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Tetrahedron 60 (2004) 9037–9042

Enantioselective oxidative coupling of methyl 3-hydroxy-2-naphthoate using mono-*N*-alkylated octahydrobinaphthyl-2,2′-diamine ligand

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Received 8 July 2004; revised 28 July 2004; accepted 30 July 2004

Available online 27 August 2004

Abstract—Mono-*N*-alkylated octahydrobinaphthyl-2,2′-diamine (H_8-BINAM) chiral ligands were employed in the catalytic and asymmetric oxidative coupling of methyl 3-hydroxy-2-naphthoate to the corresponding binaphthol derivative. The diamine ligand with one *N*-(3-pentyl) group shows highest enantioselectivity in the biaryl coupling among other BINAM derivatives, and the coupling reaction proceeds faster than the reactions using alkanediamine ligands.

1. Introduction

Chiral 1,1′-bi-2-naphthol (BINOL) and its derivatives have been very successful as chiral ligands in asymmetric transformations and catalyses.[1] Efforts to obtain these versatile ligands in enantiopure forms were mainly focused on the optical resolutions of racemic compounds.[2] However, significant developments were also made in the last decade on the oxidative asymmetric homocoupling of achiral 2-naphthols to chiral BINOL derivatives. Oxidative coupling of 2-naphthol to BINOL utilizing chiral oxovanadium(IV) complexes has been reported with reasonably high enantioselectivities.[3] Another area of intensive study is the oxidative coupling of 3-hydroxy-2-naphthoate ester catalyzed by copper-amine complexes. The ester group on the naphthol is essential for a better asymmetric induction through a bidentated chelation to the copper catalyst. Initial asymmetric study was reported by Smrcina et al. using stoichiometric copper(II) complex of chiral amines, such as sparteine (**1**) and α-methylbenzylamine.[4] Further development was made by Nakajima et al. using catalytic amount CuCl and proline-derived diamine **2** to give an improved, but still moderate, enantiselectivity.[5] Better enantioselectivity, up to 93%, was achieved using *cis*-1,5-diazadecalin (**3**) as a chiral diamine ligand and CuI as a copper(I) source.[6] The slow reaction rates of the oxidative biaryl couplings using the diamine ligands **1**–**3**, requiring heating at 40 °C for one to several days, and the formation of the *ortho*-iodinated naphthol byproduct in the case of using CuI as a copper ion source are demanding further improvements of the catalyst activity and enantioselectivity in this versatile catalytic reaction (Fig. 1).

The chiral diamines previously studied for the biaryl coupling reaction were mostly aliphatic diamines, and the use of chiral aryldiamines derived from 1,1′-binaphthyl-2,2′-diamine (BINAM) has not been reported yet. Thus, we studied the Cu-catalyzed enantioselective oxidative coupling of naphthol **4** to binaphthol **5** in the presence of BINAM derivatives.[7,8]

2. Results and discussion

The use of (*R*)-BINAM (**6a**) itself for the copper-catalyzed oxidative coupling of 3-hydroxy-2-naphthoate ester provided **5** in almost quantitative yield at room temperature under oxygen atmosphere in two days, and the reaction was slowed down, without affecting the enantioselectivity, when powdered 4 Å molecular sieves were not added (entries 1 and 2, Table 1).[6a] The coupling reaction was almost

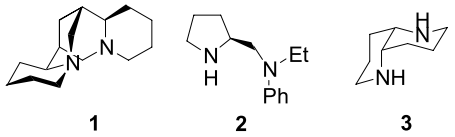

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Figure 1. Chiral diamine ligands for the asymmetric oxidative coupling of methyl 3-hydroxy-2-naphthoate

Keywords: Catalytic; Asymmetric; Oxidation; Biaryl; Coupling; Binaphthol.
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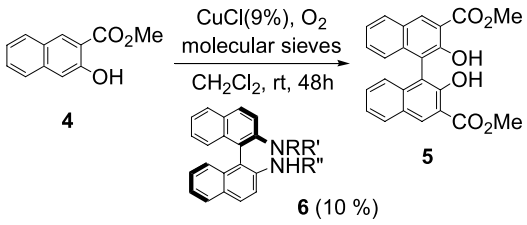
doi:10.1016/j.tet.2004.07.086

Table 1. Enantioselective oxidative coupling of **4** catalyzed by complexes between (*R*)-BINAM derivative and CuCl



Entry	Ligand	R, R′	R″	Yield[a,b] (%)	ee[c,d] (%)
1	**6a**	H, H	H	99	20 (*S*)
2	**6a**[e]	H, H	H	76	20 (*S*)
3	**6b**	*i*-Pr, H	*i*-Pr	11	11 (*S*)
4	**6c**	$-(CH_2)_4-$	H	56	23 (*S*)
5	**6d**	*i*-Pr, H	H	95	58 (*R*)
6	**6e**	*c*-Hex, H	H	82	51 (*R*)
7	**6f**	3-Pentyl, H	H	8	30 (*R*)

[a] Isolated yields.
[b] 0.5 M substrate concentration.
[c] Determined by chiral HPLC (Chiralpak AD-H column).
[d] Absolute configuration assigned by comparison to the literature.
[e] Without powdered molecular sieves.

completed in a day and is apparently much faster than the reported cases using aliphatic diamines. It was proposed by Kozlowski et al. that the slow step of the catalytic cycle of this oxidative coupling is the reduction of copper(II) to copper(I), and a more electrophilic copper(II) coordinates to the substrate more strongly and can undergo more facile reduction to copper(I).[6d] Thus, the decreased basicity of the biaryl diamine ligand **6a**, compared with aliphatic diamines **1**–**3**, can be the major reason for the relative rate increase. We screened a number of *N*-substituted BINAMs for an optimum *N*-substitution pattern for better enantiselectivity. *N*,*N*′-Dialkylated BINAM **6b** and *N*,*N*-dialkylated BINAM **6c** provided low reaction yields and enantioselectivities under the same condition (entries 3 and 4, Table 1). *N*-Monoalkylated BINAMs showed improved results. *N*-Isopropyl BINAM **6d** showed an improved enantioselectivity, but the change of the isopropyl group to cyclohexyl or 3-pentyl decreases the reaction yield and enantioselectivity (entries 5–7, Table 1). Racemic **5** was observed in low yield with the use of ligand **6d** in CH_3CN as a solvent, and only trace amounts of **5** were observed with the use of CuI, instead of CuCl, in CH_2Cl_2.

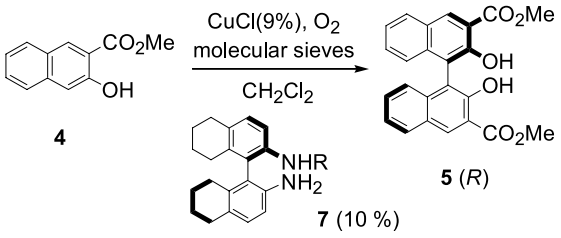
With the results that mono-*N*-alkylated derivatives are showing better enantioselectivity than other BINAM derivatives, we studied the use of enantiopure mono-*N*-alkylated 5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl-2,2′-diamine (H_8-BINAM) derivatives for the coupling reaction. (*R*)-H_8-BINAM (**7a**) can be easily obtained by partial reduction of **6a** with Ni–Al alloy in dilute aqueous alkaline solution or with Pd/C catalyst under hydrogen pressure at elevated temperature.[9] With this steric tuning, much an enhancement in the enantioselectivity was observed in the case of **7a** (entry 1, Table 2) compared with **6a** (entry 1, Table 1). *N*-Benzyl and *N*-aryl derivatives were inferior to **7a** (entries 2 and 3, Table 2), and *N*-isopropyl **7d** gave a better, but much less than desired, enantioselectivity (entry 4, Table 2). Lowering the reaction temperatures gradually improved the enantioselectivities, but with decreasing reaction yields (entries 5–7, Table 2). Unexpectedly, considering the result with ligand **6f** (entry 7, Table 1), *N*-3-pentyl derivative **7e** showed an improved result with 73% ee and 99% isolated yield in 24 h at ambient temperature. The reaction temperature was lowered to 0 °C and, much gratifyingly, the enantioselectivity was improved to 94% with 95% isolated yield which is the best result so far reported to date for the catalytic enantioselective oxidative coupling of **4** using CuCl catalyst (entry 9, Table 2). Decreasing the substrate concentration of the reaction under the same condition slowed down the coupling reaction without deteriorating the enantioselectivity of the coupling reaction (entries 10 and 11, Table 2).

The stereochemical result of this oxidative biaryl coupling can be rationalized with a tentative monomeric model of the substrate-catalyst complex (Fig. 2). The in situ generated Cu(II)–binaphthol complex from **4** and **7e** would undergo electron transfer to form a radical intermediate coordinated to tetrahedral Cu(I) center, as shown with the intermediate **8** (Fig. 2). The ketoester–Cu(I) complex **8** is likely favored over the more congested **9** due to the steric interaction between the *N*-3-pentyl group and the substrate. The approach of the second substrate in the carbon–carbon bond formation step is preferred from the top *si*-face since the bottom face is blocked by the *N*-3-pentyl group. Subsequent transformation of the central chirality of the coupling product to axial chirality through keto-enol tautomerization would provide the binaphthol (*R*)-**5**.

3. Conclusions

In conclusion, enantiopure *N*-(3-pentyl)-octahydrobinaphthyl-2,2′-diamine [*N*-(3-pentyl)-H_8-BINAM] has shown to be a highly selective diamine ligand in Cu(I)-catalyzed asymmetric oxidative biaryl coupling of

Table 2. Enantioselective oxidative coupling of **4** with the use of monoalkylated (*R*)-H_8-BINAM ligands



7a R = H **7d** R = *i*-Pr
7b R = $PhCH_2$ **7e** R = 3-pentyl
7c R = 3,5-xylyl

Entry	Ligand	Conc.(M)[a]	Temp. (time)	Yield[b] (%)	ee[c,d] (%)
1	**7a**	0.5	rt (24 h)	98	42
2	**7b**	0.5	rt (24 h)	95	4
3	**7c**	0.5	rt (24 h)	60	12
4	**7d**	0.5	rt (24 h)	92	66
5	**7d**	0.5	0 °C (48 h)	97	71
6	**7d**	0.5	−20 °C (48 h)	83	78
7	**7d**	0.5	−40 °C (24 h)	10	90
8	**7e**	0.5	rt (24 h)	99	73
9	**7e**	0.5	0 °C (48 h)	95	94
10	**7e**	0.4	0 °C (48 h)	88	94
11	**7e**	0.2	0 °C (48 h)	72	94

[a] Substrate concentration.
[b] Isolated yields.
[c] Determined by chiral HPLC (Chiralpak AD-H column).
[d] Absolute configuration assigned by comparison to the literature.

methyl 3-hydroxy-2-naphthoate to the corresponding binaphthol derivative. This catalytic system using the easily available chiral binaphthyl-based aryldiamine ligand provides an excellent enantioselectivity and a much improved catalytic activity in the biaryl coupling reaction compared with the other alkanediamine ligands. Further studies to address the scope of this catalyst in the other biaryl couplings are in progress.

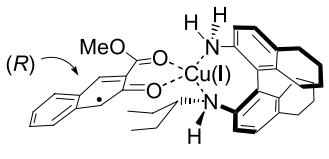
4. Experimental

4.1. General

IR spectra were recorded on a Bomem MB-104 spectrophotometer. Optical rotations were measured with a Rudolph Research Autopol III polarimeter. ^{1}H NMR spectra were recorded on a Varian Germini 300 (300 MHz) with TMS as an internal reference. ^{13}C NMR spectra were recorded on a Bruker AMX 400 (100 MHz) with TMS or $CDCl_3$ as an internal reference. Elemental analyses were obtained from Sogang Organic Chemistry Research Center, Seoul. Chiral HPLC analysis was performed on a Jasco LC-1500 Series HPLC system with a UV detector. TLC was performed on Merck silica gel 60 F_{254} precoated glass backed plates. All reactions were carried out in oven-dried glassware under an argon or oxygen atmosphere. Dichloromethane (CaH_2), THF (Na, benzophenone), toluene (CaH_2) were dried by distillation before use.

4.2. General procedure for the synthesis of diamine ligands 6d–f and 7d–e

To a solution of the corresponding ketone (21.9 mmol) in THF was added 20% H_2SO_4 (2 ml per 1 mmol of diamine). The reaction mixture was stirred for 30 min at rt, and the binaphthyl diamine[10] (1.37 mmol, 0.1 M substrate concentration) was added slowly followed by the addition of $NaBH_4$ (21.9 mmol). The resulting mixture was stirred for 1 h at room temperature and quenched by the addition of 1 N KOH (40 ml). The mixture was extracted with ethyl acetate (40 ml×3), and the combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel



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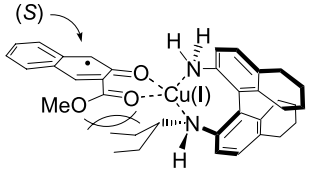

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Figure 2. Tentative stereochemical models for the coupling of **4** using the diamine ligand **7e**.

eluted with ethyl acetate/hexanes to give the enantiomerically pure *N*,*N*′-dialkylated diamines and *N*-monoalkylated diamines.

4.2.1. (*R*)-*N*-Isopropyl-1,1-binaphthyl-2,2′-diamine (6d). 74% yield as a white solid (mp 158–159 °C); $[\alpha]_D^{25}$ 137.3 (*c* 1.33, THF) {lit.[8] $[\alpha]_D$137 (*c* 0.2, THF)}; IR ($CHCl_3$) 3473, 3380 (NH_2), 1620, 1596 (C=C, aromatic) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.01 (d, J=6.3 Hz, 3H), 1.08 (d, J=6.3 Hz, 3H), 3.44 (br, 1H), 3.68 (br, 2H), 3.83 (m, 1H), 6.99 (d, J=7.5 Hz, 1H), 7.07 (d, J=8.1 Hz, 1H), 7.15–7.24 (m, 4H), 7.31 (d, J=9.0 Hz, 2H), 7.78–7.91 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.45, 23.60, 45.02, 112.53, 113.09, 115.55, 118.48, 122.17, 122.62, 124.06, 124.35, 126.90, 126.95, 127.89, 128.28, 128.32, 128.68, 129.72, 129.81, 133.96, 134.17, 143.15, 144.28. Anal. Calcd for $C_{23}H_{22}N_2$: C, 84.63; H, 6.79; N, 8.58. Found: C, 84.57; H, 6.88; N, 8.60.

4.2.2. (*R*)-*N*-Cyclohexyl-1,1-binaphthyl-2,2′-diamine (6e). 32% yield as a white solid (mp 223–224 °C); $[\alpha]_D^{25}$ 121.9 (*c* 1.0, THF) {lit.[8] $[\alpha]_D$122 (*c* 0.4, THF)}; IR ($CHCl_3$) 3475, 3377 (NH_2), 1618, 1597 (C=C, aromatic) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.76–1.11 (m, 3H), 1.19–1.37 (m, 2H), 1.52–1.66 (m, 3H), 1.86–1.98 (m, 2H), 3.41 (m, 1H), 3.65 (br, 3H), 6.98 (d, J=6.6 Hz, 1H), 7.06 (d, J=8.1 Hz, 1H), 7.13–7.31 (m, 6H), 7.76–7.88 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.19, 25.26, 25.90, 33.85, 34.02, 52.39, 112.59, 112.90, 115.51, 118.47, 122.07, 122.60, 124.00, 124.39, 126.86, 126.93, 127.84, 128.26, 128.28, 128.67, 129.64, 129.64, 134.01, 134.18, 143.13, 144.00.

4.2.3. (*R*)-*N*-(3-Pentyl)-1,1-binaphthyl-2,2′-diamine (6f). 61% yield as a yellowish solid (mp 133–134 °C); $[\alpha]_D^{25}$ 174.8 (*c* 1.0, THF); IR ($CHCl_3$) 3460, 3376 (NH_2), 1617, 1594 (C=C, aromatic) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.70 (t, J=7.5 Hz, 3H), 0.88 (t, J=7.2 Hz, 3H), 1.24–1.60 (m, 4H), 3.46 (m, 1H), 3.61 (br, 1H), 3.71 (br, 1H), 7.01 (d, J=6.6 Hz, 1H), 7.14–7.31 (m, 7H), 7.81–7.92 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.15, 10.36, 27.37, 27.50, 55.64, 111.93, 112.72, 114.75, 118.51, 121.80, 122.65, 123.90, 124.54, 126.93, 126.96, 127.52, 128.29, 128.35, 128.71, 129.71, 129.77, 134.16, 134.29, 143.30, 144.59. Anal. Calcd for $C_{25}H_{26}N_2$: C, 84.70; H, 7.39; N, 7.90. Found: C, 84.77; H, 7.36; N, 7.75.

4.2.4. (*R*)-*N*-Isopropyl-5,5′,6,6′,7,7′,8,8′-octahydro-1,1-binaphthyl-2,2′-diamine (7d). 79% yield as a pale yellow oil; $[\alpha]_D^{25}$ 80.7 (*c* 0.32, THF); IR ($CHCl_3$) 3461, 3369 (NH_2), 1680, 1597 (C=C, aromatic) cm^{-1}; ^1H NMR(300 MHz, $CDCl_3$) δ 1.07 (d, J=3.0 Hz, 3H), 1.09 (d, J=3.1 Hz, 3H), 1.62–1.77 (m, 8H), 2.16–2.30 (m, 4H), 2.74 (m, 4H), 3.28 (br, 3H), 3.62 (m, 1H), 6.61 (d, J=9.0 Hz, 1H), 6.64 (d, J=8.1 Hz, 1H), 6.94 (d, J=8.1 Hz, 1H), 7.01 (d, J=8.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.38, 23.40, 23.57, 23.63, 23.72, 23.82, 27.21, 27.41, 29.56, 29.63, 44.48, 109.78, 113.31, 121.93, 122.09, 126.15, 127.77, 129.40, 129.47, 136.33, 136.61, 142.04, 143.03. Anal. Calcd for $C_{23}H_{32}N_2$: C, 82.59; H, 9.04; N, 8.37. Found: C, 82.40; H, 9.15; N, 8.17.

4.2.5. (*R*)-*N*-(3-Pentyl)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1-binaphthyl-2,2′-diamine (7e). 63% yield as a pale yellow oil; $[\alpha]_D^{25}$ 88.5 (*c* 0.37, THF); IR ($CHCl_3$) 3459, 3367 (NH_2), 1619, 1597 (C=C, aromatic) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.80 (td, J=7.2, 2.1 Hz, 6H), 1.23–1.38 (m, 4H), 1.47 (m, 1H), 1.58–1.75 (m, 8H), 2.11–2.30 (m, 4H), 2.72 (m, 4H), 3.19 (br, 3H), 6.51 (d, J=8.1 Hz, 1H), 6.63 (d, J=8.4 Hz, 1H), 6.91 (d, J=8.1 Hz, 1H), 6.99 (d, J=8.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.16, 10.34, 23.56, 23.67 (2C), 23.84, 26.99, 27.01, 27.19, 27.37, 29.51, 29.65, 54.99, 108.31, 113.26, 121.31, 122.05, 127.37, 127.79, 129.30, 129.44, 136.42, 136.79, 142.08, 143.23. Anal. Calcd for $C_{25}H_{34}N_2$: C, 82.82; H, 9.45; N, 7.73. Found: C, 82.961; H, 9.61; N, 7.79.

4.3. Procedures for the synthesis of diamine ligands 6c, 7b and 7c.

4.3.1. (*R*)-2-Amino-2′-(1-pyrrolinyl)-1,1′-binaphthyl (6c). To a solution of (*R*)-BINAM (**6a**)[10a] (300 mg, 1.056 mmol), NaI (16 mg, 0.1056 mmol), and potassium carbonate (365 mg, 2.64 mmol) in DMF (22 ml) was added 1,4-dibromobutane (126 μl, 1.506 mmol) slowly. The reaction mixture was stirred for 36 h at 70 °C. After cooling the mixture to room temperature, the reaction mixture was added with brine followed by extraction with dichloromethane (30 ml×3). The combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel eluted with ethyl acetate/hexanes (1:16) to give **6c** (71 mg, 20% yield) as a white solid (mp 99–100 °C): $[\alpha]_D^{25}$ 180.0 (*c* 1.0, THF); IR ($CHCl_3$) 3464, 3374 (NH_2), 1618, 1596 (C=C, aromatic) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.62–1.70 (m, 4H), 2.90 (m, 2H), 3.14 (m, 2H), 3.75 (br, 2H), 7.03–7.27 (m, 6H), 7.32 (d, J=9.0 Hz, 2H), 7.75–7.84 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.01 (2C), 49.99 (2C), 112.70, 117.50, 117.99, 118.07, 122.00, 122.26, 124.29, 125.59, 126.61, 126.78, 127.84, 128.03, 128.09, 128.11, 129.01, 129.27, 134.65, 135.42, 142.96, 146.46. Anal. Calcd for $C_{24}H_{22}N_2$: C, 85.17; H, 6.55; N, 8.28. Found: C, 85.18; H, 6.54; N, 8.18.

4.3.2. (*R*)-*N*-Benzyl-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl-2,2′-diamine (7b). To a solution of the diamine **7a**[10b] (300 mg, 1.019 mmol) in 10 ml of dichloromethane was added a solution of acetic anhydride (0.11 ml, 1.12 mmol) in 10 ml of dichloromethane slowly for 2 h. The reaction mixture was stirred for another 1 h and quenched with 1 N NaOH (20 ml). The mixture was extract with dichloromethane (20 ml×3), and the combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel eluted with ethyl acetate/hexanes (1:3) to give (*R*)-*N*-acetyl-H_8-BINAM (202.6 mg, 68%). The (*R*)-*N*-acetyl-(H_8)-BINAM (100 mg, 0.3 mmol) was dissolved with DMF (3 ml), and K_2CO_3 (42 mg, 0.3 mmol) was added to the reaction mixture. Benzyl bromide (36 μl, 0.3 mmol) was added slowly to the reaction mixture, and the mixture was stirred overnight. The mixture was added with 1 N NaOH (10 ml) and extracted with ethyl acetate (20 ml×3). The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. The residue was dissolved with MeOH (5 ml) and 4 N HCl (5 ml) and the reaction mixture was heated to reflux overnight. The reaction mixture was quenched by 1 N NaOH (20 ml),

extracted with ethyl acetate (20 ml×3). The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel eluted with ethyl acetate/hexanes (1:7) to give **7b** (40.5 mg, 71% yield based on the (*R*)-*N*-acetyl-H_8-BINAM) as a pale yellow oil: $[\alpha]_D^{25}$ 70.7 (*c* 0.35, THF); IR ($CHCl_3$) 3459, 3360 (NH_2), 1677, 1597 (C=C, aromatic) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.63–1.78 (m, 8H), 2.14–2.34 (m, 4H), 2.69–2.75 (m, 4H), 3.37 (br, 2H), 3.89 (br, 1H), 4.29 (s, 2H), 6.50 (d, J=8.1 Hz, 1H), 6.64 (d, J=7.8 Hz, 1H), 6.94 (d, J=8.1 Hz, 2H), 7.17–7.31 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.50, 23.58, 23.66, 23.76, 27.27, 27.33, 29.53, 29.61, 48.07, 109.07, 113,37, 121.80, 121.85, 126.61, 126.98, 127.10, 127.15, 127.37, 127.92, 128.63, 129.37, 129.59, 136.25, 136.77, 140.56, 142.07, 143.19. Anal. Calcd for $C_{27}H_{30}N_2$: C, 84.77; H, 7.90; N, 7.32. Found: C, 84.86; H, 7.86; N, 7.26.

4.3.3. (*R*)-*N*-(3,5-Xylyl)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl-2,2′-diamine (7c). (*R*)-*N*-Acetyl-1,1′-binaphthyl-2,2′-diamine (prepared during the synthesis of **7b**) in toluene (0.5 ml) was added to a solution of $Pd(OAc)_2$ (2 mg, 9×10^{-3} mmol), (*o*-biphenyl)P(*t*-Bu)$_2$[11] (3.6 mg, 1.2×10^{-2} mmol), bromo-*m*-xylene (40 μl, 0.30 mmol) in toluene (0.5 ml). The reaction mixture was stirred for 12 h and diluted with ethyl acetate. The organic layer was washed with brine (10 ml), dried (Na_2SO_4), and concentrated in vacuo. After the deacetylation as above, the desired product was purified by flash column chromatography on silca gel eluted with ethyl acetate/hexanes (1:6) to give **7c** (51 mg, yield: 43%) as a pale yellow oil: $[\alpha]_D^{25}$ 47.3 (*c* 0.34, THF); IR ($CHCl_3$) 3464, 3371 (NH_2), 1615, 1589 (C=C, aromatic) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.63–1.74 (m, 8H), 2.14–2.33 (m, 10H), 2.68–2.78 (m, 4H), 3.31 (br, 2H), 5.16 (br, 1H), 6.52–6.63 (m, 4H), 6.91 (d, J=6.6 Hz, 1H), 7.01 (d, J=8.1 Hz, 1H), 7.21 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.58(2C), 23.07, 23.30, 23.34, 23.51, 27.39, 27.57, 29.63, 29.77, 110.36, 116.71, 123.40, 123.67, 124.75, 124.90, 127.75, 127.95, 129.78, 129.94, 130.03, 130.13, 131.59, 133.65, 136.33, 139.14, 139.43, 143.16. Anal. Calcd for $C_{28}H_{32}N_2$: C, 84.80; H, 8.13; N, 7.06.Found: C, 84.75; H. 8.17; N, 7.15.

4.4. General procedure for the oxidative biaryl coupling

CuCl (0.09 equiv) and the diamine ligand (0.1 equiv) were dissolved in dichloromethane and stirred for 30 min. The color of solution was changed to dark brown. Substrate **4** (0.5 M substrate concentration) was added and the mixture was stirred for 48 h in O_2 atmosphere. The reaction mixture was treated with aqueous ammonia to decompose the copper complexes. The reaction mixture was extracted with dichloromethane (20 ml×3), and the combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel eluted with ethyl acetate/hexanes (1:8) to give **5**: IR ($CHCl_3$) 3207 (OH), 1680 (carbonyl), 1599, 1577 (C=C, aromatic) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.06 (s, 6H), 7.17–7.39 (m, 6H), 7.92–7.95 (m, 2H), 8.71 (s, 2H), 10.76 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 52.99, 114.38, 117.21, 124.22, 124.92, 127.42, 129.70, 130.03, 133.13, 137.42, 154.24, 170.81. Anal. Calcd for $C_{24}H_{18}O_6$: C, 71.64; H, 4.51; O, 23.86. Found: C, 71.61; H, 4.66; N, 0.00.

4.4.1. Asymmetric synthesis of 5 from the coupling of 4 using ligand 7e. 95% yield; $[\alpha]_D^{25}$ 161.5 (*c* 1.0, THF) {lit.[5b] $[\alpha]_D$ −125.0 (*c* 1.0, THF) for 78% (*S*) of ee}, 94% ee by HPLC analysis (Chiralpak AD-H column, hexane:2-propanol=9:1, 1 ml/min, 254 nm UV detector), t_R=11.47 min for (*S*) and t_R=20.56 min for (*R*).

Acknowledgements

This work was financially supported by the Center for Molecular Design and Synthesis (CMDS) at KAIST.

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