Nickel-Catalyzed Alkyne Annulation by Anilines: Versatile Indole Synthesis by C–H/N–H Functionalization

Weifeng Song, Lutz Ackermann*

Institut für Organische und Biomolekulare Chemie

Georg-August-Universität

Tammannstrasse 2, 37077 Göttingen (Germany)

Fax: (+49)551-39-6777 E-mail: Lutz.Ackermann@chemie.uni-goettingen.de

Contents

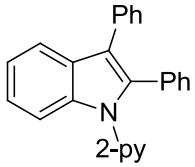
General remarks

Catalytic reactions were carried out under a N_2 atmosphere using pre-dried glassware. The following starting materials were prepared according to modified literature procedures: *N*-phenyl pyridine **1a**,[1] *N*-aryl pyrimidines **1b**–**1o**,[2] **1l**,[1] $[D]_5$-**1b**,[3] Diarylalkynes **2b**–**2d**[4] and **2f**.[2] Other chemicals were obtained from commercial sources, and were used without further purification. Yields refer to isolated compounds, estimated to be >95 % pure as determined by ^{1}H-NMR and GC. Flash chromatography: Macherey-Nagel silica gel 60 (70-230 mesh). NMR: Spectra were recorded on a Varian-NMR 300 and a Varian-NMR 500 instrument in the solvent indicated; chemical shifts (δ) are provided in ppm. All IR spectra were recorded on a Bruker FT-IR Alpha device. MS: EI-MS: Finnigan MAT 95, 70eV; ESI-MS: Finnigan LCQ. High resolution mass spectrometry (HR-MS): APEX IV 7T FTICR, Bruker Daltonic. M.p.: StuartR® melting point apparatus SMP3, Barlworld Scientific, values are uncorrected.

Represenatative Procedure: Nickel-catalyzed Alkyne Annulation by Anilines 1.

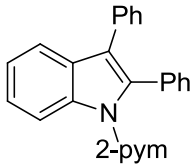
1a (85.5 mg, 0.50 mmol), **2a** (446 mg, 2.50 mmol), $Ni(cod)_2$ (13.8 mg, 10.0 mol %), and dppf (55.4 mg, 20.0 mol %) were stirred at 160 ℃ for 20 h in a sealed tube. After cooling the reaction mixture to ambient temperature, the crude product was purified by column chromatography on silica gel (*n*-hexane/EtOAc: 10:1→5:1) to yield **3aa** as a white solid (142 mg, 82%).

2,3-Diphenyl-1-(pyridin-2-yl)-1*H*-indole (3aa)



The general procedure was followed using **1a** (85.5 mg, 0.50 mmol) and **2a** (446 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→5:1) **3aa** (142 mg, 82%) was obtained as a white solid (m.p. 159–160 ℃). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.61 (ddd, J = 4.8, 2.0, 0.9 Hz, 1H), 7.78–7.65 (m, 2H), 7.59–7.52 (m, 1H), 7.42–7.06 (m, 13H), 6.82 (dt, J = 8.0, 0.9 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 151.8 (C_q), 149.1 (CH), 137.6 (CH), 137.4 (C_q), 135.9 (C_q), 134.6 (C_q), 131.7 (C_q), 130.9 (CH), 130.3 (CH), 128.3 (C_q), 128.2 (CH), 128.1 (CH), 127.4 (CH), 126.1 (CH), 123.4 (CH), 122.2 (CH), 121.6 (CH), 121.5 (CH), 119.6 (CH), 118.2 (C_q), 111.5 (CH). IR (neat): 3050, 1582, 1464, 1388, 1028, 696 cm^{-1}. MS (EI) m/z (relative intensity) 346 (100) [M^+], 267 (25), 165 (11), 78 (15), 51 (11). HR-MS (EI) m/z calcd for $[C_{25}H_{18}N_2]^+$ 346.1470, found 346.1478. The spectral data were in accordance with those reported in the literature.[1]

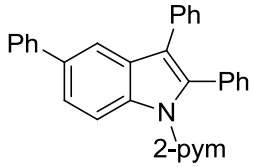
2,3-Diphenyl-1-(pyrimidin-2-yl)-1*H*-indole (3ba)



The general procedure was followed using **1b** (86 mg, 0.50 mmol) and **2a** (446 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→5:1) **3ba** (141 mg, 81%) was obtained as a white solid (m.p. 148–149 ℃). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.62 (d, J = 4.9 Hz, 2H), 8.28–8.20 (m, 1H), 7.83–7.76 (m, 1H), 7.47–7.29 (m, 7H), 7.24 (m, 5H), 7.01 (t, J = 4.9 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.9 (CH), 157.8 (C_q), 136.9 (C_q), 136.0 (C_q), 134.1 (C_q), 132.7 (C_q), 130.2 (CH), 130.1 (CH), 129.1 (C_q), 128.1 (CH), 127.7 (CH), 126.9 (CH), 126.3 (CH), 123.8 (CH), 122.1 (CH), 120.1 (C_q), 119.6 (CH), 117.4 (CH), 112.6 (CH). IR (neat): 3054, 1556, 1416, 1257, 1027, 847 cm^{-1}. MS (EI) m/z (relative intensity) 347 (100) [M^+], 267 (16), 165 (5), 77 (3), 53 (3). HR-MS (EI) m/z calcd for $[C_{24}H_{17}N_3]^+$ 347.1422, found 347.1417. The spectral data were in accordance with those

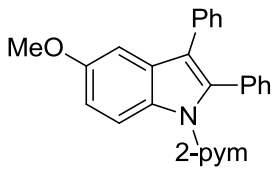
reported in the literature.[5]

2,3,5-Triphenyl-1-(pyrimidin-2-yl)-1*H*-indole (3ca)



The general procedure was followed using **1c** (124 mg, 0.50 mmol) and **2a** (446 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→5:1) **3ca** (144 mg, 68%) was obtained as a white solid (m.p. 207–208 ℃). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.64 (d, J = 4.9 Hz, 2H), 8.27 (dd, J = 8.6, 0.6 Hz, 1H), 7.94 (dd, J = 1.9, 0.6 Hz, 1H), 7.74–7.67 (m, 2H), 7.64 (dd, J = 8.6, 1.9 Hz, 1H), 7.51–7.31 (m, 8H), 7.27–7.16 (m, 5H), 7.06 (t, J = 4.9 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.0 (CH), 157.9 (C_q), 142.0 (C_q), 136.7 (C_q), 136.4 (C_q), 135.7 (C_q), 134.0 (C_q), 132.7 (C_q), 130.4 (CH), 130.2 (CH), 129.7 (C_q), 128.6 (CH), 128.3 (CH), 127.8 (CH), 127.3 (CH), 127.1 (CH), 126.6 (CH), 126.5 (CH), 123.5 (CH), 120.5 (C_q), 118.1 (CH), 117.6 (CH), 112.9 (CH). IR (neat): 3041, 1560, 1417, 1228, 915, 722 cm^{-1}. MS (EI) m/z (relative intensity) 423 (100) [M^+], 346 (10), 264 (3), 77 (3), 43 (2). HR-MS (EI) m/z calcd for $[C_{30}H_{21}N_3]^+$ 423.1735, found 423.1743.

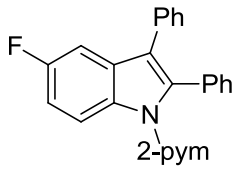
5-Methoxy-2,3-diphenyl-1-(pyrimidin-2-yl)-1*H*-indole (3da)



The general procedure was followed using **1d** (101 mg, 0.50 mmol) and **2a** (446 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→3:1) **3da** (127 mg, 67%) was obtained as a white solid (m.p. 186–187 ℃) . ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.59 (d, J = 4.9 Hz, 2H), 8.10 (dd, J = 9.0, 0.6 Hz, 1H), 7.36–7.23 (m, 5H), 7.21–7.11 (m, 6H), 7.03 (t, J = 4.9 Hz, 1H), 6.98 (dd, J = 9.0, 2.6 Hz, 1H), 3.83 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.9 (CH), 155.8 (C_q), 136.7 (C_q), 134.3 (C_q), 134.3 (C_q), 132.9 (C_q), 131.9 (C_q), 130.3 (CH), 130.2 (CH), 129.9 (C_q), 128.2 (CH), 127.7 (CH), 126.9 (CH), 126.4 (CH), 120.3 (C_q), 117.3 (CH), 113.7 (CH), 113.2 (CH), 101.6 (CH), 55.8 (CH_3). IR (neat): 3052, 2988,

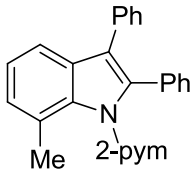
1572, 1420, 1161, 730 cm^{-1}. MS (EI) m/z (relative intensity) 377 (100) [M^+], 334 (35), 254 (10), 79 (4), 53 (3). HR-MS (EI) m/z calcd for $[C_{25}H_{19}N_3O]^+$ 377.1528, found 377.1522.

5-Fluoro-2,3-diphenyl-1-(pyrimidin-2-yl)-1*H*-indole (3ea)



The general procedure was followed using **1e** (95 mg, 0.50 mmol) and **2a** (446 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→5:1) **3ea** (149 mg, 82%) was obtained as a white solid (m.p. 176–177 ℃). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.60 (d, J = 4.9 Hz, 2H), 8.12 (dd, J = 9.0, 4.6 Hz, 1H), 7.40–7.09 (m, 11H), 7.09–7.02 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.2 (C_q, $^1J_{C\text{-}F}$ = 237.8 Hz), 158.0 (CH), 157.8 (C_q), 137.6 (C_q), 133.7 (C_q), 133.3 (C_q), 132.5 (C_q), 130.2 (CH), 130.1 (CH), 129.9 (C_q, $^3J_{C\text{-}F}$ = 10.0 Hz), 128.3 (CH), 127.8 (CH), 127.2 (CH), 126.6 (CH), 120.0 (C_q, $^4J_{C\text{-}F}$ = 4.6 Hz), 117.7 (CH), 113.8 (CH, $^3J_{C\text{-}F}$ = 9.4 Hz), 111.7 (CH, $^2J_{C\text{-}F}$ = 25.8 Hz), 104.8 (CH, $^2J_{C\text{-}F}$ = 24.4 Hz). ^{19}F-NMR (283 MHz, $CDCl_3$): δ = -(121.4–121.6) (m). IR (neat): 3051, 1561, 1418, 1178, 913, 731 cm^{-1}. MS (EI) m/z (relative intensity) 365 (100) [M^+], 285 (14), 181 (4), 79 (2), 53 (3). HR-MS (EI) m/z calcd for $[C_{24}H_{16}FN_3]^+$ 365.1328, found 365.1315.

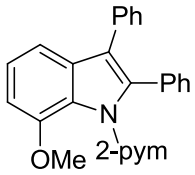
7-Methyl-2,3-diphenyl-1-(pyrimidin-2-yl)-1*H*-indole (3fa)



The general procedure was followed using **1f** (93 mg, 0.50 mmol) and **2a** (446 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→5:1) **3fa** (117 mg, 65%) was obtained as a white solid (m.p. 151–152 ℃). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.70 (d, J = 4.9 Hz, 2H), 7.63 (dt, J = 7.9, 0.6 Hz, 1H), 7.40–7.09 (m, 12H), 7.03 (d, J = 7.2 Hz, 1H), 1.96 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.7 (C_q), 157.9 (CH), 137.8 (C_q), 136.6 (C_q), 134.6 (C_q), 131.7 (C_q), 131.0 (CH), 130.3 (CH), 128.7 (C_q), 128.1 (CH), 127.7 (CH), 127.4 (CH), 126.1 (CH), 125.9 (CH), 121.5 (C_q), 121.4 (CH), 119.7 (CH), 118.0 (C_q),

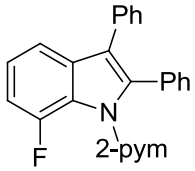
117.9 (CH), 19.4 (CH_3). IR (neat): 3024, 1560, 1442, 1231, 920, 786 cm^{-1}. MS (EI) m/z (relative intensity) 361 (100) [M^+], 284 (20), 178 (3), 77 (2), 53 (4). HR-MS (EI) m/z calcd for $[C_{25}H_{19}N_3]^+$ 361.1579, found 361.1566. The spectral data were in accordance with those reported in the literature.[2]

7-Methoxy-2,3-diphenyl-1-(pyrimidin-2-yl)-1*H*-indole (3ga)



The general procedure was followed using **1g** (101 mg, 0.50 mmol) and **2a** (446 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→3:1) **3ga** (125 mg, 66%) was obtained as a white solid (m.p. 190–191 ℃). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.68 (d, J = 4.9 Hz, 2H), 7.39–7.25 (m, 5H), 7.23–7.06 (m, 8H), 6.71 (d, J = 7.9 Hz, 1H), 3.62 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.7 (C_q), 157.6 (CH), 146.9 (C_q), 137.6 (C_q), 134.7 (C_q), 131.5 (C_q), 131.0 (CH), 130.2 (CH), 130.0 (C_q), 128.2 (CH), 127.8 (CH), 127.6 (C_q), 127.4 (CH), 126.0 (CH), 121.7 (CH), 119.3 (CH), 117.9 (C_q), 112.8 (CH), 105.0 (CH), 55.9 (CH_3). IR (neat): 3046, 1561, 1433, 1242, 924, 702 cm^{-1}. MS (EI) m/z (relative intensity) 377 (100) [M^+], 334 (32), 256 (25), 79 (6), 53 (6). HR-MS (EI) m/z calcd for $[C_{25}H_{19}N_3O]^+$ 377.1528, found 377.1523. The spectral data were in accordance with those reported in the literature.[2]

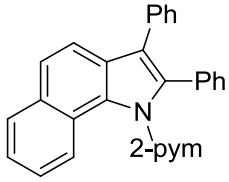
7-Fluoro-2,3-diphenyl-1-(pyrimidin-2-yl)-1*H*-indole (3ha)



The general procedure was followed using **1h** (95 mg, 0.50 mmol) and **2a** (446 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→5:1) **3ha** (131 mg, 72%) was obtained as a white solid (m.p. 201–202 ℃). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.69 (d, J = 4.9 Hz, 2H), 7.50 (dd, J = 8.0, 0.8 Hz, 1H), 7.38–7.06 (m, 12H), 6.96 (ddd, J = 12.1, 8.0, 0.8 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.3 (C_q), 158.2 (CH), 149.7 (C_q,

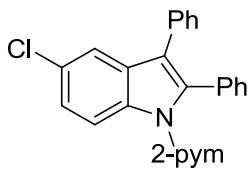
$^{1}J_{C\text{-}F}$ = 245.6 Hz), 137.9 (C_q), 134.0 (C_q), 132.0 (C_q, $^{3}J_{C\text{-}F}$ = 4.3 Hz), 131.2 (C_q), 130.8 (CH), 130.2 (CH), 128.3 (CH), 127.9 (CH), 127.7 (CH), 126.4 (CH), 124.9 (C_q, $^{2}J_{C\text{-}F}$ = 9.8 Hz), 121.6 (CH, $^{3}J_{C\text{-}F}$ = 7.0 Hz), 119.4 (CH), 118.7 (C_q, $^{4}J_{C\text{-}F}$ = 2.3 Hz), 115.6 (CH, $^{4}J_{C\text{-}F}$ = 3.3 Hz), 109.3 (CH, $^{2}J_{C\text{-}F}$ = 18.1 Hz). ^{19}F-NMR (283 MHz, $CDCl_3$): δ = -127.9 (dd, J = 12.2, 4.7 Hz). IR (neat): 3033, 1559, 1432, 1224, 979, 727 cm^{-1}. MS (EI) m/z (relative intensity) 365 (100) [M$^+$], 288 (20), 181 (4), 79 (5), 43 (18). HR-MS (EI) m/z calcd for $[C_{24}H_{16}FN_3]^+$ 365.1328, found 365.1318.

2,3-Diphenyl-1-(pyrimidin-2-yl)-1*H*-benzo[g]indole (3ia)



The general procedure was followed using **1i** (110 mg, 0.50 mmol) and **2a** (446 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→5:1) **3ia** (178 mg, 90%) was obtained as a white solid (m.p. 180–181 ℃). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.76 (d, J = 4.9 Hz, 2H), 7.99 (d, J = 8.0 Hz, 1H), 7.95 (d, J = 8.7 Hz, 1H), 7.71 (d, J = 8.7 Hz, 1H), 7.56–7.47 (m, 2H), 7.46–7.35 (m, 3H), 7.35–7.15 (m, 8H), 6.92 (d, J = 8.7 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.9 (C_q), 158.8 (CH), 137.0 (C_q), 134.3 (C_q), 131.9 (C_q), 131.4 (C_q), 131.3 (C_q), 131.1 (CH), 130.3 (CH), 129.1 (CH), 128.2 (CH), 127.7 (CH), 127.3 (CH), 126.1 (CH), 125.1 (CH), 124.8 (C_q), 123.6 (CH), 122.8 (CH), 122.0 (C_q), 120.6 (CH), 120.3 (CH), 119.3 (CH), 118.9 (C_q). IR (neat): 3047, 2948, 1560, 1267, 911, 736 cm^{-1}. MS (EI) m/z (relative intensity) 397 (100) [M$^+$], 317 (10), 213 (4), 98 (6), 43 (8). HR-MS (EI) m/z calcd for $[C_{28}H_{19}N_3]^+$ 397.1579, found 397.1574. The spectral data were in accordance with those reported in the literature.[2]

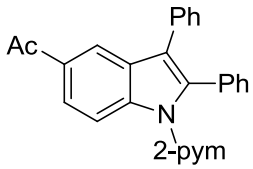
5-Chloro-2,3-diphenyl-1-(pyrimidin-2-yl)-1*H*-indole (3ja)



The general procedure was followed using **1j** (103 mg, 0.50 mmol) and **2a** (446 mg, 2.50

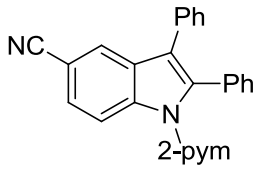
mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→5:1) **3ja** (104 mg, 55%) was obtained as a white solid (m.p. 169–170 ℃). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.61 (d, J = 4.9 Hz, 2H), 8.07 (d, J = 8.9 Hz, 1H), 7.64 (d, J = 2.0 Hz, 1H), 7.40–7.10 (m, 11H), 7.08 (t, J = 4.9 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.1 (CH), 157.7 (C_q), 137.3 (C_q), 135.3 (C_q), 133.5 (C_q), 132.4 (C_q), 130.4 (C_q), 130.2 (CH), 130.2 (CH), 128.3 (CH), 127.8 (CH), 127.7 (C_q), 127.3 (CH), 126.8 (CH), 123.9 (CH), 119.7 (C_q), 119.1 (CH), 117.8 (CH), 113.9 (CH). IR (neat): 3051, 1603, 1415, 1069, 956 cm^{-1}. MS (EI) m/z (relative intensity) 381 (100) [M^+], 345 (25), 172 (15), 79 (2), 53 (3). HR-MS (EI) m/z calcd for $[C_{24}H_{16}ClN_3]^+$ 381.1033, found 381.1035.

1-(2,3-Diphenyl-1-(pyrimidin-2-yl)-1*H*-indol-5-yl) ethanone (3ka)



The general procedure was followed using **1k** (107 mg, 0.50 mmol) and **2a** (446 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→5:1) **3ka** (132 mg, 68%) was obtained as a white solid (m.p. 171–172 ℃). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.63 (d, J = 4.9 Hz, 2H), 8.31 (d, J = 1.2 Hz, 1H), 8.11 (d, J = 8.8 Hz, 1H), 7.98 (dd, J = 8.9, 1.6 Hz, 1H), 7.45–7.02 (m, 11H), 2.64 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 198.0 (C_q), 158.2 (CH), 157.4 (C_q), 139.4 (C_q), 137.5 (C_q), 133.3 (C_q), 132.0 (C_q), 131.8 (C_q), 130.2 (CH), 130.1 (CH), 128.7 (C_q), 128.4 (CH), 127.8 (CH), 127.3 (CH), 126.7 (CH), 123.9 (CH), 121.2 (CH), 120.7 (C_q), 118.2 (CH), 112.4 (CH), 26.7 (CH_3). IR (neat): 3053, 1672, 1467, 1180, 948 cm^{-1}. MS (EI) m/z (relative intensity) 389 (100) [M^+], 346 (36), 172 (5), 79 (4), 43 (12). HR-MS (EI) m/z calcd for $[C_{26}H_{19}N_3O]^+$ 389.1528, found 389.1531.

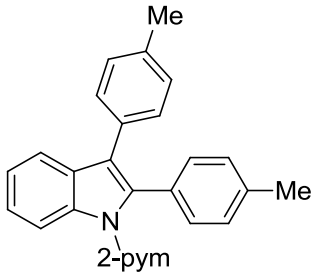
2,3-Diphenyl-1-(pyrimidin-2-yl)-1*H*-indole-5-carbonitrile (3la)



The general procedure was followed using **1l** (98 mg, 0.50 mmol) and **2a** (446 mg, 2.50 mmol).

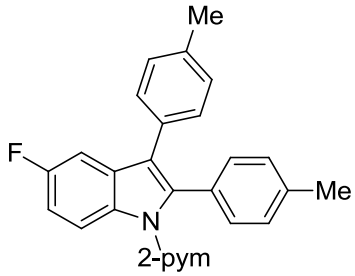
After purification by column chromatography (*n*-hexane/EtOAc 10:1→3:1) **3la** (130 mg, 70%) was obtained as a white solid (m.p. 193–194 ℃). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.65 (d, *J* = 4.9 Hz, 2H), 8.13 (dd, *J* = 8.6, 0.8 Hz, 1H), 8.02 (dd, *J* = 1.7, 0.7 Hz, 1H), 7.54 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.40–7.06 (m, 11H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.3 (CH), 157.2 (C_q), 138.4 (C_q), 138.2 (C_q), 132.7 (C_q), 131.5 (C_q), 130.1 (CH), 130.0 (CH), 128.9 (C_q), 128.4 (CH), 127.9 (CH), 127.7 (CH), 127.0 (CH), 126.5 (CH), 124.9 (CH), 120.2 (C_q), 119.7 (C_q), 118.5 (CH), 113.5 (CH), 105.1 (C_q). IR (neat): 3051, 2221, 1561, 1204, 971 cm^{-1}. MS (EI) m/z (relative intensity) 372 (100) [M^+], 292 (12), 186 (7), 79 (2), 53 (3). HR-MS (EI) m/z calcd for $[C_{25}H_{16}N_4]^+$ 372.1375, found 372.1364.

1-(Pyrimidin-2-yl)-2,3-di-*p*-tolyl-1*H*-indole (3bb)



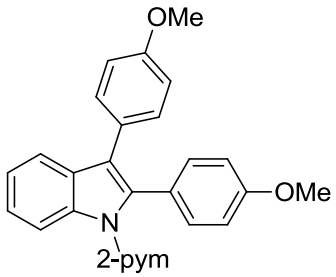
The general procedure was followed using **1b** (86 mg, 0.50 mmol) and **2b** (515 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→5:1) **3bb** (129 mg, 69%) was obtained as a white solid (m.p. 161–162 ℃). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.63 (d, *J* = 4.9 Hz, 2H), 8.20–8.12 (m, 1H), 7.80–7.67 (m, 1H), 7.41–7.25 (m, 4H), 7.23–6.99 (m, 7H), 2.41 (s, 3H), 2.33 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.0 (C_q), 157.9 (CH), 136.9 (C_q), 136.5 (C_q), 135.9 (C_q), 135.8 (C_q), 131.2 (C_q), 130.1 (CH), 130.0 (CH), 129.8 (C_q), 129.3 (C_q), 128.9 (CH), 128.5 (CH), 123.6 (CH), 122.0 (CH), 119.7 (C_q), 119.6 (CH), 117.4 (CH), 112.4 (CH), 21.2 (CH_3), 21.2 (CH_3). IR (neat): 3017, 2196, 1519, 1318, 980, 760 cm^{-1}. MS (EI) m/z (relative intensity) 375 (100) [M^+], 286 (10), 172 (3), 79 (2), 43 (3). HR-MS (EI) m/z calcd for $[C_{26}H_{21}N_3]^+$ 375.1735, found 375.1731.

5-Fluoro-1-(pyrimidin-2-yl)-2,3-di-*p*-tolyl-1*H*-indole (3eb)



The general procedure was followed using **1e** (90 mg, 0.50 mmol) and **2b** (515 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→5:1) **3eb** (132 mg, 67%) was obtained as a white solid (m.p. 141–142 ℃). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.62 (d, J = 4.9 Hz, 2H), 8.04 (q, J = 4.5 Hz, 1H), 7.30 (dd, J = 9.4, 2.6 Hz, 1H), 7.22–6.95 (m, 10H), 2.36 (s, 3H), 2.29 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.2 (C_q, $^{1}J_{C\text{-}F}$ = 236.3 Hz), 158.1 (CH), 157.9 (C_q), 137.5 (C_q), 136.9 (C_q), 136.1 (C_q), 133.3 (C_q), 130.8 (C_q), 131.1 (C_q, $^{3}J_{C\text{-}F}$ = 9.9 Hz), 130.0 (CH), 129.9 (CH), 129.6 (C_q), 129.1 (CH), 128.6 (CH), 119.7 (C_q, $^{4}J_{C\text{-}F}$ = 4.8 Hz), 117.6 (CH), 113.5 (CH, $^{3}J_{C\text{-}F}$ = 9.9 Hz), 111.4 (CH, $^{2}J_{C\text{-}F}$ = 25.8 Hz), 104.8 (CH, $^{2}J_{C\text{-}F}$ = 24.9 Hz), 21.3 (CH_3), 21.2 (CH_3). ^{19}F-NMR (283 MHz, $CDCl_3$): δ = -(121.8–122.2) (m). IR (neat): 2921, 1614, 1520, 1419, 1153, 976 cm^{-1}. MS (EI) m/z (relative intensity) 393 (100) [M^+], 302 (8), 181 (3), 79 (3), 43 (7). HR-MS (EI) m/z calcd for $[C_{26}H_{20}FN_3]^+$ 393.1641, found 393.1643.

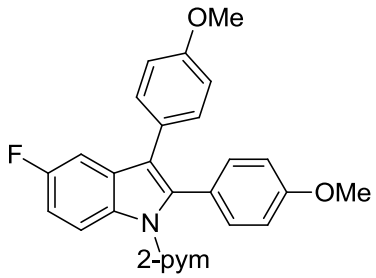
2,3-Bis(4-methoxyphenyl)-1-(pyrimidin-2-yl)-1*H*-indole (3bc)



The general procedure was followed using **1b** (86 mg, 0.50 mmol) and **2c** (595 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→3:1) **3bc** (136 mg, 67%) was obtained as a white solid (m.p. 166–167 ℃). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.63 (d, J = 4.9 Hz, 2H), 8.14–8.04 (m, 1H), 7.71–7.60 (m, 1H), 7.36–7.18 (m, 4H), 7.12–7.00 (m, 3H), 6.94–6.83 (m, 2H), 6.80–6.66 (m, 2H), 3.81 (s, 3H), 3.76 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.5 (C_q), 158.1 (C_q), 158.1 (C_q), 158.0 (CH), 136.8 (C_q), 135.6 (C_q), 131.4

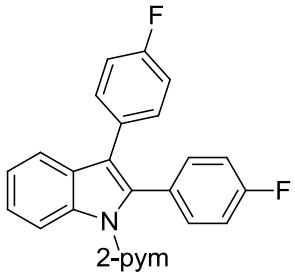
(CH), 131.3 (CH), 129.4 (C_q), 126.6 (C_q), 125.2 (C_q), 123.5 (CH), 122.0 (CH), 119.5 (CH), 119.3 (C_q), 117.4 (CH), 113.7 (CH), 113.3 (CH), 112.4 (CH), 55.1 (CH_3), 55.0 (CH_3). IR (neat): 2930, 1558, 1416, 1241, 1029, 727 cm^{-1}. MS (EI) m/z (relative intensity) 407 (100) [M^+], 392 (20), 241 (9), 79 (2), 43 (5). HR-MS (EI) m/z calcd for $[C_{26}H_{21}N_3O_2]^+$ 407.1634, found 407.1631.

5-Fluoro-2,3-bis(4-methoxyphenyl)-1-(pyrimidin-2-yl)-1*H*-indole (3ec)



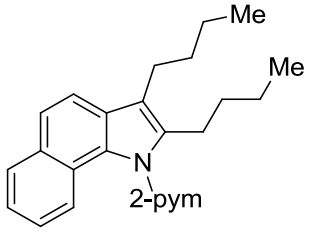
The general procedure was followed using **1e** (90 mg, 0.50 mmol) and **2c** (595 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→3:1) **3ec** (127 mg, 60%) was obtained as a white solid (m.p. 159–160 ℃). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.62 (d, J = 4.9 Hz, 2H), 8.02 (ddd, J = 9.0, 4.6, 0.4 Hz, 1H), 7.27 (ddd, J = 9.4, 2.6, 0.4 Hz, 1H), 7.24–7.17 (m, 2H), 7.08 (t, J = 4.9 Hz, 1H), 7.05–6.96 (m, 3H), 6.91–6.83 (m, 2H), 6.75–6.68 (m, 2H), 3.81 (s, 3H), 3.76 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.3 (C_q, $^1J_{C\text{-}F}$ = 237.2 Hz), 158.7 (C_q), 158.3 (C_q), 158.1 (CH), 158.0 (C_q), 137.2 (C_q), 133.2 (C_q), 131.4 (CH), 131.2 (CH), 130.2 (C_q, $^3J_{C\text{-}F}$ = 9.8 Hz), 126.2 (C_q), 125.0 (C_q), 119.2 (C_q, $^4J_{C\text{-}F}$ = 4.8 Hz), 117.6 (CH), 113.9 (CH), 113.5 (CH, $^3J_{C\text{-}F}$ = 8.9 Hz), 113.4 (CH), 111.4 (CH, $^2J_{C\text{-}F}$ = 25.1 Hz), 104.7 (CH, $^2J_{C\text{-}F}$ = 25.1 Hz), 55.2 (CH_3), 55.1 (CH_3). ^{19}F-NMR (283 MHz, $CDCl_3$): δ = -(121.7–122.2) (m). IR (neat): 2931, 1609, 1560, 1134, 975, 759 cm^{-1}. MS (EI) m/z (relative intensity) 425 (100) [M^+], 350 (8), 259 (9), 79 (2), 43 (5). HR-MS (EI) m/z calcd for $[C_{26}H_{20}FN_3O_2]^+$ 425.1540, found 425.1544.

2,3-Bis(4-fluorophenyl)-1-(pyrimidin-2-yl)-1*H*-indole (3bd)



The general procedure was followed using **1b** (86 mg, 0.50 mmol) and **2d** (536 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→5:1) **3bd** (109 mg, 57%) was obtained as a white solid (m.p. 199–200 ℃). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.63 (d, J = 4.9 Hz, 2H), 8.16 (dt, J = 8.1, 0.9 Hz, 1H), 7.62 (ddd, J = 7.9, 1.3, 0.7 Hz, 1H), 7.38–7.31 (m, 1H), 7.30–7.23 (m, 3H), 7.15–6.98 (m, 5H), 6.94-6.84 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.0 (C_q, $^{1}J_{C\text{-}F}$ = 247.7 Hz), 161.6 (C_q, $^{1}J_{C\text{-}F}$ = 245.8 Hz), 158.1 (CH), 157.8 (C_q), 136.8 (C_q), 135.1 (C_q), 131.9 (CH, $^{3}J_{C\text{-}F}$ = 8.2 Hz), 131.8 (CH, $^{3}J_{C\text{-}F}$ = 8.2 Hz), 129.9 (C_q, $^{4}J_{C\text{-}F}$ = 3.6 Hz), 129.0 (C_q), 128.8 (C_q, $^{4}J_{C\text{-}F}$ = 4.2 Hz), 124.1 (CH), 122.4 (CH), 129.5 (C_q), 119.4 (CH), 117.6 (CH), 115.3 (CH, $^{2}J_{C\text{-}F}$ = 21.2 Hz), 115.0 (CH, $^{2}J_{C\text{-}F}$ = 21.2 Hz), 112.8 (CH). ^{19}F-NMR (283 MHz, $CDCl_3$): δ = -(113.8–114.8) (m), -(115.3–116.3) (m). IR (neat): 3052, 1561, 1419, 1221, 946, 746 cm^{-1}. MS (EI) m/z (relative intensity) 383 (100) [M^+], 303 (14), 181 (8), 79 (3), 43 (5). HR-MS (EI) m/z calcd for $[C_{24}H_{15}F_2N_3]^+$ 383.1234, found 383.1231.

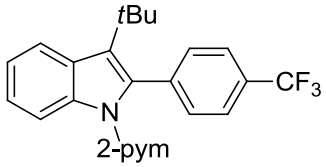
2,3-Di-*n*-butyl-1-(pyrimidin-2-yl)-1*H*-benzo[g]indole (3ie)



The general procedure was followed using **1i** (110 mg, 0.50 mmol) and **2e** (345 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 20:1→10:1) **3ie** (112 mg, 63%) was obtained as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.90 (d, J = 4.9 Hz, 2H), 7.89 (d, J = 8.5 Hz, 1H), 7.71 (d, J = 8.5 Hz, 1H), 7.60 (d, J = 8.5 Hz, 1H), 7.37–7.22 (m, 2H), 7.20–7.10 (m, 1H), 6.78 (d, J = 8.5 Hz, 1H), 2.91–2.72 (m, 4H), 1.80–1.61 (m, 2H), 1.58–1.40 (m, 2H), 1.40–1.17 (m, 4H), 0.99 (t, J = 7.3 Hz, 3H), 0.81 (t, J = 7.3 Hz, 3H).

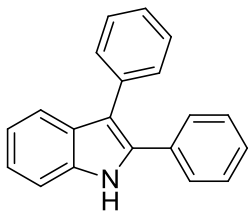
^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.2 (C_q), 159.1 (CH), 137.4 (C_q), 131.3 (C_q), 130.5 (C_q), 129.1 (CH), 126.4 (C_q), 124.5 (CH), 122.8 (CH), 122.0 (C_q), 121.9 (CH), 120.9 (CH), 119.8 (CH), 118.6 (CH), 116.2 (C_q), 33.3 (CH_2), 32.4 (CH_2), 24.6 (CH_2), 24.1 (CH_2), 22.8 (CH_2), 22.4 (CH_2), 14.1 (CH_3), 13.7 (CH_3). IR (neat): 2954, 1558, 1417, 1274, 926, 740 cm^{-1}. MS (EI) m/z (relative intensity) 357 (65) [M^+], 314 (100), 272 (78), 165 (6), 43 (7). HR-MS (EI) m/z calcd for $[C_{24}H_{27}N_3]^+$ 357.2205, found 357.2200.

3-(*tert*-Butyl)-1-(pyrimidin-2-yl)-2-{4-(trifluoromethyl)phenyl}-1*H*-indole (3bf)



The general procedure was followed using **1b** (86 mg, 0.50 mmol) and **2f** (565 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→5:1) **3bf** (108 mg, 55%) was obtained as a white solid (m.p. 178–179 ℃). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.47 (dd, J = 4.9, 0.9 Hz, 2H), 8.02–7.87 (m, 2H), 7.78 (s, 4H), 7.37–7.16 (m, 2H), 6.95 (td, J = 4.9, 0.9 Hz, 1H), 1.34 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.8 (CH), 157.3 (C_q), 139.7 (C_q), 136.9 (C_q), 132.8 (CH), 132.8 (C_q), 129.6 (C_q, $^2J_{C\text{-}F}$ = 32.6 Hz), 128.1 (C_q), 126.6 (C_q), 126.0 (C_q, $^1J_{C\text{-}F}$ = 271.3 Hz), 123.4 (CH, $^3J_{C\text{-}F}$ = 3.8 Hz), 123.2 (CH), 122.5 (CH), 121.0 (CH), 117.5 (CH), 112.4 (CH), 33.5 (C_q), 32.3 (CH_3). ^{19}F-NMR (283 MHz, $CDCl_3$): δ = -62.8 (s). IR (neat): 2955, 1619, 1421, 1106, 955 cm^{-1}. MS (EI) m/z (relative intensity) 395 (43) [M^+], 380 (100), 286 (14), 183 (20), 79 (3). HR-MS (EI) m/z calcd for $[C_{23}H_{20}F_3N_3]^+$ 395.1609, found 395.1619.

2,3-Diphenyl-1*H*-indole (4)

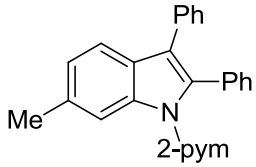


A mixture of **3ba** (174 mg, 0.50 mmol), NaOEt (102 mg, 1.50 mmol) and DMSO (2.0 mL) was stirred at 120 ℃ under a nitrogen atmosphere for 24 h. After cooling to ambient temperature, the reaction mixture was diluted with EtOAc (75 mL) and washed with brine (30

mL). The aqueous phase was extracted with EtOAc (2×30 mL), and the combined organic phase was dried over Na_2SO_4. After filtration and evaporation of the solvents in vacuum, the crude product was purified by column chromatography on silica gel (*n*-hexane/EtOAc 10:1) to yield **4** (124 mg, 92%) as a white solid (m.p. 120–121 ℃).

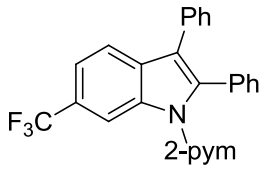
^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.19 (s_{br}, 1H), 7.70 (d, J = 7.9 Hz, 1H), 7.50–7.22 (m, 12H), 7.21–7.12 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 135.9 (C_q), 135.0 (C_q), 134.1 (C_q), 132.7 (C_q), 130.1 (CH), 128.8 (C_q), 128.7 (CH), 128.5 (CH), 128.2 (CH), 127.7 (CH), 126.2 (CH), 122.7 (CH), 120.4 (CH), 119.7 (CH), 115.1 (C_q), 110.9 (CH). IR (neat): 3055, 1504, 1250, 1147, 956, 737 cm^{-1}. MS (EI) m/z (relative intensity) 269 (100) [M^+], 165 (18), 105 (19), 77 (14), 51 (4). HR-MS (EI) m/z calcd for $[C_{20}H_{15}N]^+$ 269.1204, found 269.1199. The spectral data were in accordance with those reported in the literature.[6]

6-Methyl-2,3-diphenyl-1-(pyrimidin-2-yl)-1*H*-indole (3ma')



The general procedure was followed using **1m** (93 mg, 0.50 mmol) and **2a** (446 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→5:1) **3ma'** (110 mg, 61%) was obtained as a white solid (m.p. 154–155 ℃). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.65 (d, J = 4.9 Hz, 2H), 7.99 (s, 1H), 7.61 (d, J = 8.1 Hz, 1H), 7.39–7.11 (m, 11H), 7.06 (t, J = 4.9 Hz, 1H), 2.55 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.0 (C_q), 158.0 (CH), 137.3 (C_q), 135.4 (C_q), 134.3 (C_q), 133.8 (C_q), 132.9 (C_q), 130.3 (CH), 130.2 (CH), 128.1 (CH), 127.7 (CH), 127.0 (C_q), 126.8 (CH), 126.3 (CH), 123.7 (CH), 120.1 (C_q), 119.3 (CH), 117.4 (CH), 112.4 (CH), 21.9 (CH_3). IR (neat): 3025, 2916, 1556, 1418, 1196, 920 cm^{-1}. MS (EI) m/z (relative intensity) 361 (100) [M^+], 284 (9), 172 (6), 79 (5), 53 (5). HR-MS (EI) m/z calcd for $[C_{25}H_{19}N_3]^+$ 361.1579, found 361.1576.

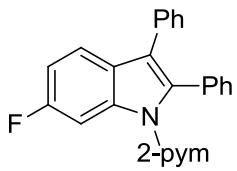
2,3-Diphenyl-1-(pyrimidin-2-yl)-6-(trifluoromethyl)-1*H*-indole (3na')



The general procedure was followed using **1n** (120 mg, 0.50 mmol) and **2a** (446 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→5:1) **3na'** (175 mg, 84%) was obtained as a white solid (m.p. 175–176 ℃). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.66 (dd, J = 4.9, 0.6 Hz, 2H), 8.44 (s, 1H), 7.76 (dd, J = 8.3, 0.6 Hz, 1H), 7.50 (ddd, J = 8.3, 1.0, 0.6 Hz, 1H), 7.39–7.03 (m, 11H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.3 (CH), 157.5 (C_q), 138.7 (C_q), 135.9 (C_q), 133.4 (C_q), 132.1 (C_q), 131.5 (C_q), 130.2 (CH), 130.2 (CH), 128.4 (CH), 127.9 (CH), 127.5 (CH), 126.9 (C_q, $^{1}J_{C\text{-}F}$ = 272.0 Hz), 126.8 (CH), 125.6 (C_q, $^{2}J_{C\text{-}F}$ = 32.1 Hz), 120.1 (CH), 120.0 (C_q), 118.8 (CH, $^{3}J_{C\text{-}F}$ = 3.6 Hz), 118.1 (CH), 110.4 (CH, $^{3}J_{C\text{-}F}$ = 4.3 Hz). ^{19}F-NMR (283 MHz, $CDCl_3$): δ = -60.6 (s). IR (neat): 3064, 2920, 1564, 1420, 1157, 917 cm^{-1}. MS (EI) m/z (relative intensity) 415 (100) [M^+], 338 (11), 239 (4), 79 (7), 53 (8). HR-MS (EI) m/z calcd for $[C_{25}H_{16}F_3N_3]^+$ 415.1296, found 415.1284.

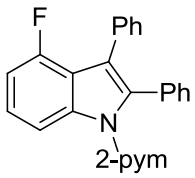
6-Fluoro-2,3-diphenyl-1-(pyrimidin-2-yl)-1*H*-indole (3oa') and
4-Fluoro-2,3-diphenyl-1-(pyrimidin-2-yl)-1*H*-indole (3oa")

The general procedure was followed using **1o** (95 mg, 0.50 mmol) and **2a** (446 mg, 2.50 mmol). After purification by column chromatography (*n*-hexane/EtOAc 10:1→5:1) **3oa'** (78 mg, 43%) was obtained as a white solid (m.p. 160–161 ℃) and **3oa"** (52 mg, 29%) was obtained as a white solid (m.p. 124–125 ℃).



6-Fluoro-2,3-diphenyl-1-(pyrimidin-2-yl)-1*H*-indole (3oa'): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.61 (d, J = 4.9 Hz, 2H), 7.91 (dd, J = 10.4, 2.3 Hz, 1H), 7.59 (dd, J = 8.7, 5.7 Hz, 1H), 7.38–7.10 (m, 10H), 7.07 (t, J = 4.9 Hz, 1H), 7.01 (td, J = 9.0, 2.3 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.7 (C_q, $^{1}J_{C\text{-}F}$ = 237.2 Hz), 158.1 (CH), 157.8 (C_q), 137.0 (C_q, $^{3}J_{C\text{-}F}$ =

12.5 Hz), 136.3 (C_q, $^4J_{C\text{-}F}$ = 4.2 Hz), 133.8 (C_q), 132.6 (C_q), 130.2 (CH), 130.1 (CH), 128.3 (CH), 127.8 (CH), 127.1 (CH), 126.6 (CH), 125.7 (C_q), 120.4 (CH, $^3J_{C\text{-}F}$ = 10.4 Hz), 120.1 (C_q), 117.7 (CH), 110.5 (CH, $^2J_{C\text{-}F}$ = 24.4 Hz), 99.8 (CH, $^2J_{C\text{-}F}$ = 28.2 Hz). ^{19}F-NMR (283 MHz, $CDCl_3$): δ = -(118.1–118.4) (m). IR (neat): 3056, 1979, 1562, 1416, 1122, 974 cm^{-1}. MS (EI) m/z (relative intensity) 365 (100) [M^+], 285 (14), 172 (3), 79 (2), 53 (3). HR-MS (EI) m/z calcd for $[C_{24}H_{16}FN_3]^+$ 365.1328, found 365.1327.



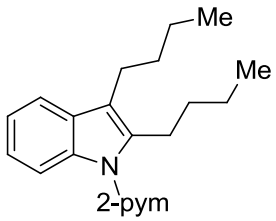
4-Fluoro-2,3-diphenyl-1-(pyrimidin-2-yl)-1*H*-indole (3oa"): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.63 (d, *J* = 4.9 Hz, 2H), 7.86 (dd, *J* = 8.3, 0.7 Hz, 1H), 7.37-7.05 (m, 12H), 6.90 (ddd, *J* = 11.0, 7.9, 0.7 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.2 (CH), 157.8 (C_q), 156.7 (C_q, $^1J_{C\text{-}F}$ = 246.7 Hz), 139.0 (C_q, $^3J_{C\text{-}F}$ = 9.6 Hz), 136.6 (C_q, $^4J_{C\text{-}F}$ = 1.4 Hz), 134.1 (C_q, $^4J_{C\text{-}F}$ = 1.4 Hz), 132.1 (C_q), 131.0 (CH, $J_{C\text{-}F}$ = 2.1 Hz), 130.3 (CH), 127.7 (CH), 127.5 (CH), 127.2 (CH), 126.5 (CH), 124.0 (CH, $^3J_{C\text{-}F}$ = 8.1 Hz), 118.1 (CH), 117.9 (C_q, $^3J_{C\text{-}F}$ = 3.1 Hz), 117.5 (C_q, $^2J_{C\text{-}F}$ = 17.8 Hz), 108.4 (CH, $^4J_{C\text{-}F}$ = 3.9 Hz), 107.7 (CH, $^2J_{C\text{-}F}$ = 19.5 Hz). ^{19}F-NMR (283 MHz, $CDCl_3$): δ = -(118.5–119.5) (m). IR (neat): 3036, 1562, 1433, 1264, 973, 761 cm^{-1}. MS (EI) m/z (relative intensity) 365 (100) [M^+], 285 (15), 182 (2), 79 (3), 53 (4). HR-MS (EI) m/z calcd for $[C_{24}H_{16}FN_3]^+$ 365.1328, found 365.1314.

Competition Experiments

Intermolecular competition experiment between alkynes 2a and 2e (Scheme 6a):

1b (86 mg, 0.50 mmol), **2a** (267 mg, 1.50 mmol), **2e** (207 mg, 1.50 mmol), $Ni(cod)_2$ (13.8 mg, 10.0 mol %), and dppf (55.4 mg, 20.0 mol %) were stirred at 160 ℃ for 20 h in a sealed tube. After cooling the reaction mixture to ambient temperature, the crude product was purified by column chromatography on silica gel (*n*-hexane/EtOAc: 10:1→5:1) to yield **3ba** (77 mg, 44%) and **3be** (50 mg, 32%).

2,3-Di-*n*-butyl-1-(pyrimidin-2-yl)-1*H*-indole (3be)



^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.76 (d, J = 4.9 Hz, 2H), 8.22–8.13 (m, 1H), 7.55–7.46 (m, 1H), 7.22–7.13 (m, 2H), 7.10 (t, J = 4.9 Hz, 1H), 3.15 (t, J = 7.7 Hz, 2H), 2.73 (t, J = 7.7 Hz, 2H), 1.70–1.23 (m, 8H), 0.95 (t, J = 7.3 Hz, 3H), 0.84 (t, J = 7.3 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.4 (C_q), 158.1 (CH), 137.3 (C_q), 136.4 (C_q), 130.0 (C_q), 122.4 (CH), 121.2 (CH), 118.1 (CH), 117.7 (C_q), 116.7 (CH), 113.4 (CH), 32.9 (CH_2), 32.3 (CH_2), 25.6 (CH_2), 24.1 (CH_2), 22.9 (CH_2), 22.6 (CH_2), 14.1 (CH_3), 13.8 (CH_3). IR (neat): 2954, 2927, 1558, 1419, 1224, 988 cm^{-1}. MS (EI) m/z (relative intensity) 307 (75) [M^+], 364 (100), 222 (88), 79 (8), 43 (12). HR-MS (EI) m/z calcd for $[C_{20}H_{25}N_3]^+$ 307.2048, found 307.2057.

Intermolecular competition experiment between anilines 1d and 1e (Scheme 6b):

1d (101 mg, 0.50 mmol), **1e** (90 mg, 0.50 mmol), **2a** (178 mg, 1.00 mmol), $Ni(cod)_2$ (13.8 mg, 10.0 mol %), and dppf (55.4 mg, 20.0 mol %) were stirred at 160 ℃ for 20 h in a sealed tube. After cooling the reaction mixture to ambient temperature, the crude product was purified by column chromatography on silica gel (*n*-hexane/EtOAc: 10:1→3:1) to yield **3da** (22 mg, 23%) and **3ea** (30 mg, 32%).

Deuterium-Labelling Experiment

$[D]_5$-**1b** (88 mg, 0.50 mmol), **2a** (345 mg, 2.50 mmol), $Ni(cod)_2$ (13.8 mg, 10.0 mol %), and dppf (55.4 mg, 20.0 mol %) were stirred at 160 ℃ for 3 h in a sealed tube. After cooling the reaction mixture to ambient temperature, the crude product was purified by column chromatography on silica gel (*n*-hexane/EtOAc: 20:1→10:1) to yield $[D]_n$-**3be** (23 mg, 15%) as a colorless oil with 22% H incorporation into the *ortho*-position, as estimated by ^{1}H NMR spectroscopy. Additionally, $[D]_n$-**1b** (72 mg, 82%) was recovered as a white solid with 34% H incorporation into the *ortho*-positions, as estimated by ^{1}H NMR spectroscopy.

References

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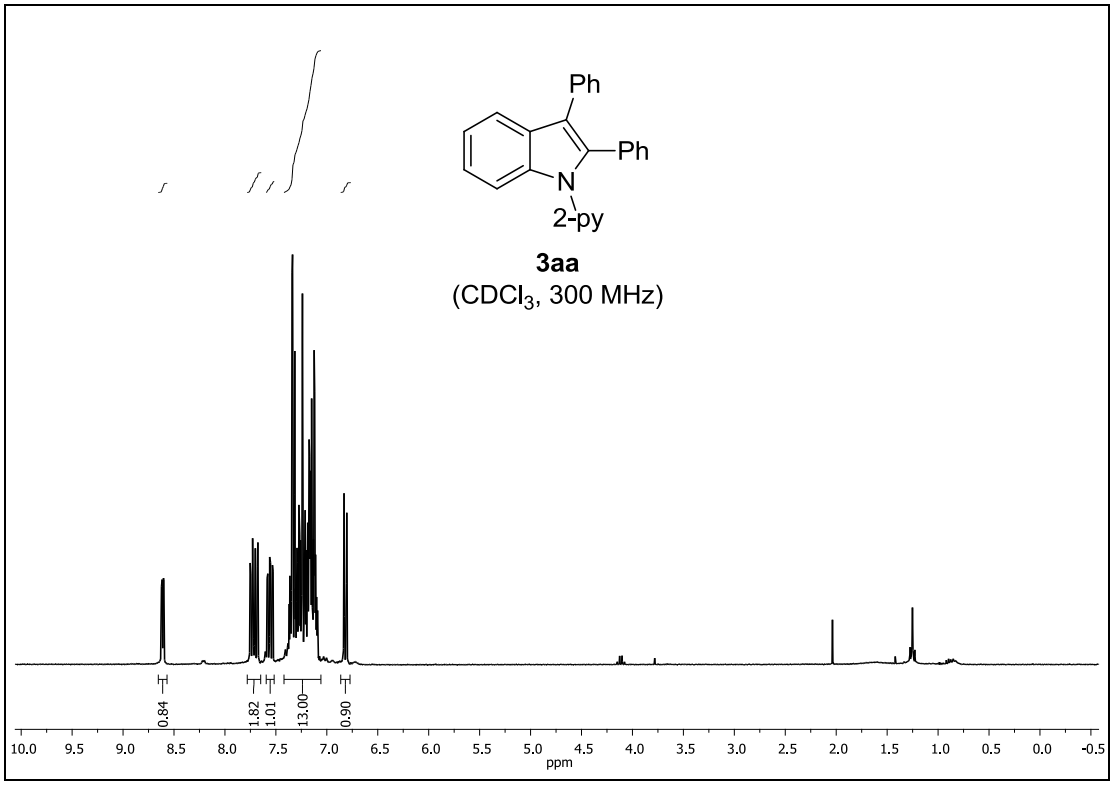
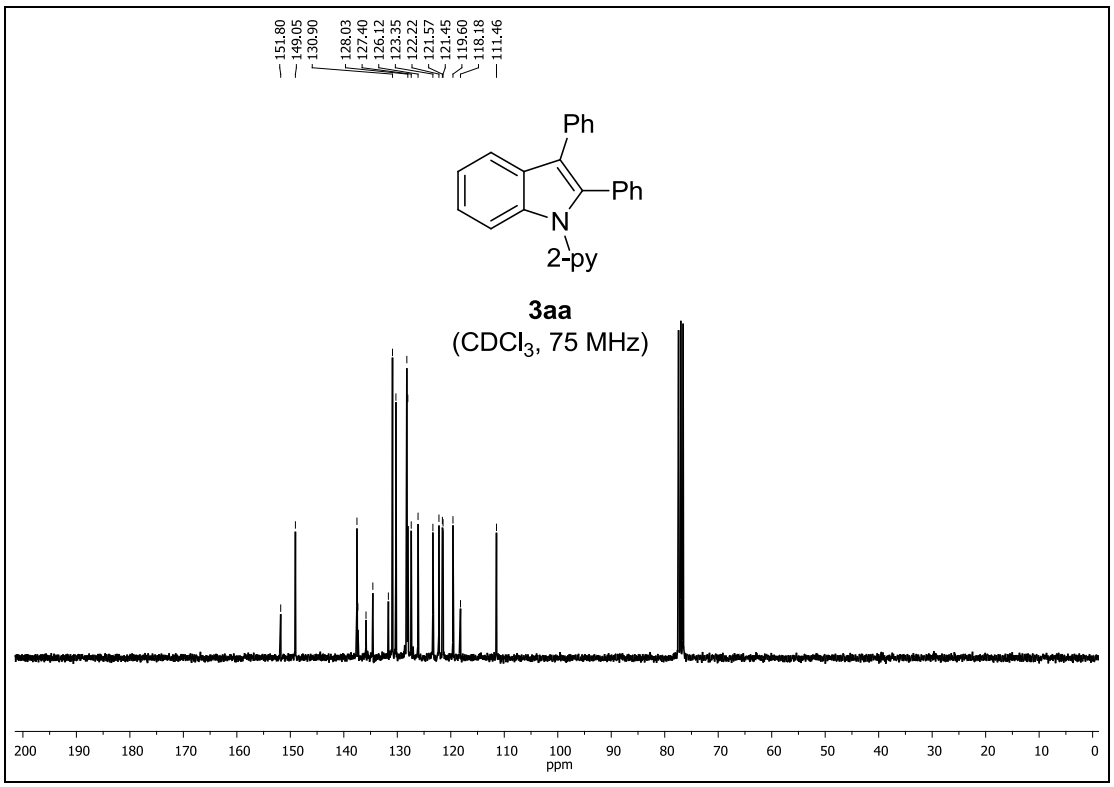
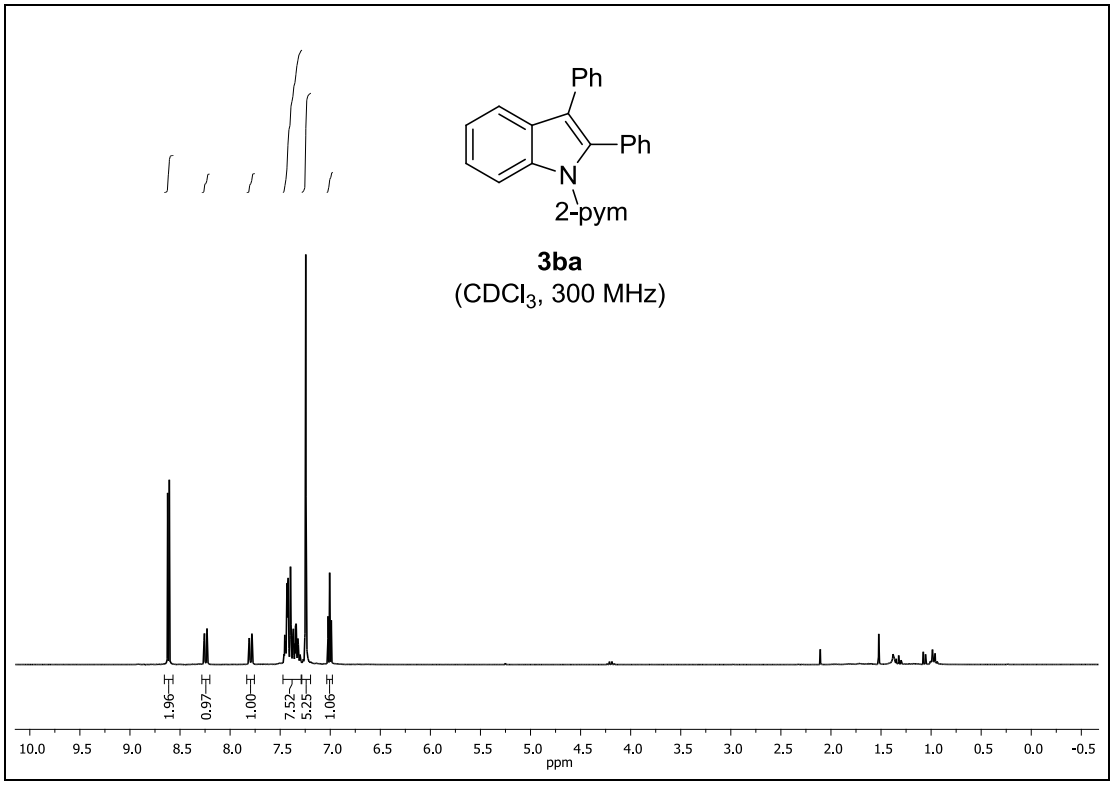
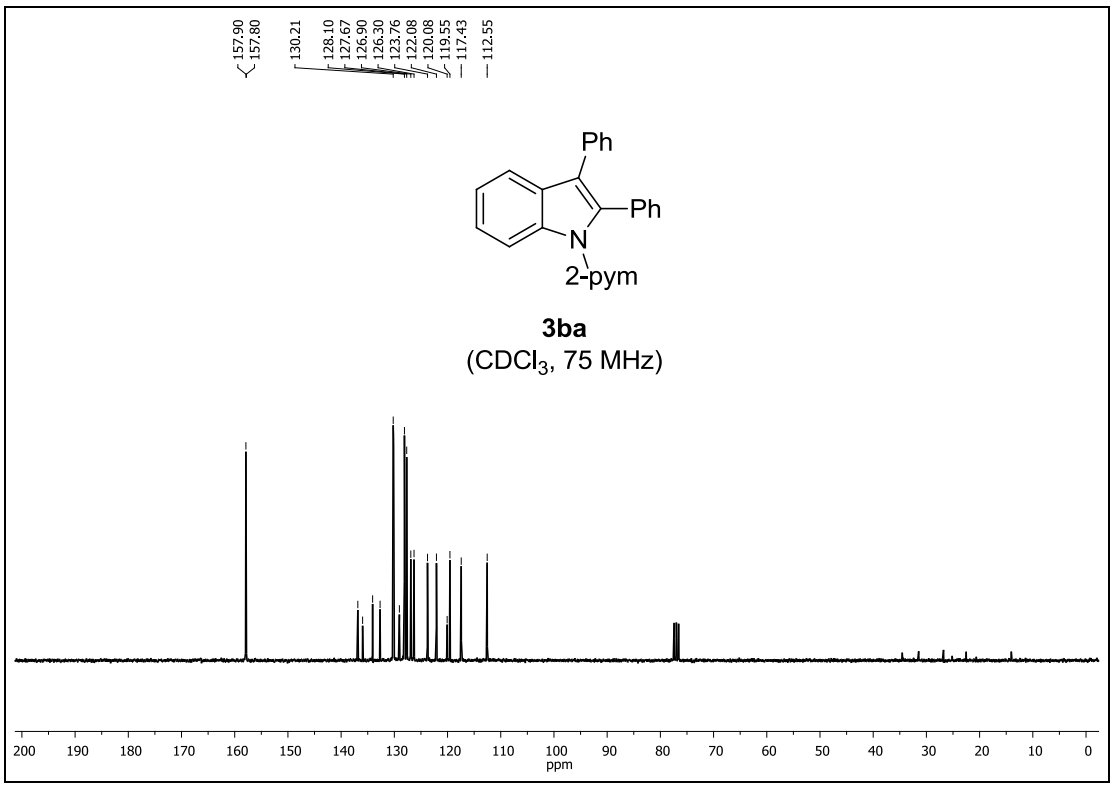


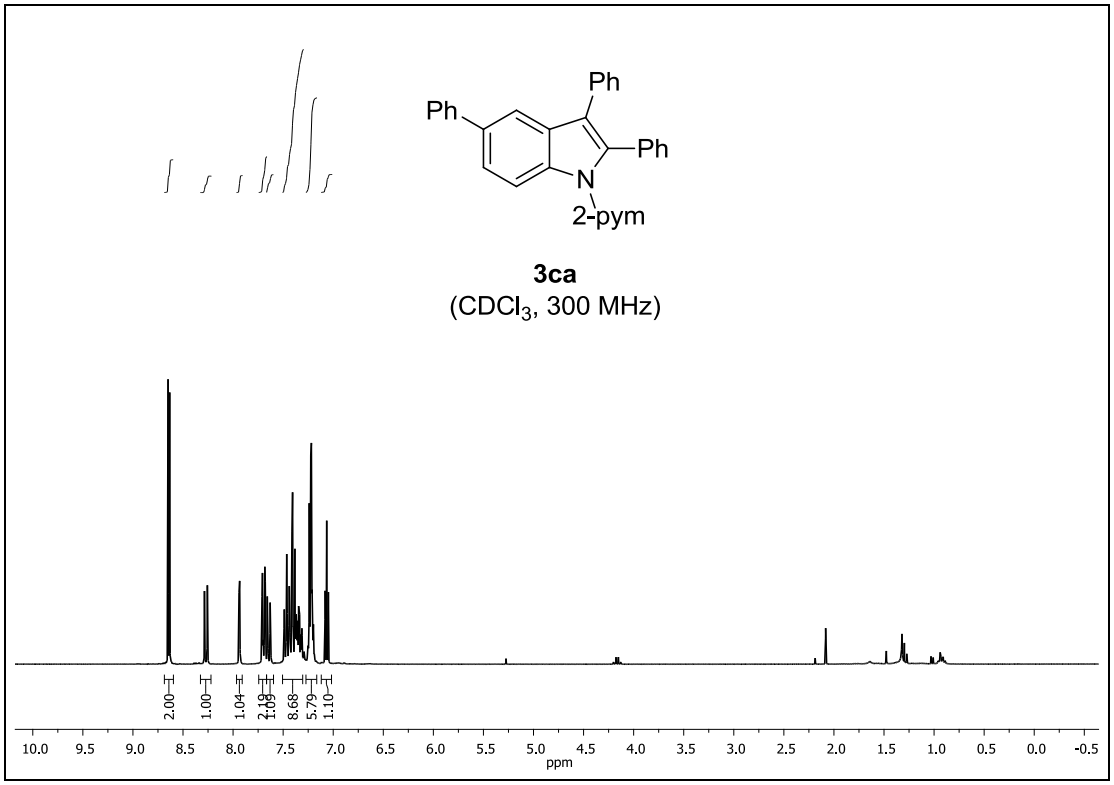


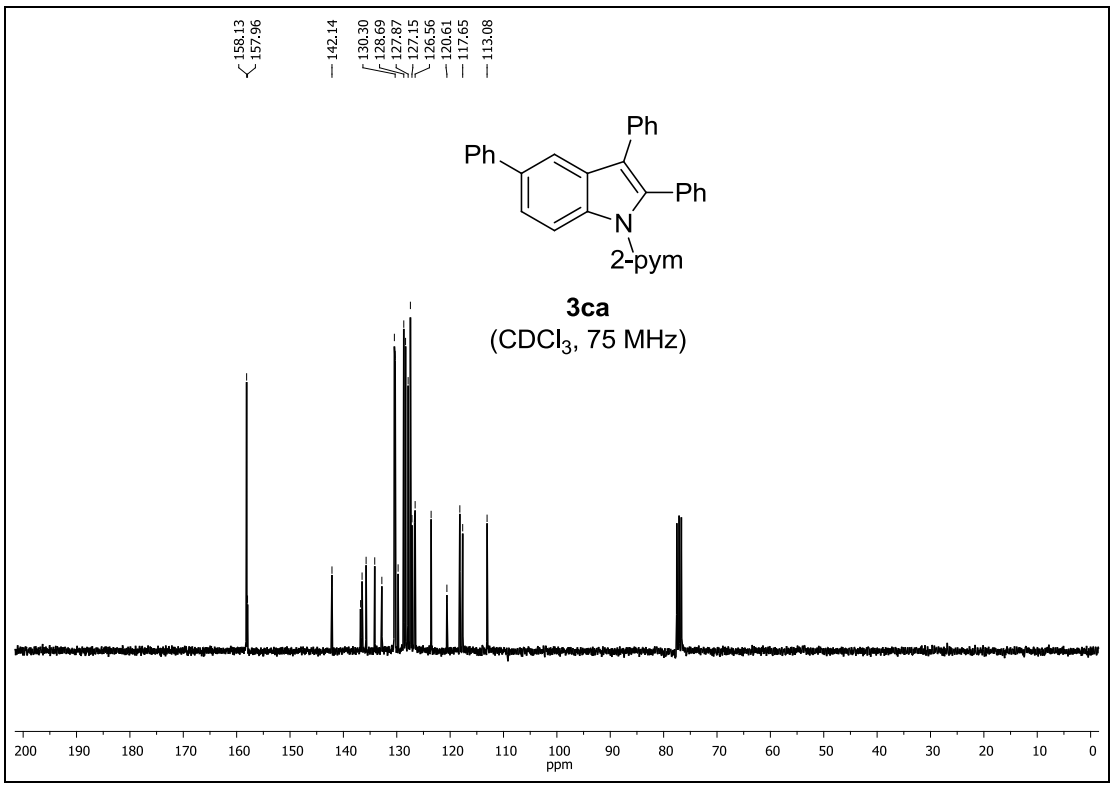


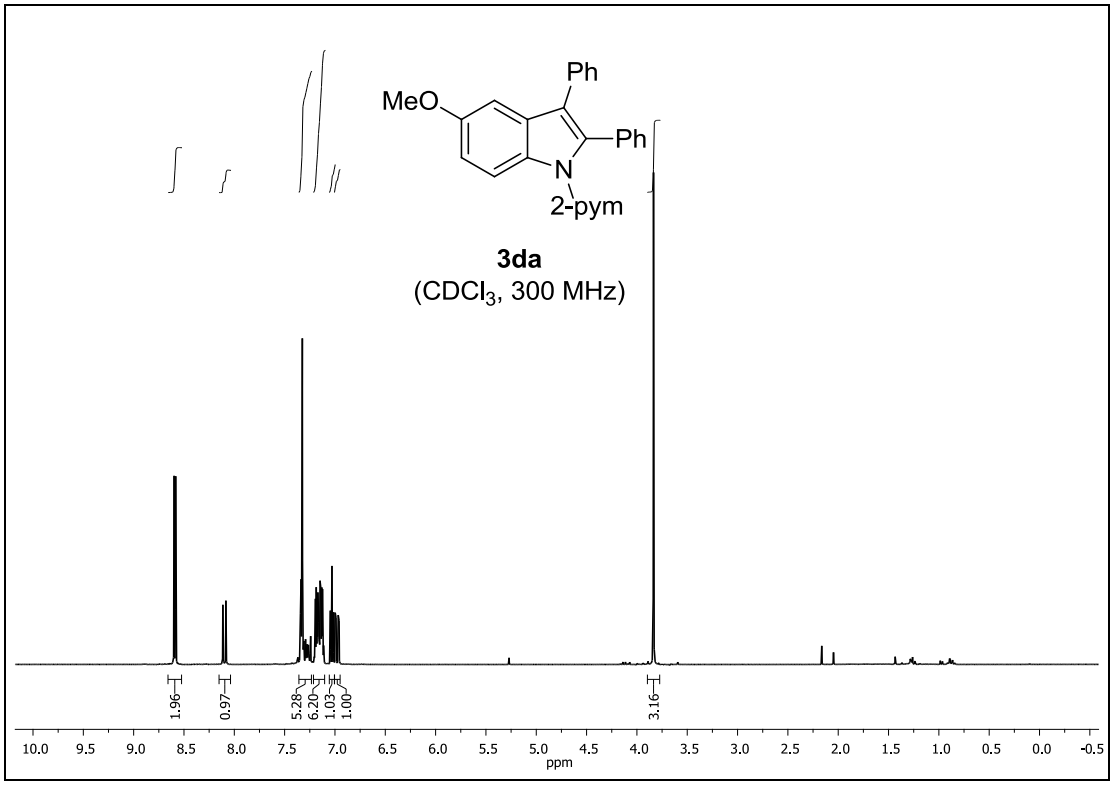
3ba
($CDCl_3$, 300 MHz)

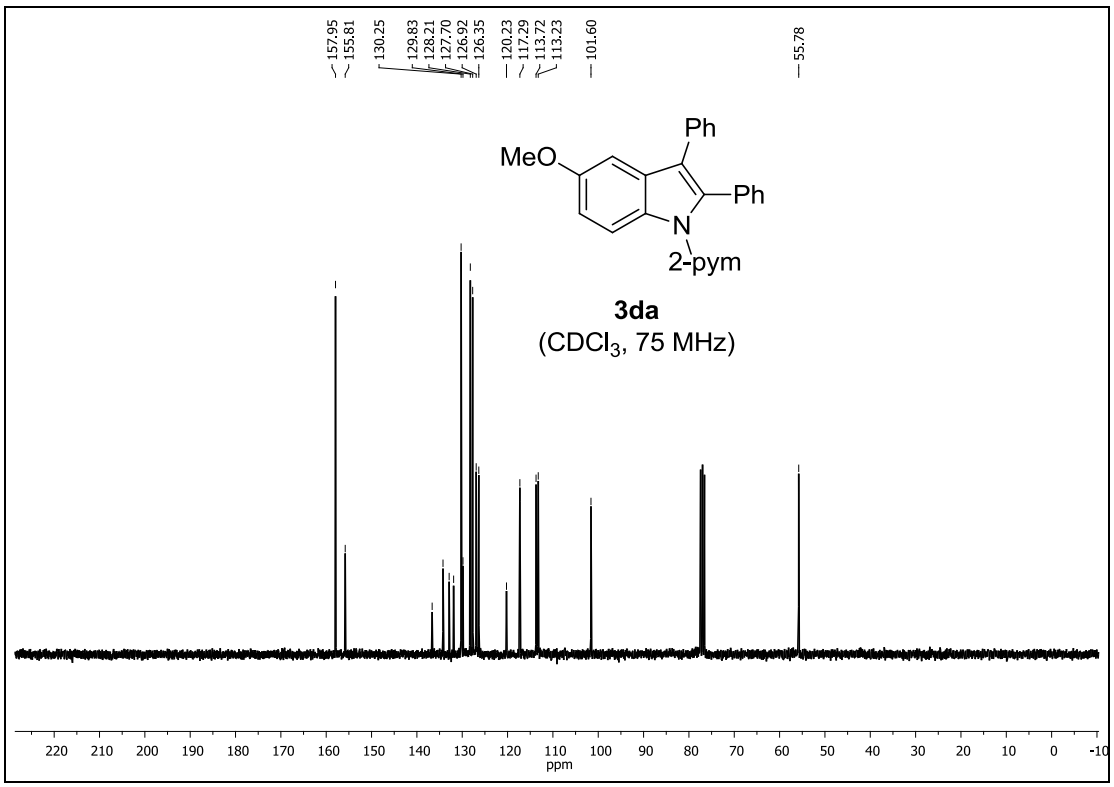


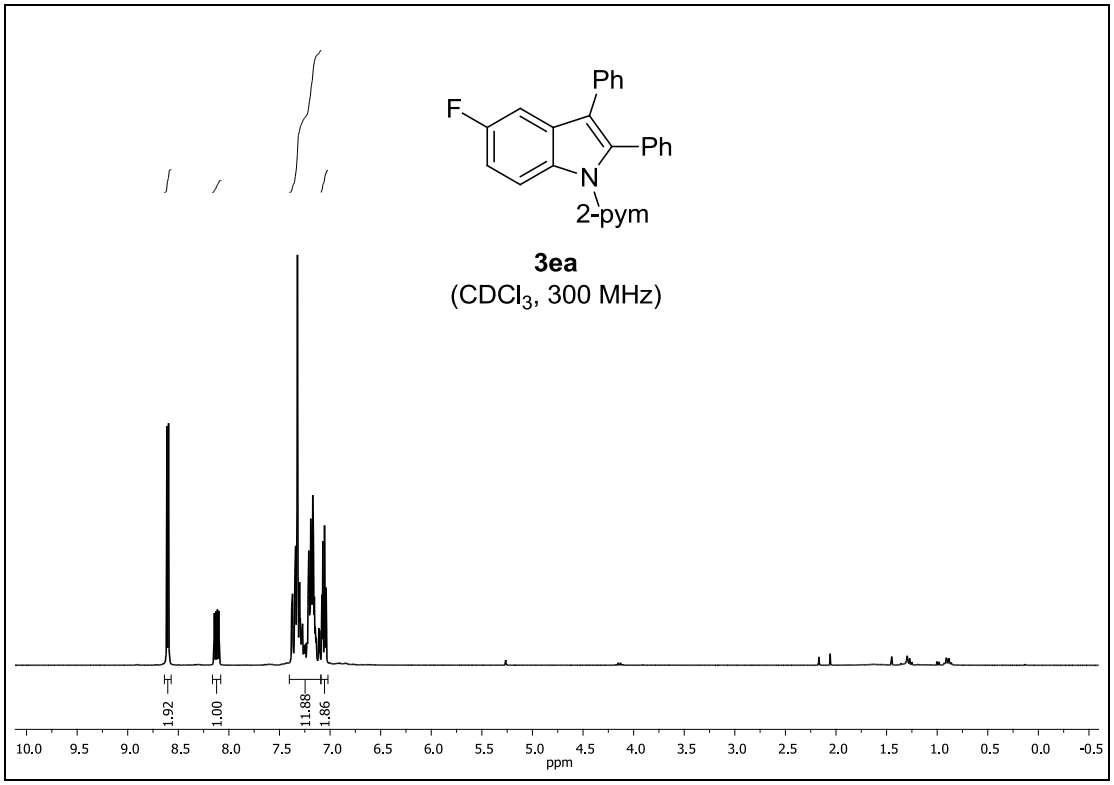
3ba
($CDCl_3$, 75 MHz)

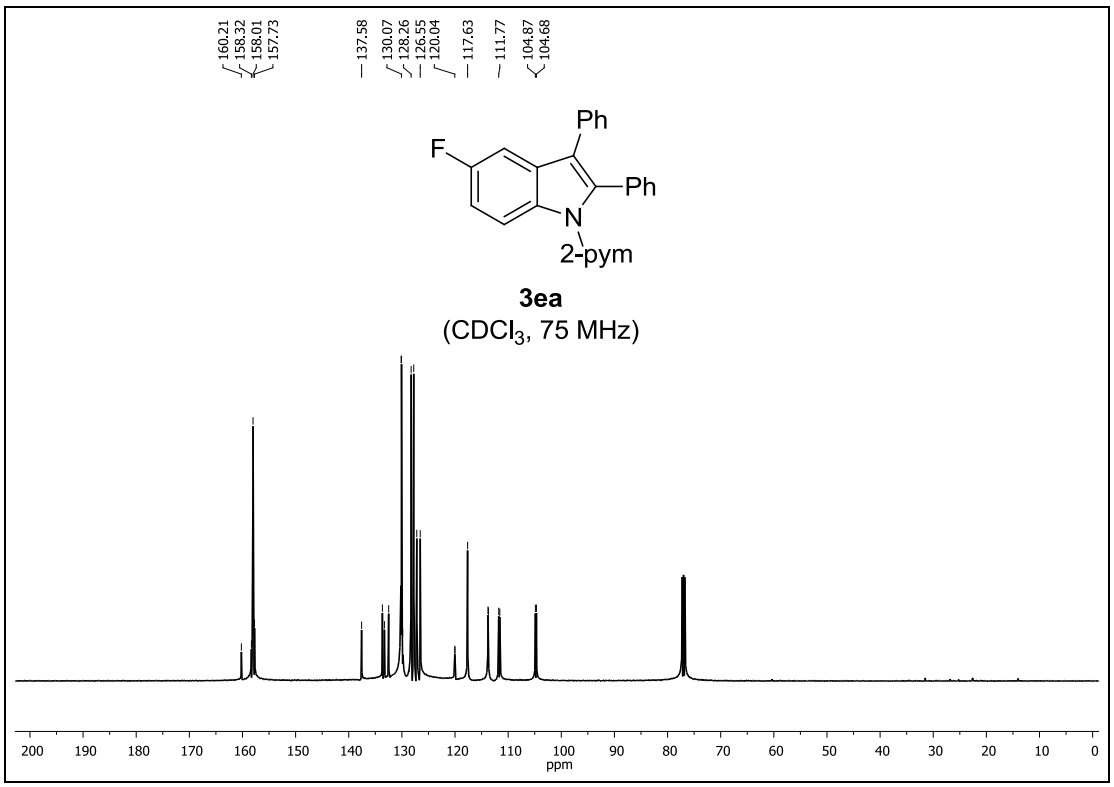


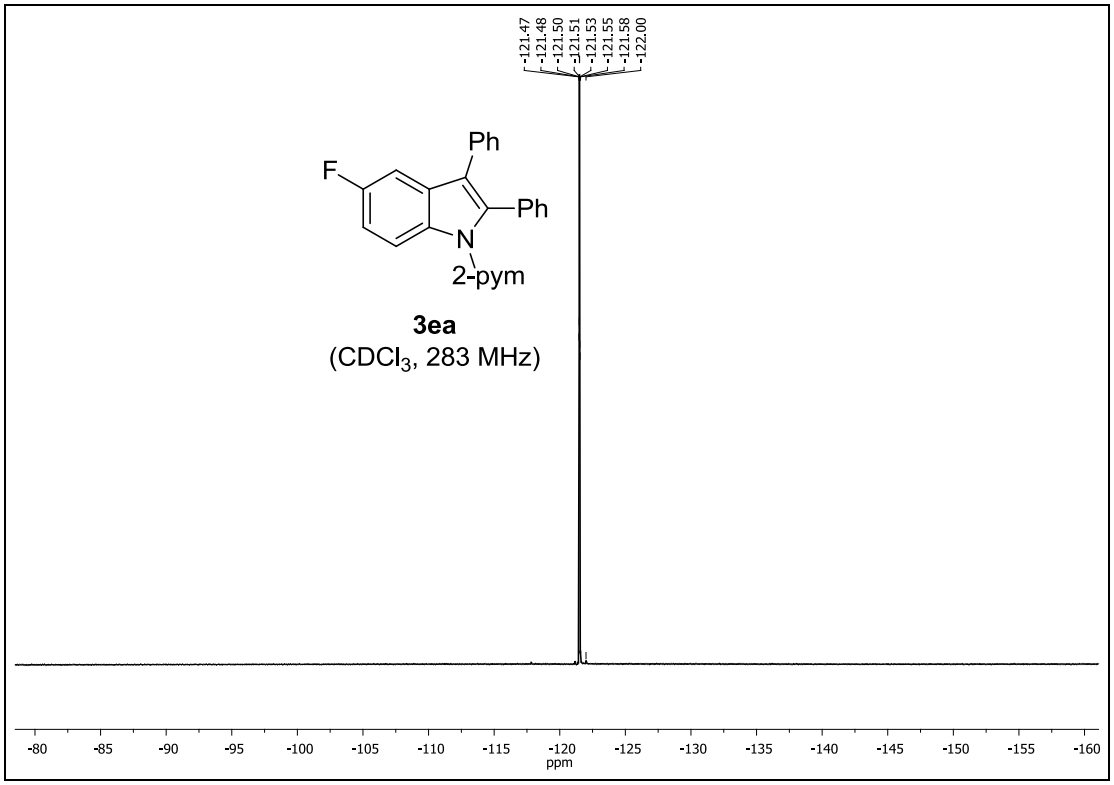



Ph
MeO
Ph
N
2-pym
3da
(CDCl3, 300 MHz)
1.96
0.97
5.28
6.20
1.03
1.00
3.16
ppm

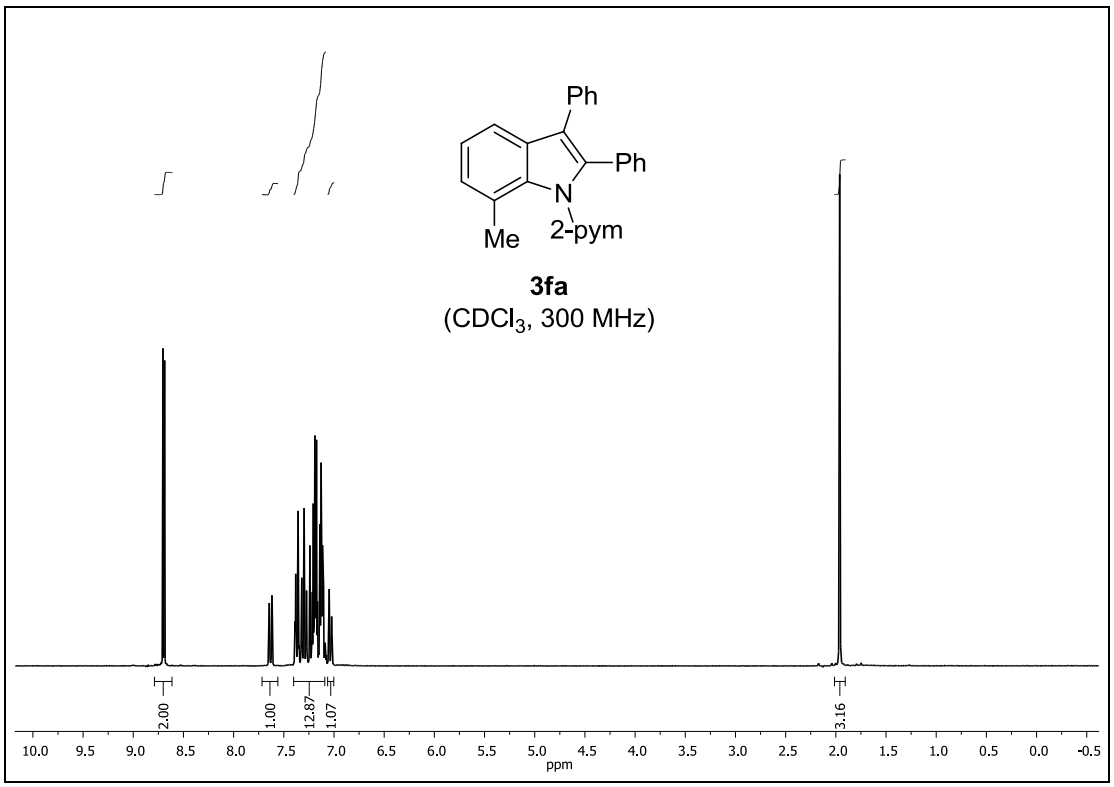

157.95
155.81
130.25
129.83
128.21
127.70
126.92
126.35
120.23
117.29
113.72
113.23
101.60
55.78
Ph
MeO
Ph
N
2-pym
3da
(CDCl3, 75 MHz)
ppm


Ph
F
Ph
N
2-pym
3ea
(CDCl3, 300 MHz)
1.92
1.00
11.88
1.86
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm

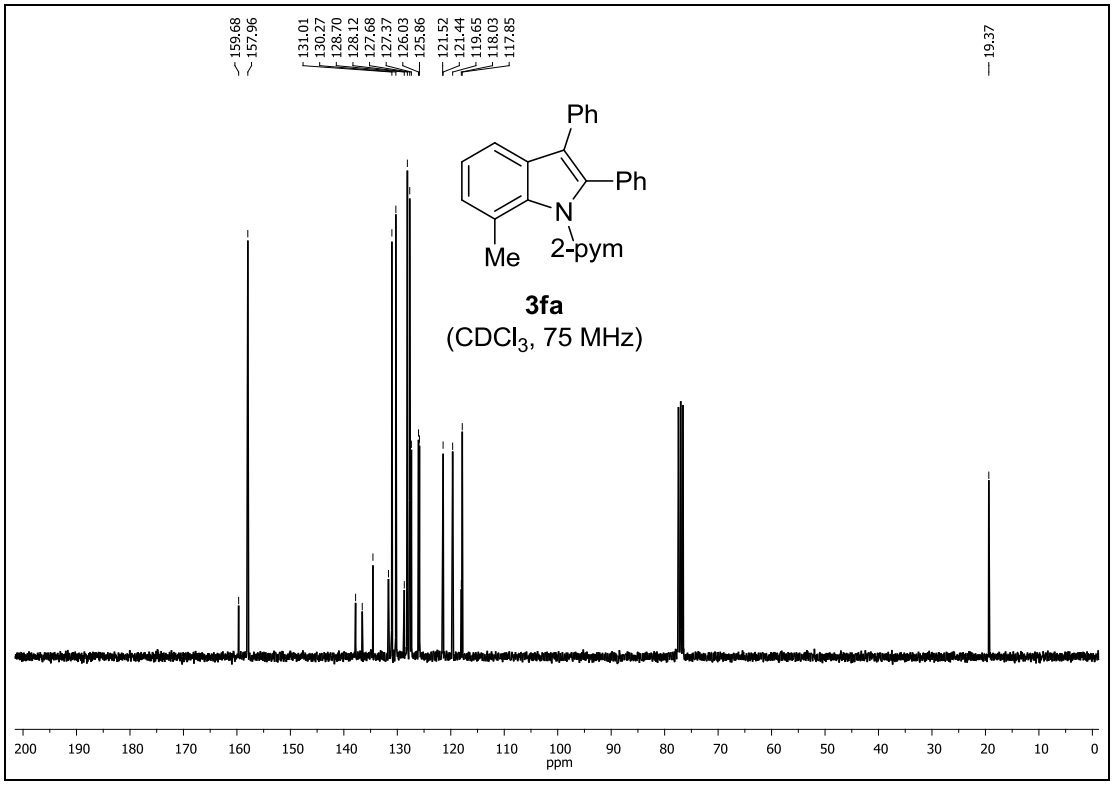

160.21
158.32
158.01
157.73
137.58
130.07
128.26
126.55
120.04
117.63
111.77
104.87
104.68
Ph
F
Ph
N
2-pym
3ea
(CDCl3, 75 MHz)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm

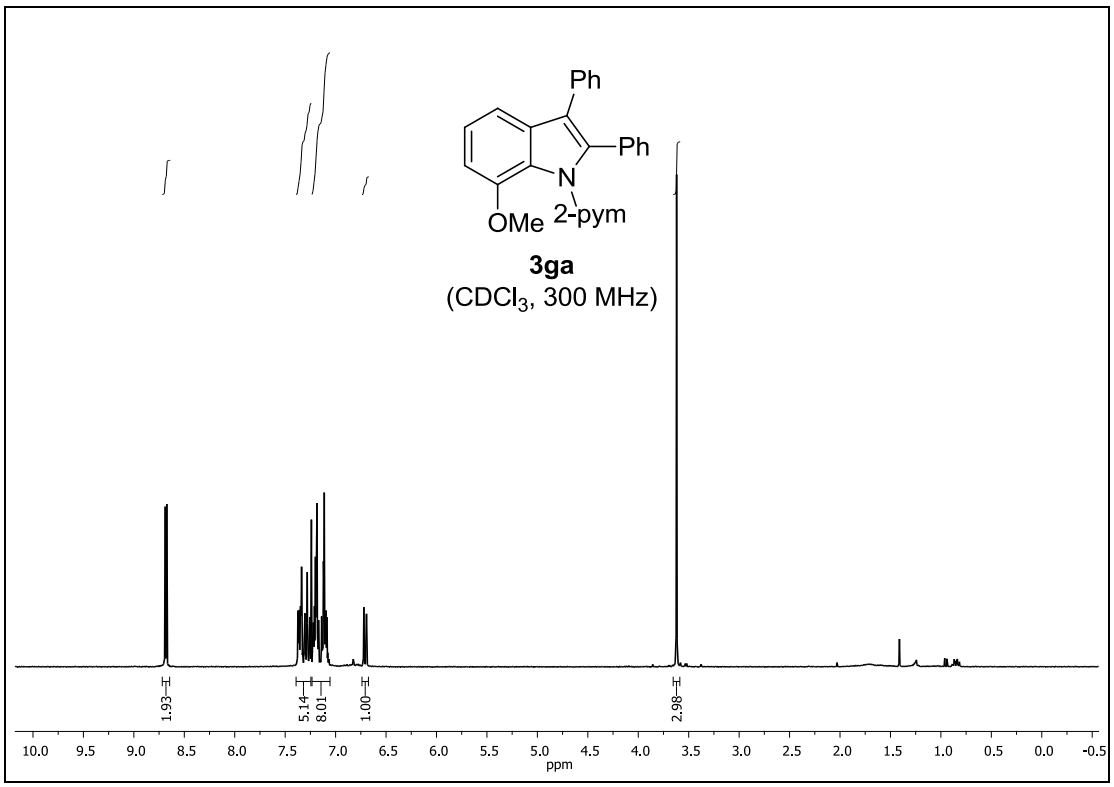


3ea
($CDCl_3$, 283 MHz)



3fa
($CDCl_3$, 300 MHz)


159.68
157.96
131.01
130.27
128.70
128.12
127.68
127.37
126.03
125.86
121.52
121.44
119.65
118.03
117.85
19.37
Ph
Ph
N
2-pym
Me
3fa
(CDCl3, 75 MHz)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm


Ph
Ph
N
2-pym
OMe
3ga
(CDCl3, 300 MHz)
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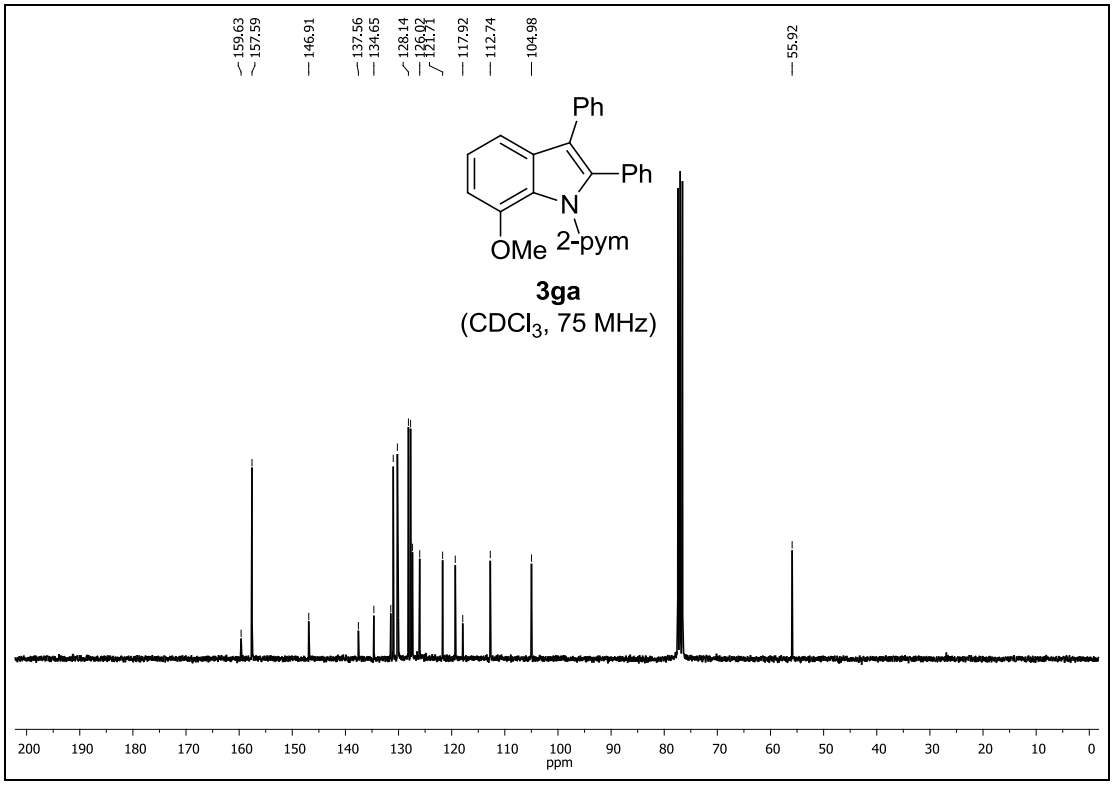
5.14
8.01
1.00
2.98
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm


159.63
157.59
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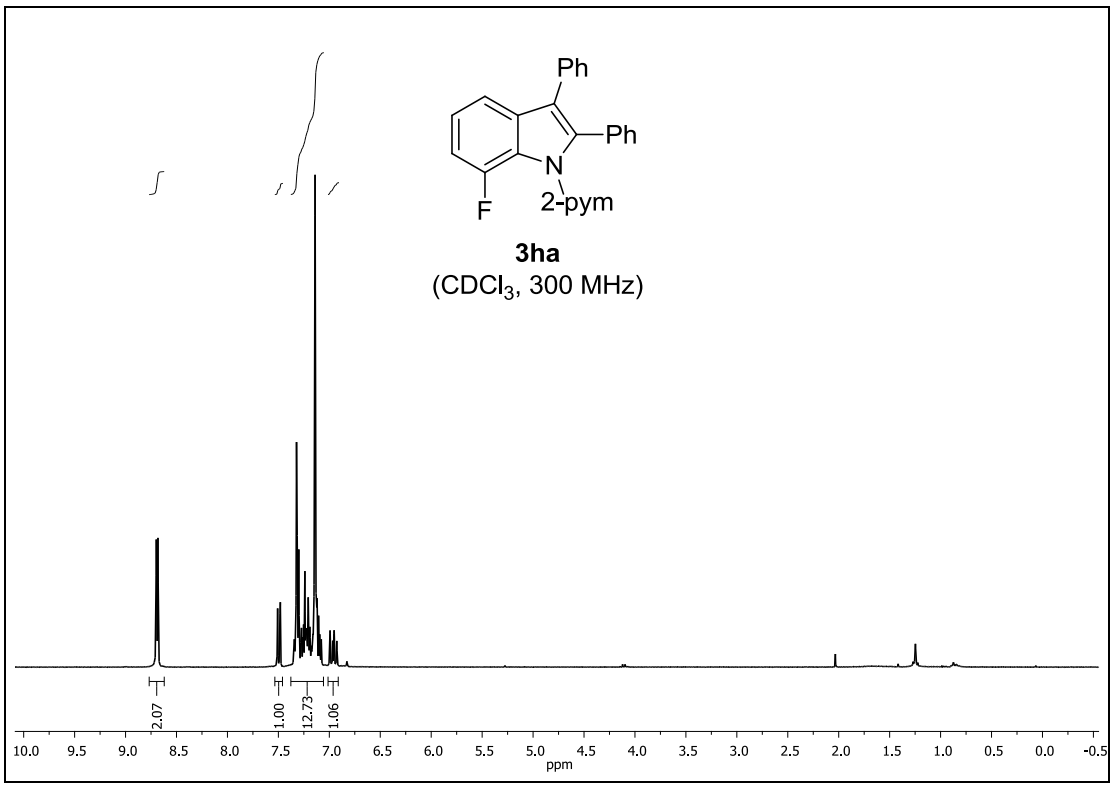
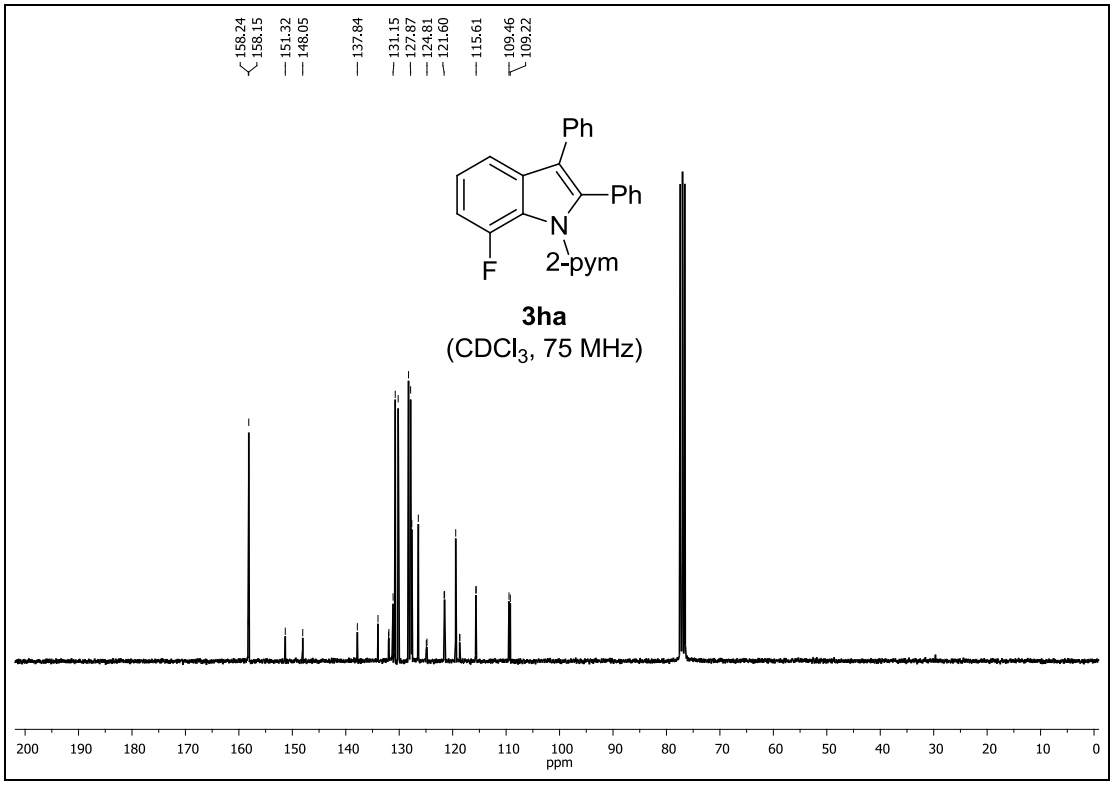
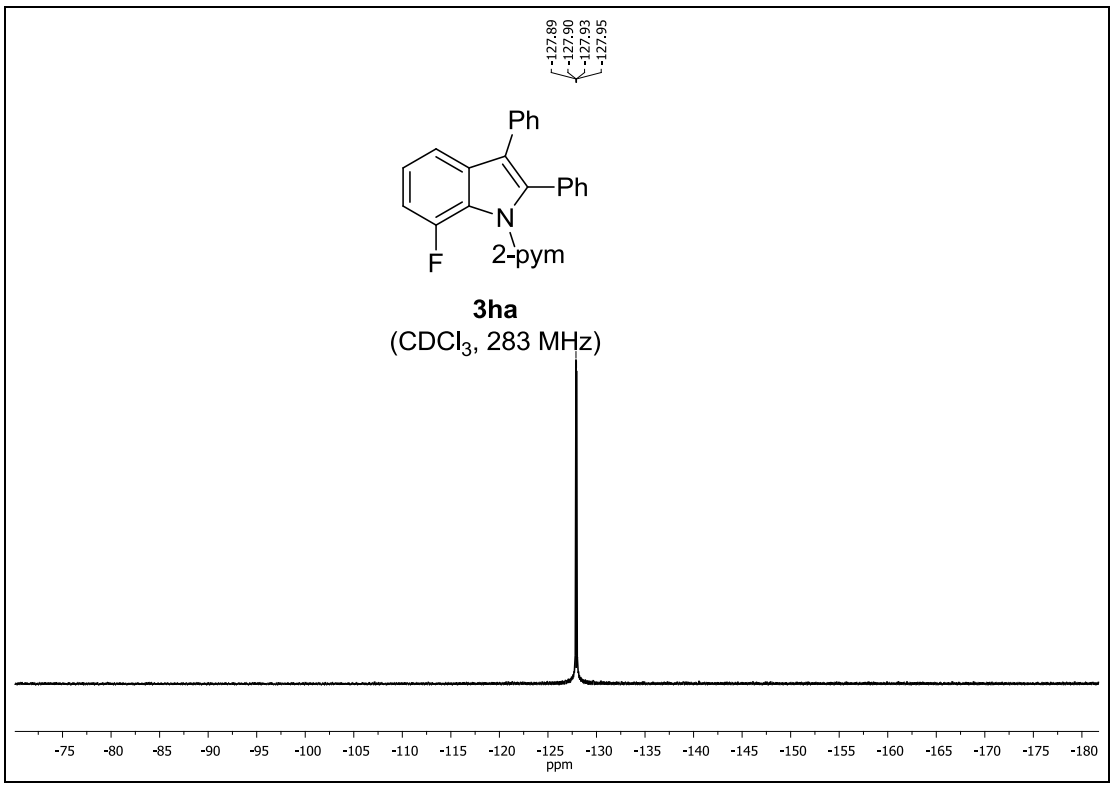
134.65
128.14
126.02
121.71
117.92
112.74
104.98
55.92
Ph
Ph
N
OMe
2-pym
3ga
(CDCl3, 75 MHz)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm


Ph
Ph
N
F
2-pym
3ha
(CDCl3, 300 MHz)
2.07
1.00
12.73
1.06
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm


158.24
158.15
151.32
148.05
137.84
131.15
127.87
124.81
121.60
115.61
109.46
109.22
Ph
Ph
N
F
2-pym
3ha
(CDCl3, 75 MHz)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm


-127.89
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Ph
Ph
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(CDCl3, 283 MHz)
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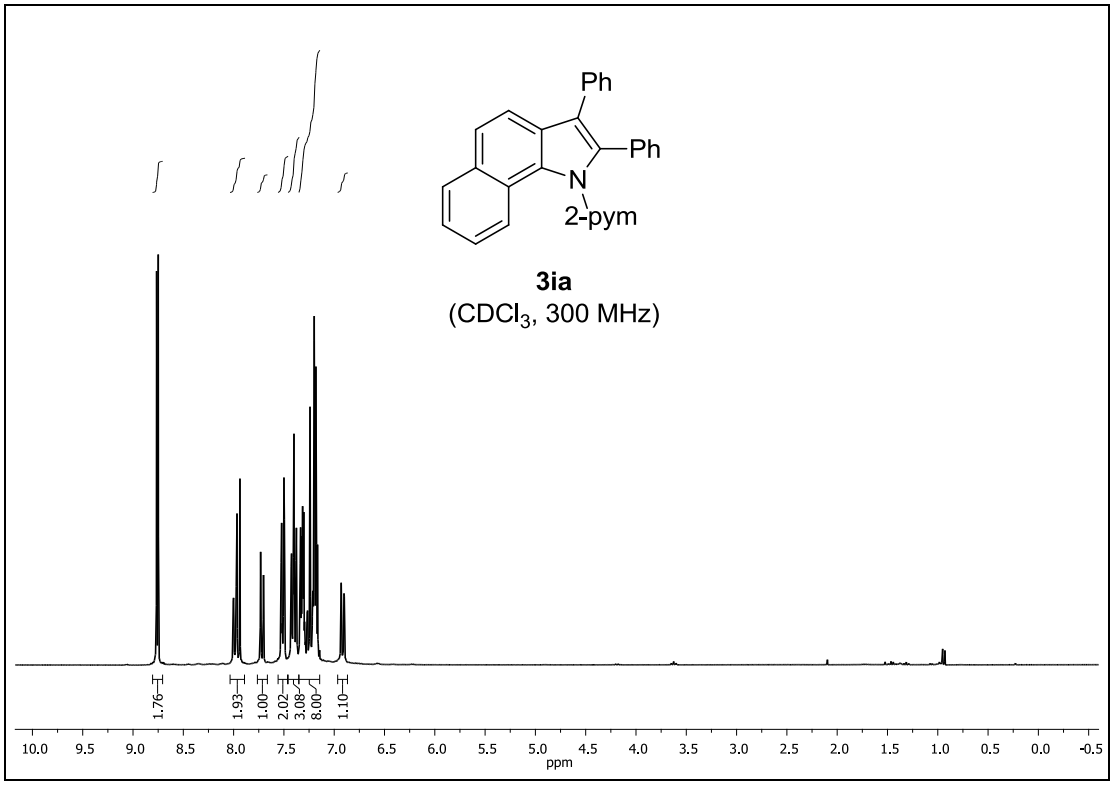
ppm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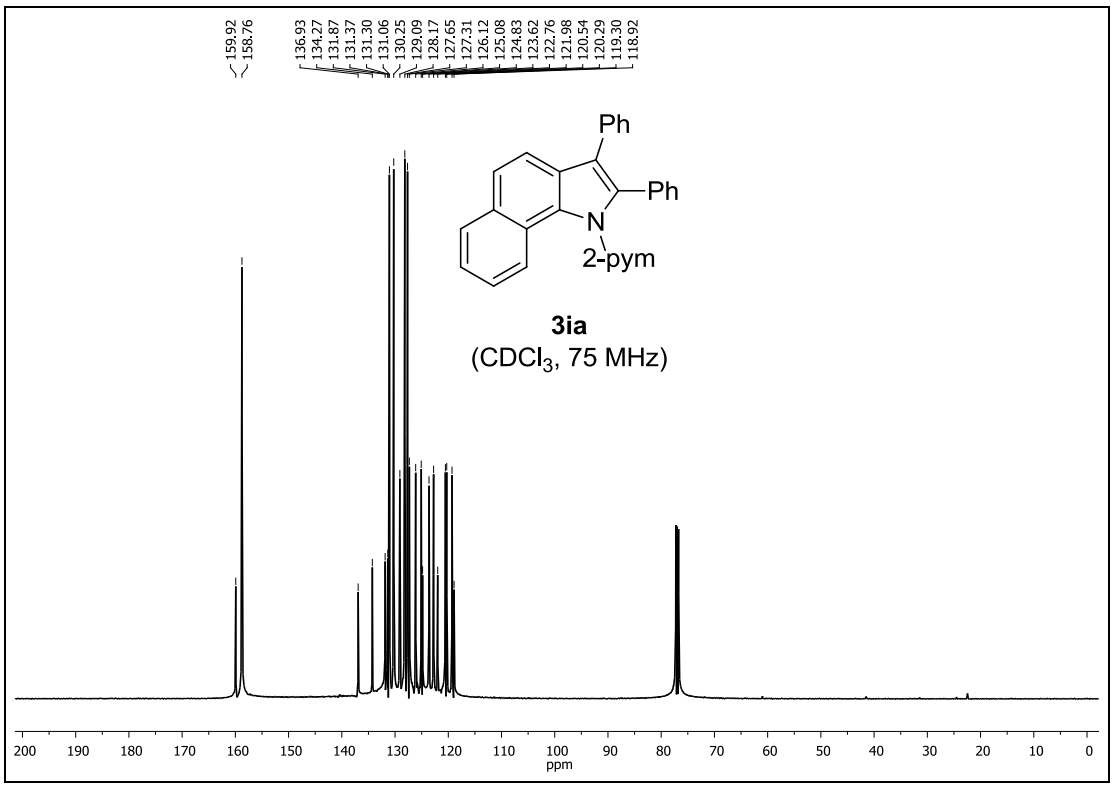
3.08
8.00
1.10
ppm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131.06
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129.09
128.17
127.65
127.31
126.12
125.08
124.83
123.62
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120.29
119.30
118.92
Ph
Ph
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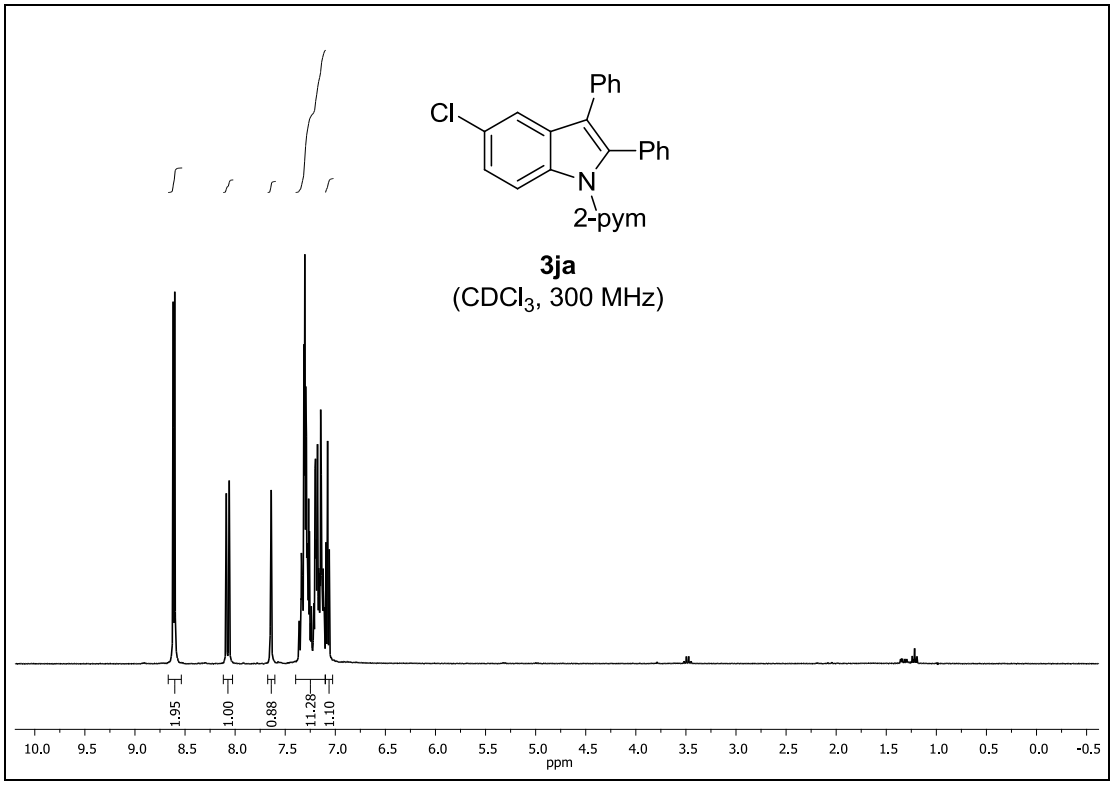
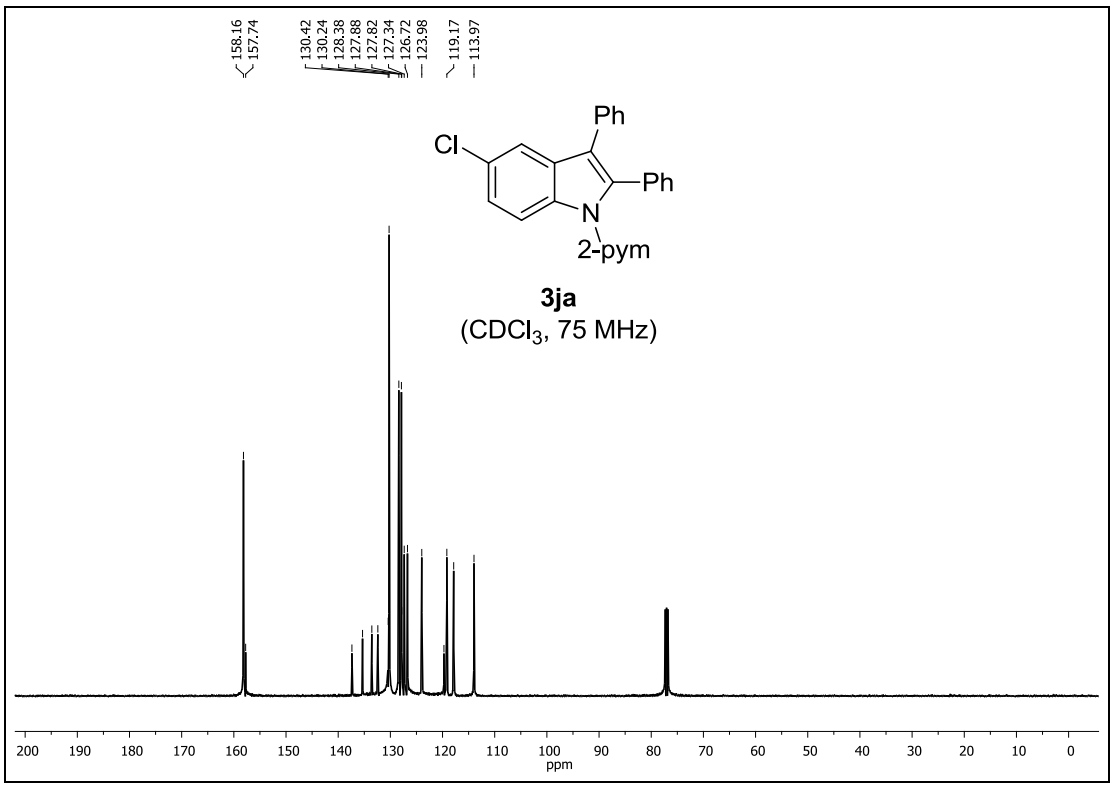
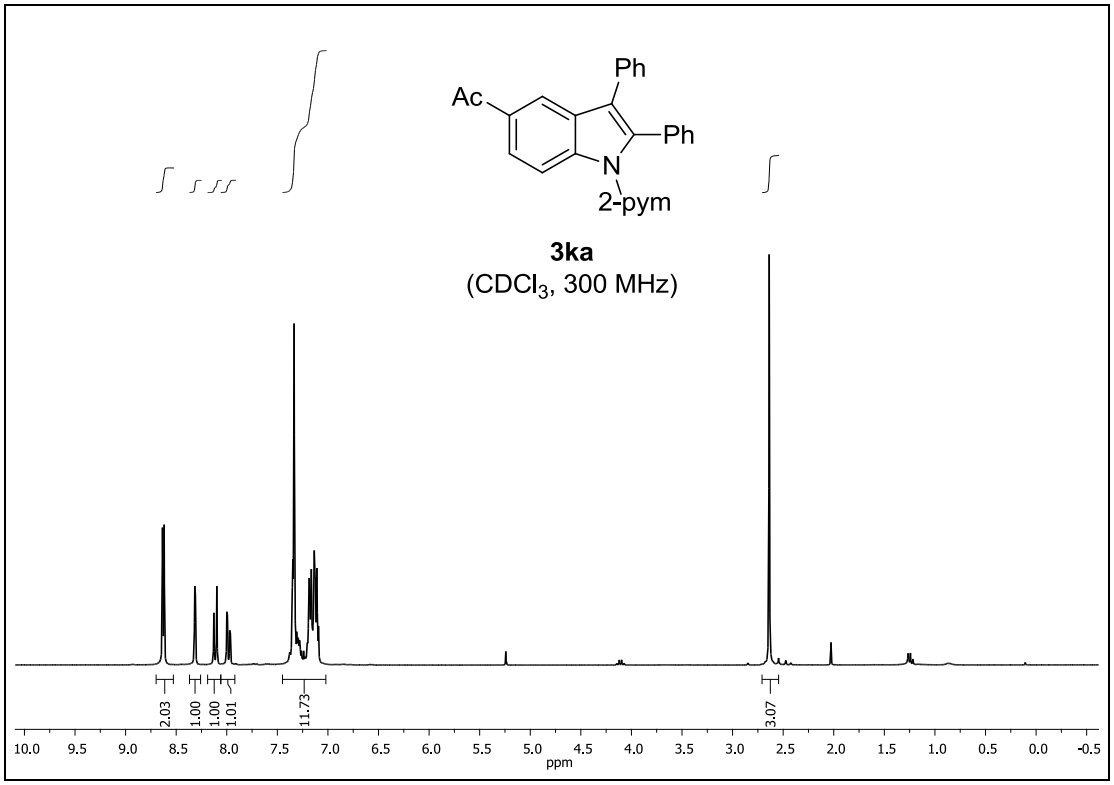
2-pym
3ia
(CDCl3, 75 MHz)
ppm






Ac
Ph
Ph
N
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3ka
(CDCl3, 300 MHz)
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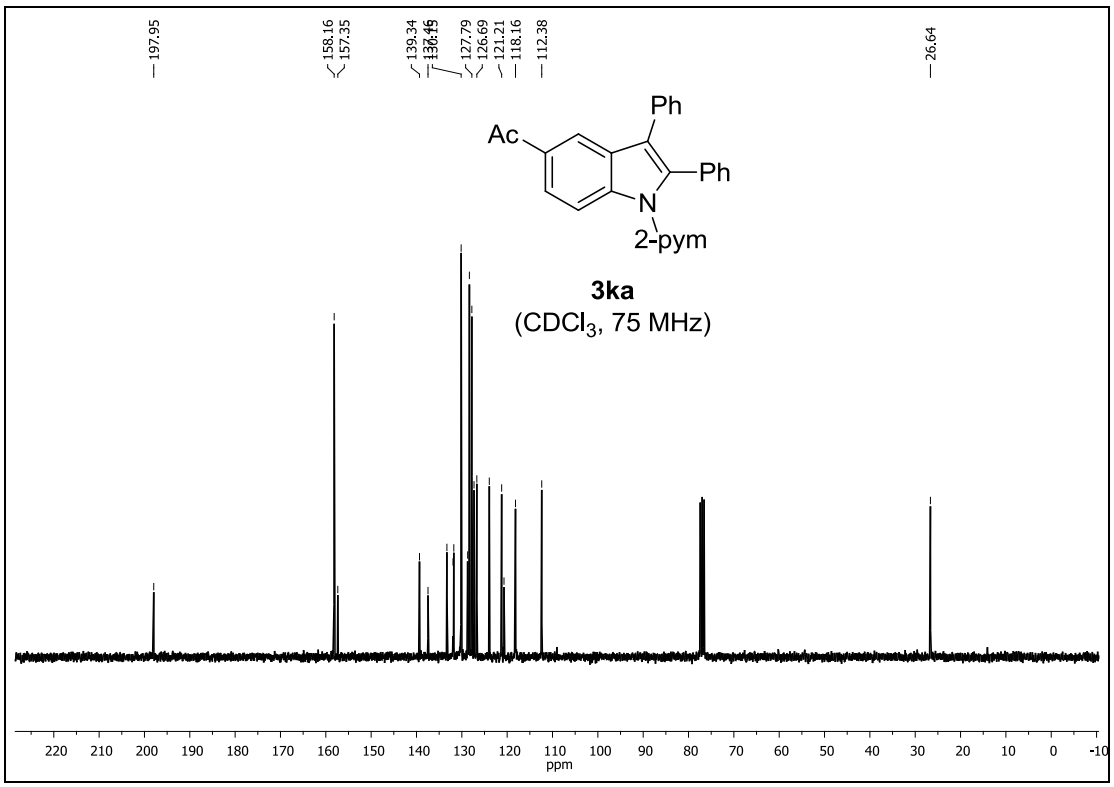
1.00
1.00
1.01
11.73
3.07
ppm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112.38
26.64
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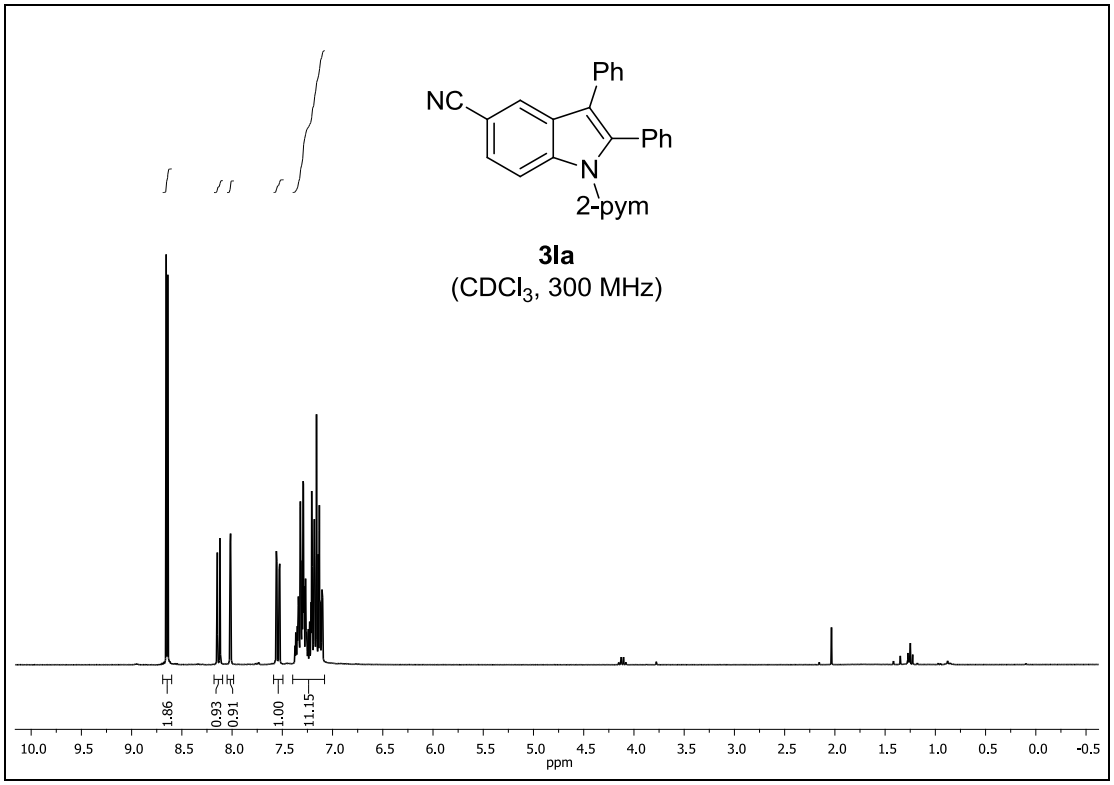
Ph
Ph
N
2-pym
3ka
(CDCl3, 75 MHz)
ppm


NC
Ph
Ph
N
2-pym
3la
(CDCl3, 300 MHz)
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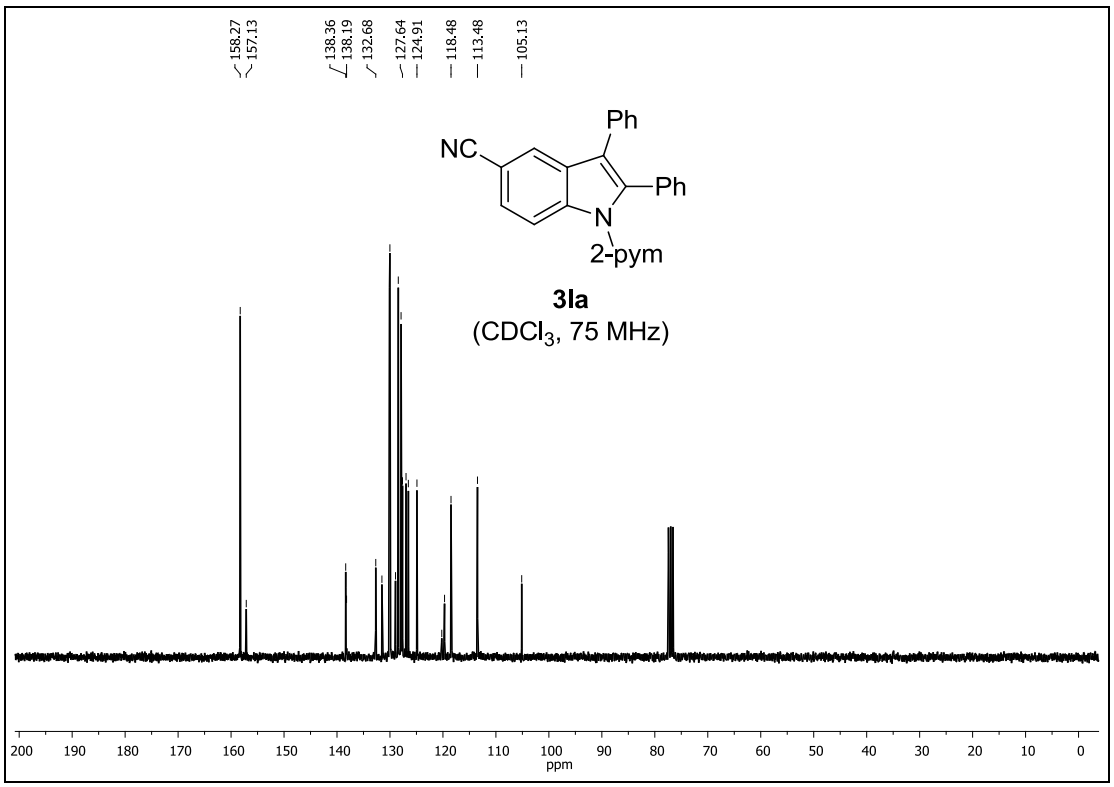
0.93
0.91
1.00
11.15
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm


158.27
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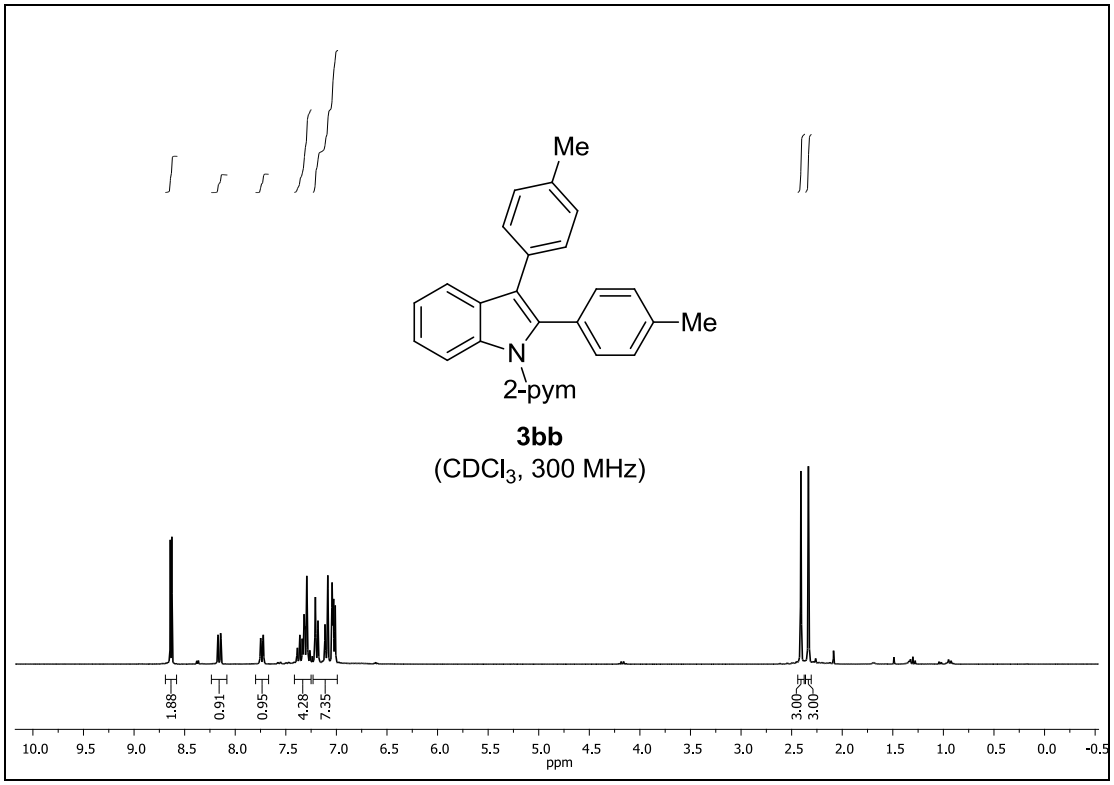
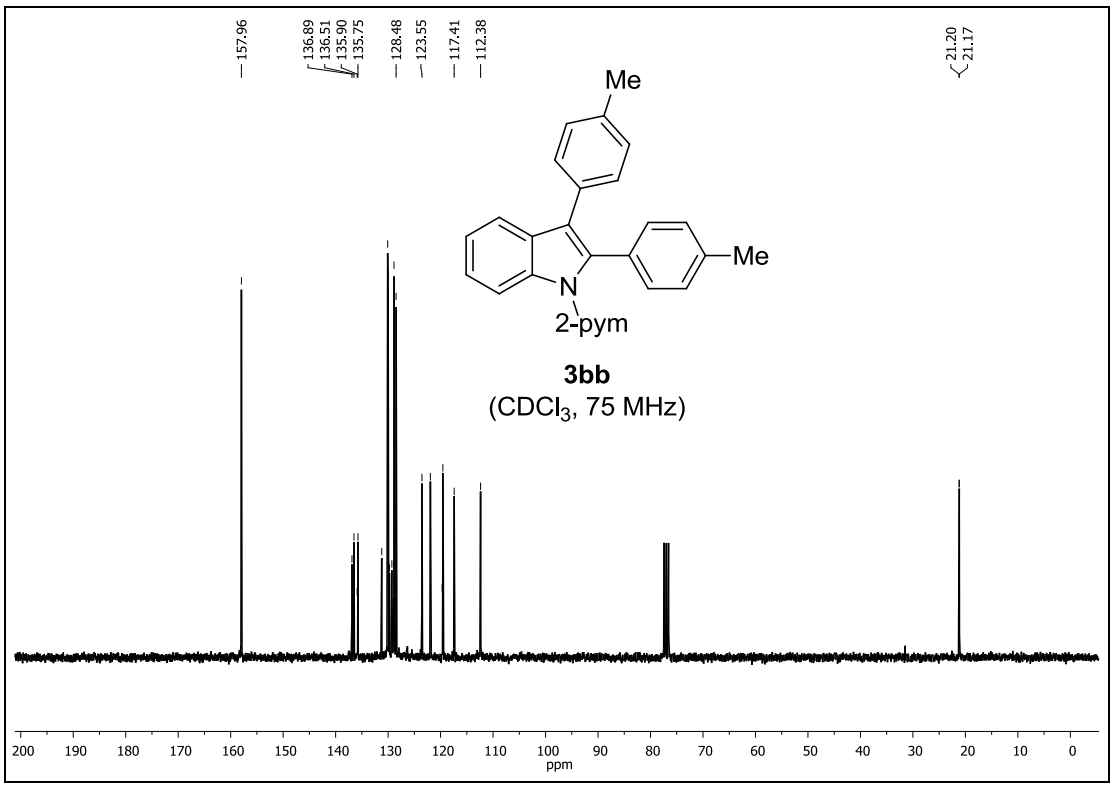
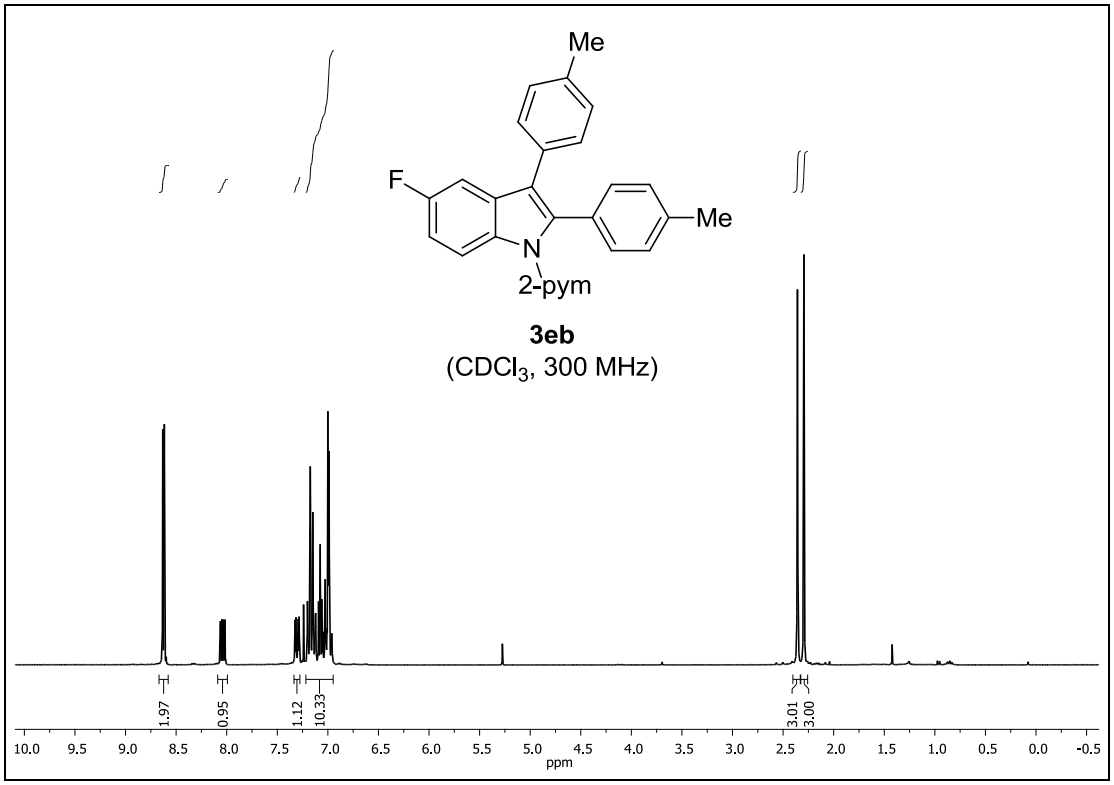
138.19
132.68
127.64
124.91
118.48
113.48
105.13
NC
Ph
Ph
N
2-pym
3la
(CDCl3, 75 MHz)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm

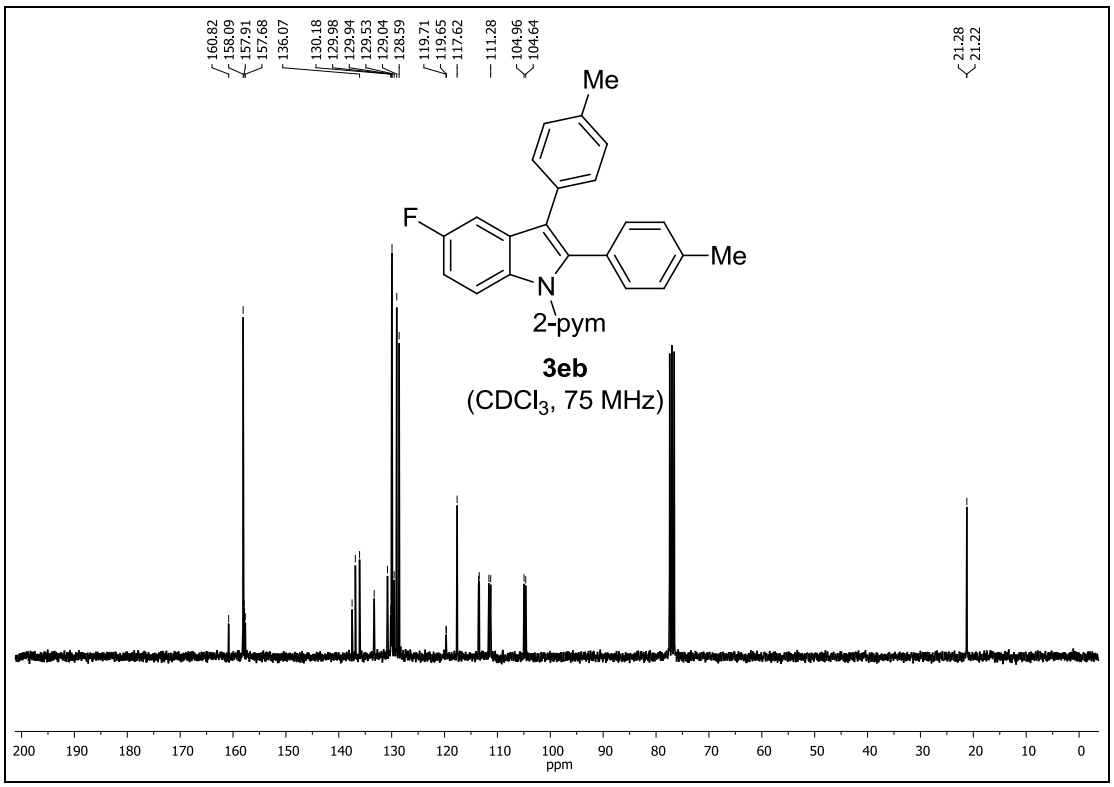


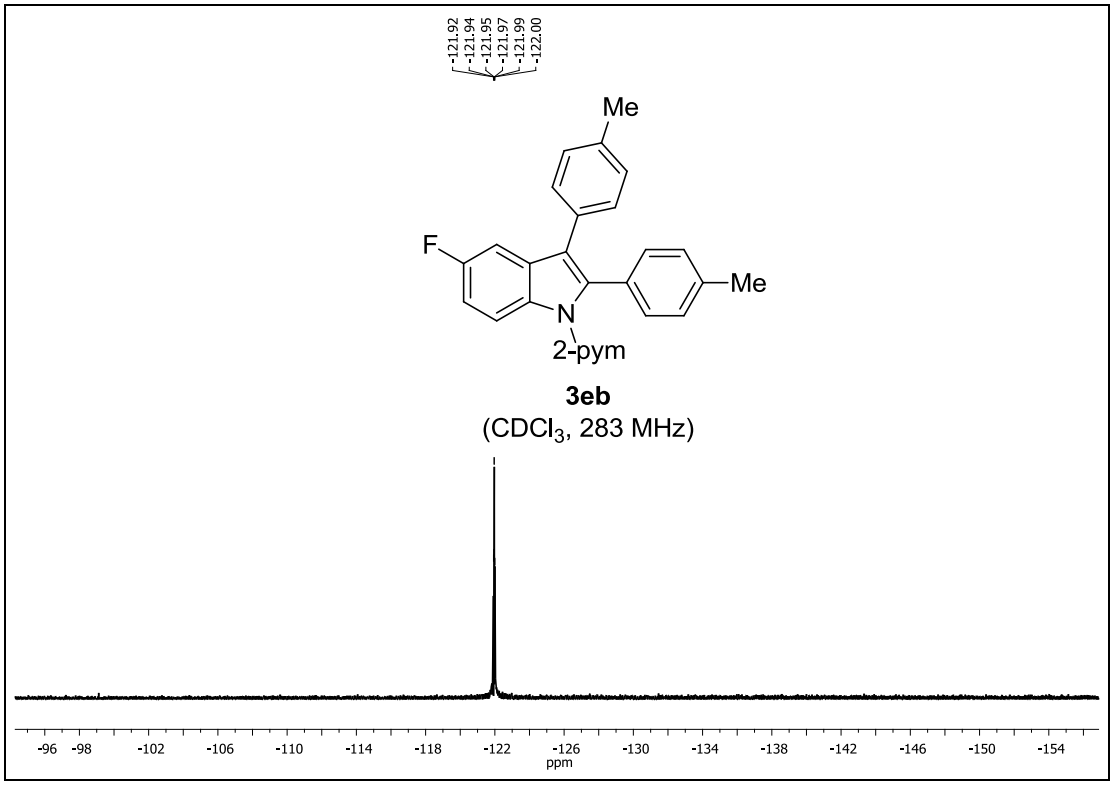
3bb
($CDCl_3$, 300 MHz)



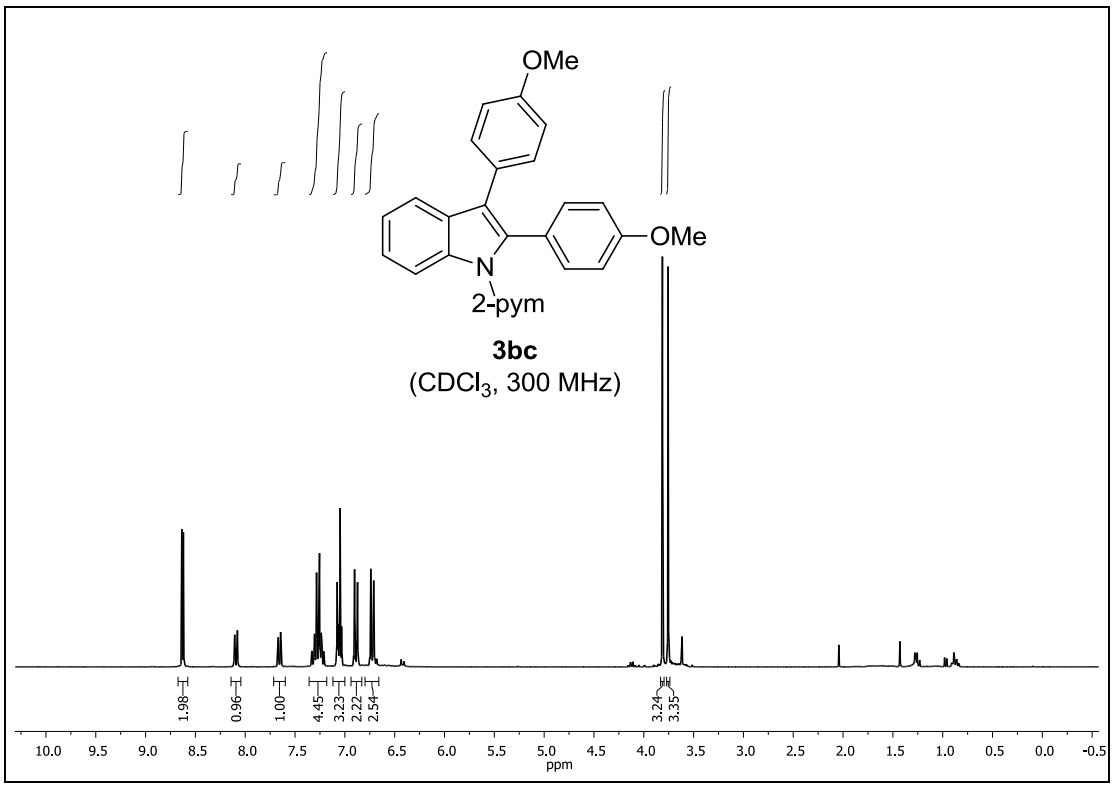
3bb
($CDCl_3$, 75 MHz)


Me
F
Me
N
2-pym
3eb
(CDCl3, 300 MHz)
1.97
0.95
1.12
10.33
3.01
3.00
ppm

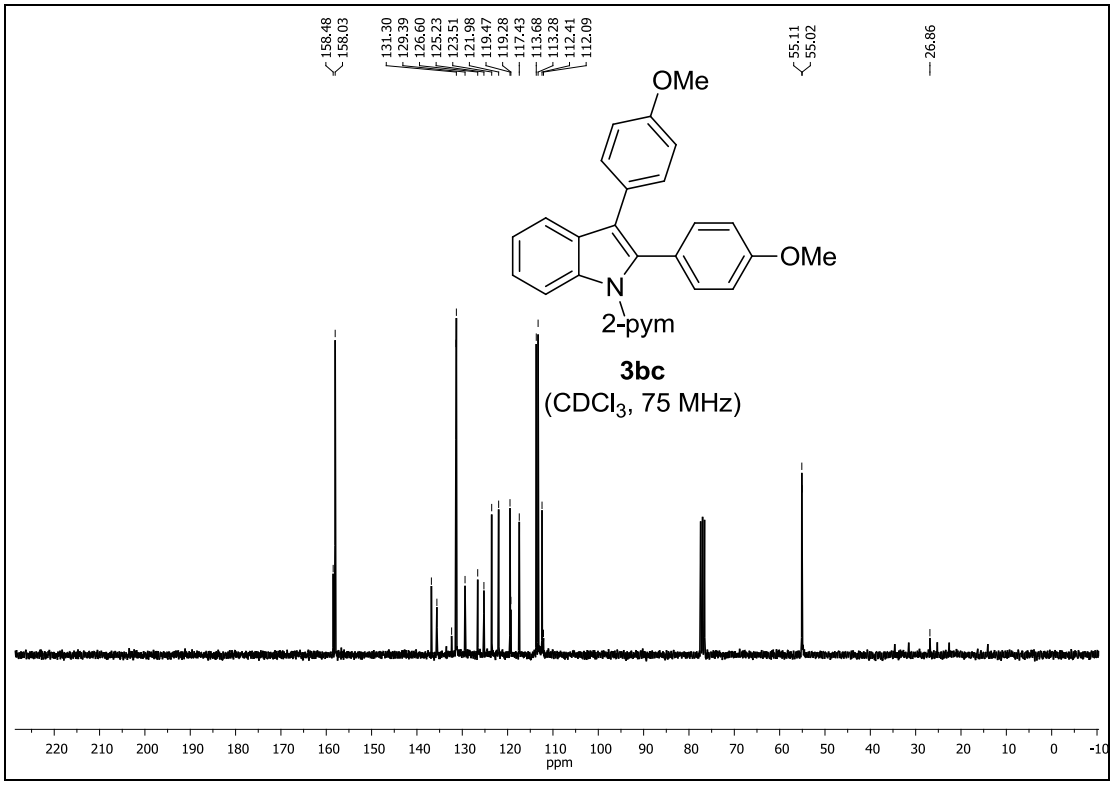

160.82
158.09
157.91
157.68
136.07
130.18
129.98
129.94
129.53
129.04
128.59
119.71
119.65
117.62
111.28
104.96
104.64
21.28
21.22
Me
F
Me
N
2-pym
3eb
(CDCl3, 75 MHz)
ppm

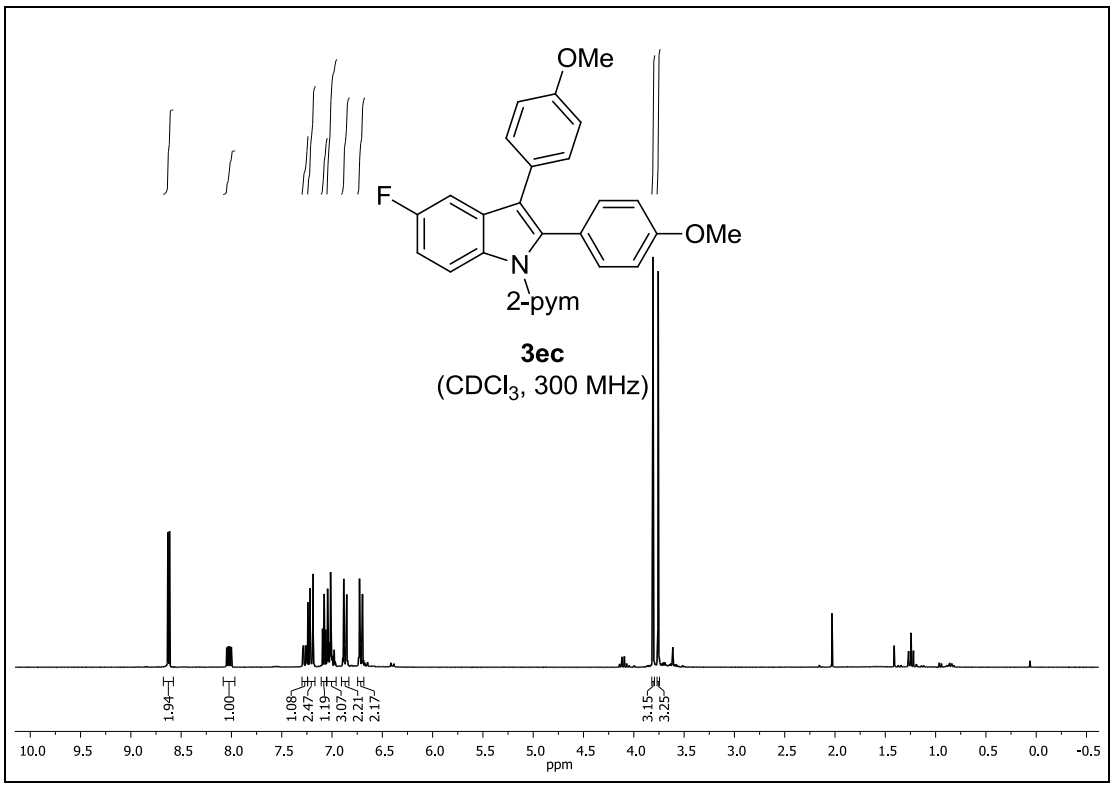


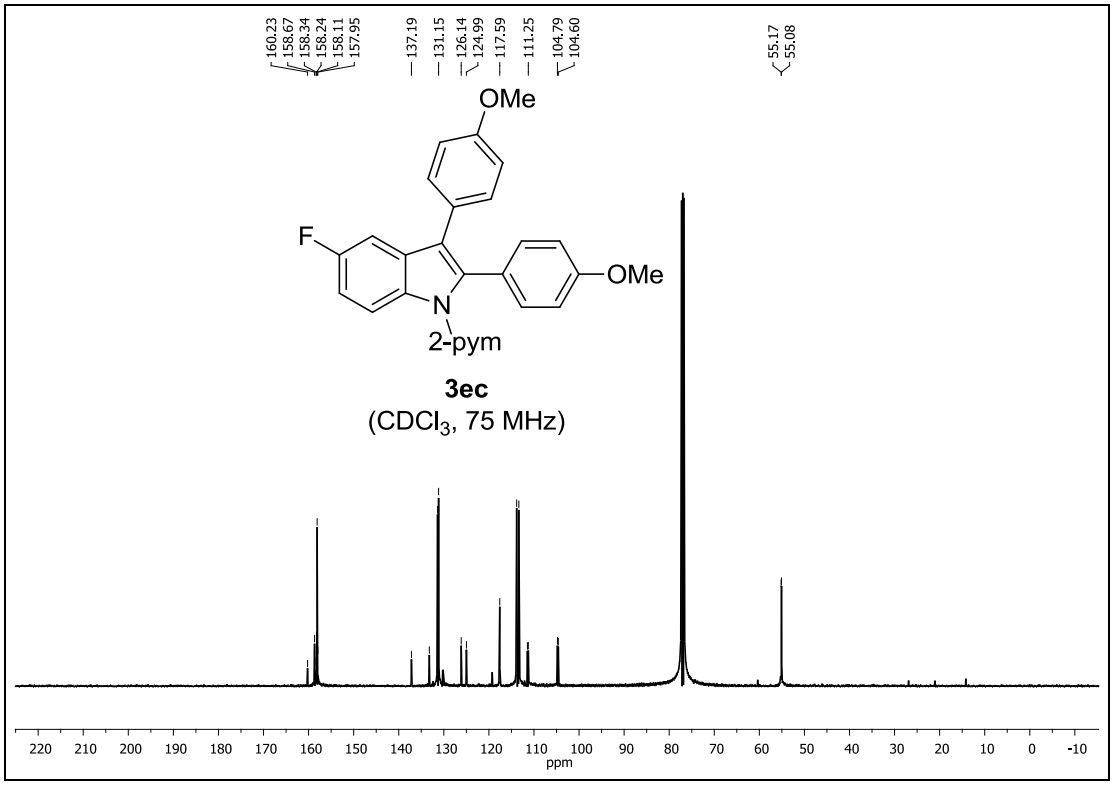
3eb
($CDCl_3$, 283 MHz)

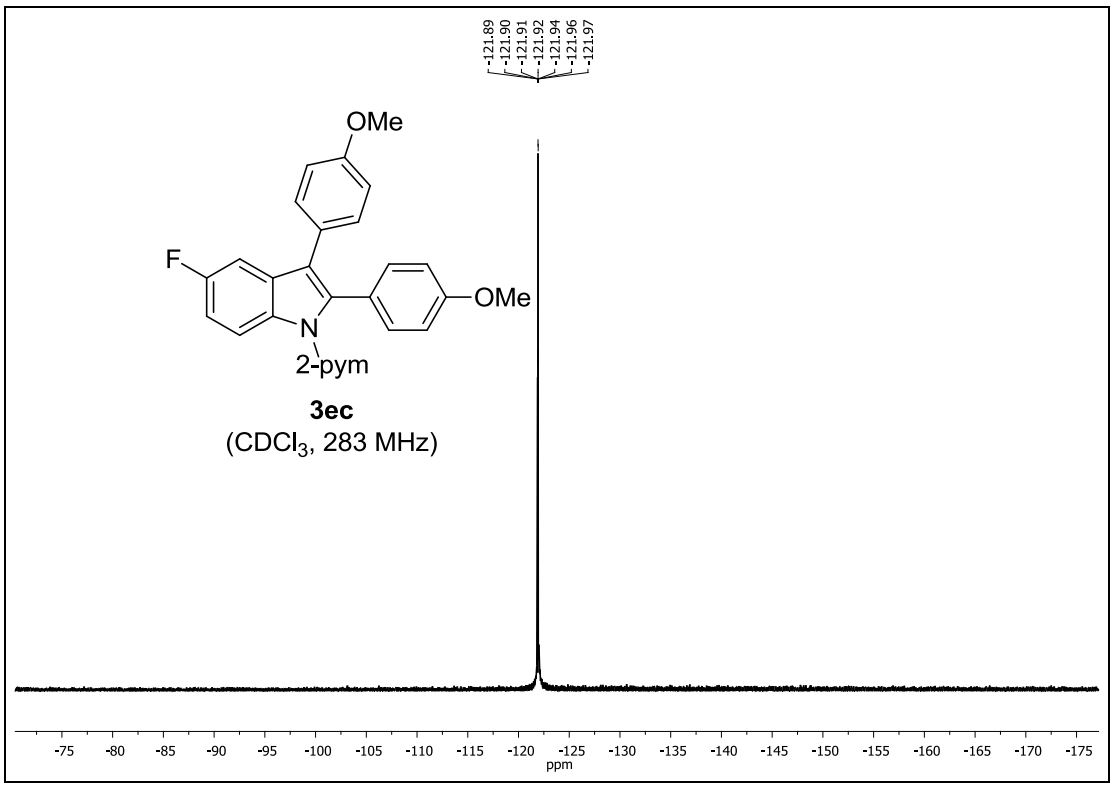


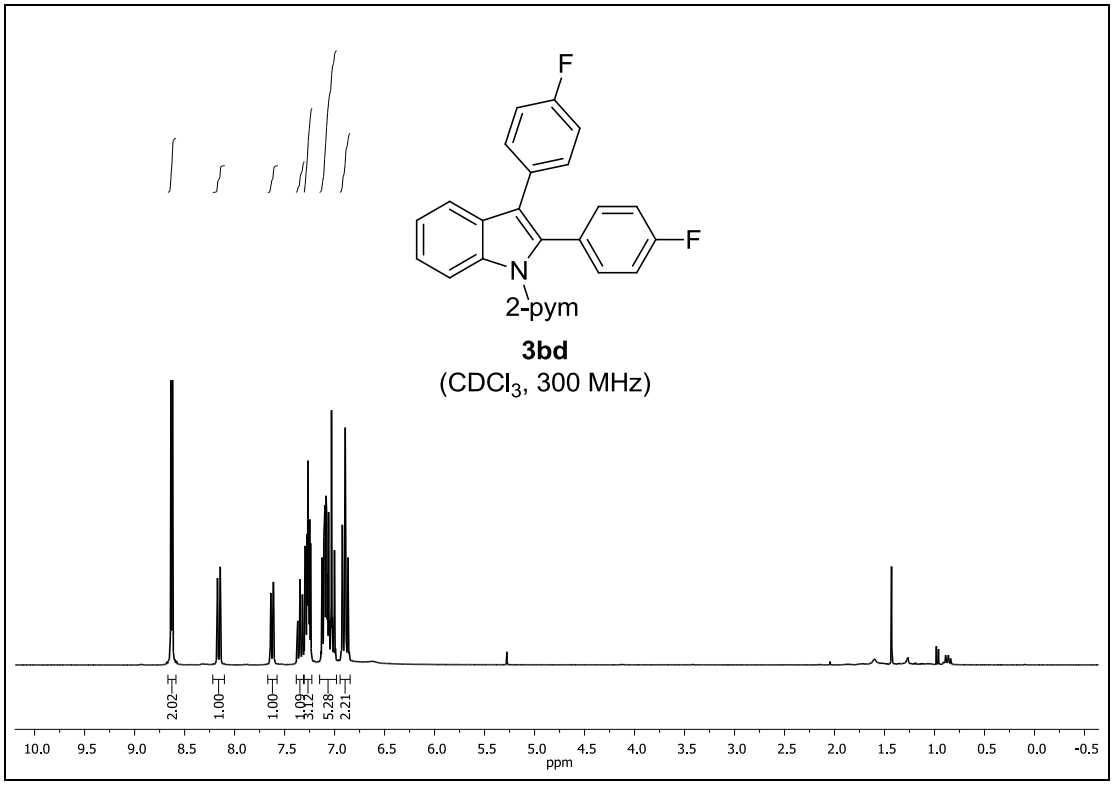
3bc
($CDCl_3$, 300 MHz)

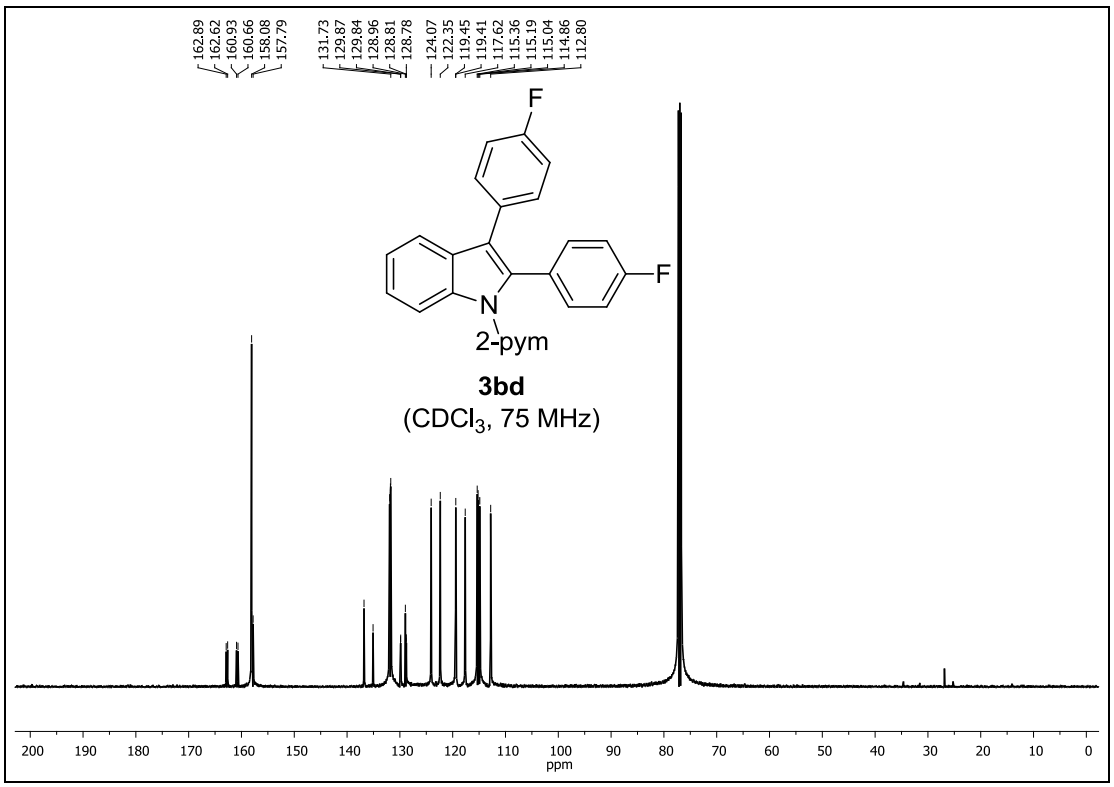

158.48
158.03
131.30
129.39
126.60
125.23
123.51
121.98
119.47
119.28
117.43
113.68
113.28
112.41
112.09
55.11
55.02
26.86
OMe
OMe
N
2-pym
3bc
(CDCl3, 75 MHz)
ppm

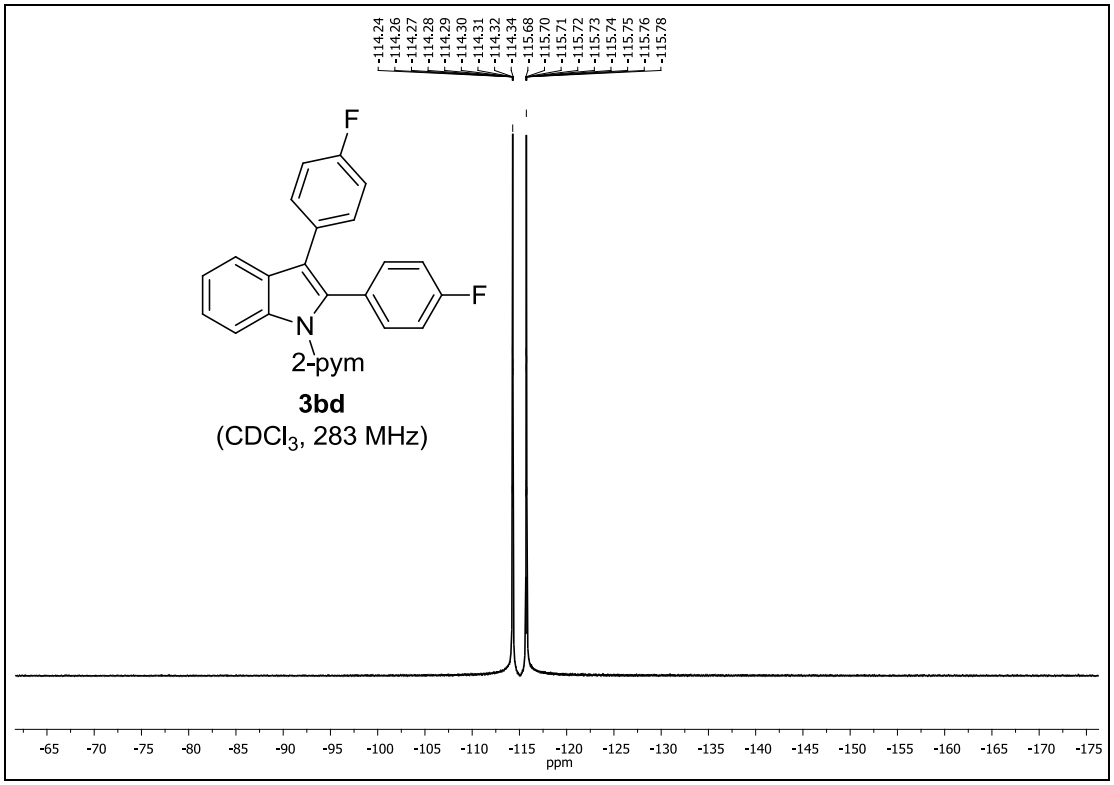

OMe
F
OMe
N
2-pym
3ec
(CDCl3, 300 MHz)
1.94
1.00
1.08
2.47
1.19
3.07
2.21
2.17
3.15
3.25
ppm

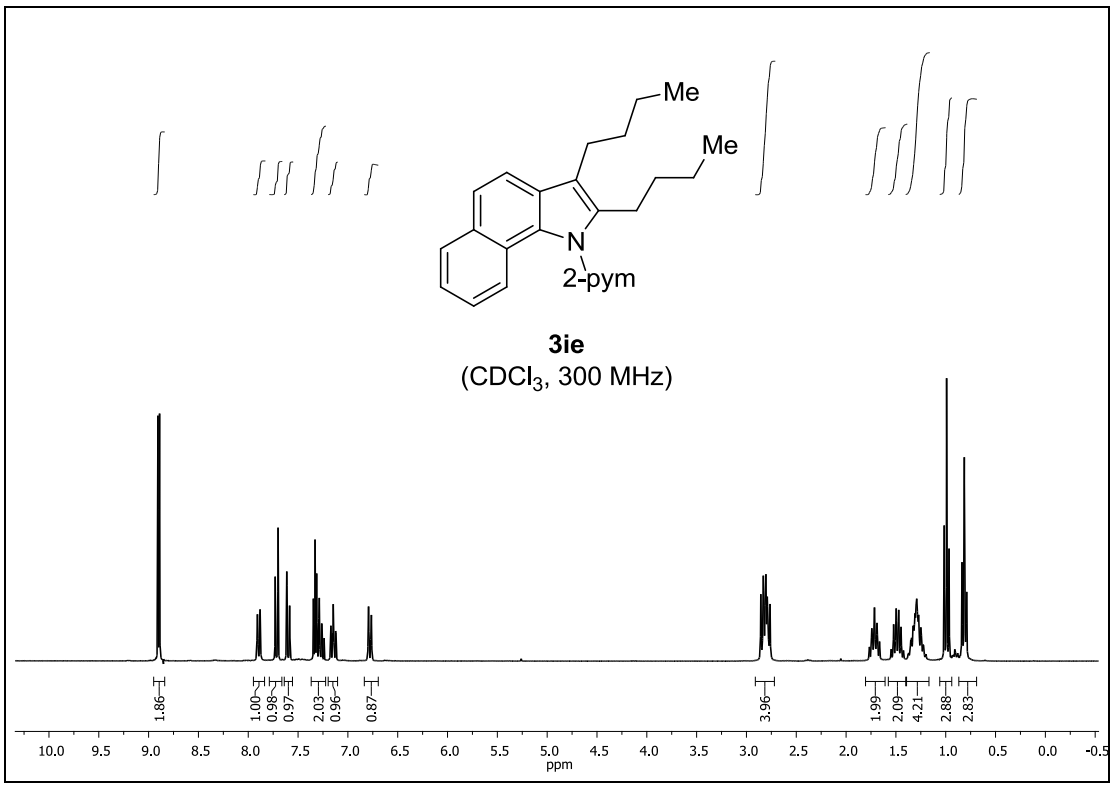

160.23
158.67
158.34
158.24
158.11
157.95
137.19
131.15
126.14
124.99
117.59
111.25
104.79
104.60
55.17
55.08
OMe
F
OMe
N
2-pym
3ec
(CDCl3, 75 MHz)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
ppm

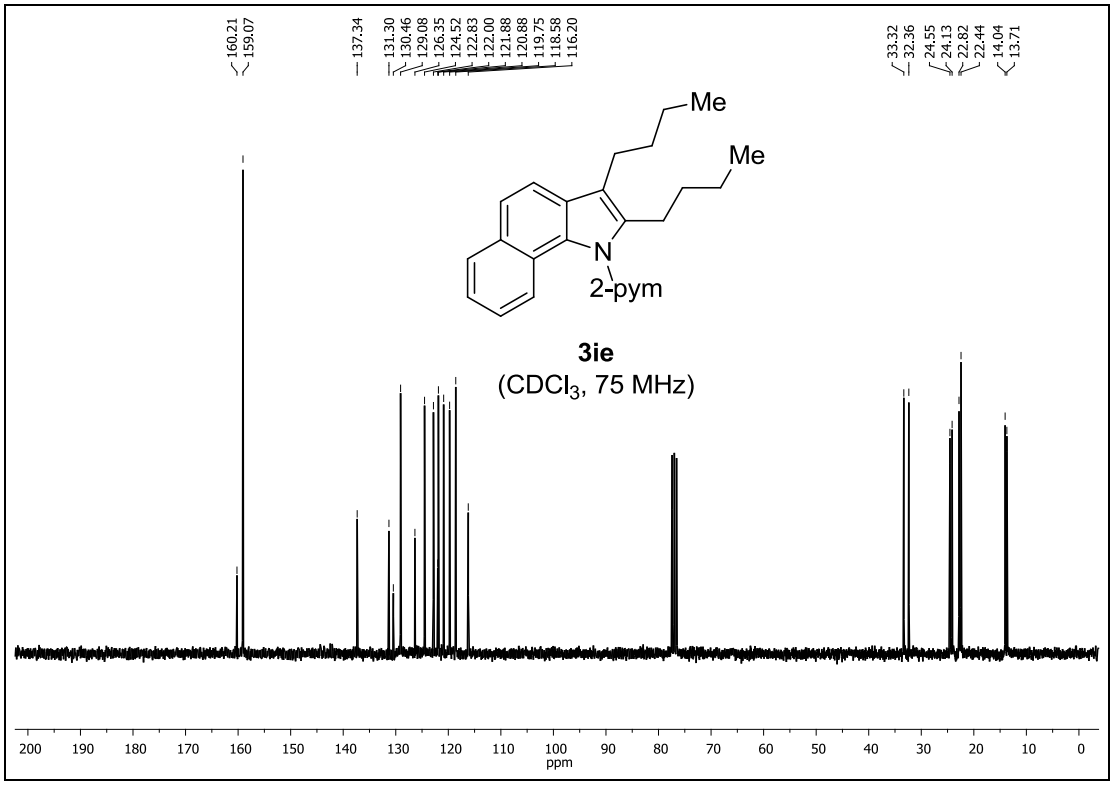

-121.89
-121.90
-121.91
-121.92
-121.94
-121.96
-121.97
OMe
F
OMe
N
2-pym
3ec
(CDCl3, 283 MHz)
-75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150 -155 -160 -165 -170 -175
ppm


F
F
N
2-pym
3bd
(CDCl3, 300 MHz)
2.02
1.00
1.00
1.09
3.12
5.28
2.21
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm

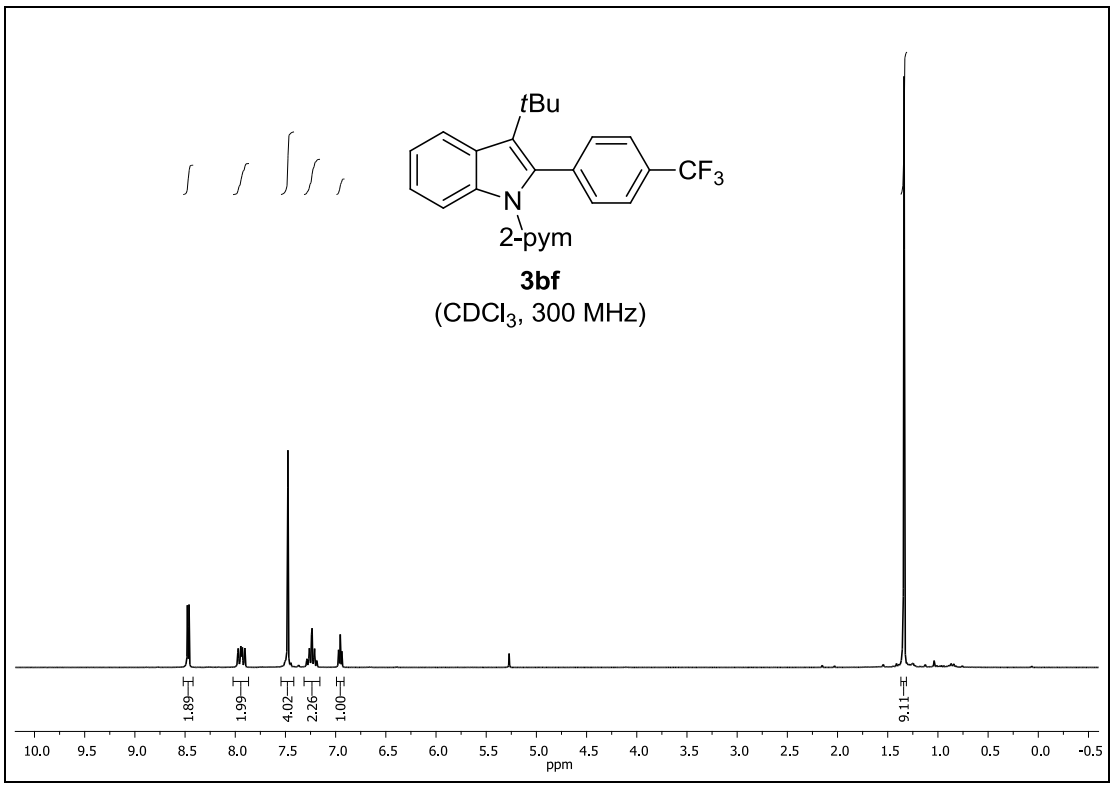

162.89
162.62
160.93
160.66
158.08
157.79
131.73
129.87
129.84
128.96
128.81
128.78
124.07
122.35
119.45
119.41
117.62
115.36
115.19
115.04
114.86
112.80
F
F
N
2-pym
3bd
(CDCl3, 75 MHz)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm


-114.24
-114.26
-114.27
-114.28
-114.29
-114.30
-114.31
-114.32
-114.34
-115.68
-115.70
-115.71
-115.72
-115.73
-115.74
-115.75
-115.76
-115.78
F
F
N
2-pym
3bd
(CDCl3, 283 MHz)
-65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150 -155 -160 -165 -170 -175
ppm

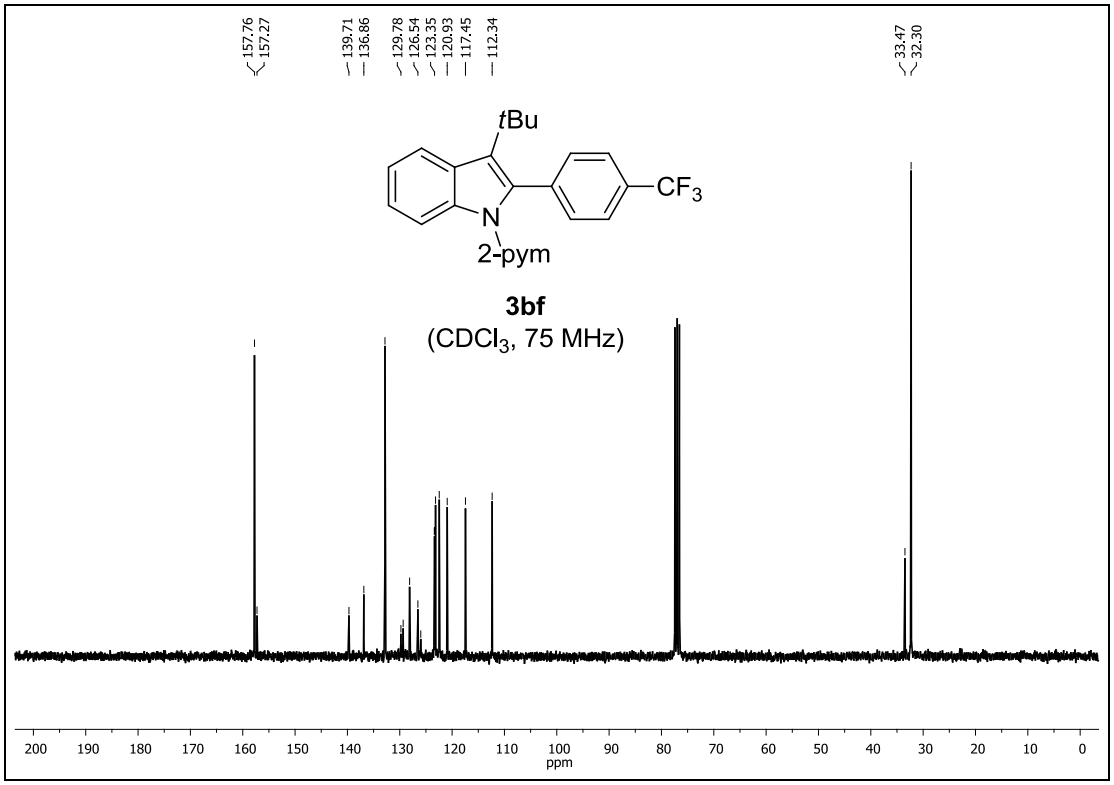

Me
Me
N
2-pym
3ie
(CDCl3, 300 MHz)
1.86
1.00
0.98
0.97
2.03
0.96
0.87
3.96
1.99
2.09
4.21
2.88
2.83
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm

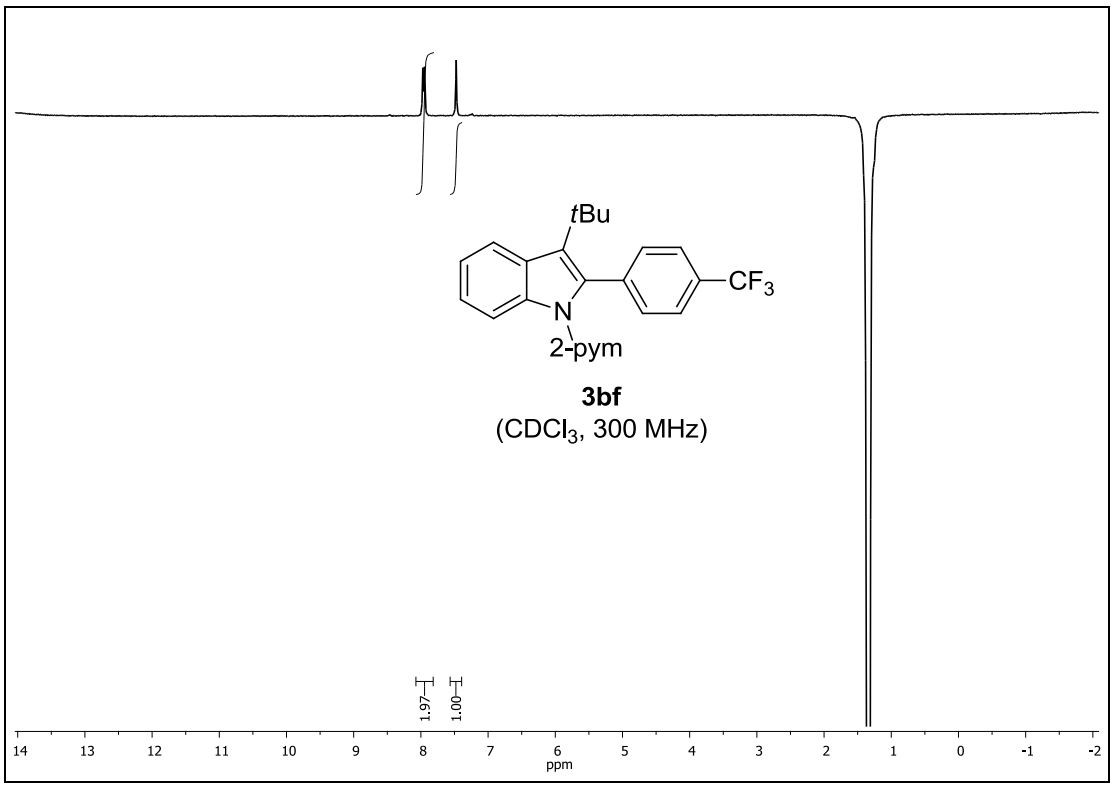


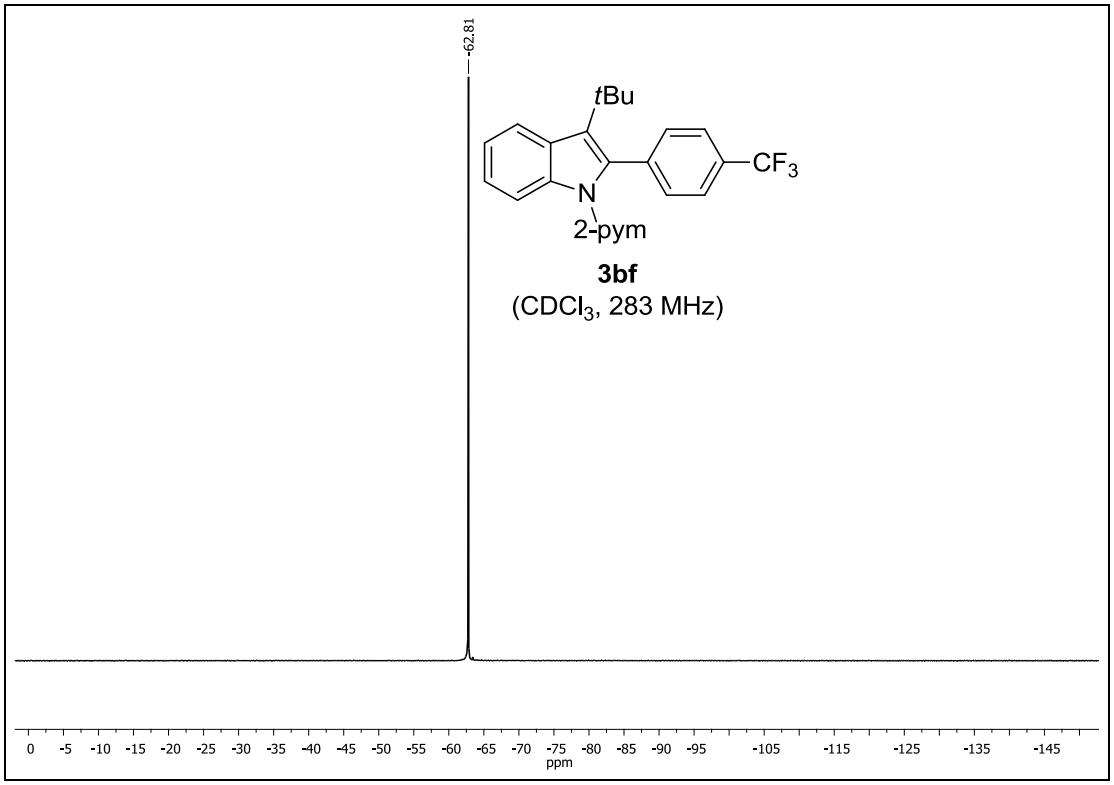
3ie
($CDCl_3$, 75 MHz)

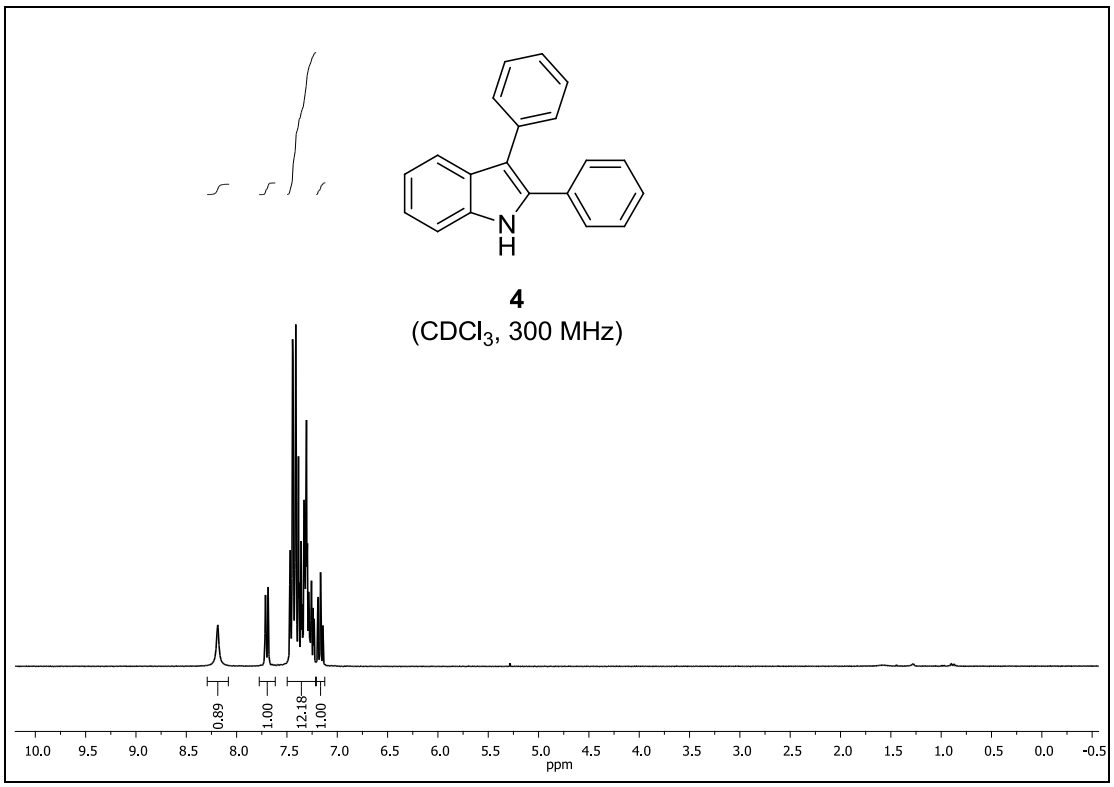


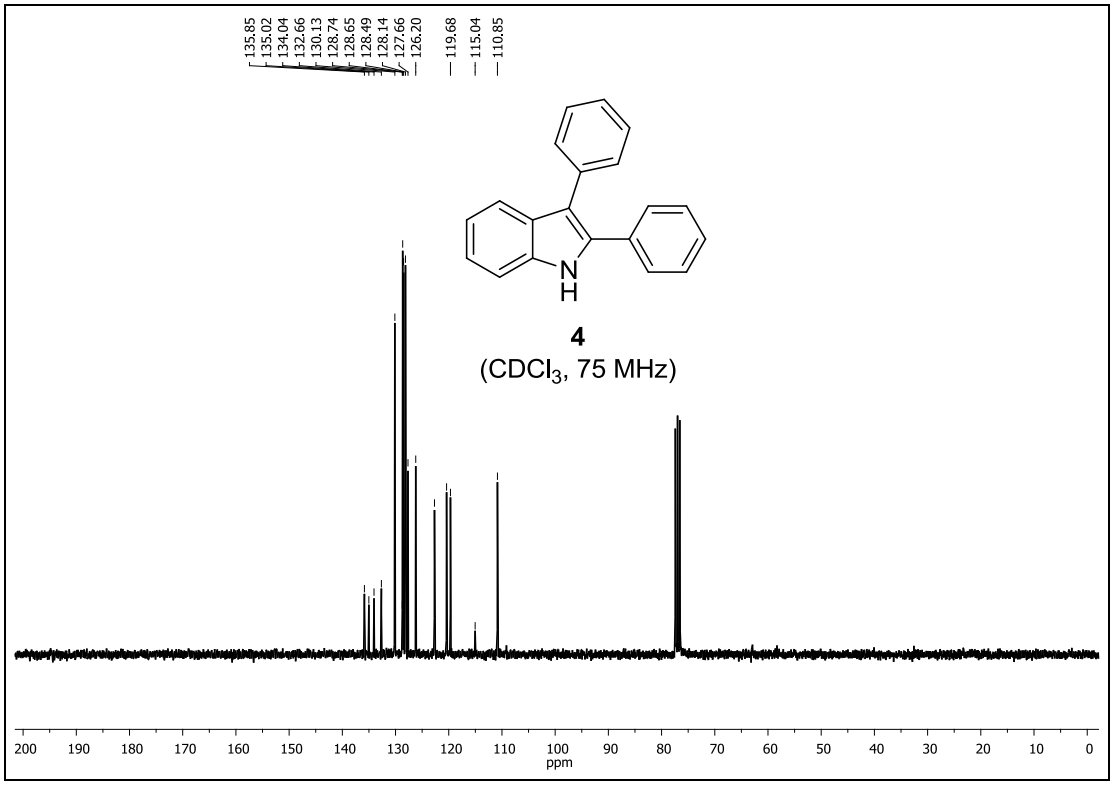
3bf
($CDCl_3$, 300 MHz)

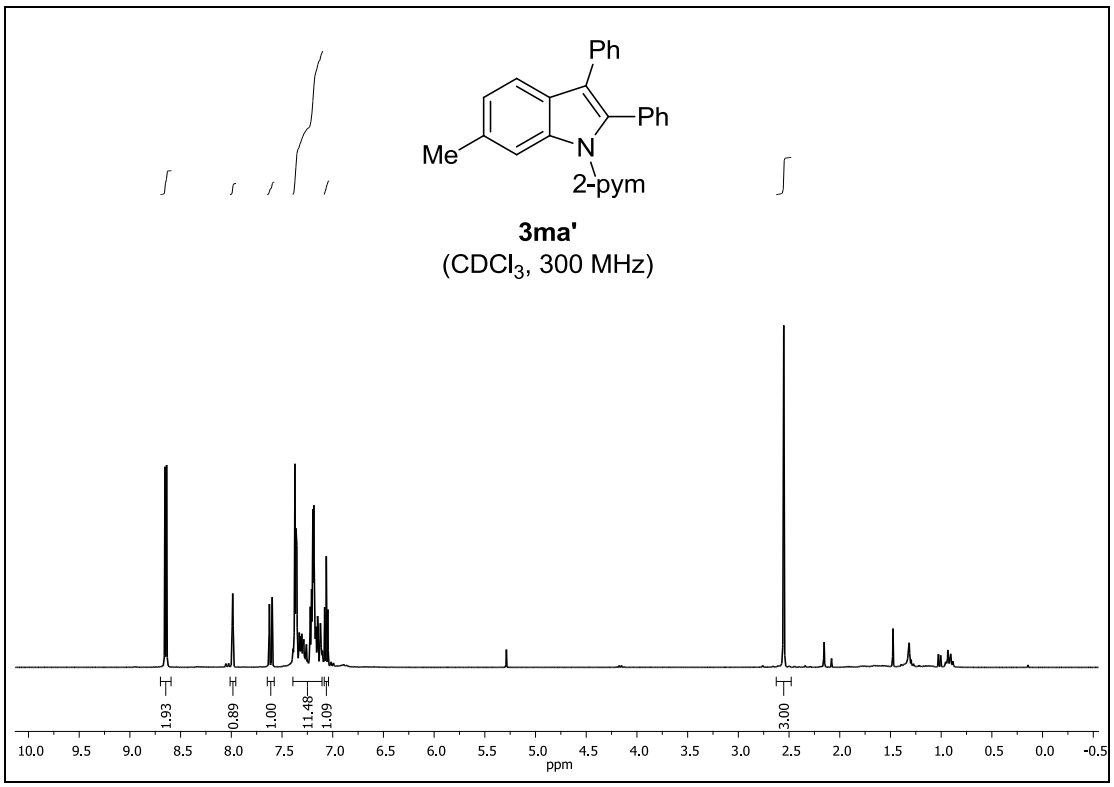

157.76
157.27
139.71
136.86
129.78
126.54
123.35
120.93
117.45
112.34
33.47
32.30
tBu
CF3
N
2-pym
3bf
(CDCl3, 75 MHz)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm

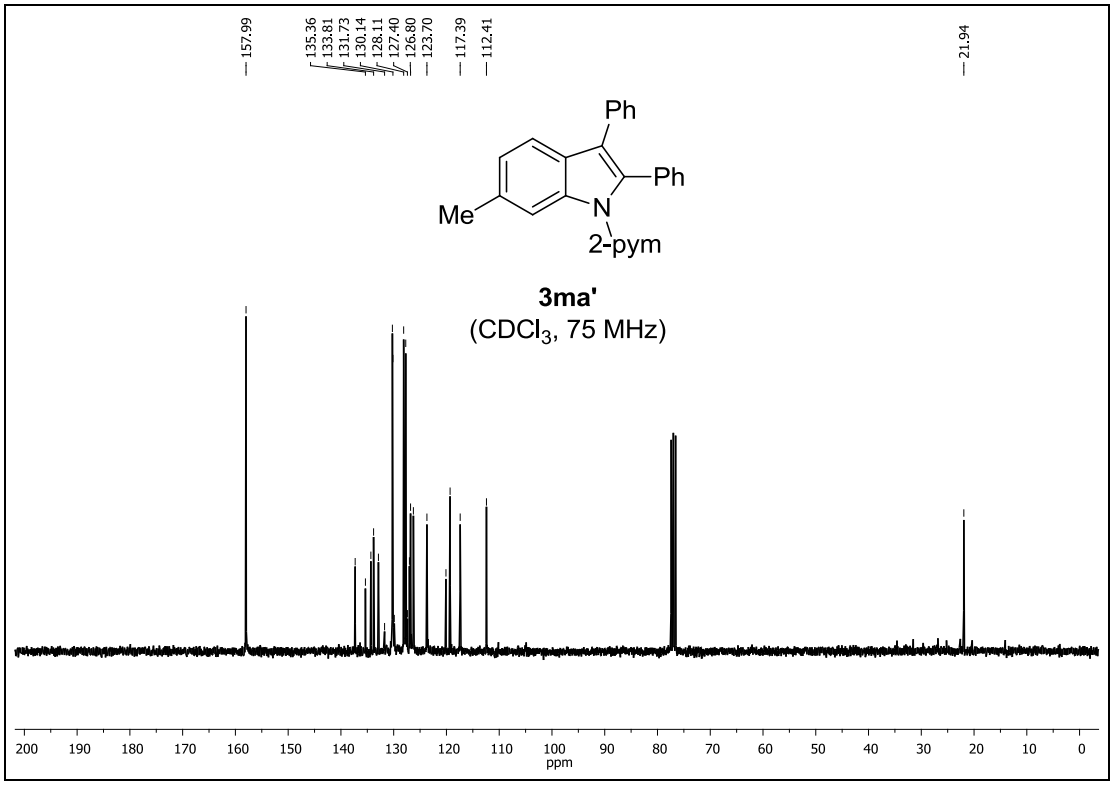

tBu
CF3
N
2-pym
3bf
(CDCl3, 300 MHz)
1.97
1.00
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2
ppm


-62.81
tBu
CF3
N
2-pym
3bf
(CDCl3, 283 MHz)
0 -5 -10 -15 -20 -25 -30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -105 -115 -125 -135 -145
ppm

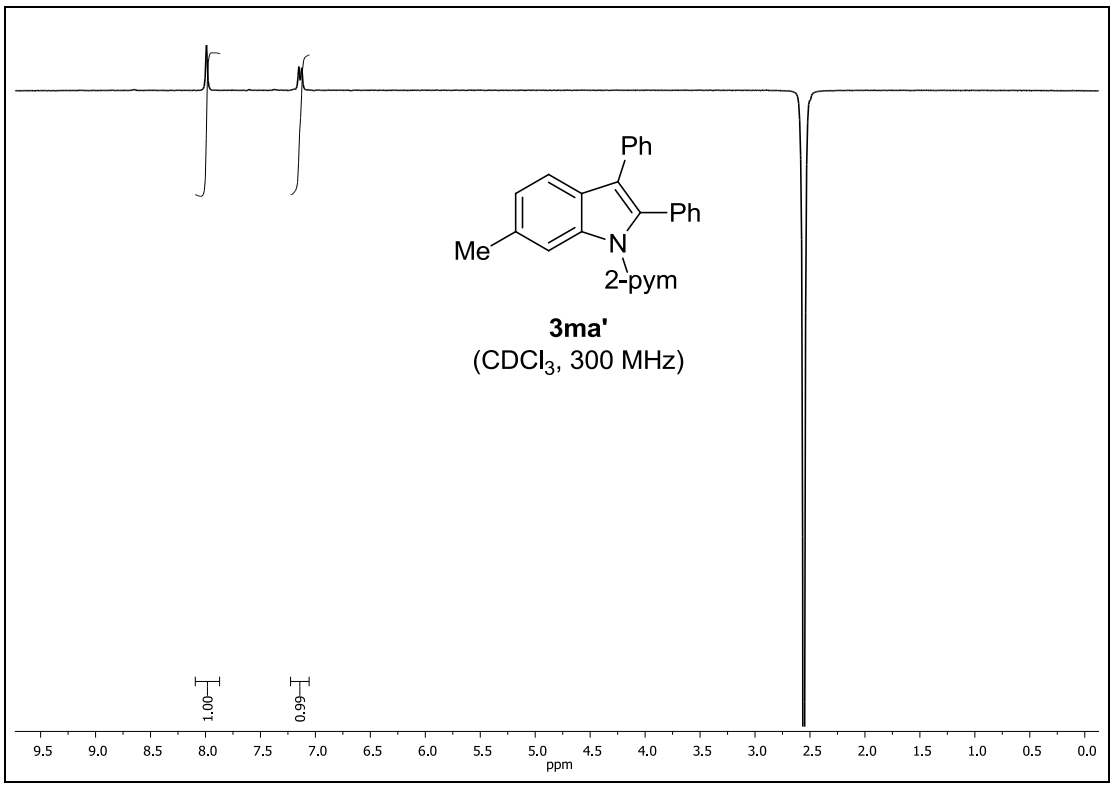

N
H
4
(CDCl3, 300 MHz)
0.89
1.00
12.18
1.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm


135.85
135.02
134.04
132.66
130.13
128.74
128.65
128.49
128.14
127.66
126.20
119.68
115.04
110.85
N
H
4
(CDCl3, 75 MHz)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm

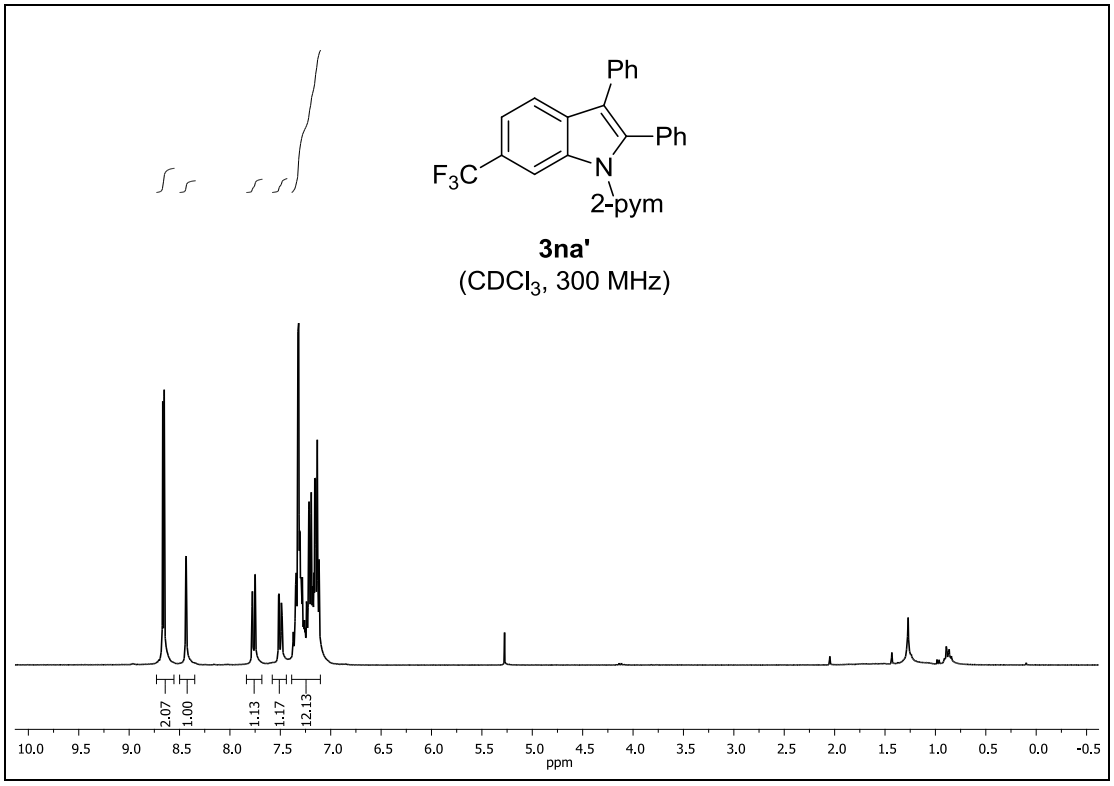

Ph
Ph
Me
N
2-pym
3ma'
(CDCl3, 300 MHz)
1.93
0.89
1.00
11.48
1.09
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm

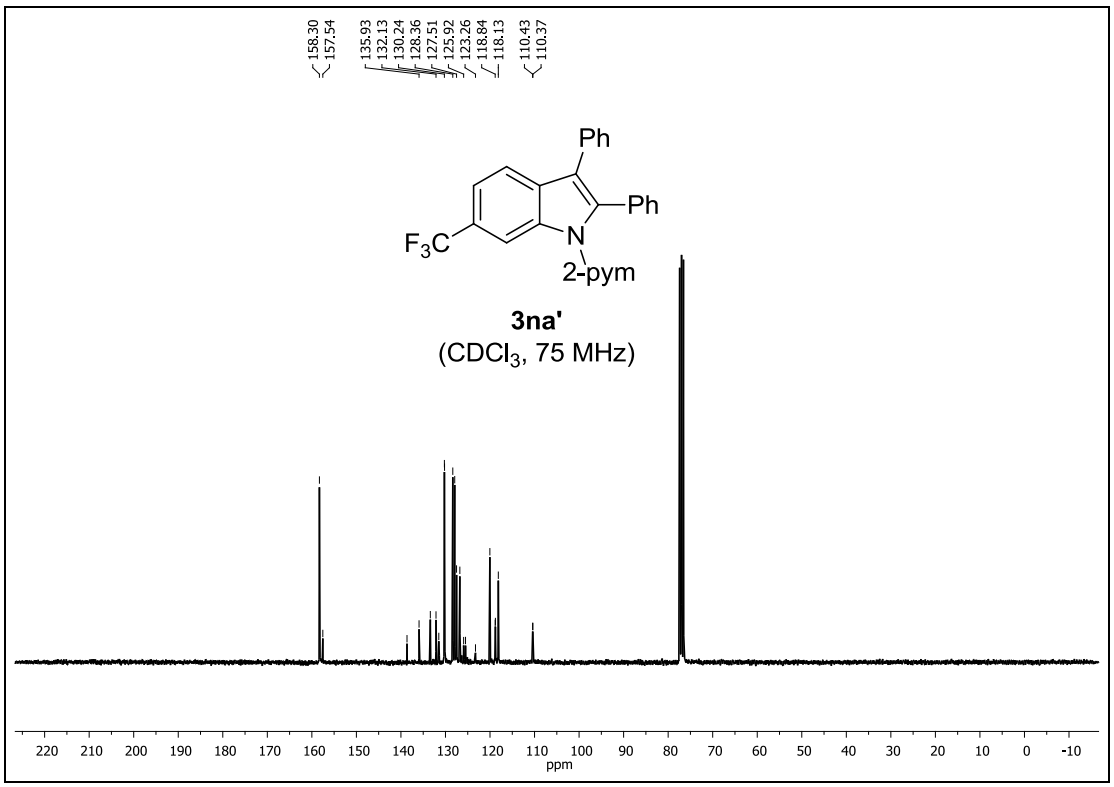


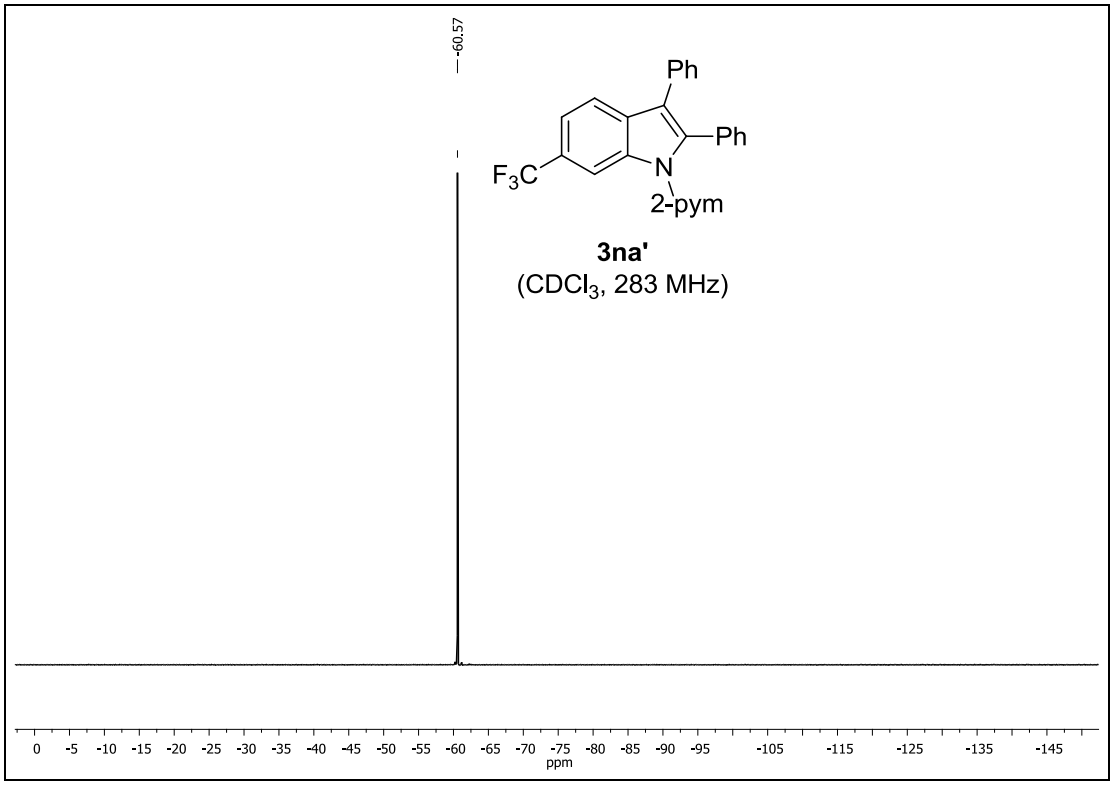
3ma'
($CDCl_3$, 75 MHz)



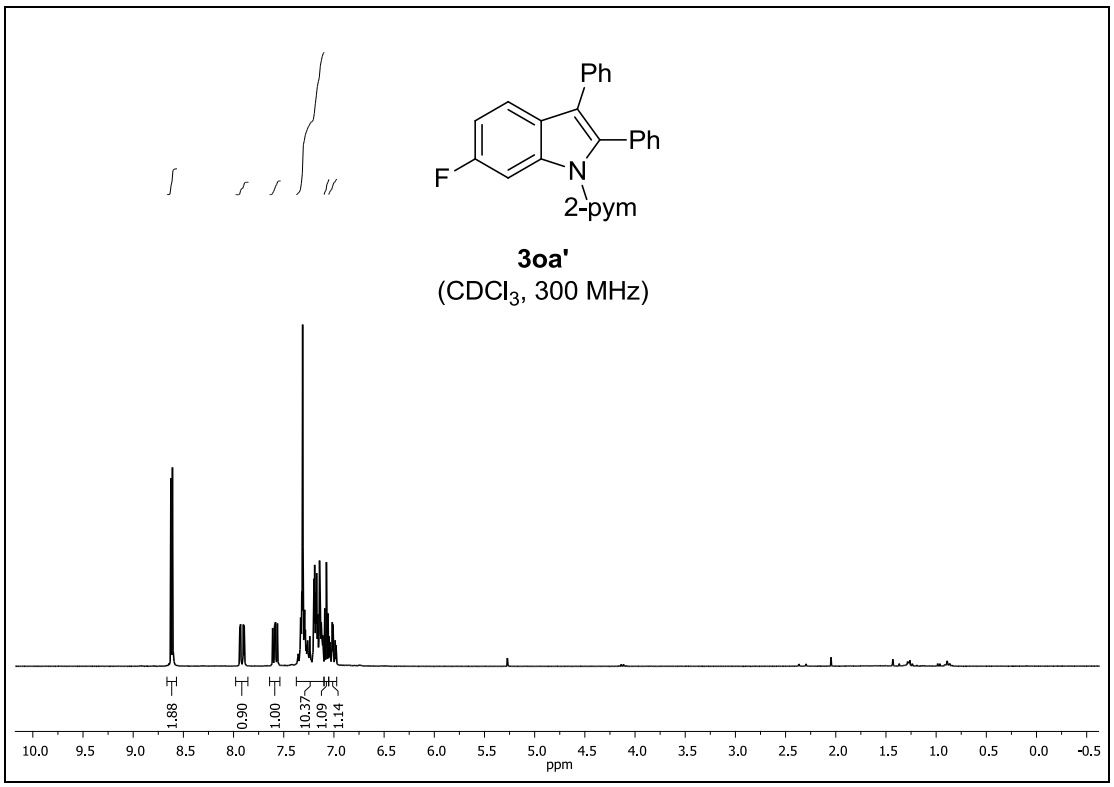
3ma'
($CDCl_3$, 300 MHz)



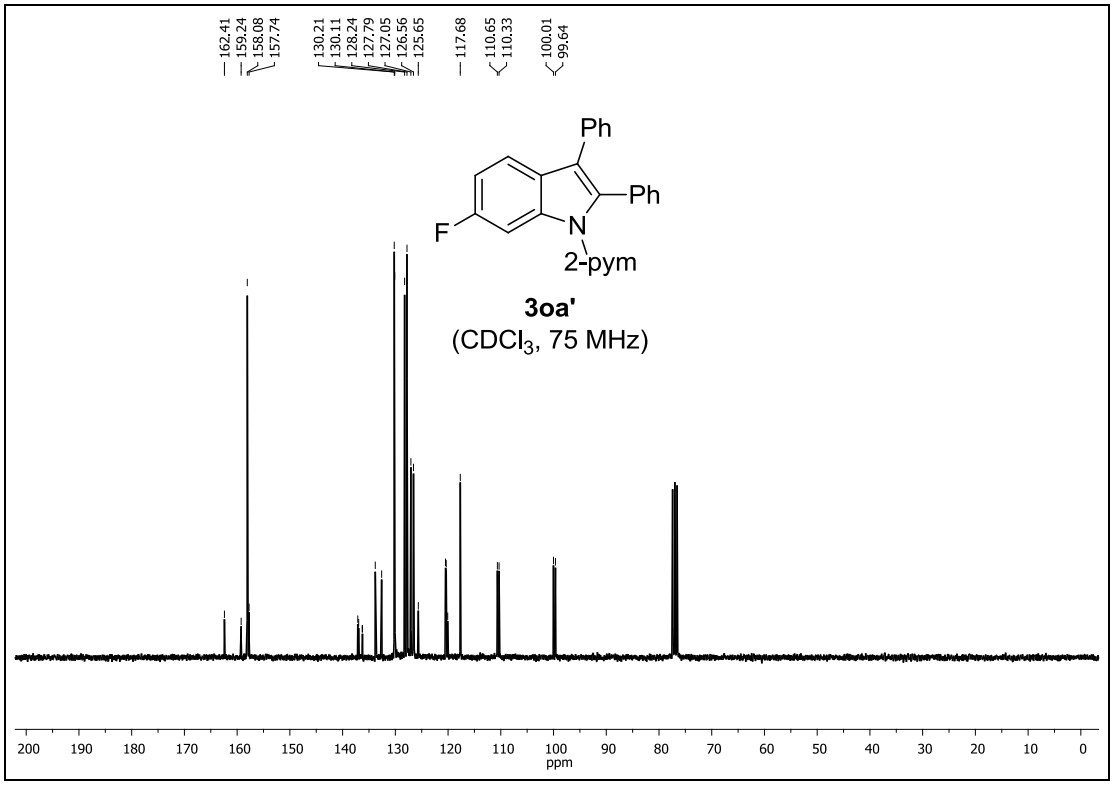


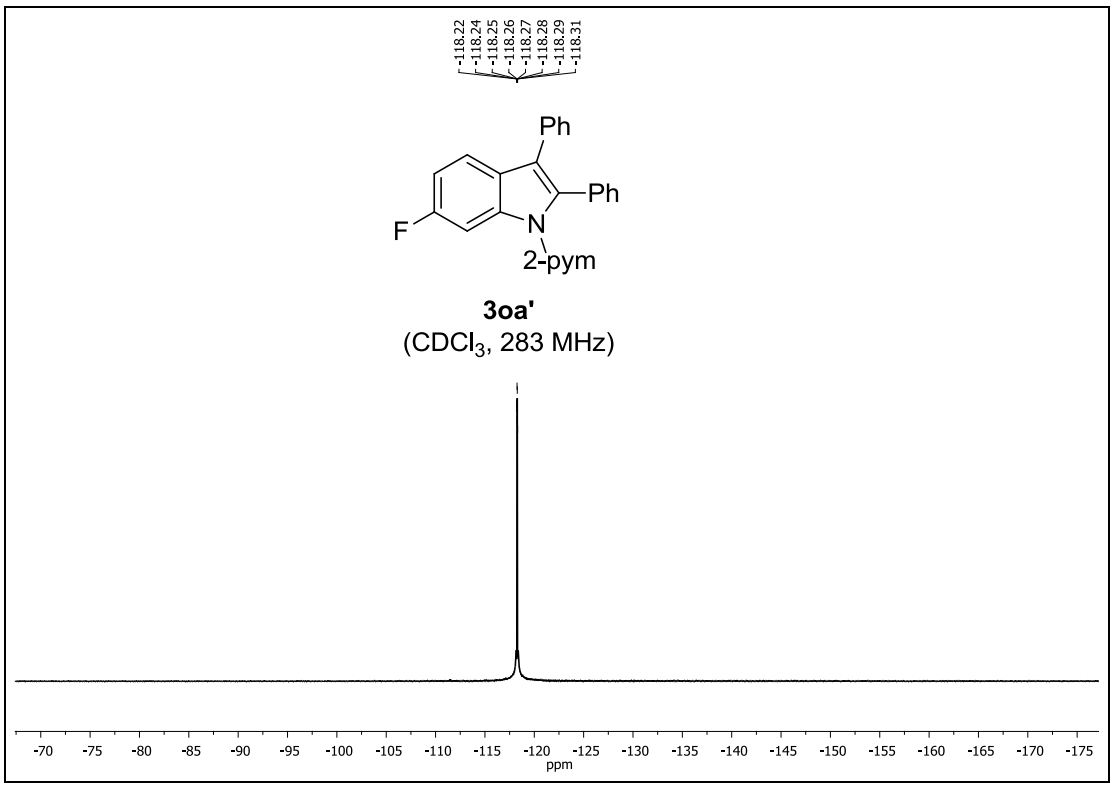


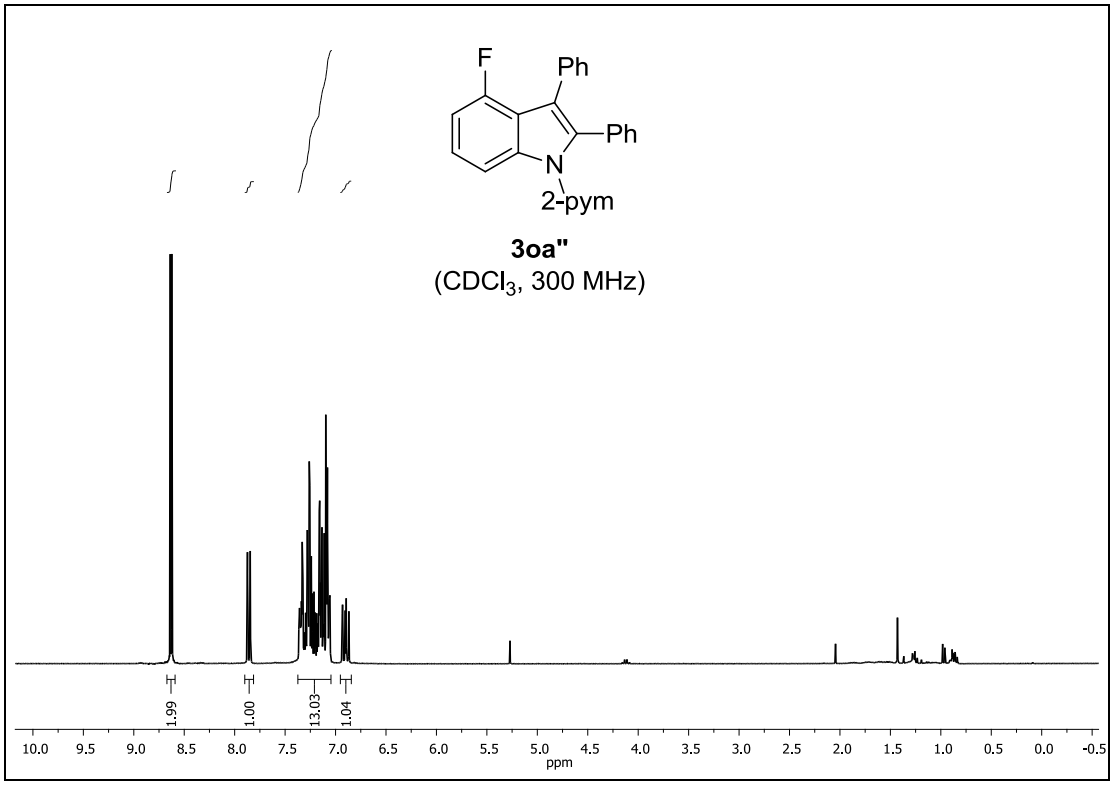
3na'
($CDCl_3$, 283 MHz)

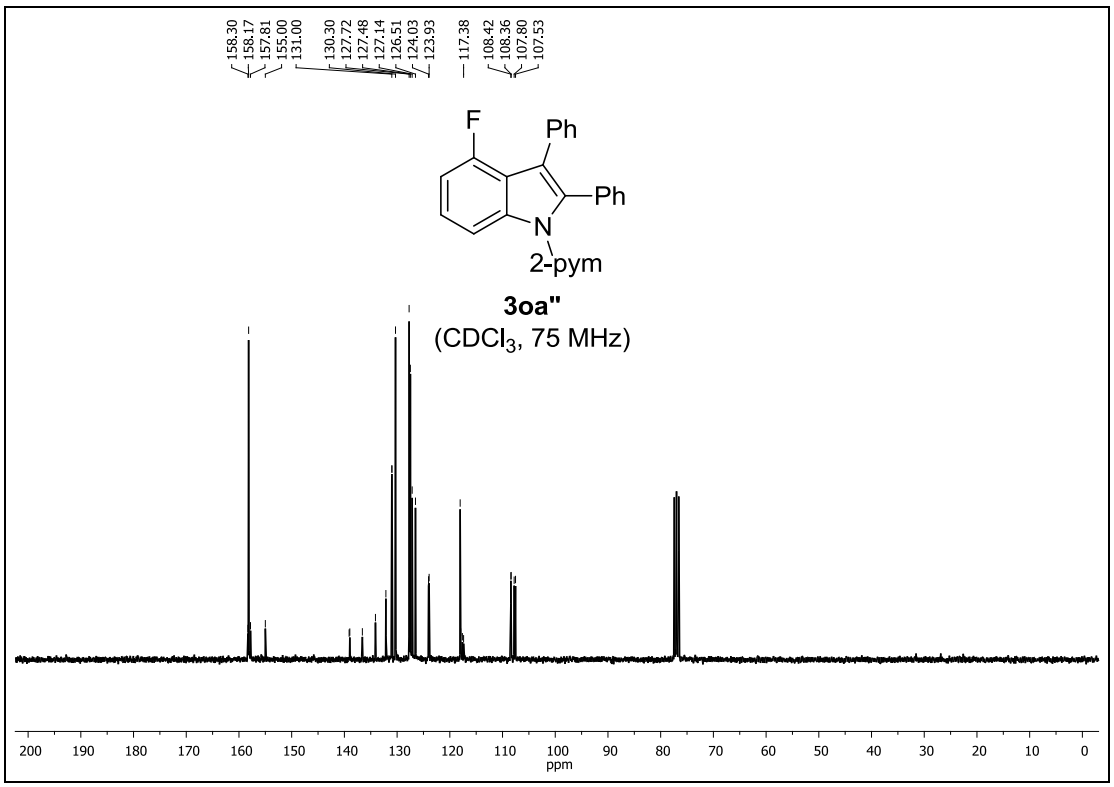


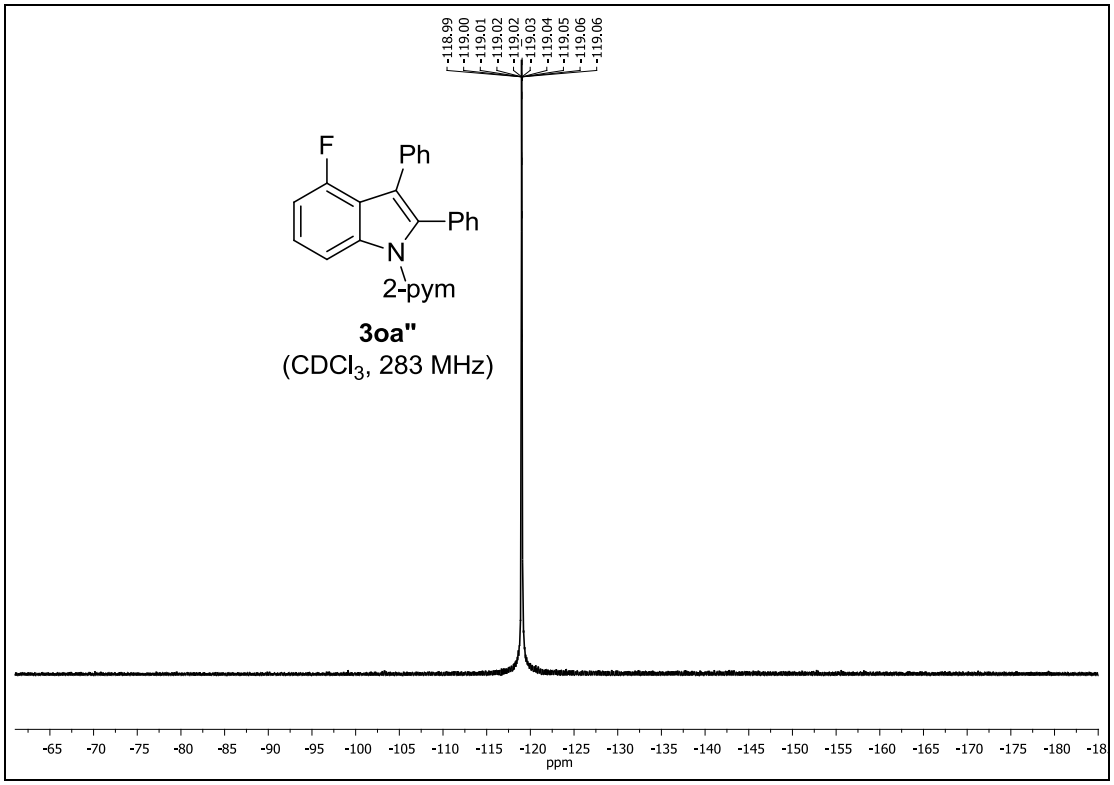
3oa'
($CDCl_3$, 300 MHz)

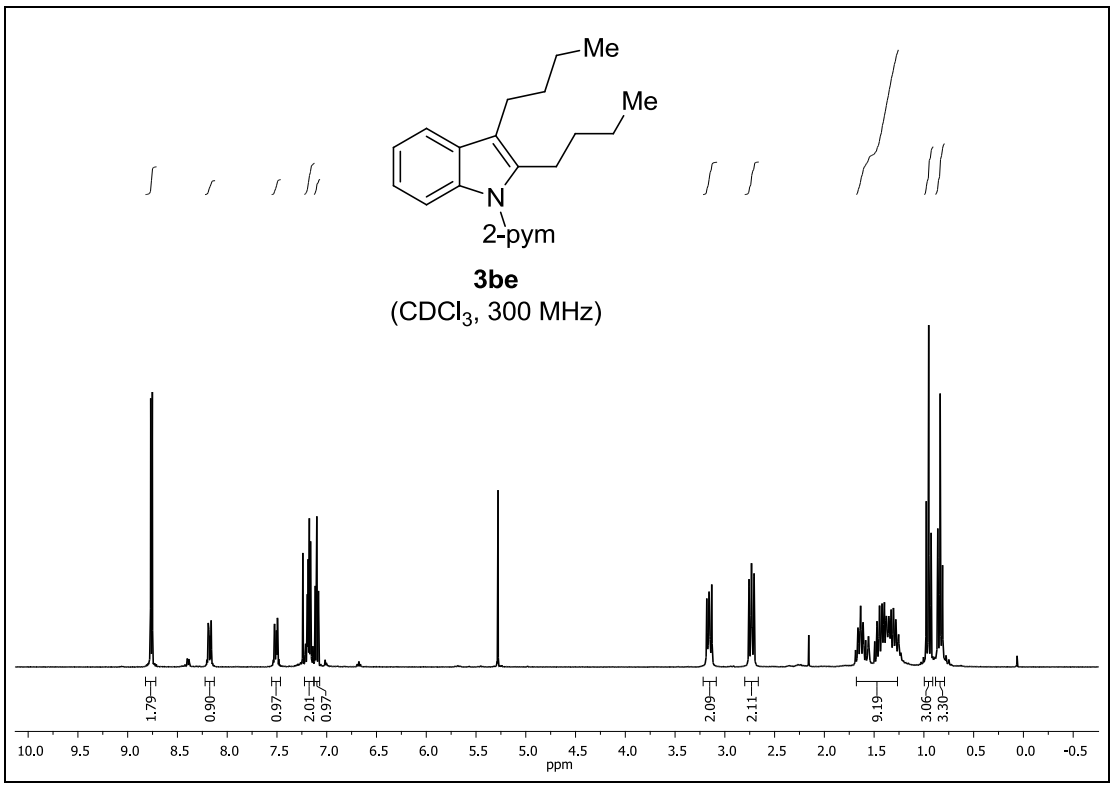

162.41
159.24
158.08
157.74
130.21
130.11
128.24
127.79
127.05
126.56
125.65
117.68
110.65
110.33
100.01
99.64
Ph
Ph
F
N
2-pym
3oa'
(CDCl3, 75 MHz)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm

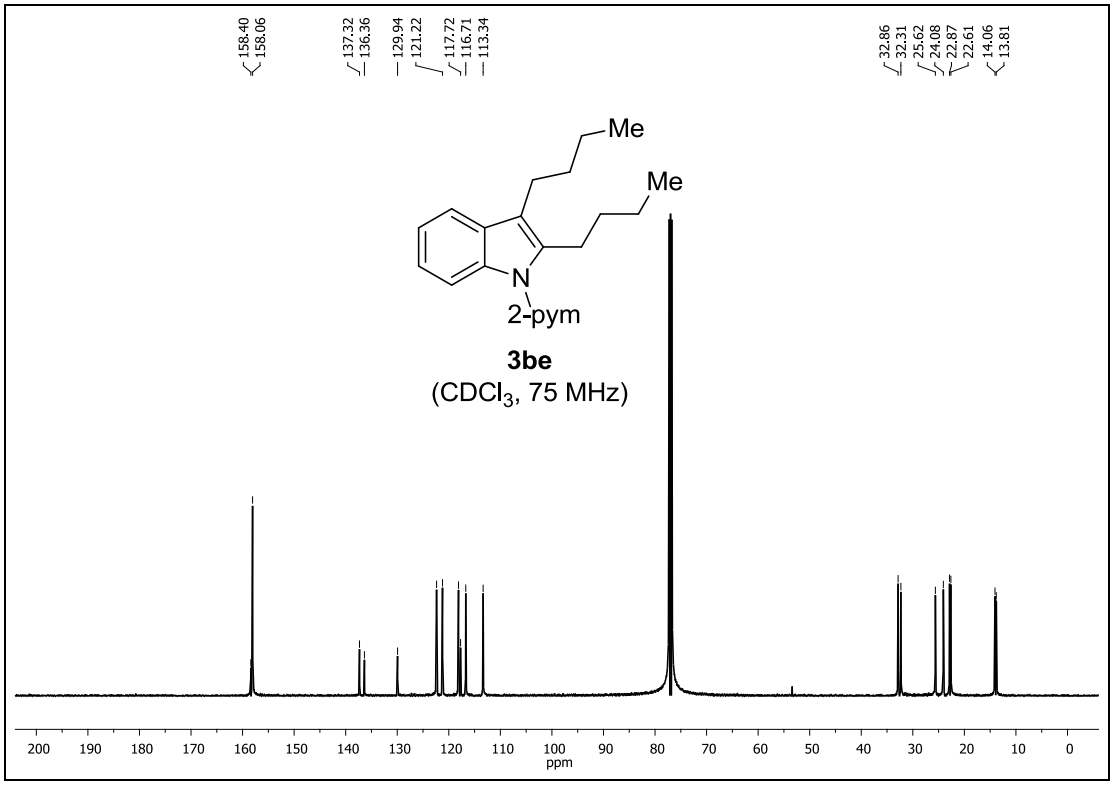

-118.22
-118.24
-118.25
-118.26
-118.27
-118.28
-118.29
-118.31
Ph
Ph
F
N
2-pym
3oa'
(CDCl3, 283 MHz)
-70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150 -155 -160 -165 -170 -175
ppm

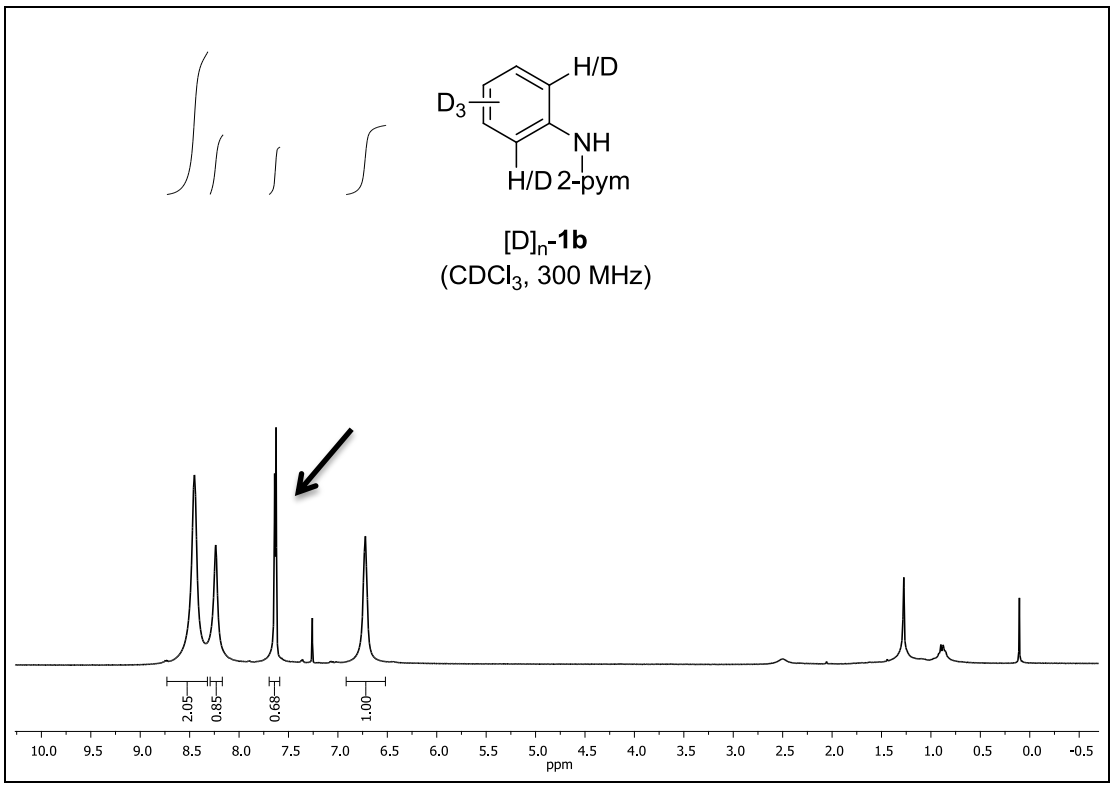

F
Ph
Ph
N
2-pym
3oa"
(CDCl3, 300 MHz)
1.99
1.00
13.03
1.04
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm


158.30
158.17
157.81
155.00
131.00
130.30
127.72
127.48
127.14
126.51
124.03
123.93
117.38
108.42
108.36
107.80
107.53
F
Ph
Ph
N
2-pym
3oa"
(CDCl3, 75 MHz)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm


-118.99
-119.00
-119.01
-119.02
-119.02
-119.03
-119.04
-119.05
-119.06
-119.06
F
Ph
Ph
N
2-pym
3oa"
(CDCl3, 283 MHz)
-65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150 -155 -160 -165 -170 -175 -180 -18
ppm


Me
Me
N
2-pym
3be
(CDCl3, 300 MHz)
1.79
0.90
0.97
2.01
0.97
2.09
2.11
9.19
3.06
3.30
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm


158.40
158.06
137.32
136.36
129.94
121.22
117.72
116.71
113.34
32.86
32.31
25.62
24.08
22.87
22.61
14.06
13.81
Me
Me
N
2-pym
3be
(CDCl3, 75 MHz)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm


H/D
D3
NH
H/D 2-pym
[D]n-1b
(CDCl3, 300 MHz)
2.05
0.85
0.68
1.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm