Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting information

Regioselective 1,2-Carbosulfenylation of Unactivated Alkenes via Directed Nickel Catalysis

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1. General remarks

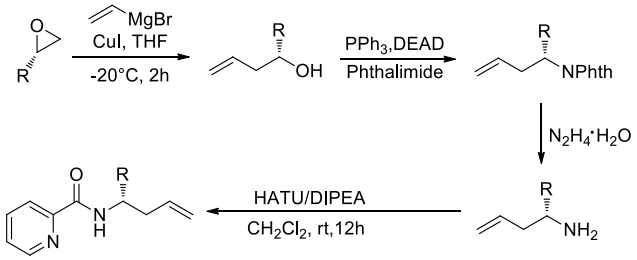
All the manipulations were performed in an argon-filled glovebox, unless mentioned otherwise. Anhydrous solvent was purchased from commercial sources and transferred under argon atmosphere. Alkene substrates and Amine benzoate substrates were prepared according to previously reported procedures, all arylboronic acids were purchased from commercial sources and used without further purification. All reagents were purchased from Energy Chemicals and used as received.

^{1}H NMR, ^{13}C NMR spectra were recorded using Bruker 400 MHz NMR spectrometer. ^{1}H NMR and ^{13}C NMR spectra were referenced to resonances of the residual protons in the deuterated solvents. Multiplicities are recorded as: s = singlet, d = doublet, t = triplet, m = doublet of doublets, br = broad singlet and m = multiplet. GC-MS analysis was performed on Shimadzu GC-2010 gas chromatography coupled to a Shimadzu QP2010 mass selective detector. Analytical HPLC/MS was performed with an Agilent 6520 Series HPLC. Agilent 1200 Series HPLC. High-pressure liquid chromatography (HPLC) was performed on Shimadzu Essentia LC-16 Series chromatographs using a chiral column (25 cm) as noted for each compound.

2. Alkene substrate synthesis

Picolinamide-containing alkene substrates were synthesized according to the literature.[1]

Synthesis of substrates bearing a α-chiral center:



To a 100 mL schlenk flask was added CuI (5 mmol, 0.1 eq, 2.0 M in THF), anhydrous THF (10 mL) under Ar atmosphere. The resulting solution was submerged in a -20 °C dry ice bath. A solution of vinyl magnesium bromide (75 mmol, 1.5 eq, 1.0 M in THF) was added dropwise over 10 min, and a solution of chiral ethylene oxide (50 mmol, 1 eq) in 10 mL THF was added dropwise

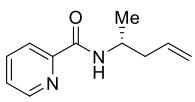
over 5 min. After 2 h at this temperature, The aqueous layer was transferred to a separatory funnel and washed with Et_2O (50 mL × 2) before being charged back into the schlenk flask. Hydrochloric acid was added dropwise into the vigorously stirring solution at 0 °C until pH = 3. The milky solution was then extracted with EtOAc (100 mL × 2). The combined organic extracts were washed with brine (50 mL), dried over Na_2SO_4, concentrated, and carried forward to the next step without further purification.[2]

To a mixture of triphenylphosphine (50 mmol, 1.0 eq), phthalimide (50 mmol, 1.0 eq) and the corresponding allyl alcohol (50 mmol, 1.0 eq) in THF (60 mL) was slowly added diethyl azodicarboxylate (DEAD) (50 mmol, 1.0 eq) at 0 °C. The mixture was stirred at 0 ºC for 12 h. After the completion of the reaction, the reaction mixture was diluted with *n*-hexane and filtered. The filtrate was dried over Na_2SO_4 and concentrated in vacuo to give the crude product, which was used without further purification.

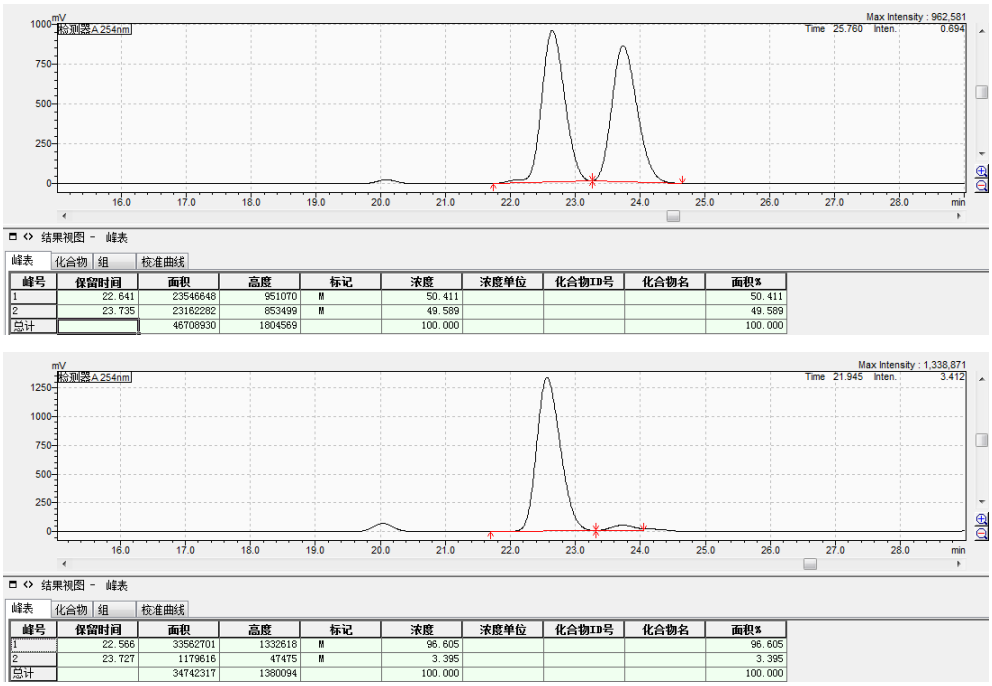
To the solution of phthalimide product in ethanol (100 mL) was added hydrazine monohydrate (50 mmol) at 50 ºC. The mixture was stirred for 1 h and quenched with 6 M HCl (40 mL). The precipitates formed were removed by filtration, and the resultant filtrate was dried over Na_2SO_4 and concentrated in vacuo to give an unsaturated amine hydrochloride. Aqueous NaOH (6.0 M, 20 mL) was added to the amine salt, and the resulting solution was extracted with CH_2Cl_2 (50 mL × 3). The combined organic extracts was then washed again with brine (20 mL), dried over Na_2SO_4, and filtered. The amine solution was used without further purification.

To the solution of amine (100 mmol, 1.0 eq) was successively added picolinic acid (120 mmol, 1.2 eq), HATU (110 mmol, 1.1 eq) and DIPEA (100 mmol, 2.0 eq). The resultant mixture was stirred at room temperature overnight. Water was added and the mixture was extracted with CH_2Cl_2 (50 mL × 3). The combined organic layers were washed with water and brine, dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The resulting residue was purified by silica gel flash chromatography (ethyl acetate:hexanes = 1:8) to give the desired product.

(R)-N-(pent-4-en-2-yl)picolinamide **(1b)**

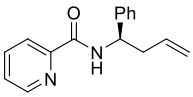


HPLC analysis (OD-H, nHexane: i-Propanol = 95:5 as eluent, 0.3 mL/min, 254 nm) indicated 93% ee: tR (minor) = 23.7 min, tR (major) = 22.6 min.

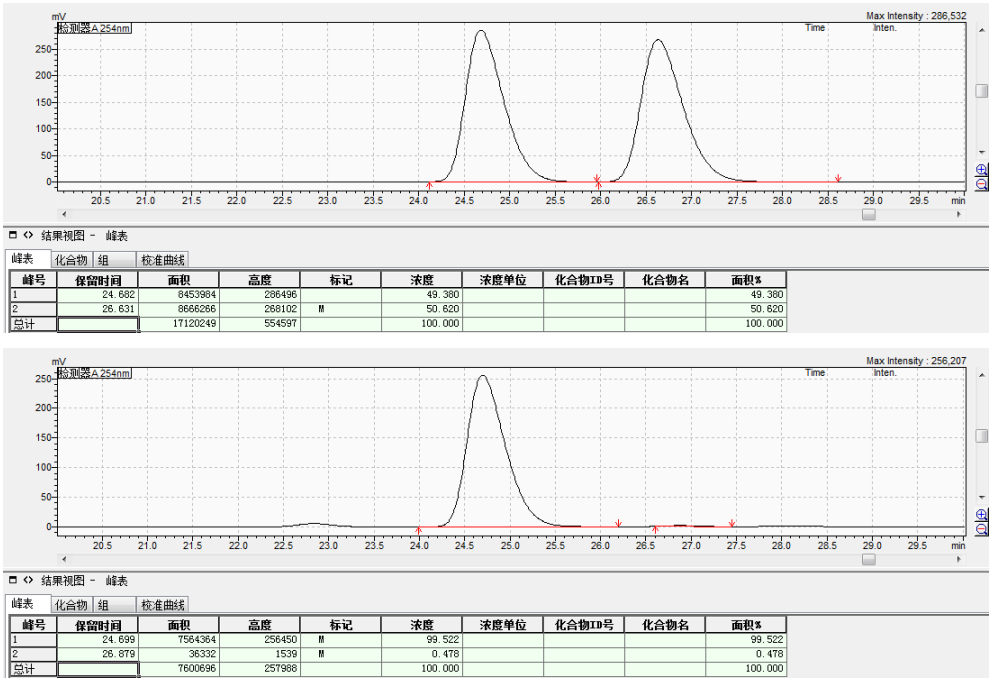


Supplementary Figure 1. HPLC spectra for **1b**

***(R)-N-(1-phenylbut-3-en-1-yl)picolinamide* (1c)**



HPLC analysis (OD-H, nHexane: i-Propanol = 95:5 as eluent, 0.4 mL/min, 254 nm) indicated 99% ee: tR (minor) = 26.9 min, tR (major) = 24.7 min.

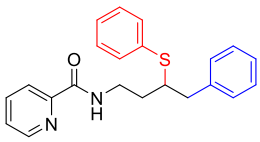


Supplementary Figure 2. HPLC spectra for **1c**

3. Procedure for the Ni-catalyzed 1,2-carbosulfenylation of unactivated alkenes

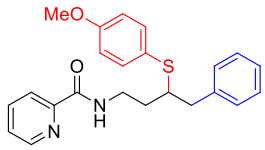
In an argon-filled glovebox, $NiBr_2$•DME (0.04 mmol, 20 mol%), K_3PO_4 (0.6 mmol, 3.0 eq), alkene substrate (0.2 mmol, 1.0 eq), appropriate arylboronic acid (0.3 mmol, 1.5 eq), appropriate phenyl disulfide (0.5 mmol, 2.5 eq), DMF/MeOH (1 mL /0.5 mL) were added to a 10 mL schlenk flask. The reaction mixture was stirred at 100 °C for 18 h. After the reaction time, the vessel was allowed to silica gel column chromatography. The crude product was purified by column chromatography on silica gel with a mixture of ethyl acetate and petroleum ether as eluent. The conditions for flash chromatography and data for characterization of the products are listed below.

***N-(4-phenyl-3-(phenylthio)butyl)picolinamide* (2a)**



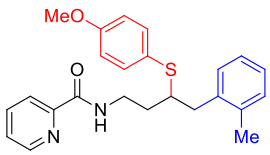
The title compound was isolated as a yellow oil (87% yield) after chromatography on silica with ethyl acetate/hexane (1:12). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (s, 1H), 8.16 (d, *J* = 7.9 Hz, 1H), 8.10 (d, *J* = 5.9 Hz, 1H), 7.77 (d, *J* = 8.2 Hz, 1H), 7.41 (d, *J* = 7.5 Hz, 2H), 7.34 (s, 1H), 7.27–7.13 (m, 8H), 3.75 (m, 1H), 3.59 (m, 1H), 3.41 (m, 1H), 2.99 (m, 1H), 2.85 (m, 1H), 1.98 (m, 1H), 1.78 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.3, 149.9, 148.0, 138.8, 137.4, 134.7, 132.5, 129.3, 129.0, 128.4, 127.2, 126.5, 126.1, 122.2, 48.6, 41.7, 37.3, 33. 7. HRMS (ESI) m/z calculated for $C_{22}H_{23}N_2OS$ $[M+H]^+$ 363.1526, found: 363.1526.

***N-(3-((4-methoxyphenyl)thio)-4-phenylbutyl)picolinamide* (2b)**



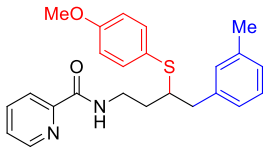
The title compound was isolated as a yellow oil (85% yield) after chromatography on silica with ethyl acetate/hexane (1:10). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, *J* = 4.7 Hz, 1H), 8.18 (d, *J* = 7.8 Hz, 1H), 8.08 (s, 1H), 7.83 (t, *J* = 7.7 Hz, 1H), 7.42 (m, 3H), 7.26 (m, 3H), 7.10 (d, *J* = 8.0 Hz, 2H), 6.80 (d, *J* = 7.9 Hz, 2H), 3.79–3.70 (m, 4H), 3.58 (m, 1H), 3.41–3.32 (m, 1H), 2.95 (m, 1H), 2.81 (m, 1H), 2.04–1.95 (m, 1H), 1.81–1.74 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.2, 158.2, 149.9, 148.0, 137.3, 134.8, 132.3, 130.8, 130.2, 128.9, 127.0, 126.1, 122.1, 113.8, 55.2, 48.7, 40.6, 37.2, 33.5. HRMS (ESI) m/z calculated for $C_{23}H_{25}N_2O_2S$ $[M+H]^+$ 393.1631, found: 393.1642.

***N-(3-((4-methoxyphenyl)thio)-4-(o-tolyl)butyl)picolinamide* (2c)**



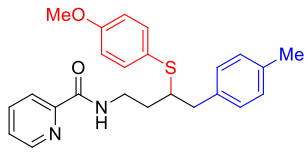
The title compound was isolated as a yellow oil (77% yield) after chromatography on silica with ethyl acetate/hexane (1:10). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (d, *J* = 4.5 Hz, 1H), 8.09 (d, *J* = 7.8 Hz, 1H), 8.00 (s, 1H), 7.74 (m, 1H), 7.35–7.30 (m, 3H), 7.04–6.97 (m, 4H), 6.77–6.73 (m, 2H), 3.72–3.65 (m, 4H), 3.52 (m, 1H), 3.08 (m, 1H), 2.94 (m, 1H), 2.68 (m, 1H), 2.07 (s, 3H), 1.90–1.81 (m, 1H), 1.73–1.62 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.2, 159.7, 150.0, 148.0, 137.3, 136.3, 136.2, 130.4, 130.1, 126.6, 126.1, 125.8, 124.5, 122.2, 114.5, 55.4, 49.0, 39.6, 37.5, 33.5, 19.4. HRMS (ESI) m/z calculated for $C_{24}H_{27}N_2O_2S$ $[M+H]^+$ 407.1788, found: 407.1790.

***N-(3-((4-methoxyphenyl)thio)-4-(m-tolyl)butyl)picolinamide* (2d)**



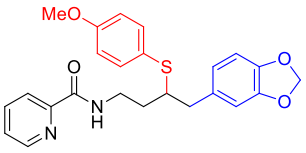
The title compound was isolated as a yellow oil (82% yield) after chromatography on silica with ethyl acetate/hexane (1:10). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (d, *J* = 4.5 Hz, 1H), 8.10 (d, *J* = 7.8 Hz, 1H), 8.00 (s, 1H), 7.75 (m, 1H), 7.36–7.30 (m, 3H), 7.06 (t, *J* = 7.8 Hz, 1H), 6.92 (d, *J* = 7.6 Hz, 1H), 6.89–6.83 (m, 2H), 6.79–6.72 (m, 2H), 3.72 (m, 4H), 3.53 (m, 1H), 3.13 (m, 1H), 2.89 (m, 1H), 2.65 (m, 1H), 2.21 (s, 3H), 1.84–1.79 (m, 1H), 1.65 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.3, 159.6, 150.0, 148.0, 139.0, 137.9, 137.3, 136.0, 130.0, 128.3, 127.2, 126.3, 126.1, 124.4, 122.2, 114.6, 55.4, 49.6, 41.7, 37.4, 33.3, 21.5. HRMS (ESI) m/z calculated for $C_{24}H_{27}N_2O_2S$ $[M+H]^+$ 407.1788, found: 407.1787.

***N-(3-((4-methoxyphenyl)thio)-4-(p-tolyl)butyl)picolinamide* (2e)**



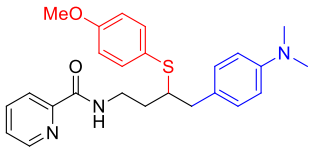
The title compound was isolated as a yellow oil (85% yield) after chromatography on silica with ethyl acetate/hexane (1:10). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (d, *J* = 4.7 Hz, 1H), 8.09 (d, *J* = 7.8 Hz, 1H), 7.99 (s, 1H), 7.74 (m, 1H), 7.36–7.30 (m, 3H), 7.01–6.94 (m, 4H), 6.75 (d, *J* = 8.6 Hz, 2H), 3.71 (s, 4H), 3.52 (m, 1H), 3.17–3.05 (m, 1H), 2.87 (m, 1H), 2.66 (m, 1H), 2.22 (s, 3H), 1.88–1.80 (m, 1H), 1.69–1.59 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.2, 159.6, 150.0, 148.0, 137.3, 135.9, 135.9, 129.1, 129.1, 126.1, 124.5, 122.2, 114.6, 114.5, 55.3, 49.7, 41.2, 37.4, 33.3, 21.1. HRMS (ESI) m/z calculated for $C_{24}H_{27}N_2O_2S$ $[M+H]^+$ 407.1788, found: 407.1780.

***N-(4-(2,3-dihydrobenzofuran-5-yl)-3-((4-methoxyphenyl)thio)butyl)picolinamide* (2f)**



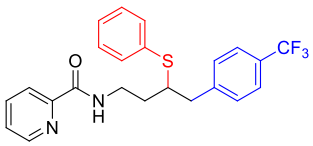
The title compound was isolated as a brown oil (70% yield) after chromatography on silica with ethyl acetate/hexane (1:8). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47–8.41 (m, 1H), 8.10 (d, *J* = 7.8 Hz, 1H), 8.01 (s, 1H), 7.75 (m, 1H), 7.35–7.30 (m, 3H), 6.78–6.73 (m, 2H), 6.61 (d, *J* = 7.9 Hz, 1H), 6.57–6.49 (m, 2H), 5.82 (s, 2H), 3.72–3.64 (m, 4H), 3.53 (m, 1H), 3.07 (m, 1H), 2.80 (m, 1H), 2.62 (m, 1H), 1.85–1.82 (m, 1H), 1.68–1.59 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.3, 159.6, 149.8, 148.0, 147.7, 137.7, 137.3, 135.8, 130.6, 126.1, 124.2, 122.1, 121.7, 120.8, 114.5, 55.3, 49.7, 40.9, 37.2, 33.7. HRMS (ESI) m/z calculated for $C_{24}H_{25}N_2O_4S$ $[M+H]^+$ 437.1530, found: 437.1532.

***N-(4-(4-(dimethylamino)phenyl)-3-((4-methoxyphenyl)thio)butyl)picolinamide* (2g)**



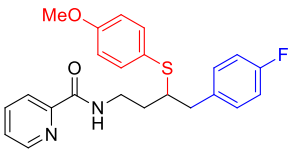
The title compound was isolated as a dark brown oil (69% yield) after chromatography on silica with ethyl acetate/hexane (1:6). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (d, *J* = 4.7 Hz, 1H), 8.09 (d, *J* = 7.8 Hz, 1H), 7.99 (s, 1H), 7.76–7.70 (m, 1H), 7.36–7.28 (m, 3H), 6.94 (d, *J* = 8.6 Hz, 2H), 6.77–6.73 (m, 2H), 6.57 (d, *J* = 8.6 Hz, 2H), 3.70 (m, 4H), 3.52 (m, 1H), 3.09 (m, 1H), 2.85 (s, 1H), 2.81 (s, 6H), 2.60 (m, 1H), 1.87–1.79 (m, 1H), 1.64 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.2, 159.4, 150.0, 149.3, 148.0, 137.3, 135.8, 129.9, 126.9, 126.0, 124.7, 122.1, 114.5, 112.7, 55.3, 49.9, 40.7, 40.7, 37.4, 33.2. HRMS (ESI) m/z calculated for $C_{25}H_{30}N_3O_2S$ $[M+H]^+$ 436.2053, found: 436.2055.

***N-(3-(phenylthio)-4-(4-(trifluoromethyl)phenyl)butyl)picolinamide* (2h)**



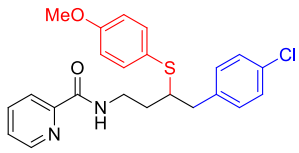
The title compound was isolated as a colorless oil (52% yield) after chromatography on silica with ethyl acetate/hexane (1:12). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, *J* = 4.7 Hz, 1H), 8.19 (d, *J* = 7.7 Hz, 1H), 8.10 (s, 1H), 7.85 (t, *J* = 7.6 Hz, 1H), 7.50 (d, *J* = 7.9 Hz, 2H), 7.46–7.35 (m, 3H), 7.30–7.26 (m, 5H), 3.79 (m, 1H), 3.63 (m, 1H), 3.45–3.37 (m, 1H), 3.05–2.92 (m, 2H), 1.99 (m, 1H), 1.80 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.4, 149.8, 148.0, 142.8, 137.4, 134.3, 132.5, 129.6, 129.0, 127.3, 126.2, 125.6, 125.2, 125.2, 122.2, 48.3, 41.3, 37.1, 33.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.40. HRMS (ESI) m/z calculated for $C_{23}H_{22}F_3N_2OS$ $[M+H]^+$ 431.1399, found: 431.1392.

***N-(4-(4-fluorophenyl)-3-((4-methoxyphenyl)thio)butyl)picolinamide* (2i)**



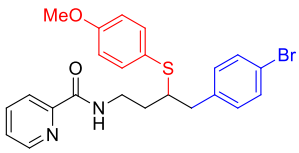
The title compound was isolated as a yellow oil (65% yield) after chromatography on silica with ethyl acetate/hexane (1:10). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, *J* = 4.8 Hz, 1H), 8.18 (d, *J* = 7.8 Hz, 1H), 8.09 (s, 1H), 7.83 (d, *J* = 7.9 Hz, 1H), 7.39 (m, 3H), 7.13–7.09 (m, 2H), 6.93 (t, *J* = 8.0 Hz, 2H), 6.83 (d, *J* = 7.7 Hz, 2H), 3.81–3.72 (m, 4H), 3.62 (m, 1H), 3.16 (m, 1H), 2.92 (m, 1H), 2.78 (m, 1H), 1.93 (m, 1H), 1.79–1.71 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.2, 162.8, 160.3, 159.6, 149.9, 147.9, 137.3, 135.8, 134.7, 130.7, 130.6, 126.0, 124.4, 122.1, 115.2, 115.0, 114.6, 55.3, 49.8, 40.8, 37.3, 33.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -116.74. HRMS (ESI) m/z calculated for $C_{23}H_{24}FN_2O_2S$ $[M+H]^+$ 411.1537, found: 411.1535.

***N*-(4-(4-chlorophenyl)-3-((4-methoxyphenyl)thio)butyl)picolinamide (2j)**



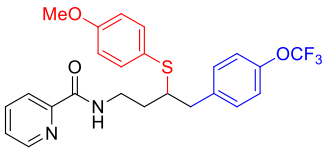
The title compound was isolated as a yellow oil (42% yield) after chromatography on silica with ethyl acetate/hexane (1:10). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (d, *J* = 4.2 Hz, 1H), 8.10 (d, *J* = 7.8 Hz, 1H), 8.01 (s, 1H), 7.77 (m, 1H), 7.37–7.28 (m, 3H), 7.14 (d, *J* = 8.4 Hz, 2H), 7.01 (d, *J* = 8.4 Hz, 2H), 6.78–6.73 (m, 2H), 3.72 (m, 4H), 3.54 (m, 1H), 3.14–3.04 (m, 1H), 2.84 (m, 1H), 2.70 (m, 1H), 1.87–1.78 (m, 1H), 1.67 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.3, 159.6, 149.8, 148.0, 137.4, 137.3, 135.9, 132.2, 130.6, 128.4, 126.1, 124.2, 122.1, 114.6, 55.3, 49.5, 40.9, 37.3, 33.5. HRMS (ESI) m/z calculated for $C_{23}H_{24}ClN_2O_2S$ $[M+H]^+$ 427.1242, found: 427.1243.

***N*-(4-(4-bromophenyl)-3-((4-methoxyphenyl)thio)butyl)picolinamide (2k)**



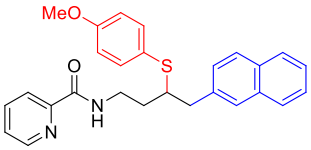
The title compound was isolated as a yellow oil (36% yield) after chromatography on silica with ethyl acetate/hexane (1:10). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (d, *J* = 4.0 Hz, 1H), 8.10 (d, *J* = 7.6 Hz, 1H), 8.04 (s, 1H), 7.77 (t, *J* = 7.6 Hz, 1H), 7.36–7.33 (m, 1H), 7.31–7.26 (m, 4H), 6.94 (d, *J* = 7.9 Hz, 2H), 6.75 (d, *J* = 8.2 Hz, 2H), 3.72 (m, 4H), 3.52 (m, 1H), 3.08 (m, 1H), 2.81 (m, 1H), 2.68 (m, 1H), 1.82 (m, 1H), 1.65 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.6, 148.6, 147.0, 136.9, 136.3, 134.8, 134.7, 130.3, 129.9, 125.1, 123.1, 121.1, 119.2, 113.5, 54.3, 48.4, 40.0, 36.3, 32.4. HRMS (ESI) m/z calculated for $C_{23}H_{24}BrN_2O_2S$ $[M+H]^+$ 471.0736, found: 471.0745.

***N*-(3-((4-methoxyphenyl)thio)-4-(4-(trifluoromethoxy)phenyl)butyl)picolinamide (2l)**



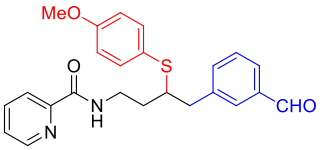
The title compound was isolated as a yellow oil (45% yield) after chromatography on silica with ethyl acetate/hexane (1:10). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (d, J = 4.4 Hz, 1H), 8.11 (d, J = 7.7 Hz, 1H), 8.02 (s, 1H), 7.77 (m, 1H), 7.35 (m, 1H), 7.28 (d, J = 8.7 Hz, 2H), 7.10 (d, J = 8.6 Hz, 2H), 7.02 (d, J = 8.2 Hz, 2H), 6.75 (d, J = 8.7 Hz, 2H), 3.72 (m, 4H), 3.55 (m, 1H), 3.09 (m, 1H), 2.86 (m, 1H), 2.76 (m, 1H), 1.90–1.81 (m, 1H), 1.70 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.3, 159.6, 149.8, 148.0, 147.7, 137.7, 137.3, 135.8, 130.6, 126.1, 124.2, 122.1, 121.7, 120.8, 114.5, 55.3, 49.7, 40.9, 37.2, 33.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -57.84. HRMS (ESI) m/z calculated for $C_{24}H_{24}F_3N_2O_3S$ $[M+H]^+$ 477.1454, found: 477.1455.

N-(3-((4-methoxyphenyl)thio)-4-(naphthalen-2-yl)butyl)picolinamide **(2m)**



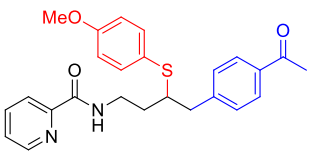
The title compound was isolated as a red oil (42% yield) after chromatography on silica with ethyl acetate/hexane (1:6). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (d, *J* = 4.5 Hz, 1H), 8.16 (d, *J* = 7.8 Hz, 1H), 8.07 (s, 1H), 7.82–7.71 (m, 4H), 7.59 (s, 1H), 7.41 (m, 5H), 7.27 (m, 1H), 6.85–6.79 (m, 2H), 3.78 (m, 4H), 3.63 (m, 1H), 3.36–3.28 (m, 1H), 3.15 (m, 1H), 2.95 (m, 1H), 1.95 (m, 1H), 1.82–1.76 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.3, 159.6, 149.8, 148.0, 137.3, 136.5, 136.0, 133.4, 132.2, 128.0, 127.8, 127.6, 127.5, 126.1, 125.9, 125.4, 124.3, 122.1, 114.6, 114.5, 55.3, 49.5, 41.9, 37.4, 33.4. HRMS (ESI) m/z calculated for $C_{27}H_{27}N_2O_2S$ $[M+H]^+$ 443.1788, found:443.1788.

N-(4-(3-formylphenyl)-3-((4-methoxyphenyl)thio)butyl)picolinamide **(2n)**



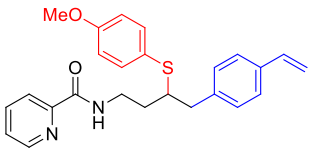
The title compound was isolated as a yellow oil (65% yield) after chromatography on silica with ethyl acetate/hexane (1:6). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.88 (s, 1H), 8.45 (d, *J* = 4.6 Hz, 1H), 8.10 (d, *J* = 7.8 Hz, 1H), 8.03 (s, 1H), 7.77 (m, 1H), 7.64 (m, 1H), 7.59 (s, 1H), 7.38–7.33 (m, 3H), 7.32–7.28 (m, 2H), 6.76 (d, *J* = 8.7 Hz, 2H), 3.72 (m, 4H), 3.59–3.50 (m, 1H), 3.20–3.13 (m, 1H), 2.94 (m, 1H), 2.84 (m, 1H), 1.89–1.80 (m, 1H), 1.71–1.68 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.4, 164.3, 159.7, 149.8, 148.0, 140.1, 137.3, 136.5, 135.9, 135.5, 130.3, 129.0, 128.0, 126.1, 124.0, 122.1, 114.6, 55.3, 49.3, 41.2, 37.2, 33.7. HRMS (ESI) m/z calculated for $C_{24}H_{25}N_2O_3S$ $[M+H]^+$ 421.1580, found: 421.1580.

N-(4-(4-acetylphenyl)-3-((4-methoxyphenyl)thio)butyl)picolinamide **(2o)**



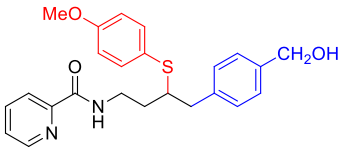
The title compound was isolated as a yellow oil (42% yield) after chromatography on silica with ethyl acetate/hexane (1:6). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, *J* = 4.4 Hz, 1H), 8.18 (d, *J* = 7.8 Hz, 1H), 8.08 (s, 1H), 7.84 (t, *J* = 7.3 Hz, 3H), 7.44–7.37 (m, 3H), 7.25 (d, *J* = 8.6 Hz, 2H), 6.83 (d, *J* = 8.7 Hz, 2H), 3.80 (m, 4H), 3.65–3.58 (m, 1H), 3.28–3.17 (m, 1H), 3.00 (m, 1H), 2.88 (m, 1H), 2.57 (s, 3H), 1.92 (m, 1H), 1.77 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.8, 164.3, 159.7, 149.8, 148.0, 144.8, 137.3, 136.0, 135.4, 129.5, 128.5, 126.1, 124.0, 122.1, 114.6, 55.3, 49.2, 41.5, 37.2, 33.6, 26.6. HRMS (ESI) m/z calculated for $C_{25}H_{27}N_2O_3S$ $[M+H]^+$ 435.1737, found: 435.1750.

***N-(3-((4-methoxyphenyl)thio)-4-(4-vinylphenyl)butyl)picolinamide* (2p)**



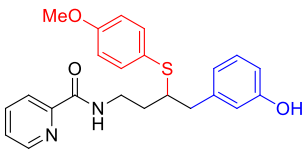
The title compound was isolated as a yellow oil (54% yield) after chromatography on silica with ethyl acetate/hexane (1:8). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (d, *J* = 4.5 Hz, 1H), 8.10 (d, *J* = 7.8 Hz, 1H), 8.01 (s, 1H), 7.77 (t, *J* = 7.6 Hz, 1H), 7.33 (m, 3H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.04 (d, *J* = 7.9 Hz, 2H), 6.77–6.75 (m, 2H), 6.60 (m, 1H), 5.62 (d, *J* = 17.6 Hz, 1H), 5.13 (d, *J* = 10.9 Hz, 1H), 3.72 (m, 4H), 3.54 (m, 1H), 3.16–3.10 (m, 1H), 2.89 (m, 1H), 2.70 (m, 1H), 1.84 (m, 1H), 1.67 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.3, 159.6, 149.9, 148.0, 142.7, 140.2, 140.1, 137.3, 135.9, 126.1, 124.2, 122.1, 121.6, 114.5, 111.4, 111.3, 55.3, 48.4, 37.3, 33.4, 30.4. HRMS (ESI) m/z calculated for $C_{25}H_{27}N_2O_2S$ $[M+H]^+$ 419.1788, found: 419.1788.

***N-(3-((4-methoxyphenyl)thio)-4-(4-(trifluoromethoxy)phenyl)butyl)picolinamide* (2q)**



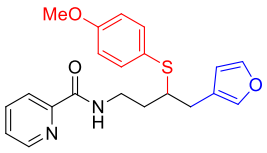
The title compound was isolated as a brown oil (55% yield) after chromatography on silica with ethyl acetate/hexane (1:3). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (d, *J* = 4.1 Hz, 1H), 8.07 (d, *J* = 7.9 Hz, 1H), 8.00 (s, 1H), 7.74 (t, *J* = 7.7 Hz, 1H), 7.35–7.30 (m, 3H), 7.19–7.15 (m, 2H), 7.05 (d, *J* = 7.9 Hz, 2H), 6.76 (d, *J* = 8.6 Hz, 2H), 4.55 (d, *J* = 4.0 Hz, 2H), 3.71 (m, 4H), 3.50 (m, 1H), 3.12 (m, 1H), 2.89 (m, 1H), 2.69 (m, 1H), 2.19–2.09 (m, 1H), 1.82 (m, 1H), 1.64 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.3, 159.6, 149.9, 148.0, 139.1, 138.5, 137.4, 135.9, 129. 5, 127.2, 126.1, 124.3, 122.2, 114.6, 65.2, 55.3, 49.5, 41.4, 37.3, 33.4. HRMS (ESI) m/z calculated for $C_{24}H_{27}N_2O_3S$ $[M+H]^+$ 423.1737, found: 423.1740.

***N-(4-(3-hydroxyphenyl)-3-((4-methoxyphenyl)thio)butyl)picolinamide* (2r)**



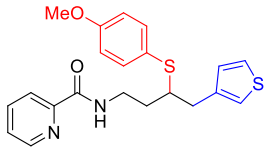
The title compound was isolated as a brown oil (70% yield) after chromatography on silica with ethyl acetate/hexane (1:3). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (d, *J* = 4.4 Hz, 1H), 8.09 (m, 2H), 7.74(m, 1H), 7.33 (m, 3H), 7.01 (t, *J* = 8.1 Hz, 1H), 6.74 (d, *J* = 8.7 Hz, 2H), 6.65 (d, *J* = 6.0 Hz, 2H), 6.57 (d, *J* = 7.5 Hz, 1H), 3.70 (m, 4H), 3.51 (m, 1H), 3.11 (m, 1H), 2.84 (m, 1H), 2.60 (m, 1H), 1.89 (s, 1H), 1.81 (m, 1H), 1.67–1.59 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.6, 159.6, 156.3, 149.6, 148.1, 140.7, 137.5, 135.9, 129.5, 126.3, 124.4, 122.3, 121.2, 116.3, 114.6, 113.6, 55.3, 49.4, 41.4, 37.4, 33.1. HRMS (ESI) m/z calculated for $C_{23}H_{25}N_2O_3S$ $[M+H]^+$ 409.1580, found: 409.1574.

***N-(4-(furan-3-yl)-3-((4-methoxyphenyl)thio)butyl)picolinamide* (2s)**



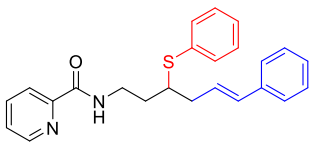
The title compound was isolated as a brown oil (75% yield) after chromatography on silica with ethyl acetate/hexane (1:8). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, *J* = 4.4 Hz, 1H), 8.19 (d, *J* = 7.8 Hz, 1H), 8.11 (s, 1H), 7.84 (t, *J* = 7.7 Hz, 1H), 7.45–7.40 (m, 3H), 7.32 (d, *J* = 14.9 Hz, 2H), 6.84 (d, *J* = 8.6 Hz, 2H), 6.30 (s, 1H), 3.81–3.72 (m, 4H), 3.62 (m, 1H), 3.13 (m, 1H), 2.77 (m, 1H), 2.65 (m, 1H), 1.96 (m, 1H), 1.77–1.72 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.3, 159.6, 149.9, 148.0, 142.8, 140.2, 137.3, 135.9, 126.1, 124.2, 122.1, 121.6, 114.6, 111.4, 55.3, 48.4, 37.3, 33.4, 30.5. HRMS (ESI) m/z calculated for $C_{21}H_{23}N_2O_3S$ $[M+H]^+$ 383.1424, found: 383.1423.

***N-(3-((4-methoxyphenyl)thio)-4-(thiophen-3-yl)butyl)picolinamide* (2t)**



The title compound was isolated as a green oil (68% yield) after chromatography on silica with ethyl acetate/hexane (1:8). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, *J* = 4.3 Hz, 1H), 8.19 (d, *J* = 7.7 Hz, 1H), 8.10 (s, 1H), 7.84 (t, *J* = 7.6 Hz, 1H), 7.41 (d, *J* = 8.5 Hz, 3H), 7.22 (m, 1H), 7.03 (s, 1H), 6.94 (d, *J* = 4.9 Hz, 1H), 6.84 (d, *J* = 8.5 Hz, 2H), 3.80 (m, 4H), 3.63 (m, 1H), 3.20 (m, 1H), 2.98 (m, 1H), 2.85 (m, 1H), 1.93 (m, 1H), 1.75 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.3, 159.6, 149.9, 148.0, 139.1, 137.3, 135.9, 128.5, 126.1, 125.4, 124.3, 122.2, 122.0, 114.5, 55.2, 48.9, 37.3, 35.8, 33.5. HRMS (ESI) m/z calculated for $C_{21}H_{23}N_2O_2S_2$ $[M+H]^+$ 399.1195, found: 399.1204.

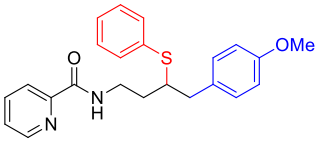
***(E)-N-(6-phenyl-3-(phenylthio)hex-5-en-1-yl)picolinamide* (2u)**



The title compound was isolated as a yellow oil (61% yield) after chromatography on silica with ethyl acetate/hexane (1:12). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (d, *J* = 4.8 Hz, 1H), 8.12 (d, *J* = 7.8 Hz, 1H),

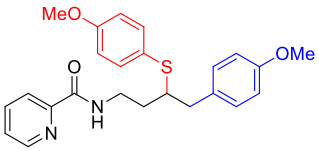
8.08 (s, 1H), 7.77 (m, 1H), 7.47–7.37 (m, 2H), 7.35 (m, 1H), 7.26–7.12 (m, 8H), 6.37 (d, *J* = 15.7 Hz, 1H), 6.21 (m, 1H), 3.70 (m, 1H), 3.57 (m, 1H), 3.25 (m, 1H), 2.56–2.39 (m, 2H), 1.99 (m, 1H), 1.86–1.75 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.3, 149.8, 148.0, 137.3, 137.2, 134.5, 132.6, 129.0, 128.6, 128.5, 127.2, 126.6, 126.2, 126.1, 126.1, 122.2, 46.9, 38.4, 37.2, 33.9. HRMS (ESI) m/z calculated for $C_{24}H_{25}N_2OS$ $[M+H]^+$ 389.1682, found: 389.1682.

***N-(4-(4-methoxyphenyl)-3-(phenylthio)butyl)picolinamide* (2v)**



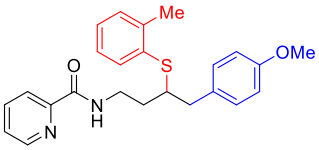
The title compound was isolated as a yellow oil (92% yield) after chromatography on silica with ethyl acetate/hexane (1:10). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (d, *J* = 4.2 Hz, 1H), 8.09 (d, *J* = 7.8 Hz, 1H), 7.99 (s, 1H), 7.73 (m, 1H), 7.37–7.28 (m, 3H), 7.21–7.11 (m, 3H), 7.01 (d, *J* = 8.6 Hz, 2H), 6.72 (t, *J* = 6.9 Hz, 2H), 3.70–3.63 (m, 4H), 3.50 (m, 1H), 3.33–3.23 (m, 1H), 2.86 (m, 1H), 2.72 (m, 1H), 1.94–1.85 (m, 1H), 1.69 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.3, 158.3, 149.9, 148.0, 137.3, 134.9, 132.4, 130.8, 130.3, 129.0, 127.1, 126.1, 122.2, 113.8, 55.2, 48.8, 40.7, 37.3, 33.6.HRMS (ESI) m/z calculated for $C_{23}H_{25}N_2O_2S$ $[M+H]^+$ 393.1631, found: 393.1633.

***N-(4-(4-methoxyphenyl)-3-((4-methoxyphenyl)thio)butyl)picolinamide* (2w)**



The title compound was isolated as a yellow oil (73% yield) after chromatography on silica with ethyl acetate/hexane (1:8). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (d, *J* = 4.7 Hz, 1H), 8.10 (d, *J* = 7.7 Hz, 1H), 8.01 (s, 1H), 7.75 (m, 1H), 7.35–7.30 (m, 3H), 6.99 (d, *J* = 8.5 Hz, 2H), 6.73 (m, 4H), 3.70 (m, 7H), 3.56–3.48 (m, 1H), 3.14–3.03 (m, 1H), 2.84 (m, 1H), 2.65 (m, 1H), 1.88–1.79 (m, 1H), 1.68–1.60 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.3, 159.5, 158.1, 149.8, 148.0, 137.3, 135.8, 131.0, 130.2, 126.1, 124.5, 122.1, 114.5, 113.7, 55.2, 49.9, 40.7, 39.4, 37.4, 33.3. HRMS (ESI) m/z calculated for $C_{24}H_{27}N_2O_3S$ $[M+H]^+$ 423.1737, found: 423.1739.

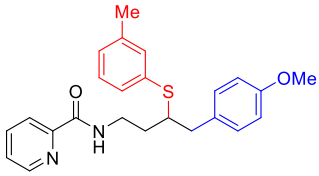
***N-(4-(4-methoxyphenyl)-3-(o-tolylthio)butyl)picolinamide* (2x)**



The title compound was isolated as a yellow oil (80% yield) after chromatography on silica with ethyl acetate/hexane (1:10). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, *J* = 4.7 Hz, 1H), 8.17 (d, *J* = 7.8 Hz, 1H), 8.05 (s, 1H), 7.83 (m, 1H), 7.44–7.37 (m, 2H), 7.18 (m, 1H), 7.15–7.05 (m, 4H), 6.80 (d, *J* = 8.5 Hz, 2H), 3.78 (s, 3H), 3.75–3.68 (m, 1H), 3.61–3.52 (m, 1H), 3.44–3.36 (m, 1H), 2.95 (m, 1H), 2.83 (m, 1H), 2.40 (s, 3H), 2.00 (m, 1H), 1.80 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ

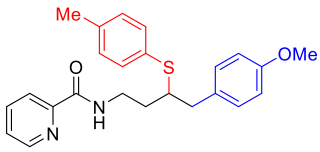
164.2, 158.2, 149.9, 148.0, 139.6, 137.3, 134.5, 131.4, 130.9, 130.4, 130.3, 126.8, 126.4, 126.1, 122.2, 113.8, 55.3, 47.7, 40.5, 37.3, 33.6, 20.8. HRMS (ESI) m/z calculated for $C_{24}H_{27}N_2O_2S$ $[M+H]^+$ 407.1788, found: 407.1791.

N-(4-(4-methoxyphenyl)-3-(m-tolylthio)butyl)picolinamide (2y)



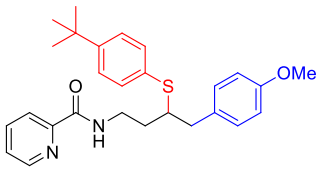
The title compound was isolated as a yellow oil (82% yield) after chromatography on silica with ethyl acetate/hexane (1:10). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53–8.51 (m, 1H), 8.18 (d, *J* = 7.8 Hz, 1H), 8.09 (s, 1H), 7.85–7.80 (m, 1H), 7.42–7.38 (m, 1H), 7.22 (d, *J* = 9.2 Hz, 2H), 7.16 (t, *J* = 7.5 Hz, 1H), 7.12–7.08 (m, 2H), 7.02 (d, *J* = 7.4 Hz, 1H), 6.82–6.79 (m, 2H), 3.78–3.72 (m, 4H), 3.59 (m, 1H), 3.36 (m, 1H), 2.94 (m, 1H), 2.82 (m, 1H), 2.29 (s, 3H), 2.03–1.94 (m, 1H), 1.78 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.2, 158.2, 149.9, 148.0, 138.7, 137.3, 134.6, 132.9, 130.9, 130.3, 129.2, 128.7, 127.9, 126.0, 122.1, 113.7, 55.2, 48.7, 40.7, 37.2, 33.6, 21.2. HRMS (ESI) m/z calculated for $C_{24}H_{27}N_2O_2S$ $[M+H]^+$ 407.1788, found: 407.1798.

N-(4-(4-methoxyphenyl)-3-(p-tolylthio)butyl)picolinamide (2z)



The title compound was isolated as a yellow oil (90% yield) after chromatography on silica with ethyl acetate/hexane (1:10). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (d, *J* = 4.4 Hz, 1H), 8.09 (d, *J* = 7.8 Hz, 1H), 8.00 (s, 1H), 7.73 (m, 1H), 7.31 (m, 1H), 7.25 (d, *J* = 8.1 Hz, 2H), 7.00 (m, 4H), 6.71 (d, *J* = 8.5 Hz, 2H), 3.68–3.63 (m, 4H), 3.51 (m, 1H), 3.26–3.14 (m, 1H), 2.85 (m, 1H), 2.68 (m, 1H), 2.23 (s, 3H), 1.90–1.82 (m, 1H), 1.67 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.2, 158.2, 149.9, 148.0, 137.3, 137.3, 133.1, 130.9, 130.8, 130.2, 129.7, 126.1, 122.1, 113.7, 55.2, 49.1, 40.6, 37.3, 33.4, 21.1. HRMS (ESI) m/z calculated for $C_{24}H_{27}N_2O_2S$ $[M+H]^+$ 407.1788, found: 407.1793.

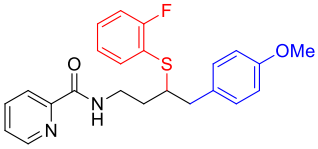
***N-(3-((4-(tert-butyl)phenyl)thio)-4-(4-methoxyphenyl)butyl)picolinamide* (2aa)**



The title compound was isolated as a colorless oil (80% yield) after chromatography on silica with ethyl acetate/hexane (1:10). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, *J* = 4.4 Hz, 1H), 8.18 (d, *J* = 7.7 Hz, 1H), 8.09 (s, 1H), 7.83 (m, 1H), 7.42–7.34 (m, 3H), 7.29 (d, *J* = 8.4 Hz, 2H), 7.10 (d, *J* = 8.5 Hz, 2H), 6.80 (d, *J* = 8.5 Hz, 2H), 3.79–3.71 (m, 4H), 3.63–3.56 (m, 1H), 3.37–3.28 (m, 1H), 2.96 (m, 1H), 2.79 (m, 1H), 1.97 (m, 1H), 1.76 (m, 1H), 1.30 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.2, 158.2, 150.3, 150.0, 148.0, 137.3, 132.5, 131.0, 130.9, 130.2, 126.0, 126.0,

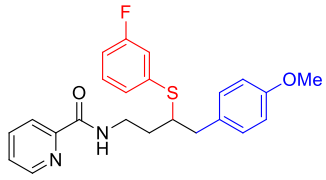
122.1, 113.7, 55.2, 48.8, 40.7, 37.3, 34.5, 33.5, 31.2.HRMS (ESI) m/z calculated for $C_{27}H_{33}N_2O_2S$ $[M+H]^+$ 449.2257, found: 449.2257.

***N-(3-((2-fluorophenyl)thio)-4-(4-methoxyphenyl)butyl)picolinamide* (2ab)**



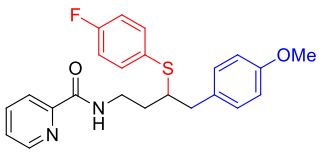
The title compound was isolated as a colorless oil (82% yield) after chromatography on silica with ethyl acetate/hexane (1:10). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45–8.42 (m, 1H), 8.09 (d, *J* = 7.8 Hz, 1H), 8.02 (s, 1H), 7.76–7.72 (m, 1H), 7.37–7.30 (m, 2H), 7.19–7.14 (m, 1H), 7.03–6.94 (m, 4H), 6.72–6.67 (m, 2H), 3.70–3.64 (m, 4H), 3.56–3.49 (m, 1H), 3.41–3.33 (m, 1H), 2.85 (m, 1H), 2.73 (m, 1H), 1.95–1.85 (m, 1H), 1.73–1.62 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.3, 163.7, 161.2, 158.2, 149.9, 148.0, 137.3, 135.2, 130.6, 130.2, 129.5, 129.5, 126.0, 124.4, 122.1, 121.6, 121.5, 116.0, 115.8, 113.8, 55.2, 48.1, 40.9, 37.2, 33.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -107.22. HRMS (ESI) m/z calculated for $C_{23}H_{24}FN_2O_2S$ $[M+H]^+$ 411.1537, found: 411.1537.

***N-(3-((3-fluorophenyl)thio)-4-(4-methoxyphenyl)butyl)picolinamide* (2ac)**



The title compound was isolated as a colorless oil (90% yield) after chromatography on silica with ethyl acetate/hexane (1:10). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, *J* = 4.4 Hz, 1H), 8.18 (d, *J* = 7.8 Hz, 1H), 8.10 (s, 1H), 7.82 (m, 1H), 7.40 (m, 1H), 7.24–7.14 (m, 2H), 7.08 (m, 3H), 6.92–6.85 (m, 1H), 6.80 (d, *J* = 8.5 Hz, 2H), 3.79–3.71 (m, 4H), 3.63–3.55 (m, 1H), 3.42 (m, 1H), 2.89 (m, 2H), 2.06–1.98 (m, 1H), 1.80 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.3, 163.9, 161.4, 158.3, 149.8, 148.0, 137.6, 137.5, 137.3, 130.5, 130.3, 130.2, 130.1, 127.1, 127.1, 126.1, 122.1, 118.3, 118.1, 113.9, 113.8, 113.7, 55.2, 48.7, 40.6, 37.1, 33.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -112.16. HRMS (ESI) m/z calculated for $C_{23}H_{24}FN_2O_2S$ $[M+H]^+$ 411.1537, found: 411.1540.

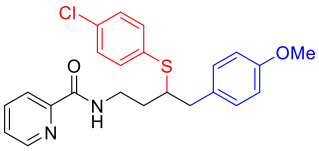
***N-(3-((4-fluorophenyl)thio)-4-(4-methoxyphenyl)butyl)picolinamide* (2ad)**



The title compound was isolated as a colorless oil (80% yield) after chromatography on silica with ethyl acetate/hexane (1:10). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, *J* = 4.4 Hz, 1H), 8.18 (d, *J* = 7.8 Hz, 1H), 8.06 (s, 1H), 7.83 (m, 1H), 7.43–7.38 (m, 3H), 7.07 (d, *J* = 8.5 Hz, 2H), 6.97 (t, *J* = 8.6 Hz, 2H), 6.80 (d, *J* = 8.5 Hz, 2H), 3.79–3.71 (m, 4H), 3.60 (m, 1H), 3.29–3.20 (m, 1H), 2.90 (m, 1H), 2.78 (m, 1H), 2.01–1.92 (m, 1H), 1.76 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.2, 163.6, 161.1, 158.2, 149.8, 148.0, 137.3, 135.4, 135.3, 130.7, 130.2, 129.6, 126.1, 122.1, 116.1, 115.9, 113.8,

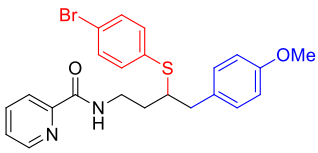
55.2, 49.8, 40.7, 37.2, 33.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -114.07. HRMS (ESI) m/z calculated for $C_{23}H_{24}FN_2O_2S$ $[M+H]^+$ 411.1537, found: 411.1543.

***N-(3-((4-chlorophenyl)thio)-4-(4-methoxyphenyl)butyl)picolinamide* (2ae)**



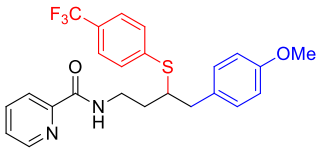
The title compound was isolated as a colorless oil (77% yield) after chromatography on silica with ethyl acetate/hexane (1:10). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (d, *J* = 4.2 Hz, 1H), 8.10 (d, *J* = 7.8 Hz, 1H), 7.99 (s, 1H), 7.78–7.74 (m, 1H), 7.34 (m, 1H), 7.27–7.21 (m, 2H), 7.18–7.12 (m, 2H), 7.00 (d, *J* = 8.6 Hz, 2H), 6.74–6.70 (m, 2H), 3.69 (m, 4H), 3.54–3.47 (m, 1H), 3.24 (m, 1H), 2.87–2.69 (m, 2H), 1.95–1.86 (m, 1H), 1.73–1.64 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.3, 158.3, 149.8, 148.0, 137.3, 133.7, 133.4, 133.2, 130.6, 130.2, 129.0, 126.1, 122.1, 113.8, 55.2, 49.3, 40.7, 37.2, 33.7. HRMS (ESI) m/z calculated for $C_{23}H_{24}ClN_2O_2S$ $[M+H]^+$ 427.1242, found: 427.1239.

***N-(3-((4-bromophenyl)thio)-4-(4-methoxyphenyl)butyl)picolinamide* (2af)**



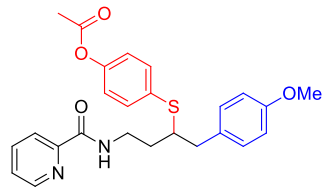
The title compound was isolated as a red oil (72% yield) after chromatography on silica with ethyl acetate/hexane (1:10). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, *J* = 4.2 Hz, 1H), 8.18 (d, *J* = 7.8 Hz, 1H), 8.07 (s, 1H), 7.84 (m, 1H), 7.43–7.39 (m, 1H), 7.39–7.34 (m, 2H), 7.27–7.23 (m, 2H), 7.08 (d, *J* = 8.6 Hz, 2H), 6.80 (d, *J* = 8.6 Hz, 2H), 3.77 (m, 4H), 3.58 (m, 1H), 3.32 (m, 1H), 2.90 (m, 1H), 2.82 (m, 1H), 2.02–1.95 (m, 1H), 1.82–1.73 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.3, 158.3, 149.8, 148.0, 137.3, 134.1, 133.8, 132.0, 130.5, 130.2, 126.1, 122.1, 121.1, 113.8, 55.2, 49.1, 40.7, 37.2, 33.7. HRMS (ESI) m/z calculated for $C_{23}H_{24}BrN_2O_2S$ $[M+H]^+$ 471.0736, found: 471.0730.

***N-(4-(4-methoxyphenyl)-3-((4-(trifluoromethyl)phenyl)thio)butyl)picolinamide* (2ag)**



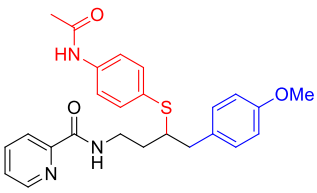
The title compound was isolated as a colorless oil (89% yield) after chromatography on silica with ethyl acetate/hexane (1:10). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53–8.51 (m, 1H), 8.19–8.17 (m, 1H), 8.08 (s, 1H), 7.84 (m, 1H), 7.43 (m, 5H), 7.12–7.09 (m, 2H), 6.82–6.78 (m, 2H), 3.78–3.73 (m, 4H), 3.59 (m, 1H), 3.50 (m, 1H), 2.92 (d, *J* = 7.3 Hz, 2H), 2.09–2.01 (m, 1H), 1.88–1.82 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.3, 158.4, 149.8, 148.0, 140.8, 137.3, 130.4, 130.3, 130.3, 126.2, 125.7, 125.6, 125.6, 125.6, 122.2, 113.8, 55.2, 48.1, 40.6, 37.1, 33.9;^{19}F NMR (376 MHz, $CDCl_3$) δ -62.49. HRMS (ESI) m/z calculated for $C_{24}H_{24}FN_2O_2S$ $[M+H]^+$ 461.1505, found: 461.1518.

***4-((1-(4-methoxyphenyl)-4-(picolinamido)butan-2-yl)thio)phenyl acetate* (2ah)**



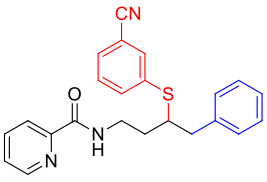
The title compound was isolated as a brown oil (57% yield) after chromatography on silica with ethyl acetate/hexane (1:6). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (d, *J* = 4.3 Hz, 1H), 8.09 (d, *J* = 7.9 Hz, 2H), 7.76 (m, 1H), 7.36–7.32 (m, 1H), 7.24 (d, *J* = 8.4 Hz, 2H), 6.97 (d, *J* = 8.6 Hz, 2H), 6.73 (m, 4H), 3.69 (m, 4H), 3.57–3.48 (m, 1H), 3.11–2.98 (m, 1H), 2.88–2.81 (m, 1H), 2.62 (m, 1H), 1.88–1.74 (m, 2H), 1.68–1.61 (m, 1H), 1.19 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.6, 158.1, 156.6, 149.5, 148.1, 137.5, 136.1, 131.1, 130.2, 126.3, 123.6, 122.2, 116.2, 113.8, 55.2, 49.9, 40.8, 37.6, 33.2, 29.7. HRMS (ESI) m/z calculated for $C_{25}H_{27}N_2O_4S$ $[M+H]^+$ 451.1686, found: 451.1688.

***N-(3-((4-acetamidophenyl)thio)-4-(4-methoxyphenyl)butyl)picolinamide* (2ai)**



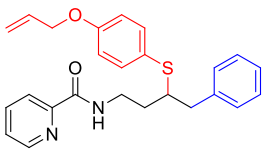
The title compound was isolated as a yellow oil (60% yield) after chromatography on silica with ethyl acetate/hexane (1:6). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (m, 1H), 8.14 (d, *J* = 8.3 Hz, 3H), 7.82 (m, 1H), 7.49 (d, *J* = 8.3 Hz, 2H), 7.41 (m, 1H), 7.38–7.34 (m, 2H), 7.10–7.03 (m, 2H), 6.81–6.75 (m, 2H), 3.76 (m, 4H), 3.58 (m, 1H), 3.31–3.19 (m, 1H), 2.91 (m, 1H), 2.74 (m, 1H), 2.14 (s, 3H), 1.93 (m, 1H), 1.73 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.7, 164.4, 158.2, 149.7, 148.1, 137.8, 137.3, 134.0, 130.8, 130.2, 128.9, 126.2, 122.0, 120.2, 113.8, 55.2, 49.3, 40.7, 37.3, 33.3, 24.5. HRMS (ESI) m/z calculated for $C_{25}H_{28}N_3O_3S$ $[M+H]^+$ 450.1846, found: 450.1844.

***N-(3-((3-cyanophenyl)thio)-4-phenylbutyl)picolinamide* (2aj)**



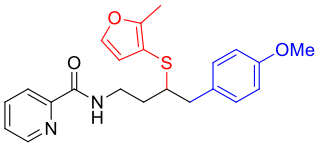
The title compound was isolated as a yellow oil (72% yield) after chromatography on silica with ethyl acetate/hexane (1:6). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (d, *J* = 4.8 Hz, 1H), 8.09 (d, *J* = 7.7 Hz, 1H), 8.00 (s, 1H), 7.81–7.77 (m, 1H), 7.75–7.69 (m, 2H), 7.43–7.35 (m, 5H), 7.35–7.27 (m, 2H), 7.20–7.16 (m, 1H), 3.53 (m, 2H), 3.29 (m, 1H), 3.00 (m, 1H), 2.94–2.90 (m, 1H), 2.22 (m, 1H), 1.89–1.81 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.4, 149.4, 148.1, 139.3, 137.5, 137.4, 133.3, 132.0, 131.6, 130.5, 129.8, 129.5, 126.3, 122.2, 117.9, 113.4, 113.3, 48.7, 38.2, 36.7, 32.6.HRMS (ESI) m/z calculated for $C_{23}H_{22}N_3OS$ $[M+H]^+$ 388.1478, found: 388.1480.

***N-(3-((4-(allyloxy)phenyl)thio)-4-phenylbutyl)picolinamide* (2ak)**



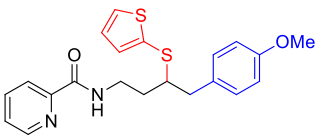
The title compound was isolated as a yellow oil (73% yield) after chromatography on silica with ethyl acetate/hexane (1:8). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (d, *J* = 4.4 Hz, 1H), 8.09 (d, *J* = 7.9 Hz, 1H), 7.99 (s, 1H), 7.76–7.71 (m, 1H), 7.31 (d, *J* = 8.7 Hz, 3H), 7.17 (t, *J* = 7.2 Hz, 2H), 7.09 (m, 3H), 6.76 (d, *J* = 8.6 Hz, 2H), 5.96 (m, 1H), 5.36–5.28 (m, 1H), 5.20 (d, *J* = 10.5 Hz, 1H), 4.43 (d, *J* = 5.2 Hz, 2H), 3.67 (m, 1H), 3.53 (m, 1H), 3.13 (m, 1H), 2.90 (m, 1H), 2.70 (m, 1H), 1.84 (m, 1H), 1.66 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.2, 158.6, 149.9, 148.0, 139.0, 137.3, 135.8, 133.0, 129.2, 128.3, 126.4, 126.0, 124.7, 122.1, 117.8, 115.3, 68.8, 49.7, 41.7, 37.3, 33.4. HRMS (ESI) m/z calculated for $C_{25}H_{27}N_2O_2S$ $[M+H]^+$ 419.1788, found: 419.1791.

N-(4-(4-methoxyphenyl)-3-((2-methylfuran-3-yl)thio)butyl)picolinamide **(2al)**



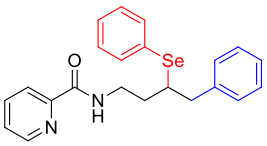
The title compound was isolated as a dark brown oil (22% yield) after chromatography on silica with ethyl acetate/hexane (1:8). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, *J* = 4.6 Hz, 1H), 8.18 (d, *J* = 7.8 Hz, 1H), 8.06 (s, 1H), 7.84 (m, 1H), 7.43–7.41 (m, 1H), 7.29 (d, *J* = 1.7 Hz, 1H), 7.07 (d, *J* = 8.5 Hz, 2H), 6.80 (d, *J* = 8.6 Hz, 2H), 6.36 (d, *J* = 1.7 Hz, 1H), 3.78 (m, 4H), 3.59–3.55 (m, 1H), 2.99–2.90 (m, 2H), 2.70 (m, 1H), 2.33 (s, 3H), 1.91–1.85 (m, 1H), 1.73–1.68 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.2, 158.1, 156.0, 149.8, 147.9, 140.6, 137.3, 131.1, 130.1, 126.1, 122.2, 115.7, 113.8, 108.6, 55.2, 49.0, 41.0, 37.4, 33.2, 11.9. HRMS (ESI) m/z calculated for $C_{22}H_{25}N_2O_3S$ $[M+H]^+$ 397.1580, found: 397.1579.

N-(4-(4-methoxyphenyl)-3-(thiophen-2-ylthio)butyl)picolinamide **(2am)**



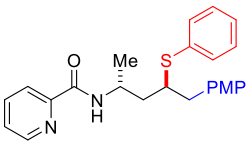
The title compound was isolated as a dark brown oil (30% yield) after chromatography on silica with ethyl acetate/hexane (1:8). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (d, *J* = 4.4 Hz, 1H), 8.11 (d, *J* = 7.8 Hz, 1H), 8.03 (s, 1H), 7.77 (m, 1H), 7.33 (m, 2H), 7.11 (d, *J* = 3.5 Hz, 1H), 7.03 (d, *J* = 8.5 Hz, 2H), 6.94 (m, 1H), 6.74 (d, *J* = 8.5 Hz, 2H), 3.71 (m, 4H), 3.54 (m, 1H), 3.05–2.97 (m, 1H), 2.90 (m, 1H), 2.68 (m, 1H), 1.84 (m, 1H), 1.73–1.65 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.3, 158.2, 149.8, 148.0, 137.3, 135.7, 131.5, 130.8, 130.2, 127.7, 127.6, 126.1, 122.2, 113.8, 55.2, 51.1, 40.6, 37.3, 33.0. HRMS (ESI) m/z calculated for $C_{21}H_{23}N_2O_2S$$[M+H]^+$ 399.1195, found: 399.1203.

N-(4-phenyl-3-(phenylselanyl)butyl)picolinamide **(2an)**



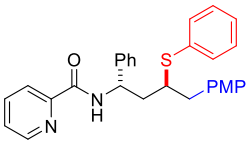
The title compound was isolated as a yellow oil (65% yield) after chromatography on silica with ethyl acetate/hexane (1:12). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47–8.42 (m, 1H), 8.10 (d, *J* = 7.7 Hz, 1H), 7.97 (s, 1H), 7.75 (t, *J* = 7.5 Hz, 1H), 7.47 (d, *J* = 6.1 Hz, 2H), 7.35–7.31 (m, 1H), 7.18 (d, *J* = 7.2 Hz, 5H), 7.11 (m, 3H), 3.68 (m, 1H), 3.50 (m, 1H), 3.41–3.32 (m, 1H), 3.01 (m, 1H), 2.88 (m, 1H), 1.95 (m, 1H), 1.78 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.9, 148.0, 139.4, 137.3, 135.2, 129.2, 129.0, 128.8, 128.3, 127.7, 126.5, 126.1, 122.1, 44.6, 42.5, 38.0, 34.4. HRMS (ESI) m/z calculated for $C_{22}H_{23}N_2OSe$ $[M+H]^+$ 408.2651, found: 408.2650.

***N-((2R,4S)-5-(4-methoxyphenyl)-4-(phenylthio)pentan-2-yl)picolinamide* (2ao)**



The title compound was isolated as a yellow oil (62% yield) after chromatography on silica with ethyl acetate/hexane (1:10). This product was isolated as a 12:1 mixture of diastereomers. The reported dr was determined by ^{1}H NMR analysis. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, *J* = 4.5 Hz, 0.08H), 8.50 (d, *J* = 4.4 Hz, 0.92H), 8.23 (d, *J* = 7.5 Hz, 0.08H), 8.20 (d, *J* = 7.8 Hz, 0.92H), 7.93–7.86 (m, 0.16H), 7.86–7.77 (m, 1.84H), 7.41 (m, 2.77H), 7.38–7.33 (m, 0.24H), 7.28–7.20 (m, 2.76H), 7.20 (s, 0.24H), 7.12 (d, *J* = 8.6 Hz, 0.16H), 7.04 (d, *J* = 8.5 Hz, 1.84H), 6.83–6.79 (m, 0.16H), 6.77 (d, *J* = 8.6 Hz, 1.84H), 4.65–4.48 (m, 1H), 3.77 (s, 3H), 3.46–3.26 (m, 1H), 2.93 (m, 0.93H), 2.75 (m, 0.08H), 1.98–1.80 (m, 1H), 1.74–1.60 (m, 1H), 1.26–1.19 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.6, 158.1, 150.0, 147.9, 137.3, 134.7, 132.8, 130.9, 130.2, 128.8, 127.1, 126.0, 122.2, 113.7, 55.2, 47.8, 43.5, 41.0, 40.7, 21.2. HRMS (ESI) m/z calculated for $C_{24}H_{27}N_2O_2S$ $[M+H]^+$ 407.1788, found: 407.1789.

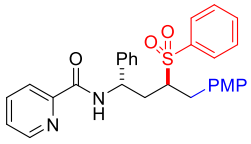
***N-((1S,3S)-4-(4-methoxyphenyl)-1-phenyl-3-(phenylthio)butyl)picolinamide* (2ap)**



The title compound was isolated as a colourless oil (43% yield) after chromatography on silica with ethyl acetate/hexane (1:10). This product was isolated as a >20:1 mixture of diastereomers. The reported dr was determined by ^{1}H NMR analysis. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (d, *J* = 4.3 Hz, 1H), 8.33 (d, *J* = 8.5 Hz, 1H), 8.17 (d, *J* = 7.8 Hz, 1H), 7.82 (m, 1H), 7.41 (m, 1H), 7.33–7.20 (m, 10H), 7.03 (d, *J* = 8.6 Hz, 2H), 6.78 (d, *J* = 8.6 Hz, 2H), 5.52 (q, *J* = 8.4 Hz, 1H), 3.78 (s, 3H), 3.26 (m, 1H), 2.95 (m, 1H), 2.87 (m, 1H), 2.21 (m, 1H), 2.06 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.6, 158.2, 149.8, 148.0, 141.6, 137.3, 134.5, 132.7, 130.7, 130.2, 128.8, 128.7, 127.4, 127.1, 126.5, 126.1, 122.3,

113.8, 55.2, 51.5, 47.4, 40.6, 40.5. HRMS (ESI) m/z calculated for $C_{29}H_{29}N_2O_2S$ $[M+H]^+$ 469.1944, found: 469.1946.

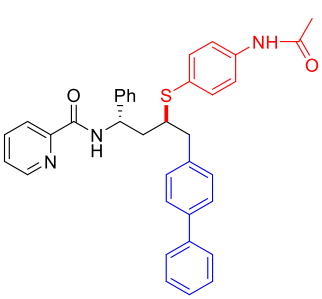
***N-((1S,3S)-4-(4-methoxyphenyl)-1-phenyl-3-(phenylsulfonyl)butyl)picolinamide* (2ap')**



In an 10 mL vial charged with a magnetic stir bar, **2ap** (0.2 mmol) was dissolved in DCM (3 mL). m-CPBA (0.5 mmol, 2.5 equiv) was dissolved in 2mL DCM, and was added to the reaction mixture dropwise. The resulting mixture was stirred at room temperature for 3h. The reaction mixture was then poured into 20 mL DCM, followed by washing with 1.0 M NaOH solution (20 mL) and brine (20 mL ×3). The organic phase was dried over $MgSO_4$ and concentrated in vacuo. The solvent was removed under reduced pressure to give the crude. After that, The title compound were purified by column chromatography.[6]

The title compound was isolated as a white solid (60% yield) after chromatography on silica with ethyl acetate/hexane (1:2).This product was isolated as a >20:1 mixture of diastereomers. The reported dr was determined by ^{1}H NMR analysis. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 4.4 Hz, 1H), 8.03 (d, *J* = 7.8 Hz, 1H), 7.84 (t, *J* = 9.2 Hz, 3H), 7.73 (t, *J* = 7.5 Hz, 1H), 7.59 (t, *J* = 7.3 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 2H), 7.30 (m, 1H), 7.16–7.11 (m, 3H), 6.88 (t, *J* = 7.6 Hz, 4H), 6.57 (d, *J* = 8.4 Hz, 2H), 4.87 (q, *J* = 8.6 Hz, 1H), 3.65 (s, 3H), 3.30–3.21 (m, 2H), 2.68–2.58 (m, 1H), 2.47 (m, 1H), 2.08 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.6, 158.4, 149.4, 147.9, 140.1, 137.6, 137.2, 133.8, 130.2, 129.3, 129.0, 128.8, 128.4, 127.7, 126.5, 126.2, 122.1, 114.1, 62.8, 55.1, 51.7, 34.8, 34.1. HRMS (ESI) m/z calculated for $C_{29}H_{29}N_2O_4S$ $[M+H]^+$ 501.1843, found: 501.1845.

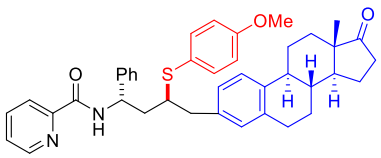
N-((1S,3S)-4-([1,1'-biphenyl]-4-yl)-3-((4-acetamidophenyl)thio)-1-phenylbutyl)picolinamide (2aq)



The title compound was isolated as a colourless oil (52% yield) after chromatography on silica with ethyl acetate/hexane (1:3). This product was isolated as a >20:1 mixture of diastereomers. The reported dr was determined by 1H NMR analysis. 1H NMR (400 MHz, $CDCl_3$) δ 8.44–8.40 (m, 1H), 8.32 (d, J = 8.9 Hz, 1H), 8.10 (d, J = 7.8 Hz, 1H), 7.77–7.73 (m, 1H), 7.60 (s, 1H), 7.52–7.49 (m, 2H), 7.40–7.33 (m, 7H), 7.27–7.17 (m, 8H), 7.08 (d, J = 7.9 Hz, 2H), 5.52 (m, 1H), 3.25–3.14 (m, 1H), 2.95 (m, 1H), 2.82 (m,

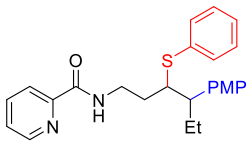
1H), 2.12 (m, 1H), 2.03 (s, 3H), 2.00–1.93 (m, 1H); 13C NMR (101 MHz, $CDCl_3$) δ 168.5, 163.8, 149.6, 148.1, 141.6, 140.9, 139.3, 137.8, 137.8, 137.4, 134.5, 134. 5, 129. 7, 128.8, 128.7, 127.5, 127.2, 127.1, 127.0, 126.5, 126.3, 122.3, 120.1, 51. 5, 47.8, 41.3, 40.6, 24.6. HRMS (ESI) m/z calculated for $C_{36}H_{34}N_3O_2S$ $[M+H]^+$ 572.2366, found: 572.2363.

N-((1S,3S)-3-((4-methoxyphenyl)thio)-4-((8R,9S,13S,14S)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-3-yl)-1-phenylbutyl)picolinamide **(2ar)**



The title compound was isolated as a colourless oil (52% yield) after chromatography on silica with ethyl acetate/hexane (1:3). This product was isolated as a >20:1 mixture of diastereomers. The reported dr was determined by ^{1}H NMR analysis. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (m, 1H), 8.37 (m, 1H), 8.20 (d, *J* = 7.8 Hz, 1H), 7.85 m, 1H), 7.43 (m, 1H), 7.34 (m, 2H), 7.27 (m, 5H), 7.16 (m, 1H), 6.88 (m, 1H), 6.79 (m, 3H), 5.58 (m, 1H), 3.79 (s, 3H), 3.22–3.06 (m, 1H), 2.94 (m, 1H), 2.81 (m, 3H), 2.51 (m, 1H), 2.40 m, 1H), 2.32–2.22 (m, 1H), 2.18–1.94 (m, 6H), 1.70–1.40 (m, 7H), 0.92 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.5, 159.5, 149.9, 147.9, 141.7, 137.7, 137.3, 136.3, 136.1, 136.0, 129.7, 129.6, 128.6, 127.3, 126.6, 126.5, 126.1, 125.3, 122.4, 114.4, 55.3, 51.4, 50.5, 48.0, 47.8, 44.3, 41.0, 40.2, 38.1, 35.8, 31.6, 29.3, 26.5, 25.7, 21.6, 13.8. HRMS (ESI) m/z calculated for $C_{41}H_{45}N_2O_3S$ $[M+H]^+$ 645.3145, found: 645.3142.

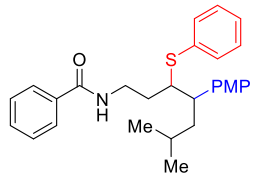
N-(4-(4-methoxyphenyl)-3-(phenylthio)hexyl)picolinamide **(2as) (2at)**



The title compound was isolated as a yellow oil (**2as**, 81% yield; **2at**, 71% yield) after chromatography on silica with ethyl acetate/hexane (1:10). This product was isolated as a 1:1 mixture of diastereomers. The reported dr was determined by ^{1}H NMR analysis. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (s, 0.5H), 8.49 (s, 0.5H), 8.16 (s, 0.5H), 8.15 (d, 0.5H), 7.98 (s, 1H), 7.81 (m, 1H), 7.47–7.41 (m, 1.5H), 7.41–7.36 (m, 1.5H), 7.27 (m, 2H), 7.21 (m, 1H), 7.16–7.11 (m, 1H), 7.11–7.07 (m, 1H), 6.84–6.82 (m, 1H), 6.81 (m, 1H), 3.78 (d, *J* = 1.5 Hz, 3H), 3.74–3.62 (m, 1H), 3.61–3.48 (m, 1H), 3.39 (m, 0.5H), 3.30 (m, 0.5H), 2.85–2.75 (m, 0.5H), 2.65 (m, 0.5H), 2.22–2.12 (m, 0.5H), 2.08–1.92 (m, 1.5H), 1.80–1.52 (m, 2H), 0.78 (t, *J* = 7.3 Hz, 1.5H), 0.72 (t, *J* = 7.3 Hz, 1.5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.2, 164.2, 158.3, 158.2, 149.9, 149.9, 147.9, 137.3, 137.2, 136.5, 135.9, 133.9, 133.3, 131.8, 131.7, 129.7, 129.5, 129.0, 128.9, 128.5, 126.8, 126.7, 126.0, 122.1, 122.1, 113.8, 113.6, 113.5,

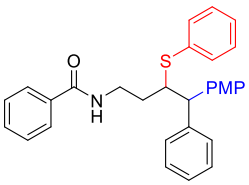
55.1, 55.1, 54.3, 53.9, 51.2, 50.5, 37.7, 37.5, 32.8, 32.6, 26.3, 24.5, 12.4, 12.2. HRMS (ESI) m/z calculated for $C_{25}H_{29}N_2O_2S$ $[M+H]^+$ 421.1944, found: 421.1942.

N-(4-(4-methoxyphenyl)-6-methyl-3-(phenylthio)heptyl)benzamide **(2au)**



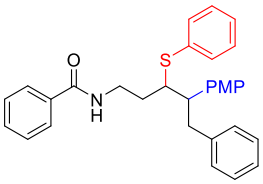
The title compound was isolated as a yellow oil (66% yield) after chromatography on silica with ethyl acetate/hexane (1:10). This product was isolated as a 1:1 mixture of diastereomers. The reported dr was determined by ^{1}H NMR analysis. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, *J* = 4.8 Hz, 1H), 8.16 (d, *J* = 8.0 Hz, 1H), 7.97 (d, *J* = 6.1 Hz, 1H), 7.81 (t, *J* = 7.8 Hz, 1H), 7.50–7.42 (m, 1H), 7.41–7.35 (m, 2H), 7.32–7.17 (m, 3H), 7.14–7.06 (m, 2H), 6.86–6.76 (m, 2H), 3.84–3.74 (m, 3H), 3.71–3.62 (m, 1H), 3.61–3.50 (m, 1H), 3.39–3.30 (m, 0.5H), 3.24 (m, 0.5H), 2.98 (m, 0.5H), 2.88 (m, 0.5H), 2.13–1.92 (m, 1H), 1.90–1.77 (m, 1H), 1.75–1.49 (m, 2.5H), 0.94–0.82 (m, 2H), 0.77 (m, 4.5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.2, 158.2, 149.9, 149.9, 147.9, 137.8, 137.2, 137.2, 136.5, 135.9, 134.0, 133.5, 131.8, 131.8, 129.6, 129.5, 129.0, 128.9, 128.5, 126.7, 126.7, 126.0, 122.1, 122.1, 113.9, 113.7, 113.6, 113.5, 55.1, 55.0, 54.6, 46.7, 46.0, 42.2, 40.0, 37.8, 37.5, 32.8, 32.5, 25.4, 25.3, 23.8, 21.4, 21.2. HRMS (ESI) m/z calculated for $C_{27}H_{33}$ N_2O_2S $[M+H]^+$ 449.2257, found: 449.2265.

N-(4-(4-methoxyphenyl)-4-phenyl-3-(phenylthio)butyl)benzamide **(2av)**



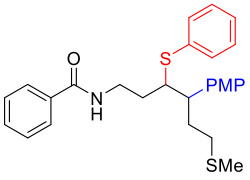
The title compound was isolated as a yellow oil (65% yield) after chromatography on silica with ethyl acetate/hexane (1:10). This product was isolated as a 1:1 mixture of diastereomers. The reported dr was determined by ^{1}H NMR analysis. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (d, *J* = 4.1 Hz, 1H), 8.11 (d, *J* = 7.8 Hz, 1H), 7.94 (s, 1H), 7.76 (t, *J* = 7.7 Hz, 1H), 7.33 (m, 1H), 7.24–7.15 (m, 5H), 7.15–7.00 (m, 7H), 6.69 (d, *J* = 8.6 Hz, 2H), 3.96 (d, *J* = 9.7 Hz, 1H), 3.80 (m, 1H), 3.73–3.51 (m,5H), 1.93 (m, 1H), 1.67 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.2, 158.2, 158.1, 150.0, 147.9, 142.9, 142.8, 137.3, 134.8, 134.8, 134.7, 134.6, 133.0, 133.0, 129.4, 129.2, 128.8, 128.8, 128.7, 128.6, 128.4, 128.4, 128.3, 128.1, 127.7, 127.2, 127.1, 126.6, 126.4, 126.1, 126.0, 122.1, 114.0, 113.8, 113.7, 55.8, 55.8, 55.2, 55.1, 52.3, 52.1, 39.3, 37.3, 33.2, 33.1. HRMS (ESI) m/z calculated for $C_{29}H_{29}$ N_2O_2S $[M+H]^+$ 469.1944, found: 469.1945.

N-(4-(4-methoxyphenyl)-5-phenyl-3-(phenylthio)pentyl)benzamide **(2aw)**



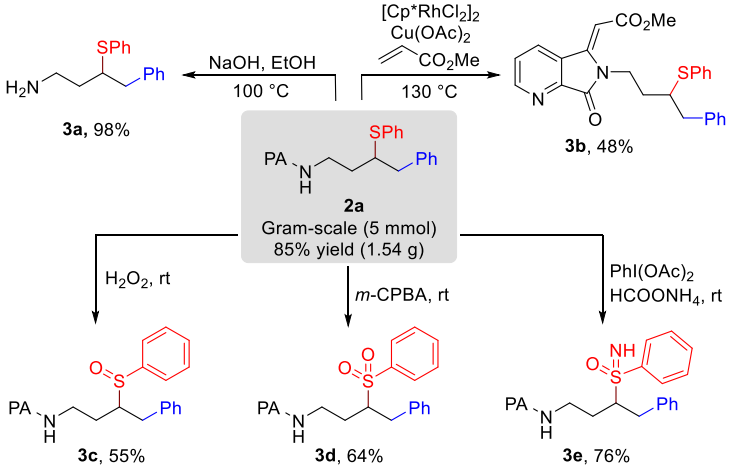
The title compound was isolated as a yellow oil (65% yield) after chromatography on silica with ethyl acetate/hexane (1:10). This product was isolated as a 1:1 mixture of diastereomers. The reported dr was determined by ^{1}H NMR analysis. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (d, *J* = 4.7, 0.5H), 8.38 (d, *J* = 4.8, 0.5H), 8.10 (d, *J* = 7.8 Hz, 0.5H), 8.04 (d, *J* = 7.8 Hz, 0.5H), 7.93 (s, 0.5H), 7.81 (s, 0.5H), 7.77–7.72 (m, 0.5H), 7.72–7.67 (m, 0.5H), 7.34–7.29 (m, 1H), 7.27 (m, 1H), 7.19–7.08 (m, 5H), 6.97 (m, 5H), 6.85 (m, 1H), 6.73–6.69 (m, 1H), 6.69–6.66 (m, 1H), 3.65 (s, 1.5H), 3.65 (s, 1.5H), 3.45 (m, 1.5H), 3.27 (m, 2H), 3.21–3.14 (m, 0.5H), 3.06–2.92 (m, 1H), 2.79 (m, 0.5H), 2.07 (m, 0.5H), 2.01–1.93 (m, 0.5H), 1.70–1.59 (m, 0.5H), 1.40–1.26 (m, 0.5H), 0.76 (m, 0.5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.3, 164.2, 158.4, 158.3, 149.9, 149.8, 148.0, 147.9, 140.2, 140.1, 137.3, 137.2, 136.2, 135.7, 133.0, 132.6, 131.4, 131.0, 129.9, 129.8, 129.3, 129.2, 129.0, 129.0, 128.1, 128.1, 128.0, 126.7, 126.5, 126.1, 126.0, 125.8, 122.1, 122.1, 113.8, 113.7, 113.5, 113.4, 55.1, 55.1, 52.5, 50.6, 50.5, 49.7, 39.5, 37.9, 37.6, 37.4, 33.3, 31.0. HRMS (ESI) m/z calculated for $C_{30}H_{31}N_2O_2S$ $[M+H]^+$ 483.2101, found: 483.2101.

N-(4-(4-methoxyphenyl)-6-(methylthio)-3-(phenylthio)hexyl)benzamide **(2ax)**

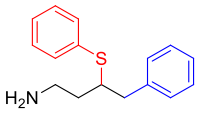


The title compound was isolated as a yellow oil (57% yield) after chromatography on silica with ethyl acetate/hexane (1:10). This product was isolated as a 1:1 mixture of diastereomers. The reported dr was determined by ^{1}H NMR analysis. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45–8.41 (m, 1H), 8.08 (d, *J* = 7.8 Hz, 1H), 7.96–7.85 (m, 1H), 7.75 (m, 1H), 7.41–7.35 (m, 1.5H), 7.35–7.30 (m, 2H), 7.24–7.18 (m, 1.5H), 7.18–7.11 (m, 1H), 7.09–7.01 (m, 2H), 6.76 (s, 1H), 6.73 (s, 1H), 3.71 (t, *J* = 2.2 Hz, 3H), 3.65–3.55 (m, 1H), 3.54–3.42 (m, 1H), 3.35–3.26 (m, 0.5H), 3.20 (m, 0.5H), 3.01 (m, 0.5H), 2.86 (m, 0.5H), 2.47–2.31 (m, 1H), 2.30–2.16 (m, 1.5H), 2.15–2.07 (m, 1.5H), 1.95 (s, 1.5H), 1.94 (s, 1.5H), 1.90–1.79 (m, 1.5H), 1.57–1.46 (m, 0.5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.3, 164.2, 158.5, 158.4, 149.9, 149.8, 147.9, 147.9, 137.3, 136.2, 135.5, 133.2, 132.3, 132.0, 131.8, 129.7, 129.4, 129.0, 129.0, 126.9, 126.9, 126.0, 126.0, 122.1, 122.1, 114.0, 113.9, 113.7, 55.2, 55.1, 54.4, 54.0, 48.3, 47.4, 37.6, 37.4, 32.9, 32.7, 32.6, 32.3, 32.2, 30.7, 15.4, 15.3. HRMS (ESI) m/z calculated for $C_{26}H_{31}N_2O_2S$ $[M+H]^+$ 467.1821, found: 467.1829.

4. Scaling up, auxiliary removal and synthetic applications

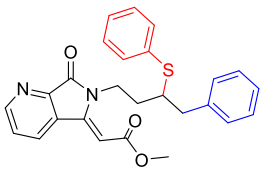


4-phenyl-3-(phenylthio)butan-1-amine **(3a)**



The title compound was isolated as a yellow oil (98% yield) after chromatography on silica with ethyl acetate/hexane (1:1). Removal of picolinic acid directing group was carried out by adapting a literature procedure[3]. To an oven-dried schlenk flask was added the aryl dulfide product **2a** (0.2 mmol, 1.0 eq), NaOH (1 mmol, 5 eq), and EtOH (1 mL). The resulting mixture was stirred at 100 °C for 12 h. After this time, the reaction mixture was allowed to cool to room temperature, diluted by amition of EtOAc (5 mL) and H_2O (2 mL × 2). The aqueous layers were combined and extracted with EtOAc (10 mL × 2). The organic layers were combined, dried over Na_2SO_4, and concentrated in vacuo to give pure orimary dulfide product. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.29 (m, 2H), 7.21–7.16 (m, 4H), 7.12 (m, 2H), 7.06 (d, *J* = 7.0 Hz, 2H), 3.34–3.28 (m, 1H), 2.90 (m, 1H), 2.86–2.79 (m, 1H), 2.75 (m, 1H), 2.66 (m, 1H), 2.39 (m, 2H), 1.73–1.66 (m, 1H), 1.59–1.50 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.0, 134.9, 132.2, 129.2, 128.9, 128.3, 127.0, 126.4, 48.2, 41.9, 39.5, 36.8. HRMS (ESI) m/z calculated for $C_{16}H_{20}NS$ $[M+H]^+$ 258.1311, found: 258.1313.

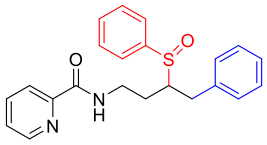
methyl (Z)-2-(7-oxo-6-(4-phenyl-3-(phenylthio)butyl)-6,7-dihydro-5H-pyrrolo[3,4-b]pyridin-5-ylidene)acetate **(3b)**



The title compound was isolated as a colourless oil (48% yield) after chromatography on silica with ethyl acetate/hexane (1:3). A 25 mL sealed tube was charged with the mixture of **2a** (0.2 mmol), $[Cp^*RhCl_2]_2$ (10

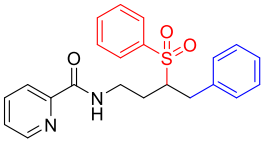
mol %), $Cu(OAc)_2$ (3 equiv). Under nitrogen atmosphere, methyl acrylate (1.5 equiv) and toluene (1 mL) was added, then the tube was sealed and the mixture was allowed to stir at 130 °C for 12 h. After completion, the mixture was cooled to room temperature, then H_2O (5 mL) was added and the mixture was extracted with EtOAc (5 mL x 3), dried by anhydrous Na_2SO_4.[4] The solvent was removed under reduced pressure to give the crude. After that, The title compound were purified by column chromatography.^{1}H NMR (400 MHz, CDCl3) δ 9.32 (m, 1H), 8.82 (m, 1H), 7.53 (m, 1H), 7.43 (m, 2H), 7.25 (m, 5H), 7.16 (t, *J* = 6.1 Hz, 3H), 5.75 (s, 1H), 4.15–3.97 (m, 2H), 3.82 (s, 3H), 3.43–3.34 (m, 1H), 3.01 (m, 1H), 2.85 (m, 1H), 2.00 (m, 1H), 1.86–1.78 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.2, 165.0, 152.9, 148.6, 145.4, 138.5, 136.1, 134.5, 132.6, 129.3, 129.2, 129.1, 128.6, 127.5, 126.7, 126.5, 100.1, 51.9, 48.8, 41.6, 37.9, 31.6. HRMS (ESI) m/z calculated for $C_{26}H_{25}N_2O_3S$ $[M+H]^+$ 445.1580, found: 445.1582.

***N-(4-phenyl-3-(phenylsulfinyl)butyl)picolinamide* (3c)**



The title compound was isolated as a yellow oil (55% yield) after chromatography on silica with ethyl acetate/hexane (1:2). To an 10 mL vial charged with a magnetic stir bar, **2a** (0.2 mmol) was added, followed by MeOH (5 mL). The resulting solution was then treated with 30 wt.% aq. H_2O_2 (0.8 mmol, 4.0 equiv), and stirred overnight. The reaction mixture was then poured into water and extracted with DCM (20 mL × 3). The combined organic phase was dried over $MgSO_4$ and concentrated in vacuo.[5] The solvent was removed under reduced pressure to give the crude. After that, The title compound were purified by column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (d, *J* = 4.7 Hz, 1H), 8.10 (d, *J* = 7.8 Hz, 1H), 8.01–7.92 (m, 3H), 7.83 (m, 1H), 7.66–7.62 (m, 1H), 7.55 (t, *J* = 7.6 Hz, 2H), 7.42 (m, 1H), 7.20–7.11 (m, 3H), 7.09–7.05 (m, 2H), 3.45–3.30 (m, 4H), 2.70 (m, 1H), 2.24–2.16 (m, 1H), 1.92 m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.3, 149.6, 148.0, 137.5, 137.2, 136.5, 133.8, 129.2, 128.9, 128.7, 128.5, 126.9, 126.1, 122.1, 63.6, 37.1, 35.0, 27.9. HRMS (ESI) m/z calculated for $C_{22}H_{23}N_2O_2S$ $[M+H]^+$ 379.1475, found: 379.1472

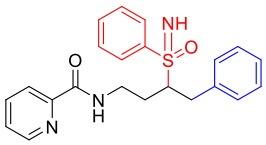
***N-(4-phenyl-3-(phenylsulfonyl)butyl)picolinamide* (3d)**



The title compound was isolated as a colourless oil (64% yield) after chromatography on silica with ethyl acetate/hexane (1:1). In an 10 mL vial charged with a magnetic stir bar, **2a** (0.2 mmol) was dissolved in DCM (3 mL). m-CPBA (0.4 mmol, 2.0 equiv) was dissolved in 1 mL DCM, and was added to the reaction

mixture dropwise. The resulting mixture was stirred at room temperature for 3h. The reaction mixture was then poured into 20 mL DCM, followed by washing with 1.0 M NaOH solution (20 mL) and brine (20 mL × 3).[6] The organic phase was dried over $MgSO_4$ and concentrated in vacuo. The solvent was removed under reduced pressure to give the crude. After that, The title compound were purified by column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (d, *J* = 4.4 Hz, 1H), 8.08 (d, *J* = 7.8 Hz, 1H), 8.05 (t, *J* = 6.0 Hz, 1H), 7.96 (d, *J* = 7.5 Hz, 2H), 7.78 m, 1H), 7.60 (t, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.6 Hz, 2H), 7.38 (m, 1H), 7.16–7.04 (m, 5H), 3.52–3.30 (m, 4H), 2.71 (m, 1H), 2.23 (m, 1H), 1.97–1.87 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.3, 149.5, 147.9, 137.4, 137.2, 136.5, 133.8, 129.2, 128.9, 128.9, 128.7, 126.9, 126.2, 122.1, 63.5, 37.1, 34.9, 27.9. HRMS (ESI) m/z calculated for $C_{22}H_{23}N_2O_3S$ $[M+H]^+$: 395.1424, found: 395.1422

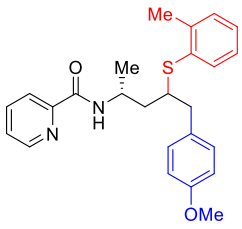
N-(4-phenyl-3-(phenylsulfonimidoyl)butyl)picolinamide (3e)



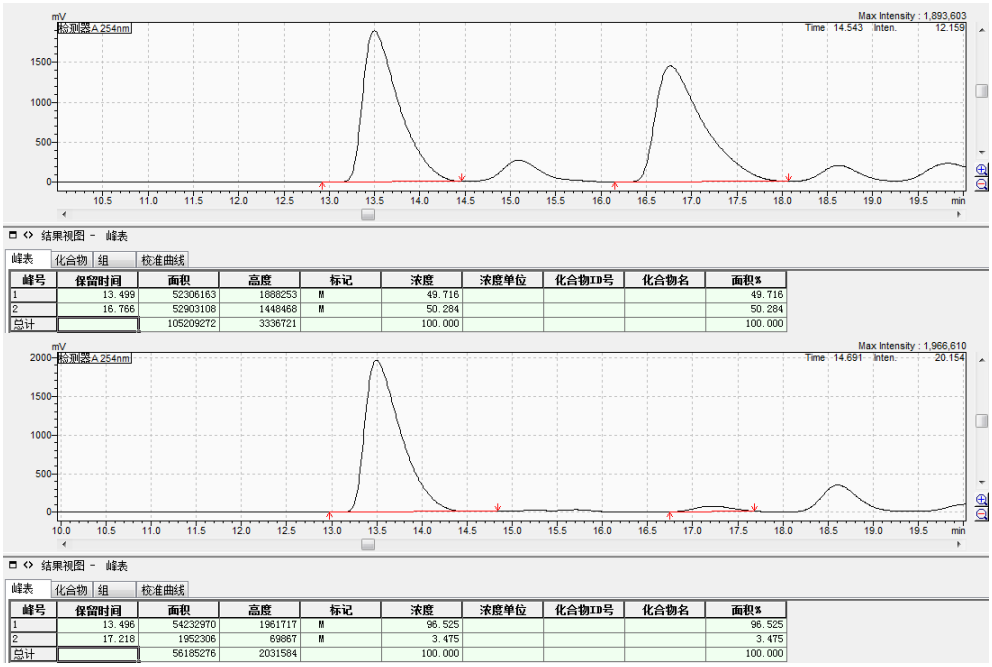
The title compound was isolated as a colourless oil (76% yield) after chromatography on silica with ethyl acetate/hexane (1:1). Compound **2a** (0.2 mmol, 1 equiv), (diacetoxyiodo)benzene (0.46 mmol, 2.3 equiv) and ammonium formate (0.3 mmol, 1.5 equiv) were added to a flask with a stirrer bar. MeOH (2 mL) was added and the reaction was stirred at room temperature for 3 h.[7] The solvent was removed under reduced pressure to give the crude. After that, The title compound were purified by column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53–8.50 (m, 1H), 8.13 (s, 1H), 8.09 (d, *J* = 7.8 Hz, 1H), 8.02 (d, *J* = 8.0 Hz, 2H), 7.84–7.80 (m, 1H), 7.60 (m,= 1H), 7.53 (m, 2H), 7.41 (m, 1H), 7.23–7.01 (m, 6H), 3.47–3.30 (m, 4H), 2.76–2.67 (m, 1H), 2.25 (m, 1H), 1.97–1.89 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.3, 149.8, 148.00, 140. 5, 137.2, 136.9, 133.2, 129.3, 129.2, 129.2, 129.02, 128.7, 126.9, 126.1, 122.2, 64.8, 37.3, 35.4, 28.2. HRMS (ESI) m/z calculated for $C_{22}H_{24}N_3O_2S$ $[M+H]^+$ 394.1584, found: 394.1586.

5. Access to enantioenriched α,γ-difunctionalized thiolamines

***N-((2R)-5-(4-methoxyphenyl)-4-(o-tolylthio)pentan-2-yl)picolinamide* (4a)**

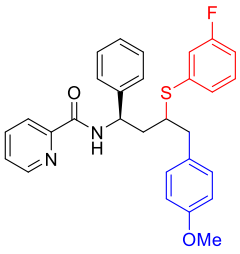


The title compound was isolated as a yellow oil (75% yield) after chromatography on silica with ethyl acetate/hexane (1:10). This product was isolated as a 15:1 mixture of diastereomers. The reported dr was determined by GC-MS analysis. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (d, *J* = 4.3 Hz, 1H), 8.11 (d, *J* = 7.8 Hz, 1H), 7.79–7.70 (m, 2H), 7.37–7.30 (m, 2H), 7.10–7.06 (m, 1H), 7.05–7.00 (m, 2H), 6.97 (d, *J* = 8.4 Hz, 2H), 6.69 (d, *J* = 8.4 Hz, 2H), 4.48–4.34 (m, 1H), 3.70 (s, 3H), 3.32 (m, 1H), 2.85 (m, 1H), 2.69 (m, 1H), 2.29 (s, 3H), 1.84 (m, 1H), 1.64 (m, 1H), 1.14 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.5, 157.1, 149.0, 146.8, 138.8, 136.2, 133.3, 130.9, 129.9, 129.2, 129.1, 125.7, 125.2, 124.9, 121.1, 112.7, 54.1, 45.6, 42.5, 39.7, 39.6, 20.2, 19.8. HRMS (ESI) m/z calculated for $C_{25}H_{29}N_2O_2S$ $[M+H]^+$ 421.1944, found: 421.1944. HPLC analysis (OD-H, nHexane: i-Propanol = 95:5 as eluent, 0.9 mL/min, 254 nm) indicated 93% ee: tR (minor) = 17.2 min, tR (major) = 13.5 min.

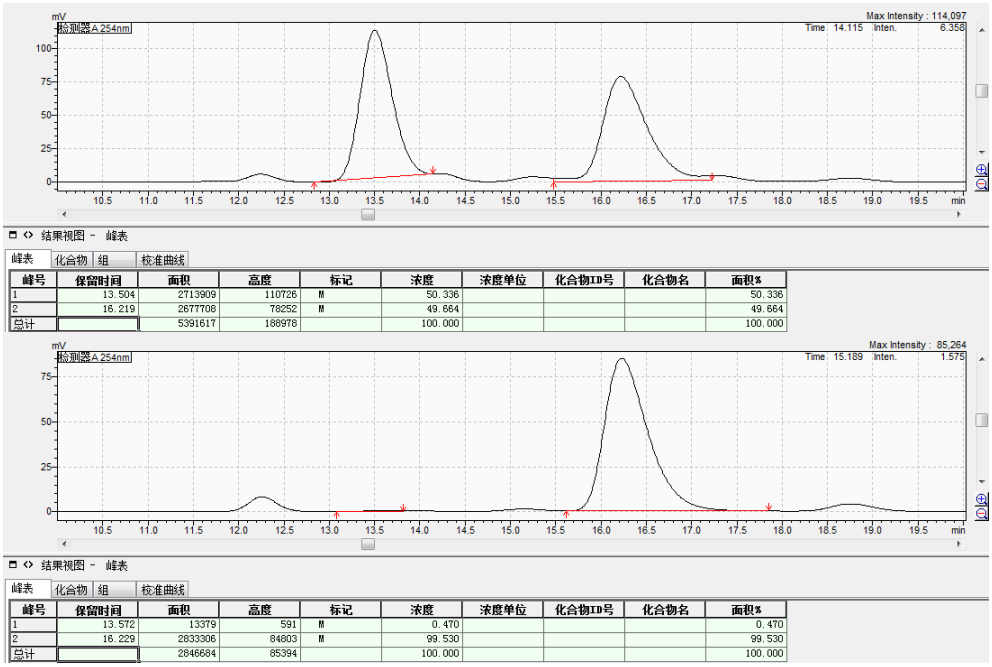


Supplementary Figure 3. HPLC spectra for **4a**

***N-((1R)-3-((3-fluorophenyl)thio)-4-(4-methoxyphenyl)-1-phenylbutyl)picolinamide* (4b)**

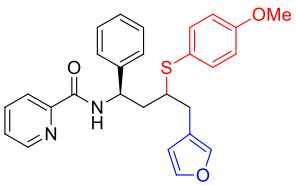


The title compound was isolated as a yellow oil (55% yield) after chromatography on silica with ethyl acetate/hexane (1:10). This product was isolated as a >20:1 mixture of diastereomers. The reported dr was determined by ^{1}H NMR analysis. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (d, *J* = 4.5 Hz, 1H), 8.26 (d, *J* = 8.7 Hz, 1H), 8.10 (d, *J* = 7.8 Hz, 1H), 7.75 (m, 1H), 7.36–7.32 (m, 1H), 7.27–7.23 (m, 2H), 7.22–7.18 (m, 3H), 7.11–7.05 (m, 1H), 6.96 (m, 3H), 6.86 (m, 1H), 6.78 (m, 1H), 6.71 (d, *J* = 8.5 Hz, 2H), 5.44 (m, 1H), 3.70 (s, 3H), 3.21 (m, 1H), 2.86 (d, *J* = 7.0 Hz, 2H), 2.18 (m, 1H), 2.00 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.5, 160.3, 157.2, 148.6, 146.9, 140.4, 136.3, 129.3, 129.2, 129.0, 128.9, 127.7, 126.5, 126.3, 126.3, 125.5, 125.1, 121.2, 117.4, 117.2, 112.8, 112.7, 112.6, 54.1, 50.4, 46.4, 39.8, 39.3. ^{19}F NMR (376 MHz, $CDCl_3$) δ -112.44. HRMS (ESI) m/z calculated for $C_{29}H_{28}FN_2O_2S$ $[M+H]^+$ 487.1850, found: 487.1850. HPLC analysis (OD-H, nHexane: i-Propanol = 90:10 as eluent, 0.8 mL/min, 254nm) indicated 99% ee: tR (minor) = 16.2 min, tR (major) = 13.6 min.

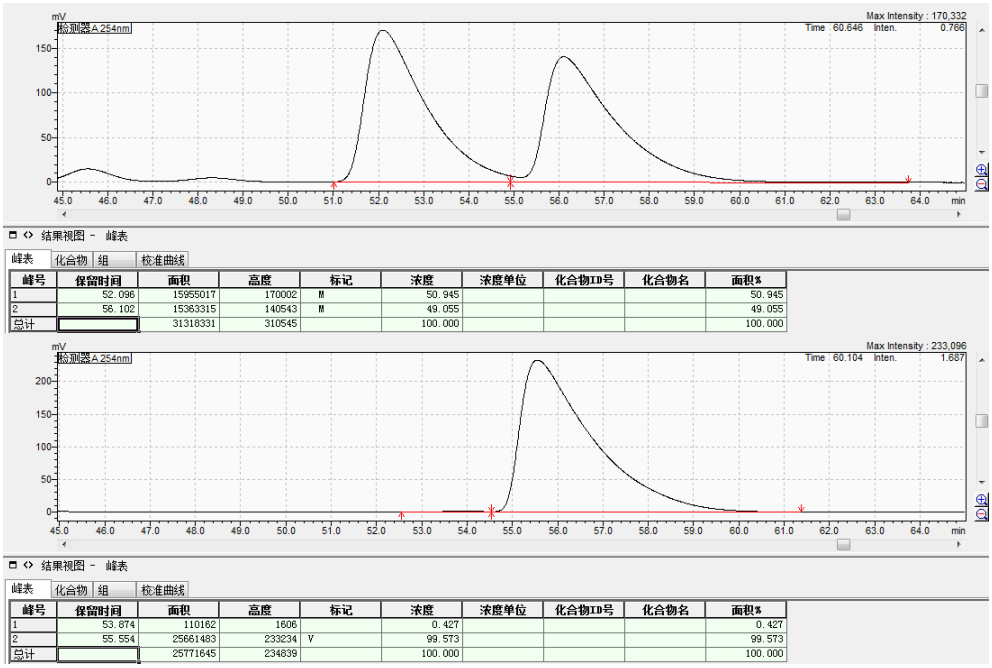


Supplementary Figure 4. HPLC spectra for **4b**

***N-((1R)-4-(furan-3-yl)-3-((4-methoxyphenyl)thio)-1-phenylbutyl)picolinamide* (4c)**

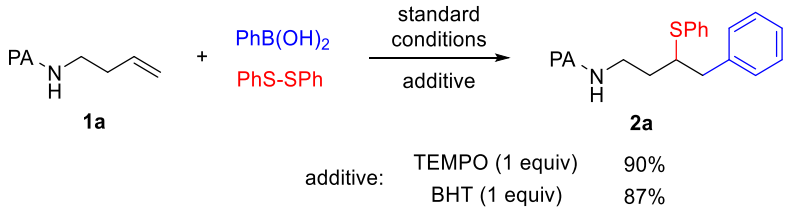


The title compound was isolated as a yellow oil (51% yield) after chromatography on silica with ethyl acetate/hexane (1:10). This product was isolated as a >20:1 mixture of diastereomers. The reported dr was determined by 1H NMR analysis. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, *J* = 4.4 Hz, 1H), 8.41 (d, *J* = 8.7 Hz, 1H), 8.19 (d, *J* = 7.8 Hz, 1H), 7.86–7.81 (m, 1H), 7.43–7.40 (m, 1H), 7.37–7.33 (m, 3H), 7.30 (d, *J* = 6.3 Hz, 5H), 7.26–7.24 (m, 1H), 6.79 (d, *J* = 8.6 Hz, 2H), 6.24 (s, 1H), 5.56 (m, 1H), 3.78 (s, 3H), 3.08–2.99 (m, 1H), 2.79 (m, 1H), 2.68 (m, 1H), 2.16 (m, 1H), 2.01 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.6, 159.6, 149.7, 148.0, 142.8, 141.7, 140.2, 137.4, 136.1, 128.7, 127.4, 126.5, 126.2, 124.0, 122.3, 121.5, 114.4, 111.4, 55.3, 51.5, 47.0, 40.3, 30.5. HRMS (ESI) m/z calculated for $C_{27}H_{27}N_2O_3S$ $[M+H]^+$ 459.1737, found: 459.1740. HPLC analysis (OD-H, nHexane: i-Propanol = 95:5 as eluent, 0.4 mL/min, 254 nm) indicated 99% ee: tR (minor) = 53.9 min, tR (major) = 55.6 min.



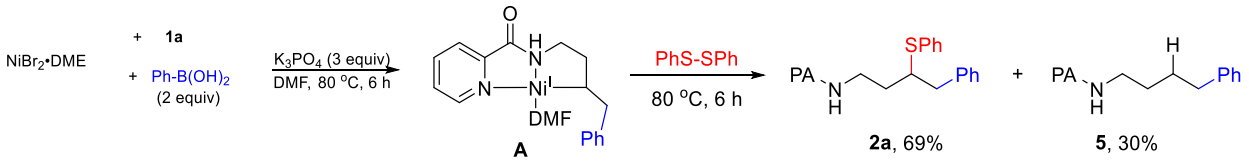
Supplementary Figure 5. HPLC spectra for **4c**

6. Radical scavenger experiment

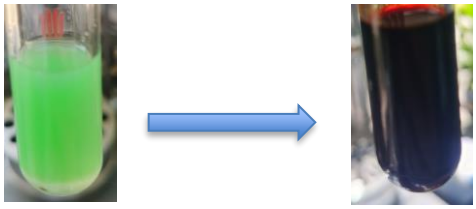


Procedure: To a 10 mL Schlenk tube were added $NiBr_2$•DME (0.04 mmol, 20 mol%), K_3PO_4 (0.6 mmol, 3 eq), alkene substrate (0.2 mmol, 1.0 eq), diaryl sulfide substrates (0.5 mmol, 2.5 eq), phenylboronic acid (0.3 mmol, 1.5 eq), additive (0.2mmol, 1 equiv) and DMF/MeOH (1 mL /0.5 mL). The resulting mixture was stired for 18 h at 100 °C. The products were separately obtained with a isolated yield of 90% and 88%.

7. Control experiment with *in-situ* prepared Ni(I) intermediate



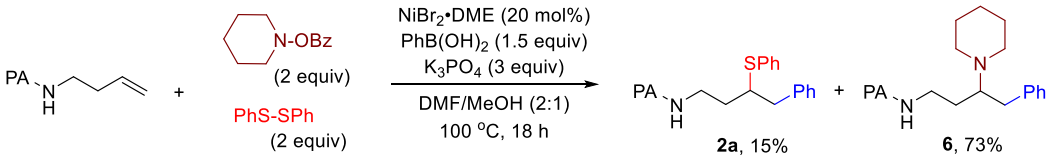
In a nitrogen-filled glovebox, DMF (2 mL) was added to a 10 mL schlenk tube that contained **1a** (35.2 mg, 0.2 mmol), phenylboronic acid (48.8 mg, 0.4mmol), K_3PO_4 (127.3 mg, 0.6 mmol) and $NiBr_2$·DME (61.7 mg, 0.2 mmol). The mixture was stirred for 6 h at 80 °C. During the reaction, the color of the solution changes from green to blood red. Next, diphenyl disulfide (109.2 mg, 2.5 eq, 0.5 mmol) was added to this solution and the reaction continued for 6 h. The products were afforded **2a** in 69% yield along with 30% hydroarylation product **5**.



Color of Ni(I) intermediate **A**

Supplementary Figure 6. Color changes during the *in-situ* preparation of **A**.

8. Competition experiment: arylsulfenylation *vs* arylamination



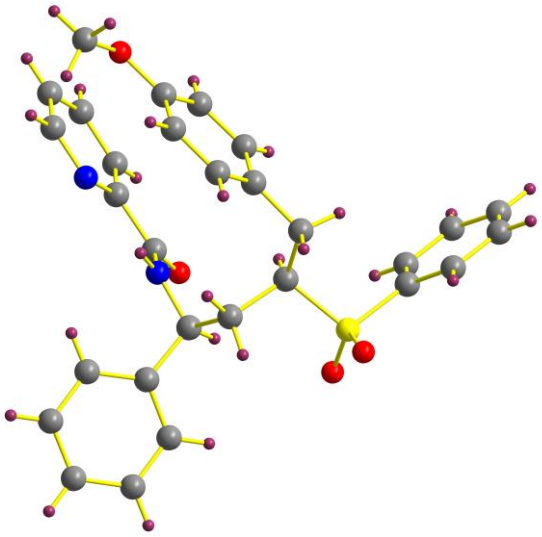
According to the reviewer's suggestions, we have run a competition experiment between piperidino benzoate and PhSSPh as the substrate to compare the coupling rate of amination and thiolation. The reaction afforded the arylsulfenylation product in 15% yield and arylamination[1] product in 73% yield, indicating that amination proceeds much faster than thiolation, and the lower coupling rate of thiolation with aryl disulfides might be one factor in determining the diastereoselectivity.

Procedure: In an argon-filled glovebox, $NiBr_2$•DME (0.04 mmol, 20 mol%), K_3PO_4 (0.6 mmol, 3.0 eq), alkene substrate (0.2 mmol, 1.0 eq), phenylboronic acid (0.3 mmol, 1.5 eq), phenyl disulfide (0.4 mmol, 2 eq), piperidino benzoate (0.4 mmol, 2 eq), DMF/MeOH (1 mL /0.5 mL) were added to a 10 mL schlenk flask. The reaction mixture was stirred at 100 °C for 18 h.

9. X-ray crystallographic data

Single crystals for X-ray studies were grown by slow evaporation of a solution of compound **2ap'** in a mixture of petroleum ether and ethyl acetate at room temperature. X-Ray structural analysis of single crystal **2ap'** was obtained to confirm the absolute configuration. The X-ray data of **2ap'** is deposited in the Cambridge Crystallographic Data Centre with a number of **CCDC 2143338**.

Crystal Data for $C_{29}H_{28}N_2O_4S$ (M =500.59 g/mol): monoclinic, space group $P2_1/n$ (no. 14), a = 9.65941(16) Å, b = 24.1219(4) Å, c = 10.92538(17) Å, β = 97.3866(15)°, V = 2524.52(7) Å^3, Z = 4, T = 113.8(6) K, μ(CuKα) = 1.451 mm^{-1}, *Dcalc* = 1.317 g/cm^3, 9747 reflections measured (7.33° ≤ 2Θ ≤ 134.144°), 4508 unique (R_{int} = 0.0203, R_{sigma} = 0.0240) which were used in all calculations. The final R_1 was 0.0371 (I > 2σ(I)) and wR_2 was 0.0972 (all data).



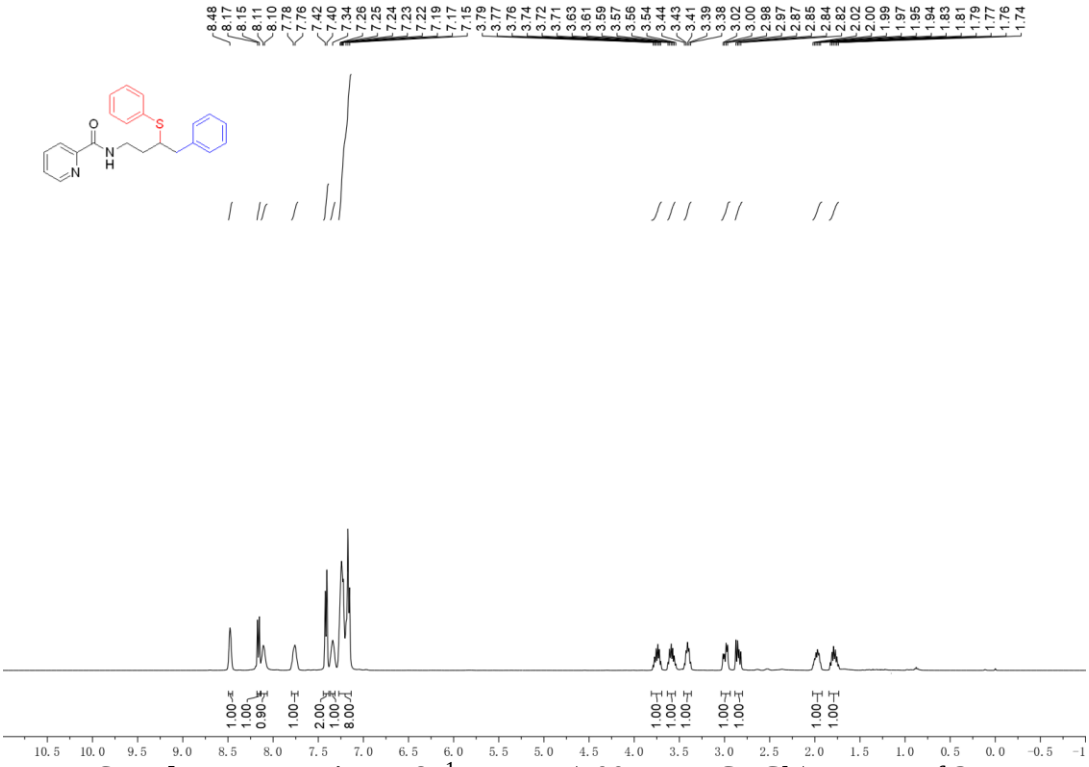
Supplementary Figure 7. X-ray structure of compound **2ap'** (CCDC 2143338)

Supplementary Table 1. Crystal data and structure refinement for **2ap'**

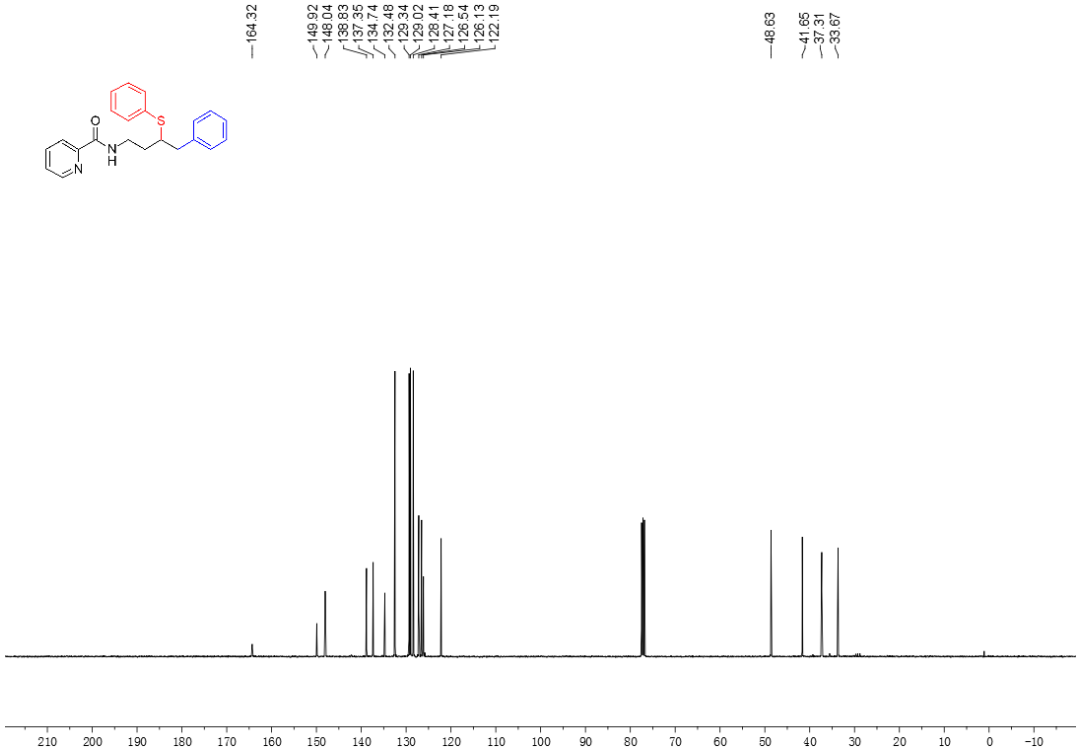
Identification code	**2ap'**
Empirical formula	$C_{29}H_{28}N_2O_4S$
Formula weight	500.59
Temperature/K	113.8(6)
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	9.65941(16)
b/Å	24.1219(4)
c/Å	10.92538(17)
α/°	90
β/°	97.3866(15)
γ/°	90
Volume/Å^3	2524.52(7)
Z	4

ρ_{calc}g/cm^3	1.317
μ/mm^{-1}	1.451
F(000)	1056.0
Crystal size/mm^3	0.3 × 0.25 × 0.24
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	7.33 to 134.144
Index ranges	$-11 \leq h \leq 11$, $-28 \leq k \leq 27$, $-13 \leq l \leq 6$
Reflections collected	9747
Independent reflections	4508 [R_{int} = 0.0203, R_{sigma} = 0.0240]
Data/restraints/parameters	4508/0/326
Goodness-of-fit on F^2	1.046
Final R indexes [I>=2σ (I)]	R_1 = 0.0371, wR_2 = 0.0939
Final R indexes [all data]	R_1 = 0.0406, wR_2 = 0.0972
Largest diff. peak/hole / e Å^{-3}	0.30/-0.45

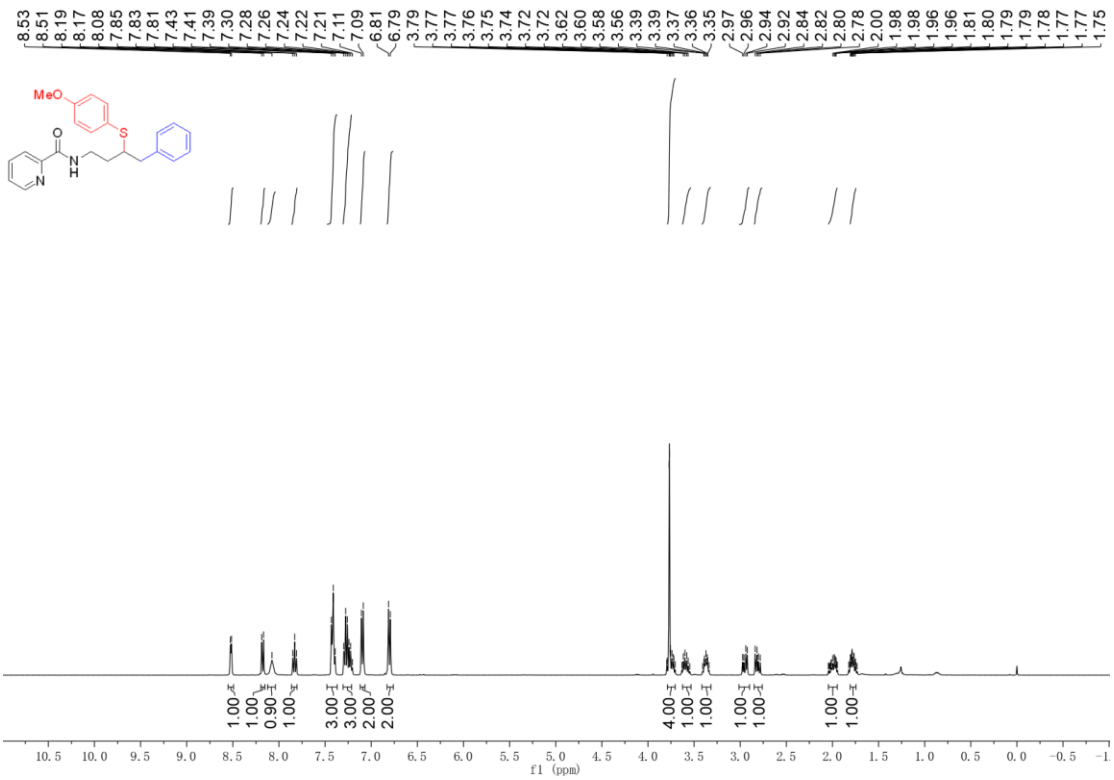
10. NMR spectra



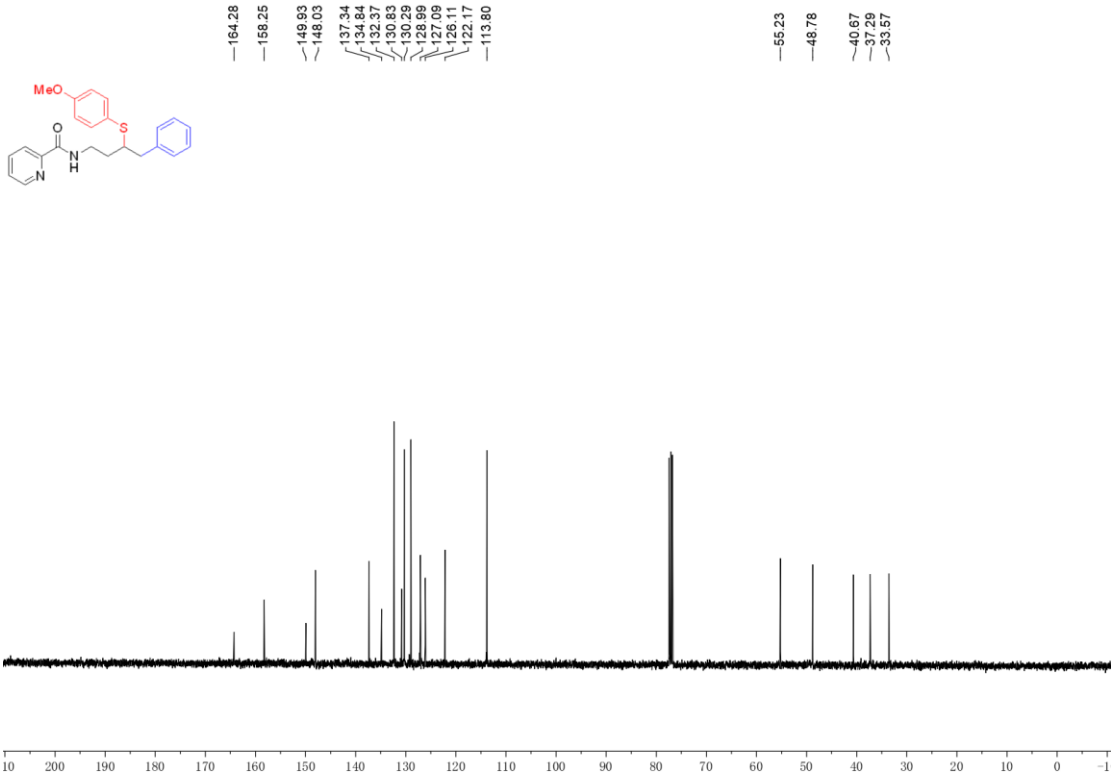
Supplementary Figure 8. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2a**



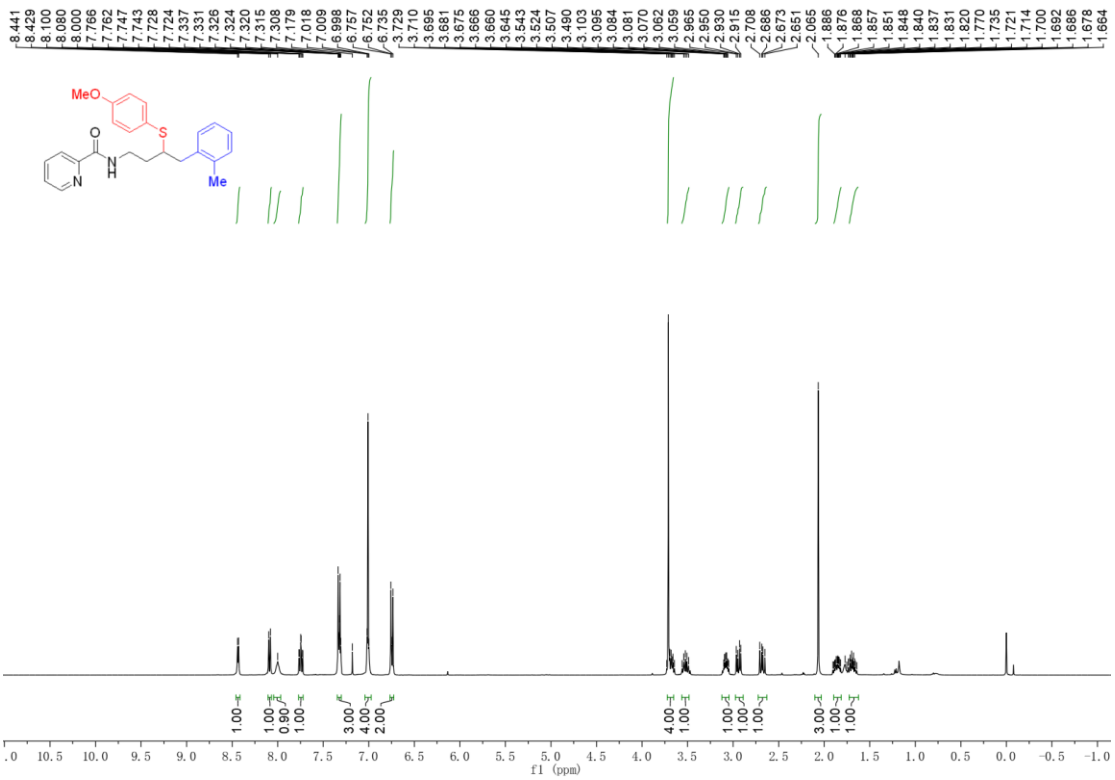
Supplementary Figure 9. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2a**



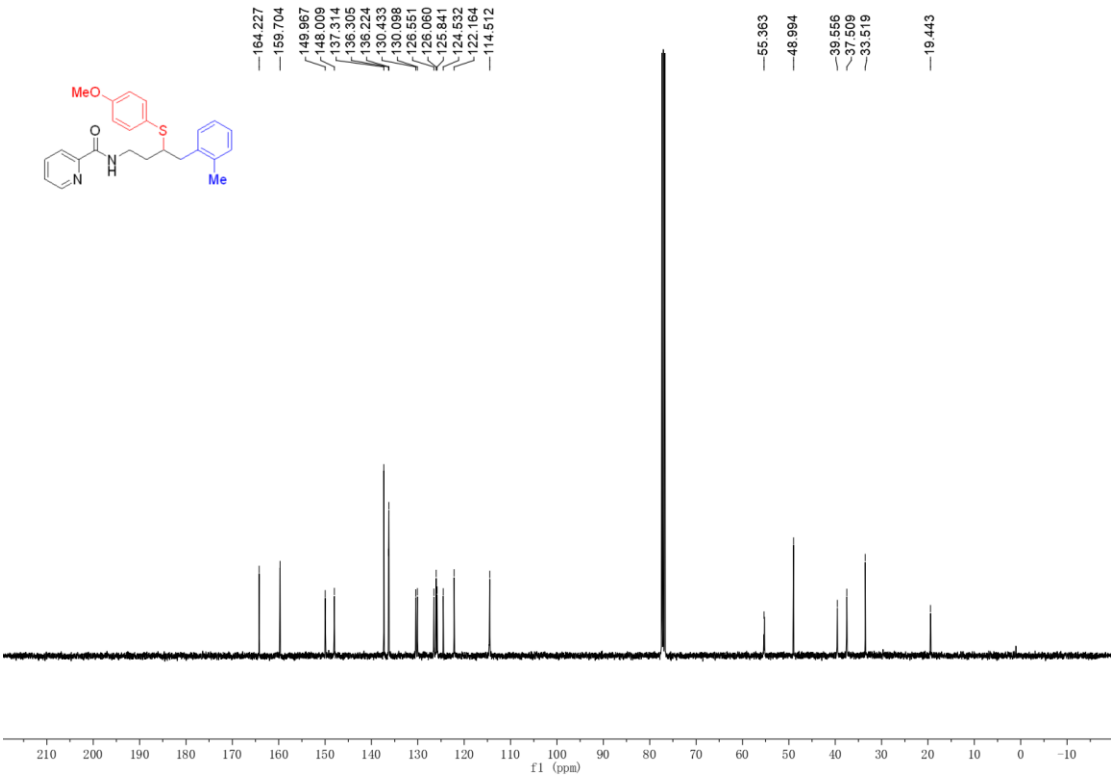
Supplementary Figure 10. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2b**



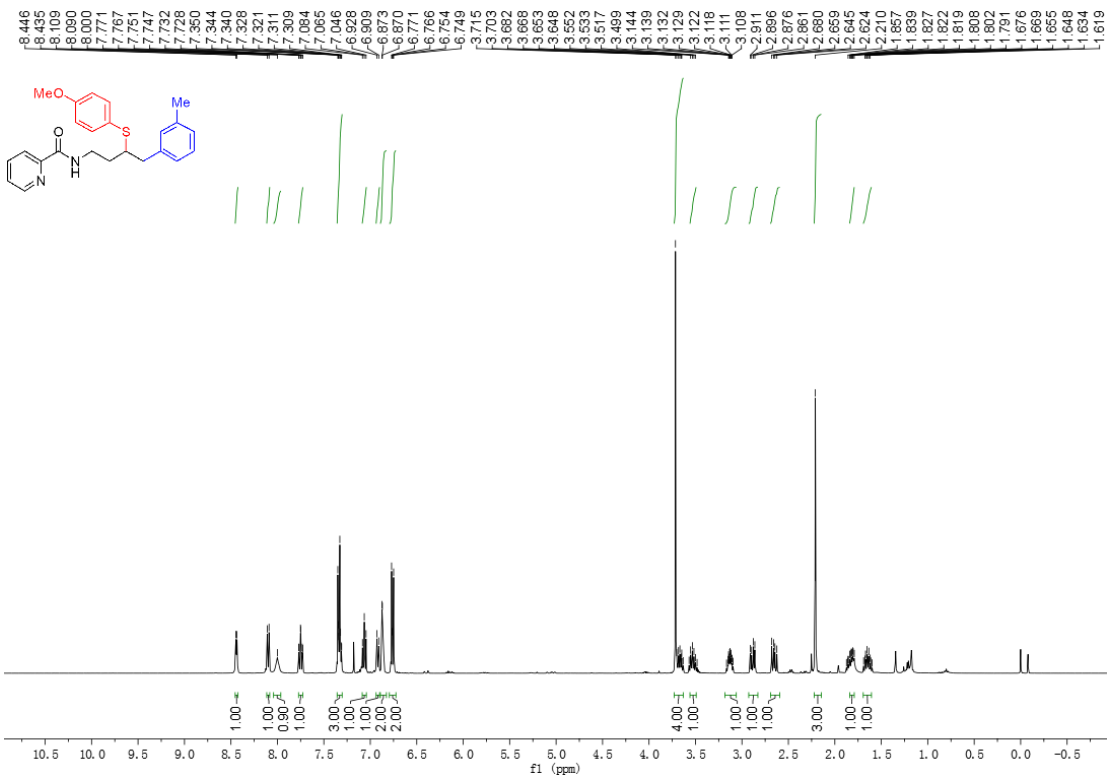
Supplementary Figure 11. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2b**



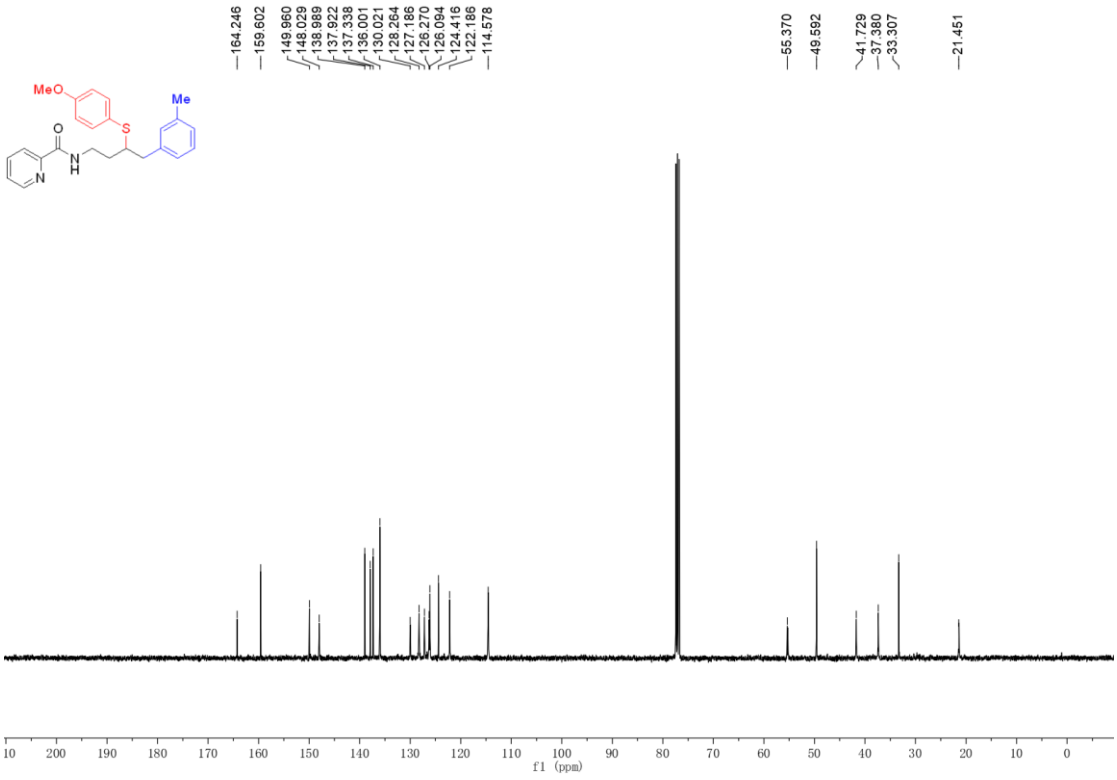
Supplementary Figure 12. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2c**



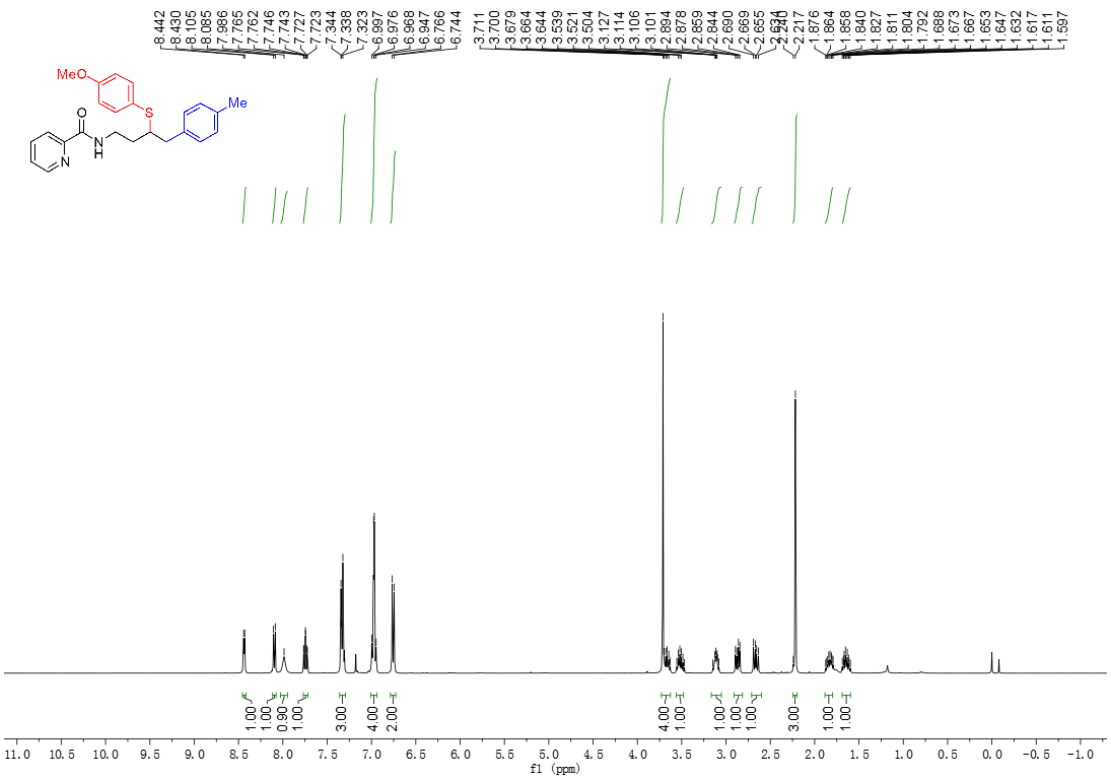
Supplementary Figure 13. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2c**



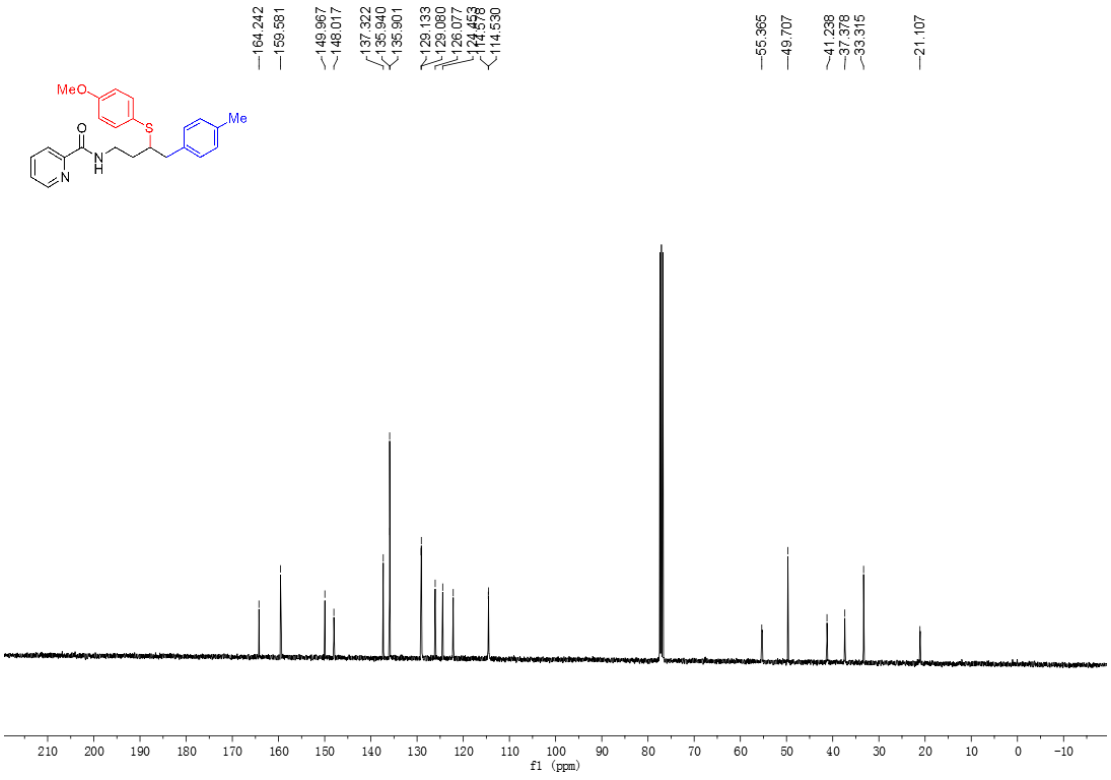
Supplementary Figure 14. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2d**



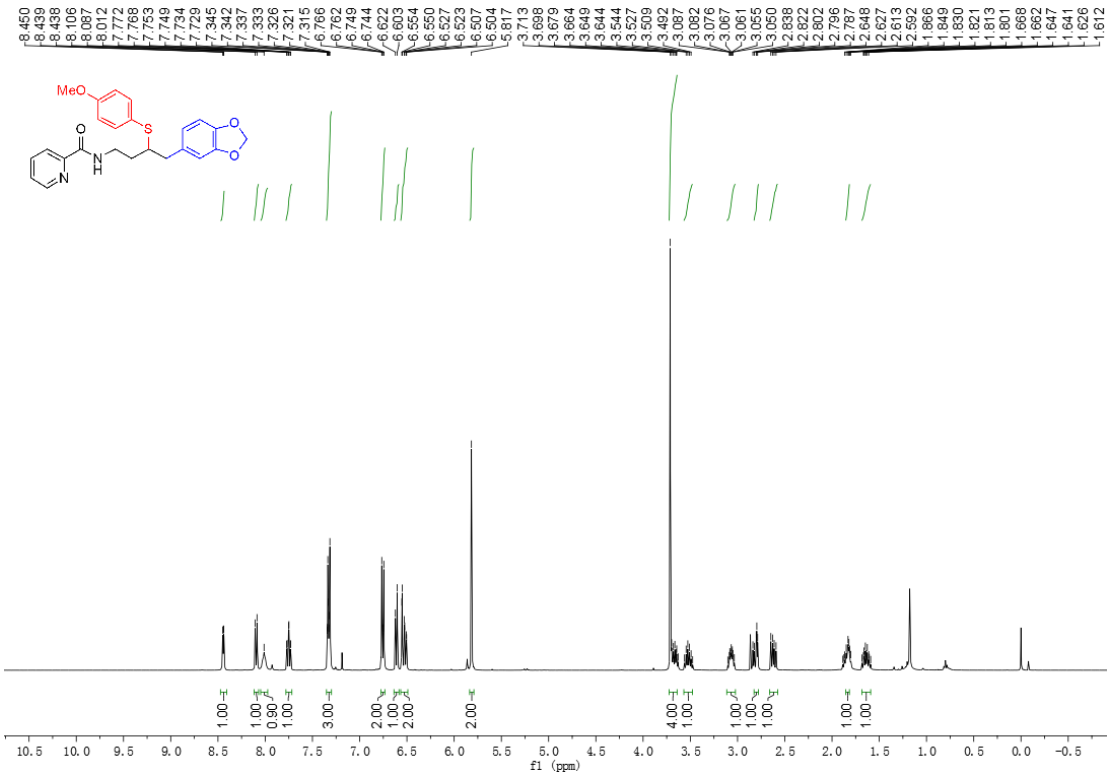
Supplementary Figure 15. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2d**



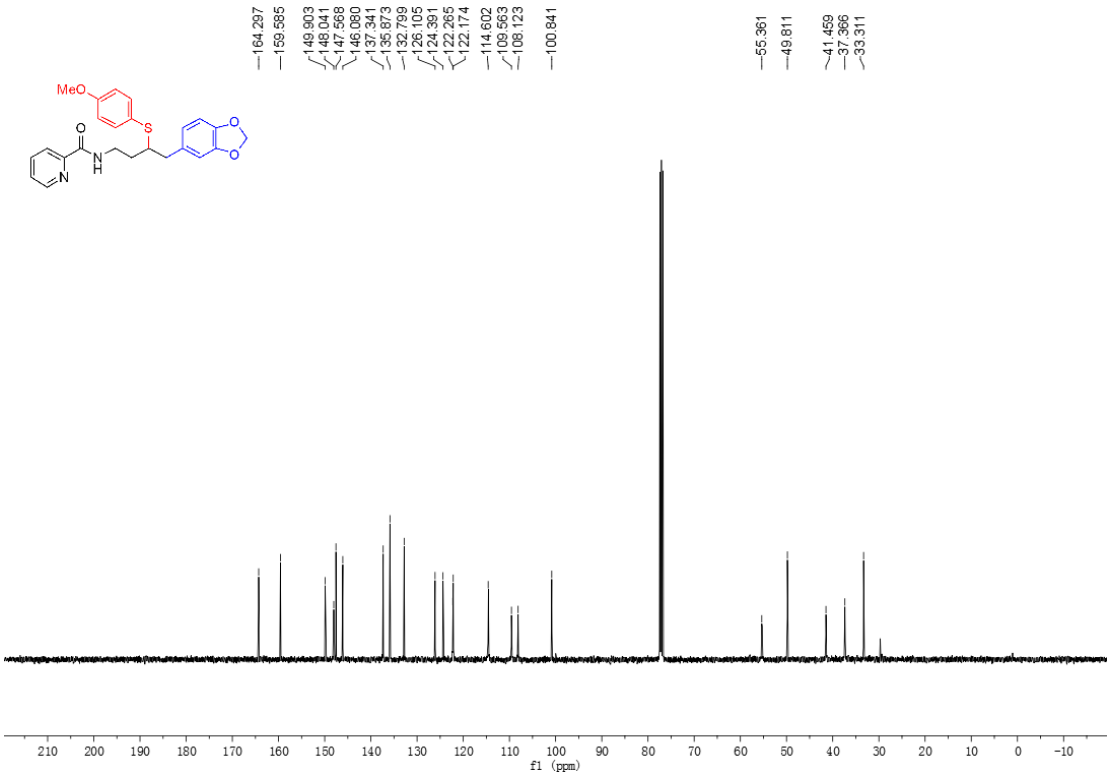
Supplementary Figure 16. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2e**



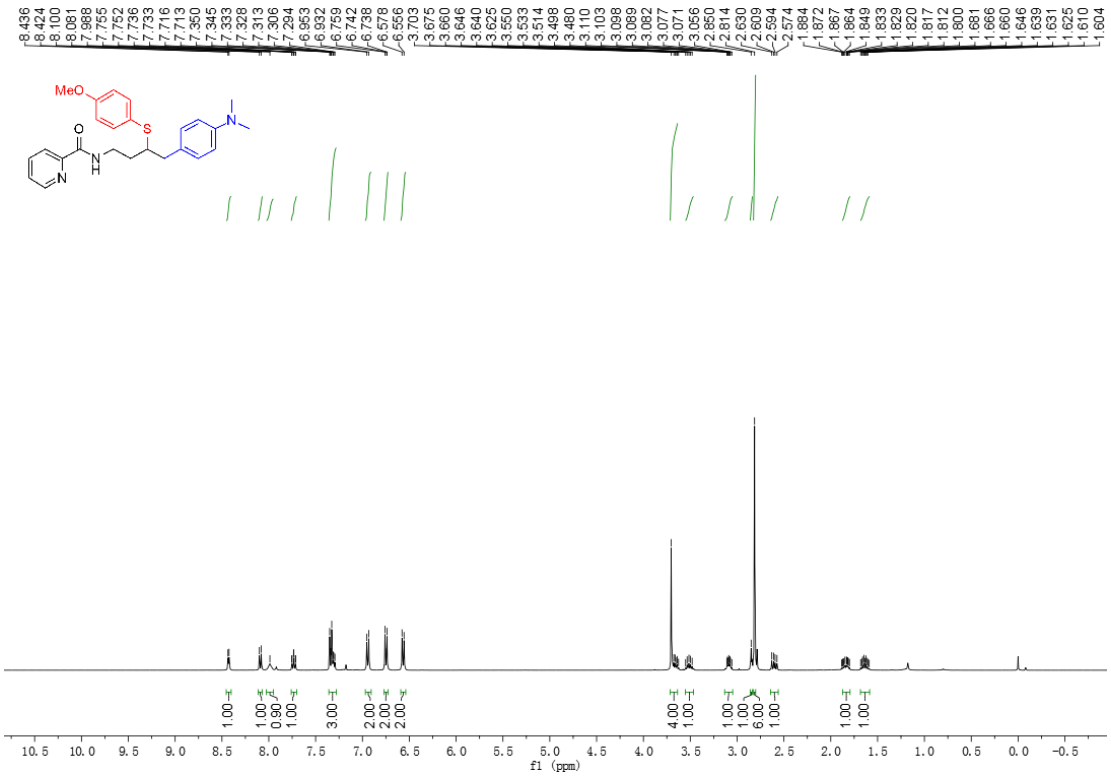
Supplementary Figure 17. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2e**



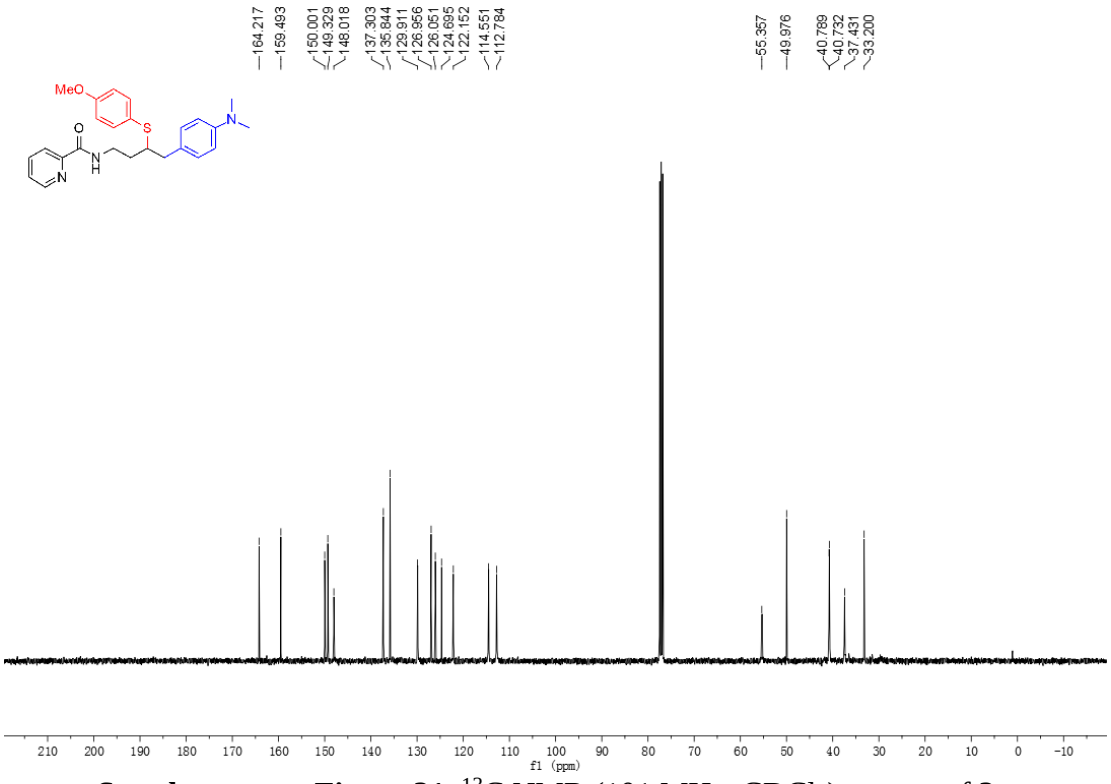
Supplementary Figure 18. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2f**



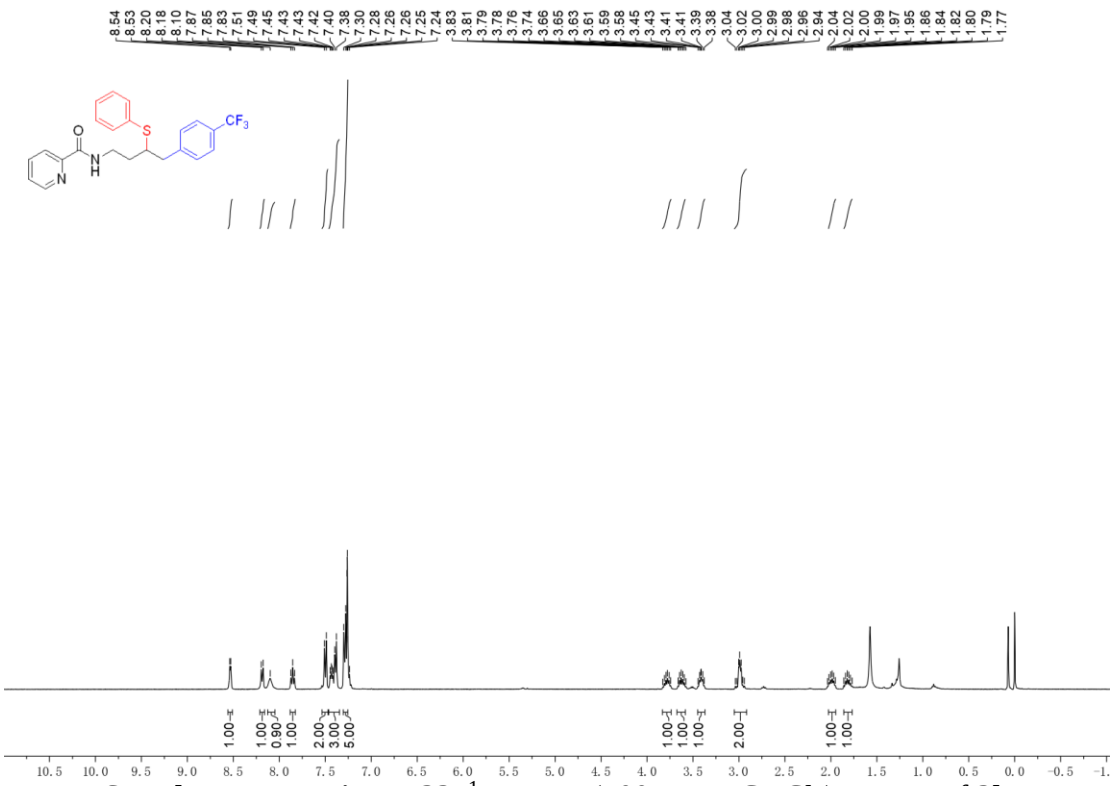
Supplementary Figure 19. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2f**



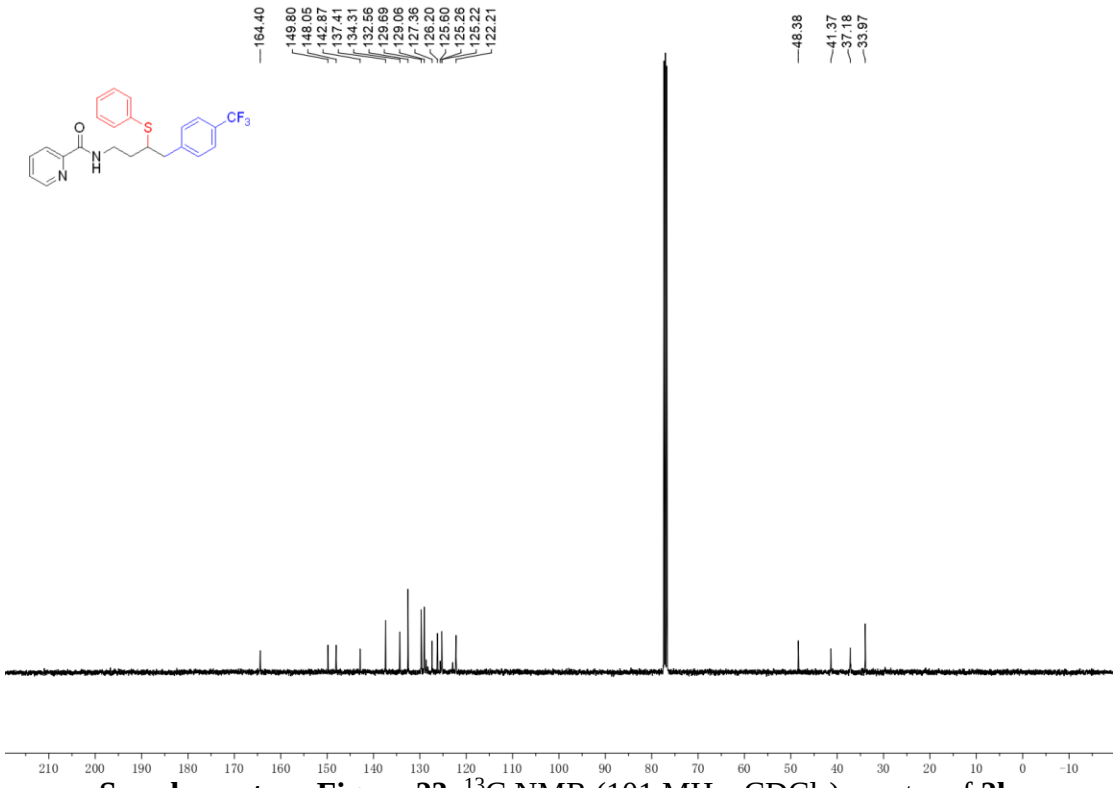
Supplementary Figure 20. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2g**



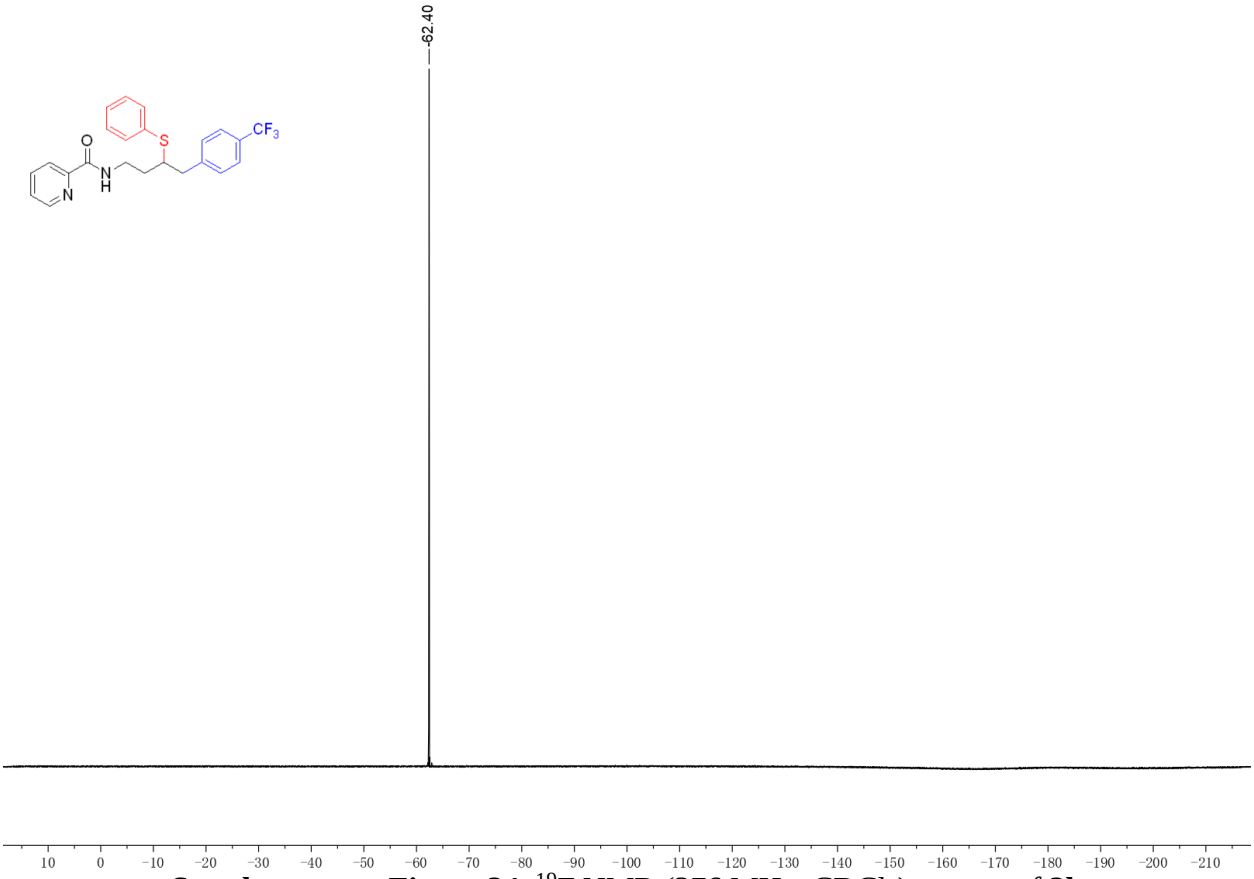
Supplementary Figure 21. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2g**



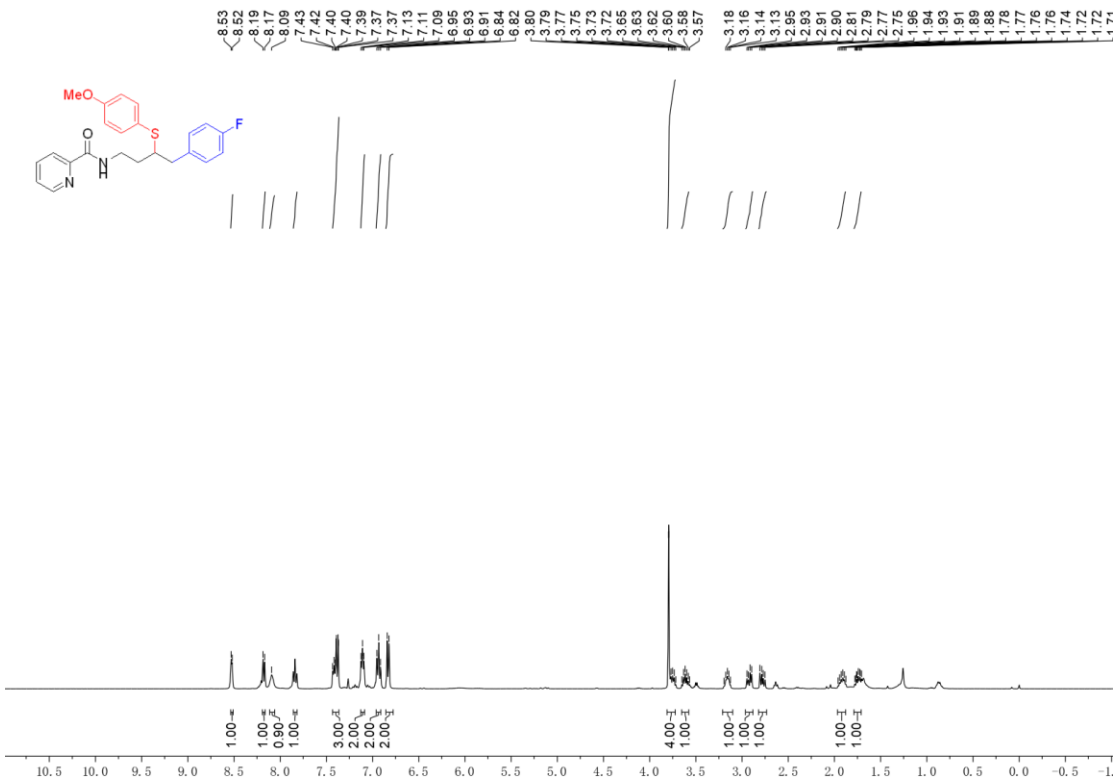
Supplementary Figure 22. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2h**



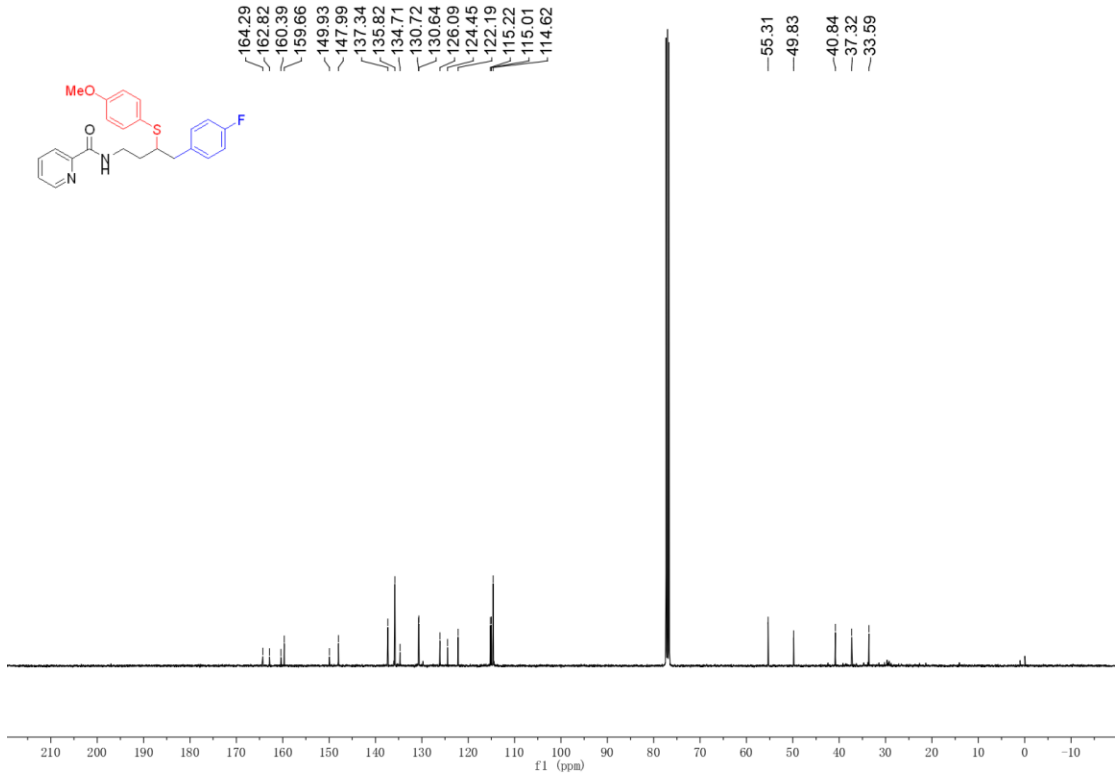
Supplementary Figure 23. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2h**



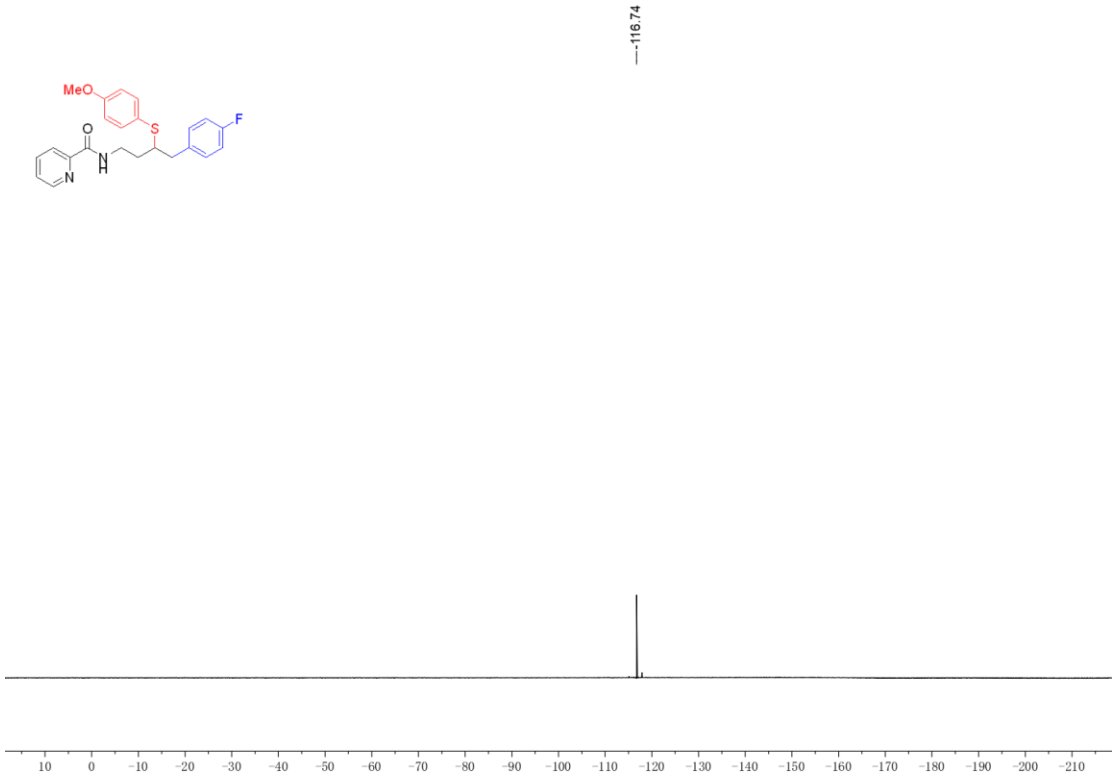
Supplementary Figure 24. ^{19}F NMR (376 MHz, $CDCl_3$) spectra of **2h**



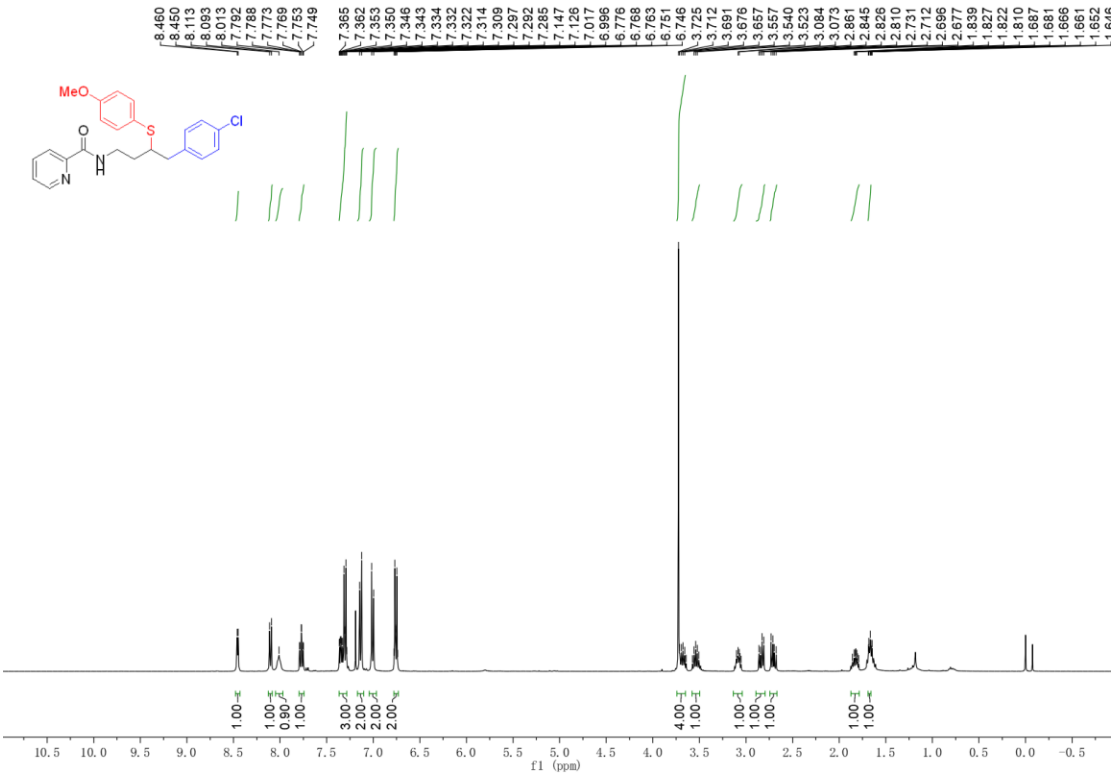
Supplementary Figure 25. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2i**



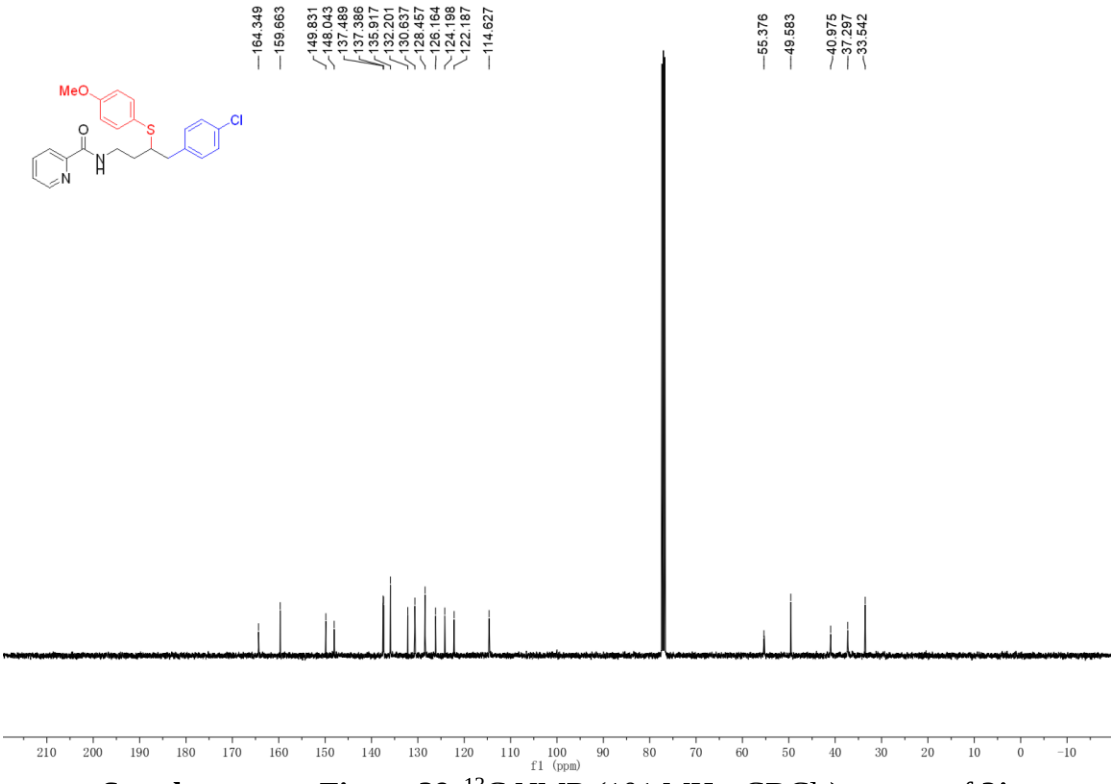
Supplementary Figure 26. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2i**



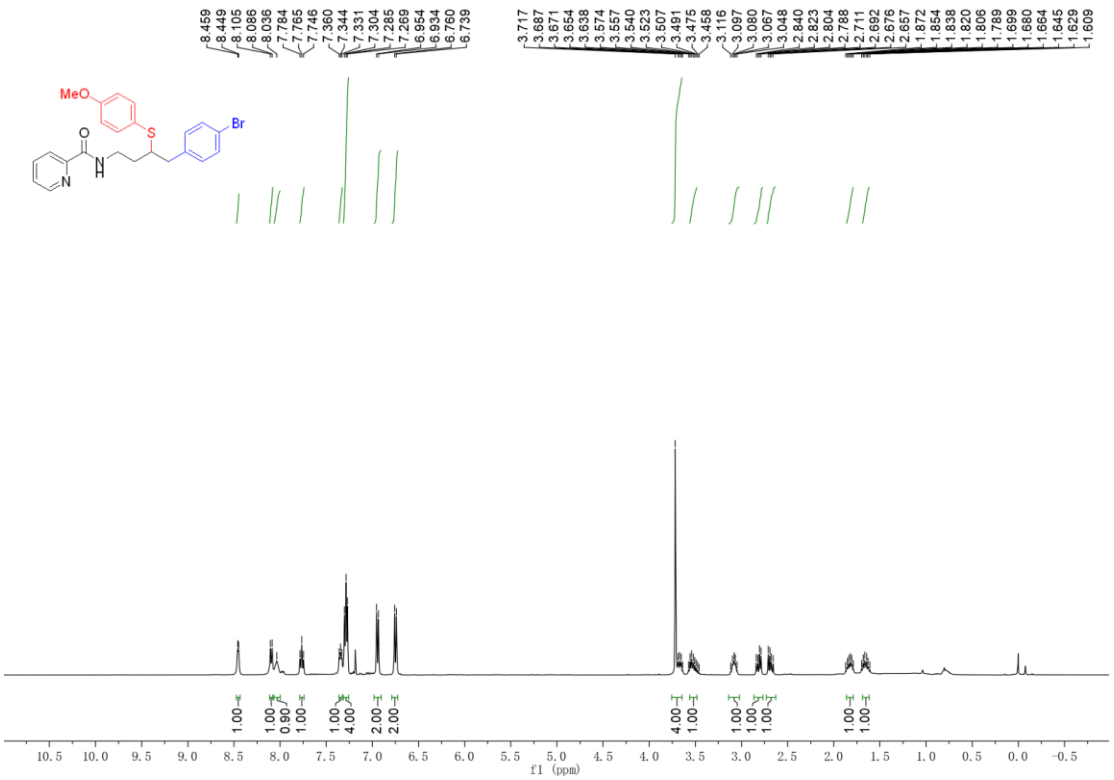
Supplementary Figure 27. ^{19}F NMR (376 MHz, $CDCl_3$) spectra of **2i**



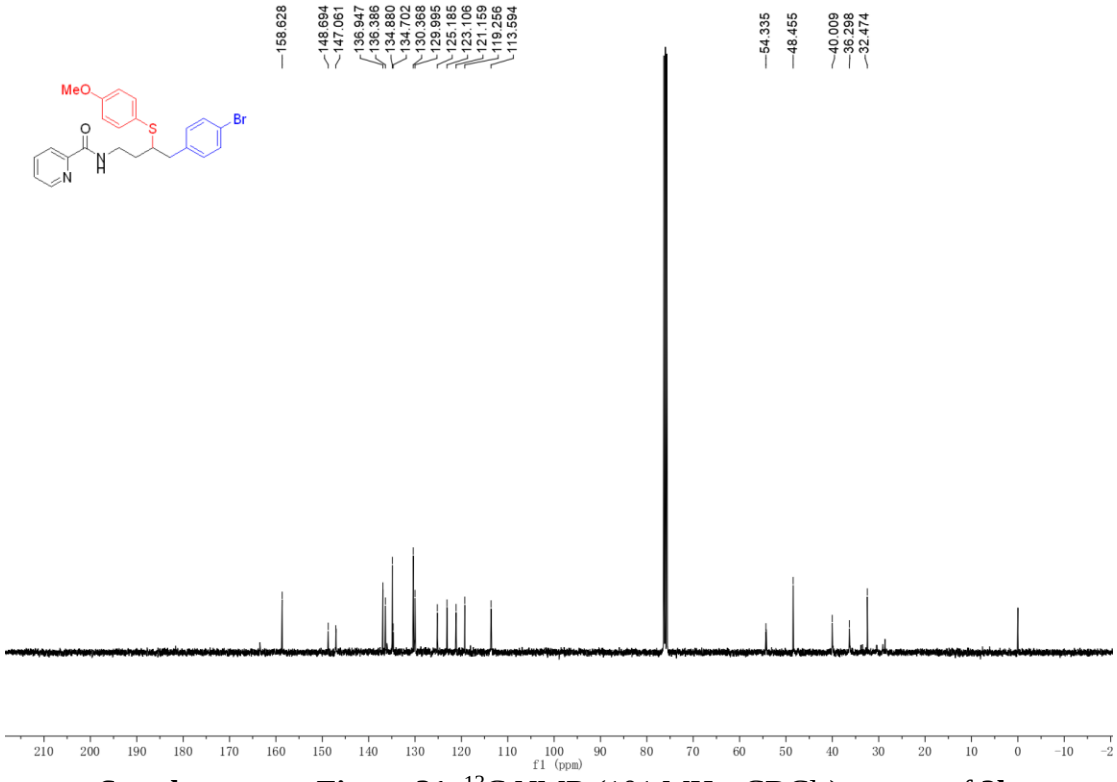
Supplementary Figure 28. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2j**



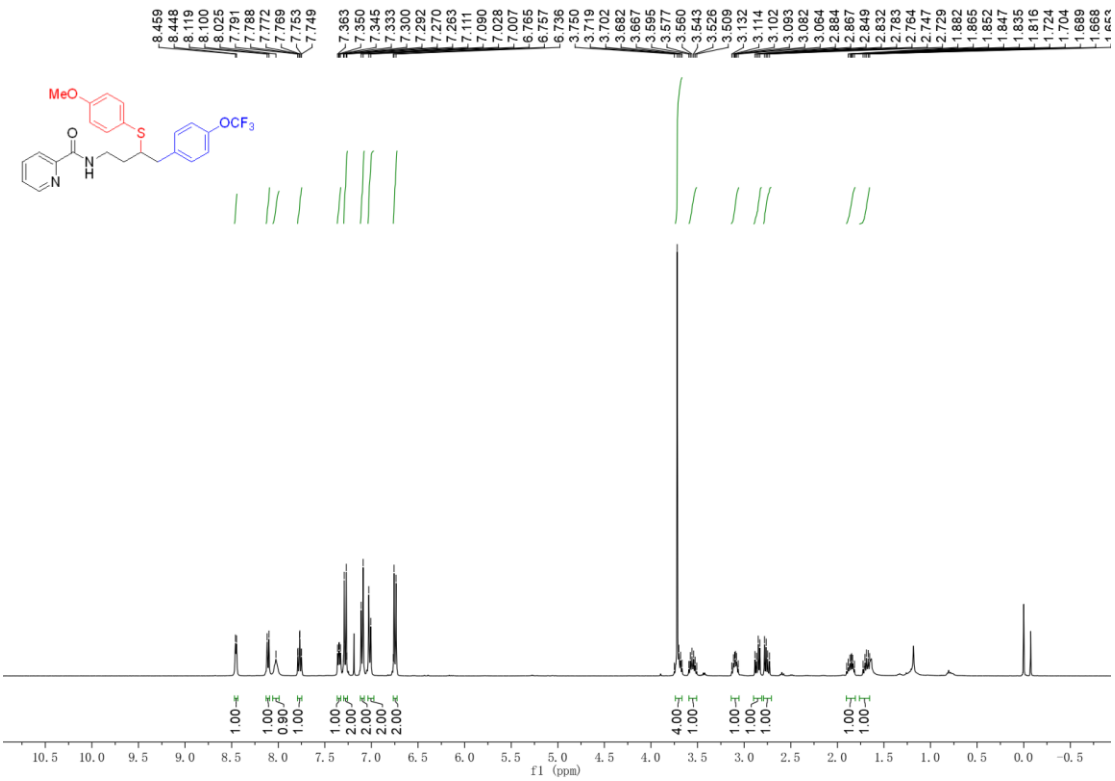
Supplementary Figure 29. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2j**



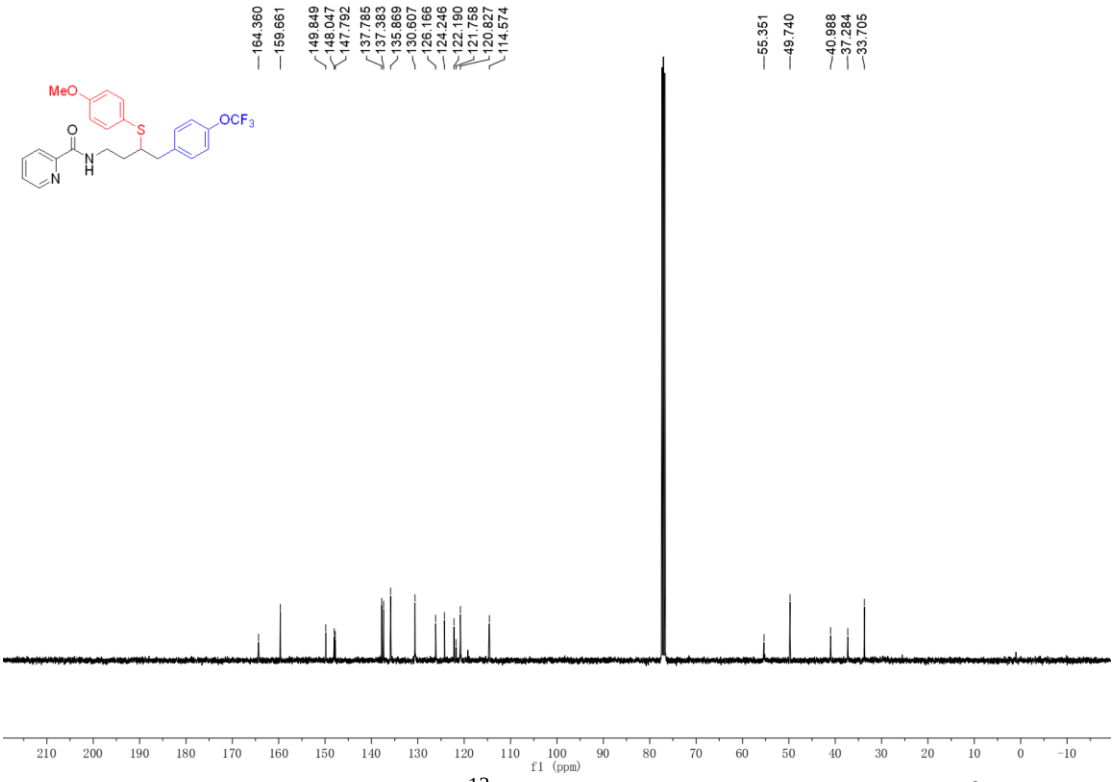
Supplementary Figure 30. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2k**



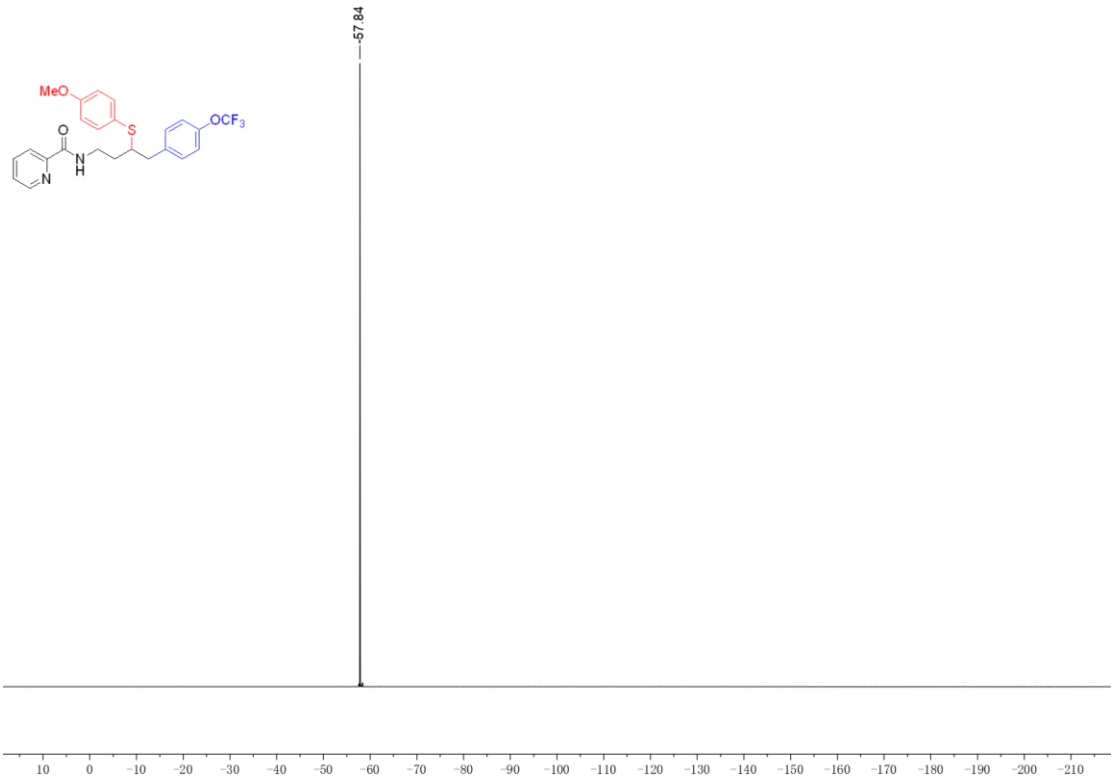
Supplementary Figure 31. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2k**



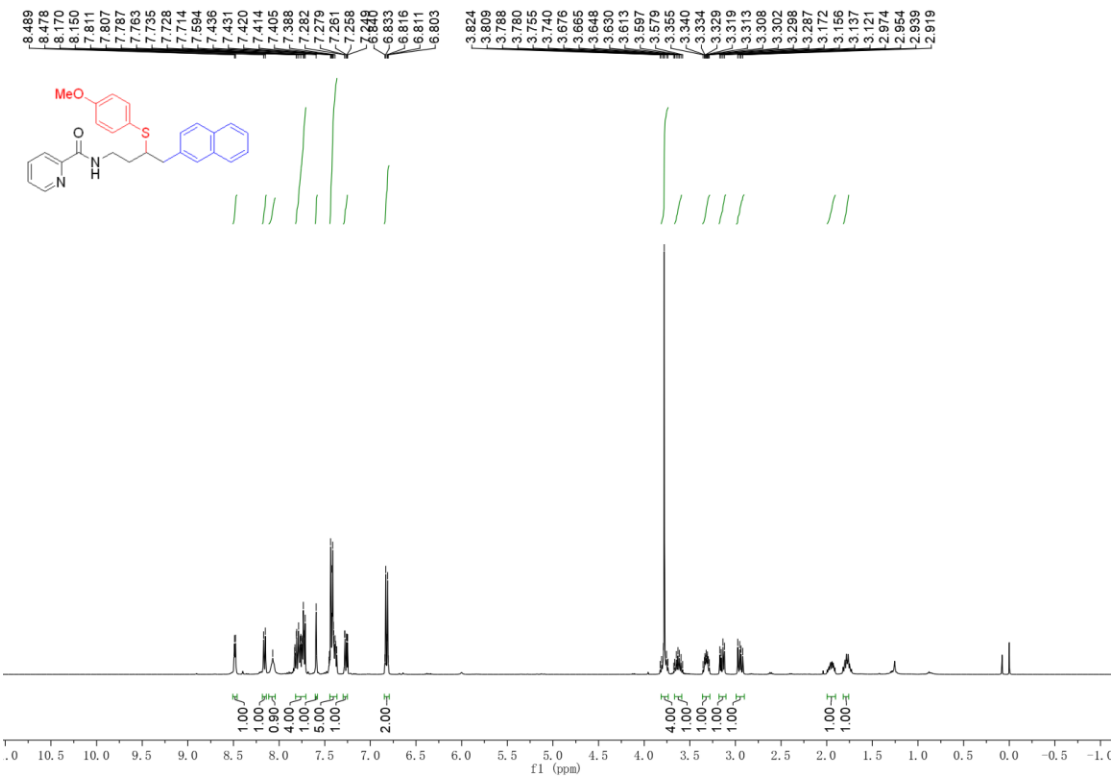
Supplementary Figure 32. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2l**



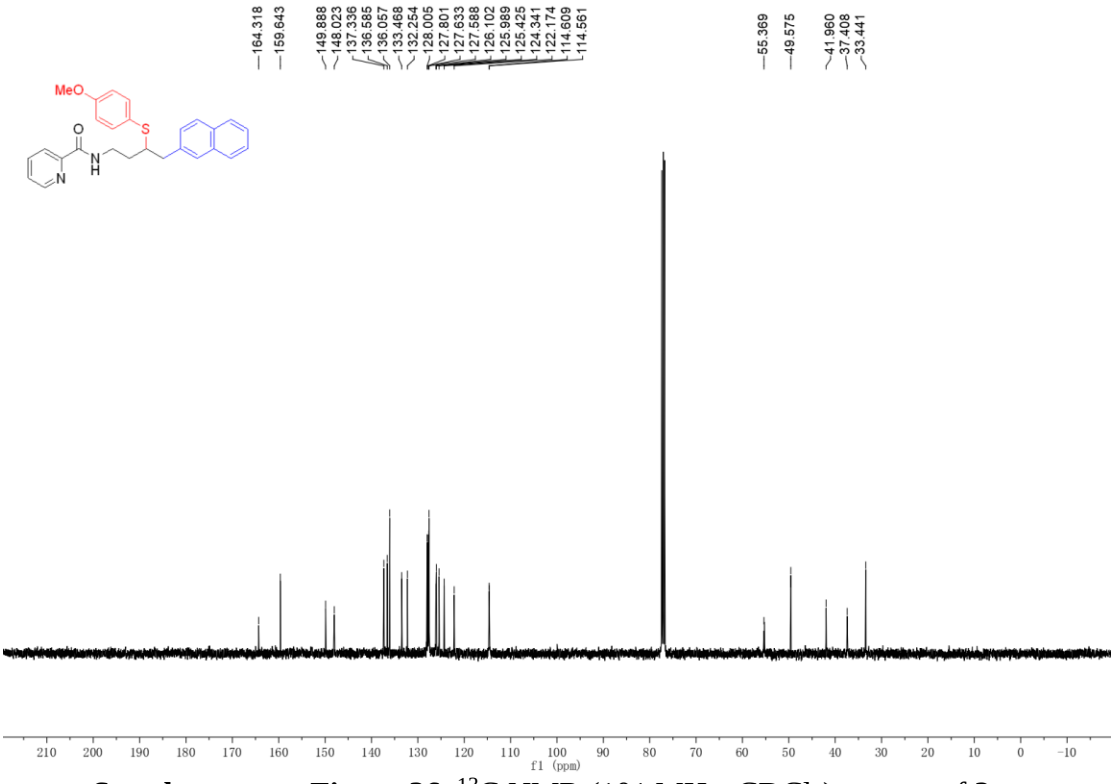
Supplementary Figure 33. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2l**



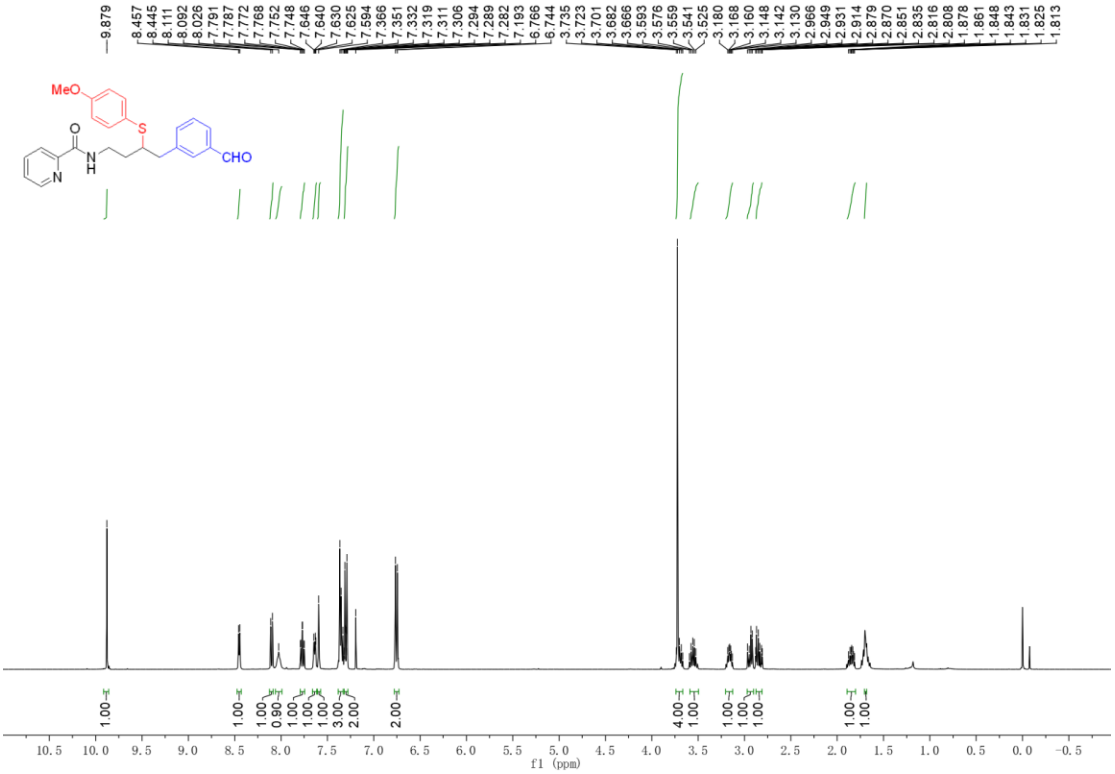
Supplementary Figure 34. ^{19}F NMR (376 MHz, $CDCl_3$) spectra of **2l**



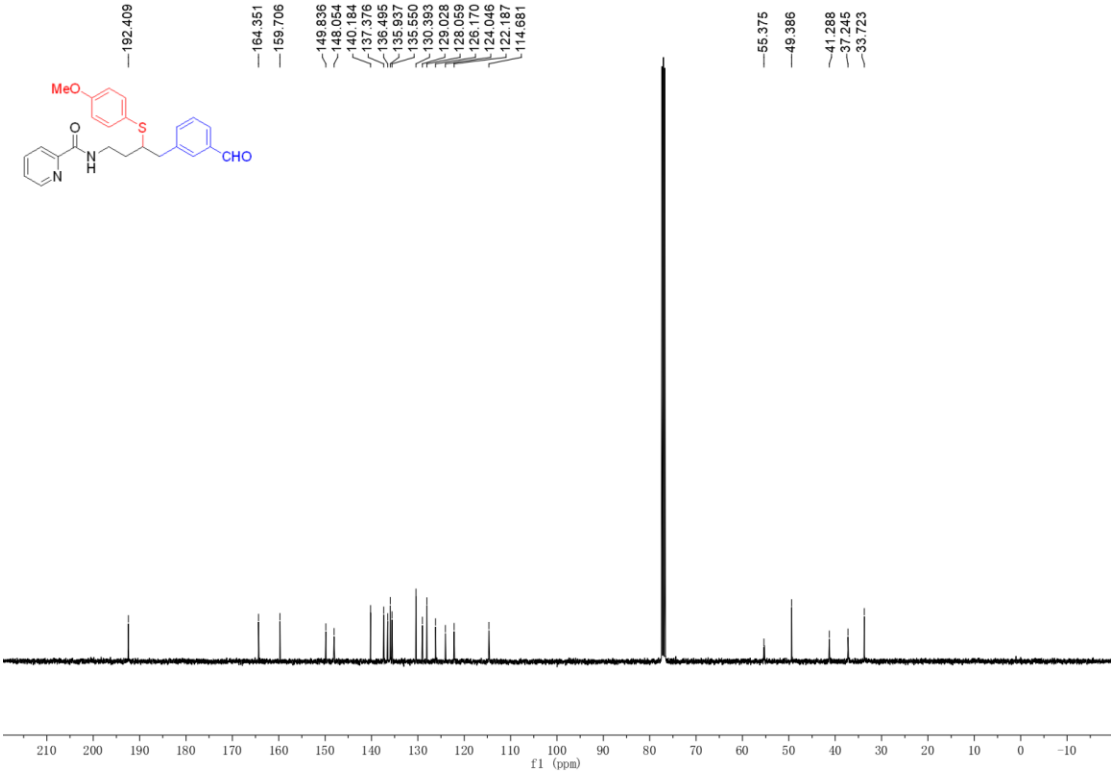
Supplementary Figure 35. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2m**



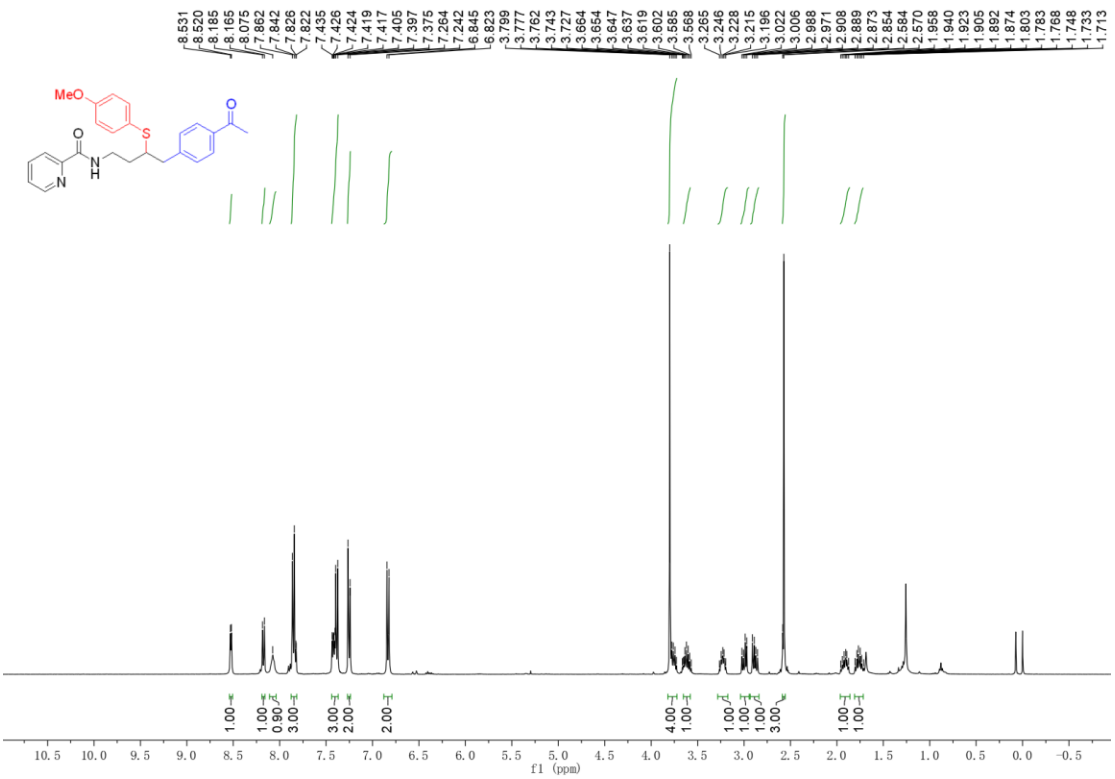
Supplementary Figure 36. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2m**



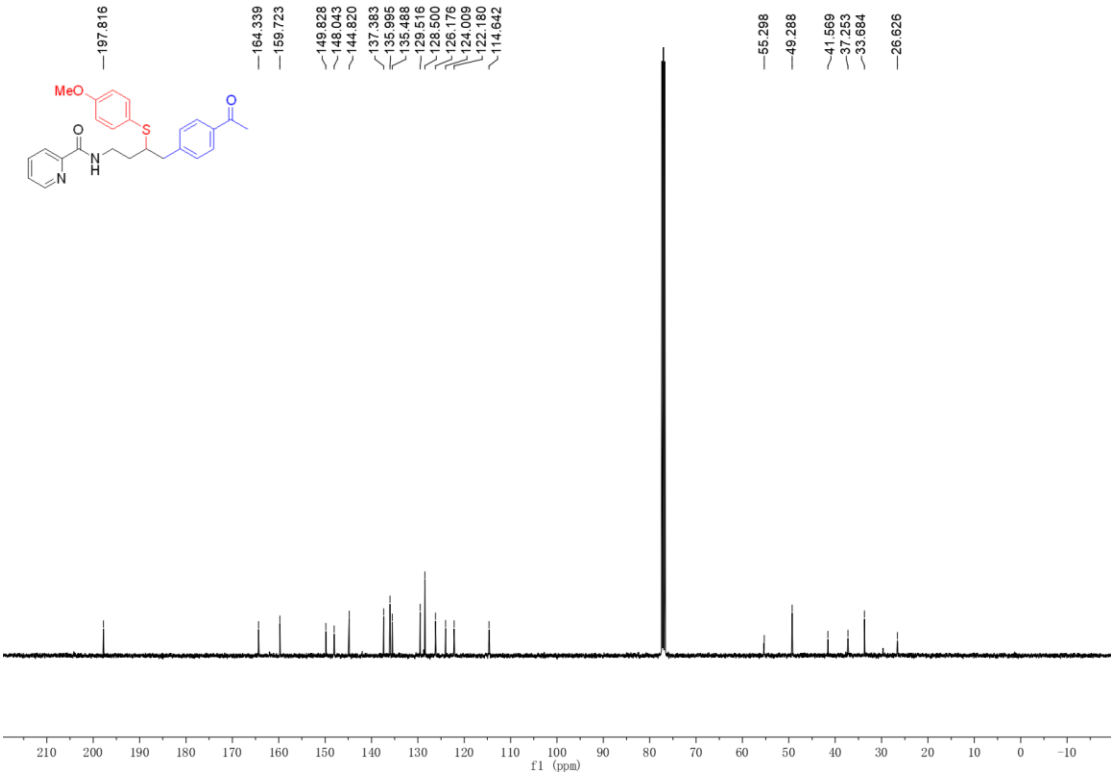
Supplementary Figure 37. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2n**



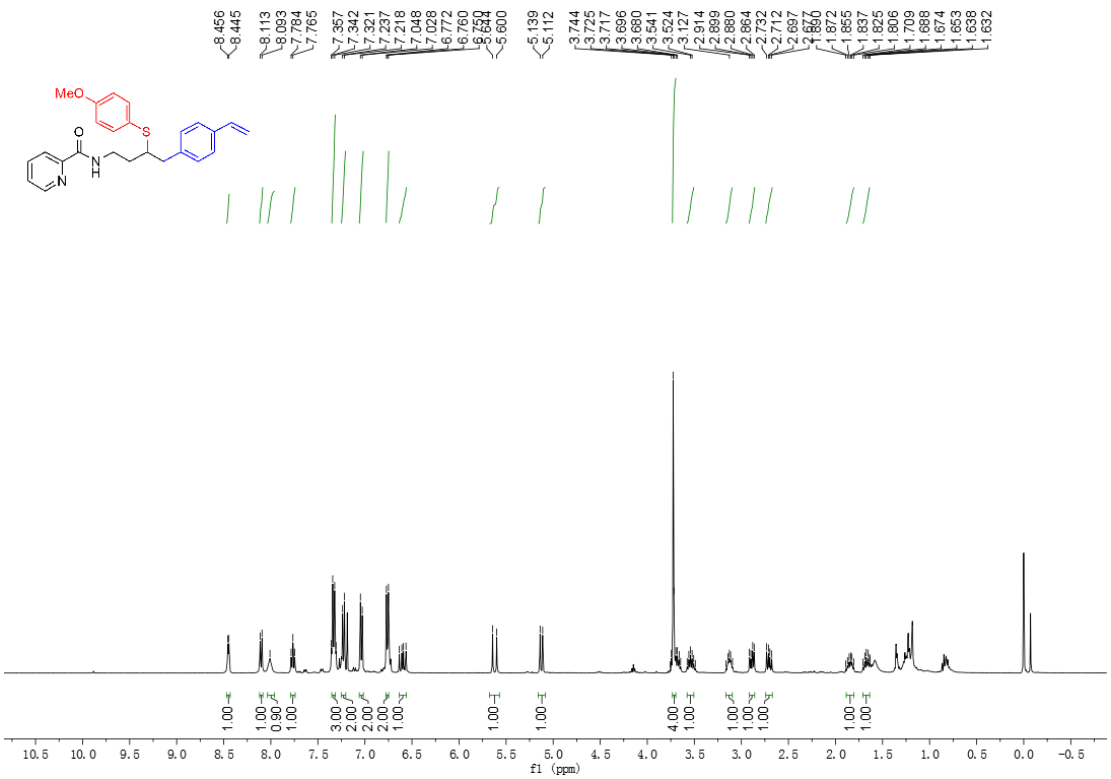
Supplementary Figure 38. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2n**



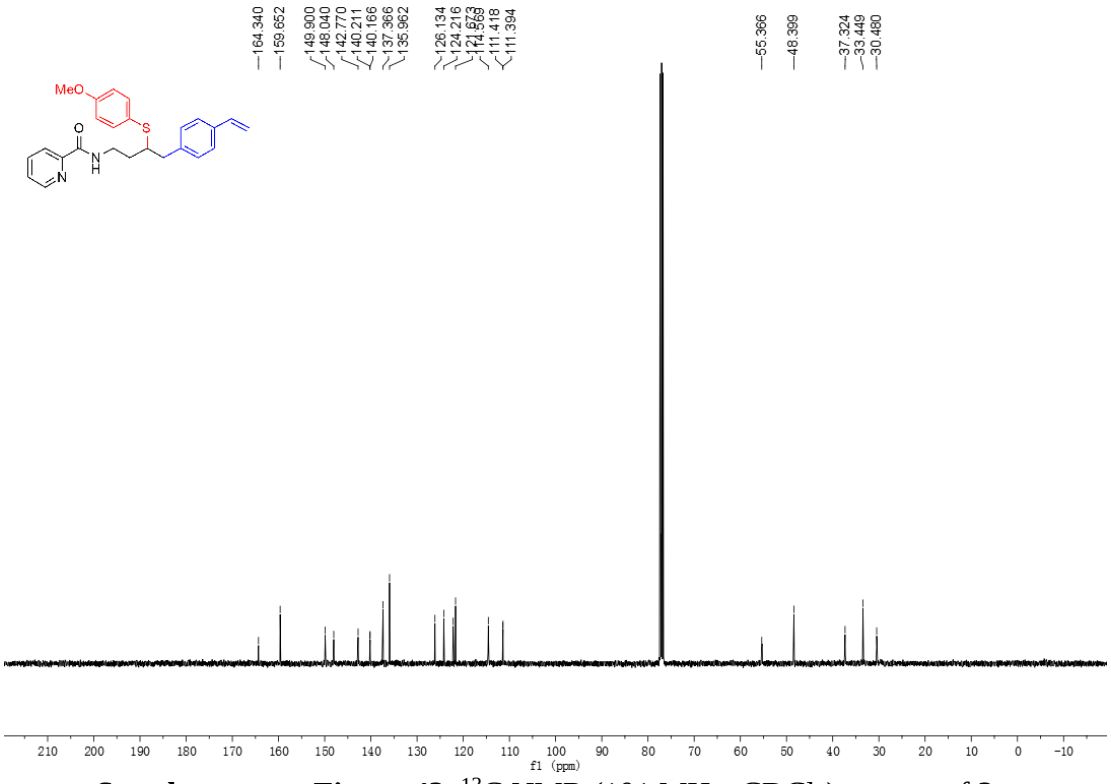
Supplementary Figure 39. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2o**



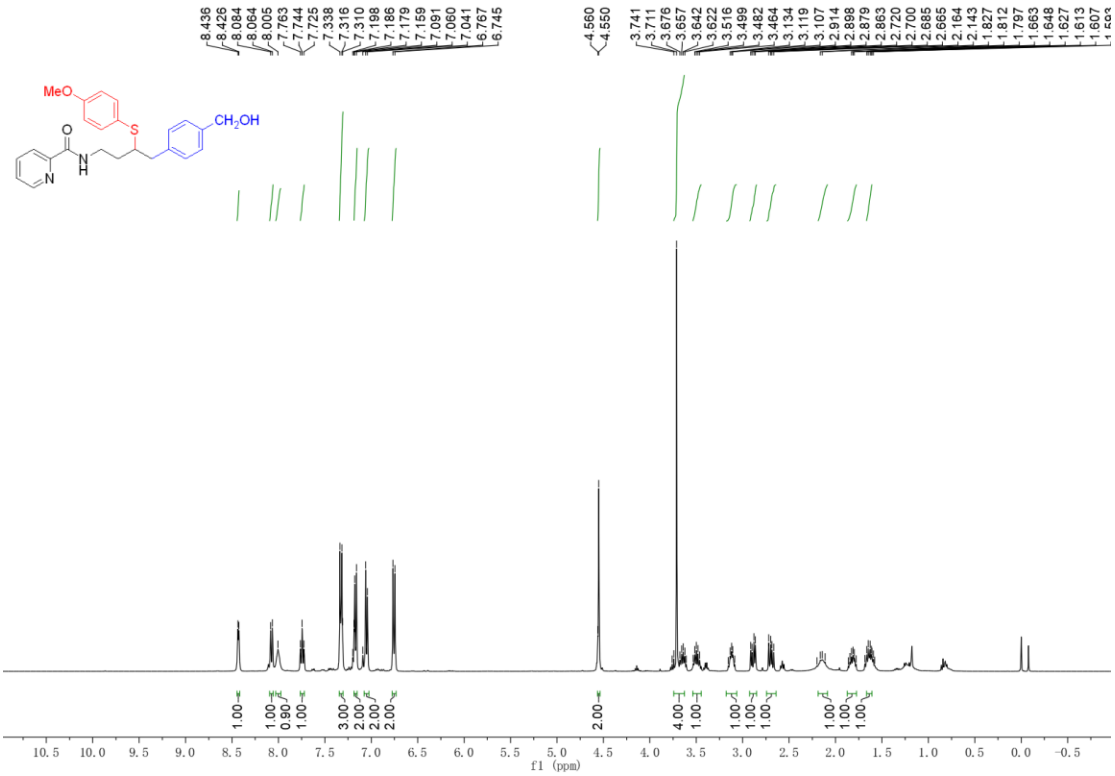
Supplementary Figure 40. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2o**



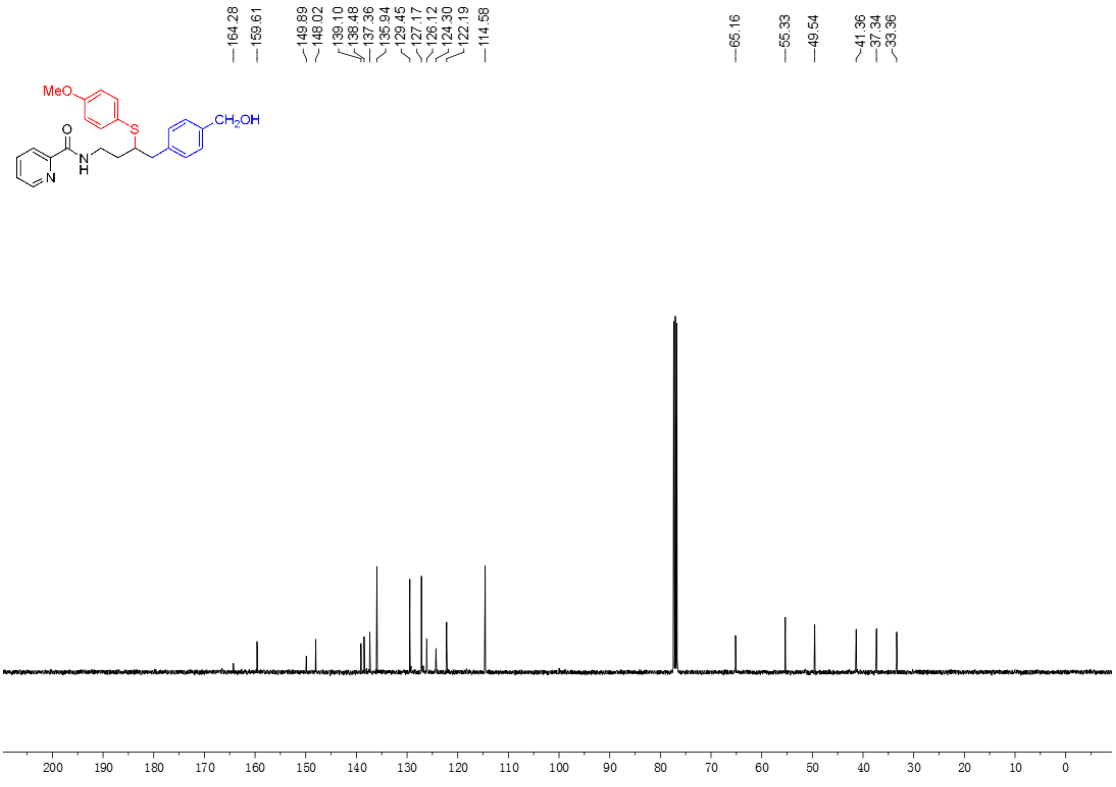
Supplementary Figure 41. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2p**



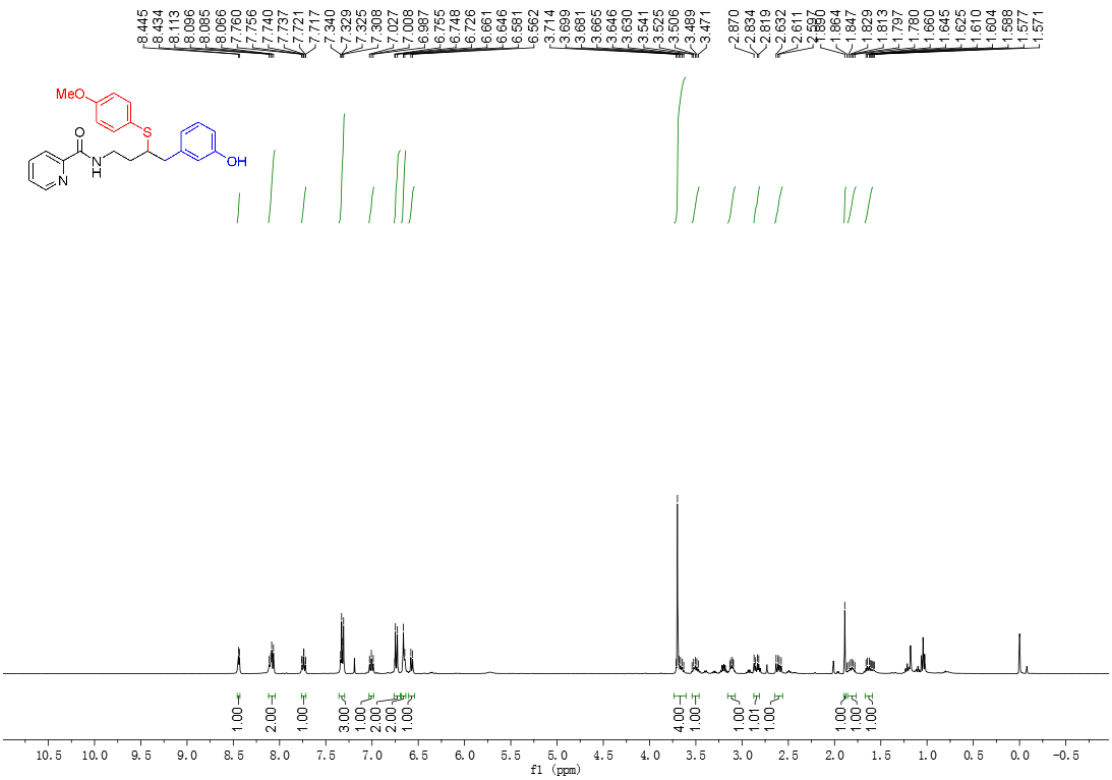
Supplementary Figure 42. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2p**



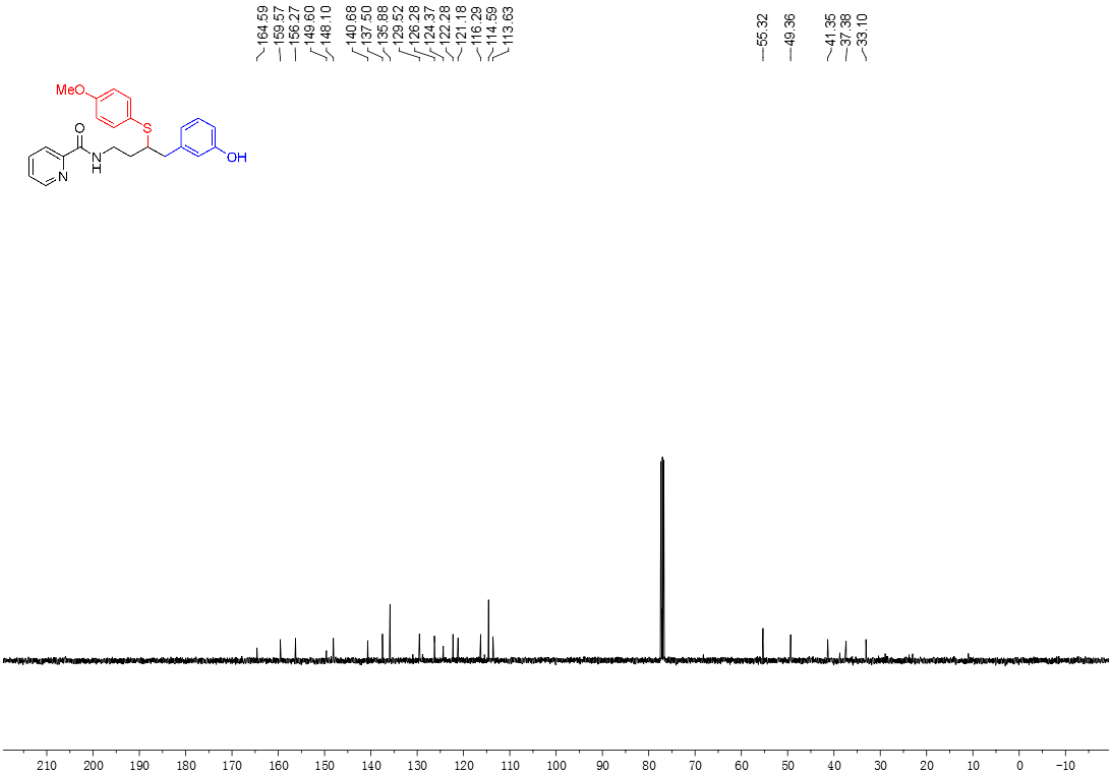
Supplementary Figure 43. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2q**



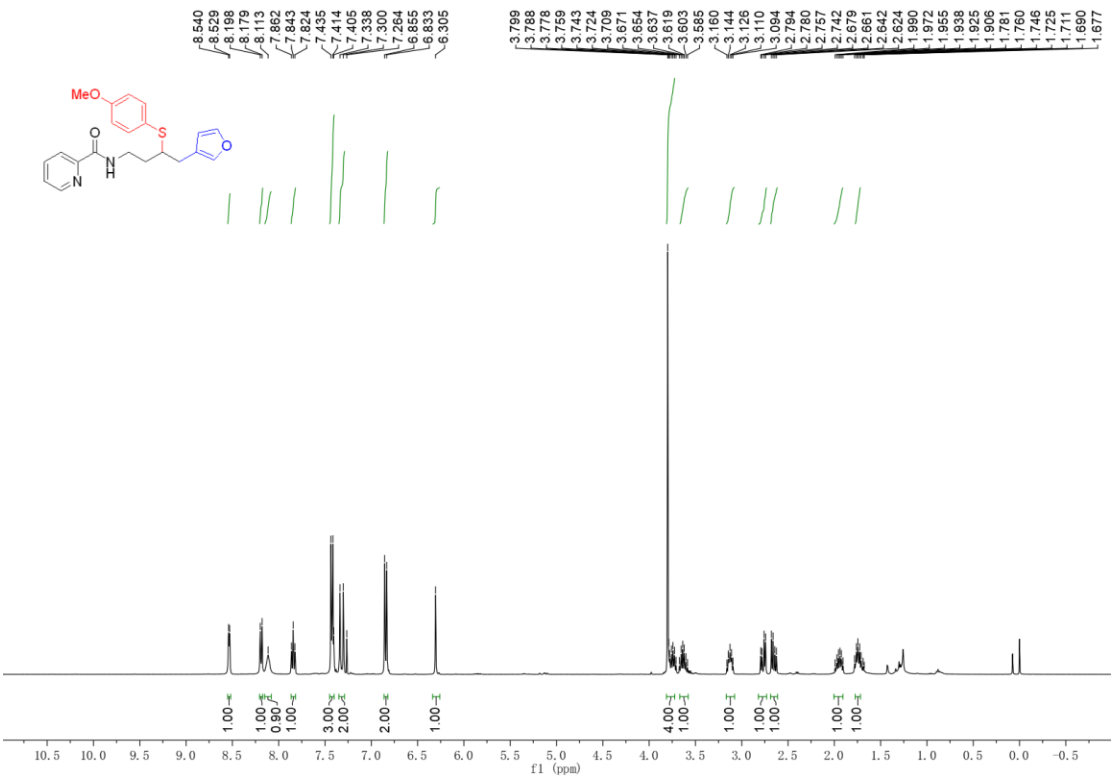
Supplementary Figure 44. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2q**



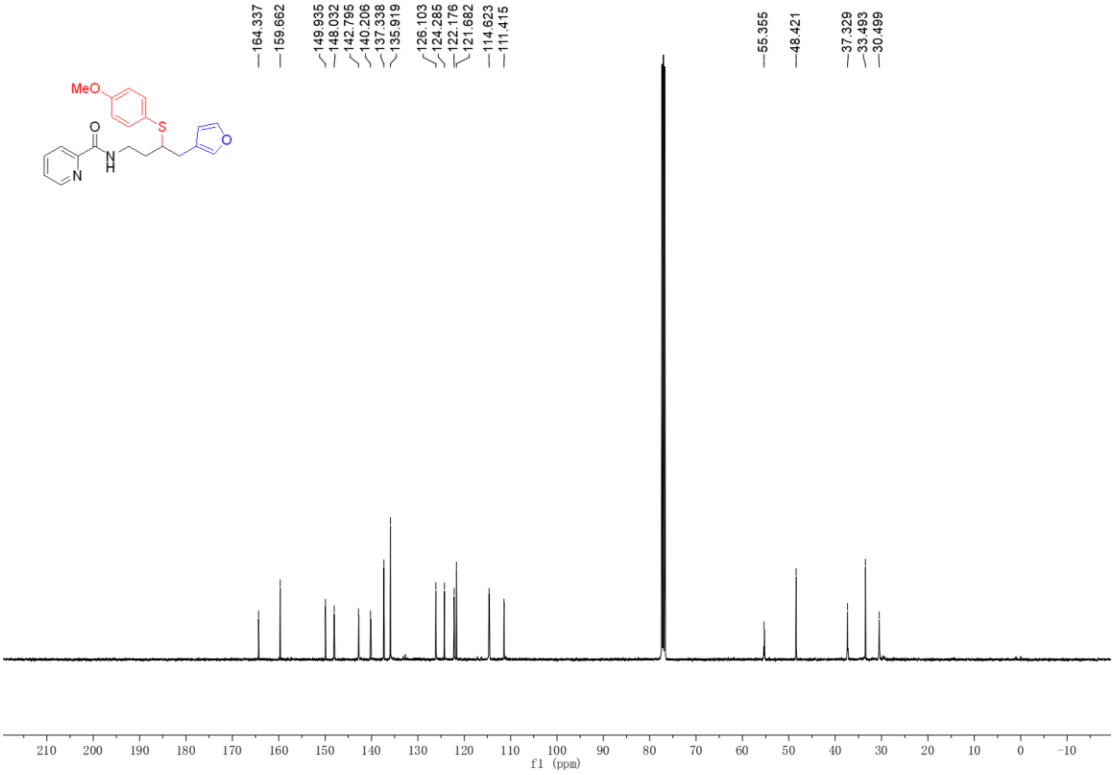
Supplementary Figure 45. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2r**



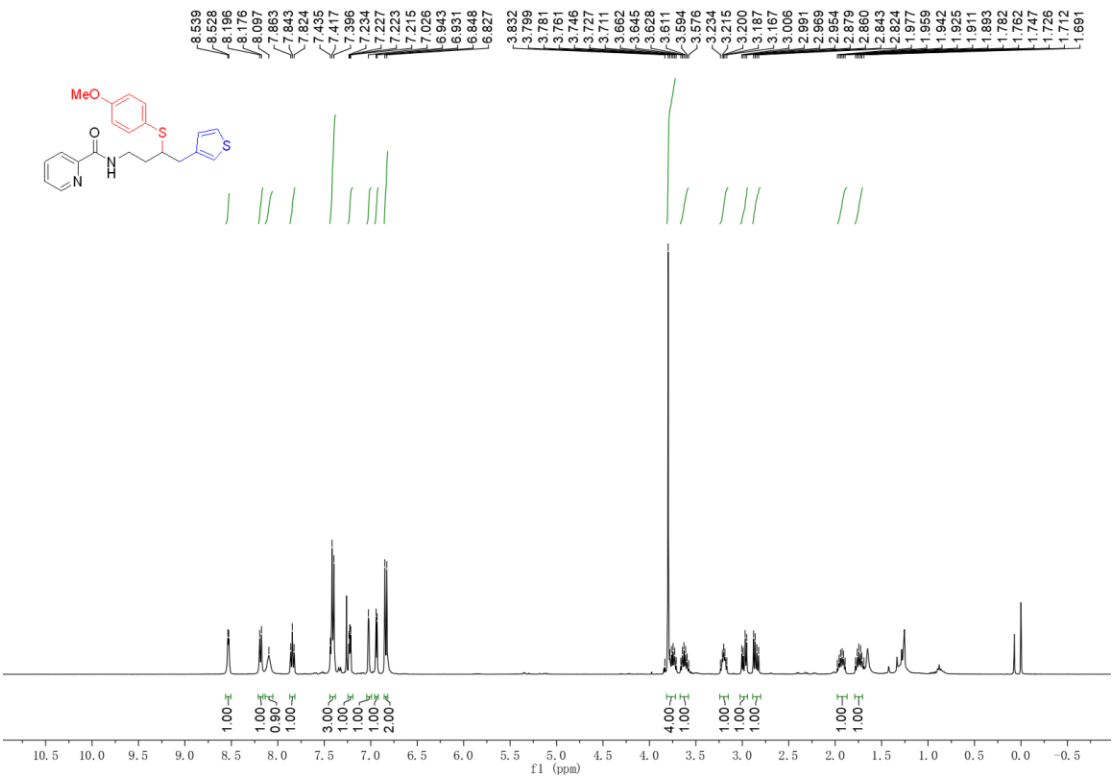
Supplementary Figure 46. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2r**



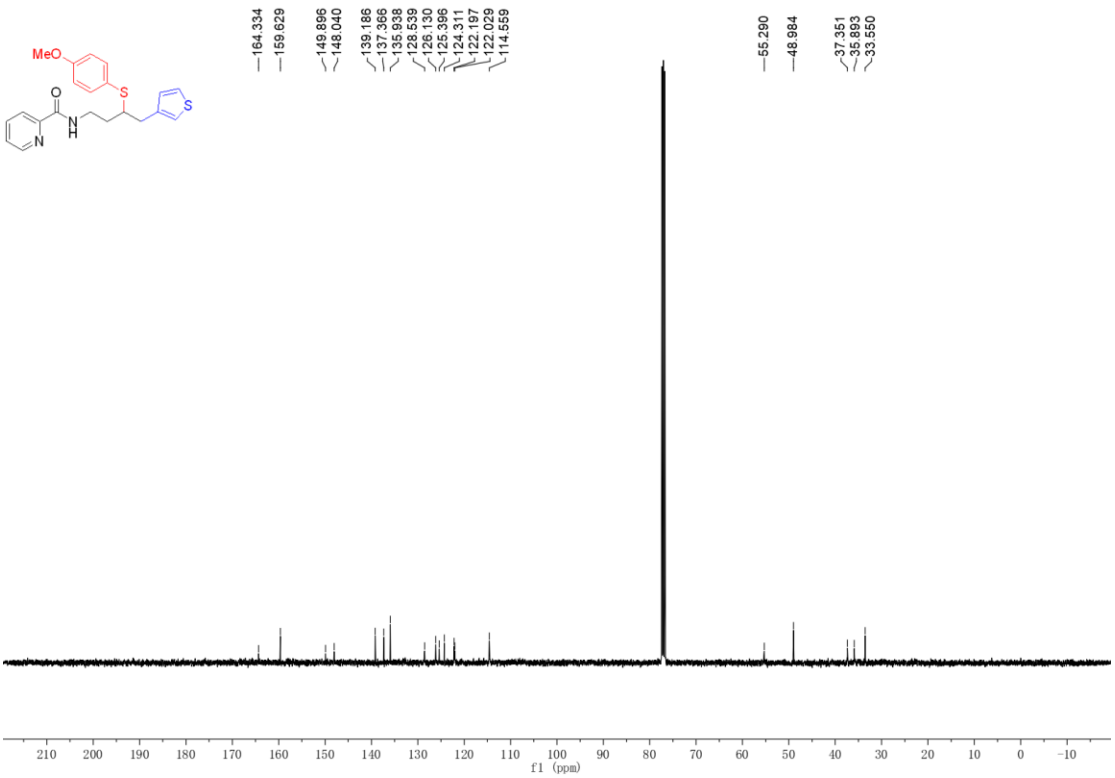
Supplementary Figure 47. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2s**



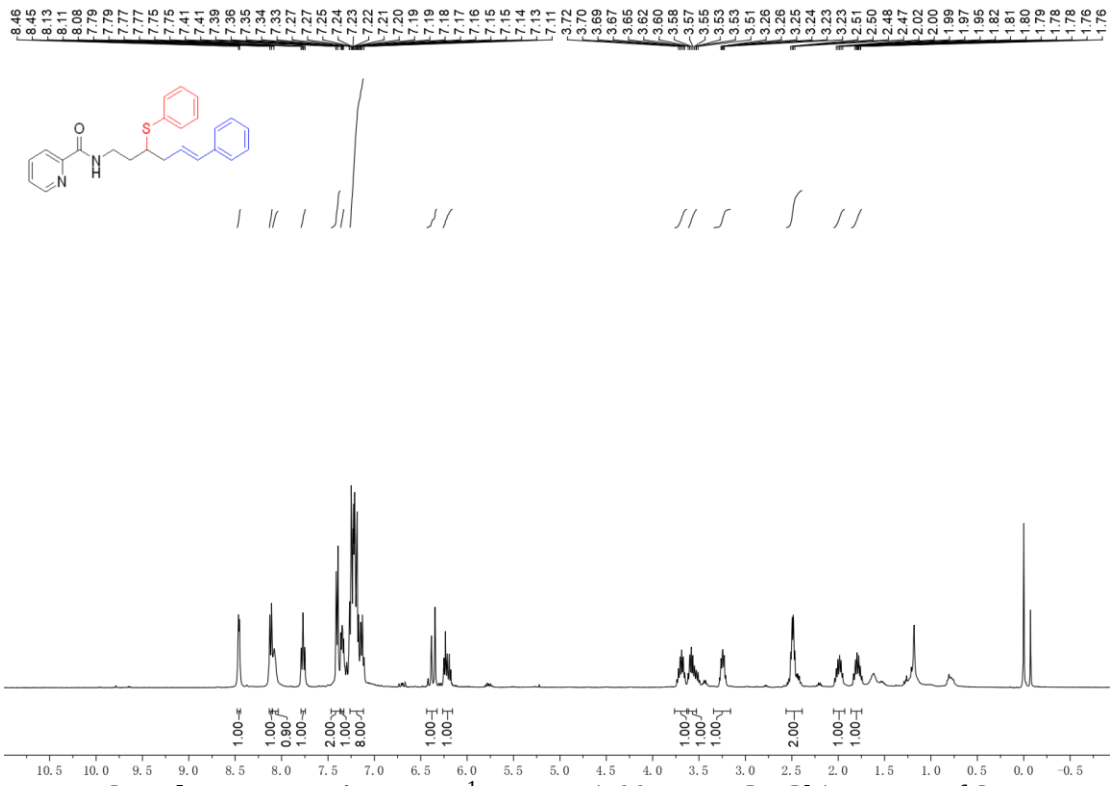
Supplementary Figure 48. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2s**



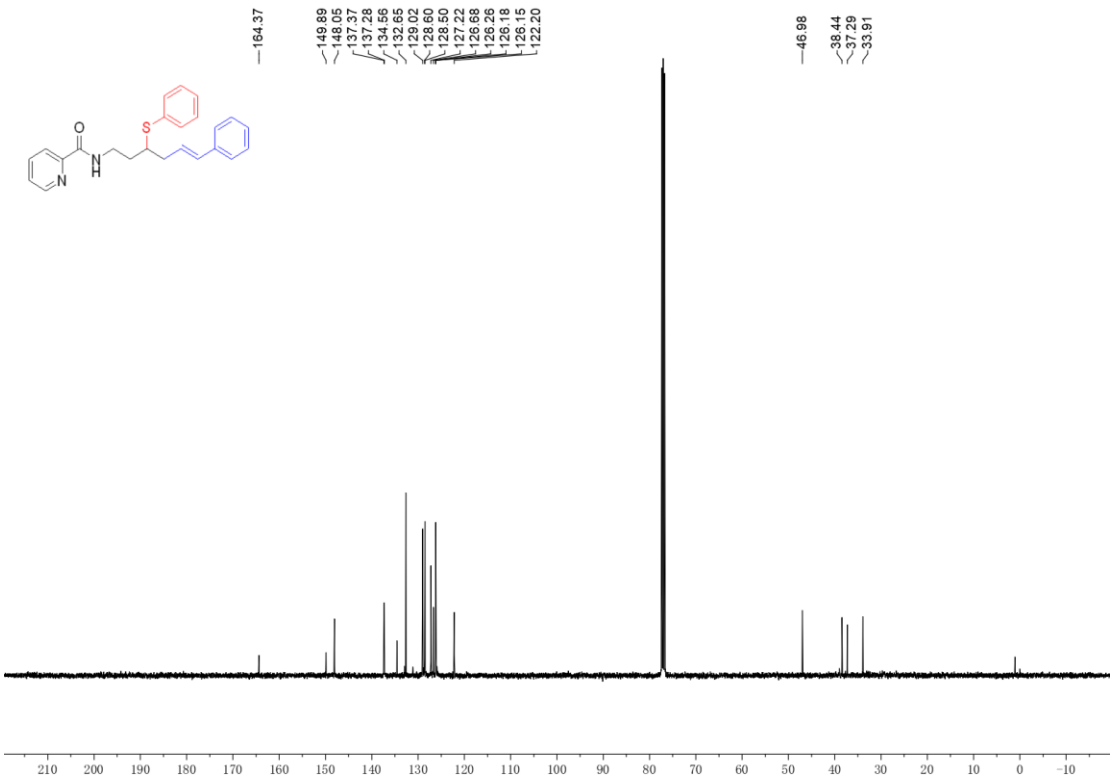
Supplementary Figure 49. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2t**



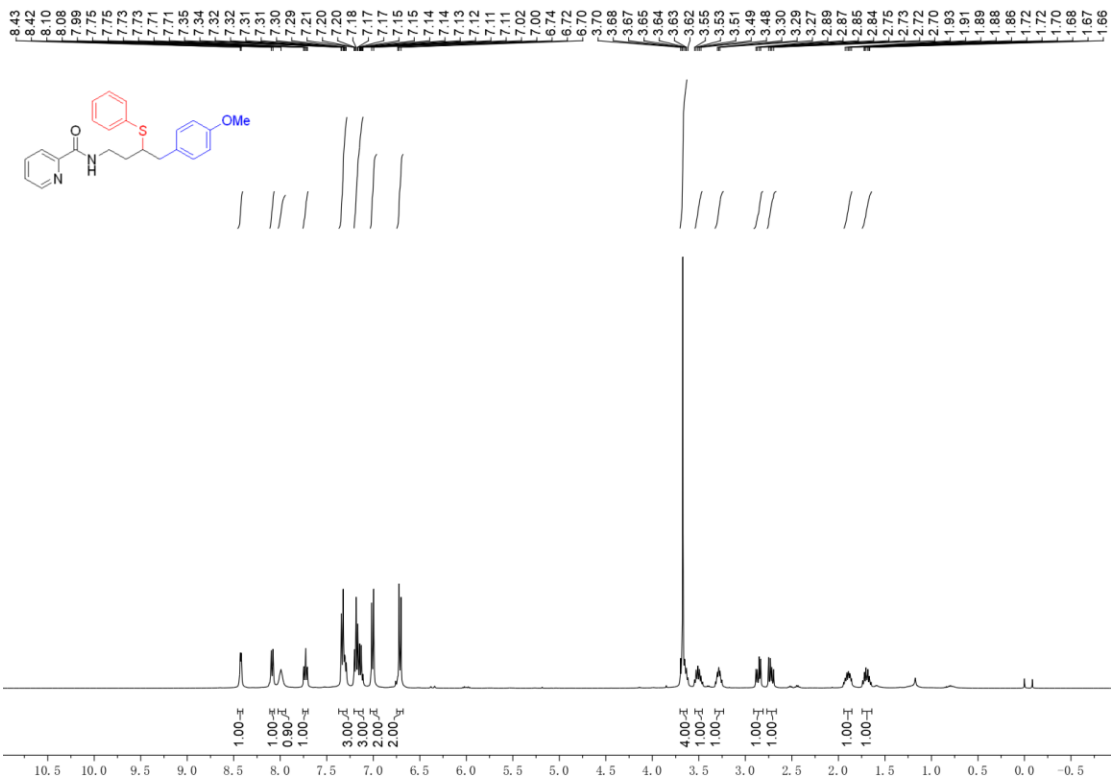
Supplementary Figure 50. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2t**



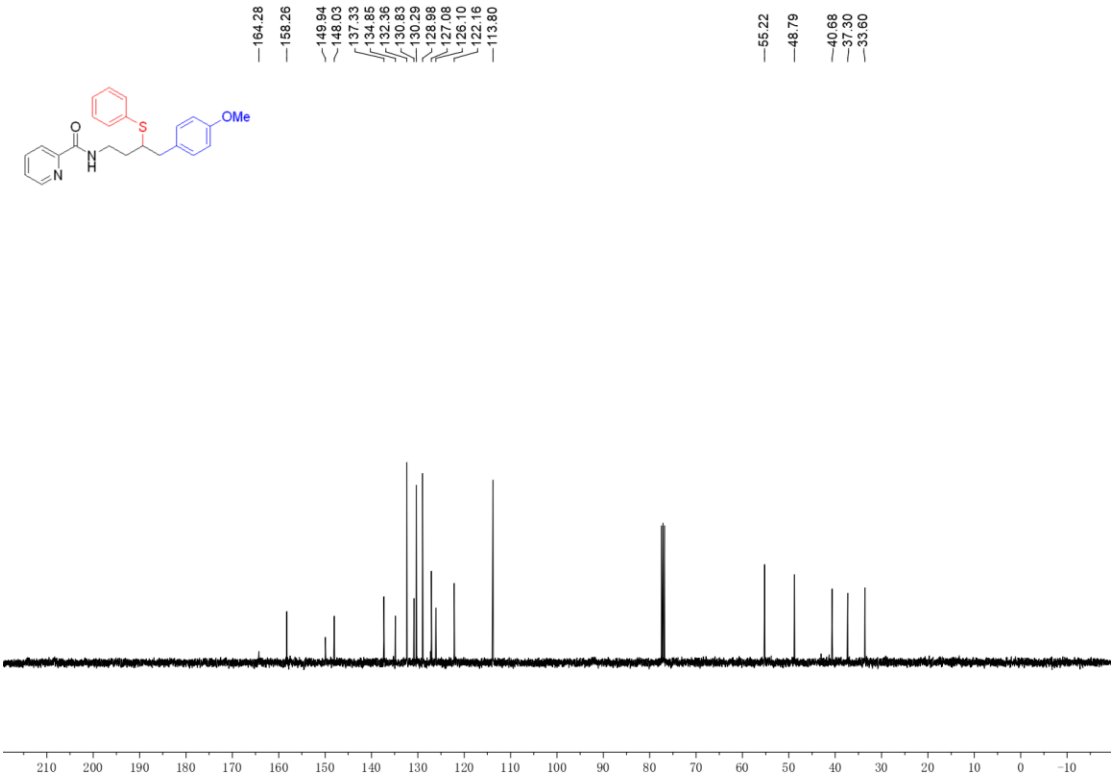
Supplementary Figure 51. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2u**



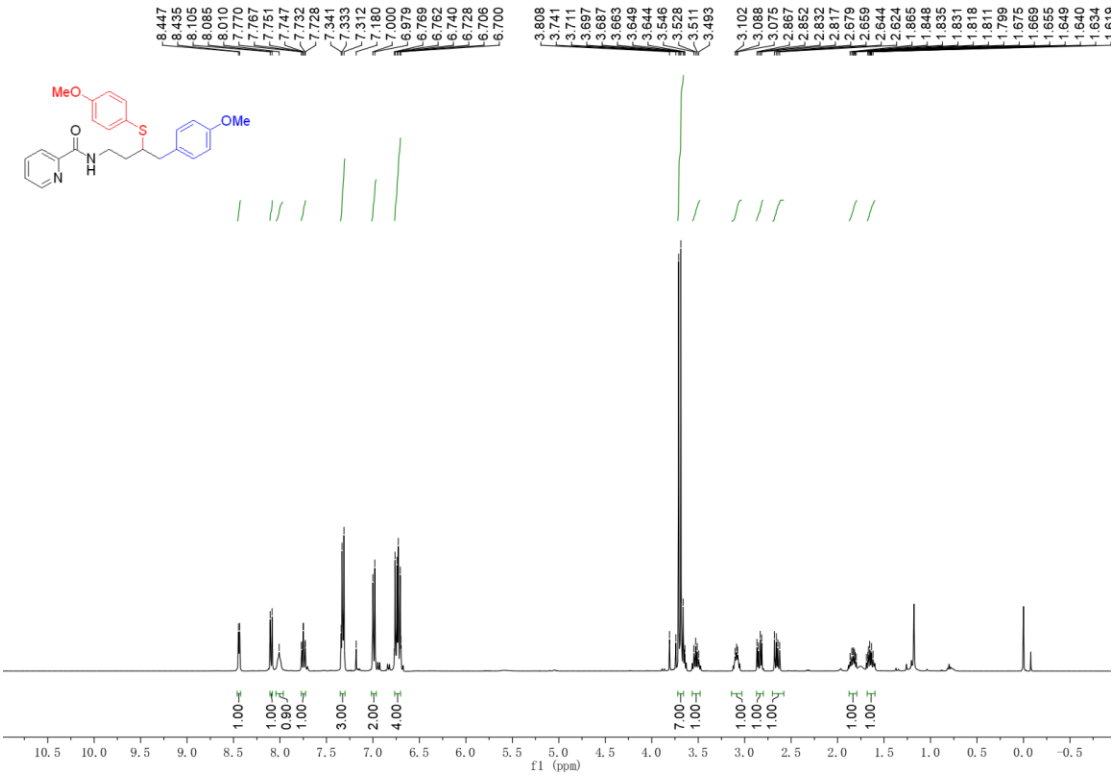
Supplementary Figure 52. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2u**



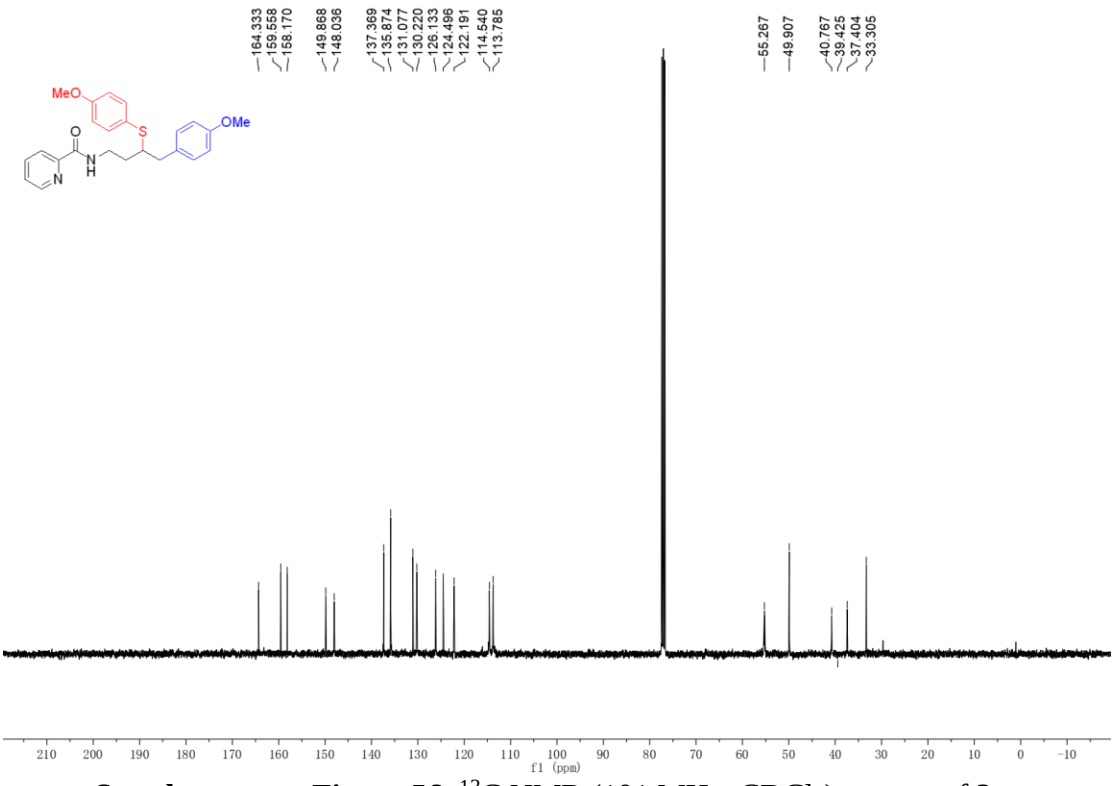
Supplementary Figure 53. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2v**



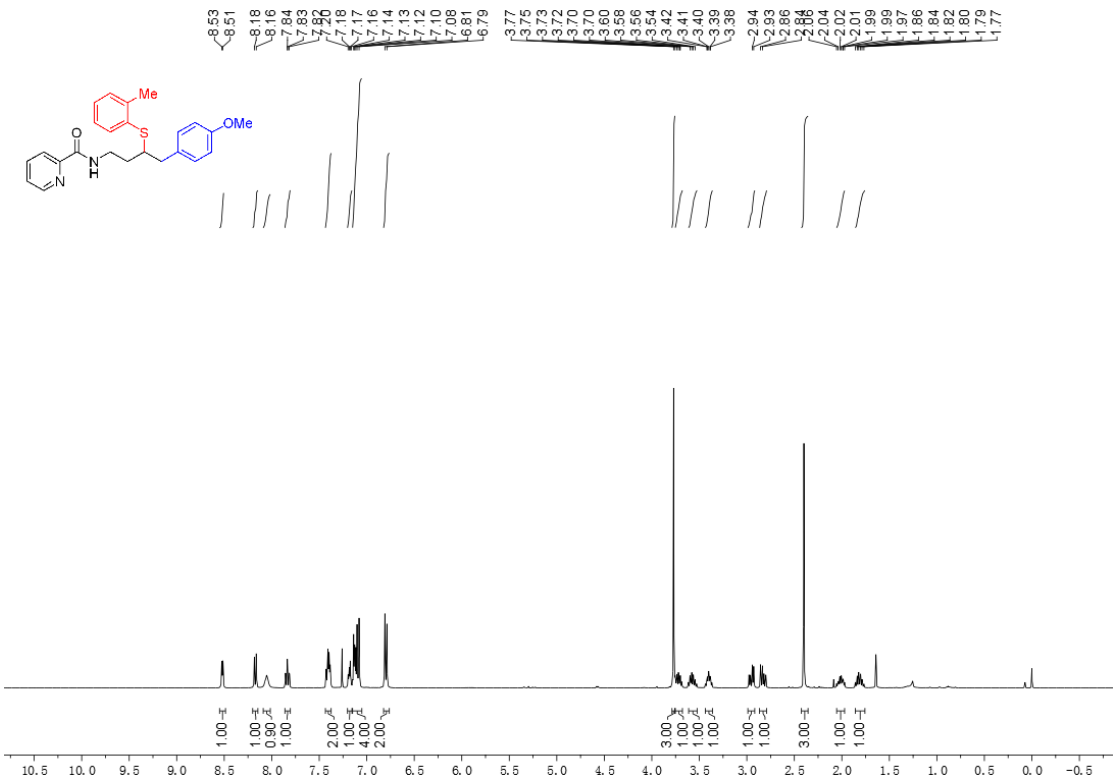
Supplementary Figure 54. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2v**



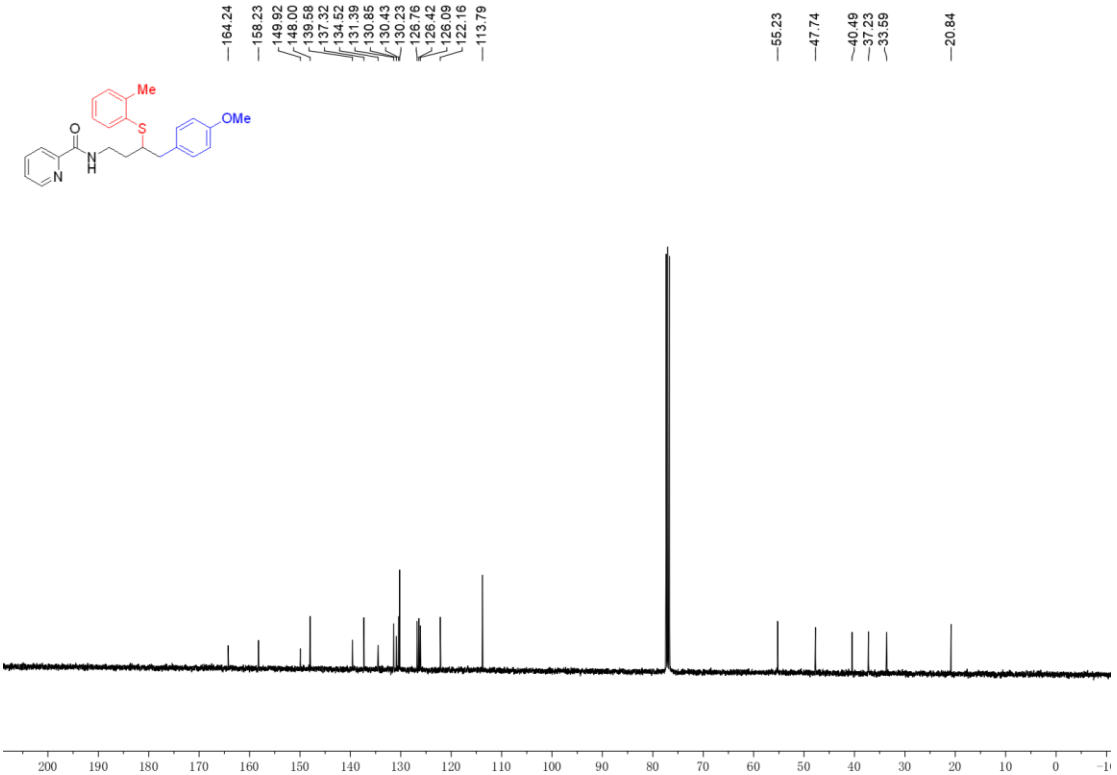
Supplementary Figure 55. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2w**



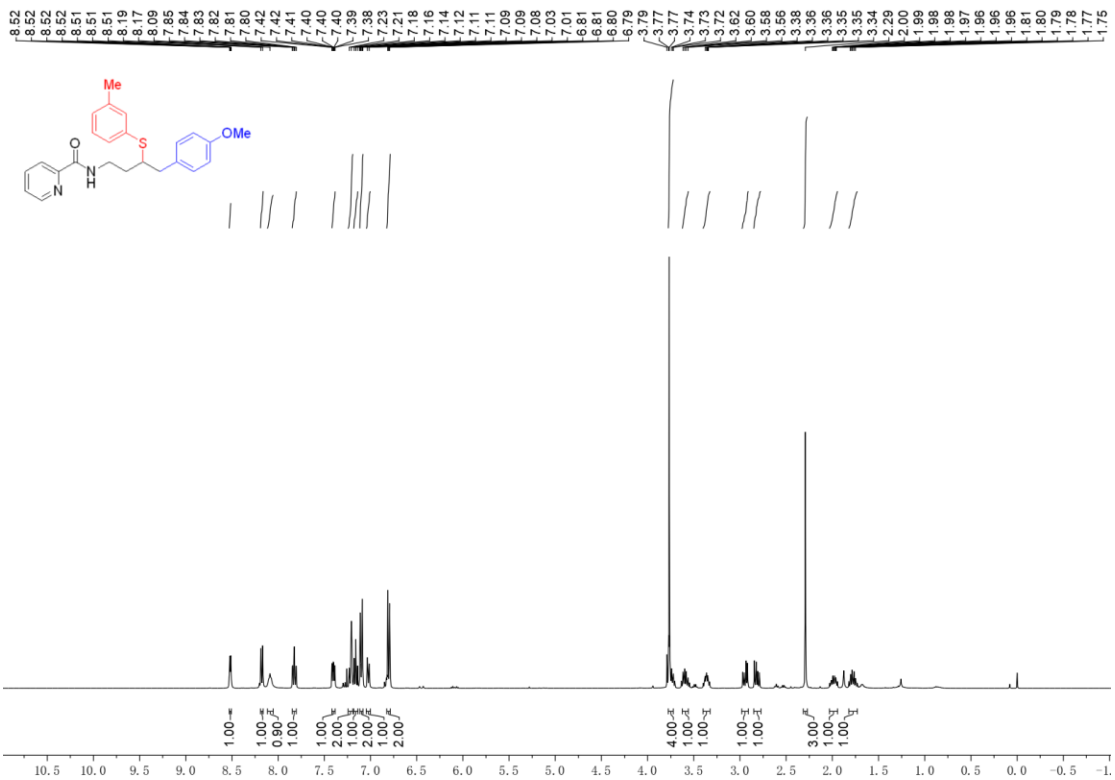
Supplementary Figure 56. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2w**



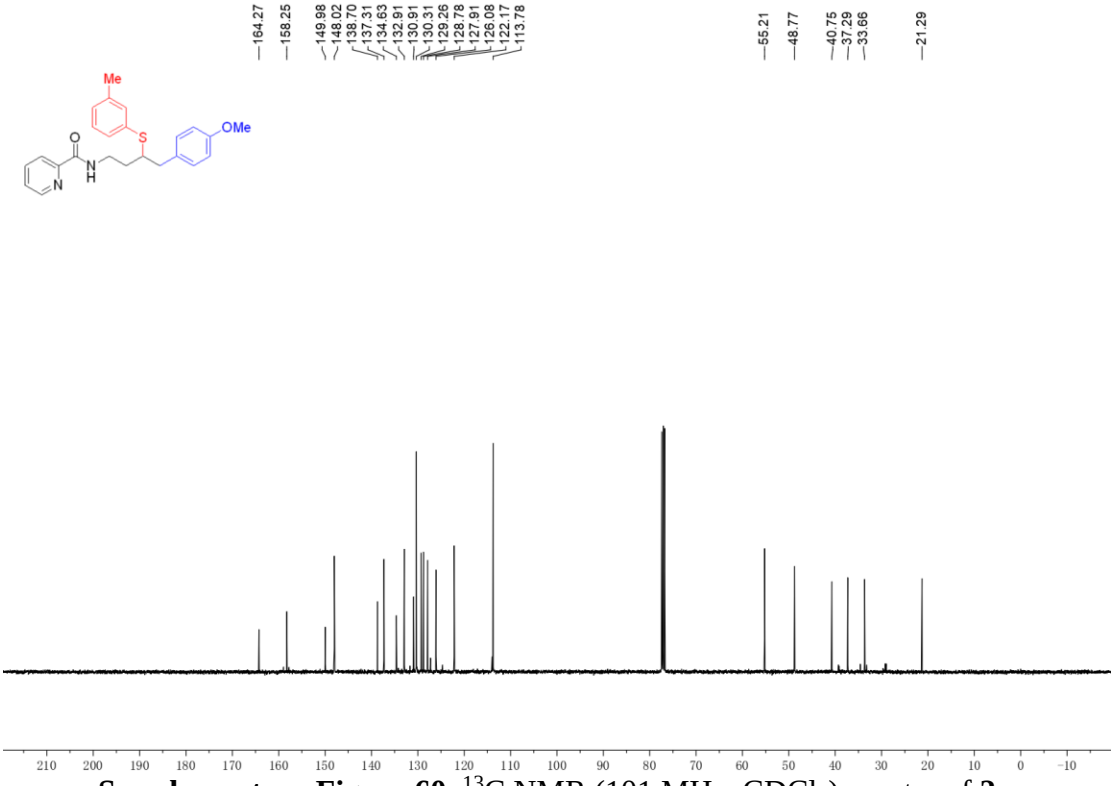
Supplementary Figure 57. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2x**



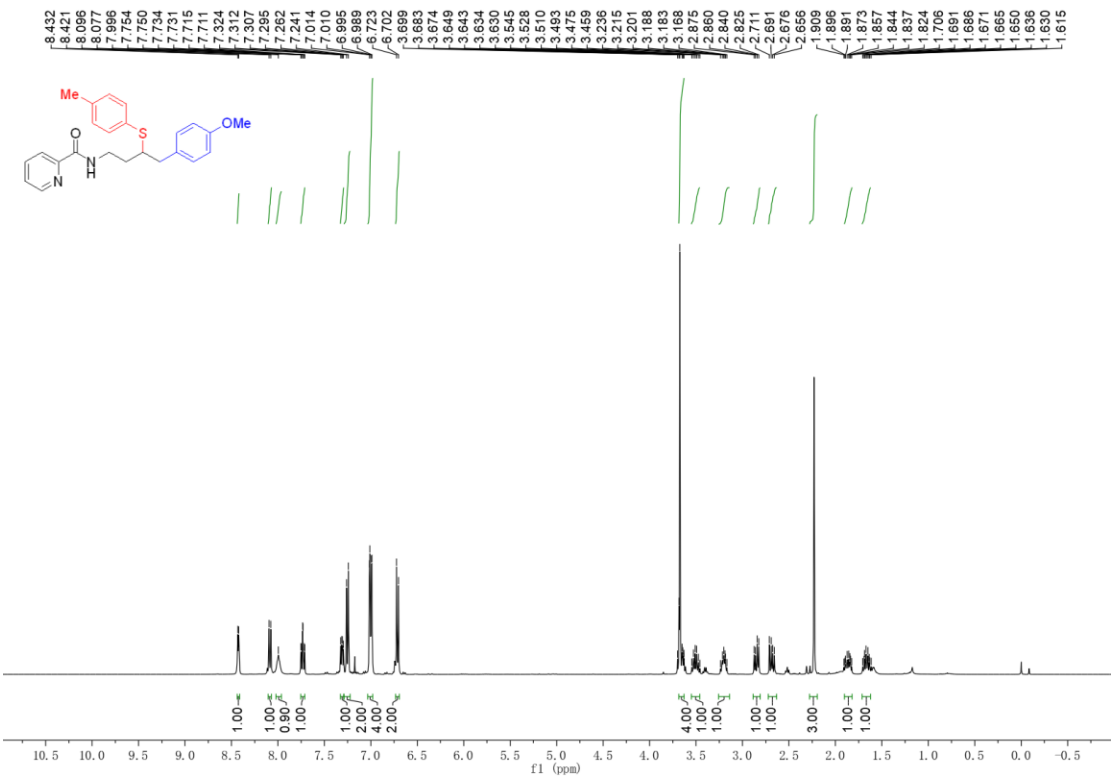
Supplementary Figure 58. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2x**



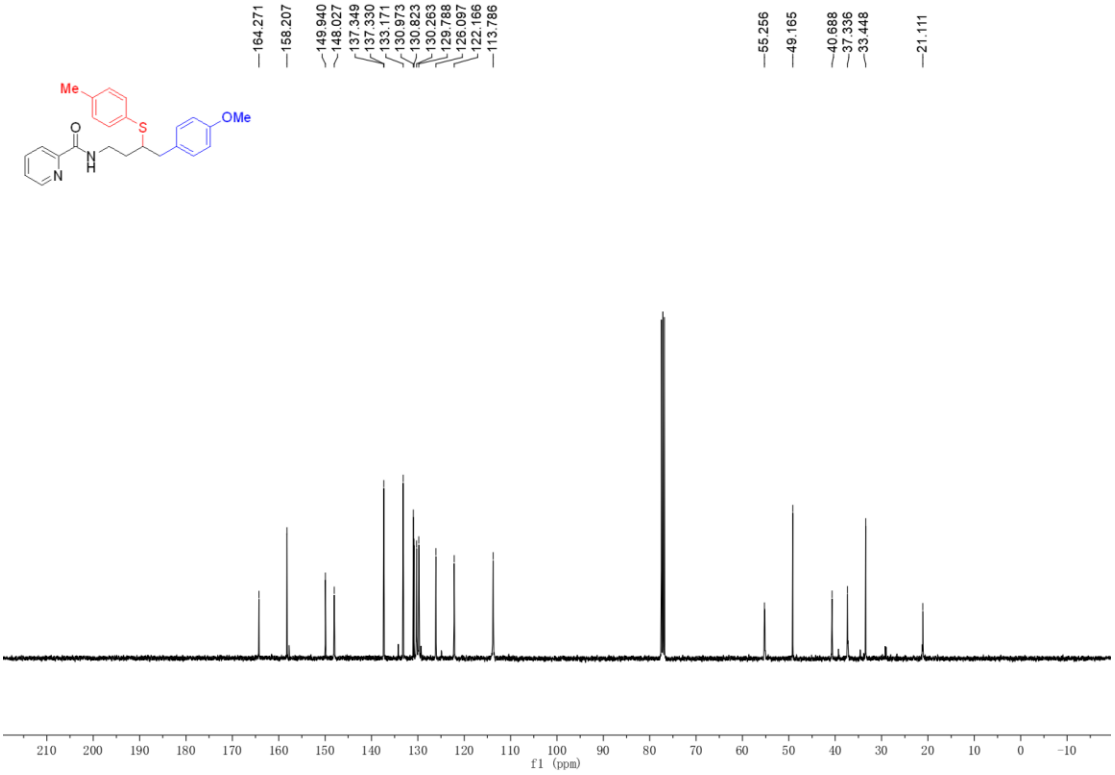
Supplementary Figure 59. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2y**



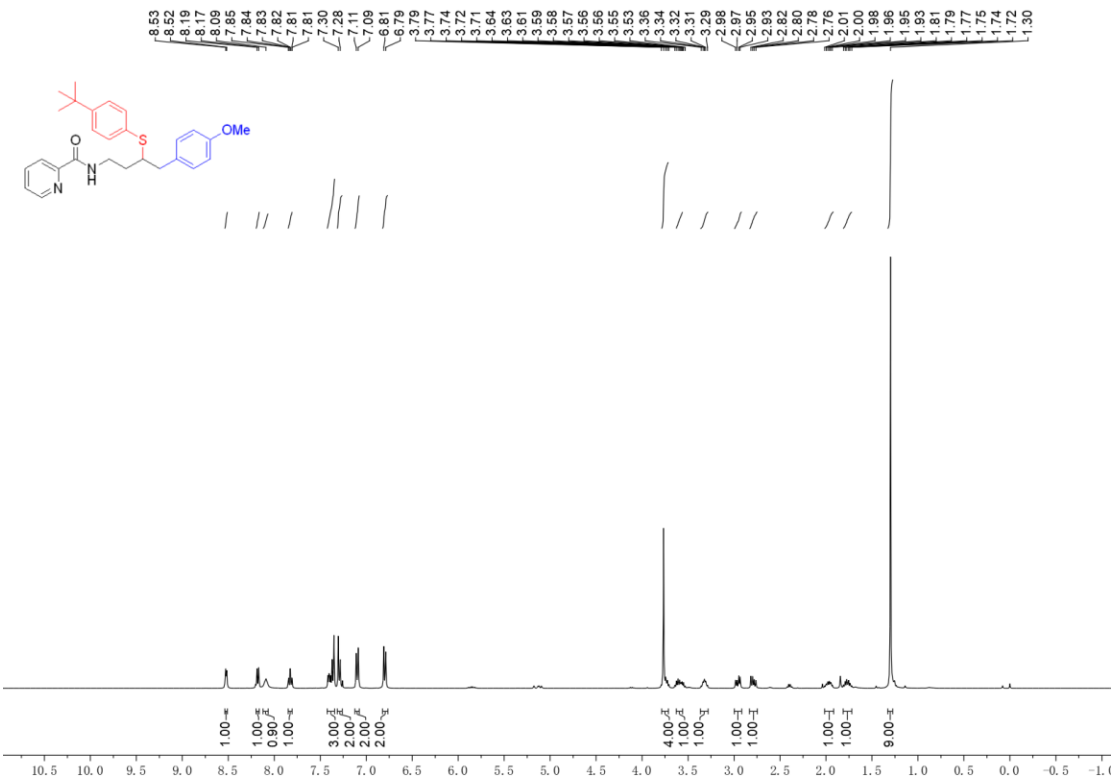
Supplementary Figure 60. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2y**



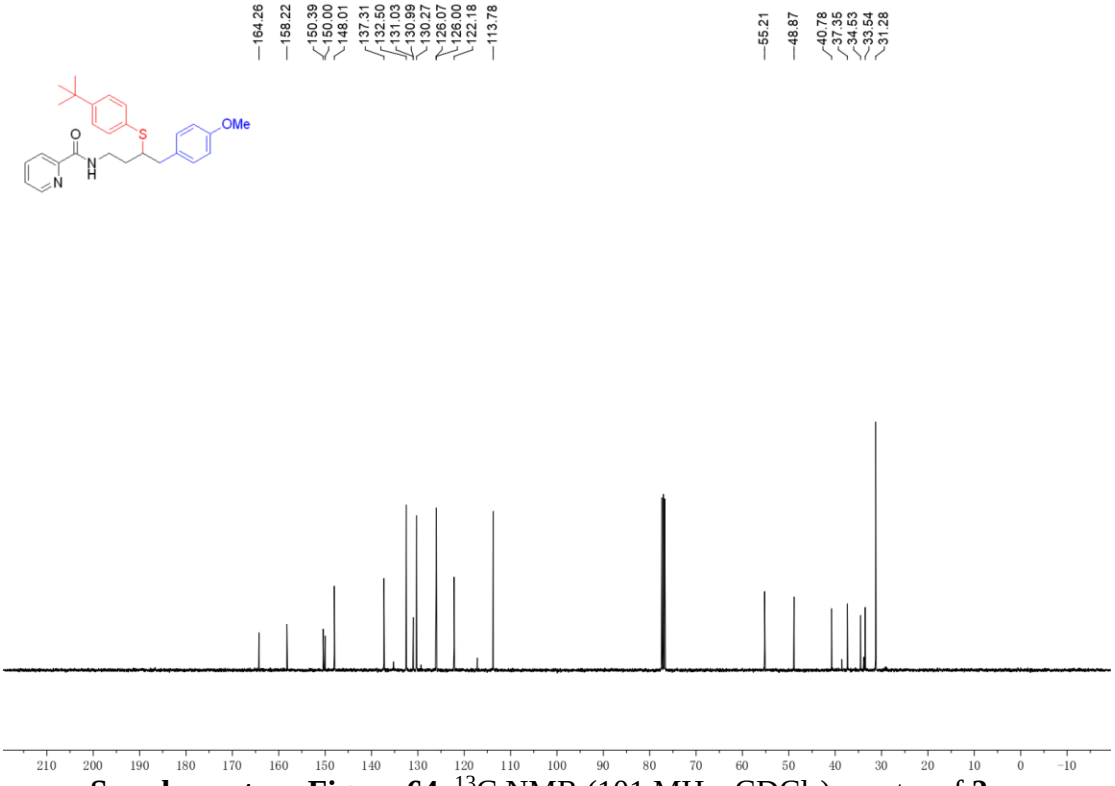
Supplementary Figure 61. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2z**



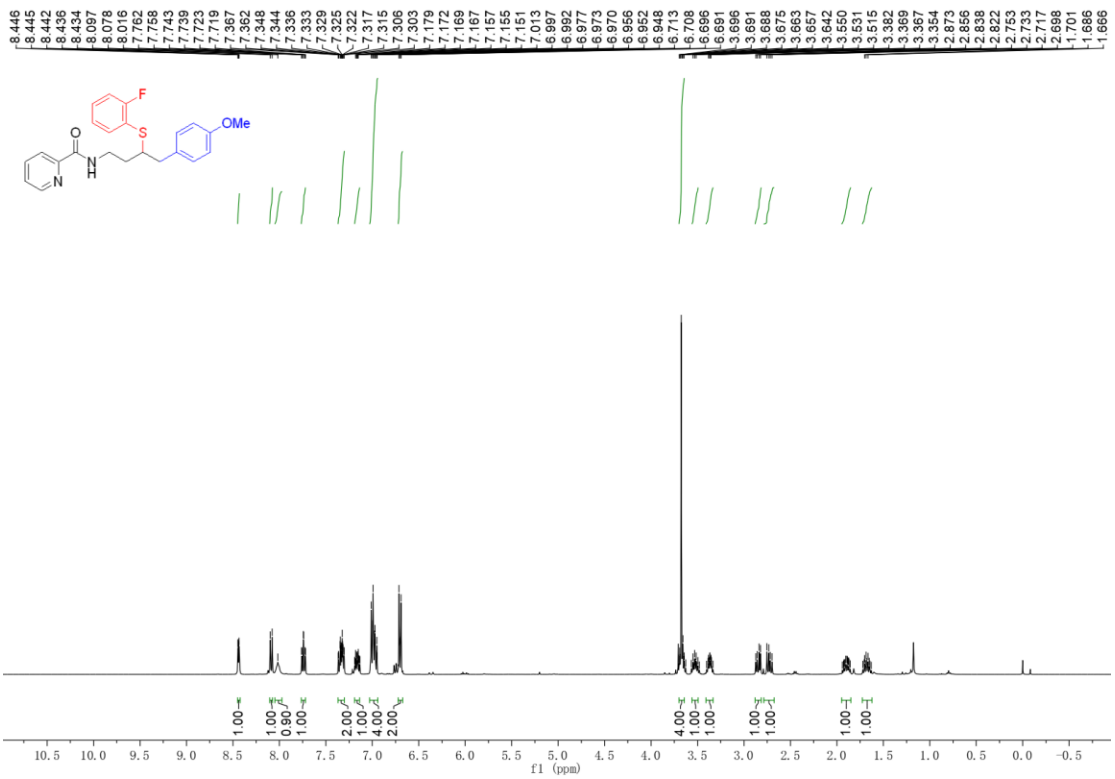
Supplementary Figure 62. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2z**



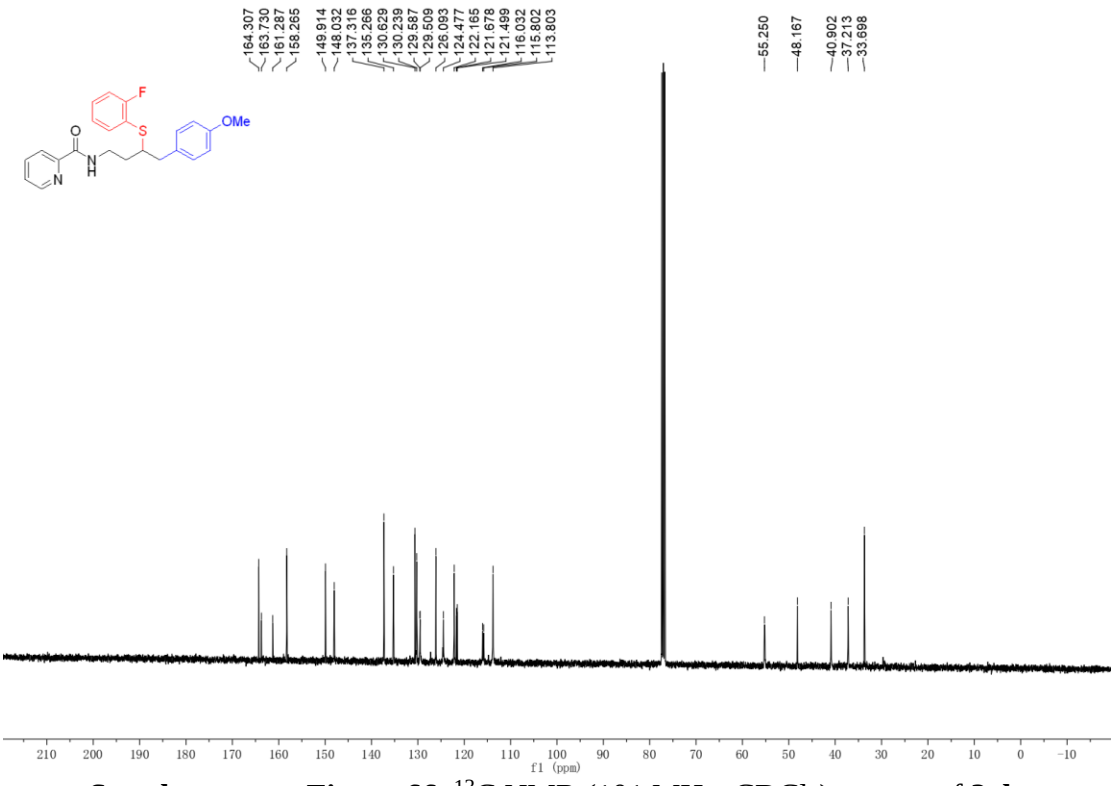
Supplementary Figure 63. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2aa**



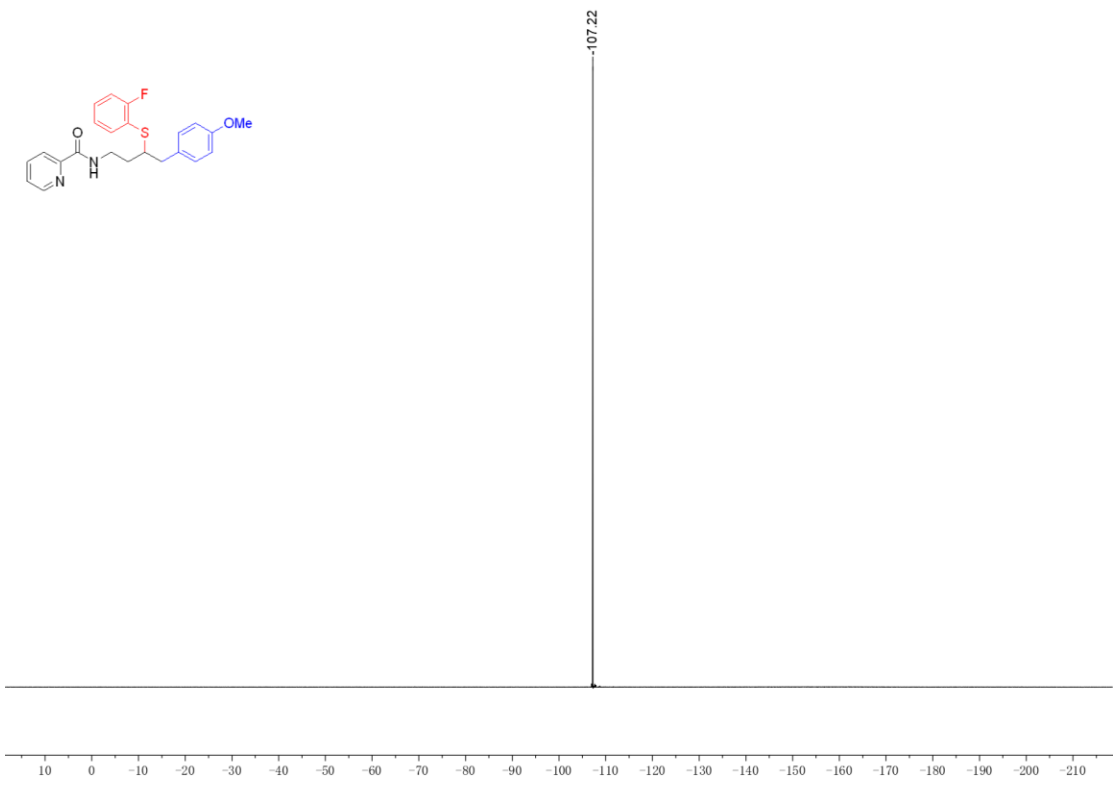
Supplementary Figure 64. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2aa**



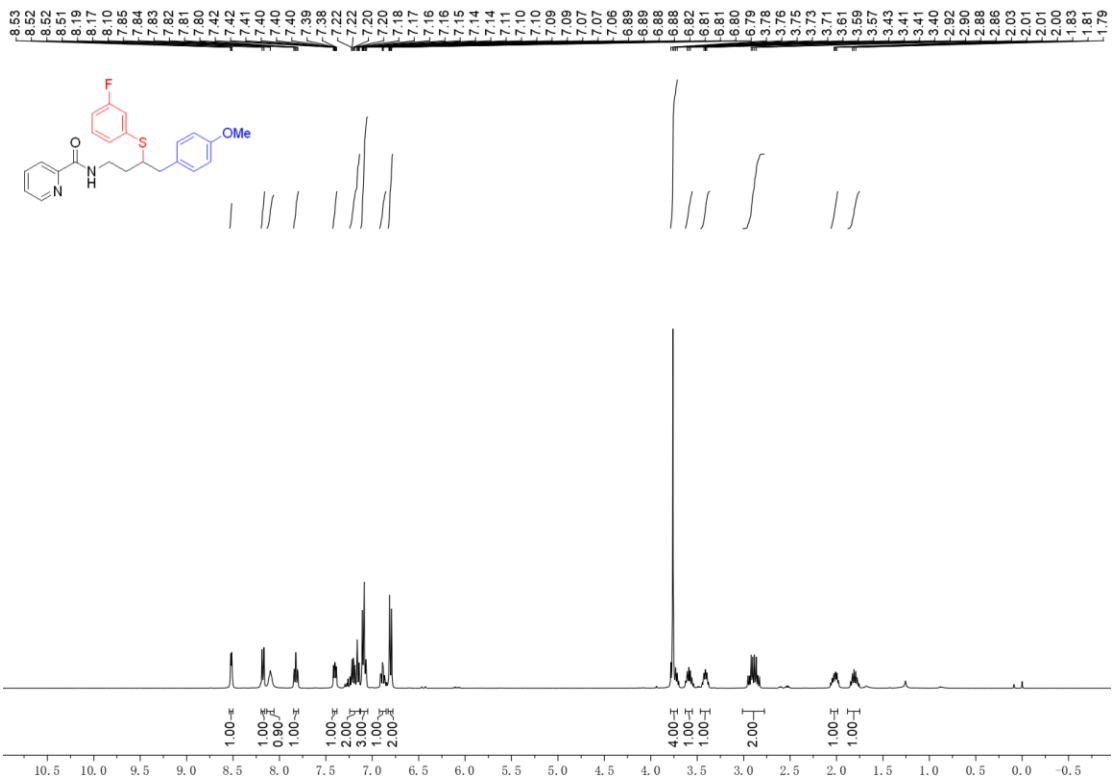
Supplementary Figure 65. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2ab**



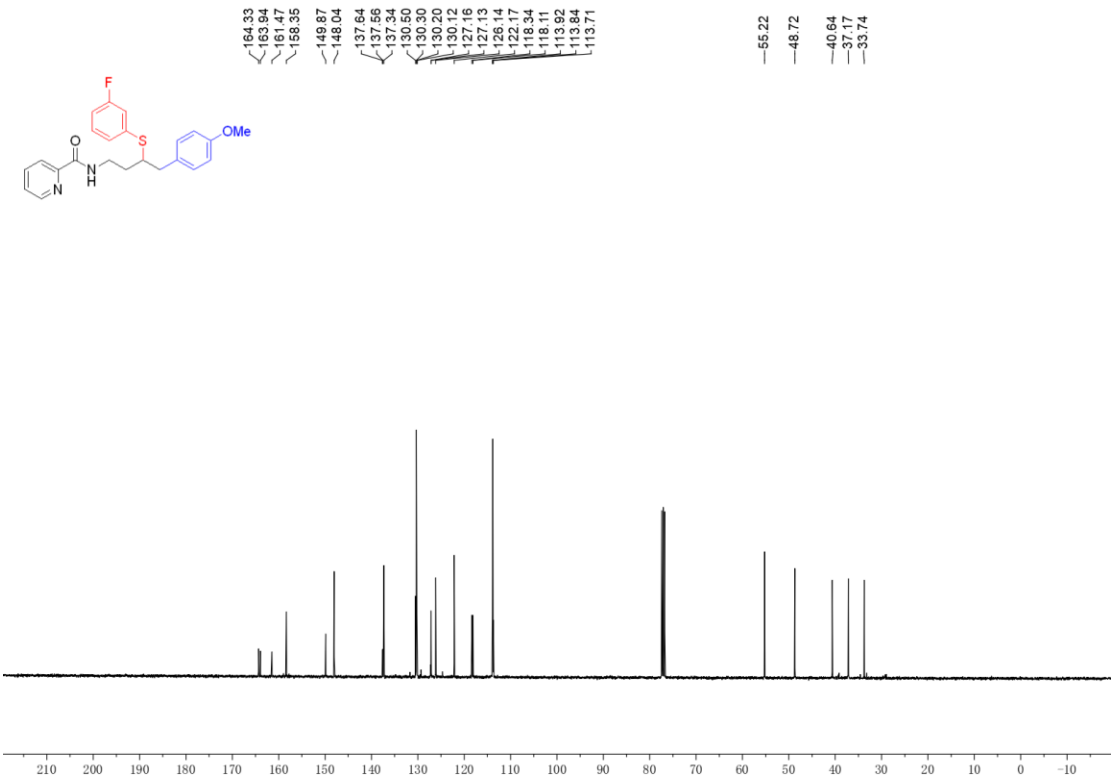
Supplementary Figure 66. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2ab**



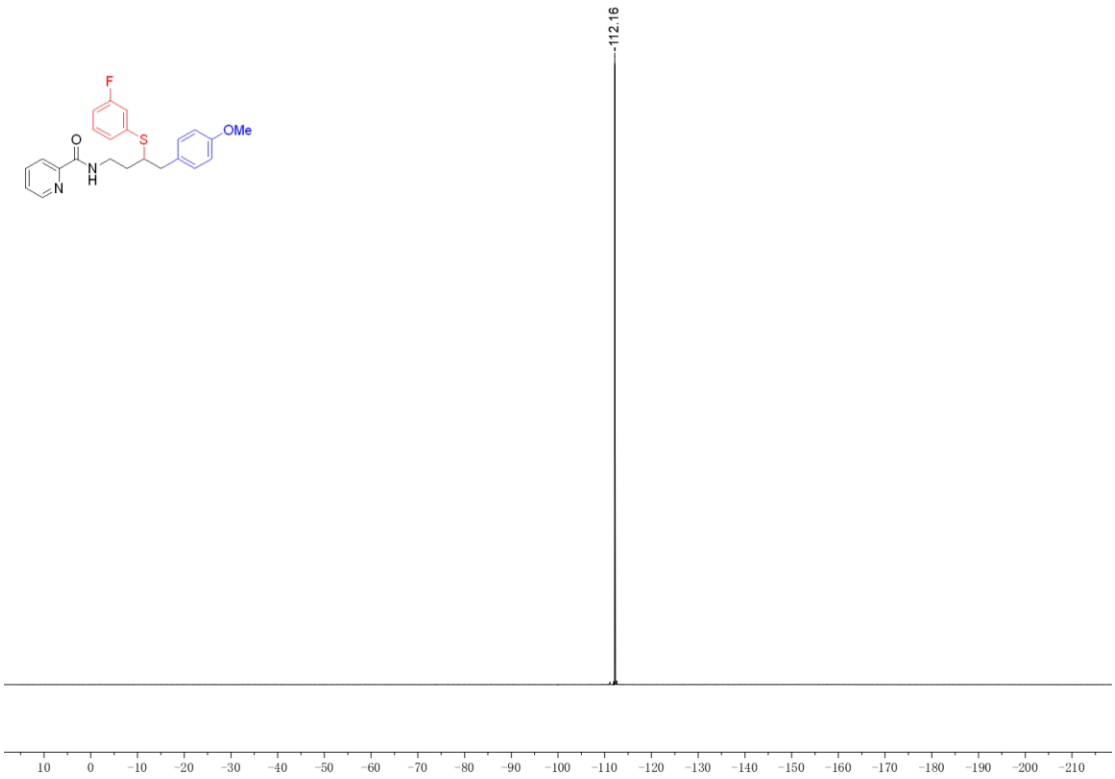
Supplementary Figure 67. ^{19}F NMR (376 MHz, $CDCl_3$) spectra of **2ab**



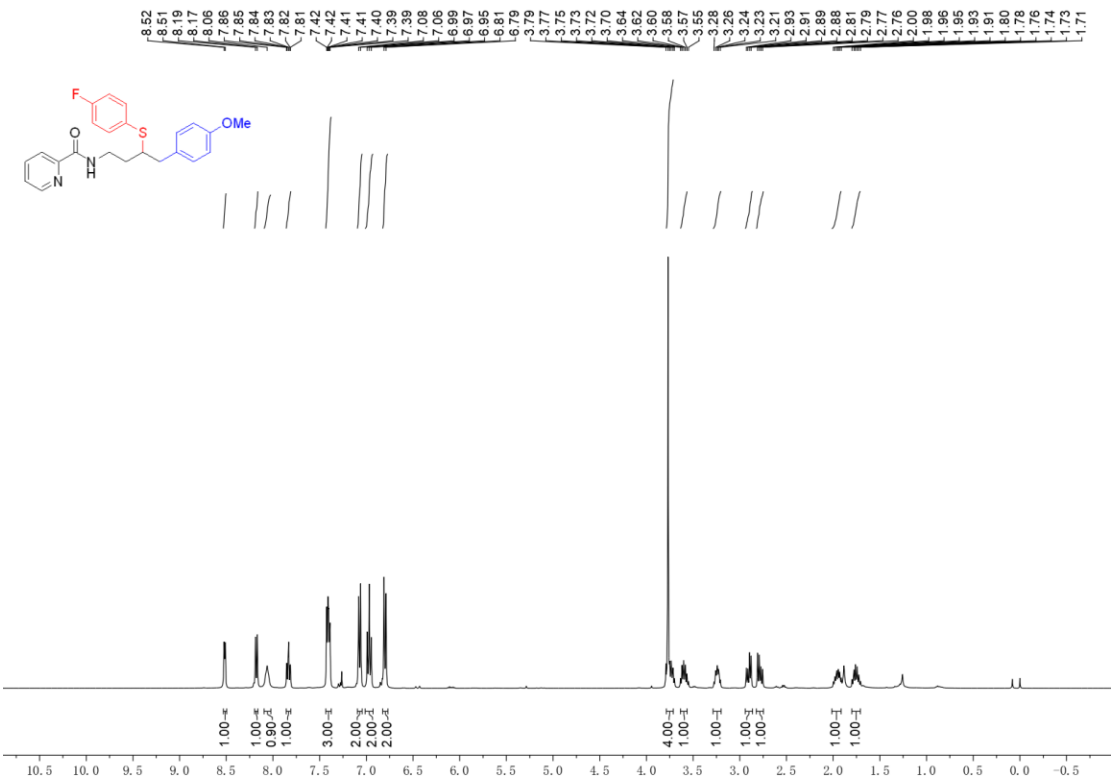
Supplementary Figure 68. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2ac**



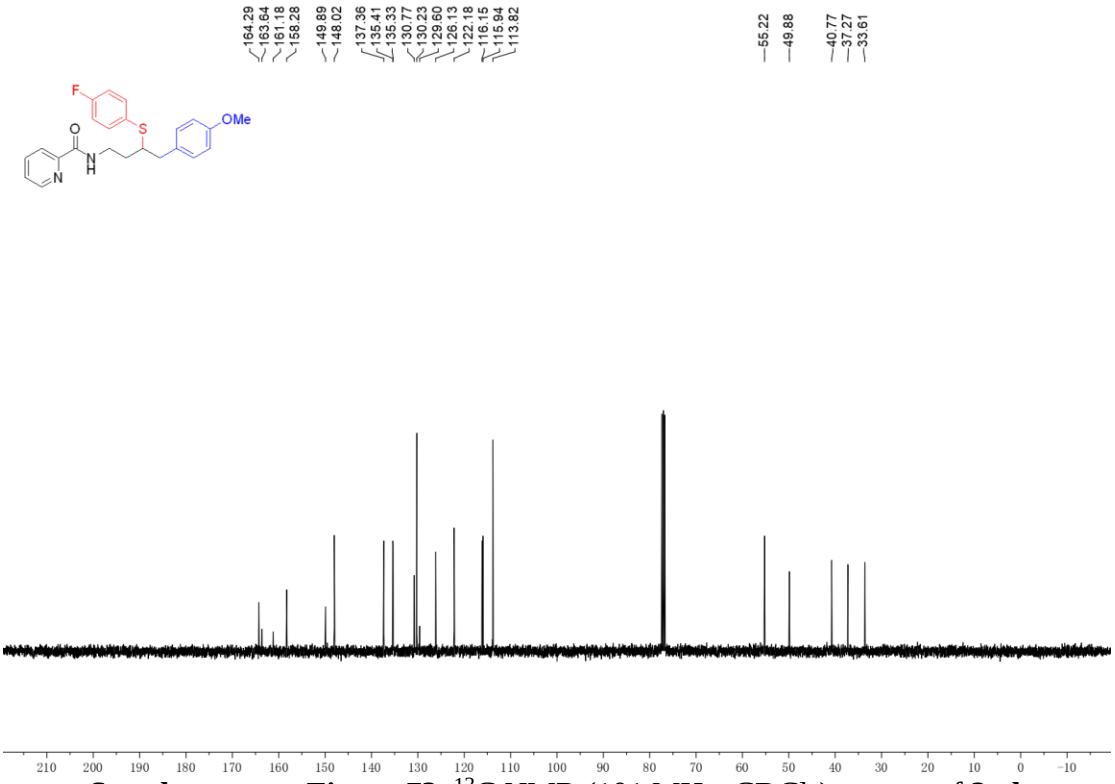
Supplementary Figure 69. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2ac**



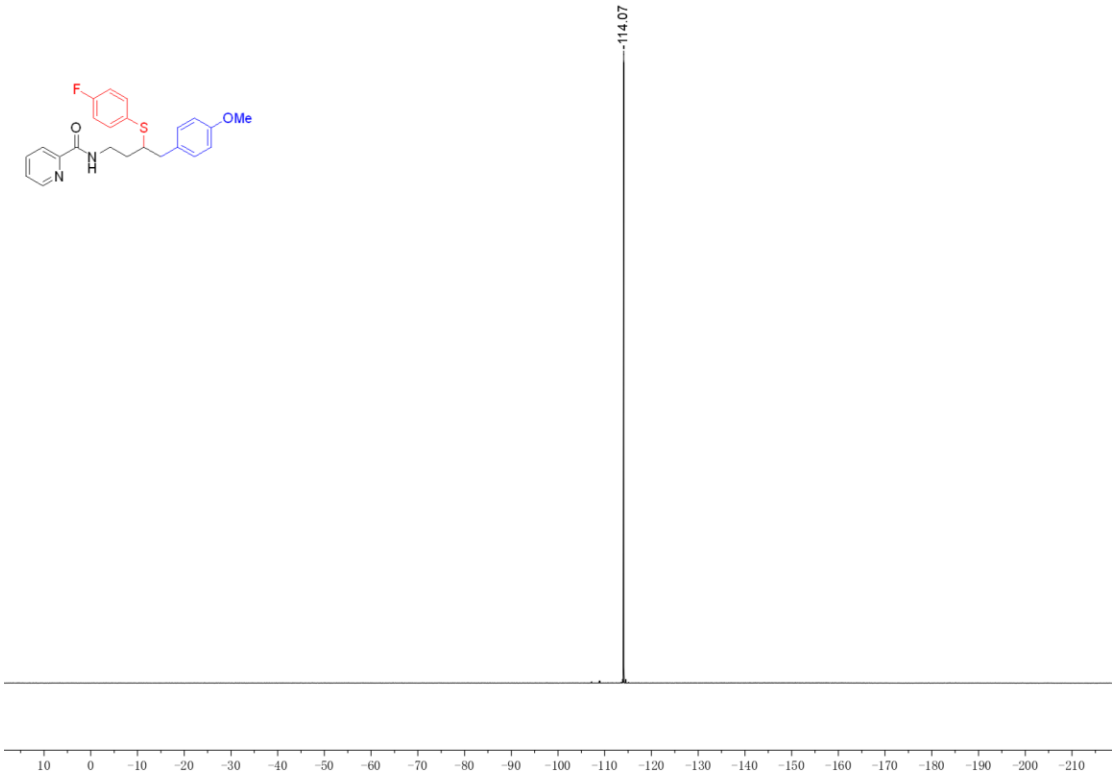
Supplementary Figure 70. ^{19}F NMR (376 MHz, $CDCl_3$) spectra of **2ac**



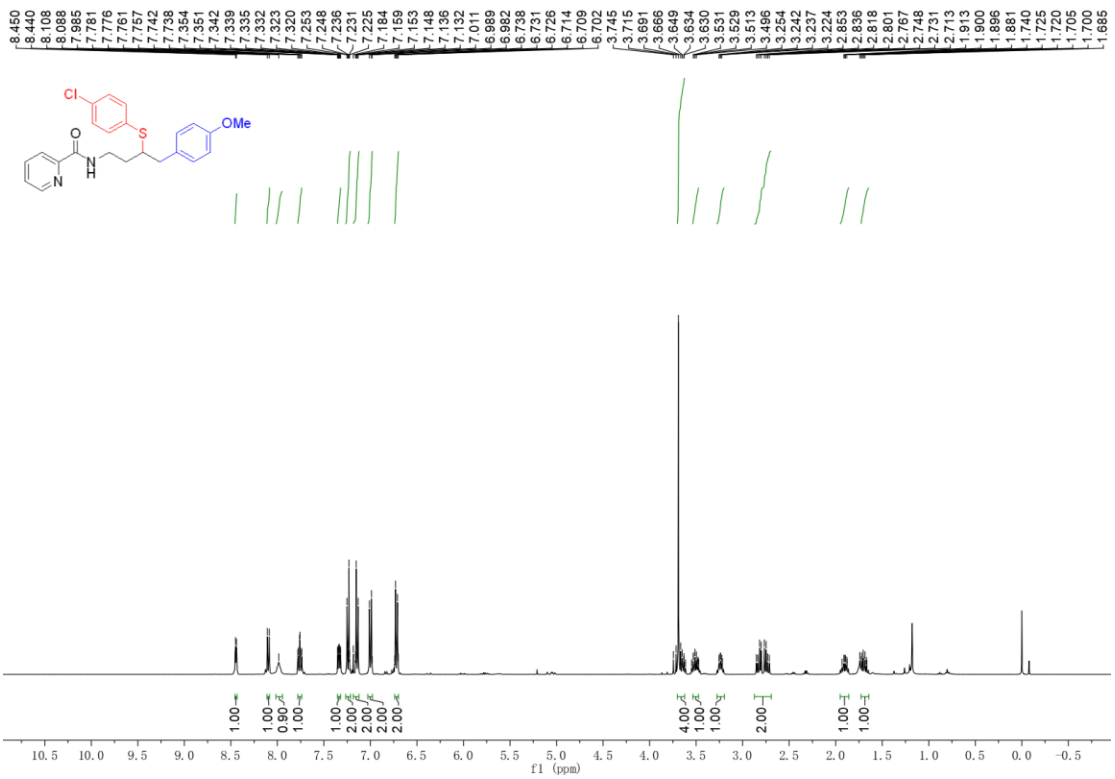
Supplementary Figure 71. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2ad**



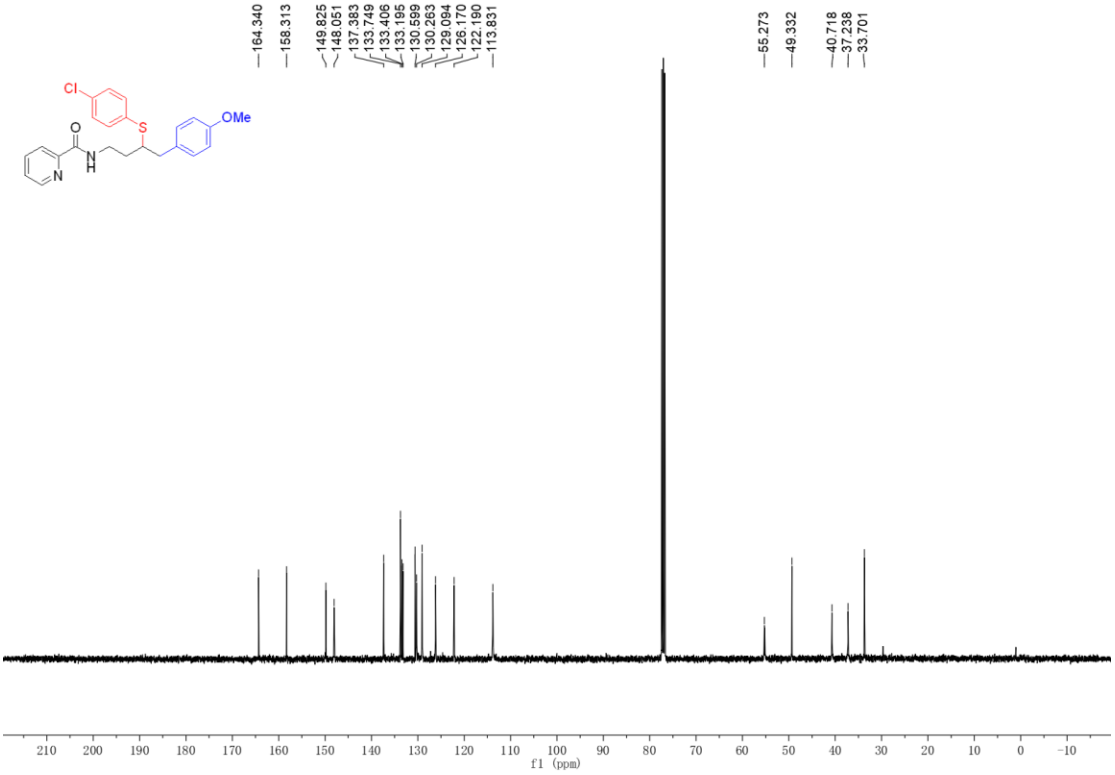
Supplementary Figure 72. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2ad**



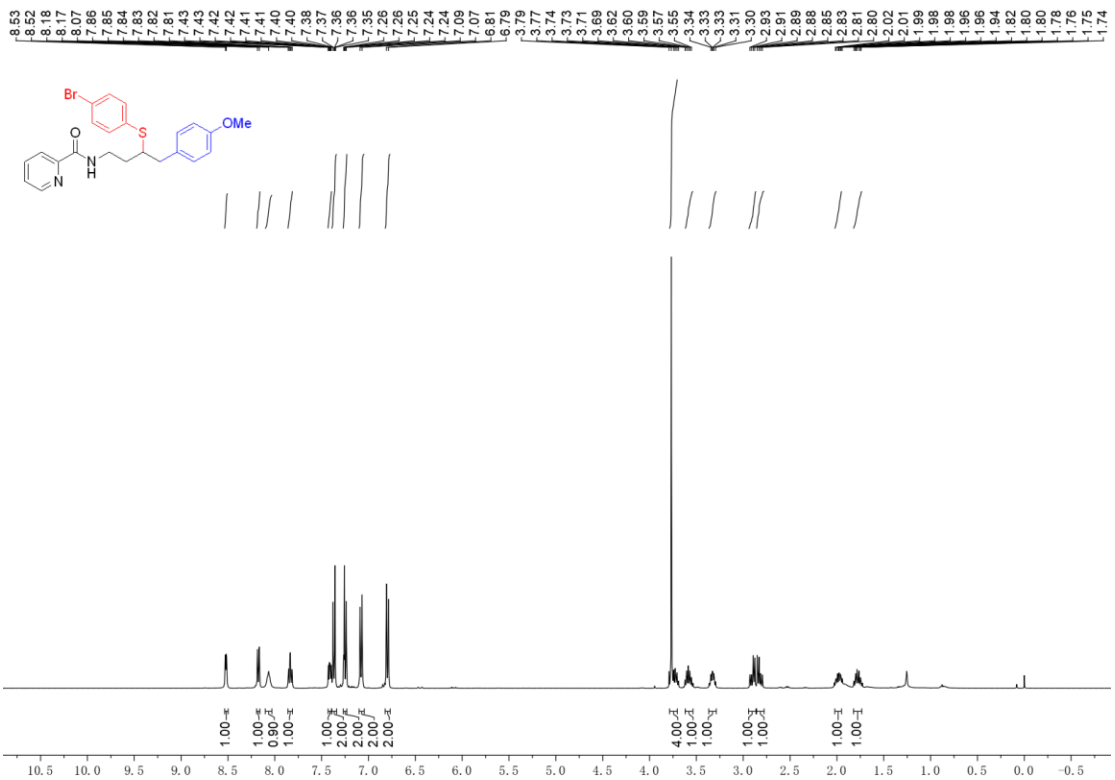
Supplementary Figure 73. ^{19}F NMR (376 MHz, $CDCl_3$) spectra of **2ad**



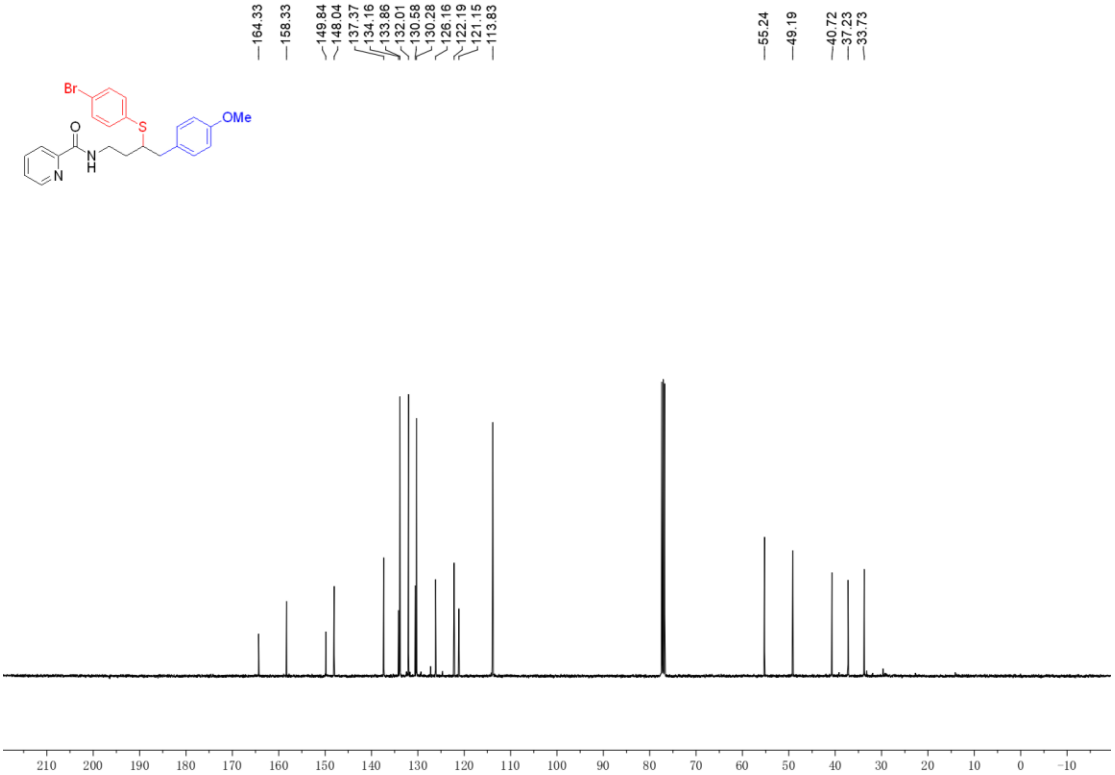
Supplementary Figure 74. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2ae**



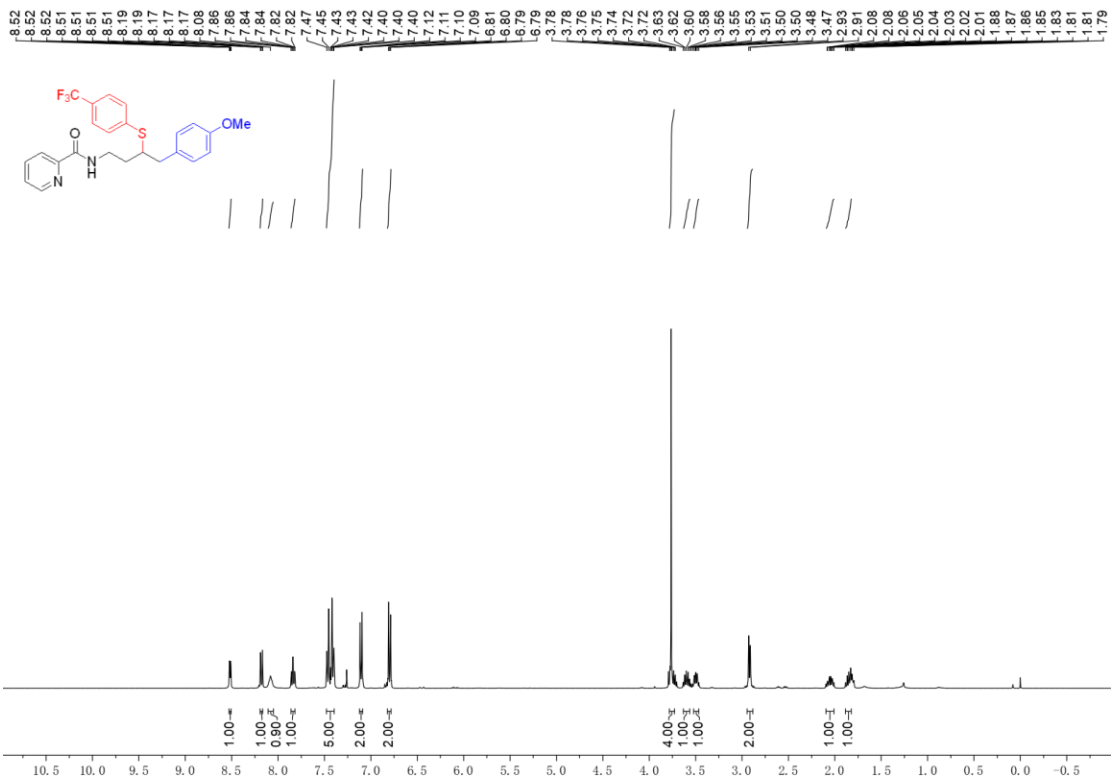
Supplementary Figure 75. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2ae**



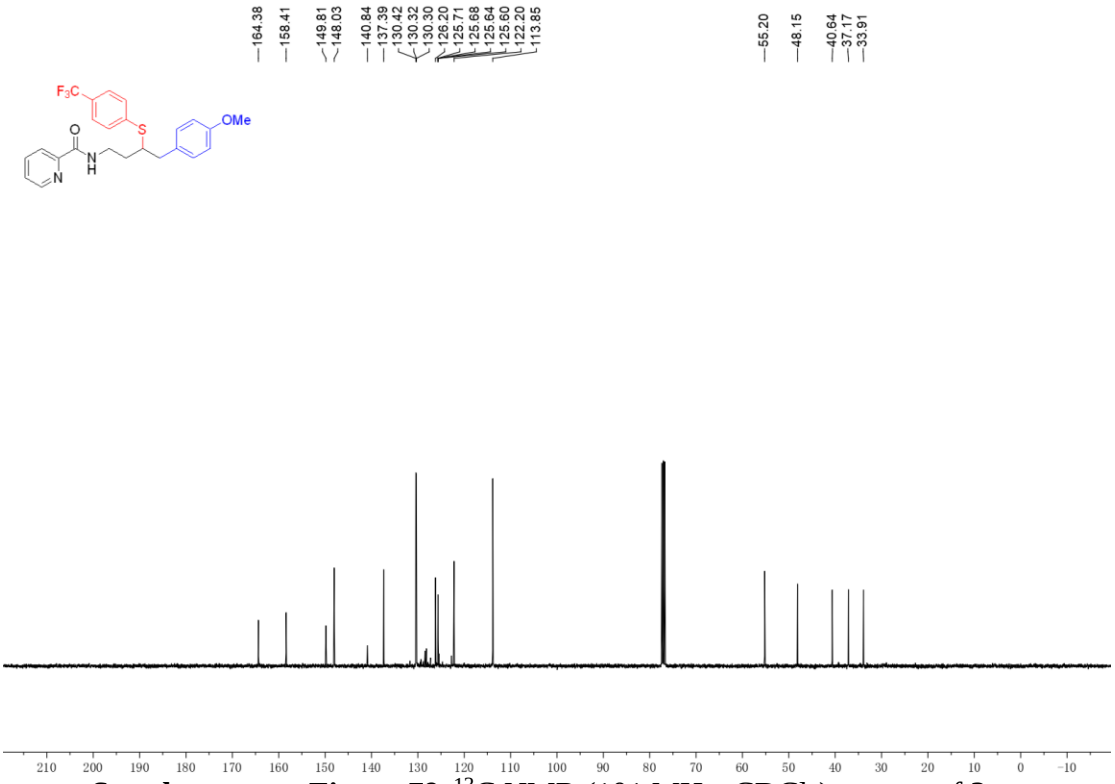
Supplementary Figure 76. ^{1}H NMR and ^{13}C NMR spectra of **2af**



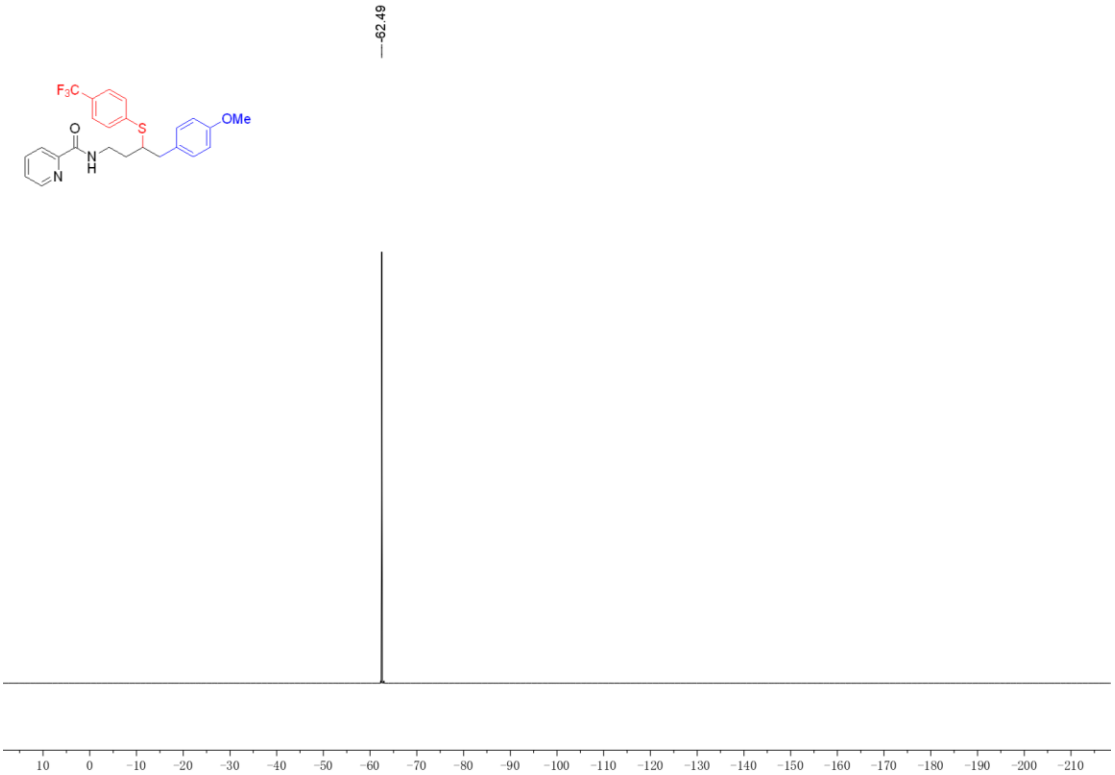
Supplementary Figure 77. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2af**



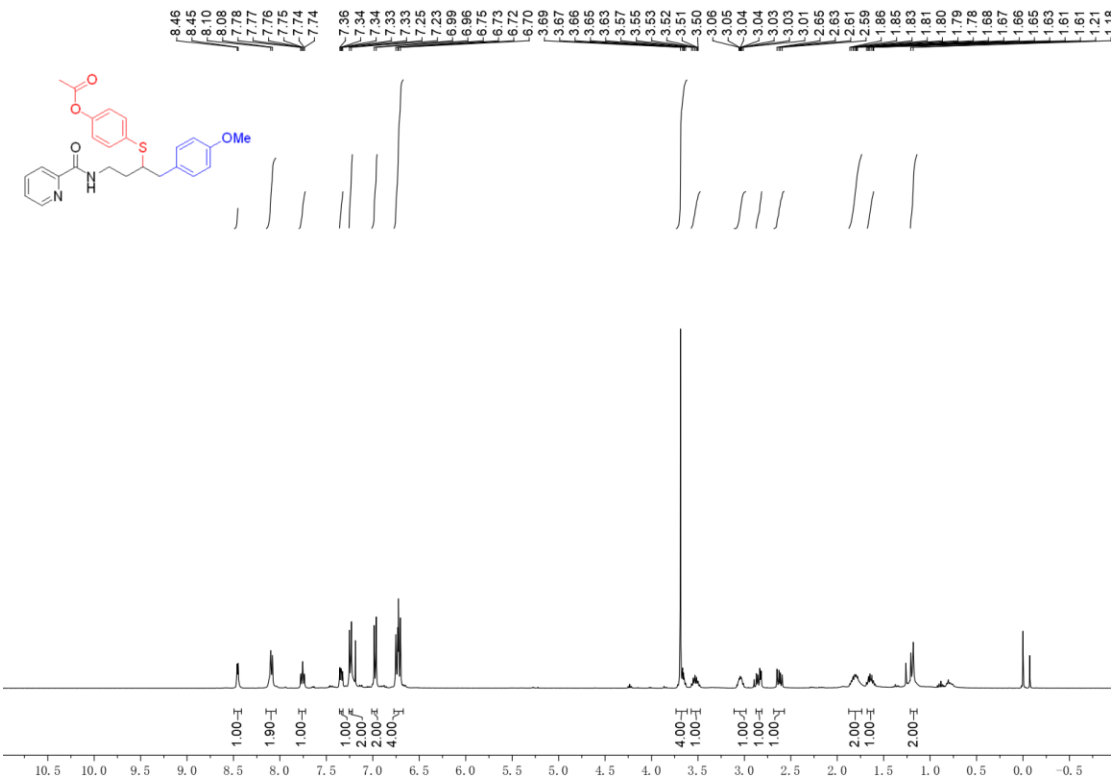
Supplementary Figure 78. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2ag**



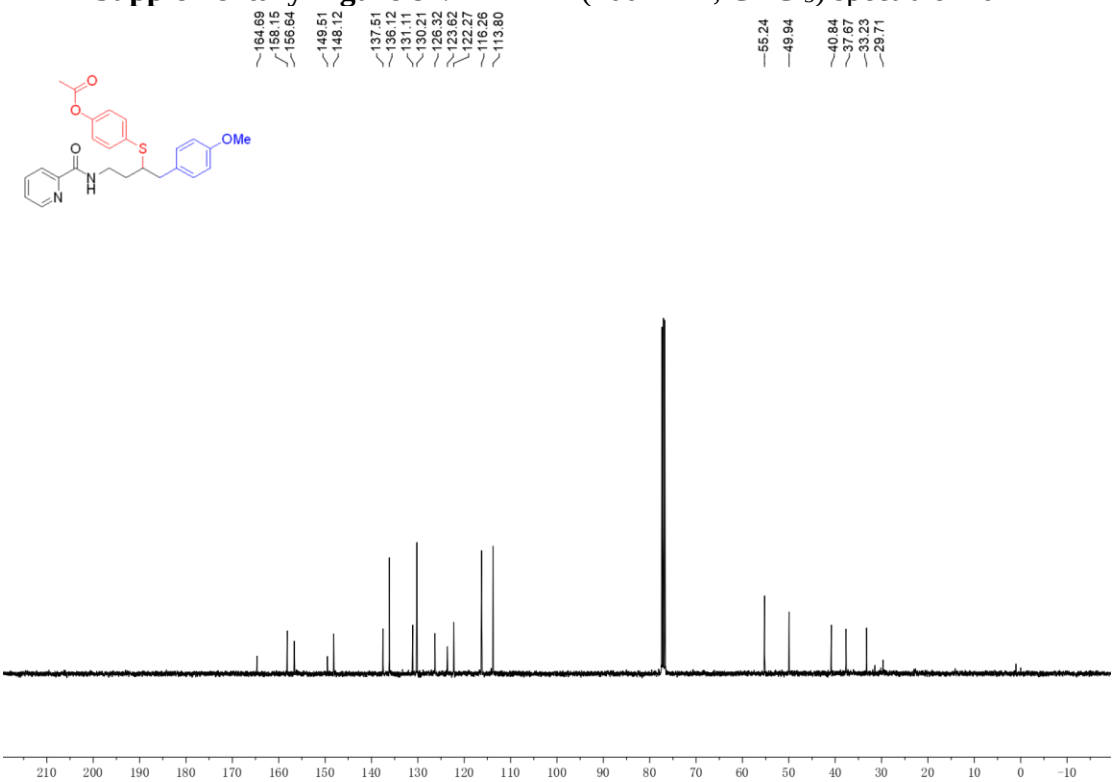
Supplementary Figure 79. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2ag**



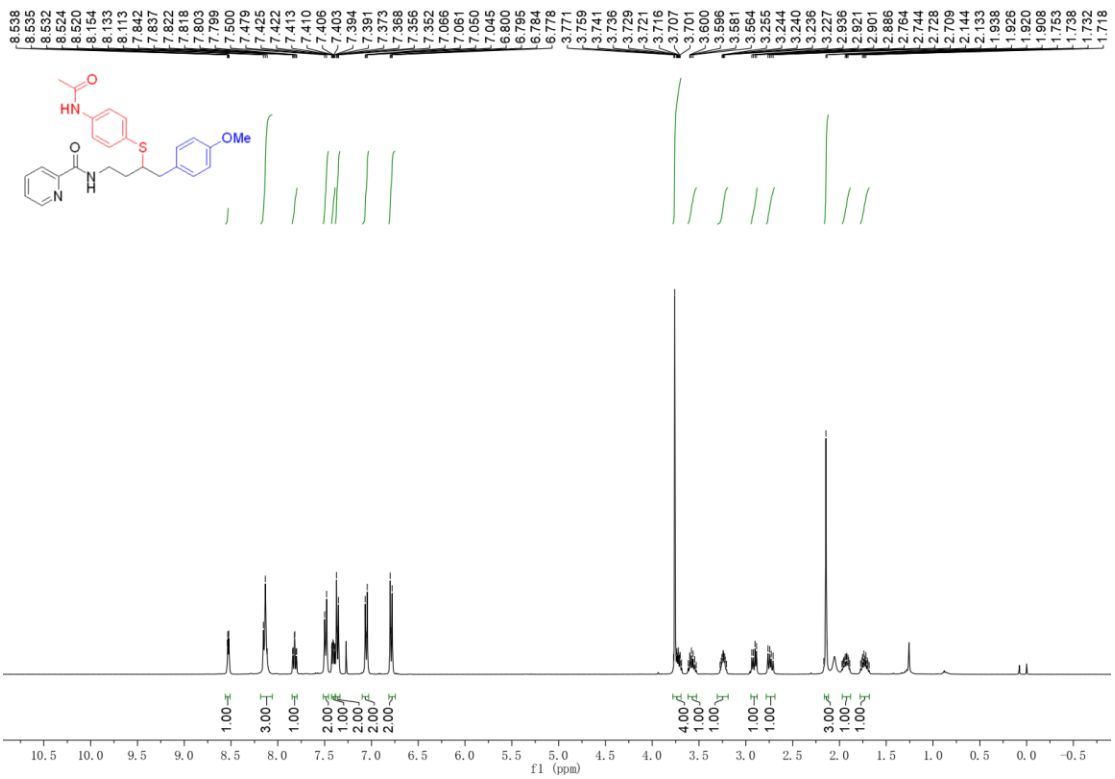
Supplementary Figure 80. ^{19}F NMR (376 MHz, $CDCl_3$) spectra of **2ag**



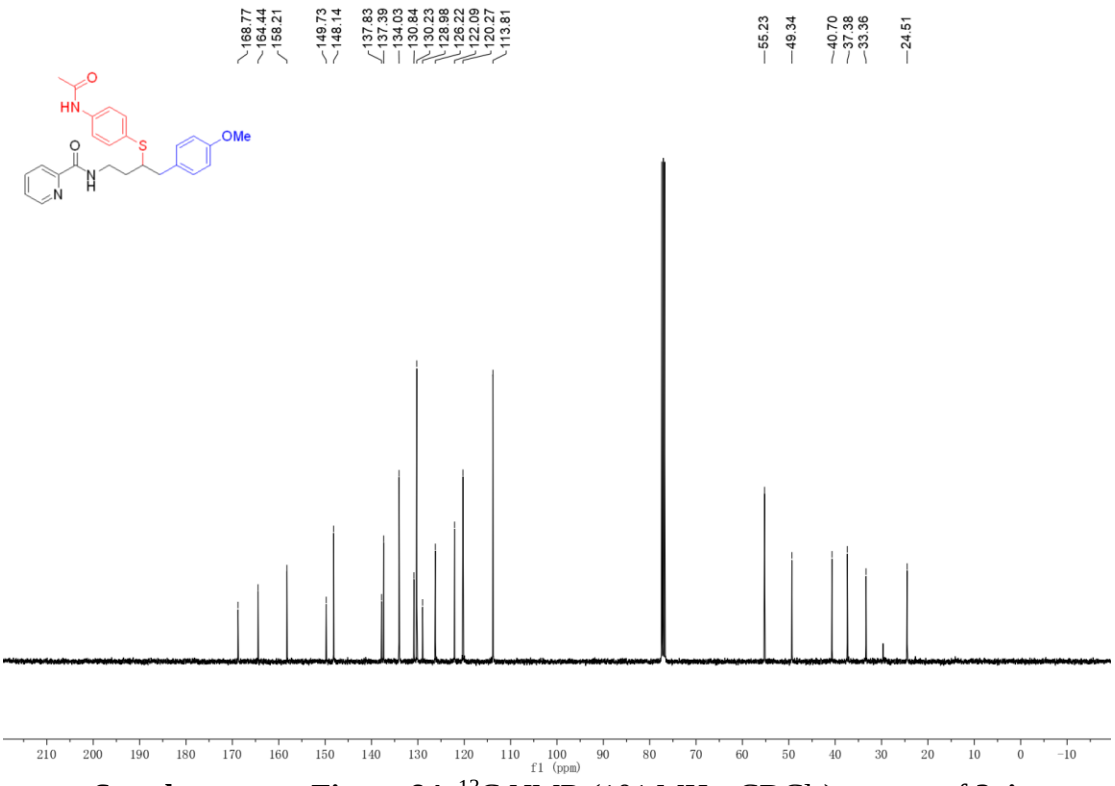
Supplementary Figure 81. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2ah**



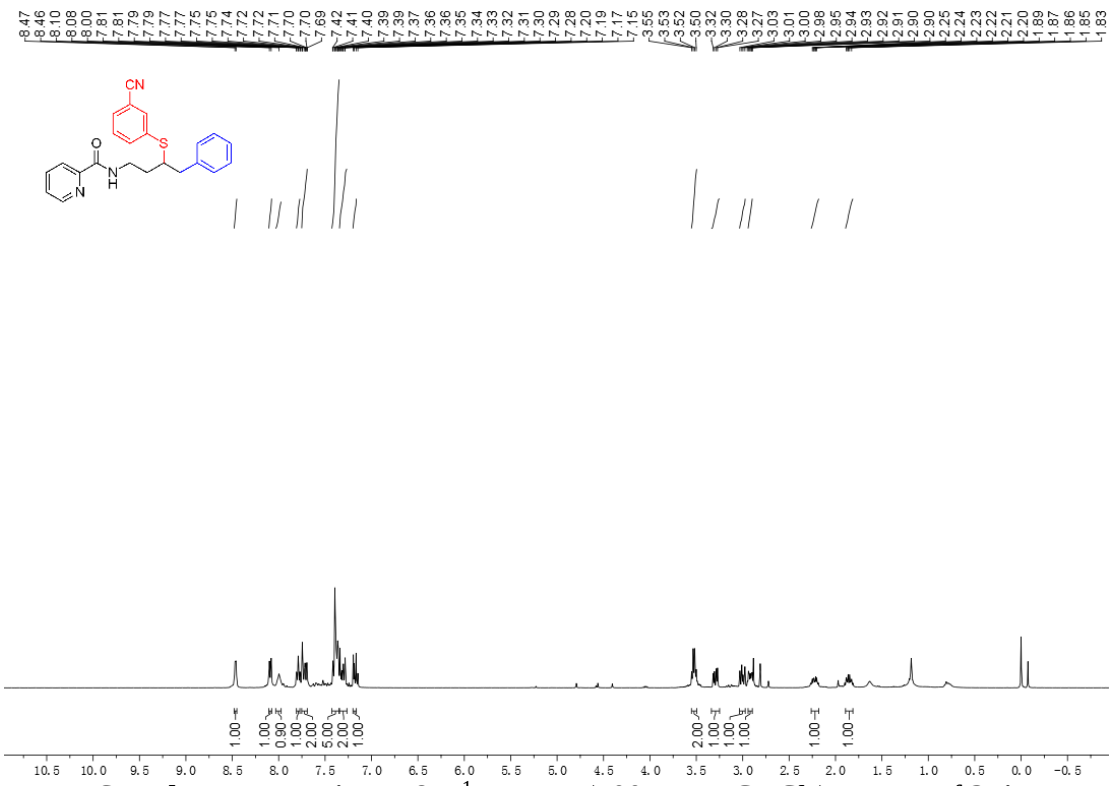
Supplementary Figure 82. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2ah**



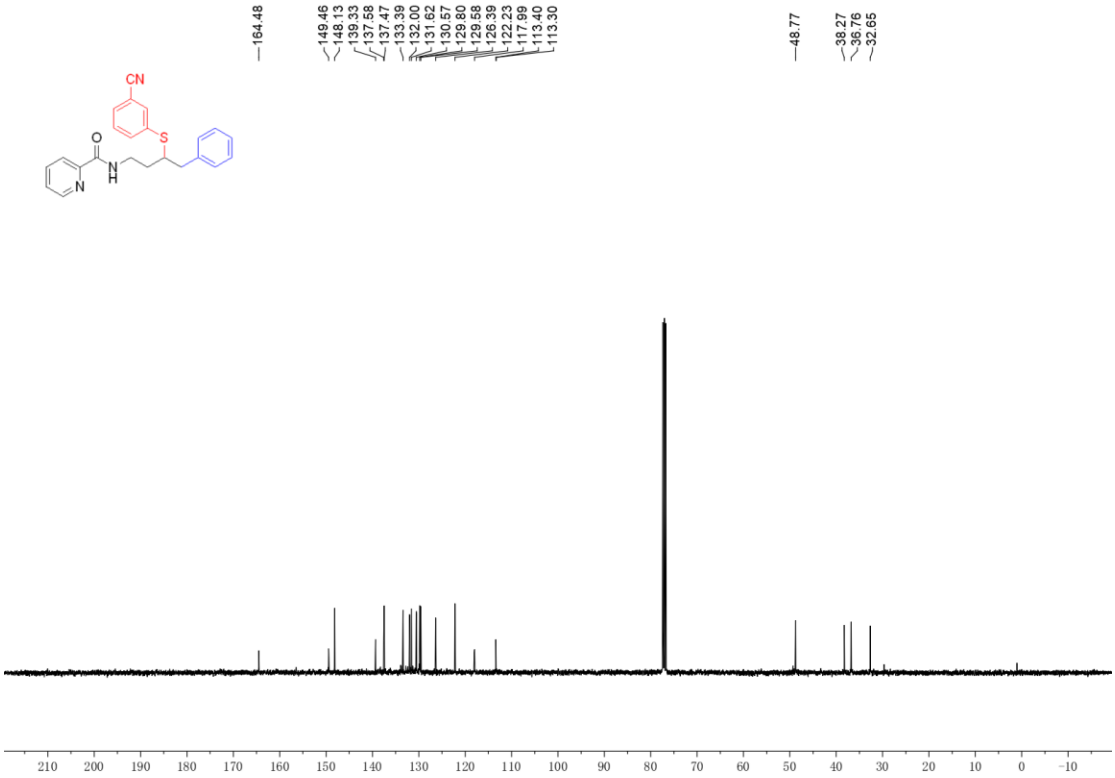
Supplementary Figure 83. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2ai**



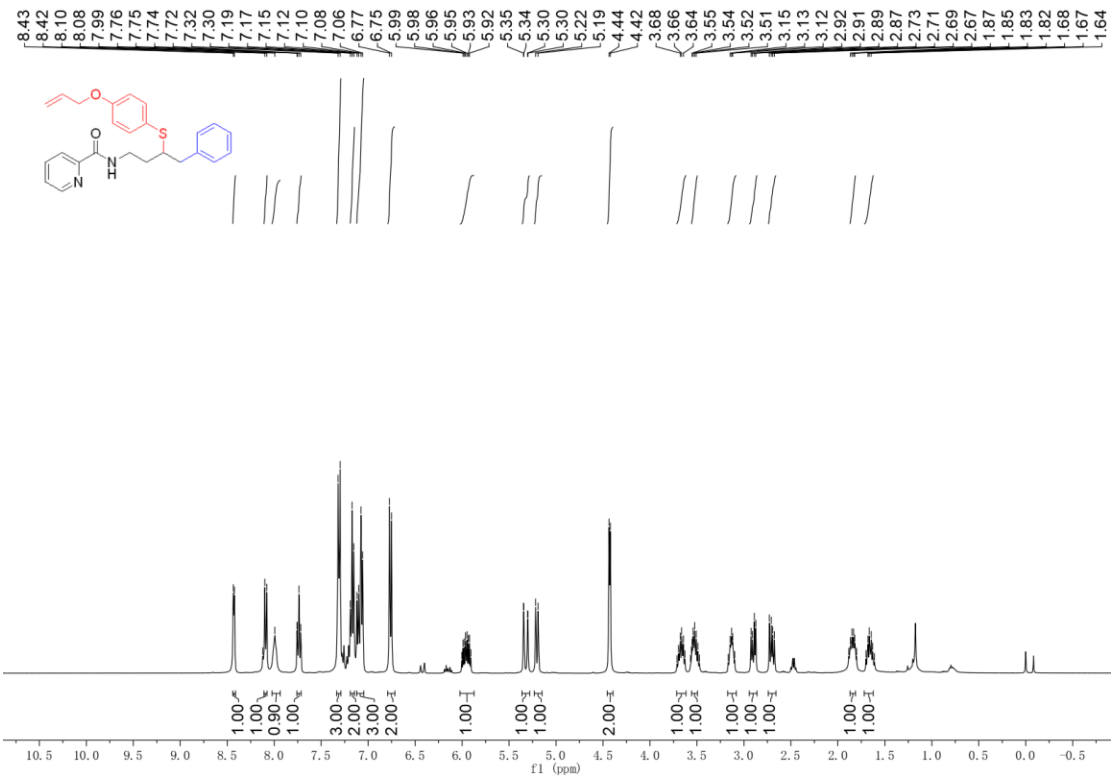
Supplementary Figure 84. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2ai**



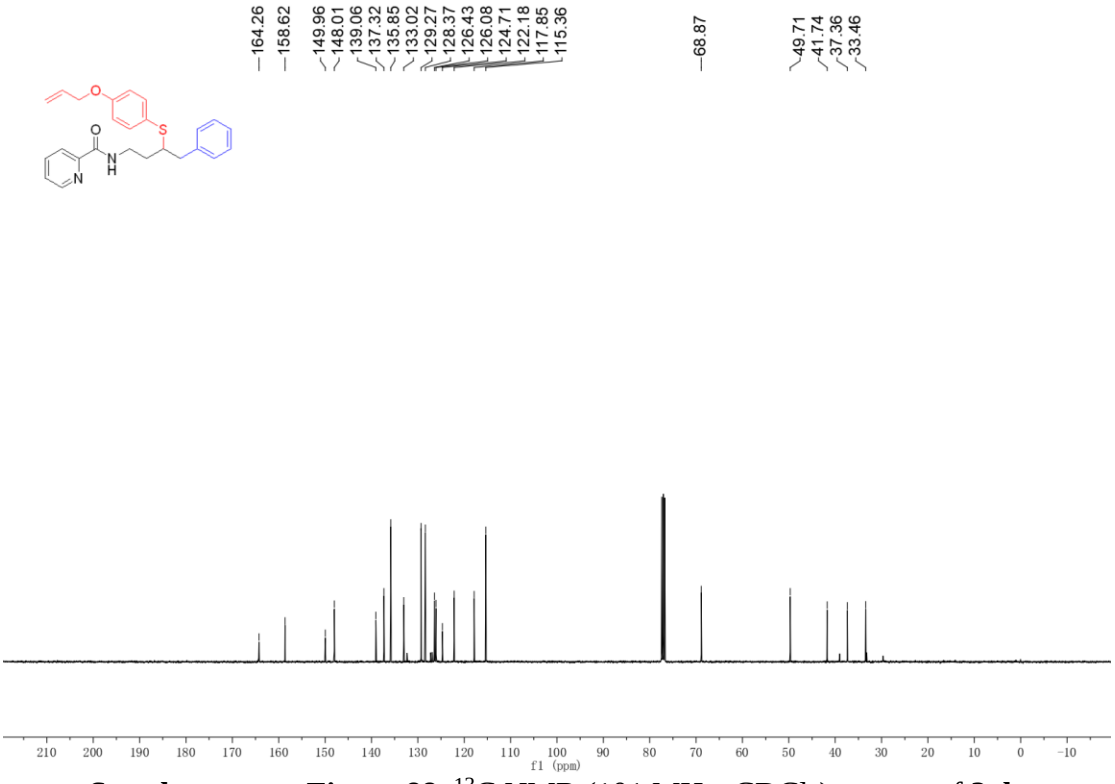
Supplementary Figure 85. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2aj**



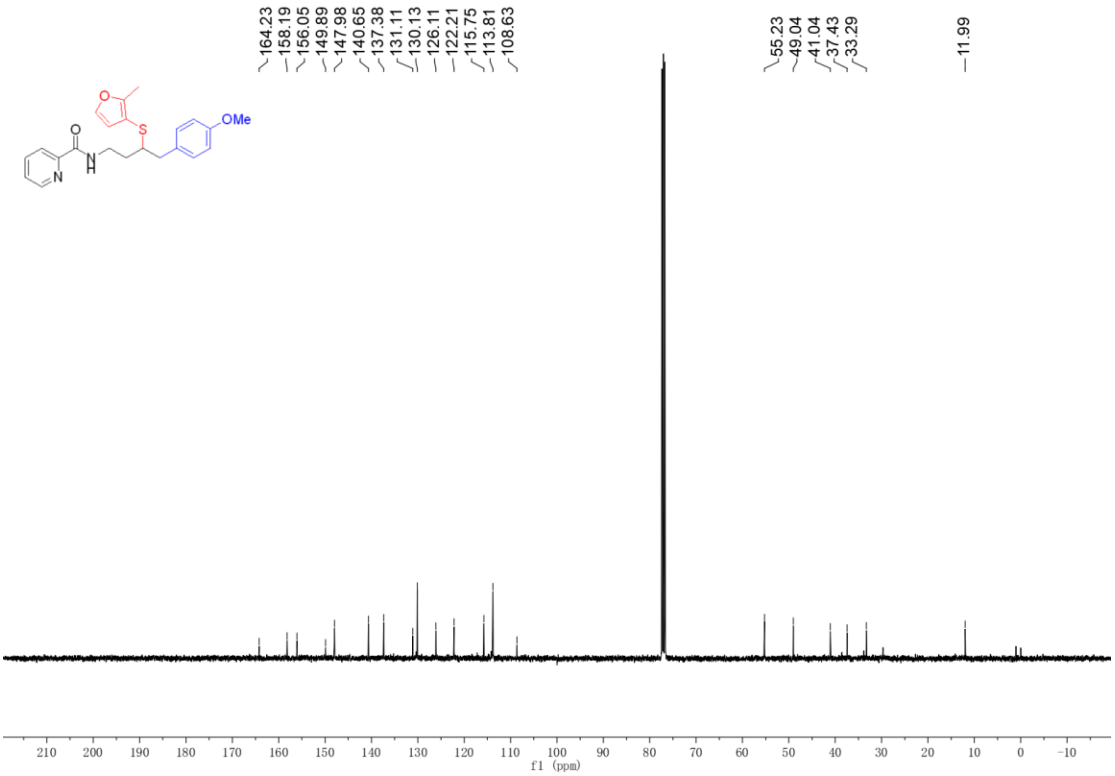
Supplementary Figure 86. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2aj**



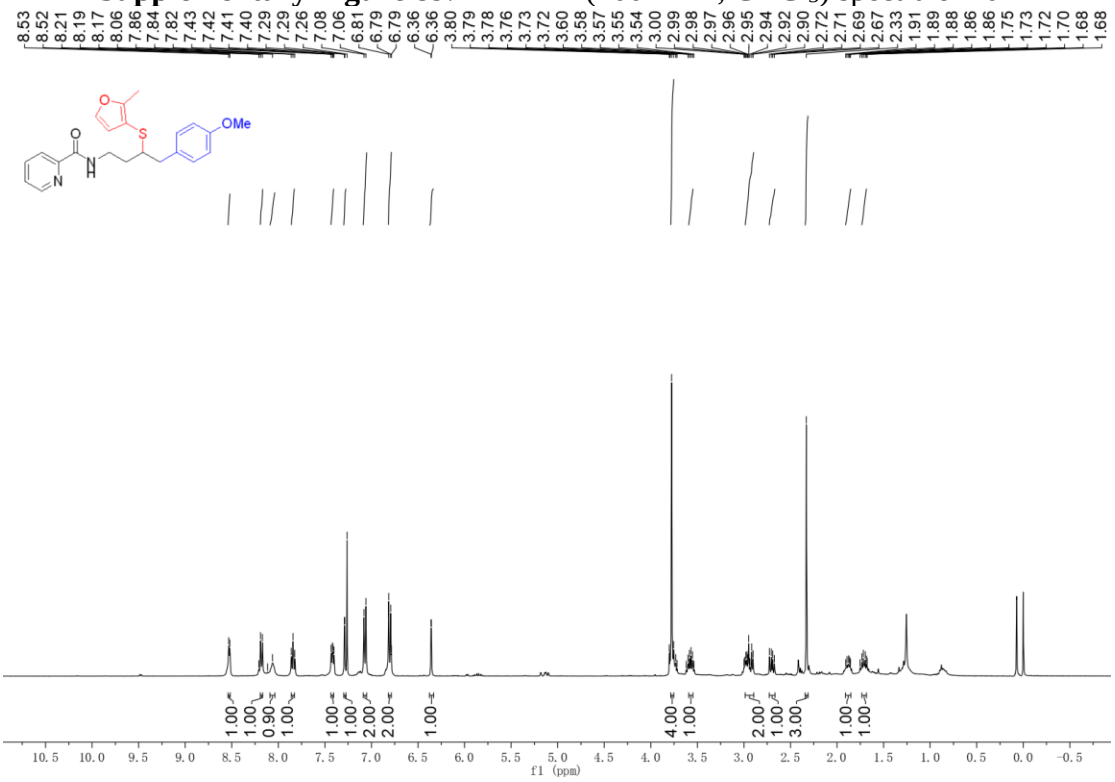
Supplementary Figure 87. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2ak**



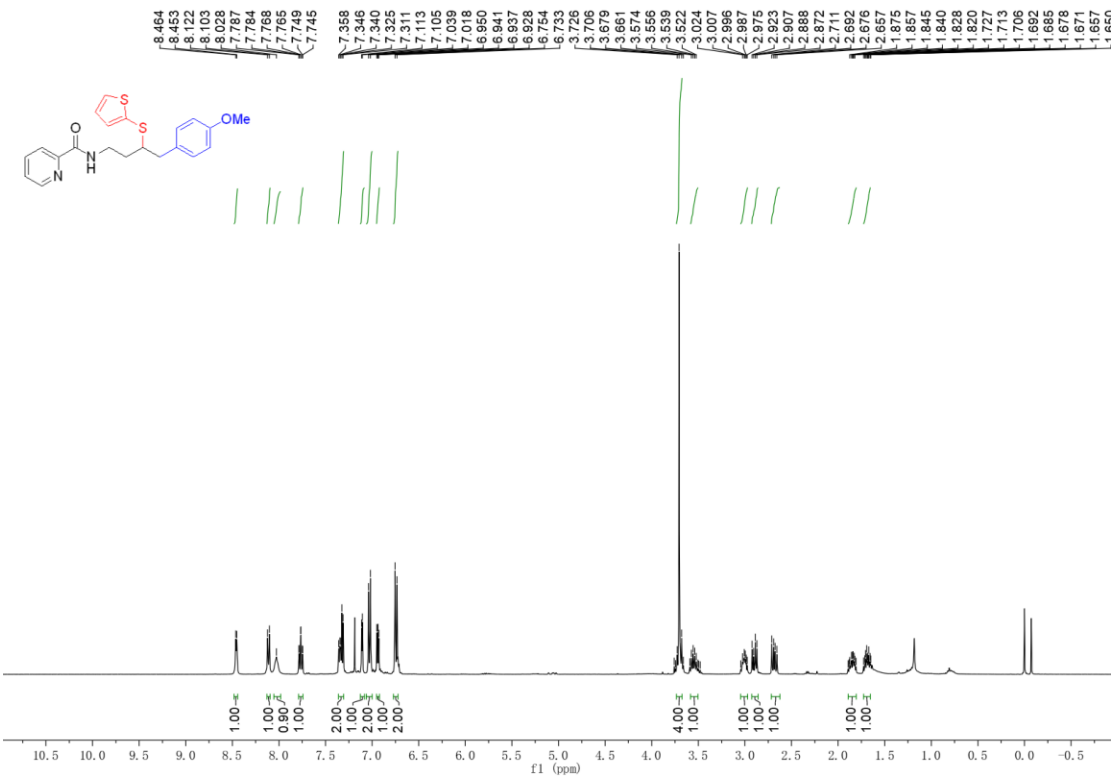
Supplementary Figure 88. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2ak**



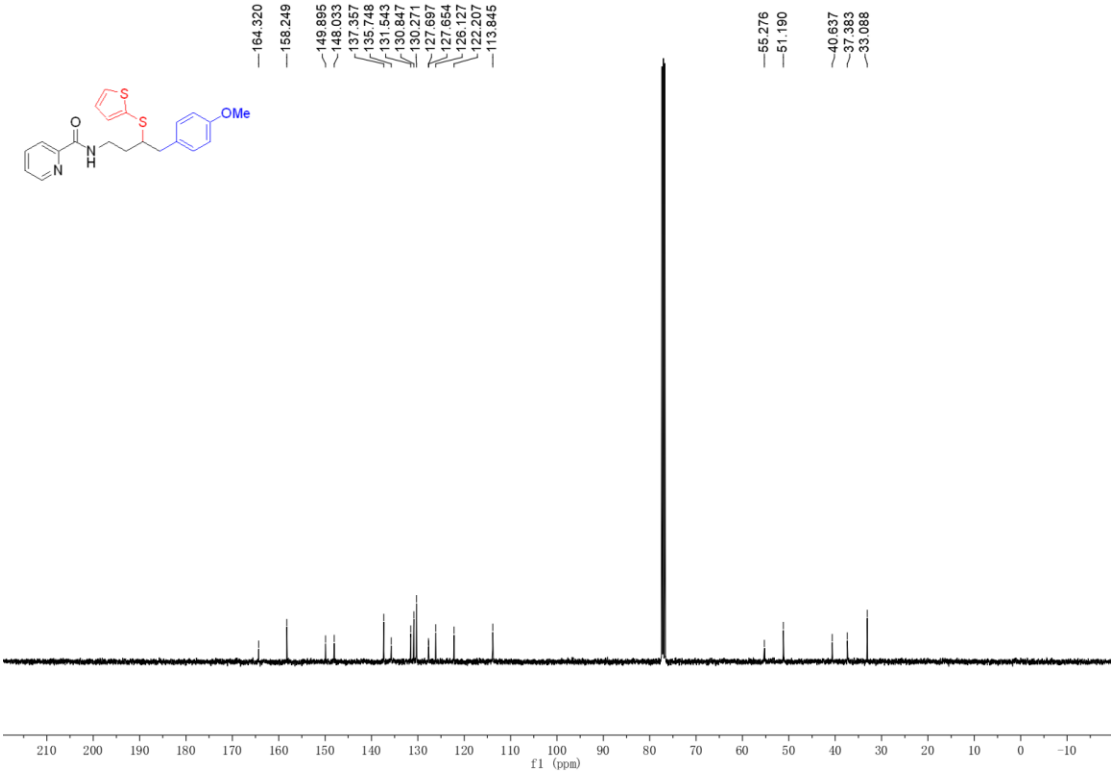
Supplementary Figure 89. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2al**



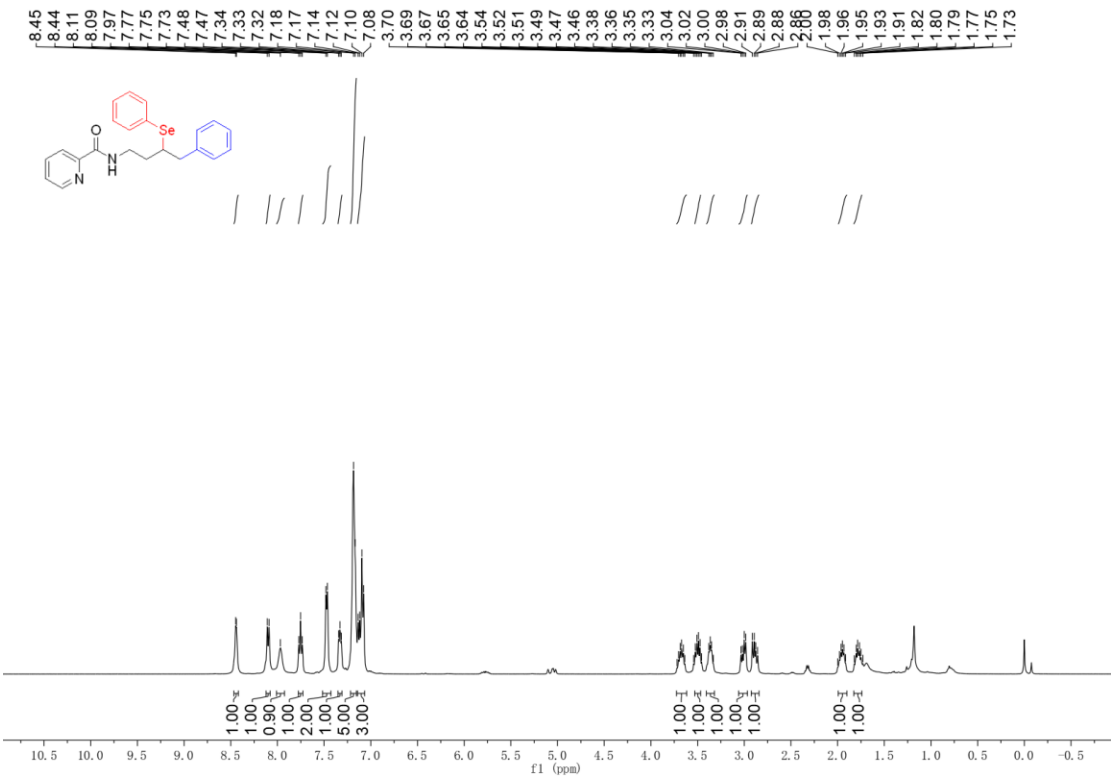
Supplementary Figure 90. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2al**



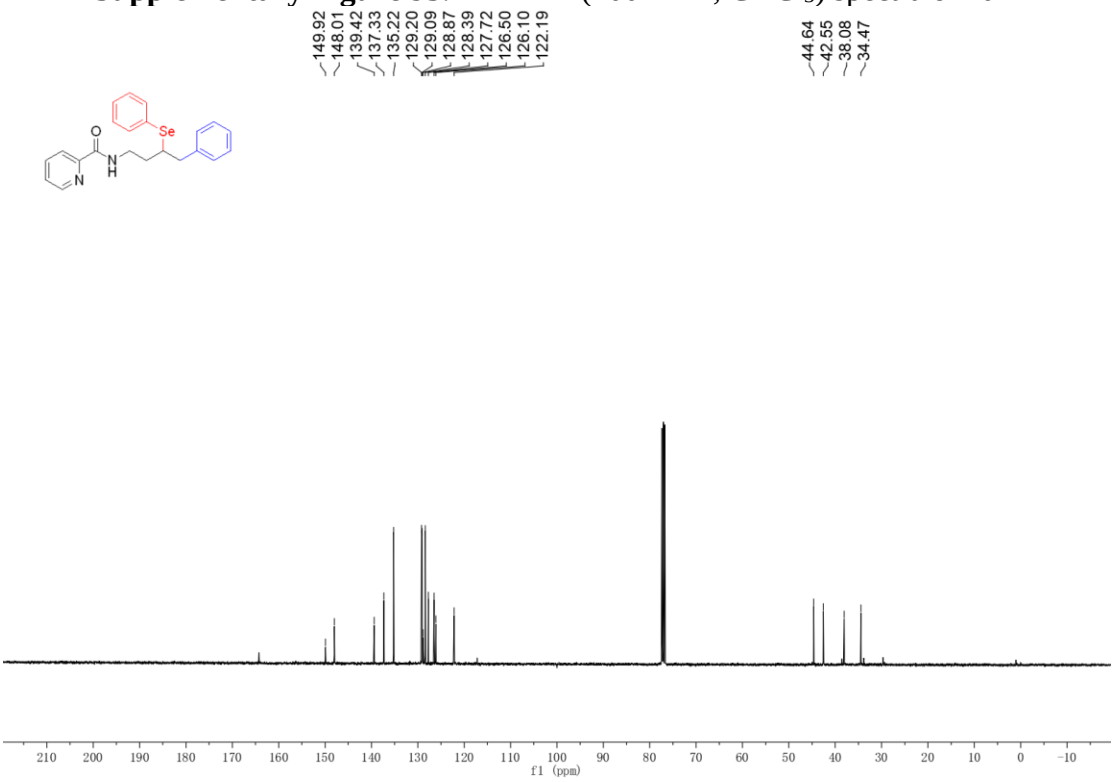
Supplementary Figure 91. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2am**



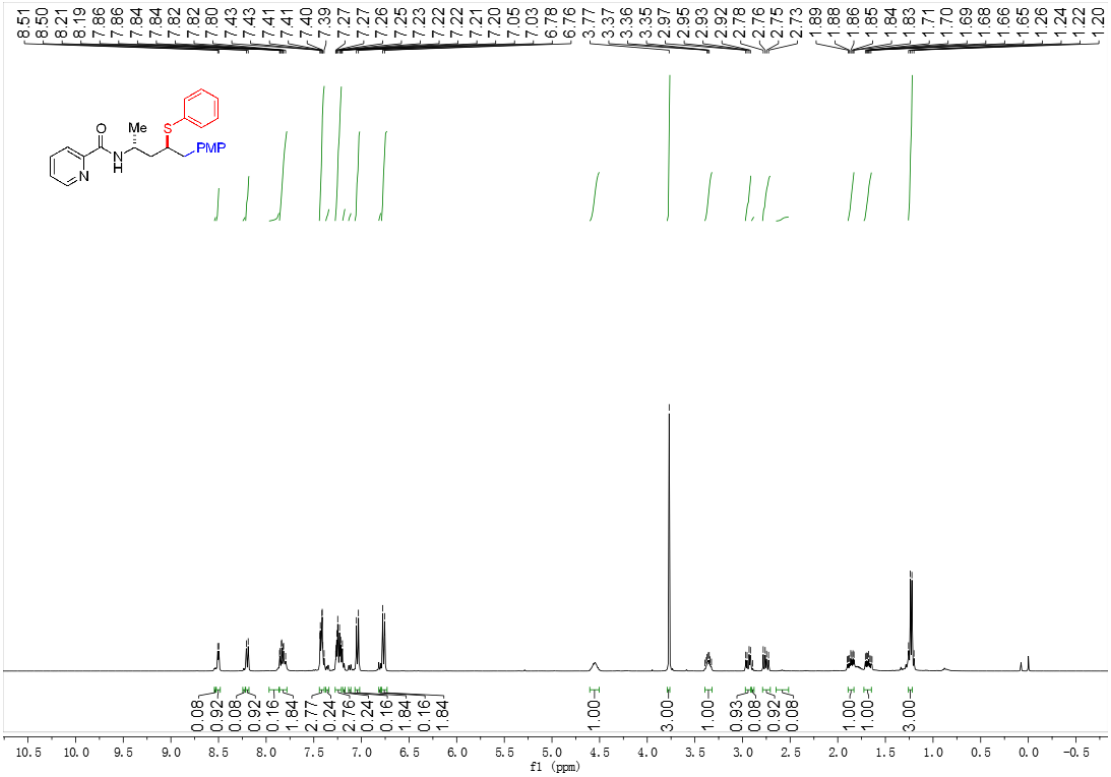
Supplementary Figure 92. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2am**



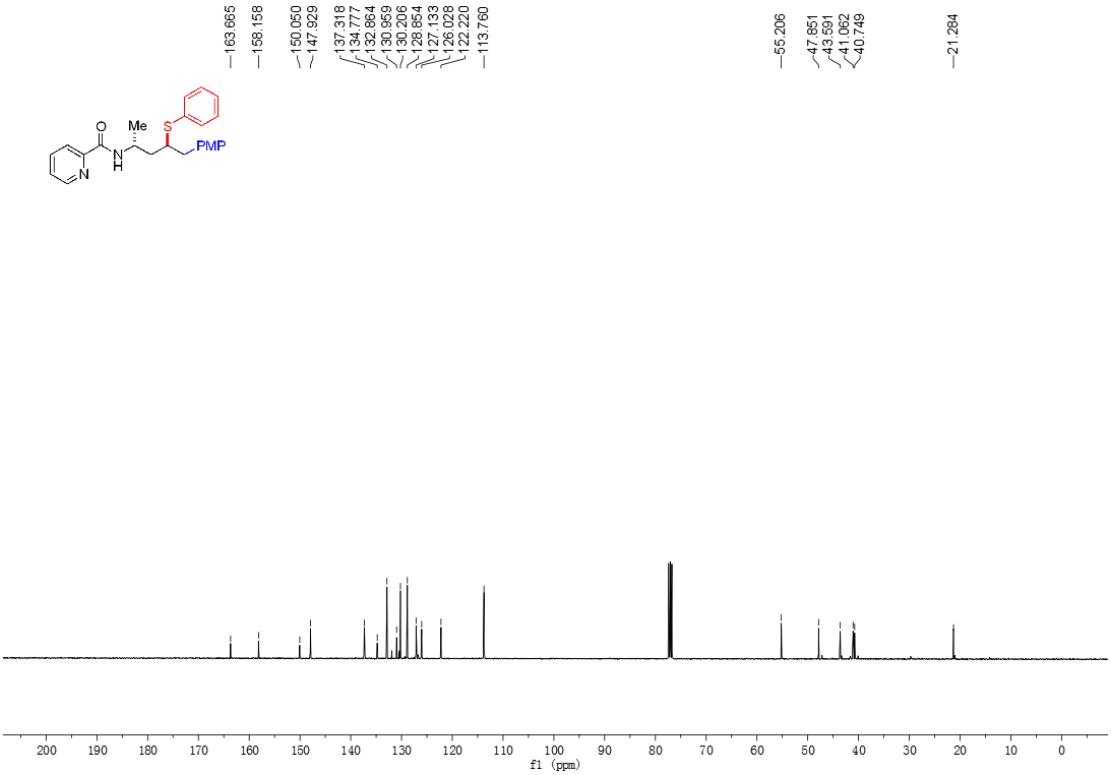
Supplementary Figure 93. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2an**



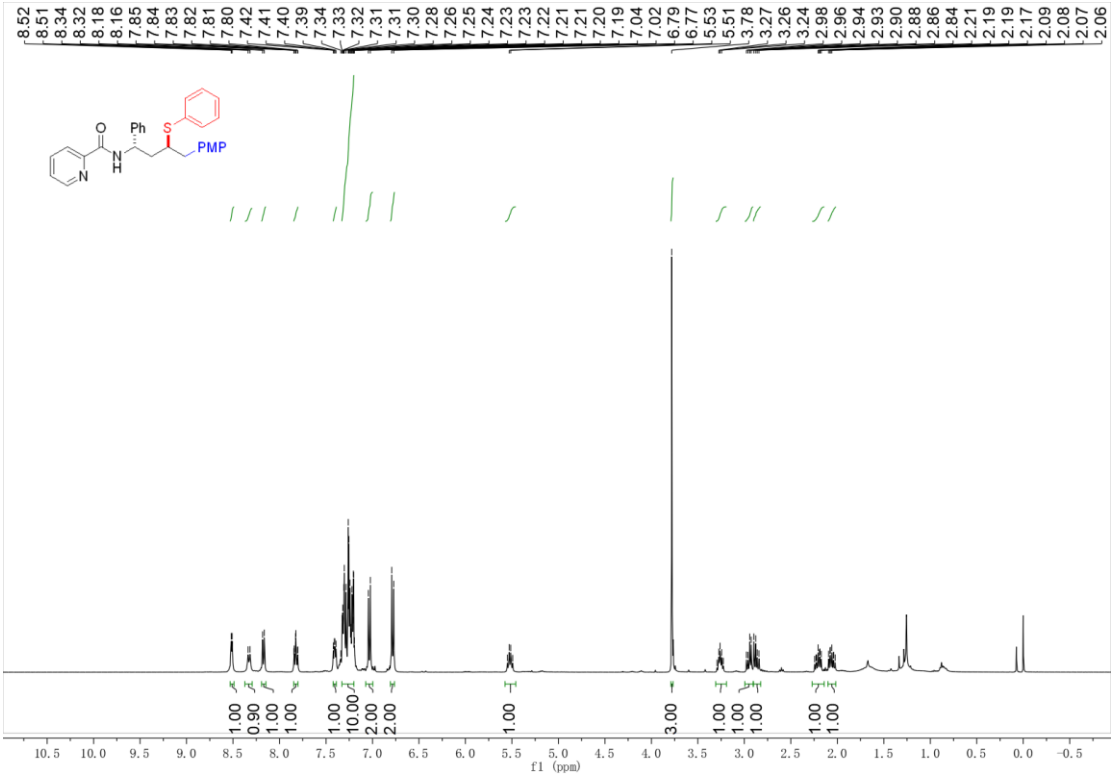
Supplementary Figure 94. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2an**



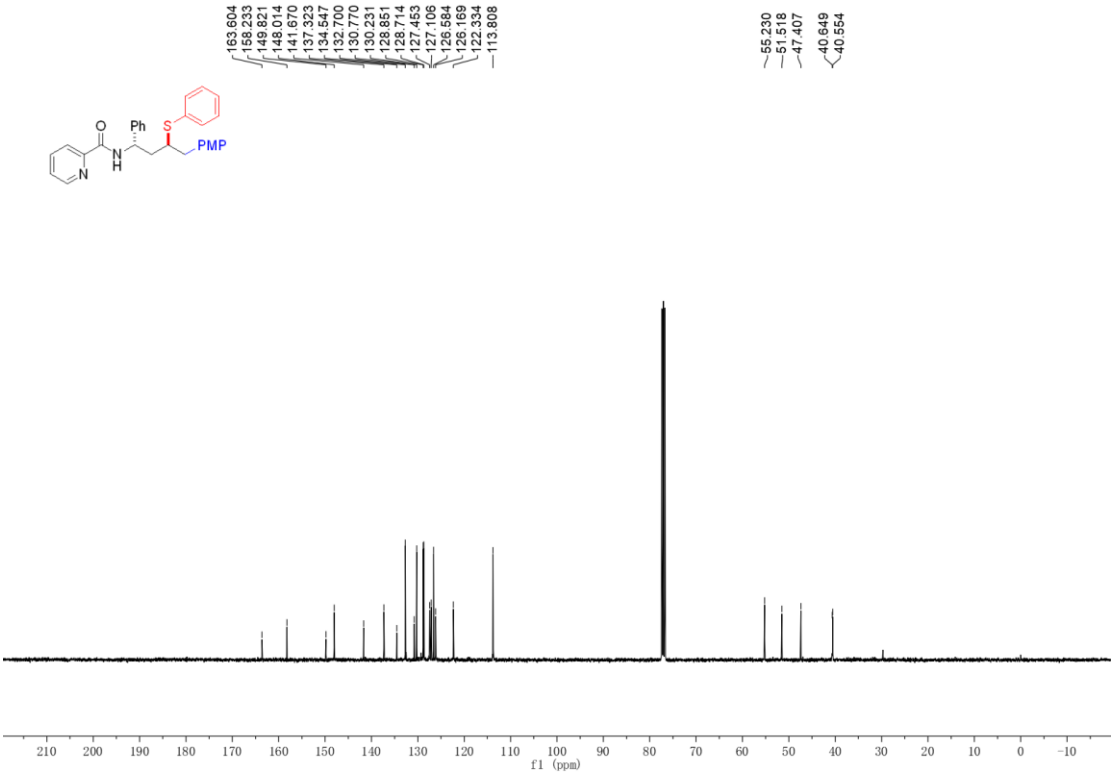
Supplementary Figure 95. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2ao**



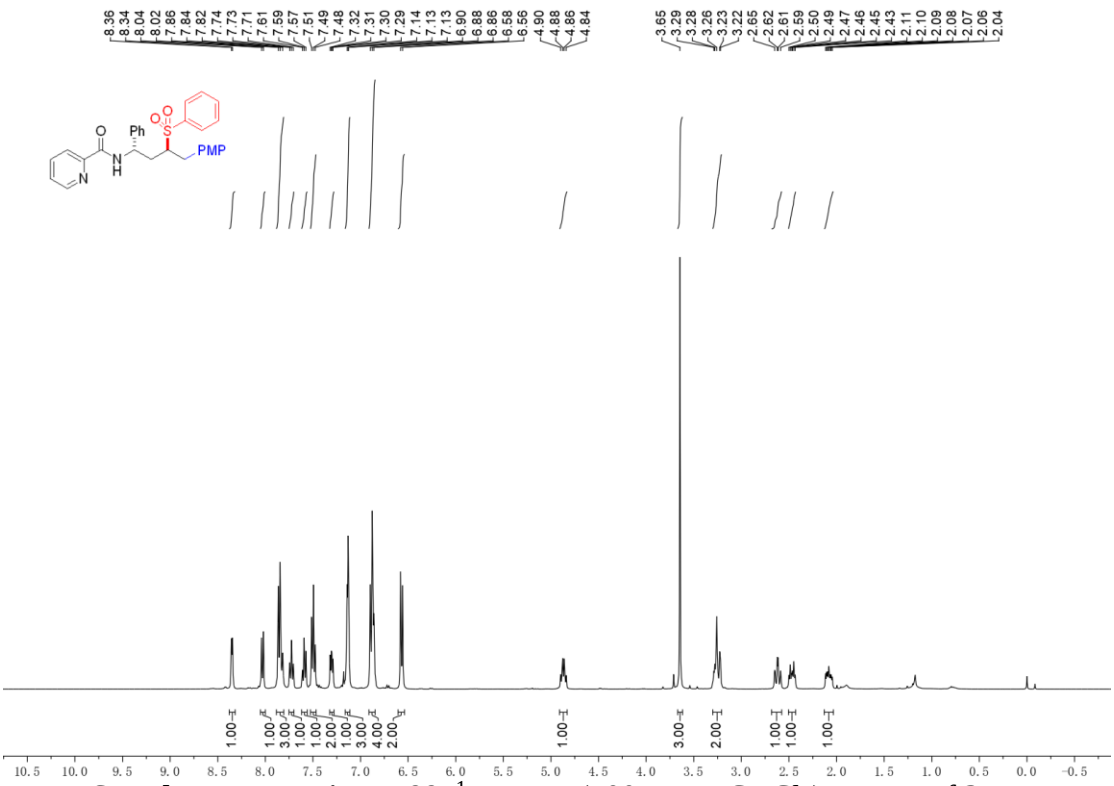
Supplementary Figure 96. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2ao**



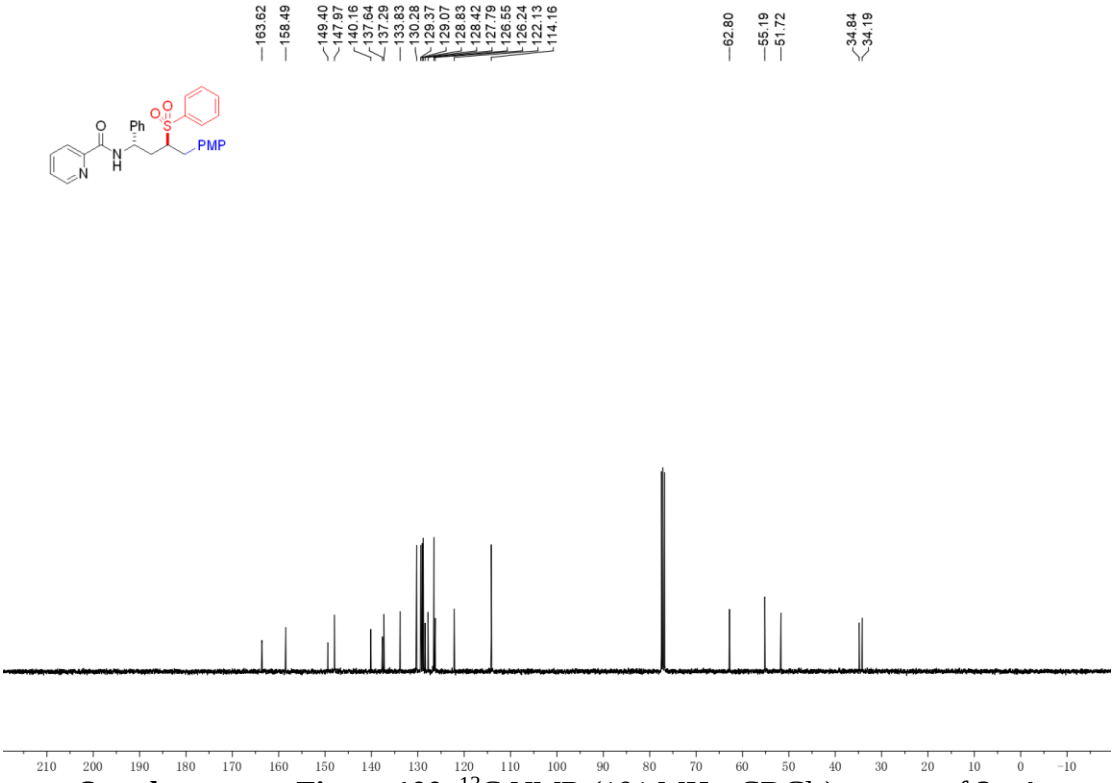
Supplementary Figure 97. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2ap**



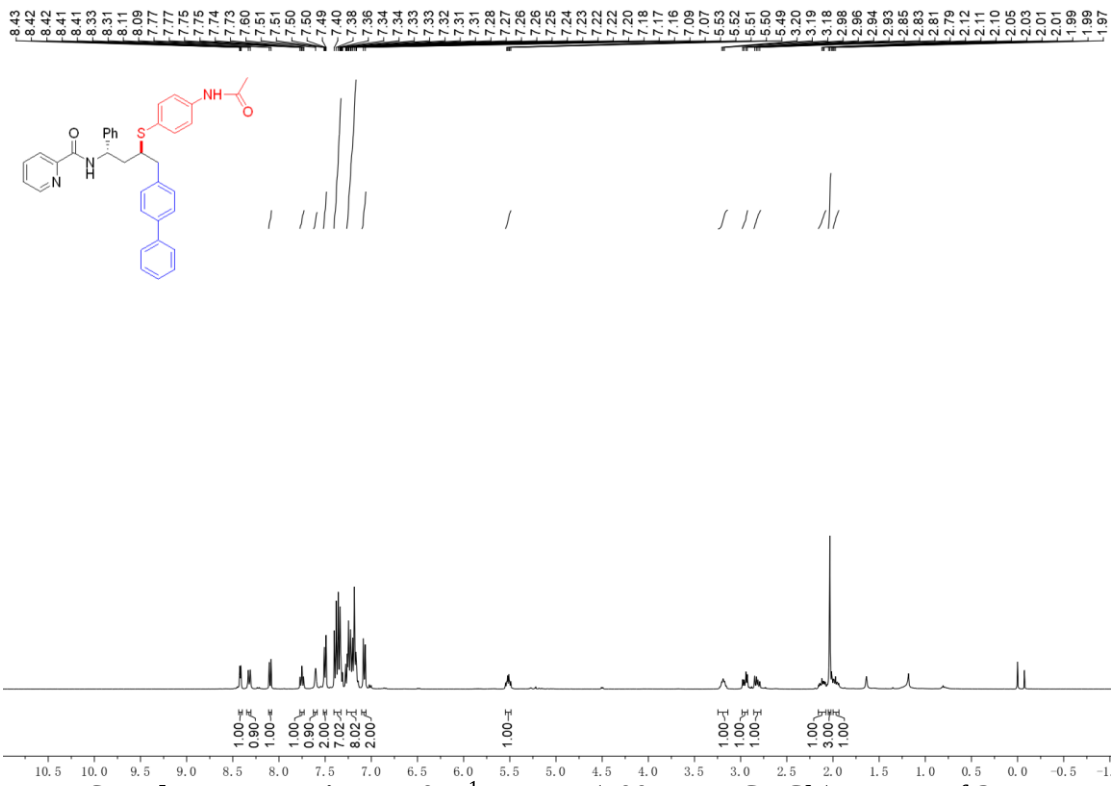
Supplementary Figure 98. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2ap**



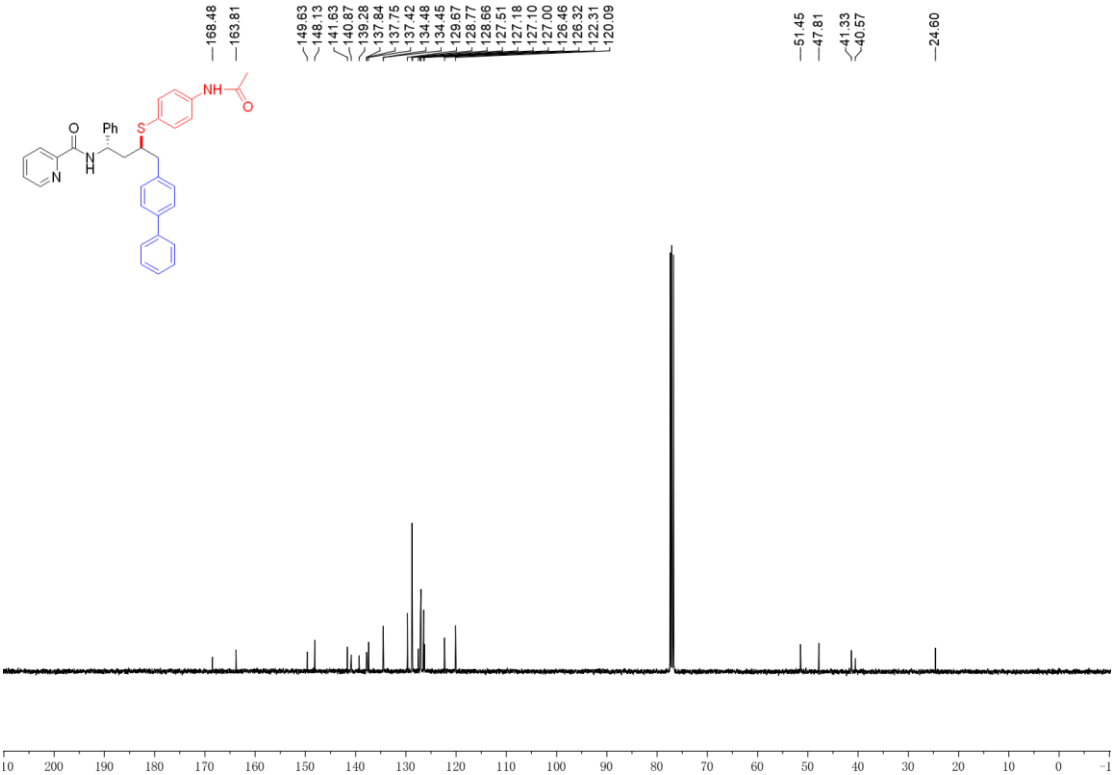
Supplementary Figure 99. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2ap'**



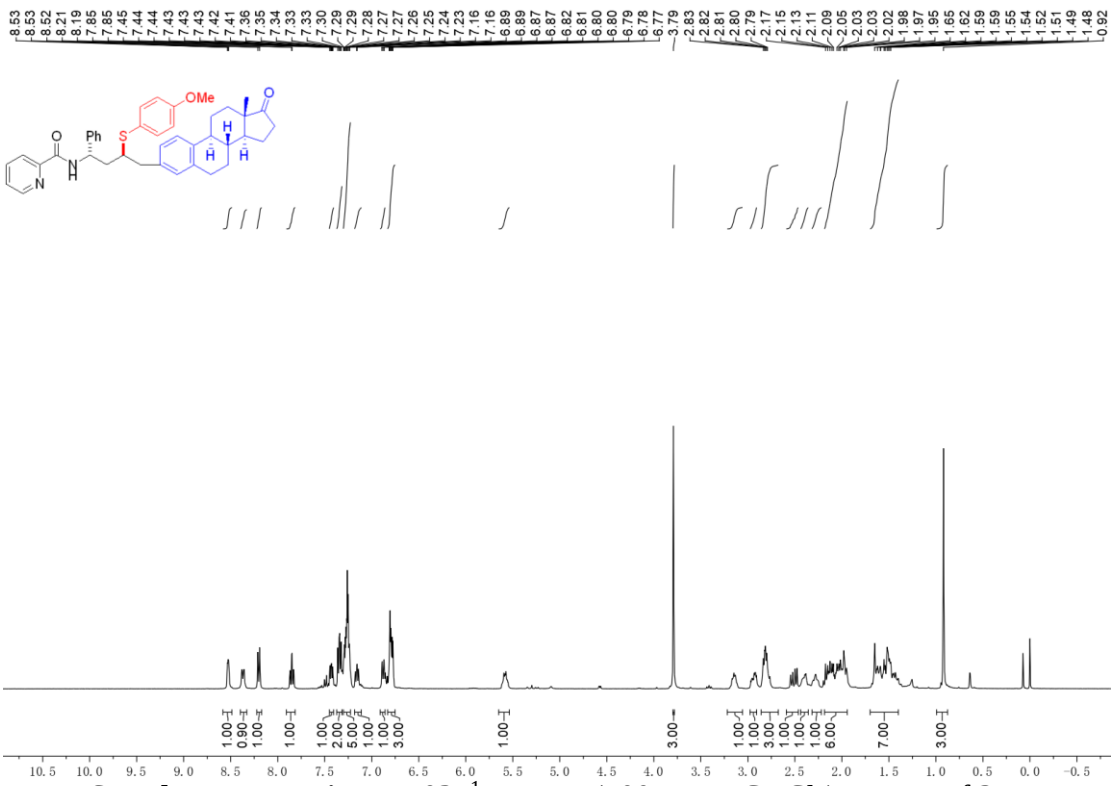
Supplementary Figure 100. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2ap'**



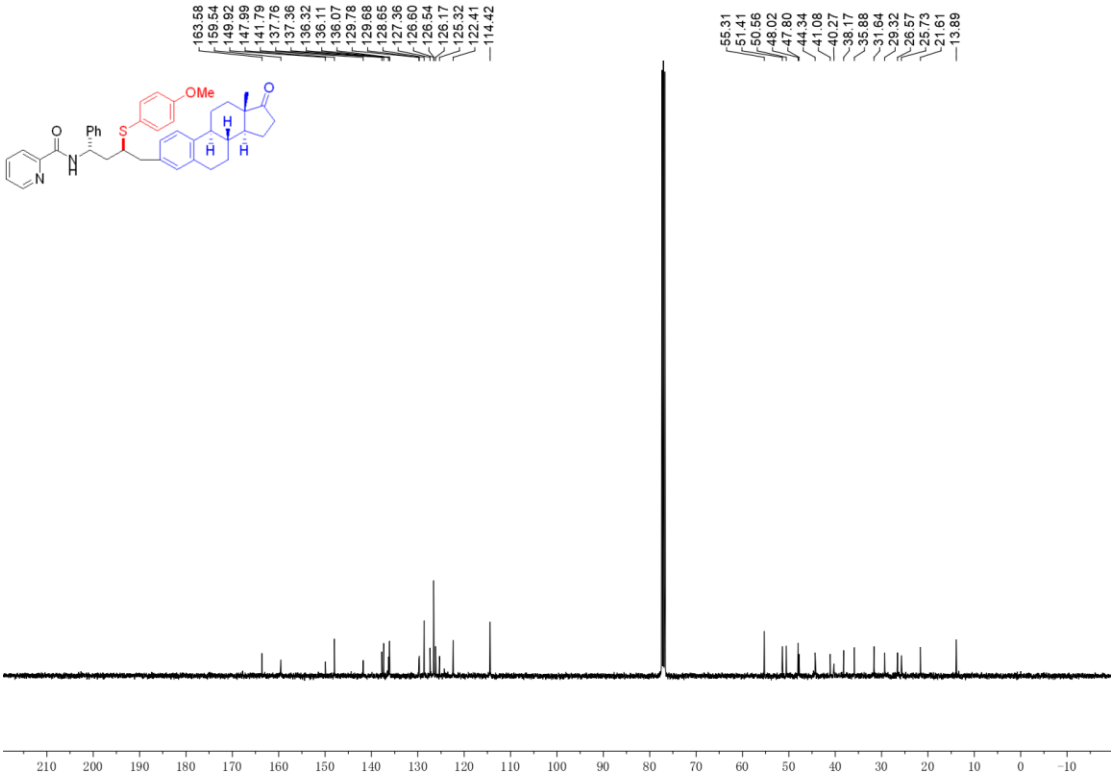
Supplementary Figure 101. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2aq**



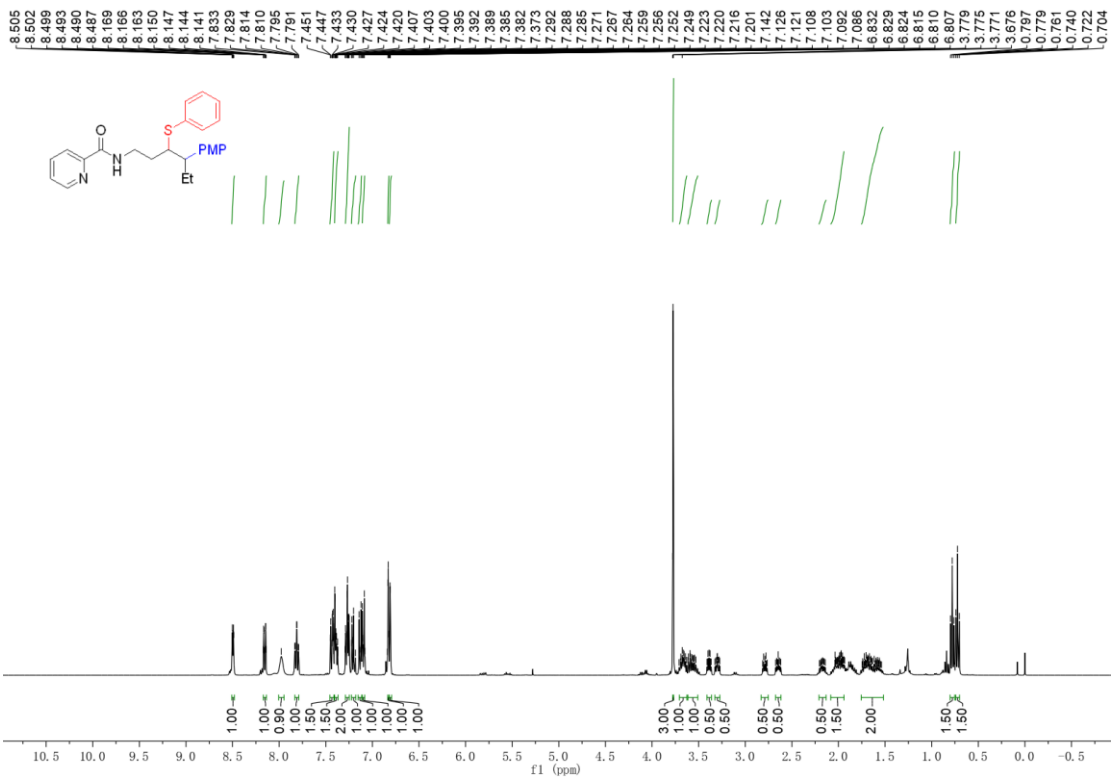
Supplementary Figure 102. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2aq**



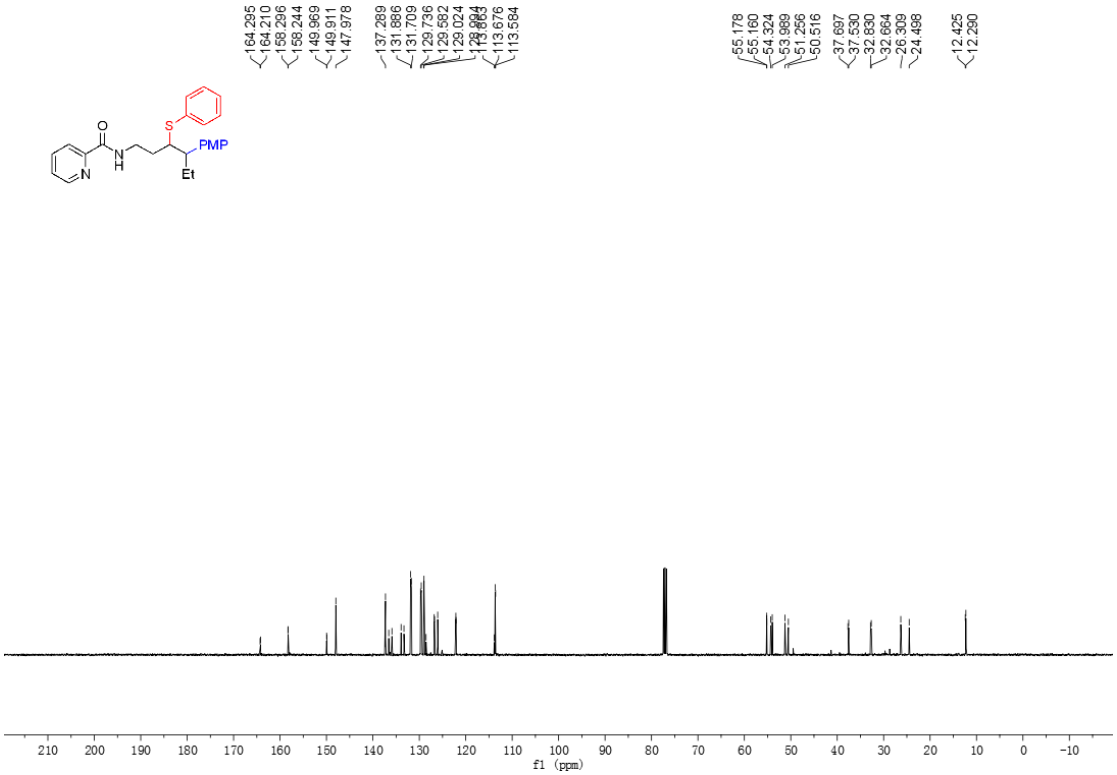
Supplementary Figure 103. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2ar**



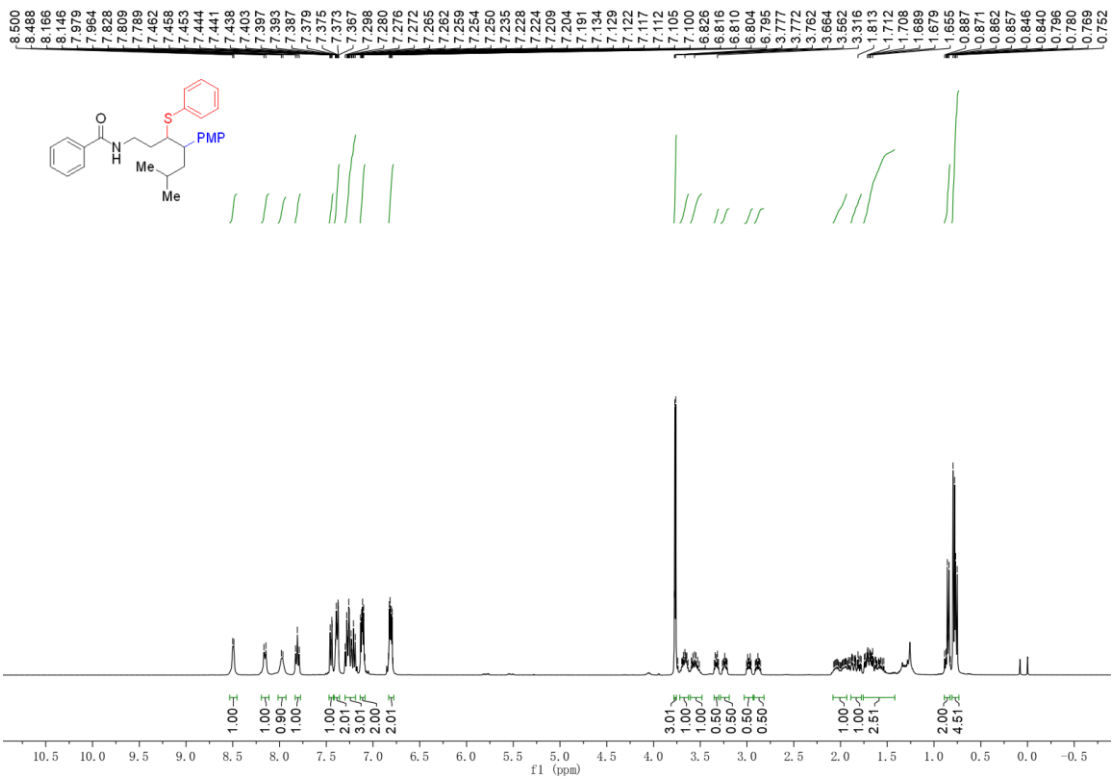
Supplementary Figure 104. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2ar**



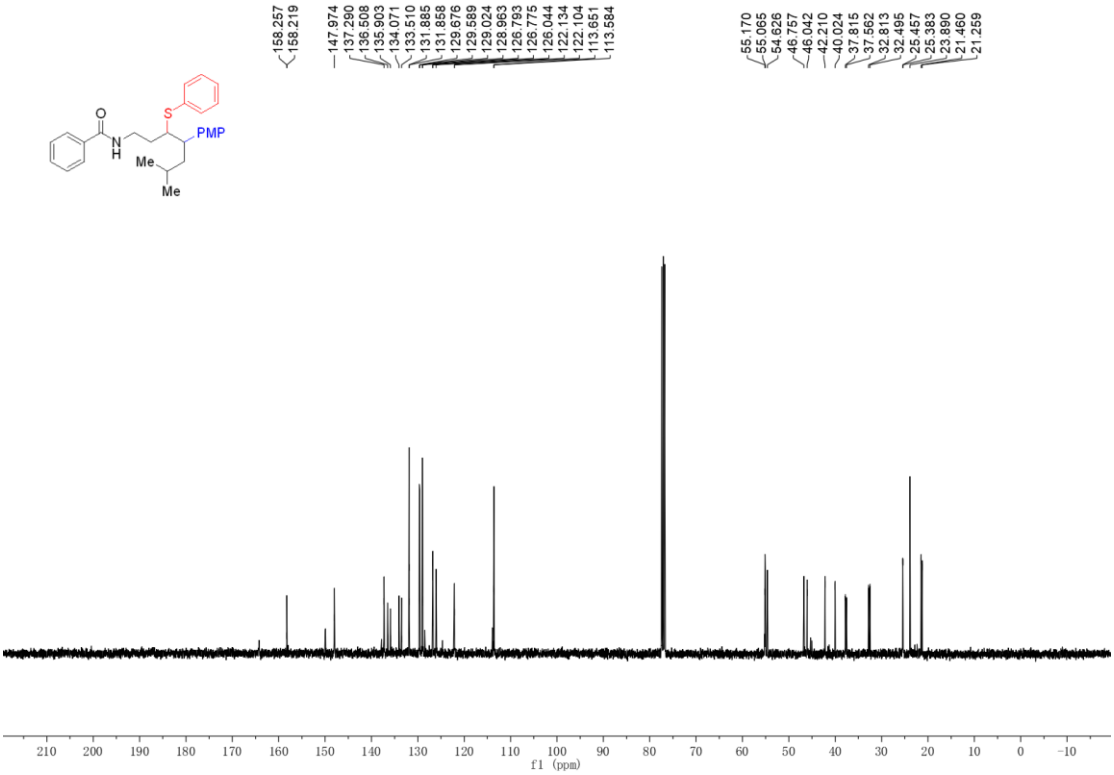
Supplementary Figure 105. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2as (2at)**



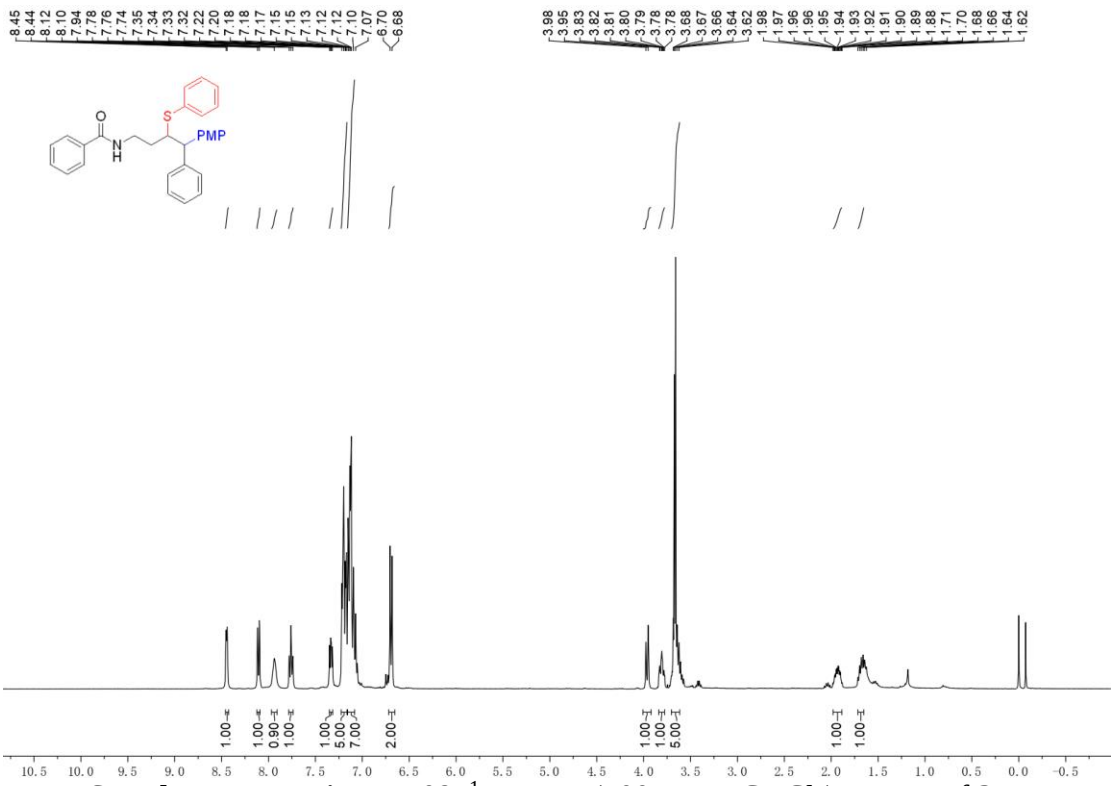
Supplementary Figure 106. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2as (2at)**



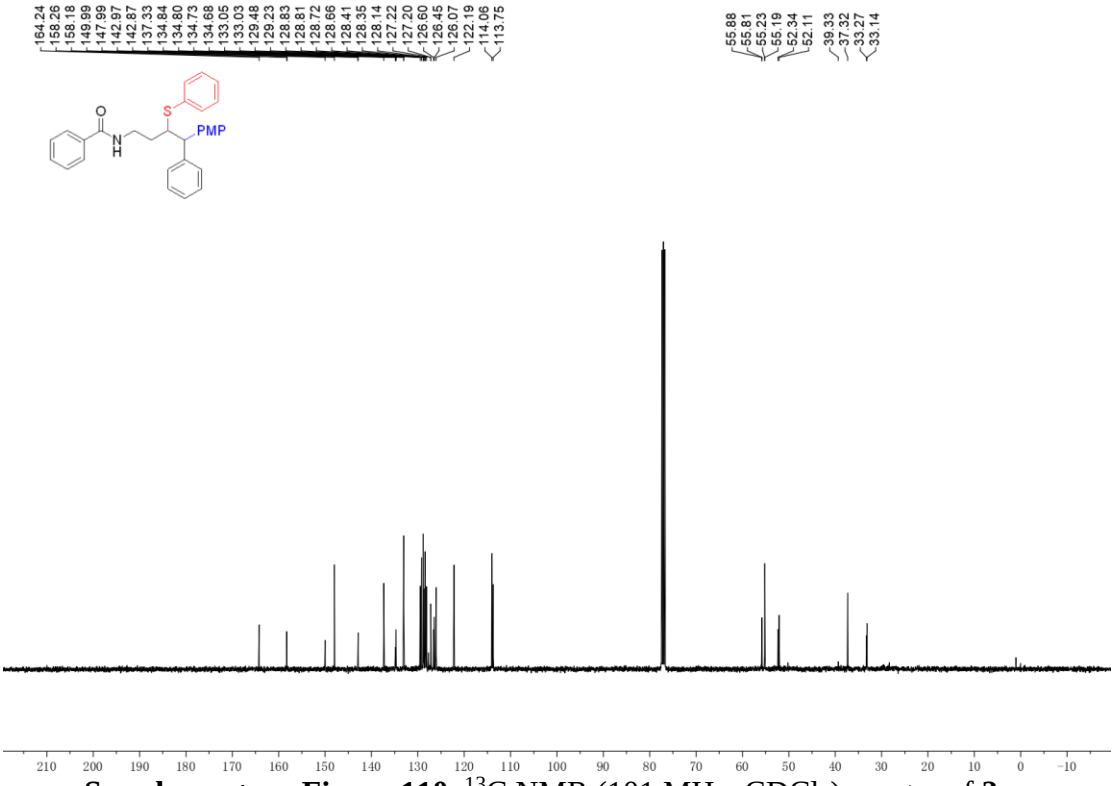
Supplementary Figure 107. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2au**



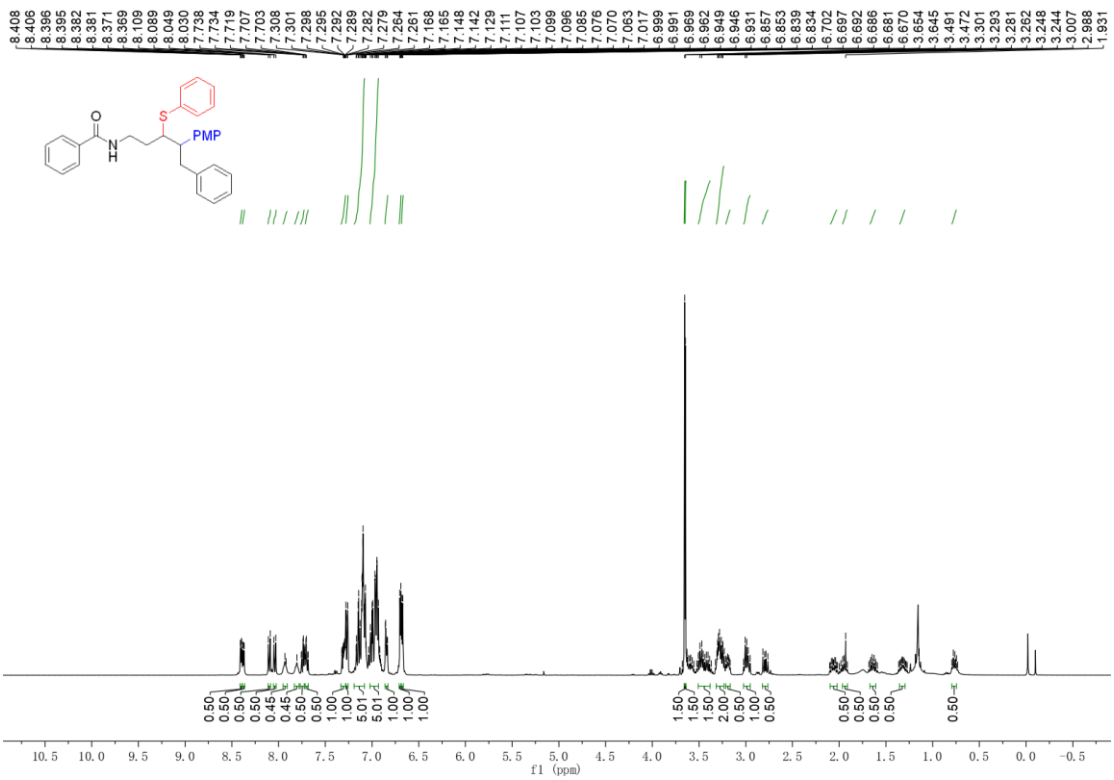
Supplementary Figure 108. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2au**



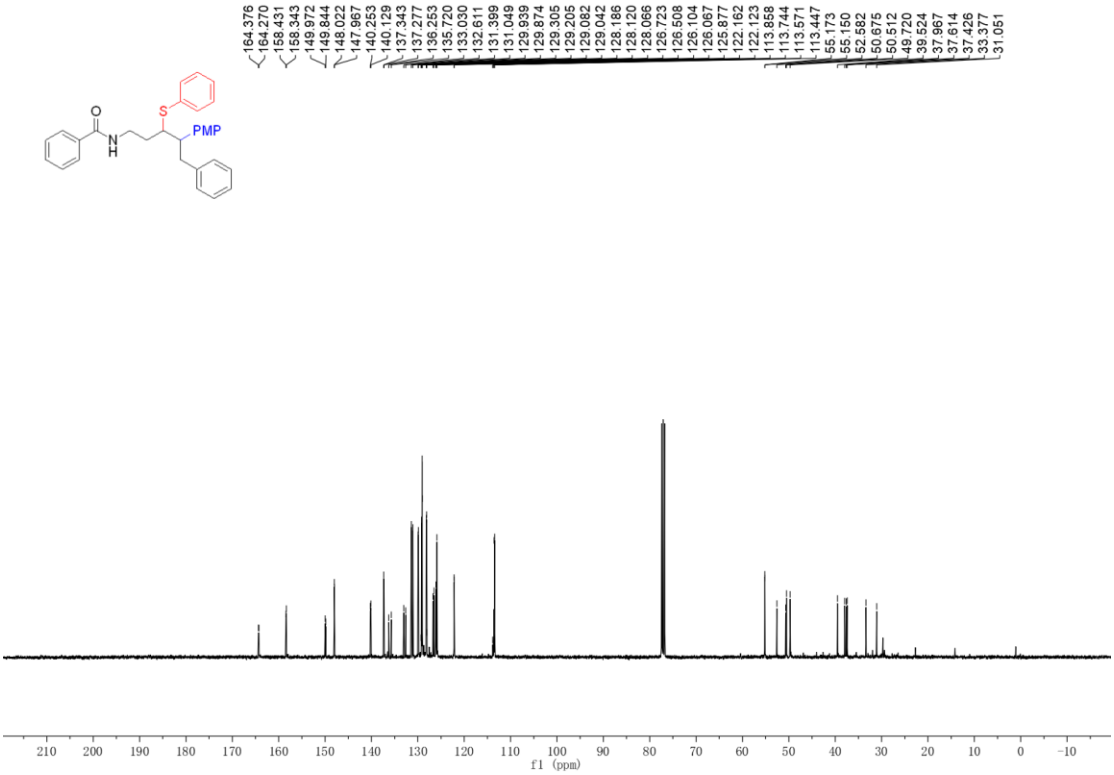
Supplementary Figure 109. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2av**



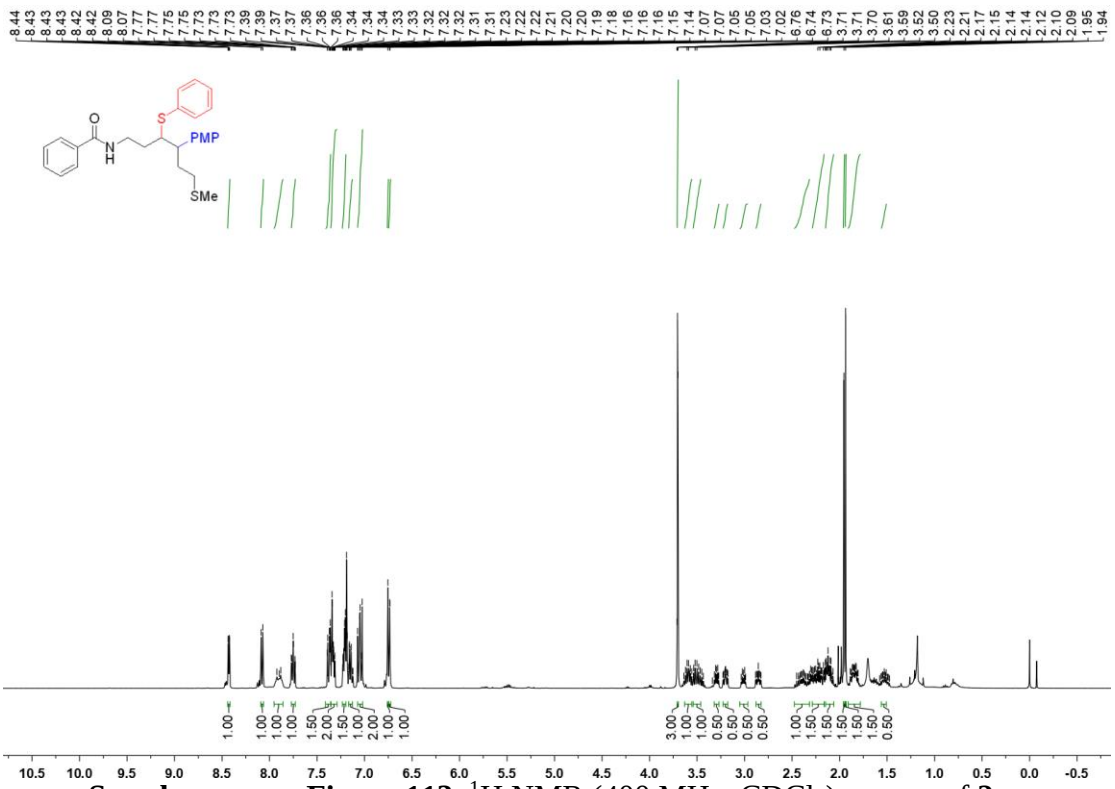
Supplementary Figure 110. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2av**



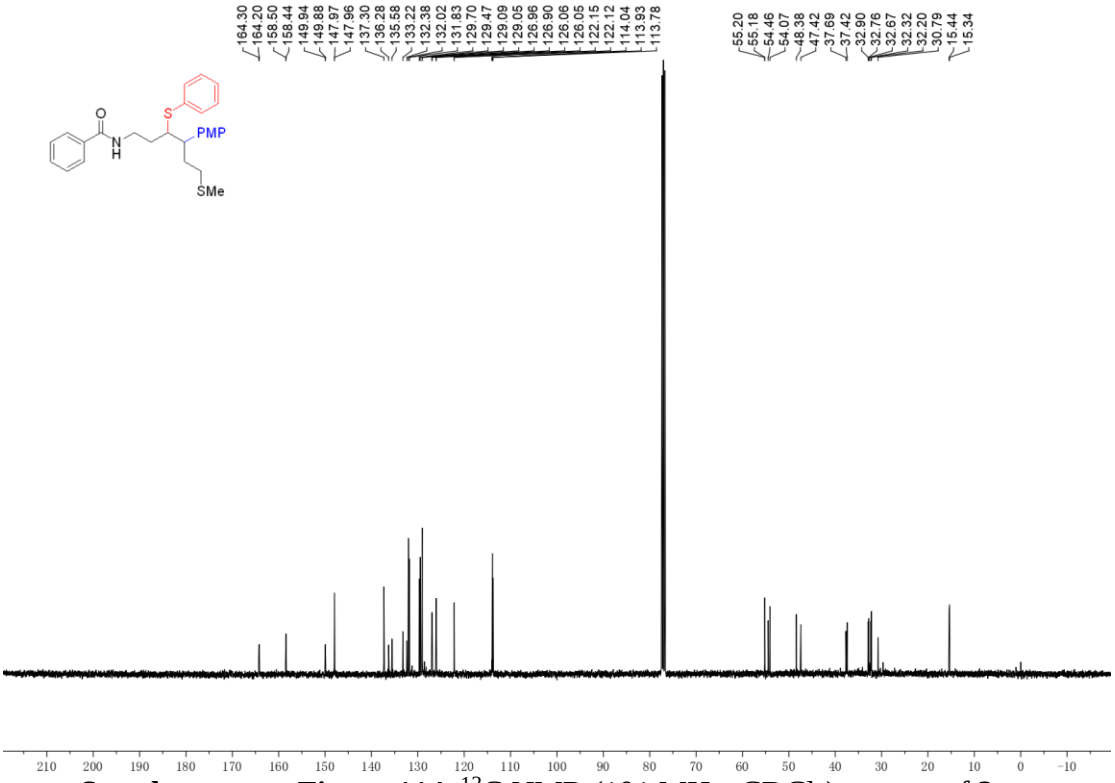
Supplementary Figure 111. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2aw**



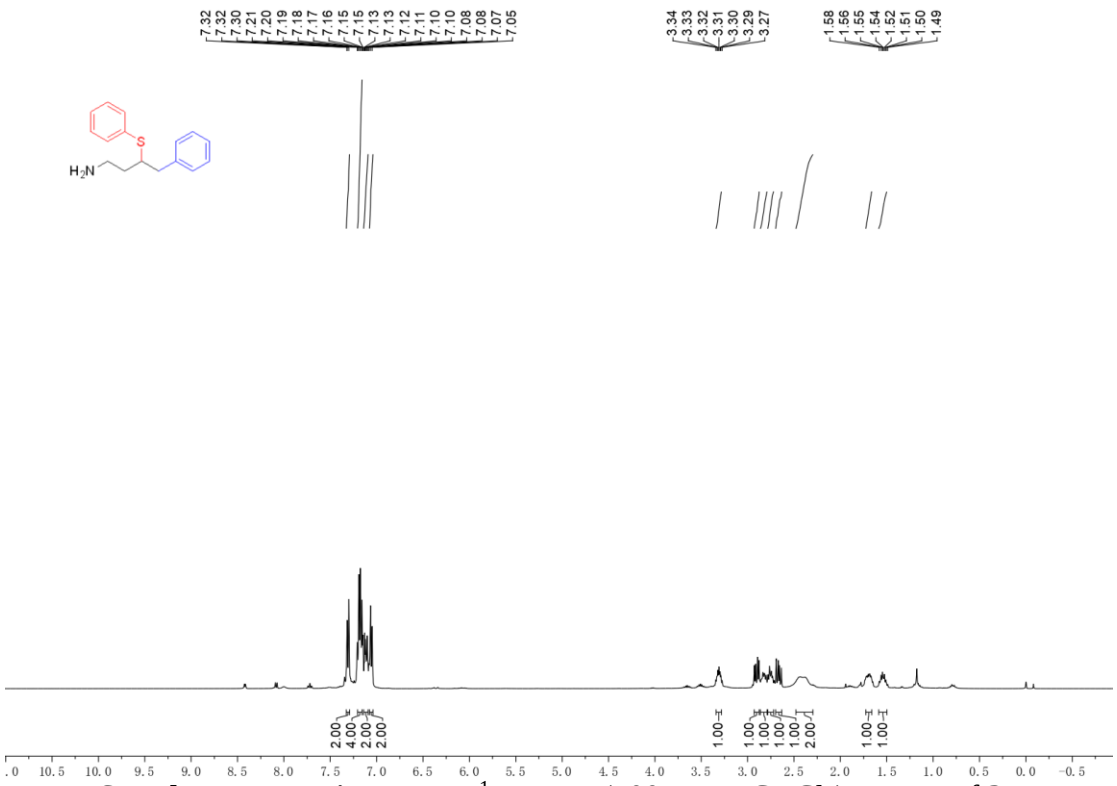
Supplementary Figure 112. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2aw**



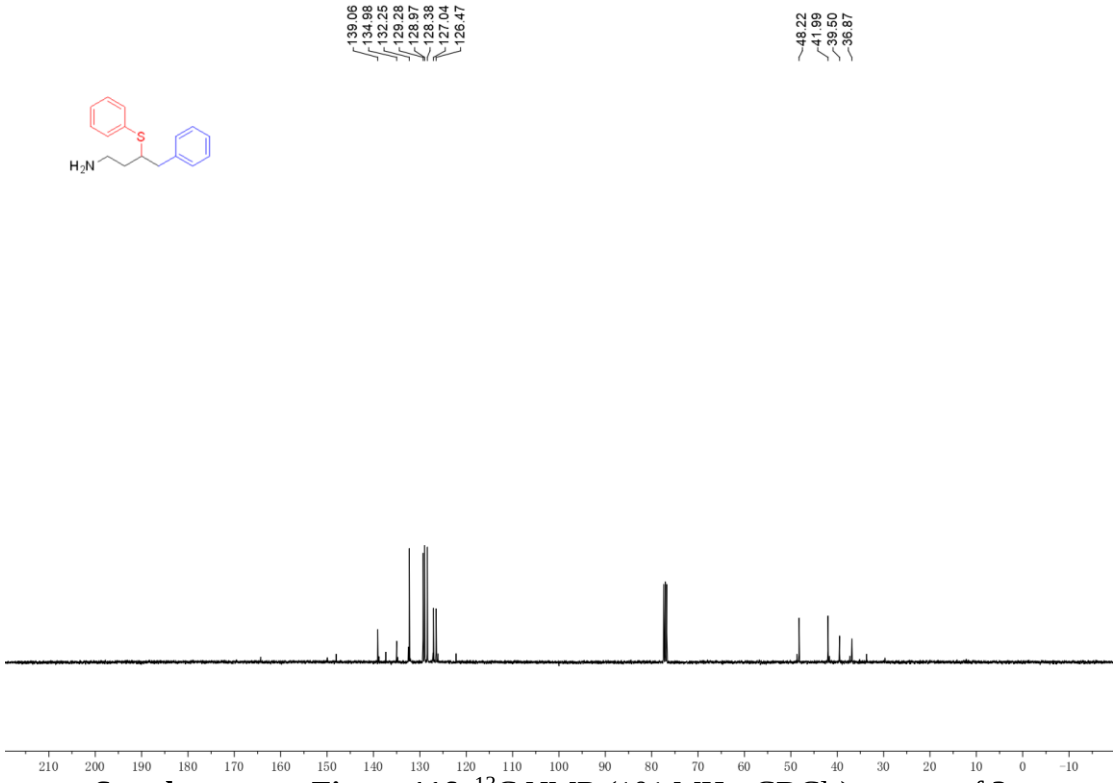
Supplementary Figure 113. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **2ax**



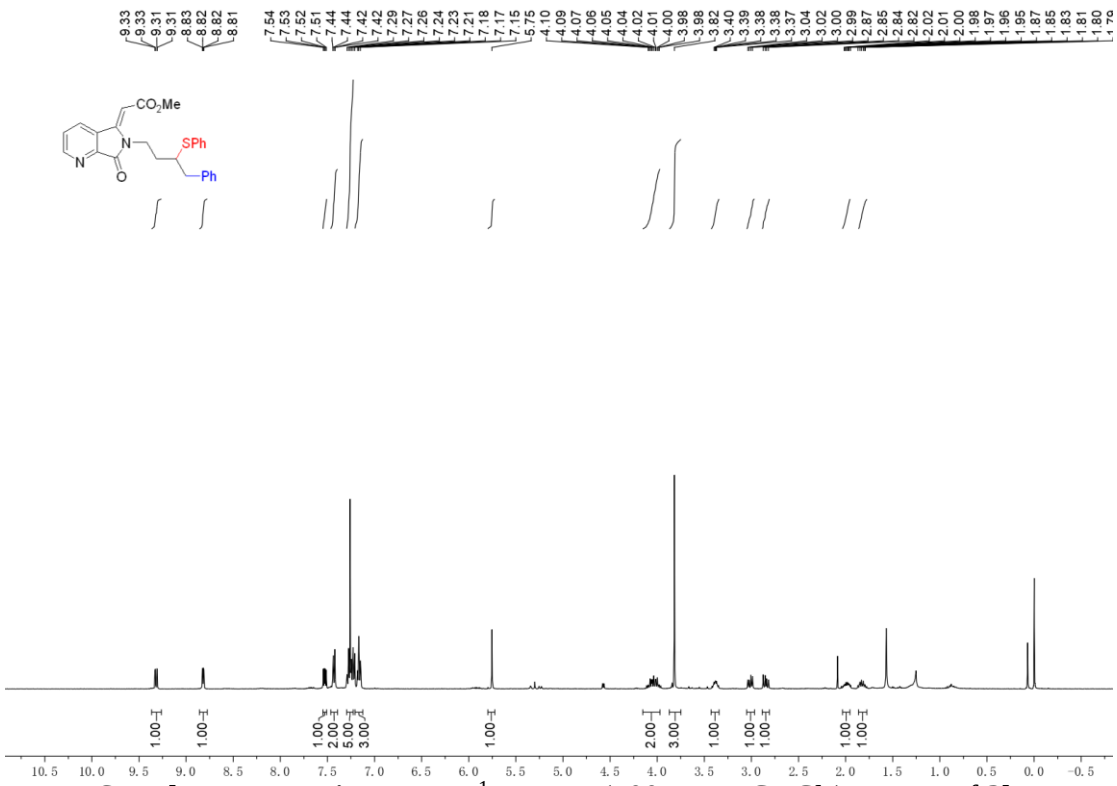
Supplementary Figure 114. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **2ax.**



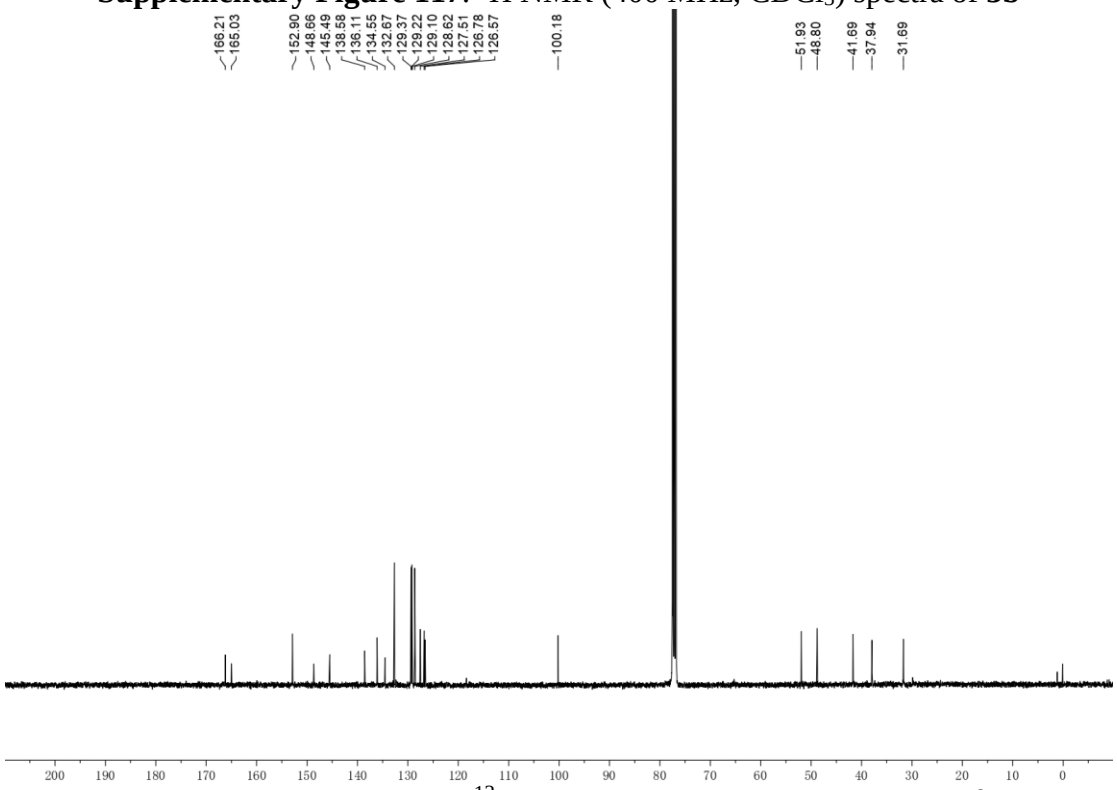
Supplementary Figure 115. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **3a**



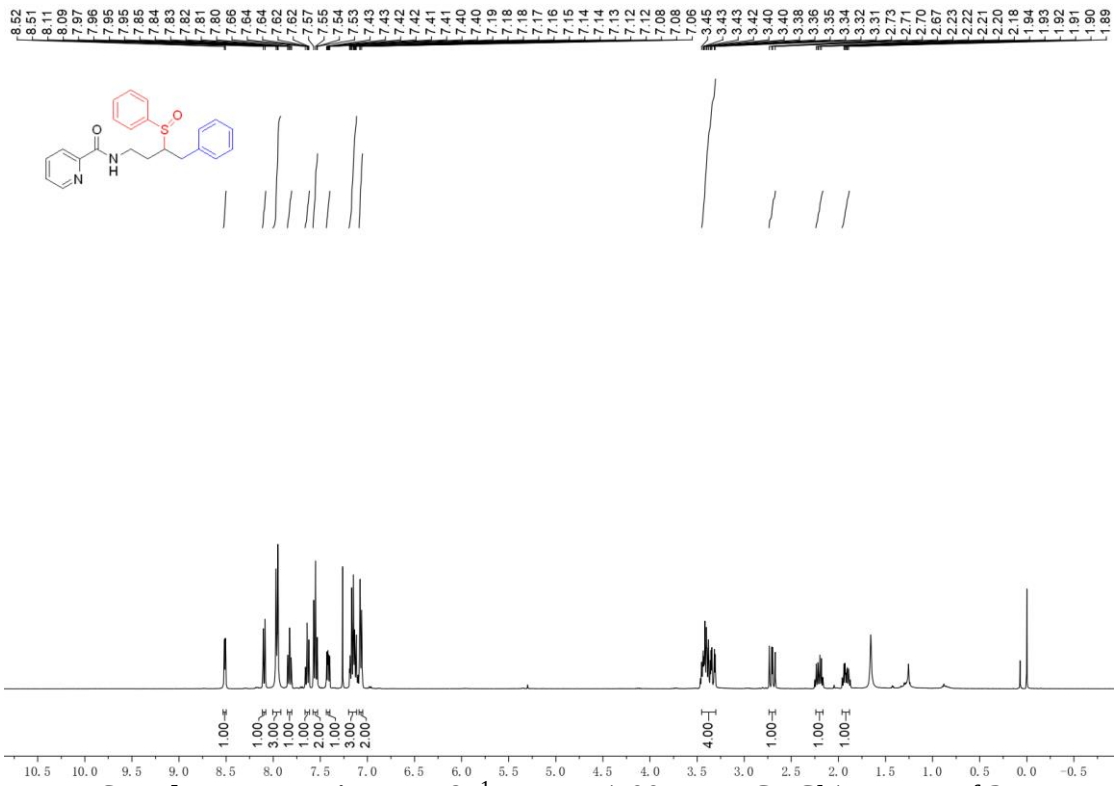
Supplementary Figure 116. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **3a**



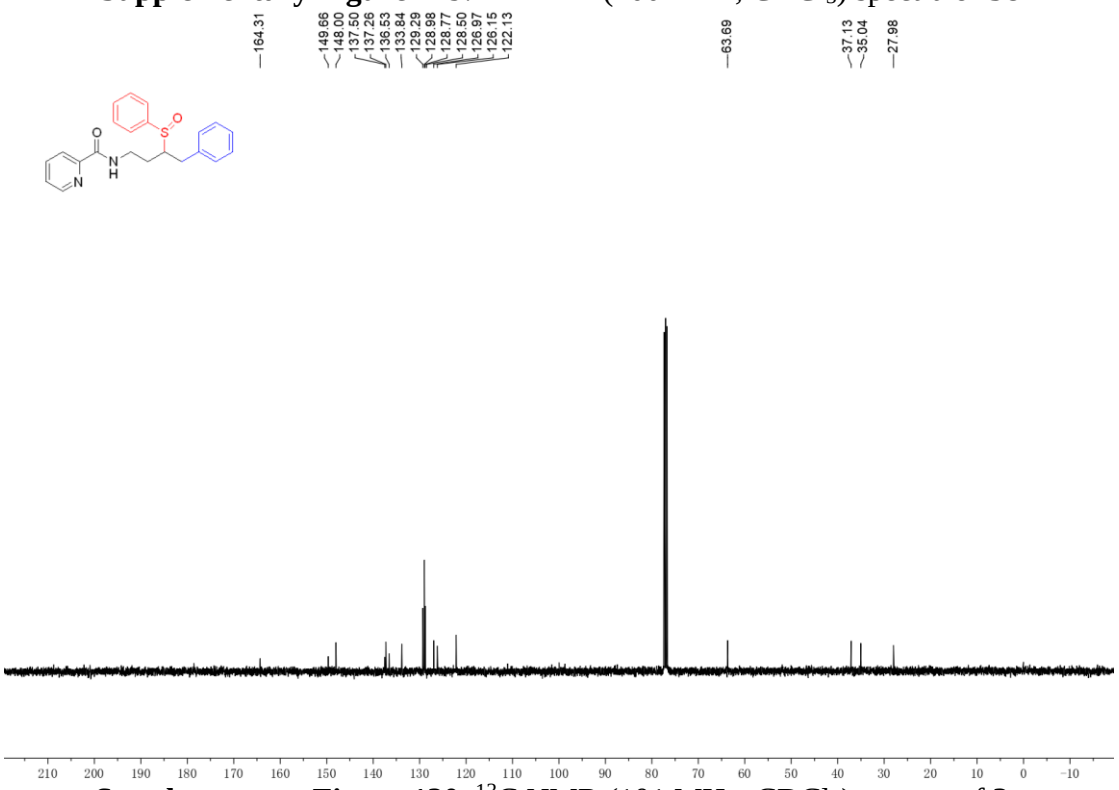
Supplementary Figure 117. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **3b**



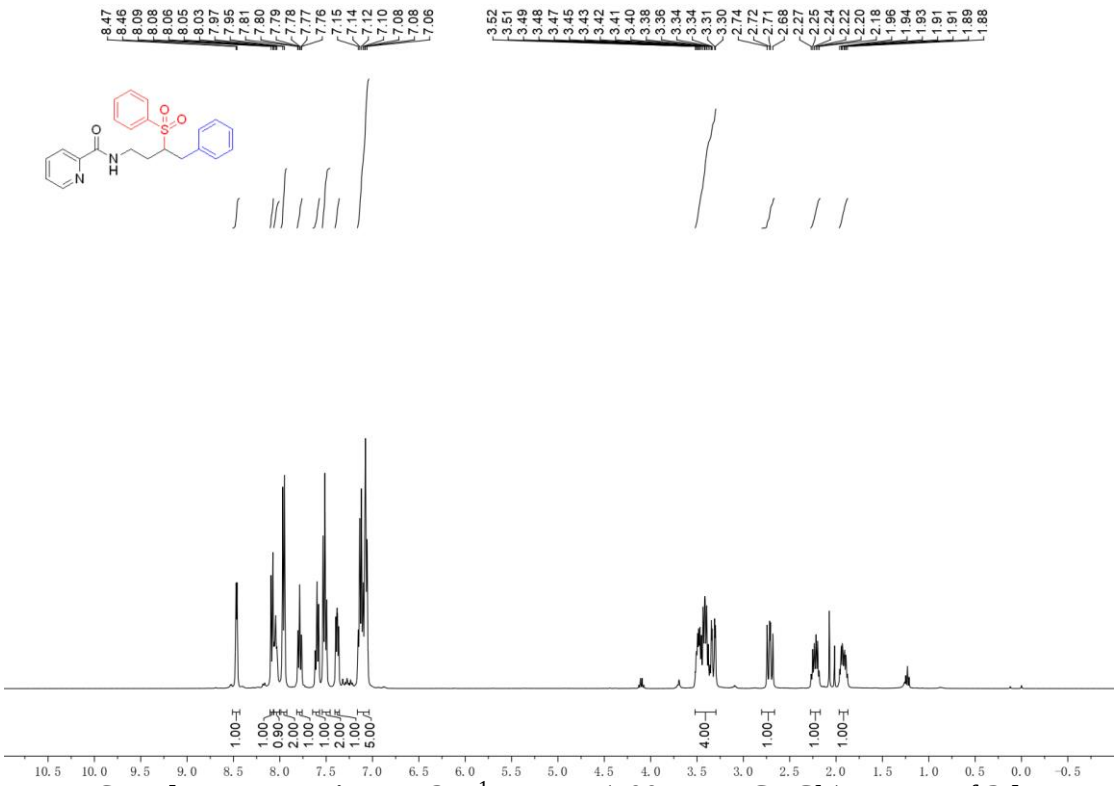
Supplementary Figure 118. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **3b**



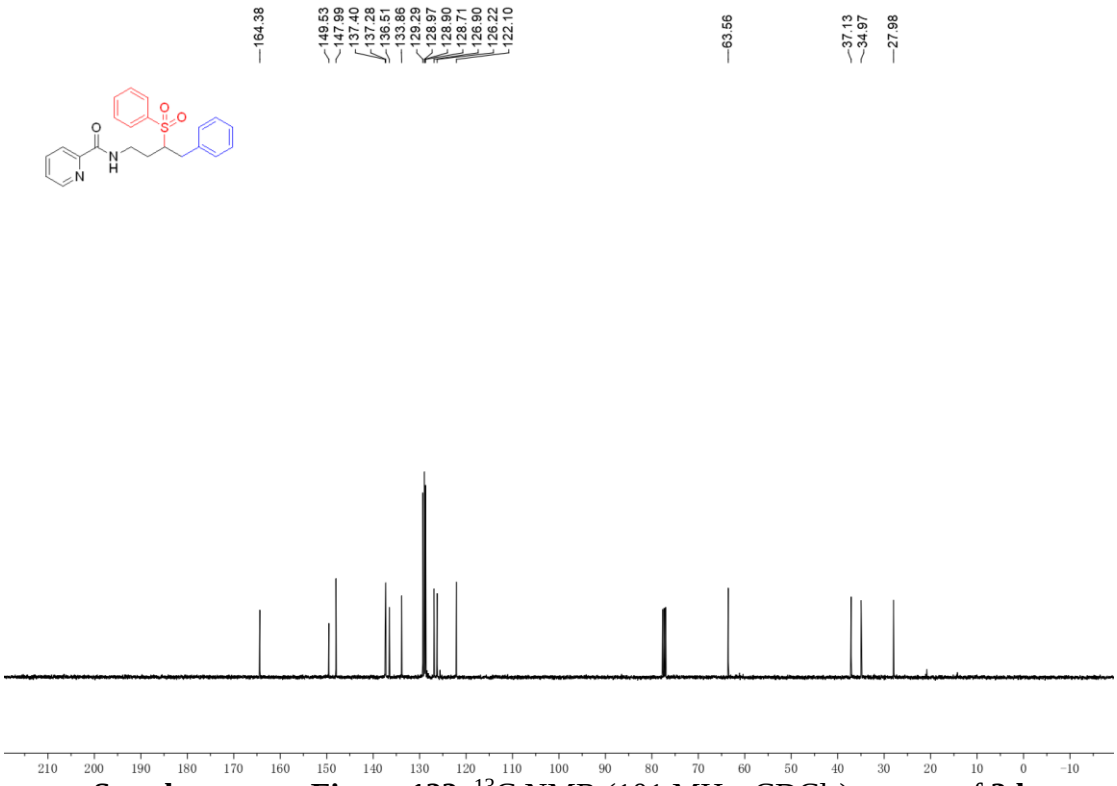
Supplementary Figure 119. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **3c**



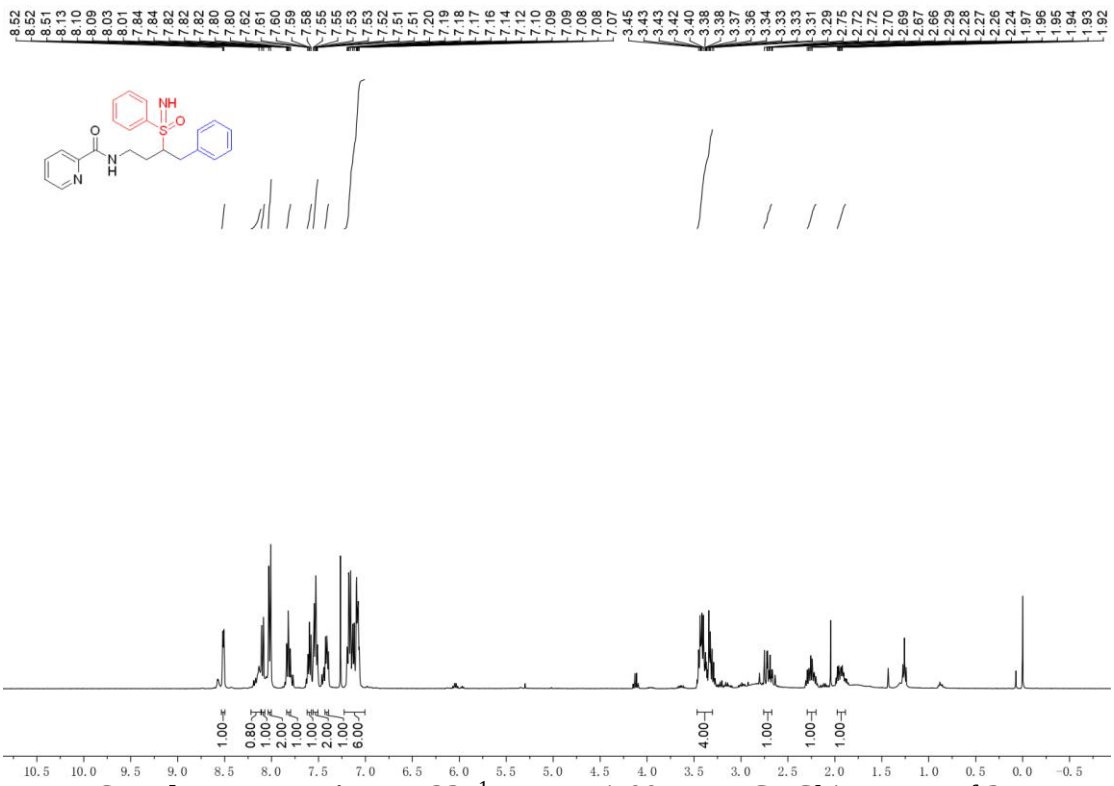
Supplementary Figure 120. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **3c**



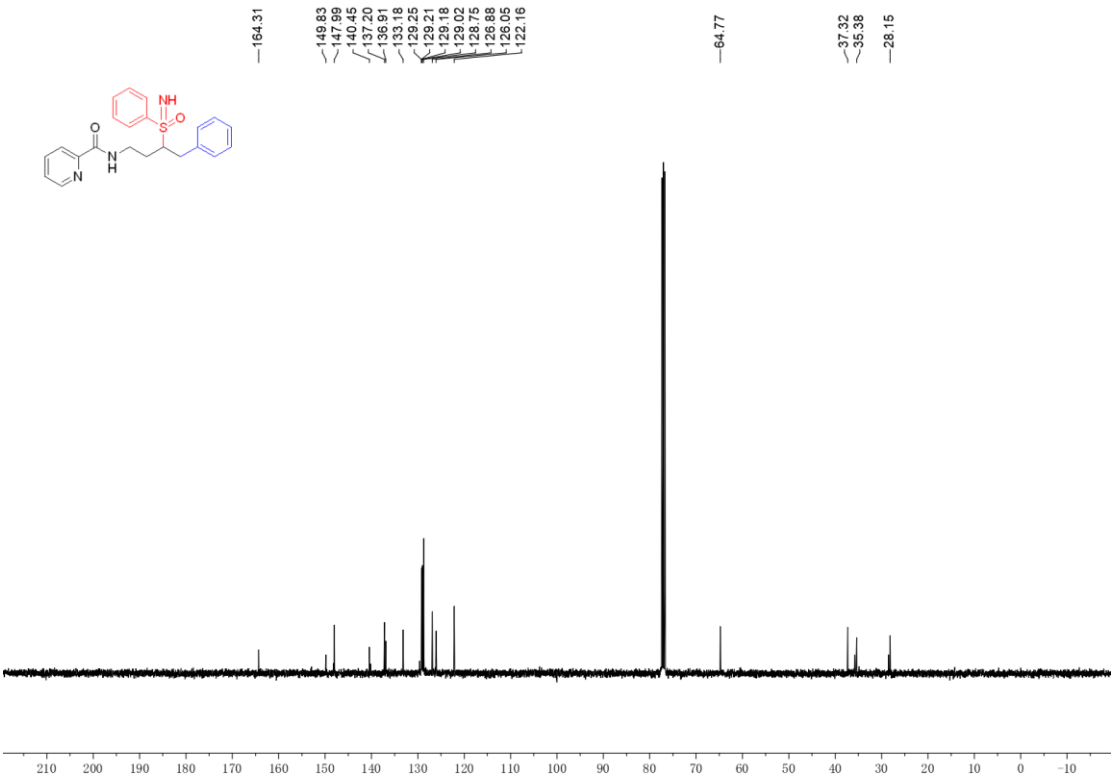
Supplementary Figure 121. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **3d**



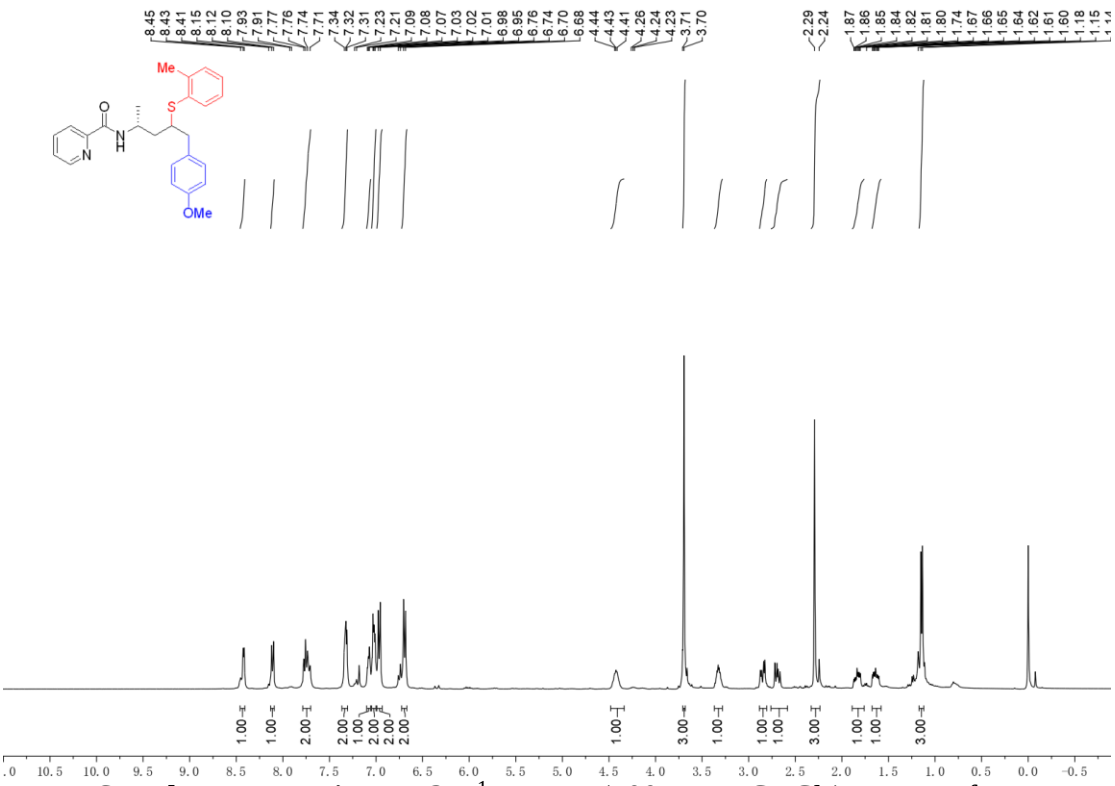
Supplementary Figure 122. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **3d**



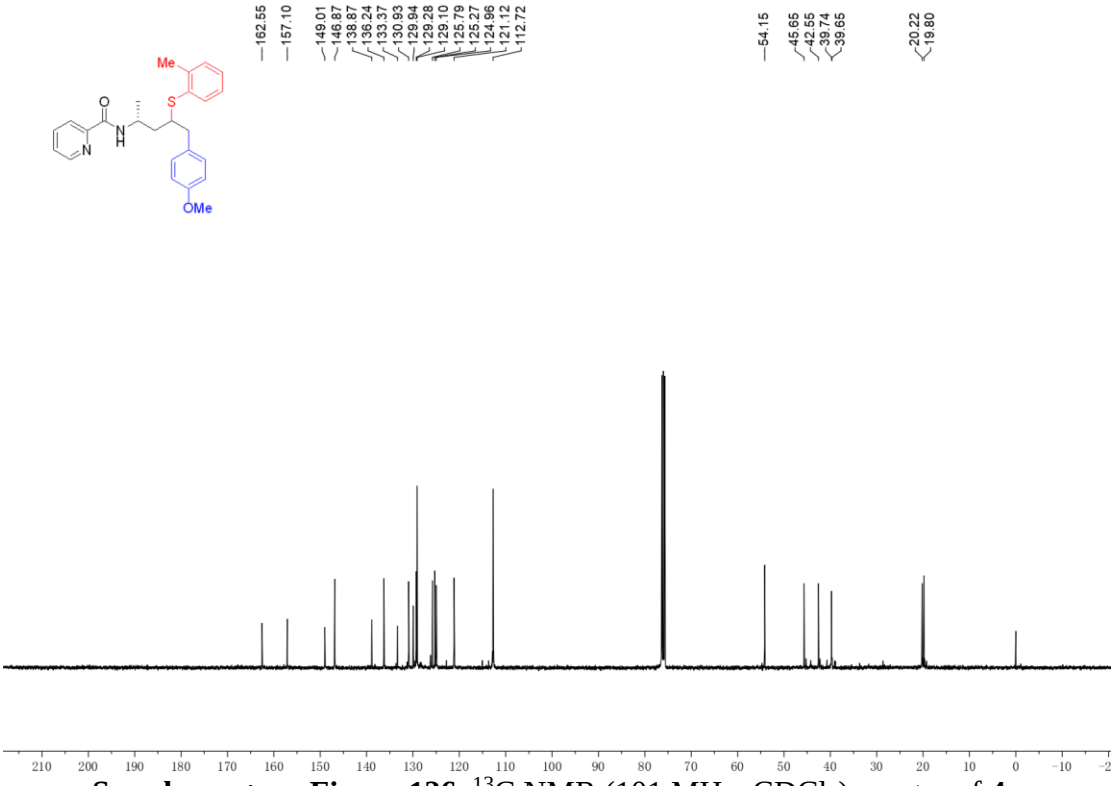
Supplementary Figure 123. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **3e**



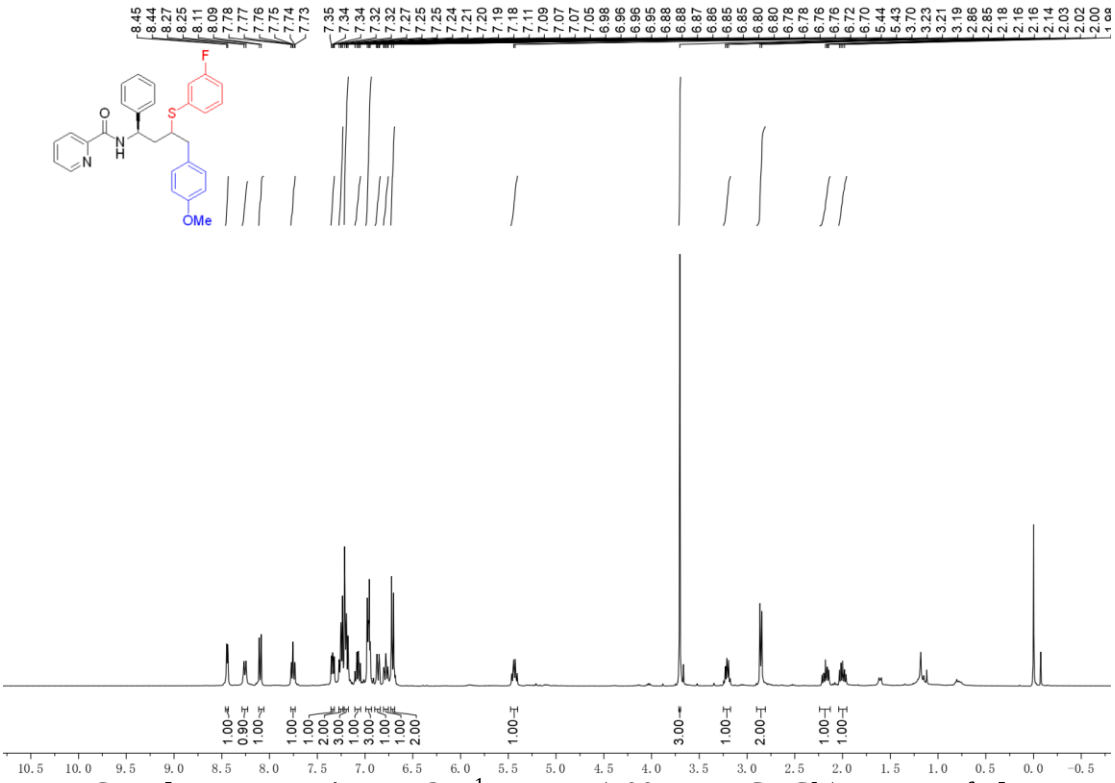
Supplementary Figure 124. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **3e**



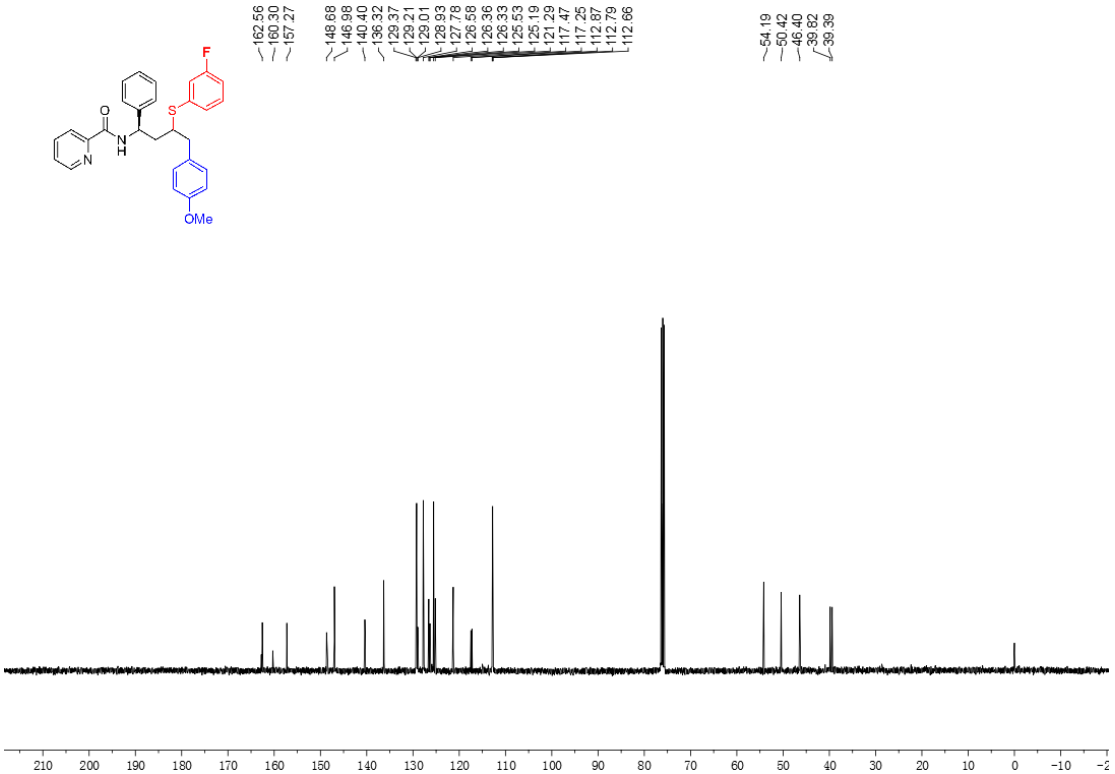
Supplementary Figure 125. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **4a**



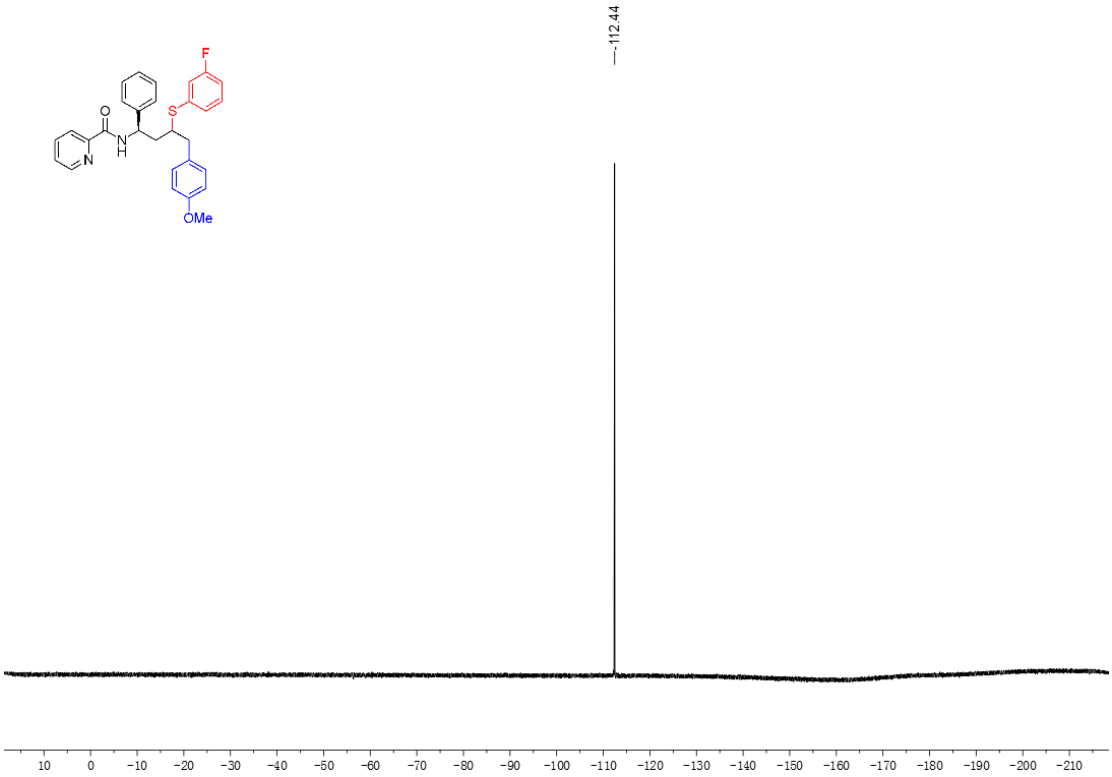
Supplementary Figure 126. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **4a**



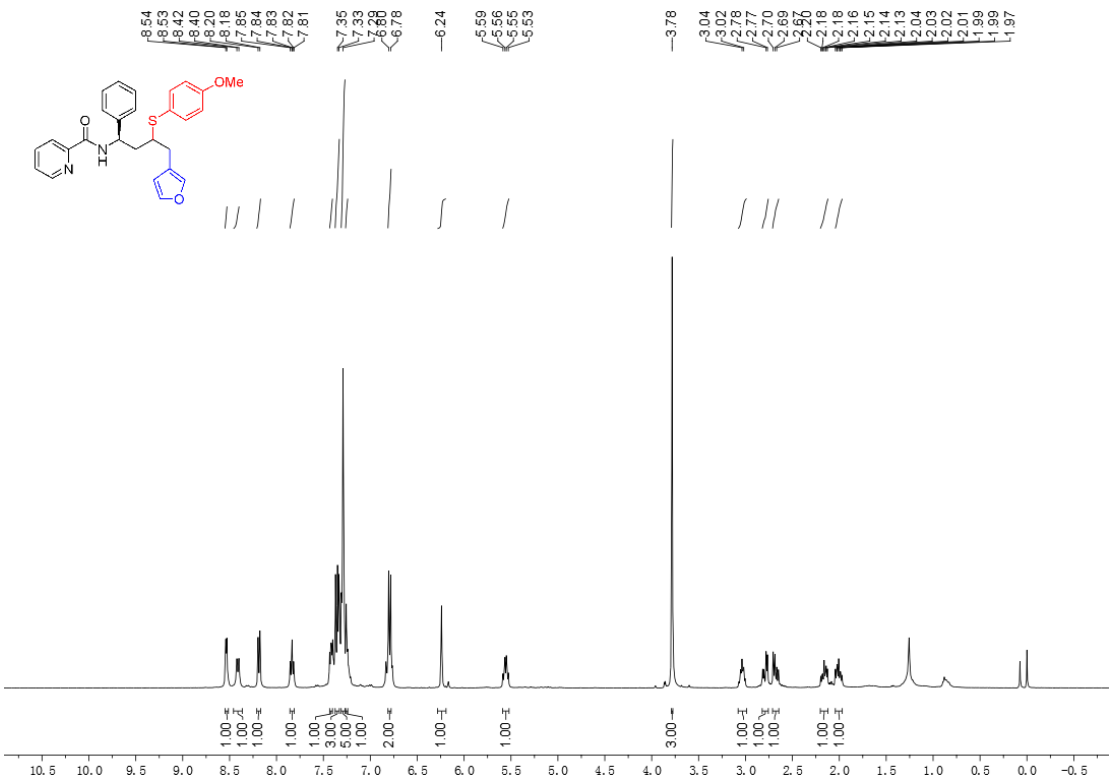
Supplementary Figure 127. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **4b**



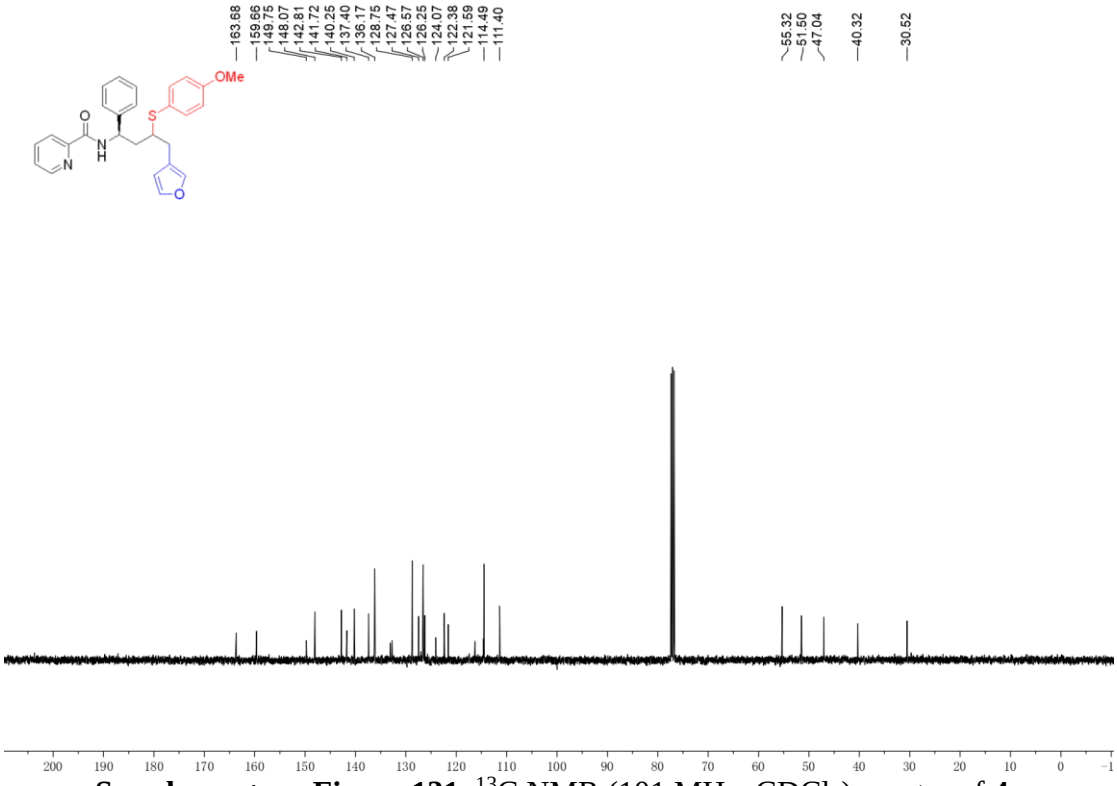
Supplementary Figure 128. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **4b**



Supplementary Figure 129. ^{19}F NMR (376 MHz, $CDCl_3$)ff spectra of **4b**



Supplementary Figure 130. ^{1}H NMR (400 MHz, $CDCl_3$) spectra of **4c**



Supplementary Figure 131. ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **4c**

11. Supplementary references

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