Supporting information

One pot synthesis of thioethers from indoles and *p*-quinone methides using thiourea as a sulfur source

---

Table of contents

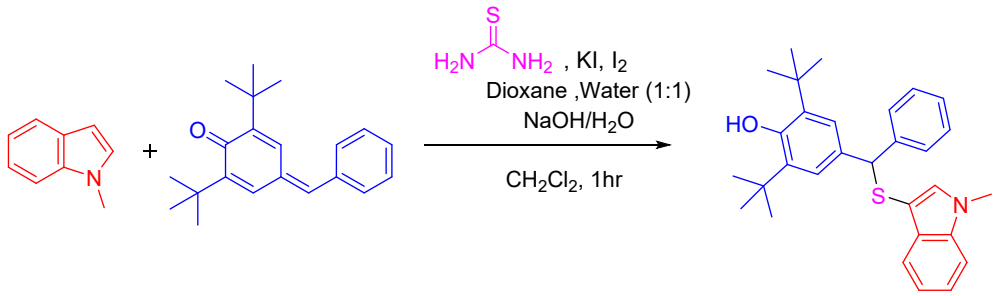
General information

Most of the reagents and starting materials were purchased from commercial sources and used as such. The progress of the reaction was monitored by analytical TLC on silica gel G/GF 254 plates. The column chromatography was performed with silica gel 100-200 mesh using EtOAc/hexane as an eluent. NMR ($^{1}H$and ^{13}C) spectra were recorded either on a 400 MHz using TMS as an internal standard and chemical shifts (δ ppm) (multiplicity, coupling constant (Hz), integration). The abbreviations for multiplicity are as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets. Melting points are uncorrected were determined in capillary tubes on a hot stage melting point apparatus containing silicon oil. High resolution mass spectra were taken with a 3000 mass spectrometer and Q-TOF Analyzer. IR spectra were recorded using a FTIR spectrophotometer.

(a). General procedure for synthesis of starting materials *p*-quinone methides

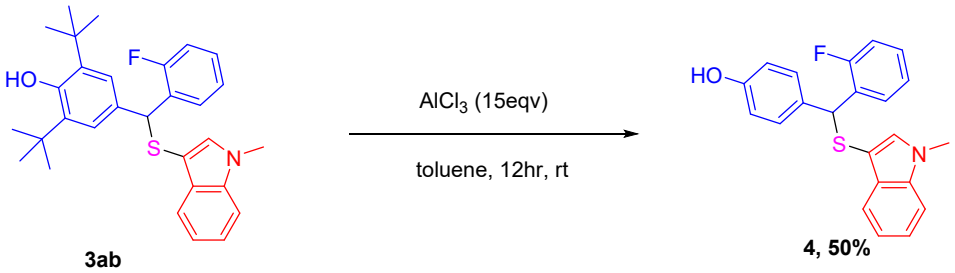
In a Dean-Stark apparatus, a solution of phenols (10.0 mmol) and the corresponding aldehydes (10.0 mmol) in toluene (40 mL) was heated to reflux. Piperidine (20.0 mmol, 2.0 mL) was drop wise added over 0.5 h. The reaction mixture was continued to reflux for overnight. After cooling just below the boiling point of the reaction mixture, acetic anhydride (20.0 mmol, 2.0 mL) was added, and stirring was continued for 30 min. Then, the reaction mixture was poured on ice-water (200 mL) and extracted with EtOAc (4 × 50 mL). The combined organic phases were dried over anhydrous Na_2SO_4, and the solvent of the filtrate was removed under reduced pressure. The crude products were purified by column chromatography, affording the desired substrate *p*-QMs.

(b). General Procedure for Synthesis of diarylmethyl thioether :



A mixture of indole (0.5 mmol), thiourea (76.1 mg, 1 mmol), iodine (126.9 mg, 0.5 mmol) and potassium iodide (83 mg, 0.5 mmol) in dioxane (1 mL) with water (1 mL) were taken in a round bottom flask. Subsequently, NaOH (0.2 g in 1mL water) and *p*-quinone methides (149.25.5 mg, 0.5 mmol) was added with dichloromethane and the mixture was stirred at room temperature for 1hr. Upon completion, DCM (10 mL) was added, and the mixture was washed with water (20 X 3mL), dried with Na_2SO_4 and concentrated under vacuum to give the crude product. Further column chromatography on silica gel (ethyl acetate/petroleum ether) was needed to afford the pure desired product.

(c). Procedure for synthesis of de-tert-butyl product 4:

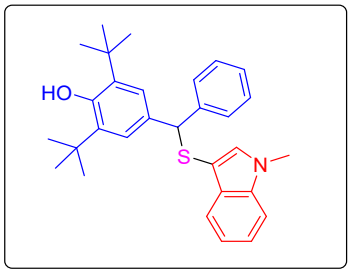


3ab **4, 50%**

In an oven-dried 50 mL round-bottom flask 3ab (0.5 mmol, 1.0eqv) and $AlCl_3$ (15eqv) were mixed. The flask was degassed, and toluene (2mL) was added. The reaction mixture was further stirred at 25 ^{0}C for 12 hr. The reaction mixture was then quenched with water 2mL. Then, the reaction mixture was extracted with EtOAc (3 × 20 mL). The combined organic phases were dried over anhydrous Na_2SO_4, and the solvent of the filtrate was removed under reduced pressure. The crude products were purified by column chromatography, affording the desired product 4.

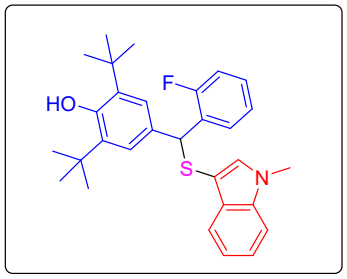
2. ^{1}H and ^{13}C NMR Spectral data of all the compounds

2,6-di-tert-butyl-4-(((1-methyl-1H-indol-3-yl)thio)(phenyl)methyl)phenol (3aa)



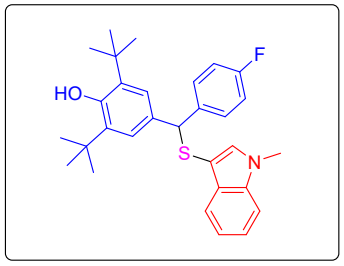
Yield 90% (205mg); Light brown solid; mp 120-122 °C; (KBr) cm^{-1}: 2953, 1583, 1431, 1234, 1152, 738, 697; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58 (d, J = 7.8 Hz, 1H), 7.42 (d, J =7.42 Hz, 2H), 7.29-7.23 (m, 3H), 7.22-7.16 (m, 2H), 7.11 (t, J = 7.2 Hz, 1H), 7.04 (s, 2H), 6.7 (s, 1H), 5.1 (s, 1H), 5.0 (s, 1H), 3.63 (s, 3H), 1.32 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.6, 142.3, 136.9, 135.6, 134.3, 132.2, 130.3, 128.5, 128.1, 126.7, 125.1, 121.9, 119.9, 119.5, 109.3, 103.9, 59.0, 34.2, 32.8, 30.2; mass (ES-) HRMS (ESI-TOF) calcd for $C_{30}H_{34}NOS$ 456.2361 $(M-H)^-$ Found 456.2381.

2,6-di-tert-butyl-4-((2-fluorophenyl)((1-methyl-1H-indol-3-yl)thio)methyl)phenol (3ab)



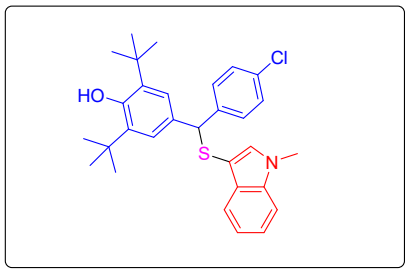
Yield 92% (218mg); light yellow solid; mp 130-132 °C; (KBr) cm^{-1}: 2445, 1505, 1359, 1234, 1136, 740, 670; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85-7.82 (d, m, 1H), 7.62 (d, J = 7.90 Hz, 1H), 7.28-7.19 (m, 4H), 7.16-7.13 (m, 1H), 7.11 (s, 2H), 6.97-6.93 (m, 1H), 6.86 (s, 1H), 5.57 (s, 1H), 5.08 (s, 1H), 3.69 (s, 3H), 1.36 (s, 18H); ^{13}C NMR (100MHz, $CDCl_3$): δ 161.1, 159.1, 152.7, 136.9, 135.4, 134.6, 131.3, 130.3, 129.89, 129.87, 129.7, 129.6, 128.3, 128.2, 125.0, 123.90, 123.88, 122.04, 120.0, 119.5, 115.35, 115.17, 109.28, 103.67, 51.20, 51.18, 34.2, 32.8, 30.2; mass (ES-) HRMS (ESI-TOF) calcd for $C_{30}H_{33}FNOS$ 474.2272 $(M-H)^-$ Found 474.2287.

2,6-di-tert-butyl-4-((4-fluorophenyl)((1-methyl-1H-indol-3-yl)thio)methyl)phenol (3ac)



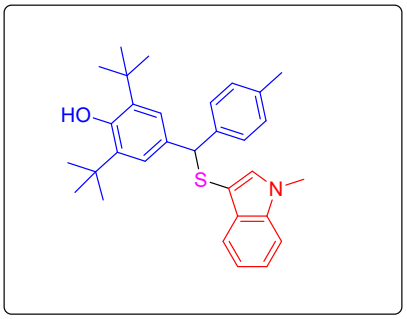
Yield 91% (216mg); light yellow solid; mp 110-112 °C; (KBr) cm^{-1}: 2929, 2556, 1458, 1429, 1212, 739, 631; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (d, J=*7.83*, 1H), 7.37-7.35 (m, 1H) ,7.24-7.19 (m, 2H), 7.12 (t, J = 7.06 Hz, 1H), 7.02 (s, 2H), 6.94 (t, J=8.75 Hz, 2H), 6.73 (s, 1H), 5.17 (s, 1H), 5.06 (s, 1H), 3.65 (s, 3H), 1.33 (s, 18H); ^{13}C NMR (100MHz, $CDCl_3$): δ 162.6, 152.7, 138.16, 138.13, 136.98, 135.48, 134.68, 131.96, 130.3, 130.1, 130.07, 125.07, 122.0, 120.0, 119.4, 114.9, 114.7, 109.3, 103.7, 58.2, 34.2, 32.8, 30.2; mass (ES-) HRMS (ESI-TOF) calcd for $C_{30}H_{33}FNOS$ 474.2272 $(M-H)^-$ Found 474.2287.

2,6-di-tert-butyl-4-((4-chlorophenyl)((1-methyl-1H-indol-3-yl)thio)methyl)phenol (3ad)



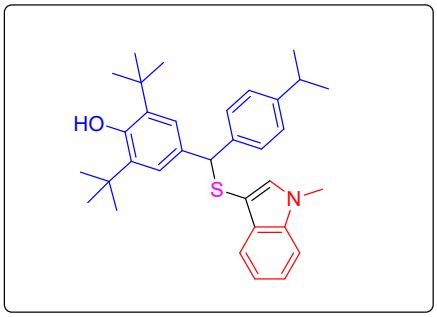
Yield 90% (221mg); Colourless solid; mp 112-114 °C; (KBr) cm^{-1}: 3341, 2900, 2213, 1487, 782, 626; ^1H NMR (400 MHz, $CDCl_3$): δ 7.58 (d, J = 7.63 Hz, 1H), 7.33 (d, J = 8.44 Hz, 2H), 7.23 (t, J = 8.3 Hz, 4H), 7.12 (t, J = 7.82 Hz, 1H), 7.02 (s, 2H), 6.7 (s, 1H), 5.15 (s, 1H), 5.07 (s, 1H), 3.65 (s, 3H), 1.33 (s, 18H); ^{13}C NMR (100MHz, $CDCl_3$): δ 152.7, 141.0, 136.9, 135.6, 134.6, 132.4, 131.6, 130.2, 129.9, 128.2, 125.0, 122.1, 120.1, 119.4, 109.4, 103.5, 58.3, 34.3, 32.9, 30.2; mass (ES-) HRMS (ESI-TOF) calcd for $C_{30}H_{33}ClNOS$ 490.1977 $(M-H)^-$ Found 490.1994.

2,6-di-tert-butyl-4-(((1-methyl-1H-indol-3-yl)thio)(p-tolyl)methyl)phenol (3ae)



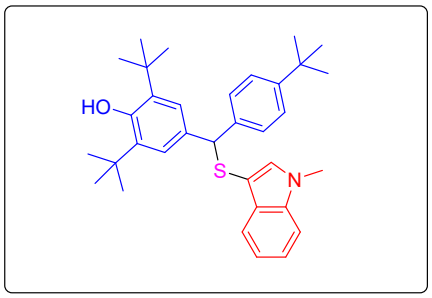
Yield 88% (207mg); Light yellow solid; mp 112-114 °C; (KBr) cm^{-1}: 3366, 2891, 2200, 1457, 737, 618; ^1H NMR (400 MHz, $CDCl_3$): δ 7.51 (d, J = 7.87 Hz, 1H), 7.25 (d, J = 8.02 Hz, 2H), 7.17-7.11 (m, 2H), 7.05-7.00 (m, *3*H), 6.9 (s, 2H), 6.6 (s, 1H), 5.0 (s, 1H), 4.9 (s, 1H), 3.5 (s, 3H), 2.2 (s, 3H), 1.24 (s, 18H); ^{13}C NMR (100MHz, $CDCl_3$): δ 152.5, 139.2, 136.9,136.2, 135.2, 134.6, 132.4, 130.3, 128.8, 128.3, 125.1, 121.9, 119.9, 119.5, 109.2, 104.1, 58.8, 34.2, 32.8, 30.2, 21.0; mass (ES-) HRMS (ESI-TOF) calcd for $C_{31}H_{36}NOS$ 470.2523 $(M-H)^-$ Found 470.2538.

2,6-di-tert-butyl-4-((4-isopropylphenyl)((1-methyl-1H-indol-3-yl)thio)methyl)phenol (3af)



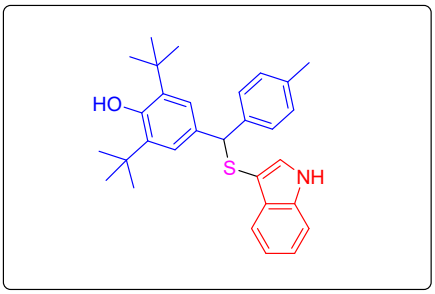
Yield 86% (214mg); Light yellow solid; mp 104-106 °C; (KBr) cm^{-1}: 3360, 2682, 2343, 785, 629; ^1H NMR (400 MHz, $CDCl_3$): δ 7.54 (d, J = 7.83 Hz, 1H), 7.33 (d, J = 7.79 Hz, 2H) , 7.24-7.17 (m, 2H), 7.1-7.0 (m, *3*H), 7.0 (s, 2H), 6.7 (s, 1H), 5.1 (s, 1H), 5.0 (s, 1H), 3.6 (s, 3H), 2.86 (m, 1H), 1.3 (s, 18H), 1.22 (d, J = 7, 6H); ^{13}C NMR (100MHz, $CDCl_3$): δ 152.5, 147.3, 139.6, 136.9, 135.2, 134.7, 132.4, 130.4, 128.4, 126.2, 125.2, 121.9, 119.9, 119.5, 109.2, 104.1, 58.9, 34.2, 33.7, 32.7, 30.2, 24.0; mass (ES-) HRMS (ESI-TOF) calcd for $C_{33}H_{40}NOS$ 498.2836 $(M-H)^-$ Found 498.2852.

2,6-di-tert-butyl-4-((4-(tert-butyl)phenyl)((1-methyl-1H-indol-3-yl)thio)methyl)phenol (3ag)



Yield 85% (218mg); light Brown solid; mp 130-132 °C; (KBr) cm^{-1}: 2270, 1505, 1484, 693, 639; ^1H NMR (400 MHz, $CDCl_3$): δ 7.53 (d, J = 7.89 Hz, 1H), 7.34 (d, J = 7.89 Hz, 2H), 7.28 (d, J = 8.33 Hz, 2H), 7.24-7.17 (m, *2*H), 7.10-7.07 (m, 1H), 7.05 (s, 2H), 6.69 (s, 1H), 5.1 (s, 1H), 5.0 (s, 1H), 3.6 (s, 3H), 1.3 (s, 18H), 1.29(s, 9H); ^{13}C NMR (100MHz, $CDCl_3$): δ 152.5, 149.5, 139.2, 136.9, 135.2, 134.7, 132.4, 130.4, 128.0, 125.2, 125.0, 121.9, 119.9, 119.5, 109.2, 104.1, 58.9, 34.4, 34.2, 32.7, 31.3, 30.2; mass (ES-) HRMS (ESI-TOF) calcd for $C_{34}H_{42}NOS$ 512.2993 $(M-H)^-$ Found 512.3011.

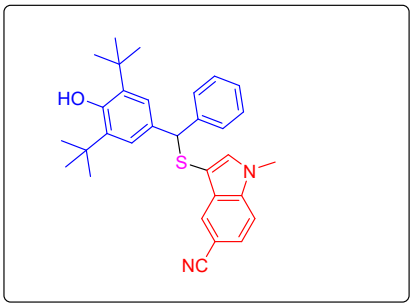
4-(((1H-indol-3-yl)thio)(p-tolyl)methyl)-2,6-di-tert-butylphenol (3be)



Yield 20% (45mg); Colourless solid; mp 120-122 °C; (KBr) cm^{-1}: 3341, 2900, 2213, 1487, 1429,782, 626; ^1H NMR (400 MHz, $CDCl_3$): δ 8.08 (s, 1H), 7.62 (d, J = 7.85 Hz, 1H), 7.32-7.29 (m, 3H), 7.20-7.16 (m, 1H), 7.15-7.11 (m, 1H), 7.09-7.07 (m, *4*H), 6.88 (d, J = 2.88Hz, 1H), 5.18 (s, 1H), 45.04 (s, 1H), 2.31 (s, 3H), 1.34 (s, 18H); ^{13}C NMR (100MHz, $CDCl_3$): δ 152.6, 139.2, 136.2, 135.9, 132.3, 130.0, 129.6, 128.8, 128.3, 125.1, 122.4, 120.3, 119.4, 111.2, 106.1, 58.5, 34.2, 30.2, 21.08; mass (ES-) HRMS (ESI-TOF) calcd for $C_{30}H_{34}NOS$ 456.2367 $(M-H)^-$ Found 456.2375.

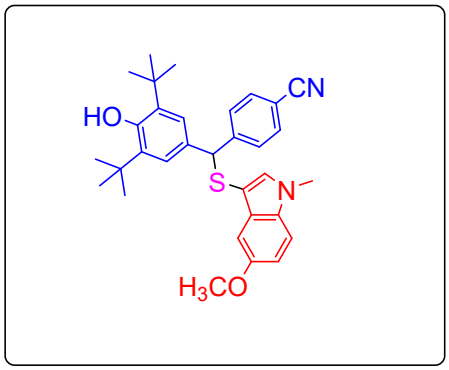
.

3-(((3,5-di-tert-butyl-4-hydroxyphenyl)(phenyl)methyl)thio)-1-methyl-1H-indole-5-carbonitrile (3ca)



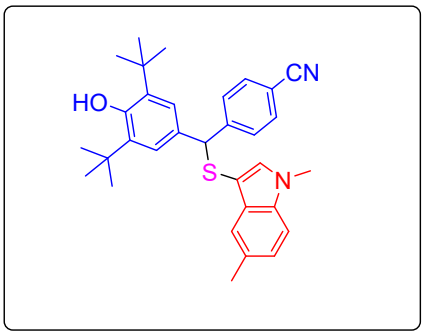
Yield 85% (204mg); Colourless solid; mp 124-126 °C; (KBr) cm^{-1}: 2924,1917 1612, 1454, 619; ^1H NMR (400 MHz, $CDCl_3$): δ 7.6 (s, 1H), 7.43-7.37 (m, 4H),7.29-7.26 (m, 3H), 7.03 (s, 2H), 6.95 (s, 1H), 5.12 (s, 1H), 5.10 (s, 1H), 3.70 (s, 3H), 1.32 (s, 18H); ^{13}C NMR (100MHz, $CDCl_3$): δ 152.8, 141.7, 138.3, 136.8, 135.7, 131.8, 130.2, 128.4, 128.4 128.2, 127.0, 125.2, 125.0, 124.9, 120.4, 110.2, 105.9, 103.2, 59.7, 34.3, 33.1, 30.2; mass (ES-) HRMS (ESI-TOF) calcd for $C_{31}H_{33}N_2OS$ 481.2319 $(M-H)^+$ Found 481.2327.

4-((3,5-di-tert-butyl-4-hydroxyphenyl)((5-methoxy-1-methyl-1H-indol-3-yl)thio)methyl)benzonitrile (3dh)



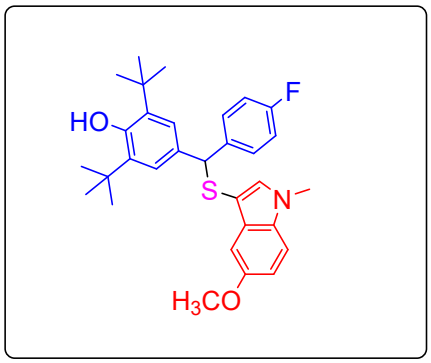
Yield 96% (245mg); Colourless solid; mp 122-124 °C; (KBr) cm^{-1}: 3841, 1973, 1621, 1485; ^1H NMR (400 MHz, $CDCl_3$): δ 7.54-7.51 (m, 2H), 7.46-7.44 (m, 2H), 7.16 (d, J = 8.78 Hz, 1H), 7.05 (s, *2*H), 6.95 (d, J = 2.40 Hz, 1H), 6.89-6.86 (m, 1H), 5.15 (s, 1H), 6.72(s, 1H, 5.15 (s, 1H), 3.8 (s, 3H), 3.6 (s, 3H), 1.35 (s, 18H); ^{13}C NMR (100MHz, $CDCl_3$): δ 154.9, 153.0, 148.3, 135.8, 135.2, 132.2, 131.8, 130.79, 130.77, 129.3, 124.9, 118.9, 112.6, 110.4, 110.3, 102.1, 100.8, 58.7, 55.8, 34.3, 33.1, 30.1, 21.4; mass (ES-) HRMS (ESI-TOF) calcd for $C_{32}H_{35}N_2O_2S$ 511.2425 $(M-H)^-$ Found 511.2434.

4-((3,5-di-tert-butyl-4-hydroxyphenyl)((1,5-dimethyl-1H-indol-3-yl)thio)methyl)benzonitrile (3eh)



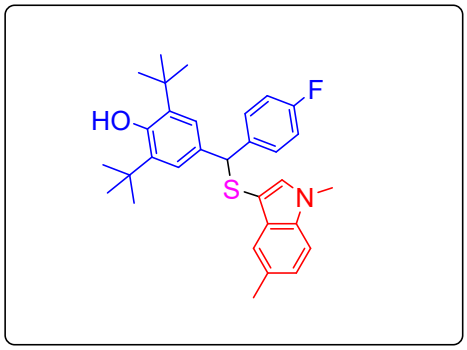
Yield 95% (235mg); Light yellow solid; mp 118-120 °C; (KBr) cm^{-1}: 2361, 1927, 1604, 1431, 615; ^1H NMR (400 MHz, $CDCl_3$): δ 7.53-7.51 (m, 2H), 7.45-7.43 (m, 2H), 7.24-7.23 (m, 1H), 7.15 (d, J = 8.32 Hz, 1H), 7.05 (s, *3*H), 6.73 (s, 1H), 5.15 (s, 1H), 5.14 (s, 1H), 3.6 (s, 3H), 2.4 (s, 3H), 1.35 (s, 18H); ^{13}C NMR (100MHz, $CDCl_3$): δ 153.0, 148.3, 135.8, 135.4, 134.8, 131.8, 130.7, 130.3, 129.6, 129.3, 125.0, 123.9, 119.0, 118.8, 110.3, 109.2, 102.1, 58.8, 34.4, 34.3, 32.9, 30.1, 21.4; mass (ES-) HRMS (ESI-TOF) calcd for $C_{32}H_{35}N_2OS$ 495.2476 $(M-H)^-$ Found 495.2481.

2,6-di-tert-butyl-4-((4-fluorophenyl)((5-methoxy-1-methyl-1H-indol-3-yl)thio)methyl)phenol (3dc)



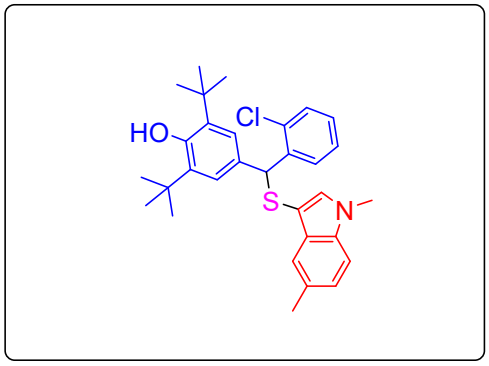
Yield 95% (239mg); Light Yellow solid; mp 124-126 °C; (KBr) cm^{-1}: 3880, 2262, 1502, 1427, 649; ^1H NMR (400 MHz, $CDCl_3$): δ 7.37-7.33 (m, 2H), 7.14 (d, J = 8.82 Hz, 1H), 7.03 (s, *2*H), 6.96-6.92 (m, 3H), 6.87-6.84 (m, 1H), 6.71 (s, 1H), 5.11 (s, 1H), 5.09 (s, 1H), 3.8 (s, 3H), 3.6 (s, 3H), 1.34 (s, 18H); ^{13}C NMR (100MHz, $CDCl_3$): δ 162.8, 160.4, 154.7, 152.7, 138.3, 135.5, 135.1, 132.17, 132.10, 130.9, 130.1, 130.04, 125.0, 114.9, 114.7, 112.5, 110.2, 102.9, 100.8, 58.3, 55.8, 34.3, 33.0, 30.2; mass (ES-) HRMS (ESI-TOF) calcd for $C_{31}H_{35}FNO_2S$ 504.2378 $(M-H)^-$ Found 504.2387.

2,6-di-tert-butyl-4-(((1,5-dimethyl-1H-indol-3-yl)thio)(4-fluorophenyl)methyl)phenol (3de)



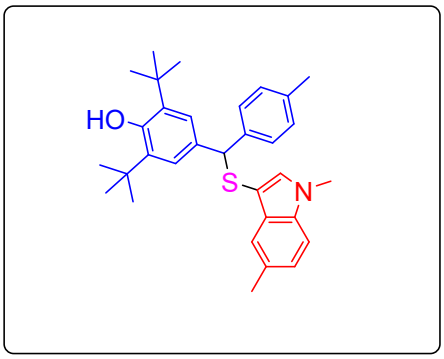
Yield 94% (229mg); Colourless solid; mp 118-120 °C; (KBr) cm^{-1}: 3675, 1926, 1503, 1429, 1143, 789; ^1H NMR (400 MHz, $CDCl_3$): δ 7.37-7.24 (m, 3H), 7.13 (d, J = 8.42 Hz, 1H), 7.03-7.01 (m, 3H), 6.96-6.92 (m, 2H), 6.71 (s, 1H), 5.12 (s, 1H), 5.07 (s, 1H), 3.6 (s, 3H), 2.4 (s, 3H), 1.33 (s, 18H); ^{13}C NMR (100MHz, $CDCl_3$): δ 162.9, 160.4, 152.6, 138.33, 135.30, 135.46, 135.40, 134.76, 132.11, 130.5, 130.16, 130.08, 129.42, 125.05, 123.7, 119.09, 114.92, 114.71, 109.08, 102.9, 58.3, 55.8, 34.3, 32.9, 30.2, 21.4; mass (ES-) HRMS (ESI-TOF) calcd for $C_{31}H_{35}FNOS$ 488.2429 $(M-H)^-$ Found 488.2436.

2,6-di-tert-butyl-4-((2-chlorophenyl)((1,5-dimethyl-1H-indol-3-yl)thio)methyl)phenol (3ei)



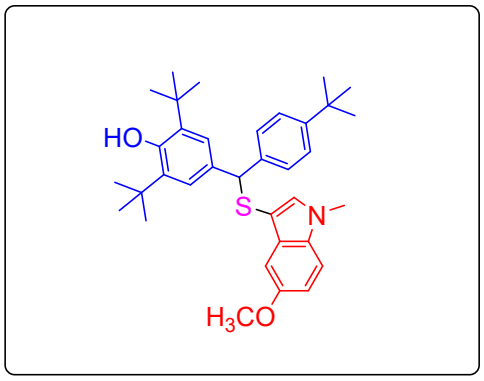
Yield 93% (234mg); Colourless solid; mp 126-128 °C; (KBr) cm^{-1}: 3610, 1895, 1432, 1119, 695, 646; ^1H NMR (400 MHz, $CDCl_3$): δ 7.89 (dd, J = 7.78 Hz and 1.59 Hz, 1H), 7.31-7.24 (m, 3H), 7.15-7.09 (m, 4H), 7.00 (dd, J = 8.36 Hz and 1.38 Hz, 1H), 6.82 (s, 1H), 5.67 (s, 1H), 5.05 (s, 1H), 3.6 (s, 3H), 2.4 (s, 3H), 1.33 (s, 18H); ^{13}C NMR (100MHz, $CDCl_3$): δ 152.6, 140.1, 135.36, 135.32, 134.5, 133.7, 131.3, 130.5, 130.0, 129.4, 129.3, 127.8, 126.7, 125.2, 123.6, 119.2, 108.9, 102.9, 55.2, 34.2, 32.9, 30.2, 21.4; mass (ES-) HRMS (ESI-TOF) calcd for $C_{31}H_{35}ClNOS$ 504.2133 $(M-H)^-$ Found 504.2143.

2,6-di-tert-butyl-4-(((1,5-dimethyl-1H-indol-3-yl)thio)(p-tolyl)methyl)phenol (3ee)



Yield 89% (215mg); Colourless solid; mp 120-122 °C; (KBr) cm^{-1}: 3666, 1924, 1506, 1359, 768, 654; ^1H NMR (400 MHz, $CDCl_3$): δ 7.30-7.26 (m, 3H), 7.11-7.04 (m, 6H), 6.70 (s, 1H), 5.1 (s, 1H), 5.0 (s, 1H), 3.6 (s, 3H), 2.6 (s, 3H), 2.4 (s, 3H), 1.32 (s, 18H); ^{13}C NMR (100MHz, $CDCl_3$): δ 152.5, 139.4, 136.2, 135.3, 135.2, 134.7, 132.6, 130.6, 129.2, 128.8, 128.4, 125.1, 123.5, 119.2, 108.9, 103.4, 59.0, 34.2, 32.8, 30.2, 21.4, 21.0; mass (ES-) HRMS (ESI-TOF) calcd for $C_{32}H_{38}NOS$ 484.2680 $(M-H)^-$ Found 484.2687.

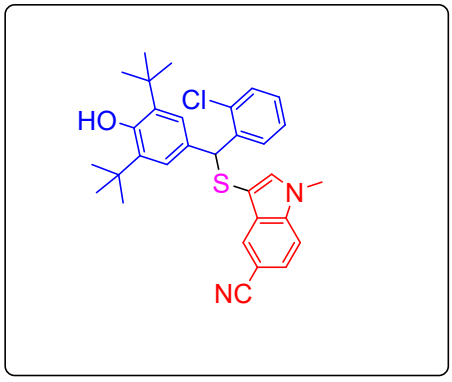
2,6-di-tert-butyl-4-((4-(tert-butyl)phenyl)((5-methoxy-1-methyl-1H-indol-3-yl)thio)methyl)phenol (3dg)



Yield 87% (236mg); Brown solid; mp 124-126 °C; (KBr) cm^{-1}: 3567, 2025, 1509, 788, 631; ^1H NMR (400 MHz, $CDCl_3$): δ 7.34-7.32 (m, 2H), 7.29-7.27 (m, 2H), 7.13 (d, J = 8.78 Hz, 1H), 7.06 (s, 2H), 6.96 (d, J = 2.43 Hz, 1H), 6.85 (d, J = 2.52 Hz, 1H), 6.83 (d, J = 2.52 Hz, 1H), 6.6 (s, 1H), 5.08 (s, 1H), 5.05 (s, 1H), 3.78 (s, 3H), 3.61 (s, 3H), 1.33 (s, 18H), 1.29 (s, 9H); ^{13}C NMR (100MHz, $CDCl_3$): δ 154.6, 152.5, 149.5, 139.4, 135.3, 135.2, 132.6, 132.1, 131.0, 128.0, 125.1, 125.0, 112.4, 110.1, 103.4, 101.0, 59.0, 55.8, 34.4, 34.2, 32.9, 31.3, 30.2; mass (ES-) HRMS (ESI-TOF) calcd for $C_{35}H_{44}NO_2S$ 542.3098 $(M-H)^-$ Found 542.3109.

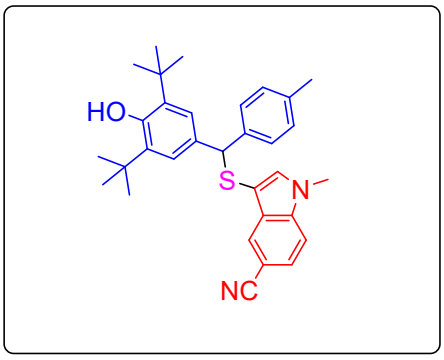
.

3-(((2-chlorophenyl)(3,5-di-tert-butyl-4-hydroxyphenyl)methyl)thio)-1-methyl-1H-indole-5-carbonitrile (3ci)



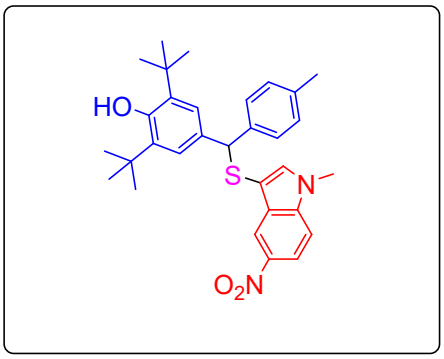
Yield 86% (258mg); light yellow solid; mp 126-128 °C; (KBr) cm^{-1}: 3567, 1896, 1431, 1117, 890, 757, 642; ^1H NMR (400 MHz, DMSO): δ 7.95-7.93 (dd, J = 7.82 Hz, 1.46Hz, 1H), 7.66 (s, 1H), 7.61-7.56 (m, 2H), 7.48-7.44 (m, 2H), 7.35-7.33 (m, 1H), 7.28-7.24 (m, 1H), 6.99 (s, 2H), 6.88 (s, 1H), 5.65 (s, 1H), 3.77 (s, 3H), 3.33 (s, 3H), 1.25 (s, 18H); ^{13}C NMR (100MHz, DMSO): δ 153.4, 139.3, 139.1, 138.8, 138.7, 132.9, 130.8, 130.2, 129.9, 129.8, 129.1, 127.8, 124.8, 124.2, 120.6, 112.1, 103.8, 102.6, 55.5, 34.8, 33.3, 30.6; mass (ES-) HRMS (ESI-TOF) calcd for $C_{31}H_{32}ClN_2OS$ 515.1929 $(M-H)^-$ Found 515.1938.

2,6-di-tert-butyl-4-(((1,5-dimethyl-1H-indol-3-yl)thio)(p-tolyl)methyl)phenol (3ce)



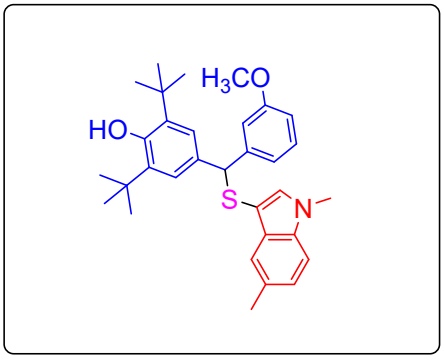
Yield 68% (168mg); Colourless solid; mp 128-130 °C; (KBr) cm^{-1}: 3841, 2199, 1872, 1425, 766, 636; ^1H NMR (400 MHz, $CDCl_3$): δ 7.58 (s, 1H), 7.42-7.26 (m, 5H), 7.0 (d, J = 8.52 Hz, 1H), 7.02 (s, 2H), 6.96 (s, 1H), 5.08 (s, 2H), 3.7 (s, 3H), 2.3 (s, 3H), 1.32 (s, 18H); ^{13}C NMR (100MHz, $CDCl_3$): δ 152.8, 138.7, 138.3, 136.79, 136.74, 135.6, 132.0, 130.3, 128.9, 128.3, 125.4, 125.3, 125.0, 124.9, 120.5, 110.1, 106.1, 103.1, 59.5, 34.2, 33.1, 30.2, 21.0; mass (ES-) HRMS (ESI-TOF) calcd for $C_{32}H_{35}N_2OS$ 495.2476 $(M-H)^-$ Found 495.2483.

2,6-di-tert-butyl-4-(((1-methyl-5-nitro-1H-indol-3-yl)thio)(p-tolyl)methyl)phenol (3fe)



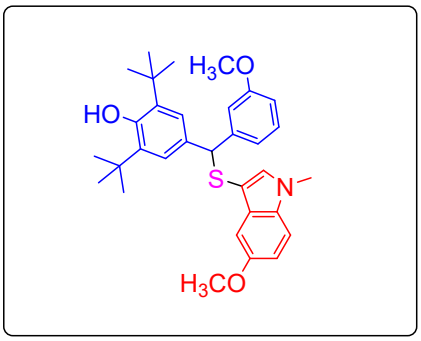
Yield 60% (154mg); Colourless solid; mp 126-128 °C; (KBr) cm^{-1}: 3740, 2067, 1543, 661; ^1H NMR (400 MHz, $CDCl_3$): δ 8.3 (d, J = 2.14 Hz, 1H), 8.22 (dd, J = 8.98 Hz and 2.22 Hz, 1H), 7.3 (d, J = 7.99 Hz, 2H), 7.2 (d, J = 4.85 Hz, 1H), 7.08-7.04 (m, 4H) , 6.95 (s, 1H), 5.14 (s, 1H), 5.06 (s, 1H), 3.7 (s, 3H), 2.2 (s, 3H), 1.32 (s, 18H); ^{13}C NMR (100MHz, $CDCl_3$): δ 152.8, 142.2, 139.5, 138.6, 137.5, 136.7, 135.6, 131.8, 129.9, 128.9, 125.0, 117.6, 117.0, 109.3, 108.6, 59.5, 34.2, 33.3, 30.2, 21.0; mass (ES-) HRMS (ESI-TOF) calcd for $C_{31}H_{35}N_2O_3S$ 515.2374 $(M-H)^-$ Found 515.2380.

2,6-di-tert-butyl-4-(((1,5-dimethyl-1H-indol-3-yl)thio)(3-methoxyphenyl)methyl)phenol (3ej)



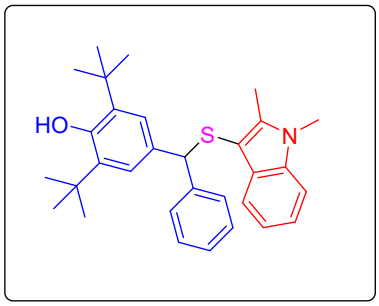
Yield 75% (188mg); Colourless solid; mp 120-122 °C; (KBr) cm^{-1}: 3629, 1963, 1597, 1432, 769, 699; ^1H NMR (400 MHz, $CDCl_3$): δ 7.29-7.28 (m, 1H), 7.18-7.12 (m, 2H), 7.06 (s, 2H), 7.03-7.01 (m, 2H), 6.97 (t, J = 2.33 Hz, 1H) , 6.76-6.72 (m, 2H), 5.10 (s, 1H), 5.05 (s, 1H), 3.7 (s, 3H), 3.6 (s, 3H), 2.4 (s, 3H), 1.33 (s, 18H); ^{13}C NMR (100MHz, $CDCl_3$): δ 159.3, 152.6, 144.02, 135.38, 135.32, 134.7, 132.2, 130.5, 129.3, 129.04, 125.1, 123.6, 121.0, 119.2, 113.9, 112.5, 109.0, 103.2, 59.2, 55.1, 34.2, 32.8, 30.2, 21.4; mass (ES-) HRMS (ESI-TOF) calcd for $C_{32}H_{38}NO_2S$ 500.2629 $(M-H)^+$ Found 500.2638.

2,6-di-tert-butyl-4-(((5-methoxy-1-methyl-1H-indol-3-yl)thio)(3-methoxyphenyl)methyl)phenol (3dj)



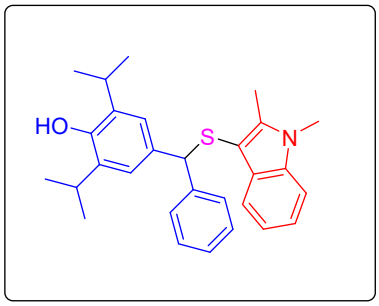
Yield 78% (201mg); Colourless solid; mp 122-124 °C; (KBr) cm^{-1}: 3585, 2270, 1999, 1452, 687, 629; ^1H NMR (400 MHz, $CDCl_3$): δ 7.20-7.12 (m, 2H), 7.06(s, 2H) , 7.01 (d, J = 7.52 Hz, 1H), 6.97-6.95 (m, 2H), 6.85 (dd, J = 8.89 Hz and 2.51 Hz, 1H), 6.77-6.71 (m, 2H), 5.08 (s, 1H), 5.07 (s, 1H), 3.79 (s, 3H), 3.73 (s, 3H), 3.63 (s, 3H), 1.33 (s, 18H); ^{13}C NMR (100MHz, $CDCl_3$): δ 159.3, 154.7, 152.6, 144.1, 135.38, 135.2, 132.24, 132.14, 131.0, 129.0, 125.0, 120.9, 113.9, 112.5, 110.2, 103.2, 100.9, 59.3, 55.7, 55.1, 34.3, 33.0, 30.2; mass (ES-) HRMS (ESI-TOF) calcd for $C_{32}H_{38}NO_3S$ 516.2578 $(M-H)^-$ Found 516.2585.

2,6-di-tert-butyl-4-(((1,2-dimethyl-1H-indol-3-yl)thio)(phenyl)methyl)phenol (3ga)



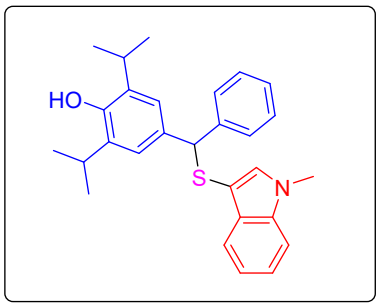
Yield 90% (212mg); White solid; mp 124-126 °C; (KBr) cm^{-1}: 2887, 1529, 1470, 1236, 700; ^1H NMR (400 MHz, DMSO-d^6): δ 7.50 (d, J = 7.24 Hz, 1H), 7.45-7.43 (m, 2H), 7.39 (d, J = 8.01 Hz, 1H), 7.32 (td, J = 7.14 Hz, 1.14 Hz, 3H), 7.25-7.21 (m, 1H), 7.12 (td, J = 7.08 Hz, 1.2 Hz, 1H), 7.32 (td, J = 7.8 Hz, 1.04 Hz, 1H), 6.85 (s, 2H), 6.80 (s, 1H), 5.11 (s, 1H), 3.58 (s, 3H), 1.99 (s, 3H), 1.24 (s, 18H); ^{13}C NMR (100MHz, DMSO-d^6): δ 153.0, 142.6, 142.2, 138.9, 136.9, 132.6, 130.0, 128.67, 128.63, 127.2, 124.8, 121.4, 120.2, 118.3, 109.9, 100.2, 57.7, 34.8, 30.6, 30.4, 10.4; mass (ES-) ESMS (ESI-TOF) calcd for $C_{31}H_{36}NOS^-$ 470.2 $(M-H)^-$ Found 470.6.

4-(((1,2-dimethyl-1H-indol-3-yl)thio)(phenyl)methyl)-2,6-diisopropylphenol (3gk)



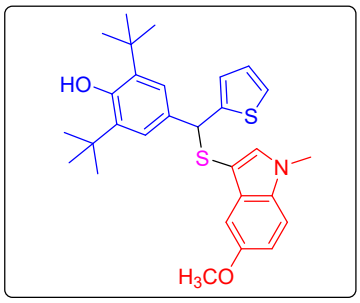
Yield 88% (195mg); White solid; mp 122-124 °C; (KBr) cm^{-1}: 2900, 1529, 1141, 736, 698; ^1H NMR (400 MHz, DMSO-d^6): δ 7.95 (s, 1H), 7.53 (d, J = 7.12 Hz, 1H), 7.39-7.35 (m, 3H), 7.29-7.26 (m, 2H), 7.22-7.18 (m, 1H), 7.14-7.04 (m, 2H), 6.85 (s, 2H), 5.13 (s, 1H), 3.58 (s, 3H), 3.22 (sep, J = 6.83 Hz, 2H), 2.05 (s, 3H), 1.06 (d, J = 6.83 Hz 6H), 1.01 (d, J = 6.83 Hz 6H); ^{13}C NMR (100MHz, DMSO-d^6): δ 150.0, 143.4, 142.6, 136.9, 135.1, 132.8, 129.9, 128.56, 128.54, 127.1, 123.3, 121.4, 120.1, 118.4, 109.9, 100.3, 57.9, 30.4, 26.5, 23.3, 23.2, 10.5; mass (ES-) ESMS (ESI-TOF) calcd for $C_{29}H_{32}NOS^-$ 442.2 $(M-H)^-$ Found 442.6

2,6-di-tert-butyl-4-(furan-2-yl((1-methyl-1H-indol-3-yl)thio)methyl)phenol (3ak)



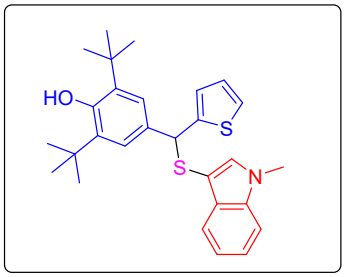
Yield 85% (182mg); White solid; mp 120-122 °C; (KBr) cm^{-1}: 3607, 3105, 2958, 1457, 693; ^1H NMR (400 MHz, DMSO-d^6): δ 7.96 (s, 1H), 7.51 (d, J = 7.86 Hz, 1H), 7.41-7.37 (m, 3H), 7.27 (t, J = 7.73 Hz, 2H), 7.20-7.14 (m, 3H), 7.06 (t, J = 7.10 Hz, 1H), 6.97 (s, 2H), 5.33 (s, 1H), 3.67 (s, 3H), 3.26-3.19 (m, 2H), 1.09 (d, J = 6.93 Hz 6H), 1.05 (d, J = 6.93 Hz 6H); ^{13}C NMR (100MHz, DMSO-d^6): δ 150.0, 142.9, 137.1, 135.4, 135.2, 132.9, 130.0, 128.6, 128.5, 127.1, 123.2, 122.0, 120.0, 119.2, 110.5, 102.9, 58.5, 32.9, 26.6, 23.3, 23.2; mass (ES-) ESMS (ESI-TOF) calcd for $C_{28}H_{30}NOS^-$ 428.2 $(M-H)^-$ Found 428.5.

2,6-di-tert-butyl-4-(((1-methyl-1H-indol-3-yl)thio)(thiophen-2-yl)methyl)phenol (3dl)



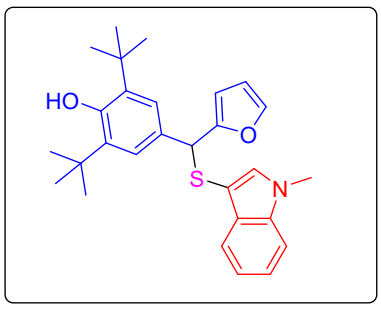
Yield 85% (219mg); light yellow solid ; mp 106-108 °C; (KBr) cm^{-1}: 3624, 2954, 1734, 1430, 1234, 788, 695; ^1H NMR (400 MHz, $CDCl_3$): δ 7.23 (m, 1H), 7.19 (m, 1H), 7.13-7.11 (d, J = 7.96 Hz, 1H), 7.06 (s, 2H), 7.02-6.99 (dd, J = 8.32 Hz, 1.33 Hz, 1H), 6.87-6.86 (m, 2H), 6.78 (s, 1H) , 5.32 (s, 1H), 5.07 (s, 1H), 3.63 (s, 3H), 2.40 (s, 3H), 1.32 (s, 18H); ^{13}C NMR (100MHz, $CDCl_3$): δ 152.9, 146.6, 135.3, 135.1, 132.18, 130.6, 129.4, 126.3, 125.8, 125.0, 124.6, 123.6, 119.1, 109.0, 102.9, 54.6, 34.2, 32.9, 30.2, 21.4; mass (ES^+) calcd for $C_{29}H_{35}NO_2SNa$ 516.2 $(M+Na)^+$ Found 516.5.

2,6-di-tert-butyl-4-(((1-methyl-1H-indol-3-yl)thio)(thiophen-2-yl)methyl)phenol (3dk)



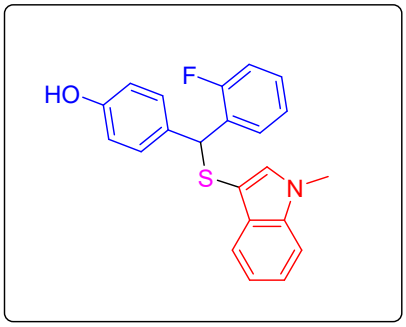
Yield 83% (192mg);Llight Brown solid; mp 104-106 °C; (KBr) cm^{-1}: 3784, 2161, 1525, 660, 621; ^1H NMR (400 MHz, $CDCl_3$): δ 7.53-7.52 (m, 1H), 7.25-7.24 (m, 1H), 7.22-7.17 (m, 2H), 7.12-7.08 (m, 1H), 7.05 (s, 2H), 6.88-6.86 (m, 2H), 6.81 (s, 1H) , 5.35 (s, 1H), 5.06 (s, 1H), 3.66 (s, 3H), 1.32 (s, 18H); ^{13}C NMR (100MHz, $CDCl_3$): δ 152.9, 146.5, 136.9, 135.4, 135.0, 131.9, 130.4, 126.3, 125.8, 125.0, 124.6, 122.0, 120.1, 119.4, 109.3, 103.6, 54.4, 34.2, 32.8, 30.2; mass (ES-) HRMS (ESI-TOF) calcd for $C_{28}H_{32}NOS_2$ 462.1931 $(M-H)^-$ Found 462.1947.

2,6-di-tert-butyl-4-(furan-2-yl((1-methyl-1H-indol-3-yl)thio)methyl)phenol (3am)



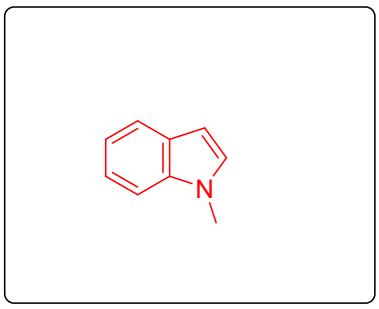
Yield 80% (178mg); Light Yellow solid; mp 124-126 °C; (KBr) cm^{-1}: 3697, 2238, 1541, 719, 635; ^1H NMR (400 MHz, $CDCl_3$): δ 7.49 (d, J = 7.88 Hz, 1H), 7.389-7.386 (m, 1H), 7.25-7.24 (m, 1H), 7.21-7.18 (m, 1H), 7.11-7.08 (m, 1H), 7.0 (s, 2H), 6.8 (s, 1H), 6.28-6.27 (m, 1H), 6.20-6.19 (m, 1H), 5.13 (s, 1H), 5.06 (s, 1H), 3.68 (s, 3H), 1.31 (s, 18H); ^{13}C NMR (100MHz, $CDCl_3$): δ 154.4, 152.9, 141.8, 136.9, 135.4, 135.3, 130.5, 130.0, 125.1, 122.0, 120.0, 119.5, 110.2, 109.2, 107.8, 103.0, 52.3, 34.1, 32.8, 30.1; mass (ES-) HRMS (ESI-TOF) calcd for $C_{28}H_{32}NO_2S$ 446.2159 $(M-H)^-$ Found 446.2165.

4-((2-fluorophenyl)((1-methyl-1H-indol-3-yl)thio)methyl)phenol (4)



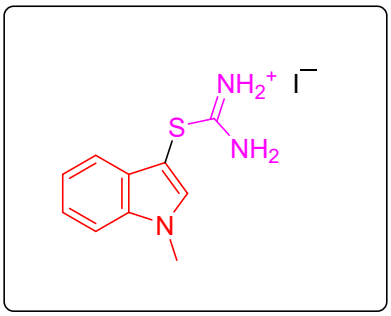
Yield 50% (90mg); Pale Yellow oil; (KBr) cm^{-1}: 2844, 1689, 1470, 1221, 730; ^1H NMR (400 MHz, $CDCl_3$): δ 7.29-7.28 (m, 1H), 7.21-7.16 (m, 3H), 7.10-6.95 (m, 7H), 7.75-6.73 (m, 2H), 6.42 (s, 1H), 5.90 (s, 1H, 3.69 (s, 3H); ^{13}C NMR (100MHz, $CDCl_3$): δ 161.8, 159.4, 154.0, 137.5, 135.1, 131.4, 131.2, 130.48, 130.44, 129.9, 128.6, 127.90, 127.82, 127.19, 123.85, 123.81, 121.6, 119.8, 118.8, 117.1, 115.3, 109.1, 40.34, 40.31, 32.69; mass (ES+) ESMS (ESI-TOF) calcd for $C_{22}H_{18}FNOSNa$ 386.0 $(M+Na)^-$ Found 385.6.

1-methyl-1H-indole(1a)



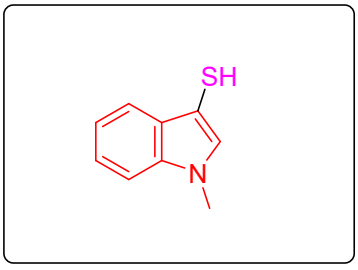
Light Brown oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.62 (dt, J = 7.94 Hz, 0.94Hz 1H), 7.31 (dd, J = 8.25 Hz, 0.83Hz 1H), 7.23-7.19 (m, 1H), 7.12-7.08 (m, 1H), 7.03(d, J = 3.05 Hz 1H), 6.47(dd, J = 3.12 Hz, 0.85 Hz 1H), 3.77(s, 3H); ^{13}C NMR (100MHz, $CDCl_3$): δ 136.7, 128.7, 128.5, 121.5, 120.8, 119.2, 109.1, 100.9, 32.3 mass (ES+) ESMS (ESI-TOF) calcd for $C_9H_{10}N^+$ 132.08 $(M+H)^+$ Found 132.2.

2-(1-methyl-1H-indol-3-yl)isothiouronium iodide (I)



Light Yellow Solid; ^1H NMR (400 MHz, DMSO-d^6): δ 8.88(s, 2H), 8.55(s, 2H), 7.98(s, 1H), 7.64 (d, J = 7.98 Hz, 1H), 7.5(d, J = 7.59 Hz, 1H), 7.34 (dd, J = 7.13 Hz, 1.07 Hz 1H), 7.27-7.23 (m, 1H), 3.88(s, 3H) ; ^{13}C NMR (100MHz, $CDCl_3$): δ 171.2, 139.9, 138.0, 129.2, 123.2, 121.7, 118.2, 111.6, 89.1, 33.8.

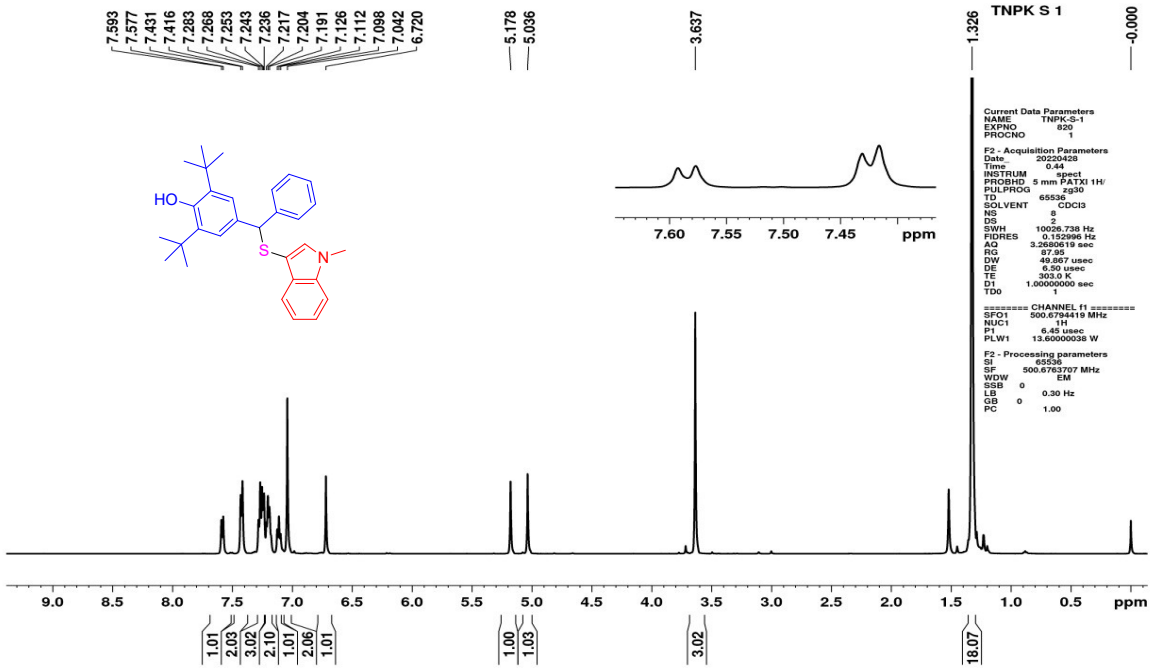
1-methyl-1H-indole-3-thiol (II)



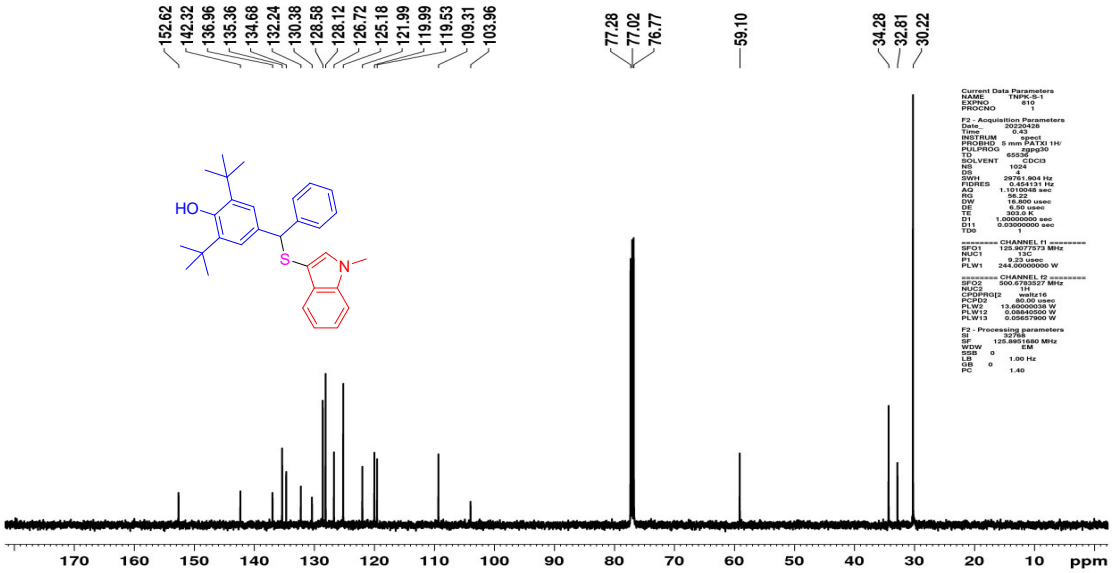
Light Yellow oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.51 (d, J = 7.72 Hz, 1H), 7.31-7.27 (m, 2H), 7.17-7.09 (m, 1H), 6.94 (s, 1H), 3.68(s, 3H); ^{13}C NMR (100MHz, $CDCl_3$): δ 137.4, 134.9, 129.5, 122.5, 120.39, 120.16, 109.5, 107.2, 33.0; mass (ES+) ESMS (ESI-TOF) calcd for $C_9H_{10}NS^+$ 164.05 $(M+H)^+$ Found 164.

3. Copies of ^{1}H and ^{13}C NMR spectra

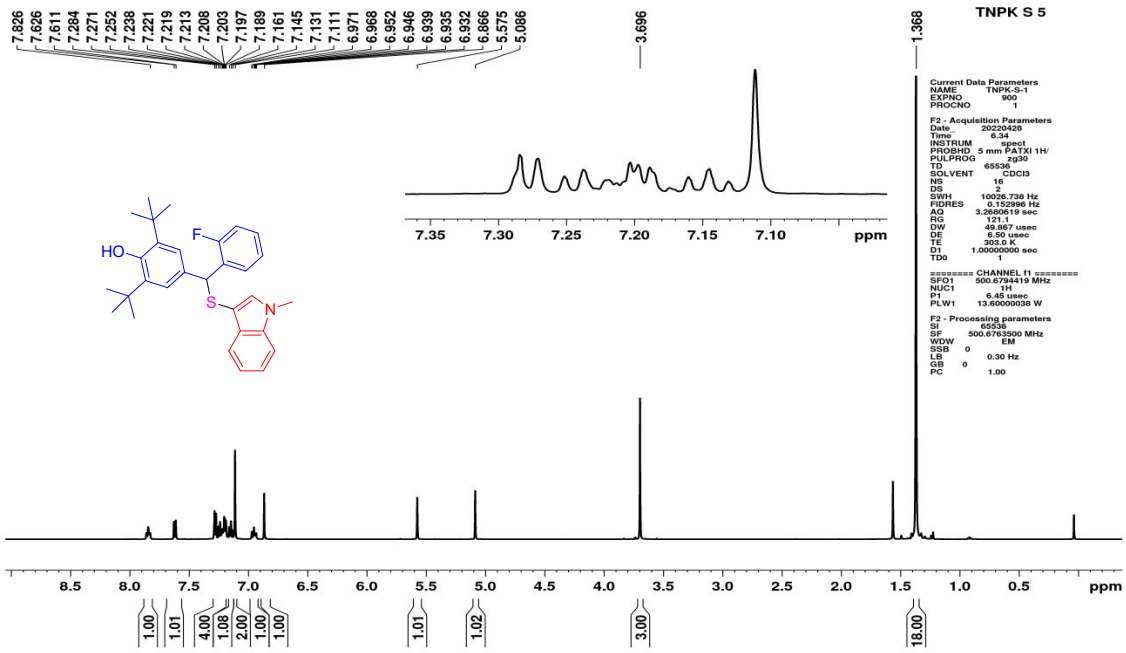
^{1}H NMR spectrum of compound- 3aa (400 Mz, $CDCl_3$)



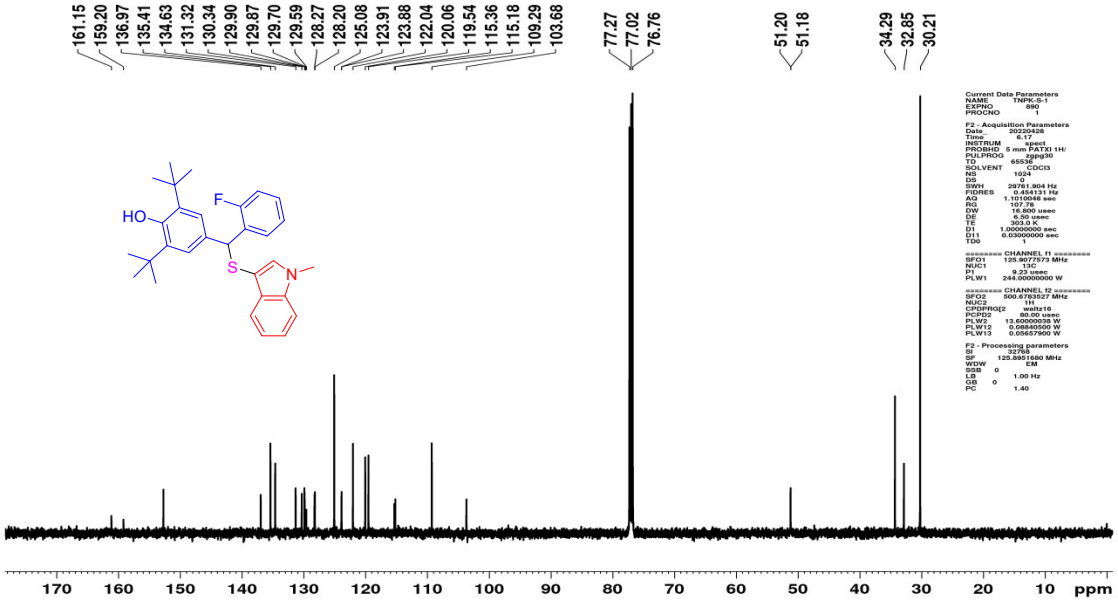
^{13}C NMR spectrum of compound- 3aa (100 Mz, $CDCl_3$)



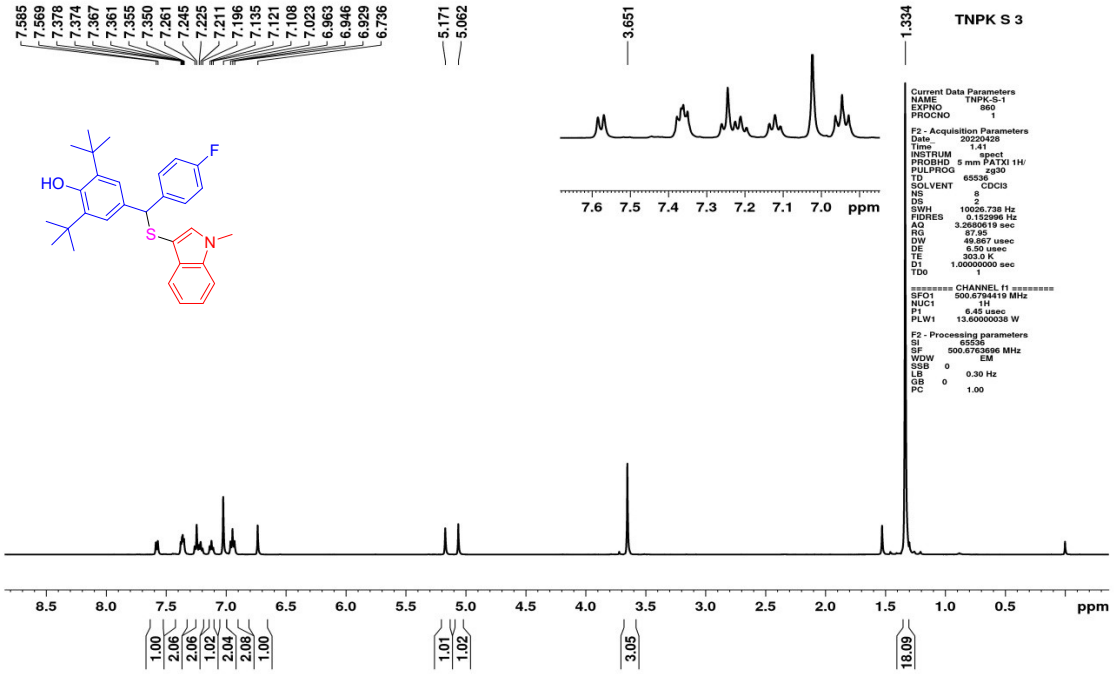
^{1}H NMR spectrum of compound- 3ab (400 Mz, $CDCl_3$)



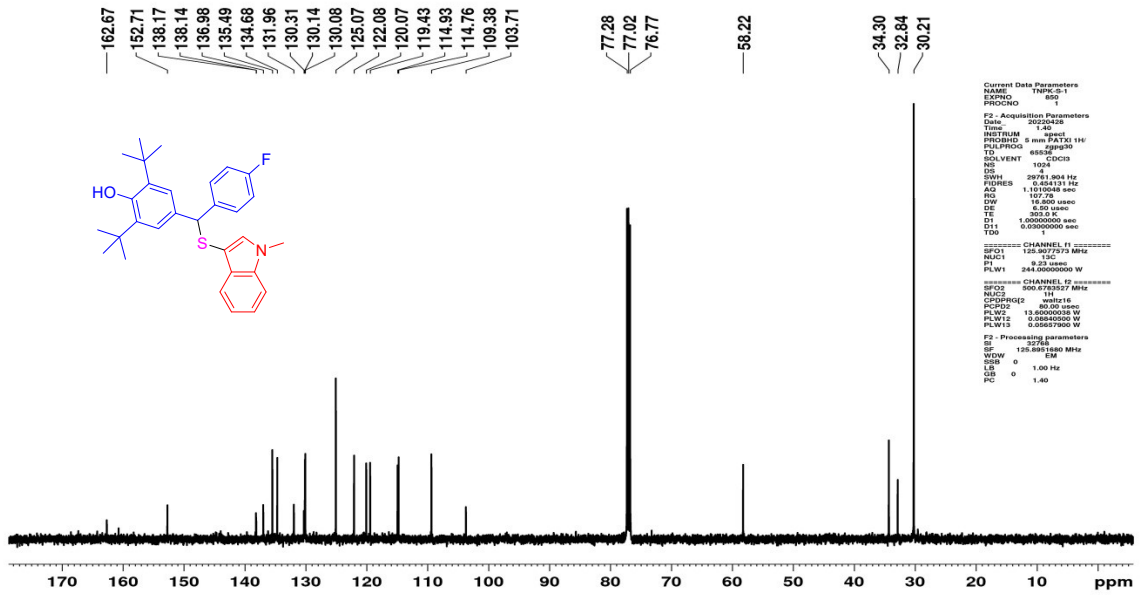
^{13}C NMR spectrum of compound- 3ab (100 Mz, $CDCl_3$)



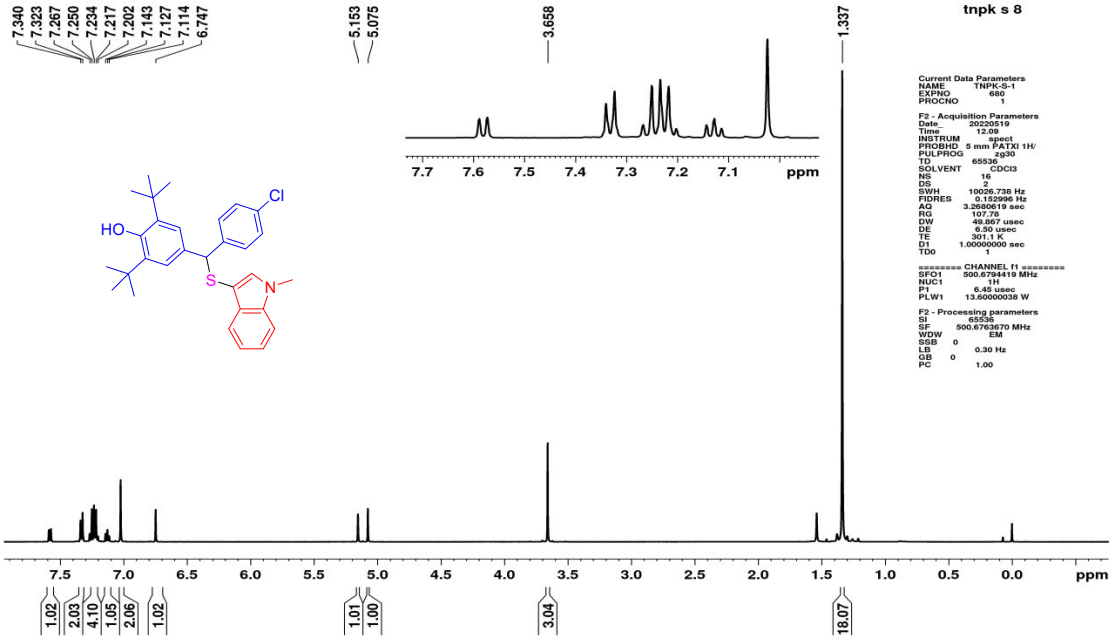
^{1}H NMR spectrum of compound- 3ac (400 Mz, $CDCl_3$)



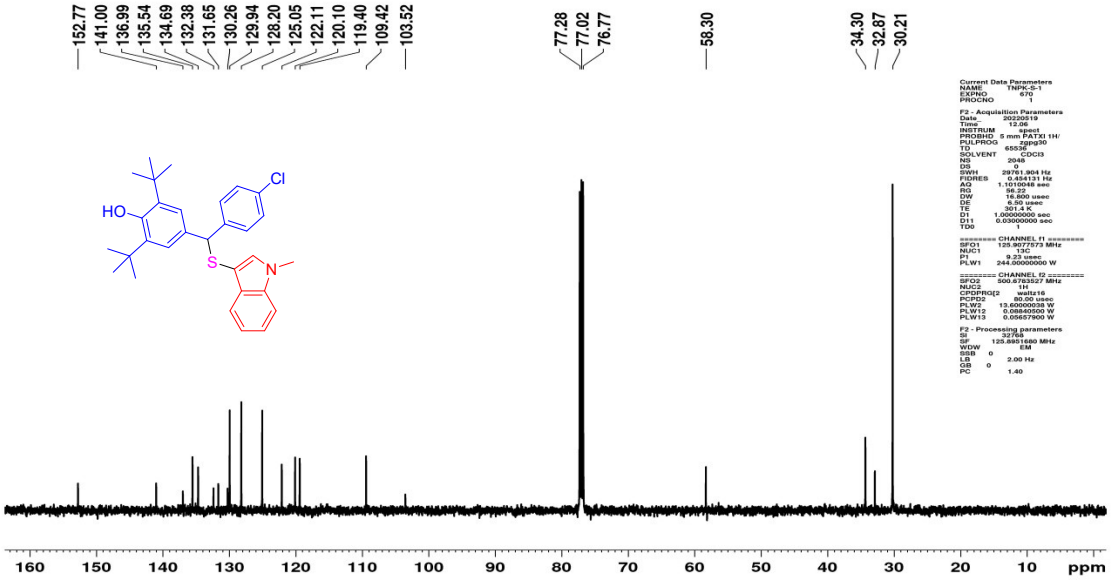
^{13}C NMR spectrum of compound- 3ac (100 Mz, $CDCl_3$)



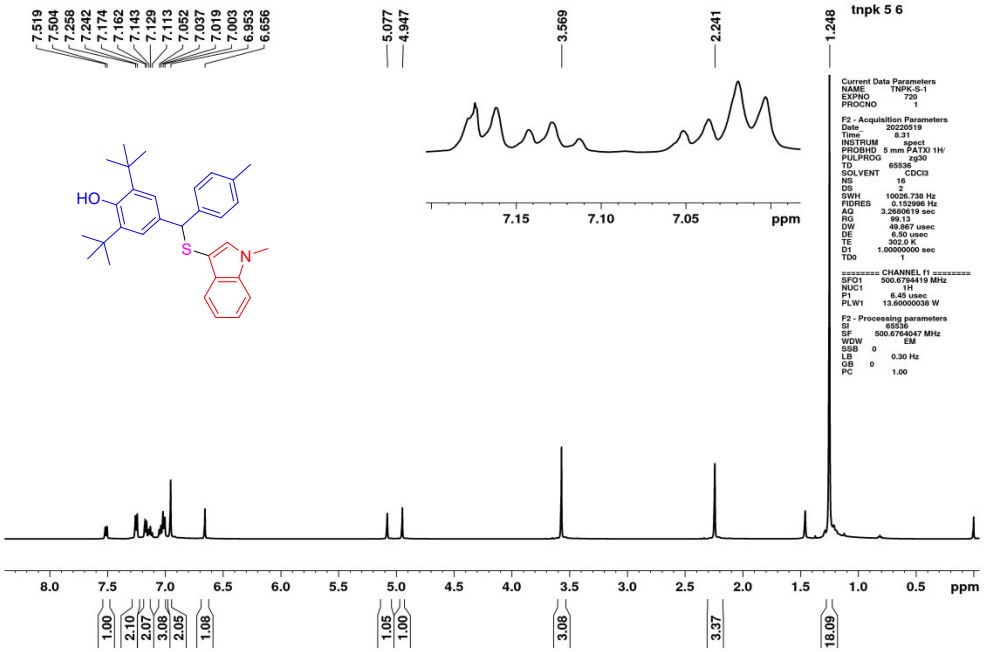
^{1}H NMR spectrum of compound- 3ad (400 Mz, $CDCl_3$)



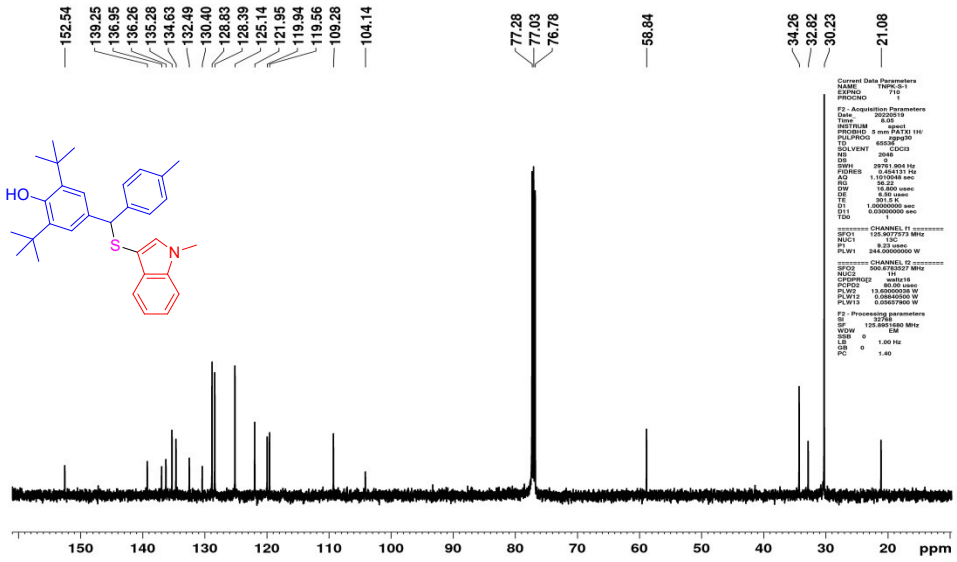
^{13}C NMR spectrum of compound- 3ad (100 Mz, $CDCl_3$)



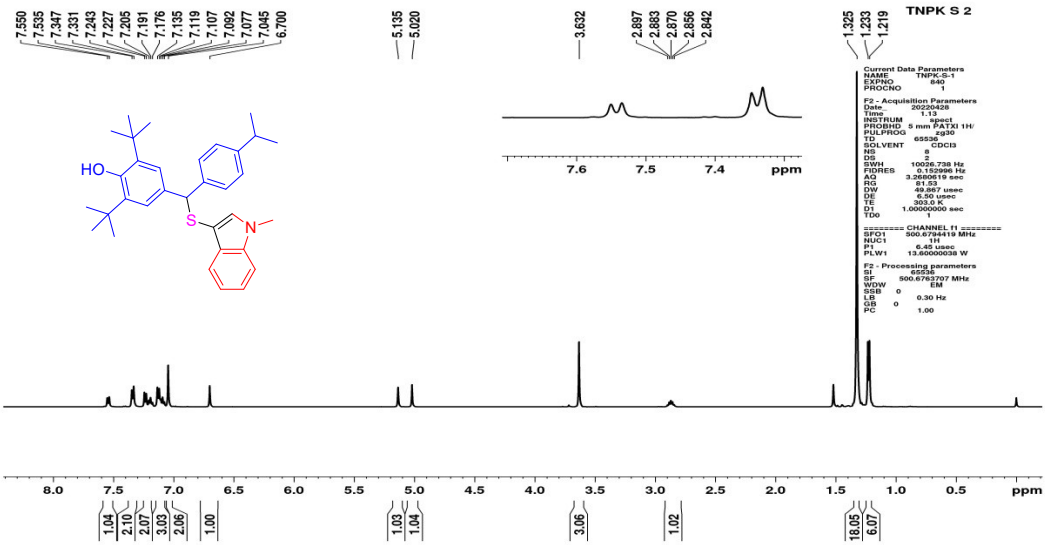
^{1}H NMR spectrum of compound- 3ae (400 Mz, $CDCl_3$)



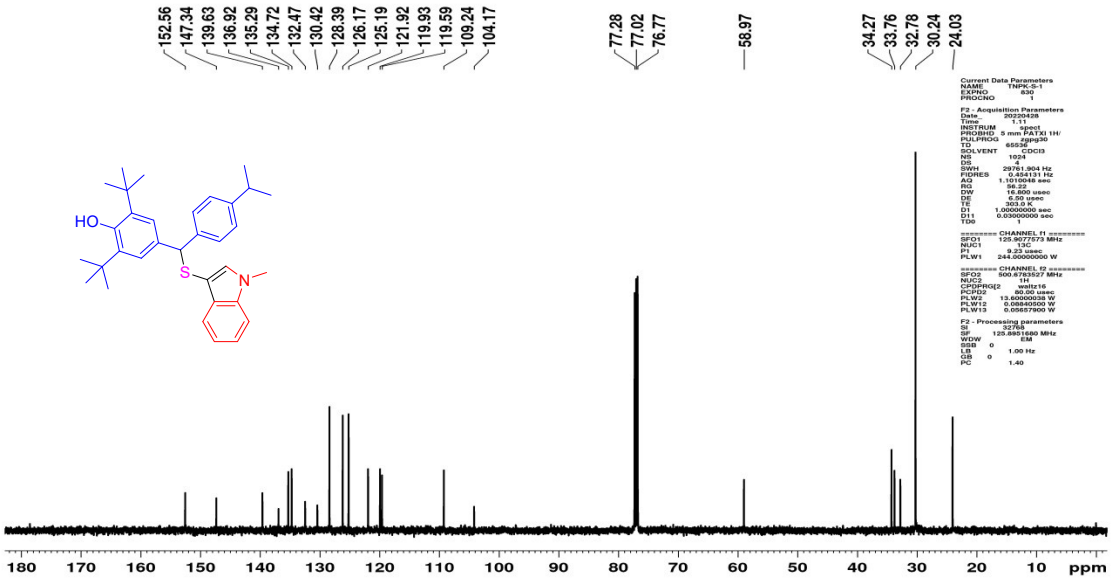
^{13}C NMR spectrum of compound- 3ae (100 Mz, $CDCl_3$)



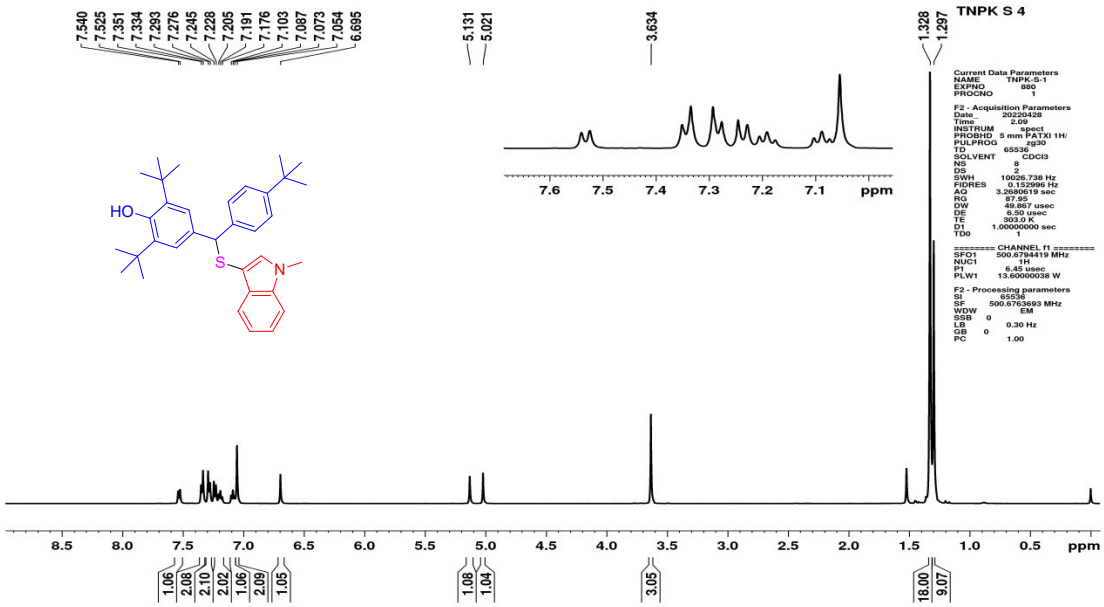
^{1}H NMR spectrum of compound- 3af (400 Mz, $CDCl_3$)



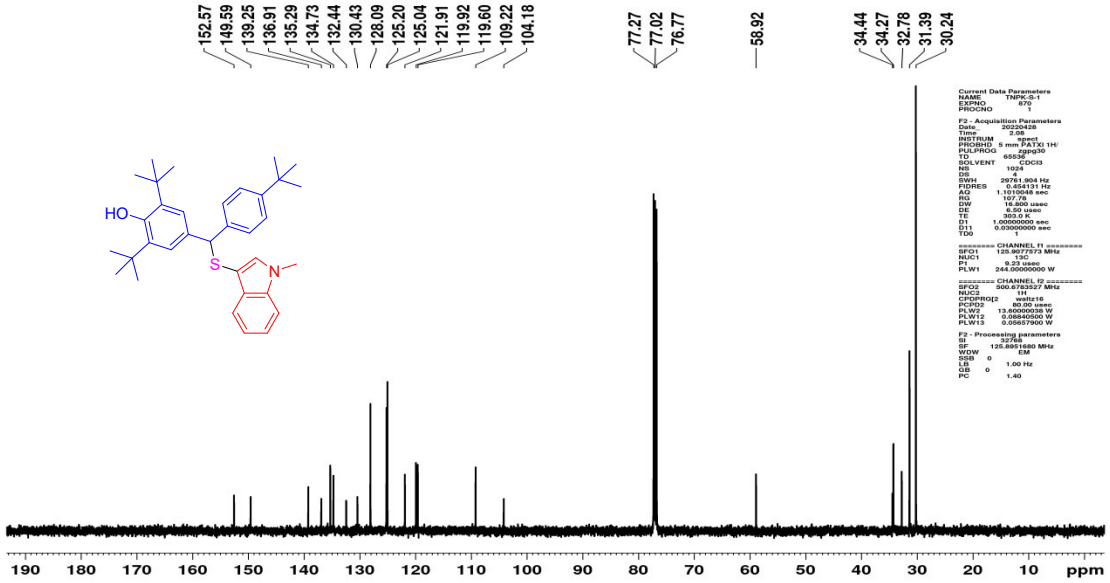
^{13}C NMR spectrum of compound- 3af (100 Mz, $CDCl_3$)



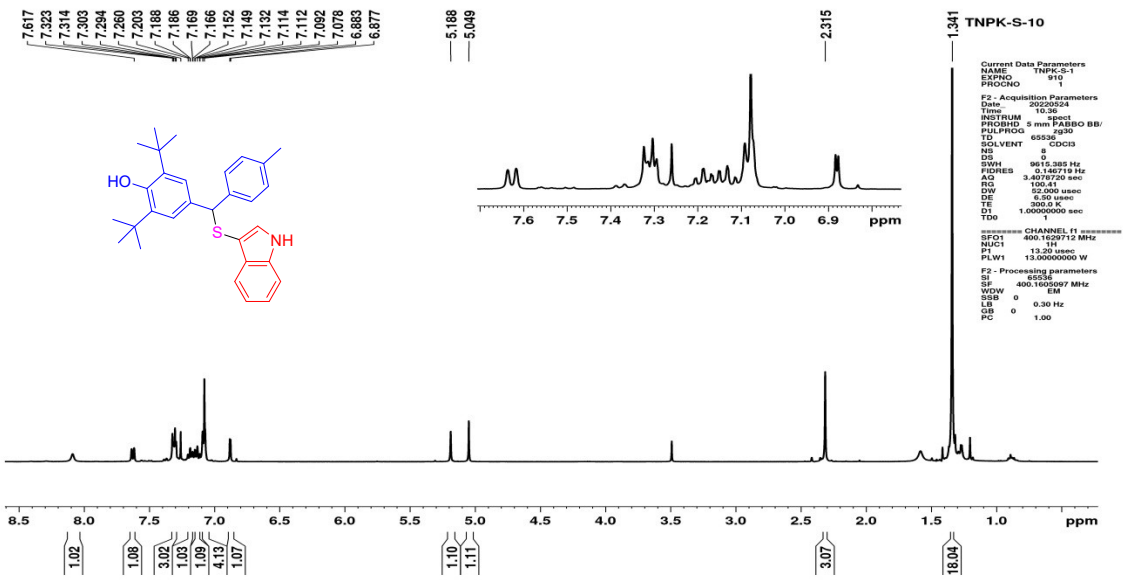
^{1}H NMR spectrum of compound- 3ag (400 Mz, $CDCl_3$)



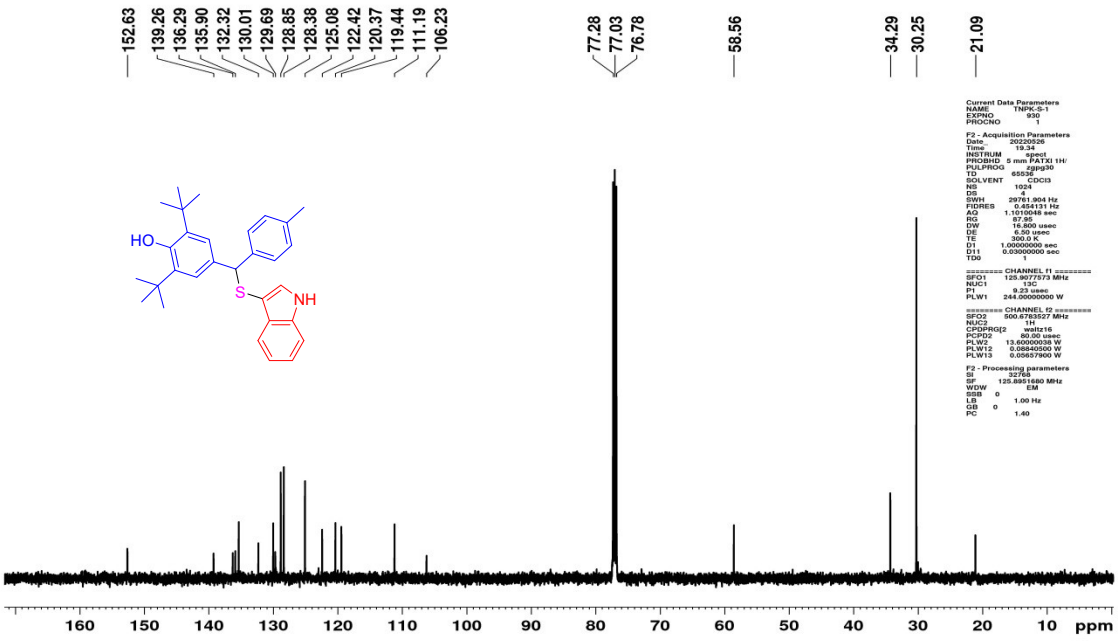
^{13}C NMR spectrum of compound- 3ag (100 Mz, $CDCl_3$)



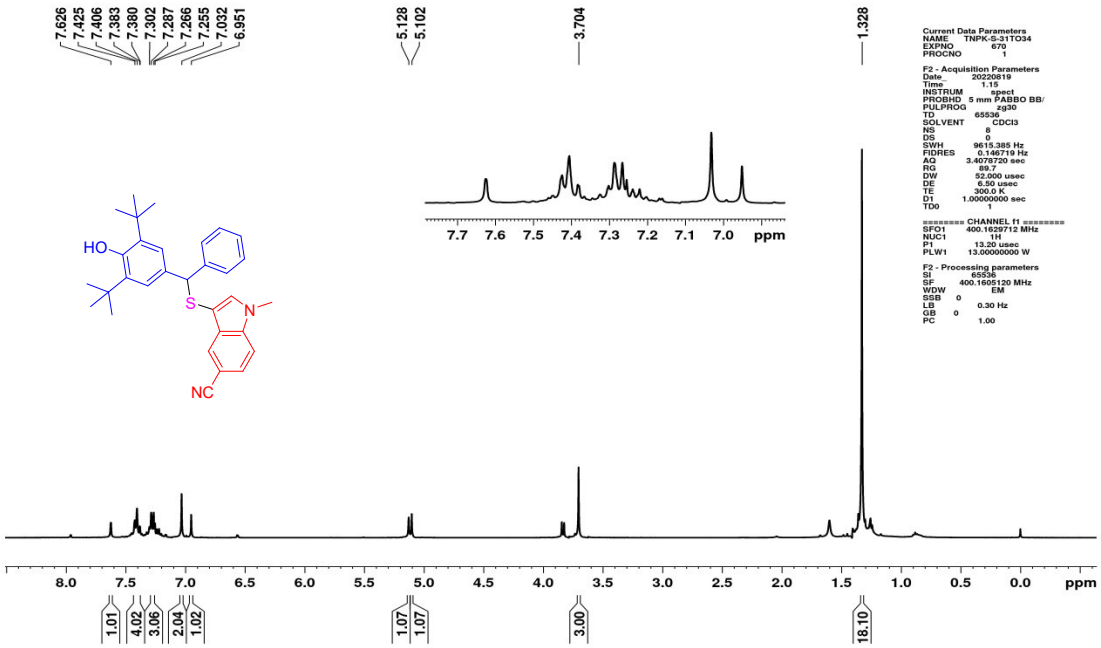
^{1}H NMR spectrum of compound- 3be (400 Mz, $CDCl_3$)



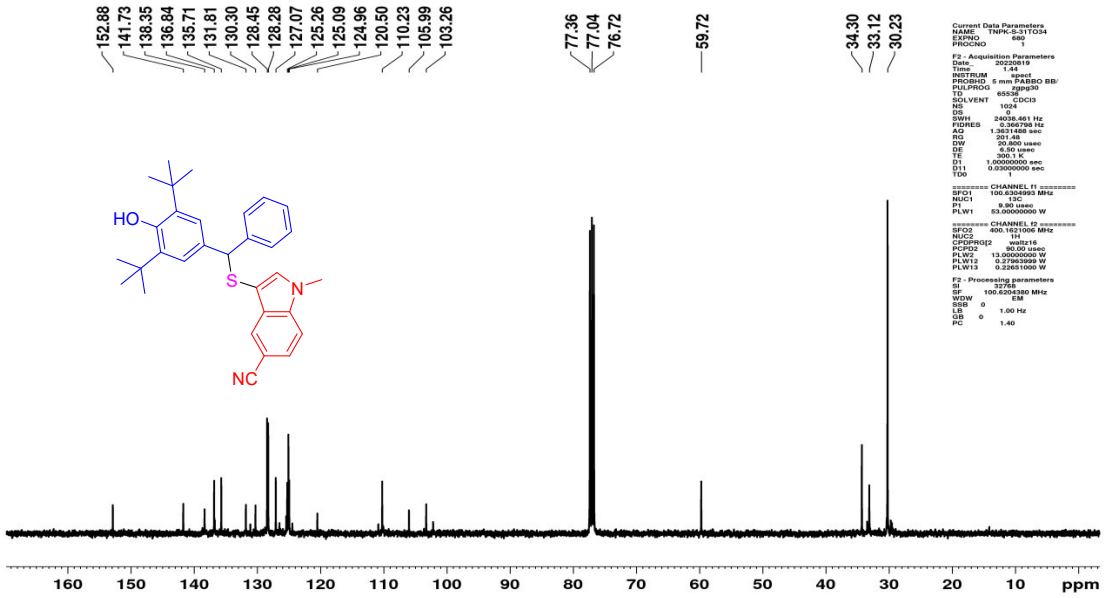
^{13}C NMR spectrum of compound- 3be (100 Mz, $CDCl_3$)



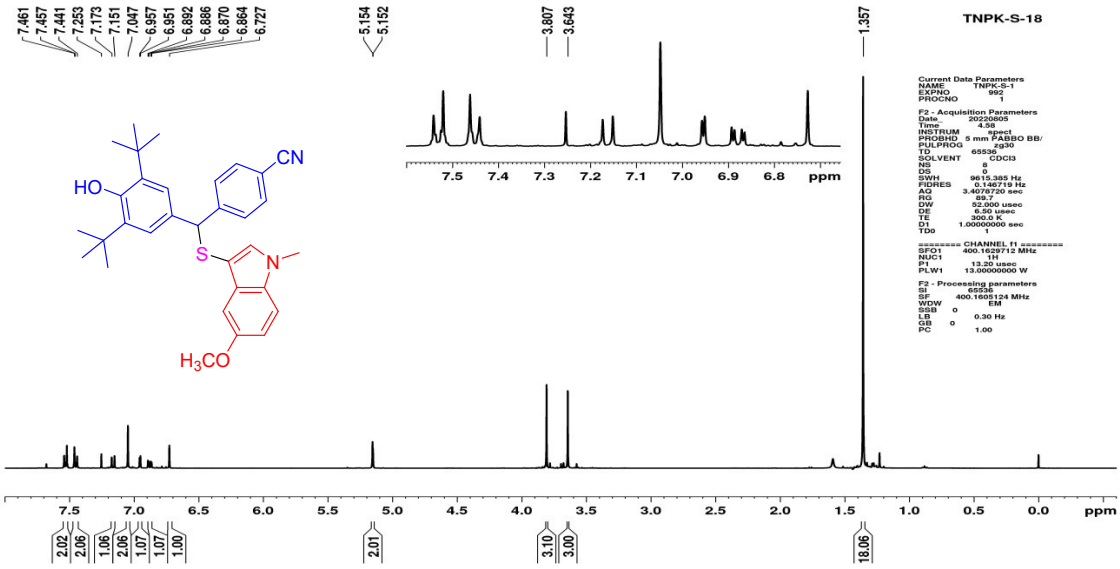
^{1}H NMR spectrum of compound- 3ca (400 Mz, $CDCl_3$)



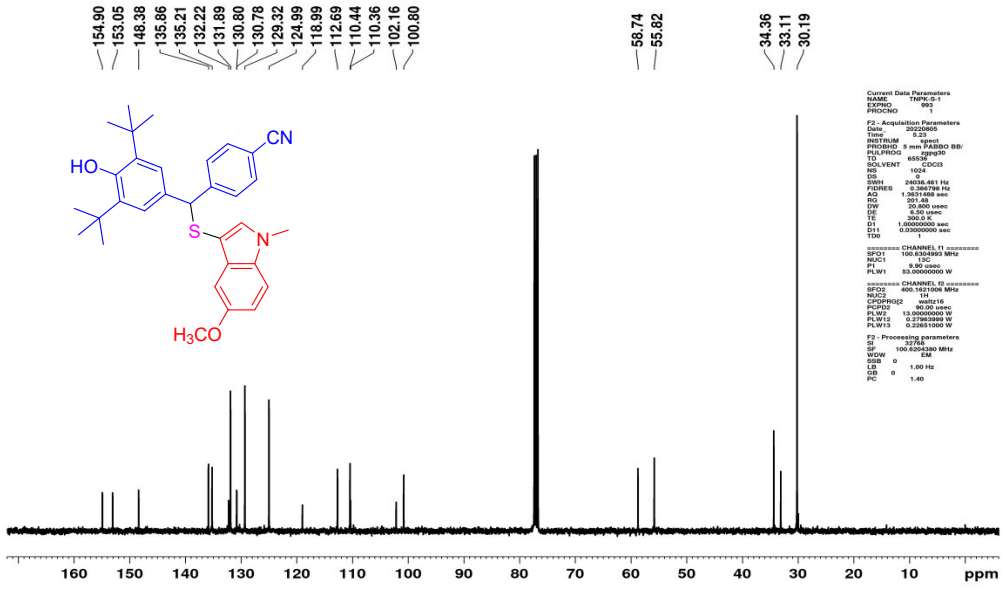
^{13}C NMR spectrum of compound- 3ca (100 Mz, $CDCl_3$)



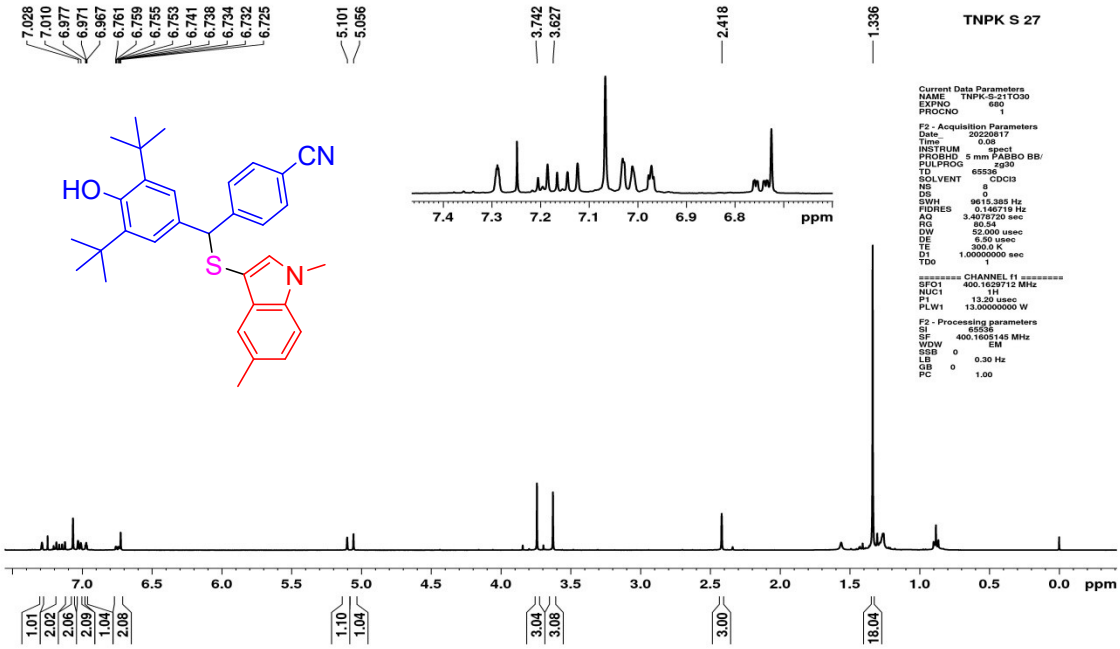
^{1}H NMR spectrum of compound- 3dh (400 Mz, $CDCl_3$)



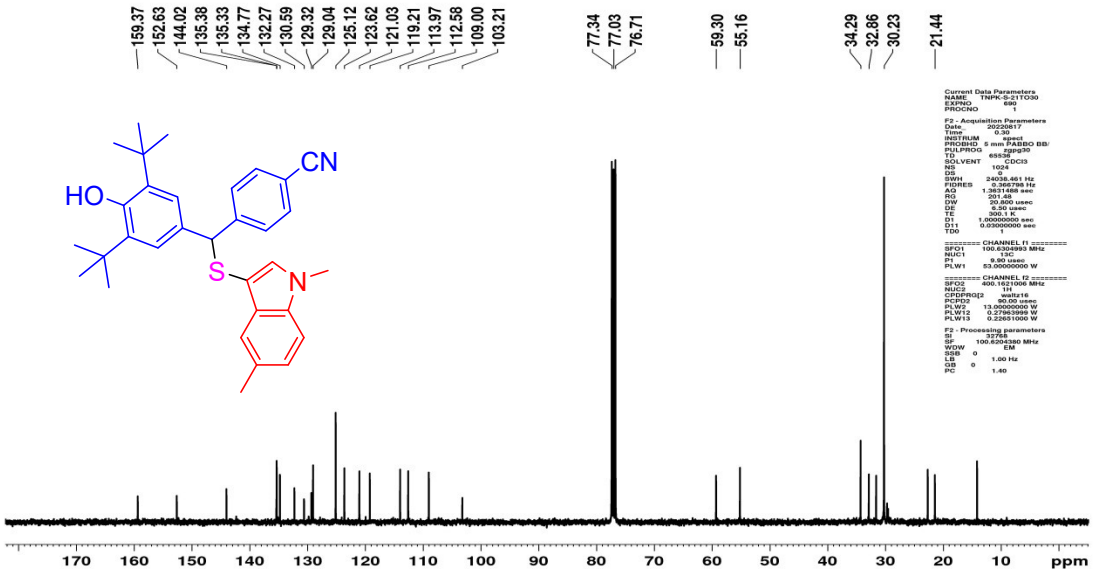
^{13}C NMR spectrum of compound- 3dh (100 Mz, $CDCl_3$)



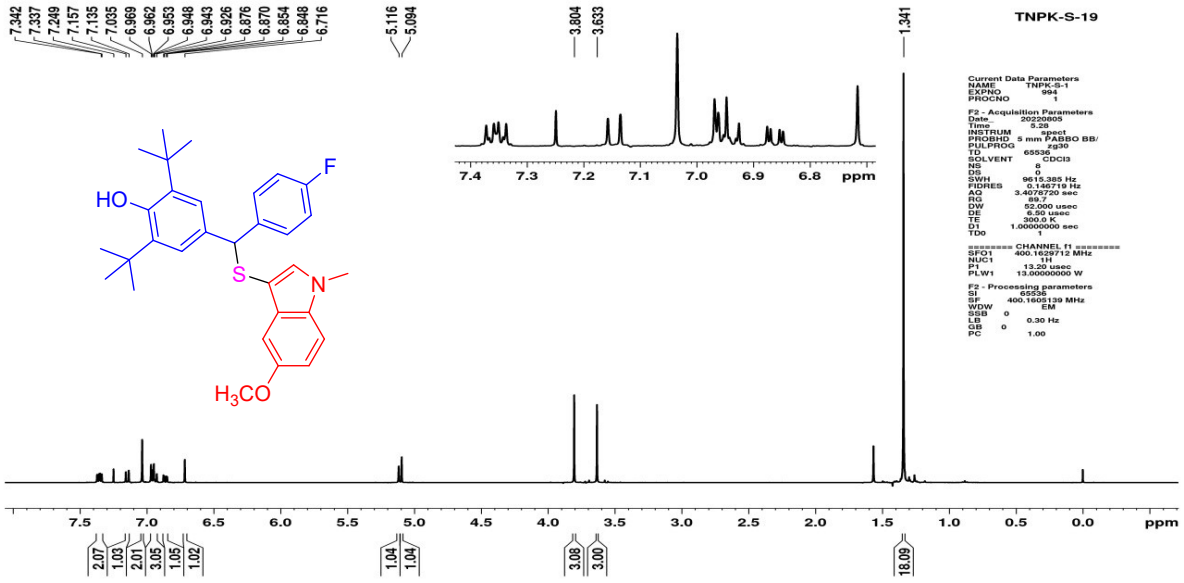
^{1}H NMR spectrum of compound- 3eh (400 Mz, $CDCl_3$)



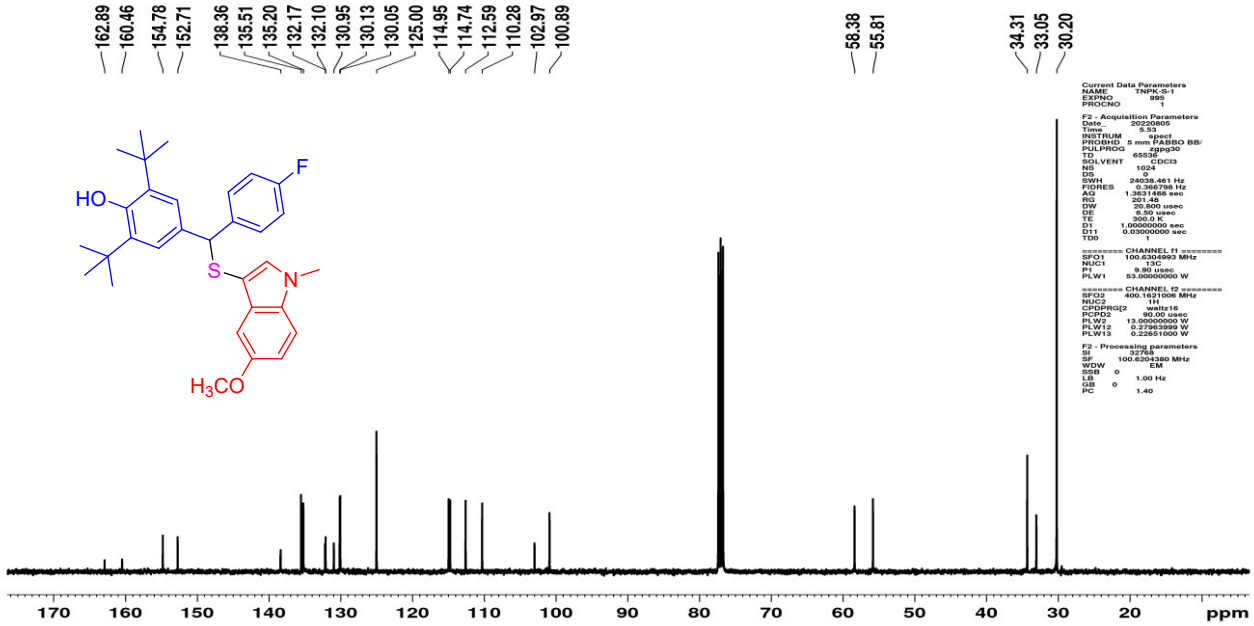
^{13}C NMR spectrum of compound- 3eh (100 Mz, $CDCl_3$)



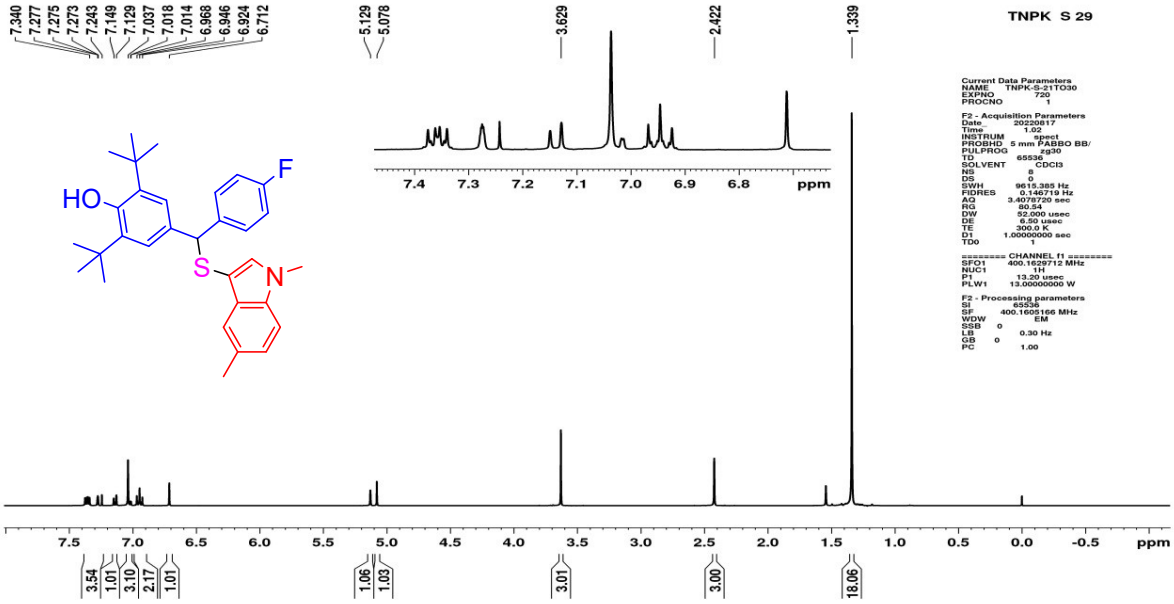
^{1}H NMR spectrum of compound- 3dc (100 Mz, $CDCl_3$)



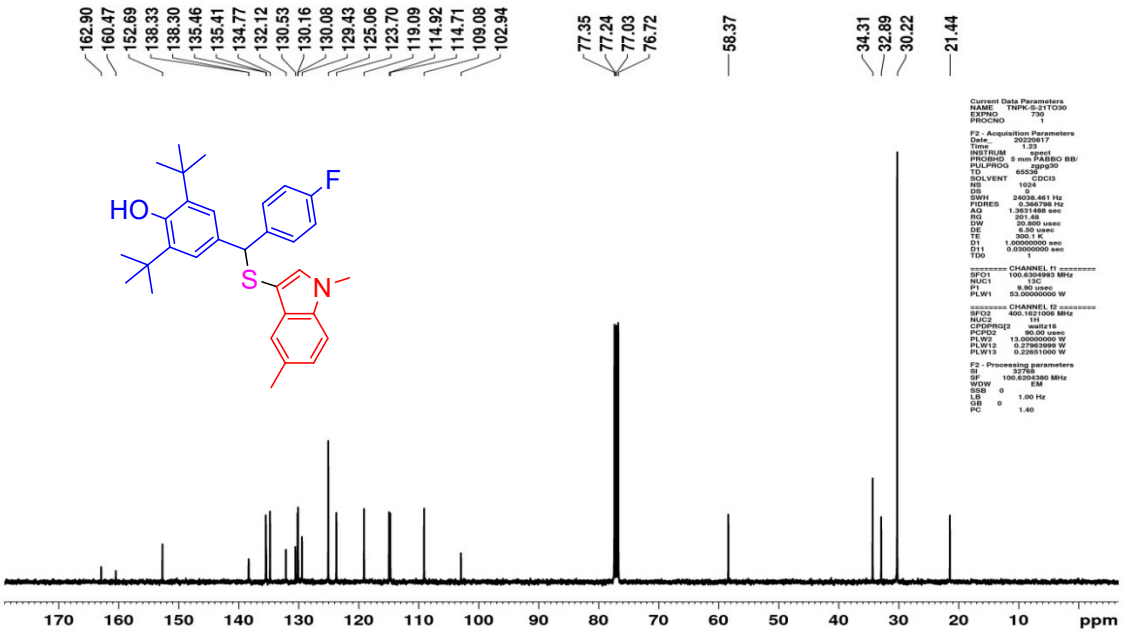
^{13}C NMR spectrum of compound- 3dc (100 Mz, $CDCl_3$)



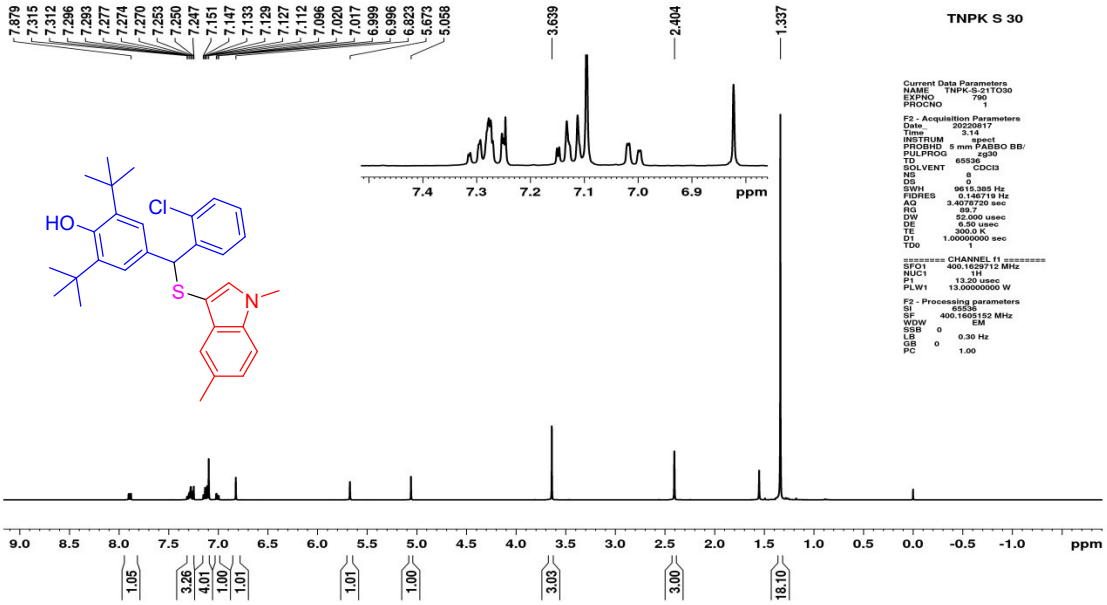
^{1}H NMR spectrum of compound- 3de (400 Mz, $CDCl_3$)



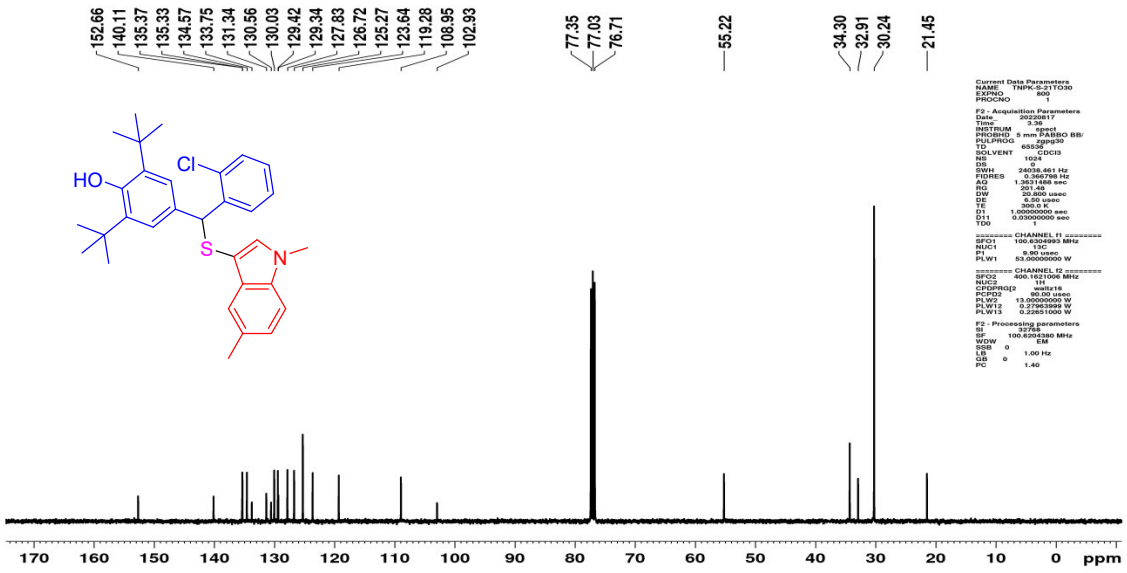
^{13}C NMR spectrum of compound- 3de (100 Mz, $CDCl_3$)



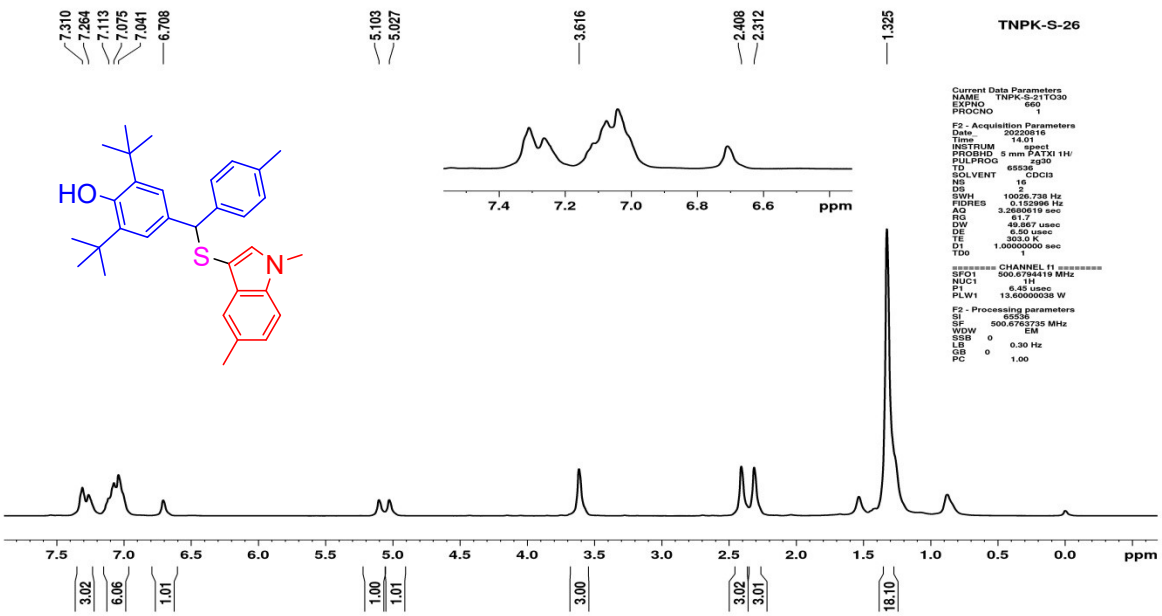
^{1}H NMR spectrum of compound- 3ei (400 Mz, $CDCl_3$)



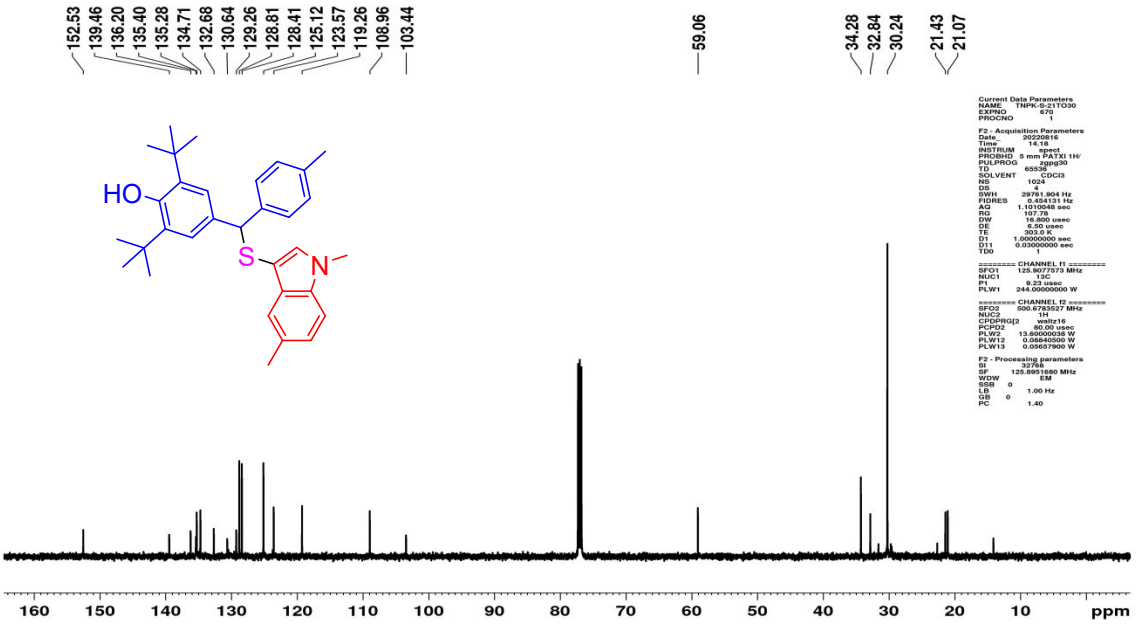
^{13}C NMR spectrum of compound- 3ei (100 Mz, $CDCl_3$)



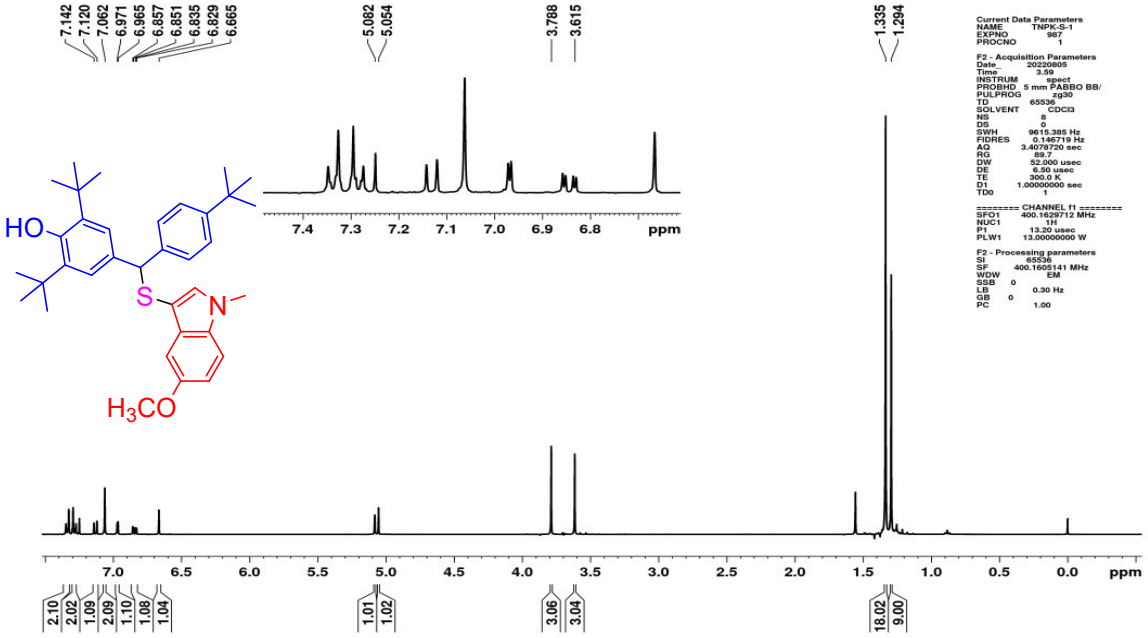
^{1}H NMR spectrum of compound- 3ee (400 Mz, $CDCl_3$)



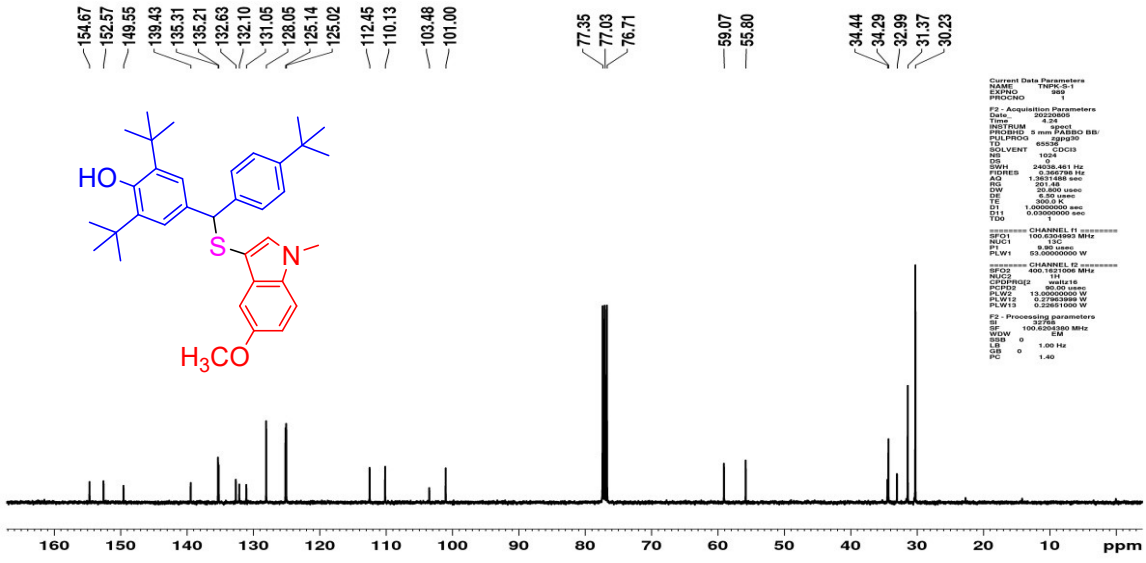
^{13}C NMR spectrum of compound- 3ee (100 Mz, $CDCl_3$)



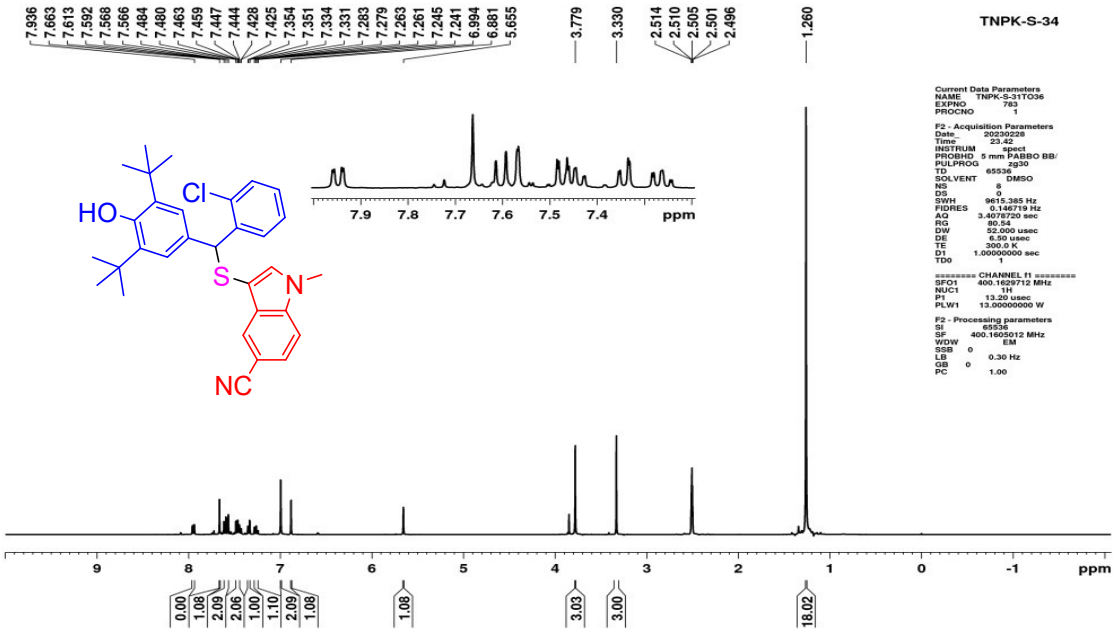
^{1}H NMR spectrum of compound- 3dg (400 Mz, $CDCl_3$)



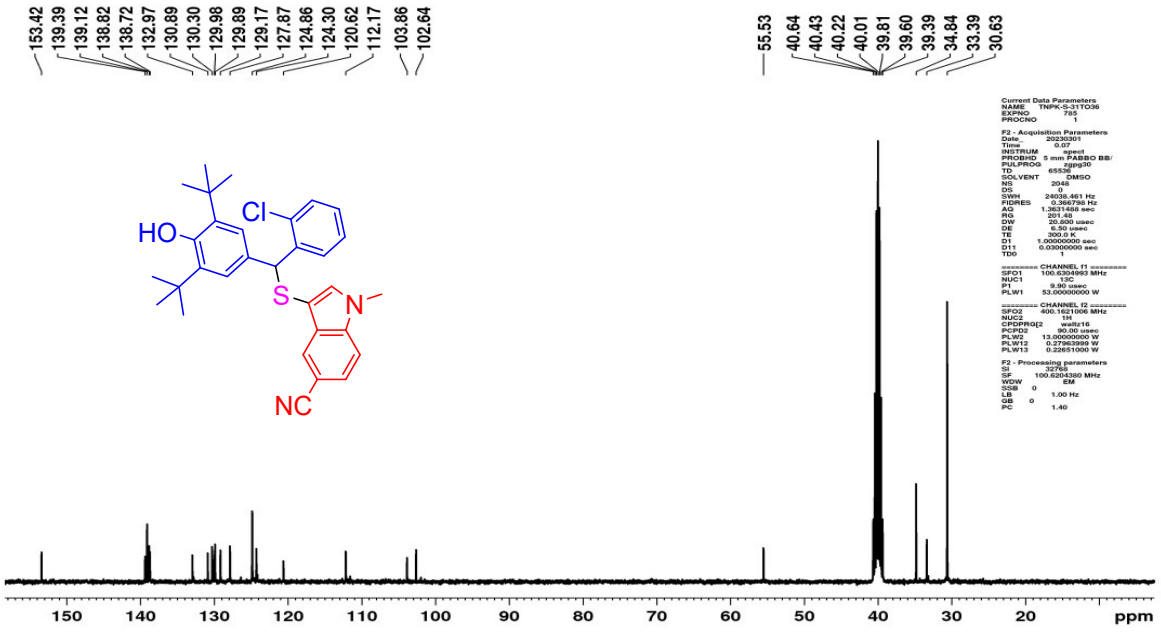
^{13}C NMR spectrum of compound- 3dg (100 Mz, $CDCl_3$)



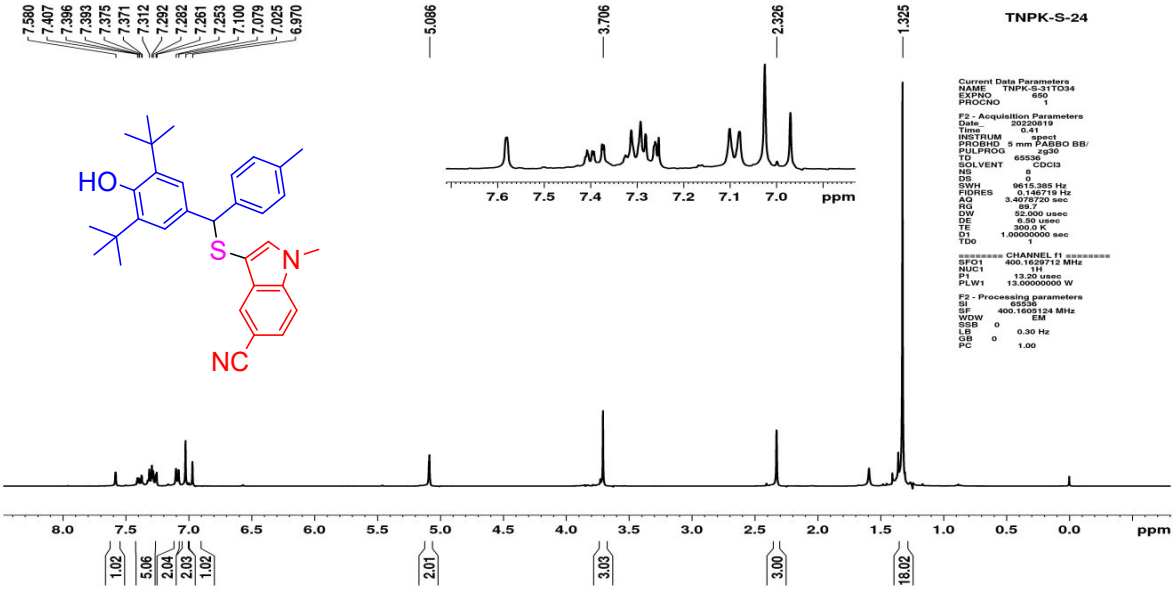
^{1}H NMR spectrum of compound- 3ci (400 Mz, $CDCl_3$)



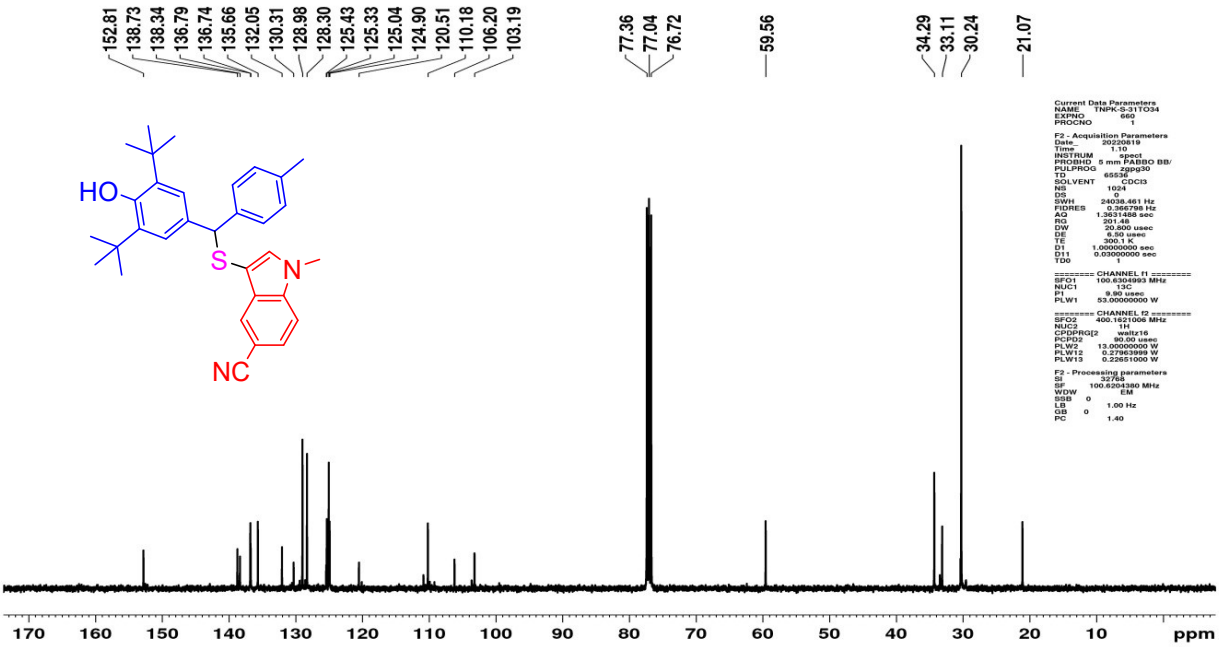
^{13}C NMR spectrum of compound- 3ci (100 Mz, $CDCl_3$)



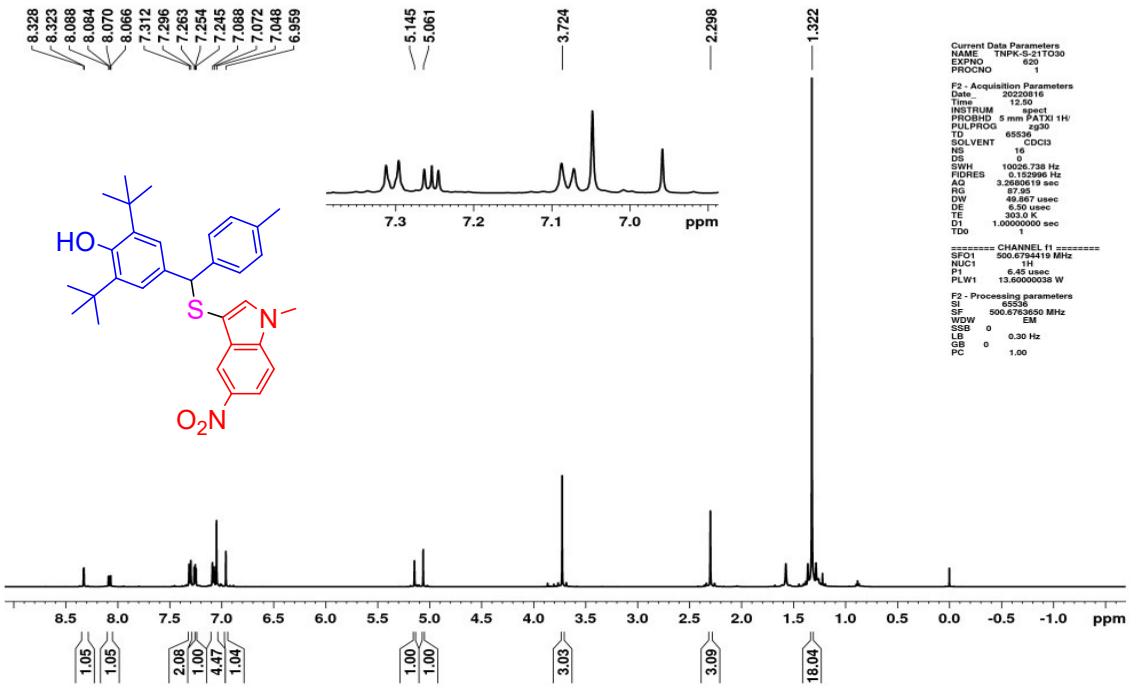
^{1}H NMR spectrum of compound- 3ce (400 Mz, $CDCl_3$)



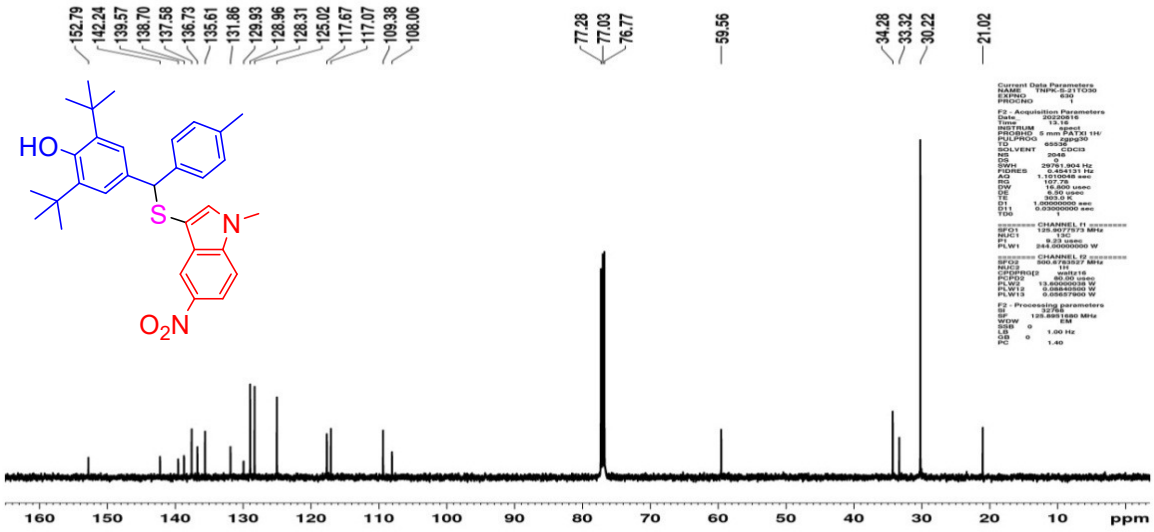
^{13}CNMR spectrum of compound- 3ce (100 Mz, $CDCl_3$)



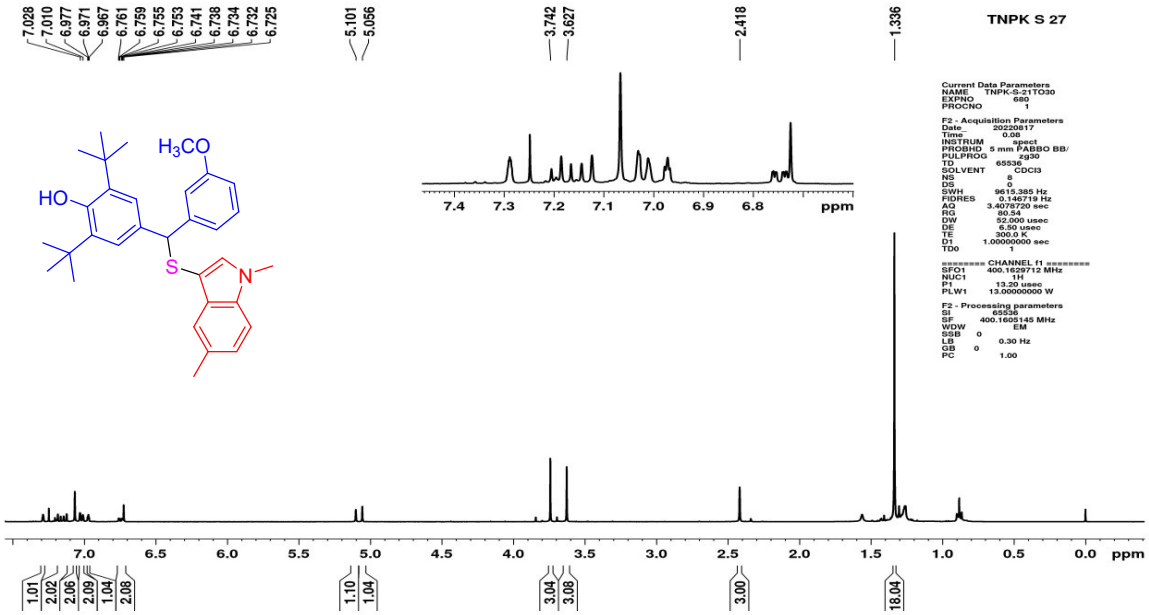
^{1}H NMR spectrum of compound- 3fe (400 Mz, $CDCl_3$)



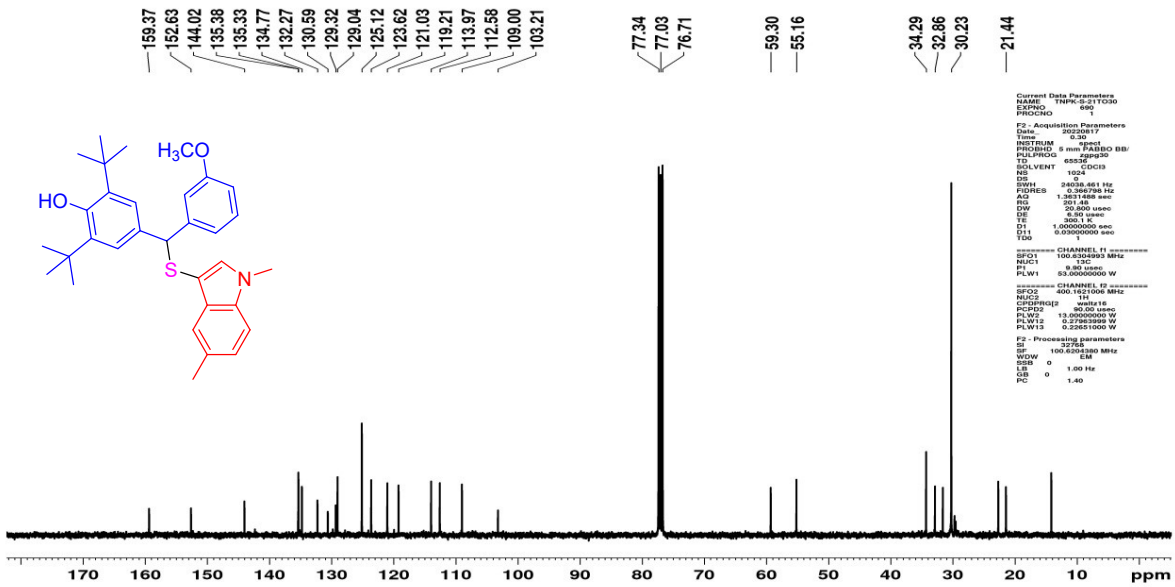
^{13}C NMR spectrum of compound- 3fe (100 Mz, $CDCl_3$)



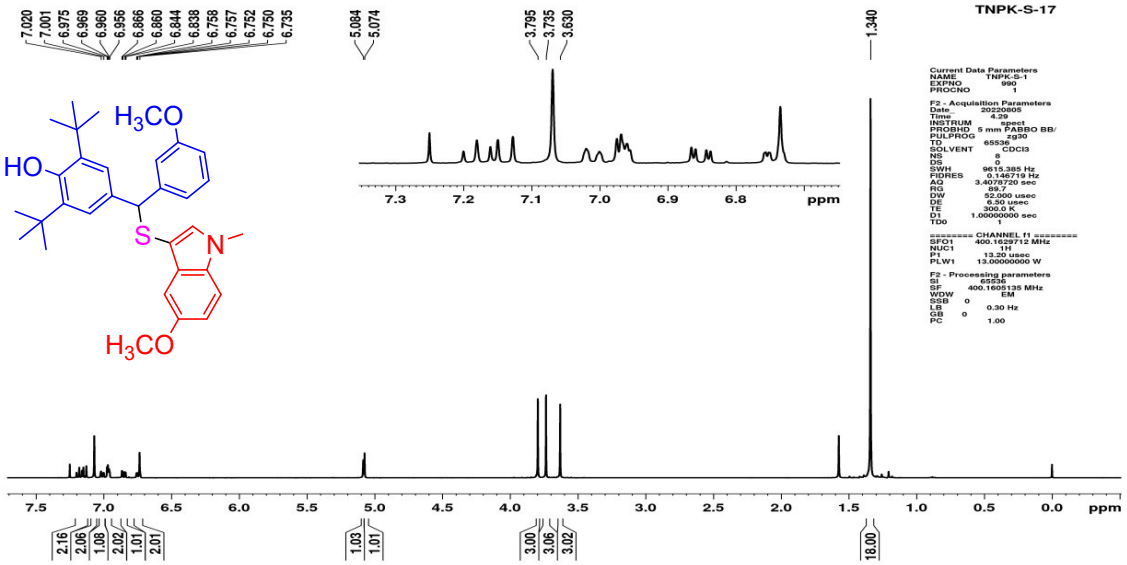
^{1}H NMR spectrum of compound- 3ej (400 Mz, $CDCl_3$)



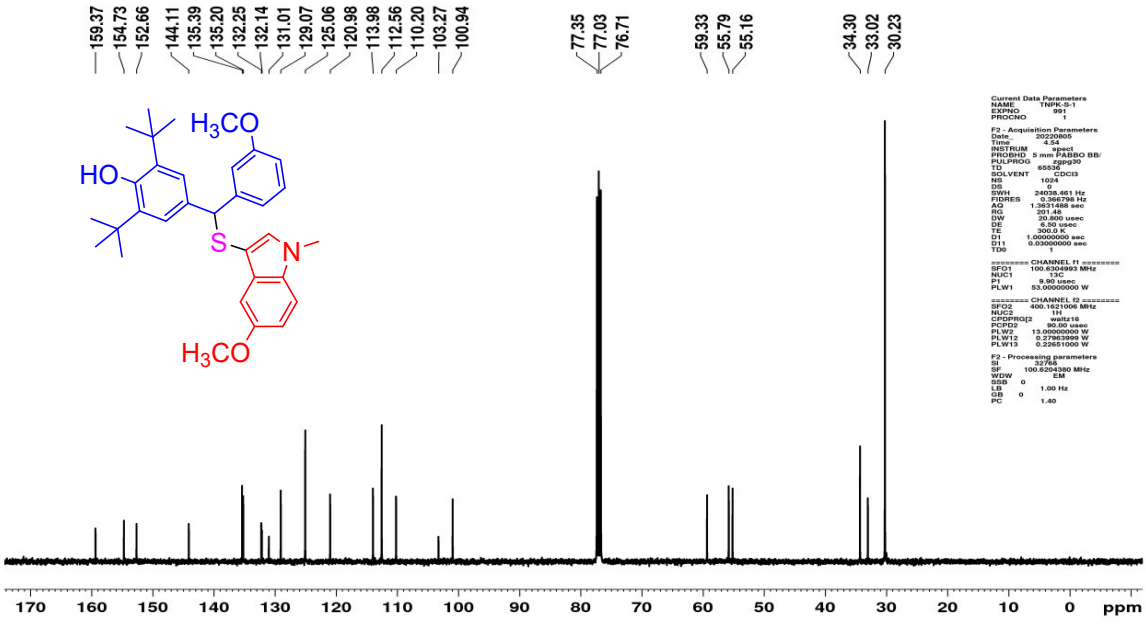
^{13}C NMR spectrum of compound- 3ej (100 Mz, $CDCl_3$)



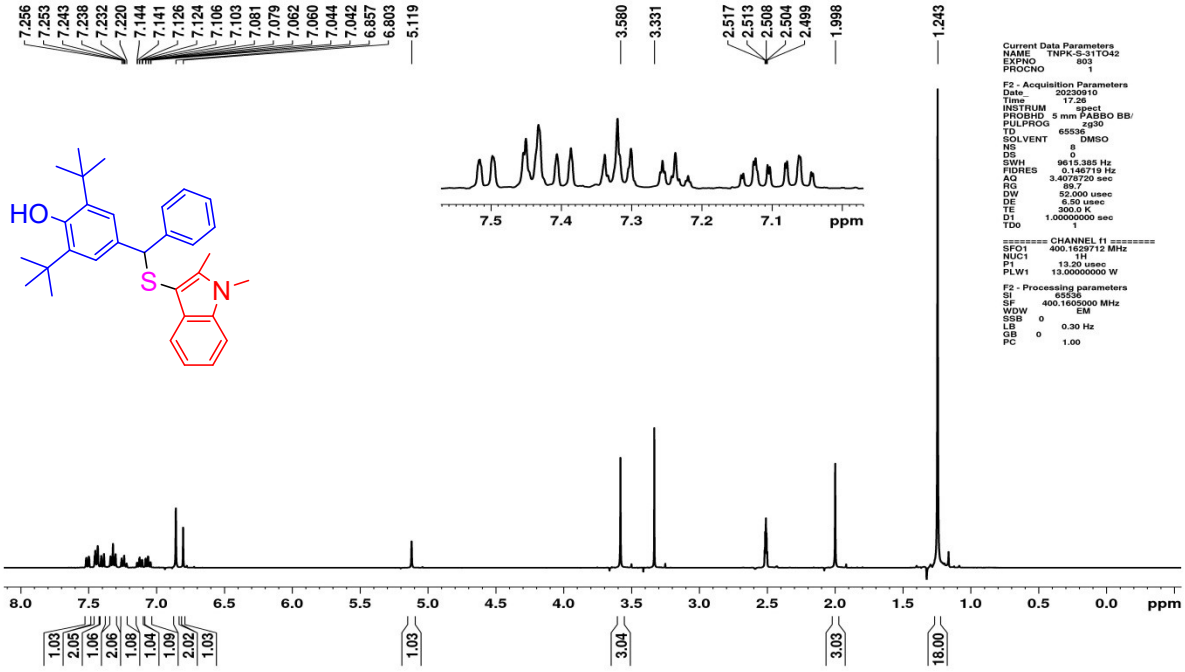
^{1}H NMR spectrum of compound- 3dj (400 Mz, $CDCl_3$)



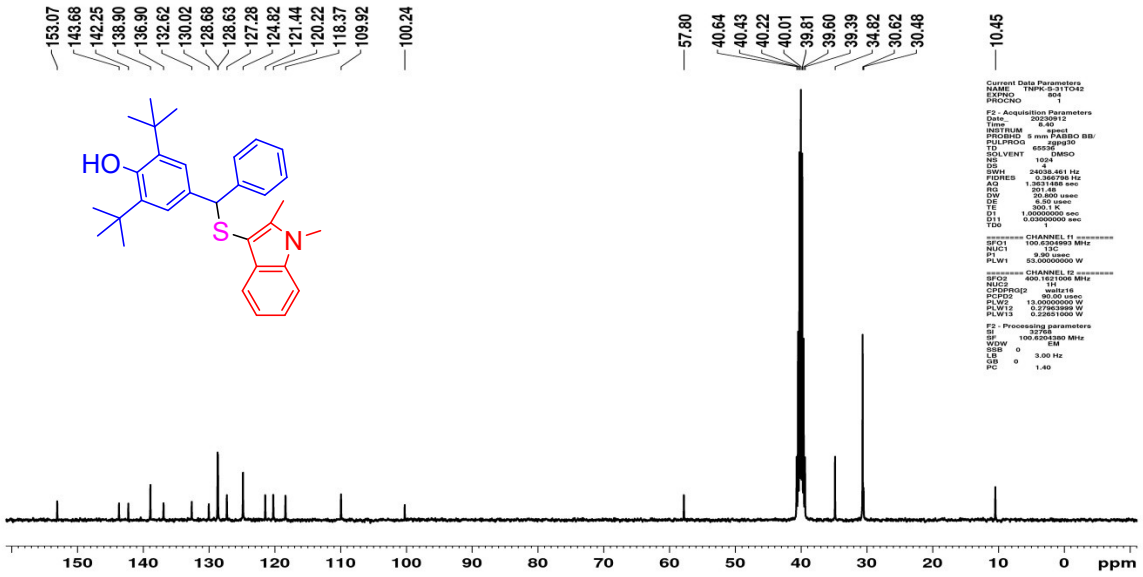
^{13}C NMR spectrum of compound- 3dj (100 Mz, $CDCl_3$)



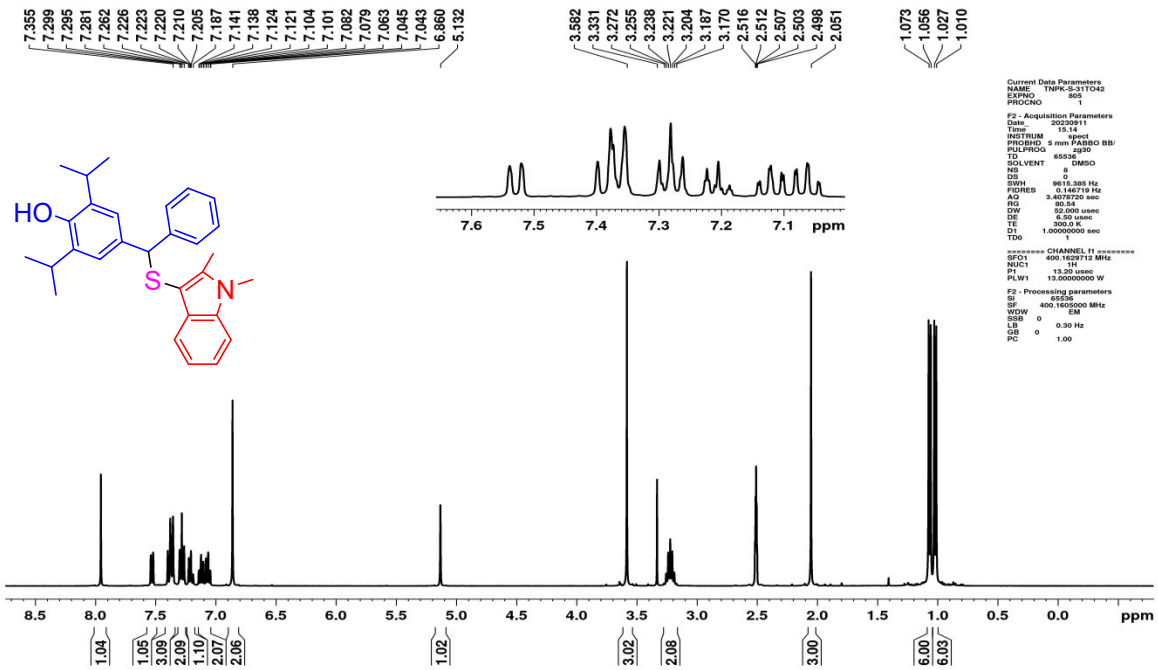
^{1}H NMR spectrum of compound- 3ga (400 Mz, DMSO-d^{6})



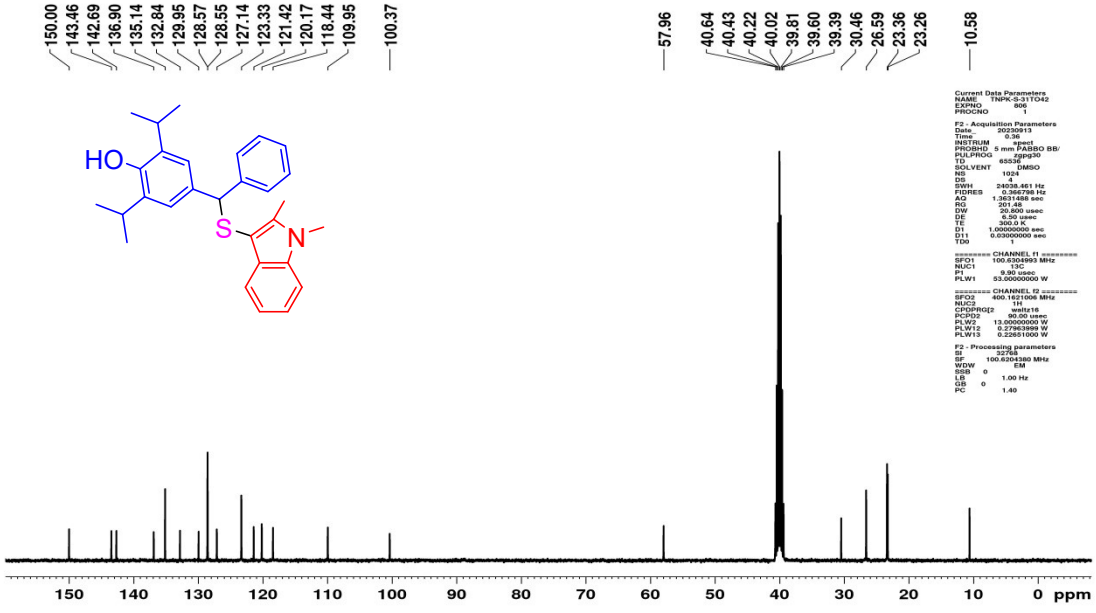
^{13}C NMR spectrum of compound- 3ga (100 Mz, DMSO-d^{6})



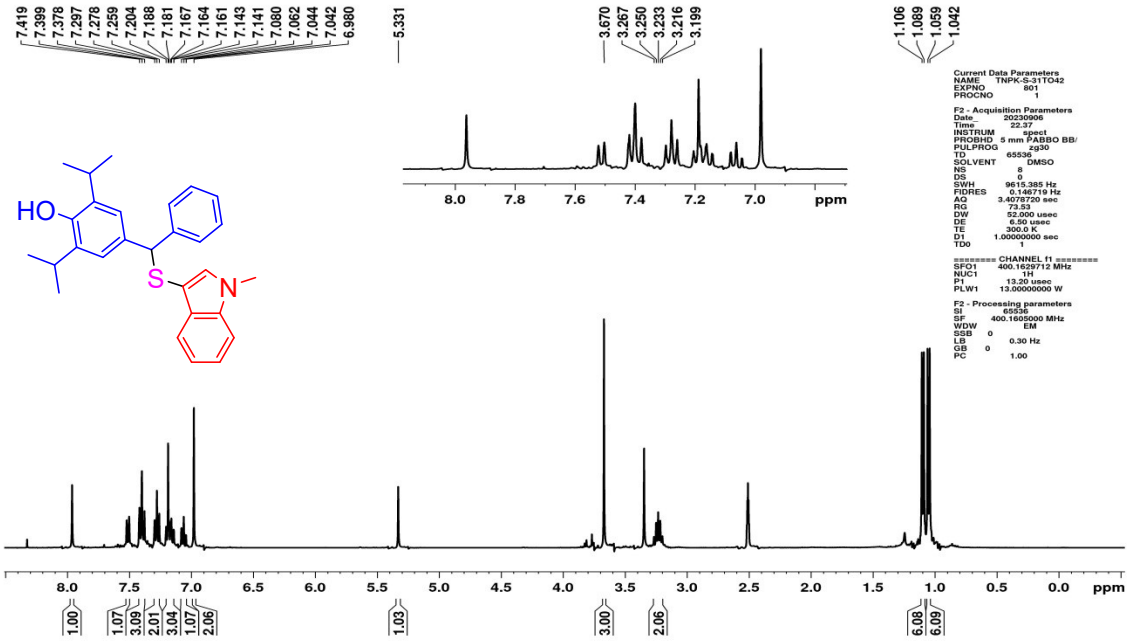
^{1}H NMR spectrum of compound- 3gk (400 Mz, DMSO-d^{6})



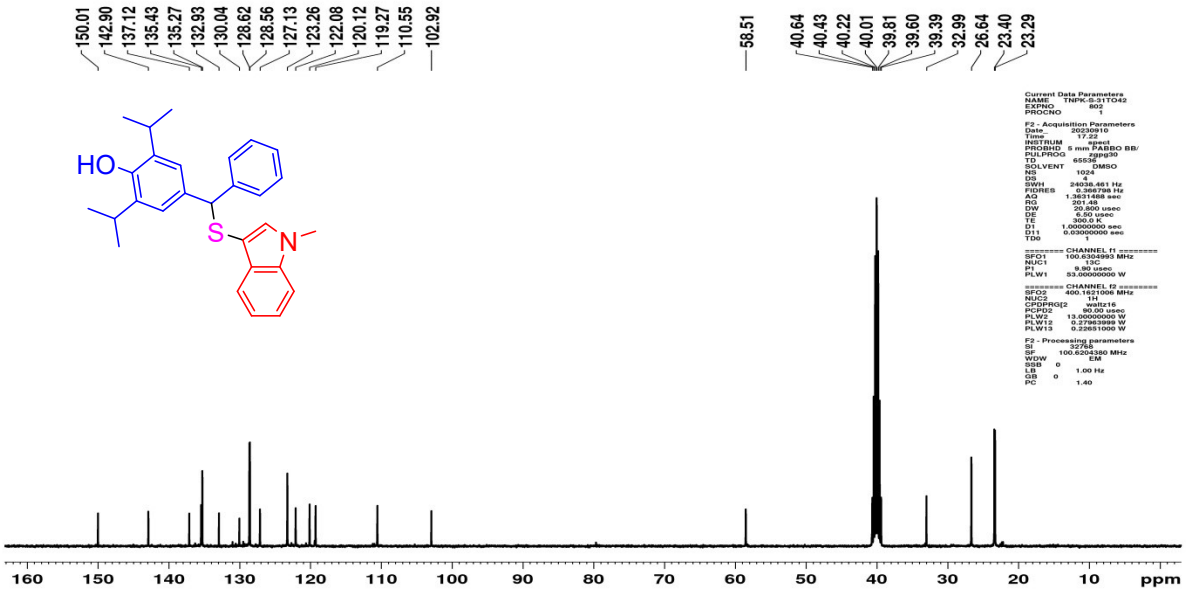
^{13}C NMR spectrum of compound- 3gk (100 Mz, DMSO-d^{6})



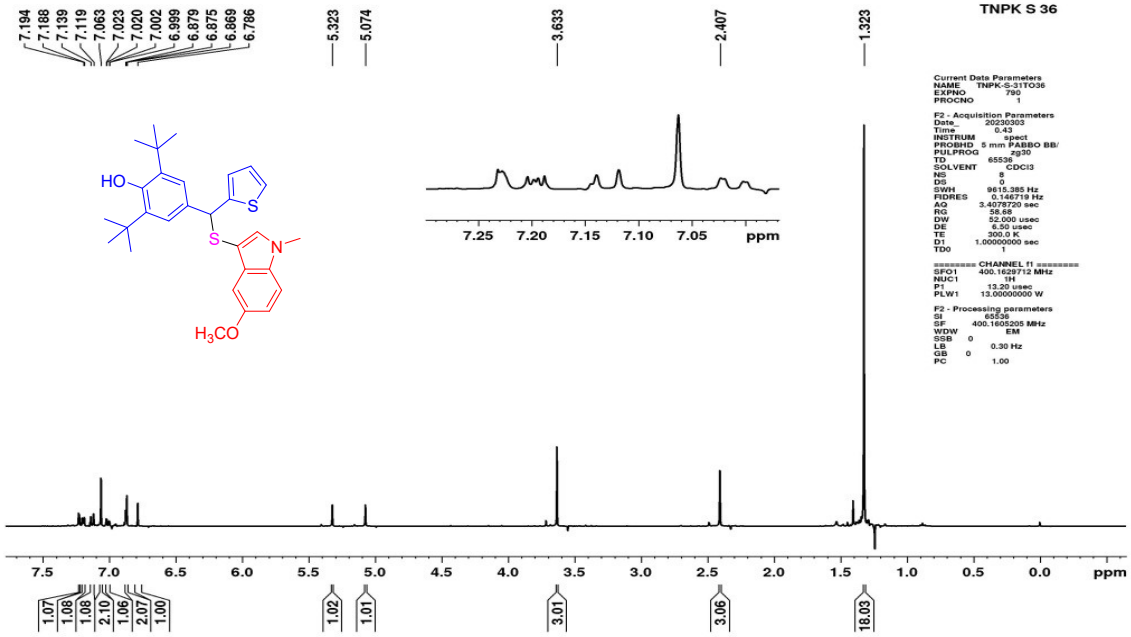
^{1}H NMR spectrum of compound- 3ak (400 Mz, DMSO-d^{6})



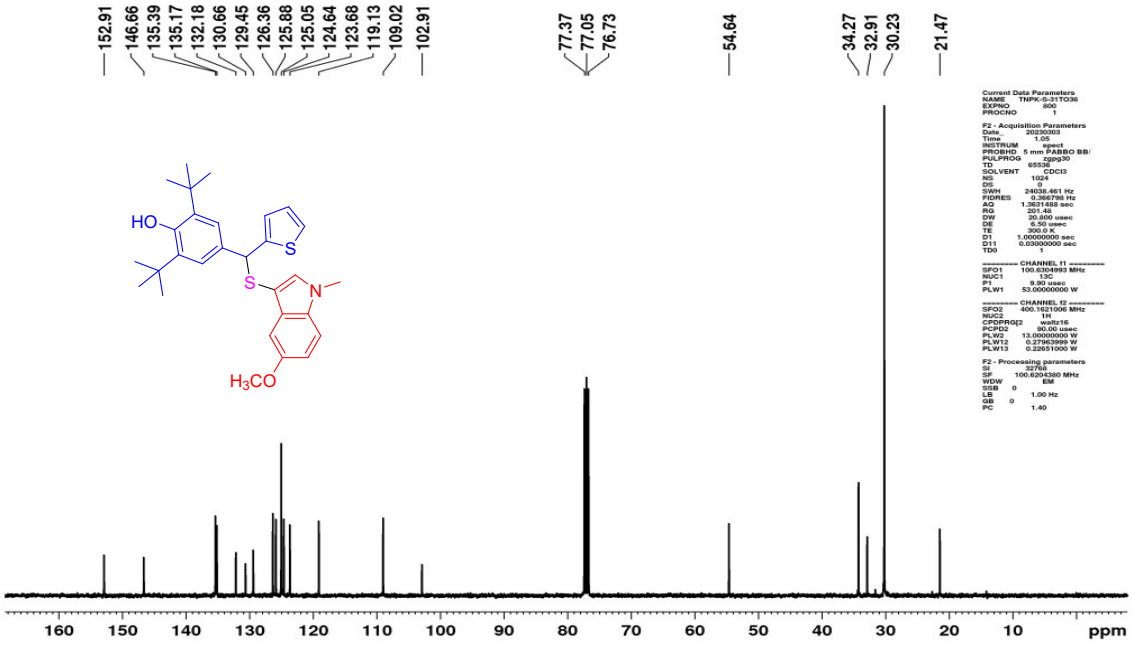
^{13}C NMR spectrum of compound- 3ak (100 Mz, DMSO-d^{6})



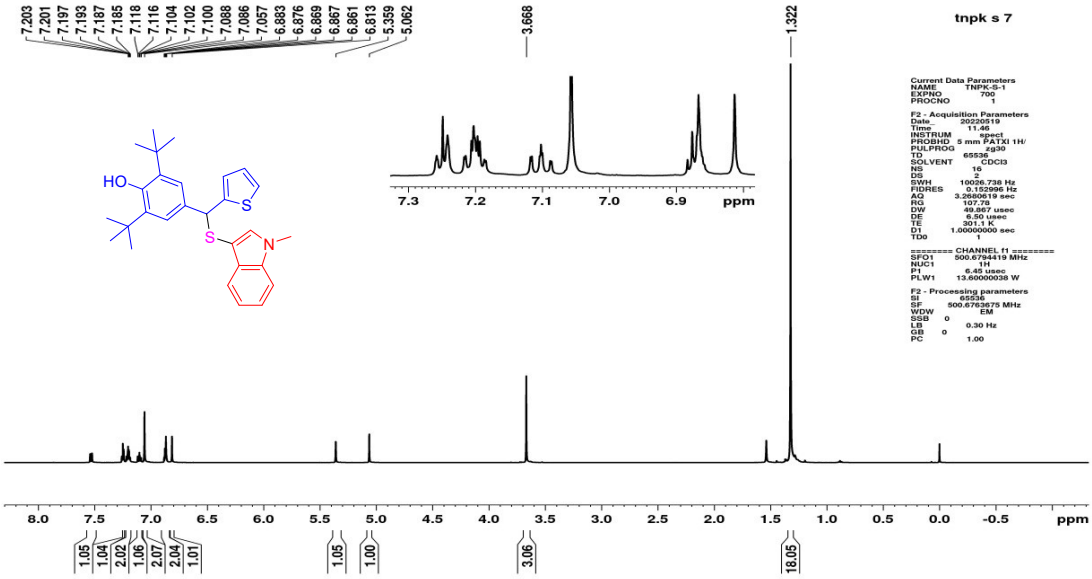
^{1}H NMR spectrum of compound- 3dl (400 Mz, $CDCl_3$)



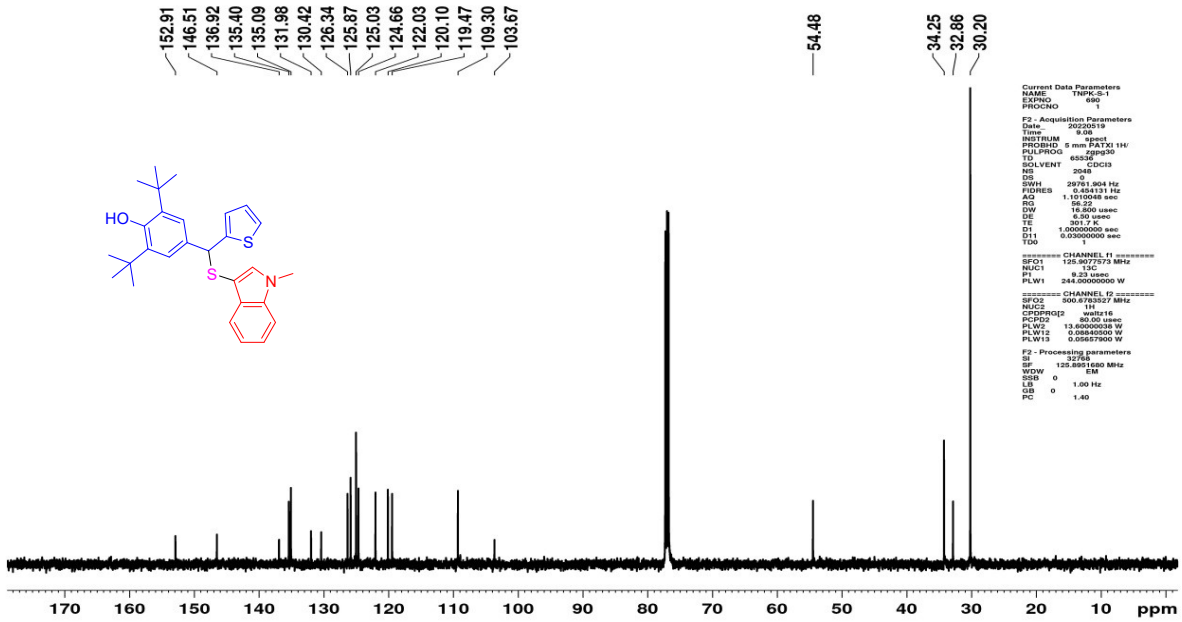
^{13}C NMR spectrum of compound- 3dl (100 Mz, $CDCl_3$)



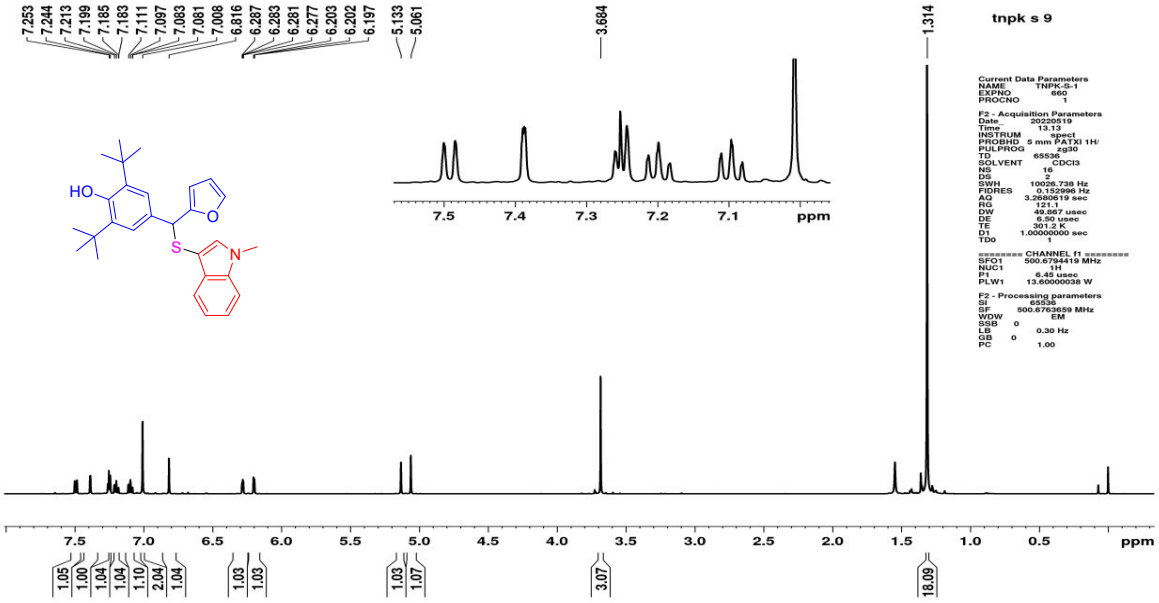
^{1}H NMR spectrum of compound- 3al (400 Mz, $CDCl_3$)



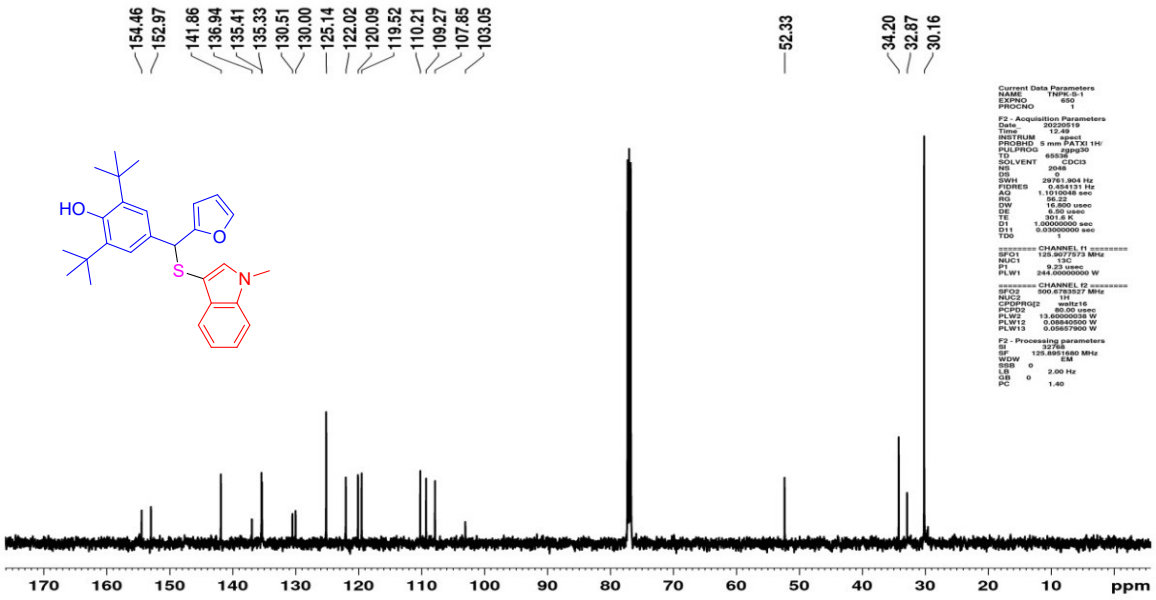
^{13}C NMR spectrum of compound- 3al (100 Mz, $CDCl_3$)



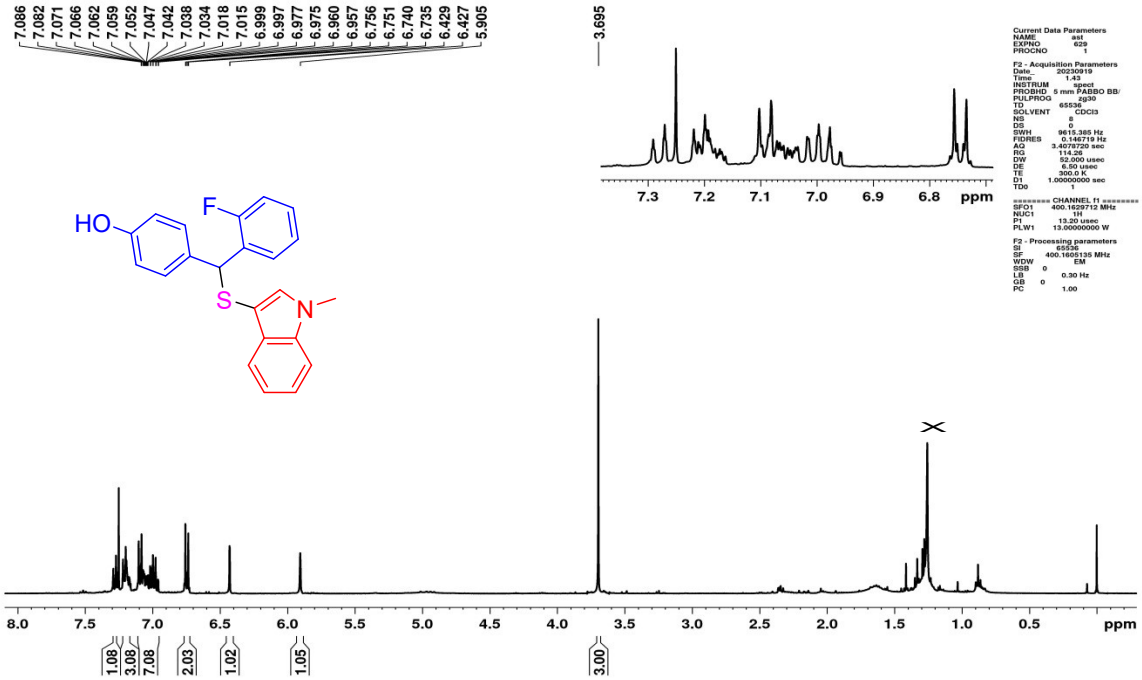
^{1}H NMR spectrum of compound- 3am (400 Mz, $CDCl_3$)



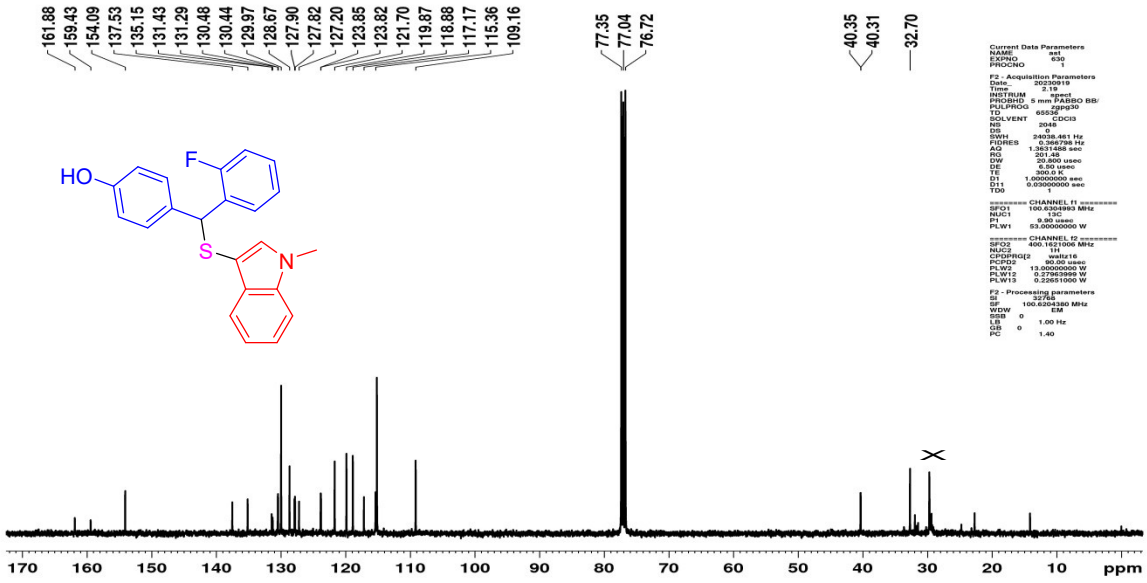
^{13}C NMR spectrum of compound- 3am (100 Mz, $CDCl_3$)



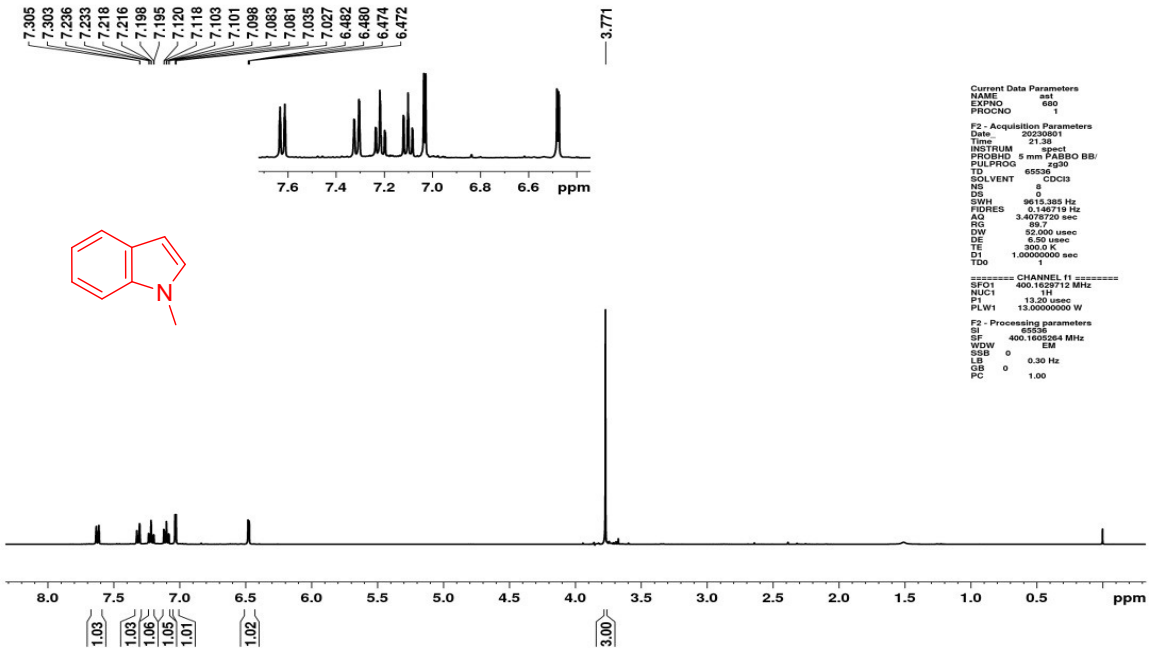
^{1}H NMR spectrum of compound- 4 (400 Mz, $CDCl_3$, X = grease)



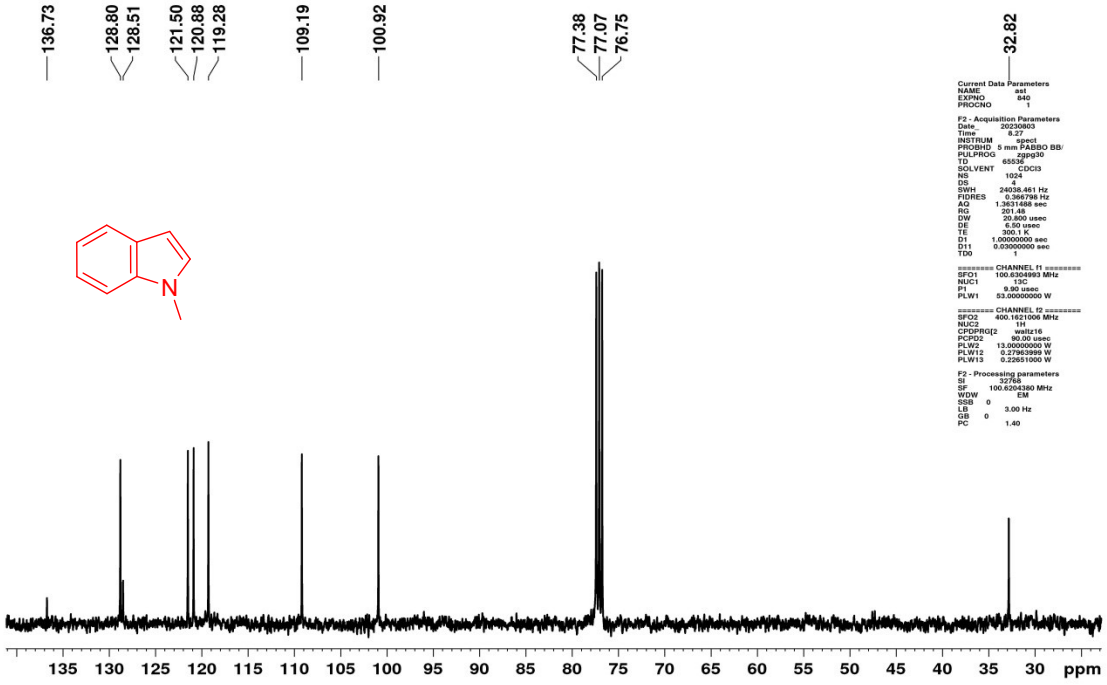
^{13}C NMR spectrum of compound- 4 (100 Mz, $CDCl_3$, X = grease)



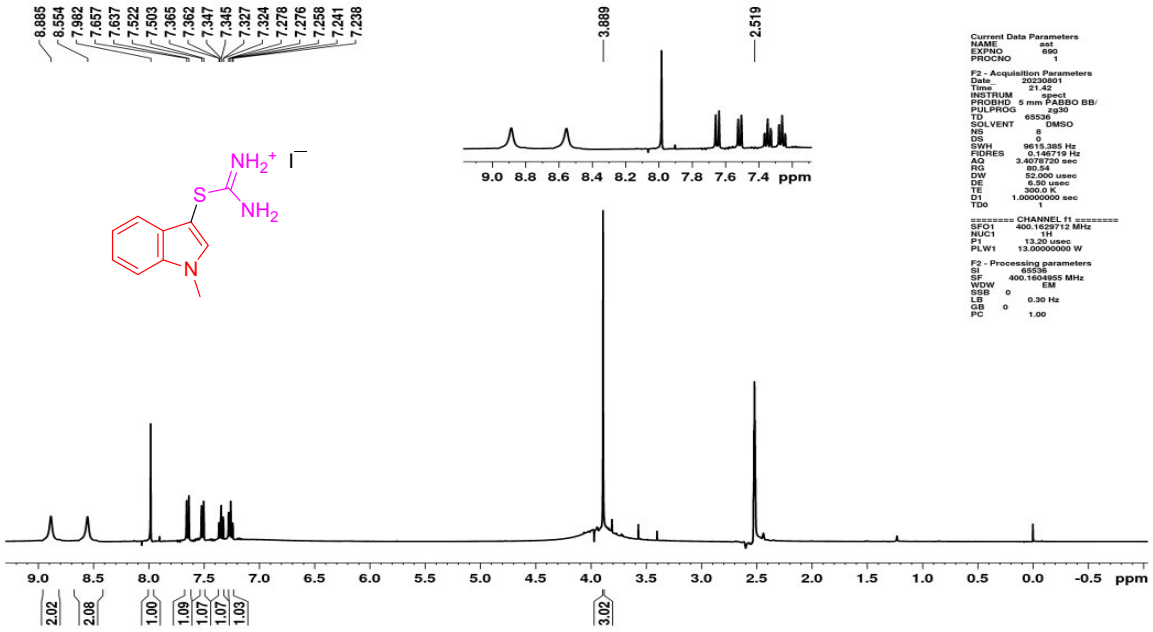
^{1}H NMR spectrum of compound- 1a (400 Mz, $CDCl_3$)



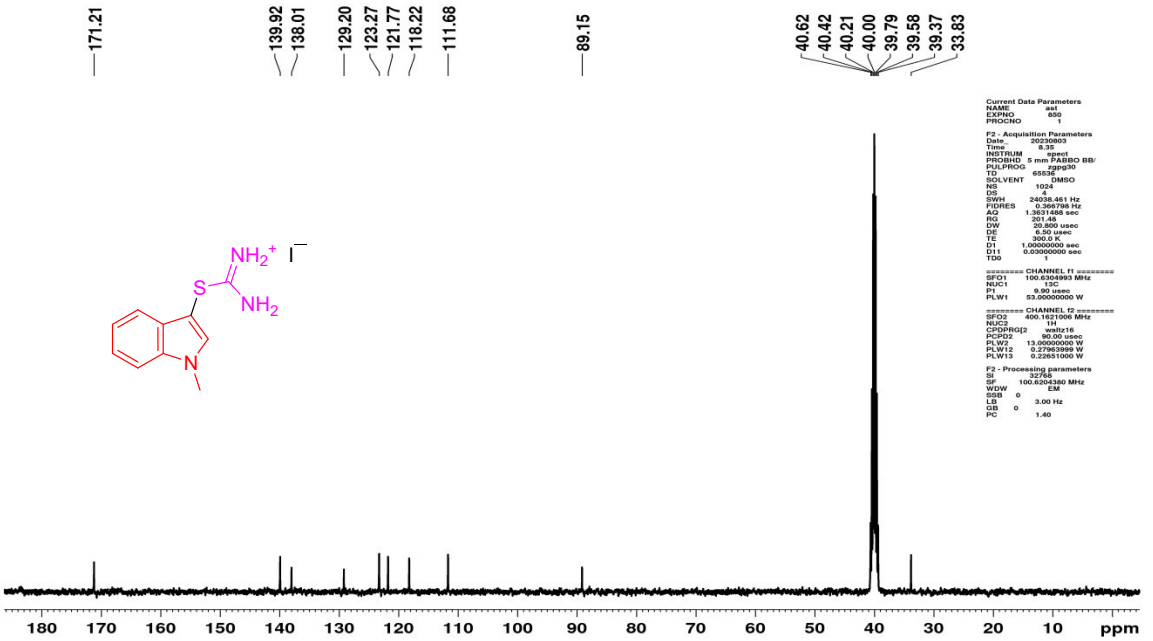
^{13}C NMR spectrum of compound- 1a (100 Mz, $CDCl_3$)



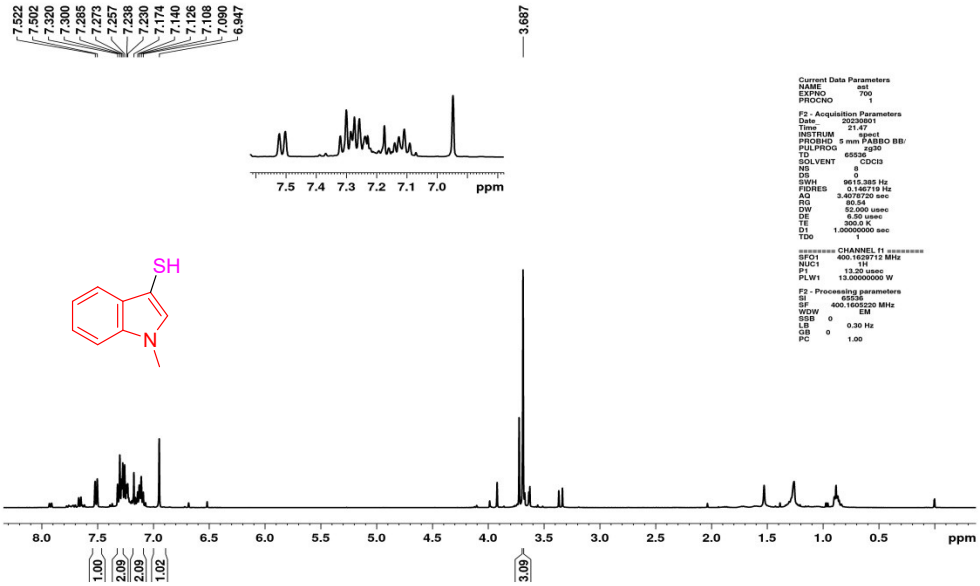
^{1}H NMR spectrum of intermediate compound- I (400 Mz, DMSO-d^{6})



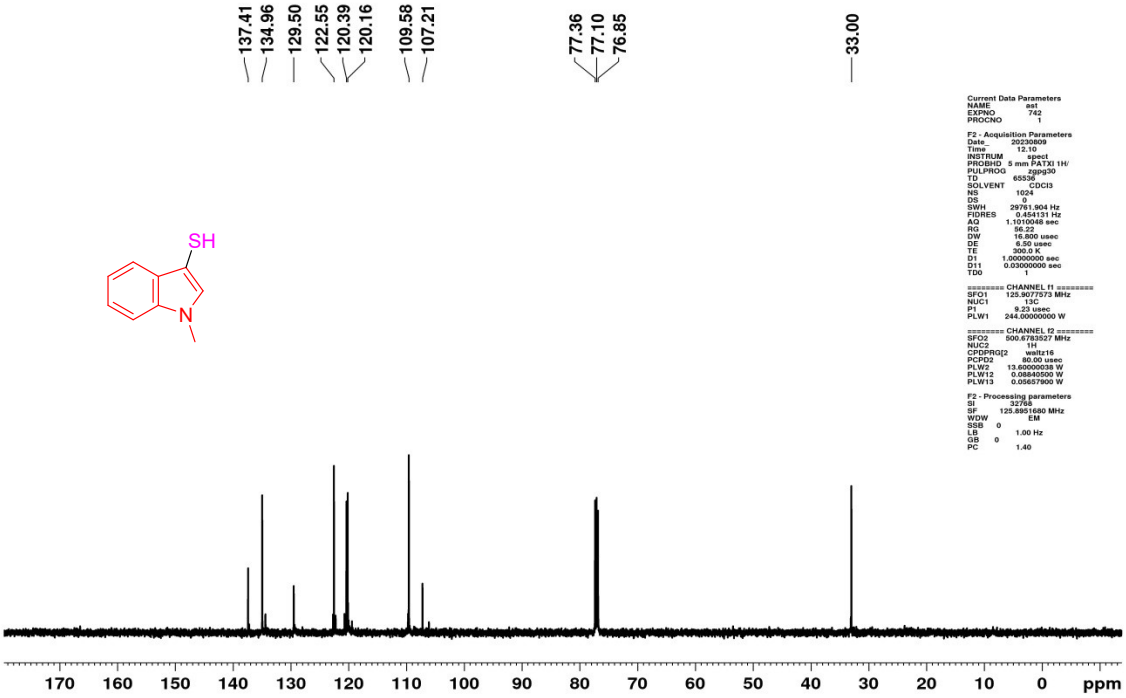
^{13}C NMR spectrum of intermediate compound- I (100 Mz, DMSO-d^{6})



^{1}H NMR spectrum of intermediate compound- II (400 Mz, $CDCl_3$)

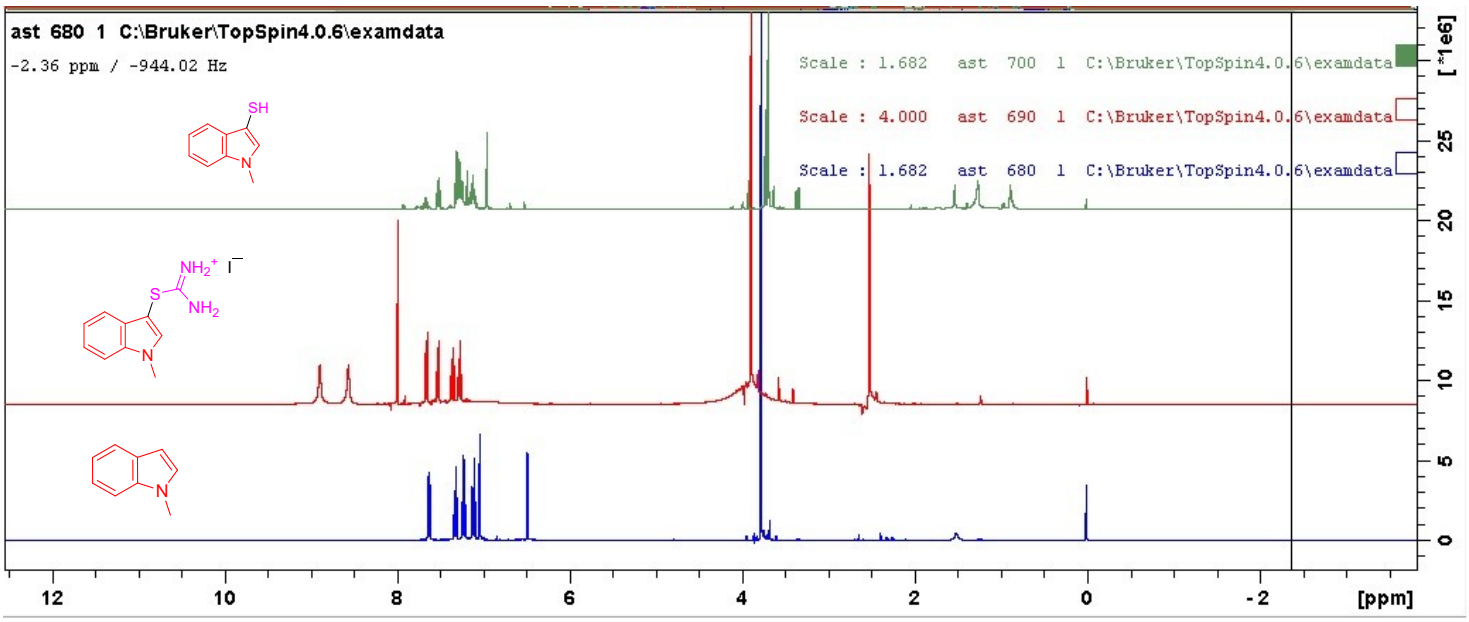


^{13}C NMR spectrum of intermediate compound- II (100 Mz, $CDCl_3$)

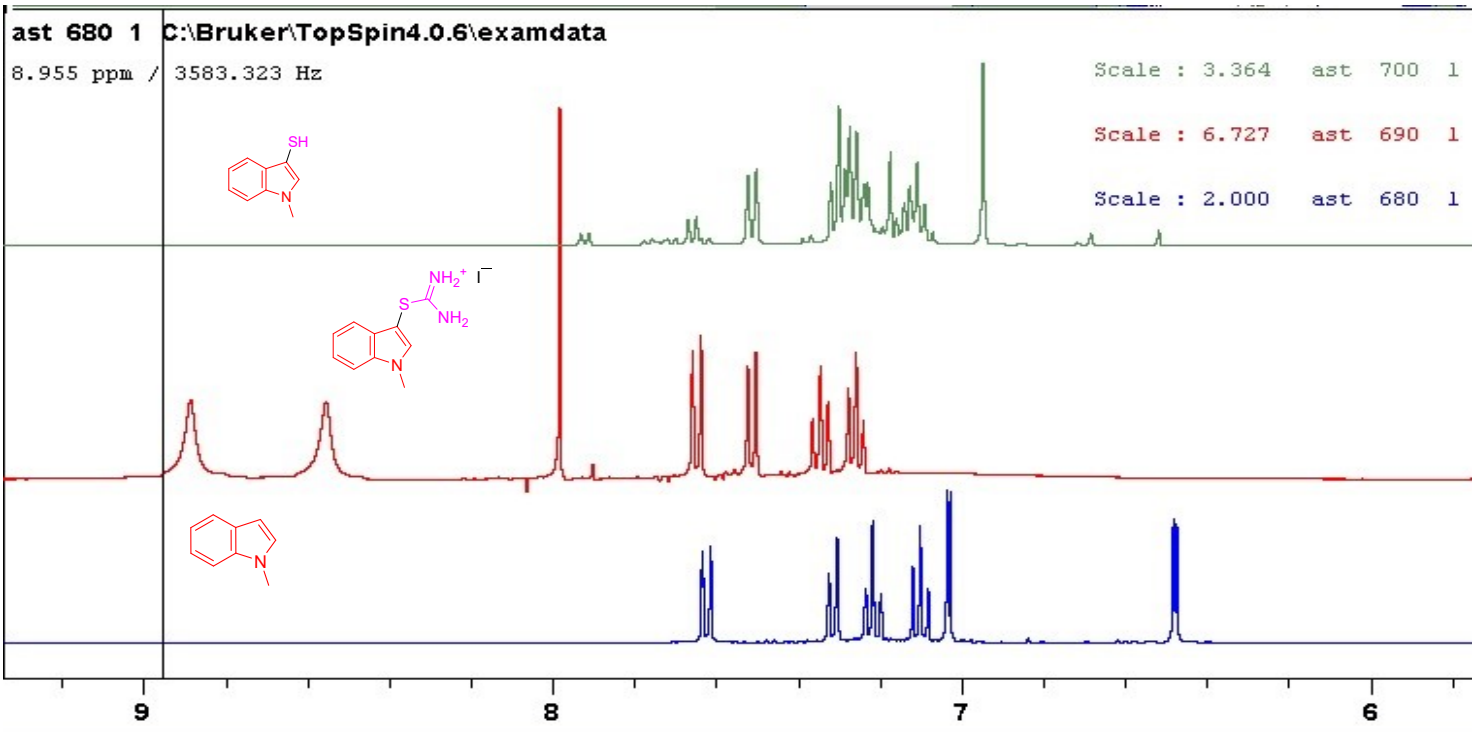


4. Comparative data of mechanistic study

^{1}H NMR spectrum of 1a, intermediate compound I and II



^{1}H NMR spectrum of 1a, intermediate compound I and II (expanded spectra)



5. Antimicrobial activity data

Material and Methods

Growth media, reagents and bacterial strains

All bacterial media and supplements including Mueller–Hinton cation supplemented broth II (MHBII) and Mueller–Hinton agar (MHA) were purchased from Becton-Dickinson (Franklin Lakes, NJ, USA). All other chemicals and antibiotics were procured from Sigma-Aldrich (St. Louis, MO, USA). While performing the experiments all the relevant guidelines and regulations were followed. All the synthesized compounds were primarily screened by following Clinical and Laboratory Standard Institute (CLSI) guidelines[1], against *E. coli* ATCC 25922, *S. aureus* ATCC 29213, *K. pneumoniae* BAA 1705, *A. baumannii* BAA-1605 and *P. aeruginosa* ATCC 27853. The further screening includes drug-resistant clinical strains of *S. aureus* including those resistant to vancomycin and other clinically utilized antibiotics. These strains were procured from Biodefense and Emerging Infections Research Resources Repository/Network on Antimicrobial Resistance in *Staphylococcus aureus*/American Type Culture Collection (BEI/NARSA/ATCC, USA), and routinely cultivated on MHA and MHBII. To obtain the starter culture, a single colony was picked from MHA plate, inoculated in MHBII, and incubated overnight at 37°C with shaking for 18–24h.

Cell cytotoxicity against Vero cells (ATCC CCL-81)

3am was tested for cytotoxicity against Vero cells using MTT assay as described earlier[2]. ~10^3 cells/well were seeded in 96 well plate and incubated at 37°C with 5% CO_2 atmosphere. After 24 h, compound was added ranging from 100–5 mg/L and incubated for 72 h at 37°C. After the incubation was over, MTT was added at 5 mg/L in each well, incubated at 37°C for further 4 hours, residual medium was discarded, 0.1 mL of DMSO was added to solubilize the formazan crystals and OD_{540} for the calculation of CC_{50}. CC_{50} is defined as the lowest concentration of compound, which leads to a 50% reduction in cell viability. Doxorubicin was used as positive control and each experiment was repeated in triplicate.

Tables:

Table1: MIC values (mg/L)of synthesized compounds against gram-positive and gram-negative pathogen.

S. No	compounds	*Escherichia coli* ATCC 25922	*S. aureus* ATCC 29213	*K. pneumoniae* BAA-1705	*A. baumannii* BAA-1605	*P. aeruginosa* ATCC 25923
1	**3aa**	>64	>64	>64	>64	>64
2	**3ab**	>64	>64	>64	>64	>64
3	**3ac**	>64	>64	>64	>64	>64
4	**3ad**	>64	>64	>64	>64	>64
5	**3ae**	>64	>64	>64	>64	>64
6	**3af**	>64	>64	>64	>64	>64
7	**3ag**	>64	>64	>64	>64	>64
8	**3de**	>64	>64	>64	>64	>64
9	**3ei**	>64	>64	>64	>64	>64
10	**3dg**	>64	>64	>64	>64	>64
11	**3dl**	>64	>64	>64	>64	>64
12	**3al**	>64	>64	>64	>64	>64
13	**3am**	>64	2	>64	>64	>64
14	**Levofloxacin**	0.0156	0.25	64	8	1

Table 2: MIC (mg/L) of 3al against clinical MDR MRSA and VRSA isolates

Organisms		3am	Levofloxacin	Meropenem	Vancomycin
MSSA	ATCC 29213	2	0.25	0.125	1
MRSA	NRS 100	4	0.25	32	2
	NRS 119	4	16	64	2
	NRS 129	2	0.25	8	1
VRSA	VRS 1	4	32	64	>64

Table 3: Cytotoxicity profile and selectivity Index of **3al** against Vero cells (ATCC CCL-81)

Compound	MIC (mg/L)	SI (CC_{50}/MIC)
3am	2	>100

References:

1. Wayne, P., Clinical and Laboratory Standards Institute: Performance standards for antimicrobial susceptibility testing: 20th informational supplement. *CLSI document M100-S21* **2012**.
2. 2.Twentyman, P. R.; Luscombe, M., A study of some variables in a tetrazolium dye (MTT) based assay for cell growth and chemosensitivity. *British journal of cancer* **1987,***56* (3), 279-285.