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# Highly Enantioselective Epoxidation of *cis*-Alkenylsilanes

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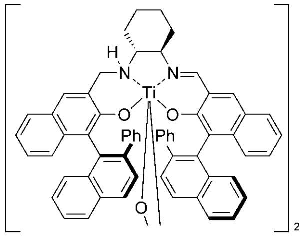
Since the development of the titanium/tartrate-catalyzed asymmetric epoxidation of allyl alcohols in 1980, significant progress has been made in the field of asymmetric epoxidation of olefins, and now most olefins can be transformed to epoxides with high optical purity.[1–3] However, there are no satisfactory methods available thus far for the asymmetric epoxidation of terminal olefins such as styrene.[4] While epoxysilanes are a synthetic equivalent of epoxides, a highly enantioselective epoxidation of simple alkenylsilanes is also quite rare in the literature.[5,6] Although Shi and co-workers applied their sugar-derived ketone catalyst to the epoxidation of 2,2-disubstituted alkenylsilanes and obtained the epoxysilanes with high enantioselectivity up to 94% *ee*, the method has a major drawback that it requires a substoichiometric amount of the catalyst.[7,8] While the introduction of a sterically more demanding silyl group at the vinyl position is expected to further facilitate the enantioface-differentiation, there is a concern that the steric hindrance strongly inhibits the reaction progress.[5] Thus, in order to implement the catalytic asymmetric epoxidation of alkenylsilanes, the utilization of a more refined epoxidation catalyst in terms of catalytic activity, asymmetric induction and durability is necessary.

We have reported that the di-μ-oxo-Ti(salalen) complex **1** (Figure 1) is an effective catalyst for the asymmetric epoxidation of olefins with aqueous hydrogen peroxide as the oxidant.[9] Not only conjugate olefins but also non-conjugate olefins, which still are the most challenging substrate for asymmetric epoxidation with regard to both reactivity and enantioselectivity, underwent the epoxidation to give the epoxides with high enantioselectivity. Thus, we expected that Ti(salalen) **1** would best meet the requirements for the epoxidation of alkenylsilanes. Herein, we report the catalytic asymmetric epoxidation of *cis*-alkenylsilanes, in which the *cis*-epoxysilanes are obtained with complete enantioelectivity using 0.5–2 mol% of the catalyst.



**1**

Figure 1. Di-μ-oxo-Ti(salalen) complex **1**.

*cis*-Alkenylsilanes were readily prepared by simple reduction of the corresponding alkynylsilanes with diisobutylaluminum hydride.[10] We first examined the scope of alkenylsilanes in the presence of Ti(salalen) **1** (Table 1). The complex **1** effectively promoted the epoxidation of *cis*-alkenylsilanes bearing aromatic groups. Silicon substituents have little effect on the enantioselectivity (entries 1 and 2). The reactions furnished both the trimethylsilyl- and dimethylphenylsilyl epoxides with *ee* values of >99%. Substituted alkenylsilanes with electron-donating methoxy and electron-withdrawing bromide groups on the aromatic ring also underwent the epoxidation with complete enantioselectivity (entries 3–7). However, the substitution at the *ortho*-position decreased the reaction rate (entries 3 and 5). The reaction with methoxy group at this position required a longer reaction time, and an *ortho*-bromide group significantly impeded the reaction progress. Alkenylsilanes with other groups, such as biphenyl and naphthyl groups, were also good substrates (entries 8–10). Noteworthy the epoxysilanes were effectively desilylated by TBAF to give the corresponding styrene oxide derivatives without erosion of the enantioselectivity.[11]

A combination of $Ti(OiPr)_4$ and salan ligand **2** was also effective for the epoxidation.[12] In the reaction of dimethylphenyl(styryl)silane, the epoxysilane was obtained in 59% with >99% *ee* (Scheme 1). Although the *ee* value is

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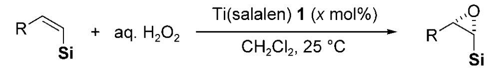
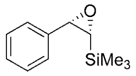
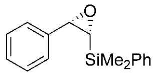
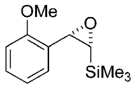
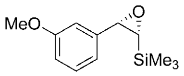
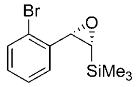
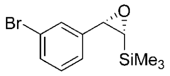
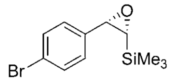
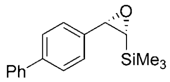
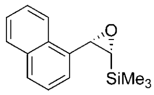
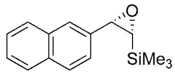
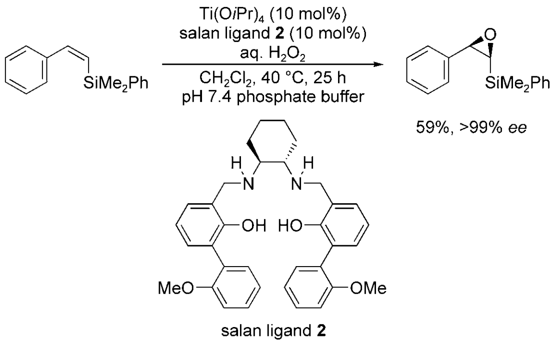
Table 1. Asymmetric epoxidation of *cis*-alkenylsilanes with Ti(salalen) **1**.



| Entry | Epoxysilane[a] | $x$ [mol %] | $t$ [h] | Yield [%][b] | *ee* [%][c,d] |
|---|---|---|---|---|---|
| 1 |  | 0.5 | 9 | 87 | >99 (>99) |
| 2 |  | 2 | 9 | 95 | >99 (>99) |
| 3 |  | 2 | 18 | 94 | >99 (>99) |
| 4 |  | 0.5 | 7 | 96 | >99 (>99) |
| 5 |  | 2 | 24 | 10 | >99 (>99) |
| 6 |  | 2 | 4 | 98 | >99 (>99) |
| 7 |  | 1 | 4 | 91 | >99 (>99) |
| 8 |  | 0.5 | 6 | 99 | >99 (>99) |
| 9 |  | 1 | 9 | 92 | >99 (>99) |
| 10 |  | 0.5 | 6 | 96 | >99 (>99) |

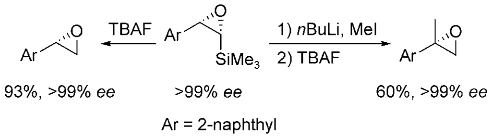
[a] Absolute configuration was determined after desilylation. [b] Isolated yield. [c] Enantiomeric excess was determined by chiral HPLC analysis. [d] Numbers in the parentheses correspond to enantiomeric excesses after desilylation.



Scheme 1. Asymmetric epoxidation with an in-situ prepared titanium/salan **2** catalyst.

still high, the reaction was significantly slow compared to that with Ti(salalen) **1**.

Synthetic application of the *cis*-epoxysilanes is illustrated in Scheme 2. As mentioned above, treatment of epoxysilanes with TBAF cleanly cleaved the silyl group to give the optically pure styrene oxide derivatives.[11,13] Regioselective alkylation and the subsequent desilylation afforded the corresponding 2,2-disubstituted terminal epoxides.[6,14] Although highly enantioselective epoxidation of styrene derivatives and geminally disubstituted alkenes is still difficult at present, our procedure can provide these epoxides in enantiopure form.[15] These transformations enhance the synthetic value of the titanium-catalyzed asymmetric epoxidation.



Scheme 2. Synthetic application of epoxysilanes.

It is noteworthy that the absolute configuration of styrene oxide obtained by the desilylation of dimethyl(phenyl)(3-phenyloxiran-2-yl)silane was consistent with that of the styrene oxide obtained by the epoxidation of styrene. These results indicate that the active oxidant derived from Ti(salalen) **1** and hydrogen peroxide recognizes the same enantioface of alkenylsilanes and styrene.

In summary, we developed a general and highly enantioselective method for the epoxidation of *cis*-alkenylsilanes, in which the epoxysilanes were obtained with complete enantioselectivity in the presence of 0.5–2 mol % of Ti(salalen) complex **1**. The combination of this epoxidation method and the following transformations is a powerful approach that provides synthetically important epoxides such as styrene oxides and geminally disubstituted epoxides in enantiopure form.

## Experimental Section

**General procedure for asymmetric epoxidation of *cis*-alkenylsilanes**: Ti(salalen) **1** [4.5 mg (0.5 mol %) to 18 mg (2.0 mol %)] and *cis*-alkenylsilane (0.50 mmol) were dissolved in $CH_2Cl_2$ (0.50 mL). Then, aqueous $H_2O_2$ (30–35 % in water, 85 µL,) was added and the reaction mixture was stirred at 25 °C. After the reaction completion, the mixture was purified by chromatography on basic silica gel (*n*-pentane or *n*-hexane) to give the desired epoxysilane. The *ee* value was determined by chiral HPLC analysis.

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