Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

A cascade of indolyl-migratory isocyanide insertion, scaffold rearrangement and redox-neutral event with isocyanide as a C(sp^3)H–N synthon efficiently constructs indolylisoindolinones

Shailendra Sisodiya,[a] Ayan Acharya,[a†] Mithilesh Nagpure,[a†] Nibedita Roy,[a] Santosh K. Giri,[a] Hare Ram Yadav,[b] Angshuman R. Choudhury,[b] Sankar K. Guchhait,[a*]

[a]Department of Medicinal Chemistry, National Institute of Pharmaceutical Education and Research (NIPER), Sector 67, S.A.S. Nagar, Mohali, Punjab 160062, India

[b]Department of Chemistry, Indian Institute of Science Education and Research, Mohali, Sector 81, S.A.S. Nagar, Manauli PO, Mohali, Punjab 140306, India

*S. K. Guchhait: Tel.: +91 (0)172 2214683; fax: +91 (0)172 2214692; E-mail address: skguchhait@niper.ac.in

†The authors have equally contributed

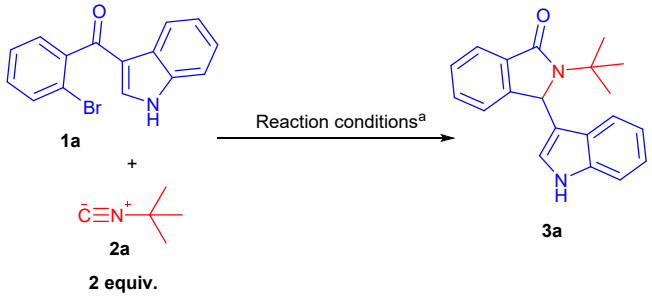
1. Table of Contents

1. General method

Infrared (IR) spectra were recorded using the PerkinElmer instrument ATR spectrometer. Melting points were determined on a Büchi melting point apparatus. ^{1}H NMR spectra were taken on Bruker 400, JEOL 500 and 600 MHz spectrometers. Data were reported as follows: chemical shifts in ppm from tetramethylsilane as an internal standard in DMSO-d_6 and $CDCl_3$ integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet, dt = doublet of triplet, dd = doublet of doublet, dt = doublet of triplet, br. = broad), and J = coupling constants (Hz). ^{13}C NMR spectra were taken on a 100, 126, and 151 MHz spectrometer with complete proton decoupling and ^{19}F NMR were taken on a 565 MHz in JEOL 600 MHz instrument. Chemical shifts were reported in ppm. The single crystal X-ray diffraction data of the compound (**3a**) was recorded using Rigaku XtaLabmini X-ray diffractometer equipped with Mo Kα radiation (0.7107 Å) at room temperature (298(2)K). High-resolution mass spectra of unknown products were obtained using Agilent Q-TOF spectrometer in positive (ESI^+ and $APCI^+$) ion mode and mass spectra were taken with Thermo Scientific LTQ-XL instrument. Thin-layer chromatography (TLC) analysis were done using commercially received pre-coated TLC plates (silica gel 60 GF434, 0.43 mm). The products were purified by column chromatography silica gel 100−200 (silica gel 100−200 mesh, neutral, spherical). Chemicals and solvents were purchased from Alfa Aesar®, Sigma-Aldrich®, Avra®, Acros®, TCI®, and were used as received without further purification, unless otherwise mentioned in the procedure or manuscript.

2. Optimization study:

Table S1: Optimization of Base and Temperature:

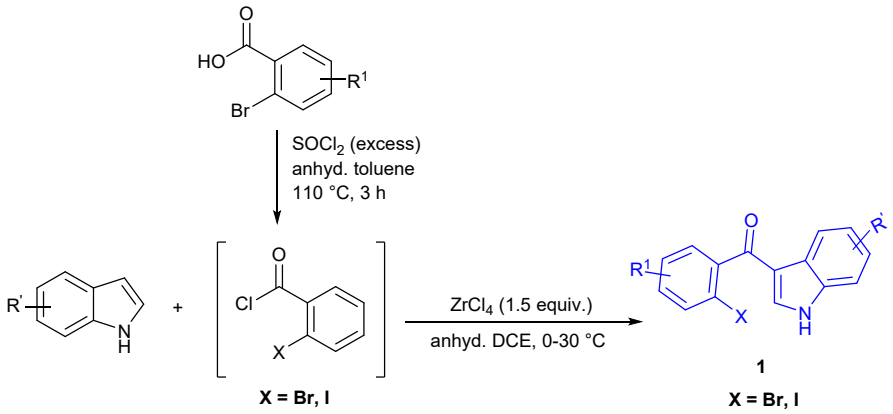


Entry	Variable	Time[b] (h)	Yield[c] (%)
$Pd(OAc)_2$ (5 mol%), P(*o*-tolyl)$_3$ (20 mol%), **Base (2 equiv.)**, anhyd. DMF (2 mL), 80 °C			
1.	**Cs_2CO_3**	**18**	**82**
2.	KOAc	48	0
3.	^{t}-BuOK	48	0
4.	K_2CO_3	36	59
$Pd(OAc)_2$ (5 mol%), P(*o*-tolyl)$_3$ (20 mol%), Cs_2CO_3 (2 equiv.), anhyd. DMF (2 mL), **Temperature (°C)**			
5.	30	48	0
6.	60	48	15
7.	**80**	**18**	**82**

[a]Reactions were performed at 0.25 mmol scale, [b]Reaction was continued for certain time to obtain optimum conversion, [c]Isolated yield.

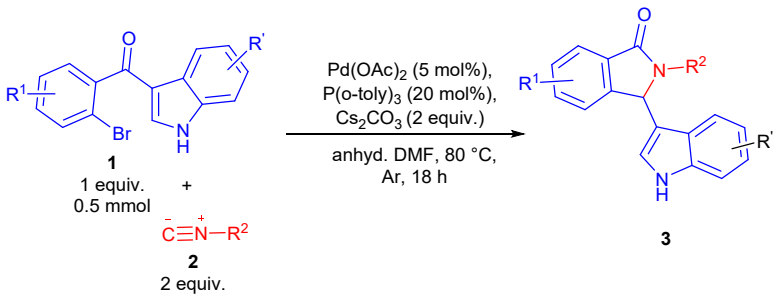
3. Representative experimental procedures:

(2-Bromophenyl)(1*H*-indol-3-yl)methanones **(1)** were synthesized following our previously reported method.[1]



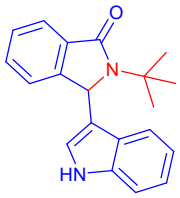
Scheme 1: Synthesis of (2-Bromophenyl)(1*H*-indol-3-yl)methanones

Synthesis of 2-(*tert*-Butyl)-3-(1*H*-indol-3-yl)isoindolin-1-one **(3a):**

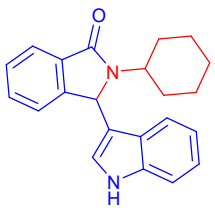


In an oven-dried sealed tube, 3-(2-Bromo)benzoylindole (**1a**) (150 mg, 0.5 mmol), $Pd(OAc)_2$ (6 mg, 0.05 mmol), P(*o*-tolyl)$_3$ (32 mg, 0.2 mmol) and Cs_2CO_3 (325 mg, 1 mmol) were taken under argon. DMF (3 mL, anhyd.) was added. The mixture was degassed using argon. Then, *tert*-Butyl isocyanide (**2a**) (0.11 mL, 1 mmol) was added to the mixture. The tube was capped and the mixture was stirred and heated at 80 °C. After completion of the reaction as indicated by TLC, the mixture was extracted with EtOAc, and washed twice with water. The organic layer was dried with anhyd. Na_2SO_4, filtered and concentrated under vacuum. The crude mixture obtained was subjected to column chromatography using EtOAc-Hexane (30:70) as eluent. The pure product (compound **3a**) was obtained in 82% yield. Compounds **3b-q** were prepared following this general procedure.

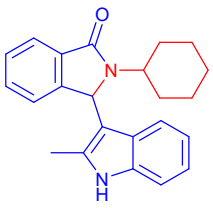
2-(tert-Butyl)-3-(1H-indol-3-yl)isoindolin-1-one ***(3a)****:* White solid; 125 mg, 82%; m.p = 280 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.09 (s, 1H), 7.68 (s, 1H), 7.39 (dd, J = 5.4, 3.0 Hz, 2H), 7.34 (d, J = 7.8 Hz, 1H), 7.10 – 7.09 (m, 1H), 7.00-6.74 (m, 3H), 6.23 (s, 1), 1.40 (s, 9H) ppm; ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6): δ 169.1, 147.2, 137.1, 132.5, 131.9, 128.2, 125.2, 124.9, 123.2, 122.47, 121.7, 119.2, 118.9, 113.6, 112.3, 59.1, 55.7, 28.3 ppm; IR ν_{max} 3192, 2962, 1654, 1547, 1455, 1434, 1353, 1280, 1247, 1215, 1193, 1146, 1008, 780, 759, 741, 729.48 cm^{-1}; HRMS (ESI-TOF) *m/z* [M+Na]$^+$ calculated for $C_{20}H_{20}N_2ONa$ 327.1473 found: 327.1471.



2-Cyclohexyl-3-(1H-indol-3-yl)isoindolin-1-one ***(3b)****:* White solid; 125 mg, 82%; m.p = 281°C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.08 (s, 1H), 7.71 (dd, J = 6.0, 1.9 Hz, 1H), 7.63 (s, 1H), 7.44 – 7.40 (m, 2H), 7.30 (d, J = 8.0 Hz, 1H), 7.09 (dd, J = 6.5, 1.6 Hz, 1H) 6.94 (t, J = 7.7 Hz, 1H), 6.68 (t, J = 7.4 Hz, 1H), 6.52 (s, 1H), 5.95 (s, 1H), 3.68 (tt, J = 15.6, 12.1, 3.5 Hz, 1H), 2.01 – 1.93 (m, 1H), 1.62 (d, J = 13.2 Hz, 1H), 1.52 (d, J = 12.0 Hz, 1H), 1.48 - 1.43 (m, 3H), 1.22 – 1.15 (m, 1H), 1.10 – 1.05 (m, 2H), 0.89 – 0.81 (m, 1H) ppm; ^{13}C{^{1}H} NMR (151 MHz, DMSO-d_6): δ 167.4, 147.3, 137.4, 132.6, 132.0, 128.5, 123.6, 122.8, 121.7, 121.7, 121.7, 119.2, 118.9, 112.4, 111.3, 58.0, 53.1, , 30.6, 30.4, 26.2, 26.0, 25.6 ppm; IR ν_{max} 3192, 2967, 1654, 1547, 1453, 1434, 1353, 1275, 1247, 1212, 1193, 1146, 1006, 780, 759, 741, 729.48 cm^{-1}; HRMS (ESI-TOF) *m/z* [M+H]$^+$ calculated for $C_{22}H_{22}N_2O$ 331.1810 found: 331.1806.



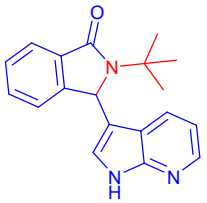
2-(tert-Butyl)-3-(2-phenyl-1H-indol-3-yl)isoindolin-1-one ***(3c)****:* White solid, 150 mg, 79% yield, m.p = 289 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.47 (s, 1H), 7.75 (dd, J = 8.2, 1.05 H, 2H), 7.71 (dd, J = 6.7, 1.5 H, 1H), 7.58 (t, J = 7.6 Hz, 2H), 7.50 – 7.43 (m, 3H), 7.39 (d, J = 7.1 Hz, 1H), 7.30 (d, J = 8.2 Hz, 1H), 6.98 – 6.96 (m, 1H), 6.74 – 6.71 (m, 1H), 6.67 (d, J = 8.0 Hz, 1H), 6.16 (s, 1H), 1.11 (s, 9H) ppm; ^{13}C{^{1}H} NMR (151 MHz, DMSO-d_6) δ 168.6, 147.1, 137.2, 136.8, 133.4, 132.7, 132.2, 129.6, 129.2, 128.9, 128.6, 125.8, 123.4, 122.7, 122.2, 119.5, 112.0, 109.7, 57.7, 55.3, 28.13 ppm; IR ν_{max} 3153, 2971, 2341, 1647, 1611, 1455, 1381, 1366, 1306, 1214, 1158, 781, 742, 723, 693 cm^{-1}; HRMS (ESI-TOF) *m/z* [M+H]$^+$ calculated for $C_{21}H_{19}N_3O$ 381.1967; found 381.1973.



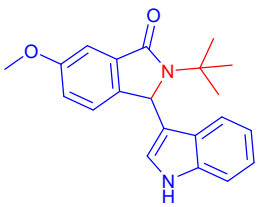
2-Cyclohexyl-3-(2-methyl-1H-indol-3-yl)isoindolin-1-one ***(3d)****:* White solid, 139 mg, 81% yield, m.p = 198 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ ; 11.02 (s, 1H), 7.75

(dd, J = 6.1, 1.6 Hz, 1H) 7.48 – 7.42 (m, 2H), 7.21 (d, J = 8.0 Hz, 1H), 7.12 (d, J = 6.8 Hz, 1H), 6.89 – 6.86 (m, 1H), 6.62 – 6.60 (m, 1H), 6.32 (d, J = 7.9 Hz, 1H), 5.97 (s, 1H), 3.72-3.67 (m, 1H), 2.63 (s, 3H), 1.84 (qd, J = 12.5, 3.6 Hz, 1H), 1.69 – 1.62 (m, 2H), 1.49 (d, J = 9.4 Hz, 3H), 1.15 – 1.09 (m, 3H), 0.92 – 0.85 (m, 1H) ppm; $^{13}C\{^{1}H\}$ NMR (151 MHz, DMSO-d_6) δ 167.4, 147.4, 136.1, 135.3, 132.7, 131.9, 128.4, 126.4, 123.6, 122.7, 120.8, 118.9, 118.2, 111.2, 106.6, 56.8, 53.0, 30.6, 26.2, 26.0, 25.6, 11.9 ppm; IR ν_{max} 3160, 2980, 2341, 1650, 1611, 1455, 1323, 1366, 1306, 1214, 1158, 742, 723cm^{-1}; HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{23}H_{24}N_2O$ 345.1967; found 345.1961.

*2-(tert-Butyl)-3-(1H-pyrrolo[2,3-b]pyridin-3-yl)isoindolin-1-one (**3e**):* White solid, 115 mg, 76% yield, m.p = 182 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.63 (s, 1H), 8.10 (s, 1H), 7.65 – 7.64 (m, 2H), 7.39 – 7.36 (m, 2H), 7.09 – 7.08 (m, 2H), 6.84 (s, 1H), 6.20 (s, 1H), 1.35 (s, 9H) ppm; $^{13}C\{^{1}H\}$ NMR (151 MHz, DMSO-d_6) δ 168.8, 149.3, 143.3, 132.6, 132.1, 132.0, 128.4, 127.1, 123.3, 122.6, 115.77, 113.0, 55.6, 28.5 ppm; IR ν_{max} 3163, 3043, 1658, 1591, 1449, 1414, 1216, 964, 761, 735 HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{19}H_{19}N_3O$ 306.1606; found 306.1605.

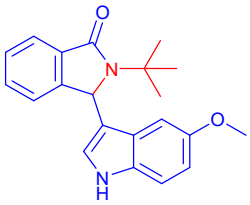


*2-(tert-Butyl)-3-(1H-indol-3-yl)-6-methoxyisoindolin-1-one (**3f**):* White solid; 128 mg, 77%, m.p = 198 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.08 (s, 1H), 7.59 (d, J = 8.3 Hz, 2H), 7.34 (d, J = 7.9 Hz, 1H), 6.99 – 6.76 (m, 4H), 6.56 (d, J = 1.6 Hz, 2H), 6.13 (s, 1H), 3.66 (s, 3H), 1.37 (s, 9H) ppm; $^{13}C\{^{1}H\}$ NMR (151 MHz, DMSO-d_6): δ 168.1, 162.1, 148.9, 136.8, 124.7, 123.5, 121.1, 118.7, 114.4, 113.5, 111.8, 107.3, 58.2, 55.4, 54.9, 28.0 ppm; IR ν_{max} 3786, 3397, 3155, 1602, 1580, 1566, 1515, 1492, 1443, 1420, 1404, 1313, 1289, 1274, 1234, 1195, 1085, 1045, 737 cm^{-1}; HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{21}H_{22}N_2O_2$ 335.1760; found 335.1766.



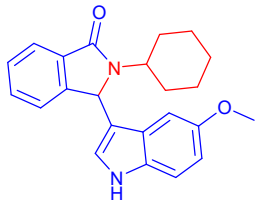
*2-(tert-Butyl)-6-fluoro-3-(1H-indol-3-yl)isoindolin-1-one (**3g**):* White solid; 135 mg, 84%, m.p = 230 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.19 (s, 1H), 7.79 (dd, J = 8.4, 5.1 Hz, 1H), 7.68 (s, 1H), 7.41 (d, J = 8.2 Hz, 1H), 7.31-7.26 (m, 1H), 7.07 (s, 1H), 6.99 – 6.58 (m, 3H), 6.30 (s, 1H), 1.43 (s, 9H) ppm; $^{13}C\{^{1}H\}$ NMR (151 MHz, DMSO-d_6): δ 167.59, 165.51 ($^{1}J_{C\text{-}F}$ = 244.0 Hz), 137.1, 129.1, 125.5, 124.8, 121.6, 119.2, 118.8, 115.9 ($^{2}J_{C\text{-}F}$ = 20.0 Hz), 112.8, 112.2, 110.1, 58.6, 55.6, 28.3 ppm; ^{19}F NMR (565 MHz, DMSO-d_6) δ 108.7 ppm; IR ν_{max} 3318, 3158, 2928, 2851, 1653, 1622, 1576, 1437, 1403, 1358, 1341, 1324, 1245, 1196, 1088, 1007, 893, 798, 758, 728, 692 cm^{-1}; HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{21}H_{22}FN_2O$ 323.1554; found 323.1563.

2-(tert-Butyl)-3-(5-methoxy-1H-indol-3-yl)isoindolin-1-one ***(3h)****:* White solid; 142 mg, 85%,



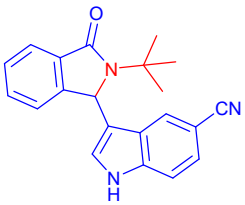
m.p = 185 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.92 (s, 1H), 7.67-7.54 (m, 2H), 7.42 – 7.38 (m, 2H), 7.23 (d, J = 8.7 Hz, 1H), 7.11 (d, J = 6.1 Hz, 1H), 6.67 (s, 1H), 6.20 (s, 1H), 3.48 (s, 3H), 1.41 (s, 9H) ppm; ^{13}C{^{1}H} NMR (151 MHz, DMSO-d_6): δ 168.2, 152.6, 146.4, 131.9, 131.3, 127.6, 125.4, 124.7, 122.7, 121.8, 112.2, 110.6, 100.9, 58.5, 55.0, 27.9 ppm; IR ν_{max} 3185, 2934, 2341, 1745,1600, 1509, 1461, 1420, 1373, 1292, 1208, 1194, 1134, 1082, 919, 891, 878, 780, 756 cm^{-1}; HRMS (ESI-TOF) *m/z* [M+Na]$^+$ calculated for $C_{21}H_{22}N_2O_2Na$ 357.1579 found: 357.1574.

2-Cyclohexyl-3-(5-methoxy-1H-indol-3-yl)isoindolin-1-one ***(3i)***: White solid; 142 mg, 78%,



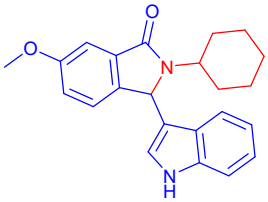
m.p = 189 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.93 (s, 1H) 7.75 (dd, J = 7.2, 3.8 Hz, 1H), 7.60 (s, 1H), 7.48 – 7.45 (m, 2H), 7.22 (d, J = 8.8 Hz, 1H), 7.15 (t, J = 5.0 Hz, 1H), 6.66 (dd, J = 8.8, 2.2 Hz, 1H), 5.97 (s, 2H), 3.69 (tt, J = 15.5, 12.0, 3.5 Hz, 1H), 3.41 (s, 3H), 2.04 – 1.94 (m, 1H), 1.64 (d, J = 13.3 Hz, 1H), 1.55 – 1.45 (m, 4H), 1.26 – 1.22 (m, 1H), 1.14 – 1.04 (m, 2H), 0.90 – 0.82 (m, 1H) ppm; ^{13}C{^{1}H} NMR (151 MHz, DMSO-d_6) δ 167.3, 153.2, 147.3, 132.7, 132.5, 131.9, 128.5, 123.7, 122.7, 112.9, 111.1, 101.4, 57.9, 55.7, 55.5, 53.2, 26.2, 25.9, 25.6 ppm; IR ν_{max} 3135, 2928, 2320, 1785,1608, 1530, 1461, 1440, 1373, 1282, 1208, , 1134, 1019, 955, 891, 780, cm^{-1}; HRMS (ESI-TOF) *m/z* [M+Na]$^+$ calculated for $C_{23}H_{24}N_2O_2$ 361.1911 found: 361.1909.

3-(2-(tert-Butyl)-3-oxoisoindolin-1-yl)-1H-indole-5-carbonitrile ***(3j)****:* White solid; 118 mg,



72%, m.p = 212 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.73 (s, 1H), 7.90 – 7.72 (m, 2H), 7.55 (d, J = 8.4 Hz, 1H), 7.44 (s, 3H), 7.13 – 6.99 (m, 2H), 6.32 (s, 1H), 1.40 (s, 9H) ppm; ^{13}C{^{1}H} NMR (151 MHz, DMSO-d_6): δ 168.2, 138.4, 131.5, 127.8, 123.8, 123.5, 122.6, 122.1, 120.4, 113.1, 100.8, 57.7, 55.0, 27.8 ppm; IR ν_{max} 3176, 2936, 1602, 1579, 1505, 1457, 1360, 1261, 1216, 1195, 1169, 1146, 1089, 963, 795, 771 cm^{-1}; HRMS (ESI-TOF) *m/z* [M+H]$^+$ calculated for $C_{21}H_{19}N_3O$ 329.1528; found 329.1537.

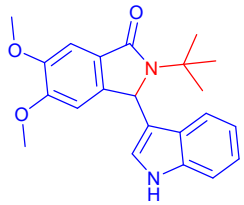
2-Cyclohexyl-3-(1H-indol-3-yl)-6-methoxyisoindolin-1-one ***(3k)****:* Off-white solid; 146 mg,



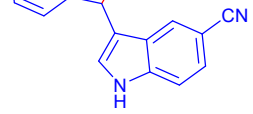
81%, m.p = 213 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.12 (s, 1H), 7.67 (d, J = 8.8 Hz, 2H), 7.35 (d, J = 8.1 Hz, 2H), 7.02 (d, J = 9.5 Hz, 2H), 6.68-6.61 (m, 2H), 5.92 (s, 1H), 3.69 (s, 3H), 1.68 – 1.49 (m, 5H),

1.23 – 1.10 (m, 4H), 0.88-0.86 (m, 1H) ppm; $^{13}C\{^{1}H\}$ NMR (101 MHz, DMSO-d_6): δ 166.7, 162.2, 149.0, 136.8, 125.9, 125.0, 124.7, 123.7, 121.2, 118.7, 118.5, 114.6, 111.8, 111.0, 107.6, 57.1, 55.4, 52.4, 30.2, 29.9, 25.7, 25.4, 25.0 ppm; IR ν_{max} 3161, 2958, 2338, 1572, 1493, 1463, 1351, 1292, 1200, 1117, 1005, 936, 825, 760 cm^{-1}; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calculated for $C_{23}H_{24}N_2O_2$ 360.1838; found 360.1847.

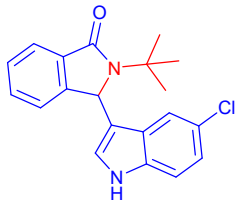
2-(tert-Butyl)-3-(1H-indol-3-yl)-5,6-dimethoxyisoindolin-1-one ***(3l)****:* White solid; 136 mg, 75%, m.p = 140 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.05 (s, 1H), 7.59 (s, 1H), 7.33 (d, J = 8.2 Hz, 1H), 7.15 (s, 1H), 7.00 (s, 1H), 6.77 (s, 2H), 6.58 (s, 1H), 6.07 (s, 1H), 3.82 (s, 3H), 3.62 (s, 3H), 1.36 (s, 9H) ppm; $^{13}C\{^{1}H\}$ NMR (151 MHz, DMSO-d_6) δ 168.5, 152.2, 149.1, 140.0, 136.8, 124.8, 124.3, 121.1, 118.9, 118.5, 111.7, 105.0, 104.0, 58.0, 55.7, 54.9, 28.0 ppm; IR ν_{max} 3255, 2936, 1649, 1615, 1491, 1457, 1421, 1361, 1294, 1213, 1096, 1019, 996, 860, 777, 739 cm^{-1}; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calculated for $C_{22}H_{24}N_2O_3$ 365.1860; found 365.1869.



3-(2-Cyclohexyl-3-oxoisoindolin-1-yl)-1H-indole-5-carbonitrile ***(3m)****:* Off-white solid; 126 mg, 71%, m.p = 228 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.77 (s, 1H), 7.91 (s, 1H), 7.81 (d, J = 6.8 Hz, 1H), 7.56 (d, J = 8.5 Hz, 1H), 7.54 – 7.48 (m, 3H), 7.39 (d, J = 8.1 Hz, 1H), 7.17 (d, J = 7.1 Hz, 2H), 3.79 – 3.75 (m, 1H), 1.99 – 1.94 (m, 1H), 1.69 (d, J = 13.2 Hz, 1H), 1.59 (d, J = 11.5 Hz, 1H), 1.54 – 1.49 (m, 3H), 1.19 – 1.11 (m, 3H), 0.93 – 0.87 (m, 1H) ppm; $^{13}C\{^{1}H\}$ NMR (151 MHz, DMSO-d_6) δ 166.8, 146.2, 138.5, 131.6, 128.1, 124.7, 123.9, 123.3, 122.9, 122.3, 120.2, 113.2, 112.1, 100.8, 56.4, 52.5, 30.08, 29.8, 25.4, 25.2, 24.8 ppm; IR ν_{max} 3316, 3155, 2927, 2851, 1654, 1623, 1574, 1437, 1404, 1361, 1243, 1088, 892, 758, 729 cm^{-1}; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calculated for $C_{23}H_{21}N_3O$ 356.1757; found 356.1566.

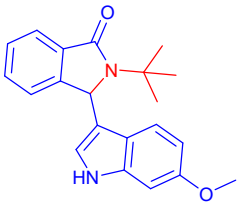


2-(tert-Butyl)-3-(5-chloro-1H-indol-3-yl)isoindolin-1-one ***(3n)****:* White solid; 130 mg, 77%, m.p = 275 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.32 (s, 1H), 7.69 (s, 1H), 7.44 – 7.42 (m, 2H), 7.37 (d, J = 8.6 Hz, 1H), 7.12 – 7.09 (m, 1H), 7.02 (s, 1H), 6.61 (s, 1H), 6.26 (s, 1H), 1.39 (s, 9H) ppm; $^{13}C\{^{1}H\}$ NMR (151 MHz, DMSO-d_6) δ 168.6, 135.6, 131.9, 128.1, 128.0, 127.1, 123.3,

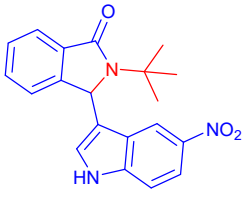


123.1, 122.4, 121.6, 117.9, 113.7, 58.6, 55.5, 28.3 ppm; IR ν_{max} 3187, 2973, 1656, 1614, 1457, 1438, 1377, 1356, 1248, 1223, 1151, 1013, 915, 801, 775, 754 cm^{-1}; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calculated for $C_{20}H_{19}ClN_2O$ 339.1259; found 339.1264.

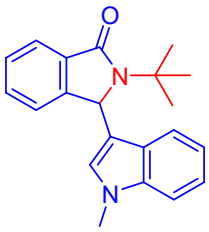
*2-(tert-Butyl)-3-(6-methoxy-1H-indol-3-yl)isoindolin-1-one (**3o**):* White solid; 114 mg, 68%, m.p = 200 °C; ^1H NMR (600 MHz, $CDCl_3$) δ 10.18 (s, 1H), 8.25 (d, J = 8.7 Hz, 1H), 7.73 – 7.71 (m, 1H), 7.50 – 7.47 (m, 2H), 7.46 – 7.44 (m, 1H), 6.94 (dd, J = 8.8, 2.4 Hz, 1H), 6.92 (d, *J* = 2.9 Hz, 1H), 6.85 (d, *J* = 2.3 Hz, 1H), 3.83 (s, 3H), 1.07 (s, 9H) ppm; $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) *δ* 168.7, 157.4, 140.0, 138.0, 135.9, 135.1, 130.3, 129.7, 128.1, 127.9, 122.7, 119.9, 118.1, 112.5, 95.4, 55.6, 52.2, 28.1 ppm; IR ν_{max} 3257, 2931, 1623, 1523, 1158 cm-1; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calculated for $C_{21}H_{21}N_2O_2$, 333.1603; found, 333.1581.



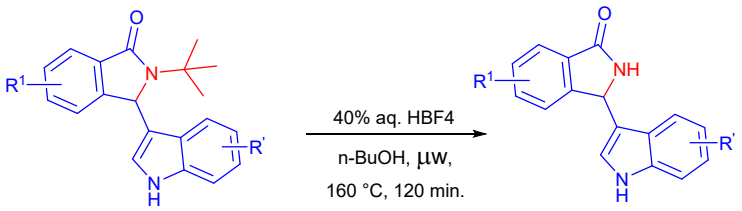
*2-(tert-Butyl)-3-(5-nitro-1H-indol-3-yl)isoindolin-1-one (**3p**):* White solid; 105 mg, 67%, m.p = 292 °C; ^1H NMR (600 MHz, DMSO-d_6) *δ* 2.52 (s, 1H), 9.02 (d, *J* = 2.3 Hz, 1H), 8.10 (dd, *J* = 9.0, 2.3 Hz, 1H), 7.88 (s, 1H), 7.81 (d, *J* = 2.6 Hz, 1H), 7.64 (d, *J* = 9.0 Hz, 1H), 7.54 - 7.53 (m, 3H), 7.49 - 7.48 (m, 1H), 1.03 (s, 9H) ppm; $^{13}C\{^1H\}$ NMR (151 MHz, DMSO-d_6) *δ* 191.3, 168.0, 143.2, 140.4, 140.4, 138.9, 138.2, 130.1, 128.4, 128.2, 125.6, 118.9, 118.6, 118.3, 113.5, 51.1 ppm. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd. for $C_{20}H_{19}N_3O_3$, 350.1499; found, 350.1505.



*2-(tert-Butyl)-3-(1-methyl-1H-indol-3-yl)isoindolin-1-one (**3q**)*: White solid, 126 mg, 79% yield, m.p = 162 °C; ^1H NMR (600 MHz, $CDCl_3$) *δ* 7.57 (s, 2H), 7.27 (d, *J* = 10 Hz, 2H), 7.15 – 7.09 (m, 4H), 6.86 (s, 1H), 6.85 (s, 1H), 3.72 (s, 3H), 1.50 (s, 9H) ppm; $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) *δ* 155.8, 146.0, 136.7, 131.4, 131.3, 128.6, 126.0, 122.8, 121.6, 119.5, 112.0, 109.2, 93.0, 53.7, 33.0, 30.4 ppm; HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{21}H_{22}N_2O$ 319.1810 found: 319.1798.

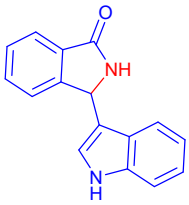


Synthesis of 3-(1*H*-indol-3-yl)isoindolin-1-one (4a)[2]

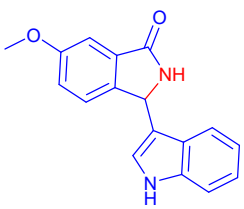


To a solution of 2-(*tert*-Butyl)-3-(1*H*-indol-3-yl)isoindolin-1-one (**3**) (152 mg, 0.5 mmol) in *n*-BuOH (1 mL) taken in a microwave vial, was added 40% aqueous HBF_4 (0.1 mL, 0.5 mmol). The vessel was sealed with a cap. The reaction mixture was then irradiated in a Monomode microwave synthesizer (Biotage Initiator™ EXP) at 160 °C for 20 min. After cooling to RT (25 °C) in the microwave cavity, the vial cap was removed and the resultant mixture was added to an aqueous ammonia solution (10%) to basify (pH = 8). The mixture was then extracted with EtOAc (30 mL x 2) and the solution was washed with H_2O (10 mL x 3). The organic solution was dried with anhyd. Na_2SO_4, filtered, and concentrated under reduced pressure. The column chromatographic purification of the crude product was done using silica gel (mesh size: 100–200) with EtOAc–hexane (70:30) as eluent. Compounds **4b-c** were prepared following this general method.

*3-(1H-Indol-3-yl)isoindolin-1-one (**4a**):* Brown semi-solid; 58 mg, 47%, m.p = 182 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.08 (s, 1H), 8.94 (s, 1H), 7.76 (dd, J = 6.1, 2.6 Hz, 2H), 7.52 – 7.49 (m, 2H), 7.46 (d, J = 2.3 Hz, 1H), 7.36 (d, J = 8.2 Hz, 1H), 7.30 (d, J = 6.2 Hz, 1H), 7.03 (t, J = 7.2 Hz, 1H), 6.89 (d, J = 7.8 Hz, 1H), 6.82 (t, J = 7.4 Hz, 1H), 5.97 (s, 1H) ppm; ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 169.8, 148.8, 137.3, 132.6, 132.1, 128.4, 125.5, 124.9, 123.9, 123.14, 121.8, 119.1, 119.0, 112.2, 54.3 ppm; IR ν_{max} 3540, 3046, 1590, 1562, 1484, 1448, 1411, 1367, 1317, 1264, 1216, 1011, 963, 927, 881, 850, 782, 762, 740, 727 cm^{-1}; HRMS (ESI-TOF) m/z: $[M + H]^+$ calculated for $C_{16}H_{12}N_2O$ was 249.1022; found, 249.1026.

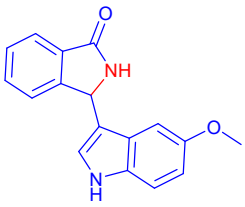


*3-(1H-Indol-3-yl)-6-methoxyisoindolin-1-one (**4b**):* Brown semi-solidS; 57 mg, 41%, m.p = 129 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.91 (s, 1H), 8.92 (s, 1H), 7.76 (dd, J = 6.4, 1.4 Hz, 1H), 7.56 – 7.49 (m, 2H), 7.35 – 7.33 (m, 2H), 7.26 (d, J = 8.8 Hz, 1H), 6.71 (dd, J = 8.8, 2.4 Hz, 1H), 6.42 (d, J = 2.4 Hz, 1H), 5.96 (s, 1H), 3.56 (s, 3H) ppm; ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 169.8, 153.3, 148.7, 132.7, 132.4, 132.1, 128.4, 126.0, 125.3, 124.0, 123.1, 112.8, 111.9, 111.4, 101.3, 55.6, 54.1 ppm; IR ν_{max} 3450, 3326, 3062,



1551, 1457, 1428, 1379, 1342, 1226, 1101, 1022 cm^{-1}; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{17}H_{14}N_2O_2$, 279.1128; found, 279.1132.

*3-(5-Methoxy-1H-indol-3-yl)isoindolin-1-one (**4c**):* Brown semi-solid; 58 mg, 42%, m.p = 212 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 10.91 (s, 1H), 8.92 (s, 1H), 7.76 (d, J = 6.52 Hz, 1H), 7.54-7.50 (m, 2H), 7.35-7.33 (m, 2H), 7.26 (d, J = 8.76 Hz, 1H), 6.71 (dd, J = 8.76, 2.4 Hz, 1H), 6.42 (d, J = 2.36 Hz, 1H), 5.95 (s, 1H), 3.56 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-d_6): δ 169.7, 153.3, 148.7, 132.7, 132.4, 132.1, 128.4, 126.0, 125.3, 124.0, 123.1, 112.8, 111.9, 111.4, 101.3, 55.6, 54.1; IR ν_{max} 3540, 3214, 2926, 2851, 1665, 1623, 1603, 1482, 1437, 1369, 1238, 1201, 1086, 892, 868, 838, 821, 806, 765, 738 cm^{-1}; HRMS (ESI-TOF) m/z: $[M + H]^+$ calculated for $C_{16}H_{12}N_2O$, 249.1022; found, 249.1027.



4. X-ray crystallographic study:

The single crystal X-ray diffraction data of the compound (3a) was recorded using Rigaku XtaLabmini X-ray diffractometer equipped with Mo Kα radiation (0.7107 Å) at room temperature (298(2)K). The unit cell determination, data collection and the data reduction were

done using CrystalClear package. The crystal structure was solved using XT and refined using XL packages respectively using Olex2 suite. The compound was found to crystallize in the triclinic $P\ \bar{1}$ space group with two molecules in the asymmetric unit (Fig S1 below).

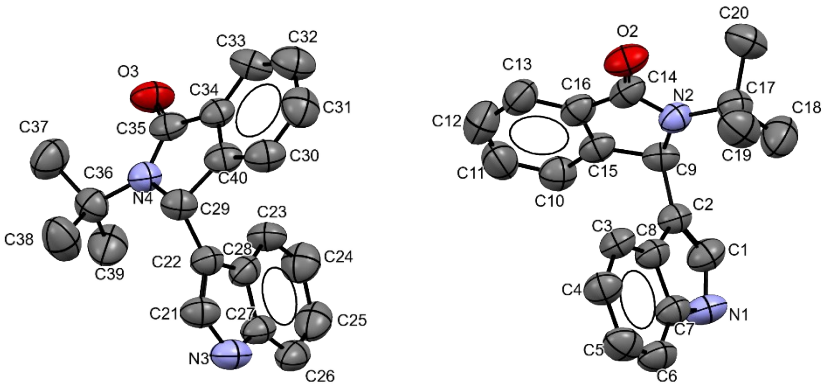


Figure S1: ORTEP diagram of **3a** using 50% probability ellipsoid. H atoms are removed for clarity

The structure has been deposited to CCDC and the depository number is 2192321.

The CIF and checkcif files are enclosed as additional supporting information.

Table S2: X-ray diffraction data of 2-(tert-Butyl)-3-(1H-indol-3-yl)isoindolin-1-one (**3a**)

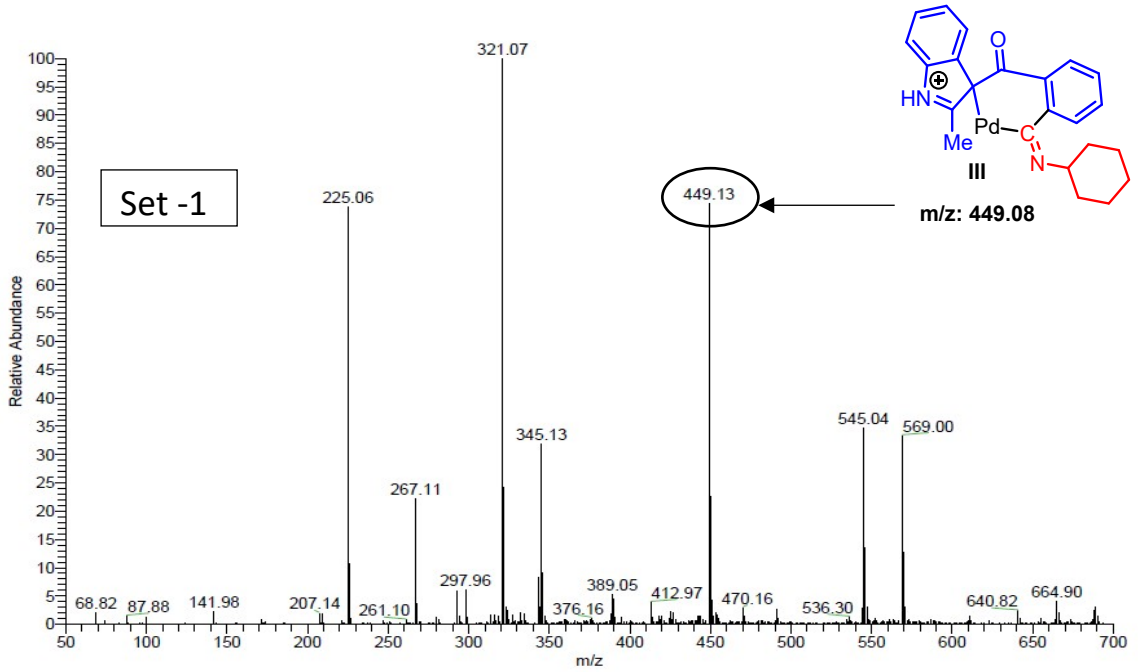
Parameter	***2-(tert-Butyl)-3-(1H-indol-3-yl)isoindolin-1-one (3a)***
Empirical formula	$C_{20}H_{20}N_2O$
CCDC number	2192321
Formula weight	304.38
Crystal system	Triclinic
Space group	$P\ \bar{1}$
a (Å)	10.581(6)
b (Å)	11.314(5)
c (Å)	14.595(9)

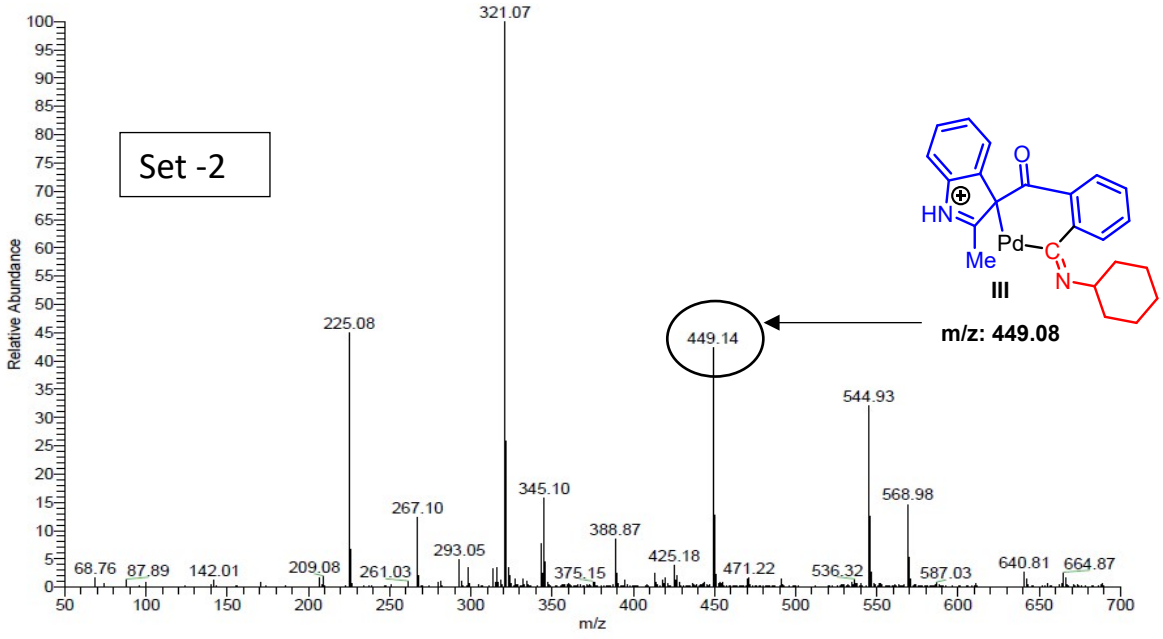
α (°)	91.596(14)
β (°)	106.105(17)
γ (°)	99.60(2)
V (Å^3)	1650.0(16)
Z	4
ρ_{calc} (g/cm^{-3})	1.225
Temperature (K)	298(2)
μ/ mm^{-1}	0.076
$2\theta_{min,\ max}$ ()	2.2, 27.3
F (000)	648
$h_{min,max}$; $k_{min,max}$; $l_{min,max}$	-13, 12; -14, 14; -18, 18
Total no. of reflections	7521
R_{int}	0.0821
No. of unique reflections	2678
R_1 [I>2σ(I)]	0.1109
wR2 (all data)	0.3776
GooF on F²	1.074
$\Delta\rho_{max,min}$/eÅ^{-3}	0.3/-0.3

5. Figure S2: Mass Spectrometry study of reaction mixtures withdrawn at different time interval of various sets of reactions for identification of intermediates (III, IV, V or VI and VII) involved in the proposed mechanism:

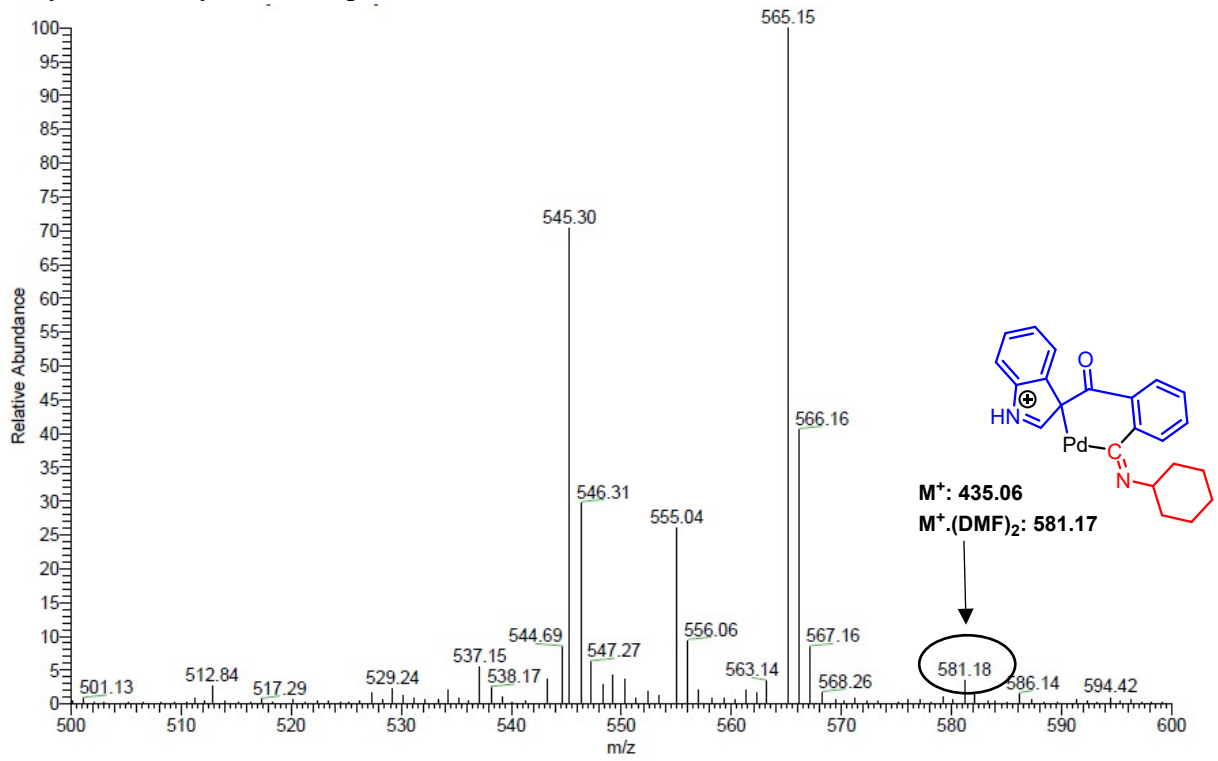
A. Identification of intermediate-III

A.1. Reaction of (2-Bromophenyl)(2-methyl-1*H*-indol-3-yl) methanone **(1c)** with Cyclohexyl isocyanide for synthesis of product **3d**:

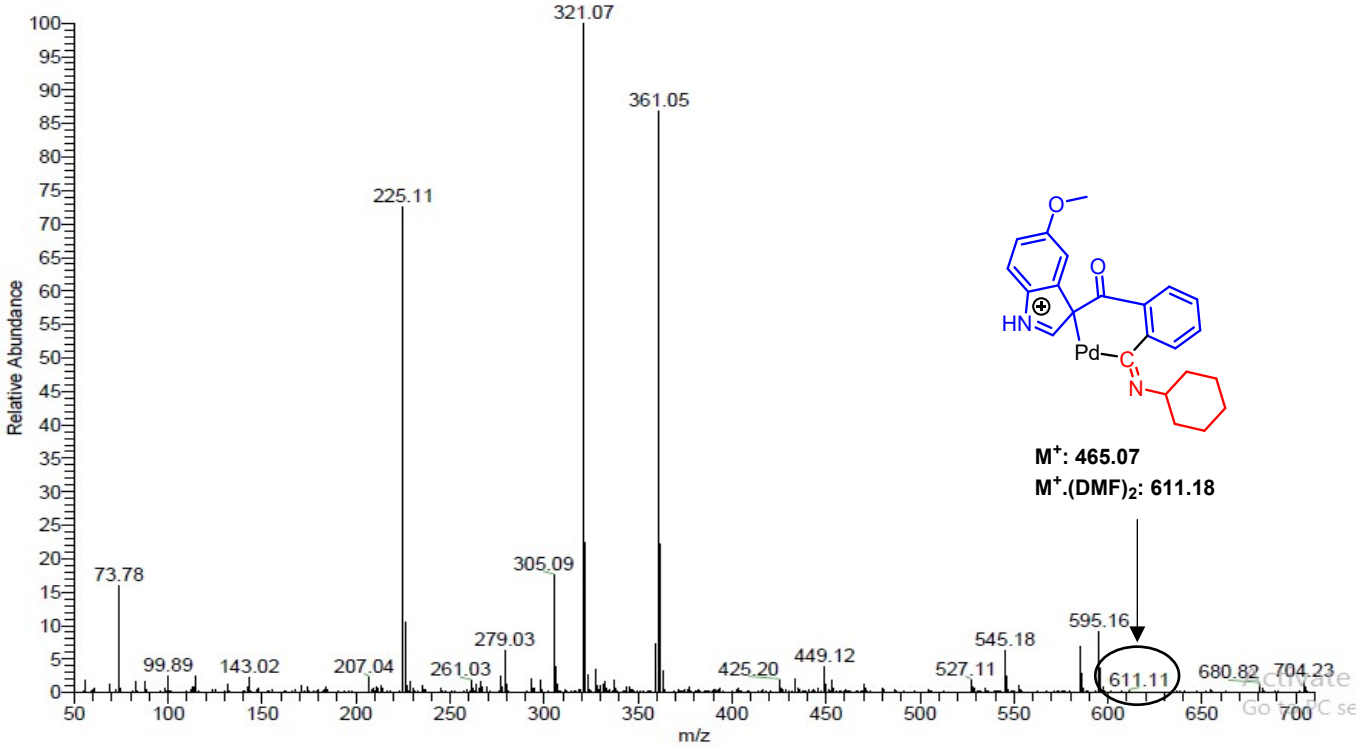




A.2. Reaction of (2-Bromophenyl)(1*H*-indol-3-yl)methanone **(1a)** with Cyclohexyl isocyanide for synthesis of product **3b**:

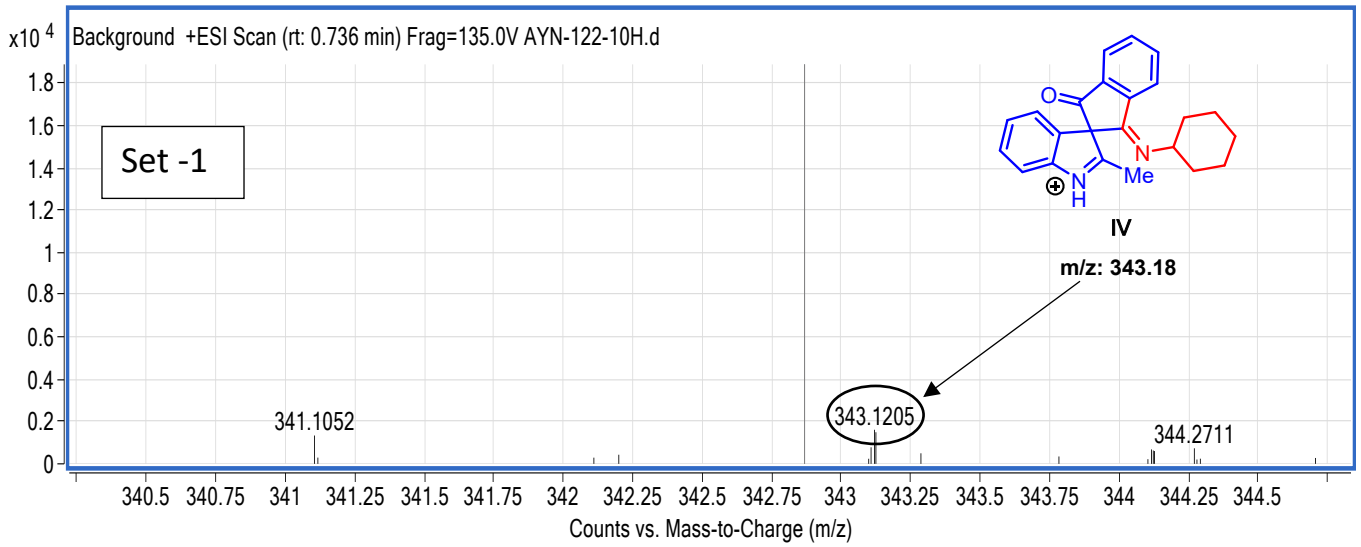


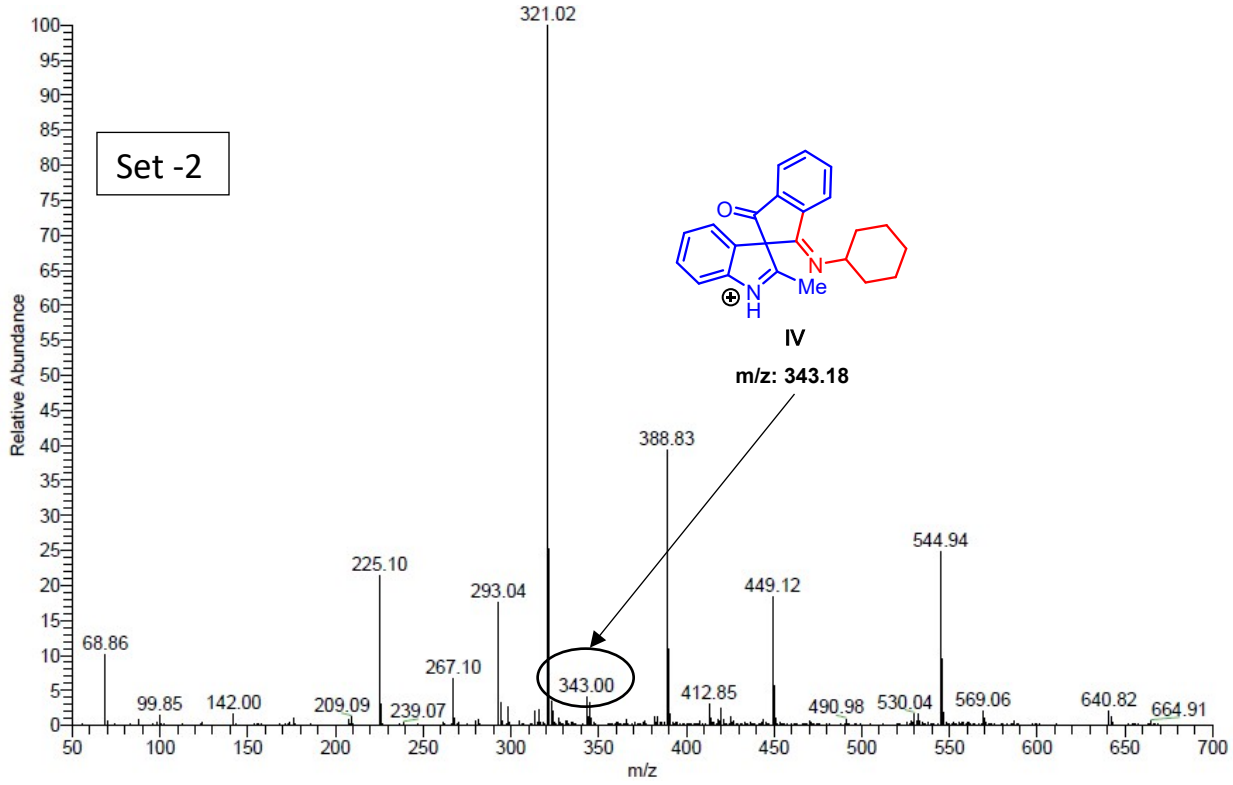
A.3. Reaction of (2-Bromophenyl)(5-methoxy-1*H*-indol-3-yl)methanone **(1g)** with Cyclohexyl isocyanide for synthesis of product **3i**:



B. Identification of intermediate-IV

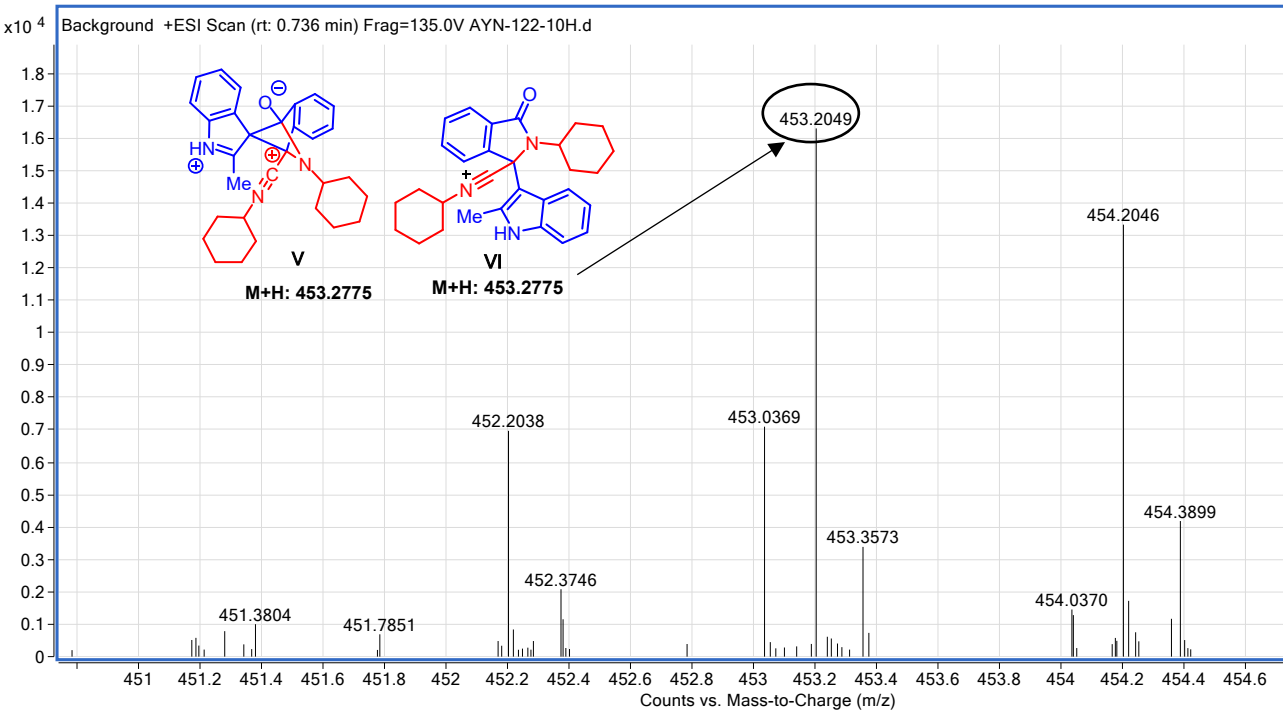
B.1. Reaction of (2-Bromophenyl)(2-methyl-1*H*-indol-3-yl)methanone **(1c)** with Cyclohexyl isocyanide for synthesis of product **3d**



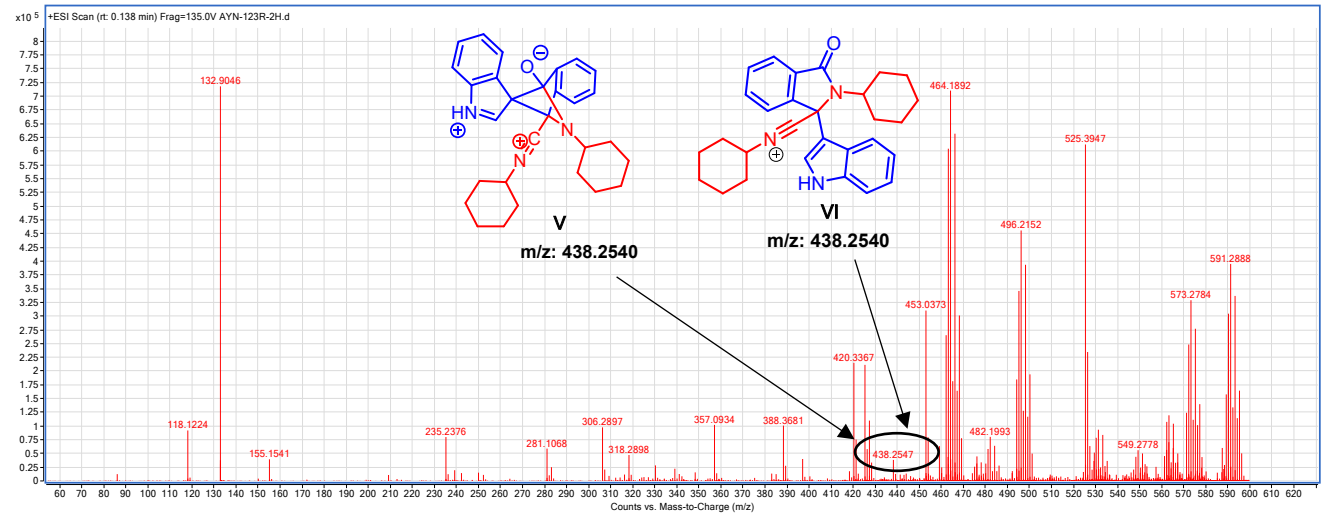


C. Identification of intermediate-V or VI:

C.1. Reaction of (2-Bromophenyl)(2-methyl-1*H*-indol-3-yl)methanone **(1c)** with Cyclohexyl isocyanide for synthesis of product **3d**

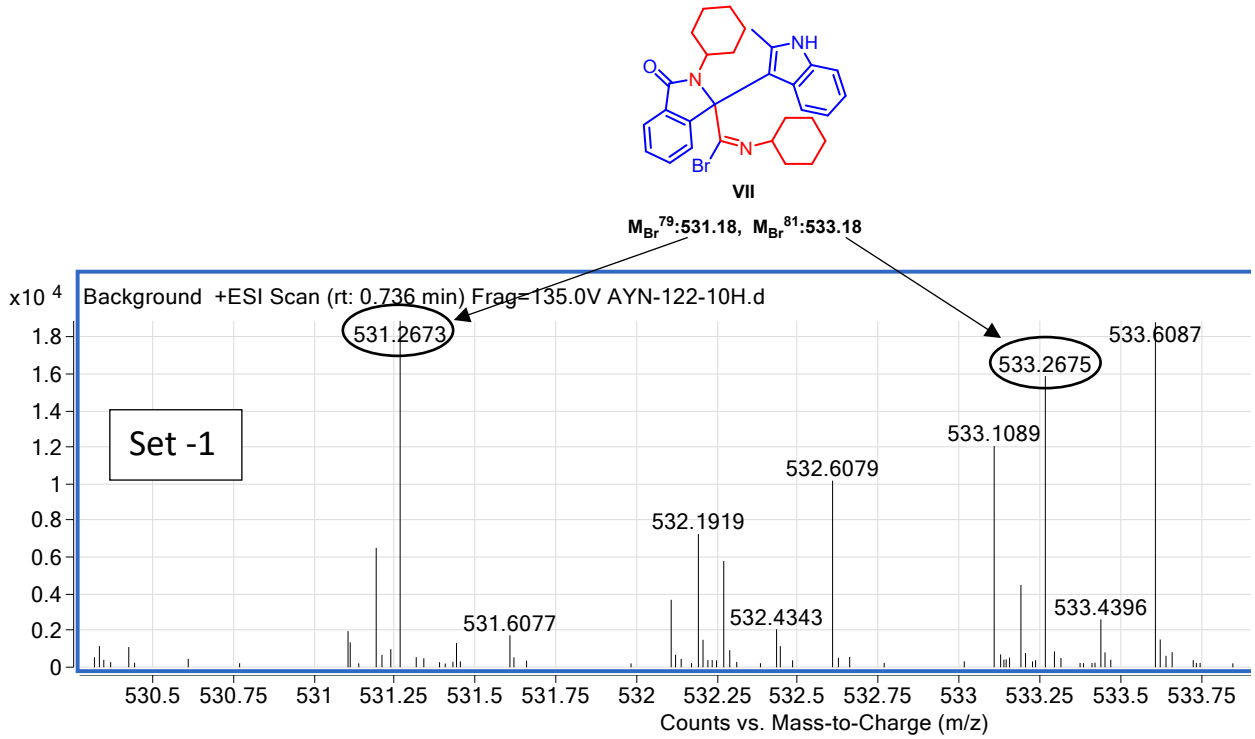


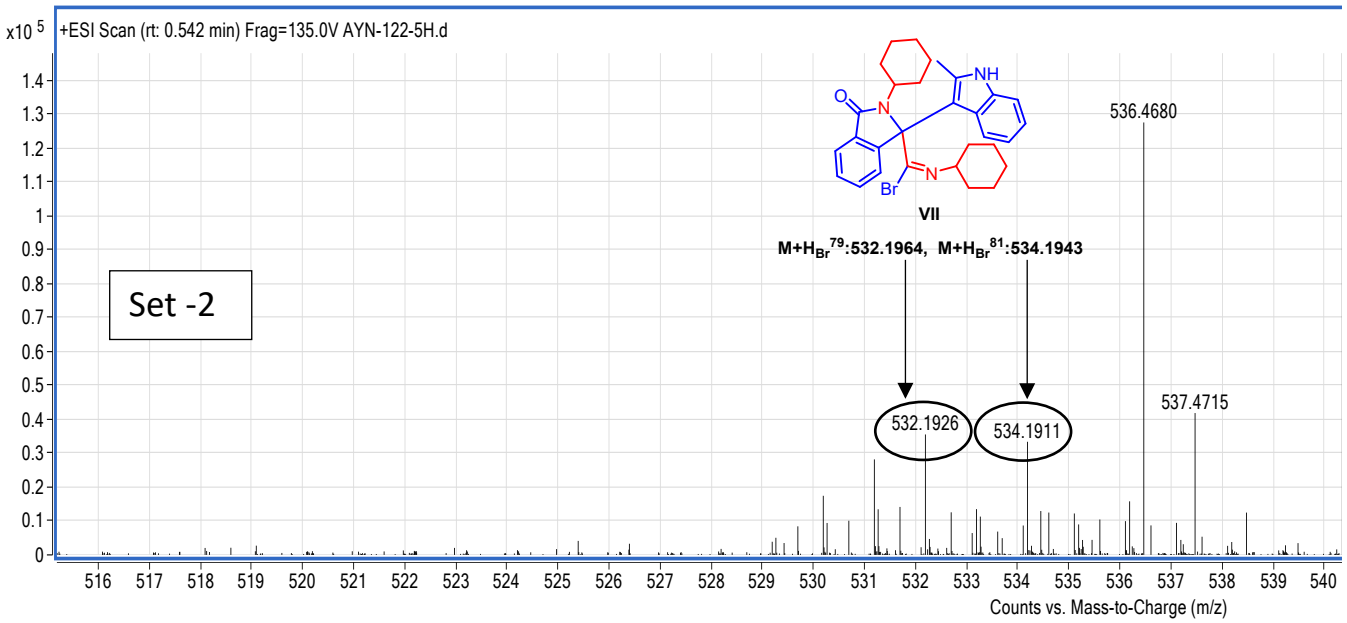
C.2. Reaction of (2-Bromophenyl)(1*H*-indol-3-yl)methanone **(1a)** with Cyclohexyl isocyanide for synthesis of product **3b**



D. Identification of intermediate-VII:

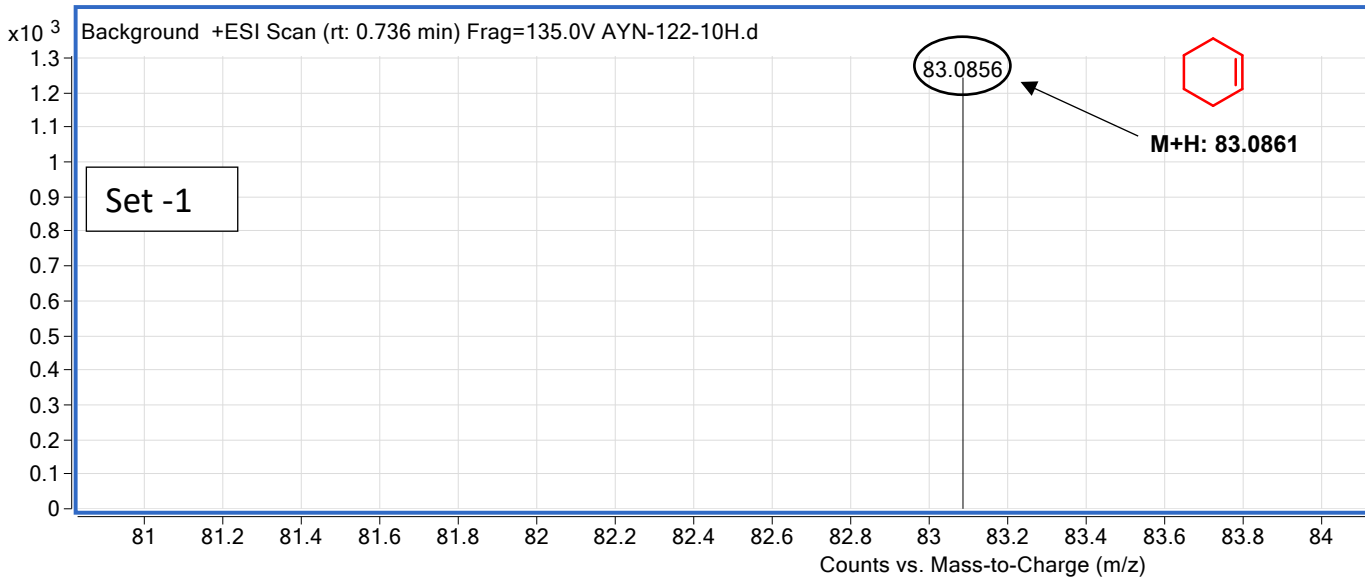
Reaction of (2-Bromophenyl)(2-methyl-1*H*-indol-3-yl)methanone (**1c**)with Cyclohexyl isocyanide for synthesis of product **3d**

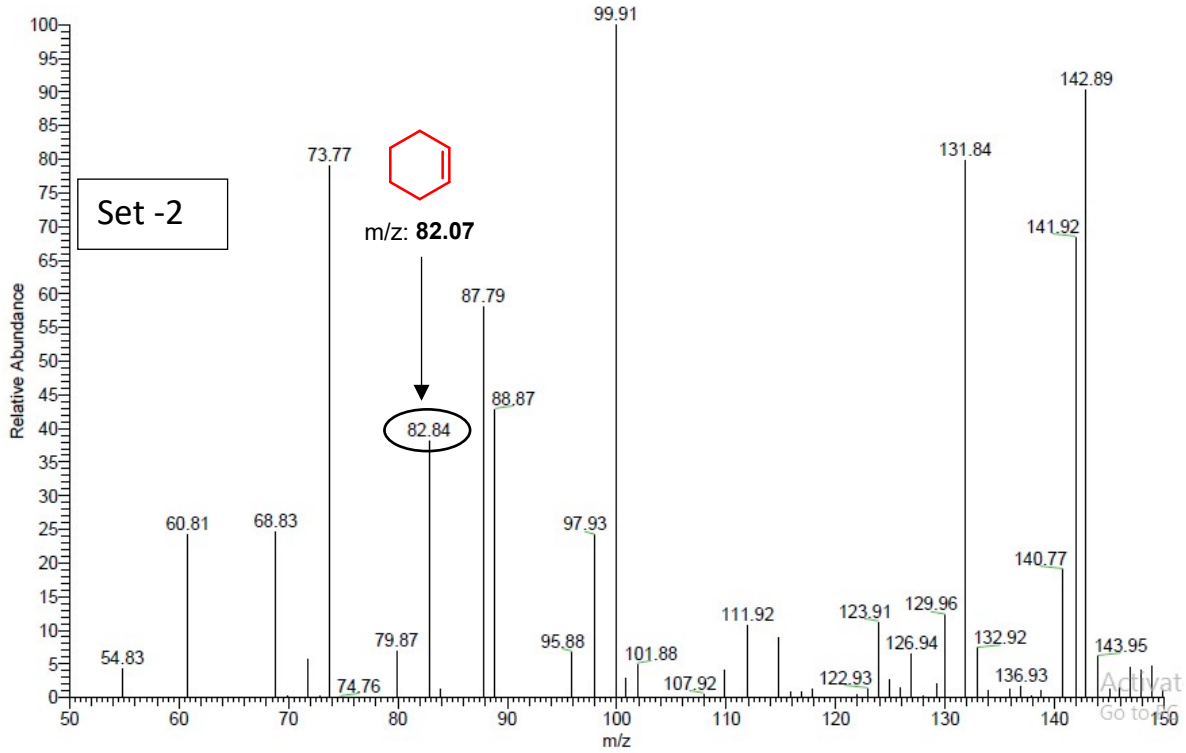




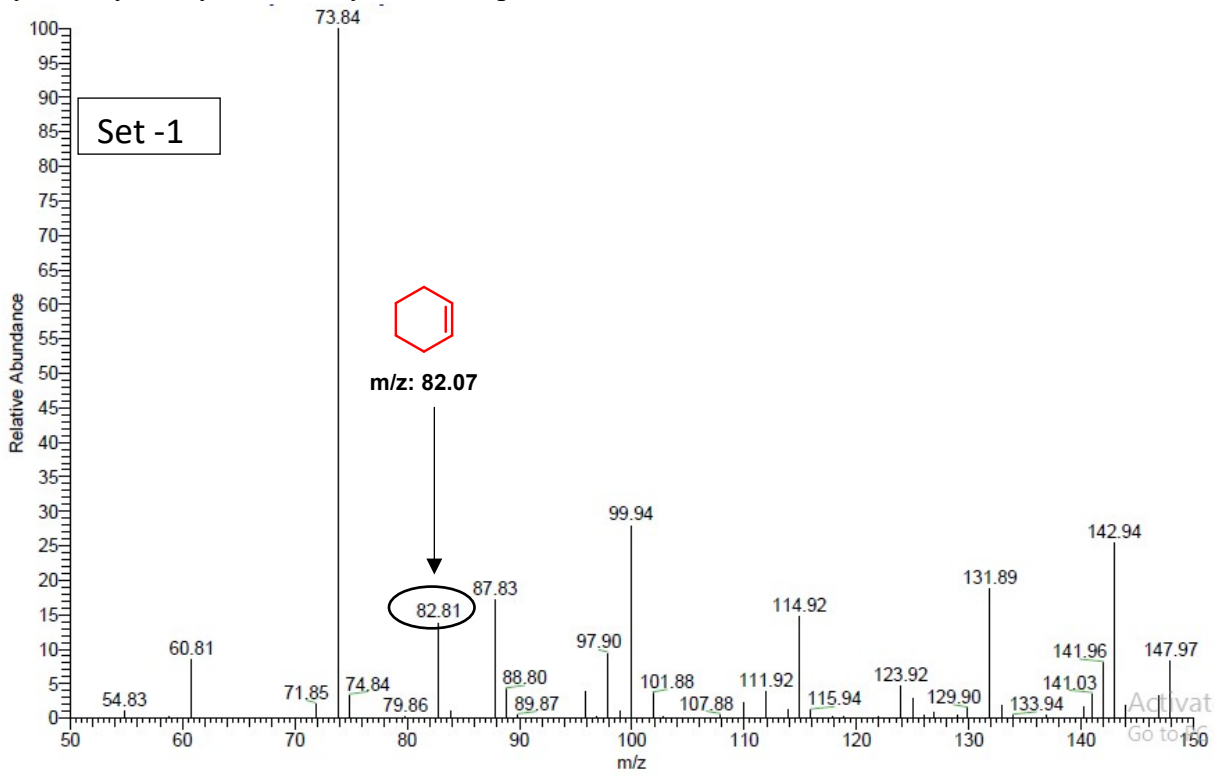
6. Figure S3: Identification of by-product cyclohexene and BrCN:

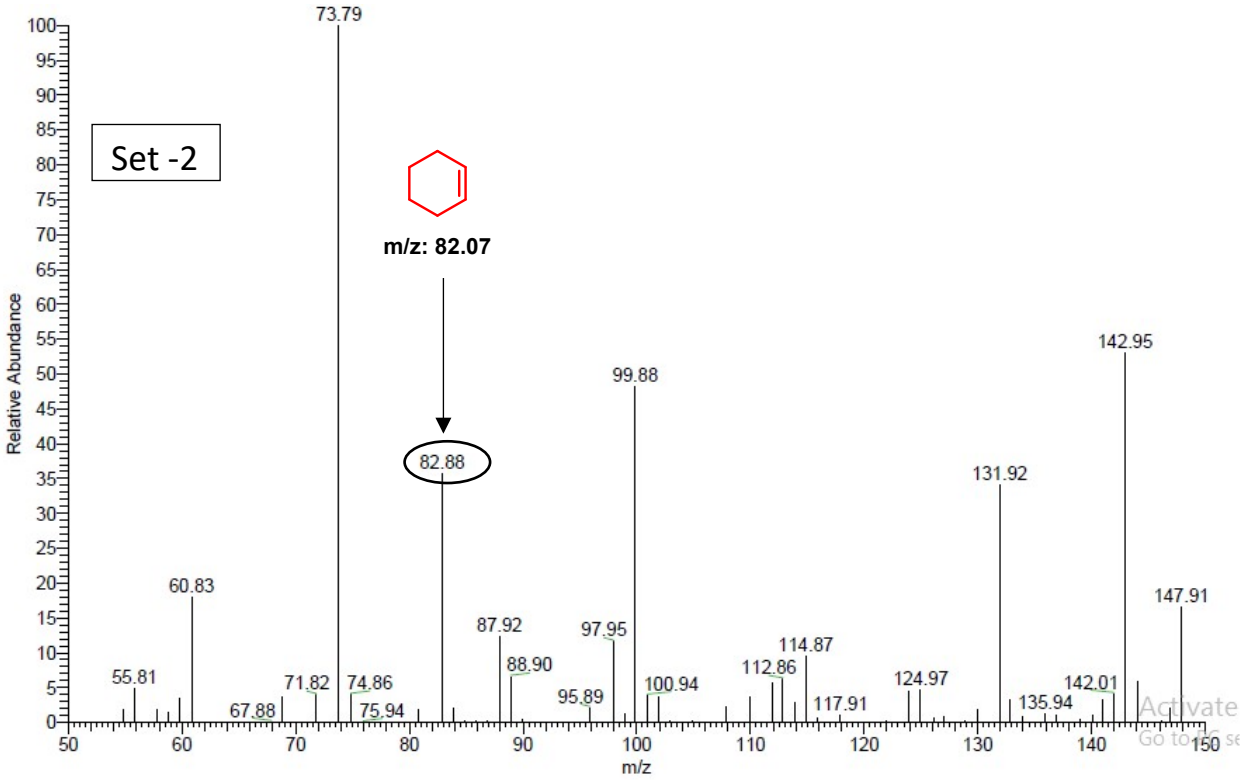
A.1. Reaction of (2-Bromophenyl)(2-methyl-1*H*-indol-3-yl)methanone (**1c**) with Cyclohexyl isocyanide for synthesis of product **3d**



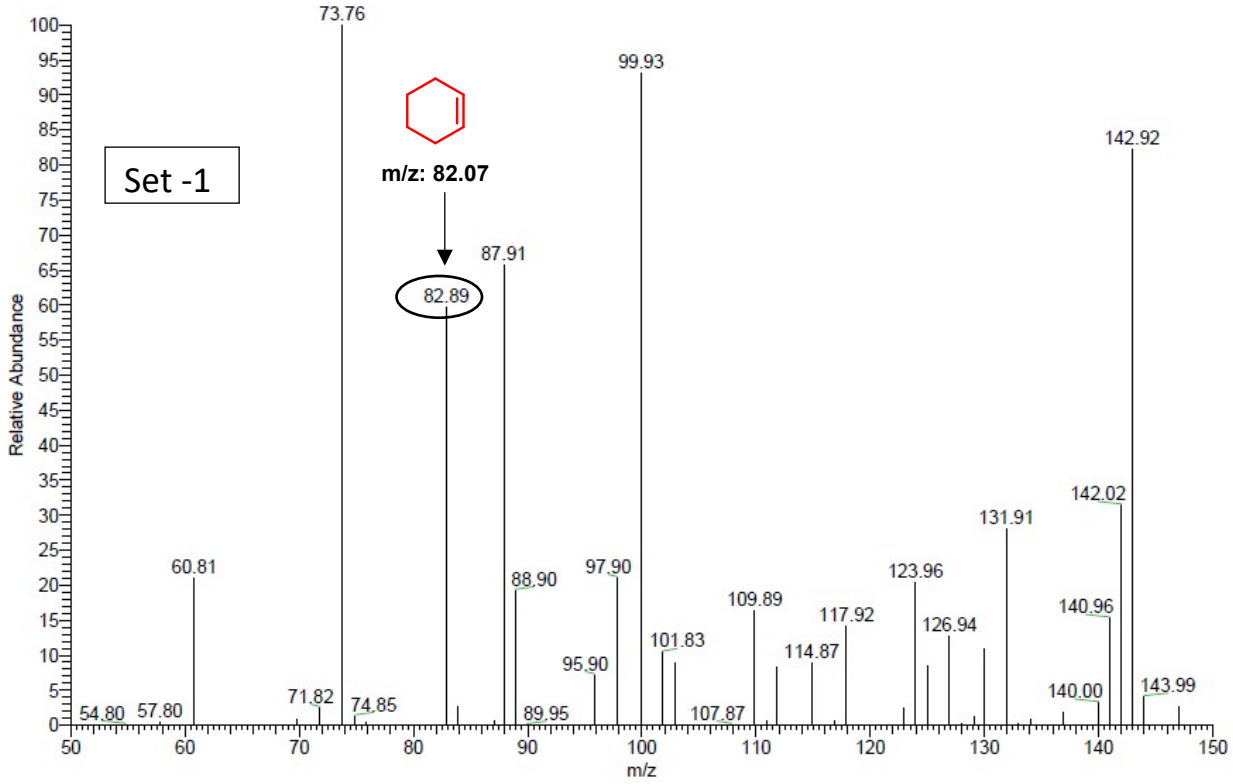


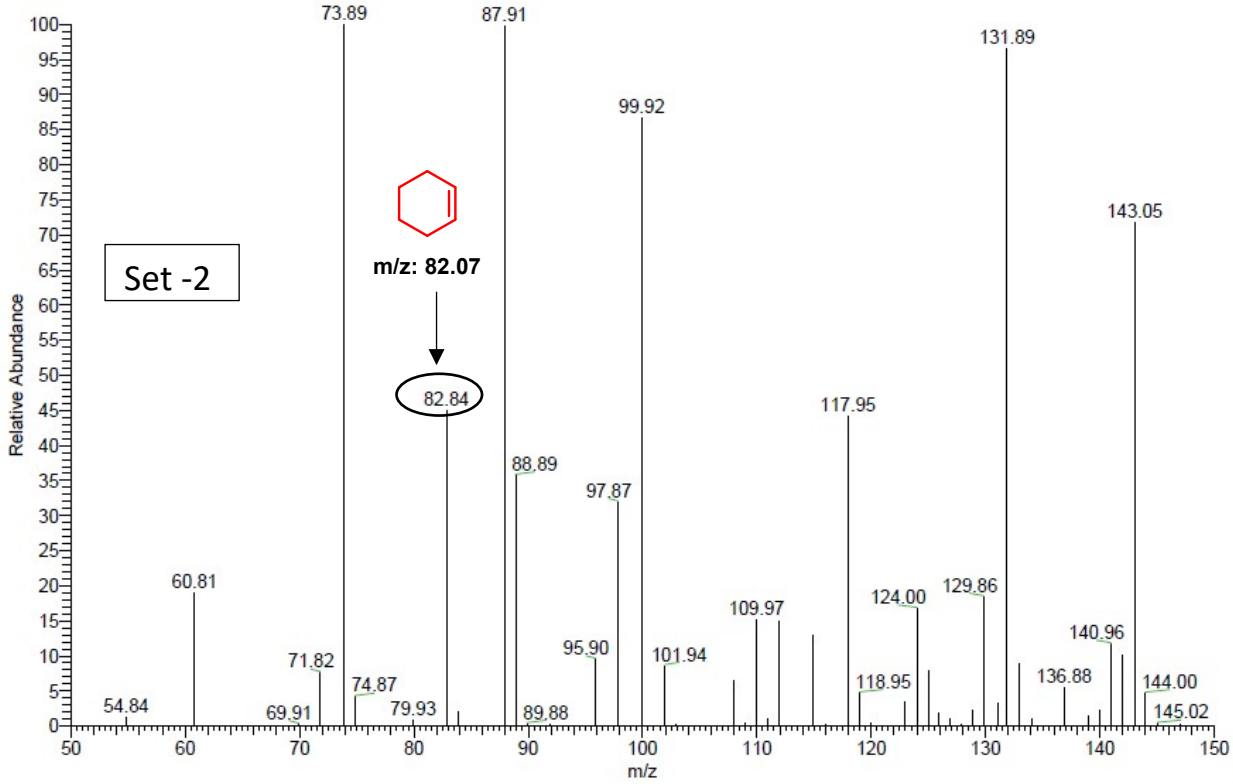
A.2. Reaction of (2-Bromophenyl)(5-methoxy-1*H*-indol-3-yl)methanone (**1g**) with Cyclohexyl isocyanide for synthesis of product **3i**



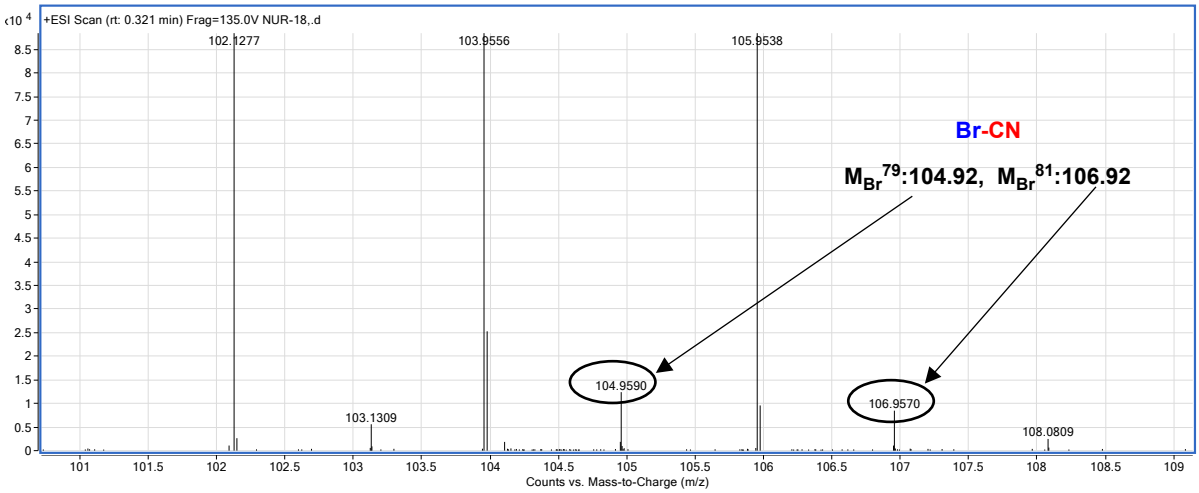


A.3. Reaction of (2-Bromophenyl)(1*H*-indol-3-yl)methanone (**1a**) with Cyclohexyl isocyanide for synthesis of product **3b**

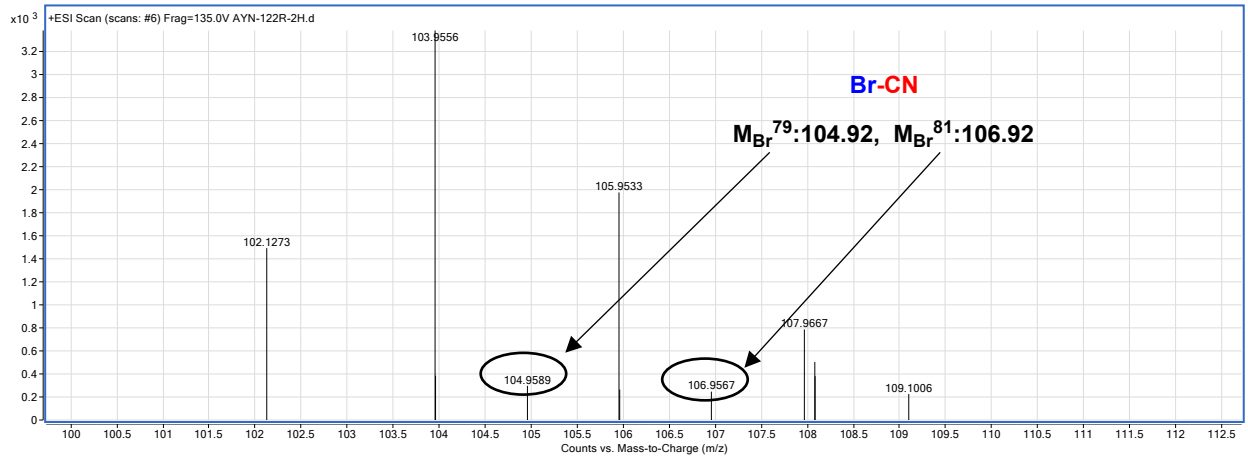




B.1. Reaction of (2-Bromophenyl)(1*H*-indol-3-yl)methanone (**1a**) with Cyclohexyl isocyanide for BrCN detection:

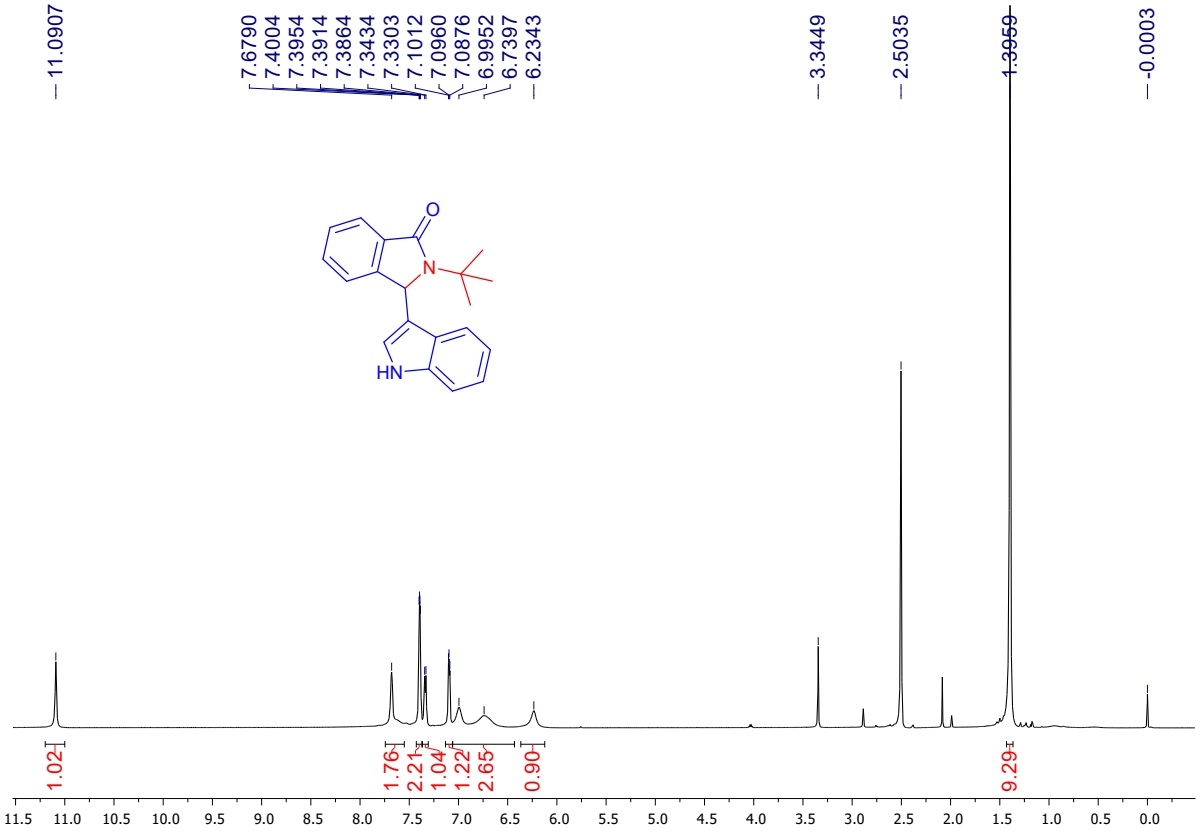


B.2. Reaction of (2-Bromophenyl)(2-methyl-1*H*-indol-3-yl)methanone (**1c**) with Cyclohexyl isocyanide for BrCN detection:

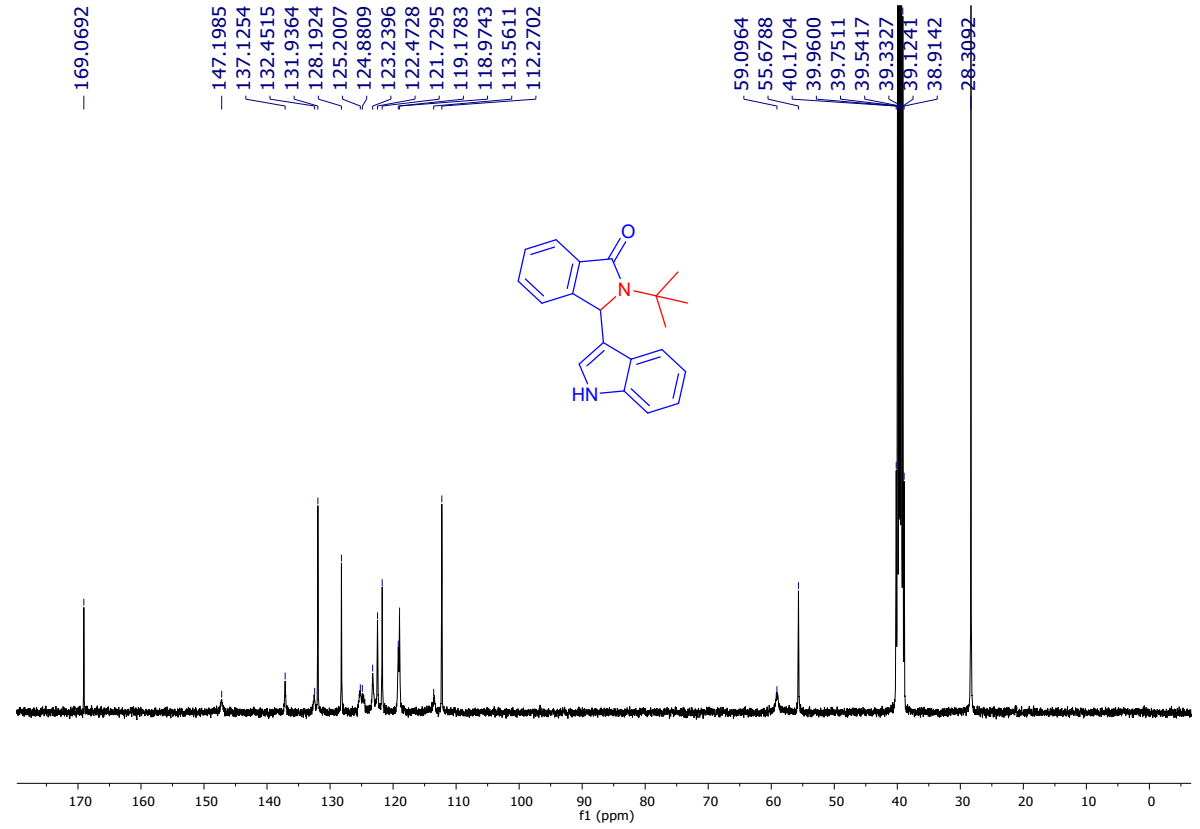


7. NMR spectra

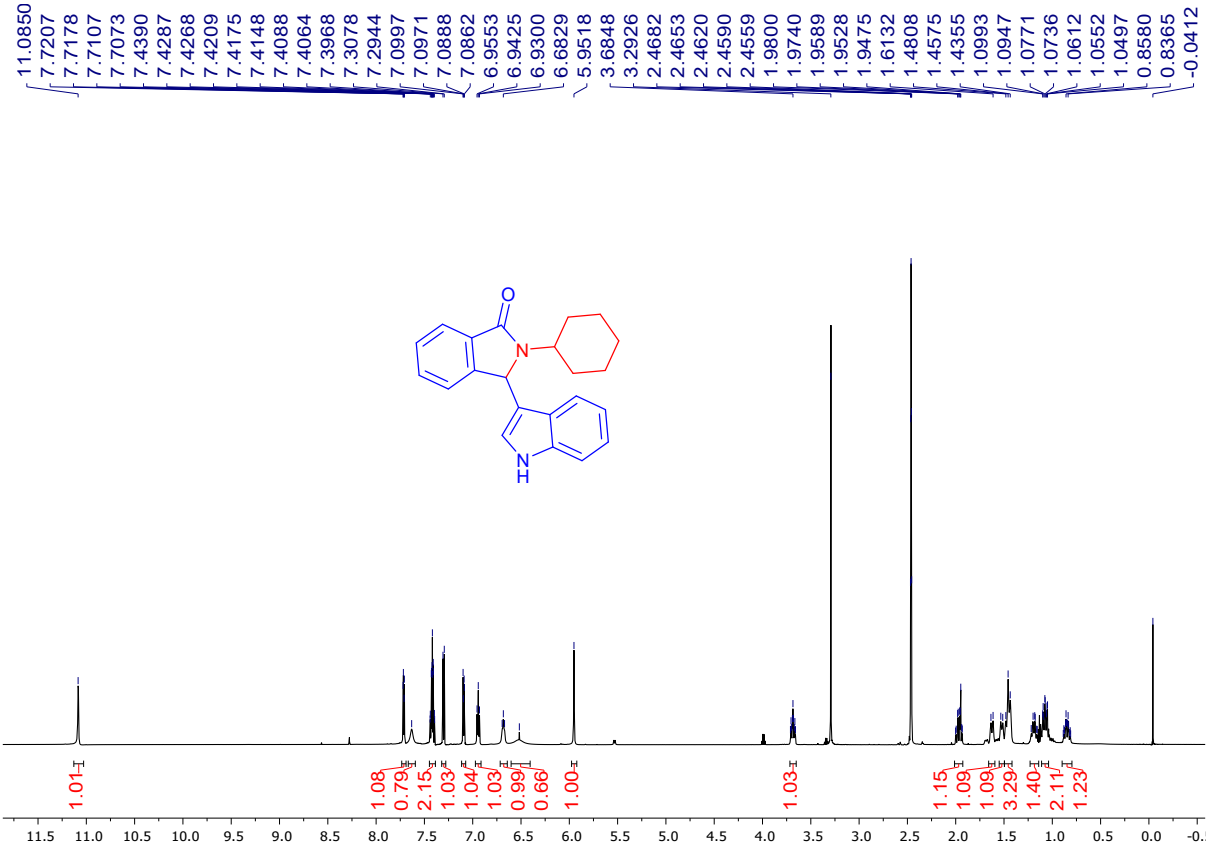
^{1}H NMR of **3a** (600 MHz, DMSO-d_6)



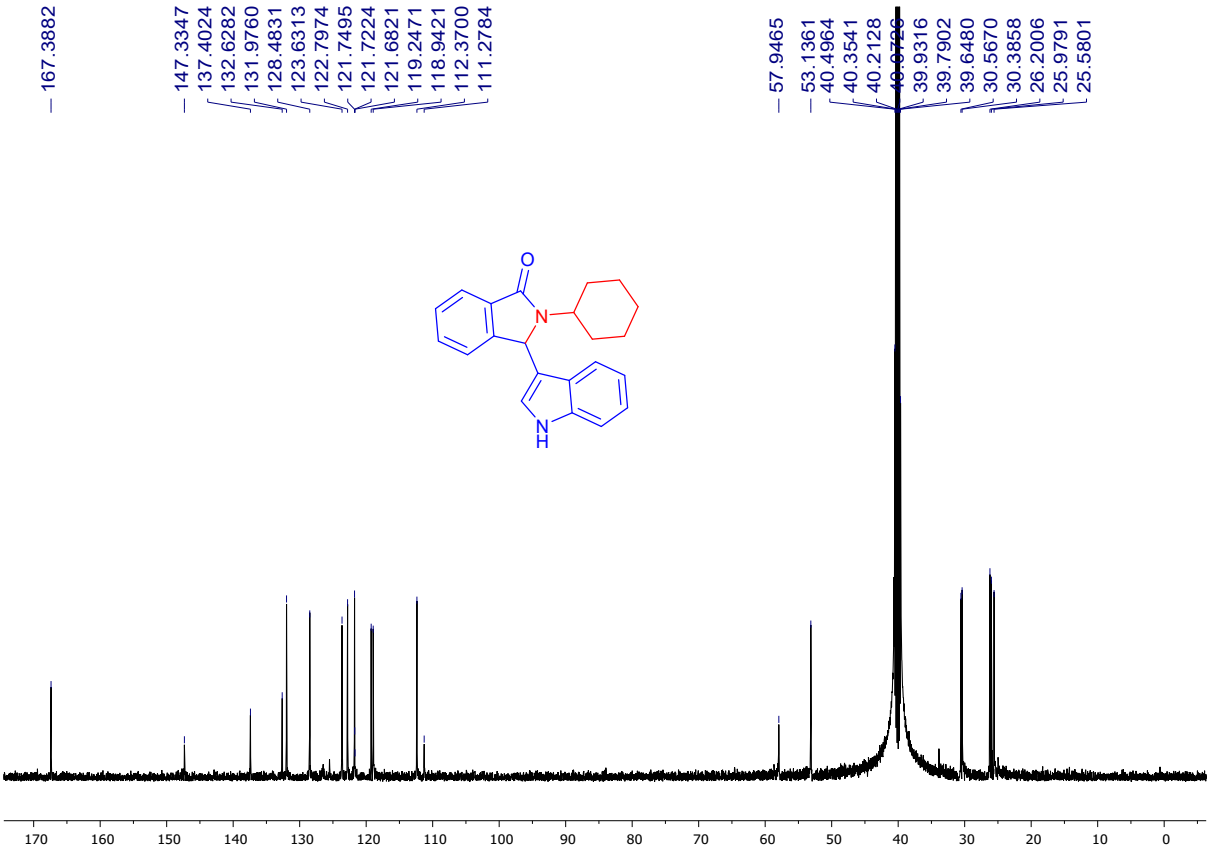
^{13}C{^{1}H} NMR of **3a** (101 MHz, DMSO-d_6)



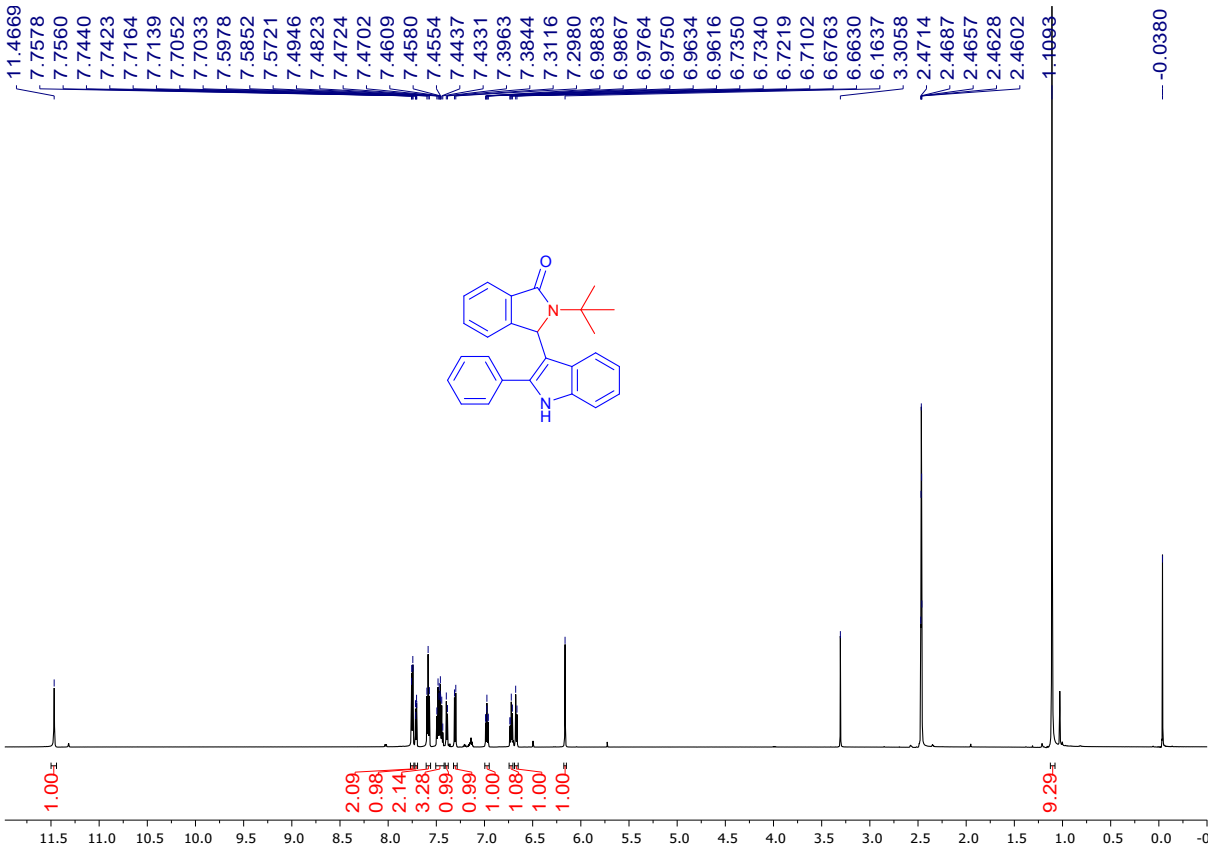
^{1}H NMR of **3b** (600 MHz, DMSO-d_6)



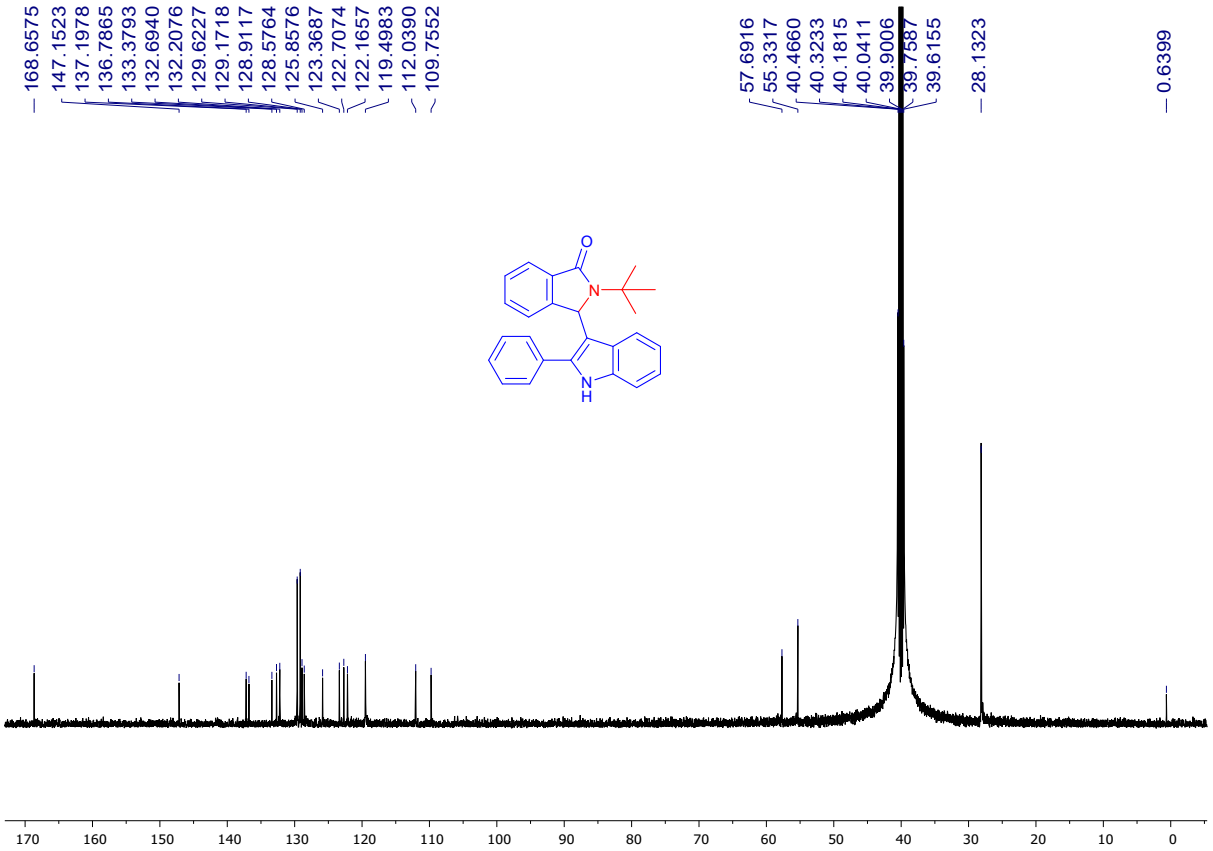
^{13}C{^{1}H} NMR of **3b** (151 MHz, DMSO-d_6)



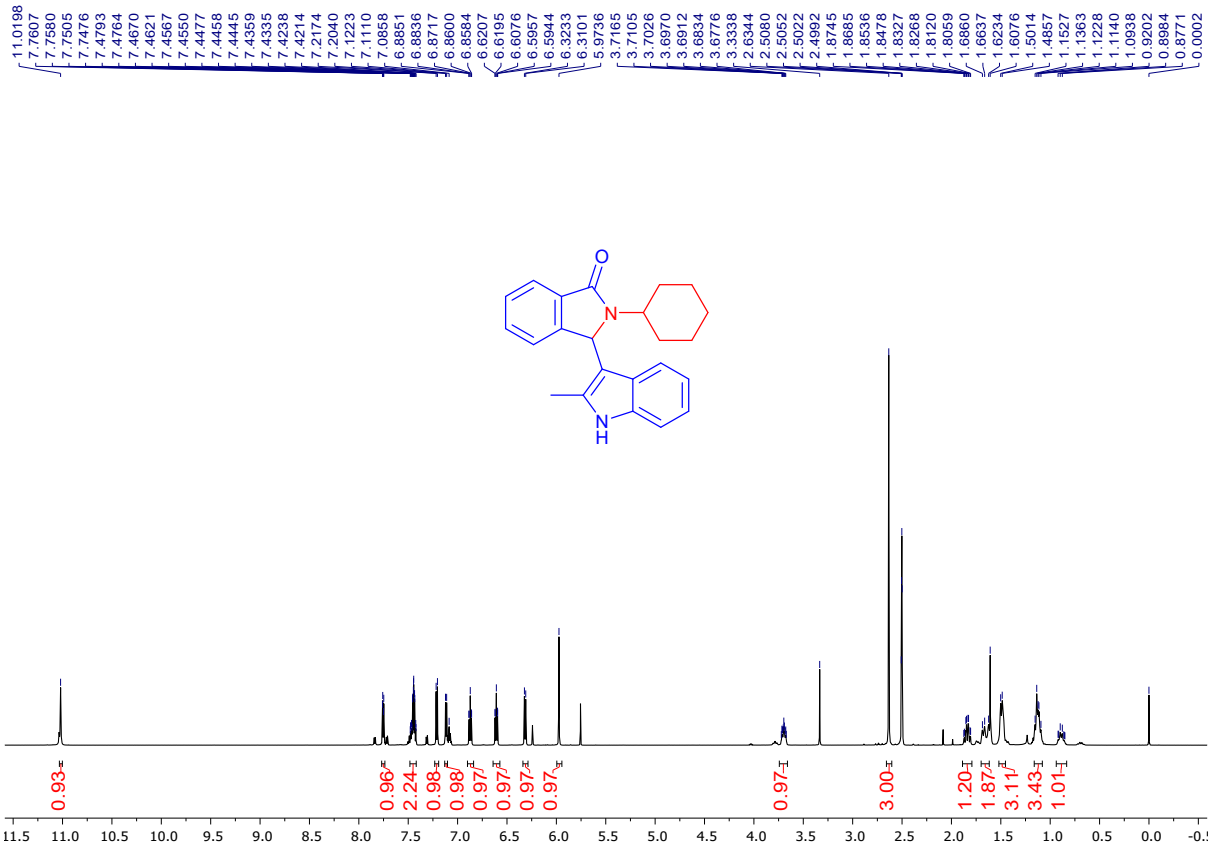
^{1}H NMR of **3c** (600 MHz, DMSO-d_6)



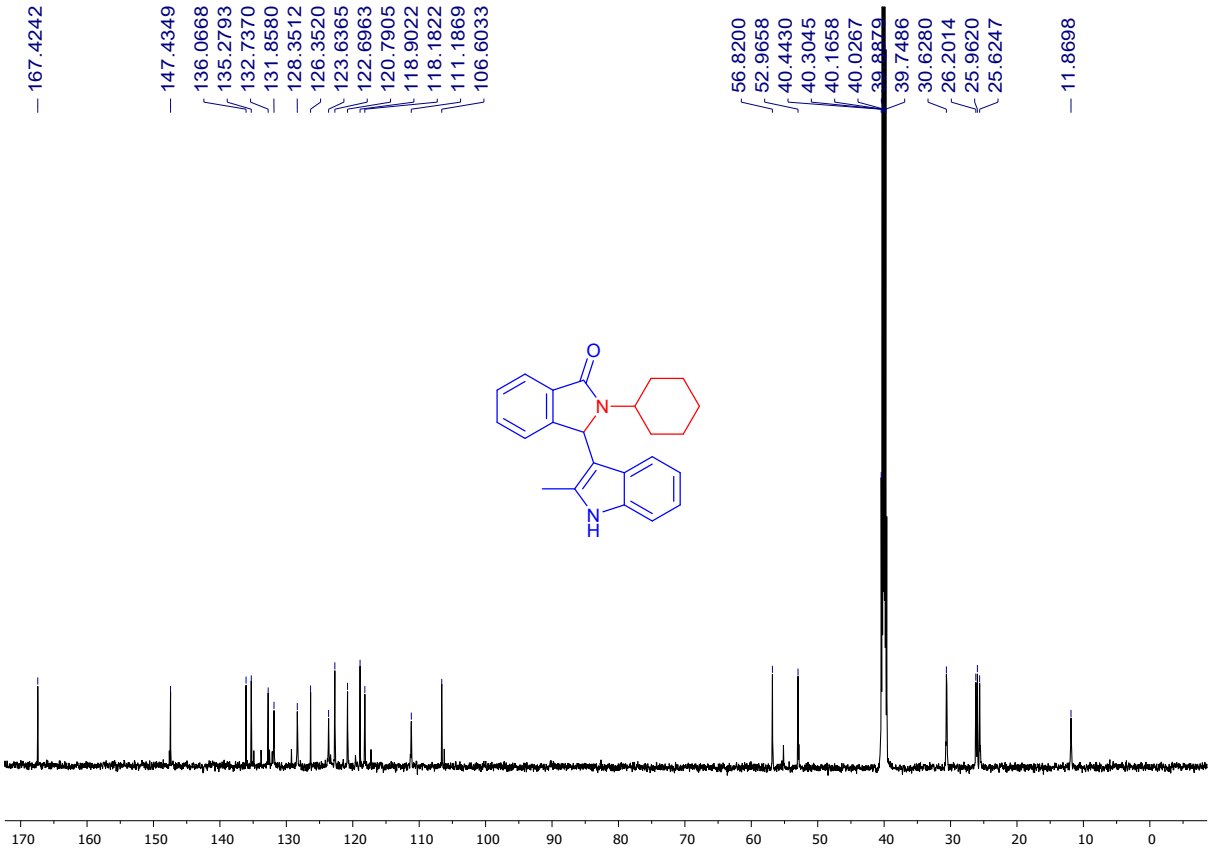
^{13}C{^{1}H} NMR of **3c** (151 MHz, DMSO-d_6)



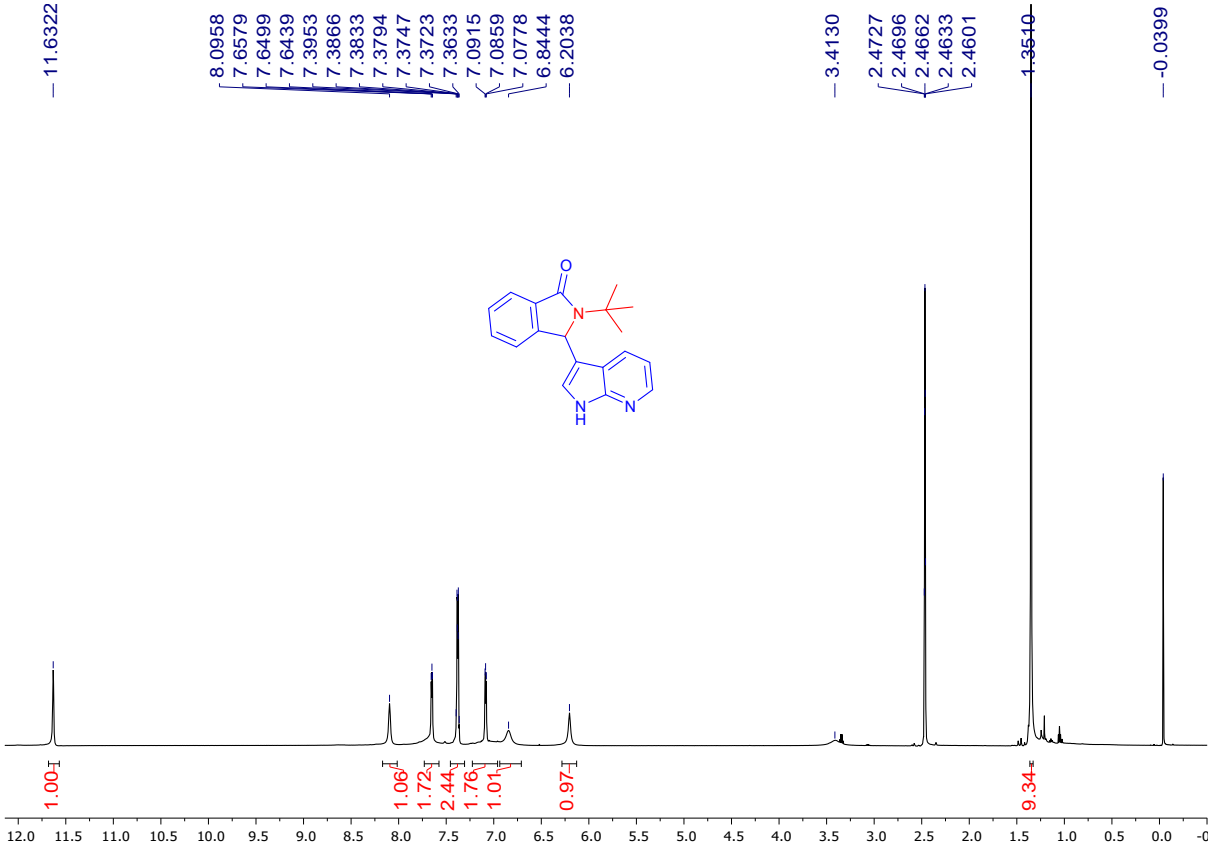
^{1}H NMR of **3d** (600 MHz, DMSO-d_6)



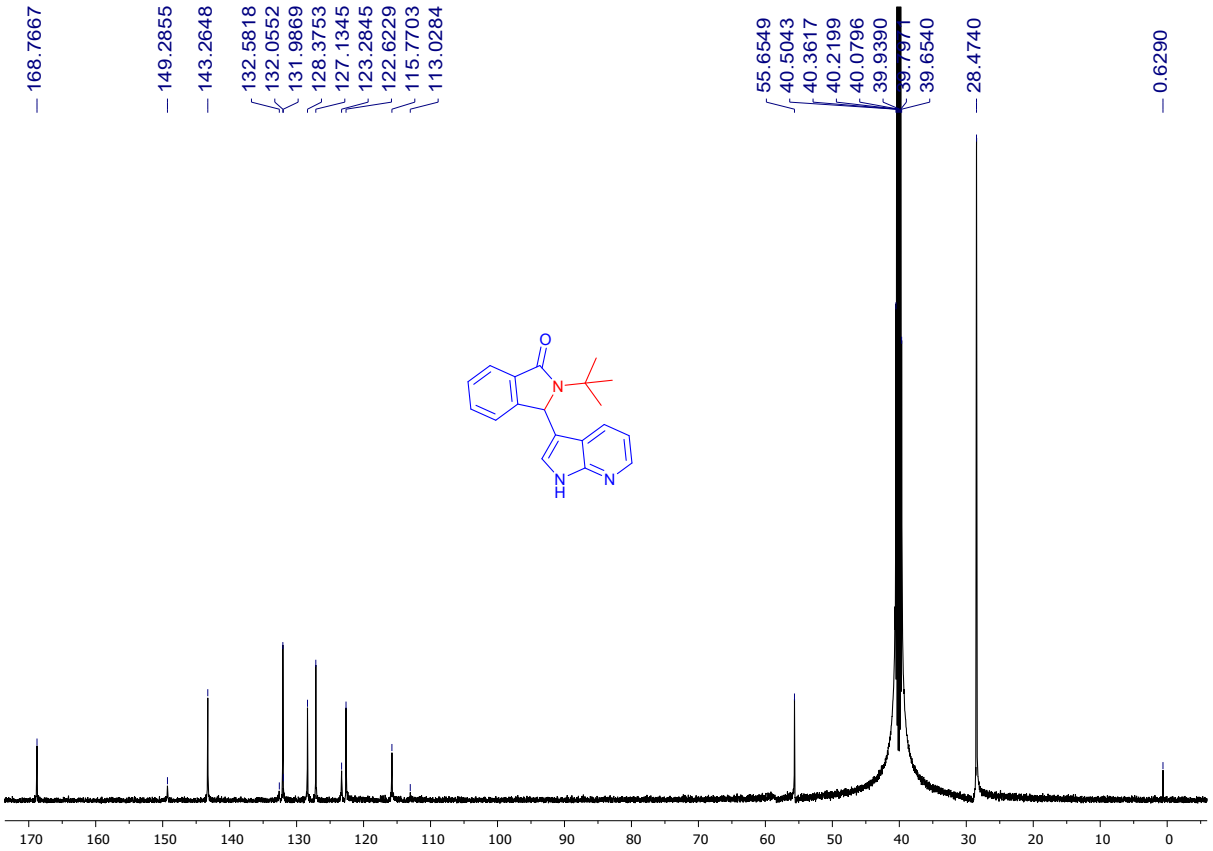
^{13}C NMR of **3d** (151 MHz, DMSO-d_6)



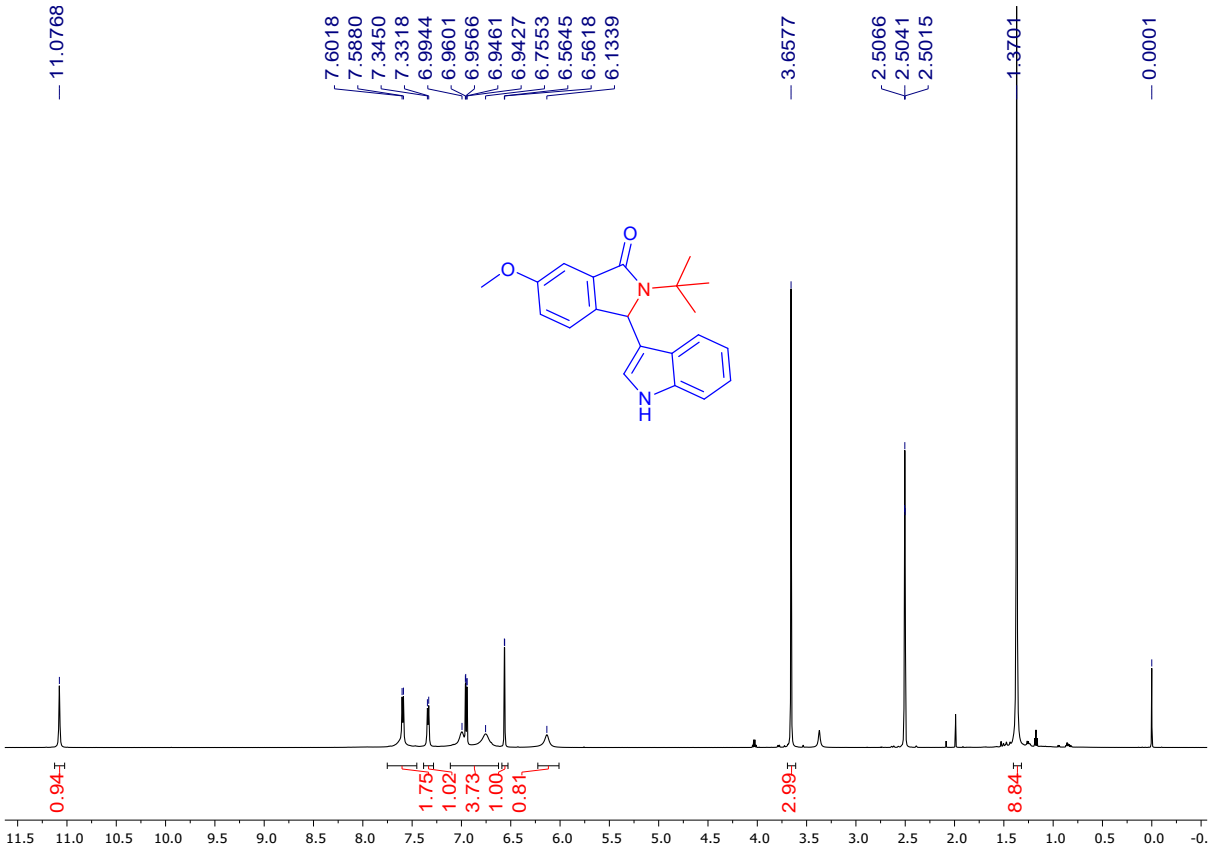
^{1}H NMR of **3e** (600 MHz, DMSO-d_6)



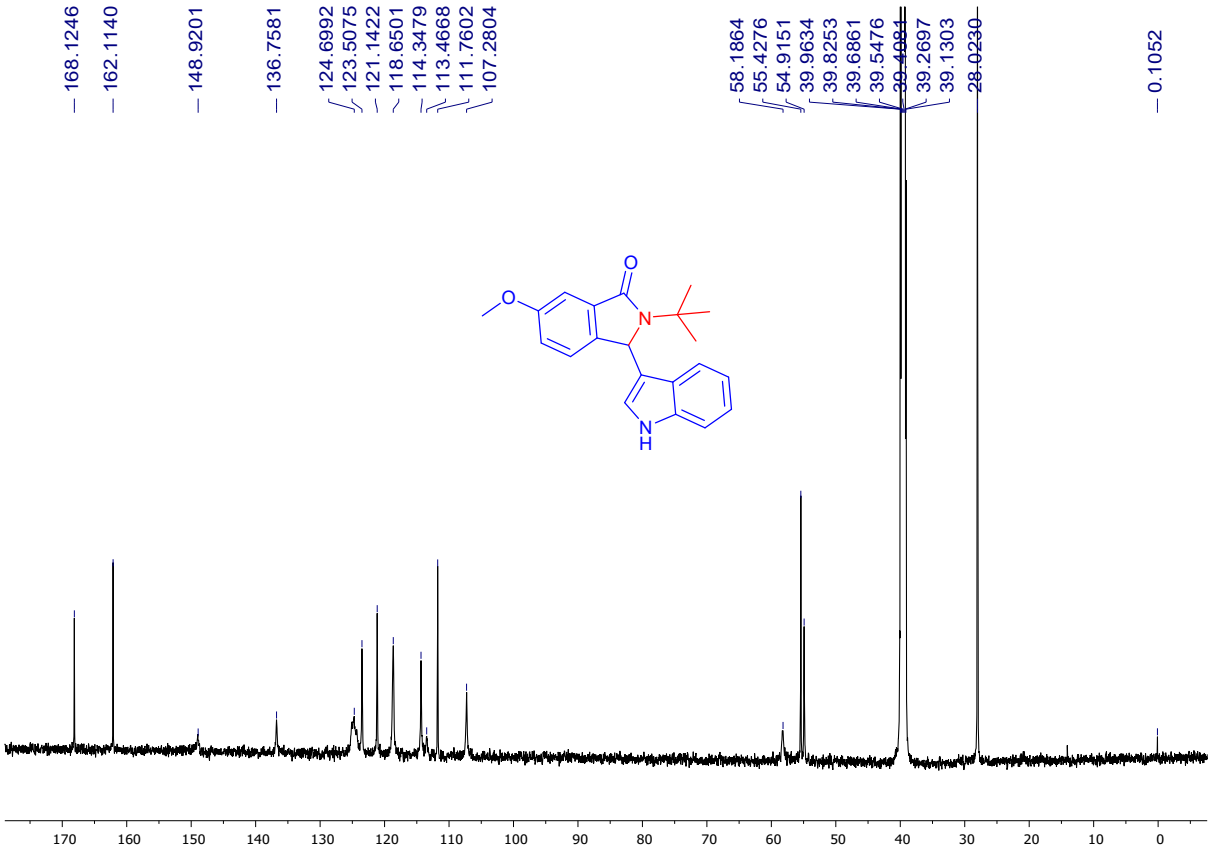
^{13}C{^{1}H} NMR of **3e** (151 MHz, DMSO-d_6)



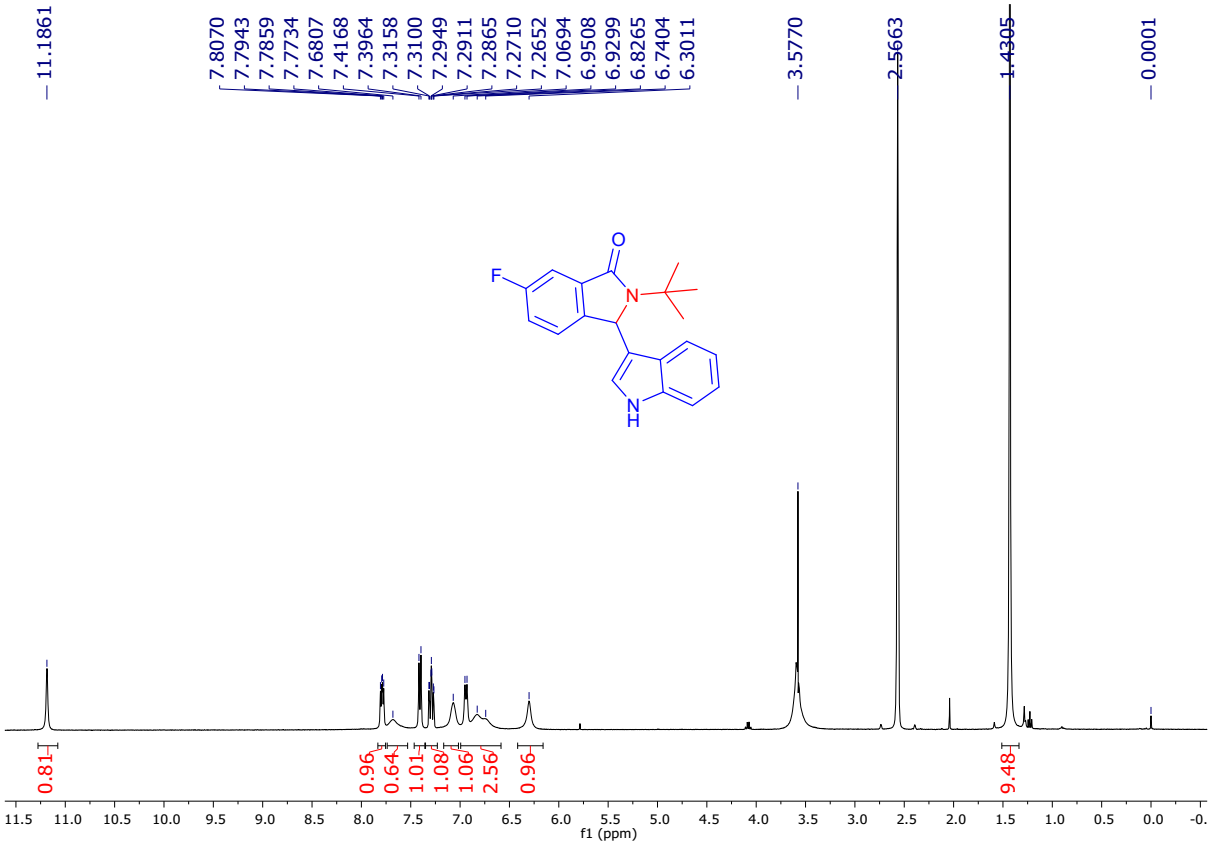
^{1}H NMR of **3f** (600 MHz, DMSO-d_6)



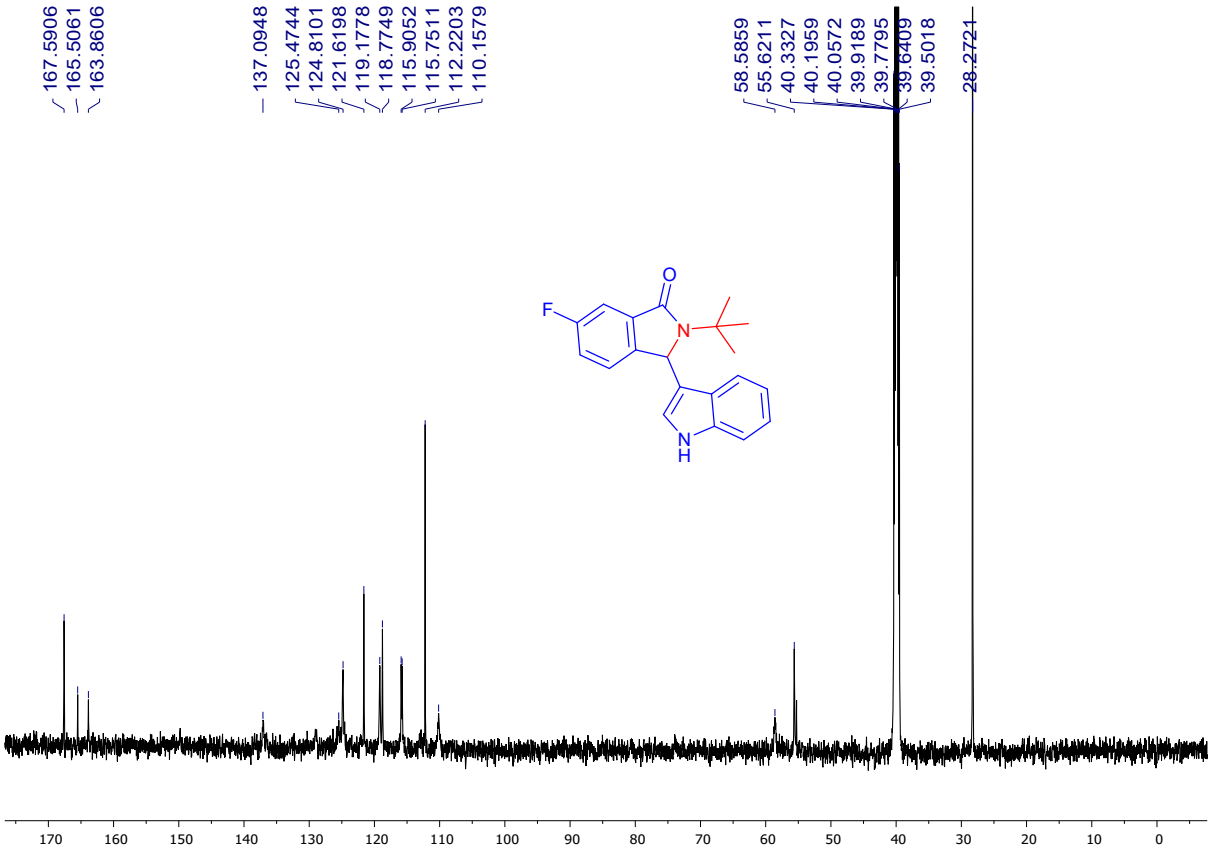
^{13}C NMR of **3f** (151 MHz, DMSO-d_6)



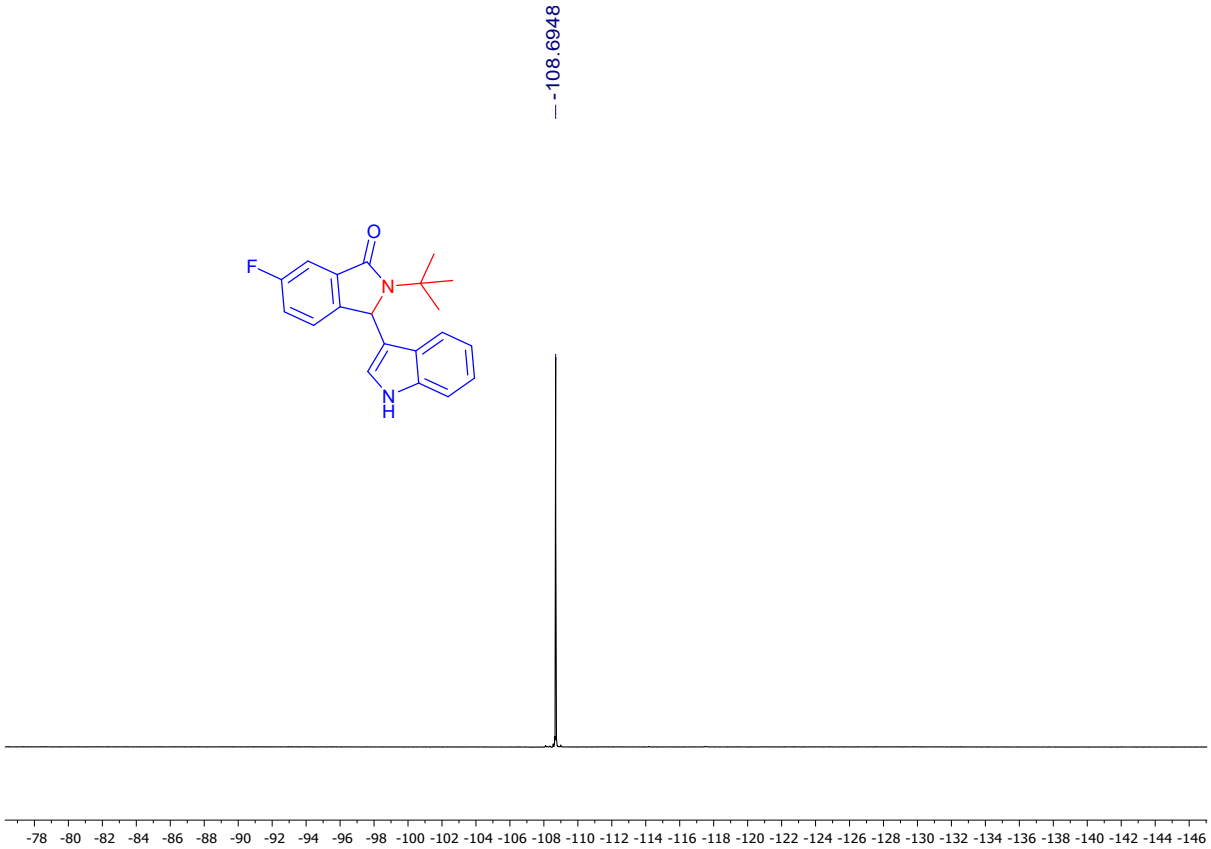
^{1}H NMR of **3g** (400 MHz, DMSO-d_6)



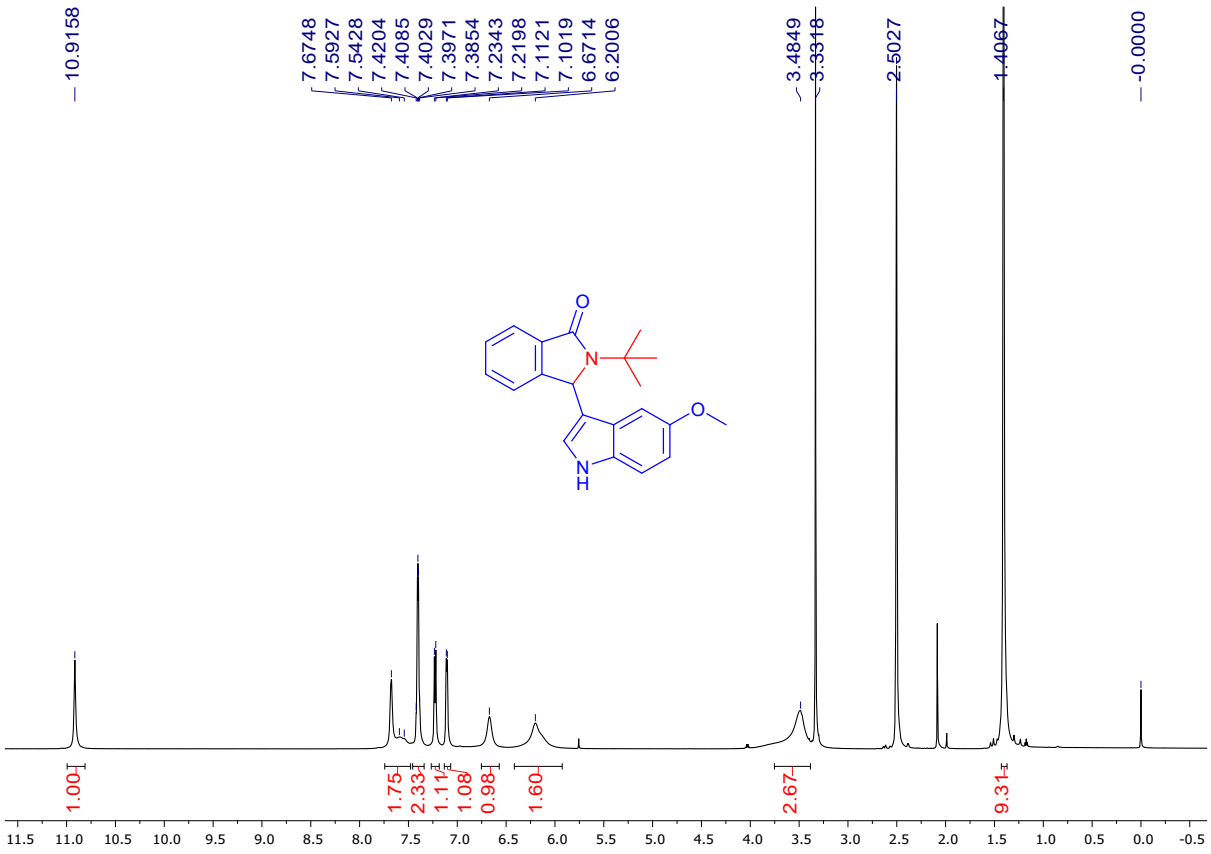
^{13}C{^{1}H} NMR of **3g** (151 MHz, DMSO-d_6)



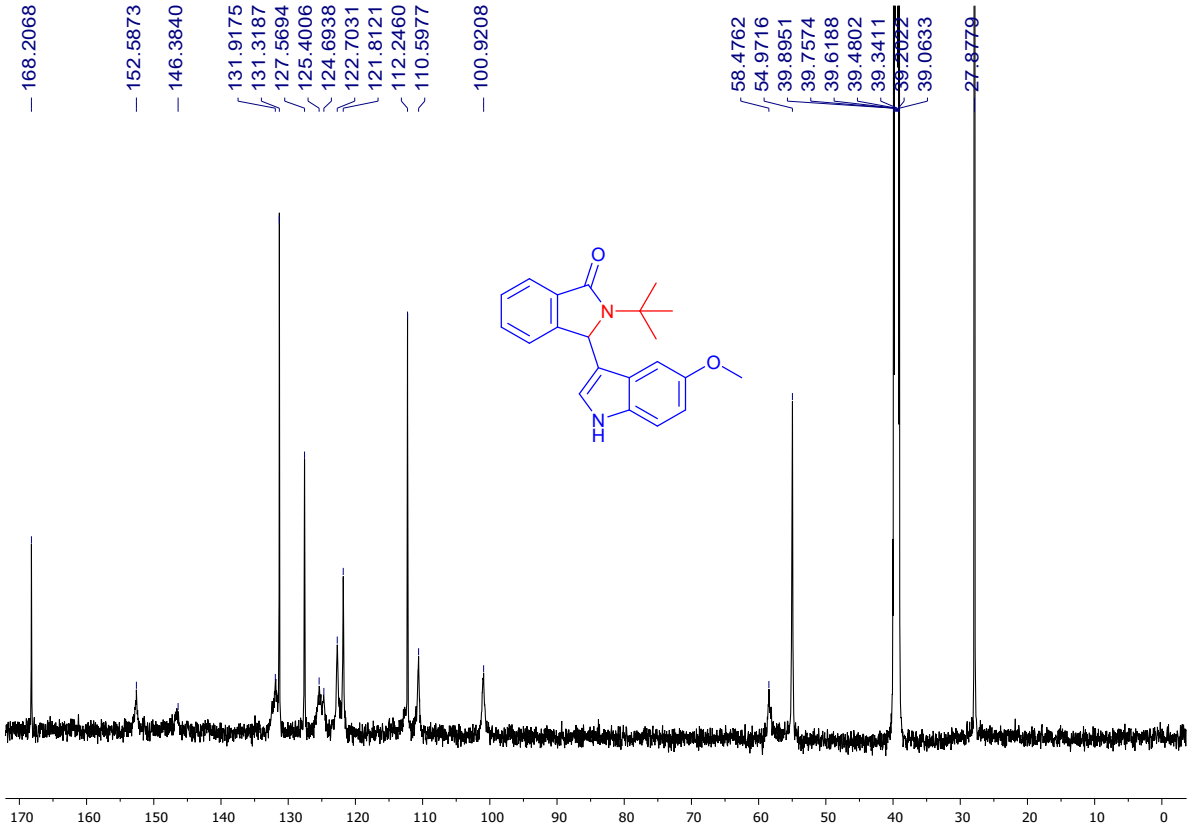
^{19}F NMR of **3g** (565 MHz, DMSO-d_6)



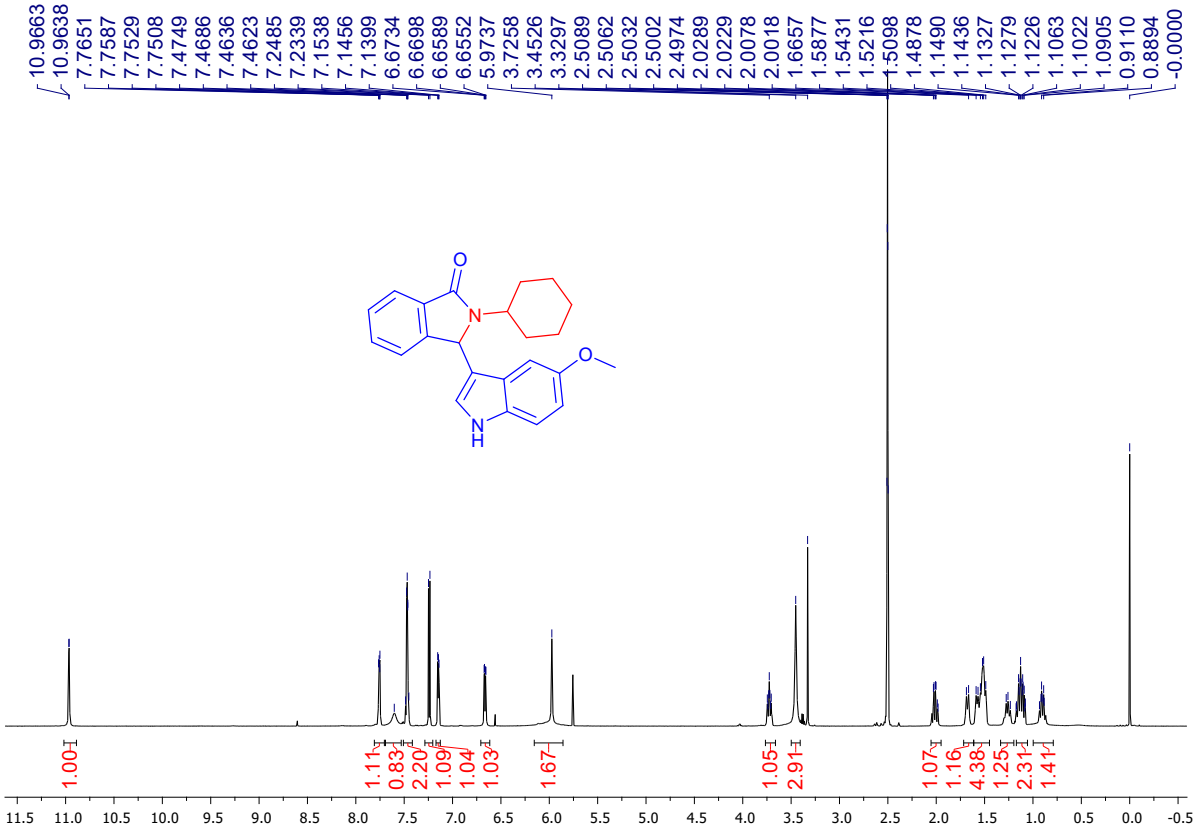
^{1}H NMR of **3h** (600 MHz, DMSO-d_6)



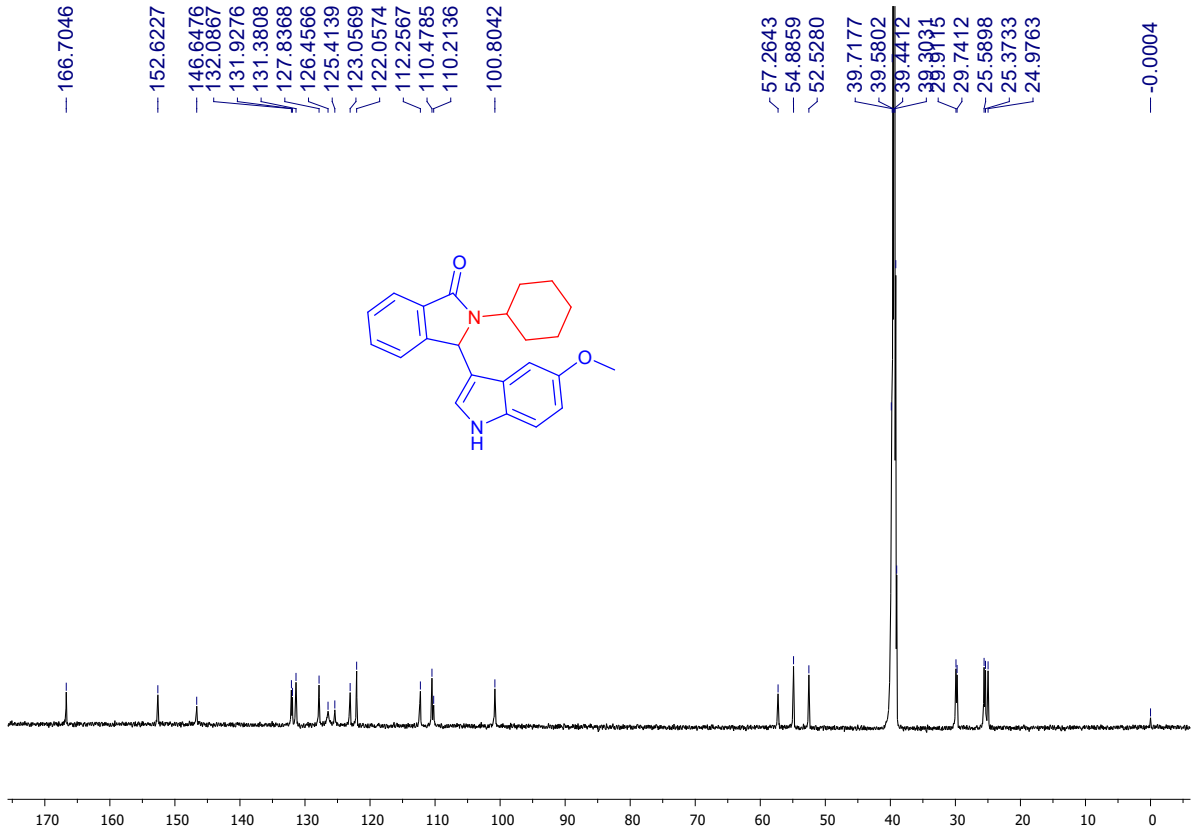
^{13}C NMR of **3h** (151 MHz, DMSO-d_6)



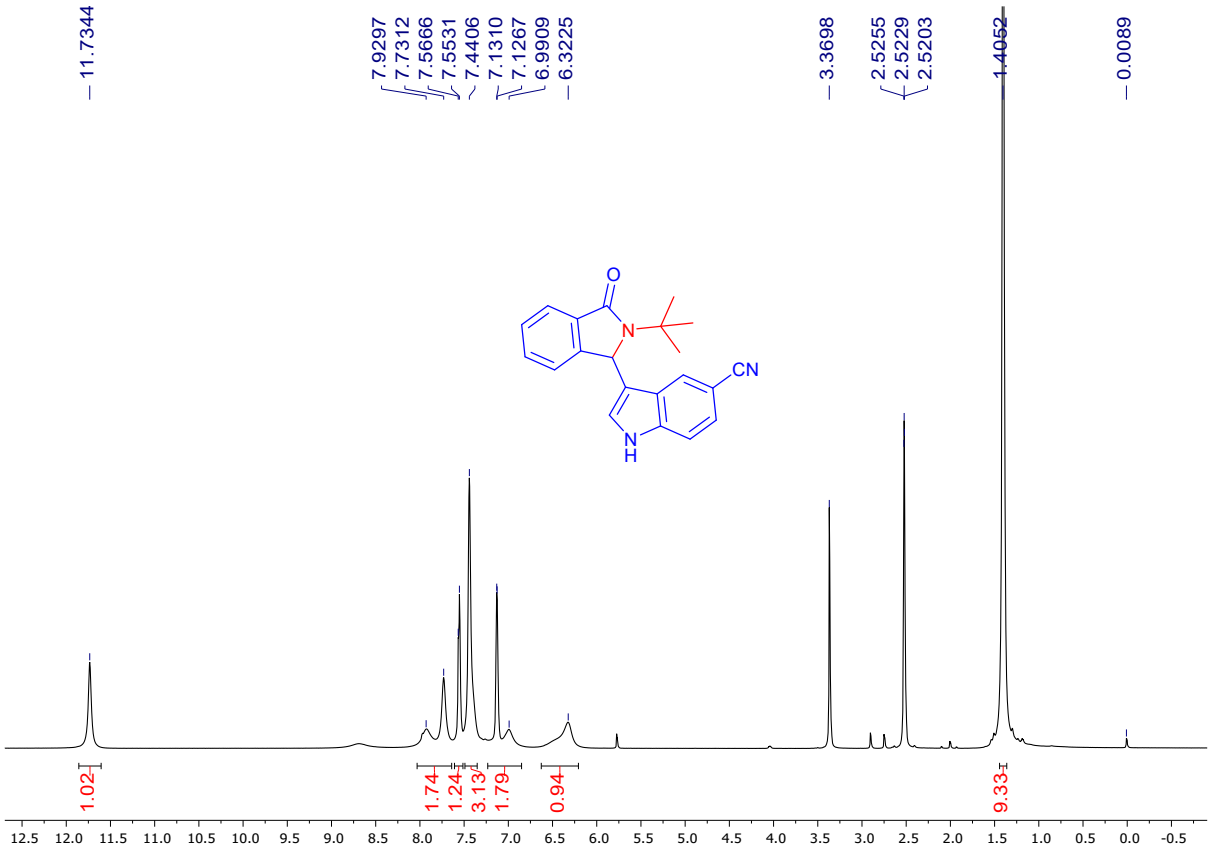
^{1}H NMR of **3i** (600 MHz, DMSO-d_6)



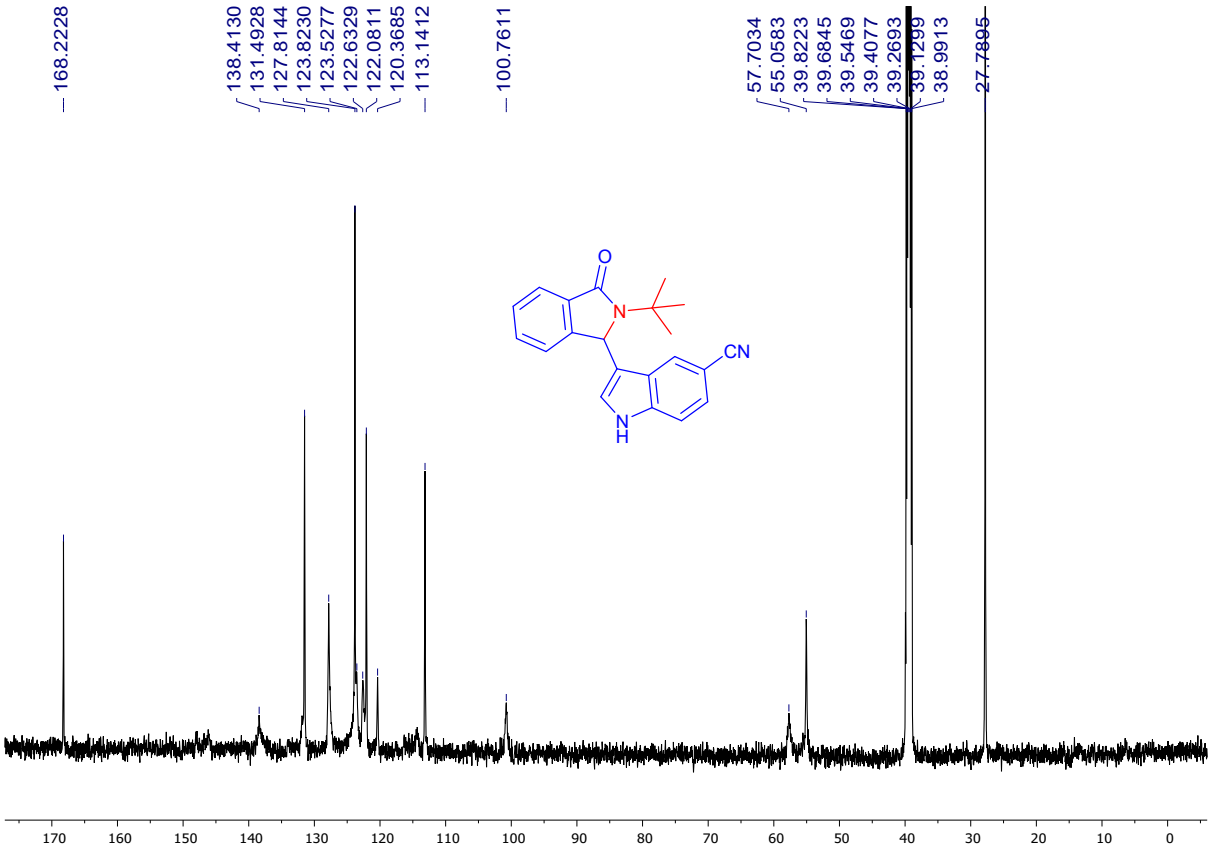
$^{13}C\{^{1}H\}$ NMR of **3i** (151 MHz, DMSO-d_6)



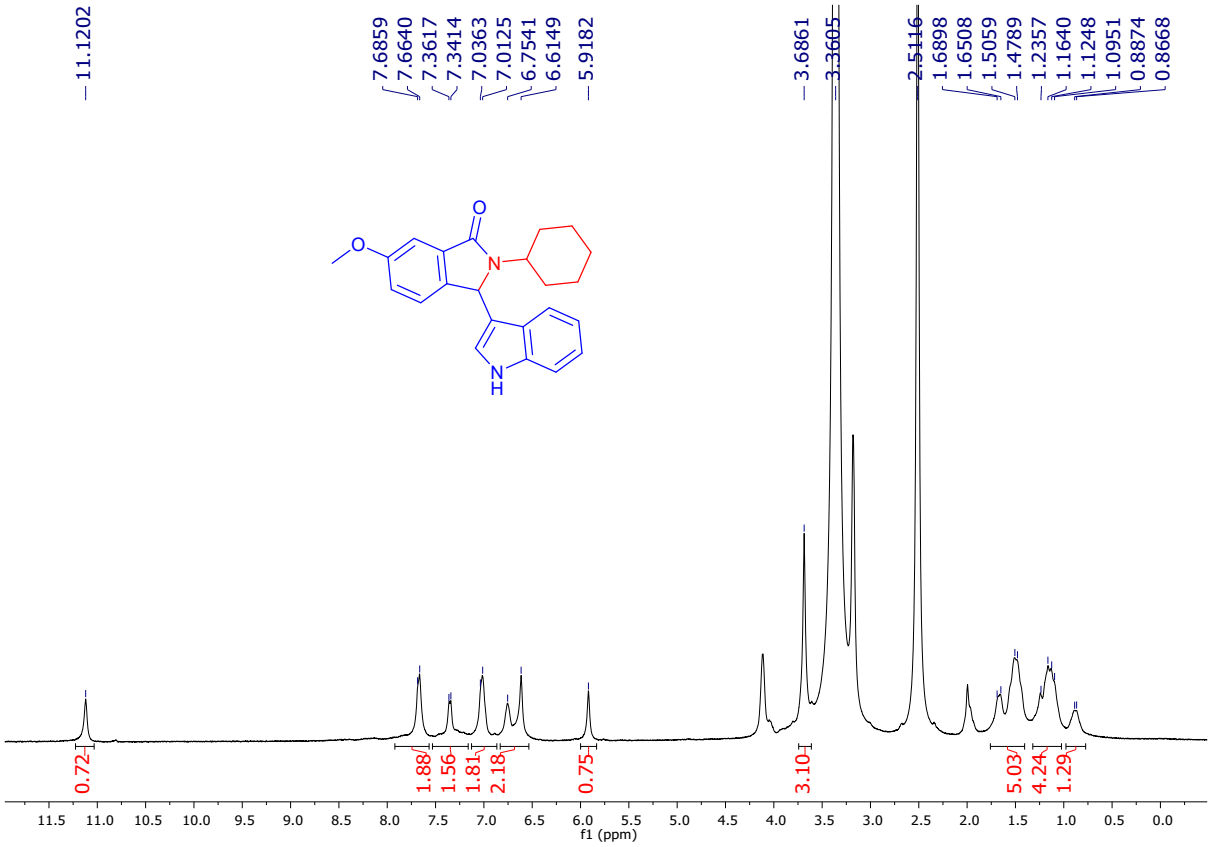
^{1}H NMR of **3j** (600 MHz, DMSO-d_6)



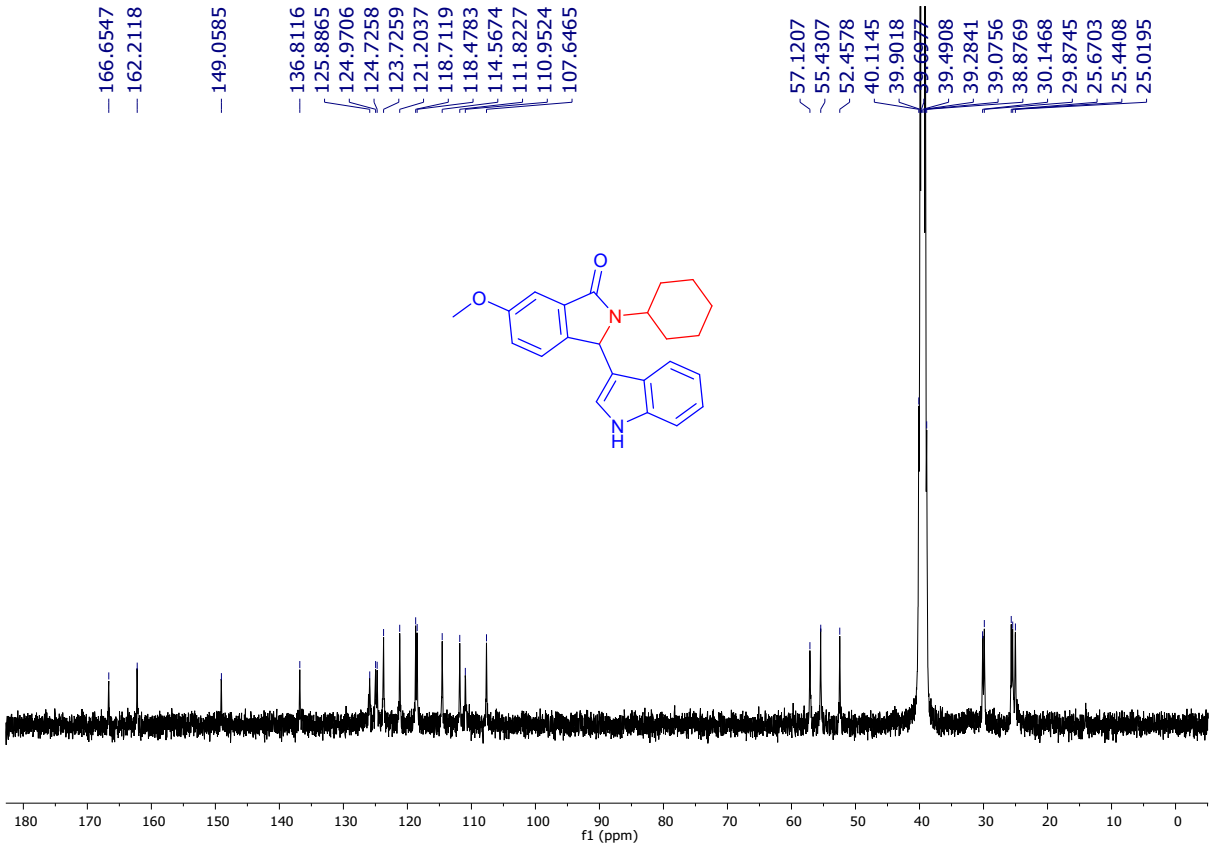
^{13}C NMR of **3j** (151 MHz, DMSO-d_6)



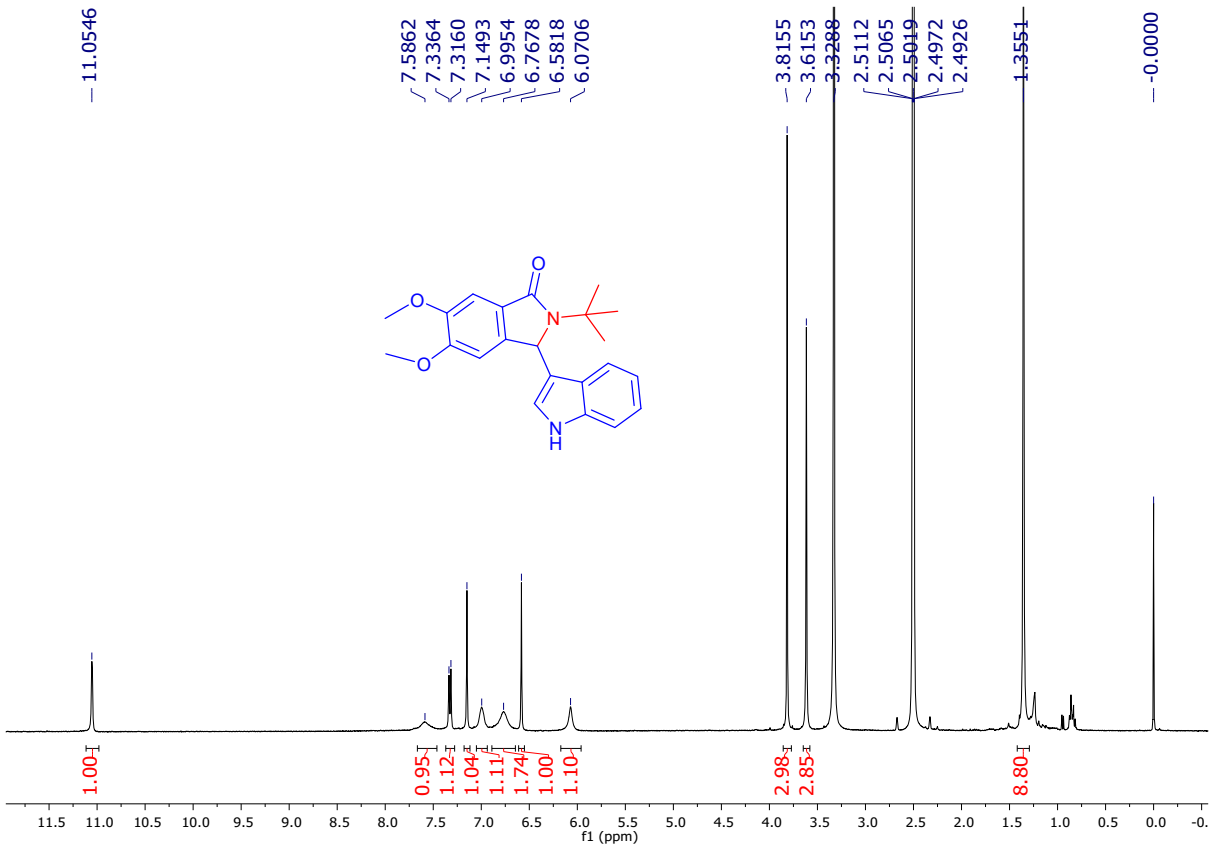
^{1}H NMR of **3k** (400 MHz, DMSO-d_6)



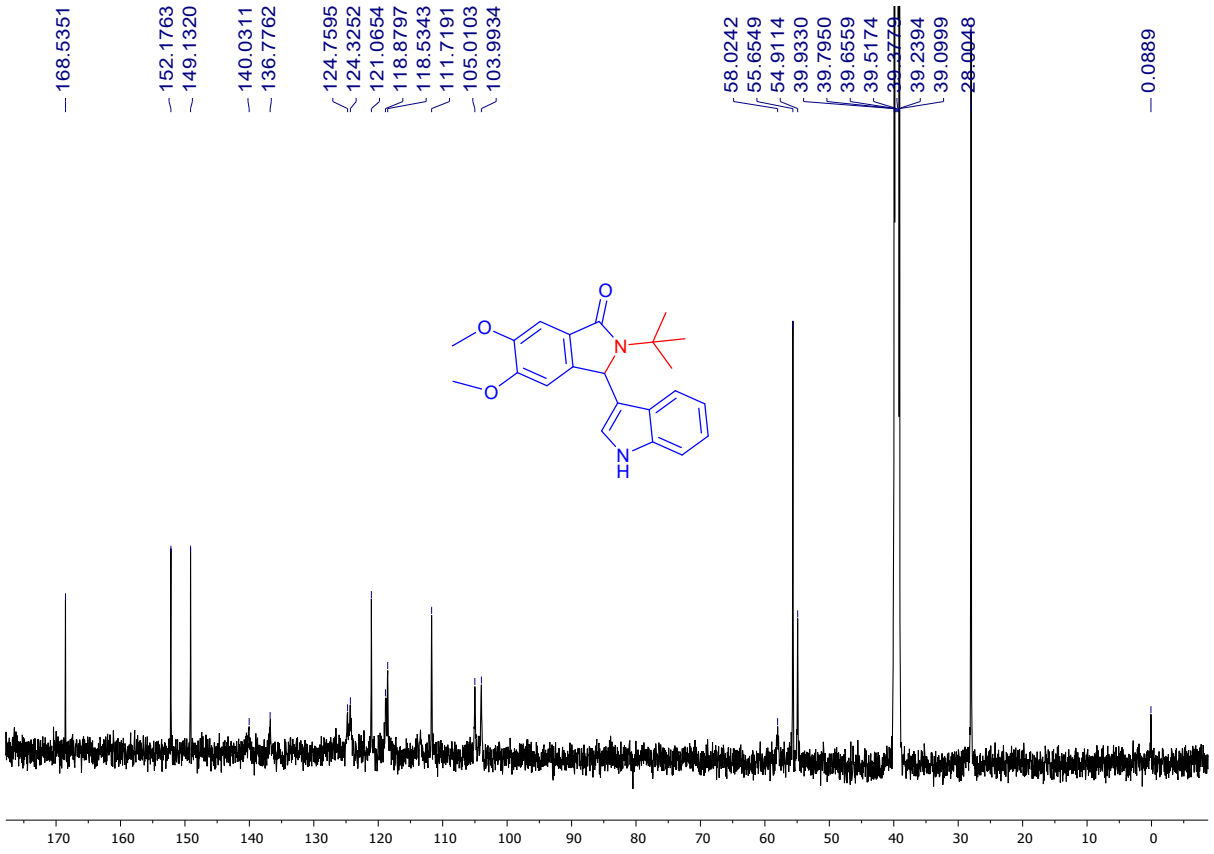
$^{13}C\{^{1}H\}$ NMR of **3k** (101 MHz, DMSO-d_6)



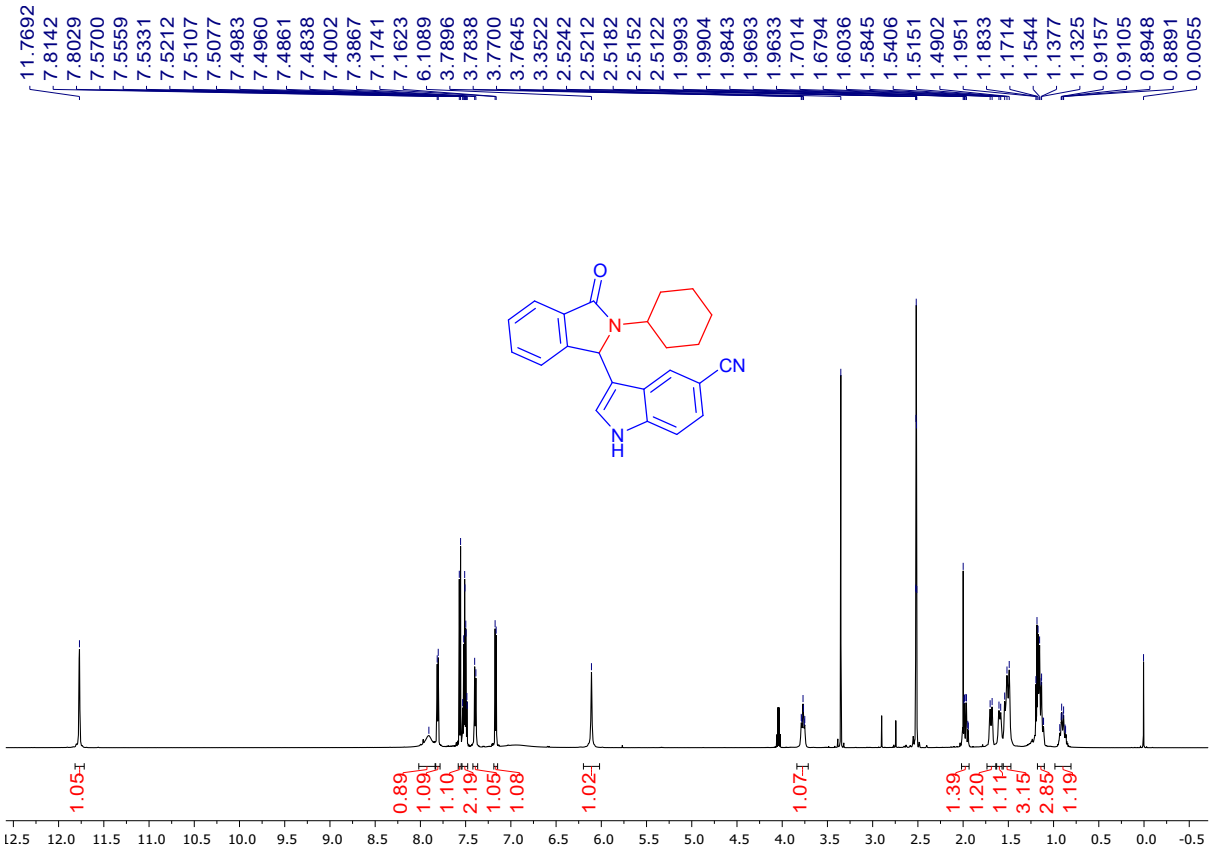
^{1}H NMR of **3l** (400 MHz, DMSO-d_6)



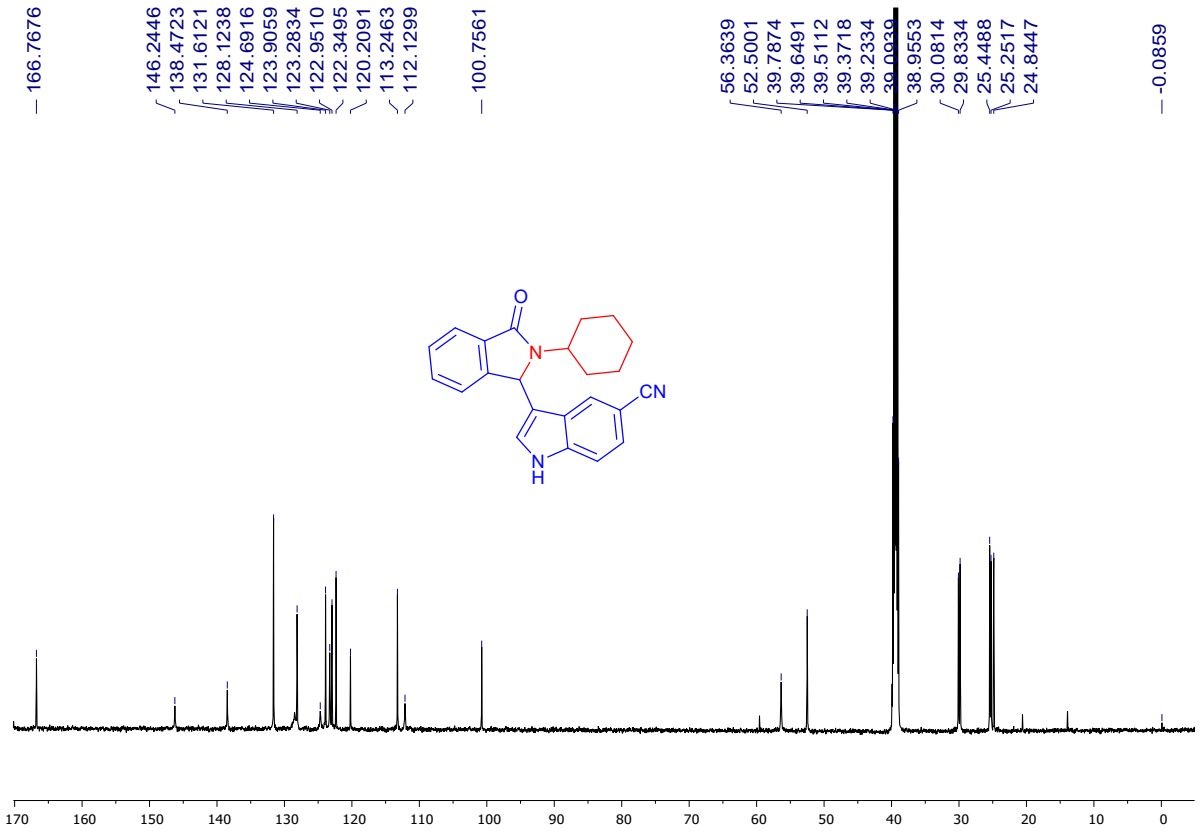
$^{13}C\{^{1}H\}$ NMR of **3l** (151 MHz, DMSO-d_6)



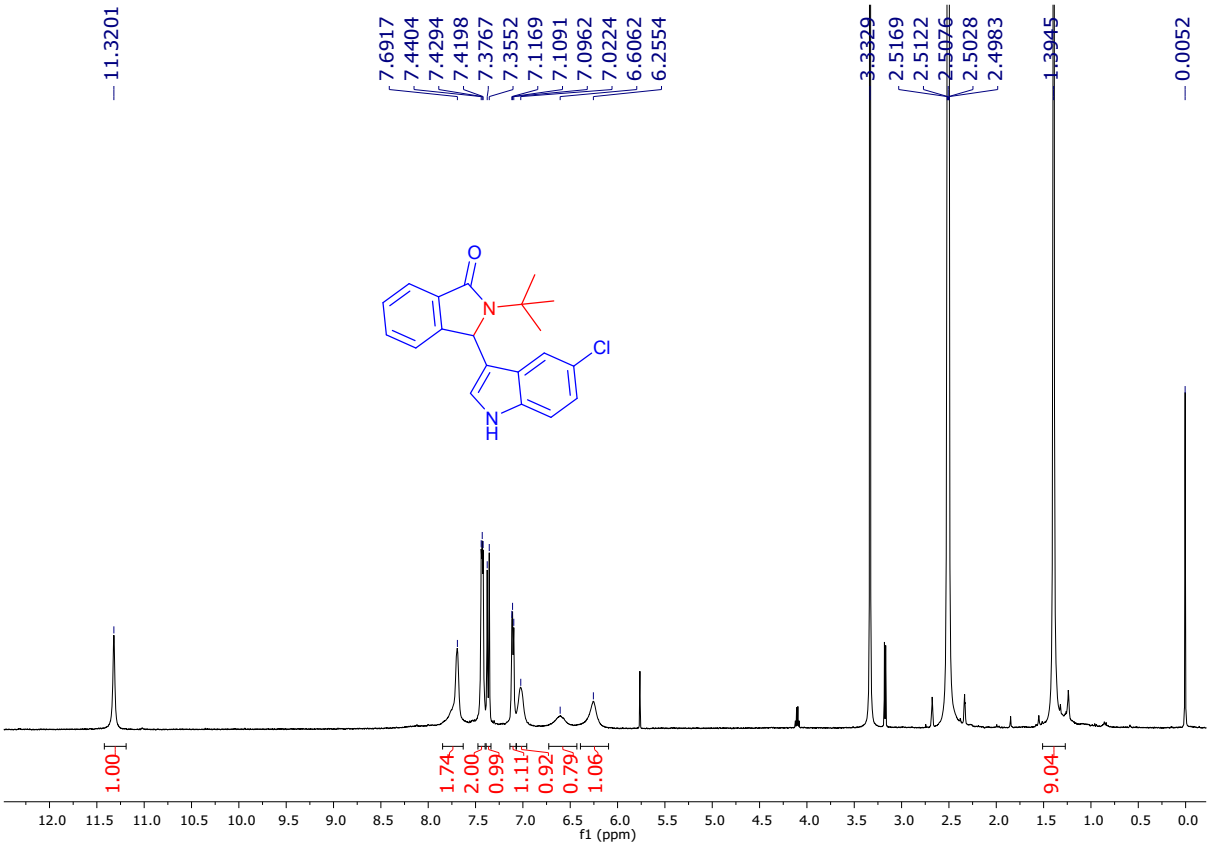
^{1}H NMR of **3m** (600 MHz, DMSO-d_6)



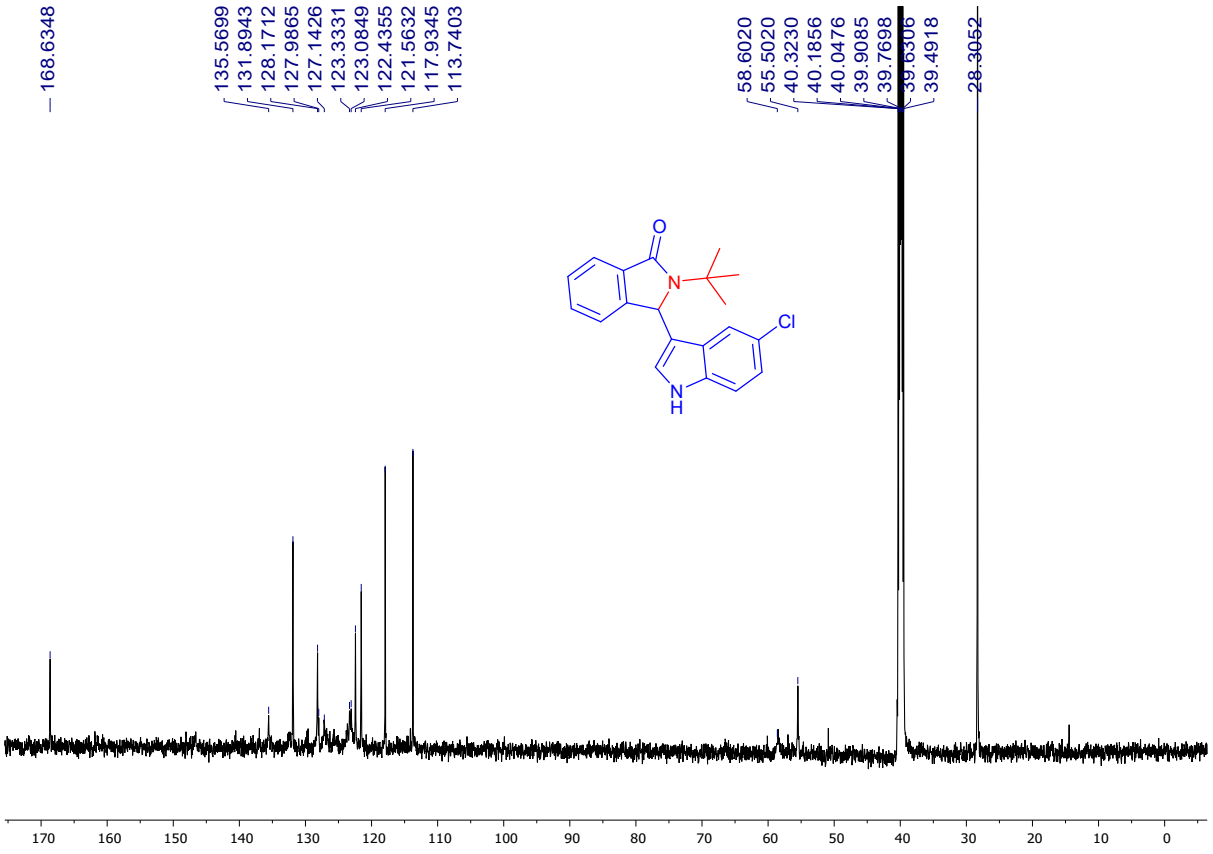
^{13}C NMR of **3m** (151 MHz, DMSO-d_6)



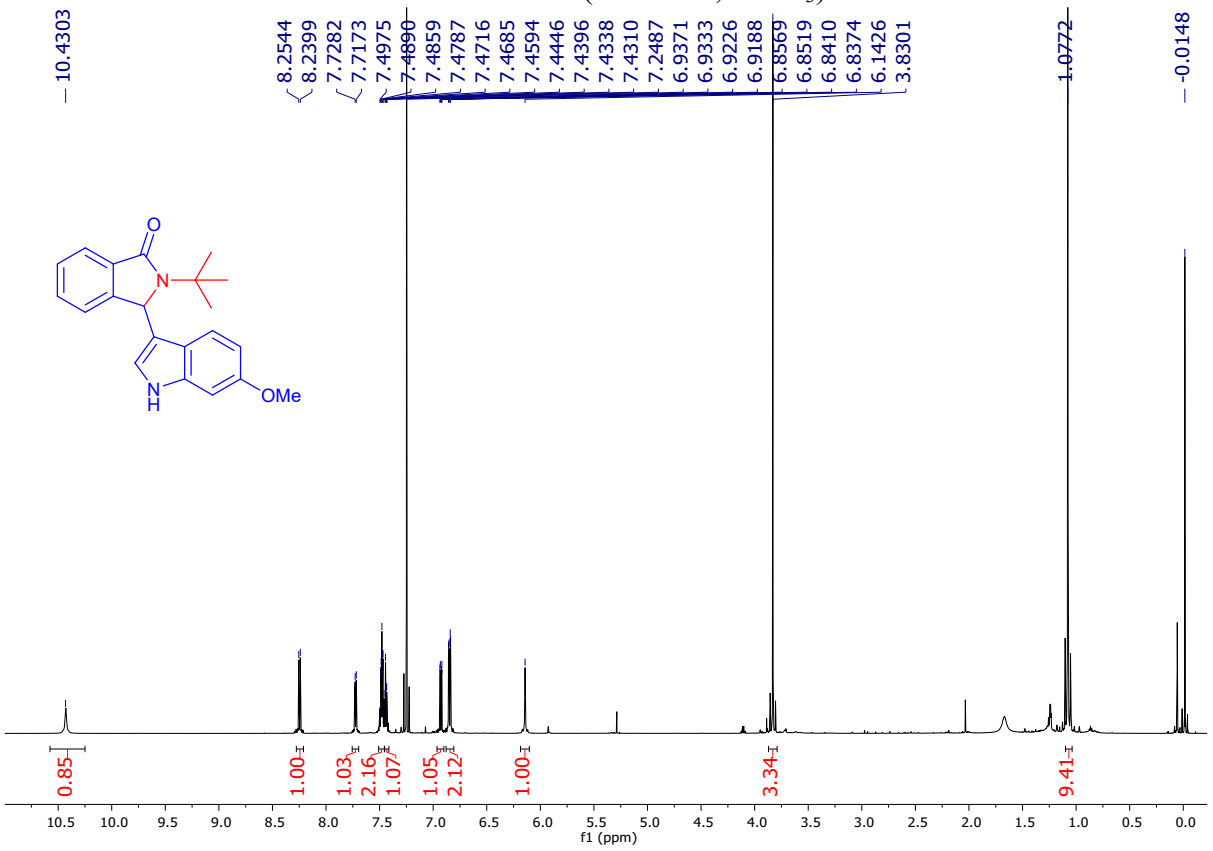
^{1}H NMR of **3n** (400 MHz, DMSO-d_6)



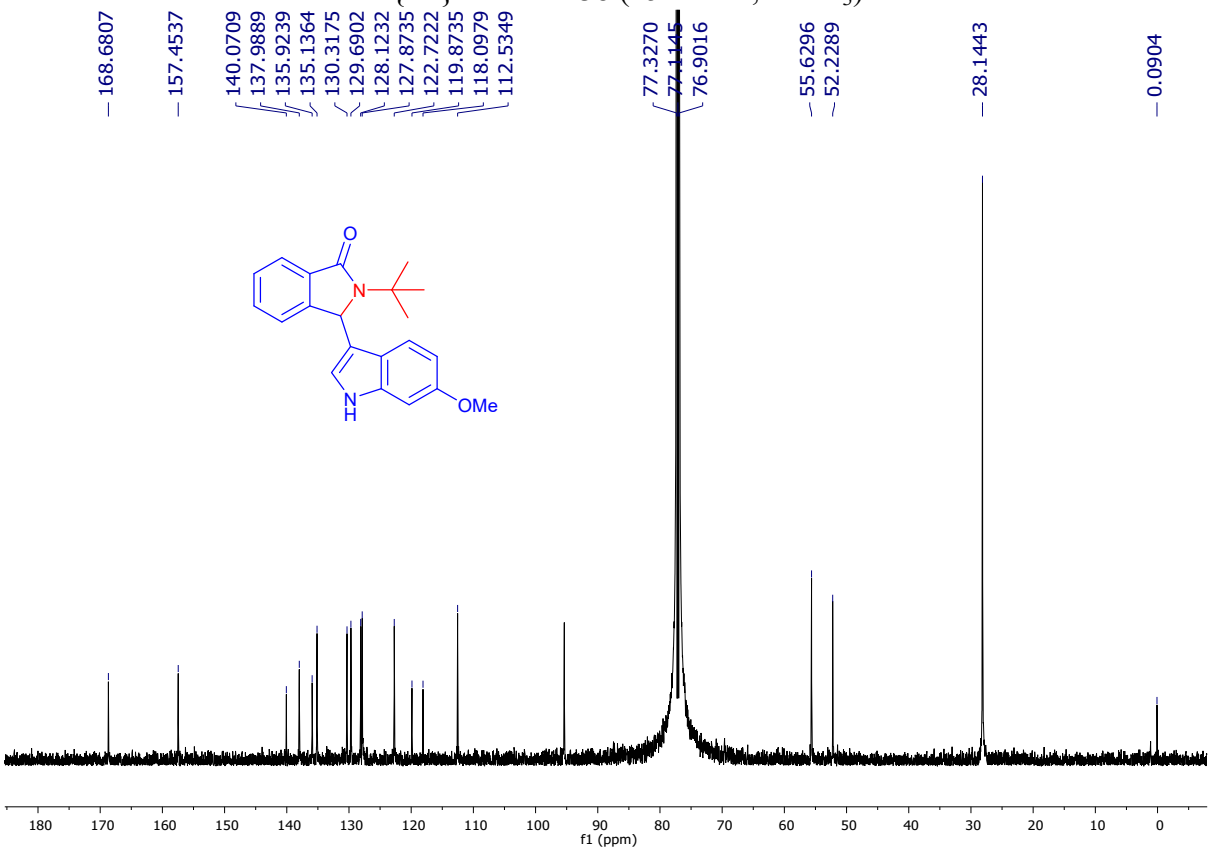
$^{13}C\{^{1}H\}$ NMR of **3n** (151 MHz, DMSO-d_6)



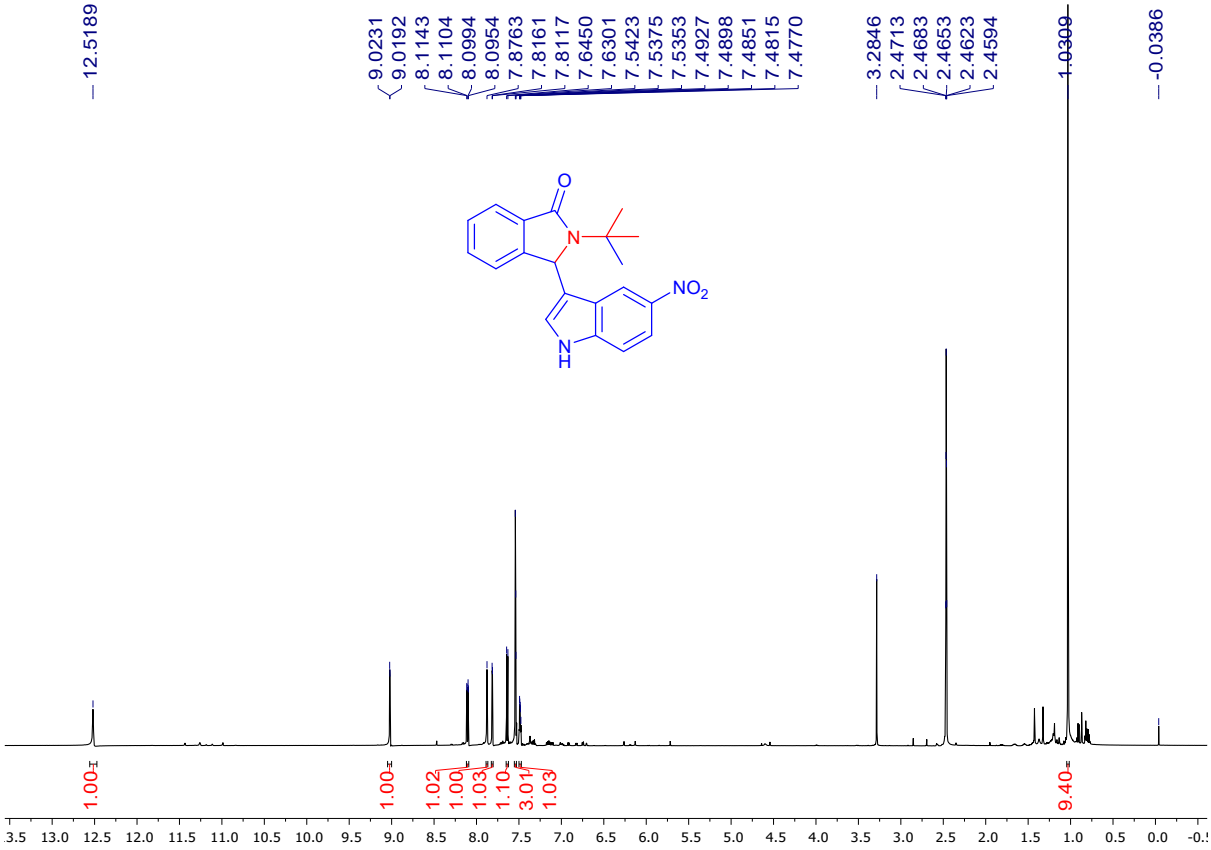
^{1}H NMR of **3o** (600 MHz, $CDCl_3$)



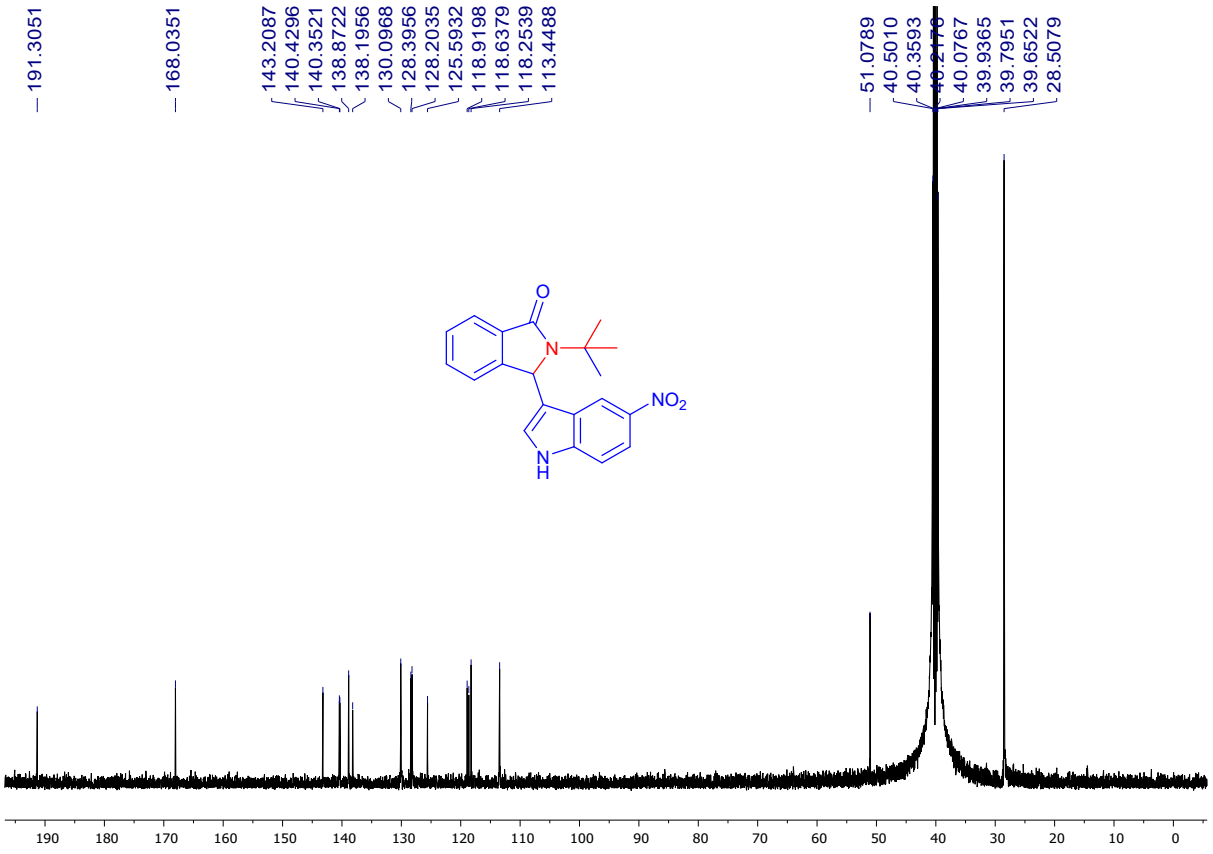
$^{13}C\{^{1}H\}$ NMR of **3o** (151 MHz, $CDCl_3$)



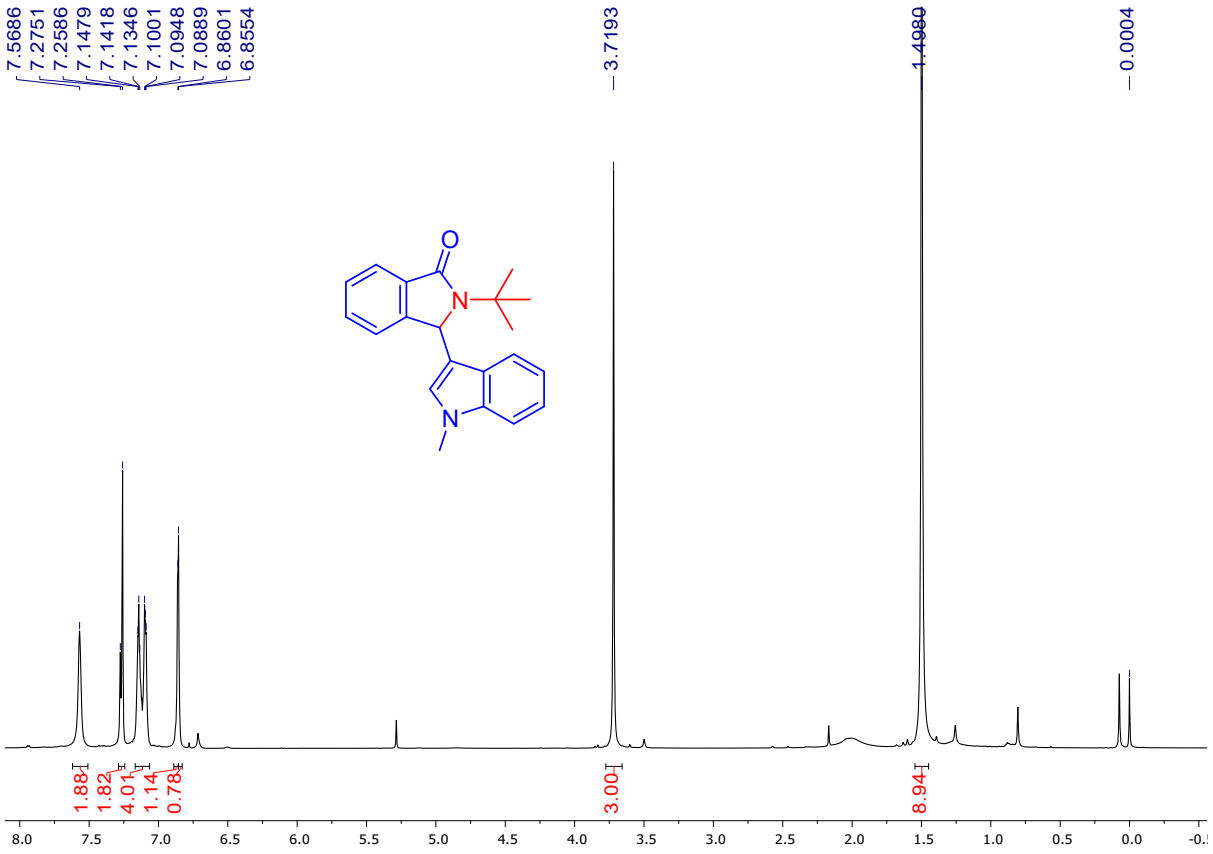
^{1}H NMR of **3p** (600 MHz, DMSO-d_6)



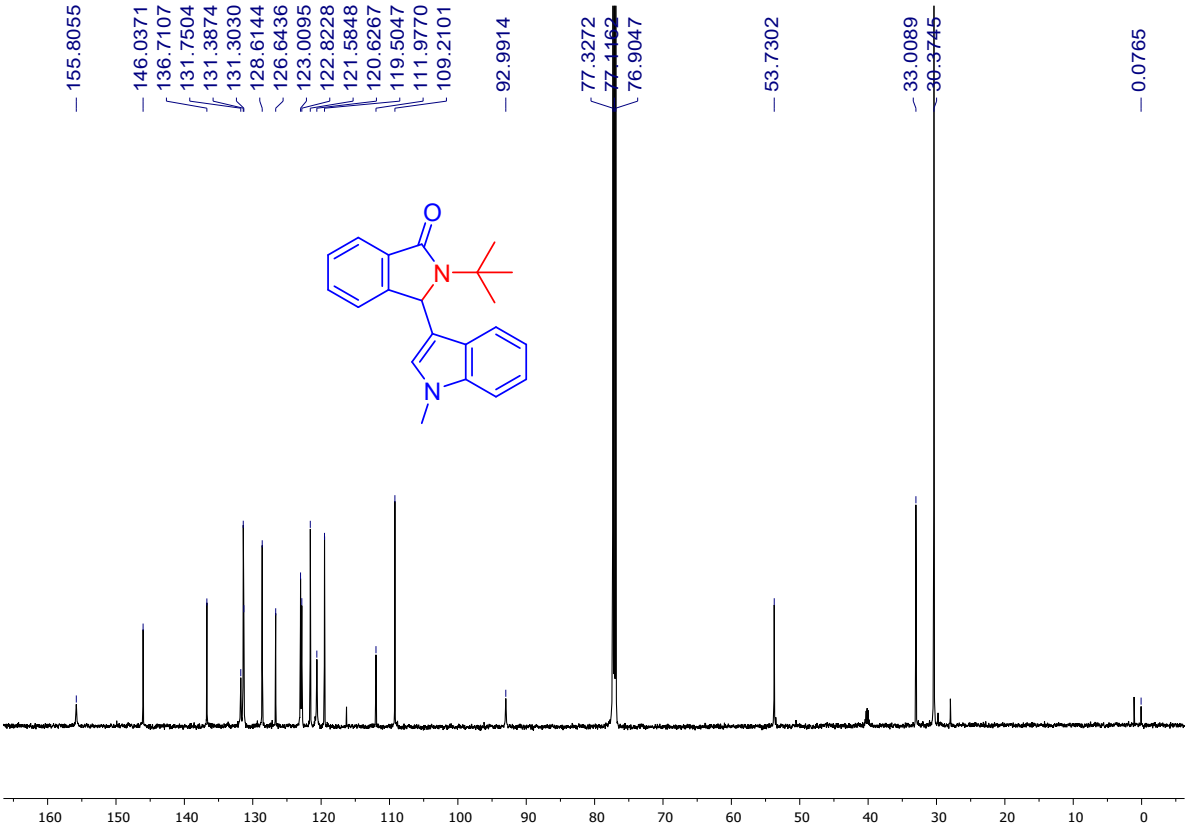
$^{13}C\{^{1}H\}$ NMR of **3p** (151 MHz, DMSO-d_6)



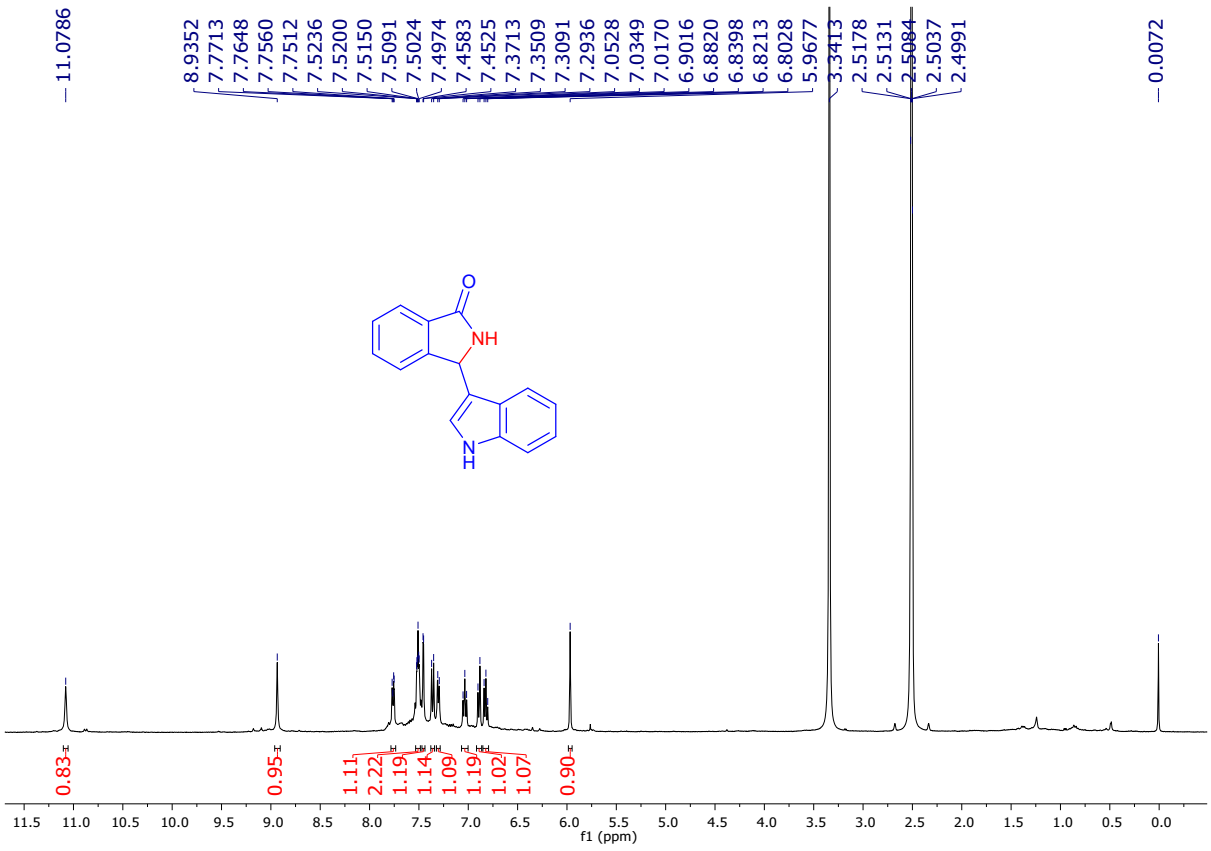
^{1}H NMR of **3q** (600 MHz, $CDCl_3$)



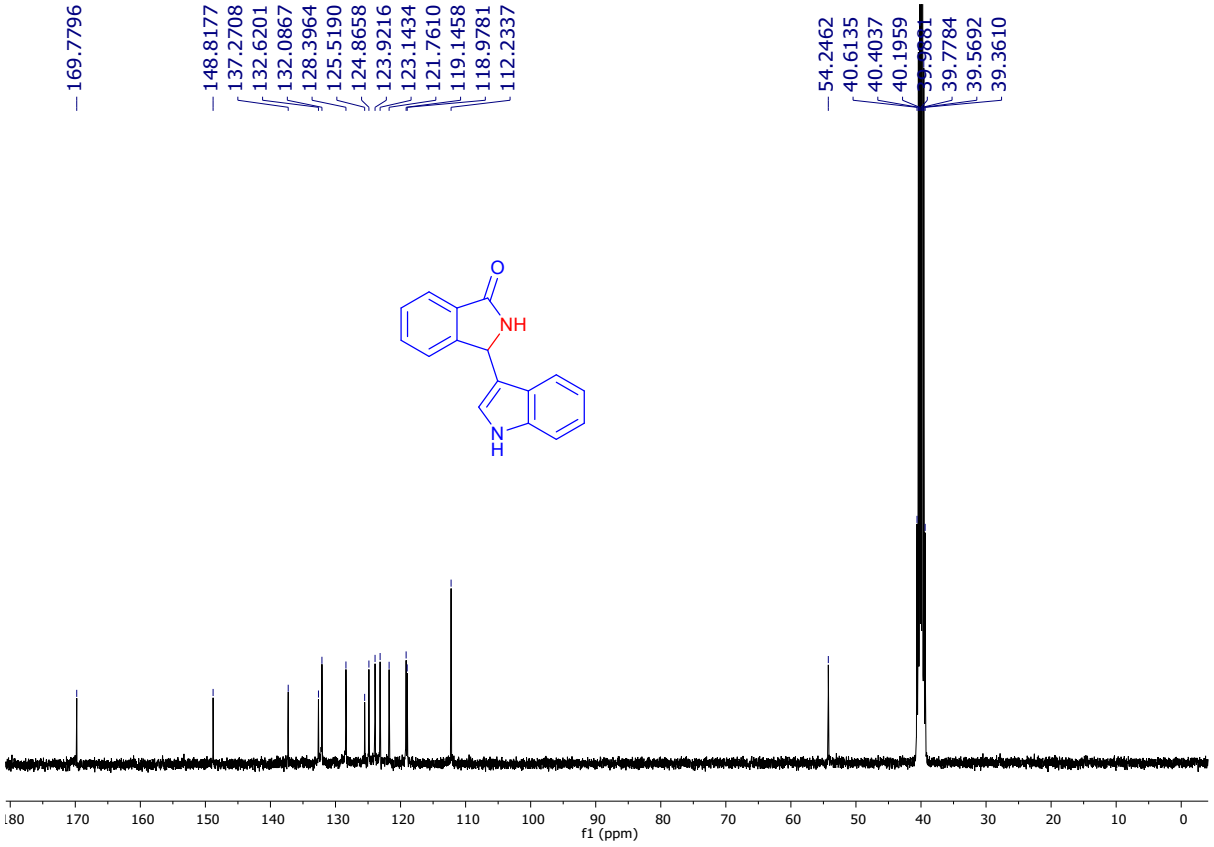
^{13}C NMR of **3q** (151 MHz, $CDCl_3$)



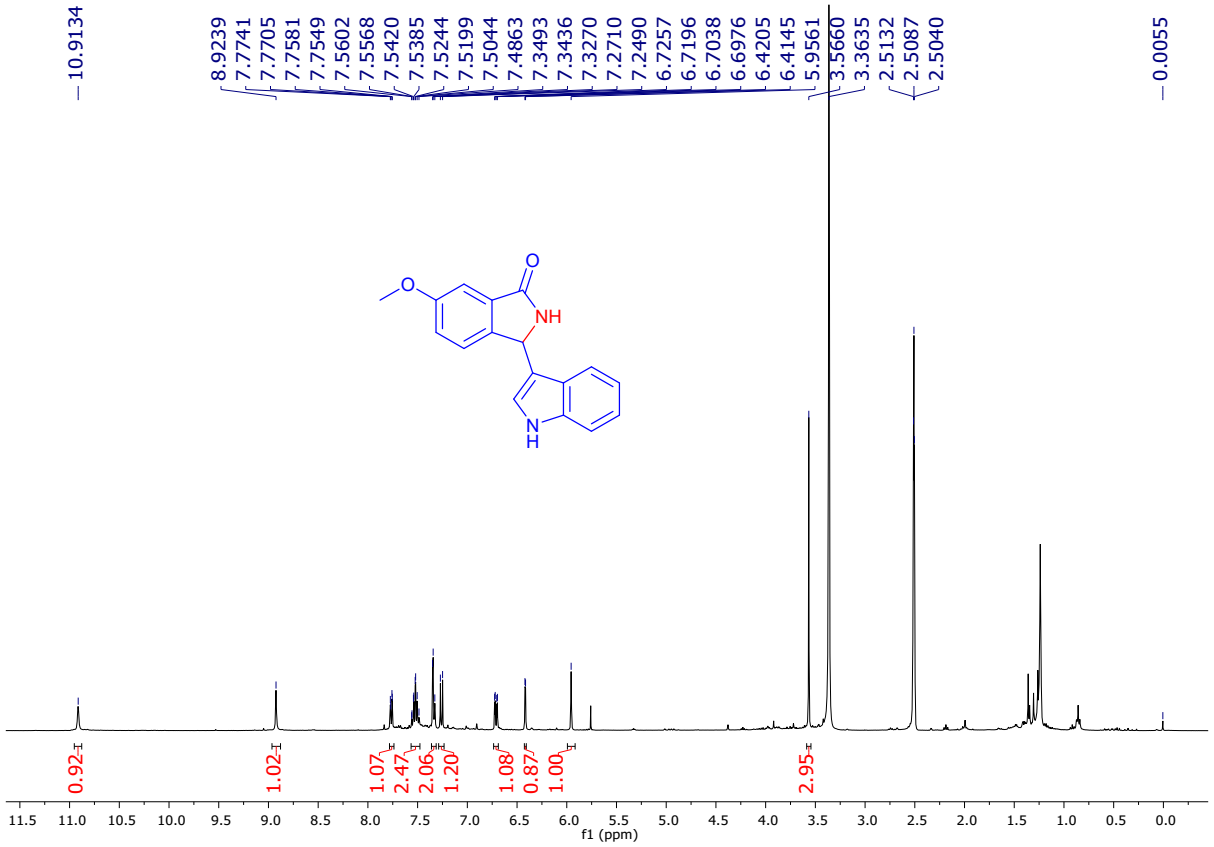
^{1}H NMR of **4a** (400 MHz, DMSO-d_6)



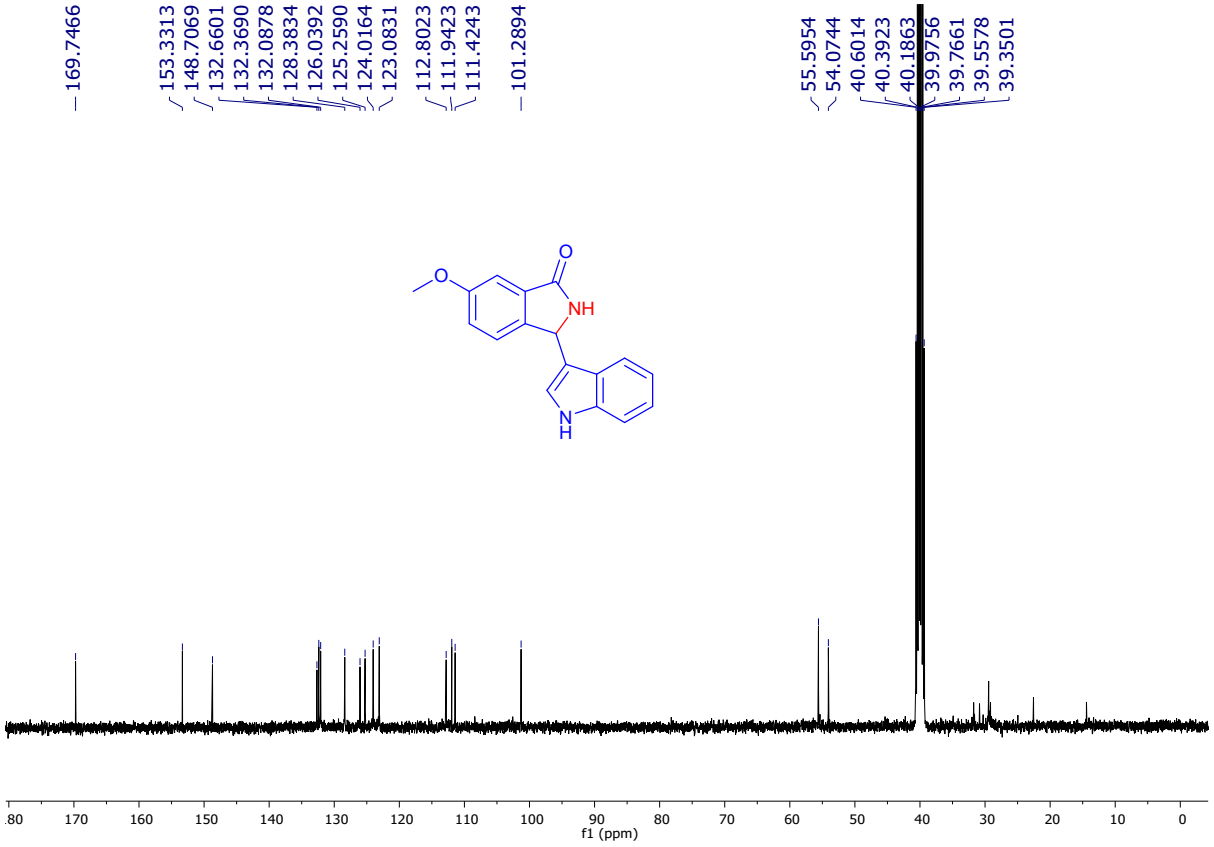
$^{13}C\{^{1}H\}$ NMR of **4a** (101 MHz, DMSO-d_6)



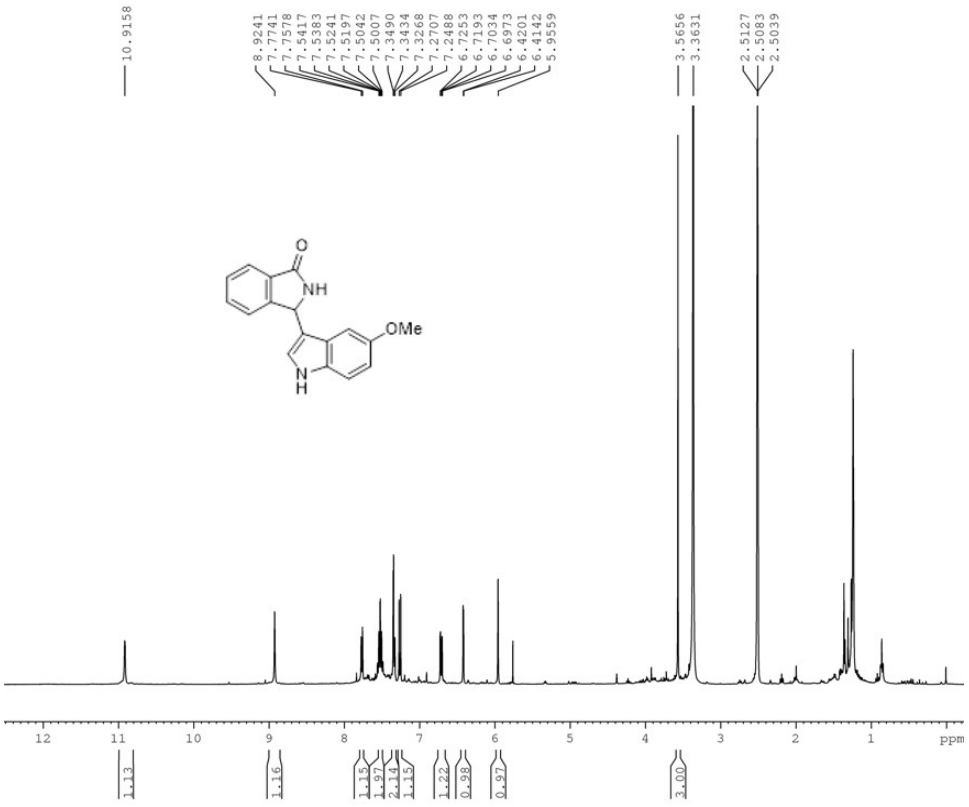
^{1}H NMR of **4b** (400 MHz, DMSO-d_6)



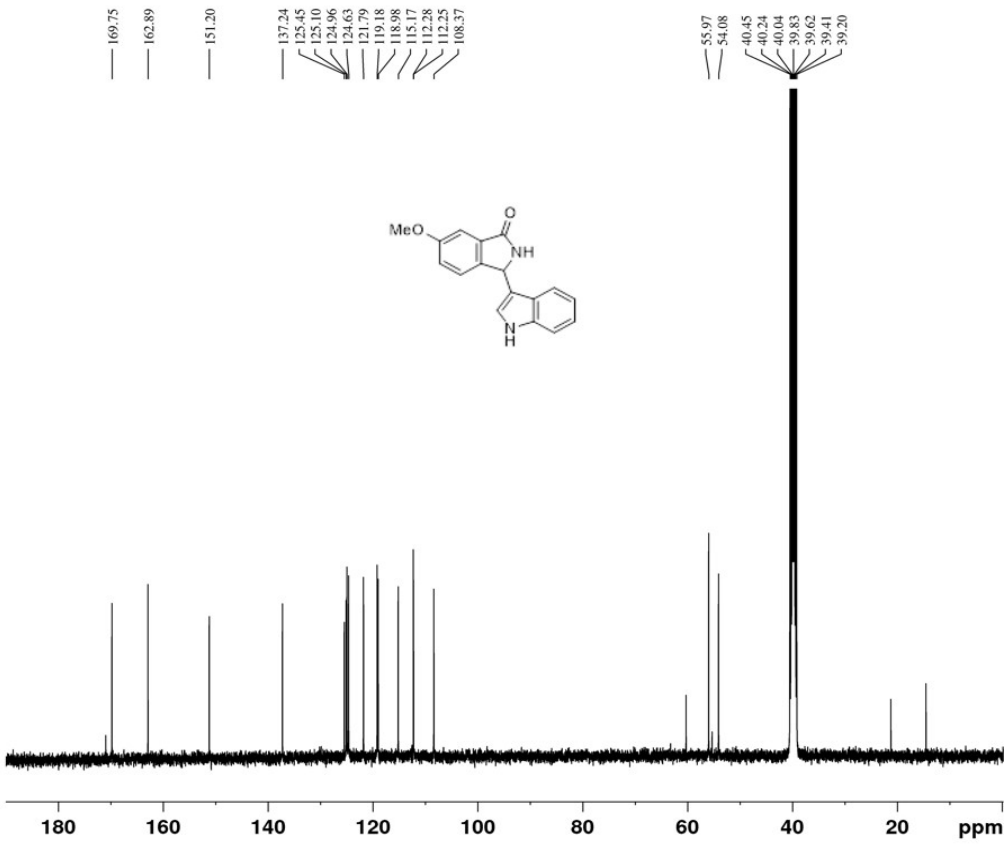
$^{13}C\{^{1}H\}$ NMR of **4b** (101 MHz, DMSO-d_6)



^{1}H NMR of **4c** (400 MHz, DMSO-d_6)



$^{13}C\{^{1}H\}$ NMR of **4c** (101 MHz, DMSO-d_6)



8. References:

1. S. K. Guchhait, M. Kashyap and H. Kamble, *J. Org. Chem*, 2011, **76**, 4753-4758.
2. S. K. Guchhait, C. Madan, *Org. Biomol. Chem*., 2010, **8**, 3631–3634.