[6] with saturated sodium bicarbonate at 0 °C followed by flash column chromatography afforded the addition products mainly as the ene-type allylic silane **4b**, along with the "usual" non-allylic silane product **5** and non-ene-type allylic silane **6b**. The enantiomeric

purity and absolute stereochemistry of each product were determined by the modified Mosher method[7] on the basis of ^{1}H NMR (300 MHz) spectral analysis of the (S)-(-)- and (R)-(+)-MTPA ester derivatives. Thus, the sense of asymmetric induction in the present reactions is consistent with that previously observed in the glyoxylate-ene reaction:[4] (R)-1 provides the (2R)-products. The high level of enantiomeric excess of the desilylated combined product 7 was further confirmed, after protodesilylation of those products (Table I).

This asymmetric catalytic process is characterized by the intriguing ene regioselectivity and high level of asymmetric induction (Table I). The ene-type product was obtained via the hydrogen shift preferentially from the non-silylated position of the methallylsilane. The observed regioselectivity is in sharp contrast to that reported in the quite recent communication on the ZnI_2-promoted Michael-type acetylene-ene[3g] reaction with butynone.[8] However, their observation on the ene regioselectivity for the methylene hydrogen-shift from the α-silyl position may reflect the cyclic situation of the allylic silane employed.[9] Remarkably high level of enantiofacial selectivity for the ene-type product 4 was obtained either in toluene or in dichloromethane. Interestingly, the enhancement of enantiomeric excess of the "usual" product 5 was observed in less polar solvent, toluene as compared to dichloromethane, and might imply the concertedness of the "usual" pathway in less polar solvents. Furthermore, the high level of asymmetric induction was confirmed in the desilylated form of combined product 7, after protodesilylation of those products (4, 4', 5, 6, and 6'). In sharp contrast, the allyl(trimethyl)silane afforded the "usual" product rather than the ene-type product (eq. (2)),[10] apparently because of the less ene-reactivity of mono-substituted olefins.[4]

$$Me_3Si\diagdown\diagup\diagdown\diagup \quad + \quad \underset{H}{\overset{O}{\|}}CO_2Me \quad \xrightarrow[\substack{CH_2Cl_2 \\ 0\ ^\circ C, 2h \\ (44\%)}]{\substack{(R)-1 \\ (10\ mol\%)}} \quad \overset{OH}{\diagdown\diagup\diagdown}CO_2Me \quad (2)$$

In summary, we have disclosed herein that the ene-type process does involve in the asymmetric catalytic Sakurai-Hosomi reaction with allylic silanes. Further studies along these lines are now underway and will be reported in a full paper format.

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