

Supporting Information

COPPER-MEDIATED REGIOSELECTIVE HOMOCOUPLING OF THIOPHENES AND INDOLES VIA DIRECTED C–H CLEAVAGE

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Instrumentation and Chemicals

¹H and ¹³C NMR spectra were recorded at 400 MHz and 100 or 150 MHz, respectively, for CDCl₃ solutions. MS data were obtained by EI, FAB, or APCI. GC analysis was carried out using a silicon OV-17 column (i. d. 2.6 mm x 1.5 m) or a CBP-1 capillary column (i. d. 0.5 mm x 25 m). TLC analyses were performed on commercial glass plates bearing 0.25-mm layer of Merck Silica gel 60F₂₅₄. Silica gel (Wakogel 200 mesh) was used for column chromatography.

Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. *o*-Xylene was stored on slices of sodium. Anhydrous Cu(OAc)₂ was purchased from Wako Pure Chemical Co. All thiophenecarboxamides **1** were synthesized from the corresponding thiophenecarboxylic acids or thiophenecarbonyl chlorides and 8-aminoquinoline.¹ *N*-(2-pyrimidyl)indoles and *N*-(2-pyridyl)indole were prepared according to the literature.²

¹ M. Nishino, K. Hirano, T. Satoh, and M. Miura, *Angew. Chem., Int. Ed.* 2013, **52**, 4457.

² M. Nishino, K. Hirano, T. Satoh, and M. Miura, *Angew. Chem., Int. Ed.* 2012, **51**, 6993.

Experimental Procedures

Copper-mediated homocoupling of thiophenecarboxamides

The reaction of **1a** is representative (Table 1, entry 1). Cu(OAc)₂ (91 mg, 0.50 mmol) and *N*-(quinolin-8-yl)thiophene-2-carboxamide (**1a**, 64 mg, 0.25 mmol) were placed in a 20 mL two-necked reaction flask equipped with a reflux condenser. The flask was filled with nitrogen by using the Standard Schrenk technique. *o*-Xylene (1.5 mL) was added dropwise via a syringe, and the solution was stirred at 165 °C for 3 h. The resulting mixture was then quenched with water. The mixture was extracted with ethyl acetate, and the combined organic layer was dried over sodium sulfate. Concentration in vacuo followed by silica gel column purification with hexane/ethyl acetate (1:1, v/v) gave *N,N'*-di(quinolin-8-yl)-[3,3'-bithiophene]-2,2'-dicarboxamide (**2a**, 43 mg, 0.085 mmol) in 67% yield.

Copper-mediated homocoupling of indoles

Synthesis of **4e** is representative (Scheme 3). Cu(OAc)₂ (23 mg, 0.125 mmol) and *N*-(2-pyridyl)indole (49 mg, 0.25 mmol) were placed in a 20 mL two-necked reaction flask equipped with a reflux condenser and a drying tube lined with calcium chloride. *o*-Xylene (1.5 mL) and AcOH (0.014 mL, 0.25 mmol) were added dropwise via a syringe, and the solution was stirred at 165 °C for 15 h. The resulting mixture was then quenched with water. The mixture was extracted with ethyl acetate, and the combined organic layer was dried over sodium sulfate. Concentration in vacuo followed by silica gel column purification with hexane/ethyl acetate (2:1, v/v) gave 1,1'-di(pyridin-2-yl)-1*H*,1'*H*-2,2'-biindole (**3b**, 23 mg, 0.058 mmol) in 46% yield.

Characterization Data for Products

¹H and ¹³C NMR spectra for all compounds are attached in the last part.

***N*², *N*^{2'}-Di(quinolin-8-yl)-[3,3'-bithiophene]-2,2'-dicarboxamide (2a)** m.p. 197-198 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.15 (d, *J* = 4.8 Hz, 2H), 7.32 (dd, *J* = 4.4 Hz, 8.0 Hz, 2H), 7.37-7.45 (m, 4H), 7.64 (d, *J* = 4.8 Hz, 2H), 7.99 (dd, *J* = 1.6 Hz, 4.4 Hz, 2H), 8.67 (dd, *J* = 1.6 Hz, 4.4 Hz, 2H), 8.77 (dd, *J* = 1.6 Hz, 7.6 Hz, 2H), 10.33 (s, 2H); ¹³C NMR (400 MHz, CDCl₃) δ 116.76, 121.61, 121.85, 127.20, 127.81, 131.07, 131.41, 134.32, 134.41, 136.02, 138.68, 139.87, 148.31, 159.85; HRMS (EI) *m/z* (*M*⁺) calcd for C₂₈H₁₈N₄O₂S₂: 506.0871, found: 506.0864.

5,5'-Dichloro-*N*²,*N*^{2'}-di(quinolin-8-yl)-[3,3'-bithiophene]-2,2'-dicarboxamide (2c) m.p. 260-262 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.03 (s, 2H), 7.38-7.45 (m, 6H), 8.06 (d, *J* = 8.4 Hz, 2H), 8.70-8.77 (m, 4H), 10.29 (s, 2H); ¹³C NMR (400 MHz, CDCl₃) δ 116.95, 121.86, 122.29, 127.19, 127.92, 130.02, 132.45, 134.04, 136.21, 137.16, 138.65, 138.94, 148.58, 158.52; HRMS (EI) *m/z* (*M*⁺) calcd for C₂₈H₁₆Cl₂N₄O₂S₂: 574.0092, found: 574.0076.

A 78:22 mixture of *N*³, *N*^{3'}-di(quinolin-8-yl)-[2,2'-bithiophene]-3,3'-dicarboxamide (2e) and *N*³, *N*^{4'}-di(quinolin-8-yl)-[2,3'-bithiophene]-3,4'-dicarboxamide (2e') m.p. 222-223 °C for mixture; ¹H NMR (400 MHz, CDCl₃) for mixture: δ 7.30-7.41 (m, 6H), 7.42 (d, *J* = 5.6 Hz, 0.22 × 1H for **2e'**), 7.51 (d, *J* = 5.2 Hz, 0.78 × 2H for **2e**), 7.63 (d, *J* = 3.2 Hz, 0.22 × 1H for **2e'**), 7.78 (d, *J* = 5.6 Hz, 0.22 × 1H for **2e'**), 7.85 (d, *J* = 5.2 Hz, 0.78 × 2H for **2e**), 8.00-8.03 (m, 0.22 × 2H for **2e'**), 8.02 (dd, *J* = 1.6 Hz, 8.8 Hz, 0.78 × 2H for **2e**), 8.32 (d, *J* = 3.6 Hz, 0.22 × 1H for **2e'**), 8.54-8.57 (m, 0.22 × 2H for **2e'**), 8.56 (dd, *J* = 2.0 Hz, 4.0 Hz, 0.78 × 2H for **2e**), 8.69-8.73 (m, 0.22 × 2H for **2e'**), 8.78 (dd, *J* = 1.6 Hz, 7.2 Hz, 0.78 × 2H for **2e**), 10.22 (s, 0.22 × 2H for **2e'**), 10.41 (s, 0.78 × 2H for **2e**); ¹³C NMR for **2e** (400 MHz, CDCl₃) δ 116.67, 121.55, 121.62, 127.31, 127.84, 127.90, 129.84, 133.27, 134.68, 136.08, 138.72, 138.99, 148.04, 160.92; HRMS (EI) *m/z* (*M*⁺) calcd for C₂₈H₁₈N₄O₂S₂: 506.0871, found: 506.0871.

5,5'-Diphenyl-*N*⁴,*N*^{4'}-di(quinolin-8-yl)-[3,3'-bithiophene]-4,4'-dicarboxamide (2f) m.p. 227-228 °C; ¹H NMR (400 MHz, CDCl₃) δ 6.99-7.26 (m, 12H), 7.43 (s, 2H), 7.53 (d, *J* = 8.4 Hz, 4H), 7.86 (d, *J* = 8.4 Hz, 2H), 8.26 (d, *J* = 4.0 Hz, 2H), 8.47 (d, *J* = 7.2 Hz, 2H), 10.14 (s, 2H); ¹³C NMR (400 MHz, CDCl₃) δ 117.20, 121.11, 121.46, 124.05, 126.64, 127.47, 128.42, 128.62, 129.10, 133.18, 134.26,

134.57, 135.76, 136.90, 138.36, 144.14, 147.64, 164.05; HRMS (FAB) m/z (M^+) calcd for $C_{40}H_{26}N_4O_2S_2$: 658.1497, found: 659.1583.

4,4'-Diphenyl- $N^3,N^{3'}$ -di(quinolin-8-yl)-[2,2'-bithiophene]-3,3'-dicarboxamide (2g) m.p. 254-255 °C; 1H NMR (400 MHz, $CDCl_3$) δ 7.18-7.22 (m, 2H), 7.20 (dd, $J = 4.0$ Hz, $J = 8.0$ Hz, 2H), 7.25-7.30 (m, 10H), 7.45 (s, 2H), 7.47 (d, $J = 1.6$ Hz, 2H), 7.96 (dd, $J = 1.6$ Hz, $J = 8.0$ Hz, 2H), 8.31 (dd, $J = 1.6$ Hz, $J = 4.0$ Hz, 2H), 8.63 (dd, $J = 2.4$ Hz, $J = 6.8$ Hz, 2H), 10.29 (s, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 117.40, 121.26, 121.80, 125.06, 127.06, 127.77, 128.47, 128.65, 134.44, 135.34, 135.50, 135.94, 137.60, 138.63, 142.16, 147.87, 161.53, 163.32; HRMS (APCI) m/z ($[M+1]^+$) calcd for $C_{40}H_{27}N_4O_2S_2$: 659.1575, found: 659.1570.

5,5'-Diphenyl- $N^3,N^{3'}$ -di(quinolin-8-yl)-[2,2'-bithiophene]-3,3'-dicarboxamide (2h) m.p. 200-202 °C; 1H NMR (400 MHz, $CDCl_3$) δ 7.25 (dd, $J = 4.0$ Hz, $J = 8.4$ Hz, 2H), 7.36-7.45 (m, 10H), 7.67 (dd, $J = 1.6$ Hz, $J = 7.2$ Hz, 4H), 8.00 (dd, $J = 1.6$ Hz, $J = 8.0$ Hz, 2H), 8.07 (s, 2H), 8.45 (dd, $J = 1.6$ Hz, $J = 4.4$ Hz, 2H), 8.79 (dd, $J = 2.0$ Hz, $J = 7.6$ Hz, 2H), 10.55 (s, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 116.72, 121.58, 121.70, 125.62, 126.06, 127.27, 127.86, 128.67, 129.31, 131.61, 133.16, 134.71, 136.02, 138.74, 139.73, 146.42, 148.08, 160.74; HRMS (EI) m/z (M^+) calcd for $C_{40}H_{26}N_4O_2S_2$: 658.1497, found: 658.1504.

5,5'-Bis(4-methoxyphenyl)- $N^3,N^{3'}$ -di(quinolin-8-yl)-[2,2'-bithiophene]-3,3'-dicarboxamide (2i) m.p. 222-224 °C; 1H NMR (400 MHz, $CDCl_3$) δ 3.84 (s, 6H), 6.94 (d, $J = 8.8$ Hz, 4H), 7.24 (dd, $J = 4.4$ Hz, $J = 8.4$ Hz, 2H), 7.35-7.43 (m, 4H), 7.58 (d, $J = 8.8$ Hz, 4H), 7.96 (s, 2H), 7.98 (dd, $J = 1.6$ Hz, $J = 8.4$ Hz, 2H), 8.44 (dd, $J = 1.6$ Hz, $J = 4.4$ Hz, 2H), 8.79 (dd, $J = 1.6$ Hz, $J = 7.6$ Hz, 2H), 10.56 (s, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 55.57, 114.70, 116.71, 121.61, 121.66, 124.60, 126.00, 127.29, 127.39, 127.88, 130.67, 134.81, 136.01, 138.79, 139.68, 146.36, 148.12, 160.09, 160.87; HRMS (APCI) m/z ($[M+1]^+$) calcd for $C_{42}H_{31}N_4O_2S_2$: 719.1787, found: 719.1781.

$N^{3''},N^{4'}$ -Di(quinolin-8-yl)-[3,2':5',2'':5'',3'''-quaterthiophene]-3'',4'-dicarboxamide (2j) m.p. 166-167 °C; 1H NMR (400 MHz, $CDCl_3$) δ 7.25 (dd, $J = 4.0$ Hz, $J = 8.0$ Hz, 2H), 7.35-7.41 (m, 8H), 7.48 (dd, $J = 1.2$ Hz, $J = 2.8$ Hz, 2H), 7.94 (s, 2H), 7.99 (dd, $J = 2.0$ Hz, $J = 8.4$ Hz, 2H), 8.45 (dd, $J = 1.2$ Hz, $J = 4.0$ Hz, 2H), 8.78 (dd, $J = 1.6$ Hz, $J = 7.2$ Hz, 2H), 10.54 (s, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 116.72, 121.23, 121.60, 121.73, 125.65, 125.92, 127.16, 127.26, 127.86, 130.46, 134.31,

134.68, 136.03, 138.73, 139.57, 141.25, 148.07, 160.65; HRMS (FAB) m/z (M^+) calcd for $C_{36}H_{22}N_4O_2S_4$: 670.0626, found: 671.0706.

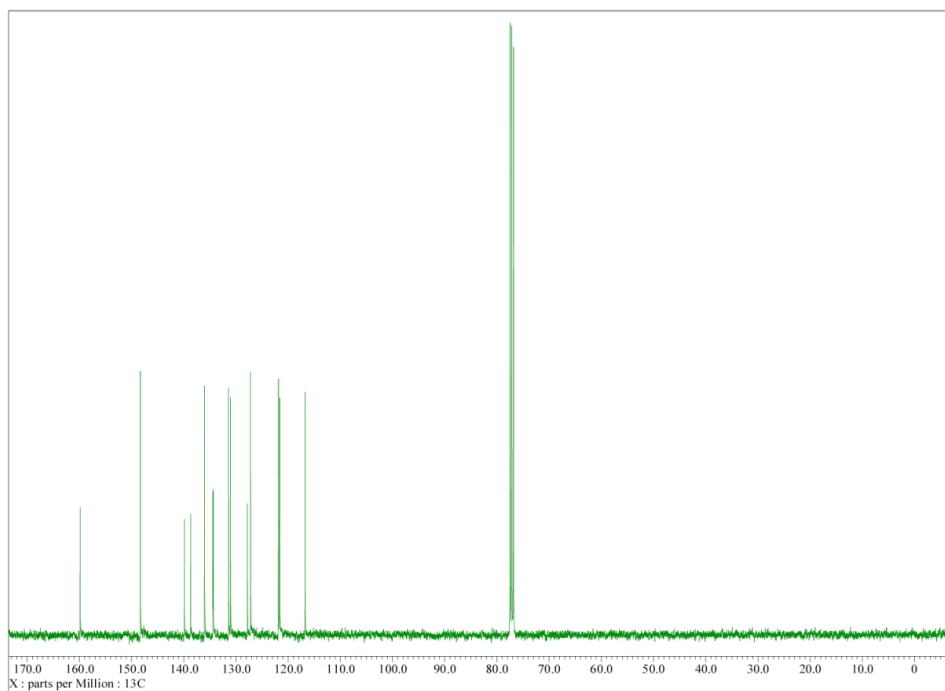
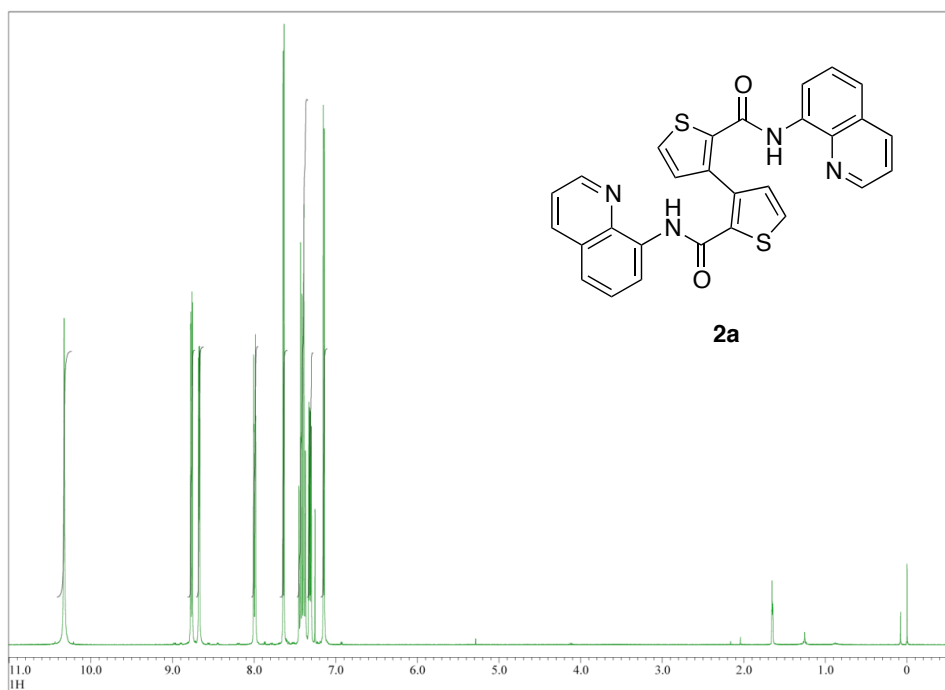
1,1'-Di(pyrimidin-2-yl)-1*H*,1'*H*-2,2'-biindole (3a) m.p. 226-228 °C; 1H NMR (400 MHz, $CDCl_3$) δ 6.81 (t, $J = 4.8$ Hz, 2H), 7.01 (s, 2H), 7.24-7.33 (m, 4H), 7.69 (d, $J = 8.0$ Hz, 2H), 8.30 (d, $J = 8.0$ Hz, 2H), 8.34 (d, $J = 4.8$ Hz, 4H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 109.99, 114.36, 116.55, 120.97, 122.19, 123.90, 129.43, 133.29, 136.93, 157.55, 157.87; HRMS (EI) m/z (M^+) calcd for $C_{24}H_{16}N_6$: 388.1436, found: 388.1437.

1,1'-Di(pyridin-2-yl)-1*H*, 1*H*'-2,2'-biindole (3b) m.p. 169-170 °C; 1H NMR (400 MHz, $CDCl_3$) δ 6.79 (d, $J = 8.0$ Hz, 2H), 6.90 (s, 2H), 7.05 (dd, $J = 5.2$ Hz, 7.6 Hz, 2H), 7.17-7.22 (m, 4H), 7.47 (ddd, $J = 2.0$ Hz, 7.6 Hz, 8.0 Hz, 2H), 7.62-7.68 (m, 4H), 8.26 (dd, $J = 2.0$ Hz, 5.2 Hz, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 108.02, 112.04, 119.98, 120.83, 121.30, 121.543, 123.59, 128.52, 131.07, 137.48, 137.99, 148.60, 151.07; HRMS (EI) m/z (M^+) calcd for $C_{26}H_{18}N_4$: 386.1531, found: 386.1534.

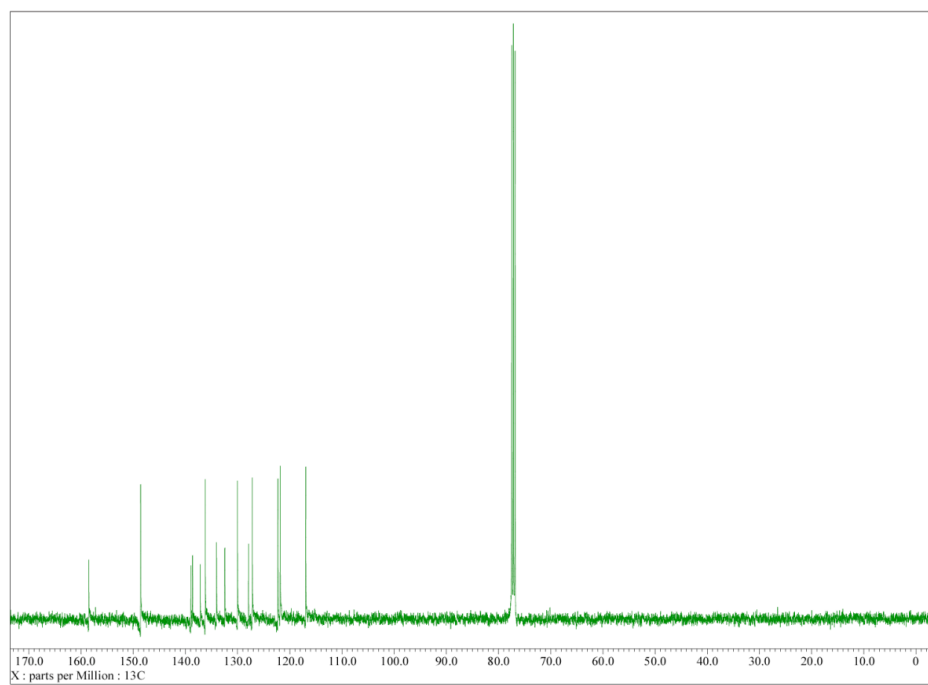
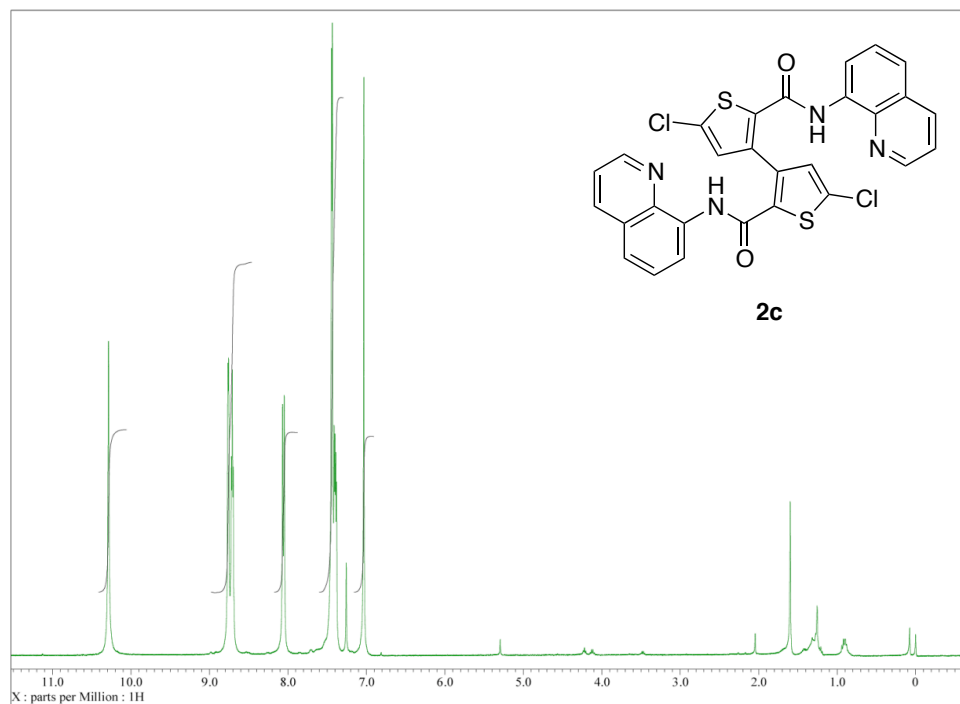
5,5'-Dimethoxy-1,1'-di(pyrimidin-2-yl)-1*H*,1'*H*-2,2'-biindole (3c) m.p. 250-252 °C; 1H NMR (400 MHz, $CDCl_3$) δ 3.90 (s, 6H), 6.76 (t, $J = 4.4$ Hz, 2H), 6.90 (s, 2H), 6.94 (dd, $J = 2.4$ Hz, $J = 9.2$ Hz, 2H), 7.14 (d, $J = 2.4$ Hz, 2H), 8.31 (d, $J = 4.4$ Hz, 4H), 8.49 (d, $J = 9.2$ Hz, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 55.88, 102.87, 109.80, 113.22, 115.62, 116.24, 130.14, 131.88, 133.90, 155.62, 157.55, 157.78; HRMS (EI) m/z (M^+) calcd for $C_{26}H_{20}N_6O_2$: 448.1648, found: 448.1650.

6,6'-Dichloro-1,1'-di(pyrimidin-2-yl)-1*H*,1'*H*-2,2'-biindole (3d) m.p. 276-278 °C; 1H NMR (400 MHz, $CDCl_3$) δ 6.84 (t, $J = 4.8$ Hz, 2H), 6.95 (s, 2H), 7.24 (dd, $J = 1.6$ Hz, $J = 8.4$ Hz, 2H), 7.59 (d, $J = 8.4$ Hz, 2H), 8.35 (d, $J = 4.8$ Hz, 4H), 8.41 (d, $J = 1.6$ Hz, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 109.82, 114.91, 116.87, 121.68, 122.88, 127.87, 129.84, 133.61, 137.19, 157.26, 157.96; HRMS (EI) m/z (M^+) calcd for $C_{24}H_{14}Cl_2N_6$: 456.0657, found: 456.0658.

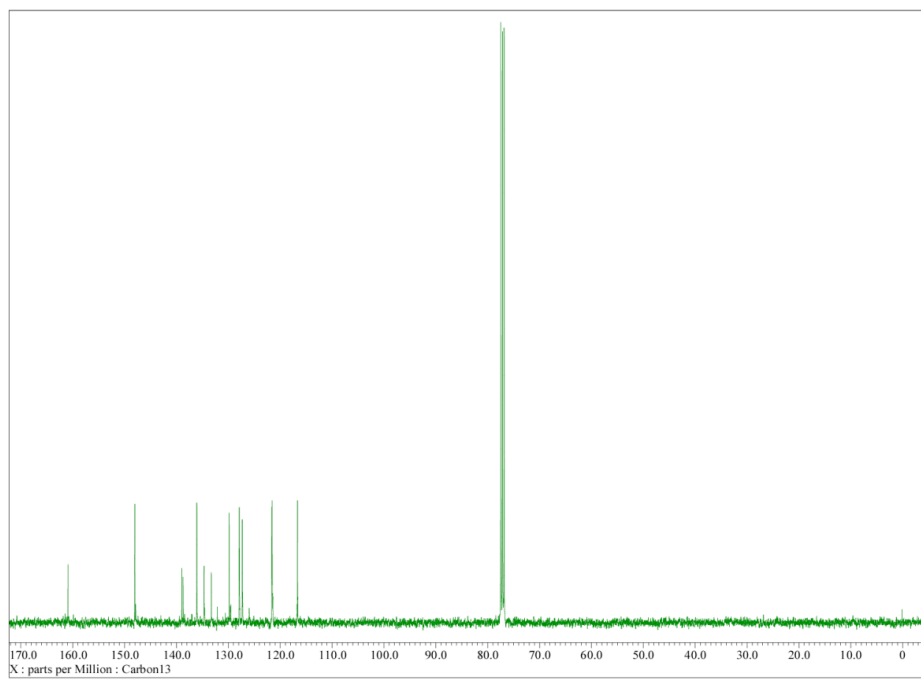
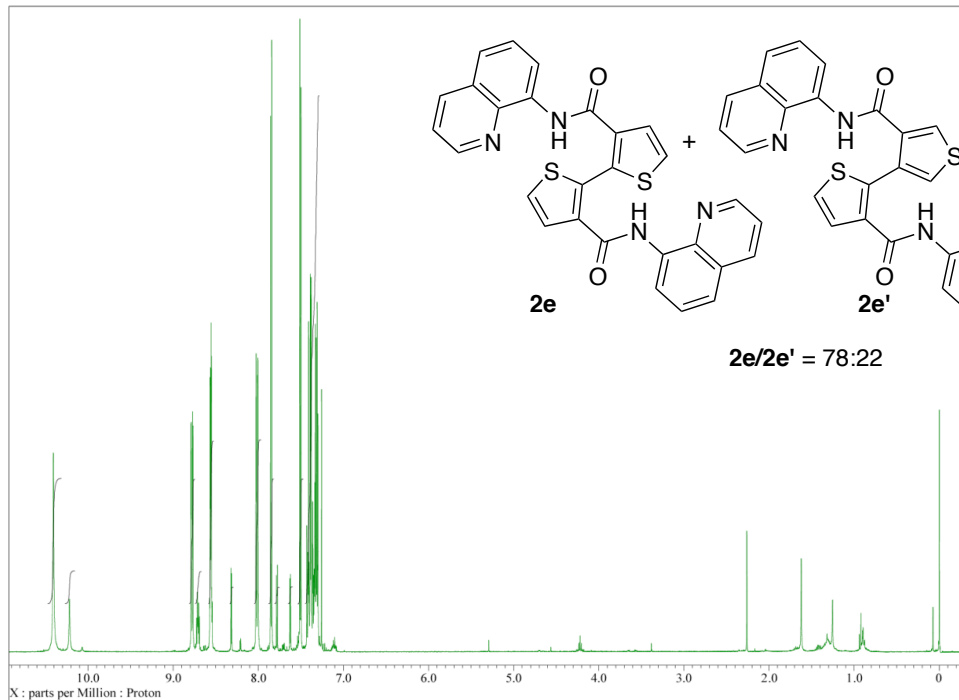
[^1H and ^{13}C NMR Spectra of **2a**]



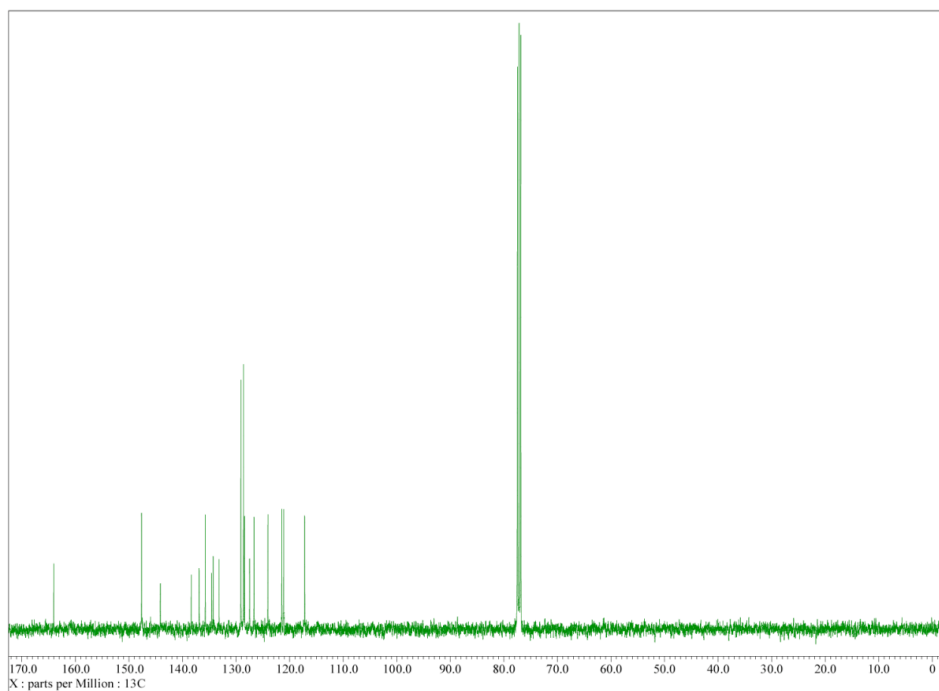
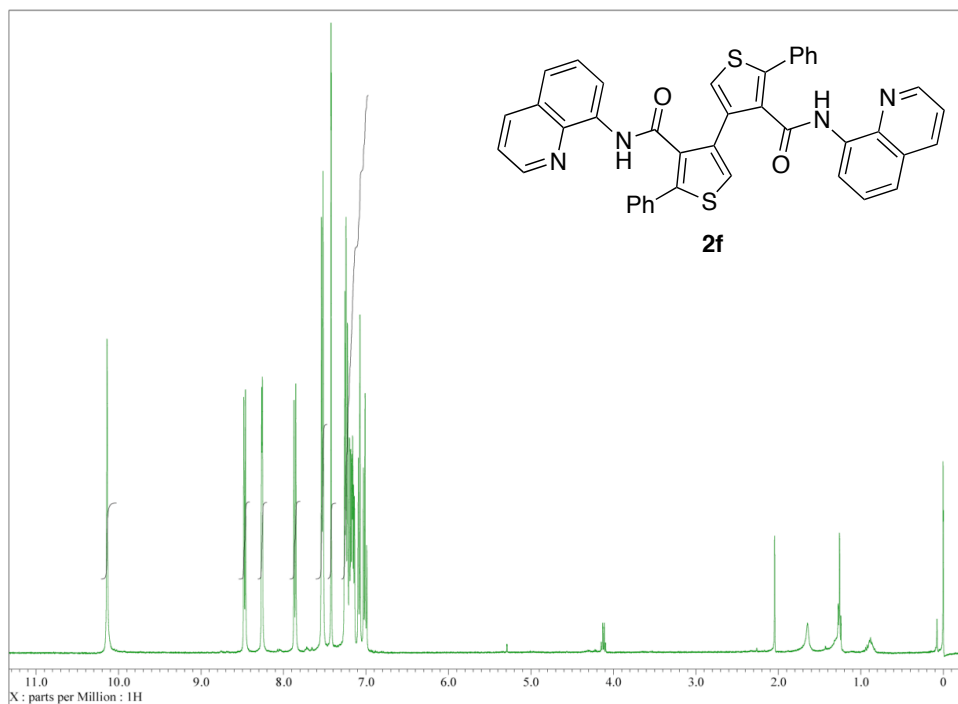
[¹H and ¹³C NMR Spectra of **2c**]



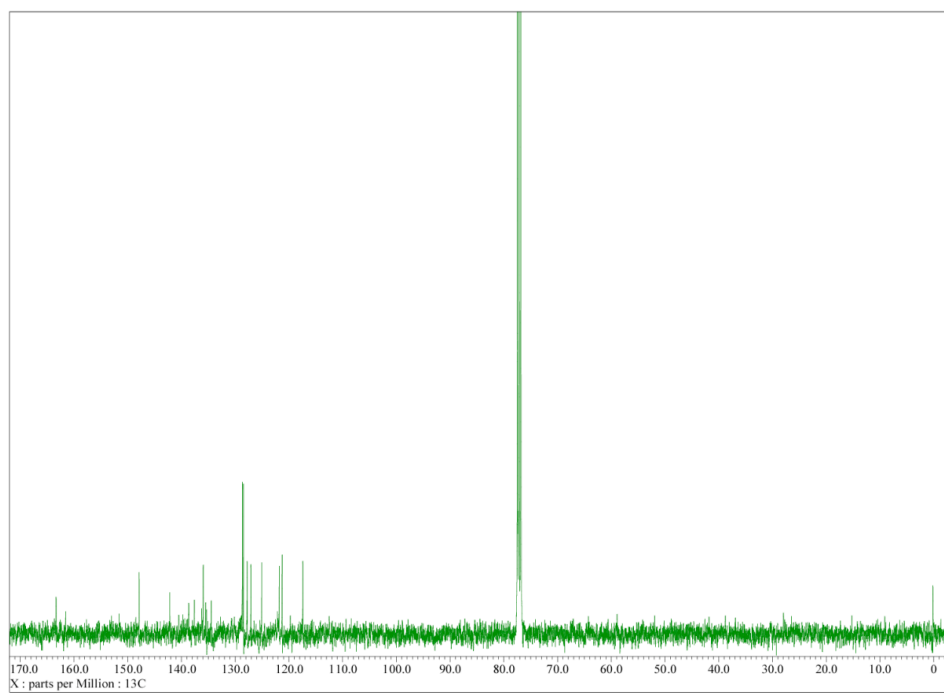
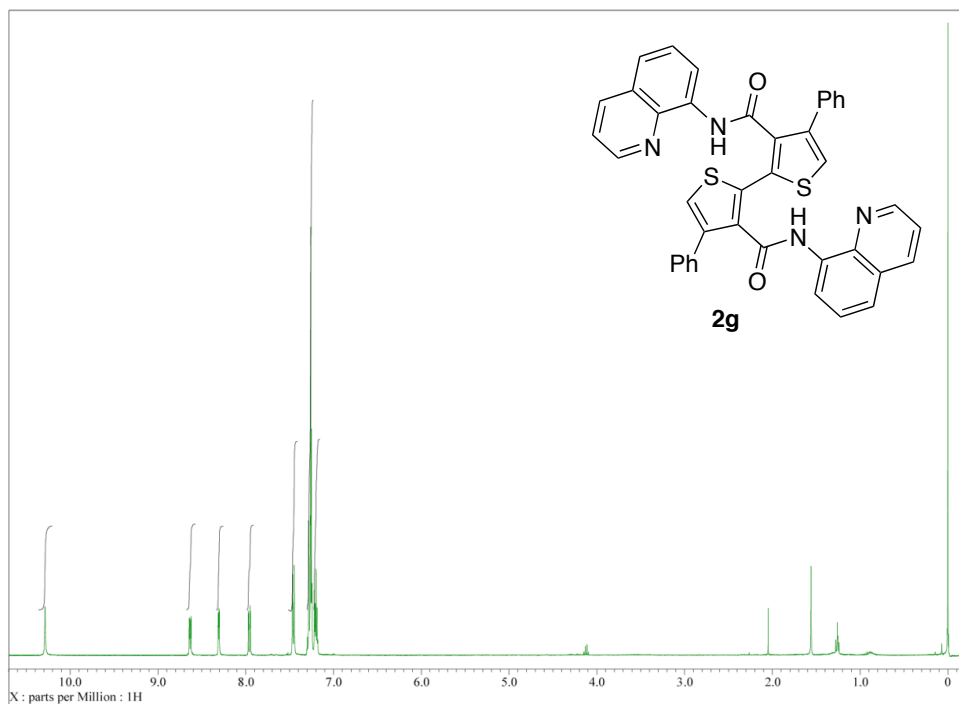
[¹H and ¹³C NMR Spectra of a 78:22 mixture of **2e** and **2e'**]



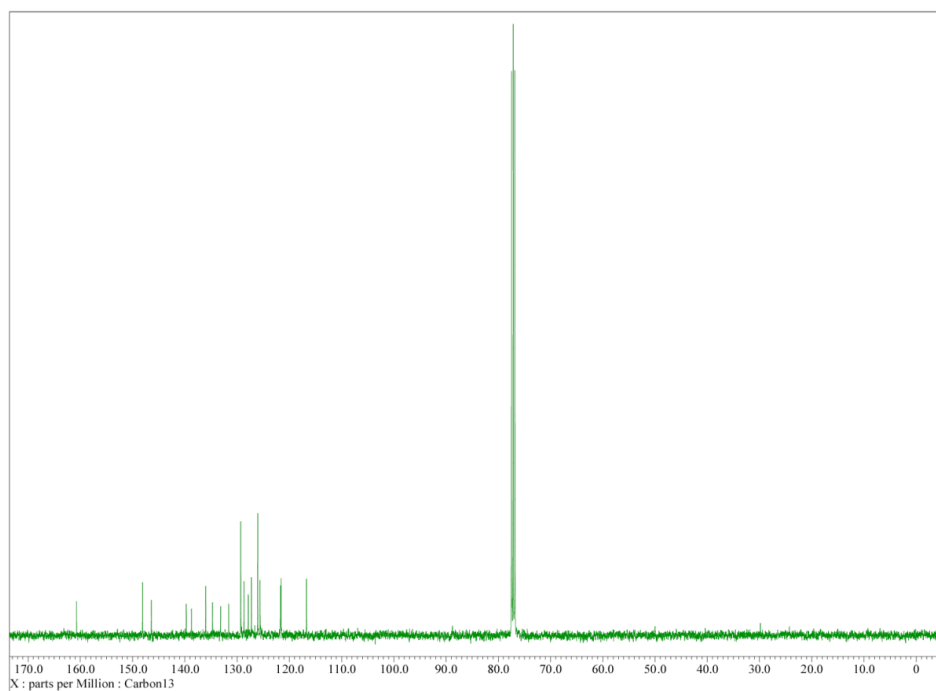
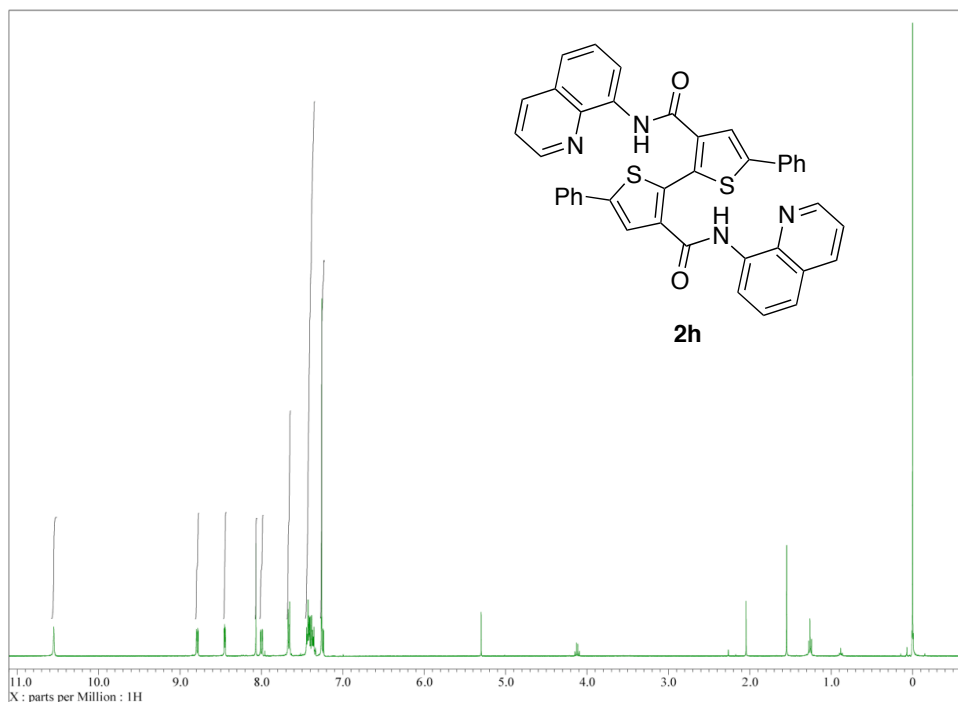
[¹H and ¹³C NMR Spectra of **2f**]



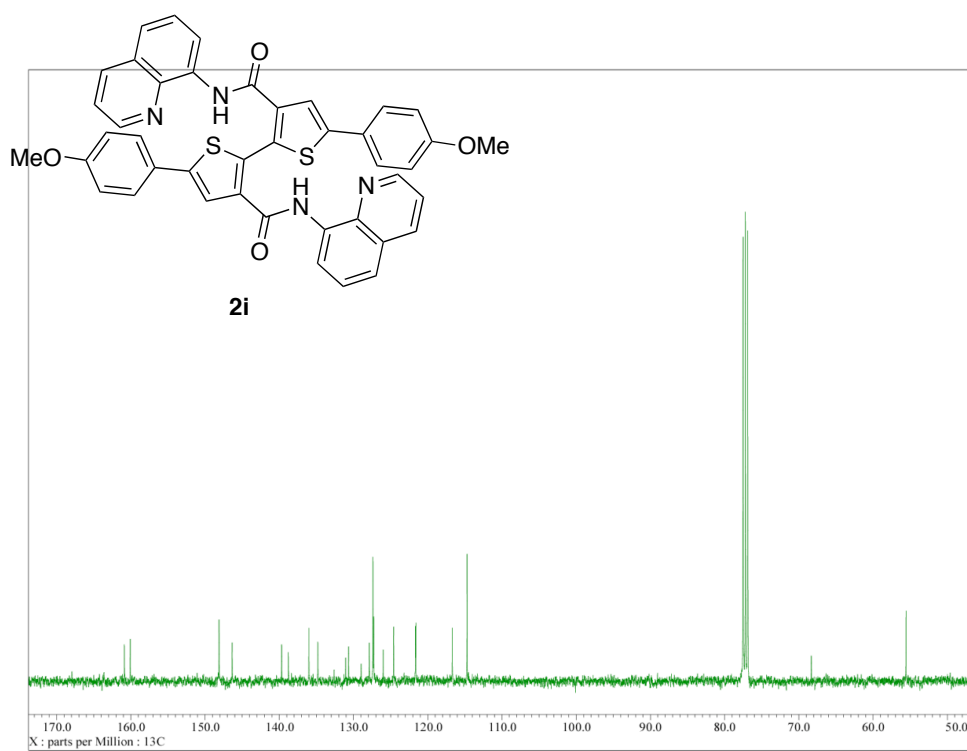
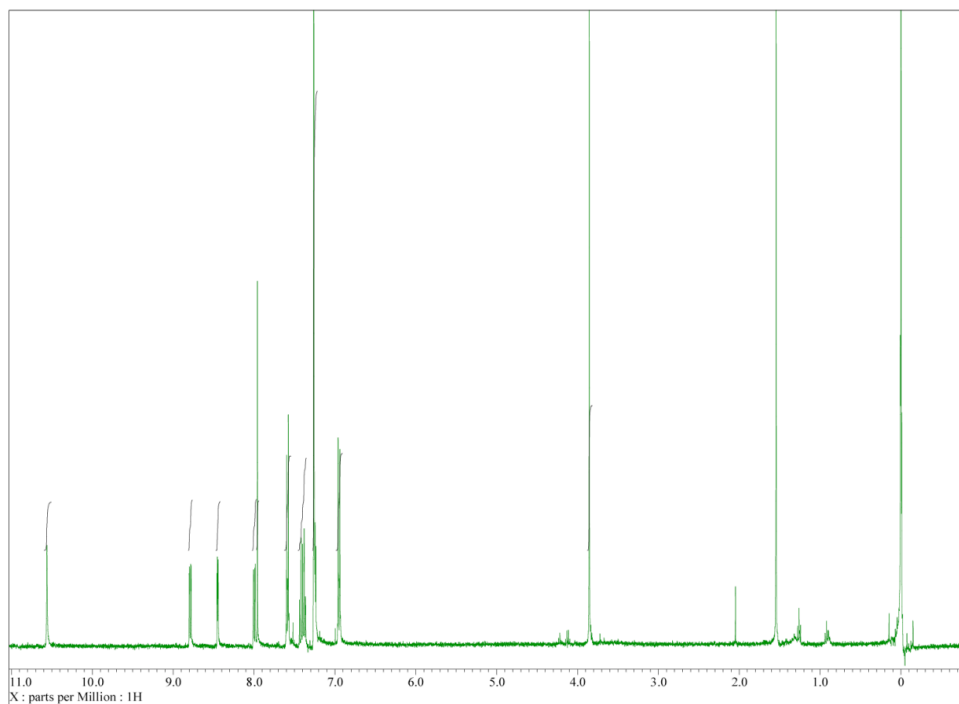
[¹H and ¹³C NMR Spectra of **2g**]



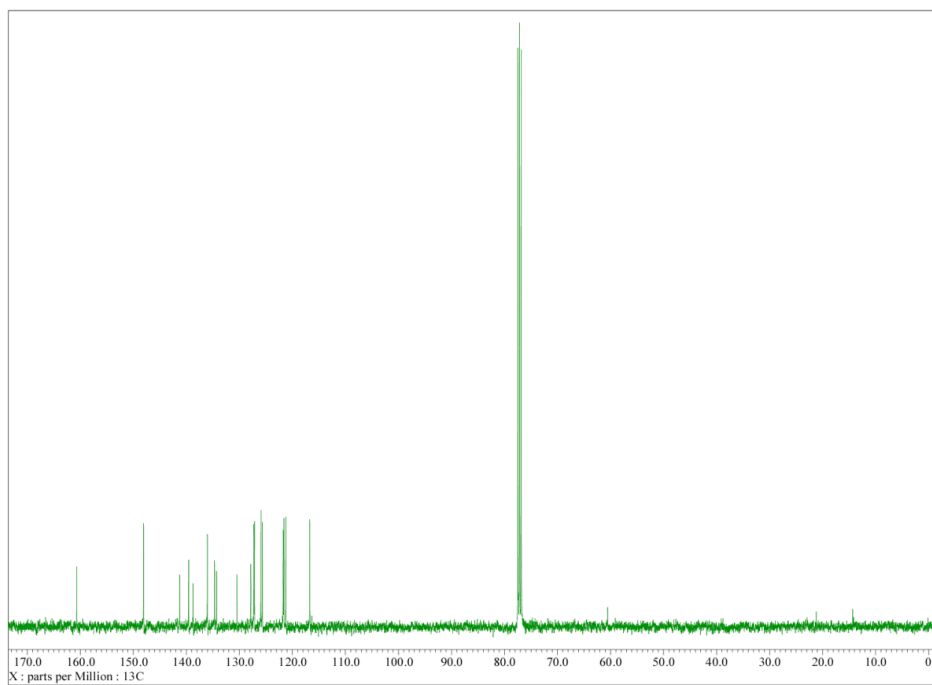
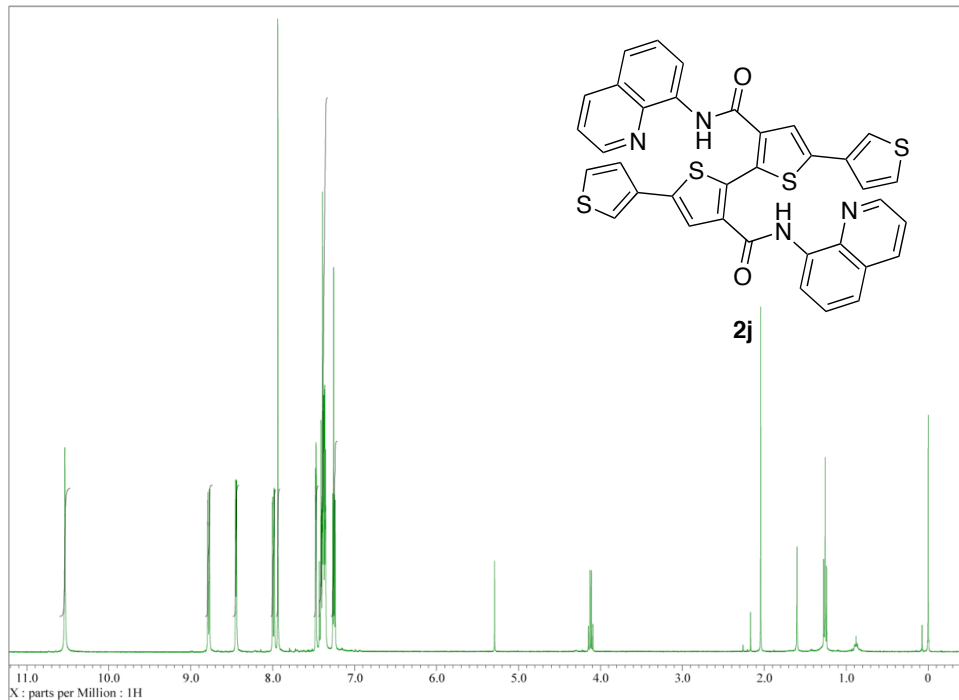
[¹H and ¹³C NMR Spectra of **2h**]



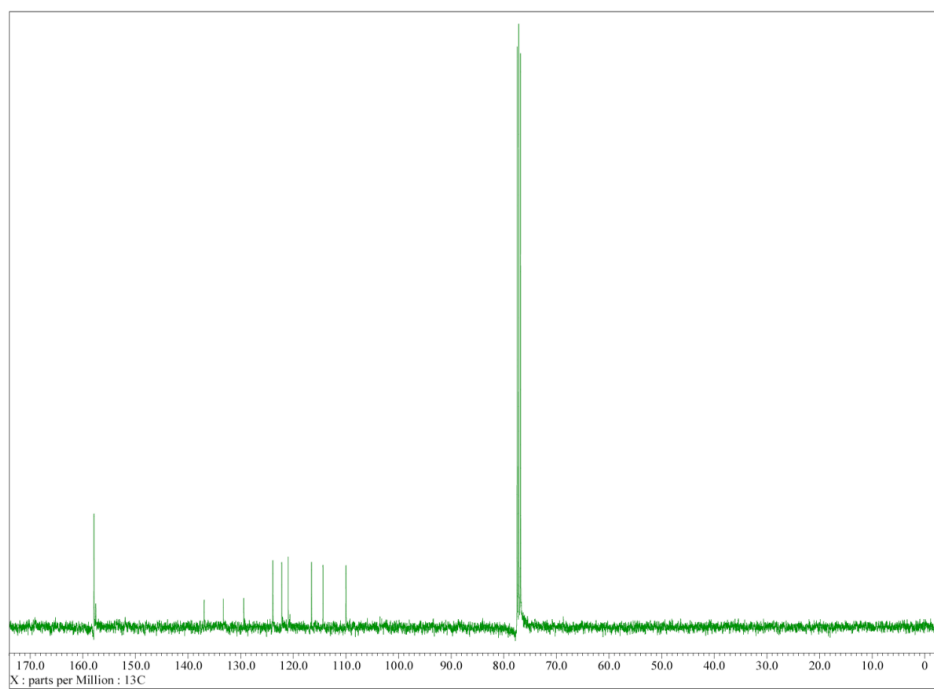
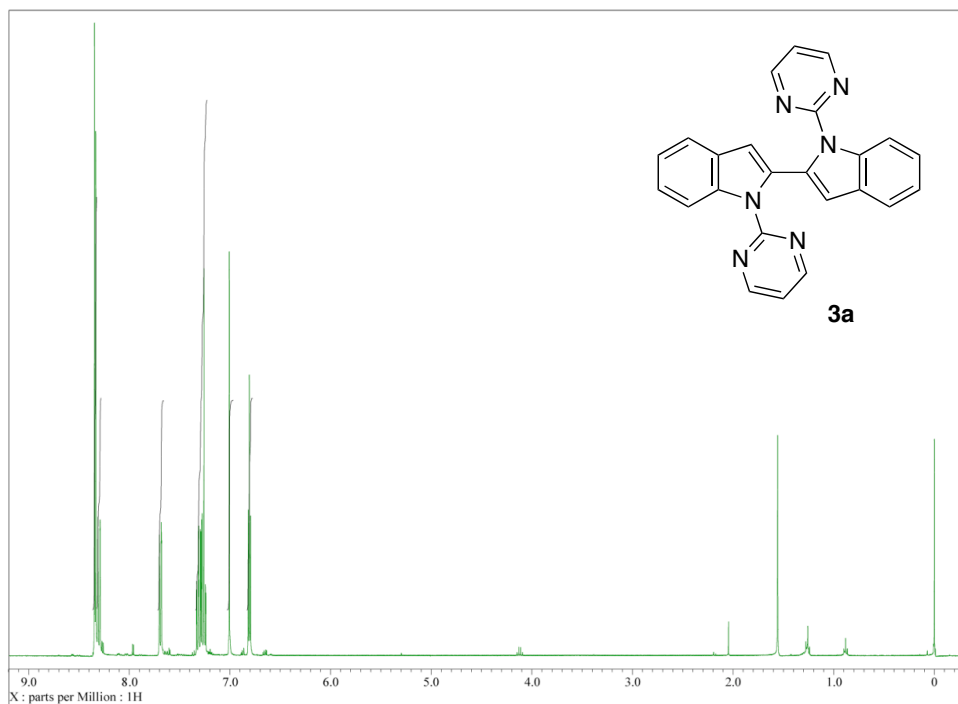
[¹H and ¹³C NMR Spectra of **2i**]



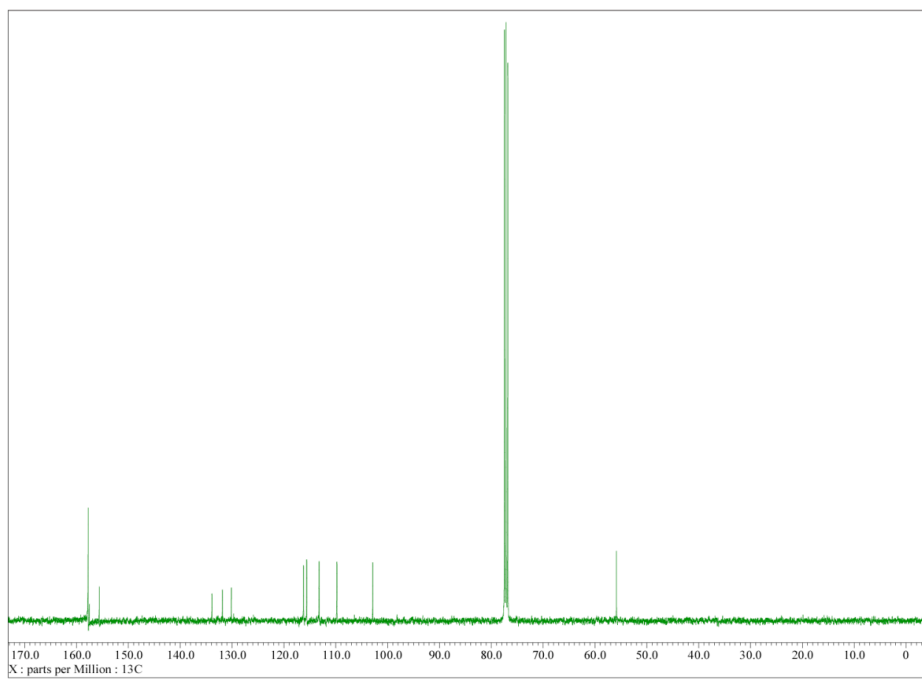
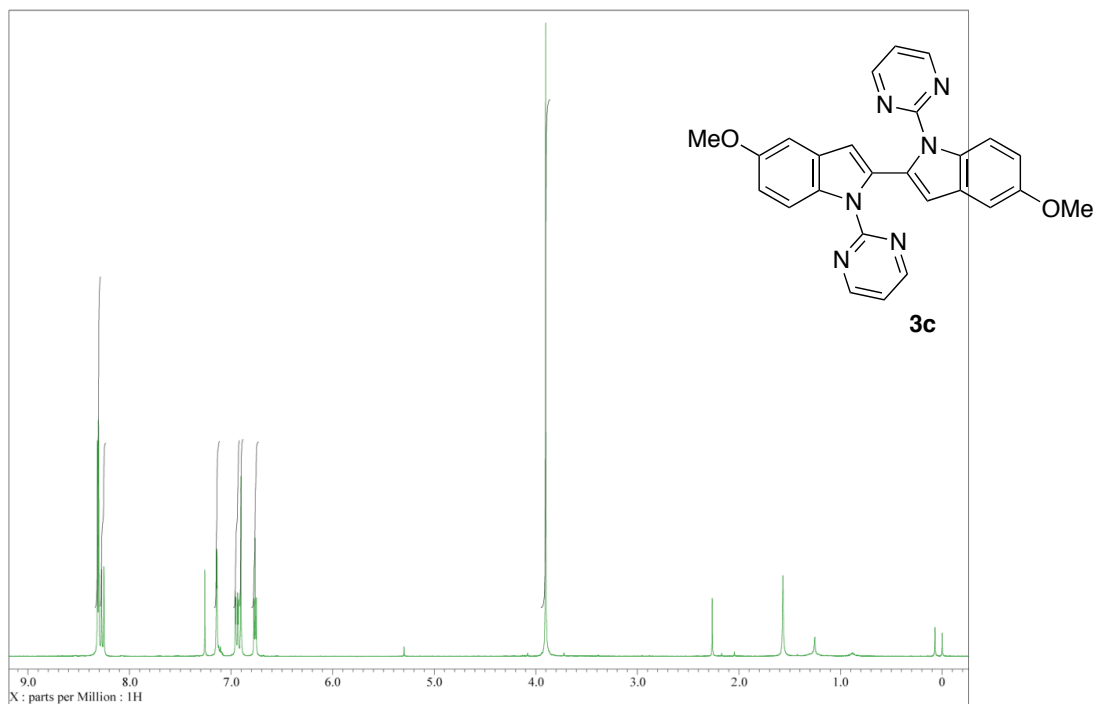
[¹H and ¹³C NMR Spectra of **2j**]



[¹H and ¹³C NMR Spectra of **3a**]



[¹H and ¹³C NMR Spectra of **3c**]



[¹H and ¹³C NMR Spectra of **3d**]

