Chinese Chemical Letters Vol. 13, No. 12, pp 1143 – 1146, 2002
http://www.imm.ac.cn/journal/ccl.html

Asymmetric Cyclopropanation Catalyzed by Four Stereoisomers of a Copper-(Schiff-base) Complex with Double Chiral Centers

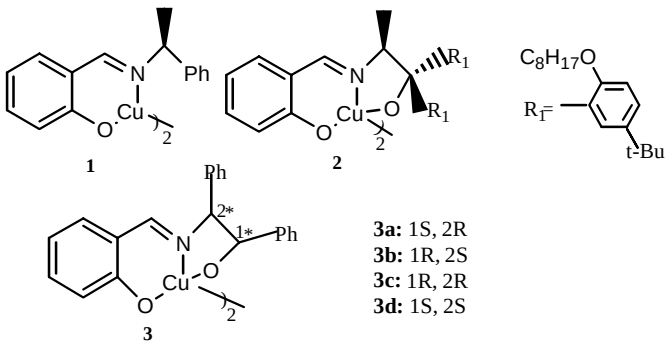
Chang Sheng JIANG, You Gui LI, Chen JIANG, Fang WANG, Tian Pa YOU*

Department of Chemistry, Universtity of Science & Technology of China, Hefei 230026

Abstract: Four stereoisomers of a copper-(Schiff-base) complex with double chiral centers were applied to catalyze the asymmetric cyclopropanation. Two of the stereoisomers were also efficient catalysts affording high enantiomeric excess of up to 91.8%. A mechanism that predicts the observed results accurately was proposed.

Keywords: Asymmetric cyclopropanation, copper-(Schiff-base), olefins, diazoacetates.

Catalytic asymmetric cyclopropanation of diazoacetates with olefins has attracted much attention. Those catalysts containing various metals and optically active ligands have been employed for this reaction[1,2]. The first catalytic asymmetric cyclopropanation reaction was reported in 1966 by Nozaki *et al.*[3]. The author used the copper(II) complex **1** bearing a salicyladimine ligand as catalyst though with a low e.e. value of 6%. Aratani and his coworkers designed the copper-(Schiff-base) complex nearly 10 years later that gave dramatic improvements in optical yields[4,5]. Some other efficient copper-(Schiff-base) complexes were reported by Z.L. Li[6,7] and Cai *et al*[8] . Recently these complexes were prepared by modification of Aratani's catalyst **2**.

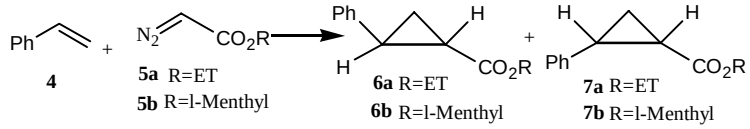


However, the mechanism of the asymmetric cyclopropanation catalyzed by this kind of Schiff-base complex is still not very clear. Aratani has proposed a mechanism[5] that can predict the configuration of predominant cyclopropane, but it does not adequately

*E-mail: ytp@ustc.edu.cn

account for the preferential *trans* stereochemistry that is observed in most cases. It will be helpful to know the mechanism more thoroughly for designing novel efficient catalyst. Up to now, all the copper-(Schiff-base) complexes, that have been applied to catalyze this reaction, have only one chiral center, which attached to the nitrogen atom. If the carbon attached to the oxygen also has chirality, how does it affect the enantioselectivity and which of the two chiral centers displays main effect? To explore the answers and to know more details about the catalytic mechanism, complexes **3a-d** were synthesized and the efficacies of them in catalyzing the asymmetric cyclopropanation were investigated in this paper.

The ligands of complexes **3a-d** were derived from salicyclaldehyde and four stereoisomers of 1,2-diphenyl-2-aminoethanol that were obtained according to the reference[9] with some modifications.

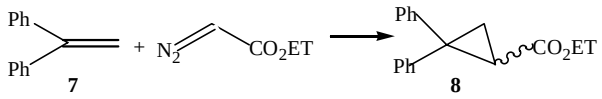


Initially, the complexes **3a-d** were applied to catalyze the reaction of styrene **4** with diazoesters **5** (**Table1**). In the cases of using **3a** or **3c** as catalyst, the *1S, 2R* for **6a** and **6b** and the *1S, 2S* for **7a** and **7b** are the major enantiomers respectively, though the configurations of C_1 in **3a** and **3c** are different. While using **3b** or **3d** as a catalyst, the *1R, 2S* for **6a** and **6b** and *1R, 2R* for **7a** and **7b** turn out to be the major enantiomers respectively, despite the configurations of C_1 in **3b** and **3d** are different too. This indicates that the configuration of C_2 in complex **3** dominates the configuration of predominant cyclopropane in **6a** and **6b** and **7a** and **7b**. It is noteworthy that the degree of enantioselectivity for **3c** and **3d** are much lower than that for **3a** and **3b**. This suggests that the configuration of C_1 in complexes **3a-d** affect mainly on the degree of enantioselectivity.

Table 1 Asymmtric cyclopropanation of styene **4** (1 mol% of **3** as catalyst) [a]

Run	3	5	Yield(%)[b]	6:7[c]	e.e.% of 6[d]	e.e.% of 7[d]
1	a	a	63	30/70	63.2(1S, 2R)	32.8(1S, 2S)
2	b	a	65	31/69	60.6(1R, 2S)	32.3(1R, 2R)
3	c	a	54	27/73	12.1(1S, 2R)	23.4(1S, 2S)
4	d	a	57	27/73	12.9(1R, 2S)	22.7(1R, 2R)
5	a	b	54	21/79	65.4(1S, 2R)	55.3(1S, 2S)
6	b	b	59	22/78	63.9(1R, 2S)	56.7(1R, 2R)
7	c	b	60	15/85	11.3(1S, 2R)	17.2(1S, 2S)
8	d	b	51	18/82	11.4(1R, 2S)	17.8(1R, 2R)

[a]All reactions were carried out at 40°C in benzene. [b]Isolated yields of purified **6** and **7**. [c]Determined by GC(Column: PE-5, length: 20.00 M,ID:0.18mm,film thickness:0.18 um, column temp.: 250°C). [d]For entry1-4: the e.e. % of **7** was determined by HPLC (Chiracel OD column, elution with hexane/isopropanol 9.75:0.25, 0.4 ml/min), the determination of e.e. % of **6** was effected by polarimetry of it's corresponding acid since chiral HPLC did not give sufficiently resolved peaks[10]; for entry 5-8 the e.e. % was determined by GC(Column: PE-5, length: 20.00 M,ID:0.18 mm,film thickness:0.18 um, column temp.: 250°C). The configuration in parentheses is of the excess enatiomer, which was established on the basis of the sign of the specific rotation of the corresponding acid[10].



7 **8**

Table 2 Asymmetric cyclopropanation of **7** with ethyl diazoacetate (1 mol% of **3**)[a]

Run	**3**	Yield[b]	e.e.%[c]
1	a	53	90.1
2	b	54	91.8
3	c	58	13.4
4	d	51	13.1

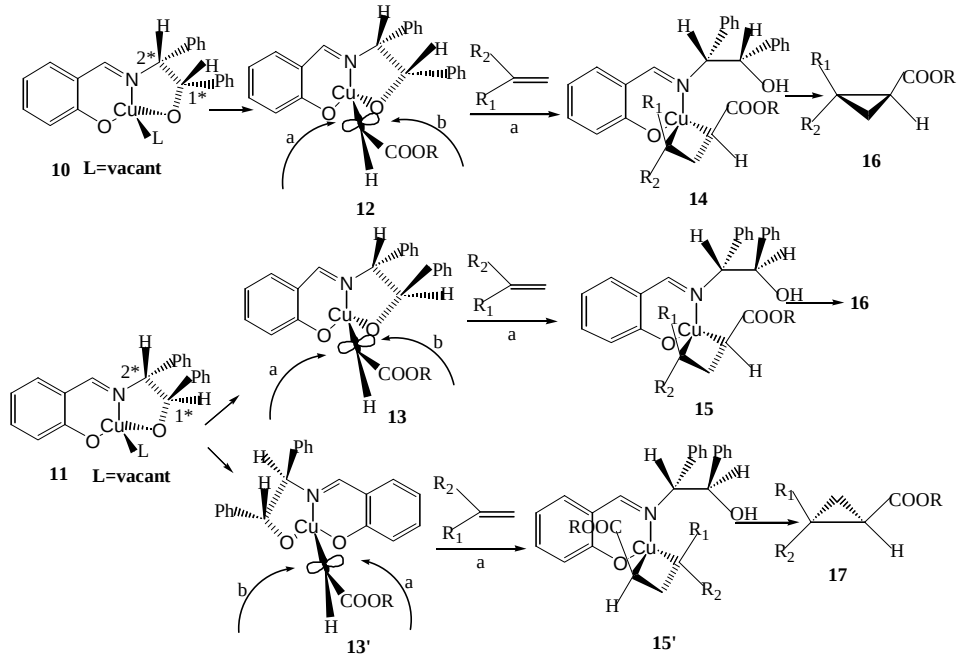
[a]Same as **Table 1**. [b]Isolated yields. [c]The %e.e. of 10 was determined by HPLC (Chiracel OD column, elution with hexane/isopropanol 9.75:0.25, 0.4 ml/min). The configuration in parentheses is of the excess enatiomer, which was established on the basis of the sign of the specific rotation of the corresponding acid[1].

The similar behavior was observed when complexes **3a-d** were used to catalyze the asymmetric cyclopropanation of 1,1-diphenylethylene **7** with ethyl diazoacetate (**Table 2**). The complexes **3a** and **3b** were efficient catalyst for cyclopropanation of 1,1-diphenylethene with ethyl diazoacetate, affording high enantiomeric excesses of up to 91.8%.

A possible mechanism (**Scheme 1**) is proposed. The reactions employing the catalysts **3a** and **3c** are considered throughout the following discussions. There have been strong evidences that the actual catalyst responsible for the asymmetric induction is a mononuclear cuprous complex such as **10** and **11**, in which copper is supposed to have a tetrahedral configuration and one of four coordination sites is left vacant[5]. In the case of **10,** two phenyl groups in the catalyst are *syn*, and the alkyldiazoacetate will take the vacant site from the less hindered front side to give **12**. The carbene carbon bears sp^2 hybridization and the out side orientation of the alkoxycarbonyl group is selected to minimize steric repulsion. The olefin will approach the carbene from the less hindered **a** side and the metallacyclobutanes **14** is the main product. The copper atom forms a bond with α-carbon atom of the alkene rather than β-carbon atom, because the carbonium ion at the α-position is more stable than that of the β-position. Collapse of the metallacycles **14** into the products **16** regenerates the true catalyst **10** to complete a catalysis cycle. In the case of **11**, the difference of the steric repulsion from rear or front is not obvious. Alkyldiazoacetate can approach the copper either from rear or front, thus **13** and **13′** are given. The **13** is somewhat predominant for the C_2 lives a little closer to the alkoxycarbonyl group of carbene than C_1. The olefin will attack **13** or **13′** in the similar manner as that of **10** to give **16** and **17** (**16** somewhat predominant). This model explains the most of the results that we derived and reported early very well: The configuration of C_2 of the catalyst dominates the configuration of predominant cyclopropanes by governing the side the alkyldiazoacetate approach to the catalyst. A bulky group on C_1 is in favor of the enantioselectivity[6]. The enantioselectivity is diminished when two phenyl groups are *anti* in the catalyst such as **3c** and **3d,** since the difference for the diazoacetates to approach the catalyst from rear or front is diminished. If R_2 is a more bulky group than R_1, and the R_2 is at the bottom, the approach of the

olefins to the carbene is easier and the metallacycles are more stable. This leads to preference of the *trans* cyclopropane in the most cases and a bulky group in the diazoacetates favors the diastereoselectivity.

Scheme 1



Acknowledgment

This work was supported by the National Natural Science Foundation of China (No.29872035).

References

1. D. A. Evans, K. A. Woerpel, M. M. Hinman, M. M. Faul, *J. Am. Chem. Soc*., **1991**, *113***,** 726.
2. I. Seiji, T. Futoshi, T. Yasunori, N. Hisao, *Chem. Commun*., **2001**,59.
3. H.Nozaki, S.Moriuti, T. Nagase, *Tetra. Lett*., **1966**, 5239.
4. T. Aratani, Y. Yoneyoshi, T. Nagase, *Tetra. Lett*., **1975**,1707.
5. T. Aratani, *Pure & Appl. Chem*., **1985**, *57***,** 1839.
6. Z. N. Lin, Z. Zheng, H.L.Chen, *Tetrahedron: Asymmetry*, **2000**, *11*, 1157.
7. Z. N. Li, Z. Zheng, B.S.Wan, H. L. Chen, *J. Mol. Catal. A: Chem.*, **2001**, *165*, 67
8. L.Cai, H.Mahmoud, Y.Han, *Tetrahedron: Asymmetry*., **1999**, *10*, 411.
9. J.Weijlard, K.Pfister, S.Edward, *J. Am. Chem. Soc*., **1951**, *73*, 1216.
10. T.Aratani, Y. Nakanisi, H. Nozaki, *Tetrahedron*, **1970**, *26*, 1675.

Received 7 March, 2002