Electronic Supplementary Material (ESI) for Chemical Communications.

Synthesis of Pyrimido[2,1-*a*]isoindolone and Isoindolo[2,1-*a*]quinazolinone *via* Intramolecular Aza-Prins Type Reaction

Subhamoy Biswas, Bikoshita Porashar, Pallav Jyoti Arandhara and Anil K. Saikia

Department of Chemistry, Indian Institute of Technology Guwahati, Guwahati-781039, Assam, India

Table of content

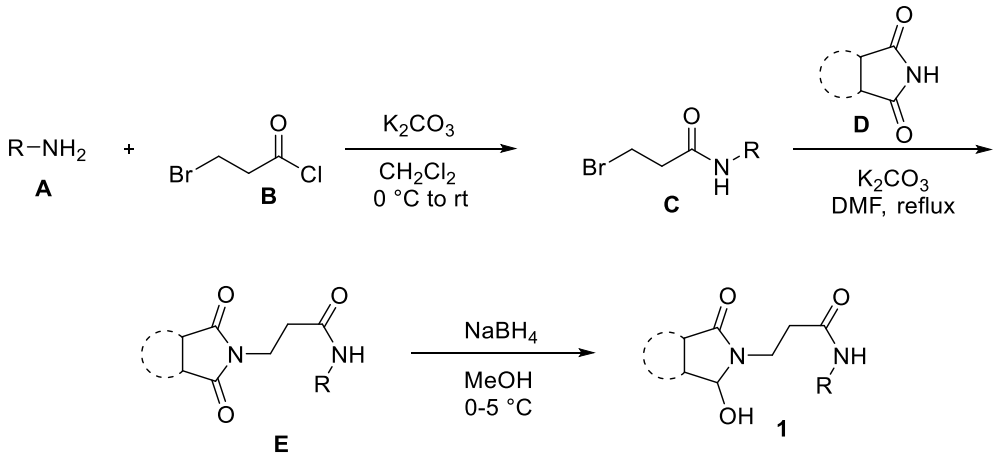
Experimental section:

General information:

All the reagents were of reagent grade (AR grade) and were used as purchased without further purification. Silica gel (60-120 mesh size) was used for column chromatography. Reactions were monitored by TLC on silica gel GF254 (0.25 mm). Melting points were recorded in an open capillary tube and are uncorrected. Fourier transform-infra red (FT-IR) spectra were recorded as neat liquid or KBr pellets. NMR spectra were recorded in $CDCl_3$ with tetramethylsilane as the internal standard for ^1H (600, 500, and 400 MHz) or ^{13}C (150, 125, and 100 MHz) NMR. Chemical shifts (δ) are reported in ppm and spin-spin coupling constants (*J*) are given in Hz. HRMS spectra were recorded using Q-TOF mass spectrometer.

General experimental procedure and characterization data of the compounds (1a-1u):[1]

Schematic representation of starting materials **1a-1u**:



To an ice-cold suspension of substituted amine **A** (5.0 mmol, 1.0 equiv.) and K_2CO_3 (1.3 equiv.) in DCM under N_2 atmosphere, 3-bromopropanoyl chloride (**B**) (1.2 equiv.) was added dropwise. The reaction mixture was allowed to stir at 0 °C for 5 minutes, which was then warmed to room temperature. The progress of the reaction was monitored by TLC analysis. After completion of the

reaction, the reaction mixture was quenched with saturated $NaHCO_3$ solution and the organic layer was extracted with dichloromethane (2 x 15 mL). The combined organic layers were further washed with brine, followed by drying over anhydrous Na_2SO_4. The organic phase was concentrated in a rotary evaporator to give the crude product, which was then subjected to column chromatography over silica gel to provide the desired product **C**.

To a stirred suspension of imide **D** (1.2 equiv.) and K_2CO_3 (1.5 equiv.) in DMF under N_2 atmosphere, *N*-substituted bromo anilide **C** (3.0 mmol, 1.0 equiv.) dissolved in DMF was added. The reaction was then refluxed until the starting material was fully consumed, monitored by TLC analysis. The reaction mixture was diluted with ice-cold water and the organic layer was extracted with ethyl acetate (20 mL). The organic layer was further washed with brine (2 x 20 mL), followed by drying over anhydrous Na_2SO_4. The organic phase was concentrated in a rotary evaporator to give the crude product, which was then subjected to column chromatography over silica gel to provide the desired product **E**.

To an ice-cold solution of imide substituted *N*-alkyl/aryl propanamide **E** (1.0 mmol, 1.0 equiv.) in methanol, $NaBH_4$ (1.5 equiv.) was added. The reaction was allowed to stir at the same temperature (0 °C) until the starting material was entirely consumed as evident by TLC analysis. After completion of the reaction, the solvent was removed under reduced pressure and diluted with saturated $NaHCO_3$ solution. The organic layer was extracted with dichloromethane (2 x 20 mL), and the combined organic layers were further washed with brine, followed by drying over anhydrous Na_2SO_4. The organic phase was concentrated in a rotary evaporator to give the crude product, which was then subjected to column chromatography over silica gel to provide the desired product **1**.

3-(1-Hydroxy-3-oxoisoindolin-2-yl)-*N*-phenylpropanamide (1a):

White solid; R_f (Hexane:EtOAc, 1:4) 0.50; mp 176-178 ºC. Yield 253 mg, 85%; ^{1}H NMR (400 MHz, $CDCl_3$/DMSO-d_6) δ 2.46-2.90 (m, 2 H), 3.91-3.99 (m, 2 H), 5.89 (s, 1 H), 6.12 (s, 1 H), 7.06 (t, *J* = 7.2 Hz, 1 H), 7.28-7.33 (m, 2 H), 7.46 (t, *J* = 7.2 Hz, 1 H), 7.53-7.60 (m, 4 H), 7.74 (d, *J* = 7.2 Hz, 1 H), 9.22 (brs, 1 H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d6) δ 35.8, 36.4, 82.2, 119.9, 122.7, 123.2, 123.8, 128.6, 129.2, 131.6, 131.9, 138.3, 144.3, 167.6, 170.2; IR (KBr, neat) 3251, 1661, 1543, 1316, 1193, 1064, 743 cm^{-1}; HRMS (ESI) calcd. for $C_{17}H_{16}N_2NaO_3$ $(M + Na)^+$ 319.1053, found 319.1053.

3-(1-Hydroxy-3-oxoisoindolin-2-yl)-*N*-(*p*-tolyl)propanamide (1b):

White solid; R_f (Hexane EtOAc, 1:4) 0.50; mp 189-191 ºC. Yield 220 mg, 71%; ^{1}H NMR (400 MHz, $CDCl_3$/MeOH-d_4) δ 2.26 (s, 3 H), 2.71-2.74 (m, 4 H), 3.80-3.88 (m, 2 H), 5.85 (s, 1 H), 7.07 (t, *J* = 7.2 Hz, 2 H), 7.36-7.38 (m, 2 H), 7.43-7.46 (m, 1 H), 7.52-7.55 (m, 2 H), 7.70 (d, *J* = 7.2 Hz, 1 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$/MeOH-d_4) δ 20.8, 36.4 (2C), 82.2, 120.1, 120.2, 122.9, 123.4, 129.4, 129.6, 131.3, 132.4, 134.1, 135.2, 144.0, 168.5, 170.4; IR (KBr, neat) 3395, 1687, 1653, 1543, 1302, 1116, 1065, 747 cm^{-1}; HRMS (ESI) calcd. for $C_{18}H_{19}N_2O_3$ $(M + H)^+$ 311.1390, found 311.1389.

***N*-(4-fluorophenyl)-3-(1-hydroxy-3-oxoisoindolin-2-yl)propanamide (1c):**

White solid; R_f (Hexane:EtOAc, 1:4) 0.50; mp 182-184 ºC. Yield 198 mg, 63%; ^{1}H NMR (600 MHz, $CDCl_3$/MeOH-d_4) δ 2.72-2.75 (m, 2 H), 3.79-3.89 (m, 2 H), 5.85 (s, 1 H), 6.94-6.97 (m, 2 H), 7.45-7.48 (m, 3 H), 7.54-7.55 (m, 2 H), 7.69 (d, *J* = 7.2 Hz, 1 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$/MeOH-d_4) δ 36.2, 36.4, 82.2, 115.4 (d, *J* = 22.2 Hz), 121.7, 121.8, 122.9, 123.4, 129.6, 132.4, 133.9 (d, *J* = 2.8 Hz), 144.0, 159.3 (d, *J* = 241.9 Hz), 168.5, 170.4; ^{19}F NMR (564 MHz, $CDCl_3$/MeOH-d_4/C_6F_6) δ -121.09 (m, -CF-); IR (KBr, neat) 3249, 2936, 1659, 1618, 1504, 1381,

1209, 1062, 784 cm^{-1}; HRMS (ESI) calcd. for $C_{17}H_{15}FN_2NaO_3$ $(M + Na)^+$ 337.0959, found 337.0959.

***N*-benzyl-3-(1-hydroxy-3-oxoisoindolin-2-yl)propanamide (1d):**

White solid; R_f (EtOAc, 100%) 0.50; mp 158-160 °C. Yield 248 mg, 80%; ^1H NMR (400 MHz, $CDCl_3$) δ 2.59-2.74 (m, 2 H), 3.75-3.90 (m, 2 H), 4.28-4.40 (m, 2 H), 5.80-5.85 (m, 2 H), 6.91 (t, *J* = 5.8 Hz, 1 H), 7.16-7.22 (m, 5 H), 7.39-7.45 (m, 1 H), 7.51-7.56 (m, 2 H), 7.59 (d, *J* = 7.4 Hz, 1 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 35.3, 36.2, 43.8, 82.7, 123.0, 123.4, 127.5, 127.8, 128.7, 129.5, 131.4, 132.3, 137.7, 144.1, 168.1, 172.2; IR (KBr, neat) 3286, 2934, 1673, 1632, 1413, 1386, 1047, 747 cm^{-1}; HRMS (ESI) calcd. for $C_{18}H_{19}N_2O_3$ $(M + H)^+$ 311.1390, found 311.1389.

3-(1-Hydroxy-3-oxoisoindolin-2-yl)-*N*-(4-methylbenzyl)propanamide (1e):

White solid; R_f (EtOAc, 100%) 0.50; mp 157-159 °C. Yield 247 mg, 76%; ^1H NMR (400 MHz, $CDCl_3$) δ 2.25 (s, 3 H), 2.63 (t, *J* = 6.4 Hz, 2 H), 3.71-3.85 (m, 2 H), 4.18-4.30 (m, 2 H), 5.78(s, 1 H), 6.23 (brs, 1 H), 6.97 (d, *J* = 7.8 Hz, 2 H), 7.02 (d, *J* = 7.8 Hz, 2 H), 7.22-7.28 (m, 1 H), 7.35-7.39 (m, 1 H), 7.49-7.52 (m, 3 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 21.1, 35.2, 36.2, 43.5, 82.6, 123.0, 123.4, 127.8, 129.3, 129.4, 131.4, 132.2, 134.7, 137.1, 144.1, 168.1, 172.1; IR (KBr, neat) 3338, 2856, 1670, 1634, 1546, 1385, 1051, 745 cm^{-1}; HRMS (ESI) calcd. for $C_{19}H_{20}N_2NaO_3$ $(M + Na)^+$ 347.1366, found 347.1377.

***N*-(4-chlorobenzyl)-3-(1-hydroxy-3-oxoisoindolin-2-yl)propanamide (1f):**

White solid; R_f (EtOAc, 100%) 0.60; mp 147-149 °C. Yield 241 mg, 70%; ^1H NMR (400 MHz, $CDCl_3$) δ 2.61-2.75 (m, 2 H), 3.74-3.80 (m, 1 H), 3.83-3.90 (m, 1 H), 4.22-4.34 (m, 2 H), 5.69 (d, *J* = 6.2 Hz, 1 H), 5.78 (d, *J* = 6.2 Hz, 1 H), 7.07-7.10 (m, 3 H), 7.13-7.16 (m, 2 H), 7.41-7.46 (m, 1 H), 7.52-7.57 (m, 3 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 35.3, 36.3, 43.0, 82.8, 122.9, 123.4, 128.8, 129.1, 129.6, 131.3, 132.4, 133.3, 136.4, 144.0, 168.2, 172.3; IR (KBr, neat) 3393, 2944,

1688, 1621, 1571, 1062, 746 cm^{-1}; HRMS (ESI) calcd. for $C_{18}H_{17}ClN_2NaO_3$ $(M + Na)^+$ 367.0820, found 367.0825.

3-(1-Hydroxy-3-oxoisoindolin-2-yl)-*N*-(1-phenylethyl)propanamide (diastereomeric mixture , 1:1, 1g):

White solid; R_f (Hexane:EtOAc, 1:4) 0.40; mp 148-150 ^oC. Yield 266 mg, 82%; ^1H NMR (400 MHz, $CDCl_3$) δ 1.38 (d, *J* = 7.0 Hz, 3 H), 1.40 (d, *J* = 7.0 Hz, 3 H), 2.58-2.63 (m, 2 H), 3.70-3.83 (m, 2 H), 4.94-5.04 (m, 1 H), 5.65 (d, *J* = 5.2 Hz, 1 H), 5.82 (d, *J* = 5.6 Hz, 1 H), 6.08 (brs, 1 H), 7.14-7.24 (m, 5 H), 7.38-7.43 (m, 1 H), 7.46-7.50 (m, 2 H), 7.52-7.62 (m, 1 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 21.7, 21.8, 35.3, 34.0, 36.1, 49.1, 49.2, 82.4, 82.6, 122.8, 122.9, 123.3, 123.4, 126.0, 126.1, 127.1, 127.2, 128.4, 128.5, 129.4, 129.5, 132.2, 143.0, 143.2, 144.1, 168.0, 168.1, 171.1, 171.2; IR (KBr, neat) 3292, 2881, 1681, 1641, 1067, 744 cm^{-1}; HRMS (ESI) calcd. for $C_{19}H_{21}N_2O_3$ $(M + H)^+$ 325.1547, found 325.1546.

***N*-butyl-3-(1-hydroxy-3-oxoisoindolin-2-yl)propanamide (1h):**

White semi solid; R_f (EtOAc, 100%) 0.60; Yield 260 mg, 94%; ^1H NMR (600 MHz, $CDCl_3$) δ 0.84 (t, *J* = 7.4 Hz, 3 H), 1.22-1.28 (m, 2 H), 1.38-1.43 (m, 2 H), 2.58-2.69 (m, 2 H), 3.11-3.19 (m, 2 H), 3.77-3.82 (m, 1 H), 3.84-3.88 (m, 1 H), 5.86 (d, *J* = 6.4 Hz, 1 H), 6.25 (d, *J* = 6.6 Hz, 1 H), 6.71 (t, *J* = 5.6 Hz, 1 H), 7.42 (t, *J* = 7.4 Hz, 1 H), 7.52 (t, *J* = 7.4 Hz, 1 H), 7.55 (d, *J* = 7.4 Hz, 1 H), 7.65 (t, *J* = 7.4 Hz, 1 H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 13.7, 20.0, 31.3, 35.3, 36.2, 39.5, 82.6, 122.9, 123.4, 129.5, 131.4, 132.3, 144.1, 168.1, 172.1; IR (KBr, neat) 3303, 2932, 1683, 1636, 1462, 1208, 1054, 737 cm^{-1}; HRMS (ESI) calcd. for $C_{15}H_{21}N_2O_3$ $(M + H)^+$ 277.1547, found 277.1547.

3-(1-Hydroxy-3-oxoisoindolin-2-yl)-*N*-octylpropanamide (1i):

White semi solid; R_f (EtOAc, 100%) 0.60; Yield 249 mg, 75%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.86 (t, *J* = 7.0 Hz, 3 H), 1.20-1.25 (m, 10 H), 1.40-1.43 (m, 2 H), 2.59-2.63 (m, 1 H), 2.65-2.68 (m, 1 H), 3.14-3.19 (m, 2 H), 3.78-3.90 (m, 2 H), 5.86 (d, *J* = 6.2 Hz, 1 H), 6.01 (d, *J* = 6.8 Hz, 1 H), 6.47 (brs, 1 H), 7.44 (t, *J* = 7.2 Hz, 1 H), 7.52-7.59 (m, 2 H), 7.68 (d, *J* = 7.2 Hz, 1 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 14.1, 22.6, 26.9, 29.1, 29.2, 29.3, 31.8, 35.4, 36.1, 39.9, 82.6, 123.0, 123.4, 129.5, 131.5, 132.3, 144.1, 168.1, 172.3; IR (KBr, neat) 3258, 2856, 1660, 1629, 1449, 1061, 738 cm^{-1}; HRMS (ESI) calcd. for $C_{19}H_{29}N_2O_3$ $(M + H)^+$ 333.2173, found 333.2174.

3-(1-Hydroxy-3-oxoisoindolin-2-yl)-*N*-isopropylpropanamide (1j):

White solid; R_f (EtOAc, 100%) 0.40; mp 127-129 ºC. Yield 236 mg, 90%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.07 (d, *J* = 7.4 Hz, 3 H), 1.08 (d, *J* = 7.4 Hz, 3 H), 2.55-2.66 (m, 2 H), 3.76-3.81 (m, 1 H), 3.83-3.88 (m, 1 H), 3.93-3.99 (m, 1 H), 5.86 (d, *J* = 6.2 Hz, 1 H), 6.22-6.32 (m, 1 H), 6.45-6.58 (m, 1 H), 7.44 (t, *J* = 7.2 Hz, 1 H), 7.45-7.58 (m, 2 H), 7.64-7.68 (m, 1 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 22.5, 22.51, 35.5, 36.0, 41.8, 82.7, 123.0, 123.4, 129.5, 131.5, 132.3, 144.0, 168.1, 171.5; IR (KBr, neat) 3295, 2872, 1680, 1642, 1549, 1057, 751 cm^{-1}; HRMS (ESI) calcd. for $C_{14}H_{19}N_2O_3$ $(M + H)^+$ 263.1390, found 263.1384.

***N*-cyclopropyl-3-(1-hydroxy-3-oxoisoindolin-2-yl)propanamide (1k):**

White semi solid; R_f (EtOAc, 100%) 0.40; Yield 184 mg, 71%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.45-0.47 (m, 2 H), 0.67-0.69 (m, 2 H), 2.58-2.63 (m, 3 H), 3.74-3.78 (m, 1 H), 3.82-3.88 (m, 1 H), 5.86 (d, *J* = 6.0 Hz, 1 H), 6.24-6.26 (m, 1 H), 7.08-7.15 (m, 1 H), 7.42 (t, *J* = 7.4 Hz, 1 H), 7.51-7.53 (m, 1 H), 7.56 (d, *J* = 7.4 Hz, 1 H), 7.62-7.64 (m, 1 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 6.3, 6.4, 22.8, 35.3, 36.1, 82.7, 123.0, 123.4, 129.6, 131.4, 132.4, 144.1, 168.2, 173.9; IR (KBr,

neat) 3255, 2857, 1673, 1638, 1454, 1020, 741cm^{-1}; HRMS (ESI) calcd. for $C_{14}H_{17}N_2O_3$ $(M + H)^+$ 261.1234, found 261.1235.

***N*-cyclohexyl-3-(1-hydroxy-3-oxoisoindolin-2-yl)propanamide (1l):**

White solid; R_f (EtOAc, 100%) 0.60; mp 158-160 ^{o}C. Yield 189 mg, 63%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.06-1.13 (m, 3 H), 1.23-1.29 (m, 2 H), 1.54-1.58 (m, 1 H), 1.62-1.68 (m, 2 H), 1.76-1.82 (m, 2 H), 2.53-2.67 (m, 2 H), 3.60-3.69 (m, 1 H), 3.74-3.88 (m, 2 H), 5.85 (d, *J* = 5.8 Hz, 1 H), 6.27-6.31 (m, 1 H), 6.53-7.59 (m, 1 H), 7.41 (t, *J* = 7.2 Hz, 1 H), 7.44-7.56 (m, 2 H), 7.65 (d, *J* = 7.2 Hz, 1 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 24.8, 25.4, 32.8, 35.5, 36.1, 48.6, 82.5, 122.9, 123.4, 129.4, 131.4, 132.2, 144.1, 168.1, 171.2; IR (KBr, neat) 3280, 2927, 1671, 1838, 1550, 1059, 742 cm^{-1}; HRMS (ESI) calcd. for $C_{17}H_{23}N_2O_3$ $(M + H)^+$ 303.1703, found 303.1708.

3-(2-Hydroxy-5-oxopyrrolidin-1-yl)-*N*-phenylpropanamide (1m):

White solid; R_f (CH_2Cl_2:MeOH, 23:2) 0.40; mp 79-81 ^{o}C. Yield 144 mg, 58%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.89-1.93 (m, 1 H), 2.24-2.30 (m, 2 H), 2.55-2.61 (m, 1 H), 2.68-2.73 (m, 1 H), 2.79-2.85 (m, 1 H), 3.58-3.63 (m, 1 H), 3.71-3.77 (m, 1 H), 5.29 (d, *J* = 5.6 Hz, 1 H), 5.55 (brs, 1 H), 7.08 (t, *J* = 8.2 Hz, 1 H), 7.27 (d, *J* = 8.4 Hz, 2 H), 7.52 (d, *J* = 8.4 Hz, 2 H), 9.08 (brs, 1 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 27.9, 29.3, 35.8, 37.1, 84.6, 120.2, 124.5, 127.8, 128.9, 129.7, 137.8, 171.0, 176.0; IR (KBr, neat) 3280, 2927, 1671, 1638, 1550, 1059, 742 cm^{-1}; HRMS (ESI) calcd. for $C_{13}H_{17}N_2O_3$ $(M + H)^+$ 249.1234, found 249.1229.

3-(2-Hydroxy-5-oxopyrrolidin-1-yl)-*N*-(4-methylbenzyl)propanamide (1n):

White solid; R_f (CH_2Cl_2:MeOH, 23:2) 0.50; mp 113-115 ^{o}C. Yield 169 mg, 61%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.85-1.92 (m, 1 H), 2.16-2.24 (m, 2 H), 2.32 (s, 3 H), 2.44-2.57 (m, 2 H), 2.64-2.72 (m, 1 H), 3.48-3.56 (m, 1 H), 3.64-3.69 (m, 1 H), 4.29-4.41 (m, 2 H), 5.21 (d, *J* = 5.2 Hz, 1

H), 5.49 (brs, 1 H), 6.52 (brs, 1 H), 7.10-7.15 (m, 4 H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 21.1, 27.8, 29.2, 34.7, 37.1, 43.6, 84.5, 127.9, 129.4, 134.6, 137.5, 172.6, 175.6; IR (KBr, neat) 3292, 2852, 1652, 1157, 1070, 752 cm^{-1}; HRMS (ESI) calcd. for $C_{15}H_{20}N_2NaO_3$ $(M + Na)^+$ 299.1366, found 299.1366.

3-(1-Hydroxy-3-oxoisoindolin-2-yl)-*N*-phenethylpropanamide (1o):

White solid; R_f (EtOAc, 100%) 0.40; mp 138-140 °C. Yield 190 mg, 59%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.52-2.65 (m, 2 H), 2.75 (t, *J* = 7.2 Hz, 2 H), 3.41-3.47 (m, 2 H), 3.74-3.79 (m, 1 H), 3.80-3.85 (m, 1 H), 5.82 (d, *J* = 6.6 Hz, 1 H), 6.08 (brs, 1 H), 6.69 (brs, 1 H), 7.11 (d, *J* = 7.5 Hz, 2 H), 7.14 (d, *J* = 7.2 Hz, 1 H), 7.21 (t, *J* = 7.5 Hz, 2 H), 7.44 (t, *J* = 7.2 Hz, 1 H), 7.51-7.57 (m, 2 H), 7.65 (d, *J* = 7.5 Hz, 1 H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 35.3, 35.4, 36.1, 40.9, 82.6, 123.0, 123.4, 126.5, 128.6, 128.7, 129.5, 131.4, 132.3, 138.6, 144.1, 168.1, 172.3; IR (KBr, neat) 3293, 2867, 1676, 1646, 1550, 1055, 748 cm^{-1}; HRMS (ESI) calcd. for $C_{19}H_{21}N_2O_3$ $(M + H)^+$ 325.1547, found 325.1548.

***N*-benzyl-3-(1-hydroxy-3-oxo-3*a*,4,7,7*a*-tetrahydro-1*H*-isoindol-2(3*H*)-yl)propanamide (1p):**

White semi solid; R_f (EtOAc, 100%) 0.40; Yield 188 mg, 57%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.69-1.76 (m, 1 H), 1.90-1.98 (m, 1 H), 2.14-2.30 (m, 2 H), 2.32 (s, 3 H), 2.33-2.38 (m, 1 H), 2.42-2.49 (m, 1 H), 2.64-2.71 (m, 1 H), 2.89-2.94 (m, 1 H), 3.43-3.50 (m, 1 H), 3.64-3.71 (m, 1 H), 4.28-4.39 (m, 2 H), 4.76 (t, *J* = 2.6 Hz, 1 H), 5.47 (brs, 1 H), 5.64-5.72 (m, 2 H), 6.68 (brs, 1 H), 7.09-7.13 (m, 4 H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 21.1, 21.9, 24.3, 34.7, 37.4, 37.7, 38.2, 43.6, 89.5, 125.2, 126.4, 127.9, 129.4, 134.6, 137.4, 172.6, 177.6; IR (KBr, neat) 3297, 2850, 1652, 1459, 1050, 740 cm^{-1}; HRMS (ESI) calcd. for $C_{19}H_{25}N_2O_3$ $(M + H)^+$ 329.1860, found 329.1858.

3-(1-Hydroxy-3-oxo-3*a*,4,7,7*a*-tetrahydro-1*H*-isoindol-2(3*H*)-yl)-*N*-phenylpropanamide (1q, diastereomeric mixture, 9:1; only major isomer is considered):

White semi solid; R_f (EtOAc, 100%) 0.50; Yield 188 mg, 63%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.74-1.82 (m, 1 H), 2.14-2.30 (m, 3 H), 2.38-2.44 (m, 1 H), 2.67-2.73 (m, 1 H), 2.82-2.89 (m, 1 H), 2.98-3.03 (m, 1 H), 3.54-3.61 (m, 1 H), 3.72-3.78 (m, 1 H), 4.84 (d, *J* = 6.0 Hz, 1 H), 5.43-5.56 (m, 1 H), 5.62-5.78 (m, 2 H), 7.09 (t, *J* = 7.2 Hz, 1 H), 7.28 (t, *J* = 7.2 Hz, 2 H), 7.51 (d, *J* = 8.0 Hz, 2 H), 9.04 (brs, 1 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 22.0, 24.3, 35.8, 37.7, 37.72, 38.4, 89.7, 120.3, 124.6, 125.4, 126.2, 128.9, 137.8, 171.0, 178.1; IR (KBr, neat) 3301, 2850, 1667, 1601, 1545, 1038, 755 cm^{-1}; HRMS (ESI) calcd. for $C_{17}H_{20}N_2NaO_3$ $(M + Na)^+$ 323.1366, found 323.1366.

3-(1-Hydroxy-3-oxohexahydro-1*H*-isoindol-2(3*H*)-yl)-*N*-(4-methoxybenzyl)propanamide (1r, diastereomeric mixture, 9:1; only major isomer is considered):

White semi solid; R_f (EtOAc, 100%) 0.40; Yield 219 mg, 63%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.94-1.04 (m, 2 H), 1.16-1.19 (m, 1 H), 1.43-1.51 (m, 3 H), 1.72-1.75 (m, 1 H), 1.86-1.90 (m, 1 H), 2.16-2.18 (m, 1 H), 2.45-2.50 (m, 1 H), 2.64-2.70 (m, 1 H), 2.72-2.76 (m, 1 H), 3.41-3.46 (m, 1 H), 3.65-3.71 (m, 1 H), 3.76 (s, 3 H), 4.25-4.71 (m, 2 H), 4.71 (s, 1 H), 5.41 (s, 1 H), 6.82 (d, *J* = 6.5 Hz, 2 H), 6.91 (s, 1 H), 7.15 (d, *J* = 6.5 Hz, 2 H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 23.0, 23.1, 23.3, 26.2, 34.7, 38.0, 39.1, 41.0, 43.3, 55.3, 88.4, 114.1, 129.2, 130.0, 159.1, 172.6, 177.3; IR (KBr, neat) 3294, 2855, 1650, 1513, 1246, 1027, 745 cm^{-1}; HRMS (ESI) calcd. for $C_{19}H_{27}N_2O_4$ $(M + H)^+$ 347.1965, found 347.1974.

3-(1-Hydroxy-3-oxo-3*a*,4,7,7*a*-tetrahydro-1*H*-4,7-methanoisoindol-2(3*H*)-yl)-*N*-(4-methylbenzyl)propanamide (1s):

White solid; R_f (CH_2Cl_2:MeOH, 23:2) 0.40; mp 139-141 ^oC. Yield 248 mg, 73%; ^1H NMR (400 MHz, $CDCl_3$) δ 1.31 (d, *J* = 10.5 Hz, 1 H), 1.51 (d, *J* = 10.5 Hz, 1 H), 2.30 (s, 3 H), 2.36-2.41 (m, 1 H), 2.42-2.52 (m, 1 H), 2.59-2.63 (m, 1 H), 3.03-3.10 (m, 3 H), 3.32-3.39 (m, 1 H), 3.43-3.50 (m, 1 H), 4.29 (d, *J* = 5.6 Hz, 2 H), 4.55 (d, *J* = 4.8 Hz, 1 H), 5.68 (d, *J* = 5.0 Hz, 1 H), 5.93-5.98 (m, 2 H), 7.07-7.16 (m, 5 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 21.1, 34.6, 36.7, 43.4, 44.7, 44.8, 46.3, 49.3, 51.1, 85.8, 127.8, 129.3, 133.7, 134.9, 135.7, 137.2, 172.0, 176.3; IR (KBr, neat) 3289, 2887, 1651, 1546, 1057, 722 cm^{-1}; HRMS (ESI) calcd. for $C_{20}H_{25}N_2O_3$ $(M + H)^+$ 341.1860, found 341.1872.

***N*-(2-(1*H*-indol-3-yl)ethyl)-3-(1-hydroxy-3-oxoisoindolin-2-yl)propanamide (1t):**

Brown solid; R_f (EtOAc, 100%) 0.50; mp 68-70 ^oC. Yield 252 mg, 69%; ^1H NMR (600 MHz, $CDCl_3$) δ 2.44-2.49 (m, 1 H), 2.54-2.59 (m, 1 H), 2.90 (t, *J* = 6.8 Hz, 2 H), 3.48-3.57 (m, 2 H), 3.72-3.76 (m, 1 H), 3.80-3.84 (m, 1 H), 5.78 (brs, 1 H), 5.87 (brs, 1 H), 6.28 (t, *J* = 5.8 Hz, 1 H), 6.92 (d, *J* = 2.4 Hz, 1 H), 7.05 (t, *J* = 7.0 Hz, 1 H), 7.14 (t, *J* = 7.0 Hz, 1 H), 7.28 (d, *J* = 8.0 Hz, 1 H), 7.42 (t, *J* = 7.2 Hz, 1 H), 7.50-7.56 (m, 3 H), 7.66 (d, *J* = 7.2 Hz, 1 H), 8.25 (s, 1 H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 25.0, 35.3, 36.1, 39.9, 82.6, 111.3, 112.5, 118.6, 119.4, 122.1, 122.2, 123.0, 123.4, 127.2, 129.6, 131.4, 132.3, 136.3, 144.0, 168.0, 172.4; IR (KBr, neat) 3281, 2854, 1642, 1540, 1042, 740 cm^{-1}; HRMS (ESI) calcd. for $C_{21}H_{22}N_3O_3$ $(M + H)^+$ 364.1656, found 364.1655.

3-(1-Hydroxy-3-oxoisoindolin-2-yl)-*N*-(prop-2-yn-1-yl)propanamide (1u):

White solid; R_f (Hexane:EtOAc,1:4) 0.40; mp 146-147 ^oC. Yield 190 mg, 74%; ^1H NMR (400 MHz, $CDCl_3$/MeOH-d_4) δ 2.14 (t, *J* = 2.4 Hz, 1 H), 2.53-2.66 (m, 2 H), 2.89 (brs, 1 H), 3.73-3.83 (m, 2 H), 3.86-3.99 (m, 2 H), 5.81 (s, 1 H), 7.39-7.43 (m, 1 H), 7.49-7.54 (m, 2 H), 7.64-7.68 (m, 1 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$/MeOH-d_4) δ 29.0, 35.2, 36.3, 71.3, 79.1, 82.2, 122.9, 123.3, 129.5, 131.3, 132.3, 144.1, 168.3, 171.9; IR (KBr, neat) 3287, 2924, 1657, 1421, 1313, 1058, 745 cm^{-1}; HRMS (ESI) calcd. for $C_{14}H_{15}N_2O_3$ $(M + H)^+$ 259.1077, found 259.1077.

Experimental procedure and Characterization data of the compound 1v:

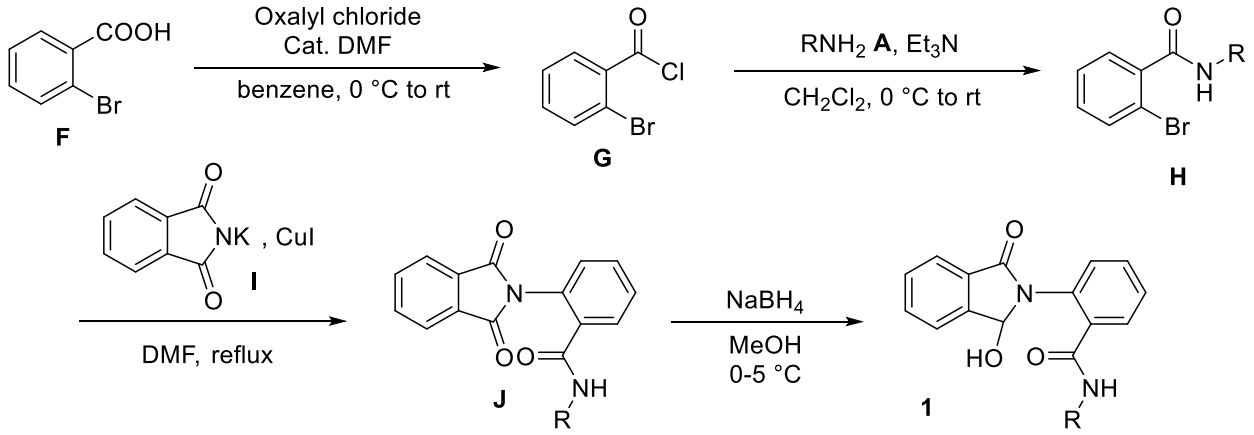
To a mixture of $Pd(PPh_3)_2Cl_2$ (25 mg, 0.036 mmol) and CuI (3.0 mg, 0.018 mmol) under inert atmosphere, triethylamine (3.0 mL) was added, followed by the dropwise addition of iodobenzene (184 mg, 0.9 mmol). The reaction mixture was stirred for 10 minutes at room temperature, after which the amido alcohol **1u** (258 mg, 1.0 mmol) was added dropwise over a period of 5 minutes. The reaction mixture was stirred for 8 hours (monitored by TLC analysis) before filtering through a pad of celite. The solids were washed with ethyl acetate, and the combined filtrates were concentrated in a rotary evaporator. The crude product was then purified by column chromatography to provide the corresponding product **1v**.

3-(1-Hydroxy-3-oxoisoindolin-2-yl)-*N*-(3-phenylprop-2-yn-1-yl)propanamide (1v):

White semi solid; R_f (Hexane:EtOAc,1:4) 0.40; Yield 272 mg, 81%; ^1H NMR (500 MHz, $CDCl_3$) δ 2.64-2.76 (m, 2 H), 3.80-3.92 (m, 2 H), 4.16 (dd, *J* = 17.6 and 5.0 Hz, 1 H), 4.24 (dd, *J* = 17.6 and 5.2 Hz, 1 H), 5.67 (brs, 1 H), 5.85 (d, *J* = 6.2 Hz, 1 H), 7.05 (brs, 1 H), 7.22-7.28 (m, 3 H), 7.32-7.38 (m, 3 H), 7.46-7.51 (m, 2 H), 7.66 (d, *J* = 7.4 Hz, 1 H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 30.2, 35.2, 36.1, 82.7, 83.4, 84.5, 122.5, 123.1, 123.4, 128.3, 128.5, 129.5, 131.4, 131.8, 132.3,

144.1, 168.2, 172.1; IR (KBr, neat) 3288, 2923, 1678, 1649, 1443, 1237, 1060, 748 cm^{-1}; HRMS (ESI) calcd. for $C_{20}H_{19}N_2O_3$ $(M + H)^+$ 335.1390, found 335.1370.

General experimental procedure and Characterization data of the compounds (1w-1z and 1aa):[2]



To an ice-cold solution of 2-bromobenzoic acid (**F**) (5.0 mmol, 1.0 equiv.) in anhydrous benzene, oxalyl chloride (1.5 equiv.) was added dropwise, followed by the addition of catalytic amount of DMF (2-3 drops). After the evolution of gas has ceased, the reaction mixture was concentrated in a rotary evaporator to provide the crude 2-bromobenzoyl chloride (**G**), which was further used without purification.

To an ice-cold solution of substituted amine **A** (5.0 mmol, 1.0 equiv.) and Et_3N (3.0 equiv.) in dichloromethane under N_2 atmosphere, 2-bromobenzoyl chloride (**G**)(1.0 equiv.) was added slowly. The reaction mixture was stirred at room temperature until the starting material was entirely consumed as evident by TLC analysis. After completion of the reaction, the reaction mixture was quenched with saturated $NaHCO_3$ solution and the organic layer was extracted with dichloromethane (2 x 15 mL). The combined organic layers were further washed with brine, followed by drying over anhydrous Na_2SO_4. The organic phase was concentrated in a rotary

evaporator to give the crude product, which was then subjected to column chromatography over silica gel to provide the desired product amide **H**.

A stirred suspension of *N*-substituted 2-bromobenzamide (**H**) (3.0 mmol, 1.0 equiv.), potassium salt of phthalimide (**I**) (1.2 equiv.) and copper(I) iodide (1.2 equiv.) in DMF under N_2 atmosphere was refluxed. The solution was homogeneous unless high amounts of copper(I) iodide was used. Upon completion of the reaction (checked by TLC analysis), the reaction mixture was cooled and diluted with ice-cold saturated ammonium chloride solution. The organic layer was extracted with ethyl acetate (20 mL). The organic layer was further washed with brine (2 x 20 mL), followed by drying over anhydrous Na_2SO_4. The organic phase was concentrated in a rotary evaporator to give the crude product, which was then subjected to column chromatography over silica gel to provide the desired product amide **J**.

To an ice-cold solution of phthalimide substituted *N*-alkyl/aryl benzamide **J** (1.0 mmol, 1.0 equiv.) in methanol, $NaBH_4$ (1.5 equiv.) was added. The reaction was allowed to stir at the same temperature (0 °C) until the starting material was entirely consumed as evident by TLC analysis. After completion of the reaction, the solvent was removed under reduced pressure and diluted with saturated $NaHCO_3$ solution. The organic layer was extracted with dichloromethane (2 x 20 mL), and the combined organic layers were further washed with brine, followed by drying over anhydrous Na_2SO_4. The organic phase was concentrated in a rotary evaporator to give the crude product, which was then subjected to column chromatography over silica gel to provide the desired product **1**.

***N*-benzyl-2-(1-hydroxy-3-oxoisoindolin-2-yl)benzamide (1w):**

Light yellow solid; R_f (Hexane:EtOAc,1:4) 0.60; mp 120-122 °C. Yield 227 mg, 63%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.35 (dd, *J* = 14.8 and 5.6 Hz, 1 H), 4.45 (dd, *J* = 14.8 and 6.0 Hz, 1 H), 6.13 (brs, 1 H), 6.95 (t, *J* = 6.0 Hz, 1 H), 7.22-7.24 (m, 5 H), 7.37-7.39 (m, 2 H), 7.53-7.57 (m, 3 H), 7.63-7.65 (m, 2 H), 7.78 (d, *J* = 7.6 Hz, 1 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 44.1, 85.1, 123.6, 123.8, 127.5, 127.8, 128.2, 128.7, 129.6, 129.7, 130.9, 131.8, 132.8, 134.2, 135.9, 137.5, 145.3, 167.7, 169.1; IR (KBr, neat) 3309, 2851, 1694, 1621, 1380, 1036, 739 cm^{-1}; HRMS (ESI) calcd. for $C_{22}H_{18}N_2NaO_3$ $(M + Na)^+$ 381.1210, found 381.1210.

2-(1-Hydroxy-3-oxoisoindolin-2-yl)-*N*-phenylbenzamide (1x):

White solid; R_f (Hexane:EtOAc,1:4) 0.60; mp 181-183 °C. Yield 232 mg, 68%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.75 (d, *J* = 10.2 Hz, 1 H), 6.17 (d, *J* = 9.8 Hz, 1 H), 7.06 (t, *J* = 7.4 Hz, 1 H), 7.21 (t, *J* = 7.8 Hz, 2 H), 7.33 (d, *J* = 7.8 Hz, 1 H), 7.36-7.42 (m, 3 H), 7.47-7.52 (m, 2 H), 7.60-7.63 (m, 2 H), 7.69 (d, *J* = 7.4 Hz, 1 H), 7.76 (d, *J* = 7.4 Hz, 1 H), 8.74 (brs, 1 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 85.2, 120.9, 123.7, 123.8, 124.9, 128.5, 128.6, 128.8, 129.4, 129.8, 130.8, 131.9, 132.9, 134.0, 136.1, 137.6, 145.1, 167.1, 167.8; IR (KBr, neat) 3290, 2855, 1688, 1651, 1541, 1050, 753 cm^{-1}; HRMS (ESI) calcd. for $C_{21}H_{16}N_2NaO_3$ $(M + Na)^+$ 367.1053, found 367.1046.

***N*-butyl-2-(1-hydroxy-3-oxoisoindolin-2-yl)benzamide (1y):**

White solid; R_f (EtOAc, 100%) 0.60; mp 138-140 °C. Yield 223 mg, 93%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.84 (t, *J* = 7.2 Hz, 3 H) 1.24-1.31 (m, 2 H), 1.39-1.44 (m, 2 H), 3.12-3.18 (m, 1 H), 3.21-3.26 (m, 1 H), 6.13 (d, *J* = 10.2 Hz, 1 H), 6.66 (brs, 1 H), 7.36-7.42 (m, 2 H), 7.50-7.56 (m, 3 H), 7.62 (t, *J* = 7.4 Hz, 1 H), 7.67 (d, *J* = 7.2 Hz, 1 H), 7.78 (d, *J* = 7.4 Hz, 1 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 13.7, 20.0, 31.1, 39.9, 85.0, 123.4, 123.7, 128.2, 128.5, 129.5, 130.9, 131.4,

131.5, 132.7, 134.0, 136.2, 145.4, 167.6, 167.0 ; IR (KBr, neat) 3302, 2867, 1697, 1632, 1388, 1055, 752 cm^{-1}; HRMS (ESI) calcd. for $C_{19}H_{20}N_2NaO_3$ $(M + Na)^+$ 347.1366, found 347.1343.

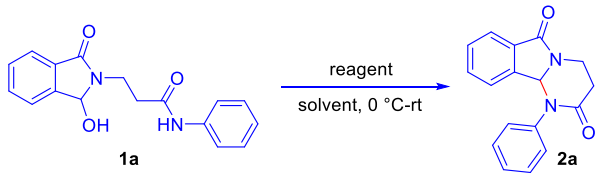
2-(1-Hydroxy-3-oxoisoindolin-2-yl)-*N*-phenethylbenzamide (1z):

White solid; R_f (Hexane:EtOAc, 1:1) 0.40; mp 160-162 ^oC. Yield 258 mg, 69%; ^1H NMR (500 MHz, $CDCl_3$) δ 2.73-2.77 (m, 2 H), 3.38-3.45 (m, 1 H), 3.46-3.53 (m, 1 H), 6.16 (s, 1 H), 7.14-7.19 (m, 3 H), 7.22-7.27 (m, 2 H), 7.34-7.38 (m, 2 H), 7.42-7.43 (m, 1 H), 7.49-7.53 (m, 2 H), 7.60-7.66 (m, 2 H), 7.77-7.79 (m, 1 H); $^{13}C\{1H\}$ NMR (125 MHz, $CDCl_3$) δ 35.3, 41.3, 85.1, 123.5, 123.8, 126.5, 128.1, 128.5, 128.6, 128.8, 129.5, 129.7, 131.0, 131.7, 132.8, 134.3, 136.0, 138.8, 145.4, 167.6, 169.1; IR (KBr, neat) 3299, 2931, 1696, 1635, 1388, 1054, 753 cm^{-1}; HRMS (ESI) calcd. for $C_{23}H_{20}N_2NaO_3$ $(M + Na)^+$ 395.1366, found 395.1358.

***N*-cyclopropyl-2-(1-hydroxy-3-oxoisoindolin-2-yl)benzamide (1aa):**

White solid; R_f (Hexane:EtOAc, 2:3) 0.40; mp 187-189 ^oC. Yield 220 mg, 71%; ^1H NMR (500 MHz, $CDCl_3$) δ 0.42-0.46 (m, 2 H), 0.64-0.68 (m, 2 H), 2.20 (brs, 1 H), 2.61-2.65 (m, 1 H), 6.14 (s, 1 H), 7.32-7.39 (m, 2 H), 7.48-7.53 (m, 3 H), 7.59-7.65 (m, 2 H), 7.76-7.79 (m, 1 H); $^{13}C\{1H\}$ NMR (125 MHz, $CDCl_3$) δ 6.2, 6.5, 23.0, 85.0, 123.5, 123.8, 128.2, 128.4, 129.2, 129.7, 130.9, 131.6, 132.9, 133.8, 135.7, 145.2, 167.7, 170.8; IR (KBr, neat) 3283, 2945, 1697, 1639, 1392, 1052, 752 cm^{-1}; HRMS (ESI) calcd. for $C_{18}H_{16}N_2NaO_3$ $(M + Na)^+$ 331.1053, found 331.1076.

Table S17: Optimization of the reaction



Entry[a]	Reagent	Equiv.	Solvent	Time/h	Yield[b]
1	BF_3•OEt_2	1.0	DCM	24	92%
2	BF_3•OEt_2	1.2	DCM	0.25	99%
3	BF_3•OEt_2	1.2	Toluene	14	93%
4	BF_3•OEt_2	1.2	DCE	0.25	92%
5	BF_3•OEt_2	1.2	CH_3CN	0.25	96%
6	TMSOTf	1.2	DCM	24	91%
7	$Zn(OTf)_2$	0.1	DCM	24	–
8	$Cu(OTf)_2$	0.1	DCM	24	–
9	$Sc(OTf)_3$	0.1	DCM	24	–
10	$Bi(OTf)_3$	0.1	DCM	24	85%
11	$In(OTf)_3$	0.1	DCM	24	80%
12	$InCl_3$	0.1	DCM	24	–
13	$InBr_3$	0.1	DCM	24	–
14	$FeCl_3$	1.2	DCM	05	75%
15	TFA	1.2	DCM	04	94%
16	TfOH	1.2	DCM	24	69%
17	*p*-TsOH	1.2	DCM	24	72%

[a]Reactions were conducted with **1a** (0.2 mmol) under N_2 atmosphere.
[b]Yields refer to isolated yield.

General experimental procedure and Characterization data of the compounds (2a-2v):

To an ice-cold solution of *N*-alkyl/aryl propanamide amido alcohol (0.5 mmol, 1.0 equiv.) in dichloromethane (3.0 mL), borontrifluoride diethyl etherate (1.2 equiv.) was added under inert atmosphere. The reaction was continued to stir at room temperature till all the starting material was consumed as evident by TLC. Then it was treated with saturated $NaHCO_3$ solution, and the organic layer was extracted with dichloromethane (2 x 10 mL). The combined organic layers were further washed with brine, followed by drying over anhydrous Na_2SO_4. The organic phase was concentrated in a rotary evaporator to give the crude product, which was then subjected to column chromatography over silica gel to provide the final product.

1-Phenyl-1,3,4,10*b*-tetrahydropyrimido[2,1-*a*]isoindole-2,6-dione (2a):

White solid; R_f (EtOAc, 100%) 0.60; mp 168-170 ^oC. Yield 139 mg, 99%; ^1H NMR (400 MHz, $CDCl_3$) δ 2.69 (ddd, *J* = 17.0, 4.8 and 2.2 Hz, 1 H), 2.80 (ddd, *J* = 18.4, 9.8 and 7.2 Hz, 1 H), 3.60 (ddd, *J* = 16.2, 11.2 and 4.8 Hz, 1 H), 4.63 (ddd, *J* = 13.6, 7.0 and 2.4 Hz, 1 H), 6.12 (d, *J* = 7.6 Hz, 1 H, Ar-H), 6.22 (s, 1 H), 7.15-7.18 (m, 2 H), 7.24 (t, *J* = 7.6 Hz, 1 H), 7.43-7.50 (m, 4 H), 7.85 (dt, *J* = 7.6 and 1.0 Hz, 1 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 32.2, 35.6, 72.4, 124.0, 124.5, 128.7, 129.0, 129.6, 130.0, 131.6, 131.7, 138.4, 140.6, 167.3, 167.7; IR (KBr, neat) 2877, 1713, 1658, 1121, 732 cm^{-1}; HRMS (ESI) calcd. for $C_{17}H_{15}N_2O_2$ $(M + H)^+$ 279.1128, found 279.1129.

1-(*p*-Tolyl)-1,3,4,10*b*-tetrahydropyrimido[2,1-*a*]isoindole-2,6-dione (2b):

White semi solid; R_f (EtOAc, 100%) 0.60; Yield 141 mg, 96%; ^1H NMR (400 MHz, $CDCl_3$) δ 2.42 (s, 3 H), 2.68 (ddd, *J* = 17.2, 3.0 and 1.2 Hz, 1 H), 2.78 (ddd, *J* = 17.2, 11.2 and 7.2 Hz, 1 H), 3.59 (ddd, *J* = 16.2, 11.2 and 4.8 Hz, 1 H), 4.61 (ddd, *J* = 13.4, 6.8 and 1.4 Hz, 1 H), 6.19 (s,

1 H), 6.20 (d, *J* = 7.6 Hz, 1 H, Ar-H), 7.03 (d, *J* = 7.8 Hz, 2 H), 7.27-7.29 (m, 3 H), 7.46 (t, *J* = 7.6 Hz, 1 H), 7.84 (dd, *J* = 7.8 and 1.2 Hz, 1 H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 21.2, 32.2, 35.5, 72.3, 123.9, 124.6, 128.6, 129.9, 130.2, 131.6, 131.7, 135.6, 138.6, 140.6, 167.2, 167.8; IR (KBr, neat) 2854, 1693, 1646, 1426, 1149, 729 cm^{-1}; HRMS (ESI) calcd. for $C_{18}H_{17}N_2O_2$ $(M + H)^+$ 293.1285, found 293.1286.

1-(4-Fluorophenyl)-1,3,4,10*b*-tetrahydropyrimido[2,1-*a*]isoindole-2,6-dione (2c):

White solid; R_f (EtOAc, 100%) 0.60; mp 152-154 °C. Yield 144 mg, 97%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.70 (ddd, *J* = 17.4, 4.8 and 2.6 Hz, 1 H), 2.75 (ddd, *J* = 17.6, 11.2 and 2.2 Hz, 1 H), 3.60 (ddd, *J* = 16.2, 11.4 and 4.8 Hz, 1 H), 4.62 (ddd, *J* = 13.6, 7.2 and 4.2 Hz, 1 H), 6.18 (s, 1 H), 6.20 (d, *J* = 7.6 Hz, 1 H, Ar-H), 7.11-7.18 (m, 4 H), 7.29 (t, *J* = 7.6 Hz, 1 H), 7.48 (t, *J* = 7.6 Hz, 1 H), 7.86 (d, *J* = 7.6 Hz, 1 H); $^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$) δ 32.2, 35.6, 72.5, 116.7 (d, *J* = 22.5 Hz), 124.2, 124.4, 130.2, 130.8, 131.7 (d, *J* = 3.8 Hz), 134.3, 140.4, 162.2 (d, *J* = 247.4 Hz), 167.3, 167.9; ^{19}F NMR (564 MHz, $CDCl_3/C_6F_6$) δ -115.31 (m, -CF-); IR (KBr, neat) 2856, 1696, 1640, 1434, 727 cm^{-1}; HRMS (ESI) calcd. for $C_{17}H_{13}FN_2NaO_2$ $(M + Na)^+$ 319.0853, found 319.0855.

1-Benzyl-1,3,4,10*b*-tetrahydropyrimido[2,1-*a*]isoindole-2,6-dione (2d):

White solid; R_f (Hexane:EtOAc, 1:4) 0.40; mp 149-151 °C. Yield 144 mg, 98%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.74 (ddd, *J* = 13.4, 10.0 and 7.0 Hz, 2 H), 3.48 (ddd, *J* = 15.6, 9.2 and 6.2 Hz, 1 H), 4.46 (ddd, *J* = 13.4, 6.2 and 2.2 Hz, 1 H), 4.55 (d, *J* = 16.2 Hz, 1 H), 5.44 (d, *J* = 16.2 Hz, 1 H), 5.86 (s, 1 H), 7.20 (d, *J* = 7.4 Hz, 2 H), 7.25 (t, *J* = 7.2 Hz, 1 H), 7.27-7.35 (m, 2 H), 7.51-7.55 (m, 3 H), 7.85-7.88 (m, 1 H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 32.3, 35.8, 46.0, 70.1, 124.5, 124.7, 127.0, 127.5, 129.0, 130.3, 132.0, 132.3, 136.1, 140.5, 167.5, 168.5; IR (KBr, neat) 2857,

1699, 1633, 1402, 740 cm^{-1}; HRMS (ESI) calcd. for $C_{18}H_{17}N_2O_2$ $(M + H)^+$ 293.1285, found 293.1285.

1-(4-Methylbenzyl)-1,3,4,10*b*-tetrahydropyrimido[2,1-*a*]isoindole-2,6-dione (2e):

White solid; R_f (Hexane:EtOAc, 1:4) 0.40; mp 141-143 ºC. Yield 151 mg, 98%; ^1H NMR (400 MHz, $CDCl_3$) δ 2.32 (s, 3 H), 2.71 (ddd, *J* = 11.6, 7.6 and 2.0 Hz, 2 H), 3.44 (ddd, *J* = 15.6, 9.4 and 6.2 Hz, 1 H), 4.42 (d, *J* = 16.0 Hz, 1 H), 4.45 (ddd, *J* = 13.4, 6.0 and 4.2 Hz, 1 H), 5.47 (d, *J* = 16.0 Hz, 1 H), 5.83 (s, 1 H), 7.09-7.15 (m, 4 H), 7.51-7.55 (m, 3 H), 7.84-7.87 (m, 1 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 21.1, 32.3, 35.7, 45.7, 69.9, 124.4, 124.7, 127.0, 129.6, 130.2, 132.0, 132.3, 132.9, 137.2, 140.6, 167.5, 168.3; IR (KBr, neat) 2921, 1685, 1660, 1422, 1091, 796 cm^{-1}; HRMS (ESI) calcd. for $C_{19}H_{19}N_2O_2$ $(M + H)^+$ 307.1441, found 307.1442.

1-(4-Chlorobenzyl)-1,3,4,10*b*-tetrahydropyrimido[2,1-*a*]isoindole-2,6-dione (2f):

White solid; R_f (EtOAc, 100%) 0.60; mp 172-174 ºC. Yield 161 mg, 98%; ^1H NMR (400 MHz, $CDCl_3$) δ 2.74 (ddd, *J* = 15.0, 9.8 and 6.6 Hz, 2 H), 3.48 (ddd, *J* = 15.4, 9.8 and 5.8 Hz, 1 H), 4.47 (ddd, *J* = 13.5, 6.4 and 3.8 Hz, 1 H), 4.65 (d, *J* = 16.2 Hz, 1 H), 5.22 (d, *J* = 16.2 Hz, 1 H), 5.85 (s, 1 H), 7.08 (d, *J* = 8.2 Hz, 2 H), 7.27 (d, *J* = 8.2 Hz, 2 H), 7.44-7.57 (m, 3 H), 7.87 (d, *J* = 7.0 Hz, 1 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 32.2, 35.7, 45.8, 70.4, 124.5, 124.6, 128.2, 129.1, 130.4, 132.0, 132.3, 133.3, 134.9, 140.2, 167.4, 168.6; IR (KBr, neat) 2940, 1697, 1646, 1418, 1212, 737cm^{-1}; HRMS (ESI) calcd. for $C_{18}H_{16}ClN_2O_2$ $(M + H)^+$ 327.0895, found 327.0895.

1-(1-Phenylethyl)-1,3,4,10*b*-tetrahydropyrimido[2,1-*a*]isoindole-2,6-dione (diastereomeric mixture, 1:1, 2g):

White solid; R_f (EtOAc, 100%) 0.50; mp 131-133 ºC. Yield 151 mg, 98%; ^1H NMR (400 MHz, $CDCl_3$) δ 1.40 (d, *J* = 6.4 Hz, 3 H), 1.41 (d, *J* = 6.4 Hz, 3 H), 2.56-2.68 (m, 2 H), 3.73-3.84 (m, 2

H), 4.99-5.03 (m, 1 H), 5.66 (d, *J* = 4.2 Hz, 0.5 H), 5.83 (s, 1 H), 5.90 (d, *J* = 4.2 Hz, 0.5 H), 6.93-7.00 (m, 1 H), 7.16-7.25 (m, 5 H), 7.42-7.45 (m, 1 H), 7.48-7.55 (m, 2 H), 7.62-7.65 (m, 1 H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 21.7, 21.8, 35.3, 35.4, 35.9, 36.1, 49.2, 49.3, 82.5, 82.6, 122.9, 123.0, 123.4, 123.5, 126.0, 126.2, 127.2, 127.3, 128.5, 128.6, 129.4, 129.5, 131.4, 131.5, 132.2, 132.3, 142.9, 143.0, 144.0, 144.1, 168.1, 168.2, 171.2, 171.4; IR (KBr, neat) 2926, 1681, 1637, 1557, 1285, 741cm^{-1}; HRMS (ESI) calcd. for $C_{19}H_{19}N_2O_2$ $(M + H)^+$ 307.1441, found 307.1441.

1-Butyl-1,3,4,10*b*-tetrahydropyrimido[2,1-*a*]isoindole-2,6-dione (2h):

White semi solid; R_f (EtOAc, 100%) 0.50; Yield 128 mg, 99%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.92 (t, *J* = 6.6 Hz, 3 H), 1.31-1.39 (m, 3 H), 1.63-1.70 (m, 1 H), 2.55 (ddd, *J* = 14.2, 5.8 and 2.8 Hz, 2 H), 2.62 (ddd, *J* = 17.0, 7.4 and 6.2 Hz, 1 H), 3.41 (ddd, *J* = 15.8, 10.4 and 5.0 Hz, 1 H), 3.59 (ddd, *J* = 14.2, 9.2 and 5.2 Hz, 1 H), 4.38-4.44 (m, 1 H), 5.82 (s, 1 H), 7.56-7.63 (m, 3 H), 7.88 (d, *J* = 7.2 Hz, 1 H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 13.8, 20.1, 29.8, 32.0, 35.6, 43.4, 70.3, 124.2, 124.4, 130.2, 132.0, 132.3, 140.6, 167.1, 167.8; IR (KBr, neat) 2930, 1700, 1639, 1430, 732 cm^{-1}; HRMS (ESI) calcd. for $C_{15}H_{19}N_2O_2$ $(M + H)^+$ 259.1441, found 259.1435.

1-Octyl-1,3,4,10*b*-tetrahydropyrimido[2,1-*a*]isoindole-2,6-dione (2i):

White semi solid; R_f (EtOAc, 100%) 0.50; Yield 140 mg, 89%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.87 (t, *J* = 6.6 Hz, 3 H), 1.22-1.33 (m, 11 H), 1.64-1.71 (m, 1 H), 2.52-2.67 (m, 2 H), 3.42 (ddd, *J* = 15.6, 10.2 and 5.4 Hz, 1 H), 3.57-3.70 (m, 2 H), 4.41 (ddd, *J* = 13.4, 6.6 and 3.6 Hz, 1 H), 5.83 (s, 1 H), 7.60-7.63 (m, 3 H), 7.89 (d, *J* = 7.6 Hz, 1 H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 14.1, 22.6, 26.9, 27.8, 29.1, 29.2, 31.8, 32.1, 35.7, 43.8, 70.4, 124.2, 124.6, 130.3, 132.1, 132.5, 140.7, 167.2, 167.8; IR (KBr, neat) 2855, 1705, 1646, 1427, 1208, 730, cm^{-1}; HRMS (ESI) calcd. for $C_{19}H_{27}N_2O_2$ $(M + H)^+$ 315.2067, found 315.2066.

1-Isopropyl-1,3,4,10*b*-tetrahydropyrimido[2,1-*a*]isoindole-2,6-dione (2j):

White solid; R_f (EtOAc, 100%) 0.50; mp 96-98 ºC. Yield 65 mg, 53%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.41 (d, *J* = 7.0 Hz, 3 H), 1.58 (d, *J* = 7.0 Hz, 3 H), 2.42-2.46 (m, 1 H), 2.47-2.54 (m, 1 H), 3.29 (ddd, *J* = 16.0, 11.4 and 3.0 Hz, 1 H), 3.83-3.88 (m, 1 H), 4.42 (ddd, *J* = 13.4, 6.4 and 2.2 Hz, 1 H), 5.77 (s, 1 H), 7.57 (t, *J* = 7.4 Hz, 1 H), 7.62 (t, *J* = 7.4 Hz, 1 H), 7.70 (d, *J* = 7.4 Hz, 1 H), 7.89 (d, *J* = 7.4 Hz, 1 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 19.4, 20.3, 33.8, 35.6, 51.5, 71.6, 123.8, 124.5, 130.2, 132.3, 132.4, 141.9, 167.6, 167.7; IR (KBr, neat) 2926, 1697, 1640, 1410, 735 cm^{-1}; HRMS (ESI) calcd. for $C_{14}H_{17}N_2O_2$ $(M + H)^+$ 245.1285, found 245.1285.

1-Cyclopropyl-1,3,4,10*b*-tetrahydropyrimido[2,1-*a*]isoindole-2,6-dione (2k):

White semi solid; R_f (EtOAc, 100%) 0.40; Yield 184 mg, 71%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.86-0.93 (m, 1 H), 1.02-1.09 (m, 2 H), 1-22-1.28 (m, 1 H), 2.45-2.50 (m, 1 H), 2.55-2.65 (m, 2 H), 3.29 (ddd, *J* = 16.0, 11.8 and 6.8 Hz, 1 H), 4.45 (dd, *J* = 13.6 and 6.8 Hz, 1 H), 5.79 (s, 1 H), 7.55-7.62 (m, 2 H), 7.89 (d, *J* = 7.0 Hz, 2 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 7.05, 11.0, 26.6, 32.8, 35.4, 70.9, 124.3, 124.4, 130.2, 132.0, 132.2, 141.5, 167.8, 168.8; IR (KBr, neat) 2856, 1695, 1645, 1412, 729 cm^{-1}; HRMS (ESI) calcd. for $C_{14}H_{15}N_2O_2$ $(M + H)^+$ 243.1128, found 243.1128.

1-Cyclohexyl-1,3,4,10*b*-tetrahydropyrimido[2,1-*a*]isoindole-2,6-dione (2l):

White solid; R_f (EtOAc, 100%) 0.50; mp 219-121 ºC. Yield 36 mg, 25%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.25-1.33 (m, 2 H), 1.49-1.55 (m, 1 H), 1-62-1.68 (m, 2 H), 1.75-1.84 (m, 2 H), 1.90-1.95 (m, 1 H), 2.34-2.49 (m, 2 H), 2.51-2.61 (m, 2 H), 3.25-3.36 (m, 2 H), 4.42 (ddd, *J* = 13.4, 6.2 and 2.4 Hz, 1 H), 5.78 (s, 1 H), 7.59-7.62 (m, 2 H), 7.67 (d, *J* = 7.4 Hz, 1 H), 7.89 (d, *J* = 7.4 Hz, 1 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 25.2, 26.5, 26.8, 28.7, 29.9, 33.9, 35.7, 60.4, 71.7, 123.6,

124.5, 130.2, 132.3, 132.4, 142.1, 167.6, 167.7; IR (KBr, neat) 2854, 1692, 1640, 1405, 733 cm^{-1}; HRMS (ESI) calcd. for $C_{17}H_{21}N_2O_2$ $(M + H)^+$ 285.1598, found 285.1599.

1-Phenylhexahydropyrrolo[1,2-*a*]pyrimidine-2,6-dione (2m):

White semi solid; R_f (EtOAc, 100%) 0.40; Yield 112 mg, 97%; ^1H NMR (400 MHz, $CDCl_3$) δ 1.80-1.86 (m, 1 H), 2.02-2.08 (m, 1 H), 2.38-2.48 (m, 2 H), 2.59 (ddd, *J* = 16.8, 4.7 and 1.8 Hz, 1 H), 2.74 (ddd, *J* = 17.4, 10.8 and 7.4 Hz, 1 H), 3.23-3.32 (m, 1 H), 4.30-4.35 (m, 1 H), 5.49 (t, *J* = 5.7 Hz, 1 H), 7.18 (d, *J* = 7.6 Hz, 2 H), 7.34 (t, *J* = 7.6 Hz, 1 H), 7.44 (t, *J* = 7.6 Hz, 2 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 25.7, 29.1, 31.9, 35.7, 72.8, 127.9, 128.1, 129.7, 137.9, 168.0, 173.2; IR (KBr, neat) 2857, 1686, 1645, 1396, 758 cm^{-1}; HRMS (ESI) calcd. for $C_{13}H_{15}N_2O_2$ $(M + H)^+$ 231.1128, found 231.1128.

1-(4-Methylbenzyl)hexahydropyrrolo[1,2-*a*]pyrimidine-2,6-dione (2n):

White semi solid; R_f (EtOAc, 100%) 0.40; Yield 123 mg, 95%; ^1H NMR (400 MHz, $CDCl_3$) δ 1.83-1.91 (m, 1 H), 2.27-2.37 (m, 1 H), 2.31 (s, 3 H), 2.38-2.48 (m, 2 H), 2.51-2.65 (m, 2 H), 2.98-3.06 (m, 1 H), 4.22 (d, *J* = 15.2 Hz, 1 H), 4.21-4.27 (m, 1 H), 4.92 (t, *J* = 6.2 Hz, 1 H), 5.04 (d, *J* = 15.2 Hz, 1 H), 7.12-7.15 (m, 4 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 21.1, 26.2, 29.5, 32.0, 35.2, 45.2, 70.5, 127.8, 129.6, 133.4, 137.5, 167.6, 172.4; IR (KBr, neat) 2856, 1691, 1643, 1420, 1012, 790 cm^{-1}; HRMS (ESI) calcd. for $C_{15}H_{19}N_2O_2$ $(M + H)^+$ 259.1441, found 259.1443.

1-Phenethyl-1,3,4,10*b*-tetrahydropyrimido[2,1-*a*]isoindole-2,6-dione (2o):

White solid; R_f (EtOAc, 100%) 0.50; mp 115-117 ºC. Yield 146 mg, 95%; ^1H NMR (400 MHz, $CDCl_3$) δ 2.55-2.67 (m, 3 H), 3.06 (ddd, *J* = 16.5, 13.4 and 8.2 Hz, 1 H), 3.33 (ddd, *J* = 13.4, 10.2 and 5.2 Hz, 1 H), 4.89 (t, *J* = 7.8 Hz, 2 H), 4.36 (ddd, *J* = 10.3, 6.8 and 3.6 Hz, 1 H), 5.61 (s, 1 H), 7.20-7.25 (m, 3 H), 7.31 (t, *J* = 7.4 Hz, 2 H), 7.58 (t, *J* = 7.2 Hz, 1 H), 7.61-7.66 (m, 2 H), 7.88

(d, *J* = 7.4 Hz, 1 H); $^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$) δ 32.3, 34.0, 35.7, 45.5, 70.8, 124.3, 124.6, 126.8, 128.7, 128.8, 130.3, 132.1, 132.5, 138.6, 140.7, 167.2, 168.1; IR (KBr, neat) 2860, 1704, 1647, 1427, 734 cm^{-1}; HRMS (ESI) calcd. for $C_{19}H_{19}N_2O_2$ $(M + H)^+$ 307.1441, found 307.1452.

1-(4-Methylbenzyl)-1,3,4,6*a*,7,10,10*a*,10*b*-octahydropyrimido[2,1-*a*]isoindole-2,6-dione (2p): White solid; R_f (EtOAc, 100%) 0.50; mp 112-114 ºC. Yield 143 mg, 92%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.86-1.94 (m, 1 H), 2.11-2.23 (m, 2 H), 2.32 (s, 3 H), 2.36-2.42 (m, 1 H), 2.49 (dd, *J* = 17.0 and 4.8 Hz, 1 H), 2.58-2.73 (m, 3 H), 3.06 (ddd, *J* = 17.0, 12.5 and 4.8 Hz, 1 H), 4.24 (dd, *J* = 13.4 and 7.2 Hz, 1 H), 4.46 (d, *J* = 15.4 Hz, 1 H), 4.54 (s, 1 H), 4.88 (d, *J* = 15.4 Hz, 1 H), 5.70-5.75 (m, 1 H), 5.80-5.85 (m, 1 H), 7.09-7.15 (m, 4 H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 21.1, 22.9, 26.0, 32.0, 34.7, 36.0, 39.0, 45.6, 125.7, 127.3, 127.8, 129.6, 133.7, 137.3, 168.5, 176.3; IR (KBr, neat) 2850, 1698, 1647, 1428, 753 cm^{-1}; HRMS (ESI) calcd. for $C_{19}H_{23}N_2O_2$ $(M + H)^+$ 311.1754, found 311.1755.

1-Phenyl-1,3,4,6*a*,7,10,10*a*,10*b*-octahydropyrimido[2,1-*a*]isoindole-2,6-dione (2q):

White solid; R_f (EtOAc, 100%) 0.40; mp 136-138 ºC. Yield 130 mg, 92%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.52-1.58 (m, 1 H), 1.85-1.93 (m, 1 H), 2.25-2.28 (m, 1 H), 2.37-2.44 (m, 2 H), 2.53-2.55 (m, 1 H), 2.58-2.73 (m, 1 H), 2.80-2.84 (m, 1 H), 3.25 (ddd, *J* = 16.2, 8.4 and 1.4 Hz, 1 H), 4.35 (ddd, *J* = 16.2, 9.0 and 2.4 Hz, 1 H), 5.06 (d, *J* = 3.6 Hz, 1 H), 5.64-5.69 (m, 1 H), 5.80-5.84 (m, 1 H), 7.20 (d, *J* = 8.4 Hz, 2 H), 7.38 (t, *J* = 8.4 Hz, 1 H), 7.45 (t, *J* = 8.4 Hz, 2 H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 23.1, 25.3, 31.9, 35.8, 36.0, 39.0, 78.7, 125.8, 127.6, 128.0, 128.2, 129.8, 138.3, 168.2, 176.2; IR (KBr, neat) 2848, 1693, 1658, 1459, 753 cm^{-1}; HRMS (ESI) calcd. for $C_{17}H_{18}N_2NaO_2$ $(M + Na)^+$ 305.1260, found 305.1240.

1-(4-Methoxybenzyl)decahydropyrimido[2,1-*a*]isoindole-2,6-dione (2r):

White solid; R_f (EtOAc, 100%) 0.50; mp 124-126 ^oC. Yield 135 mg, 82%; ^1H NMR (400 MHz, $CDCl_3$) δ 1.02-1.21 (m, 3 H), 1.41-1.57 (m, 3 H), 1.61-1.66 (m, 1 H), 2.01-2.08 (m, 1 H), 2.40-2.47 (m, 3 H), 2.57-2.67 (m, 1 H), 3.06 (ddd, *J* = 17.4, 12.6 and 4.8 Hz, 1 H),3.77 (s, 3 H), 4.21 (ddd, *J* = 13.0, 8.6 and 7.0 Hz, 1 H), 4.43 (d, *J* = 15.0 Hz, 1 H), 4.45 (s, 1 H), 4.81 (d, *J* = 15.0 Hz, 1 H), 6.84 (d, *J* = 8.6 Hz, 2 H), 7.12 (d, *J* = 8.4 Hz, 2 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 22.5, 23.0, 23.3, 27.4, 31.8, 34.9, 36.5, 39.4, 45.5, 55.2, 75.6, 114.2, 128.7, 128.9, 159.0, 168.9, 176.6; IR (KBr, neat) 2855, 1706, 1649, 1422, 1249, 753 cm^{-1}; HRMS (ESI) calcd. for $C_{19}H_{25}N_2O_3$ $(M + H)^+$ 329.1860, found 329.1834.

1-(4-Methoxybenzyl)decahydropyrimido[2,1-*a*]isoindole-2,6-dione (2s):

White solid; R_f (EtOAc, 100%) 0.40; mp 122-124 ^oC. Yield 152 mg, 94%; ^1H NMR (400 MHz, $CDCl_3$) δ 1.34-1.41 (m, 1 H), 1.56-1.62 (m, 1 H), 2.33 (s, 3 H), 2.42 (ddd, *J* = 17.0, 4.7 and 1.6 Hz, 1 H), 2.51(ddd, *J* = 17.0, 12.0 and 7.0 Hz, 1 H), 2.81 (dd, *J* = 16.8 and 4.8 Hz, 1 H), 2.85-2.90 (m, 1 H), 3.01-3.05 (m, 1 H), 3.13 (dd, *J* = 9.4 and 4.4 Hz, 1 H), 3.22-3.25 (m, 1 H), 4.11 (ddd, *J* = 13.2, 7.0 and 1.8 Hz, 1 H), 4.26 (s, 1 H), 4.30 (d, *J* = 15.2 Hz, 1 H), 5.07 (d, *J* = 15.2 Hz, 1 H), 5.96 (dd, *J* = 5.8 and 3.0 Hz, 1 H), 6.16 (dd, *J* = 5.8 and 3.0 Hz, 1 H), 7.12-7.17 (m, 4 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 21.1, 32.4, 35.2, 43.7, 44.7, 45.2, 45.4, 50.2, 51.5, 72.9, 127.8, 129.6, 133.6, 133.8, 136.8, 137.4, 168.0, 173.6; IR (KBr, neat) 2870, 1693, 1648, 1427, 754 cm^{-1}; HRMS (ESI) calcd. for $C_{20}H_{22}N_2O_2K$ $(M + K)^+$ 361.1313, found 361.1309.

1-(Prop-2-yn-1-yl)-1,3,4,10*b*-tetrahydropyrimido[2,1-*a*]isoindole-2,6-dione (2u):

White solid; R_f (Hexane:EtOAc, 1:4) 0.60; mp 159-161 ^oC. Yield 116 mg, 97%; ^1H NMR (500 MHz, $CDCl_3$) δ 2.44 (t, *J* = 2.6 Hz, 1 H), 2.57-2.64 (m, 2 H), 3.41-3.47 (m, 1 H), 3.81 (dd, *J* = 17.8 and 2.5 Hz, 1 H), 4.45-4.50 (m, 1 H), 5.32 (dd, *J* = 17.8 and 2.6 Hz, 1 H), 6.12 (s, 1 H), 7.56-

7.61 (m, 2 H), 7.62-7.65 (m, 1 H), 7.86-7.90 (m, 1 H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 31.7, 32.0, 35.4, 69.7, 74.3, 77.8, 124.6, 124.7, 130.4, 132.2, 132.3, 140.1, 167.4; IR (KBr, neat) 2931, 1705, 1652, 1436, 1092, 734 cm^{-1}; HRMS (ESI) calcd. for $C_{14}H_{13}N_2O_2$ $(M + H)^+$ 241.0972, found 241.0972.

1-(3-Phenylprop-2-yn-1-yl)-1,3,4,10*b*-tetrahydropyrimido[2,1-*a*]isoindole-2,6-dione (2v):

White semi solid; R_f (Hexane:EtOAc, 1:4) 0.50; Yield 148 mg, 93%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.58-2.71 (m, 2 H), 3.44-3.50 (m, 1 H), 4.06 (d, *J* = 17.8 Hz, 1 H), 4.47-4.53 (m, 1 H), 5.56 (dd, *J* = 17.8 and 2.1 Hz, 1 H), 6.21 (s, 1 H), 7.29-7.34 (m, 3 H), 7.44 (d, *J* = 7.0 Hz, 2 H), 7.60 (t, *J* = 7.4 Hz, 1 H), 7.66 (t, *J* = 7.4 Hz, 1 H), 7.91 (d, *J* = 7.8 Hz, 1 H), 7.98 (d, *J* = 7.8 Hz, 1 H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 32.0, 32.5, 35.4, 69.8, 82.9, 86.2, 122.1, 124.6, 124.7, 128.4, 128.9, 130.4, 131.8, 132.2, 132.3, 140.3, 167.3, 167.4; IR (KBr, neat) 2928, 1710, 1654, 1438, 732 cm^{-1}; HRMS (ESI) calcd. for $C_{20}H_{17}N_2O_2$ $(M + H)^+$ 317.1285, found 317.1264.

General experimental procedure and Characterization data of the compounds (2w-2z and 2aa):

To an ice-cold solution of *N*-alkyl/aryl benzamide amido alcohol (0.5 mmol, 1.0 equiv.) in dichloromethane (3.0 mL) and acetonitrile (0.5 ml), borontrifluoride diethyl etherate (2.0 equiv.) was added under inert atmosphere. The reaction was continued to stir at room temperature till all the starting material was consumed as evident by TLC. Then it was treated with saturated $NaHCO_3$ solution, and the organic layer was extracted with dichloromethane (2 x 10 mL). The combined organic layers were further washed with brine, followed by drying over anhydrous Na_2SO_4. The organic phase was concentrated in a rotary evaporator to give the crude product, which was then subjected to column chromatography over silica gel to provide the product.

6-Benzyl-6,6*a*-dihydroisoindolo[2,1-*a*]quinazoline-5,11-dione (2w):

White solid; R_f (Hexane:EtOAc, 1:4) 0.70; mp 153-155 ºC. Yield 154 mg, 91%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.62 (d, *J* = 16.6 Hz, 1 H), 5.51 (d, *J* = 16.6 Hz, 1 H), 6.36 (s, 1 H), 7.20 (d, *J* = 7.6 Hz, 2 H), 7.25 (d, *J* = 7.6 Hz, 1 H), 7.32-7.38 (m, 3 H), 7.41 (d, *J* = 7.6 Hz, 1 H), 7.54 (t, *J* =7.6 Hz, 1 H), 7.59 (t, *J* = 7.4 Hz, 1 H), 7.66 (t, *J* = 7.6 Hz, 1 H), 7.96 (d, *J* = 7.4 Hz, 1 H), 8.12 (d, *J* = 7.6 Hz, 1 H), 8.22 (t, *J* = 7.6 Hz, 1 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 46.6, 70.7, 120.1, 120.2, 125.0, 125.3, 125.4, 126.3, 127.3, 129.1, 129.5, 130.6, 132.5, 132.6, 133.8, 136.1, 136.9, 137.7, 164.1, 164.9; IR (KBr, neat) 2854, 1717, 1657, 1410, 735 cm^{-1}; HRMS (ESI) calcd. for $C_{22}H_{17}N_2O_2$ $(M + H)^+$ 341.1285, found 341.1286.

6-Phenyl-6,6*a*-dihydroisoindolo[2,1-*a*]quinazoline-5,11-dione (2x):

White solid; R_f (EtOAc, 100%) 0.70; mp 200-202 ºC. Yield 156 mg, 96%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.15 (d, *J* = 7.6 Hz, 1 H), 6.54 (s, 1 H), 7.26 (t, *J* = 7.4 Hz, 2 H), 7.35 (d, *J* = 7.6 Hz, 2 H), 7.45-7.53 (m, 4 H), 7.68 (t, *J* = 7.6 Hz, 1 H), 7.96 (d, *J* = 7.6 Hz, 1 H), 8.18-8.21 (m, 2 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 72.3, 120.3, 120.33, 124.5, 125.3, 125.4, 129.2, 129.5, 129.8, 130.3, 132.1, 132.2, 133.9, 137.1, 138.2, 138.7, 164.2, 165.3; IR (KBr, neat) 2926, 1716, 1665, 1404, 739 cm^{-1}; HRMS (ESI) calcd. for $C_{21}H_{15}N_2O_2$ $(M + H)^+$ 327.1128, found 327.1118.

6-Butyl-6,6*a*-dihydroisoindolo[2,1-*a*]quinazoline-5,11-dione (2y):

White solid; R_f (Hexane:EtOAc, 1:4) 0.60; mp 136-138 ºC. Yield 142 mg, 93%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.91 (t, *J* = 7.2 Hz, 3 H), 1.28-1.37 (m, 2 H), 1.41-1.50 (m, 1 H), 1.52-1.60 (m, 1 H), 3.69 (ddd, *J* = 15.0, 7.6 and 5.6 Hz, 1 H), 3.88 (ddd, *J* = 14.2, 10.2 and 5.6 Hz, 1 H), 6.21 (s, 1 H), 7.29 (t, *J* = 7.6 Hz, 1 H), 7.59 (t, *J* = 7.6 Hz, 1 H), 7.64-7.69 (m, 1 H), 7.70-7.73 (m, 2 H), 8.01 (d, *J* = 7.0 Hz, 1 H), 8.07 (d, *J* = 8.0 Hz, 1 H), 8.11 (d, *J* = 8.0 Hz, 1 H); ^{13}C{^{1}H} NMR (100

MHz, $CDCl_3$) δ13.8, 20.1, 30.4, 42.9, 70.6, 120.1, 120.6, 125.0, 125.1, 125.2, 129.1, 130.6, 132.7, 130.0, 133.3, 136.7, 138.3, 163.7, 164.8; IR (KBr, neat) 2868, 1717, 1657, 1416, 756 cm^{-1}; HRMS (ESI) calcd. for $C_{19}H_{19}N_2O_2$ $(M + H)^+$ 307.1441, found 307.1416.

6-Phenethyl-6,6*a*-dihydroisoindolo[2,1-*a*]quinazoline-5,11-dione (2z):

White solid; R_f (Hexane:EtOAc, 1:1) 0.60; mp 145-147 ºC. Yield 157 mg, 88%; ^1H NMR (500 MHz, $CDCl_3$) δ 2.62-2.68 (m, 1 H), 2.91-2.97 (m, 1 H), 3.92-3.99 (m, 1 H), 4.05-4.12 (m, 1 H), 6.17 (s, 1 H), 7.10-7.12 (m, 2 H), 7.18-7.20 (m, 1 H), 7.22-7.26 (m, 2 H), 7.32-7.35 (m, 1 H), 7.61-7.71 (m, 4 H), 7.97-7.99 (m, 1 H), 8.07-8.10 (m, 1 H), 8.15-8.17 (m, 1 H); $^{13}C\{1H\}$ NMR (125 MHz, $CDCl_3$) δ 34.5, 44.8, 70.8, 120.2, 120.6, 125.3, 125.33, 125.4, 126.6, 128.7, 128.8, 129.0, 130.7, 132.6, 133.1, 133.5, 136.8, 138.1, 138.3, 163.8, 164.7; IR (KBr, neat) 2856, 1716, 1653, 1411, 735 cm^{-1}; HRMS (ESI) calcd. for $C_{23}H_{19}N_2O_2$ $(M + H)^+$ 355.1441, found 355.1461.

6-Cyclopropyl-6,6*a*-dihydroisoindolo[2,1-*a*]quinazoline-5,11-dione (2aa):

White solid; R_f (Hexane:EtOAc, 2:3) 0.60; mp 160-162 ºC. Yield 142 mg, 97%; ^1H NMR (500 MHz, $CDCl_3$) δ 0.03-0.08 (m, 1 H), 0.65-0.71 (m, 1 H), 0.84-0.90 (m, 1 H), 1.11-1.17 (m, 1 H), 2.68-2.72 (m, 1 H), 6.17 (s, 1 H), 7.29 (t, *J* = 7.6 Hz, 1 H), 7.29 (t, *J* = 7.6 Hz, 1 H), 7.65-7.70 (m, 2 H), 7.91 (d, *J* = 7.2 Hz, 1 H), 7.99 (d, *J* = 7.2 Hz, 1 H), 8.13-8.17 (m, 2 H); $^{13}C\{1H\}$ NMR (125 MHz, $CDCl_3$) δ 9.6, 11.6, 26.2, 72.1, 119.6, 120.5, 124.7, 125.0, 126.6, 129.1, 130.3, 132.0, 132.6, 133.6, 137.1, 138.4, 164.9, 165.6; IR (KBr, neat) 2923, 2853, 1714, 1664, 1409, 756 cm^{-1}; HRMS (ESI) calcd. for $C_{18}H_{15}N_2O_2$ $(M + H)^+$ 291.1128, found 291.1140.

Experimental procedure and Characterization data of the compound 3a:

To a stirred solution of benzyl bromide (56 mg, 0.33 mmol) in H_2O (2 ml)/*t*-BuOH (2 ml) under N_2 atmosphere, sodium azide (20 mg, 0.3 mmol) and Et_3N (40 mg, 0.39 mmol) were added. The reaction was allowed to stir at room temperature for an hour. Later on, 1-(prop-2-yn-1-yl)-1,3,4,10*b*-tetrahydropyrimido[2,1-*a*]isoindole-2,6-dione (**2u**) (72 mg, 0.3 mmol), sodium ascorbate (30 mg, 0.15 mmol), and $CuSO_4$ (5.0 mg, 0.03 mmol) were added to the freshly prepared benzyl azide. The reaction mixture was then stirred at room temperature for 10 h. Upon completion of the reaction (checked by TLC analysis), the reaction mixture was diluted with saturated $NaHCO_3$ solution. The crude product was extracted with ethyl acetate (2 x 10 mL). The combined organic layers were further washed with brine and dried over anhydrous Na_2SO_4. The organic phase was concentrated in a rotary evaporator to give the crude product, which was then subjected to column chromatography over silica gel to provide the corresponding product **3a**.

1-((2-Benzyl-2*H*-1,2,3-triazol-4-yl)methyl)-1,3,4,10*b*-tetrahydropyrimido[2,1-*a*]isoindole-2,6-dione (3a):

White solid; R_f (EtOAc, 100%) 0.40; mp 198-200 ^oC. Yield 89 mg, 79%; ^1H NMR (400 MHz, $CDCl_3$) δ 2.49-2.56 (m, 1 H), 2.60-2.68 (m, 1 H), 3.32-3.40 (m, 1 H), 4.37-4.44 (m, 1 H), 4.65 (d, *J* = 15.6 Hz, 1 H), 5.19 (d, *J* = 15.6 Hz, 1 H), 5.40 (d, *J* = 14.8 Hz, 1 H), 5.52 (d, *J* = 14.8 Hz, 1 H), 6.02 (s, 1 H), 7.20-7.23 (m, 2 H), 7.33-7.35 (m, 3 H), 7.45 (s, 1 H), 7.51-7.60 (m, 2 H), 7.85 (d, *J* = 7.2 Hz, 1 H), 8.15 (d, *J* = 7.2 Hz, 1 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 32.1, 35.5, 38.2, 54.3, 70.5, 123.2, 124.3, 125.8, 128.1, 128.8, 129.1, 130.2, 132.1, 134.4, 140.5, 144.2, 167.5, 168.4; IR (KBr, neat) 2927, 1705, 1650, 1425, 1294, 730 cm^{-1}; HRMS (ESI) calcd. for $C_{21}H_{19}N_5NaO_2$ $(M + Na)^+$ 396.1431, found 396.1432.

Experimental procedure and Characterization data of the compound 3b:

To an ice-cold solution of 1-(prop-2-yn-1-yl)-1,3,4,10*b*-tetrahydropyrimido[2,1-*a*]isoindole-2,6-dione (**2u**) (96 mg, 0.4 mmol) in benzene (0.5 mL) under N_2 atmosphere, triflic acid (1.5 mL) was added. The reaction was then refluxed at 80 °C in an oil bath for 2.5 h. Upon completion of the reaction (checked by TLC analysis), the reaction mixture was made basic with 50% NaOH solution and extracted with ethyl acetate (2 x 10 mL). The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. The organic phase was concentrated in a rotary evaporator to give the crude product, which was then subjected to column chromatography over silica gel to provide the corresponding product **3b**.

8-Methyl-8-phenyl-2,3,8,9-tetrahydro-1*H*-3*a*,9*a*-diazacyclopenta[*def*]phenanthrene-1,4(9*a*1*H*)-dione (3b):

White semi solid; R_f (Hexane:EtOAc, 2:3) 0.50; Yield 108 mg, 84%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.21 (s, 3 H), 2.88-2.94 (m, 1 H), 3.03-3.10 (m, 1 H), 3.29-3.35 (m, 1 H), 4.21-4.27 (m, 1 H), 5.43 (s, 1 H), 6.57 (t, *J* = 1.4 Hz, 1 H), 7.08-7.10 (m, 2 H), 7.11-7.13 (m, 1 H), 7.28-7.34 (m, 3 H), 7.40-7.45 (m, 2 H), 7.84-7.88 (m, 1 H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 10.8, 27.4, 38.1, 64.8, 122.6, 123.1, 123.5, 127.6, 128.3, 128.7, 129.1, 131.3, 131.8, 136.8, 146.4, 148.8, 160.8, 168.7; IR (KBr, neat) 2926, 1692, 1403, 1217, 740 cm^{-1}; HRMS (ESI) calcd. for $C_{20}H_{19}N_2O_2$ (M + H)$^+$ 319.1441, found 319.1438.

Experimental procedure and Characterization data of the compound 3c:

To a stirred solution of 1-(prop-2-yn-1-yl)-1,3,4,10*b*-tetrahydropyrimido[2,1-*a*]isoindole-2,6-dione (**2u**) (96 mg, 0.4 mmol) in toluene (3.0 mL) under inert atmosphere, $In(OTf)_3$ (34 mg, 0.06 mmol) was added. The reaction mixture was refluxed in an oil bath for 5 h. Upon completion of

the reaction (checked by TLC analysis), the solvent was removed under reduced pressure and diluted with saturated $NaHCO_3$ solution. The organic layer was extracted with ethyl acetate (2 x 10 mL). The combined organic layers were further washed with brine and dried over anhydrous Na_2SO_4. The organic phase was concentrated in a rotary evaporator to give the crude product, which was then subjected to column chromatography over silica gel to provide the corresponding product **3c**.

1-(2-Oxopropyl)-1,3,4,10*b*-tetrahydropyrimido[2,1-*a*]isoindole-2,6-dione (3c):

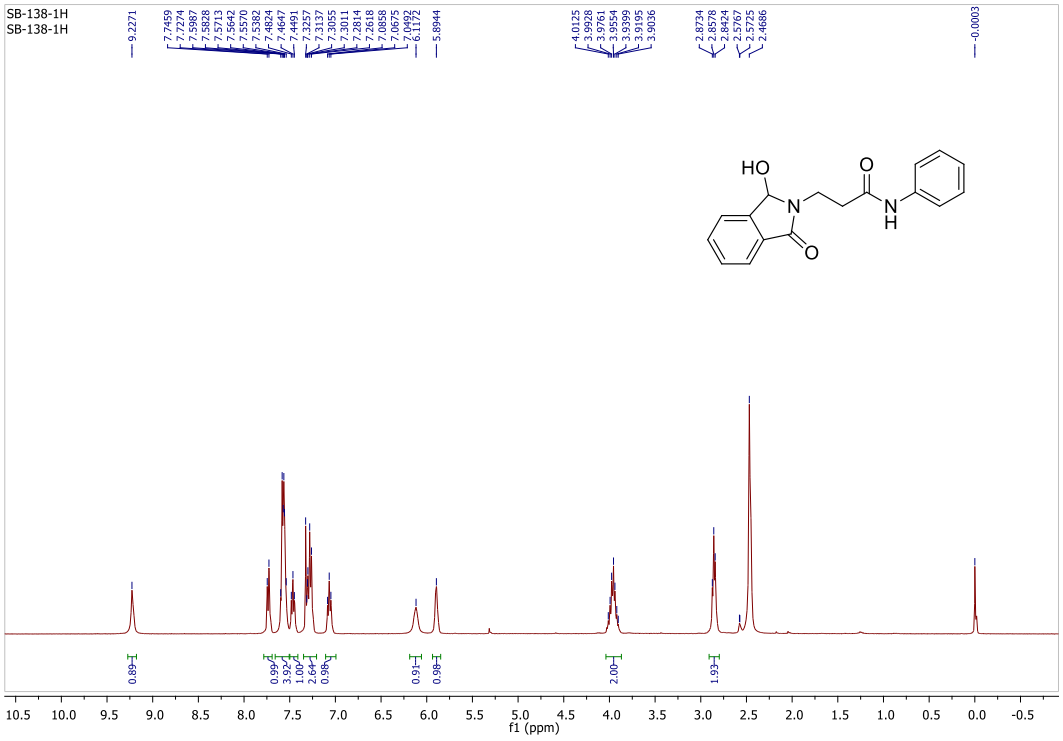
White solid; R_f (EtOAc, 100%) 0.40; mp 159-161 ^oC. Yield 78 mg, 75%; ^1H NMR (500 MHz, $CDCl_3$) δ 2.16 (s, 3 H), 2.69 (dd, *J* = 7.4 and 5.8 Hz, 2 H), 3.59 (dt, *J* = 13.2 and 7.4 Hz, 1 H), 4.08 (d, *J* = 18.2 Hz, 1 H), 4.36 (dt, *J* = 11.5 and 5.8 Hz, 1 H), 4.81 (d, *J* = 18.2 Hz, 1 H), 6.00 (s, 1 H), 7.37-7.41 (m, 1 H), 7.56-7.59 (m, 2 H), 7.87-7.91 (m, 1 H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 27.3, 31.6, 35.8, 53.0, 70.7, 123.8, 124.8, 130.5, 132.1, 132.7, 140.0, 167.2, 169.0, 203.2; IR (KBr, neat) 2925, 1702, 1650, 1412, 1295, 735 cm^{-1}; HRMS (ESI) calcd. for $C_{14}H_{15}N_2O_3$ $(M + H)^+$ 259.1077, found 259.1102.

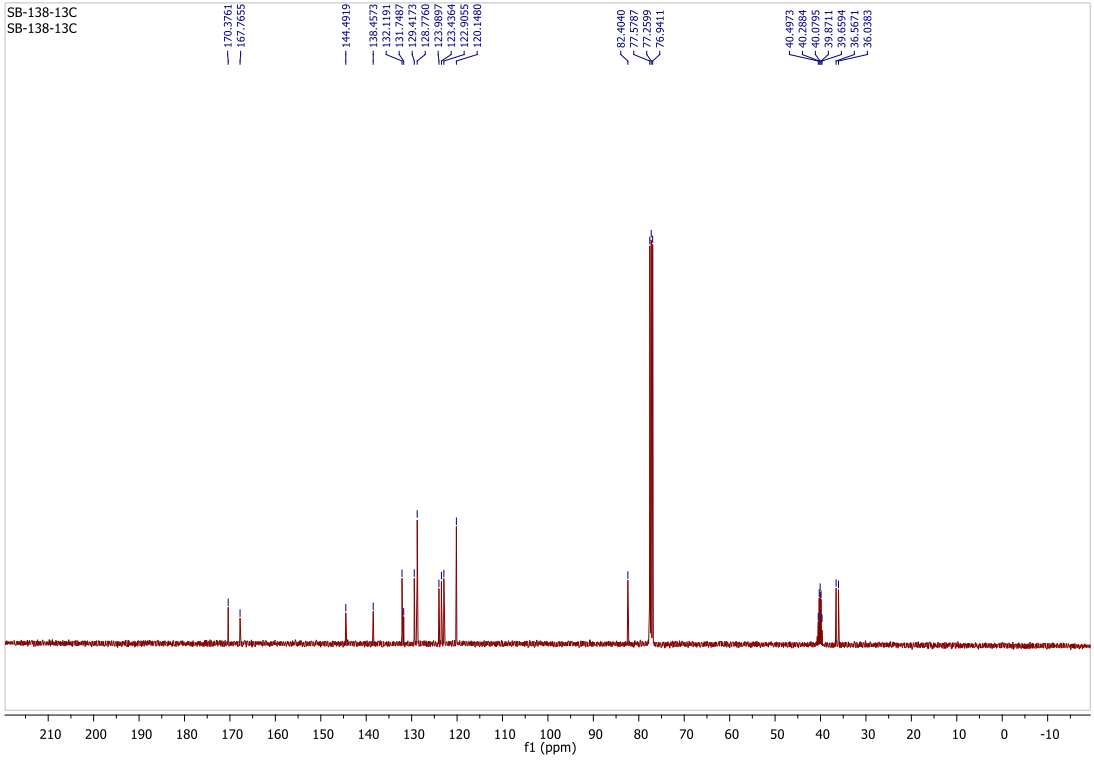
References:

1. (a) R. G. Schmidt, E. K. Bayburt, S. P. Latshaw, J. R. Koenig, J. F. Daanen, H. A. McDonald, B. R. Bianchi, C. Zhong, S. Joshi, P. Honore, K. C. Marsh, C.-H. Lee, C. R. Faltynek and A. Gomtsyan, *Bioorg. Med. Chem. Lett.*, 2011, **21**, 1338–1341; (b) P. A. Tenthorey, R. L. DiRubio, H. S. Feldman, B. H. Takman, E. W. Byrnes and P. D. McMaster, *J. Med. Chem*., 1979, **22**, 1182-1186.

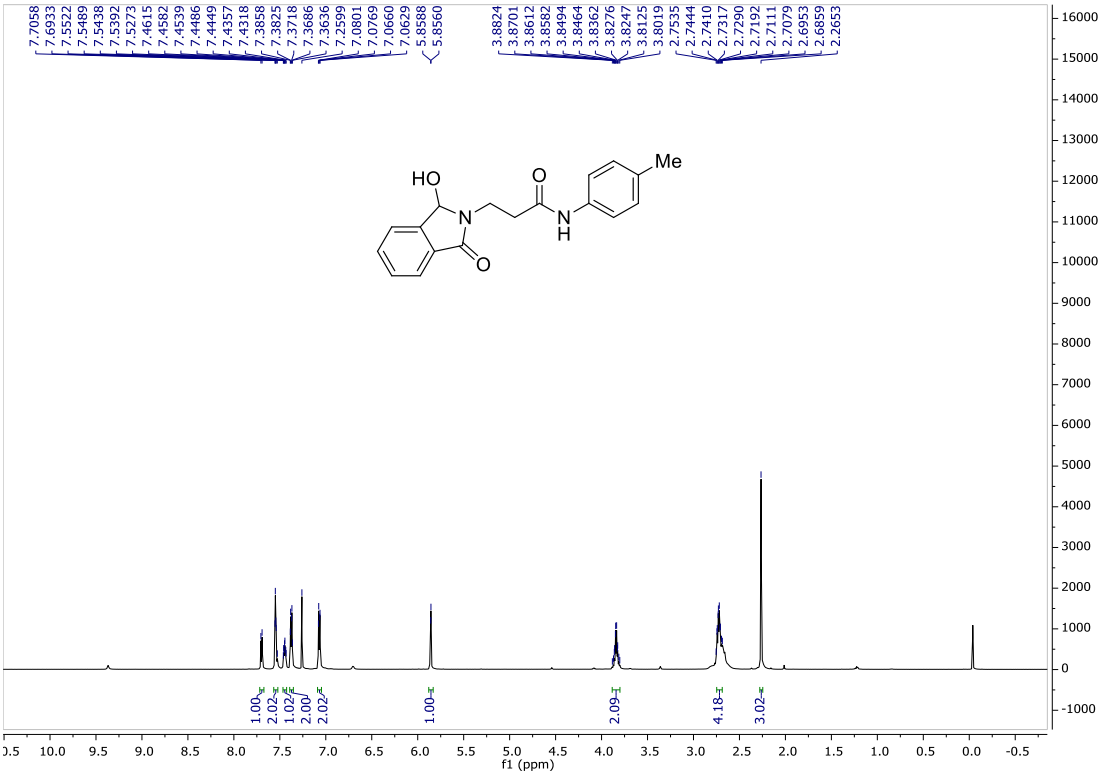
2. (a) M. Hellal and G. D. Cuny, *Tetrahedron Lett.*, 2011, **52**, 5508–5511; (b) R. G. R. Bacon and A. Karim, *J. Chem. Soc., Perkin Trans. 1*, 1973, 272-278.

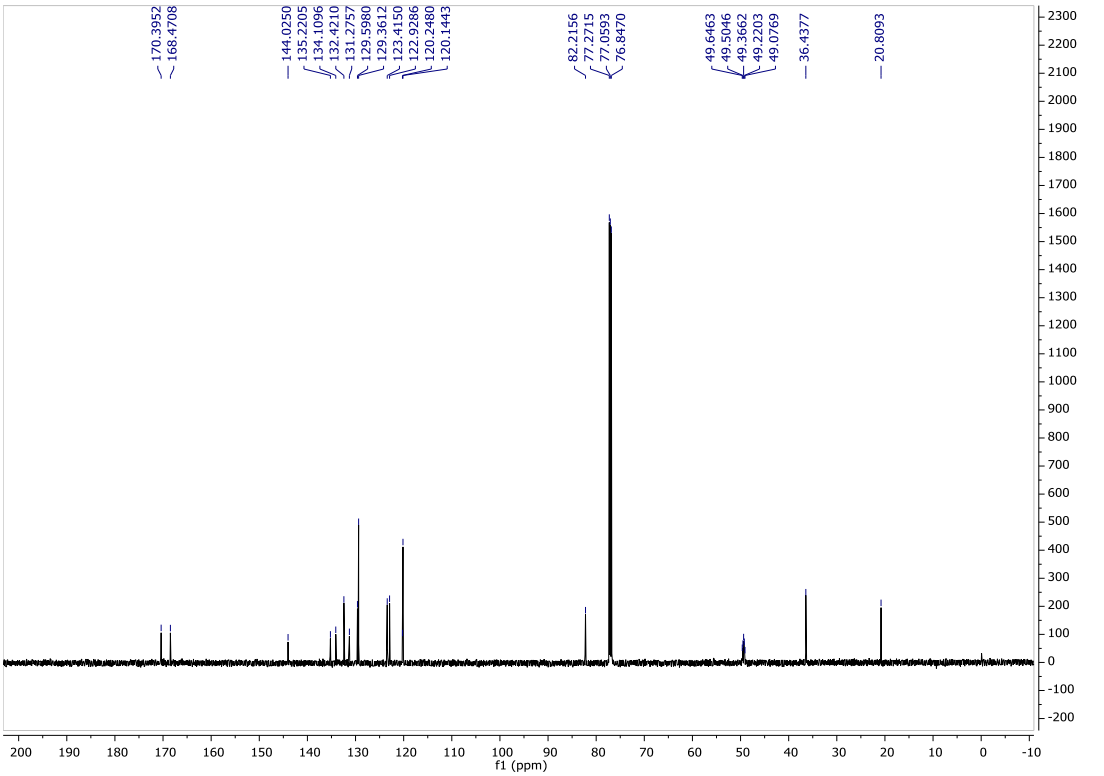
^{1}H and ^{13}C NMR spectra of **1a** (400 and 100 MHz, DMSO-d_6)



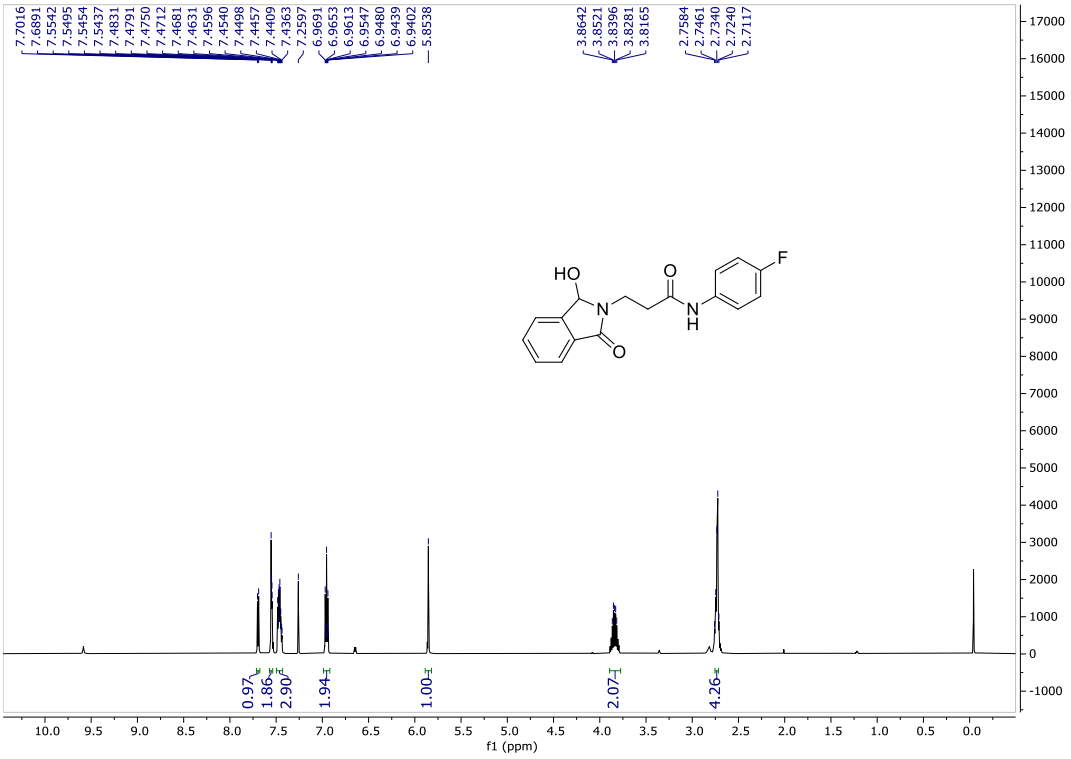


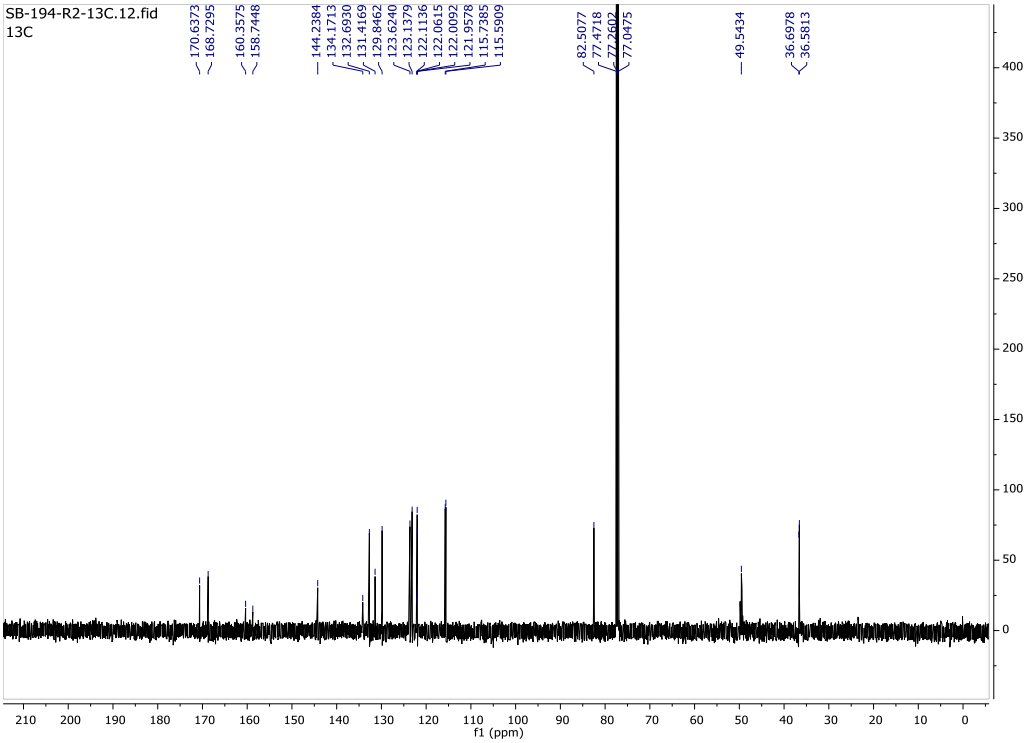
^{1}H and ^{13}C NMR spectra of **1b** (400 and 100 MHz, $CDCl_3$/MeOH-d_4)



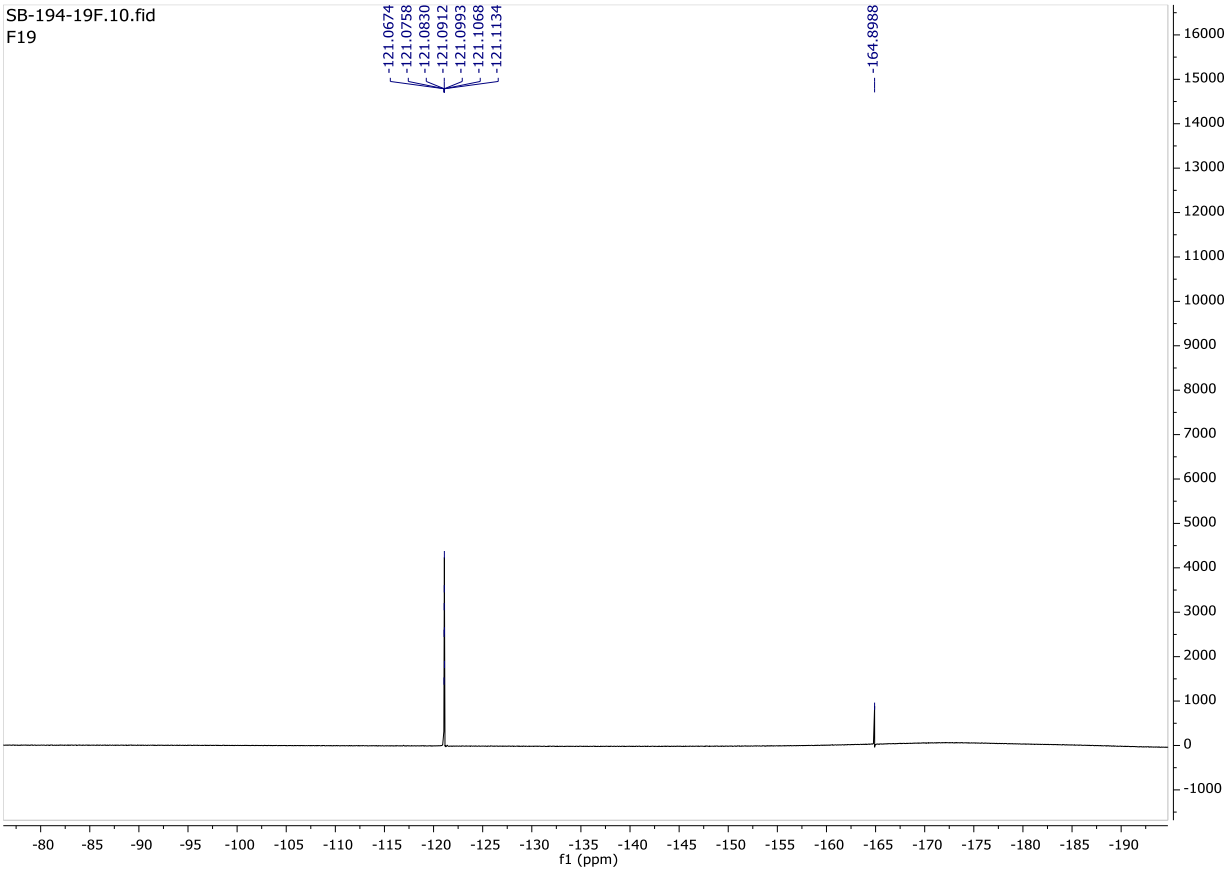


^{1}H and ^{13}C NMR spectra of **1c** (600 and 150 MHz, $CDCl_3$/MeOH-d_4)

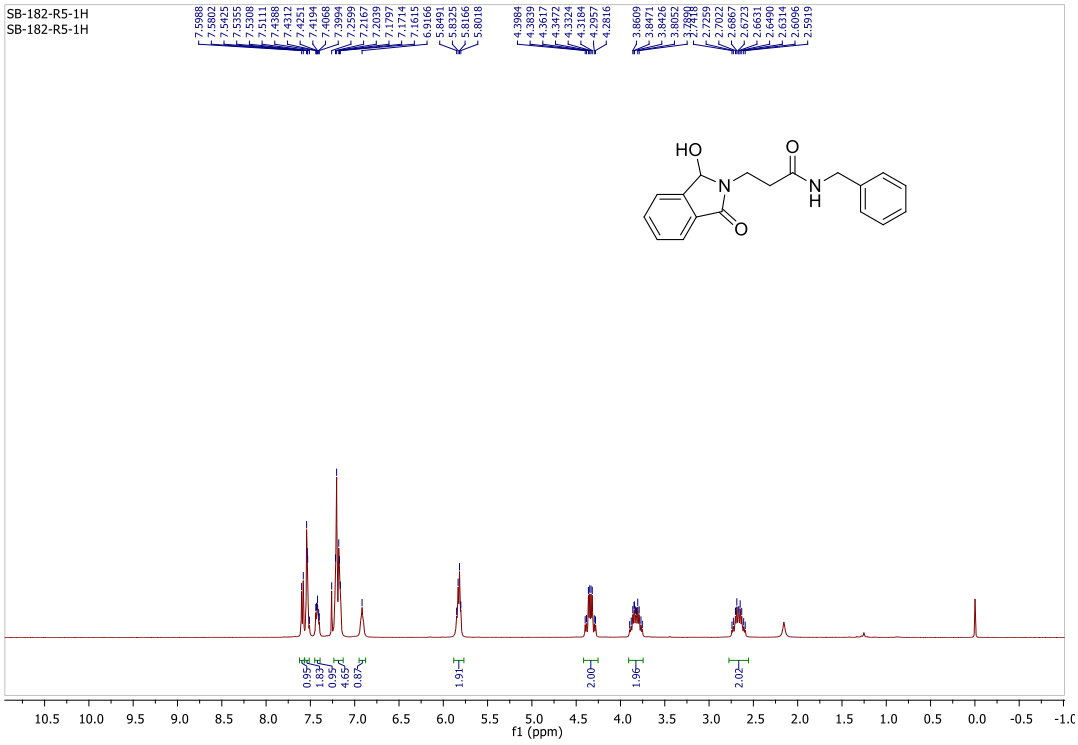


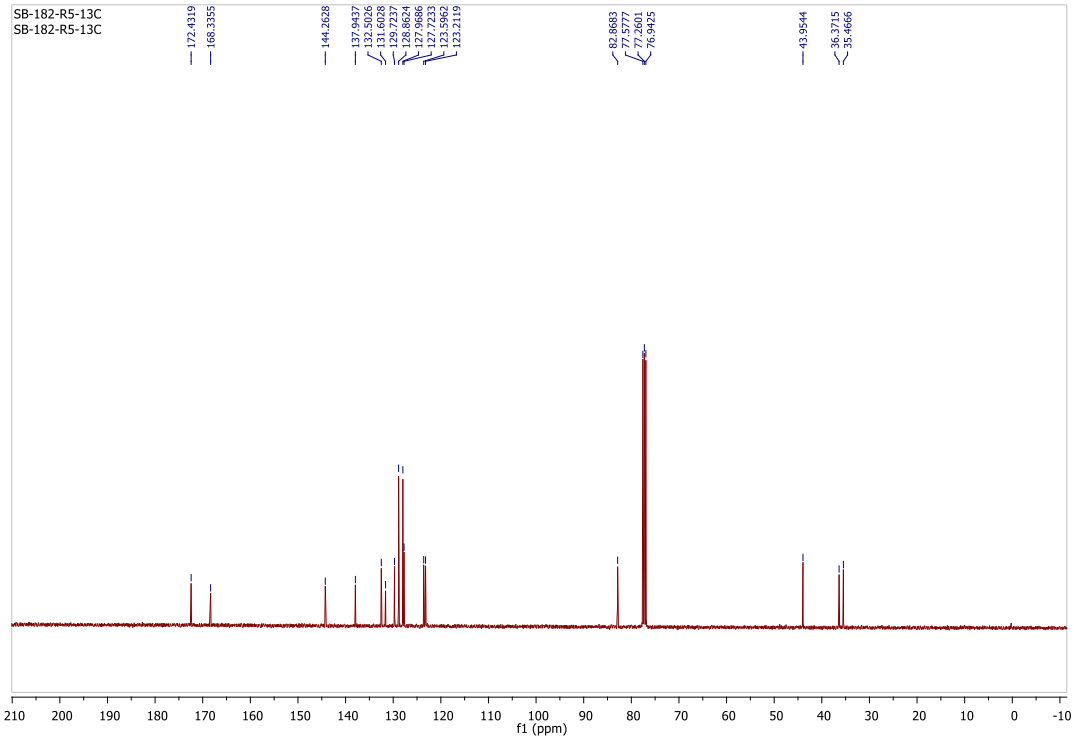


^{19}F NMR spectrum of **1c** (564 MHz, $CDCl_3$/MeOH-d_4/C_6F_6)

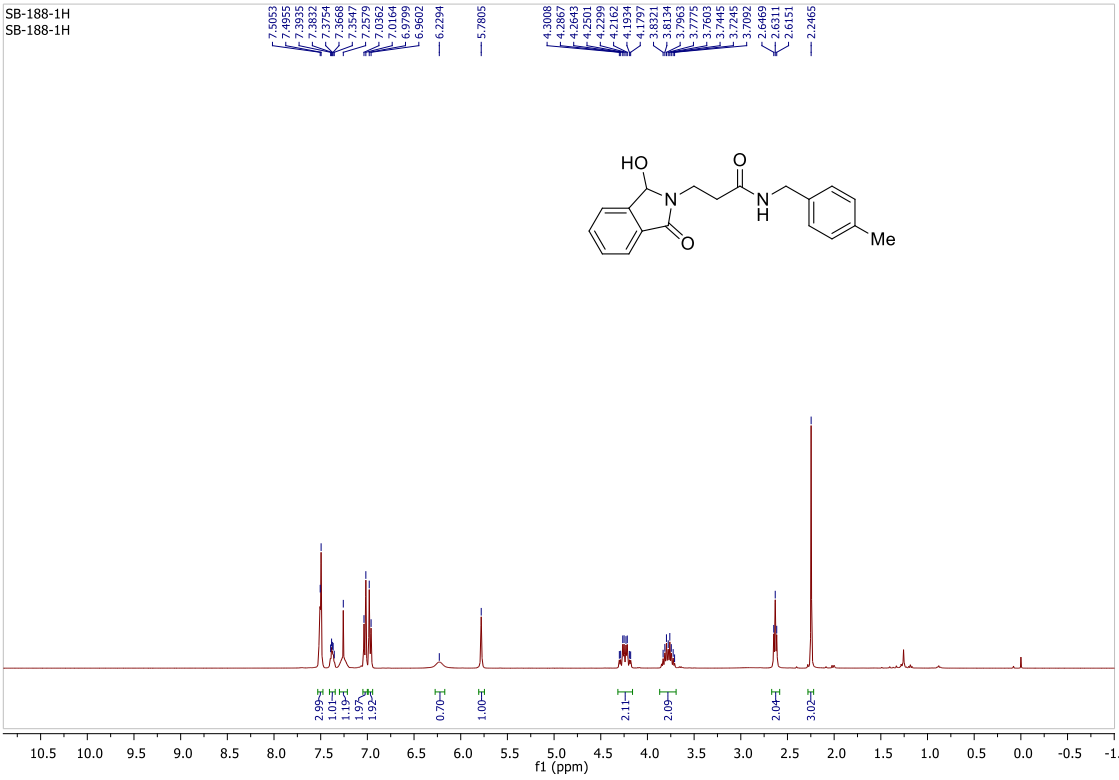


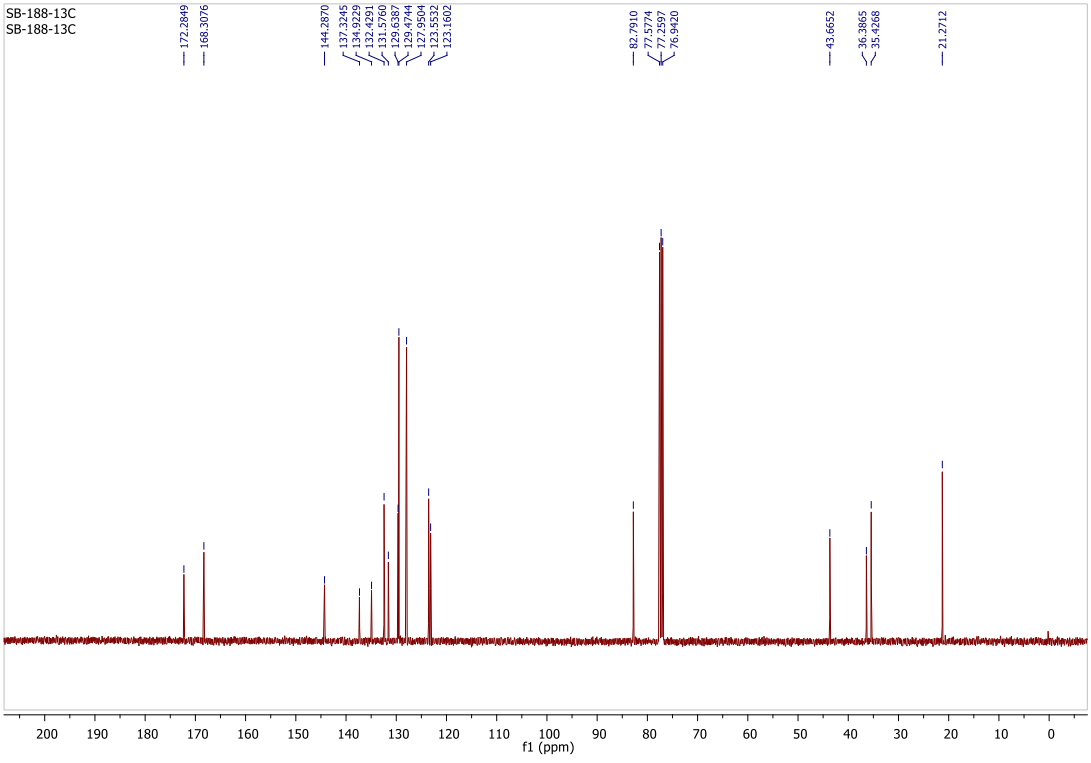
^{1}H and ^{13}C NMR spectra of **1d** (400 and 100 MHz, $CDCl_3$)



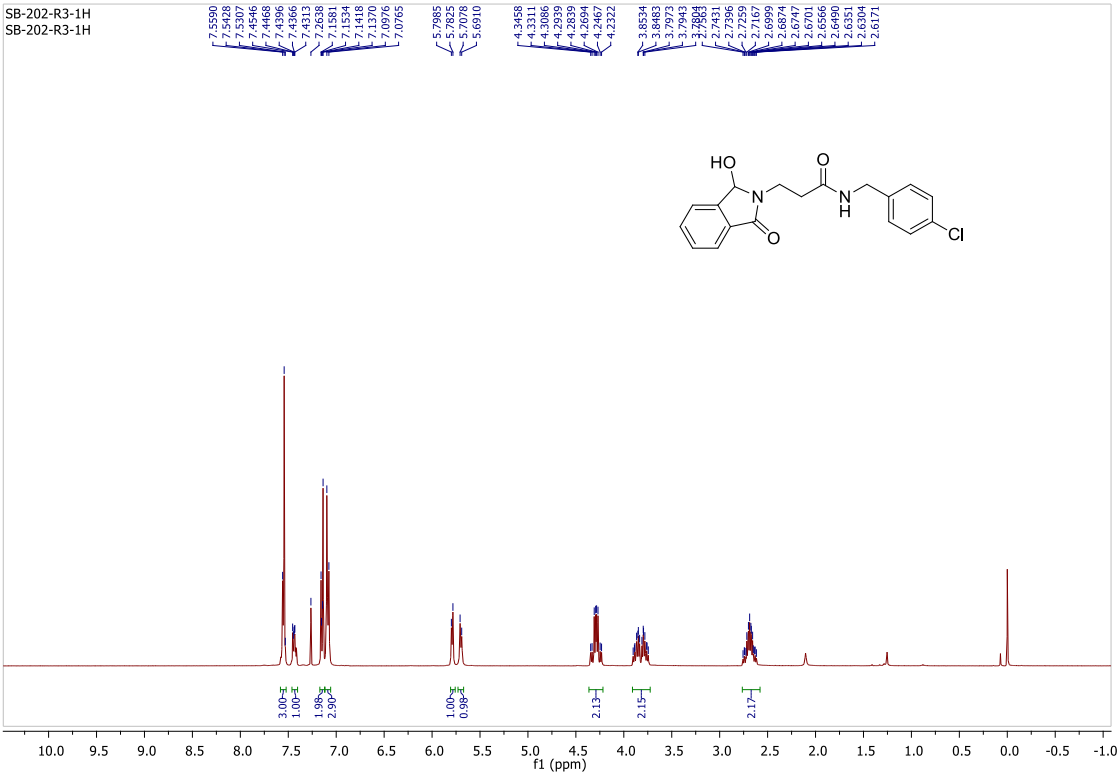


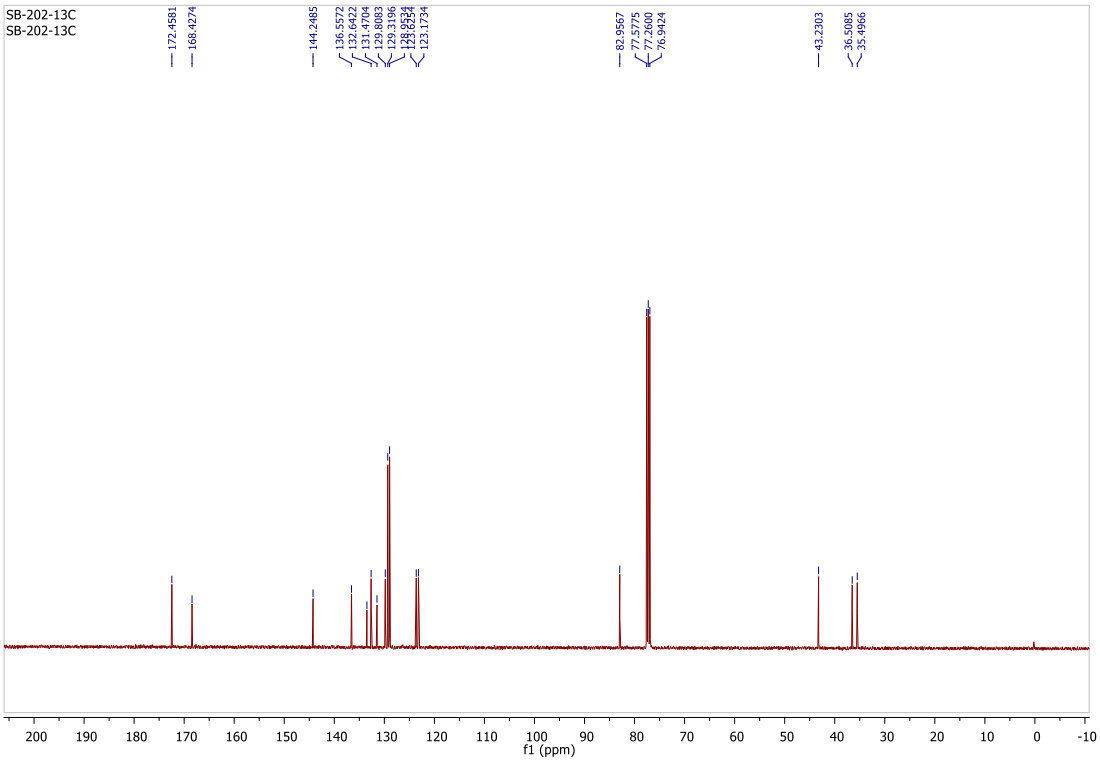
^{1}H and ^{13}C NMR spectra of **1e** (400 and 100 MHz, $CDCl_3$)



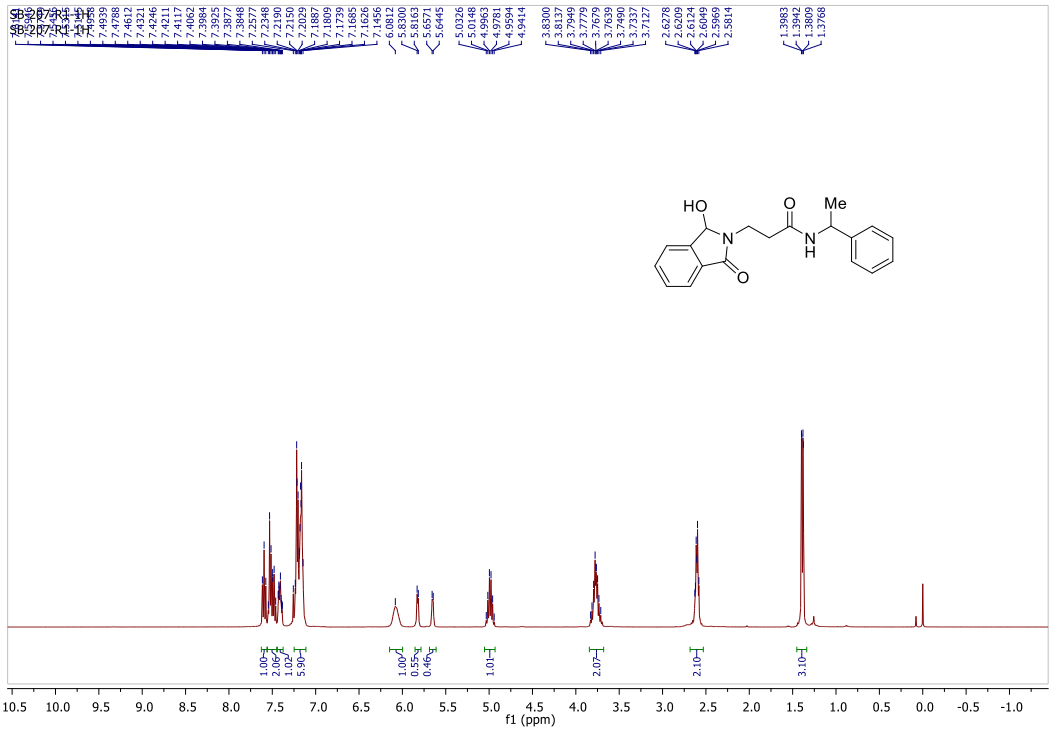


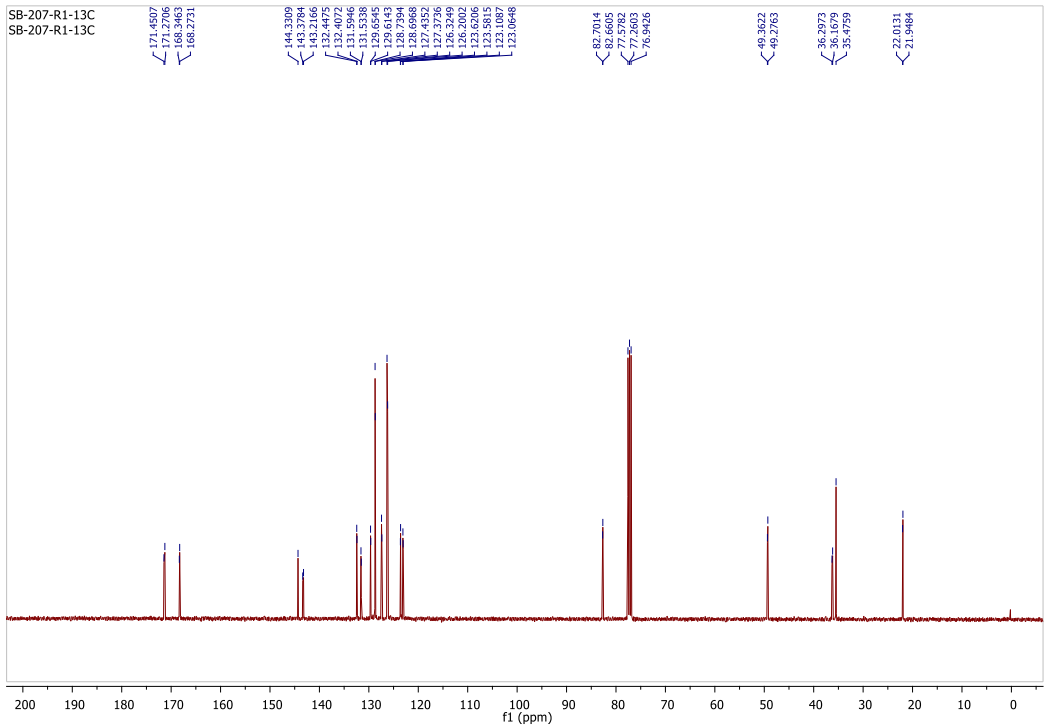
^{1}H and ^{13}C NMR spectra of **1f** (400 and 100 MHz, $CDCl_3$)



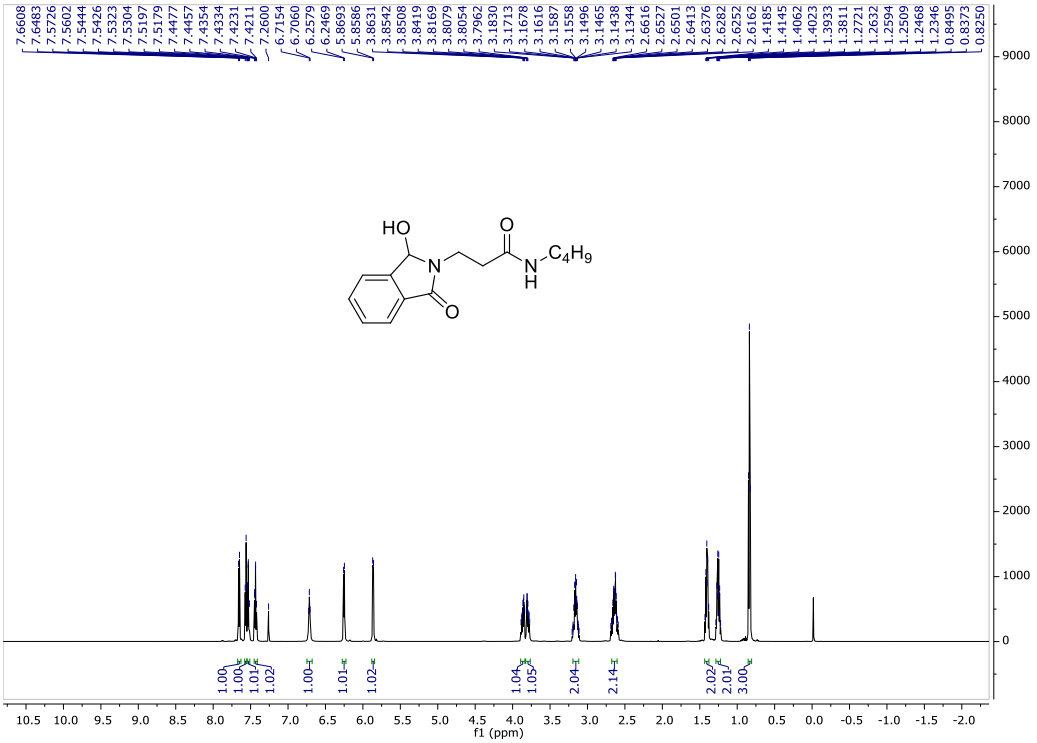


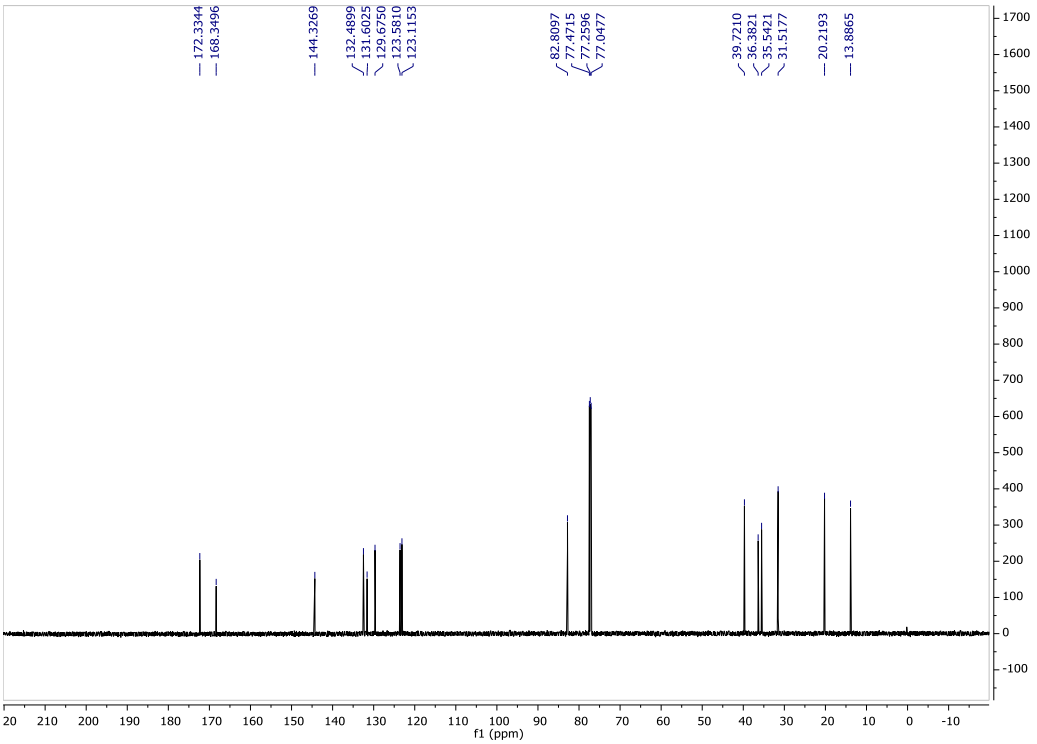
^{1}H and ^{13}C NMR spectra of **1g** (400 and 100 MHz, $CDCl_3$)



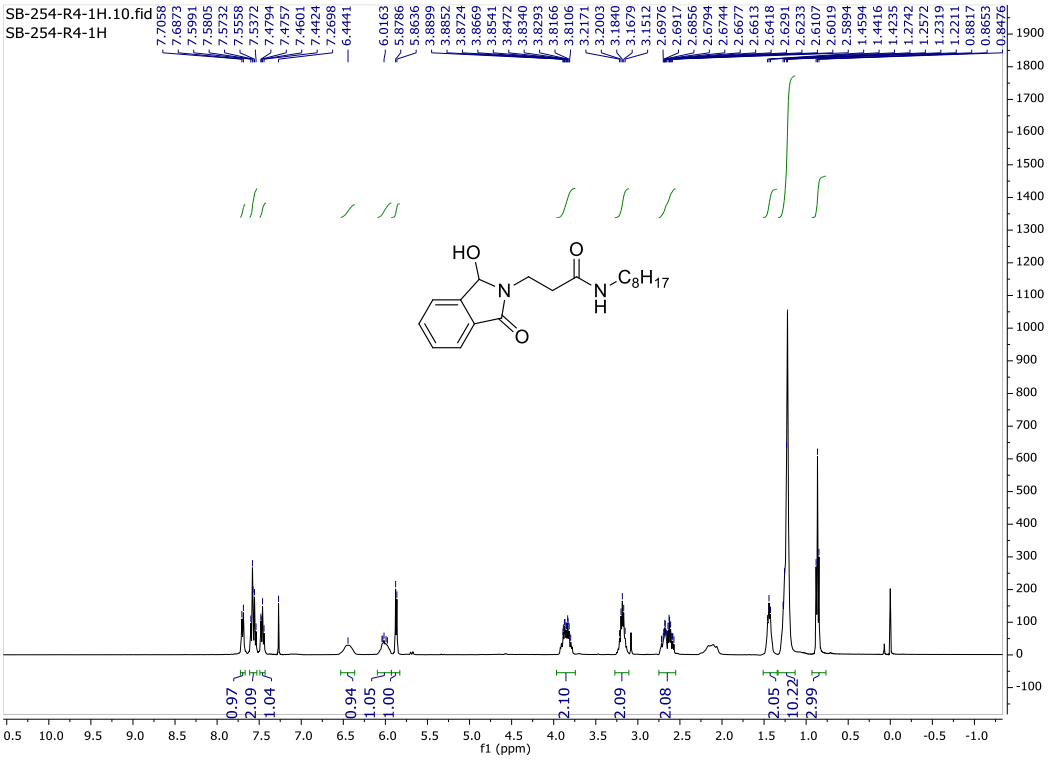


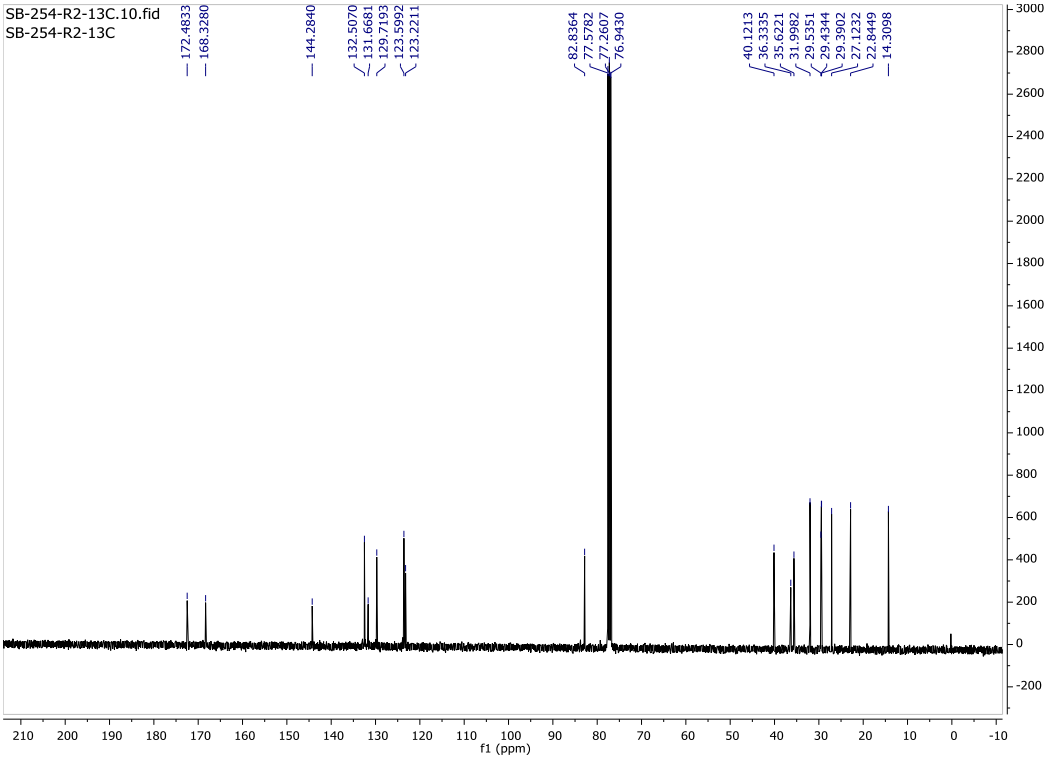
^{1}H and ^{13}C NMR spectra of **1h** (600 and 150 MHz, $CDCl_3$)



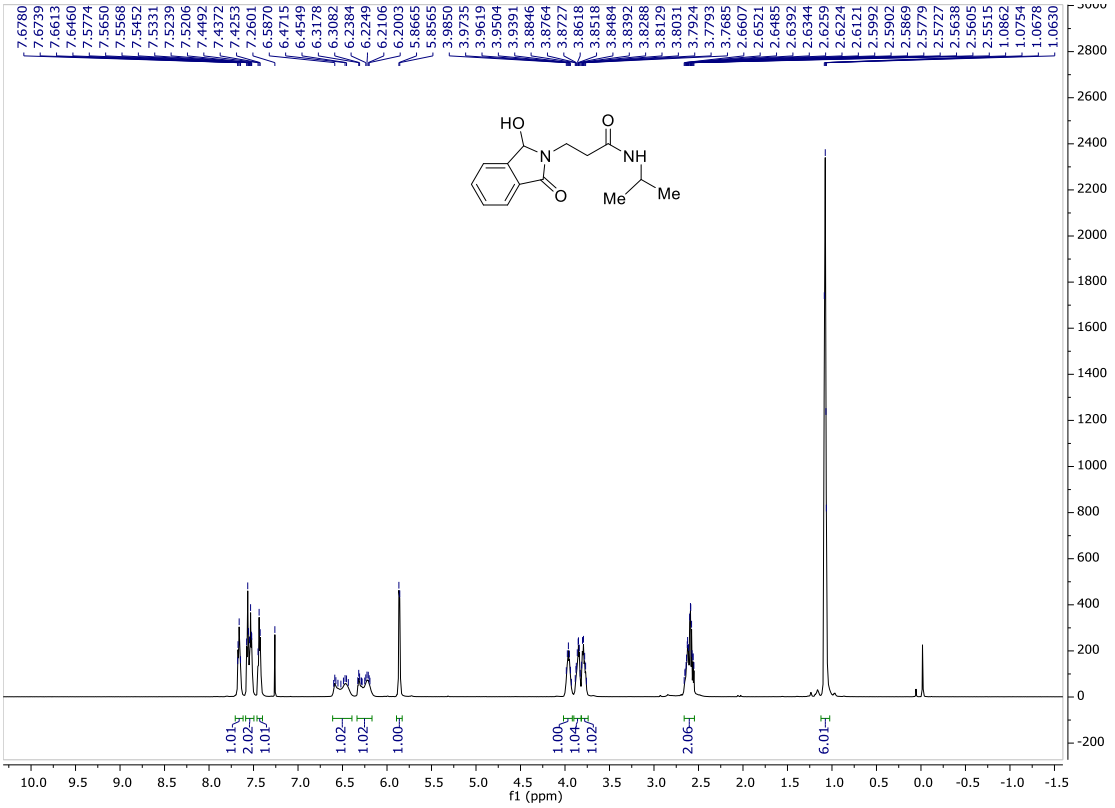


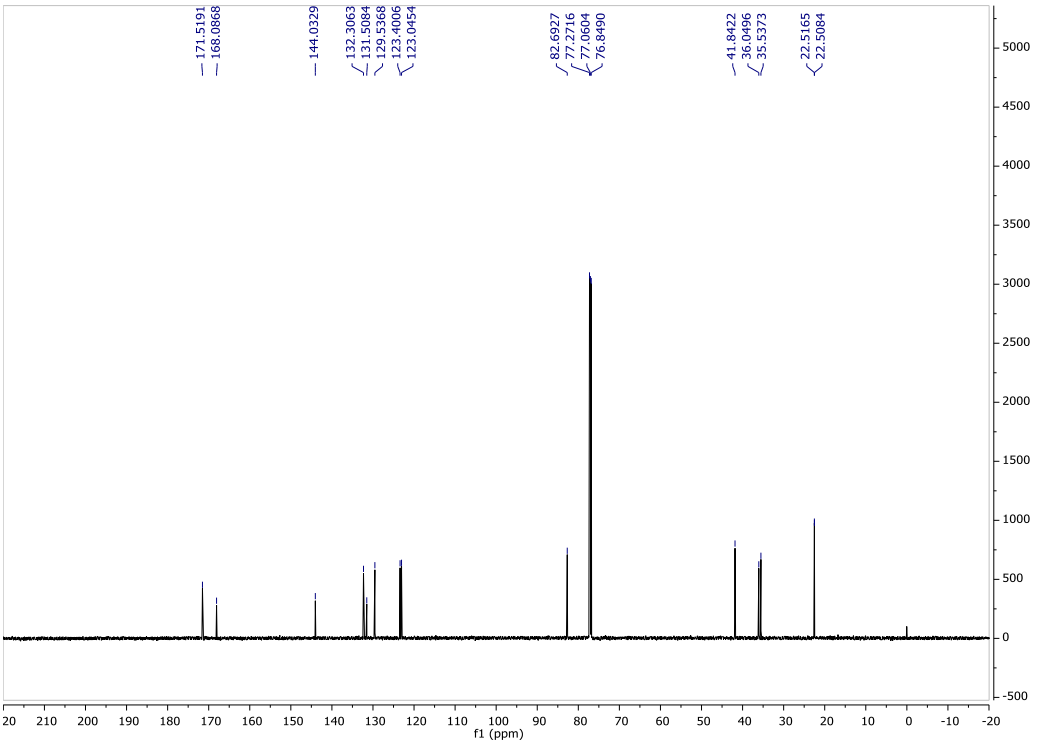
^{1}H and ^{13}C NMR spectra of **1i** (400 and 100 MHz, $CDCl_3$)



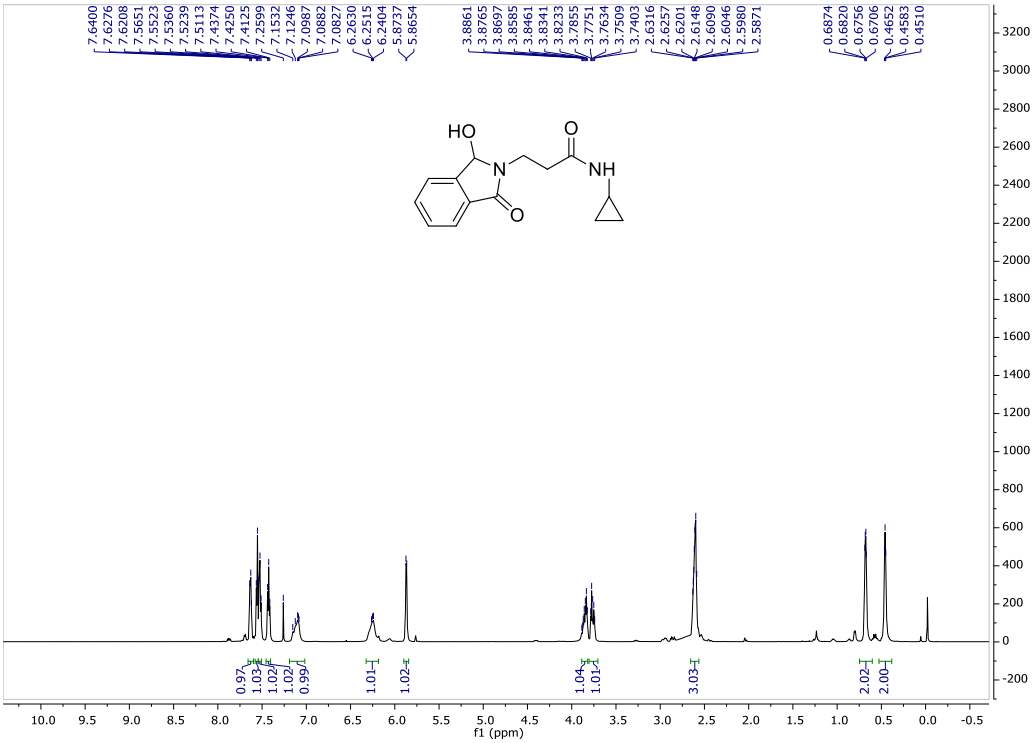


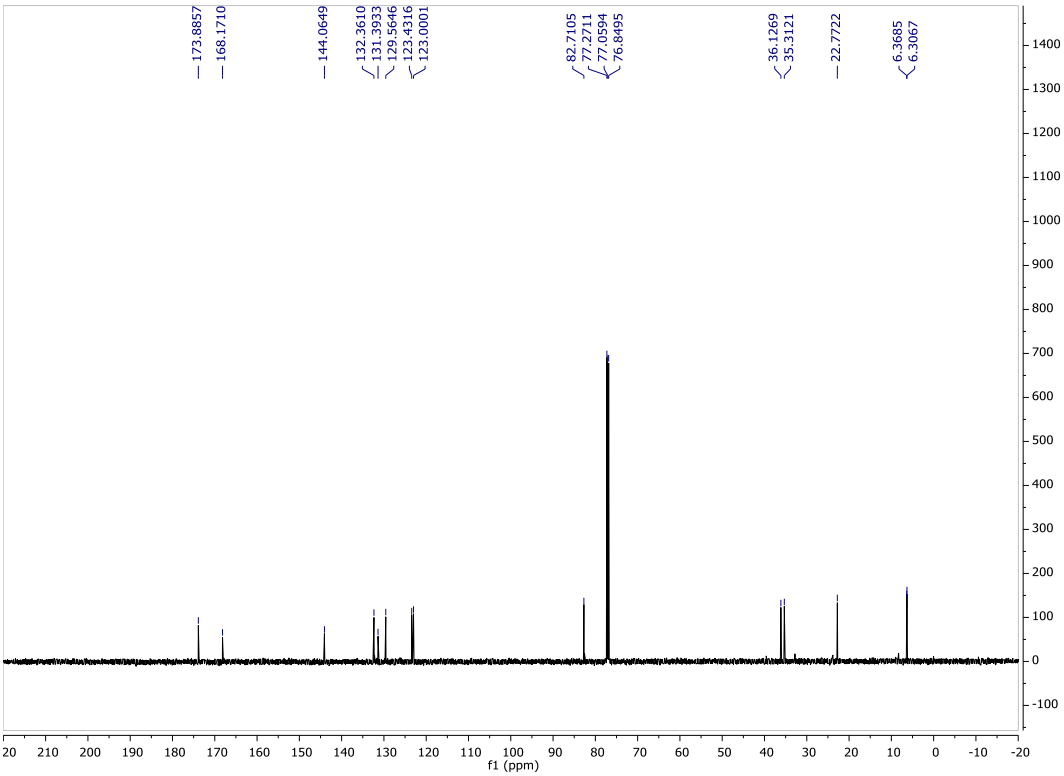
^{1}H and ^{13}C NMR spectra of **1j** (600 and 150 MHz, $CDCl_3$)



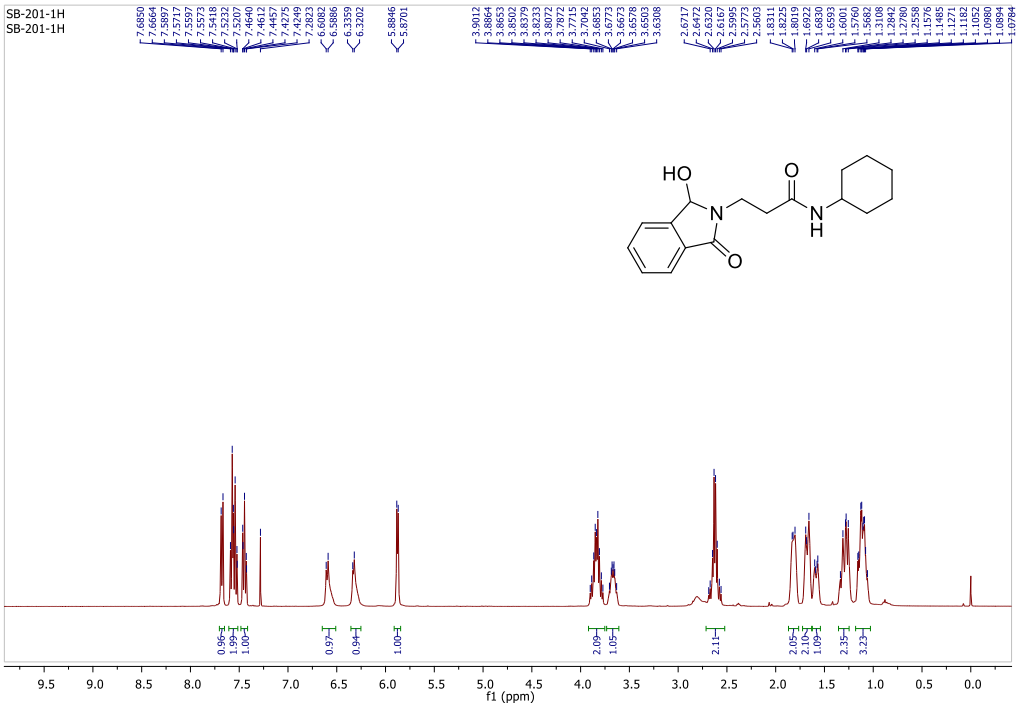


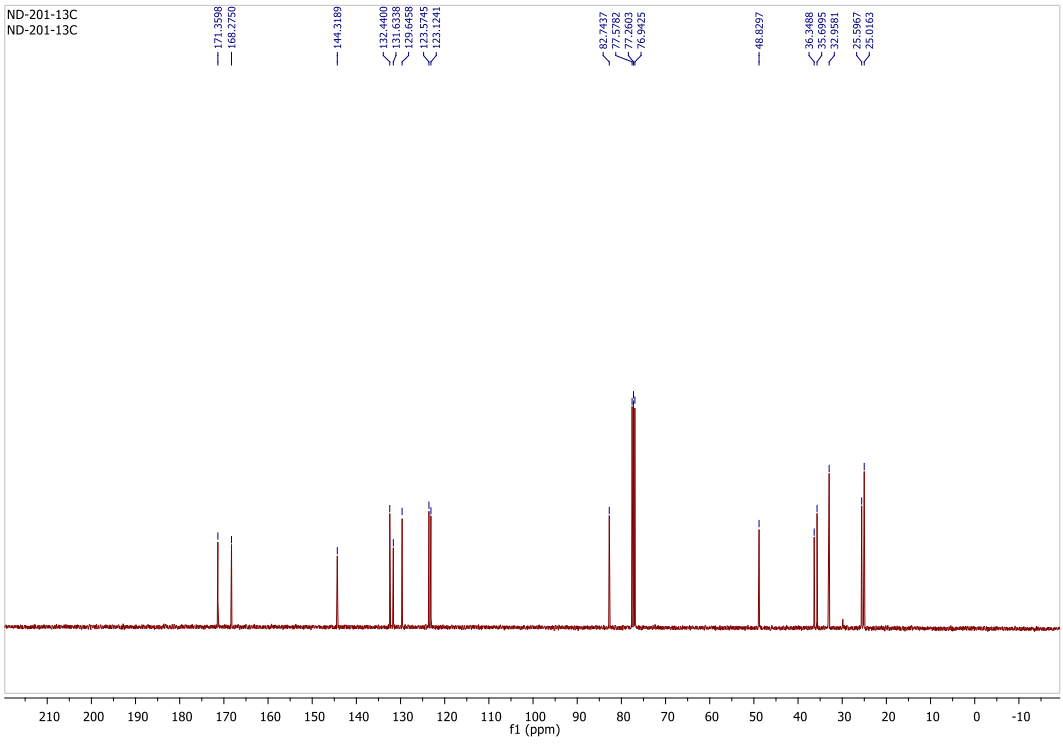
^{1}H and ^{13}C NMR spectra of **1k** (600 and 150 MHz, $CDCl_3$)



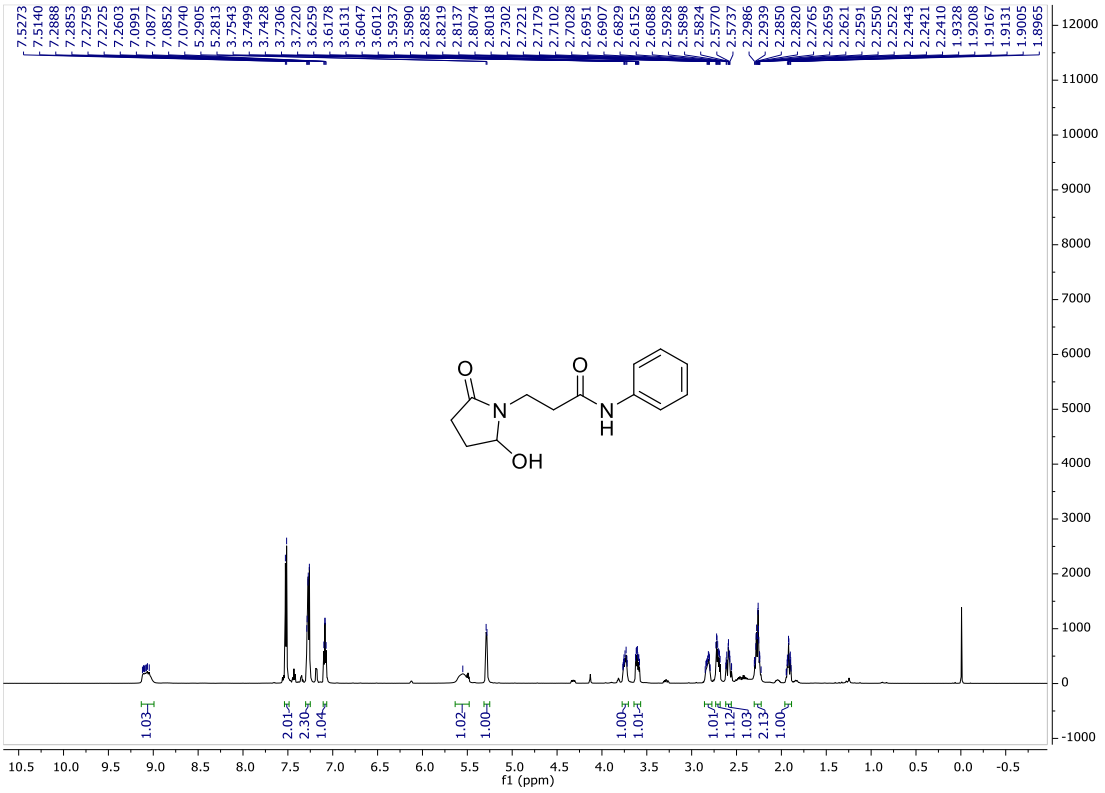


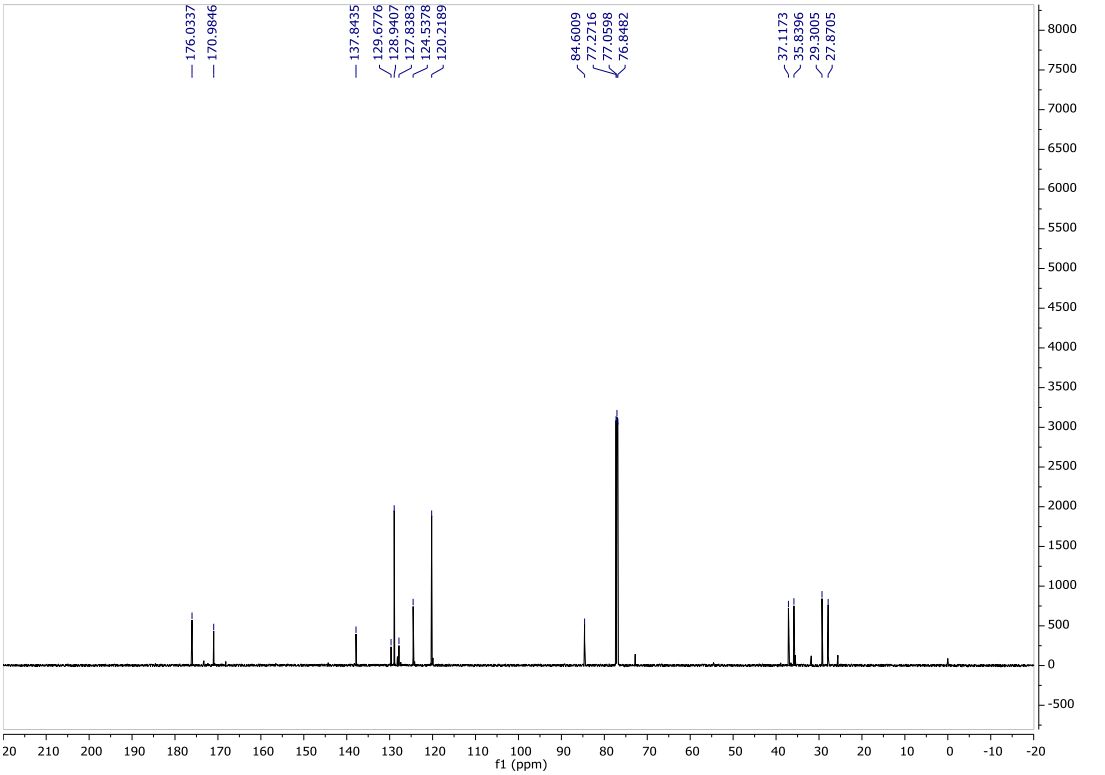
^{1}H and ^{13}C NMR spectra of **1l** (400 and 100 MHz, $CDCl_3$)



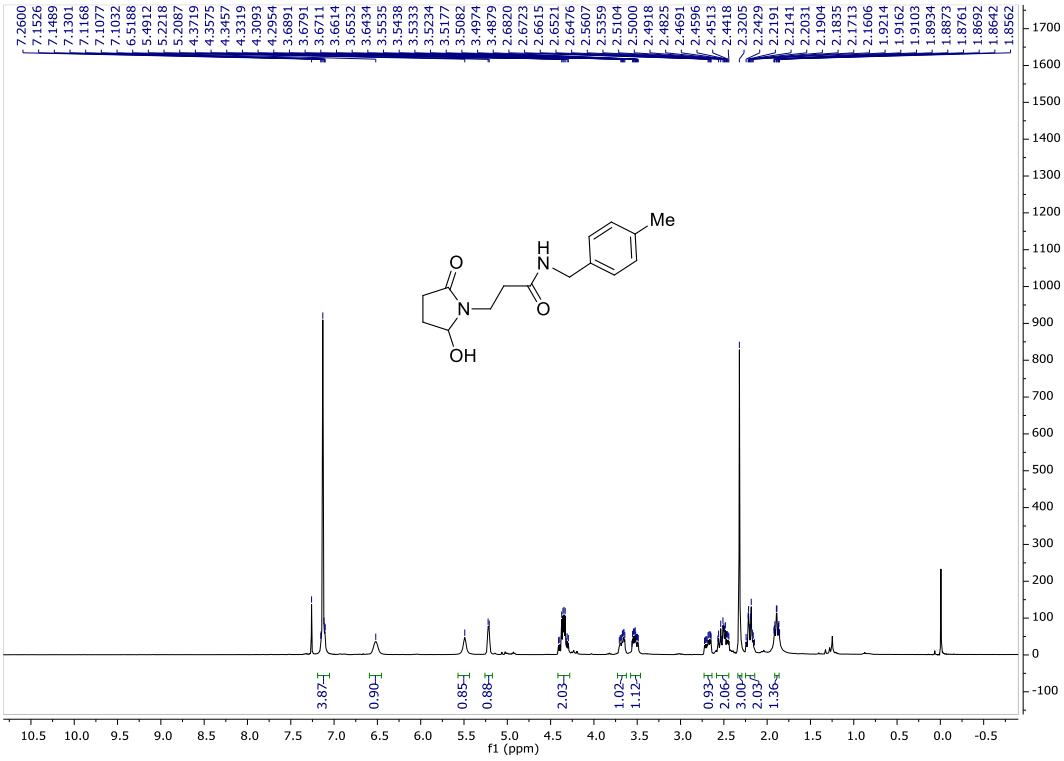


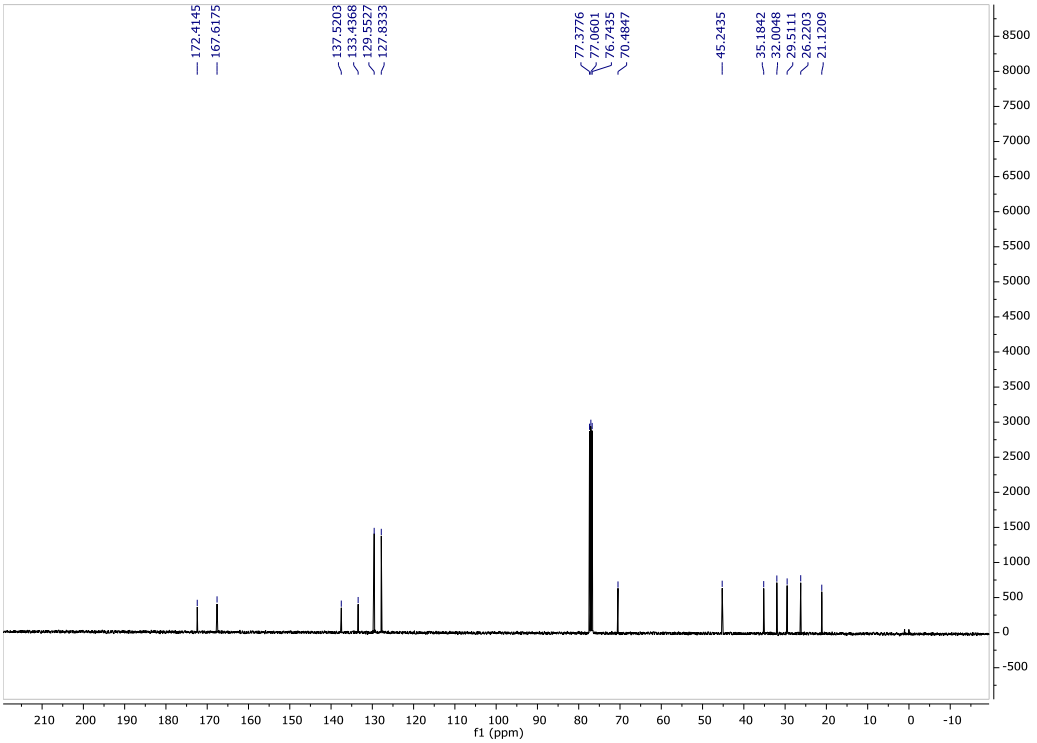
^{1}H and ^{13}C NMR spectra of **1m** (600 and 150 MHz, $CDCl_3$)



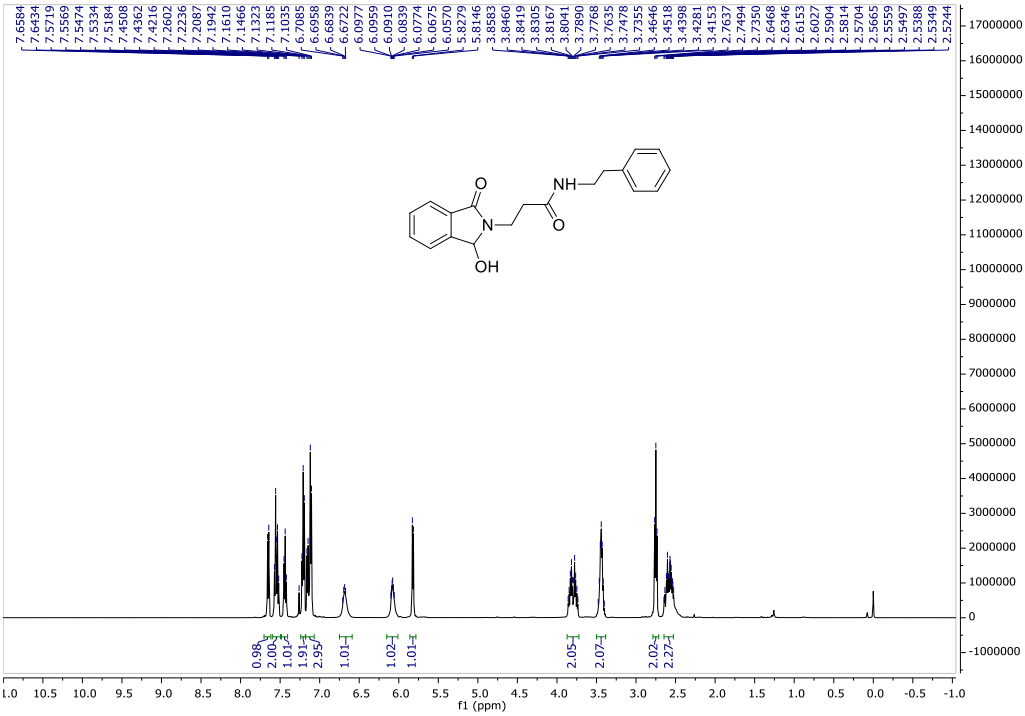


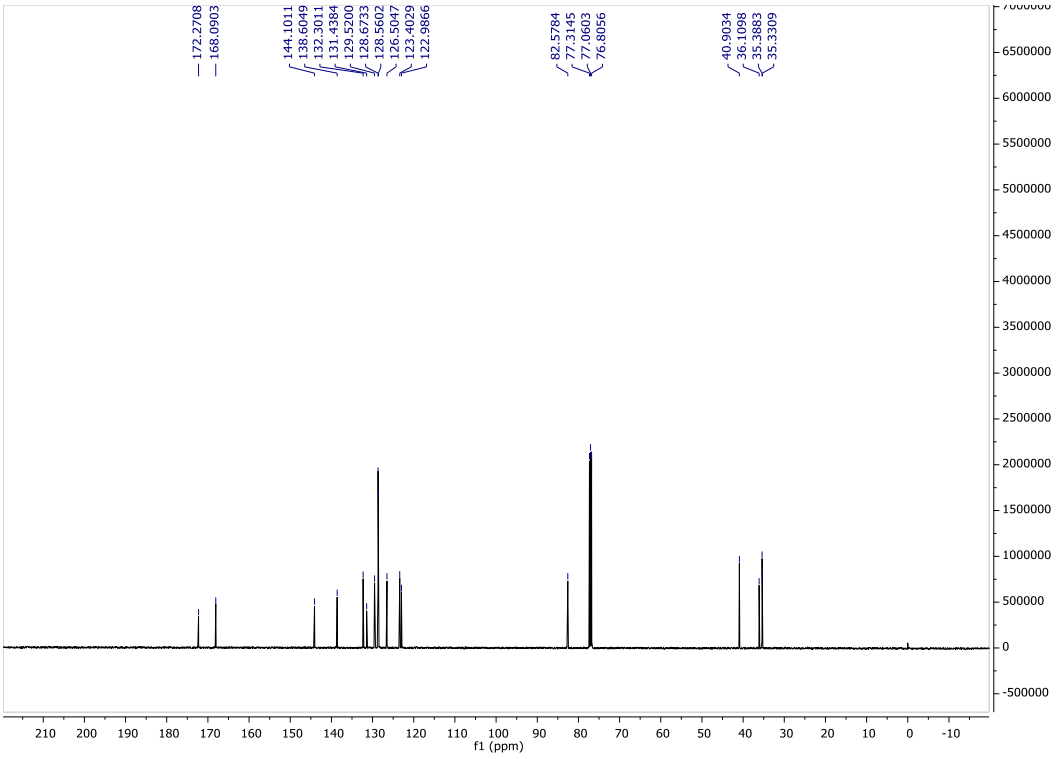
^{1}H and ^{13}C NMR spectra of **1n** (400 and 100 MHz, $CDCl_3$)



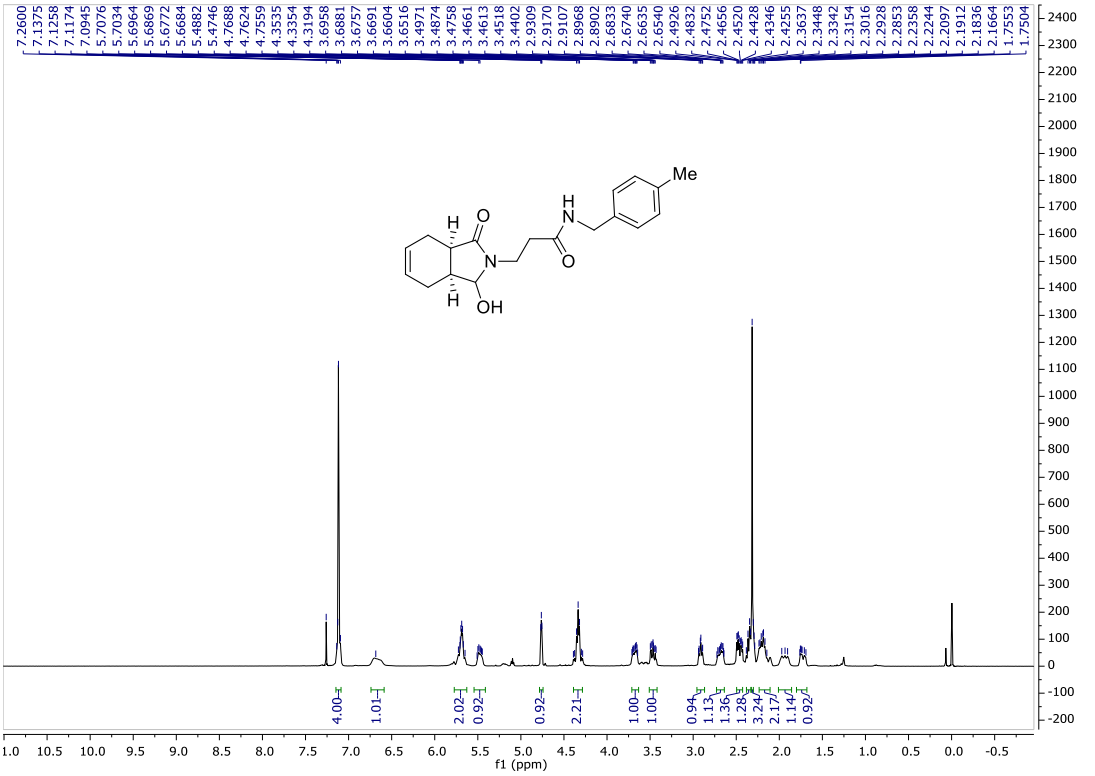


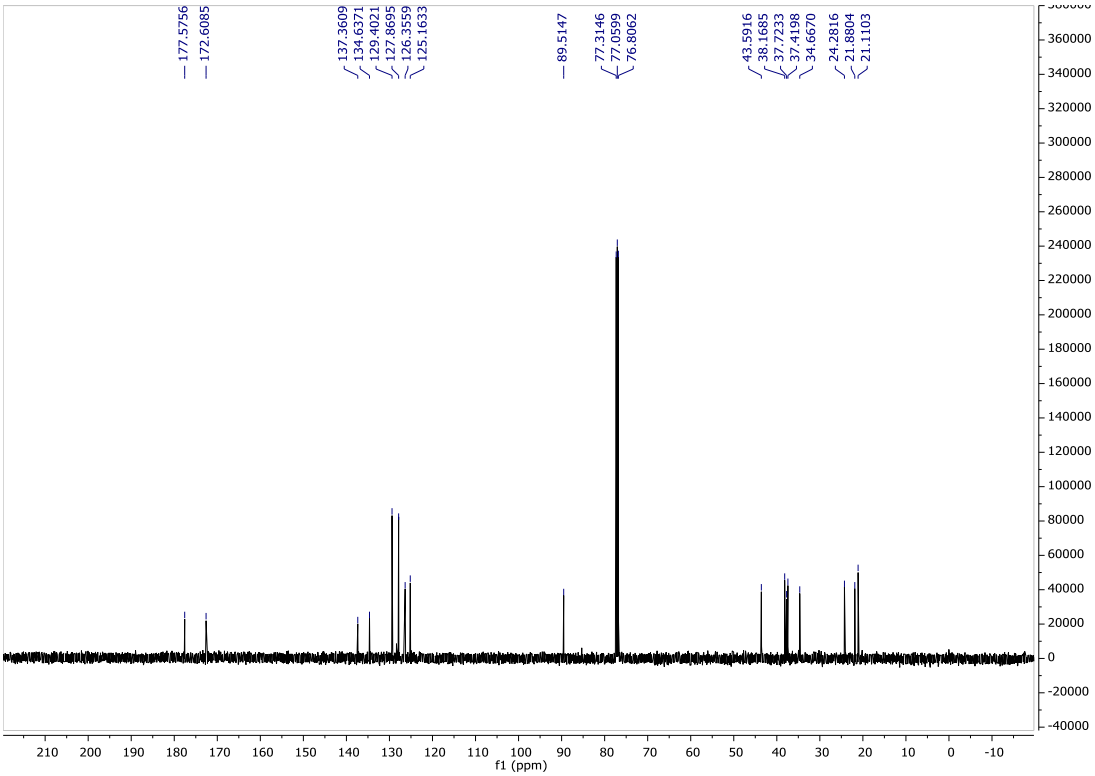
^{1}H and ^{13}C NMR spectra of **1o** (500 and 125 MHz, $CDCl_3$)



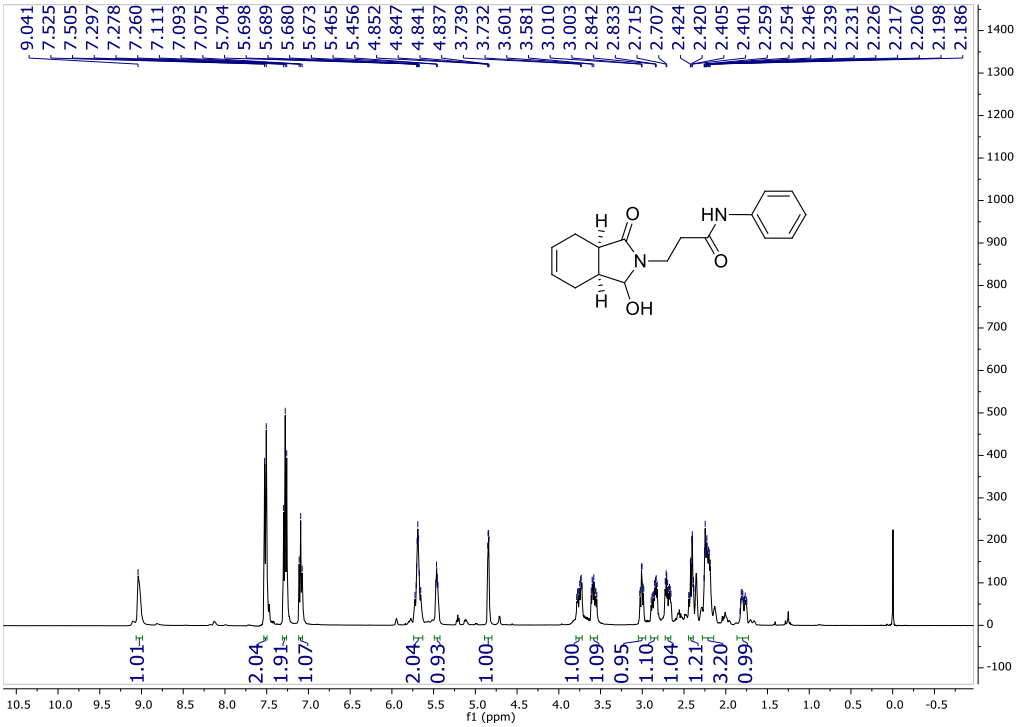


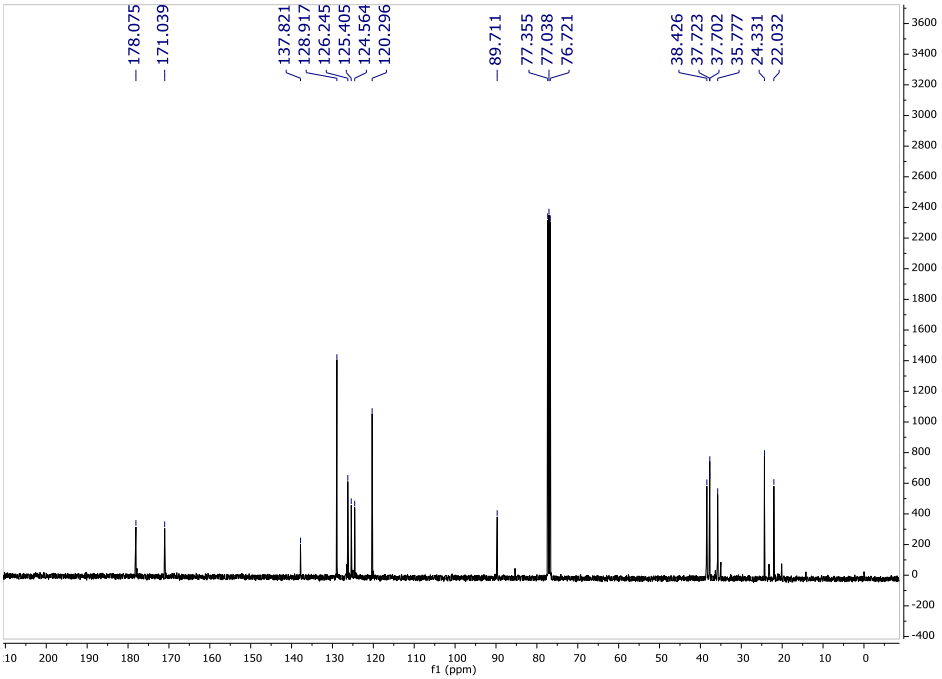
^{1}H and ^{13}C NMR spectra of **1p** (400 and 100 MHz, $CDCl_3$)



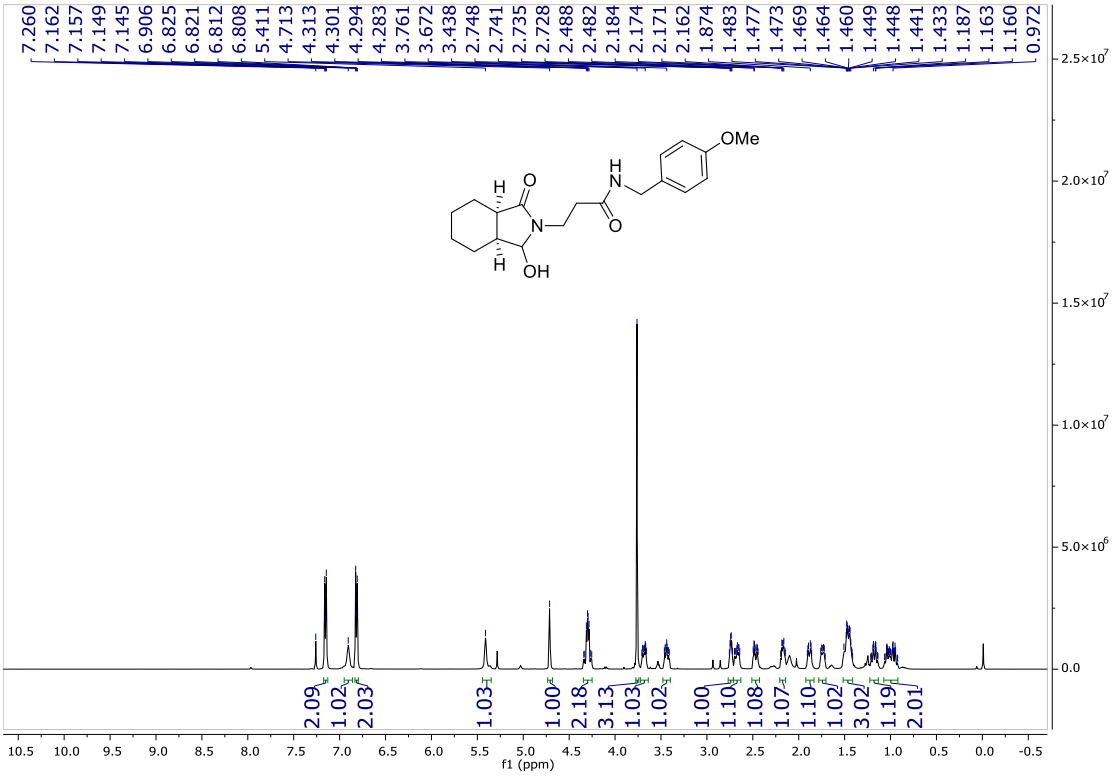


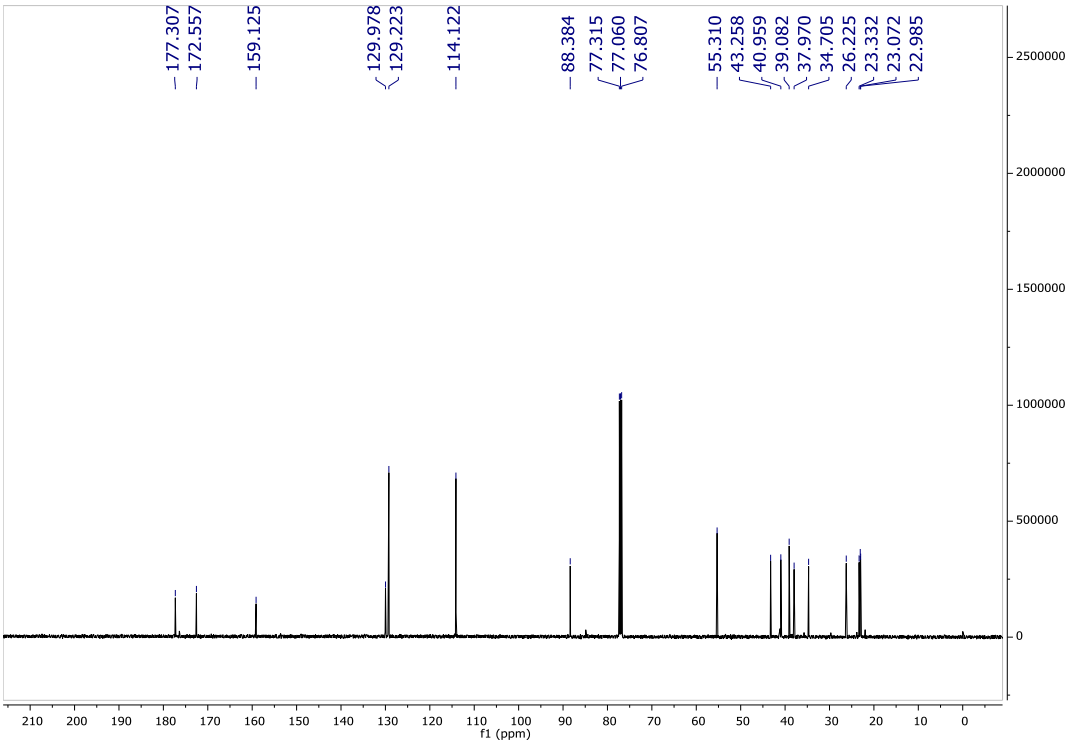
^{1}H and ^{13}C NMR spectra of **1q** (400 and 100 MHz, $CDCl_3$)



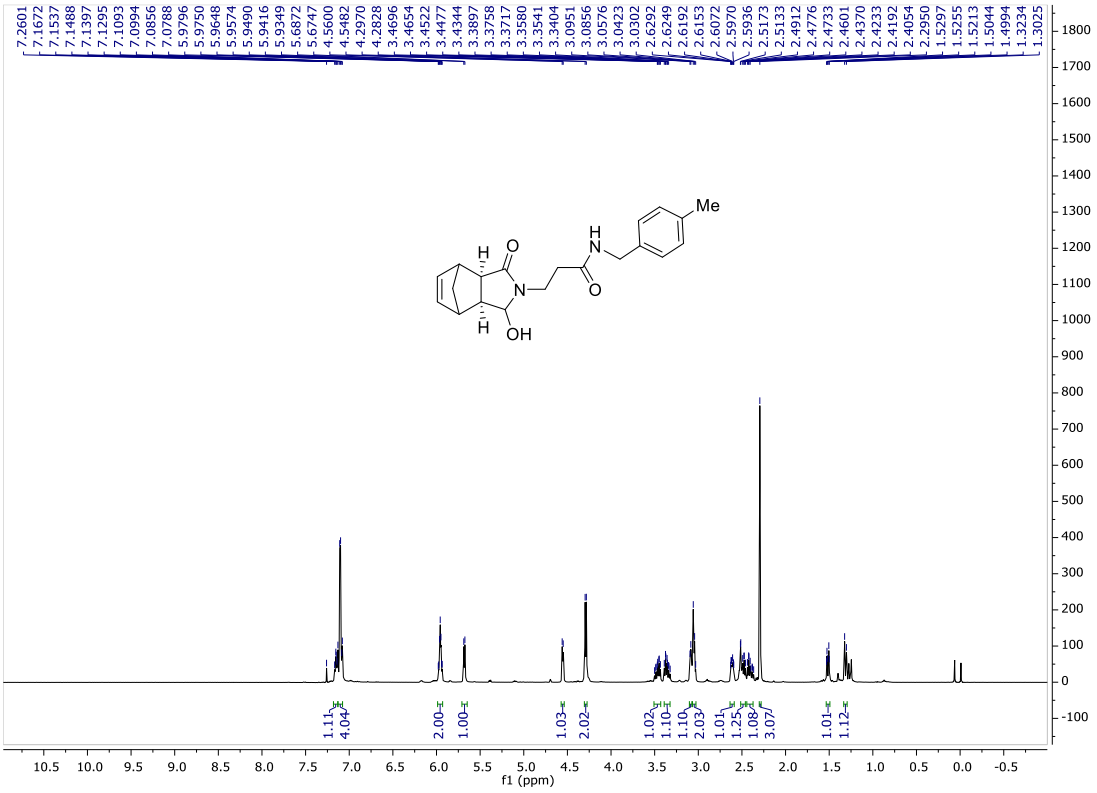


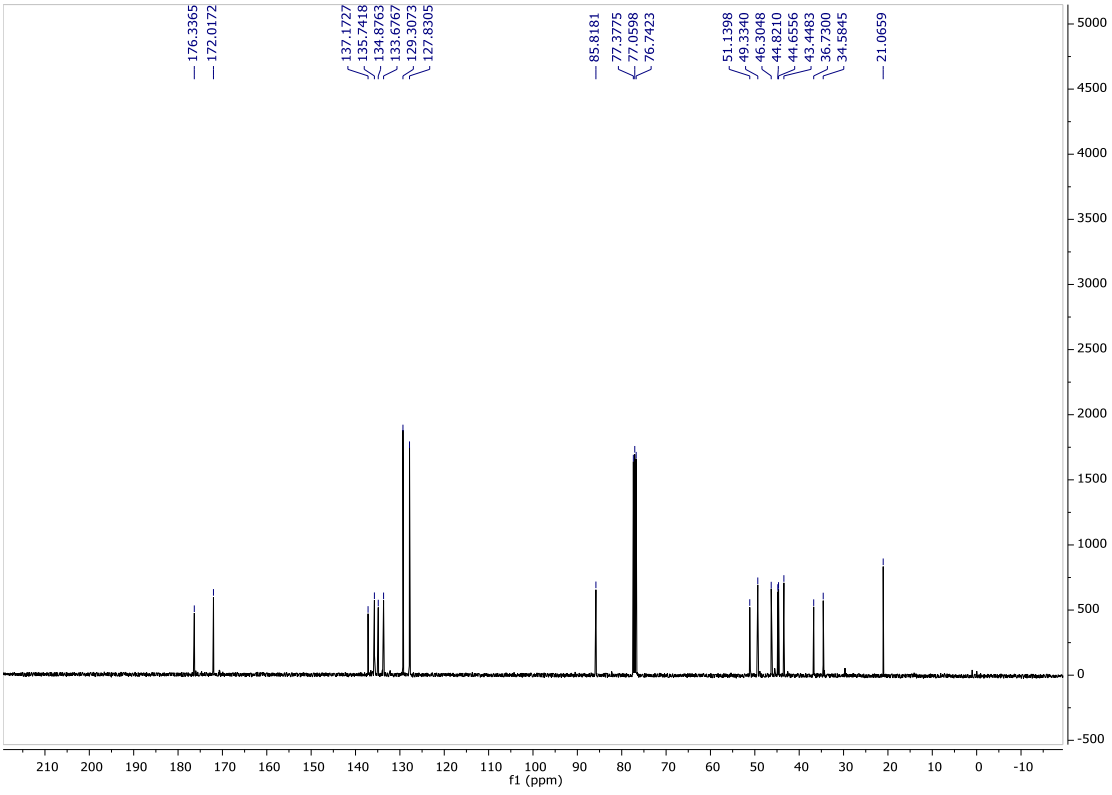
^{1}H and ^{13}C NMR spectra of **1r** (500 and 125 MHz, $CDCl_3$)



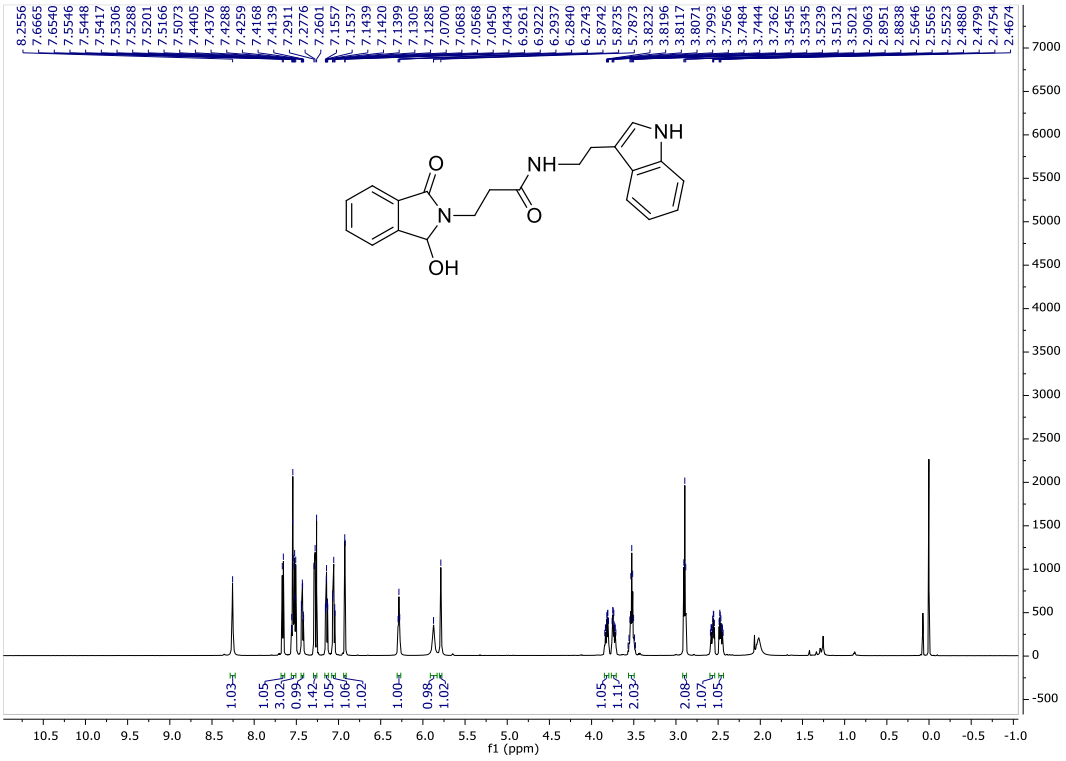


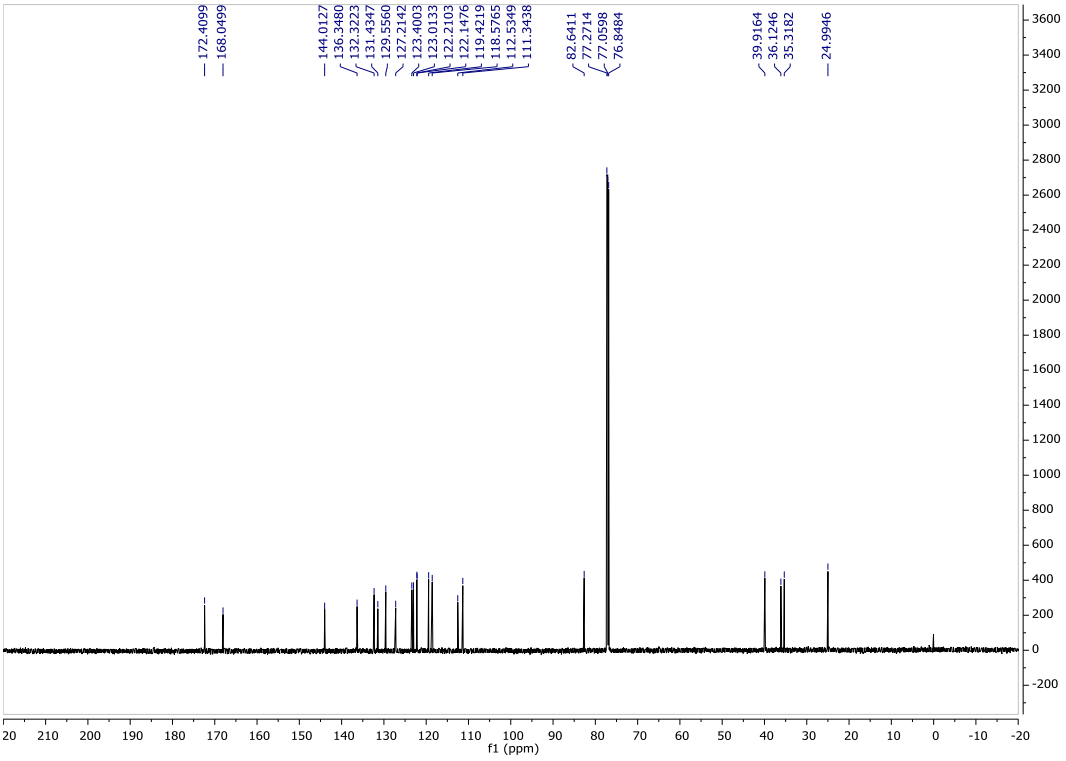
^{1}H and ^{13}C NMR spectra of **1s** (400 and 100 MHz, $CDCl_3$)



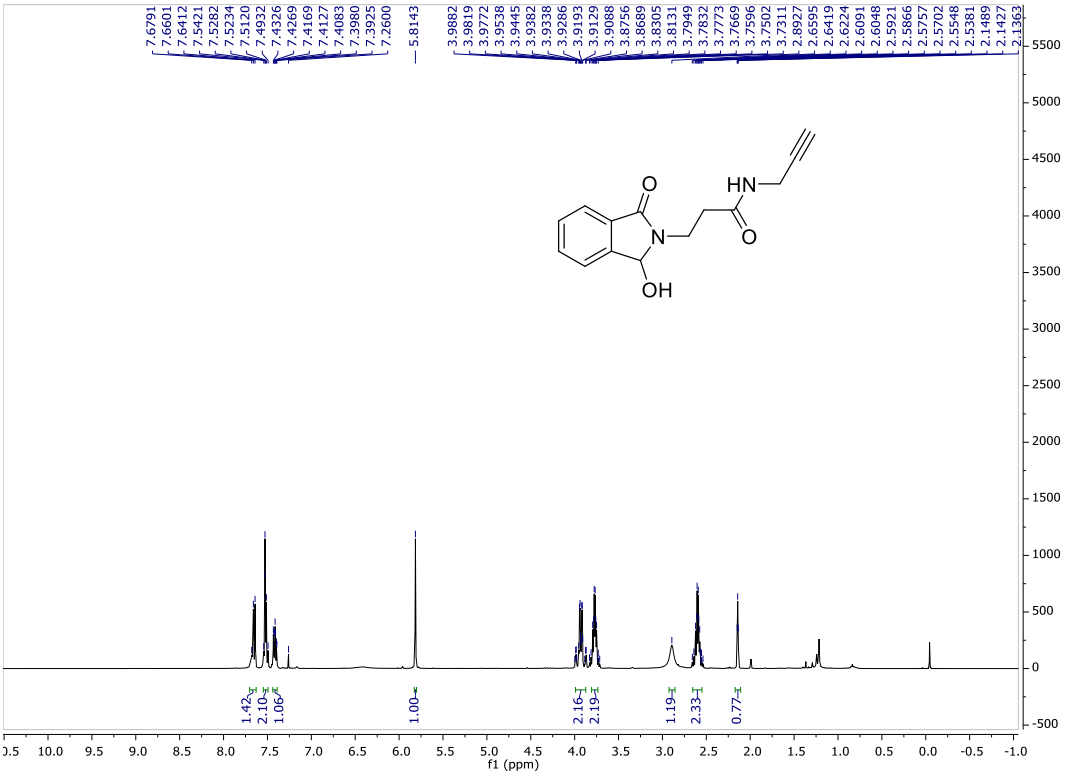


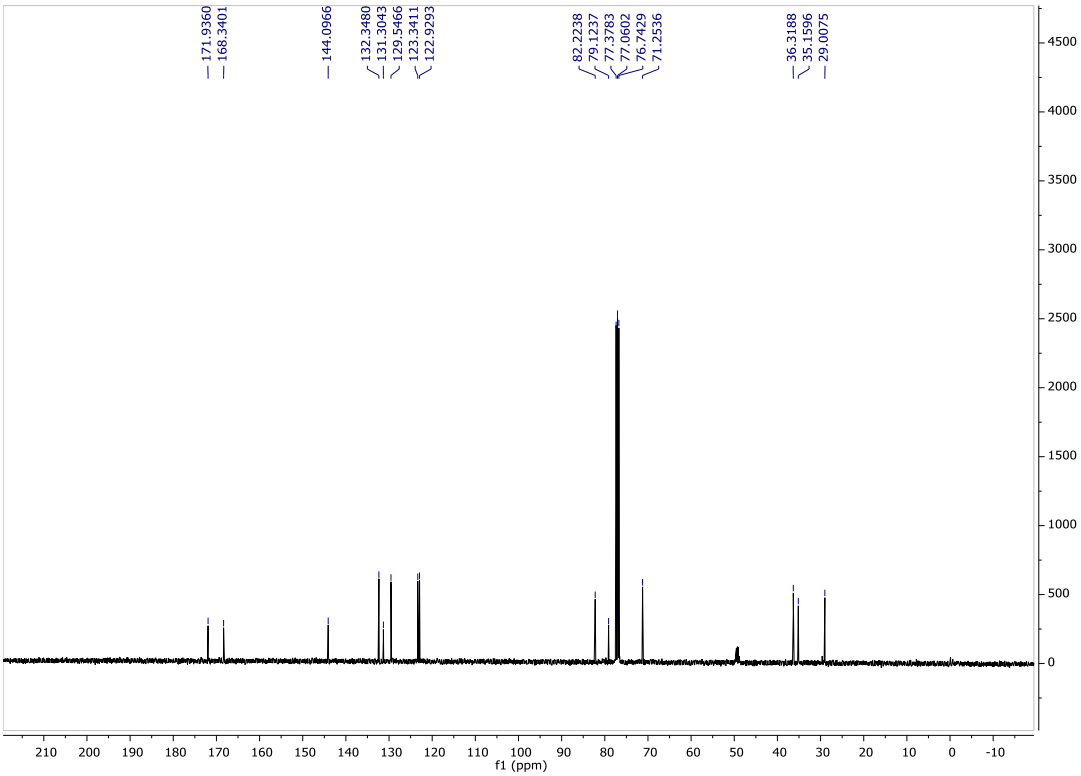
^{1}H and ^{13}C NMR spectra of **1t** (600 and 150 MHz, $CDCl_3$)



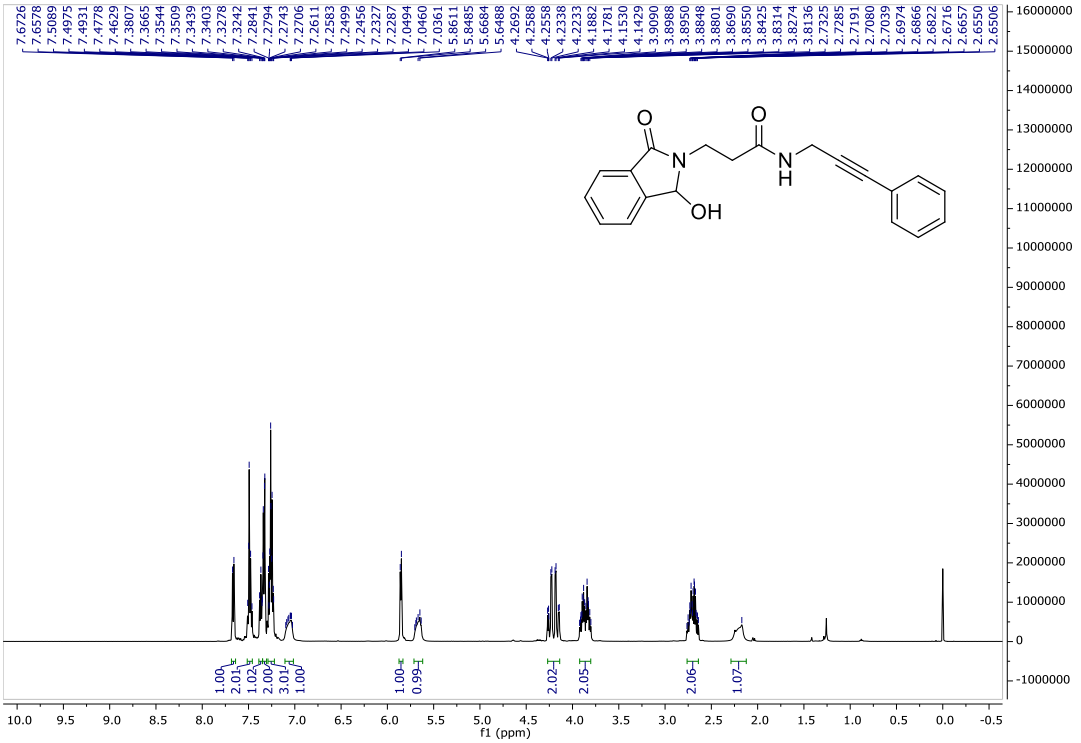


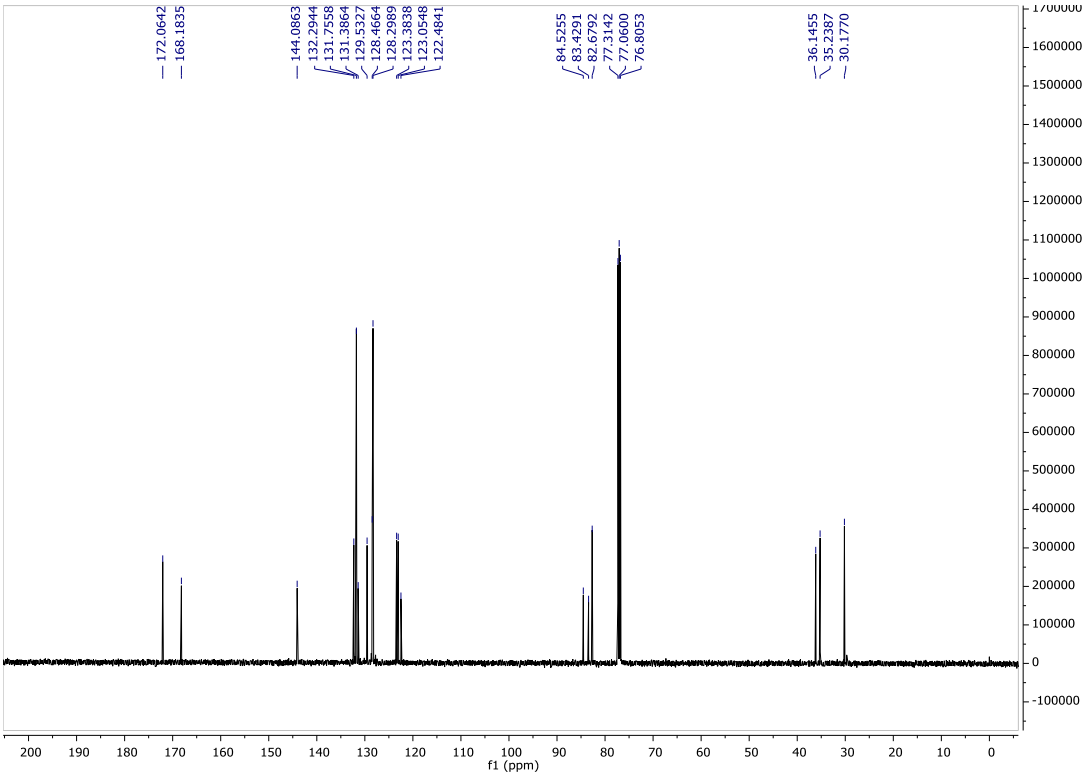
^{1}H and ^{13}C NMR spectra of **1u** (400 and 100 MHz, $CDCl_3$/MeOH-d_4)



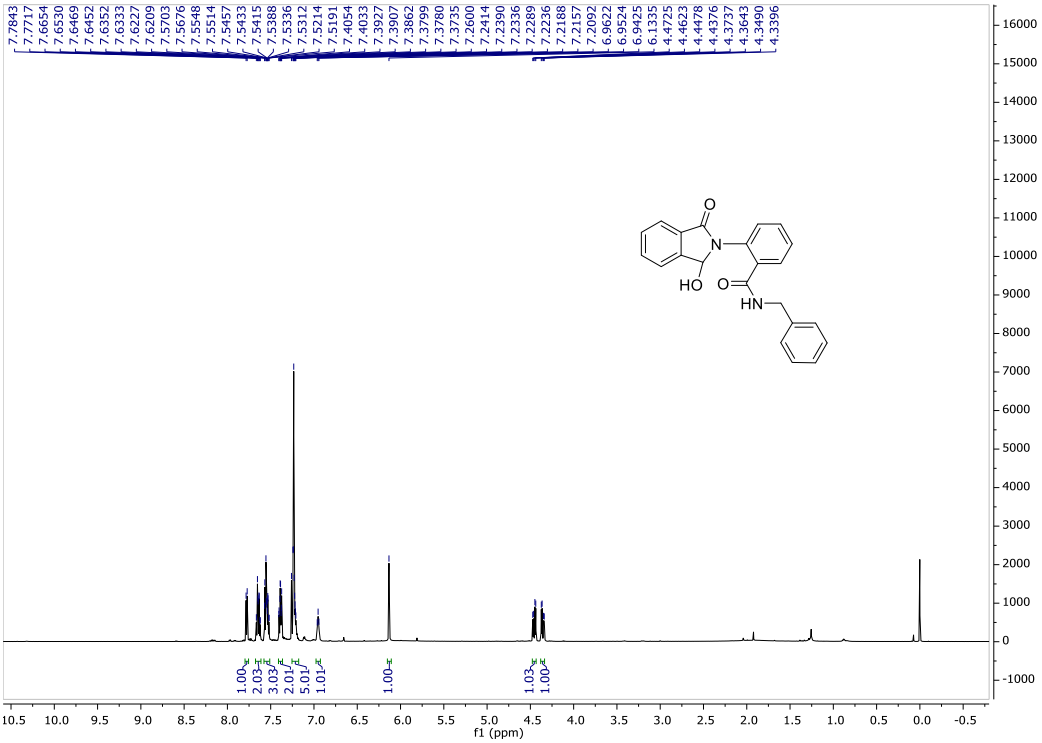


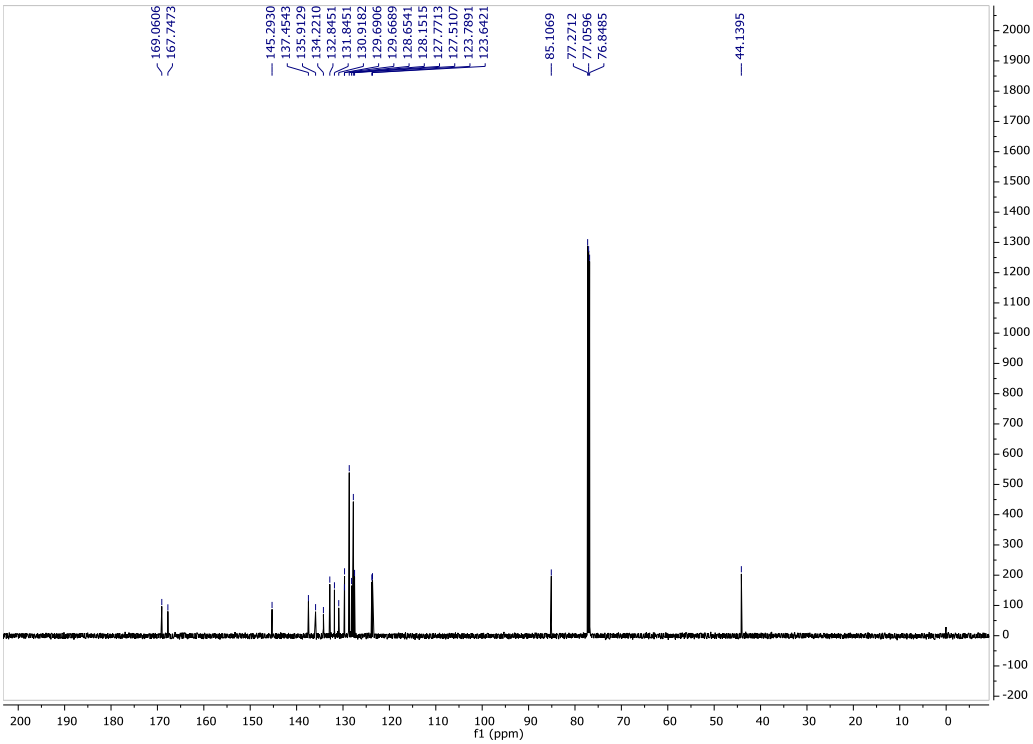
^{1}H and ^{13}C NMR spectra of **1v** (400 and 100 MHz, $CDCl_3$)



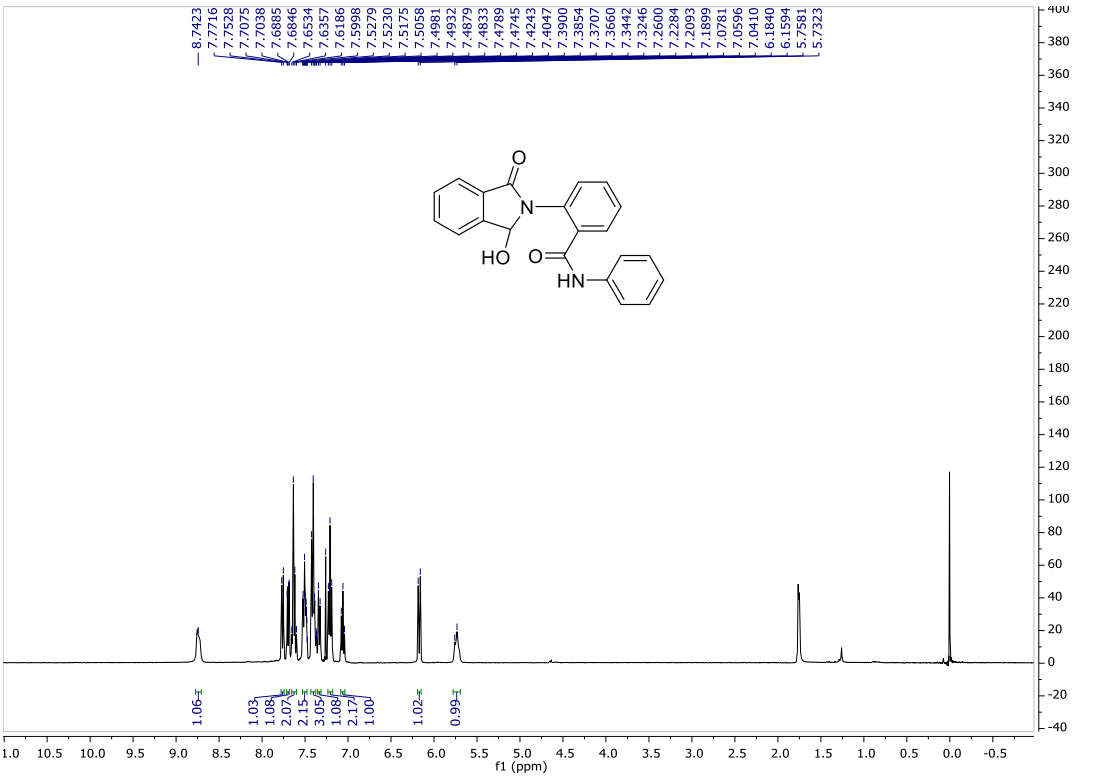


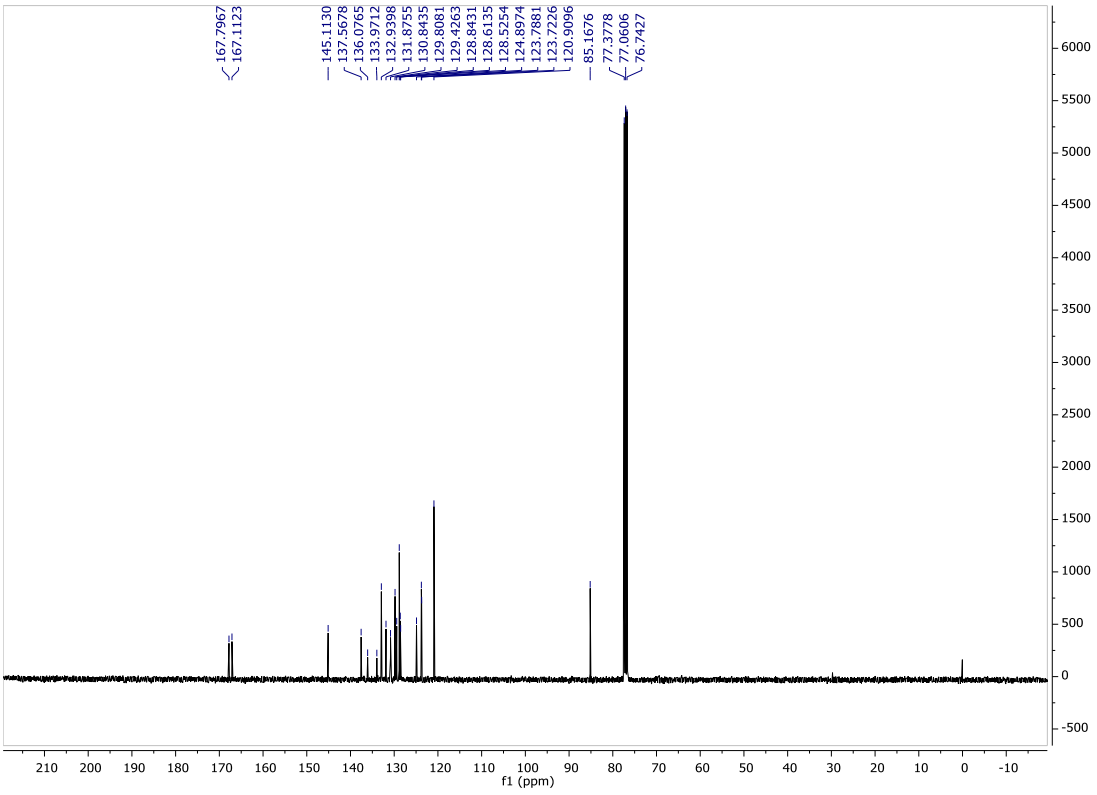
^{1}H and ^{13}C NMR spectra of **1w** (600 and 150 MHz, $CDCl_3$)



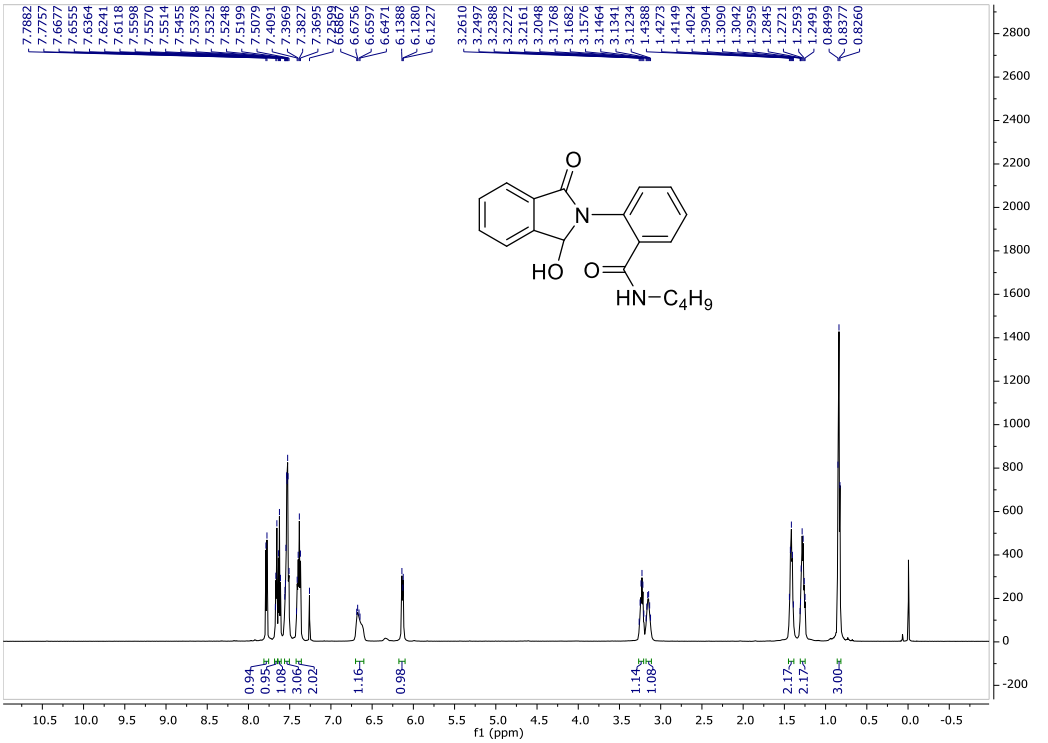


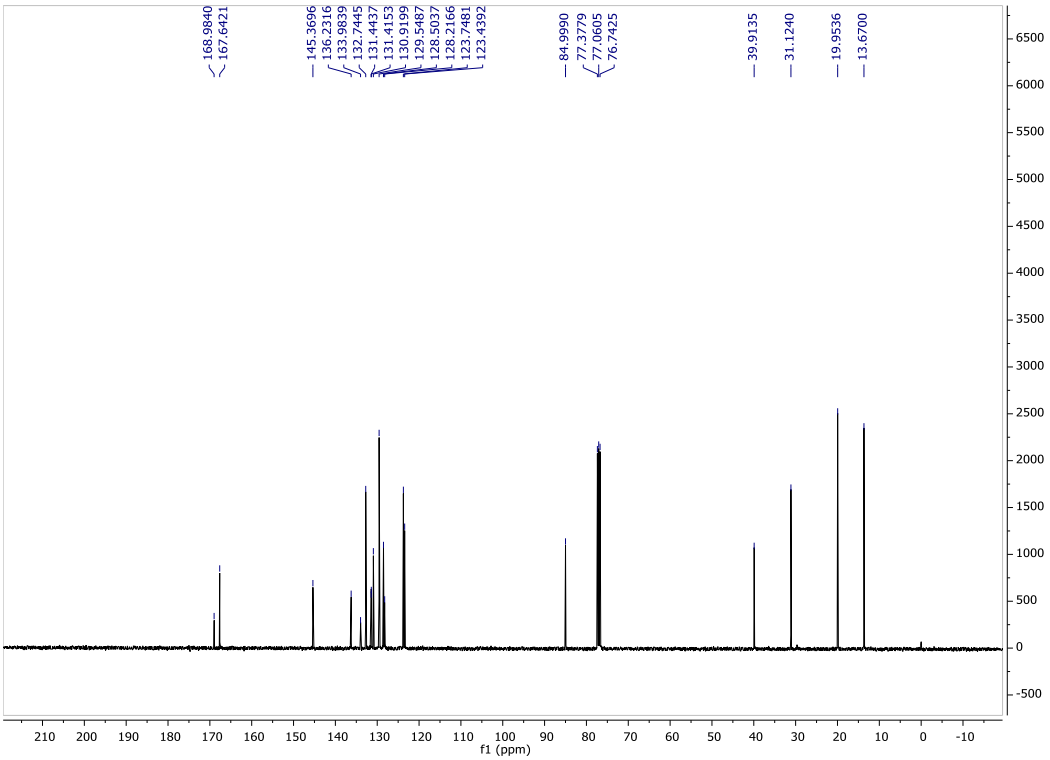
^{1}H and ^{13}C NMR spectra of **1x** (400 and 100 MHz, $CDCl_3$)



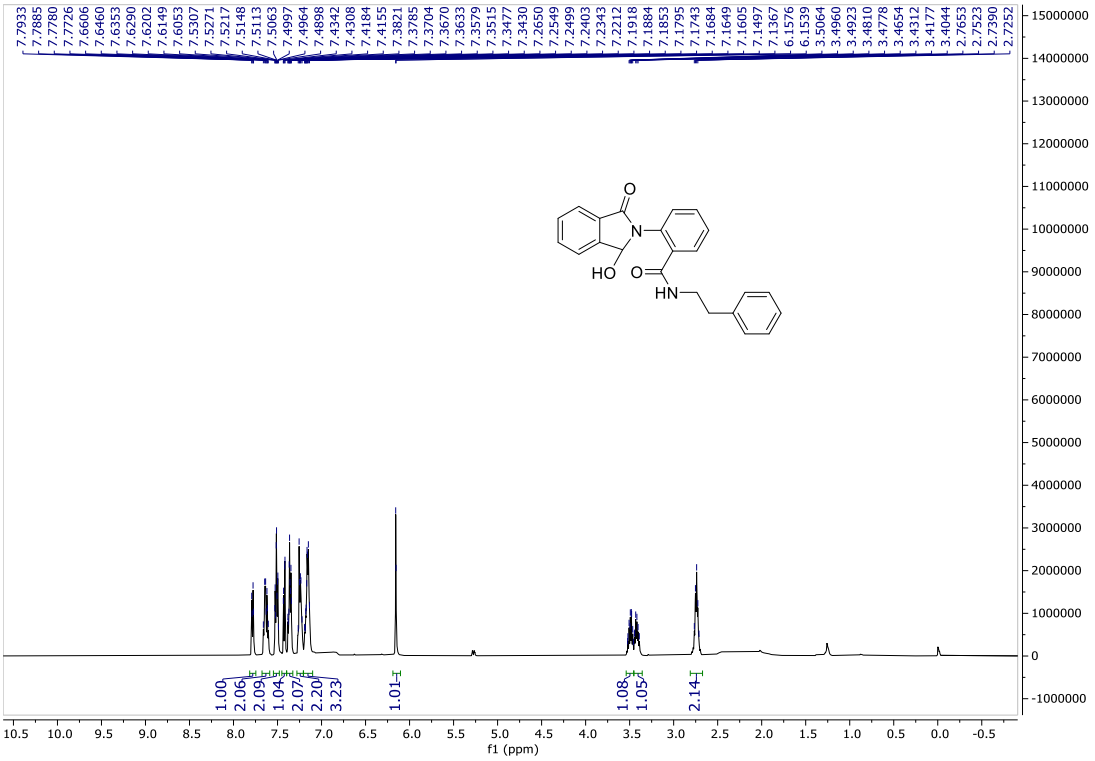


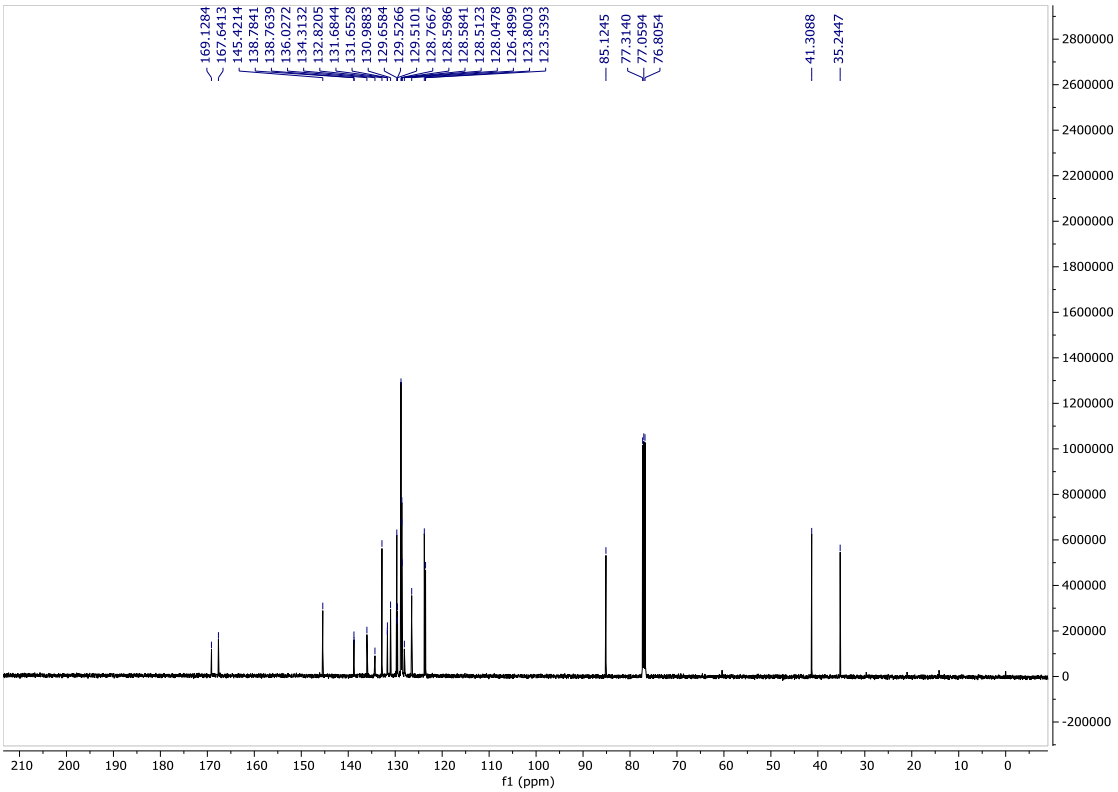
^{1}H and ^{13}C NMR spectra of **1y** (600 and 150 MHz, $CDCl_3$)



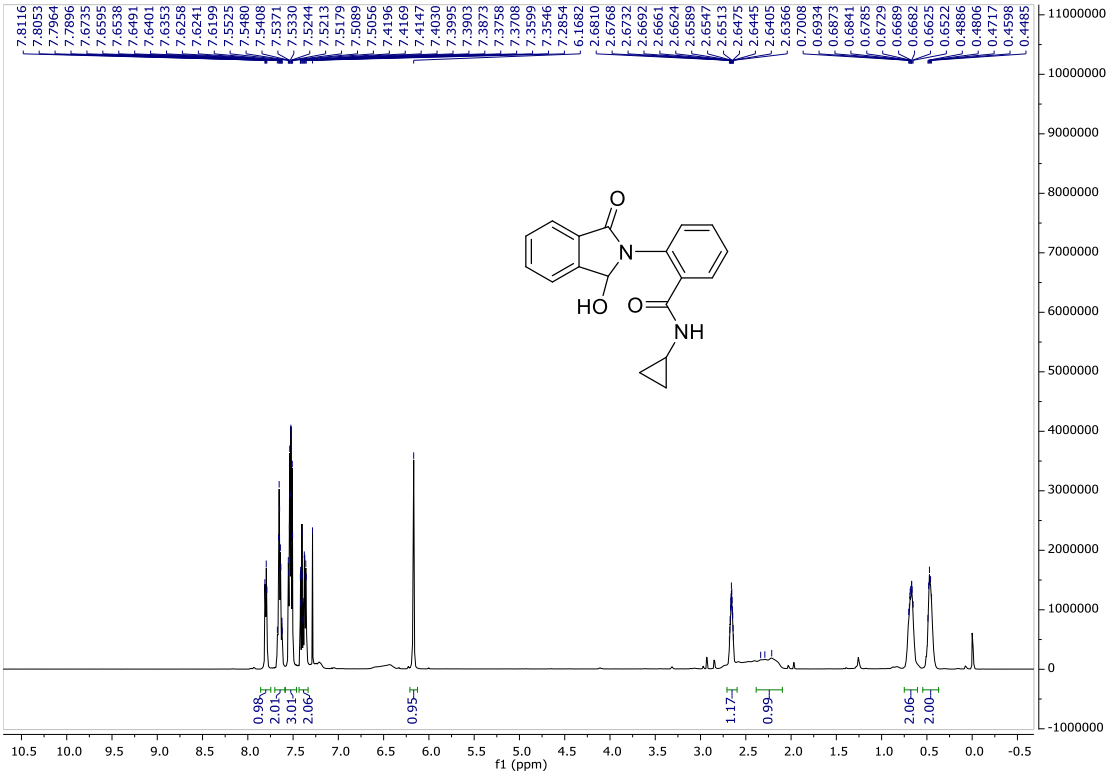


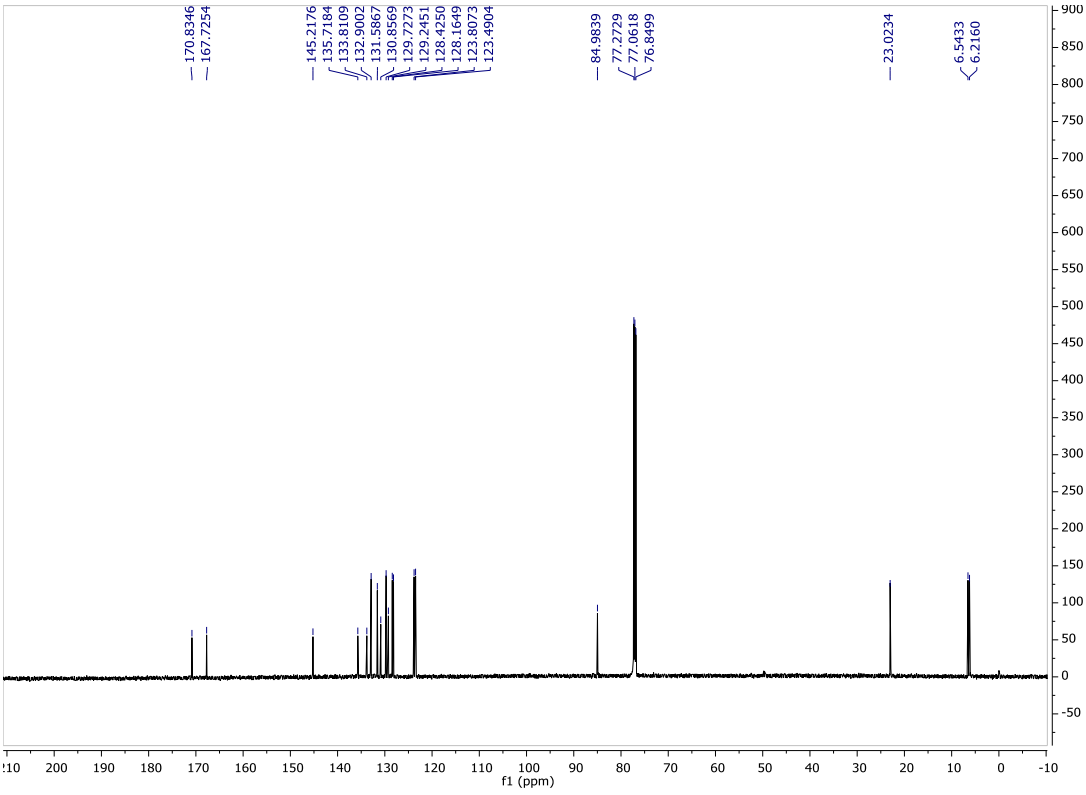
^{1}H and ^{13}C NMR spectra of **1z** (500 and 125 MHz, $CDCl_3$)



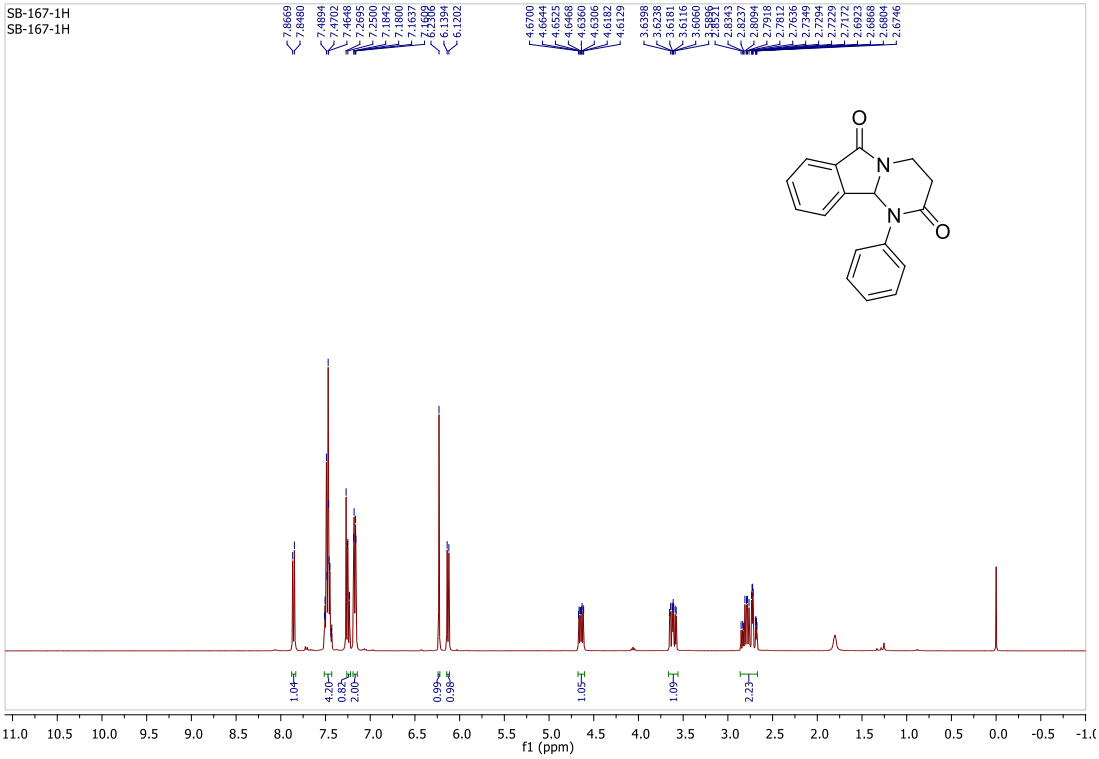


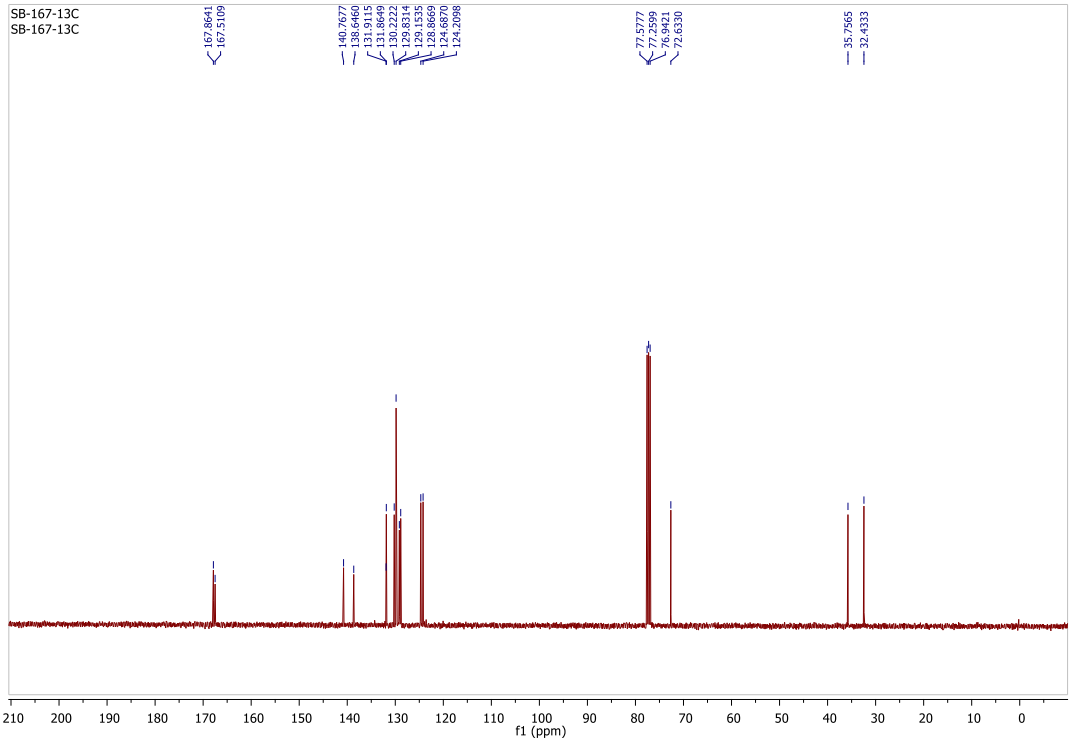
^{1}H and ^{13}C NMR spectra of **1aa** (500 and 125 MHz, $CDCl_3$)



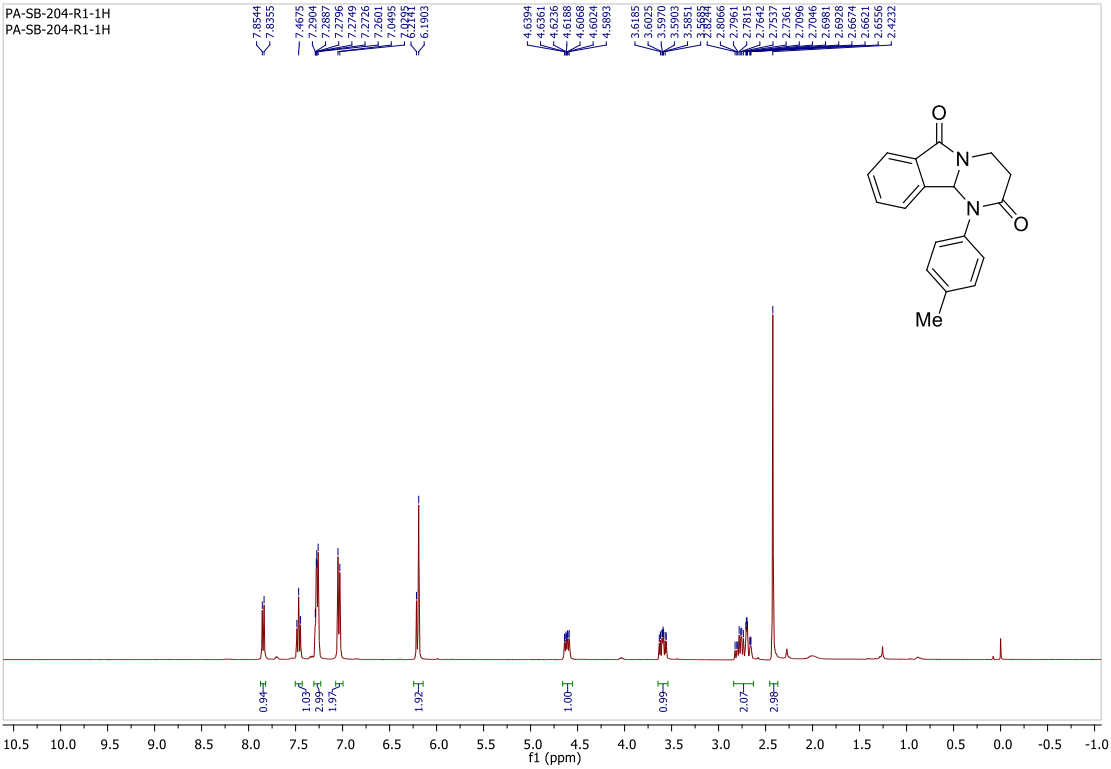


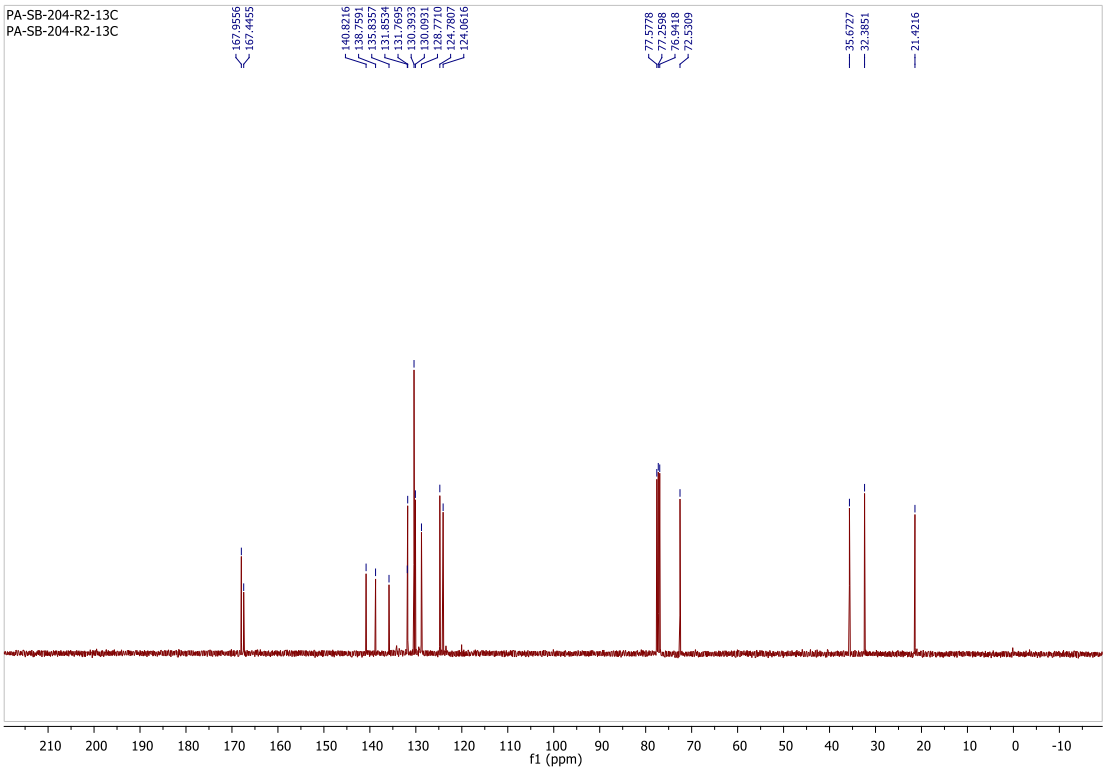
^{1}H and ^{13}C NMR spectra of **2a** (400 and 100 MHz, $CDCl_3$)



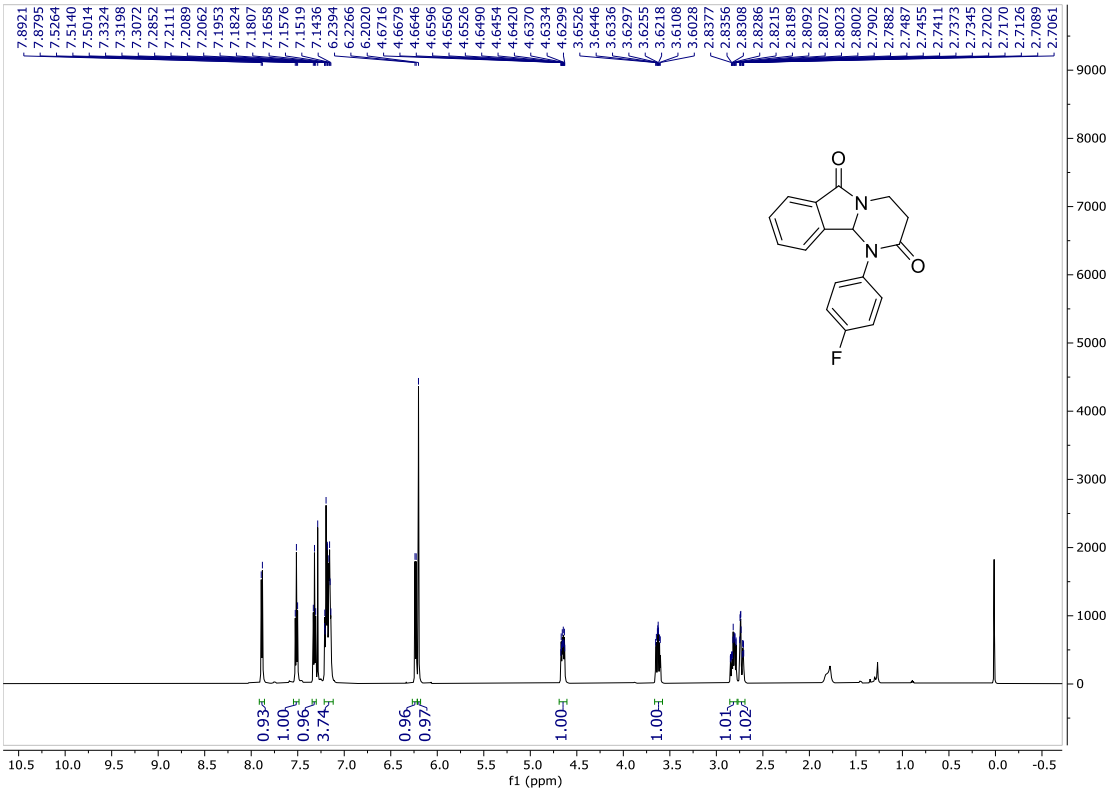


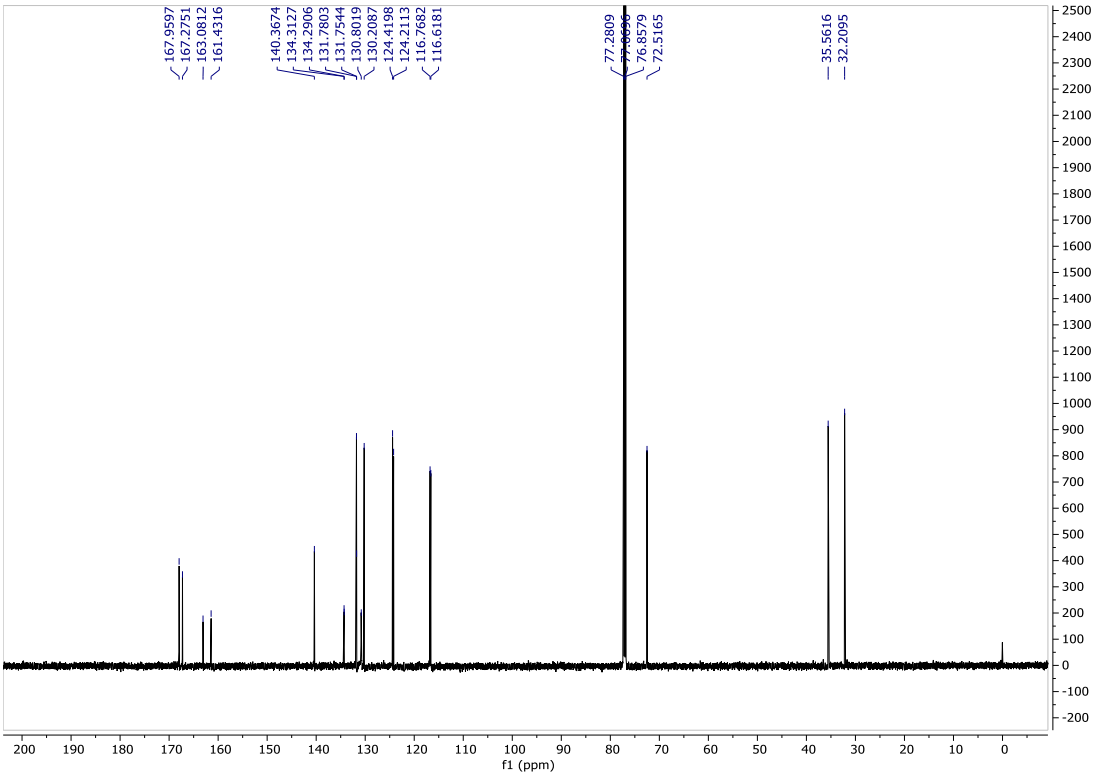
^{1}H and ^{13}C NMR spectra of **2b** (400 and 100 MHz, $CDCl_3$)



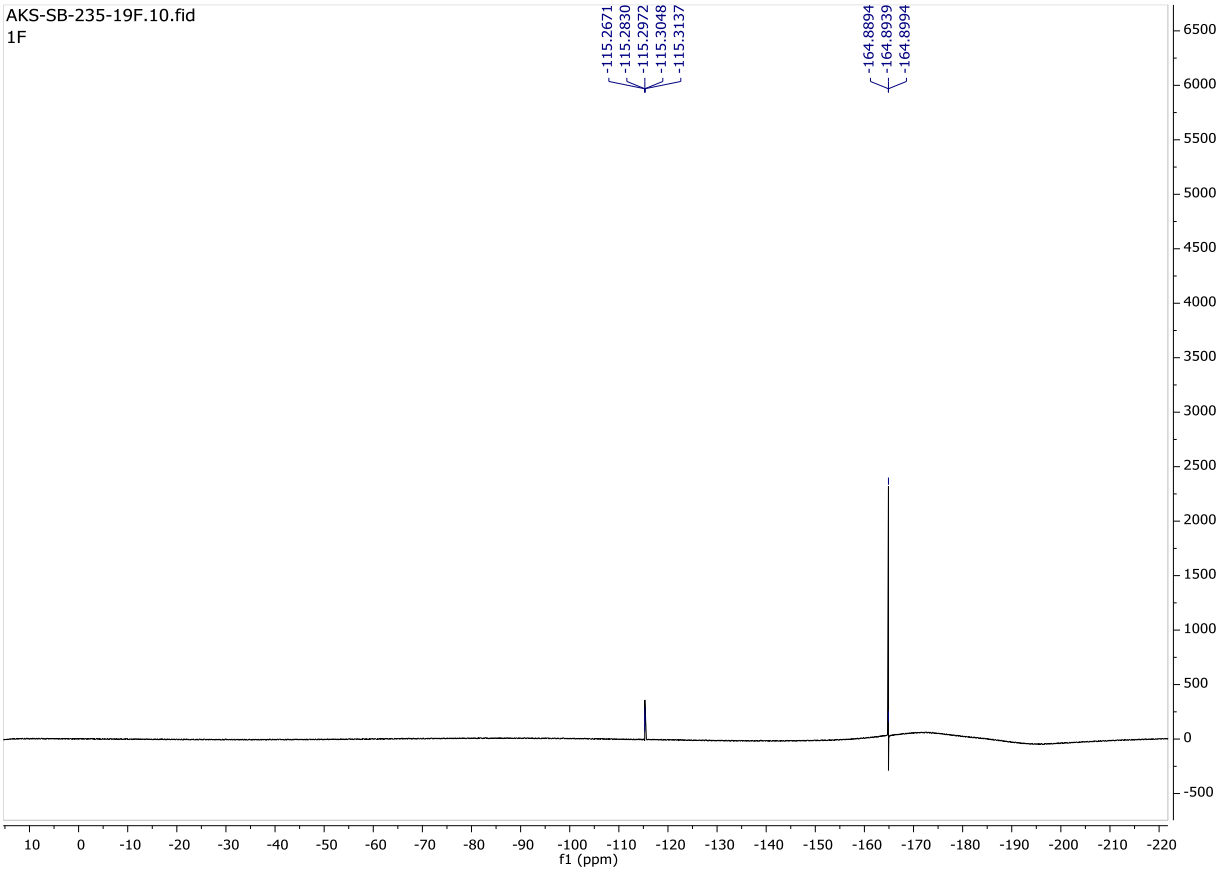


^{1}H and ^{13}C NMR spectra of **2c** (600 and 150 MHz, $CDCl_3$)

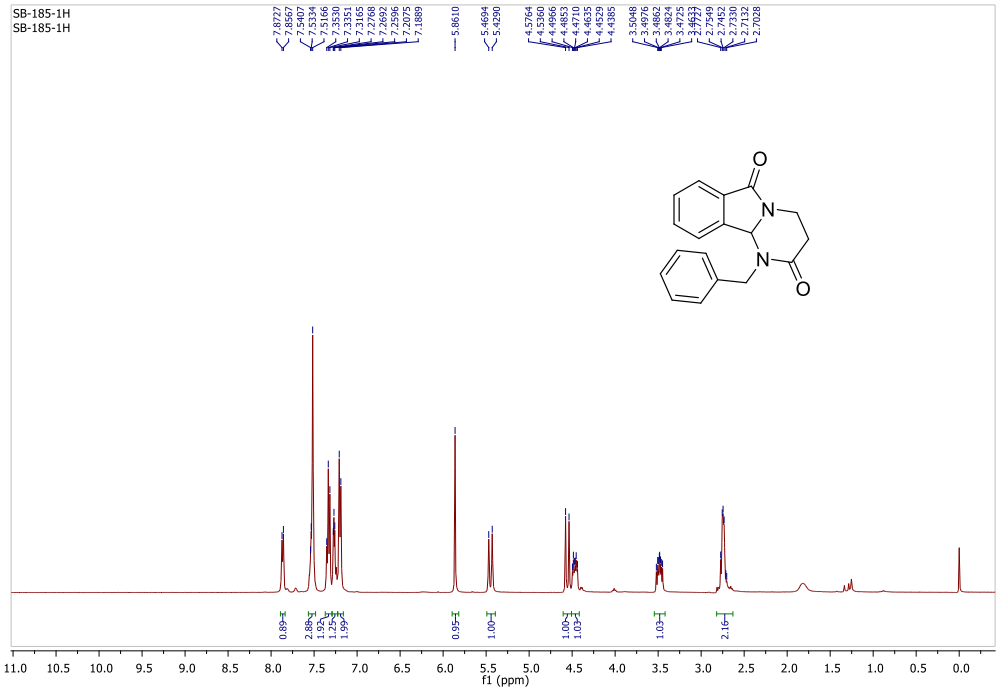


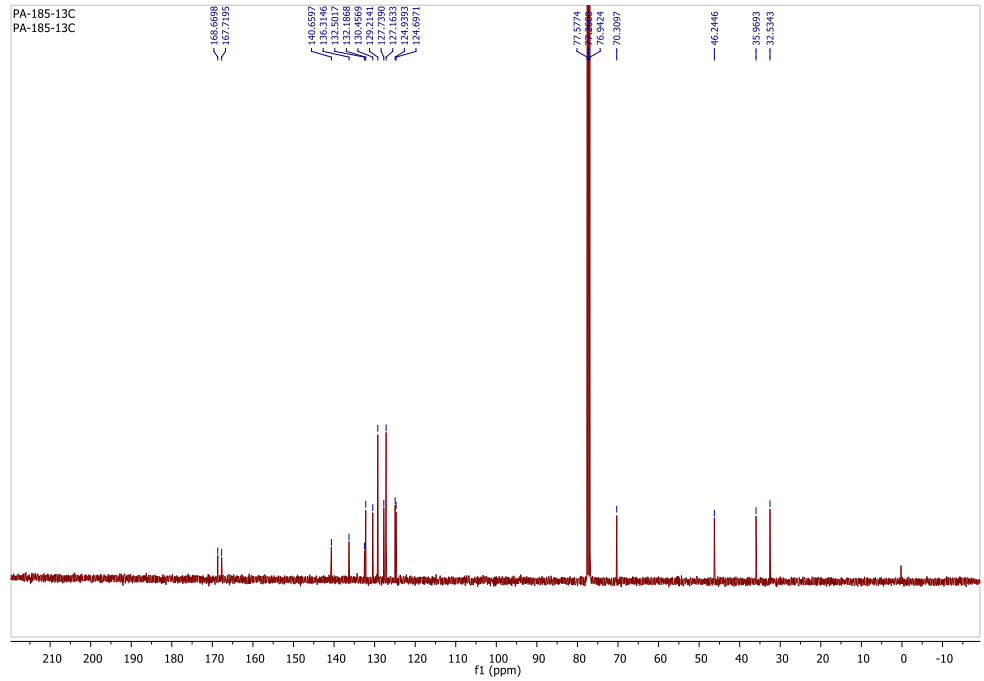


^{19}F NMR spectrum of **2c** (564 Mhz, $C_6F_6/CDCl_3$)

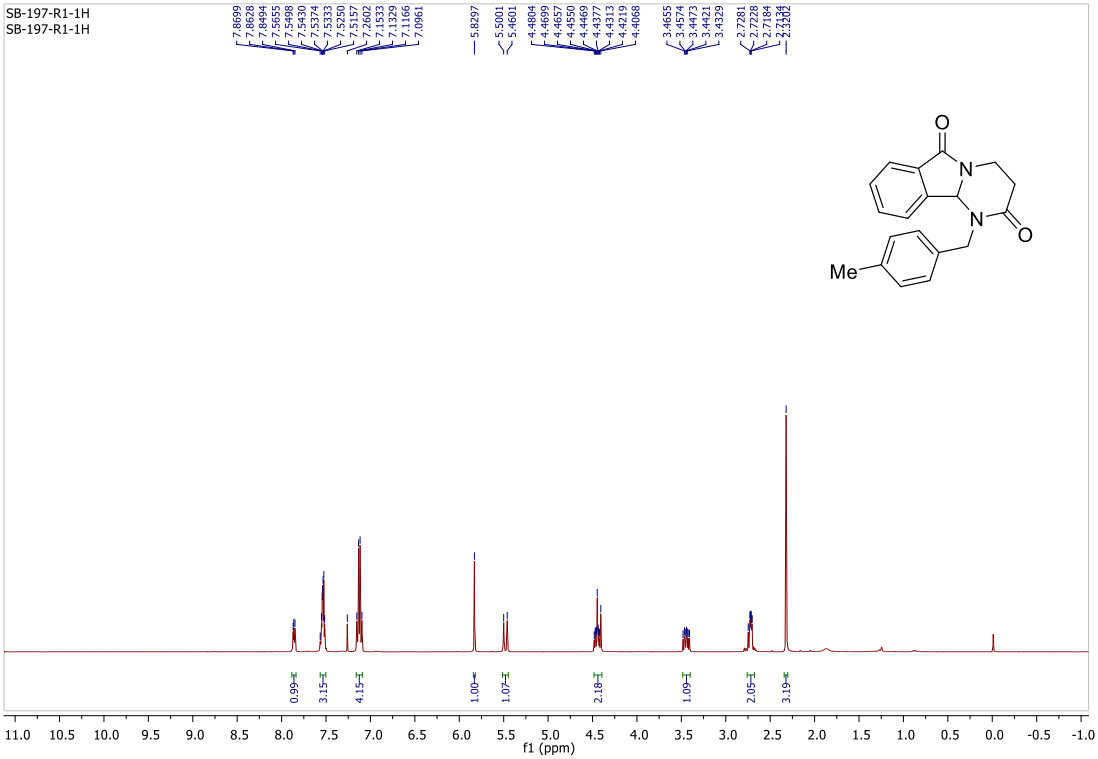


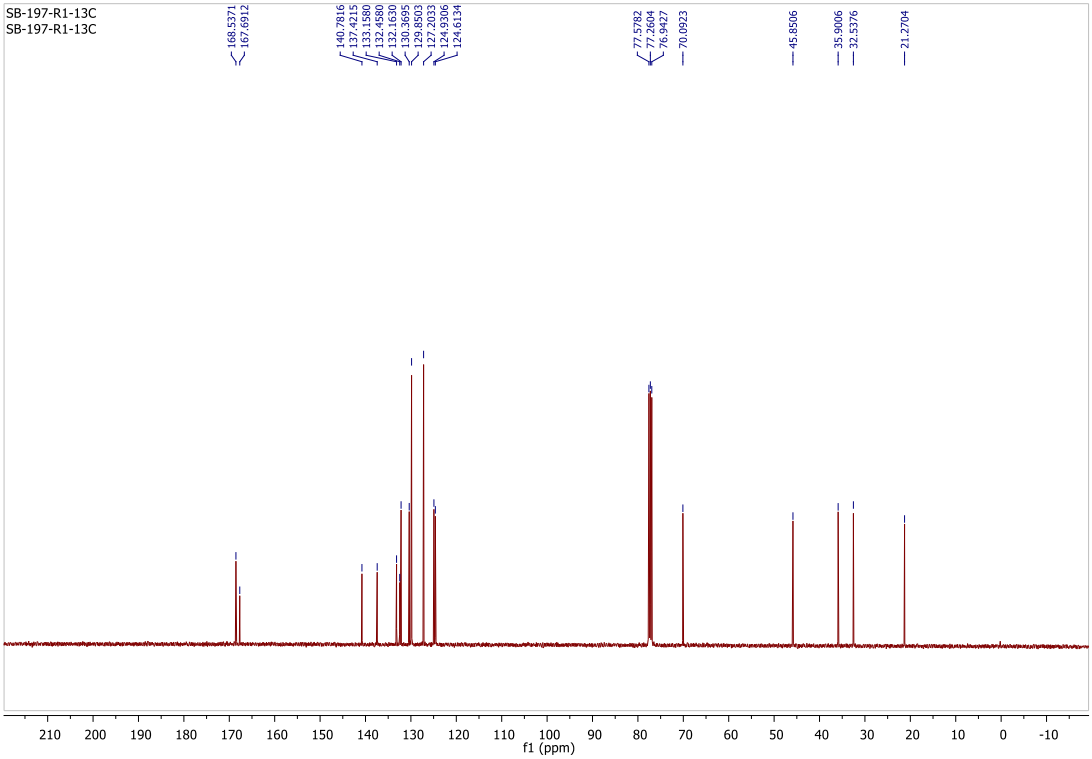
^{1}H and ^{13}C NMR spectra of **2d** (400 and 100 MHz, $CDCl_3$)



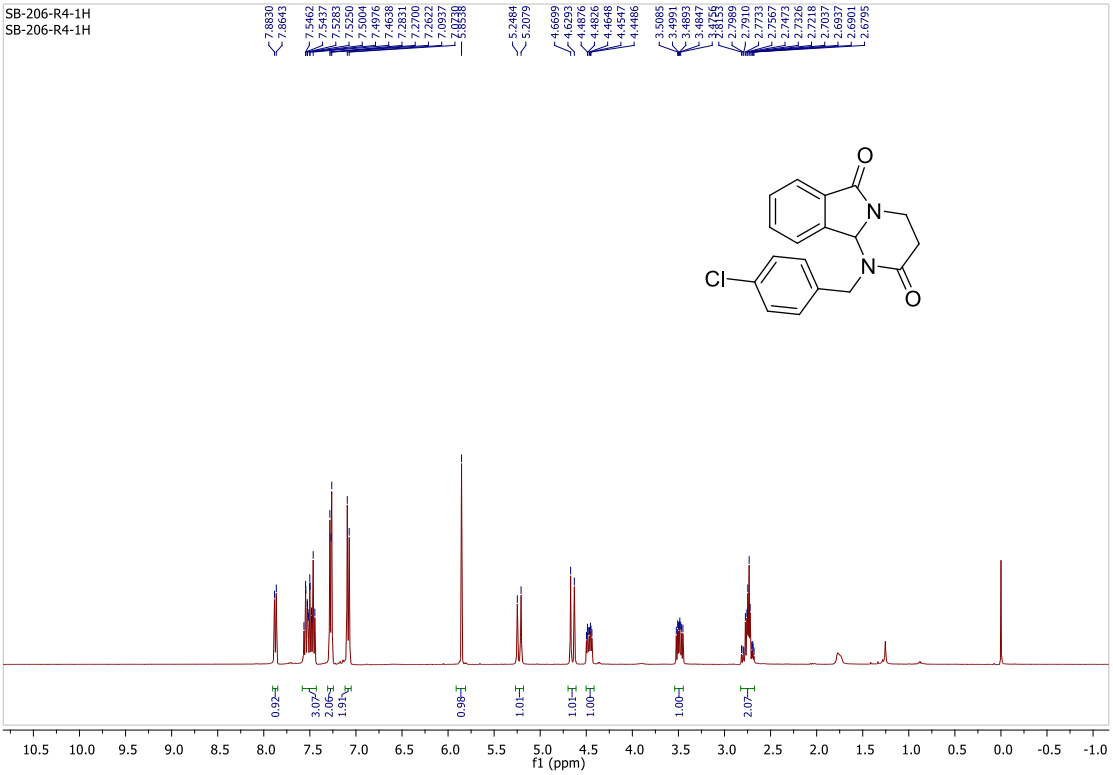


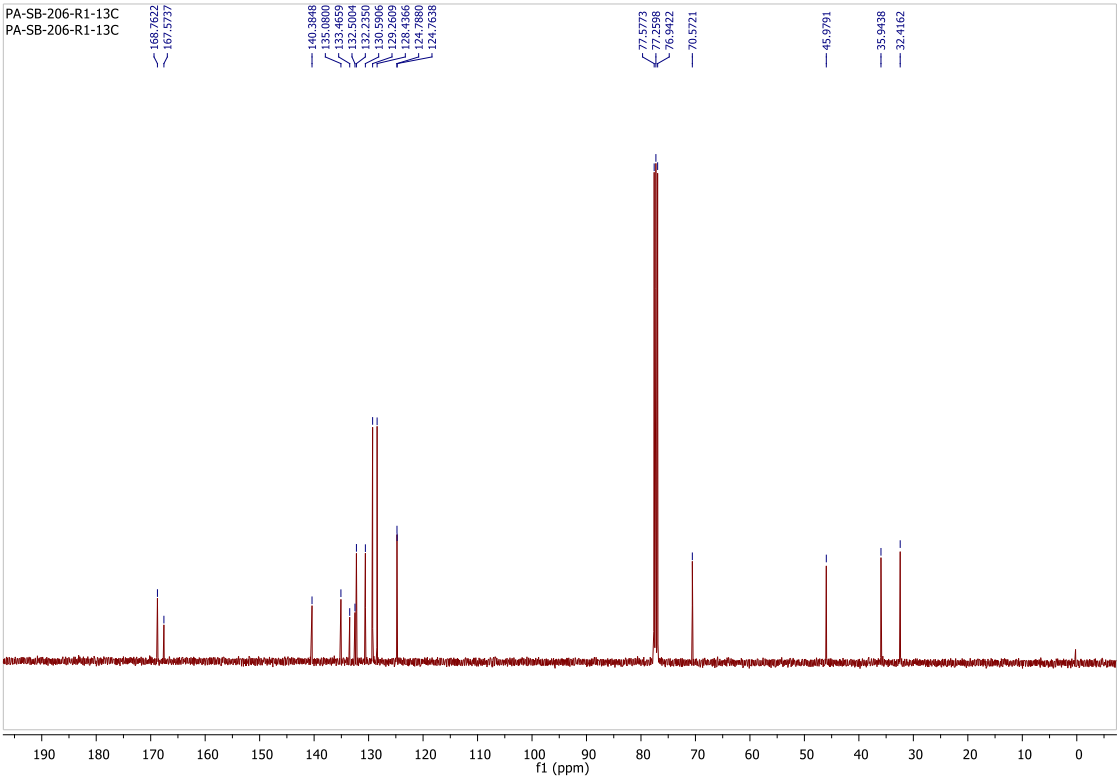
^{1}H and ^{13}C NMR spectra of **2e** (400 and 100 MHz, $CDCl_3$)



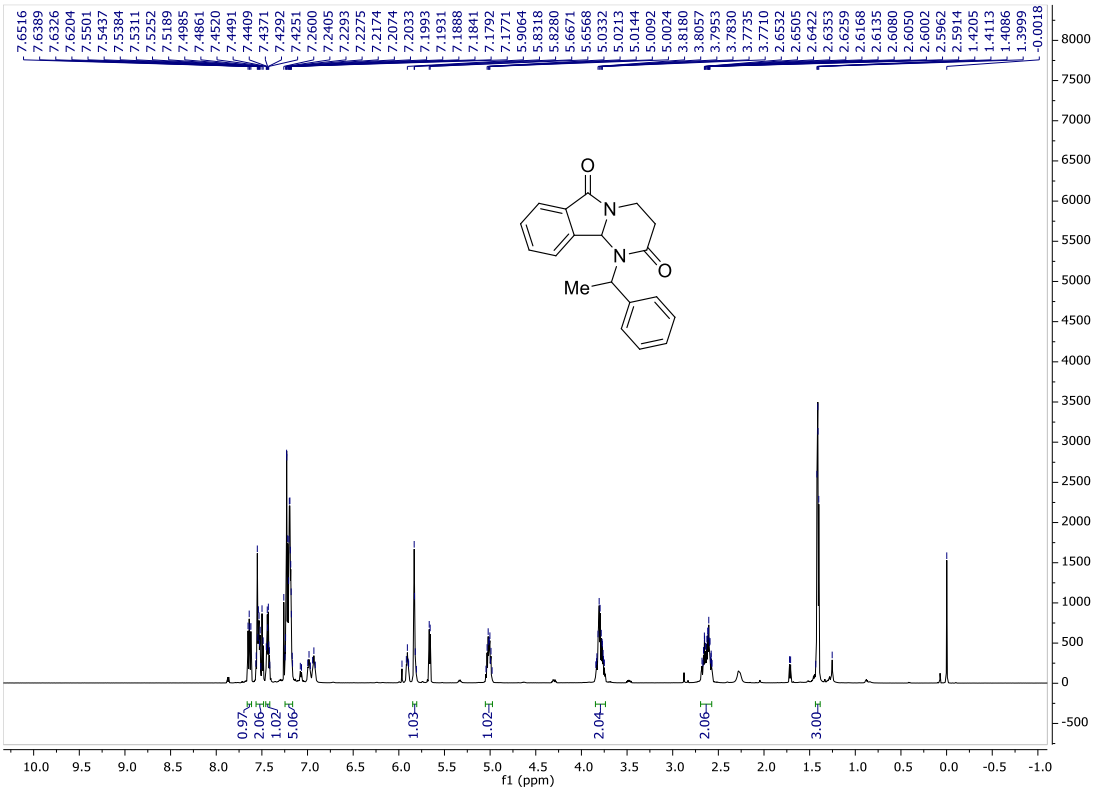


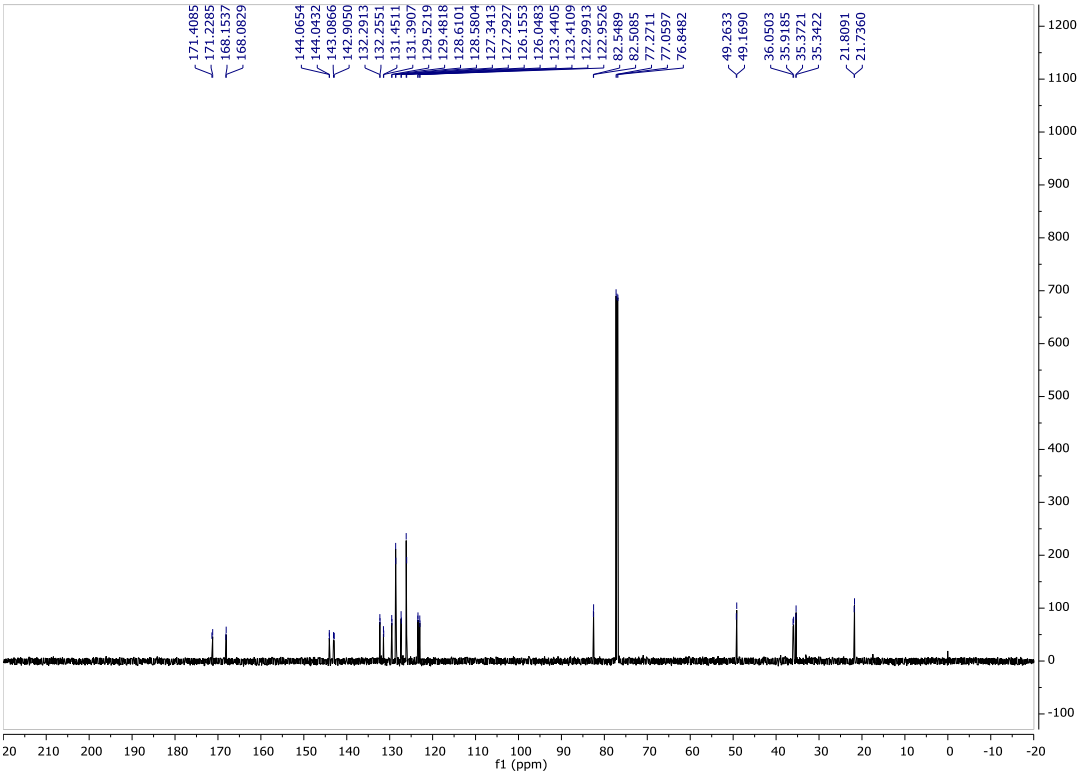
^{1}H and ^{13}C NMR spectra of **2f** (400 and 100 MHz, $CDCl_3$)



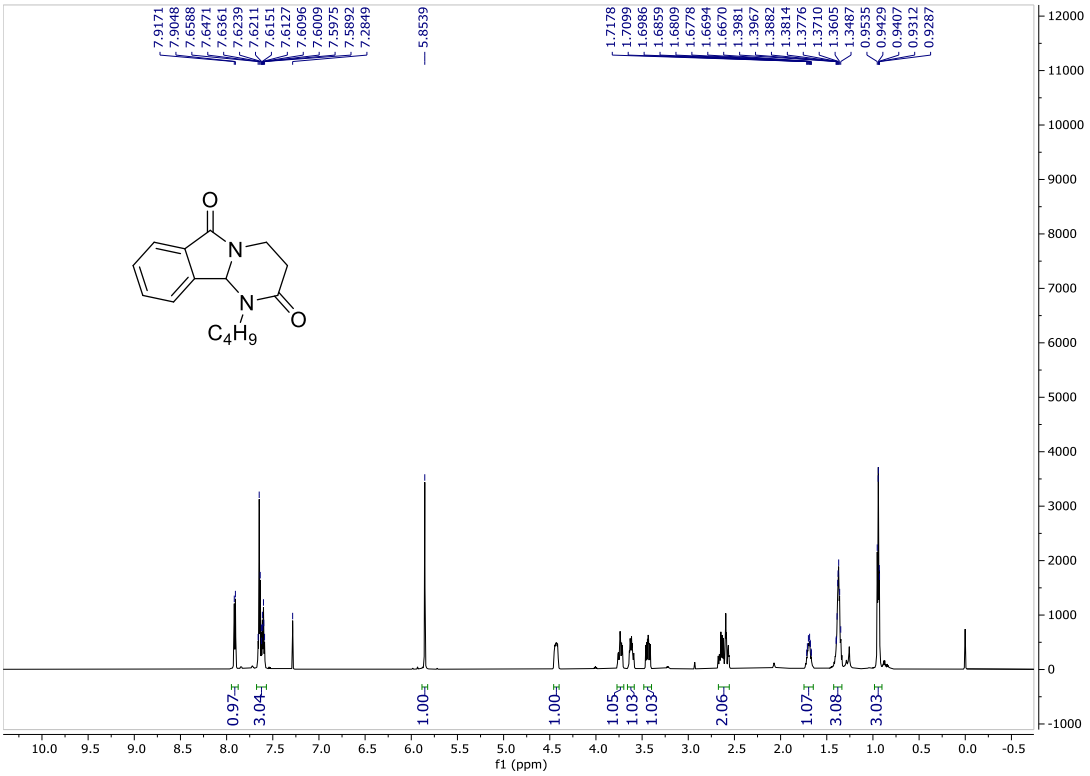


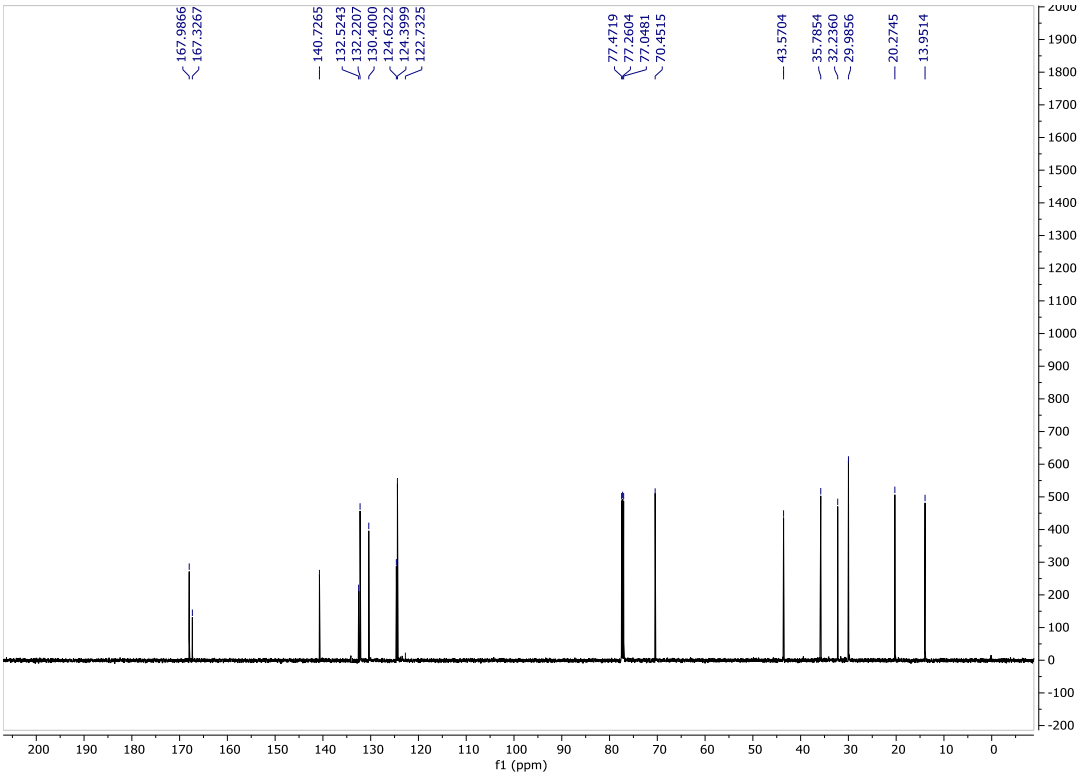
^{1}H and ^{13}C NMR spectra of **2g** (400 and 100 MHz, $CDCl_3$)



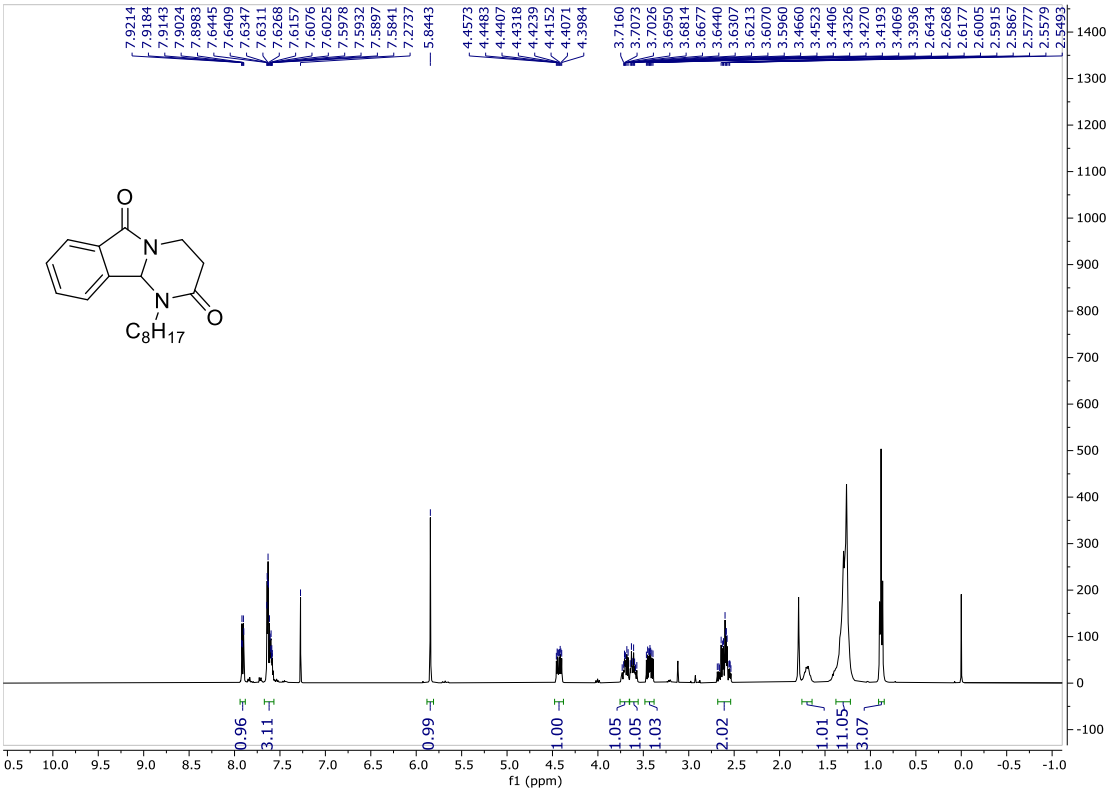


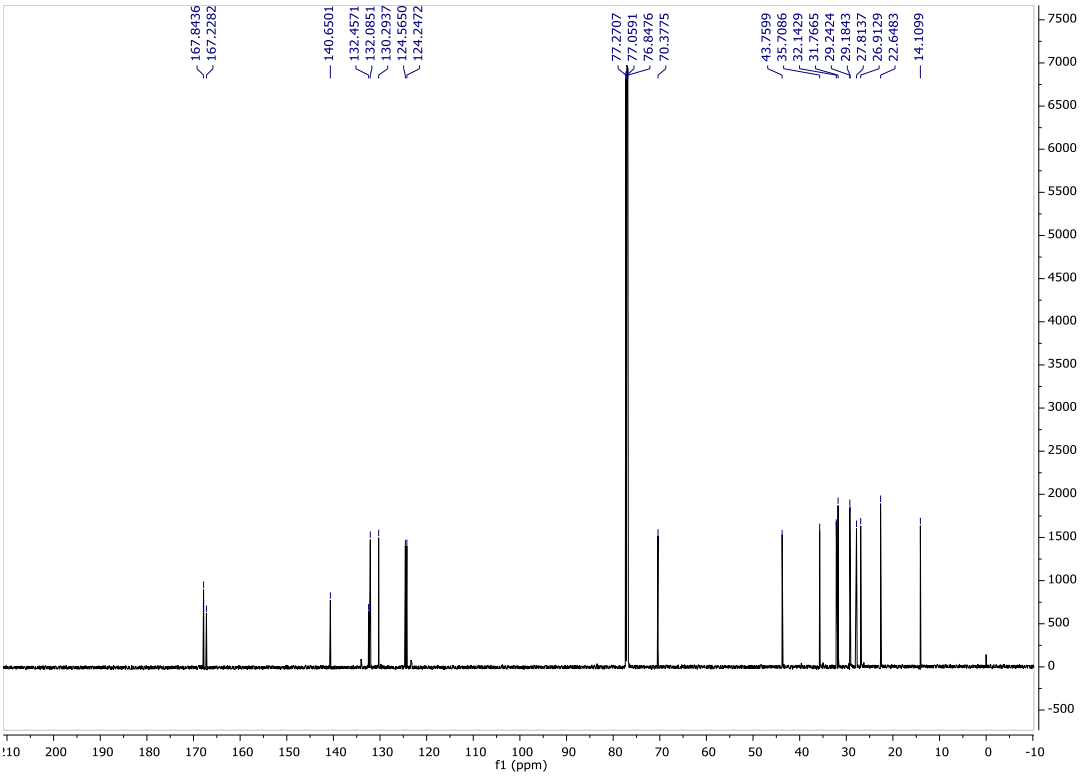
^{1}H and ^{13}C NMR spectra of **2h** (600 and 150 MHz, $CDCl_3$)



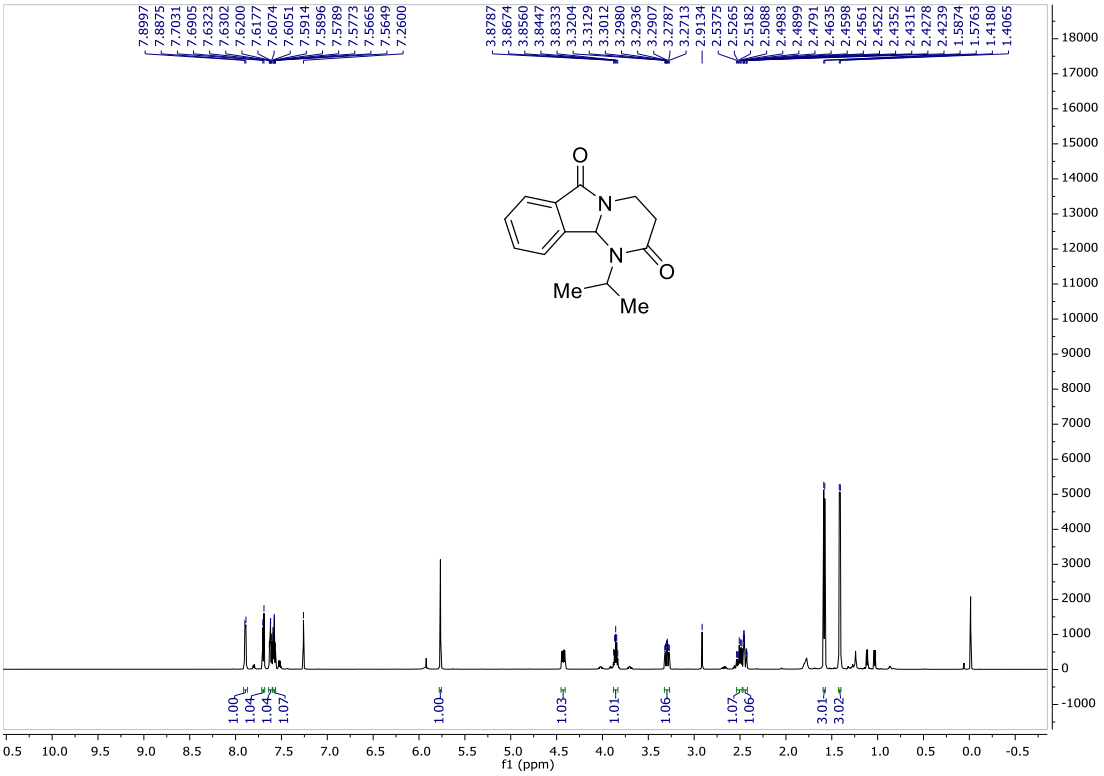


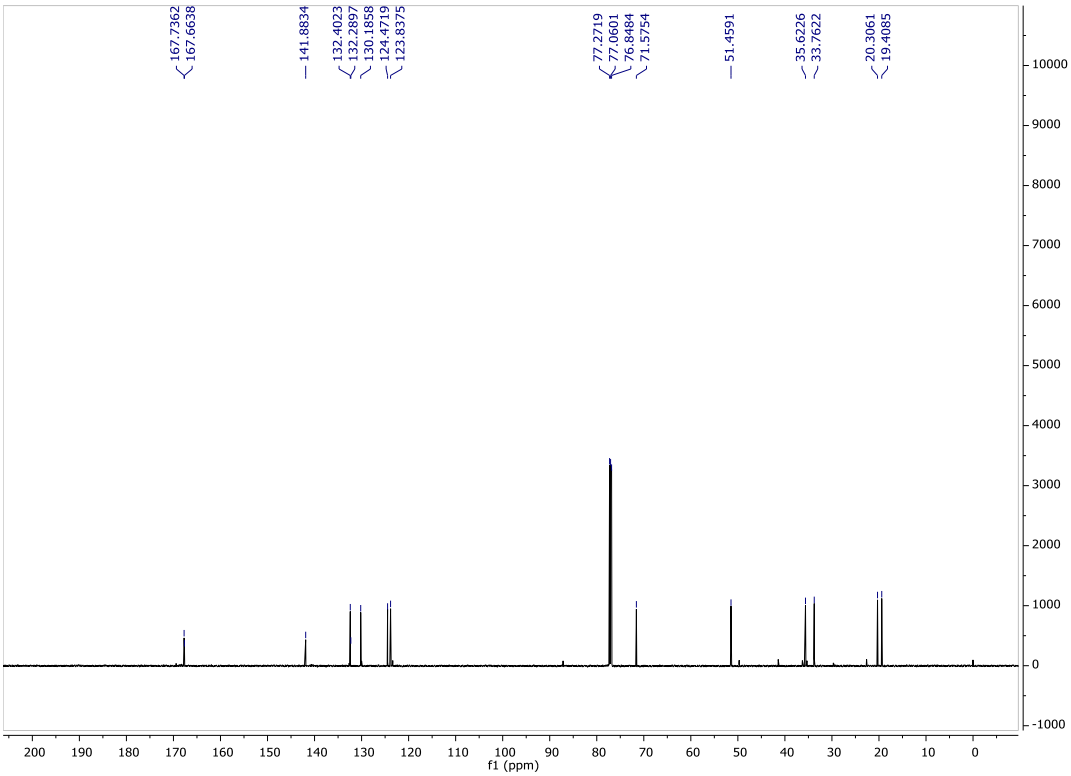
^{1}H and ^{13}C NMR spectra of **2i** (400 and 100 MHz, $CDCl_3$)



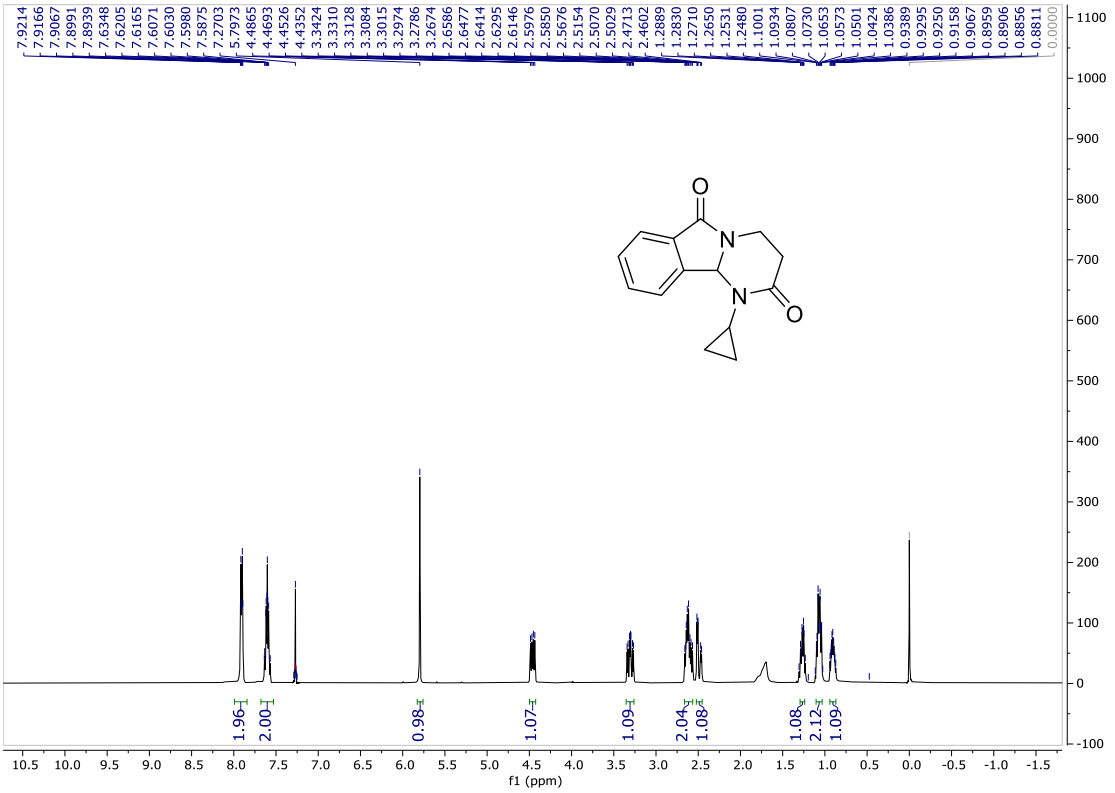


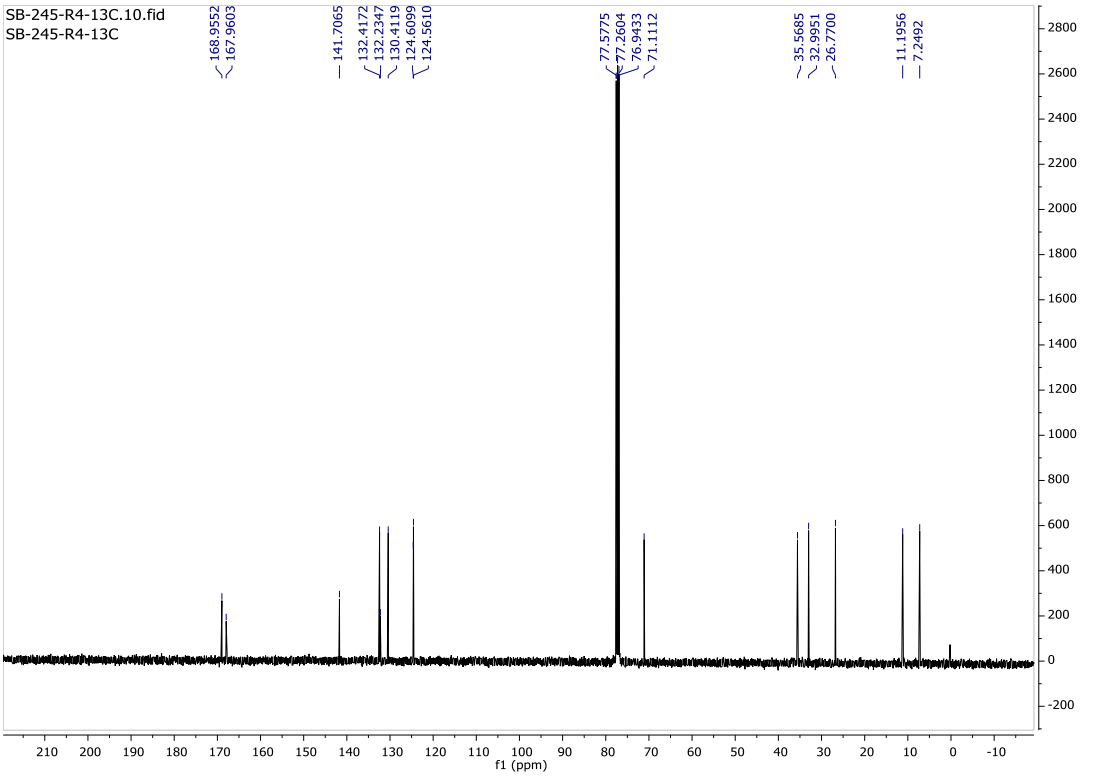
^{1}H and ^{13}C NMR spectra of **2j** (600 and 150 MHz, $CDCl_3$)



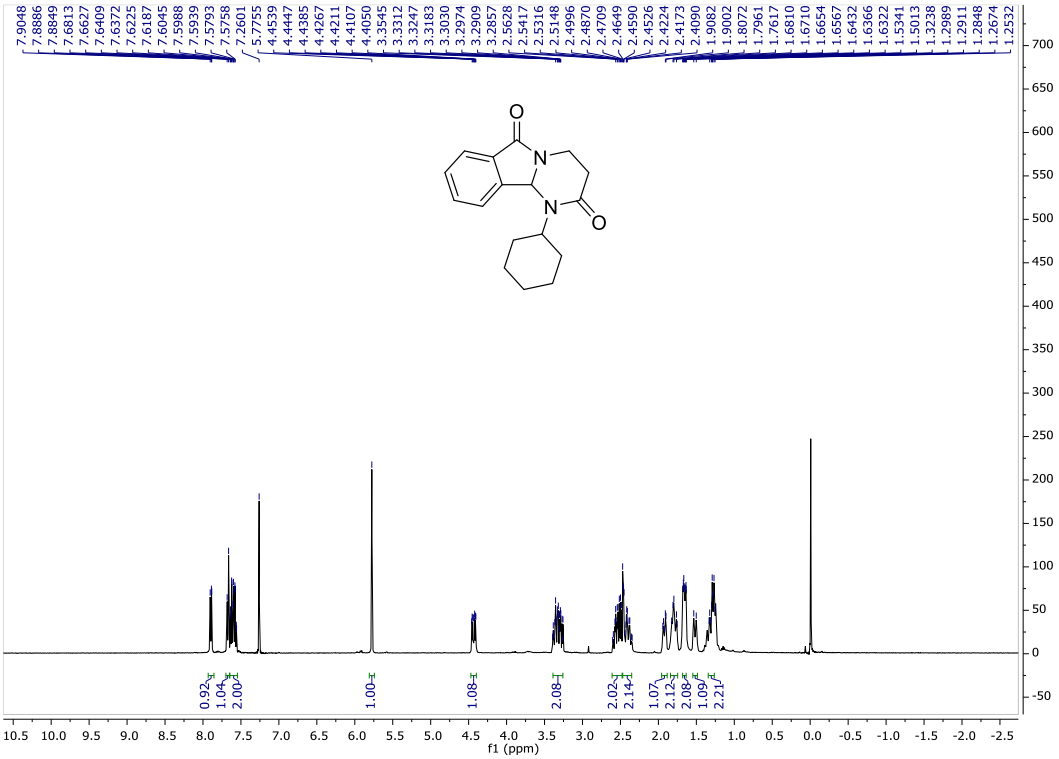


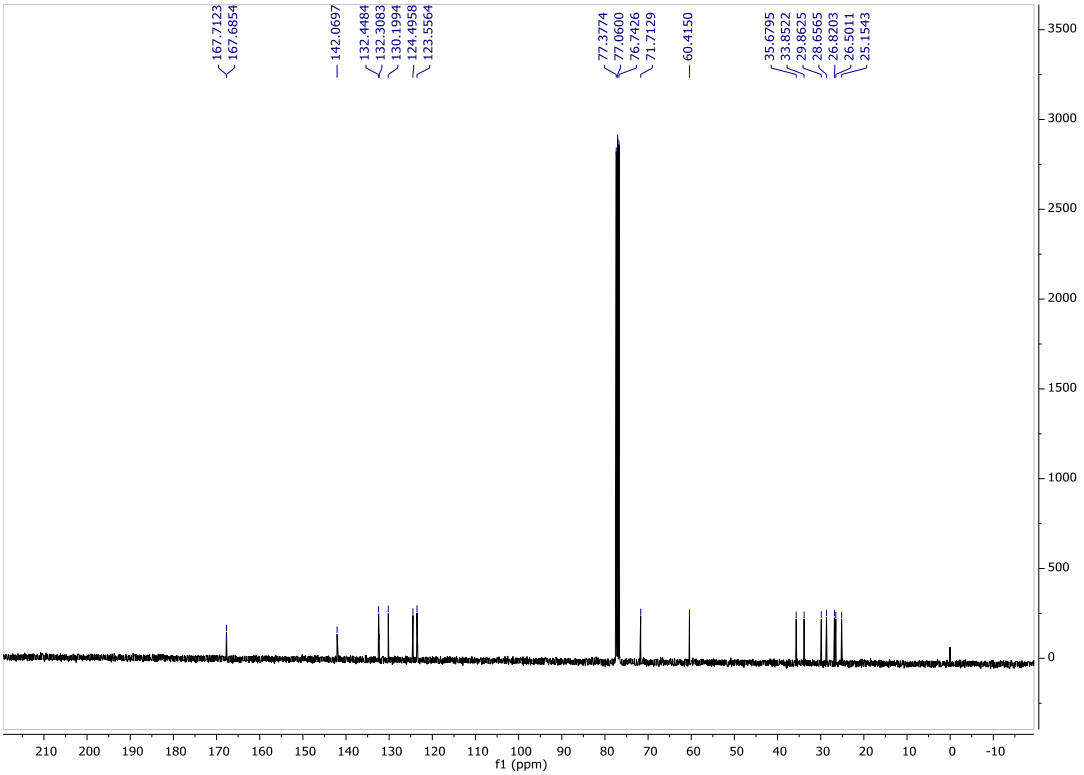
^{1}H and ^{13}C NMR spectra of **2k** (400 and 100 MHz, $CDCl_3$)



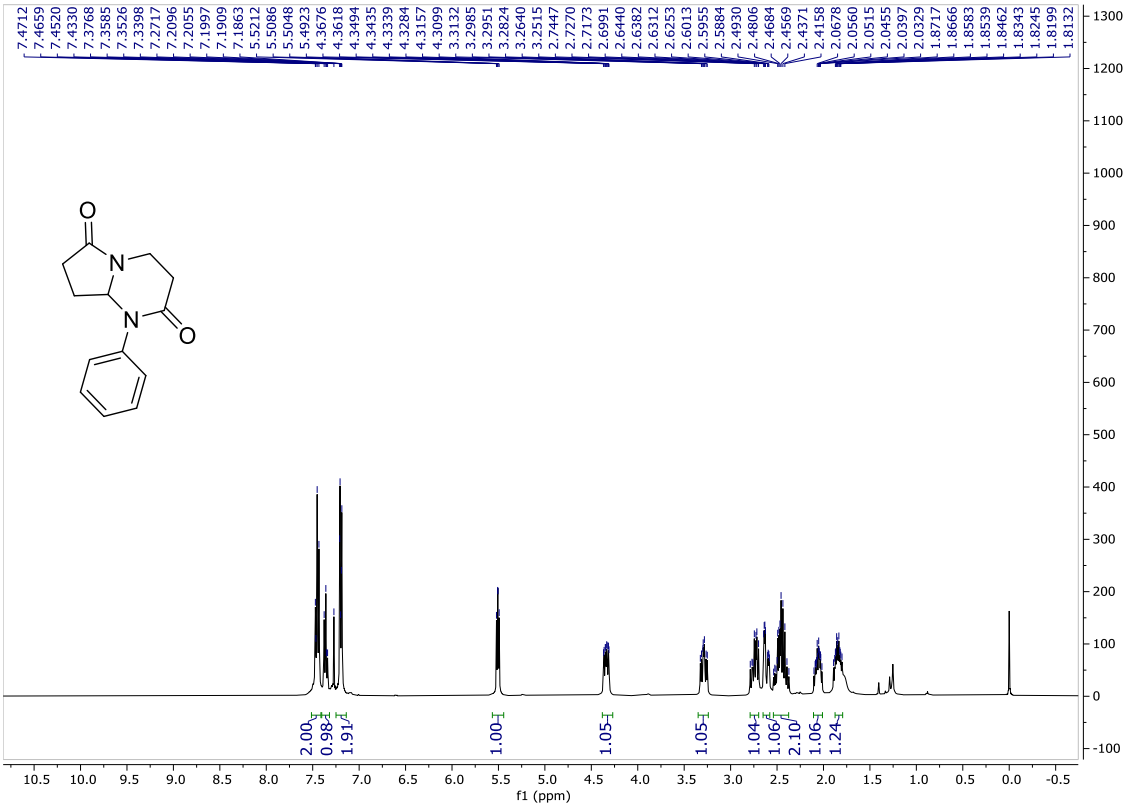


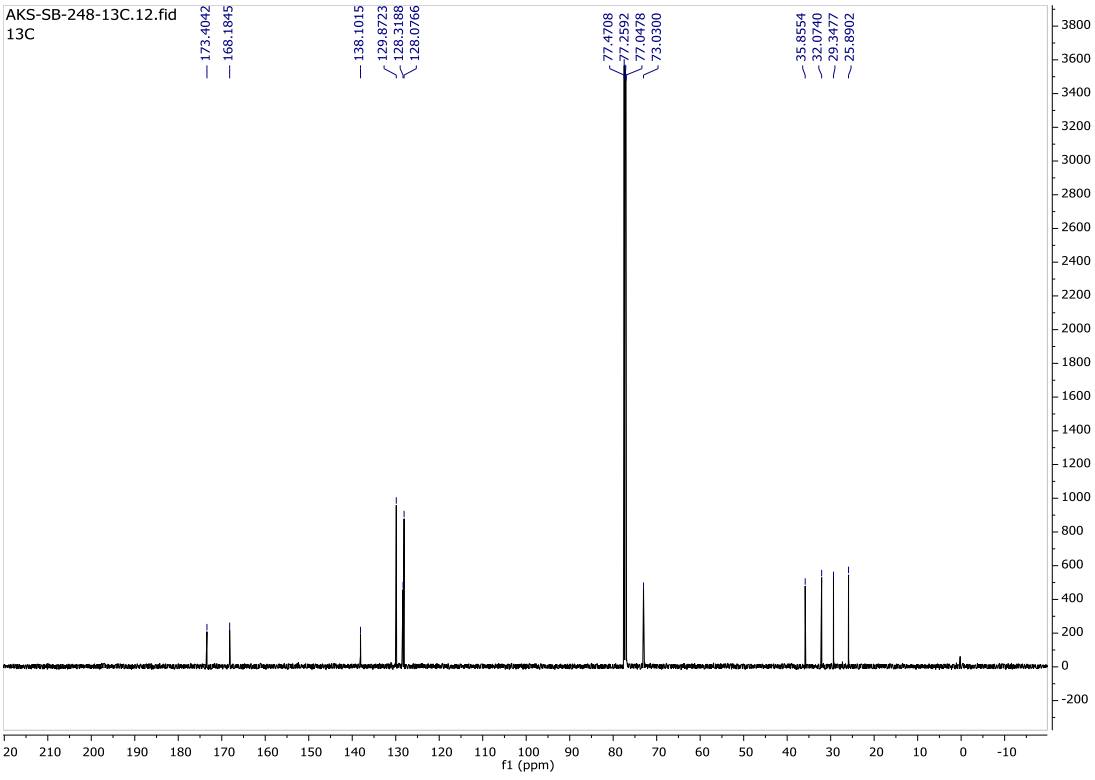
^{1}H and ^{13}C NMR spectra of **2l** (400 and 100 MHz, $CDCl_3$)



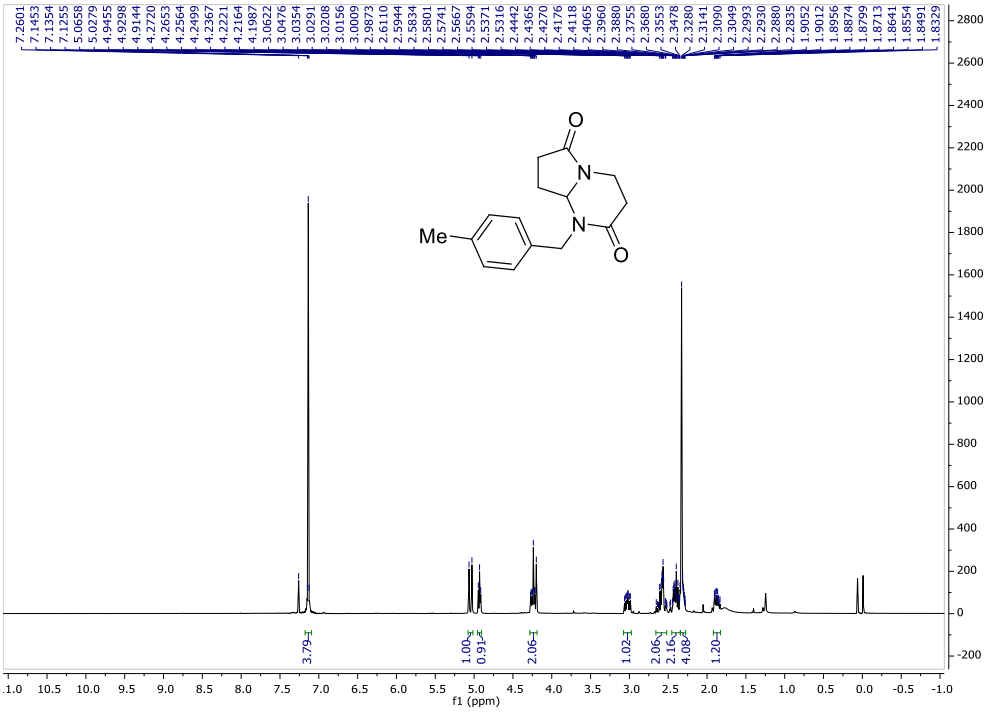


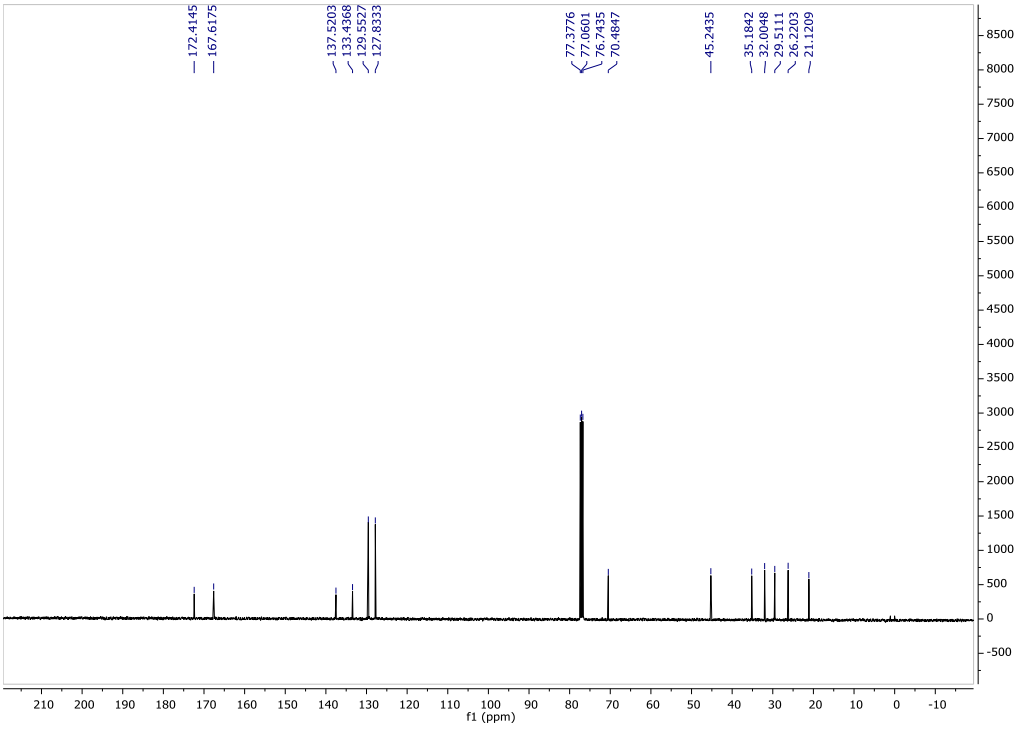
^{1}H and ^{13}C NMR spectra of **2m** (400 and 100 MHz, $CDCl_3$)



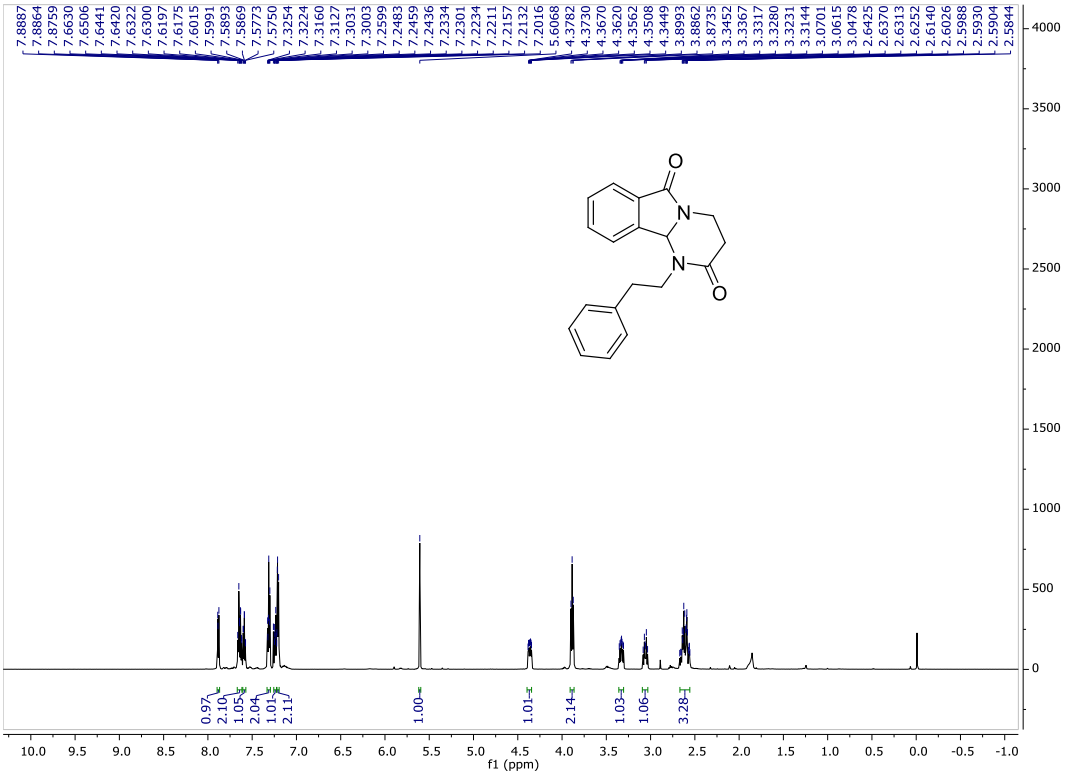


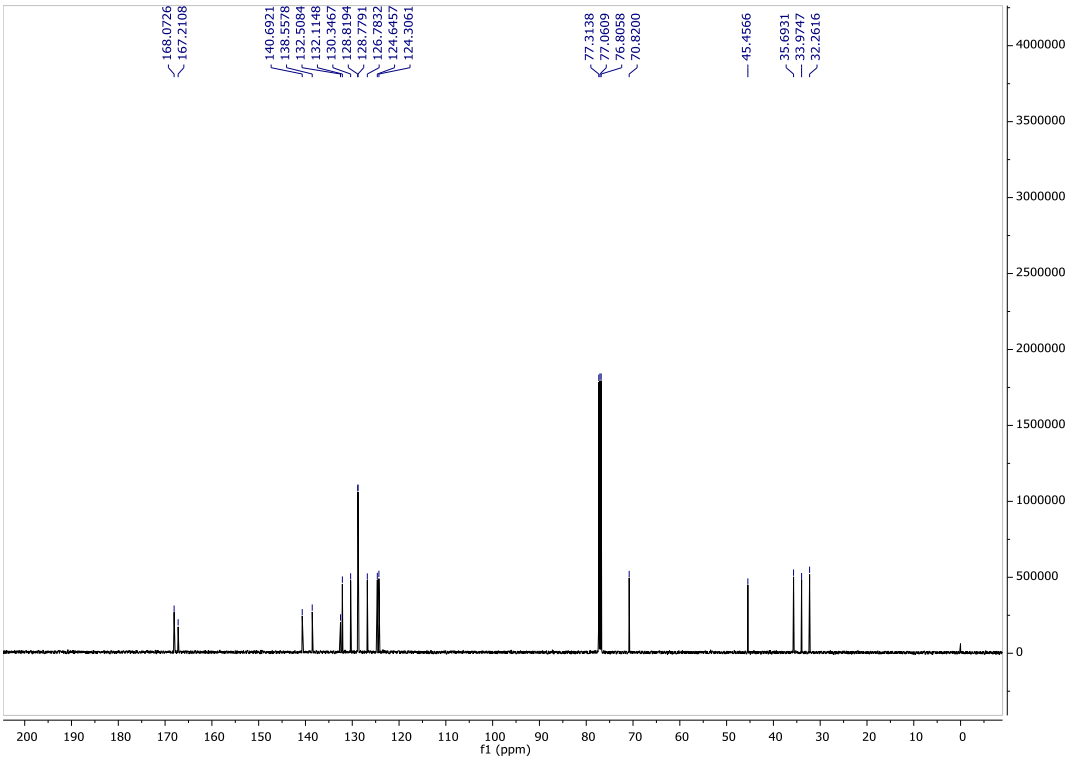
^{1}H and ^{13}C NMR spectra of **2n** (400 and 100 MHz, $CDCl_3$)



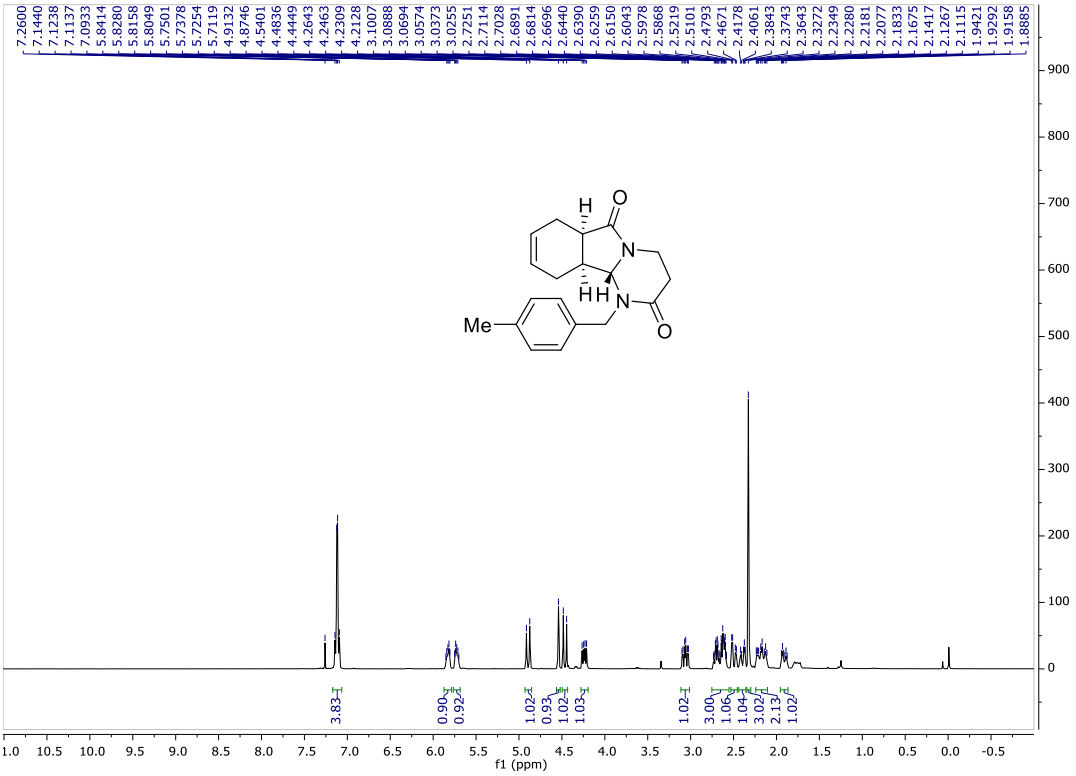


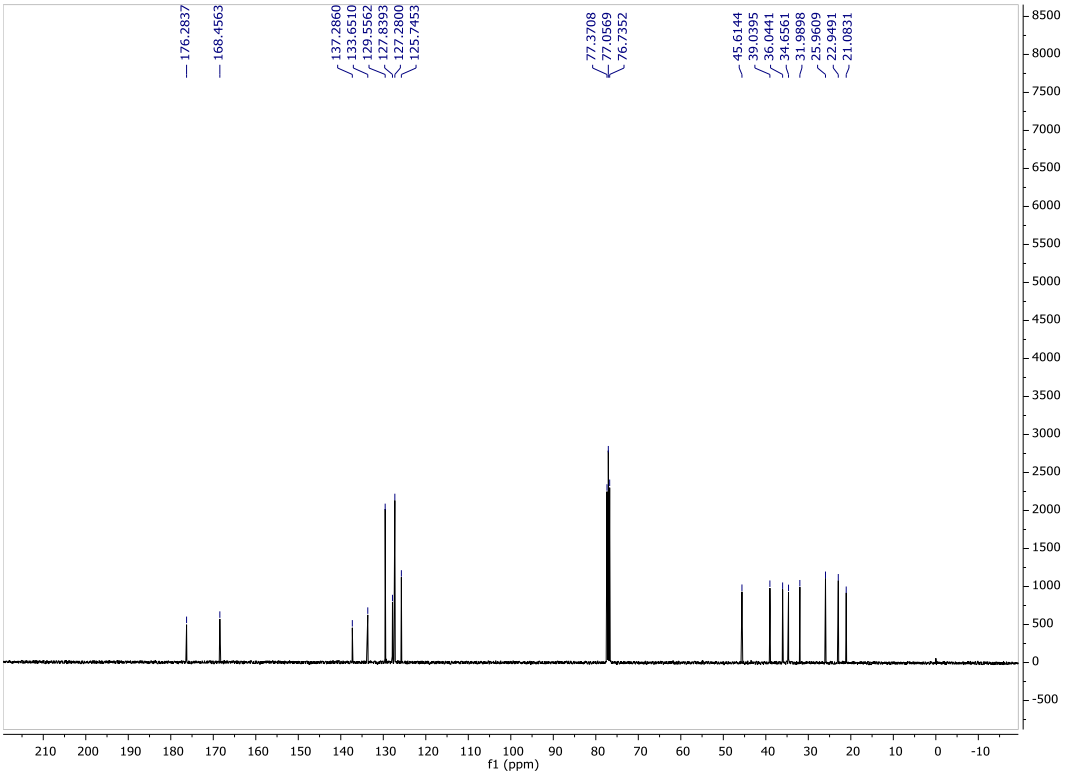
^{1}H and ^{13}C NMR spectra of **2o** (400 and 100 MHz, $CDCl_3$)



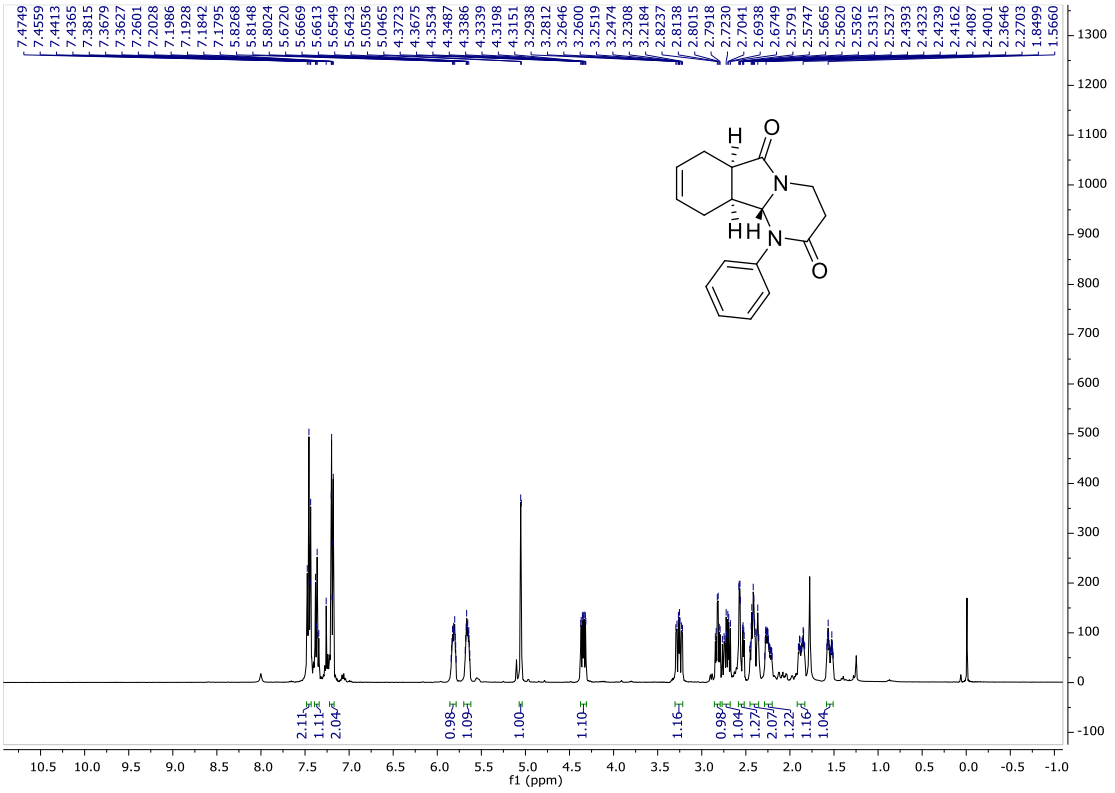


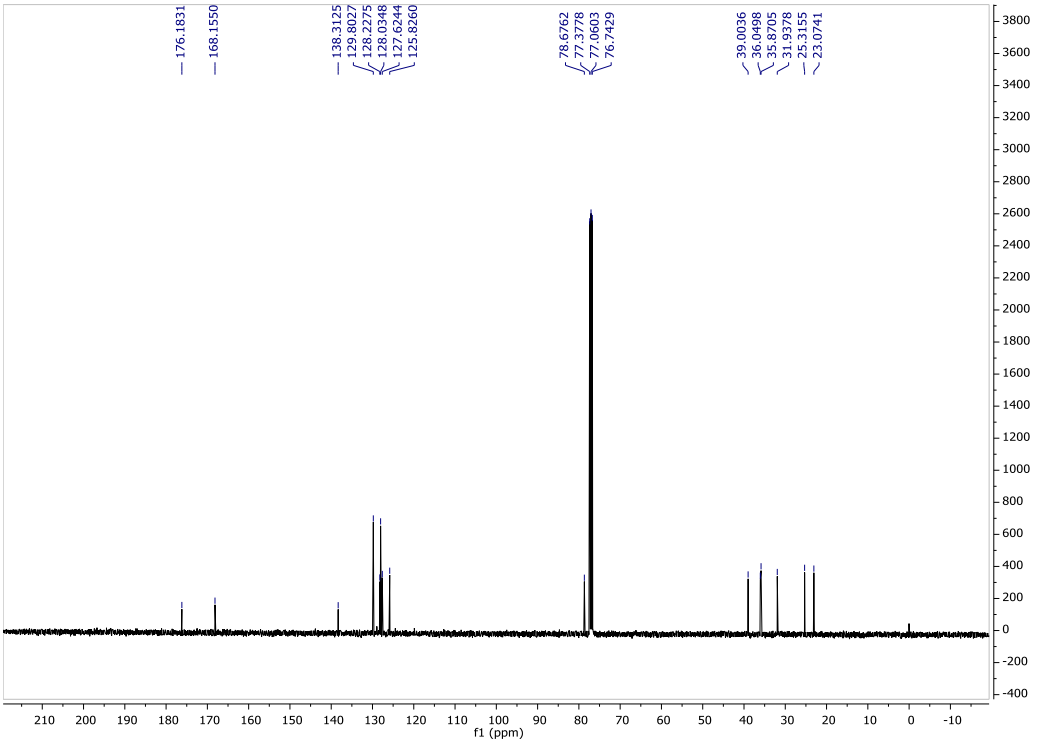
^{1}H and ^{13}C NMR spectra of **2p** (400 and 100 MHz, $CDCl_3$)



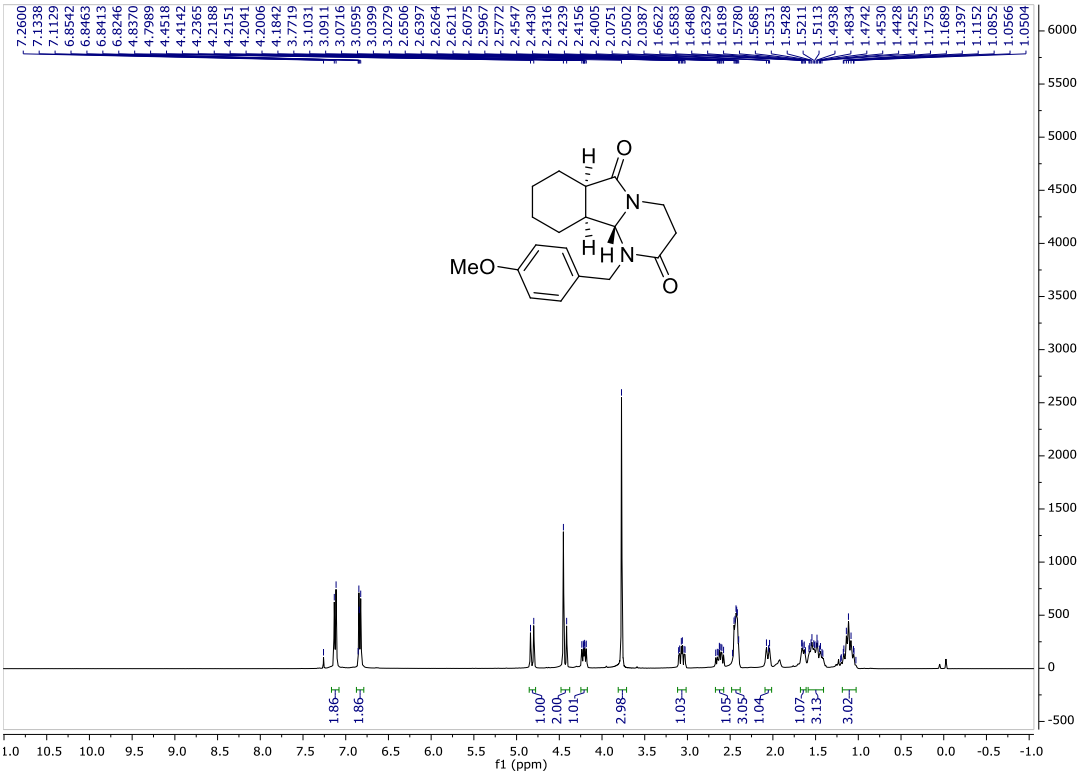


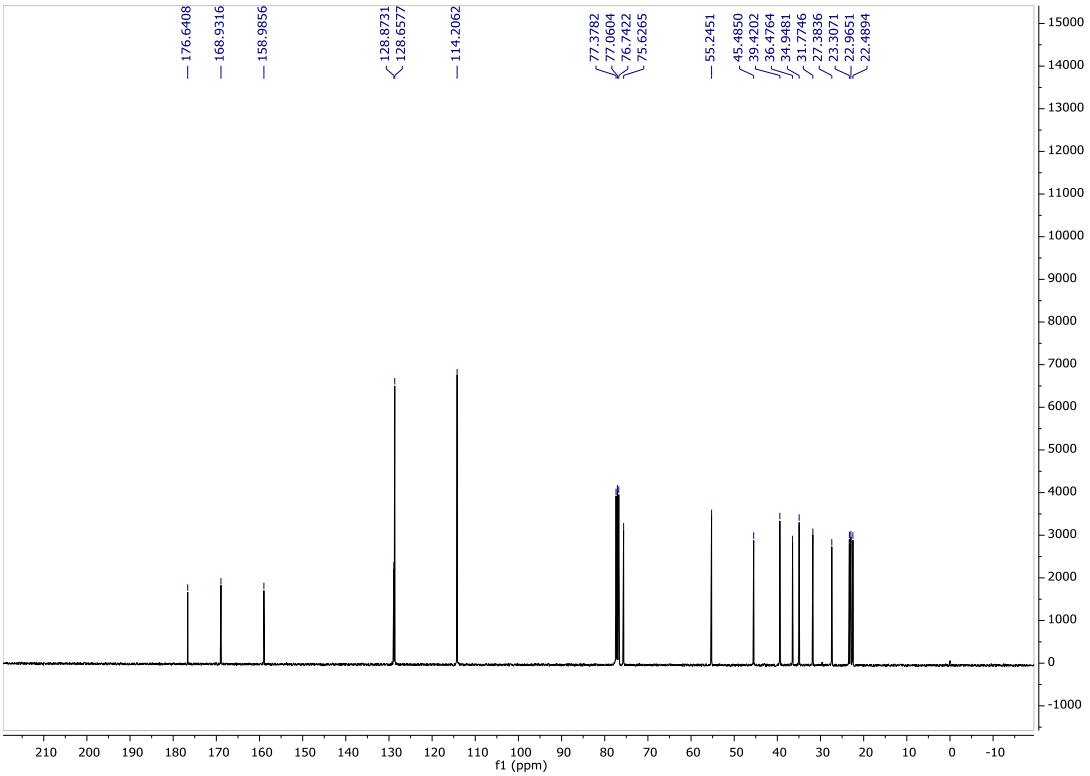
^{1}H and ^{13}C NMR spectra of **2q** (600 and 150 MHz, $CDCl_3$)



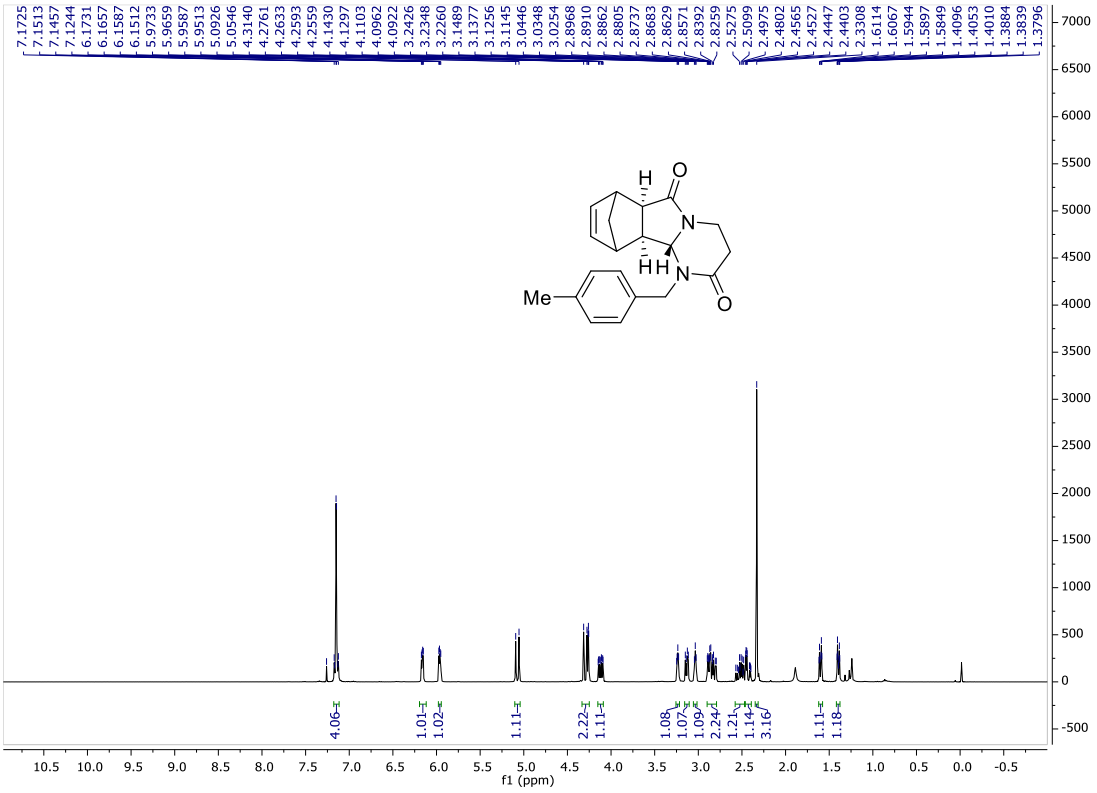


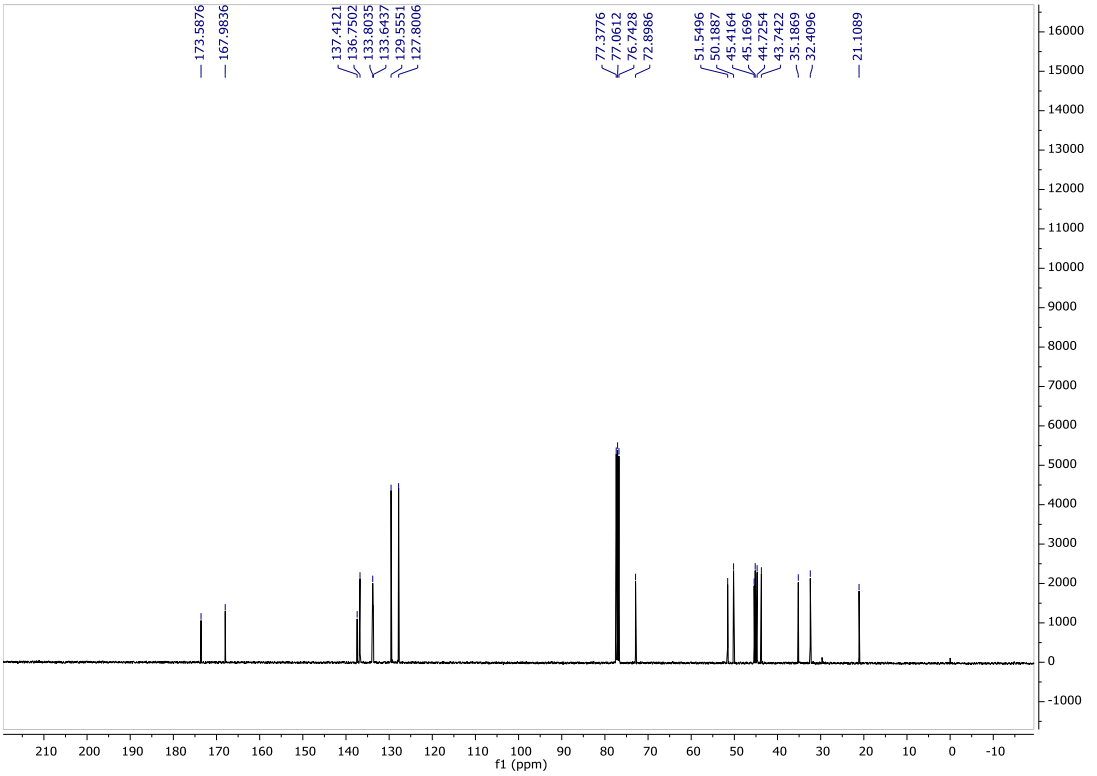
^{1}H and ^{13}C NMR spectra of **2r** (400 and 100 MHz, $CDCl_3$)



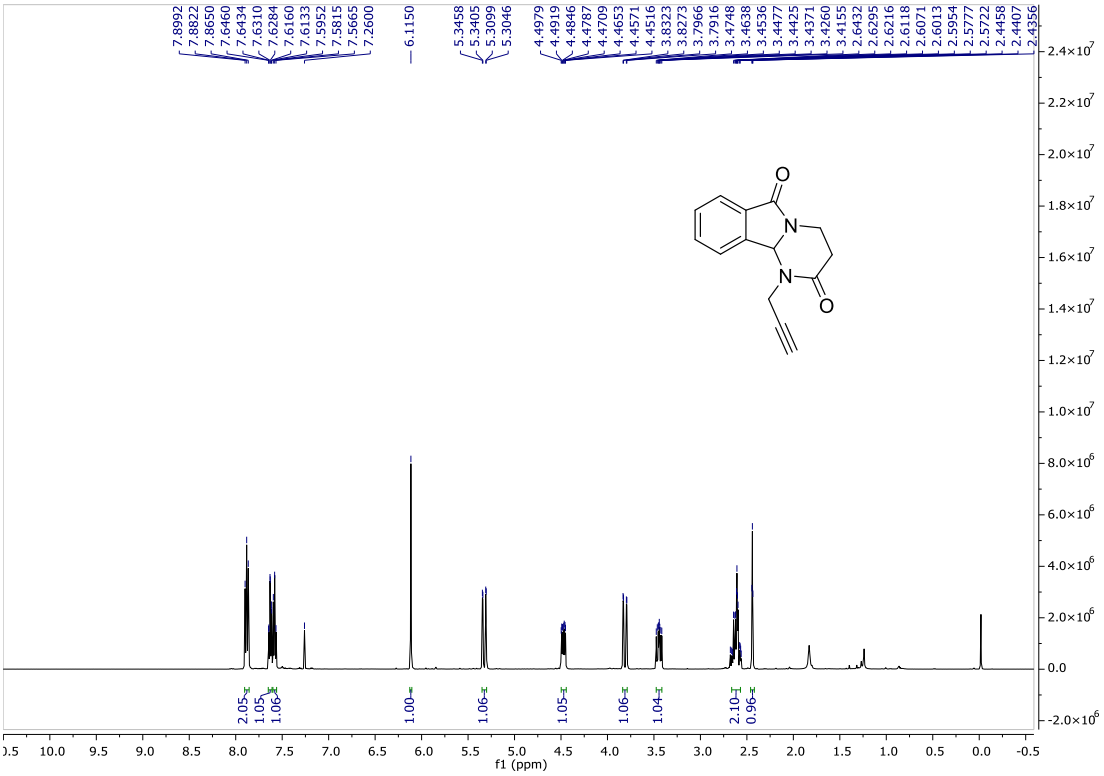


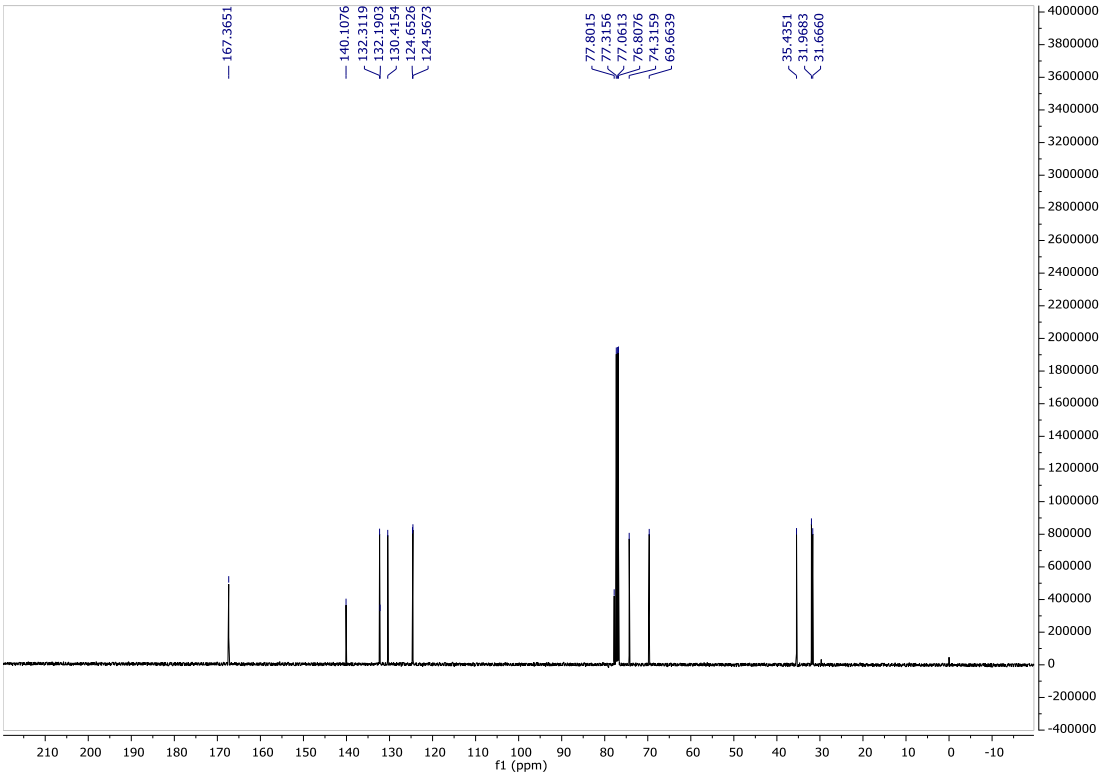
^{1}H and ^{13}C NMR spectra of **2s** (400 and 100 MHz, $CDCl_3$)



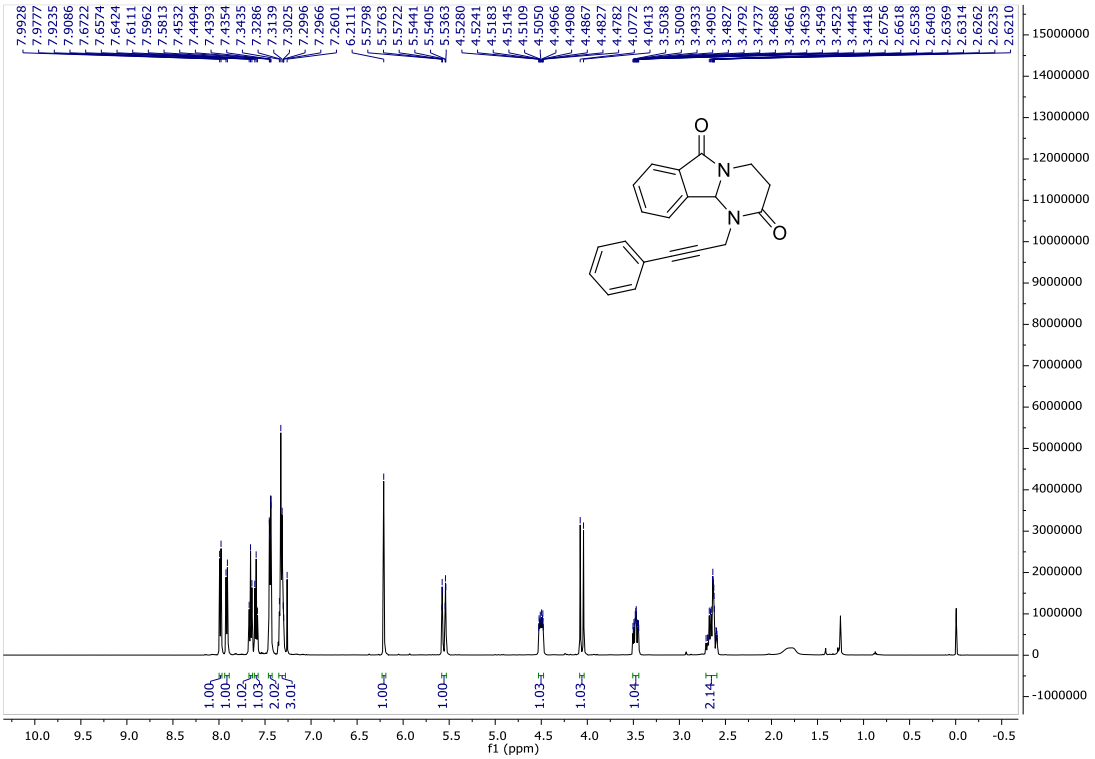


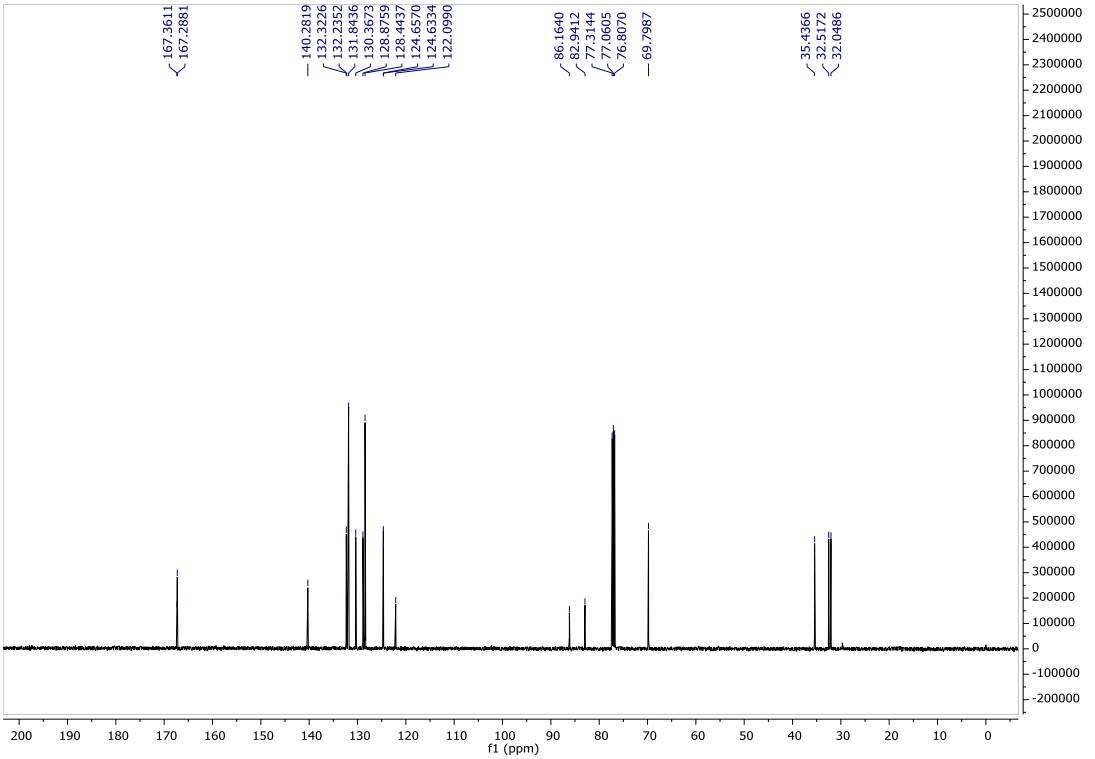
^{1}H and ^{13}C NMR spectra of **2u** (500 and 125 MHz, $CDCl_3$)



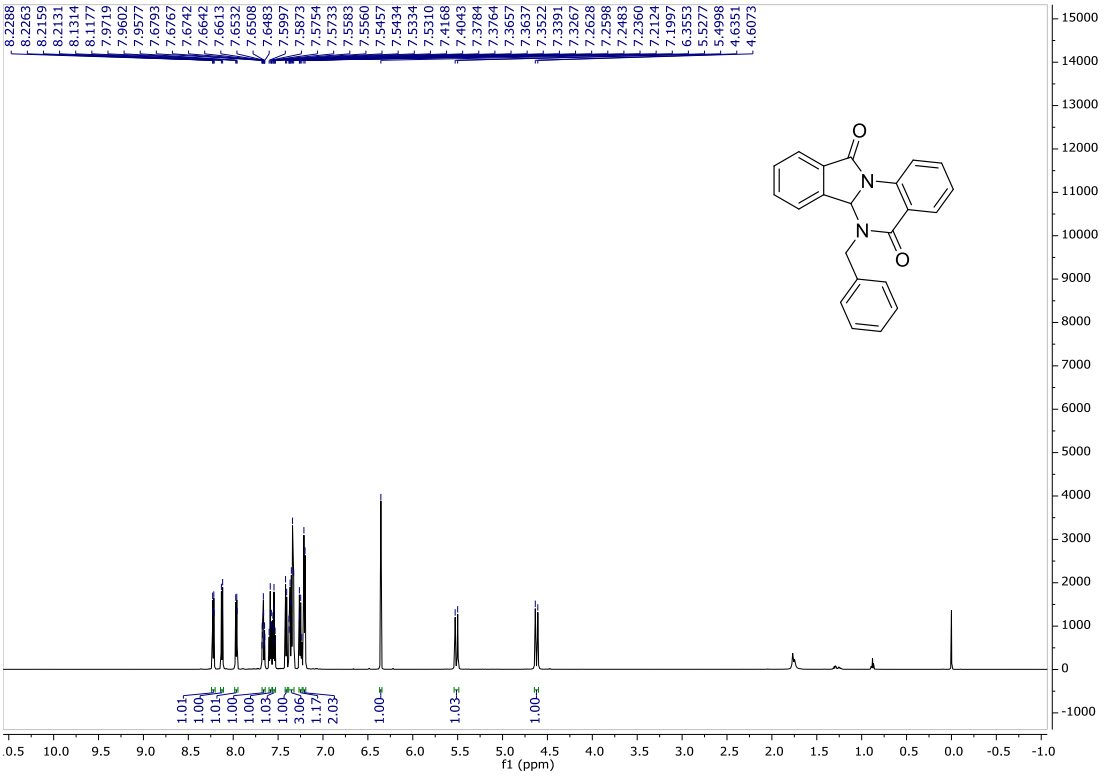


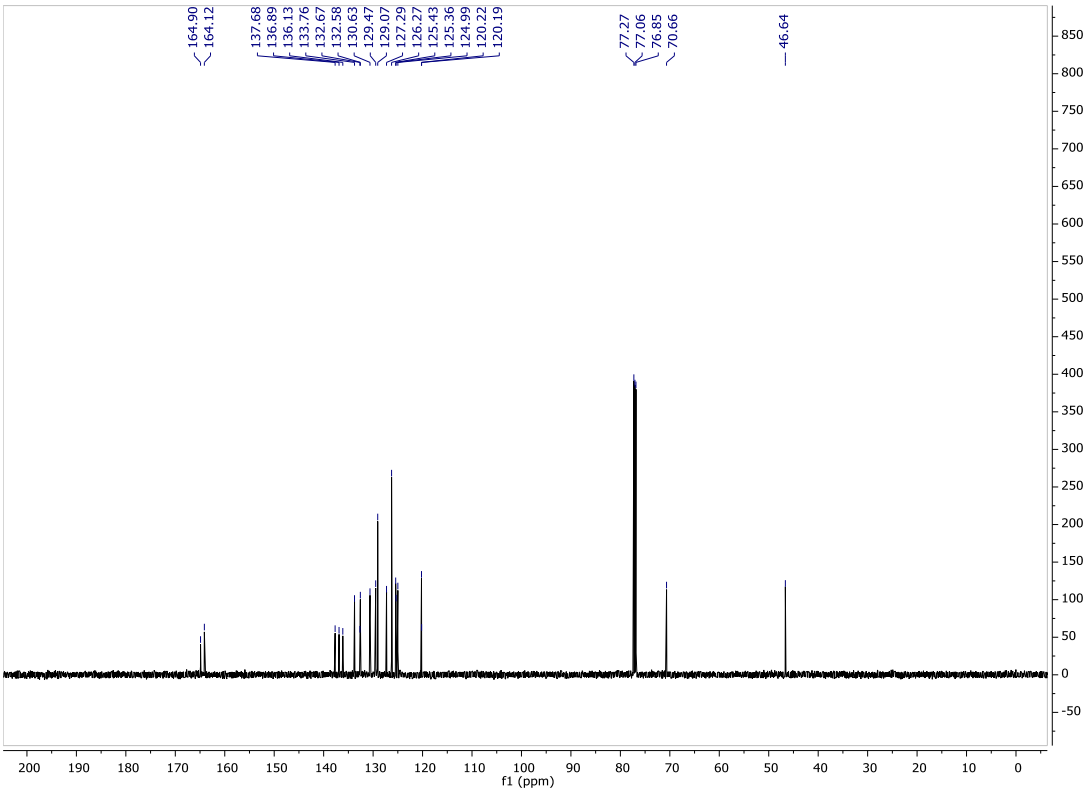
^{1}H and ^{13}C NMR spectra of **2v** (600 and 150 MHz, $CDCl_3$)



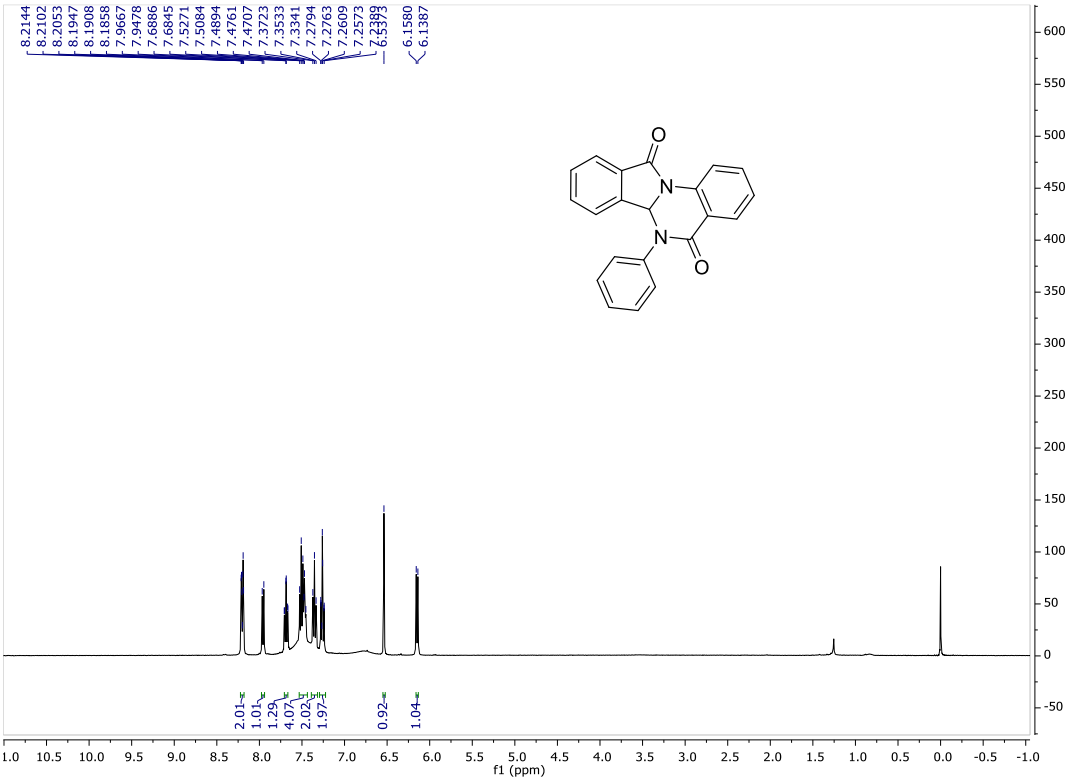


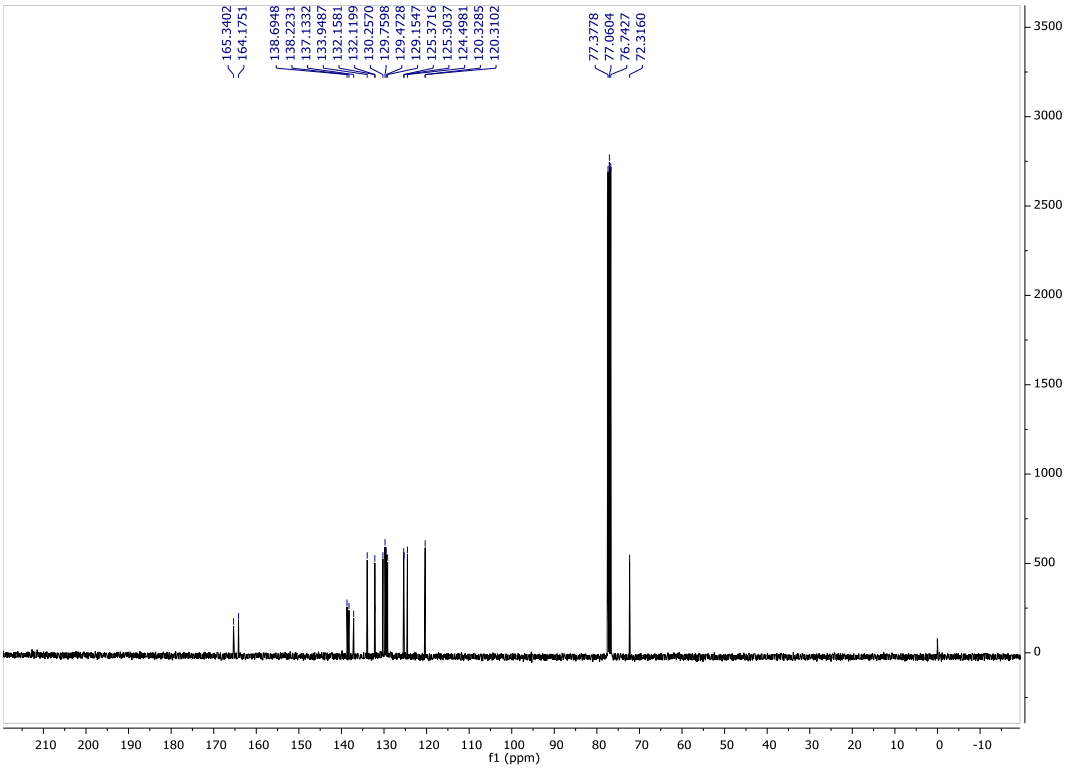
^{1}H and ^{13}C NMR spectra of **2w** (600 and 150 MHz, $CDCl_3$)



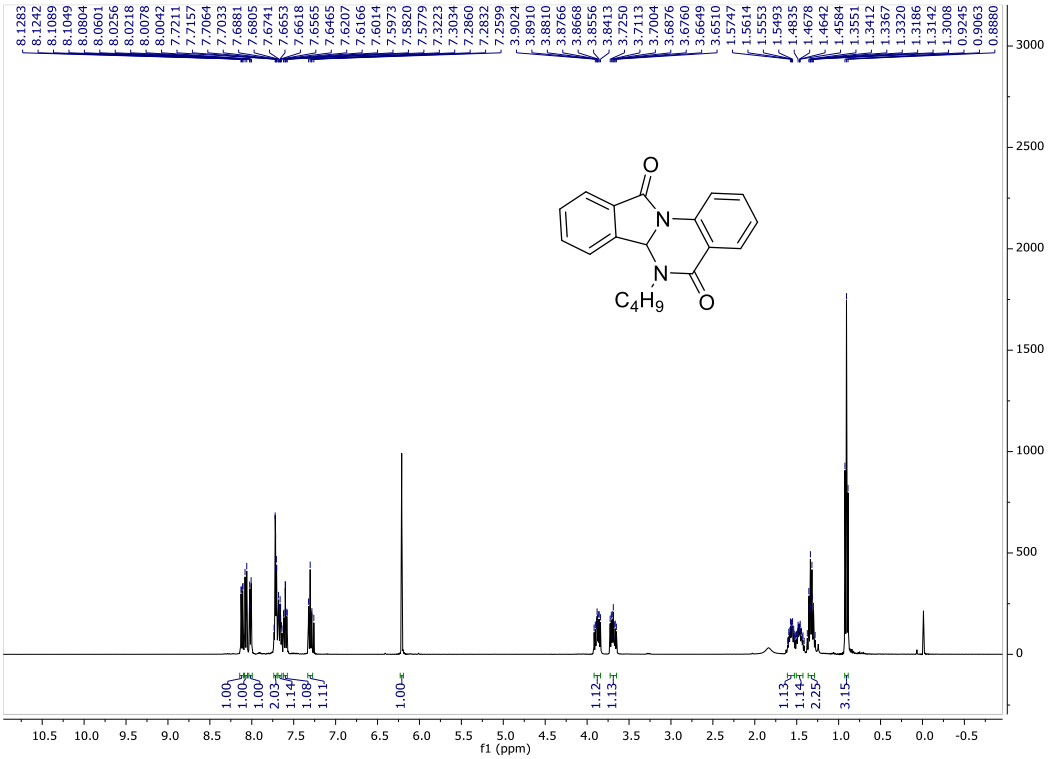


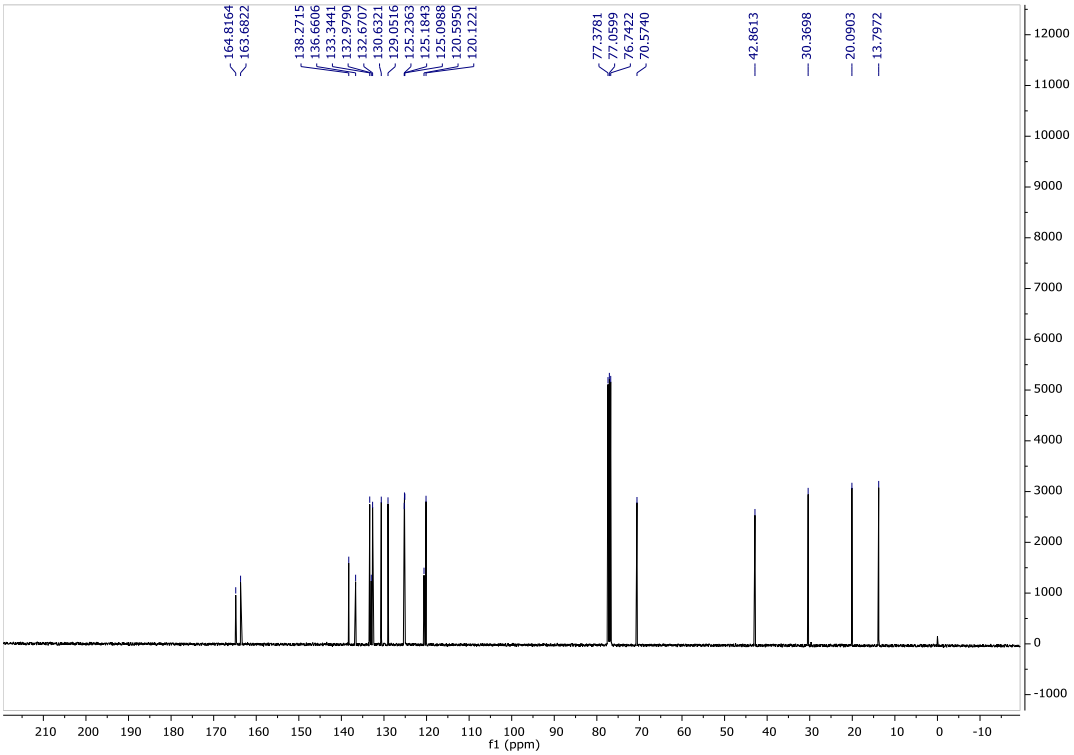
^{1}H and ^{13}C NMR spectra of **2x** (400 and 100 MHz, $CDCl_3$)



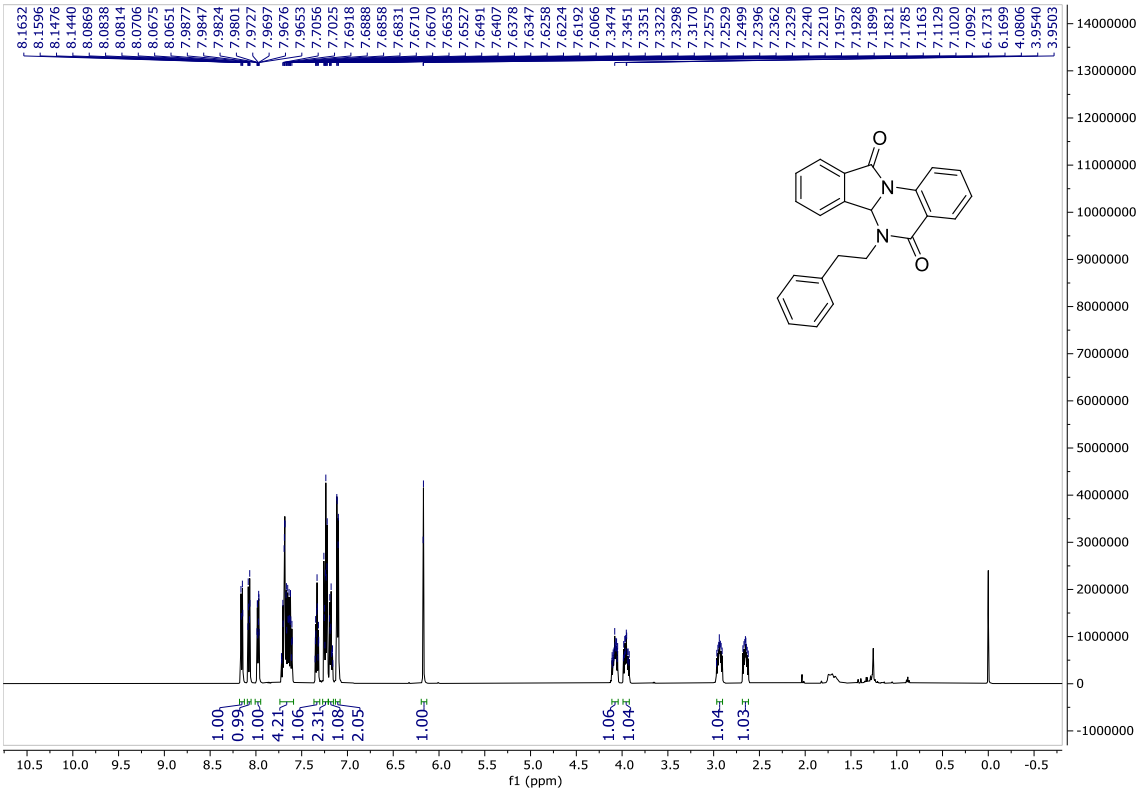


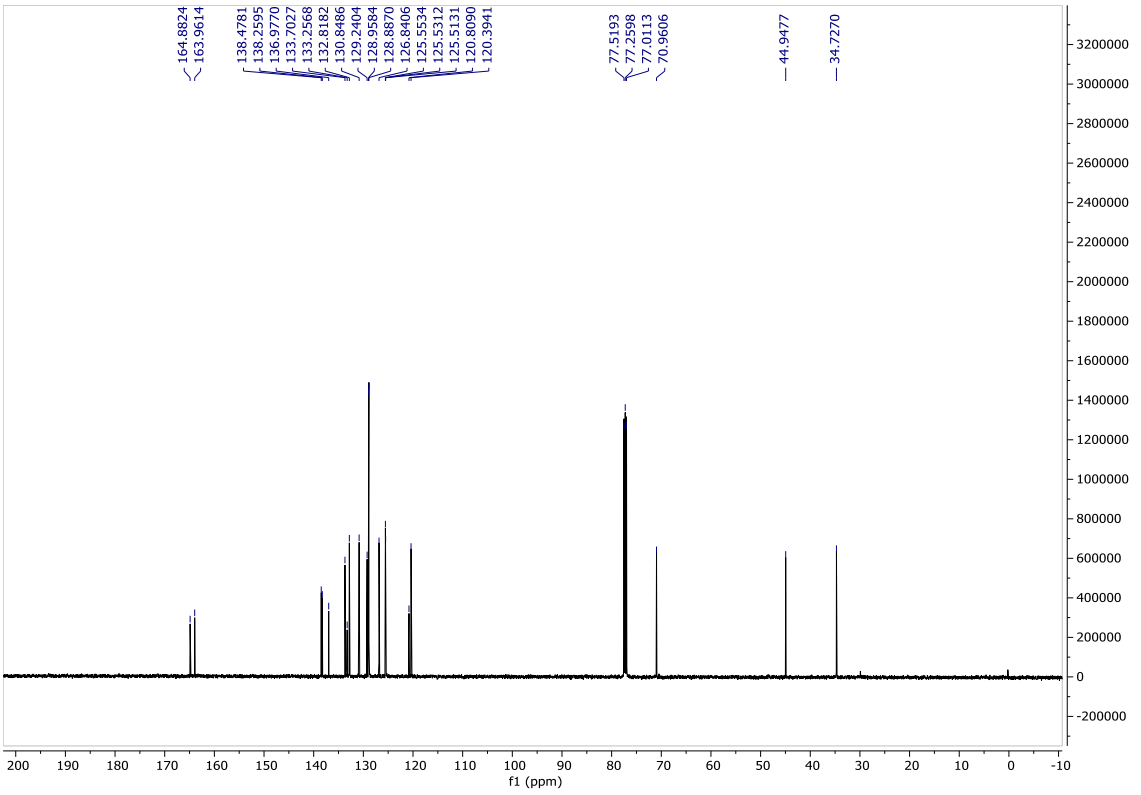
^{1}H and ^{13}C NMR spectra of **2y** (400 and 100 MHz, $CDCl_3$)



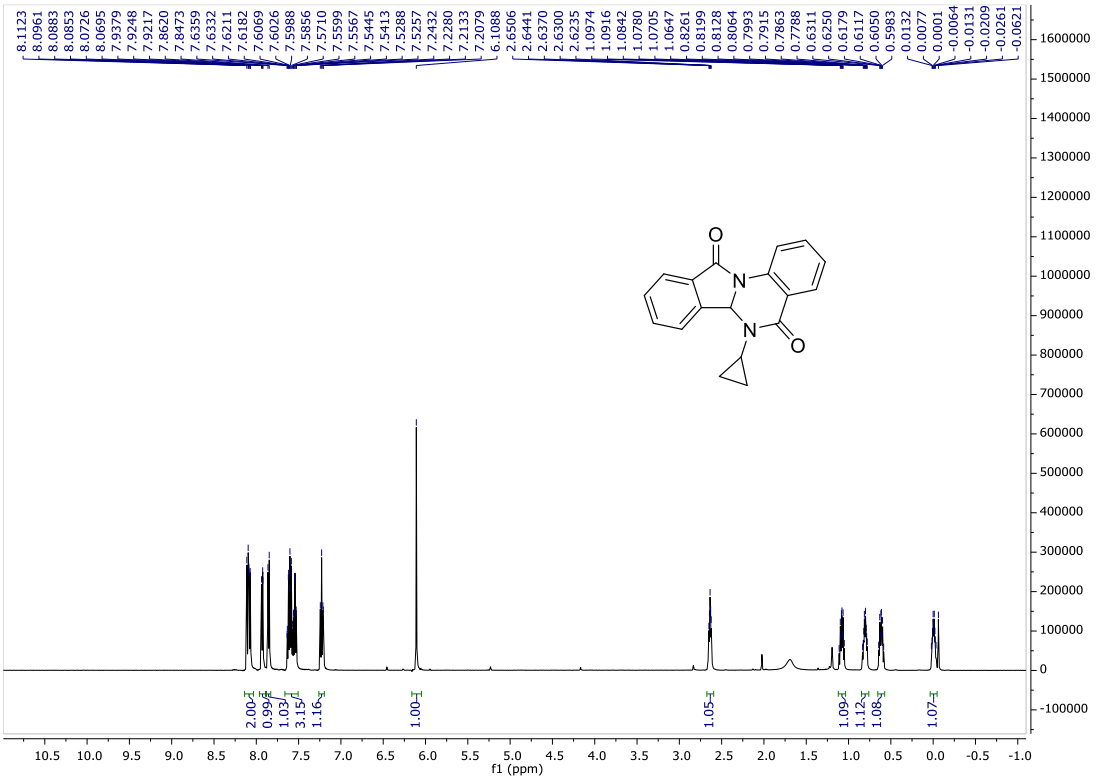


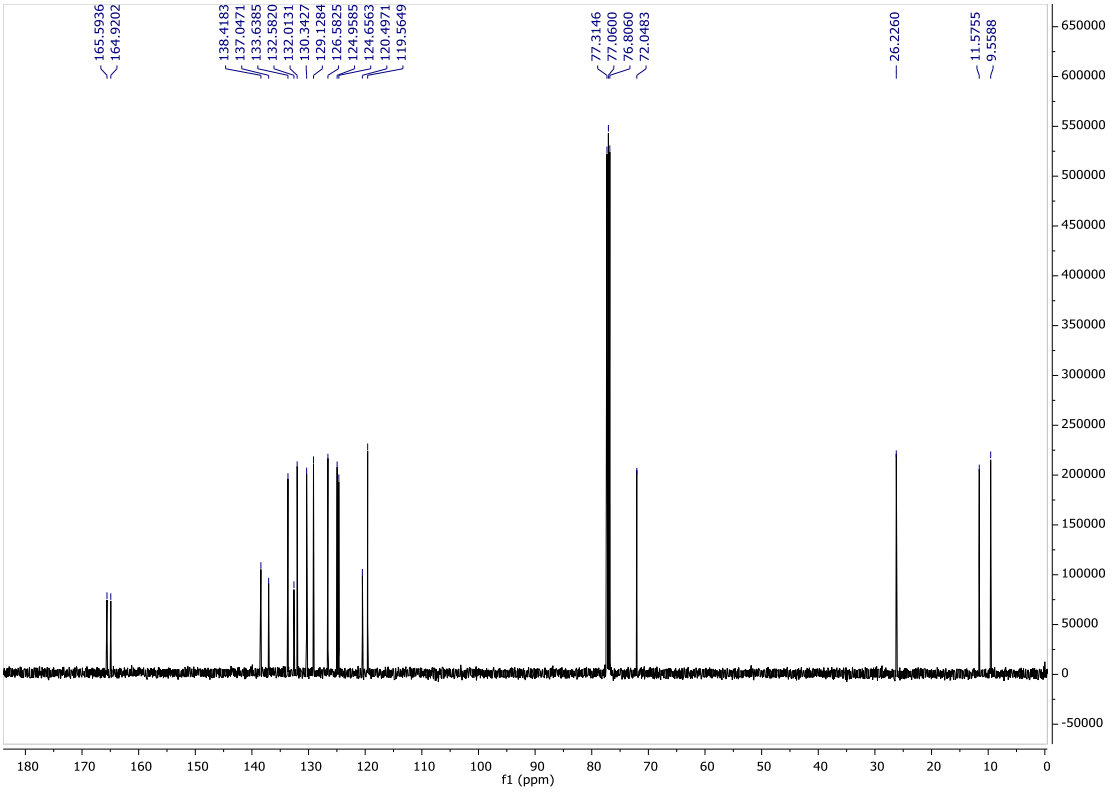
^{1}H and ^{13}C NMR spectra of **2z** (500 and 125 MHz, $CDCl_3$)



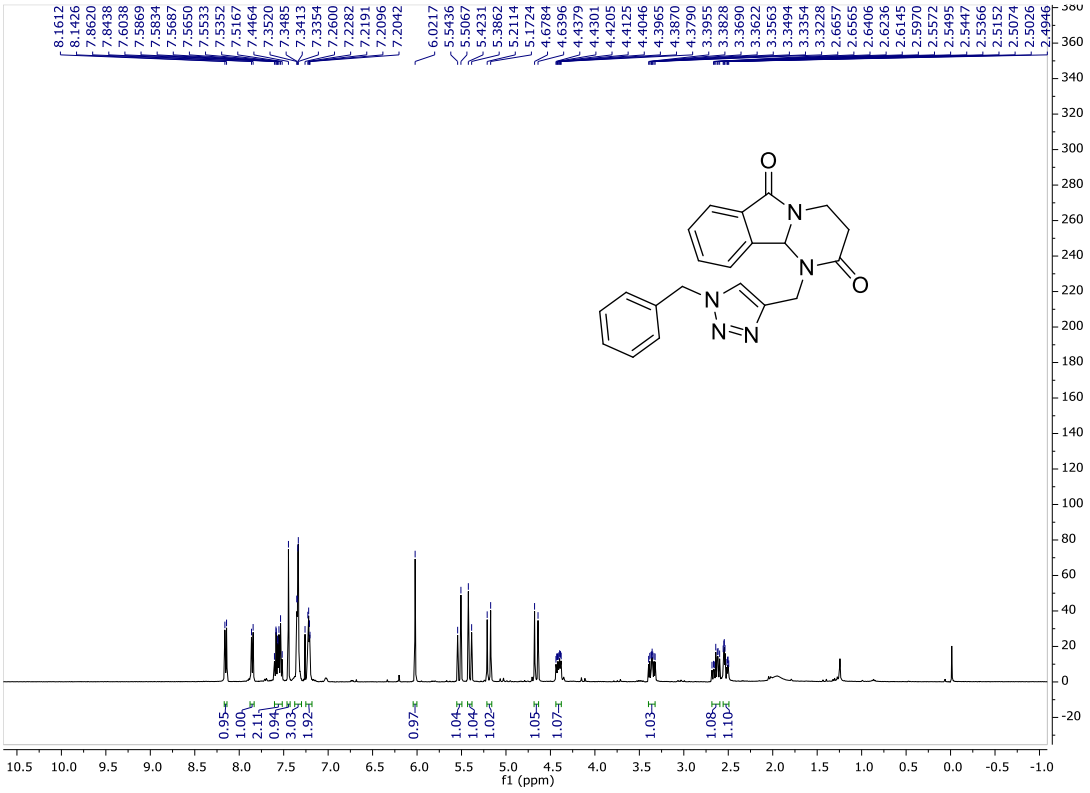


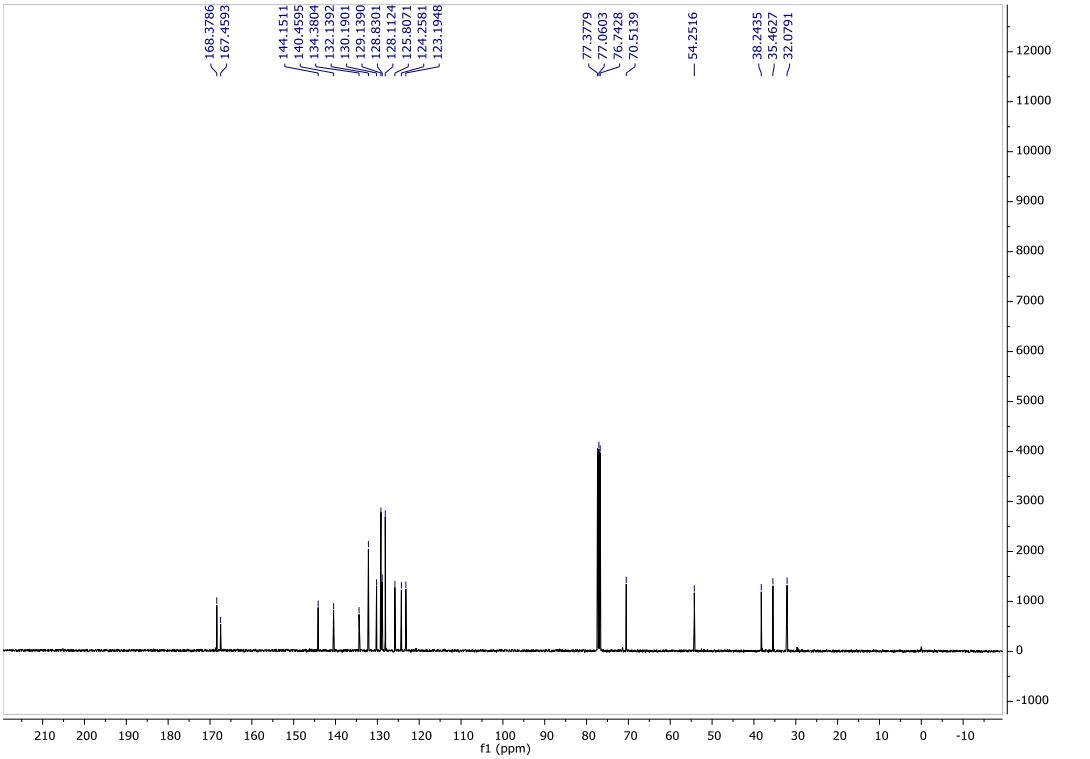
^{1}H and ^{13}C NMR spectra of **2aa** (500 and 125 MHz, $CDCl_3$)



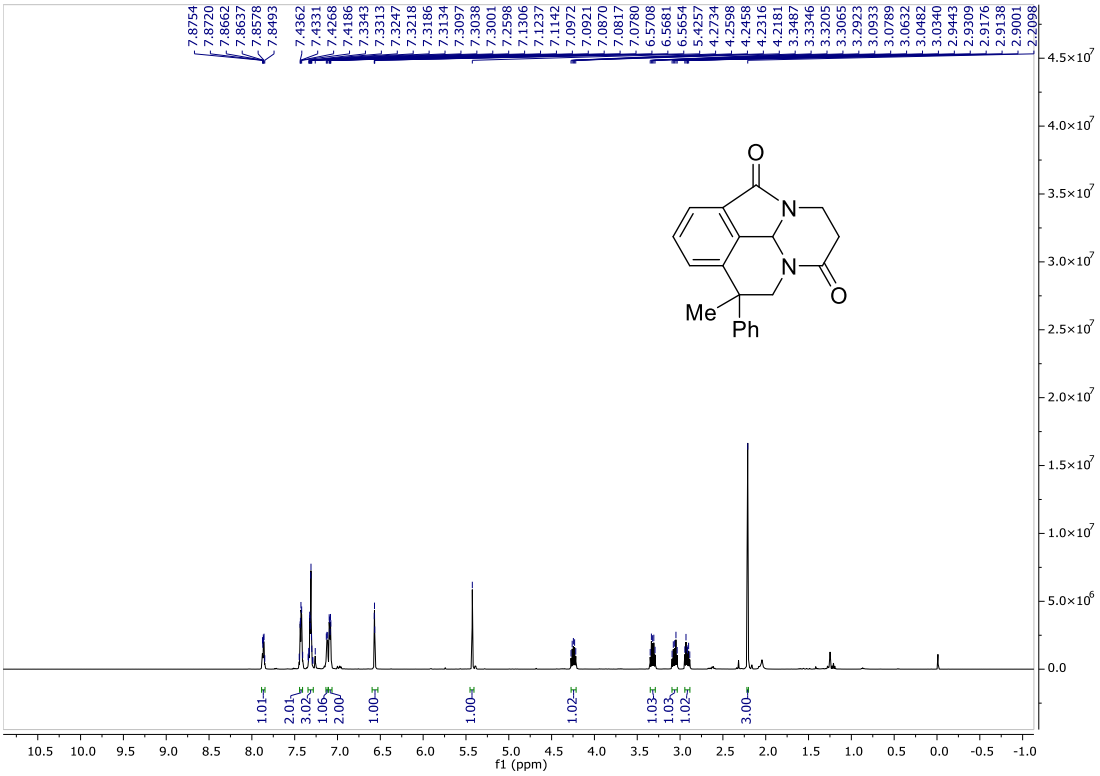


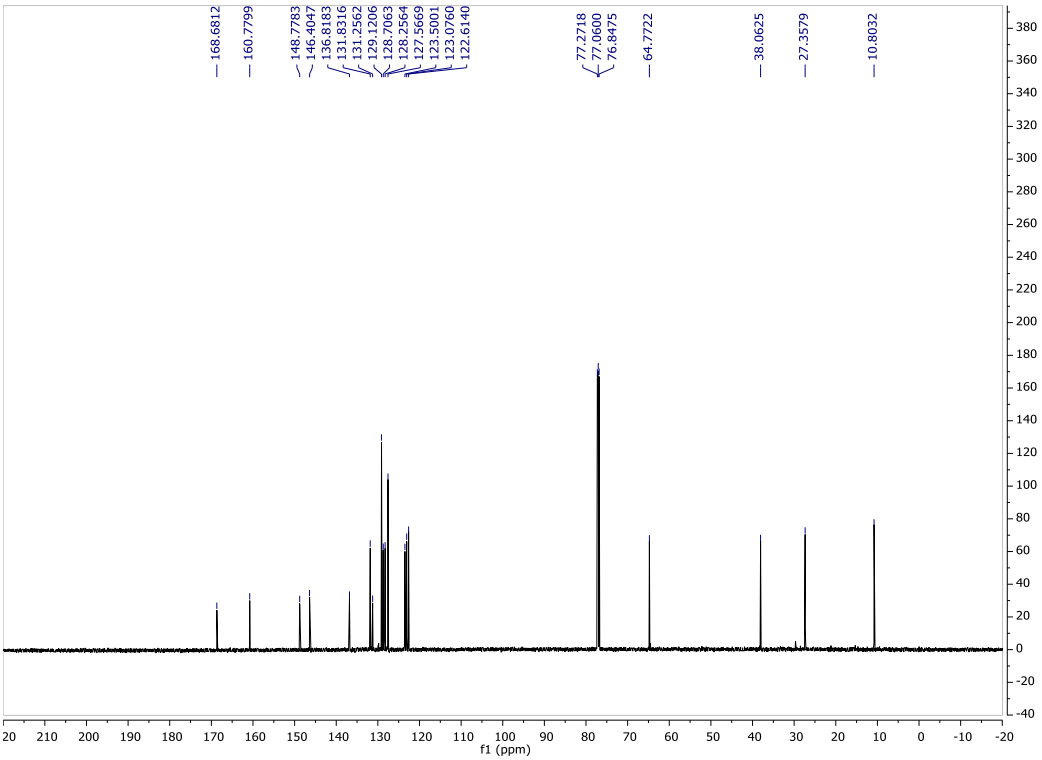
^{1}H and ^{13}C NMR spectra of **3a** (400 and 100 MHz, $CDCl_3$)



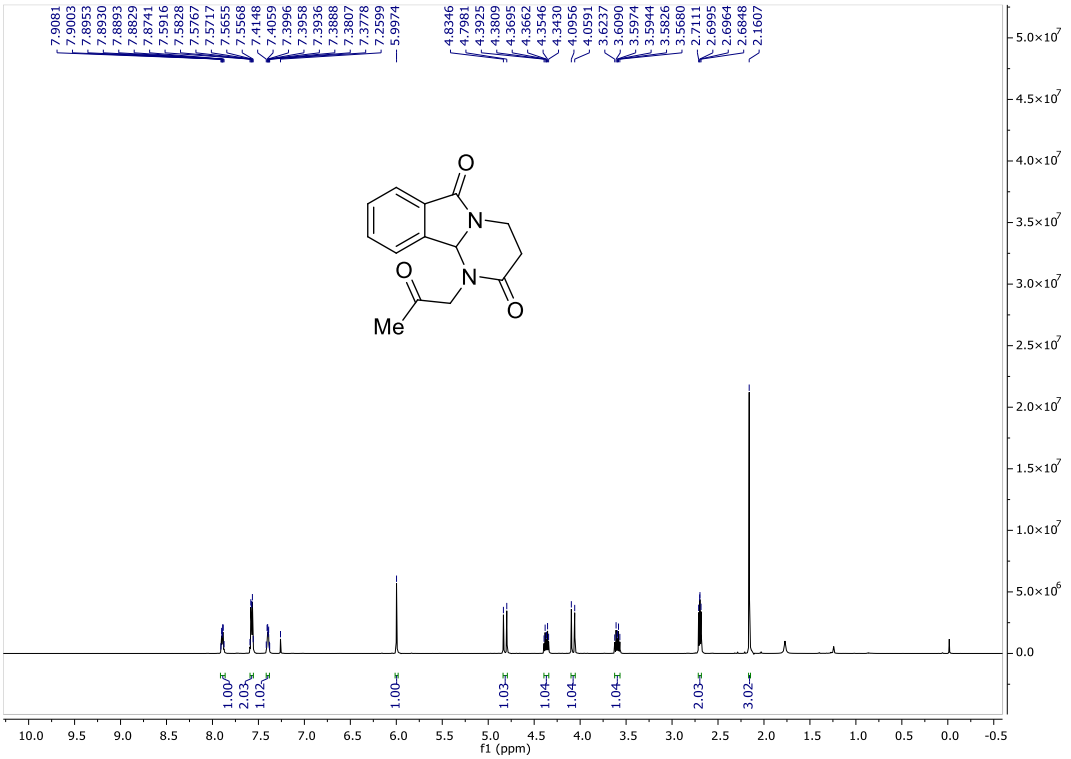


^{1}H and ^{13}C NMR spectra of **3b** (500 and 125 MHz, $CDCl_3$)





^{1}H and ^{13}C NMR spectra of **3c** (500 and 125 MHz, $CDCl_3$)



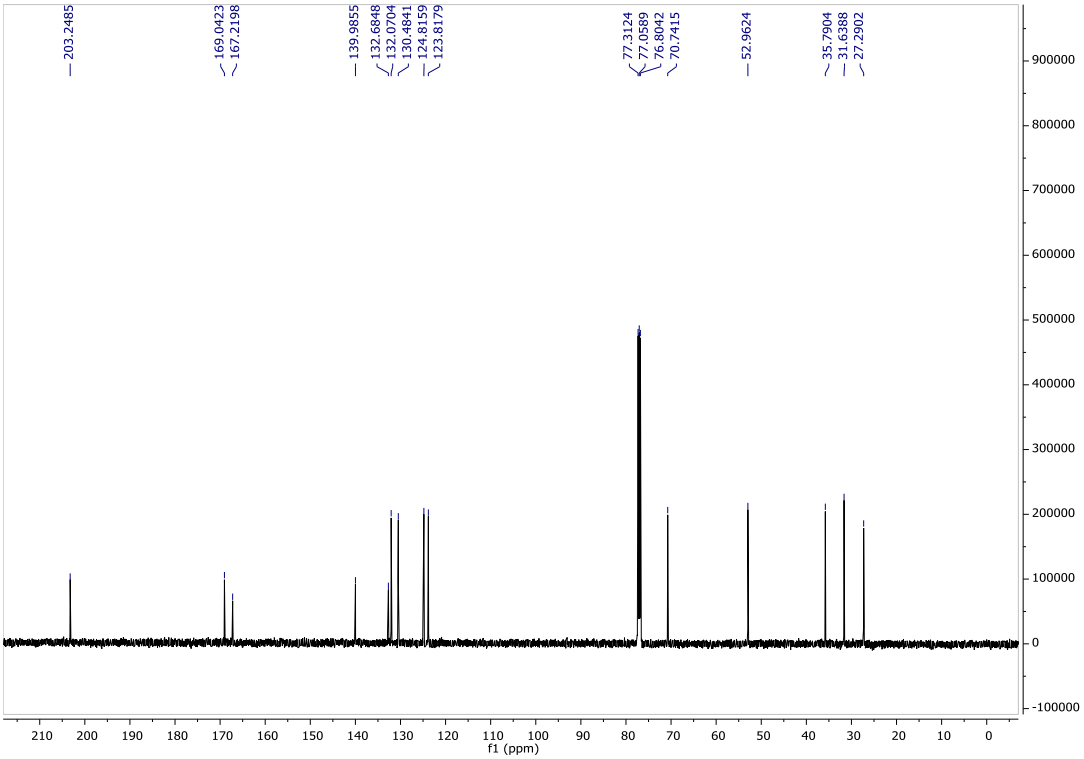


Table S90: The crystal parameters of compound **2a**

	CCDC 2096075
Formula	$C_{17}H_{14}N_2O_2$
Formula weight	278.30
T/K	296(2)
Crystal system	monoclinic
Space group	P 21/n
a/Å	9.5567(6)
b/Å	9.7212(6)
c/Å	15.0352(9)
α/°	90
β/°	93.695(2)
γ/°	90
V/Å^3	1393.91(15)
Z	4
Abs. Coeff./mm^{-1}	0.089
Abs. Correction	multi-scan
GOF on F^2	1.048
Final *R* indices [$I > 2\sigma(I)$]	*R1* = 0.0499
R indices [all data]	*wR2* = 0.1424 *R1* = 0.0800 *wR2* = 0.1768

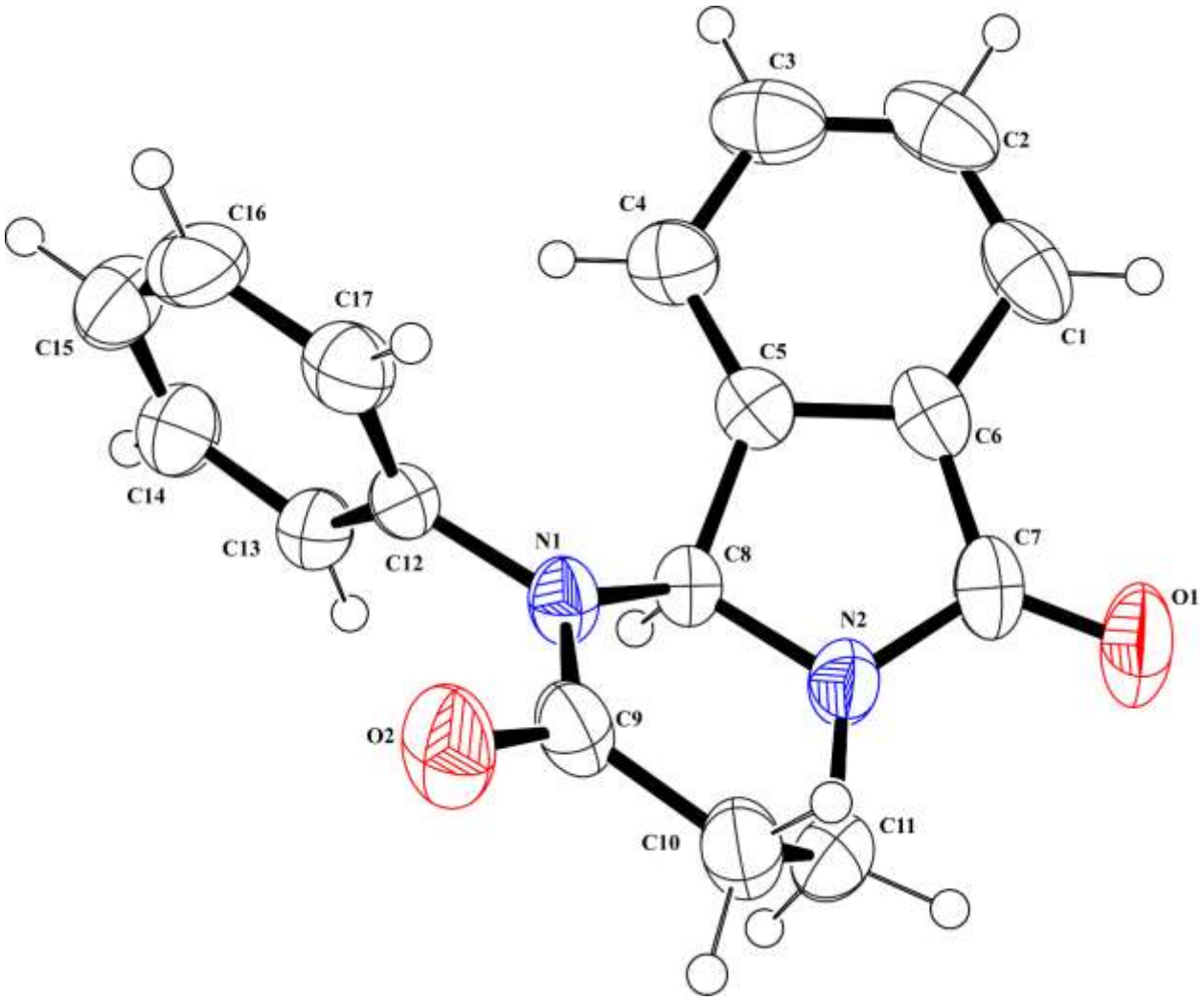


Figure S91: ORTEP diagram of compound 2a using thermal ellipsoids of 30% probability

Table S92: The crystal parameters of compound **2q**

	CCDC 2096084
Formula	$C_{17}H_{18}N_2O_2$
Formula weight	282.33
T/K	296(2)
Crystal system	orthorhombic
Space group	P21 21 21
a/Å	8.9929(8)
b/Å	9.6220(10)
c/Å	17.0576(19)
α/°	90
β/°	90
γ/°	90
V/Å^3	1476.0(3)
Z	4
Abs. Coeff./mm^{-1}	0.084
Abs. Correction	none
GOF on F^2	0.866
Final *R* indices [$I > 2\sigma(I)$]	*R1* = 0.0426
	wR2 = 0.1245
R indices [all data]	*R1* = 0.0512
	wR2 = 0.1334

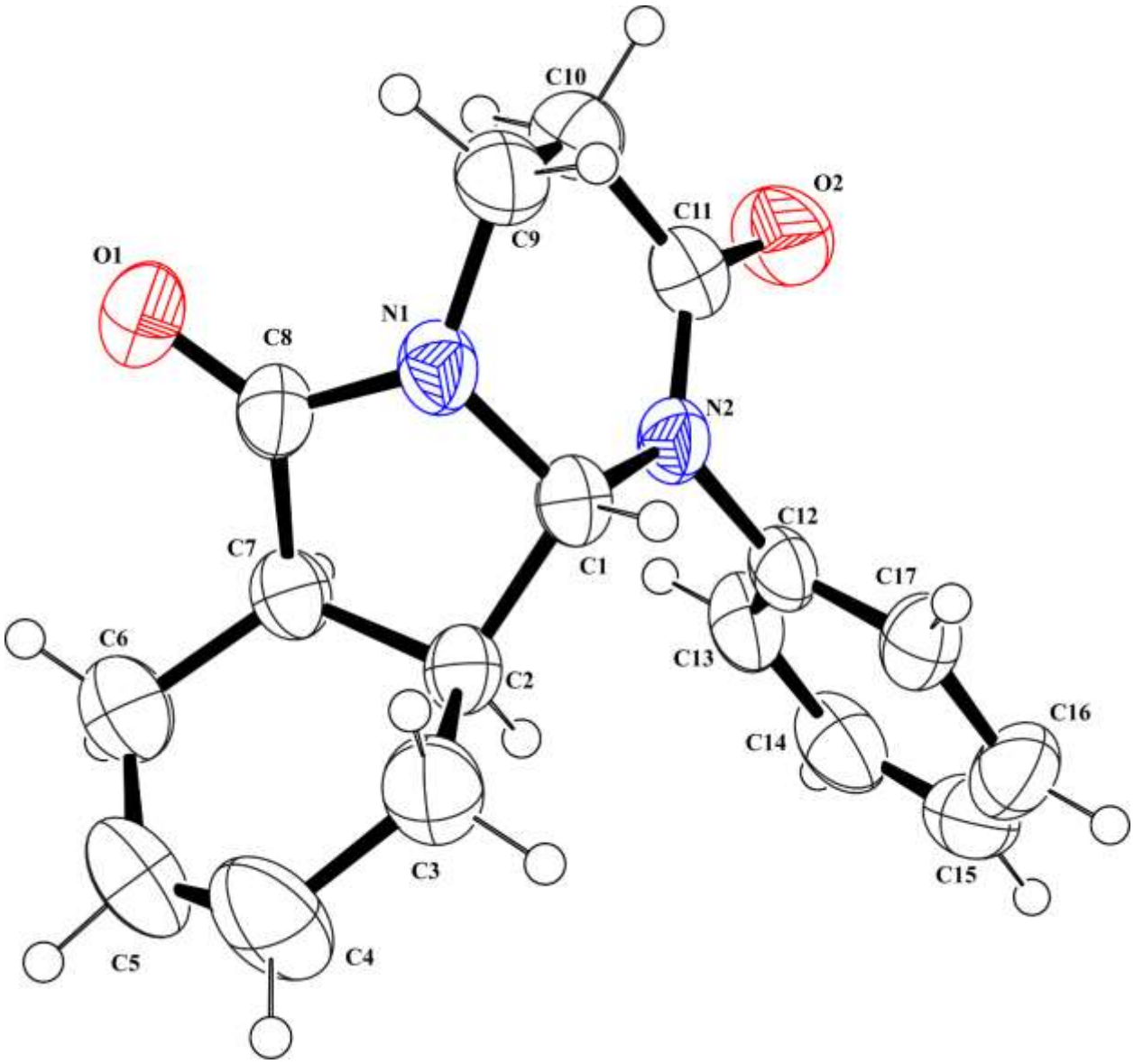


Figure S93: ORTEP diagram of compound 2q using thermal ellipsoids of 30% probability