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Studies of Copper−Bisoxazoline-Catalyzed Asymmetric Cyclopropanation of 2,5-Dimethyl-2,4-hexadiene

Makoto Itagaki,*,† Katsuhisa Masumoto,† Katsuhiro Suenobu,‡ and Yohsuke Yamamoto§

Organic Synthesis Research Laboratory, Sumitomo Chemical Co., Ltd., 3-1-98, Kasugade-naka, Konohana-ku, Osaka 554-8558, Japan, Tsukuba Research Laboratory, Sumitomo Chemical Co., Ltd., 6, Kitahara, Tsukuba, Ibaraki 300-3294, Japan, and Department of Chemistry, Graduate School of Science, Hiroshima University 1-3-1, Kagamiyama, Higashi-Hiroshima, Hiroshima 739-8526, Japan

Abstract:

In the [bis{(4*R*)-(1-naphthyl)-5,5-dimethyloxazoline}/copper]-catalyzed asymmetric cyclopropanation of 2,5-dimethyl-2,4-hexadiene with *tert*-butyl diazoacetate, the effects of a counterion of the copper complex were studied. The[CuCl/bisoxazoline/Ph_3CPF_6] catalyst was found to enhance both the catalytic efficiency and the stereoselectivity (the catalyst 0.2 mol %, yield 92%, trans/cis = 88/12, 96% ee for the trans product), compared to our previously reported CuOTf/bisoxazoline catalyst. The density functional calculations were performed to elucidate the effects of the counterion as well as the effects of the gem-dimethyl groups at the 5-position on the bisoxazoline ligand.

Introduction

3-(1-Isobutenyl)-2,2-dimethyl cyclopropanecarboxylic acid (chrysanthemic acid) is a key intermediate of pyrethroid insecticides, and the (1*R*,3*R*) isomer ((+)-trans isomer)) shows the highest insecticidal activity among the four isomers of the chrysanthemate.[1−3] Therefore, we have been engaged in industrially applicable asymmetric catalysis for the cyclopropanation of 2,5-dimethyl-2,4-hexadiene (DMHD) with diazoacetate, which is one of the most efficient methods in the synthesis of the optically active chrysanthemic acid esters.[4−8] The industrially applicable process for us needs the following: (1) good enantioselectivity and trans selectivity, (2) use of a simple alkyl diazoacetate such as ethyl or *tert*-butyl diazoacetate, by which chrysanthemic acid is cheaply and readily obtained with a strong acid or a strong base from the corresponding chrysanthemic acid ester, (3) low catalyst loading (high catalyst efficiency).

Although previously reported copper catalysts **1**−**3** achieved high stereoselectivities (Scheme 1 and Table 1), high catalyst loading (1 mol %) or an industrially expensive diazoacetate (*l*-menthyl diazoacetate or dicyclohexylmethyl diazoacetate) was needed.[3,9−12] Scott et al. reported the asymmetric cyclopropanation of DMHD with *tert*-butyl diazoacetate catalyzed by the copper complex with biaryl Schiff-base ligand **4**, but the trans selectivity and the enantioselectivity were moderate (Table 1).[13]

We recently disclosed two new catalysts; a combination catalyst composed of a 5-nitro-substituted salicylaldimine−copper complex **5** with an equivalent of $Al(OEt)_3$[14] and CuOTf/2,2-bis{2-[(4*R*)-(1-naphthyl)-5,5-dimethyloxazolinyl]}-propane **6** catalyst.[15] However, although the **5**/$Al(OEt)_3$ catalyst shows high catalytic efficiency (0.1 mol % catalyst, 90% yield) and achieves >90% ee of the trans product,[14] the trans selectivity still remains moderate (trans/cis = 78/22). In addition, the CuOTf/**6** catalyst achieved higher trans selectivity and enantioselectivity (trans/cis = 87/13, 96%ee for the trans product) than those with the **5**/$Al(OEt)_3$ catalyst, but the catalyst loading is high (0.5 mol %).[15] When the catalyst loading of CuOTf/**6** is low (0.2 mol %), the chemical yield, the trans selectivity, and the enantioselectivity were decreased (see Table 3).

Therefore, we needed to look for a more efficient catalyst than the CuOTf/**6** catalyst for the asymmetric cyclopropanation of DMHD with a simple alkyl diazoacetate. In this article, we especially describe the full details of the asymmetric cyclopropanation with the Cu(I)/bisoxazoline catalyst system. After the effect of the bridge moiety in the bisoxazoline ligands and the effects of a counteranion were examined, we found that the CuCl/**6**/Ph_3CPF_6 catalyst shows higher catalytic efficiency (0.2 mol %, Y 92%, trans/cis = 88/12, 96%ee for the trans product) than the CuOTf/**6** catalyst. Furthermore, density functional (DFT) calculations for the Cu(I)/**6** system were carried out to elucidate the effects of the substituents and the counteranions.

* Corresponding author. E-mail: itagakim@sc.sumitomo-chem.co.jp.
† Organic Synthesis Research Laboratory, Sumitomo Chemical Co., Ltd.
‡ Tsukuba Research Laboratory, Sumitomo Chemical Co., Ltd.
§ Hiroshima University.

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Scheme 1. **Structures of Aratani's catalyst 1, Masamune's $CuClO_4$/2 catalyst, Kanemasa's CuOTf/3 catalyst, Scott's CuOTf/4 catalyst, and Itagaki's 5/$Al(OEt)_3$ and CuOTf/6 catalysts**

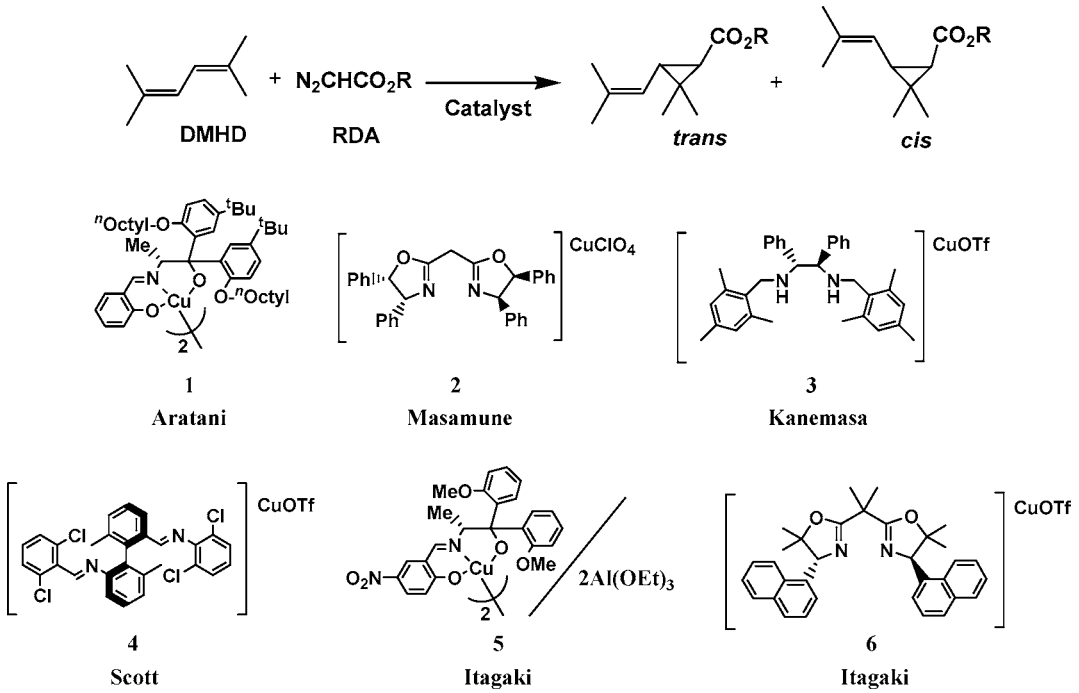

Table 1. **Previously reported asymmetric cyclopropanation of DMHD with diazoacetate (RDA) catalyzed by the copper complexes in Scheme 1**

catalyst	*T*/°C	catalyst loading[a]/ mol %	R = in RDA	yield (%)	trans/cis	ee (%) trans[b]	ee (%) cis[c]
1	40	1	*l*-menthyl	75	93/7	94	46
2	0	1	$(C_6H_{11})_2CH$	78	95/5	94	ND[d]
3	0	1	*l*-menthyl	47	88/12	88	ND[d]
4	20	1	^{t}Bu	98	75/25	72	ND[d]
5	20	0.1	^{t}Bu	90	78/22	91	62
6	0	0.5	^{t}Bu	83	87/13	96	71

[a] Based on RDA. [b] 1*R*,3*R* as a major enantiomer. [c] 1*R*,3*S* as a major enantiomer. [d] Not determined.

Results and Discussion

Effect of the Bridge Moiety in the Bisoxazoline Compounds. We recently reported that 0.5 mol % of CuOTf/**6** catalyst provided 83% yield, an 87/13 trans/cis ratio, and 96%ee at 0 °C with *tert*-butyl diazoacetate as the major (1*R*,3*R*)-isomer of the *tert*-butyl chrysanthemate in a communication.[15] However, 0.5 mol % catalyst loading still remains high for industrial application. We therefore synthesized new bis{(4*R*)-(1-naphthyl)-5,5-dimethyloxazoline} ligands (**7** and **8** in Scheme 2) and investigated the effects of the bridge moiety in the bisoxazoline for high catalytic efficiency and high stereoselectivities. Bisoxazoline ligands (**7** and **8**) were synthesized in the same manner as our recently reported procedure.[15] The results of asymmetric cyclopropanation of DMHD with *tert*-butyl diazoacetate are shown in Table 2, using 0.5 mol % catalyst at 0 °C. In comparison with the CuOTf/**6** catalyst (entry 1), the copper-methylene-bridged-bisoxazoline **7** catalyst slightly decreased in both the trans/cis ratio and the enantioselectivity (entry 2), while the CuOTf/cyclopropylidene-bridged-bisoxazoline **8** catalyst provided almost the same stereoselectivities as the CuOTf/isopropylidene-bridged bisoxazoline **6** catalyst (entries 1 and 3).

Effect of a Counterion in the Copper(I)−Bisoxazoline Complex on the Catalytic Activity and Stereoselectivity. Since successful results were not obtained by change of the bridge moiety in the bisoxazoline ligands, we focused on the effects of counterions in the Cu(I)/**6** catalyst system. In general, CuOTf is often used as a catalyst precursor for the copper−bisoxazoline-catalyzed asymmetric cyclopropanation.[7] However, Evans' research group demonstrated that the counterions of the Cu(II)−bisoxazoline complex catalyst remarkably affected the reaction rate in a Lewis acid catalyzed Diels−Alder reaction and that [Cu(II)−bisoxazoline]$(SbF_6)_2$ shows higher reactivity than Cu(II)−bisoxazoline]$(OTf)_2$.[16] In addition, Fraile et al. studied counterion effects in the asymmetric cyclopropanation of styrene catalyzed by Cu(I)- or Cu(II)−bisoxazoline catalyst systems.[17] We therefore prepared Cu(I)/**6** complex catalysts with various kinds of counterions (**X**) as shown in Scheme 3 and examined the chemical yield and the stereoselectivities for the cyclopropanation of DMHD.

Shown in Table 3 are the results of cyclopropanation of DMHD with *tert*-butyl diazoacetate at 0 °C using the Cu(I)/**6** catalysts. Under 0.5 mol % catalyst loading, CuCl/**6**/$AgPF_6$ and CuCl/**6**/$AgSbF_6$ provided higher chemical yield (87%) and slightly higher trans selectivity (*t*/*c* = 88/12) than CuOTf/**6** (83%, *t*/*c* = 87/13 (entries 1, 4, and 5). Meanwhile,

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Scheme 2. **Structures of bisoxazoline ligands 7 and 8**

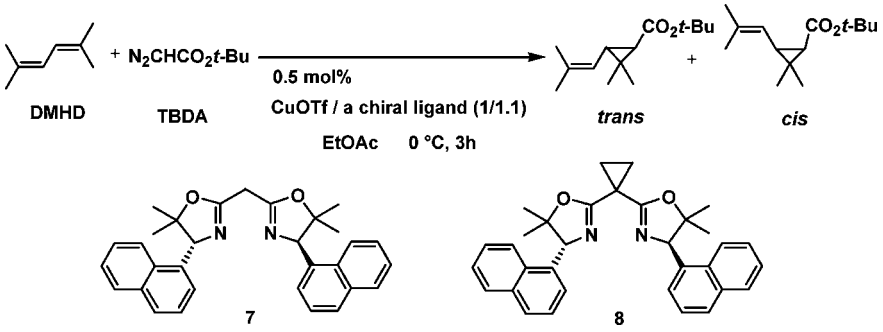
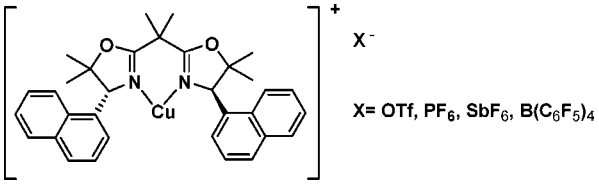


Table 2. **Asymmetric cyclopropanation of 2,5-dimethyl-2,4-hexadiene (DMHD) with *tert*-butyl diazoacetate (TBDA) catalyzed by copper−bisoxazoline complexes**

entry	ligand in Cu-cat.	solvent	*T*/°C	yield (%)	trans/cis[b]	ee[c] (%) trans[d]	ee[c] (%) cis[e]
1	**6**	EtOAc	0	83	87/13	96	71
2	**7**	EtOAc	0	84	85/15	90	60
3	**8**	EtOAc	0	80	87/13	95	70

[a] Based on TBDA and determined by GC analysis with *n*-decane as an internal standard (DB-1, 30 m × 0.25 mm ID, 0.25 mm film, column temp 100 °C). [b] Determined by GC analysis (DB-1, 30 m × 0.25 mm ID, 0.25 mm film, column temp 100 °C). [c] Determined by GC analysis (DB-210, 30 m × 0.25 mm ID, 0.25 mm film, column temp 115 °C) after transformation into *l*-menthyl chrysanthemate. [d] 1*R*,3*R* as a major enantiomer. [e] 1*R*,3*S* as a major enantiomer.

Scheme 3. **Tentative structures of [Cu(I)/6]X complexes**



Ph_3CPF_6 was used in place of $AgPF_6$, because Ph_3CPF_6 is much easier to handle in air for the catalyst preparation than $AgPF_6$. As a result of the use of Ph_3CPF_6, a higher chemical yield (91%) with *t*/*c* = 88/12 and 96%ee for the trans product was obtained than that with the use of $AgPF_6$ (entries 4 and 6). Subsequently, [Cu/**6**]$B(C_6F_5)_4$ from $Ph_3CB(C_6F_5)_4$ provided the highest chemical yield, but both the trans selectivity and the enantioselectivity were decreased (entry 9).

When the catalyst loading was reduced from 0.5 mol % to 0.2 mol % in the case of CuOTf/**6**, both the chemical yield and the stereoselectivities were decreased (entries 1 and 2). Meanwhile, it should be noted that 0.2 mol % of CuCl/**6**/Ph_3CPF_6 catalyst loading gave the same level of the yield and stereoselectivity as those with 0.5 mol % (entries 6 and 7) and that the yield and stereoselectivity were just slightly decreased under 0.1 mol % CuCl/**6**/Ph_3CPF_6 catalyst, compared to 0.5 mol % (entry 8). These results show that Cu(I)/bisoxazoline with the PF_6 complex has a higher catalytic efficiency for asymmetric cyclopropanation of DMHD.

Theoretical Study on the Effect of the Introduction of *gem*-Dimethyl Groups at the 5-Position on the Oxazoline Moiety. We already disclosed that the introduction of *gem*-dimethyl groups at the 5-position on the bisoxazoline moiety enhances trans selectivity and enantioselectivity (for example, in the case of $N_2CHCO_2{}^tBu$: 2,2-bis{2-[(4*R*)-phenyloxazolinyl]}propane (trans/cis = 80/20, ee of trans = 80%) vs 2,2-bis{2-[(4*R*)-phenyl-5,5-dimethyloxazolinyl]}propane (trans/cis = 84/16, ee of trans = 88%)).[15] To clarify the effects of the *gem*-dimethyl groups at the 5-position of the oxazoline ring in the copper−bisoxazoline catalyst, DFT calculations employing simplified models of the Cu/bis{(4*R*)-phenyloxazolinyl}methane complex and the Cu/bis{(4*R*)-phenyl-5,5-dimethyloxazolinyl}methane complex were carried out. Based on theoretical studies about the copper-catalyzed cyclopropanation with diazo compounds reported by several groups[18−20] including us,[21] the catalytic key intermediates for determining the stereoselectivities can be considered to be a copper−bisoxazoline−carbene complex. Scheme 4 shows the most energetically favored conformation of **carbene A** for the unsubstituted bisoxazoline and **carbene B** for the 5,5-*gem*-dimethyl substituted bisoxazoline based

Table 3. **Asymmetric cyclopropanation of DMHD with *tert*-butyl diazoacetate[f] (TBDA) catalyzed by Cu(I)/6 complexes with various kinds of counterions with in EtOAc at 0 °C**

entry	catalyst system	catalyst mol %	yield[a] (%)	trans/cis[b]	ee[c] (%) trans[d]	ee[c] (%) cis[e]
1	CuOTf/**6**	0.5	83	87/13	96	71
2	CuOTf/**6**	0.2	72	85/15	89	61
3	$Cu(CH_3CN)_4PF_6$/**6**	0.5	82	87/13	95	70
4	CuCl/$AgPF_6$/**6**	0.5	87	88/12	96	74
5	CuCl/$AgSbF_6$/**6**	0.5	88	88/12	94	73
6	CuCl/Ph_3CPF_6/**6**	0.5	91	88/12	96	74
7	CuCl/Ph_3CPF_6/**6**	0.2	92	88/12	96	71
8	CuCl/Ph_3CPF_6/**6**	0.1	87	87/13	93	67
9	CuCl/$Ph_3CB(C_6F_5)_4$/**6**	0.5	94	82/18	85	61

[a] Based on TBDA and determined by GC analysis with *n*-decane as an internal standard (DB-1, 30 m × 0.25 mm ID, 0.25 mm film, column temp 100 °C). [b] Determined by GC analysis (DB-1, 30 m × 0.25 mm ID, 0.25 mm film, column temp 100 °C). [c] Determined by GC analysis (DB-210, 30 m × 0.25 mm ID, 0.25 mm film, column temp 115 °C) after transformation into *l*-menthyl chrysanthemate. [d] 1*R*,3*R* as a major enantiomer. [e] 1*R*,3*S* as a major enantiomer. [f] TBDA was added to the solution containing DMHD and the catalyst over 3 h at 0 °C.

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Scheme 4. **Minimized structures of the unsubstituted bisoxazoline−copper−carbene complex (carbene A) on the left side and the *gem*-dimethyl substituted bisoxazoline−copper−carbene complex (carbene B) on the right based on the DFT calculations (B3LYP/6-31G(d))**

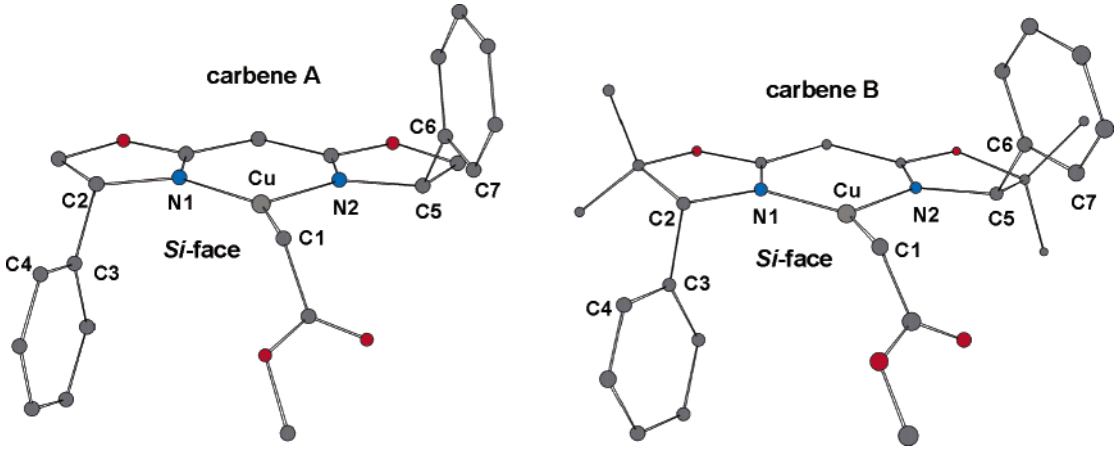

Table 4. **Calculated dihedral angles (deg) for carbene A and carbene B**

parameter	**carbene A**	**carbene B**
N1−C2−C3−C4	121.3	140.0
N2−C5−C6−C7	116.1	34.8

on the DFT calculations. It is noted that an attack of DMHD at the carbene carbon on the *Si*-face side produces the (1*R*)-chrysanthemate.

The electronic energy barriers of rotation for the C2−C3 bond on each carbene complex **A** and **B** were calculated (B3LYP/6-31G(d)). The calculated energy barriers are found to be 9 kcal/mol for the **carbene A** and 50 kcal/mol for the **carbene B**.

These results indicated that the conformation is relatively rigid especially in **carbene B** and that the most stable conformation in the carbene complex determines the stereoselectivities. Thus, the dihedral angles of the copper carbene complexes **A** and **B** with the most favored conformation are summarized in Table 4. It is clear that the dihedral angle N1−C2−C3−C4 in **carbene B** (140.0°) is remarkably larger than that of **carbene A** (121.3°). These results suggest that the *Si*-face side of the carbene carbon in **carbene B** might be more spacious than that in **carbene A** and that the energy of the transition state in the reaction of **carbene B** with the diene on the *Si*-face side could be more stabilized than that of **carbene A**. Consequently, the higher selectivity for the (1*R*,3*R*) isomer could be attributed to the introduction of the *geminal*-dimethyl groups in the case of **carbene B** when compared with **carbene A**.

Calculations of the Structural Parameters of the [Copper−Carbene]OTf and of [Copper−Carbene]PF_6. Comparisons of LUMO energy on the carbene carbon between the copper carbene complex with OTf and that with PF_6 were performed based on the DFT calculations (B3LYP/6-31G(d)) employing the simplified models (ligand: an unsubstituted bisoxazoline at the 5-position), in which the counterion is assumed to coordinate to the copper atom. Shown in Scheme 5 is a minimized structure of the [copper−carbene]OTf complex (**carbene C**) on the left side and the [copper−carbene]PF_6 complex (**carbene** D) on the right.

Scheme 5. **Minimized structures of the [copper−carbene−bisoxazoline]OTf complex (carbene C) and the [copper−carbene−bisoxazoline]PF_6 complex (carbene D) based on the DFT calculations (B3LYP/6-31G(d))**

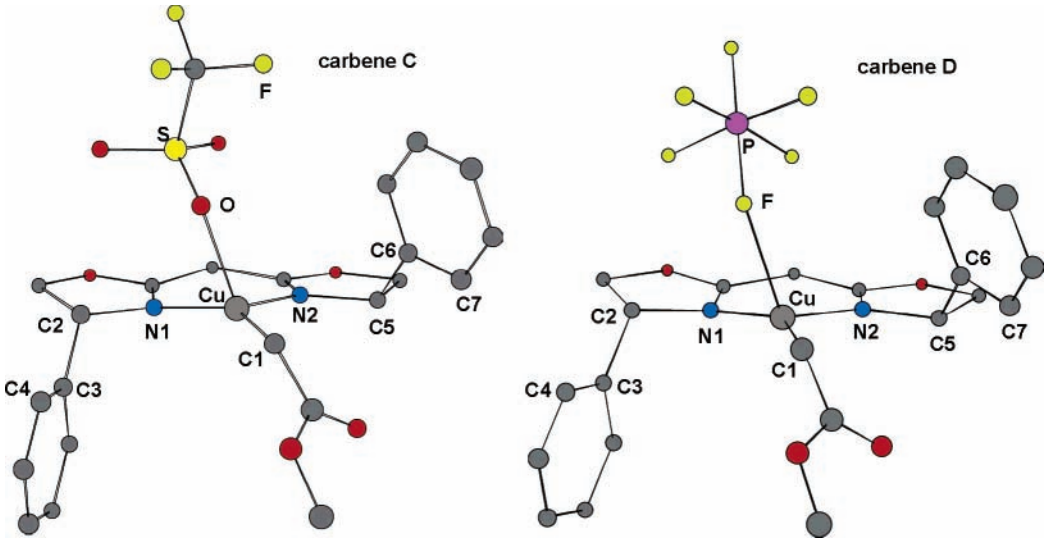

Table 5. **Calculated energies of LUMO (eV) on the C1 and bond distances (Å) for the [copper−carbene]OTf complex and the [copper−carbene]PF6 complex**

parameter	carbene C	carbene D
LUMO	−2.6789	−3.0050
Cu−C1	1.795	1.786
Cu−N1	1.974	1.950
Cu−N2	1.946	1.929

Subsequently, structural parameters of those complexes are summarized in Table 5.

As a result, the LUMO energy of **carbene D** is found to be lower than that of **carbene C** (−2.6789 eV for OTf and −3.0050 eV for PF_6). These results are consistent with the fact that the copper carbene complex with PF_6 has higher electrophilic reactivity toward DMHD than that with OTf. Furthermore, **carbene D** is found to be a more compact complex than **carbene C**, because the bond distances (Cu−C1, Cu−N1, and Cu−N2) around the copper atom in **carbene D** were shorter than those in **carbene C**. The enhancement of the stereoselectivities of the cyclopropanation might be due to the fact that the chiral carbon in the bioxazoline ligand of **carbene D** could be closer to the carbene carbon than that of **carbene C**.

Conclusions

In conclusion, the effects of the structure of the bridge moiety in the bisoxazoline ligands and a counterion X in the [Cu(I)/bisoxazoline]X complex catalysts were examined for asymmetric cyclopropanation of 2,5-dimethyl-2,4-hexadiene with *tert*-butyl diazoacetate. The structure of the bridge moiety did not affect the catalyst efficiency nor the stereoselectivities. Meanwhile, the Cu/2,2-bis{(4*R*)-(1-naphthyl)-5,5-dimethyloxazoline}propane **6** /Ph_3CPF_6 catalyst prepared in situ was found to show higher catalytic efficiency and slightly higher stereoselectivities than the CuOTf/**6** catalyst. The CuCl/**6**/Ph_3CPF_6 catalyst gave 92% yield, an 88/12 trans/cis ratio, and 96%ee for the trans product using 0.2 mol % at 0 °C. A theoretical study with DFT calculations (B3LYP/6-31G(d)) clarified the effects of the *gem*-dimethyl groups at the 5-position on the oxazoline ring and the counterion in the copper(I)−carbene complex.

Experimental Section

General. Unless otherwise noted, all reactions were carried out under a nitrogen atmosphere. AcOEt, CH_2Cl_2, and xylene as the solvents were dehydrated by molecular sieves 4A before use. Et_3N was dried over sodium hydroxide. $Ti(O^iPr)_4$, dimethylmalonate, and 1,1-cyclopropane dicarboxylic acid dichloride were purchased from Tokyo Kasei Kogyo Co., Ltd. (TCI), and CuOTf was purchased from Aldrich. *tert*-Butyl diazoacetate was prepared according to literature prpcedure.[22] The bisoxazoline compound **6** was prepared based on our previously reported procedure.[15] (*R*)-1-Amino-1-(1-naphthyl)-2-methyl-2-propanol as the intermediate for bisoxazoline compounds **6**, **7**, and **8** was also prepared based on our previously reported procedure.[15] Optical rotations were measured on a JASCO DIP-370. Melting points were measured with a METTLER TOLEDO TYPE FP62. The absolute configurations of enantiomerically pure bisoxazolines **7** and **8** were determined by the absolute configurations of the major enantiomers of the trans products in the copper−bisoxazoline catalyzed cyclopropanation, based on the results in which the (*R*)-configured ligand **6** predominantly provided the (1*R*,3*R*)-isomer of trans chrysanthemate.

General Procedure for Preparation of Bisoxazolines (7) and (8). Preparation of *N*,*N*′-Bis[2-hydroxy-2-methyl-(1*R*)-(1-naphthyl)propyl]cyclopropane-1,1-dicarboxamide (9). A solution of (*R*)-1-amino-1-(1-naphthyl)-2-methyl-2-propanol (1.50 g, 6.97 mmol) and Et_3N (0.84 g, 8.29 mmol) in CH_2Cl_2 (13 mL) was cooled to −10 °C. 1,1-Cyclopropane dicarboxylic acid dichloride (0.58 g, 3.48 mmol) prepared by the reaction of 1,1-cyclopropane dicarboxylic acid with 2.5 equiv of $SOCl_2$ was then added dropwise over 3 min. The reaction mixture was allowed to warm to 20 °C and stirred for 7 h. Subsequently, aqueous HCl (1 N, 15 mL) was added in one portion. The organic phase was separated, washed with aqueous $NaHCO_3$ (5%, 20 mL), washed with H_2O (5 mL), dried over Na_2SO_4, and concentrated under reduced pressure to give compound **9** as a white solid which was used in the next step without further purification (1.91 g, quant). ^{1}H NMR (300 MHz, CD_3OD) δ 8.31 (d, J = 9.0 Hz, 2H), 7.85 (d, J = 9.0 Hz, 2H), 7.76 (d, J = 9.0 Hz, 2H), 7.54−7.32 (m, 8H), 5.86 (s, 2H), 4.87 (s, 4H), 1.35 (s, 6H), 1.32 (s, 4H), 0.97 (s, 6H); ^{13}C NMR (75 MHz, CD_3OD) δ 172.4, 137.6, 135.5, 134.0, 130.2, 129.2, 127.9, 127.5, 127.1, 126.8, 126.7, 125.3, 74.0, 57.2, 30.8, 29.1, 27.7, 16.4. HRMS-EI (*m*/*z*): [MH^+] calcd for $C_{33}H_{37}N_2O_4$, 525.2747; found, 525.2773.

Preparation of Bis{2-[(4*R*)-(1-naphthyl)-5,5-dimethyl-oxazolinyl]}methane (7). (*R*)-1-Amino-1-(1-naphthyl)-2-methyl-2-propanol (1.20 g, 5.57 mmol), dimethyl malonate (0.368 g, 2.79 mmol), and xylene (anhydrous, 60 mL) were charged into a Schlenk tube, and the reaction mixture was heated to reflux for 13 h. $Ti(O^iPr)_4$ (79 mg, 0.28 mmol) was then added to the solution in one portion, and the reaction mixture was refluxed for 31 h with removal of the water byproduct. After the reaction mixture was cooled to 20 °C, the solution was concentrated under reduced pressure. The resulting pale yellow oil was purified by column chromatography (alumina neutral, hexane: AcOEt = 10:1 to 2:1) to give a white solid **7**, which appeared pure by ^{1}H NMR. The solid was recrystallized from CH_2Cl_2/hexane to give a white powder (0.7 g, 54%). Mp 201.6−202.2 °C; $[\alpha]_D$ = −240 (*c* = 0.11, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95−7.87 (m, 4H), 7.77 (d, J = 9.0 Hz, 2H), 7.59−7.43 (m, 8H), 5.81 (s, 2H), 3.61 (s, 2H), 1.82 (s, 6H), 0.84 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.3, 134.9, 133.6, 131.6, 129.1, 127.8, 126.2, 125.4, 125.3, 122.7, 88.1, 73.6, 29.6, 29.1, 23.5. Anal. Calcd for $C_{31}H_{30}N_2O_2$: C, 80.49%; H, 6.54%; N, 6.06%. Found: C, 79.9%; H, 6.3%; N, 5.5%. HRMS-EI (*m*/*z*): [MH^+] calcd for $C_{31}H_{31}N_2O_2$, 463.2380; found, 463.2396.

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1,1-Bis{2-[(4*R*)-(1-naphthyl)-5,5-dimethyloxazolinyl]}-cyclopropane (8). Bisamide alcohol **9** (1.83 g, 3.49 mmol) and xylene (anhydrous, 100 mL) were charged into a Schlenk tube, and the reaction mixture was heated to reflux to dissolve the alcohol completely. $Ti(O^iPr)_4$ (99 mg, 0.35 mmol) was then added to the solution in one portion, and the reaction mixture was refluxed for 48 h with removal of the water byproduct. After the reaction mixture was cooled to 20 °C, the solution was concentrated under reduced pressure. The resulting pale yellow oil was purified by column chromatography (alumina basic, hexane/AcOEt = 4:1) to give a white solid, which appeared pure by ^{1}H NMR. The solid was recrystallized from CH_2Cl_2/hexane to give a white powder (1.23 g, 72%). Mp 54.0−56.0 °C; $[\alpha]_D = -194$ (*c* = 0.11, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94−7.86 (m, 4H), 7.78 (d, *J* = 9.0 Hz, 2H), 7.54−7.46 (m, 8H), 5.76 (s, 2H), 1.77 (s, 6H), 1.75−1.69 (m, 2H), 1.61−1.53 (m, 6H), 0.83 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.0, 135.2, 133.6, 131.6, 129.0, 127.7, 126.1, 125.5, 125.3, 122.8, 87.8, 73.2, 28.9, 23.4, 19.2, 14.6. Anal. Calcd for $C_{33}H_{32}N_2O_2$: C, 81.12%; H, 6.60%; N, 5.73%. Found: C, 80.4%; H, 6.3%; N, 5.3%. HRMS-EI (*m*/*z*): [MH^+] calcd for $C_{33}H_{33}N_2O_2$, 489.2536; found, 489.2532.

General Procedure for Cyclopropanation. CuCl (1.98 mg, 0.02 mmol), the bisoxazoline ligand **6** (0.022 mmol), and Ph_3CPF_6 (0.022 mmol) were dissolved in 5 mL of EtOAc, and the solution was stirred for 30 min. 2,5-Dimethyl-2,4-hexadiene (3.86 g, 70 mmol) was added to the solution, and the reaction mixture was cooled to 0 °C. A solution of *tert*-butyl diazoacetate (1.41 g, 10 mmol) in 5 mL of ethyl acetate was added dropwise to the solution over a period of 3 h at 0 °C, and then the mixture was further stirred at the same temperature for 0.5 h. The reaction mixture was filtered through silica gel and then analyzed by GC (DB-1, 30 m × 0.25 mm ID, 0.25 mm film, column temp 100 °C − 10 min to 250 °C) using the internal method with *n*-decane as a standard for determining the yield and trans/cis ratio. After concentration of the reaction mixture under reduced pressure, part of the residue containing 1.13 g of *tert*-butyl chrysanthemate (5 mmol) was dissolved in 10 mL of toluene. Trifluoroacetic acid (57 mg, 0.5 mmol) was then added to the solution, and the solution was refluxed for 3 h to afford chrysanthemic acid, which was analyzed by GC (DB-210, 30 m × 0.25 mm ID, 0.25 mm film, column temp 115 °C) after transformation into the *l*-menthyl chrysanthemate with $SOCl_2$, pyridine, and *l*-menthol. The absolute configurations of the products were determined by comparison of the GC elution order of the enantiomers with authentic samples.

Computational Methods

Geometry optimizations of all stable structures reported here were performed with the B3LYP hybrid density functional method implemented in the Gaussian 03 program.[23,24] The 6-31G(d) basis set was used for all atoms. Normal coordinate analysis confirmed that all stationary points discussed in this article are stable structures. Each optimized structure shown in Schemes 4 and 5 is the most stable conformer with respect to the Gibbs free energy (25 °C) among several conformers obtained for each calculation model.

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Supporting Information Available

Cartesian coordinates of stationary points of the **carbenes A**, **B**, **C**, and **D** based on the DFT calculations. This material is available free of charge via the Internet at http://pubs.acs.org.

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