New chiral dinitrogen ligands containing sp^{2}N–sp^{3}N in the enantioselective cyclopropanation of olefins

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Abstract

The dihydrodinaphthazepinyl-oxazoline ligands **3** have been synthesized and tested in the copper-catalyzed enantioselective cyclopropanation of olefins with diazoacetates. The ligands **3** were efficient in the cyclopropanations of styrene derivatives with up to 90% ee. The match of chiralities of binaphthyl and oxazoline in the ligands **3** is crucial for obtaining high enantioselectivity. The absolute configurations of cyclopropanation products were controlled mainly by the configuration of binaphthyl.
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1. Introduction

The enantioselective cyclopropanation of olefins with diazoacetates catalyzed by copper complexes bearing chiral ligands, initiated by Nozaki et al. [1], is one of the most useful reactions in the synthesis of optically active cyclopropanes [2]. Of the large number of chiral catalysts, the copper complex of dinitrogen ligands is a predominant and efficient class. Excellent dinitrogen ligands include chiral semicorrins [3], bisoxazolines [4], bipyridines [5] and binaphthyldiimines [6], etc. Most of the reported dinitrogen ligands that have been observed to induce high enantioselectivities contain sp^{2}N–sp^{2}N type of nitrogen functionalities, which are soft bases. Kanemasa

et al. have described that the C$_2$-symmetric secondary 1,2-diamine (with sp^{3}N–sp^{3}N), a hard base, also has good asymmetric induction in the cyclopropanation reaction [7]. We recently reported the synthesis of quinolinyl-dihydrodinaphthazepine (**1**) that provided the first example of efficient dinitrogen ligand with sp^{2}N–sp^{3}N in the copper-catalyzed cyclopropanation reaction [8]. In order to modify ligand **1** we prepared quinolinyl-pyrrolidine ligand **2** in which the chiral dihydrodinaphthazepine part was replaced by 2,5-dimethylpyrrolidine. It was disappointed that the ligand **2** showed a very low enantioselectivity (<20% ee) in the cyclopropanation of styrene. As a continuing modification of ligand **1**, we describe here the synthesis of ligands **3** in which the quinoline part of ligand **1** was changed to a chiral oxazoline. We expect to enhance the level of chiral discrimination of ligands **3** by finding a match of central chirality of

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oxazoline and axial chirality of binaphthyl.
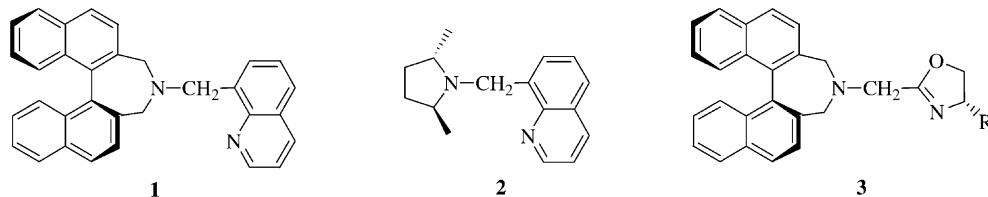
2. Experimental

2.1. General

All reactions were carried out under an N_2 atmosphere. Melting points were measured with a Yanaco MP-500 apparatus and uncorrected. ^{1}H NMR spectra were recorded on a Bruker AC-P200 instrument using tetramethylsilane as an internal standard in deuterochloroform. IR spectra were recorded as KBr plates on a Shimadzu 435 spectrophotometer. Mass spectra were measured on a VG-7070E spectrometer using a solid probe at 70 eV. High resolution mass spectra (HRMS) were measured on a APEX2 spectrometer (FAB). Enantiomeric excesses of cyclopropanation products were determined by GC analysis on a HP-6890 gas chromatography equipped with a flame ionization detector. Optical rotations were measured on a Perkin-Elmer 241 rotation apparatus. Chloroform was distilled over calcium sulfate. THF was dried and distilled from sodium-benzophenone ketyl under nitrogen.

2.2. Synthesis of ligand 2

2.2.1. (2R,5R)-2,5-Ditosyloxymethyl-1-tosylpyrrolidine (5)

To a mixture of (2R,5R)-2,5-dihydroxylmethylpyrrolidine **4** [9] (3.55 g, 19.5 mmol), dry CH_2Cl_2 (60 ml) and Et_3N (10 ml) was added dropwise a solution of *p*-toluenesulfonyl chloride (14.5 g, 76 mmol) in CH_2Cl_2 (50 ml) at $-5\,^\circ$C. The reaction mixture was stirred for 12 h at this temperature and then washed successively with dilute acid, dilute base, water and brine. After removal of solvent under reduced pressure the crude product was purified by silica gel column chromatography with petroleum ether/EtOAc (1:1) to give 9.8 g (85%) of (2R,5R)-**5** as a white

solid, m.p. 93 °C. TLC (PE/EtOAc 1:1): $R_f = 0.57$. $[\alpha]_D^{20} = +47.6$ (c 1.0, CHCl$_3$). IR (KBr): 3436, 1359, 1329, 1175, 1096, 865, 721 cm^{-1}. ^{1}H NMR: δ 1.86 (m, 2H), 2.03 (m, 2H), 2.44 (s, 3H), 2.46 (s, 6H), 3.98 (q, J = 6.3 Hz, 4H), 4.18 (q, J = 6.3 Hz, 2H), 7.25 (d, J = 8.1 Hz, 2H), 7.36 (d, J = 8.4 Hz, 4H), 7.55 (d, J = 8.1 Hz, 2H), 7.71 (d, J = 8.4 Hz, 4H). MS: 593 (42, M^+), 422 (90), 408 (54), 268 (25), 254 (26), 91 (100). Anal. calcd. for $C_{27}H_{31}S_3O_8N$: C 54.77, H 5.30, N 2.45, S 16.05. Found: C 54.64, H 5.23, N 2.36, S 16.19.

2.2.2. (2S,5S)-2,5-Dimethyl-1-tosylpyrrolidine (6)

A solution of (2R,5R)-**5** (3.97 g, 6.7 mmol) in THF (10 ml) was added dropwise to a suspension of LiAlH$_4$ (0.79 g, 21 mmol) in ether (40 ml). The mixture was stirred at 40 °C for 2 h and then was added MeOH (2.2 ml), 15% NaOH (0.9 ml) and H$_2$O (2.8 ml) successively with ice-cooling. The precipitate was filtered out and washed with CH$_2$Cl$_2$ (50 ml). The filtrates were combined and concentrated. The crude product was re-crystallized with ethyl acetate (30 ml) to give 1.47 g (87%) of (2R,5R)-**6** as a white solid, m.p. 124–125 °C. TLC (PE/EtOAc 4:1): $R_f = 0.50$. $[\alpha]_D^{20} = +40.3$ (c 1.0, CHCl$_3$). ^{1}H NMR: δ 1.33–1.44 (m, 6H), 1.67–1.85 (m, 2H), 2.0–2.16 (m, 2H), 2.397 (s, 3H), 3.95–4.15 (m, 2H), 7.26 (d, J = 8.4 Hz, 3H), 7.79 (d, J = 8.4 Hz, 2H). IR (KBr): 2973, 1601, 1495, 1345, 1212, 1158, 815. MS: 253 (4, M^+), 238 (100), 155 (54), 91 (68). Anal. calcd. for $C_{13}H_{19}NSO_2$: C 61.66, H 7.51, N 5.53, S 12.65. Found: C 61.65, H 7.50, N 5.40, S 12.76.

2.2.3. (2S,5S)-2,5-Dimethylpyrrolidine hydrochloride (7)

To a solution of (2S,5S)-**6** (0.76 g, 3 mmol) in dry DME (50 ml) was added dropwise a sodium naphthalene solution [made by naphthalene (5.6 g, 43 mmol) and sodium (0.99 g, 30 mmol) in 50 ml of DME] over

15 min at $-78\,^{\circ}$C under nitrogen. The mixture was stirred at $-78\,^{\circ}$C for 2 h and 3 ml of saturated NaHCO$_3$ was added to quench the reaction. After being acidified with concentrated HCl at $0\,^{\circ}$C the mixture was extracted with ether to remove organic impurity. The aqueous layer was treated with 40% NaOH and extracted with ether (3×50 ml). The ethereal phase was acidified with concentrated HCl. The aqueous layer was separated out and evaporated to dryness under reduced pressure to give 0.35 g (86%) of (2S,5S)-**7** as a white solid which was used directly in the next step.

2.2.4. (2S,5S)-2,5-Dimethyl-1-(8-quinolinylmethyl) pyrrolidine (2)

A mixture of 8-bromomethylquinoline (1.8 g, 8.1 mmol), (2S,5S)-2,5-dimethylpyrrolidine hydrochloride (1.1 g, 8.1 mmol), and K$_2$CO$_3$ (1.8 g, 13 mmol) in dry CH$_3$CN (25 ml) was stirred at room temperature for 3 days. The reaction mixture was then diluted with ethyl acetate (50 ml), filtered, and evaporated to dryness under reduced pressure. The crude product was purified by silica gel column chromatography with petroleum ether/EtOAc (5:1) to give 1.05 g (92%) of (2S,5S)-**2** as a yellow oil. TLC (PE/EtOAc 4:1): $R_f = 0.20$. $[\alpha]_D^{20} = +125.5$ (c 1.7, CH$_2$Cl$_2$). IR (film): 3047, 2796, 1612, 1596, 1498, 1178, 823, 791 cm^{-1}. ^{1}H NMR: δ 1.0 (d, $J = 6$ Hz, 6H), 1.36–1.48 (m, 2H), 2.0–2.18 (m, 2H), 3.18–3.40 (m, 2H), 4.28 (d, $J = 15.6$ Hz, 1H), 4.70 (d, $J = 15.6$ Hz, 1H), 7.42 (d, $J = 7.5$ Hz, 1H), 7.54 (t, $J = 8.1$ Hz, 1H), 7.72 (d, $J = 7.5$ Hz, 1H), 7.99 (t, $J = 7.5$ Hz, 1H), 8.16 (dd, $J = 1.5$ Hz, 8.1 Hz, 1H), 8.93 (dd, $J = 1.5$ Hz, 8.1 Hz, 1H). ^{13}C NMR: δ 17.7 (CH$_3$), 17.9 (CH$_3$), 31.4 (CH$_2$), 31.5(CH$_2$), 45.9 (CH$_2$), 55.7 (CH), 120.6/126.0/126.5/128.1/128.9/136.4/138.5/146.4/149.1 (aromatic). MS: 240 (9, M^+), 197 (25), 183 (27), 156 (32), 155 (50), 143 (100), 142 (58), 98 (54). HRMS (FAB): calcd. for C$_{16}$H$_{21}$N$_2$ + H: 241.1699. Found: 241.1698.

2.3. Syntheses of ligands 3

2.3.1. (S,S)-4-(4,5-Dihydro-4-phenyloxazol-2-ylmethyl)-3,5-dihydrodinaphth[2,1-c:1',2'-e]-azepine, (S,S)-3a

General procedure. A mixture of (S)-3,5-dihydro-4H-binaphth[2,1-c:1',2'-e]-azepine (230 mg, 0.78 mmol), (S)-2-chloromethyl-4,5-dihydro-4-phenyloxazole (152 mg, 0.78 mmol), and K$_2$CO$_3$ (215 mg,

1.56 mmol) in dry THF (10 ml) was stirred at room temperature for 18 h. The reaction mixture was then diluted with ethyl acetate (20 ml), filtered, and evaporated to dryness under reduced pressure. The crude product obtained was purified by silica gel column chromatography with petroleum ether/EtOAc (1:1) to give 248 mg (70%) of (S,S)-**3a** as a white solid, m.p. 54–56 $^{\circ}$C. TLC (PE/EtOAc 1:1): $R_f = 0.38$. $[\alpha]_D^{25} = +140.0$ (c 0.3, EtOAc). IR (KBr): 3036, 2905, 1638, 1451, 1148, 975 cm^{-1}. ^{1}H NMR: δ 3.36–3.52 (m, 4H), 3.89 (d, $J = 12.3$ Hz, 2H), 4.19 (t, $J = 8.4$ Hz, 1H), 4.74 (dd, $J = 8.4$ and 10.2 Hz, 1H), 5.29 (t, $J = 10.2$ Hz, 1H), 7.25–7.63 (m, 13H), 7.95 (d, $J = 8.7$ Hz, 4H). ^{13}C NMR: δ 51.9 (CH$_2$), 55.5 (CH$_2$), 69.8 (CH), 75.0 (CH$_2$), 125.6/125.8/126.6/126.8/127.0/127.5/127.6/128.1/128.4/128.8/131.4/132.8/133.3/135.1/142.1 (aromatic), 165.8 (N=C). MS: 455 (100, $M + 1$), 294 (80), 295 (32), 281 (60), 221 (40), 207 (51), 147 (35). HRMS (FAB): calcd. for C$_{32}$H$_{26}$N$_2$O + H: 455.2119. Found: 455.2118.

2.3.2. (S,R)-4-(4,5-Dihydro-4-phenyloxazol-2-ylmethyl)-3,5-dihydrodinaphth[2,1-c:1',2'-e]-azepine, (S,R)-3a

White solid, 74% yield, m.p. 60–61 $^{\circ}$C. TLC (PE/EtOAc 1:3): $R_f = 0.50$. $[\alpha]_D^{25} = +153.3$ (c 0.3, EtOAc). IR (KBr): 3036, 2905, 1638, 1451, 1148, 975, 813 cm^{-1}. ^{1}H NMR: δ 3.37–3.87 (m, 4H), 3.88 (d, $J = 12.3$ Hz, 2H), 4.19 (dd, $J = 7.5$ and 8.7 Hz, 1H), 4.68 (dd, $J = 8.7$ and 10.2 Hz, 1H), 5.65 (t, $J = 10.2$ Hz, 1H), 7.22–7.65 (m, 13H), 7.95 (d, $J = 8.7$ Hz, 4H). ^{13}C NMR: δ 52.1 (CH$_2$), 55.5 (CH$_2$), 69.9 (CH), 75.0 (CH$_2$), 125.7/125.7/126.0/126.2/126.7/126.8/127.7/127.8/128.0/128.2/128.3/128.5/128.6/128.7/128.8/129.0/141.8 (aromatic), 166.2 (N=C). MS: 455 (100, $M+1$), 294 (80), 295 (32), 281 (60), 221 (40), 207 (51), 147 (35). HRMS (FAB): calcd. for C$_{32}$H$_{26}$N$_2$O + H: 455.2119. Found: 455.2118.

2.3.3. (S,S)-4-(4,5-Dihydro-4-benzyloxazol-2-ylmethyl)-3,5-dihydrodinaphth[2,1-c:1',2'-e]-azepine, (S,S)-3b

White solid, 75% yield, m.p. 55–56 $^{\circ}$C. TLC (PE/EtOAc 1:3): $R_f = 0.42$. $[\alpha]_D^{25} = +130.0$ (c 0.3, EtOAc). IR (KBr): 3019, 2902, 1657, 1381, 1068, 975, 812 cm^{-1}. ^{1}H NMR: δ 2.70–2.80 (m, 1H),

3.08–3.37 (m, 5H), 3.72 (d, $J = 12.3$ Hz, 2H), 4.06 (dd, $J = 7.5$ and 8.7 Hz, 1H), 4.27 (t, $J = 8.7$ Hz, 1H), 4.44–4.54 (m, 1H), 7.21–7.59 (m, 13H), 7.95 (d, $J = 8.7$ Hz, 4H). ^{13}C NMR: δ 41.6 (CH_2), 51.9 (CH_2), 55.5 (CH_2) 67.4 (CH), 71.9 (CH_2), 125.4/125.6/126.5/127.3/128.0/128.2/128.5/129.3/131.2/132.8/133.1/134.9/137.5 (aromatic), 165.0 (N=C). MS: 469 (6, $M + 1$), 377 (10), 294 (100), 295 (32), 252 (8), 175 (6). HRMS (FAB): calcd. for $C_{33}H_{28}N_2O + H$: 469.2275. Found: 469.2274.

2.3.4. (S,S)-4-(4,5-Dihydro-4-isopropyloxazol-2-ylmethyl)-3,5-dihydrodinaphth[2,1-c:1′,2′-e]-azepine, (S,S)-3c

White solid, 65% yield, m.p. 58–60 °C. TLC (PE/EtOAc 1:3): $R_f = 0.51$. $[\alpha]_D^{25} = +156.7$ (c 0.3, EtOAc). IR (KBr): 3048, 2955, 1665, 1463, 1121, 983, 817 cm^{-1}. ^1H NMR: δ 0.90 (d, $J = 6.6$ Hz, 3H), 1.00 (d, $J = 6.6$ Hz, 3H), 1.80–1.89 (m, 1H), 3.26–3.42 (m, 4H), 3.76 (d, $J = 12.3$ Hz, 2H), 3.95–4.12 (m, 2H), 4.32–4.38 (m, 1H), 7.26–7.60 (m, 8H), 7.93 (d, $J = 8.7$ Hz, 4H). ^{13}C NMR: δ 18.2 (CH_3), 19.0 (CH_3), 32.6 (CH), 52.0 (CH_2), 55.6 (CH_2), 70.3 (CH_2), 72.2 (CH), 125.7/126.0/127.6/128.2/128.5/129.0/130.7/131.8/132.2 (aromatic), 165.5 (N=C). MS: 421 (5, $M + 1$), 294 (100), 295 (50), 265 (16), 127 (18). HRMS (FAB): calcd. for $C_{29}H_{28}N_2O + H$: 421.2276. Found: 421.2274.

### 2.4. General procedure for copper-catalyzed cyclopropanation

To a two-neck round-bottom flask were added Cu(OTf)·(C$_6$H$_6$)$_{0.5}$ (7.5 mg, 0.03 mmol), chloroform (20 ml) and ligand (0.06 mmol) under nitrogen. The solution was stirred at room temperature for 2 h and filtered through a syringe-tip filter (0.45 μm). After addition of alkene (10 mmol), the solution was heated to reflux, and diazoacetate (1 mmol) in chloroform (15 ml) was slowly added over 4 h at refluxing temperature. The resulting mixture was refluxed for an additional 5–10 h. The mixture was then worked up and the crude product obtained was purified by a silica gel column chromatography. All the cyclopropanes obtained are known compounds and were characterized by ^1H NMR. Diastereoselectivities (cis/trans ratio) of cyclopropanation products were measured by GC analysis using a capillary column (HP-1, 30 m × 0.32 mm i.d.). The enantiomeric excesses of cyclopropanes were determined, after re-esterification with (−)-menthol, by GC analysis using a capillary column (HP-1, 30 m × 0.32 mm i.d. or CP-SIL 24CB, 30 m × 0.25 mm i.d.).

3. Results and discussion

3.1. Synthesis of quinolinyl-pyrrolidine ligand 2

Quinolinyl-pyrrolidine 2 was synthesized from 8-bromomethylquinoline and (2S,5S)-2,5-dimethylpyrrolidine prepared readily from (2S,5S)-2,5-dihydromethylpyrrolidine (4) [9] in four steps as illustrated in Scheme 1. The tosylations of compound 4 gave fully protected product 5 in 85% yield. The reduction of compound 5 with LiAlH$_4$ followed by the deprotection of nitrogen atom with sodium naphthalene afforded (2S,5S)-2,5-dimethylpyrrolidine as a hydrochloride 7 in 75% yield. The ligand 2 was
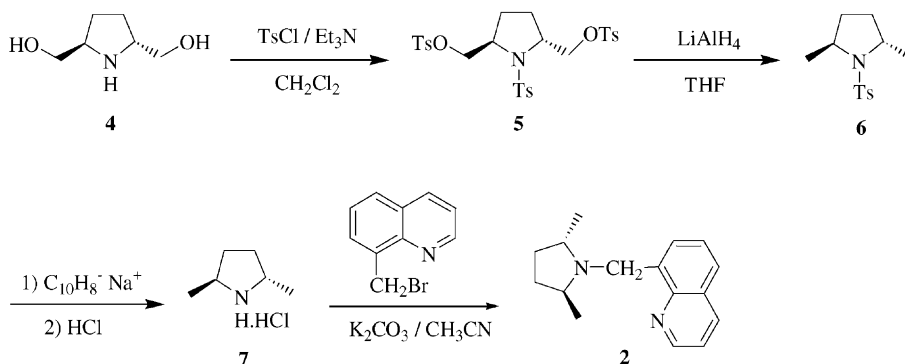
Scheme 1.
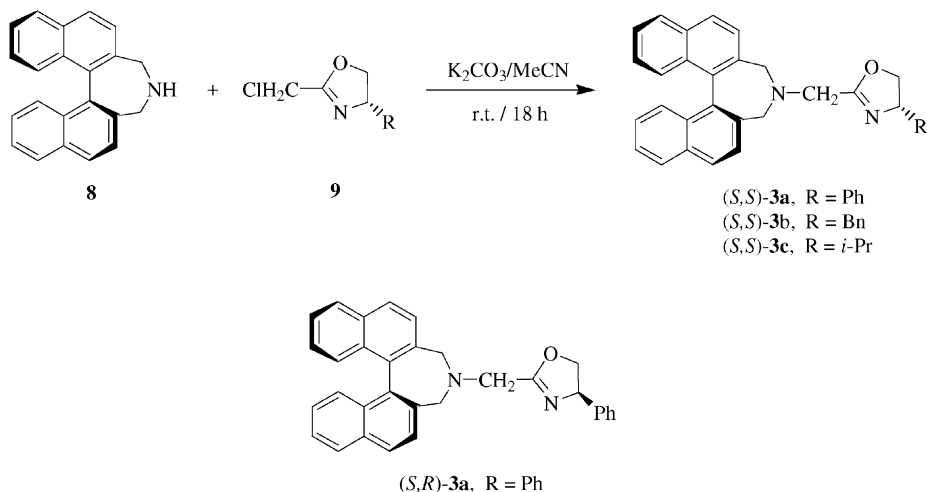
Scheme 2.

prepared by reaction of **7** with 8-bromomethylquinoline in the presence of K_2CO_3 in 92% yield.

3.2. Synthesis of dihydrodinaphthazepinyl-oxazoline ligands 3

Dihydrodinaphthazepinyl-oxazolines **3** were easily synthesized from dihydrodinaphthazepine [10] and 2-chloromethyloxazolines [11] derived from chiral amino alcohols as shown in Scheme 2. The treatment of (*S*)-**8** with (*S*)-**9** in acetonitrile in the presence of K_2CO_3 at room temperature for 18 h afforded ligands (*S*,*S*)-**3** in 65–75% yield. Ligand (*S*,*R*)-**3a** was prepared by the same method using (*R*)-**9** in 74% yield. Starting from commercially available amino alcohols, a variety of dihydrodinaphthazepinyl-oxazoline ligands with different substituents and different configurations are readily accessible in enantiomerically pure form by this route. The compounds **3** are white solids and are air stable.

3.3. Copper(I)-catalyzed asymmetric cyclopropanation

The cyclopropanation reactions were carried out in refluxing chloroform, and the catalysts were prepared

in situ from $[Cu(OTf)\cdot(C_6H_6)_{0.5}]$ and the ligands (Cu/L 1:2). The results are summarized in Table 1. By comparison with ligand **1**, ligand **2** gave much lower enantioselectivities in the cyclopropanation of styrene with ethyl diazoacetate. In a sharp contrast, ligand (*S*,*S*)-**3a** has higher enantioselectivity than ligand **1** (entries 1–3). As the volume of R′ in diazo esters increased from ethyl to dicyclohexylmethyl (DCM), the enantiomeric excesses of cyclopropanation products were further improved to 82% ee for *cis*-isomer and 74% ee for *trans*-isomer. By using (−)-menthyl diazoacetates, a double asymmetric induction effect from catalyst and substrate was observed (entry 7 versus entry 9). For all the substrates tested, (*S*,*S*)-**3a** gave much higher enantioselectivities than (*S*,*R*)-**3a**, showing that (*S*)-dihydrodinaphthazepine matched with (*S*)-oxazoline in the ligands **3**. Ligand (*S*,*S*)-**3b**, with a benzyl group at the oxazoline ring, provided a similar level of asymmetric induction to the ligand (*S*,*S*)-**3a**, whereas the bulkier isopropyl derivative (*S*,*S*)-**3c** gave slightly lower enantioselectivities (entries 11 and 12 versus entry 7).

Examination of catalyst loading demonstrated that the enantiomeric excess of cyclopropanation product is sensitive to the catalyst amount used, and a much
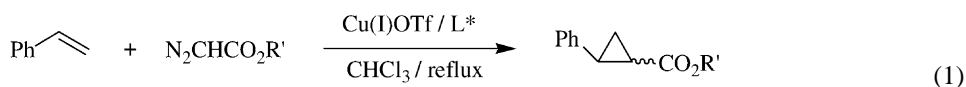

(1)

Table 1
Copper(I)-catalyzed cyclopropanation of styrene with diazoacetates[a]

Entry	Ligand	N_2CHCO_2R'	Yield (%)[b]	cis/trans[c]	cis (% ee)[d]	trans (% ee)[d]
1	**1**	R' = Et	60	28/72	43 (1S,2R)	45 (1R,2R)
2	**2**	R' = Et	88	52/48	11 (1R,2S)	15 (1S,2S)
3	(S,S)-**3a**	R' = Et	60	40/60	62 (1S,2R)	66 (1R,2R)
4	(S,R)-**3a**	R' = Et	66	39/61	18 (1S,2R)	45 (1R,2R)
5	(S,S)-**3a**	R' = DCM	82	21/79	82 (1S,2R)	74 (1R,2R)
6	(S,R)-**3a**	R' = DCM	82	17/83	69 (1S,2R)	45 (1R,2R)
7	(S,S)-**3a**	R' = (−)-menthol	96	25/75	87 (1S,2R)	83 (1R,2R)
8	(S,R)-**3a**	R' = (−)-menthol	88	25/75	74 (1S,2R)	58 (1R,2R)
9	(S,S)-**3a**	R' = (+)-menthol	81	19/81	70 (1R,2S)	78 (1S,2S)
10	(S,R)-**3a**	R' = (+)-menthol	84	20/80	29 (1R,2S)	52 (1S,2S)
11	(S,S)-**3b**	R' = (−)-menthol	93	25/75	86 (1S,2R)	81 (1R,2R)
12	(S,S)-**3c**	R' = (−)-menthol	85	23/77	77 (1S,2R)	76 (1R,2R)

[a] 3 mol% catalyst was used, the reactions were completed within 10 h.
[b] Isolated yield.
[c] Determined by GC analysis using a capillary column (HP-1, 30 m × 0.32 mm i.d.).
[d] Determined by GC analysis using a capillary column (HP-1, 30 m × 0.32 mm i.d.) (for entries 1–6, after re-esterification with (−)-menthol). The configurations were determined by chiroptical comparison with the published data [12].

lower ee was obtained in the reaction with 1 or 2 mol% of catalyst (Table 2, entries 1 and 2). In the most of our experiments 3 mol% of catalyst was used although 5 mol% catalyst provided slightly higher enantioselectivities. Investigation of the ratio of ligand to Cu(I) showed that two equivalent of ligand to Cu(I) is necessary to achieve high yield and enantioselectivity. In the optimized condition, the cyclopropanations of different styrene derivatives were carried out with good enantioselectivities (entries 5–8).

The ligands (S,S)-**3a**, (S,R)-**3a** and **1** provided the cyclopropanation products with the same absolute configurations (Table 1, entries 1, 3 and 4) implying that the configurations of products are mainly controlled by binaphthyl unit, instead of oxazoline group, in the ligands **3**. It is reasonable to believe that the
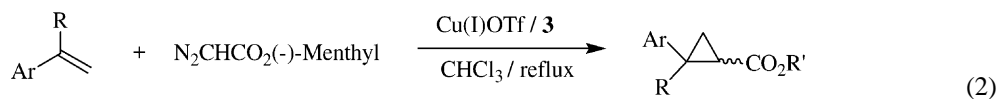
$$\text{Ar} \diagdown \text{R} \quad + \quad N_2CHCO_2(\text{-})\text{-Menthyl} \quad \xrightarrow[\text{CHCl}_3 \text{ / reflux}]{\text{Cu(I)OTf / } \mathbf{3}} \quad \text{Ar} \diagup\hspace{-0.3em}\triangle\hspace{-0.3em}\diagdown CO_2R' \quad \quad (2)$$

Table 2
Asymmetric cyclopropanation of styrene derivatives

Entry	Ligand	Catalyst (mol%)	Olefin	Yield (%)	cis/trans[a]	cis (% ee)[b]	trans (% ee)[b]
1	(S,S)-**3b**	1	Styrene	80	22/78	52	41
2	(S,S)-**3b**	2	Styrene	83	26/74	66	63
3	(S,S)-**3b**	3	Styrene	93	25/75	86	81
4	(S,S)-**3b**	5	Styrene	92	23/77	90	86
5	(S,S)-**3a**	3	4-Methylstyrene	80	30/70	87	71
6	(S,S)-**3a**	3	4-Methoxystyrene	85	33/67	79	65
7	(S,S)-**3a**	3	4-Chlorostyrene	95	29/71	90	79
8	(S,S)-**3a**	3	α-Methylstyrene	60	42/58	88	79

[a] Determined by GC analysis using a capillary column HP-1 (30 m × 0.32 mm i.d.).
[b] Determined by GC analysis using a capillary column HP-1 (30 m × 0.32 mm i.d.) for entries 1–4 and CP-SIL 24 CB (30 m × 0.25 mm i.d.) for entries 5–8. The configurations are (1S,2R) for cis-isomer and (1R,2R) for trans-isomer for entries 1–4. The configurations for entries 5–8 are not determined.
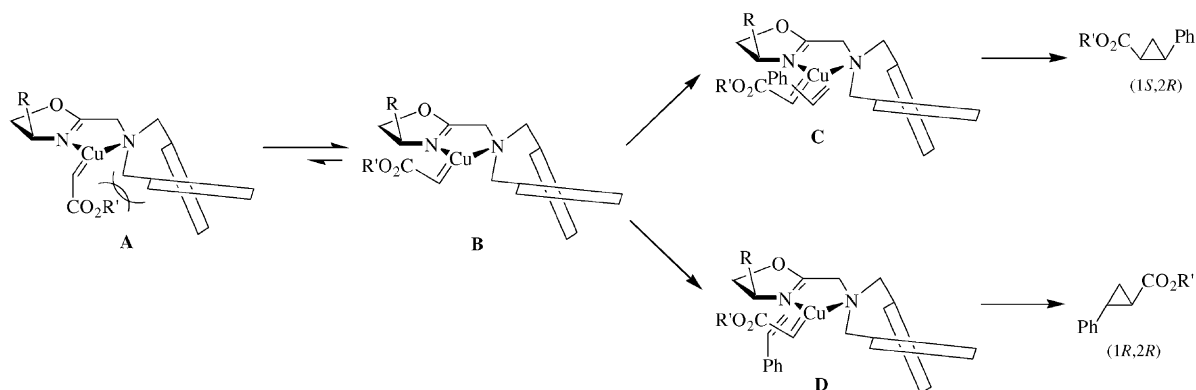
Scheme 3.

cyclopropanation reactions with ligands **3** proceeded through the same intermediates as in the reactions with ligand **1**, with carbene complex **B** being a major intermediate (Scheme 2) [8]. The olefin preferentially approaches to the carbene carbon from the direction with less steric hindrance as shown in **C** and **D** in Scheme 3 to generate *cis*-product with (1*S*,2*R*)-configuration and *trans*-product with (1*R*,2*R*)-configuration, respectively, which are consistent with the experimental results.

In summary, chiral dihydrodinaphthazepinyl-oxazolines, a new type of dinitrogen ligands containing sp^2N–sp^3N, were demonstrated to be effective in the copper(I)-catalyzed cyclopropanation of styrene and its derivatives. It is obviously necessary to modify the structure of ligands **3** substantially for improving the activities and selectivities in the cyclopropanations of styrene derivatives and other olefins. The ready access to dihydrodinaphthazepinyl-oxazolines and the variety of chiral amino alcohols available as starting materials will facilitate such studies.

Acknowledgements

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