

Chiral Copper–Schiff Base Catalyst for Asymmetric Henry Reaction*

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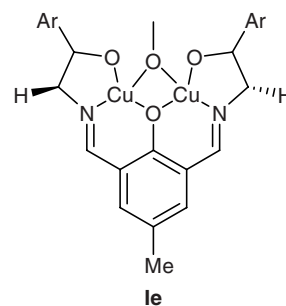
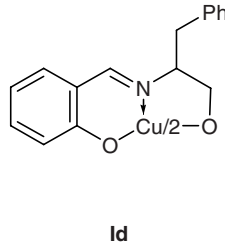
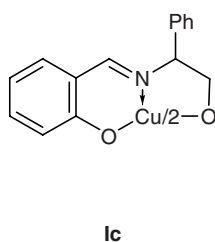
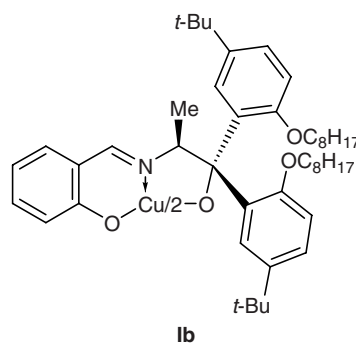
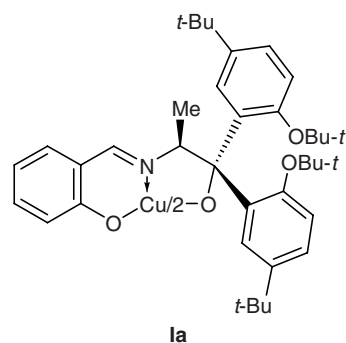
Abstract—Five copper–Schiff base complexes were synthesized conveniently from copper(II) acetate monohydrate, salicylaldehydes, and amino alcohols. The complexes were shown to be effective as catalysts in the asymmetric Henry reaction affording nitro alkanols in up to 98% yield with moderate and good enantiomeric excess (up to ee 38.6%).

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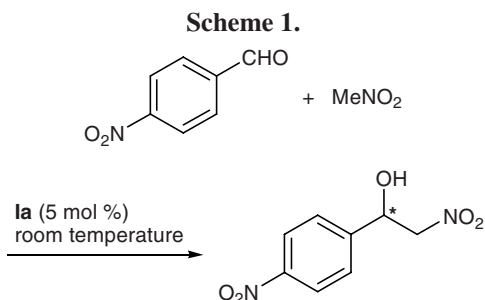
Syntheses of nitro alcohols via the Henry reaction have been extensively studied during the last decade [1–3]. Recent contributions to this area have been highlighted by Shibasaki and Trost [4–11]. Among efficient catalysts for the Henry reaction, bimetallic zinc complexes [6, 7], rare-earth lithium BINOL complexes [2, 4, 5, 12–15], chiral quaternary ammonium salts [10, 11], and complexes derived from bis(dihydrooxazole) and bis(dihydrothiazole) ligands [1, 3, 8, 9, 16] were shown to be potent. On the other hand, copper

complexes with Schiff bases have seldom been reported for asymmetric Henry reaction. In the present communication we report on the use of copper–Schiff base complexes in asymmetric Henry reaction.

Five copper–Schiff base complexes were synthesized according to the procedures described in [17, 18]. Their structures are shown below. Initially, we examined the Henry reaction of *p*-nitrobenzaldehyde with nitromethane, catalyzed by complex **1a** in various solvents (Scheme 1), and some representative results



* The text was submitted by the authors in English.



are summarized in Table 1. The reactions were carried out in different solvents at room temperature using 5 mol % of **Ia**. The results showed that ethanol was the best solvent: the corresponding nitro alcohols were obtained in high yield with moderate enantiomeric excess (ee 25.4% for the *R* enantiomer, Table 1). Compounds **Ia–Ie** were then tested in the same reaction using ethanol as solvent (Table 2). The reactions were complete within 24 h at room temperature. It is seen that complexes **Ia** and **Ib** ensure high yields of 2-nitro-1-(4-nitrophenyl)ethanol and moderate ee values (25.4 and 19%, respectively). We also performed the Henry reaction of nitromethane with different aromatic aldehydes [12] with a view to estimate its scope. Complex **Ia** worked well with the examined benzaldehydes (Table 3), but better enantioselectivity was observed with substituted benzaldehydes compared to unsubstituted. The product obtained from *p*-chlorobenzaldehyde was characterized by higher optical purity than that formed from *p*-nitrobenzaldehyde. On the other hand, the chemical yield in the reaction with *p*-nitrobenzaldehyde was greater than in the reaction with *p*-chlorobenzaldehyde.

EXPERIMENTAL

The ee values were determined by HPLC using a Chiralcel™ OD-H column (eluent propan-2-ol–hexane). The ¹H NMR spectra were recorded on a Bruker AV-400 spectrometer at a frequency of 400 MHz using chloroform-*d* as solvent and tetramethylsilane as internal reference.

General procedure for the Henry reaction.

A mixture of 5 mol % of catalyst **Ia–Ie** and 2.5 mmol of nitromethane in 5 ml of the corresponding solvent was stirred for an hour at room temperature, 0.5 mmol of aromatic aldehyde was added, the mixture was stirred for 24 h at room temperature, the solvent was evaporated under reduced pressure, and the crude product was purified by column chromatography (15% of ethyl acetate in petroleum ether).

Table 1. Henry reaction of *p*-nitrobenzaldehyde with nitromethane in the presence of complex **Ia** (5 mol %) in different solvents (reaction time 24 h, room temperature)

| Solvent | Yield, ^a % | ee, ^b % (<i>R</i>) |
|--------------------|-----------------------|---------------------------------|
| Tetrahydrofuran | 20 | 10.9 |
| Nitromethane | 90 | 1.4 |
| Acetonitrile | 90 | 19.0 |
| Toluene | 30 | 1.1 |
| Diethyl ether | 40 | 10.6 |
| Ethyl acetate | 93 | 15.0 |
| Methylene chloride | 85 | 17.2 |
| Ethanol | 87 | 25.4 |

^a Hereinafter, the yield of the isolated product is given.

^b Hereinafter, determined by HPLC; the absolute configuration was assigned by comparison of the retention time with published data [1].

Table 2. Henry reaction of *p*-nitrobenzaldehyde with nitromethane in the presence of complexes **Ia–Ie** (5 mol %) in ethanol (reaction time 24 h, room temperature)

| Catalyst no. | Yield, % | ee, % (<i>R</i>) |
|--------------|----------|--------------------|
| Ia | 87 | 25.4 |
| Ib | 98 | 19.0 |
| Ic | 40 | 7.4 |
| Id | 45 | 9.0 |
| Ie | 50 | 3.1 |

Table 3. Henry reaction of nitromethane with substituted benzaldehydes in the presence of complex **Ia** (5 mol %) in ethanol (reaction time 24 h, room temperature)

| Aldehyde | Yield, % | ee, % (<i>R</i>) |
|------------------------------|----------|--------------------|
| Benzaldehyde | 65 | 6.6 |
| <i>o</i> -Chlorobenzaldehyde | 50 | 30.2 |
| <i>p</i> -Chlorobenzaldehyde | 70 | 38.6 |
| <i>p</i> -Nitrobenzaldehyde | 87 | 25.4 |

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