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Novel chiral dibenzo[*a*,*c*]cycloheptadiene bis(oxazoline) and catalytic enantioselective cyclopropanation of styrene

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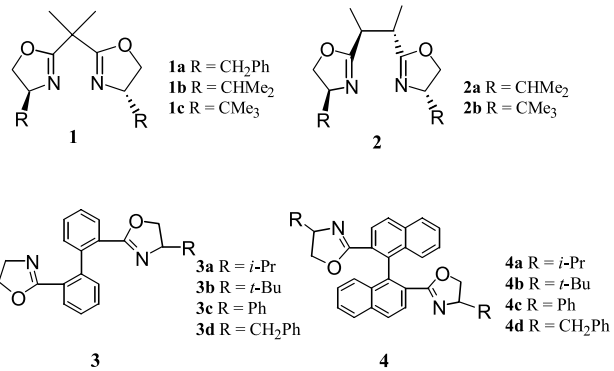
Abstract—A series of chiral C_2-symmetric bis(oxazoline) ligands containing dibenzo[*a*,*c*]cycloheptadiene units were synthesized. The copper complexes, prepared in situ from copper (I)-triflate and the new enantiopure oxazoline ligands, were assessed as chiral catalysts in the enantioselective cyclopropanation of styrene with diazoacetate. Enantioselectivities up to 82 and 62%, respectively, for *trans*- and *cis*-2-phenylcyclopropanecarboxylate were observed.

1. Introduction

The transition metal catalyzed cyclopropanation of alkenes with diazoacetates is the effective method developed for the synthesis of enantioenriched cyclopropanes.[1] Over the last decade, C_2-symmetric chiral oxazoline metal complexes have been recognized as an effective class of chiral catalyst in a variety of transition metal catalyzed asymmetric reactions.[2] High catalytic activities and enantiomeric excesses have been obtained for example in hydrosilylation of ketone,[3] allylic alkylation,[4] Michael addition,[5] Diels–Alder cycloaddition,[6] and cyclopropanation[7] mainly using C_2-symmetric chiral ligands in conjunction with suitable transition metal ion. Thus, the design and synthesis of new chiral oxazoline ligands has inspired many scientists to work with great efforts.

This type of ligands most studied were the ligand **1** with a one carbon spacer and **2** with a two carbon spacer between the bis(oxazoline) rings.[8,9] In their molecular structure, only the central chirality element in the oxazoline moiety and the asymmetric induction was controlled only by the central chirality element in the oxazoline moiety. Later, Ikeda,[10] Hayashi[11] and their co-workers developed bis(oxazoline) ligands **3** and **4** which include an axially flexible and rigid chiral biaryl skeleton and high enantioselectivity for cyclopropanation of olefin were obtained. However, in their studies chiral biaryl bis(oxazoline) need separation of the two diastereomers of the ligand, and only one of the two diastereomers shows high enantioselectivity.[11]

Continuing on our ongoing project on the synthesis, structure and catalytic enantioselective cyclopropanation of styrene by novel chiral bis(oxazoline) ligands containing 2,5-diaryl-1,3,4-oxadizole units and other reactions using heterocyclic ligands,[12] in this paper, we report the synthesis and the catalytic enantioselective cyclopropanation of styrene by copper (I) complex of a series of new bis(oxazoline) ligands **5** containing axial biaryl of dibenzo-[*a*,*c*]cycloheptadiene and chiral center of bis(oxazoline). We expect the combination of dibenzo[*a*,*c*]cycloheptadiene unit and chiral oxazoline unit in new ligands may result in unique characteristics for catalytic reaction.



2. Results and discussion

The usual method for preparation of chiral bis(oxazoline) is the reaction of diacid derivatives with chiral β-amino alcohol. The cyclic diethyl carboxylate **6** was synthesized according to literature procedure from 2,2′-bis(bromomethyl)biphenyl.[13] The cyclic diethyl carboxylate **6** was transformed into dihydroxy diamide **7** by the following

Keywords: bis(oxazoline); synthesis; dibenzo[*a*,*c*]cycloheptadiene; enantioselective cyclopropanation; styrene.

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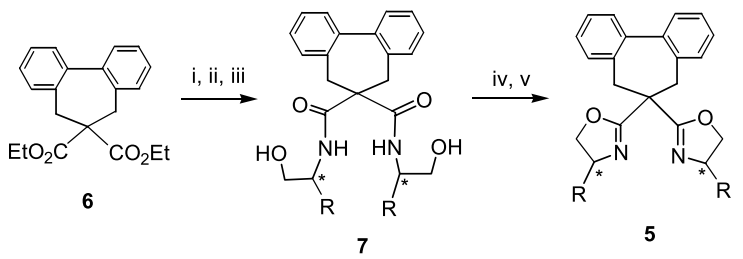
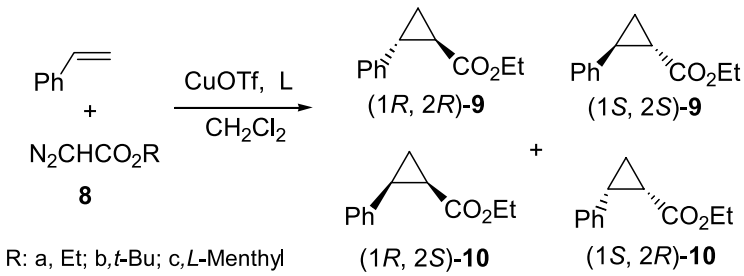


Scheme 1. Synthesis of new bis(oxazoline) **5a**–**e**.

reaction sequence. Hydrolysis of diethyl carboxylate **6** in an alcohol solution of NaOH gave the corresponding dicarboxylate, which was refluxed with thionyl chloride to afford the diacyl chloride. The diacyl chloride was treated with β-amino alcohols and triethylamine to afford the corresponding chiral intermediate dihydroxy diamides **7** as solids in 65–73% yields. In the present work, the procedure developed by Denmark[14] was selected to synthesize the desired ligands **5a**–**e**. The dihydroxy diamides were treated with methanesulfonyl chloride (MsCl) (2.2 equiv.) and Et_3N (4.4 equiv.) in dichloromethane to afford the corresponding bismesylates, which were treated with an aqueous methanolic solution of NaOH (8 equiv.) to furnish the bis(oxazoline) **5** in good yields (70–82%) (Scheme 1). In all cases, the intermediate bismesylates were too unstable to tolerate chromatographic purification, thus the intermediate bismesylates were not isolated and directly cyclized in situ. The structures of new ligands were characterized by ^1H NMR, MS, IR and elemental analysis.

Although compounds **5** possess an axial chirality, they cannot be isolated in enantiomerically pure state of chiral configuration, because fast interconversion between (*R*) and (*S*) enantiomers of biphenyl occurs at room temperature owing to the low rotation barrier energy along the 1,1′ bond of biphenyl moiety.[15] Then, the chirality of **5** only came from chiral oxazoline, this reduce the difficulty in separating the diastereoisomers resulting from the double chirality of biphenyl skeleton and oxazoline.

These ligands were then examined for the copper-catalyzed cyclopropanation of styrene with diazoacetate which is the model reaction most often investigated with chiral oxazoline ligands.[16] The asymmetric cyclopropanation was carried out in dichloromethane in the presence of 1% mol of copper (I) catalyst generated by mixing $Cu(OTf).1/2C_6H_6$ and the bis(oxazoline) ligands **5** to give 2-phenyl-cyclopropanecarboxylate as a mixture of *trans* and *cis* isomers (Scheme 2). The ratio of *trans* and *cis* isomer were



Scheme 2. Cyclopropanation reaction of styrene and diazoacetate.

Table 1. Asymmetric cyclopropanation of styrene with diazoacetates catalyzed by copper (I)-bis(oxazoline)

Entry	Ligands	Diazoacetate	Temp. (°C)	Yields[a] (%)	*trans*/*cis*[b]	ee%[c] (*trans*)	Config.[d]	ee%[c] (*cis*)	Config.[d]
1	**5a**	**8a**	20	72	61:39	63	1*R*, 2*R*	54	1*R*, 2*S*
2	**5b**	**8a**	20	76	64:36	42	1*R*, 2*R*	28	1*R*, 2*S*
3	**5c**	**8a**	20	68	56:44	41	1*R*, 2*R*	32	1*R*, 2*S*
4	**5d**	**8a**	20	70	62:38	61	1*R*, 2*R*	41	1*R*, 2*S*
5	**5e**	**8a**	20	71	60:40	60	1*S*, 2*S*	38	1*S*, 2*R*
6	**5a**	**8a**	0	74	62:38	68	1*R*, 2*R*	55	1*R*, 2*S*
7	**5a**	**8b**	0	72	66:34	76	1*R*, 2*R*	61	1*R*, 2*S*
8	**5a**	**8c**	0	75	68:32	82	1*R*, 2*R*	64	1*R*, 2*S*

[a] Isolated yield of a mixture of *trans* and *cis* by chromatographic purification.
[b] The ratio of *trans* and *cis* was determined by ^1H NMR.
[c] ee values were determined by HPLC (Chiracel Daicel OD and OJ Column, elution with hexane–isopropanol 90:10, 0.5 ml/min).
[d] Based on the sign of optical rotation.

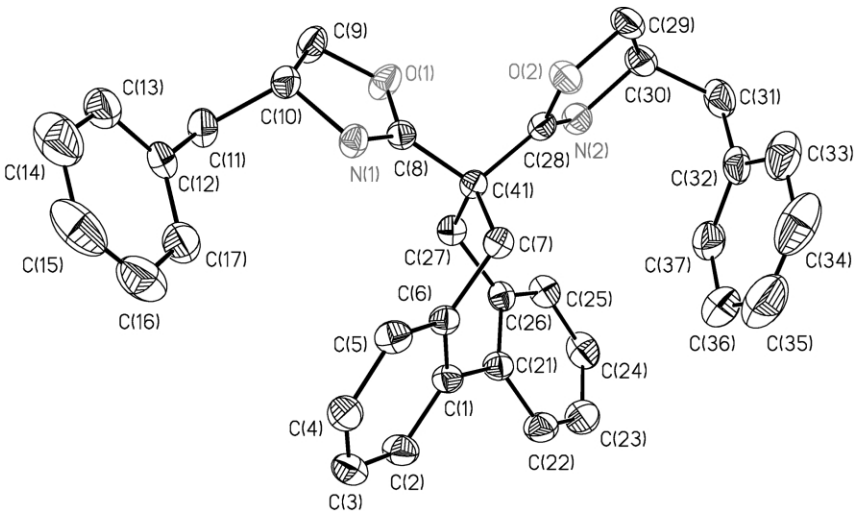


Figure 1. Perspective view of compound **5c**, showing 30% probability ellipsoids for the non-hydrogen atoms and the numbering scheme of the atoms in the molecule.

determined by ^{1}H NMR analysis, and the enantiomeric excesses were determined by HPLC analysis using a chiral column (Chiracel OD and OJ). The representative results are summarized in Table 1.

Among the bis(oxazoline) ligands, **5a** containing isobutyl substitutent on its oxazolines gave the highest enantiomeric excess for *trans* **9** in 63% ee and *cis* **10** in 52% ee (entry 1), the ligands **5b** and **5c** containing isopropyl and benzyl group afforded comparably lower enantioselectivity (*trans* 42 and 41% ee, respectively, entry 2, 3). Also, the ligands **5d** and **5e** with phenyl substituent present good enantioselectivity for cyclopropanation in 61 and 60% ee (entry 4, 5).

Meanwhile we examined the effect of temperature and different diazoacetate for cyclopropanation of the ligand **5a** as shown in Table 1. The reactions were carried out under the same condition as above, except addition of diazoacetate for 5 h and reaction proceeding for 16 h at 0°C, the ee value of copper (I)-catalyzed cyclopropanation rise to 68% (entry 6). As expected, the enantioselectivity was improved by use of steric bulkier diazoacetate ester. The reaction of L-menthyl diazoacetate with styrene in the presence of Cu(I)-ligand **5a** catalyst gave *trans* menthyl cyclopropanecarboxylates up to 82% ee and *cis* isomer in 64% ee (entry 8). The best advantage is that our new ligand can give good enantioselectivity using the very cheap ligand derivated from L-leucinol. In contrast, very expensive ligands derivated from L-*t*-leucinol were usually used in literature.[8,9]

In order to obtain a direct understanding of the structure of new dibenzo[*a*,*c*]cycloheptadiene bis(oxazoline) ligands, the stereostructure of ligand **5c** was determined by X-ray crystal diffraction analysis.[17] Compound **5c** was obtained as air-stable, colorless crystal upon slow evaporation of a solution of **5c** in ethyl acetate–petroleum ether (v/v 1:3). A perspective view of compound **5c** was shown in Figure 1. The dibenzo[*a*,*c*]cycloheptadiene is twist conformation in compound **5c**. The C1–C2–C3–C4–C5–C6 benzene ring has a dihedral angle with C21–C22–C23–C24–C25–C26 benzene ring of 44.2°. The φ angle of bis(oxazoline) is 107.12°. From the crystal structure of **5c**, it turns out that the twist conformation of biphenyl may has effect on the chiral environment of two oxazoline units in corresponding copper (I) complex. The conformation of biphenyl unit may be affected by temperature and thus the dibenzo[*a*,*c*]cycloheptadiene bis(oxazoline) copper (I) complex will result in different enantioselectivity on different temperatures.

In conclusion, we have synthesized a series of new chiral dibenzo[*a*,*c*]cycloheptadiene bis(oxazoline) ligands. Preliminary results in asymmetric cyclopropanation of styrene with diazoacetate have been obtained. The C_2-symmetric bis(oxazoline) **5** derived from dibenzo[*a*,*c*]cycloheptadiene showed different reactivity in the asymmetric copper-catalyzed cyclopropanation. The highest enantioselectivity has been obtained with isobutyl substituted bis(oxazoline) **5a**. Although the *trans*/*cis* stereoselectivity and enantioselectivity are moderate to good, the preliminary results at least suggest that these novel dibenzo[*a*,*c*]cycloheptadiene bis(oxazoline) ligands have much potential as new catalyst system for asymmetric reaction. Further studies on other asymmetric reactions are undergoing in our research group.

3. Experimental

3.1. General

Melting points were measured on an XT-4 melting point apparatus and were uncorrected. ^{1}H NMR spectra were recorded on a Mercury 200 spectrometer with tetramethylsilane serving as internal standard. Infrared spectra were obtained on a Bruker Vector 22 spectrometer. Mass spectra were obtained on a VG-ZAB-HS mass spectrometer. Optical rotations were measured on a Perkin–Elmer 341 LC spectrometer. Elemental analyses were carried out on an Elementar Vario EL instrument. The optical purities of *trans*- and *cis*-cyclopropanes were determined by HPLC analysis using a chiral column (Daicel Chiralcel OD and OJ; eluent, hexane–isopropyl alcohol 90:10; flow rate, 0.5 mL/min; UV detector, 220 nm). The absolute configuration of the major enantiomer was assigned according to

the sign of the specific rotation.[18] Solvents used were purified and dried by standard procedures.

3.1.1. 6,6-Bis[*N*-(1′*S*)-(1′-isobutylhydroxyethyl)amido]-dibenzo[*a*,*c*]-1,3-cycloheptadiene (7a). *General procedure I*. To a solution of diethyl dibenzo[*a*,*c*]-1,3-cycloheptadiene-6,6-dicarboxylate **6** (1.0 g, 2.96 mmol) in CH_3OH (10 mL) was added NaOH solution (10 mL, 2N). The mixture was refluxed for 8 h, then the methanol was removed in vacuo. The residue was cooled to 0°C and acidified with aqueous HCl (6N). The acidified mixture was extracted with ether (10 mL×3), the organic layer was dried with anhydrous Na_2SO_4 and evaporated. The obtained white solid was directly refluxed with $SOCl_2$ (5 mL) for 2 h, the excess $SOCl_2$ was removed in vacuo. Benzene (10 mL) was added and the solvent was removed again to dryness to remove the trace of $SOCl_2$ and afford the diacyl dichloride. The diacyl dichloride in CH_2Cl_2 (20 mL) was added dropwise to a solution of L-leucinol (0.75 g, 6.4 mmol) and Et_3N (4 mL, 28.9 mmol) in CH_2Cl_2 (20 mL) at 0°C and stirred at room temperature for 4 h. The reaction mixture was washed with water (5 mL×2). The organic layer was dried over anhydrous Na_2SO_4 and concentrated to give crude solid. Purification by silica gel column chromatography (40% ethyl acetate in petroleum ether) afforded the dihydroxy diamide **7a** 0.96 g (67.6%). Mp 162–163.5°C. $[\alpha]_D^{20}=-6.8$ (c=0.8, $CHCl_3$). IR (KBr): ν 3406, 2958, 1639, 1534, 1451, 1262 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.39–7.20 (m, 8H), 6.20 (br s, 2H), 4.02–4.18 (m, 2H), 3.73 (t, J=6.4 Hz, 2H), 3.41–3.25 (m, 6H), 2.80 (br s, 2H), 1.55–1.25 (m, 6H), 0.86 (d, J=7.0 Hz, 12H). ^{13}C (50 MHz, $CDCl_3$): δ 172.0, 140.6, 135.6, 127.8, 127.3, 65.3, 58.1, 49.8, 36.9, 24.8, 22.7, 21.7, 18.2. MS (FAB): 481 (M+1). Anal. for $C_{29}H_{40}O_4N_2$ Calcd (%) C, 72.50; H, 8.33; N, 5.83. Found (%): C, 72.44; H, 8.20; N, 5.68.

3.1.2. 6,6-Bis[*N*-(1′*S*)-(1′-isopropylhydroxyethyl)amido]-dibenzo[*a*,*c*]-1,3-cycloheptadiene (7b). Following general procedure I, from diethyl dibenzo[*a*,*c*]-1,3-cycloheptadiene-6,6-dicarboxylate **6** (1.0 g, 2.96 mmol), L-valinol (0.66 g, 6.4 mmol) and Et_3N (4 mL, 28.9 mmol) to afford the dihydroxy diamide **7b** 0.88 g (65.7%). Mp 170–172°C. $[\alpha]_D^{20}=-14.6$ (c=0.24, $CHCl_3$). IR (KBr): ν 3406, 2960, 1637, 1539, 1451, 1262 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.42–7.25 (m, 8H), 6.24 (br s, 2H), 3.83–3.70 (m, 4H), 3.60–3.25 (m, 4H), 3.05–2.70 (m, 4H), 1.82–1.73 (m, 2H), 0.92 (d, J=7.0 Hz, 6H), 0.88 (d, J=8.8 Hz, 6H). ^{13}C ($CDCl_3$): δ 172.5, 140.3, 135.5, 130.4, 128.0, 127.6, 65.9, 63.8, 57.4, 37.2, 28.9, 19.6, 19.0. MS (FAB): 453 (M+1). Anal. for $C_{27}H_{36}O_4N_2$ Calcd (%) C, 71.68; H, 7.96; N, 6.19. Found (%): C, 71.73; H, 7.82; N, 6.06.

3.1.3. 6,6-Bis[*N*-(1′*S*)-(1′-benzylhydroxyethyl)amido]-dibenzo[*a*,*c*]-1,3-cycloheptadiene (7c). Following general procedure I, from diethyl dibenzo[*a*,*c*]-1,3-cycloheptadiene-6,6-dicarboxylate **6** (1.0 g, 2.96 mmol), L-phenylalaninol (0.97 g, 6.4 mmol) and Et_3N (4 mL, 28.9 mmol) to afford the dihydroxy diamide **7c** 1.15 g (70.8%). Mp 196–198°C. $[\alpha]_D^{20}=+74.2$ (c=0.48, $CHCl_3$). IR (KBr): ν 3406, 2932, 1640, 1539, 1453, 1262 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.34–7.12 (m, 18H), 6.31 (br s, 2H), 4.38–4.20 (m, 2H), 3.85–3.70 (m, 2H), 3.50–3.44 (m, 2H), 2.90–2.56 (m, 8H). ^{13}C ($CDCl_3$): δ 171.9, 140.2, 137.2, 135.3, 128.5, 127.9, 127.4, 127.2, 126.6, 65.4, 63.4, 58.2, 36.6. MS (FAB): 549 (M+1). Anal. for $C_{35}H_{36}O_4N_2$ Calcd (%) C, 76.64; H, 6.56; N, 5.11. Found (%): C, 76.72; H, 6.66; N, 5.20.

3.1.4. 6,6-Bis[*N*-(1′*S*)-(1′-phenylhydroxyethyl)amido]-dibenzo[*a*,*c*]-1,3-cycloheptadiene (7d). Following general procedure I, diethyl dibenzo[*a*,*c*]-1,3-cycloheptadiene-6,6-dicarboxylate **6** (1.0 g, 2.96 mmol), L-phenylglycinol (0.88 g, 6.4 mmol) and Et_3N (4 mL, 28.9 mmol) to afford the dihydroxy diamide **7d** 1.08 g (70.1%). Mp 181–183°C. $[\alpha]_D^{20}=-50.0$ (c=0.44, $CHCl_3$). IR (KBr): ν 3406, 2936, 1641, 1539, 1453, 1262 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.37–7.16 (m, 18H), 6.90 (br s, 2H), 5.16–5.09 (m, 2H), 3.91–3.80 (m, 4H), 3.50–2.80 (m, 6H). ^{13}C ($CDCl_3$): δ 171.8, 140.4, 135.3, 129.8, 127.9, 127.8, 127.6, 127.5, 126.6, 65.9, 65.6, 55.9, 37.5. MS (FAB): 521 (M+1). Anal. for $C_{33}H_{32}O_4N_2$ Calcd (%) C, 76.15; H, 6.15; N, 5.38. Found (%): C, 76.34; H, 6.20; N, 5.14.

3.1.5. 6,6-Bis[*N*-(1′*R*)-(1′-phenylhydroxyethyl)amido]-dibenzo[*a*,*c*]-1,3-cycloheptadiene (7e). Following general procedure I, diethyl dibenzo[*a*,*c*]-1,3-cycloheptadiene-6,6-dicarboxylate **6** (1.0 g, 2.96 mmol), D-phenylglycinol (0.88 g, 6.4 mmol) and Et_3N (4 mL, 28.9 mmol) to afford the dihydroxy diamide **7e** 1.12 g (72.7%). Mp 175–177°C. $[\alpha]_D^{20}=+69.6$ (c=0.56, $CHCl_3$). IR (KBr): ν 3406, 2936, 1640, 1536, 1456, 1262 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.38–7.16 (m, 18H), 6.91 (br s, 2H), 5.18–5.09 (m, 2H), 3.91–3.80 (m, 4H), 3.40–2.80 (m, 6H). ^{13}C ($CDCl_3$): δ 171.7, 140.3, 135.2, 129.9, 127.8, 127.7, 127.6, 127.5, 126.5, 65.7, 65.5, 55.8, 37.2. MS (FAB): 521 (M+1). Anal. for $C_{33}H_{32}O_4N_2$ Calcd (%) C, 76.15; H, 6.15; N, 5.38. Found (%): C, 76.38; H, 6.28; N, 5.19.

3.1.6. 6,6-Bis[(4′*S*)-4′-isobutyloxazolin-2′-yl]-dibenzo-[*a*,*c*]-1,3-cycloheptadiene (5a). *General procedure II*. To an ice cold solution of the dihydroxy diamide **7a** (1.20 g, 2.5 mmol) and Et_3N (2 mL, 14 mmol) in CH_2Cl_2 (20 mL) was added MsCl (0.60 g, 5.2 mmol) slowly. The mixture was allowed to warm to room temperature and was stirred for 1 h. The mixture was washed with water (5 ml). The organic layer was dried over anhydrous Na_2SO_4 and concentrated to dryness in vacuo to give the crude bismesylate as a yellow oil. The crude bismesylate was dissolved in CH_3OH (20 mL) and was treated with NaOH solution (4 mL, 1N) at room temperature for 12 h. The methanol was removed in vacuo and 30 mL CH_2Cl_2 was added to it. The solution was washed with water (5 mL×2). The organic layer was dried over anhydrous Na_2SO_4 and concentrated in vacuo to give a pale yellow oil. Purification by silica gel column chromatography (petroleum ether–ethyl acetate 5:1) to afford colorless viscous oil **5a** 0.91 g (81.9% yield). $[\alpha]_D^{20}=-28.9$ (c=0.95, $CHCl_3$). IR (KBr): ν 3010, 2966, 1654, 1508, 1482 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.25–7.44 (m, 8H), 4.36 (t, J=8.4 Hz, 2H), 4.22–4.07 (m, 2H), 3.89 (s, 2H), 3.26–2.90 (m, 4H), 1.86–1.42 (m, 4H), 1.36–1.19 (m, 2H), 0.88 (d, J=3.8 Hz, 12H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 166.1, 140.9, 138.1, 127.9, 127.4, 127.1, 73.5, 65.8, 64.6, 45.6, 37.6, 25.3, 22.8. MS (EI): 444 (M^+, 100), 429 (7), 387 (20), 318 (45), 304 (32). HRMS (EI): calcd for $C_{29}H_{36}O_2N_2$ 444.2777, found: 444.2777.

3.1.7. 6,6-Bis[(4′*S*)-4′-isopropyloxazolin-2′-yl]-dibenzo-[*a*,*c*]-1,3-cycloheptadiene (5b). Following general procedure II, from dihydroxy diamide **7b** (0.91 g, 2.0 mmol), MsCl (0.50 g, 4.4 mmol) and Et_3N (2 mL, 14 mmol) to afford the crude bismesylate. The crude bismesylate was treated with a NaOH/MeOH–H_2O solution as the above to afford **5b** (0.64 g, 76.4%) as a colorless viscous oil after purification by column chromatography on silica gel (ethyl acetate–petroleum ether 1:6). $[\alpha]_D^{20}=-17.5$ (c=0.80, $CHCl_3$). IR (KBr): ν 2966, 1654, 1508, 1482 cm^{-1}. ^1H NMR ($CDCl_3$): 7.41–7.23 (m, 8H), 4.26 (t, J=8.2 Hz, 2H), 4.13–3.90 (m, 4H), 3.42–2.80 (m, 4H), 1.78–1.68 (m, 2H), 0.87 (t, J=4.0 Hz, 12H). ^{13}C NMR ($CDCl_3$): δ 166.1, 140.7, 135.8, 130.4, 127.7, 127.1, 126.9, 126.8, 71.7, 70.8, 53.2, 37.4, 32.2, 18.4, 17.7. MS (EI): 416 (M^+, 8), 304 (58), 191 (38), 127 (100). HRMS (EI) calcd for $C_{27}H_{32}O_2N_2$ 416.2464. Found: 416.2463.

3.1.8. 6,6-Bis[(4′*S*)-4′-benzyloxazolin-2′-yl]-dibenzo[*a*,*c*]-1,3-cycloheptadiene (5c). Following general procedure II, from dihydroxy diamide **7c** (1.60 g, 2.92 mmol), MsCl (0.70 g, 6.1 mmol) and Et_3N (2 mL, 14 mmol) to afford the crude bismesylate. The crude bismesylate was treated with a NaOH/MeOH–H_2O solution as the above to afford **5c** (1.06 g, 70.8%) as a colorless solid after purification by column chromatography on silica gel (ethyl acetate–petroleum ether 1:3). Mp 82–83.5°C. $[\alpha]_D^{20}=-19.0$ (c=0.35, $CHCl_3$). IR (KBr): ν 3010, 1656, 1452 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.46–7.14 (m, 18H), 4.42–4.30 (m, 2H), 4.23 (t, J=7.8 Hz, 2H), 4.15–3.98 (m, 2H), 3.25–3.02 (m, 4H), 3.00–2.48 (m, 4H). ^{13}C NMR ($CDCl_3$): δ 166.1, 140.8, 137.7, 135.8, 129.3, 127.9, 127.3, 127.2, 126.3, 72.2, 67.1, 53.2, 37.5. MS (EI): 512 (M^+, 90), 421 (100), 334 (46). Anal. for $C_{35}H_{32}O_2N_2$ Calcd (%): C. 82.10; H. 6.48; N, 5.46. Found (%): C, 82.31; H, 6.52; N, 5.40.

3.1.9. 6,6-Bis[(4′*S*)-4′-phenyloxazolin-2′-yl]-dibenzo[*a*,*c*]-1,3-cycloheptadiene (5d). Following general procedure II, from dihydroxy diamide **7d** (0.84 g, 1.62 mmol), MsCl (0.40 g, 3.5 mmol) and Et_3N (2 mL, 14 mmol) to afford the crude bismesylate. The crude bismesylate was treated with a NaOH/MeOH–H_2O solution as the above to afford **5d** (0.78 g, 78.2%) as a colorless viscous oil after purification by column chromatography on silica gel (ethyl acetate–petroleum ether 1:6). $[\alpha]_D^{20}=-19.0$ (c=1.80, $CHCl_3$). IR (KBr): ν 3010, 2964, 1656, 1482 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.46–7.17 (m, 18H), 5.30 (dd, J=8.2, 8.2 Hz, 2H), 4.72 (dd, J=8.2, 8.4 Hz, 2H), 4.17 (t, J=8.4 Hz, 2H), 3.41–3.12 (m, 4H). ^{13}C NMR ($CDCl_3$): δ 168.0, 140.9, 135.7, 130.2, 128.5, 128.1, 127.5, 127.4, 127.3, 126.7, 75.5, 69.5, 53.7, 37.8. MS (EI): 484 (M^+, 64), 380 (12), 306 (100). HRMS (EI): $C_{33}H_{28}O_2N_2$ Calcd 484.2139. Found: 484.2150.

3.1.10. 6,6-Bis[(4′*R*)-4′-phenyloxazolin-2′-yl]-dibenzo-[*a*,*c*]-1,3-cycloheptadiene (5e). Following general procedure II, from dihydroxy diamide **7e** (0.92 g, 2.5 mmol), MsCl (0.45 g, 3.94 mmol) and Et_3N (2 mL, 14 mmol) to afford the crude bismesylate. The crude bismesylate was treated with a NaOH/MeOH–H_2O solution as the above to afford **5e** (0.70 g, 81.7%) as a colorless viscous oil after purification by column chromatography on silica gel (ethyl acetate–petroleum ether 1:6). $[\alpha]_D^{20}=+41.1$ (c=0.45, $CHCl_3$). IR (KBr): ν 3010, 2966, 1650, 1508 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.46–7.06 (m, 18H), 5.26 (dd, J=9.6, 8.2 Hz, 2H), 4.72 (dd, J=8.0, 9.6 Hz, 2H), 4.18 (dd, J=8.2, 8.0 Hz, 2H), 3.28–2.90 (m, 4H). ^{13}C NMR ($CDCl_3$): δ 168.0, 140.9, 135.7, 130.2, 128.6, 128.2, 127.6, 127.5, 127.3, 126.7, 75.5, 69.6, 53.7, 37.8. MS (EI): 484 (M^+, 74), 380 (14), 306 (100). HRMS (EI): calcd for $C_{33}H_{28}O_2N_2$ 484.2150. Found: 484.2151.

3.2. General procedure for the asymmetric cyclopropanation

A mixture of CuOTf-1/2C_6H_5 (6.0 mg, 0.024 mmol) and ligand **5a** (12.0 mg, 0.027 mmol) was stirred in dry CH_2Cl_2 (2 mL) under nitrogen for 30 min Styrene (1.60 g, 15.4 mmol) was added at room temperature or 0°C. Followed by slow addition of a CH_2Cl_2 solution (2 mL) of ethyl (or *t*-butyl, L-menthyl) diazoacetate (310 mg, 2.72 mmol) over 5 h by syringe. The reaction mixture was stirred for an addition 16 h at room temperature or 0°C. The solution was diluted with Et_2O (20 mL). The solution was then washed with water (5 mL) and brine (5 mL), dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure, the residue was purified by column chromatography on silica gel (petroleum ether–ethyl acetate 50:1) to afford the mixture of *trans*- and *cis*-2-phenyl-cyclopropane-1-carboxylates as colorless oil. The *trans*/*cis* ratio of this mixture was determined by ^1H NMR (200 MHz) in $CDCl_3$. The enantiomeric excess was determined by HPLC with a chiral column (Daicel Chiralcel OD and OJ; eluent, hexane–isopropyl alcohol 90:10; flow rate 0.5 mL/min).

3.3. X-Ray crystallographic analysis

A colorless crystal was selected and mounted on a fine-focus sealed tube and used for data collection. Cell constants and an orientation matrix for data collection were obtained by least-squares refinement of the diffraction data from 25 reflections in the 2θ range from 1.50 to 28.05 degree in a Rigaku AFC6S diffractometer equipped with a graphite crystal incident beam monochromator. Data were collected at 293 K using Mo Kα radiation (λ=0.71073 Å) and the ω–2θ variable-scan mode. The intensity data obtained were corrected for Lorentz and polarization effects. An empirical absorption correction based on ψ-scan data was applied. The crystal structure was resolved by the direct method using SHELXS97, and full-matrix least-squares refinement on F^2 was performed with SHELXL97 program. All the non-hydrogen atoms were deduced from an E-map and refined anisotropically. The positions of hydrogen atoms were generated geometrically and included in structure factor calculations with assigned isotropic thermal parameters. All computations were performed on a FOUNDER FP^+ 5-166 586 personal computer.

5c: $C_{35}H_{32}N_2O_2$, F_W=512.63, monoclinic, space group P(2)1, a=9.9894 (2), b=10.2532 (4), c=13.7784 (7) Å; α=90°, β=99.981 (2)°, γ=90°, V=1389.8 (5) $Å^3$, Z=2, $F(000)$=544, Dc=1.225 Mg/m^3, μ=0.076 mm^{-1}. Crystal size 0.60×0.50×0.25 mm; Index ranges $-12\le h\le 12$, $-13\le k\le 13$, $-17\le l\le 17$; Reflections collected/unique, 1272/3367 (f_{int}=0.0485); Data/restraints/parameters, 3367/1/353; Goodness-of-fit on F^2 0.833; Final R indices

$[I>2\sigma(I)]$: $R1=0.0352$, $wR2=0.0624$; Extinction coefficient 0.0293 (17); Largest diff. peak and hole, 0.134 and -0.171 e $\AA^{-3}$.

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17. Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC-195273. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK [fax: +44-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].
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