

Letter

Asymmetric trimethylsilylcyanation of benzaldehyde catalyzed by novel Ti(IV)-chiral Schiff base complexes

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Abstract

Benzaldehyde has been trimethylsilylcyanated with a catalyst prepared in situ from titanium tetraisopropoxide and chiral Schiff bases. Cyanohydrin is obtained in high optical yield (up to 67.5%). © 1998 Elsevier Science B.V. All rights reserved.

Keywords: Ti(IV)-complexes; Chiral schiff bases; Asymmetric trimethylsilylcyanation

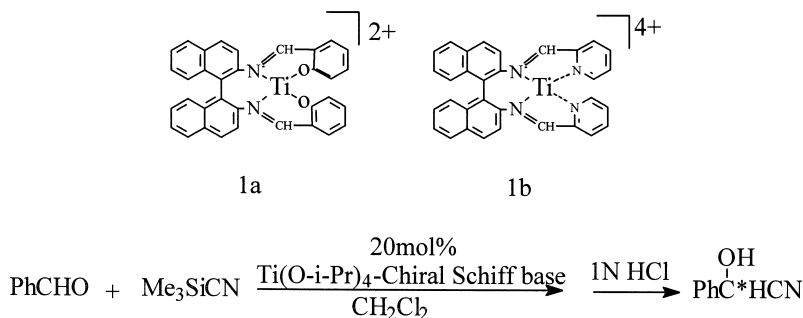
1. Introduction

Asymmetric hydrocyanation of aldehydes is very important in organic synthesis, and there have been many approaches to the catalytic asymmetric synthesis of this class of compounds reported in the literature [1]. Recently, Hayashi et al. [2–4] and Hayashi and Oguni [5] developed a new catalytic system based on Ti(IV)-tridentate Schiff's base complexes, for trimethylsilylcyanation of aldehyde. Enantiomeric excesses of the corresponding reaction products up to 96% were reported by this group [2,3,5,4]. Some experimental evidence was presented to support the reaction mechanism, including as a key step the substitution by the aldehyde carbonyl group of the isopropanol molecule in the coordination sphere of the catalytic complex [2]. It is noteworthy that chiral Schiff's base complexes of transition metals have been found to become very effective catalysts for asymmetric cyclopropanation [6], epoxidation of alkenes [7]. A possible mechanism involving the nucleophile delivery to the epoxide reactive group via coordination of the nucleophile with the central metal ion was tentatively suggested by the authors [7].

Recently, we reported the highly enantioselective transfer hydrogenation of aceto-phenone by Ir(I)/Rh(I) complexes [8]. In this paper, we describe the use of the titanium tetraisopropoxide [Ti(OPrⁱ)₄]-chiral Schiff's base as a catalyst for the asymmetric silylcyanation of benzaldehyde to give optically active cyanohydrin.

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We supposed that chiral Ti(IV) catalysts (1a and 1b) prepared in situ from titanium tetraisopropoxide and ligand 1a (or 1b) might become efficient in the asymmetric trimethylsilylcyanation of benzaldehyde if the key step of the addition reaction is the cyanide coordination to the metal ion. Herein we describe the successful application of this idea.



2. Results and discussion

The Schiff's bases were prepared by the condensation of salicylaldehyde or pyridine-2-carboxaldehyde with chiral 2,2'-diamino-1,1'-binaphthyl in ethanol, as described in the literature [6,8]. The chiral Schiff's base–titanium complexes were obtained by mixing the corresponding chiral Schiff's bases and $\text{Ti}(\text{OPr}^i)_4$ in dichloromethane. The reaction of the aldehyde with trimethylsilylcyanide was carried out essentially at -40°C in dichloromethane, using 20 mol% of the in situ prepared catalyst, as outlined by Hayashi et al. [2–4] and Hayashi and Oguni [5]. In addition, a special experiment (entry 1) was conducted to check if the free ligand was an efficient asymmetric catalyst of trimethylsilylcyanation reaction under the experimental conditions.

The results on enantioselective silylcyanation of benzaldehyde with trimethylsilyl-cyanide catalyzed by the mixture of titanium tetraisopropoxide [$\text{Ti}(\text{OPr}^i)_4$] and chiral Schiff's bases (20 mol% per aldehyde) are summarized in Table 1. The data clearly indicated that the free Schiff's base ligands might serve as catalysts of the reaction but no asymmetric induction was detected in the product (entry 1). Nevertheless, there were no doubt that the Ti(IV) complexes, 1a and 1b, were both efficient

Table 1
Enantioselective trimethylsilylcyanation of benzaldehyde

Entry	Ligand ^a	Temperature ($^\circ\text{C}$)	Time (h)	Yield ^b (%)	E.e. ^c (%)	OP ^d (%) (configuration)
1	1a	-40	60	83.1	—	—
2	1a	-40	60	86.1	67.5	69.8(<i>R</i>)
3	1b	-40	60	71.6	42.8	45.1(<i>R</i>)
4	1a	-20	48	83.7	58.2	60.0(<i>R</i>)
5	1b	-20	48	72.5	33.1	33.7(<i>R</i>)
6	1a	0	36	86.4	36.5	38.9(<i>R</i>)
7	1b	0	36	78.3	12.7	13.2(<i>R</i>)

^aAll Schiff's base have *S* configuration.

^bIsolated yield.

^cDetermined by HPLC analysis of its MTPA ester.

^dDetermined by the comparison of the specific rotation values for the (*R*)-cyanodrin [4].

asymmetric catalysts of trimethylsilylcyanation of benzaldehyde. 1a seemed to be a more promising catalyst, having produced a larger e.e. of the reaction. The temperature dependence of the e.e. of the reaction was noticeable and predictably favored low temperatures, although to a lesser extent than reported by Hayashi et al. [2–4] and Hayashi and Oguni [5] for his type of catalysts.

The mechanism of the catalysis by 1a and 1b appears to be different from that suggested by Hayashi et al. [2–4] and Hayashi and Oguni [5] for his tridentate ligand based catalysts. All the coordination sites in the complexes 1a or 1b are occupied either by the tetradentate ligand or by alkoxide molecules. There are no vacant sites or sites occupied by the solvent or neutral alcohol molecule left in the coordination sphere of the catalytic complex. The mechanism, involving the substitution of such strong ligands as alkoxide or a fragment of the tetradentate ligand by such a relatively weak base as the carbonyl group of aldehyde, looks unlikely because of the very low probability of the substitution event. We suggest that the preliminary interaction of trimethylsilylcyanide with the complex, generating $\text{Me}_3\text{SiOPr}^i$ and the coordinated CN at the apical position of the complex, might be the first step in the catalytic cycle. The stereo differentiating step would then be nucleophilic delivery of CN from the chiral complex to the carbonyl group of the aldehyde, taking place inside the coordination sphere of the complex. Further discussion should be postponed until after new experimental facts emerge. The reported e.e. of the cyanosilylation reaction were not optimized and probably could be further improved by the appropriate choice of the reaction conditions. Furthermore, the enantioselectivity of the reaction was influenced considerably by the central metal. Although Schiff base 1a–Zn(II) catalyze the reaction effectively, the e.e. value was only 2.1% (*R*).

3. Conclusion

The enantioselectivity of the reaction was dependent upon the ligand structure, reaction temperature, central metal; using the catalyst system consisting of $\text{Ti}(\text{OPr}^i)_4$ and chiral Schiff's base provides a new, efficient synthetic road for the preparation of optically active cyanohydrins. Further investigation to improve the enantioselectivity is in progress.

4. Experimental

Melting points were determined by using a Yanaco mp-500 micro melting point apparatus and uncorrected. ^1H NMR spectra were obtained with a JEOL-FX90Q NMR spectrometer and recorded in deuterio-chloroform containing tetramethylsilane as the internal standard; and IR spectra were recorded with a HITACHI 260-50 Infrared spectrometer; elemental analysis data were determined with a Perkin-Elmer 240C instrument; optical rotations were measured with a Perkin-Elmer 241MC instrument; HPLC analyses were determined with a 880-PU instrument.

Dichloromethane was dried over P_2O_5 and distilled prior to use; aldehydes were distilled prior to use.

4.1. Preparation of $\text{Ti}(\text{OPr}^i)_4$

$\text{Ti}(\text{OPr}^i)_4$ was prepared according to the patent [9].

4.2. Preparation of $(\text{CH}_3)_3\text{SiCN}$

$(\text{CH}_3)_3\text{SiCN}$ was prepared according to the procedure in the literature [10].

4.3. Preparation of 2,2'-diamino-1,1' binaphthyl

2,2'-Diamino-1,1' binaphthyl was prepared according to the procedure in the literature [11].

4.4. Preparation of Schiff bases (1a and 1b)

1a and 1b was prepared according to the procedure in the literature [6,8].

4.5. General procedure for the trimethylsilylcyanation of benzaldehyde

To a solution of Schiff base 1a(0.4 mmol) in dichloromethane (2 ml) was added $\text{Ti}(\text{OPr}^i)_4$ (0.36 mmol) and stirred for 2 h at room temperature. The reaction mixture was cooled to -78°C , followed by addition of freshly distilled benzaldehyde (2 mmol) and trimethylsilylcyanide (4.56 mmol). Stirring was continued at -40°C for 60 h, then the mixture was poured into a mixture of 1 N HCl(30 ml) and ethyl acetate (60 ml) and stirred for 6 h at room temperature. The usual extractive work up and silica gel column chromatography (hexane–ethyl acetate, 5:1) of the residue gave (*R*)-cyanohydrin (229 mg, 86.1%). The e.e. of the product was determined by analysis of its MTPA ester. The t_{R} of (*R*)-(+)-isomer: 12.5 min; t_{R} of (*S*)-(–)-isomer: 15.0 min (hexane–ethyl acetate 100:5, 1.0 ml min^{-1}).

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