Supplementary Information

Visible-light-induced sulfonylarylation of unactivated alkenes via 1,4-(hetero)aryl migration from oxygen or nitrogen to carbon

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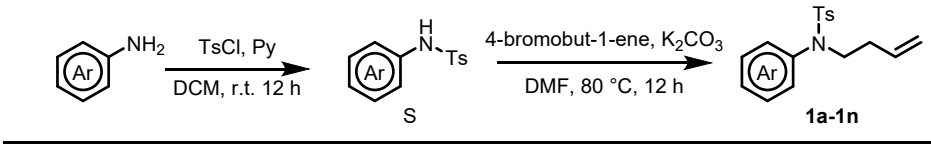
1. General Information

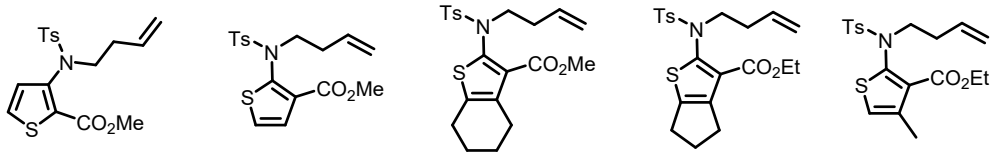
All commercially available reagents were used without further purification unless mentioned otherwise. ^{1}H and ^{13}C Nuclear Magnetic Resonance (NMR) spectra were recorded on Bruker Avance 400 Ultrashield NMR spectrometer. Chemical shifts (δ) were given in parts per million (ppm) and were measured downfield from internal tetramethylsilane. High-resolution mass spectrometry (HRMS) data were obtained on an FTICR-MS instrument (Ionspec 7.0 T, ESI/ Quadrupole Mass Analyzer, ESI-QMA). The melting points were determined on an X-4 microscope melting point apparatus and are uncorrected. Conversion was monitored by thin layer chromatography (TLC). Flash column chromatography was performed over silica gel (100-200 mesh). 200 mesh). Blue LED (30 W, λ max = 470 nm) was purchased from JIADENG (LS) was used for blue light irradiation. A fan attached to the apparatus was used to maintain the reaction temperature at room temperature.

2. Preparation of substrates

2.1 General procedure for synthesis of distal olefinic aromatic amines 1a-1j



1a-1n



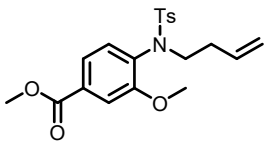
1a

1b

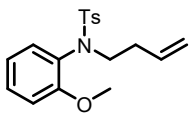
1c

1d

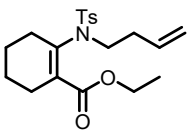
1e



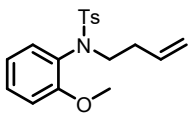
1f



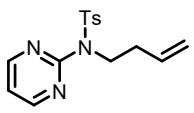
1g



1h



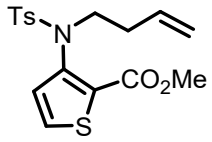
1i



1j

According to literature reports[1, 2], step 1: to a 100 mL round-bottom flask was added aromatic amine (10.0 mmol), tosyl chloride (2.29 g, 12 mmol, 1.2 equiv), pyridine (2.41 mL, 30.0 mmol, 3 equiv), and 30 mL DCM. The mixture was stirred at room temperature for 12 h. This organic solution was washed with 1N HCl, water and brine, dried over anhydrous Na_2SO_4 and concentrated in vacuo. The crude product was washed three times with petroleum ether (15 mL) to obtain the compound **S**. Step 2: The compound **S** that the product of the first step, 4-bromobut-1-ene (2 mL, 20 mmol), and K_2CO_3 (2.7 g, 20 mmol) were dispersed in DMF (20 mL). The mixture was stirred for 12 h at 80 ℃ and quenched with H_2O (20 mL), extracted with EA (50 mL × 2). The combined organic layer was washed with brine (30 mL × 3), dried over Na_2SO_4, and concentrated. The residue was purified by flash chromatography on a silica gel using petroleum ether and ethyl acetate (20/1~10/1, v/v) as the eluent to give substrate **1a-1j**.

Methyl 3-((*N*-(but-3-en-1-yl)-4-methylphenyl)sulfonamido)thiophene-2-carboxylate (1a)



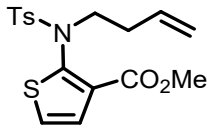
White solid, yield 89% (3.25 g). M.p. = 82–83 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, J = 8.2 Hz, 2H), 7.44 (d, J = 5.3 Hz, 1H), 7.23 (d, J = 8.1 Hz, 2H), 6.99 (d, J = 5.3 Hz, 1H), 5.72 (ddt, J = 17.1, 10.3, 6.8 Hz, 1H), 5.07 – 4.97 (m, 2H), 3.69 (t, J = 7.5 Hz, 2H), 3.59 (s, 3H), 2.40 (s, 3H), 2.28 (q, J = 7.4 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 143.4, 141.0, 136.7, 134.9, 131.3, 129.4, 129.3, 128.6, 127.6, 117.1, 52.0, 51.1, 33.9, 21.6.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{17}H_{20}NO_4S_2^+$ 366.0828; found 366.0833.

Methyl 2-((*N*-(but-3-en-1-yl)-4-methylphenyl)sulfonamido)thiophene-3-carboxylate (1b)



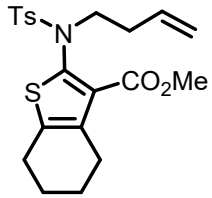
White solid, yield 77% (2.81 g). M.p. = 83–84 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J = 8.3 Hz, 2H), 7.32 (d, J = 5.9 Hz, 1H), 7.26 (d, J = 8.1 Hz, 2H), 7.17 (d, J = 5.9 Hz, 1H), 5.74 (ddt, J = 17.0, 10.2, 6.7 Hz, 1H), 5.10 – 4.99 (m, 2H), 3.77 – 3.71 (m, 2H), 3.58 (s, 3H), 2.42 (s, 3H), 2.39 – 2.32 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 162.1, 146.2, 143.8, 136.0, 134.5, 129.9, 129.6, 128.1, 128.0, 124.1, 117.4, 52.6, 51.7, 33.4, 21.7.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{17}H_{20}NO_4S_2^+$ 366.0828; found 366.0832.

Methyl 2-((*N*-(but-3-en-1-yl)-4-methylphenyl)sulfonamido)-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylate (1c)



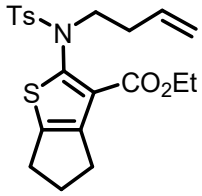
White solid, yield 89% (3.67 g). M.p. = 116–117 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, J = 8.1 Hz, 2H), 7.27 (d, J = 7.1 Hz, 2H), 5.74 (ddt, J = 17.0, 10.2, 6.8 Hz, 1H), 5.11 – 4.97 (m, 2H), 3.65 – 3.58 (m, 5H), 2.72 (t, J = 5.3 Hz, 2H), 2.67 (t, J = 5.7 Hz, 2H), 2.42 (s, 3H), 2.40 – 2.34 (m, 2H), 1.85 – 1.75 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3, 143.6, 141.8, 136.2, 135.5, 134.7, 134.6, 130.3, 129.6, 127.9, 117.2, 52.7, 51.4, 33.2, 25.8, 25.3, 22.9, 22.5, 21.7.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{21}H_{26}NO_4S_2^+$ 420.1298; found 420.1305.

Ethyl 2-((*N*-(but-3-en-1-yl)-4-methylphenyl)sulfonamido)-5,6-dihydro-4*H*-cyclopenta[*b*]thiophene-3-carboxylate (1d)



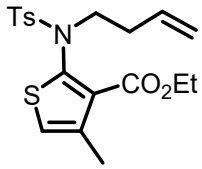
White solid, yield 89% (3.68 g). M.p. = 72–73 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J = 8.3 Hz, 2H), 7.26 (d, J = 8.1 Hz, 2H), 5.73 (ddt, J = 17.1, 10.3, 6.8 Hz, 1H), 5.09 – 4.98 (m, 2H), 4.06 (q, J = 7.1 Hz, 2H), 3.73 – 3.65 (m, 2H), 2.95 – 2.84 (m, 4H), 2.42 (s, 3H), 2.40 – 2.32 (m, 4H), 1.26 (t, J = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 162.2, 146.7, 144.9, 143.6, 139.7, 136.4, 134.7, 129.5, 128.0, 126.7, 117.2, 60.5, 52.6, 33.3, 30.6, 30.0, 27.3, 21.7, 14.2.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{21}H_{26}NO_4S_2^+$ 420.1298; found 420.1292.

Methyl 2-((*N*-(but-3-en-1-yl)-4-methylphenyl)sulfonamido)-4-methylthiophene-3-carboxylate (1e)



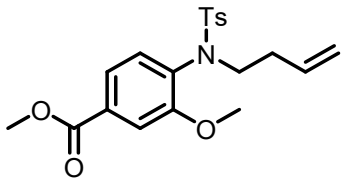
White solid, yield 86% (3.37 g). M.p. = 52–53 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J = 8.3 Hz, 2H), 7.26 (d, J = 8.1 Hz, 2H), 6.79 (q, J = 0.9 Hz, 1H), 5.74 (ddt, J = 17.1, 10.3, 6.8 Hz, 1H), 5.09 – 4.98 (m, 2H), 4.16 (q, J = 7.1 Hz, 2H), 3.71 – 3.61 (m, 2H), 2.42 (s, 3H), 2.41 – 2.36 (m, 2H), 2.34 (d, J = 0.9 Hz, 3H), 1.33 (t, J = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 163.2, 144.9, 143.8, 137.7, 135.7, 134.5, 131.6, 129.6, 128.0, 120.2, 117.3, 60.9, 52.8, 33.2, 21.7, 17.2, 14.2.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{18}H_{22}NO_4S_2^+$ 394.1141; found 394.1146.

Methyl 4-((N-(but-3-en-1-yl)-4-methylphenyl)sulfonamido)-3-methoxybenzoate (1f)



Colorless oil, yield 85% (3.32 g).

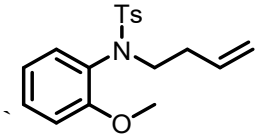
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (dd, J = 8.1, 1.4 Hz, 1H), 7.53 (d, J = 8.2 Hz, 2H), 7.46 (d, J = 1.5 Hz, 1H), 7.36 (d, J = 8.1 Hz, 1H), 7.23 (d, J = 8.2 Hz, 2H), 5.79 – 5.66

(m, 1H), 5.06 – 4.96 (m, 2H), 3.92 (s, 3H), 3.66 (t, *J* = 7.1 Hz, 2H), 3.43 (s, 3H), 2.41 (s, 3H), 2.18 (q, *J* = 7.1 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 156.5, 143.0, 137.2, 134.9, 133.5, 131.3, 131.0, 129.1, 127.5, 122.0, 117.0, 112.6, 55.2, 52.4, 49.1, 33.5, 21.5.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{20}H_{24}NO_5S^+$ 390.1370; found 390.1375.

***N*-(but-3-en-1-yl)-*N*-(2-methoxyphenyl)-4-methylbenzenesulfonamide (1g)**



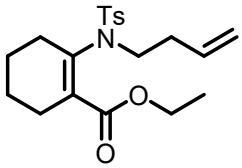
Colorless oil, yield 88% (2.92 g).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.2 Hz, 2H), 7.30 – 7.25 (m, 2H), 7.22 (d, *J* = 8.1 Hz, 2H), 6.92 (t, *J* = 7.6 Hz, 1H), 6.78 (d, *J* = 8.1 Hz, 1H), 5.74 (ddt, *J* = 17.1, 10.4, 6.7 Hz, 1H), 5.06 – 4.95 (m, 2H), 3.63 (br, 2H), 3.35 (s, 3H), 2.39 (s, 3H), 2.20 (q, *J* = 7.2 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 156.7, 142.7, 137.5, 135.1, 133.5, 129.8, 129.0, 127.5, 126.5, 120.6, 116.7, 111.7, 54.9, 49.2, 33.5, 21.5.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{18}H_{22}NO_3S^+$ 332.1315; found 332.1319.

Ethyl 2-((*N*-(but-3-en-1-yl)-4-methylphenyl)sulfonamido)cyclohex-1-ene-1-carboxylate (1h)



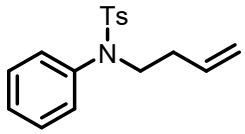
White solid, yield 59% (2.21 g). M.p. = 59–60 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.3 Hz, 2H), 7.27 (d, *J* = 8.0 Hz, 2H), 5.75 (ddt, *J* = 17.0, 10.3, 6.7 Hz, 1H), 5.11 – 4.99 (m, 2H), 4.09 (q, *J* = 7.1 Hz, 2H), 3.56 – 3.16 (m, 2H), 2.52 – 2.30 (m, 7H), 1.95 (br, 2H), 1.61 (br, 4H), 1.28 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 167.9, 143.3, 138.8, 137.8, 135.0, 133.3, 129.6, 127.5, 116.9, 60.8, 48.1, 33.5, 28.5, 27.5, 22.5, 21.7, 21.6, 14.2.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{20}H_{28}NO_4S^+$ 378.1734; found 378.1739.

***N*-(but-3-en-1-yl)-4-methyl-*N*-phenylbenzenesulfonamide (1i)**

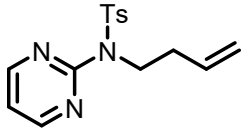


White solid, yield 89% (2.68 g). M.p. = 65–66 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, J = 8.3 Hz, 2H), 7.34 – 7.28 (m, 3H), 7.24 (d, J = 8.0 Hz, 2H), 7.06 – 7.02 (m, 2H), 5.73 (ddt, J = 17.1, 10.5, 6.7 Hz, 1H), 5.06 – 4.96 (m, 2H), 3.62 – 3.57 (m, 2H), 2.42 (s, 3H), 2.21 – 2.15 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 143.5, 139.1, 135.4, 134.6, 129., 129.10, 129.07, 128.1, 127.8, 117.2, 50.1, 32.9, 21.7.

***N*-(but-3-en-1-yl)-4-methyl-*N*-(pyrimidin-2-yl)benzenesulfonamide (1j)**

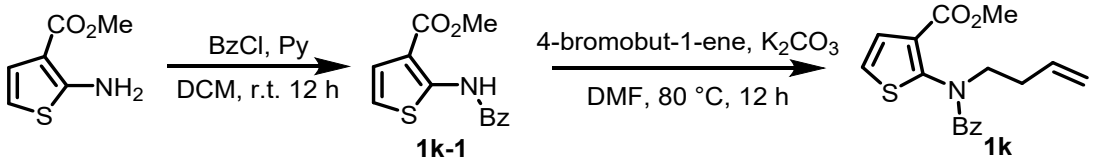


White solid, yield 73% (2.21 g). M.p. = 66–67 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (d, J = 4.8 Hz, 2H), 7.97 (d, J = 8.2 Hz, 2H), 7.26 (d, J = 7.9 Hz, 2H), 6.85 (t, J = 4.8 Hz, 1H), 5.88 (ddt, J = 17.0, 10.2, 6.8 Hz, 1H), 5.14 (d, J = 17.2 Hz, 1H), 5.07 (d, J = 10.2 Hz, 1H), 4.36 – 4.26 (m, 2H), 2.69 – 2.57 (m, 2H), 2.39 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 158.3, 157.5, 143.7, 137.9, 134.9, 129.0, 128.7, 117.1, 115.4, 46.7, 34.0, 21.6.

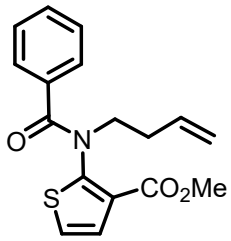
2.2 General procedure for synthesis of 1k



According to literature reports[2], step 1: to a 100 mL round-bottom flask was added methyl 2-aminothiophene-3-carboxylate (1.57g, 10.0 mmol), benzoyl chloride (2.29 g, 12 mmol, 1.2 equiv), pyridine (2.41 mL, 30.0 mmol, 3 equiv), and 30 mL DCM. The mixture was stirred at room temperature for 12 h. This organic solution was washed with 1N HCl, water and brine, dried over anhydrous Na_2SO_4 and concentrated in vacuo.

The crude product was washed with petroleum ether (15 mL x 3) to obtain the pure compound **1k-1**. Step 2: The compound **1k-1**, 4-bromobut-1-ene (2 mL, 20 mmol), and K_2CO_3 (2.7 g, 20 mmol) were dispersed in DMF (20 mL). The mixture was stirred for 12 h at 80 ℃ and quenched with H_2O (20 mL), extracted with EA (50 mL × 2). The combined organic layer was washed with brine (30 mL × 3), dried over Na_2SO_4, and concentrated. The residue was purified by flash chromatography on a silica gel using petroleum ether and ethyl acetate (20/1, v/v) as the eluent to give substrate **1k**.

Methyl 2-(*N*-(but-3-en-1-yl)benzamido)thiophene-3-carboxylate (1k)



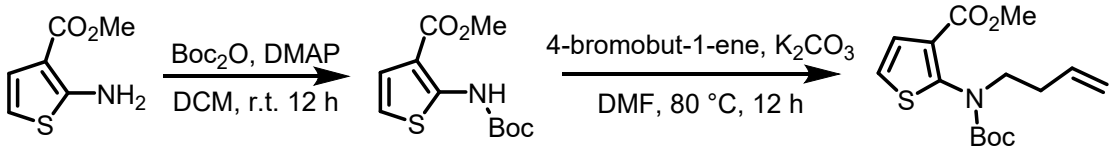
White solid, yield 83% (2.61 g). M.p. = 54–56 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, J = 7.1 Hz, 2H), 7.27 – 7.11 (m, 4H), 7.03 (d, J = 5.8 Hz, 1H), 5.92 – 5.75 (m, 1H), 5.17 – 5.05 (m, 2H), 4.19 – 3.76 (m, 5H), 2.48 (br, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 161.9, 152.3, 135.8, 135.0, 130.0, 127.8, 127.7, 127.3, 122.3, 117.1, 51.8, 51.3, 32.0.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{17}H_{18}NO_3S^+$ 316.1002; found 316.1006.

2.3 General procedure for synthesis of 1l

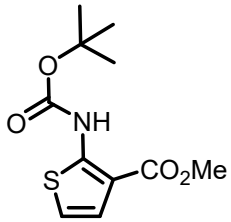


1l-1 **1l**

According to literature reports[2], Step 1: to a 100 mL round-bottom flask was added methyl 2-aminothiophene-3-carboxylate (1.57g, 10.0 mmol), Boc_2O (2.4 g, 11 mmol) and DMAP (0.12 g, 1 mmol) were dissolved in DCM (20 mL). The mixture was stirred for 12 h at room temperature. This organic solution was washed with water and brine, dried over anhydrous Na_2SO_4 and concentrated in vacuo. The product was purified by flash column chromatography on silica gel (hexane/ethyl acetate = 20:1) to give **1l-1**.

Step 2: The compound **1l-1** (1.29 g, 5 mmol), 4-bromobut-1-ene (1 mL, 10 mmol), and K_2CO_3 (1.35 g, 10 mmol) were dispersed in DMF (10 mL). The mixture was stirred for 12 h at 80 ℃ and quenched with H_2O (10 mL), extracted with EA (20 mL × 2). The combined organic layer was washed with brine (20 mL × 3), dried over Na_2SO_4, and concentrated. The residue was purified by flash chromatography on a silica gel using petroleum ether and ethyl acetate (20/1, v/v) as the eluent to give substrate **1l**.

Methyl 2-((*tert*-butoxycarbonyl)amino)thiophene-3-carboxylate (1l-1)

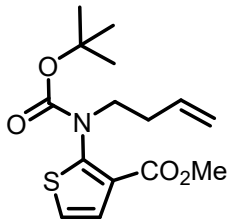


Colorless oil, yield 74% (1.91 g).

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.02 (s, 1H), 7.11 (d, J = 5.8 Hz, 1H), 6.62 (d, J = 5.7 Hz, 1H), 3.83 (s, 3H), 1.51 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 152.2, 151.3, 124.2, 114.6, 111.0, 82.2, 51.6, 28.2.

Methyl 2-(but-3-en-1-yl(tert-butoxycarbonyl)amino)thiophene-3-carboxylate (1l)



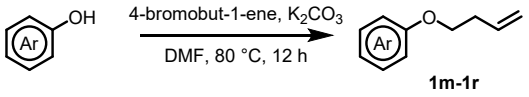
Colorless oil, yield 87% (1.35 g).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, J = 5.8 Hz, 1H), 7.03 (d, J = 5.9 Hz, 1H), 5.74 (ddt, J = 17.1, 10.2, 6.8 Hz, 1H), 5.10 – 4.97 (m, 2H), 3.79 (s, 3H), 3.64 (t, J = 7.4 Hz, 2H), 2.37 – 2.30 (m, 2H), 1.51 (br, 3H), 1.31 (br, 6H).

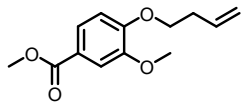
^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5, 154.0, 151.4, 135.2, 127.5, 126.6, 121.5, 116.9, 80.8, 51.7, 50.7, 32.5, 28.3, 28.1.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{15}H_{22}NO_4S^+$ 312.1264; found 312.1260.

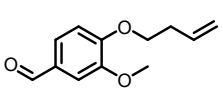
2.4 General procedure for synthesis of distal olefinic aryl ether



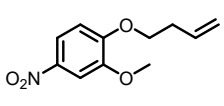
1m-1r



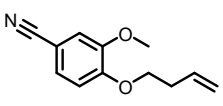
1m



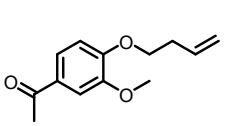
1n



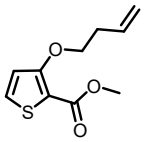
1o



1p



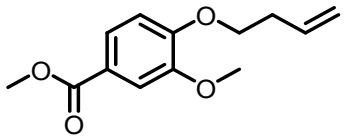
1q



1r

According to literature reports[2], The aromatic alcohol (5 mmol), 4-bromobut-1-ene (1 mL, 10 mmol), and K_2CO_3 (1.38 g, 10 mmol) were dispersed in DMF (10 mL). The mixture was stirred for 12 h at 80 ℃ and quenched with H_2O (10 mL), extracted with EA (30 mL × 2). The combined organic layer was washed with brine (20 mL × 3), dried over Na_2SO_4, and concentrated. The residue was purified by flash chromatography on a silica gel using petroleum ether and ethyl acetate (20/1 ~ 15/1, v/v) as the eluent to give substrate **1m-1r**.

Methyl 4-(but-3-en-1-yloxy)-3-methoxybenzoate (1m)



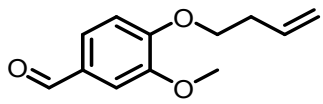
Colorless oil, yield 83% (0.98 g).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (dd, J = 8.4, 2.0 Hz, 1H), 7.52 (d, J = 1.9 Hz, 1H), 6.85 (d, J = 8.5 Hz, 1H), 5.88 (ddt, J = 17.1, 10.2, 6.8 Hz, 1H), 5.21 – 5.12 (m, 1H), 5.12 – 5.06 (m, 1H), 4.09 (t, J = 7.0 Hz, 2H), 3.88 (s, 3H), 3.86 (s, 3H), 2.60 (q, J = 6.9 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 152.4, 148.9, 133.8, 123.5, 122.7, 117.5, 112.5, 111.6, 68.2, 56.1, 52.0, 33.5.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{13}H_{17}O_4^+$ 237.1121; found 237.1126.

4-(but-3-en-1-yloxy)-3-methoxybenzaldehyde (1n)



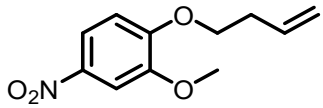
Colorless oil, yield 90% (0.93 g).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.77 (s, 1H), 7.36 (dd, J = 8.2, 1.9 Hz, 1H), 7.33 (d, J = 1.8 Hz, 1H), 6.90 (d, J = 8.2 Hz, 1H), 5.84 (ddt, J = 17.1, 10.2, 6.8 Hz, 1H), 5.17 – 5.09 (m, 1H), 5.09 – 5.03 (m, 1H), 4.07 (t, J = 7.0 Hz, 2H), 3.84 (s, 3H), 2.57 (q, J = 6.9 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 190.8, 153.8, 149.8, 133.6, 130.0, 126.6, 117.5, 111.5, 109.3, 68.2, 55.9, 33.2.

The data is in accordance with the literature[3].

1-(but-3-en-1-yloxy)-2-methoxy-4-nitrobenzene (1o)



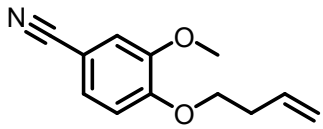
White solid, yield 80% (0.98 g). M.p. = 51–52 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (dd, J = 8.9, 1.0 Hz, 1H), 7.73 (d, J = 1.1 Hz, 1H), 6.89 (d, J = 8.9 Hz, 1H), 5.89 (ddt, J = 16.9, 10.4, 6.8 Hz, 1H), 5.24 – 5.10 (m, 2H), 4.15 (t, J = 6.9 Hz, 2H), 3.93 (s, 3H), 2.63 (q, J = 6.5 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 154.0, 149.2, 141.5, 133.5, 117.9, 117.8, 111.0, 106.9, 68.7, 56.4, 33.4.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{11}H_{14}NO_4^+$ 224.0917; found 224.0913.

4-(but-3-en-1-yloxy)-3-methoxybenzonitrile (1p)



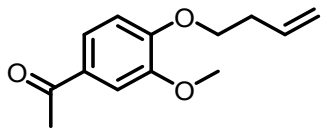
White solid, yield 81% (0.82 g). M.p. = 36–37 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (dd, J = 8.3, 1.9 Hz, 1H), 7.05 (d, J = 1.8 Hz, 1H), 6.87 (d, J = 8.4 Hz, 1H), 5.87 (ddt, J = 17.0, 10.2, 6.8 Hz, 1H), 5.21 – 5.07 (m, 2H), 4.08 (t, J = 6.9 Hz, 2H), 3.85 (s, 3H), 2.59 (q, J = 6.9 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 152.3, 149.5, 133.6, 126.4, 119.3, 117.7, 114.4, 112.5, 103.9, 68.3, 56.2, 33.3.

The data is in accordance with the literature[3].

1-(4-(but-3-en-1-yloxy)-3-methoxyphenyl)ethan-1-one (1q)



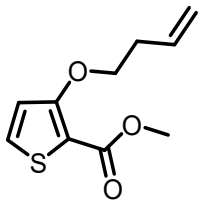
Colorless oil, yield 73% (0.80 g).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (dd, J = 8.3, 2.0 Hz, 1H), 7.47 (d, J = 1.9 Hz, 1H), 6.83 (d, J = 8.3 Hz, 1H), 5.86 (ddt, J = 17.0, 10.2, 6.8 Hz, 1H), 5.19 – 5.11 (m, 1H), 5.11 – 5.03 (m, 1H), 4.08 (t, J = 7.0 Hz, 2H), 3.86 (s, 3H), 2.59 (q, J = 6.9 Hz, 2H), 2.51 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 196.8, 152.7, 149.2, 133.7, 130.4, 123.2, 117.5, 111.2, 110.5, 68.1, 56.0, 33.4, 26.2.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{13}H_{17}O_3^+$ 221.1172; found 221.1177.

Methyl 3-(but-3-en-1-yloxy)thiophene-2-carboxylate (1r)



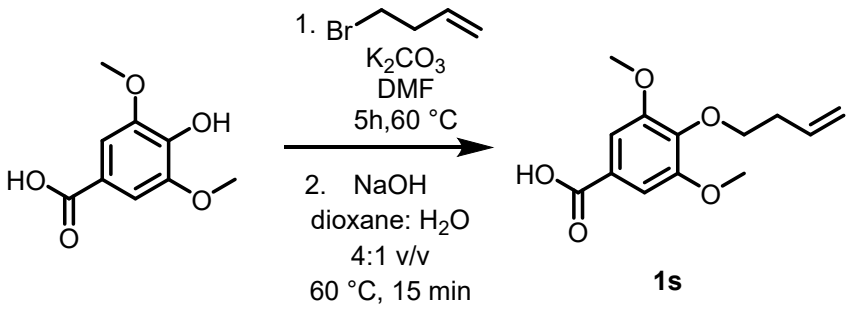
White solid, yield 93% (0.99 g). M.p. = 35–36 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, J = 5.5 Hz, 1H), 6.83 (d, J = 5.5 Hz, 1H), 5.91 (ddt, J = 17.1, 10.2, 6.8 Hz, 1H), 5.27 – 5.15 (m, 1H), 5.15 – 5.06 (m, 1H), 4.17 (t, J = 6.9 Hz, 2H), 3.83 (s, 3H), 2.59 (q, J = 6.8 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 162.3, 161.3, 133.9, 130.7, 117.6, 117.1, 110.1, 71.3, 51.7, 33.9.

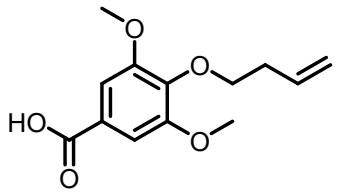
HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{10}H_{13}O_3S^+$ 213.0580; found 213.0580.

2.5 General procedure for synthesis of 1s



According to literature reports[4], 4-hydroxy-3,5-dimethoxybenzoic acid (1.98g, 10 mmol), anhydrous K_2CO_3 (5.53 g, 40 mmol, 4 eq) and 4-bromobut-1-ene (4 mL, 40 mmol, 4 eq) were reacted in DMF (25 mL). The mixture was stirred for 3 h at 60 ℃. Flask was allowed to cool to RT and then the reaction mixture was filtered through celite. The celite was washed three times with methanol and all organic solvents were removed in vacuum. The obtained oily residue was redissolved with dioxane:H_2O = 4:1 v/v (60 mL), NaOH (2eq) was added and the flask was heated to 60°C for 15 minutes. Then, pH was neutralized with 1N HCl, organic solvents were removed in vacuum, and the residue was transferred into a separation funnel using EA (100mL). This organic phase was washed with 1N HCl (2x50mL) and brine (2x50mL), dried over Na_2SO_4, filtered and evaporated to dryness. The residue was purified by flash chromatography on a silica gel using petroleum ether and ethyl acetate (2/1, v/v) + 1% AcOH as the eluent to give substrate **1s (**white solid, 1.54 g, 61%).

4-(but-3-en-1-yloxy)-3,5-dimethoxybenzoic acid (1s)



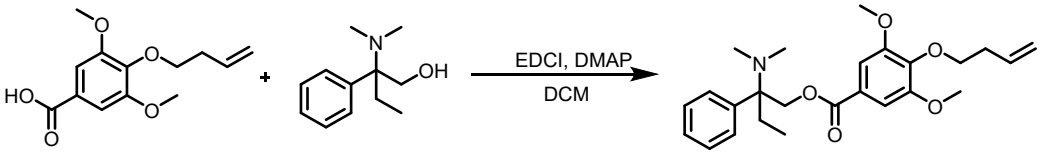
White solid, yield 61% (1.54 g). M.p. = 88–89 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (s, 2H), 5.91 (ddt, J = 17.0, 10.3, 6.7 Hz, 1H), 5.19 – 5.11 (m, 1H), 5.11 – 5.04 (m, 1H), 4.12 (t, J = 7.0 Hz, 2H), 3.91 (s, 6H), 2.54 (q, J = 6.9 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.0, 153.3, 142.2, 134.8, 124.2, 116.8, 107.5, 72.7, 56.4, 34.7.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{13}H_{17}O_5^+$ 253.1071; found 253.1076.

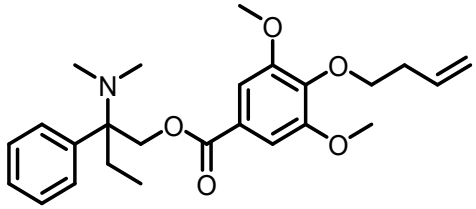
2.6 General procedure for synthesis of 1t



1t,92%

According to literature reports[5], Compounds **1s** (0.50 g, 2 mmol), 1-ethyl-(3-(3-dimethylamino)propyl)-carbodiimide hydrochloride (0.58 g, 3 mmol) and 4-dimethylaminopyridine (0.024 g, 0.2 mmol) were dissolved in DCM (10 mL). The mixture was stirred for 1 h at room temperature. Then the mixture was added 2-(dimethylamino)-2-phenylbutan-1-ol (0.58 g, 3 mmol) and then the mixture was stirred for 5 h at room temperature and quenched with H_2O (10 mL), extracted with DCM (20 mL × 2). The combined organic layer was washed with brine (30 mL), dried over Na_2SO_4, and concentrated. The residue was purified by flash chromatography on a silica gel using petroleum ether and ethyl acetate (4/1 ~ 2/1, v/v) as the eluent to give substrate **1t** (Colorless oil, 0.79g, 92%)

2-(dimethylamino)-2-phenylbutyl 4-(but-3-en-1-yloxy)-3,5-dimethoxybenzoate (1t)



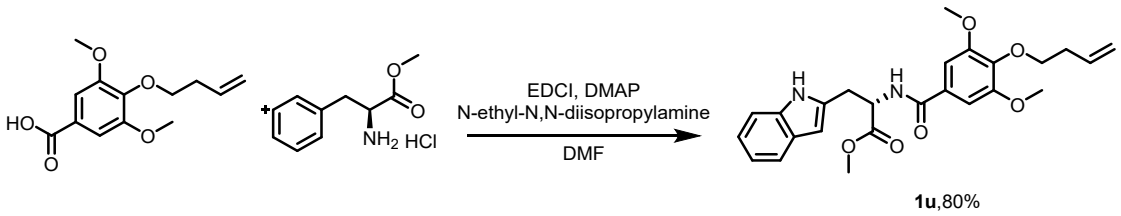
Colorless oil, yield 92% (0.79 g).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, J = 7.4 Hz, 2H), 7.33 (t, J = 7.7 Hz, 2H), 7.22 (t, J = 7.3 Hz, 1H), 7.19 (s, 2H), 5.89 (ddt, J = 17.0, 10.3, 6.7 Hz, 1H), 5.19 – 5.09 (m, 1H), 5.08 – 5.02 (m, 1H), 4.84 (d, J = 11.9 Hz, 1H), 4.74 (d, J = 11.9 Hz, 1H), 4.06 (t, J = 7.0 Hz, 2H), 3.79 (s, 6H), 2.50 (q, J = 6.9 Hz, 2H), 2.39 (s, 6H), 1.94 – 1.83 (m, 2H), 0.71 (t, J = 7.4 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 153.2, 142.5, 141.4, 134.7, 127.9, 127.6, 126.5, 125.2, 116.7, 106.9, 72.6, 64.9, 64.7, 56.1, 39.7, 34.6, 29.6, 8.7.

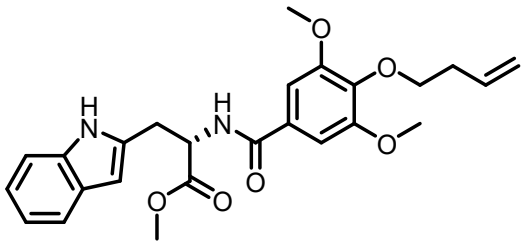
HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{25}H_{34}NO_5^+$ 428.2431; found 428.2435.

2.7 General procedure for synthesis of 1u



According to literature reports[6], Compounds **1s** (0.50 g, 2 mmol), 1-ethyl-(3-(3-dimethylamino)propyl)-carbodiimide hydrochloride (0.58 g, 3 mmol), 4-dimethylaminopyridine (0.024 g, 0.2 mmol), Methyl L-tryptophanate hydrochloride (1.02g, 4 mmol) and N-ethyl-N,N-diisopropylamine (0.70 mL, 4 mmol) were dissolved in DMF (10 mL). The mixture was stirred for 5 h at room temperature and quenched with H_2O (10 mL), extracted with EA (20 mL × 2). The combined organic layer was washed with brine (20 mL x 3), dried over Na_2SO_4, and concentrated. The residue was purified by flash chromatography on a silica gel using petroleum ether and ethyl acetate (4/1 ~ 2/1, v/v) as the eluent to give substrate **1u** (Colorless oil, 0.72g, 80%)

Methyl (4-(but-3-en-1-yloxy)-3,5-dimethoxybenzoyl)-L-tryptophanate (1u)



Colorless oil, yield 80% (0.72 g).

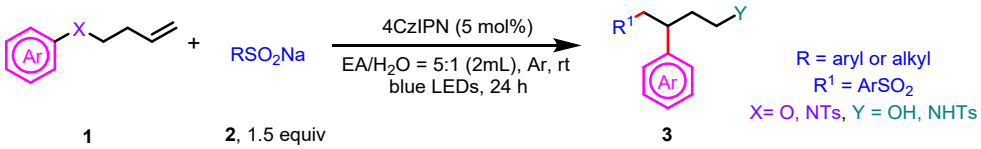
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.85 (s, 1H), 7.56 (d, J = 7.8 Hz, 1H), 7.30 (d, J = 8.0 Hz, 1H), 7.13 (t, J = 7.5 Hz, 1H), 7.05 (t, J = 7.4 Hz, 1H), 6.95 (s, 1H), 6.81 (s, 2H), 6.66 (d, J = 7.6 Hz, 1H), 5.87 (ddt, J = 13.5, 10.2, 6.7 Hz, 1H), 5.16 – 5.01 (m, 3H), 4.02 (t, J = 6.9 Hz, 2H), 3.72 (s, 3H), 3.68 (s, 6H), 3.49 – 3.37 (m, 2H), 2.48 (q, J = 6.7 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 167.0, 153.3, 139.9, 136.2, 134.7, 129.1, 127.8, 123.1, 122.1, 119.7, 118.3, 116.7, 111.6, 109.5, 104.4, 72.5, 56.1, 53.9, 52.5, 34.5, 27.2.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{25}H_{29}N_2O_6^+$ 453.2020; found 453.2020.

3. Experimental procedures and product characterization

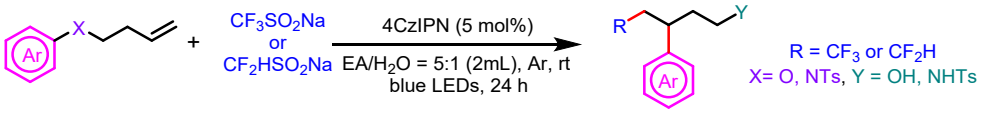
3.1 General procedure for synthesis of 3a-3q, 4a-4s and 5



1 **2**, 1.5 equiv **3**

To a 4 mL glass vial equipped with a magnetic stir bar was added **1** (0.2 mmol), **2** (0.3 mmol, 1.5 equiv), and 4CzIPN (5 mol%) in 5:1 (v/v) ethyl acetate (EA)/H_2O (2 mL). The reaction mixture was degassed by bubbling with argon for 10 s with an outlet needle and the vial was sealed with PTFE cap. The mixture was then stirred rapidly and irradiated with a 30 W Blue LED at room temperature for 24 h. When the reaction is completed, extracted with ethyl acetate, washed with brine, dried over anhydrous sodium sulfate, concentrated in vacuo, and purified by column chromatography (hexane/ethyl acetate = 5/1~1/1 (v/v)) to afford the corresponding target compounds **3a-3q, 4a-4s** and **5**.

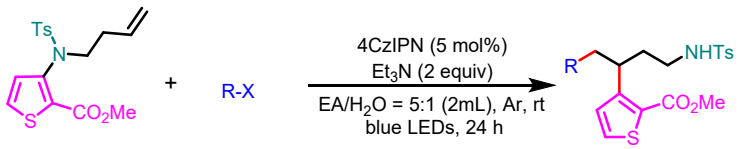
3.2 General procedure for synthesis of 3r-3u and 4t-4u



1 **2**, 1.5 equiv **3**

To a 4 mL glass vial equipped with a magnetic stir bar was added **1** (0.2 mmol), **2** (0.3 mmol, 1.5 equiv), and 4CzIPN (5 mol%) in 10:1 (v/v) ethyl acetate (EA)/H_2O (2 mL). The reaction mixture was degassed by bubbling with argon for 10 s with an outlet needle and the vial was sealed with PTFE cap. The mixture was then stirred rapidly and irradiated with a 30 W Blue LED at room temperature for 16 h. When the reaction is completed, extracted with ethyl acetate, washed with brine, dried over anhydrous sodium sulfate, concentrated in vacuo, and purified by column chromatography (hexane/ethyl acetate) to afford the corresponding target compounds **3r-3u** and **4t-4u**

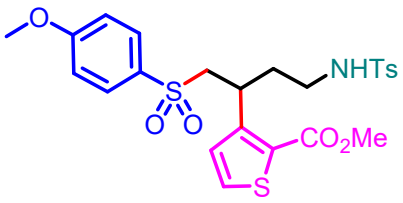
3.3 General procedure for synthesis of 3w-3y.



1a **2**, 1.5 equiv **3w-3y**

To a 4 mL glass vial equipped with a magnetic stir bar was added **1a** (0.2 mmol), **2** (0.3 mmol, 1.5 equiv), Et_3N (0.4 mmol, 2 equiv) and 4CzIPN (5 mol%) in 10:1 (v/v) ethyl acetate (EA)/H_2O (2 mL). The reaction mixture was degassed by bubbling with argon for 10 s with an outlet needle and the vial was sealed with PTFE cap. The mixture was then stirred rapidly and irradiated with a 30 W Blue LED at room temperature for 20 h. When the reaction is completed, extracted with ethyl acetate, washed with brine, dried over anhydrous sodium sulfate, concentrated in vacuo, and purified by column chromatography (hexane/ethyl acetate) to afford the corresponding target compounds **3w-3y**.

Methyl 3-(1-((4-methoxyphenyl)sulfonyl)-4-((4-methylphenyl)sulfonamido)butan-2-yl)thiophene-2-carboxylate (3a)



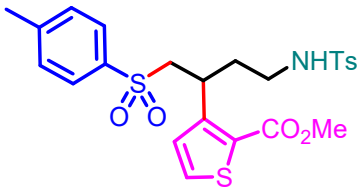
Colorless oil, yield 93% (100.0 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, J = 8.2 Hz, 2H), 7.61 (d, J = 8.9 Hz, 2H), 7.32 (d, J = 5.2 Hz, 1H), 7.26 (d, J = 8.0 Hz, 2H), 6.89 (d, J = 8.9 Hz, 2H), 6.78 (d, J = 5.2 Hz, 1H), 5.47 (dd, J = 7.5, 4.4 Hz, 1H), 4.32 – 4.21 (m, 1H), 3.86 (s, 6H), 3.47 (dd, J = 14.5, 8.2 Hz, 1H), 3.29 (dd, J = 14.5, 5.3 Hz, 1H), 2.98 – 2.87 (m, 1H), 2.52 – 2.44 (m, 1H), 2.41 (s, 3H), 2.03 – 1.91 (m, 1H), 1.77 – 1.64 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7, 163.2, 148.4, 143.3, 137.3, 131.7, 130.6, 130.1, 129.7, 128.0, 127.8, 127.0, 114.4, 61.3, 55.8, 52.5, 40.4, 35.6, 31.2, 21.6.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{24}H_{28}NO_7S_3^+$ 538.1022; found 538.1018.

Methyl 3-(4-((4-methylphenyl)sulfonamido)-1-tosylbutan-2-yl)thiophene-2-carboxylate (3b)



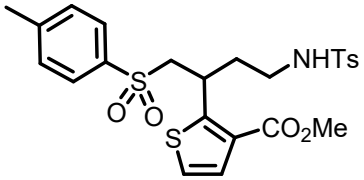
White solid, yield 96% (100.0 mg). M.p. = 113–114 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, J = 8.2 Hz, 2H), 7.56 (d, J = 8.2 Hz, 2H), 7.30 (d, J = 5.2 Hz, 1H), 7.25 (d, J = 8.1 Hz, 2H), 7.22 (d, J = 8.1 Hz, 2H), 6.78 (d, J = 5.2 Hz, 1H), 5.48 (dd, J = 7.3, 4.5 Hz, 1H), 4.37 – 4.21 (m, 1H), 3.85 (s, 3H), 3.49 (dd, J = 14.4, 8.3 Hz, 1H), 3.29 (dd, J = 14.5, 5.2 Hz, 1H), 2.97 – 2.87 (m, 1H), 2.54 – 2.38 (m, 7H), 2.02 – 1.92 (m, 1H), 1.79 – 1.66 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 163.1, 148.2, 144.6, 143.3, 137.3, 136.2, 131.7, 129.8, 129.7, 128.0, 127.9, 127.0, 61.1, 52.4, 40.4, 35.6, 31.1, 21.7, 21.6.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{24}H_{28}NO_6S_3^+$ 522.1073; found 522.1072.

Methyl 2-(4-((4-methylphenyl)sulfonamido)-1-tosylbutan-2-yl)thiophene-3-car-Boxylate (3c)



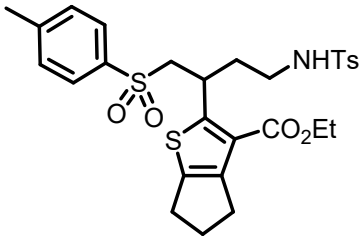
Colorless oil, yield 94% (98.1 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 8.2 Hz, 2H), 7.60 (d, J = 8.2 Hz, 2H), 7.28 – 7.23 (m, 4H), 7.18 (d, J = 5.4 Hz, 1H), 7.05 (d, J = 5.3 Hz, 1H), 5.50 (dd, J = 7.2, 4.3 Hz, 1H), 4.57 – 4.43 (m, 1H), 3.86 (s, 3H), 3.49 (dd, J = 14.5, 7.9 Hz, 1H), 3.31 (dd, J = 14.5, 5.5 Hz, 1H), 3.08 – 2.96 (m, 1H), 2.65 – 2.53 (m, 1H), 2.41 (s, 6H), 2.14 – 2.03 (m, 1H), 1.76 – 1.71 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2, 153.2, 144.8, 143.3, 137.5, 136.2, 129.9, 129.9, 129.8, 129.0, 128.0, 127.0, 123.6, 62.9, 52.3, 40.2, 37.5, 31.7, 21.7, 21.6.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{24}H_{28}NO_6S_3^+$ 522.1073; found 522.1068.

Ethyl 2-(4-((4-methylphenyl)sulfonamido)-1-tosylbutan-2-yl)-5,6-dihydro-4H-cyclopenta[*b*]thiophene-3-carboxylate (3d)



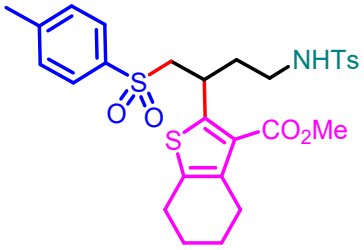
Colorless oil, yield 76% (88.0 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, J = 8.2 Hz, 2H), 7.55 (d, J = 8.2 Hz, 2H), 7.26 (d, J = 7.9 Hz, 2H), 7.21 (d, J = 8.1 Hz, 2H), 5.78 (d, J = 4.6 Hz, 1H), 4.53 – 4.36 (m, 1H), 4.31 (q, J = 7.1 Hz, 2H), 3.48 (dd, J = 14.5, 8.7 Hz, 1H), 3.20 (dd, J = 14.5, 4.9 Hz, 1H), 3.11 – 3.01 (m, 1H), 2.87 – 2.77 (m, 1H), 2.75 – 2.56 (m, 4H), 2.41 (s, 6H), 2.38 – 2.30 (m, 2H), 2.02 – 1.93 (m, 1H), 1.68 – 1.57 (m, 1H), 1.39 (t, J = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4, 155.3, 146.6, 144.4, 143.2, 140.2, 137.8, 136.4, 129.7, 129.5, 128.0, 127.0, 125.9, 63.2, 61.1, 40.2, 37.4, 32.5, 30.3, 29.0, 28.4, 21.7, 21.6, 14.3.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{28}H_{34}NO_6S_3^+$ 576.1543; found 576.1538.

Methyl 2-(4-((4-methylphenyl)sulfonamido)-1-tosylbutan-2-yl)-4,5,6,7-tetrahydro benzo[*b*]thiophene-3-carboxylate (3e)



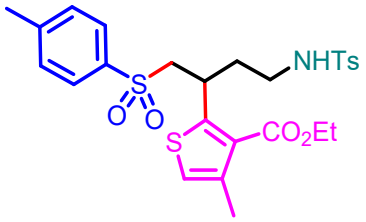
Colorless oil, yield 87% (100.3 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J = 7.7 Hz, 2H), 7.51 (d, J = 7.7 Hz, 2H), 7.27 (d, J = 7.9 Hz, 2H), 7.21 (d, J = 7.9 Hz, 2H), 5.95 (dd, J = 8.7, 3.7 Hz, 1H), 4.33 – 4.22 (m, 1H), 3.90 (s, 3H), 3.39 (dd, J = 14.5, 9.0 Hz, 1H), 3.15 (dd, J = 14.6, 4.8 Hz, 1H), 3.12 – 3.03 (m, 1H), 2.71 – 2.56 (m, 2H), 2.54 – 2.38 (m, 9H), 2.03 – 1.93 (m, 1H), 1.83 – 1.72 (m, 2H), 1.71 – 1.54 (m, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 147.8, 144.1, 143.2, 137.8, 136.5, 135.5, 134.7, 130.5, 129.7, 129.5, 127.9, 127.0, 63.4, 52.2, 40.0, 37.2, 32.0, 26.1, 25.0, 22.9, 22.5, 21.6, 21.6.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{28}H_{34}NO_6S_3^+$ 576.1543; found 576.1539.

Ethyl 4-methyl-2-(4-((4-methylphenyl)sulfonamido)-1-tosylbutan-2-yl)thiophene-3-carboxylate (3f)



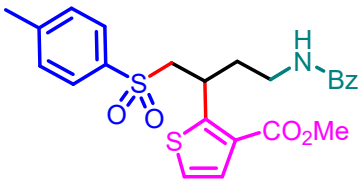
Colorless oil, yield 83% (91.0 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, J = 8.0 Hz, 2H), 7.56 (d, J = 7.9 Hz, 2H), 7.26 (d, J = 8.1 Hz, 2H), 7.22 (d, J = 8.0 Hz, 2H), 6.64 (s, 1H), 5.90 (dd, J = 8.6, 4.1 Hz, 1H), 4.43 – 4.28 (m, 3H), 3.41 (dd, J = 14.5, 8.3 Hz, 1H), 3.21 (dd, J = 14.5, 5.2 Hz, 1H), 3.10 – 3.00 (m, 1H), 2.62 – 2.53 (m, 1H), 2.40 (s, 6H), 2.23 (s, 3H), 2.09 – 2.00 (m, 1H), 1.71 – 1.60 (m, 1H), 1.42 (t, J = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.0, 151.8, 144.5, 143.2, 138.1, 137.7, 136.4, 131.2, 129.7, 127.9, 127.0, 120.5, 63.3, 61.6, 40.1, 37.4, 32.1, 21.7, 21.6, 17.0, 14.3.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{26}H_{32}NO_6S_3^+$ 550.1386; found 550.1381.

Methyl 2-(4-benzamido-1-tosylbutan-2-yl)thiophene-3-carboxylate (3g)



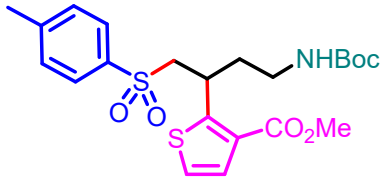
Colorless oil, yield 90% (85.4 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, J = 7.3 Hz, 2H), 7.60 (d, J = 8.2 Hz, 2H), 7.51 (t, J = 7.2 Hz, 1H), 7.44 (t, J = 7.4 Hz, 2H), 7.37 – 7.33 (m, 1H), 7.26 (d, J = 5.3 Hz, 1H), 7.13 (d, J = 8.2 Hz, 2H), 7.11 (d, J = 5.4 Hz, 1H), 4.77 – 4.62 (m, 1H), 3.84 (s, 3H), 3.80 – 3.66 (m, 1H), 3.58 (dd, J = 14.6, 8.0 Hz, 1H), 3.48 (dd, J = 14.6, 5.2 Hz, 1H), 2.93 – 2.80 (m, 1H), 2.31 (s, 3H), 2.25 – 2.15 (m, 1H), 1.92 – 1.81 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 164.5, 154.6, 144.7, 136.0, 134.4, 131.4, 129.8, 129.6, 128.8, 128.4, 127.9, 127.2, 123.5, 63.0, 52.0, 37.9, 36.6, 31.9, 21.6.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{24}H_{26}NO_5S_2^+$ 472.1247; found 472.1248.

Methyl 2-(4-((*tert*-butoxycarbonyl)amino)-1-tosylbutan-2-yl)thiophene-3-carboxylate (3h)



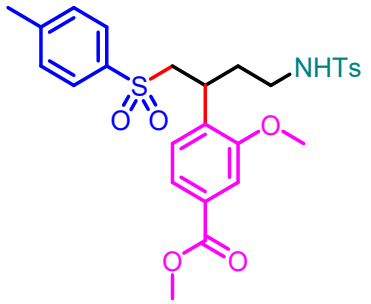
Colorless oil, yield 76% (70.8 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.1 Hz, 2H), 7.25 – 7.19 (m, 3H), 7.05 (d, *J* = 5.3 Hz, 1H), 5.03 (s, 1H), 4.55 (s, 1H), 3.82 (s, 3H), 3.57 (dd, *J* = 14.4, 7.6 Hz, 1H), 3.44 (dd, *J* = 14.5, 5.7 Hz, 1H), 3.22 – 3.09 (m, 1H), 2.82 – 2.72 (m, 1H), 2.39 (s, 3H), 2.17 – 2.08 (m, 1H), 1.85 – 1.81 (m, 1H), 1.42 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 163.8, 155.9, 153.9, 144.6, 136.5, 129.8, 129.5, 129.2, 128.0, 123.2, 79.2, 62.8, 51.9, 37.8, 32.2, 28.5, 21.7.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{22}H_{29}NNaO_6S_2^+$ 490.1329; found 490.1325.

Methyl 3-methoxy-4-(4-((4-methylphenyl)sulfonamido)-1-tosylbutan-2-yl)benzoate (3i)



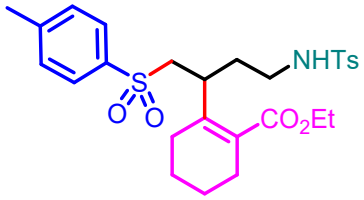
Colorless oil, yield 92% (100.0 mg).

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.61 (d, *J* = 7.9 Hz, 2H), 7.51 (d, *J* = 7.9 Hz, 2H), 7.39 (d, *J* = 7.8 Hz, 1H), 7.25 – 7.20 (m, 3H), 7.14 (d, *J* = 7.9 Hz, 2H), 6.91 (d, *J* = 7.8 Hz, 1H), 4.97 (t, *J* = 6.1 Hz, 1H), 3.88 (s, 3H), 3.68 (s, 3H), 3.61 (dd, *J* = 14.2, 7.3 Hz, 1H), 3.54 – 3.43 (m, 1H), 3.35 (dd, *J* = 14.3, 5.7 Hz, 1H), 2.79 – 2.69 (m, 1H), 2.68 – 2.58 (m, 1H), 2.38 (s, 3H), 2.34 (s, 3H), 1.99 – 1.90 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) *δ* 166.7, 156.8, 144.5, 143.4, 136.8, 136.3, 133.2, 130.3, 129.7, 129.6, 129.5, 127.9, 127.1, 122.2, 111.5, 59.6, 55.4, 52.3, 40.9, 34.3, 33.6, 21.5.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{27}H_{32}NO_7S_2^+$ 546.1615; found 546.1615.

Ethyl 2-(4-((4-methylphenyl)sulfonamido)-1-tosylbutan-2-yl)cyclohex-1-ene-1-carboxylate (3j)



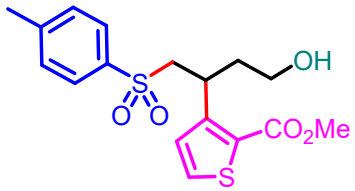
Colorless oil, yield 84% (90.0 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 – 7.65 (m, 4H), 7.33 (d, J = 8.1 Hz, 2H), 7.27 (d, J = 8.0 Hz, 2H), 6.49 (dd, J = 9.5, 2.8 Hz, 1H), 4.25 (q, J = 7.1 Hz, 2H), 3.82 – 3.71 (m, 1H), 3.19 (dd, J = 14.5, 9.1 Hz, 1H), 3.14 – 3.03 (m, 1H), 2.83 (dd, J = 14.6, 4.8 Hz, 1H), 2.63 – 2.51 (m, 1H), 2.44 (s, 3H), 2.41 (s, 3H), 2.32 – 2.21 (m, 1H), 1.96 – 1.86 (m, 1H), 1.68 – 1.56 (m, 3H), 1.54 – 1.46 (m, 1H), 1.37 – 1.23 (m, 5H), 1.19 – 1.08 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1, 144.7, 143.0, 141.4, 137.7, 136.8, 130.7, 129.8, 129.6, 128.1, 127.1, 61.4, 58.9, 40.1, 33.8, 31.8, 27.0, 23.6, 21.7, 21.6, 21.5, 21.2, 14.3.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{27}H_{36}NO_6S_2^+$ 534.1979; found 534.1977.

Methyl 3-(4-hydroxy-1-tosylbutan-2-yl)thiophene-2-carboxylate (3m)



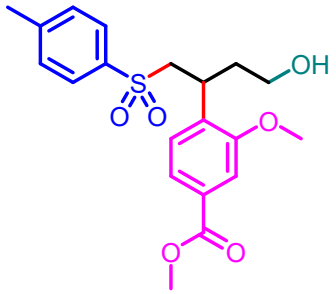
Colorless oil, yield 68% (50.0 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, J = 8.3 Hz, 2H), 7.33 (d, J = 5.2 Hz, 1H), 7.20 (d, J = 8.0 Hz, 2H), 6.84 (d, J = 5.2 Hz, 1H), 4.47 – 4.36 (m, 1H), 3.84 (s, 3H), 3.60 (dd, J = 14.5, 8.7 Hz, 1H), 3.50 – 3.43 (m, 2H), 3.24 (ddd, J = 11.8, 9.7, 3.6 Hz, 1H), 2.75 (s, 1H), 2.39 (s, 3H), 2.11 – 2.03 (m, 1H), 1.77 – 1.68 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5, 149.3, 144.5, 136.3, 131.5, 129.7, 128.0, 127.8, 61.5, 59.4, 52.4, 39.2, 30.8, 21.7.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{17}H_{21}O_5S_2^+$ 369.0825; found 369.0823.

Methyl 4-(4-hydroxy-1-tosylbutan-2-yl)-3-methoxybenzoate (3n)



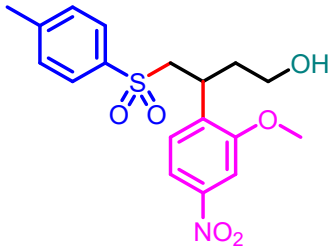
Colorless oil, yield 70% (55.0 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, J = 8.0 Hz, 2H), 7.47 (d, J = 7.8 Hz, 1H), 7.28 (s, 1H), 7.15 (d, J = 8.0 Hz, 2H), 7.06 (d, J = 7.8 Hz, 1H), 3.90 (s, 3H), 3.78 – 3.66 (m, 5H), 3.55 – 3.45 (m, 2H), 3.40 – 3.32 (m, 1H), 2.36 (s, 3H), 2.11 – 2.04 (m, 1H), 1.98 – 1.90 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 156.9, 144.4, 136.5, 134.1, 130.2, 129.7, 129.5, 127.9, 122.2, 111.5, 60.1, 59.9, 55.4, 52.3, 37.0, 33.8, 21.6.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{20}H_{25}O_6S^+$ 393.1366; found 393.1362.

3-(2-methoxy-4-nitrophenyl)-4-tosylbutan-1-ol (3o)



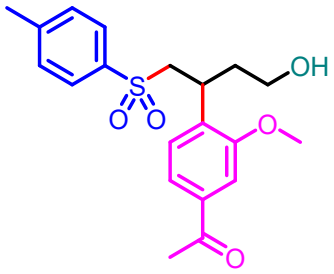
White solid, yield 46% (35.0 mg). M.p. = 95–96 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (dd, J = 8.3, 2.0 Hz, 1H), 7.52 (d, J = 8.2 Hz, 2H), 7.43 (d, J = 1.9 Hz, 1H), 7.17 (t, J = 8.8 Hz, 3H), 3.81 – 3.69 (m, 5H), 3.56 – 3.45 (m, 2H), 3.39 – 3.31 (m, 1H), 2.36 (s, 3H), 2.05 – 1.93 (m, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 157.5, 147.9, 144.8, 136.5, 136.4, 130.5, 129.5, 127.9, 115.9, 105.7, 59.9, 59.3, 55.8, 36.5, 34.2, 21.6.

HRMS(ESI) m/z: $[M+H]^+$Calcd for$C_{18}H_{22}NO_6S^+$ 380.1162; found 380.1161.

1-(4-(4-hydroxy-1-tosylbutan-2-yl)-3-methoxyphenyl)ethan-1-one (3p)



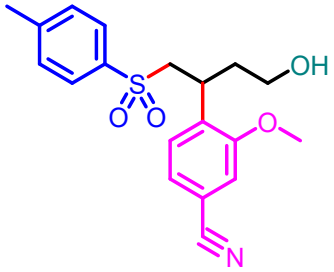
Colorless oil, yield 85% (64.0 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, J = 8.1 Hz, 2H), 7.35 (d, J = 7.7 Hz, 1H), 7.21 (s, 1H), 7.13 (d, J = 8.1 Hz, 2H), 7.09 (d, J = 7.8 Hz, 1H), 3.76 – 3.61 (m, 5H), 3.52 – 3.43 (m, 2H), 3.37 – 3.28 (m, 1H), 2.52 (s, 3H), 2.33 (s, 3H), 2.12 (s, 1H), 2.08 – 2.00 (m, 1H), 1.98 – 1.88 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 197.6, 157.3, 144.4, 137.3, 136.5, 134.5, 129.9, 129.4, 127.9, 121.7, 109.4, 60.0, 59.7, 55.4, 36.9, 33.9, 26.6, 21.6.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{20}H_{25}O_5S^+$ 377.1417; found 377.1415

4-(4-hydroxy-1-tosylbutan-2-yl)-3-methoxybenzonitrile (3q)



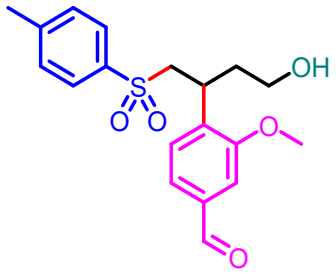
White solid, yield 70% (51.0 mg). M.p. = 144–146 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, J = 8.3 Hz, 2H), 7.20 (d, J = 8.0 Hz, 2H), 7.17 – 7.08 (m, 2H), 6.85 (s, 1H), 3.79 – 3.66 (m, 5H), 3.57 – 3.44 (m, 2H), 3.40 – 3.31 (m, 1H), 2.41 (s, 3H), 2.09 – 2.01 (m, 2H), 1.99 – 1.88 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 157.2, 144.6, 136.4, 134.7, 130.8, 129.5, 127.9, 124.8, 118.6, 113.7, 111.7, 59.9, 59.4, 55.6, 36.6, 34.2, 21.6.

HRMS(ESI) m/z: $[M+Na]^+$Calcd for $C_{19}H_{21}NNaO_4S^+$ 382.1083; found 382.1082.

4-(4-hydroxy-1-tosylbutan-2-yl)-3-methoxybenzaldehyde (3r)



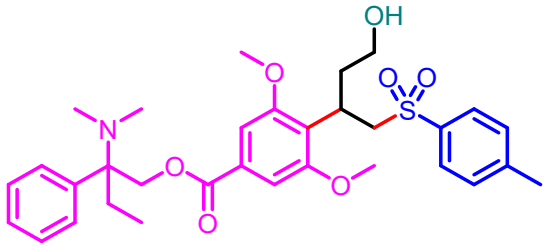
Colorless oil, yield 86% (62.0 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.89 (s, 1H), 7.54 (d, J = 8.1 Hz, 2H), 7.31 (d, J = 7.6 Hz, 1H), 7.22 (d, J = 7.6 Hz, 1H), 7.15 (d, J = 8.8 Hz, 3H), 3.82 – 3.68 (m, 5H), 3.57 – 3.47 (m, 2H), 3.41 – 3.32 (m, 1H), 2.36 (s, 3H), 2.20 (s, 1H), 2.13 – 2.04 (m, 1H), 2.02 – 1.90 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 191.7, 157.6, 144.5, 136.6, 136.3, 136.2, 130.5, 129.4, 127.9, 124.4, 109.0, 60.0, 59.6, 55.4, 36.7, 34.2, 21.6.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{19}H_{23}O_5S^+$ 363.1261; found 363.1259.

2-(dimethylamino)-2-phenylbutyl 4-(4-hydroxy-1-tosylbutan-2-yl)-3,5-dimethoxybenzoate (3s)



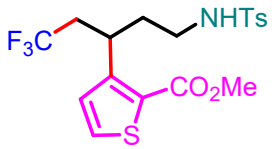
Colorless oil, yield 93% (108.8 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, J = 8.1 Hz, 2H), 7.49 (d, J = 7.8 Hz, 2H), 7.35 (t, J = 7.6 Hz, 2H), 7.24 (t, J = 7.2 Hz, 1H), 7.13 (dd, J = 8.1, 2.0 Hz, 2H), 7.02 (s, 1H), 6.89 (s, 1H), 4.91 – 4.66 (m, 2H), 4.10 – 4.01 (m, 1H), 3.95 (dd, J = 14.5, 8.3 Hz, 1H), 3.73 (s, 3H), 3.63 (s, 3H), 3.48 – 3.38 (m, 2H), 3.30 – 3.21 (m, 1H), 2.39 (s, 6H), 2.34 (s, 1H), 2.15 (s, 1H), 1.98 – 1.83 (m, 4H), 0.73 (t, J = 7.3 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 158.4, 157.6, 144.2, 142.2, 136.4, 130.1, 129.2, 127.9, 127.9, 127.5, 126.6, 121.6, 105.4, 105.2, 64.8, 60.5, 59.1, 56.3, 55.3, 39.7, 36.1, 29.4, 30.0, 21.6, 8.7.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{32}H_{42}NO_7S^+$ 584.2676; found 584.2678.

Methyl 3-(1,1,1-trifluoro-5-((4-methylphenyl)sulfonamido)pentan-3-yl)thiophene -2-carboxylate (3t)



Colorless oil, yield 87% (75.9 mg).

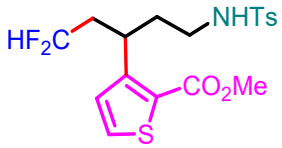
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, J = 8.2 Hz, 2H), 7.47 (d, J = 5.2 Hz, 1H), 7.26 (d, J = 8.1 Hz, 2H), 6.93 (d, J = 5.2 Hz, 1H), 5.49 (dd, J = 8.0, 3.8 Hz, 1H), 4.30 – 4.12 (m, 1H), 3.90 (s, 3H), 3.07 – 2.96 (m, 1H), 2.57 – 2.47 (m, 1H), 2.42 – 2.32 (m, 4H), 2.26 – 2.17 (m, 1H), 1.96 – 1.87 (m, 1H), 1.71 – 1.62 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 163.6, 149.6, 143.4, 137.6, 132.0, 129.7, 127.8, 127.2, 127.0, 126.1 (q, J = 277.6 Hz), 52.5, 40.6, 40.0 (q, J = 27.7 Hz), 35.8, 29.5, 21.6.

^{19}F NMR (376 MHz, $CDCl_3$) δ -64.02 (t, J = 10.6 Hz).

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{18}H_{21}F_3NO_4S_2^+$ 436.0859; found 436.0854.

Methyl 3-(1,1-difluoro-5-((4-methylphenyl)sulfonamido)pentan-3-yl)thiophene-2-carboxylate (3u)



Colorless oil, yield 85% (71.8 mg).

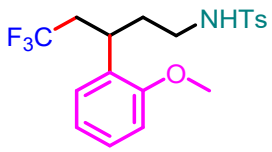
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, J = 7.9 Hz, 2H), 7.48 (d, J = 5.1 Hz, 1H), 7.27 (d, J = 7.7 Hz, 2H), 6.95 (d, J = 5.1 Hz, 1H), 5.62 – 5.28 (m, 2H), 4.11 – 3.99 (m, 1H), 3.89 (s, 3H), 3.08 – 2.95 (m, 1H), 2.60 – 2.49 (m, 1H), 2.41 (s, 3H), 2.10 – 1.83 (m, 3H), 1.71 – 1.58 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 163.55, 150.33, 143.33, 137.64, 132.19, 129.72, 127.86, 127.10, 126.98, 116.1 (t, J = 240.0 Hz), 52.51, 40.64, 40.59 (t, J = 21.1 Hz), 36.12, 29.8 (dd, J = 7.0, 4.0 Hz), 21.58.

^{19}F NMR (376 MHz, $CDCl_3$) δ -113.50 – -116.63 (m).

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{18}H_{22}F_2NO_4S_2^+$ 418.0953; found 418.0947.

4-methyl-N-(5,5,5-trifluoro-3-(2-methoxyphenyl)pentyl)benzenesulfonamide (3v)



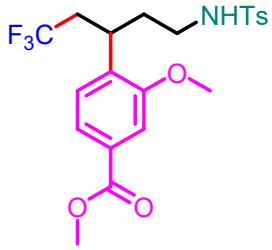
Colorless oil, yield 82% (66.0 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, J = 8.1 Hz, 2H), 7.26 (d, J = 8.0 Hz, 2H), 7.20 (t, J = 7.5 Hz, 1H), 6.99 (d, J = 7.0 Hz, 1H), 6.89 (t, J = 7.4 Hz, 1H), 6.84 (d, J = 8.2 Hz, 1H), 4.73 (t, J = 6.0 Hz, 1H), 3.81 (s, 3H), 3.38 – 3.27 (m, 1H), 2.91 – 2.80 (m, 1H), 2.65 – 2.56 (m, 1H), 2.54 – 2.44 (m, 1H), 2.41 (s, 3H), 2.34 – 2.24 (m, 1H), 1.91 – 1.75 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 157.1, 143.4, 137.2, 129.8, 129.3, 128.4, 128.4, 127.1, 126.7 (d, J = 277.5 Hz), 121.3, 55.6, 41.2, 39.0 (q, J = 27.3 Hz), 34.7, 31.2, 21.6.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{19}H_{23}F_3NO_3S^+$ 402.1345; found 402.1341.

Methyl 3-methoxy-4-(1,1,1-trifluoro-5-((4-methylphenyl)sulfonamido)pentan- 3-yl)benzoate (3w)



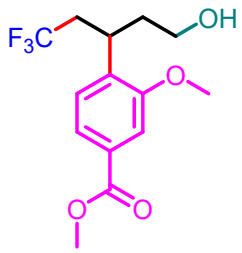
Colorless oil, yield 71% (65.0 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, J = 8.2 Hz, 2H), 7.54 (dd, J = 7.8, 1.2 Hz, 1H), 7.48 (d, J = 1.0 Hz, 1H), 7.24 (d, J = 8.2 Hz, 2H), 7.06 (d, J = 7.9 Hz, 1H), 4.90 (t, J = 6.2 Hz, 1H), 3.90 (s, 3H), 3.84 (s, 3H), 3.41 – 3.30 (m, 1H), 2.84 – 2.75 (m, 1H), 2.63 – 2.47 (m, 2H), 2.39 (s, 3H), 2.34 – 2.22 (m, 1H), 1.89 – 1.82 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 157.1, 143.5, 136.9, 134.7, 130.6, 130.3, 129.8, 128.7, 127.0, 126.5 (q, J = 277.6 Hz), 122.5, 111.9, 55.8, 52.3, 41.0, 38.5 (q, J = 27.3 Hz), 34.3, 31.8, 21.5.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{21}H_{25}F_3NO_5S^+$ 460.1400; found 460.1401.

Methyl 3-methoxy-4-(1,1,1-trifluoro-5-hydroxypentan-3-yl)benzoate (3x)



Colorless oil, yield 82% (50.0 mg).

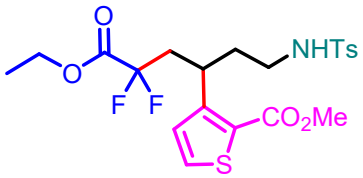
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, J = 7.9 Hz, 1H), 7.54 (s, 1H), 7.19 (d, J = 7.9 Hz, 1H), 3.90 (s, 3H), 3.89 (s, 3H), 3.60 – 3.46 (m, 2H), 3.38 – 3.27 (m, 1H), 2.66 – 2.54 (m, 1H), 2.53 – 2.41 (m, 1H), 2.06 – 1.98 (m, 1H), 1.97 – 1.88 (m, 1H), 1.76 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 157.3, 135.7, 130.1, 128.8, 126.8 (q, J = 277.5 Hz), 122.6, 111.9, 60.4, 55.9, 52.3, 38.7 (q, J = 27.5 Hz), 37.5, 31.1.

^{19}F NMR (376 MHz, $CDCl_3$) δ -64.03 (t, J = 11.0 Hz).

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{14}H_{18}F_3O_4^+$ 307.1152; found 307.1151.

Methyl 3-(6-ethoxy-5,5-difluoro-1-((4-methylphenyl)sulfonamido)-6-oxohexan- 3-yl)thiophene-2-carboxylate (3y)



Colorless oil, yield 51% (50.0 mg).

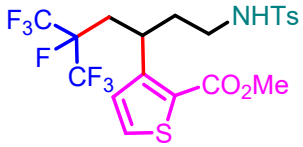
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J = 8.2 Hz, 2H), 7.44 (d, J = 5.2 Hz, 1H), 7.26 (d, J = 8.1 Hz, 2H), 6.92 (d, J = 5.2 Hz, 1H), 5.58 – 5.45 (br, 1H), 4.18 – 4.05 (m, 3H), 3.90 (s, 3H), 3.04 – 2.94 (m, 1H), 2.49 – 2.38 (m, 5H), 2.27 – 2.15 (m, 1H), 1.95 – 1.86 (m, 1H), 1.70 – 1.61 (m, 1H), 1.27 (t, J = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 163.8 (t, J = 32.5 Hz), 163.6, 149.8, 143.3, 137.5, 131.6, 129.7, 128.0, 127.5, 126.9, 115.4 (t, J = 252.4 Hz), 63.1, 52.5, 40.7 (t, J = 22.8 Hz), 40.6, 36.4, 29.2, 21.6, 13.9.

^{19}F NMR (376 MHz, $CDCl_3$) δ -101.93 (dt, J = 261.5, 15.0 Hz), -104.86 (dt, J = 261.4, 16.7 Hz).

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{21}H_{26}F_2NO_6S_2^+$ 490.1164; found 490.1162.

Methyl 3-(5,6,6,6-tetrafluoro-1-((4-methylphenyl)sulfonamido)-5-(trifluoromethyl)hexan-3-yl)thiophene-2-carboxylate (3z)



Colorless oil, yield 42% (45.0 mg).

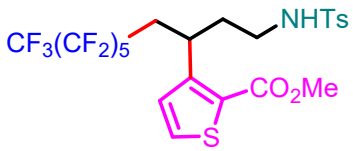
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.3 Hz, 2H), 7.47 (d, *J* = 5.2 Hz, 1H), 7.26 (d, *J* = 8.1 Hz, 2H), 6.94 (d, *J* = 5.2 Hz, 1H), 5.59 (s, 1H), 4.29 (s, 1H), 3.89 (s, 3H), 3.06 – 2.96 (m, 1H), 2.50 – 2.38 (m, 5H), 2.27 – 2.16 (m, 1H), 1.96 – 1.87 (m, 1H), 1.68 – 1.60 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7, 149.9, 143.3, 137.6, 131.9, 129.7, 127.7, 127.0, 122.97 – 118.79 (m), 93.38 – 89.74 (m), 52.5, 40.4, 37.4, 34.6 (d, *J* = 18.7 Hz), 29.5, 21.5.

^{19}F NMR (376 MHz, $CDCl_3$) δ -76.37 – -77.35 (m, 3F), -185.00 – -185.31 (m, 1F).

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{20}H_{21}F_7NO_4S_2^+$ 536.0795; found 536.0795.

Methyl 3-(5,5,6,6,7,7,8,8,9,9,10,10,10-tridecafluoro-1-((4-methylphenyl)sulfonamido)decan-3-yl)thiophene-2-carboxylate (3ab)



Colorless oil, yield 55% (75.0 mg).

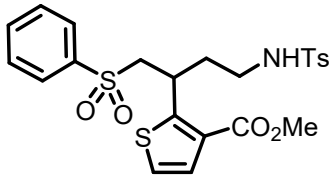
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 7.8 Hz, 2H), 7.47 (d, *J* = 5.1 Hz, 1H), 7.26 (d, *J* = 7.7 Hz, 2H), 6.94 (d, *J* = 5.1 Hz, 1H), 5.58 (br, 1H), 4.32 (m, 1H), 3.91 (s, 3H), 3.13 – 3.01 (m, 1H), 2.56 – 2.47 (m, 1H), 2.43 – 2.31 (m, 4H), 2.23 – 2.09 (m, 1H), 1.94 – 1.85 (m, 1H), 1.72 – 1.65 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7, 149.9, 143.4, 137.8, 132.0, 129.7, 127.7, 127.1, 126.9, 122.1– 110.1(m), 52.6), 40.6, 36.6 (t, *J* = 20.8 Hz), 36.4, 28.1, 21.5.

^{19}F NMR (376 MHz, $CDCl_3$) δ -80.85 (t, *J* = 10.8 Hz, 3F), -112.61 – -113.54 (m, 2F), -121.35 – -122.16 (m, 2F), -122.95 (d, *J* = 8.7 Hz, 2F), -123.42 – -123.93 (m, 2F), -125.79 – -126.68 (m, 2F).

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{23}H_{21}F_{13}NO_4S_2^+$ 686.0699; found 686.0696.

Methyl 2-(4-((4-methylphenyl)sulfonamido)-1-(phenylsulfonyl)butan-2-yl)thiophene-3-carboxylate (4a)



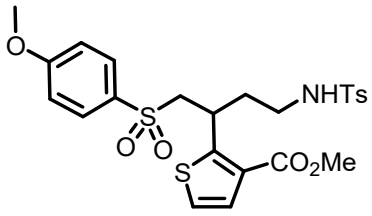
Colorless oil, yield 91% (92.4 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J = 7.3 Hz, 2H), 7.69 (d, J = 8.2 Hz, 2H), 7.58 (t, J = 7.5 Hz, 1H), 7.46 (t, J = 7.7 Hz, 2H), 7.27 (d, J = 8.1 Hz, 2H), 7.18 (d, J = 5.4 Hz, 1H), 7.04 (d, J = 5.3 Hz, 1H), 5.48 (dd, J = 7.6, 4.6 Hz, 1H), 4.57 – 4.45 (m, 1H), 3.86 (s, 3H), 3.52 (dd, J = 14.5, 8.0 Hz, 1H), 3.32 (dd, J = 14.5, 5.5 Hz, 1H), 3.08 – 2.97 (m, 1H), 2.66 – 2.55 (m, 1H), 2.41 (s, 3H), 2.15 – 2.05 (m, 1H), 1.79 – 1.72 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2, 152. 9, 143.3, 139.2, 137.4, 133.7, 129.9, 129.3, 129.0, 127.9, 127.0, 123.7, 62.6, 52.3, 40.2, 37.3, 31.7, 21.6.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{23}H_{26}NO_6S_3^+$ 508.0917; found 508.0916.

methyl 2-(1-((4-methoxyphenyl)sulfonyl)-4-((4-methylphenyl)sulfonamido)butan-2-yl)thiophene-3-carboxylate (4b)



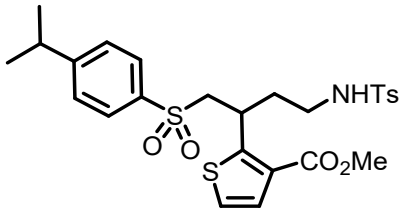
Colorless oil, yield 97% (104.4 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J = 8.2 Hz, 2H), 7.64 (d, J = 8.9 Hz, 2H), 7.25 (d, J = 8.0 Hz, 2H), 7.18 (d, J = 5.3 Hz, 1H), 7.05 (d, J = 5.3 Hz, 1H), 6.91 (d, J = 8.8 Hz, 2H), 5.56 (dd, J = 7.3, 4.6 Hz, 1H), 4.53 – 4.41 (m, 1H), 3.86 (s, 3H), 3.85 (s, 3H), 3.49 (dd, J = 14.4, 7.8 Hz, 1H), 3.32 (dd, J = 14.5, 5.4 Hz, 1H), 3.04 – 2.93 (m, 1H), 2.62 – 2.53 (m, 1H), 2.40 (s, 3H), 2.15 – 2.05 (m, 1H), 1.79 – 1.69 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2, 163.7, 153.3, 143.3, 137.3, 130.5, 130.1, 129.7, 128.9, 126.9, 123.6, 114.5, 62.9, 55.8, 52.2, 40.2, 37.4, 31.8, 21.5.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{24}H_{28}NO_7S_3^+$ 538.1022; found 538.1017.

Methyl 2-(1-((4-isopropylphenyl)sulfonyl)-4-((4-methylphenyl)sulfonamido) butan-2-yl)thiophene-3-carboxylate (4c)



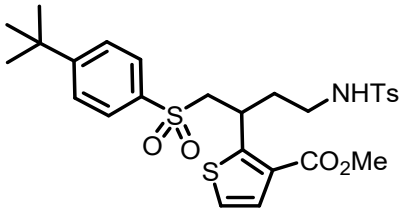
Colorless oil, yield 93% (102.0 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 8.2 Hz, 2H), 7.61 (d, J = 8.4 Hz, 2H), 7.26 (n, J = 8.1, 3.4 Hz, 4H), 7.14 (d, J = 5.4 Hz, 1H), 7.01 (d, J = 5.3 Hz, 1H), 5.53 (dd, J = 7.5, 4.8 Hz, 1H), 4.57 – 4.44 (m, 1H), 3.85 (s, 3H), 3.53 (dd, J = 14.5, 8.1 Hz, 1H), 3.31 (dd, J = 14.5, 5.3 Hz, 1H), 3.04 – 2.90 (m, 2H), 2.64 – 2.55 (m, 1H), 2.16 – 2.05 (m, 1H), 1.81 – 1.69 (m, 1H), 1.25 (s, 3H), 1.24 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 155.3, 153.1, 143.3, 137.4, 136.4, 129.8, 129.7, 129.0, 128.1, 127.3, 127.0, 123.5, 62.7, 52.2, 40.2, 37.4, 34.3, 31.8, 23.7, 23.6, 21.6.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{26}H_{32}NO_6S_3^+$ 550.1386; found 550.1379.

Methyl 2-(1-((4-(tert-butyl)phenyl)sulfonyl)-4-((4-methylphenyl)sulfonamido) butan-2-yl)thiophene-3-carboxylate (4d)



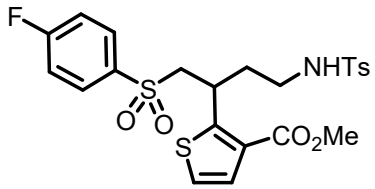
Colorless oil, yield 94% (106.2 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 8.2 Hz, 2H), 7.61 (d, J = 8.5 Hz, 2H), 7.42 (d, J = 8.5 Hz, 2H), 7.26 (d, J = 8.1 Hz, 2H), 7.13 (d, J = 5.4 Hz, 1H), 7.00 (d, J = 5.3 Hz, 1H), 5.54 (dd, J = 7.0, 4.8 Hz, 1H), 4.57 – 4.45 (m, 1H), 3.85 (s, 3H), 3.55 (dd, J = 14.5, 8.2 Hz, 1H), 3.32 (dd, J = 14.5, 5.2 Hz, 1H), 3.06 – 2.95 (m, 1H), 2.65 – 2.56 (m, 1H), 2.40 (s, 3H), 2.15 – 2.05 (m, 1H), 1.81 – 1.70 (m, 1H), 1.32 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 157.5, 153.1, 143.3, 137.4, 136.0, 129.7, 129.0, 127.7, 127.0, 126.2, 123.4, 62.6, 52.2, 40.2, 37.4, 35.2, 31.8, 31.1, 21.6.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{27}H_{34}NO_6S_3^+$ 564.1543; found 564.1537.

Methyl 2-(1-((4-fluorophenyl)sulfonyl)-4-((4-methylphenyl)sulfonamido)butan-2-yl)thiophene-3-carboxylate (4e)



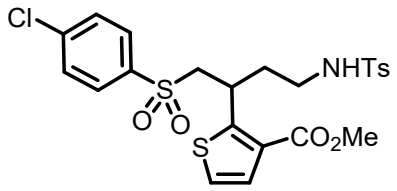
Colorless oil, yield 90% (94.6 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 – 7.70 (m, 2H), 7.68 (d, J = 8.2 Hz, 2H), 7.27 (d, J = 8.7 Hz, 2H), 7.18 (d, J = 5.3 Hz, 1H), 7.11 (t, J = 8.5 Hz, 2H), 7.05 (d, J = 5.3 Hz, 1H), 5.55 (dd, J = 7.2, 4.8 Hz, 1H), 4.56 – 4.43 (m, 1H), 3.86 (s, 3H), 3.55 (dd, J = 14.5, 8.2 Hz, 1H), 3.37 (dd, J = 14.6, 5.3 Hz, 1H), 3.06 – 2.95 (m, 1H), 2.63 – 2.54 (m, 1H), 2.41 (s, 3H), 2.19 – 2.08 (m, 1H), 1.83 – 1.71 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7 (d, J = 256.4 Hz), 164.2, 143.4, 137.3, 135.2 (d, J = 3.0 Hz), 130.9 (d, J = 9.7 Hz), 129.9, 129.8, 129.0, 127.0, 123.8, 116.5 (d, J = 22.7 Hz), 62.7, 52.3, 40.2, 37.32, 31.8, 21.6.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{23}H_{25}FNO_6S_3^+$ 526.0823; found 526.0819.

Methyl 2-(1-((4-chlorophenyl)sulfonyl)-4-((4-methylphenyl)sulfonamido)butan-2-yl)thiophene-3-carboxylate (4f)



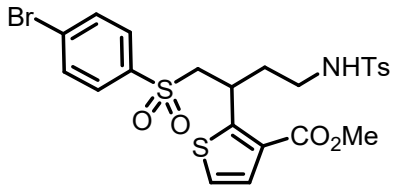
Colorless oil, yield 94% (102.0 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 8.2 Hz, 2H), 7.63 (d, J = 8.6 Hz, 2H), 7.40 (d, J = 8.6 Hz, 2H), 7.26 (d, J = 8.1 Hz, 2H), 7.18 (d, J = 5.4 Hz, 1H), 7.06 (d, J = 5.3 Hz, 1H), 5.58 (dd, J = 7.3, 4.9 Hz, 1H), 4.55 – 4.42 (m, 1H), 3.85 (s, 3H), 3.56 (dd, J = 14.5, 8.3 Hz, 1H), 3.37 (dd, J = 14.6, 5.3 Hz, 1H), 3.04 – 2.94 (m, 1H), 2.66 – 2.55 (m, 1H), 2.40 (s, 3H), 2.17 – 2.07 (m, 1H), 1.83 – 1.71 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 152.7, 143.3, 140.3, 137.6, 137.3, 129.9, 129.7, 129.4, 129.0, 127.0, 123.8, 62.6, 52.2, 40.2, 37.2, 31.8, 21.5.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{23}H_{25}ClNO_6S_3^+$ 542.0527; found 542.0519.

Methyl 2-(1-((4-bromophenyl)sulfonyl)-4-((4-methylphenyl)sulfonamido)butan-2-yl)thiophene-3-carboxylate (4g)



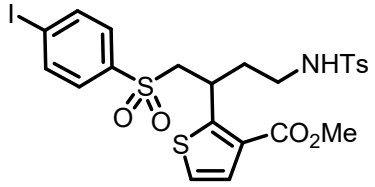
White solid, yield 93% (109.0 mg).M.p. = 117–119 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 8.2 Hz, 2H), 7.55 (s, 4H), 7.26 (d, J = 8.1 Hz, 2H), 7.18 (d, J = 5.4 Hz, 1H), 7.06 (d, J = 5.3 Hz, 1H), 5.57 (dd, J = 7.4, 4.9 Hz, 1H), 4.49 (m, 1H), 3.85 (s, 3H), 3.56 (dd, J = 14.6, 8.3 Hz, 1H), 3.36 (dd, J = 14.6, 5.3 Hz, 1H), 3.06 – 2.93 (m, 1H), 2.64 – 2.54 (m, 1H), 2.40 (s, 3H), 2.18 – 2.07 (m, 1H), 1.82 – 1.71 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 152.6, 143.3, 138.1, 137.3, 132.4, 129.9, 129.7, 129.5, 129.0, 129.0, 127.0, 123.8, 62.6, 52.3, 40.2, 37.3, 31.8, 21.6.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{23}H_{25}BrNO_6S_3^+$ 586.0022; found 586.0017.

Methyl 2-(1-((4-iodophenyl)sulfonyl)-4-((4-methylphenyl)sulfonamido)butan- 2-yl)t-hiophene-3-carboxylate (4h)



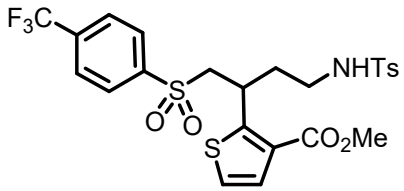
Colorless oil, yield 92% (117.0 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, J = 8.4 Hz, 2H), 7.69 (d, J = 8.1 Hz, 2H), 7.39 (d, J = 8.4 Hz, 2H), 7.27 (d, J = 8.1 Hz, 2H), 7.19 (d, J = 5.3 Hz, 1H), 7.06 (d, J = 5.3 Hz, 1H), 5.50 (dd, J = 7.0, 4.8 Hz, 1H), 4.56 – 4.42 (m, 1H), 3.87 (s, 3H), 3.53 (dd, J = 14.6, 8.3 Hz, 1H), 3.33 (dd, J = 14.6, 5.2 Hz, 1H), 3.09 – 2.97 (m, 1H), 2.64 – 2.54 (m, 1H), 2.41 (s, 3H), 2.18 – 2.06 (m, 1H), 1.78 – 1.73 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2, 152.7, 143.4, 138.8, 138.5, 137.5, 130.0, 129.8, 129.3, 129.1, 127.0, 123.8, 101.7, 62.7, 52.4, 40.2, 37.4, 31.8, 21.6.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{23}H_{25}INO_6S_3^+$ 633.9883; found 633.9876.

Methyl 2-(4-((4-methylphenyl)sulfonamido)-1-((4-(trifluoromethyl)phenyl)sulfonyl)butan-2-yl)thiophene-3-carboxylate (4i)



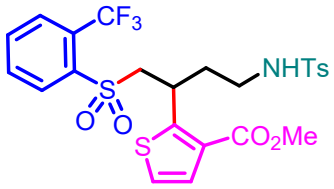
Colorless oil, yield 91% (105.7 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, J = 8.2 Hz, 2H), 7.72 – 7.66 (m, 4H), 7.27 (d, J = 8.1 Hz, 2H), 7.13 (d, J = 5.4 Hz, 1H), 7.02 (d, J = 5.3 Hz, 1H), 5.51 (dd, J = 7.0, 5.1 Hz, 1H), 4.51 (s, 1H), 3.84 (s, 3H), 3.62 (dd, J = 14.8, 8.7 Hz, 1H), 3.39 (dd, J = 14.7, 5.1 Hz, 1H), 3.06 – 2.96 (m, 1H), 2.65 – 2.56 (m, 1H), 2.41 (s, 3H), 2.19 – 2.08 (m, 1H), 1.82 – 1.74 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 152.4, 143.4, 142.6, 137.4, 135.2 (q, J = 33.1 Hz), 130.1, 129.8, 129.1, 128.6, 127.0, 126.2 (q, J = 3.6 Hz), 123.9, 123.2 (d, J = 273.1 Hz), 62.4, 52.3, 40.2, 37.3, 31.8, 21.6.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{24}H_{25}F_3NO_6S_3^+$ 576.0791; found 576.0785.

Methyl 2-(4-((4-methylphenyl)sulfonamido)-1-((2-(trifluoromethyl)phenyl)sulfonyl)butan-2-yl)thiophene-3-carboxylate (4j)



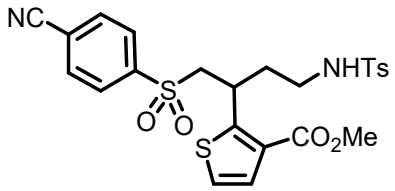
Colorless oil, yield 91% (105.0 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, J = 7.7 Hz, 1H), 7.82 (d, J = 7.6 Hz, 1H), 7.73 – 7.62 (m, 4H), 7.27 (d, J = 8.4 Hz, 2H), 7.18 (d, J = 5.3 Hz, 1H), 7.03 (d, J = 5.3 Hz, 1H), 5.55 (br, 1H), 4.58 (br, 1H), 3.87 (s, 3H), 3.71 (dd, J = 14.5, 8.1 Hz, 1H), 3.43 (dd, J = 14.6, 5.4 Hz, 1H), 3.08 – 2.96 (m, 1H), 2.61 (ddt, J = 14.2, 9.7, 4.7 Hz, 1H), 2.40 (s, 3H), 2.16 – 2.06 (m, 1H), 1.81 – 1.71 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2, 152.6, 143.4, 138.0, 137.4, 133.9, 132.8, 132.7, 130.0, 129.8, 129.0, 128.6 (q, *J* = 33.1 Hz), 128.4 (q, *J* = 6.2 Hz), 127.0, 123.8, 122.68 (q, *J* = 274.0 Hz), 63.1, 52.3, 40.2, 37.3, 31.8, 21.5.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{24}H_{25}F_3NO_6S_3^+$ 576.0791; found 576.0785.

Methyl 2-(1-((4-cyanophenyl)sulfonyl)-4-((4-methylphenyl)sulfonamido)butan-2-yl)thiophene-3-carboxylate (4k)



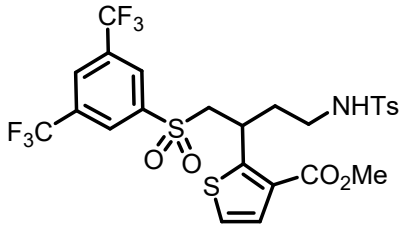
White solid, yield 47% (50.0 mg). M.p. = 166–167 °C.

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.82 (d, *J* = 8.4 Hz, 2H), 7.73 (d, *J* = 8.4 Hz, 2H), 7.69 (d, *J* = 8.2 Hz, 2H), 7.28 (d, *J* = 8.1 Hz, 2H), 7.17 (d, *J* = 5.3 Hz, 1H), 7.05 (d, *J* = 5.3 Hz, 1H), 5.46 (dd, *J* = 6.9, 5.2 Hz, 1H), 4.51 (s, 1H), 3.86 (s, 3H), 3.62 (dd, *J* = 14.6, 8.4 Hz, 1H), 3.42 (dd, *J* = 14.7, 5.3 Hz, 1H), 3.08 – 2.96 (m, 1H), 2.64 – 2.55 (m, 1H), 2.41 (s, 3H), 2.21 – 2.10 (m, 1H), 1.83 – 1.75 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) *δ* 164.1, 152.3, 143.5, 143.2, 137.3, 132.9, 130.1, 129.8, 129.1, 128.7, 127.0, 124.0, 117.3, 117.2, 62.4, 52.4, 40.2, 37.2, 31.8, 21.6.

HRMS(ESI) m/z: $[M+Na]^+$Calcd for $C_{24}H_{24}N_2NaO_6S_3^+$ 555.0689; found 555.0682.

Methyl 2-(1-((3,5-bis(trifluoromethyl)phenyl)sulfonyl)-4-((4-methylphenyl)sulfonamido)butan-2-yl)thiophene-3-carboxylate (4l)



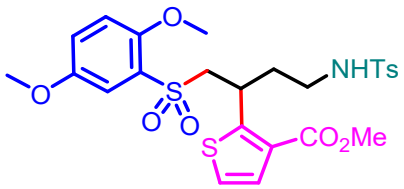
Colorless oil, yield 81% (105.0 mg).

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.08 (s, 2H), 7.98 (s, 1H), 7.70 (d, *J* = 8.1 Hz, 2H), 7.28 (d, *J* = 9.0 Hz, 2H), 7.08 (d, *J* = 5.3 Hz, 1H), 6.96 (d, *J* = 5.3 Hz, 1H), 5.42 (s, 1H), 4.51 (s, 1H), 3.95 – 3.74 (m, 4H), 3.44 (dd, *J* = 15.0, 4.2 Hz, 1H), 3.02 (dd, *J* = 13.2, 7.6 Hz, 1H), 2.68 – 2.55 (m, 1H), 2.42 (s, 3H), 2.13 – 2.04 (m, 1H), 1.88 – 1.76 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0, 151.0, 143.6, 142.1, 137.4, 132.8 (q, J = 34.6 Hz), 130.4, 129.9, 129.4, 128.3 (q, J = 3.1 Hz), 127.2 (q, J = 3.3 Hz), 127.1, 124.0, 122.4 (q, J = 273.4 Hz), 60.9, 52.4, 40.2, 36.6, 32.1, 21.6.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{25}H_{24}F_6NO_6S_3^+$ 644.0664; found 644.0660.

Methyl 2-(1-((2,5-dimethoxyphenyl)sulfonyl)-4-((4-methylphenyl)sulfonamido) butan-2-yl)thiophene-3-carboxylate (4m)



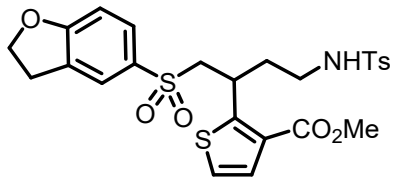
Colorless oil, yield 96% (110.0 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J = 8.1 Hz, 2H), 7.29 – 7.24 (m, 2H), 7.15 (d, J = 3.0 Hz, 1H), 7.06 (d, J = 5.3 Hz, 1H), 7.01 (dd, J = 9.0, 3.0 Hz, 1H), 6.97 (d, J = 5.3 Hz, 1H), 6.80 (d, J = 9.0 Hz, 1H), 5.72 – 5.58 (m, 1H), 4.44 (br, 1H), 3.93 – 3.81 (m, 7H), 3.76 (s, 3H), 3.44 (dd, J = 14.6, 4.0 Hz, 1H), 3.06 – 2.96 (m, 1H), 2.60 – 2.51 (m, 1H), 2.39 (s, 3H), 2.08 – 1.99 (m, 1H), 1.80 – 1.68 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 153.2, 152.8, 151.0, 143.3, 137.5, 130.0, 129.7, 128.6, 126.9, 126.8, 123.5, 122.0, 113.9, 113.7, 61.0, 56.7, 55.9, 52.1, 40.1, 37.8, 31.8, 21.5.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{25}H_{30}NO_8S_3^+$ 568.1128; found 568.1133.

Methyl 2-(1-((2,3-dihydrobenzofuran-5-yl)sulfonyl)-4-((4-methylphenyl)sulfonamido)butan-2-yl)thiophene-3-carboxylate (4n)



Colorless oil, yield 93% (103.0 mg).

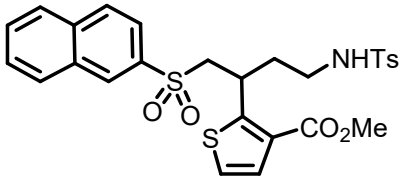
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J = 8.2 Hz, 2H), 7.56 – 7.45 (m, 2H), 7.26 (d, J = 8.1 Hz, 2H), 7.19 (d, J = 5.3 Hz, 1H), 7.06 (d, J = 5.3 Hz, 1H), 6.75 (d, J = 8.3 Hz, 1H), 5.56 (dd, J = 7.7, 4.7 Hz, 1H), 4.66 (t, J = 8.8 Hz, 2H), 4.54 – 4.42 (m, 1H), 3.85 (s, 3H), 3.48 (dd, J = 14.5, 7.9 Hz, 1H), 3.32 (dd, J = 14.5, 5.5 Hz, 1H), 3.22 (t, J = 8.8

Hz, 2H), 3.04 – 2.93 (m, 1H), 2.63 – 2.53 (m, 1H), 2.40 (s, 3H), 2.16 – 2.05 (m, 1H), 1.79 – 1.67 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7, 164.2, 153.5, 143.3, 137.3, 130.4, 129.7, 129.7, 128.8, 128.7, 127.0, 125.4, 123.5, 109.6, 72.6, 63.0, 52.2, 40.2, 37.5, 31.9, 28.9, 21.6.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{25}H_{28}NO_7S_3^+$ 550.1022; found 550.1017.

Methyl 2-(4-((4-methylphenyl)sulfonamido)-1-(naphthalen-2-ylsulfonyl)butan-2-yl)thiophene-3-carboxylate (4o)



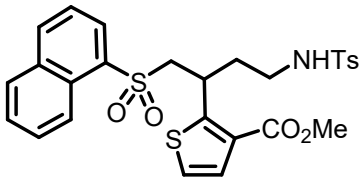
Colorless oil, yield 89% (99.0 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (s, 1H), 7.92 (d, J = 8.0 Hz, 1H), 7.88 (d, J = 8.6 Hz, 2H), 7.70 – 7.58 (m, 5H), 7.24 (d, J = 8.1 Hz, 2H), 7.03 (d, J = 5.3 Hz, 1H), 6.88 (d, J = 5.3 Hz, 1H), 5.52 (dd, J = 7.6, 4.6 Hz, 1H), 4.56 (s, 1H), 3.74 (s, 3H), 3.59 (dd, J = 14.6, 8.2 Hz, 1H), 3.39 (dd, J = 14.6, 5.3 Hz, 1H), 3.08 – 2.97 (m, 1H), 2.64 – 2.54 (m, 1H), 2.39 (s, 3H), 2.18 – 2.07 (m, 1H), 1.80 – 1.74 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 152.8, 143.3, 137.4, 135.9, 135.2, 132.0, 130.0, 129.9, 129.7, 129.5, 129.5, 129.4, 128.9, 127.9, 127.6, 127.0, 123.5, 122.4, 62.6, 52.1, 40.2, 37.4, 31.8, 21.5.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{27}H_{28}NO_6S_3^+$ 558.1073; found 558.1067.

Methyl 2-(4-((4-methylphenyl)sulfonamido)-1-(naphthalen-1-ylsulfonyl)butan- 2-yl)thiophene-3-carboxylate (4p)



Colorless oil, yield 87% (97.0 mg).

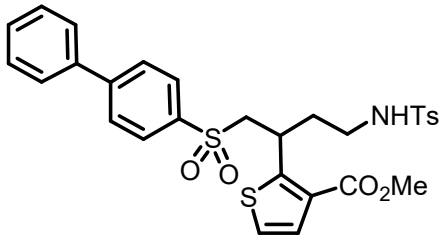
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (d, J = 8.6 Hz, 1H), 8.09 – 7.96 (m, 2H), 7.89 (d, J = 8.1 Hz, 1H), 7.65 (dd, J = 13.2, 4.7 Hz, 3H), 7.58 (t, J = 7.3 Hz, 1H), 7.43 (t, J = 7.8 Hz, 1H), 7.24 (d, J = 8.1 Hz, 2H), 7.01 (d, J = 5.3 Hz, 1H), 6.82 (d, J = 5.3 Hz, 1H),

5.47 (s, 1H), 4.53 (s, 1H), 3.85 – 3.74 (m, 4H), 3.44 (dd, *J* = 14.6, 5.0 Hz, 1H), 3.04 – 2.93 (m, 1H), 2.62 – 2.51 (m, 1H), 2.39 (s, 3H), 2.09 – 1.99 (m, 1H), 1.76 – 1.67 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0, 152.3, 143.3, 137.4, 135.2, 134.0, 130.6, 129.7, 129.7, 129.3, 128.8, 128.5, 127.0, 124.5, 123.9, 123.3, 62.0, 52.1, 40.2, 37.2, 32.0, 21.6.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{27}H_{28}NO_6S_3^+$ 558.1073; found 558.1071.

Methyl 2-(1-([1,1'-biphenyl]-4-ylsulfonyl)-4-((4-methylphenyl)sulfonamido)butan-2-yl)thiophene-3-carboxylate (4q)



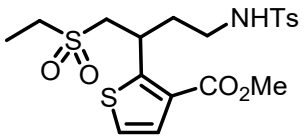
Colorless oil, yield 84% (98.0 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.4 Hz, 2H), 7.69 (d, *J* = 8.2 Hz, 2H), 7.62 (d, *J* = 8.4 Hz, 2H), 7.57 (d, *J* = 7.2 Hz, 2H), 7.48 (t, *J* = 7.3 Hz, 2H), 7.43 (t, *J* = 7.2 Hz, 1H), 7.26 (d, *J* = 8.0 Hz, 2H), 7.16 (d, *J* = 5.3 Hz, 1H), 7.02 (d, *J* = 5.3 Hz, 1H), 5.52 (s, 1H), 4.61 – 4.49 (m, 1H), 3.84 (s, 3H), 3.57 (dd, *J* = 14.5, 8.1 Hz, 1H), 3.36 (dd, *J* = 14.6, 5.3 Hz, 1H), 3.09 – 2.97 (m, 1H), 2.65 – 2.57 (m, 1H), 2.40 (s, 3H), 2.18 – 2.07 (m, 1H), 1.76 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2, 153.1, 146.6, 143.3, 139.3, 137.6, 137.5, 130.0, 129.8, 129.2, 129.0, 128.8, 128.5, 127.9, 127.5, 127.0, 123.7, 62.9, 52.3, 40.2, 37.5, 31.8, 21.6.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{29}H_{30}NO_6S_3^+$ 584.1230; found 584.1226.

Methyl 2-(1-(ethylsulfonyl)-4-((4-methylphenyl)sulfonamido)butan-2-yl)thiophene-3-carboxylate (4r)



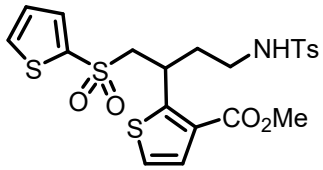
Colorless oil, yield 50% (46.0 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, J = 8.2 Hz, 2H), 7.34 (d, J = 5.4 Hz, 1H), 7.27 (d, J = 8.0 Hz, 2H), 7.19 (d, J = 5.3 Hz, 1H), 5.39 (dd, J = 7.0, 5.7 Hz, 1H), 4.68 – 4.57 (m, 1H), 3.89 (s, 3H), 3.36 (dd, J = 14.5, 7.2 Hz, 1H), 3.15 (dd, J = 14.5, 6.2 Hz, 1H), 3.09 – 2.99 (m, 1H), 2.82 (q, J = 7.5 Hz, 2H), 2.77 – 2.68 (m, 1H), 2.41 (s, 3H), 2.28 – 2.18 (m, 1H), 1.92 – 1.82 (m, 1H), 1.30 (t, J = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2, 153.3, 143.4, 137.3, 129.9, 129.8, 129.3, 127.1, 123.7, 58.5, 52.3, 47.9, 40.5, 36.9, 31.4, 21.6, 6.5.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{19}H_{26}NO_6S_3^+$ 460.0917; found 460.0910.

Methyl 2-(4-((4-methylphenyl)sulfonamido)-1-(thiophen-2-ylsulfonyl)butan-2-yl)thiophene-3-carboxylate (4s)



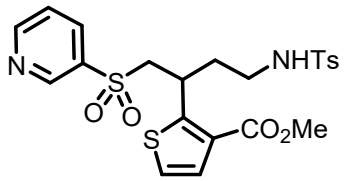
Colorless oil, yield 95% (98.0 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 – 7.65 (m, 3H), 7.50 (d, J = 3.6 Hz, 1H), 7.26 (d, J = 8.2 Hz, 2H), 7.22 (d, J = 5.3 Hz, 1H), 7.09 (d, J = 5.3 Hz, 1H), 7.05 (t, J = 4.4 Hz, 1H), 5.57 (dd, J = 7.4, 4.8 Hz, 1H), 4.62 – 4.52 (m, 1H), 3.87 (s, 3H), 3.62 (dd, J = 14.6, 7.9 Hz, 1H), 3.43 (dd, J = 14.6, 5.4 Hz, 1H), 3.06 – 2.97 (m, 1H), 2.66 – 2.56 (m, 1H), 2.40 (s, 3H), 2.15 – 2.06 (m, 1H), 1.83 – 1.72 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 152.9, 143.3, 140.1, 137.4, 134.5, 134.4, 129.9, 129.7, 129.0, 128.0, 127.0, 123.8, 64.1, 52.3, 40.2, 37.3, 31.9, 21.6.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{21}H_{24}NO_6S_4^+$ 514.0481; found 514.0485.

Methyl 2-(4-((4-methylphenyl)sulfonamido)-1-(pyridin-3-ylsulfonyl)butan-2-yl)thiophene-3-carboxylate (4t)



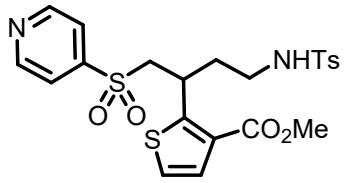
Colorless oil, yield 83% (85.0 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.87 (d, J = 2.1 Hz, 1H), 8.77 (d, J = 3.8 Hz, 1H), 7.98 (d, J = 8.0 Hz, 1H), 7.68 (d, J = 8.2 Hz, 2H), 7.39 (dd, J = 8.0, 4.9 Hz, 1H), 7.27 (d, J = 8.1 Hz, 2H), 7.17 (d, J = 5.3 Hz, 1H), 7.04 (d, J = 5.3 Hz, 1H), 5.64 (dd, J = 7.2, 5.2 Hz, 1H), 4.53 (s, 1H), 3.86 (s, 3H), 3.65 (dd, J = 14.5, 8.5 Hz, 1H), 3.42 (dd, J = 14.7, 5.1 Hz, 1H), 3.08 – 2.96 (m, 1H), 2.68 – 2.57 (m, 1H), 2.41 (s, 3H), 2.15 – 2.10 (m, 1H), 1.88 – 1.71 (m, 1H).

^{13}C NMR (10 MHz, $CDCl_3$) δ 164.1, 154.0, 152.1, 148.9, 143.4, 137.3, 135.8, 135.7, 130.1, 129.8, 129.1, 1270, 123.9, 123.7, 62.7, 52.3, 40.2, 37.1, 31.8, 21.6.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{22}H_{25}N_2O_6S_3^+$ 509.0869; found 509.0868.

Methyl 2-(4-((4-methylphenyl)sulfonamido)-1-(pyridin-4-ylsulfonyl)butan-2-yl) thiophene-3-carboxylate (4u)



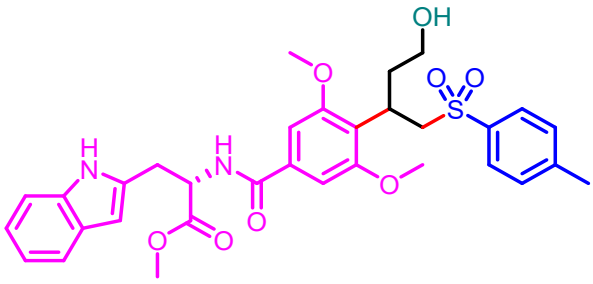
Colorless oil, yield 59% (60.0 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, J = 5.5 Hz, 2H), 7.69 (d, J = 8.1 Hz, 2H), 7.53 (d, J = 5.5 Hz, 2H), 7.27 (d, J = 8.3 Hz, 2H), 7.17 (d, J = 5.3 Hz, 1H), 7.04 (d, J = 5.3 Hz, 1H), 5.63 (dd, J = 6.6, 5.5 Hz, 1H), 4.52 (s, 1H), 3.86 (s, 3H), 3.64 (dd, J = 14.7, 8.8 Hz, 1H), 3.40 (dd, J = 14.8, 5.2 Hz, 1H), 3.06 – 2.98 (m, 1H), 2.69 – 2.58 (m, 1H), 2.41 (s, 3H), 2.18 – 2.11 (m, 1H), 1.85 – 1.75 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 164.07, 151.91, 151.04, 147.23, 143.41, 137.33, 130.22, 129.78, 129.11, 126.98, 124.03, 120.94, 62.01, 52.36, 40.17, 37.02, 31.73, 21.57.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{22}H_{25}N_2O_6S_3^+$ 509.0869; found 509.0868.

Methyl (4-(4-hydroxy-1-tosylbutan-2-yl)-3,5-dimethoxybenzoyl)-L-tryptophanate (5, dr = 1:1**)**



5 was obtained as a 1:1 mixture of inseparable diastereomers as a colorless oil (yield 89%, 108.0 mg) by column chromatography on silica gel (petroleum ether : ethyl acetate = 2:1).

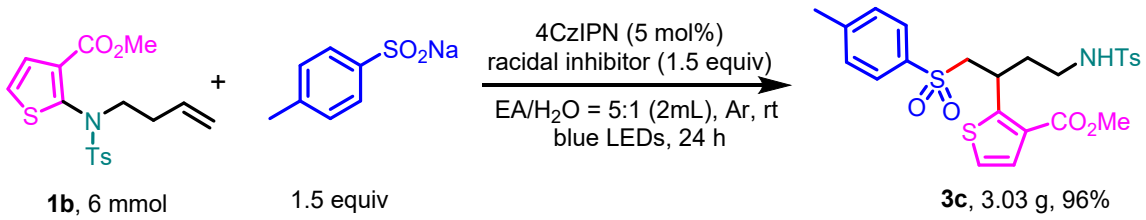
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (s, 0.5H), 8.87 (s, 0.5H), 7.55 (dd, J = 7.8, 3.1 Hz, 1H), 7.45 (d, J = 8.1 Hz, 2H), 7.33 (d, J = 8.1 Hz, 1H), 7.14 (t, J = 7.5 Hz, 1H), 7.07 – 7.00 (m, 3H), 6.98 (t, J = 2.3 Hz, 1H), 6.65 – 6.55 (m, 2H), 6.50 (s, 0.5H), 6.45 (s, 0.5H), 5.09 – 5.02 (m, 1H), 4.02 – 3.88 (m, 2H), 3.74 (s, 1.5H), 3.74 (s, 1.5H), 3.60 – 3.47 (m, 6H), 3.44 – 3.33 (m, 4H), 3.24 – 3.15 (m, 1H), 2.23 (s, 1.5H), 2.22 (s, 1.5H), 2.20 (brs, 1H), 1.92 – 1.83 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 166.84/166.78, 158.4/157.6, 144.38/144.36, 136.28/136.26, 136.14, 134.17/134.06, 129.24, 127.80/127.78, 127.71, 123.26/123.23, 122.14, 119.82/119.81, 119.73, 118.24/118.20, 111.75, 109.48/109.46, 103.2/103.1, 102.9/102.7, 60.39/60.37, 59.1, 56.3, 55.3, 53.88/53.87, 52.5, 36.0, 27.18/27.17, 26.8, 21.38/21.36.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{32}H_{37}N_2O_8S^+$ 609.2265; found 609.2266.

4. Synthetic applications

4.1 Procedure for synthesis of 3c at 6 mmol scale

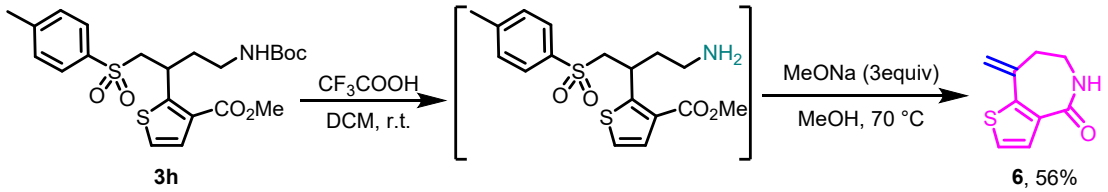


1b, 6 mmol　　1.5 equiv　　**3c**, 3.03 g, 96%

To an oven-dried 100 mL Schlenk Tube with a stirring bar was added **1b** (6 mmol), sodium 4-methylbenzenesulfinate (9 mmol, 1.5 equiv), and 4CzIPN (5 mol%). Then,

air was withdrawn and backfilled with Ar (three times). 5:1 (v/v) EA/H_2O (60 mL) was added and the mixture was irradiated under 30 W× 2 blue LED at room temperature for 24 h. When the reaction is completed, extracted with ethyl acetate, washed with brine, dried over anhydrous sodium sulfate, concentrated in vacuo, and purified by column chromatography (hexane/ethyl acetate = 5:1~4:1, v/v) to afford the corresponding target compounds **3c** (3.03g, 96%). Meanwhile, we recovered to the photocatalyst 4CzIPN (0.18g, 76%).

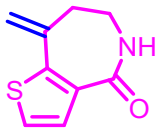
4.2 Further transformations of representative products



3h **6**, 56%

To an 4 mL glass vial equipped with a magnetic stir bar was added **3h** (94.0 mg, 0.2 mmol) and Trifluoroacetic acid (TFA, 0.15 mL, 2 mmol) in DCM (2mL), it was stirred for 6 h at RT. The reaction mixture was added to sat. $NaHCO_3$/EtOAc and extracted with EtOAc (3x), dried over Na_2SO_4 and concentrated in vacuo. The residue was redissolved in 2.0 mL of MeOH, 49.1 mg (0.6 mmol) of NaOMe were added and it was heated to 70 °C for 24 h. The reaction mixture was poured into water, extracted with EtOAc (3x), dried over Na_2SO_4 and concentrated in vacuo and purified by column chromatography (hexane/ethyl acetate) to afford the corresponding target compound **6**.

4-methylene-4,5,6,7-tetrahydro-8H-thieno[2,3-*c*]azepin-8-one (6)



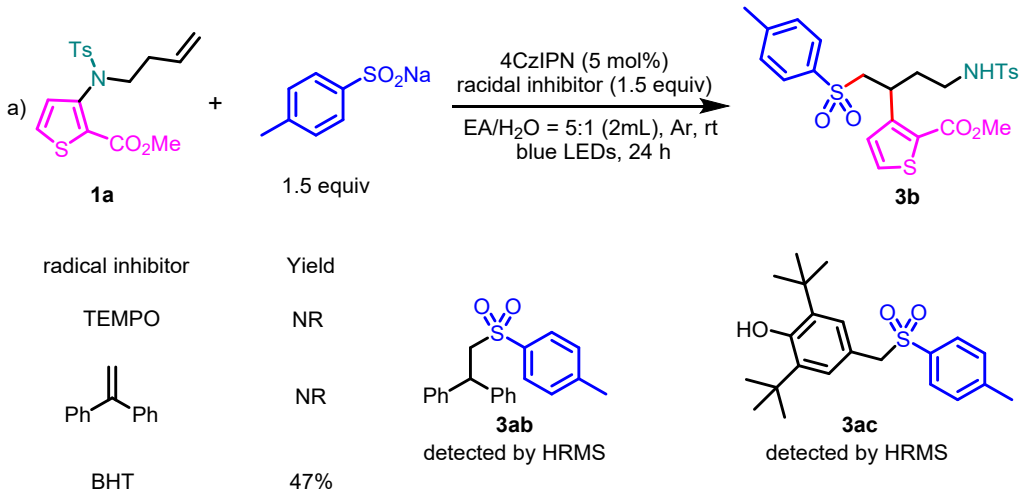
White solid, yield 56% (20.0 mg). M.p. = 92–93 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, J = 5.4 Hz, 1H), 7.10 (d, J = 5.4 Hz, 1H), 7.02 (s, 1H), 5.52 (s, 1H), 5.04 (s, 1H), 3.42 – 3.37 (m, 2H), 2.91 – 2.85 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 145.5, 140.0, 132.2, 131.7, 123.3, 115.4, 40.4, 38.0.

HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_9H_{10}OS^+$ 180.0478; found 180.0476.

5. Investigation of the mechanism



To a 4 mL glass vial equipped with a magnetic stir bar was added **1a** (0.2 mmol), sodium 4-methylbenzenesulfinate (0.3 mmol, 1.5 equiv), 4CzIPN (5 mol%) in 5:1 (v/v) ethyl acetate (EA)/H_2O (2 mL) and additive (TEMPO (48 mg, 0.3 mmol) or 1,1-diphenylethylene (53 μL, 0.3 mmol). The reaction mixture was degassed by bubbling with argon for 10 s with an outlet needle and the vial was sealed with PTFE cap. The mixture was then stirred rapidly and irradiated with a 30 W Blue LED at room temperature for 24 h.

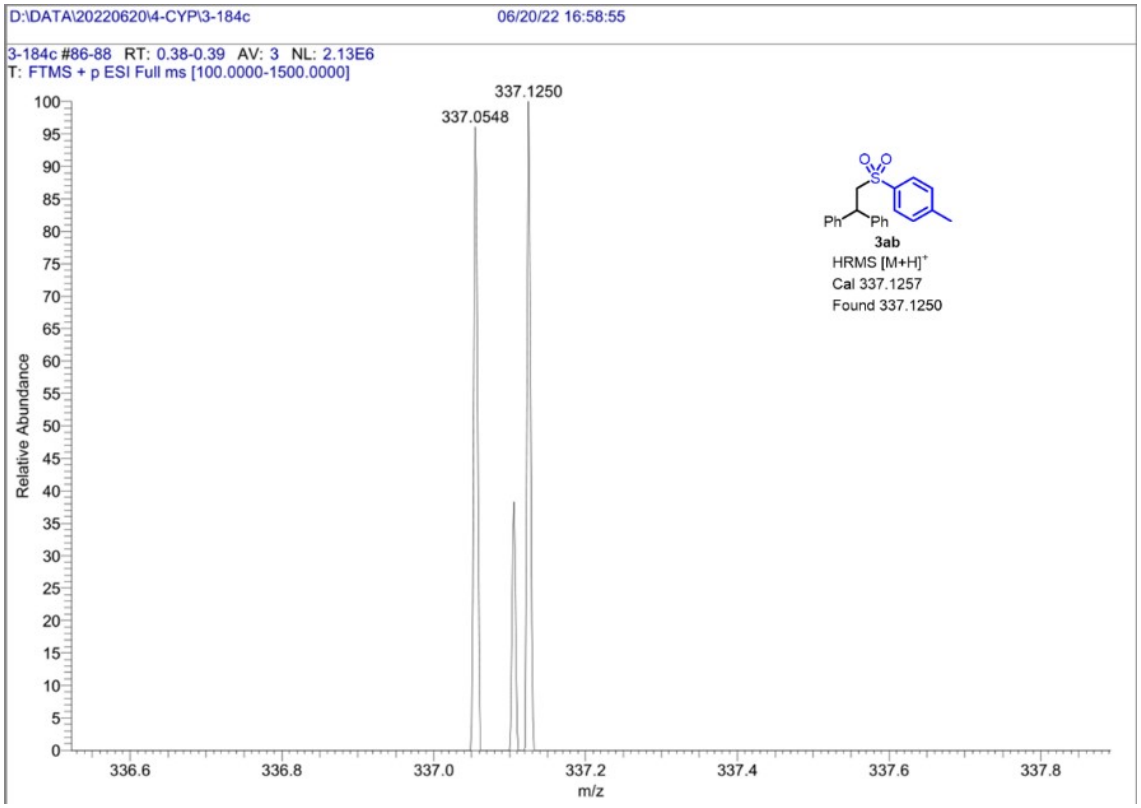


Figure S1 High resolution mass spectrum of 1,1-diphenylethylene capture product.

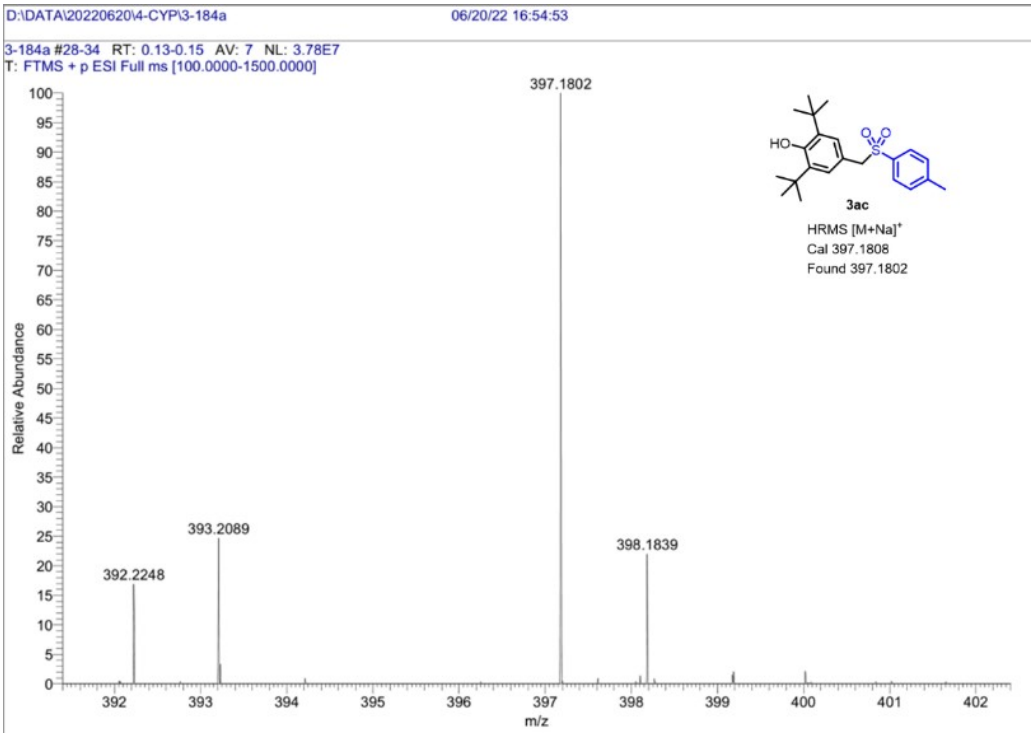


Figure S2 High resolution mass spectrum of BHT capture product.

6. Reference

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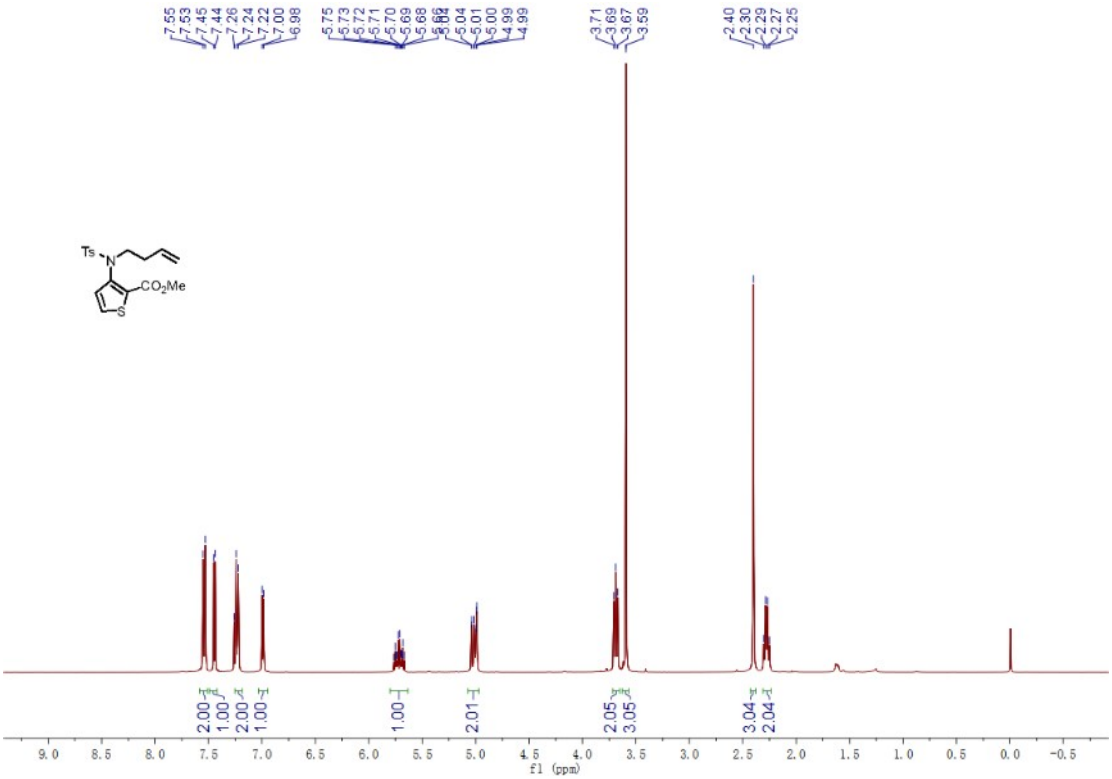
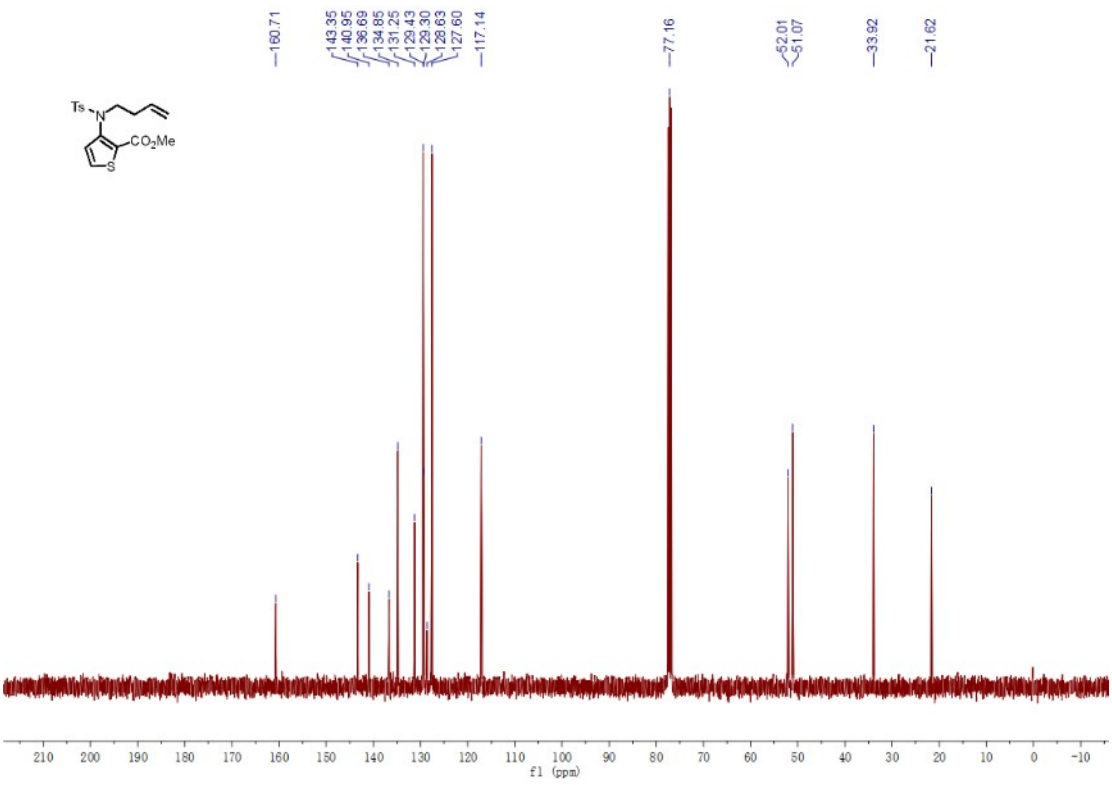
7. NMR spectrum

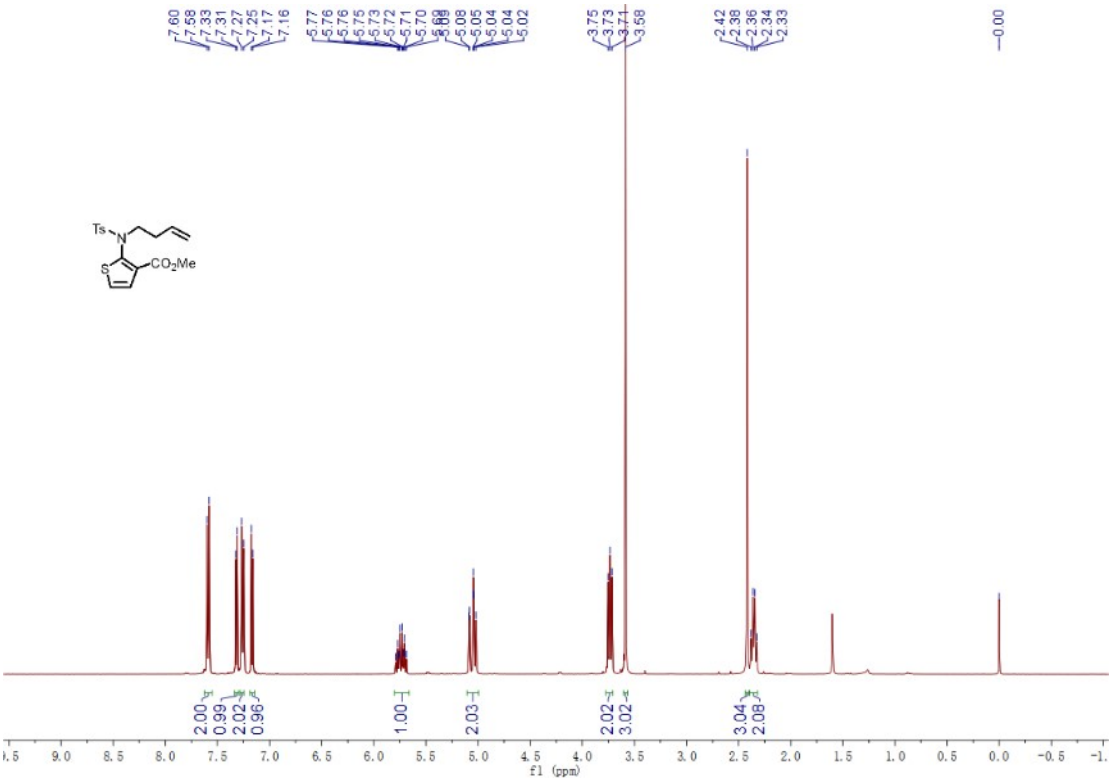
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 1a



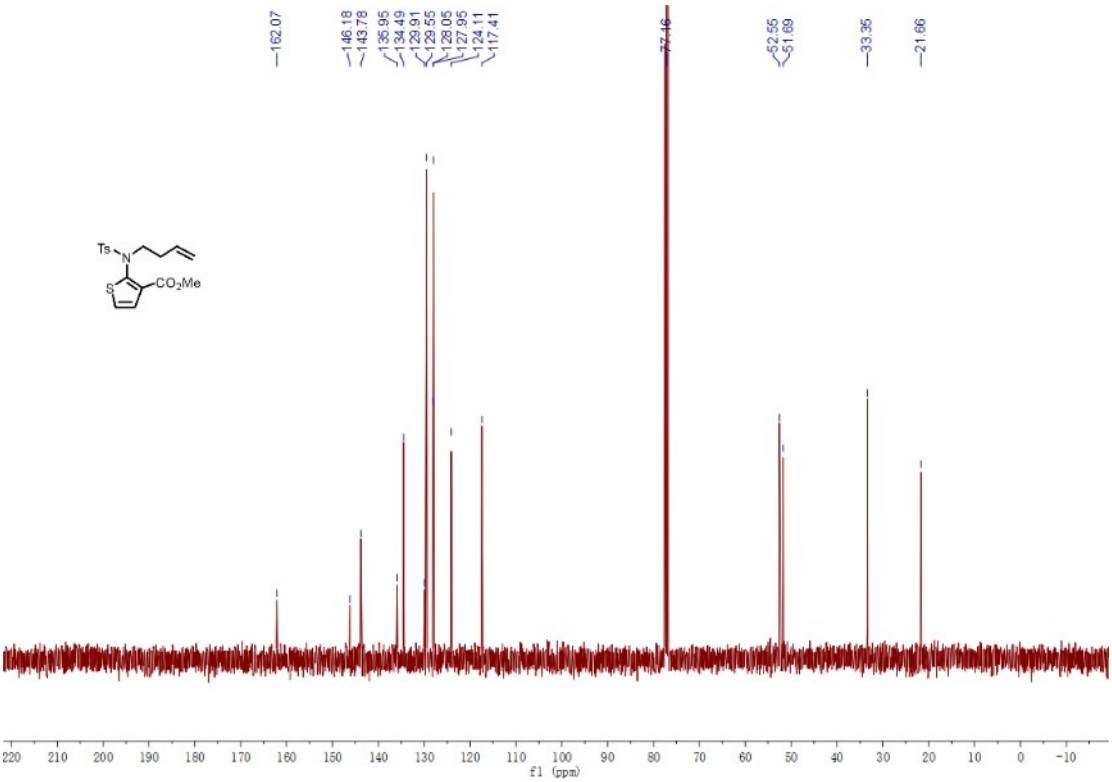
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 1a



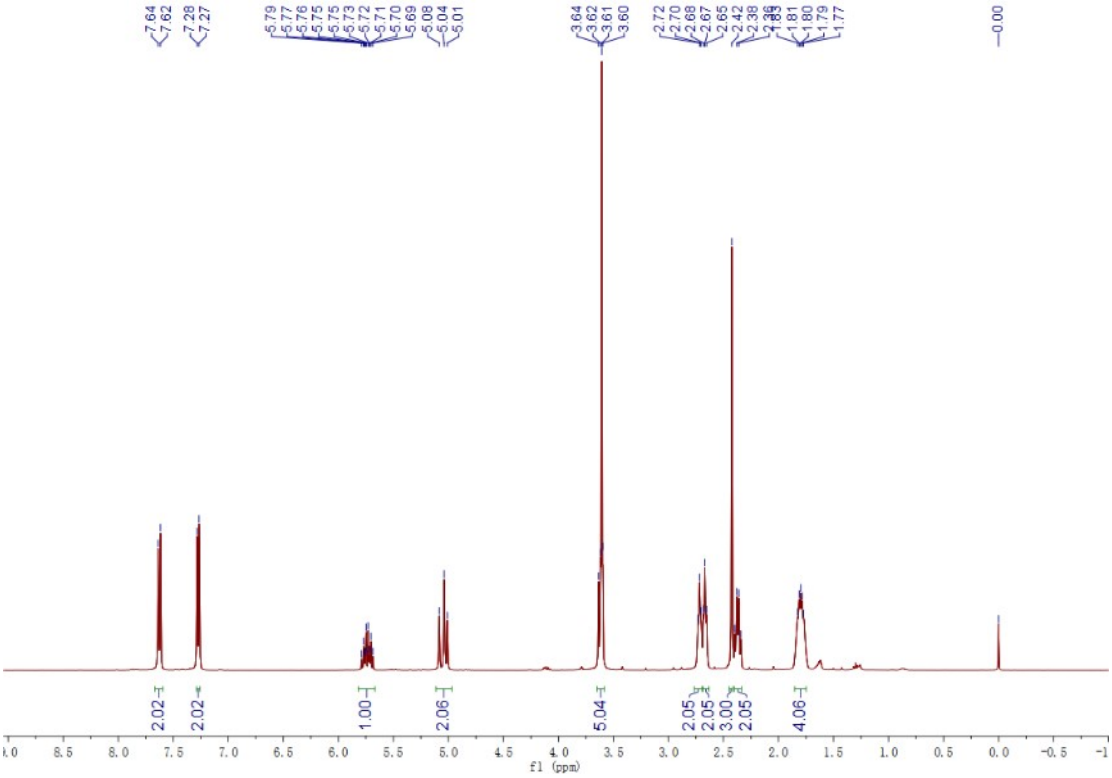
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 1b



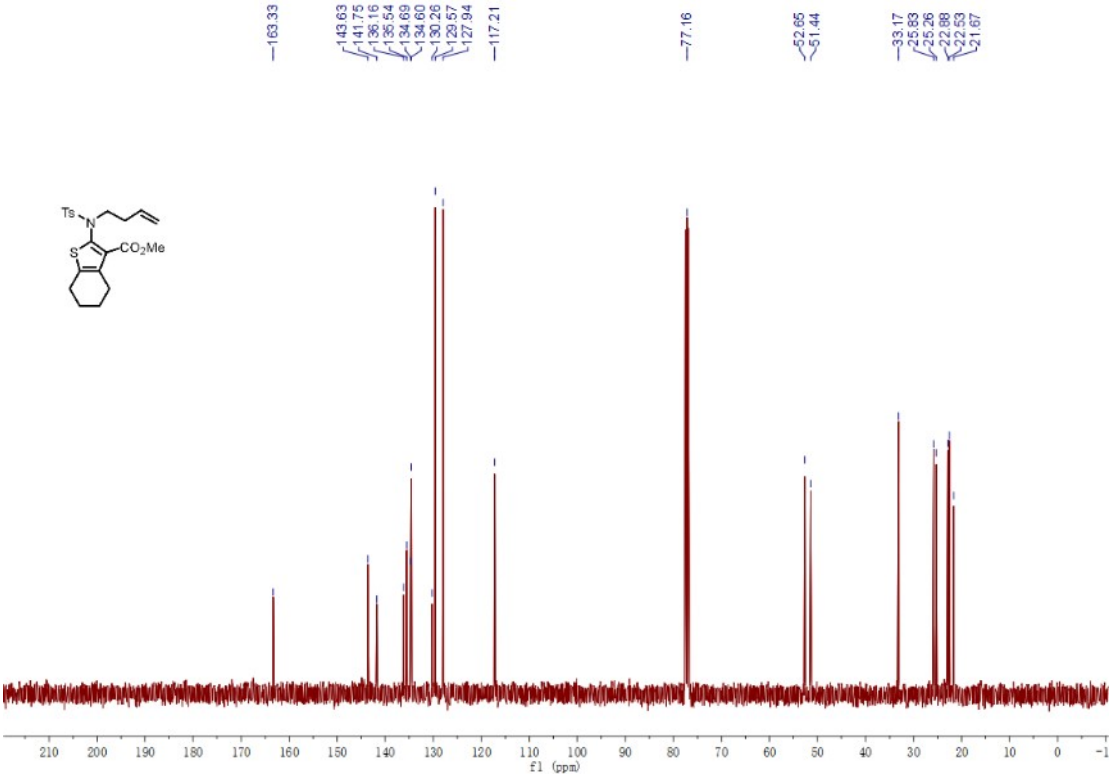
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 1b



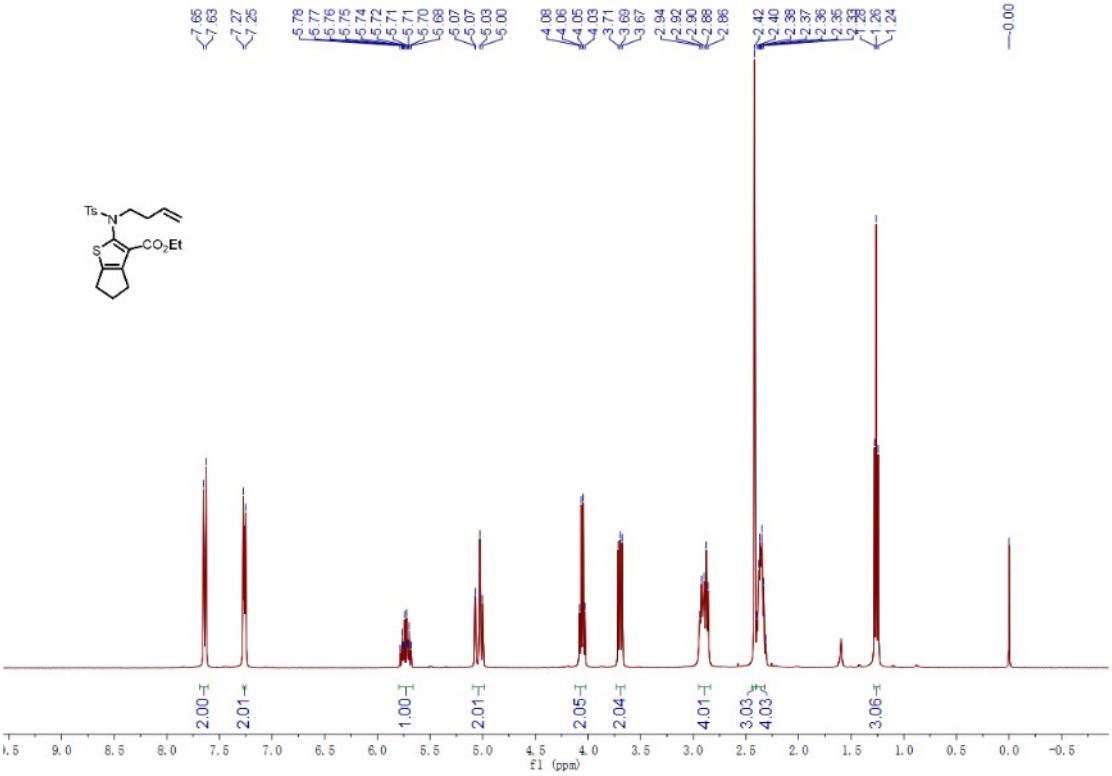
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 1c



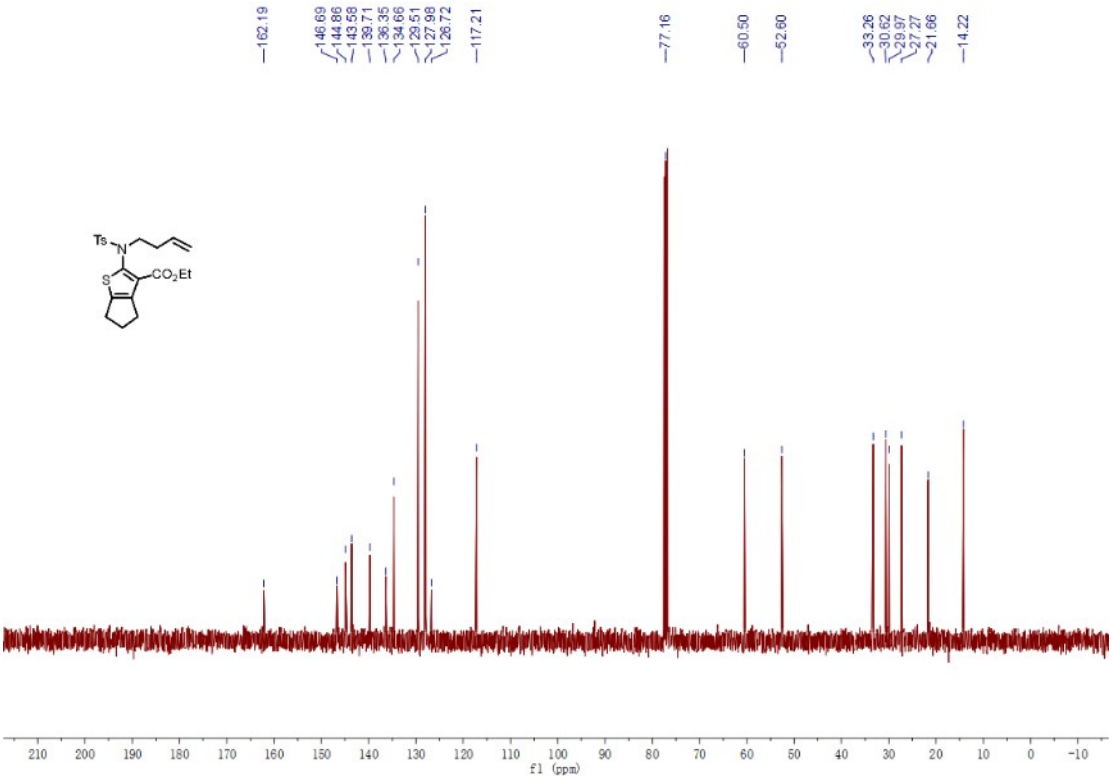
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 1c



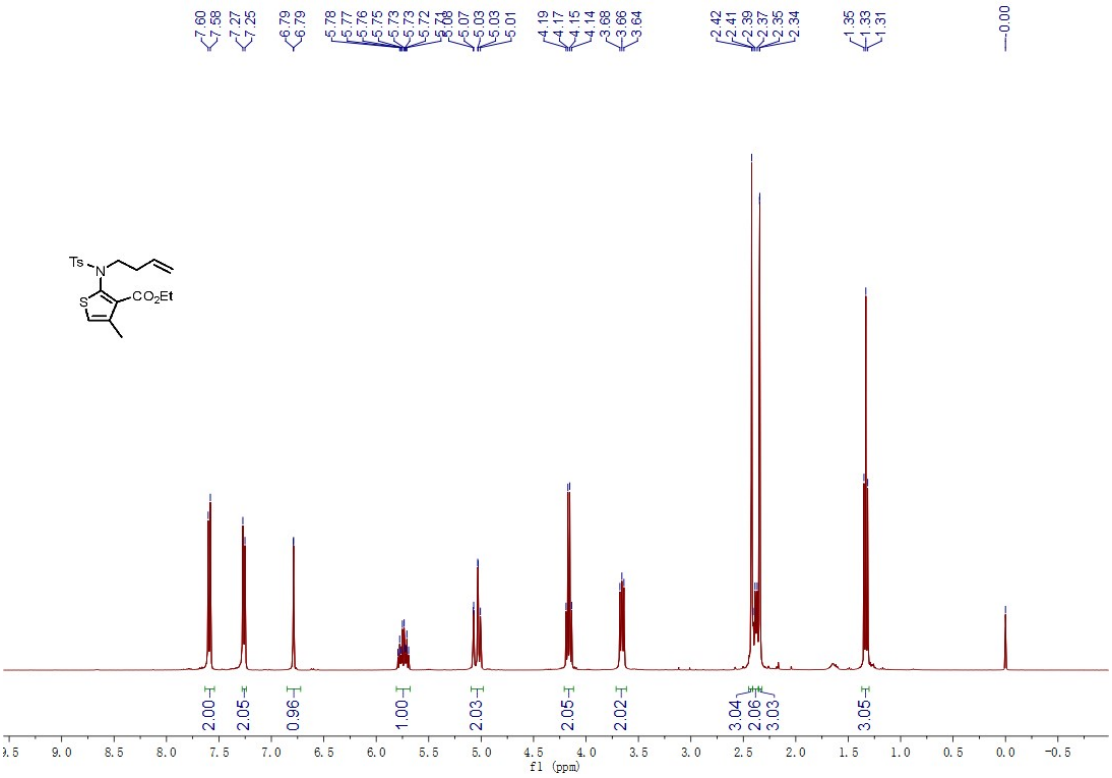
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 1d



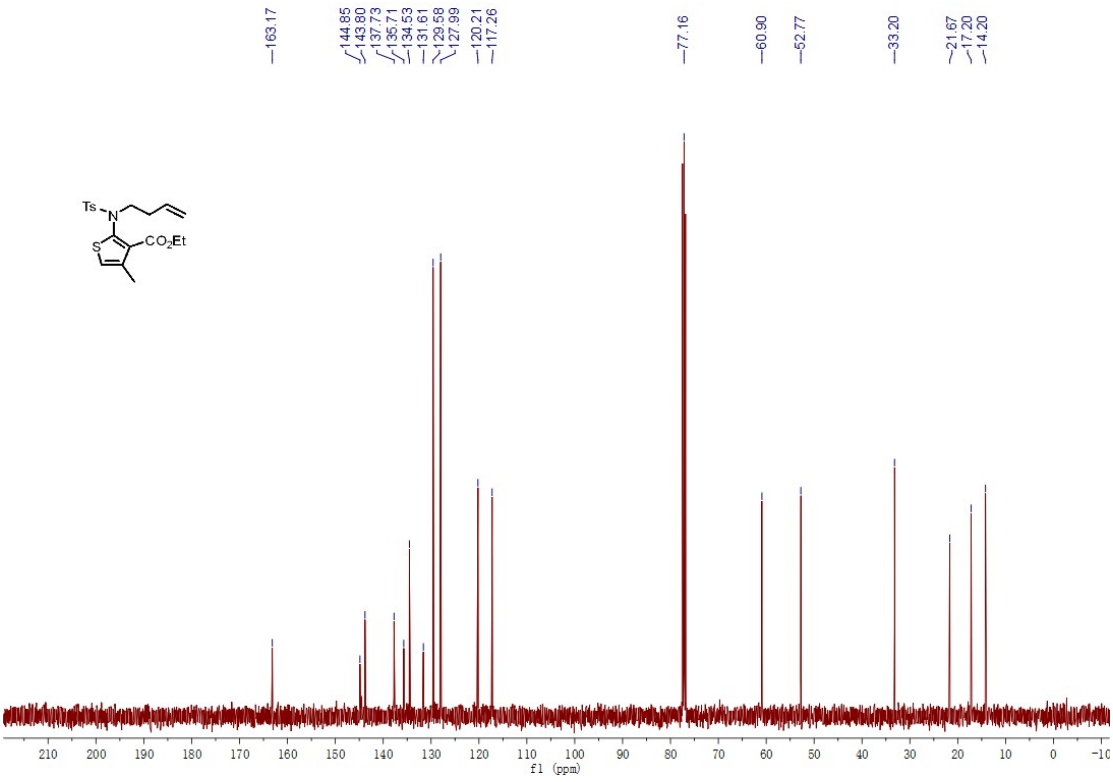
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 1d



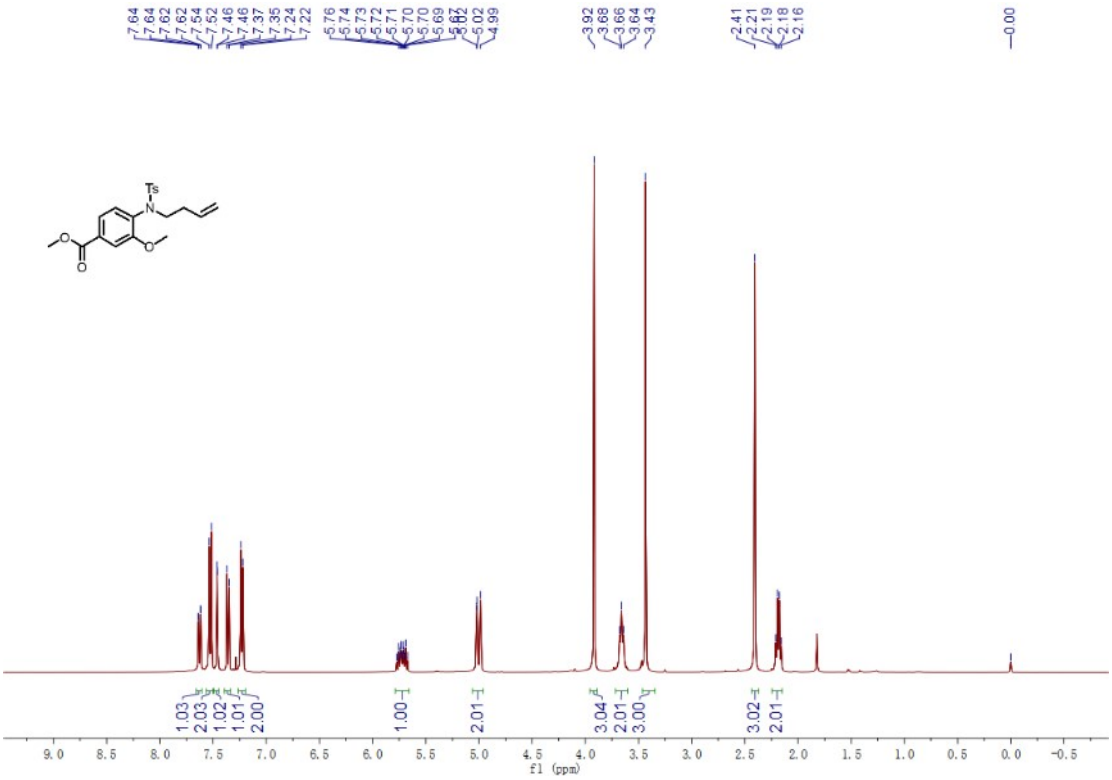
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 1e



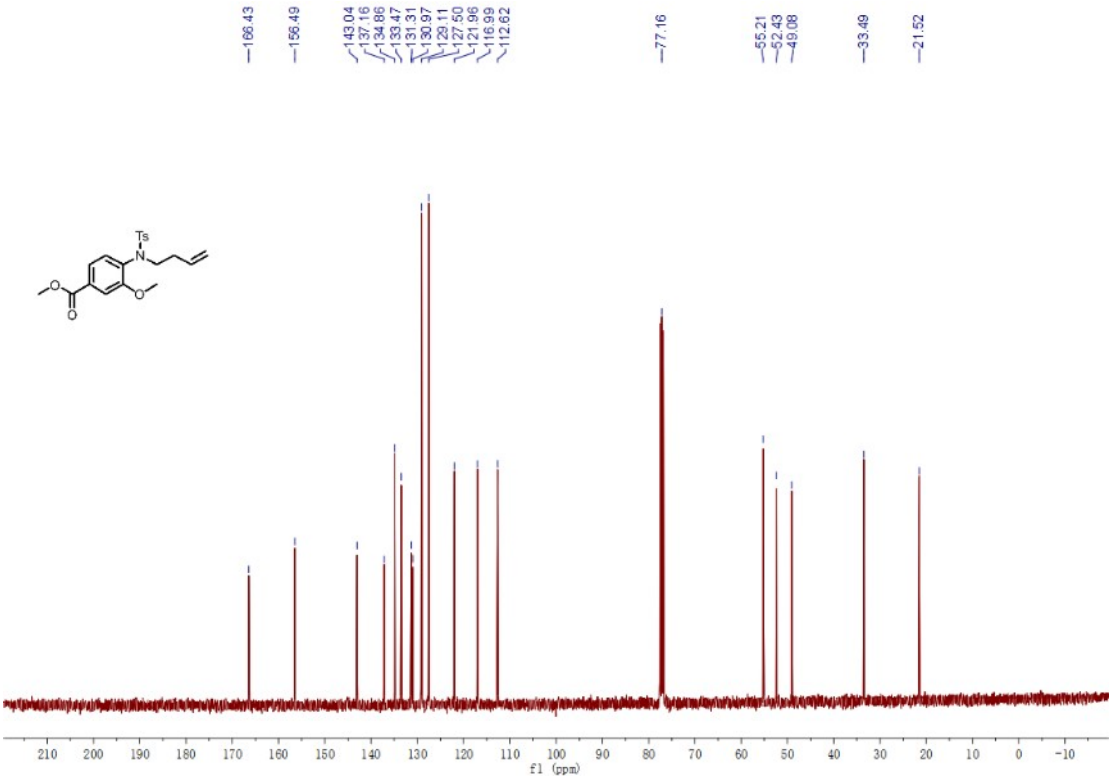
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 1e



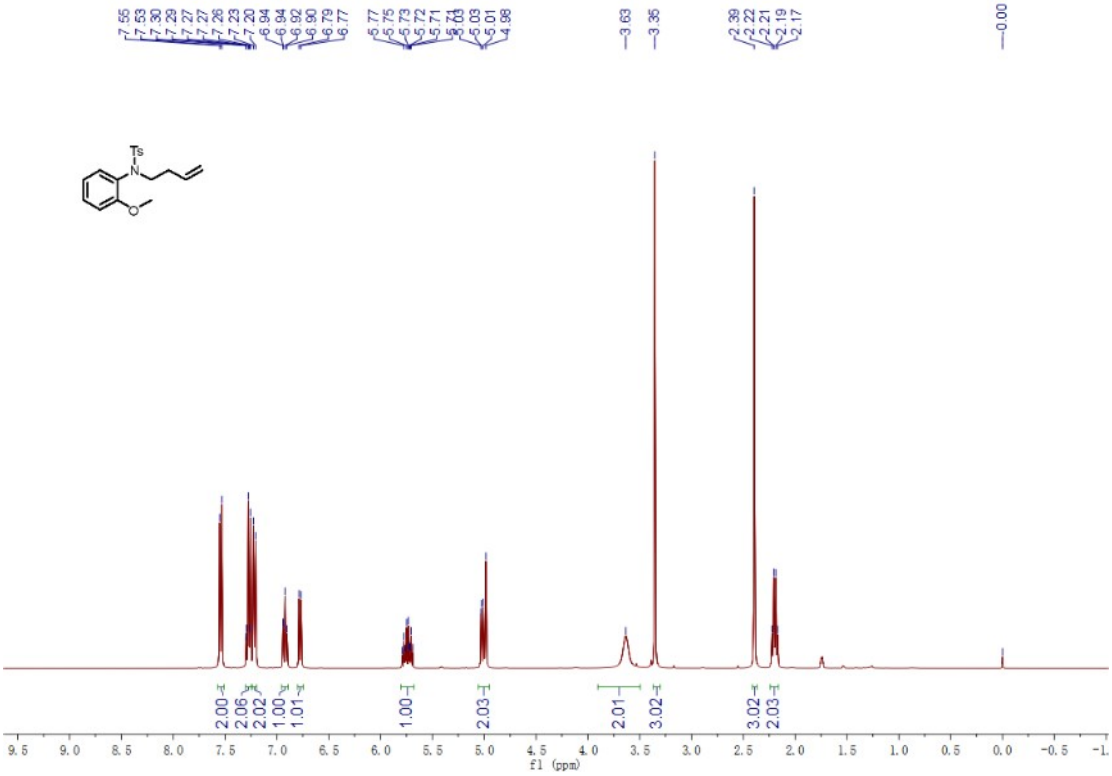
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 1f



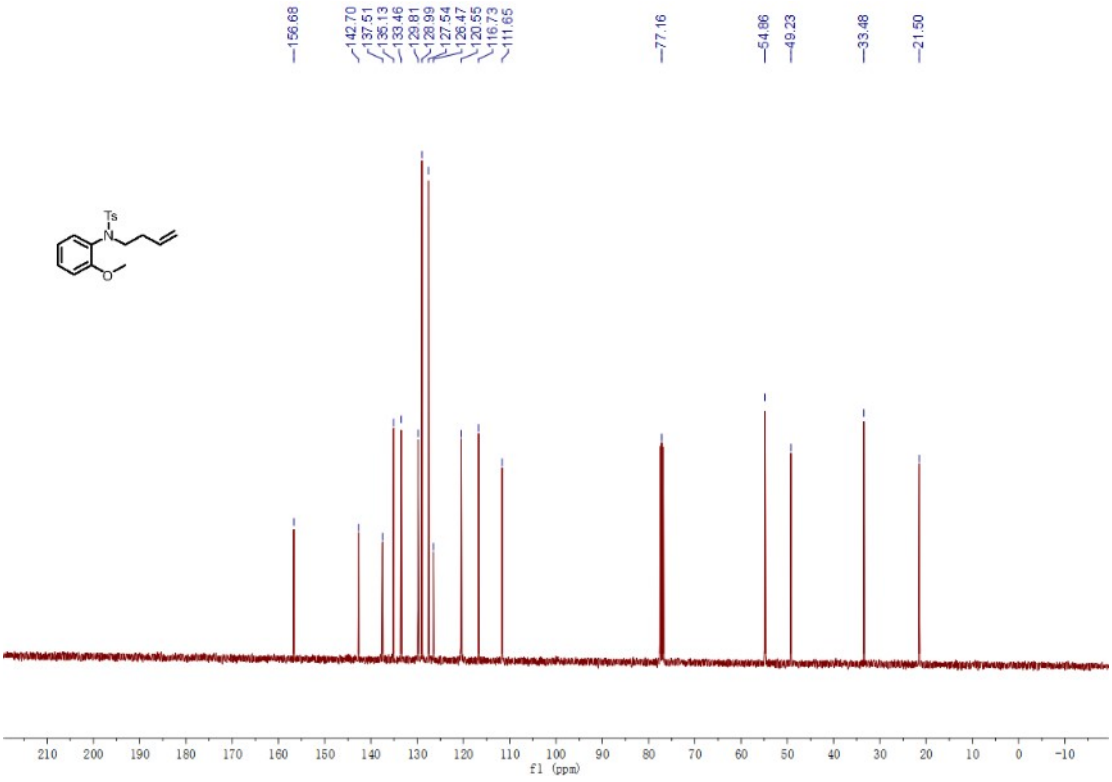
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 1f



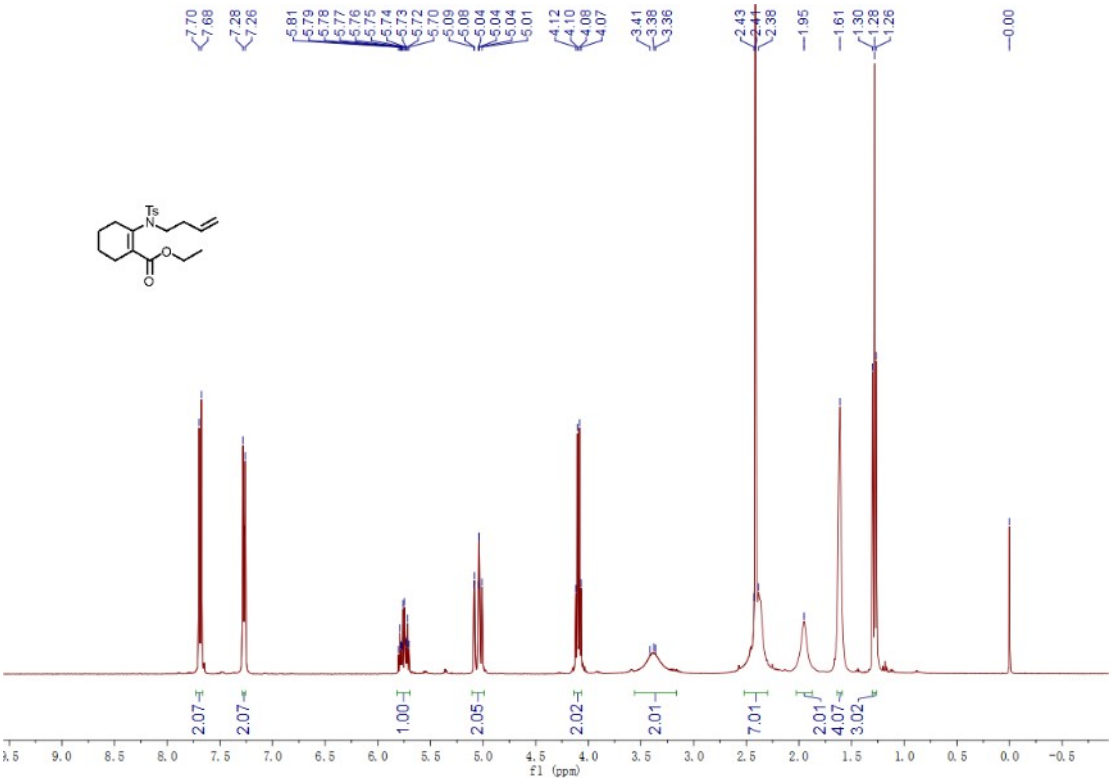
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 1g



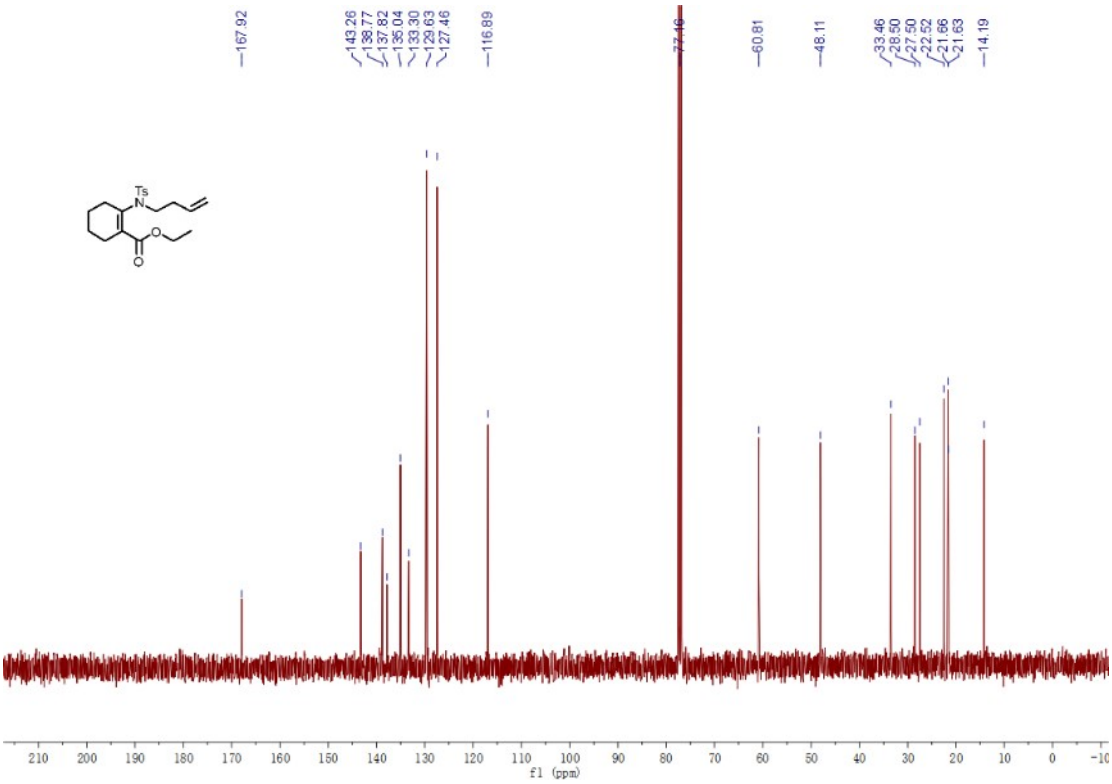
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 1g



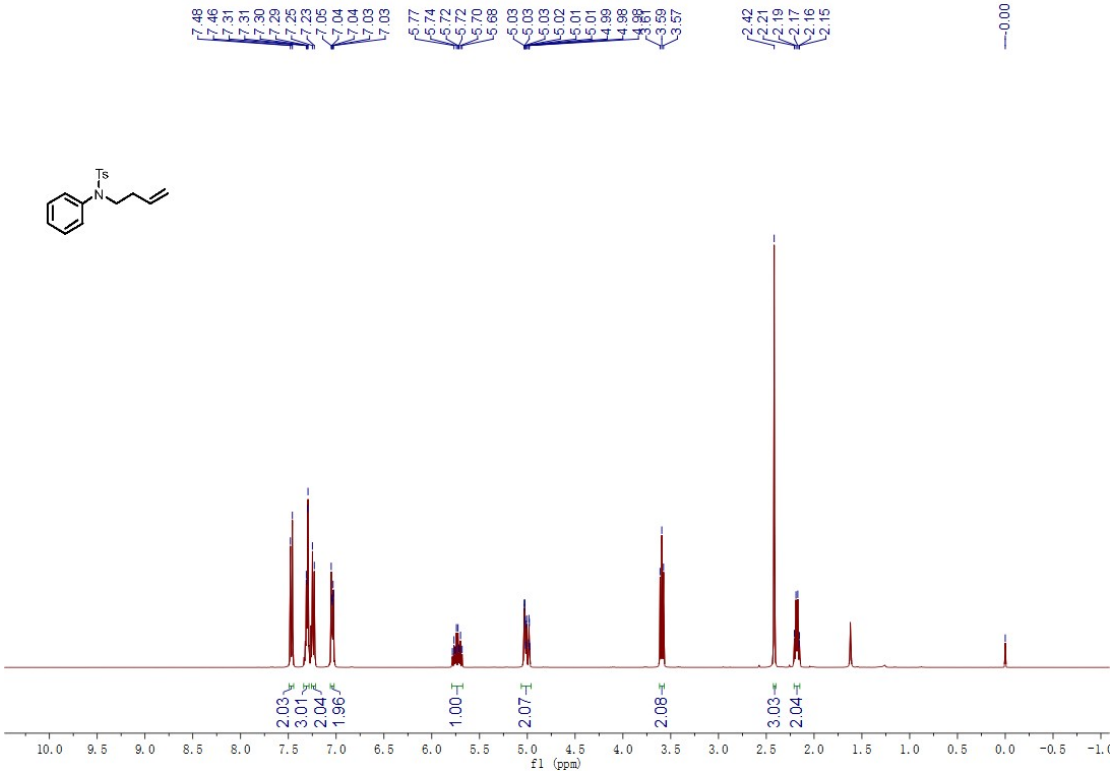
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 1h



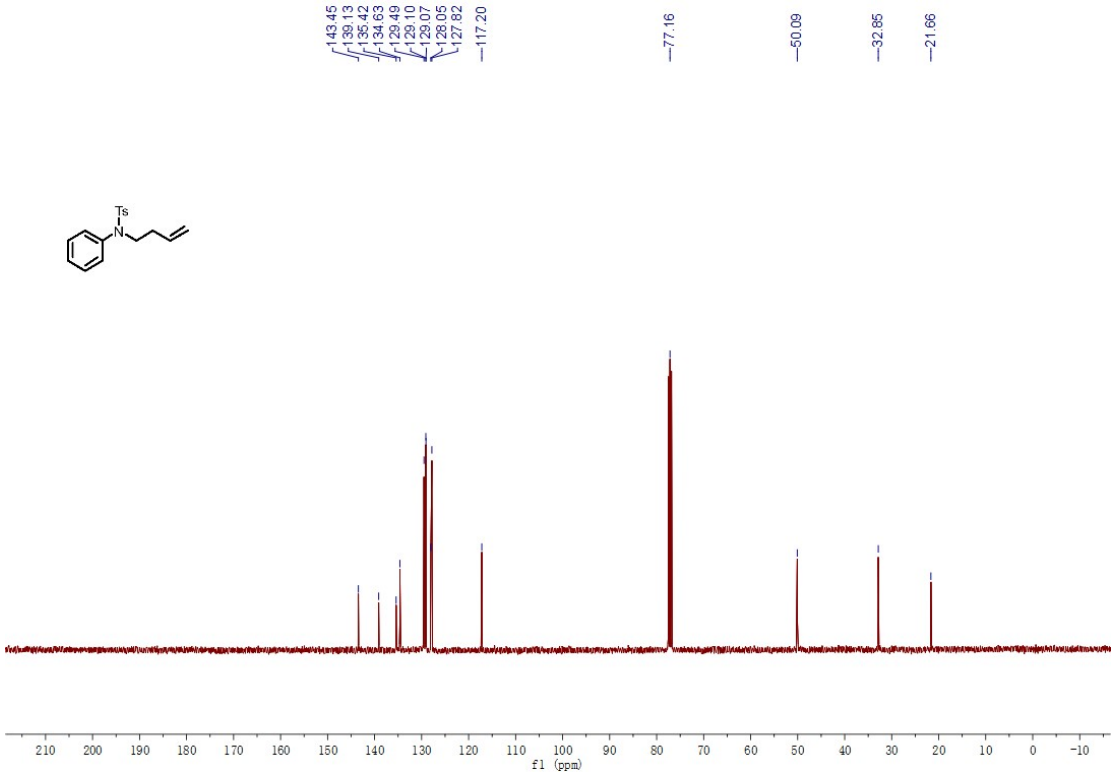
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 1h



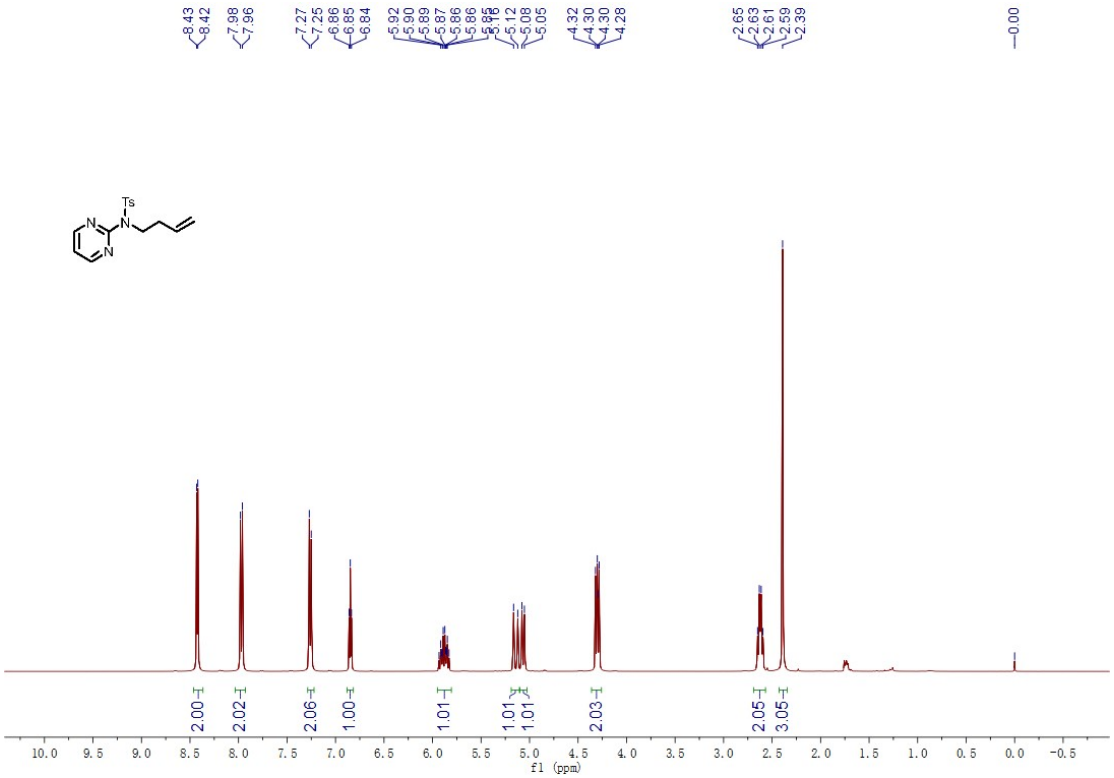
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 1i



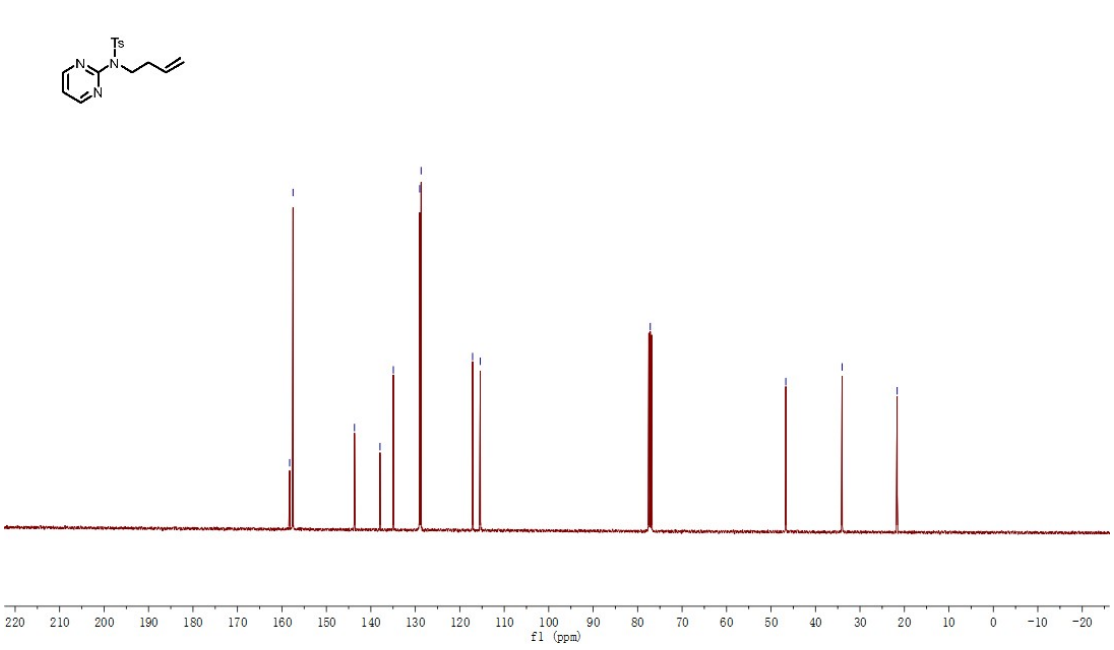
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 1i



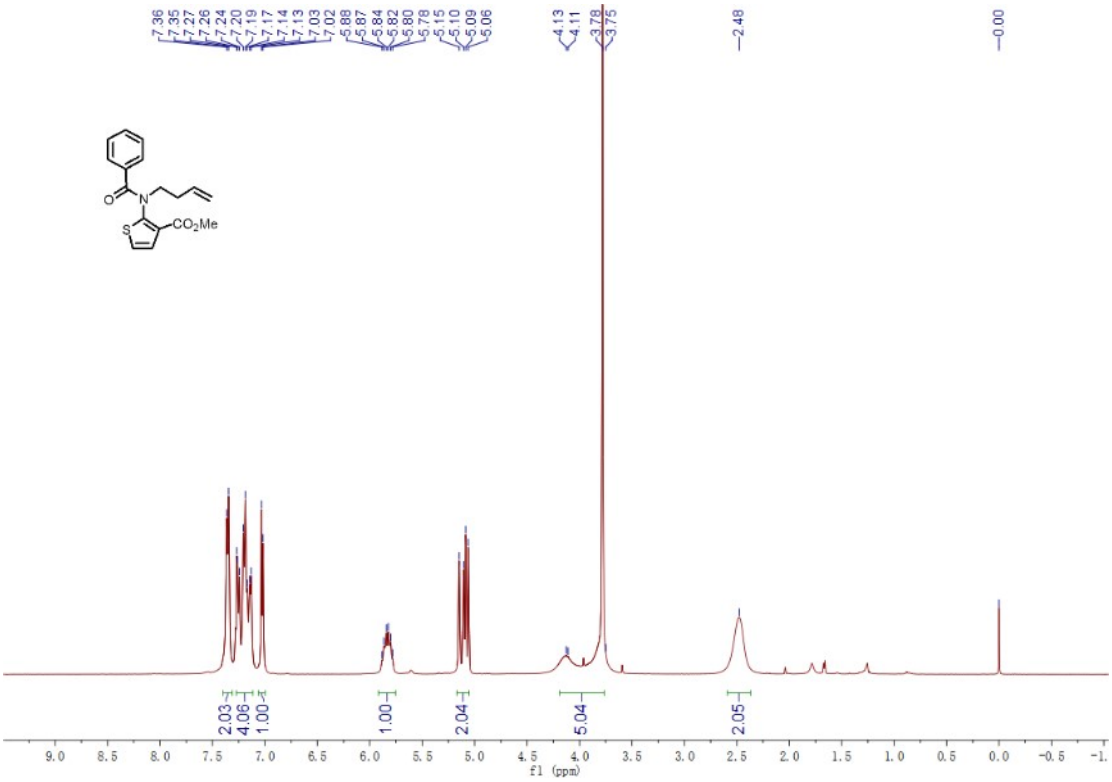
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 1j



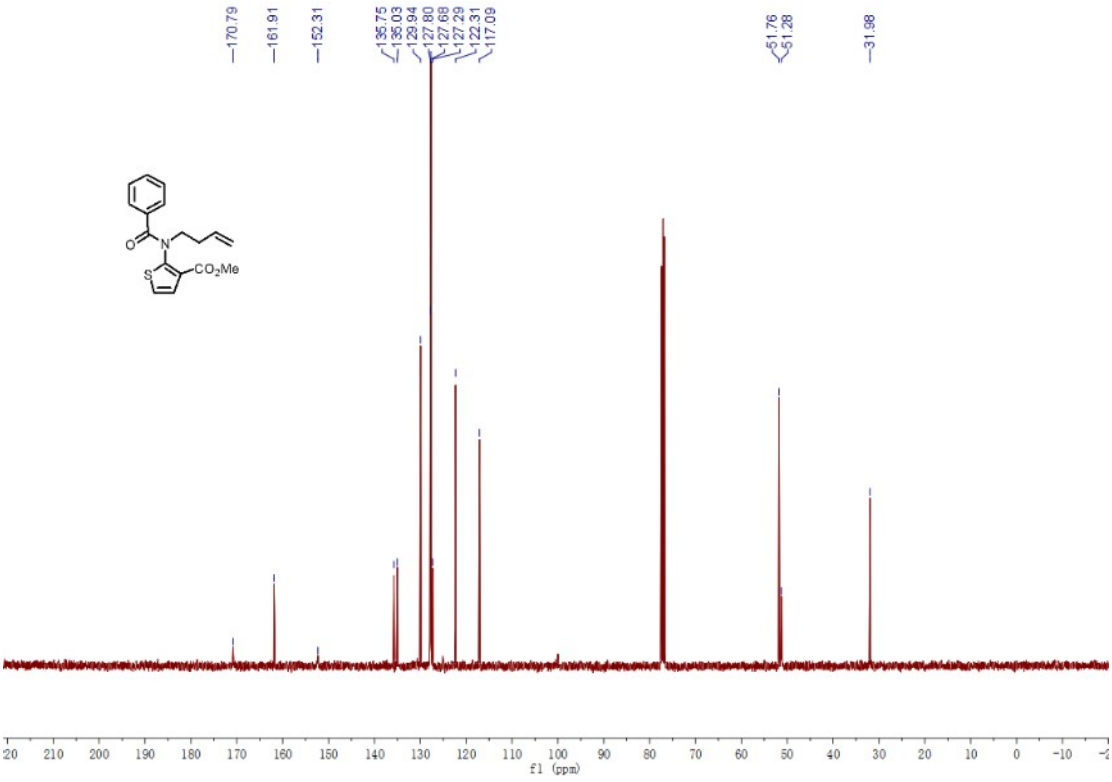
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 1j



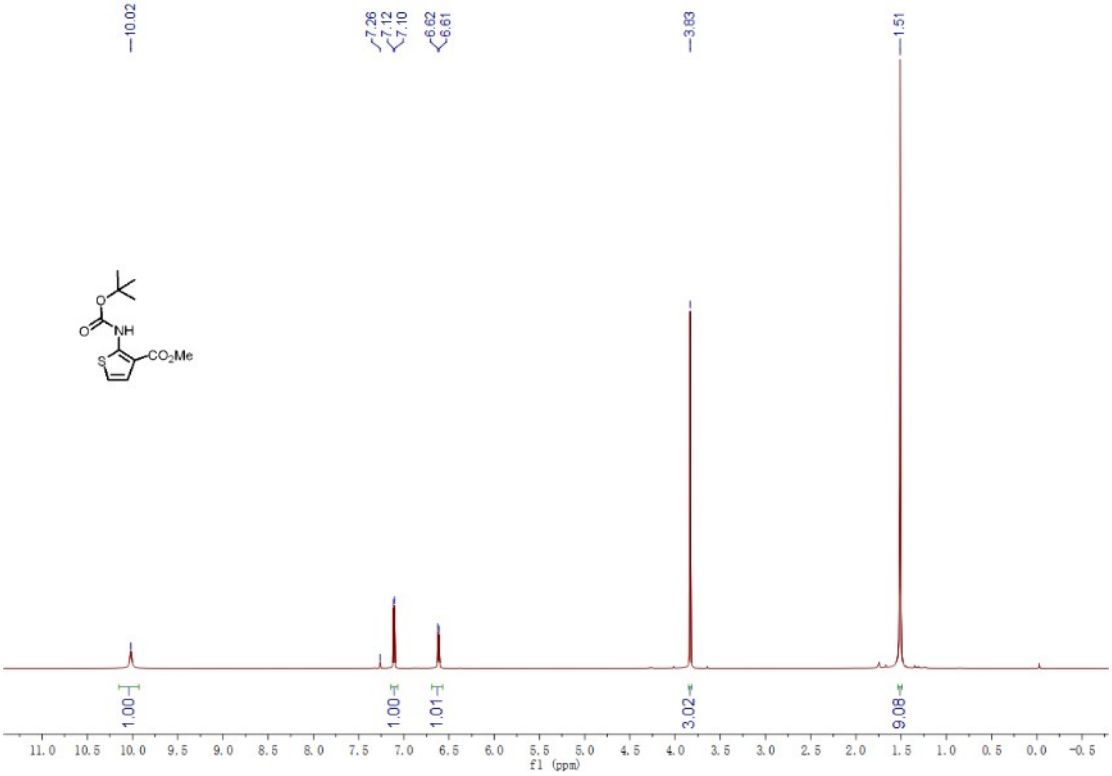
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 1k



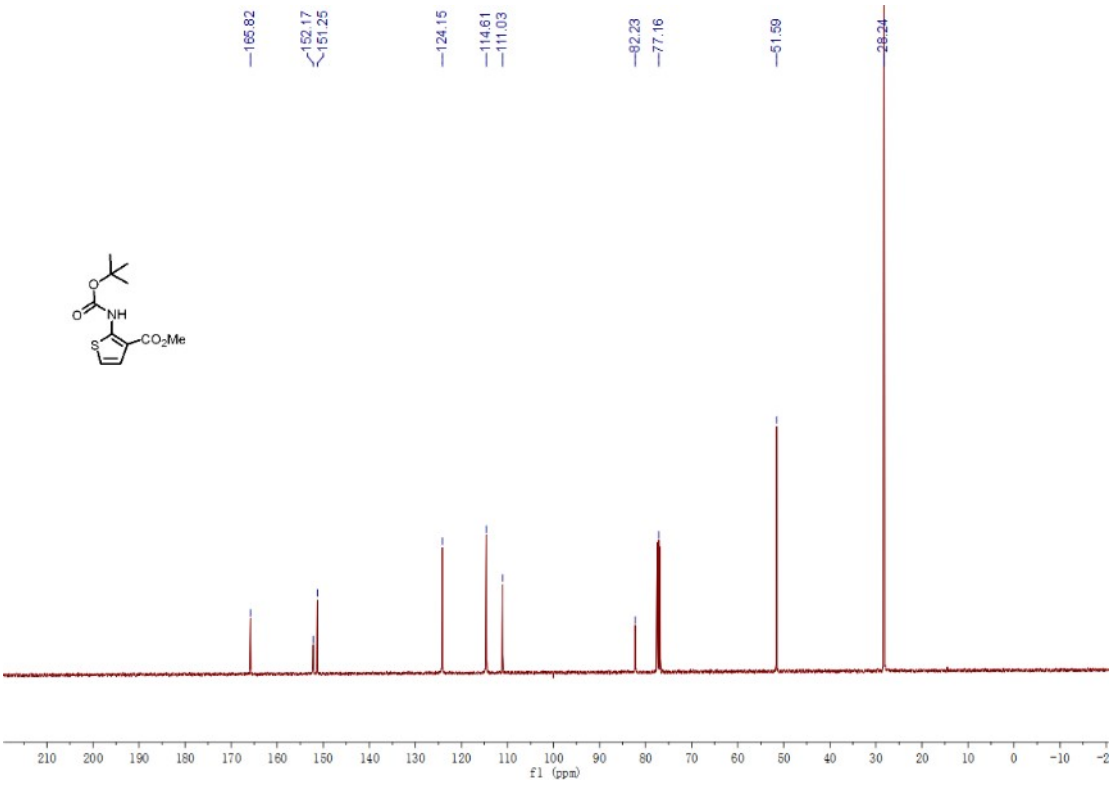
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 1k



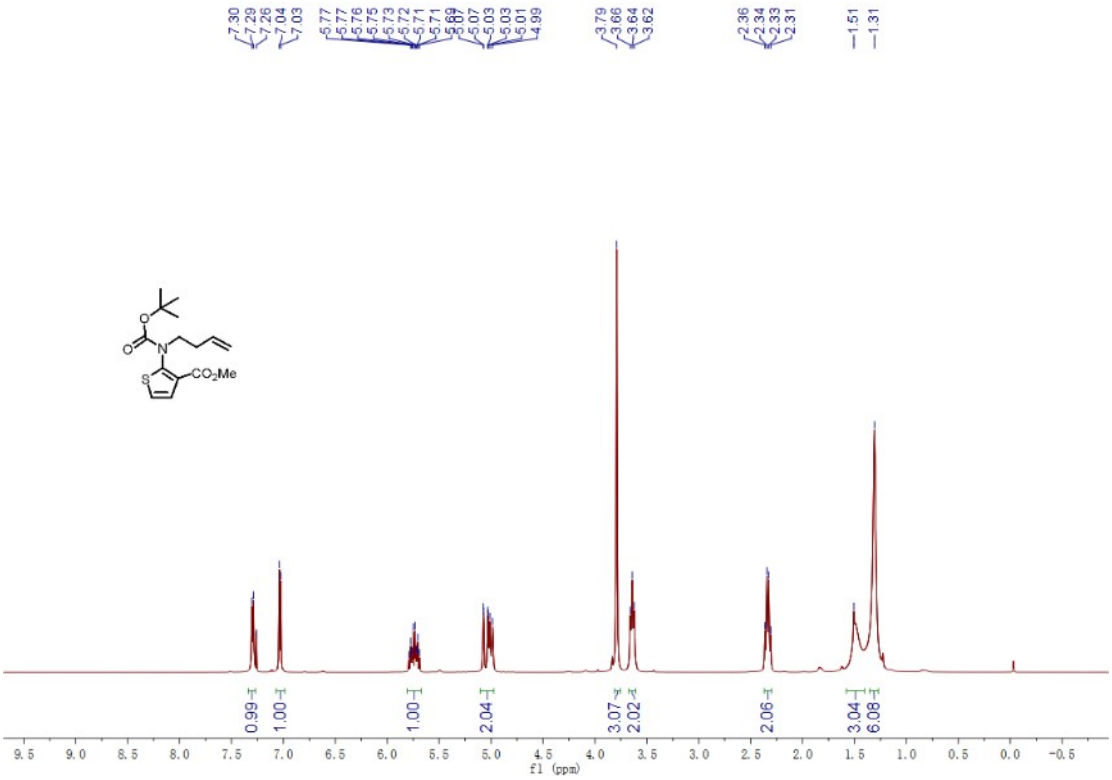
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 1l-1



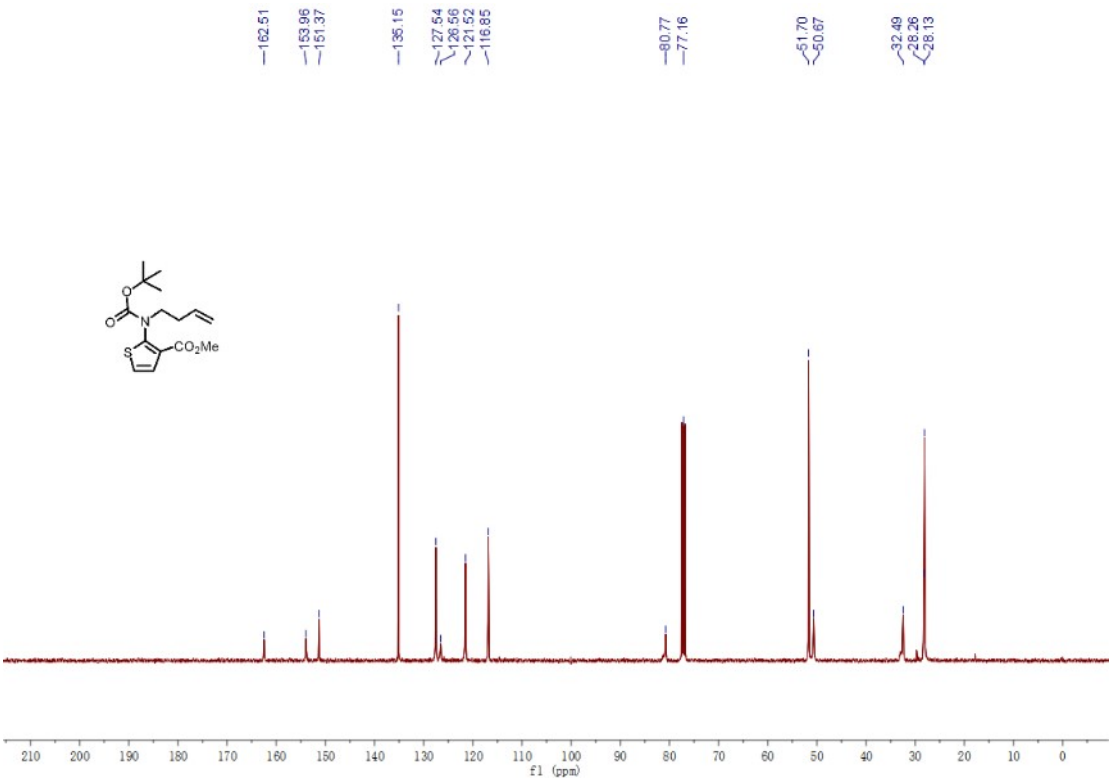
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 1l-1



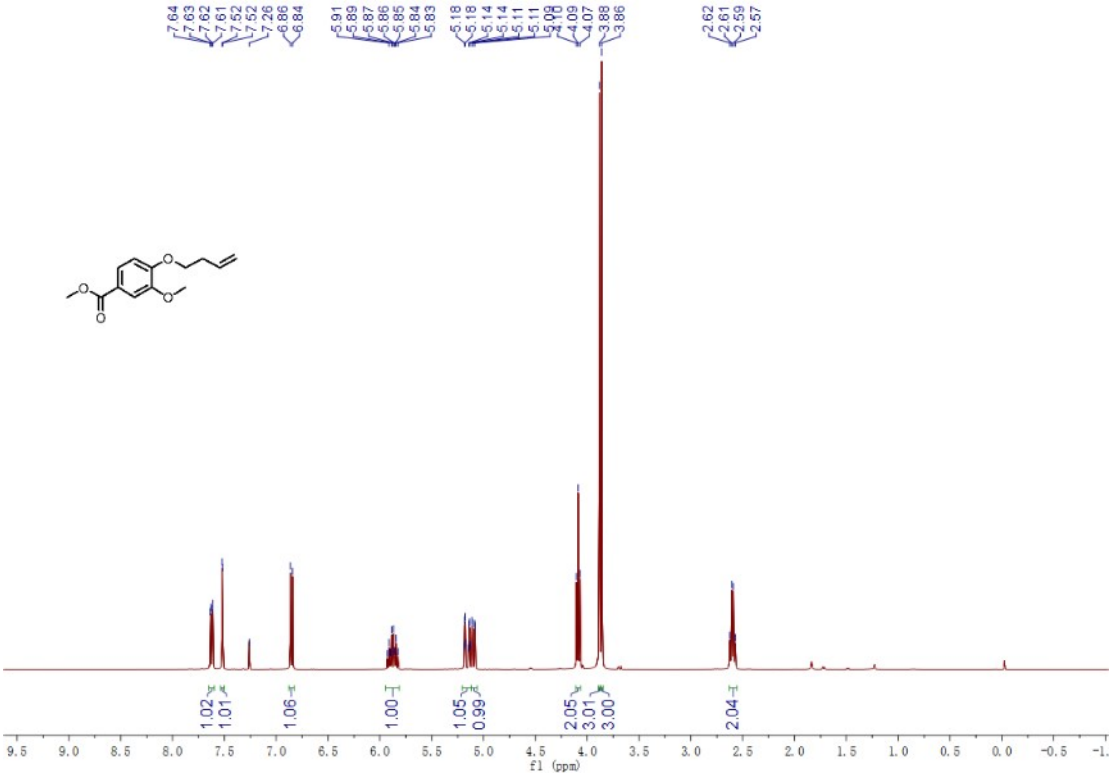
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 1l



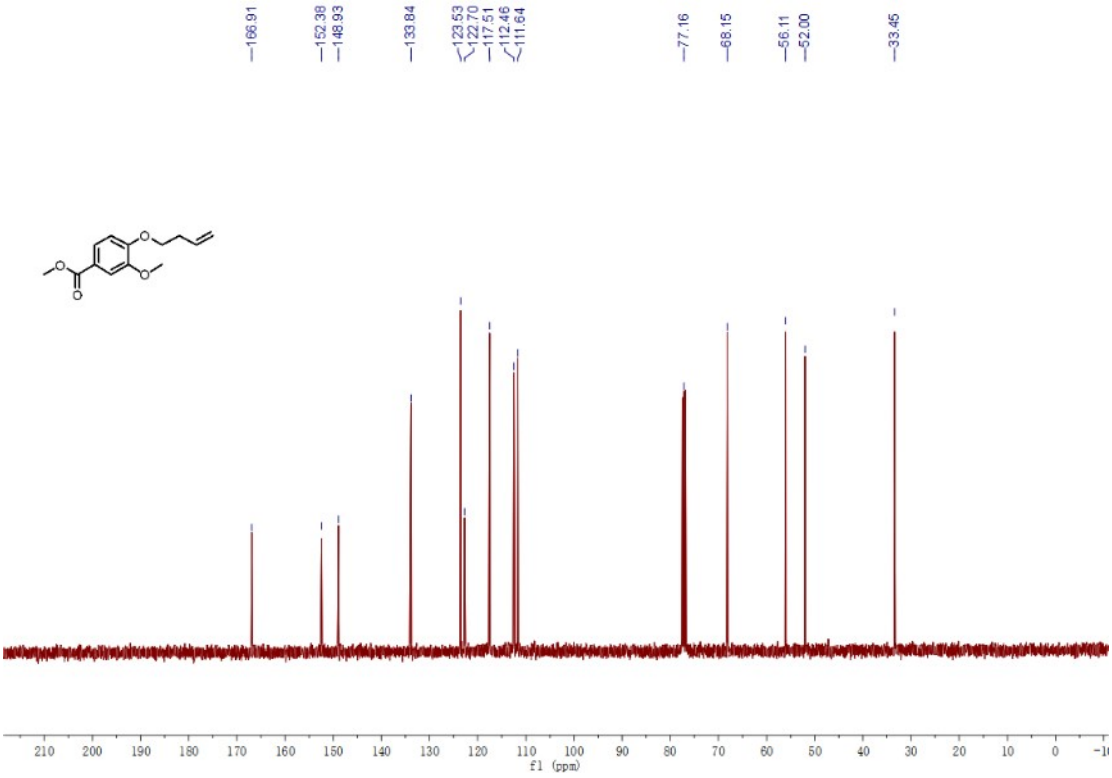
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 1l



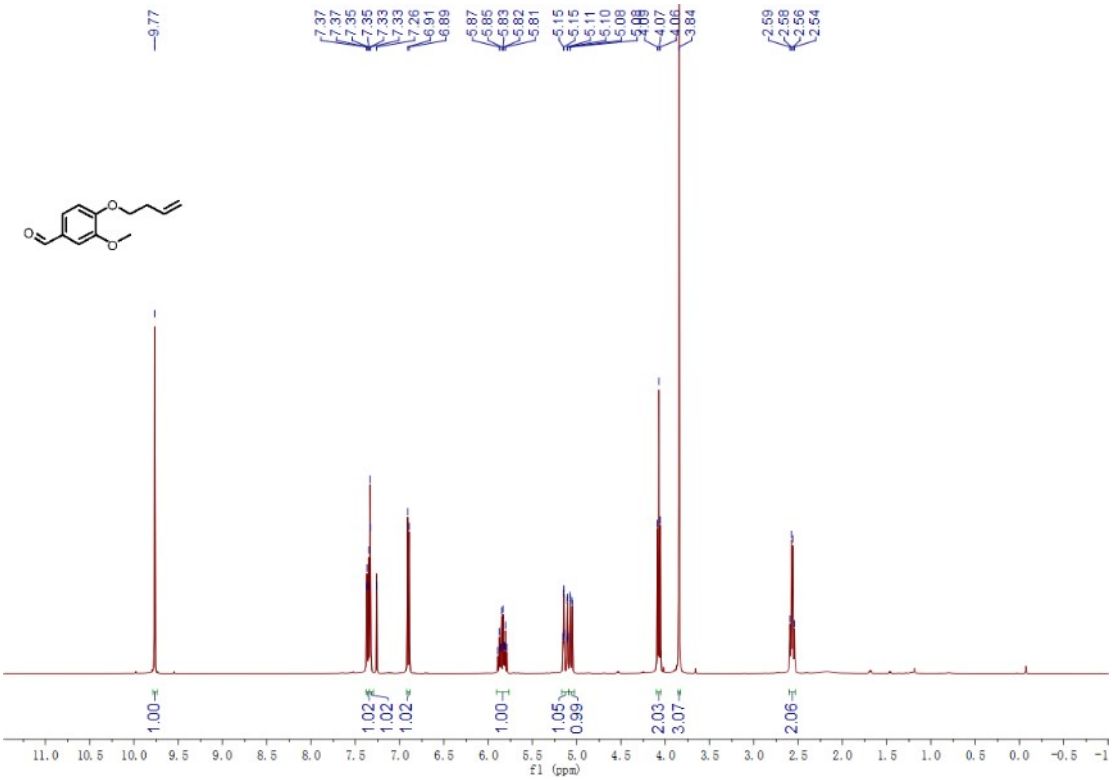
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 1m



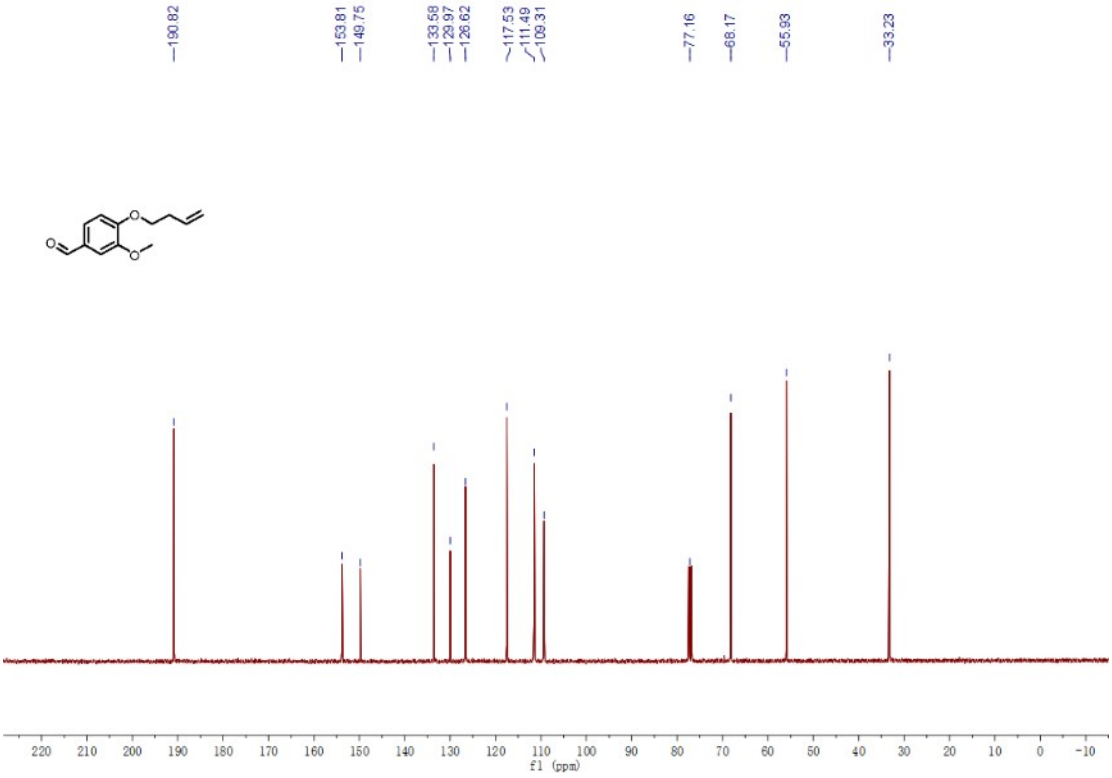
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 1m



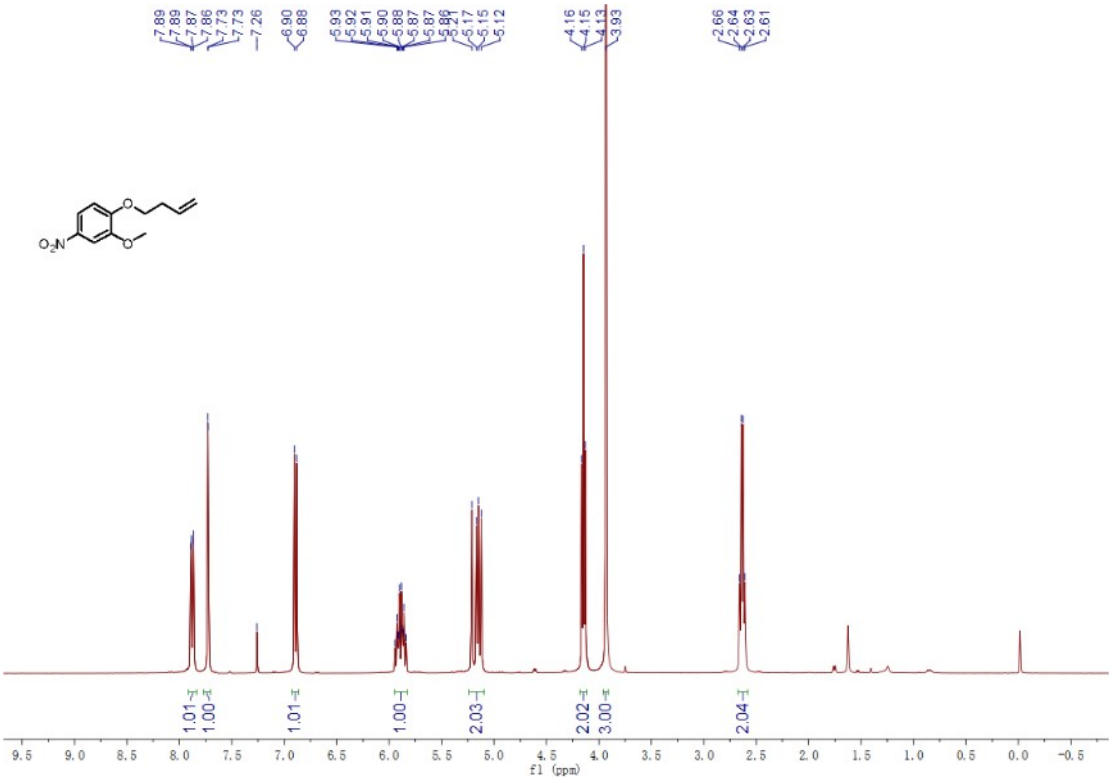
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 1n



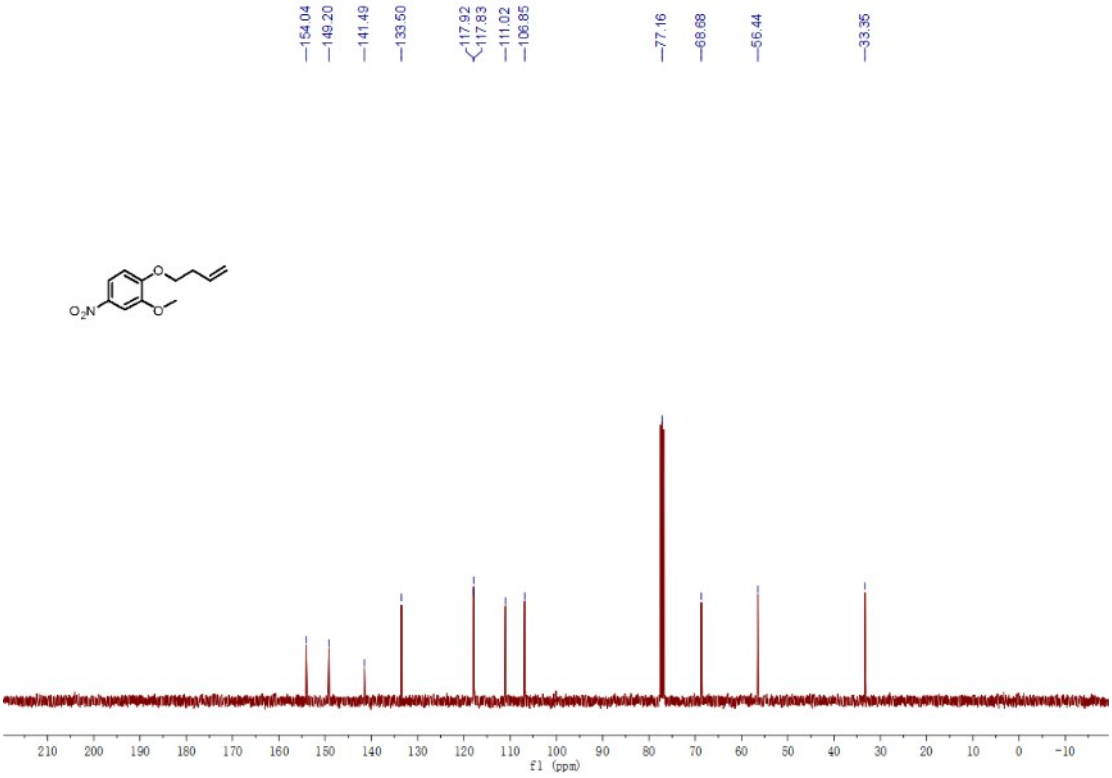
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 1n



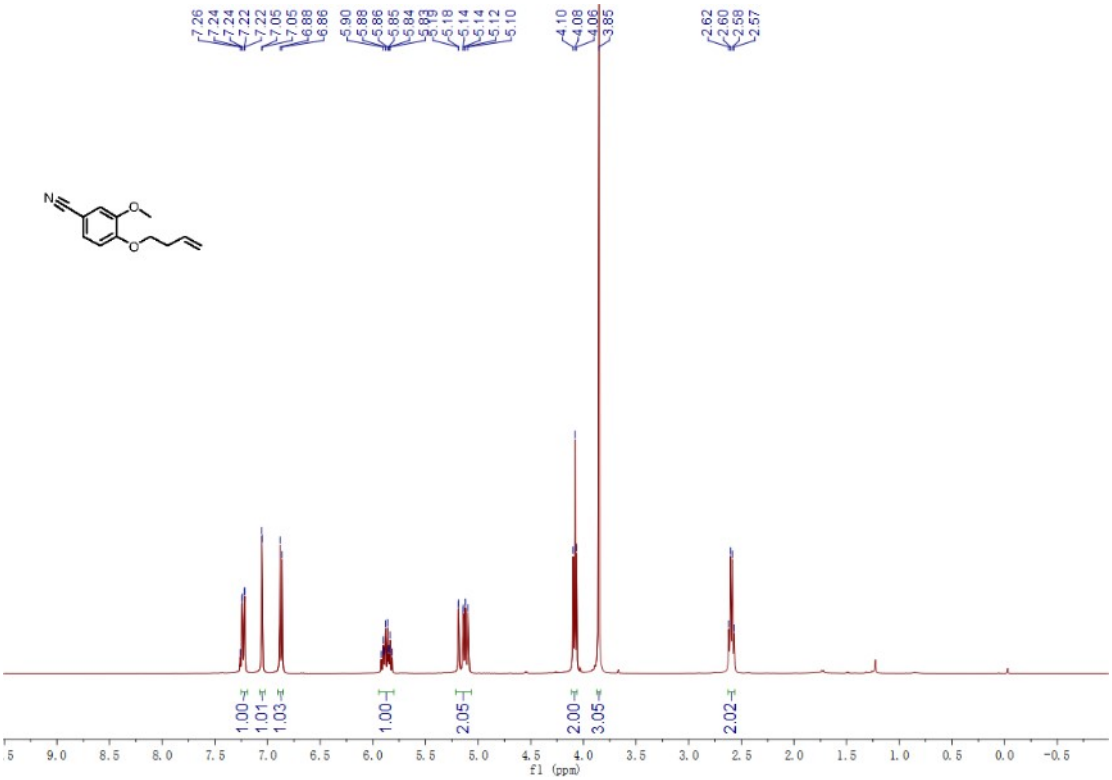
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 1o



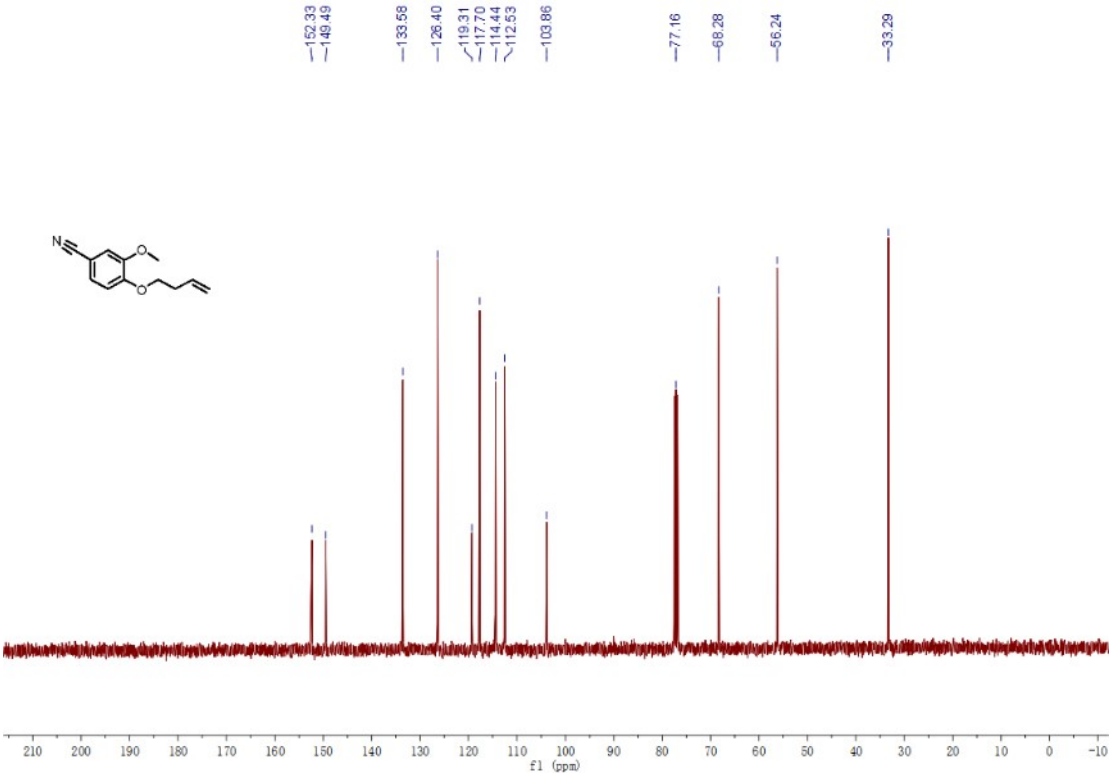
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 1o



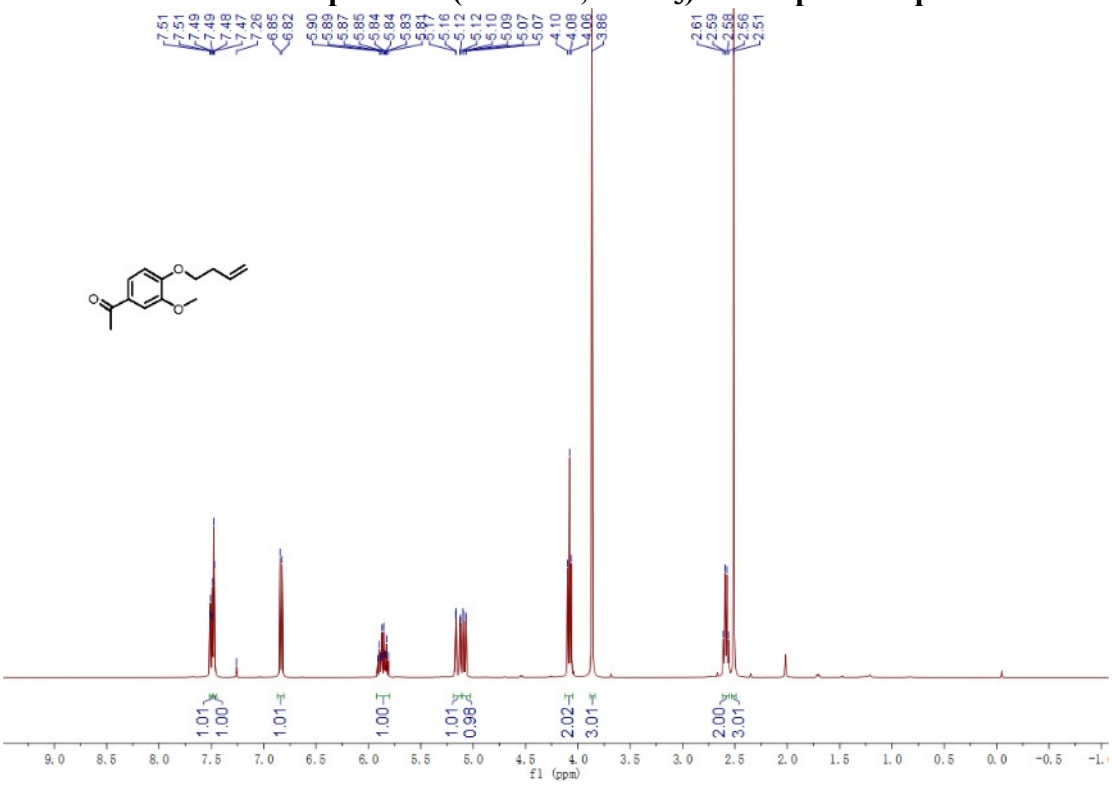
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 1p



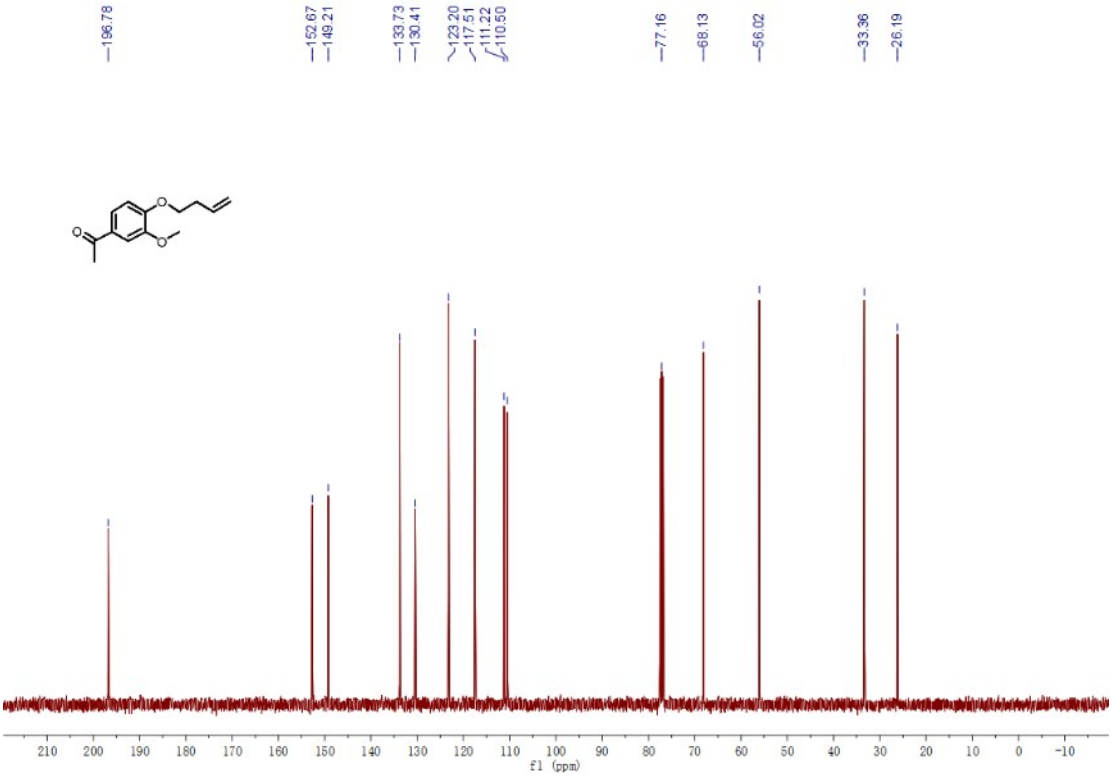
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 1p



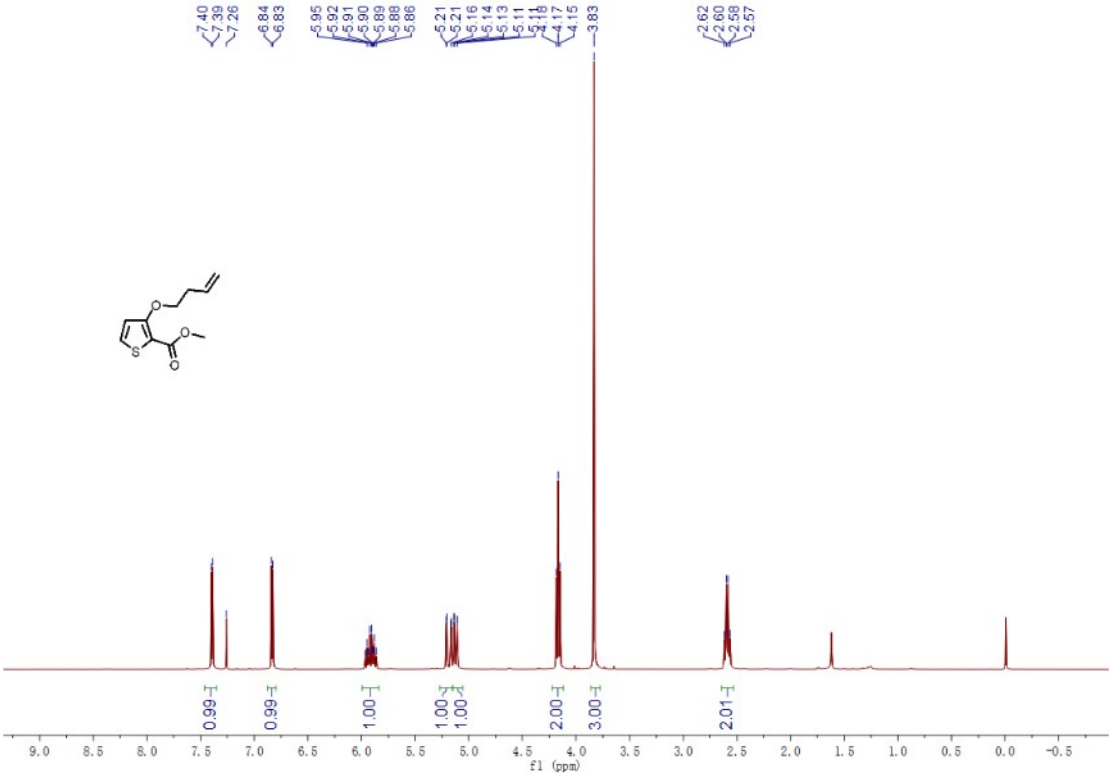
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 1q



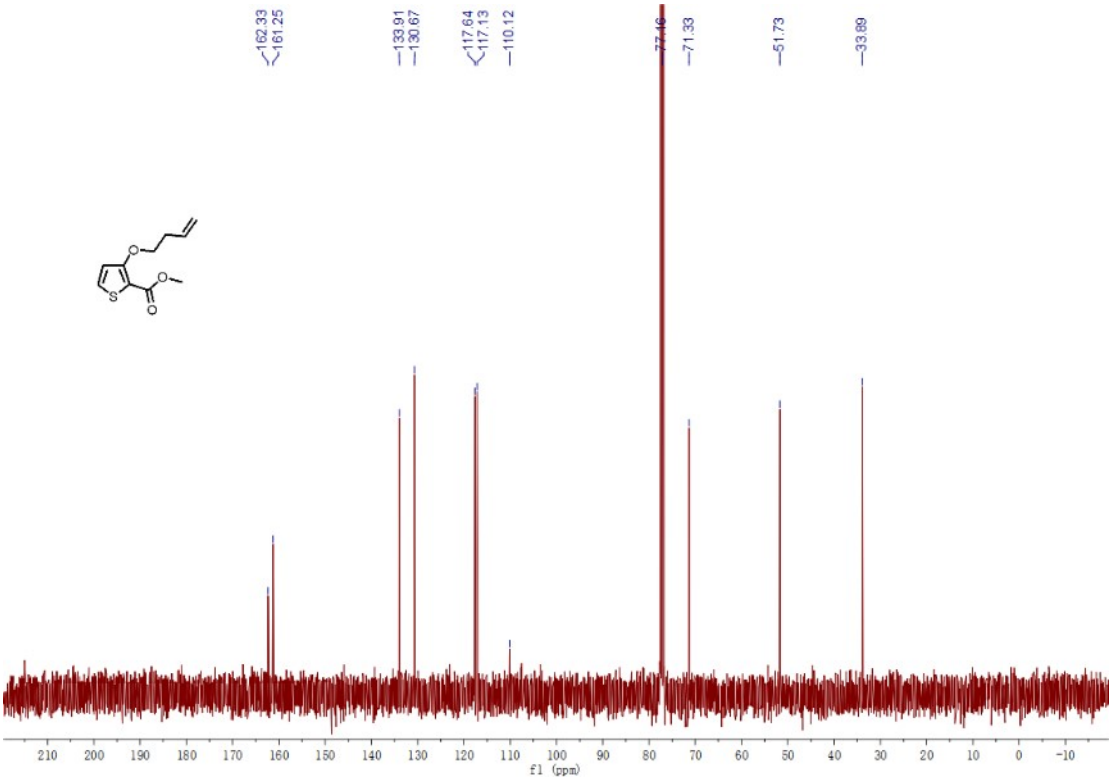
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 1q



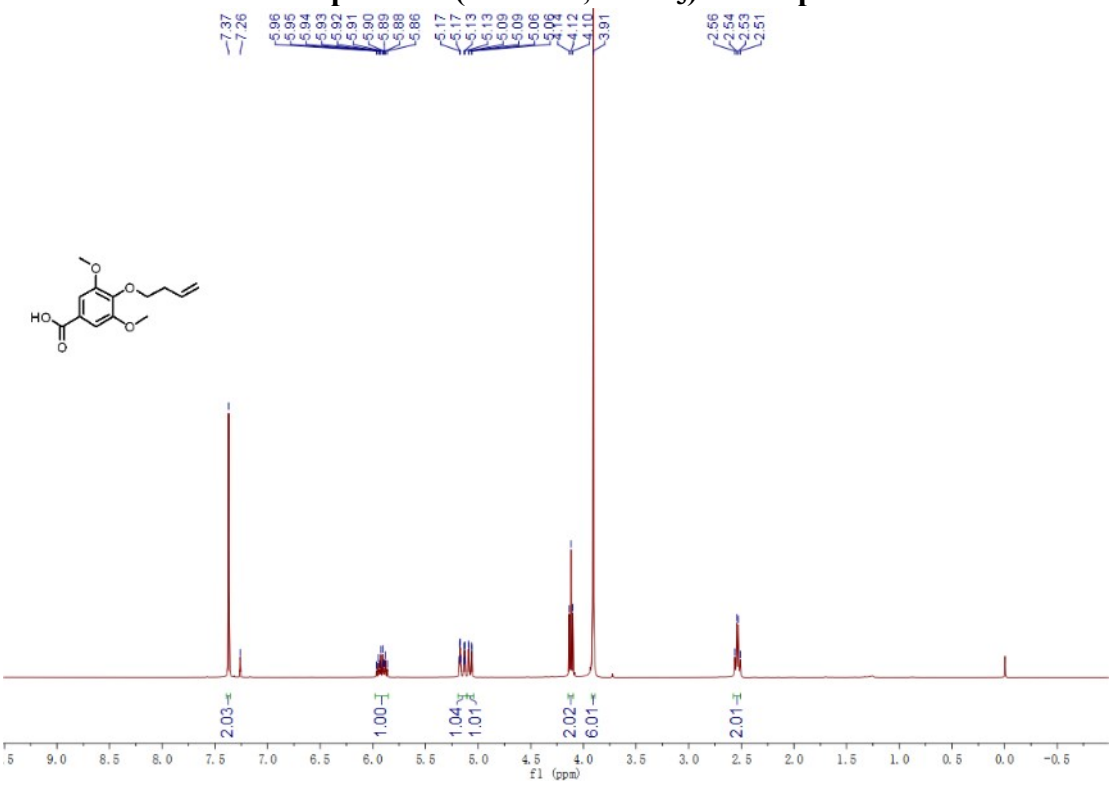
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 1r



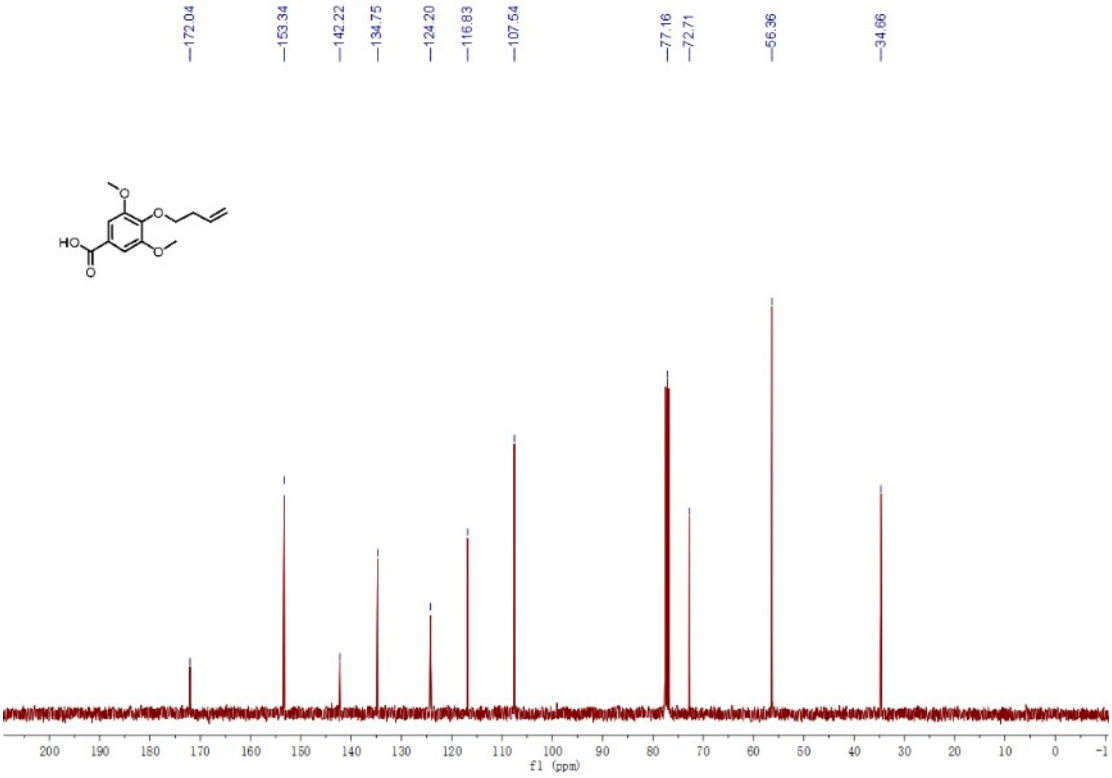
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 1r



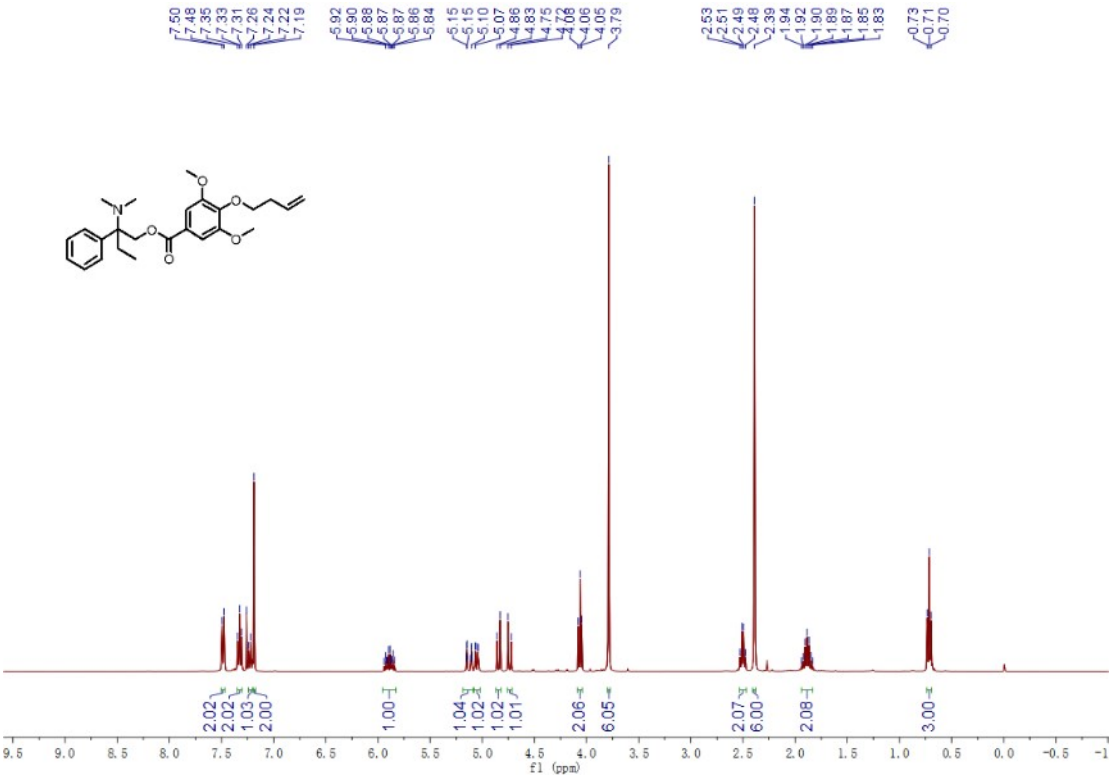
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 1s



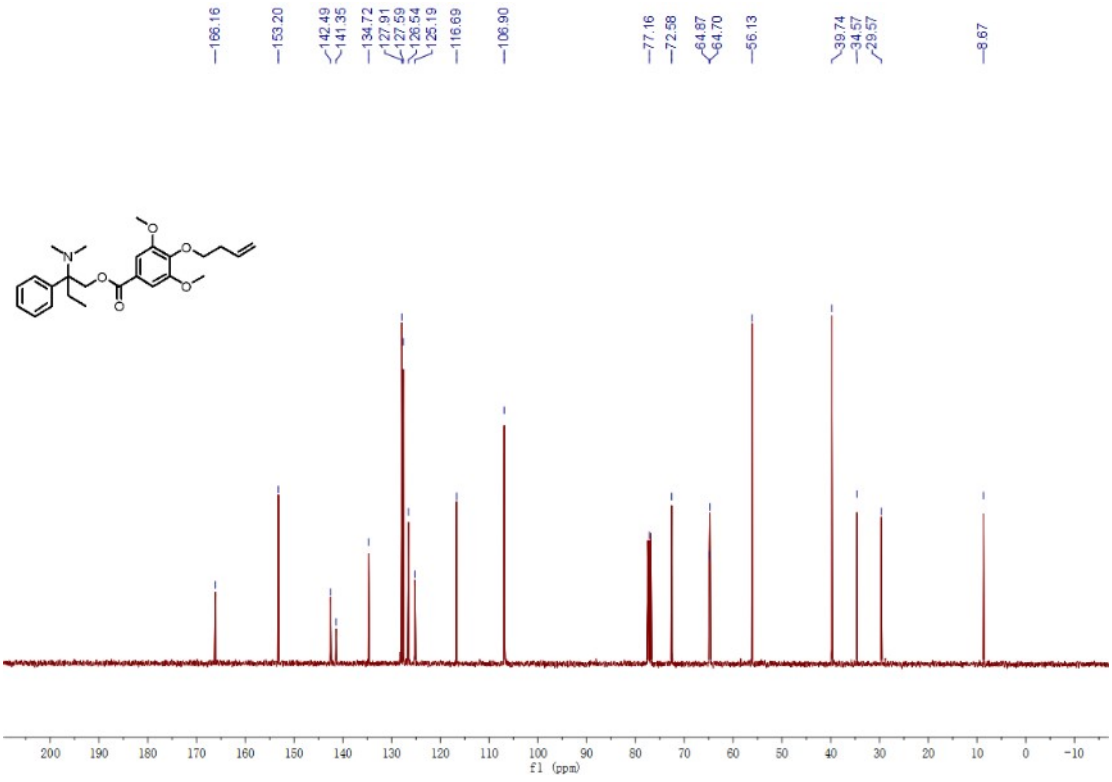
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 1s



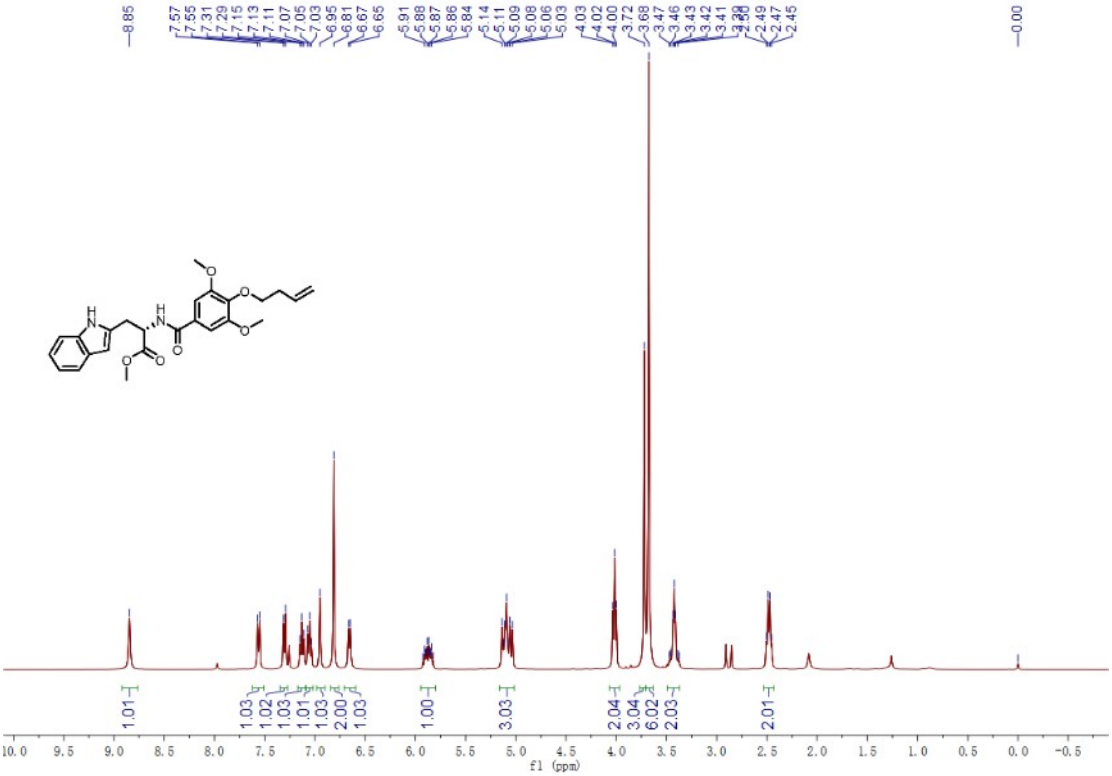
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 1t



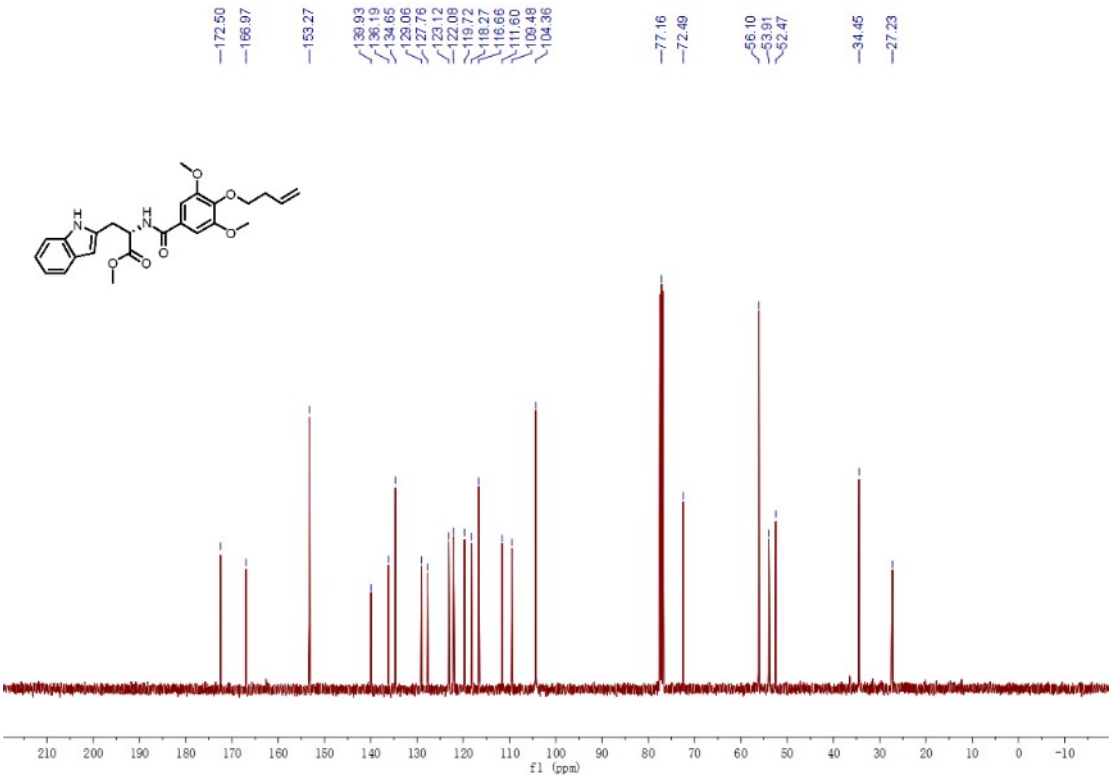
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 1t



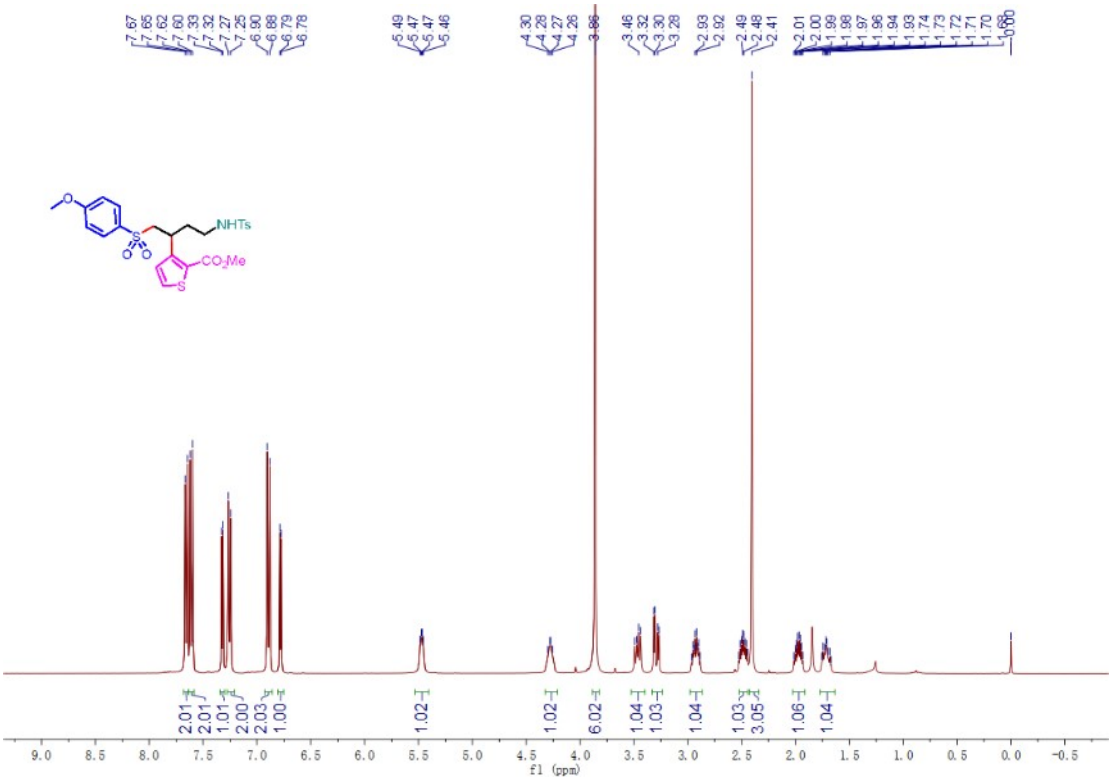
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 1u



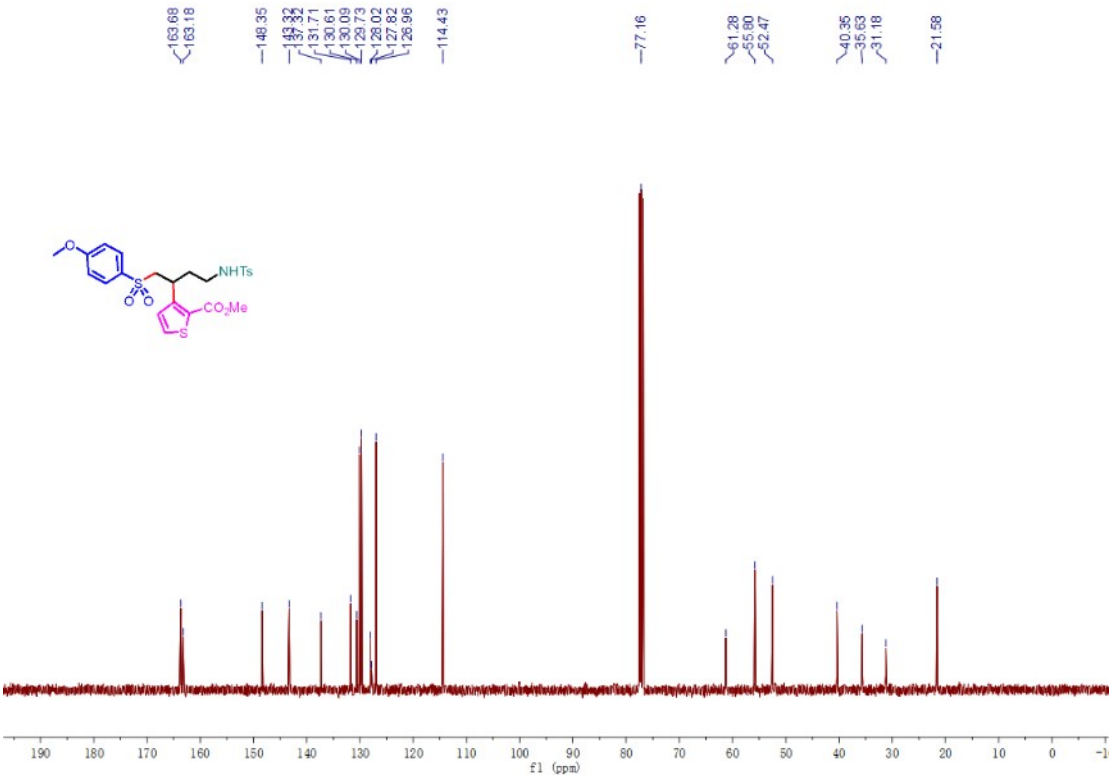
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 1u



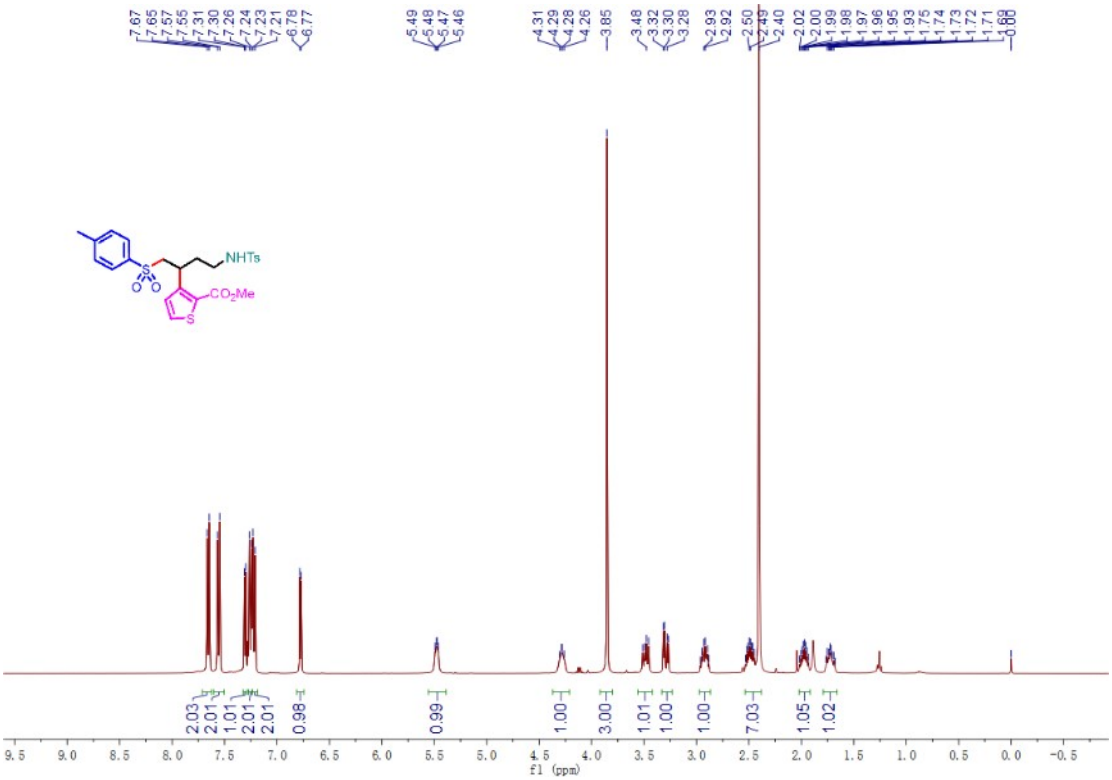
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 3a



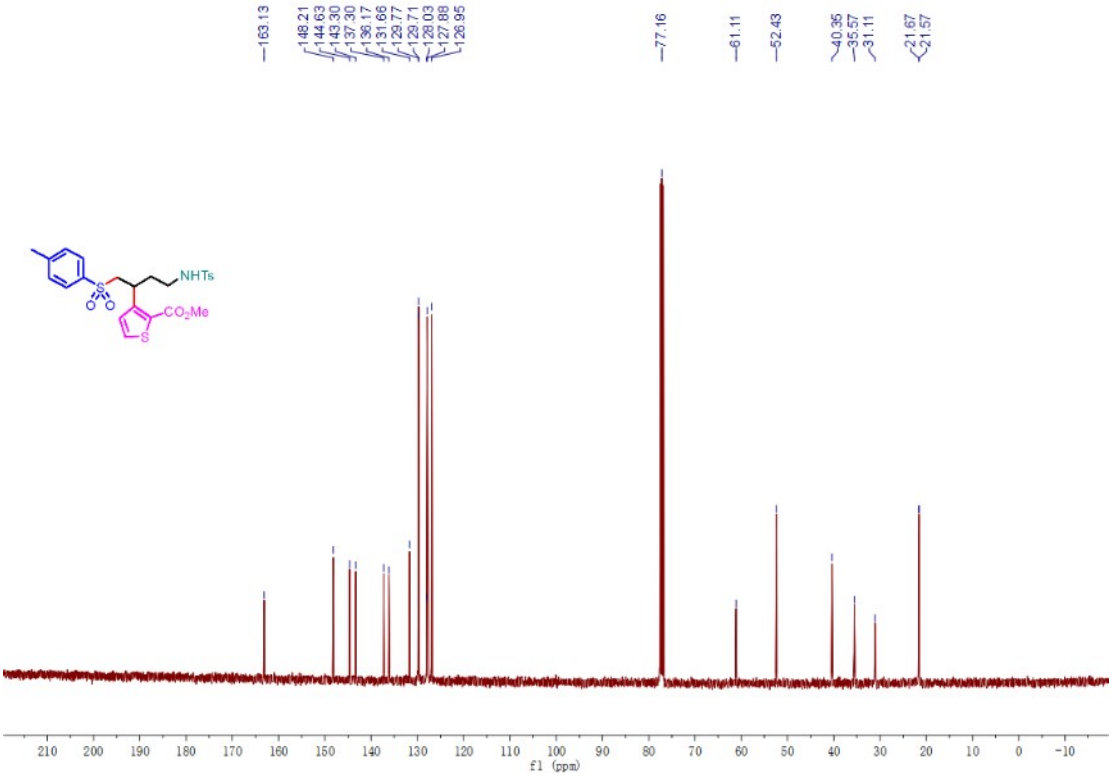
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 3a



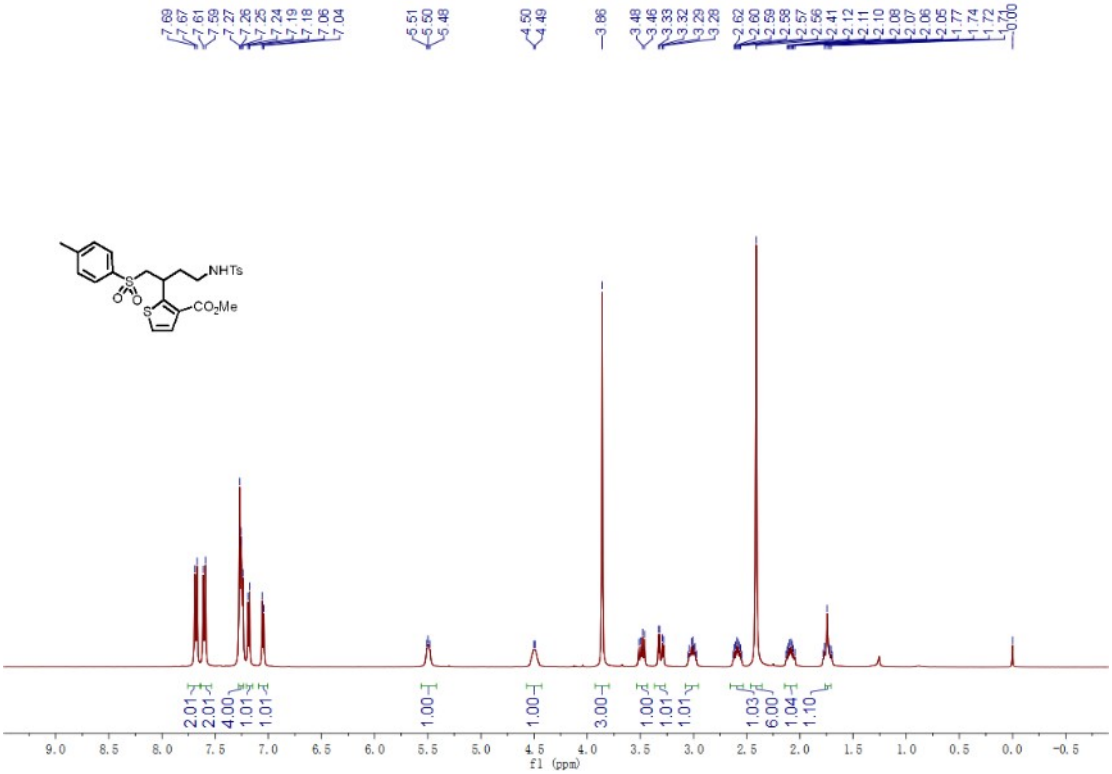
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 3b



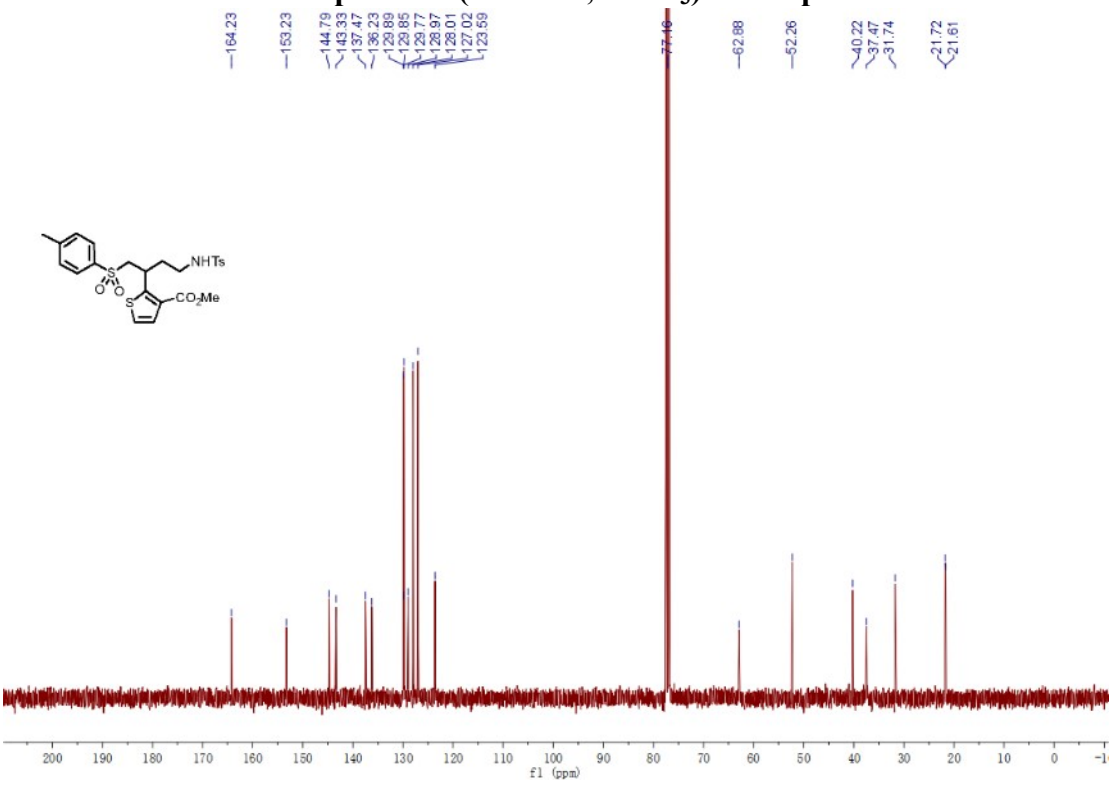
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 3b



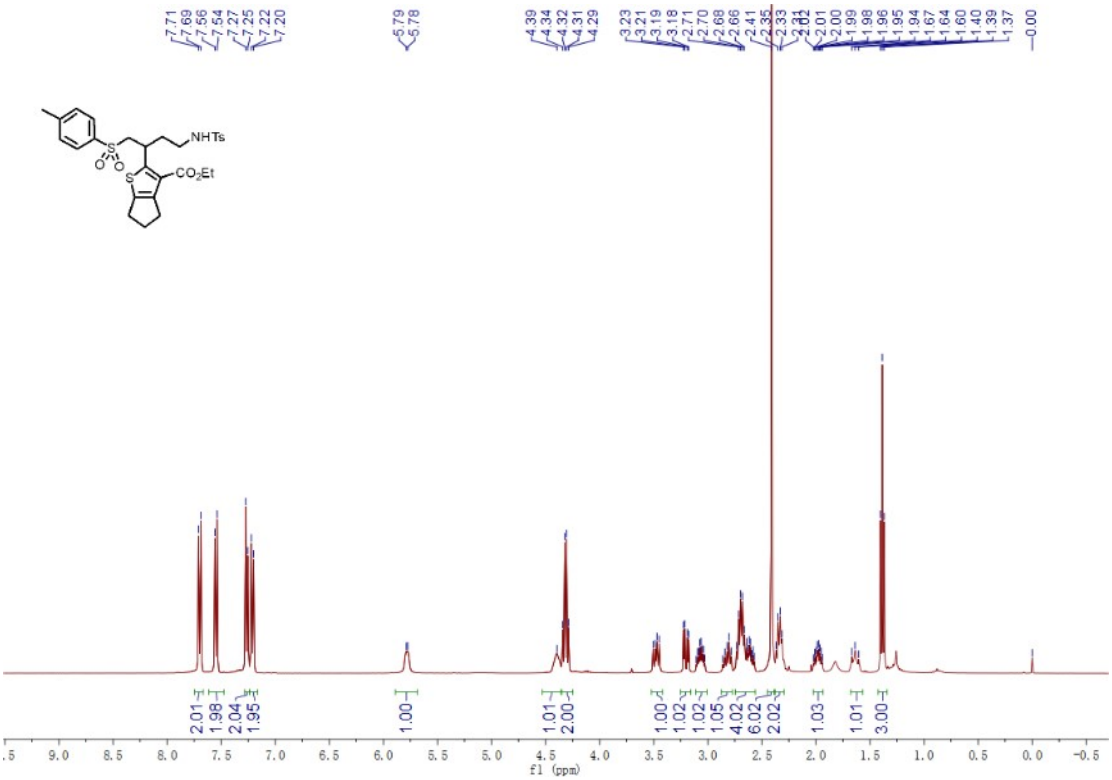
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 3c



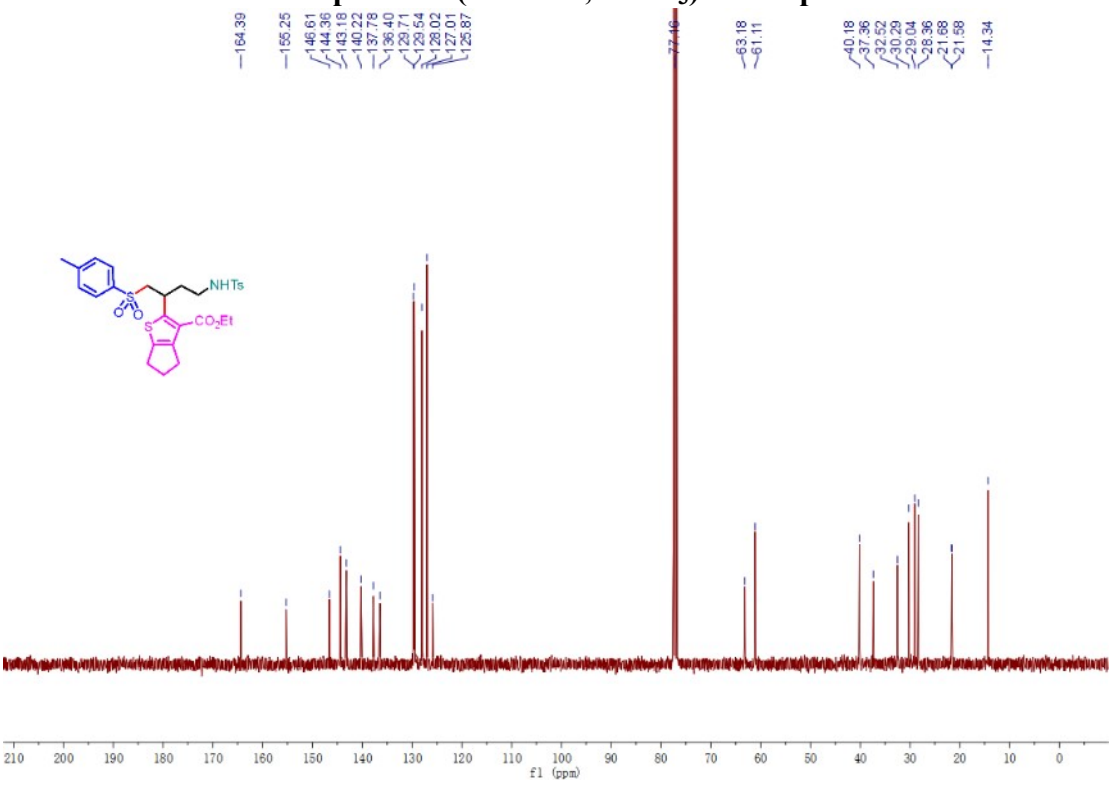
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 3c



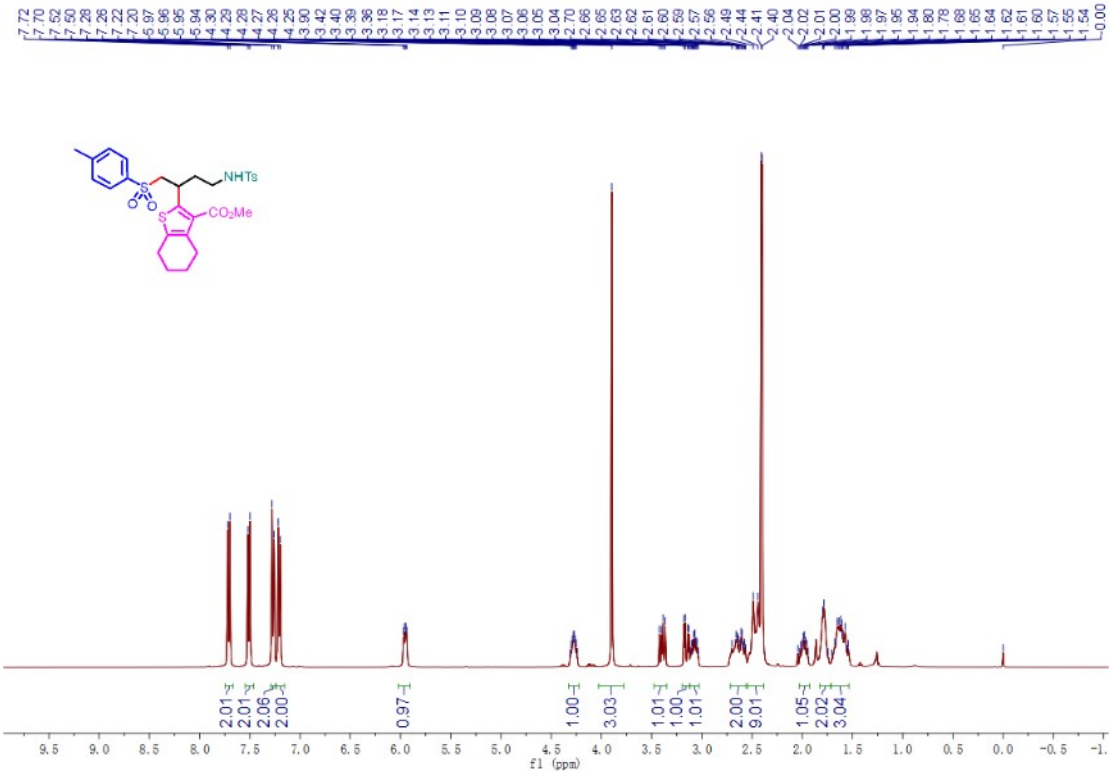
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 3d



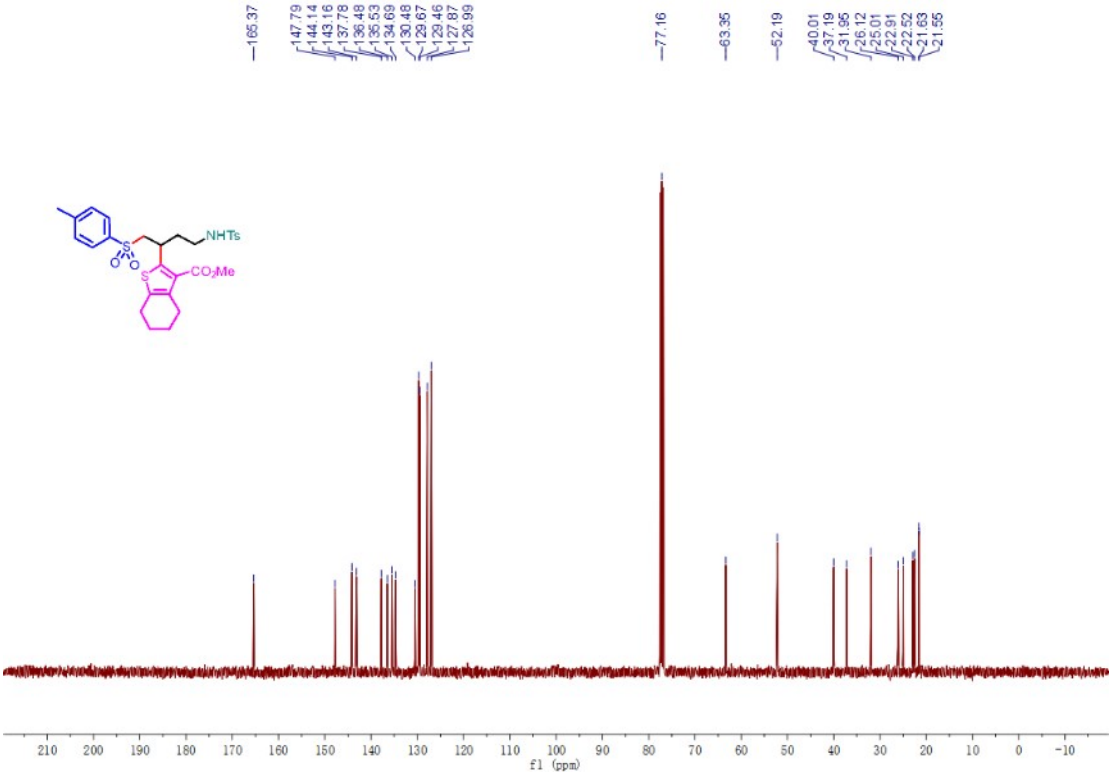
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 3d



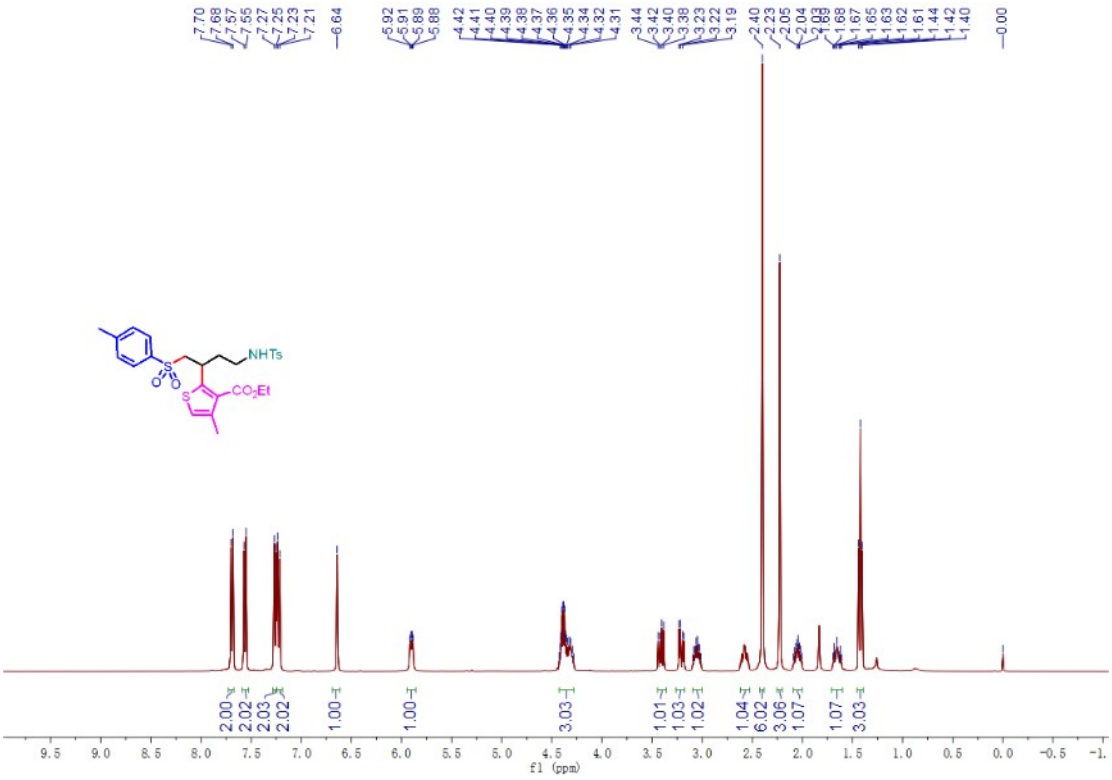
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 3e



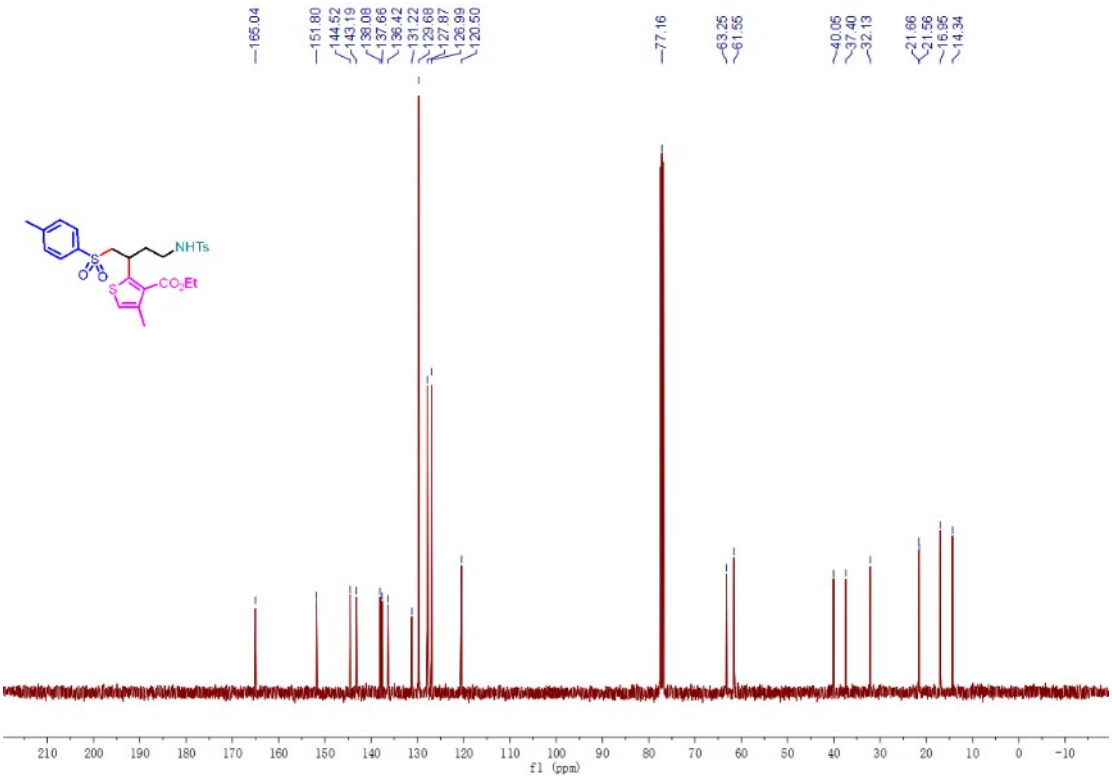
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 3e



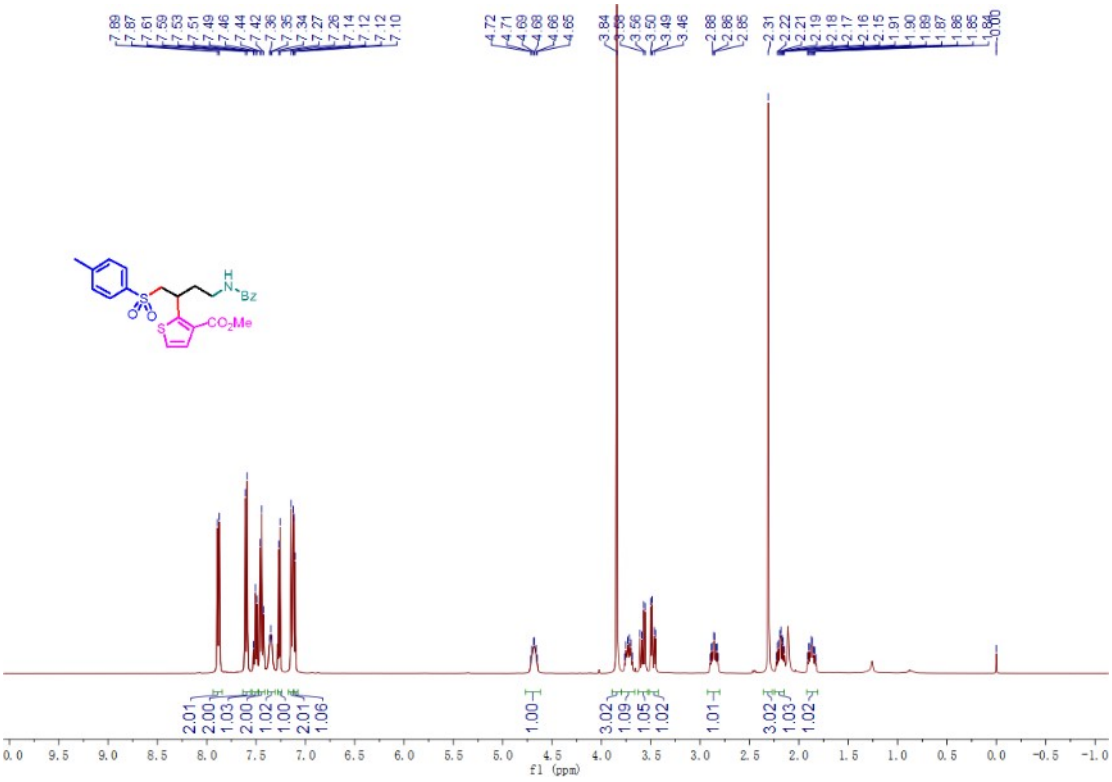
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 3f



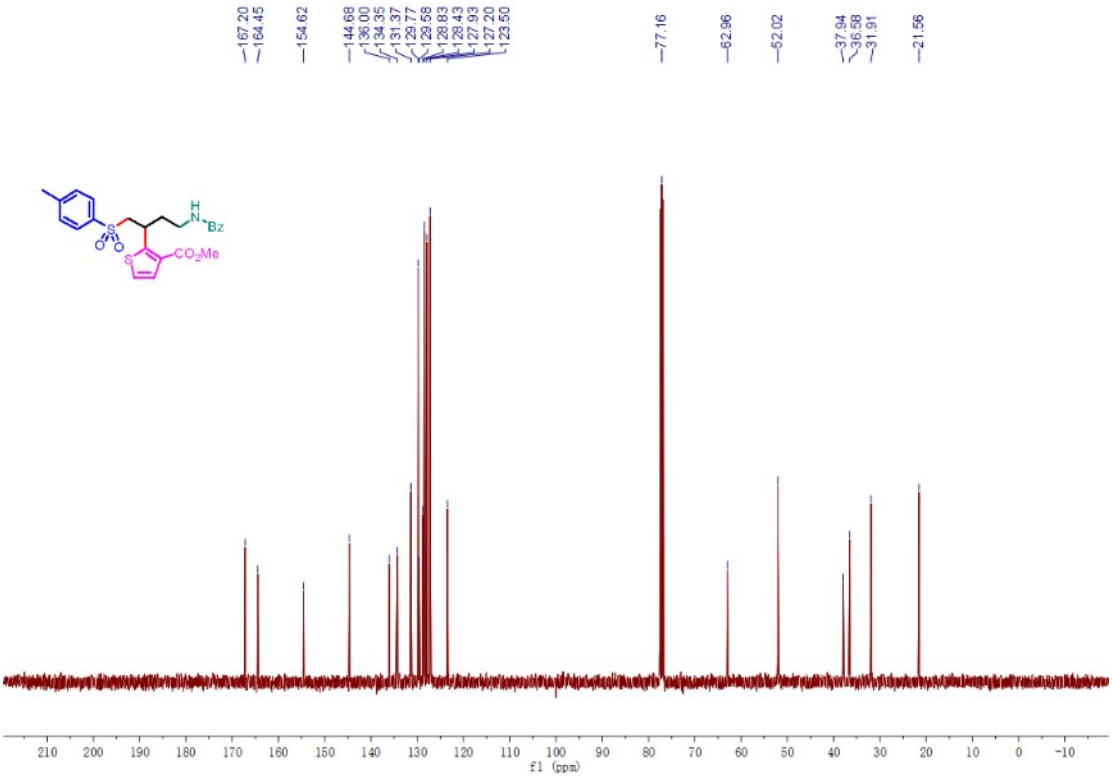
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 3f



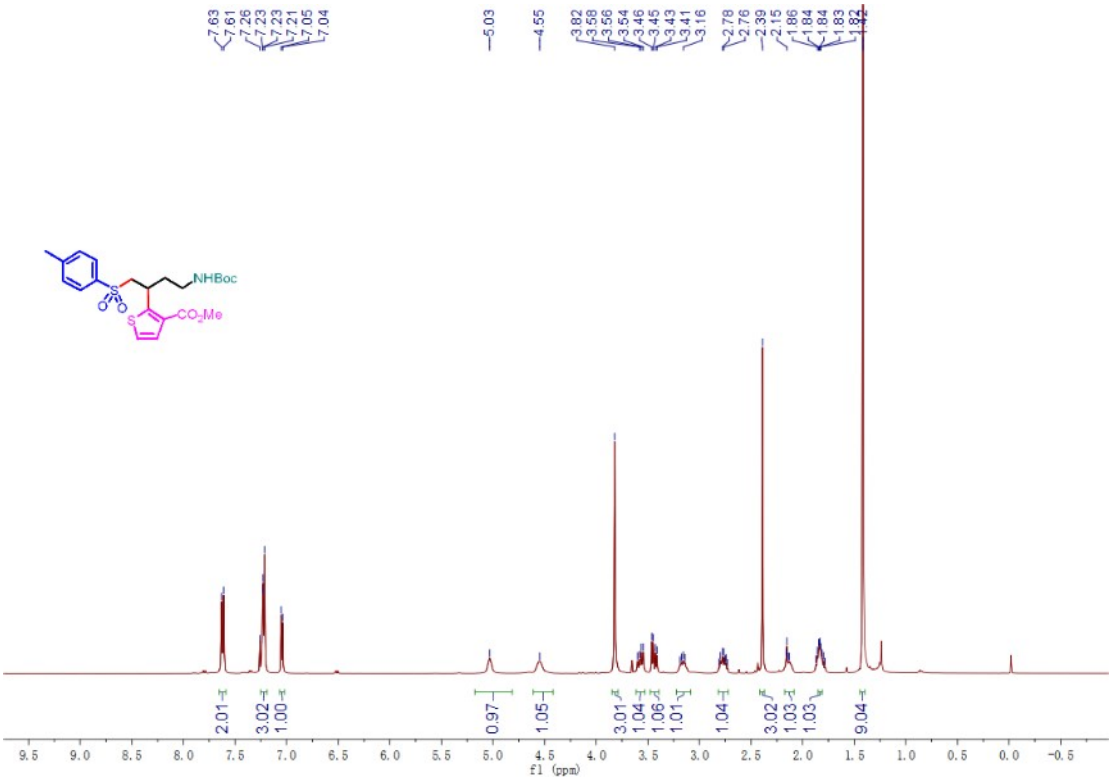
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 3g



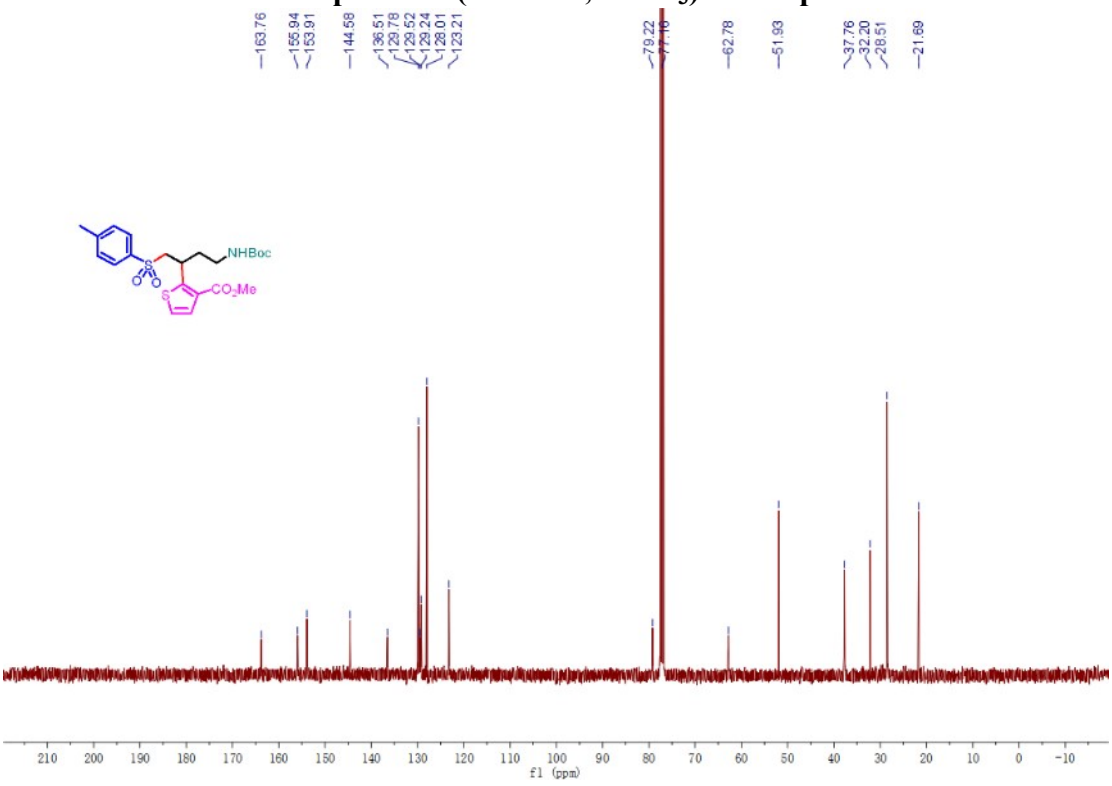
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 3g



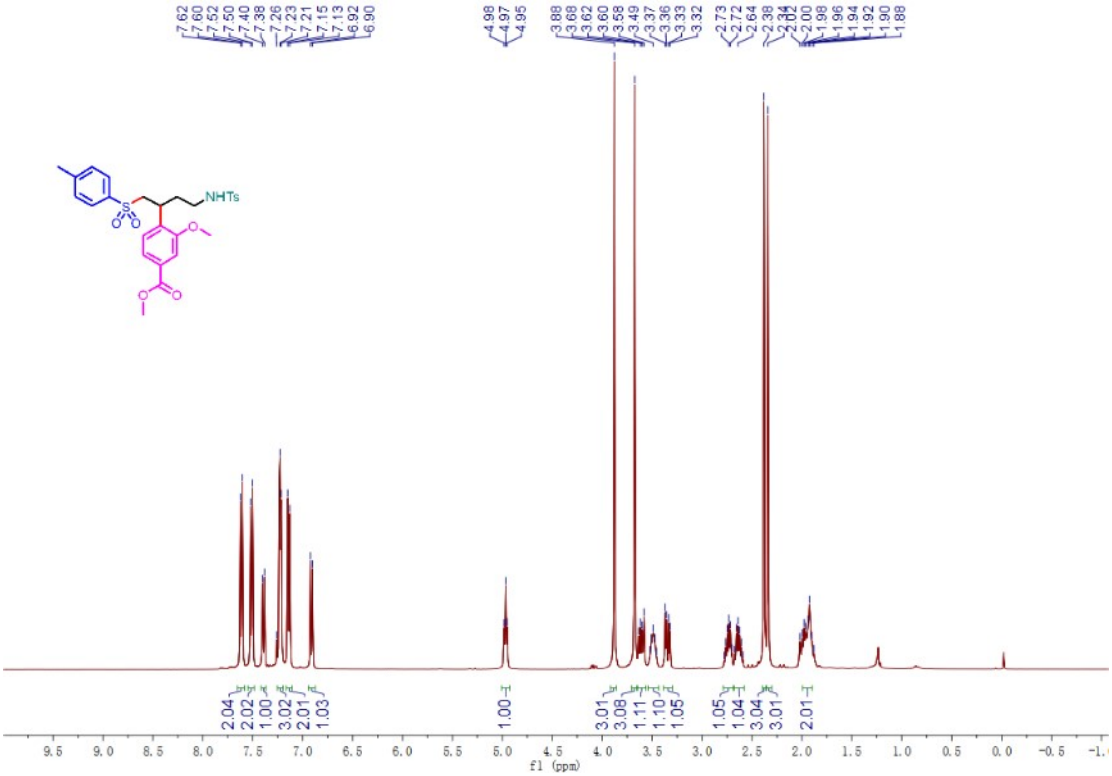
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 3h



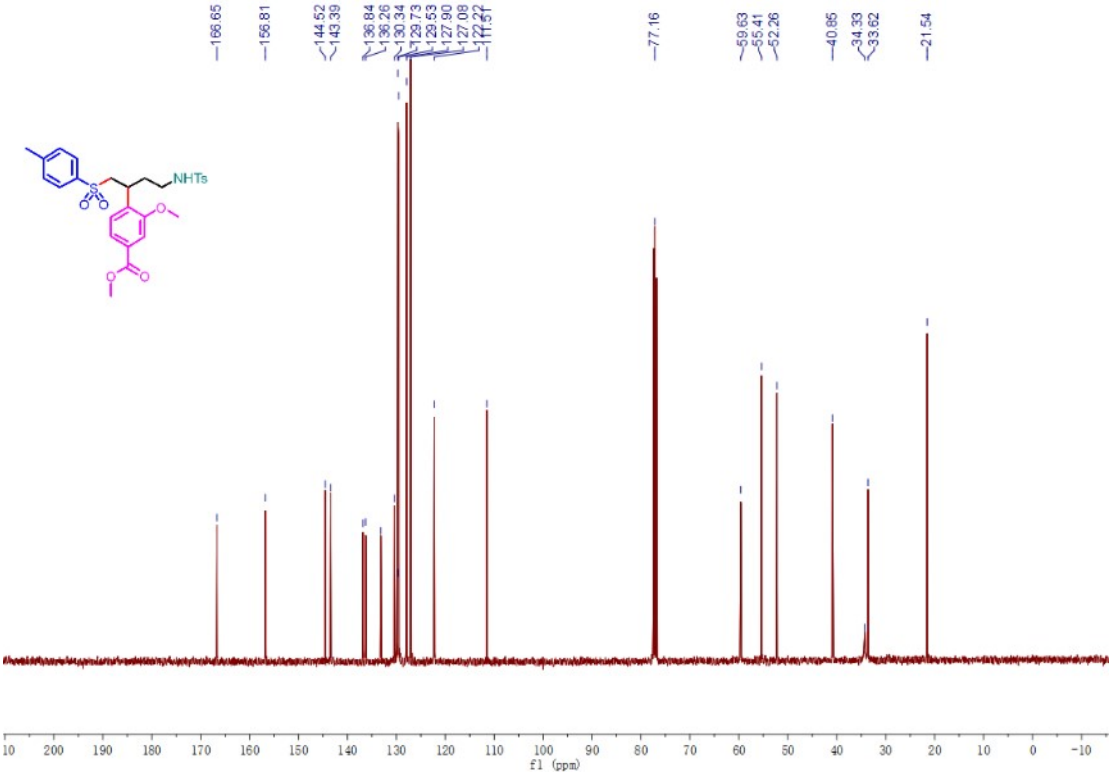
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 3h



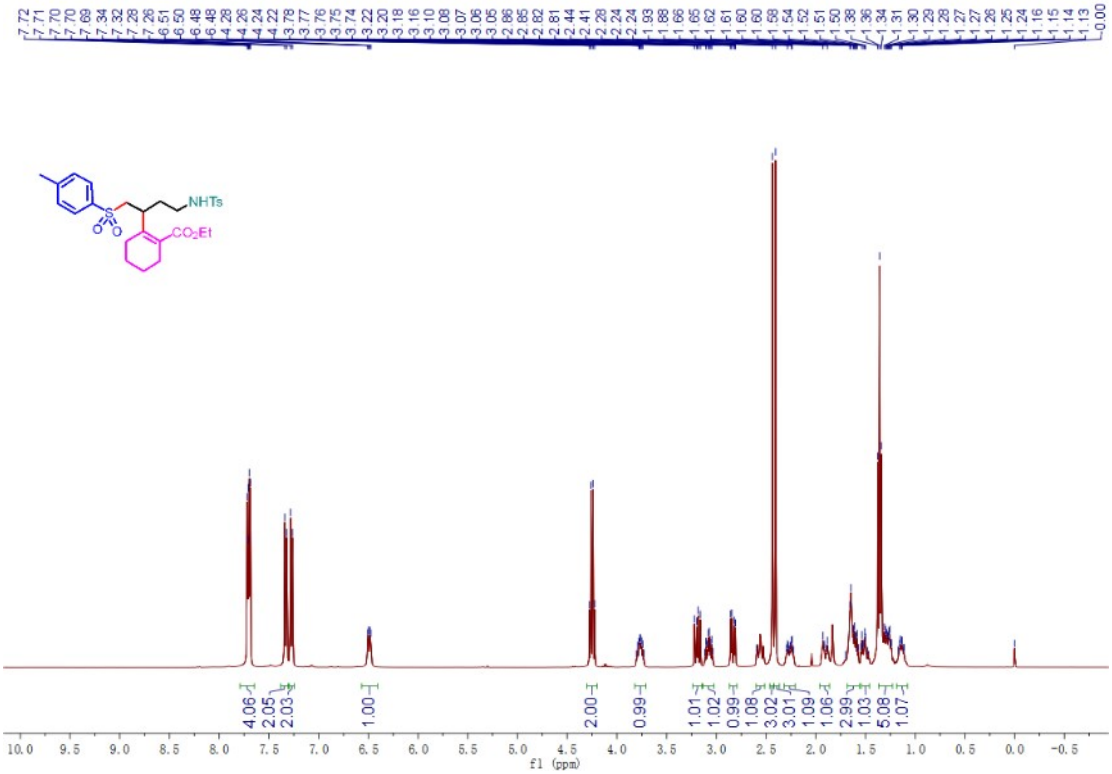
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 3i



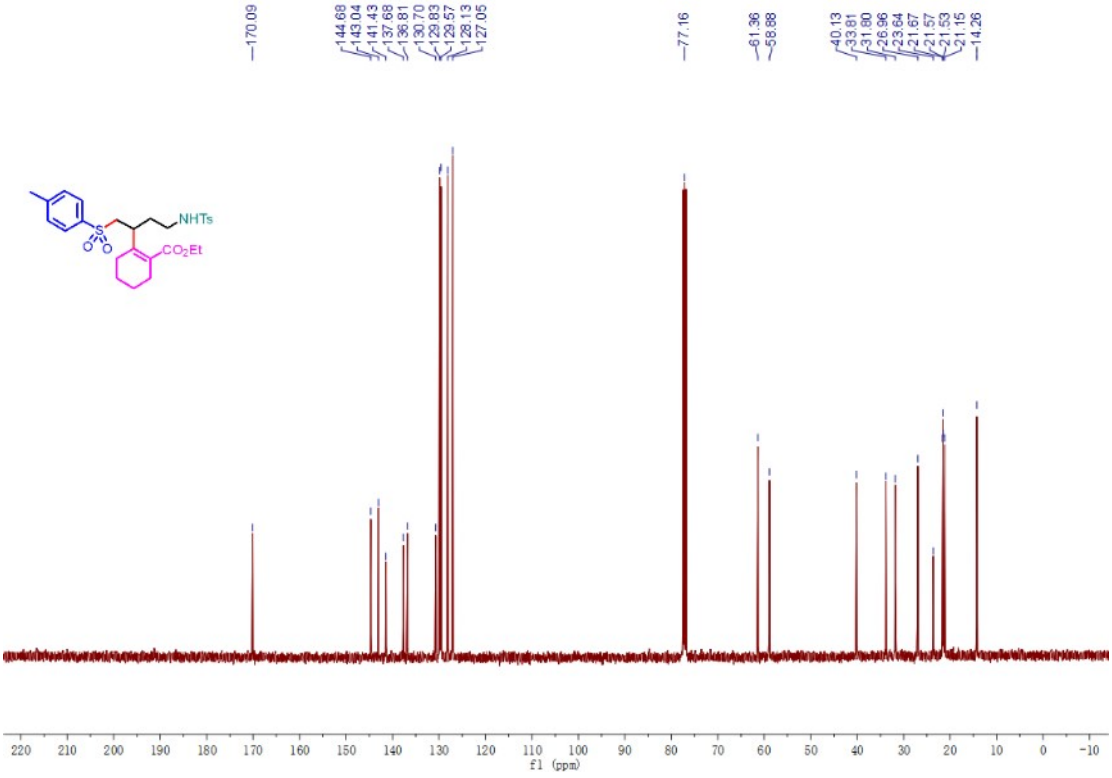
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 3i



^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 3j



^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 3j



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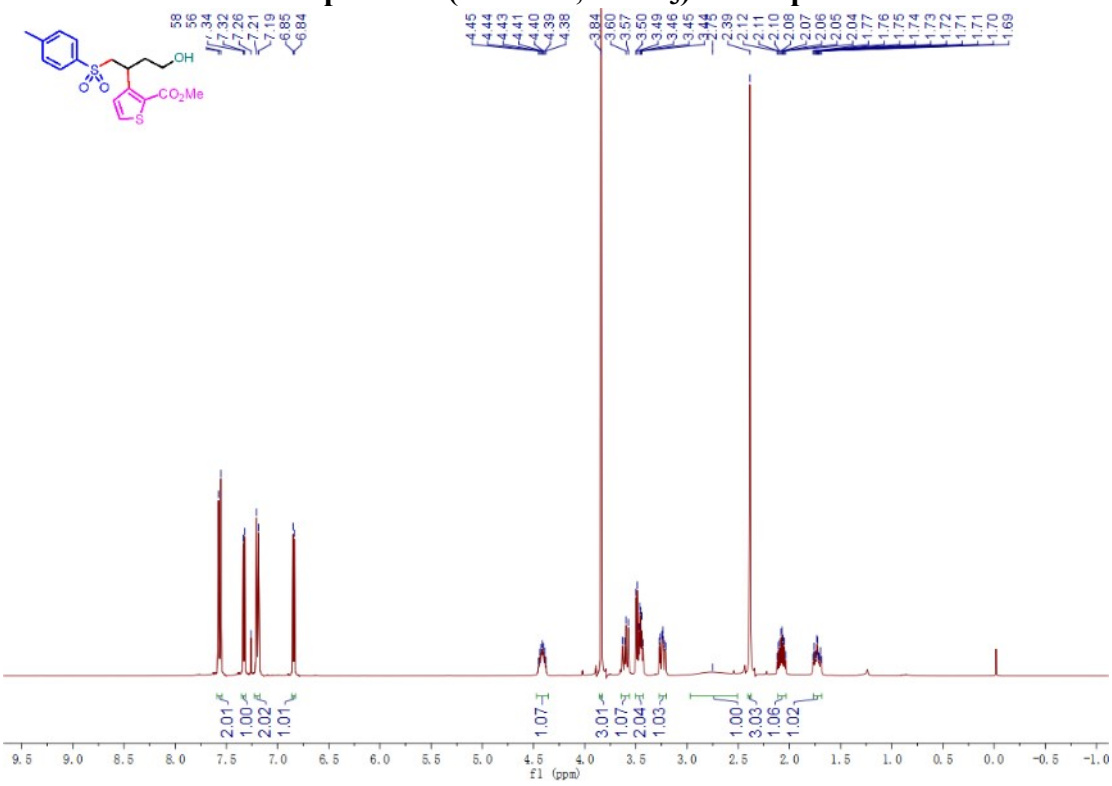
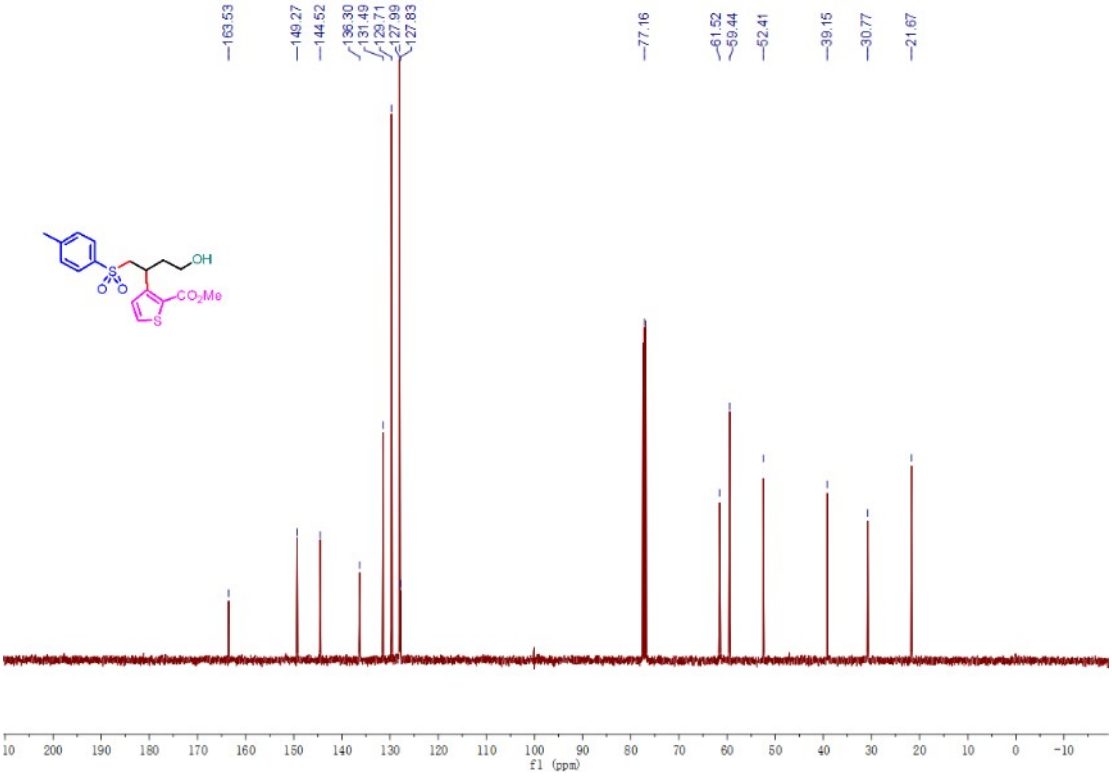
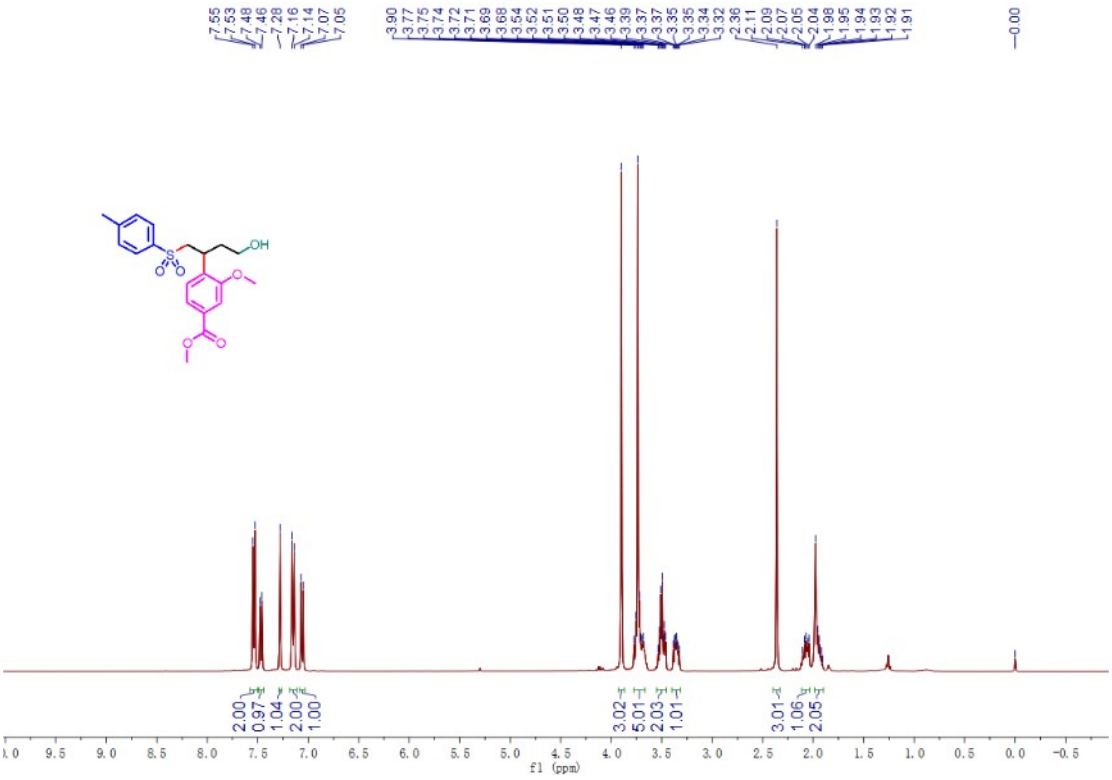


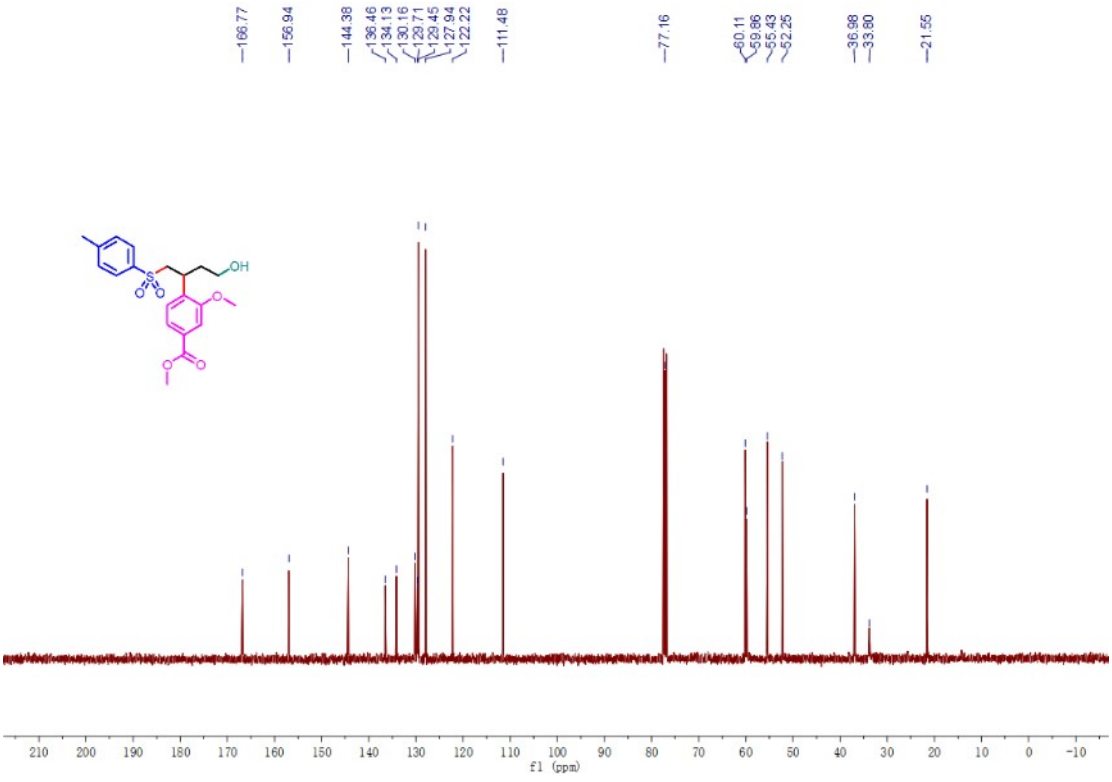
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 3m



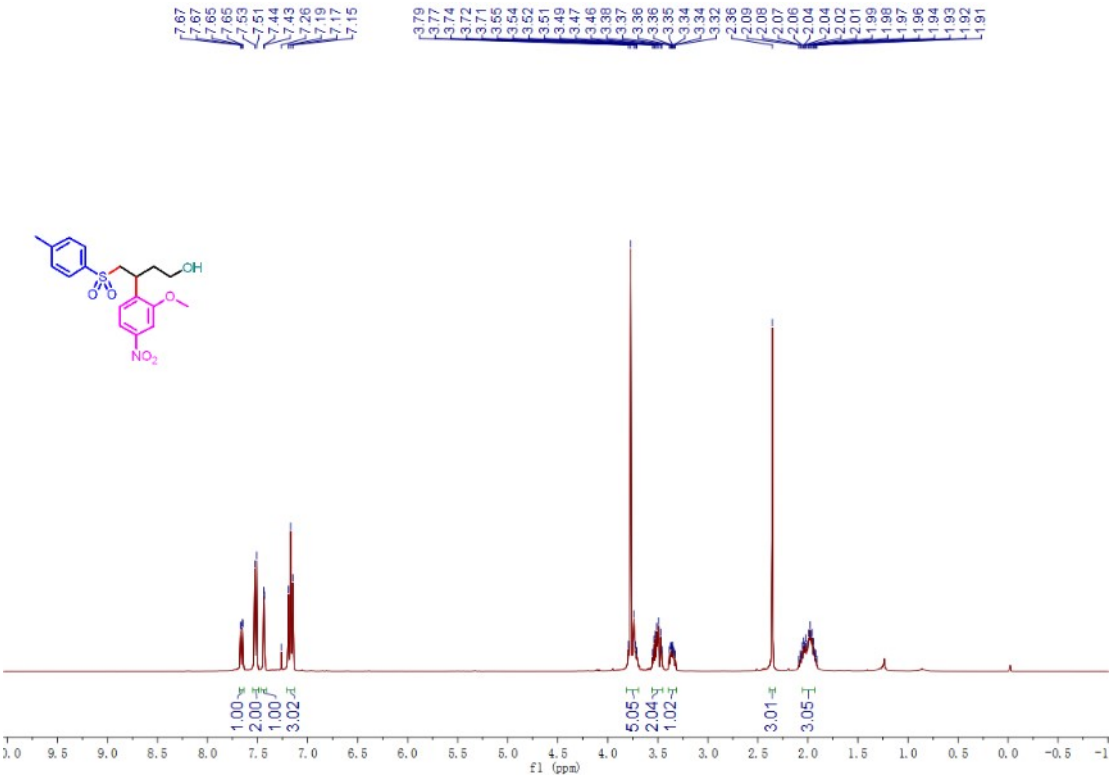
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 3n



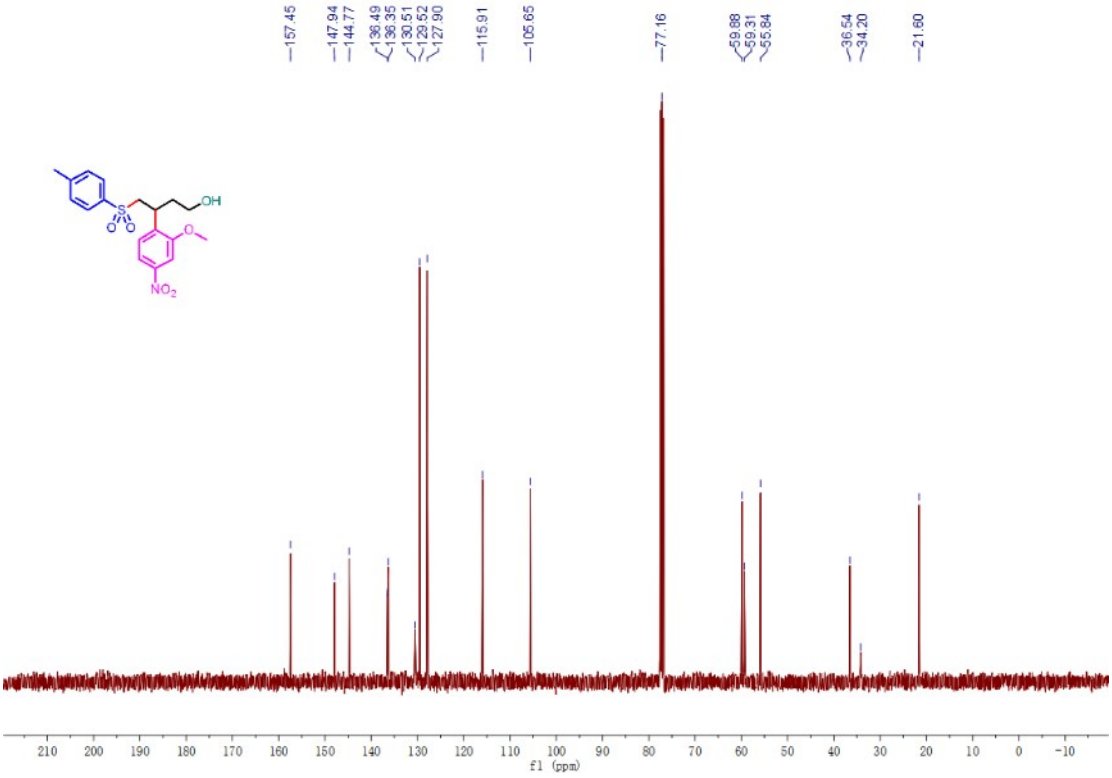
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 3n



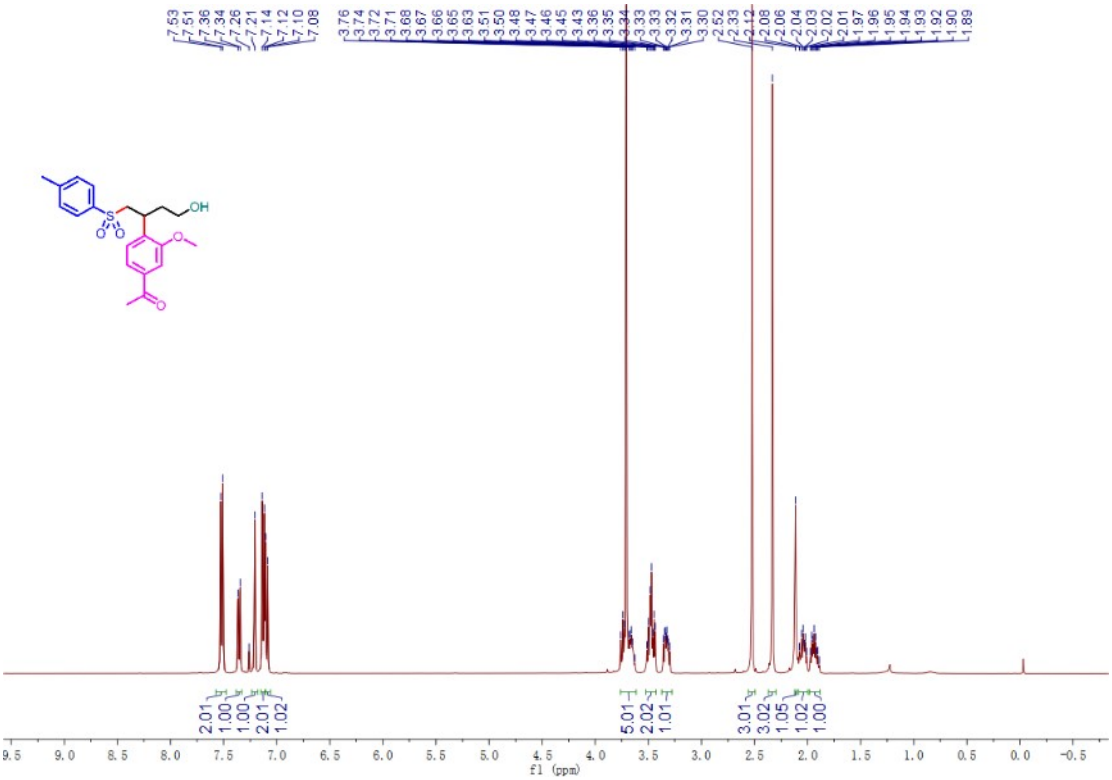
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 3o



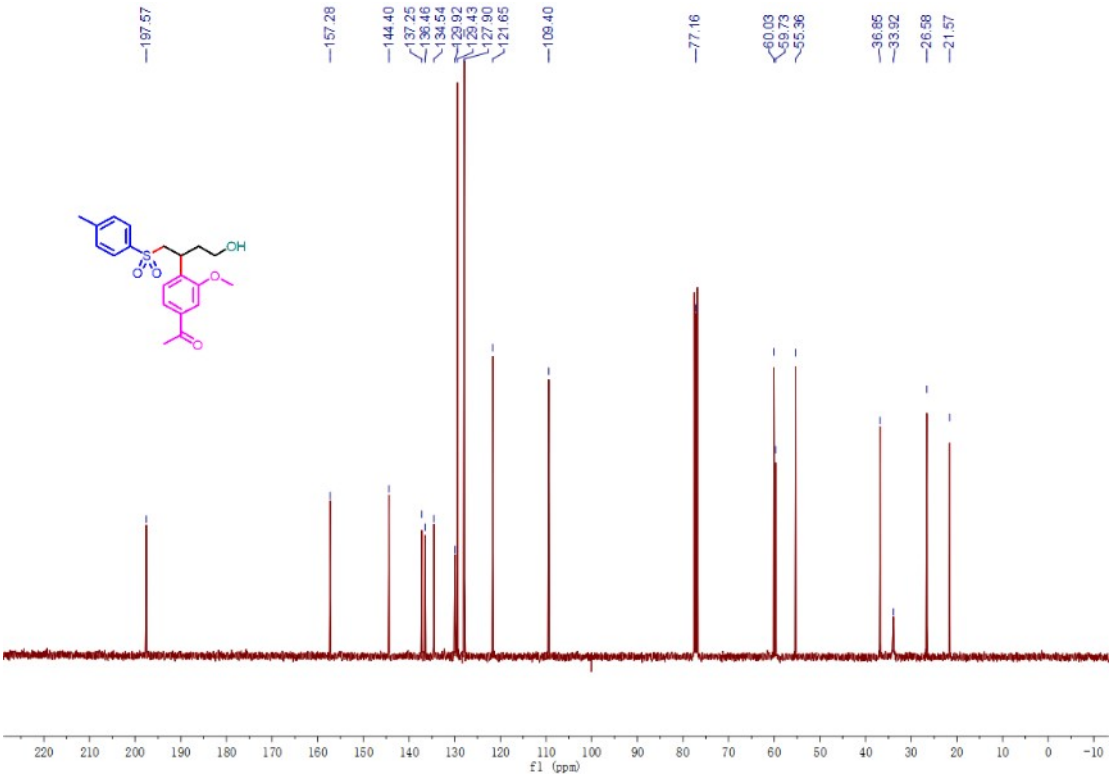
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 3o



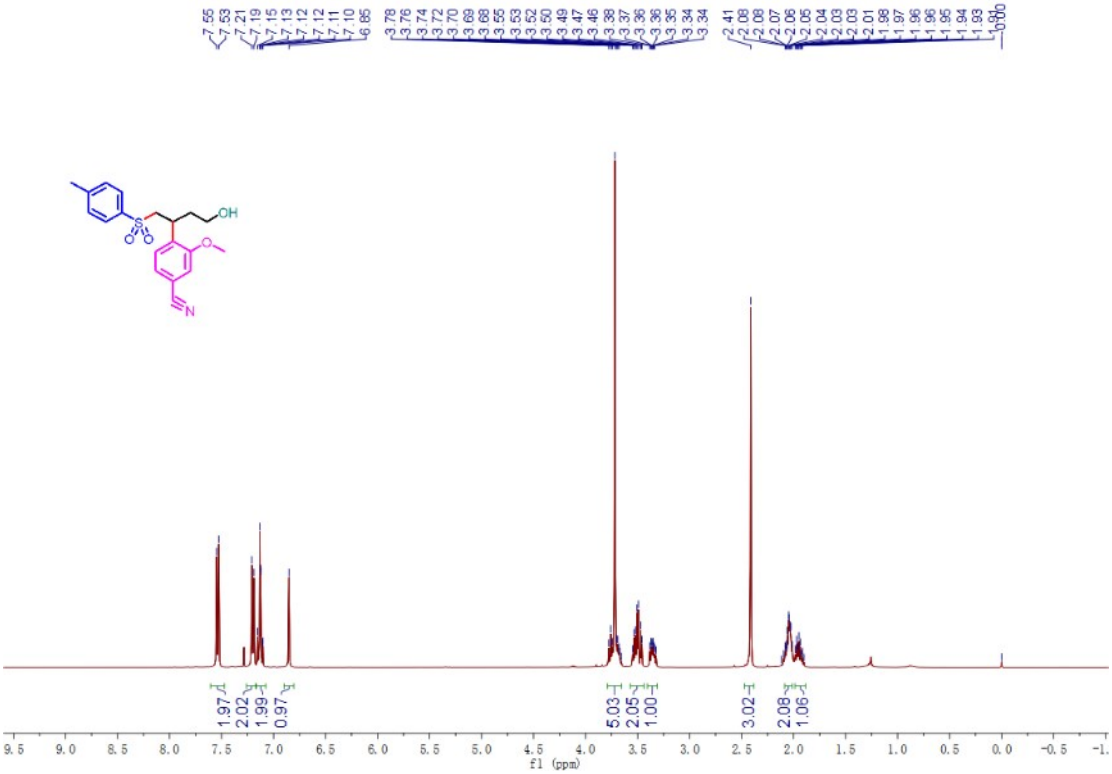
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 3p



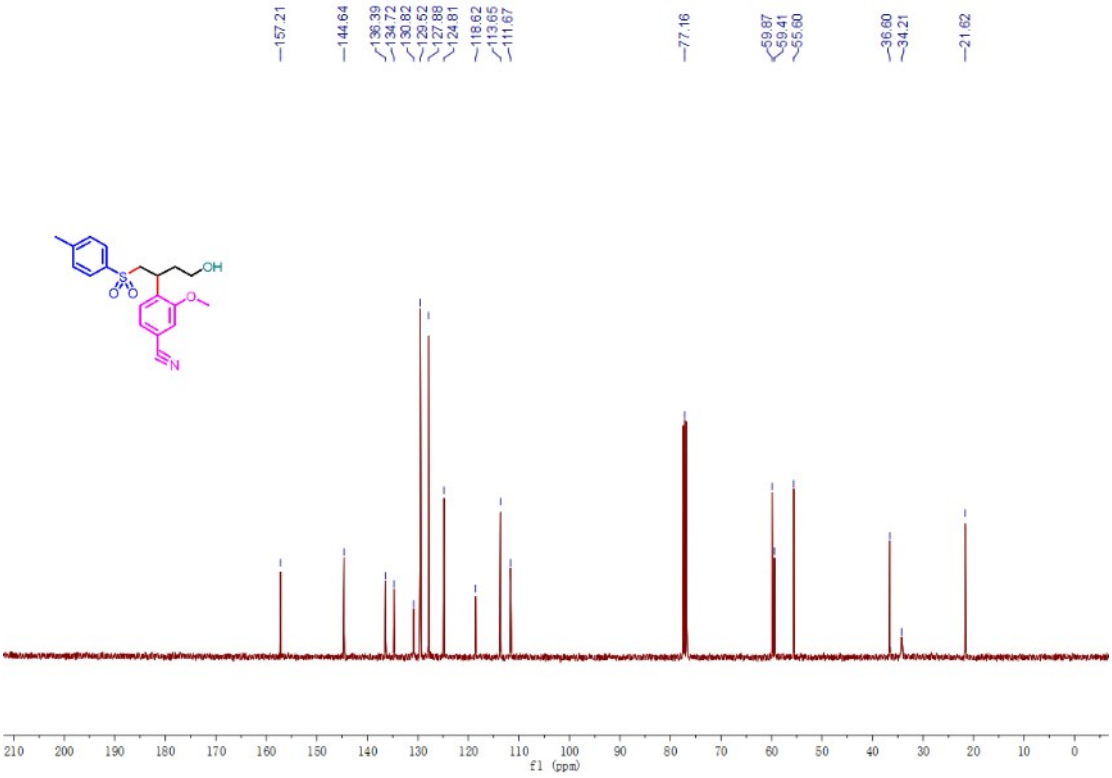
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 3p



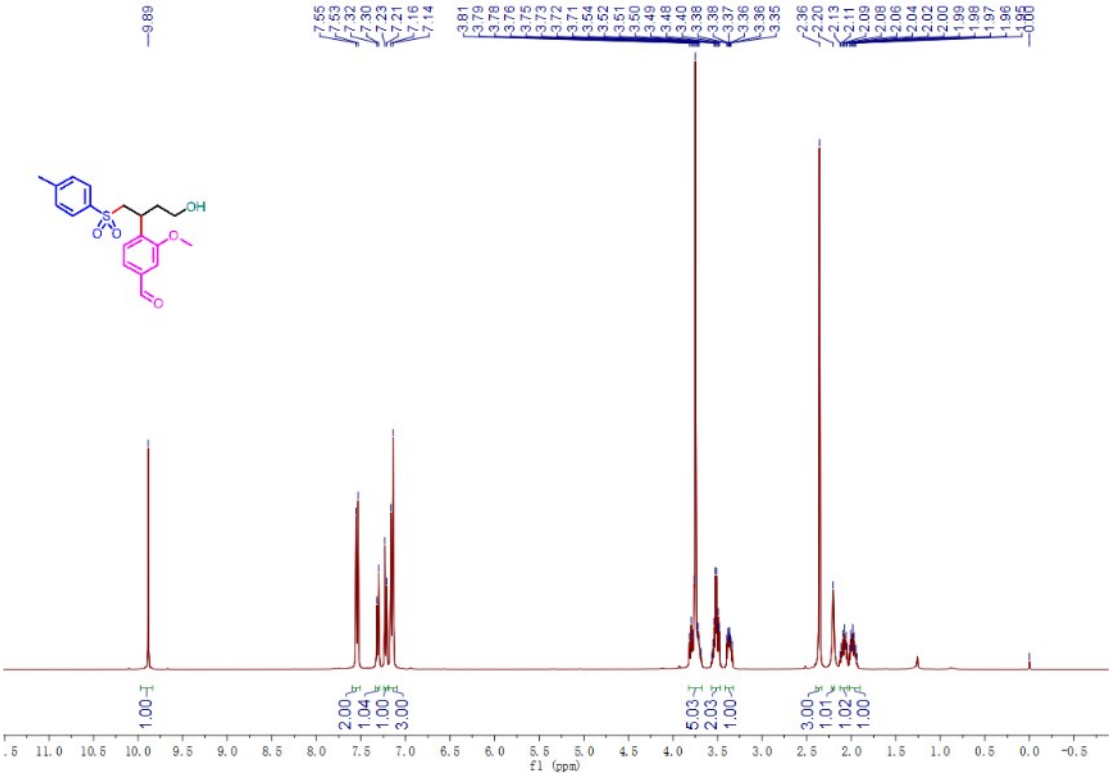
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 3q



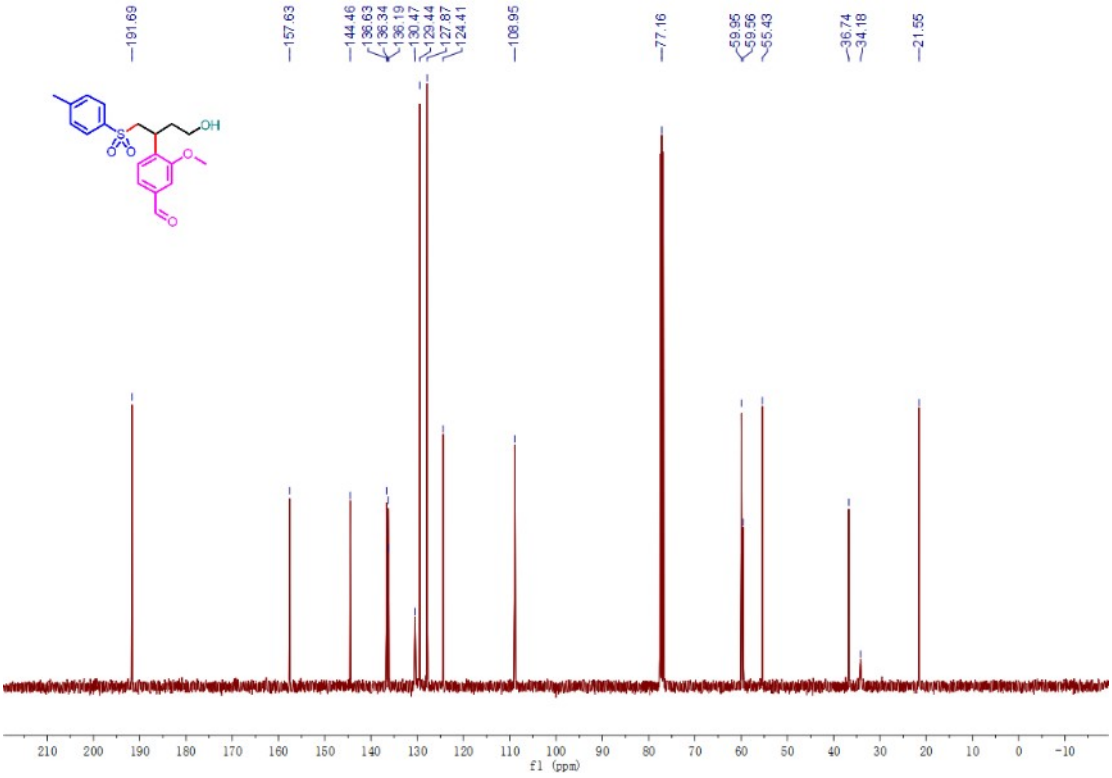
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 3q



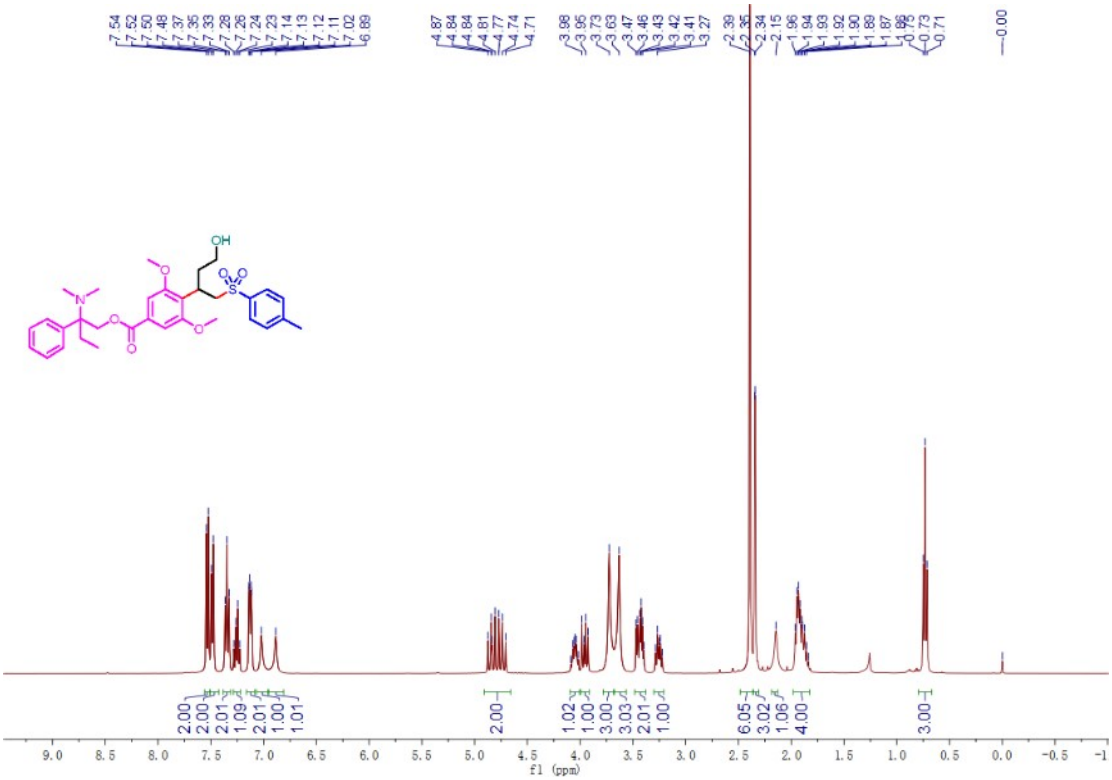
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 3r



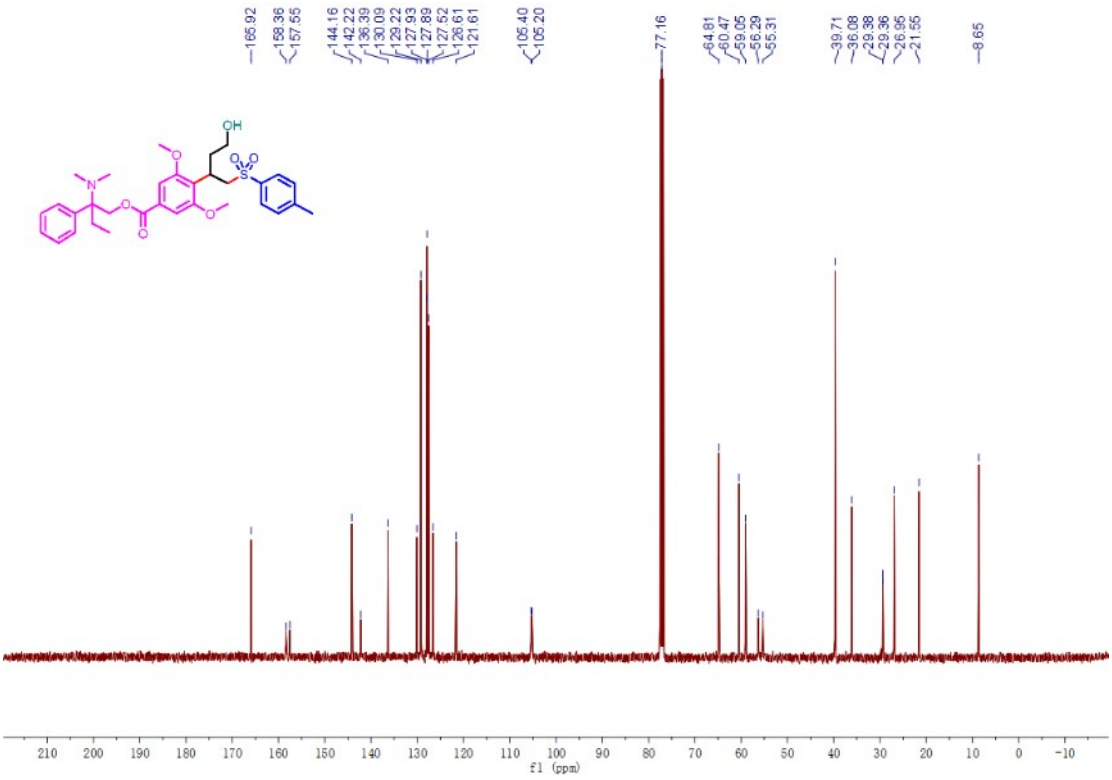
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 3r



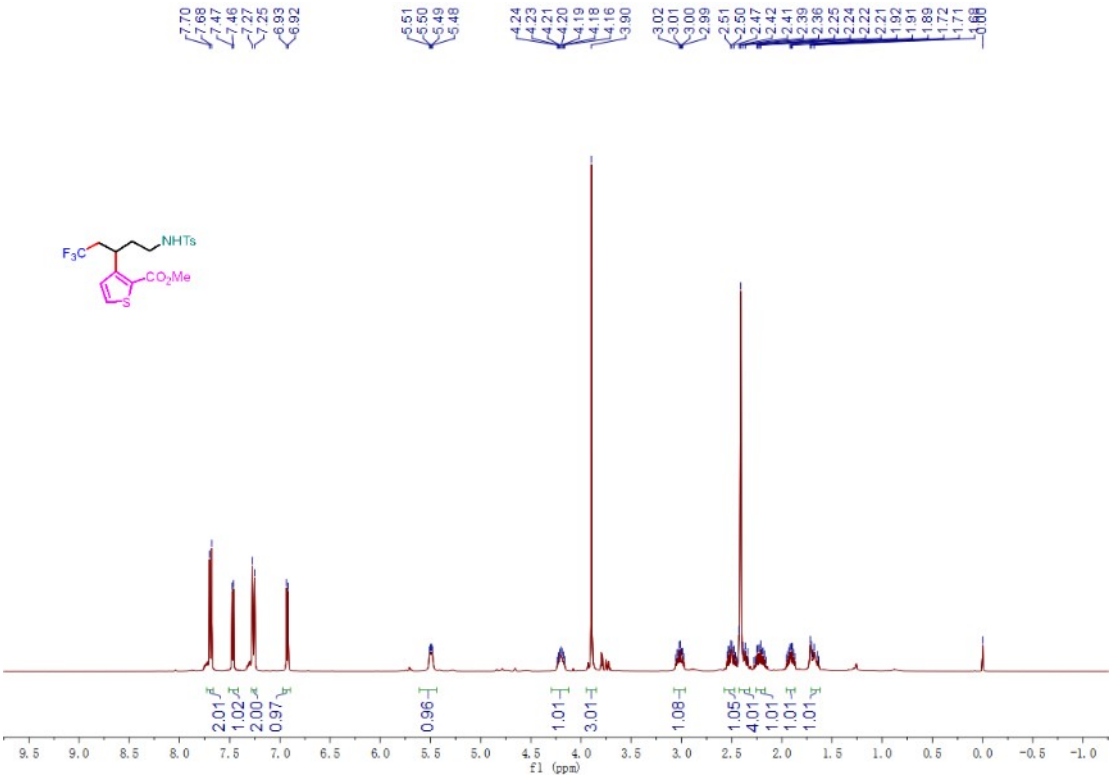
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 3s



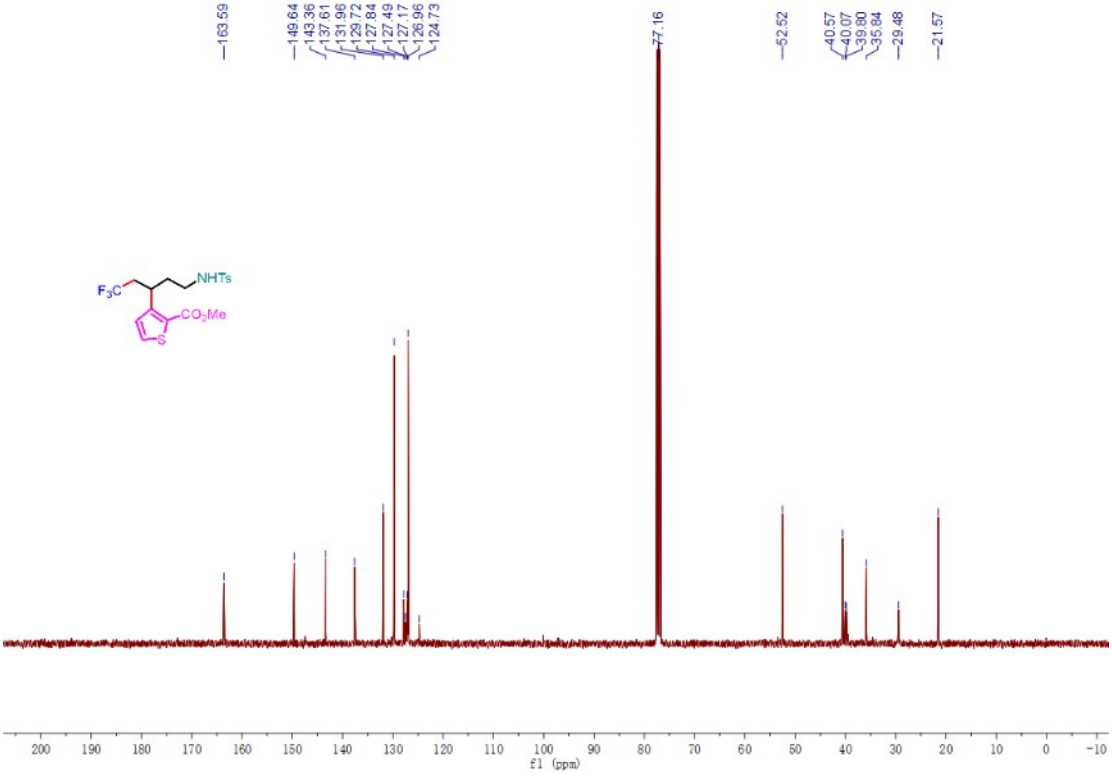
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 3s



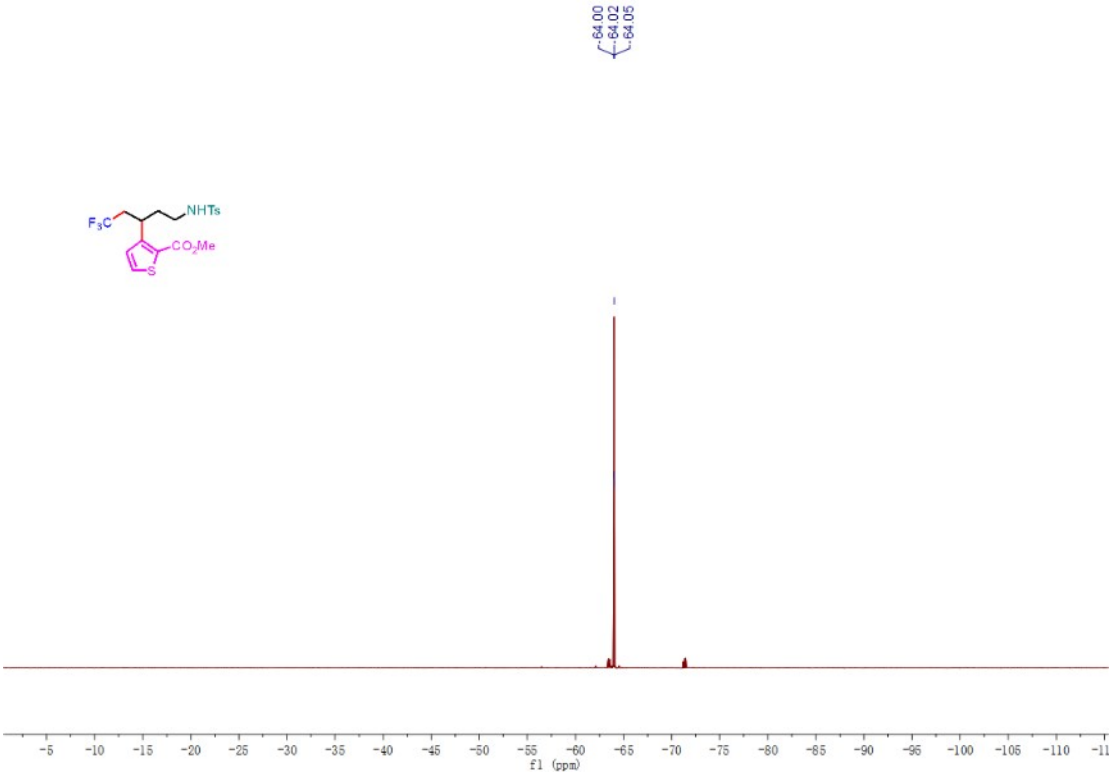
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 3t



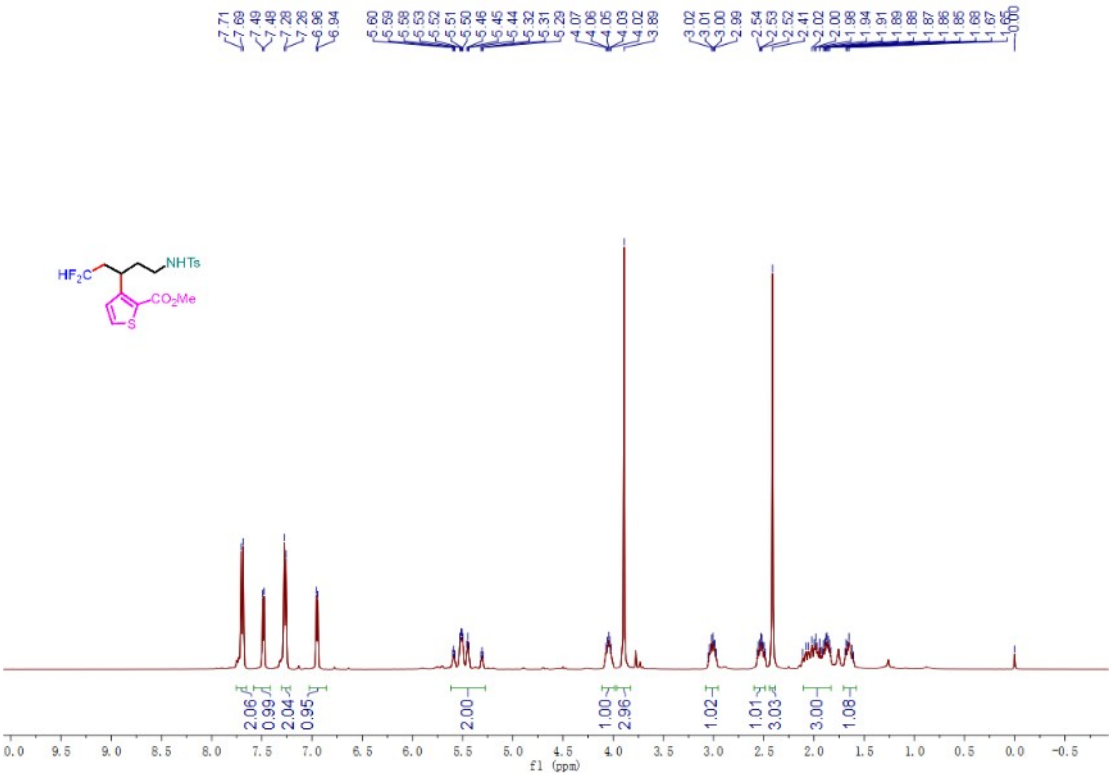
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 3t



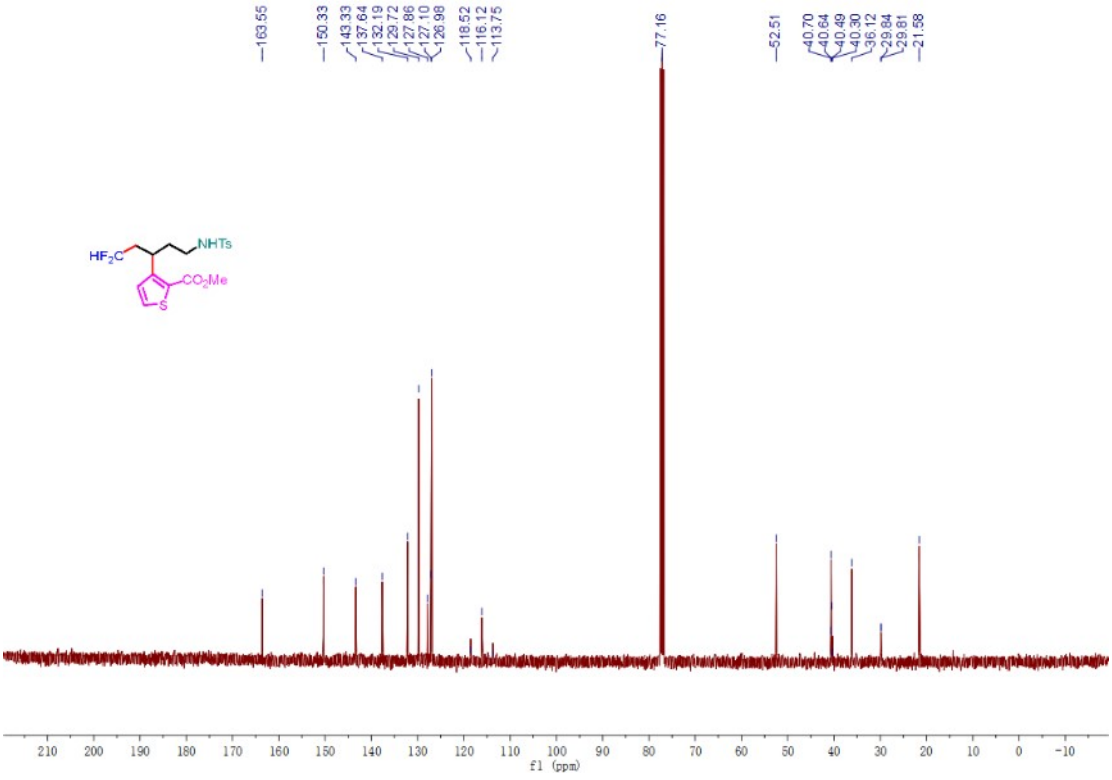
^{19}F NMR spectrum (376MHz, $CDCl_3$) of compound 3t



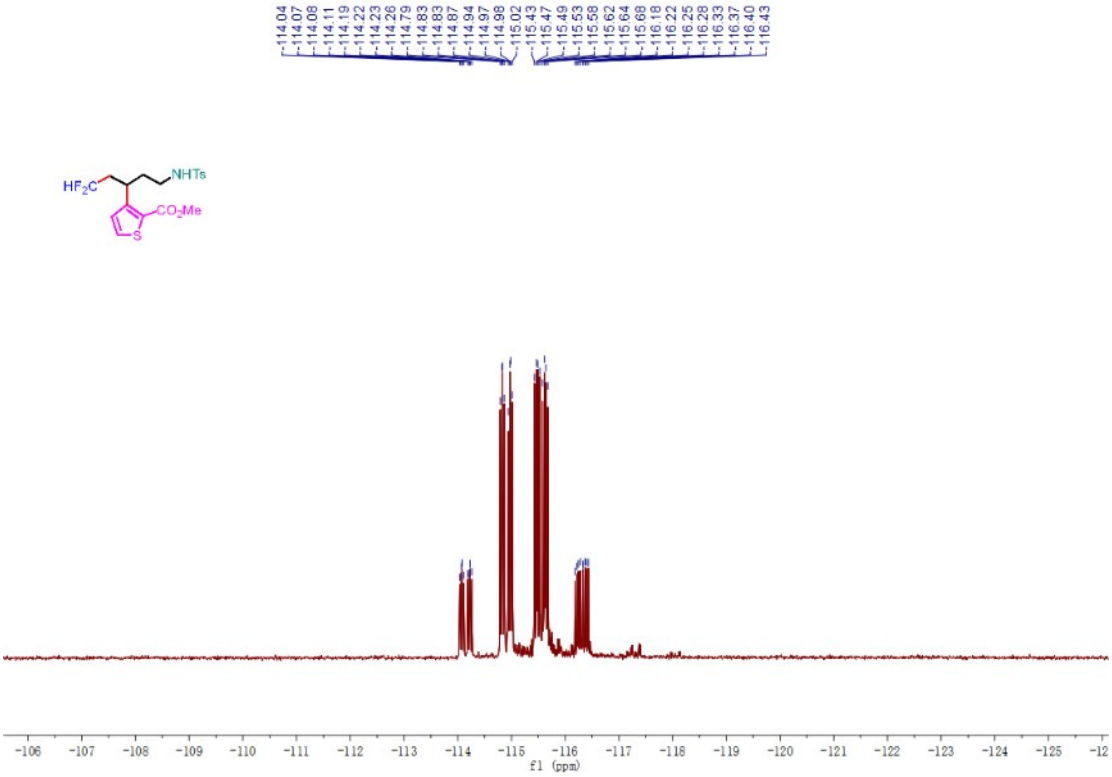
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 3u



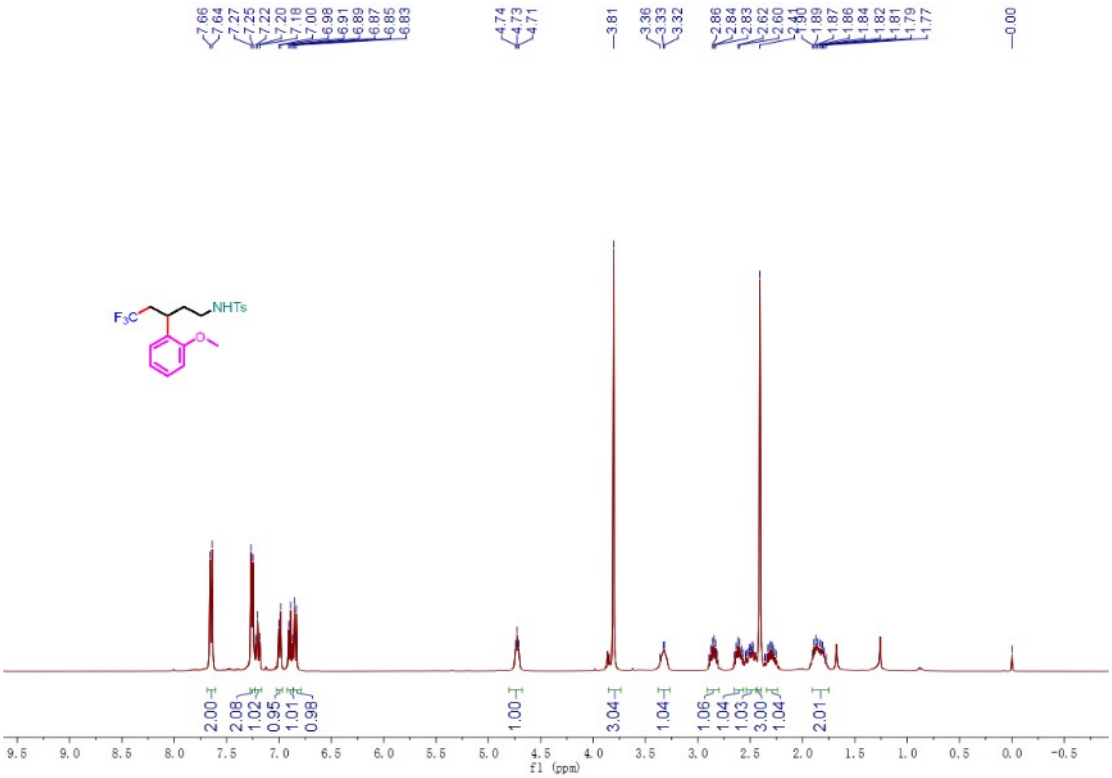
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 3u



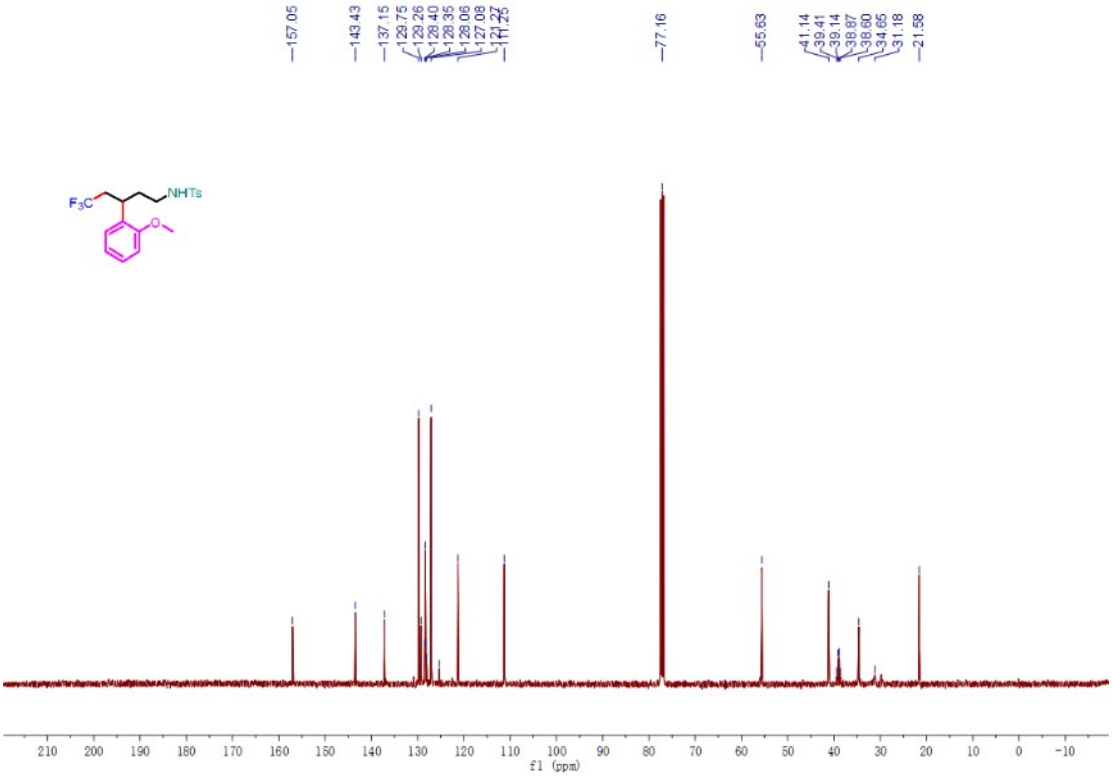
^{19}F NMR spectrum (376MHz, $CDCl_3$) of compound 3u



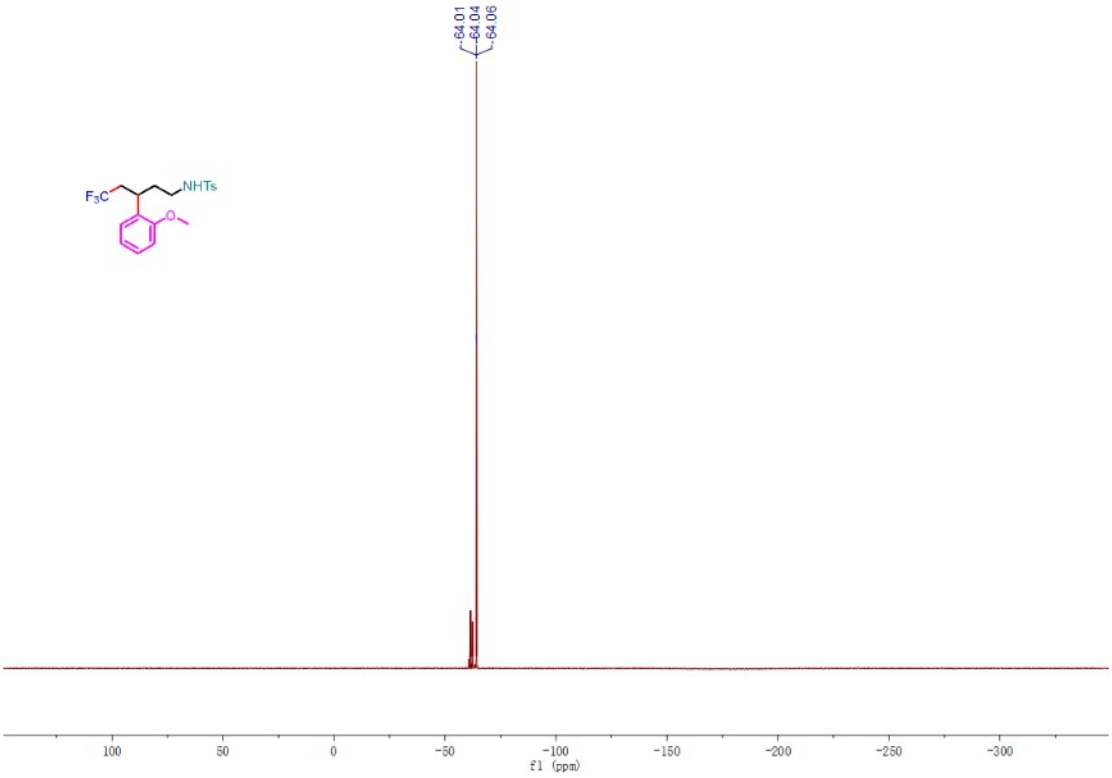
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 3v



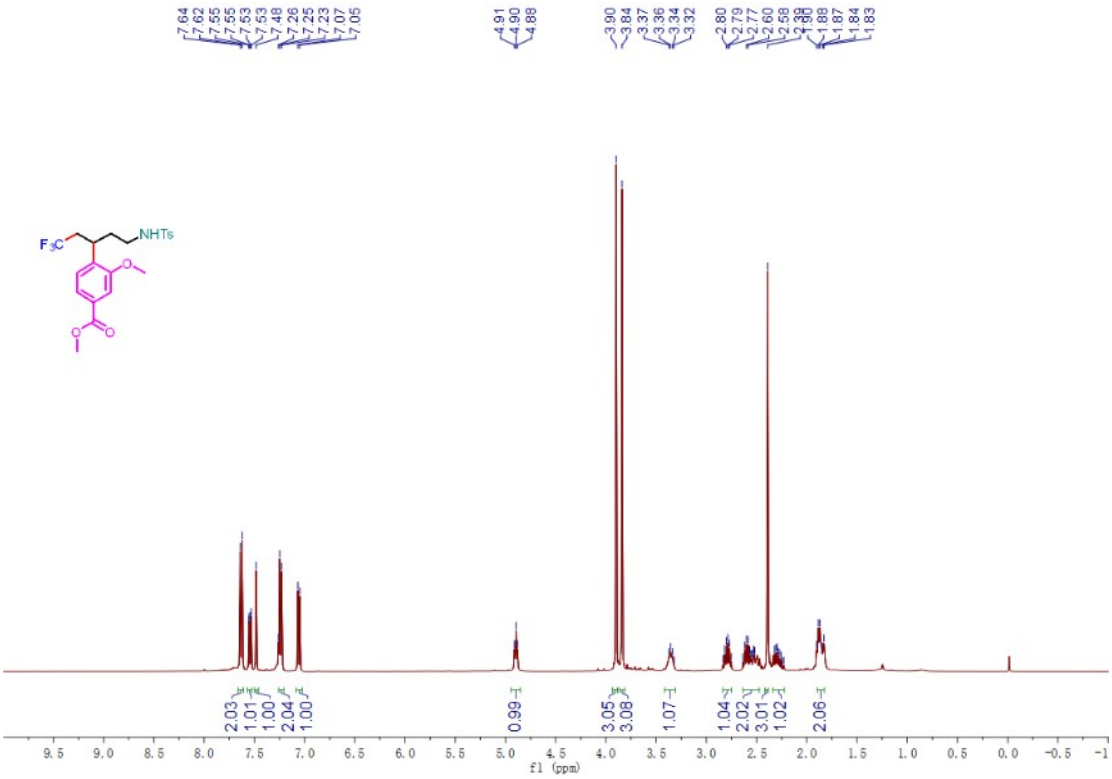
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 3v



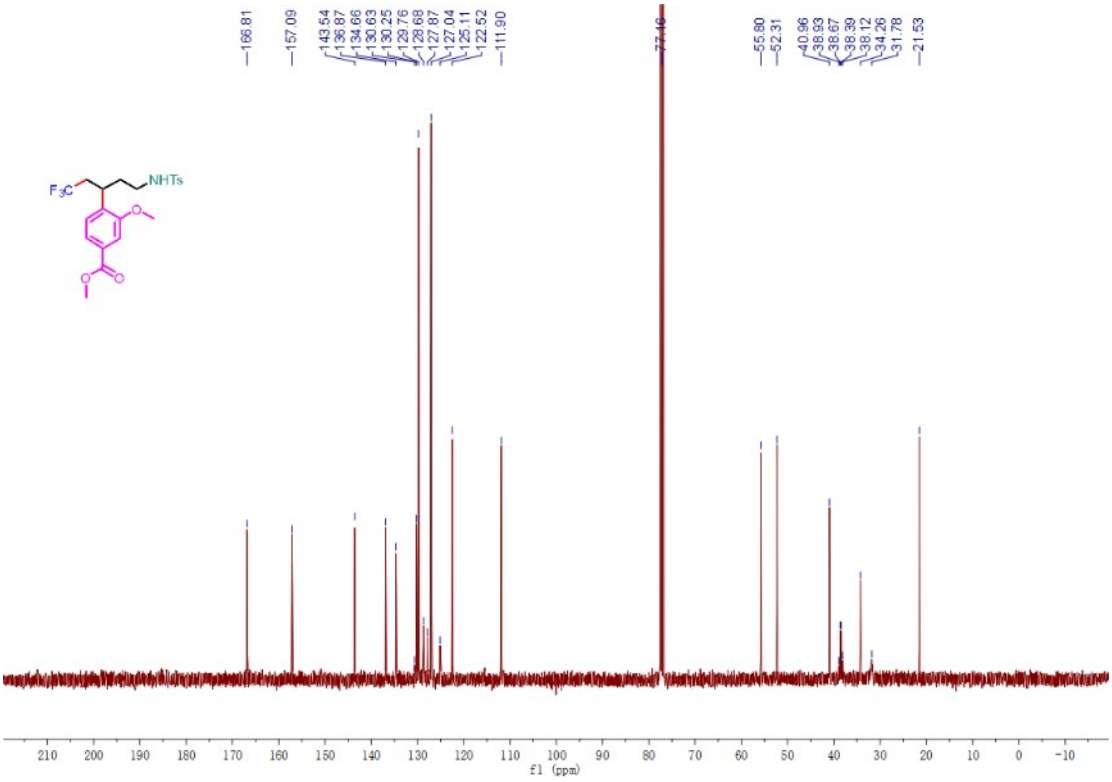
^{19}F NMR spectrum (376MHz, $CDCl_3$) of compound 3v



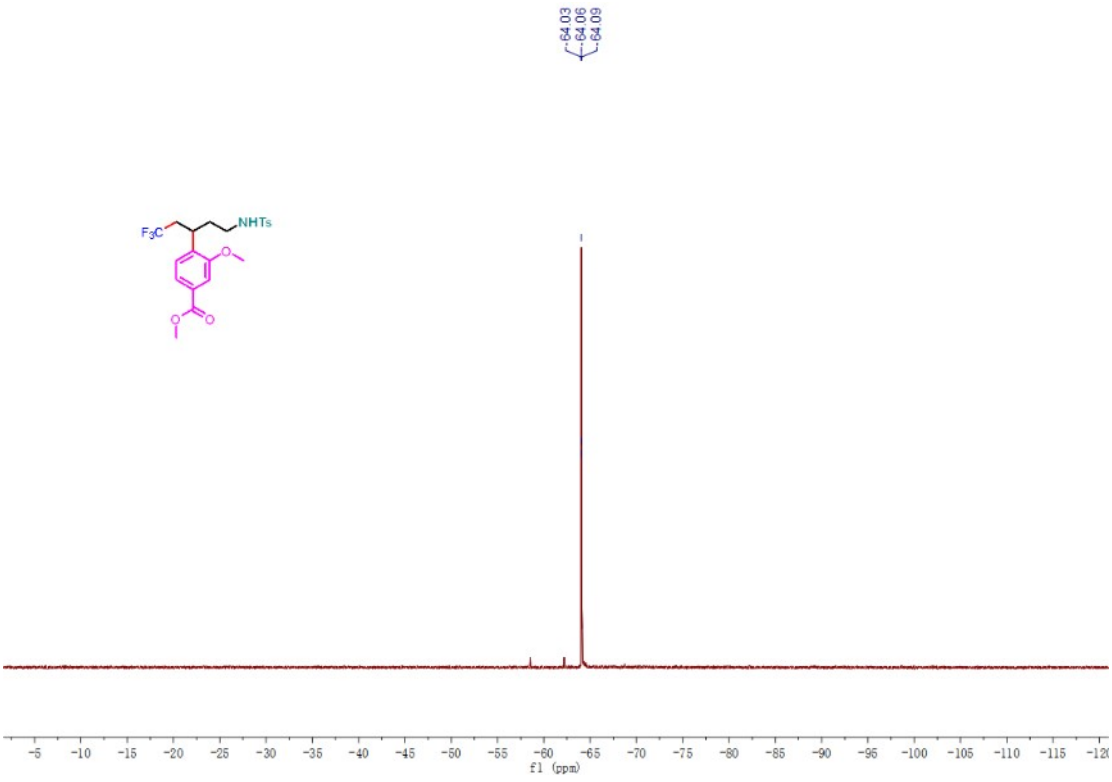
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 3w



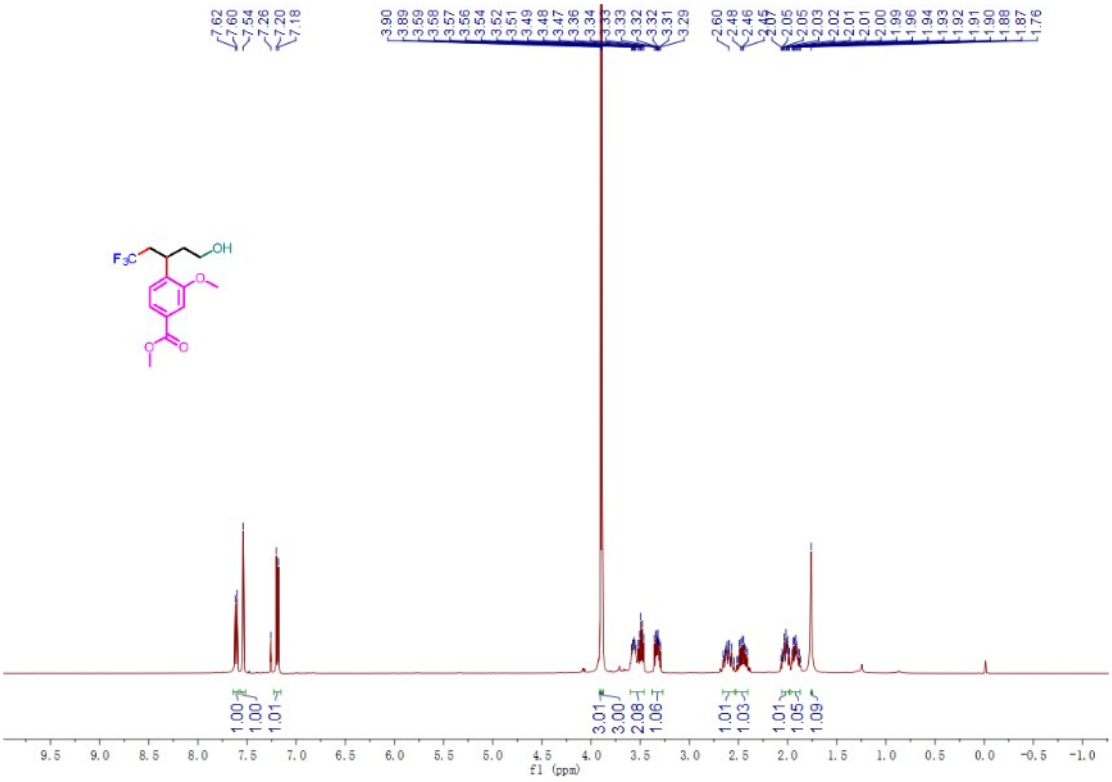
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 3w



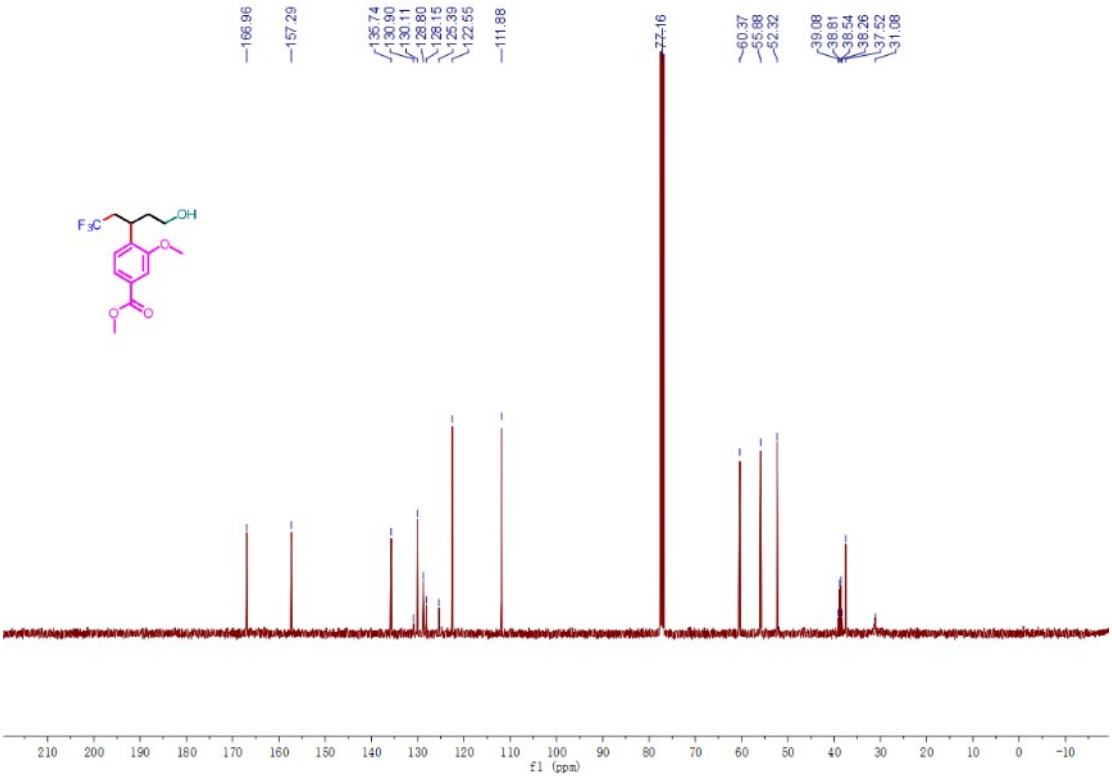
^{19}F NMR spectrum (376MHz, $CDCl_3$) of compound 3w



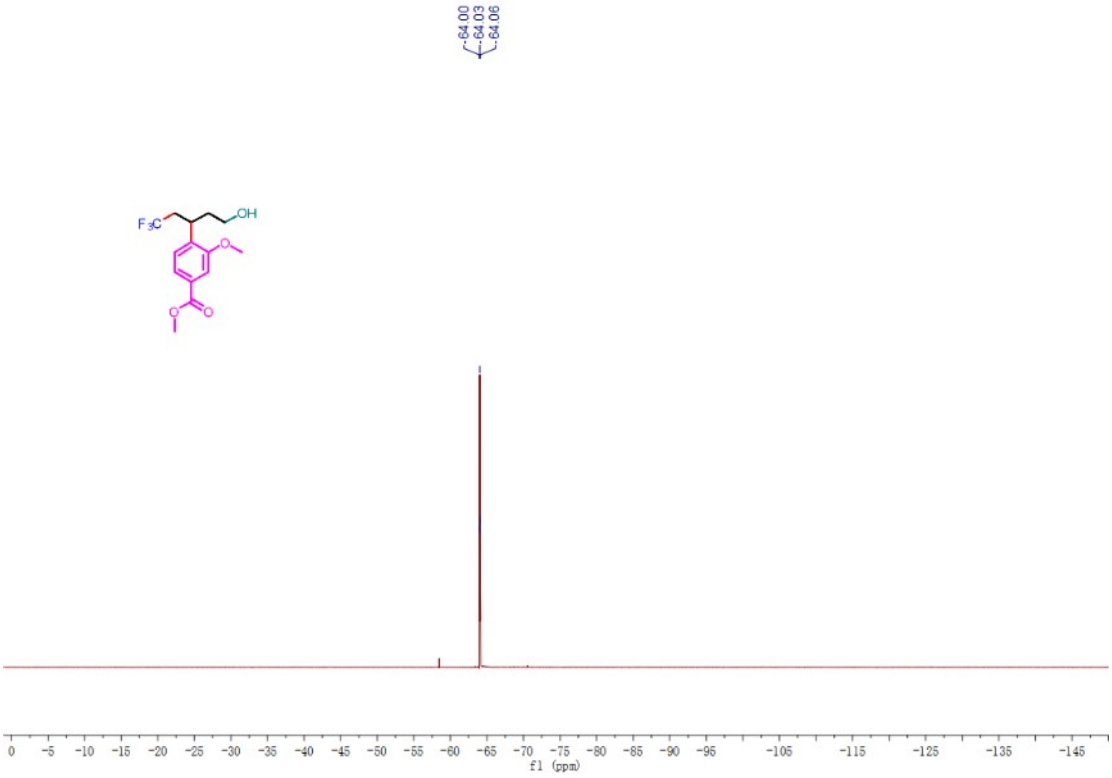
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 3x



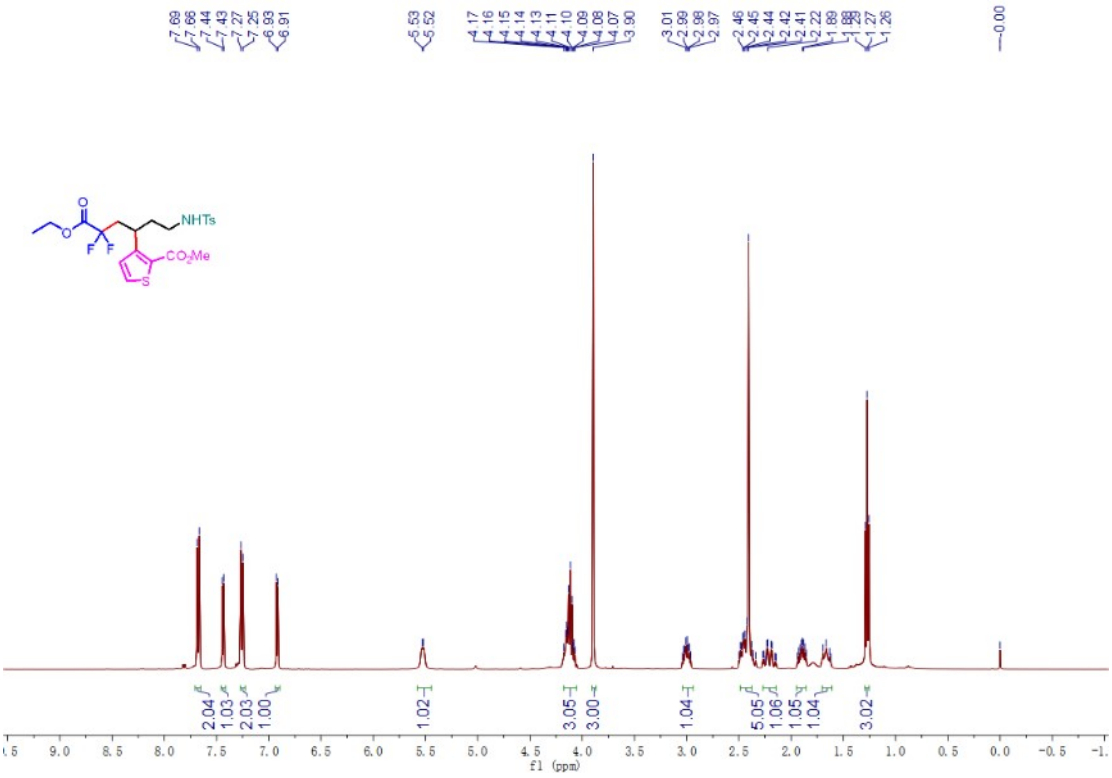
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 3x



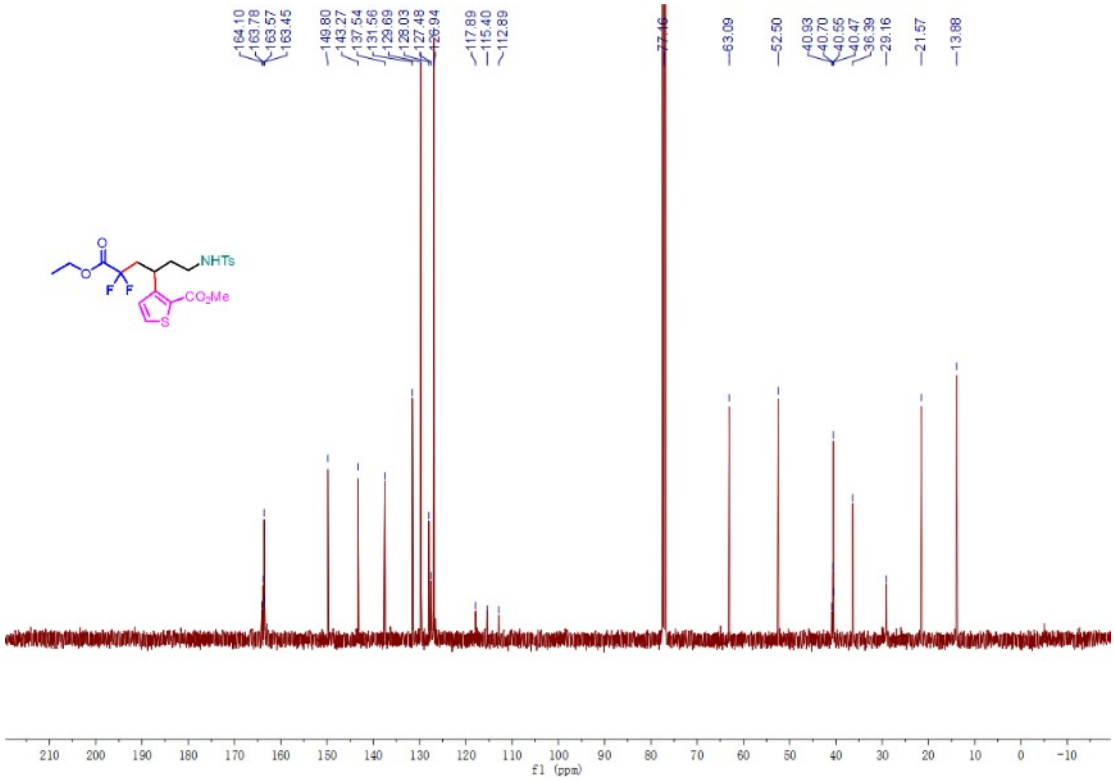
^{19}F NMR spectrum (376MHz, $CDCl_3$) of compound 3x



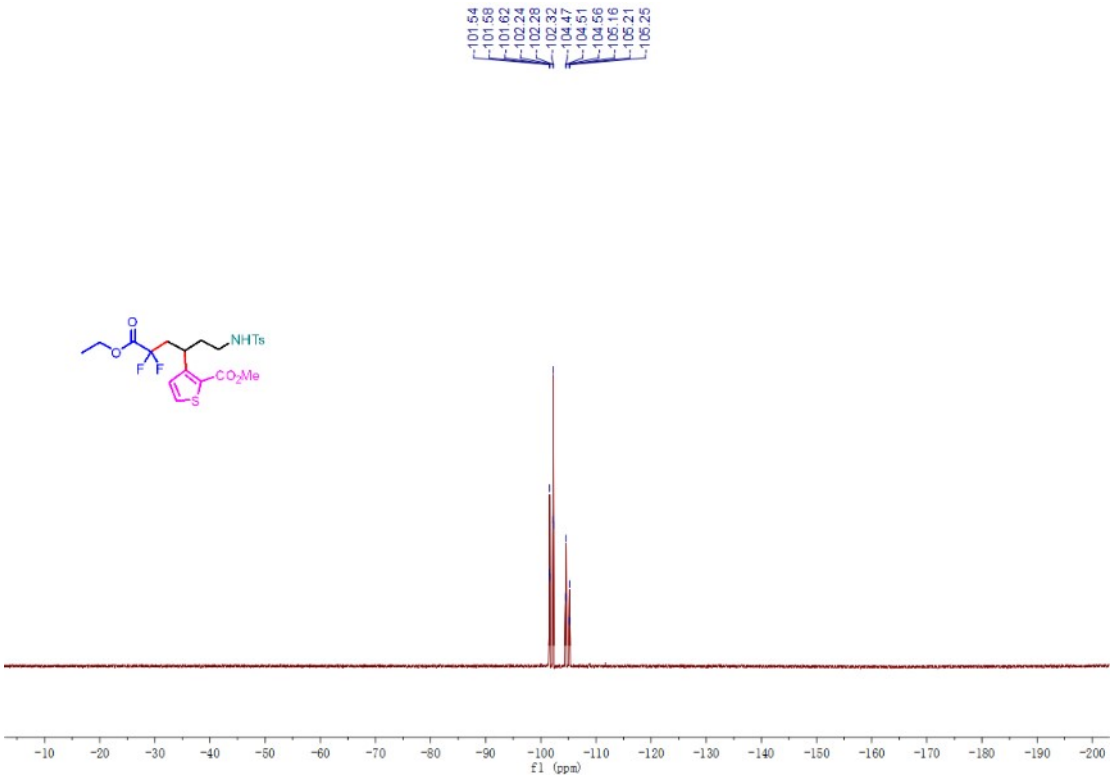
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 3y



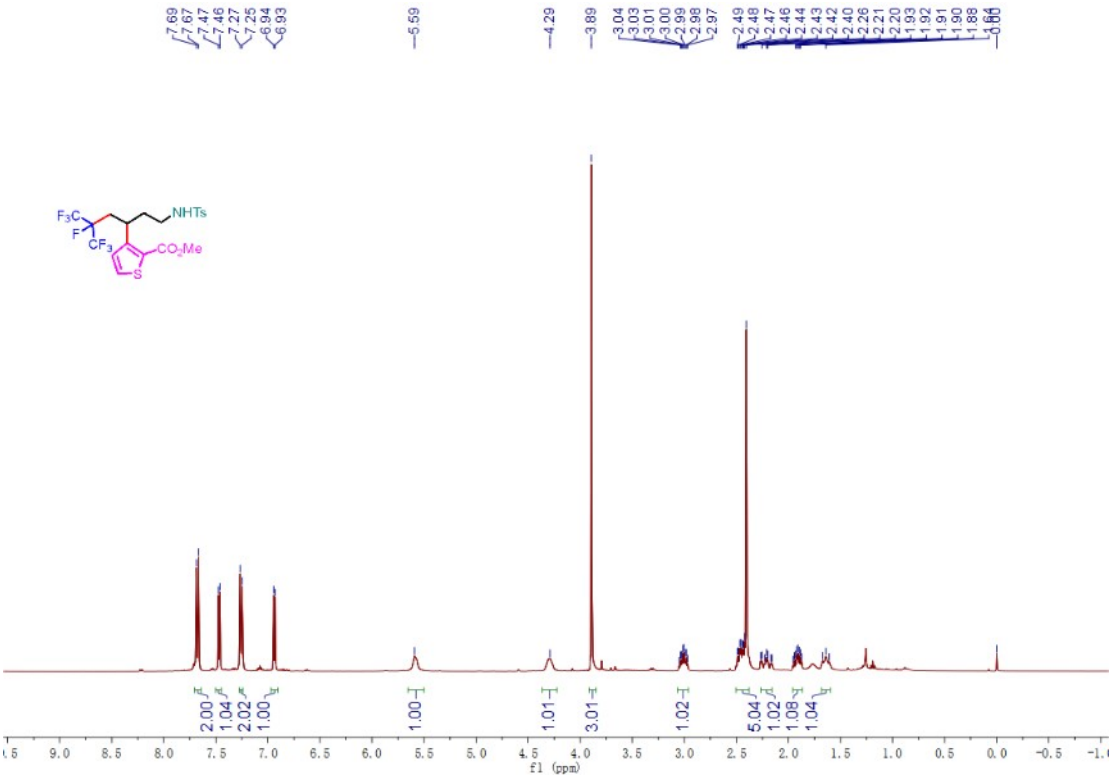
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 3y



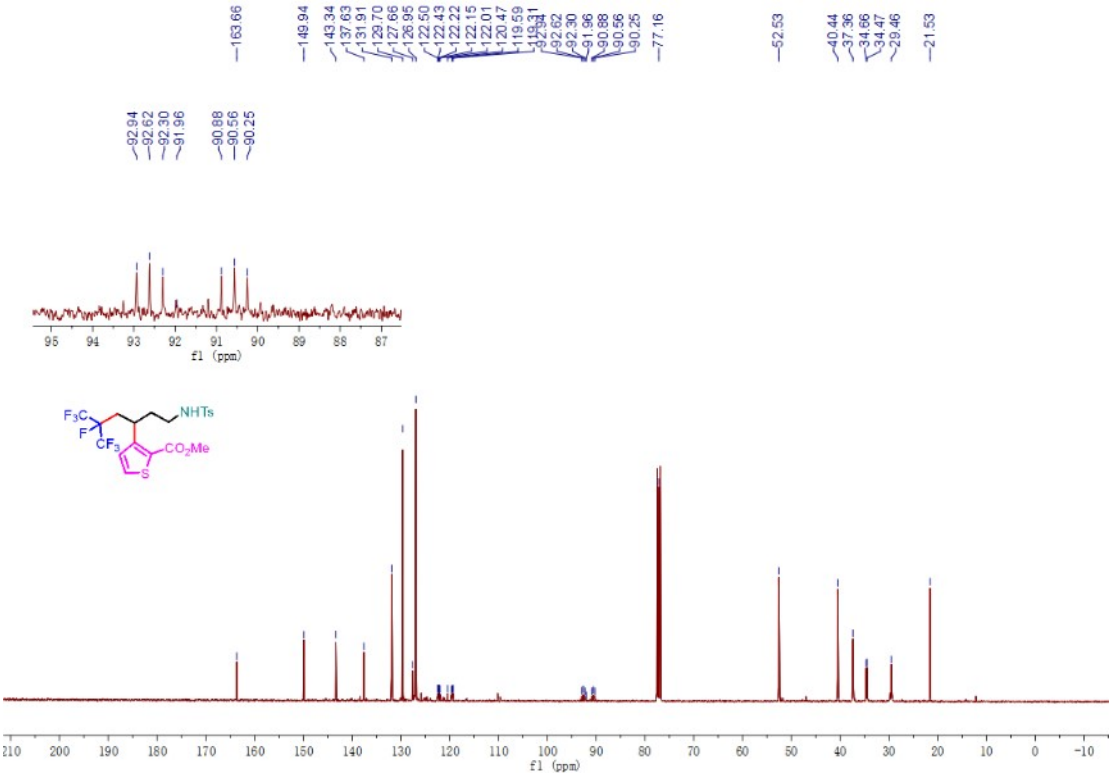
^{19}F NMR spectrum (376MHz, $CDCl_3$) of compound 3y



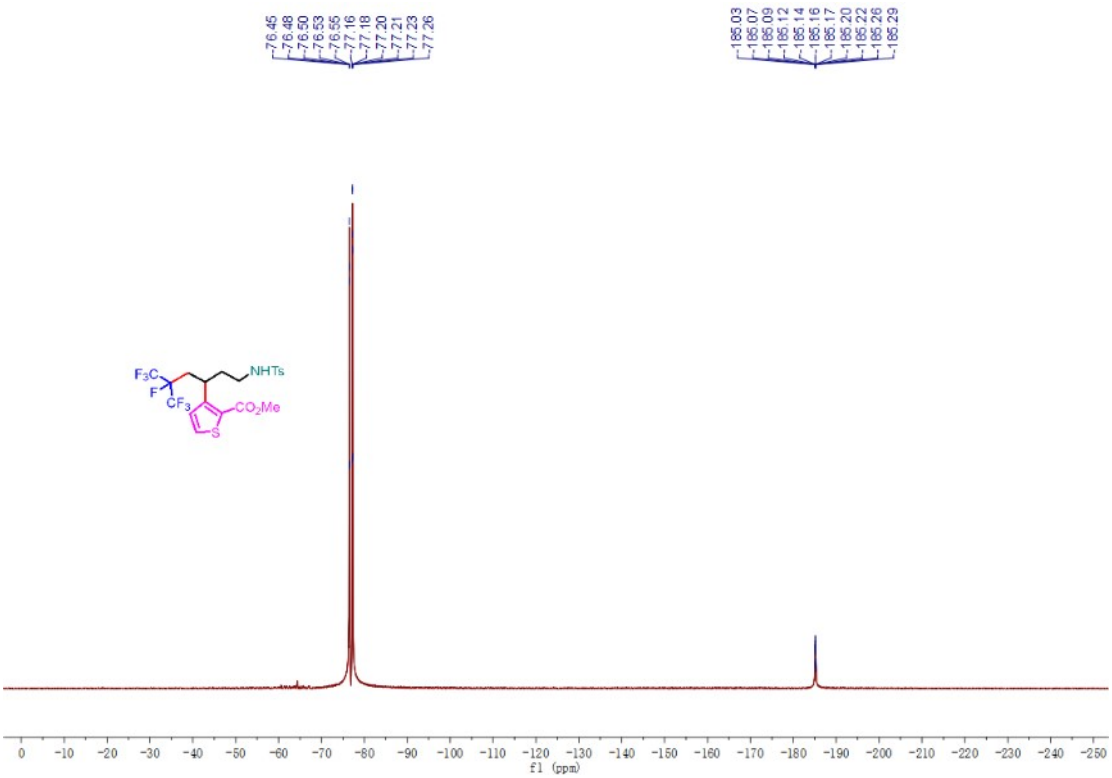
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 3z



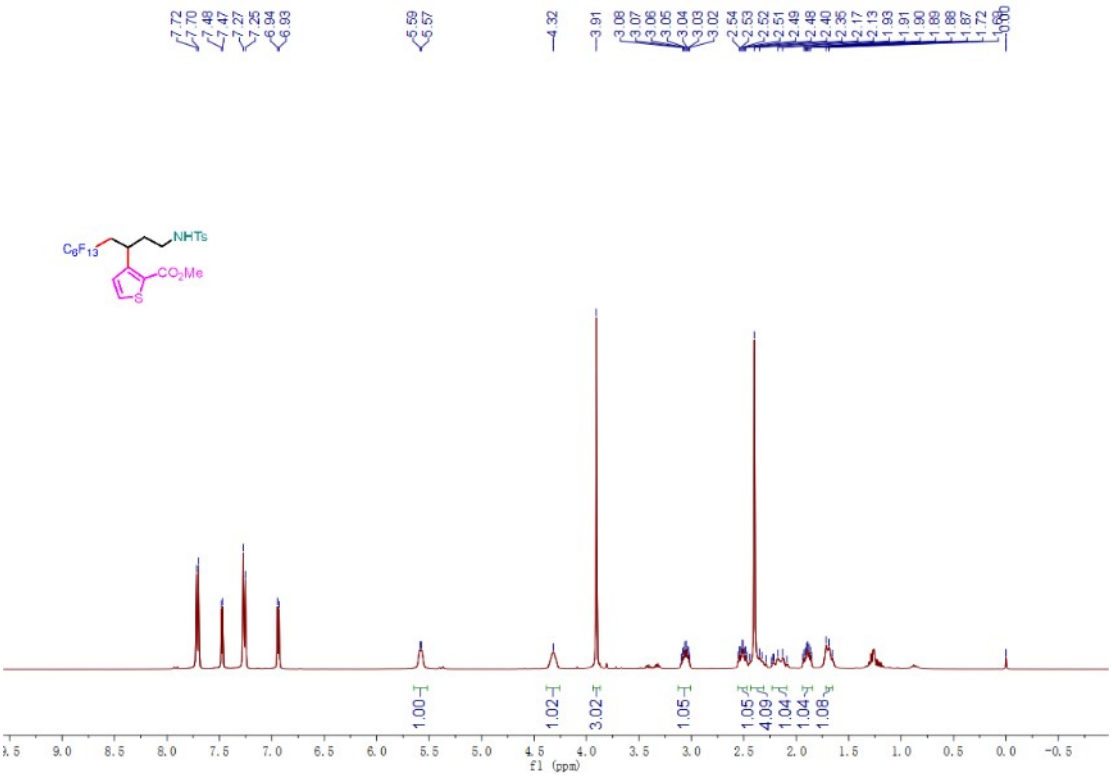
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 3z



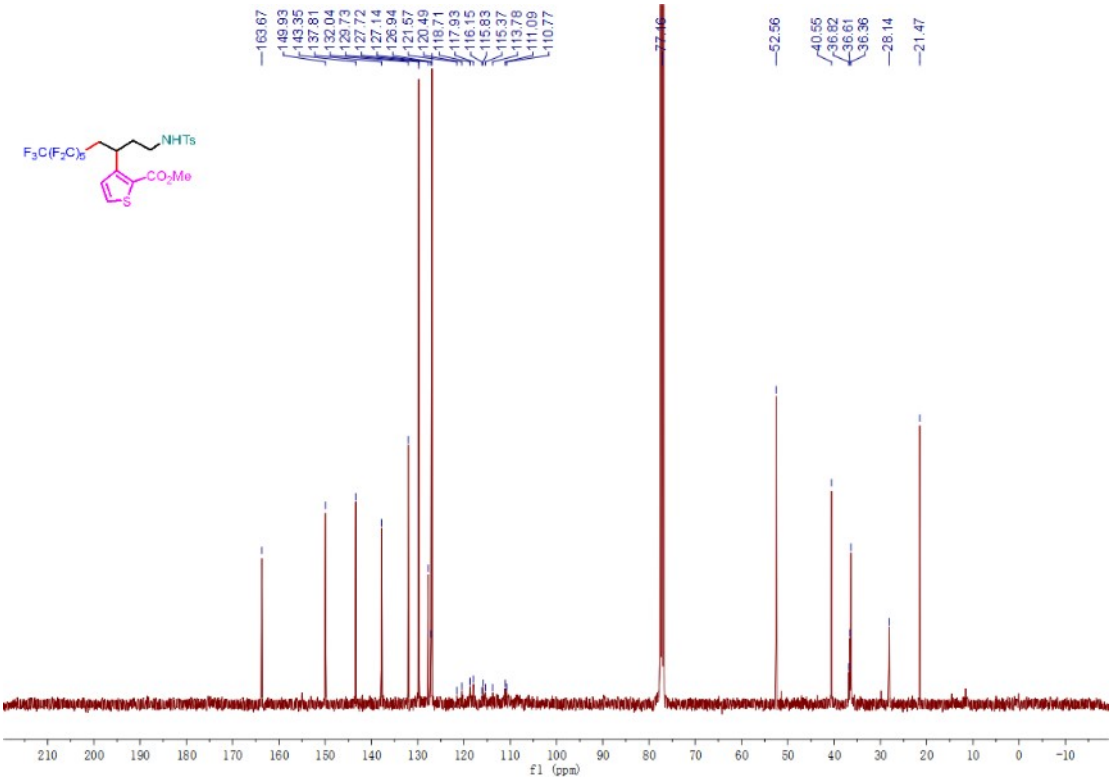
^{19}F NMR spectrum (376MHz, $CDCl_3$) of compound 3z



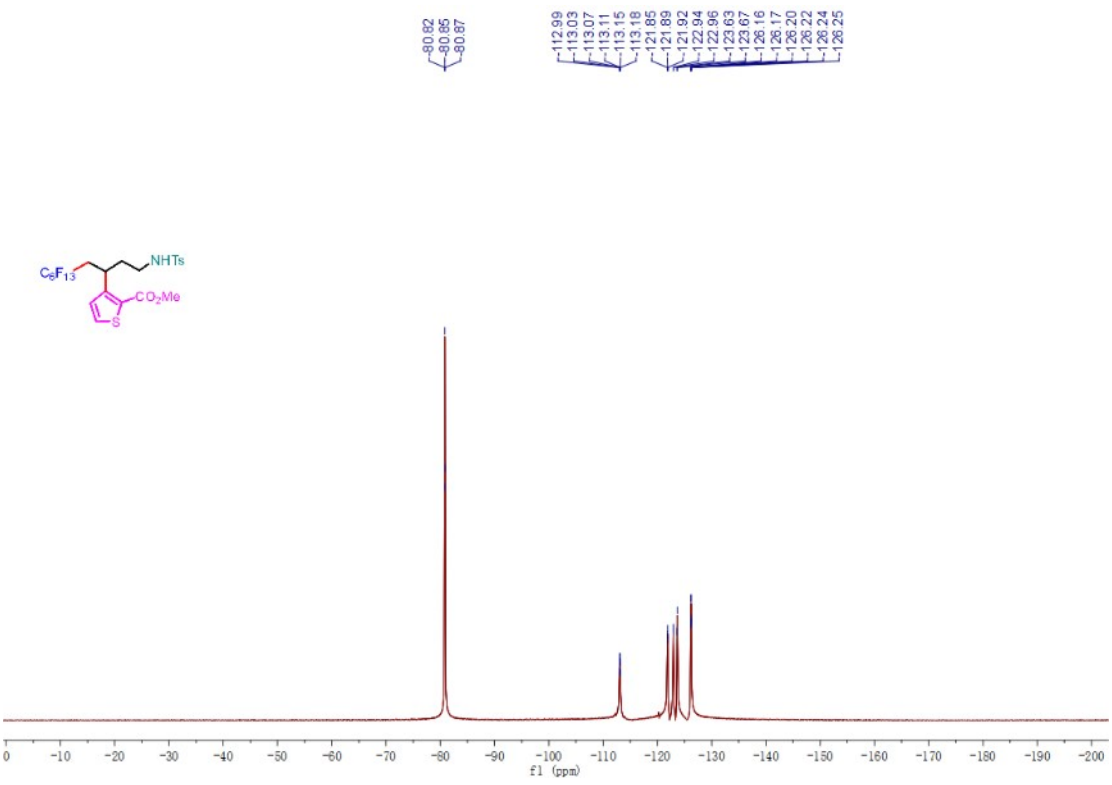
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 3ab



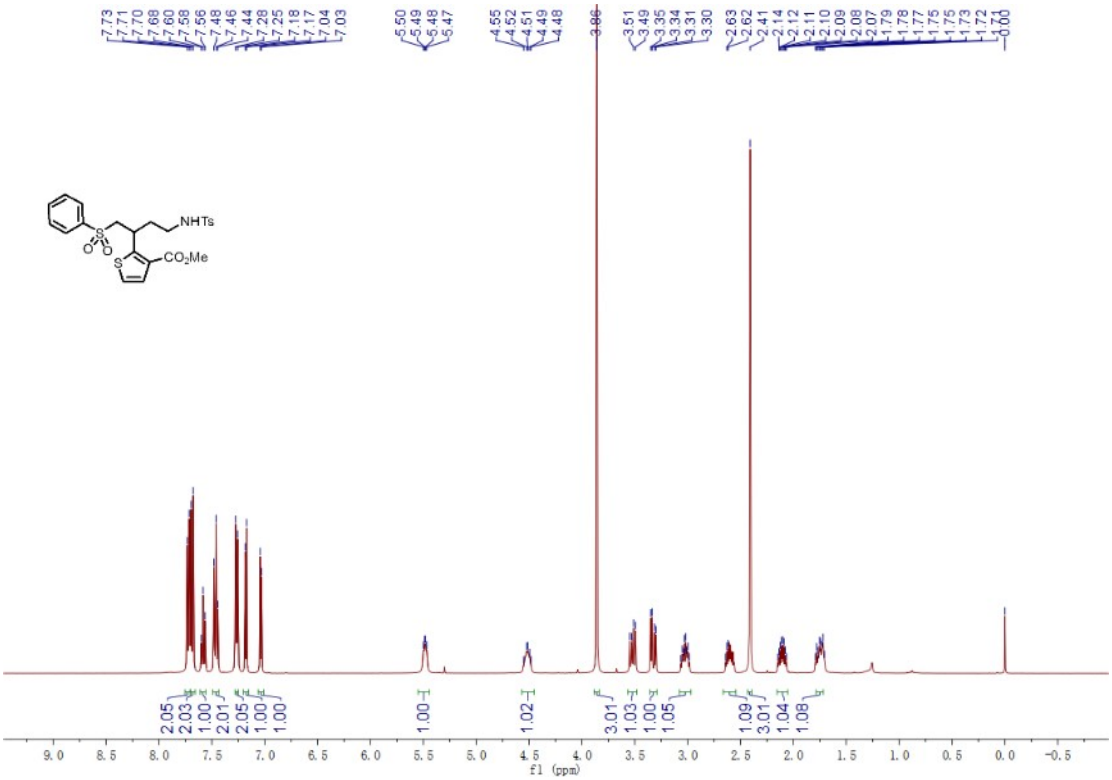
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 3ab



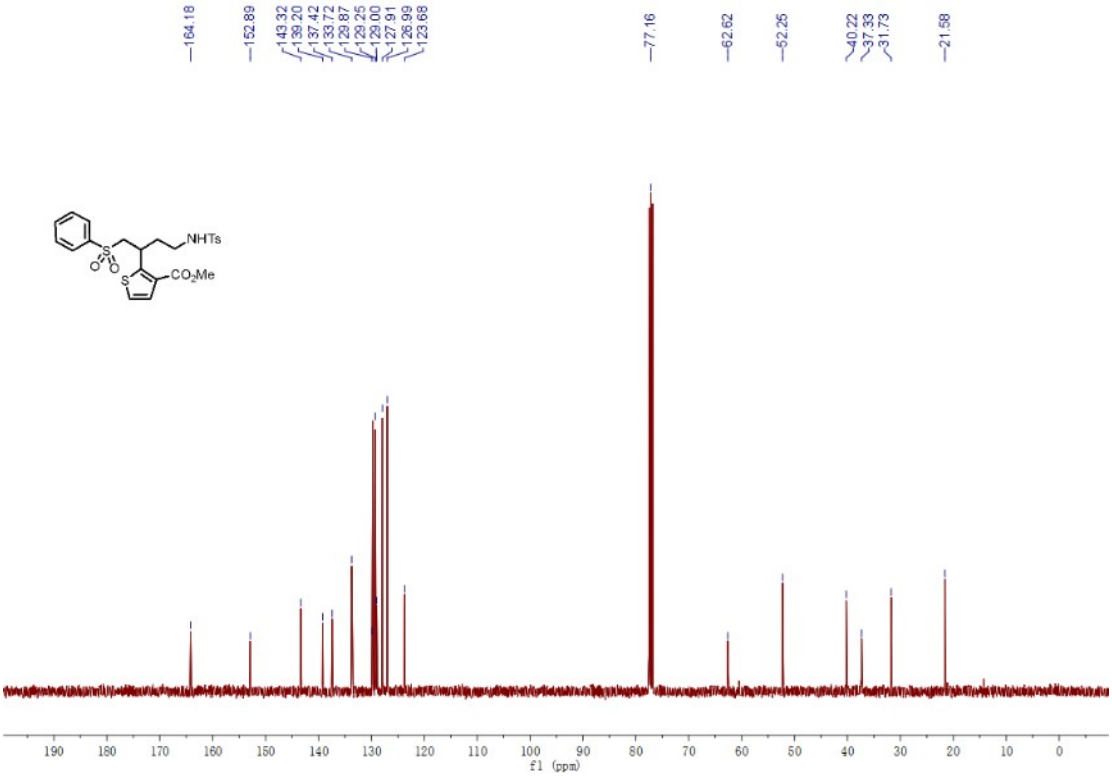
^{19}F NMR spectrum (376MHz, $CDCl_3$) of compound 3ab



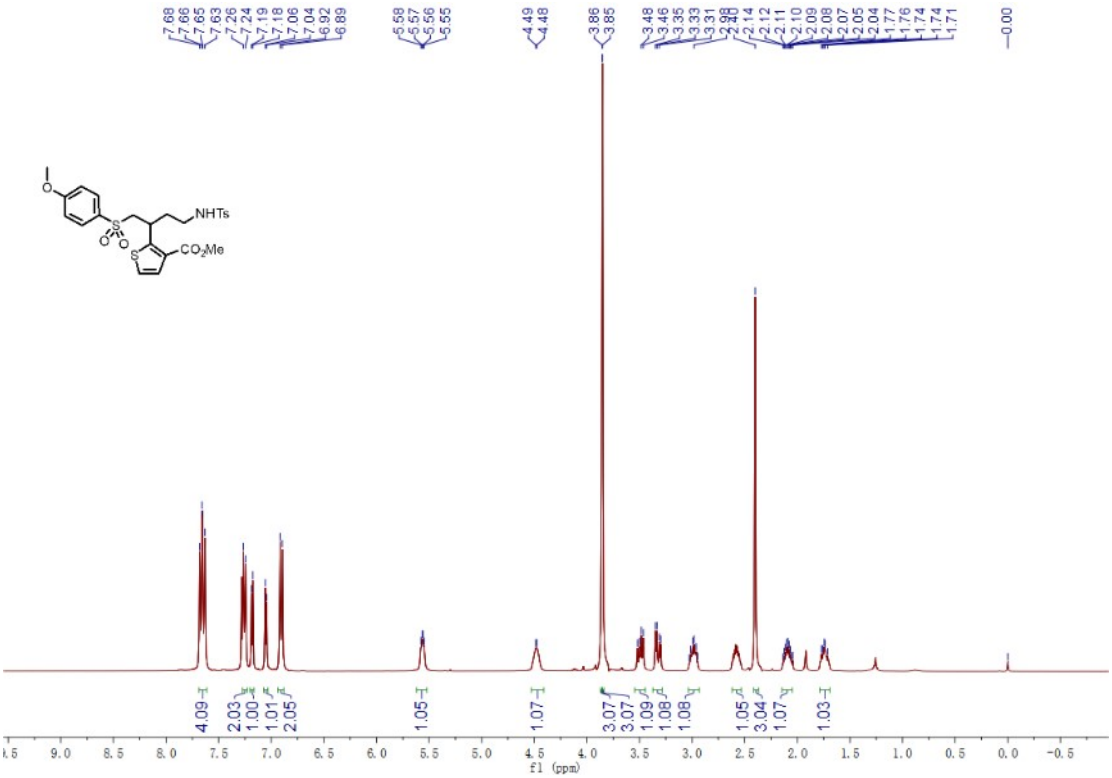
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 4a



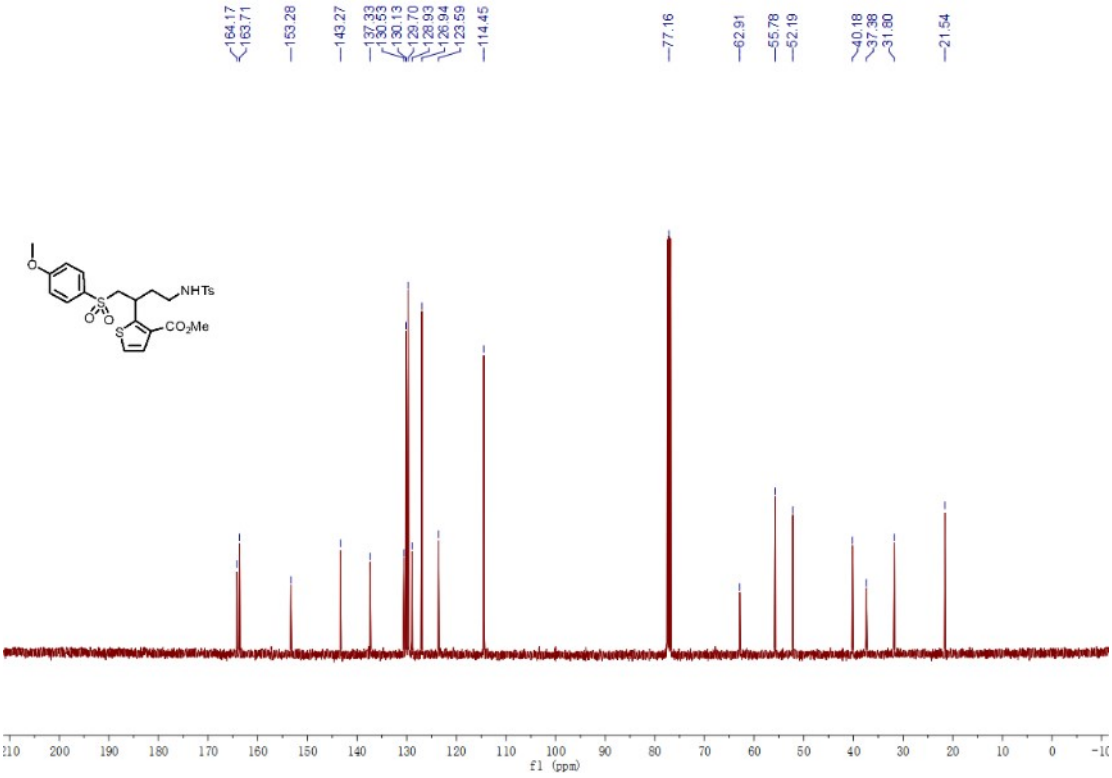
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 4a



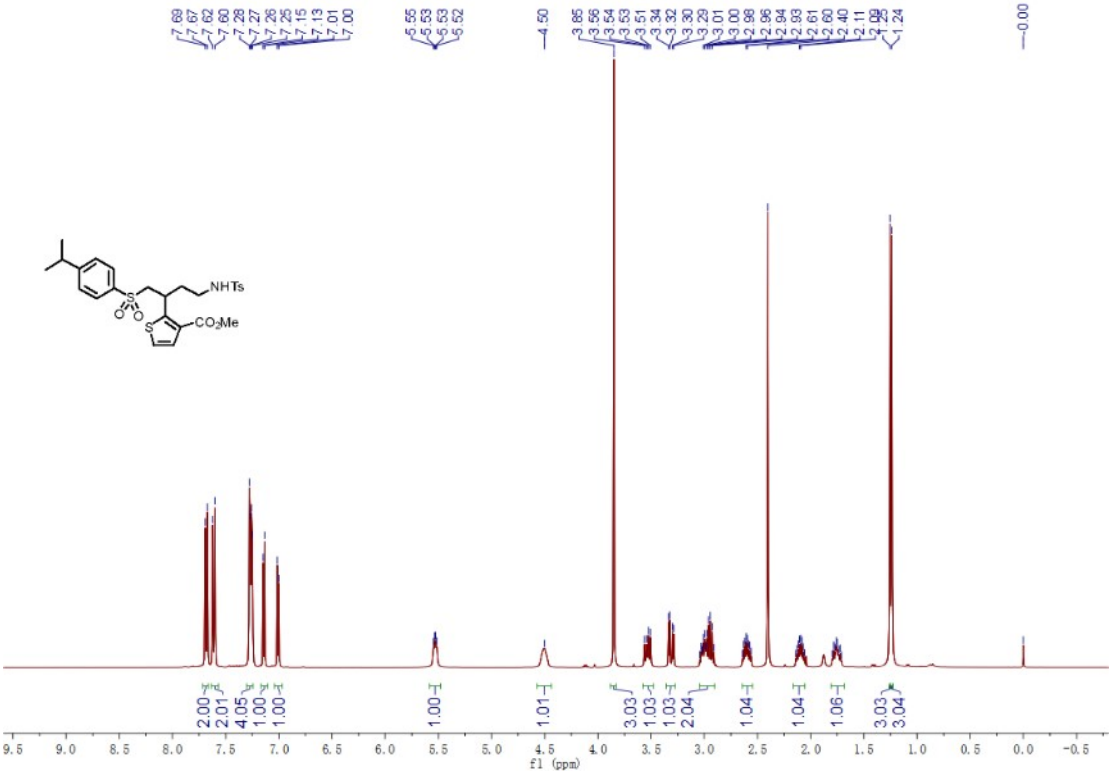
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 4b



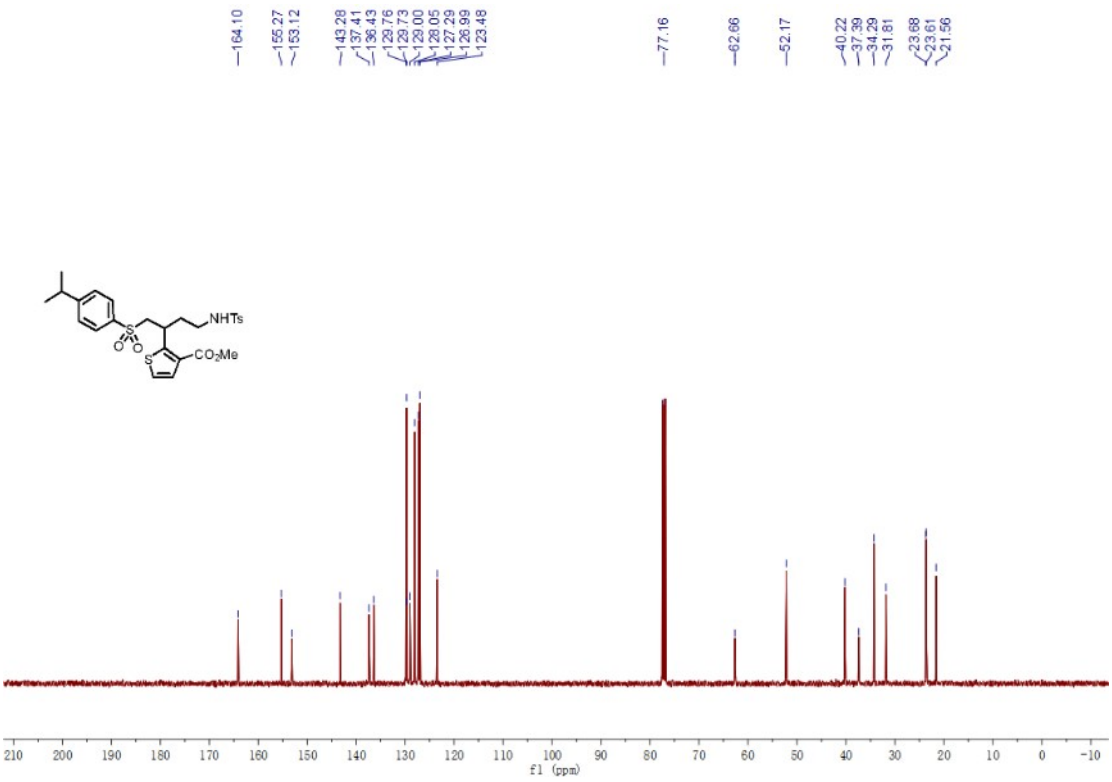
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 4b



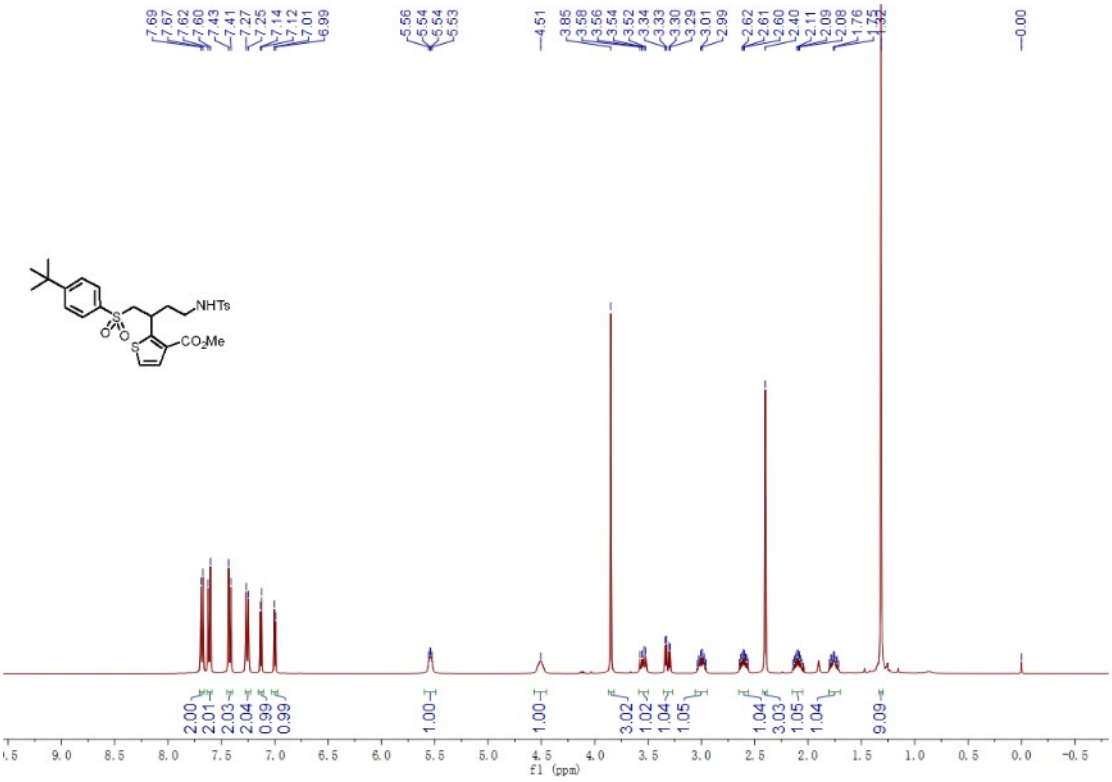
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 4c



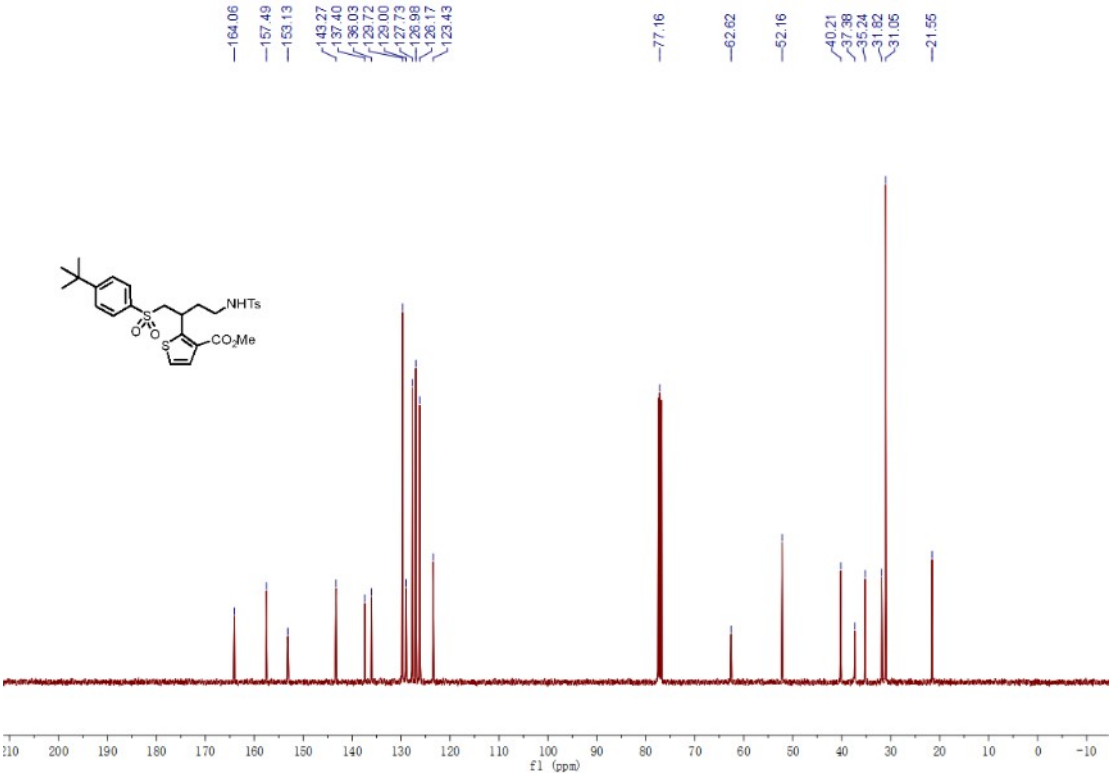
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 4c



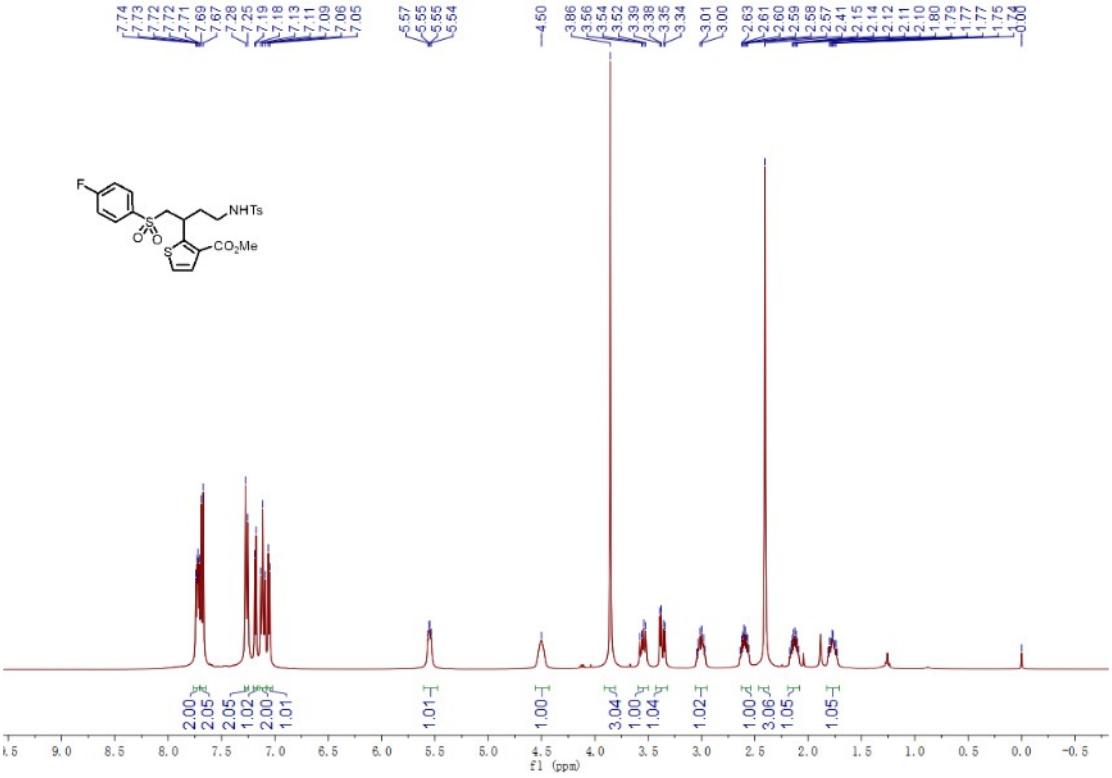
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 4d



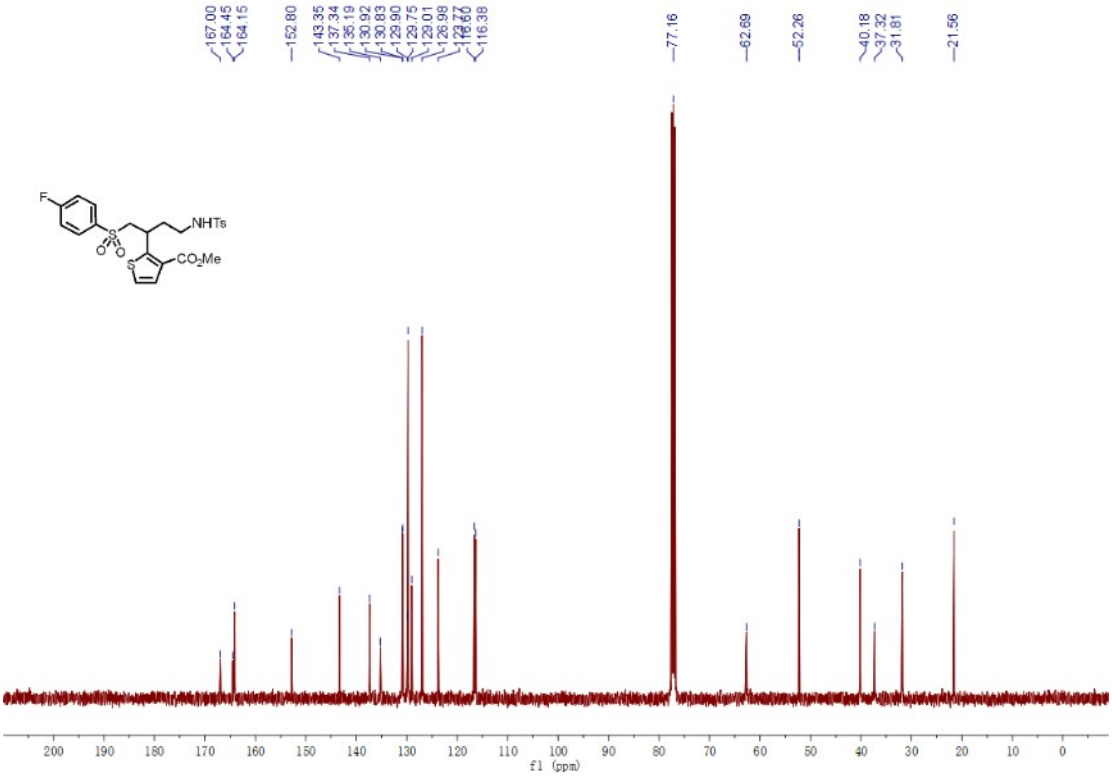
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 4d



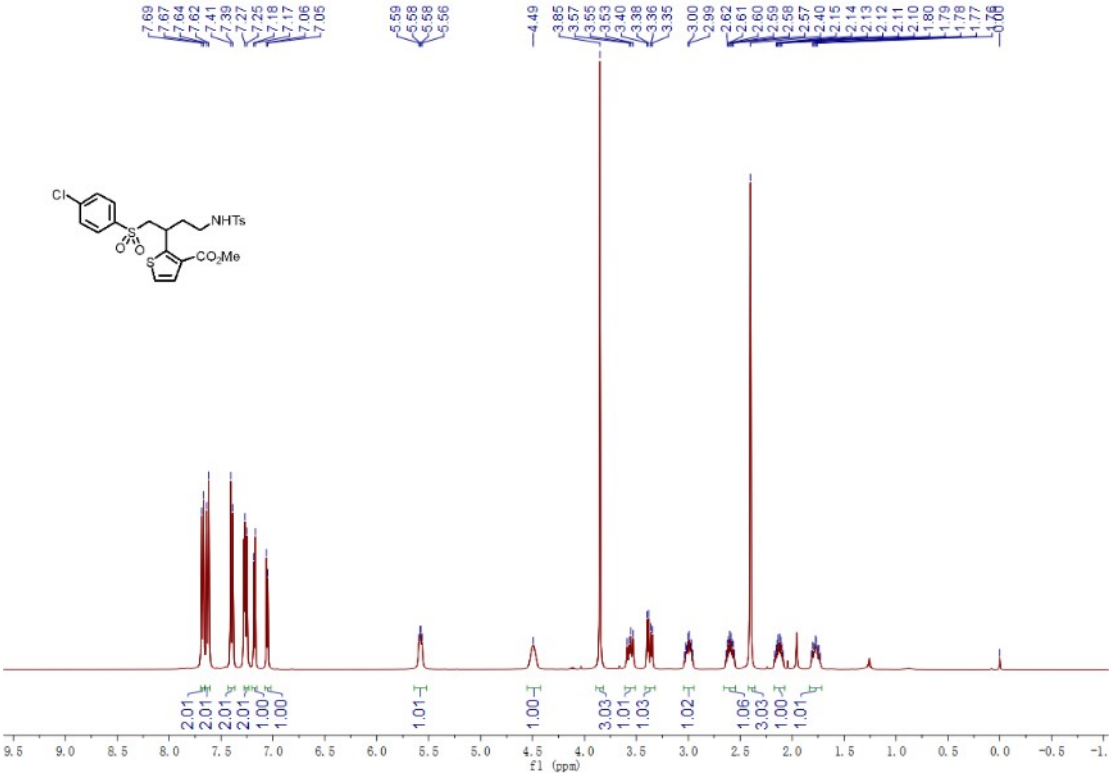
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 4e



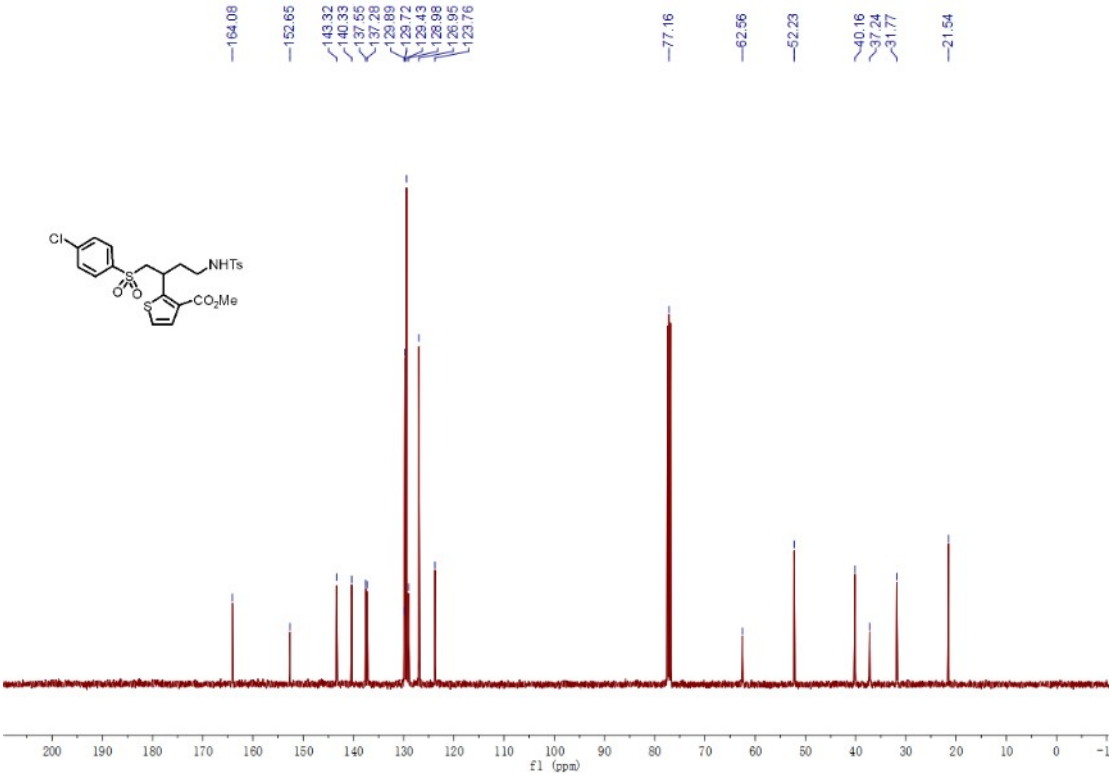
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 4e



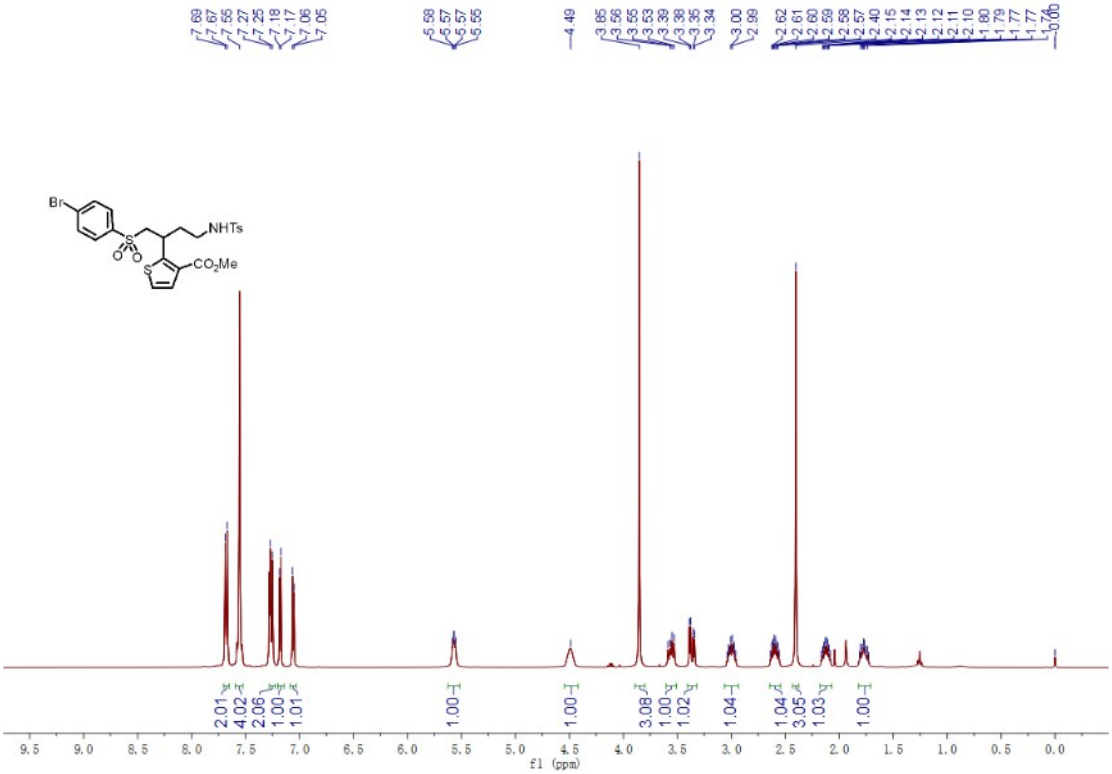
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 4f



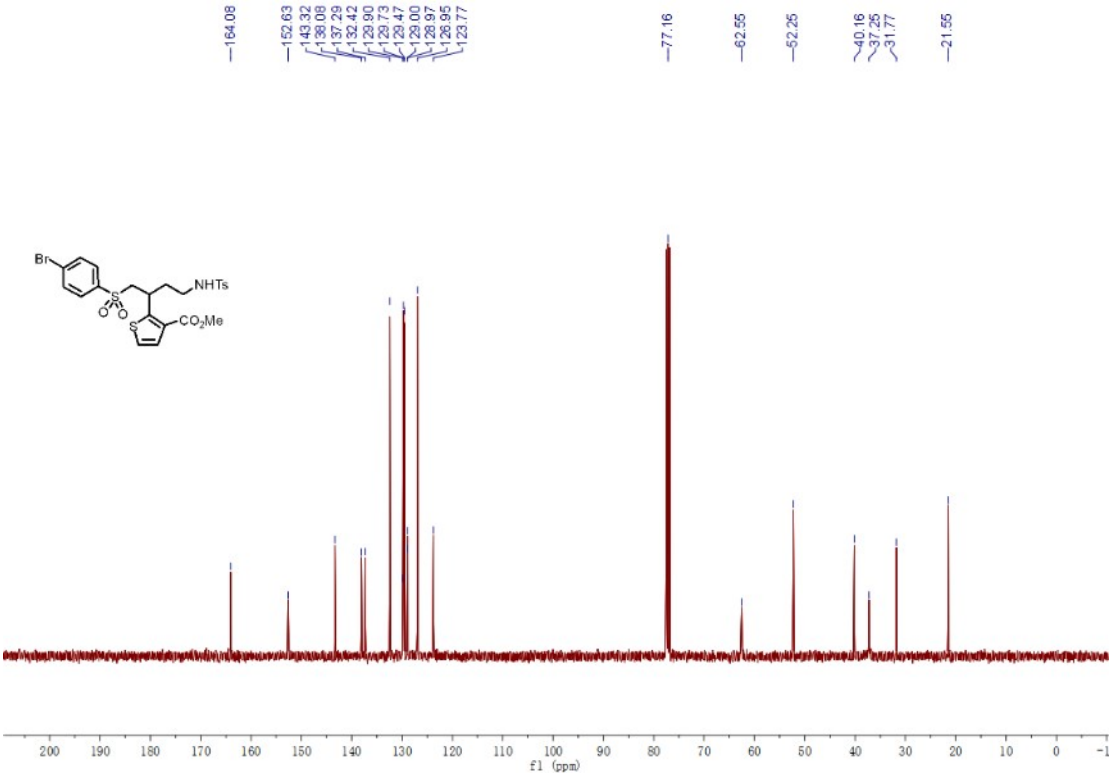
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 4f



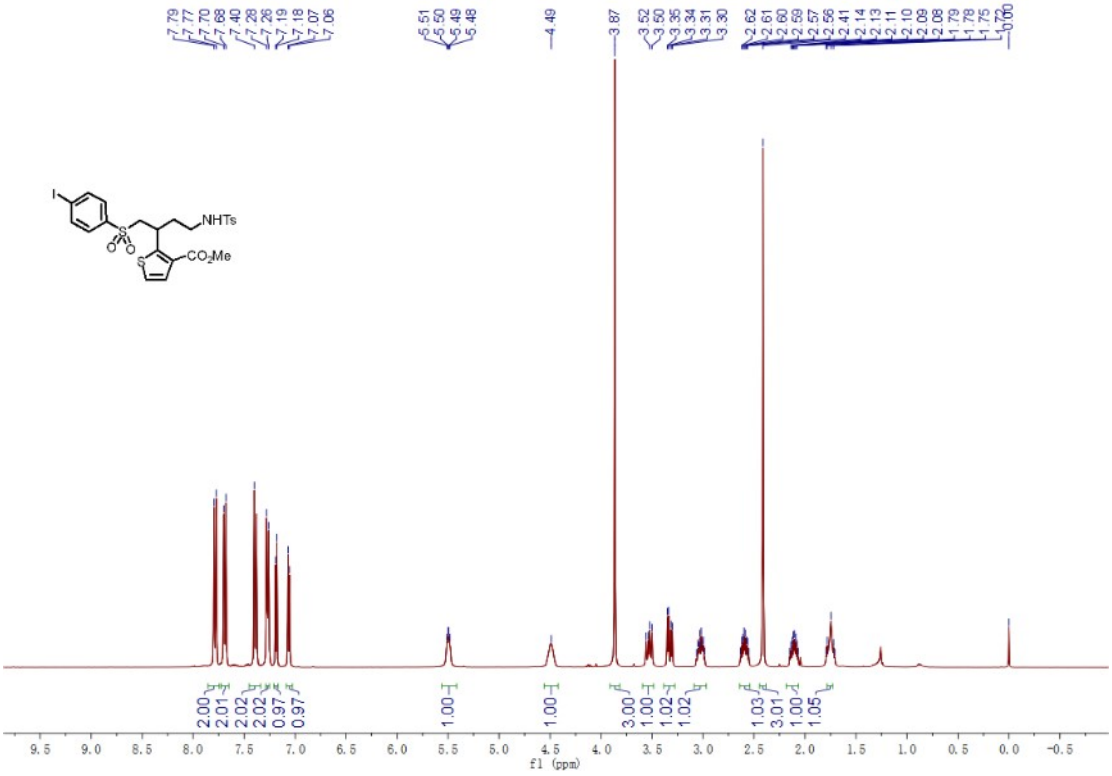
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 4g



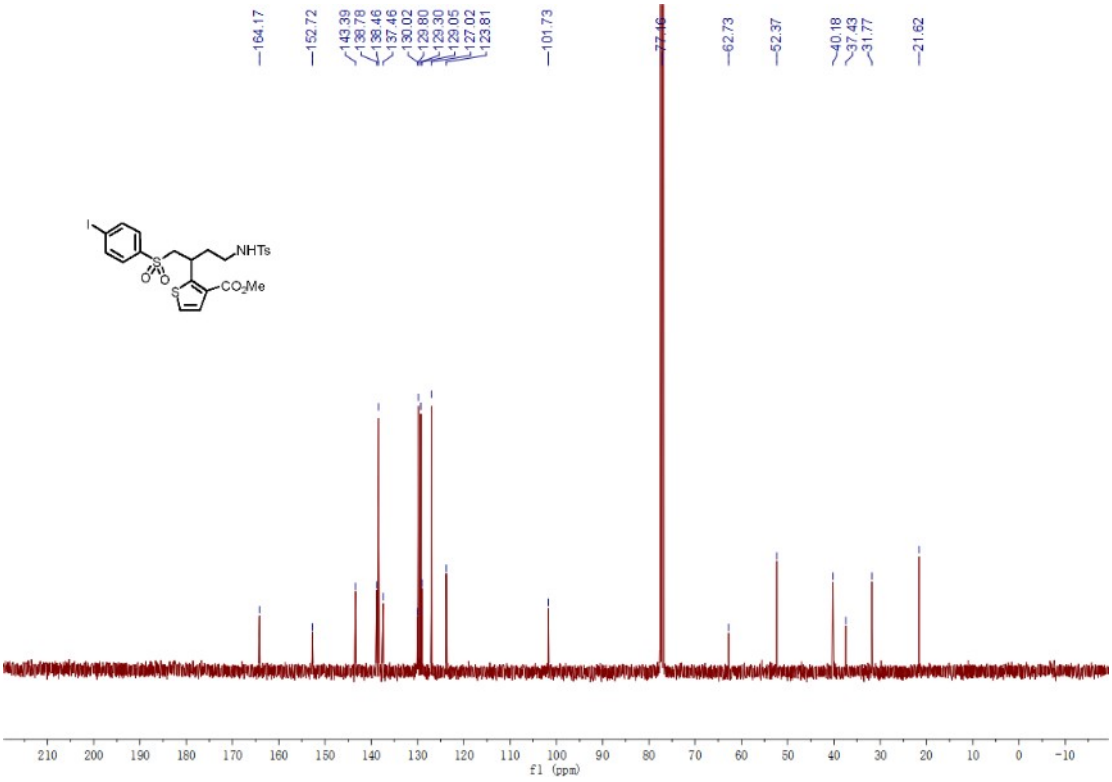
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 4g



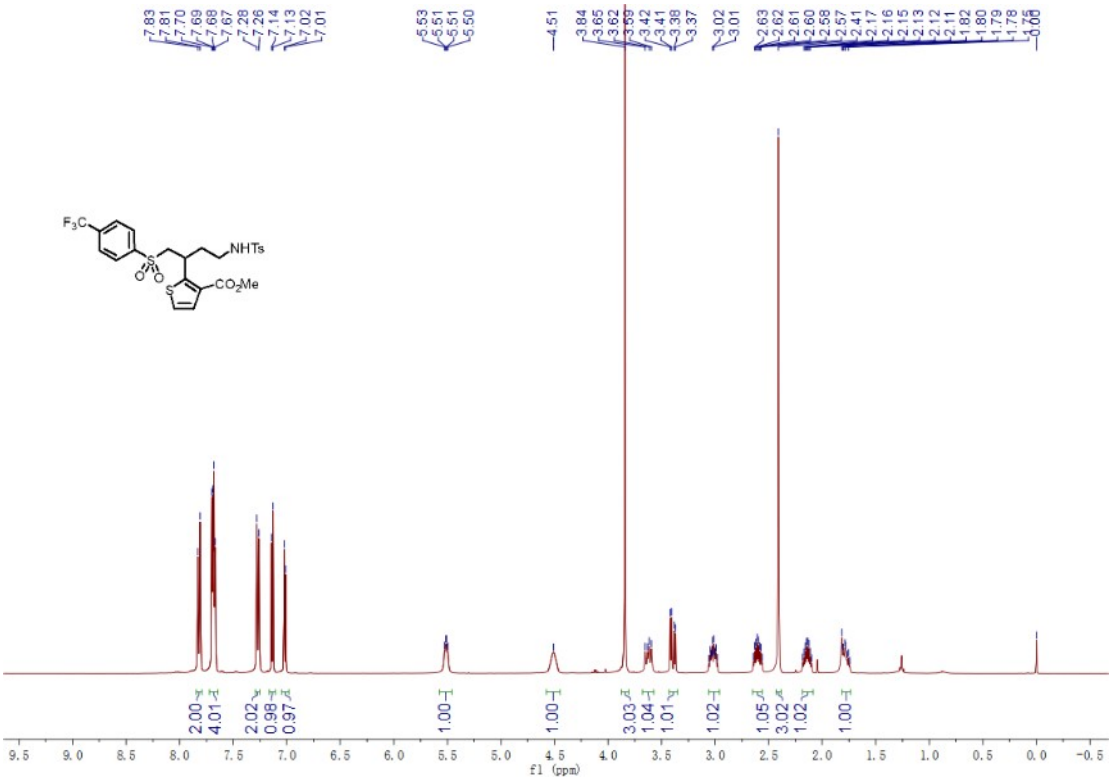
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 4h



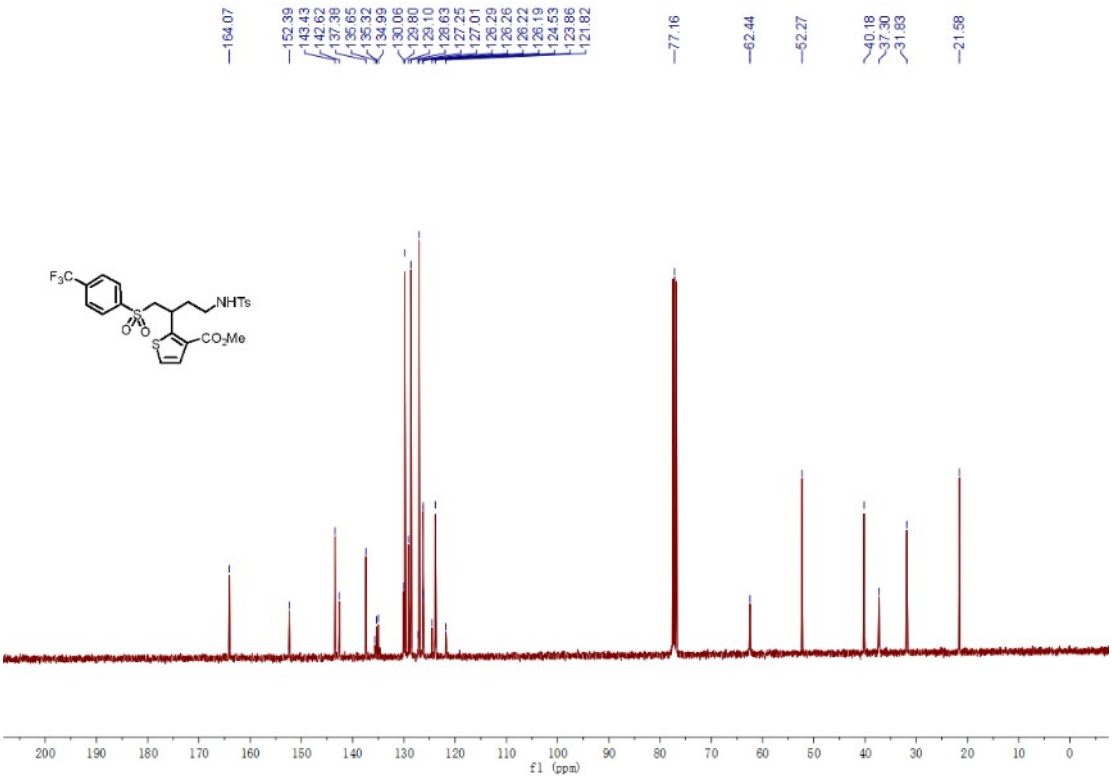
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 4h



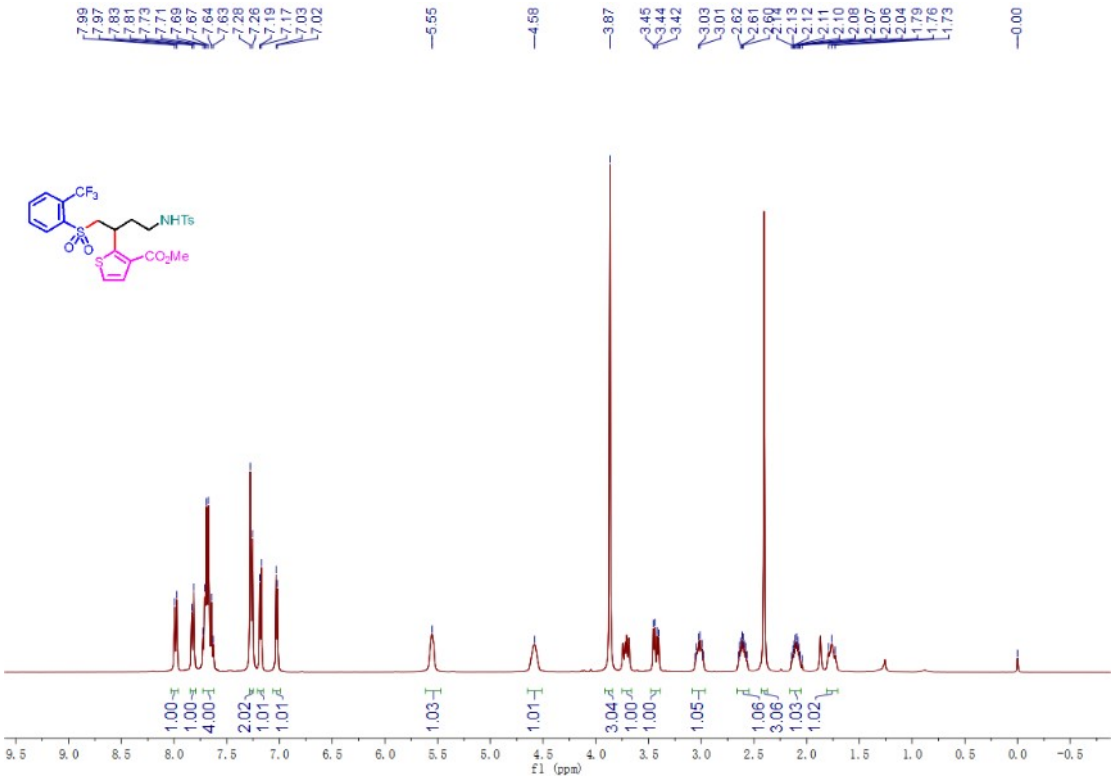
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 4i



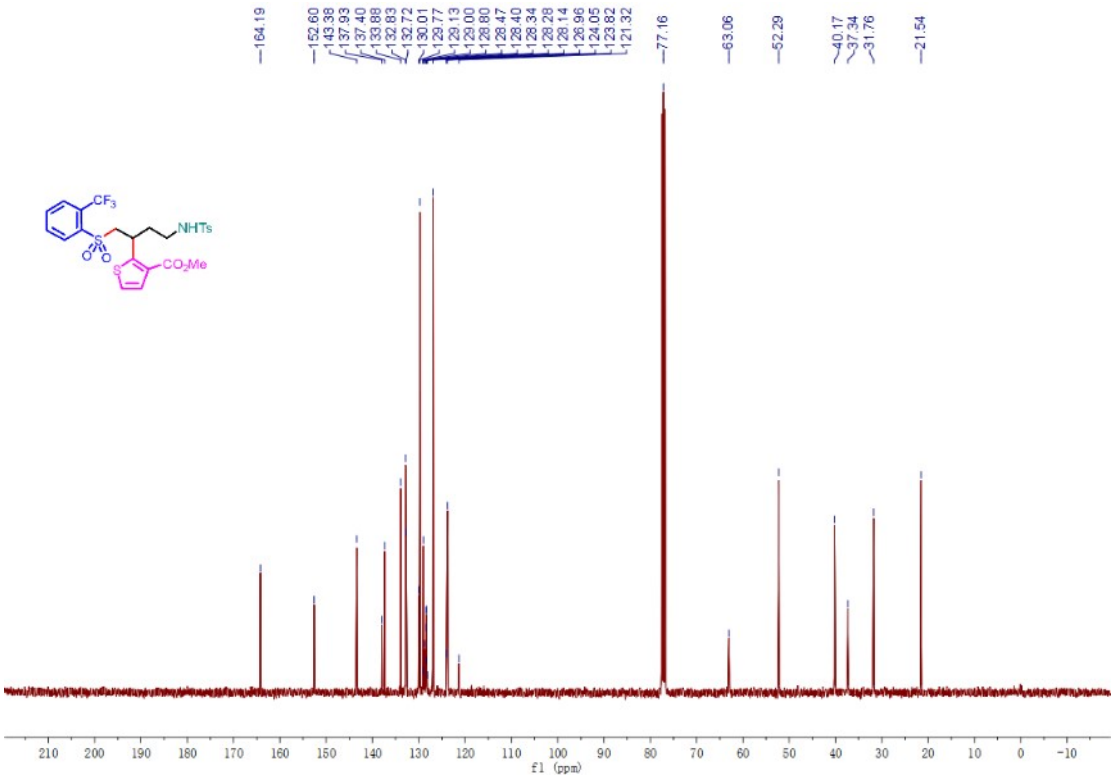
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 4i



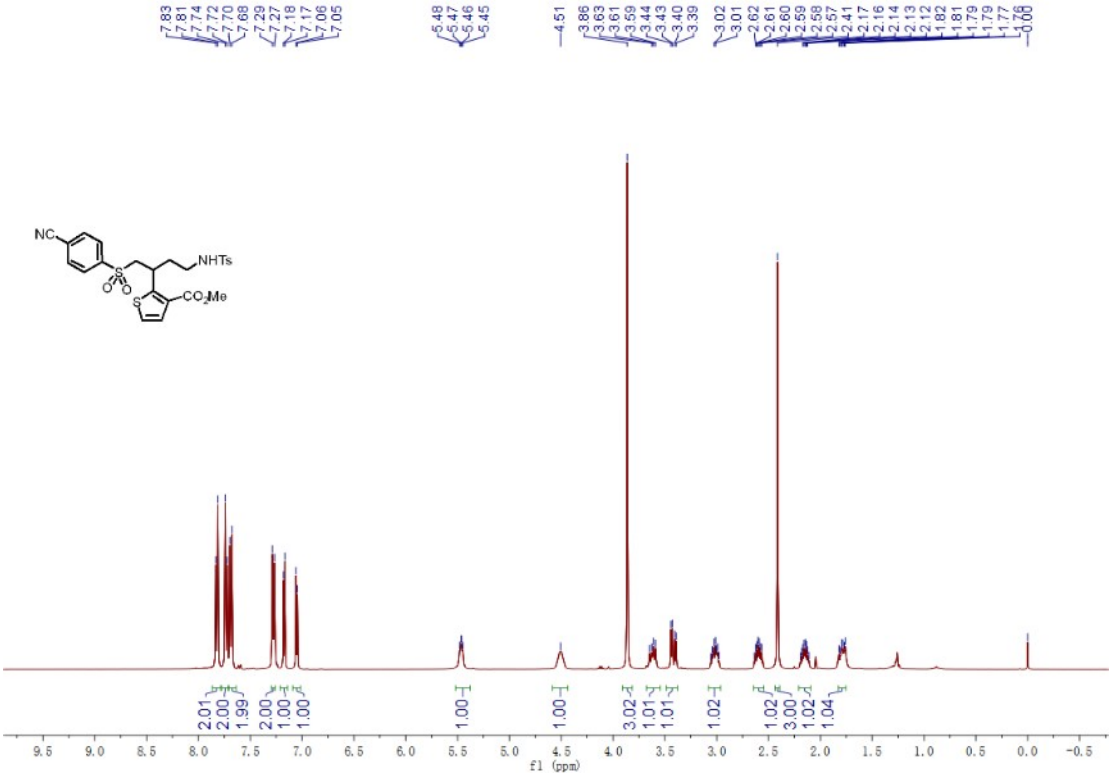
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 4j



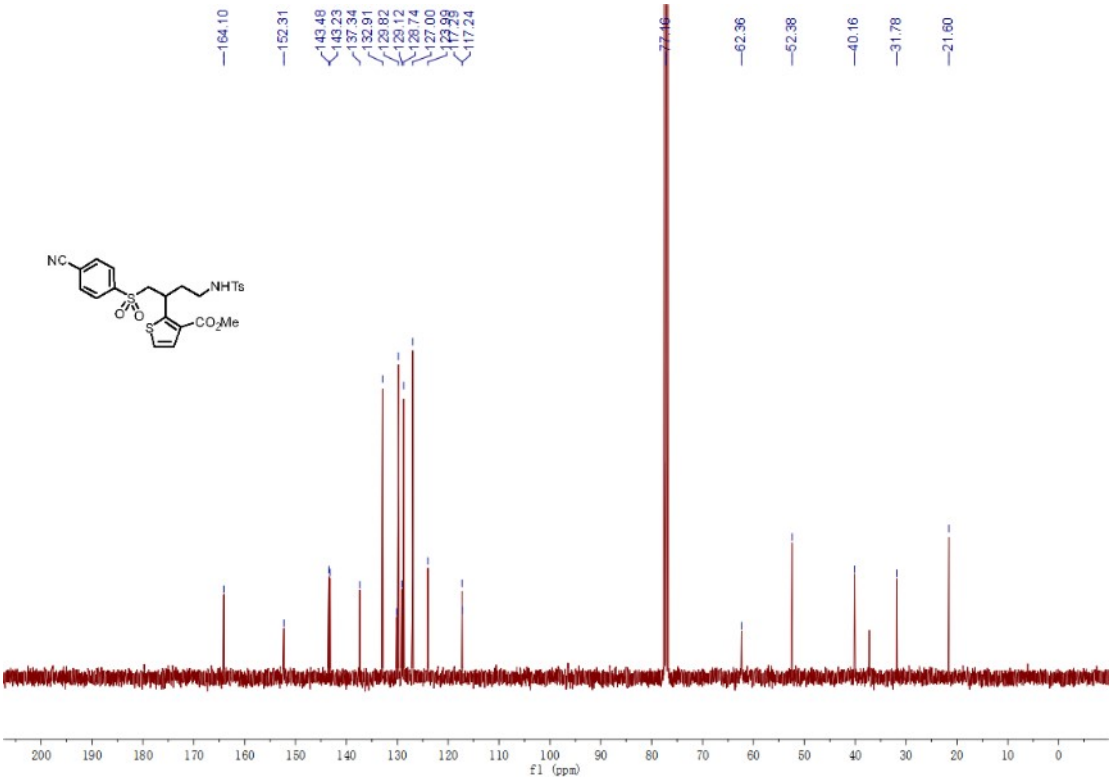
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 4j



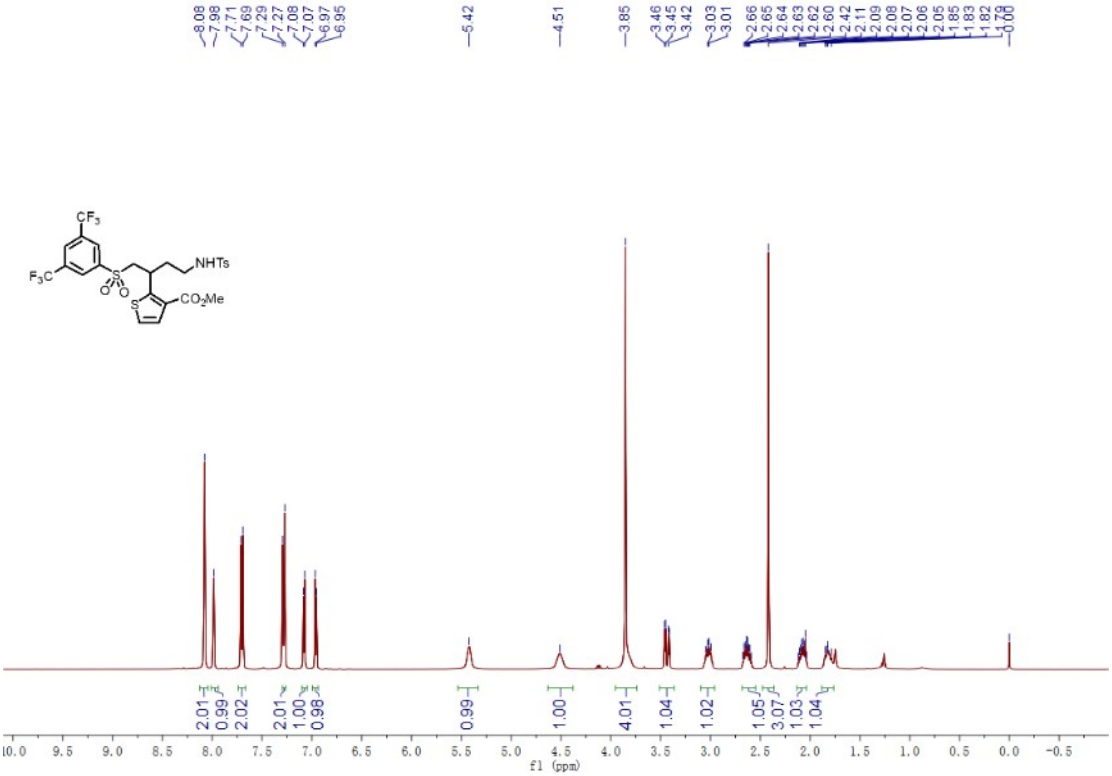
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 4k



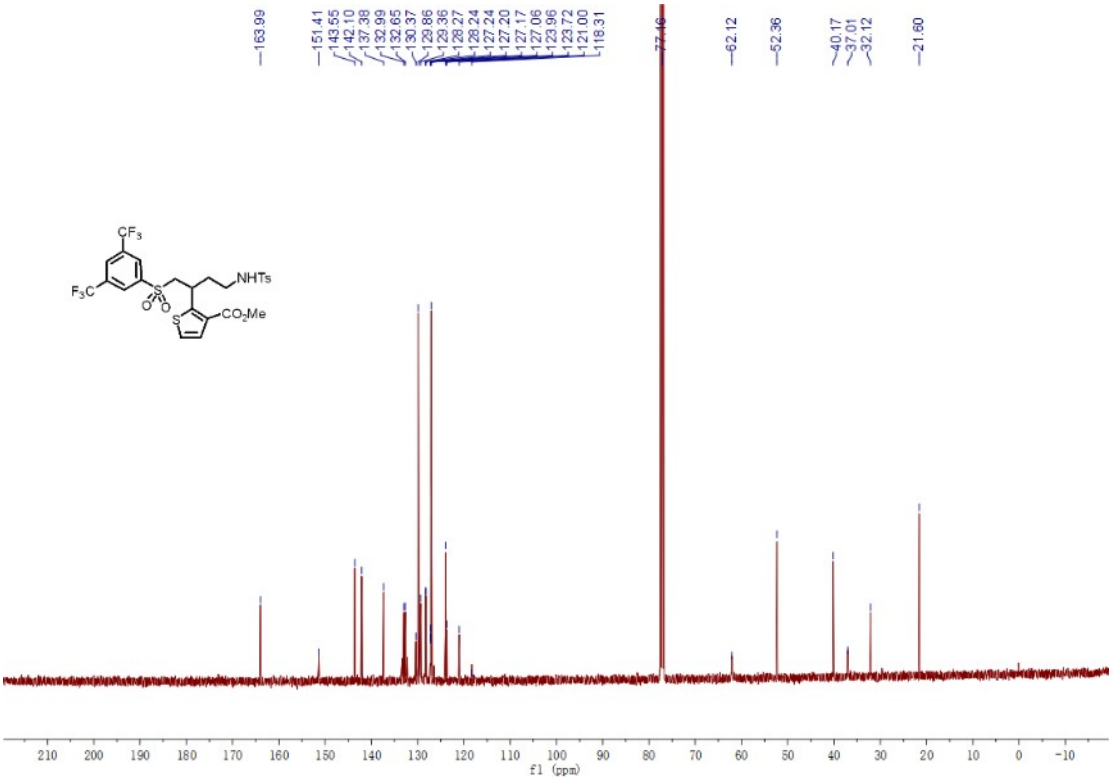
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 4k



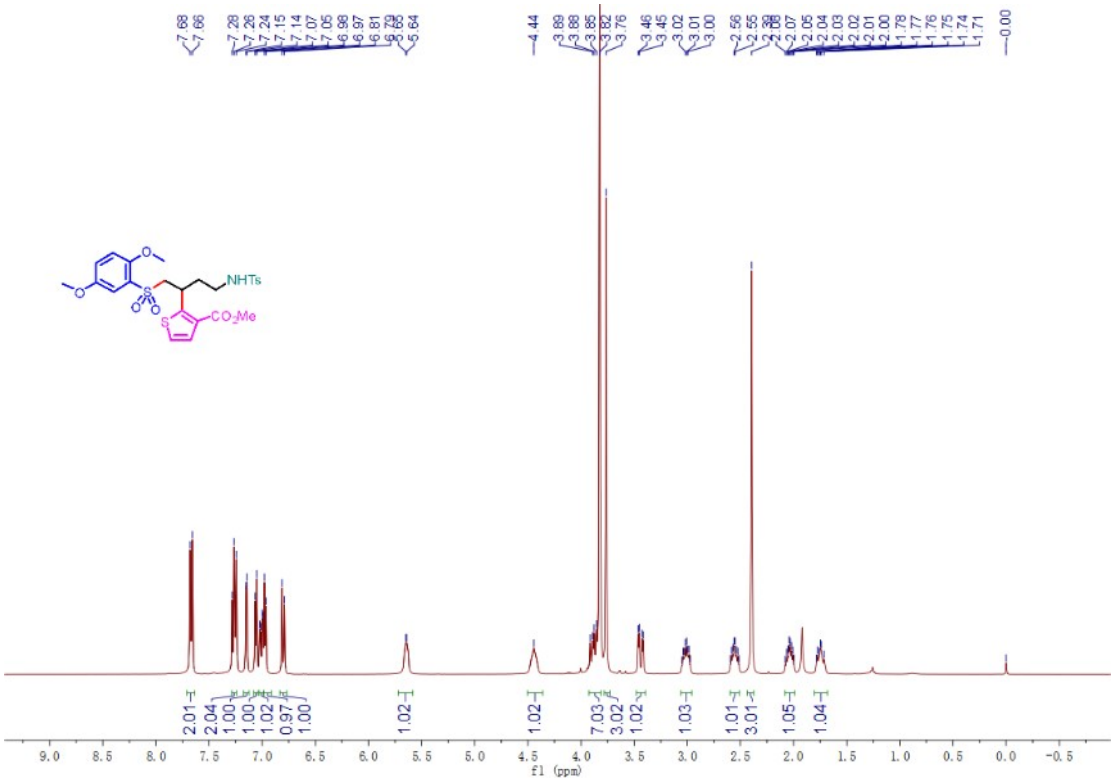
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 4l



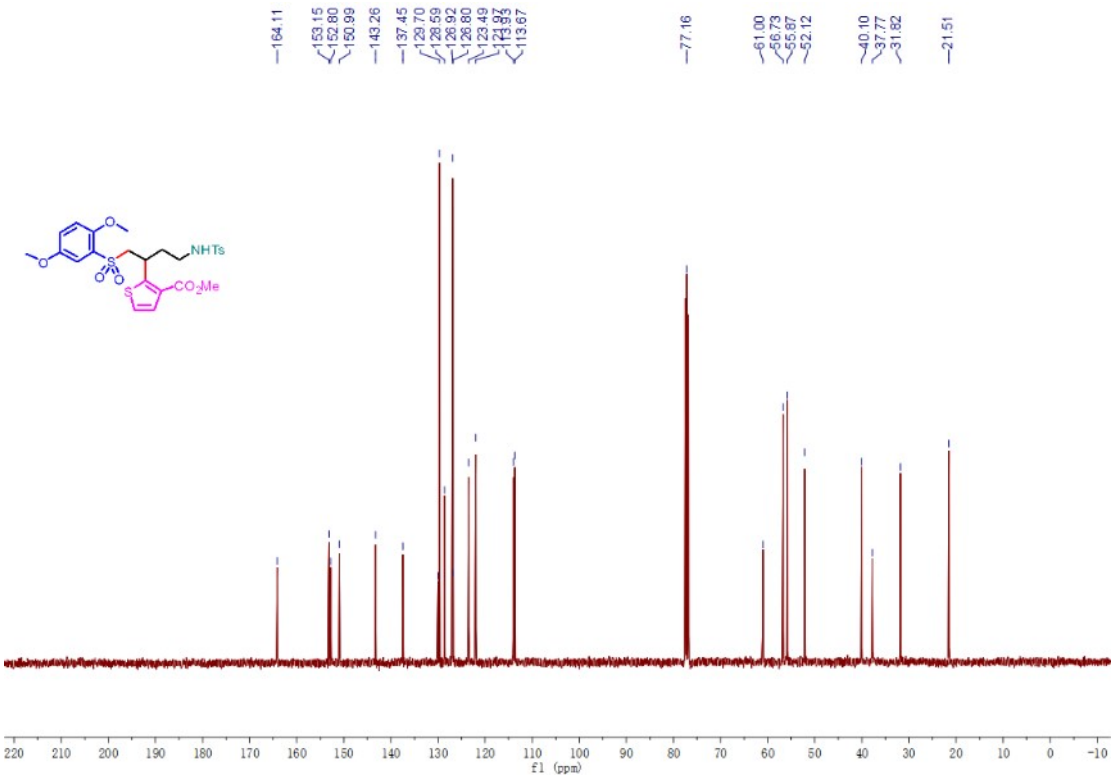
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 4l



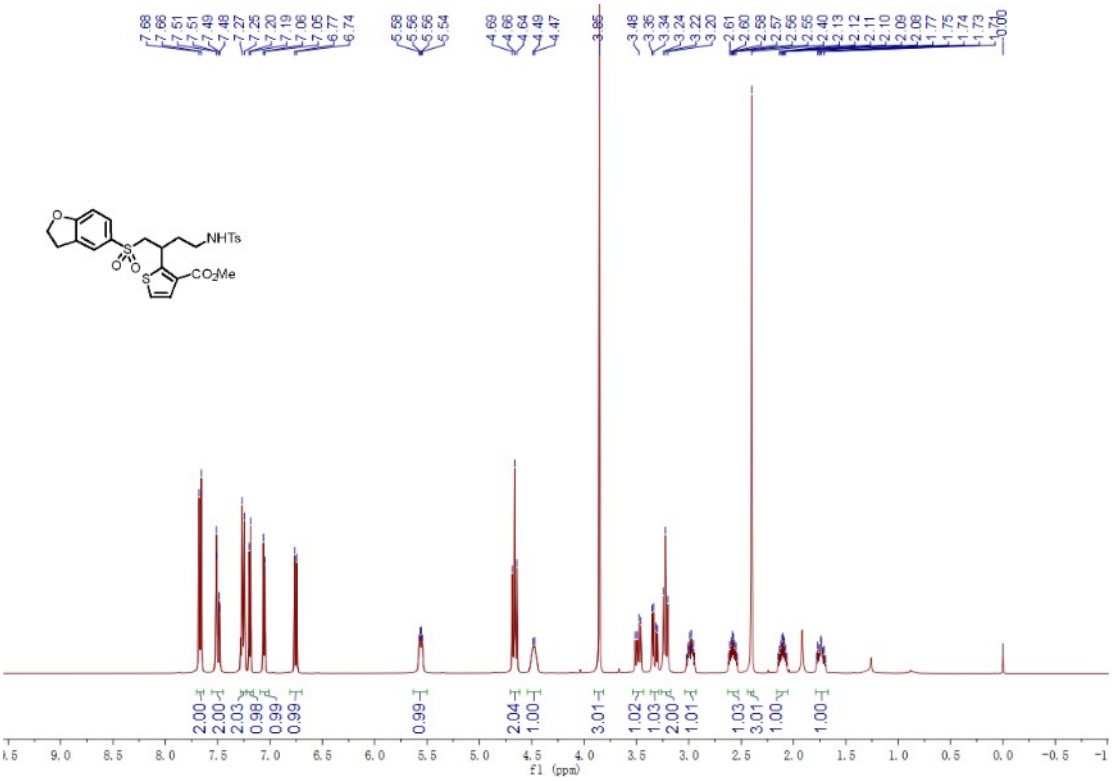
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 4m



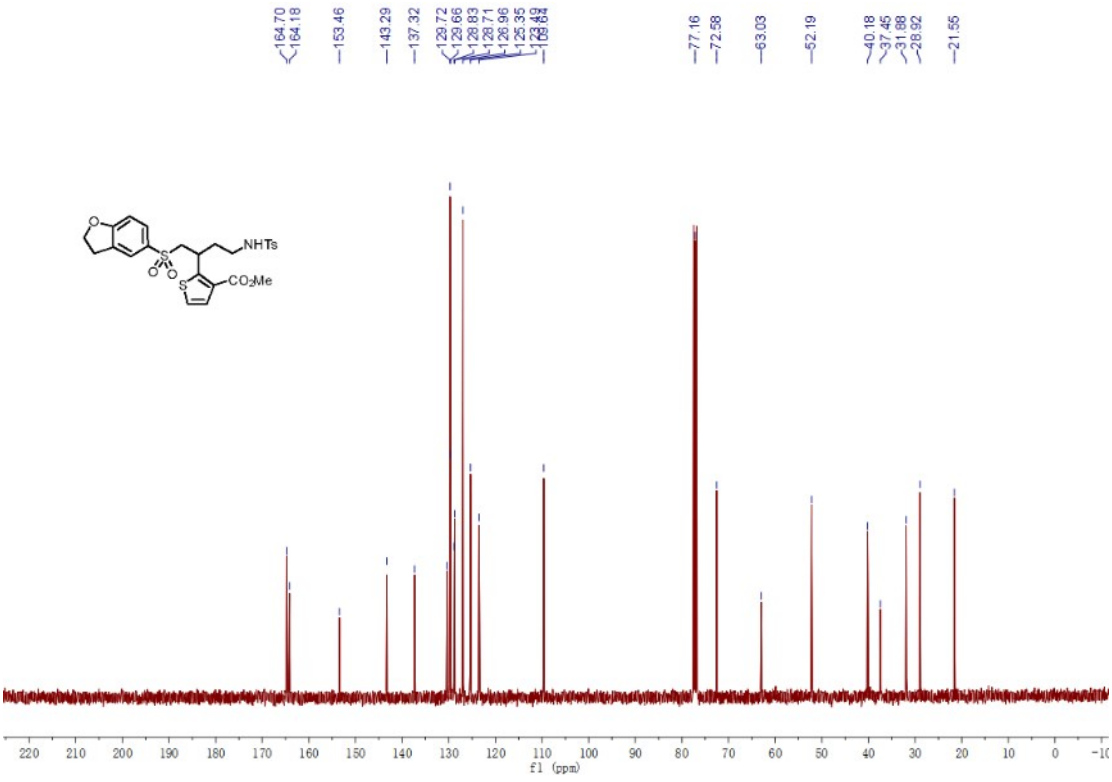
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 4m



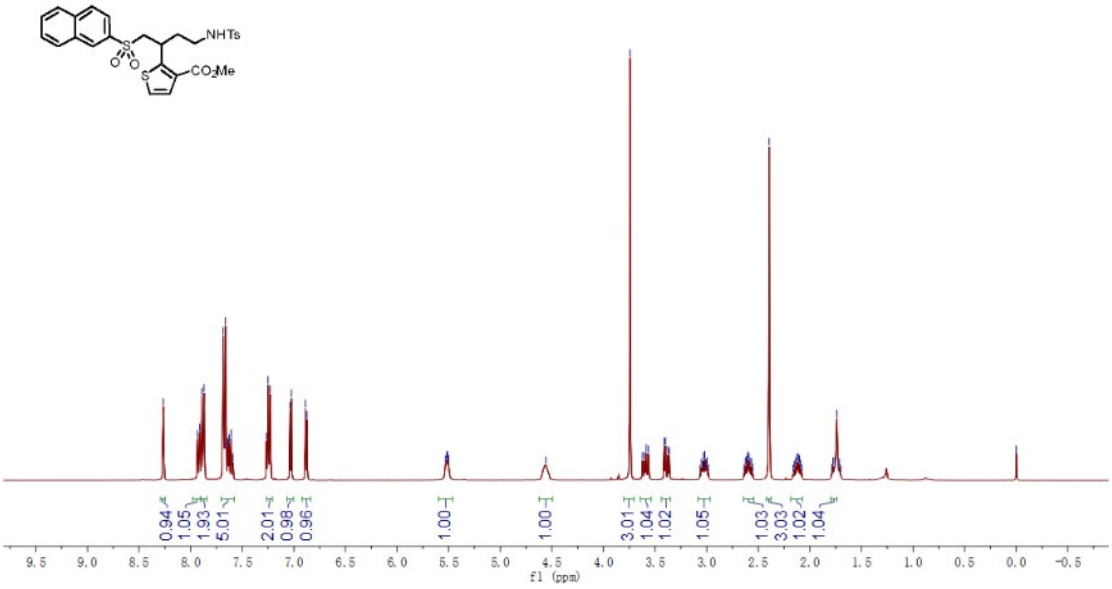
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 4n



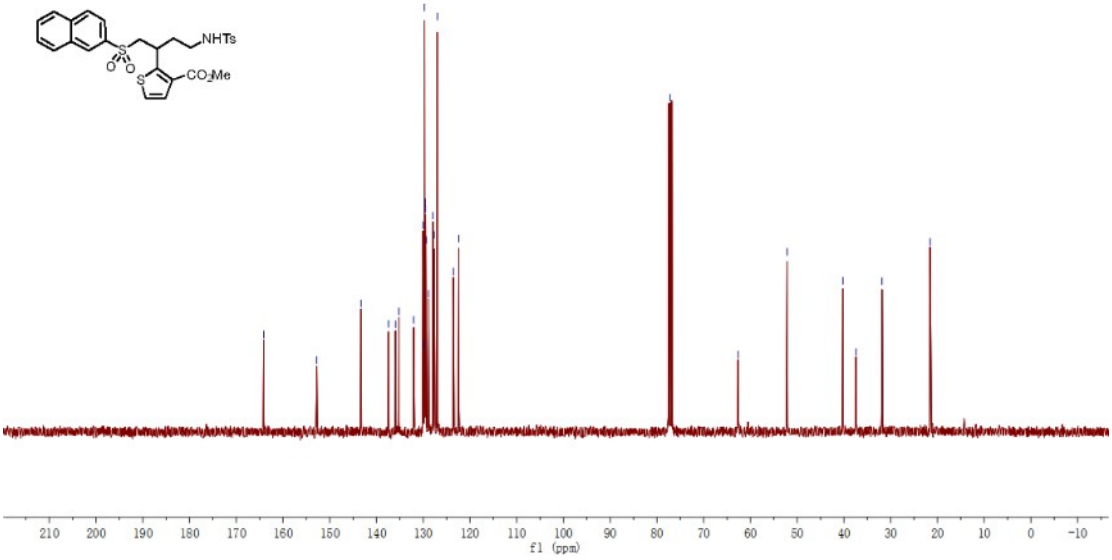
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 4n



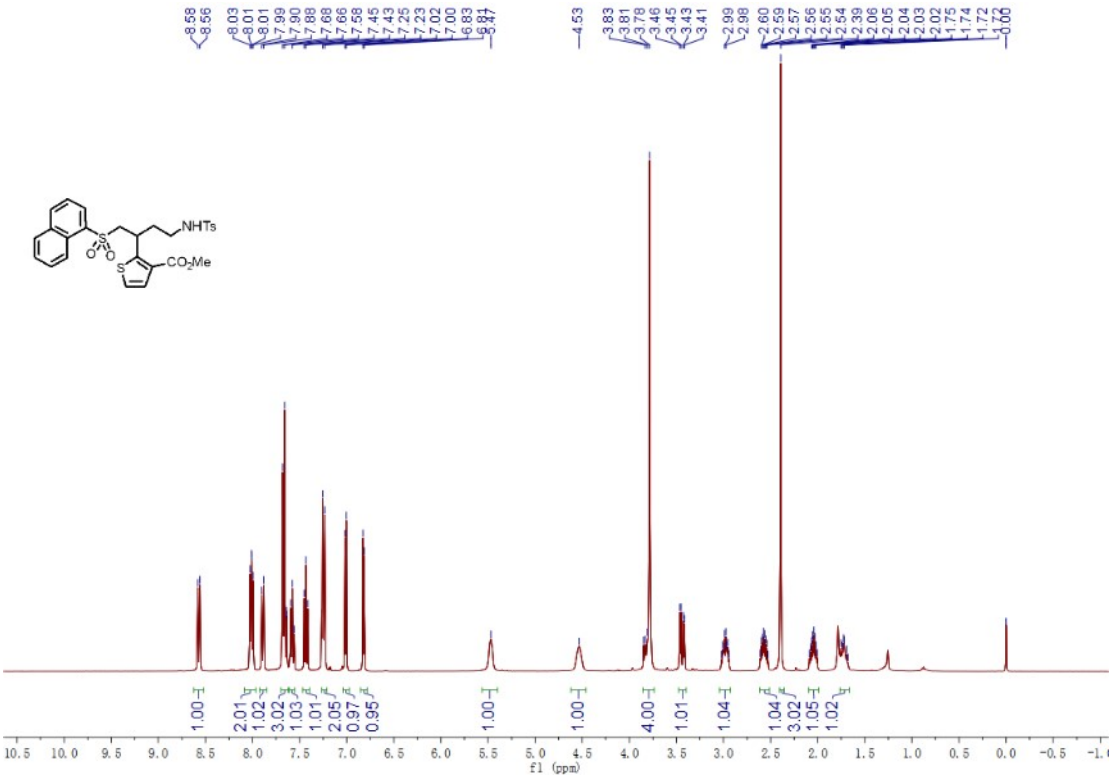
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 4o



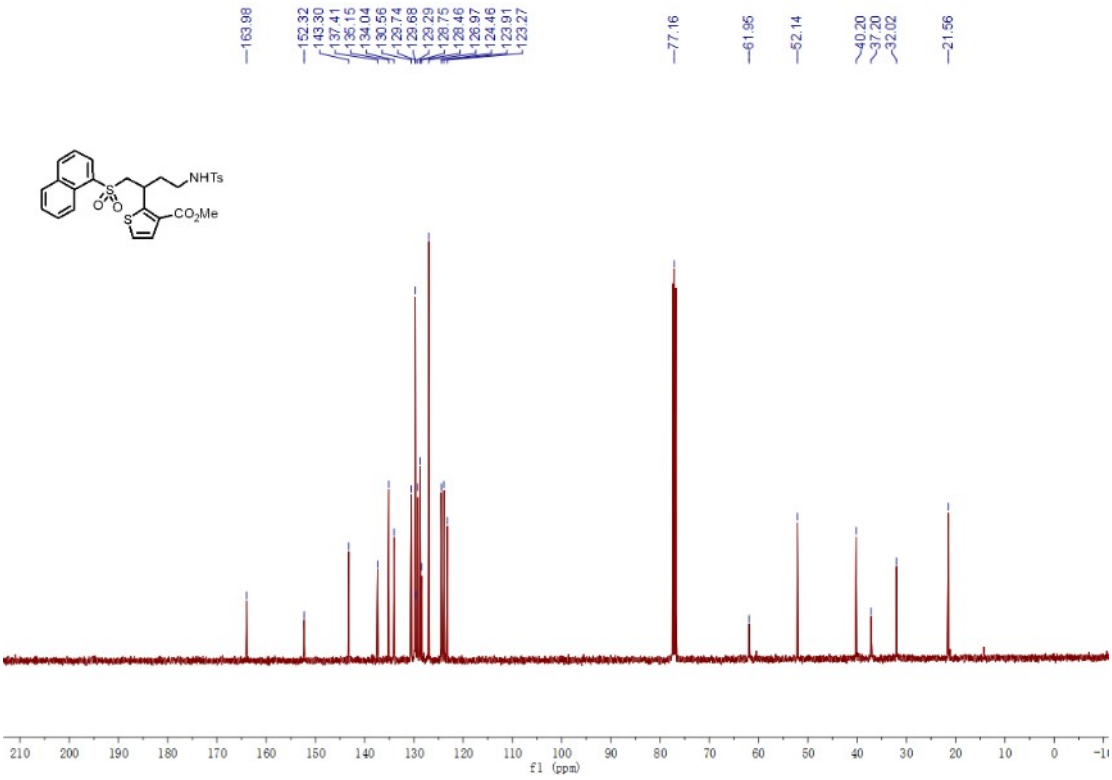
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 4o



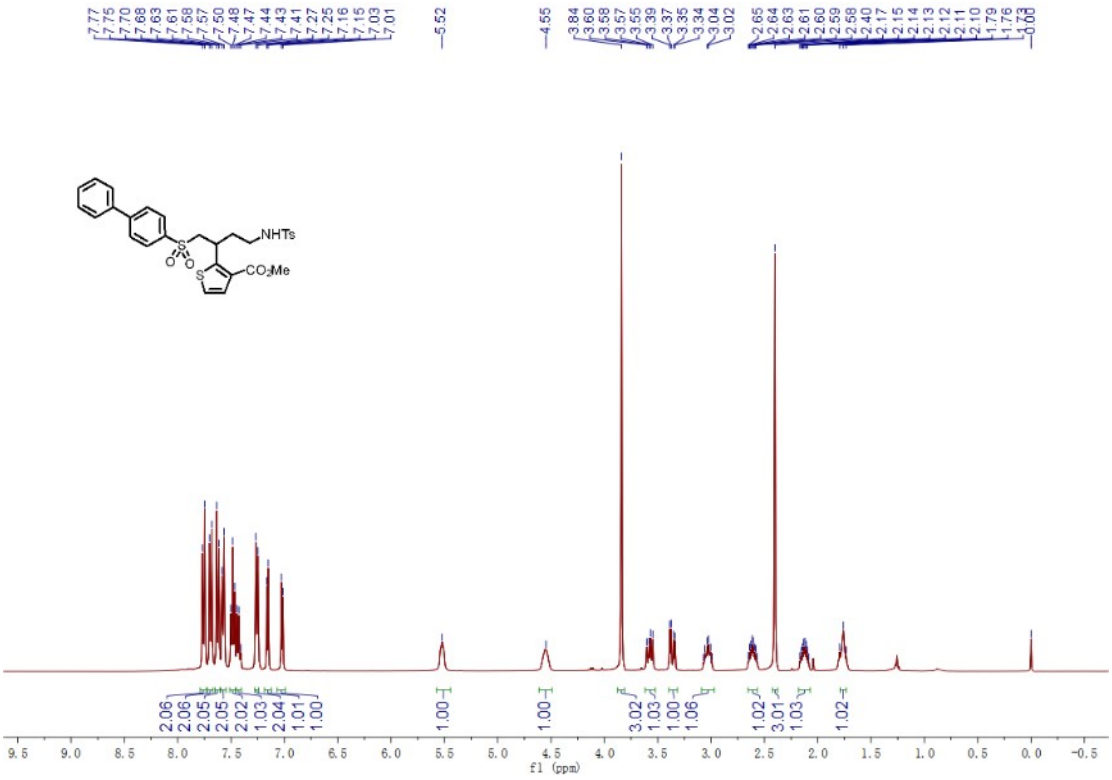
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 4p



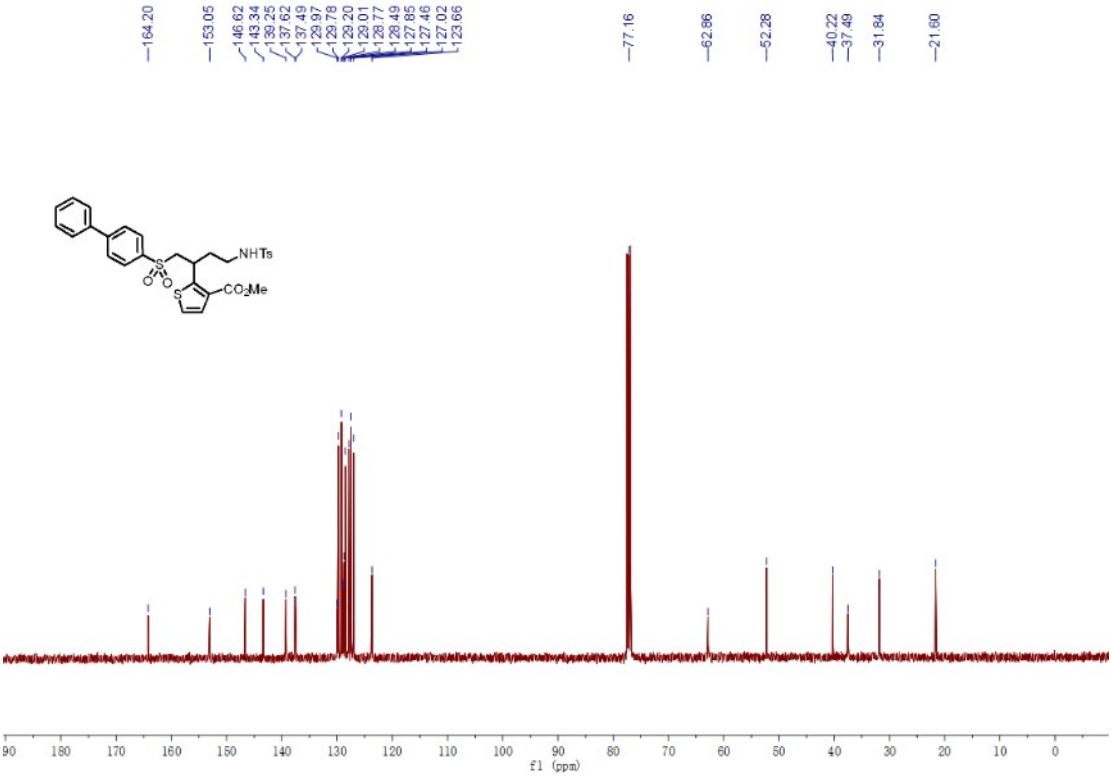
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 4p



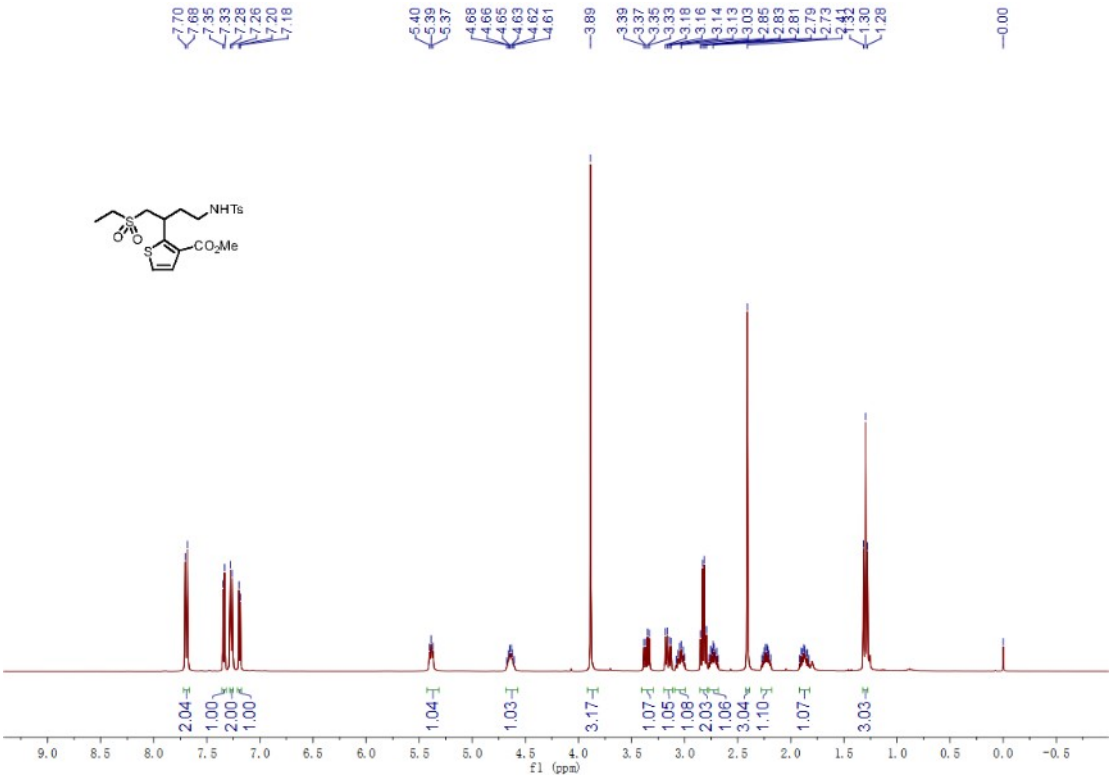
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 4q



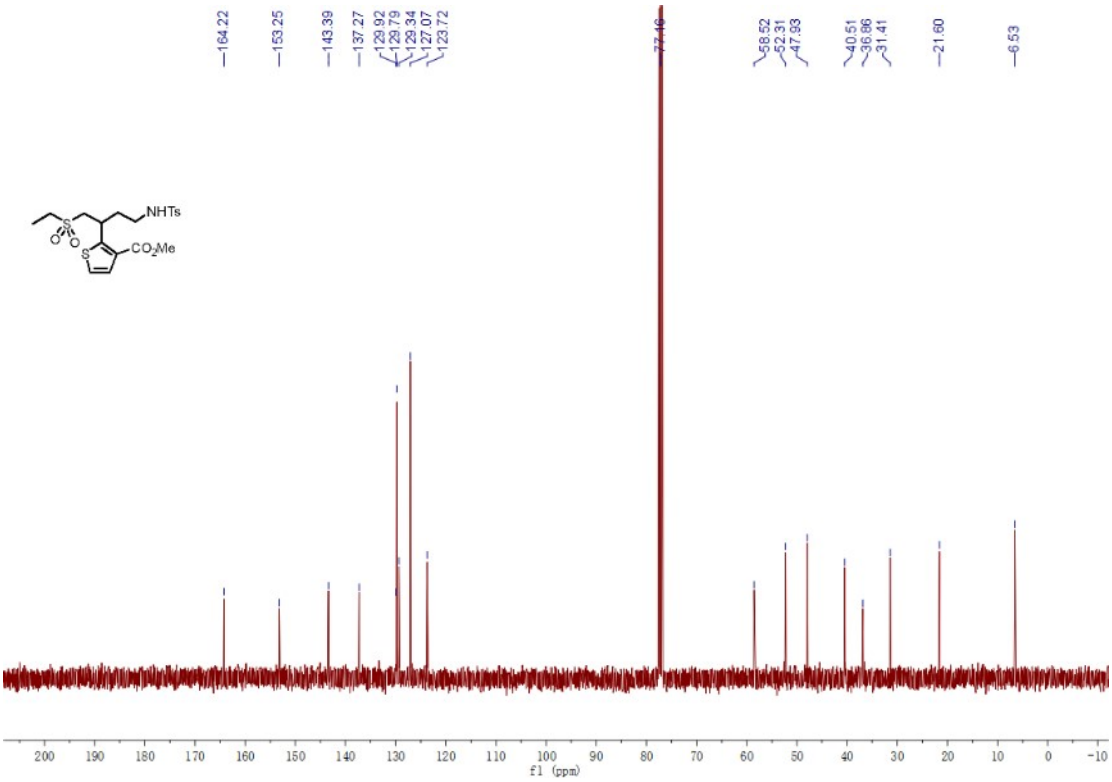
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 4q



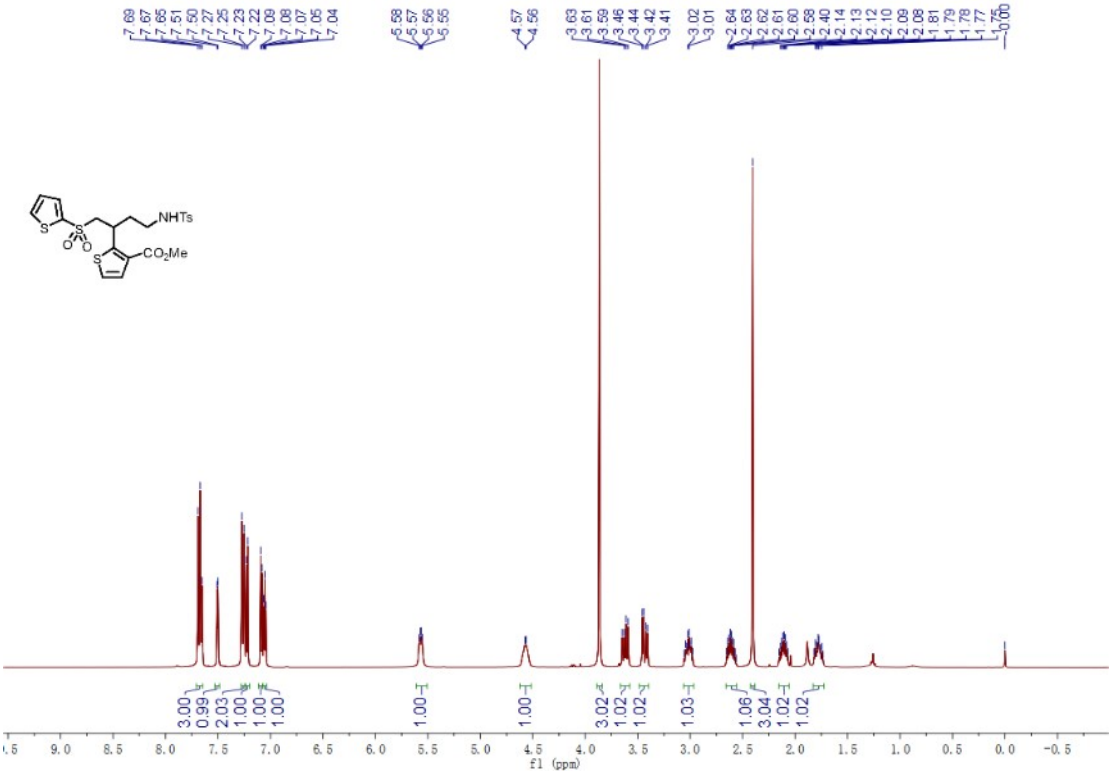
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 4r



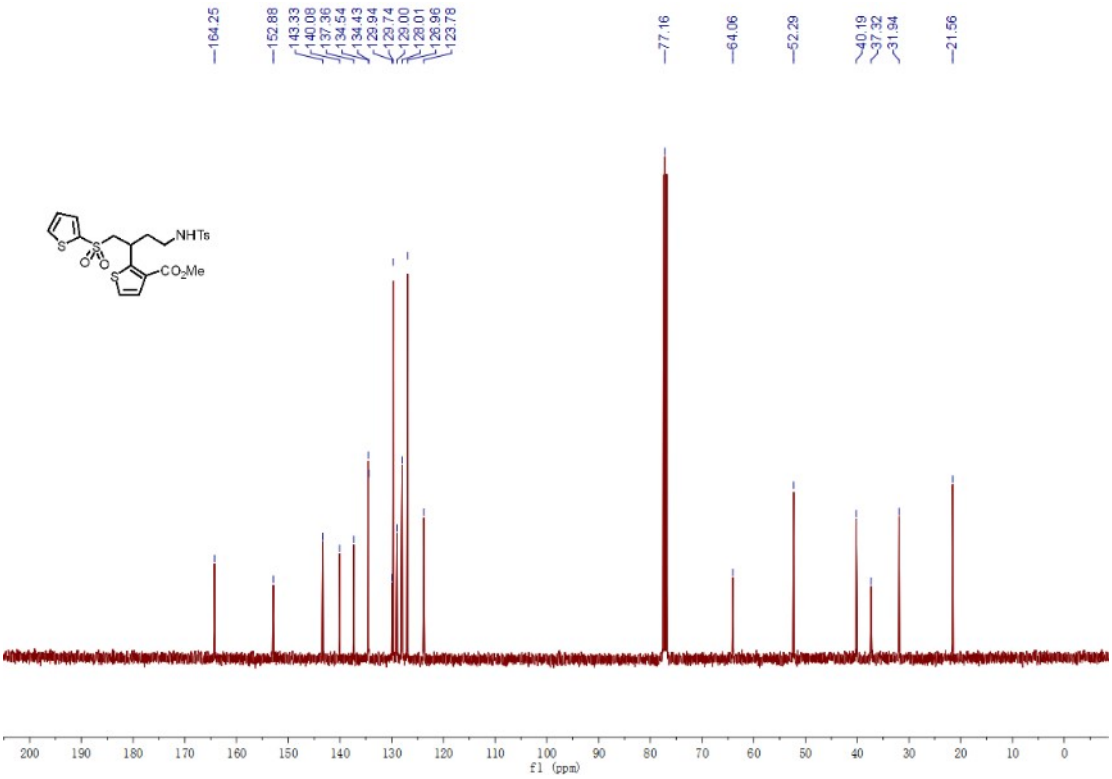
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 4r



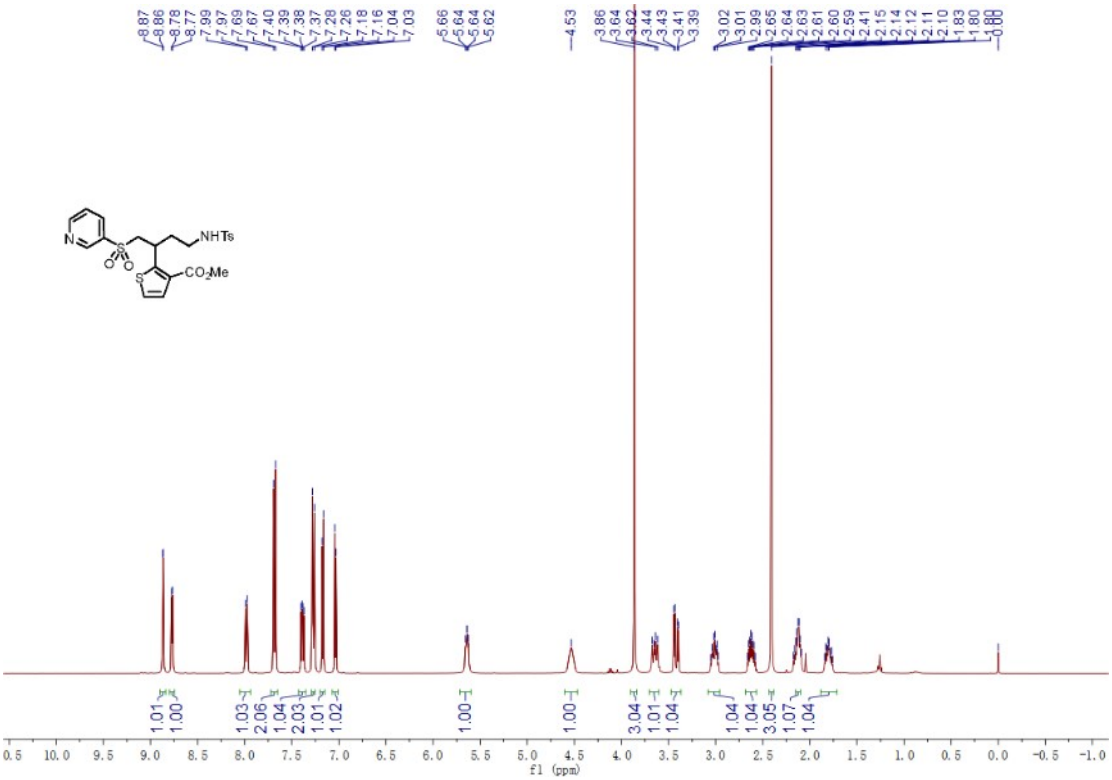
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 4s



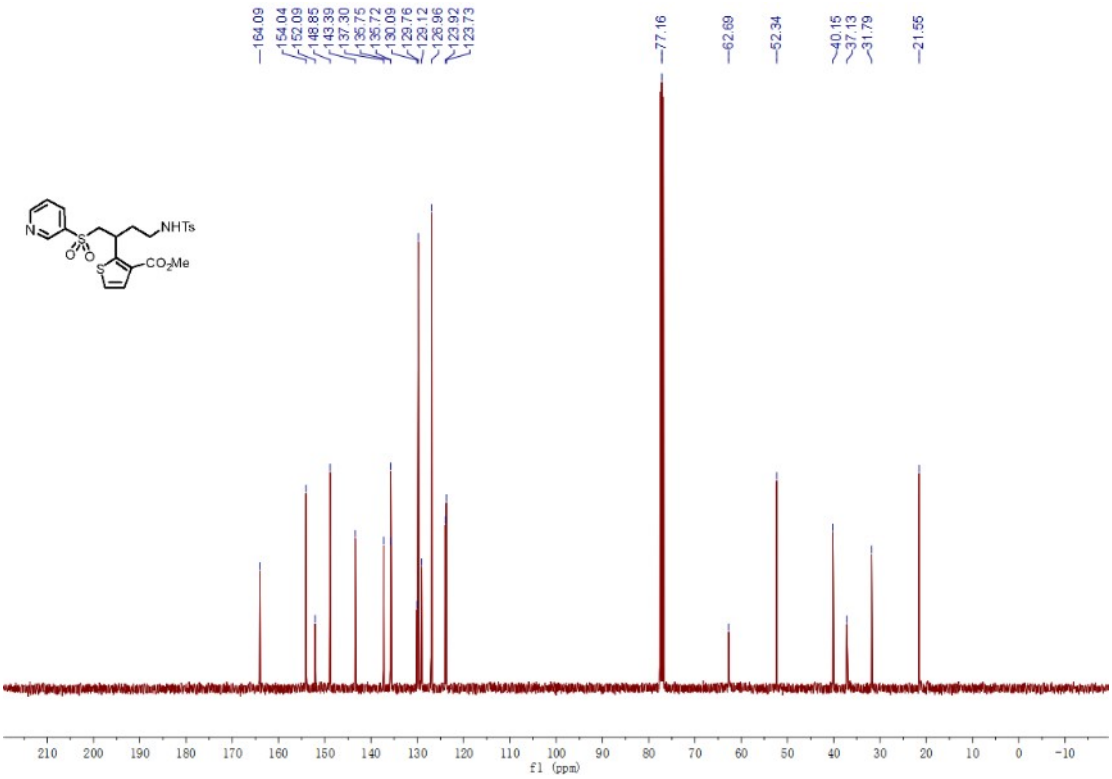
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 4s



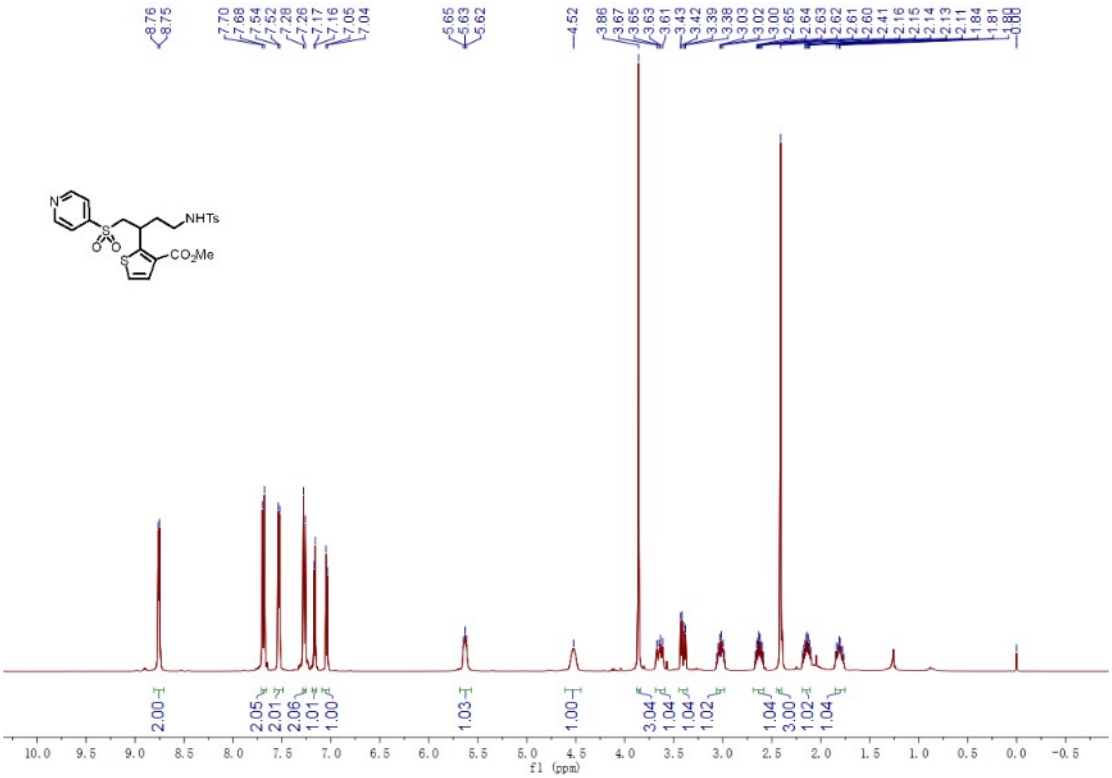
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 4t



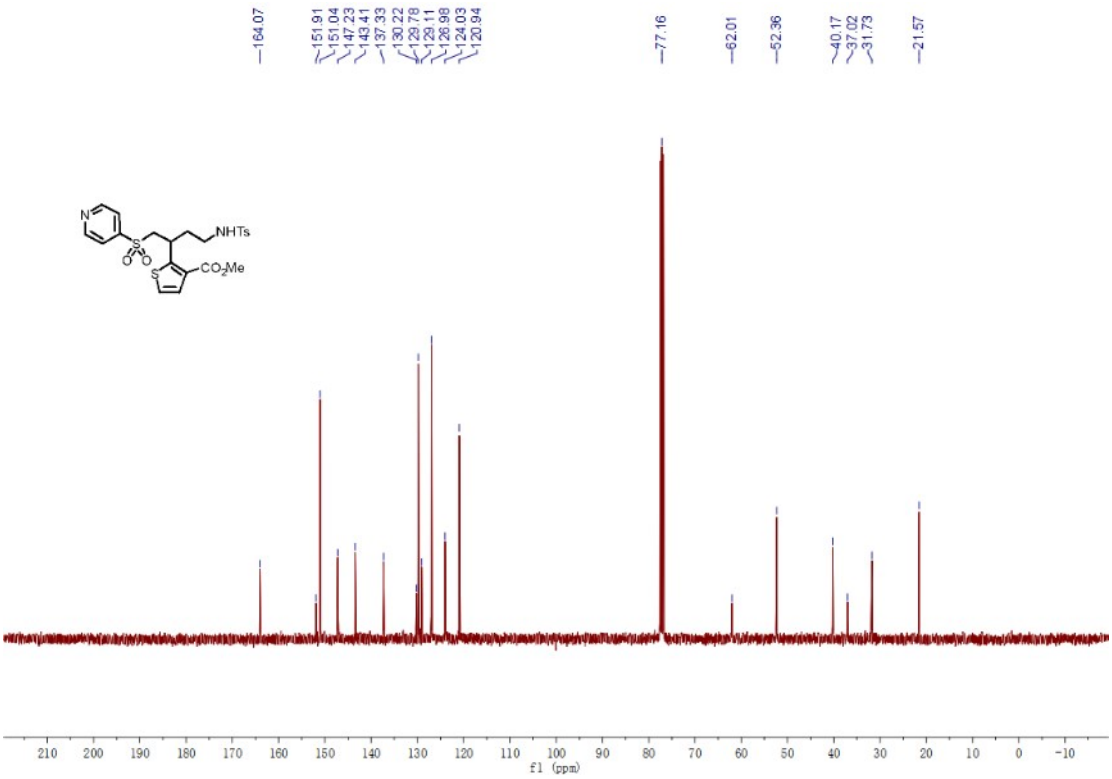
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 4t



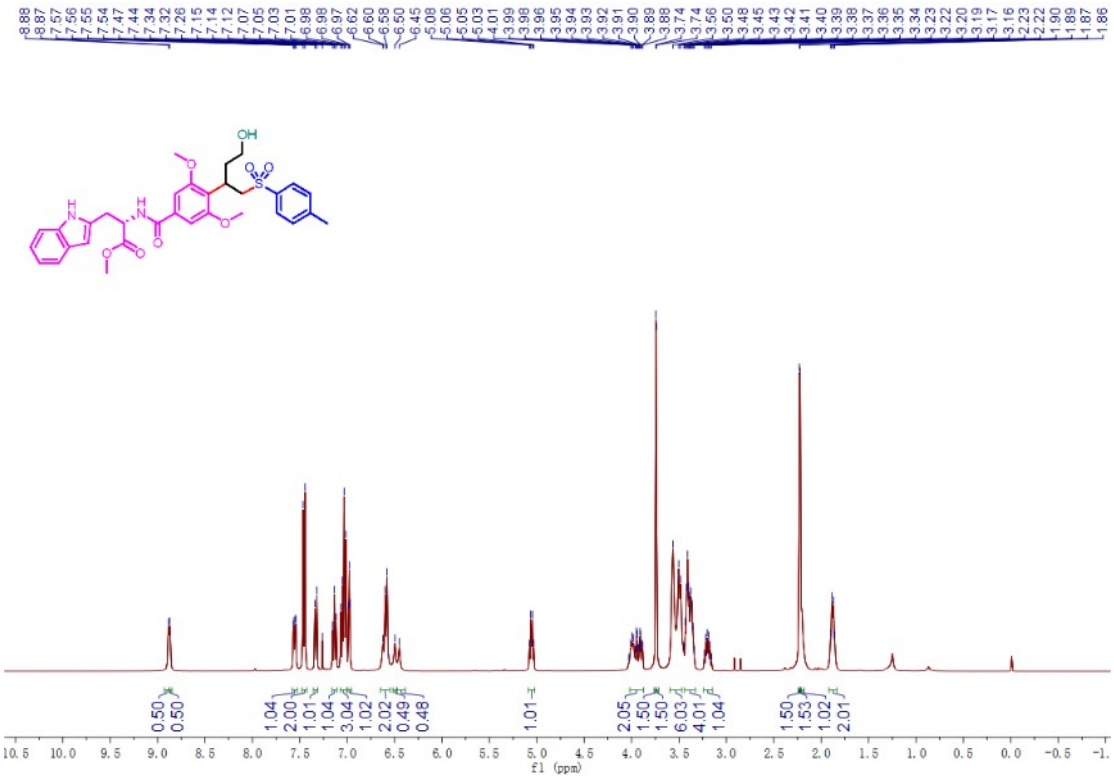
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 4u



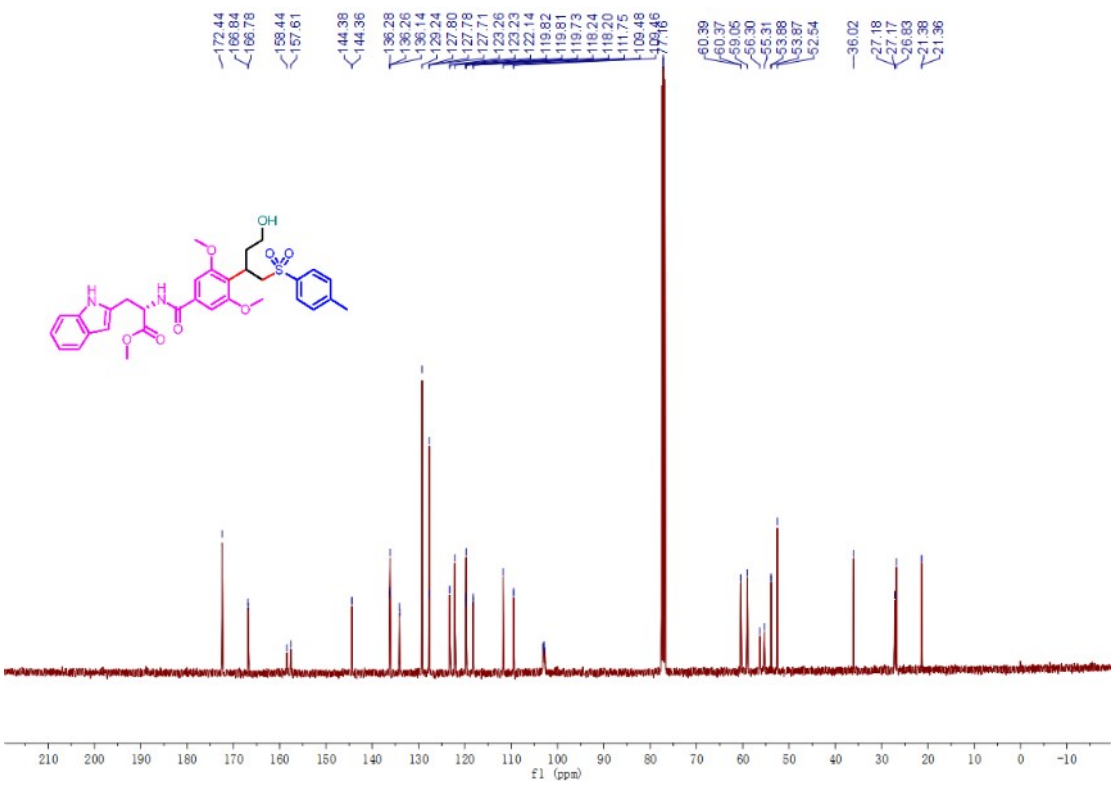
^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 4u



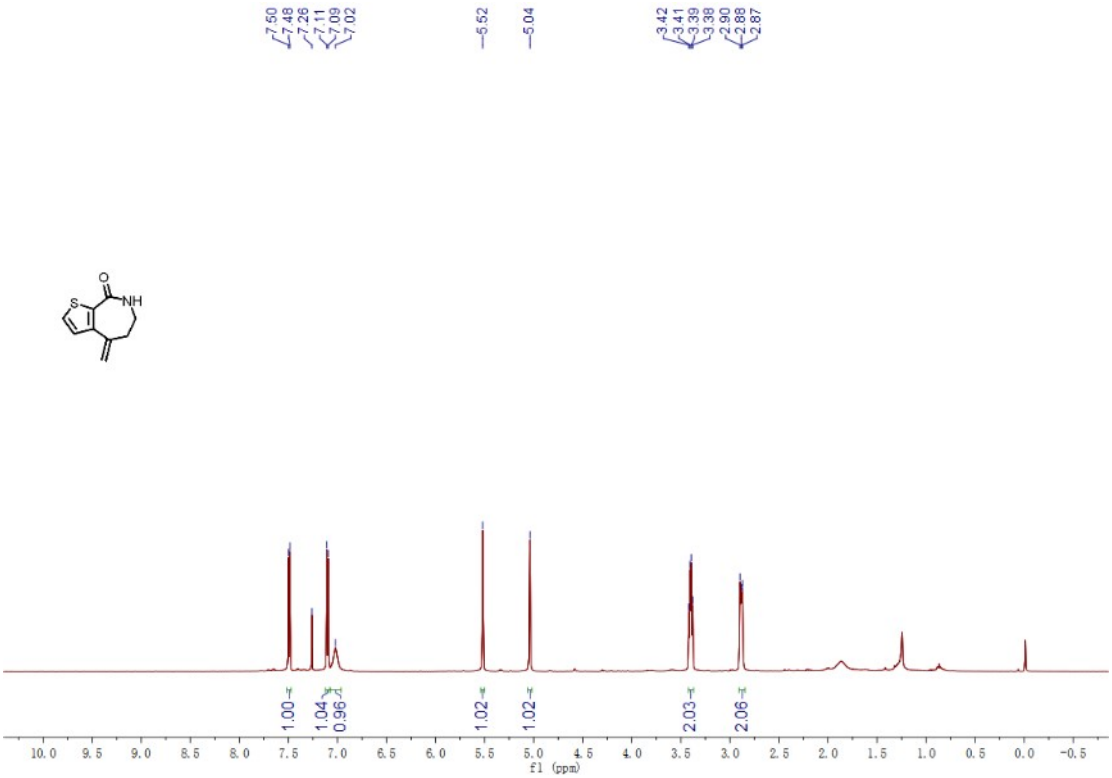
^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 5



^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 5



^{1}H NMR spectrum (400MHz, $CDCl_3$) of compound 6



^{13}C NMR spectrum (100MHz, $CDCl_3$) of compound 6