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Chiral quinolinyl-oxazolines as ligands for copper(I)-catalyzed asymmetric cyclopropanation

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Abstract

Chiral quinolinyl-oxazoline compounds have been synthesized from enantiomerically pure amino alcohols and 8-quinoline-carboxylic acid using a convenient procedure. Asymmetric cyclopropanation of styrene with diazoacetates in the presence of 1 mol% of CuOTf and quinolinyl-oxazolines gave 2-phenylcyclopropane carboxylates in moderate enantiomeric excesses.

1. Introduction

Over the last decade the chiral oxazolines derived from readily available amino acids have emerged as an efficient class of ligands in an increasing number of asymmetric transformations.[1] In particular, the oxazoline ligands with C_2 symmetry have achieved extremely high enantioselectivities in various catalytic processes.[1c] However, there have been few reports on applications of catalysts with unsymmetric oxazoline ligands which also have two coordinating nitrogen atoms. Brunner has reported that pyridinyl-oxazoline **1** is a good chiral ligand in asymmetric hydrosilylation reactions.[2] Fujisawa has demonstrated that the aminoaryl-oxazoline **2** has excellent asymmetric induction in cyclopropanation[3] and Diels–Alder reactions.[4] During our studies on the design of new nitrogen-containing chiral reagents, we became interested in the chiral quinolinyl-oxazoline ligands **3**. Ligands **3** have similar electronic properties to pyridinyl-oxazoline ligands, but they have a different size chelate ring in the metal complexes formed in the reaction, which will influence the stability, stereochemistry and enantioselectivities of catalysts.[5] Herein, we wish to report the preparation of **3** and their applications as ligands in copper(I)-catalyzed asymmetric cyclopropanation.

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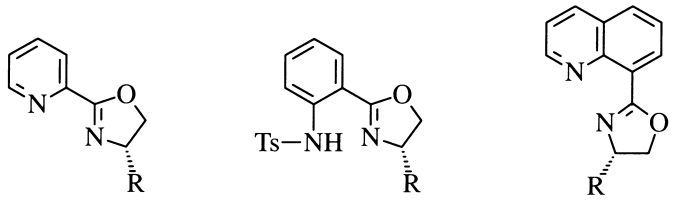
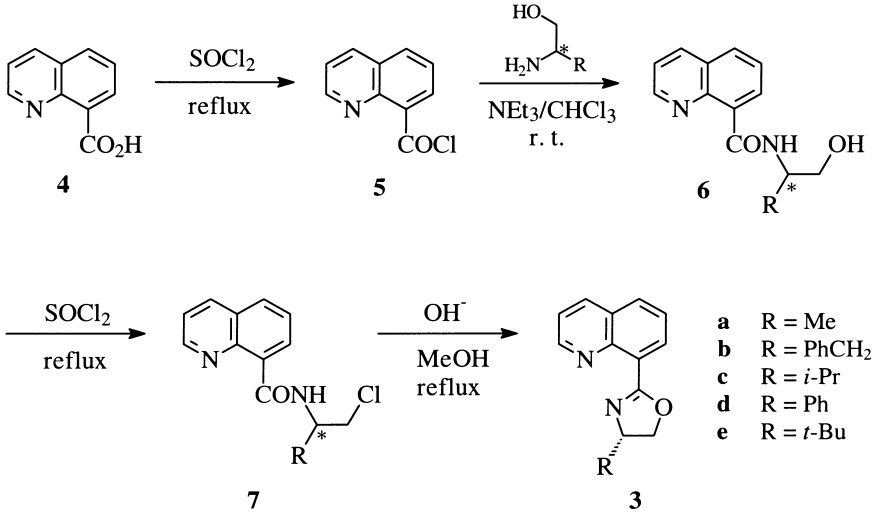


1 2 3

2. Results and discussion

2.1. Synthesis of quinolinyl-oxazoline ligands

Quinolinyl-oxazolines **3** were synthesized from enantiomerically pure amino alcohols and 8-quinolinecarboxylic acid in four steps as shown in Scheme 1. 8-Quinolinecarboxylic acids were converted to the corresponding chlorides **5** with $SOCl_2$. After evaporation of excess $SOCl_2$, the chlorides were reacted with the amino alcohols in the presence of triethylamine in chloroform to provide 8-quinolinecarboxamides **6** in 70–81% yield. The hydroxy groups of the 8-quinolinecarboxamides **6** were converted to chlorides in 52–85% yield by refluxing with $SOCl_2$. The cyclization of chlorides **7** with NaOH in refluxing methanol gave the desired ligands **3** in 30–94% yield.



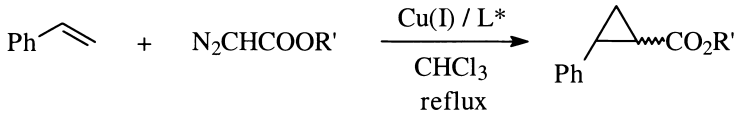
4 5 6 7 3

Scheme 1.

2.2. Copper(I)-catalyzed asymmetric cyclopropanation

Recently, copper(I)-catalyzed asymmetric cyclopropanation of olefins with diazoacetates, an important synthetic reaction, has been investigated using various oxazoline compounds as chiral ligands, and very high enantiomeric excesses have been achieved in some cases.[6] To evaluate the new class of oxazoline ligands **3**, we first tested the copper(I)-catalyzed cyclopropanation of styrene with diazoacetates using **3** as chiral ligands (Eq. 1), and the results are reported in Table 1. The reaction was carried out in $CHCl_3$ by slow addition of the diazoacetate to a refluxing solution of styrene and copper(I)-oxazoline catalyst prepared in situ from copper(I) triflate and ligands **3**. It was found that almost the same yields

and selectivities were given in 1,2-dichloroethane and benzene as in chloroform. The reaction did not occur in refluxing methylene chloride. In the reaction 1.0 mol% of catalyst was used, and no differences in the chemical yield or enantioselectivity have been found when up to 2.5 mol% of catalyst was used. As shown in Table 1, the R-group at the chiral center of the oxazoline ring has a significant effect on the enantioselectivity. For all diazoacetates, ligand **3e**, having the bulker *tert*-butyl group, provided the highest enantioselectivities, whereas ligand **3a**, having the small methyl group, gave the lowest enantioselectivities. The low chemical yield using ligand **3a** is due to decomposition of the catalyst during reaction. Different substituents on the oxazoline ring of the ligand did not change the *cis*/*trans* ratio of the cyclopropanation products, which only appears to depend on the ester group of the diazoacetate, corresponding to the results reported by others.[3,6,7]



(1)

Table 1
Asymmetric cyclopropanation of styrene with diazoacetates catalyzed by copper(I)-ligands **3**

N_2CHCO_2R'	Ligand	Solvent	Yield(%)[a]	*cis*/*trans*[b]	ee%(*cis*)[c]	ee%(*trans*)[c]
R' = Et	**3a**	$(ClCH_2)_2$	23	31:69	3	10
R' = Et	**3b**	$CHCl_3$	71	31:69	23	38
R' = Et	**3b**	$(ClCH_2)_2$	65	31:69	22	28
R' = Et	**3b**	C_6H_6	69	28:72	25	35
R' = Et	**3c**	$CHCl_3$	63	32:68	22	34
R' = Et	**3c**	C_6H_6	75	31:69	28	32
R' = Et	**3d**	$CHCl_3$	91	28:72	22	27
R' = Et	**3e**	$CHCl_3$	77	35:65	26	45
R' = (-)- menthyl	**3b**	$CHCl_3$	81	23:77	55	52
R' = (-)-menthyl	**3e**	$CHCl_3$	63	25:75	64	54
R' = DCM[d]	**3b**	$CHCl_3$	64	14:86	47	45
R' = DCM	**3e**	$CHCl_3$	54	14:86	63	64
R' = *t*-Bu	**3b**	$CHCl_3$	55	20:80	21	31
R' = *t*-Bu	**3e**	$CHCl_3$	38	26:74	34	52

[a] Isolated yield. [b] Determined by GC analysis on a 30 m capillary column (Supelco 2-4318). [c] Determined, after re-esterification with (-)-menthol[6c], by GC analysis on a 30 m capillary column (Supelco 2-4318) at 210°C constant [T_R = 7.82 and 8.04 min. for *cis* isomer, and 8.98 and 9.31 min for *trans* isomer]. [d] Dicyclohexylmethyl diazoacetate.

In summary, new enantiomerically pure quinolinyl-oxazoline compounds have been synthesized and were used as chiral ligands in asymmetric cyclopropanation. The scope and limitation of this type of

ligand in cyclopropanation and their applications in other metal-catalyzed asymmetric reactions are under investigation in our laboratory.

3. Experimental

3.1. General

1,2-Dichloroethane was distilled from CaH_2. C_6H_6 was distilled from Na. $CHCl_3$ was distilled from $CaSO_4$. All optically pure amino alcohols were prepared by reduction of the corresponding commercially available amino acids with $NaBH_4/I_2$ in THF.[8] IR (film): selected bands in cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ in ppm (TMS), *J* in Hz. MS (EI): selected peaks, *m*/*z* (%).

3.2. Synthesis of 8-quinolinecarboxamides **6**

3.2.1. (1′S)-N-(1′-Benzyl-2′-hydroxyethyl)-8-quinolinecarboxamide (**6b**)

General procedure: 8-Quinoline-carboxylic acid (3.46 g, 20 mmol) was treated with $SOCl_2$ (29 ml) at reflux temperature for 8 h, and the excess $SOCl_2$ was removed under reduced pressure. The residue was dissolved in 65 ml of $CHCl_3$, and 3.32 g (22 mmol) of L-phenylalaninol in $CHCl_3$ (15 ml) was added at −10°C, then 14 ml (100 mmol) of triethylamine in $CHCl_3$ (20 ml) was added at −10°C over 2 h. The resulting mixture was stirred at rt for 24 h and washed with water (2×50 ml), aqueous $NaHCO_3$ (0.2 M, 2×50 ml) and saturated NaCl solution. After drying over anhydrous Na_2SO_4 and concentrating under reduced pressure, the crude product was purified by column chromatography on silica gel with PE:EtOAc (1:2) to give 4.28 g (14 mmol, 70%) of **6b** as a pale yellow oil. $[\alpha]_D^{20}$ −116 (*c* 0.4, EtOH). IR: 1730w, 1641s, 1607m, 1592m, 1572s, 1546s, 1498m, 1456m, 1424w, 1382w, 1318w, 1280m, 1200w, 1146w, 1134w, 1097w, 1071w, 1044m, 914w. ^1H NMR ($CDCl_3$): δ 2.16 (s, 1H), 3.01 (m, 2H), 3.77 (m, 2H), 4.47 (m, 1H), 7.08–7.32 (m, 5H), 7.35 (dd, *J*=8.4 and 4.4 Hz, 1H), 7.50 (t, *J*=7.8 Hz, 1H), 7.82 (dd, *J*=8.1 and 1.3 Hz, 1H), 8.24 (dd, *J*=8.4 and 1.7 Hz, 1H), 8.69 (m, 2H), 11.48 (d, *J*=6.5 Hz, 1H). MS (EI): 274 (29), 260 (63), 244 (41), 243 (39), 157 (29), 156 (100), 155 (26), 128 (75), 101 (24), 89 (25). TLC (PE:EtOAc 1:2): R_f=0.4. Anal. calcd for $C_{19}H_{18}N_2O_2$: C, 74.49; H, 5.92; N, 9.14. Found: C, 73.82; H, 5.82; N, 9.14.

3.2.2. (1′S)-N-(1′-Methyl-2′-hydroxyethyl)-8-quinolinecarboxamide (**6a**)

Colorless oil, 80% yield. $[\alpha]_D^{20}$ +22 (*c* 1.0, EtOH). IR: 1642s, 1608w, 1591m, 1571s, 1498w, 1455w, 1380w, 1289w, 1203w, 1130w, 1074w, 1060m, 947w, 885w. ^1H NMR ($CDCl_3$): δ 1.40 (d, *J*=6.8 Hz, 3H), 3.75 (dd, *J*=10.9 and 4.0 Hz, 1H), 3.86 (dd, *J*=10.9 and 3.5 Hz, 1H), 3.91 (s, 1H), 4.37–4.45 (m, 1H), 7.50 (dd, *J*=8.4 and 4.3 Hz, 1H), 7.67 (t, *J*=7.7 Hz, 1H), 7.97 (dd, *J*=8.1 and 1.5 Hz, 1H), 8.28 (dd, *J*=8.4 and 1.8 Hz, 1H), 8.83 (dd, *J*=7.3 and 1.5 Hz, 1H), 8.93 (dd, *J*=4.3 and 1.8 Hz, 1H), 11.45 (s, 1H). MS (EI): 213 (13), 200 (42), 199 (96), 157 (45), 155 (100), 128 (79), 102 (24), 101 (31). TLC (PE:EtOAc 1:1): R_f=0.29. Anal. calcd for $C_{13}H_{14}N_2O_2$: C, 67.81; H, 6.13; N, 12.17. Found: C, 67.49; H, 6.08; N, 12.00.

3.2.3. (1′S)-N-(1′-Isopropyl-2′-hydroxylethyl)-8-quinolinecarboxamide (**6c**)

Pale yellow oil, 75% yield. $[\alpha]_D^{20}$ −24 (*c* 0.4, EtOH). IR: 1730s, 1652s, 1609w, 1592m, 1573s, 1551s, 1499w, 1462w, 1384w, 1370w, 1342w, 1277m, 1199m, 1145m, 1073w, 1026w, 885w. ^1H NMR ($CDCl_3$): δ 1.02 (dd, *J*=6.8 and 4.3 Hz, 6H), 2.07 (m, 1H), 3.78 (m, 2H), 4.04 (m, 2H), 7.40 (dd, *J*=8.4 and 4.2

Hz, 1H), 7.56 (t, *J*=7.8 Hz, 1H), 7.85 (dd, *J*=8.1 and 1.5 Hz, 1H), 8.18 (dd, *J*=8.4 and 1.7 Hz, 1H), 8.75 (dd, *J*=8.4 and 1.4 Hz, 1H), 8.84 (dd, *J*=4.2 and 1.7 Hz, 1H), 11.54 (d, *J*=5.9 Hz, 1H). MS (EI): 227 (8), 226 (31), 197 (10), 155(100), 128 (25), 127 (32), 101 (10). TLC (PE:EtOAc 1:2): R_f=0.2. Anal. calcd for $C_{15}H_{18}N_2O_2$: C, 69.74; H, 7.02; N, 10.84. Found: C, 70.13; H, 6.74; N, 10.43.

*3.2.4. (1′S)-N-(1′-Phenyl-2′-hydroxyethyl)-8-quinolinecarboxamide (**6d**)*

White solid, 70% yield, mp 152–155°C. $[\alpha]_D^{20}$ −158 (*c* 0.24, EtOH). IR: 1644s, 1613w, 1586m, 1566s, 1497w, 1463w, 1453w, 1384w, 1333w, 1300w, 1202w, 1091w, 1070m, 1053m, 980w. ^{1}H NMR ($CDCl_3$): δ 3.53 (s, 1H), 4.06 (m, 2H), 5.48 (m, 1H), 7.25–7.62 (m, 6H), 7.46 (t, *J*=7.7 Hz, 1H), 7.98 (d, *J*=8.1 Hz, 1H), 8.30 (dd, *J*=8.3 and 1.2 Hz, 1H), 8.86 (d, *J*=7.3 Hz, 1H), 8.91 (d, *J*=4.1 Hz, 1H), 12.18 (d, *J*=5.9 Hz, 1H). MS (EI): 292 (67, M^+), 275 (99), 261 (59), 157 (100), 155 (48), 129 (97), 128 (68), 106 (48), 102 (42), 101 (49). TLC (PE:EtOAc 1:1): R_f=0.2. Anal. calcd for $C_{18}H_{16}N_2O_2$: C, 73.96; H, 5.52; N, 9.58. Found: C, 74.29, H, 5.53; N, 9.58.

*3.2.5. (1′S)-N-(1′-tert-Butyl-2′-hydroxyethyl)-8-quinolinecarboxamide (**6e**)*

White solid, 81% yield, mp 148–150°C. $[\alpha]_D^{20}$ +4 (*c* 1.0, EtOH). IR: 1643s, 1610w, 1590m, 1572s, 1498w, 1462w, 1424w, 1382w, 1364w, 1298w, 1244w, 1200w, 1137w, 1099w, 1060m, 1018w, 944w. ^{1}H NMR ($CDCl_3$) δ 1.16 (d, *J*=6.1 Hz, 9H), 3.70–3.80 (m, 2H), 4.00–4.20 (m, 2H), 7.52 (dd, *J*=8.3 and 4.3 Hz, 1H), 7.70 (t, *J*=7.8 Hz, 1H), 7.98 (dd, *J*=8.1 and 1.6 Hz, 1H), 8.32 (dd, *J*=8.3 and 1.8 Hz, 1H), 8.86 (dd, *J*=7.4 and 1.6 Hz, 1H), 8.93 (dd, *J*=4.3 and 1.8 Hz, 1H), 11.70 (d, *J*=5.5 Hz, 1H). MS (EI): 241(7), 215(12), 156(100), 129(25), 128(32). TLC (PE:EtOAc 1:1): R_f=0.2, Anal. calcd for $C_{16}H_{20}N_2O_2$: C, 70.56; H, 7.04; N, 10.29. Found: C, 70.31; H, 7.39; N, 10.24.

*3.3. Synthesis of 8-quinolinecarboxamides **7***

*3.3.1. (1′S)-N-(1′-Benzyl-2′-chloroethyl)-8-quinolinecarboxamide (**7b**)*

General procedure: To a solution of **6b** (3.06 g, 10 mmol) in chloroform (75 ml) was added a solution of $SOCl_2$ (3.7 ml, 50 mmol) in chloroform (25 ml) in 1 h, and the mixture was refluxed for 1 h. After cooling to rt, 20 ml of water was added slowly. The organic layer was separated, and the aqueous layer was extracted with chloroform (2×20 ml). The combined organic layer was washed with aqueous $NaHCO_3$ and saturated NaCl solution, and dried over anhydrous Na_2SO_4. After filtration and concentration under reduced pressure, the crude material was purified by column chromatography on silica gel with PE:EtOAc (1:2) to give 2.47 g (7.6 mmol, 76%) of **7b** as a pale yellow oil. $[\alpha]_D^{20}$ −70 (*c* 0.4, EtOH). IR: 1652s, 1611w, 1592m, 1574s, 1538s, 1498s, 1455m, 1435w, 1382w, 1343w, 1281m, 1200w, 1134w, 1079w, 1030w. ^{1}H NMR ($CDCl_3$) δ 3.05 (dd, *J*=13.6 and 7.7 Hz, 1H), 3.15 (dd, *J*=13.6 and 6.3Hz, 1H), 3.70 (m, 2H), 4.72 (m, 1H), 7.08–7.40 (m, 5H), 7.46 (dd, *J*=8.0 and 4.3 Hz, 1H), 7.60 (t, *J*=7.8 Hz, 1H), 7.90 (d, *J*=7.4 Hz, 1H), 8.26 (d, *J*=8.0 Hz, 1H), 8.84 (d, *J*=7.4 Hz, 1H), 8.88 (d, *J*=3.0 Hz, 1H), 11.62 (d, *J*=7.0 Hz, 1H). MS (EI): 324 (34, M^+), 289 (58), 235 (72), 233 (100), 198 (34), 197 (67), 157 (47), 142 (62), 129 (56), 128 (92), 91 (59). TLC (PE:EtOAc 1:2): R_f=0.79. Anal. calcd for $C_{19}H_{17}N_2OCl$: C, 70.26; H, 5.28; N, 8.62. Found: C, 69.83; H, 5.26; N, 8.60.

*3.3.2. (1′S)-N-(1′-Methyl-2′-chloroethyl)-8-quinolinecarboxamide (**7a**)*

7a was prepared in 64% yield according to the general procedure described above except that the aqueous layer was neutralized with solid $NaHCO_3$ before extracting by chloroform. The product was obtained as an oil after purification by column chromatography. $[\alpha]_D^{20}$ +21 (*c* 1.0, EtOH). IR: 1652s, 1612w, 1593w, 1573m, 1552m, 1454w, 1438w, 1378m, 1344w, 1319w, 1277w, 1214w, 1200w, 1168w,

1139w, 1090w, 1069w, 1039w. ^{1}H NMR ($CDCl_3$) δ 1.48(d, *J*=6.8 Hz, 3H), 3.80 (dd, *J*=10.9 and 3.8 Hz, 1H), 3.87 (dd, *J*=10.9 and 4.7 Hz, 1H), 4.70 (m, 1H), 7.50 (dd, *J*=8.4 and 4.2 Hz, 1H), 7.69 (t, *J*=7.9 Hz, 1H), 7.97 (dd, *J*=8.1 and 1.4 Hz, 1H), 8.29 (dd, *J*=8.4 and 1.8 Hz, 1H), 8.86 (dd, *J*=7.2 and 1.4 Hz, 1H), 8.96 (dd, *J*=4.2 and 1.7 Hz, 1H), 11.67 (d, *J*=3.8 Hz, 1H). MS (EI): 250 (16, M+2), 233 (16), 231 (49), 214 (100), 199 (32), 156 (25). TLC (PE:EtOAc 2:1): R_f=0.47. Anal. calcd for $C_{13}H_{13}NOCl$: C, 62.78; H, 5.27; N, 11.26. Found: C, 62.78; H, 5.42; N, 10.79.

*3.3.3. (1′S)-N-(1′-Isopropyl-2′-chloroethyl)-8-quinolinecarboxamide (**7c**)*

Yellow oil, 65% yield. $[\alpha]_D^{20}$ −8 (*c* 0.4, EtOH). IR: 1727m, 1656s, 1610m, 1574s, 1543s, 1500w, 1462w, 1438w, 1384w, 1318w, 1282w, 1198w, 1135w, 1075w, 1040w, 1028w, 1011w. ^{1}H NMR ($CDCl_3$) δ 0.99 (d, *J*=6.8 Hz, 3H), 1.02 (d, *J*=6.9 Hz, 3H), 2.18 (m, 1H), 3.72 (dd, *J*=11.0 and 5.0 Hz, 1H), 3.80 (dd, *J*=11.0 and 4.0 Hz, 1H), 4.28 (m, 1H), 7.40 (dd, *J*=8.3 and 4.2 Hz, 1H), 7.57 (t, *J*=7.6 Hz, 1H), 7.86 (dd, *J*=8.1 and 1.5 Hz, 1H), 8.17 (dd, *J*=8.3 and 1.8 Hz,1H), 8.76 (dd, *J*=7.6 and 1.5 Hz, 1H), 8.83 (dd, *J*=4.2 and 1.8 Hz, 1H), 11.54 (d, *J*=6.1 Hz, 1H). MS (EI): 235 (24), 232 (73), 226 (13), 197 (40), 157 (26), 156 (100), 142 (17), 129 (32), 128 (69), 102 (15), 101 (21). TLC (PE:EtOAc 1:1): R_f=0.73. Anal. calcd for $C_{15}H_{17}N_2OCl$: C, 65.10; H, 6.19; N, 10.12. Found: C, 64.70; H, 6.21; N, 10.18.

*3.3.4. (1′S)-N-(1′-Phenyl-2-chloroethyl)-8-quinolinecarboxamide (**7d**)*

White solid, 65% yield, mp 99–102°C. $[\alpha]_D^{20}$ −102 (*c* 0.4, EtOH). IR: 1657s, 1612w, 1593w, 1575m, 1543s, 1497m, 1455w, 1442w, 1380w, 1353w, 1288w, 1254w, 1199w, 1148w, 1076w. ^{1}H NMR ($CDCl_3$) δ 4.06 (m, 2H), 5.75 (m, 1H), 7.25–7.61 (m, 6H), 7.70 (t, *J*=7.8 Hz, 1H), 8.00 (dd, *J*=8.1 and 1.5 Hz, 1H), 8.33 (dd, *J*=8.4 and 1.8 Hz, 1H), 8.89 (dd, *J*=7.2 and 1.5 Hz, 1H), 9.00 (dd, *J*=4.3 and 1.8 Hz, 1H), 12.38 (d, *J*=6.0 Hz, 1H). MS (EI): 307 (15), 290 (22), 289 (100), 215 (24), 156 (15). TLC (PE:EtOAc 1:1): R_f=0.73. Anal. calcd for $C_{18}H_{15}N_2OCl$: C, 69.57; H, 4.86; N, 9.01. Found: C, 69.69; H, 4.85; N, 8.99.

*3.3.5. (1′S)-N-(1′-tert-Butyl-2′-chloroethyl)-8-quinolinecarboxamide (**7e**)*

White solid, 52% yield, mp 132–134°C. $[\alpha]_D^{20}$ +8 (*c* 1.0, EtOH). IR: 1659s, 1610w, 1593w, 1573m, 1552s, 1496w, 1462w, 1434w, 1398w, 1380w, 1372w, 1316w, 1284w, 1271w, 1216w, 1134w, 1100w, 1068w, 995w. ^{1}H NMR ($CDCl_3$) δ 1.13 (d, *J*=4.5 Hz, 9H), 3.72 (dd, *J*=11.3 and 7.9 Hz, 1H), 4.00 (dd, *J*=11.3 and 3.7 Hz, 1H), 4.52 (ddd, *J*=9.7, 7.9 and 3.6 Hz, 1H), 7.51 (dd, *J*=8.3 and 4.3 Hz, 1H), 7.70 (dd, *J*=7.9 and 7.5 Hz, 1H), 7.97 (dd, *J*=8.1 and 1.6 Hz, 1H), 8.30 (dd, *J*=8.3 and 1.8 Hz, 1H), 8.90 (dd, *J*=7.5 and 1.6 Hz, 1H), 8.94 (dd, *J*=4.3 and 1.8 Hz, 1H), 11.74 (d, *J*=8.9 Hz,1H). MS (EI): 232 (34), 198 (17), 197 (92), 196 (13), 169 (14), 168 (12), 157 (12), 156 (100), 155 (17), 142 (34), 129 (12), 128 (34). TLC (PE:EtOAc 1:1): R_f=0.67. Anal. calcd for $C_{16}H_{19}N_2OCl$: C, 66.09; H, 6.60; N, 9.63. Found: C, 66.11; H, 6.64; N, 9.67.

*3.4. Synthesis of quinolinyl-oxazoline ligands **3***

*3.4.1. (4S)-4,5-Dihydro-2-(8′-quinolinyl)-4-benzyl-oxazole (**3b**)*

General procedure: A mixture of **7b** (3.24 g, 10 mmol) and NaOH (0.6 g, 15 mmol) in methanol (80 ml) was refluxed for 15 h. After removal of methanol, 20 ml of water and 20 ml of chloroform were added to the residue, the organic layer was separated, and the aqueous layer was extracted with chloroform (2×20 ml). The combined organic layer was dried over anhydrous K_2CO_3, and concentrated. The pure product was obtained by column chromatography on silica gel with PE:EtOAc (1:2). Yield: 1.99 g (6.9 mmol, 69%), mp 94–98°C. $[\alpha]_D^{20}$ −8 (*c* 0.8, EtOH). IR: 1656s, 1612w, 1602w, 1592m,

1578m, 1494s, 1471w, 1451w, 1389w, 1367w, 1356m, 1303w, 1286m, 1258m, 1194s, 1138w, 1017s, 1005s, 959s. ^{1}H NMR ($CDCl_3$) δ 2.80 (dd, *J*=13.7 and 9.0 Hz, 1H), 3.30 (dd, *J*=13.7 and 8.9 Hz, 1H), 4.22 (dd, *J*=8.5 and 7.5 Hz, 1H), 4.43 (dd, *J*=9.5 and 8.5 Hz, 1H), 4.65–4.80 (m, 1H), 7.10–7.32 (m, 5H), 7.38 (dd, *J*=8.3 and 4.2 Hz, 1H), 7.49 (dd, *J*=8.0 and 7.3 Hz, 1H), 7.85 (dd, *J*=8.3 and 1.3 Hz, 1H), 8.04 (dd, *J*=7.3 and 1.2 Hz, 1H), 8.11 (dd, *J*=8.3 and 1.8 Hz, 1H), 9.02 (dd, *J*=4.2 and 1.8 Hz, 1H). MS (EI): 289 (37, M+1), 198 (88), 197 (89), 169 (75), 168 (62), 155 (70), 144 (27), 143 (100), 128 (60), 91 (86), 77 (33), 65 (30). TLC (PE:EtOAc 2:1): R_f=0.16. Anal. calcd for $C_{19}H_{16}N_2O$: C, 79.14; H, 5.59; N, 9.72. Found: C, 78.70; H, 5.60; N, 9.44.

*3.4.2. (4S)-4,5-Dihydro-2-(8′-quinolinyl)-4-methyl-oxazole (**3a**)*

3a was prepared according to the general procedure described above except that aqueous $NaHCO_3$ (0.2 M, 20 ml), instead of water, was added to the residue. White solid, 30% yield, mp 119–122°C. $[\alpha]_D^{20}$ −42 (*c* 0.6, EtOH). IR: 1650s, 1594m, 1574m, 1546w, 1499s, 1473w, 1451w, 1388w, 1374w, 1355m, 1342m, 1296m, 1262w, 1192s, 1142m, 1131w, 1061m. ^{1}H NMR ($CDCl_3$) δ 1.46 (d, *J*=6.3 Hz, 3H), 4.08 (t, *J*=7.6 Hz, 1H), 4.50–4.75 (m, 2H), 7.43 (dd, *J*=8.3 and 4.2 Hz, 1H), 7.56 (t, *J*=7.8 Hz, 1H), 7.91 (dd, *J*=8.2 and 1.4 Hz, 1H), 8.16 (m, 2H), 9.07 (dd, *J*=4.2 and 1.8 Hz, 1H). MS (EI): 212 (61, M^+), 197 (63), 181 (24), 171 (20), 156 (100), 155 (58), 154 (27), 142 (54), 129 (78), 128 (45), 127 (25), 101 (24). TLC (PE:EtOAc 1:2): R_f=0.13. Anal. calcd for $C_{13}H_{12}N_2O$: C, 73.56; H, 5.70; N, 13.20. Found: C, 73.77; H, 5.96; N, 13.24.

*3.4.3. (4S)-4,5-Dihydro-2-(8′-quinolinyl)-4-isopropyl-oxazole (**3c**)*

Dark yellow oil, 94% yield. $[\alpha]_D^{20}$ −59 (*c* 0.8, EtOH). IR: 1657s, 1610w, 1594m, 1575m, 1498s, 1468m, 1387m, 1352m, 1298m, 1284m, 1256w, 1192s, 1140m, 1128m, 1066w. ^{1}H NMR ($CDCl_3$): δ 0.92 (d, *J*=6.8 Hz, 3H), 1.01 (d, *J*=6.8 Hz, 3H), 1.82–2.00 (m, 1H), 4.15–4.30 (m, 2H), 4.43–4.60 (m, 1H), 7.33 (dd, *J*=8.3 and 4.2 Hz, 1H), 7.46 (dd, *J*=8.0 and 1.3 Hz, 1H), 7.80 (dd, *J*=8.3 and 1.4 Hz, 1H), 8.02 (dd, *J*=7.2 and 1.3 Hz, 1H), 8.07 (dd, *J*=8.3 and 1.7 Hz, 1H), 8.96 (dd, *J*=4.2 and 1.7 Hz, 1H). MS (EI): 197 (82), 198 (49), 168 (23), 156 (63), 155 (42), 144 (15), 143 (100), 128 (48), 101 (21). TLC (PE:EtOAc 1:2): R_f=0.2. Anal. calcd for $C_{15}H_{16}N_2O$: C, 74.97; H, 6.71; N, 11.66. Found: C, 75.19; H, 6.74; N, 11.73.

*3.4.4. (4S)-4,5-Dihydro-2-(8′-quinolinyl)-4-phenyl-oxazole (**3d**)*

White solid, 50% yield, mp 73–76°C. $[\alpha]_D^{20}$ −50 (*c* 0.8, EtOH). IR: 1649s, 1611w, 1592w, 1577w, 1495m, 1472m, 1454w, 1387w, 1353m, 1320w, 1292m, 1277w, 1250w, 1191m, 1126m, 1011s, 938m. ^{1}H NMR ($CDCl_3$): δ 4.45 (t, *J*=8.3 Hz, 1H), 4.98 (dd, *J*=10.2 and 1.7 Hz, 1H), 5.58 (dd, *J*=10.2 and 8.1 Hz, 1H), 7.20–7.55 (m, 6H), 7.60 (t, *J*=7.8 Hz, 1H), 7.96 (dd, *J*=8.2 and 1.3 Hz, 1H), 8.21 (dd, *J*=8.3 and 1.7 Hz, 1H), 8.25 (dd, *J*=7.2 and 1.3 Hz, 1H), 9.11 (dd, *J*=4.3 and 1.7 Hz, 1H). MS (EI): 274 (16, M^+), 244 (57), 243 (67), 242 (15), 170 (24), 156 (100), 155 (27), 128 (22), 118 (16), 91 (23), 90 (26), 89 (44). TLC (PE:EtOAc 1:2): R_f=0.22. Anal. calcd for $C_{18}H_{14}N_2O$: C, 78.81; H, 5.14; N, 10.21. Found: C, 78.80; H, 5.22; N, 10.10.

*3.4.5. (4S)-4,5-Dihydro-2-(8′-quinolinyl)-4-*tert*-butyl-oxazole (**3e**)*

White solid, 50% yield, mp 138–140°C. $[\alpha]_D^{24}$ −72 (*c* 1.0, EtOH). IR: 1656s, 1610w, 1594m, 1574m, 1550w, 1499m, 1478m, 1393w, 1363m, 1354m, 1339w, 1297m, 1260m, 1208w, 1192m, 1139w, 1129w, 1066w, 1046w, 1012s, 957m. ^{1}H NMR ($CDCl_3$): δ 1.05 (d, *J*=3.4 Hz, 9H), 4.20 (dd, *J*=10.1 and 8.0 Hz, 1H), 4.39 (t, *J*=8.0 Hz, 1H), 4.57 (dd, *J*=10.1 and 8.6 Hz, 1H), 7.42 (dd, *J*=8.3 and 4.2 Hz, 1H), 7.56 (dd, *J*=8.2 and 7.2 Hz, 1H), 7.90 (dd, *J*=8.2 and 1.5 Hz, 1H), 8.08 (dd, *J*=7.1 and 1.5 Hz, 1H), 8.16 (dd,

J=8.3 and 1.8 Hz, 1H), 9.03 (dd, J=4.2 and 1.8 Hz, 1H). MS (EI): 256 (37, M+2), 254 (100, M^+), 198 (15), 197 (84), 196 (11), 169 (31), 168 (18), 156 (29), 155 (14), 142 (35). TLC (PE:EtOAc 1:2): R_f=0.25. Anal. calcd for: $C_{16}H_{18}N_2O$: C, 75.56; H, 7.13; N, 11.02. Found: C, 75.33; H, 7.83; N, 11.01.

3.5. Copper(I)-catalyzed asymmetric cyclopropanation of styrene with diazoacetates

General procedure: To a suspension of 5.0 mg (0.02 mmol) of $CuOTf(C_6H_6)_{0.5}$ in 10 ml of dry chloroform, a solution of 10.2 mg (0.04 mmol) of ligand **3e** in 10 ml of dry chloroform was added at rt. The mixture was stirred for 1.5 h and filtered through a syringe-tip filter (0.45 μm). After addition of 2.3 ml (20 mmol) of styrene, the solution was heated to reflux, and 228.2 mg (2 mmol) of ethyl diazoacetate in 10 ml of dry chloroform was slowly added over 2 h at reflux temperature. The resulting mixture was refluxed for an additional 6 h, and then was passed through a silica gel plug to remove the catalyst. The filtrate was concentrated under reduced pressure, and the residue was chromatographed on silica gel with petroleum ether:ethyl acetate (PE:EtOAc 95:5) to afford 298 mg (77%) of ethyl 2-phenylcyclopropane carboxylate. The *cis*:*trans* ratio (35:65) was determined by GC analysis on a 30 m capillary column (Supelco 2-4318) operated at 100°C for 5 min, then programmed at 4°C/min to 200°C [T_R=13.22 min (*cis* isomer) and 15.13 min (*trans* isomer)]. Enantiomeric excesses (26% ee for the *cis* isomer and 45% ee for the *trans* isomer) were determined, after re-esterification with (−)-menthol,[6c] by GC analysis on a 30 m capillary column (Supelco 2-4318) at 210°C constant [T_R=7.82 and 8.04 min for the *cis* isomer, and 8.98 and 9.31 min for the *trans* isomer].

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References

1. For recent reviews, see: (a) Pfaltz, A. *Acc. Chem. Res*. **1993**, *26*, 339. (b) Togni, A.; Venanzi, L. M. *Angew. Chem., Int. Ed. Engl*. **1994**, *33*, 497. (c) Ghosh, A. K.; Mathivanan, P.; Cappiello, J. *Tetrahedron: Asymmetry* **1998**, *9*, 1.
2. Brunner, H.; Obermann, U. *Chem. Ber*. **1989**, *122*, 499.
3. Ichiyanagi, T.; Shimizu, M.; Fujisawa, T. *Tetrahedron* **1997**, *53*, 9599.
4. Ichiyanagi, T.; Shimizu, M.; Fujisawa, T. *J. Org. Chem*. **1997**, *62*, 7937.
5. Brunner has reported an example of 2-quinolinyl-oxazoline and used it as a chiral ligand in the asymmetric hydrosilylation reaction. See Brunner, H.; Brandl, P. *Tetrahedron: Asymmetry* **1991**, *2*, 919.
6. (a) Lawenthal, R. E.; Abiko, A.; Masamune, S. *Tetrahedron Lett*. **1990**, *31*, 6005. (b) Evans, D. A.; Woepel, K. A.; Hinman, M. M.; Faul, M. M. *J. Am. Soc. Chem*. **1991**, *113*, 726. (c) Müller, D.; Umbrich, G.; Weber, B.; Pfaltz, A. *Helv. Chim. Acta* **1991**, *74*, 232.
7. Kim, S.-G.; Cho, C.-W.; Ahn, K.-H. *Tetrahedron: Asymmetry* **1997**, *8*, 1023.
8. Mckennon, M. J.; Meyers, A. I. *J. Org. Chem*. **1993**, *58*, 3568.