Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting Information

Rapid access to *N*-(indol-2-yl)amides and *N*-(indol-3-yl)amides as unexplored pharmacophores

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S1. General Procedures

Unless otherwise stated, reactions were conducted under atmospheric pressure of dry nitrogen or argon atmosphere. Temperatures of 0 ^{o}C, –10 ^{o}C and –78 ^{o}C were obtained by cooling the reaction vessel in baths of ice/water, ice/acetone and dry ice/actone respectively. Tetrahydrofuran was dried over sodium wire and distilled from sodium benzophenone. *N,N*-dimethylformamide and triethylamine were distilled from calcium hydride and stored over activated 3Å molecular sieves. Dichloromethane was distilled from calcium hydride. Toluene was dried over and distilled from sodium. Unless noted otherwise, commercially available reagents were used as purchased without further purification.

Analytical thin layer chromatography (TLC) was performed using Merck aluminium backed silica gel 60 F254 (0.2mm) plates, which were visualized using shortwave (254nm) ultra-violet fluorescence. Flash column chromatography employed Merck Kieselgel 60 (230–400 mesh) silica gel unless otherwise stated. Solvents for chromatography are quoted as volume/volume mixtures where applicable.

Melting points were measured in open capillaries using a Stanford Research Systems Optimelt Automated melting point apparatus and are uncorrected.

Infrared absorption spectra were recorded on a Bruker ALPHA FT-IR Vertex 80v spectrometer using a zinc-selenium (ZnSe) built-in cell, and the data are reported as vibrational frequency (cm^{-1}).

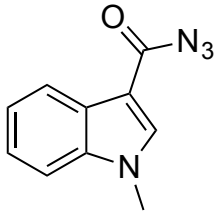
^{1}H and ^{13}C NMR spectra were recorded at 300 K on Bruker Avance DRX200 (200 MHz), DRX300 (300MHz), DRX 400 (400MHz) or AVANCE III 500 Ascend (500.1 MHz) spectrometers. The data is reported as chemical shift (δ ppm) relative to tetramethylsilane or the residual nondeuterated solvent resonance, relative integral, multiplicity (s = singlet; br s = broad singlet; d = doublet; dd = doublet of doublets; ddd = doublet of doublets of doublets; t = triplet; dt = doublet of triplets; q = quartet; quin. = quintet; m = multiplet), coupling constant (J Hz).

Low and high resolution mass spectra (LRMS and HRMS, respectively) were recorded by the Mass Spectrometry Unit of the School of Chemistry, using either electrospray ionization (ESI) or atmospheric pressure chemical ionisation (APCI) recorded on a Finnigan LCQ ion trap spectrometer, or electron impact gas chromatography mass spectrometry (GC/MS). The molecular ion, designated M^+, and major fragment peaks are quoted as percentages relative to the base peak intensity.

S2. Synthetic Procedures and Characterization

General Procedure A: The indole carboxazide in anhydrous PhMe (0.5 M) was treated with the appropriate carboxylic acid (2.0 equiv.) and DMAP (0.10 equiv.) and refluxed for 1-3 h, at which time TLC revealed completion. The reaction mixture was allowed to cool to r.t., the solvent was removed *in vacuo* and the crude residue was purified by silica gel chromatography.

1-Methyl-1*H*-indole-3-carbonyl azide (6a)

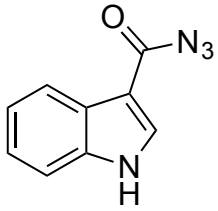


6a

1-Methyl-*1H*-indole-3-carboxylic acid (873 mg, 4.98 mmol) in CH_2Cl_2 (25 mL) was treated with Et_3N (1.39 mL, 9.96 mmol, 2.0 equiv.) and stirred for 15 min at r.t. The solution was treated with diphenylphosphoryl azide (965 μL, 4.48 mmol, 0.9 equiv.) and stirring continued for 1 h. The solvent was removed *in vacuo* and the crude residue was purified by silica gel chromatography (SiO_2; EtOAc/hexane 1:9 v/v) to afford **6a** (843 mg, 94%) as white crystals.

R_f = 0.17 (SiO_2; EtOAc/hexane 1:9); m.p. 111–112 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.17 (m, 1H), 7.68 (s, 1H,), 7.34–7.20 (m, 3H), 3.74 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.9, 137.7, 136.5, 126.6, 123.6, 122.8, 121.9, 110.1, 108.6, 33.7 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3116, 2125, 1667, 1419, 1195, 1079, 899 cm^{-1}.

1*H*-Indole-3-carboxazide (6b)

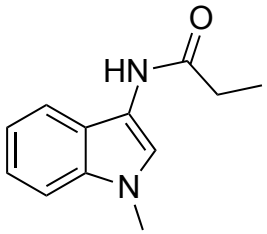


6b

1*H*-Indole-3-carboxylic acid (1.01 g, 6.27 mmol) in CH_2Cl_2 (31 mL) was treated with Et_3N (1.75 mL, 12.5 mmol, 2.0 equiv.) and stirred for 15 min at r.t. The solution was treated with diphenylphosphoryl azide (1.22 mL, 5.64 mmol, 0.9 equiv.) and stirring continued for 1 h. The solvent was removed *in vacuo* and the crude residue was purified by silica gel chromatography (SiO_2; EtOAc/hexane 1:1 v/v) to afford **6b** (1.01 g, 97%) as white crystals.

R_f = 0.65 (SiO_2; EtOAc/hexane 1:1); m.p. 125–126 °C; ^{1}H NMR (300 MHz, d_6-acetone): δ = 11.22 (br s, 1H), 8.18 (m, 1H), 8.12 (s, 1H), 7.56 ppm (m, 1H), 7.30-7.24 (m, 2H); ^{13}C NMR (75 MHz, d_6-acetone): δ = 168.4, 138.1, 134.6, 126.8, 124.2, 123.1, 121.8, 113.3, 109.9 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3256, 2142, 1652, 1516, 1434, 1197, 924 cm^{-1}.

***N*-(1-methyl-1*H*-indol-3-yl)propionamide (1a)**

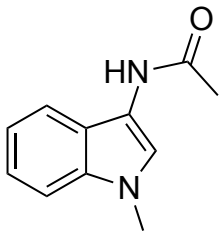


1a

Compound **1a** was prepared from **6a** (100 mg, 0.500 mmol) and propionic acid (64 µL, 1.00 mmol), according to general procedure A, and obtained as a white crystalline solid (87 mg, 86%) after column chromatography (SiO_2; EtOAc/hexane 3:1 v/v).

R_f = 0.42 (SiO_2; EtOAc/hexane 1:1); m.p. 148 °C (decomp); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.66 (s, 1H), 7.64 (br s, 1H), 7.52 (d, J = 7.8 Hz, 1H), 7.34–7.15 (m, 2H), 7.08 (ddd, J = 7.8, 6.6, 1.2 Hz, 1H), 3.69 (s, 3H), 2.45 (q, J = 7.5 Hz, 2H), 1.27 ppm (t, J = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.5, 134.5, 122.1, 121.1, 120.5, 118.8, 116.8, 113.8, 109.4, 32.8, 30.0, 10.1 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3263, 2936, 1643, 1547, 1376, 1326, 1228 cm^{-1}; ESI-MS *m*/*z* (%): 225 (100, [M + Na]$^+$), HR-ESI-MS *m*/*z* (%): Calc. for $C_{12}H_{14}N_2O$ [M + Na]$^+$: 225.1004, found 225.1000.

***N*-(1-Methyl-1*H*-indol-3-yl)acetamide (1b)**

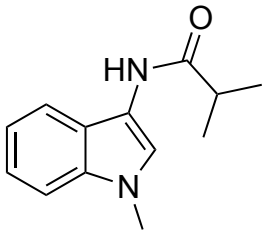


1b

Compound **1b** was prepared from **6a** (100 mg, 0.500 mmol) and acetic acid (58 μL, 1.00 mmol), according to general procedure A, and obtained as a yellow crystalline solid (65 mg, 69%) after column chromatography (SiO_2; EtOAc/hexane 4:1 v/v).

R_f = 0.38 (SiO_2; EtOAc/hexane 4:1); m.p. 162–165 °C (decomp); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.64 (s, 1H), 7.55 (br s, 1H), 7.51 (d, J = 7.8 Hz, 1H), 7.36-7.16 (m, 2H), 7.10 (ddd, J = 7.8, 6.9, 1.2 Hz, 1H), 3.73 (s, 3H), 2.23 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.7, 134.5, 122.2, 121.1, 120.7, 119.0, 116.7, 113.7, 109.5, 32.8, 23.8 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3273, 1650, 1571, 1474, 1380, 1329, 1245, 908 cm^{-1}; ESI-MS m/z (%): 211 (100, $[M + Na]^+$).

***N*-(1-Methyl-1*H*-indol-3-yl)isobutyramide (1c)**



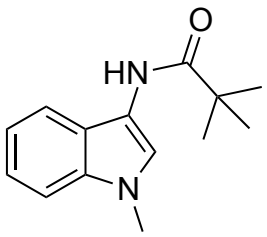
1c

Compound **1c** was prepared from **6a** (100 mg, 0.500 mmol) and isobutyric acid (91 μL, 1.00 mmol), according to general procedure A, and obtained as a yellow crystalline solid (63 mg, 58%) after column chromatography (SiO_2; EtOAc/hexane 1:1 v/v).

R_f = 0.56 (SiO_2; EtOAc/hexane 1:1); m.p. 117 °C (decomp); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.69 (s, 1H), 7.48 (d, J = 7.8 Hz, 1H), 7.44 (br s, 1H), 7.29–7.19 (m, 2H), 7.08 (ddd, J = 7.8, 6.6, 1.2 Hz,

1H), 3.71 (s, 3H), 2.61 (hept, J = 6.9 Hz, 1H), 1.28 ppm (d, J = 6.9 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.5, 134.5, 122.2, 120.9, 120.4, 118.9, 116.6, 113.8, 109.5, 36.1, 32.8, 20.0 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3280, 2967, 1645, 1538, 1455, 1380, 1329, 1226 cm^{-1}; ESI-MS m/z (%): 455 (100, $[2M + Na]^+$), 239 (11, $[M + Na]^+$), HR-ESI-MS m/z (%): Calc. for $C_{13}H_{16}N_2O$ $[M + Na]^+$: 239.1160, found 239.1156.

***N*-(1-Methyl-1*H*-indol-3-yl)pivalamide (1d)**

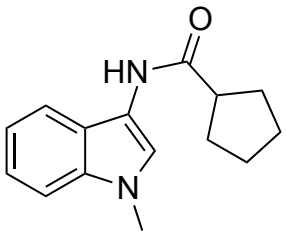


1d

Compound **1d** was prepared from **6a** (100 mg, 0.500 mmol) and trimethylacetic acid (102 mg, 1.00 mmol), according to general procedure A, and obtained as a white crystalline solid (3 mg, 3%) after column chromatography (SiO_2; EtOAc/hexane 1:1 v/v).

R_f = 0.76 (SiO_2; EtOAc/hexane 1:1); m.p. 147 °C (decomp); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.71 (s, 1H), 7.49 (br s, 1H), 7.43 (d, J = 7.8 Hz, 1H), 7.29-7.19 (m, 2H), 7.09 (ddd, J = 8.0, 6.6, 1.2 Hz, 1H), 3.72 (s, 3H), 1.34 ppm (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 175.7, 134.5, 122.2, 120.9, 120.2, 118.9, 116.2, 113.8, 109.6, 39.4, 32.9, 27.9 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3317, 2970, 1645, 1538, 1476, 1379, 1213 cm^{-1}; ESI-MS m/z (%): 483 (100, $[2M + Na]^+$), 253 (10, $[M + Na]^+$), HR-ESI-MS m/z (%): Calc. for $C_{14}H_{18}N_2O$ $[M + H]^+$: 231.1492, found 231.1429.

***N*-(1-Methyl-1*H*-indol-3-yl)cyclopentanecarboxamide (1e)**

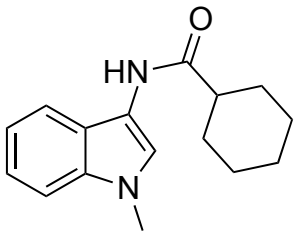


1e

Compound **1e** was prepared from **6a** (100 mg, 0.500 mmol) and cyclopentanecarboxylic acid (108 µL, 1.00 mmol), according to general procedure A, and obtained as a beige powder (91 mg, 75%) after column chromatography (SiO_2; EtOAc/hexane 1:1 v/v).

R_f = 0.58 (SiO_2; EtOAc/hexane 1:1); m.p. 162 °C (decomp); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.71 (s, 1H), 7.50 (dt, *J* = 8.0*,* 0.8 Hz, 1H), 7.47 (br s, 1H), 7.29 (dt, *J* = 8.4, 0.8 Hz, 1H), 7.23 (ddd, *J* = 8.0, 6.8, 1.0 Hz, 1H), 7.1 (ddd, *J* 8.0, 6.8, 1.2 Hz, 1H), 3.72 (s, 3H), 2.79 (quin., *J* = 8.0 Hz, 1H), 1.96 (m, 4H), 1.81 (m, 2H), 1.64 ppm (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.9, 134.5, 122.1, 120.9, 120.3, 118.8, 116.6, 114.0, 109.4, 46.2, 32.8, 30.9, 26.1 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3648, 3244, 2950, 1643,1427, 1231, 1012, 879 cm^{-1}; ESI-MS *m*/*z* (%): 507 (10, $[2M + Na]^+$), 265 (100, $[M + Na]^+$), HR-ESI-MS *m*/*z* (%): Calc. for $C_{15}H_{18}N_2O$ $[M + Na]^+$: 265.1317, found 265.1311.

***N*-(1-methyl-1*H*-indol-3-yl)cyclohexanecarboxamide (1f)**

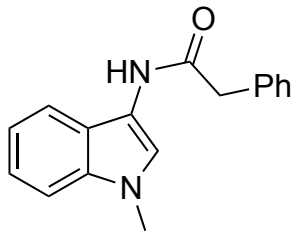


1f

Compound **1f** was prepared from **6a** (100 mg, 0.500 mmol) and cyclohexanecarboxylic acid (128 mg, 1.00 mmol), according to general procedure A, and obtained as a light brown powder (55 mg, 43%) after column chromatography (SiO_2; EtOAc/hexane 1:1 v/v).

R_f = 0.67 (SiO_2; EtOAc/hexane 1:1); m.p. 181 °C (decomp); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.72, (s, 1H), 7.48 (d, *J* = 8.0 Hz, 1H), 7.35 (br s, 1H,), 7.30 (d, *J* = 8.4 Hz), 7.24 (ddd, *J* = 8.6, 7.6, 1.4 Hz, 1H), 7.11 (ddd, *J* = 8.0, 6.8, 1.2 Hz, 1H), 3.74 (s, 3H), 2.34 (m, 1H), 2.01 (m, 2H), 1.86 (m, 2H), 1.72–1.55 (m, 3H), 1.38–1.29 ppm (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.5, 134.5, 122.2, 120.9, 120.4, 118.8, 116.5, 113.8, 109.5, 45.9, 32.8, 30.0, 25.9 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3257, 2924, 2850, 1652, 1541, 1382, 1246 cm^{-1}; ESI-MS *m*/*z* (%): 535 (100, $[2M + Na]^+$), 279 (20, $[M + Na]^+$), HR-ESI-MS *m*/*z* (%): Calc. for $C_{16}H_{20}N_2O$ $[M + Na]^+$: 279.1473, found 279.1468.

***N*-(1-Methyl-1*H*-indol-3-yl)-2-phenylacetamide (1g)**

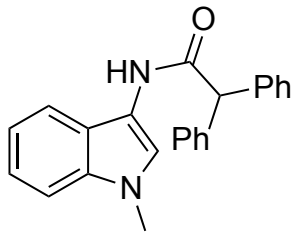


1g

Compound **1g** was prepared from **6a** (100 mg, 0.500 mmol) and phenylacetic acid (136 mg, 1.00 mmol), according to general procedure A, and obtained as a white crystalline solid (116 mg, 88%) after column chromatography (SiO_2; EtOAc/hexane 1:1 v/v).

R_f = 0.65 (SiO_2; EtOAc/hexane 1:1); m.p. 144 °C (decomp); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.69 (s, 1H), 7.52 (br s, 1H), 7.47-7.34 (m, 5H), 7.30–7.21 (m, 3H), 7.06 (ddd, J = 7.8, 7.2, 1.1 Hz, 1H), 3.82 (s, 2H), 3.72 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.4, 135.1, 134.5, 129.6, 129.3, 127.7, 122.2, 120.9, 120.3, 118.9, 116.4, 113.5, 109.5, 44.1, 32.8 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3238, 3061, 1590, 1558, 1454, 1379, 1327, 1245, 1146 cm^{-1}; ESI-MS m/z (%): 551 (100, [2M + Na]$^+$), 287 (20, [M + Na]$^+$), HR-ESI-MS m/z (%): Calc. for $C_{17}H_{16}N_2O$ [M + Na]$^+$: 287.1160, found 287.1155.

_N_-(1-Methyl-1_H_-indol-3-yl)-2,2-diphenylacetamide (1h)

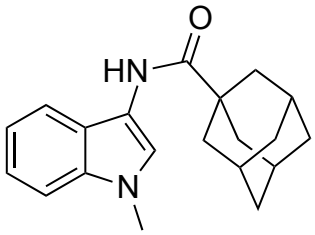


1h

Compound **1h** was prepared from **6a** (100 mg, 0.500 mmol) and diphenylacetic acid (212 mg, 1.00 mmol), according to general procedure A, and obtained as a white crystalline solid (106 mg, 62%) after column chromatography (SiO_2; EtOAc/hexane 1:1 v/v).

R_f = 0.73 (SiO_2; EtOAc/hexane 1:1); m.p. 223 °C (decomp); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.69, (s, 1H), 7.44 (br s, 1H), 7.31–7.09 (m, 12H), 7.04 (d, J = 7.8 Hz, 1H), 6.93 (ddd, J = 7.8, 6.9, 0.6 Hz, 1H), 5.10 (s, 1H), 3.60 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.1, 139.6, 134.5, 129.1, 129.1, 127.6, 122.3, 120.7, 120.2, 119.0, 116.2, 113.6, 109.6, 59.6, 32.9 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3285, 2937, 1667, 1591, 1380, 1328, 1227 cm^{-1}; ESI-MS m/z (%): 703 (100, [2M + Na]$^+$), 363 (82, [M + Na]$^+$), HR-ESI-MS m/z (%): Calc. for $C_{23}H_{20}N_2O$ [M + Na]$^+$: 363.1473, found 363.1468.

***N*-(1-Methyl-1*H*-indol-3-yl)adamantan-1-ylcarboxamide (1i)**

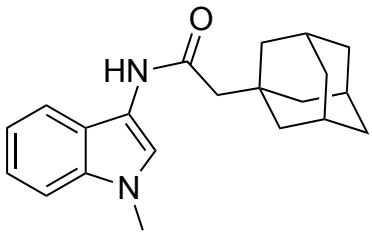


1i

Compound **1i** was prepared from **6a** (100 mg, 0.500 mmol) and 1-adamantanecarboxylic acid (180 mg, 1.00 mmol), according to general procedure A, and obtained as a light brown powder (9 mg, 6%) after column chromatography (SiO_2; EtOAc/hexane 1:1 v/v).

R_f = 0.65 (SiO_2; EtOAc/hexane 1:1); m.p. 242 °C (decomp); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.76 (s, 1H), 7.48 (br s, 1H), 7.46 (d, *J* = 7.9 Hz, 1H), 7.31-7.22 (m, 2H), 7.12 (t, *J* = 7.8 Hz, 1H), 3.76 (s, 3H), 2.13 (m, 3H), 2.04 (m, 6H), 1.79 ppm (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 175.2, 134.5, 122.2, 120.9, 120.2, 118.8, 116.3, 113.8, 109.6, 41.3, 39.6, 36.7, 32.9, 29.9, 28.4 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3273, 2896, 2848, 1638, 1530, 1377, 1245, 1159 cm^{-1}; ESI-MS *m*/*z* (%): 639 (100, $[2M + Na]^+$), 331 (17, $[M + Na]^+$), HR-ESI-MS *m*/*z* (%): Calc. for $C_{20}H_{24}N_2O$ $[M + Na]^+$: 331.1786, found 331.1782.

2-(Adamantan-1-yl)-*N*-(1-methyl-1*H*-indol-3-yl)acetamide (1j)

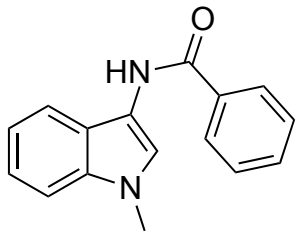


1j

Compound **1j** was prepared from **6a** (100 mg, 0.500 mmol) and 1-adamantaneacetic acid (194 mg, 1.00 mmol), according to general procedure A, and obtained as a light brown solid (66 mg, 41%) after column chromatography (SiO_2; EtOAc/hexane 1:1 v/v).

R_f = 0.71 (SiO_2; EtOAc/hexane 1:1); m.p. 168–170 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.69 (s, 1H), 7.50 (d, *J* = 8.0 Hz, 1H), 7.38 (br s, 1H), 7.28–7.20 (m, 2H), 7.08 (ddd, *J* = 8.0, 6.6, 1.3 Hz, 1H), 3.70 (s, 3H), 2.15 (s, 2H), 1.97 (m, 3H), 1.71–1.62 ppm (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.6, 134.5, 122.2, 121.0, 120.4, 118.9, 116.6, 113.7, 109.5, 52.2, 42.8, 36.9, 33.3, 32.8, 28.8 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3296, 2897, 1637, 1569, 1550, 1381, 1327 cm^{-1}; ESI-MS *m*/*z* (%): 667 (100, [2*M* + Na]$^+$), 345 (17, [*M* + Na]$^+$), HR-ESI-MS *m*/*z* (%): Calc. for $C_{21}H_{26}N_2O$ [M + Na]$^+$: 345.1943, found 345.1939.

_N_-(1-Methyl-1_H_-indol-3-yl)benzamide (1k)

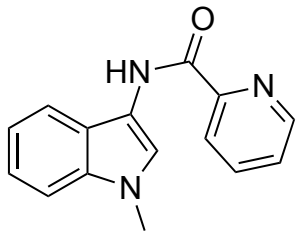


1k

Compound **1k** was prepared from **6a** (100 mg, 0.500 mmol) and benzoic acid (97 µL, 1.00 mmol), according to general procedure A, and obtained as a light yellow crystals (35 mg, 28%) after column chromatography (SiO_2; EtOAc/hexane 1:1 v/v).

R_f = 0.68 (SiO_2; EtOAc/hexane 1:1); m.p. 159–161 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.03 (br s, 1H), 7.87 (d, *J* = 8.0 Hz, 2H), 7.78 (s, 1H), 7.53 (dt, *J* = 8.0, 1.0 Hz, 1H, 7.49-7.40 (m, 3H), 7.27 (d, d, *J* = 8.1 Hz, 1H), 7.21 (ddd, *J* = 8.0, 6.9, 0.9 Hz, 1H), 7.08 (ddd, $^=$*J* = 8.0, 6.8, 1.2 Hz, 1H), 3.71 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.9, 134.8, 134.6, 131.6, 128.8, 127.1, 122.3, 121.1, 120.7, 119.1, 116.7, 113.8, 109.6, 32.9 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3839, 3270, 1628, 1542, 1472, 1379, 1287, 1244 cm^{-1}; ESI-MS *m*/*z* (%): 523 (100, [2*M* + Na]$^+$), 273 (25, [*M* + Na]$^+$), HR-ESI-MS *m*/*z* (%): Calc. for $C_{16}H_{14}N_2O$ [M + Na]$^+$: 273.1004, found 273.1000.

***N*-(1-Methyl-1*H* -indol-3-yl)picolinamide (1l)**

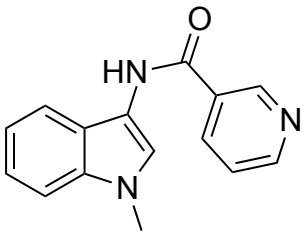


1l

Compound **1l** was prepared from **6a** (100 mg, 0.500 mmol) and picolinic acid (123 mg, 1.00 mmol), according to general procedure A, and obtained as a bright yellow solid (64 mg, 51%) after column chromatography (SiO_2; EtOAc/hexane 1:1 v/v).

R_f = 0.62 (SiO_2; EtOAc/hexane 1:1); m.p. 189 °C (decomp); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 10.10 (br s, 1H), 8.56 (d, *J* = 4.5 Hz, 1H), 8.21 (d, *J* = 7.8 Hz, 1H), 7.84 (s, 1H), 7.81 (td, *J* = 10.2, 1.6 Hz, 1H), 7.64 (d, *J* = 8.1 Hz, 1H), 7.37 (m, 1H), 7.26–7.16 (m, 2H), 7.08 (t, *J* = 7.2 Hz, 1H), 3.72 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.2, 150.1, 148.3, 137.7, 134.6, 126.2, 122.4, 122.2, 121.0, 120.0, 119.1, 117.0, 113.9, 109.5, 33.0 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3361, 1666, 1526, 1461, 1431, 1377, 1326 cm^{-1}; ESI-MS *m*/*z* (%): 525 (15, $[2M + Na]^+$), 274 (100, $[M + Na]^+$), HR-ESI-MS *m*/*z* (%): Calc. for $C_{15}H_{13}N_3O$ $[M + Na]^+$: 274.0956, found: 274.0951.

***N*-(1-methyl-1*H*-indol-3-yl)nicotinamide (1m)**

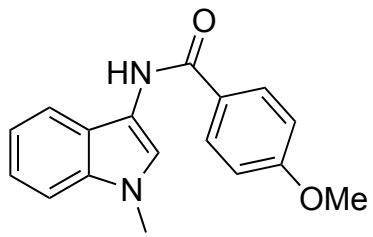


1m

Compound **1m** was prepared from **6a** (100 mg, 0.500 mmol) and nicotinic acid (123 mg, 1.00 mmol), according to general procedure A, and obtained as a bright yellow solid (51 mg, 41%) after column chromatography (SiO_2; MeOH/$CHCl_3$ 1:19 v/v).

R_f = 0.48 (SiO_2; MeOH/$CHCl_3$ 1:9); m.p. 172–173 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.09 (s, 1H), 8.68 (d, *J* = 4.2 Hz, 1H), 8.29 (br s, 1H), 8.17 (d, *J* = 8.0 Hz, 2H), 7.75 (s, 1H), 7.52 (d, *J* = 8.1 Hz), 7.35 (dd, *J* = 8.0, 4.9 Hz, 1H), 7.29–7.19 (m, 2H), 7.08 (t, *J* = 7.6 Hz, 1H), 3.72 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.0, 152.3, 148.0, 135.4, 134.7, 130.6, 123.7, 122.5, 121.1, 119.3, 116.8, 113.4, 109.7, 33.0 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3149, 2920, 1650, 1539, 1423, 1374, 1242 cm^{-1}; ESI-MS *m*/*z* (%): 252 (100, $[M + H]^+$), HR-ESI-MS *m*/*z* (%): Calc. for $C_{15}H_{13}N_3O$ $[M + Na]^+$: 274.0951, found: 274.0951.

4-Methoxy-*N*-(1-methyl-1*H*-indol-3-yl)benzamide (1o)

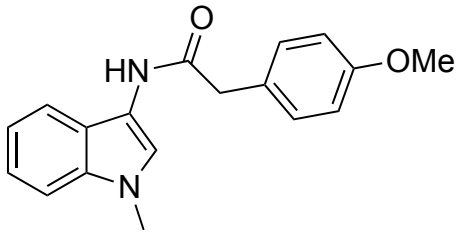


1o

Compound **1o** was prepared from **6a** (100 mg, 0.500 mmol) and 4-methoxybenzoic acid (152 mg, 1.00 mmol), according to general procedure A, and obtained as a yellow solid (44 mg, 32%) after column chromatography (SiO_2; EtOAc/hexane 1:1 v/v).

R_f = 0.50 (SiO_2; EtOAc/hexane 1:1); m.p. 145 °C (decomp); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.93 (br s, 1H), 7.90 (d, *J* = 8.8 Hz, 2H), 7.83 (s, 1H), 7.56 (d, *J* = 7.8 Hz, 1H), 7.33 (d, *J* = 8.4 Hz, 1H), 7.27 (ddd, *J* = 7.8, 6.9, 0.9 Hz, 1H), 7.14 (ddd, *J* = 7.8, 6.9, 0.9 Hz, 1H), 6.99 (d, *J* = 8.4 Hz, 2H3), 3.88 (s, 3H), 3.79 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.4, 162.4, 134.7, 128.9, 127.1, 122.3, 121.1, 120.5, 119.0, 116.6, 114.1, 114.0, 109.7, 55.6, 33.0 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3267, 2925, 1632, 1504, 1240, 1175 cm^{-1}; ESI-MS *m*/*z* (%): 583 (100, $[2M + Na]^+$), 303 (33, $[M + Na]^+$), 281 (17, $[M + H]^+$), HR-ESI-MS *m*/*z* (%): Calc. for $C_{17}H_{16}N_2O_2$ $[M + H]^+$: 281.1290, found: 281.1285.

2-(4-Methoxyphenyl)-*N*-(1-methyl-1*H*-indol-3-yl)acetamide (1p)

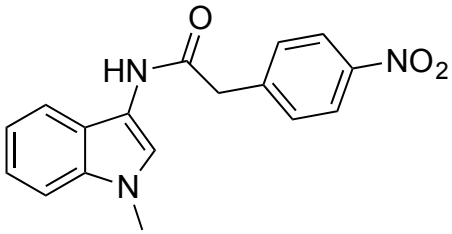


1p

Compound **1p** was prepared from **6a** (100 mg, 0.500 mmol) and 4-methoxyphenylacetic acid (166 mg, 1.00 mmol), according to general procedure A, and obtained as a pale brown powder (167 mg, 90%) after column chromatography (SiO_2; EtOAc/hexane 1:1 v/v).

R_f = 0.38 (SiO_2; EtOAc/hexane 1:1); m.p. 114 °C (decomp); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.66 (s, 1H), 7.52 (br s, 1H), 7.20–7.17 (m, 5H), 7.03 (ddd, *J* = 7.8, 6.6, 1.1 Hz, 1H), 6.93 (d, *J* = 8.7 Hz, 2H), 3.83 (s, 3H), 3.72 (s, 2H), 3.69 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 68.9, 159.1, 134.5, 130.7, 127.0, 122.2, 120.9, 120.3, 118.9, 116.5, 114.7, 113.6, 109.4, 55.4, 43.2, 32.8 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3266, 2926, 1740, 1646, 1513, 1379, 1235, 1174 cm^{-1}; ESI-MS *m*/*z* (%): 611 (100, $[2M + Na]^+$), 317 (95, $[M + Na]^+$), 295 (25, $[M + H]^+$), HR-ESI-MS *m*/*z* (%): Calc. for $C_{18}H_{18}N_2O$ $[M + H]^+$: 295.1447, found: 295.1441.

***N*-(1-Methyl-1*H* -indol-3-yl)-2-(4-nitrophenyl)acetamide (1r)**

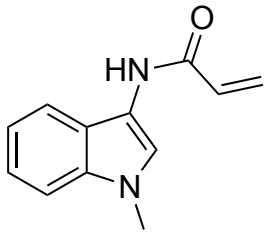


1r

Compound **1r** was prepared from **6a** (100 mg, 0.500 mmol) and 4-nitrophenylacetic acid (181 mg, 1.00 mmol), according to general procedure A, and obtained as bright yellow crystals (104 mg, 67%) after recrystallization from EtOH.

R_f = 0.34 (SiO_2; EtOAc/hexane 1:1); m.p. 228 °C (decomp); ^{1}H NMR (400 MHz, d_6-DMSO): δ = 10.19 (br s, 1H), 8.21 (d, J = 8.7 Hz, 2H), 7.80 (d, J = 8.0 Hz, 1H), 7.71 (s, 1H), 7.64 (d, J = 8.7 Hz, 2H), 7.39 (d, J = 8.3 Hz, 1H), 7.17 (ddd, J = 8.2, 7.0, 1.2 Hz, 1H), 7.05 (ddd, J = 8.0, 7.0, 1.0 Hz, 1H), 3.91 (s, 2H), 3.73 ppm (s, 3H); ^{13}C NMR (100 MHz, d_6-DMSO): δ = 166.5, 146.3, 144.5, 133.9, 130.4, 123.3, 121.6, 120.5, 119.8, 118.2, 118.0, 114.1, 109.5, 41.9, 32.3 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3257, 3063, 1644, 1539, 1514, 1329, 1237 cm^{-1}; ESI-MS m/z (%): 641 (100, $[2M + Na]^+$), 310 (10, $[M + H]^+$), HR-ESI-MS m/z (%): Calc. for $C_{17}H_{15}N_3O_3$ $[M + Na]^+$: 332.1011, found: 332.1005.

_N_-(1-Methyl-1_H_-indol-3-yl)acrylamide (1s)

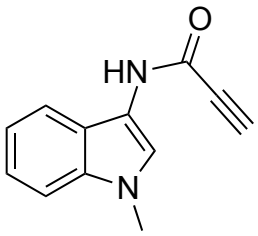


1s

Compound **1s** was prepared from **6a** (100 mg, 0.500 mmol) and acrylic acid (69 μL, 1.00 mmol), according to general procedure A, and obtained as a white powder (40 mg, 40%) after column chromatography (SiO_2; EtOAc/hexane 1:1 v/v).

R_f = 0.64 (SiO_2; EtOAc/hexane 1:1); m.p. 149 °C (decomp); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.95 (br s, 1H), 7.81 (s, 1H), 7.57 (d, J = 8.0 Hz, 1H), 7.30–7.22 (m, 2H), 7.09 (t, J = 8.0 Hz, 1H), 6.47–6.35 (m, 2H), 5.71 (dd, J = 9.0, 2.6 Hz, 1H), 3.72 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.0, 134.5, 130.7, 126.9, 122.3, 120.9, 120.8, 119.0, 116.8, 113.6, 109.5, 32.9 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3855, 3695, 3243, 3096, 1650, 1551, 1328, 1232, 1013 cm^{-1}; ESI-MS m/z (%): 423 (100, $[2M + Na]^+$), 223 (10, $[M + Na]^+$), HR-ESI-MS m/z (%): Calc. for $C_{12}H_{12}N_2O$ $[M + H]^+$: 201.1028, found: 201.1023.

***N*-(1-Methyl-1*H*-indol-3-yl)propiolamide (1t)**

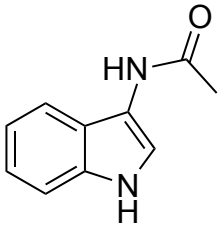


1t

Compound **1t** was prepared from **6a** (100 mg, 0.500 mmol) and propiolic acid (62 µL, 1.00 mmol), according to general procedure A, and obtained as a yellow solid (45 mg, 45%) after column chromatography (SiO_2; EtOAc/hexane 1:1 v/v).

R_f = 0.62 (SiO_2; EtOAc/hexane 1:1); m.p. 110 °C (decomp); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.05 (br s, 1H), 7.71 (s, 1H), 7.56 (d, J = 7.8 Hz, 1H), 7.35–7.21 (m, 2H), 7.13 (ddd, J = 7.8, 6.6, 1.5 Hz, 1H), 3.73 (s, 3H), 2.95 ppm (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 148.9, 134.5, 122.5, 121.4, 120.4, 119.4, 116.8, 112.9, 109.6, 77.7, 74.4, 32.9 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3215, 2926, 2108, 1614, 1540, 1374, 1329, 1241 cm^{-1}; ESI-MS m/z (%): 419 (100, [2M + Na]$^+$), 221 (25, [M + Na]$^+$), HR-ESI-MS m/z (%): Calc. for $C_{12}H_{10}N_2O$ [M + Na] $^+$: 221.0691, found: 221.0685.

***N*-(1*H*-Indol-3-yl)acetamide (1u)**

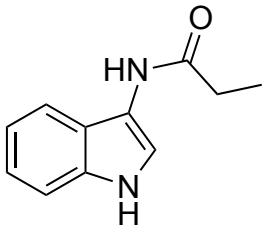


1u

Compound **1u** was prepared from **6b** (100 mg, 0.500 mmol) and acetic acid (57 µL, 1.00 mmol), according to general procedure A, and obtained as a light grey powder (65 mg, 75%) after column chromatography (SiO_2; EtOAc/hexane 1:1 v/v).

R_f = 0.21 (SiO_2; EtOAc/hexane 1:1); m.p. 150 °C (decomp); ^{1}H NMR (300 MHz, MeOD): δ = 7.65 (d, *J* = 7.9 Hz, 1H), 7.61 (s, 1H), 7.32 (d, *J* = 8.2 Hz, 1H), 7.12 (t, *J* = 7.4 Hz, 1H), 7.02 (t, *J* = 7.5 Hz, 1H), 2.18 ppm (s, 3H), NH signal not observed; ^{13}C NMR (75 MHz, MeOD): δ = 171.1, 135.6, 122.8, 122.5, 119.8, 118.4, 117.6, 115.6, 112.3, 22.8 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3288, 3026, 2456, 1619, 1374, 1240 cm^{-1}; ESI-MS *m*/*z* (%): 371 (45, [2*M* + Na]$^+$), 197 (100, [*M* + Na]$^+$), HR-ESI-MS *m*/*z* (%): Calc. for $C_{10}H_{10}N_2O$ [M + Na]$^+$: 197.0685, found: 197.0686.

_N_-(1_H_-Indol-3-yl)propionamide (1v)

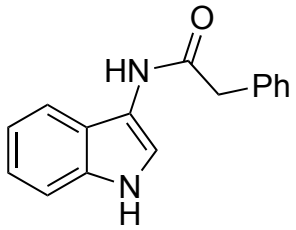


1v

Compound **1v** was prepared from **6b** (100 mg, 0.500 mmol) and propionic acid (75 µL, 1.00 mmol), according to general procedure A, and obtained as a white powder (60 mg, 64%) after column chromatography (SiO_2; EtOAc/hexane 1:3 v/v).

R_f = 0.30 (SiO_2; EtOAc/hexane 1:1); m.p. 165 °C (decomp); ^{1}H NMR (300 MHz, d_6-acetone): δ = 9.95 (br s, 1H), 9.08 (br s, 1H), 7.90 (d, *J* = 2.4 Hz, 1H), 7.78–7.66 (m, 1H), 7.38 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.11 (ddd, *J* = 8.1, 6.9, 1.2 Hz, 1H), 6.99 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 1H), 2.44 (q, *J* = 7.6 Hz, 2H), 1.19 ppm (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (75 MHz, d_6-acetone): δ = 171.6, 135.0, 122.6, 121.8, 119.2, 118.2, 116.9, 116.1, 115.9, 112.2, 10.4 (one peak obscured by solvent) ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3312, 2977, 1630, 1512, 1373, 1245, 1105 cm^{-1}; ESI-MS *m*/*z* (%): 399 (37, [2*M* + Na]$^+$), 211 (100, [*M* + Na]$^+$), 189 (22, [*M* + H]$^+$), HR-ESI-MS *m*/*z* (%): Calc. for $C_{11}H_{12}N_2O$ [M + Na]$^+$: 211.0847, found: 211.0842.

***N*-(1*H*-indol-3-yl)-2-phenylacetamide (1w)**

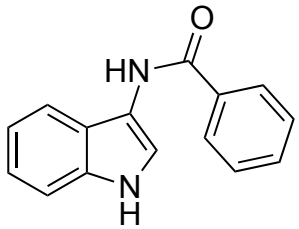


1w

Compound **1w** was prepared from **6b** (100 mg, 0.500 mmol) and phenylacetic acid (136 mg, 1.00 mmol), according to general procedure A, and obtained as a white crystalline solid (80 mg, 64%) after column chromatography (SiO_2; EtOAc/hexane 1:1 v/v).

R_f = 0.43 (SiO_2; EtOAc/hexane 1:1); m.p. 203 °C (decomp); ^{1}H NMR (400 MHz, MeOD): δ = 7.63 (dt, *J* = 8.0, 0.8 Hz, 1H), 7.61 (s, 1H), 7.40 (m, 2H), 7.35–7.31 (m, 3H), 7.26 (m, 1H), 7.12 (ddd, *J* = 8.0, 7.0, 0.8 Hz, 1H), 7.02 (ddd, *J* = 8.0, 6.8, 1.0 Hz, 1H), 3.78 ppm (s, 2H), NH signal not observed; ^{13}C NMR (100 MHz, MeOD): δ = 171.8, 137.3, 135.6, 130.1, 129.6, 127.9, 122.9, 122.6, 119.8, 118.4, 117.7, 115.6, 112.3, 43.8 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3392, 3030, 2525, 1631, 1581, 1441, 1241 cm^{-1}; ESI-MS *m*/*z* (%): 523 (100, $[2M + Na]^+$), 273 (82, $[M + Na]^+$), HR-ESI-MS *m*/*z* (%): Calc. for $C_{16}H_{14}N_2O$ $[M + Na]^+$: 273.1004, found: 273.0997.

***N*-(1*H*-Indol-3-yl)benzamide (1x)**

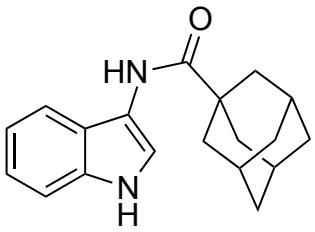


1x

Compound **1x** was prepared from **6b** (100 mg, 0.500 mmol) and benzoic acid (166 mg, 1.00 mmol), according to general procedure A, and obtained as a white crystalline solid (28 mg, 24%) after column chromatography (SiO_2; EtOAc/hexane 1:1 v/v).

R_f = 0.55 (SiO_2; EtOAc/hexane 1:1); m.p. 212 °C (decomp); ^{1}H NMR (400 MHz, d_6-acetone): δ = 8.09 – 8.04 (m, 3H), 8.02 (s, 1H), 7.90 (d, *J* = 7.8 Hz, 1H), 7.6 –7.47 (m, 4H), 7.42 (d, *J* = 8.1 Hz, 1H), 7.15 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 7.04 ppm (ddd, *J* = 8.0, 6.9, 1.0 Hz, 1H), NH signals not observed; ^{13}C NMR (100 MHz, d_6-acetone): δ = 165.5, 136.2, 135.0, 133.5, 131.9, 130.4, 129.2, 129.2, 128.4, 122.6, 122.1, 119.3, 118.8, 117.0, 116.4, 112.2 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3392, 3030, 2525, 1631, 1581, 1441, 1241 cm^{-1}; ESI-MS *m*/*z* (%): 495 (100, [2*M* + Na]$^+$), 259 (83, [*M* + Na]$^+$), HR-ESI-MS *m*/*z* (%): Calc. for $C_{15}H_{12}N_2O$ [M + Na]$^+$: 259.0847, found: 259.0842.

_N_-(1_H_-Indol-3-yl)adamantan-1-ylcarboxamide (1y)

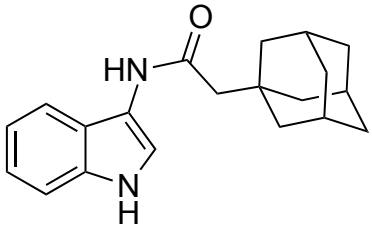


1y

Compound **1y** was prepared from **6b** (100 mg, 0.500 mmol) and 1-adamantanecarboxylic acid (180 mg, 1.00 mmol), according to general procedure A, and obtained as a white crystalline solid (46 mg, 31%) after column chromatography (SiO_2; EtOAc/hexane 1:1 v/v).

R_f = 0.50 (SiO_2; EtOAc/hexane 1:1); m.p. 225 °C (decomp); ^{1}H NMR (300 MHz, MeOD): δ = 7.52 (d, *J* = 8.1 Hz, 1H), 7.40 (s, 1H), 7.33 (d, *J* = 8.1 Hz, 1H), 7.11 (t, *J* = 7.5 Hz, 1H), 7.02 (t, *J* = 7.5 Hz, 1H), 2.09–2.01 (m, 9H), 1.83 ppm (m, 6H), NH signals not observed; ^{13}C NMR (75 MHz, MeOD): δ = 179.6, 136.1, 123.8, 122.8, 119.8, 119.3, 118.7, 115.1, 112.4, 42.4, 40.4, 37.6, 29.8 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3402, 2903, 2851, 2540, 1631, 1452, 1239 cm^{-1}; ESI-MS *m*/*z* (%): 611 (100, [2*M* + Na]$^+$), 317 (31, [*M* + Na]$^+$), 295 (19, [*M* + H]$^+$), HR-ESI-MS *m*/*z* (%): Calc. for $C_{19}H_{22}N_2O$ [M + Na]$^+$: 317.1629, found: 317.1623.

2-(adamantan-1-yl)-*N*-(1*H*-indol-3-yl)acetamide (1z)

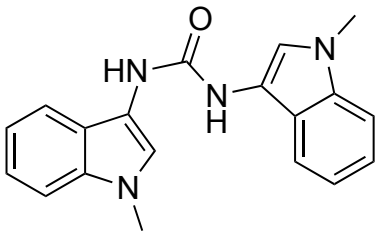


1z

Compound **1z** was prepared from **6b** (100 mg, 0.500 mmol) and 1-adamantaneacetic acid (194 mg, 1.00 mmol), according to general procedure A, and obtained as a white crystalline solid (40 mg, 26%) after column chromatography (SiO_2; EtOAc/hexane 1:1 v/v).

R_f = 0.50 (SiO_2; EtOAc/hexane 1:1); m.p. 225 °C (decomp); ^{1}H NMR (300 MHz, d_6-acetone): δ = 9.97 (br s, 1H), 8.98 (br s, 1H), 7.90 (d, *J* = 2.1 Hz, 1H), 7.72 (d, *J* = 7.8 Hz, 1H), 7.37 (d, *J* = 8.4 Hz, 1H), 7.10 (t, *J* = 7.4 Hz, 1H), 6.99 (t, *J* = 7.4 Hz, 1H), 2.19 (s, 2H), 1.95 (m, 3H), 1.71 ppm (m, 12H); ^{13}C NMR (75 MHz, d_6-acetone): δ = 168.8, 135.0, 122.5, 121.9, 119.2, 118.3, 116.8, 116.1, 112.2, 51.5, 43.4, 37.7, 33.8, 29.7 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3309, 2904, 1620, 1546, 1238 cm^{-1}; ESI-MS *m*/*z* (%): 639 (100, $[2M + Na]^+$), 331 (34, $[M + Na]^+$), 309 (16, $[M + Na]^+$), HR-ESI-MS *m*/*z* (%): Calc. for $C_{20}H_{24}N_2O$ $[M + Na]^+$: 331.1786, found: 331.1780.

1,3-bis(1-methyl-1*H* -indol-3-yl)urea (9)

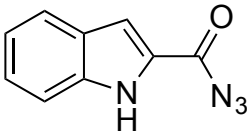


9

Compound **9** was isolated from the Curtius rearrangement reactions with various yields depending on the carboxylic substrate used.

R_f = 0.25 (SiO_2; EtOAc/hexane 1:1); m.p. 270–271 °C; ^{1}H NMR (400 MHz, d_6-DMSO): δ = 8.42 (br s, 2H), 7.54 (d, *J* = 7.9 Hz, 1H), 7.51 (s, 2H), 7.40 (d, *J* = 8.3 Hz, 2H), 7.17 (ddd, *J* = 8.3, 6.9, 1.1 Hz, 2H), 7.05 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 2H), 3.75 ppm (s, 6H); ^{13}C NMR (100 MHz, d_6-DMSO): δ = 152.8, 134.1, 121.4, 120.9, 118.0, 117.0, 115.0, 109.5, 32.3 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3295, 1633, 1572, 1555, 1377, 1328, 1218, 1125 cm^{-1}; ESI-MS *m*/*z* (%): 659 (100, [2*M* + Na]$^+$), 341 (39, [*M* + Na]$^+$), HR-ESI-MS *m*/*z* (%): Calc. for $C_{19}H_{18}N_4O$ [M + Na] $^+$: 341.1378, found: 341.1373.

1*H*-Indole-2-carboxazide (13a)

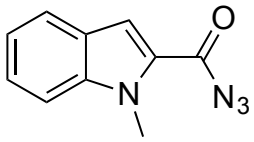


13a

1*H*-Indole-2-carboxylic acid (1.00 g, 6.20 mmol) in CH_2Cl_2 (31 mL) was treated with Et_3N (1.72 mL, 12.4 mmol, 2.0 equiv.) and stirred for 15 min at r.t. The solution was treated with diphenylphosphoryl azide (1.20 mL, 5.58 mmol, 0.9 equiv.) and stirring continued for 1 h. The solvent was removed *in vacuo* and the crude residue was purified by silica gel chromatography (SiO_2; EtOAc/hexane 3:7 v/v) to afford **13a** (970 mg, 93%) as white crystals.

R_f = 0.38 (SiO_2; $CHCl_3$/hexane 3:7); m.p. 163–166 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.96 (br s, 1H), 7.70 (dd, *J* = 8.1, 1.1 Hz, 1H), 7.51–7.28 (m, 2H), 7.29 (dd, *J* = 2.1, 0.9 Hz, 1H), 7.18 (ddd, *J* = 8.0, 6.7, 1.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.4, 138.2, 128.3, 127.5, 126.8, 123.2, 121.5, 112.3, 111.1 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3306, 2145, 1648, 1516, 1340, 1240, 1186, 940, 820, 735, 653 cm^{-1}.

1-Methyl-1*H*-indole-2-carbonyl azide (13b)

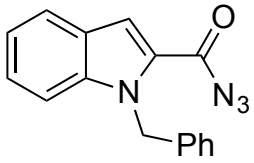


13b

A solution of compound **13a** (600 mg, 3.22 mmol) in THF (32 mL) at 0 °C was treated with 60% NaH (155 mg, 3.87 mmol, 1.2 equiv.), stirred for 0.5 h and treated with MeI (241 µL, 3.87 mmol, 1.2 equiv.). The solution was warmed to r.t. and stirred for 16 h then treated with NH_4Cl (30 mL sat. aq. solution) and extracted with EtOAc (3 x 30 mL) before being dried ($MgSO_4$), filtered and the solvent removed *in vacuo*. Purification by silica gel chromatography (SiO_2; EtOAc/hexane 1:19 v/v) to afforded **13b** (413 mg, 64%) as white crystals.

R_f = 0.67 (SiO_2; EtOAc/hexane 1:19); m.p. 84–85 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.68 (d, J = 8.1 Hz, 1H), 7.42 – 7.33 (m, 3H), 7.16 (ddd, J = 7.9, 4.7, 3.1 Hz, 1H), 4.09 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.7, 141.1, 128.4, 126.5, 125.9, 123.3, 121.2, 112.8, 110.5, 31.9 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 2922, 2135, 1662, 1510, 1464, 1393, 1324, 1202, 988, 808, 734 cm^{-1}.

1-benzyl-1*H*-indole-2-carbonyl azide (13c)



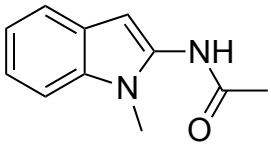
13c

A solution of compound **13a** (1.00 g, 5.37 mmol) in THF (54 mL) at 0 °C was treated with 60% NaH (258 mg, 6.44 mmol, 1.2 equiv.), stirred for 0.5 h and treated with BnBr (765 µL, 6.44 mmol, 1.2 equiv.) and tetrabutylammonium iodide (198 mg, 0.54 mmol, 0.1 equiv.). The solution was warmed to r.t. and stirred for 16 h then treated with NH_4Cl (50 mL sat. aq. solution) and extracted with EtOAc (3 x 40 mL) before being dried ($MgSO_4$), filtered and the solvent removed *in vacuo*.

Purification by silica gel chromatography (SiO_2; EtOAc/hexane 1:19 v/v) to afforded **13c** (812 mg, 55%) as white crystals.

R_f = 0.60 (SiO_2; EtOAc/hexane 1:19); m.p. 172–175 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.70 (d, *J* = 8.0 Hz, 1H), 7.44 (s, 1H), 7.39 – 7.31 (m, 2H), 7.26 – 7.13 (m, 4H), 7.15 – 6.95 (m, 2H), 5.82 ppm (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.3, 141.0, 137.9, 128.8, 128.0, 127.5, 126.8, 126.4, 126.1, 123.4, 121.5, 113.7, 111.1, 48.1 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3062, 3031, 2131, 1672, 1613, 1512, 1477, 1453, 1406, 1353, 1321, 1236, 1186, 1133, 1029, 956, 818, 724, 694 cm^{-1}.

_N_-(1-methyl-1_H_-indol-2-yl)acetamide (2a)

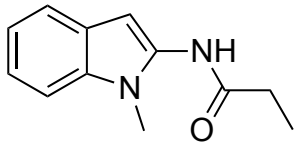


2a

Compound **2a** was prepared from **13b** (50 mg, 0.250 mmol) and acetic acid (29 μL, 0.500 mmol), according to general procedure A, and obtained as a white crystalline solid (24 mg, 52%) after column chromatography (SiO_2; EtOAc/hexane 1:1 v/v).

R_f = 0.32 (SiO_2; EtOAc/hexane 1:1); m.p. 198 °C (decomp); ^{1}H NMR (300 MHz, MeOD): δ = 7.46 (d, *J* = 7.8 Hz, 1H), 7.30 (d, *J* = 8.2 Hz, 1H), 7.17 – 7.09 (m, 1H), 7.03 (d, *J* = 7.5 Hz, 1H), 6.34 (s, 1H), 3.60 (s, 3H), 2.20 ppm (s, 3H), NH signal not observed; ^{13}C NMR (75 MHz, MeOD): δ = 173.1, 136.3, 134.1, 128.3, 122.2, 121.0, 120.6, 110.1, 95.7, 29.2, 22.8 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3289, 3056, 2923, 1656, 1525, 1457, 1376, 978, 763, 741 cm^{-1}; ESI-MS *m*/*z* (%): 187 (100, [*M* – H]$^-$), HR-ESI-MS *m*/*z* (%): Calc. for $C_{11}H_{12}N_2O$ [M + Na]$^+$: 211.0842, found: 211.0842.

***N*-(1-methyl-1*H*-indol-2-yl)propionamide (2b)**

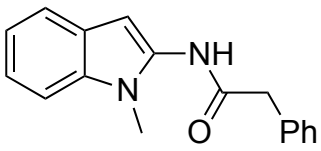


2b

Compound **2b** was prepared from **13b** (50 mg, 0.250 mmol) and propionic acid (37 μL, 0.500 mmol), according to general procedure A, and obtained as a white crystalline solid (28 mg, 55%) after column chromatography (SiO_2; EtOAc/hexane 1:1 v/v).

R_f = 0.49 (SiO_2; EtOAc/hexane 1:1); m.p. 132 °C (decomp.); ^{1}H NMR (300 MHz, MeOD): δ = 7.46 (d, J = 7.8 Hz, 1H), 7.28 (d, J = 8.2 Hz, 1H), 7.13 (t, J = 7.6 Hz, 1H), 7.02 (t, J = 7.5 Hz, 1H), 6.33 (s, 1H), 3.57 (s, 3H), 2.47 (q, J = 7.6 Hz, 2H), 1.24 ppm (t, J = 7.6 Hz, 3H), NH signal not observed; ^{13}C NMR (75 MHz, MeOD): δ = 176.8, 136.3, 134.2, 128.3, 122.1, 121.0, 120.6, 110.1, 95.8, 30.1, 29.2, 10.2 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3264, 3051, 2975, 2395, 1659, 1537, 1460, 1336, 1220, 732 cm^{-1}; ESI-MS m/z (%): 225 (100, $[M + Na]^+$), 203 (33, $[M + H]^+$), HR-ESI-MS m/z (%): Calc. for $C_{12}H_{14}N_2O$ $[M + Na]^+$: 225.0998, found: 225.0998.

***N*-(1-methyl-1*H*-indol-2-yl)-2-phenylacetamide (2c)**



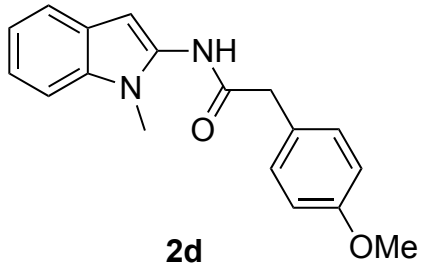
2c

Compound **2c** was prepared from **13b** (50 mg, 0.250 mmol) and phenylacetic acid (68 mg, 0.500 mmol), according to general procedure A, and obtained as a white crystalline solid (45 mg, 68%) after column chromatography (SiO_2; EtOAc/hexane 1:4 v/v).

R_f = 0.15 (SiO_2; EtOAc/hexane 1:4); m.p. 149–151 °C; ^{1}H NMR (300 MHz, MeOD): δ = 7.45 (d, J = 7.8 Hz, 1H), 7.43 – 7.23 (m, 6H), 7.12 (ddd, J = 8.3, 7.0, 1.3 Hz, 1H), 7.01 (ddd, J = 8.0, 7.0, 1.1

Hz, 1H), 6.33 (d, J = 0.8 Hz, 1H), 3.75 (s, 2H), 3.49 ppm (s, 3H); ^{13}C NMR (75 MHz, MeOD): δ = 173.9, 136.6, 136.4, 133.9, 130.2, 129.7, 128.2, 128.1, 122.3, 121.1, 120.6, 110.1, 96.1, 43.8, 29.2 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3242, 3029, 2917, 1666, 1533, 1466, 1331, 1224, 1192, 963, 769, 742, 693 cm^{-1}; ESI-MS m/z (%): 263 (100, [M – H]$^-$), HR-ESI-MS m/z (%): Calc. for $C_{17}H_{16}N_2O$ [M + Na]$^+$: 287.1155, found: 287.1156.

***N*-(1-methyl-1*H*-indol-2-yl)-2-(4-methoxyphenyl)acetamide (2d)**

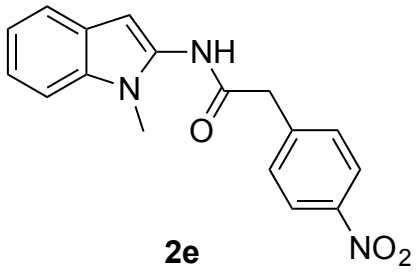


2d

Compound **2d** was prepared from **13b** (50 mg, 0.250 mmol) and 4-methoxylphenylacetic acid (83 mg, 0.500 mmol), according to general procedure A, and obtained as a white crystalline solid (37 mg, 50%) after column chromatography (SiO_2; EtOAc/hexane 1:1 v/v).

R_f = 0.10 (SiO_2; EtOAc/hexane 1:4); m.p. 154–158 °C; ^{1}H NMR (300 MHz, MeOD): δ = 7.45 (d, J = 7.9 Hz, 1H), 7.29 (m, 3H), 7.12 (t, J = 7.6 Hz, 1H), 7.01 (t, J = 7.6 Hz, 1H), 6.90 (d, J = 8.1 Hz, 2H), 6.32 (s, 1H), 3.78 (s, 3H), 3.68 (s, 2H), 3.50 ppm (s, 3H), NH proton not observed; ^{13}C NMR (75 MHz, MeOD): δ = 174.4, 160.3, 131.2, 128.5, 128.3, 122.3, 121.1, 120.6, 118.2, 115.1, 111.4, 110.1, 96.1, 55.7, 43.0, 29.2 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3226, 2926, 2852, 1651, 1542, 1508, 1434, 1301, 1246, 1176, 1025, 795, 767, 749 cm^{-1}; ESI-MS m/z (%): 293 (100, [M – H]$^-$), HR-ESI-MS m/z (%): Calc. for $C_{18}H_{18}N_2O_2$ [M + Na]$^+$: 317.1261, found: 317.1261.

***N*-(1-methyl-1*H*-indol-2-yl)-2-(4-nitrophenyl)acetamide (2e)**

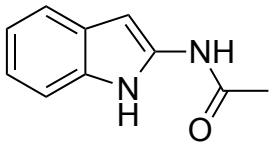


2e

Compound **2e** was prepared from **13b** (50 mg, 0.250 mmol) and 4-nitrophenylacetic acid (90 mg, 0.500 mmol), according to general procedure A, and obtained as a white crystalline solid (55 mg, 71%) after column chromatography (SiO_2; EtOAc/hexane 1:1 v/v).

R_f = 0.30 (SiO_2; EtOAc/hexane 1:1); m.p. 192 °C (decomp.); ^{1}H NMR (300 MHz, d_6-DMSO): δ = 10.27 (s, 1H), 8.23 (d, J = 8.2 Hz, 2H), 7.65 (d, J = 8.2 Hz, 2H), 7.44 (d, J = 7.8 Hz, 1H), 7.36 (d, J = 8.1 Hz, 1H), 7.09 (t, J = 7.4 Hz, 1H), 7.00 (t, J = 7.3 Hz, 1H), 6.39 (s, 1H), 3.95 (s, 2H), 3.59 ppm (s, 3H); ^{13}C NMR (75 MHz, d_6-DMSO): δ = 168.7, 146.4, 143.7, 134.1, 133.8, 130.6, 126.5, 123.4, 120.5, 119.5, 119.3, 109.3, 93.0, 41.9, 29.0 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3255, 3060, 3028, 1660, 1511, 1461, 1341, 1246, 1177, 1030, 728, 696 cm^{-1}; ESI-MS m/z (%): 332 (100, $[M + Na]^+$), HR-ESI-MS m/z (%): Calc. for $C_{17}H_{15}N_3O_3$ $[M + Na]^+$: 332.1006, found: 332.1007.

***N*-(1*H*-indol-2-yl)acetamide (2f)**



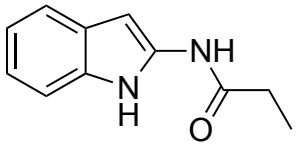
2f

Compound **2f** was prepared from **13a** (50 mg, 0.269 mmol) and acetic acid (31 µL, 0.537 mmol), according to general procedure A, and obtained as a white crystalline solid (22 mg, 47%) after column chromatography (SiO_2; EtOAc/hexane 1:1 v/v).

R_f = 0.46 (SiO_2; EtOAc/hexane 1:1); m.p. 228 °C (decomp); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 10.35 (br s, 1H), 7.92 (br s, 1H), 7.56–7.45 (m, 1H), 7.37–7.30 (m, 1H), 7.17–7.04 (m, 2H), 5.92–5.82 (m,

1H), 2.21 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.7, 135.2, 132.5, 126.7, 120.9, 120.4, 119.3, 111.0, 85.5, 24.1 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3373, 3313, 1655, 1572, 1455, 1366, 1266, 738 cm^{-1}; ESI-MS *m*/*z* (%): 173 (66, [*M* – H]$^-$), 131 (100), HR-ESI-MS *m*/*z* (%): Calc. for $C_{10}H_{10}N_2O$ [M + Na]$^+$: 197.0685, found: 197.0685.

***N*-(1*H*-indol-2-yl)propionamide (2g)**

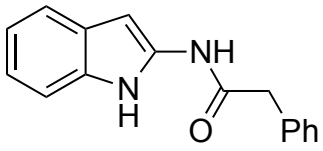


2g

Compound **2g** was prepared from **13a** (50 mg, 0.269 mmol) and propionic acid (41 μL, 0.537 mmol), according to general procedure A, and obtained as a white crystalline solid (23 mg, 45%) after column chromatography (SiO_2; EtOAc/hexane 1:1 v/v).

R_f = 0.46 (SiO_2; EtOAc/hexane 1:4); m.p. 121–123 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 10.41 (br s, 1H), 7.80 (br s, 1H), 7.53–7.42 (m, 1H), 7.36–7.28 (m, 1H), 7.17–6.98 (m, 2H), 5.86 (d, *J* = 2.0 Hz, 1H), 2.45 (q, *J* = 7.6 Hz, 2H), 1.28 ppm (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.4, 135.3, 132.5, 126.7, 120.8, 120.3, 119.3, 111.0, 85.3, 30.4, 9.6 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3419, 3191, 2966, 1632, 1571, 1457, 1332, 1224, 1075, 923, 766, 744, 659 cm^{-1}; ESI-MS *m*/*z* (%): 187 (33, [*M* – H]$^-$), 131 (100), HR-ESI-MS *m*/*z* (%): Calc. for $C_{11}H_{12}N_2O$ [M + Na]$^+$: 211.0842, found: 211.0842.

***N*-(1*H*-indol-2-yl)-2-phenylacetamide (2h)**

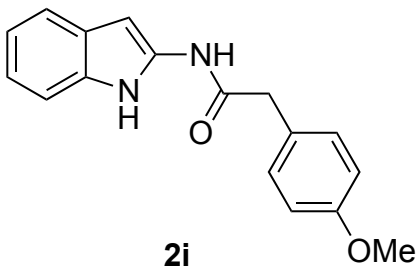


2h

Compound **2h** was prepared from **13a** (50 mg, 0.269 mmol) and phenylacetic acid (74 mg, 0.537 mmol), according to general procedure A, and obtained as a white crystalline solid (38 mg, 56%) after column chromatography (SiO_2; EtOAc/hexane 1:4 v/v).

R_f = 0.35 (SiO_2; EtOAc/hexane 1:4); m.p. 154–157 °C; ^{1}H NMR (300 MHz, d_6-acetone): δ = 10.67 (br s, 1H), 10.11 (br s, 1H), 7.44 – 7.21 (m, 7H), 6.95 (ddd, J = 6.4, 3.8, 1.5 Hz, 2H), 5.92 (s, 1H), 3.72 ppm (s, 2H); ^{13}C NMR (75 MHz, d_6-acetone): δ = 170.0, 136.8, 136.4, 133.7, 130.1, 129.3, 128.2, 127.7, 120.8, 120.5, 119.6, 111.9, 86.7, 44.1 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3389, 3283, 2999, 1631, 1556, 1491, 1453, 1348, 1135 cm^{-1}; ESI-MS *m*/*z* (%): 249 (100, [M – H]$^-$), HR-ESI-MS *m*/*z* (%): Calc. for $C_{16}H_{14}N_2O$ [M + Na]$^+$: 273.0998, found: 273.0999.

***N*-(1*H*-indol-2-yl)-2-(4-methoxyphenyl)acetamide (2i)**



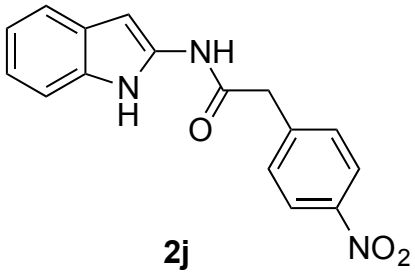
2i

Compound **2i** was prepared from **13a** (50 mg, 0.269 mmol) and 4-methoxylphenylacetic acid (90 mg, 0.537 mmol), according to general procedure A, and obtained as a white crystalline solid (69 mg, 91%) after column chromatography (SiO_2; EtOAc/hexane 3:7 v/v).

R_f = 0.15 (SiO_2; EtOAc/hexane 3:7); m.p. 164 °C (decomp.); ^{1}H NMR (300 MHz, d_6-acetone): δ = 10.67 (br s, 1H), 10.02 (br s, 1H), 7.42 – 7.30 (m, 2H), 7.26 (d, J = 8.4 Hz, 2H), 6.97 – 6.90 (m, 2H), 6.88 – 6.82 (m, 2H), 5.91 (d, J = 1.9 Hz, 1H), 3.73 (s, 3H), 3.64 ppm (s, 2H); ^{13}C NMR (75

MHz, d_6-acetone): δ = 170.5, 159.8, 137.0, 133.8, 131.2, 128.3, 128.2, 120.8, 120.5, 119.6, 114.8, 111.9, 86.6, 55.6, 43.3 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3385, 3294, 3003, 1631, 1558, 1509, 1453, 1349, 1298, 1243, 1174, 1029, 811, 741 cm^{-1}; ESI-MS *m*/*z* (%): 279 (100, $[M - H]^-$), HR-ESI-MS *m*/*z* (%): Calc. for $C_{17}H_{16}N_2O_2$ $[M + Na]^+$: 313.1104, found: 303.1104.

_N_-(1_H_-indol-2-yl)-2-(4-nitrophenyl)acetamide (2j)

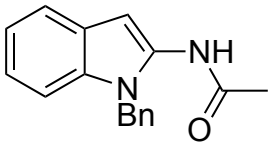


2j

Compound **2j** was prepared from **13a** (50 mg, 0.269 mmol) and 4-nitrophenylacetic acid (98 mg, 0.537 mmol), according to general procedure A, and obtained as a white crystalline solid (72 mg, 91%) after column chromatography (SiO_2; EtOAc/hexane 3:7 v/v).

R_f = 0.30 (SiO_2; EtOAc/hexane 1:3); m.p. 185 °C (decomp.); ^{1}H NMR (300 MHz, d_6-acetone): δ = 10.63 (br s, 1H), 10.26 (br s, 1H), 8.18 (d, *J* = 8.7 Hz, 2H), 7.65 (d, *J* = 8.7 Hz, 2H), 7.53 – 7.28 (m, 2H), 6.95 (ddd, *J* = 6.8, 4.7, 1.7 Hz, 2H), 5.94 (s, 1H), 3.93 ppm (s, 2H); ^{13}C NMR (75 MHz, d_6-acetone): δ = 168.8, 148.1, 144.1, 136.5, 133.8, 131.6, 128.2, 124.3, 121.0, 120.6, 119.7, 112.0, 87.0, 43.4 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3420, 3269, 2876, 1660, 1626, 1554, 1510, 1458, 1341, 1226, 925, 767, 744 cm^{-1}; ESI-MS *m*/*z* (%): 294 (100, $[M - H]^-$), HR-ESI-MS *m*/*z* (%): Calc. for $C_{16}H_{13}N_3O_3$ $[M + Na]^+$: 318.0849, found: 318.0850.

***N*-(1-benzyl-1*H*-indol-2-yl)acetamide (2k)**

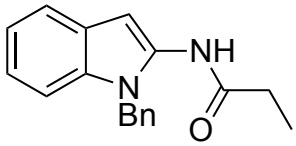


2k

Compound **2k** was prepared from **13c** (100 mg, 0.362 mmol) and acetic acid (41 µL, 0.724 mmol), according to general procedure A, and obtained as a white crystalline solid (69 mg, 72%) after column chromatography (SiO_2; EtOAc/hexane 1:4 v/v).

R_f = 0.10 (SiO_2; EtOAc/hexane 1:4); m.p. 168–171 °C; ^{1}H NMR (300 MHz, d_6-DMSO) as a mixture of rotamers: δ = 10.01 (s, 1H), 8.89 (s, 0.2H), 7.99 (s, 0.7H), 7.56 – 7.44 (m, 1.6H), 7.26 (m, 5.8H), 7.14 (m, 1.1H), 7.08 – 6.90 (m, 5.5H), 6.48 (s, 1H), 5.36 (m, 3.2H), 2.45 (s, 1H), 2.08 ppm (s, 2.6H); ^{13}C NMR (75 MHz, d_6-DMSO) as a mixture of rotamers: δ = 168.8, 154.0, 138.0, 136.6, 134.4, 134.1, 133.7, 133.5, 128.6, 128.5, 128.4, 127.3, 127.0, 126.6, 126.5, 126.4, 125.9, 121.4, 120.5, 120.3, 119.7, 119.5, 117.7, 109.9, 109.7, 109.0, 93.5, 50.3, 45.2, 43.7, 29.7, 23.1 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3275, 3059, 3029, 1663, 1613, 1461, 1342, 1158, 730, 695 cm^{-1}; ESI-MS *m*/*z* (%): 551 (90, $[2M + Na]^+$), 287 (100, $[M + Na]^+$), 265 (25, $[M + H]^+$), HR-ESI-MS *m*/*z* (%): Calc. for $C_{17}H_{16}N_2O$ $[M + Na]^+$: 287.1155, found: 287.1157.

***N*-(1-benzyl-1*H*-indol-2-yl)propionamide (2l)**

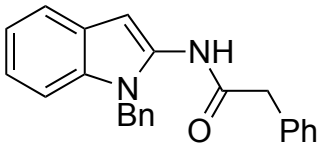


2l

Compound **2l** was prepared from **13c** (100 mg, 0.362 mmol) and propionic acid (54 µL, 0.724 mmol), according to general procedure A, and obtained as a white crystalline solid (71 mg, 70%) after column chromatography (SiO_2; EtOAc/hexane 1:4 v/v).

R_f = 0.25 (SiO_2; EtOAc/hexane 1:4); m.p. 139–143 °C; ^{1}H NMR (300 MHz, d_6-DMSO) as a mixture of rotamers: δ = 9.93 (s, 0.6H), 8.88 (s, 0.7H), 8.01 (s, 0.6H), 7.47 (d, J = 4.0 Hz, 1.5H), 7.33 – 7.14 (m, 8H), 7.09 – 6.95 (m, 5H), 6.48 (2 s, 1H), 5.36 (2 s, 2.7H), 2.81 (q, J = 7.4 Hz, 0.6H), 2.37 (q, J = 7.5 Hz, 1.2H), 1.15 (t, J = 7.4 Hz, 0.9H), 1.07 ppm (t, J = 7.5 Hz, 1.5H); ^{13}C NMR (75 MHz, d_6-DMSO) as a mixture of rotamers: δ = 172.6, 154.1, 152.5, 138.0, 137.8, 136.6, 134.4, 134.1, 133.5, 128.6, 128.5, 128.4, 127.2, 127.0, 126.6, 126.5, 126.4, 121.4, 120.5, 120.3, 119.5, 119.4, 117.9, 109.9, 109.7, 109.0, 95.0, 93.6, 92.5, 45.2, 33.9, 28.7, 9.6, 8.5 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3261, 3058, 3030, 2978, 2937, 1668, 1538, 1460, 1341, 1221, 1159, 1074, 730, 695 cm^{-1}; ESI-MS m/z (%): 579 (80, $[2M + Na]^+$), 301 (100, $[M + Na]^+$), 279 (30, $[M + H]^+$), HR-ESI-MS m/z (%): Calc. for $C_{18}H_{18}N_2O$ [M + Na] $^+$: 301.1311, found: 301.1313.

_N_-(1-benzyl-1_H_-indol-2-yl)-2-phenylacetamide (2m)

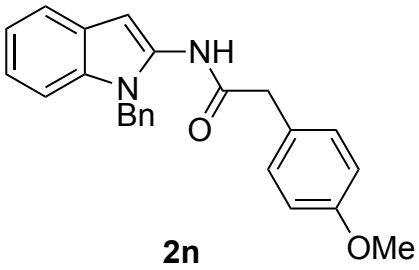


2m

Compound **2m** was prepared from **13c** (100 mg, 0.362 mmol) and phenylacetic acid (98 mg, 0.724 mmol), according to general procedure A, and obtained as a white crystalline solid (81 mg, 66%) after column chromatography (SiO_2; EtOAc/hexane 1:4 v/v).

R_f = 0.40 (SiO_2; EtOAc/hexane 1:4); m.p. 155–160 °C; ^{1}H NMR (300 MHz, d_6-DMSO): δ = 10.23 (s, 1H), 7.47 (dd, J = 6.7, 2.1 Hz, 1H), 7.36 – 7.17 (m, 9H), 7.05 – 6.96 (m, 4H), 6.50 (s, 1H), 5.36 (s, 2H), 3.71 ppm (s, 2H); ^{13}C NMR (75 MHz, d_6-DMSO): δ = 169.7, 141.1, 137.9, 135.7, 133.8, 133.6, 129.0, 128.4, 128.3, 128.0, 127.1, 126.9, 126.5, 120.6, 119.6, 109.9, 93.8, 45.2, 42.4 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3255, 3027, 1659, 1534, 1495, 1452, 1345, 1227, 1191, 770, 733, 695 cm^{-1}; ESI-MS m/z (%): 703 (70, $[2M + Na]^+$), 363 (100, $[M + Na]^+$), 341 (25, $[M + H]^+$), HR-ESI-MS m/z (%): Calc. for $C_{23}H_{20}N_2O$ [M + Na] $^+$: 363.1468, found: 363.1468.

***N*-(1-benzyl-1*H*-indol-2-yl)-2-(4-methoxyphenyl)acetamide (2n)**

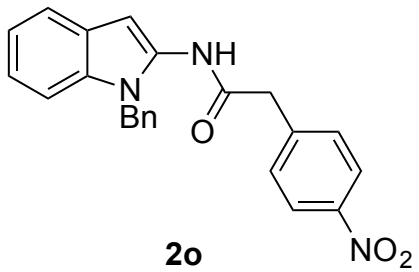


2n

Compound **2n** was prepared from **13c** (100 mg, 0.362 mmol) and 4-methoxyphenylacetic acid (120 mg, 0.724 mmol), according to general procedure A, and obtained as a white crystalline solid (83 mg, 62%) after column chromatography (SiO_2; EtOAc/hexane 3:7 v/v).

R_f = 0.15 (SiO_2; EtOAc/hexane 1:4); m.p. 131 °C (decomp.); ^{1}H NMR (300 MHz, d_6-DMSO): δ = 10.16 (s, 1H), 7.48 (dd, J = 6.7, 2.1 Hz, 1H), 7.33 – 7.16 (m, 6H), 7.00 (m, 4H), 6.85 (d, J = 8.6 Hz, 2H), 6.49 (s, 1H), 5.35 (s, 2H), 3.73 (s, 3H), 3.63 ppm (s, 2H); ^{13}C NMR (75 MHz, d_6-DMSO): δ = 170.0, 158.0, 137.9, 133.8, 133.6, 130.0, 128.5, 128.4, 127.6, 127.1, 126.9, 126.5, 120.6, 119.6, 113.7, 109.9, 93.8, 55.0, 45.2, 41.5 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3263, 3029, 1659, 1509, 1452, 1340, 1242, 1176, 1029, 775, 725, 694, 440 cm^{-1}; ESI-MS *m*/*z* (%): 763 (50, $[2M + Na]^+$), 393 (100, $[M + Na]^+$), 271 (15, $[M + H]^+$), HR-ESI-MS *m*/*z* (%): Calc. for $C_{24}H_{22}N_2O_2$ $[M + Na]^+$: 393.1574, found: 393.1573.

***N*-(1-benzyl-1*H*-indol-2-yl)-2-(4-nitrophenyl)acetamide (2o)**

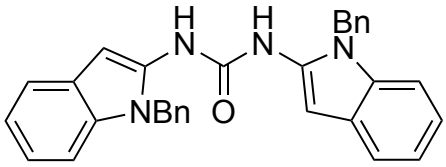


2o

Compound **2o** was prepared from **13c** (100 mg, 0.362 mmol) and 4-nitrophenylacetic acid (130 mg, 0.724 mmol), according to general procedure A, and obtained as a white crystalline solid (83 mg, 59%) after column chromatography (SiO_2; EtOAc/hexane 3:7 v/v).

R_f = 0.30 (SiO_2; EtOAc/hexane 1:3); m.p. 180 °C (decomp.); ^{1}H NMR (300 MHz, d_6-DMSO) only major rotamer is reported: δ = 10.34 (s, 1H), 8.16 (d, J = 8.7 Hz, 2H), 7.56 (d, J = 8.7 Hz, 2H), 7.51 – 7.42 (m, 1H), 7.33 – 7.15 (m, 4H), 7.08 – 6.96 (m, 4H), 6.53 (s, 1H), 5.38 (s, 2H), 3.90 ppm (s, 2H); ^{13}C NMR (75 MHz, d_6-DMSO) only major rotamer is reported: δ = 168.6, 146.4, 143.7, 137.9, 133.7, 133.5, 130.5, 128.5, 128.4, 127.0, 126.9, 126.4, 123.4, 120.8, 119.7, 119.6, 109.9, 94.0, 45.2, 42.0 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3264, 3059, 3030, 1606, 1517, 1462, 1343, 1157, 1107, 734 cm^{-1}; ESI-MS m/z (%): 509 (15, [2M + K]$^+$), 492 (20, [2M + Na]$^+$), 408 (100, [M + Na]$^+$), 386 (12, [M + H.]$^+$), HR-ESI-MS m/z (%): Calc. for $C_{23}H_{19}N_3O_3$ [M + Na] $^+$: 4081319, found: 408.1319.

1,3-bis(1-benzyl-1*H*-indol-2-yl)urea (S1)



S1

Compound **S1** was isolated from the Curtius rearrangement reactions with various yields depending on the carboxylic substrate used.

R_f = 0.05 (SiO_2; EtOAc/hexane 1:1); m.p. 189 °C (decomp.); ^{1}H NMR (300 MHz, d_6-DMSO): δ = 8.89 (s, 2H), 7.51 – 7.42 (m, 2H), 7.24 (qd, J = 6.6, 3.8 Hz, 8H), 7.10 – 7.04 (m, 4H), 7.02 – 6.92 (m, 4H), 6.48 (s, 2H), 5.35 ppm (s, 4H); ^{13}C NMR (75 MHz, d_6-DMSO): δ = 152.5, 137.8, 134.4, 133.5, 128.5, 127.1, 126.4, 120.3, 119.5, 119.3, 109.7, 92.5, 45.1 ppm; IR (neat, diamond cell): $\tilde{\nu}$ = 3264, 3030, 1660, 1511, 1461, 1341, 1247, 1177, 1030, 731, 695 cm^{-1}; ESI-MS m/z (%): 963 (5, [2M + Na]$^+$), 509 (5, [M + K]$^+$), 493 (100, [M + Na]$^+$), 471 (7, [M + H]$^+$).

S3. Crystallographic Data

Crystals of compound **1r** were measured on a Bruker APEX-II diffractometer. Sealed-tube graphite-monochromated MoKα radiation (λ = 0.71073 Å) was used and the samples kept at 150 K during data collection. Using OLEX2,[1] the structures were solved with the SHELX-S [2] structure solution program and refined with the SHELXL[2] refinement package. All hydrogen atoms were constrained to ideal geometries and refined with fixed isotropic displacement parameters (in terms of a riding model). CCDC (1508492 (**1r**)), contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44(1223)-336-033; e-mail: deposit@ccdc.cam.ac.uk), or *via* www.ccdc.cam.ac.uk/getstructures.

Crystal Data for 1r

Crystal data at 150 K for $C_{17}H_{15}N_3O_3$, M = 309.32 g mol^{-1}, monoclinic, space group Pc, a = 4.7845(14) Å, b = 7.017(2) Å, c = 21.720(6) Å, β = 92.133(4)°, V = 728.7(4) Å^3, Z = 2, D_c = 1.410 g/cm^3, μ(MoKα) = 0.099 mm^{-1}. Clear yellow needles (linear dimensions approx. 0.25 mm x 0.15 mm x 0.15 mm) were grown from slow evaporation of ethanol at 25 °C. Number of measured and unique reflections 4556 and 2409, respectively (R_{int} = 0.0375). Final R_1 = 0.0395, wR_2 = 0.0674 for 2409 independent reflections with $I > 2\sigma(I)$, 213 parameters and 3.752 < 2θ < 51.368° (corresponding R values based on all 4556 reflections are 0.0650 and 0.0754, respectively).

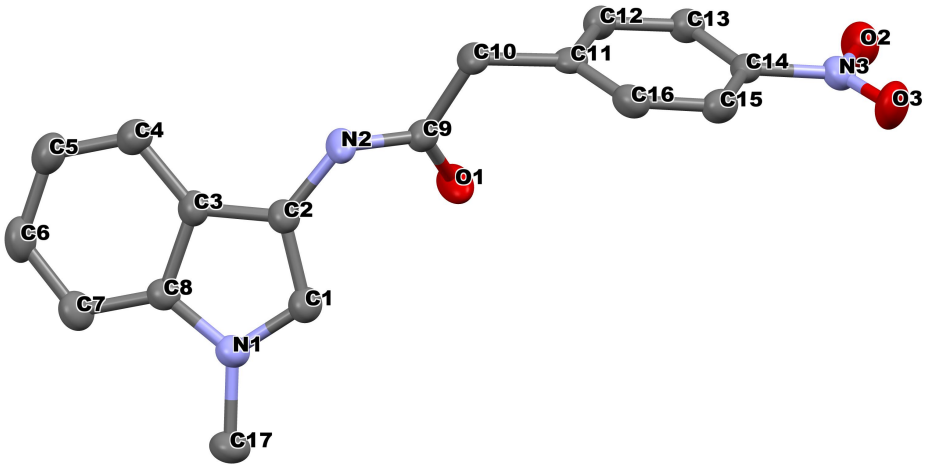


Figure S1. ORTEP plot of **1r**, arbitrary numbering, H-atoms omitted for clarity. Atomic displacement parameters at 100 K are drawn at 50% probability level. Selected bond lengths (Å), angles (°), and torsional angles (°): N1–C1 1.366(4), C1–C2 1.379(5), C2–N2 1.427(5), N2–C9 1.337(5), C2-C9-N2 29.0(2), N2-C9-C10 114.8(3), C2-N2-C9-C10 –176.8(3).

S4. Search Filters, History and Results

The SciFinder search by substructure feature was applied to the structures shown in **Figure S2** on 16th September 2016. All searches applied the single component filter and excluded ring fusion between the amide chain and the indole moiety.

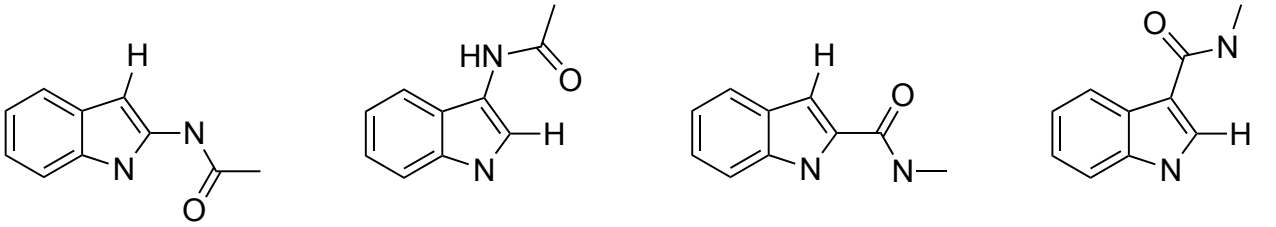


Figure S2. Structures used in the SciFinder search on 16th September 2016.

S5. Spectral Data

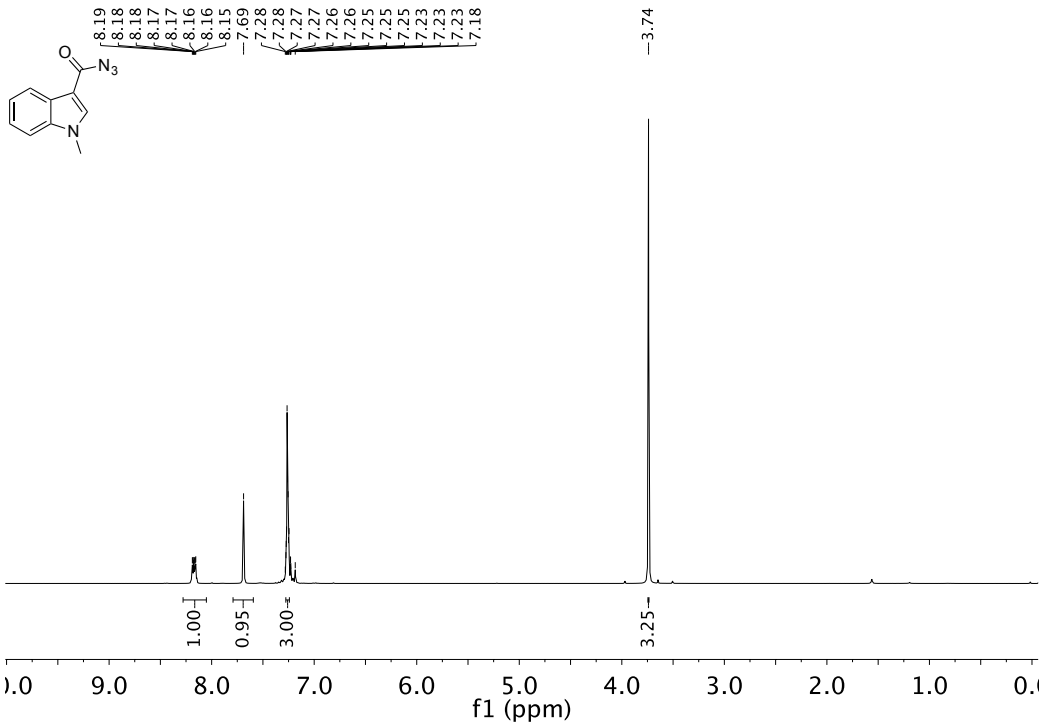


Figure S3. ^{1}H NMR spectrum of compound **6a** in $CDCl_3$ solution (300 MHz).

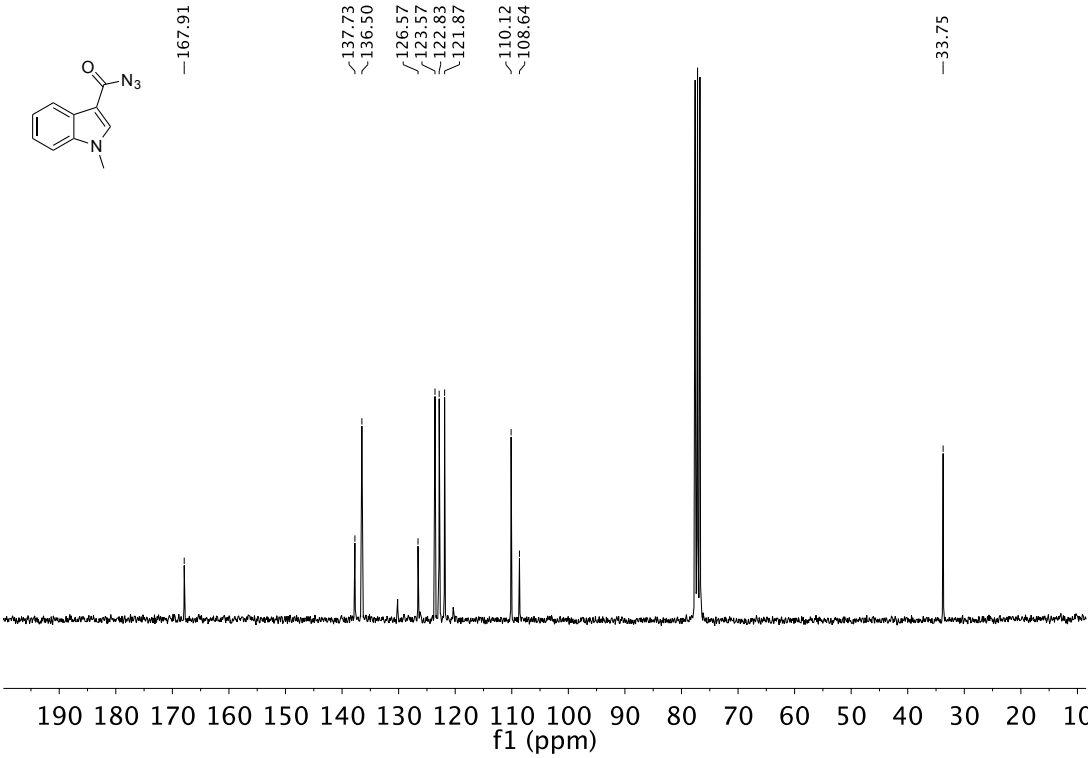


Figure S4. ^{13}C NMR spectrum of compound **6a** in $CDCl_3$ solution (75 MHz).

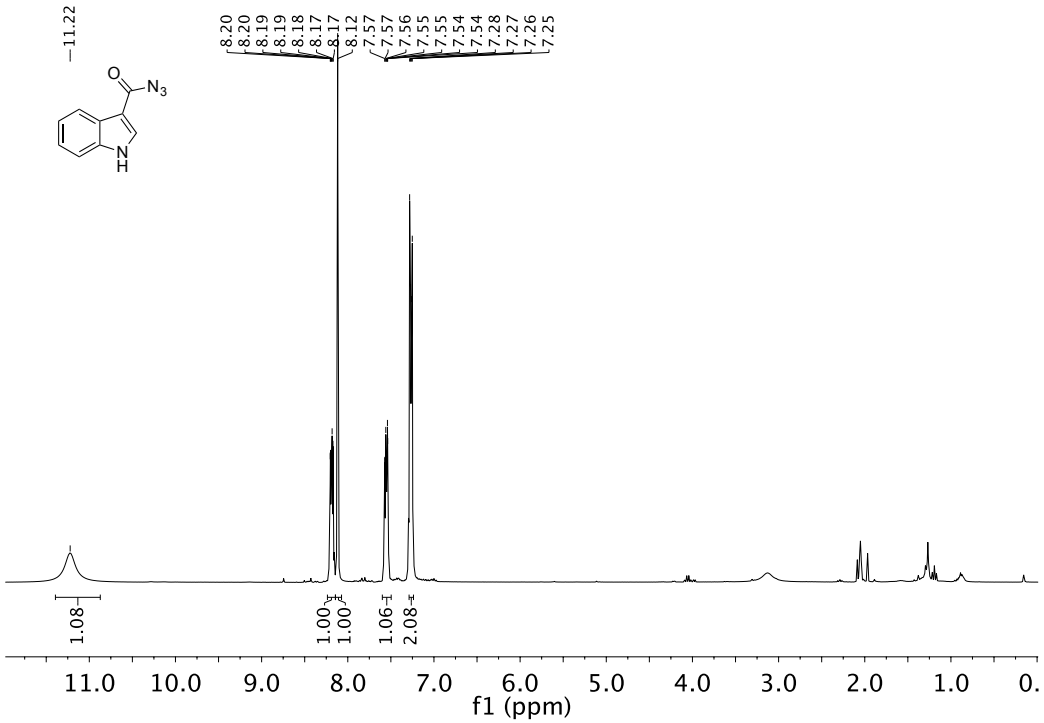


Figure S5. ^{1}H NMR spectrum of compound **6b** in d_6-acetone solution (300 MHz).

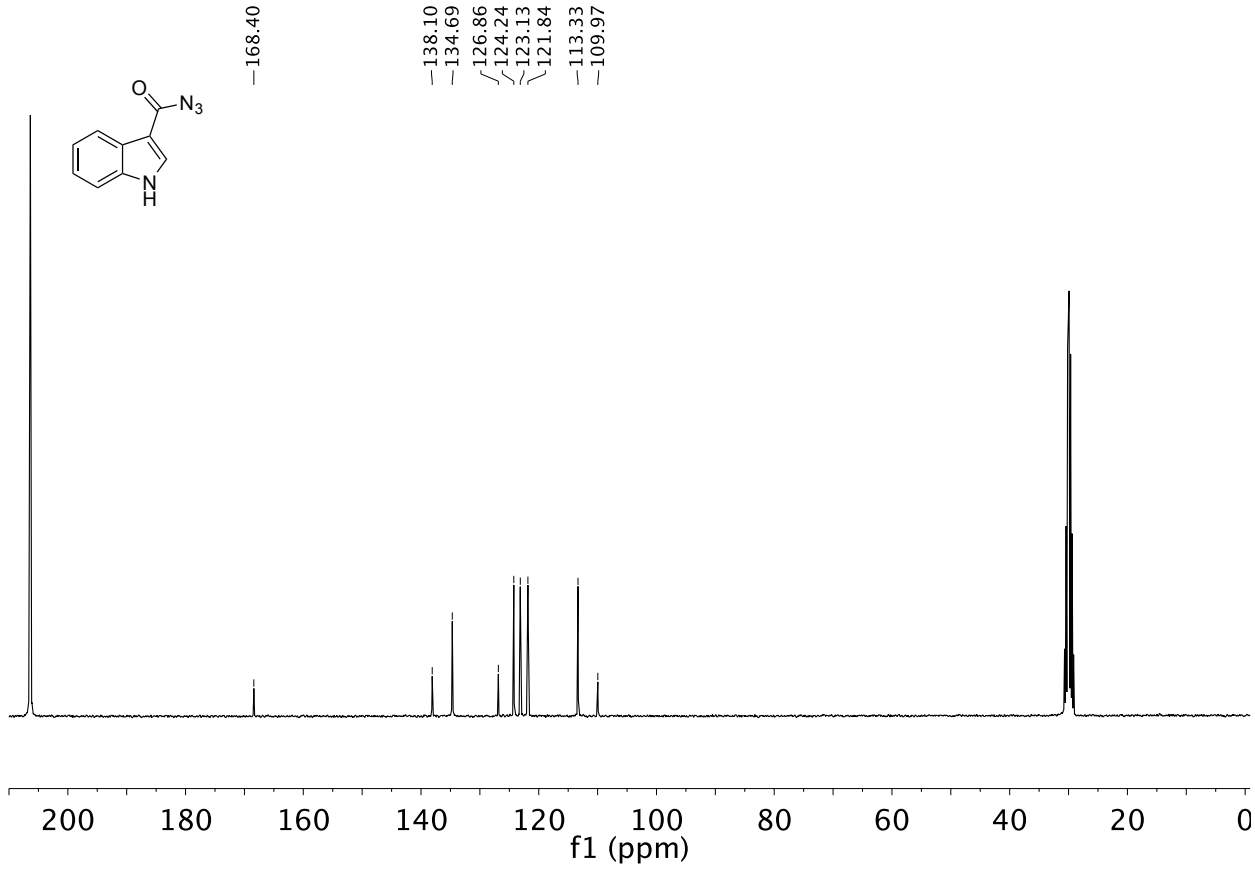


Figure S6. ^{13}C NMR spectrum of compound **6b** in d_6-acetone solution (75 MHz).

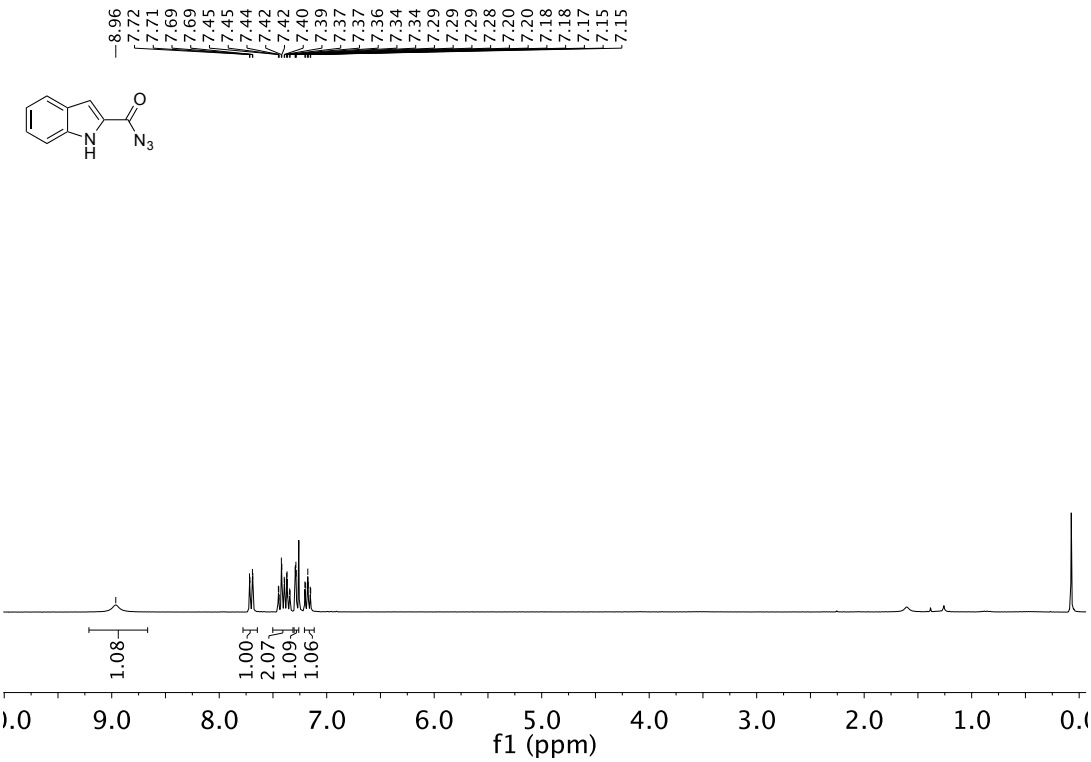


Figure S7. ^{1}H NMR spectrum of compound **13a** in $CDCl_3$ solution (300 MHz).

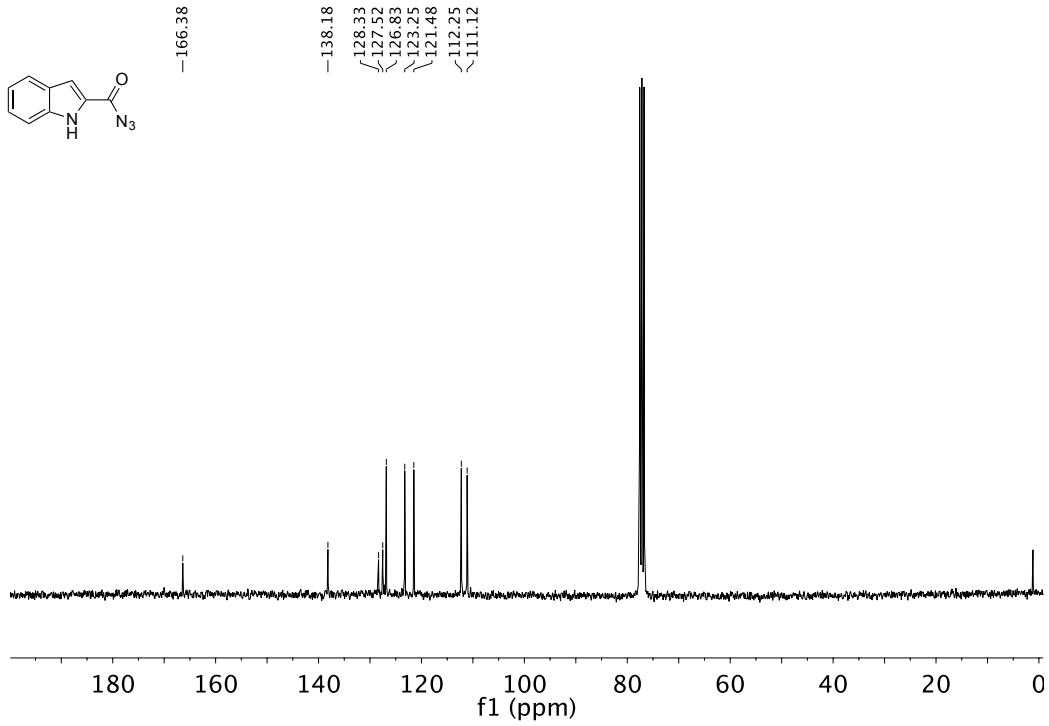


Figure S8. ^{13}C NMR spectrum of compound **13a** in $CDCl_3$ solution (75 MHz).

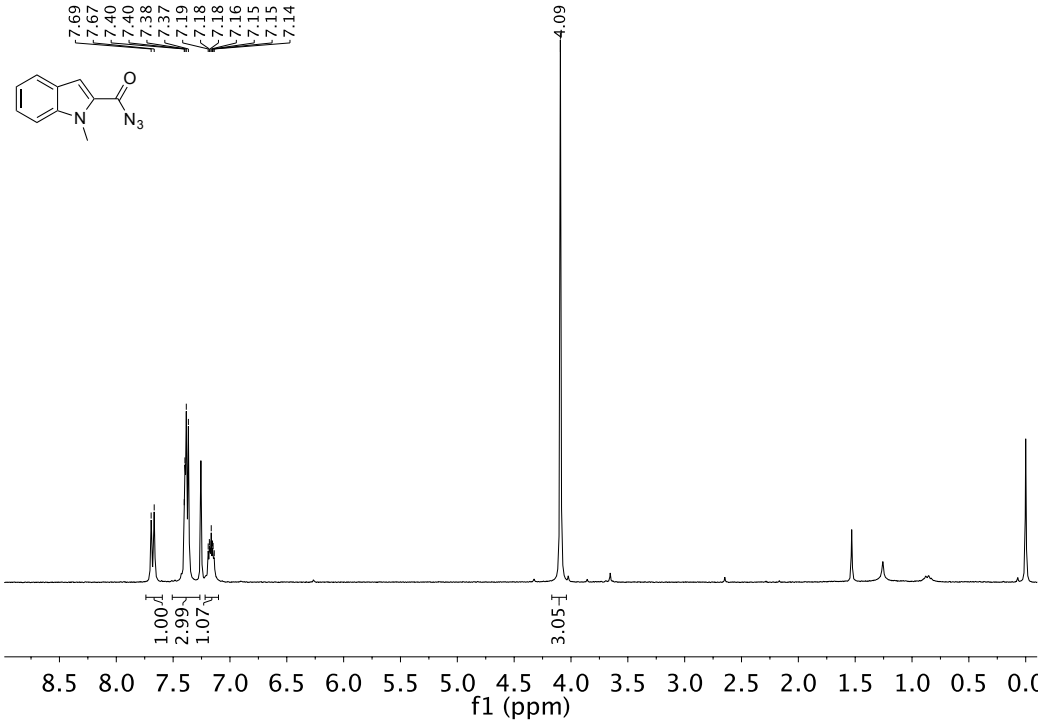


Figure S9. ^{1}H NMR spectrum of compound **13b** in $CDCl_3$ solution (300 MHz).

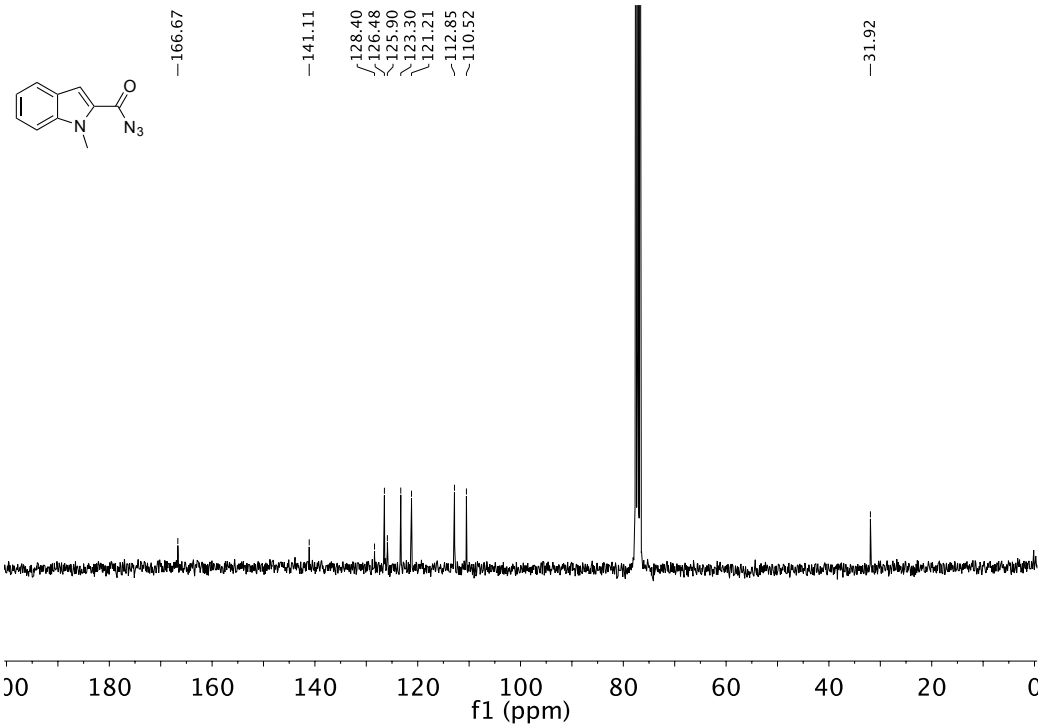


Figure S10. ^{13}C NMR spectrum of compound **13b** in $CDCl_3$ solution (75 MHz).

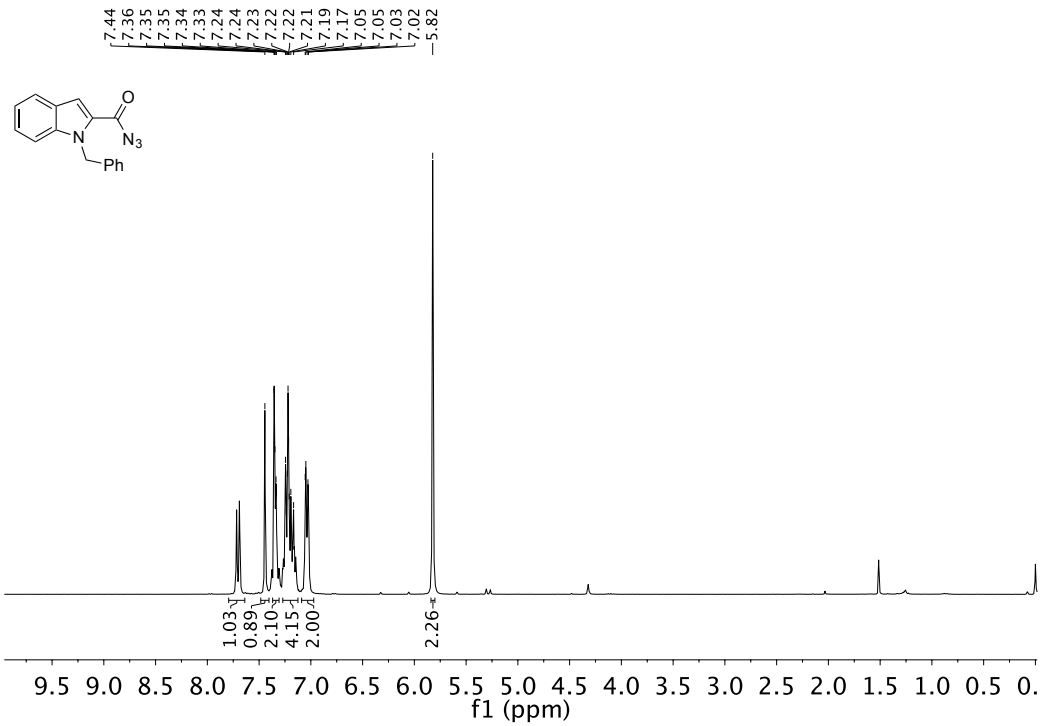


Figure S11. ^{1}H NMR spectrum of compound **13c** in $CDCl_3$ solution (300 MHz).

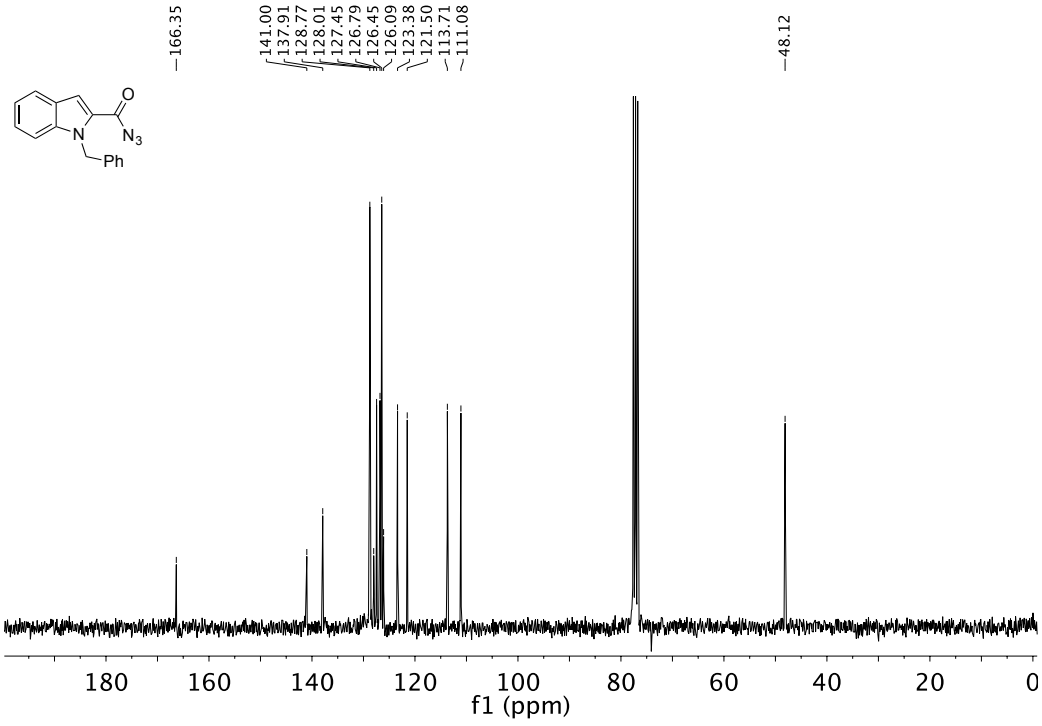


Figure S12. ^{13}C NMR spectrum of compound **13c** in $CDCl_3$ solution (75 MHz).

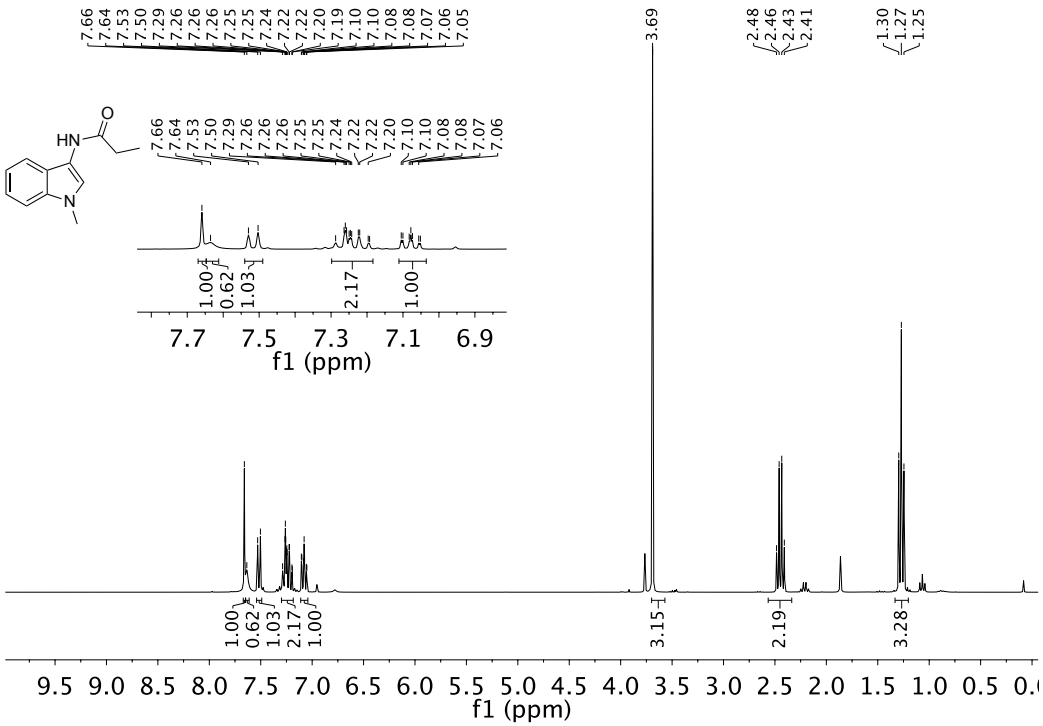


Figure S13. ^{1}H NMR spectrum of compound **1a** in $CDCl_3$ solution (300 MHz).

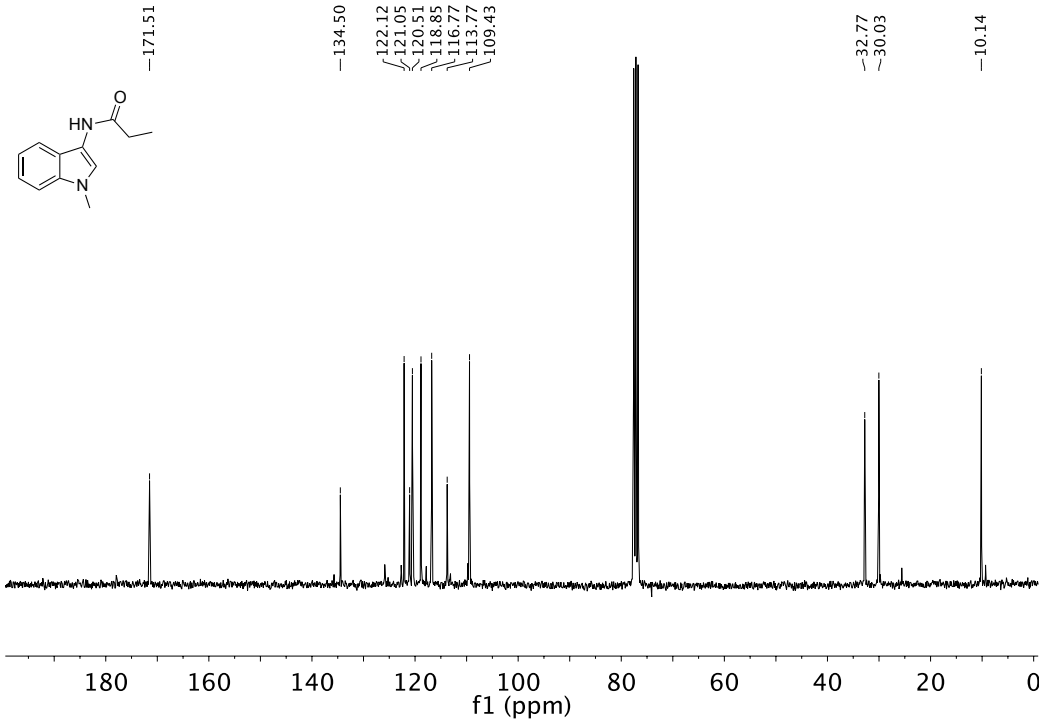


Figure S14. ^{13}C NMR spectrum of compound **1a** in $CDCl_3$ solution (75 MHz).

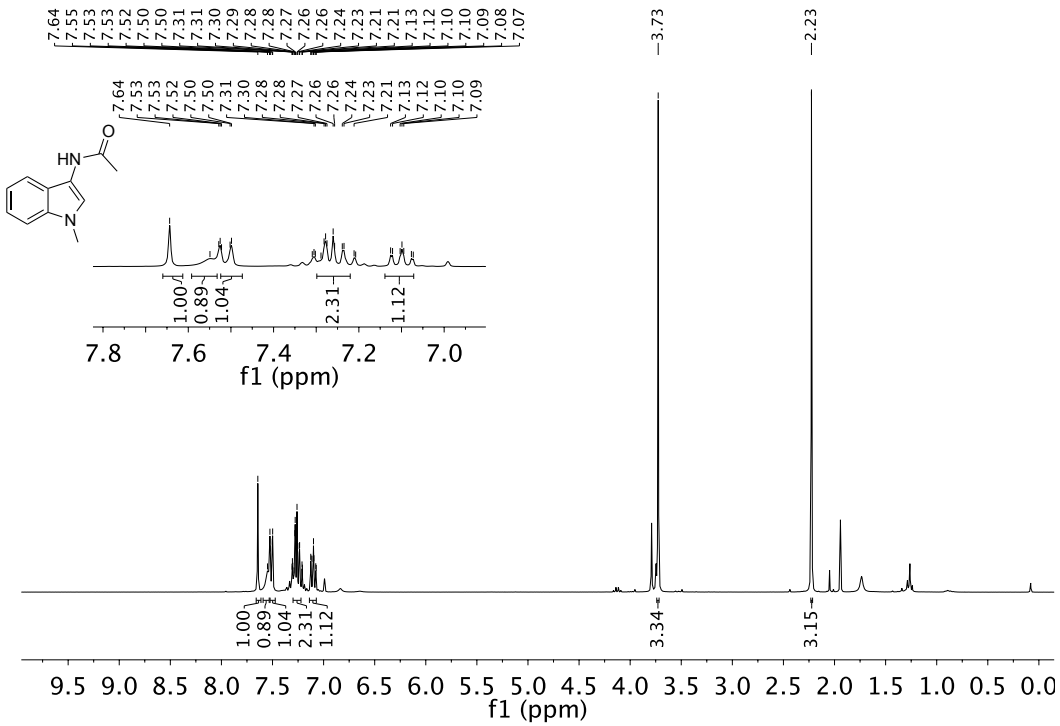


Figure S15. ^{1}H NMR spectrum of compound **1b** in $CDCl_3$ solution (300 MHz).

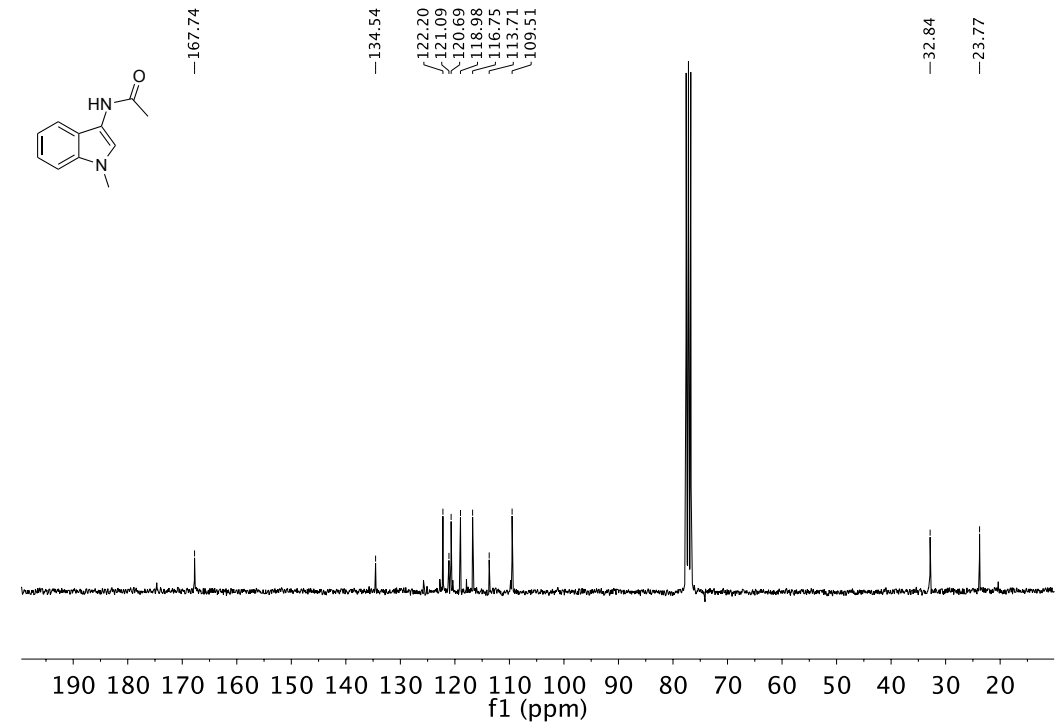


Figure S16. ^{13}C NMR spectrum of compound **1b** in $CDCl_3$ solution (75 MHz).

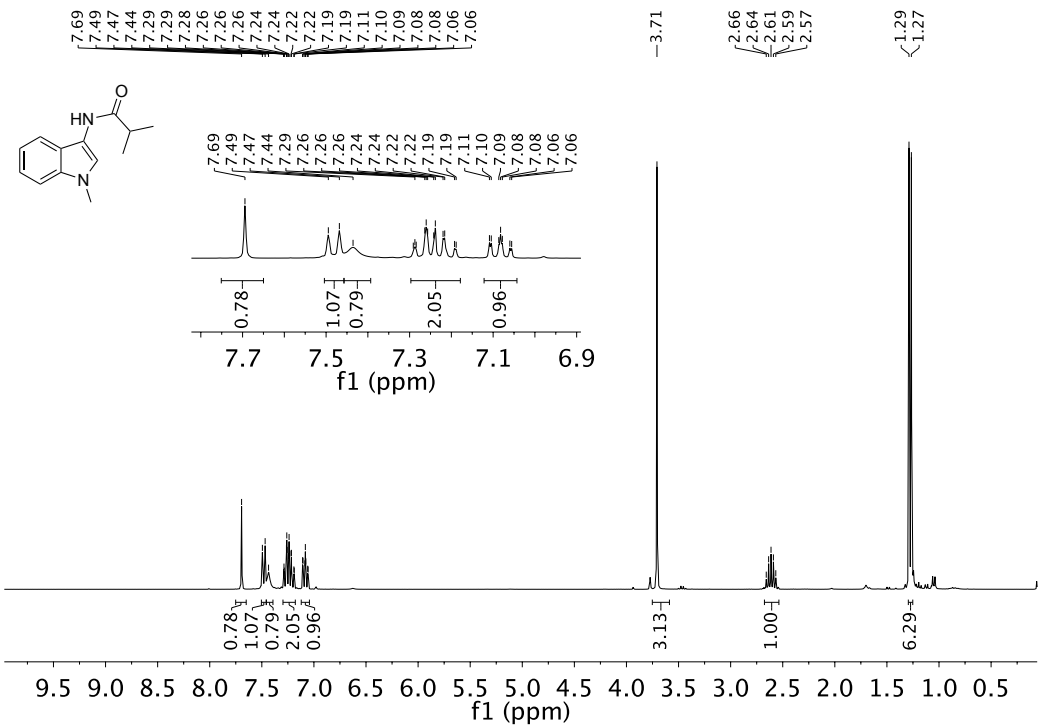


Figure S17. ^{1}H NMR spectrum of compound **1c** in $CDCl_3$ solution (300 MHz).

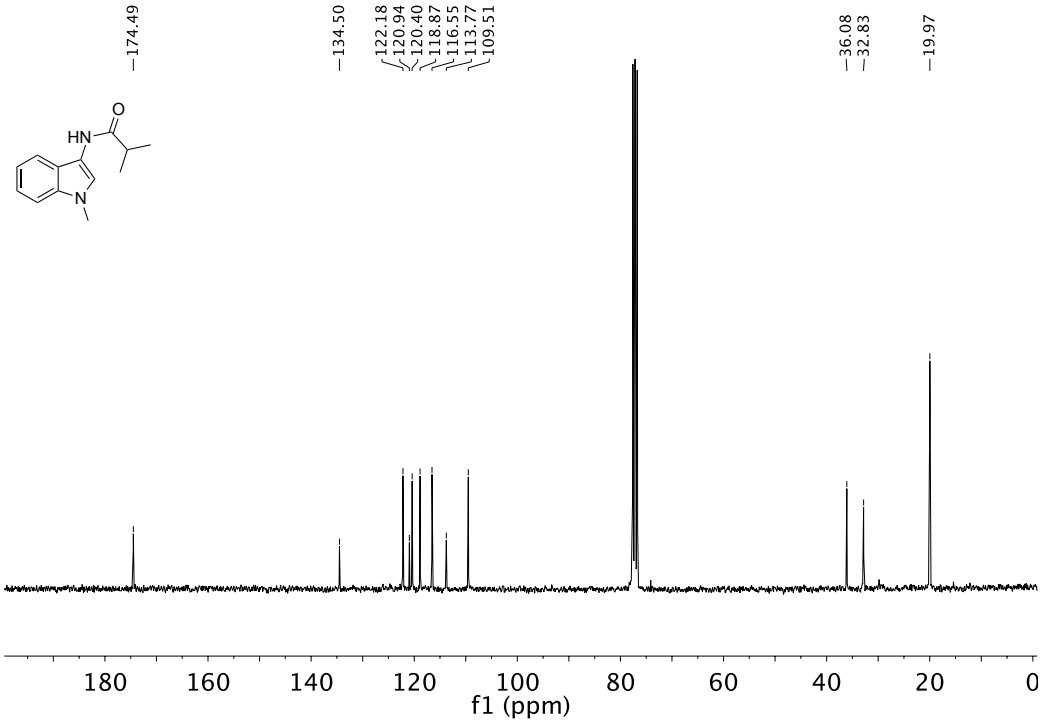


Figure S18. ^{13}C NMR spectrum of compound **1c** in $CDCl_3$ solution (75 MHz).

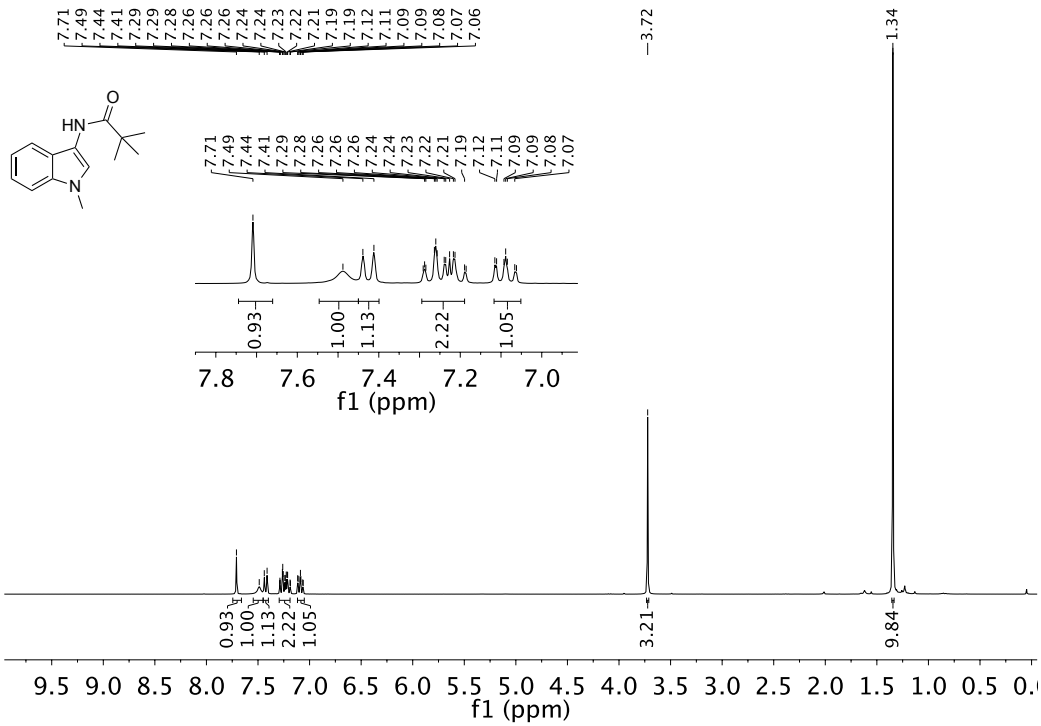


Figure S19. ^{1}H NMR spectrum of compound **1d** in $CDCl_3$ solution (300 MHz).

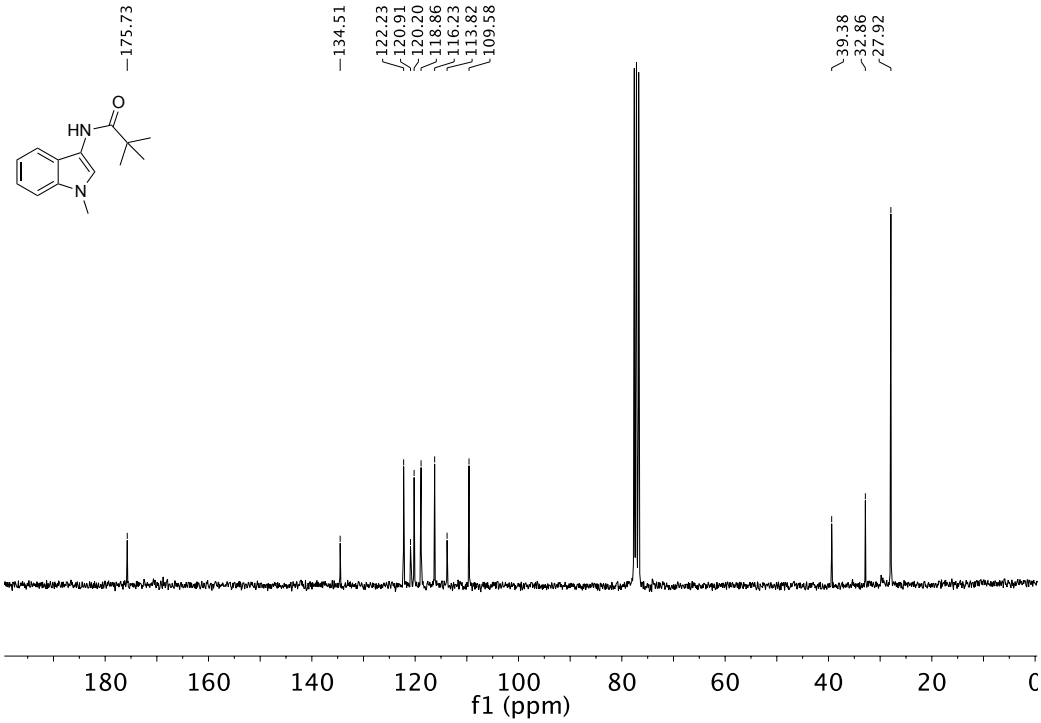


Figure S20. ^{13}C NMR spectrum of compound **1d** in $CDCl_3$ solution (75 MHz).

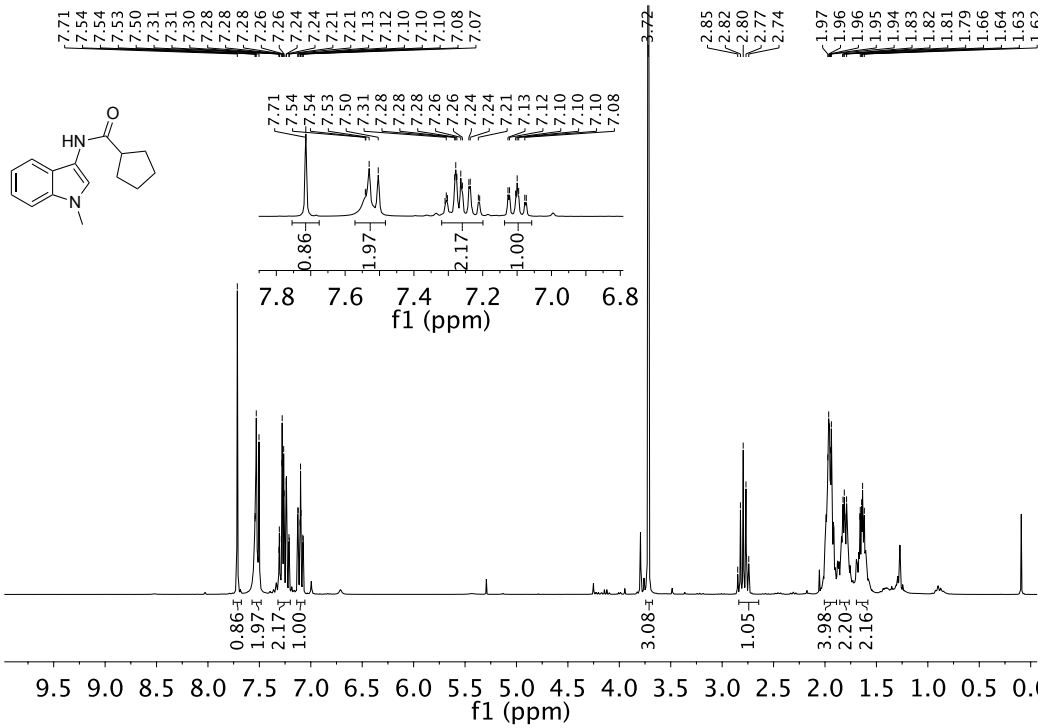


Figure S21. ^{1}H NMR spectrum of compound **1e** in $CDCl_3$ solution (300 MHz).

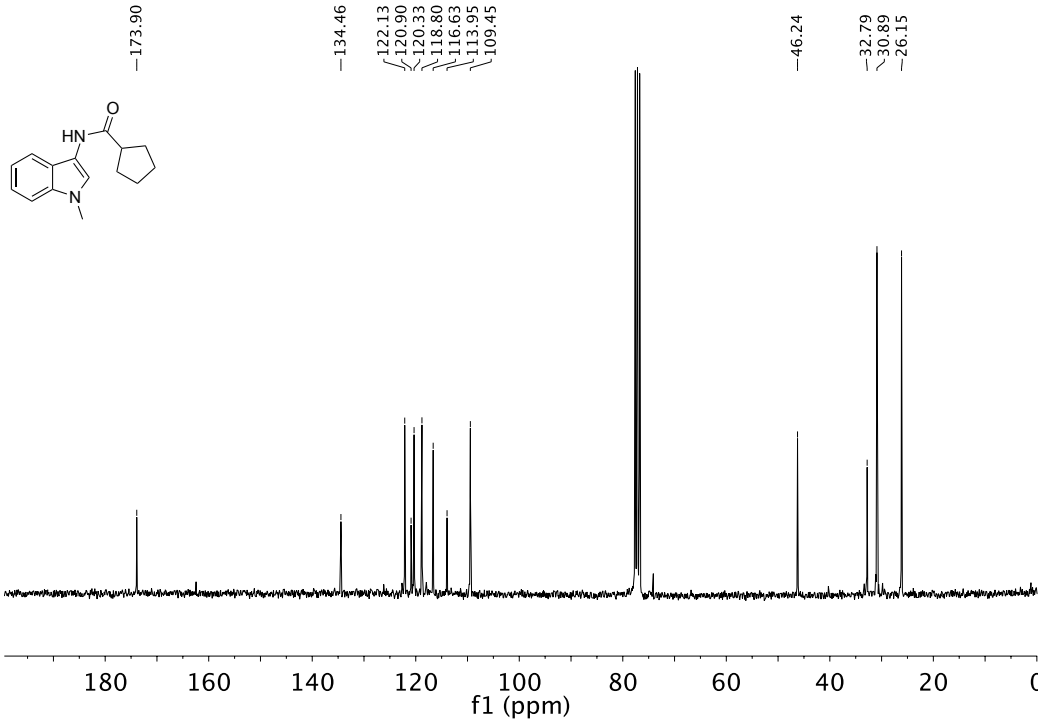


Figure S22. ^{13}C NMR spectrum of compound **1e** in $CDCl_3$ solution (75 MHz).

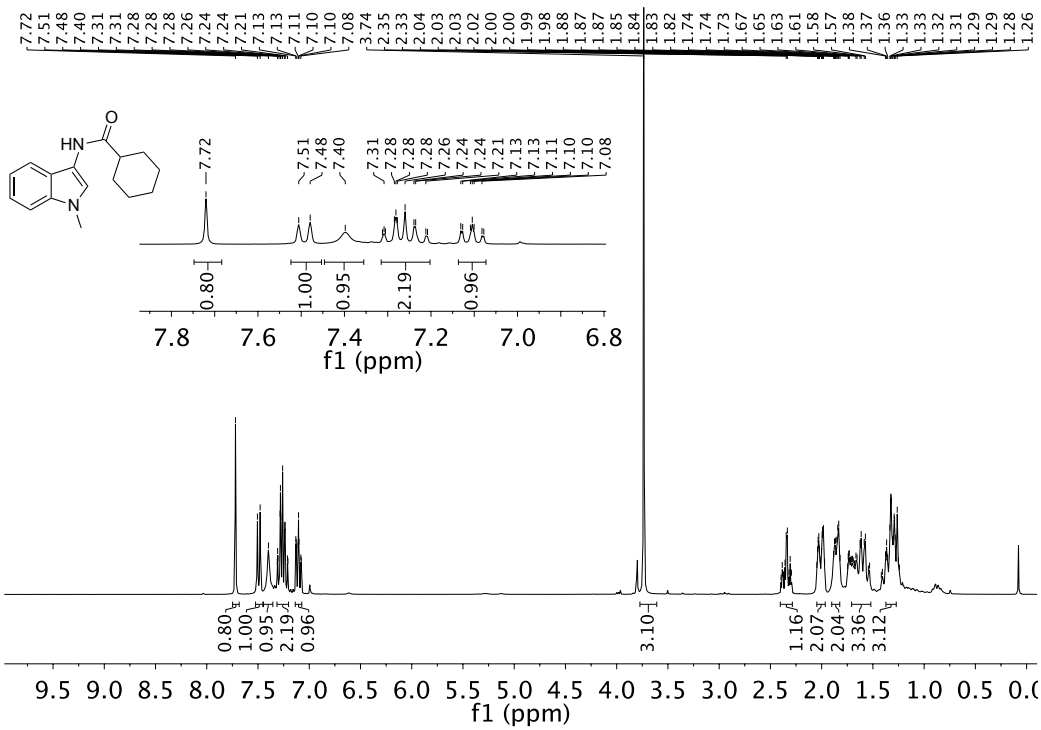


Figure S23. ^{1}H NMR spectrum of compound **1f** in $CDCl_3$ solution (300 MHz).

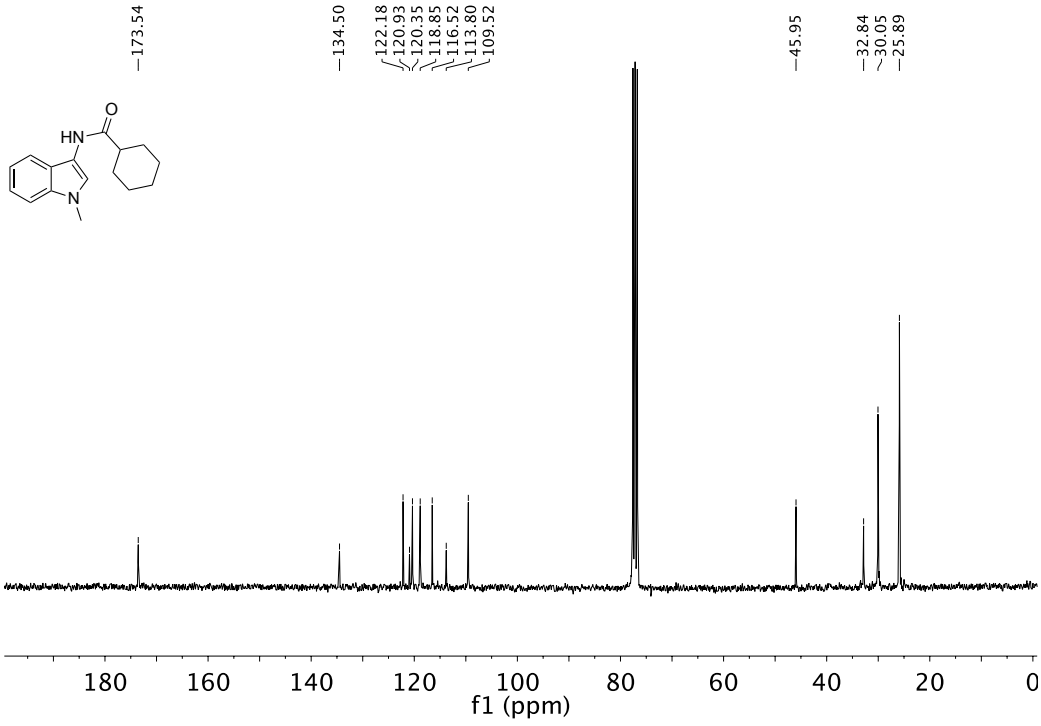


Figure S24. ^{13}C NMR spectrum of compound **1f** in $CDCl_3$ solution (75 MHz).

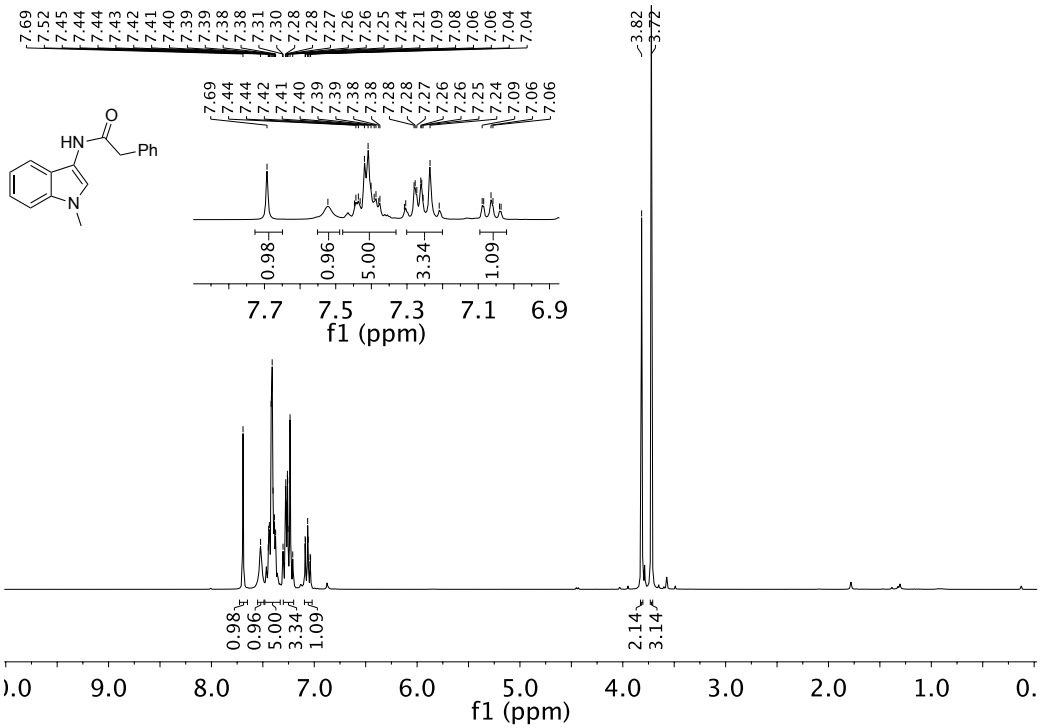


Figure S25. ^{1}H NMR spectrum of compound **1g** in $CDCl_3$ solution (300 MHz).

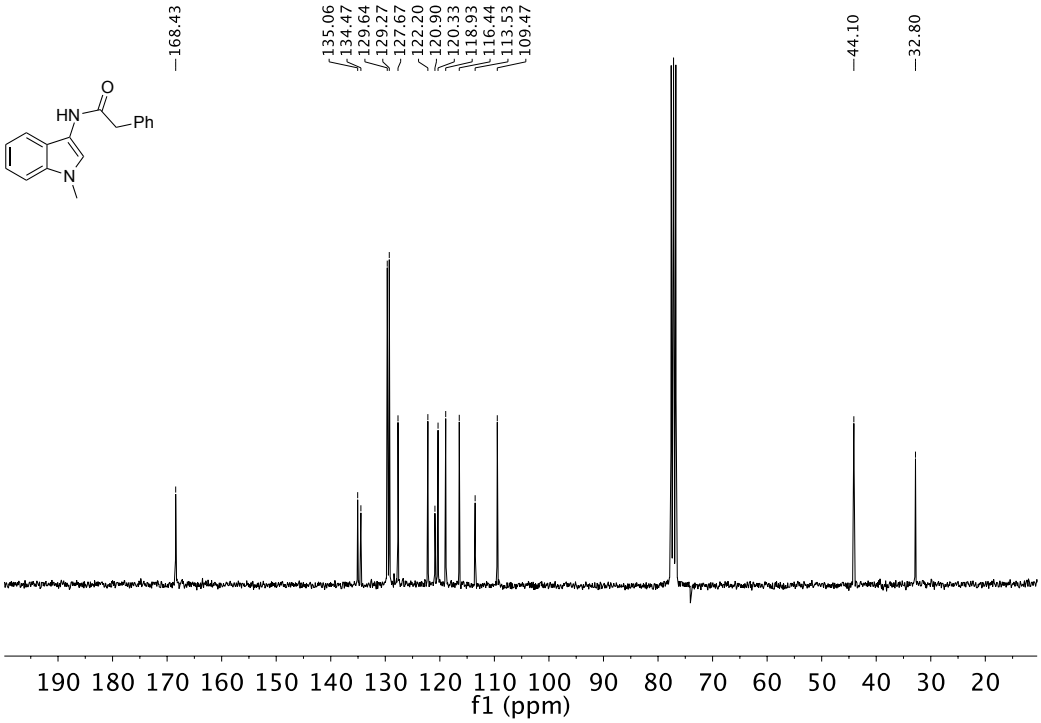


Figure S26. ^{13}C NMR spectrum of compound **1g** in $CDCl_3$ solution (75 MHz).

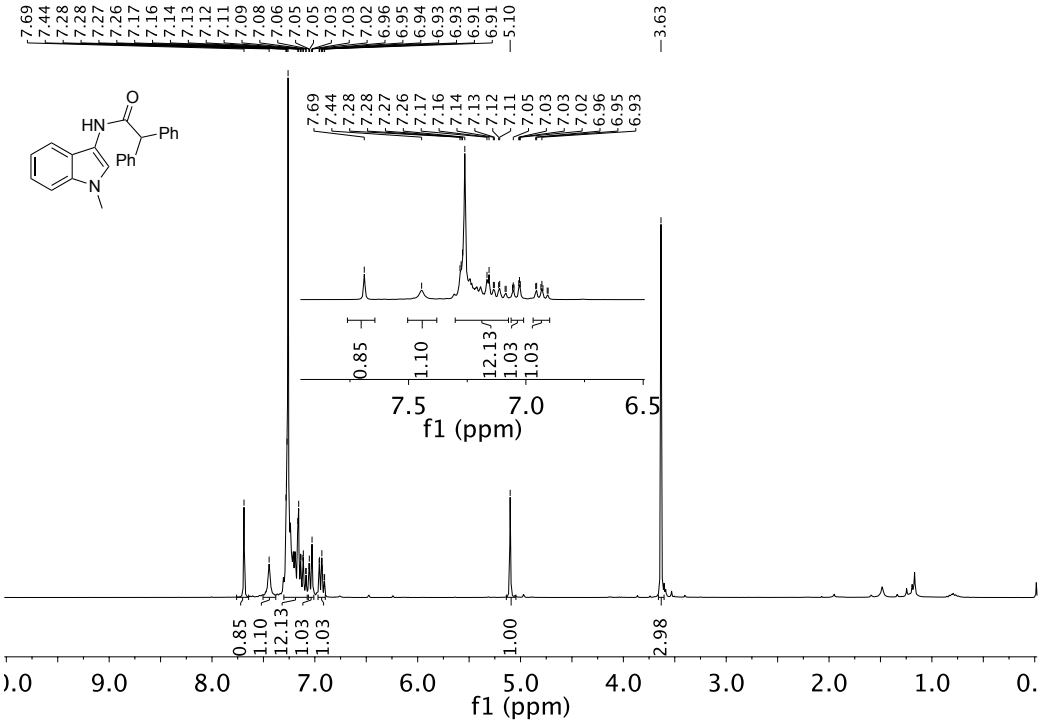


Figure S27. ^{1}H NMR spectrum of compound **1h** in $CDCl_3$ solution (300 MHz).

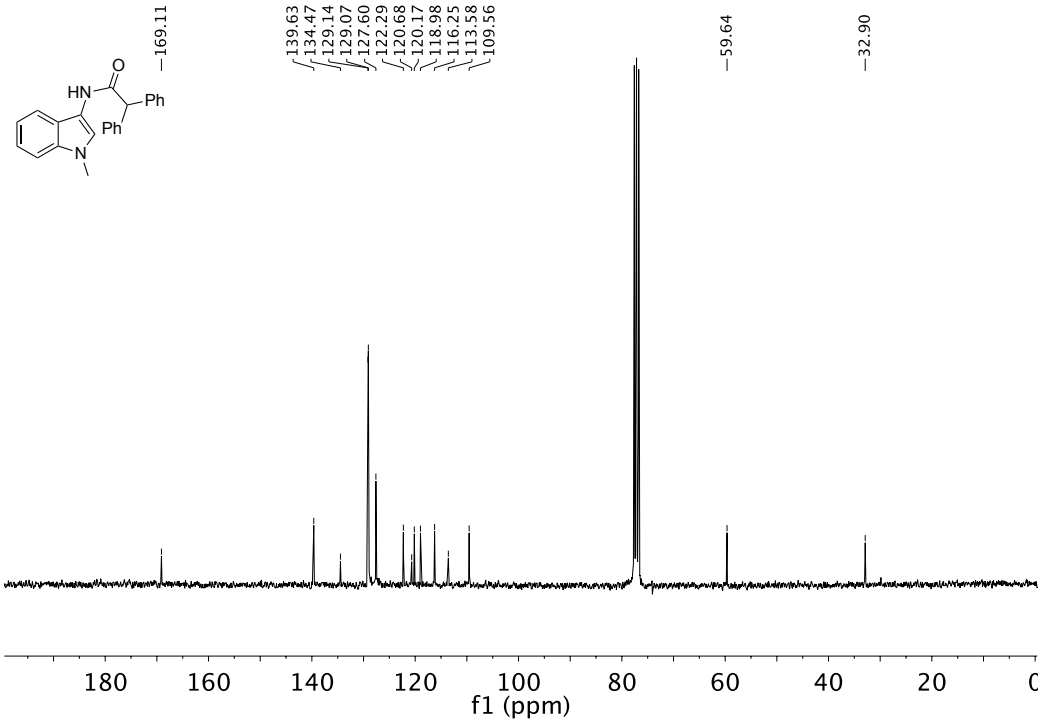


Figure S28. ^{13}C NMR spectrum of compound **1h** in $CDCl_3$ solution (75 MHz).

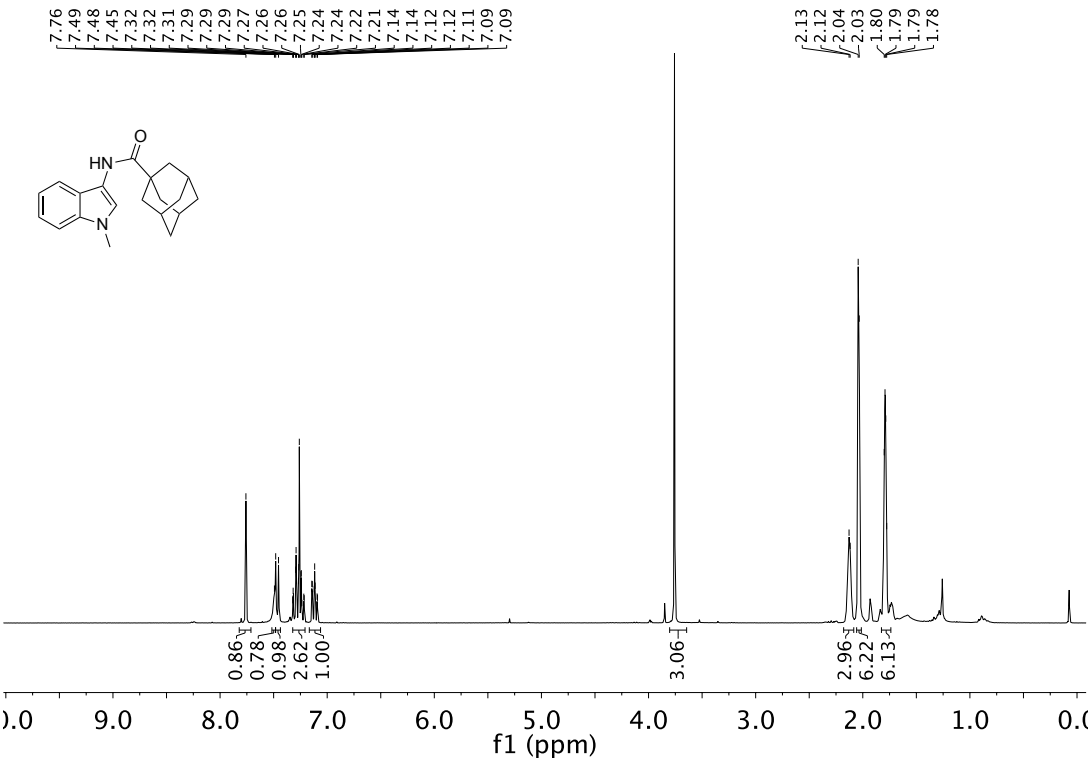


Figure S29. ^{1}H NMR spectrum of compound **1i** in $CDCl_3$ solution (300 MHz).

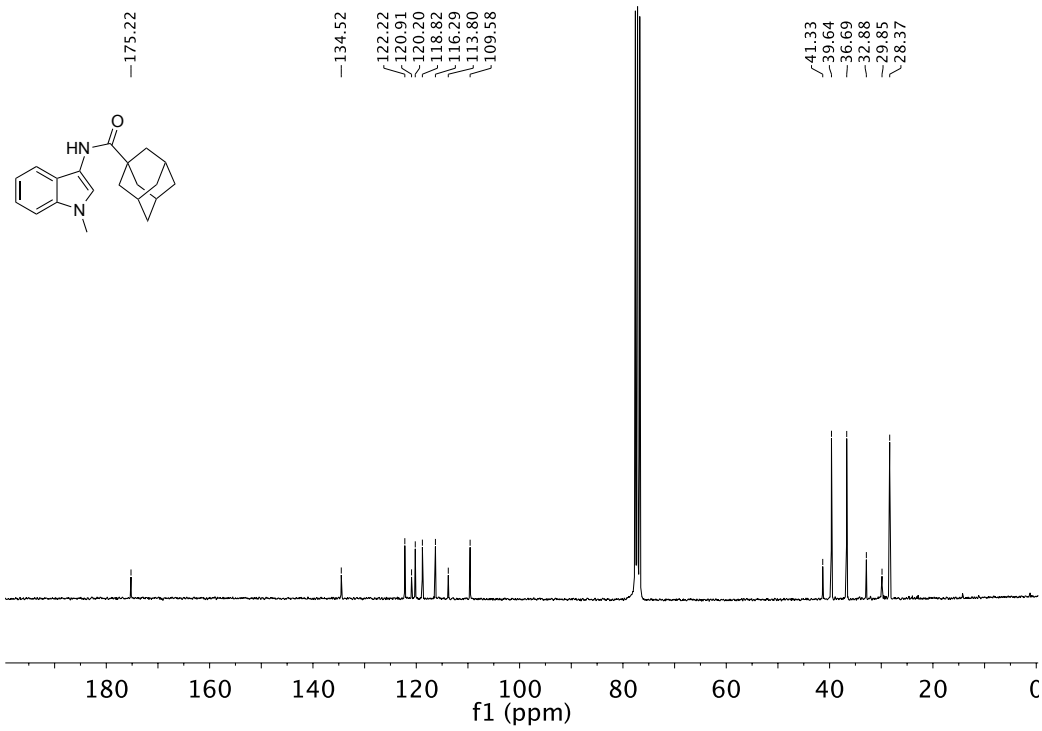


Figure S30. ^{13}C NMR spectrum of compound **1i** in $CDCl_3$ solution (75 MHz).

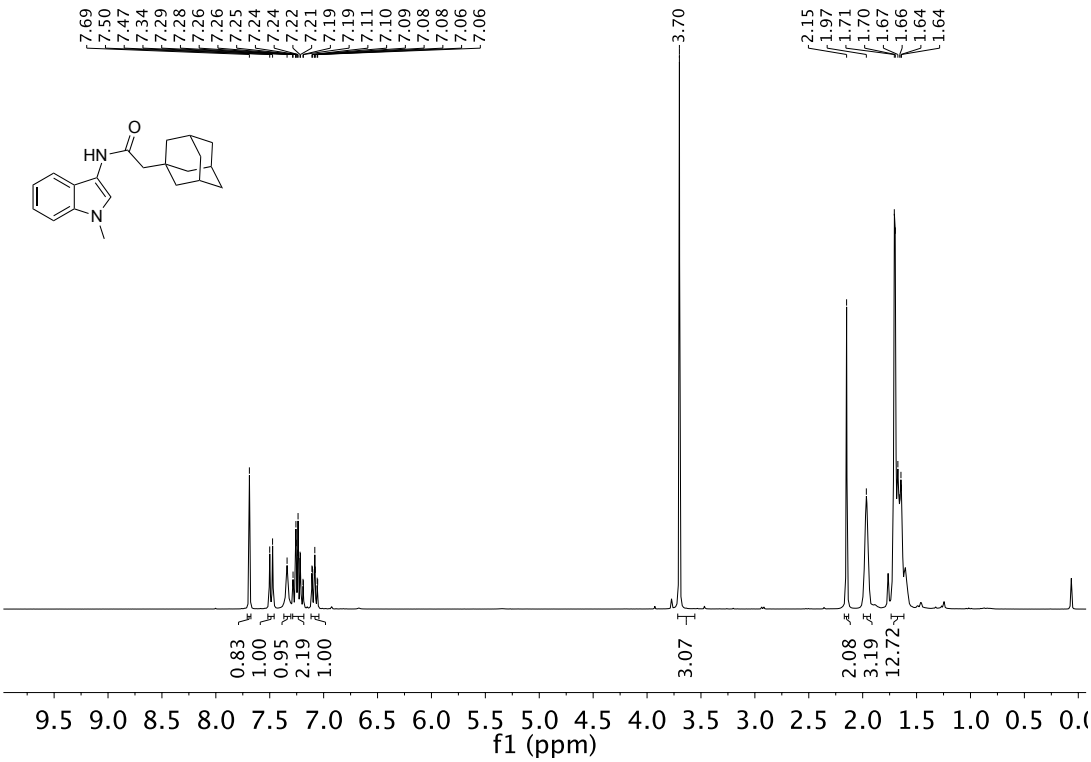


Figure S31. ^{1}H NMR spectrum of compound **1j** in $CDCl_3$ solution (300 MHz).

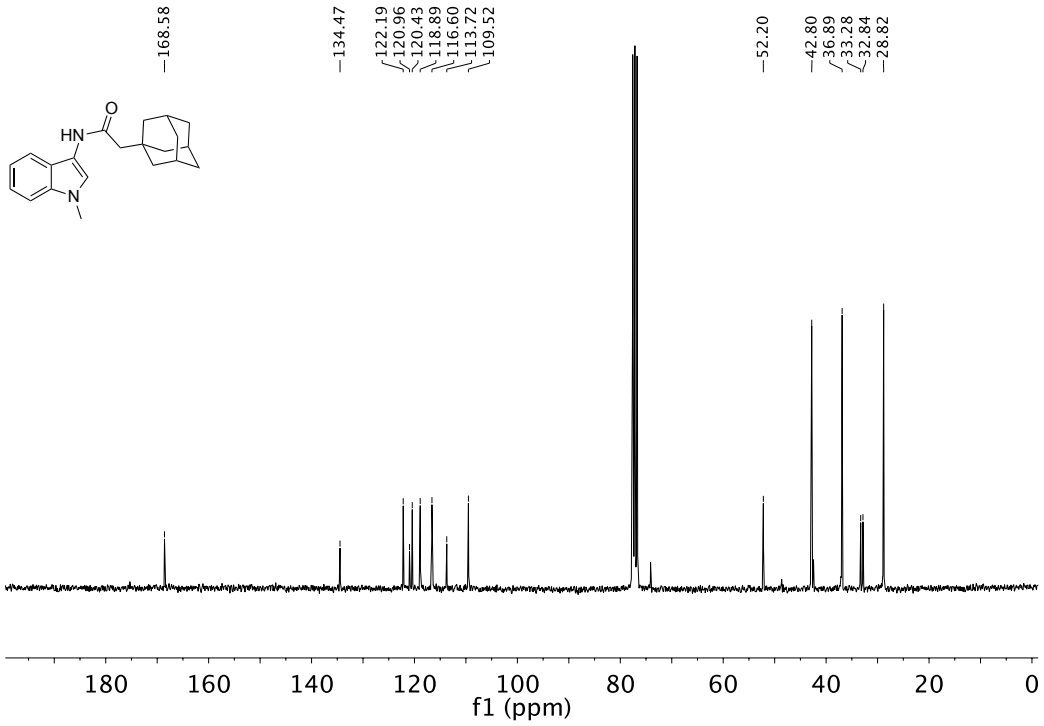


Figure S32. ^{13}C NMR spectrum of compound **1j** in $CDCl_3$ solution (75 MHz).

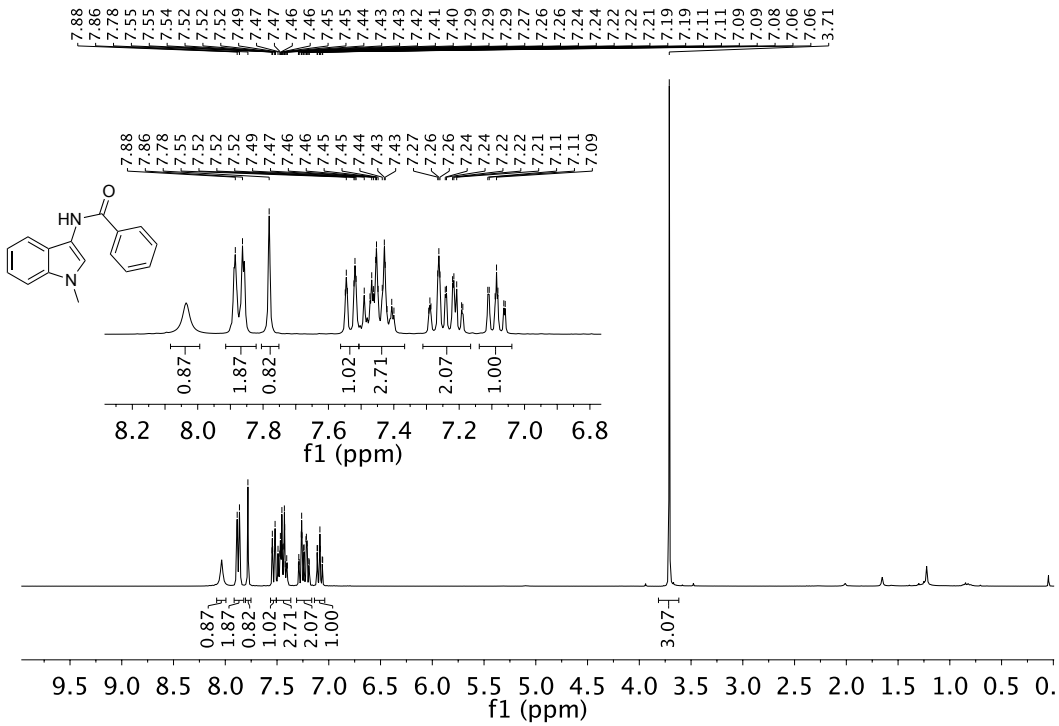


Figure S33. ^{1}H NMR spectrum of compound **1k** in $CDCl_3$ solution (300 MHz).

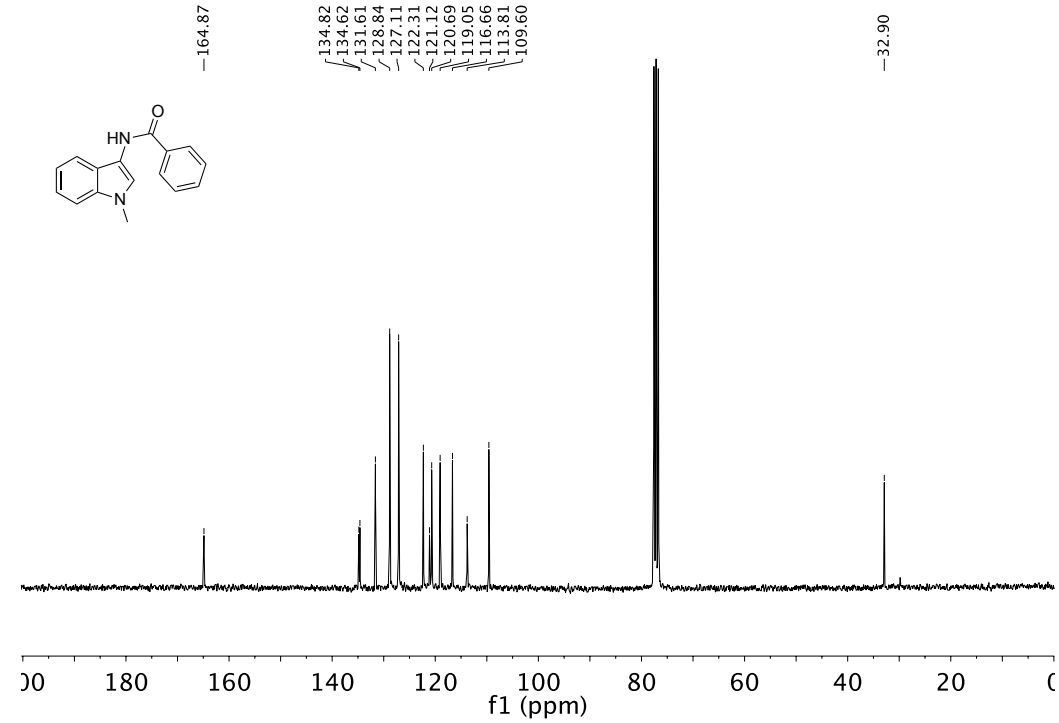


Figure S34. ^{13}C NMR spectrum of compound **1k** in $CDCl_3$ solution (75 MHz).

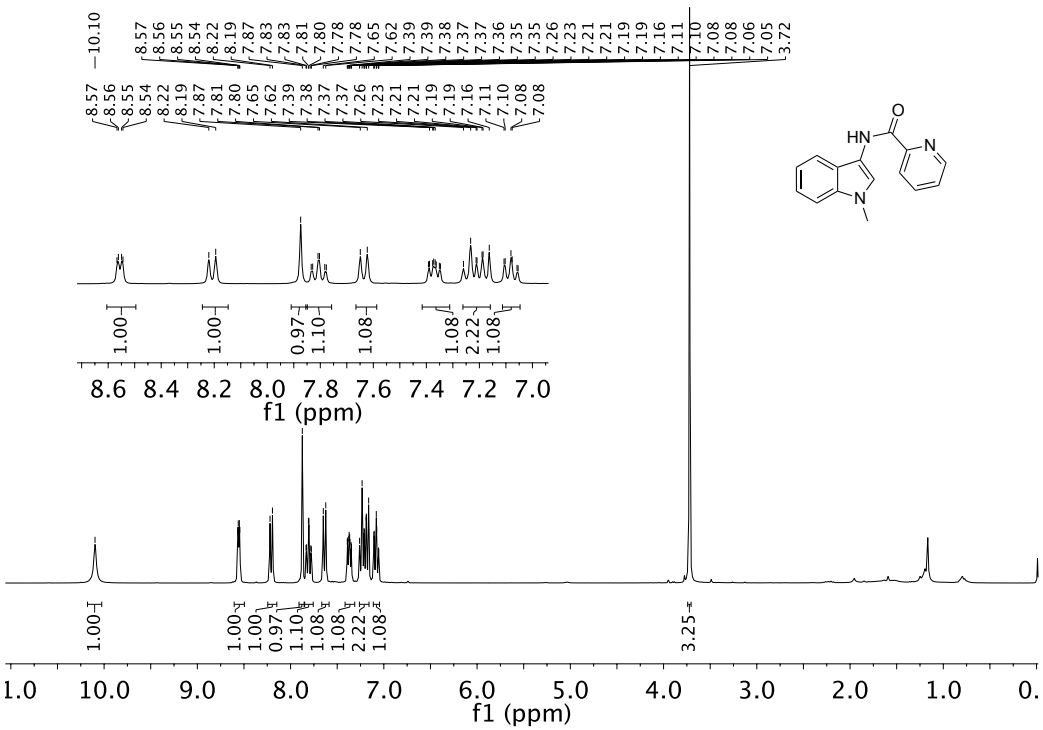


Figure S35. ^{1}H NMR spectrum of compound **1l** in $CDCl_3$ solution (300 MHz).

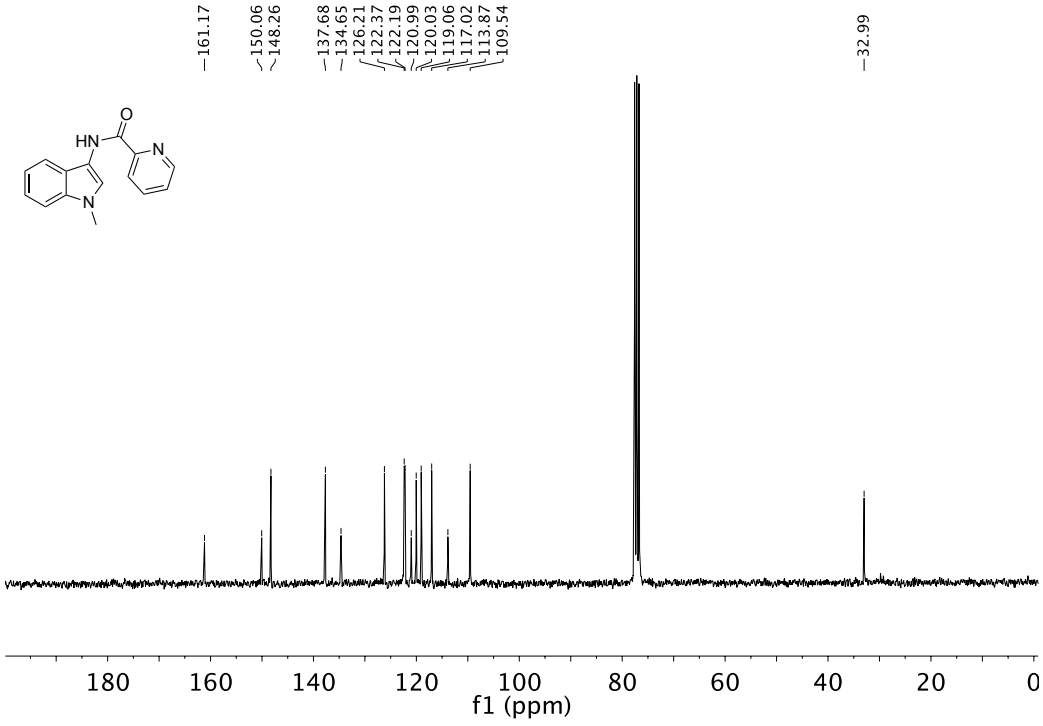


Figure S36. ^{13}C NMR spectrum of compound **1l** in $CDCl_3$ solution (75 MHz).

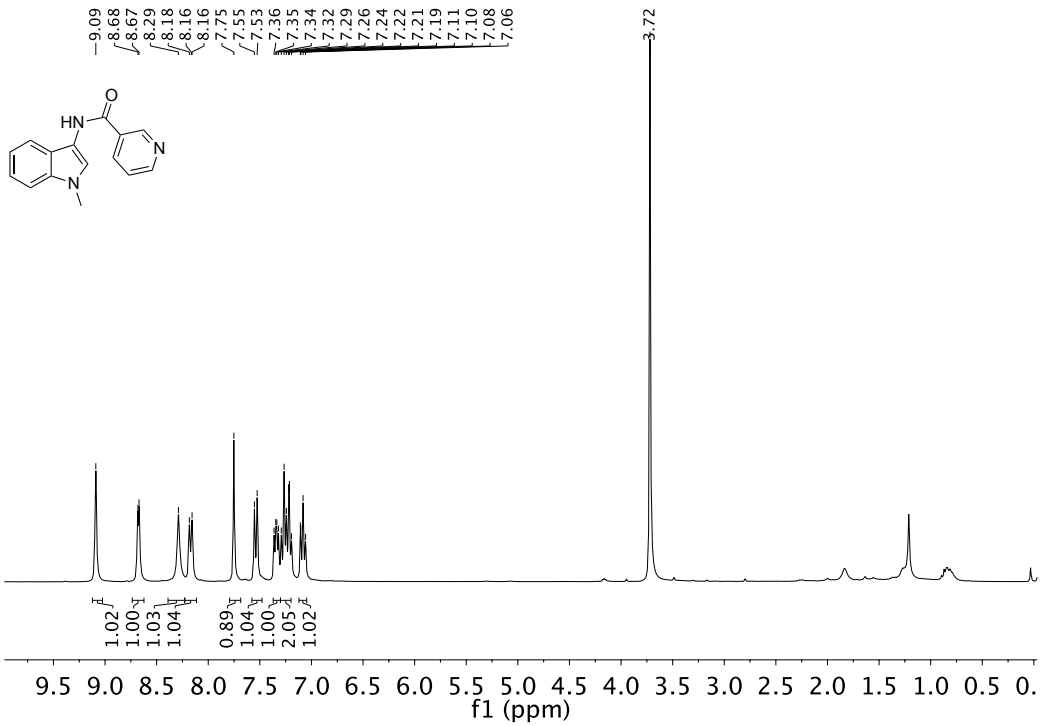


Figure S37. ^{1}H NMR spectrum of compound **1m** in $CDCl_3$ solution (300 MHz).

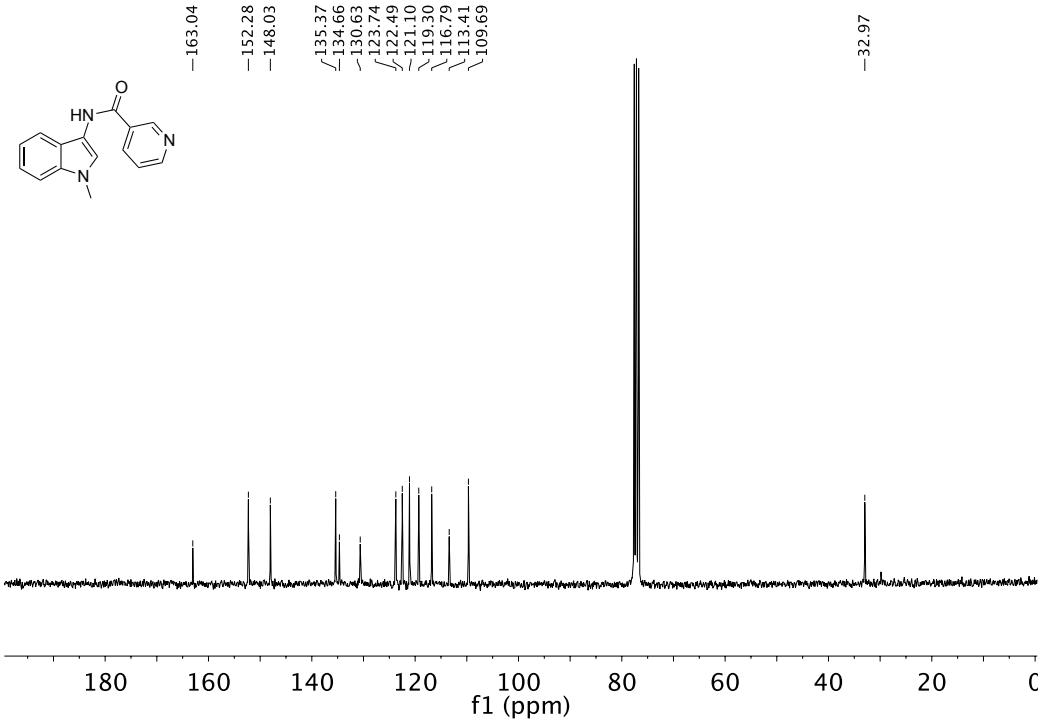


Figure S38. ^{13}C NMR spectrum of compound **1m** in $CDCl_3$ solution (75 MHz).

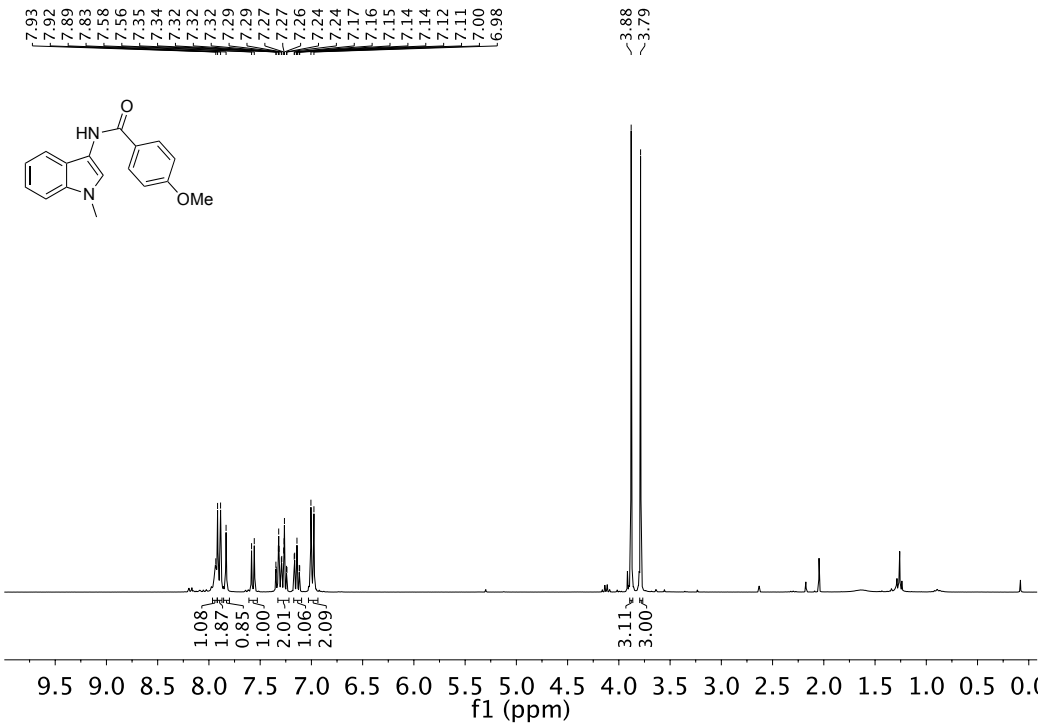


Figure S39. ^{1}H NMR spectrum of compound **1o** in $CDCl_3$ solution (300 MHz).

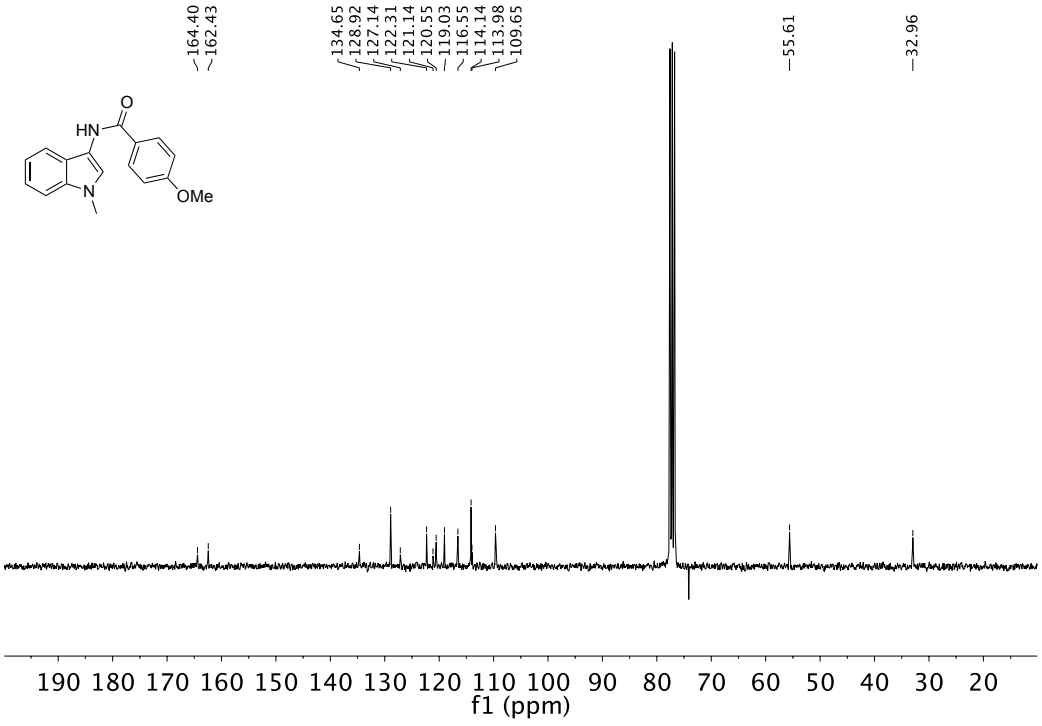


Figure S40. ^{13}C NMR spectrum of compound **1o** in $CDCl_3$ solution (75 MHz).

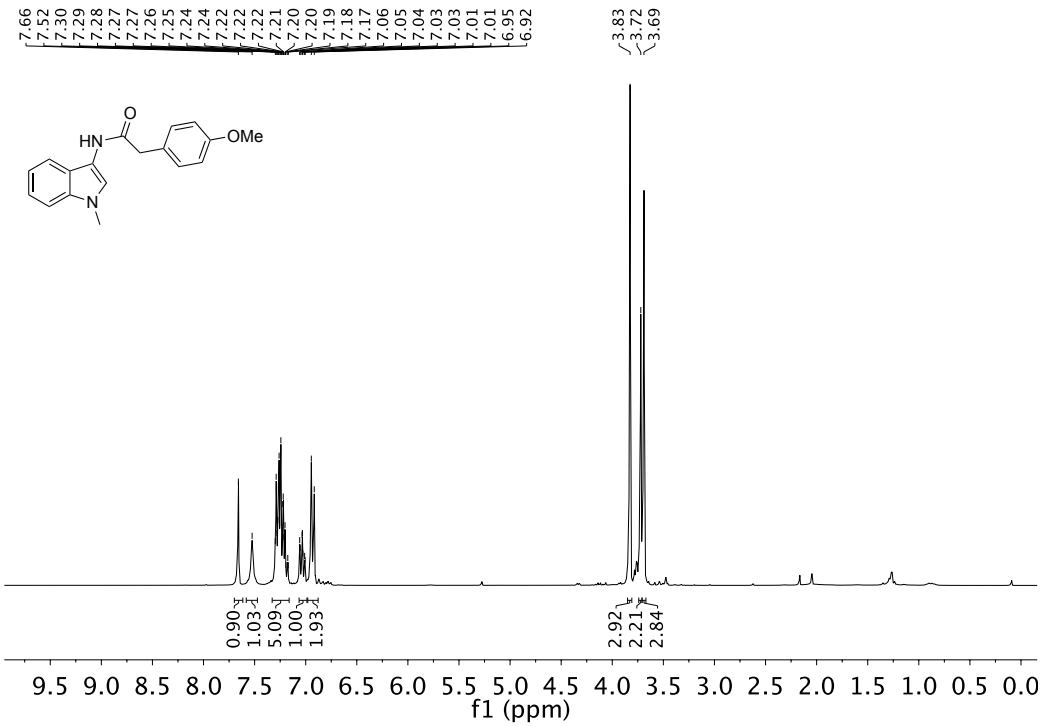


Figure S41. ^{1}H NMR spectrum of compound **1p** in $CDCl_3$ solution (300 MHz).

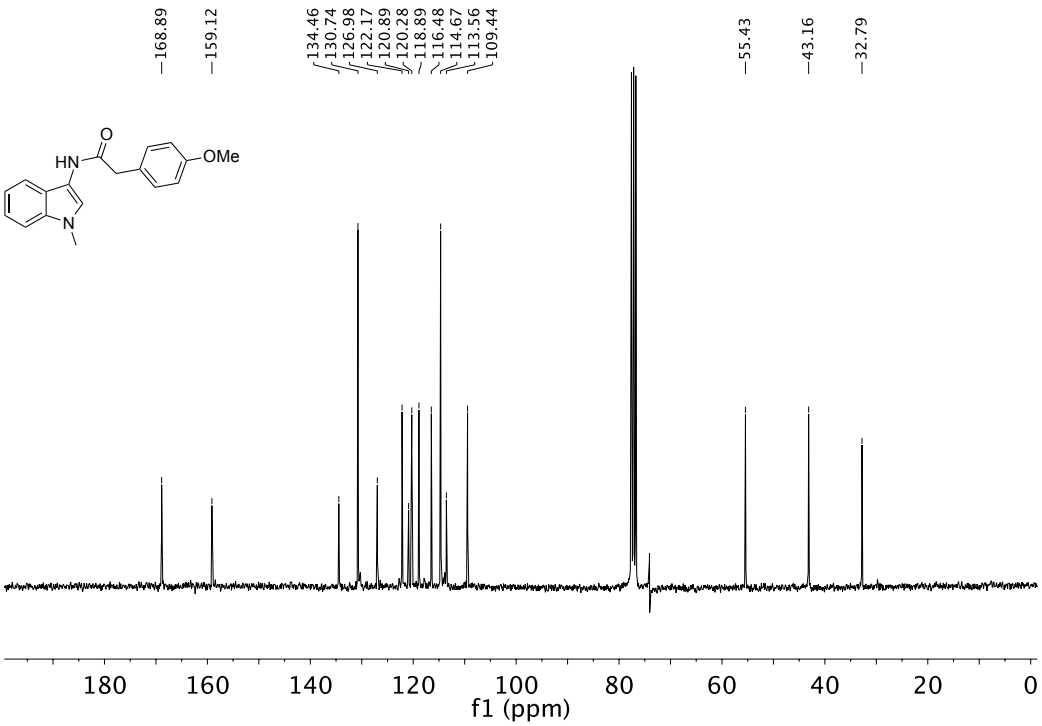


Figure S42. ^{13}C NMR spectrum of compound **1p** in $CDCl_3$ solution (75 MHz).

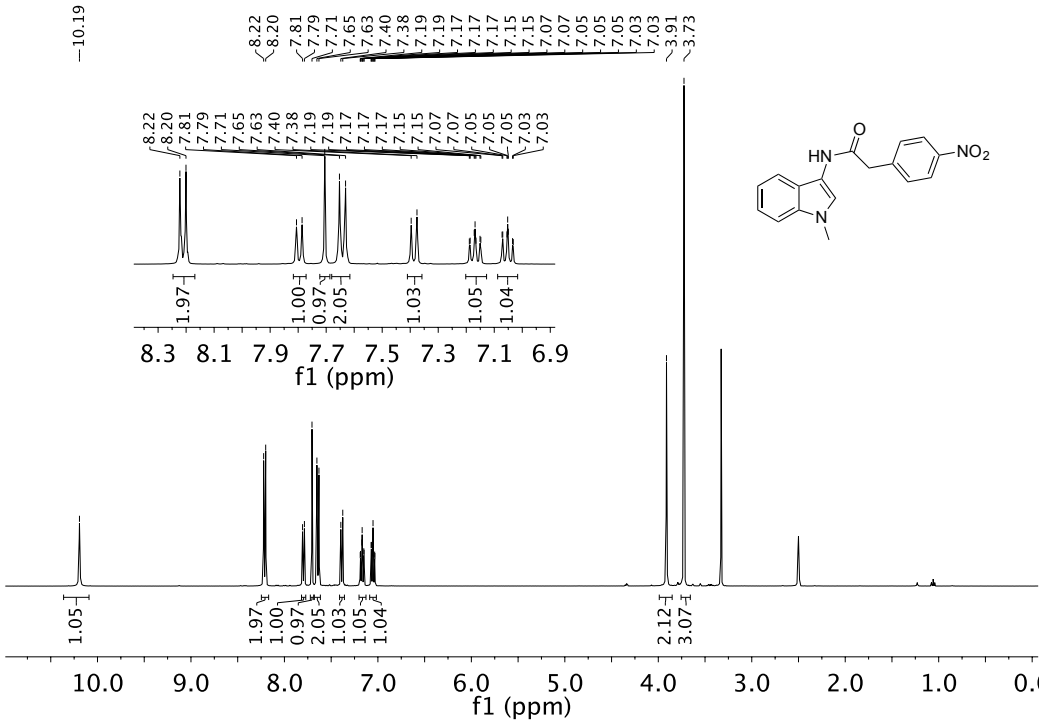


Figure S43. ^{1}H NMR spectrum of compound **1r** in d_6-DMSO solution (400 MHz).

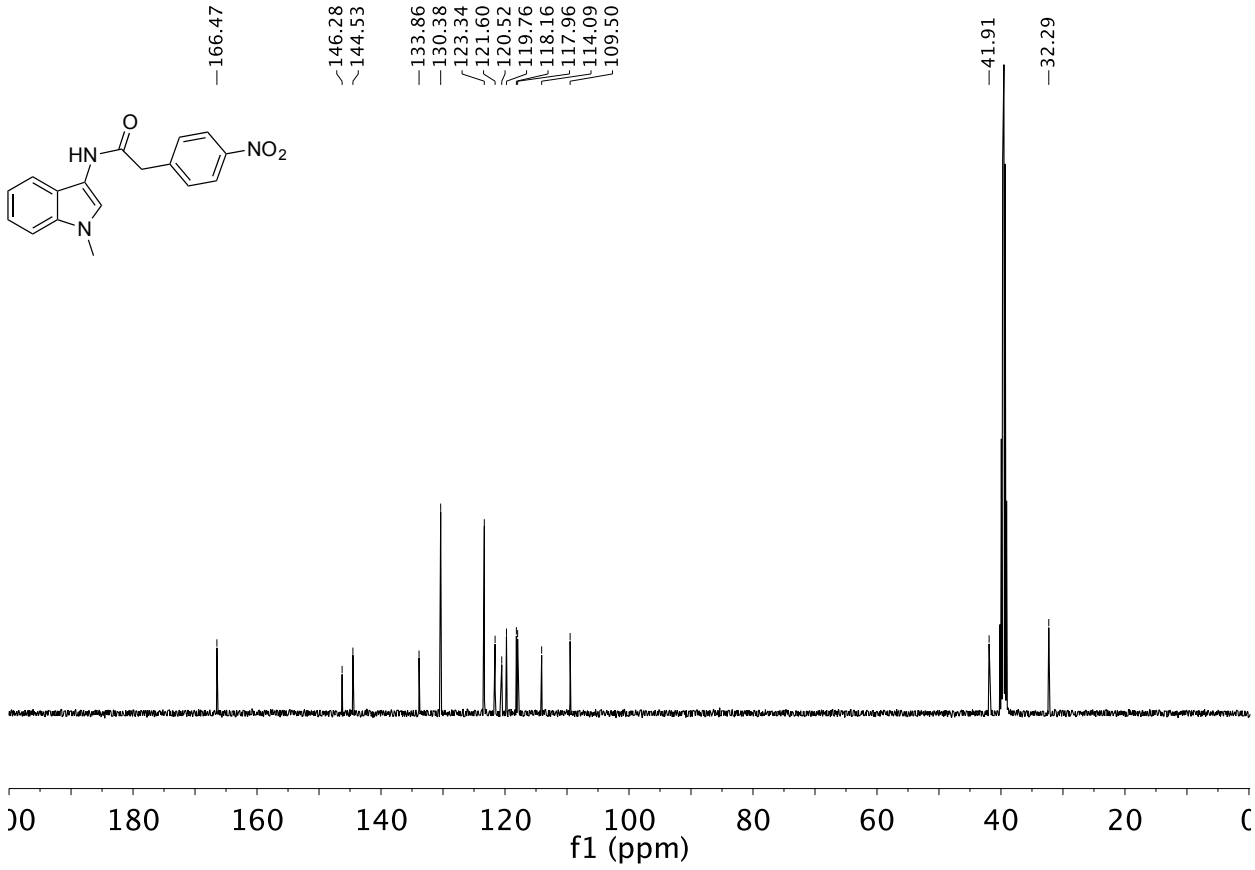


Figure S44. ^{13}C NMR spectrum of compound **1r** in d_6-DMSO solution (100 MHz).

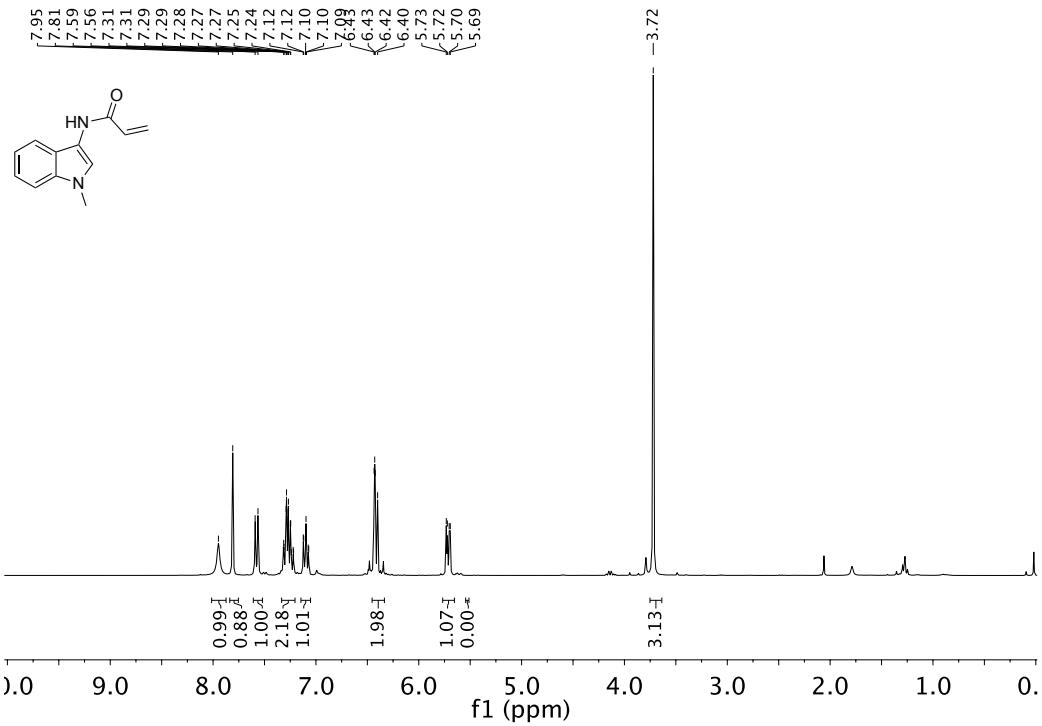


Figure S45. ^{1}H NMR spectrum of compound **1s** in $CDCl_3$ solution (75 MHz).

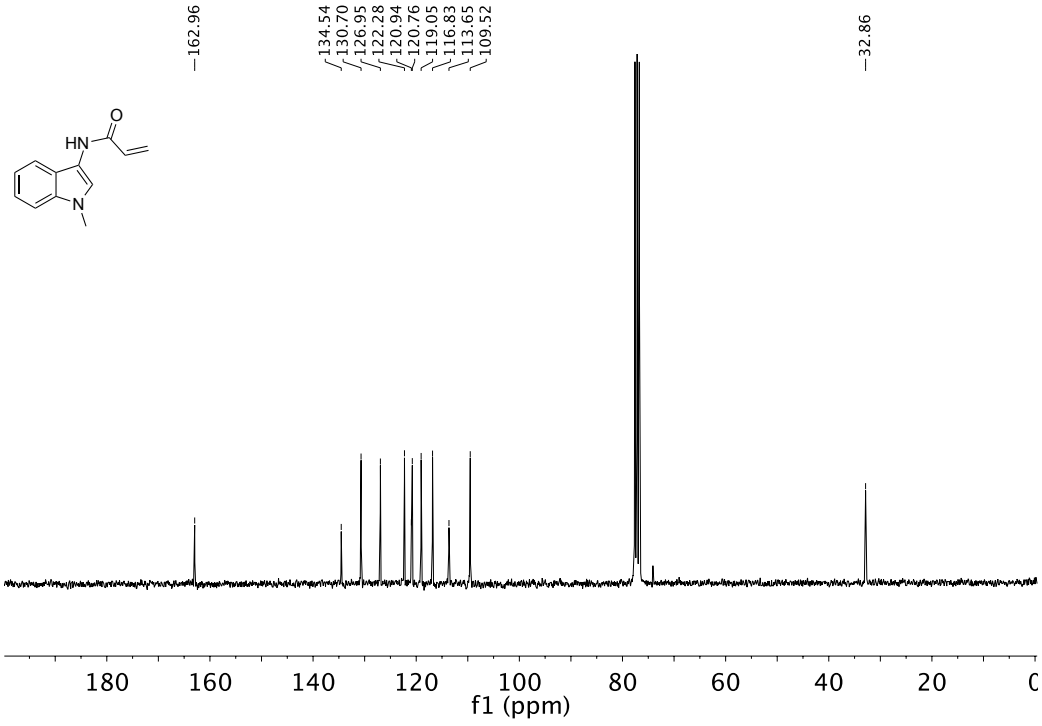


Figure S46. ^{13}C NMR spectrum of compound **1s** in $CDCl_3$ solution (75 MHz).

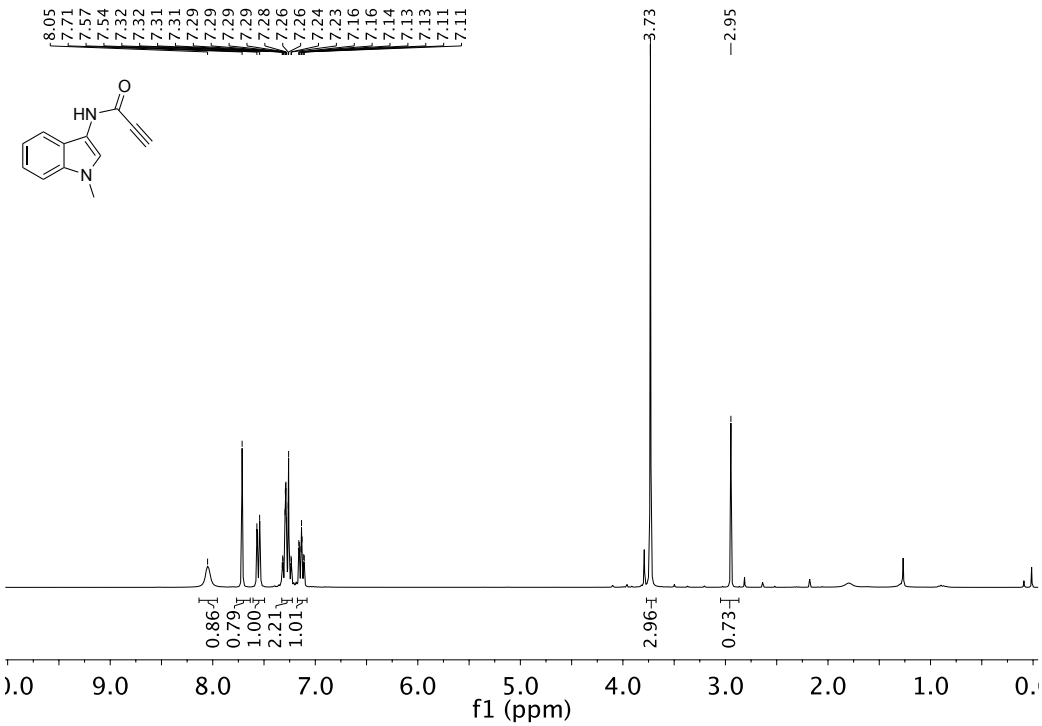


Figure S47. ^{1}H NMR spectrum of compound **1t** in $CDCl_3$ solution (300 MHz).

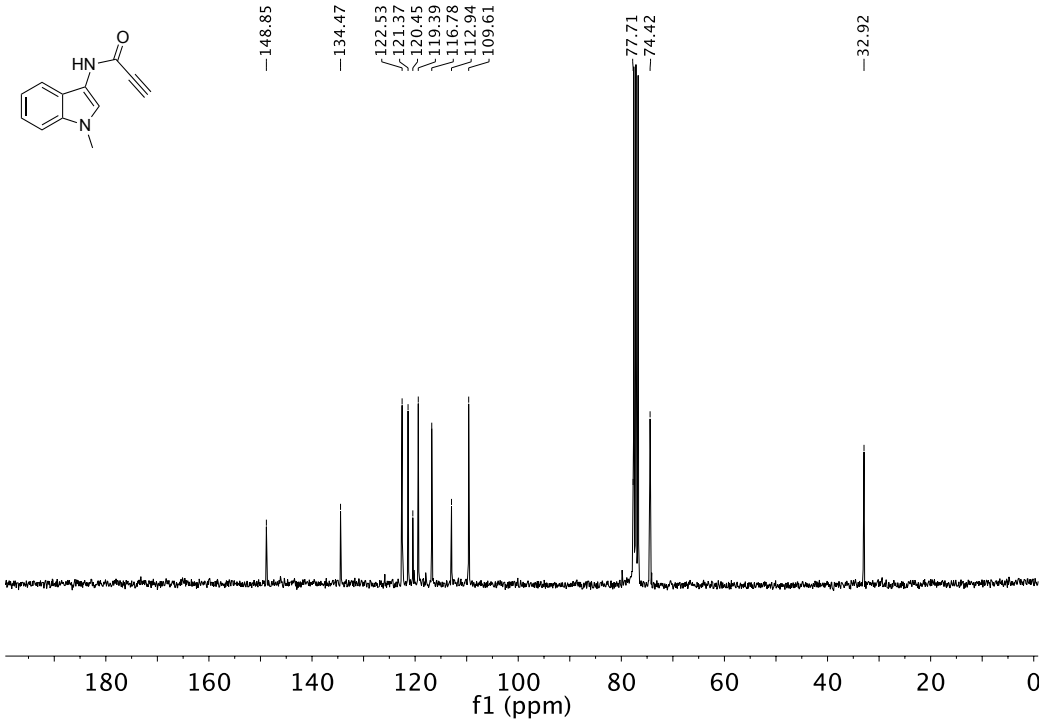


Figure S48. ^{13}C NMR spectrum of compound **1t** in $CDCl_3$ solution (75 MHz).

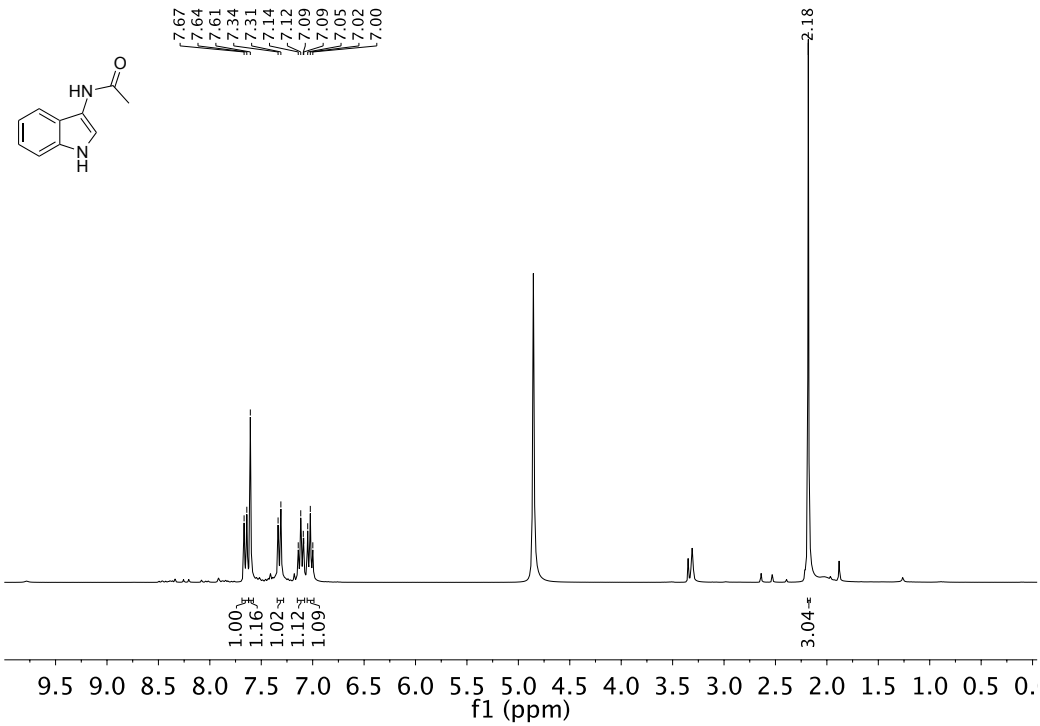


Figure S49. ^{1}H NMR spectrum of compound **1u** in MeOD solution (300 MHz).

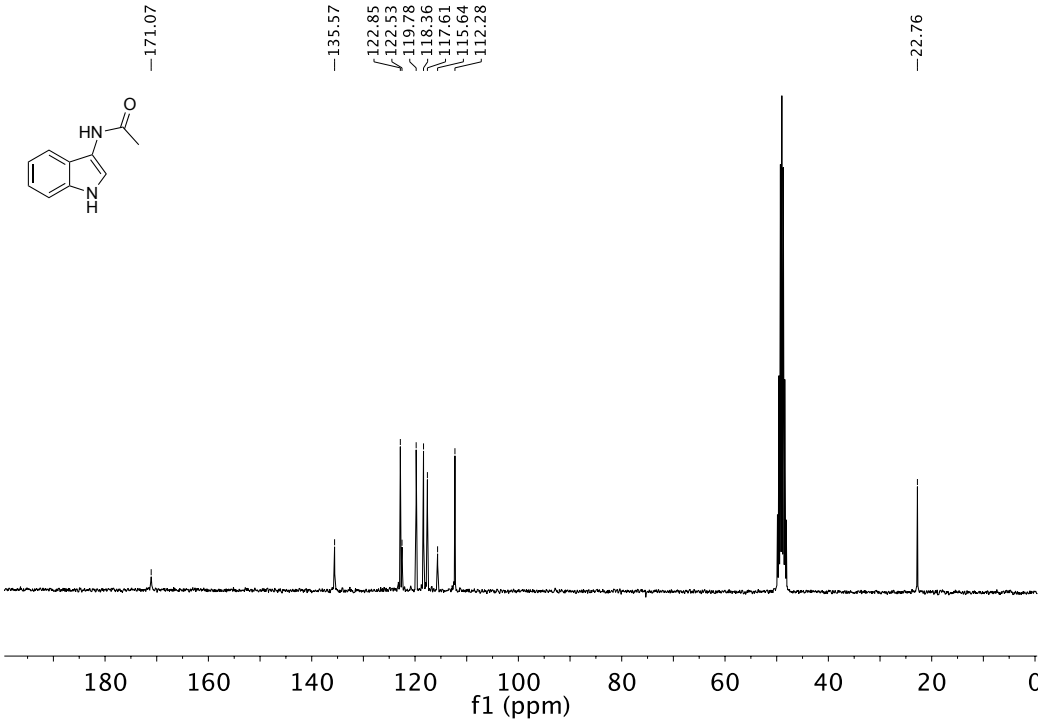


Figure S50. ^{13}C NMR spectrum of compound **1u** in MeOD solution (75 MHz).

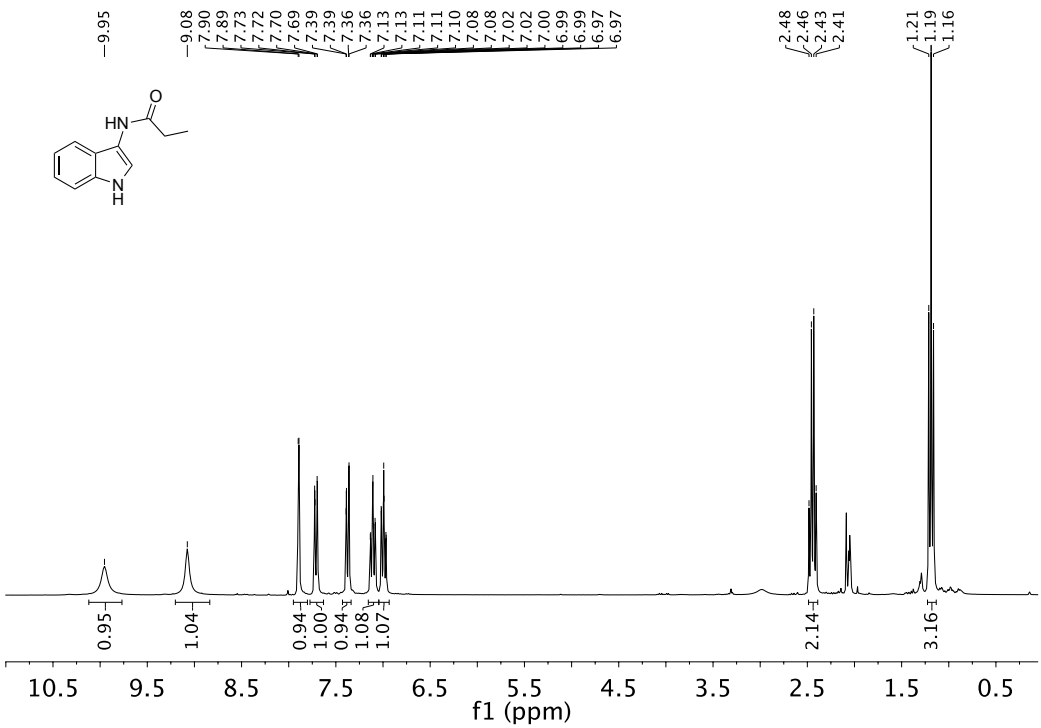


Figure S51. ^{1}H NMR spectrum of compound **1v** in d_6-acetone solution (300 MHz).

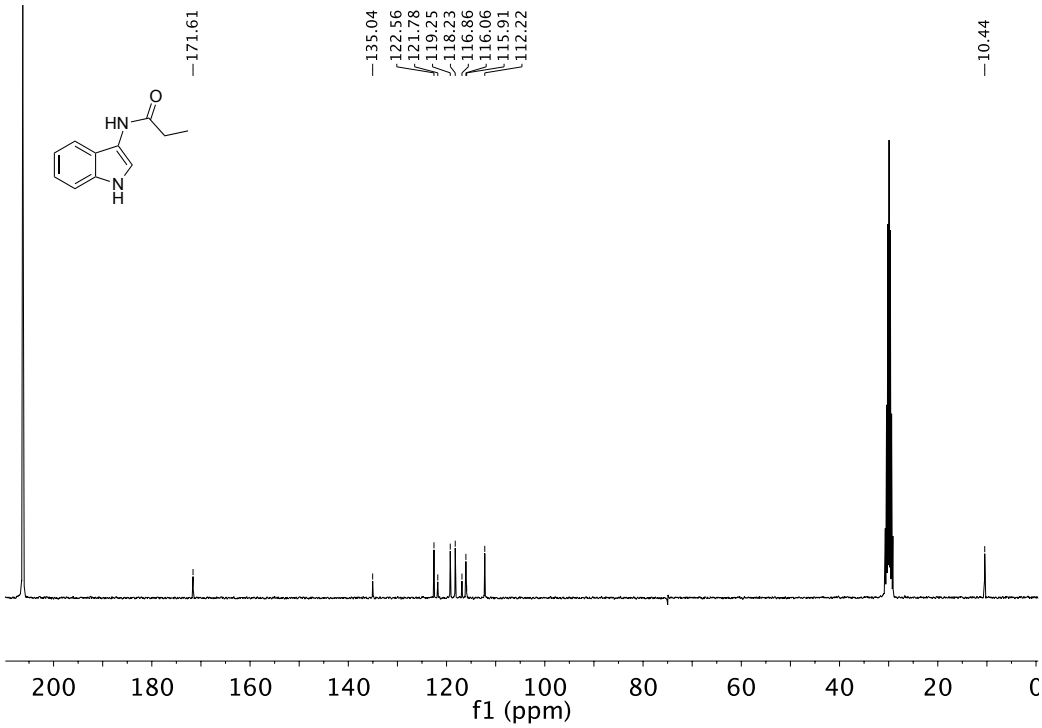


Figure S52. ^{13}C NMR spectrum of compound **1v** in d_6-acetone solution (75 MHz).

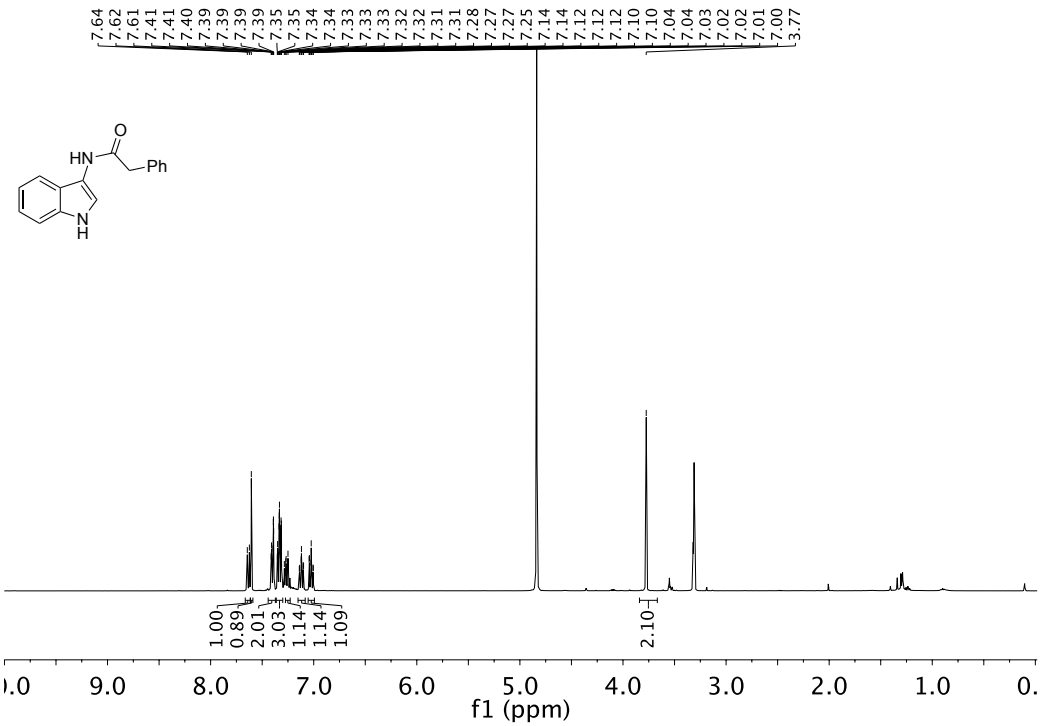


Figure S53. [1]H NMR spectrum of compound **1w** in MeOD solution (400 MHz).

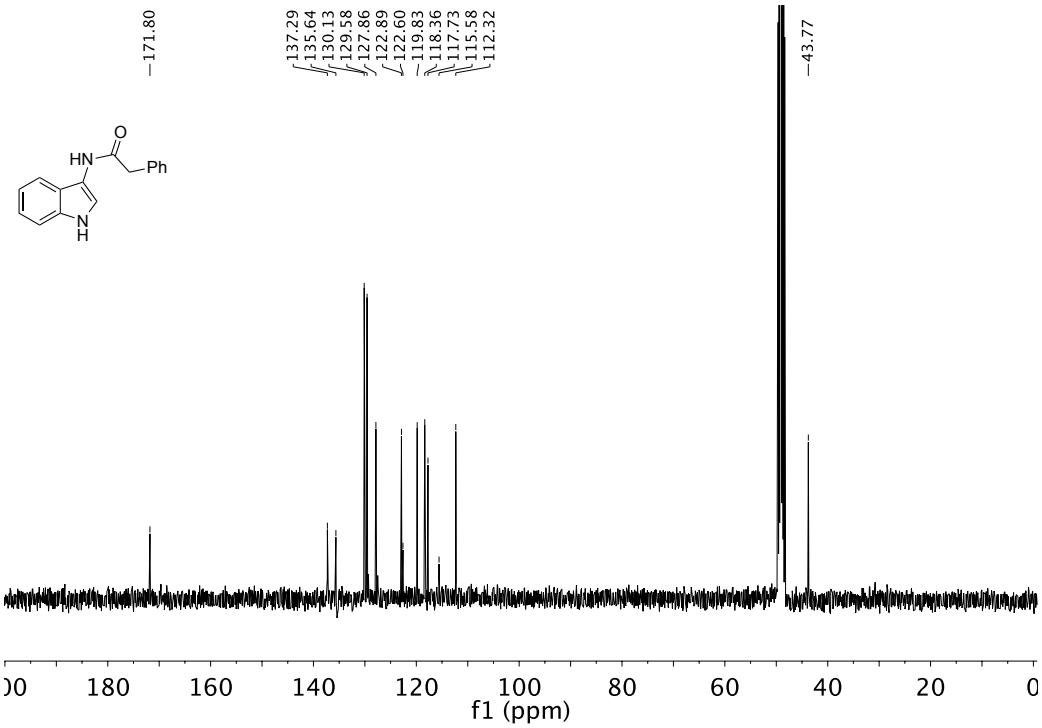


Figure S54. [13]C NMR spectrum of compound **1w** in MeOD solution (100 MHz).

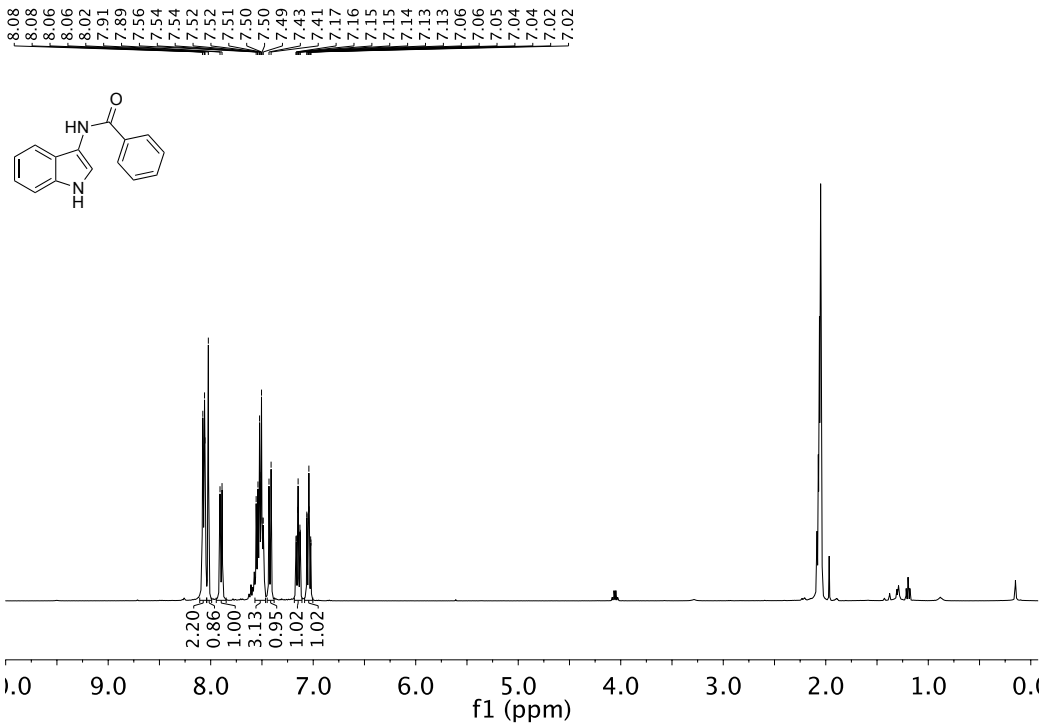


Figure S55. ^{1}H NMR spectrum of compound **1x** in d_6-acetone solution (400 MHz).

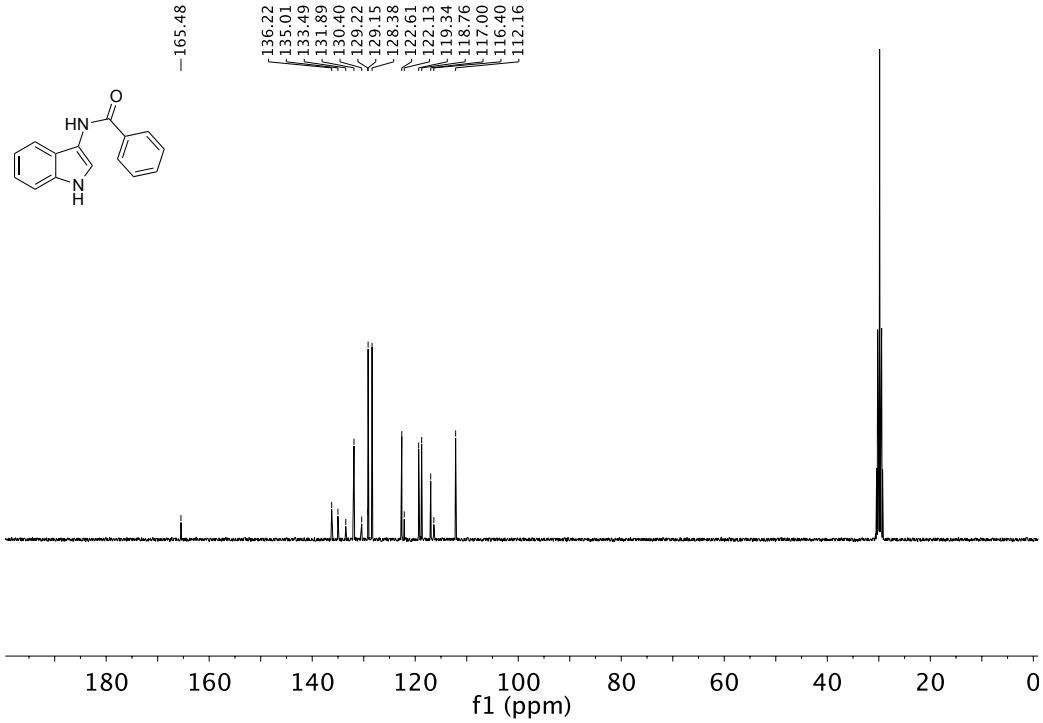


Figure S56. ^{13}C NMR spectrum of compound **1x** in d_6-acetone solution (100 MHz).

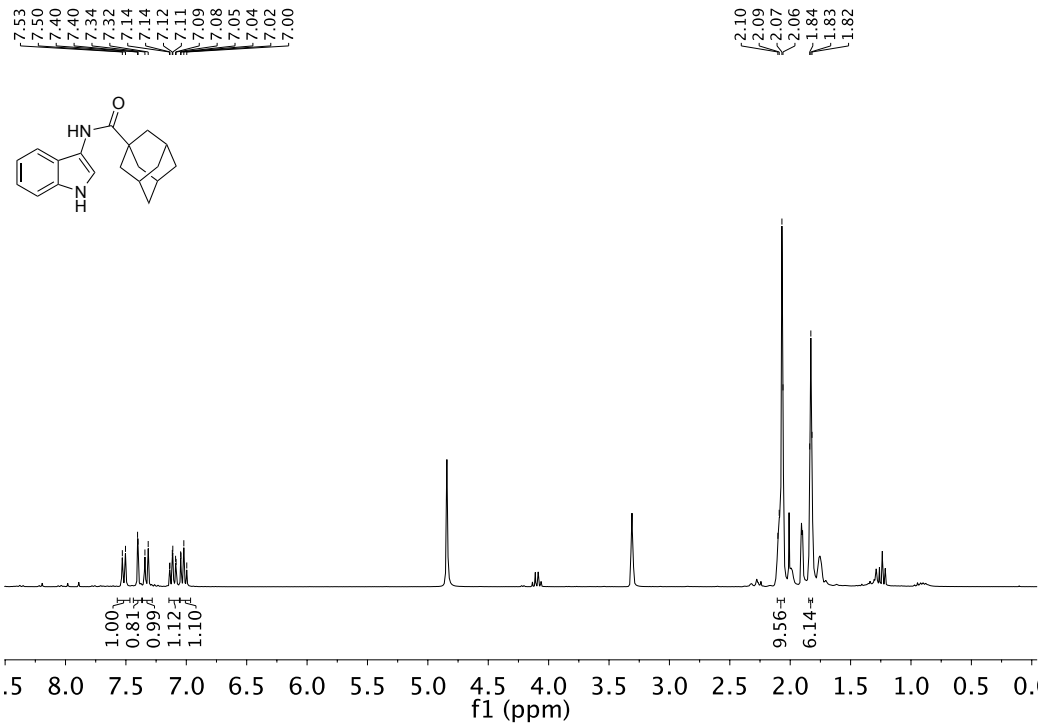


Figure S57. [1]H NMR spectrum of compound **1y** in MeOD solution (300 MHz).

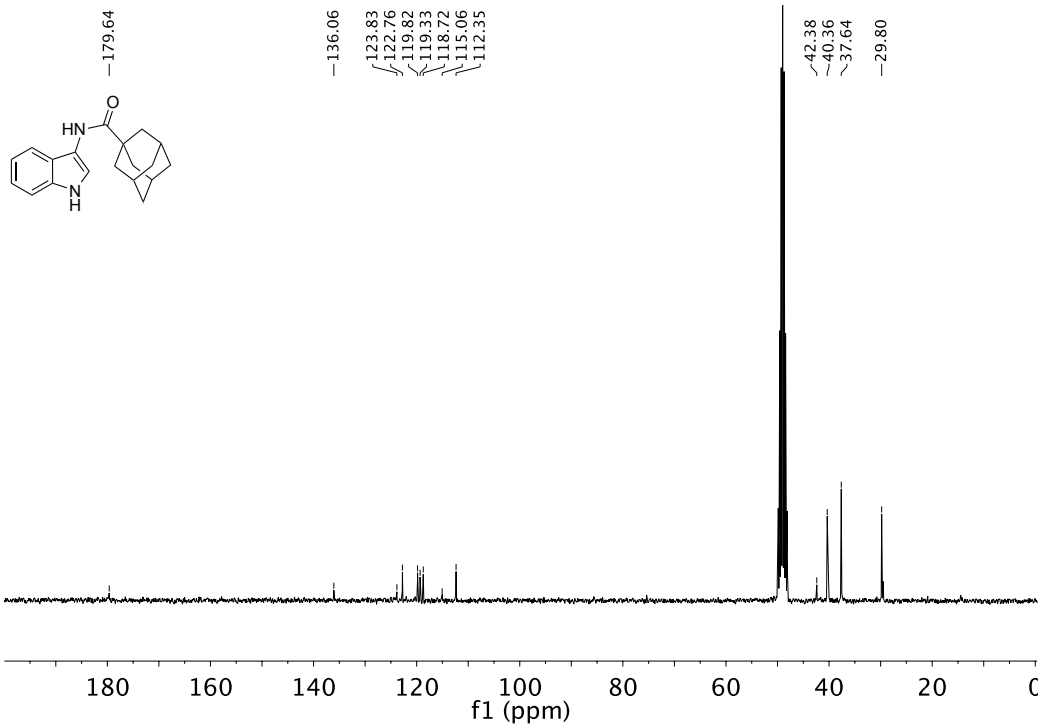


Figure S58. [13]C NMR spectrum of compound **1y** in MeOD solution (75 MHz).

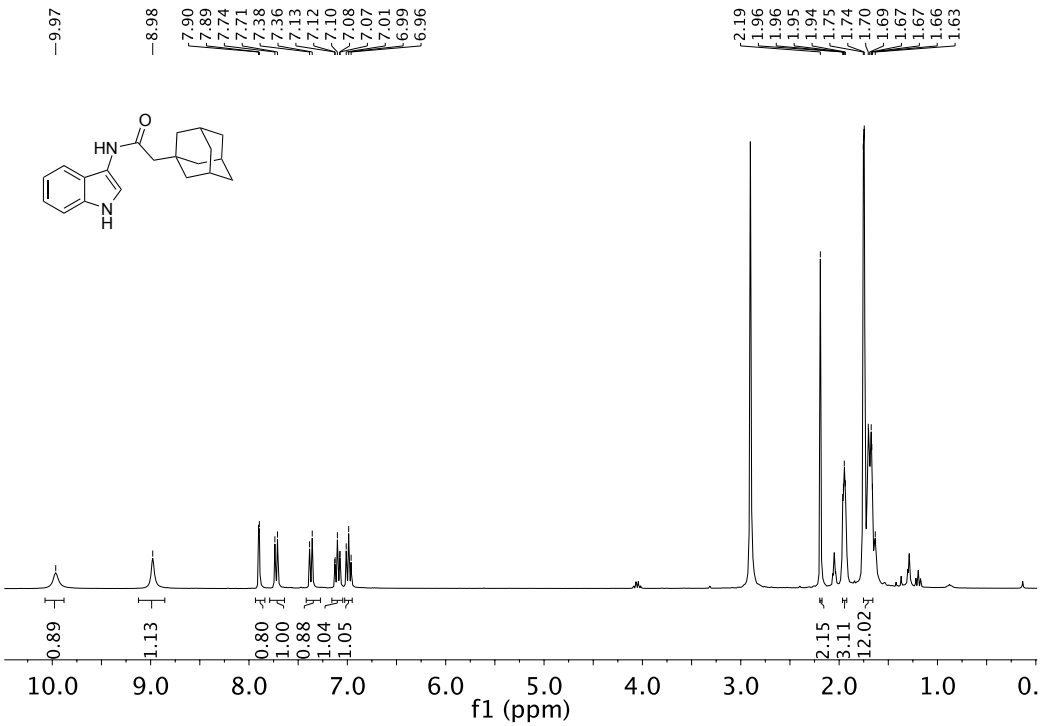


Figure S59. ^{1}H NMR spectrum of compound **1z** in d_6-acetone solution (300 MHz).

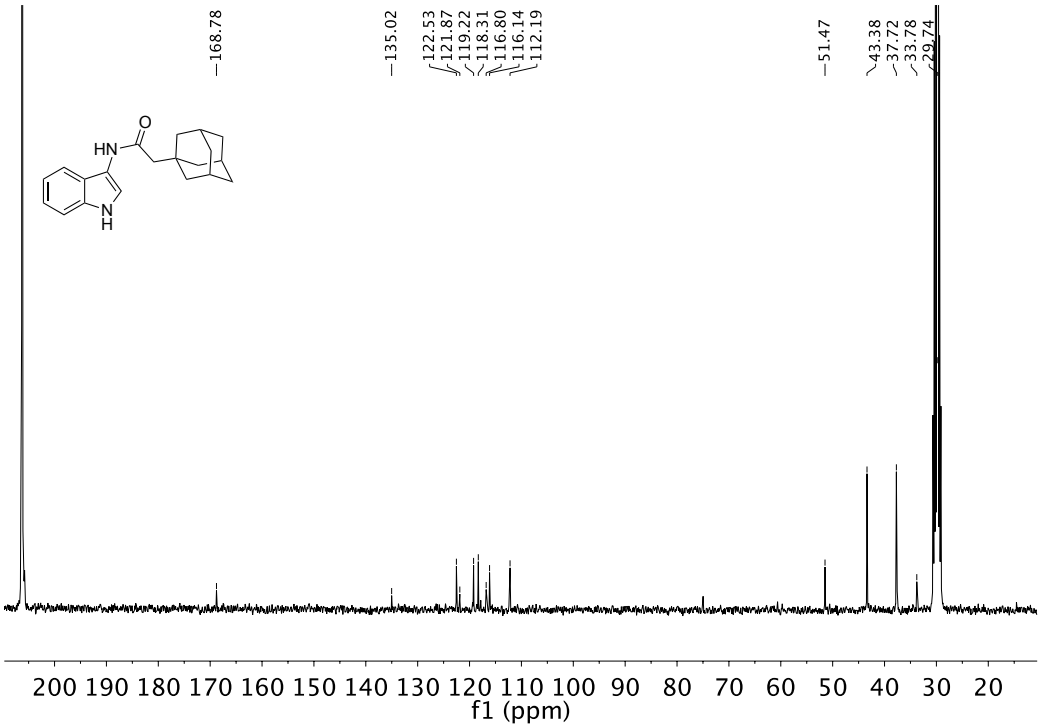


Figure S60. ^{13}C NMR spectrum of compound **1z** in d_6-acetone solution (75 MHz).

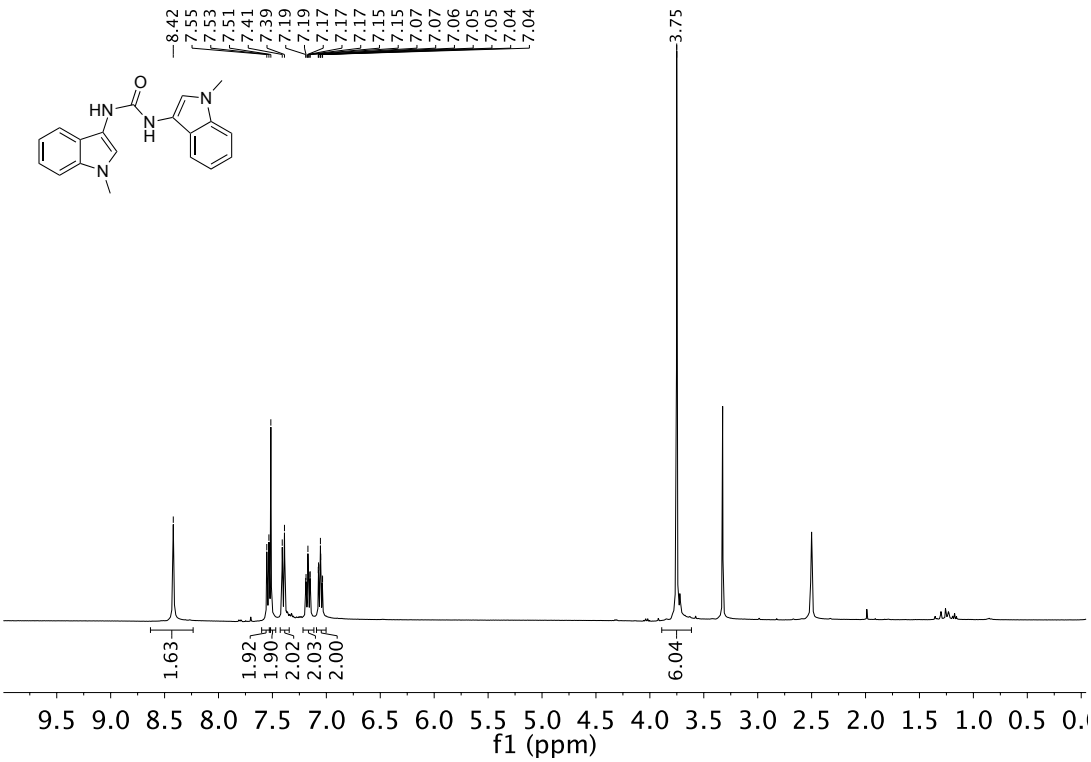


Figure S61. ^{1}H NMR spectrum of compound **9** in $CDCl_3$ solution (300 MHz).

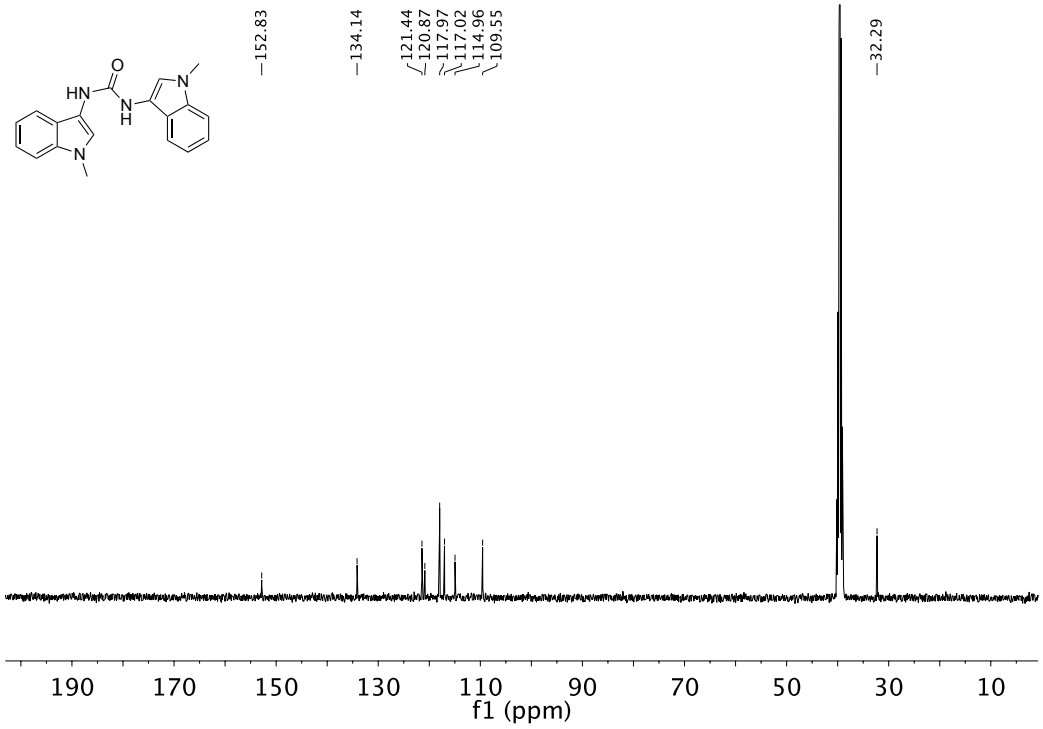


Figure S62. ^{13}C NMR spectrum of compound **9** in $CDCl_3$ solution (75 MHz).

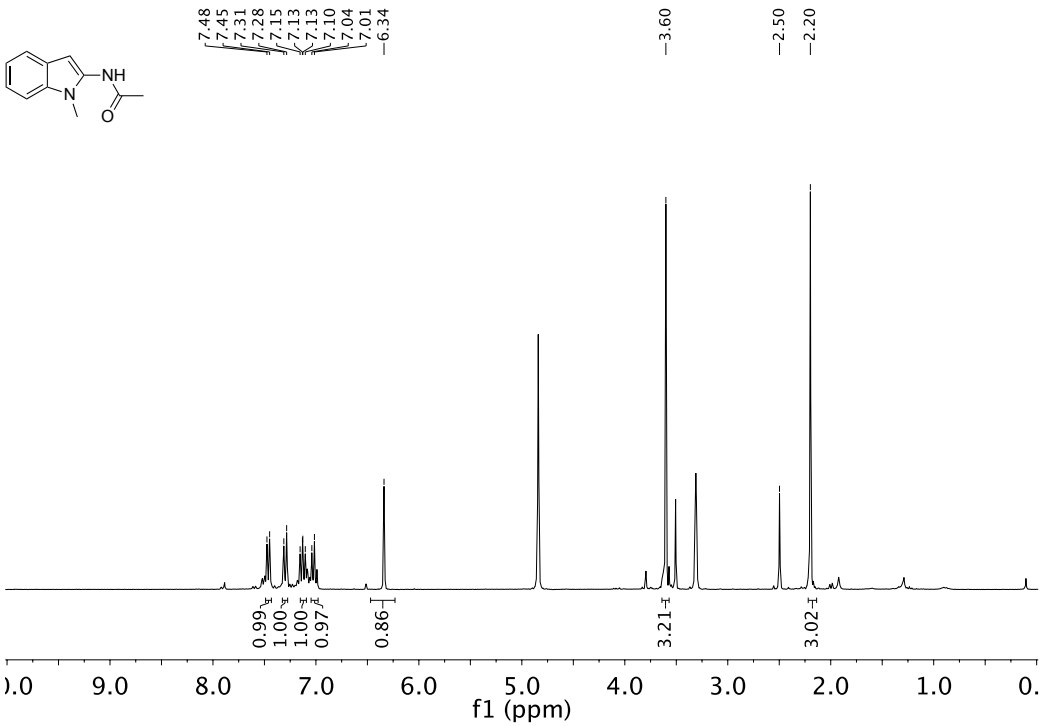


Figure S63. ^{1}H NMR spectrum of compound **2a** in MeOD solution (300 MHz).

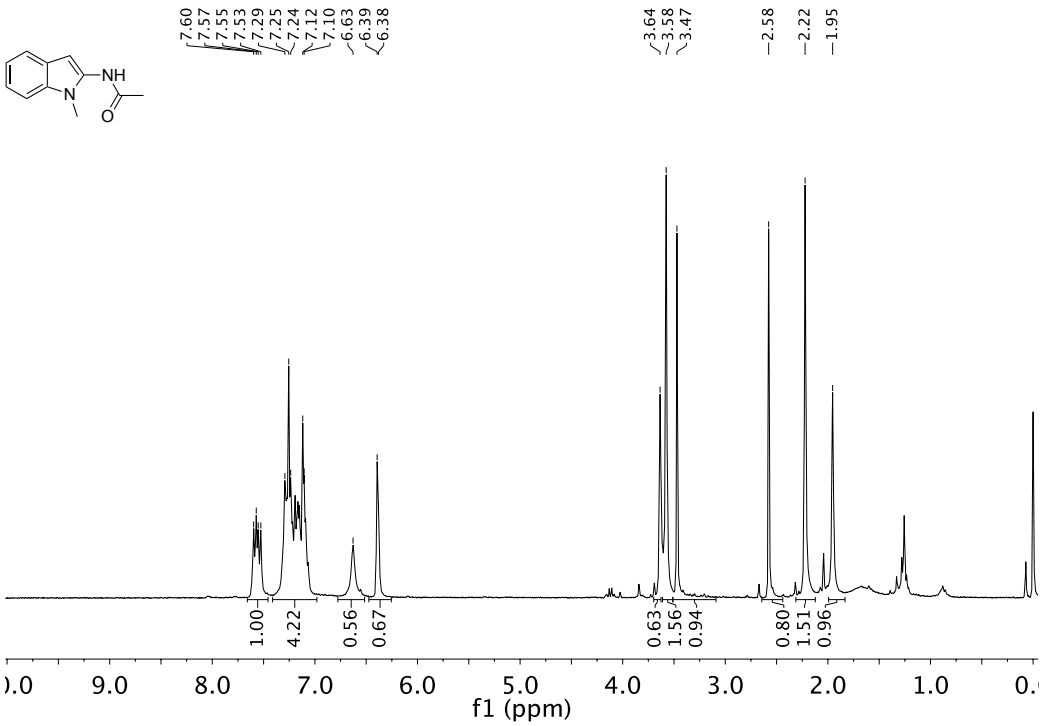


Figure S64. ^{1}H NMR spectrum of compound **2a** in $CDCl_3$ solution showing rotamers (300 MHz).

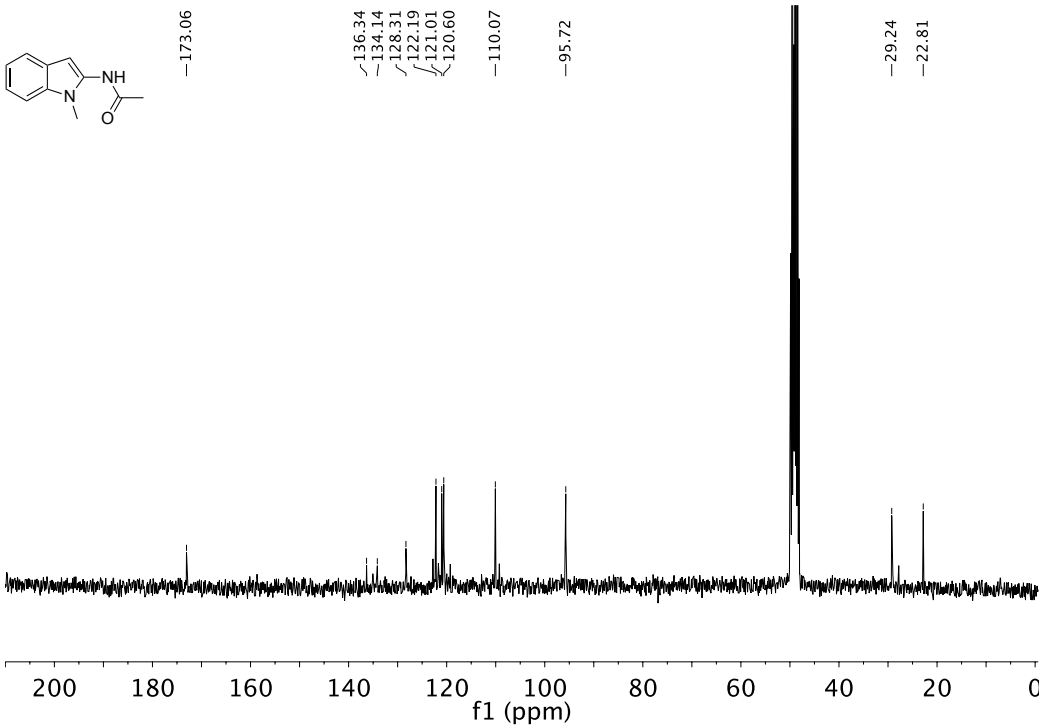


Figure S65. ^{13}C NMR spectrum of compound **2a** in MeOD solution (75 MHz).

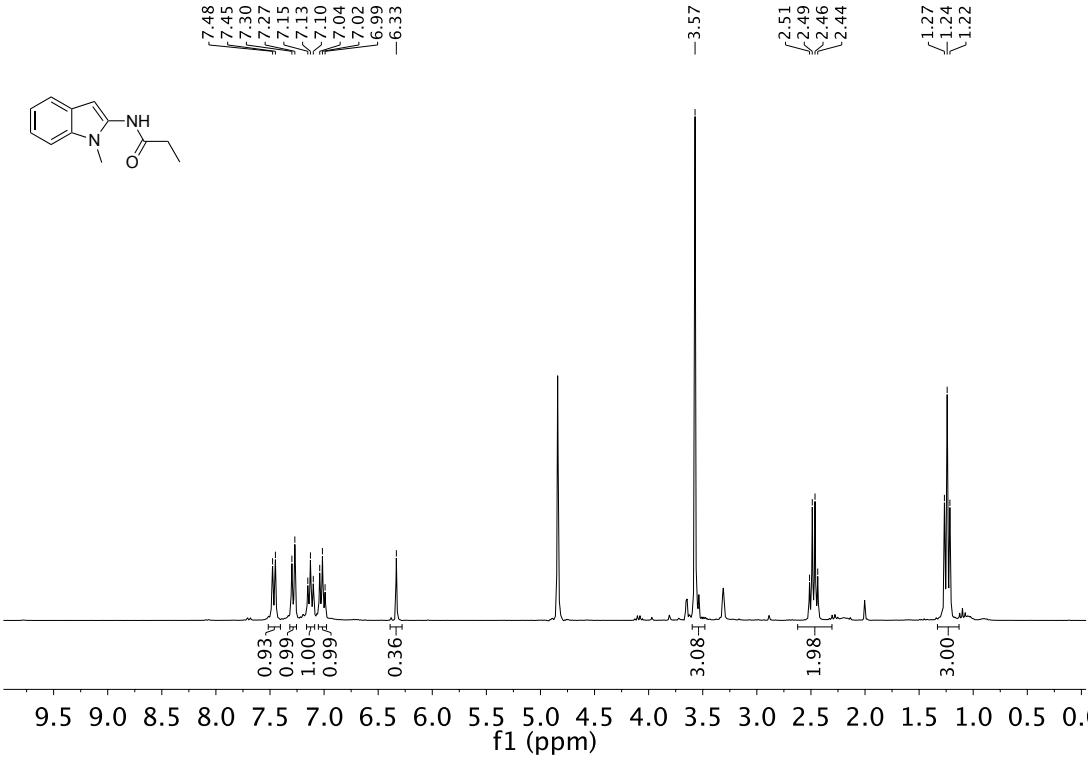


Figure S66. ^{1}H NMR spectrum of compound **2b** in MeOD solution (300 MHz).

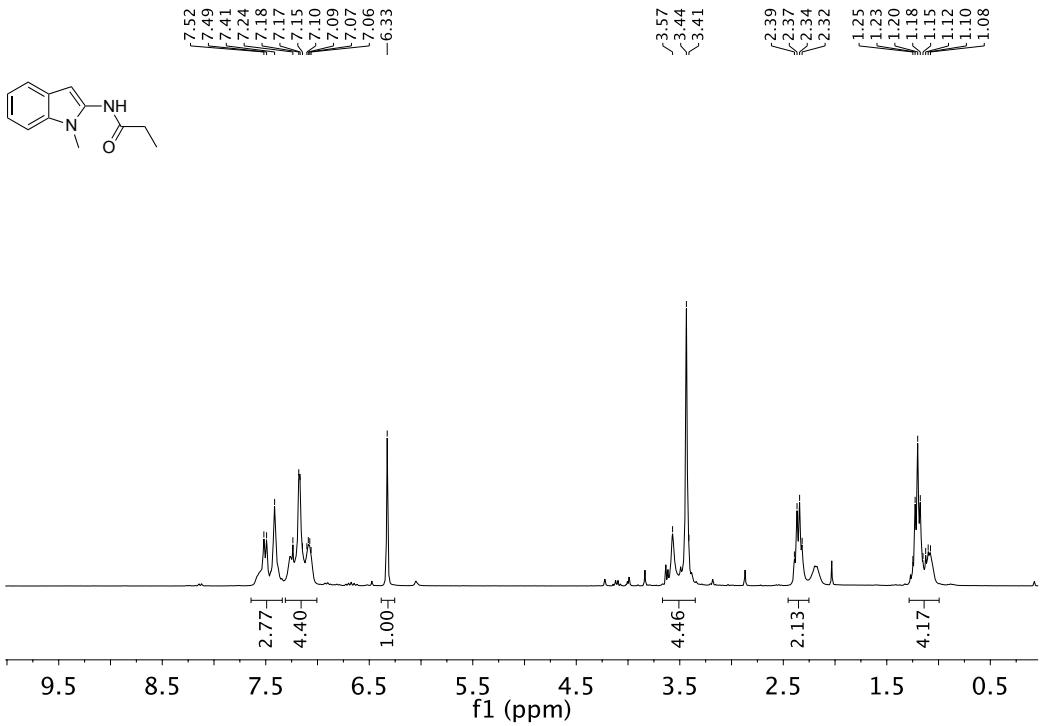


Figure S67. ^{1}H NMR spectrum of compound **2b** in $CDCl_3$ solution showing rotamers (300 MHz).

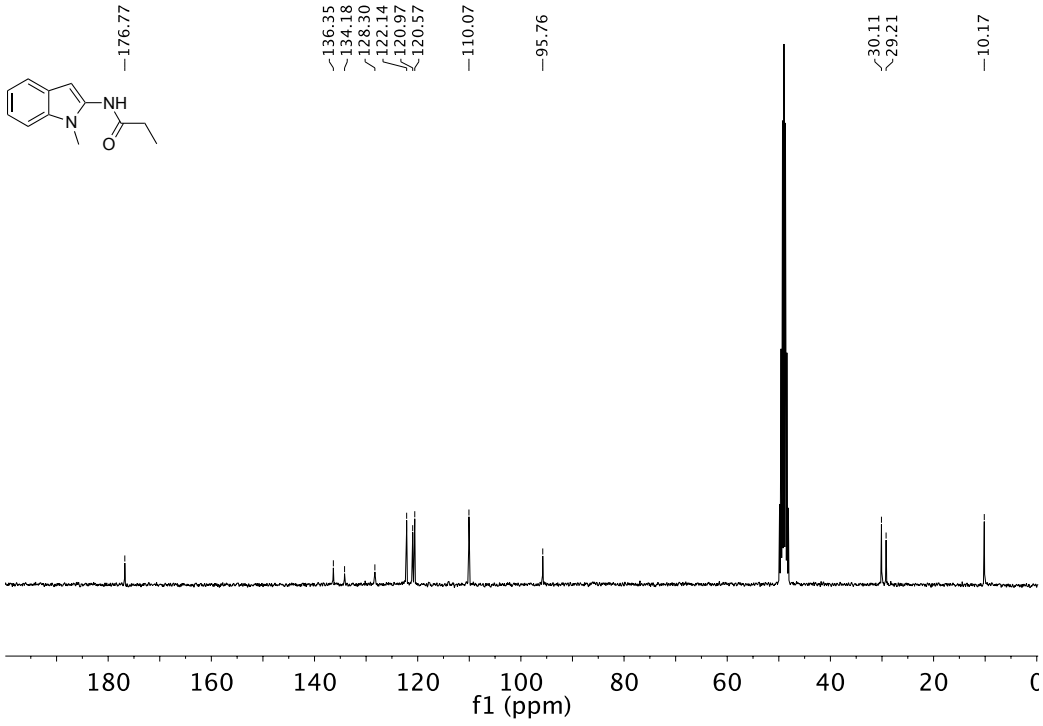


Figure S68. ^{13}C NMR spectrum of compound **2b** in $CDCl_3$ solution (75 MHz).

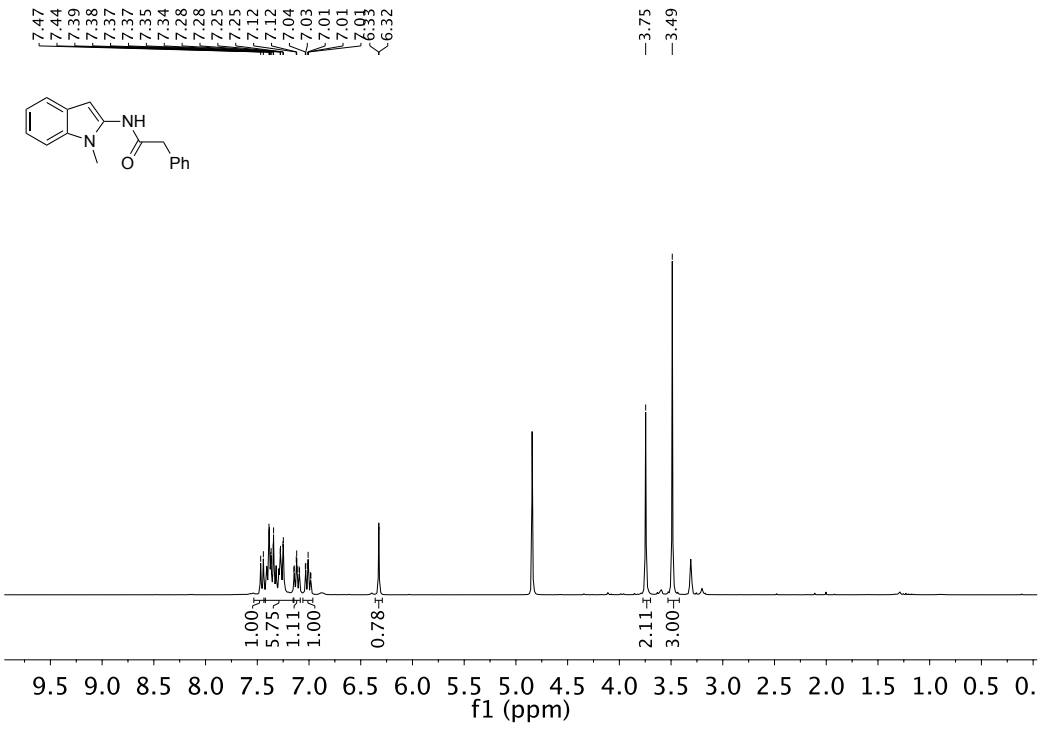


Figure S69. ^{1}H NMR spectrum of compound **2c** in MeOD solution (300 MHz).

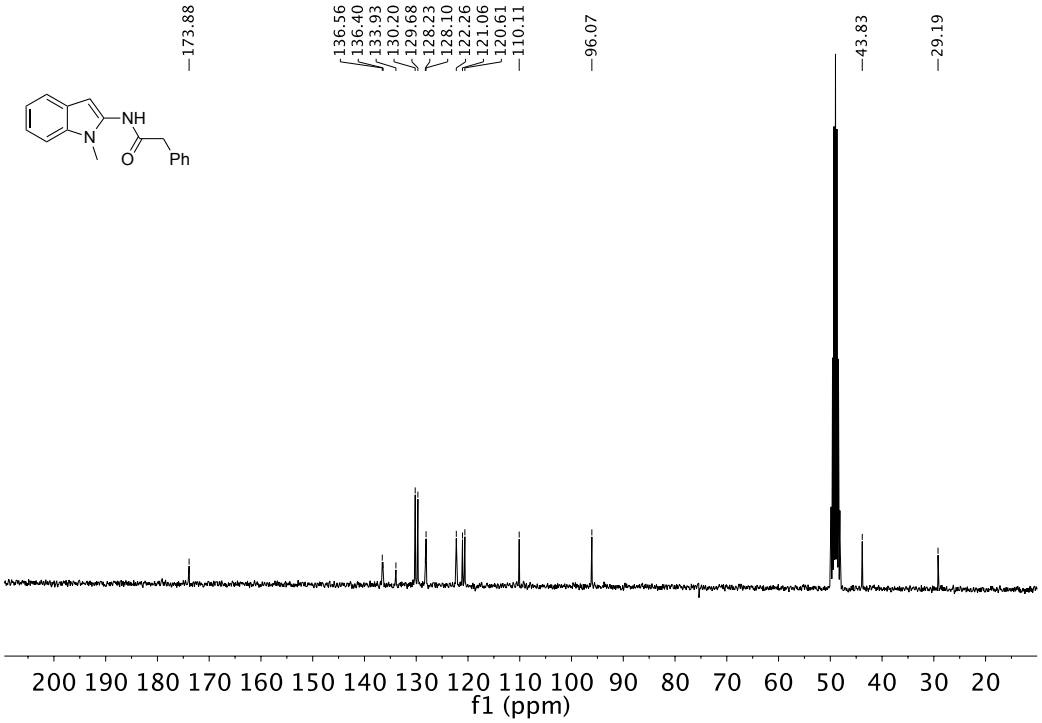


Figure S70. ^{13}C NMR spectrum of compound **2c** in MeOD solution (75 MHz).

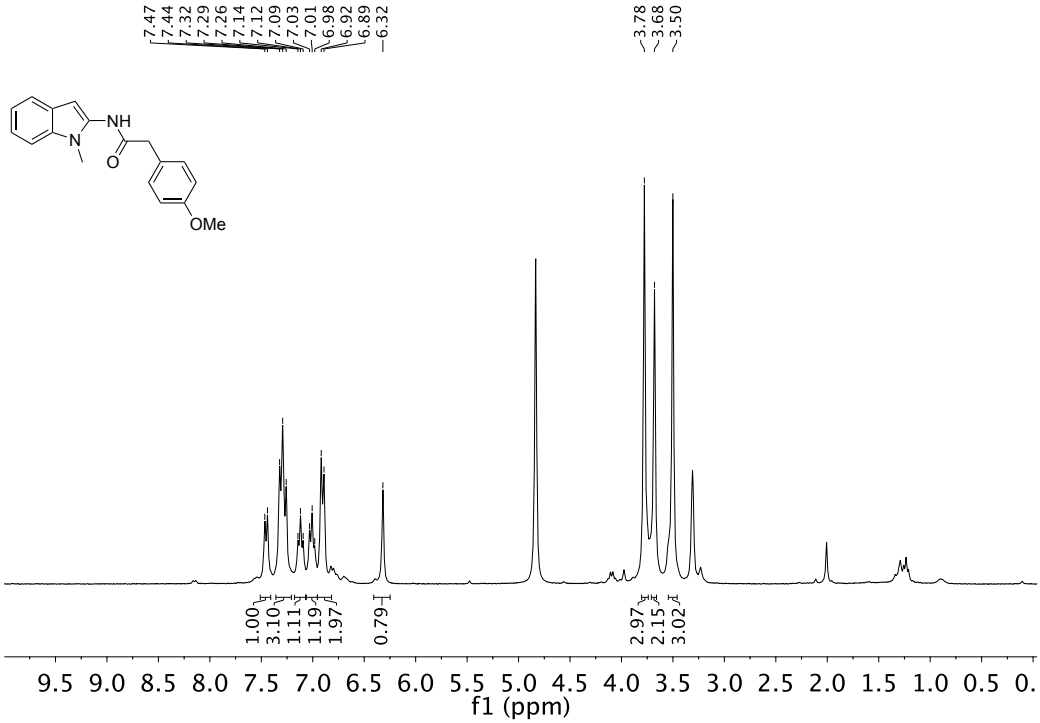


Figure S71. [1]H NMR spectrum of compound **2d** in MeOD solution (300 MHz).

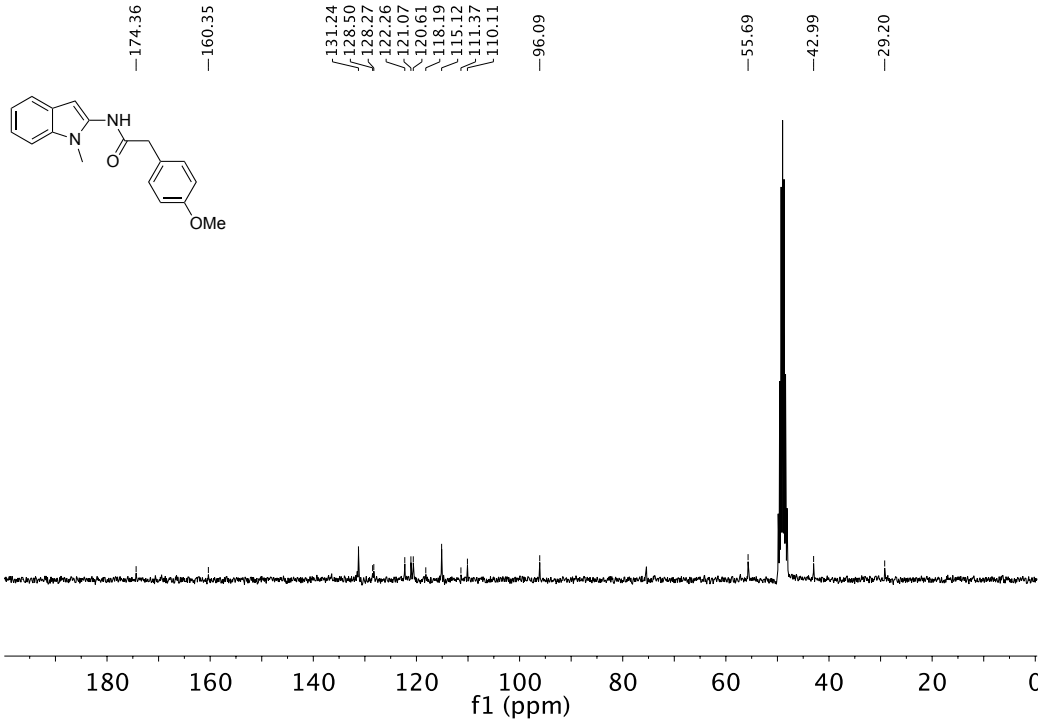


Figure S72. [13]C NMR spectrum of compound **2d** in MeOD solution (75 MHz).

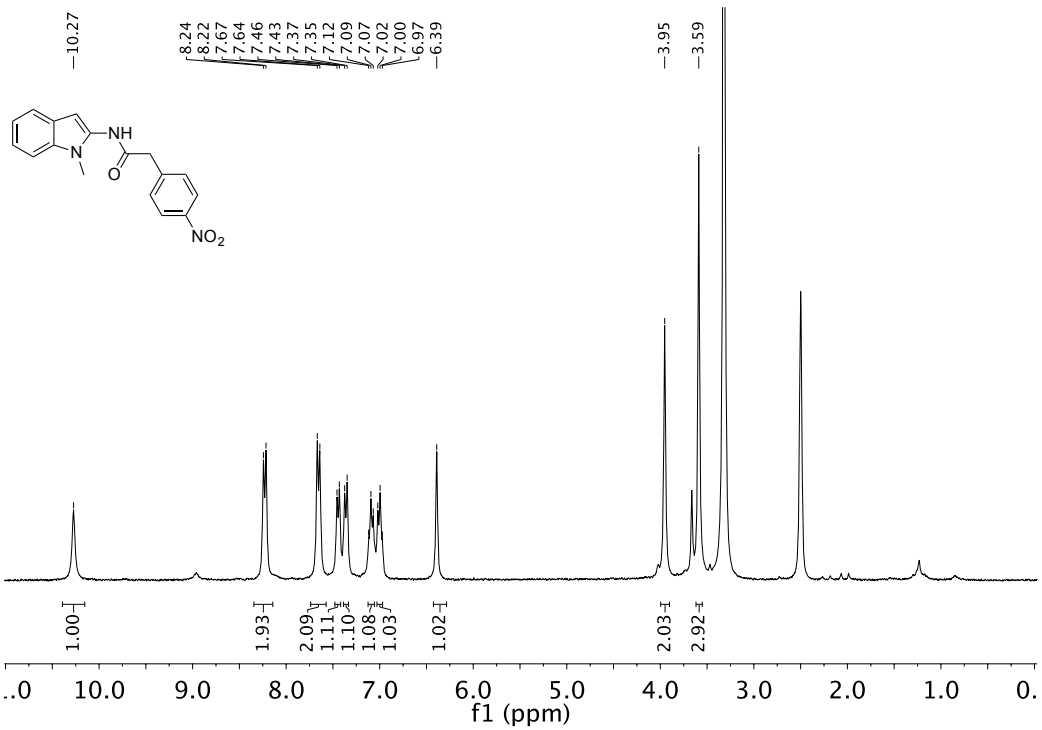


Figure S73. ^{1}H NMR spectrum of compound **1e** in d_6-DMSO solution (300 MHz).

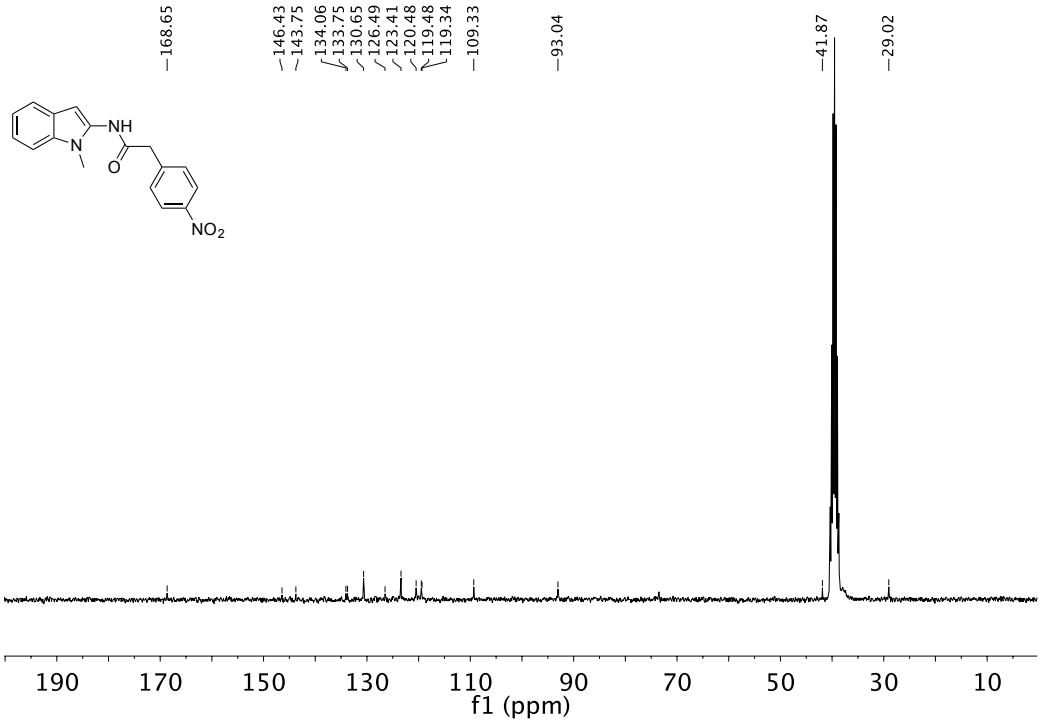


Figure S74. ^{13}C NMR spectrum of compound **2e** in d_6-DMSO solution (75 MHz).

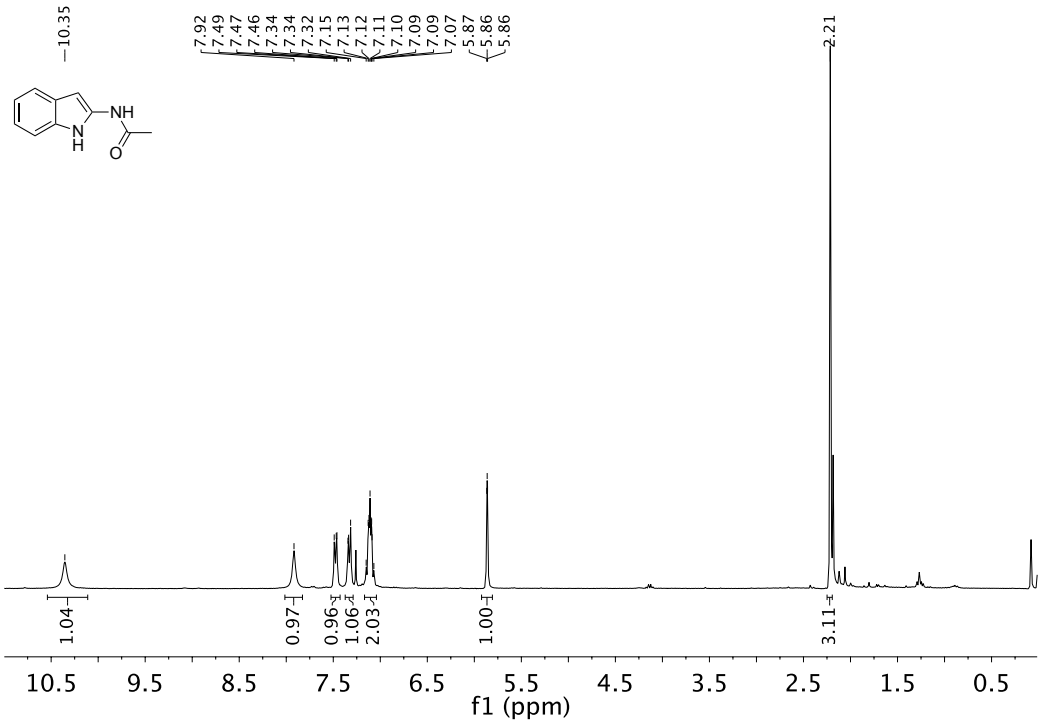


Figure S75. ^{1}H NMR spectrum of compound **2f** in $CDCl_3$ solution (300 MHz).

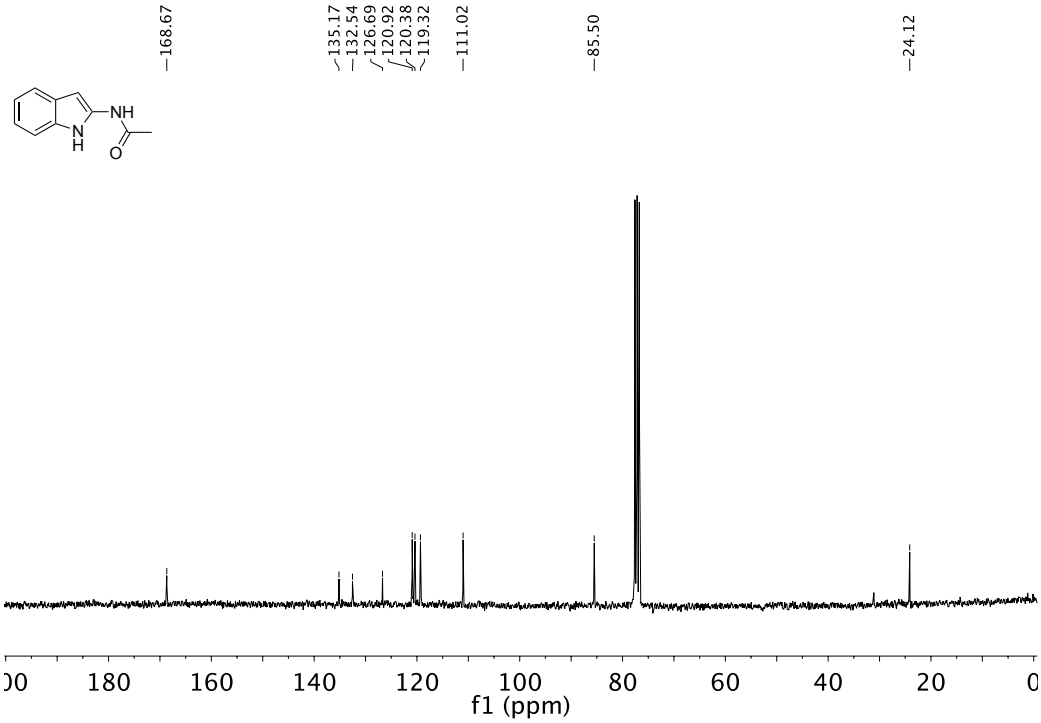


Figure S76. ^{13}C NMR spectrum of compound **2f** in $CDCl_3$ solution (75 MHz).

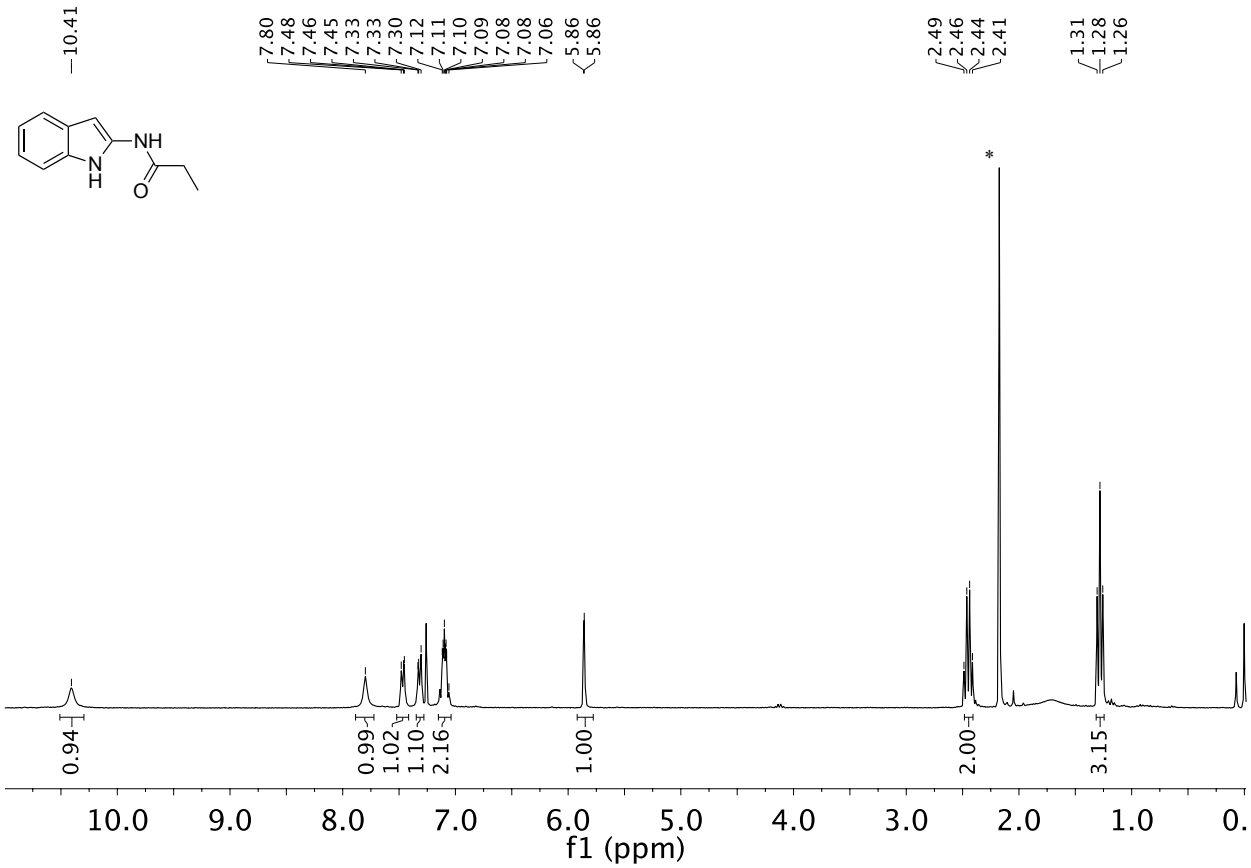


Figure S77. ^{1}H NMR spectrum of compound **2g** in $CDCl_3$ solution (300 MHz). * acetone

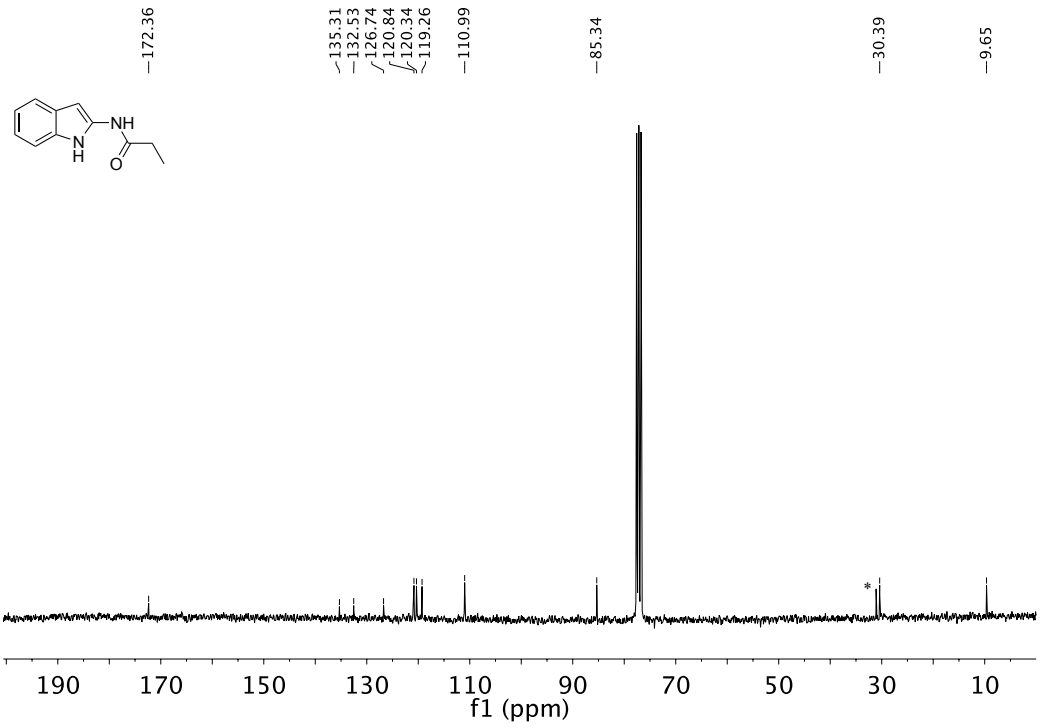


Figure S78. ^{13}C NMR spectrum of compound **2g** in $CDCl_3$ solution (75 MHz). *acetone

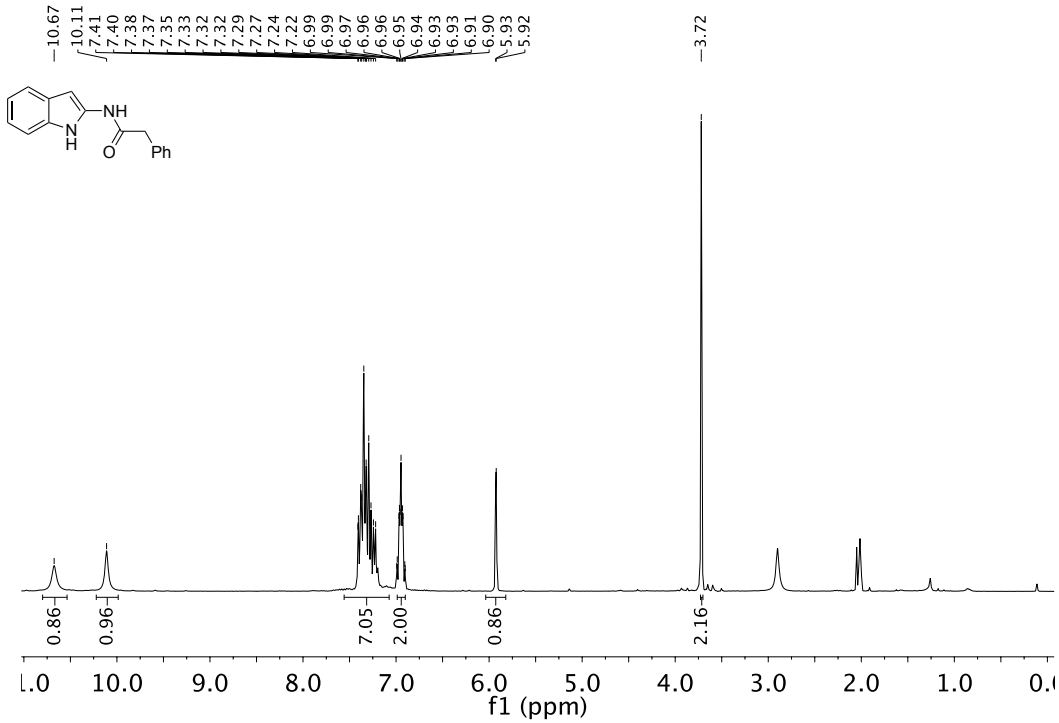


Figure S79. ^{1}H NMR spectrum of compound **2h** in d_6-acetone solution (300 MHz).

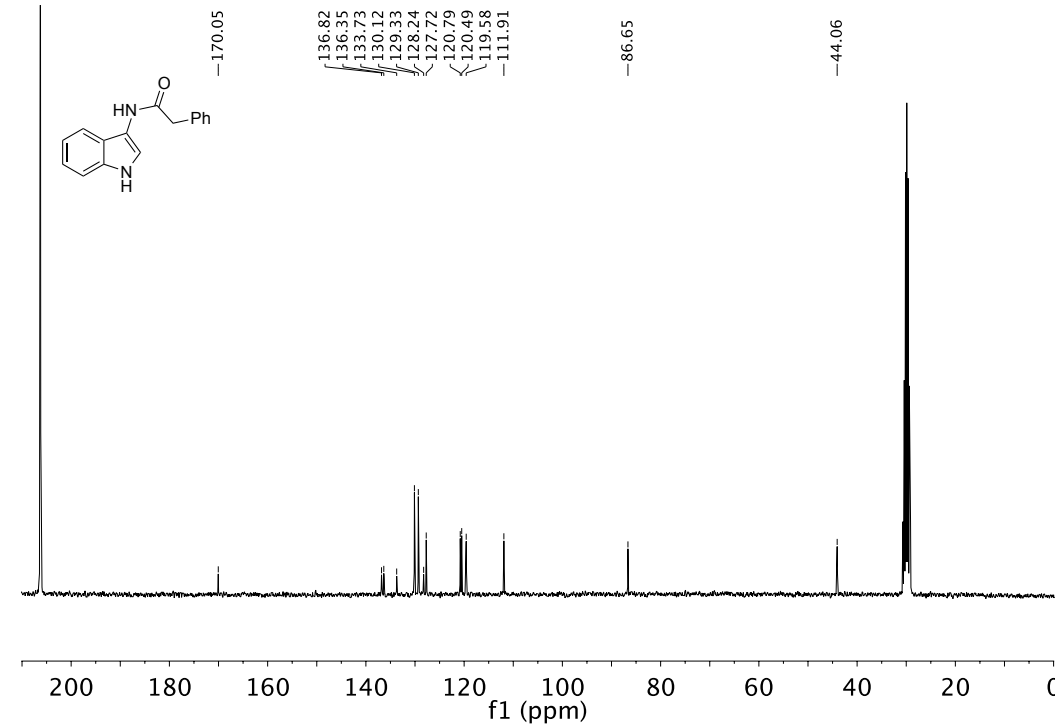


Figure S80. ^{13}C NMR spectrum of compound **2h** in d_6-acetone solution (75 MHz).

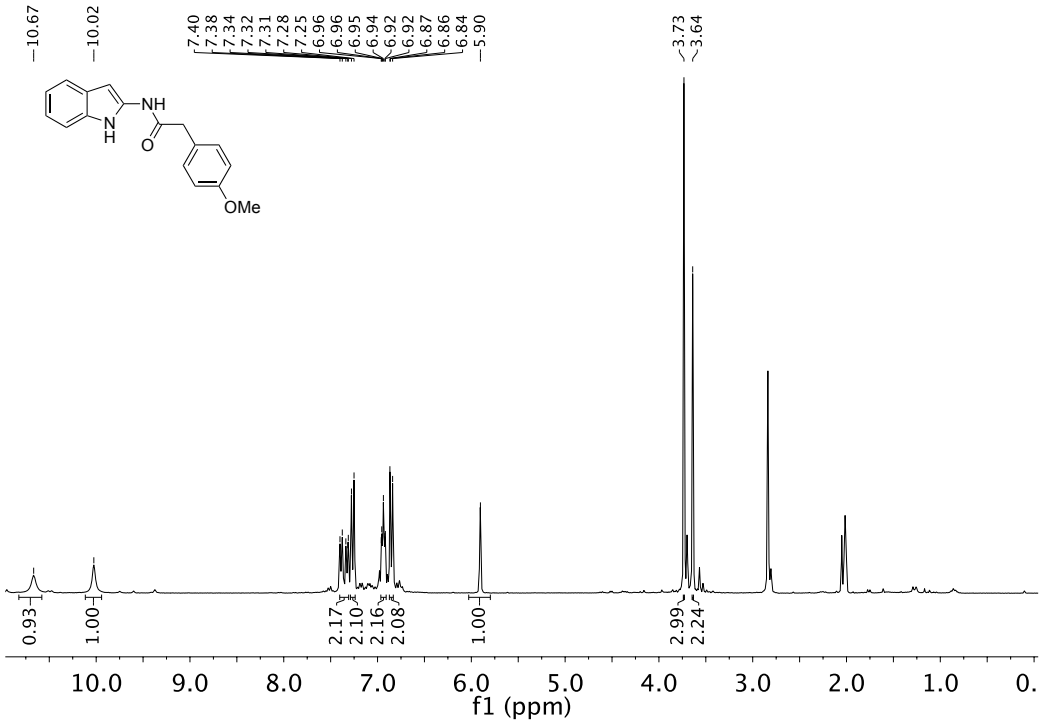


Figure S81. [1]H NMR spectrum of compound **2i** in d_6-acetone solution (300 MHz).

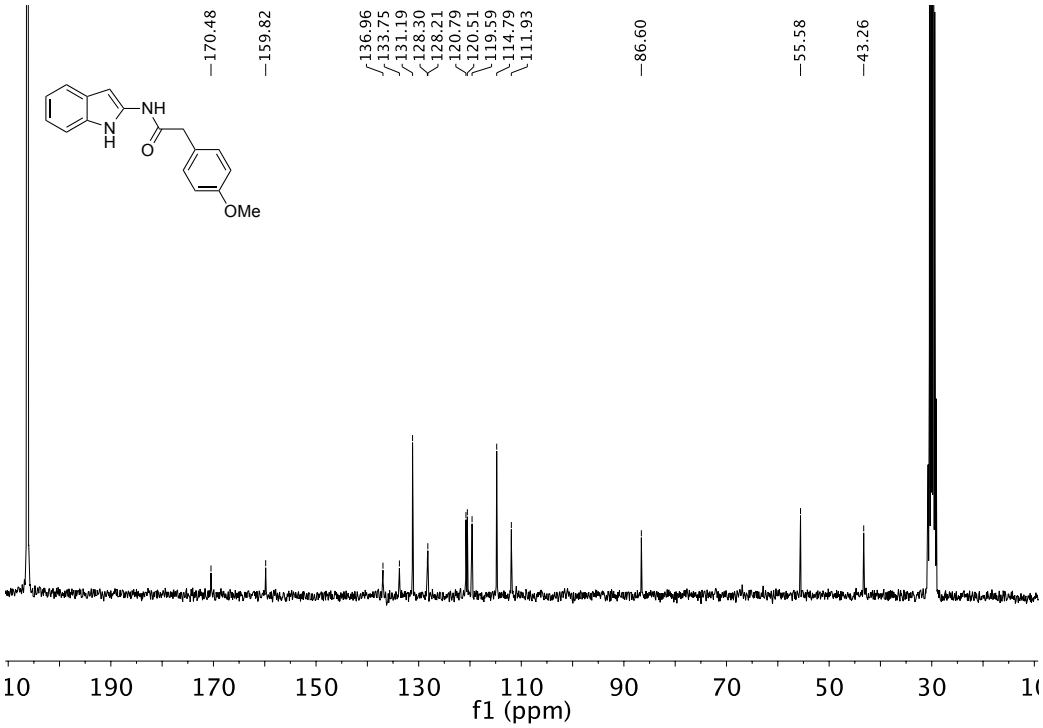


Figure S82. [13]C NMR spectrum of compound **2i** in d_6-acetone solution (75 MHz).

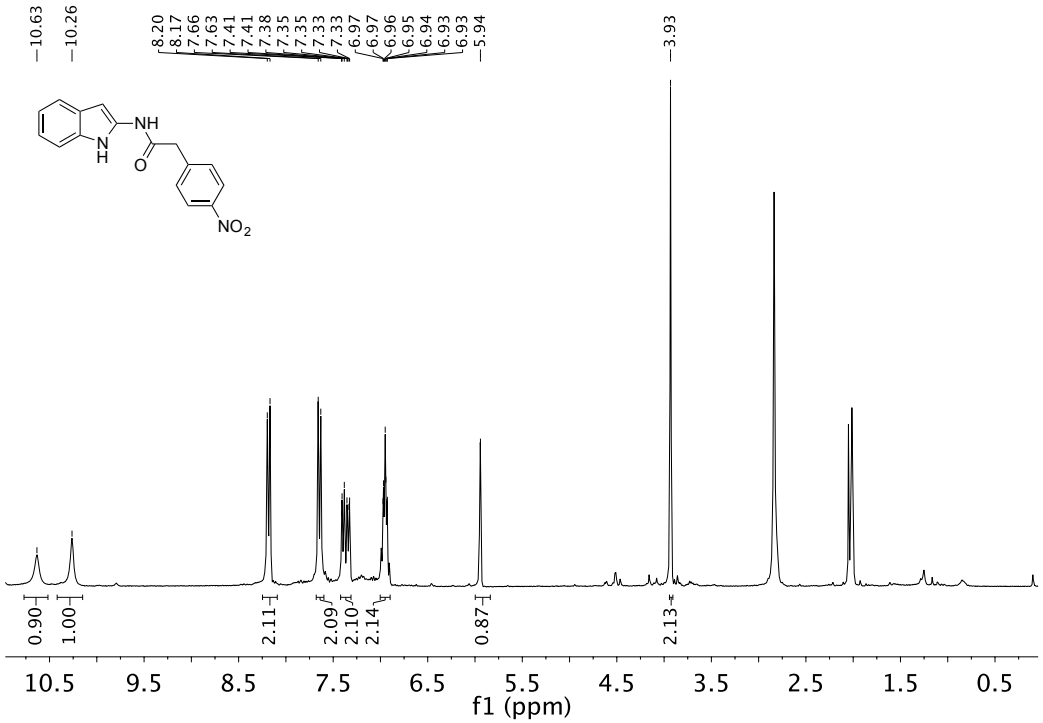


Figure S83. [1]H NMR spectrum of compound **2j** in d_6-acetone solution (300 MHz).

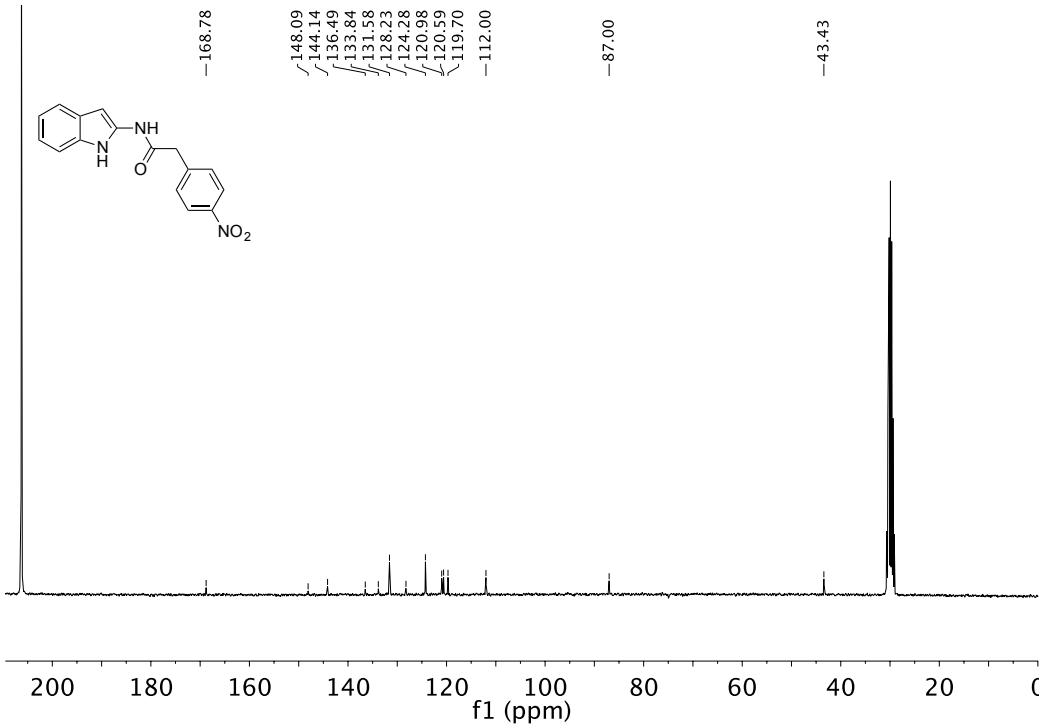


Figure S84. [13]C NMR spectrum of compound **2j** in d_6-acetone solution (75 MHz).

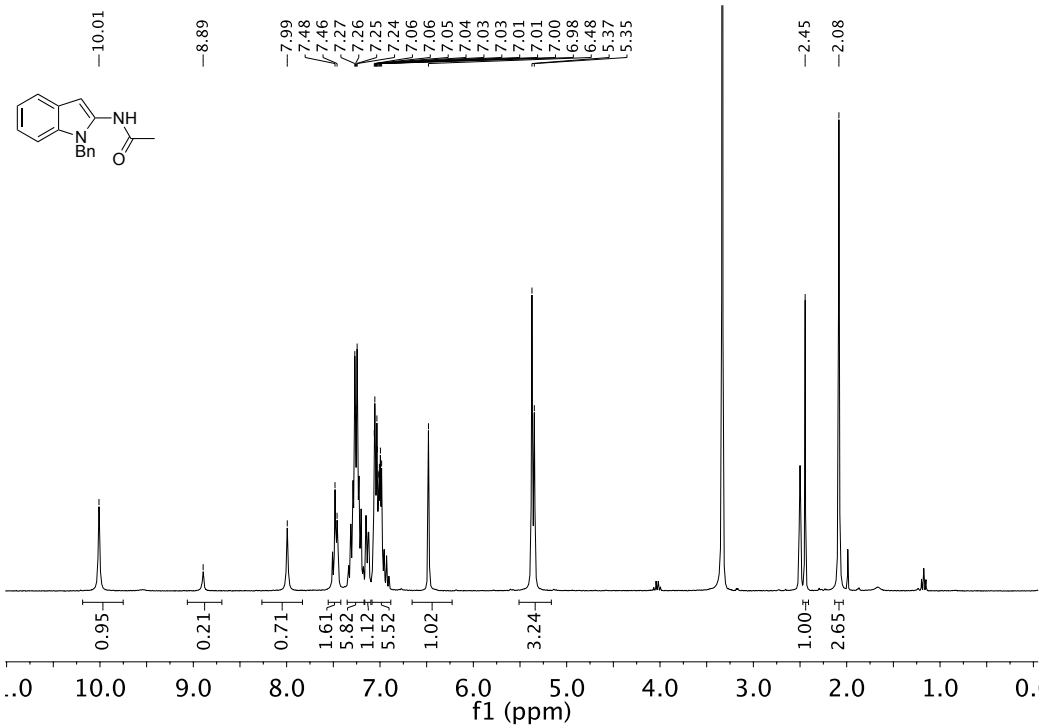


Figure S85. [1]H NMR spectrum of compound **2k** in d_6-DMSO solution (300 MHz).

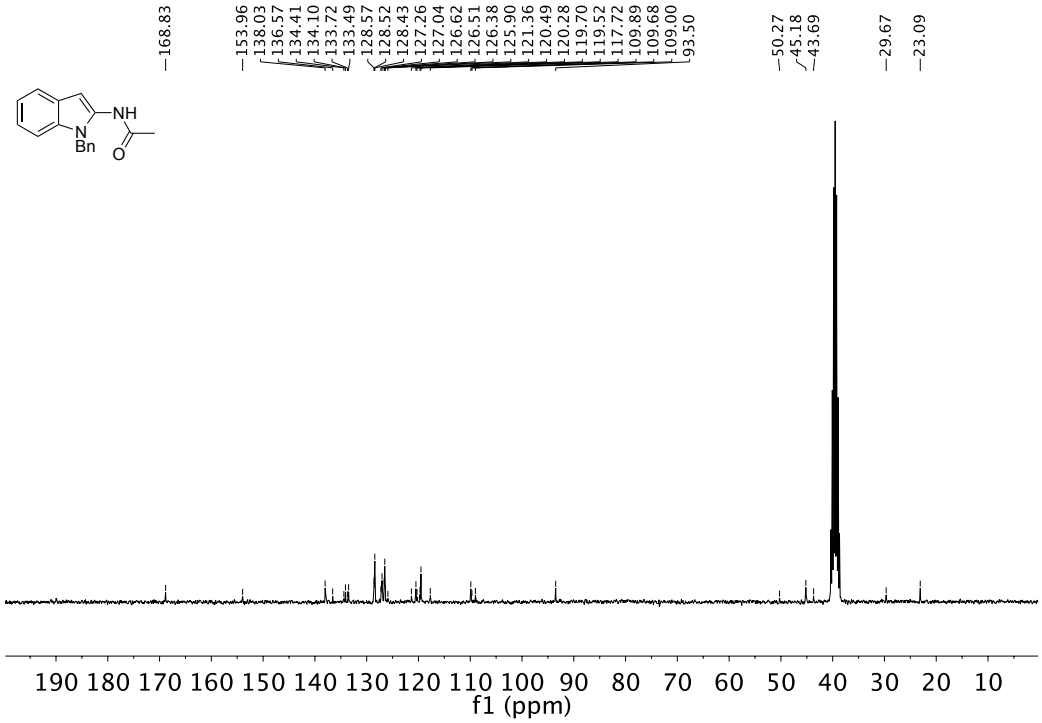


Figure S86. [13]C NMR spectrum of compound **2k** in d_6-DMSO solution (75 MHz).

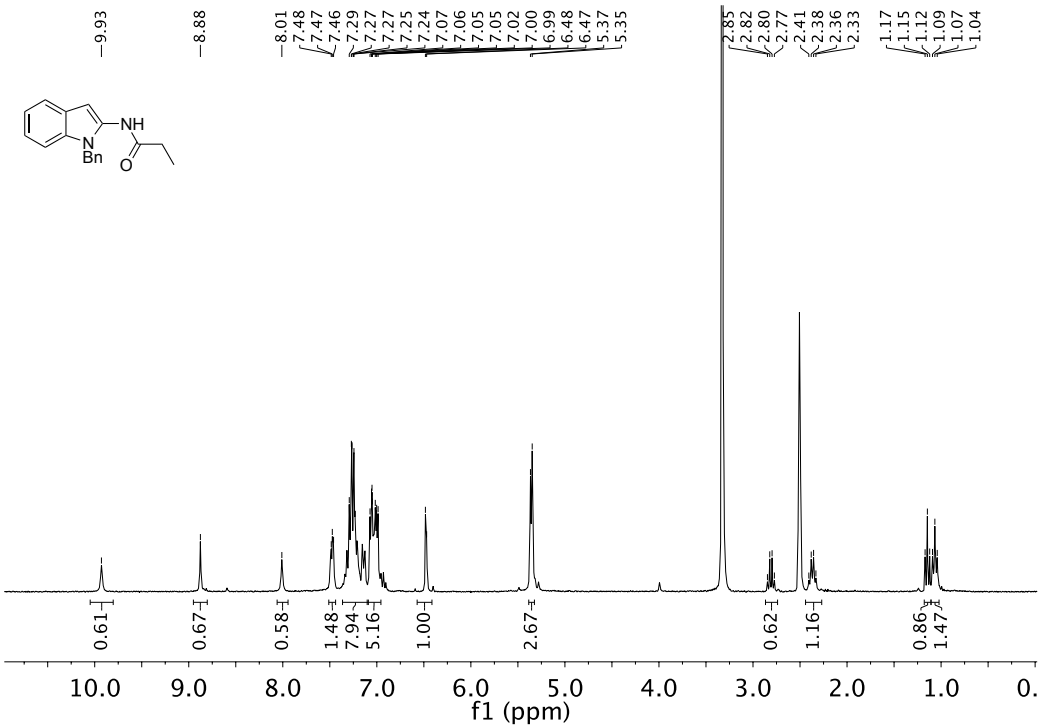


Figure S87. [1]H NMR spectrum of compound **2l** in d_6-DMSO solution (300 MHz).

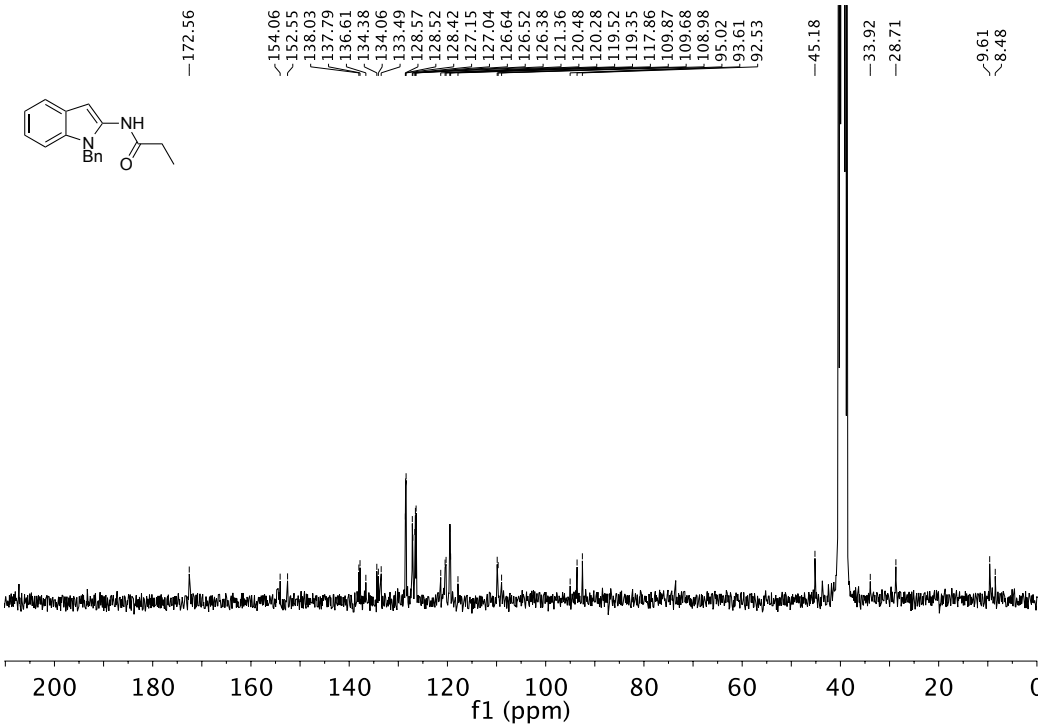


Figure S88. [13]C NMR spectrum of compound **2l** in d_6-DMSO solution (75 MHz).

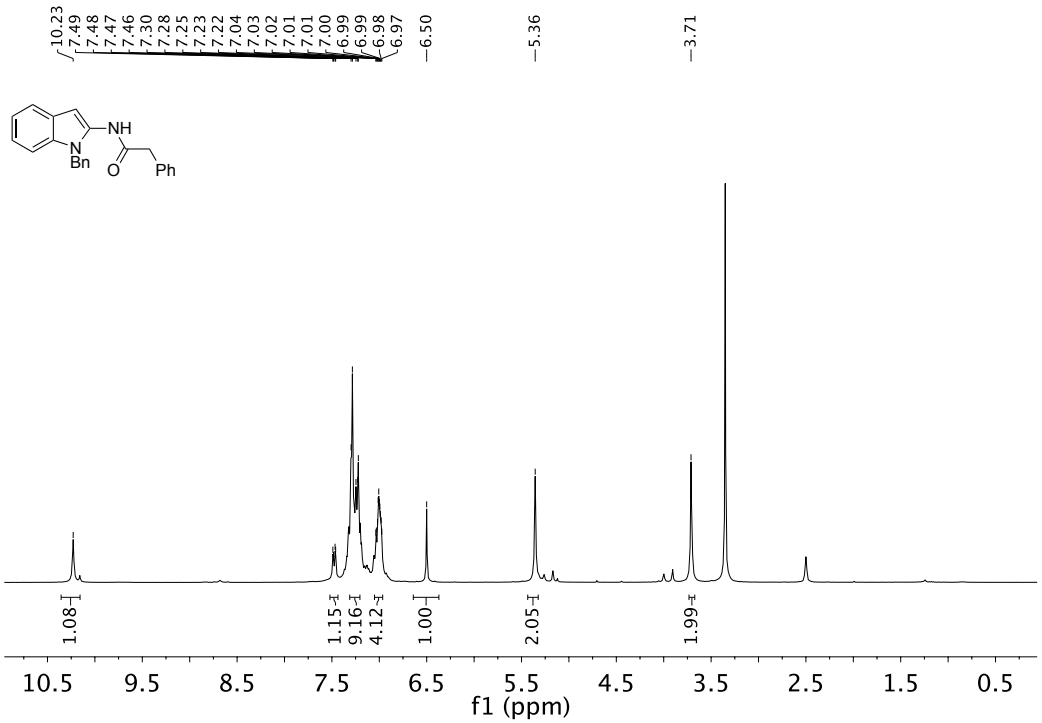


Figure S89. ^{1}H NMR spectrum of compound **2m** in d_6-DMSO solution (300 MHz).

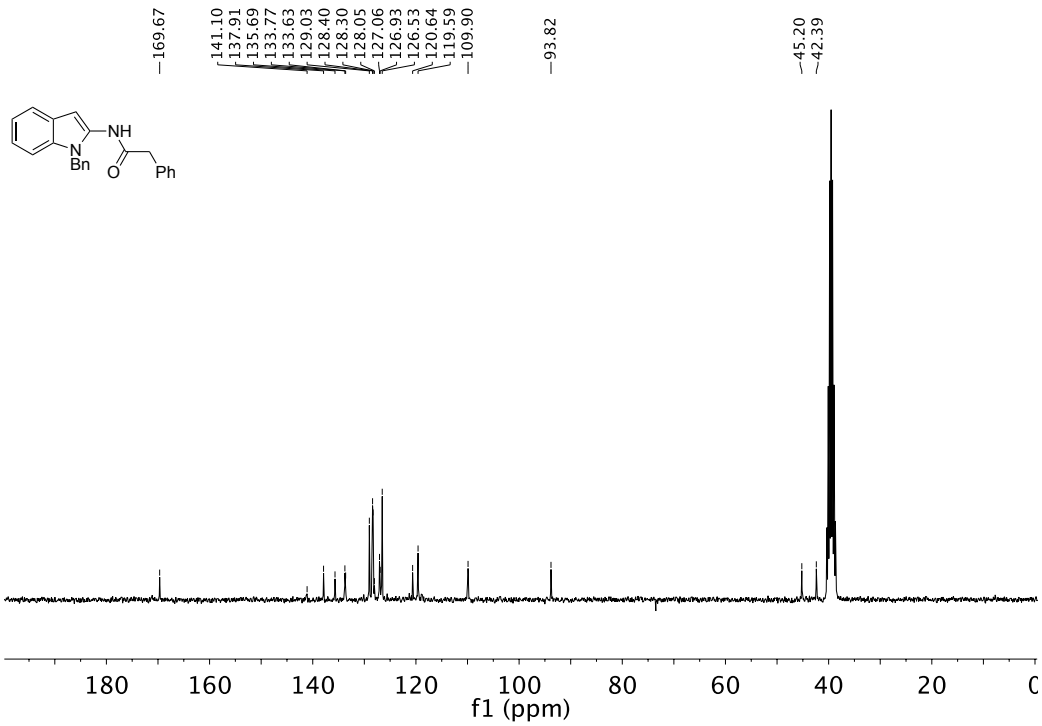


Figure S90. ^{13}C NMR spectrum of compound **2m** in d_6-DMSO solution (75 MHz).

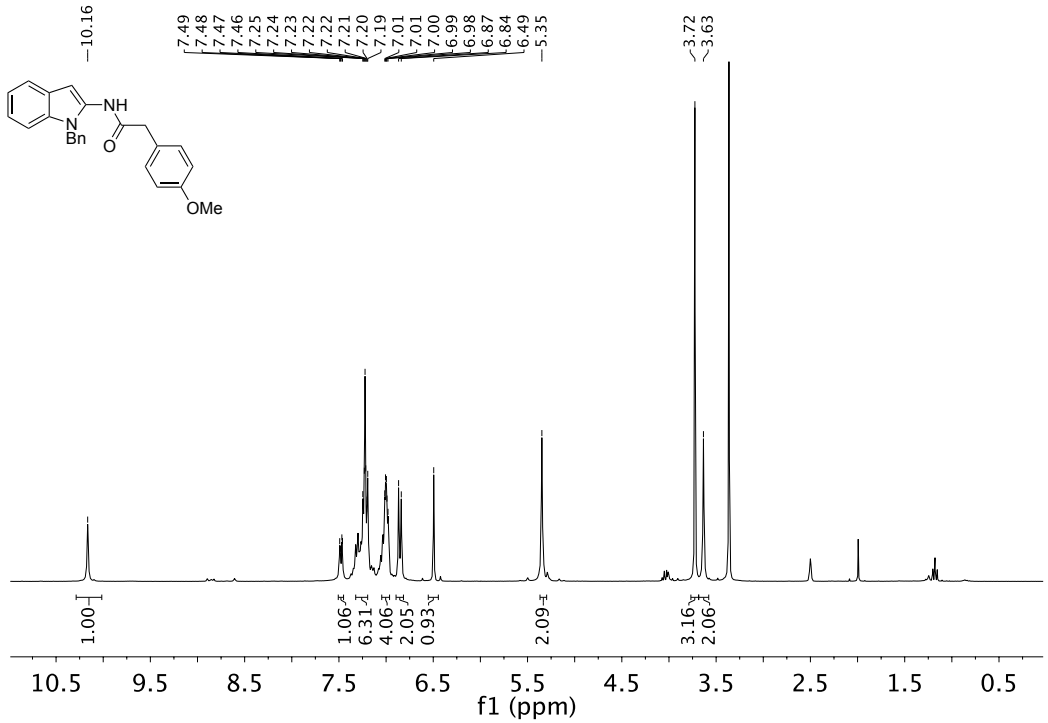


Figure S91. [1]H NMR spectrum of compound **2n** in d_6-DMSO solution (300 MHz).

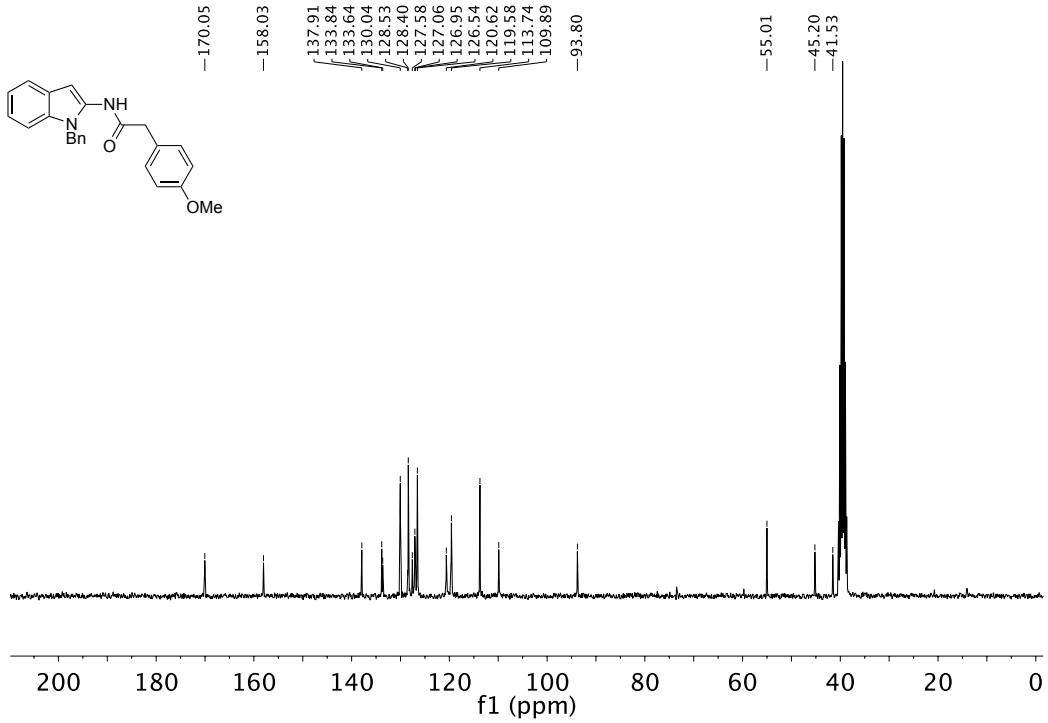


Figure S92. [13]C NMR spectrum of compound **2n** in d_6-DMSO solution (75 MHz).

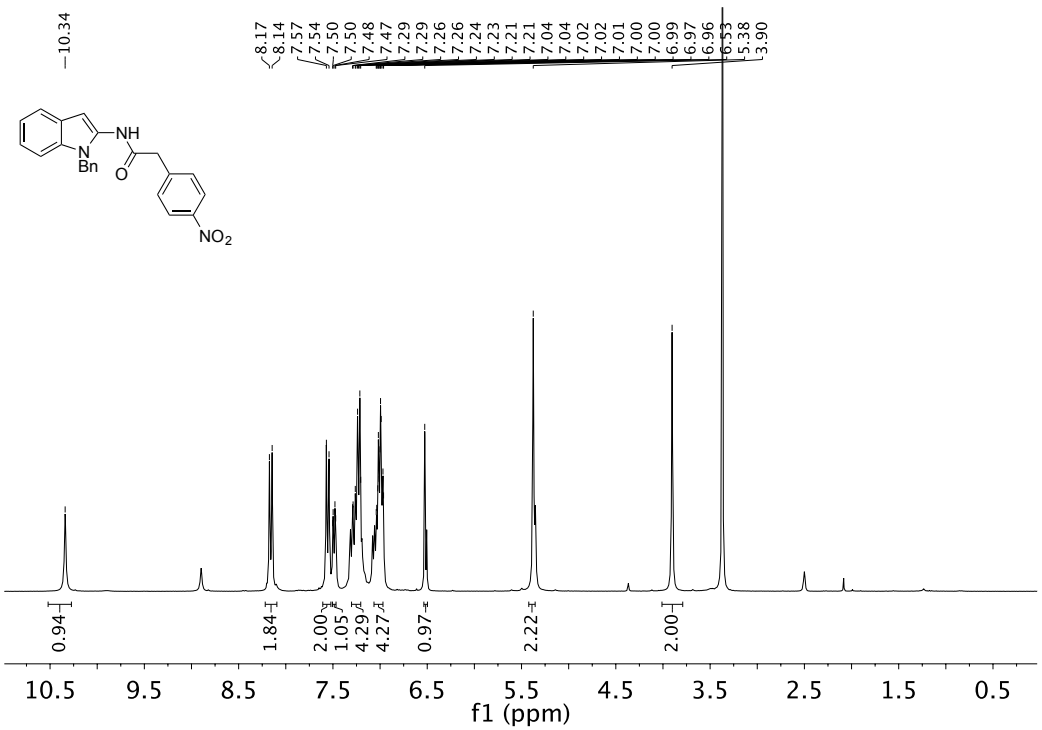


Figure S93. [1]H NMR spectrum of compound **2o** in d_6-DMSO solution (300 MHz).

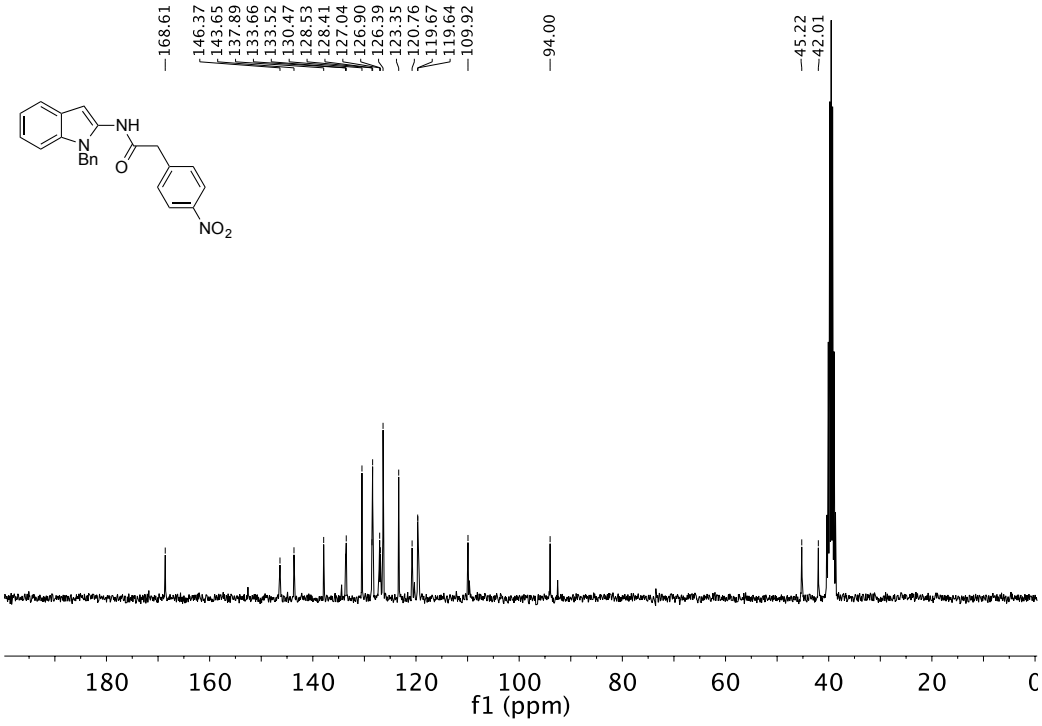


Figure S94. [13]C NMR spectrum of compound **2o** in d_6-DMSO solution (75 MHz).

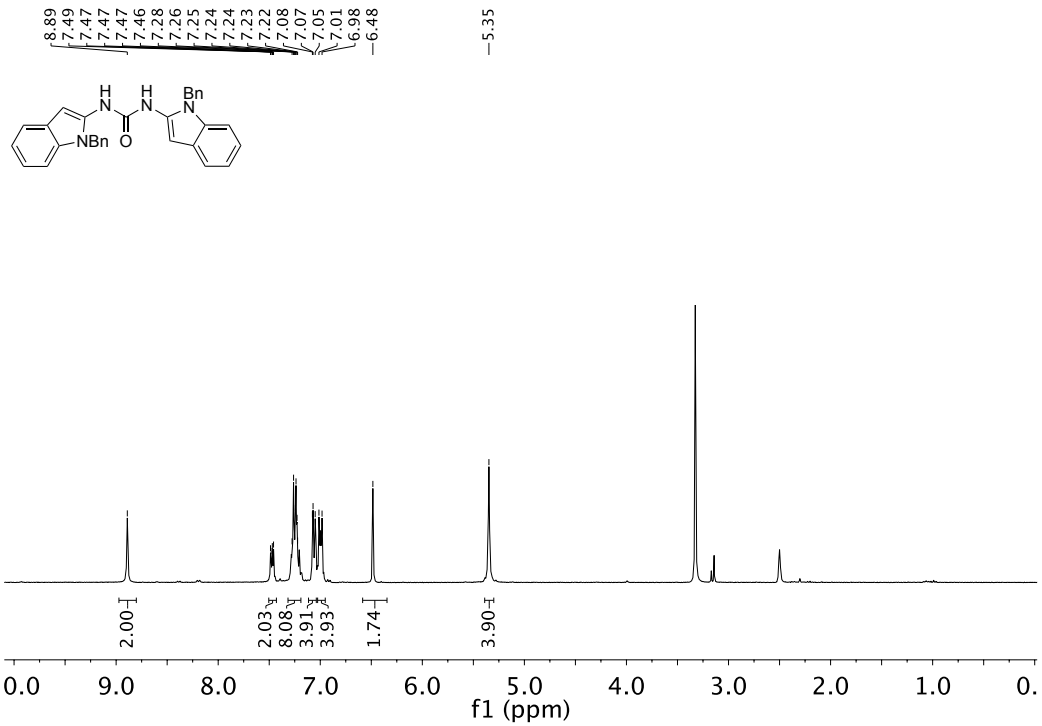


Figure S95. [1]H NMR spectrum of compound **S1** in d_6-DMSO solution (300 MHz).

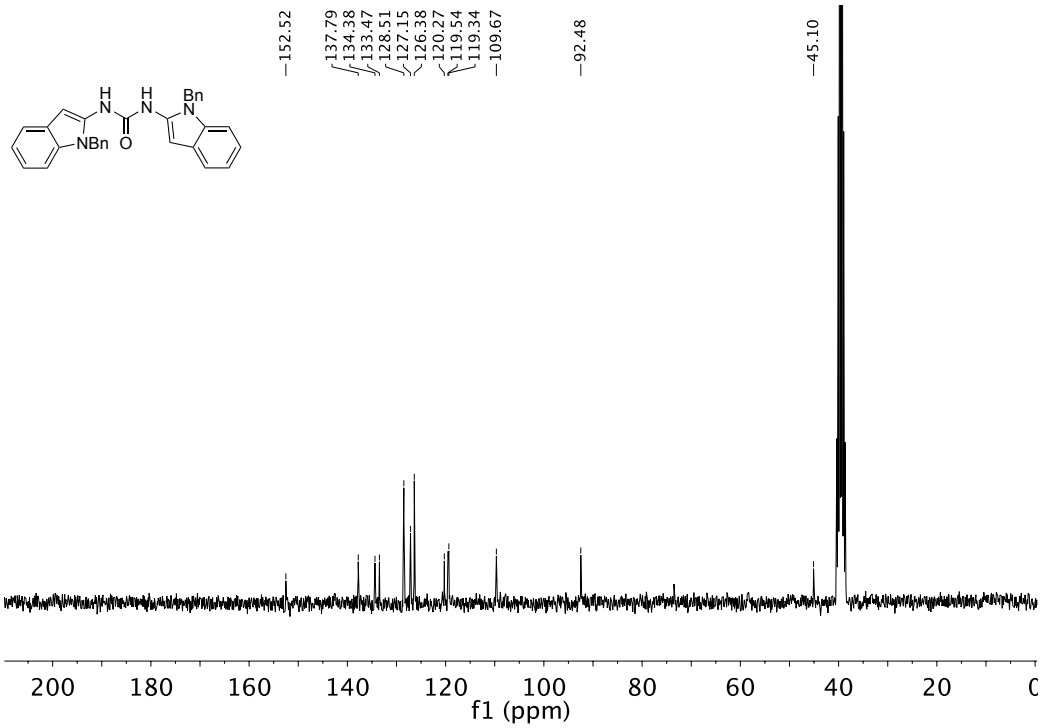


Figure S96. [13]C NMR spectrum of compound **S1** in d_6-DMSO solution (75 MHz).

S6. References

(1) Dolomanov, O. V.; Bourhis, L. J.; Gildea, R. J.; Howard, J. A. K.; Puschmann, H. *J. Appl. Crystallogr.* **2009**, *42*, 339–341.

(2) Sheldrick, G. M. *Acta Cryst.* **2008**, *A64*, 112–122.