Supporting Information

Assembly of 1*H*-Isoindole Derivatives by Selective Carbon-Nitrogen Triple Bond Activation: Access to Aggregation-Induced Emission Fluorophores for Lipid Droplets Imaging

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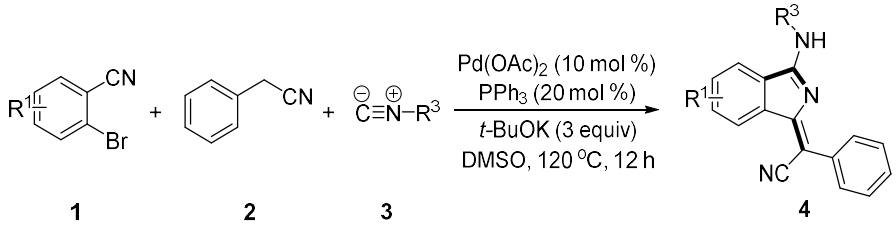
General Information

Melting points were determined with a Buchi Melting Point B-545 instrument. ^{1}H and ^{13}C NMR spectra were recorded using a Bruker DRX-400 spectrometer using DMSO-d_6 as solvent. The chemical shifts are referenced to signals at 2.50 and 44.0 ppm, respectively, and DMSO-d_6 is solvent with TMS as the internal standard. IR spectra were obtained either as potassium bromide pellets or as liquid films between two potassium bromide pellets with a Bruker TENSOR 27 spectrometer. Mass spectra were recorded on a Thermo Scientific ISQ gas chromatograph-mass spectrometer. The data of HRMS was carried out on a high-resolution mass spectrometer (LCMSIT-TOF). TLC was performed by using commercially prepared 100–400 mesh silica gel plates and visualization was effected at 254 nm. Absorption spectra were measured on a Shimadzu UV-2600 spectrophotometer. Photoluminescence spectra were obtained on a Horiba Fluoromax-4 spectrofluorometer. The absolute fluorescence quantum yield was collected using a Hamamatsu quantum yield spectrometer C11347 Quantaurus_QY. Phosphate buffered saline (PBS), streptomycin, Penicillin, Dublecco's Minimum Eagle's Medium (DMEM) and fetal bovine serum (FBS) were purchased from Thermo Fisher Scientific. HCS LipidTOX™ Deep Red neutral lipid stain was purchased from Invitrogen (Art. No.: H34477). Bodipy and Nile red were purchased from Aladdin. The HeLa was purchased from the Cell Resource Center, Peking Union Medical College. Confocal lasing scanning microscopic (CLSM) images were obtained on the confocal microscope (Zeiss Laser Scanning Confocal Microscope. Fluorescence images were obtained on the fluorescence optical microscope (Zeiss Axio Vert.A1). Automated cell counter (Countess II) was employed for cell counting. The cell viability analysis for estimating cytotoxicity was collected using a microplate reader (Tecan Infinite M200PRO) at a wavelength of 570 nm. The HPLC profiles were acquired on a Waters e2695 instrument with a SunFire C18 column (4.6 mm × 250 mm, 5 μm) and UV–Visible detector (Waters 2489) set at 315 nm, acetonitrile was used as the eluent with the flow rate of 0.6 mL min^{-1}. CH_2Cl_2 was purified by refluxing over CaH_2. Unless otherwise noted, all reagents and solvents were obtained from commercial suppliers and used without further purification.

General Experimental Procedure

A. General procedure for the synthesis of 1*H*-isoindol derivatives

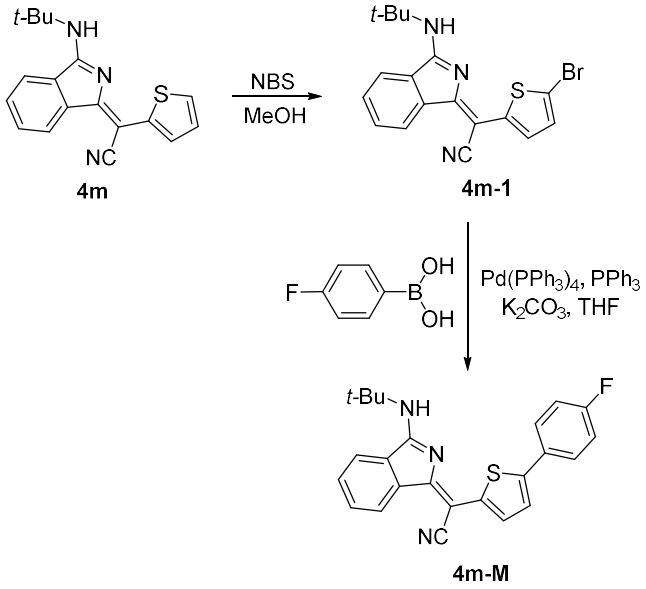


A mixture of 2-bromobenzonitriles (0.2 mmol), 2-phenylacetonitriles (0.4 mmol), and isocyanides (0.4 mmol), PPh_3 (20 mol %), $Pd(OAc)_2$ (10 mol %), *t*-BuOK (0.6 mol) was dissolved in 1.0 mL dry DMSO and stirred at 120 °C under air for 12 h. After finished, the reaction mixture was cooled to room temperature and quenched by water,

the product was extracted with ethyl acetate. The organic phase was dried over Na_2SO_4 and concentrated in vacuum, and the resulting residue was purified by silica gel column chromatography using petroleum ether/ethyl acetate/ triethylamine (5:1:1) as eluent to afford the corresponding product.

B. General procedure for the synthesis of 4m-1 and 4m-M

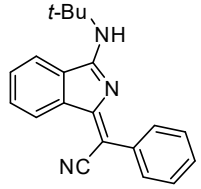
The synthesis of 4m-1: To a solution of (*Z*)-2-(3-(*tert*-butylamino)-1*H*-isoindol-1-ylidene)-2-(thiophen-2-yl)acetonitrile (61.4 mg, 0.2 mmol) in 2 mL methanol at 0 ℃ was added NBS (53.4 mg, 0.75 mmol). The reaction was stirred overnight. After finished, the reaction mixture was raised to room temperature, then Na_2SO_3 aqueous solution was added to quench the reaction. The mixture was partitioned between dichloromethane and water. The organic phase was dried ($MgSO_4$) and concentrated in vacuum. The resulting residue was purified by silica gel column chromatography using petroleum ether/dichloromethane (5:2) as eluent to afford the corresponding product **4m-1** (53.9 mg, 70% yield).



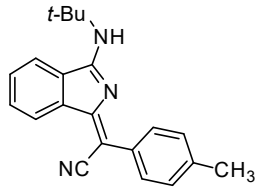
The synthesis of 4m-M: A mixture of **4m-1** (53.9 mg, 0.14 mmol), (4-fluorophenyl)boronic acid (1.5 equiv), $Pd(PPh_3)_4$ (10 mol %), PPh_3 (20 mol %), K_2CO_3 (2.5 equiv) was dissolved in 1.5 mL THF and was stirred at 80 °C for 12 h. When the reaction was complete, water was added to the reaction solution, and the mixture was extracted with dichloromethane and then, filtered after removing moisture with anhydrous $MgSO_4$ and concentrated under a reduced pressure. Then, a residue obtained therefrom was separated and purified through column chromatography using petroleum ether/ethyl acetate/ triethylamine (5:1:1) as eluent to afford the corresponding product **4m-M** (47.7 mg, 85% yield).

Characterization Data for All Products

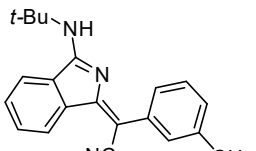
(*E*)-2-(3-(*tert*-Butylamino)-1*H*-isoindol-1-ylidene)-2-phenylacetonitrile (4a): Yield: 47 mg (79%), yellow solid. M.p.: 189 – 190 ºC. ^{1}H NMR (400 MHz, DMSO) δ ppm 8.49 (s, 1H), 8.44 (d, J = 7.7 Hz, 1H), 8.23 (d, J = 7.6 Hz, 2H), 8.19 (d, J = 7.5 Hz, 1H), 7.63 (t, J = 7.4 Hz, 1H), 7.55 (t, J = 7.4 Hz, 1H), 7.44 (t, J = 7.8 Hz, 2H), 7.30 (t, J = 7.3 Hz, 1H), 1.56 (s, 9H); ^{13}C NMR (100 MHz, DMSO) δ ppm 165.2, 158.9, 138.4, 134.3, 134.2, 130.6, 129.4, 128.9, 128.2, 127.4, 122.9, 121.5, 120.5, 92.5, 53.2, 28.6; IR (KBr, cm^{-1}): ν = 3336, 2924, 2857, 2199, 1615, 1544, 1516, 1265, 1201, 757; HRMS (ESI) calc. $C_{20}H_{19}N_3$ [M+H]$^+$: 302.1652, found: 302.1657.



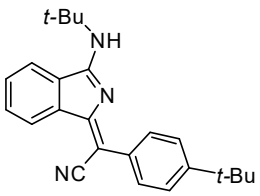
(*E*)-2-(3-(*tert*-Butylamino)-1*H*-isoindol-1-ylidene)-2-(*p*-tolyl)acetonitrile (4b): Yield: 43 mg (69%), yellow solid. M.p.: 221 – 222 ºC. ^{1}HNMR (400 MHz, DMSO) δ ppm 8.43 (d, J = 7.0 Hz, 2H), 8.18 (d, J = 7.5 Hz, 1H), 8.13 (d, J = 8.2 Hz, 2H), 7.62 (t, J = 7.5 Hz, 1H), 7.55 (t, J = 7.4 Hz, 1H), 7.26 (d, J = 8.2 Hz, 2H), 2.33 (s, 3H), 1.56 (s, 9H); ^{13}C NMR (100 MHz, DMSO) δ ppm 165.5, 158.7, 138.9, 137.5, 134.8, 131.9, 131.0, 129.8, 129.4, 123.3, 122.2, 121.1, 93.2, 53.6, 29.1, 21.2; IR (KBr, cm^{-1}): ν = 3351, 2922, 2855, 2197, 1764, 1609, 1507, 1248, 756; HRMS (ESI) calc. $C_{21}H_{21}N_3$ [M+H]$^+$: 316.1808, found: 316.1809.

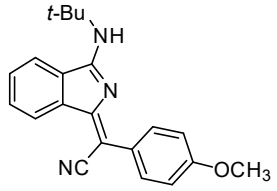


(*E*)-2-(3-(*trt*-Butylamino)-1*H*-isoindol-1-ylidene)-2-(*m*-tolyl)acetonitrile (4c): Yield: 35 mg (56%), yellow solid. M.p.: 190 – 191 ºC. ^{1}H NMR (400 MHz, DMSO) δ ppm 8.49 (s, 1H), 8.43 (d, J = 7.7 Hz, 1H), 8.24 (s, 1H), 8.18 (d, J = 7.5 Hz, 1H), 7.92 (d, J = 7.9 Hz, 1H), 7.63 (t, J = 7.5 Hz, 1H), 7.56 (t, J = 7.4 Hz, 1H), 7.33 (t, J = 7.7 Hz, 1H), 7.13 (d, J = 7.5 Hz, 1H), 2.35(s, 3H), 1.57 (s, 9H); ^{13}C NMR (100 MHz, DMSO) δ ppm 165.6, 159.3, 138.9, 137.7, 134.8, 134.6, 131.1, 130.4, 129.9, 128.6, 126.4, 123.4, 122.0, 121.0, 93.1, 53.7, 29.0, 21.6; IR (KBr, cm^{-1}): ν = 3348, 2925, 2859, 2198, 1758, 1612, 1543, 1457, 1241, 1209, 771, 693; HRMS (ESI) calc. $C_{21}H_{21}N_3$ [M+H]$^+$: 316.1808, found: 316.1811.

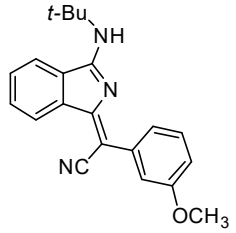


(*E*)-2-(4-(*tert*-Butyl)phenyl)-2-(3-(*tert*-butylamino)-1*H*-isoindol-1-ylidene)acetonitrile (4d): Yield: 44 mg (61%), yellow solid. M.p.: 189 – 190 ºC. ^{1}H NMR (400 MHz, DMSO) δ ppm 8.45 (d, J = 8.1 Hz, 2H), 8.26 – 8.11 (m, 3H), 7.62 (t, J = 7.5 Hz, 1H), 7.55 (t, J = 7.4 Hz, 1H), 7.46 (d, J = 8.6 Hz, 2H), 1.58(s, 9H), 1.29(s, 9H); ^{13}C NMR (100 MHz, DMSO) δ ppm 165.5, 158.8, 150.6, 139.0, 134.8, 131.9, 131.0, 129.7, 129.2, 125.5, 123.3, 122.0, 121.0, 93.2, 53.6, 34.8, 31.5, 29.2; IR (KBr, cm^{-1}): ν = 3343, 2924, 2860, 2200, 1758, 1611, 1516, 1458, 1240, 762, 697; HRMS (ESI) calc. $C_{24}H_{27}N_3$ [M+H]$^+$: 358.2278, found: 358.2278.

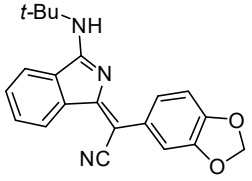


(*E*)-2-(3-(*tert*-Butylamino)-1*H*-isoindol-1-ylidene)-2-(4-methoxyphenyl)acetonitrile (4e): 

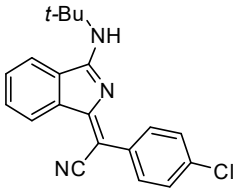
Yield: 48 mg (73%), yellow solid. M.p.: 188 – 189 ºC. ^{1}H NMR (400 MHz, DMSO) δ ppm 8.44 (d, J = 7.7 Hz, 1H), 8.37 (s, 1H), 8.23 (d, J = 8.8 Hz, 2H), 8.19 (d, J = 7.5 Hz, 1H), 7.63 (t, J = 7.5 Hz, 1H), 7.55 (t, J = 7.4 Hz, 1H), 7.04 (d, J = 8.9 Hz, 2H), 3.83 (s, 3H), 1.59 (s, 9H); ^{13}C NMR (100 MHz, DMSO) δ ppm 165.2, 159.2, 157.6, 138.9, 134.7, 130.9, 130.9, 129.6, 127.1, 123.2, 121.9, 121.1, 114.3, 93.2, 55.7, 53.5, 29.1; IR (KBr, cm^{-1}): v = 3348, 2926, 2854, 2199, 1608, 1544, 1512, 1260, 1181, 756; HRMS (ESI) calc. $C_{21}H_{21}N_3O$ $[M+H]^+$: 332.1757, found: 332.1763.

(*E*)-2-(3-(*tert*-Butylamino)-1*H*-isoindol-1-ylidene)-2-(3-methoxyphenyl)acetonitrile (4f): 

Yield: 41 mg (62%), yellow solid. M.p.: 167 – 168 ºC. ^{1}H NMR (400 MHz, DMSO) δ ppm 8.50 (s, 1H), 8.45 (d, J = 7.7 Hz, 1H), 8.17 (d, J = 8.5 Hz, 2H), 7.61 (d, J = 7.1 Hz, 2H), 7.54 (t, J = 7.4 Hz, 1H), 7.35 (t, J = 8.0 Hz, 1H), 6.88 (d, J = 8.0 Hz, 1H), 3.80 (s, 3H), 1.56 (s, 9H); ^{13}C NMR (100 MHz, DMSO) δ ppm 165.7, 159.6, 159.5, 138.9, 136.0, 134.7, 131.1, 129.9, 129.7, 123.5, 122.0, 121.5, 121.0, 114.6, 114.5, 93.0, 55.7, 53.7, 29.0; IR (KBr, cm^{-1}): v = 3344, 2966, 2854, 2199, 1764, 1610, 1542, 1318, 1233, 766; HRMS (ESI) calc. $C_{21}H_{21}N_3O$ $[M+H]^+$: 332.1757, found: 332.1753.

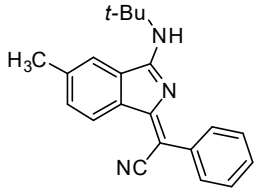
(*E*)-2-(Benzo[*d*][1,3]dioxol-5-yl)-2-(3-(*tert*-butylamino)-1*H*-isoindol-1-ylidene)acetonitrile (4h): 

Yield: 38 mg (55%), yellow solid. M.p.: 186 – 187 ºC. ^{1}H NMR (400 MHz, DMSO) δ ppm 8.44 (s, 1H), 8.41 (d, J = 7.7 Hz, 1H), 8.26 (d, J = 1.8 Hz, 1H), 8.18 (d, J = 7.5 Hz, 1H), 7.62 (t, J = 8.0 Hz, 1H), 7.55 (t, J = 7.1 Hz, 1H), 7.48 (dd, J = 8.3, 1.8 Hz, 1H), 7.02 (d, J = 8.3 Hz, 1H), 6.08 (s, 2H), 1.57 (s, 9H); ^{13}C NMR (100 MHz, DMSO) δ ppm 165.2, 157.9, 147.9, 147.2, 138.9, 134.6, 131.1, 129.7, 128.8, 123.3, 123.1, 122.0, 121.0, 109.9, 108.6, 101.9, 93.1, 53.6, 29.0; IR (KBr, cm^{-1}): v = 3358, 2988, 2861, 2199, 1764, 1376, 1242, 1055; HRMS (ESI) calc. $C_{21}H_{19}N_3O_2$ $[M+H]^+$: 346.1550, found: 346.1547.

(*E*)-2-(3-(*tert*-Butylamino)-1*H*-isoindol-1-ylidene)-2-(4-chlorophenyl)acetonitrile (4i): 

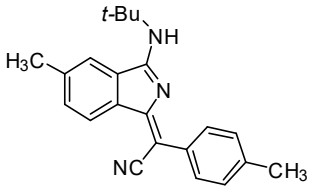
Yield: 39 mg (58%), yellow solid. M.p.: 224 – 225 ºC. ^{1}H NMR (400 MHz, DMSO) δ ppm 8.55 (s, 1H), 8.40 (d, J = 7.6 Hz, 1H), 8.22 (d, J = 8.6 Hz, 2H), 8.18 (d, J = 7.4Hz, 1H), 7.61 (t, J = 7.5 Hz, 1H), 7.55 (t, J = 7.4 Hz, 1H), 7.47 (d, J = 8.6 Hz, 2H), 1.55 (s, 9H); ^{13}C NMR (100 MHz, DMSO) δ ppm 165.9, 159.9, 138.7, 134.8, 133.7, 132.3, 131.2, 130.9, 130.0, 128.6, 123.4, 122.1, 120.7, 91.6, 53.8, 29.0; IR (KBr, cm^{-1}): v = 3352, 2926, 2859, 1759, 1608, 1540, 1505, 1251, 1120, 758; HRMS (ESI) calc. $C_{20}H_{18}ClN_3$ $[M+H]^+$: 336.1262, found: 336.1267.

(*E*)-2-(3-(*tert*-Butylamino)-5-methyl-1*H*-isoindol-1-ylidene)-2-phenylacetonitrile



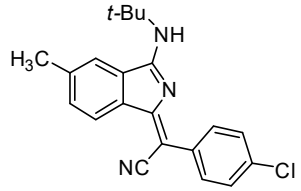
(4j): Yield: 34 mg (54%), yellow solid. M.p.: 213 – 214 ºC. ^{1}H NMR (400 MHz, DMSO) δ ppm 8.41 (s, 1H), 8.28 (d, J = 7.9 Hz, 1H), 8.21 (d, J = 8.2 Hz, 2H), 8.01 (s, 1H), 7.44 (t, J = 7.6 Hz, 3H), 7.29 (t, J = 7.3 Hz, 1H), 2.44 (s, 3H), 1.55 (s, 9H); ^{13}C NMR (100 MHz, DMSO) δ ppm 165.8, 159.6, 140.0, 136.4, 135.3, 134.8, 131.6, 129.3, 128.7, 127.8, 123.2, 122.5, 121.1, 92.4, 53.6, 29.0, 21.6; IR (KBr, cm^{-1}): ν = 2991, 2198, 1764, 1377, 1243, 1056; HRMS (ESI) calc. $C_{21}H_{21}N_3$ $[M+H]^+$: 316.1808, found: 316.1812.

(*E*)-2-(3-(*tert*-Butylamino)-5-methyl-1*H*-isoindol-1-ylidene)-2-(*p*-tolyl)acetonitrile



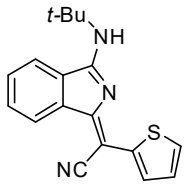
(4k): Yield: 34 mg (51%), yellow solid. M.p.: 214 – 215 ºC. ^{1}H NMR (400 MHz, DMSO) δ ppm 8.35 (s, 1H), 8.27 (d, J = 7.9 Hz, 1H), 8.11 (d, J = 8.2 Hz, 2H), 8.00 (s, 1H), 7.42 (d, J = 8.0 Hz, 1H), 7.25 (d, J = 8.1 Hz, 2H), 2.43 (s, 3H), 2.33 (s, 3H), 1.55 (s, 9H); ^{13}C NMR (100 MHz, DMSO) δ ppm 165.5, 158.8, 139.8, 137.4, 136.4, 135.2, 131.9, 131.6, 129.3, 129.3, 123.1, 122.4, 121.1, 92.7, 53.6, 29.0, 21.6, 21.2; IR (KBr, cm^{-1}): ν = 3346, 2926, 2857, 2199, 1763, 1242, 1057; HRMS (ESI) calc. $C_{22}H_{23}N_3$ $[M+H]^+$: 330.1965, found: 330.1967.

(*E*)-2-(3-(*tert*-Butylamino)-5-methyl-1*H*-isoindol-1-ylidene)-2-(4-chlorophenyl)acetonitrile (4l):

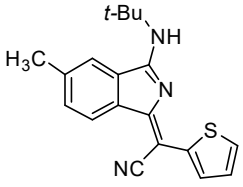


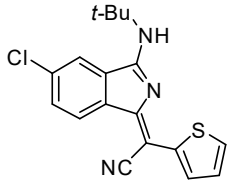
Yield: 33 mg (47%), yellow solid. M.p.: 157 – 158 ºC. ^{1}H NMR (400 MHz, DMSO) δ ppm 8.51 (s, 1H), 8.26 (d, J = 8.0 Hz, 1H), 8.22 (d, J = 8.3 Hz, 2H), 8.03 (s, 1H), 7.50 (d, J = 8.4 Hz, 2H), 7.45 (d, J = 8.0 Hz, 1H), 2.44 (s, 3H), 1.55 (s, 9H); ^{13}C NMR (100 MHz, DMSO) δ ppm 165.9, 160.1, 140.3, 136.2, 135.3, 133.8, 132.2, 131.8 130.9, 128.7, 123.2, 122.7, 120.8, 91.0, 53.8, 29.1, 21.6; IR (KBr, cm^{-1}): ν = 2926, 2859, 2202, 1764, 1378, 1242, 1057, 697; HRMS (ESI) calc. $C_{21}H_{20}ClN_3$ $[M+H]^+$: 350.1419, found: 350.1423.

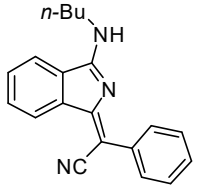
(*Z*)-2-(3-(*tert*-Butylamino)-1*H*-isoindol-1-ylidene)-2-(thiophen-2-yl)acetonitrile

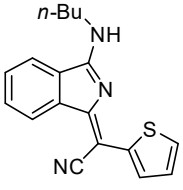


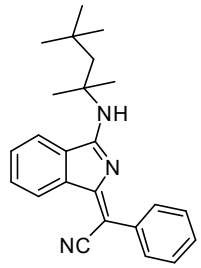
(4m): Yield: 45 mg (74%), orange solid. M.p.: 205 – 206 ºC. ^{1}H NMR (400 MHz, DMSO) δ ppm 8.58 (s, 1H), 8.29 (d, J = 7.7 Hz, 1H), 8.20 (d, J = 7.52 Hz, 1H), 7.67 (d, J = 5.12 Hz, 1H), 7.62 (t, J = 7.5 Hz, 1H), 7.54 (t, J = 7.4 Hz, 1H), 7.38 (d, J = 3.6 Hz, 1H), 7.13 (t, J = 4.4 Hz, 1H), 1.65 (s, 9H); ^{13}C NMR (100 MHz, DMSO) δ ppm 164.4, 155.7, 137.9, 137.6, 135.3, 131.1, 130.5, 129.7, 126.9, 126.8, 122.6, 122.4, 119.3, 89.5, 53.8, 28.6; IR (KBr, cm^{-1}): ν = 3345, 2923, 2856, 2201, 1614, 1549, 1511, 1267, 1203, 755; HRMS (ESI) calc. $C_{18}H_{17}N_3S$ $[M+H]^+$: 308.1216, found: 308.1219.

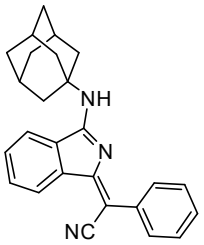
(*Z*)-2-(3-(*tert*-Butylamino)-5-methyl-1*H*-isoindol-1-ylidene)-2-(thiophen-2-yl)acetonitrile (4n): 
Yield: 32 mg (50%), orange solid. M.p.: 258 – 259 ºC. ^{1}H NMR (400 MHz, DMSO) δ ppm 8.50 (s, 1H), 8.12 (d, J = 7.9 Hz, 1H), 8.01 (s, 1H), 7.64 (d, J = 5.1 Hz, 1H), 7.41 (d, J = 7.9 Hz, 1H), 7.34 (d, J = 3.6 Hz, 1H), 7.11 (dd, J = 5.1, 3.8 Hz, 1H), 2.43 (s, 3H), 1.63 (s, 9H); ^{13}C NMR (100 MHz, DMSO) δ ppm 164.5, 155.9, 139.8, 137.6, 135.7, 135.4, 131.7, 130.3, 126.9, 126.5, 122.9, 122.4, 119.3, 88.9, 53.7, 28.5, 21.6; IR (KBr, cm^{-1}): ν = 2924, 2856, 1764, 1377, 1242, 1055; HRMS (ESI) calc. $C_{19}H_{19}N_3S$ $[M+H]^+$: 322.1372, found: 322.1378.

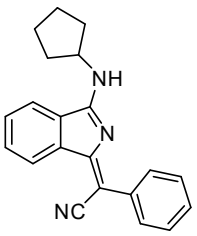
(*Z*)-2-(3-(*tert*-Butylamino)-5-chloro-1*H*-isoindol-1-ylidene)-2-(thiophen-2-yl)acetonitrile (4o): 
Yield: 31 mg (45%), orange solid. M.p.: 263 – 264 ºC. ^{1}H NMR (400 MHz, DMSO) δ ppm 8.61 (s, 1H), 8.35 (s, 1H), 8.22 (d, J = 8.3 Hz, 1H), 7.74 – 7.63 (m, 2H), 7.38 (d, J = 3.7 Hz, 1H), 7.12 (t, J = 4.4 Hz, 1H), 1.63 (s, 9H); ^{13}C NMR (100 MHz, DMSO) δ ppm 162.9, 154.4, 137.3, 137.0, 136.5, 134.5, 131.0, 130.8, 127.3, 127.1, 123.9, 122.6, 119.0, 90.4, 53.9, 28.4; IR (KBr, cm^{-1}): ν = 2989, 2856, 1764, 1376, 1242, 1055; HRMS (ESI) calc. $C_{18}H_{16}ClN_3S$ $[M+H]^+$: 342.0826, found: 342.0823.

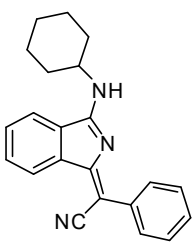
(*E*)-2-(3-(Butylamino)-1*H*-isoindol-1-ylidene)-2-phenylacetonitrile (4p): 
Yield: 50 mg (84%), yellow solid. M.p.: 196 – 197 ºC. ^{1}H NMR (400 MHz, DMSO) δ ppm 9.16 (s, 1H), 8.45 (d, J = 7.6 Hz, 1H), 8.28 (d, J = 7.7 Hz, 2H), 8.01 (d, J = 7.3 Hz, 1H), 7.65 (t, J = 7.5 Hz, 1H), 7.58 (t, J = 7.3 Hz, 1H), 7.44 (t, J = 7.6 Hz, 2H), 7.31 (t, J = 7.1 Hz, 1H), 3.64 (dd, J = 12.7, 6.4 Hz, 2H), 1.88 – 1.61 (m, 2H), 1.57 – 1.31 (m, 2H), 0.95 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, DMSO) δ ppm167.2, 159.6, 140.1, 134.8, 133.7, 131.3, 130.1, 129.5, 128.7, 127.8, 123.6, 121.6, 121.1, 92.6, 42.7, 31.3, 20.1, 14.1; IR (KBr, cm^{-1}): ν = 2989, 2856, 2199, 1764, 1376, 1242, 1054; HRMS (ESI) calc. $C_{20}H_{19}N_3$ $[M+H]^+$: 302.1652, found: 302.1657.

(*Z*)-2-(3-(Butylamino)-1*H*-isoindol-1-ylidene)-2-(thiophen-2-yl)acetonitrile (4q): 
Yield: 48 mg (78%), orange solid. M.p.: 187 – 188 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 9.27 (s, 1H), 8.26 (d, J = 7.7 Hz, 1H), 7.99 (d, J = 7.4 Hz, 1H), 7.63 (dd, J = 9.6, 5.3 Hz, 2H), 7.55 (t, J = 7.4 Hz, 1H), 7.38 (d, J = 3.6 Hz, 1H), 7.11 (t, J = 4.4 Hz, 1H), 3.77 – 3.62 (m, 2H), 1.83 – 1.64 (m, 2H), 1.52 – 1.33 (m, 2H), 0.95 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm 170.8, 160.7, 143.8, 142.8, 138.8, 136.1, 135.3, 134.6, 131.6, 131.3, 127.5, 126.7, 124.0, 93.8, 47.8, 35.8, 25.0, 18.9; IR (KBr, cm^{-1}): ν = 3267, 2957, 2860, 2199, 1764, 1377, 1243, 1055; HRMS (ESI) calc. $C_{18}H_{17}N_3S$ $[M+H]^+$: 308.1216, found: 308.1219.

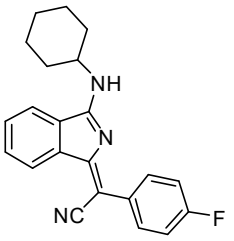
(*E*)-2-Phenyl-2-(3-((2,4,4-trimethylpentan-2-yl)amino)-1*H*-isoindol-1-ylidene)acetonitrile (4r): 
Yield: 38 mg (53%), yellow oil. ^{1}H NMR (400 MHz, DMSO) δ ppm 8.45 (d, J = 7.7 Hz, 1H), 8.34 (s, 1H), 8.23 (t, J = 8.5 Hz, 3H), 7.63 (t, J = 7.5 Hz, 1H), 7.56 (t, J = 7.4 Hz, 1H), 7.42 (t, J = 7.7 Hz, 2H), 7.30 (t, J = 7.3 Hz, 1H), 2.09 (s, 2H), 1.57 (s, 6H), 0.92 (s, 9H); ^{13}C NMR (100 MHz, DMSO) δ ppm 165.7, 159.5, 138.9, 135.0, 134.8, 131.1, 129.9, 129.5, 128.6, 127.9, 123.4, 122.0, 121.1, 92.8, 57.5, 50.3, 31.9, 31.5, 29.9; IR (KBr, cm^{-1}): ν = 2924, 2857, 2200, 1764, 1377, 1243, 1057; HRMS (ESI) calc. $C_{24}H_{27}N_3$ $[M+H]^+$: 358.2278, found: 358.2276.

2-((*E*)-3-((Adamantan-1-yl)amino)-1*H*-isoindol-1-ylidene)-2-phenylacetonitrile (4s): 
Yield: 38 mg (50%), yellow solid. M.p.: 236 – 237 ºC. ^{1}H NMR (400 MHz, DMSO) δ ppm 8.47 (s, 1H), 8.42 (d, J = 7.7 Hz, 1H), 8.28 (d, J = 7.7 Hz, 2H), 8.19 (d, J = 7.5 Hz, 1H), 7.63 (t, J = 7.5 Hz, 1H), 7.55 (t, J = 7.4 Hz, 1H), 7.42 (t, J = 7.7 Hz, 2H), 7.31 (t, J = 7.3 Hz, 1H), 2.28 (s, 7H), 2.12 (s, 3H), 1.70 (s, 7H); ^{13}C NMR (100 MHz, DMSO) δ ppm 165.3, 159.3, 138.9, 134.8, 134.7, 131.1, 129.9, 129.4, 128.6, 127.9, 123.4, 122.1, 121.0, 92.7, 54.4, 41.1, 36.4, 29.5; IR (KBr, cm^{-1}): ν = 2991, 2856, 2199, 1764, 1377, 1243, 1058; HRMS (ESI) calc. $C_{26}H_{25}N_3$ $[M+H]^+$: 380.2121, found: 380.2127.

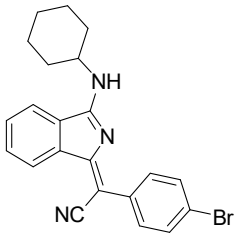
(*E*)-2-(3-(Cyclopentylamino)-1*H*-isoindol-1-ylidene)-2-phenylacetonitrile (4t): 
Yield: 47 mg (75%), yellow solid. M.p.: 193 – 194 ºC. ^{1}H NMR (400 MHz, DMSO) δ ppm 9.00 (d, J = 6.8 Hz, 1H), 8.44 (d, J = 7.7 Hz, 1H), 8.27 (d, J = 8.1 Hz, 2H), 8.07 (d, J = 7.4 Hz, 1H), 7.64 (t, J = 7.5 Hz, 1H), 7.57 (t, J = 7.5 Hz, 1H), 7.45 (t, J = 7.7 Hz, 2H), 7.30 (t, J = 7.1 Hz, 1H), 4.56 – 4.44 (m, 1H), 2.06 (dd, J = 13.5, 5.2 Hz, 2H), 1.81 – 1.68 (m, 4H), 1.67 – 1.54 (m, 2H); ^{13}C NMR (100 MHz, DMSO) δ ppm 166.5, 159.5, 140.0, 134.8, 133.8, 131.2, 129.9, 129.6, 128.7, 127.8, 123.5, 121.8, 121.1, 92.7, 54.9, 32.8, 24.4; IR (KBr, cm^{-1}): ν = 3262, 2956, 2867, 2197, 1764, 1621, 1550, 1510, 1246, 1054, 762, 695; HRMS (ESI) calc. $C_{21}H_{19}N_3$ $[M+H]^+$: 314.1652, found: 314.1653.

(*E*)-2-(3-(Cyclohexylamino)-1*H*-isoindol-1-ylidene)-2-phenylacetonitrile (4u): 
Yield: 54 mg (83%), yellow solid. M.p.: 206 – 207 ºC. ^{1}H NMR (400 MHz, DMSO) δ ppm 8.99 (s, 1H), 8.44 (d, J = 7.7 Hz, 1H), 8.26 (d, J = 7.8 Hz, 2H), 8.08 (d, J = 7.3 Hz, 1H), 7.64 (t, J = 7.5 Hz, 1H), 7.57 (t, J = 7.4 Hz, 1H), 7.44 (t, J = 7.7 Hz, 2H), 7.30 (t, J = 7.3 Hz, 1H), 4.04 (dd, J = 12.4, 8.8 Hz, 1H), 2.07 (d, J = 11.2 Hz, 2H), 1.81 (d, J = 12.6 Hz, 2H), 1.66 (d, J = 12.7 Hz, 1H), 1.53 – 1.30 (m, 4H), 1.21 (dd, J = 23.7, 12.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO) δ ppm 166.2, 159.6, 140.0, 134.8, 133.8, 131.3, 130.0, 129.5, 128.7, 127.8, 123.5, 121.8, 121.1, 92.5, 52.9, 32.5, 25.7, 25.2; IR (KBr, cm^{-1}): ν = 2933, 2197, 1764, 1377, 1243, 1056; HRMS

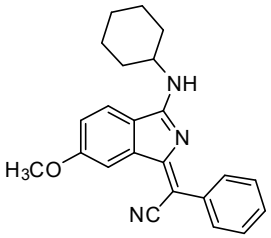
(ESI) calc. $C_{22}H_{21}N_3$ $[M+H]^+$: 328.2121, found: 328.1811.

(*E*)-2-(3-(Cyclohexylamino)-1*H*-isoindol-1-ylidene)-2-(4-fluorophenyl)acetonitrile (4v): 

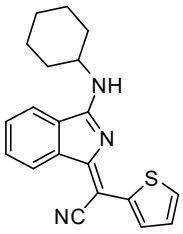
Yield: 47 mg (68%), yellow solid. M.p.: 227 – 228 ºC. ^{1}H NMR (400 MHz, DMSO) δ ppm 8.99 (d, J = 7.2 Hz, 1H), 8.40 (d, J = 7.6 Hz, 1H), 8.29 (dd, J = 7.9, 5.7 Hz, 2H), 8.06 (d, J = 7.2 Hz, 1H), 7.63 (t, J = 7.5 Hz, 1H), 7.56 (t, J = 7.3 Hz, 1H), 7.27 (t, J = 8.6 Hz, 2H), 4.02 (d, J = 6.9 Hz, 1H), 2.06 (d, J = 9.6 Hz, 2H), 1.80 (d, J = 11.0 Hz, 2H), 1.65 (d, J = 12.1 Hz, 1H), 1.54 – 1.30 (m, 4H), 1.31 – 1.08 (m, 1H); ^{13}C NMR (100 MHz, DMSO) δ ppm 166.2, 161.6 (d, J = 245.0 Hz), 159.4, 139.9, 133.7, 131.5 (d, J = 8.0 Hz), 131.3, 131.2 (d, J = 3.2 Hz), 130.0, 123.5, 121.8, 121.0, 115.6 (d, J = 21.4 Hz), 91.3, 52.9, 32.5, 25.6, 25.2; IR (KBr, cm^{-1}): v = 2991, 2192, 1764, 1377, 1243, 1056; HRMS (ESI) calc. $C_{22}H_{20}FN_3$ $[M+H]^+$: 346.1714, found: 346.1718.

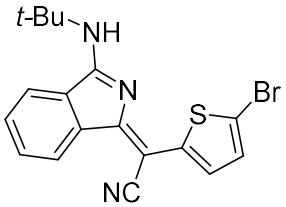
(*E*)-2-(4-Bromophenyl)-2-(3-(cyclohexylamino)-1*H*-isoindol-1-ylidene)acetonitrile (4w): 

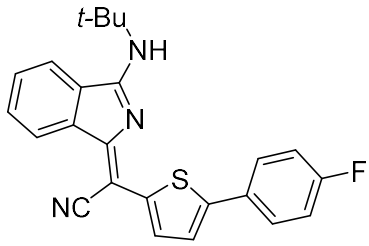
Yield: 43 mg (53%), yellow solid. M.p.: 254 – 255 ºC.^{1}H NMR (400 MHz, DMSO) δ ppm 9.09 (d, J = 7.5 Hz, 1H), 8.40 (d, J = 7.7 Hz, 1H), 8.21 (d, J = 8.7 Hz, 2H), 8.07 (d, J = 7.4 Hz, 1H), 7.64 (t, J = 8.8 Hz, 3H), 7.57 (t, J = 7.4 Hz, 1H), 4.04 (dd, J = 7.0, 2.9 Hz, 1H), 2.06 (d, J = 9.3 Hz, 2H), 1.80 (d, J = 11.6 Hz, 2H), 1.66 (d, J = 12.3 Hz, 1H), 1.51 – 1.36 (m, 4H), 1.24 (dd, J = 22.2, 12.1 Hz, 1H). ^{13}C NMR (100 MHz, DMSO) δ ppm 166.3, 160.2, 139.9, 134.1, 133.8, 131.6, 131.4, 131.3, 130.1, 123.6, 121.9, 120.8, 120.7, 91.1, 53.0, 32.5, 25.6, 25.2; IR (KBr, cm^{-1}): v = 3303, 2925, 2886, 2199, 1764, 1458, 1377, 1243, 1057; HRMS (ESI) calc. $C_{22}H_{20}BrN_3$ $[M+H]^+$: 406.0913, found: 406.0919.

(*E*)-2-(3-(Cyclohexylamino)-6-methoxy-1*H*-isoindol-1-ylidene)-2-phenylacetonitrile (4x): 

Yield: 31 mg (44%), yellow solid. M.p.: 231 – 232 ºC. ^{1}H NMR (400 MHz, DMSO) δ ppm 8.87 (d, J = 7.5 Hz, 1H), 8.25 (d, J = 7.5 Hz, 2H), 7.95 (d, J = 8.7 Hz, 2H), 7.42 (t, J = 7.8 Hz, 2H), 7.28 (t, J = 7.3 Hz, 1H), 7.11 (dd, J = 8.4, 2.2 Hz, 1H), 4.07 – 3.92 (m, 1H), 3.86 (s, 3H), 2.05 (d, J = 10.7 Hz, 2H), 1.79 (d, J = 12.5 Hz, 2H), 1.64 (d, J = 12.8 Hz, 1H), 1.49 – 1.28 (m, 4H), 1.27 – 1.11 (m, 1H); ^{13}C NMR (100 MHz, DMSO) δ ppm 166.1, 162.3, 159.5, 142.3, 134.8, 129.4, 128.7, 127.6, 126.4, 122.9, 121.2, 114.8, 110.0, 91.7, 56.2, 52.8, 32.6, 25.6, 25.2; IR (KBr, cm^{-1}): v = 2991, 1764, 1377, 1243, 1056, 798; HRMS (ESI) calc. $C_{23}H_{23}N_3O$ $[M+H]^+$: 358.1914, found: 358.1916.

(*Z*)-2-(3-(Cyclohexylamino)-1*H*-isoindol-1-ylidene)-2-(thiophen-2-yl)acetonitrile (4y): 
Yield: 51 mg (76%), orange solid. M.p.: 220 – 221 ºC. ^{1}H NMR (400 MHz, DMSO) δ ppm 9.09 (d, J = 6.3 Hz, 1H), 8.26 (d, J = 7.7 Hz, 1H), 8.05 (d, J = 7.4 Hz, 1H), 7.72 – 7.58 (m, 2H), 7.58 – 7.51 (m, 1H), 7.37 (d, J = 2.4 Hz, 1H), 7.15 – 7.06 (m, 1H), 4.12 (s, 1H), 2.13 (t, J = 11.6 Hz, 2H), 1.85 (t, J = 11.7 Hz, 2H), 1.69 (d, J = 12.4 Hz, 1H), 1.58 – 1.34 (m, 4H), 1.24 (dd, J = 21.4, 10.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO) δ ppm 165.0, 155.9, 138.9, 138.1, 134.2, 131.2, 130.6, 129.8, 126.8, 126.5, 122.7, 122.2, 119.3, 89.1, 53.4, 32.2, 25.7, 25.4; IR (KBr, cm^{-1}): v = 2926, 2856, 2204, 1764, 1486, 1380, 1243, 1059, 696; HRMS (ESI) calc. $C_{20}H_{19}N_3S$ $[M+H]^+$: 334.1372 , found: 334.1373.

(*Z*)-2-(5-bromothiophen-2-yl)-2-(3-(tert-butylamino)-1*H*-isoindol-1-ylidene)acetonitrile (4m-1): Yield: 53.9 mg (70%), orange solid. M.p.: 201 – 202 ºC. 
^{1}H NMR (400 MHz, DMSO) δ ppm 8.74 (s, 1H), 8.30 – 8.13 (m, 2H), 7.64 (t, J = 7.5 Hz, 1H), 7.57 (t, J = 7.2 Hz, 1H), 7.23 (s, 1H), 7.13 (s, 1H), 1.65 (s, 9H); ^{13}C NMR (100 MHz, DMSO) δ ppm 164.5, 156.2, 139.1, 137.4, 135.3, 131.4, 130.0, 123.0, 126.4, 122.7, 118.4, 116.1, 88.7, 53.9, 28.4; IR (KBr, cm^{-1}): v = 3341, 2922, 2204, 1632, 1539, 1430, 1205, 1041, 754; HRMS (ESI) calc. $C_{18}H_{16}BrN_3S$ $[M+H]^+$: 386.0321, found: 386.0317.

(*Z*)-2-(3-(*tert*-Butylamino)-1*H*-isoindol-1-ylidene)-2-(5-(4-fluorophenyl)thiophen-2-yl)acetonitrile (4m-M): 
Yield: 48 mg (60%), orange red solid. M.p.: 255 – 256 ºC. ^{1}H NMR (400 MHz, DMSO) δ ppm 8.66 (s, 1H), 8.27 (d, J = 7.6 Hz, 1H), 8.20 (d, J = 7.5 Hz, 1H), 7.67 (dd, J = 8.5, 5.4 Hz, 2H), 7.62 (t, J = 7.5 Hz, 1H), 7.54 (t, J = 7.4 Hz, 1H), 7.47 (d, J = 3.9 Hz, 1H), 7.33 (d, J = 3.9 Hz, 1H), 7.28 (t, J = 8.8 Hz, 2H), 1.69 (s, 9H); ^{13}C NMR (100 MHz, DMSO) δ ppm 164.2, 162.2(d, J = 244.2), 155.7, 145.2, 137.7, 137.3, 135.2, 131.2, 131.0 (d, J = 3.2), 129.8, 127.8, 127.3 (d, J = 8.2), 123.7, 122.6, 122.5, 118.8, 116.7 (d, J = 21.9), 89.3, 53.9, 28.5; IR (KBr, cm^{-1}): v = 3328, 2991, 2203, 1764, 1408, 1242, 1057; HRMS (ESI) calc. $C_{24}H_{20}FN_3S$ $[M+H]^+$: 402.1435, found: 402.1431.

Photophysical Properties of All Products

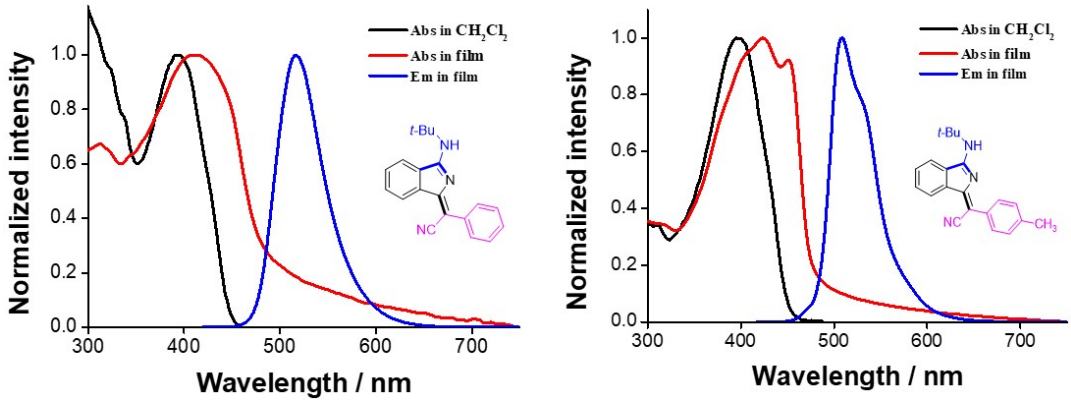
Photophysical data and spectra of all products in CH_2Cl_2 and film

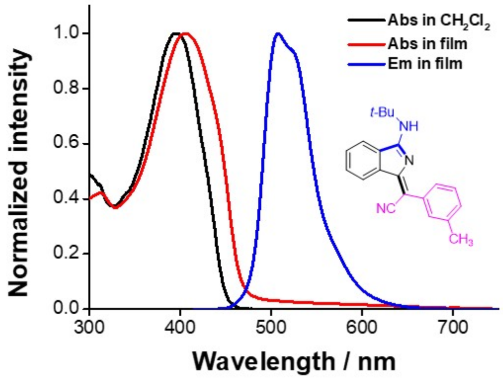
Table S1. Photophysical data of compounds in CH_2Cl_2 and film

compound	λ_{abs} (nm)[a]	λ_{em} (nm)[e]	Stokes shift	Φ_F (%)[g]

	in CH_2Cl_2 [b] (ε (10^4 M^{-1} cm^{-1})[c])	in film [d]	in film	(cm^{-1})[f]	in CH_2Cl_2	in film
4a	394 (1.76)	411	518	5026	0.2	25.0
4b	399 (1.67)	425	509	3883	0.5	16.7
4c	396 (1.87)	406	508	4946	0.7	8.9
4d	404 (2.89)	415	511	4527	0.6	2.4
4e	407 (1.90)	419	524	4782	0.6	8.3
4f	401 (2.16)	435	529	4085	0.7	7.9
4h	415 (1.17)	425	521	4336	1.1	2.7
4i	397 (1.74)	426	514	4019	0.8	17.8
4j	392 (2.24)	400	521	5806	0.6	7.6
4k	396 (2.22)	432	511	3579	0.7	13.9
4l	396 (1.88)	437	511	3314	0.7	1.9
4m	423 (3.44)	431	553	5119	0.5	2.7
4n	421 (2.61)	438	543	4415	0.6	4.2
4o	424 (1.65)	426	540	4956	0.6	2.8
4p	396 (2.27)	423	526	4629	0.6	13.5
4q	422 (2.78)	440	528	3788	0.5	2.7
4s	400 (2.00)	409	520	5219	0.5	13.2
4t	396 (2.16)	435	529	4085	0.9	12.2
4u	400 (2.30)	401	520	5707	0.7	10.1
4v	396 (2.58)	419	518	4561	0.5	26.3
4w	401 (1.27)	436	529	4032	0.5	6.0
4x	402 (1.71)	436	538	4348	0.4	14.8
4y	423 (2.66)	432	555	5130	0.3	1.9
4m-M	453 (3.17)	456	589	4952	0.9	2.6

[a]Maximum absorption wavelength; [b]Measured in CH_2Cl_2 at 10.0 μM; [c]Molar absorption coefficient; [d] Measured in drop-cast film on a quartz plate; [e]Emission peak (excited using the maximum absorption wavelength in CH_2Cl_2 as excitation wavelength); [f]Stokes shift = $1/\lambda_{abs\ (in\ film)} - 1/\lambda_{em\ (in\ film)}$; [g]Absolute fluorescence quantum yield measured by a calibrated integrating.

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Wavelength / nm
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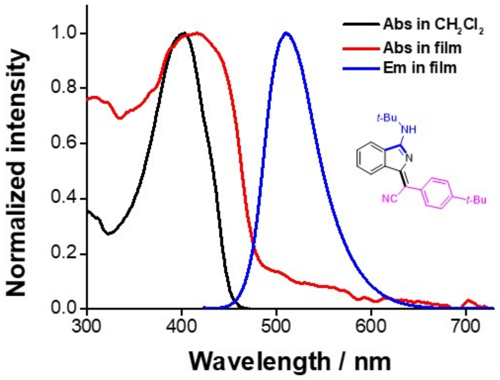
Abs in film
Em in film
t-Bu
NH
N
NC
CH_3

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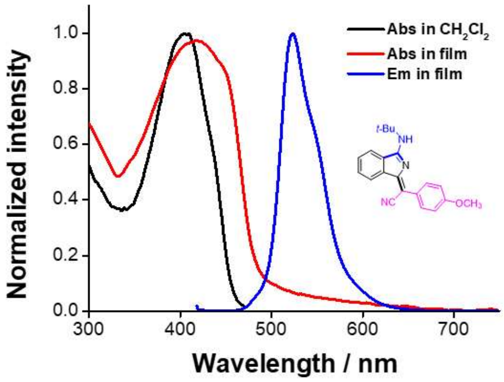
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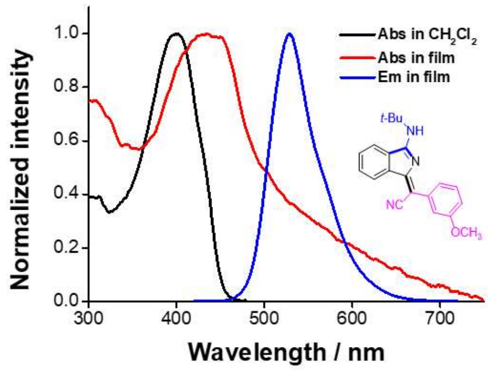
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Wavelength / nm
Abs in CH_2Cl_2
Abs in film
Em in film
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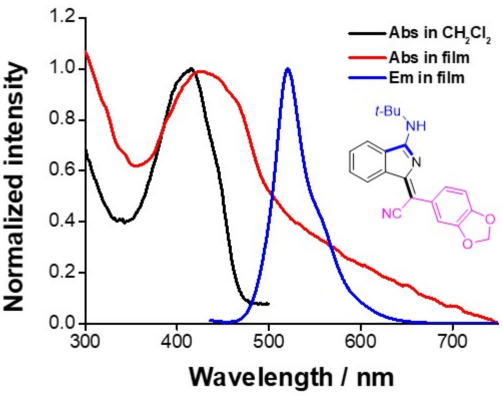
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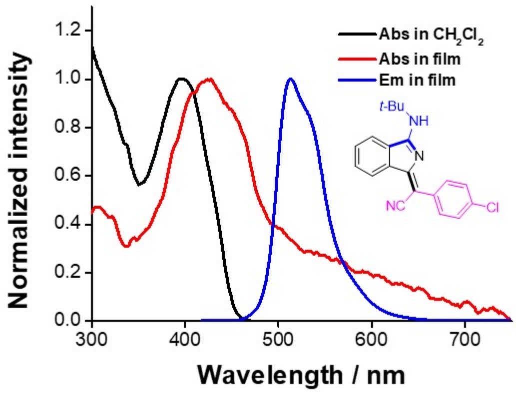
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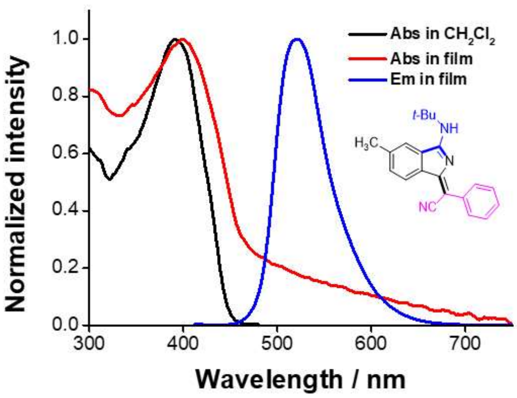
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H_3C
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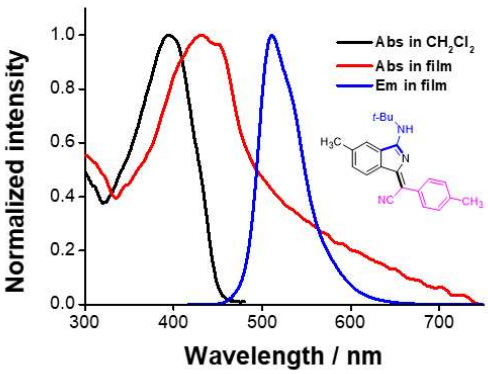
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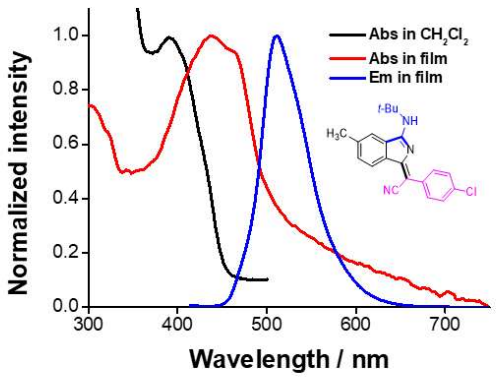
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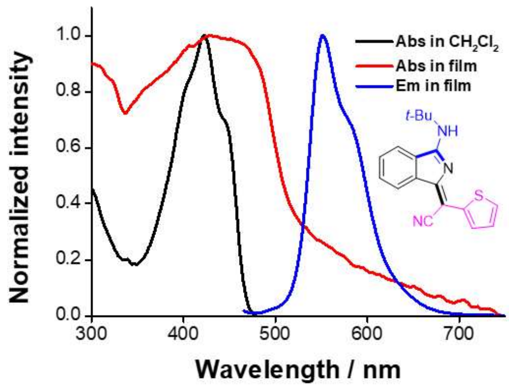
H3C
N
NC
Cl
Normalized intensity
Wavelength / nm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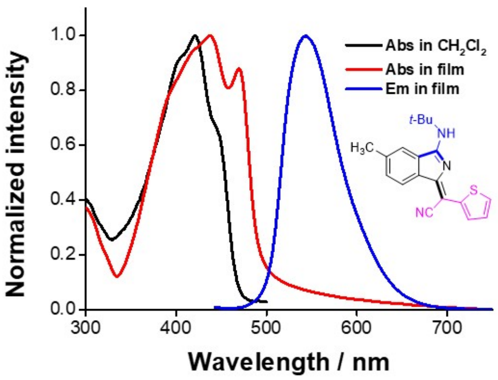
Abs in film
Em in film
t-Bu
NH
N
S
NC
Normalized intensity
Wavelength / nm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Em in film
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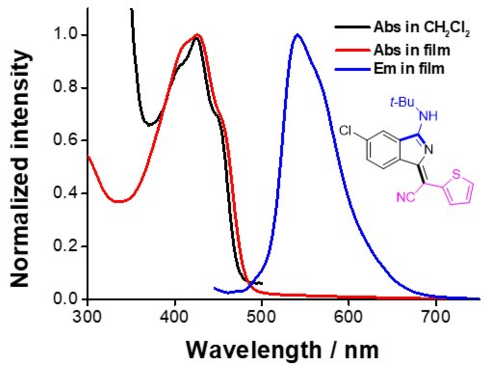
NH
H3C
N
S
NC
Normalized intensity
Wavelength / nm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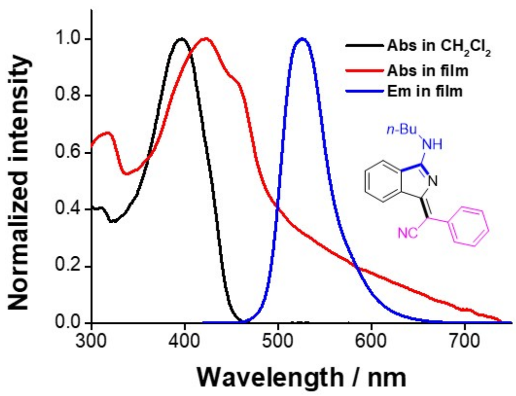
Wavelength / nm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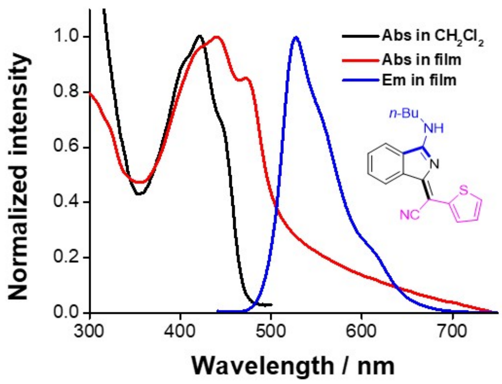
Wavelength / nm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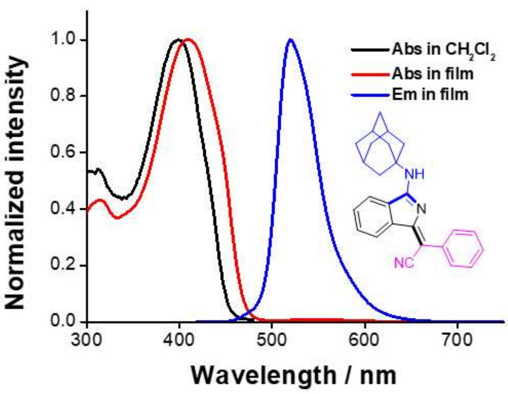
Abs in film
Em in film
n-Bu
NH
N
S
NC
Normalized intensity
Wavelength / nm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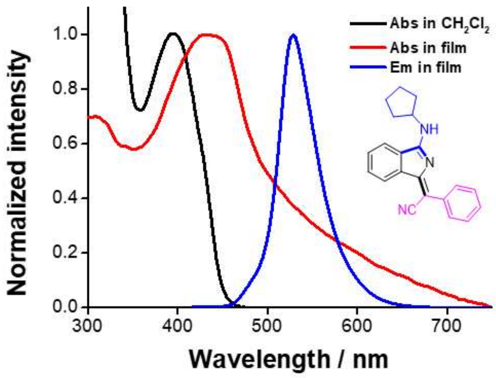
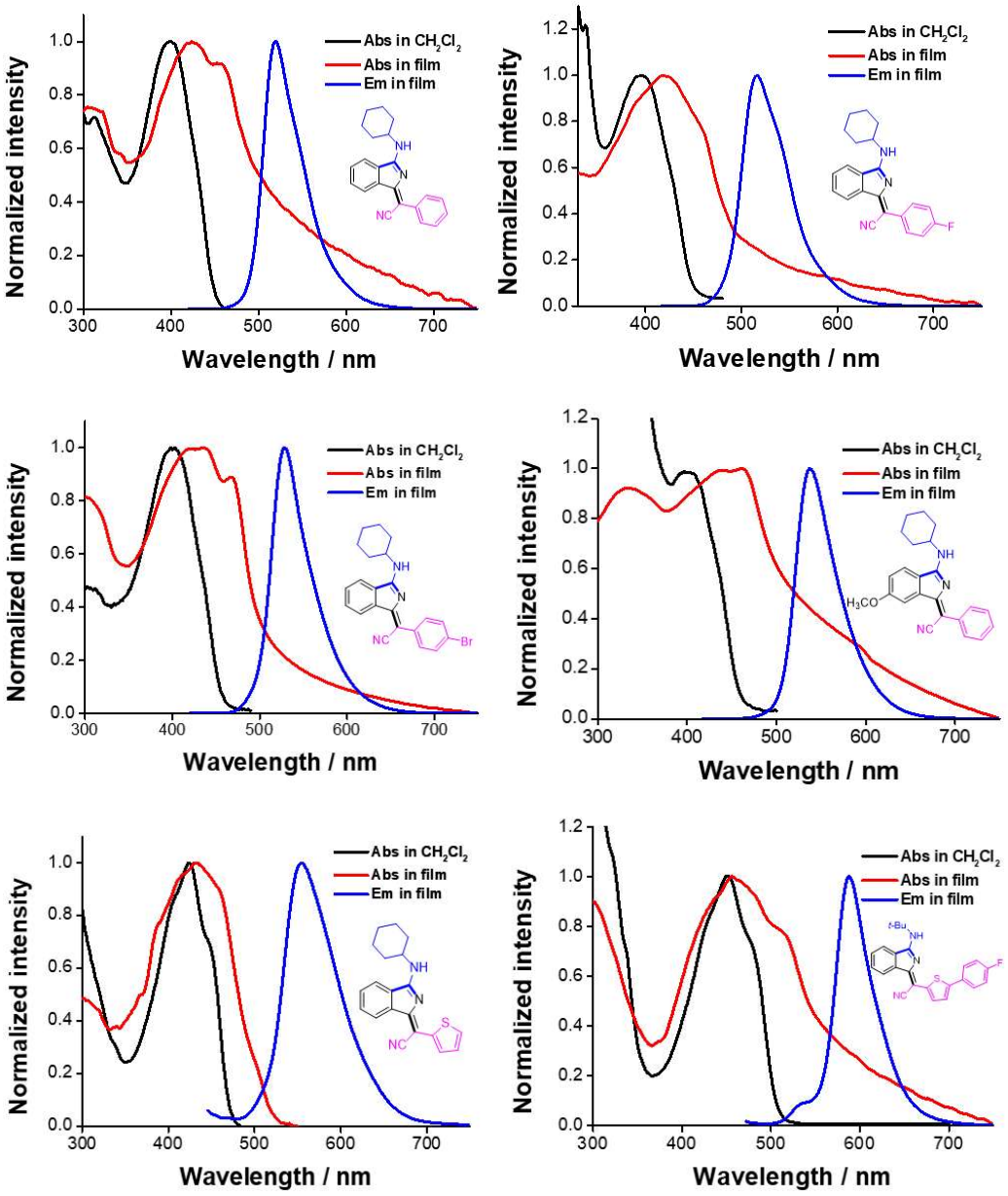
Em in film
NH
N
NC
Normalized intensity
Wavelength / nm


Abs in CH_2Cl_2
Abs in film
Em in film
NH
N
NC
Normalized intensity
Wavelength / nm



Studies of Aggregation-Induced Emission Characteristics

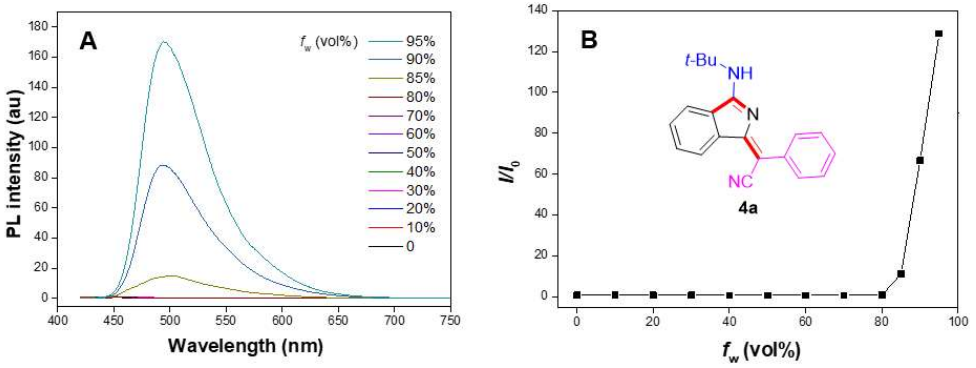


Figure S1. (A) PL spectra of **4a** in MeOH-water mixtures with different water fraction (f_w). Concentration: 10 μM. (B) Plots of (I/I_0) *vs.* f_w, where I_0 is the PL intensity in pure

MeOH solution.

Cell Imaging Experiments, Photostability, Cytotoxicity Assays and Measurement

A. Cell culture and bio-imaging experiments

HeLa cells were cultured in DMEM medium containing 100 μg/mL streptomycin, 100 U/mL penicillin, and 10% FBS in a humidified incubator with 5% CO_2 at 37 °C in confocal imaging dishes. After pretreated with 250 μg/mL oleic acid for 6 h at 37 ºC, HeLa cells were washed twice with PBS. Then 1, 3, 5 μL of DMSO solution of **4a** or **4a-M** (1 mM) (final concentration: 1, 3, 5 μM) were added into 999, 997, 995 μL of DMEM medium, respectively. The cells were further incubated for 15 min at 37 ºC, which washed and imaged by a confocal microscope.

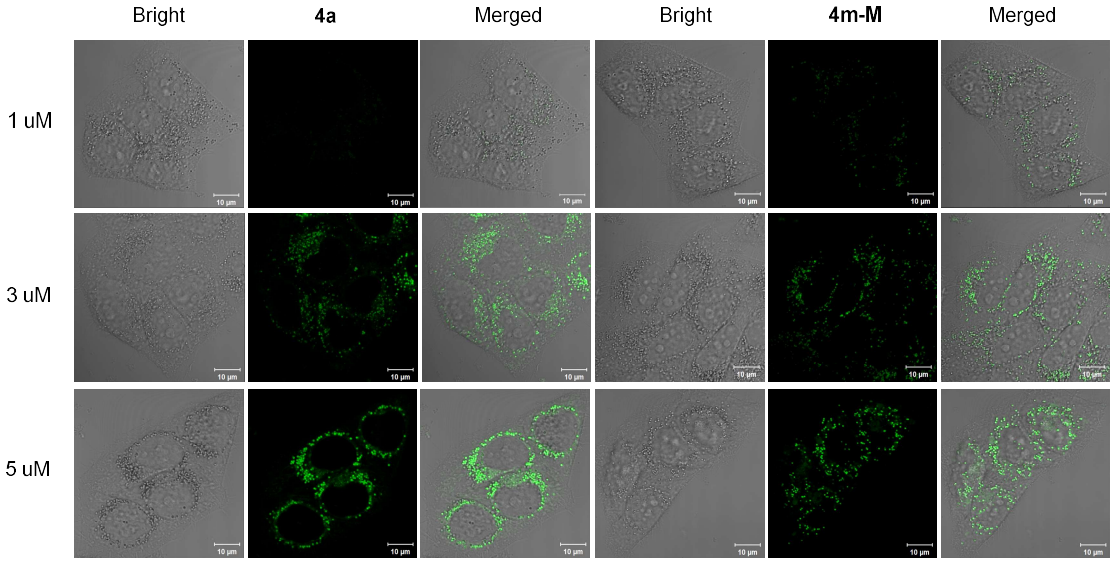


Figure S2. HeLa cells pretreated with oleic acid and then stained with different concentrations (1 μM, 3 μM, and 5 μM) **4a** or **4m-M** for 15 min: bright-field images, images from **4a** and **4m-M** (**4a**: λ_{ex} = 405, λ_{em} = 410–580; **4m-M**: λ_{ex} = 405, λ_{em} = 480–600), and merged images from bright and **4a** or **4m-M**, respectively.

For co-localization experiments, after pretreated with 250 μg/mL oleic acid for 6 h at 37 ºC, HeLa cells were washed twice with PBS. Then 5 μL of DMSO solution of **4a** or **4a-M** (1 mM) (final concentration: 5 μM) were added into 995 μL of DMEM medium. The cells were further incubated for 15 min at 37 ºC, and then washed twice with PBS and 1:1000 dilution of DMSO solution of HCS LipidTOX™ Deep Red neutral lipid stain-was added to incubate for 30 min at room temperature, which were washed twice with PBS and imaged by a confocal microscope.

For the photostability evaluation, after pretreated with 250 μg/mL oleic acid for 6 h at

37 ºC, HeLa cells were washed twice with PBS. Then, 5 μM of **4a**, **4m-M**, Bodipy or Nile Red or a 1:1000 dilution of HCS LipidTOX™ Deep Red neutral lipid stain-was added to the DMEM medium and incubate Hela cells for 30 min at room temperature, which were washed twice with PBS and imaged by a confocal microscope. A selected area of confocal imaging was scanned continuously for 30 times, where the cells were exposed to 405 nm CLSM laser with power of 10% for 10 s in every interval. The emission at 450−570 nm excited by 405 nm for **4a**, 480−600 nm excited by 405 nm for **4m-M**, 500−550 nm excited by 488 nm for Bodipy, 550−650 nm excited by 514 nm for Nile red, and 640−740 nm excited by 405 nm for HCS LipidTOX™ Deep Red neutral lipid stain, of the selected area are recorded and analyzed (manuscript, Figure 3A).

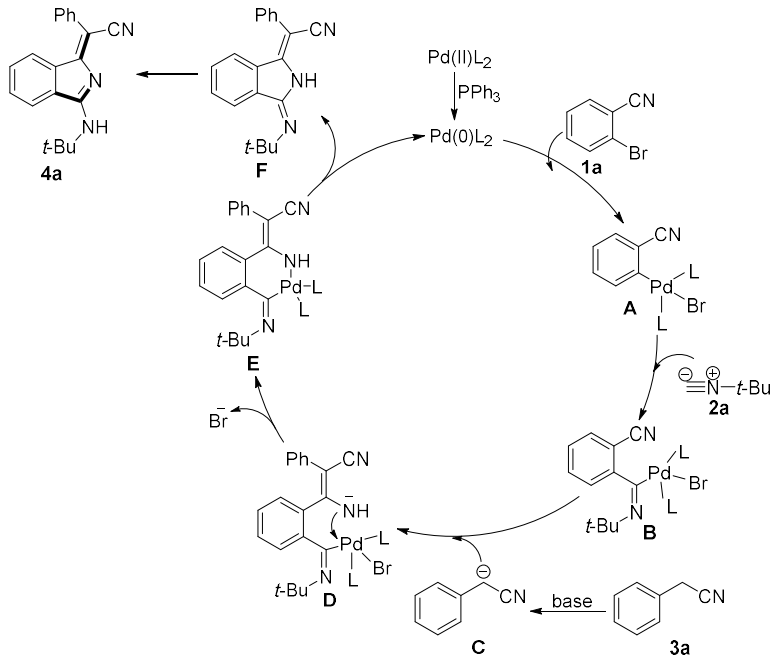
B. Cytotoxicity assays

The cells were seeded in a 96-well plate at a density of 1×10^5 cells/mL. After 24 h of culture, different concentrations of compound **4a** or **4m-M** were added and further incubated for 24 h at 37 ºC. The sample and control wells were washed twice with PBS and added with freshly prepared MTT solution (0.5 mg/mL, 100 μL). After incubation at 37 ºC for 4 h, the MTT solution was removed and washed twice with PBS buffer. DMSO (100 μL) was then added into each well and the plate was gently shaken for 10 min at room temperature to dissolve all the precipitates formed. The absorbance of sample and control wells at 570 nm was then measured by a microplate Reader. Cell viability was then calculated by the ratio of the absorbance of sample wells to control cells.

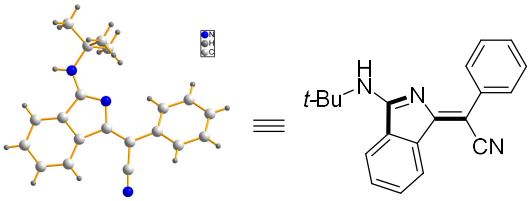
Plausible Mechanism

On the basis of the above results and previous reports, we proposed a plausible reaction mechanism for this transformation detailed in Scheme S1. Initially, oxidative addition of **1a** to the $L_2Pd(0)$ catalyst facilitates the formation of aryl palladium species **A**, followed by the insertion of **2a** to give intermediate **B**. Then, the nucleophilic addition of **C** formed by **3a** in the presence of base to the nitrile forms intermediate **D**. Subsequently, reductive elimination of **E** provides intermediate F and $L_2Pd(0)$. Immediately, the unstable product **F** would be isomerized to give the final product **4a**.

Scheme S1. Plausible mechanism



X-ray Crystallographic Analysis for Product 4a



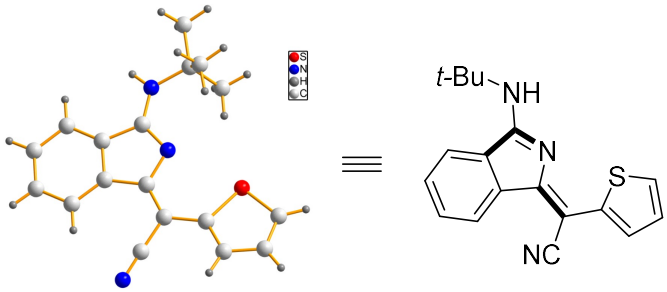
CCDC 1868897 4a

Table S2. Crystal data and structure refinement for **4a**

Empirical formula	$C_{20}H_{19}N_3$
Formula weight	301.38
Temperature	100(10) K
Wavelength	1.54184 Å
Crystal system	orthorhombic
Space group	C_{2221}
Unit cell dimensions	a = 7.32208(15) Å, α = 90.00°
	b = 18.4404(4) Å, β = 90.00°
	c = 23.9475(4) Å, γ = 90.00°
Density (calculated)	1.238
Absorption coefficient	0.576 mm^{-1}
$F(000)$	1280.0
Crystal size	0.2 × 0.16 × 0.11
Theta range for data collection	7.384 to 147.086
Index ranges	$-8 \le h \le 5$, $-16 \le k \le 22$, $-29 \le l \le 29$
Reflections collected	4173
Independent reflections	2798 [R_{int} = 0.0150, R_{sigma} = 0.0250]

Completeness to theta	66.97%
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	2798/0/211
Goodness-of-fit on F^2	1.027
Final R indices [$I > 2sigma(I)$]	$R_1 = 0.0299$, $wR_2 = 0.0783$
Final R indices (all data)	$R_1 = 0.0305$, $wR_2 = 0.0790$

X-ray Crystallographic Analysis for Product 4m



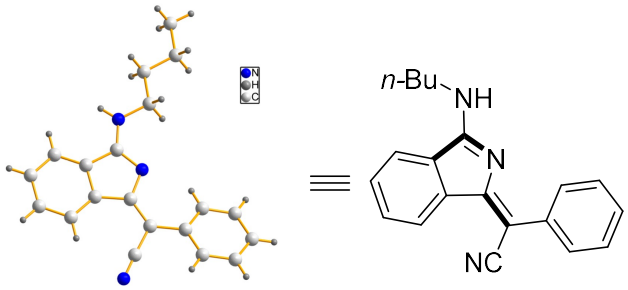
CCDC 1880913 **4m**

Table S3. Crystal data and structure refinement for **4m**

Empirical formula	$C_{18}H_{17}N_3S$
Formula weight	307.40
Temperature	170.0 K
Wavelength	0.71073 Å
Crystal system	orthorhombic
Space group	C_{2221}
Unit cell dimensions	$a = 7.306(3)$ Å, $\alpha = 90.00^o$
	$b = 18.404(8)$ Å, $\beta = 90.00^o$
	$c = 23.763(9)$ Å, $\gamma = 90.00^o$
Density (calculated)	1.278
Absorption coefficient	0.202 mm^{-1}
$F(000)$	1296.0
Crystal size	0.19 × 0.16 × 0.13 mm^3
Theta range for data collection	3.428 to 52.744
Index ranges	$-8 \leqslant h \leqslant 9, -22 \leqslant k \leqslant 22, -29 \leqslant l \leqslant 29$
Reflections collected	11257
Independent reflections	3269 [$R_{int} = 0.0702$, $R_{sigma} = 0.0755$]
Completeness to theta	99.9%
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	3269/0/202
Goodness-of-fit on F^2	1.041
Final R indices [$I > 2sigma(I)$]	$R_1 = 0.0529$, $wR_2 = 0.1034$

Final *R* indexes [all data]	$R_1 = 0.0807$, $wR_2 = 0.1158$

X-ray Crystallographic Analysis for Product 4p

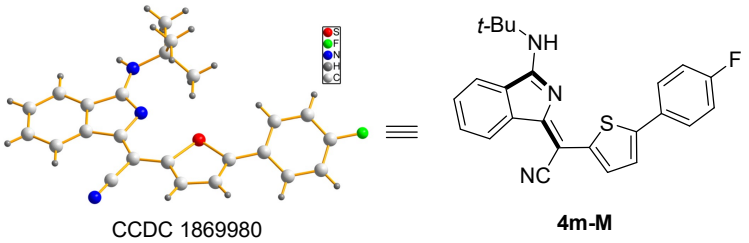


CCDC 1880930 **4p**

Table S4. Crystal data and structure refinement for **4p**

Empirical formula	$C_{23}H_{25}N_3$
Formula weight	343.46
Temperature	100(10) K
Wavelength	1.54184 Å
Crystal system	monoclinic
Space group	$P_{2/n}$
Unit cell dimensions	$a = 7.6842(19)$ Å, $\alpha = 90.00°$
	$b = 15.222(4)$ Å, $\beta = 94.247(16)$
	$c = 15.865(2)$ Å, $\gamma = 90.00°$
Density (calculated)	1.233
Absorption coefficient	0.563 mm^{-1}
F(000)	736.0
Crystal size/mm^3	0.13 × 0.12 × 0.11
Theta range for data collection	5.806 to 147.386
Index ranges	$-6 \leqslant h \leqslant 9, -18 \leqslant k \leqslant 17, -19 \leqslant l \leqslant 16$
Reflections collected	11307
Independent reflections	3629 [$R_{int} = 0.0964$, $R_{sigma} = 0.1702$]
Completeness to theta	66.97%
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	3629/0/236
Goodness-of-fit on F^2	1.027
Final *R* indices [*I* > *2sigma(I)*]	$R_1 = 0.0795$, $wR_2 = 0.4114$
Final *R* indexes [all data]	$R_1 = 0.2253$, $wR_2 = 0.1468$

X-ray Crystallographic Analysis for Product 4m-M



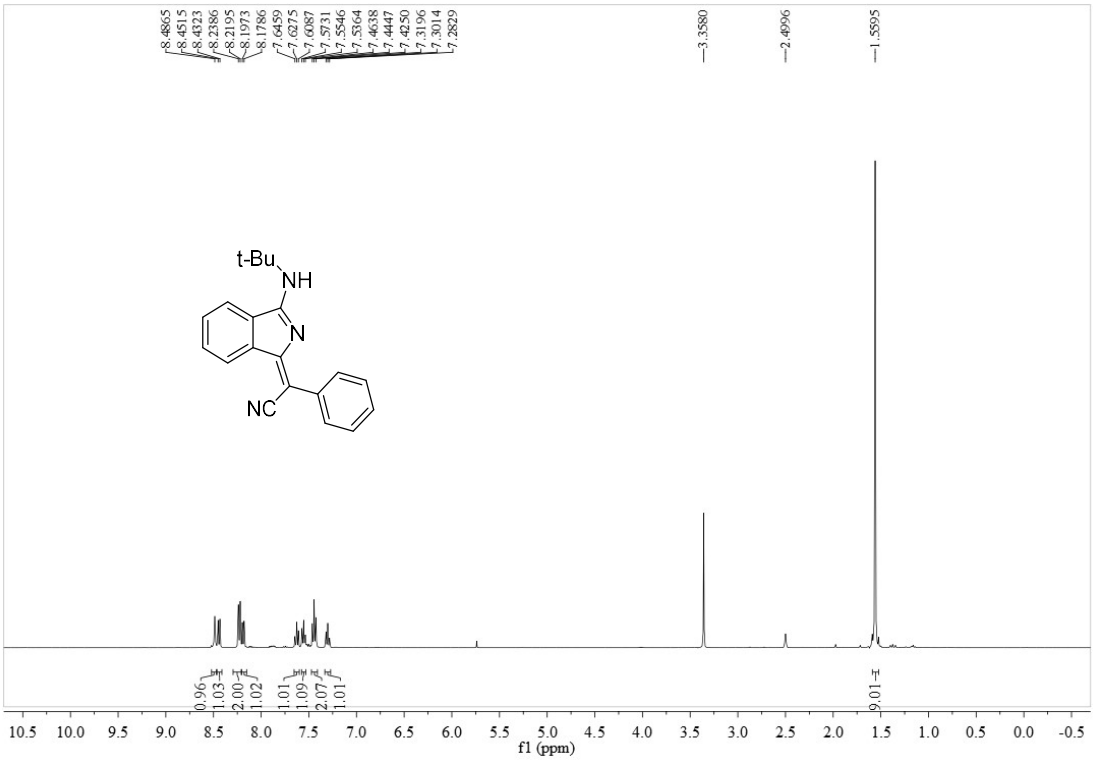
CCDC 1869980 **4m-M**

Table S5. Crystal data and structure refinement for **4m-M**

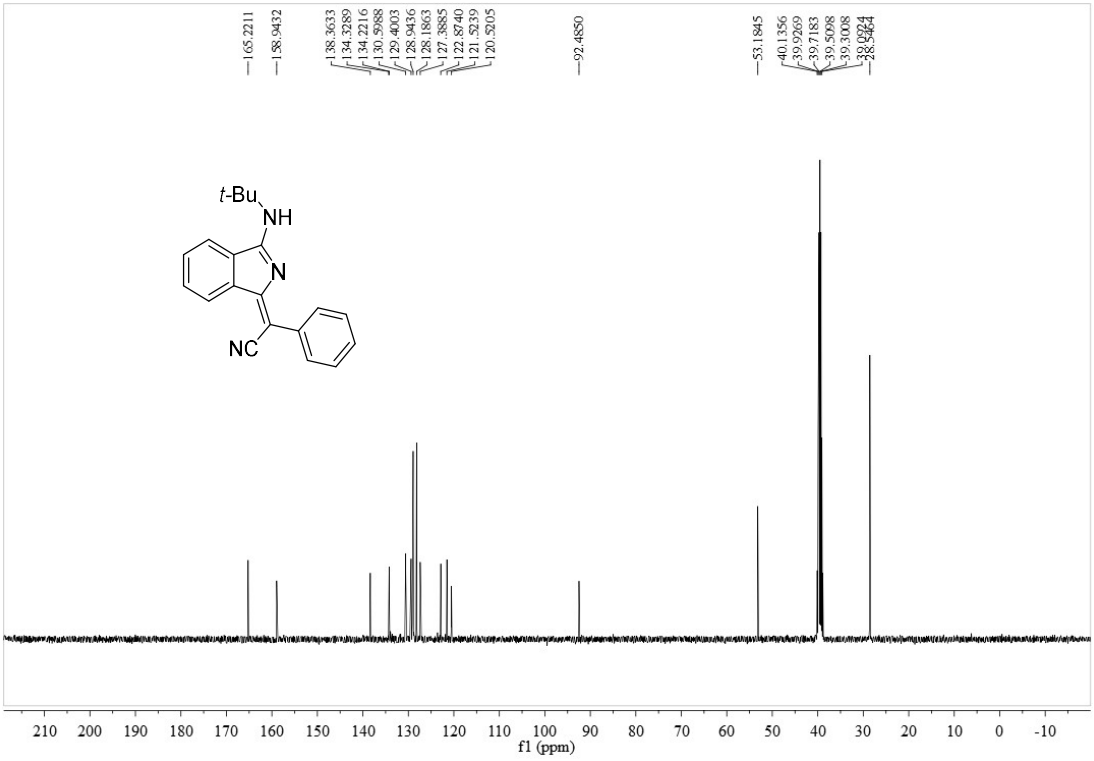
Empirical formula	$C_{24}H_{20}FN_3S$
Formula weight	401.49
Temperature	100(10) K
Wavelength	1.54184 Å
Crystal system	monoclinic
Space group	$P_{21/c}$
Unit cell dimensions	a = 13.52460(10) Å, α = 90.00°
	b = 15.58000(10) Å, β = 100.2070(10)
	c = 9.81710(10) Å, γ = 90.00°
Density (calculated)	1.310
Absorption coefficient	1.603 mm^{-1}
F(000)	840.0
Crystal size	0.13 × 0.12 × 0.11
Theta range for data collection	8.738 to 147.156
Index ranges	$-16 \leqslant h \leqslant 16, -19 \leqslant k \leqslant 18, -7 \leqslant l \leqslant 12$
Reflections collected	13713
Independent reflections	4043 [R_{int} = 0.0547, R_{sigma} = 0.0425]
Completeness to theta	66.97%
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	4043/0/265
Goodness-of-fit on F^2	1.067
Final R indices [$I > 2sigma(I)$]	R_1 = 0.0464, wR_2 = 0.1267
Final R indexes [all data]	R_1 = 0.0490, wR_2 = 0.1316

NMR Spectra for All the Compounds

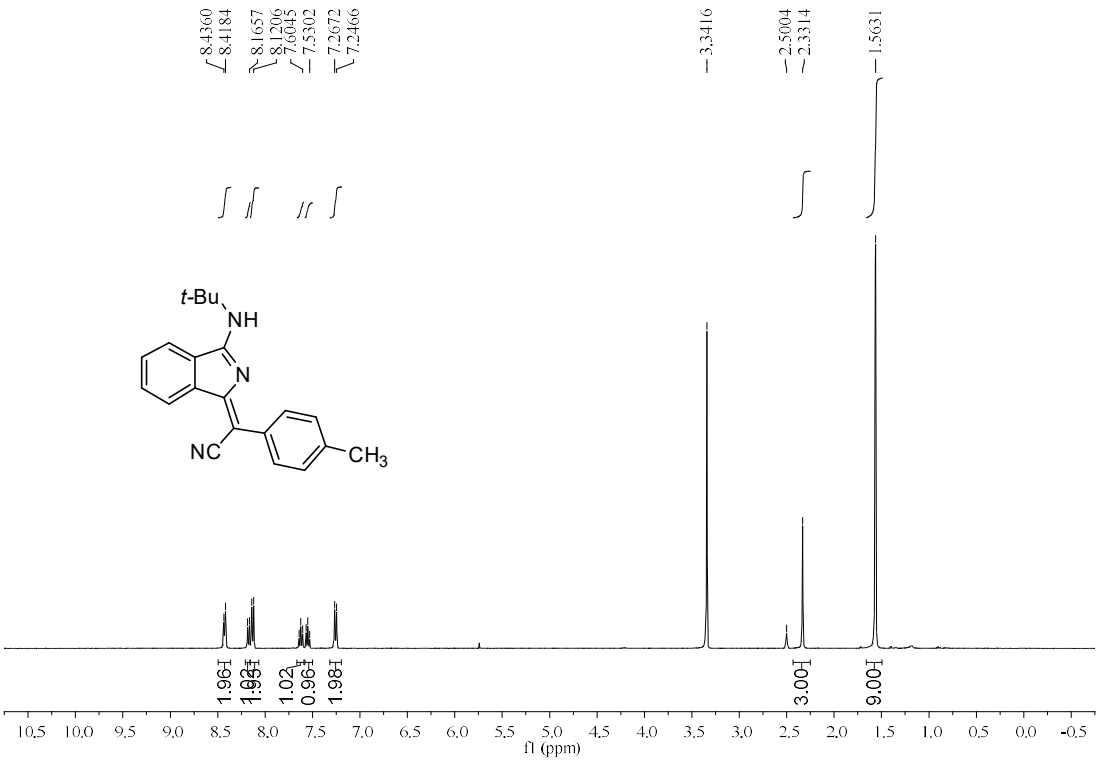
^{1}H NMR (400 MHz, DMSO) spectrum of compound 4a



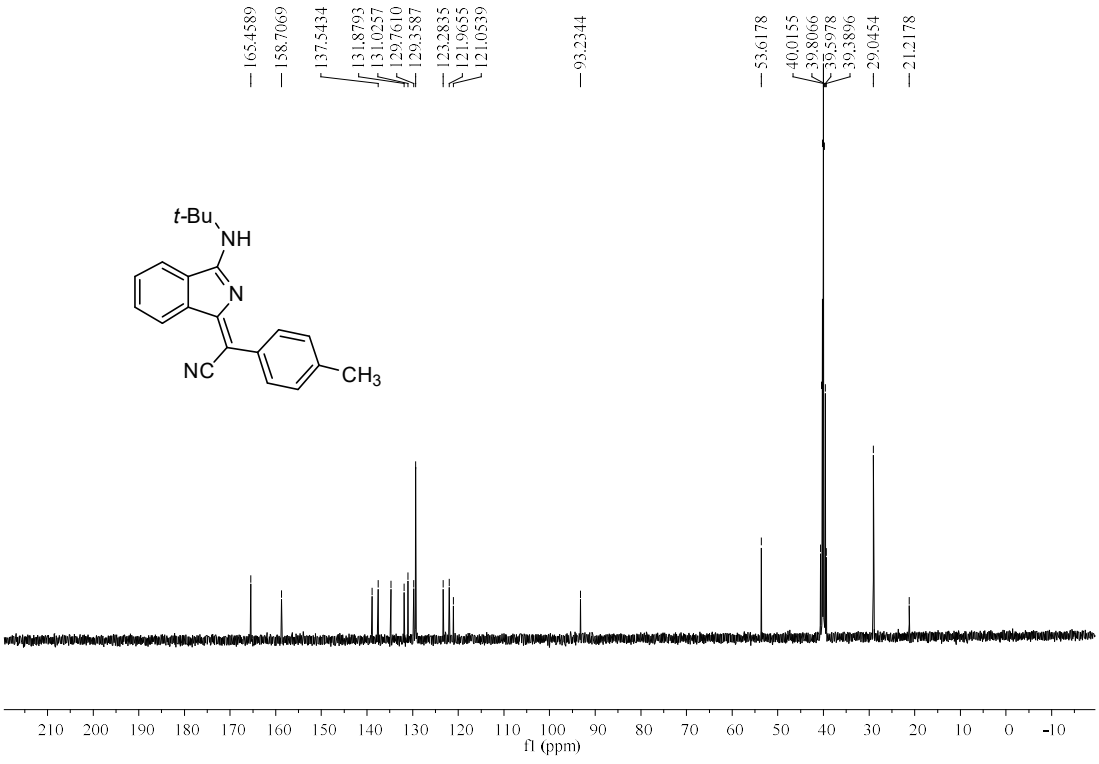
^{13}C NMR (100 MHz, DMSO) spectrum of compound 4a



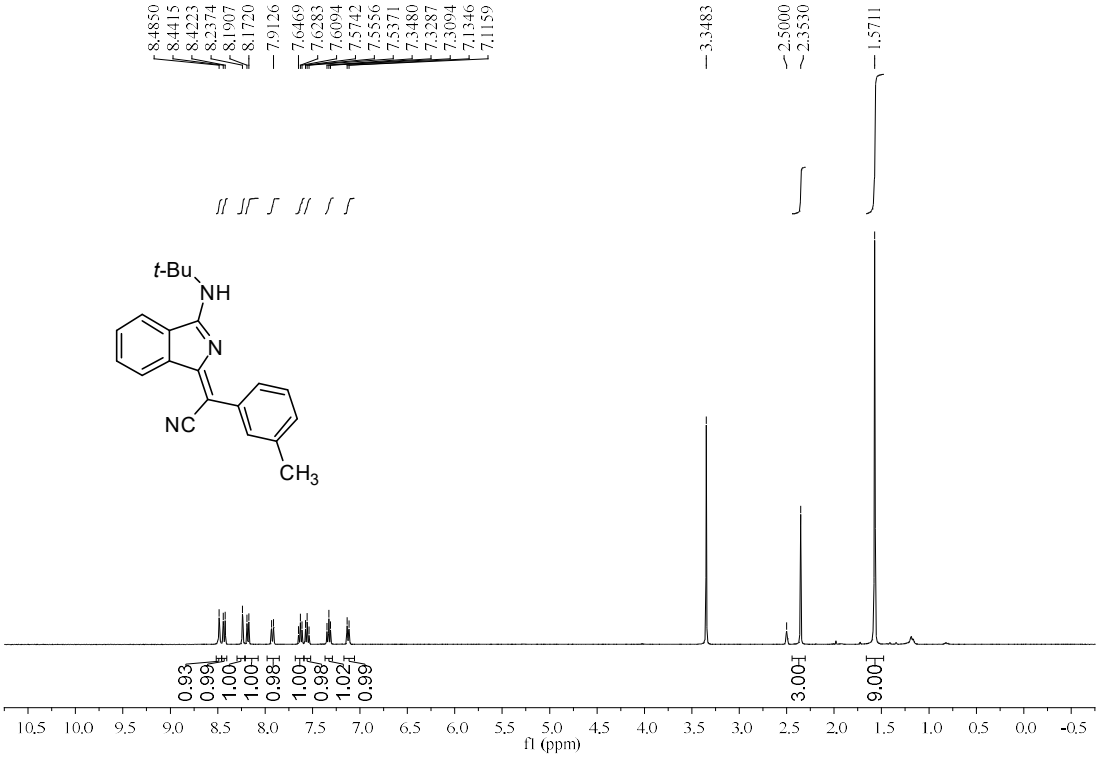
^{1}H NMR (400 MHz, DMSO) spectrum of compound 4b



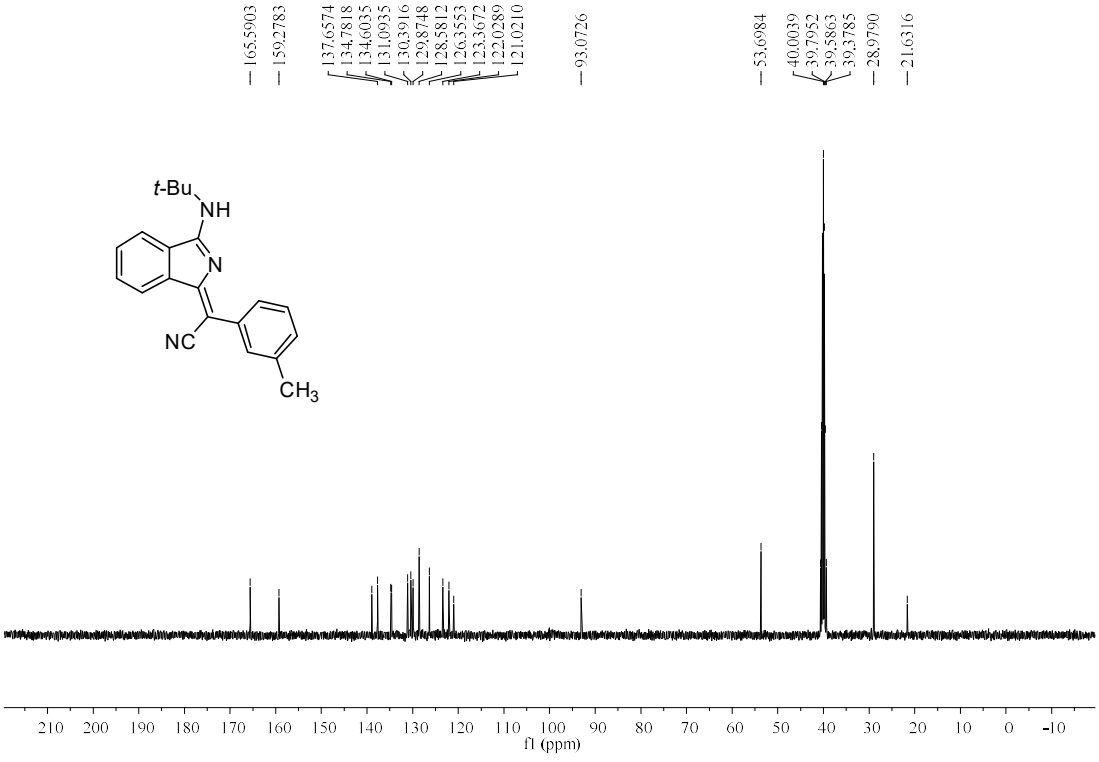
^{13}C NMR (100 MHz, DMSO) spectrum of compound 4b



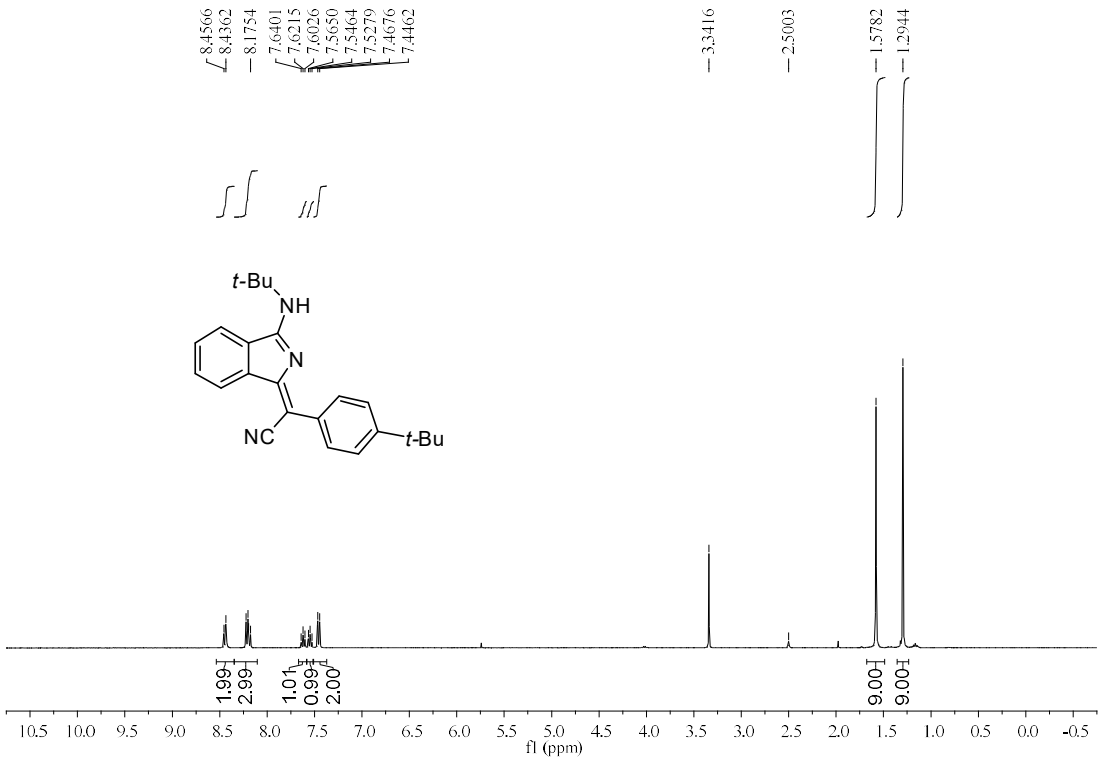
^{1}H NMR (400 MHz, DMSO) spectrum of compound 4c



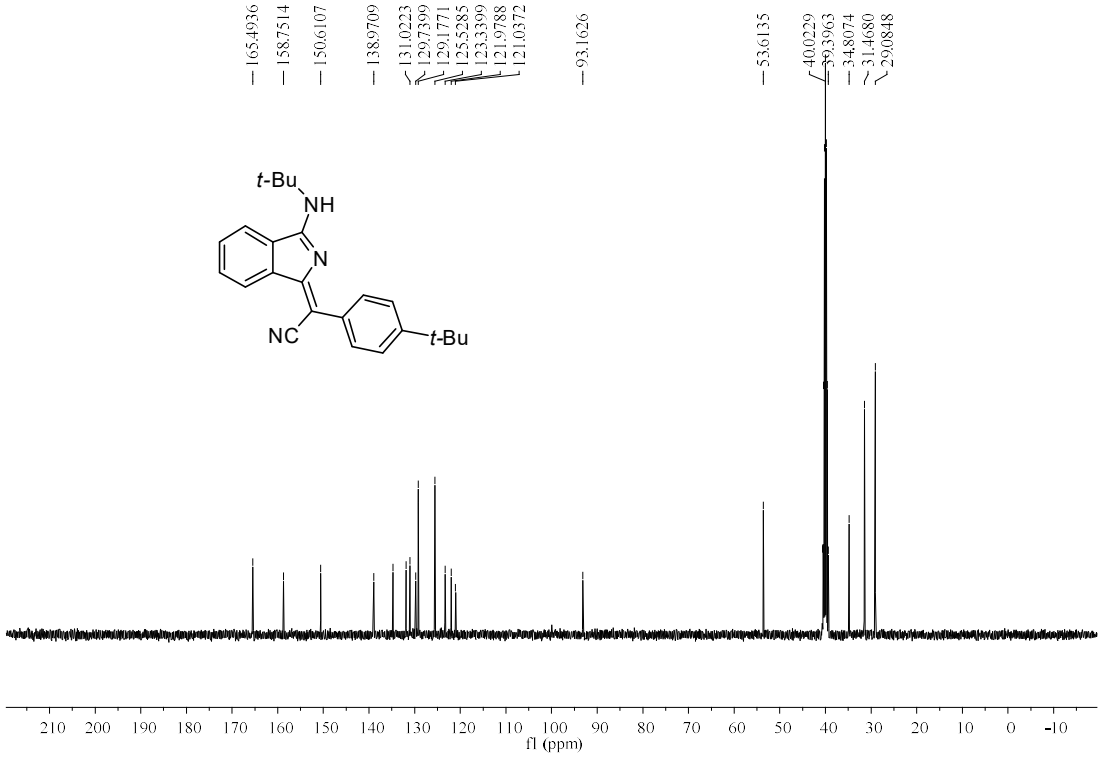
^{13}C NMR (100 MHz, DMSO) spectrum of compound 4c



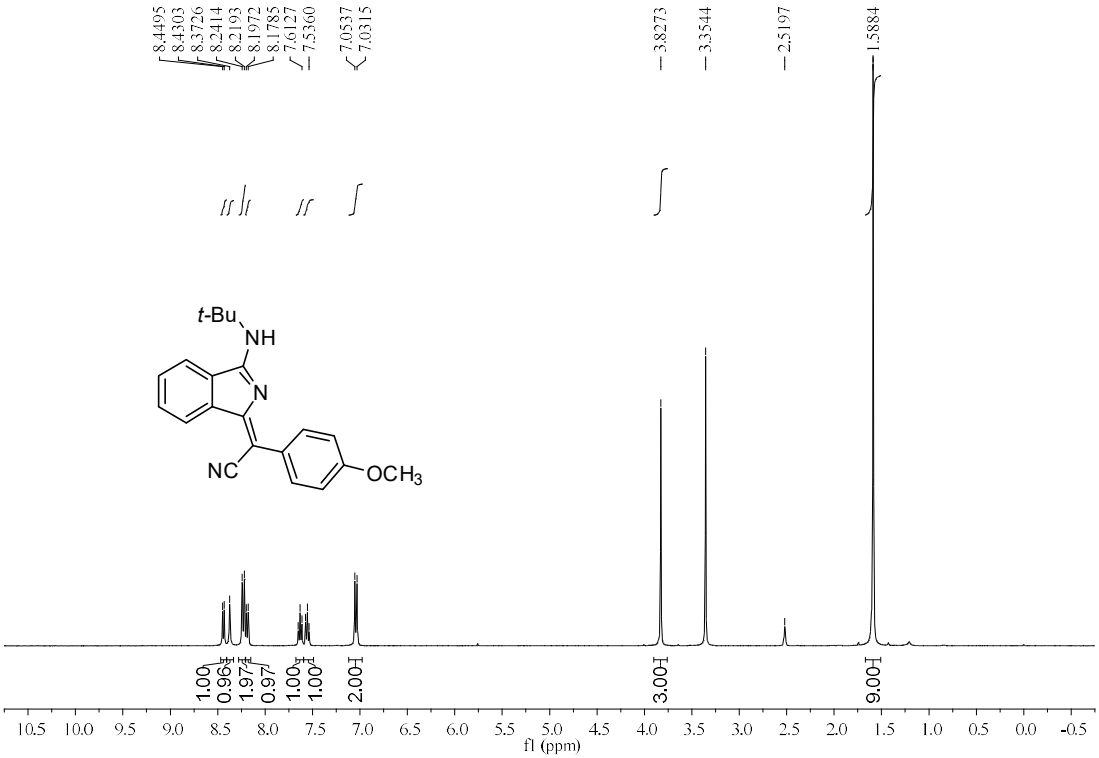
^{1}H NMR (400 MHz, DMSO) spectrum of compound 4d



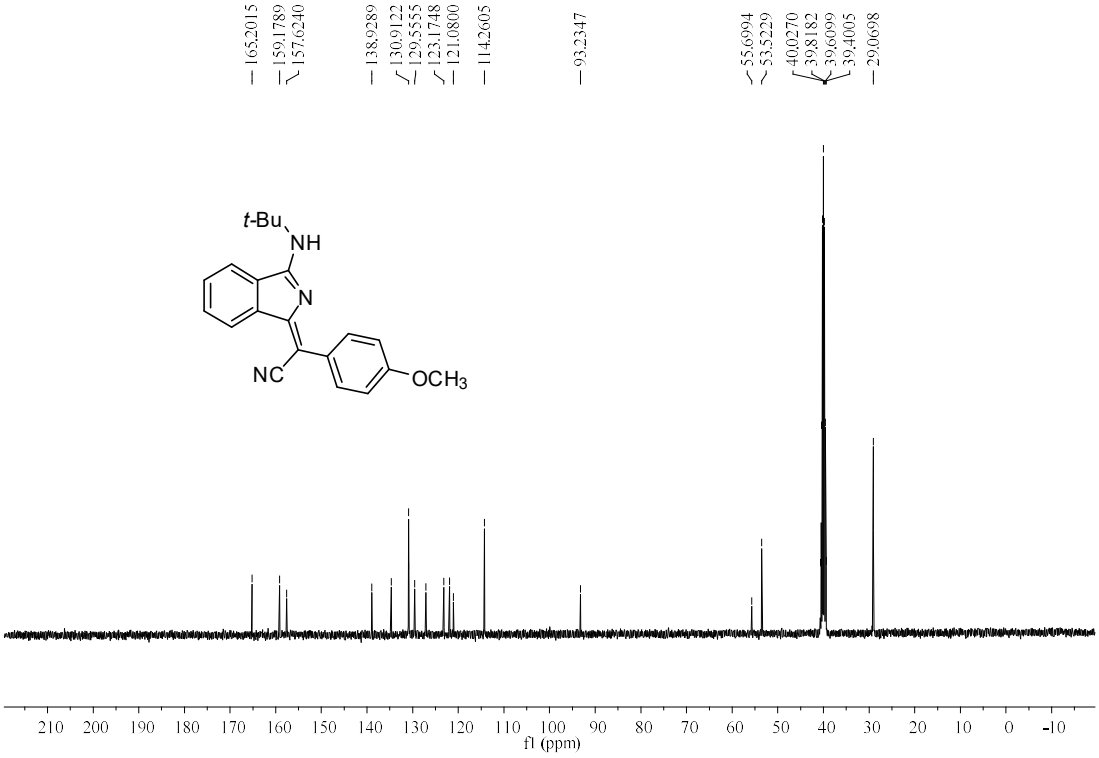
^{13}C NMR (100 MHz, DMSO) spectrum of compound 4d



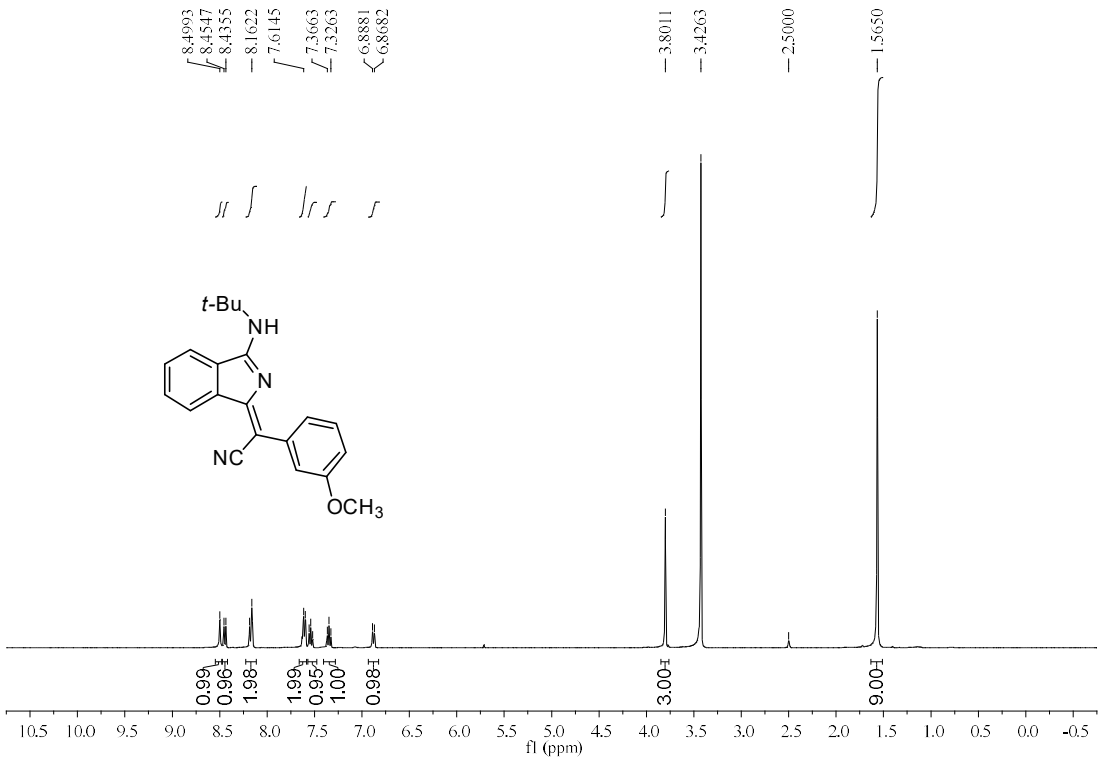
^{1}H NMR (400 MHz, DMSO) spectrum of compound 4e



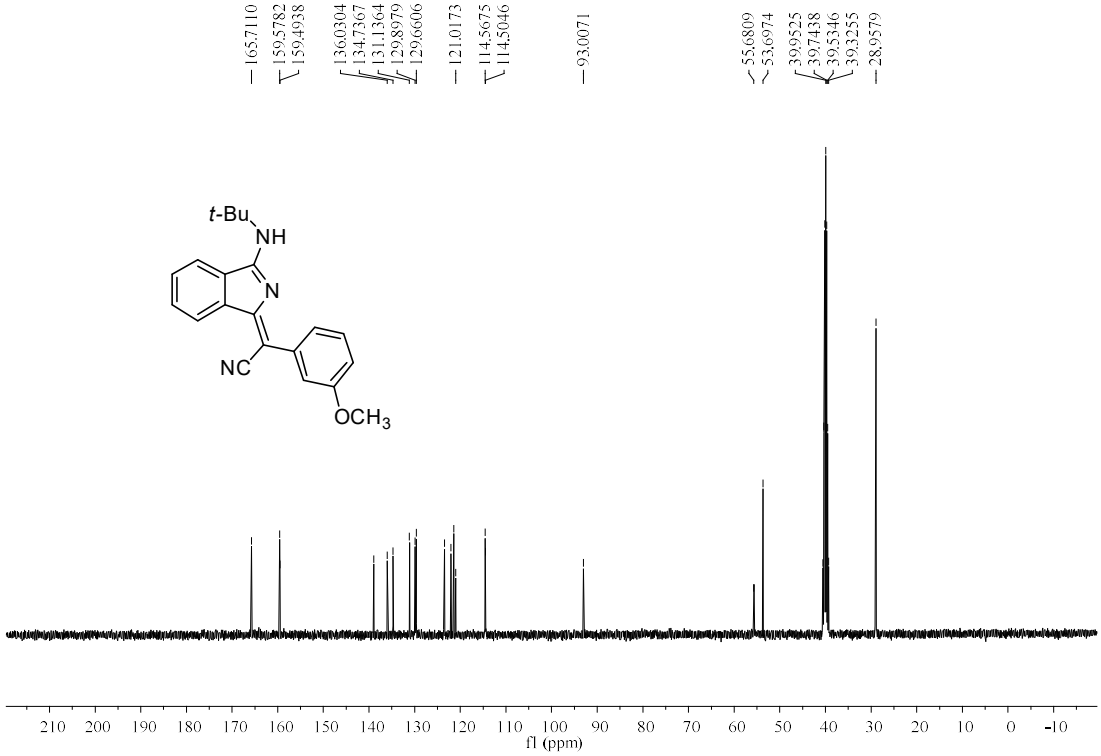
^{13}C NMR (100 MHz, DMSO) spectrum of compound 4e



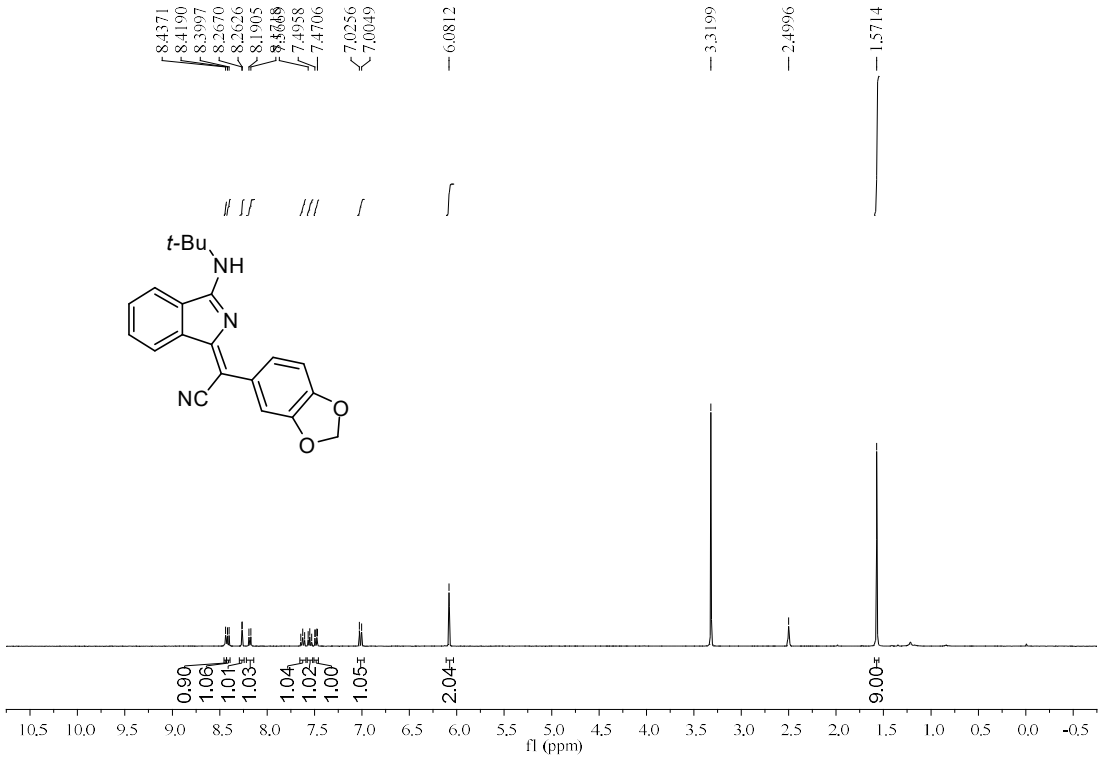
^{1}H NMR (400 MHz, DMSO) spectrum of compound 4f



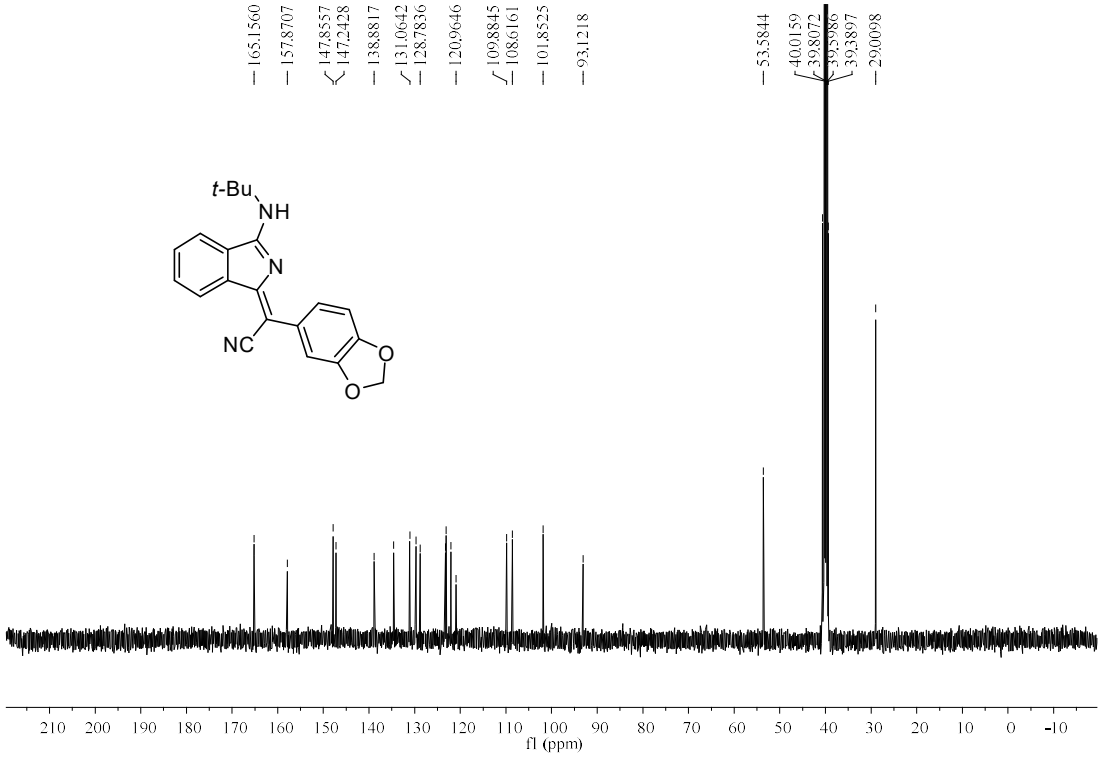
^{13}C NMR (100 MHz, DMSO) spectrum of compound 4f



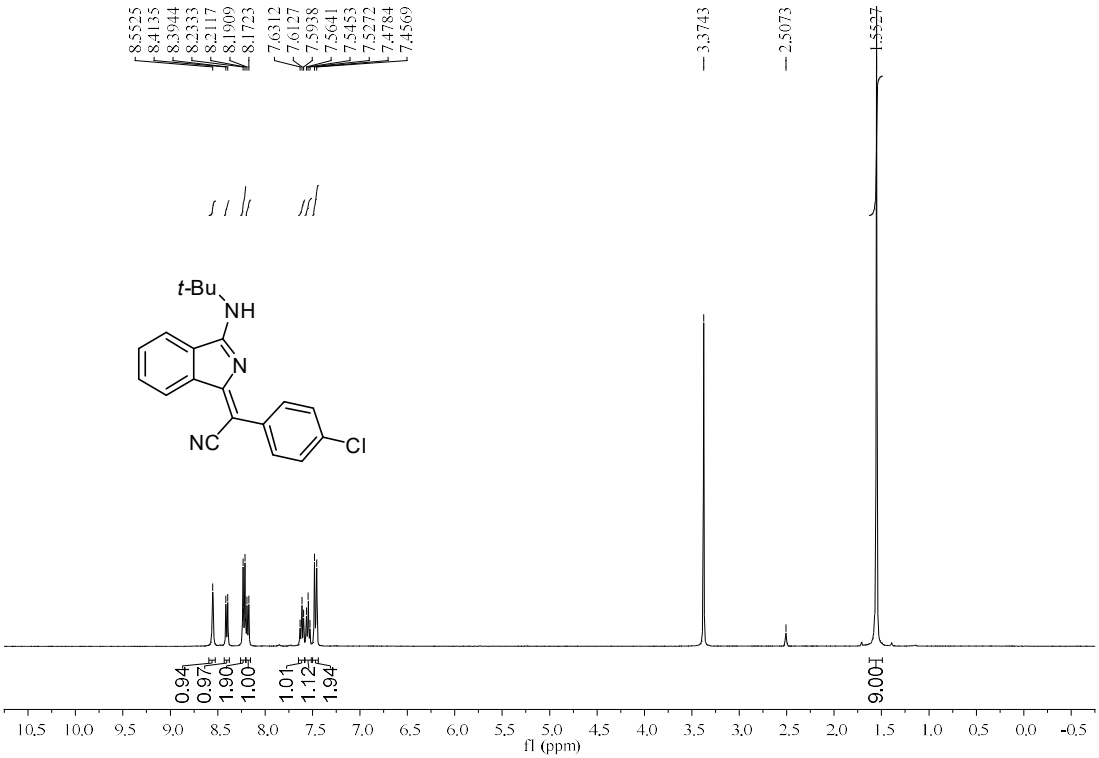
^{1}H NMR (400 MHz, DMSO) spectrum of compound 4h



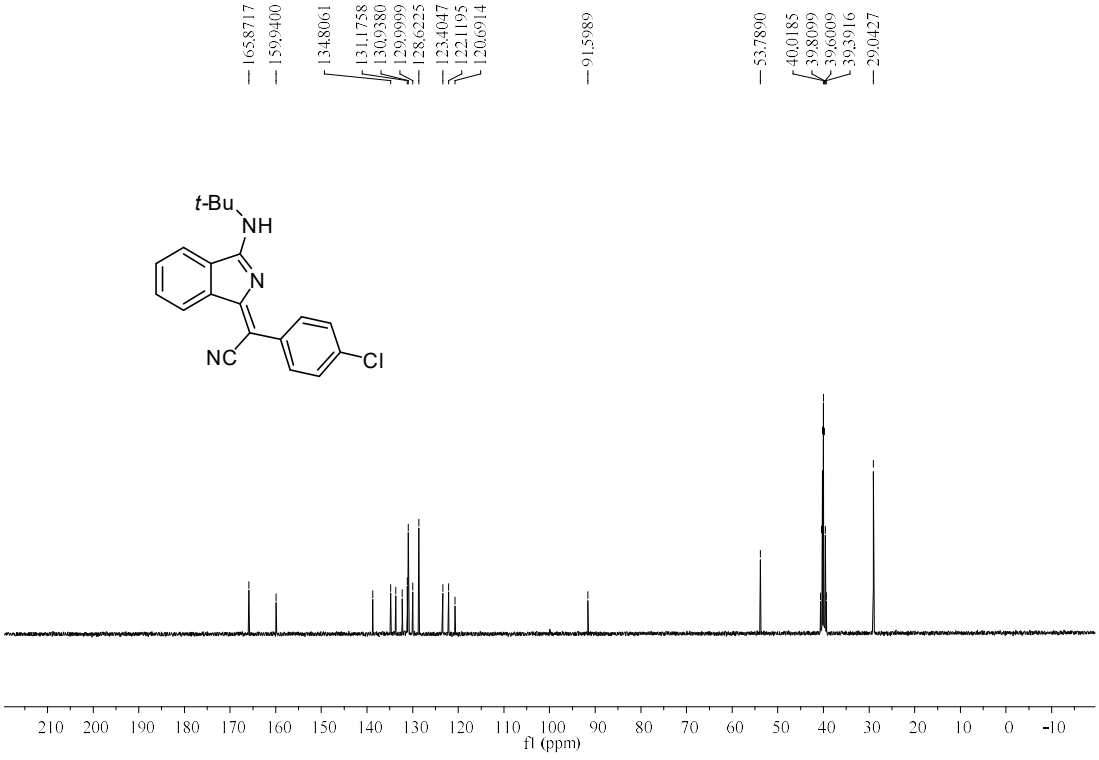
^{13}C NMR (100 MHz, DMSO) spectrum of compound 4h



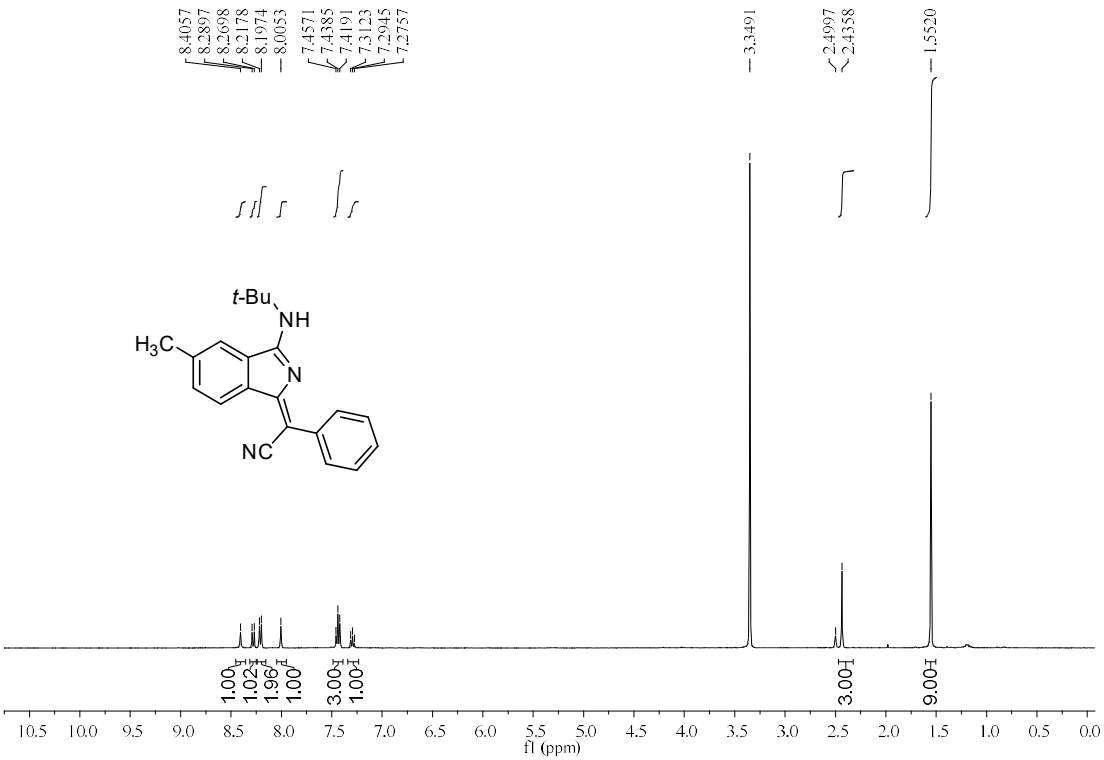
^{1}H NMR (400 MHz, DMSO) spectrum of compound 4i



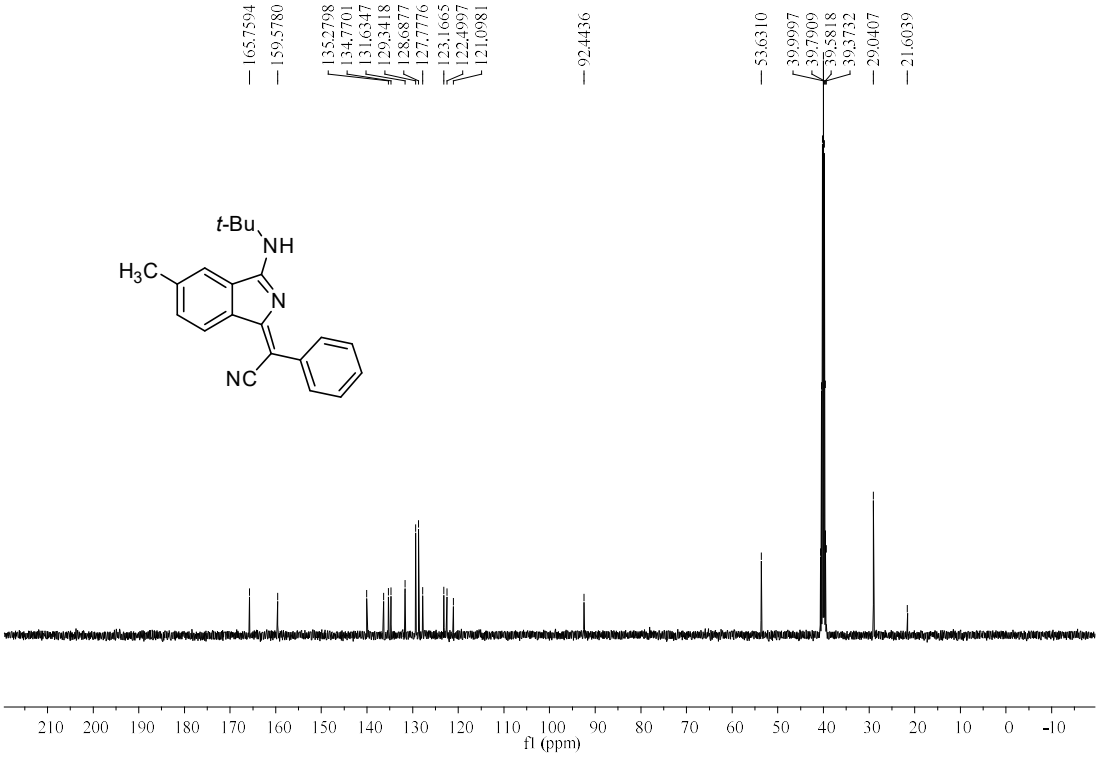
^{13}C NMR (100 MHz, DMSO) spectrum of compound 4i



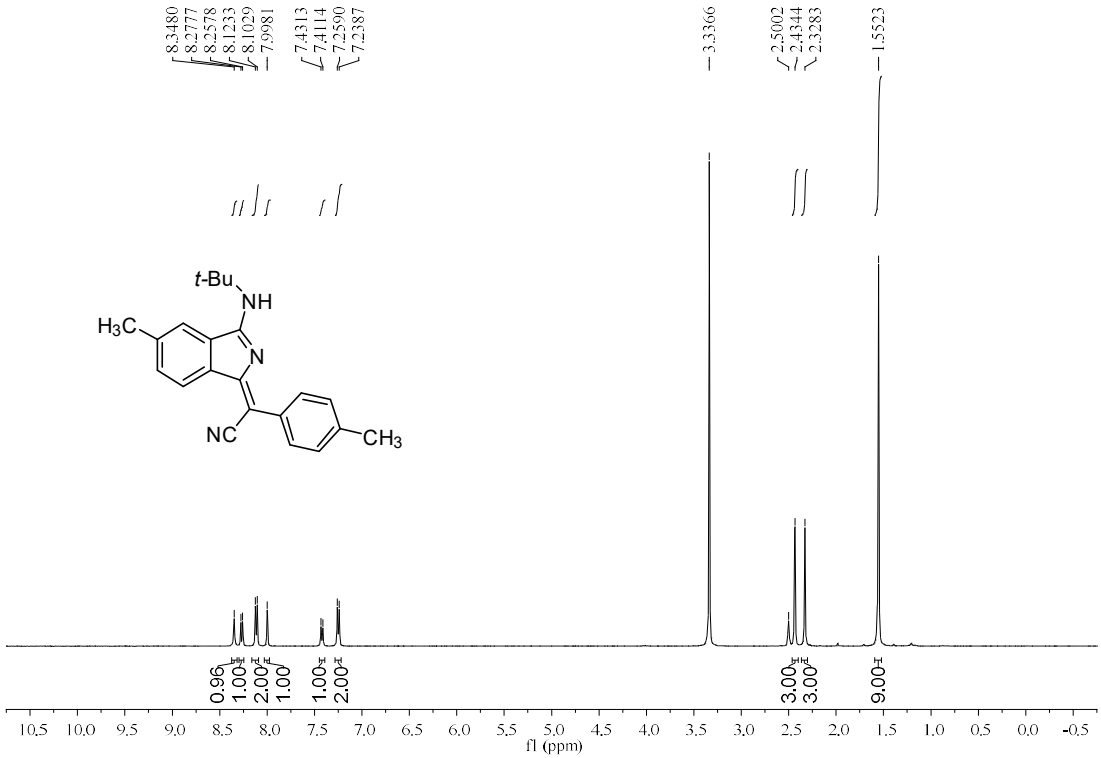
^{1}H NMR (400 MHz, DMSO) spectrum of compound 4j



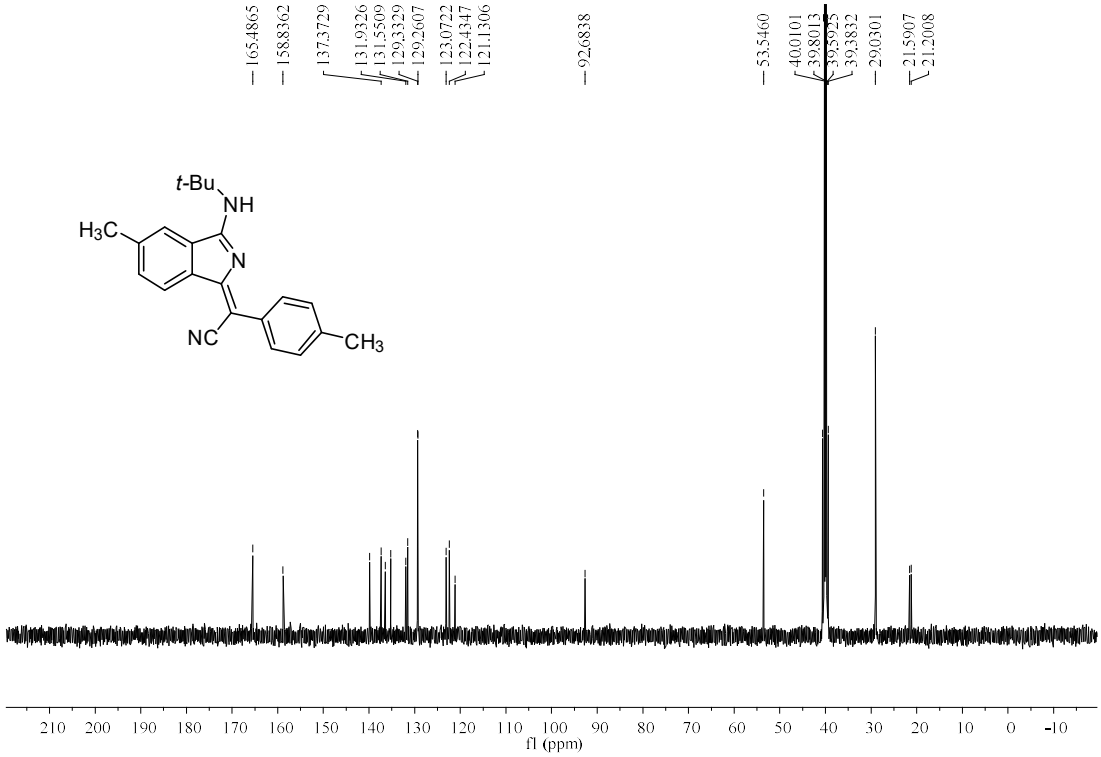
^{13}C NMR (100 MHz, DMSO) spectrum of compound 4j



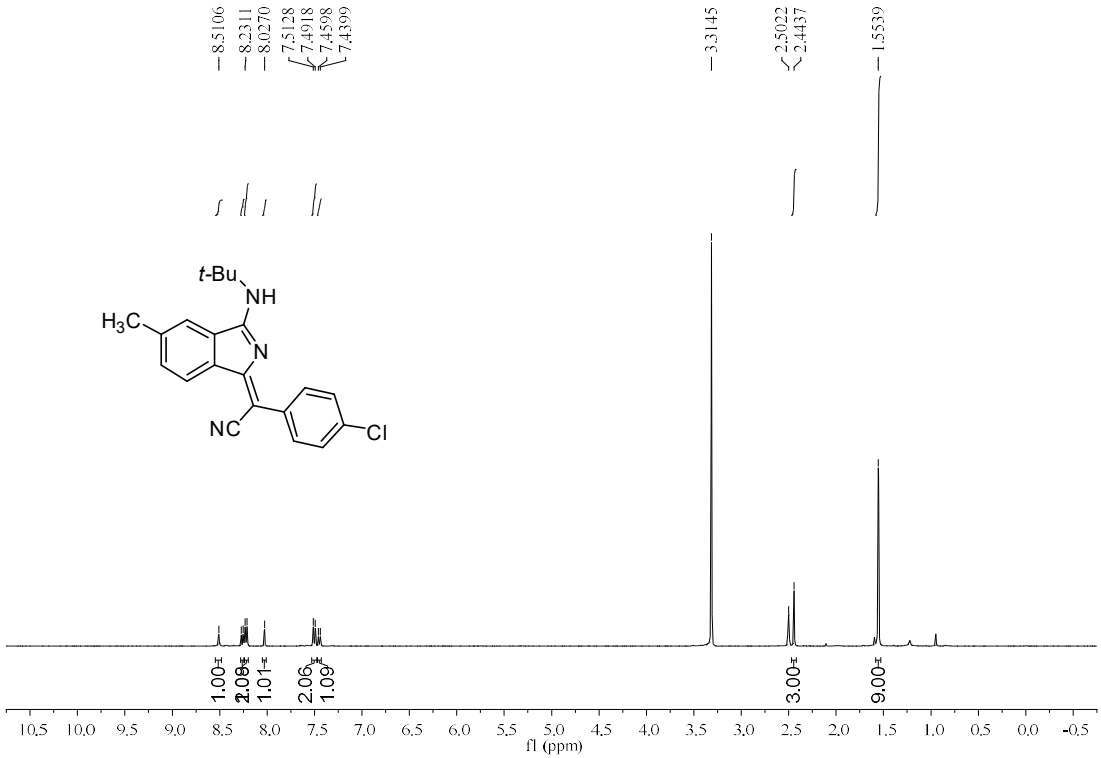
^{1}H NMR (400 MHz, DMSO) spectrum of compound 4k



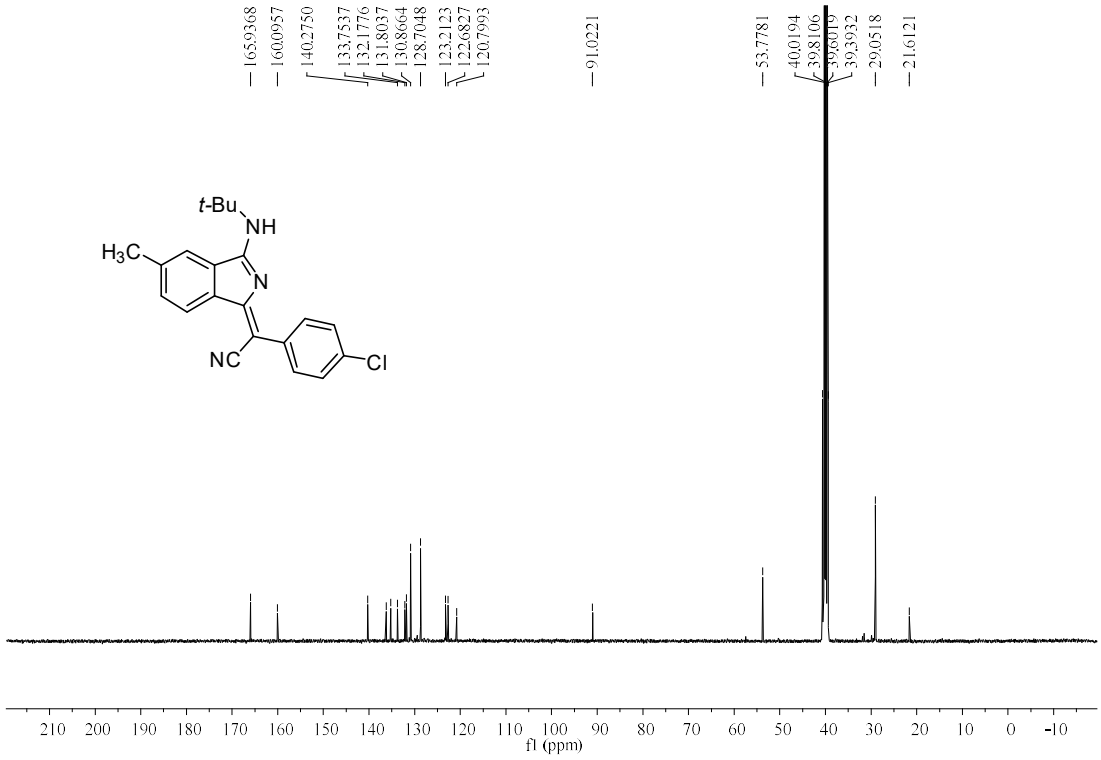
^{13}C NMR (100 MHz, DMSO) spectrum of compound 4k



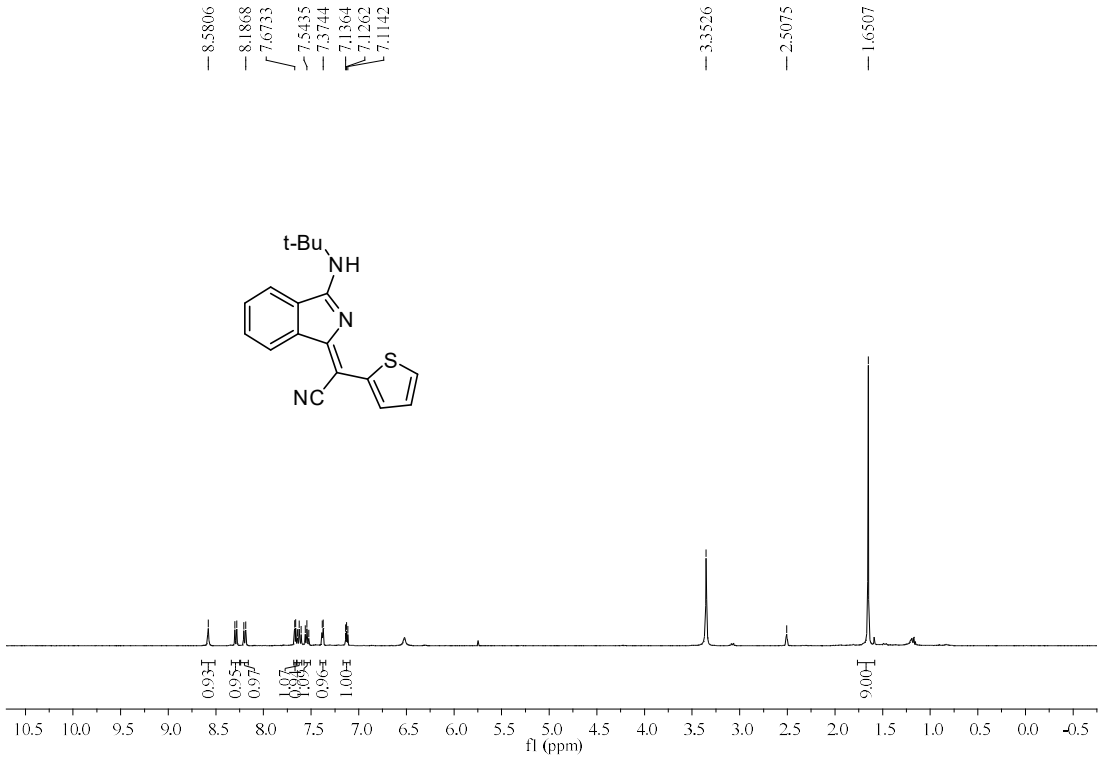
^{1}H NMR (400 MHz, DMSO) spectrum of compound 4l



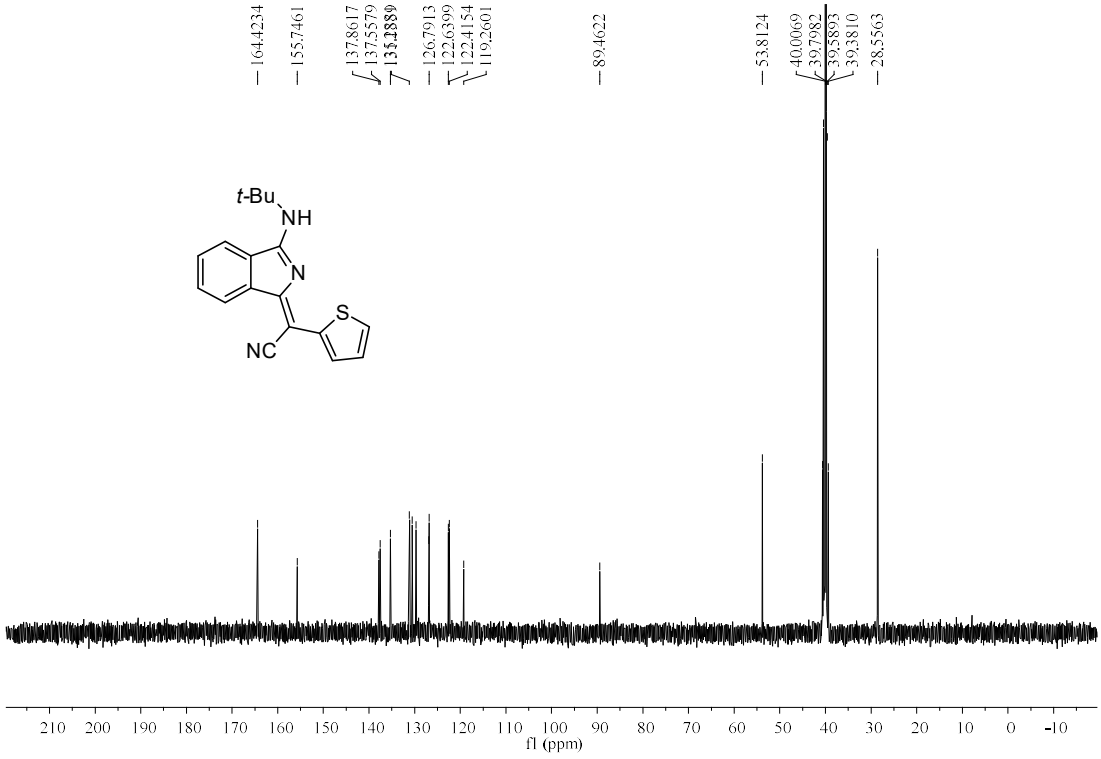
^{13}C NMR (100 MHz, DMSO) spectrum of compound 4l



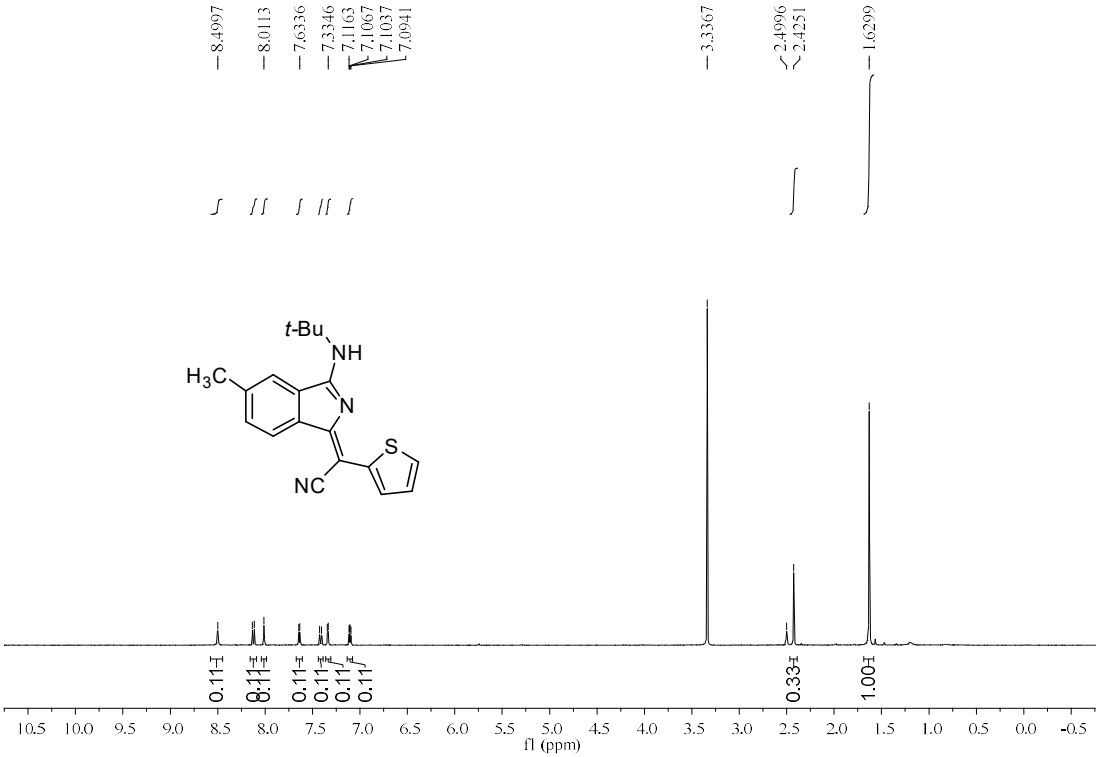
^{1}H NMR (400 MHz, DMSO) spectrum of compound 4m



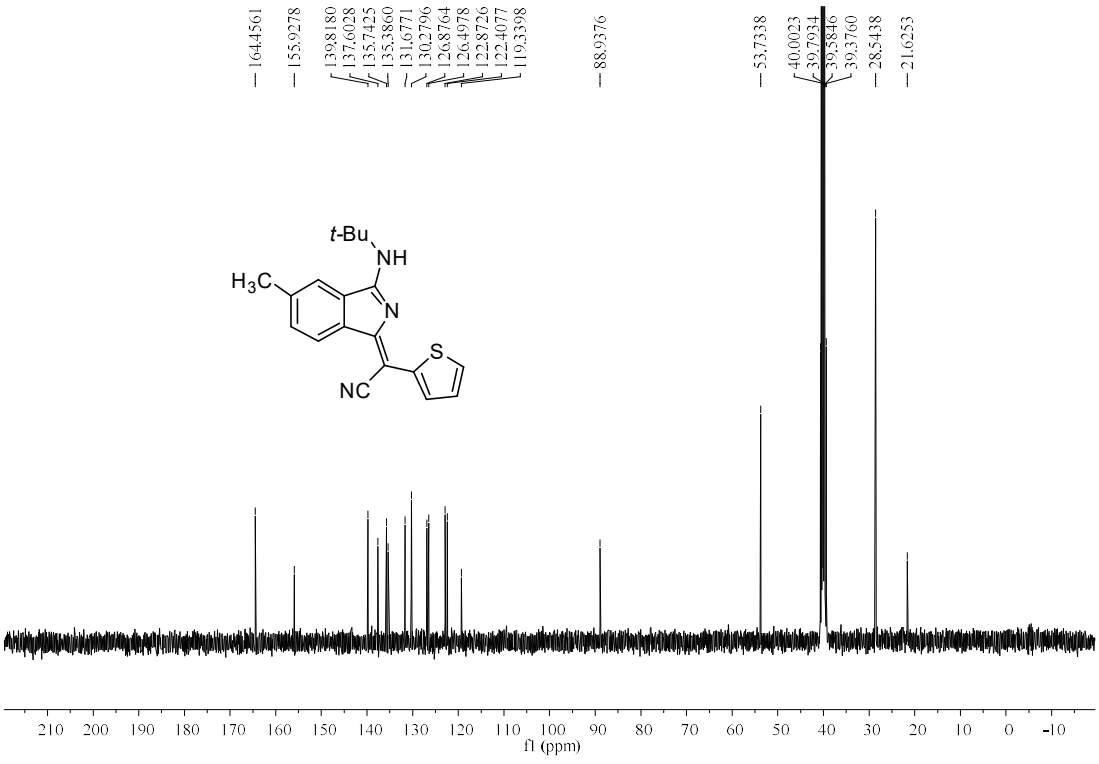
^{13}C NMR (100 MHz, DMSO) spectrum of compound 4m



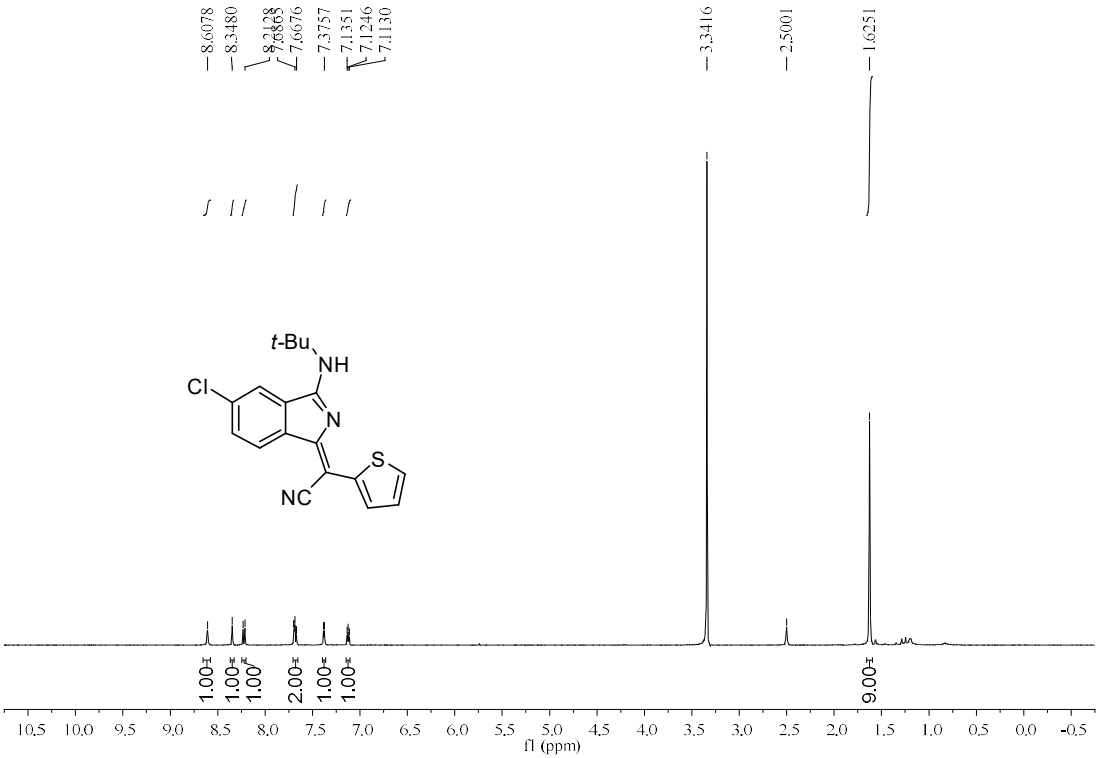
^{1}H NMR (400 MHz, DMSO) spectrum of compound 4n



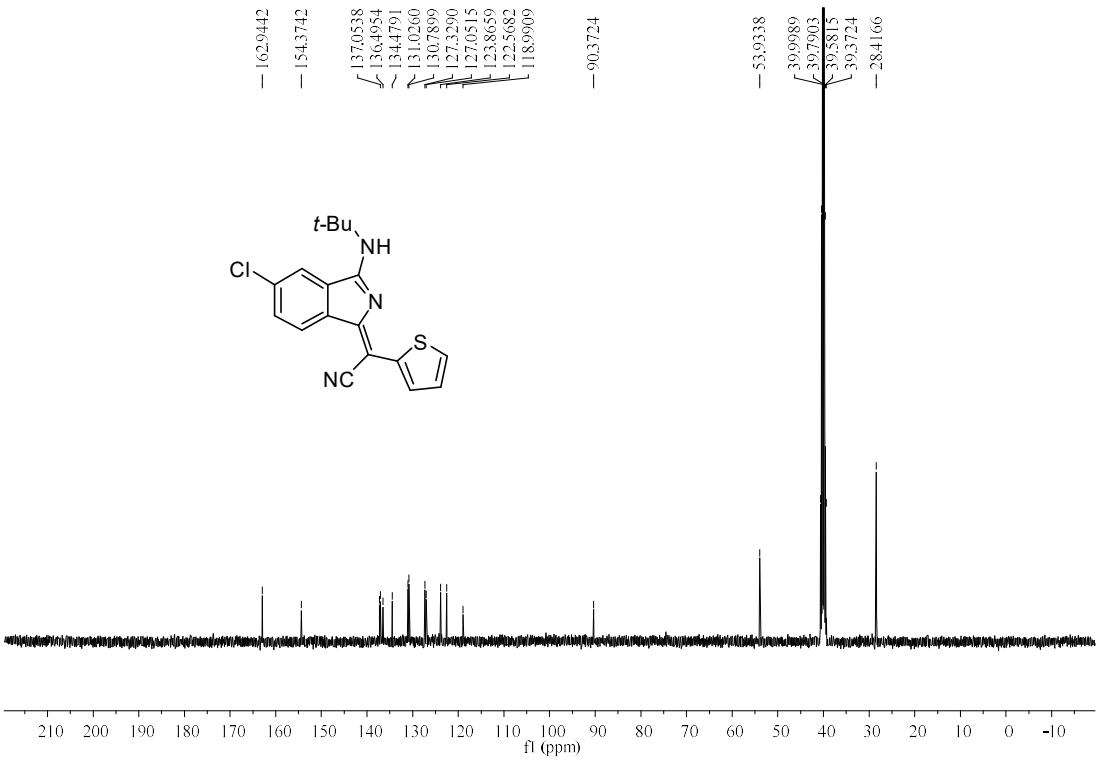
^{13}C NMR (100 MHz, DMSO) spectrum of compound 4n



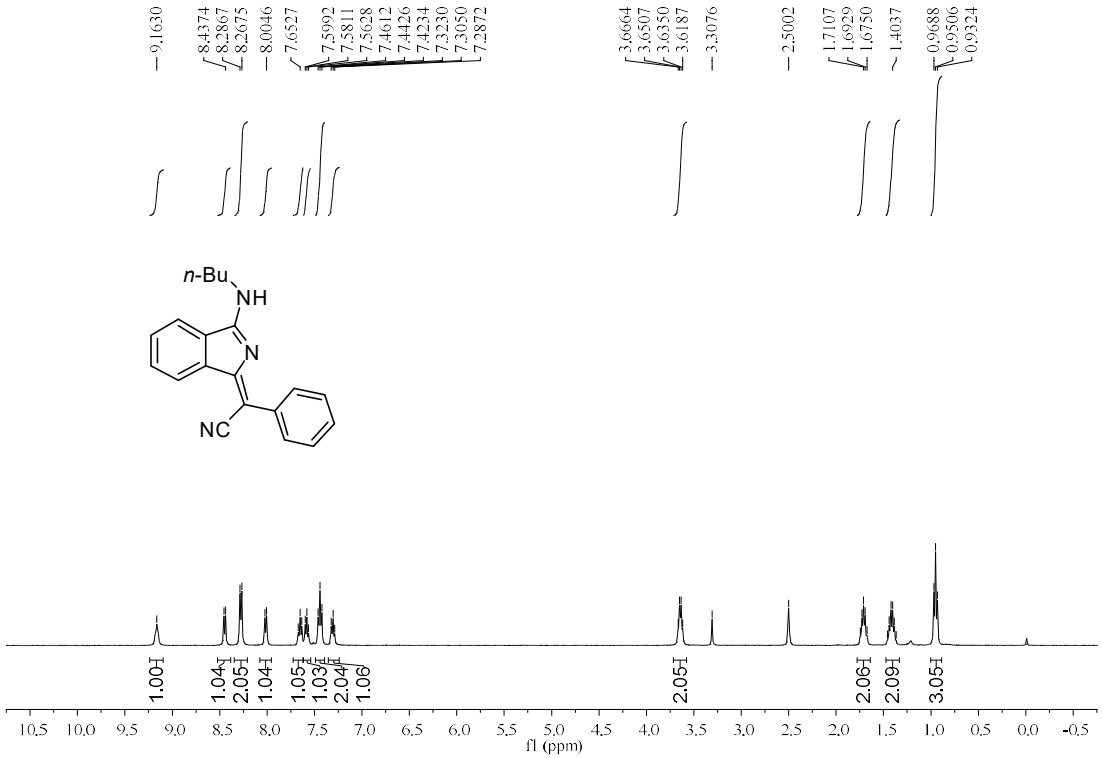
^{1}H NMR (400 MHz, DMSO) spectrum of compound 4o



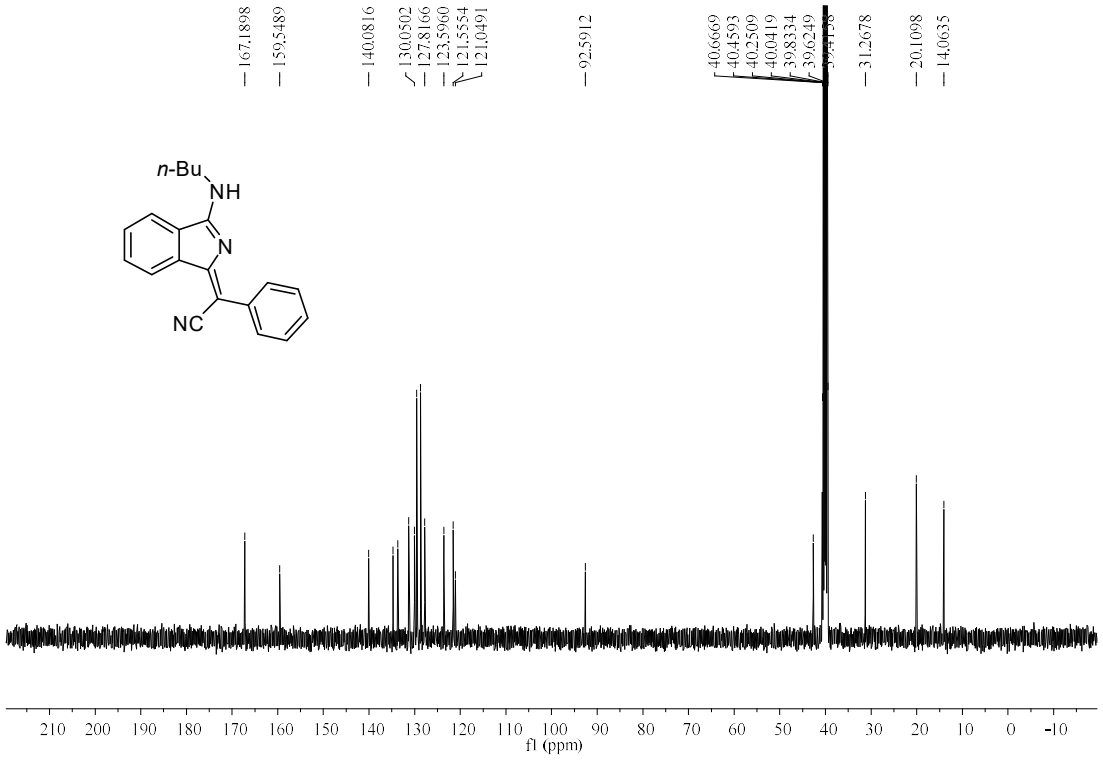
^{13}C NMR (100 MHz, DMSO) spectrum of compound 4o



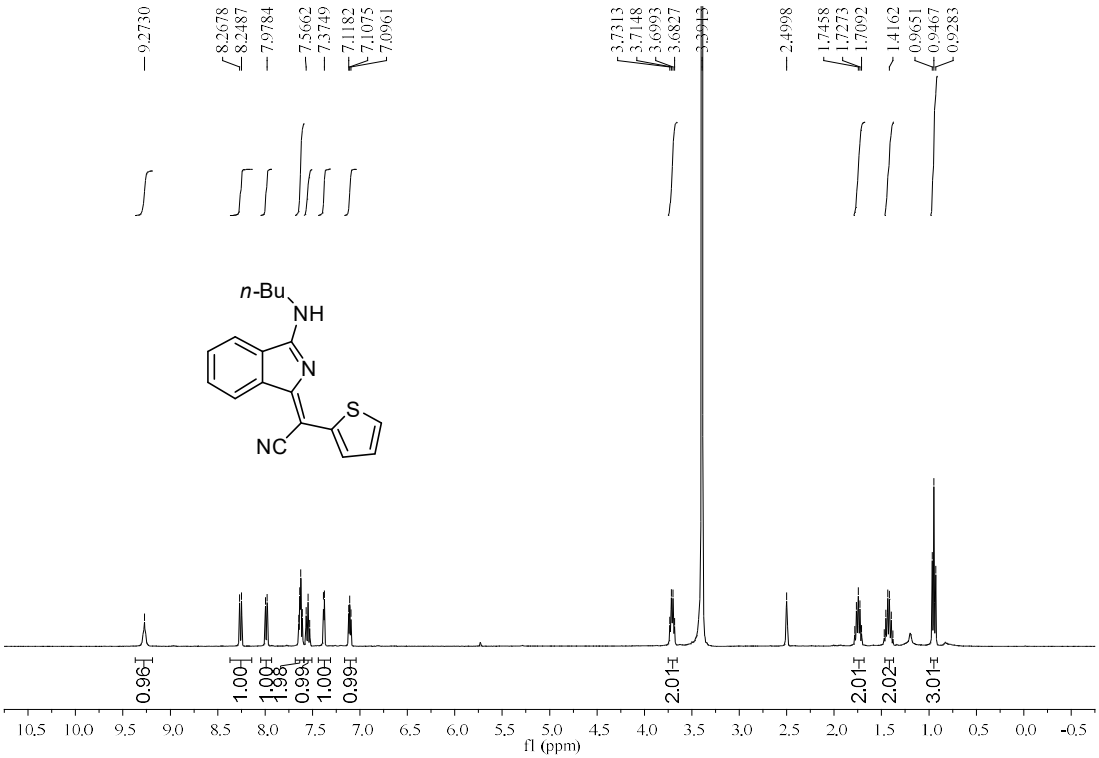
^{1}H NMR (400 MHz, DMSO) spectrum of compound 4p



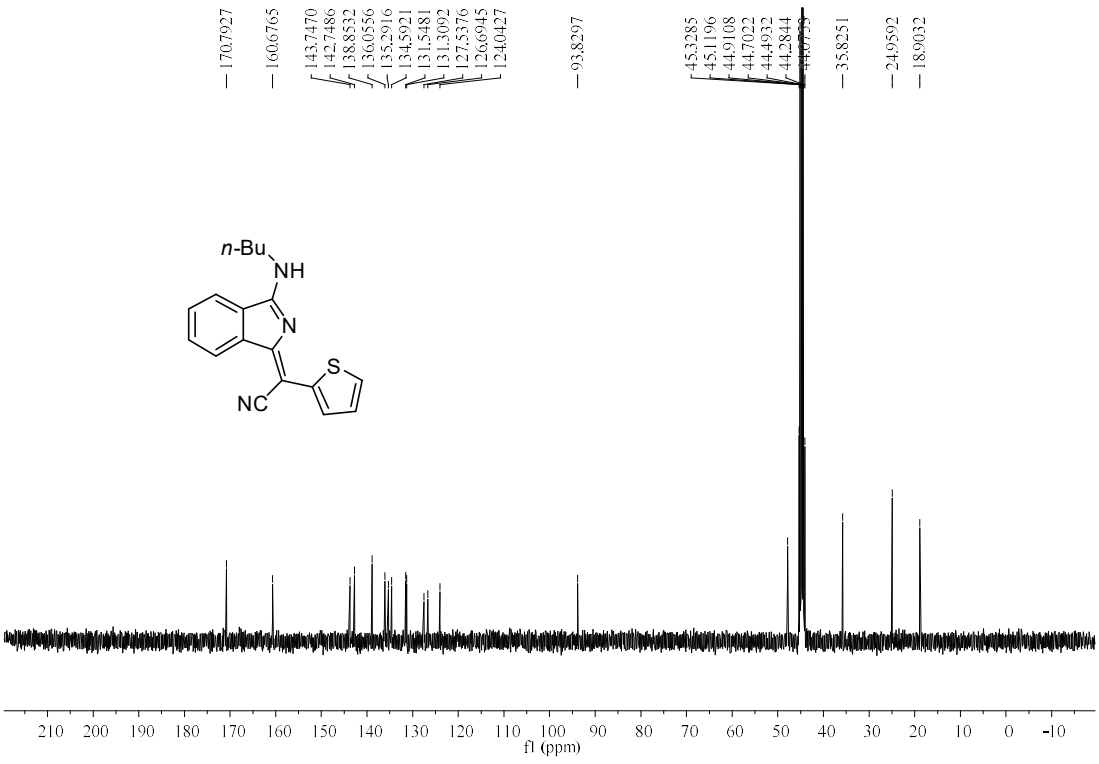
^{13}C NMR (100 MHz, DMSO) spectrum of compound 4p



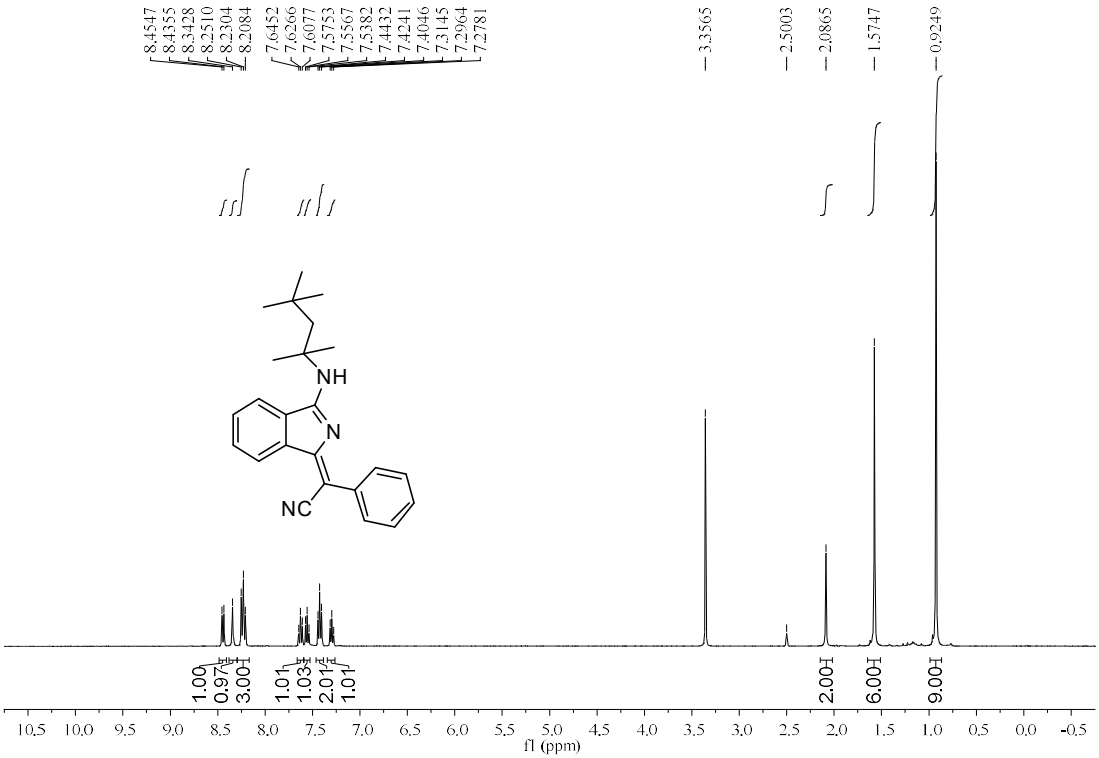
^{1}H NMR (400 MHz, DMSO) spectrum of compound 4q



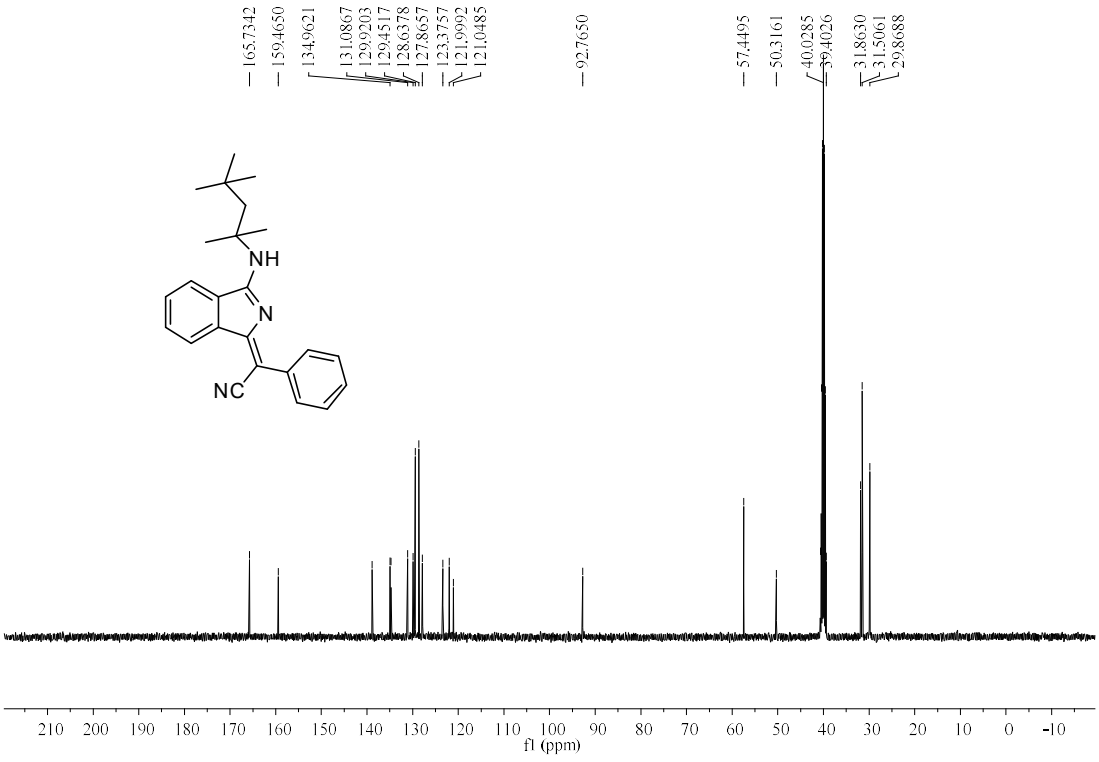
^{13}C NMR (100 MHz, DMSO) spectrum of compound 4q



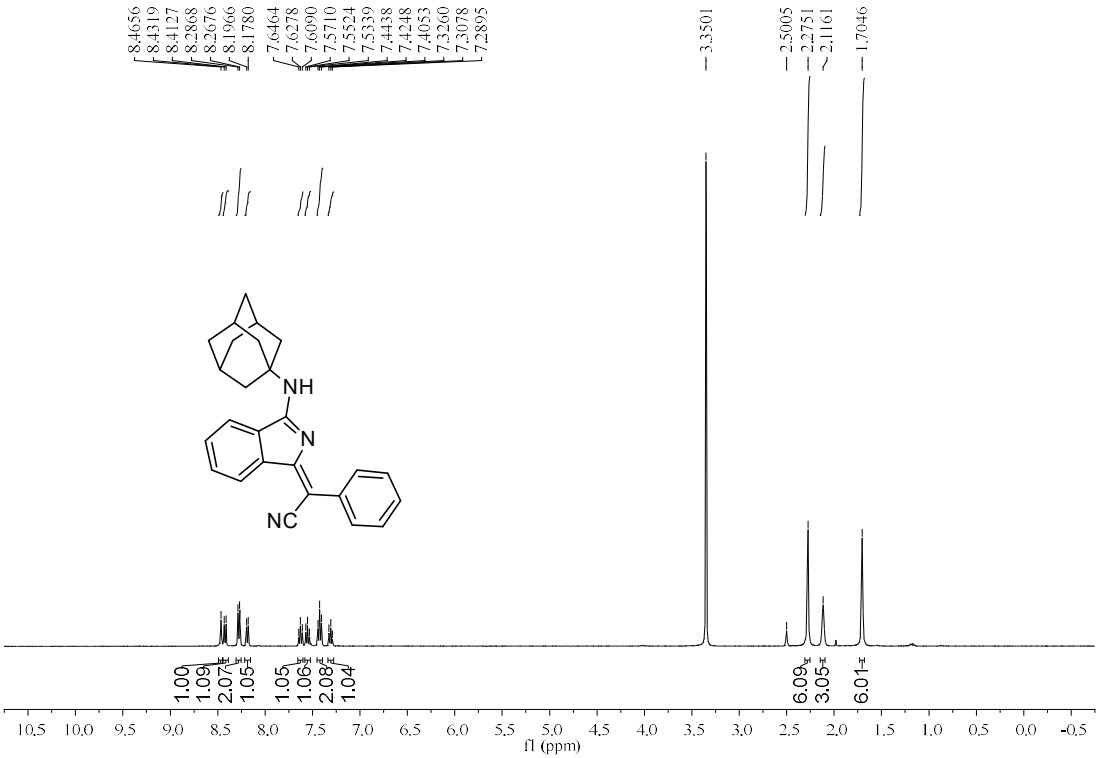
^{1}H NMR (400 MHz, DMSO) spectrum of compound 4r



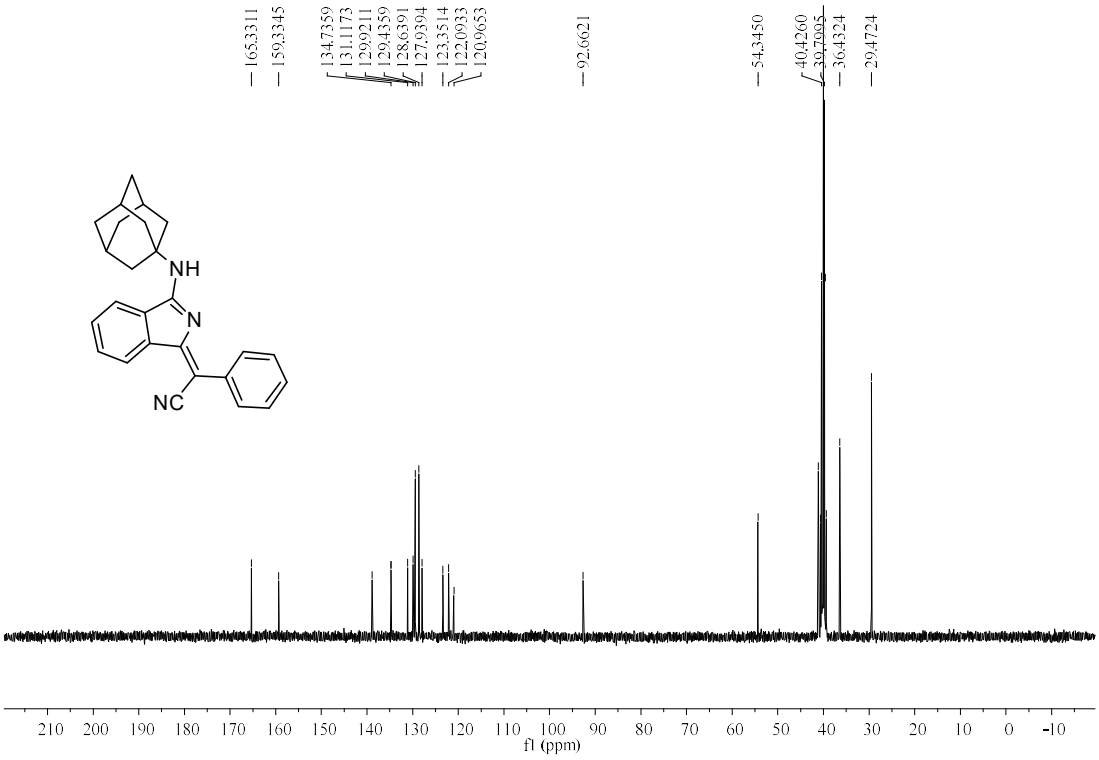
^{13}C NMR (100 MHz, DMSO) spectrum of compound 4r



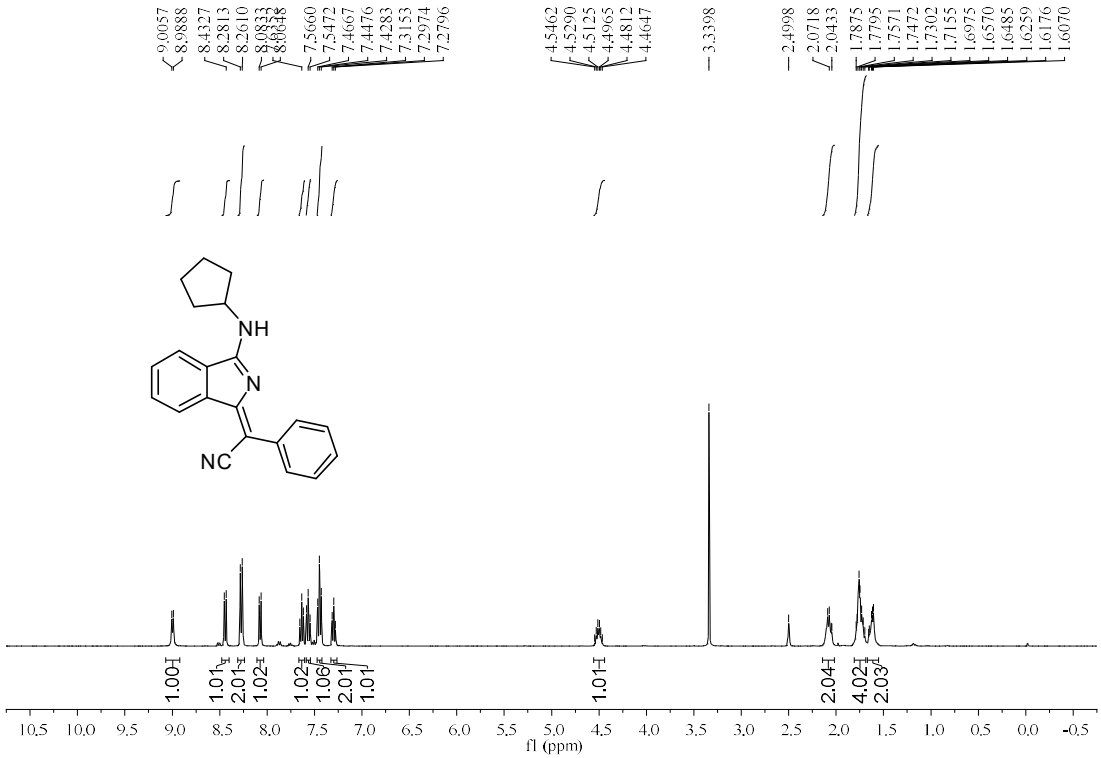
^{1}H NMR (400 MHz, DMSO) spectrum of compound 4s



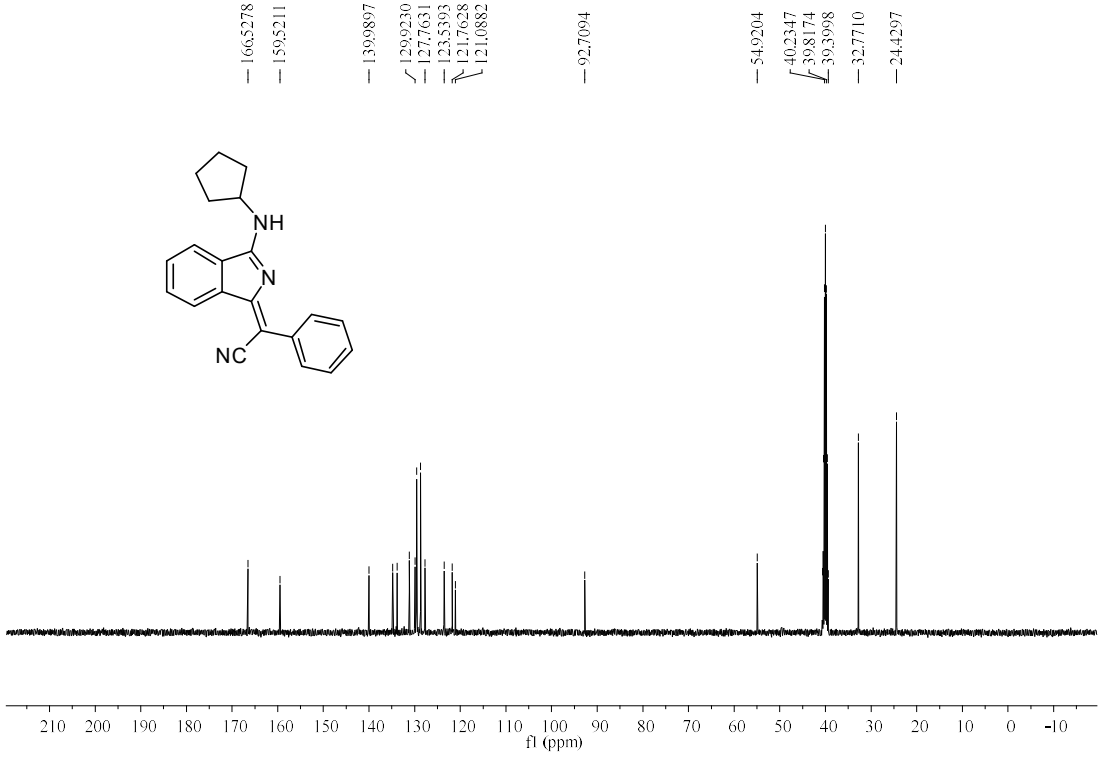
^{13}C NMR (100 MHz, DMSO) spectrum of compound 4s



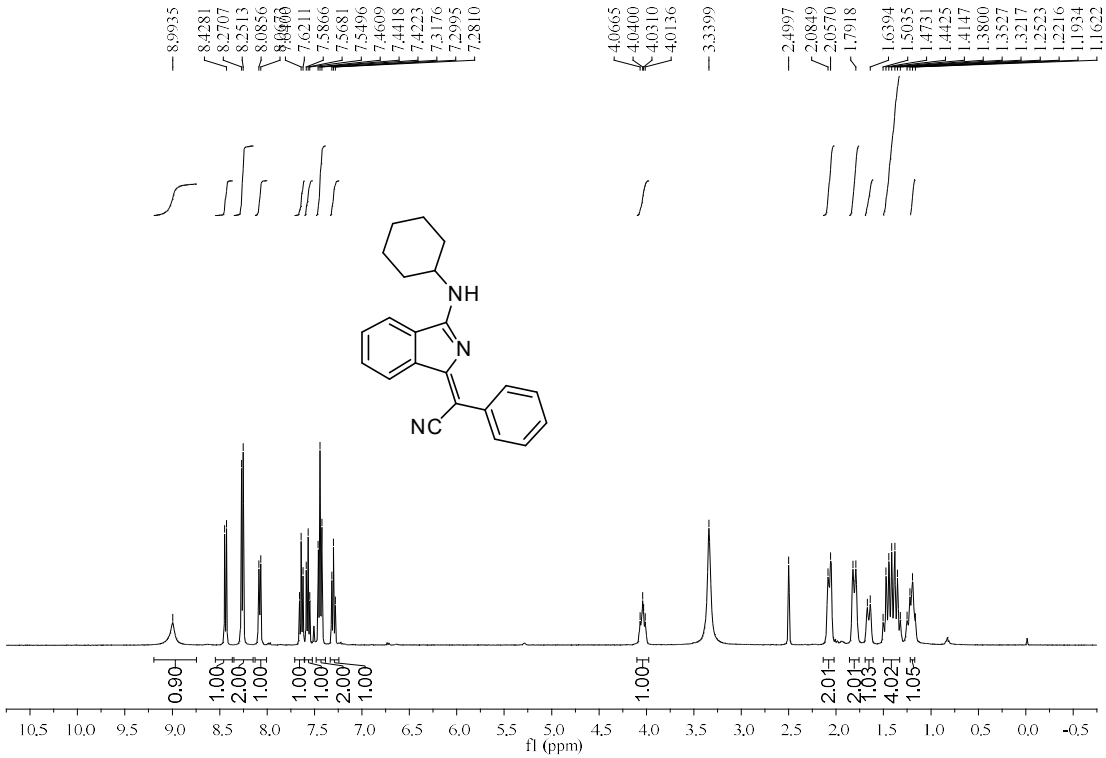
^{1}H NMR (400 MHz, DMSO) spectrum of compound 4t



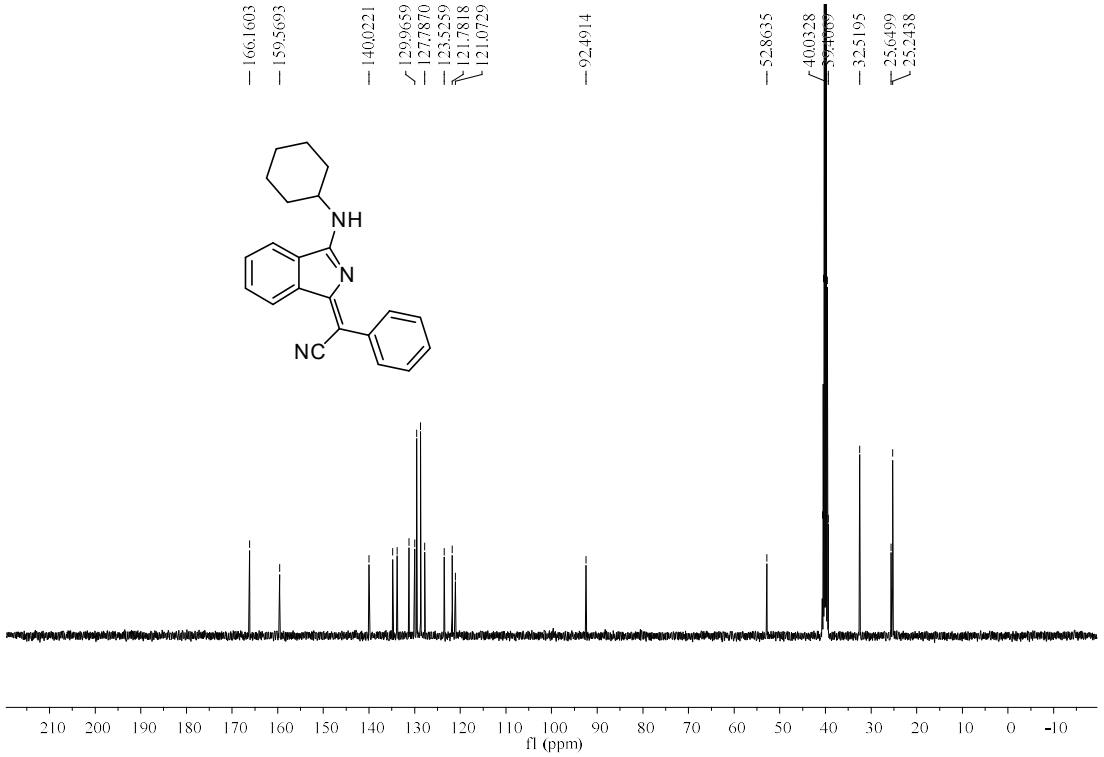
^{13}C NMR (100 MHz, DMSO) spectrum of compound 4t



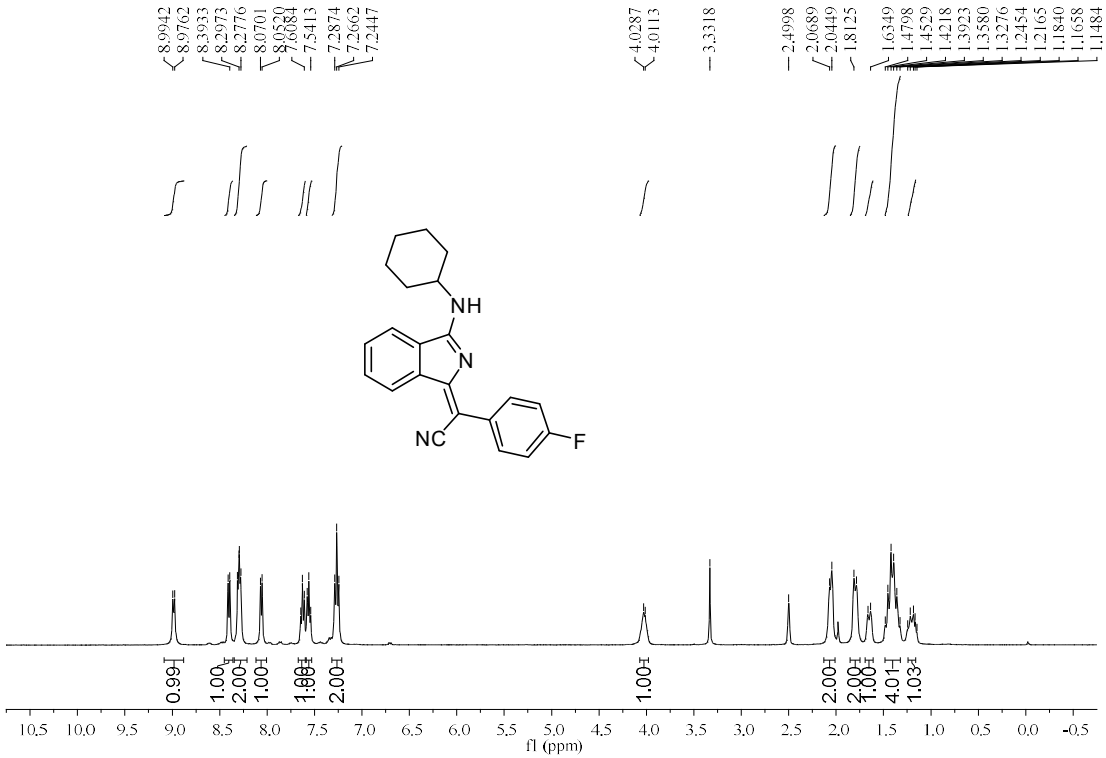
^{1}H NMR (400 MHz, DMSO) spectrum of compound 4u



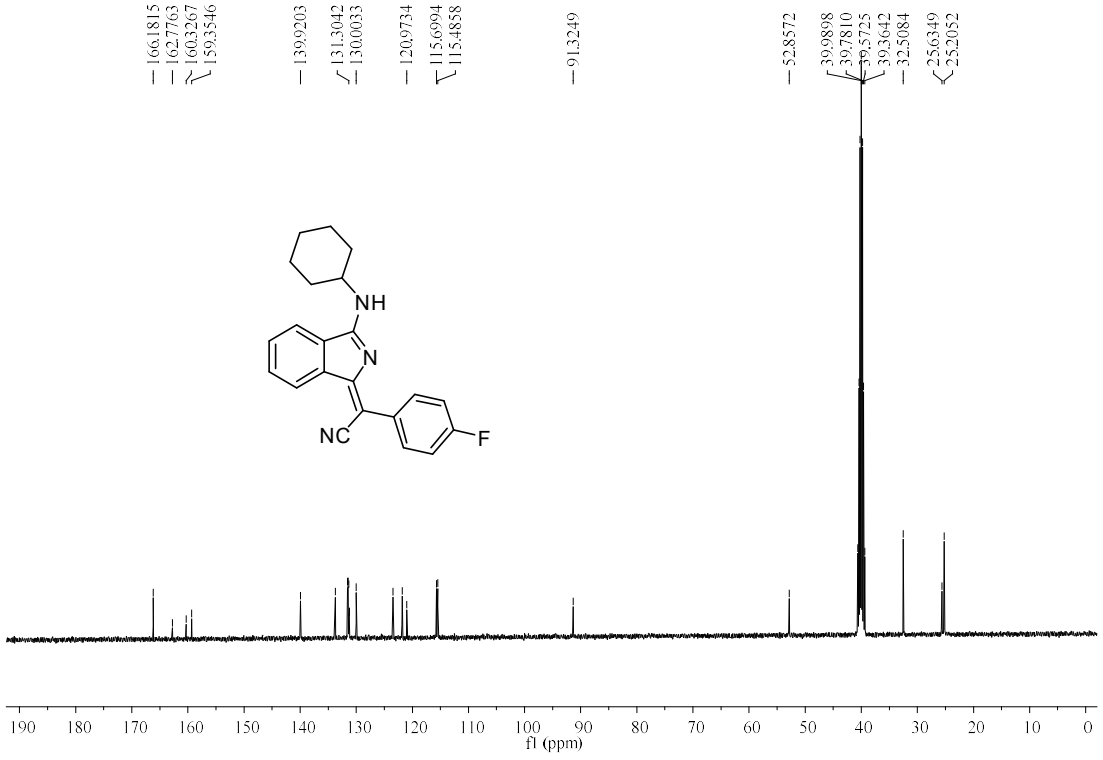
^{13}C NMR (100 MHz, DMSO) spectrum of compound 4u



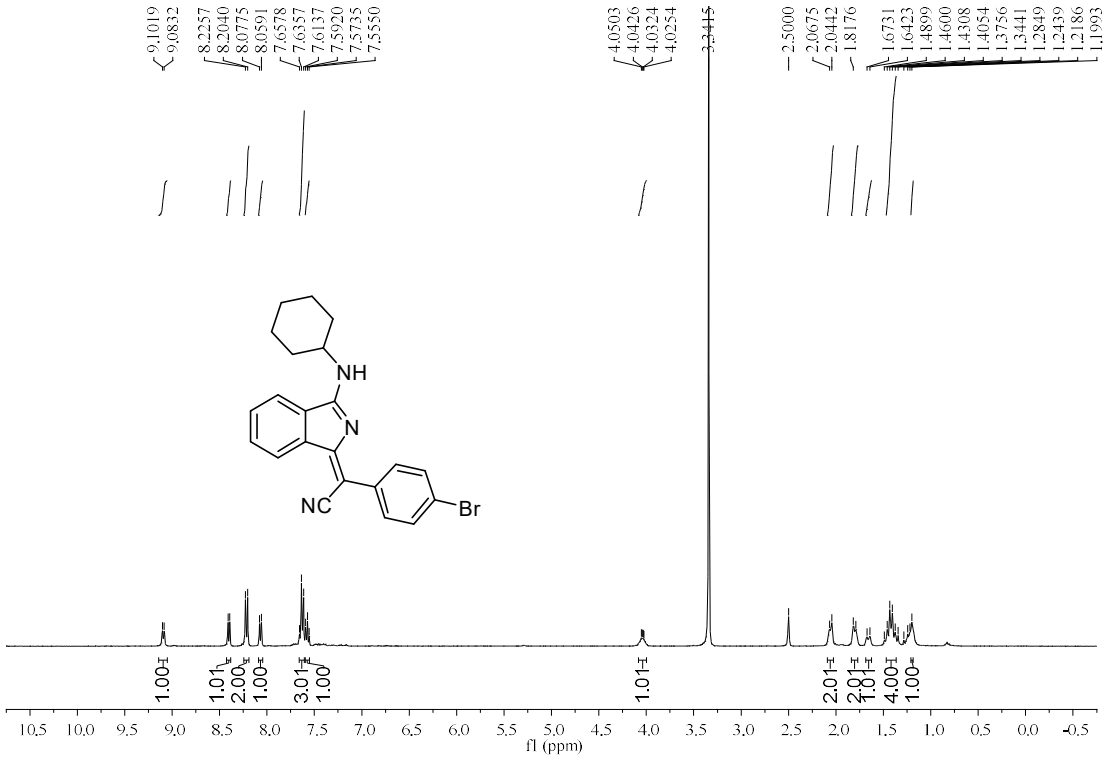
^{1}H NMR (400 MHz, DMSO) spectrum of compound 4v



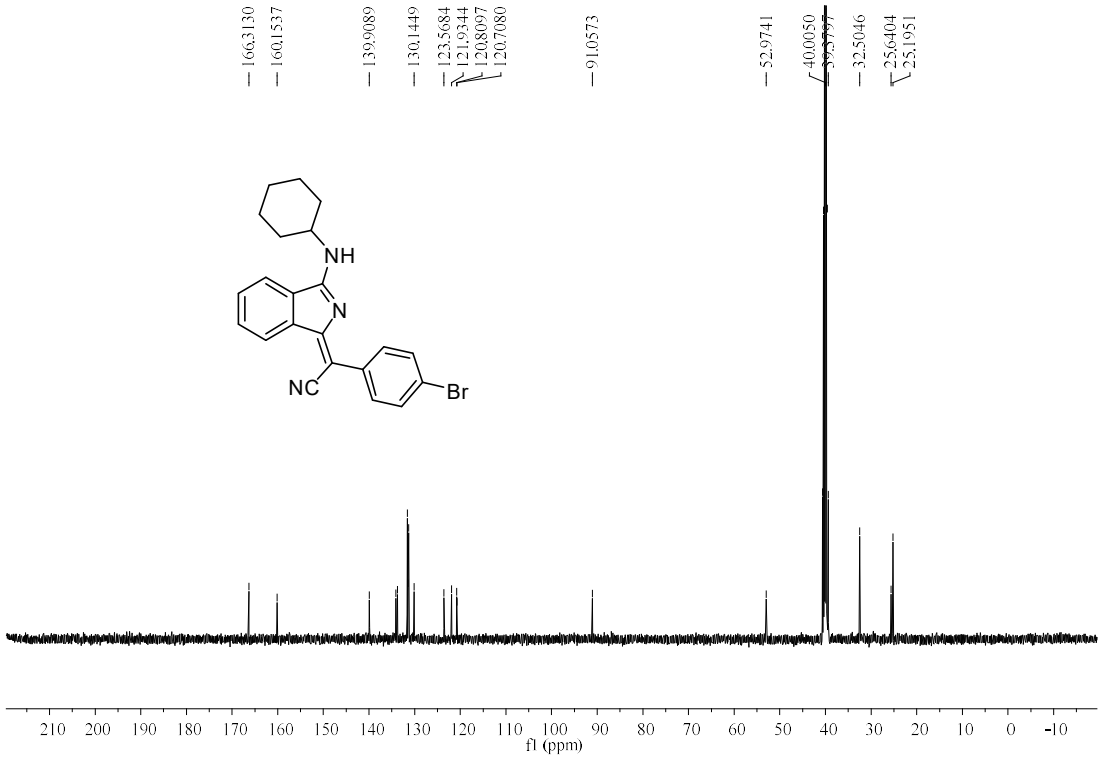
^{13}C NMR (100 MHz, DMSO) spectrum of compound 4v



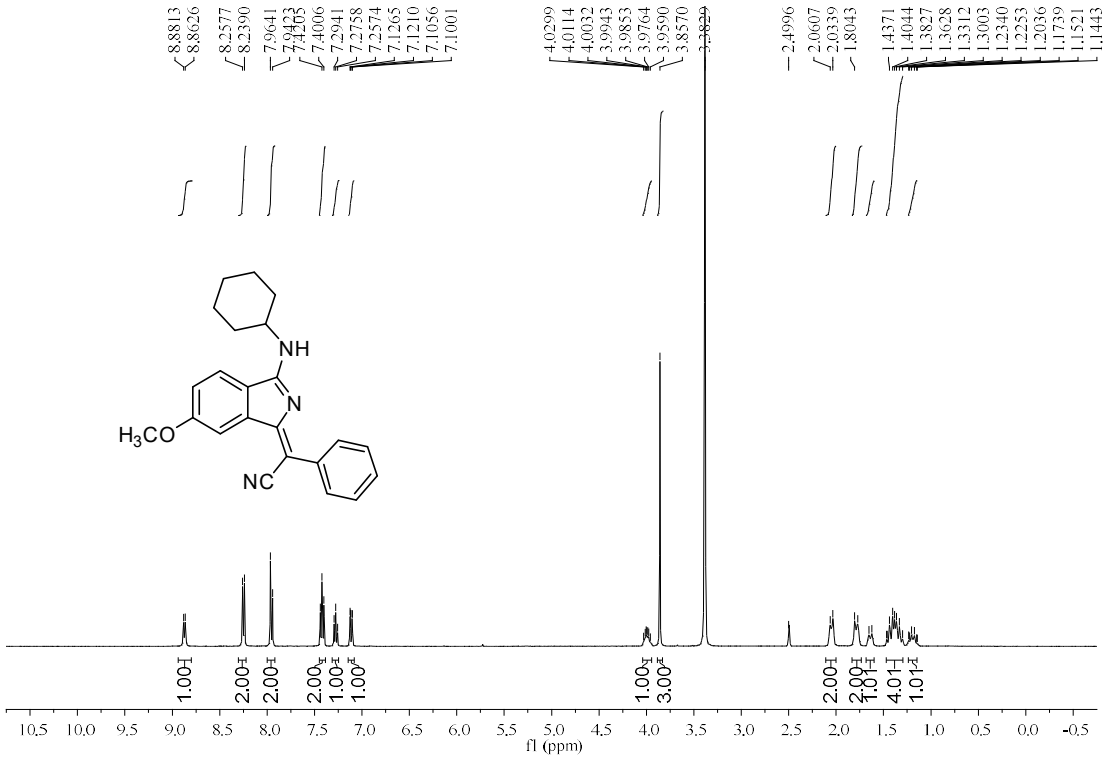
^{1}H NMR (400 MHz, DMSO) spectrum of compound 4w



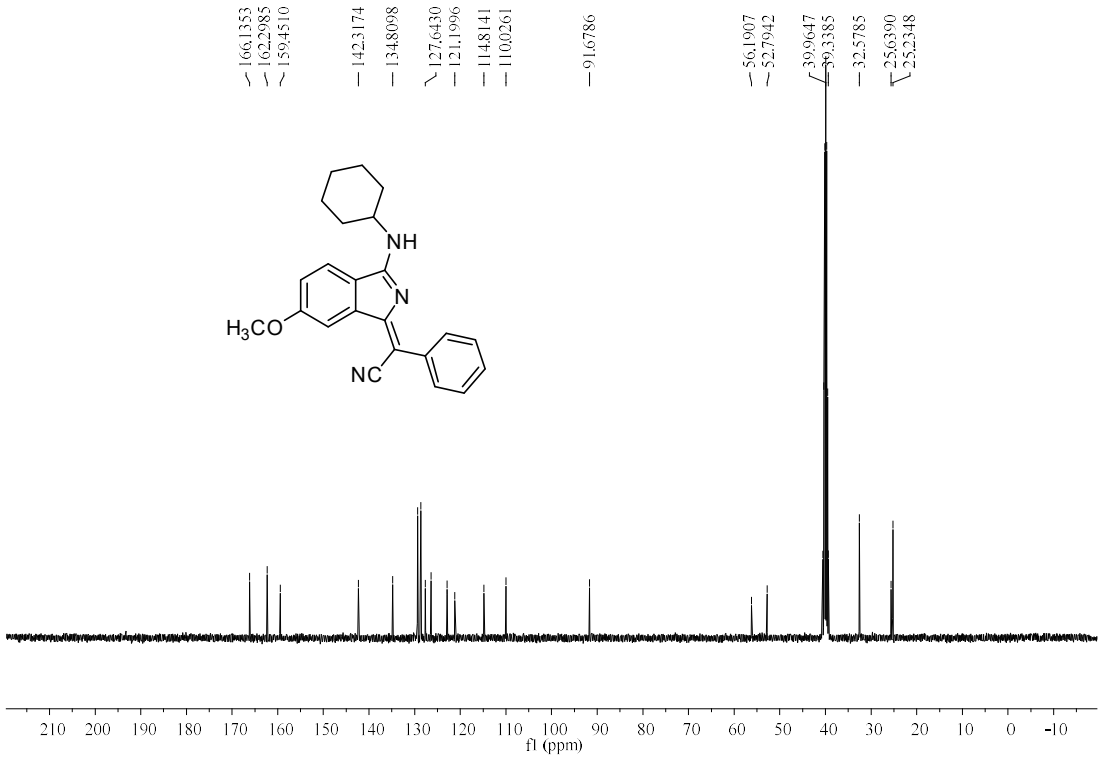
^{13}C NMR (100 MHz, DMSO) spectrum of compound 4w



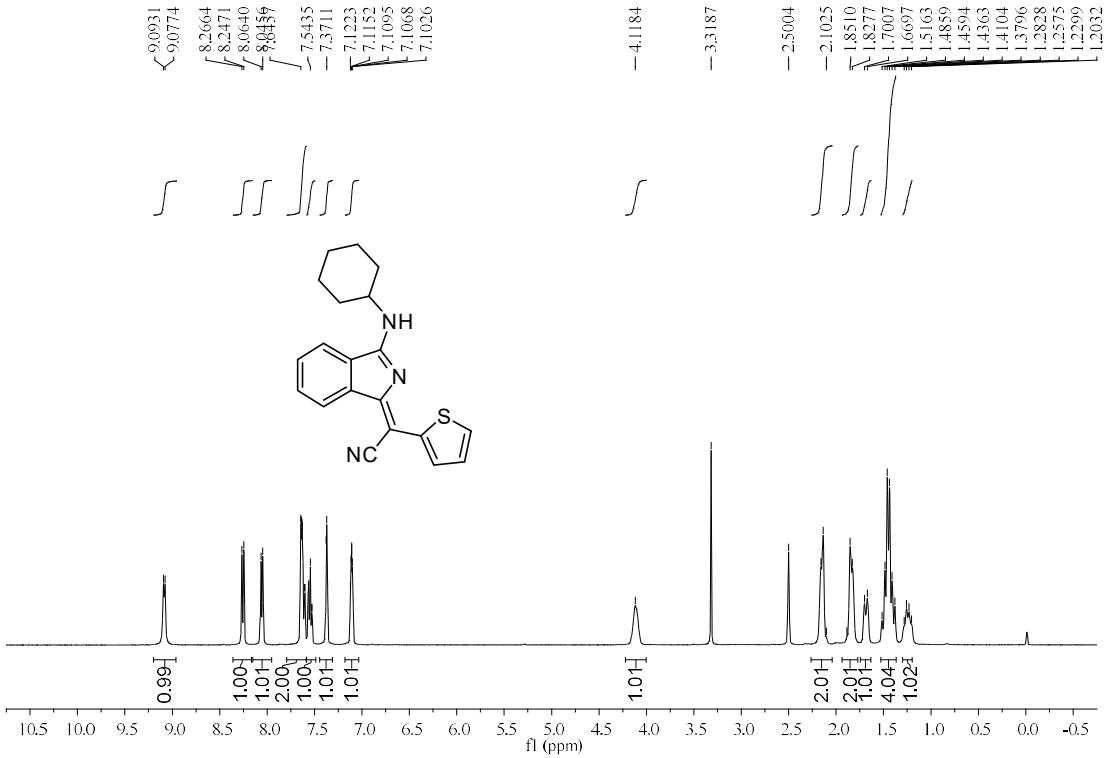
^{1}H NMR (400 MHz, DMSO) spectrum of compound 4x



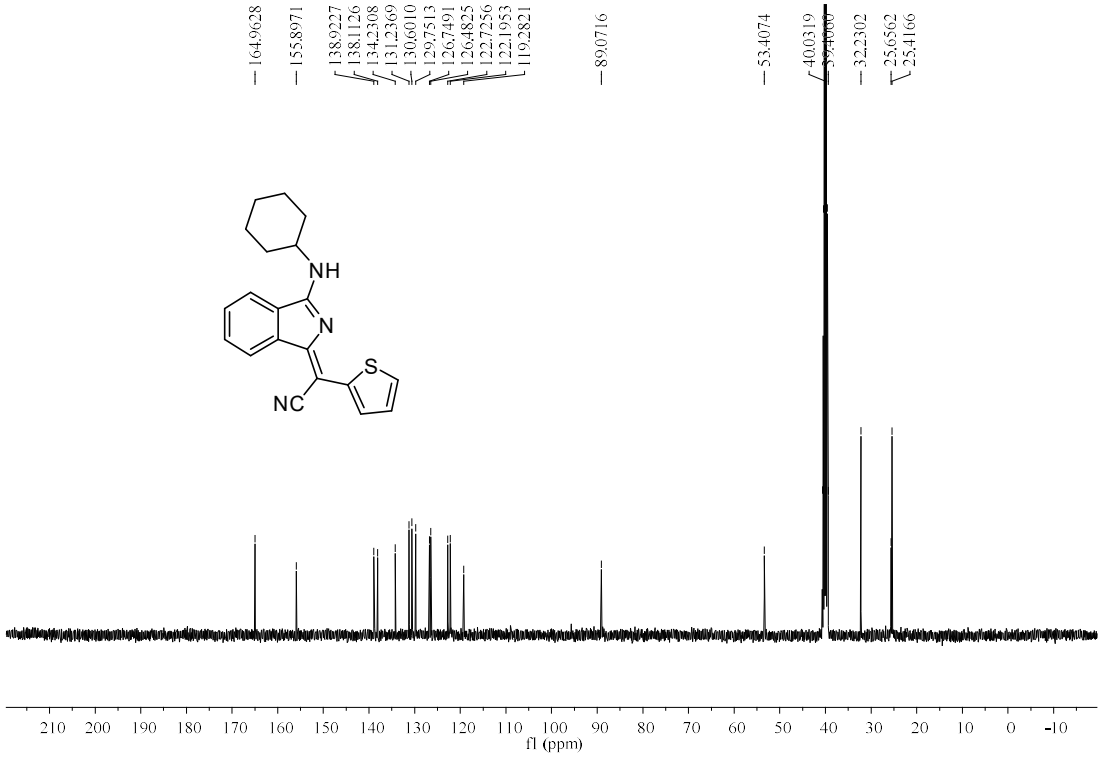
^{13}C NMR (100 MHz, DMSO) spectrum of compound 4x



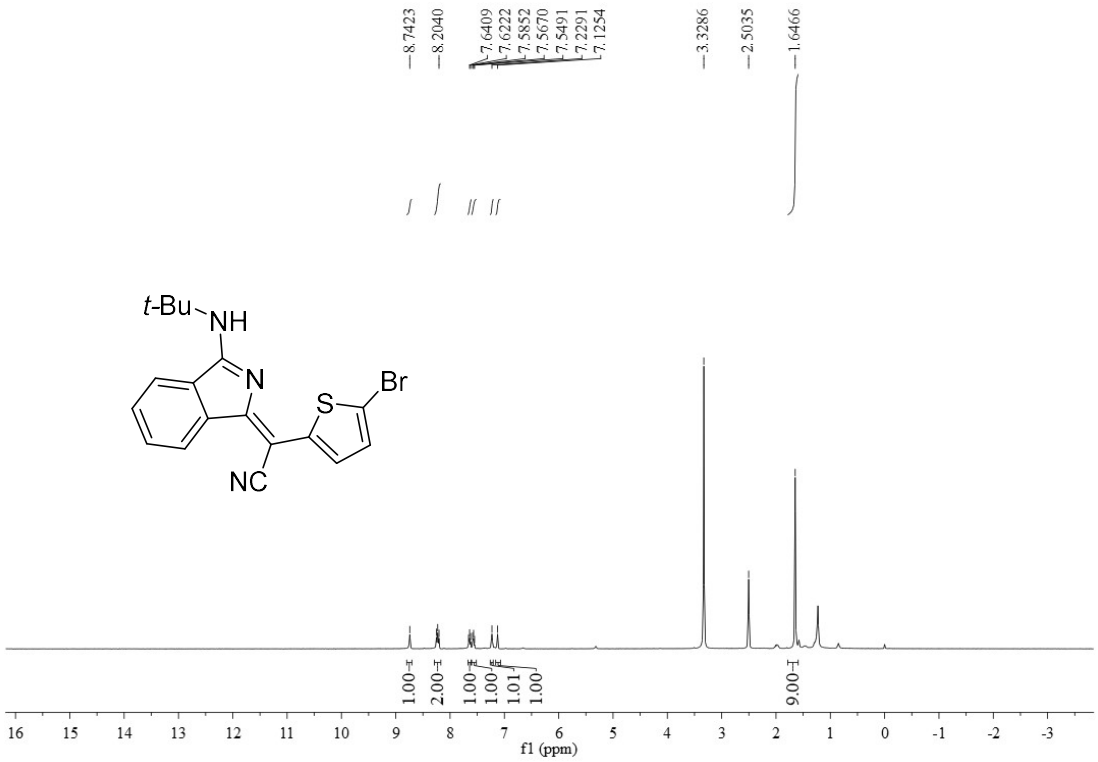
^{1}H NMR (400 MHz, DMSO) spectrum of compound 4y



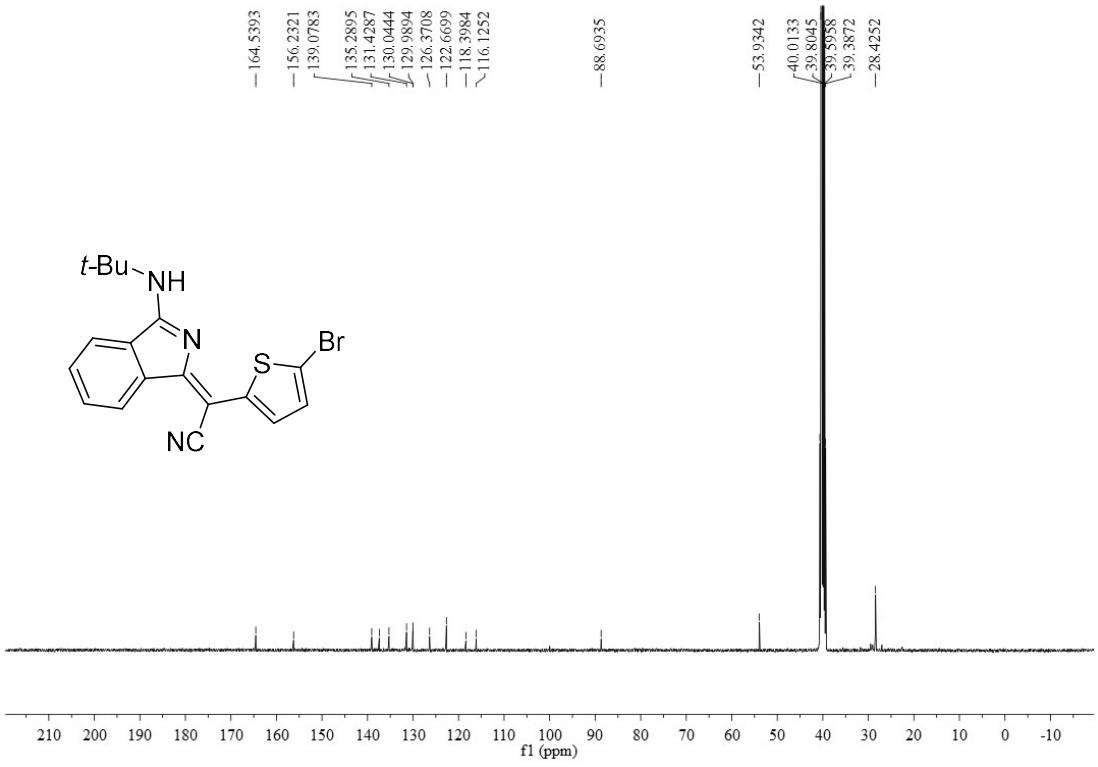
^{13}C NMR (100 MHz, DMSO) spectrum of compound 4y



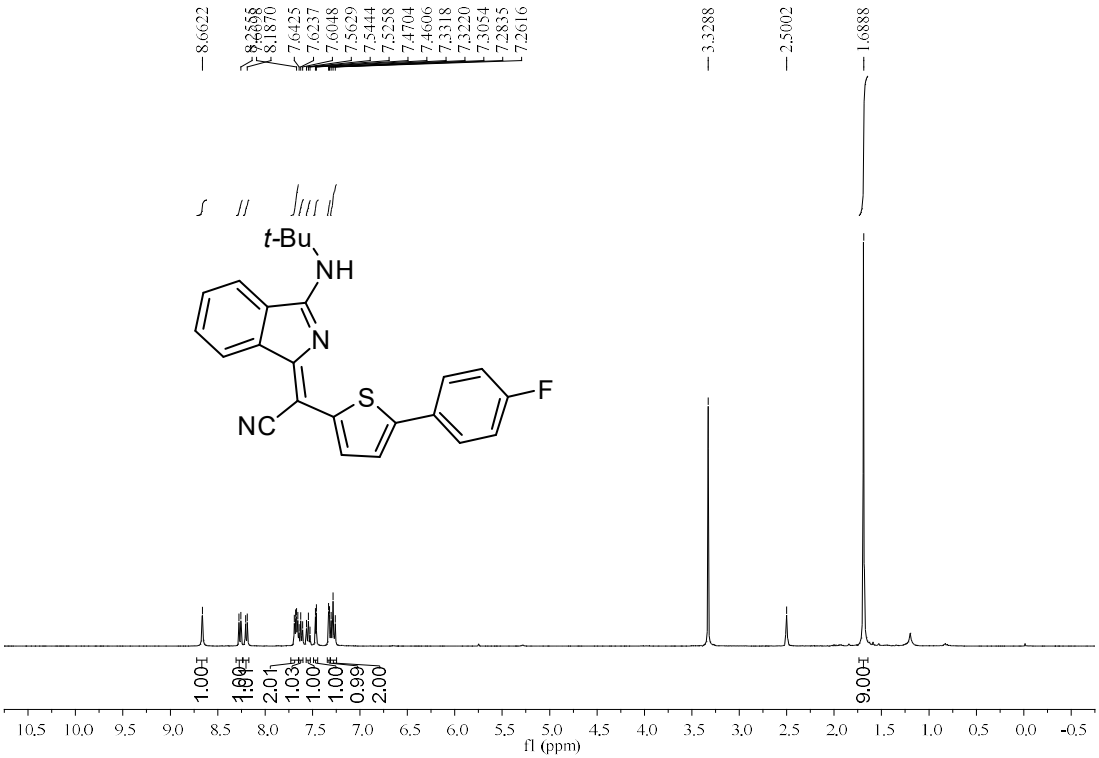
^{1}H NMR (400 MHz, DMSO) spectrum of compound 4m-1



^{13}C NMR (100 MHz, DMSO) spectrum of compound 4m-1



^{1}H NMR (400 MHz, DMSO) spectrum of compound 4m-M



^{13}C NMR (100 MHz, DMSO) spectrum of compound 4m-M