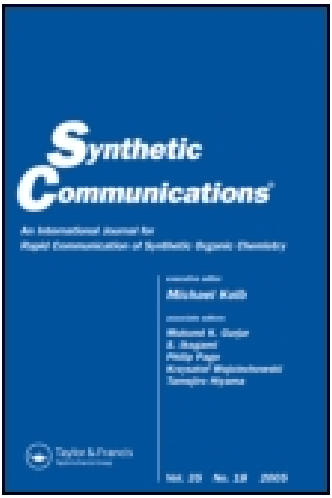

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SYNTHESIS OF BINUCLEATING LIGANDS OF PYRIDYLPHENOL

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SYNTHESIS OF BINUCLEATING LIGANDS OF PYRIDYLPHENOL

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ABSTRACT

The synthesis of pyridylphenol-type dinucleating tri- and penta-dentate ligands has been accomplished by cross-couplings.

Dinucleating ligands and bimetallic complexes play important roles in the studies of bioinorganic chemistry and homogeneous catalysis, and have continued to arouse wide interest.[1–3] Dinuleating ligands capable of binding two metal ions in close proximity serve as essential precursors for the formation of homo- and hetero- bimetallic complexes. The design of a dinucleating system determines the nature of metal ions to be incorporated, coordination environment, and metal–metal separation of the bimetallic complexes. Phenoxy-bridged Schiff-base ligands have been used as binucleating ligands, and some of the bimetallic complexes of these ligands show catalytic activities for oxidation of organic substrates.[1–3] To enhance the oxidative and hydrolytic robustness of the imine functional groups of the Schiff base type complexes, we have attempted to aromatize the imine as part of a pyridine ring[4–6] and we report the synthesis of pyridylphenol type dinucleating tri- and penta-dentate ligands.

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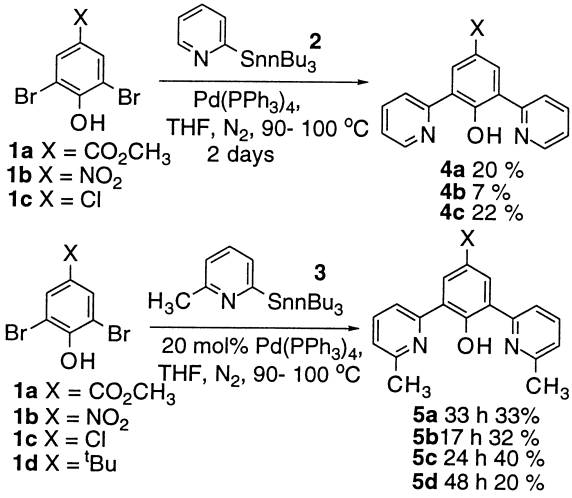


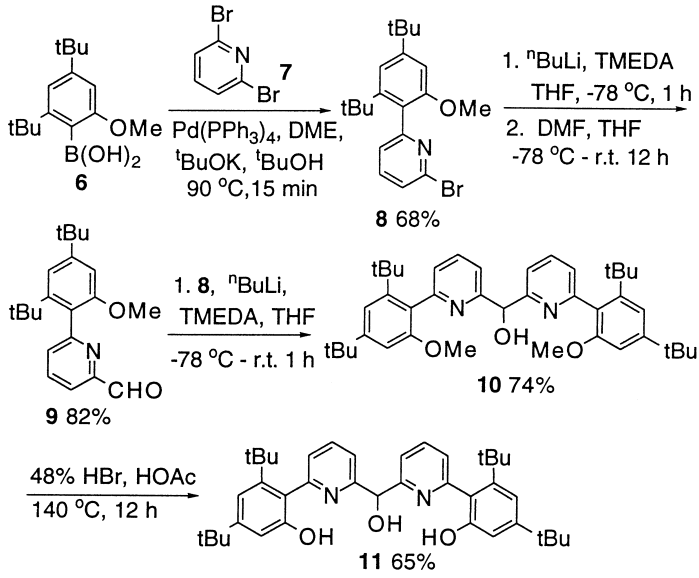
Scheme 1. Syntheses of dipyridylphenols **5** and **6**.

4-Substituted 2,6-dibromophenols[7] **1a–c** and **1a–d** underwent smooth Stille cross-couplings[8] with tributylstannylpyridine (**2**) and 2-(tributylstannyl)-6-methylpyridine (**3**), respectively, catalyzed by $Pd(PPh_3)_4$ in THF under N_2 at 90°–100°C for two days to yield 4-substituted tridentate dipyridylphenols **4a–c** and **5a–d** (Scheme 1). The yield of **4b** was very poor, possibly due to low solubility of both the starting material and final product. The yields of **5a–d** were higher than that of **4a–c**, likely due to the enhancement of nucleophilicity in **3** and the solubility of the resultant ligands.

A more lipophilic, pentadentate ligand **11** was also prepared, which resembles the structural feature of a dimanganese Schiff base complex.[9] 3,5-Di-*tert*-butyl-2-[2′-(6′-bromo)pyridyl]anisole **8** was synthesized by modified Suzuki coupling of 2,6-dibromopyridine **7** and arylboronic acid **6**, catalyzed by $Pd(PPh_3)_4$ with ^{t}BuOK in 68% yield (Scheme 2).[10] Lithiation of **9** with ^{n}BuLi,[11] followed by addition of excess DMF, gave the aldehyde **10** in 82% yield. **10** reacted with lithiated **8** to yield **10** in 74% yield. It should be noted that **10** could not be prepared directly from the reaction of lithiated **8** and DMF. **10** was then deprotected with 48% HBr in refluxing acetic acid for 12 h to give pentadentate ligand **11** in 65% yield.

In preliminary studies, ligands **4** and **5** complexed with the first row transition metal ions in both 1:1 and 1:2 ratio.

In conclusion, bidentate and pentadentate ligands of pyridylphenol were synthesized by Stille and Suzuki cross-coupling reaction in moderate yield and coordination chemistry is being studied.



Scheme 2. Synthetic route of pentadentate ligand **11**.

EXPERIMENTAL

General Procedures

All materials were obtained from commercial suppliers and used without further purification unless otherwise specified. Tetrahydrofuran (THF) was freshly distilled from sodium benzophenone ketyl under N_2. Chromatography was carried out on silica gel.

^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Bruker DPX-300 spectrometer at 300 and 75.47 MHz, respectively. Proton chemical shifts were referenced with the residual solvent protons in $CDCl_3$ (δ 7.24 ppm) or with tetramethylsilane (δ 0.00 ppm) as the internal standard. Carbon chemical shifts were referenced to the residual solvent peak of $CDCl_3$ (δ 77.0 ppm).

Mass spectra were recorded on either a VG7070F mass spectrometer, Hewlett Packard 5989B mass spectrometer, or a Bruker APEX 47e FT-ICR mass spectrometer. Fast atom bombardment spectra were obtained using 3-nitrobenzyl alcohol (NBA) as the matrix. Electrospray ionization spectra were obtained with a solvent mixture of acetone with 3% of acetic acid. IR spectra were obtained on either a Nicolet Magne-IR 550 FT-IR spectrophotometer, Perkin Elmer Paragon 500 FT-IR spectrophotometer, or a Perkin Elmer 1600 FT-IR spectrophotometer. Samples were prepared

either as neat film on KBr plates or as a KBr disk. UV-vis spectra were recorded on a Hitachi U-3300 spectrophotometer.

Preparation of Methyl 3,5-Dibromo-4-hydroxybenzoate (**1a**)[12]

To the solution of methyl 4-hydroxybenzoate (8.0 g, 53 mmol) in $CHCl_3$ (35 mL) at 0°C, Br_2 (6.4 mL, 125 mmol) in $CHCl_3$ (20 mL) was slowly added for 2 h 15 min. The reaction mixture was then raised to room temperature and stirred for 1 day. Then sat.NaS_2O_5 was added. The crude product was extracted with CH_2Cl_2, washed with water, brine, dried ($MgSO_4$), filtered, and rotary-evaporated to dryness. A white solid was obtained after recrystallization from CH_2Cl_2/hexanes. $R_f = 0.35$ (hexanes:E.A. = 3:1); ^{1}H NMR δ 3.91 (s, 3 H), 6.29 (br s, 1 H), 8.16 (s, 2 H).

Preparation of 2,6-Dibromo-4-nitrophenol (**1b**)[13,14]

Br_2 (8.7 mL, 169 mmol) in glassical acetic acid (27 mL) was added dropwise to 4-nitrophenol (10.0 g, 72 mmol) in glassical acetic acid (30 mL) for 1 h 15 m. The reaction mixture was then stirred at room temperature for 9 h. Then the reaction mixture was heated to 80°C for 1 h to remove HBr and excess Br_2. Cold water (33 mL) was then added and the reaction mixture was stirred in an ice bath for 6 h. The resulting pale yellow solid was then filtered and washed with 50% acetic acid and then water. A slightly pale yellow solid (20.6 g, 69 mmol, 96%) was obtained after being dried under high vacuum. $R_f = 0.14$ (hexanes/E.A. = 3:1); m.p. d 140°C (Lit.[13] d = 138°–140°C); ^{1}H NMR δ 6.54 (br s, 1 H), 8.41 (s, 2 H).

Preparation of 2-Tributylstannylpyridine (**2**)

^{n}BuLi (1.6 M in hexanes, 33 mL, 53 mmol) was added dropwise to a solution of 2-bromopyridine (5.0 mL, 52 mmol) in THF (20 mL) at −78°C under N_2. After addition of about 20 mL ^{n}BuLi, a brown precipitate appeared, together with a brown solution. After the addition of ^{n}BuLi, the solution was stirred for 2 h at −78°C under N_2. Then $^n Bu_3SnCl$ (15 mL, 55 mmol) was added by syringe for 30 m. It was then stirred at −78°C for 1 h and stood at room temperature for 12 h. A brown solution resulted with some white precipitate. The reaction mixture was then filtered through celite and the brown solution was rotary-evaporated to dryness and a viscous brown liquid obtained. It was then vacuum-distillated

and a colorless liquid (14.3 g, 39 mmol, 75%) was obtained. $R_f = 0.74$ (hexanes:E.A. = 6:1); b.p. 120°–122°C (0.04 mm Hg); ^{1}H NMR δ 0.88 (t, 9 H, $J = 7.3$ Hz), 1.10–1.15 (m, 6 H) 1.32–1.39 (m, 6 H), 1.51–1.62 (m, 6 H), 7.08–7.13 (m, 1 H), 7.38–7.44 (m, 1 H), 7.45–7.53 (m, 1 H), 8.73 (ddd, 1 H, $J = 1.0$, 1.6, 4.8 Hz); IR (KBr, cm^{-1}) ν 664, 690, 1376, 1448, 1567, 2927, 3392.

Preparation of 2-(Tributylstannyl)-6-methylpyridine (**3**)

^{n}BuLi (1.6 M, 29 mL, 47 mmol) was added dropwise to a solution of 2-bromo-6-methylpyridine (**3**) (8.0 g, 47 mmol) in THF (20 mL) at −78°C under N_2. Then, the solution was stirred for 2 h at −78°C under N_2 and ^{n}Bu$_3$SnCl (13.2 mL, 49 mmol) was added by syringe in 30 m. The mixture was then stirred at −78°C for 1 h and stood at room temperature for 12 h. A yellow solution with some white precipitate was resulted. The reaction mixture was then filtered through celite and the yellow solution was rotary-evaporated to dryness to yield a viscous yellow liquid. The residue was vacuum-distillated to give a colorless liquid (13.4 g mL, 35 mmol, 74%). $R_f = 0.70$ (hexanes/E.A. = 6:1); b.p. 126°–128°C (0.04 mm Hg); ^{1}H NMR δ 0.88 (t, 9 H, $J = 7.3$ Hz), 1.07–1.13 (m, 6 H) 1.27–1.39 (m, 6 H), 1.51–1.62 (m, 6 H), 2.53 (s, 3 H), 6.94 (dd, 1 H, $J = 0.7$, 7.8 Hz), 7.18 (dd, 1 H, $J = 0.5$, 7.3), 7.33–7.38 (unresolved dd, 1 H); ^{13}C NMR δ 9.81, 13.67, 24.86, 27.31, 29.07, 121.45, 133.23, 158.55, 172.99; IR (KBr, cm^{-1}) ν 665, 691, 772, 1437, 1557, 2925, 3436; FABMS: m/z (relative intensity) 384 {[(M+H)$^+$]+4, 100}, 382 {[(M+H)$^+$]+2, 75}, 380 [(M+H)$^+$, 42]; HRMS (ESIMS): Calc. for $(C_{18}H_{35}NSn)^+$: m/z 385.1791. Found: m/z 385.1789.

Preparation of 4-Substituted-2,6-di-(2′-pyridyl)phenol

General Procedure. The preparation of methyl 4-hydroxy-3,5-di-(2′-pyridyl)benzoate (**5a**) was described as a typical example for the preparation of 4-substituted-2,6-di-(2′-pyridyl)phenol.

Methyl 3,5-dibromo-4-hydroxybenzoate (**1a**) (500 mg, 0.65 mmol) and $Pd(PPh_3)_4$ (386 mg, 0.32 mmol) were charged into a side-armed, rotaflow, screw-stoppered flask. 2-Tributylstannylpyridine (**2**) (1.31 g, 3.35 mmol) in THF was then added. It was then degassed by freeze-pump-thaw method (3 cycles) and refilled with N_2. The reaction mixture was then heated to 90°–100°C. After 16 h, 2-tributylstannylpyridine (1.31 g, 3.55 mmol) was added again and the reaction mixture was heated to 90°–100°C for 1 d. After removal of solvent by rotary evaporation, the product was isolated

by column chromatography on silica gel using a solvent mixture of hexanes/E.A. (1:**1**) as the eluent. A yellow crystalline solid (101 mg, 0.33 mmol, 20%) was obtained after recrystallization from CH_2Cl_2/hexanes. $R_f = 0.29$ (hexanes:E.A. = 1:**1**); m.p. 178°–179°C; ^{1}H NMR δ 3.94 (s, 3 H), 7.30–7.35 (m, 2 H) 7.85–7.91 (m, 2 H), 8.12 (d, 2 H, $J = 8.2$ Hz), 8.61 (s, 2 H), 8.65 (d, 2 H, $J = 4.4$ Hz); ^{13}C NMR δ 51.98, 120.42, 122.22, 122.44, 131.61, 137.45, 146.95, 155.89, 162.53, 166.78, 179.47; UV-visible (CH_2Cl_2) λ_{max}, nm (log ε) 334 (4.40); IR (KBr, cm^{-1}) ν 747, 802, 1247, 1456, 1599, 1714, 3418; FABMS: m/z 307 [$(M+H)^+$]; HRMS (ESIMS): Calc. for $(C_{18}H_{15}N_2O_3)^+$: m/z 307.1077. Found: m/z 307.1063.

Preparation of 4-Nitro-2,6-di-(2′-pyridyl)phenol (**5b**)

2,6-Dibromo-4-nitrophenol (**1b**) (1.0 g, 3.4 mmol) was reacted with 2-(tributylstannyl)pyridine (**2**) (2.7 g, 7.4 mmol) and $Pd(PPh_3)_4$ (806 mg, 0.68 mmol) in THF under N_2 at 90°–100°C for 2 days. It was purified by column chromatography (70–230 mesh) using hexanes/E.A. (3:1) as the eluent. A yellow solid (71 mg, 0.24 mmol, 7%) was obtained after recrystallization from CH_2Cl_2/hexanes. $R_f = 0.12$ (hexanes/E.A. = 3:1); m.p. 205°–206°C; ^{1}H NMR δ 7.26–7.39 (m, 2 H) 7.89–7.94 (m, 2 H), 8.13–8.16 (m, 2 H), 8.66 (d, 2 H, $J = 4.9$ Hz), 8.86 (s, 2 H); ^{13}C NMR δ 122.44, 122.84, 125.37, 137.48, 139.64, 147.38, 154.88, 164.19 (due to low solubility of **53b**, only 8 peaks was found out of the expected 9); UV-visible (CH_2Cl_2) λ_{max}, nm (log ε) 338 (4.67); IR (KBr, cm^{-1}) ν 739, 802, 1339, 1599, 3436; FABMS: m/z 294 [$(M+H)^+$]; HRMS (ESIMS): Calc. for $(C_{16}H_{12}N_3O_3)^+$: m/z 294.0873. Found: m/z 294.0888.

Preparation of 4-Chloro-2,6-di-(2′-pyridyl)phenol (**5c**)

2,6-Dibromo-4-chlorophenol (**1c**) (1.0 g, 3.49 mmol) was reacted with 2-(tributylstannyl)pyridine (**2**) (2.83 g, 7.68 mmol) and $Pd(PPh_3)_4$ (835 mg, 0.70 mmol) in THF under N_2 at 90°–100°C for 2 days. The reaction mixture was purified by column chromatography using hexanes/E.A. (4:1) as the eluent. A yellow solid (253 mg, 0.89 mmol, 26%) was obtained after recrystallization from CH_2Cl_2/hexanes. $R_f = 0.22$ (hexanes/E.A. = 3:1); m.p. 127°–128°C; ^{1}H NMR δ 7.23–7.28 (m, 2 H), 7.77–7.82 (m, 2 H) 7.84 (s, 2 H), 8.00 (d, 2 H, $J = 8.2$ Hz), 8.59 (d, 2 H, $J = 4.1$ Hz); UV-visible (CH_2Cl_2) λ_{max}, nm (log ε) 347 (4.41); IR (KBr, cm^{-1}) ν 735, 794, 1264, 1456, 1598, 3418; HRMS (ESIMS): Calc. for $(C_{16}H_{12}N_2OCl)^+$: m/z 283.0633. Found: m/z 283.0625.

Preparation of Methyl 4-Hydroxy-3,5-di-[2′-(6′-methyl)pyridyl]-benzoate (**5a**)

Methyl 3,5-dibromo-4-hydroxybenzoate (**1a**) (200 mg, 0.65 mmol) was reacted with 2-(tributylstannyl)-6-methylpyridine (**3**) (543 mg, 1.42 mmol) and $Pd(PPh_3)_4$ (154 mg, 0.13 mmol) in THF under N_2 at 90°–100°C for 33 h. It was purified by column chromatography on silica gel (70–230 mesh) using hexanes/E.A. (3:1) as the eluent. A yellow solid (71 mg, 0.21 mmol, 33%) was obtained after rotary evaporation. $R_f = 0.21$ (hexanes/E.A. = 3:1); m.p. 142°–144°C; ^{1}H NMR δ 2.62 (s, 6 H), 7.13 (d, 2 H, $J = 7.5$ Hz), 7.69–7.75 (unresolved dd, 2 H), 7.85 (d, 2 H, $J = 8.0$ Hz), 8.53 (s, 2 H); ^{13}C NMR δ 24.01, 51.83, 119.18, 120.13, 121.65, 131.27, 137.26, 155.50, 156.23, 162.54, 166.86; UV-visible (CH_2Cl_2) λ_{max}, nm (log ε) 334 (4.54); IR (KBr, cm^{-1}) ν 768, 1258, 1574, 1714, 2951, 3408; FABMS: m/z 335 [$(M+H)^+$]; HRMS (ESIMS): Calc. for $(C_{20}H_{19}N_2O_3)^+$: m/z 335.1390. Found: m/z 335.1403.

Preparation of 4-Nitro-2,6-di-[2′-(6′-methyl)pyridyl]phenol (**5b**)

2,6-Dibromo-4-nitrophenol (**1b**) (200 mg, 0.67 mmol) was reacted with 2-(tributylstannyl)-6-methylpyridine (**3**) (566 mg, 1.48 mmol) and $Pd(PPh_3)_4$ (161 mg, 0.14 mmol) in THF under N_2 at 90°–100°C for 17 h. It was purified by column chromatography on silica gel (70–230 mesh) using hexanes/E.A. (3:1) as the eluent. A yellow solid (70 mg, 0.22 mmol, 32%) was obtained after recrystallization from CH_2Cl_2/Hexanes. $R_f = 0.22$ (hexanes/E.A. = 3:1); m.p. 204°–206°C; ^{1}H NMR δ 2.64 (s, 6 H), 7.19 (d, 2 H, $J = 7.5$ Hz), 7.74–7.79 (unresolved dd, 2 H), 7.88 (d, 2 H, $J = 7.9$ Hz); 8.75 (s, 2 H); ^{13}C NMR δ 23.93, 119.39, 122.53, 125.30, 137.84, 139.32, 154.15, 156.43, 164.68; UV-visible (CH_2Cl_2) λ_{max}, nm (log ε) 340 (4.43); IR (KBr, cm^{-1}) ν 808, 1328, 1471, 1574, 3501; FABMS: m/z 322 [$(M+H)^+$]; HRMS (ESIMS): Calc. for $(C_{18}H_{16}N_3O_3)^+$: m/z 322.1186. Found: m/z 322.1160.

Preparation of 4-Chloro-2,6-di-[2′-(6′-methyl)pyridyl]phenol (**5c**)

2,6-Dibromo-4-chlorophenol (**1c**) (200 mg, 0.70 mmol) was reacted with 2-(tributylstannyl)-6-methylpyridine (**3**) (587 mg, 1.54 mmol) and $Pd(PPh_3)_4$ (167 mg, 0.14 mmol) in THF under N_2 at 90°–100°C for 24 h. It was purified by column chromatography on silica gel (70–230 mesh) using hexanes/E.A. (6:1) as the eluent. A yellow solid (88 mg, 0.28 mmol, 40%) was obtained. $R_f = 0.23$ (hexanes/E.A. = 6:1); m.p. 114°–115°C; ^{1}H NMR

δ 2.60 (s, 6 H), 7.11 (d, 2 H, $J = 7.5$ Hz), 7.66–7.71 (unresolved dd, 2 H), 7.76–7.79 (m, 4 H); ^{13}C NMR δ 24.09, 119.14, 121.66, 123.48, 125.52, 129.10, 137.17, 155.90, 156.40, 156.80; UV-visible (CH_2Cl_2) λ_{max}, nm (log ε) 347 (4.54); IR (KBr, cm^{-1}) ν 725, 1456, 1574, 2925; FABMS: m/z 311 [$(M+H)^+$]; HRMS (ESIMS): Calc. for $(C_{18}H_{16}N_2OCl)^+$: m/z 311.0946. Found: m/z 311.0929.

Preparation of 4-*tert*-Butyl-2,6-di-[2′-(6′-methyl)pyridyl]phenol (**5d**)

2,6-Dibromo-4-*tert*-butylphenol (**1d**) (200 mg, 0.65 mmol) was reacted with 2-(tributylstannyl)-6-methylpyridine (**3**) (546 mg, 1.43 mmol) and $Pd(PPh_3)_4$ (155 mg, 0.13 mmol) in THF under N_2 at 90°–100°C for 2 days. The reaction mixture was purified by column chromatography on silica gel (70–230 mesh) using hexanes/E.A. (6:1) as the eluent. A yellow viscous liquid (44 mg, 0.13 mmol, 20%) was obtained. $R_f = 0.39$ (hexanes/E.A. = 6:1); ^{1}H NMR δ 1.40 (s, 9 H), 2.61 (s, 6 H), 7.08 (d, 2 H, $J = 7.5$ Hz) 7.66–7.71 (unresolved dd, 2 H), 7.78 (d, 2 H, $J = 8.0$), 7.82 (s, 2 H); ^{13}C NMR δ 24.14, 31.55, 34.24, 119.15, 121.00, 123.63, 126.79, 136.98, 140.63, 155.73, 156.27, 156.93; UV-visible (CH_2Cl_2) λ_{max}, nm (log ε) 342 (4.25); IR (KBr, cm^{-1}) ν 666, 735, 803, 1097, 1269, 1455, 1574, 2958, 3059; FABMS: m/z 333 [$(M+H)^+$]; HRMS (ESIMS): Calc. for $(C_{22}H_{25}N_2O)^+$: m/z 333.1961. Found: m/z 333.1946.

Preparation of 3,5-di-*tert*-Butyl-2-[2′-(6′-bromo)pyridyl]anisole (**8**)

2,6-Dibromopyridine (**7**) (948 mg, 4.0 mmol) and $Pd(PPh_3)_4$ (231 mg, 0.20 mmol) were dissolved in DME (8 mL). The yellow suspension was then degassed by freeze-pump-thaw method (3 cycles) and refilled with N_2. The reaction mixture was then heated at 50°C for 15–20 m until a clear yellow solution was obtained. Then 2,4-di-*tert*-butyl-6-methoxyphenylboronic acid (1.06 g, 4.0 mmol) in DME (4 mL) and ^{t}BuOK (898 mg, 8.0 mmol) in ^{t}BuOH (4 mL) were added. The reaction mixture was degassed by freeze-pump-thaw method (3 cycles) and refilled with N_2 and was then heated to 90°C for 30 m. The reaction mixture turned from a pale yellow solution with some white precipitate to an orange solution with some white precipitate. The reaction mixture was then filtered through celite. After rotary evaporation, the crude product was chromatographed on silica gel (70–230 mesh) and using hexanes/CH_2Cl_2 (3:1) to hexanes/CH_2Cl_2 (3:2) as the gradient eluent. A white solid

(1.03 g, 2.7 mmol, 68%) was obtained after rotary evaporation. $R_f = 0.60$ (hexanes/E.A. = 6:1); ^{1}H NMR δ 1.14 (s, 9 H), 1.34 (s, 9 H), 3.63 (s, 3 H), 6.83 (s, 1 H), 7.20 (s, 1, H), 7.27 (d, 1 H, $J = 7.5$ Hz), 7.41 (d, 1 H, $J = 7.3$ Hz), 7.51 (unresolved dd, 1 H); ^{13}C NMR δ 31.33, 32.46, 35.13, 36.88, 106.22, 116.50, 125.67, 126.04, 137.28, 140.40, 148.70, 151.97, 157.34, 160.23; IR (KBr, cm^{-1}) ν 665, 1070, 1237, 1432, 1545, 1604, 2954, 3036; FABMS: m/z (relative intensity) 378 {[(M+H)$^+$+2], 81}, 376 {[(M+H)$^+$, 100}; HRMS (ESIMS): Calc. for $(C_{20}H_{27}BrNO)^+$: m/z 376.1276. Found: m/z 376.1271.

Preparation of 6-(2′,4′-Di-*tert*-butyl-6′-methoxyphenyl)pyridine-2-carboxyaldehyde (**9**)

3,5-Di-*tert*-butyl-2-[2′-(6′-bromo)pyridyl]anisole (**8**) (500 mg, 1.33 mmol) and TMEDA (300 μL, 1.99 mmol) were dissolved in THF (5 mL) under N_2. 1.6 M ^{n}BuLi (1.25 mL, 1.99 mmol(was then added at -78°C by syringe under N_2. The mixture turned from colorless to deep yellow. After 1 h, DMF (1.0 mL, 13.3 mmol) was added. The solution decolorized and some white precipitate appeared. After 1 h, water was added and the crude product was extracted with ether (3 times). The organic layer was then washed with water (3 times), brine, dried ($MgSO_4$), filtered, and rotary-evaporated to dryness. The crude product was then separated by column chromatography on silica gel (230–400 mesh) using hexanes/E.A. (10:1) as the eluent. A white solid (355 mg, 1.09 mmol, 82%) was obtained after rotary evaporation. $R_f = 0.37$ (hexanes/E.A. = 9:1); ^{1}H NMR δ 1.13 (s, 9 H), 1.37 (s, 9 H), 3.64 (s, 3 H), 6.89 (d, 1 H, $J = 1.6$ Hz), 7.26 (d, 1 H), 7.27 (d, 1 H, $J = 1.6$ Hz), 7.54 (dd, 1 H, $J = 1.2$, 7.3 Hz), 7.85 (unresolved dd, 1 H), 7.93 (dd, 1 H, $J = 1.2$, 7.6 Hz), 10.11 (s, 1 H); ^{13}C NMR δ 31.35, 32.48, 35.19, 36.87, 55.76, 106.20, 116.64, 119.48, 131.68, 135.91, 148.80, 151.82, 152.11, 157.31, 160.44, 194.18; IR (KBr, cm^{-1}) ν 724, 1066, 1709, 2959, 3392; FABMS: m/z 326 [(M+H)$^+$]; HRMS (ESIMS): Calc. for $(C_{21}H_{27}NO_2)^+$: m/z 326.2120. Found: m/z 326.2112.

Preparation of bis-2-[6-(2′,6′-Di-*tert*-butyl-6′-methoxyphenyl)pyridyl]-methanol (**10**)

3,5-Di-*tert*-butyl-2-[2′-(6′-bromo)pyridyl]anisole (**58**) (350 mg, 0.93 mmol) and TMEDA (154 μL, 1.02 mmol) were dissolved in THF (5 mL) under N_2. ^{n}BuLi (1.6 M, 0.64 mL, 1.02 mmol) was then added at -78°C via syringe. The solution turned from colorless to deep yellow.

After 1 h, the reaction mixture was transferred to a solution of 6-(2′,4′-di-*tert*-butyl-6′-methoxyphenyl)pyridine-2-carboxyaldehyde (**9**) (333 mg, 1.02 mmol) in THF (2 mL) under N_2 at -78°C via a cannular. The temperature gradually rose to room temperature. Water was added to the reaction mixture after 1 h. The mixture was extracted with ether (3 times). The organic layer was dried ($MgSO_4$), filtered, and rotary-evaporated to dryness. The residue was then separated by column chromatography on silica gel using hexanes/E.A. (100:4) to hexanes/E.A. (9:1) as the gradient eluent. A mixture of yellow solids (430 mg, ~0.69 mmol, ~74%) was obtained after rotary evaporation. $R_f = 0.20$ (hexanes/E.A. = 9:1); ^{1}H NMR δ 1.09 (s, 12 H), 1.14 (s, 4 H), 1.15 (s,3 H), 1.39 (s, 12 H), 3.60 (s, 2 H), 3.63 (s, 2 H), 3.66 (s, 2 H), s5.89 (br s, 1 H), 6.02 (br s, 1 H) 6.89 (d, 2 H, $J = 2.0$ Hz), 7.13–7.19 (m, 2 H), 7.24 (d, 2 H, $J = 5.6$ Hz), 7.34–7.47 (m, 2 H), 7.55–7.60 (m, 2 H); FABMS: m/z 623 [$(M+H)^+$].

Preparation of bis-2-[6-(2′,6′-Di-*tert*-butyl-6′-hydroxphenyl)-pyridyl]-methanol (**11**)

Crude bis-2-[6-(2′,6′-di-*tert*-butyl-6′-methoxyphenyl)-pyridyl]-methanol (**10**) (300 mg, 0.48 mmol) was dissolved in acetic acid (5 mL) with 48% HBr (5mL) and then heated to 140°C for 11 h. The reaction mixture was then neutralized by sat. $NaHCO_3$ and the product was extracted with ether, dried ($MgSO_4$), filtered, and rotary-evaporated to dryness. The residue was then separated by column chromatography on silica gel using hexanes/E.A. (6:1) to hexanes/E.A. (2:1) as the gradient eluent. A white solid (187 mg, 0.31 mmol, 65%) was obtained after rotary evaporation. $R_f = 0.06$ (hexanes/E.A. = 2:1); ^{1}H NMR δ 1.07 (s, 18 H), 1.32 (s, 18 H), 5.97 (s, 1 H), 6.86 (d, 2 H, $J = 1.2$ Hz), 7.17 (d, 2 H, $J = 1.2$ Hz), 7.27 (d, 2 H, $J = 7.6$ Hz), 7.48 (d, 2 H, $J = 7.8$ Hz), 7.67 (unresolved dd, 2 H); ^{13}C NMR δ 31.26, 32.72, 34.85, 36.83, 75.06, 111.02, 116.66, 119.92, 123.80, 126.32, 137.36, 148.62, 152.26, 153.41, 157.03, 160.69; FABMS: m/z 595 [$(M+H)^+$]; HRMS (ESIMS): Calc. for $(C_{21}H_{27}NO_2)^+$: m/z 595.3894. Found: m/z 595.3924.

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