Supporting Information

Enantioselective Friedel-Crafts Alkylation Reactions Catalyzed by a Chiral Nonracemic C₂-Symmetric 2,2'-Bipyridyl Copper(II) Complex

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1. General Experimental Details

All non-aqueous reactions were performed under an atmosphere of dry nitrogen in oven- or flame-dried glassware, unless indicated otherwise. The reaction temperatures stated were those of the external bath. Diethyl ether (ether) was dried over sodium/benzophenone ketyl and distilled under an atmosphere of dry nitrogen immediately prior to use. Toluene was dried over calcium hydride and distilled under an atmosphere of dry nitrogen immediately prior to use. All other solvents and reagents were purified by standard techniques or used as supplied.¹ Silica gel column chromatography (“flash chromatography”) was carried out using *Merck silica gel 60* (230 to 400 mesh).² Melting points were measured on a *Gallenkamp* capillary melting point apparatus and are uncorrected. Optical rotations were recorded on a *Perkin Elmer 341* polarimeter. All proton and carbon nuclear magnetic resonance spectra (¹H and ¹³C NMR, respectively) were recorded using a *Bruker AMX 400 FT* spectrometer (operating frequencies: ¹H, 400.13 MHz; ¹³C, 100.61 MHz). Chemical shifts (δ) for all compounds are listed in parts per million downfield from tetramethylsilane using the NMR solvent as an internal reference. The reference values used for deuterated chloroform (CDCl₃) were 7.26 and 77.16 ppm for ¹H and ¹³C NMR spectra, respectively. The reference value used for deuterated acetone (acetone-D₆) was 30.83 ppm for ¹³C NMR spectra. Infrared spectra (IR) were recorded as either KBr pellets (KBr) or as films (neat) using a *Perkin Elmer 599B* IR spectrophotometer. Low-resolution mass spectra (MS) were recorded on a *Hewlett Packard 5985* GC-mass spectrometer. The mode of ionization used was chemical ionization (CI) with isobutane. Matrix-assisted laser desorption/ionization time-of-flight mass spectra (MALDI-TOF) were recorded on a *PerSeptive Biosystems Voyager-DE* mass spectrometer using 2,4-dihydroxybenzoic acid as the matrix. High-resolution mass spectra using fast atom bombardment (FAB HRMS) were recorded on a *Kratos Concept IH* mass spectrometer. Microanalyses were performed on a *Carlo Erba Model 1106* CHN analyzer. Analytical chiral high performance liquid chromatography (HPLC) was performed on a *Hewlett Packard Series 1050* instrument. Compounds **5a-g** were also prepared in racemic form by performing the corresponding reactions in the absence of the chiral ligand at

(1) Armarego, W. L. F.; Perrin, D. D. *Purification of Laboratory Chemicals*, 4th ed.; Oxford: Butterworth-Heinemann, 1997.

(2) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

room temperature. For compounds **5a-g**, the ^1H and ^{13}C NMR data reported herein is that of the racemic compounds. These materials were also used as reference compounds for the determination of the enantioselectivity of the corresponding asymmetric reactions.

2. Experimental Procedures and Characterization Data

*General procedure for the copper(II)-catalyzed asymmetric Friedel-Crafts reactions using ligand [(+)-1].*³

To a flame-dried Schlenk tube was added copper(II) trifluoromethanesulfonate (3.1 mg, $8.6\text{ }\mu\text{mol}$), ligand (+)-**1** (4.1 mg, $8.8\text{ }\mu\text{mol}$) and anhydrous ether (1.5 mL) and the resultant solution was stirred at room temperature for 1 h. The catalyst solution was then cooled to $0\text{ }^\circ\text{C}$ and treated with the appropriate indole **3a-f** ($94\text{ }\mu\text{mol}$) and the ethyl or methyl ester of 3,3,3-trifluoropyruvic acid **4a,b** ($86\text{ }\mu\text{mol}$). The Schlenk tube was then sealed and stirred at $0\text{ }^\circ\text{C}$ for 16 h. The reaction mixture was then concentrated *in vacuo* to afford the crude product. Flash chromatography using hexanes:ether (1:1) as the eluant afforded the desired substituted indoles **5a-g**.

(3) Zhuang, W.; Gathergood, N.; Hazell, R. G.; Jørgensen, K. A. *J. Org. Chem.* **2001**, 66, 1009.

(2S)-3,3,3-Trifluoro-2-hydroxy-(indole-3-yl)-propionic acid ethyl ester (5a)

Indole **3a** (11.0 mg, 94 μ mol) was reacted with ethyl 3,3,3-trifluoropyruvate **4a** (11 μ L, 86 μ mol) according to the general procedure to afford the *title compound* **5a** (17 mg, 68%) as a colorless oil. $[\alpha]_D^{20} + 11.3$ (*c* 1.01, chloroform) [lit.³ $[\alpha]_D^{25} + 12.3$ (*c* 1.91, chloroform), 83% ee]; **¹H NMR** (CDCl_3) δ 1.35 (3H, t, *J* = 7.1 Hz, $\text{CO}_2\text{CH}_2\text{CH}_3$), 4.33-4.39 (1H, m, $\text{CO}_2\text{CHHCH}_3$), 4.42-4.50 (1H, m, $\text{CO}_2\text{CHHCH}_3$), 7.14-7.19 (1H, m, *ArH*), 7.21-7.26 (1H, m, *ArH*), 7.39 (1H, d, *J* = 8.1 Hz, *ArH*), 7.49 (1H, d, *J* = 2.6 Hz, *ArH*), 7.91 (1H, d, *J* = 8.1 Hz, *ArH*), 8.27 (1H, broad s, *NH*); **¹³C NMR** (acetone- D_6) δ 15.2, 64.6, 79.2 (q, $^2J_{\text{C-F}} = 31$ Hz), 110.7, 113.5, 121.4, 122.9, 123.7, 126.3 (q, $^1J_{\text{C-F}} = 285$ Hz), 126.8, 127.4, 138.8, 170.3; **IR** (KBr) 3417 (broad), 1741, 1462, 1372, 1310, 1229, 1176, 1097, 1008, 909, 858, 751 cm^{-1} ; **MS** (CI) *m/z* (rel. intensity) 270 (52), 171 (100). Analytical chiral HPLC analysis using a *Daicel Chiracel OD* column [hexanes:isopropanol (90:10), flow rate at 0.5 mL/min, detection at $\lambda = 220$ nm, $t_{\text{MINOR}} = 32.5$ min, $t_{\text{MAJOR}} = 37.1$ min, ee = 74%].

(2S)-3,3,3-Trifluoro-2-hydroxy-(indole-3-yl)-propionic acid methyl ester (5b)

Indole **3a** (11.0 mg, 94 μ mol) was reacted with methyl 3,3,3-trifluoropyruvate **4b** (8.7 μ L, 86 μ mol) according to the general procedure to afford the *title compound* **5b** (18 mg, 77%) as a colorless oil. $[\alpha]_D^{20} - 24.1$ (*c* 0.99, chloroform); **¹H NMR** (CDCl_3) δ 3.94 (3H, s, CO_2CH_3), 4.35 (1H, broad s, *OH*), 7.14-7.20 (1H, m, *ArH*), 7.21-7.25 (1H, m, *ArH*), 7.36-7.41 (1H, m, *ArH*), 7.44-7.48 (1H, m, *ArH*), 7.87 (1H, d, *J* = 8.0 Hz, *ArH*), 8.29 (1H, broad s, *NH*); **¹³C NMR** (acetone- D_6) δ 58.0, 82.5 (q, $^2J_{\text{C-F}} = 31$ Hz), 113.9, 116.8, 124.9, 126.0, 127.1, 129.5 (q, $^1J_{\text{C-F}} =$

286 Hz), 130.1, 130.7, 142.0, 174.2; **IR** (neat) 3414 (broad), 3331 (broad), 1750, 1461, 1438, 1341, 1299, 1261, 1233, 1173, 1118, 1102, 1080, 999, 907, 753 cm^{-1} ; **MS** (CI) m/z (rel. intensity) 273 ($M + H$, 12), 256 (100); **Anal.** Calcd. for $\text{C}_{12}\text{H}_{10}\text{F}_3\text{NO}_3$: C, 52.75; H, 3.69; N, 5.13. Found: C, 52.90; H, 3.69; N, 5.06. Analytical chiral HPLC analysis using a *Daicel Chiracel OD* column [hexanes:isopropanol (90:10), flow rate at 0.5 mL/min, detection at $\lambda = 220$ nm, $t_{\text{MINOR}} = 44.2$ min, $t_{\text{MAJOR}} = 45.8$ min, ee = 90%].

(2S)-3,3,3-Trifluoro-2-hydroxy-(2-methylindole-3-yl)-propionic acid methyl ester (5c)

2-Methylindole **3b** (12.4 mg, 94 μmol) was reacted with methyl 3,3,3-trifluoropyruvate **4b** (8.7 μL , 86 μmol) according to the general procedure to afford the *title compound* **5c** (20 mg, 79%) as a light yellow oil. $[\alpha]_D^{20} + 7.1$ (c 1.70, chloroform); $^1\text{H NMR}$ (CDCl_3) δ 2.50 (3H, s, CH_3), 2.52 (3H, s, CO_2CH_3), 7.07-7.19 (2H, m, ArH), 7.26-7.30 (1H, m, ArH), 7.75 (1H, d, $J = 8.0$ Hz, ArH), 8.03 (1H, broad s, NH); $^{13}\text{C NMR}$ (acetone- D_6) δ 14.5, 54.1, 79.7 (q, $^2J_{\text{C-F}} = 30$ Hz), 105.9, 112.4, 121.3, 121.4, 122.7, 126.9 (q, $^1J_{\text{C-F}} = 284$ Hz), 129.1, 137.0, 137.5, 170.9; **IR** (neat) 3401 (broad), 1741, 1694, 1461, 1438, 1291, 1183, 1029, 748 cm^{-1} ; **MS** (CI) m/z (rel. intensity) 287 ($M + H$, 100), 270 (50); **FAB HRMS** Calcd. for $\text{C}_{13}\text{H}_{12}\text{F}_3\text{NO}_3$: 287.0769. Found: 287.0774. Analytical chiral HPLC analysis using a *Daicel Chiracel OD* column [hexanes:isopropanol (90:10), flow rate at 0.5 mL/min, detection at $\lambda = 220$ nm, $t_{\text{MAJOR}} = 43.9$ min, $t_{\text{MINOR}} = 63.3$ min, ee = 86%].

(2S)-3,3,3-Trifluoro-2-hydroxy-(5-methoxyindole-3-yl)-propionic acid methyl ester (5d)

5-Methoxyindole **3c** (13.9 mg, 94 μ mol) was reacted with methyl 3,3,3-trifluoropyruvate **4b** (8.7 μ L, 86 μ mol) according to the general procedure to afford the *title compound* **5d** (18 mg, 69%) as a colorless oil. $[\alpha]_D^{20}$ - 1.7 (*c* 1.30, chloroform); $^1\text{H NMR}$ (CDCl_3) δ 3.84 (3H, s, OCH_3), 3.92 (3H, s, CO_2CH_3), 6.86-6.91 (1H, m, *ArH*), 7.18 (1H, d, J = 8.9 Hz, *ArH*), 7.30-7.34 (2H, m, *ArH*), 8.33 (1H, broad s, *NH*); $^{13}\text{C NMR}$ (acetone- D_6) δ 54.8, 56.8, 79.2 (q, $^2J_{\text{C-F}}$ = 31 Hz), 104.4, 114.2, 114.9, 124.9, 127.3, 127.7 (q, $^1J_{\text{C-F}}$ = 288 Hz), 127.7, 127.9, 133.9, 170.8; **IR** (neat) 3409 (broad), 1748, 1692, 1628, 1583, 1488, 1441, 1294, 1217, 1178, 1113, 1026, 1000, 906, 794 cm^{-1} ; **MS** (CI) m/z (rel. intensity) 303 (*M* + *H*, 100), 286 (41), 244 (16), 174 (24), 147 (67); **FAB HRMS** Calcd. for $\text{C}_{13}\text{H}_{12}\text{F}_3\text{NO}_4$: 303.0718. Found: 303.0716. Analytical chiral HPLC analysis using a *Daicel Chiracel OD* column [hexanes:isopropanol (90:10), flow rate at 0.5 mL/min, detection at λ = 220 nm, t_{MINOR} = 61.5 min, t_{MAJOR} = 72.5 min, ee = 72%].

(2S)-3,3,3-Trifluoro-2-hydroxy-(5-nitroindole-3-yl)-propionic acid methyl ester (5e)

5-Nitroindole **3d** (15.3 mg, 94 μ mol) was reacted with methyl 3,3,3-trifluoropyruvate **4b** (8.7 μ L, 86 μ mol) according to the general procedure to afford the *title compound* **5e** (21 mg, 75%) as a yellow crystalline solid. **M.p.** 139-140 $^{\circ}\text{C}$, hexanes/ether; $[\alpha]_D^{20}$ - 0.5 (*c* 1.00, chloroform); $^1\text{H NMR}$ (CDCl_3) δ 4.01 (3H, s, CO_2CH_3), 4.27 (1H, broad s, *OH*), 7.45 (1H, d, J = 9.0 Hz, *ArH*), 7.67-7.70 (1H, m, *ArH*), 8.16 (1H, dd, J = 9.0, 2.2 Hz, *ArH*), 8.74 (1H, broad s, *NH*), 8.92-8.95 (1H, m, *ArH*); $^{13}\text{C NMR}$ (acetone- D_6) δ 55.2, 79.2 (q, $^2J_{\text{C-F}}$ = 30 Hz), 113.0, 114.1, 119.1, 120.1, 125.8 (q, $^1J_{\text{C-F}}$ = 285 Hz), 126.8, 130.7, 141.7, 143.9, 170.2; **IR** (KBr) 3400

(broad), 3373 (broad), 1754, 1521, 1473, 1339, 1303, 1224, 1198, 1169, 1108, 1053, 989, 941, 660 cm^{-1} ; **MS** (CI) m/z (rel. intensity) 319 ($M + H$, 100), 302 (33), 259 (51); **Anal.** Calcd. for $\text{C}_{12}\text{H}_9\text{F}_3\text{N}_2\text{O}_5$: C, 45.29; H, 2.85; N, 8.80. Found: C, 45.02; H, 3.06; N, 8.51. ^1H NMR analysis in the presence of the chiral shift reagent $\text{Eu}(\text{hfc})_3$ indicated a 3.9:1.0 ratio of enantiomers, ee = 60%.

(2S)-3,3,3-Trifluoro-2-hydroxy-(1-methylindole-3-yl)-propionic acid methyl ester (5f)

1-Methylindole **3e** (12.3 mg, 94 μmol) was reacted with methyl 3,3,3-trifluoropyruvate **4b** (8.7 μL , 86 μmol) according to the general procedure to afford the *title compound* **5f** (18 mg, 74%) as a colorless oil. $[\alpha]_D^{20} < \pm 0.5$ (c 1.00, chloroform); ^1H NMR (CDCl_3) δ 3.80 (3H, s, NCH_3), 3.94 (3H, s, CO_2CH_3), 7.13-7.19 (1H, m, ArH), 7.24-7.30 (1H, m, ArH), 7.31-7.35 (2H, m, ArH), 7.82-7.87 (1H, d, $J = 8.2$ Hz, ArH); ^{13}C NMR (acetone- D_6) δ 34.1, 54.8, 79.1 (q, $^2J_{\text{C-F}} = 31$ Hz), 109.5, 111.6, 121.6, 122.9, 123.8, 126.2 (q, $^1J_{\text{C-F}} = 286$ Hz), 127.8, 130.9, 139.2, 170.8; **IR** (neat) 3488 (broad), 1742, 1544, 1477, 1466, 1296, 1173, 1135, 745 cm^{-1} ; **MS** (CI) m/z (rel. intensity) 288 ($M + H$, 46), 270 (100); **FAB HRMS** Calcd. for $\text{C}_{13}\text{H}_{12}\text{F}_3\text{NO}_3$: 287.0769. Found: 287.0769. Analytical chiral HPLC analysis using a *Daicel Chiracel OD* column [hexanes:isopropanol (90:10), flow rate at 0.5 mL/min, detection at $\lambda = 220$ nm, $t_{\text{MINOR}} = 26.2$ min, $t_{\text{MAJOR}} = 37.1$ min, ee = 18%].

(2S)-3,3,3-Trifluoro-2-hydroxy-(1-methyl-2-phenylindole-3-yl)-propionic acid methyl ester (5g)

1-Methyl-2-phenylindole **3f** (19.5 mg, 94 μmol) was reacted with methyl 3,3,3-trifluoropropionate **4b** (8.7 μL , 86 μmol) according to the general procedure to afford the *title compound* **5g** (20 mg, 65%) as a colorless oil. $[\alpha]_D^{20} < \pm 0.5$ (*c* 1.00, chloroform); $^1\text{H NMR}$ (CDCl_3) δ 3.26 (3H, s, NCH_3), 3.36 (3H, s, CO_2CH_3), 7.17–7.42 (5H, m, *ArH*), 7.45–7.55 (3H, m, *ArH*), 8.07 (1H, d, $J = 8.1$ Hz, *ArH*); $^{13}\text{C NMR}$ (acetone- D_6) δ 53.5, 79.7 (q, $^2J_{\text{C-F}} = 30$ Hz), 111.4, 121.7, 123.9, 124.3, 126.5 (q, $^1J_{\text{C-F}} = 285$ Hz), 129.7, 129.9, 130.9, 132.7, 133.0, 133.7, 138.4, 141.2, 169.7; **IR** (neat) 3445 (broad), 1736, 1467, 1442, 1294, 1238, 1188, 1106, 1069, 984, 748 cm^{-1} ; **MS** (CI) m/z (rel. intensity) 364 ($\text{M} + \text{H}$, 93), 346 (100); **FAB HRMS** Calcd. for $\text{C}_{19}\text{H}_{16}\text{F}_3\text{NO}_3$: 363.1082. Found: 363.1083. Analytical chiral HPLC analysis using a *Daicel Chiracel OD* column [hexanes:isopropanol (96:4), flow rate at 0.5 mL/min, detection at $\lambda = 245$ nm, $t_{\text{MINOR}} = 25.6$ min, $t_{\text{MAJOR}} = 26.4$ min, ee = 18%].

(4S)-4-(Indole-3-yl)-4-phenyl-2-oxo-butanoic acid methyl ester (7)⁴

To a flame-dried Schlenk tube was added copper(II) trifluoromethanesulfonate (3.1 mg, 8.6 μmol), ligand (+)-**1** (4.1 mg, 8.8 μmol) and anhydrous ether (2.0 mL) and the resultant solution was stirred at room temperature for 1 h. The catalyst solution was then cooled to -78 $^{\circ}\text{C}$ and treated with indole **3a** (10.0 mg, 86 μmol) and (3*E*)-2-oxo-4-phenyl-3-butenic acid methyl

(4) Jensen, K. B.; Thorhauge, J.; Hazell, R. G.; Jørgensen, K. A. *Angew. Chem., Int. Ed.* **2001**, *40*, 160.

ester **6**⁵ (16.4 mg, 86 μ mol) and the resultant heterogeneous mixture was stirred at -78 °C for 16 h. The reaction mixture was then allowed to warm to room temperature and then filtered through a pad of silica gel using ether as the eluant. The filtrate was concentrated *in vacuo* to afford the desired product as the corresponding enol tautomer in pure form. The enol was smoothly converted to the desired ketone on stirring in methanol (5 mL) at room temperature for 2 h. On concentration *in vacuo*, the *title compound* **7** (25 mg, 97%) was isolated as a white crystalline solid. **M.p.** 93-94 °C, methanol (lit.⁶ 98 °C, ether/pentane); $[\alpha]_D^{20} + 14.1$ (*c* 1.00, chloroform) [lit.⁶ $[\alpha]_D^{20} - 23.9$ (*c* 1.00, chloroform), 99.5% ee]; **¹H NMR** (CDCl₃) δ 3.6 (1H, dd, *J* = 17.0, 8.0 Hz, *CHH*), 3.69 (1H, dd, *J* = 17.0, 7.1 Hz, *CHH*), 3.77 (3H, s, CO₂CH₃), 4.93 (1H, t, *J* = 7.5 Hz, *CH*), 6.99-7.46 (10H, m, *ArH*), 7.99 (1H, broad s, *NH*); **¹³C NMR** (CDCl₃) δ 38.9, 45.9, 53.2, 111.3, 116.5, 119.7, 120.2, 122.3, 126.7, 128.3, 136.2, 143.3, 161.1; **IR** (KBr) 3447 (broad), 1744, 1699, 1490, 1456, 1438, 1376, 1240, 1091, 1071, 768, 747 cm⁻¹; **MS** (CI) *m/z* (rel. intensity) 290 (25), 191 (100), 118 (34). The enantiomeric purity was determined by comparison of the optical rotation with a literature value, ee = 59%.⁶

(2*S*,4*R*)-3,4-Dihydro-4-hydroxy-7-methoxy-2-phenyl-2*H*-chromene-4-methyl carboxylate (9**)**⁷

To a flame-dried Schlenk tube was added copper(II) trifluoromethanesulfonate (9.0 mg, 0.025 mmol), ligand (+)-**1** (13.0 mg, 0.028 mmol) and anhydrous toluene (1.0 mL) and the resultant solution was stirred at room temperature for 1 h. (3*E*)-2-oxo-4-phenyl-3-butenic acid methyl ester **6**⁵ (58.0 mg, 0.25 mmol) and *N,N*-dimethylaniline (3.2 μ L, 0.025 mmol) were then added and the solution was cooled to 0 °C. 3-methoxyphenol **8** (55.0 μ L, 0.50 mmol) was added

(5) Dujardin, G.; Leconte, S.; Benard, A.; Brown, E. *Synlett* **2001**, 147.

(6) See: Ref. 4 (*Supporting Information*).

(7) van Lingen, H. L.; Zhuang, W.; Hansen, T.; Rutjes, F. P. J. T.; Jørgensen, K. A. *Org. Biomol. Chem.* **2003**, *1*, 1953.

to the resultant solution which was then stirred at 0 °C for 16 h. The reaction mixture was then concentrated *in vacuo* to afford the crude product. Purification by flash chromatography using pentane:ether (5:1) as the eluant afforded the *title compound 9* (49 mg, 62%) as a colorless oil. $[\alpha]_D^{20} + 0.75$ (*c* 1.00, chloroform) [lit.⁷ $[\alpha]_D^{20} + 1.36$ (*c* 1.55, chloroform), 80% ee]; ¹H NMR (CDCl₃) δ 2.26 (1H, dd, *J* = 13.4, 5.5 Hz, CHH), 2.45 (1H, td, *J* = 2.0, 13.2 Hz, CHH), 3.75 (3H, s, CO₂CH₃), 3.90 (3H, s, OCH₃), 4.28 (1H, dd, *J* = 13.2, 5.5 Hz, CH), 4.37 (1H, broad d, *J* = 2.0 Hz, OH), 6.40-6.47 (2H, m, ArH), 6.64 (1H, d, *J* = 8.4 Hz, ArH), 7.23-7.38 (5H, m, ArH); ¹³C NMR (CDCl₃) δ 37.1, 53.8, 55.6, 94.7, 102.0, 108.8, 118.0, 127.2, 129.0, 129.1, 130.2, 143.8, 152.4, 159.7, 170.5; IR (neat) 3450 (broad), 1750, 1621, 1581, 1504, 1442, 1256, 1161, 1123, 1032 cm⁻¹; MS (CI) *m/z* (rel. intensity) 315 (M + H, 38), 265 (100). Analytical chiral HPLC analysis using a *Daicel Chiracel OD* column [hexanes:isopropanol (98:2), flow rate at 0.75 mL/min, detection at λ = 220 nm, *t*_{MAJOR} = 34.4 min, *t*_{MINOR} = 36.7 min, ee = 42%].

3. Selected X-Ray Crystallographic Data

Procedure for the preparation and crystallization of the CuCl₂·ligand [(+)-1] complex (10).

A solution of the ligand (+)-**1** (12.4 mg, 27 μmol) and copper(II) chloride (3.8 mg, 28 μmol) in a mixture of ethanol:dichloromethane (1:1, 4 mL) was heated at reflux for 6 h. The reaction mixture was then allowed to cool to room temperature and then concentrated *in vacuo* to afford the crude product. This material was then taken up in dichloromethane (2 mL) and filtered through a pad of glass wool. Ethanol (1 mL) was added to the filtrate and upon slow evaporation, the *title compound 10* (10 mg, 62%) was obtained as X-ray quality yellow crystals. **M.p.** >210 °C (dec.), dichloromethane/ethanol; $[\alpha]_D^{20} + 1117$ (*c* 0.38, dichloromethane); IR (KBr) 3433 (broad), 3044, 2972, 2937, 2880, 1604, 1478, 1463, 1196, 1176, 1091, 1082, 929

cm⁻¹; **MS** (MALDI-TOF) *m/z* 562 (M - Cl), 465 (M - CuCl₂ + H); **Anal.** Calcd. for C₂₈H₃₆Cl₂CuN₂O₄: C, 56.14; H, 6.06; N, 4.68. Found: C, 56.31; H, 6.12; N, 4.75.

X-ray crystallographic analysis of the CuCl₂·ligand [(+)-1] complex (10).

A single crystal, a yellow platelet that had the dimensions 0.06 x 0.23 x 0.28 mm³, was mounted on a glass fiber using epoxy adhesive. The data for this crystal of the CuCl₂·ligand (+)-**1** complex **10** was acquired at 293 K on a *Rigaku RAXIS-RAPID* curved image plate area detector with graphite monochromated Cu K α radiation. Indexing for the crystal was performed using four, 5° oscillations that were exposed for 400 seconds. The following data range was recorded: 4.1° ≤ 2 θ ≤ 144.3° and a total of 54 images were collected. A sweep of data was then collected using ω scans from 0.0° to 180.0° in 10° steps, at χ = 0.0° and ϕ = 0.0°. A second sweep of data was collected using ω scans from 0.0° to 180.0° in 10° steps, at χ = 45.0° and ϕ = 0.0°. A final sweep of data was collected using ω scans from 0.0° to 180.0° in 10° steps, at χ = 45.0° and ϕ = 90.0°. The exposure rate was 100 sec/° and in each case, the crystal-to-detector distance was 127.40 mm. A numerical absorption correction was then applied which resulted in the following transmission range: 0.69 to 0.83.⁸ The coordinates and anisotropic displacement parameters for the non-hydrogen atoms were then refined. Of note, hydrogen atoms were placed in calculated positions (d C-H 0.95 Å) and their coordinate shifts were linked with those of the respective carbon atoms during refinement. Isotropic thermal parameters for the hydrogen atoms were initially assigned proportionately to the equivalent isotropic thermal parameters of their respective carbon atoms. Subsequently, the isotropic thermal parameters for the hydrogen atoms were constrained to have identical shifts during refinement. The programs used for all absorption corrections, data reduction, and processing were from the *Rigaku CrystalClear* package. The structure was refined using *CRYSTALS*.⁹ Complex scattering factors for neutral atoms were used in the calculation of structure factors.¹⁰ An *ORTEP* representation of the CuCl₂·ligand (+)-**1** complex **10** is provided below (Figure 3.1). Crystallographic data, fractional

(8) de Meulenaer, J.; Tompa, H. *Acta Cryst.* **1965**, *19*, 1014.

(9) Watkin, D. J.; Prout, C. K.; Carruthers, J. R.; Betteridge, P. W.; Cooper, R. I. *CRYSTALS* Issue 12.50; Chemical Crystallography Laboratory, University of Oxford, Oxford, England, 2003.

(10) International Union of Crystallography. *International Tables for X-Ray Crystallography*; Kynoch Press: Birmingham, England, 1952.

atomic coordinates and equivalent isotropic thermal displacement parameters, selected bond lengths, and selected bond angles for the CuCl_2 ·ligand (+)-**1** complex **10** are listed below (Table 3.1, 3.2, 3.3, and 3.4, respectively).

Figure 3.1. ORTEP representation of the CuCl_2 ·ligand (+)-**1** complex **10**.¹¹

Table 3.1. Summary of Crystallographic Data for the CuCl_2 ·Ligand (+)-**1** Complex **10**

Empirical formula	$\text{C}_{28}\text{H}_{36}\text{N}_2\text{Cl}_2\text{CuO}_4$
<i>FW</i> (g mol^{-1})	599.06
Temperature (K)	293
Wavelength (Cu $K\alpha$, Å)	1.54180
Crystal system	monoclinic

(11) The thermal ellipsoids are drawn at a 25% probability level for clarity.

Space group	$P 2_1$
a (Å)	8.7438(6)
b (Å)	7.6589(3)
c (Å)	21.3498(9)
α (°)	90
β (°)	90.022(3)
γ (°)	90
Z	2
U (Å ³)	1429.75(13)
D_{calc} (g cm ⁻³)	1.391
2θ limits (°)	4-145
Reflections collected	10274
Independent reflections	3461
Reflections observed [$I = 2.5\sigma(I)$]	3374
Goodness-of-fit on F	1.1741
R_1, R_w [$I = 2.5\sigma(I)$]	0.0436, 0.0553

Table 3.2. Fractional Atomic Coordinates (Å) and Equivalent Isotropic Thermal Displacement Parameters [$U(\text{iso})$, (Å²)] for the CuCl₂·Ligand (+)-**1** Complex **10**¹²

atom	x	y	z	U (iso)
Cu1	-0.75010(9)	-0.0208(2)	-0.25004(4)	0.0378
Cl1	-0.90802(18)	0.1773(2)	-0.28858(7)	0.0534
Cl2	-0.90612(19)	-0.2196(2)	-0.21132(8)	0.0541
O1	-0.6450(6)	-0.4482(7)	-0.4404(2)	0.0760
O2	-0.8062(5)	-0.2837(5)	-0.37837(18)	0.0509
O3	-0.6458(6)	0.4056(7)	-0.0595(2)	0.0744
O4	-0.8071(5)	0.2408(5)	-0.12236(18)	0.0475
N1	-0.5748(5)	-0.1706(6)	-0.2803(2)	0.0359
N2	-0.5728(6)	0.1282(6)	-0.2199(2)	0.0375

(12) The occupancies for all atoms listed in this table are 1.0.

C1	-0.5812(7)	-0.3224(8)	-0.3120(2)	0.0402
C2	-0.7223(7)	-0.4002(7)	-0.3385(3)	0.0382
C3	-0.6599(8)	-0.5396(9)	-0.3826(3)	0.0577
C4	-0.4985(8)	-0.5821(8)	-0.3609(3)	0.0622
C5	-0.4494(8)	-0.4181(7)	-0.3264(2)	0.0428
C6	-0.3098(7)	-0.3555(8)	-0.3135(3)	0.0479
C7	-0.1639(9)	-0.4472(10)	-0.3327(4)	0.0758
C8	-0.3037(8)	-0.1964(9)	-0.2830(3)	0.0501
C9	-0.4329(7)	-0.1067(7)	-0.2666(2)	0.0370
C10	-0.4335(7)	0.0642(7)	-0.2330(3)	0.0383
C11	-0.3009(8)	0.1522(9)	-0.2167(3)	0.0512
C12	-0.3096(9)	0.3124(9)	-0.1869(3)	0.0580
C13	-0.1669(8)	0.4070(10)	-0.1675(4)	0.0750
C14	-0.4554(8)	0.3770(8)	-0.1728(3)	0.0460
C15	-0.5007(8)	0.5403(8)	-0.1393(3)	0.0554
C16	-0.6586(8)	0.4961(9)	-0.1163(3)	0.0544
C17	-0.7272(7)	0.3574(7)	-0.1604(3)	0.0407
C18	-0.5777(7)	0.2787(7)	-0.1887(2)	0.0376
C19	-0.638(2)	-0.0177(17)	-0.4424(8)	0.2811
C20	-0.6711(19)	-0.1446(14)	-0.4632(5)	0.1753
C21	-0.7544(9)	-0.3110(10)	-0.4414(3)	0.0615
C22	-0.8884(8)	-0.3642(12)	-0.4796(3)	0.0799
C23	-0.8460(10)	-0.4058(14)	-0.5480(3)	0.1098
C24	-0.647(2)	-0.0320(16)	-0.0540(8)	0.2839
C25	-0.6678(16)	0.1087(14)	-0.0353(5)	0.1445
C26	-0.7535(9)	0.2679(10)	-0.0581(3)	0.0624
C27	-0.8975(9)	0.3198(11)	-0.0206(3)	0.0813
C28	-0.8464(12)	0.3585(14)	0.0484(4)	0.1213
H21	-0.7856(7)	-0.4475(7)	-0.3066(3)	0.050(4)
H31	-0.7222(8)	-0.6407(9)	-0.3859(3)	0.064(4)
H41	-0.4339(8)	-0.6010(8)	-0.3960(3)	0.072(4)

H42	-0.4944(8)	-0.6809(8)	-0.3340(3)	0.072(4)
H71	-0.0776(9)	-0.3829(10)	-0.3186(4)	0.085(4)
H72	-0.1614(9)	-0.4557(10)	-0.3771(4)	0.085(4)
H73	-0.1617(9)	-0.5610(10)	-0.3150(4)	0.085(4)
H81	-0.2068(8)	-0.1469(9)	-0.2733(3)	0.057(4)
H111	-0.2040(8)	0.1016(9)	-0.2255(3)	0.061(4)
H131	-0.1934(8)	0.5146(10)	-0.1482(4)	0.085(4)
H132	-0.1060(8)	0.4289(10)	-0.2034(4)	0.085(4)
H133	-0.1109(8)	0.3372(10)	-0.1387(4)	0.085(4)
H151	-0.4983(8)	0.6386(8)	-0.1664(3)	0.070(4)
H152	-0.4354(8)	0.5608(8)	-0.1045(3)	0.070(4)
H161	-0.7212(8)	0.5971(9)	-0.1130(3)	0.064(4)
H171	-0.7910(7)	0.4051(7)	-0.1921(3)	0.048(4)
H191	-0.565(2)	0.0425(17)	-0.4675(8)	0.459(4)
H192	-0.735(2)	0.0379(17)	-0.4459(8)	0.459(4)
H193	-0.606(2)	-0.0159(17)	-0.3999(8)	0.459(4)
H201	-0.6981(19)	-0.1324(14)	-0.5061(5)	0.151(4)
H202	-0.5690(19)	-0.1861(14)	-0.4601(5)	0.151(4)
H221	-0.9564(8)	-0.2675(12)	-0.4802(3)	0.097(4)
H222	-0.9378(8)	-0.4617(12)	-0.4610(3)	0.097(4)
H231	-0.9361(10)	-0.4345(14)	-0.5707(3)	0.132(4)
H232	-0.7972(10)	-0.3089(14)	-0.5673(3)	0.132(4)
H233	-0.7785(10)	-0.5031(14)	-0.5481(3)	0.132(4)
H241	-0.595(2)	-0.0981(16)	-0.0231(8)	0.397(4)
H242	-0.738(2)	-0.0910(16)	-0.0656(8)	0.397(4)
H243	-0.584(2)	-0.0183(16)	-0.0897(8)	0.397(4)
H251	-0.7255(16)	0.0803(14)	0.0009(5)	0.182(4)
H252	-0.5708(16)	0.1529(14)	-0.0232(5)	0.182(4)
H271	-0.9424(9)	0.4203(11)	-0.0391(3)	0.097(4)
H272	-0.9691(9)	0.2265(11)	-0.0210(3)	0.097(4)
H281	-0.9362(12)	0.3907(14)	0.0706(4)	0.144(4)

H282	-0.7753(12)	0.4523(14)	0.0494(4)	0.144(4)
H283	-0.8020(12)	0.2585(14)	0.0675(4)	0.144(4)

Table 3.3. Bond Lengths (Å) for the CuCl₂·Ligand (+)-**1** Complex **10**

Cu1-Cl1	2.2100(17)
Cu1-Cl2	2.2054(19)
Cu1-N1	2.021(5)
Cu1-N2	2.029(5)
O1-C3	1.423(8)
O1-C21	1.421(9)
O2-C2	1.435(6)
O2-C21	1.436(8)
O3-C16	1.403(8)
O3-C26	1.414(9)
O4-C17	1.395(7)
O4-C26	1.463(7)
N1-C1	1.347(7)
N1-C9	1.365(7)
N2-C10	1.343(7)
N2-C18	1.332(7)
C1-C2	1.482(8)
C1-C5	1.400(8)
C2-C3	1.525(8)
C3-C4	1.521(9)
C4-C5	1.519(8)
C5-C6	1.339(8)
C6-C7	1.513(8)
C6-C8	1.383(9)
C8-C9	1.368(8)
C9-C10	1.492(7)

C10-C11	1.386(8)
C11-C12	1.384(9)
C12-C13	1.501(8)
C12-C14	1.401(9)
C14-C15	1.495(8)
C14-C18	1.351(8)
C15-C16	1.504(8)
C16-C17	1.540(8)
C17-C18	1.562(8)
C19-C20	1.107(14)
C20-C21	1.540(11)
C21-C22	1.484(9)
C22-C23	1.541(9)
C24-C25	1.162(13)
C25-C26	1.512(10)
C26-C27	1.545(10)
C27-C28	1.567(10)

Table 3.4. Bond Angles (°) for the CuCl₂•Ligand (+)-**1** Complex **10**

Cl1-Cu1-Cl2	103.12(7)
Cl1-Cu1-N1	138.12(14)
Cl2-Cu1-N1	101.38(15)
Cl1-Cu1-N2	102.07(15)
Cl2-Cu1-N2	137.90(14)
N1-Cu1-N2	80.86(18)
C3-O1-C21	108.4(5)
C2-O2-C21	107.7(5)
C16-O3-C26	109.5(5)
C17-O4-C26	107.1(5)
Cu1-N1-C1	128.3(4)

Cu1-N1-C9	114.7(4)
C1-N1-C9	117.1(5)
Cu1-N2-C10	115.0(4)
Cu1-N2-C18	128.4(4)
C10-N2-C18	116.7(5)
N1-C1-C2	125.0(5)
N1-C1-C5	121.9(5)
C2-C1-C5	113.0(5)
C1-C2-O2	113.7(5)
C1-C2-C3	102.7(5)
O2-C2-C3	104.6(5)
C2-C3-O1	102.9(5)
C2-C3-C4	107.1(5)
O1-C3-C4	106.5(6)
C3-C4-C5	103.5(5)
C4-C5-C1	107.9(6)
C4-C5-C6	130.7(6)
C1-C5-C6	121.2(6)
C5-C6-C7	123.2(6)
C5-C6-C8	116.5(6)
C7-C6-C8	120.3(6)
C6-C8-C9	122.1(6)
C8-C9-N1	121.0(5)
C8-C9-C10	124.5(5)
N1-C9-C10	114.5(5)
C9-C10-N2	115.1(5)
C9-C10-C11	122.9(6)
N2-C10-C11	122.0(6)
C10-C11-C12	120.0(7)
C11-C12-C13	120.6(7)
C11-C12-C14	117.5(6)

C13-C12-C14	121.8(6)
C12-C14-C15	129.8(6)
C12-C14-C15	118.0(6)
C15-C14-C18	112.2(6)
C14-C15-C16	102.2(5)
C15-C16-O3	108.7(5)
C15-C16-C17	108.3(5)
O3-C16-C17	102.6(5)
C16-C17-O4	106.3(5)
C16-C17-C18	100.2(5)
O4-C17-C18	113.4(5)
C17-C18-C14	110.5(5)
C17-C18-N2	123.7(5)
C14-C18-N2	125.6(6)
C19-C20-C21	136.9(10)
C20-C21-O2	108.2(6)
C20-C21-O1	107.4(8)
O2-C21-O1	107.8(5)
C20-C21-C22	115.8(8)
O2-C21-C22	107.8(6)
O1-C21-C22	109.7(6)
C21-C22-C23	112.8(7)
C24-C25-C26	135.6(10)
C25-C26-O4	110.2(6)
C25-C26-O3	106.1(8)
O4-C26-O3	107.4(5)
C25-C26-C27	116.4(8)
O4-C26-C27	105.2(6)
O3-C26-C27	111.2(6)
C26-C27-C28	107.7(7)

4. ^1H and ^{13}C NMR Spectra

¹H NMR spectrum (CDCl₃) of (2S)-3,3,3-trifluoro-2-hydroxy-(indole-3-yl)-propionic acid methyl ester **5b**.

^{13}C NMR spectrum (acetone- D_6) of (2S)-3,3,3-trifluoro-2-hydroxy-(indole-3-yl)-propionic acid methyl ester **5b**.

^1H NMR spectrum (CDCl_3) of (2S)-3,3,3-trifluoro-2-hydroxy-(2-methylindole-3-yl)-propionic acid methyl ester **5c**.

^{13}C NMR spectrum (acetone- D_6) of (2S)-3,3,3-trifluoro-2-hydroxy-(2-methylindole-3-yl)-propionic acid methyl ester **5c**.

¹³C NMR spectrum (acetone-D₆) of (2S)-3,3,3-trifluoro-2-hydroxy-(5-methoxyindole-3-yl)-propionic acid methyl ester **5d**.

¹H NMR spectrum (CDCl₃) of (2S)-3,3,3-trifluoro-2-hydroxy-(5-nitroindole-3-yl)-propionic acid methyl ester **5e**.

¹³C NMR spectrum (acetone-D₆) of (2S)-3,3,3-trifluoro-2-hydroxy-(5-nitroindole-3-yl)-propionic acid methyl ester **5e**.

¹H NMR spectrum (CDCl₃) of (2S)-3,3,3-trifluoro-2-hydroxy-(1-methylindole-3-yl)-propionic acid methyl ester **5f**.

¹³C NMR spectrum (acetone-D₆) of (2S)-3,3,3-trifluoro-2-hydroxy-(1-methylindole-3-yl)-propionic acid methyl ester **5f**.

¹H NMR spectrum (CDCl₃) of (2S)-3,3,3-trifluoro-2-hydroxy-(1-methyl-2-phenylindole-3-yl)-propionic acid methyl ester **5g**.

¹³C NMR spectrum (acetone-D₆) of (2S)-3,3,3-trifluoro-2-hydroxy-(1-methyl-2-phenylindole-3-yl)-propionic acid methyl ester **5g**.