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Bisoxazoline ligands with an axial-unfixed biaryl backbone: the effects of the biaryl backbone and the substituent at oxazoline ring on Cu-catalyzed asymmetric cyclopropanation

Wanbin Zhang,[a,*] Fang Xie,[a] Shigeaki Matsuo,[b] Yuji Imahori,[b] Toshiyuki Kida,[b] Yohji Nakatsuji[b] and Isao Ikeda[b,*]

[a]*School of Chemistry and Chemical Engineering, Shanghai Jiao Tong University, 800 Dongchuan Road, Shanghai 200240, China*
[b]*Department of Applied Chemistry, Faculty of Engineering, Osaka University, Suita, Osaka 565-0871, Japan*

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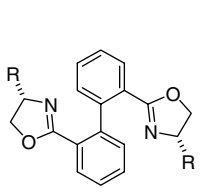
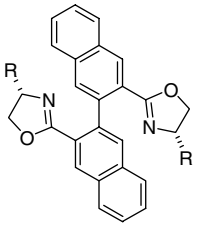
Abstract—The synthesis of novel C_2-symmetric bisoxazoline ligands with an axial-unfixed biaryl backbone and different substituents at the oxazoline ring is reported. The diastereomer equilibrium of these ligands in solution and their complexation behavior with the copper(I) ion were studied. Their application in Cu-catalyzed cyclopropanation of styrene, with diazoacetate, was carried out and the effects of the biaryl backbone and the substituent on the oxazoline ring in the catalysis were examined. The best result was obtained with the ligand having a 1,1′-binaphthyl backbone and a *t*-butyl group on the oxazoline ring, which afforded 89% de and 96% de for the *trans*- and *cis*-products of the above asymmetric cyclopropanation reaction, respectively.

1. Introduction

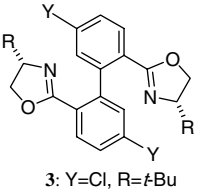
Over the last decade, chiral oxazoline ligands derived from readily available amino acids, have found widespread use in metal-catalyzed asymmetric reactions.[1] We also prepared novel oxazoline ligands with a chiral backbone, such as 1,3-dioxolane,[2] ferrocene,[3] and biaryl[4] moiety for the purpose of the development of effective asymmetric catalytic systems during recent years. By the introduction of the chiral backbone, the asymmetric induction by these ligands could be effectively controlled by a combination of the substituent on the oxazoline ring and the chiral backbone. Particularly, the oxazoline ligands with a biaryl backbone have attracted much attention and several other groups also developed this kind of ligands, independently.[5] However, one type of our bisoxazoline ligands, such as **1** is different from others,[5] and has an axis-unfixed biphenyl backbone and the two rotatory diastereomers of the ligand exist in equilibrium in solution.[4a,c] Upon complexation with a copper(I) ion however, ligand **1** afforded only one of the two possible complexes, which proved to be effective for asymmetric catalysis.[4a,c] Herein, we report the preparation, complexation and application of novel C_2-symmetric bisoxazoline ligands **2**–**4** with a biaryl backbone, such as, 2,2′-binaphthyl and a 5,5′-disubstituted 1,1′-biphenyl. Here the axis around the carbon–carbon bond between the two aryl rings is unfixed although a high activation barrier should be expected. We report also the preparation, complexation and application of novel C_2-symmetric biphenyl bisoxazoline ligands. We report **5**–**7**



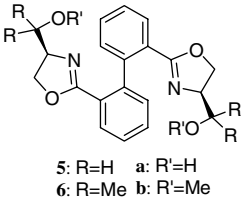
1a: R=*i*-Pr
1b: R=*t*-Bu



2: R=*t*-Bu



3: Y=Cl, R=*t*-Bu
4: Y=Ph, R=*i*-Pr



5: R=H **a**: R'=H
6: R=Me **b**: R'=Me
7: R=Et **c**: R'=Et

* Corresponding authors. Tel./fax: 86 21 54743265 (W.Z.); e-mail addresses: wanbin@sjtu.edu.cn; ikedaisa@estate.ocn.ne.jp

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with substituents of different bulkiness on the oxazoline ring.

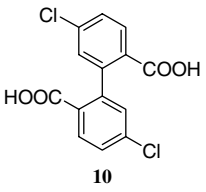
Since these ligands were expected to have the same complexation property as ligand **1**, we planned to find the best structure for this type of ligand with an axis-unfixed backbone through the investigation of the effects of the backbone and the kind of the substituent on the oxazoline ring on enantioselectivity.

2. Results and discussions

2.1. Ligand preparation

Ligand **2** was prepared from 3-amino-2-naphthoic acid and (*S*)-*t*-leucinol with ease (Scheme 1). Thus, by the diazotization of 3-amino-2-naphthoic acid with sodium nitrite followed by the coupling reaction with a Cu(I) reducing solution,[6] 2,2′-binaphthyl-3,3′-dicarboxylic acid **8** was obtained in 60% isolated yield. Then, 3,3′-bis(4-(*S*)-*t*-butyloxazolinyl)-2,2′-binaphthyl **2** was easily prepared from the dicarboxylic acid **8** and (*S*)-*t*-leucinol in 41% overall yield through the corresponding diamide **9** as the intermediate followed by the oxazoline ring closure reaction using methanesulfonyl chloride and triethylamine.[3a]

5,5′-Dichloro-2,2′-bisoxazolinyl-1,1′-biphenyl **3** was prepared from 2-amino-4-chlorobenzoic acid and (*S*)-*t*-leucinol by the same method as ligand **2** in 31% overall yield through 5,5′-dichloro-1,1′-biphenyl-2,2′-dicarboxylic acid **10** and the corresponding diamide **11** as intermediates.



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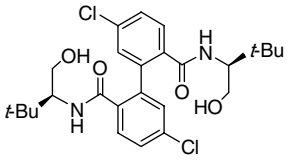
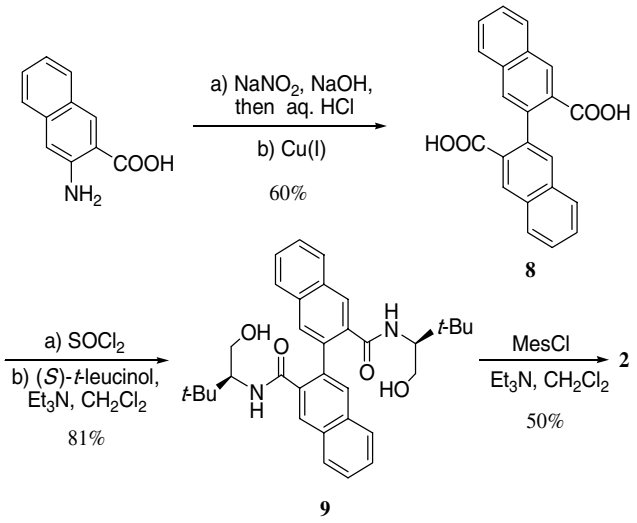


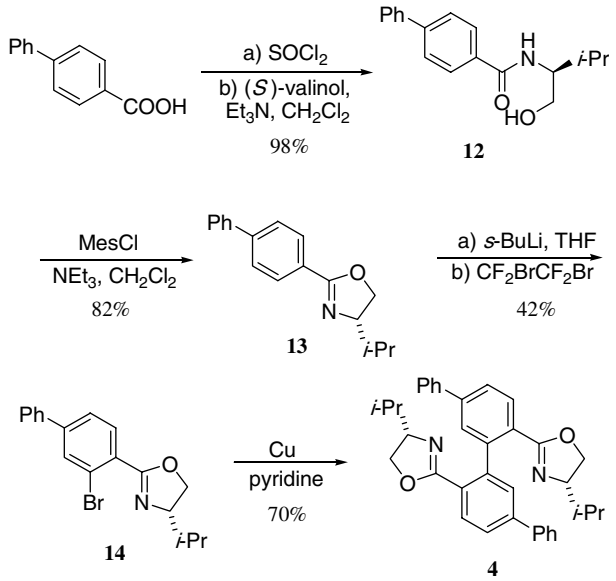
11

5,5′-Diphenyl-2,2′-bisoxazolinyl-1,1′-biphenyl **4** was prepared by a different method compared to that for ligands **2** and **3** because the corresponding 4-phenyl-2-aminobenzoic acid is commercially unavailable (Scheme 2). Thus, at first biphenyl oxazoline **13** was prepared with ease from 4-phenylbenzoic acid as a starting material through amide **12** as an intermediate. Then, ligand **4** was prepared through the intermediate 4-phenyl-2-bromophenyloxazoline **14** by *ortho*-lithiation of **13** with *s*-butyllithium followed by bromination with 1,1,2,2-tetrafluoro-1,2-dibromoethane[7] and coupling reaction with active copper powder in pyridine successively.[8]

Ligands **5**–**7** were prepared from achiral 2,2′-biphenyldicarboxylic acid and L-serine methyl ester hydrochloride (Scheme 3). Thus, a mixture of L-serine methyl ester hydrochloride, triethylamine, and 2,2′-biphenyldicarboxylic acid dichloride prepared from 2,2′-biphenyldicarboxylic acid and thionyl chloride in CH_2Cl_2 was stirred at room temperature overnight to give amide **15** in 78% yield. An attempt at oxazoline ring closure using



Scheme 1.

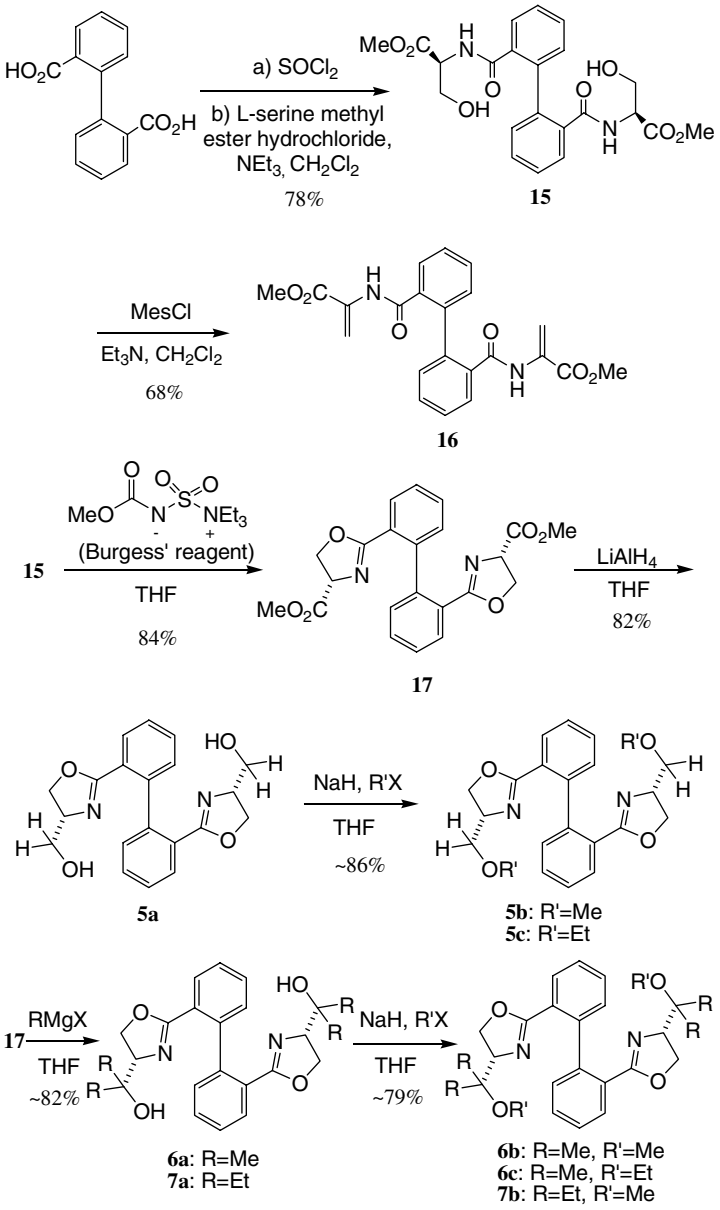


Scheme 2.

methanesulfonyl chloride in the presence of triethylamine failed, and afforded an elimination product **16** in 68% yield. However, the ring closure reaction can be carried out successfully by using Burgess' reagent [(methoxycarbonyl sulfamoyl)triethylammonium hydroxide inner salt].[9] Thus, a mixture of **15** and Burgess' reagent in THF was heated at reflux for 2 h to give bisoxazoline **17** in 84% yield. Reduction of **17** with $LiAlH_4$ in THF afforded **5a** in 82% yield, while **6a** and **7a** were afforded by the reaction of the bisoxazoline **17** with methyl- and ethylmagnesium bromide in good yields, respectively. Then the reaction of **5a**, **6a**, and **7a** with sodium hydride followed by alkylation with iodomethane and bromoethane afforded **5b**, **5c**, **6b**, **6c**, and **7b**, respectively.

2.2. Behavior of ligands in solution

As expected, all of ligands **2**–**7**, except for **5**, gave two sets of signals in ^1H NMR spectra and the ratio of the



Scheme 3.

two sets of signals changed depending on the temperature, showing that for these ligands, two rotatory diastereomers also exist in equilibrium in solution as was seen in the case of ligand **1**. In the case of **5**, the reason as to why only one set of signals was observed remains unknown. Furthermore, the dependence of the rotatory diastereomer ratio of these ligands upon temperature seems rather significant. Table 1 gives the diastereomeric ratios of ligands **1b** and **2** at different temperatures. At around room temperature, both ligands **1b** and **2** gave about the same ratio. However, at −60 °C, the ratio of ligand **2** was about 2.3 times higher than that of ligand **1b**, showing that the biaryl backbone of this type of ligand has a large effect on the equilibrium. Furthermore, while all the protons of **1b** coalesced at 40 °C, the protons of **2** did not coalesce even at 60 °C. This result shows that the activation barrier between the two diastereomers of **2** is much higher than that of the corresponding ligand **1b**.[10] This may be due to the additional steric repulsion between the *t*-Bu group at oxazoline ring and the 8′-position proton at the naphthalene ring.

Table 1. Temperature dependence of the ratio of the two diastereomers of ligand **1b** and **2**[a]

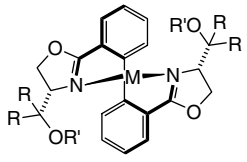
Temperature (°C)	Major:minor	
	1b	**2**
−60	4.4:1	10.1:1
−30	2.8:1	7.9:1
0	2.4:1	4.0:1
26	2.2:1	2.7:1
40	—[b]	
60		2.2:1

[a] Determined by ^{1}H NMR (400 MHz, $CDCl_3$).
[b] All signals coalesced, respectively.

2.3. Complexation behavior of ligands with copper(I) ion

The complexation behavior of ligand **2** on mixing with a copper(I) triflate benzene complex [Cu(I)OTf(C_6H_6)$_{0.5}$] and copper(I) iodide in solution was examined. Since the activation barrier between the two diastereomers of **2** was much higher than that of the corresponding ligand **1b**, the inter-conversion rate between the two diastereomers of **2** should be slower than that of **1b**. Furthermore, the complexation of ligand **1** with zinc(II) iodide may be a kinetically controlled process.[4c] Therefore, it was doubted whether this ligand could afford only one of the two possible diastereomers on complexation with Cu(I) ion such as the corresponding biphenyl ligands **1**. However, when a solution of ligand **2** in chloroform-*d* was mixed with 1 equiv of the copper(I) triflate benzene complex or copper(I) iodide at room temperature, the ^{1}H NMR spectra of the solution showed that only one diastereomer was formed. The configuration of the complex generated was deduced to be (a*S*)-**18** (Scheme 4), because the axis chirality of the corresponding complex of ligands **1** was assigned to be (a*S*).[4c]

The complexation behavior of ligands **5**–**7** having an oxygen atom in the substituent at the oxazoline ring on mixing with copper(I) triflate and iodide was next examined. With copper(I) iodide, all of these ligands were clearly proven to afford only one kind of the C_2-symmetric complex from ^{1}H NMR. With copper(I) triflate, all of these ligands also afford only one kind of the C_2-symmetric complex besides ligands **5a**, **6a**, and **7a** having hydroxyl groups, which gave broad signals in ^{1}H NMR spectra on complexation, perhaps due to the low solubility of the complexes in the solution.[11] From the little difference in the chemical shifts of the alkoxyl groups of the complex and those of the ligand in ^{1}H NMR spectra, it can be concluded that the oxygen atom in the substituent at oxazoline ring does not coordinate with the copper(I) ion. Therefore, the complexes formed should be C_2-symmetrically N,N′-coordinated, the structure of which could be deduced to be (a*R*)-**19**. (Note: the chirality at the oxazoline ring of this kind of ligands is different from that of ligand **1**.)



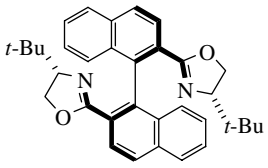
(a*R*)-**19**

(R=H, Me, Et; R'=Me, Et; M=CuOTf, CuI)

2.4. Application in Cu(I)-catalyzed asymmetric cyclopropanation

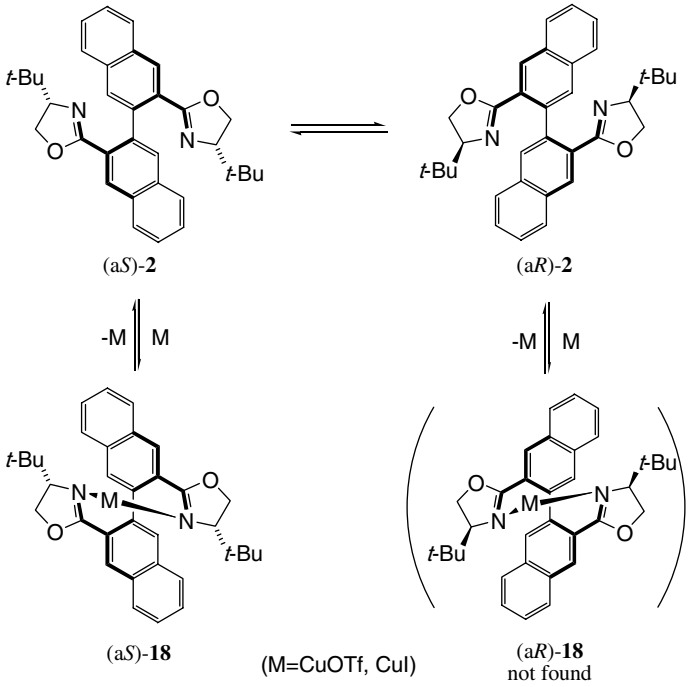
Cu(I)-catalyzed asymmetric cyclopropanation of olefin with diazoacetate is attracting considerable attention due to the demand for enantiomerically pure cyclopropanes, and some oxazoline ligands have been found to be effective for cyclopropanation of styrene with diazoacetate.[1a,b,f,g,i,12] In order to examine the effect of the axis-unfixed biaryl backbone and the kind of the substituent on the oxazoline ring on asymmetric catalysis using this new kind of ligand, the Cu(I)-catalyzed asymmetric cyclopropanation of styrene with diazoacetate was carried out.

At first, the results when using ligands **2**–**4** are shown in Table 2. It can be seen that all the ligands afford about yields of around 49–67%. This result is about the same with those with oxazoline ligands **1**[4a,c] and **20**[5b] having a biaryl backbone and several other recent examples.[12i,j] It can also be seen that the biaryl backbone has a large effect not only on *trans*/*cis* selectivity but also on diastereoselectivity, as does the substituent on the oxazoline ring,[4a,c,5b] although the reason for this remains unknown. Among ligands **2**–**4**, ligand **2** having an axis-unfixed binaphthyl backbone gave the best result and the *trans*- and *cis*-products were obtained in a ratio of 83/17 and with up to 89% de and 96% de, respectively. These results are better than those with the corresponding biphenyl derivative **1**.[4a,c] With ligand **2**, the diastereoselectivities are slightly lower but the trans/cis selectivity is higher than those with the corresponding axis-fixed binaphthyl derivative (a*S*)-**20**,[5b] which was prepared from racemic 1,1′-binaphthyl-2,2′-dicarboxylic acid using a diastereomeric separation procedure. This result suggests that ligand **2** with an axis-unfixed 2,2′-binaphthyl backbone existing as a mixture of two diastereomers in equilibrium in solution can be completely transferred to an active catalyst which affords very high diastereoselectivities and trans/cis selectivity for the Cu(I)-catalyzed asymmetric cyclopropanation of olefin with diazoacetate.



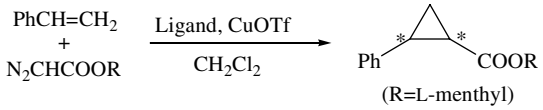
(a*S*)-**20**

The results with ligands **5**–**7** are shown in Table 3. It can be seen that the type of R group on the oxazoline substituent has a large effect on catalytic activity. When the R group is a proton, the yields are very high. However, where the R group becomes larger, the yields become lower. This may be caused by the hindrance of the large R group for the approach of the substrate to the copper(I) in the complex center. The R′ group of the ligand has a large effect on catalytic activity also. When the R′ is a proton, the yields are very low. This may be due to the low solubility of the complexes in the solution.[11] However, when the R′ group is a methyl or an ethyl group, the yield becomes higher. The R and R′ groups of the ligands also have a large effect on trans/cis selectivity and diastereoselectivity. Amongst ligands **5**–**7**, ligand **6b** afforded the best result. This result is about the same as that of ligand **1a** with an *i*-Pr group at oxazoline ring but worse than that of ligand **1b** with a *t*-Bu group.



Scheme 4.

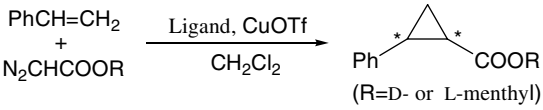
Table 2. Cu(I)-Catalyzed asymmetric cyclopropanation of styrene with menthyldiazoacetate[a]



Ligand	Yield[b] (%)	*Trans*/*cis*[c]	% de[c]	
			Cis (1*R*,2*S*)[d]	*Trans* (1*R*,2*R*)[d]
1a	60	79/21	87	70
1b	60	81/19	92	84
2	49	83/17	96	89
3	67	62/38	90	70
4	62	92/8	53	40
(a*S*)-**20**[e]	50	68/32	97	95

[a] Conducted at 20 °C with ligand (17 μmol), Cu(I)OTf$(C_6H_6)_{0.5}$ (13 μmol), styrene (1.0 mmol), and menthyl diazoacetate (1.3 mmol) in CH_2Cl_2 (2.0 mL) for 24 h.
[b] Isolated yield of a mixture of *trans*- and *cis*-product.
[c] Determined by GC.
[d] Determined by comparison of the specific rotation of their corresponding ethyl ester with the literature.[13]
[e] See, Ref. 5b.

Table 3. Cu(I)-Catalyzed asymmetric cyclopropanation of styrene with menthyldiazoacetate[a]



Ligand	Menthyl	Yield[b] (%)	*Trans*/*cis*[c]	% de[c] (config.)[d]	
				Cis	*Trans*
5a	D	48	95/5	0	15 (1*S*,2*S*)
5b	D	80	92/8	27 (1*S*,2*R*)	3 (1*S*,2*S*)
5c	D	78	81/19	20 (1*S*,2*R*)	3 (1*R*,2*R*)
6a	D	21	83/17	88 (1*S*,2*R*)	69 (1*S*,2*S*)
6b	D	69	87/13	90 (1*S*,2*R*)	63 (1*S*,2*S*)
6c	D	66	78/22	23 (1*S*,2*R*)	0
7a	D	15	84/16	83 (1*S*,2*R*)	77 (1*S*,2*S*)
7b	D	31	75/25	43 (1*S*,2*R*)	25 (1*S*,2*S*)
1a	L	60	79/21	87 (1*R*,2*S*)	70 (1*R*,2*R*)
1b	L	60	81/19	92 (1*R*,2*S*)	84 (1*R*,2*R*)

[a] Conducted at 20 °C with ligand (17 μmol), Cu(I)OTf$(C_6H_6)_{0.5}$ (13 μmol), styrene (1.0 mmol), and menthyl diazoacetate (1.3 mmol) in CH_2Cl_2 (2.0 mL) for 24 h.
[b] Isolated yield of a mixture of *trans*- and *cis*-product.
[c] Determined by GC.
[d] Determined by comparison of the specific rotation of the corresponding ethyl ester with the literature.[13]

3. Conclusion

We have prepared several new types of C_2-symmetric bisoxazoline ligands with an axis-unfixed biaryl backbone and different substituents at oxazoline ring. These ligands were proven to exist as a mixture of two diastereomers with opposite axial chirality in equilibrium in solution and upon coordination with copper(I) ion only one of the two possible rotatory diastereomer complexes formed. These ligands were applied to the Cu-catalyzed cyclopropanation of styrene with diazoacetate, and the effects of the biaryl backbone and the kind of the substituent at oxazoline ring on the catalysis were examined. The best result was obtained with the ligand having a 2,2′-binaphthyl backbone and a *t*-butyl group at oxazoline ring, which afforded 89% de and 96% de for the

trans- and *cis*-products of the above asymmetric cyclopropanation reaction, respectively.

4. Experimental

Melting points were measured on a Yanagimoto micro-melting point apparatus and are uncorrected. Optical rotations were measured on a DIP-181 digital polarimeter. ^{1}H NMR spectra were recorded on a JEOL GSX-400 spectrometer and the chemical shifts were referenced to $CHCl_3$ (δ 7.27) in $CDCl_3$. The fast atom bombardment mass spectra (FAB-MS) and high-resolution mass spectra (HRMS) were obtained on a JEOL JMS-DX303HF spectrometer.

THF was freshly distilled from sodium, dichloromethane from P_2O_5, and DMF, TMEDA, and triethylamine from CaH_2 before use. All of the other chemicals used in synthetic procedures were of reagent grade. Merck 70–230 mesh silica gel was used for column chromatography. TLC plastic sheet (Silica gel 60 F254) was used for the determination of R_f. All of the reactions were carried out under an argon atmosphere.

4.1. 2,2′-Binaphthyl-3,3′-dicarboxylic acid 8

4.1.1. Diazotization of 3-amino-2-naphthoic acid. 3-Amino-2-naphthoic acid (1.00 g, 5.34 mmol) was dissolved in a solution of sodium hydroxide (0.28 g, 7.0 mmol) in water (12.5 mL). To this solution was added sodium nitrite (0.44 g, 6.4 mmol) and the solution cooled to 10 °C. Then, this solution was added to a solution of concentrated hydrochloric acid (1.8 mL) and water (3.6 mL) at 10 °C for 2 h with efficient stirring to give a diazo solution.

4.1.2. Preparation of the reducing agent. Cupric sulfate pentahydrate (2.80 g, 11.2 mmol) was dissolved in water (9.0 mL) and then concentrated ammonium hydroxide (28%, 4.7 mL) was added with stirring and the solution cooled to 10 °C. To a solution of hydroxylamine hydrochloride (0.86 g, 12 mmol) in water (2.5 mL) was added 6 M sodium hydroxide solution (1.7 mL, 10 mmol) at 10 °C. This hydroxylamine solution was immediately added to the ammoniacal cupric sulfate solution with stirring. Reduction occurred at once with the evolution of nitrogen, and the solution becomes pale blue.

4.1.3. The coupling of the diazotized 3-amino-2-naphthoic acid. The reducing solution prepared above was cooled to 10 °C and maintained at 10–15 °C during the addition of the diazo solution, which is added by a syringe with the needle dipping well below the surface of the reducing solution. The diazo solution was added for 1 h and a lot of foaming occurred. After addition, the solution was stirred for an additional 5 h. The solution was heated to 80 °C, and rapidly acidified with concentrated hydrochloric acid with vigorous stirring. At this point acidification was continued more carefully until the solution was acid to Congo Red. The solution was allowed to stand overnight. The solid was filtered by suction and dissolved in ethyl acetate. The ethyl acetate solution was dried with magnesium sulfate and the solvent removed under reduced pressure. The residue was purified by column chromatography with ethyl acetate and then acetone as eluent to afford 2,2′-binaphthyl-3,3′-dicarboxylic acid **8** (0.53 g, 1.6 mmol, 60%). $R_f = 0.29$ (ethyl acetate). ^{1}H NMR (400 MHz, CD_3OD): δ 7.56 (dt, 2H, J 1.5, 7.6 Hz), 7.61 (dt, 2H, J 1.5, 7.6 Hz), 7.75 (s, 2H), 7.90 (br d, 2H, J 8.1 Hz), 8.01 (br d, 2H, J 8.1 Hz), 8.60 (s, 2H). FABMS (m/z) 341 ($[M-H]^-$).

4.2. 3,3′-Bis{*N*-[(1′*S*)-*tert*-butyl-2′-hydroxyethyl]carboxamido}-2,2′-binaphthyl 9

A mixture of **8** (0.53 g, 1.6 mmol) and thionyl chloride (10.0 mL, 16.3 g, 137 mmol) was refluxed for 6 h. Low boiling point chemicals were removed under reduced pressure and the residue dissolved in dichloromethane (5.0 mL). This solution was added to a solution of (*S*)-*tert*-leucinol (0.41 g, 3.5 mmol) and triethylamine (1.3 mL, 0.94 g, 9.3 mmol) in dry dichloromethane (20 mL) dropwise at 0 °C over 15 min. After being stirred for 3 h at room temperature, the resulting mixture was washed with water and then brine, dried over magnesium sulfate, and then concentrated under reduced pressure. The residue was purified by silica gel column chromatography with ethyl acetate as eluent to give **9** (0.72 g, 1.3 mmol, 81%) as a light orange solid. $R_f =$ 0.42 (ethyl acetate). The ^{1}H NMR of **9** shows two sets of signals in $CDCl_3$ (52/48). ^{1}H NMR (400 MHz, $CDCl_3$) major: δ 0.67 (s, 18H); minor: δ 0.80 (s, 18H). The other signals are overlapped.

4.3. 3,3′-Bis[(4′*S*)-*tert*-butyloxazolin-2′-yl]-2,2′-binaphthyl 2

To a solution of **9** (0.49 g, 0.91 mmol) and triethylamine (0.75 mL, 0.55 g, 5.4 mmol) in dry dichloromethane (25 mL) was added methanesulfonyl chloride (0.15 mL, 0.22 g, 1.9 mmol) dropwise by syringe for 5 min at 0 °C. After being stirred overnight at room temperature, the resulting mixture was washed with water and then brine, dried over magnesium sulfate, and then concentrated under reduced pressure. The residue was purified by silica gel column chromatography with ethyl acetate/hexane (1/4) as eluent to give **2** (0.23 g, 0.46 mmol, 50%) as a light orange solid. $R_f = 0.27$ (ethyl acetate/hexane = 1/4). The ^{1}H NMR of **2** shows two sets of signals in $CDCl_3$ (91/9, −60 °C). ^{1}H NMR (400 MHz, $CDCl_3$, −60 °C) major: δ 0.92 (s, 18H), 3.56 (t, 2H, J 8.8 Hz), 3.96 (t, 2H, J 9.9 Hz), 4.15 (t, 2H, J 9.2 Hz), 7.57 (m, 4H), 7.76 (m, 2H), 7.80 (s, 2H), 7.95 (m, 2H), 8.46 (s, 2H); minor: δ 0.80 (s, 18H), 3.83 (m, 2H), 3.92 (m, 2H), 4.00 (m, 2H), 7.35–8.00 (m, 8H), 7.83 (s, 2H), 8.43 (s, 2H). HRMS(EI) calcd for $C_{34}H_{36}N_2O_2$: 504.2818, found 504.2790. Mp: 73–76 °C. $[\alpha]_D^9 = -78.5$ (c 0.50, $CHCl_3$).

4.4. 5,5′-Dichloro-1,1′-biphenyl-2,2′-dicarboxylic acid 10

Following a procedure identical to that described for the preparation of **8**, **10** (6.60 g, 21.2 mmol, 73%) was prepared from 2-amino-4-chlorobenzoic acid (10.0 g, 58.3 mmol) as a light yellow solid. $R_f = 0.42$ (acetone/

hexane = 4/1). ^{1}H NMR (400 MHz, CD_3OD): δ 7.18 (d, 2H, J 2.2 Hz), 7.45 (dd, 2H, J 2.2, 8.4 Hz), 7.90 (d, 2H, J 8.4 Hz). IR (KBr, cm^{-1}) 1531, 1633, 3236. FABMS (m/z) 310 (M^+).

4.5. 5,5′-Dichloro-2,2′-bis{*N*-[(1′*S*)-*tert*-butyl-2′-hydroxyethyl]carboxamido}-1,1′-biphenyl 11

Following a procedure identical to that described for the preparation of **9**, **11** (1.90 g, 3.73 mmol, 89%) was prepared from **10** (1.30 g, 4.18 mmol) as a light yellow solid. $R_f = 0.35$ (ethyl acetate). The ^{1}H NMR of **11** shows two sets of signals in $CDCl_3$ (51/49). ^{1}H NMR (400 MHz, $CDCl_3$) major: δ 0.75 (s, 18H), 3.30 (dd, 2H, J 8.1, 11.4 Hz), 3.66 (dd, 2H, J 3.7, 11.4 Hz), 3.79 (m, 2H), 7.09 (br, 2H), 7.22 (d, 2H, J 2.2 Hz), 7.40 (m, 2H), 7.60 (d, 2H, J 8.1 Hz); minor : δ 0.89 (s, 18H), 3.48 (dd, 2H, J 7.5, 11.5 Hz), 3.72 (dd, 2H, J 3.7, 11.4 Hz), 3.79 (m, 2H), 7.20 (br, 2H), 7.24 (d, 2H, J 2.2 Hz), 7.40 (m, 2H), 7.50 (d, 2H, J 8.1 Hz). FABMS (m/z) 509 ([M−H]$^-$).

4.6. 5,5′-Dichloro-2,2′-bis[(4′*S*)-*tert*-butyloxazolin-2′-yl]-1,1′-biphenyl 3

Following a procedure identical to that described for the preparation of **2**, **3** (0.14 g, 0.29 mmol, 48%) was prepared from **11** (0.31 g, 0.61 mmol) as a light yellow oil. $R_f = 0.49$ (ethyl acetate/hexane = 1/2). The ^{1}H NMR of **2** shows two sets of signals in $CDCl_3$ (75/25, −60 °C). ^{1}H NMR (400 MHz, $CDCl_3$, −60 °C) major: δ 0.87 (s, 9H), 3.72 (m, 2H), 3.89 (t, 2H, J 9.9 Hz), 4.15 (t, 2H, J 9.5 Hz), 7.18 (d, 2H, J 1.8 Hz), 7.37 (dd, 2H, J 1.8, 8.4 Hz), 7.79 (d, 2H, J 8.4 Hz); minor: δ 0.73 (s, 18H), 3.88 (m, 2H), 4.02 (m, 2H), 4.09 (q, 2H, J 7.3 Hz), 7.15 (d, 2H, J 2.2 Hz), 7.34 (dd, 2H, J 2.2, 8.4 Hz), 7.82 (d, 2H, J 8.4 Hz). HRMS(EI) calcd for $C_{26}H_{30}Cl_2N_2O_2$: 472.1687, found 472.1682. $[\alpha]_D^{13} = -96.6$ (c 0.50, $CHCl_3$).

4.7. 4-{*N*-[(1′*S*)-Isopropyl-2′-hydroxyethyl]carboxamido}-1,1′-biphenyl 12

Following a procedure identical to that described for the preparation of **9**, **12** (7.00 g, 24.7 mmol, 98%) was prepared as a white solid from 4-biphenylcarboxylic acid (5.00 g, 25.2 mmol) with 4-biphenylcarbonyl chloride as intermediate followed by reaction with (*S*)-valinol (3.60 g, 35.0 mmol) in the presence of triethylamine (11.0 mL, 8.0 g, 79 mmol). $R_f = 0.43$ (ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.06 (d, 3H, J 6.6 Hz), 1.07 (d, 3H, J 7.0 Hz), 2.06 (m, 1H), 3.84 (m, 2H), 3.99 (m, 1H), 6.38 (d, 1H, J 7.7 Hz), 7.40 (tt, 1H, J 1.3, 7.3 Hz), 7.48 (tt, 2H, J 1.5, 7.3 Hz), 7.62 (m, 2H), 7.68 (td, 2H, J 1.8, 8.4 Hz), 7.87 (td, 2H, J 1.8, 8.4 Hz). FABMS (m/z) 284 ([M+1]$^+$).

4.8. 4-[(4′*S*)-Isopropyloxazolin-2′-yl]-1,1′-biphenyl 13

Following a procedure identical to that described for the preparation of **2**, **13** (2.30 g, 8.67 mmol, 82%) was prepared as a white solid by the reaction of **12** (3.00 g, 10.6 mmol) with methanesulfonyl chloride (0.98 mL, 1.45 g, 13 mmol) in the presence of triethylamine (5.9 mL, 4.3 g, 42 mmol). $R_f = 0.25$ (ethyl acetate/hexane = 1/3). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.96 (d, 3H, J 6.6 Hz), 1.06 (d, 3H, J 7.0 Hz), 1.90 (m, 1H), 4.11–4.20 (m, 2H), 4.44 (m, 1H), 7.38 (tt, 1H, J 1.5, 7.3 Hz), 7.47 (m, 2H), 7.64 (m, 4H), 8.03 (td, 2H, J 1.8, 8.4 Hz). FABMS (m/z) 266 ([M+1]$^+$).

4.9. 3-Bromo-4-[(4′*S*)-isopropyloxazolin-2′-yl]-1,1′-biphenyl 14

To a solution of **13** (1.00 g, 3.77 mmol) in dry THF (40 mL) was added dropwise over 10 min, a solution of *s*-butyllithium in hexane (1.0 M, 4.6 mL, 4.6 mmol) at −78 °C. After being stirred at this temperature for 3 h, a solution of 1,2-dibromotetrafluoroethane (0.92 mL, 2.0 g, 7.7 mmol) in dry THF (20 mL) was added to the mixture dropwise over 15 min. The mixture was stirred at −78 °C for an additional 1 h and overnight at room temperature. Then, the mixture was concentrated under reduced pressure and residue was dissolved in dichloromethane (100 mL). The solution was washed with water and brine, dried over magnesium sulfate, and then concentrated under reduced pressure. The residue was purified by silica gel column chromatography with ethyl acetate/hexane (1/5) as eluent to give **14** (0.54 g, 1.6 mmol, 42%) as a light yellow oil. $R_f = 0.30$ (ethyl acetate/hexane = 1/5). ^{1}H NMR (400 MHz, $CDCl_3$): δ1.01 (d, 3H, J 7.0 Hz), 1.08 (d, 3H, J 7.0 Hz), 1.94 (m, 1H), 4.20 (m, 2H), 4.46 (m, 1H), 7.41 (m, 1H), 7.47 (m, 2H), 7.58 (m, 3H), 7.77 (d, 1H, J 8.1 Hz), 7.88 (d, 1H, J 1.8 Hz).

4.10. 5,5′-Diphenyl-2,2′-bis[(4′*S*)-isopropyloxazolin-2′-yl]-1,1′-biphenyl 4

A mixture of **14** (97 mg, 0.28 mmol) and freshly activated copper (47 mg, 0.73 mmol) in dry pyridine (1.5 mL, 19 mmol) was heated at reflux for 12 h. After being cooled, the mixture was diluted with dichloromethane (30 mL) and washed with 25% aqueous ammonia (20 mL). The ammonia layer was extracted with dichloromethane twice (20 mL × 2). The organic layers were combined and washed with brine (50 mL). The brine layer was extracted with dichloromethane twice (40 mL × 2) and the combined organic layers were dried over magnesium sulfate, and then concentrated under reduced pressure. The residue was purified by silica gel column chromatography with ethyl acetate/hexane (1/3) as eluent to give **4** (52 mg, 0.098 mmol, 70%) as an yellow oil. $R_f = 0.10$ (ethyl acetate/hexane = 1/3). The ^{1}H NMR of **4** shows two sets of signals in $CDCl_3$ (65/35). ^{1}H NMR (400 MHz, $CDCl_3$) major: δ 0.78 (d, 6H, J 6.6 Hz), 0.82 (d, 6H, J 6.6 Hz), 1.70 (m, 2H), 3.77 (t, 2H, J 8.1 Hz), 3.89 (m, 2H), 4.17 (m, 2H), 7.34–7.48 (m, 6H), 7.54 (m, 2H), 7.60–7.71 (m, 6H), 7.95 (br d, 2H, J 8.1 Hz); minor: δ 0.78 (d, 6H, J 6.6 Hz), 0.83 (d, 6H, J 6.6 Hz), 1.64 (m, 2H), 3.90 (m, 4H), 4.06 (m, 2H), 7.34–7.48 (m, 6H), 7.54 (m, 2H), 7.60–7.71 (m, 6H), 8.01 (br d, 2H, J 8.1 Hz). HRMS(EI) calcd for $C_{36}H_{36}N_2O_2$: 528.2779, found 528.2756. $[\alpha]_D^{13} = -59.0$ (c 0.50, $CHCl_3$).

4.11. 2,2′-Bis{*N*-[(1′*S*)-methoxycarbonyl-2′-hydroxyethyl]carboxamido}-1,1′-biphenyl 15

Following a procedure identical to that described for the preparation of **9**, **15** (7.10 g, 16.0 mmol, 78%) was prepared as a light yellow solid from 2,2′-biphenyldicarboxylic acid (5.00 g, 20.6 mmol) with 2,2′-biphenyldicarbonyl chloride as intermediate followed by reaction with L-serine methyl ester hydrochloride (8.10 g, 52.1 mmol) in the presence of triethylamine (17.0 mL, 12.3 g, 122 mmol). $R_f = 0.15$ (ethyl acetate). The ^{1}H NMR of **15** shows two sets of signals in $CDCl_3$ (69/31). ^{1}H NMR (400 MHz, $CDCl_3$) major: δ 3.68 (s, 6H), 3.80 (m, 2H), 4.02 (t, 2H, J 7.0 Hz), 4.11 (m, 2H), 4.42 (m, 2H), 6.36 (d, 2H, J 5.1 Hz), 7.48 (dd, 2H, J 1.5, 7.7 Hz), 7.56 (dt, 2H, J 1.5, 7.7 Hz), 7.70 (dt, 2H, J 1.5, 7.7 Hz), 7.85 (dd, 2H, J 1.5, 7.7 Hz); minor: δ 3.59 (m, 2H), 3.76 (s, 6H), 3.78 (m, 2H), 4.14 (m, 2H), 4.59 (m, 2H), 7.31–7.38 (m, 4H), 7.43–7.54 (m, 4H), 7.69 (dt, 2H, J 1.5, 7.7 Hz). FABMS (m/z) 445 ($[M+1]^+$).

4.12. 2,2′-Bis [(4′*S*)-(methoxycarbonyl)oxazolin-2′-yl]-1,1′-biphenyl 17

4.12.1. Attempted oxazoline ring closure of 15 using methanesulfonyl chloride. Following a procedure identical to that described for the preparation of **2**, **17** was not obtained by the reaction of **15** (0.55 g, 1.2 mmol) with methanesulfonyl chloride (0.25 mL, 0.37 g, 3.2 mmol) in the presence of triethylamine (1.8 mL, 1.3 g, 13 mmol). However, an elimination product, 2,2′-bis{*N*-[1′-(methoxycarbonyl)vinyl]carboxamido}-1,1′-biphenyl **16**, was obtained as a light yellow solid by this reaction (0.33 g, 0.81 mmol, 68%). $R_f = 0.27$ (ethyl acetate/hexane = 1/1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.80 (s, 6H), 5.85 (d, 2H, J 2.0 Hz), 6.55 (s, 2H), 7.20 (m, 2H), 7.45 (m, 4H), 7.70 (m, 2H), 8.60 (s, 2H). FABMS (m/z) 409 ($[M+1]^+$).

4.12.2. Oxazoline ring closure of 15 using Burgess' reagent. A solution of **15** (6.00 g, 13.5 mmol) and Burgess' reagent [(methoxycarbonylsulfamoyl)triethylammonium hydroxide inner salt] (6.70 g, 28.1 mmol) in THF (200 mL) was refluxed for 2.5 h. The solvent was evaporated and the residue was dissolved in dichloromethane (200 mL). The solution was washed with water (100 mL) and brine (100 mL), dried over sodium sulfate, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with ethyl acetate as eluent to give **17** (4.60 g, 11.3 mmol, 84%) as a colorless viscous oil. $R_f = 0.25$ (ethyl acetate). The ^{1}H NMR of **17** shows two sets of signals in $CDCl_3$ (72/28). ^{1}H NMR (400 MHz, $CDCl_3$) major: δ 3.77 (s, 6H), 4.25 (m, 2H), 4.34 (t, 2H, J 8.4 Hz), 4.73 (m, 2H), 7.33 (br d, 2H, J 7.7 Hz), 7.41 (dt, 2H, J 1.5, 7.7 Hz), 7.54 (dt, 2H, J 1.5, 7.7 Hz), 7.88 (dd, 2H, J 1.5, 7.7 Hz); minor: δ 3.74 (s, 6H), 4.24 (m, 2H), 4.37 (m, 2H), 4.74 (m, 2H), 7.25 (m, 2H), 7.39 (m, 2H), 7.48 (dt, 2H, J 1.5, 7.7 Hz), 7.92 (dd, 2H, J 1.5, 7.7 Hz). FABMS (m/z) 409 ($[M+1]^+$). HRMS(EI) calcd for $C_{22}H_{20}N_2O_6$: 408.1322, found 408.1318.

4.13. 2,2′-Bis[(4′*R*)-(hydroxymethyl)oxazolin-2′-yl]-1,1′-biphenyl 5a

A solution of **17** (1.10 g, 2.69 mmol) in THF (50 mL) was added dropwise over 15 min to a suspension of $LiAlH_4$ (0.30 g, 7.9 mmol) in THF (40 mL) at −10 °C. The reaction mixture was stirred further for 2 h at this temperature and overnight at room temperature. Ethyl acetate (2 mL) was added to the mixture. After being stirred for several minutes, the solvent was evaporated. The residue was dissolved in dichloromethane (100 mL). The solution was washed with brine (30 mL), dried over sodium sulfate, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with acetone as eluent to give **5a** (0.79 g, 2.2 mmol, 82%) as a white solid. $R_f = 0.27$ (acetone). The ^{1}H NMR of **5a** shows only one set of signals in $CDCl_3$. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.38 (m, 2H), 3.91 (t, 2H, J 8.0 Hz), 4.06–4.23 (m, 6H), 7.39–7.46 (m, 4H), 7.51–7.58 (m, 4H). FABMS (m/z) 353 ($[M+1]^+$). HRMS(EI) calcd for $C_{20}H_{20}N_2O_4$: 352.1424, found 352.1422. $[\alpha]_D^9 = +53.4$ (c 0.51, $CHCl_3$).

4.14. 2,2′-Bis[(4′*R*)-(methoxymethyl)oxazolin-2′-yl]-1,1′-biphenyl 5b

A solution of **5a** (50 mg, 0.14 mmol) in THF (1.0 mL) was added to a suspension of NaH (29 mg, 60% in nujol, 0.73 mmol) in THF (1.0 mL) at 0 °C. After being stirred for several minutes, iodomethane (44 μL, 0.10 g, 0.71 mmol) was added and the reaction mixture stirred at room temperature overnight. The solvent was evaporated and the residue dissolved in dichloromethane (20 mL). The solution was washed with water (10 mL) and brine (10 mL), dried over sodium sulfate, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with acetone as eluent to give **5b** (46 mg, 0.12 mmol, 86%) as a colorless viscous oil. $R_f = 0.36$ (acetone). The ^{1}H NMR of **5b** shows two sets of signals in $CDCl_3$ at 0 °C (72/28). ^{1}H NMR (400 MHz, $CDCl_3$, 0 °C) major: δ 3.31 (dd, J 7.0, 9.5 Hz, 2H), 3.35 (s, 6H), 3.46 (dd, J 4.7, 9.5 Hz, 2H), 3.89 (t, J 7.8 Hz, 2H), 4.20 (dd, J 8.1, 9.5 Hz, 2H), 4.28 (m, 2H), 7.32 (dd, J 1.5, 8.0 Hz, 2H), 7.36–7.52 (m, 4H), 7.82 (dd, J 2.5, 7.7 Hz, 2H); minor: δ 3.25 (dd, J 7.6, 9.1 Hz, 2H), 3.34 (s, 6H), 3.51 (dd, J 5.2, 9.5 Hz, 2H), 3.98 (t, J 8.1 Hz, 2H), 4.11 (dd, J 7.3, 8.8 Hz, 2H), 4.28 (m, 2H), 7.25 (br d, 2H), 7.36–7.52 (m, 4H), 7.85 (m, 2H). HRMS(EI) calcd for $C_{22}H_{24}N_2O_4$: 380.1737, found 380.1738. $[\alpha]_D^{10} = +150.5$ (c 0.49, $CHCl_3$).

4.15. 2,2′-Bis [(4′*R*)-(ethoxymethyl)oxazolin-2′-yl]-1,1′-biphenyl 5c

Following a procedure identical to that described for the preparation of **5b**, **5c** (42 mg, 0.10 mmol, 77%) was obtained from **5a** (45 mg, 0.13 mmol) and bromoethane (48 μL, 0.070 g, 0.64 mmol) as a colorless viscous oil. $R_f = 0.40$ (acetone). The ^{1}H NMR of **5c** shows two sets of signals in $CDCl_3$ (64/36). ^{1}H NMR (400 MHz, $CDCl_3$) major: δ 1.16 (t, J 7.0 Hz, 6H), 3.29 (t, J 8.8 Hz, 2H), 3.42–3.59 (m, 6H), 3.90 (t, J 7.7 Hz, 2H),

4.19 (t, *J* 8.8 Hz, 2H), 4.25 (m, 2H), 7.31 (br d, *J* 7.4 Hz, 2H), 7.37 (t, *J* 7.7 Hz, 2H), 7.47 (t, *J* 7.7 Hz, 2H), 7.81 (br d, *J* 7.7 Hz, 2H); minor: δ 1.16 (t, *J* 7.0 Hz, 6H), 3.23 (t, *J* 8.8 Hz, 2H), 3.42–3.59 (m, 6H), 3.98 (t, *J* 8.1 Hz, 2H), 4.10 (t, *J* 8.5 Hz, 2H), 4.26 (m, 2H), 7.24 (br d, *J* 7.7 Hz, 2H), 7.30–7.49 (m, 4H), 7.83 (br d, *J* 7.7 Hz, 2H). HRMS(EI) calcd for $C_{24}H_{28}N_2O_4$: 408.2050, found 408.2065. $[\alpha]_D^9 = +116.4$ (*c* 0.51, $CHCl_3$).

4.16. 2,2′-Bis[(4′*S*)-(dimethylhydroxylmethyl)oxazolin-2′-yl]-1,1′-biphenyl 6a

A solution of methylmagnesium bromide in THF (0.93 M, 3.3 mL, 3.1 mmol) was added dropwise over 10 min to a solution of **17** (0.21 g, 0.51 mmol) in dry THF (10 mL) with stirring at 0 °C. After stirring at room temperature for 2 h, the solvent was removed under reduced pressure. The residue was dissolved in dichloromethane (50 mL). The solution was washed with water (30 mL) and brine (30 mL), dried over sodium sulfate, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with ethyl acetate as an eluent to give **6a** (0.17 g, 0.42 mmol, 82%) as a colorless oil. $R_f = 0.16$ (ethyl acetate). The ^{1}H NMR of **6a** shows two sets of signals in $CDCl_3$ (59/41). ^{1}H NMR (400 MHz, $CDCl_3$) major: δ 1.00 (s, 6H), 1.00 (s, 6H), 3.93 (m, 2H), 4.16 (m, 2H), 4.20 (m, 2H), 7.33–7.56 (m, 6H), 7.77 (br d, *J* 7.7 Hz, 2H); minor: δ 0.85 (s, 6H), 1.26 (s, 6H), 3.91 (dd, *J* 3.3, 8.8 Hz, 2H), 4.02 (t, *J* 8.8 Hz, 2H), 4.15 (m, 2H), 7.25 (br d, *J* 7.7 Hz, 2H), 7.33–7.56 (m, 4H), 7.77 (br d, *J* 7.7 Hz, 2H). HRMS(CI) calcd for $C_{24}H_{29}N_2O_4$: 409.2129, found 409.2117. $[\alpha]_D^{27} = +71.2$ (*c* 0.70, $CHCl_3$).

4.17. 2,2′-Bis[(4′*S*)-(dimethylmethoxymethyl)oxazolin-2′-yl]-1,1′-biphenyl 6b

Following a procedure identical to that described for the preparation of **5b**, **6b** (0.16 g, 0.37 mmol, 79%) was obtained from **6a** (0.19 g, 0.47 mmol) and iodomethane (0.43 mL, 0.98 g, 6.9 mmol) as a white solid. $R_f = 0.16$ (ethyl acetate/hexane = 1/3). The ^{1}H NMR of **6b** shows two sets of signals in $CDCl_3$ (70/30). ^{1}H NMR (400 MHz, $CDCl_3$) major: δ 0.88 (s, 6H), 1.14 (s, 6H), 3.16 (s, 6H), 3.96–4.16 (m, 6H), 7.29 (br d, *J* 7.7 Hz, 2H), 7.35–7.47 (m, 4H), 7.84 (br d, *J* 7.7 Hz, 2H); minor: δ 0.86 (s, 6H), 1.13 (s, 6H), 3.16 (s, 6H), 3.96–4.16 (m, 6H), 7.19 (br d, *J* 7.7 Hz, 2H), 7.35–7.47 (m, 4H), 7.89 (br d, *J* 7.7 Hz, 2H). FABMS (*m*/*z*) 437 ($[M+1]^+$). HRMS(EI) calcd for $C_{26}H_{32}N_2O_4$: 436.2363, found 436.2363. $[\alpha]_D^{10} = +119.9$ (*c* 0.50, $CHCl_3$).

4.18. 2,2′-Bis[(4′*S*)-(dimethylethoxymethyl)oxazolin-2′-yl]-1,1′-biphenyl 6c

Following a procedure identical to that described for the preparation of **5b**, **6c** (46 mg, 0.099 mmol, 58%) was obtained from **6a** (68 mg, 0.17 mmol) and iodoethane (0.14 mL, 0.27 g, 1.7 mmol) as a white solid. $R_f = 0.27$ (ethyl acetate/hexane = 1/1). The ^{1}H NMR of **6c** shows two sets of signals in $CDCl_3$ (72/28). ^{1}H NMR (400 MHz, $CDCl_3$) major: δ 0.88 (s, 6H), 1.08 (t, *J* 7.0 Hz, 6H), 1.17 (s, 6H), 3.34 (m, 4H), 3.96–4.18 (m, 6H), 7.28 (br d, 2H), 7.34–7.45 (m, 4H), 7.83 (br d, *J* 7.7 Hz, 2H); minor: δ 0.86 (s, 6H), 1.08 (t, *J* 7.0 Hz, 6H), 1.15 (s, 6H), 3.38 (m, 4H), 3.96–4.18 (m, 6H), 7.19 (br d, *J* 7.7 Hz, 2H), 7.34–7.45 (m, 4H), 7.88 (br d, *J* 7.7 Hz, 2H). FABMS (*m*/*z*) 465 ($[M+1]^+$). HRMS(EI) calcd for $C_{28}H_{36}N_2O_4$: 464.2677, found 464.2672. $[\alpha]_D^{10} = +102.8$ (*c* 0.50, $CHCl_3$).

4.19. 2,2′-Bis[(4′*S*)-(diethylhydroxylmethyl)oxazolin-2′-yl]-1,1′-biphenyl 7a

Following a procedure identical to that described for the preparation of **6a**, **7a** (0.17 g, 0.37 mmol, 56%) was obtained as a white solid from **17** (0.27 g, 0.66 mmol) and a solution of ethylmagnesium bromide prepared by stirring a mixture of magnesium (0.16 g, 6.6 mmol) and bromoethane (0.55 mL, 0.80 g, 7.3 mmol) in THF (5.0 mL) at room temperature for 30 min. $R_f = 0.36$ (ethyl acetate). The ^{1}H NMR of **7a** shows two sets of signals in $CDCl_3$ (70/30). ^{1}H NMR (400 MHz, $CDCl_3$): major: δ 0.74 (t, *J* 7.5 Hz, 6H), 0.85 (t, *J* 7.5 Hz, 6H), 1.25 (m, 4H), 1.35 (m, 4H), 4.01 (t, *J* 9.5 Hz, 2H), 4.15 (m, 2H), 4.23 (t, *J* 8.4 Hz, 2H), 7.33 (d, *J* 7.7 Hz, 2H), 7.39 (m, 2H), 7.52 (m, 2H), 7.75 (m, 2H); minor: δ 0.71 (t, *J* 7.5 Hz, 6H), 0.78 (t, *J* 7.5 Hz, 6H), 1.19 (m, 4H), 1.61 (m, 4H), 3.85 (t, *J* 7.9 Hz, 2H), 4.11 (m, 4H), 7.26 (d, *J* 7.7 Hz, 2H), 7.39 (m, 2H), 7.46 (m, 2H), 7.75 (m, 2H). FABMS (*m*/*z*) 465 ($[M+1]^+$). HRMS(CI) calcd for $C_{28}H_{37}N_2O_4$: 465.2755, found 465.2747. $[\alpha]_D^{27} = +83.7$ (*c* 0.13, $CHCl_3$).

4.20. 2,2′-Bis[(4′*S*)-(diethylmethoxymethyl)oxazolin-2′-yl]-1,1′-biphenyl 7b

Following a procedure identical to that described for the preparation of **5b**, **7b** (25 mg, 0.050 mmol, 51%) was obtained from **7a** (46 mg, 0.099 mmol) and iodomethane (31 μL, 0.071 g, 0.50 mmol) as a colorless oil. $R_f = 0.12$ (ethyl acetate/hexane = 1/5). The ^{1}H NMR of **7a** shows two sets of signals in $CDCl_3$ (64/36). ^{1}H NMR (400 MHz, $CDCl_3$) major: δ 0.75–0.83 (m, 12H), 1.33–1.57 (m, 8H), 3.12 (s, 6H), 4.03–4.20 (m, 6H), 7.28 (br d, *J* 7.7 Hz, 2H), 7.33–7.46 (m, 4H), 7.82 (dd, *J* 1.5, 7.7 Hz, 2H); minor: δ 0.75–0.83 (m, 12H), 1.33–1.57 (m, 8H), 3.08 (s, 6H), 4.03–4.20 (m, 6H), 7.17 (br d, *J* 7.7 Hz, 2H), 7.33–7.46 (m, 4H), 7.87 (dd, *J* 1.5, 7.7 Hz, 2H). HRMS(CI) calcd for $C_{30}H_{41}N_2O_4$: 493.3147, found 493.3185. $[\alpha]_D^9 = +67.4$ (*c* 0.52, $CHCl_3$).

4.21. 3,3′-Bis[(4′*S*)-*tert*-butyloxazolin-2′-yl]-2,2′-binaphthyl copper(I) triflate complex (a*S*)-18, M = Cu(OTf)

To a solution of ligand **2** (5.0 mg, 10 μmol) in chloroform-*d* (1.0 mL) was added 1 equiv of [Cu(I)OTf-$(C_6H_6)_{0.5}$] (2.6 mg, 10 μmol) and the suspension was stirred at room temperature under an argon atmosphere until complete dissolution. The ^{1}H NMR of this solution showed only one set of signals. (a*S*)-**18** (M = Cu(OTf)): ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.45 (s,

18H), 4.20 (dd, *J* 5.5, 10.3 Hz, 2H), 4.54 (dd, *J* 5.5, 9.2 Hz, 2H), 4.65 (dd, *J* 9.2, 10.3 Hz, 2H), 7.59–7.64 (m, 6H), 7.74 (dd, *J* 3.3, 6.3 Hz, 2H), 7.97 (dd, *J* 3.3, 6.3 Hz, 2H), 8.34 (s, 2H). FABMS (*m*/*z*) 567 ($[M-OTf]^+$).

4.22. 3,3′-Bis[(4′*S*)-*tert*-butyloxazolin-2′-yl]-2,2′-binaphthyl copper(I) iodide complex (a*S*)-18, M = CuI

The ^{1}H NMR of the solution prepared by dissolving ligand **2** and CuI following a procedure identical to that described in Section 4.21 showed only one set of signals. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.42 (s, 18H), 4.38 (dd, 2H, *J* 5.1, 9.5 Hz), 4.46 (dd, 2H, *J* 5.1, 9.2 Hz), 4.55 (t, 2H, *J* 9.3 Hz), 7.58–7.61 (m, 4H), 7.63 (s, 2H), 7.74 (t, 2H, *J* 5.2 Hz), 7.96 (t, 2H, *J* 5.2 Hz), 8.36 (s, 2H). FABMS (*m*/*z*) 567 ($[M-I]^+$).

4.23. 2,2′-Bis[(4′*S*)-(dimethylmethoxymethyl)oxazolin-2′-yl]-1,1′-biphenyl copper(I) triflate complex (a*R*)-19, R = Me, R′ = Me, M = CuOTf

The ^{1}H NMR of the solution prepared by dissolving ligand **6b** and $[Cu(I)OTf(C_6H_6)_{0.5}]$ following a procedure identical to that described in Section 4.21 shows only one set of signals. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.67 (s, 6H), 1.01 (s, 6H), 2.99 (s, 6H), 4.33 (dd, *J* 5.5, 10.3 Hz, 2H), 4.56 (dd, *J* 8.8, 10.3 Hz, 2H), 4.77 (dd, *J* 5.5, 8.8 Hz, 2H), 7.09 (m, 2H), 7.43–7.49 (m, 4H), 7.70 (m, 2H). FABMS (*m*/*z*) 499 ($[M-OTf]^+$).

4.24. 2,2′-Bis[(4′*S*)-[dimethylmethoxymethyl]oxazolin-2′-yl]-1,1′-biphenyl copper(I) iodide complex (a*R*)-19, R = Me, R′ = Me, M = CuI

The ^{1}H NMR of the solution prepared by dissolving ligand **6b** and CuI following a procedure identical to that described in Section 4.21 shows only one set of signals. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.63 (s, 6H), 1.01 (s, 6H), 3.00 (s, 6H), 4.44–4.51 (m, 4H), 4.70 (dd, *J* 1.9, 5.2 Hz, 2H), 7.09 (dd, *J* 1.8, 7.3 Hz, 2H), 7.42 (dt, *J* 1.8, 7.3 Hz, 2H), 7.45 (dt, *J* 1.8, 7.3 Hz, 2H), 7.71 (dd, *J* 1.8, 7.3 Hz, 2H). FABMS (*m*/*z*) 499 ($[M-I]^+$).

4.25. 2,2′-Bis[(4′*R*)-(methoxymethyl)oxazolin-2′-yl]-1,1′-biphenyl copper(I) triflate complex (a*R*)-19, R = H, R′ = Me, M = CuOTf

The ^{1}H NMR of the solution prepared by dissolving ligand **5b** and $[Cu(I)OTf(C_6H_6)_{0.5}]$ following a procedure identical to that described in Section 4.21 shows only one set of signals. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.02 (s, 6H), 3.08 (dd, *J* 4.8, 10.1 Hz, 2H), 3.18 (dd, *J* 3.3, 10.1 Hz, 2H), 4.49 (m, 2H), 4.58 (dd, *J* 6.6, 8.6 Hz, 2H), 4.65 (dd, *J* 8.6, 10.1 Hz, 2H), 7.12 (m, 2H), 7.46–7.51 (m, 4H), 7.63 (m, 2H). FABMS (*m*/*z*) ($[M-OTf]^+$).

4.26. 2,2′-Bis[(4′*R*)-(ethoxymethyl)oxazolin-2′-yl]-1,1′-biphenyl copper(I) triflate complex (a*R*)-19, R = H, R′ = Et, M = CuOTf

The ^{1}H NMR of the solution prepared by dissolving ligand **5c** and $[Cu(I)OTf(C_6H_6)_{0.5}]$ following a procedure identical to that described in Section 4.21 shows only one set of signals. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.03 (t, *J* 7.0 Hz, 6H), 3.02 (dd, *J* 5.6, 9.9 Hz, 2H), 3.18–3.26 (m, 6H), 4.50 (m, 2H), 4.57–4.68 (m, 4H), 7.11 (dd, *J* 3.3, 5.5 Hz, 2H), 7.48 (m, 4H), 7.65 (dd, *J* 3.3, 5.5 Hz, 2H). FABMS (*m*/*z*) ($[M-OTf]^+$).

4.27. Typical procedure for copper(I)-catalyzed asymmetric cyclopropanation of styrene

To a copper(I) triflate benzene complex $[Cu(I)OTf(C_6H_6)_{0.5}]$ (3.3 mg, 13 μmol) was added a solution of ligand **2** (8.7 mg, 17 μmol) in dichloromethane (1.0 mL) and then the suspension stirred at room temperature for 2 h under an argon atmosphere. The resulting solution was filtered through a membrane filter. After the addition of styrene (104 mg, 1.0 mmol), a solution of L-menthyl diazoacetate (290 mg, 1.3 mmol) in dichloromethane (1.0 mL) was slowly added over a period of 4 h and then the reaction solution was stirred at room temperature for an additional 24 h. The reaction mixture was filtered through an alumina short column and the filtrate was concentrated under reduced pressure to give an oil product. The ratio of the trans- and cis-products of the oil and the diastereomeric excess of them were determined by GC with DB-1. The absolute configuration of the trans- and cis-products was determined by comparison of the specific rotation of their corresponding ethyl ester after transesterification in the presence of a sulfuric acid catalyst with the reported one.[13]

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