Metal-free synthesis of 3,5-disubstituted 1*H*- and 1-aryl-1*H*-pyrazoles from 1,3-diyne-indole derivatives employing two successive hydroaminations

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General information: PEG-400 and other commercial reagents were used without further purification. In the conventional purification procedure, the crude material was submitted to flash column chromatography with silica gel 60 H (particle size 40-63 μm, 230-400 mesh), eluting isocratically with mixtures of hexane:EtOAc.

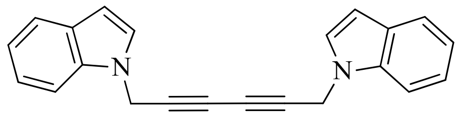
All new compounds gave single spots when run on TLC plates of Kieselgel 60 GF_{254}, employing different hexane-EtOAc solvent systems. Chromatographic spots were detected by irradiation of the plates with UV light (254 nm), followed by exposure to iodine vapors of by spraying with ethanolic vanillin/sulfuric acid reagent and careful heating.

Equipment: The melting points were measured on an MQAPF-301 (Microquímica) instrument and are reported uncorrected. The infrared spectra were acquired on a Shimadzu Prestige-21 spectrometer, with the samples prepared as KBr pellets or thin films held between NaCl disks. The NMR spectra (^{1}H and ^{13}C) were recorded in $CDCl_3$ unless otherwise noted, on Bruker DPX-400 and Bruker DPX-600 spectrometers (400 and 600 MHz for ^{1}H, respectively). Chemical shift data are reported in ppm downfield from TMS, employed as internal standard. Coupling constants (J) are informed in Hertz. Elemental analyses were recorded on a Perkin-Elmer CHN 2400 analyzer. The low resolution mass spectra were acquired on a Shimadzu QP2010 *Plus* CG-MS instrument. High-resolution mass spectral data were obtained in a Bruker microTOF-Q II instrument. Detection of the ions was performed with electrospray ionization in positive ion mode.

General procedure for the synthesis of the symmetric 1,3-diynes (1a-f)

A stirred mixture of the heterocyclic *N*-propargyl derivative (5 mmol) and CuCl (25 mg, 0.25 mmol, 5 mol%) in DMSO (5 mL) was heated to 90 ºC for 4 h. Then, the reaction was cooled to room temperature and filtered through Celite. The filtrate was diluted with water (15 mL) and extracted with EtOAc (4 × 25 mL). The combined extracts were successively washed with water (1 × 10 mL) and brine (1 × 10 mL). The organic layer was dried over $MgSO_4$, and concentrated under reduced pressure. The product was purified by column chromatography using an hexane: EtOAc:CH_2Cl_2 (80:10:10) solvent mixture as eluent.

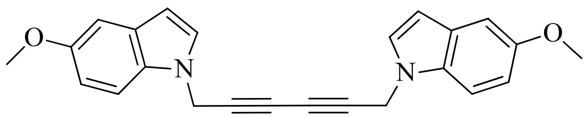
1,6-Bis(1*H*-indol-1-yl)hexa-2,4-diyne (1a)



1a

Light brown solid, m.p.: 147-149 °C; yield: 83%. ^{1}H NMR (400 MHz) δ: 4.84 (s, 4H), 6.49 (d, *J* = 3.1, 2H), 7.07 (d, *J* = 3.1, 2H), 7.10-7.13 (m, 2H), 7.19-7.23 (m, 2H), 7.31 (d, *J* = 8.2, 2H) and 7.60 (d, *J* = 7.9, 2H). ^{13}C NMR (100 MHz) δ: 36.3, 69.0, 73.3, 102.5, 109.2, 120.0, 121.1, 122.1, 127.2, 128.9 and 135.8. IR (KBr, ν): 3104, 2904, 1614, 1463, 1333, 1315, 1185, 739 and 719 cm^{-1}. MS (*m/z*, rel. int., %): 309 [12, $(M+1)^+$], 308 (51, M^+), 281 (28), 253 (17), 209 (14), 208 (21), 207 (100), 191 (100), 133 (15), 117 (38), 89 (24) and 73 (27). HRMS (ESI–TOF, *m/z*): Obsd. 331.1208; $C_{22}H_{16}N_2Na$ [$(M+Na)^+$] requires 331.1211.

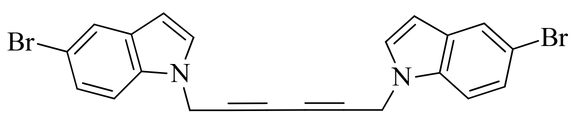
1,6-Bis(5-methoxy-1*H*-indol-1-yl)hexa-2,4-diyne (1b)



1b

Beige solid, m.p.: 166-168 °C; yield: 72%. ^{1}H NMR (400 MHz) δ: 3.82 (s, 6H), 4.84 (s, 4H), 6.42 (dd, *J* = 3.2 and 0.8, 2H), 6.88 (dd, *J* = 8.9 and 2.4, 2H), 7.06 (d, *J* = 3.2, 2H), 7.07 (d, *J* = 2.4, 2H) and 7.21 (d, *J* = 8.9, 2H). ^{13}C NMR (100 MHz) δ: 36.5, 55.9, 69.0, 73.3, 102.1, 103.0, 109.9, 112.3, 127.8, 129.3, 131.1 and 154.5. IR (KBr, ν): 3102, 2956, 2935, 2832, 1728, 1616, 1576, 1482, 1432, 1397, 1243, 1152, 1030, 802 and 726 cm^{-1}. MS (*m/z*, rel. int., %): 368 (3, M^+), 78 (99), 63 (100), 62 (13) and 61 (36). Anal. Calc.: C, 78.24; H, 5.47; N, 7.60. Found: C, 77.86; H, 5.54; N, 7.25.

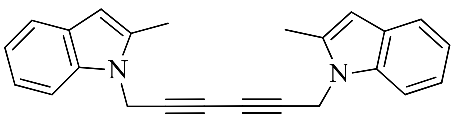
1,6-Bis(5-bromo-1*H*-indol-1-yl)hexa-2,4-diyne (1c)



1c

Beige solid, m.p.: 157-159 °C; yield: 76%. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 5.26 (s, 4H), 6.46 (dd, *J* = 3.2 and 0.7, 2H), 7.29 (dd, *J* = 8.7 and 1.9, 2H), 7.42 (d, *J* = 3.2, 2H), 7.47 (d, *J* = 8.7, 2H) and 7.75 (d, *J* = 1.9, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ: 35.6, 67.5, 75.0, 101.3, 111.8, 112.2, 122.7, 123.9, 129.8, 130.0 and 134.1. IR (KBr, ν): 3106, 1705, 1604, 1562, 1507, 1463, 1333, 1208, 793, 754 and 581 cm^{-1}. MS (*m/z*, rel. int., %): 468 [2, $(M+2)^+$], 466 (4, M^+), 235 (27), 233 (28), 197 (55), 195 (55), 154 (60), 127 (15), 116 (78) and 89 (39). Anal. Calc.: C, 56.68; H, 3.03; N, 6.01. Found: C, 57.07; H, 3.13; N, 5.87.

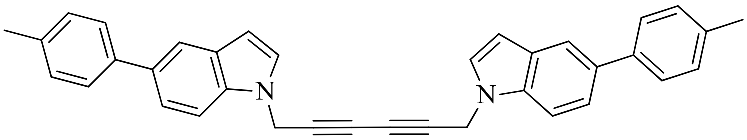
1,6-Bis(2-methyl-1*H*-indol-1-yl)hexa-2,4-diyne (1d)



1d

Brown solid, m.p.: 218 °C (dec); yield: 83%. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 2.39 (s, 6H), 5.13 (s, 4H), 6.22 (s, 2H), 6.98-7.09 (m, 4H) and 7.40-7.43 (m, 4H). ^{13}C NMR (100 MHz, DMSO-d_6) δ: 12.1, 32.4, 66.7, 75.3, 100.5, 109.3, 119.3, 119.5, 120.6, 127.7, 136.2 and 136.3. IR (KBr, ν): 2916, 1614, 1552, 1462, 1337, 787 and 745 cm^{-1}. MS (*m/z*, rel. int., %): 337 [17, (M+1)$^+$], 336 (60, M$^+$), 205 (100), 204 (88), 191 (28), 167 (18), 149 (12), 130 (44), 97 (18), 81 (26) and 69 (47). HRMS (ESI–TOF, *m/z*): Obsd. 359.1507; $C_{24}H_{20}N_2Na$ [(M+Na)$^+$] requires 359.1519.

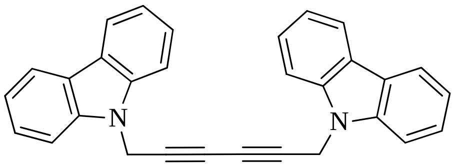
1,6-Bis(5-*p*-tolyl-1*H*-indol-1-yl)hexa-2,4-diyne (1e)



1e

Brown solid, m.p.: 175-177 °C; yield: 72%. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 2.33 (s, 6H), 5.27 (s, 4H), 6.50 (d, *J* = 3.1, 2H), 7.23 (d, *J* = 7.9, 4H), 7.38 (d, *J* = 3.1, 2H), 7.44 (dd, *J* = 8.6 and 1.6, 2H), 7.53-7.55 (m, 6H) and 7.79-7.80 (m, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ: 20.6, 35.6, 67.4, 75.4, 102.1, 110.3, 118.3, 120.8, 126.5, 128.9, 129.1, 129.4, 132.1, 134.9, 135.5 and 138.5. IR (KBr, ν): 2915, 1616, 1476, 1335, 799 and 720 cm^{-1}. MS (*m/z*, rel. int., %): 489 [20, (M+1)$^+$], 488 (50, M$^+$), 282 (22), 281 (32), 267 (28), 266 (20), 244 (17), 208 (20), 207 (100), 206 (64), 204 (25), 97 (23) and 57 (46). HRMS (ESI–TOF, *m/z*): Obsd. 511.2129; $C_{36}H_{28}N_2Na$ [(M+Na)$^+$] requires 511.2145.

1,6-Bis(9*H*-carbazol-9-yl)hexa-2,4-diyne (1f)



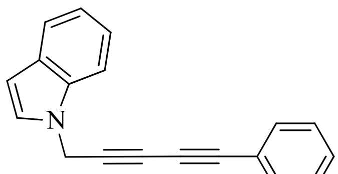
1f

White crystalline solid, m.p.: 204 °C (dec); yield: 60%. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 5.39 (s, 4H), 7.20-7.24 (m, 4H), 7.42-7.46 (m, 4H), 7.59 (d, *J* = 8.1, 4H) and 8.12 (d, *J* = 7.6, 4H). ^{13}C NMR (100 MHz, DMSO-d_6) δ: 32.2, 66.5, 74.8, 109.2, 119.4, 120.1, 122.4, 125.7 and 139.3. IR (KBr, ν): 3050, 2910, 1625, 1599, 1485, 1454, 1325, 747 and 720 cm^{-1}. MS (*m/z*, rel. int., %): 409 [16, (M+1)$^+$], 408 (50, M$^+$), 242 (36), 241 (100), 167 (18), 166 (29) and 140 (16). HRMS (ESI–TOF, *m/z*): Obsd. 431.1521; $C_{30}H_{20}N_2Na$ [(M+Na)$^+$] requires 431.1524.

General procedure for the preparation of unsymmetric 1,3-diynes (3a-f)

Solid CuI (10 mg, 0.05 mmol, 5 mol%) and $NiCl_2.6H_2O$ (12 mg, 0.05 mmol, 5 mol%) were added to a stirred solution of TMEDA (30 µL, 0.2 mmol, 20 mol%) in THF (4 mL). The aryl acetylene (5 mmol) and the *N*-propargyl indole or carbazole (1 mmol) were successively added and the system was allowed to stir at room temperature for 6 h. Then, the volatiles were evaporated under reduced pressure and the residue was chromatographically purified, eluting with hexane.

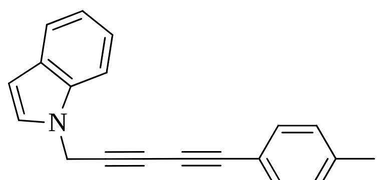
1-(5-Phenylpenta-2,4-diynyl)-1*H*-indole (3a)



3a

Light brown solid, m.p.: 68-70 °C; yield: 76%. ^1H NMR (400 MHz) δ: 4.97 (s, 2H), 6.53 (dd, *J* = 3.2 and 0.6, 1H), 7.12-7.19 (m, 2H), 7.23-7.34 (m, 4H), 7.38 (d, *J* = 8.2, 1H), 7.43-7.45 (m, 2H) and 7.63 (d, *J* = 7.8, 1H). ^{13}C NMR (100 MHz) δ: 36.6, 69.9, 73.2, 76.4, 78.2, 102.4, 109.3, 120.0, 121.1, 121.2, 122.0, 127.2, 128.4, 128.9, 129.4, 132.6 and 135.8. IR (KBr, ν): 3045, 2942, 2240, 1609, 1573, 1513, 1483, 1355, 1304, 1254, 1192, 752, 732 and 686 cm^{-1}. MS (*m/z*, rel. int., %): 256 [15, $(M+1)^+$], 255 (73, M^+), 254 (44), 140 (12), 139 (100), 113 (9) and 89 (14). HRMS (ESI–TOF, *m/z*): Obsd. 278.0948; $C_{19}H_{13}NNa$ [$(M+Na)^+$] requires 278.0946.

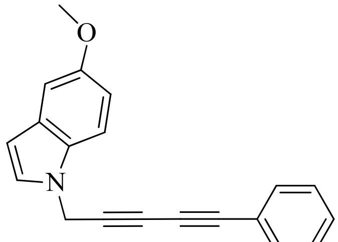
1-(5-*p*-Tolylpenta-2,4-diynyl)-1*H*-indole (3b)



3b

Light brown solid, m.p.: 83-85 °C; yield: 70%. ^1H NMR (400 MHz) δ: 2.33 (s, 3H), 4.99 (s, 2H), 6.54 (dd, *J* = 3.2 and 0.5, 1H), 7.09 (d, *J* = 8.0, 2H), 7.12-7.16 (m, 1H), 7.18 (d, *J* = 3.2, 1H), 7.24-7.27 (m, 1H), 7.35 (d, *J* = 8.1, 2H), 7.40 (d, *J* = 8.3, 1H) and 7.64 (d, *J* = 7.9, 1H). ^{13}C NMR (100 MHz) δ: 21.5, 36.7, 70.1, 72.7, 76.1, 78.6, 102.4, 109.3, 118.2, 120.0, 121.1, 122.0, 127.2, 129.0, 129.2, 132.5, 135.9 and 139.8. IR (KBr, ν): 3028, 2951, 2239, 1604, 1508, 1462, 1336, 1314, 1257, 1182, 811, 742 and 720 cm^{-1}. MS (*m/z*, rel. int., %): 270 [14, $(M+1)^+$], 269 (63, M^+), 268 (25), 207 (13), 154 (14), 153 (100) and 152 (23). HRMS (ESI–TOF, *m/z*): Obsd. 270.1255; $C_{20}H_{16}N$ [$(M+H)^+$] requires 270.1283.

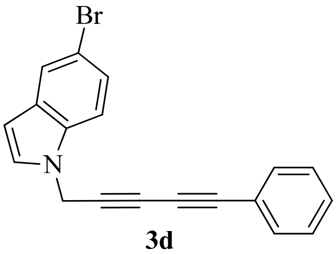
5-Methoxy-1-(5-phenylpenta-2,4-diynyl)-1*H*-indole (3c)



3c

Beige solid, m.p: 105-107 °C; yield: 83%. ^1H NMR (400 MHz) δ: 3.84 (s, 3H), 4.95 (s, 2H), 6.45 (d, *J* = 3.0, 1H), 6.91 (dd, *J* = 8.8 and 2.3, 1H), 7.09 (d, *J* = 2.3, 1H), 7.14 (d, *J* = 3.0, 1H), 7.26-7.35 (m, 4H) and 7.44-7.46 (m, 2H). ^{13}C NMR (100 MHz) δ: 36.8, 55.9, 69.8, 73.2, 76.5, 78.2, 102.0, 103.0, 110.0, 112.3, 121.2, 127.9, 128.4, 129.4, 131.2, 132.6 and 154.5. IR (KBr, ν): 2943, 2901, 2244, 1619, 1574, 1486, 1451, 1423, 1347, 1237, 1152, 1026, 801, 757, 722 and 687 cm^{-1}. MS (*m/z*, rel. int., %): 286 [16, $(M+1)^+$], 285 (69, M^+), 281 (11), 254 (11), 207 (29), 140 (13) and 139 (100). HRMS (ESI–TOF, *m/z*): Obsd. 308.1039; $C_{20}H_{15}NNaO$ [$(M+Na)^+$] requires 308.1046.

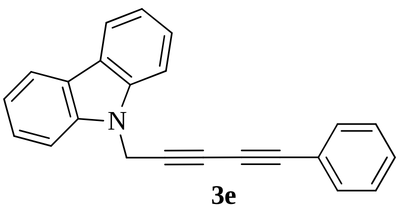
5-Bromo-1-(5-*p*-tolylpenta-2,4-diynyl)-1*H*-indole (3d)



3d

White solid, m.p.: 120-122 °C; yield: 60%. ^{1}H NMR (400 MHz) δ: 2.33 (s, 3H), 4.96 (s, 2H), 6.46 (d, *J* = 3.1, 1H), 7.09 (d, *J* = 8.0, 2H), 7.17 (d, *J* = 3.1, 1H), 7.26 (d, *J* = 8.7, 1H), 7.31-7.36 (m, 3H) and 7.74 (d, *J* = 1.6, 1H). ^{13}C NMR (100 MHz) δ: 21.6, 36.9, 70.5, 72.5, 75.4, 78.9, 102.0, 110.8, 113.4, 118.0, 123.6, 124.9, 128.5, 129.2, 130.7, 132.6, 134.6 and 140.0. IR (KBr, v): 2916, 2891, 2247, 1650, 1560, 1508, 1463, 1433, 1400, 1344, 1268, 1242, 1210, 823, 794, 755 and 723 cm^{-1}. MS (*m/z*, rel. int., %): 349 [8, $(M+2)^+$], 347 (9, M^+), 209 (12), 208 (21), 207 (100), 153 (44), 133 (15), 96 (17) and 73 (33). HRMS (ESI–TOF, *m/z*): Obsd. 370.0190; $C_{20}H_{14}BrNNa$ [$(M+Na)^+$] requires 370.0202.

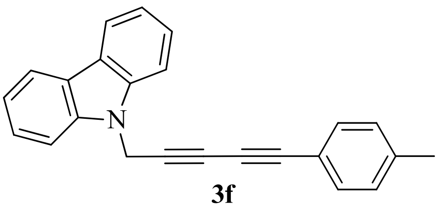
9-(5-Phenylpenta-2,4-diynyl)-9*H*-carbazole (3e)



3e

White crystalline solid, m.p: 154-155 °C; yield: 80%. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 5.58 (s, 2H), 7.25-7.28 (m, 2H), 7.34-7.44 (m, 3H), 7.47-7.53 (m, 4H), 7.72 (d, *J* = 8.2, 2H) and 8.18 (d, *J* = 7.8, 2H). ^{13}C NMR (100 MHz, DMSO-d^6) δ: 32.6, 67.0, 72.9, 77.2, 79.4, 109.4, 119.5, 119.9, 120.3, 122.5, 125.9, 128.6, 129.8, 132.3 and 139.5. IR (KBr, v): 3053, 2914, 2244, 1626, 1597, 1487, 1456, 1329, 748, 720 and 684 cm^{-1}. MS (*m/z*, rel. int., %): 305 (32, M^+), 304 (24), 166 (10), 140 (21) and 139 (100). Anal. Calc.: C, 90.46; H, 4.95; N, 4.59. Found: C, 90.10; H, 4.91; N, 4.29.

9-(5-*p*-Tolylpenta-2,4-diynyl)-9*H*-carbazole (3f)



3f

White crystalline solid, m.p: 155-156 °C; yield: 85%. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 2.27 (s, 3H), 5.57 (s, 2H), 7.15 (d, *J* = 7.9, 2H), 7.24-7.28 (m, 2H), 7.36 (d, *J* = 7.9, 2H), 7.49-7.53 (m, 2H), 7.72 (d, *J* = 8.2, 2H) and 8.17 (d, *J* = 7.7, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ: 20.9, 32.6, 67.2, 72.4, 77.5, 78.9, 109.4, 116.8, 119.5, 120.2, 122.5, 125.8, 129.2, 132.2, 139.5 and 139.9. IR (KBr, v): 3052, 2912, 2242, 1627, 1603, 1489, 1455, 1332, 812, 746 and 719 cm^{-1}. MS (*m/z*, rel. int., %): 319 (5, M^+), 170 (65), 150 (12), 135 (22), 133 (57), 103 (21), 102 (29), 86 (100), 84 (100) and 66 (80). HRMS (ESI–TOF, *m/z*): Obsd. 320.1420; $C_{24}H_{18}N$ [$(M+H)^+$] requires 320.1434.

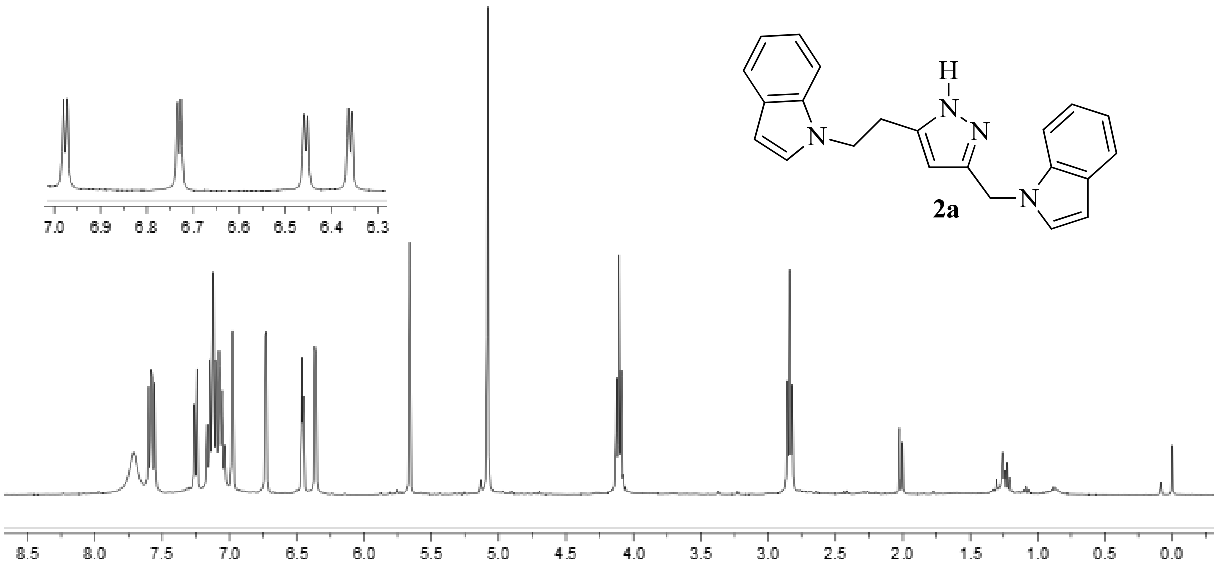


Figure S1. 400 MHz ^{1}H NMR spectrum of compound **2a** in $CDCl_3$.

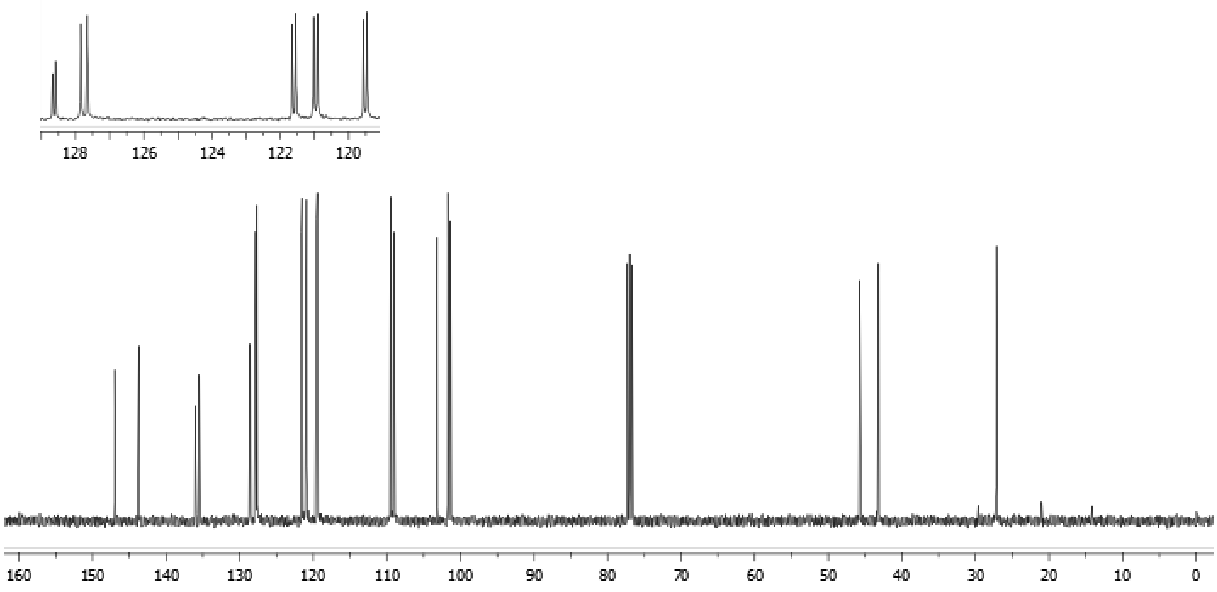


Figure S2. 100 MHz ^{13}C NMR spectrum of compound **2a** in $CDCl_3$.

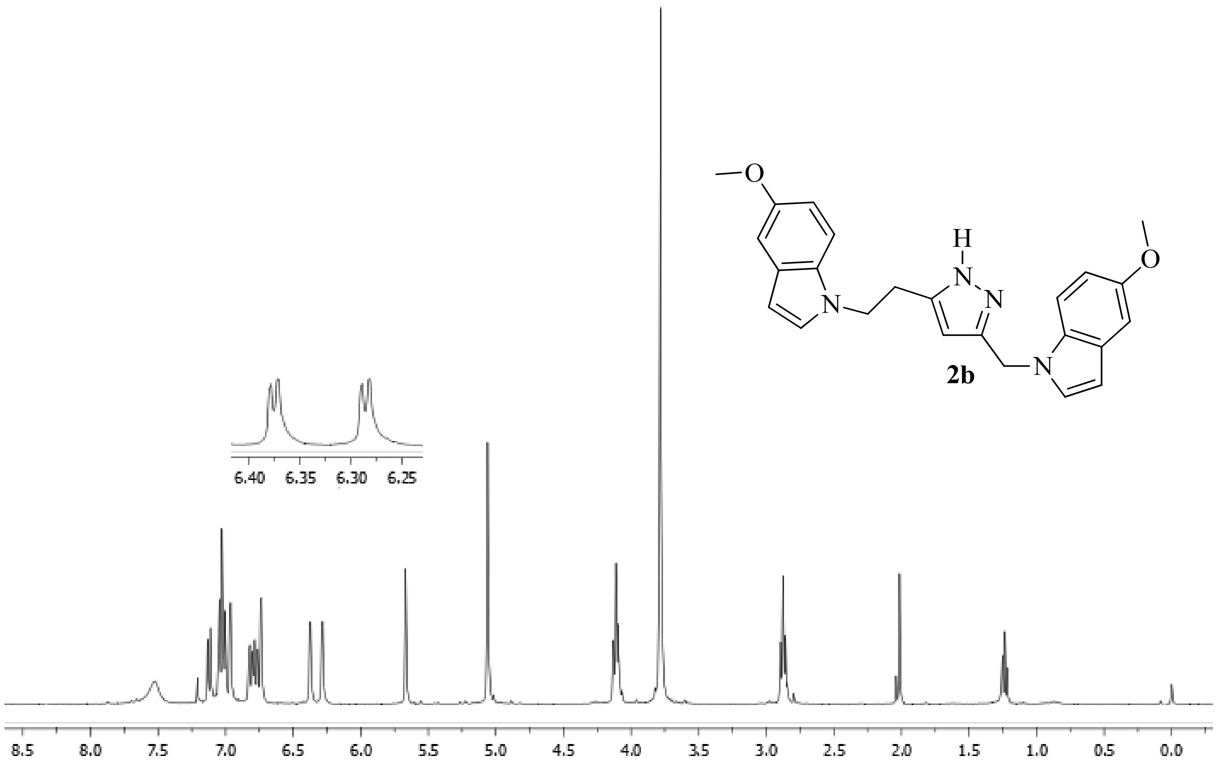


Figure S3. 400 MHz ^{1}H NMR spectrum of compound **2b** in $CDCl_3$.

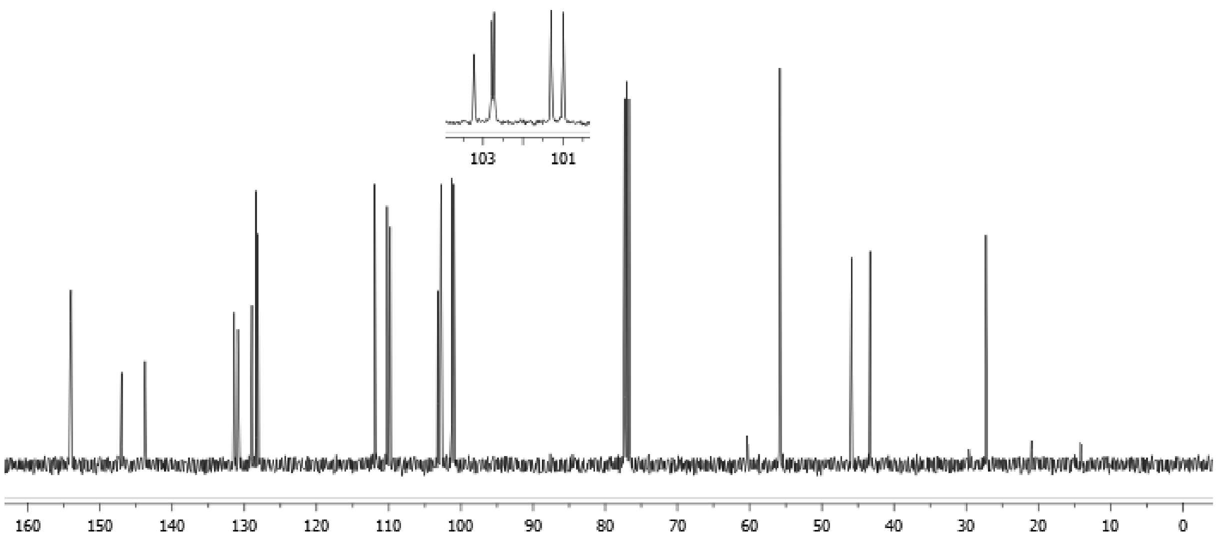


Figure S4. 100 MHz ^{13}C NMR spectrum of compound **2b** in $CDCl_3$.

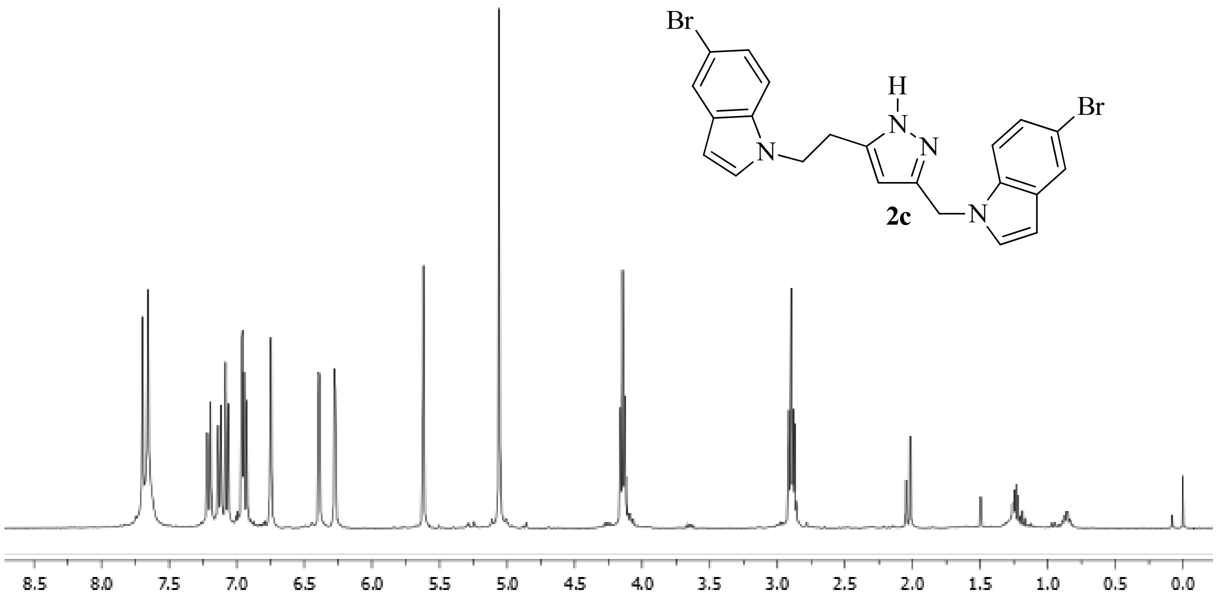


Figure S5. 400 MHz ^{1}H NMR spectrum of compound **2c** in $CDCl_3$.

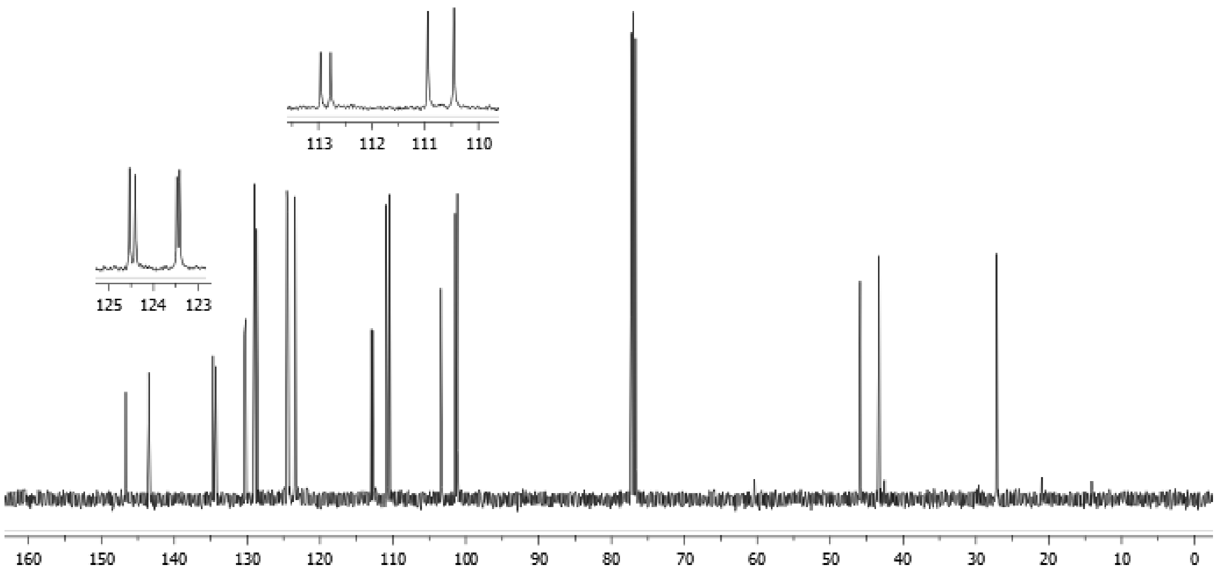


Figure S6. 100 MHz ^{13}C NMR spectrum of compound **2c** in $CDCl_3$.

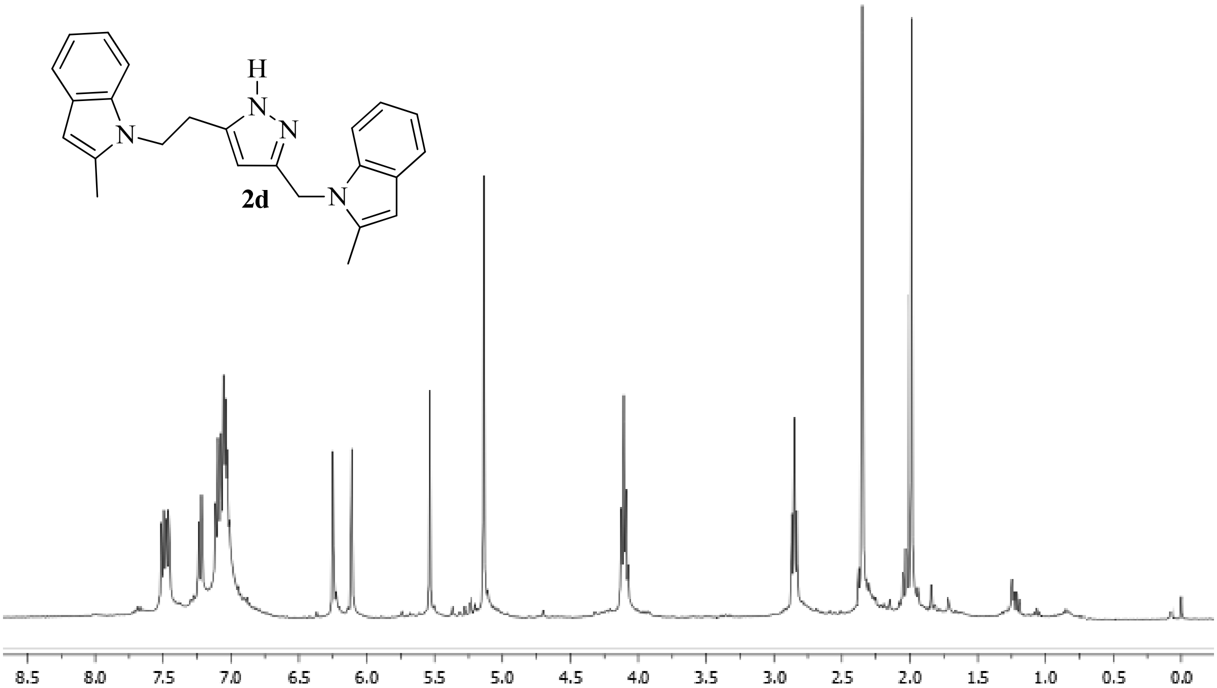


Figure S7. 400 MHz ^{1}H NMR spectrum of compound **2d** in $CDCl_3$.

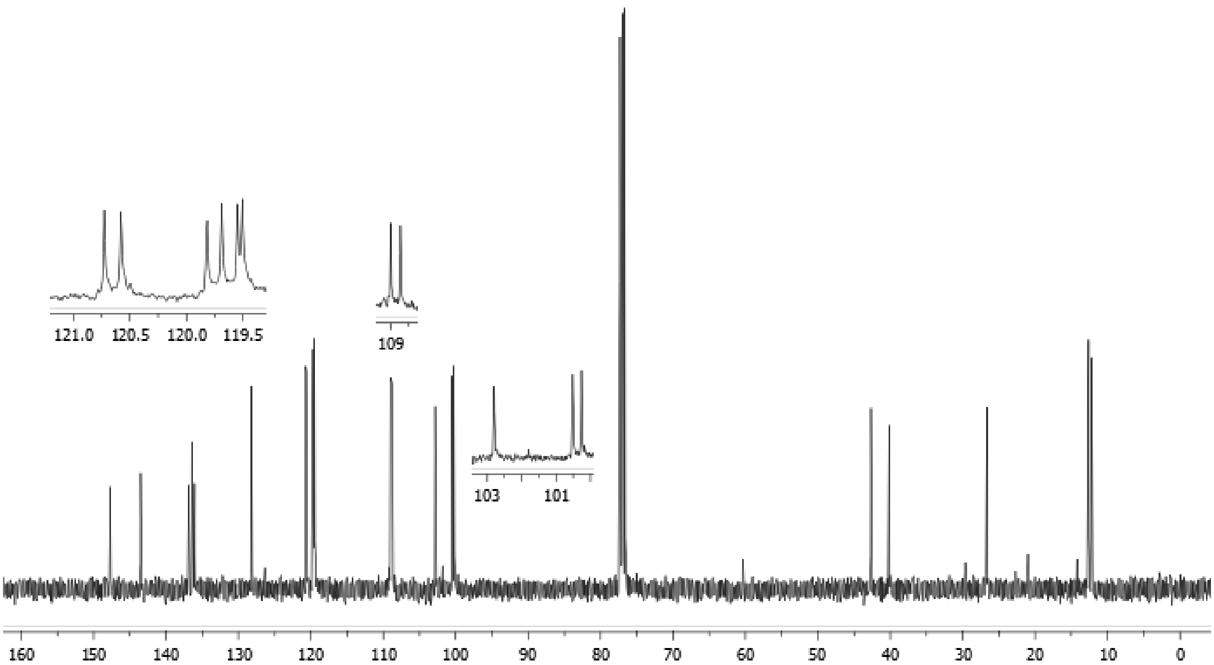


Figure S8. 100 MHz ^{13}C NMR spectrum of compound **2d** in $CDCl_3$.

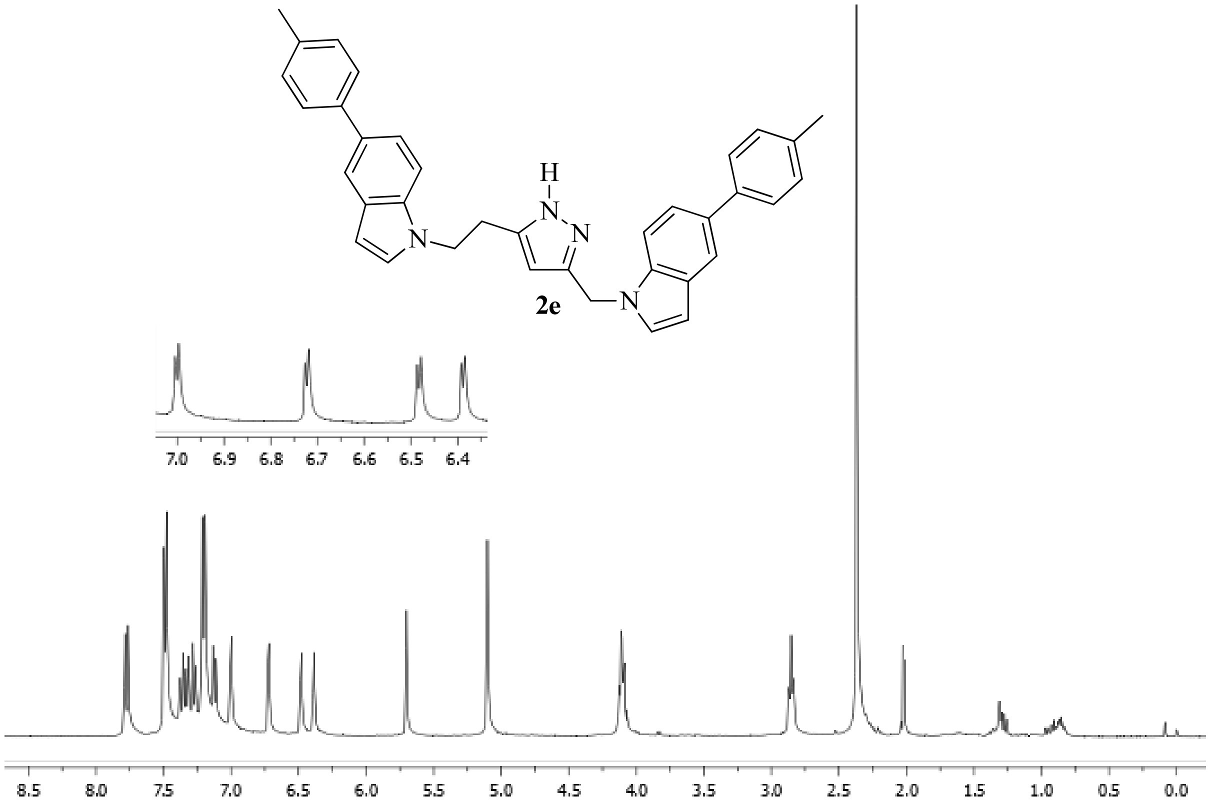


Figure S9. 400 MHz ^{1}H NMR spectrum of compound **2e** in $CDCl_3$.

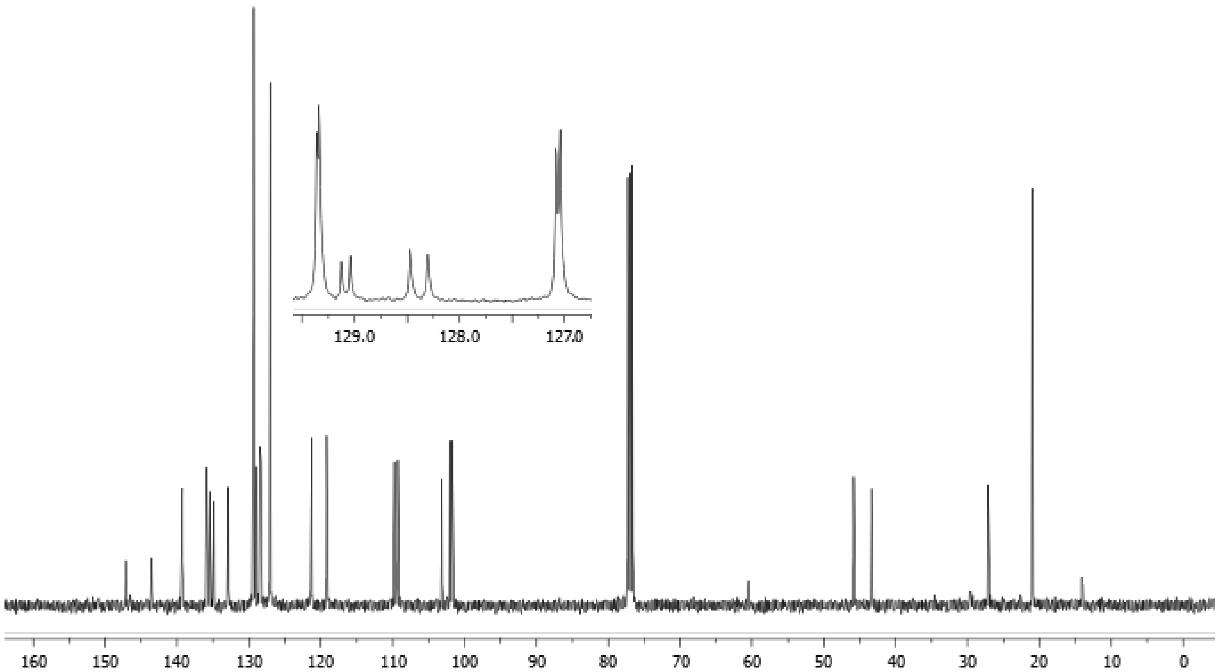


Figure S10. 100 MHz ^{13}C NMR spectrum of compound **2e** in $CDCl_3$.

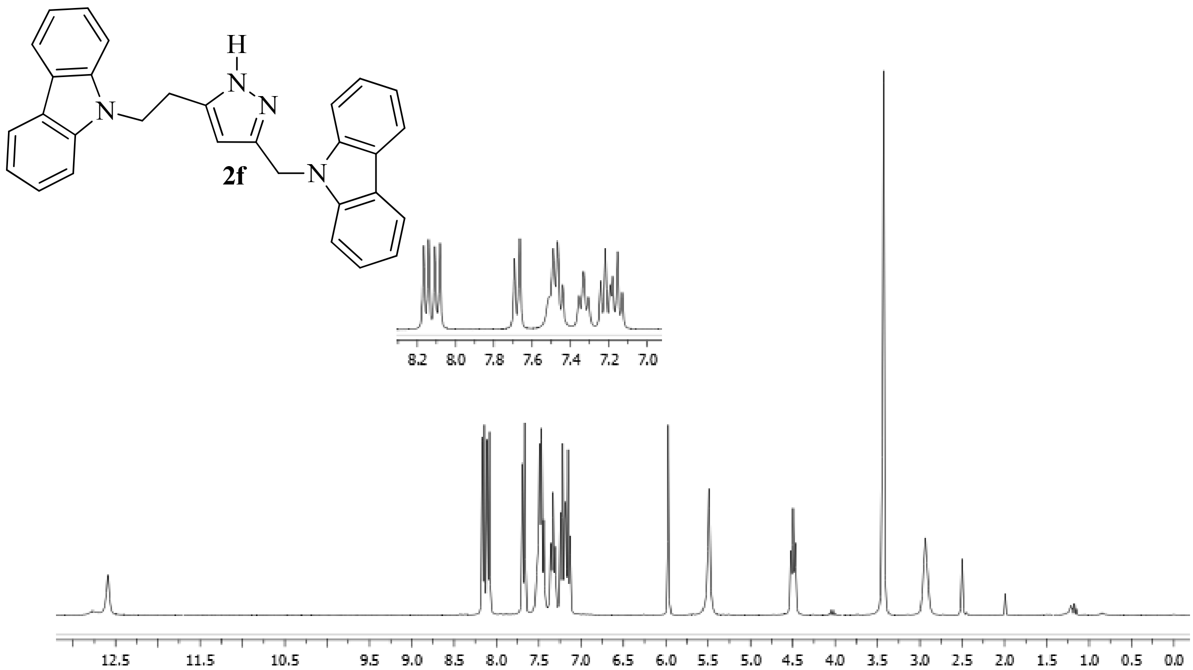


Figure S11. 300 MHz ^{1}H NMR spectrum of compound **2f** in DMSO-d_{6}.

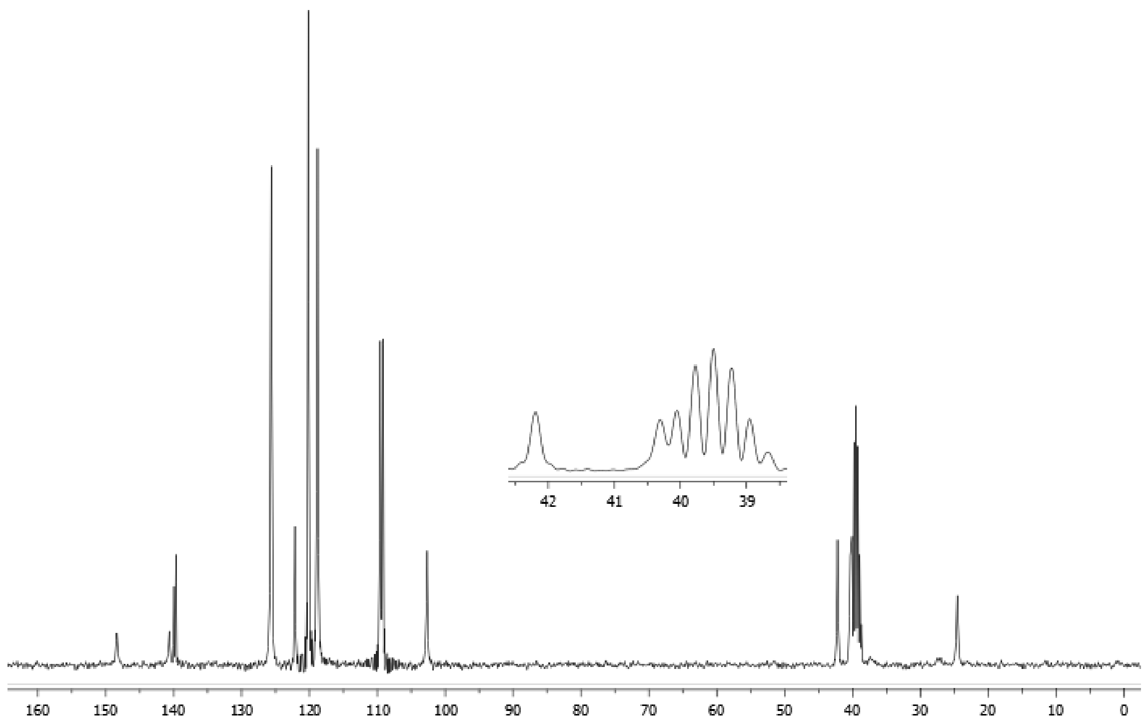


Figure S12. 75 MHz ^{13}C NMR spectrum of compound **2f** in DMSO-d_{6}.

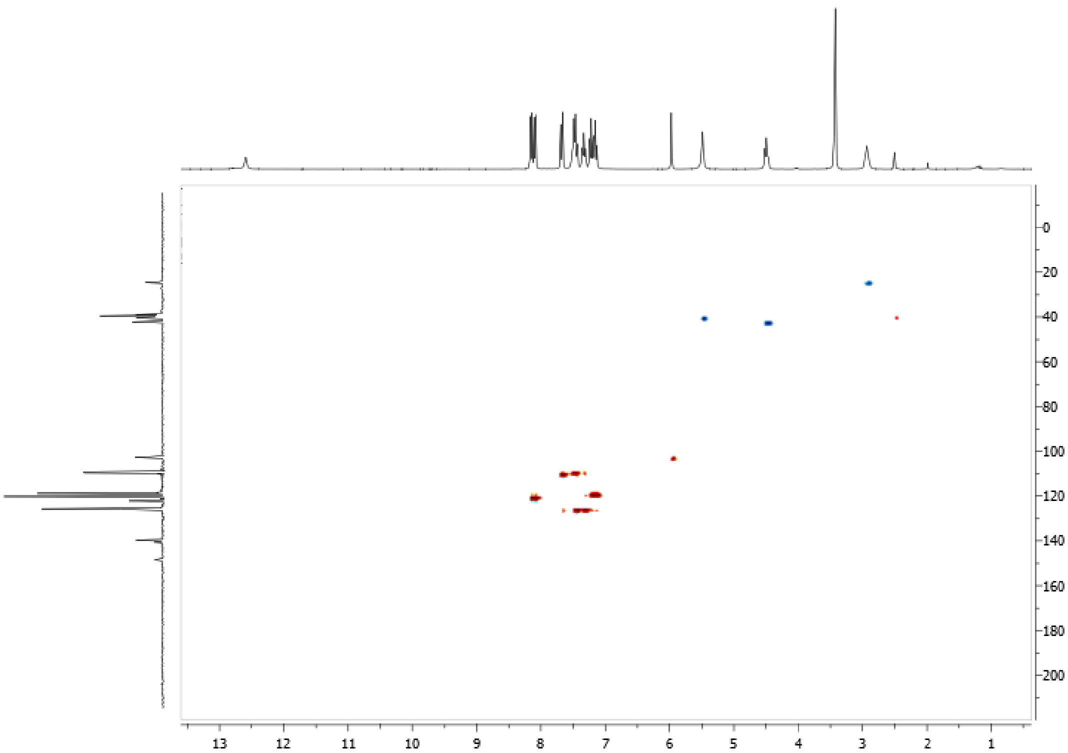


Figure S13. HSQC spectrum of compound **2f** in DMSO-d_6.

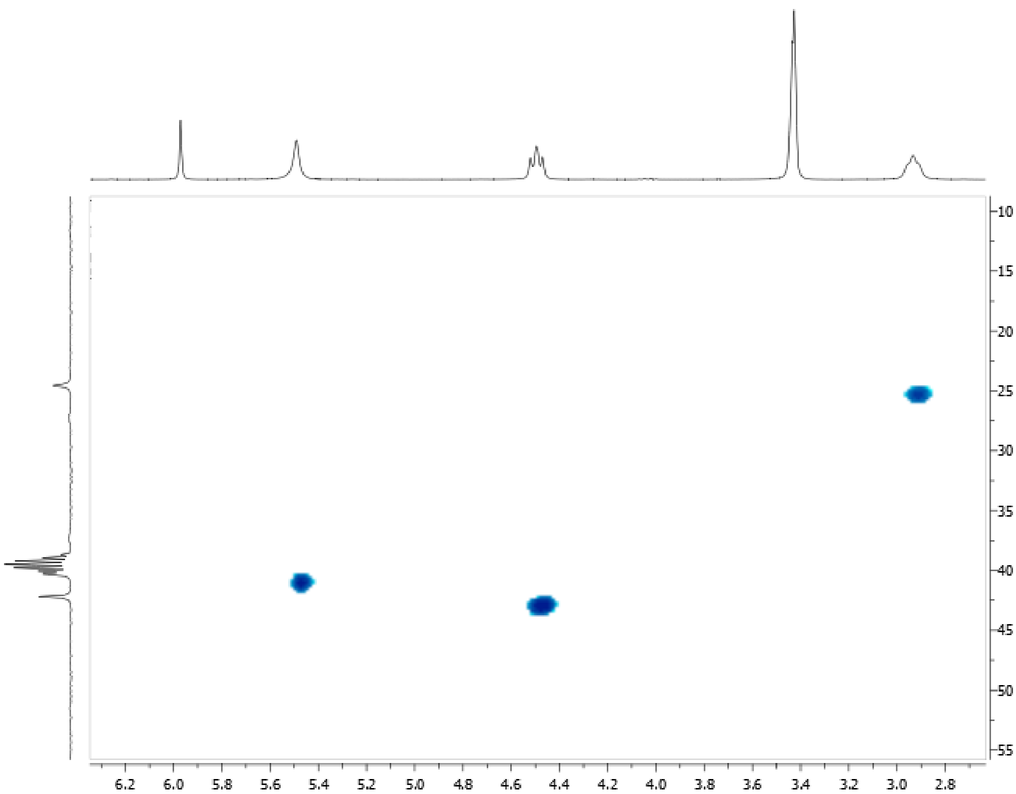


Figure S14. Expansion of HSQC spectrum of compound **2f** in DMSO-d_6.

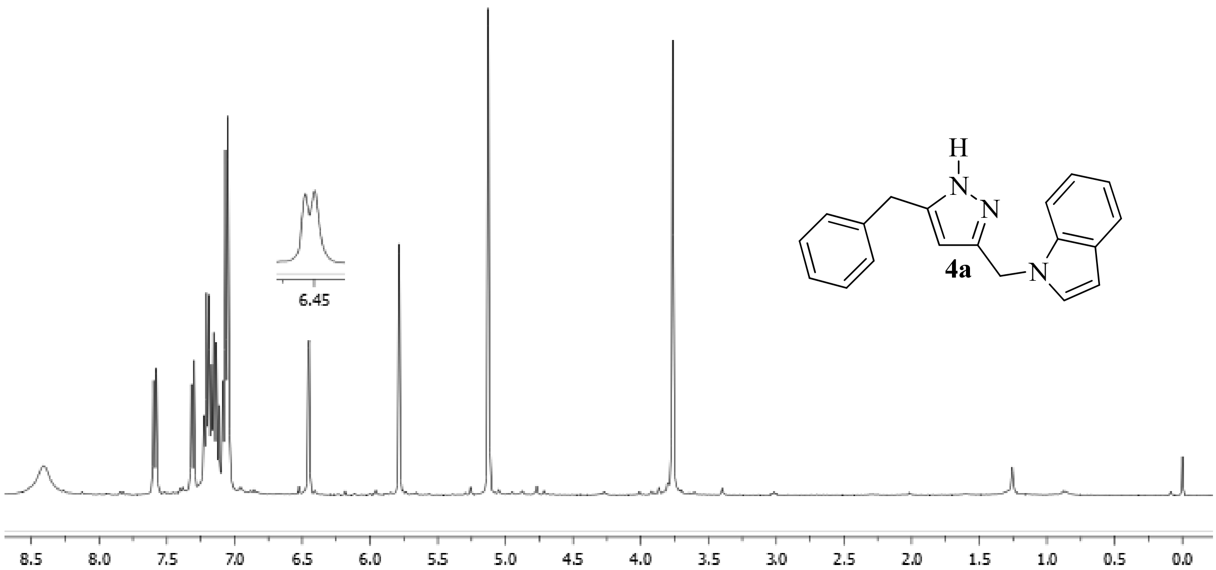


Figure S15. 400 MHz ^{1}H NMR spectrum of compound **4a** in $CDCl_3$.

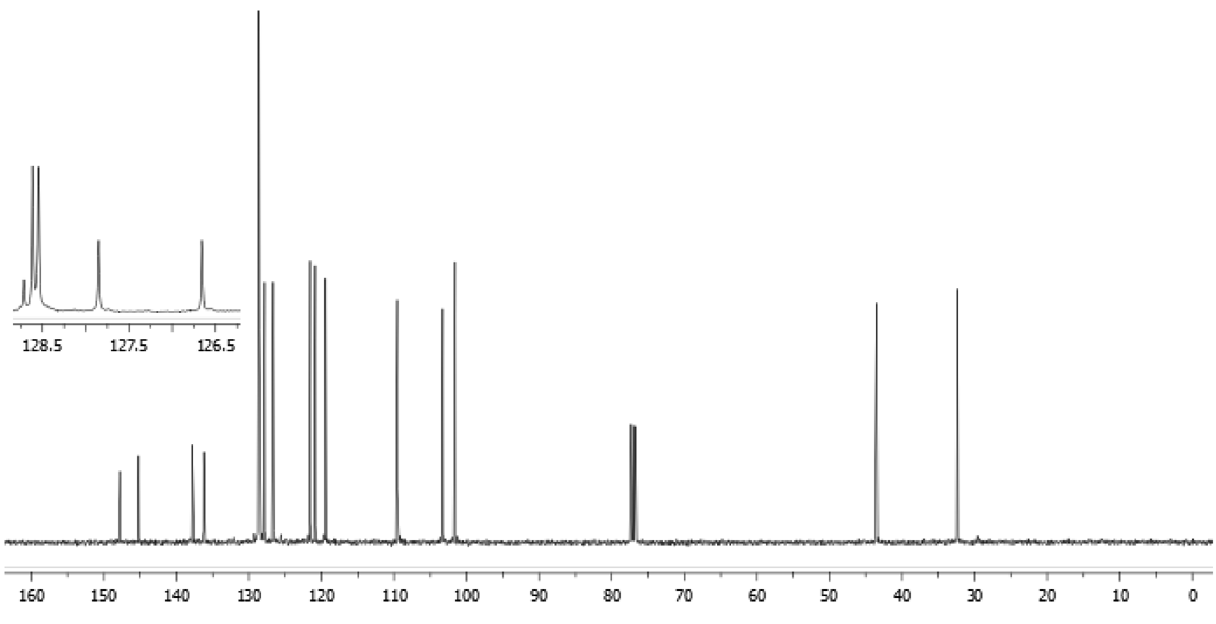


Figure S16. 100 MHz ^{13}C NMR spectrum of compound **4a** in $CDCl_3$.

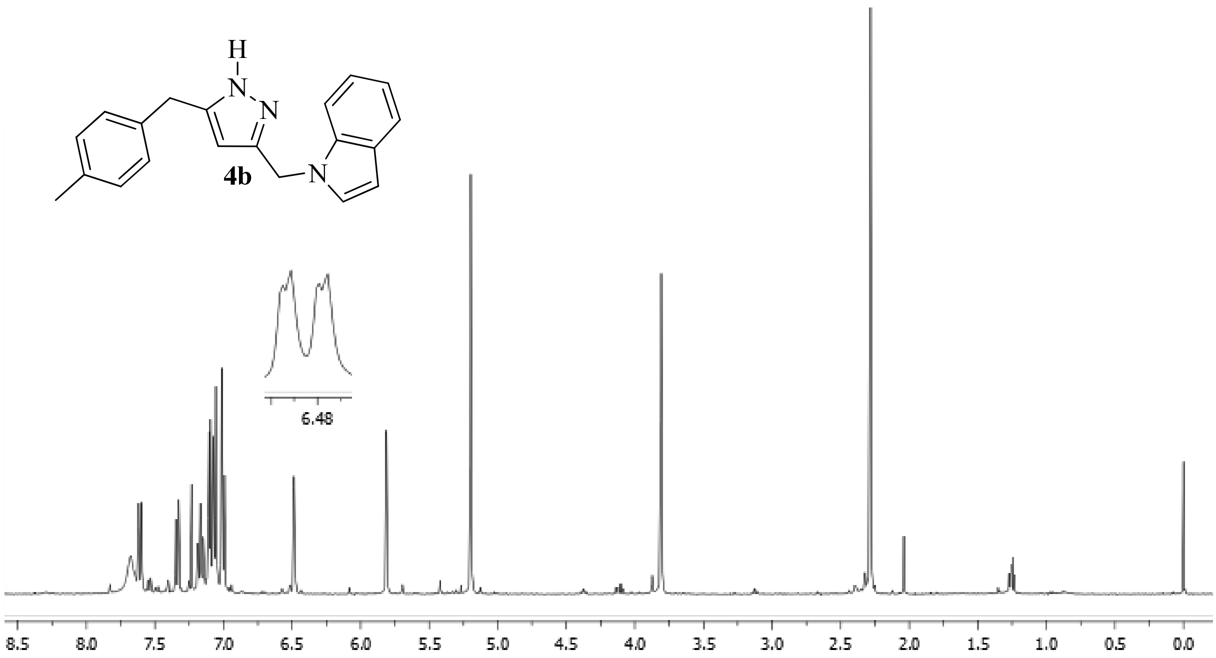


Figure S17. 400 MHz ^{1}H NMR spectrum of compound 4**b** in $CDCl_3$.

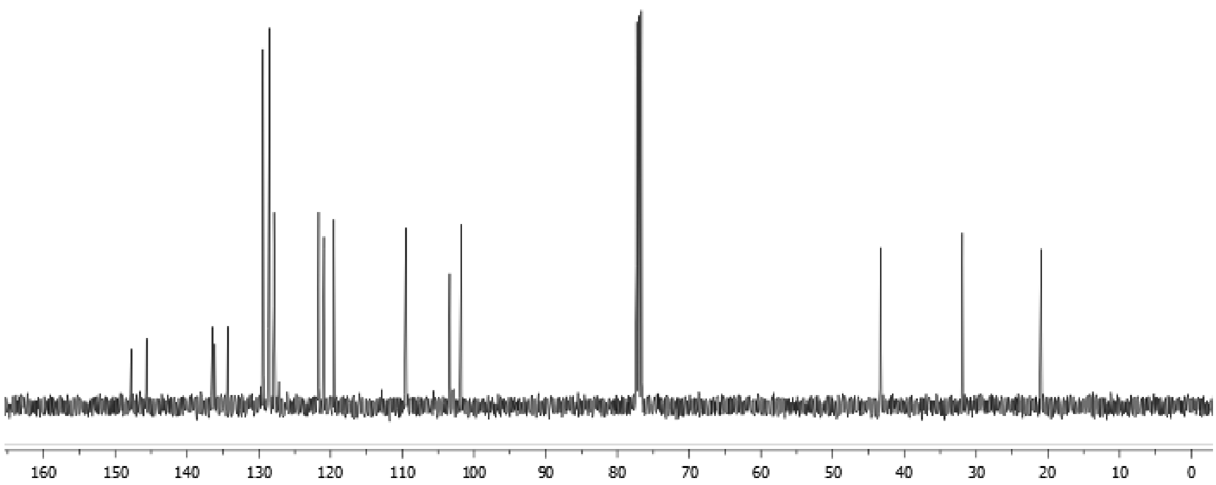


Figure S18. 100 MHz ^{13}C NMR spectrum of compound **4b** in $CDCl_3$.

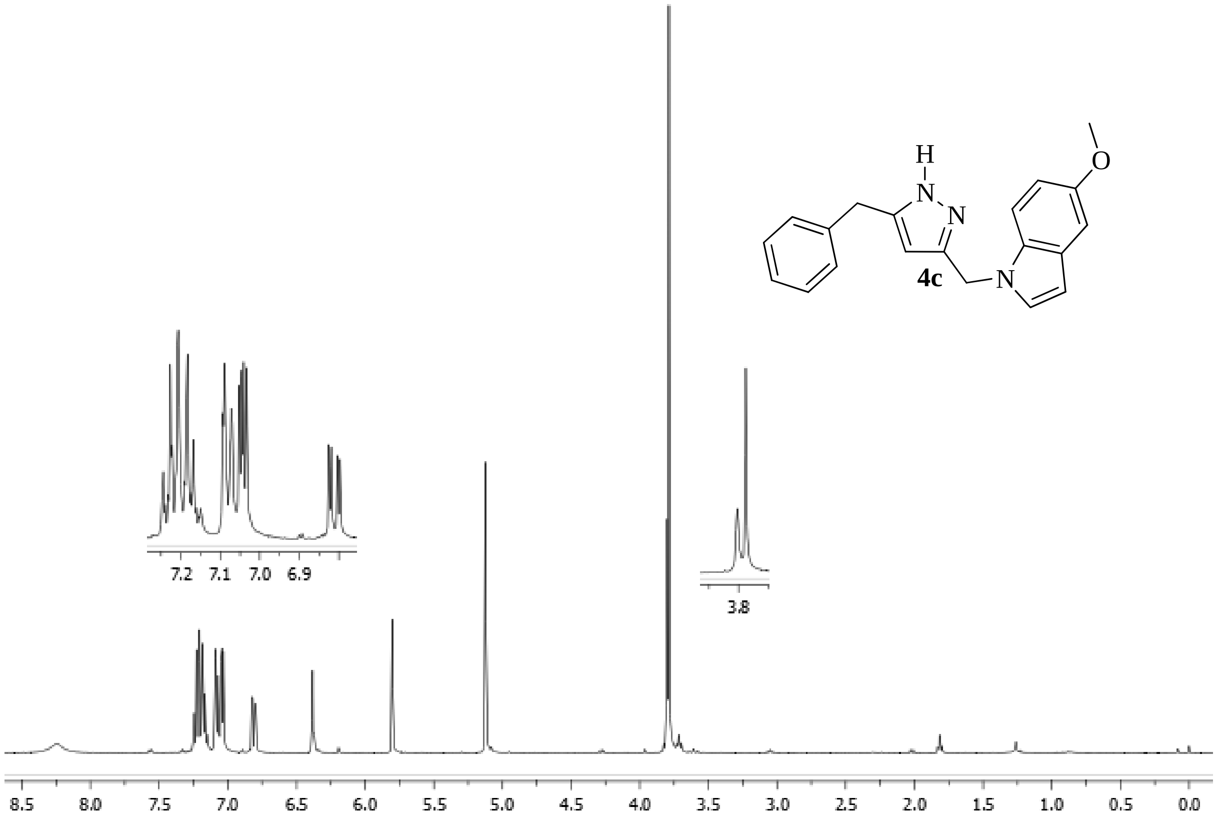


Figure S19. 400 MHz ^{1}H NMR spectrum of compound **4c** in $CDCl_3$.

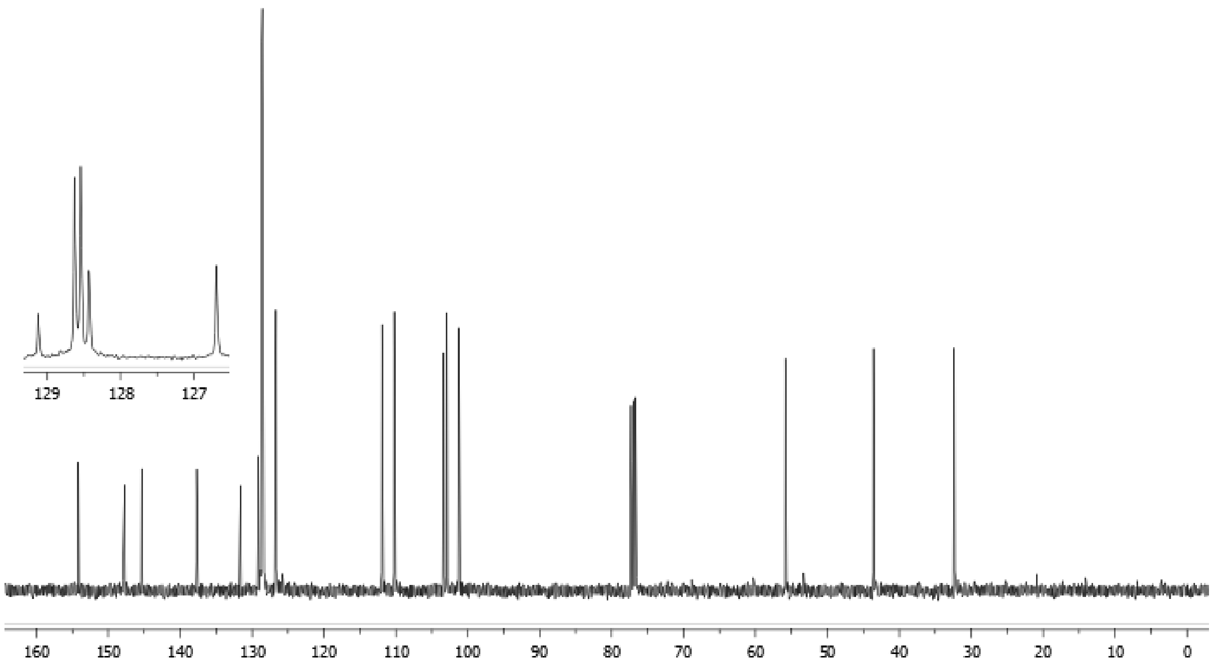


Figure S20. 100 MHz ^{13}C NMR spectrum of compound **4c** in $CDCl_3$.

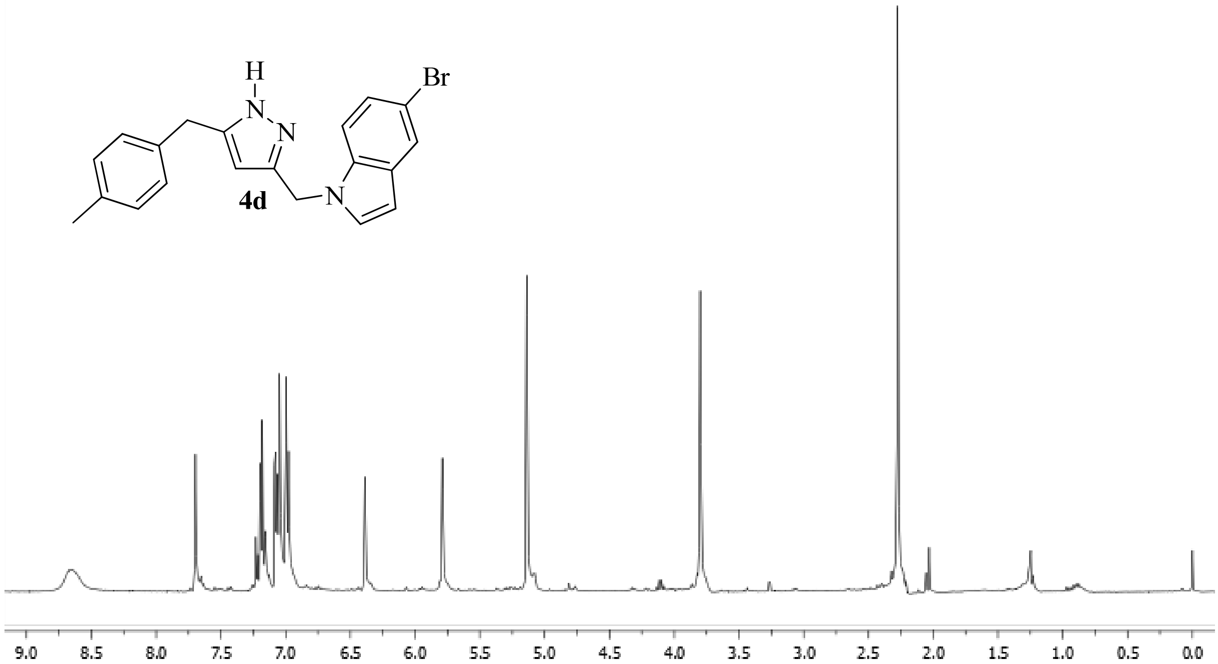


Figure S21. 400 MHz ^{1}H NMR spectrum of compound **4d** in $CDCl_3$.

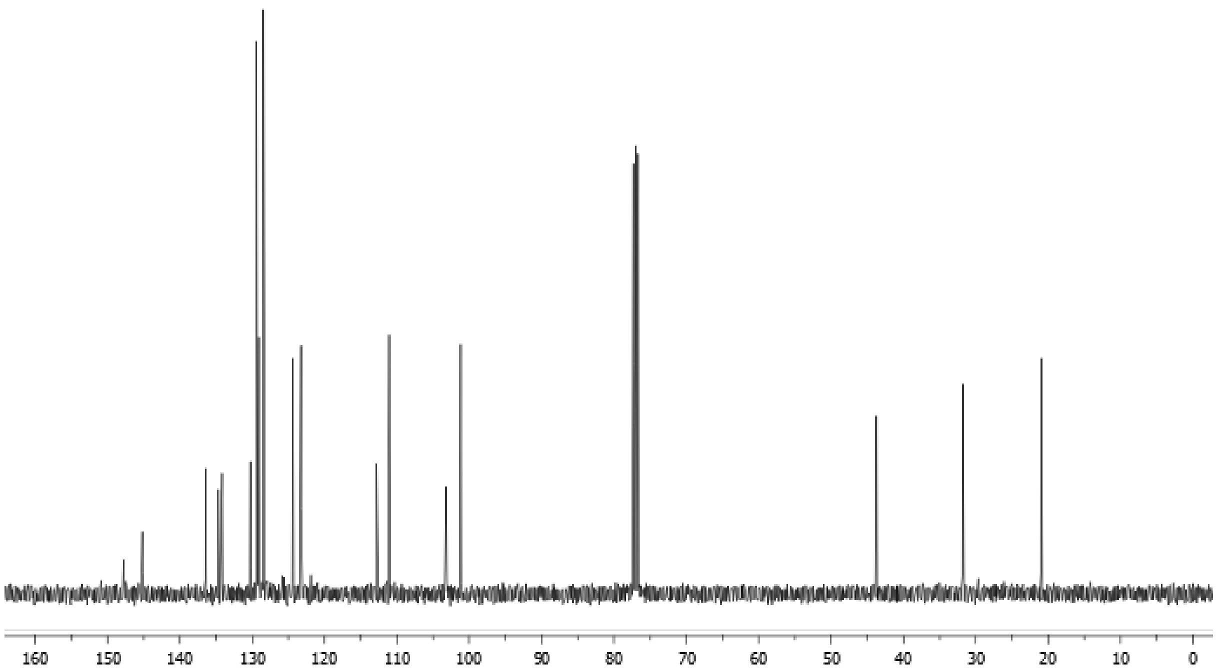


Figure S22. 100 MHz ^{13}C NMR spectrum of compound **4d** in $CDCl_3$.

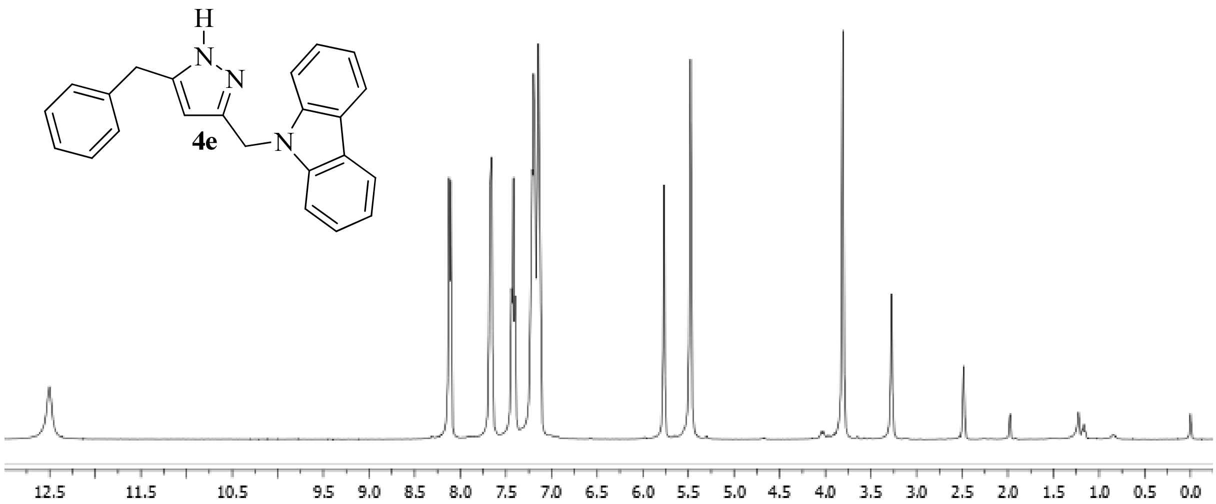


Figure S23. 400 MHz ^{1}H NMR spectrum of compound **4e** DMSO-d_6.

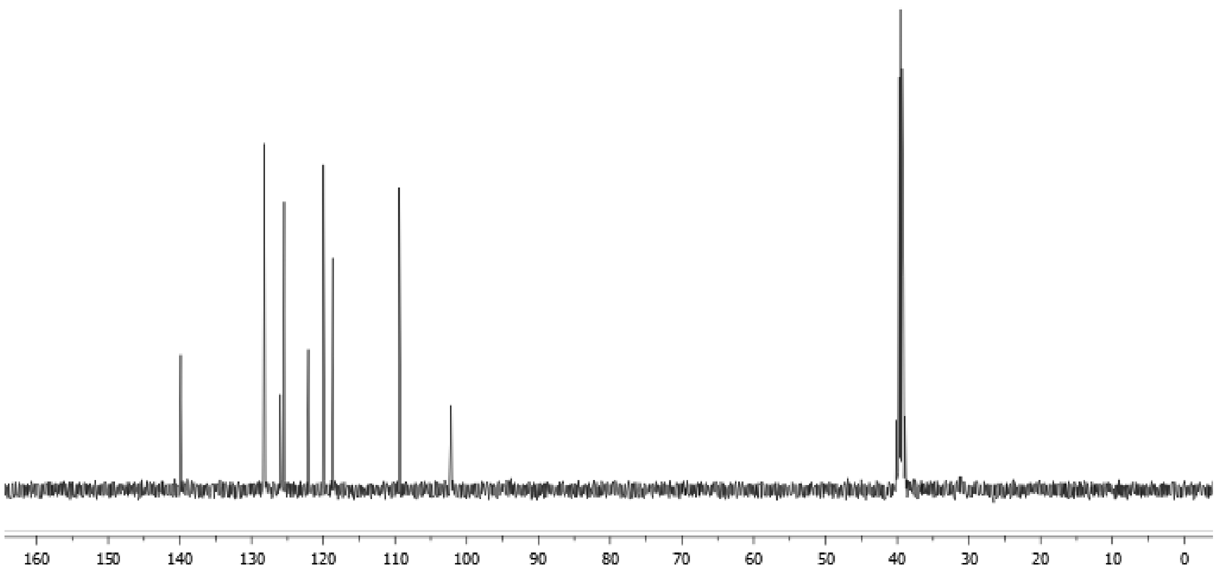


Figure S24. 100 MHz ^{13}C NMR spectrum of compound **4e** in DMSO-d_6.

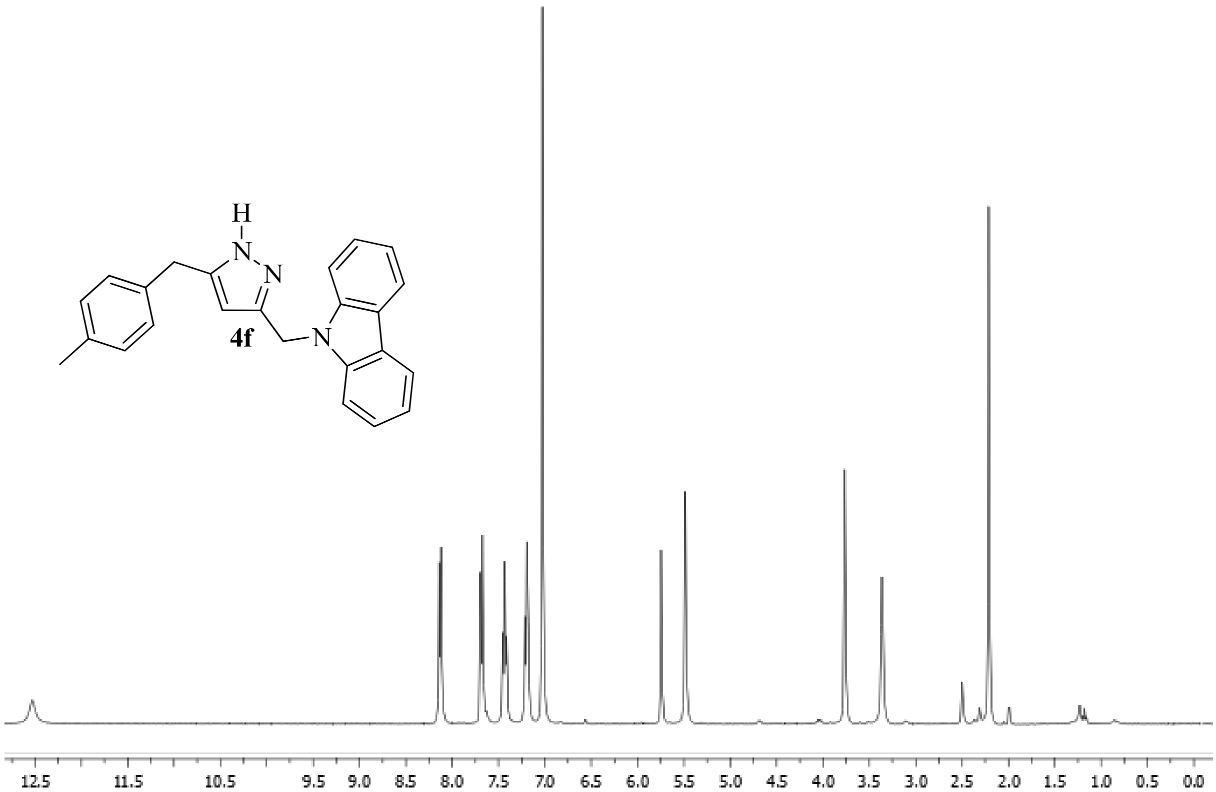


Figure S25. 300 MHz ^{1}H NMR spectrum of compound **4f** in DMSO-d_6.

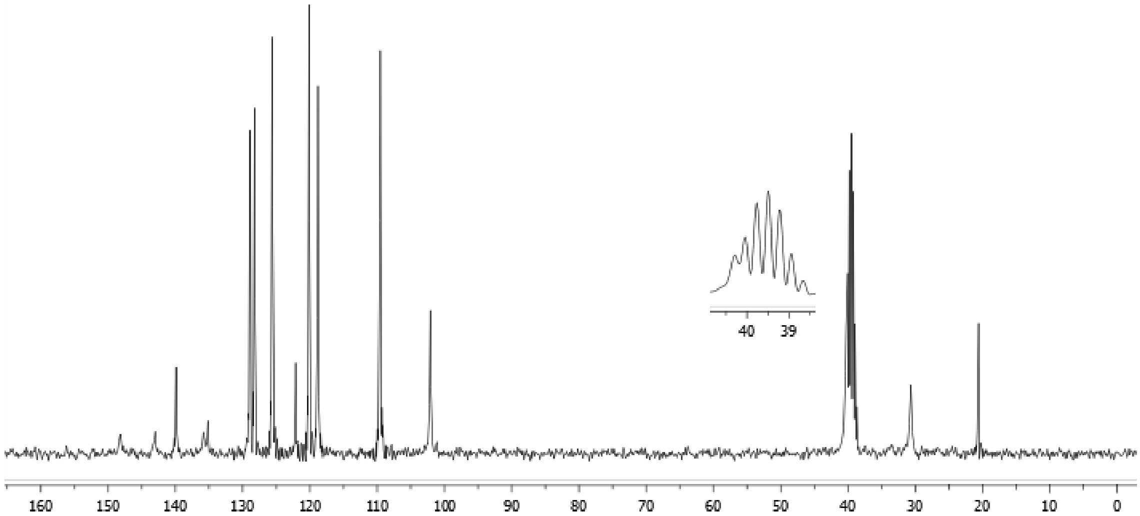


Figure S26. 75 MHz ^{13}C NMR spectrum of compound **4f** in DMSO-d_6.

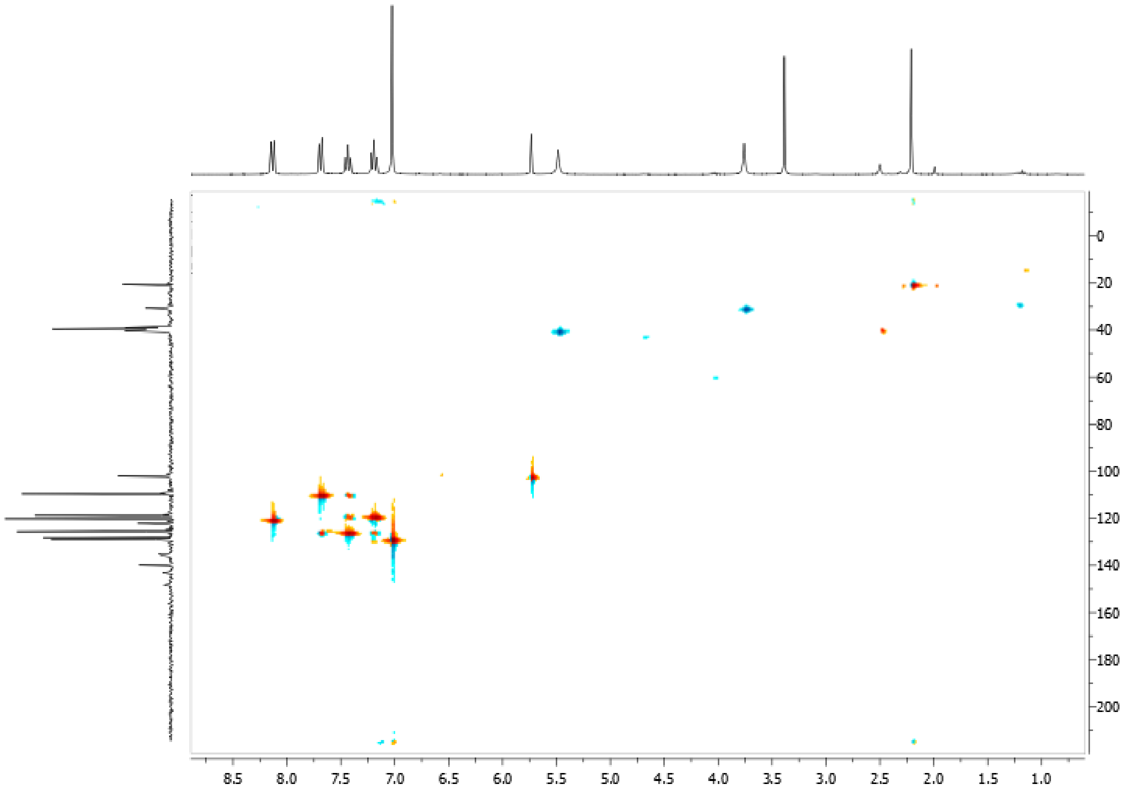


Figure S27. HSQC spectrum of compound **4f** in DMSO-d_6.

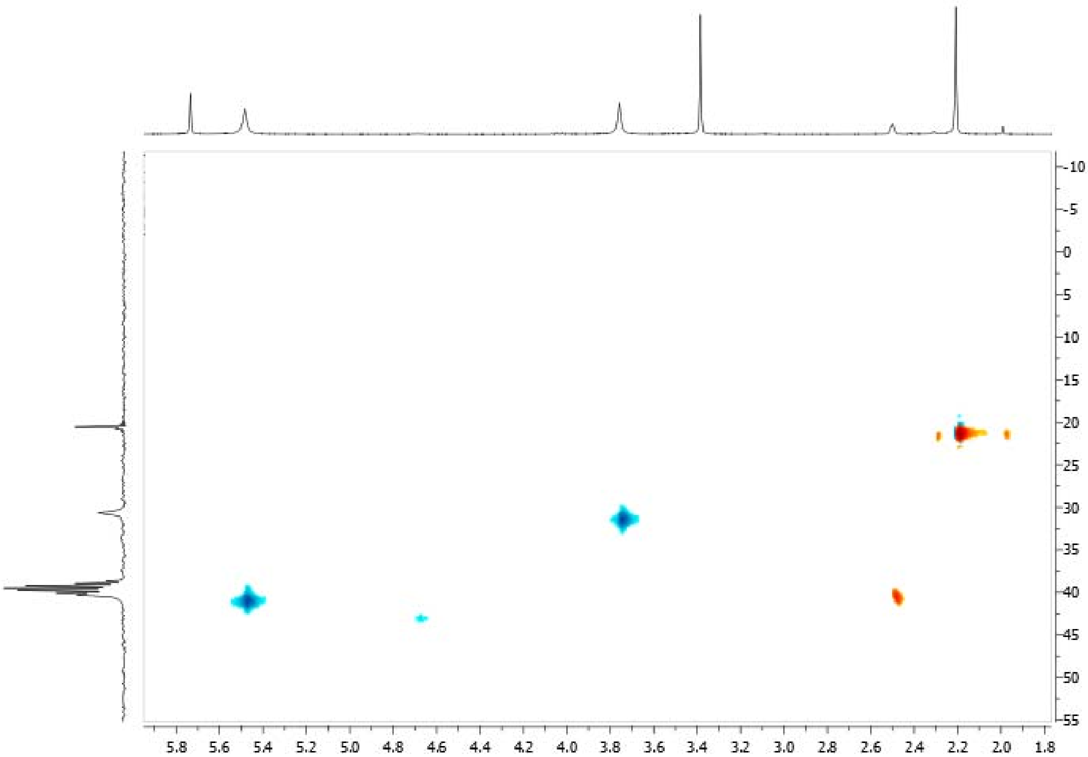


Figure S28. Expansion of the HSQC spectrum of compound **4f** in DMSO-d_6.

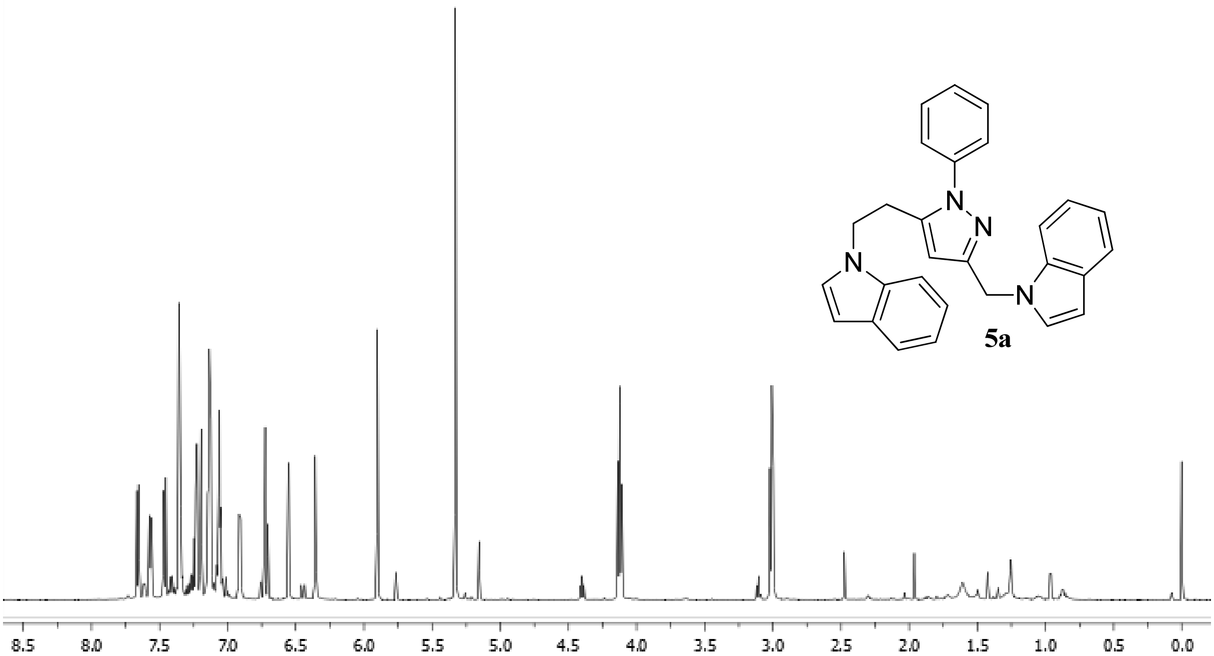


Figure S29. 600 MHz ^{1}H NMR spectrum of compound **5a** in $CDCl_3$.

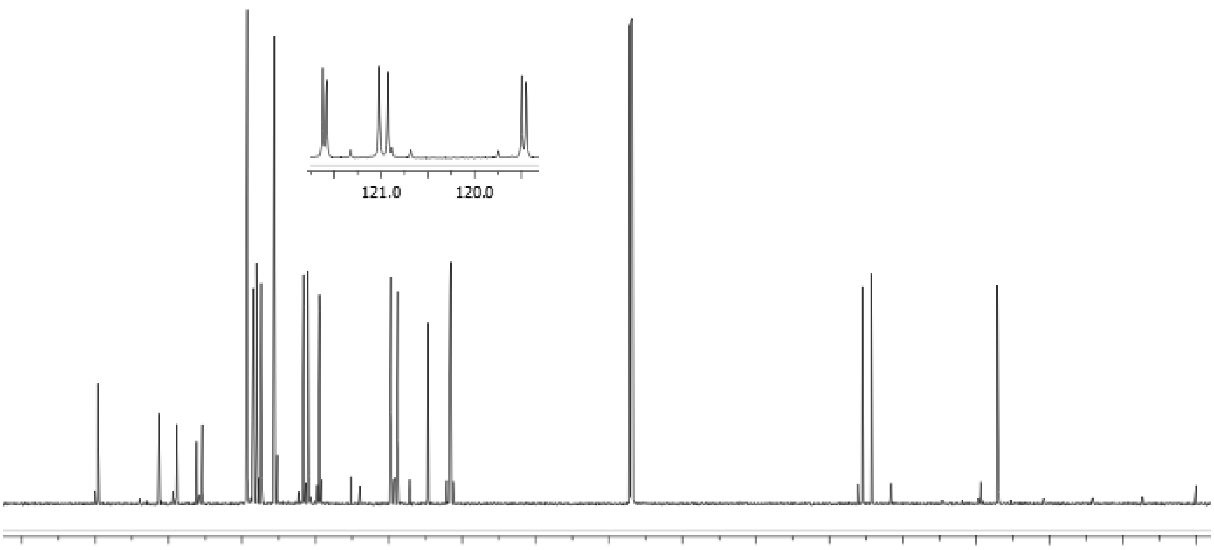


Figure S30. 150 MHz ^{13}C NMR spectrum of compound **5a** in $CDCl_3$.

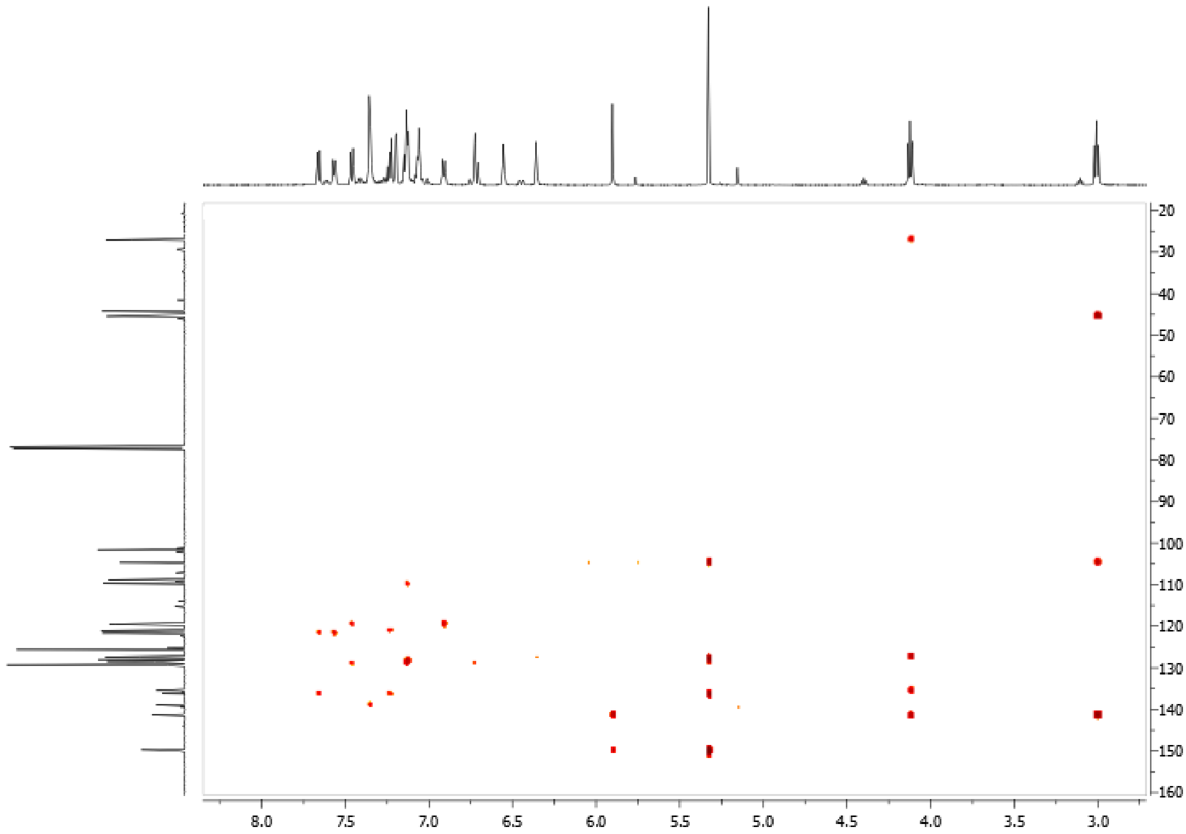


Figure S31. HMBC spectrum of compound **5a** in $CDCl_3$.

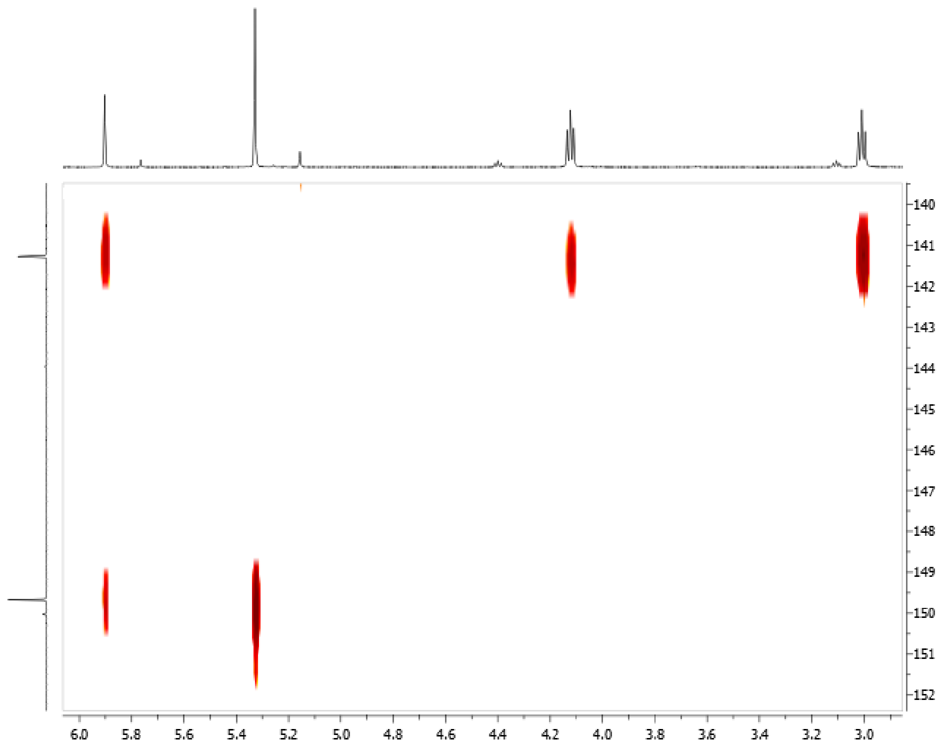


Figure S32. Expansion of the HMBC spectrum of compound **5a**.

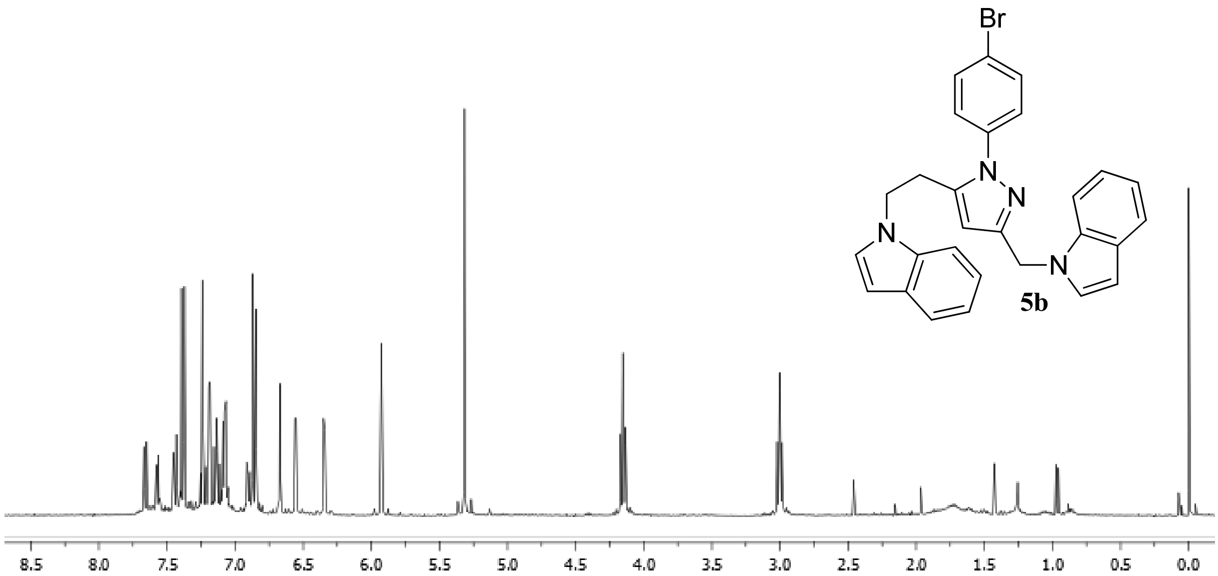


Figure S33. 400 MHz ^{1}H NMR spectrum of compound **5b** in $CDCl_3$.

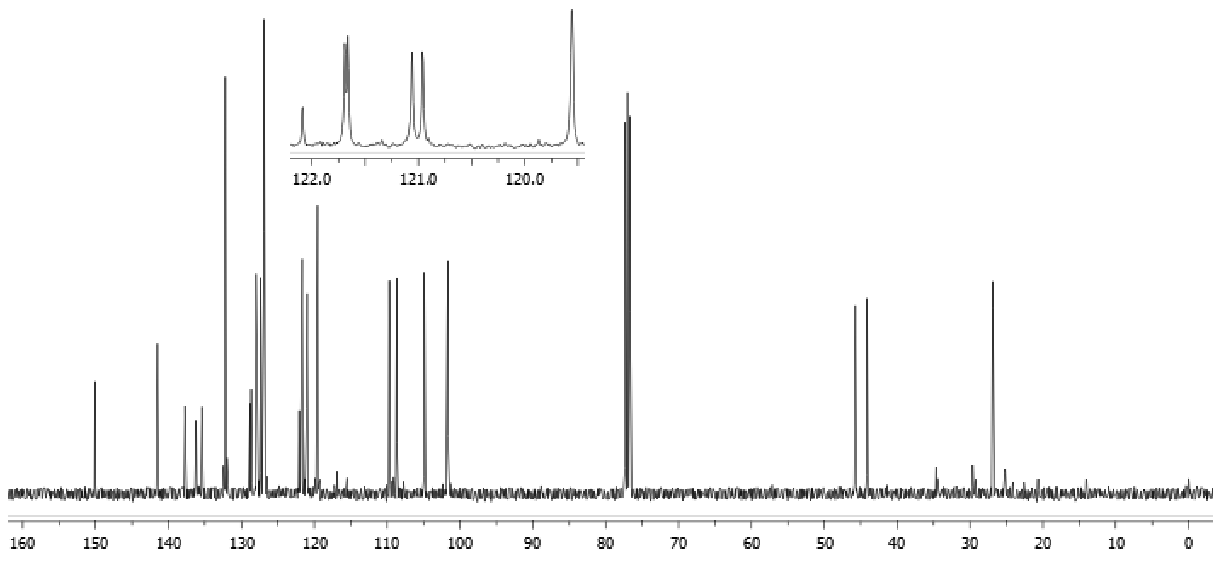


Figure S34. 100 MHz ^{13}C NMR spectrum of compound **5b** in $CDCl_3$.

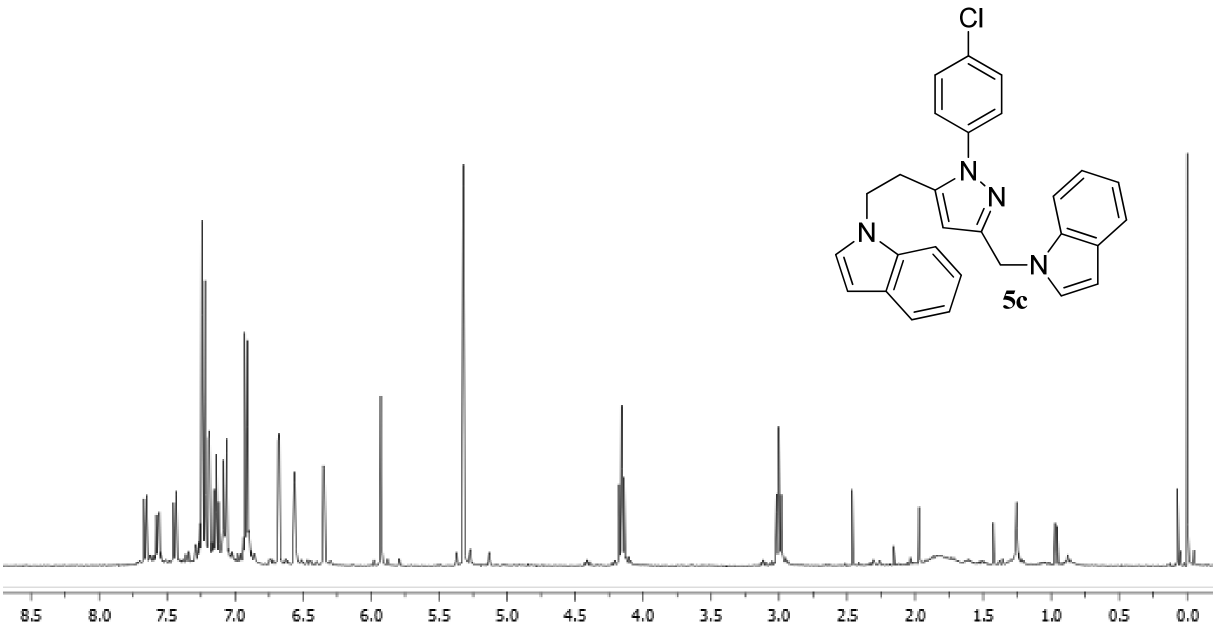


Figure S35. 400 MHz ^{1}H NMR spectrum of compound **5c** in $CDCl_3$.

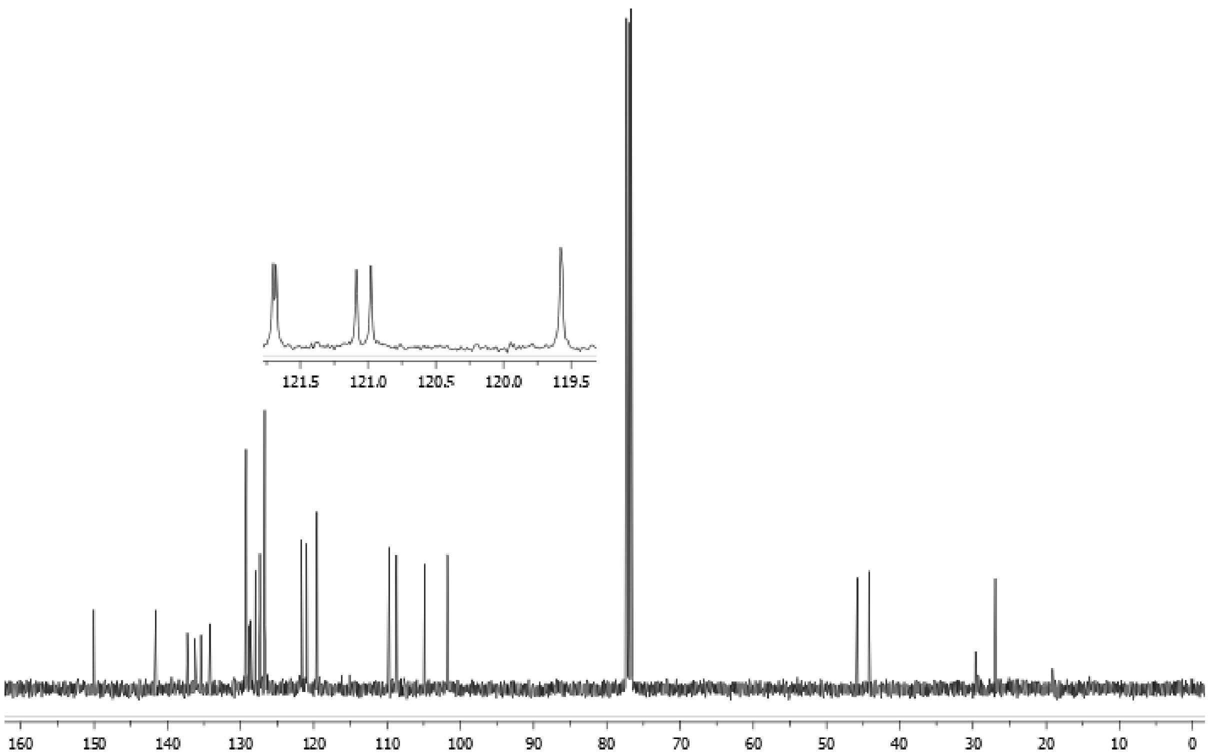


Figure S36. 100 MHz ^{13}C NMR spectrum of compound **5c** in $CDCl_3$.

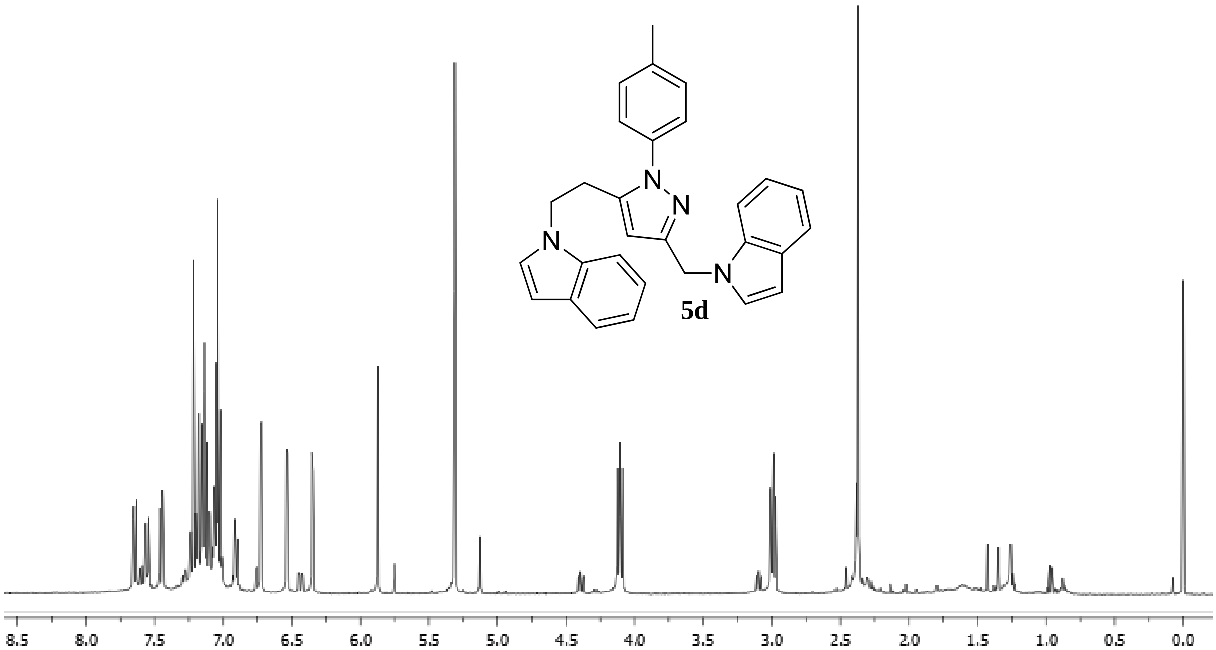


Figure S37. 400 MHz ^{1}H NMR spectrum of compound **5d** in $CDCl_3$.

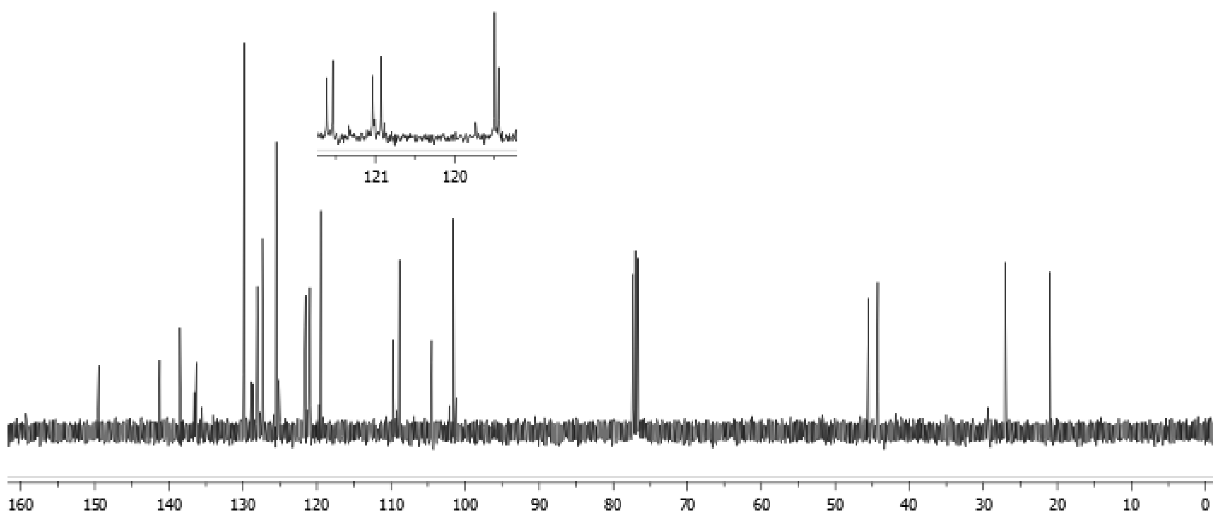


Figure S38. 100 MHz ^{13}C NMR spectrum of compound **5d** in $CDCl_3$.

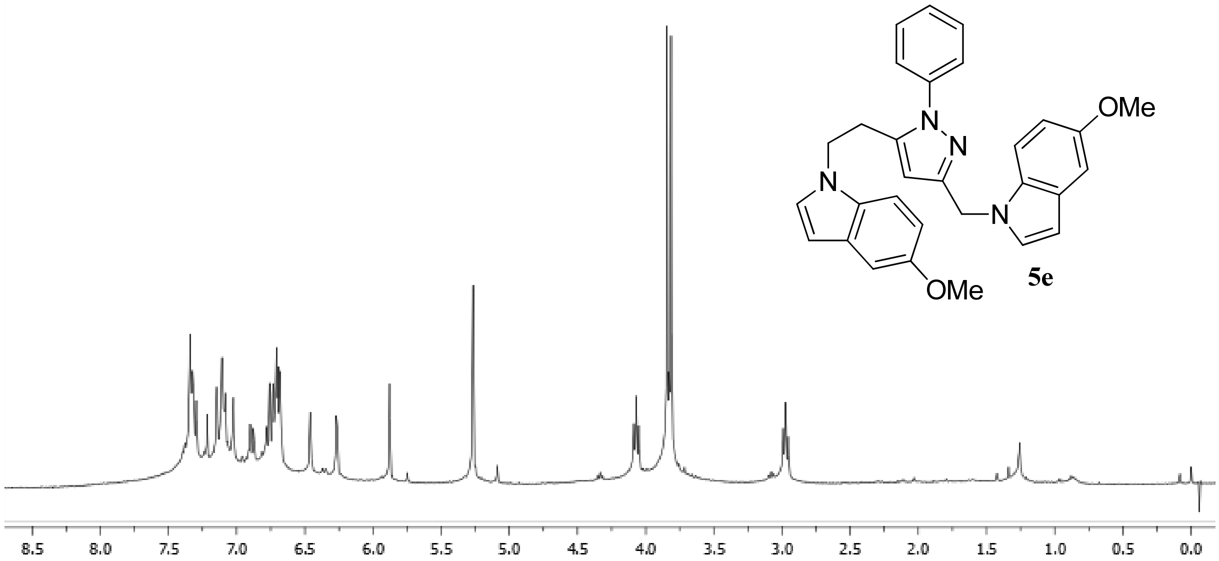


Figure S39. 400 MHz ^{1}H NMR spectrum of compound **5e** in $CDCl_3$.

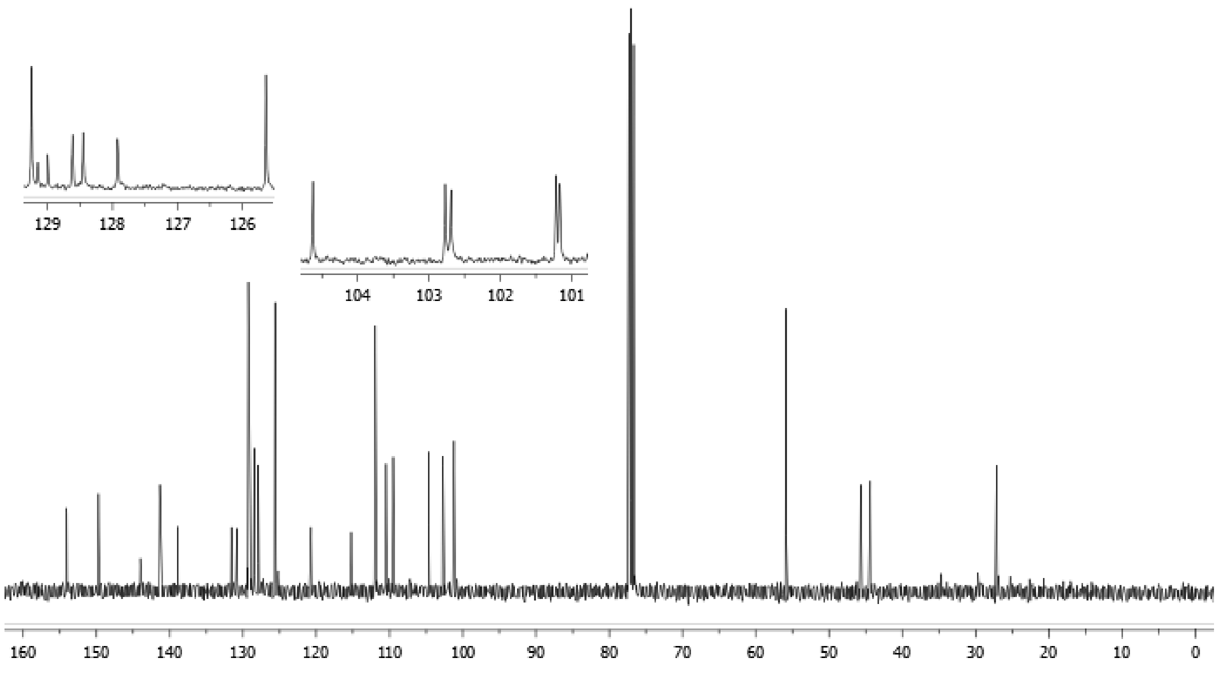


Figure S40. 100 MHz ^{13}C NMR spectrum of compound **5e** in $CDCl_3$.

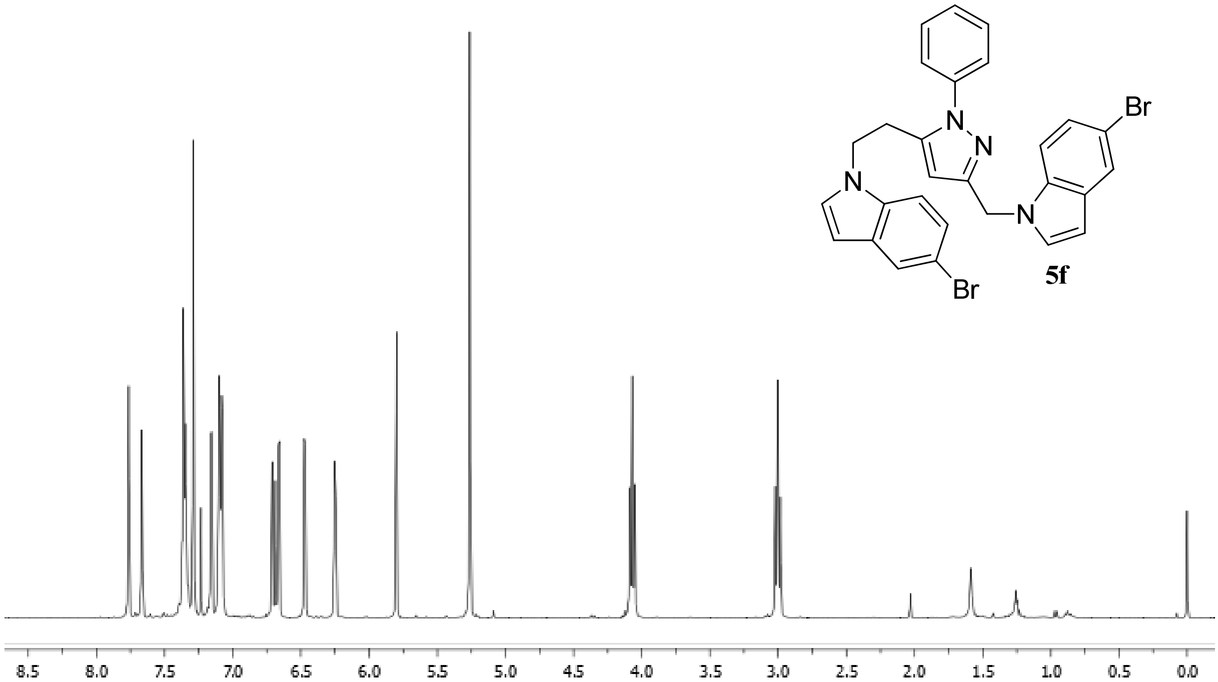


Figure S41. 400 MHz ^{1}H NMR spectrum of compound **5f** in $CDCl_3$.

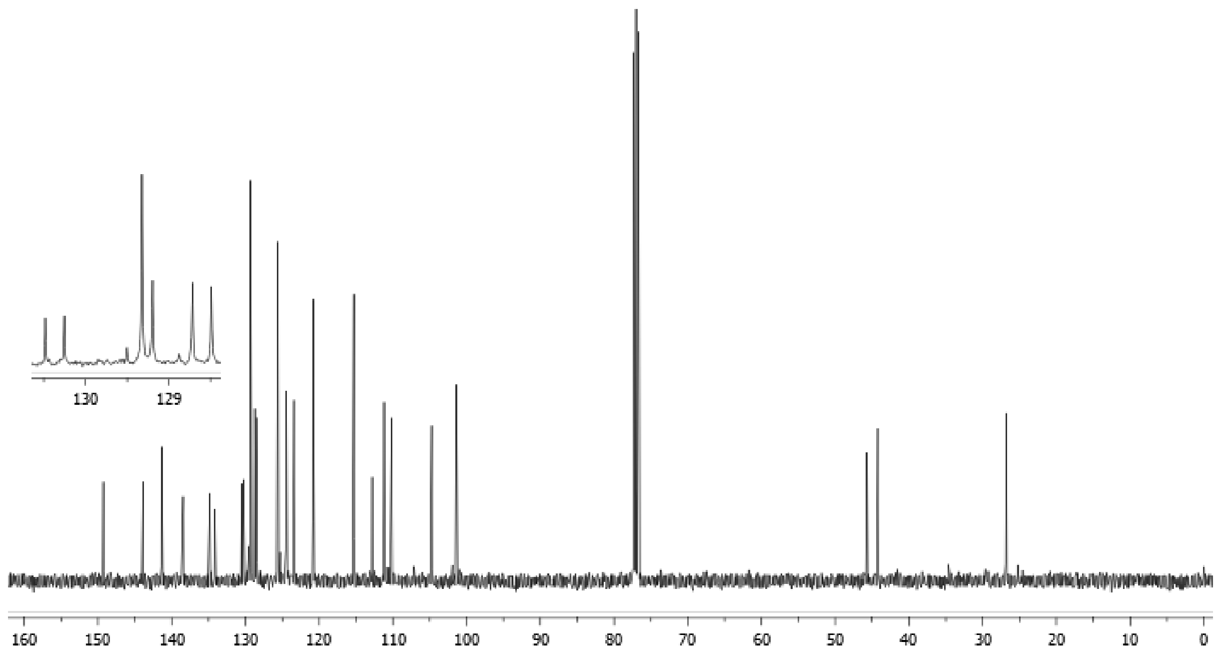


Figure S42. 100 MHz ^{13}C NMR spectrum of compound **5f** in $CDCl_3$.

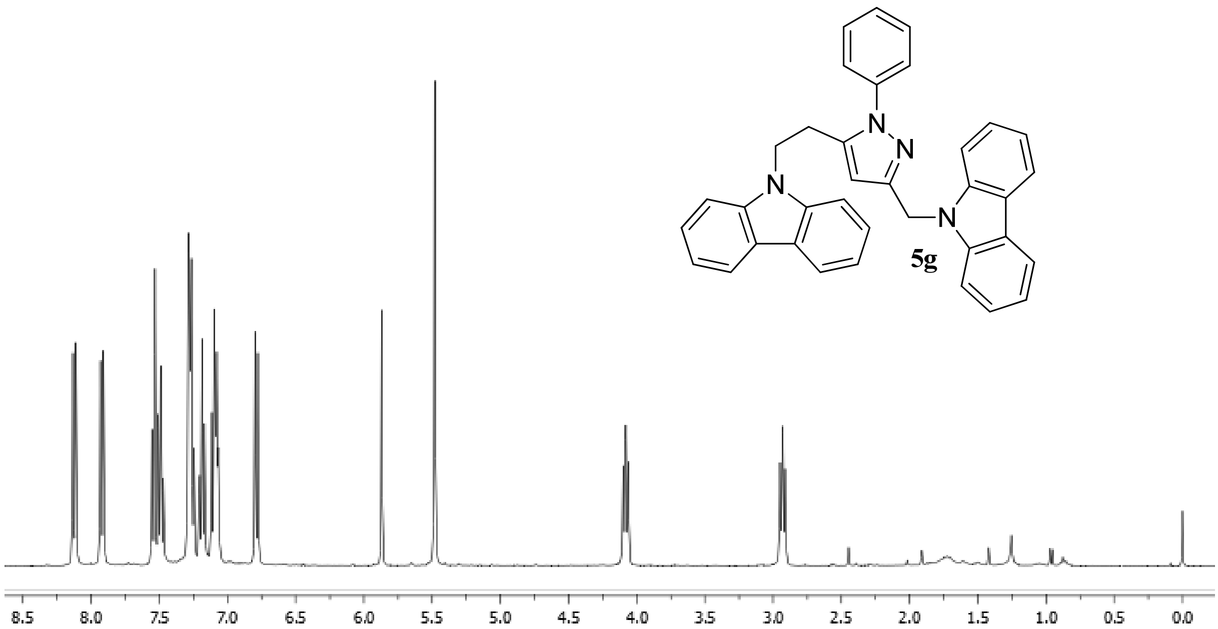


Figure S43. 400 MHz ^{1}H NMR spectrum of compound **5g** in $CDCl_3$.

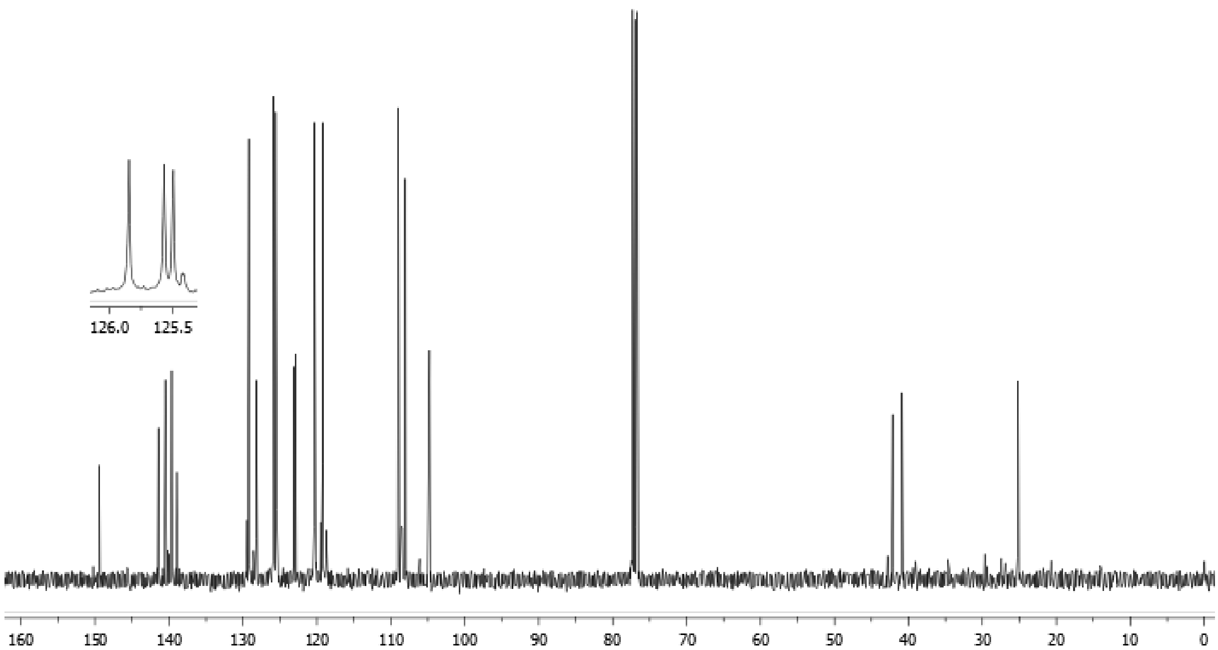


Figure S44. 100 MHz ^{13}C NMR spectrum of compound **5g** in $CDCl_3$.

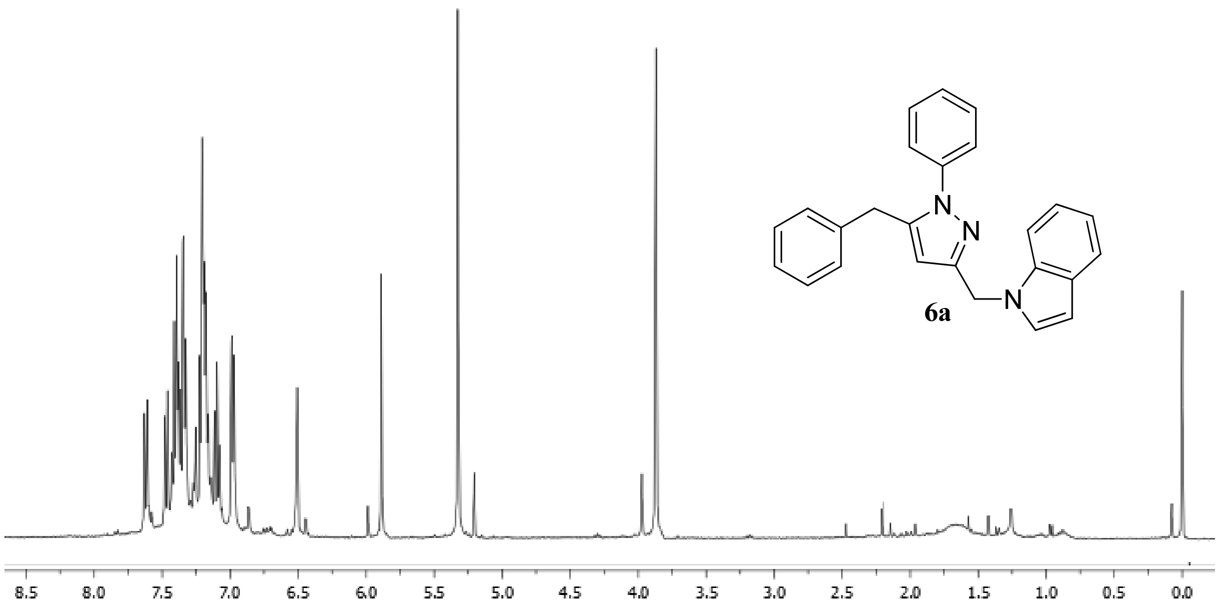


Figure S45. 400 MHz ^{1}H NMR spectrum of compound **6a** in $CDCl_3$.

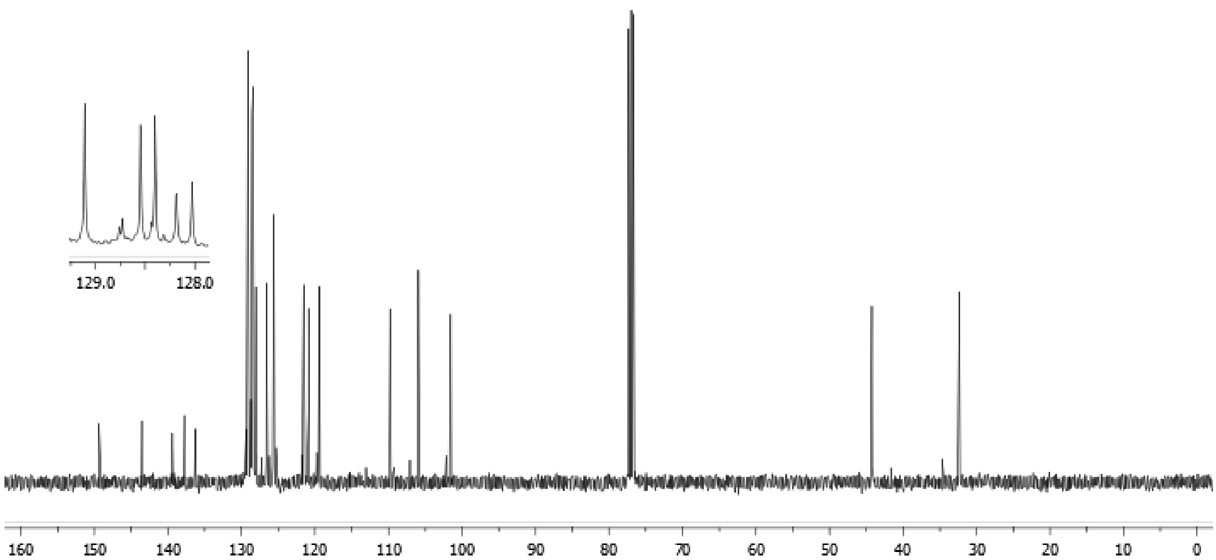


Figure S46. 100 MHz ^{13}C NMR spectrum of compound **6a** in $CDCl_3$.

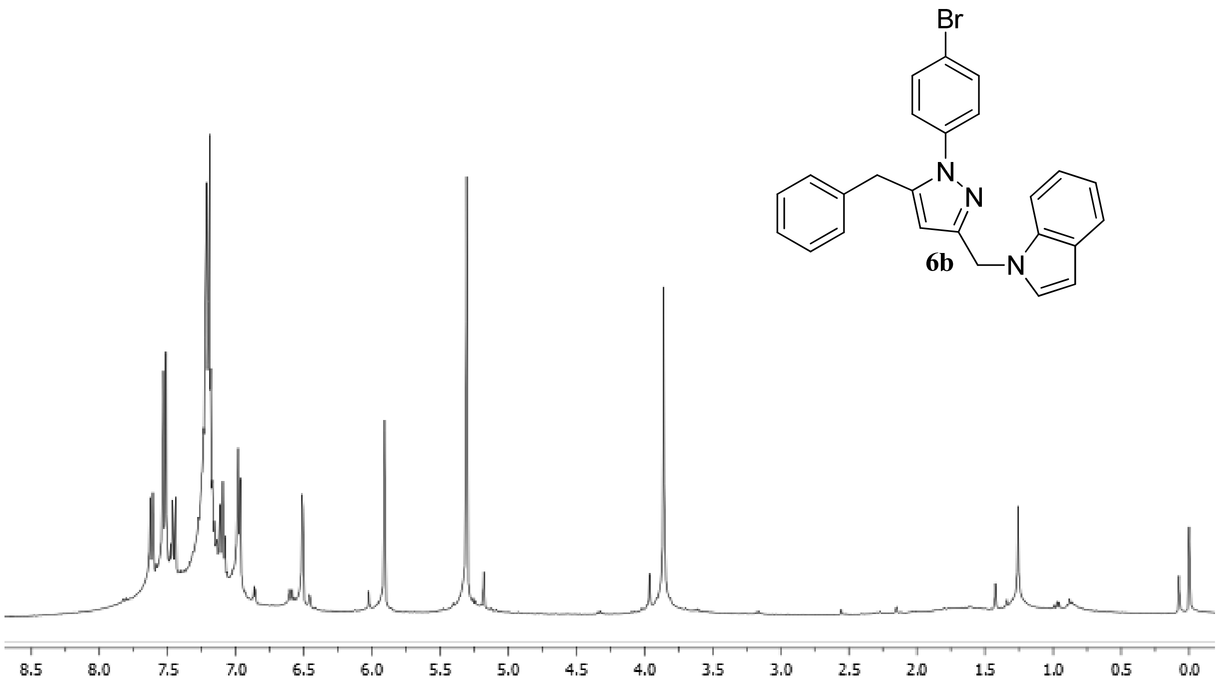


Figure S47. 400 MHz ^{1}H NMR spectrum of compound **6b** in $CDCl_3$.

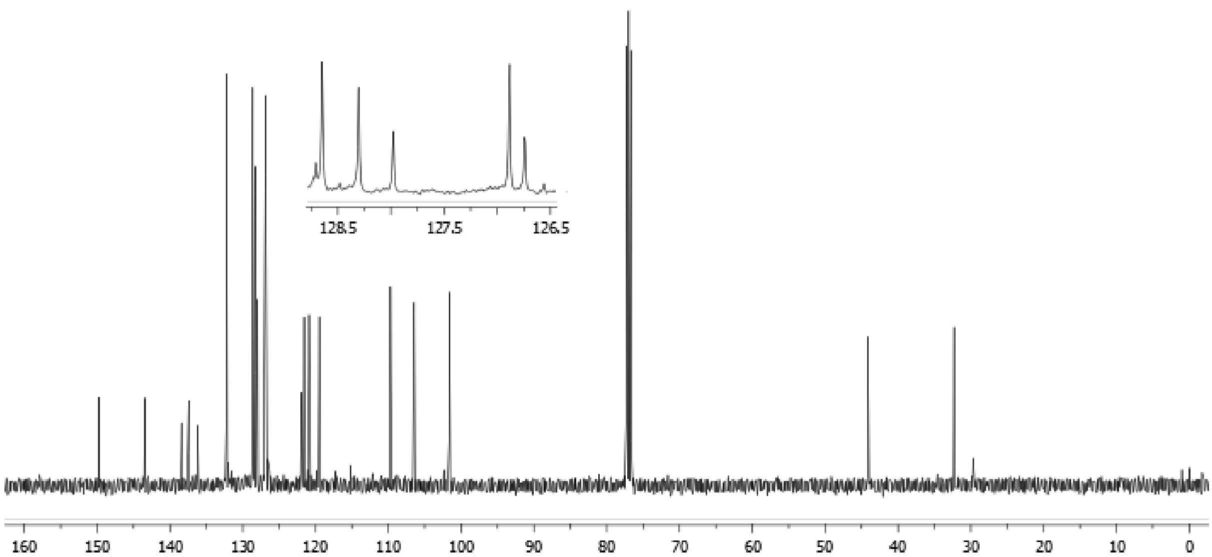


Figure S48. 100 MHz ^{13}C NMR spectrum of compound **6b** in $CDCl_3$.

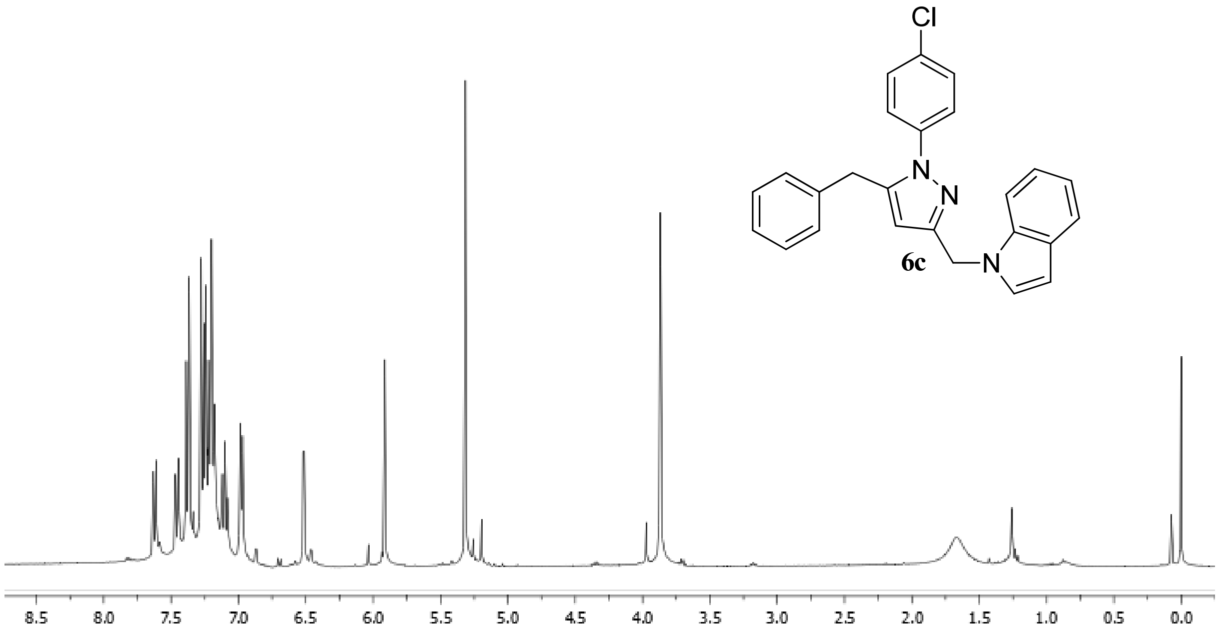


Figure S49. 400 MHz ^{1}H NMR spectrum of compound **6c** in $CDCl_3$.

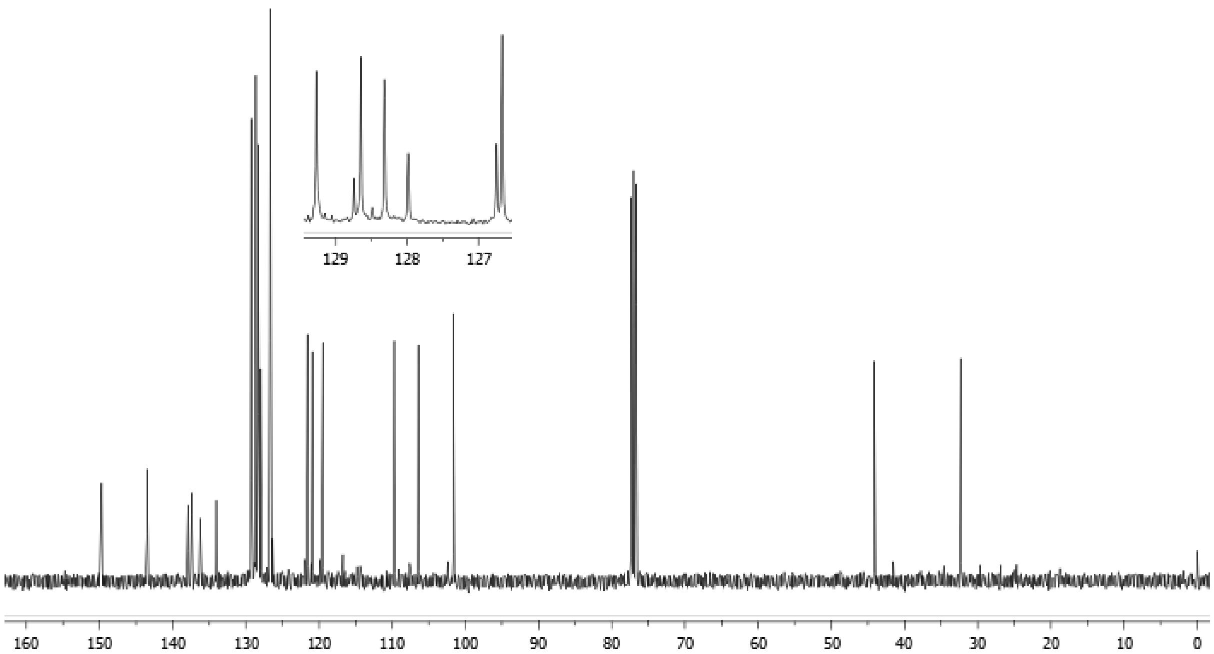


Figure S50. 100 MHz ^{13}C NMR spectrum of compound **6c** in $CDCl_3$.

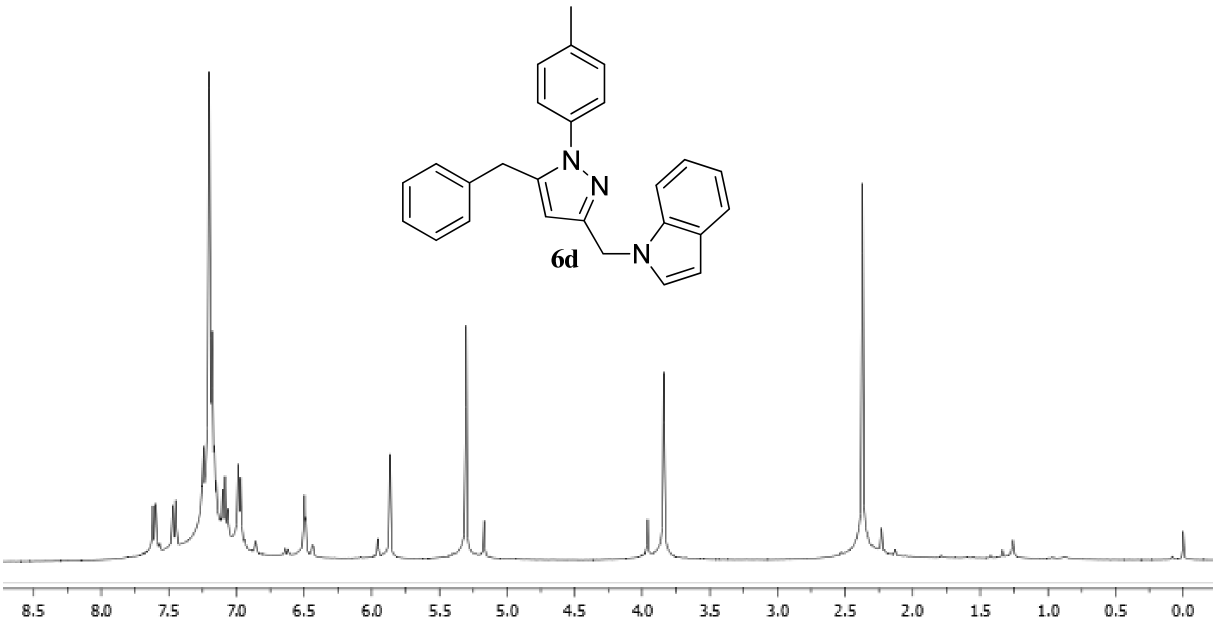


Figure S51. 400 MHz ^{1}H NMR spectrum of compound **6d** in $CDCl_3$.

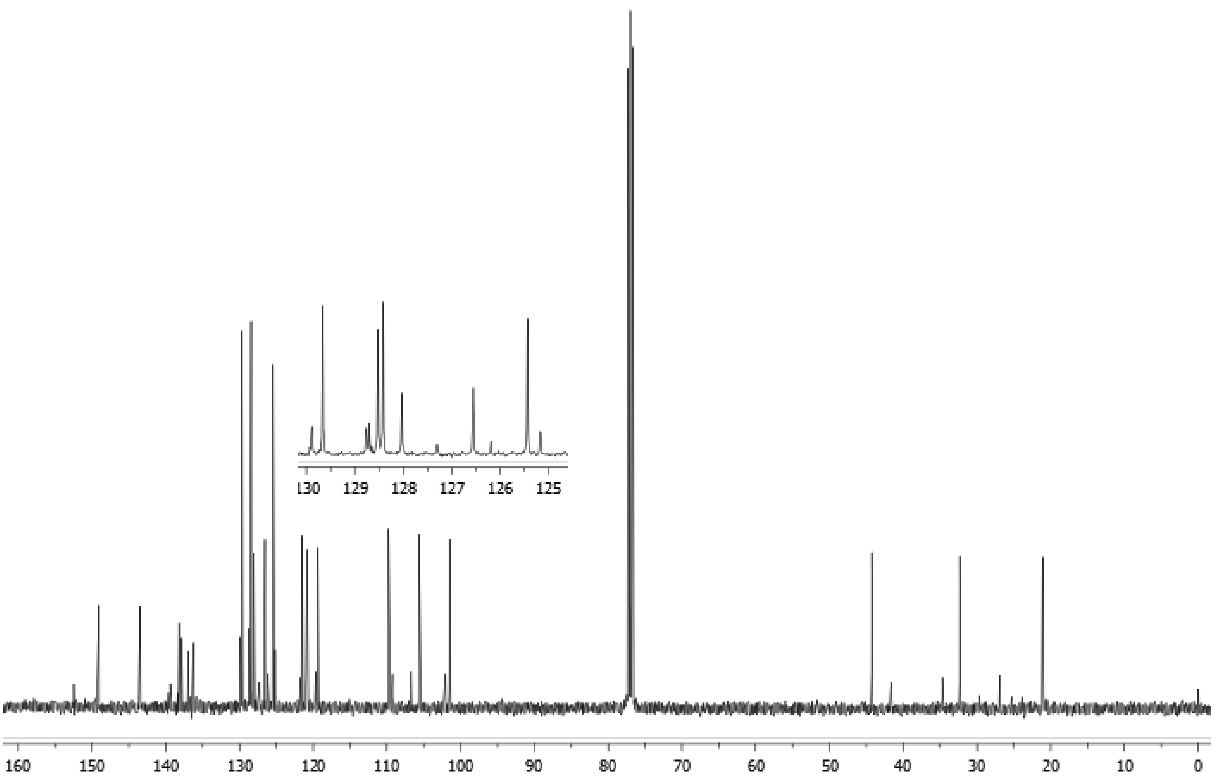


Figure S52. 100 MHz ^{13}C NMR spectrum of compound **6d** in $CDCl_3$.

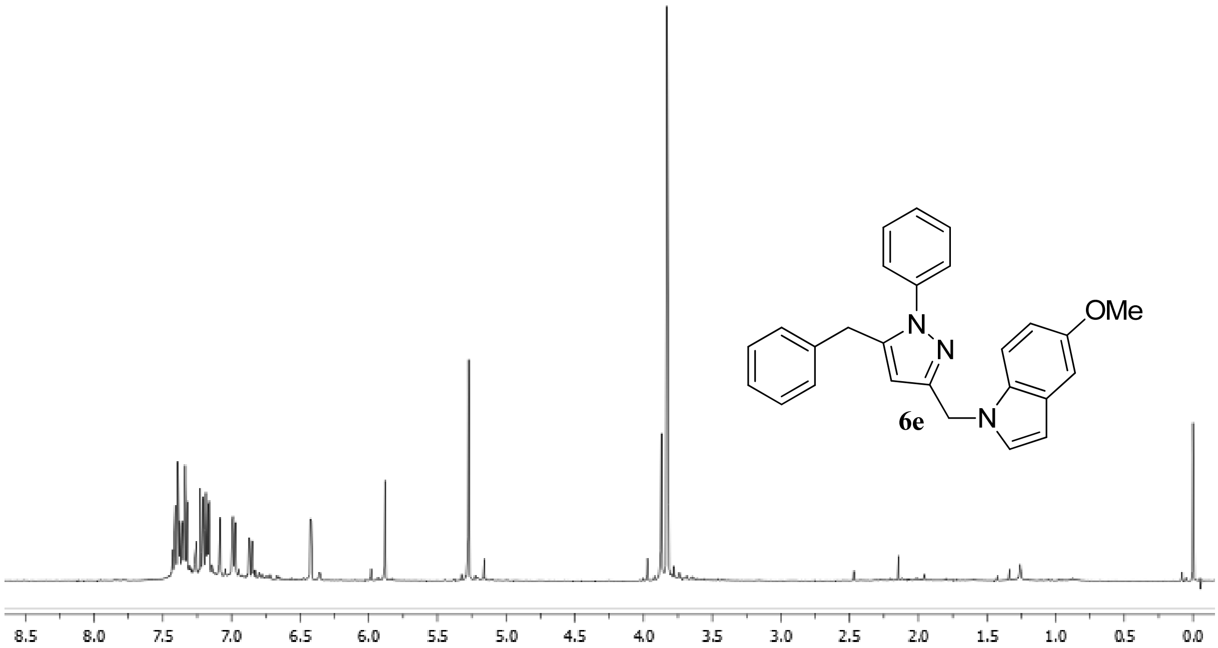


Figure S53. 400 MHz ^{1}H NMR spectrum of compound **6e** in $CDCl_3$.

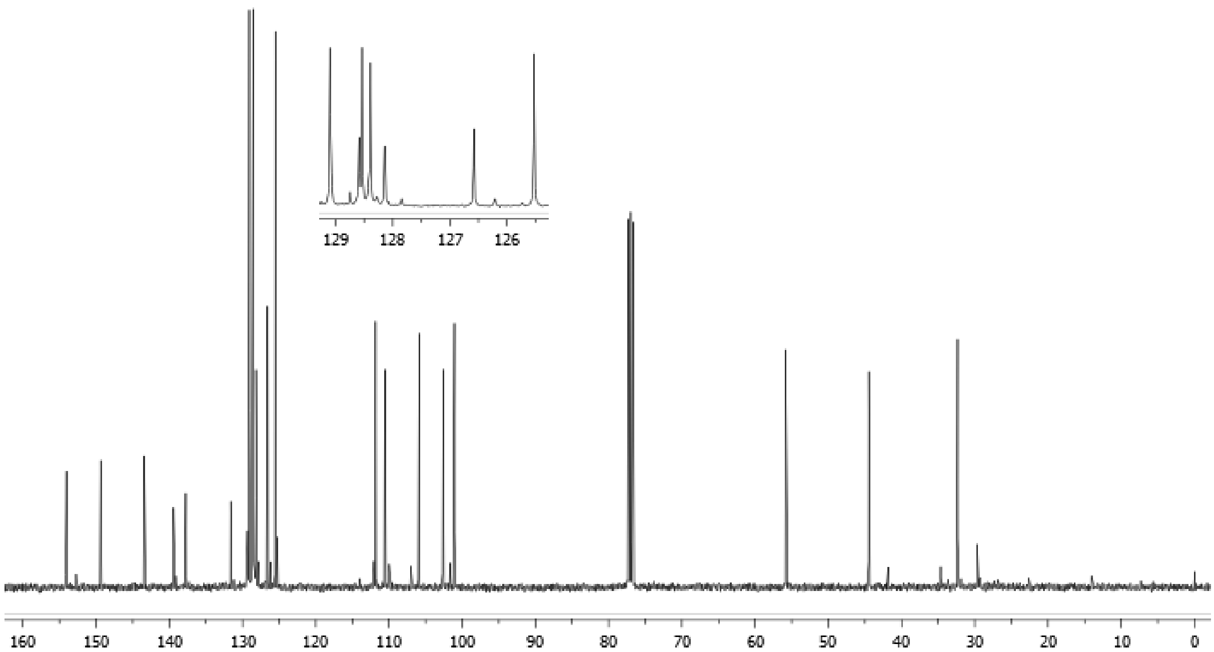


Figure S54. 100 MHz ^{13}C NMR spectrum of compound **6e** in $CDCl_3$.

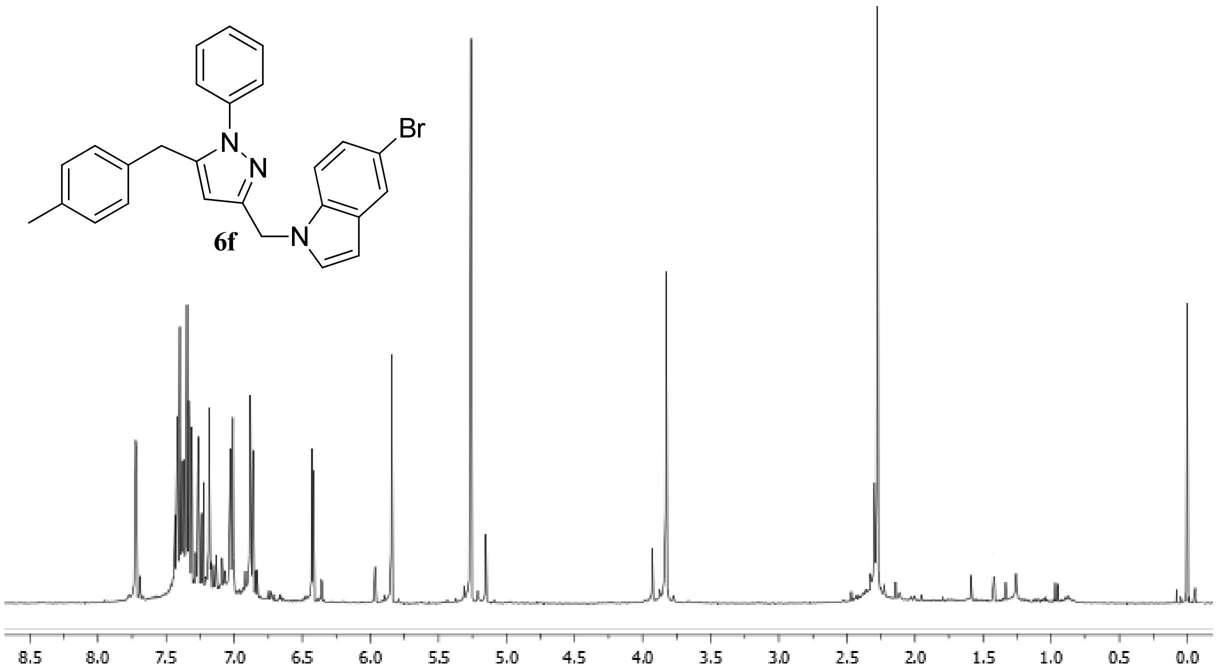


Figure S55. 400 MHz ^{1}H NMR spectrum of compound **6f** in $CDCl_3$.

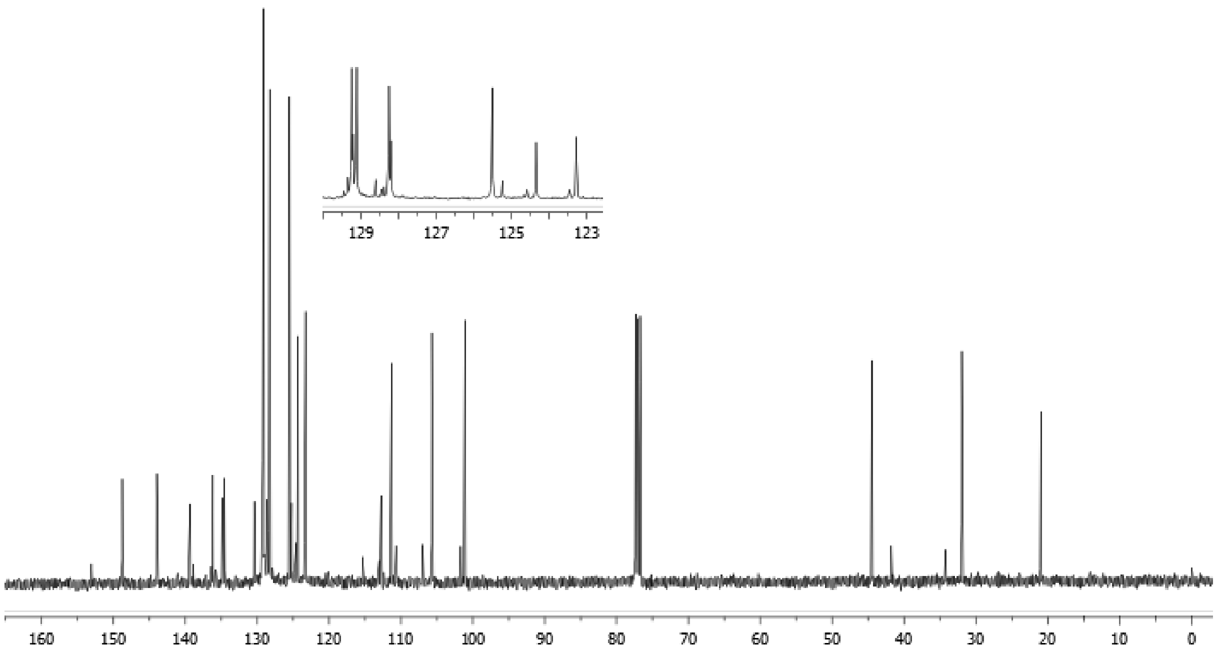


Figure S56. 100 MHz ^{13}C NMR spectrum of compound **6f** in $CDCl_3$.

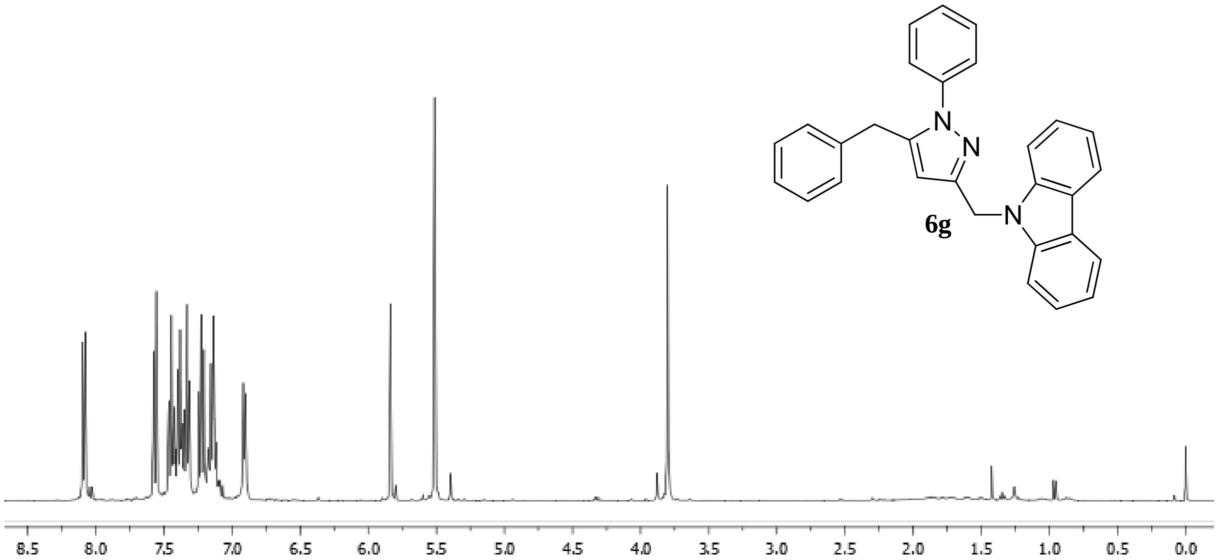


Figure S57. 400 MHz ^{1}H NMR spectrum of compound **6g** in $CDCl_3$.

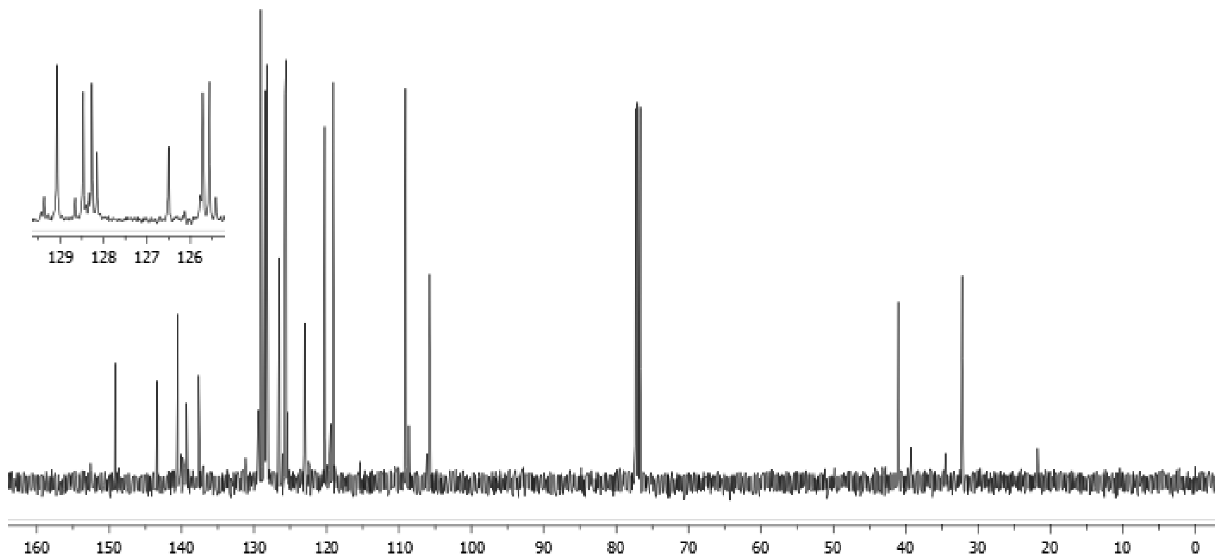


Figure S58. 100 MHz ^{13}C NMR spectrum of compound **6g** in $CDCl_3$.