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Novel bis(oxazoline) ligands derived from camphoric acid for Cu-catalyzed asymmetric cyclopropanation

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Abstract

Novel bis(oxazoline) ligands derived from camphoric acid were prepared and applied to Cu-catalyzed asymmetric cyclopropanation of styrene or 1,1-diphenylethylene with diazoacetate. Good ee values (up to 81%) were obtained for 1,1-diphenylethylene; however, the enantioselectivities for styrene were poor. The chirality of the oxazolyl group dominated the configuration of the products. The rigid structure and the chiral centers in the camphor backbone of the ligands proved to be not helpful in increasing enantioselectivity.
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Keywords: Bis(oxazoline); Oxazoline; Asymmetry; Cyclopropanation; Camphor; Camphoric acid

1. Introduction

In recent years, chiral bis(oxazoline) ligands have received a great deal of attention and become one of the most successful and versatile classes of ligands in catalytic asymmetric synthesis [1]. As a result, bis(oxazoline) ligands with lots of structural diversities have been introduced [2], while only few bis(oxazoline) ligands with additional chiral centers at the linker between the oxazolines have been prepared [3].

Since Noyori used (−)dimethylamino isoborneol as highly enantioselective catalyst for the addition of zinc alkyls to aldehydes [4], ligands derived from camphor have attracted much attention in asymmetric synthesis [5].

The rigid structure and the chiral centers of the camphor backbone prompted us to develop a new kind of camphor-based chiral bis(oxazoline) ligands **5**. To estimate their asymmetric catalytic effects, we applied them in Cu-catalyzed cyclopropanation, which is the reaction most often examined with chiral oxazolyl ligands [6].

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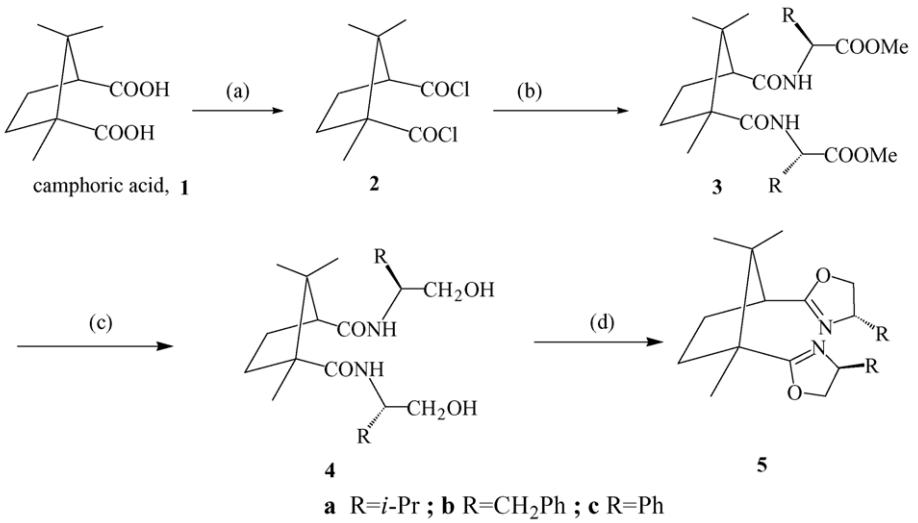
2. Results and discussion

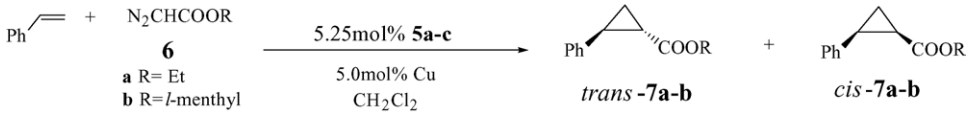
2.1. Synthesis of chiral bis(oxazoline) ligands

Camphoric acid **1** was easily transformed to **2** by reacting with PCl_5 in petroleum ether [7]. An attempt to synthesize **4** by reacting **2** with the corresponding amino alcohol failed, which is a common method for the preparation of oxazoline [1b]. Alternatively, compound **2** was treated with amino acid methyl ester hydrochloride and catalytic amount of DMAP, and then **3** were obtained as a major product, which can be easily purified by chromatography. Attempt to prepare **3** by treatment of **1** with amino acid methyl ester hydrochloride in the presence of HOBt and EDC also failed [8]. Compound **3** was then selectively reduced to **4** quantitatively by $Ca(BH_4)_2$ prepared in situ using $CaCl_2$ and $NaBH_4$ in THF and EtOH [9]. In this reaction, low temperature (below −10 °C) was necessary and EtOH can accelerate the reaction. Then **4** was easily transformed to bis(oxazoline) **5** by reacting with $SOCl_2$ followed by treatment with K_2CO_3. This method offers another convenient way of preparing oxazolines (Scheme 1).



Reagents and conditon:(a) PCl_5, Petroleum ether, 0˚C; (b) amino acid methyl ester hydrochloride, 4.0mol Et_3N, 5mol % DMAP, 0˚C, toluene; (c) $NaBH_4$, $CaCl_2$, THF-EtOH=1:1, -10˚C; (d) $SOCl_2$, then K_2CO_3.

Scheme 1. Reagents and condition: (a) PCl_5, petroleum ether, 0 °C; (b) amino acid methyl ester hydrochloride, 4.0 mol Et_3N, 5 mol% DMAP, 0 °C, toluene; (c) $NaBH_4$, $CaCl_2$, THF-EtOH = 1:1, −10 °C and (d) $SOCl_2$, then K_2CO_3.



Scheme 2.

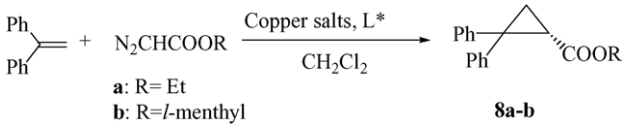
2.2. Asymmetric cyclopropanation of styrene or 1,1′-diphenylethylene with diazoacetate catalyzed by copper-bis(oxazoline) 5

Initially, bis(oxazoline) **5a–c** were used for the copper-catalyzed cyclopropanation of styrene with diazoacetate (Scheme 2). The reaction was carried out in CH_2Cl_2 at room temperature in the presence of 5.0 mol% Cu-bis(oxazoline) (1:1.05) complex prepared in situ by adding the bis(oxazoline) **5a–c** to Cu(OTf)·(1/2)C_6H_6. The results are summarized in Table 1.

The ratio of *trans*/*cis* **7a** was determined by ^{1}H NMR. Clearly, the structure of the bis(oxazoline) ligand does not effect the ratio dramatically, which is almost 2:1, while the ester groups of the diazoacetate do affect the ratio. When **6b** was used, the ratio of *trans*/*cis* **7b** was increased to 87:13 (entry 3). These results were similar to the observation of Pfalz [10]. Unfortunately, the ee of **7a** and **b** was depressed. When ethyl diazoacetate was used as the carbene source, the best result was obtained with 29% ee for *cis*-**7a** using **5c** as ligand (entry 4). Bis(oxazoline) **5a** and **b** were inferior to **5c**.

When menthyl diazoacetate **6b** was used, even lower enantioselectivities were obtained. Because there are two additional chiral centers in the backbone of camphor in bis(oxazoline) **5**, there may exist matching and mismatching problem. To investigate this, we synthesized **5c*** using the methyl amino acid (*R*)-$PhCHNH_2COOMe$ instead of (*S*)-$PhCHNH_2COOMe$. So the chiral centers of the oxazoline group of **5c*** are opposite to those of **5c**. When **5c*** was used as catalyst, the configuration of *trans* and *cis* **7a** was 1*R*, 2*R* and 1*R*, 2*S*, respectively, opposite to those obtained in the case of using **5c** (entry 8), while the ee was almost the same. The results show the chirality of the oxazoline group dominates the configuration of the products, while the matching or mismatching problem may not be important. The low enantioselectivities may be attributed to the too rigid conformation and the eight membered metal chelate formed which is not stable enough.

As reported by Gibson and co-workers [6e], complex of copper(II) triflate and **5a–c** can also catalyze the reaction with slightly lower enantioselectivity (entry 7). Addition of phenylhydrazine to reduce copper(II) to copper(I) in situ described by Masamune and co-workers [11] gave a similar result (entry 5) (Schemes 2 and 3).



Scheme 3.

Table 1
Asymmetric cyclopropanation of styrene with diazoacetate catalyzed by copper-bis(oxazoline) **5a–c**

Entry	Ligand (**5a–c**)	$N_2CHCOOR$ (**6**) (R = Et, *l*-menthyl)	Cu[a]	Yield[b]	Ratio of[c] *trans*/*cis*	ee%[d] (configuration)[e]	
						trans	*cis*
1	**5a**	Et	Cu(I)	58	67/33	5(1*S*,2*S*)	6(1*S*,2*R*)
2	**5b**	Et	Cu(I)	65	66/34	15(1*S*,2*S*)	18(1*S*,2*R*)
3	**5b**	*l*-Menthyl	Cu(I)	55	87/13	10(1*S*,2*S*)	6(1*S*,2*R*)
4	**5c**	Et	Cu(I)	68	66/34	25(1*S*,2*S*)	29(1*S*,2*R*)
5	**5c**	Et	Cu(I)[f]	58	66/34	24(1*S*,2*S*)	28(1*S*,2*R*)
6	**5c**	*l*-Menthyl	Cu(I)	58	85/15	22(1*S*,2*S*)	3(1*S*,2*R*)
7	**5c**	Et	Cu(II)	52	65/35	15(1*S*,2*S*)	18(1*S*,2*R*)
8	**5c***[g]	Et	Cu(I)	65	61/39	22(1*R*,2*R*)	25(1*R*,2*S*)

[a] Cu(I) refers to the use of $Cu(OTf)\cdot(1/2)C_6H_6$, and Cu(II) refers to $Cu(OTf)_2$.
[b] Isolated yield.
[c] Determined by ^{1}H NMR.
[d] For *trans*-**7a**, ee was determined using a Chiralcel OD column, and for *cis*-**7a**, by measurement of their specific rotation values. GC determined the ee of **7b**.
[e] Absolute configuration of *trans*-**7** and *cis*-**7** was established on the basis of the sign of the specific rotation of the corresponding acid [10].
[f] Cu(I) refers to $Cu(OTf)_2$ reduced by phenylhydrazine in this case.
[g] **5c*** was prepared from (*R*)-$PhCHNH_2COOMe$ and camphoric acid as **5c**.

Table 2
Asymmetric cyclopropanation of 1,1-diphenylethene with diazoacetate catalyzed by copper-bis(oxazoline) **5**

Entry	Ligand (**5a–c**)	$N_2CHCOOR$ (R = Et, *l*-menthyl)	Yield[a]	ee%[b] (configuration)[c]
1	**5a**	Et	48	45(*S*)
2	**5a**	*l*-Menthyl	44	12(*S*)
3	**5b**	Et	58	68(*S*)
4	**5b**	*l*-Menthyl	54	11(*S*)
5	**5c**	Et	71	81(*S*)
6	**5c**	*l*-Menthyl	65	15(*S*)
7[d]	**5c**	Et	55	55(*S*)
8	**5c***	Et	68	78(*R*)
9	**5c***	*l*-Menthyl	45	26(*R*)

[a] Isolated yield.
[b] The ee of **8a** was determined using a Chiralcel OD column and for **8b** by GC analysis.
[c] Absolute configuration of **8a** and **b** was established on the basis of the sign of the specific rotation of the corresponding acid.
[d] In this case $Cu(OTf)_2$ was used as copper salt.

The cyclopropanation of 1,1-diphenylethylene was also investigated (Scheme 3). When ethyl diazoacetate was used as carbene source, moderate to good enantioselectivities were obtained with the best result (up to 81% ee) using **5c** as the ligand (entry 5, Table 2). While when menthyl diazoacetate was used, very poor ee was obtained. Thus, **5a** and **5b** was inferior to **5c** as mentioned for styrene. Ligand **5c*** also gave good ee (78%) with *R* configuration of the product (entry 8, Table 2).

In conclusion, a series of bis(oxazoline) ligands derived from camphoric acid were conveniently synthesized and applied to the copper-catalyzed cyclopropanation of styrene and 1,1-diphenylethylene with diazoacetate. For styrene poor ee was obtained, while for 1,1-diphenylethylene up to 81% was achieved, using bis(oxazoline) **5c** as the ligand. In both cases, the use of bulky diazoacetate, such as menthyl diazoacetate as the carbene source, was not helpful in increasing the enantioselectivities of the products. The chirality of the oxazoline group dominated the configuration of the product and there were no significant matching and mismatching effects observed between the chiral centers of the camphor backbone and oxazoline groups.

3. Experimental

3.1. General

Melting points were measured on a Thomas Hoover melting point apparatus. ^{1}H NMR spectra were recorded on a Bruker AV-300 (300 MHz) spectrometer. Elemental analyses were performed on an Elementar Vario ElIII instrument. IR spectra were recorded on a Bruker Equinox55 spectrometer. Optical rotations were measured on a Wzz-1 apparatus. The enantiomeric excesses of *trans* **7a** and **8a** were determined by HPLC analysis using a chiral column (Daicel Chiralcel OD; eluent, hexane/isopropyl alcohol 99:1; flow rate, 0.5 ml/min; UV detector, 254 nm). The enantiomeric excesses of **7b** and **8b** were determined by GC analysis on a Varian Cp-sil 8CB 25 m × 0.25 mm × 0.25 μm column. Solvents used

were purified and dried by standard procedures. Camphoryl dichloride **2** was prepared according to literature [7].

3.2. General procedure for the synthesis of (**3a–c**)

The corresponding amino acid methyl ester hydrochloride (46.0 mmol) was suspended in 150 ml toluene and (13.0 ml, 93.0 mmol) Et_3N in 50 ml toluene was added dropwise. Then (0.60 g, 5.0 mmol) DMAP was added to the mixture and stirring was continued for 30 min. To the reaction mixture camphoryl dichloride **2** (5.44 g, 23.0 mmol) in 50 ml toluene was added and after the mixture was stirred for 10 h at room temperature, 50 ml EtOAc was added. Then the mixture was washed with 2N HCl (3× 80 ml), brine (2× 50 ml) and dried (Na_2SO_4). The solvent was removed in vacuo and the residue was purified by silica gel column chromatography using petroleum ether and ethyl acetate (4:1) as the eluent.

3.3. (1R,3S)-Bis[(S)-N-(1-isoproyl-2-methoxylcarbonyl-methyl)-amido]-1,2,2-trimethyl-cyclopentane(**3a**)

Yield: 38%, colorless oil. $[\alpha]_D^{20} = -12.8$ (*c* 1.5, EtOAc). ^{1}H NMR ($CDCl_3$): δ 6.17 (d, J = 8.3 Hz, 1H), 5.88 (d, J = 8.3 Hz, 1H), 4.53–4.60 (m, 2H), 3.73 (s, 3H), 3.75 (s, 3H), 2.65 (t, J = 9.5 Hz, 1H), 2.45–2.49 (m, 1H), 2.12–2.47 (m, 4H), 1.85–1.98 (m, 1H), 1.55–1.68 (m, 1H), 1.37 (s, 3H), 1.28 (s, 3H), 0.90–0.97 (m, 12H), 0.83 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 176.7, 175.1, 172.5, 172.1, 57.1, 57.0, 56.6, 53.6, 51.6, 46.5, 32.4, 30.6, 30.4, 23.0, 22.4, 21.5, 20.5, 18.6, 17.9, 17.7, 17.6. IR (KBr): 3354, 2964, 1734, 1648, 1508, 1261, 1021. Anal. calcd. for $C_{25}H_{44}N_2O_6$: C, 64.07; H, 9.46; N, 5.98. Found: C, 64.18; H, 9.52; N, 5.92.

3.4. (1R,3S)-Bis[(S)-N-(1-phenylmethyl-2-methoxylcarbonyl-methyl)-amido]-1,2,2-trimethyl-cyclopentane (**3b**)

Yield: 55%, colorless oil. $[\alpha]_D^{20} = +11.2$ (*c* 0.5, EtOAc). ^{1}H NMR ($CDCl_3$): δ 7.30–7.25 (m, 6H), 7.11–7.08 (m, 4H), 5.95 (d, J = 7.5 Hz, 1H), 5.74 (d, J = 7.5 Hz, 1H), 4.82–4.91 (m, 2H), 3.72 (s, 6H), 3.01–3.20 (m, 4H), 2.45–2.51 (t, J = 8.2 Hz, 1H), 2.10–2.32 (m, 2H), 1.69–1.82 (m, 1H), 1.35–1.48 (m, 1H), 1.16 (s, 3H), 1.08 (s, 3H), 0.70 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 176.6, 175.0, 172.1, 172.0, 136.0, 135.9, 129.0, 128.9, 128.5, 128.4, 127.1, 127.0, 60.2, 55.8, 54.9, 53.8, 52.9, 46.6, 38.0, 37.5, 32.3, 23.1, 22.4, 21.5, 20.4, 20.0, 19.2, 14.0. IR (KBr): 3348, 2953, 1742, 1656, 1508, 1499, 1211, 911, 732. Anal. calcd. for $C_{30}H_{38}N_2O_6$: C, 68.94; H, 7.33; N, 5.36. Found: C, 68.80; H, 7.38; N, 5.31.

3.5. (1R,3S)-Bis[(S)-N-(1-phenyl-2-methoxylcarbonyl-methyl)-amido]-1,2,2-trimethyl-cyclopentane (**3c**)

Yield: 47%, colorless foam. $[\alpha]_D^{20} = +110.4$ (*c* 1.1, EtOAc). ^{1}H NMR ($CDCl_3$): δ 7.31–7.34 (m, 10H), 6.60 (d, J = 6.7, 1H), 6.28 (d, J = 6.7, 1H), 5.50–5.56 (m, 2H), 3.72 (s, 6H), 2.60–2.65 (t, J = 8.5 Hz, 1H), 2.45–2.47 (m, 1H), 2.25–2.29 (m, 1H), 1.81–1.84 (m, 1H), 1.54–1.60 (m, 1H), 1.38 (s, 3H), 1.20 (s, 3H), 0.81 (m, 3H). ^{13}C NMR ($CDCl_3$): δ 176.5, 174.9, 172.2, 171.6, 136.5, 129.1, 127.5, 60.1, 56.8, 56.5, 54.2, 52.8, 47.2, 32.7, 23.7, 22.7, 21.8, 20.7, 14.1. IR (KBr): 3436, 3033, 2955, 1744, 1655, 1496, 1172, 732, 698. Anal. calcd. for $C_{28}H_{34}N_2O_6$: C, 68.00; H, 6.93; N, 5.66. Found: C, 68.08; H, 6.85; N, 5.61.

3.6. (1R,3S)-Bis[(R)-N-(1-phenyl-2-methoxylcarbonyl-methyl)-amido]-1,2,2-trimethyl-cyclopentane (**3c***)

Yield: 45%, from (*R*)-phenylglycine methyl ester hydrochloride, colorless foam. $[\alpha]_D^{20} = -50.4$ (*c* 1.1, EtOAc). ^{1}H NMR ($CDCl_3$): δ 7.31–7.35 (m, 10H), 6.54 (d, J = 6.7 Hz), 6.48 (d, J = 6.7 Hz), 5.58 (d, J = 7.0 Hz, 1H), 5.50 (d, J = 7.0 Hz, 1H), 3.71 (s, 6H), 2.65–2.68 (t, J = 7.9 Hz, 1H), 2.35–2.49 (m, 1H), 2.18–2.32 (m, 1H), 1.85–1.88 (m, 1H), 1.56–1.61 (m, 1H), 1.25 (s, 3H), 1.21 (s, 3H), 0.58 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 175.0, 172.2, 171.7, 171.6, 136.9, 136.6, 129.1, 129.1, 127.4, 127.3, 60.1, 56.5, 55.9, 54.3, 52.9, 47.2, 32.7, 23.9, 21.7, 20.8, 14.3. IR (KBr): 3328, 2965, 1741, 1656, 1496, 1436, 1173, 987, 732, 698. Anal. calcd. for $C_{28}H_{34}N_2O_6$: C, 68.00; H, 6.93; N, 5.66. Found: C, 68.01; H, 6.89; N, 5.58.

3.7. General procedure for the synthesis of (**4a–c**)

$CaCl_2$ (3.2 g, 28.8 mmol) and $NaBH_4$ (2.2 g, 55.5 mmol) in 80 ml THF were cooled below −10 °C under nitrogen, and then (4.80 mmol) **3a–c** in 30 ml THF and 110 ml EtOH was added dropwise. The reaction was kept for 3 h below −5 °C and then at room temperature overnight. The suspension was poured into 200 g crushed ice and 200 ml saturated NH_4Cl solution was added. Then 100 ml of EtOAc was added, the slurry was stirred for 30 min, and 50 ml concentrated HCl was added slowly. After 20 min, the water layer was extracted with EtOAc (3× 100 ml). The combined organic layer was washed with $NaHCO_3$ (2× 100 ml), brine (2× 100 ml) and dried (Na_2SO_4). Solvent was removed in vacuo and **4a–c** was obtained as white solid that was pure enough for subsequent reaction and analysis.

3.8. (1R,3S)-Bis[(S)-N-(1-isoproyl-2-hydroxy-ethyl)-amido]-1,2,2-trimethyl-cyclopentane (**4a**)

Yield: 92%, white solid. Mp: 153–155 °C. $[\alpha]_D^{20} = -24.2$ (*c* 0.8, EtOH). ^{1}H NMR ($CDCl_3$): δ 6.01 (d, br, 1H), 5.70 (d, br, 1H), 3.77–4.11 (m, 2H), 3.65–3.69 (m, 4H), 3.65–3.80 (s, br, 1H), 2.20–2.40 (m, 2H), 1.80–1.98 (m, 3H), 1.54–1.68 (m, 1H), 1.32 (s, 3H), 1.21 (s, 3H), 0.92–0.97 (m, 12H), 0.88 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 176.7, 174.0, 63.5, 60.5, 57.1, 56.7, 56.2, 54.8, 46.9, 33.2, 29.0, 24.4, 23.2, 22.1, 21.2, 19.6, 19.5, 18.9, 14.2. IR (KBr): 3413, 2961, 2929, 2876, 1636, 1519, 1464, 1372, 1078. Anal. calcd. for $C_{20}H_{38}N_2O_4$: C, 64.83; H, 10.34; N, 7.56. Found: C, 64.78; H, 10.38; N, 7.51.

3.9. (1R,3S)-Bis[(S)-N-(1-phenylmethyl-2-hydroxyethyl)-amido]-1,2,2-trimethyl-cyclopentane (**4b**)

Yield: 90%, white solid. Mp: 73–75 °C. $[\alpha]_D^{20} = -34.1$(*c* 0.5, EtOAc). ^{1}H NMR ($CDCl_3$): δ 7.20–7.32 (m, 10H), 5.93 (s, br, 1H), 5.74 (s, br, 1H), 4.13–4.20 (m, 2H), 3.59–3.68 (m, 4H), 2.77–2.93 (m, 4H), 2.39–2.53 (m, 1H), 2.16–2.31 (m, 2H), 2.05–2.15 (br, 2H), 1.66–1.81 (m, 1H), 1.37–1.52 (m, 1H), 1.26 (s, 3H), 1.04 (s, 3H), 0.71 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 176.4, 173.7, 137.8, 129.3, 128.6, 126.6, 64.1, 63.6, 55.9, 54.6, 52.7, 52.5, 46.7, 37.1, 37.0, 32.9, 24.2, 23.0, 21.6, 21.0. IR (KBr): 3378, 3027, 2963, 1639, 1516, 1454, 1373, 1038, 743, 701. Anal. calcd. for $C_{28}H_{38}N_2O_4$: C, 72.07; H, 8.21; N, 6.00. Found: C, 72.12; H, 8.22; N, 6.05.

3.10. (1R,3S)-Bis[(S)-N-(1-phenyl-2-hydroxyethyl)-amido]-1,2,2-trimethyl-cyclopentane (**4c**)

Yield: 88%, white solid. Mp: 98–99 °C. $[\alpha]_D^{20} = +86.6$(*c* 0.8, EtOH). ^{1}H NMR (CD_3COCD_3): δ 7.26–7.39 (m, 10H), 7.25 (d, J = 8.5 Hz, 1H), 6.95 (d, J = 8.5 Hz, 1H), 5.02–5.08 (m, 2H), 3.75–3.78 (m, 4H), 2.84–2.90 (m, 1H), 2.42–2.58 (m, 1H), 2.12–2.27 (m, 1H), 1.65–1.81 (m, 1H), 1.49–1.60 (m, 1H), 1.35 (s, 3H), 1.19 (s, 3H), 0.83 (s, 3H). ^{13}C NMR (CD_3COCD_3): 175.8, 173.2, 142.3, 142.1, 128.9, 128.8, 128.0, 127.9, 127.7, 127.6, 66.4, 66.2, 66.1, 65.9, 56.8, 56.4, 56.2, 54.4, 47.5, 33.5, 24.1, 23.5, 22.2, 21.8. IR (KBr): 3414, 3030, 2964, 1642, 1523, 1454, 1044, 757, 699. Anal. calcd. for $C_{26}H_{34}N_2O_4$: C, 71.21; H, 7.81; N, 6.39. Found: C, 71.18; H, 7.82; N, 6.28.

3.11. (1R,3S)-Bis[(R)-N-(1-phenyl-2-hydroxyethyl)-amido]-1,2,2-trimethyl-cyclopentane (**4c***)

Yield: 91%, white solid. Mp: 135–137 °C. $[\alpha]_D^{20} = -55.0$ (*c* 1.1, EtOH). ^{1}H NMR (CD_3COCD_3): 7.44(d, J = 8.5 Hz, 1H), 7.18–7.39 (m, 10H), 4.98–5.07 (m, 2H), 3.72–3.76 (m, 4H), 3.20–3.31 (s, br, 2H), 2.83 (m, 1H), 2.43–2.59 (m, 1H), 2.17–2.33 (m, 1H), 1.70–1.86 (m, 1H), 1.48–1.63 (m, 1H), 1.26 (s, 3H), 1.24 (s, 3H), 0.60 (s, 3H). ^{13}C NMR (CD_3COCD_3): 176.2, 173.7, 142.1, 128.9, 128.8, 127.9, 127.7, 127.5, 65.9, 60.0, 56.8, 56.4, 54.4, 47.7, 33.4, 24.1, 24.0, 22.1, 21.8. Anal. calcd. for $C_{26}H_{34}N_2O_4$: C, 71.21; H, 7.81; N, 6.39. Found: C, 71.18; H, 7.84; N, 6.32.

3.12. General procedure for the synthesis of (**5a**–**c**)

A solution of (10.0 mmol) **4a**–**c** in 100 ml CH_2Cl_2 was cooled to −5 °C and then (5.0 ml, 66.0 mmol) $SOCl_2$ was added dropwise. After stirring at room temperature overnight, the reaction mixture was cooled, quenched with aqueous K_2CO_3, separated and dried (Na_2SO_4). The solvent was removed and TLC showed that **5** has been obtained after this procedure. After the solvent was removed, the residue was purified by silica gel column chromatography with petroleum ether and ethyl acetate (1:1) as the eluent.

3.13. (1R,3S)-Bis[(S)-4-isoproyloxazolin-2-yl]-1,2,2-trimethyl-cyclopentane (**5a**)

Yield: 78%, colorless oil. $[\alpha]_D^{20} = -65.5$ (*c* 0.8, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 4.17–4.22 (m, 2H), 3.85–3.95 (m, 4H), 2.83 (t, J = 9.7 Hz, 1H), 2.59–2.74 (m, 1H), 2.12–2.28 (m, 1H), 1.83–1.98 (m, 1H), 1.68–1.83 (m, 2H), 1.53–1.67 (m, 1H), 1.22 (s, 3H), 1.19 (s, 3H), 0.93–0.97 (dd, J = 6.7 Hz, 6H), 0.85–0.87 (dd, J = 6.7 Hz, 6H), 0.79 (s, 3H). ^{13}C NMR ($CDCl_3$): 170.6, 167.5, 71.4, 69.3, 69.1, 50.0, 47.0, 46.4, 33.7, 32.3, 23.3, 22.6, 21.9, 20.9, 18.7, 18.5, 18.0, 17.9. IR (KBr): 2961, 1656, 1467, 1366, 1238, 1097, 986. Anal. calcd. for $C_{20}H_{34}N_2O_2$: C, 71.81; H, 10.25; N, 8.37. Found: C, 71.78; H, 10.24; N, 8.31.

3.14. (1R,3S)-Bis[(S)-4-phenylmethyloxazolin-2-yl]-1,2,2-trimethyl-cyclopentane (**5b**)

Yield: 84%, colorless oil. $[\alpha]_D^{20} = -35.5$ (*c* 0.8, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 7.17–7.29 (m, 10H), 4.29–4.36 (m, 2H), 4.14 (t, J = 8.7 Hz, 2H), 3.95 (t, J = 8.7 Hz, 2H), 3.05–3.13 (m, 2H), 2.74–2.82 (t, J = 8.5 Hz, 1H), 2.58–2.65 (m, 3H), 2.18–2.31 (m, 1H), 1.85–1.98 (m, 1H), 1.53–1.65 (m, 1H), 1.21 (s, 3H), 1.19 (s, 3H), 0.73 (s, 3H). ^{13}C NMR ($CDCl_3$): 171.6, 168.6, 137.9, 129.3, 128.4, 126.4, 71.4, 71.1, 66.9, 50.3, 47.1, 46.9, 41.8, 33.8, 23.8, 23.0, 22.0, 21.0, 14.2. IR (KBr): 2967, 1653, 1495, 1454, 1376, 984, 752, 701. Anal. calcd. for $C_{28}H_{34}N_2O_2$: C, 78.10; H, 7.96; N, 6.51. Found: C, 78.08; H, 7.98; N, 6.55.

3.15. (1R,3S)-Bis[(S)-4-phenyloxazolin-2-yl]-1,2,2-trimethyl-cyclopentane(**5c**)

Yield: 85%, colorless oil. $[\alpha]_D^{20} = -53.0$ (*c* 0.9, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 7.23–7.35 (m, 10H), 5.15–5.21 (m, 2H), 4.58–4.66 (m, 2H), 4.00–4.09 (m, 2H), 2.98 (t, J = 9.6 Hz, 1H), 2.73–2.84 (m, 1H), 2.27–2.43 (m, 1H), 1.98–2.09 (m, 1H), 1.68–1.74 (m, 1H), 1.34 (s, 3H), 1.31 (s, 3H), 0.99 (s, 3H). ^{13}C NMR ($CDCl_3$): 169.6, 172.7, 172.7, 128.7, 127.5, 126.8, 74.6, 74.5, 69.4, 50.7, 47.4, 47.2, 34.1, 24.0, 23.2, 22.4, 21.7. IR (KBr): 3029, 2969, 1650, 1603, 1493, 1454, 1173, 1100, 987, 757, 699. Anal. calcd. for $C_{26}H_{30}N_2O_2$: C, 77.85; H, 7.51; N, 6.96. Found: C, 77.81; H, 7.50; N, 6.85.

3.16. (1R,3S)-Bis[(R)-4-phenyloxazolin-2-yl]-1,2,2-trimethyl-cyclopentane (**5c***)

Yield: 84%, colorless oil. $[\alpha]_D^{20} = +80.4$ (*c* 0.9, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 7.23–7.35 (m, 10H), 5.14–5.24 (m, 2H), 4.58–4.67 (m, 2H), 4.05–4.12 (m, 2H), 2.95 (t, J = 9.4 Hz, 1H), 2.70–1.82 (m, 1H), 2.31–2.45 (m, 1H), 1.97–2.08 (m, 1H), 1.65–1.77 (m, 1H), 1.35 (s, 6H), 0.99 (s, 3H). ^{13}C NMR ($CDCl_3$): 172.2, 169.4, 142.5, 142.3, 128.5, 127.3, 126.5, 126.4, 74.4, 74.3, 69.3, 68.9, 50.5, 47.1, 46.9, 33.7, 29.5, 23.7, 23.0, 22.3, 21.4. IR (KBr): 3029, 2969, 1651, 1493, 1454, 1174, 987, 757, 699. Anal. calcd. for $C_{26}H_{30}N_2O_2$:

C, 77.85; H, 7.51; N, 6.96. Found: C, 77.87; H, 7.58; N, 6.88.

3.17. General procedure for asymmetric cyclopropanation

Under nitrogen atmosphere, $Cu(OTf)\cdot(1/2)C_6H_6$ (10 mg, 40 μmol) and **5a–c** (42 μmol) were dissolved in dry CH_2Cl_2 (5 ml) for 1 h. The solution was filtered through packed absorbent cotton under argon then styrene (or 1,1-diphenylethene) (2.5 mmol) was added at room temperature followed by addition of a CH_2Cl_2 solution (5 ml) of ethyl (or menthyl) diazoacetate (0.8 mmol) over 3 h. Stirring was continued for 10 h and the solvent was evaporated in vacuo to give a brown oil. This was purified by column chromatography on silica gel (petroleum/ethyl acetate = 20:1) to give the products that were analyzed by GC and HPLC, as described above.

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References

[1] (a) H.A. Mcmanus, P.J. Guiry, Chem. Rev. 104 (2004) 4151;
(b) A.K. Ghosh, P. Mathivanan, J. Cappiello, Tetrahedron: Asymmetry 9 (1998) 1;
(c) J.S. Johnson, D.A. Evans, Acc. Chem. Res. 33 (2000) 325;
(d) F. Fache, E. Schulz, M.L. Tommasino, M. Lemaire, Chem. Rev. 100 (2000) 2159;
(e) O.B. Sutclie, M.R. Bryce, Tetrahedron: Asymmetry 14 (2003) 2297;
(f) G. Helmchen, A. Pfaltz, Acc. Chem. Res. 33 (2000) 336.
[2] (a) E.J. Corey, N. Imai, H. Zhang, J. Am. Chem. Soc. 113 (1991) 728;
(b) D.A. Evans, K.A. Woerpel, M.M. Hinman, M.M. Faul, J. Am. Chem. Soc. 113 (1991) 726;
(c) G. Desimoni, G. Faita, M. Mella, Tetrahedron 52 (1996) 13649;
(d) G. Helmchen, K.T. Krotz, D. Hansen, Synlett (1991) 257;
(e) H. Nishiyama, S. Yamaguchi, M. Kondo, K. Itoh, J. Org. Chem. 57 (1992) 4306;
(f) J. Clariana, J. Comelles, M. Moreno-Mañas, A. Vallribera, Tetrahedron: Asymmetry 13 (2002) 1551;
(g) M. Schinnerl, C. Böhm, M. Seitz, O. Reiser, Tetrahedron: Asymmetry 14 (2003) 765;
(h) D.M. Du, B. Fu, W.T. Hua, Tetrahedron 59 (2003) 1933.
[3] (a) A.K. Ghosh, P. Mathivanan, J. Cappiello, Tetrahedron: Asymmetry 9 (1998) 1;
(b) Y. Uozumi, K. Kato, T. Hayashi, J. Am. Chem. Soc. 119 (1997) 5063;
(c) K.H. Ahn, C.W. Cho, J. Park, S. Lee, Tetrahedron: Asymmetry 8 (1997) 1179;
(d) A.V. Bedekar, P.G. Andersson, Tetrahedron Lett. 37 (1996) 4073.
[4] R. Noyori, M. Kitamura, Angew. Chem. 103 (1991) 34.
[5] (a) N. Hanyu, T. Aoki, T. Mino, M. Saka-moto, T. Fujita, Tetrahedron: Asymmetry 11 (2000) 2971;
(b) Z.H. Yang, L.X. Wang, Z.H. Zhou, Q.L. Zhou, C.C. Tang, Tetrahedron: Asymmetry 12 (2001) 1579;
(c) R.E. Lowenthal, S. Masamune, Tetrahedron Lett. 32 (1991) 7373;
(d) H.L. Kwong, W.Z. Lee, Tetrahedron: Asymmetry 10 (1999) 3791.
[6] (a) Y. Uozumi, H. Kyota, E. Kishi, K. Kitayama, T. Hayashi, Tetrahedron: Asymmetry 7 (1996) 1603;
(b) Y. Imai, W.B. Zhang, T. Kida, Y. Nakatsuji, I. Ikeda, Tetrahedron Lett. 38 (1997) 2681;
(c) R. Boulch, S. Andreas, M. Paul, R.W. Saalfrank, Tetrahedron Lett. 41 (2000) 1023;
(d) J. Clariana, J. Comelles, M.M. Marcial, A. Vallribera, Tetrahedron: Asymmetry 13 (2002) 1551;
(e) K. Alexander, S. Cook, C.L. Gibson, Tetrahedron Lett. 41 (2000) 7135;
(f) D.M. Du, B. Fu, W.T. Hua, Tetrahedron 59 (2003) 1933.
[7] (a) M.S. Toy, J. Polym. Sci. 5 (1967) 2481;
(b) G.M. Mark, R.P. Diana, M.T. Russell, W. Emma, Tetrahedron: Asymmetry 7 (1996) 2551.
[8] S.R. Gilbertson, D.J. Xie, Z. Fu, J. Org. Chem. 66 (2001) 7240.
[9] K.M.J. Brand, A.A.P. Meekel, U.K. Pandit, Tetrahedron 47 (1991) 2005.
[10] A.I. Pfaltz, in: R. Scheffold (Ed.), Modern Synthetic Methods, vol. 5, Springer, Berlin, Heidelberg, 1989, p. 199.
[11] R.E. Lowenthal, A. Abiko, S. Masamune, Tetrahedron Lett. 31 (1990) 6005.