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C_2-Symmetric 1,2-Diamine/Copper(II) Trifluoromethanesulfonate Complexes as Chiral Catalysts. Asymmetric Cyclopropanations of Styrene with Diazo Esters

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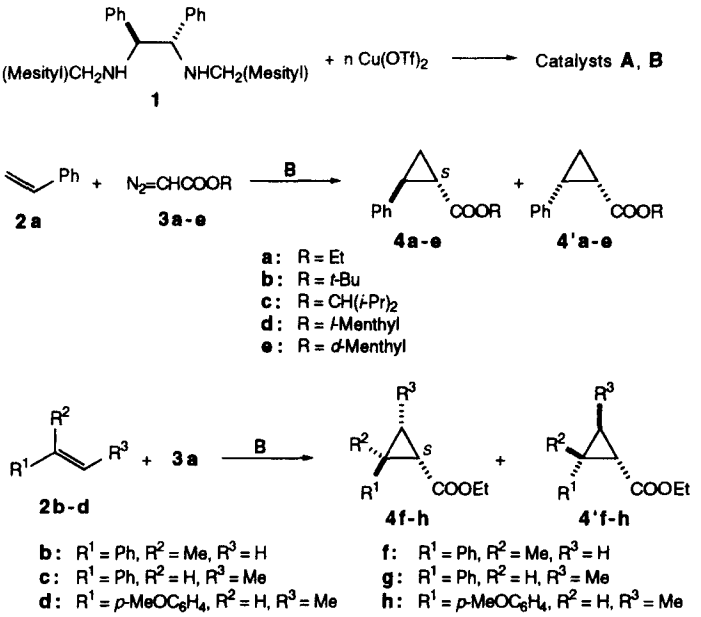
Abstract: *Styrene and diazo esters react in the presence of copper(II) trifluoromethanesulfonate (1 mol%) and (1S,2S)-N,N'-di(mesitylmethyl)-1,2-diphenyl-1,2-ethanediamine (2 - 3 mol%) to give 2-phenyl-1-cyclopropanecarboxylates in good to excellent optical yields. This reaction has been applied to the synthesis of chrythanthemic acid.*

Copper-catalyzed asymmetric cyclopropanation using both achiral diazo esters and alkenes offers one of the most direct and effective preparation method of optically active cyclopropanecarboxylic acids which often constitute key structures of organic compounds having high biological activities.[1] Chiral copper catalysts ever used in a variety of stereoselective asymmetric cyclopropanations include nitrogen ligands such as 2-(salicylideneamino)ethanols (Aratani),[2] C_2-symmetric bispyrrolines (Pfaltz),[3] bisoxazolines (Masamune and Evans),[4,5] bisimidazolines (Pfaltz),[6] and bipyridines (Katsuki).[7] Since the discovery of effective chiral copper catalysts reported by the Aratani's research group,[2a] Pfaltz has introduced C_2-symmetric chiral semicorrin ligands in 1988,[3a,b] and bisoxazolines were a little later added by the groups of Masamune[4] and Evans.[5] It is now recognized that bisoxazoline chiral ligands have powerful synthetic potentials from a viewpoint of their ready availability from β-amino alcohols, high chiral induction and enhanced reactivity of the modified metal catalysts in asymmetric cyclopropanations.[8]

All the chiral ligands previously applied to copper-catalyzed asymmetric cyclopropanations are limited to either imine alcohols or bisimine type functionalities. These ligands belong to soft bases whose complexes with highly reduced transition metals are mainly stabilized by the back donation of metal electrons to the ligand. In the course of our study on the synthetic utilization of C_2-symmetric 1,2-diamine chiral auxiliaries,[9] we became aware of a possibility that these 1,2-diamine ligands would be utilized for the effective chiral modification of copper catalysts in asymmetric cyclopropanations. To the best of our knowledge, however, successful employment of such strongly basic ligands for copper catalysts is unprecedented. Accordingly, our interest has been focussed on a point whether these 1,2-diamine-modified coppers will be able to show a sufficient catalytic activity in cyclopropanations using diazo esters. Next important is how effective these catalysts will be in chirality induction.

In the present communication, we would like to report the preparation of new chiral copper catalysts bearing secondary 1,2-diamine ligands. These copper catalysts were employed in the asymmetric cyclopropanations of alkenes with diazo esters to show a catalytic activity high enough to decompose diazo esters even below room temperature. Satisfactory levels of optical purities were observed in the cyclopropane ester derivatives as products.

(1*S*,2*S*)-*N*,*N*'-Di(mesitylmethyl)-1,2-diphenyl-1,2-ethanediamine (**1**) as C_2-symmetric 1,2-diamine, which was first synthesized by Corey for the purpose of enantio-controlled *cis*-dihydroxylation with osmium tetroxide,[10] has two identical secondary amine moieties in the same molecule. This diamine **1** provided different types of isolable complexes with copper(II) trifluoromethanesulfonate [$Cu(OTf)_2$] depending upon the molar ratio of **1**/$Cu(OTf)_2$ employed: With an equimolar amount of diamine ligand **1**, the paramagnetic blue complex **A** (mp 158 - 160 °C) was obtained. On the other hand, when two equimolar amounts of **1** were used, the diamagnetic colorless complex **B** (mp 243 - 244 °C, purified by crystallization from dichloromethane - hexane) was produced from the blue solution. The former complex **A** became diamagnetic when treated with phenylhydrazine for preactivation (color changes from blue to orange). The resulting orange solution showed a high catalytic activity in the reaction between ethyl diazoacetate and styrene (24% ee for the *trans*-isomer of the corresponding cyclopropane ester). The catalyst **B** showed a higher catalytic activity and a higher enantioselectivity in the same reaction (60% ee for the *trans*-isomer).



Scheme 1

Cyclopropanations using styrene (**2a**) and diazo esters **3a-e** were performed by the following simple procedure in which the copper catalyst was in situ prepared pripor to the reaction (Scheme 1): Excess (1*S*,2*S*)-diamine **1** (2 to 3 mol%) was treated with $Cu(OTf)_2$ (1 mol%) under nitrogen in dry 1,2-dichloroethane at room temperature for 10 min during which time the solution became deep blue. Catalyst **B** is most likely involved in this solution because of the molar ratio of **1**/$Cu(OTf)_2$ used. Phenylhydrazine (1.2 mol%) was slowly added as a reducing activator and then the mixture was stirred for additional 10 min. In this procedure the blue color changed to orange. After a large excess amount of styrene (5 to 10 equivalents) was introduced, a diazo ester was added by use of a syringe at such a rate that nitrogen gas was evolved steadily. When the reaction was complete (monitored by TLC), the reaction mixture was filtered through a short silica gel column to remove the excess styrene. Determination of the *cis*/*trans* ratios of 2-phenyl-1-

cyclopropanecarboxylates **4a-e** + **4'a-e** was based on the capillary column GLC. Optical yield of each isomer was mainly determined by the chiral HPLC using a Daicel chiral column OJ with hexane - 2-propanol = 9:1 v/v. All the results are summarized in Table 1.

Since diazo esters bearing a bulky ester moiety are known to show high enantioselectivities in the copper catalyzed cyclopropanations of styrene,[4a,b,5a,11] ethyl **3a**, *t*-butyl **3b**, 1-isopropyl-2-methylpropyl **3c**, and *d*-menthyl diazoacetates **3e** were employed to give the *trans*-isomers **4a-c,e** of 2-phenyl-1-cyclopropanecarboxylates as major diastereomers with 72 - 88% ee of enantioselectivities (entries 1-3 and 6). Although optical yields of *cis*-cyclopropanecarboxylates **4'** were lower than those of the *trans*-isomers, the absolute configuration at α-position was *S* for both diastereomers.[12] This indicates that the same enantioface of the intermediary carbenoids has been mainly involved in the reactions leading to the both diasteromers. A rather unexpected low optical and *trans/cis* selectivity was observed in the reaction of *t*-butyl ester **3b** (entry 2), no satisfactory explanation being available. Optical purities of **4b,c,e** were estimated after the two step derivatization to the ethyl ester **4a**, which consists of the trifluoroacetic acid-catalyzed hydrolysis followed by the esterification with ethanol, thionyl chloride, and triethylamine at a low temperature.

l-Menthyl diazoacetate (**3d**) provided the best optical yield where 94% ee was observed in the reaction with styrene at room temperature (entry 4) and 96% ee in the reaction at 0 °C. The relatively low optical yield was observed in the reaction of *d*-menthyl ester **3e** (entry 6), indicating that a slight double chiral induction operated as a matching pair in the reaction of **3d**.

Such high catalytic activities as well as satisfactory optical inductions is noteworthy in the present first example of asymmetric cyclopropanations on the copper catalysts **B** carrying strongly electron-donating 1,2-diamine ligand(s).[13] Alkenes other than styrene could be employed as well, 2-phenylpropene (**2b**), (*E*)-1-phenylpropene (**2c**), and (*E*)-1-(*p*-methoxyphenyl)propene (**2d**), all disubstituted styrene type alkenes, being included (entries 7-9). In these cases, poor *cis/trans* ratios were compensated with satisfactory chemical and optical yields.

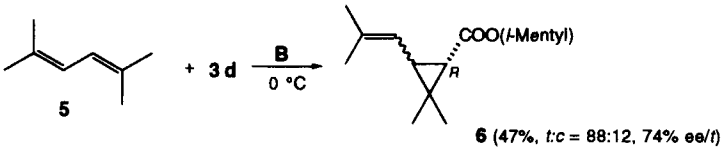
Table 1. Copper Triflate/Diamine Complex-Catalyzed Asymmetric Cyclopropanations of Alkenes **2a-d** with Diazo Esters **3a-e**[a]

Entry	Alkene **2**	Diazo Ester **3**	**1**/Cu(OTf)$_2$	Temp/°C	Product (yield/%, *t*:*c*[b])	% ee/*t*[c]	% ee/*c*[c]
1	**2a**	**3a**	3	rt	**4a** + **4'a** (88, 74:26)	86 (*S*)	58 (*S*)
2	**2a**	**3b**	3	rt	**4b** + **4'b** (55, 83:17)	72[d] (*S*)	ND
3	**2a**	**3c**	3	rt	**4c** + **4'c** (77, 89:11)	86[d] (*S*)	ND
4	**2a**	**3d**	3	rt	**4d** + **4'd** (86, 91:9)	94 (*S*)	ND
5	**2a**	**3d**	3	0	**4d** + **4'd** (50, 93:7)	96 (*S*)	66[e] (*S*)
6	**2a**	**3e**	3	rt	**4e** + **4'e** (55, 90:10)	88[d] (*S*)	ND
7	**2b**	**3a**	3	rt	**4f** + **4'f** (98, 58:42)	84 (*S*)	74 (*S*)
8	**2c**	**3a**	2	rt	**4g** + **4'g** (49, 51:49)	52 (*S*)	ND
9	**2d**	**3a**	2	rt	**4h** + **4'h** (37, 61:39)	ND	62 (ND)

[a]All reactions were performed by using 5-10 equimolar amounts of alkenes **2** and 1 mol% of Cu(OTf)$_2$ in 1,2-dichloroethane. Diamine **1** (2 - 3 mol%) was treated with Cu(OTf)$_2$ at rt for 10 min, phenylhydrazine (1.2 mol%) and alkene **2** were introdued, and then diazoacetate **3** was slowly added. [b]Determined by GLC (SE-30). [c]Determined by HPLC (Daicel chiral column OJ with hexane - 2-propanol = 9:1 v/v). [d]Determined after acid hydrolysis and conversion to the ethyl ester **4a** + **4'a**. [e]Determined by GLC.

One synthetic application of the asymmetric cyclopropanation catalyzed by 1,2-diamine/Cu(OTf)$_2$ complex **B** offers a convenient synthetic method of the naturally occurring enantiomer of chrythanthemic acid

ester.[14] This compound is known as an acid part of pyrethroid insecticides. In the presence of the copper catalyst **B** preactivated by phenylhydrazine in 1,2-dichloroethane, 2,5-dimethyl-2,4-hexadiene was allowed to react with diazo ester **3d** at room temperature to give an 88:12 mixture of *trans*- and *cis*-isomers of (*l*)-menthyl 2,2-dimethyl-3-(2-methyl-1-propenyl)-1-cyclopropanecarboxylate (*trans*-**6** and *cis*-**6**, Scheme 2). The major product *trans*-**6**, which was obtained in 74% ee, was determined as the enantiomer of natural type (1*R*-stereoisomer).



Scheme 2

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12. Their absolute configurations were determined by comparison of optical rotations with the reported values.
13. Based on the molar ratios **1**/$Cu(OTf)_2$ used for the in situ preparation of the diamine-modified copper catalyst, the catalyst precursor involved in these cyclopropanations must be of the type **B**. However, the reactive catalyst actually involved in the reaction has not been characterized.
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