



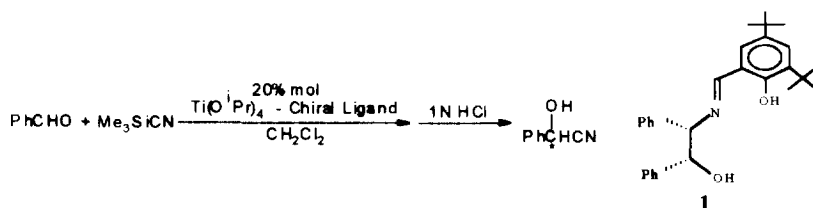
0957-4166(95)00385-1

## Asymmetric Synthesis XXVII: Asymmetric Catalytic Trimethylsilylcyanation of Aldehydes by Novel Ti-Chiral Schiff Base Complexes\*

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**Abstract:** Enantioselective catalytic trimethylsilylcyanations of aldehydes with 48% to 92% e.e. have been studied using the novel Ti-chiral Schiff base complexes. We have found that the catalyst led to high enantioselectivity when the molar ratio of the Schiff base **1** to Ti(O-i-Pr)<sub>4</sub> was 2:1.

Enantiomerically pure cyanohydrins are very versatile synthons for the preparation of a variety of valuable synthetic intermediates, which can be prepared by many biological and chemical methods.<sup>1-3</sup> Recently, Oguni and co-workers reported a novel and efficient procedure for the highly enantioselective addition of trimethylsilylcyanide to aldehydes catalyzed by chiral Schiff base-titanium alkoxide complexes.<sup>4</sup> We also reported enantioselective trimethylsilylcyanation of benzaldehyde using Ti-Schiff base complexes with 53.2% e.e. value.<sup>5</sup> Among the catalyst systems we examined, the structure of the ligand is an important factor to effect the enantioselectivity, the combination of Ti(O-i-Pr)<sub>4</sub> and the Schiff base **1** gave the product in moderate enantiomeric excess.



In this paper, we would like to report our recent progress in such a field. We found that the enantioselectivity of the reaction was influenced considerably by another factor --- mole ratio of ligand to central metal. To our knowledge, this factor is hardly mentioned in the literature.<sup>6</sup> (Results are listed in Table 1)

Table 1 Effect of mole ratio of chiral ligand to central metal <sup>a)</sup>(-80±æ)

| Entry | Schiff base <b>1</b> : Ti | C.Y.(%) <sup>b)</sup> | Time(hrs) | E.e.(%)(Config.) <sup>c)</sup> |
|-------|---------------------------|-----------------------|-----------|--------------------------------|
| 1     | 1.1:1                     | 85.3                  | 60        | 53.2(S)                        |
| 2     | 1.3:1                     | 86.5                  | 56        | 80.4(S)                        |
| 3     | 1.5:1                     | 88.7                  | 56        | 89.2(S)                        |
| 4     | 2.0:1                     | 72.0                  | 60        | 92.0(S)                        |

a) All reactions were carried out in dichloromethane using 20 mol% Ti(O-i-Pr)<sub>4</sub> per benzaldehyde.<sup>7</sup> b) Isolated yield c) determined by chiral GC after derivatisation with TFAA(Trifluo acetic anhydride)

From the table 1, we know that e.e. values increase considerably with the mole ratio of Schiff base **1** to Ti(O-i-Pr)<sub>4</sub>. It is a contrast to Oguni's result in which the reaction product of their Schiff base with Ti(OiPr)<sub>4</sub> in

molar ratio of 2:1 had no catalytic activity.<sup>8</sup> Furthermore, we have checked the relationship between the reaction time and the enantioselectivity of trimethylsilylcyanation of benzaldehyde (Schiff base 1: Ti = 1.5:1), and found that the chemical yield increases with the reaction time and enantioselectivity didn't change obviously. These results indicate that all these catalytic reactions might proceed the same transition state, though we don't know the exact component of the intermediate.

Table 2 Enantioselective addition of trimethylsilylcyanide to aldehydes catalyzed by Schiff base 1: Ti(O-*i*-Pr)<sub>4</sub> = 1.5:1(-80°C, 60hr)

| Entry | Aldehyde              | C. Y.(%) <sup>a)</sup> | $[\alpha]_D^{20}$ (c, solvent)  | E. e.(%)(config.)     |
|-------|-----------------------|------------------------|---------------------------------|-----------------------|
| 1     | 3-phenoxybenzaldehyde | 58.4                   | -8.2(1.0, CHCl <sub>3</sub> )   | 48.6(S) <sup>b)</sup> |
| 2     | 2-chlorobenzaldehyde  | 76.0                   | +3.4(0.92, CHCl <sub>3</sub> )  | 91.0(S) <sup>c)</sup> |
| 3     | (E)-cinnamaldehyde    | 59.9                   | -26.7(1.42, CHCl <sub>3</sub> ) | 54.1(S) <sup>d)</sup> |
| 4     | 4-methoxybenzaldehyde | 30.9                   | -22.0(1.12, CHCl <sub>3</sub> ) | 48.0(S) <sup>e)</sup> |

a) Isolated yield. b) determined by the comparison of the specific rotation values  $[\alpha]_D^{20} = -17.09$ (c=1.5, C<sub>6</sub>H<sub>6</sub>).<sup>9</sup> c) determined by chiral GC after derivatisation with TFAA. d) determined by the comparison of the specific rotation values  $[\alpha]_D^{20} = -26.7$ (c=1.9, CHCl<sub>3</sub>).<sup>10</sup> e) determined by the comparison of the specific rotation values  $[\alpha]_D^{20} = -45.82$  (c=1.4, CHCl<sub>3</sub>).<sup>10</sup>

At last, the trimethylsilylcyanation of several other aldehydes proceeded smoothly in the presence of 20 mol % of Schiff base 1 and Ti(O-*i*-Pr)<sub>4</sub> (1.5:1), in which the product 2-hydroxy-*o*-chlorophenylacetone nitrile was obtained in 91% e.e. (Table 2, entry 2). The further investigation to search for more efficient catalyst is in progress.

\* This project was supported by the National Natural Science Foundation of China

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(Received in Japan 12 September 1995; accepted 16 October 1995)