Supporting Information

Enantioselective Oxidative Biaryl Coupling Reactions Catalyzed Complexes

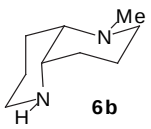
Xiaolin Li, Jaemoon Yang, and Marisa C. Kozlowski*

Department of Chemistry, Roy and Diana Vagelos Laboratories, University of Pennsylvania, Philadelphia, Pennsylvania 19104, USA

General. Unless otherwise stated all reagents and solvents were ACS reagent grade and were used without further purification. Acid-free halogenated solvents were required for the preparation of the catalyst complexes and for the oxidative coupling reactions (if necessary, trace acid can be removed by filtering through basic Al_2O_3). Naphthol **7b** was purchased from Acros and used without further purification while **7a**[1] and **7d**[2] were prepared following known procedures. The 1,5-diaza-*cis*-decalins **6a** and **6c-6e** were prepared as previously described.[3]

Analytical thin layer chromatography (TLC) was performed on EM Reagents 0.25 mm silica gel 60-F plates. Visualization was accomplished with UV light. Chromatography on silica gel was performed using a forced flow of the indicated solvent system on EM Reagents Silica Gel 60 (230-400 mesh). HPLC analyses were performed using a Waters Delta 600 system (λ = 254 nm) connected to Chiralpak AD or AS column (4.6 x 150 mm) from Daicel.

^{1}H NMR spectra were recorded on Bruker AM-500 (500 MHz), AM-250 (250 MHz), or AM-200 (200 MHz) spectrometers. ^{13}C NMR spectra were recorded on a Bruker AM-500 (125 MHz) spectrometer. Chemical shifts are reported in ppm from tetramethylsilane (0 ppm) or with the solvent resonance as the internal standard ($CDCl_3$ 7.26 ppm, DMSO-d_6 2.49 ppm, D_2O 4.80 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants, and number of protons. Mass spectra were obtained on a low resonance Micromass Platform LC in electron spray mode. IR spectra were taken on a Perkin-Elmer FT-IR spectrometer using thin films or in a cell using $CHCl_3$ solution with $CHCl_3$ as background. Optical rotations were measured on a Perkin Elmer 341 Polarimeter using a sodium lamp and are reported as follows: $[\alpha]_D^T$ (c g / 100 mL, solvent).



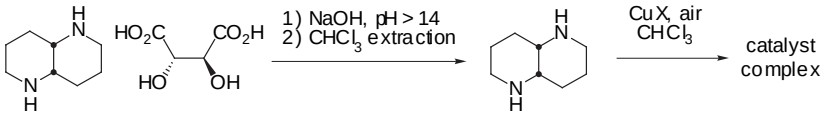
6b

***N*-Methyl-*cis*-decahydro-1,5-naphthyridine (6b).** Diamine **6a** (146 mg, 1.04 mmol) was dissolved in MeOH (30 mL) and heated to reflux. A solution of distilled MeI (65 µL, 1.04 mmol) in MeOH (1.0 mL) was added. After heating 2 h, the mixture was acidified with AcOH (1.0 mL) and cooled to rt. The solvent was removed *in vacuo* and the crude product was suspended in H_2O (2 mL), made basic (pH > 14) with NaOH, and extracted with $CHCl_3$. After drying over K_2CO_3, the extracts were filtered and concentrated to afford a crude oil. Chromatography (basic Al_2O_3: 5% MeOH / CH_2Cl_2) yielded **6b** as a yellow oil (51 mg, 32%): ^{1}H NMR

(500 MHz, $CDCl_3$) δ 3.04-3.34 (m), 2.60-2.82 (m), 2.71-2.31 (m), 2.13 (s, NC**H$_3$**), 1.89-2.0 (m), 1.18-1.69 (m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 74.7, 61.4, 60.0 (br), 57.6, 56.5 (br), 54.6, 46.5 (br), 42.3, 42.2, 30.1 (br), 29.5, 27.0 (br), 24.0 (br), 21.4, 20.8 (br). The ^{1}H NMR and ^{13}C NMR spectra of the free diamine in $CDCl_3$ were complex due to the presence of slow conformational isomerism due to chair-chair inversion. Addition of dry HCl in EtOH followed by removal of solvent *in vacuo* generated the HCl salt which existed predominantly in the "IN" conformation shown above: ^{1}H NMR (500 MHz, D_2O) "IN:OUT" = 3.5:1 δ 1.81 (m, 2H), 2.09 (m, 5.7H), 2.29 (q, J=9.2 Hz, 0.3H), 2.84 (s, 2.3H, "IN" NC**H$_3$**), 3.01 (s, 0.7H, "OUT" NC**H$_3$**), 3.15 (m, 1.8H), 3.27 (m, 2H), 3.51 (m, 0.2H), 3.72 (m, 0.2H), 3.83 (m, 0.8H), 3.91 (m, 0.8H), 4.06 (m, 0.2H);^{13}C NMR (125 MHz, $CDCl_3$) "IN" conformer δ 57.5, 50.5, 48.5, 40.7, 38.7, 21.2, 20.6, 18.0, 14.9.

3-Hydroxy-naphthalen-2-yl Benzoate (7c). The compound was prepared following the procedure for catechol monobenzoate.[4] A suspension of 2,3-dihydroxynaphthalene (16.0 g, 0.10 mol) in H_2O (260 mL) was mechanically stirred, while the mixture was made basic (pH =10) with 10% NaOH. Benzoyl chloride (15.4 g, 0.11 mol) and 10% NaOH (40 mL) were simultaneously added over 30 min maintaining pH 10.5 - 11.5. After stirring at rt for 20 min further, the solid was collected, washed with water, and dried to give the monobenzoate (5.3 g, 20%) as an off-white solid: R_f 0.14 (hexane:EtOAc = 9:1); mp 220-222 °C; ^{1}H NMR (200 MHz, DMSO-d_6) δ 10.21 (s, 1 H), 8.17 (d, J = 7.6 Hz, 2 H), 7.81-7.32 (m, 9 H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 164.3, 148.3, 140.2, 133.9, 132.5, 129.8, 128.9, 127.5, 127.1, 125.9, 125.8, 123.4, 120.4, 110.6; IR (KBr) 3387, 1718, 1527, 1400, 1278, 1152, 1114 cm^{-1}; HRMS $C_{17}H_{12}O_3$ calc'd 264.0786, found 264.0784.

Benzyl 3-Hydroxy-naphthalene-2-carboxylate (7e). A solution of 3-hydroxy-naphthalene-2-carboxylic acid (9.4 g, 50 mmol) in DMF (30 mL) was treated with K_2CO_3 (3.45 g, 25 mmol) and stirred for 1 h at 23 °C. Benzyl bromide (10.26 g, 60 mmol) was added and the mixture stirred at rt for 12 h. The product was extracted with EtOAc (3 x 50 mL), washed with brine (3 x 50 mL), dried (Na_2SO_4), and concentrated *in vacuo*. Chromatography (SiO_2: 50-60% CH_2Cl_2 / hexane) gave benzyl ester (11.2 g, 81%) as a pale yellow solid identical to that previously reported:[5] ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.40 (s, 1 H), 8.50 (s, 1 H), 7.76 (d, J = 8.2 Hz, 1 H), 7.65 (d, J = 8.3 Hz, 1 H), 7.48-7.30 (m, 8 H), 5.44 (s, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.7, 156.4, 138.0, 135.2, 132.5, 129.2, 128.7, 128.4, 127.0, 126.3, 123.9, 114.2, 111.7, 67.3.



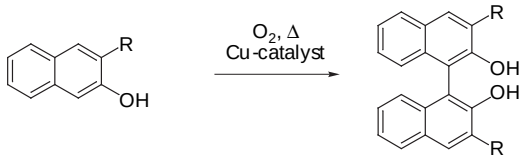
(*S,S*)-1,5-Diaza-*cis*-decalin Copper Catalysts. The tartrate salt of (*S,S*)-**6a** was dissolved in a minimum volume of water and NaOH was added until pH > 14. This solution was then extracted with $CHCl_3$ (3-4 equal volumes) and the combined $CHCl_3$ extracts were dried over K_2CO_3, filtered, and concentrated to afford a crude oil. Application of vacuum for a short time (< 1 min) afforded the chiral diamine as a waxy white solid which was weighed and used directly in the next step.

Method A: The diamine was dissolved in the reaction solvent (~0.1 M) to yield a clear solution. 0.9-1.0 equivalents of the copper source {CuCl, CuOTf, CuI} were added and the mixture was

sonicated open to the atmosphere for 10-15 min until no solids were visible. The clear solution was used directly in the reaction.

Method B: The diamine was dissolved in CH_2Cl_2 (for CuCl) or CH_3CN (for CuI) to yield a clear solution (~0.1 M). CuCl or CuI (0.9-1.0 equiv.) was added and the mixture was sonicated open to the atmosphere for 15-20 min until no solid copper salt was visible. The clear solution was filtered through a short plug of Celite in order to remove any insoluble components. A large amount of hexanes (5-10 volumes) was added to precipitate the desired complex. This solid was collected by vacuum filtration and washed with hexanes to yield the CuCl complex as a blue powder and the CuI complex as a gray powder in 76-93% yield. No difference in reactivity or selectivity was observed for the catalysts prepared using methods A or B.

General Procedure for Preparation of Chiral 1,5-Diaza-*cis*-decalin Metal Complexes. Method A described above for the copper(I) complexes was employed using the indicated metal salt.



General Procedure for the Oxidative Biaryl Coupling. To a 0.1 M solution of the catalyst (0.1 equiv.) dissolved in the indicated solvent in a disposable test-tube or vial (drying of the glassware was not necessary) was added the substrate. If necessary, the mixture was sonicated to dissolve the substrate and catalyst to yield a clear brown solution which was stirred under O_2 at the indicated temperature and time. After cooling, the reaction mixture was treated with 10% aqueous NH_4OH to decompose the copper complexes. The layers were separated and the aqueous layer was back-extracted twice with CH_2Cl_2 (for BINOL **8b**, the organic layers were then combined and washed with 1*N* HCl). The organic layers were dried over Na_2SO_4, filtered, and concentrated to afford the crude product. Purification was accomplished by SiO_2 chromatography.

Dimethyl 2,2'-Dihydroxy-1,1'-binaphthalene-3,3'-dicarboxylate (8a). Purification by SiO_2 chromatography (10% EtOAc/hexanes to remove starting naphthol followed by CH_2Cl_2 to elute the product) yielded the pure biaryl product identical to that previously reported.[6] Enantioselectivity was assayed by dissolving a small portion in MeOH completely (heating or sonicating as necessary) and analyzing by chiral HPLC: Chiralpak AD; 1.0 mL/min, 90:10 hexanes:iPrOH; t_R(SM) = 5.3 min, t_R(*S*) = 10.7 min, t_R(*R*) = 16.6 min.

The reaction course could be monitored directly by removing small aliquots (50-200 µL) and filtering through a short SiO_2 plug (5 x 20 mm) with CH_2Cl_2. The CH_2Cl_2 was removed *in vacuo* and the residue was completely dissolved in MeOH (heating or sonicating as necessary) to yield a clear solution. After filtering through a 0.22 µm filter, the sample was then subjected to chiral HPLC as described above. Conversion was also monitored by HPLC (the integration values of **7a** were multiplied by 1.2 to account for different UV absorption values of **7a** and **8a**).

1,1'-Binaphthalen-2,2'-diol (8b). The material obtained was identical to that commercially available (Aldrich). HPLC: Chiralpak AS; 1.0 mL / min, 90:10 hexanes:iPrOH; $t_R(S)$ = 10.4 min, $t_R(R)$ = 14.7 min.

3,3'-Dibenzyloxy-1,1'-binaphthalen-2,2'-diol (8d). The material obtained was identical to that previously reported.[6] ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.0 Hz, 2 H), 7.53-7.25 (m, 14 H), 7.16 (d, *J* = 3.6 Hz, 4 H), 6.00 (s, 2 H), 5.33 (s, 4 H); $[\alpha]_D^{23}$ +22.0 (c 0.80, THF) (Lit.: $[\alpha]_D^{24}$ -8.2 (c 0.80, THF), 24% ee *S*); 38% ee by HPLC: Chiralpak AS; 1.0 mL / min, 85:15 hexanes:iPrOH; $t_R(S)$ = 32.8 min, $t_R(R)$ = 39.3 min.

Dibenzyl 2,2'-Dihydroxy-1,1'-binaphthalene-3,3'-dicarboxylate (8e). The material obtained was identical to that previously reported.[6] ^{1}H NMR (200 MHz, $CDCl_3$) δ 10.71 (s, 2 H), 8.71 (s, 2 H), 7.93-7.89 (m, 2 H), 7.55-7.31 (m, 14 H), 7.16-7.12 (m, 2 H), 5.48 (s, 4 H); $[\alpha]_D^{23}$ +96.4 (c 1.0, THF); chiral HPLC: Chiralpak AD; 1.0 mL / min, 90:10 hexanes:iPrOH; $t_R(S)$ = 13.1 min, $t_R(R)$ = 18.1 min.

Prepartive Synthesis of 8a. The catalyst derived from CuI and (*S,S*)-**6a** (0.44 g, 1.26 mmol) was dissolved in 2:1 $ClCH_2CH_2Cl$:CH_3CN (100 mL) by sonicating for 5 min. Methyl ester **7a** (10.0 g, 50 mmol) and powdered 4Å molecular sieves (5.0 g) were added. The mixture was stirred for 3 d at 40-45 °C (temperature control is required; at higher temperatures the selectivity decreases slightly) under an O_2 atmosphere. After decanting, the molecular sieve residue was stirred for 30 min with 2:1 CH_2Cl_2:CH_3CN (50 mL) and the molecular sieves were filtered away. The resultant filtrate was combined with the reaction mixture and was washed with 1*N* HCl (20 mL). The aqueous layer was back-extracted with CH_2Cl_2 (2 x 50 mL). The combined organic layers were washed with 1*N* HCl (2 x 20 mL), water, and then brine. After drying over Na_2SO_4, the solvent was removed to provide the crude product (13.4 g) as a reddish brown solid. This material was treated with MeOH (100 mL). Removal of the undissolved **8a** by filtration and rinsing with further MeOH (2 x 10 mL) afforded pure **8a** (8.06 g, 81%, 93% ee) as a light-brown solid. Additional product (0.21 g, 2%, 98% ee) was obtained from the filtrate after chromatography (SiO_2: 20-80% CH_2Cl_2:hexanes).

The Effect of Water. To a solution of methyl ester **7a** (100 mg, 0.5 mmol) and the catalyst derived from CuCl and (*S,S*)-**6a** (12 mg, 0.05 mmol) in $ClCH_2CH_2Cl$ (5 mL) was added water (12 mg, 0.67 mmol, 133 mol%). The reaction was carried out as described in the general procedure and the reaction conversion was monitored by HPLC.

Cross Coupling Experiments (Eq. 4). The catalyst derived from CuCl and (*S,S*)-**6a** (25 mg, 0.1 mmol) in $ClCH_2CH_2Cl$ (8 mL) was sonicated for 3 min to obtain a homogeneous solution. A solution of methyl ester **7a** (202 mg, 0.1 mmol) and 2-naphthol **7b** (144 mg, 1.0 mmol) in $ClCH_2CH_2Cl$ (2 mL) was added. The resultant solution was stirred for 24 h at 23 °C under O_2. Water (5 mL) and 1*N* HCl (1 mL) were added. The organic layer was washed with brine, dried (Na_2SO_4), and the solvents were evaporated *in vacuo.* Chromatography (SiO_2: 50% CH_2Cl_2 / hexanes, then 50% MeOH / CH_2Cl_2) gave a fraction (A) of unreacted methyl ester **7a** (166 mg, 0.82 mmol), a mixed fraction (B) consisting of cross coupled product **8f**, BINOL **8b** , and 2-naphthol (100 mg, 1:3:2 by ^{1}H NMR), and fraction (C) of red-colored products (48 mg). Further chromatography (SiO_2: 30% MeOH+6% EtOAc / hexanes) of fraction (B) afforded BINOL **8b** (56 mg, 0.2 mmol, 7% ee) and a mixture of 2-naphthol and **8f**, which

could be separated (SiO_2: 20% EtOAc / hexanes) to provide 2-naphthol (18 mg, 0.13 mmol) and **8f**[7] (27 mg, 0.08 mmol): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.74 (s, 1 H), 7.95-7.91 (m, 2 H), 7.87 (d, *J* = 8.1 Hz, 1 H), 7.40-7.36 (m, 3 H), 7.32 (dd, *J* = 6.9, 1.1 Hz, 1 H), 7.24 (dd, *J* = 6.9, 1.2 Hz, 1 H), 7.20-7.17 (m, 1 H), 7.07 (d, *J* = 8.3 Hz, 1 H), 4.93 (s, 1 H), 4.08 (s, 3 H); $[\alpha]_D^{23}$ 16 (c 1.2, $CHCl_3$) (lit.[8]: $[\alpha]_D^{20}$ 30.5 (c 0.50, $CHCl_3$) for pure *R*-isomer); 72% ee by chiral HPLC: Chiralpak AD; 1.0 mL / min, 90:10 hexanes:iPrOH; t_R(*R*) = 21.7 min, t_R(*S*) = 26.7 min. Chromatography (SiO_2: 25% EtOAc / hexanes) of fraction (C) gave **2'-hydroxy-[1,1']-binaphthyl-3,4-dione (9)**[9] (42 mg, 0.14 mmol, 2% ee) as a red solid: R_f 0.11 (20% EtOAc / hexanes); mp 158-160 °C (dec) (hexanes-CH_2Cl_2) (lit. 148-149 °C[9a] ; 162-164 °C[9b]); ^{1}H NMR (500 MHz, $CDCl_3$ + CD_3OD) δ 8.16 (d, *J* = 7.4 Hz, 1 H), 7.89 (d, *J* = 8.9 Hz, 1 H), 7.84 (d, *J* = 7.9 Hz, 1 H), 7.60 (d, *J* = 8.3 Hz, 1 H), 7.53 (2d, *J* = 7.3 Hz, 1 H), 7.47 (2d, *J* = 7.3 Hz, 1 H), 7.36 (2d, *J* = 7.0 Hz, 1 H), 7.31 (2d, *J* = 7.0 Hz, 1 H), 7.25 (d, *J* = 8.9 Hz, 1 H), 6.83 (d, *J* = 7.6 Hz, 1 H), 6.41 (s, 1 H); ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.79 (s, 1 H), 8.06 (d, *J* = 7.3 Hz, 1 H), 7.93 (d, *J* = 8.9 Hz, 1 H), 7.87 (d, *J* = 8.1 Hz, 1 H), 7.71 (d, *J* = 8.2 Hz, 1 H), 7.56-7.50 (m, 2 H), 7.37-7.29 (m, 3 H), 6.70 (d, *J* = 7.5 Hz, 1 H), 6.35 (s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$ + CD_3OD) δ 181.9, 181.0, 155.6, 152.8, 137.1, 136.6, 133.9, 133.1, 131.9, 131.7, 131.2, 130.5, 130.1, 129.8, 129.3, 128.2, 124.9, 124.5, 119.0, 117.1; IR (film) 3393, 1651 cm^{-1}; HRMS $C_{20}H_{12}O_3$ $[M+Na]^+$ calc'd 323.0684, found 323.0683; chiral HPLC: Chiralpak AS; 1.0 mL / min, 70:30 hexanes:iPrOH; t_R = 8.4, 13.6 min.

(1) Cohen and Dudley, *J. Chem. Soc.*, **1910,** *97*, 1748

(2) Colquhoun, H. M.; Goodings, E. P.; Maud, J. M.; Stoddart, J. F.; Wolstenholme, J. B.; Williams, D. J. *J. Chem. Soc. Perkin Trans. II*, **1985**, 607.

(3) Li, X.; Schenkel, L. B.; Kozlowski, M. C. *Org. Lett.* **2000**, *2*, 975-978.

(4) Bredereck, H.; Heckh, H. *Chem. Ber.* **1958**, *91*, 1314.

(5) Okano, A.; Inaoka, M.; Funabashi, S.; Iwamoto, M.; Isoda, S.; Moroi, R.; Abiko, Y.; Hirata, M. *J. Med. Chem.* **1972,** *15*, 247.

(6) Nakajima, M.; Miyoshi, I.; Kanayama, K.; Hashimoto, S.-I. *J. Org. Chem.* **1999**, *64*, 2264-2271.

(7) Hovorka, M.; Zavada, J. *Org. Prep. Proc. Int.* **1991**, *23*, 200.

(8) Hovorka, M.; Scigel, R.; Gunterova, J.; Tichy, M.; Zavada, J. *Tetrahedron*, **1992**, *48*, 9503.

(9) (a) Bader, A. R. *J. Am. Chem. Soc.* **1951**, *73*, 3731. (b) Krohn, K.; Rieger, H.; Khanbabaee, K. *Chem. Ber.* **1989**, *122*, 2323.