

# A Facile, Metal- and Solvent Free, Autoxidative Coupling of Quinolines with Indoles and Pyrroles

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## I. General Methods.

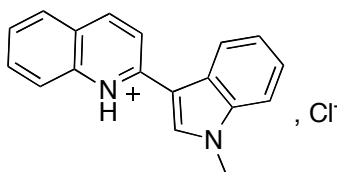
All glassware was dried overnight at 150 °C or flame-dried under vacuum immediately prior to use. Analytical thin layer chromatography (TLC) was performed on precoated silica gel 60 F254 plates and visualization on TLC was achieved by UV light (254 nm). Flash column chromatography was carried out using a Biotage SP Flash Purification System (Biotage No. SP1-B1A) with Flash+ cartridges (Biotage No. 25+M 0489-1) using hexanes/ethyl acetate gradients calculated using the TLC data recorded for each compound (vide infra). Reverse phase column chromatography was carried out using the same machine with Flash Cartridges (Biotage No. KP-C18-HS 12+M) using Acetonitrile Water gradient with 0.1% Vol. of Triflic Acid. NMR spectroscopy ( $^1\text{H}$ , and  $^{13}\text{C}\{^1\text{H}\}$ ) was conducted using a Bruker AV-300, AVQ-400 or DRX-500 spectrometer at room temperature. NMR chemical shifts are reported in ppm relative to  $\text{CHCl}_3$  (7.26 ppm for  $^1\text{H}$ , and 77.2 ppm for  $^{13}\text{C}$ ),  $\text{CD}_3\text{OD}$  (3.31 ppm for  $^1\text{H}$ , and 49.0 ppm for  $^{13}\text{C}$ ), or  $\text{DMSO-}d_6$  (2.50 ppm for  $^1\text{H}$ , and 39.5 ppm for  $^{13}\text{C}$ ). Mass spectra (HRMS) were obtained by the University of California at Berkeley Mass Spectrometry Facility using ProSpec equipped with an ESI source and an LTQ Orbitrap. Crystal structures were obtained by the University of California, Berkeley, College of Chemistry, X-ray Crystallography Facility. Unless otherwise noted, all reagents were obtained from Sigma-Aldrich and used without further purification. 1,4-Dioxane and toluene were obtained from a Seca Solvent System by GlassContour (solvent dried over alumina under a nitrogen atmosphere). HCl in dioxane, from Aldrich, was transferred to a Schlenk flask under nitrogen and was titrated with a sodium hydroxide 0.05M aqueous solution with phenolphthalein or bromothymol blue as an indicator. Three different bottles of HCl in dioxane were used and were titrated at the following concentrations, 2.1M, 2.95M and 3.25M. The quantity of HCl in the following preparations is only indicated in mmol.

## II. General procedure for optimization of Quinoline-Methylindole coupling monitored by NMR spectroscopy.

To a Schlenk tube under nitrogen were added 1-methylindole (**2a**, 62  $\mu\text{L}$ , 0.50 mmol), quinolinium chloride salt (**1a'**), previously purified by sublimation, quinoline (**1a**),

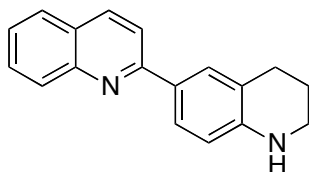
hexamethylbenzene (16.2 mg, 0.10 mmol), and solvent, dioxane or toluene, to adjust the absolute concentration of the reagents. The volume of the heterocycles is not negligible at the concentrations used and must therefore be included in the concentration calculation. The reaction vessel was sealed, submerged to the neck in a silicone oil bath, and heated at 175 °C with stirring for 24 h. The reaction mixture was then cooled to room temperature and dissolved in CH<sub>2</sub>Cl<sub>2</sub> (5 mL) and MeOH (5 mL). Two aliquots were taken, one for analysis by GCMS, and another for <sup>1</sup>H-NMR spectroscopy analysis. For samples used for NMR analysis the solvents were removed under vacuum and the residue was then dissolved in CDCl<sub>3</sub>. The yields of the expected product **3a'** were based on <sup>1</sup>H-NMR integration relative to hexamethylbenzene. The reactions also produced amounts of tetrahydroquinoline (**4**) and 1',2',3',4'-tetrahydro-2,6'-biquinoline (**5**). The quantities of these byproducts were estimated based on their <sup>1</sup>H-NMR integration relative to hexamethylbenzene.

### 2-(1-methylindol-3-yl)quinolinium chloride (**3a'**)



<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 9.83 (s, 1H), 9.33 (d, *J* = 8.7 Hz, 1H), 8.54 (d, *J* = 8.8 Hz, 1H), 8.24 (d, *J* = 9.1 Hz, 1H), 8.01 (d, *J* = 4.9 Hz, 1H), 7.90 (m, 2H), 7.66 (d, *J* = 7.9 Hz, 1H), 7.45 (m, 3H), 3.99 (s, 3H)

### 1',2',3',4'-tetrahydro-2,6'-biquinoline (**5**)



TLC (Hexane/Ethyl Acetate 3:1) *R<sub>f</sub>* = 0.44. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.20 (s, 1H), 8.16 (d, *J* = 8.8 Hz, 1H), 7.92 (s, 1H), 7.85 (dd, *J* = 8.3, 2.2 Hz, 1H), 7.84 (d, *J* = 8.7 Hz, 1H), 7.81 (dd, *J* = 8.1, 1.3 Hz, 1H), 7.72 (t, *J* = 8.4 Hz, 1H), 7.49 (t, *J* = 8.1 Hz, 1H), 6.61 (d, *J* = 8.4 Hz, 2H), 3.42 (t, *J* = 6.3 Hz, 2H), 2.94 (t, *J* = 6.3 Hz, 2H), 2.03 (m, 2H).

$^{13}\text{C}\{^1\text{H}\}$  NMR (100MHz;  $\text{CDCl}_3$ )  $\delta$  157.5, 146.3, 140.5, 136.5, 132.9, 129.5, 129.1, 128.9, 127.4, 126.7, 126.5, 125.4, 121.4, 118.4, 113.9, 42.0, 27.2, 22.0. HRMS-ESI ( $m/z$ ): calculated for  $\text{C}_{18}\text{H}_{17}\text{N}_2$ : 261.1386  $[\text{M}+\text{H}]^+$ ; observed: 261.1391.

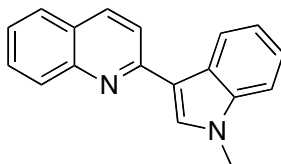
### III. Use of external oxidants

Two potential external oxidants were tested, DDQ and  $\text{O}_2$ . The use of 1 atm. of  $\text{O}_2$  in the reaction of 2 equiv. of **1d** with **2b**, and 1,2 equiv. of HCl, did not improve the yield of the reaction (**6d**, 60%) and the corresponding tetrahydroquinolines products were observed. DDQ was tested in the reaction of 1,2 equiv. of **1a** with **2b** and 1,2 equiv. of HCl. After an hour at room temperature no product was observed by NMR and GCMS; heating at 50 °C for few hours lead to partial decomposition of the indole and no product was observed. A reaction at 155 °C for 3,5 hours lead to complete decomposition of the starting material.

### IV. General simplified procedure for the synthesis of compounds 3a-3j and 6a-6f

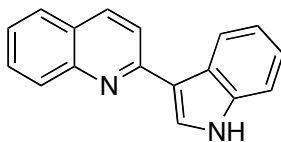
To a Schlenk tube under air were added the quinoline substrate (**1a** – **1f**, 2 equiv, 1.00 mmol), the indole substrate (**2a** – **2i**, 1 equiv, 0.50 mmol), and HCl in dioxane (1.20 equiv, 0.60 mmol). The reaction vessel was sealed, submerged to the neck in a silicone oil bath, heated at the indicated temperature without stirring, and then cooled to room temperature after the specified reaction time. The reaction mixture was transferred to a 60 mL separatory funnel using 5 mL of  $\text{CH}_2\text{Cl}_2$  and 5 mL of MeOH, and was washed with a saturated  $\text{NaHCO}_3$  aqueous solution (1 x 20 mL). The aqueous layer was then extracted with  $\text{CH}_2\text{Cl}_2$  (3 x 10 mL). The organic extracts were combined, washed with a saturated NaCl aqueous solution (1 x 20 mL), dried over  $\text{Na}_2\text{SO}_4$ , filtered and concentrated to dryness under reduced pressure. The crude product mixture was loaded onto a Biotage samplet using a minimal amount of  $\text{CH}_2\text{Cl}_2$ , and the samplet was loaded into a Biotage SP1 system. Eluting with an ethyl acetate/hexanes gradient calculated by the Biotage instrument from the  $R_f$  of the product in a specified ethyl acetate/hexanes mixture provided the desired product.

### 2-(1-methyl-1*H*-indol-3-yl)quinoline (3a)



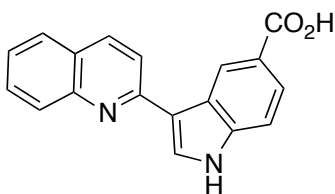
The reaction was conducted with 1-methylindole (62  $\mu\text{L}$ , 0.50 mmol), quinoline (118  $\mu\text{L}$ , 1.00 mmol) and HCl in dioxane (0.60 mmol) at 175  $^{\circ}\text{C}$  for 24 h. The crude mixture was purified by flash chromatography using an ethyl acetate/hexanes gradient to provide 95 mg (74% yield) of **3a** as a yellow solid. TLC (Hexane/Ethyl Acetate 3:1)  $R_f = 0.38$ . A portion of the product was recrystallized from  $\text{CH}_2\text{Cl}_2$  to give light yellow rods.  $^1\text{H}$  NMR (500MHz;  $\text{CDCl}_3$ )  $\delta$  8.72 (m, 1H), 8.17 (d,  $J = 8.4$  Hz, 1H), 8.10 (d,  $J = 8.6$  Hz, 1H), 7.80 (s, 1H), 7.79 (d,  $J = 8.5$  Hz, 1H), 7.76 (d,  $J = 8.1$ , 1H), 7.69 (dt,  $J = 7$  Hz, 1.5 Hz, 1H), 7.45 (dt,  $J = 7$  Hz, 1.5 Hz, 1H), 7.38 (m, 1H), 7.33 (m, 2H), 3.87 (s, 3H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (100MHz;  $\text{CDCl}_3$ )  $\delta$  155.2, 148.7, 138.0, 135.9, 130.0, 129.4, 129.2, 127.5, 126.5, 126.4, 125.2, 122.6, 122.4, 121.1, 119.5, 116.3, 109.6, 33.3. HRMS-ESI ( $m/z$ ): calculated for  $\text{C}_{18}\text{H}_{15}\text{N}_2$   $[\text{M}+\text{H}]^+$ : 259.1230; observed: 259.1236. See X-Ray structure data in section VII, page 30.

### 2-(1*H*-indol-3-yl)quinoline (3b)



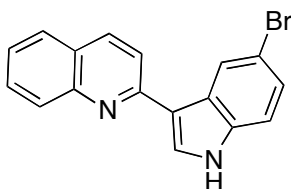
The reaction was conducted with indole (58.5 mg, 0.50 mmol), quinoline (118  $\mu\text{L}$ , 1.00 mmol) and HCl in dioxane (0.60 mmol) at 155  $^{\circ}\text{C}$  for 4 h. The crude mixture was purified by flash chromatography using an ethyl acetate/hexanes gradient to provide 90 mg (73% yield) of **3b** as a yellow solid. TLC (Hexane/Ethyl Acetate 4:1)  $R_f = 0.18$ .  $^1\text{H}$  NMR (500 MHz;  $\text{CDCl}_3$ )  $\delta$  8.78 (d,  $J = 7.9$  Hz, 1H), 8.69 (s, 1H), 8.21 (d,  $J = 8.5$  Hz, 1H), 8.16 (d,  $J = 8.6$  Hz, 1H), 7.87 (d,  $J = 2.3$  Hz, 1H), 7.82 (t,  $J = 8.1$  Hz, 2H), 7.73 (t,  $J = 8.5$  Hz, 1H), 7.50 (t,  $J = 7.5$  Hz, 1H), 7.43 (d,  $J = 7.6$  Hz, 1H), 7.35 (m, 2H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz;  $\text{CDCl}_3$ )  $\delta$  155.2, 148.5, 137.0, 136.0, 129.4, 129.2, 127.5, 126.5, 125.8, 125.3 (2C), 122.9, 122.2, 121.3, 119.6, 117.8, 111.4. HRMS-ESI ( $m/z$ ): calculated for  $\text{C}_{17}\text{H}_{13}\text{N}_2$   $[\text{M}+\text{H}]^+$ : 245.1073; observed: 245.1066.

### 3-(quinolin-2-yl)-1H-indole-5-carboxylic acid (**3c**)



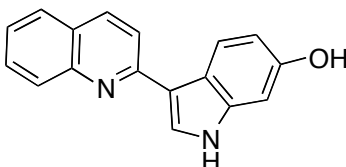
The reaction was conducted with indole-5-carboxylic acid (80.5 mg, 0.50 mmol), quinoline (118  $\mu$ L, 1.00 mmol) and HCl in dioxane (0.60 mmol) at 155  $^{\circ}$ C for 18 h. The crude mixture was purified by extraction of the product as a sodium carbonate salt. After reaction, the mixture was transferred to a 60 mL separatory funnel using 5 mL of  $\text{CH}_2\text{Cl}_2$  and 5 mL of MeOH, and to the resulting solution was added sufficient saturated NaOH aqueous solution (20 mL) until a basic pH was reached. The aqueous phase was washed with  $\text{CH}_2\text{Cl}_2$  (2 x 5 mL), and the resulting organic phases were discarded. The aqueous phase was acidified with HCl (37% wt. in water), and then neutralized with a saturated  $\text{NaHCO}_3$  aqueous solution (1 x 20 mL) to precipitate the product. The product was extracted from the aqueous phase with ethyl acetate (3 x 10 mL), the organic extracts were combined, washed with a saturated NaCl aqueous solution (1 x 20 mL), dried over  $\text{Na}_2\text{SO}_4$ , filtered and concentrated to dryness under reduced pressure. The resulting product was almost pure but was further purified by flash chromatography using an ethyl acetate/hexanes gradient to provide 66 mg (46% yield) of **3c** as a yellow solid. TLC (Hexane/Ethyl Acetate 3:1)  $R_f = 0.28$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CD}_3\text{OD}$ )  $\delta$  9.41 (d,  $J = 1.5$  Hz, 1H), 8.30 (d,  $J = 8.6$  Hz, 1H), 8.15 (s, 1H), 8.14 (d,  $J = 8.0$  Hz, 2H), 7.99 (d,  $J = 8.7$  Hz, 1H), 7.96 (dd,  $J = 8.6, 1.6$  Hz, 1H), 7.89 (dd,  $J = 8.1, 1.0$  Hz, 1H), 7.75 (ddd,  $J = 8.4, 6.9, 1.4$  Hz, 1H), 7.54 (d,  $J = 8.4$  Hz, 1H), 7.52 (d,  $J = 6.9$  Hz, 1H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CD}_3\text{OD}$ )  $\delta$  170.7, 155.2, 148.0, 140.0, 136.3, 129.3, 128.0, 127.6, 127.4, 126.5, 125.3, 125.2, 124.7, 123.6, 123.3, 119.5, 117.4, 110.9. HRMS-ESI ( $m/z$ ): calculated for  $\text{C}_{18}\text{H}_{13}\text{N}_2\text{O}_2$   $[\text{M}+\text{H}]^+$ : 289.0972; observed: 289.0968.

### 2-(5-bromo-1*H*-indol-3-yl)quinoline (3d)



The reaction was conducted with 5-bromoindole (98 mg, 0.50 mmol), quinoline (118  $\mu$ L, 1.00 mmol) and HCl in dioxane (0.60 mmol) at 155  $^{\circ}$ C for 18 h. The crude mixture was purified by flash chromatography using an ethyl acetate/hexanes gradient to provide 131 mg (81% yield) of **3d** as a yellow solid. TLC (Hexane/Ethyl Acetate 7:3)  $R_f$  = 0.28.  $^1\text{H}$  NMR (400 MHz, DMSO)  $\delta$  11.85 (s, 1H), 9.05 (d,  $J$  = 0.9 Hz, 1H), 8.40 (d,  $J$  = 2.6 Hz, 1H), 8.23 (d,  $J$  = 8.7 Hz, 1H), 8.01 (t,  $J$  = 8.2 Hz, 2H), 7.85 (d,  $J$  = 8.0 Hz, 1H), 7.69 (t,  $J$  = 7.5 Hz, 1H), 7.45 (m, 2H), 7.32 (dd,  $J$  = 8.6, 1.5 Hz, 1H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz, DMSO)  $\delta$  155.5, 148.0, 136.3, 136.3, 129.9, 129.6, 128.8, 128.1, 127.7, 126.3, 125.5, 125.2, 125.0, 119.5, 115.5, 114.2, 113.5. HRMS-ESI ( $m/z$ ): calculated for  $\text{C}_{17}\text{H}_{12}\text{BrN}_2$   $[\text{M}+\text{H}]^+$ : 323.0178; observed: 323.0176

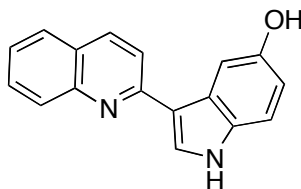
### 3-(quinolin-2-yl)-1*H*-indol-6-ol (3e)



The reaction was conducted with 6-hydroxyindole (66 mg, 0.50 mmol), quinoline (118  $\mu$ L, 1.00 mmol) and HCl in dioxane (0.60 mmol) at 155  $^{\circ}$ C for 18 h. The crude mixture was purified by flash chromatography using an ethyl acetate/hexanes gradient to provide 35 mg (27% yield) of **3e** as a brown oil. TLC (Hexane/Ethyl Acetate 3:1)  $R_f$  = 0.23. The product could also be purified by extraction as a sodium phenoxide salt. After reaction, the mixture was transferred to a 60 mL separatory funnel using 5 mL of  $\text{CH}_2\text{Cl}_2$  and 5 mL of MeOH, and to the resulting solution was added sufficient saturated NaOH aqueous solution (20 mL) until a basic pH was reached and the solution turned green. The aqueous phase was washed with  $\text{CH}_2\text{Cl}_2$  (2 x 5 mL) and the resulting organic phases were discarded. The aqueous phase was acidified with HCl (37% wt. in water) and then neutralized with a saturated  $\text{NaHCO}_3$  aqueous solution (1 x 20 mL) to precipitate the

product. The product was extracted from the aqueous phase with ethyl acetate (3 x 10 mL) and the organic extracts were combined, washed with a saturated NaCl aqueous solution (1 x 20 mL), dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated to dryness under reduced pressure. <sup>1</sup>H NMR (500 MHz, CD<sub>3</sub>OD) δ 8.39 (d, *J* = 8.6 Hz, 1H), 8.21 (d, *J* = 8.7 Hz, 1H), 8.05 (d, *J* = 8.4 Hz, 1H), 7.91 (d, *J* = 8.7 Hz, 1H), 7.88 (s, 1H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.71 (t, *J* = 7.7 Hz, 1H), 7.49 (t, *J* = 7.5 Hz, 1H), 6.90 (d, *J* = 2.1 Hz, 1H), 6.81 (dd, *J* = 8.6, 2.2 Hz, 1H). <sup>13</sup>C{<sup>1</sup>H} NMR (126 MHz, CDCl<sub>3</sub>) δ 156.1, 153.5, 148.0, 138.7, 136.0, 129.2, 127.6, 127.3, 126.4, 124.9, 124.8, 121.8, 119.6, 119.5, 116.2, 110.4, 96.5. HRMS-ESI (*m/z*): calculated for C<sub>17</sub>H<sub>13</sub>N<sub>2</sub>O [M+H]<sup>+</sup>: 261.1022; observed: 261.1020.

### 3-(quinolin-2-yl)-1H-indol-5-ol (3f)

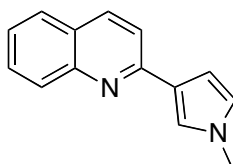


The reaction was conducted with 5-hydroxyindole (66 mg, 0.50 mmol), quinoline (118 μL, 1.00 mmol) and HCl in dioxane (0.60 mmol) at 155 °C for 18 h. The crude mixture was purified by flash chromatography using an ethyl acetate/hexanes gradient to provide 70 mg (54% yield) of **3f** as a brown oil. TLC (Hexane/Ethyl Acetate 3:1) R<sub>f</sub> = 0.34. The product could also be purified by extraction as a sodium phenoxide salt. After reaction, the mixture was transferred to a 60 mL separatory funnel using 5 mL of CH<sub>2</sub>Cl<sub>2</sub> and 5 mL of MeOH, and to the resulting solution was added sufficient saturated NaOH aqueous solution (20 mL) until a basic pH was reached and the solution turned green. The aqueous phase was washed with CH<sub>2</sub>Cl<sub>2</sub> (2 x 5 mL) and the resulting organic phases were discarded. The aqueous phase was acidified with HCl (37% wt. in water) and then neutralized with a saturated NaHCO<sub>3</sub> aqueous solution (1 x 20 mL) to precipitate the product. The product was extracted from the aqueous phase with ethyl acetate (3 x 10 mL), the organic extracts were combined, washed with a saturated NaCl aqueous solution (1 x 20 mL), dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated to dryness under reduced pressure. <sup>1</sup>H NMR (500 MHz, DMSO) δ 11.39 (s, 1H), 8.86 (s, 1H), 8.29 (d, *J* = 2.3 Hz,



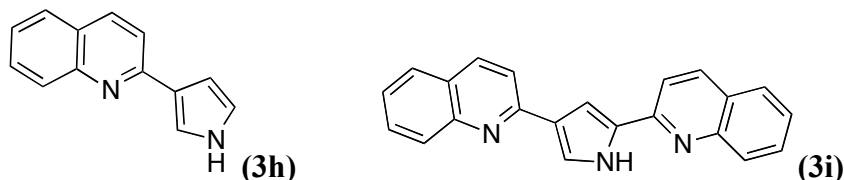
1H), 8.23 (d,  $J = 2.9$  Hz, 1H), 8.22 (d,  $J = 8.8$  Hz, 1H), 8.00 (d,  $J = 8.3$  Hz, 1H), 7.99 (d,  $J = 8.7$  Hz, 1H), 7.87 (d,  $J = 7.9$  Hz, 1H), 7.72 (dt,  $J = 7.4$  Hz,  $J = 1.25$  Hz, 1H), 7.47 (t,  $J = 7.4$  Hz, 1H), 7.28 (d,  $J = 8.6$  Hz, 1H), 6.74 (dd,  $J = 8.6, 2.4$  Hz, 1H).  $^{13}\text{C}\{^1\text{H}\}$  (126 MHz, DMSO)  $\delta$  156.3, 152.3, 148.3, 135.9, 132.10, 129.7, 128.6, 128.5, 128.1, 127.0, 126.1, 125.1, 119.6, 115.3, 112.7, 112.4, 107.4. HRMS-EI ( $m/z$ ): calculated for  $\text{C}_{17}\text{H}_{13}\text{N}_2\text{O}$   $[\text{M}+\text{H}]^+$ : 261.1022; observed: 261.1019

### 2-(1-methylpyrrol-3-yl)quinoline (**3g**)<sup>1,2</sup>



The reaction was conducted with 1-methylpyrrole (44.5  $\mu\text{L}$ , 0.50 mmol), quinoline (118  $\mu\text{L}$ , 1.00 mmol) and HCl in dioxane (0.60 mmol) at 155  $^\circ\text{C}$  for 18 h. The crude mixture was purified by flash chromatography using an ethyl acetate/hexanes gradient to provide 44 mg (42% yield) of **3g** as a yellow solid. TLC (Hexane/Ethyl Acetate 3:1)  $R_f = 0.31$ .  $^1\text{H}$  NMR (400 MHz;  $\text{CDCl}_3$ )  $\delta$  8.09 (dd,  $J = 8.4$  Hz, 1.7 Hz, 2H), 7.77 (d,  $J = 8.0$  Hz, 1H), 7.69 (td,  $J = 7.7$  Hz, 1.4 Hz, 1H), 7.65 (d,  $J = 8.6$  Hz, 1H), 7.46 (m, 2H), 6.84 (t,  $J = 2.2$  Hz, 1H), 6.72 (t,  $J = 2.5$  Hz, 1H), 3.76 (s, 3H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  154.6 148.3, 136.1, 129.3, 128.7, 127.4, 126.5, 125.3, 124.9, 123.1, 122.2, 118.6, 107.7, 36.5. HRMS-ESI ( $m/z$ ): calculated for  $\text{C}_{14}\text{H}_{13}\text{N}_2$   $[\text{M}+\text{H}]^+$ : 209.1073; observed: 209.1070.

### 2-(1H-pyrrol-3-yl)quinoline (**3h**)<sup>1</sup> and 2,2'-(1H-pyrrole-2,4-diyl)diquinoline (**3i**)

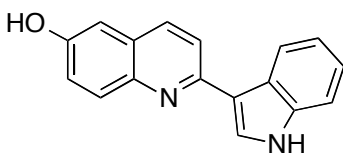


The reaction was conducted with pyrrole (34  $\mu\text{L}$ , 0.50 mmol), quinoline (118  $\mu\text{L}$ , 1.00 mmol) and HCl in dioxane (0.60 mmol) at 155  $^\circ\text{C}$  for 18 h. The crude mixture was purified by flash chromatography using an ethyl acetate/hexanes gradient to provide 21 mg (22% yield) of **3h** and 19 mg (12% yield) of **3i** as yellow solids. TLC (Hexane/Ethyl Acetate 3:1)  $R_f$  **3h** = 0.20, **3i** = 0.30.

**(3h)**  $^1\text{H}$  NMR (400 MHz, DMSO)  $\delta$  11.21 (s, 1H), 8.21 (d,  $J = 8.6$  Hz, 1H), 7.90 (d,  $J = 8.4$  Hz, 1H), 7.85 (d,  $J = 8.9$  Hz, 1H), 7.82 (d,  $J = 8.8$  Hz, 1H), 7.66 (m, 2H), 7.45 (t,  $J = 7.4$  Hz, 1H), 6.88 (dd,  $J = 4.6, 2.4$  Hz, 1H), 6.82 (dd,  $J = 4.6, 2.4$  Hz, 1H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz, DMSO)  $\delta$  155.1, 148.2, 136.4, 129.7, 128.6, 128.1, 126.6, 125.2, 124.9, 119.9, 119.4, 119.2, 107.2. HRMS-ESI ( $m/z$ ): calculated for  $\text{C}_{13}\text{H}_{11}\text{N}_2$   $[\text{M}+\text{H}]^+$ : 195.0917; observed: 195.0914.

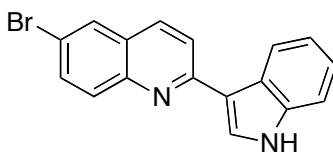
**(3i)**  $^1\text{H}$  NMR (400 MHz, DMSO)  $\delta$  12.06 (s, 1H), 8.34 (d,  $J = 8.7$  Hz, 1H), 8.29 (d,  $J = 8.6$  Hz, 1H), 8.05 (d,  $J = 8.7$  Hz, 1H), 7.94 (m, 6H), 7.73 (m, 3H), 7.53 (t,  $J = 7.1$  Hz, 1H), 7.48 (t,  $J = 7.0$  Hz, 1H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz, DMSO)  $\delta$  154.3, 150.6, 148.2, 147.9, 137.1, 136.7, 133.3, 130.3, 129.9, 128.7, 128.5, 128.4, 128.2, 126.9, 126.8, 126.7, 125.9, 125.5, 123.3, 119.1, 118.4, 108.9. HRMS-ESI ( $m/z$ ): calculated for  $\text{C}_{22}\text{H}_{16}\text{N}_3$   $[\text{M}+\text{H}]^+$ : 322.1339; observed: 322.1334

### 2-(1*H*-indol-3-yl)quinolin-6-ol (**6b**)



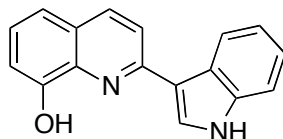
The reaction was conducted with indole (58.5 mg, 0.50 mmol), 6-hydroxyquinoline (145.1 mg, 1.00 mmol) and HCl in dioxane (0.60 mmol) at 155 °C for 18 h. The crude mixture was purified by flash chromatography using an ethyl acetate/hexanes gradient to provide 54 mg (41% yield) of **6b** as a red-brown solid. TLC (Hexane/Ethyl Acetate 1:1)  $R_f = 0.12$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CD}_3\text{OD}$ )  $\delta$  8.45 (dd,  $J = 6.6, 2.1$  Hz, 1H), 8.08 (d,  $J = 8.7$  Hz, 1H), 7.94 (s, 1H), 7.93 (d,  $J = 4.5$  Hz, 1H), 7.86 (d,  $J = 8.7$  Hz, 1H), 7.48 (dd,  $J = 6.6, 1.8$  Hz, 1H), 7.31 (dd,  $J = 9.1, 2.7$  Hz, 1H), 7.20 (m, 2H), 7.12 (d,  $J = 2.7$  Hz, 1H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CD}_3\text{OD}$ )  $\delta$  154.8, 153.1, 143.1, 137.4, 134.8, 128.9, 127.7, 125.6, 125.3, 121.8, 121.2, 120.74, 120.1, 120.0, 116.3, 111.2, 108.4. HRMS-ESI ( $m/z$ ): calculated for  $\text{C}_{17}\text{H}_{13}\text{N}_2\text{O}$   $[\text{M}+\text{H}]^+$ : 261.1022; observed: 261.1018

### 6-bromo-2-(1*H*-indol-3-yl)quinoline (**6c**)



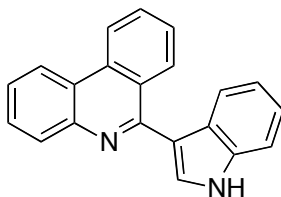
The reaction was conducted with indole (117 mg, 1.00 mmol), 6-bromoquinoline (272  $\mu$ L, 2.00 mmol) and HCl in dioxane (1.20 mmol) at 155 °C for 4 h. The crude mixture was purified by flash chromatography using an ethyl acetate/hexanes gradient to provide 239 mg (74% yield) of **6c** as a yellow solid. TLC (Hexane/Ethyl Acetate 7:3)  $R_f$  = 0.38.  $^1\text{H}$  NMR (400 MHz;  $\text{CD}_3\text{OD}$ )  $\delta$  8.63 (dt,  $J$  = 4.9 Hz, 2.2 Hz, 1H), 8.15 (d,  $J$  = 8.8 Hz, 1H), 8.06 (s, 1H), 8.03 (d,  $J$  = 2.2 Hz, 1H), 7.96 (dd,  $J$  = 8.8 Hz, 2.8 Hz, 2H), 7.79 (dd,  $J$  = 9.0 Hz, 2.3 Hz, 1H), 7.48 (dd,  $J$  = 6.1 Hz, 2.8 Hz, 1H), 7.24 (dt,  $J$  = 6.6 Hz, 2.9 Hz, 2H), 4.62 (s, 1H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz;  $\text{CD}_3\text{OD}$ )  $\delta$  156.6, 146.7, 137.6, 135.1, 132.4, 129.7, 129.4, 127.5, 126.6, 125.6, 122.1, 121.4, 120.4, 120.3, 118.0, 115.9, 111.3. HRMS-ESI ( $m/z$ ): calculated for  $\text{C}_{17}\text{H}_{12}\text{N}_2\text{Br}$  [ $\text{M}+\text{H}$ ] $^+$ : 323.0178; observed: 323.0184.

### 2-(1*H*-indol-3-yl)quinolin-8-ol (**6d**)



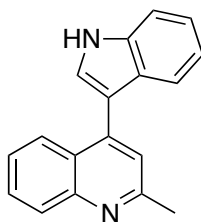
The reaction was conducted with indole (58.5 mg, 0.50 mmol), quinoline (145.1 mg, 1.00 mmol) and HCl in dioxane (0.60 mmol) at 175 °C for 18 h. The crude mixture was purified by flash chromatography using an ethyl acetate/hexanes gradient to provide 70 mg (54% yield) of **6d** as a red solid. TLC (Hexane/Ethyl Acetate 2:1)  $R_f$  = 0.34.  $^1\text{H}$  NMR (500 MHz; DMSO)  $\delta$  11.70 (s, 1H), 9.20 (s, 1H), 8.72 (t,  $J$  = 4.5 Hz, 1H), 8.46 (d,  $J$  = 2.8 Hz, 1H), 8.24 (d,  $J$  = 8.8 Hz, 1H), 8.08 (d,  $J$  = 8.7 Hz, 1H), 7.49 (m, 1H), 7.34 (m, 2H), 7.22 (m, 2H), 7.12 (dd,  $J$  = 6.8 Hz, 1.8 Hz, 1H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz; DMSO)  $\delta$  154.1, 152.8, 138.7, 137.7, 136.4, 128.6, 127.0, 126.0, 125.7, 122.5, 122.5, 120.9, 120.2, 118.3, 116.0, 112.3, 111.7. HRMS-ESI ( $m/z$ ): calculated for  $\text{C}_{17}\text{H}_{13}\text{N}_2\text{O}$  [ $\text{M}+\text{H}$ ] $^+$ : 261.1018; observed: 261.1022.

### 6-(1*H*-indol-3-yl)phenanthridine (**6e**)



The reaction was conducted with indole (58.5 mg, 0.50 mmol), phenanthridine (179 mg, 1.00 mmol) and HCl in dioxane (0.60 mmol) at 155 °C for 18 h. The crude mixture was purified by flash chromatography using an ethyl acetate/hexanes gradient to provide 76 mg (51% yield) of **6e** as a yellow solid. A portion of the product was recrystallized from CH<sub>2</sub>Cl<sub>2</sub> to give light yellow prisms. TLC (Hexane/Ethyl Acetate 4:1) *R<sub>f</sub>* = 0.14. <sup>1</sup>H NMR (500 MHz; CDCl<sub>3</sub>) δ 9.31 (s, 1H), 8.75 (d, *J* = 8.3 Hz, 1H), 8.67 (d, *J* = 8.1 Hz, 1H), 8.42 (d, *J* = 8.3 Hz, 1H), 8.30 (d, *J* = 8.1 Hz, 1H), 7.88 (dd, *J* = 7.8 Hz, 3.6 Hz, 2H), 7.78 (t, *J* = 7.5 Hz, 1H), 7.71 (t, *J* = 7.5 Hz, 1H), 7.63 (t, *J* = 7.6 Hz, 1H), 7.55 (d, *J* = 2.2 Hz, 1H), 7.37 (d, *J* = 8.0 Hz, 1H), 7.25 (t, *J* = 7.5 Hz, 1H), 7.21 (t, *J* = 7.4 Hz, 1H). <sup>13</sup>C{<sup>1</sup>H} NMR (126MHz; CDCl<sub>3</sub>) δ 156.3, 144.2, 136.3, 133.5, 130.5, 129.9, 129.0, 128.7, 127.4, 127.1, 126.4, 126.2, 126.0, 123.5, 122.7, 122.1, 122.0, 121.0, 120.7, 116.0, 111.4. HRMS-ESI (*m/z*): calculated for C<sub>21</sub>H<sub>15</sub>N<sub>2</sub> [M+H]<sup>+</sup>: 295.1230; observed: 295.1226. See X-Ray structure data in section VIII, page 38.

### 4-(1*H*-indol-3-yl)-2-methylquinoline (**6f**)



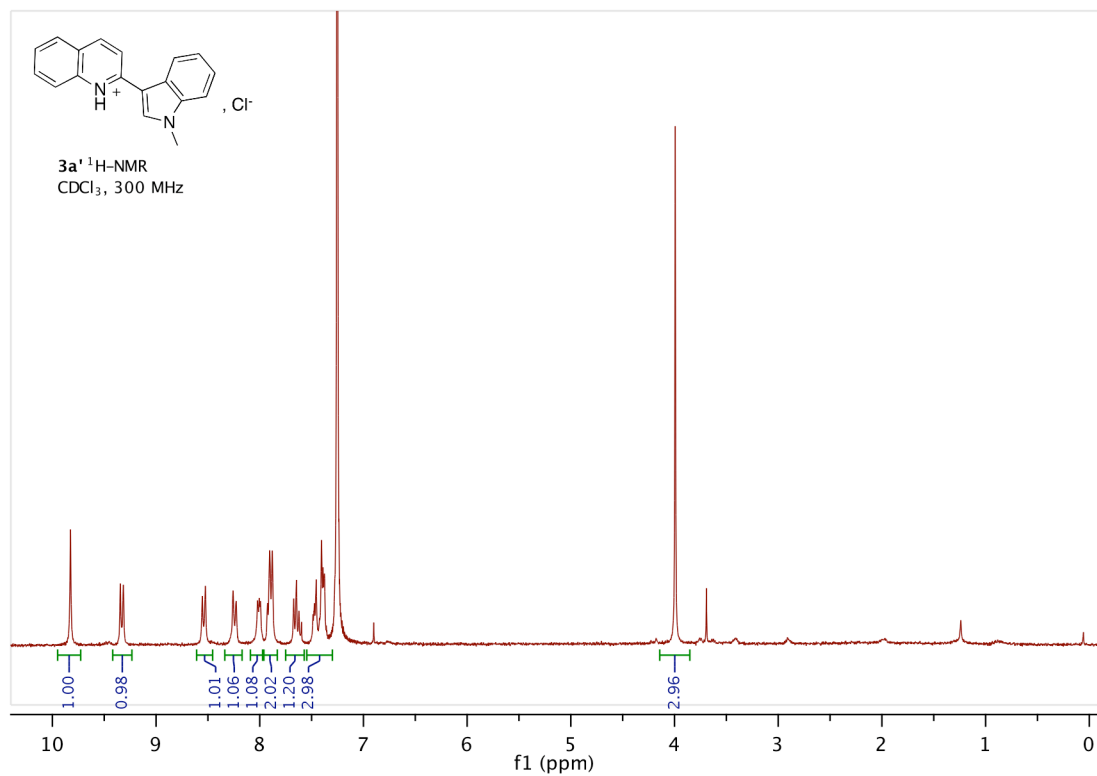
The reaction was conducted with indole (58.5 mg, 0.50 mmol), 2-picoline (135 μL, 1.00 mmol) and HCl in dioxane (0.60 mmol) at 175 °C for 36 h. The crude mixture was purified by flash chromatography using an ethyl acetate/hexanes gradient to provide 40 mg (31% yield) of **6f** as a brown oil. TLC (Hexane/Ethyl Acetate 3:1) *R<sub>f</sub>* = 0.24. <sup>1</sup>H NMR (400 MHz; CD<sub>3</sub>OD) δ 8.19 (dd, *J* = 8.4 Hz, 1.1 Hz, 1H), 8.03 (d, *J* = 8.6 Hz, 1H), 7.75 (td, *J* = 8.4 Hz, 1.1 Hz, 1H), 7.63 (s, 1H), 7.55 (s, 1H), 7.52 (d, *J* = 8 Hz, 2H), 7.50 (td, *J* = 7.5 Hz, 1.0 Hz, 1H), 7.24 (td, *J* = 7.6 Hz, 1.0 Hz, 1H), 7.12 (t, *J* = 7.5 Hz, 1H),

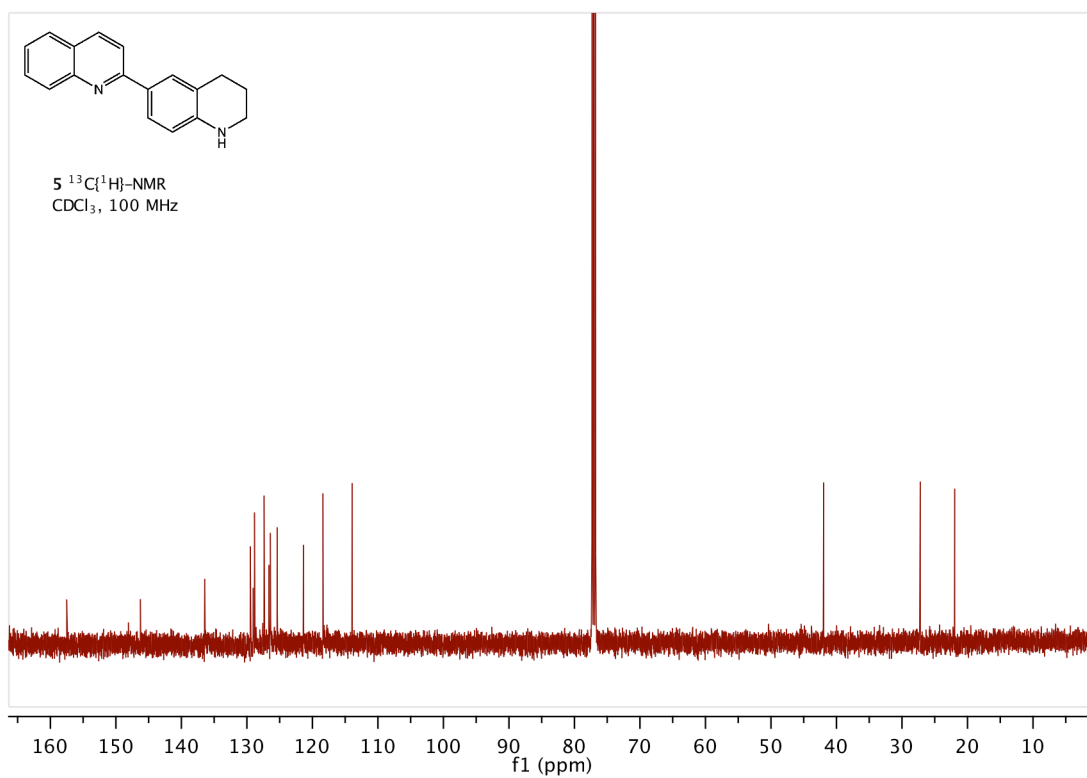
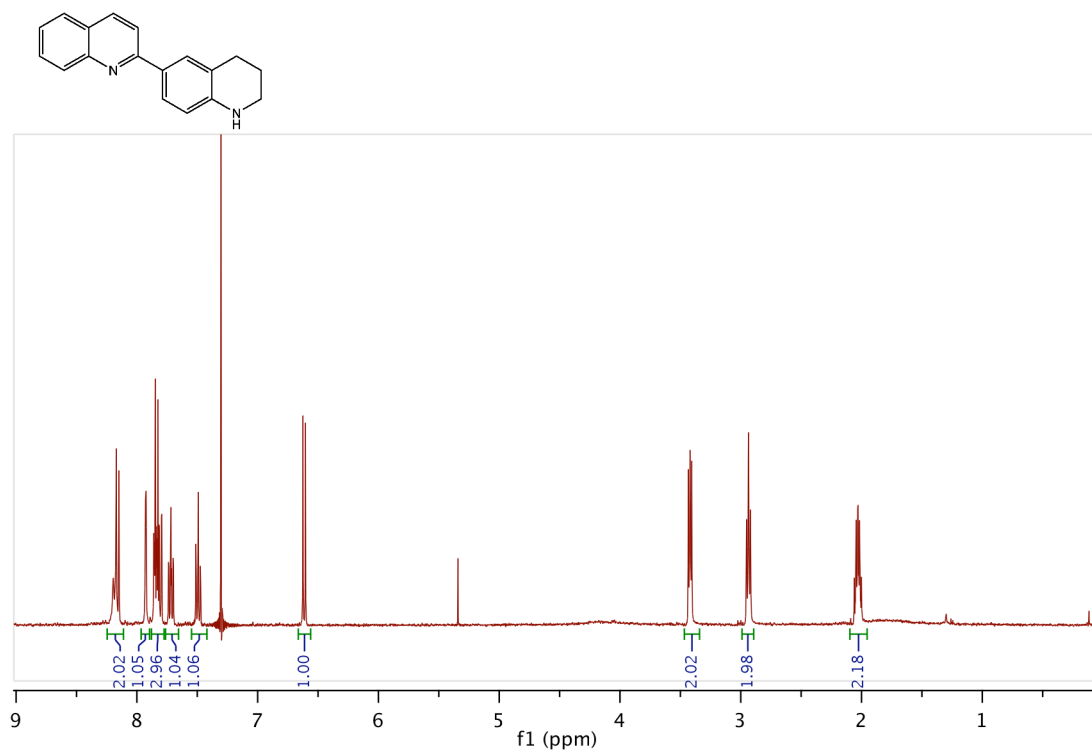
4.62 (s, 1H), 2.77 (s, 3H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz;  $\text{CD}_3\text{OD}$ )  $\delta$  158.5, 147.7, 144.0, 136.9, 129.4, 127.1, 126.5, 126.3, 125.6, 125.4, 125.3, 121.9 (2C), 119.8, 119.0, 112.3, 111.5, 23.2. HRMS-ESI ( $m/z$ ): calculated for  $\text{C}_{18}\text{H}_{15}\text{N}_2$   $[\text{M}+\text{H}]^+$ : 259.1230; observed: 259.1234.

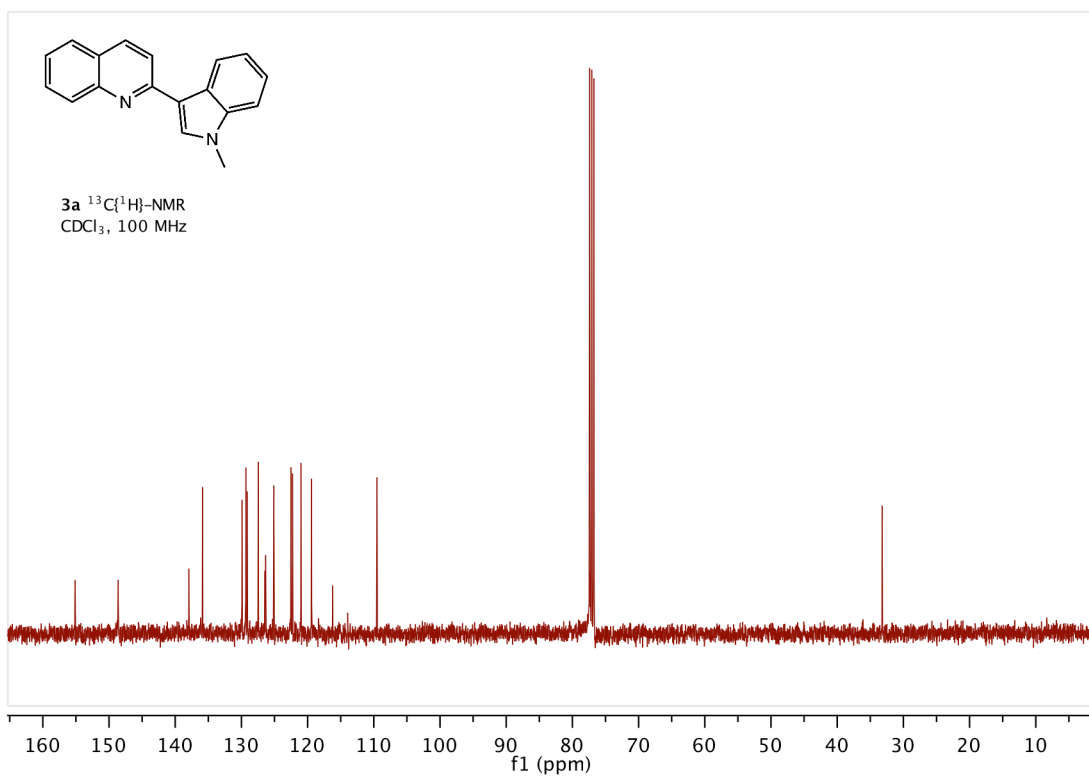
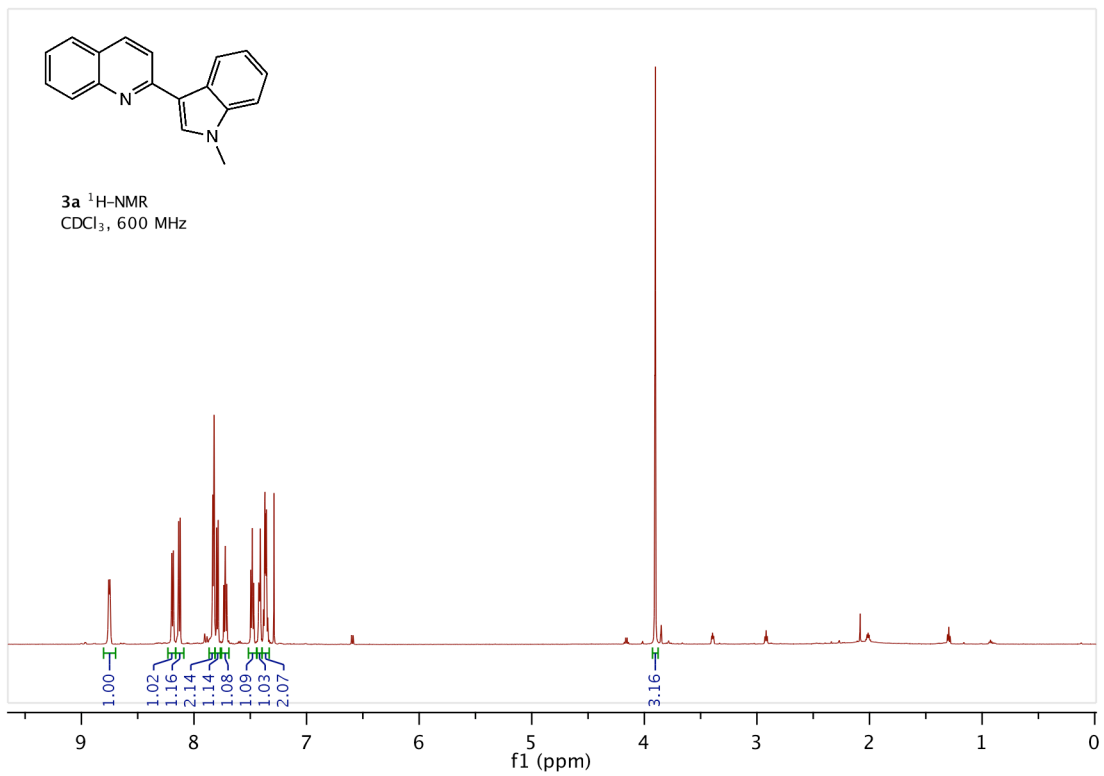
## V. References

1. K. Ohkura, K.-i. Seki, M. Terahima and Y. Kanaoka, *Heterocycles*, 1990, **30**, 957-962.
2. R. Martinez, D. Ramon and M. Yus, *Tetrahedron*, 2006, **62**, 8988-9001.

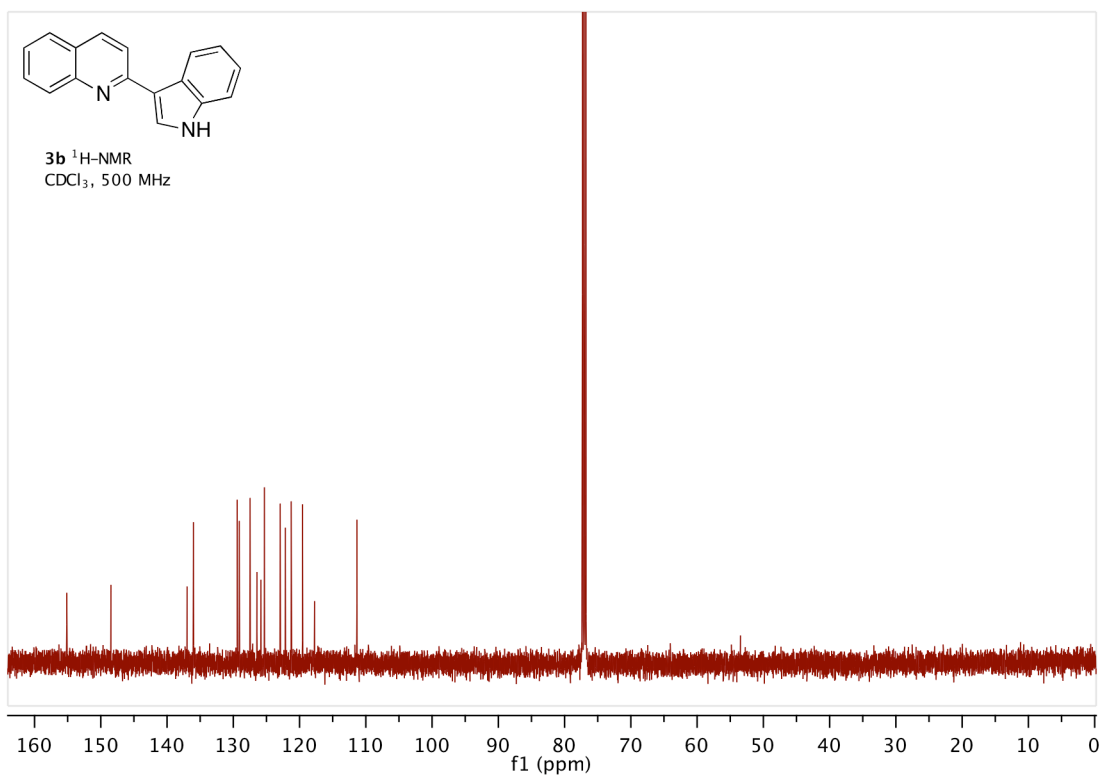
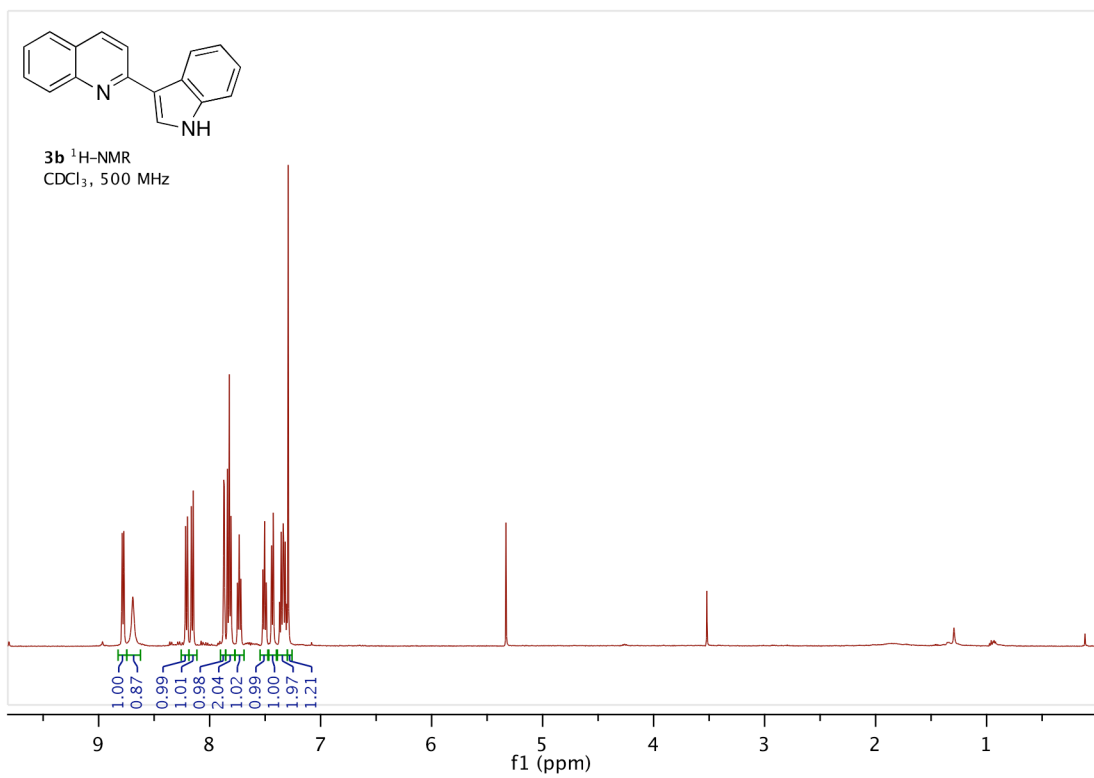
## VI. $^1\text{H}$ and $^{13}\text{C}\{^1\text{H}\}$ NMR spectra

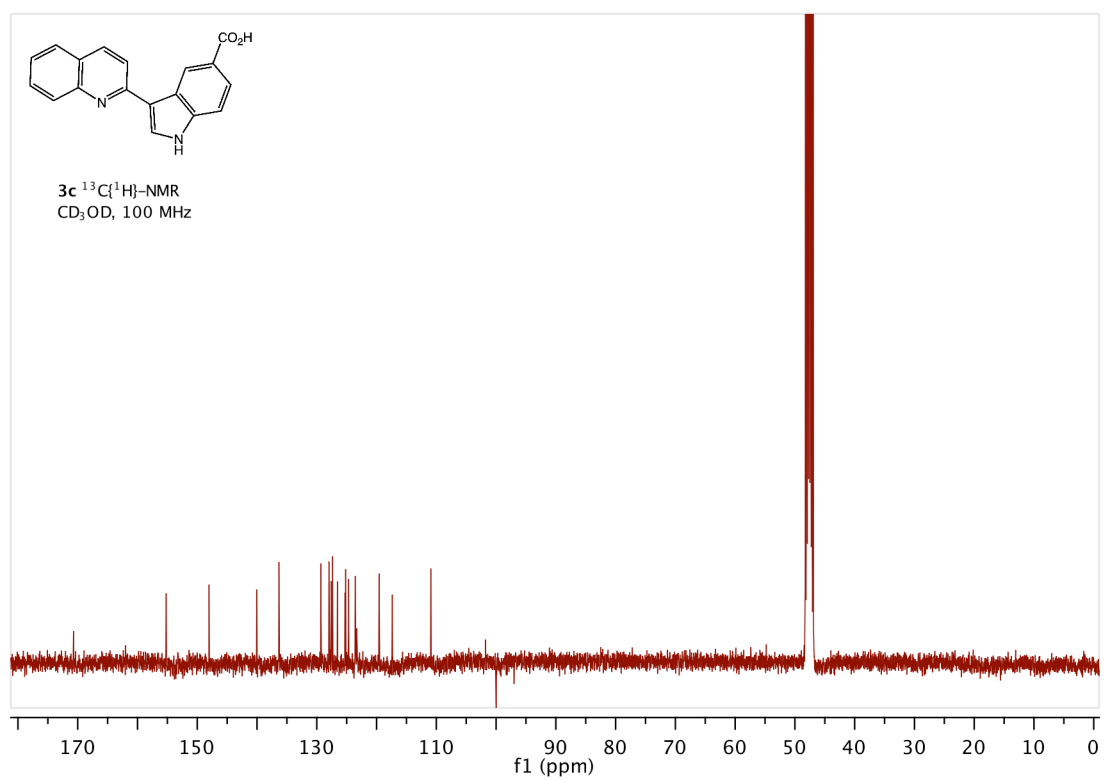
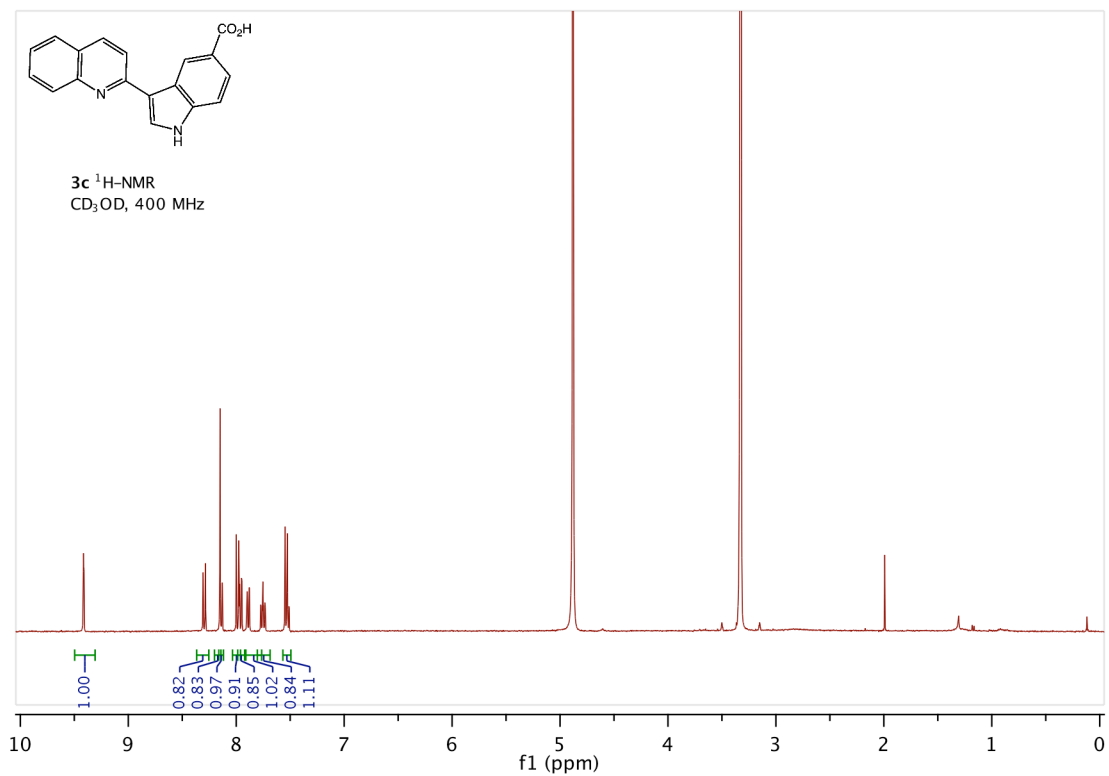


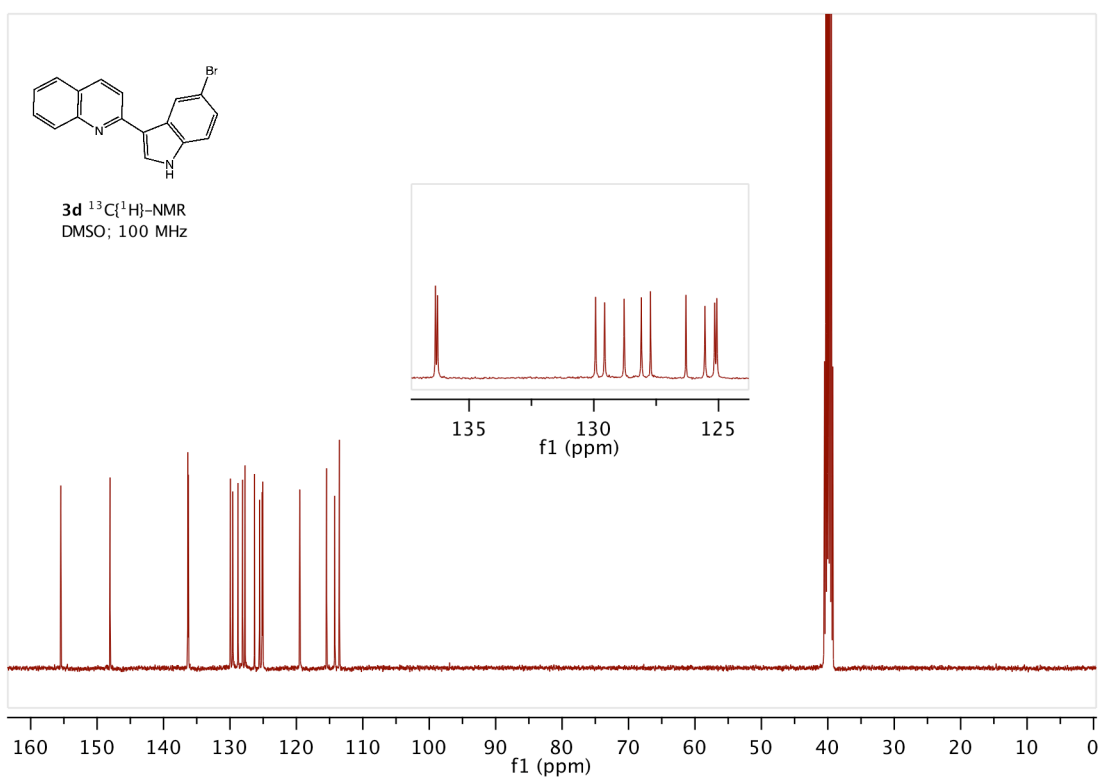
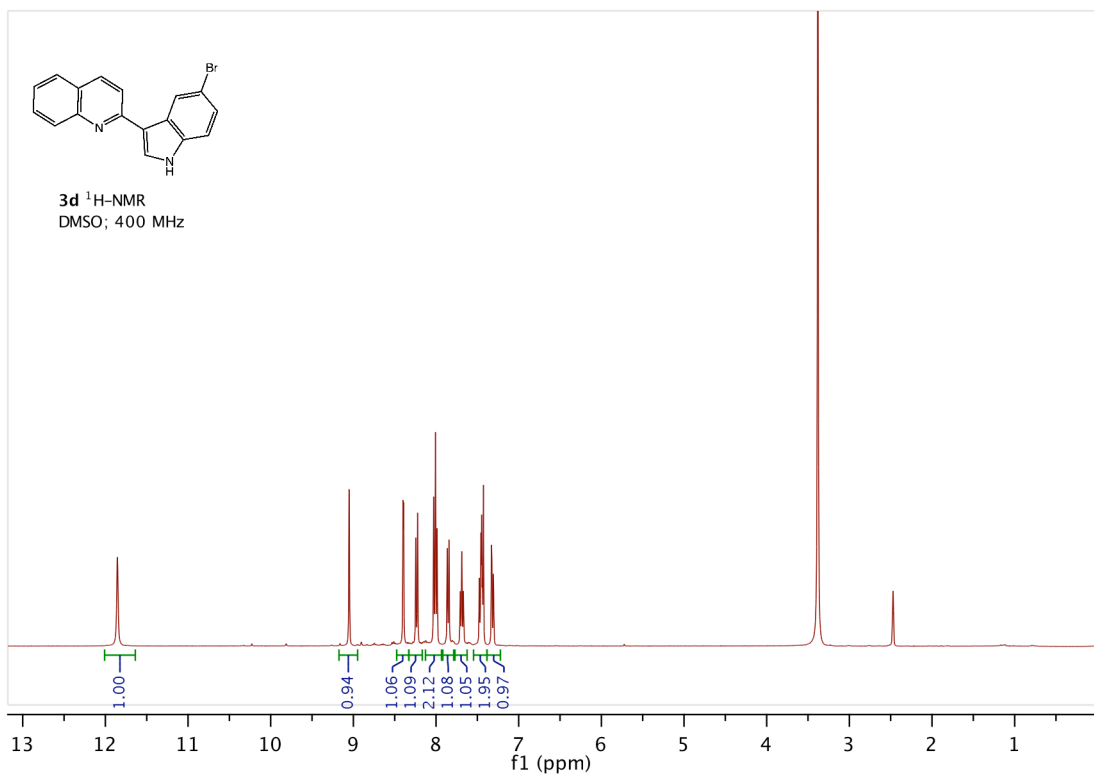


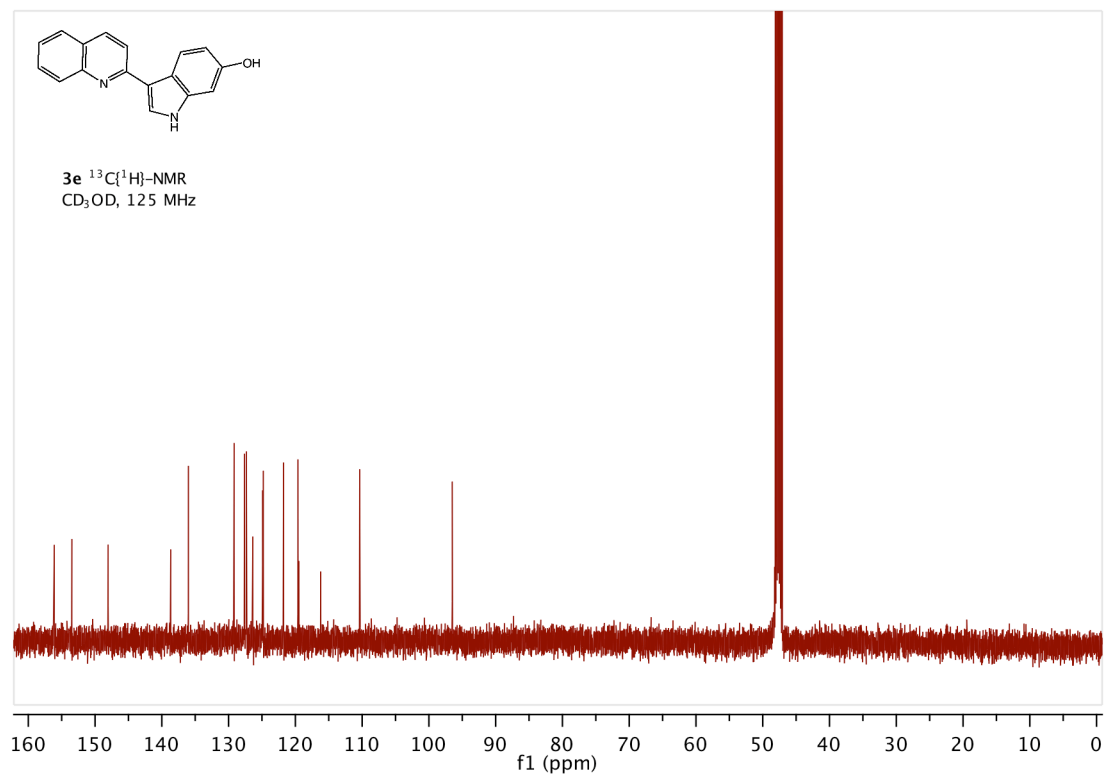
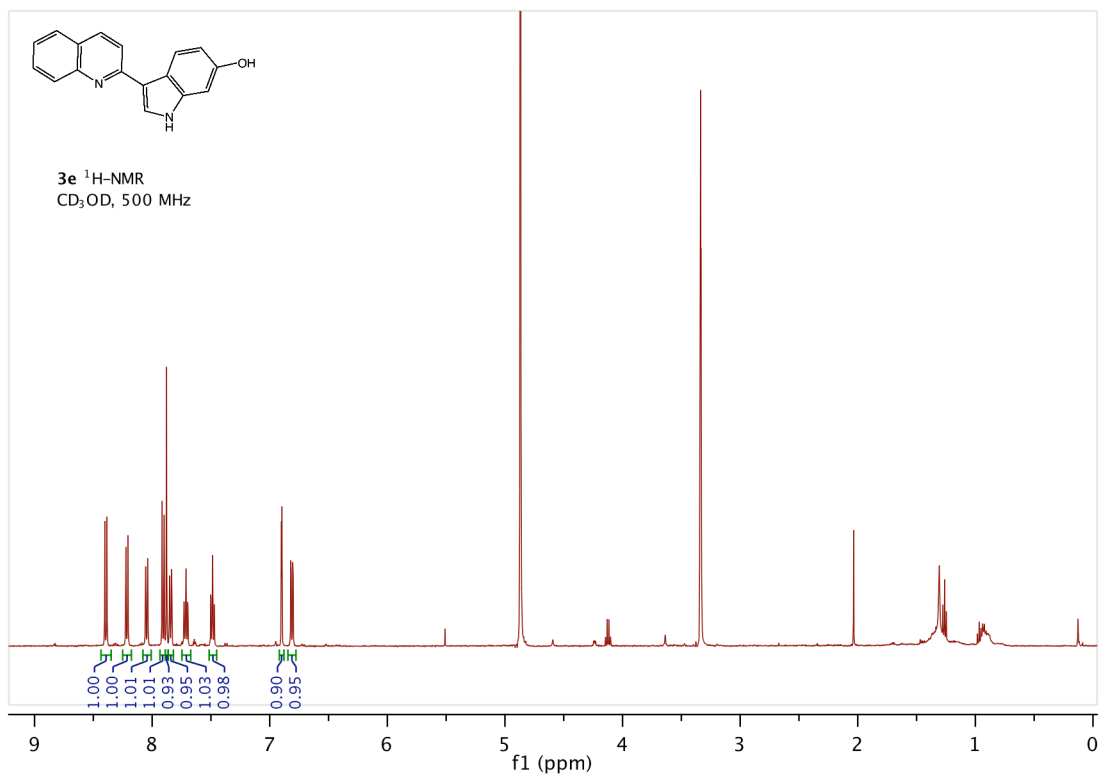


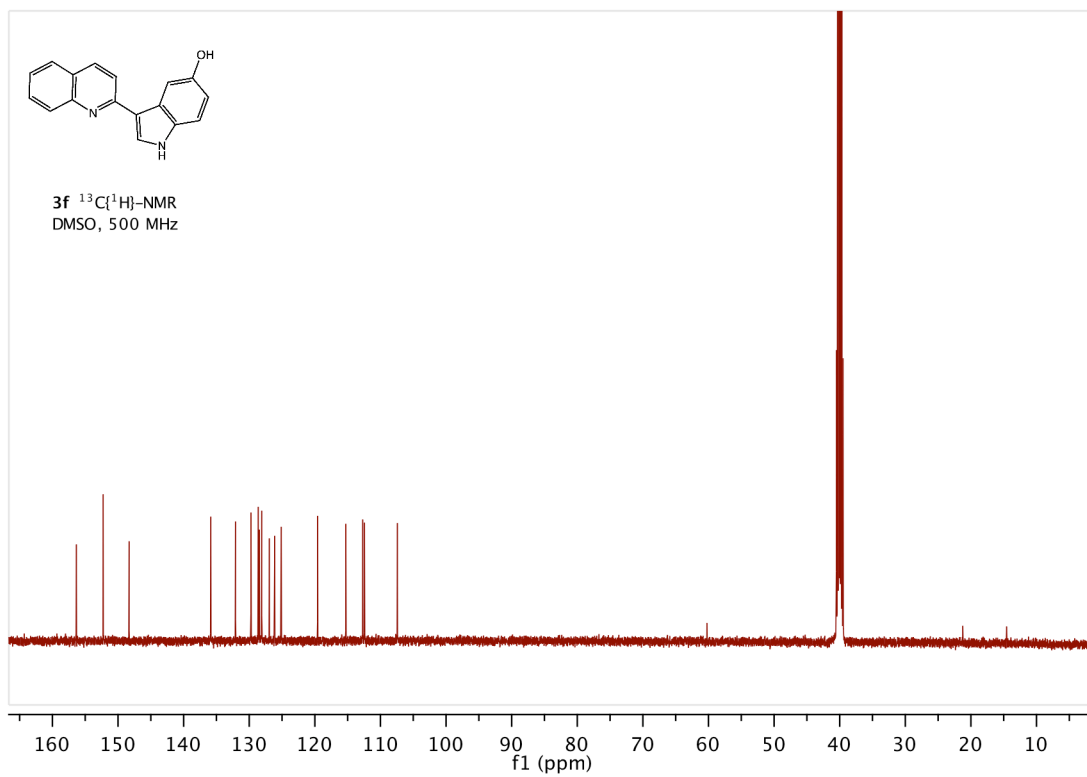
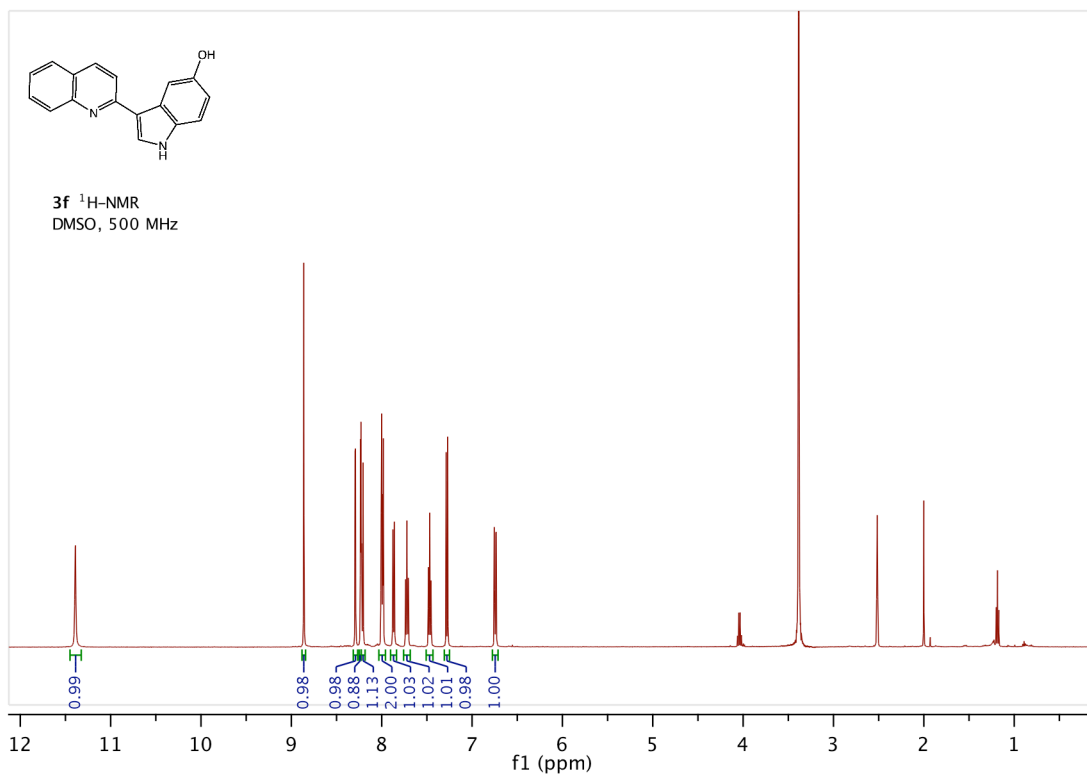


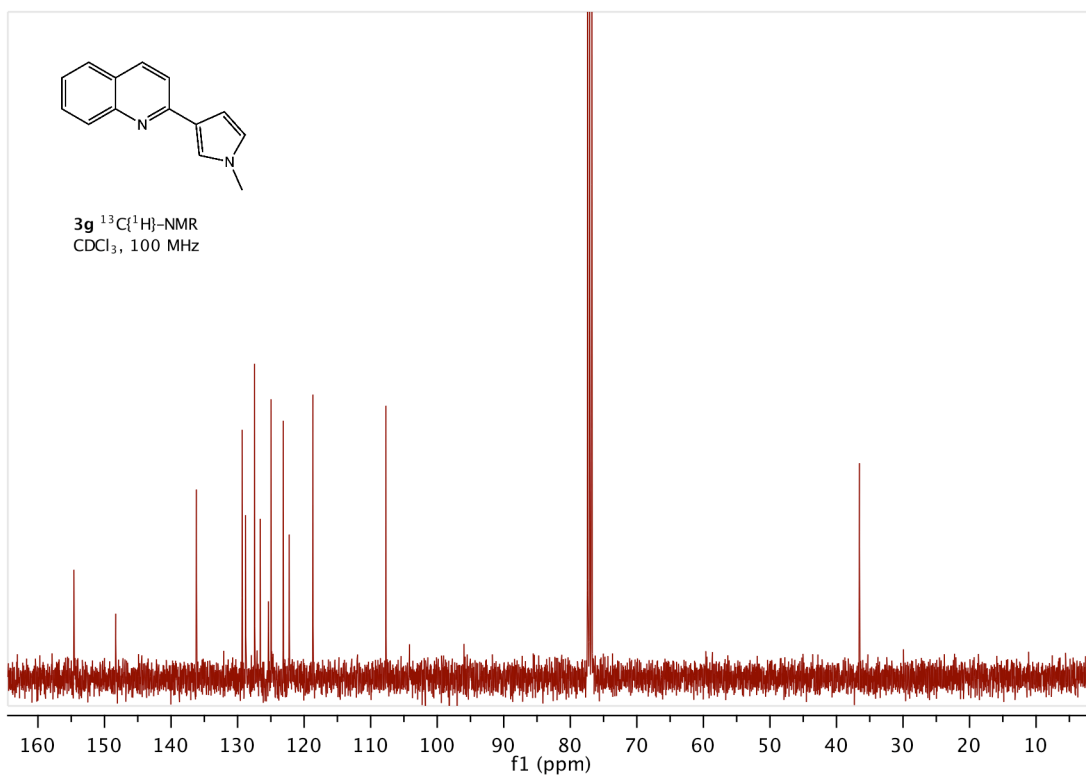
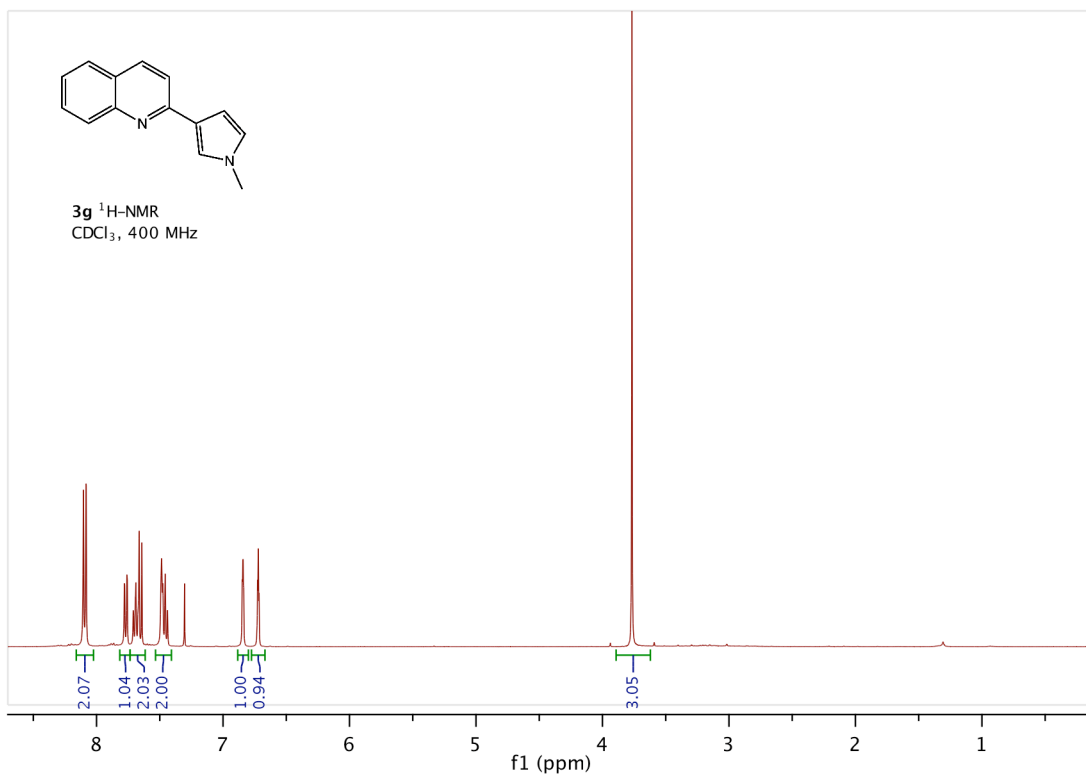


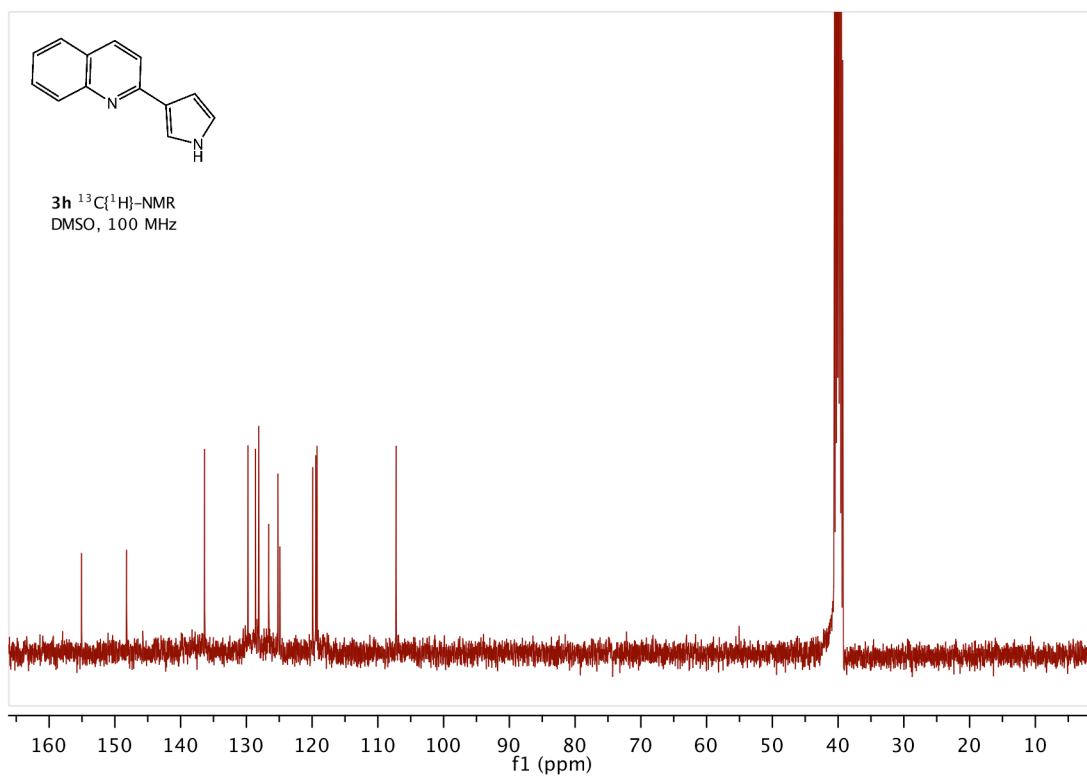
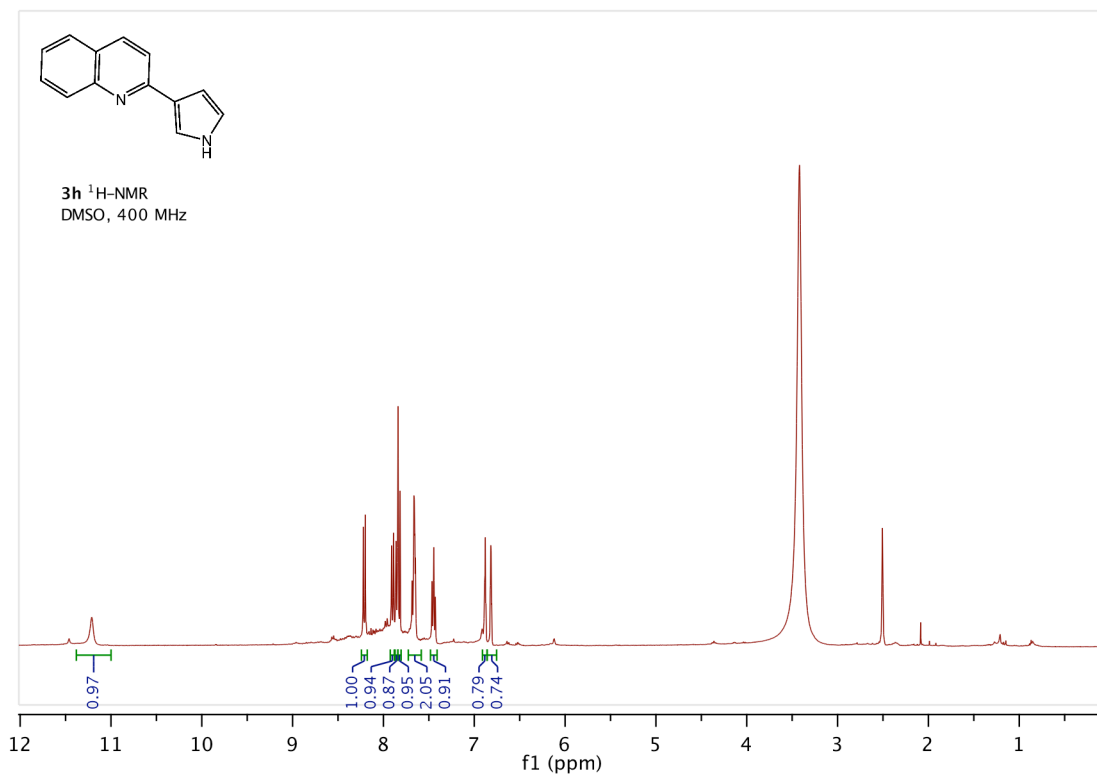


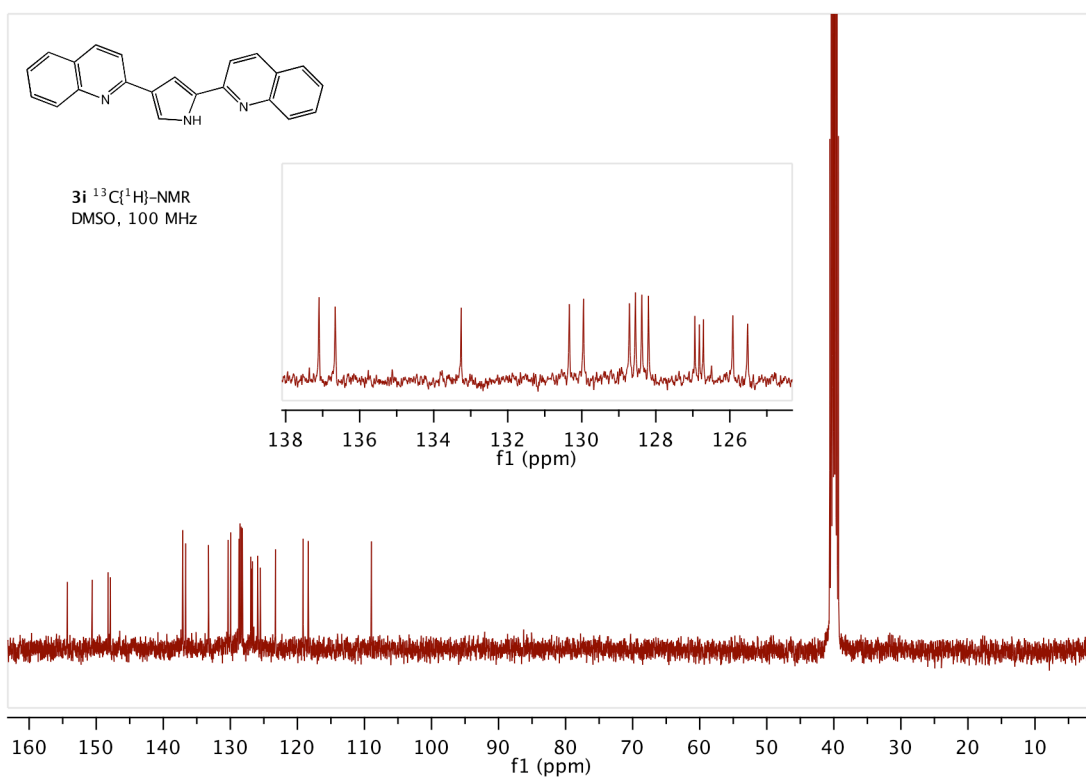
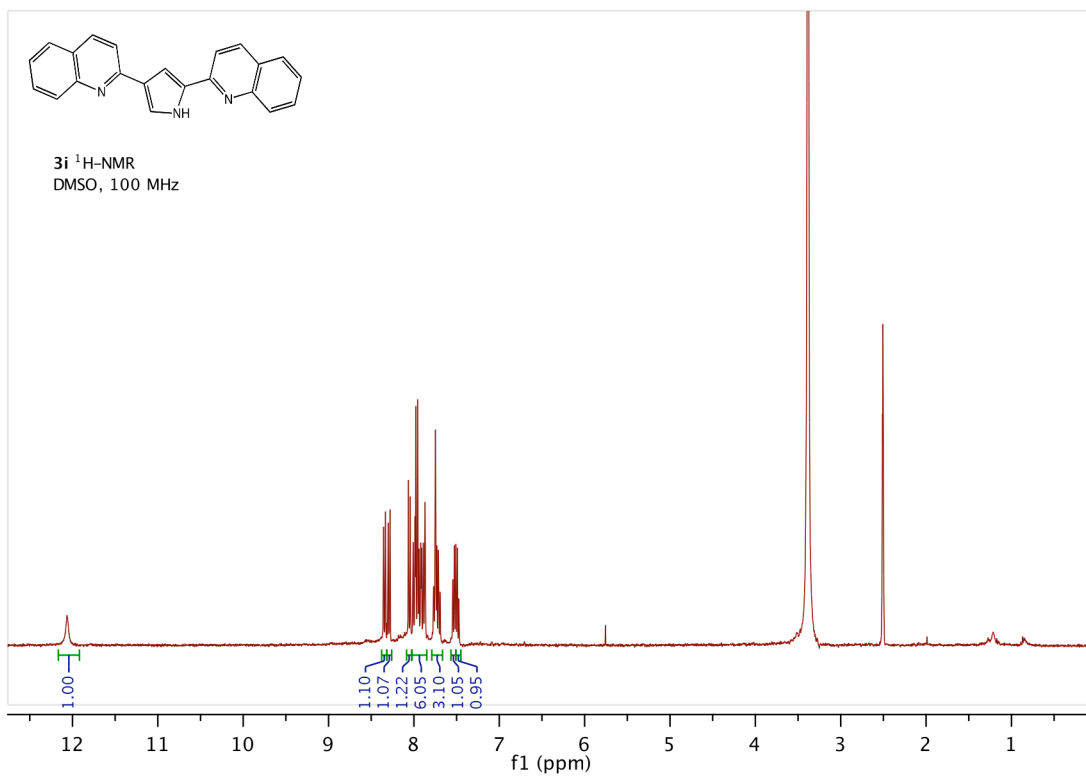




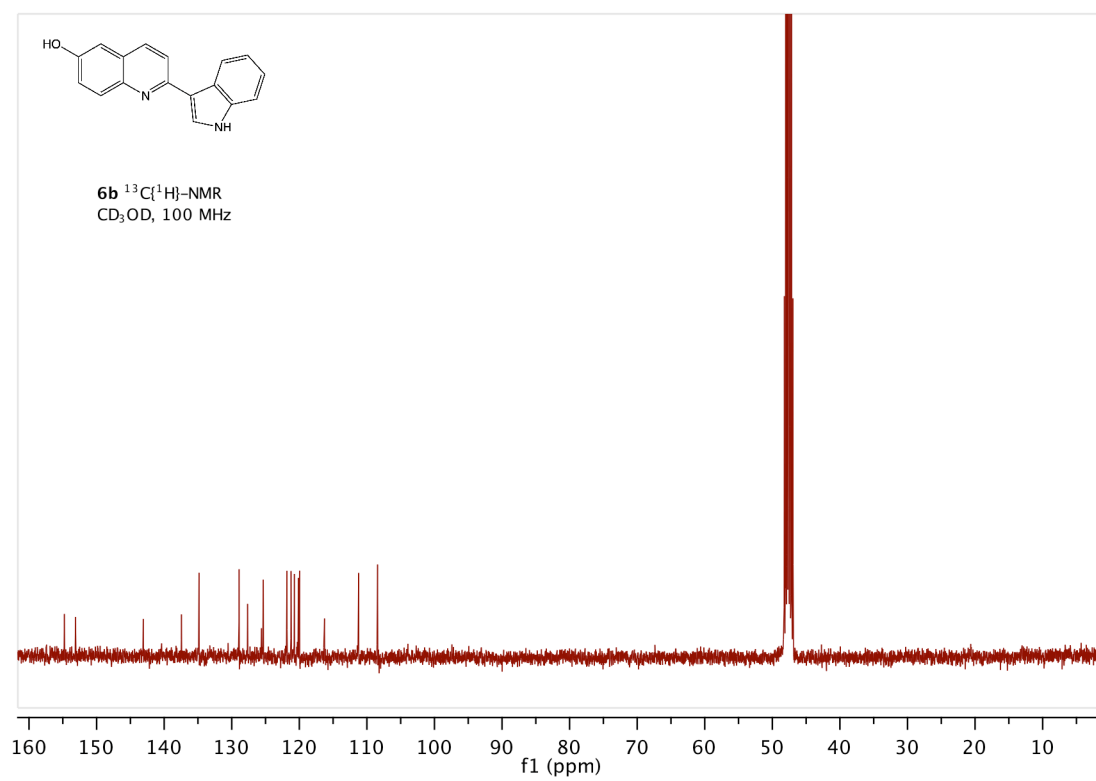
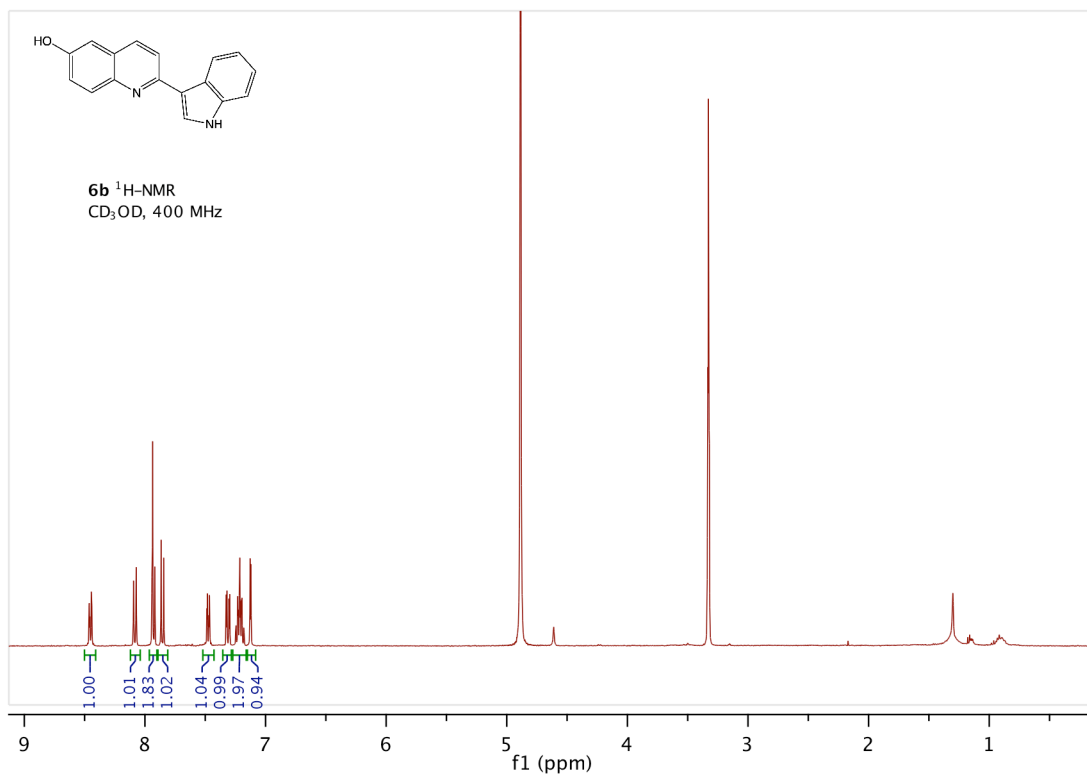


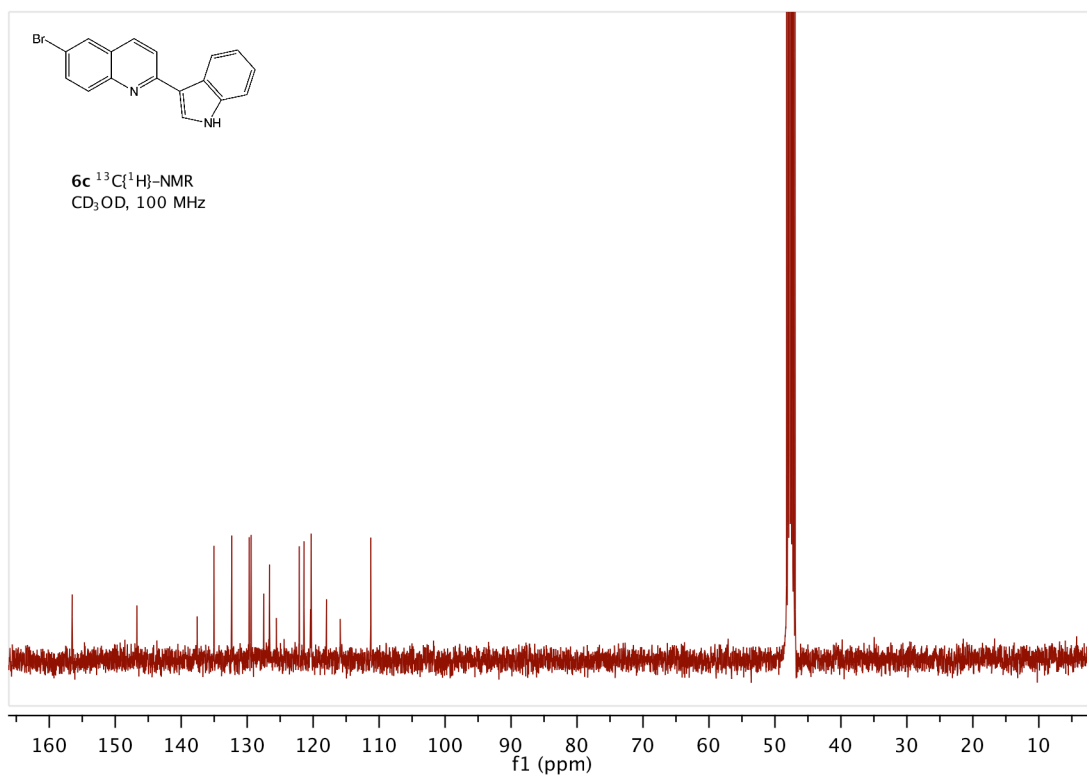
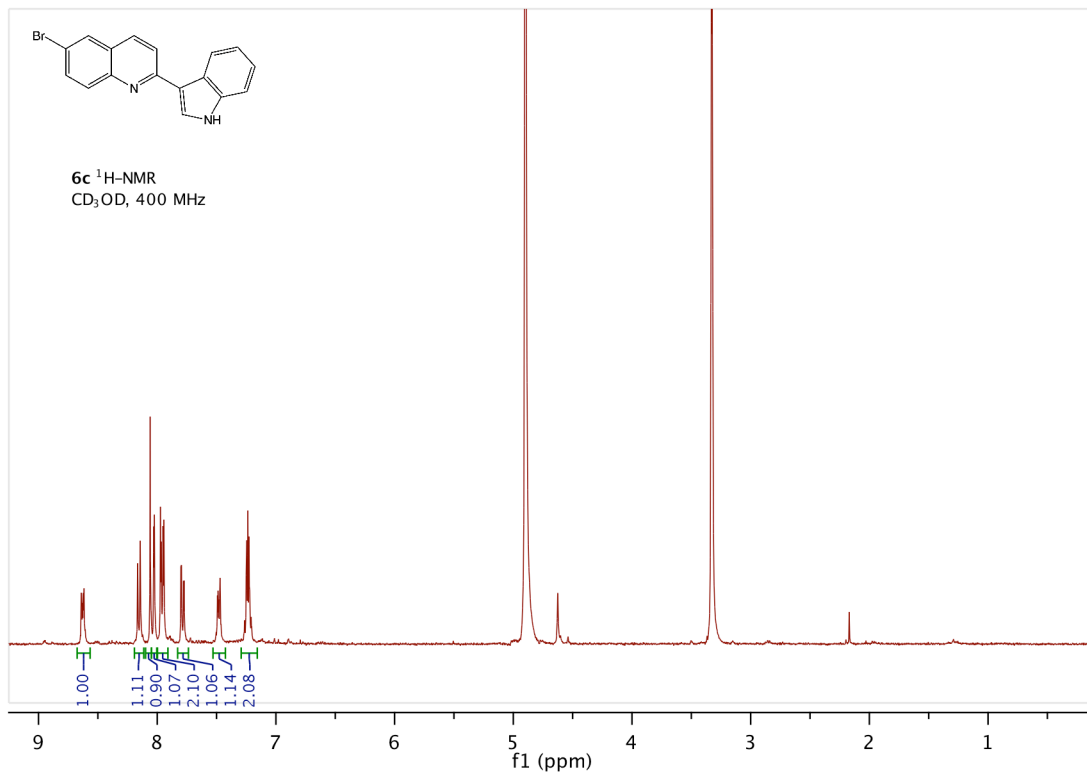


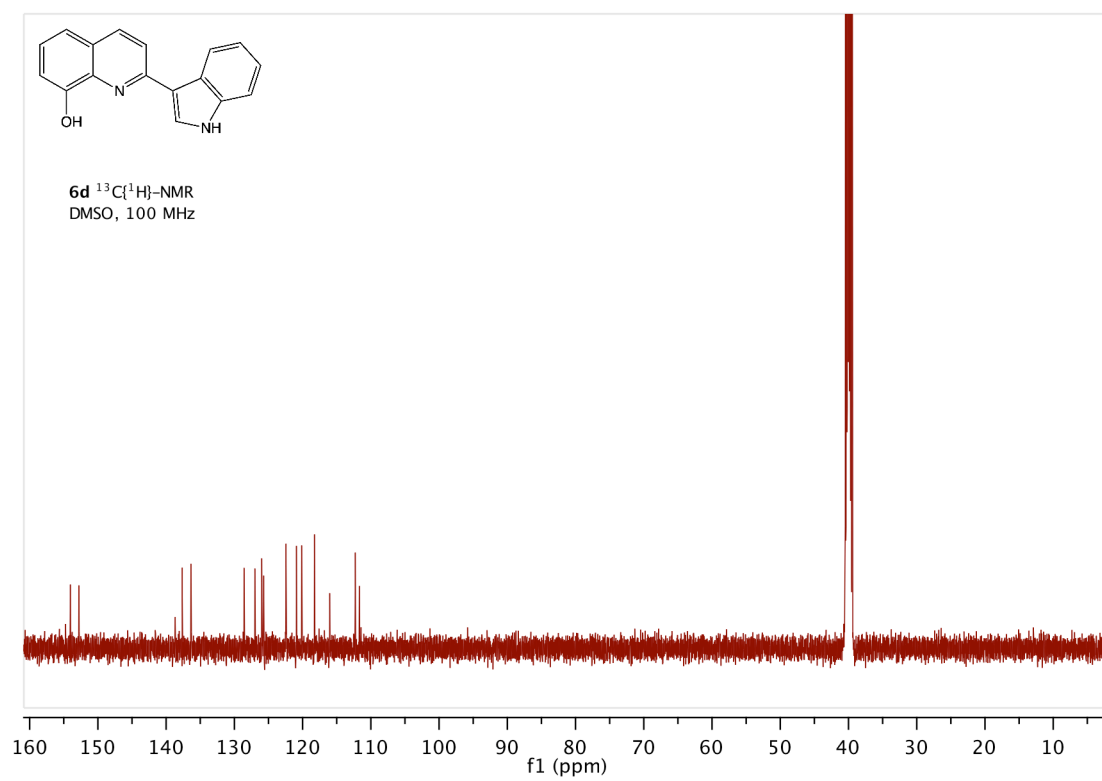
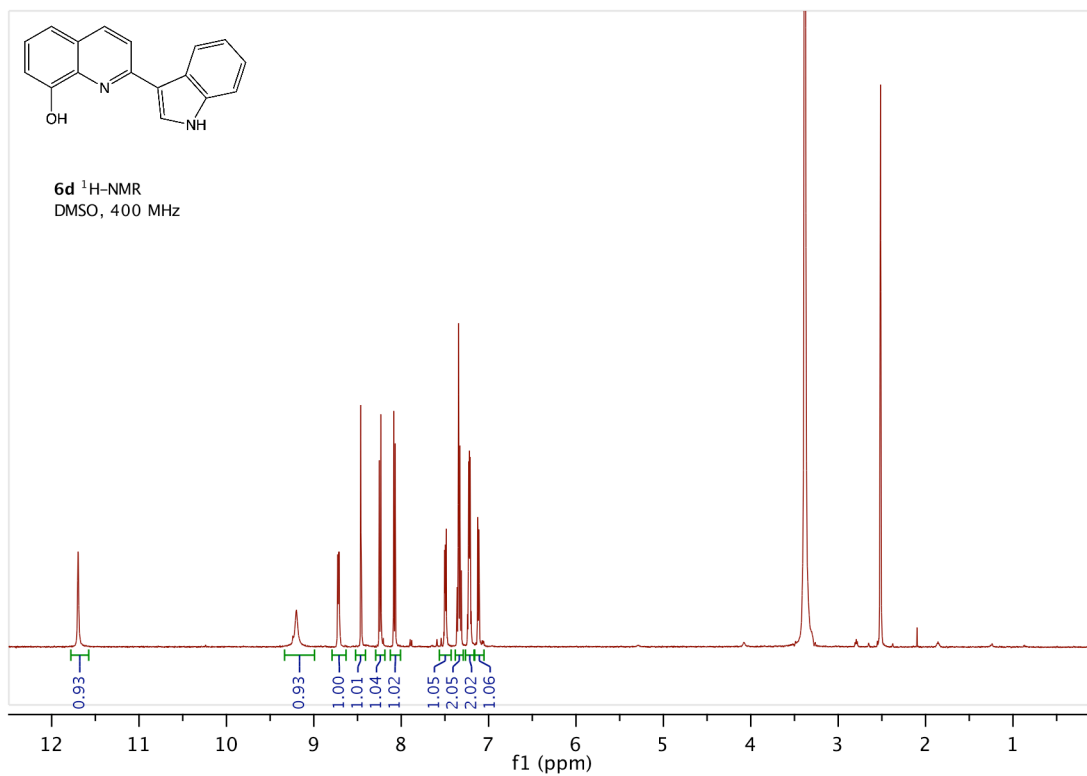


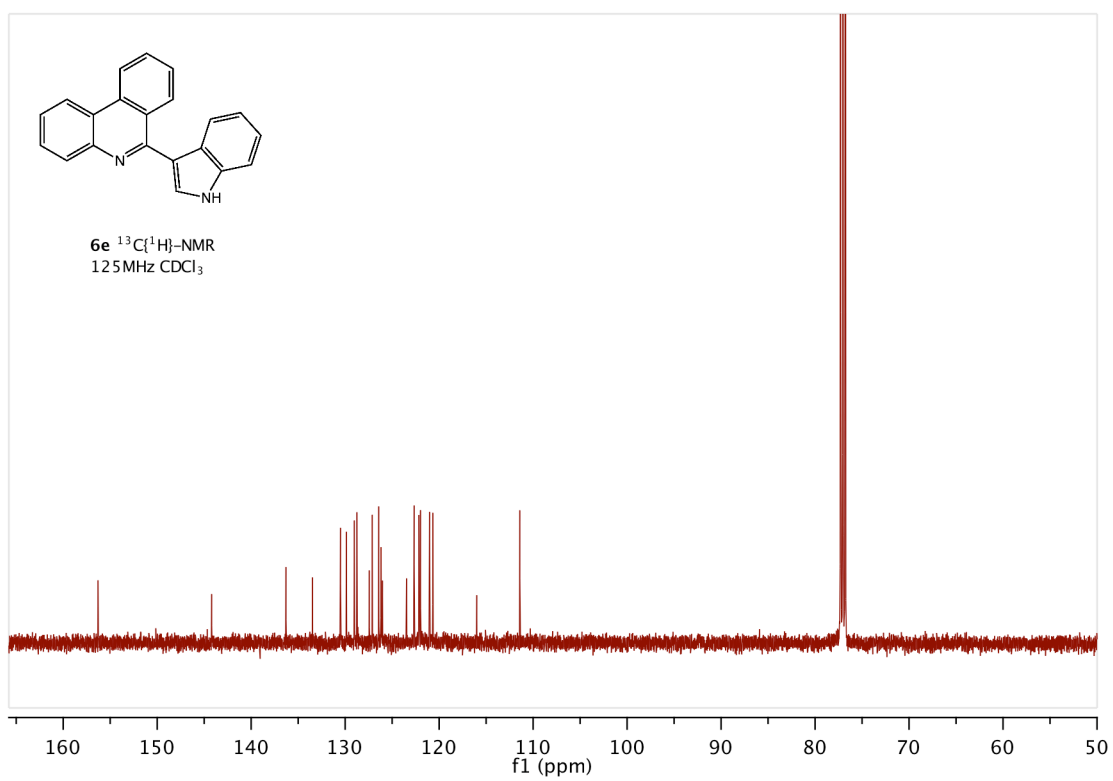
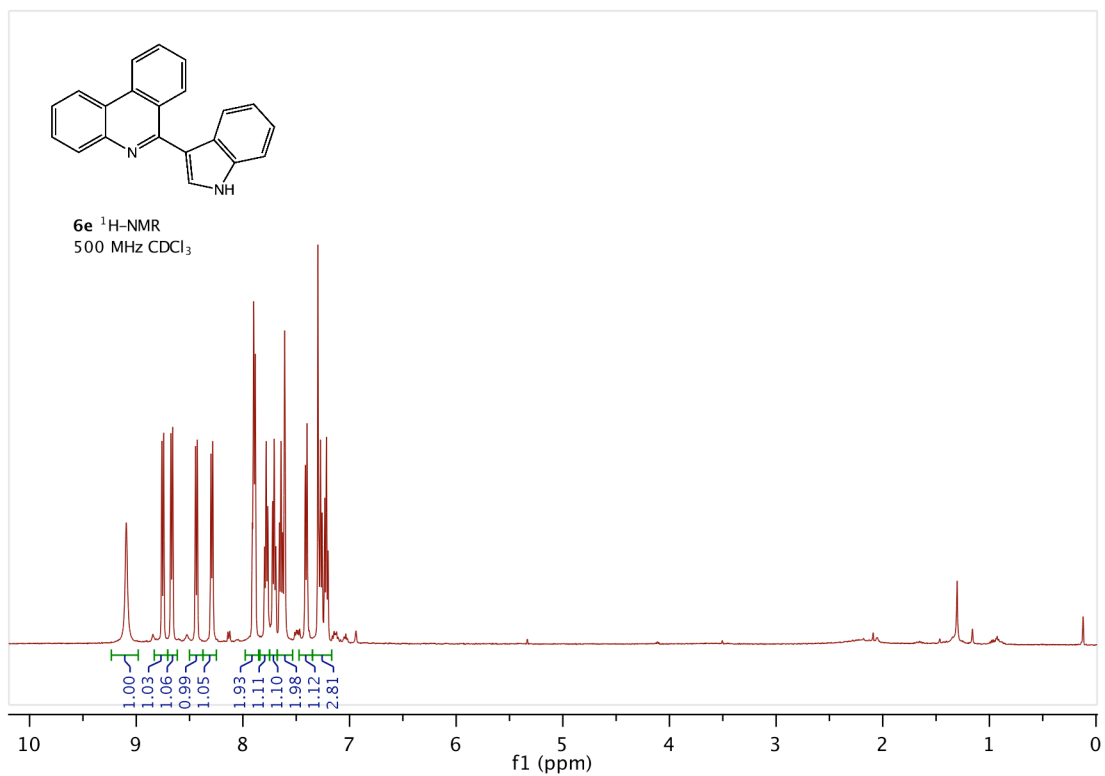


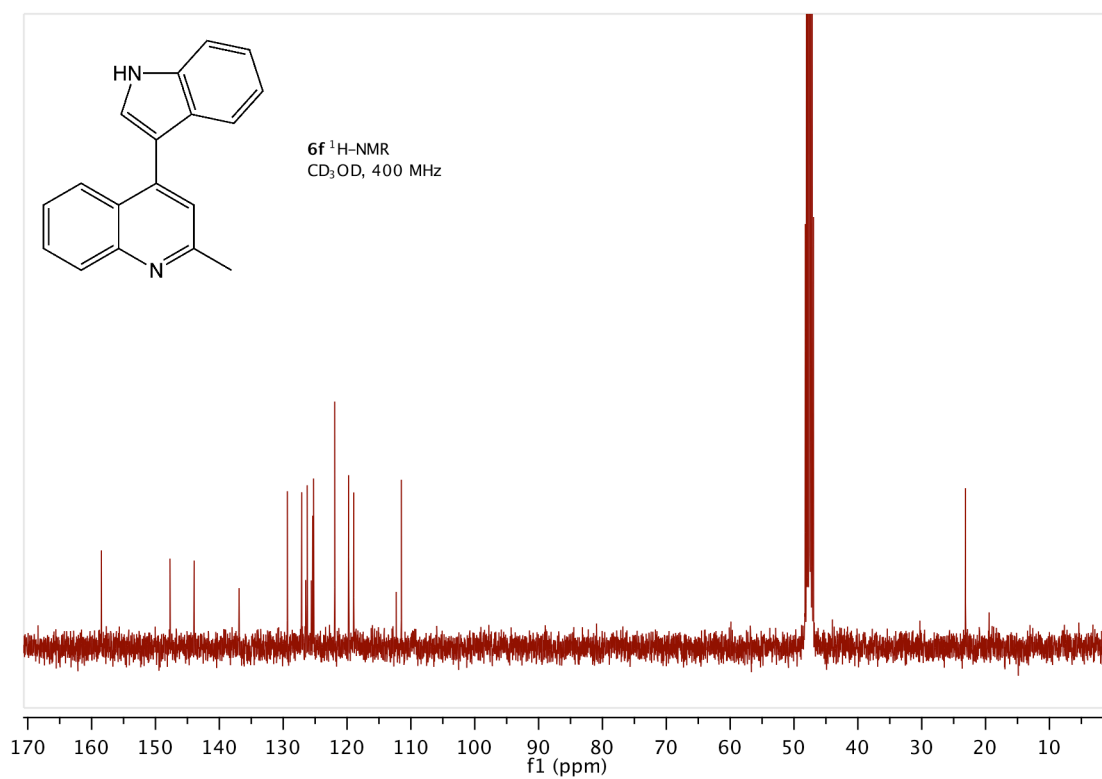
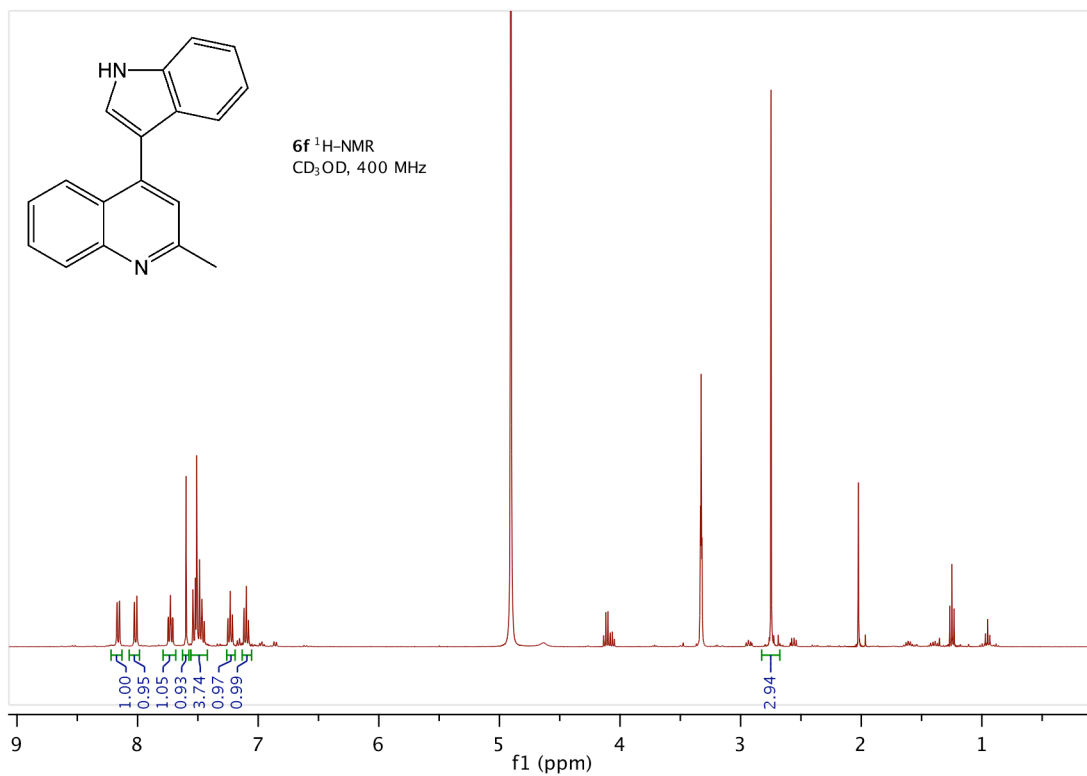




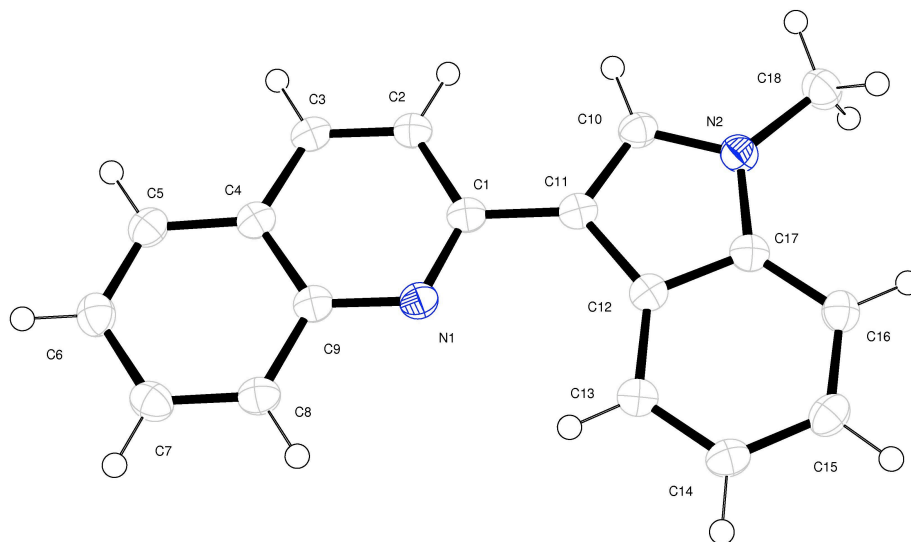








## VII. X-Ray structure report for 3a



A colorless rod 0.12 x 0.10 x 0.04 mm in size was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100(2) K using phi and omega scans. Crystal-to-detector distance was 60 mm and exposure time was 5 seconds per frame using a scan width of 0.5°. Data collection was 98.3% complete to 67.00° in  $\theta$ . A total of 16829 reflections were collected covering the indices,  $-9 \leq h \leq 9$ ,  $-6 \leq k \leq 9$ ,  $-22 \leq l \leq 22$ . 2304 reflections were found to be symmetry independent, with an  $R_{\text{int}}$  of 0.0160. Indexing and unit cell refinement indicated a primitive, monoclinic lattice. The space group was found to be P2(1)/c (No. 14). The data were integrated using the Bruker SAINT software program and scaled using the SADABS software program. Solution by direct methods (SIR-2004) produced a complete heavy-atom phasing model consistent with the proposed structure. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-97). All hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-97.

Table 1. Crystal data and structure refinement for **3a**.

X-ray ID	<b>3a</b>	
Sample/notebook ID	MB-I-47	
Empirical formula	C <sub>18</sub> H <sub>14</sub> N <sub>2</sub>	
Formula weight	258.31	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P2(1)/c	
Unit cell dimensions	a = 7.7173(3) Å	α = 90°.
	b = 8.8634(3) Å	β = 93.350(2)°.
	c = 19.0154(6) Å	γ = 90°.
Volume	1298.46(8) Å <sup>3</sup>	
Z	4	
Density (calculated)	1.321 Mg/m <sup>3</sup>	
Absorption coefficient	0.608 mm <sup>-1</sup>	
F(000)	544	
Crystal size	0.12 x 0.10 x 0.04 mm <sup>3</sup>	
Crystal color/habit	colorless rod	
Theta range for data collection	4.66 to 67.95°.	
Index ranges	-9 ≤ h ≤ 9, -6 ≤ k ≤ 9, -22 ≤ l ≤ 22	
Reflections collected	16829	
Independent reflections	2304 [R(int) = 0.0160]	
Completeness to theta = 67.00°	98.3 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9761 and 0.9306	
Refinement method	Full-matrix least-squares on F <sup>2</sup>	
Data / restraints / parameters	2304 / 0 / 182	
Goodness-of-fit on F <sup>2</sup>	1.038	
Final R indices [I > 2σ(I)]	R <sub>1</sub> = 0.0324, wR <sub>2</sub> = 0.0837	
R indices (all data)	R <sub>1</sub> = 0.0349, wR <sub>2</sub> = 0.0865	
Largest diff. peak and hole	0.197 and -0.152 e.Å <sup>-3</sup>	

Table 2. Atomic coordinates ( $\times 10^4$ ) and equivalent isotropic displacement parameters ( $\text{\AA}^2 \times 10^3$ ) for **3a**.  $U(\text{eq})$  is defined as one third of the trace of the orthogonalized  $U^{ij}$  tensor.

	x	y	z	U(eq)
C(1)	3765(1)	397(1)	7315(1)	23(1)
C(2)	4271(2)	-412(1)	7947(1)	25(1)
C(3)	3184(2)	-477(1)	8480(1)	26(1)
C(4)	1536(2)	229(1)	8404(1)	24(1)
C(5)	284(2)	135(1)	8914(1)	27(1)
C(6)	-1295(2)	829(1)	8807(1)	29(1)
C(7)	-1677(2)	1659(1)	8184(1)	29(1)
C(8)	-492(2)	1761(1)	7678(1)	27(1)
C(9)	1140(1)	1035(1)	7769(1)	24(1)
C(10)	6512(2)	-248(1)	6716(1)	25(1)
C(11)	4921(1)	452(1)	6736(1)	24(1)
C(12)	4684(1)	1278(1)	6082(1)	23(1)
C(13)	3382(2)	2222(1)	5784(1)	25(1)
C(14)	3613(2)	2860(1)	5133(1)	28(1)
C(15)	5100(2)	2575(1)	4766(1)	28(1)
C(16)	6413(2)	1659(1)	5046(1)	26(1)
C(17)	6181(1)	1025(1)	5706(1)	24(1)
C(18)	8990(2)	-390(2)	5924(1)	32(1)
N(1)	2257(1)	1119(1)	7236(1)	24(1)
N(2)	7275(1)	89(1)	6108(1)	26(1)



Table 3. Bond lengths [ $\text{\AA}$ ] and angles [ $^\circ$ ] for **3a**.

C(1)-N(1)	1.3288(15)	C(10)-C(11)	1.3780(16)
C(1)-C(2)	1.4339(16)	C(10)-H(10)	0.9500
C(1)-C(11)	1.4575(16)	C(11)-C(12)	1.4445(15)
C(2)-C(3)	1.3548(16)	C(12)-C(13)	1.4015(16)
C(2)-H(2)	0.9500	C(12)-C(17)	1.4118(16)
C(3)-C(4)	1.4173(16)	C(13)-C(14)	1.3827(16)
C(3)-H(3)	0.9500	C(13)-H(13)	0.9500
C(4)-C(5)	1.4101(16)	C(14)-C(15)	1.4008(17)
C(4)-C(9)	1.4209(16)	C(14)-H(14)	0.9500
C(5)-C(6)	1.3699(17)	C(15)-C(16)	1.3807(17)
C(5)-H(5)	0.9500	C(15)-H(15)	0.9500
C(6)-C(7)	1.4105(17)	C(16)-C(17)	1.3973(16)
C(6)-H(6)	0.9500	C(16)-H(16)	0.9500
C(7)-C(8)	1.3690(17)	C(17)-N(2)	1.3807(15)
C(7)-H(7)	0.9500	C(18)-N(2)	1.4522(15)
C(8)-C(9)	1.4159(16)	C(18)-H(18A)	0.9800
C(8)-H(8)	0.9500	C(18)-H(18B)	0.9800
C(9)-N(1)	1.3700(15)	C(18)-H(18C)	0.9800
C(10)-N(2)	1.3615(15)		
N(1)-C(1)-C(2)	121.88(11)	C(4)-C(5)-H(5)	119.7
N(1)-C(1)-C(11)	118.03(10)	C(5)-C(6)-C(7)	119.97(11)
C(2)-C(1)-C(11)	120.09(10)	C(5)-C(6)-H(6)	120.0
C(3)-C(2)-C(1)	119.90(11)	C(7)-C(6)-H(6)	120.0
C(3)-C(2)-H(2)	120.0	C(8)-C(7)-C(6)	120.64(11)
C(1)-C(2)-H(2)	120.0	C(8)-C(7)-H(7)	119.7
C(2)-C(3)-C(4)	119.77(10)	C(6)-C(7)-H(7)	119.7
C(2)-C(3)-H(3)	120.1	C(7)-C(8)-C(9)	120.62(11)
C(4)-C(3)-H(3)	120.1	C(7)-C(8)-H(8)	119.7
C(5)-C(4)-C(3)	123.40(11)	C(9)-C(8)-H(8)	119.7
C(5)-C(4)-C(9)	119.49(11)	N(1)-C(9)-C(8)	118.59(10)
C(3)-C(4)-C(9)	117.09(10)	N(1)-C(9)-C(4)	122.83(10)
C(6)-C(5)-C(4)	120.67(11)	C(8)-C(9)-C(4)	118.58(11)
C(6)-C(5)-H(5)	119.7	N(2)-C(10)-C(11)	110.78(10)

N(2)-C(10)-H(10)	124.6
C(11)-C(10)-H(10)	124.6
C(10)-C(11)-C(12)	105.84(10)
C(10)-C(11)-C(1)	126.21(10)
C(12)-C(11)-C(1)	127.91(10)
C(13)-C(12)-C(17)	118.62(10)
C(13)-C(12)-C(11)	134.60(11)
C(17)-C(12)-C(11)	106.76(10)
C(14)-C(13)-C(12)	118.67(11)
C(14)-C(13)-H(13)	120.7
C(12)-C(13)-H(13)	120.7
C(13)-C(14)-C(15)	121.64(11)
C(13)-C(14)-H(14)	119.2
C(15)-C(14)-H(14)	119.2
C(16)-C(15)-C(14)	121.22(11)
C(16)-C(15)-H(15)	119.4
C(14)-C(15)-H(15)	119.4
C(15)-C(16)-C(17)	116.99(11)
C(15)-C(16)-H(16)	121.5
C(17)-C(16)-H(16)	121.5
N(2)-C(17)-C(16)	129.22(11)
N(2)-C(17)-C(12)	107.93(10)
C(16)-C(17)-C(12)	122.85(11)
N(2)-C(18)-H(18A)	109.5
N(2)-C(18)-H(18B)	109.5
H(18A)-C(18)-H(18B)	109.5
N(2)-C(18)-H(18C)	109.5
H(18A)-C(18)-H(18C)	109.5
H(18B)-C(18)-H(18C)	109.5
C(1)-N(1)-C(9)	118.46(10)
C(10)-N(2)-C(17)	108.68(9)
C(10)-N(2)-C(18)	125.89(10)
C(17)-N(2)-C(18)	125.36(10)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ( $\text{\AA}^2 \times 10^3$ ) for **3a**. The anisotropic displacement factor exponent takes the form:  $-2\pi^2 [ h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12} ]$

	U <sup>11</sup>	U <sup>22</sup>	U <sup>33</sup>	U <sup>23</sup>	U <sup>13</sup>	U <sup>12</sup>
C(1)	25(1)	19(1)	25(1)	-2(1)	-2(1)	-2(1)
C(2)	25(1)	24(1)	27(1)	1(1)	-1(1)	1(1)
C(3)	30(1)	23(1)	24(1)	2(1)	-2(1)	0(1)
C(4)	27(1)	20(1)	24(1)	-2(1)	-1(1)	-4(1)
C(5)	31(1)	24(1)	26(1)	-1(1)	1(1)	-4(1)
C(6)	29(1)	27(1)	32(1)	-3(1)	5(1)	-5(1)
C(7)	24(1)	27(1)	36(1)	-3(1)	-1(1)	1(1)
C(8)	28(1)	26(1)	28(1)	1(1)	-2(1)	0(1)
C(9)	25(1)	20(1)	25(1)	-2(1)	-1(1)	-3(1)
C(10)	29(1)	24(1)	23(1)	0(1)	-2(1)	1(1)
C(11)	25(1)	21(1)	23(1)	-1(1)	-2(1)	-1(1)
C(12)	25(1)	20(1)	23(1)	-3(1)	-1(1)	-3(1)
C(13)	25(1)	24(1)	26(1)	-2(1)	-1(1)	-1(1)
C(14)	30(1)	26(1)	27(1)	2(1)	-4(1)	0(1)
C(15)	35(1)	28(1)	23(1)	1(1)	-1(1)	-5(1)
C(16)	28(1)	26(1)	24(1)	-4(1)	3(1)	-3(1)
C(17)	26(1)	21(1)	25(1)	-4(1)	-1(1)	-2(1)
C(18)	27(1)	37(1)	31(1)	0(1)	3(1)	6(1)
N(1)	26(1)	23(1)	24(1)	0(1)	-1(1)	0(1)
N(2)	26(1)	27(1)	25(1)	-1(1)	1(1)	2(1)

Table 5. Hydrogen coordinates ( $\times 10^4$ ) and isotropic displacement parameters ( $\text{\AA}^2 \times 10^3$ )  
for **3a**.

	x	y	z	U(eq)
H(2)	5367	-902	7991	30
H(3)	3525	-993	8903	31
H(5)	539	-417	9336	32
H(6)	-2133	751	9152	35
H(7)	-2767	2152	8115	35
H(8)	-767	2325	7261	33
H(10)	7008	-879	7078	30
H(13)	2362	2420	6025	30
H(14)	2740	3508	4929	33
H(15)	5208	3020	4316	34
H(16)	7428	1469	4801	31
H(18A)	9434	-1154	6261	47
H(18B)	9774	480	5938	47
H(18C)	8919	-820	5448	47



Table 1. Crystal data and structure refinement for **6e**.

X-ray ID	<b>6e</b>	
Sample/notebook ID	MB-II-194	
Empirical formula	C <sub>22</sub> H <sub>16</sub> Cl <sub>2</sub> N <sub>2</sub>	
Formula weight	379.27	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P2(1)/n	
Unit cell dimensions	a = 8.5493(10) Å	α = 90°.
	b = 9.3890(11) Å	β = 97.850(7)°.
	c = 22.288(2) Å	γ = 90°.
Volume	1772.3(4) Å <sup>3</sup>	
Z	4	
Density (calculated)	1.421 Mg/m <sup>3</sup>	
Absorption coefficient	3.344 mm <sup>-1</sup>	
F(000)	784	
Crystal size	0.12 x 0.10 x 0.04 mm <sup>3</sup>	
Crystal color/habit	colorless prism	
Theta range for data collection	4.00 to 68.04°.	
Index ranges	-10 ≤ h ≤ 10, -11 ≤ k ≤ 11, -25 ≤ l ≤ 26	
Reflections collected	22240	
Independent reflections	3206 [R(int) = 0.0501]	
Completeness to theta = 67.00°	99.5 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.8779 and 0.6897	
Refinement method	Full-matrix least-squares on F <sup>2</sup>	
Data / restraints / parameters	3206 / 0 / 235	
Goodness-of-fit on F <sup>2</sup>	1.071	
Final R indices [I > 2σ(I)]	R1 = 0.0371, wR2 = 0.0970	
R indices (all data)	R1 = 0.0452, wR2 = 0.1084	
Largest diff. peak and hole	0.310 and -0.334 e.Å <sup>-3</sup>	

Table 2. Atomic coordinates ( $\times 10^4$ ) and equivalent isotropic displacement parameters ( $\text{\AA}^2 \times 10^3$ ) for **6e**.  $U(\text{eq})$  is defined as one third of the trace of the orthogonalized  $U^{ij}$  tensor.

	x	y	z	U(eq)
C(1)	1585(2)	3162(2)	7392(1)	24(1)
C(2)	1762(2)	2214(2)	6934(1)	22(1)
C(3)	3419(2)	1838(2)	7003(1)	22(1)
C(4)	4355(2)	982(2)	6681(1)	25(1)
C(5)	5960(2)	902(2)	6872(1)	28(1)
C(6)	6667(2)	1673(2)	7381(1)	30(1)
C(7)	5777(2)	2536(2)	7705(1)	28(1)
C(8)	4151(2)	2608(2)	7512(1)	24(1)
C(9)	550(2)	1646(2)	6459(1)	22(1)
C(10)	-755(2)	2513(2)	6174(1)	22(1)
C(11)	-937(2)	3958(2)	6319(1)	25(1)
C(12)	-2202(2)	4738(2)	6049(1)	29(1)
C(13)	-3324(2)	4089(2)	5622(1)	32(1)
C(14)	-3163(2)	2694(2)	5460(1)	29(1)
C(15)	-1876(2)	1868(2)	5729(1)	24(1)
C(16)	-1637(2)	408(2)	5561(1)	24(1)
C(17)	-2644(2)	-348(2)	5113(1)	28(1)
C(18)	-2323(2)	-1713(2)	4960(1)	31(1)
C(19)	-971(2)	-2415(2)	5248(1)	29(1)
C(20)	26(2)	-1716(2)	5689(1)	28(1)
C(21)	-292(2)	-307(2)	5850(1)	23(1)
C(22)	5964(3)	4343(2)	3493(1)	35(1)
N(1)	3003(2)	3388(2)	7742(1)	25(1)
N(2)	758(2)	324(2)	6302(1)	23(1)
Cl(1)	7370(1)	5003(1)	4080(1)	37(1)
Cl(2)	5118(1)	2730(1)	3719(1)	33(1)



Table 3. Bond lengths [ $\text{\AA}$ ] and angles [ $^\circ$ ] for **6e**.

C(1)-N(1)	1.365(2)	C(12)-H(12)	0.9500
C(1)-C(2)	1.378(3)	C(13)-C(14)	1.370(3)
C(1)-H(1)	0.9500	C(13)-H(13)	0.9500
C(2)-C(3)	1.448(3)	C(14)-C(15)	1.411(3)
C(2)-C(9)	1.476(2)	C(14)-H(14)	0.9500
C(3)-C(4)	1.399(3)	C(15)-C(16)	1.443(3)
C(3)-C(8)	1.417(3)	C(16)-C(21)	1.409(3)
C(4)-C(5)	1.382(3)	C(16)-C(17)	1.417(3)
C(4)-H(4)	0.9500	C(17)-C(18)	1.363(3)
C(5)-C(6)	1.410(3)	C(17)-H(17)	0.9500
C(5)-H(5)	0.9500	C(18)-C(19)	1.407(3)
C(6)-C(7)	1.381(3)	C(18)-H(18)	0.9500
C(6)-H(6)	0.9500	C(19)-C(20)	1.377(3)
C(7)-C(8)	1.400(3)	C(19)-H(19)	0.9500
C(7)-H(7)	0.9500	C(20)-C(21)	1.407(3)
C(8)-N(1)	1.377(3)	C(20)-H(20)	0.9500
C(9)-N(2)	1.308(3)	C(21)-N(2)	1.387(2)
C(9)-C(10)	1.455(2)	C(22)-Cl(1)	1.762(2)
C(10)-C(11)	1.408(3)	C(22)-Cl(2)	1.780(2)
C(10)-C(15)	1.418(3)	C(22)-H(22A)	0.9900
C(11)-C(12)	1.375(3)	C(22)-H(22B)	0.9900
C(11)-H(11)	0.9500	N(1)-H(1A)	0.8800
C(12)-C(13)	1.395(3)		
N(1)-C(1)-C(2)	110.15(17)	C(5)-C(4)-H(4)	120.4
N(1)-C(1)-H(1)	124.9	C(3)-C(4)-H(4)	120.4
C(2)-C(1)-H(1)	124.9	C(4)-C(5)-C(6)	121.20(19)
C(1)-C(2)-C(3)	106.44(15)	C(4)-C(5)-H(5)	119.4
C(1)-C(2)-C(9)	128.86(17)	C(6)-C(5)-H(5)	119.4
C(3)-C(2)-C(9)	124.70(16)	C(7)-C(6)-C(5)	121.02(18)
C(4)-C(3)-C(8)	118.90(17)	C(7)-C(6)-H(6)	119.5
C(4)-C(3)-C(2)	134.83(16)	C(5)-C(6)-H(6)	119.5
C(8)-C(3)-C(2)	106.22(16)	C(6)-C(7)-C(8)	117.60(17)
C(5)-C(4)-C(3)	119.13(17)	C(6)-C(7)-H(7)	121.2

C(8)-C(7)-H(7)	121.2	C(18)-C(19)-H(19)	120.3
N(1)-C(8)-C(7)	129.81(17)	C(19)-C(20)-C(21)	120.52(18)
N(1)-C(8)-C(3)	108.05(16)	C(19)-C(20)-H(20)	119.7
C(7)-C(8)-C(3)	122.13(18)	C(21)-C(20)-H(20)	119.7
N(2)-C(9)-C(10)	122.52(16)	N(2)-C(21)-C(20)	117.26(17)
N(2)-C(9)-C(2)	115.31(16)	N(2)-C(21)-C(16)	122.38(18)
C(10)-C(9)-C(2)	122.14(17)	C(20)-C(21)-C(16)	120.36(17)
C(11)-C(10)-C(15)	119.13(17)	Cl(1)-C(22)-Cl(2)	110.63(11)
C(11)-C(10)-C(9)	122.74(16)	Cl(1)-C(22)-H(22A)	109.5
C(15)-C(10)-C(9)	118.13(17)	Cl(2)-C(22)-H(22A)	109.5
C(12)-C(11)-C(10)	121.13(18)	Cl(1)-C(22)-H(22B)	109.5
C(12)-C(11)-H(11)	119.4	Cl(2)-C(22)-H(22B)	109.5
C(10)-C(11)-H(11)	119.4	H(22A)-C(22)-H(22B)	108.1
C(11)-C(12)-C(13)	119.5(2)	C(1)-N(1)-C(8)	109.13(15)
C(11)-C(12)-H(12)	120.2	C(1)-N(1)-H(1A)	125.4
C(13)-C(12)-H(12)	120.2	C(8)-N(1)-H(1A)	125.4
C(14)-C(13)-C(12)	120.80(18)	C(9)-N(2)-C(21)	120.11(16)
C(14)-C(13)-H(13)	119.6		
C(12)-C(13)-H(13)	119.6		
C(13)-C(14)-C(15)	120.95(18)		
C(13)-C(14)-H(14)	119.5		
C(15)-C(14)-H(14)	119.5		
C(14)-C(15)-C(10)	118.40(18)		
C(14)-C(15)-C(16)	122.83(17)		
C(10)-C(15)-C(16)	118.76(16)		
C(21)-C(16)-C(17)	117.59(18)		
C(21)-C(16)-C(15)	117.99(16)		
C(17)-C(16)-C(15)	124.39(17)		
C(18)-C(17)-C(16)	121.54(18)		
C(18)-C(17)-H(17)	119.2		
C(16)-C(17)-H(17)	119.2		
C(17)-C(18)-C(19)	120.50(17)		
C(17)-C(18)-H(18)	119.7		
C(19)-C(18)-H(18)	119.7		
C(20)-C(19)-C(18)	119.48(19)		
C(20)-C(19)-H(19)	120.3		

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ( $\text{\AA}^2 \times 10^3$ ) for **6e**. The anisotropic displacement factor exponent takes the form:  $-2\pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U <sup>11</sup>	U <sup>22</sup>	U <sup>33</sup>	U <sup>23</sup>	U <sup>13</sup>	U <sup>12</sup>
C(1)	26(1)	25(1)	20(1)	2(1)	0(1)	0(1)
C(2)	24(1)	21(1)	19(1)	2(1)	0(1)	0(1)
C(3)	26(1)	21(1)	18(1)	4(1)	-2(1)	-2(1)
C(4)	28(1)	26(1)	20(1)	3(1)	1(1)	0(1)
C(5)	27(1)	32(1)	25(1)	4(1)	5(1)	2(1)
C(6)	22(1)	38(1)	29(1)	7(1)	-1(1)	-4(1)
C(7)	28(1)	32(1)	23(1)	2(1)	-4(1)	-6(1)
C(8)	29(1)	23(1)	21(1)	2(1)	1(1)	-4(1)
C(9)	22(1)	26(1)	17(1)	2(1)	2(1)	-1(1)
C(10)	21(1)	26(1)	18(1)	4(1)	3(1)	-1(1)
C(11)	24(1)	28(1)	21(1)	2(1)	3(1)	1(1)
C(12)	30(1)	29(1)	28(1)	4(1)	5(1)	6(1)
C(13)	27(1)	43(1)	26(1)	5(1)	0(1)	11(1)
C(14)	25(1)	39(1)	21(1)	1(1)	-2(1)	2(1)
C(15)	23(1)	31(1)	17(1)	4(1)	4(1)	0(1)
C(16)	22(1)	30(1)	18(1)	2(1)	2(1)	-4(1)
C(17)	25(1)	36(1)	23(1)	1(1)	-2(1)	-4(1)
C(18)	30(1)	37(1)	24(1)	-3(1)	-1(1)	-12(1)
C(19)	37(1)	25(1)	24(1)	-1(1)	4(1)	-6(1)
C(20)	31(1)	28(1)	23(1)	2(1)	0(1)	-1(1)
C(21)	26(1)	26(1)	17(1)	2(1)	1(1)	-4(1)
C(22)	47(1)	31(1)	28(1)	1(1)	7(1)	1(1)
N(1)	29(1)	25(1)	20(1)	-4(1)	-1(1)	-3(1)
N(2)	25(1)	24(1)	18(1)	1(1)	-1(1)	0(1)
Cl(1)	34(1)	35(1)	42(1)	-1(1)	5(1)	-4(1)
Cl(2)	36(1)	27(1)	35(1)	-3(1)	3(1)	2(1)

Table 5. Hydrogen coordinates ( $\times 10^4$ ) and isotropic displacement parameters ( $\text{\AA}^2 \times 10^3$ )  
for **6e**.

	x	y	z	U(eq)
H(1)	617	3595	7456	29
H(4)	3893	464	6336	30
H(5)	6598	318	6656	34
H(6)	7773	1597	7502	36
H(7)	6252	3063	8046	34
H(11)	-173	4402	6609	29
H(12)	-2311	5711	6152	35
H(13)	-4210	4622	5441	38
H(14)	-3930	2278	5163	35
H(17)	-3564	107	4914	34
H(18)	-3017	-2193	4657	37
H(19)	-748	-3364	5139	35
H(20)	936	-2189	5887	33
H(22A)	6477	4169	3128	42
H(22B)	5122	5061	3390	42
H(1A)	3160	3944	8062	30