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Supplementary Information

Copper-Mediated Construction of Benzothieno[3,2-*b*]benzofurans by Intramolecular Dehydrogenative C−O Coupling Reaction

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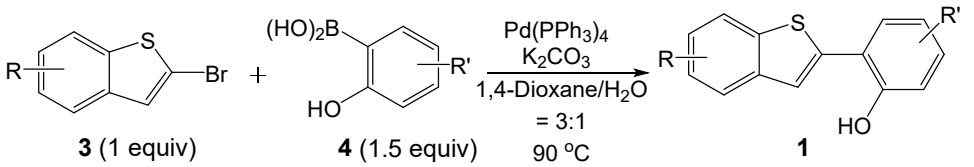
1. General Information

Chemicals were purchased from commercial suppliers such as Alfa Aesar, Aladdin, Heowns, Innochem, Meryer or Bidepharm, and used without further purification unless otherwise noted. Anhydrous toluene was obtained by distillation over CaH_2. Anhydrous dimethyl sulfoxide was refluxed for 4 h over CaH_2, and then fractionally distilled at low pressure.

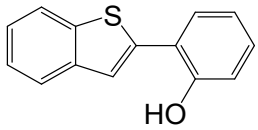
Thin-layer chromatography was done using TLC silica gel GF254 glass plates and was visualized with a UV lamp at 254 nm and 365 nm. Silica gel (200-300 mesh) was used for flash column chromatography.

Proton and carbon nuclear magnetic resonance (^{1}H NMR and ^{13}C NMR) spectra were measured on JEOL 400YH spectrometer at ambient temperature. Chemical shifts (δ) are reported in parts per million (ppm) downfield of tetramethylsilane (TMS, δ = 0), and the residual solvent peaks were used as internal references, for ^{1}H NMR: $CDCl_3$ = 7.26 ppm; for ^{13}C NMR: $CDCl_3$ = 77.16 ppm. The order of citation in parentheses is: a) multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, td = triplet of doublets, dt = doublet of triplets, ddd = doublet of doublet of doublets, m = multiplet), b) coupling constants, c) number of protons. Coupling constants (J) are reported in Hertz (Hz). The high-resolution mass spectra (HRMS) were conducted on Thermoscientific Q Exactive Focus (ESI).

2. General procedures for the 2-(benzo-[*b*]thiophen-2-yl)phenol derivatives

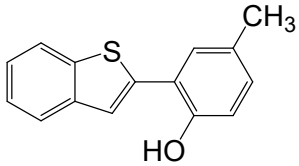


To a 25 mL Schlenk tube with a stirring bar, 2-bromobenzo[*b*]thiophene derivatives **3** (1 mmol, 1 equiv), 2-hydroxyphenylboronic acid derivatives **4** (1.5 mmol, 1.5 equiv), K_2CO_3 (2 mmol, 2 equiv) and $Pd(PPh_3)_4$ (0.05 mmol, 5 mol %) were added. The tube was evacuated and refilled with nitrogen three times. 1,4-Dioxane/H_2O (4 mL, v:v = 3:1) was added in a stream of nitrogen atmosphere. The tube was sealed and bubbled with nitrogen for 15 minutes to remove oxygen. The reaction was heated to 90 °C overnight. After being allowed to cool to room temperature, 1 M HCl (2 mL) was added to acidify the solution. By extraction with CH_2Cl_2, the organic layer was separated and dried with Na_2SO_4. After evaporation under a vacuum, the residue was purified on silica gel column chromatography with petroleum ether (PE)/ethyl acetate (EA) (v:v = 10:1) as the eluent to afford the corresponding compounds **1**.



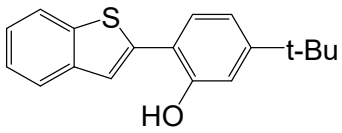
2-(benzo[*b*]thiophen-2-yl)phenol (1a)[1-2]**:** Following the general procedure, the target product was obtained after purification by column chromatography (PE/EA = 10:1) as a white solid (194.6 mg, 0.861 mmol, 86% yield).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.86 (dd, *J* = 7.3, 2.3 Hz, 1H), 7.80 (dd, *J* = 7.3, 2.3 Hz, 1H), 7.55 (s, 1H), 7.51 (dd, *J* = 7.5, 2.1 Hz, 1H), 7.43 – 7.32 (m, 2H), 7.27 (td, *J* = 7.8, 2.3 Hz, 1H), 7.00 (t, *J* = 7.3 Hz, 1H), 6.99 (d, *J* = 7.8 Hz, 1H), 5.66 (s, 1H). ^{13}C NMR (100 MHz, chloroform-*d*) δ 152.85, 140.42, 140.01, 139.33, 130.43, 130.03, 124.75, 124.67, 123.81, 122.95, 122.27, 121.17, 121.01, 116.44. HRMS (ESI$^-$) m/z: [M–H]$^-$ calcd for $C_{14}H_{10}OS$ 225.0380, found 225.0368.



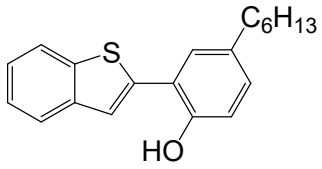
2-(benzo[*b*]thiophen-2-yl)-4-methylphenol (1b): Following the general procedure, the target product was obtained after purification by column chromatography (PE/EA = 10:1) as a white solid (232.8 mg, 0.970 mmol, 97% yield).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.96 – 7.91 (m, 1H), 7.67 – 7.62 (m, 1H), 7.47 (s, 1H), 7.44 – 7.36 (m, 2H), 7.13 (d, *J* = 7.8 Hz, 1H), 7.13 (s, 1H), 6.95 (d, *J* = 7.8 Hz, 1H), 4.91 (s, 1H), 2.33 (s, 3H). ^{13}C NMR (101 MHz, chloroform-*d*) δ 151.21, 140.68, 138.19, 132.59, 131.26, 130.38, 129.95, 125.54, 125.04, 124.76, 123.28, 123.03, 121.43, 115.77, 20.62. HRMS (ESI$^-$) m/z: [M–H]$^-$ calcd for $C_{15}H_{12}OS$ 239.0536, found 239.0531.



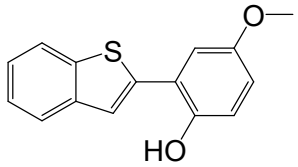
2-(benzo[*b*]thiophen-2-yl)-5-(tert-butyl)phenol (1c): Following the general procedure, the target product was obtained after purification by column chromatography (PE/EA = 10:1) as a white solid (276.4 mg, 0.979 mmol, 98% yield).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.95 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.70 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.48 (s, 1H), 7.4 – 7.36 (m, 2H), 7.27 (d, *J* = 8.0 Hz, 1H), 7.11 (s, 1H), 7.08 (d, *J* = 8.0 Hz, 1H), 5.07 (s, 1H), 1.37 (s, 9H). ^{13}C NMR (101 MHz, chloroform-*d*) δ 153.56, 153.06, 140.70, 138.30, 132.45, 130.42, 125.42, 125.03, 124.71, 123.37, 123.02, 118.70, 117.91, 113.11, 34.87, 31.41. HRMS (ESI$^-$) m/z: [M–H]$^-$ calcd for $C_{18}H_{18}OS$ 281.1005, found 281.0999.



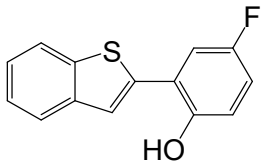
2-(benzo[*b*]thiophen-2-yl)-4-hexylphenol (1d): Following the general procedure, the target product was obtained after purification by column chromatography (PE/EA = 20:1) as a white solid (232.5 mg, 0.750 mmol, 75% yield).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.97 – 7.91 (m, 1H), 7.69 – 7.63 (m, 1H), 7.49 (s, 1H), 7.44 – 7.37 (m, 2H), 7.14 (d, *J* = 8.0 Hz, 1H), 7.13 (s, 1H), 6.97 (d, *J* = 8.0 Hz, 1H), 4.98 (s, 1H), 2.59 (t, *J* = 7.6 Hz, 2H), 1.65 – 1.57 (m, 2H), 1.34 – 1.26 (m, 6H), 0.88 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, chloroform-*d*) δ 151.31, 140.70, 138.25, 135.19, 132.67, 130.63, 129.73, 125.50, 125.04, 124.76, 123.31, 123.04, 121.32, 115.73, 35.18, 31.86, 29.11, 24.94, 22.78, 14.27. HRMS (ESI$^-$) m/z: [M−H]$^-$ calcd for $C_{20}H_{22}OS$ 309.1317, found 309.1314.



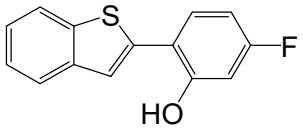
2-(benzo[*b*]thiophen-2-yl)-4-methoxyphenol (1e): Following the general procedure, the target product was obtained after purification by column chromatography (PE/EA = 20:1) as a white solid (250.9 mg, 0.980 mmol, 98% yield).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.97 – 7.92 (m, 1H), 7.70 – 7.65 (m, 1H), 7.50 (s, 1H), 7.46 – 7.35 (m, 2H), 6.99 (d, *J* = 8.7 Hz, 1H), 6.94 – 6.85 (m, 2H), 5.29 (s, 1H), 3.79 (s, 3H). ^{13}C NMR (101 MHz, chloroform-*d*) δ 153.51, 147.43, 140.66, 138.05, 132.45, 125.75, 125.09, 124.83, 123.24, 123.04, 122.19, 116.71, 115.68, 115.49, 55.95. HRMS (ESI$^-$) m/z: [M−H]$^-$ calcd for $C_{15}H_{12}O_2S$ 255.0485, found 255.0483.



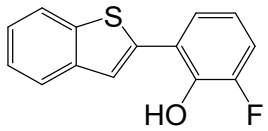
2-(benzo[*b*]thiophen-2-yl)-4-fluorophenol (1f): Following the general procedure, the target product was obtained after purification by column chromatography (PE/EA = 10:1) as a faint yellow solid (236.7 mg, 0.969 mmol, 97% yield).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.87 (d, *J* = 7.4 Hz, 1H), 7.82 (d, *J* = 7.6 Hz , 1H), 7.58 (s, 1H), 7.46 – 7.32 (m, 2H), 7.23 (dd, *J* = 9.0, 2.9 Hz, 1H), 7.05 – 6.88 (m, 2H), 5.51 (s, 1H). ^{13}C NMR (101 MHz, chloroform-*d*) δ 156.86 (d, $^1J_{C\text{-}F}$ = 238.9 Hz), 149.53 (d, $^4J_{C\text{-}F}$ = 1.9 Hz), 140.70, 137.72, 131.30, 126.24, 125.28, 125.00, 123.12, 122.99, 122.52 (d,^{3} $J_{C\text{-}F}$ = 8.7 Hz), 116.99 (d, $^2J_{C\text{-}F}$ = 23.7 Hz), 116.88 (d, $^3J_{C\text{-}F}$ = 8.2 Hz), 116.31 (d, $^2J_{C\text{-}F}$ = 22.6 Hz). HRMS (ESI$^-$) m/z: [M−H]$^-$ calcd for $C_{14}H_9FOS$ 243.0285, found 243.0282.



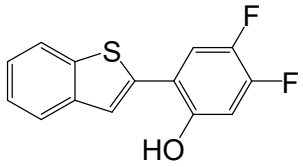
2-(benzo[*b*]thiophen-2-yl)-5-fluorophenol (1g): Following the general procedure, the target product was obtained after purification by column chromatography (PE/EA = 10:1) as a colorless oil (239.1 mg, 0.979 mmol, 98% yield).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.95 (ddd, *J* = 7.0, 2.1, 0.6 Hz, 1H), 7.60 (dd, *J* = 7.7, 1.6, 0.8 Hz, 1H), 7.49 (s, 1H), 7.47 – 7.37 (m, 2H), 7.27 (dd, *J* = 8.5, 6.5 Hz, 1H), 7.03 – 6.54 (m, 2H), 5.24 (s, 1H). ^{13}C NMR (101 MHz, chloroform-*d*) δ 163.47 (d, $^{1}J_{C\text{-}F}$ = 246.6 Hz), 154.60 (d, $^{3}J_{C\text{-}F}$ = 12.0 Hz), 140.54, 137.98, 131.64 (d, $^{3}J_{C\text{-}F}$ = 10.1 Hz), 131.23, 125.83, 125.06, 124.76, 122.95, 122.85, 117.57 (d, $^{4}J_{C\text{-}F}$ = 3.4 Hz), 107.72 (d,^{2} $J_{C\text{-}F}$ = 21.7 Hz), 103.41 (d, $^{2}J_{C\text{-}F}$ = 25.0 Hz). HRMS (ESI^{-}) m/z: [M−H]$^{-}$ calcd for $C_{14}H_9FOS$ 243.0285, found 243.0280.



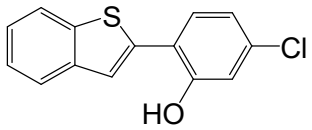
2-(benzo[*b*]thiophen-2-yl)-6-fluorophenol (1h): Following the general procedure, the target product was obtained after purification by column chromatography (PE/EA = 10:1) as a colorless oil (239.1 mg, 0.979 mmol, 98% yield).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.97 – 7.92 (m, 1H), 7.71 – 7.66 (m, 1H), 7.53 (s, 1H), 7.46 – 7.33 (m, 2H), 7.21 – 7.09 (m, 2H), 7.01 – 6.88 (m, 1H), 5.22 (s, 1H). ^{13}C NMR (101 MHz, chloroform-*d*) δ 151.41 (d, $^{1}J_{C\text{-}F}$ = 239.9 Hz), 141.60 (d, $^{2}J_{C\text{-}F}$ = 13.5 Hz), 140.23, 137.95, 131.60 (d, $^{3}J_{C\text{-}F}$ = 3.3 Hz), 126.24 (d, $^{4}J_{C\text{-}F}$ = 3.9 Hz), 125.71, 124.69, 124.44, 124.36 (d, $^{4}J_{C\text{-}F}$ = 1.9 Hz, this carbon might be the C-2 of benzothiophene, it is splitted by fluorine), 123.15, 122.83, 120.19 (d, $^{3}J_{C\text{-}F}$ = 7.7 Hz), 115.34 (d, $^{2}J_{C\text{-}F}$ = 18.8 Hz). HRMS (ESI^{-}) m/z: [M−H]$^{-}$ calcd for $C_{14}H_9FOS$ 243.0285, found 243.0278.



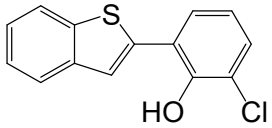
2-(benzo[*b*]thiophen-2-yl)-4,5-difluorophenol (1i): Following the general procedure, the target product was obtained after purification by column chromatography (PE/EA = 10:1) as a colorless oil (254.1 mg, 0.969 mmol, 97% yield).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.98 – 7.92 (m, 1H), 7.63 – 7.57 (m, 1H), 7.50 (s, 1H), 7.47 – 7.38 (m, 2H), 7.14 (dd, *J* = 10.5, 8.7 Hz, 1H), 6.88 (dd, *J* = 11.4, 7.0 Hz, 1H), 5.15 (s, 1H). ^{13}C NMR (101 MHz, chloroform-*d*) δ 150.49 (dd, $J_{C\text{-}F}$ = 248.8, 13.7 Hz), 149.74 (dd, $J_{C\text{-}F}$ = 9.6, 1.9 Hz), 144.61 (dd, $J_{C\text{-}F}$ = 241.1, 12.8 Hz), 140.55, 137.58, 130.26, 126.37, 125.24, 124.96, 123.04, 122.65, 118.39 (d, $J_{C\text{-}F}$ = 18.3 Hz), 117.18 (dd, $J_{C\text{-}F}$ = 5.8, 3.8 Hz), 105.19 (d, $J_{C\text{-}F}$ = 20.7 Hz). HRMS (ESI^{-}) m/z: [M−H]$^{-}$ calcd for $C_{14}H_8F_2OS$ 261.0191, found 261.0187.



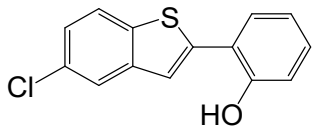
2-(benzo[*b*]thiophen-2-yl)-5-chlorophenol (1j): Following the general procedure, the target product was obtained after purification by column chromatography (PE/EA = 10:1) as a colorless oil (215.8 mg, 0.828 mmol, 83% yield).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.96 (ddd, *J* = 7.1, 2.3, 0.8 Hz, 1H), 7.61 (ddd, *J* = 7.1, 2.4, 0.6 Hz, 1H), 7.50 (s, 1H), 7.48 – 7.37 (m, 2H), 7.25 (d, *J* = 8.4 Hz, 1H), 7.09 (d, *J* = 2.1 Hz, 1H), 7.03 (dd, *J* = 8.1, 2.1 Hz, 1H), 5.19 (s, 1H). ^{13}C NMR (101 MHz, chloroform-*d*) δ 154.00, 140.60, 137.77, 134.91, 131.52, 131.01, 125.94, 125.14, 124.84, 123.00, 122.83, 120.96, 120.16, 116.28. HRMS (ESI$^-$) m/z: [M−H]$^-$ calcd for $C_{14}H_9ClOS$ 258.9990, found 258.9986.



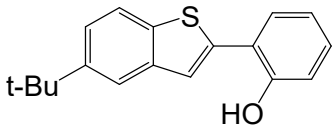
2-(benzo[*b*]thiophen-2-yl)-6-chlorophenol (1k): Following the general procedure, the target product was obtained after purification by column chromatography (PE/EA = 10:1) as a white solid (239.0 mg, 0.917 mmol, 92% yield).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.95 – 7.91 (m, 1H), 7.73 – 7.62 (m, 1H), 7.51 (s, 1H), 7.43 – 7.36 (m, 3H), 7.30 (dd, *J* = 7.7, 1.6 Hz, 1H), 6.98 (t, *J* = 7.8 Hz, 1H), 5.67 (s, 1H). ^{13}C NMR (101 MHz, chloroform-*d*) δ 149.15, 140.11, 137.99, 132.22, 129.89, 128.97, 125.65, 124.61, 124.35, 123.59, 123.18, 122.81, 120.95, 120.70. HRMS (ESI$^-$) m/z: [M−H]$^-$ calcd for $C_{14}H_9ClOS$ 258.9990, found 258.9987.



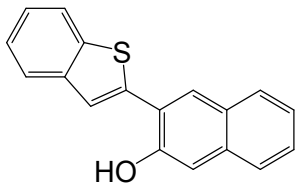
2-(5-chlorobenzo[*b*]thiophen-2-yl)phenol (1l): Following the general procedure, the target product was obtained after purification by column chromatography (PE/EA = 10:1) as a white solid (226.2 mg, 0.868 mmol, 87% yield).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.85 (dd, *J* = 8.6, 0.7 Hz, 1H), 7.62 (dd, *J* = 2.0, 0.6 Hz, 1H), 7.55 (s, 1Hz), 7.42 – 7.33 (m, 2H), 7.31 – 7.29 (m, 1H), 7.06 (d, *J* = 7.8 Hz, 1H), 7.05 (s, 1H), 5.08 (s, 1H). ^{13}C NMR (101 MHz, chloroform-*d*) δ 153.23, 139.49, 138.59, 131.88, 131.16, 130.80, 129.96, 127.28, 125.45, 123.84, 122.80, 120.98, 120.83, 116.01. HRMS (ESI$^-$) m/z: [M−H]$^-$ calcd for $C_{14}H_9ClOS$ 258.9990, found 258.9986.



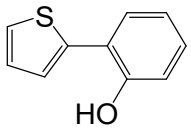
2-(5-(tert-butyl)benzo[*b*]thiophen-2-yl)phenol (1m): Following the general procedure, the target product was obtained after purification by column chromatography (PE/EA = 10:1) as a white solid (253.8 mg, 0.899 mmol, 90% yield).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.87 (dd, *J* = 8.6, 0.6 Hz, 1H), 7.62 (s, 1H), 7.51 (dd, *J* = 8.6, 1.9 Hz, 1H), 7.47 (s, 1H), 7.40 – 7.31 (m, 2H), 7.13 – 7.01 (m, 2H), 5.13 (s, 1H), 1.35 (s, 9H). ^{13}C NMR (101 MHz, chloroform-*d*) δ 153.38, 148.20, 137.93, 137.89, 132.29, 130.72, 129.63, 125.70, 123.43, 122.45, 121.72, 120.63, 119.00, 115.88, 34.81, 31.54. HRMS (ESI$^-$) m/z: [M−H]$^-$ calcd for $C_{18}H_{18}OS$ 281.1005, found 281.1000.



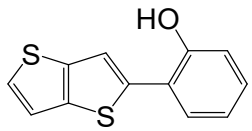
3-(benzo[*b*]thiophen-2-yl)naphthalen-2-ol (1n): Following the general procedure, the target product was obtained after purification by column chromatography (PE/EA = 10:1) as a brownish red solid (270.9 mg, 0.980 mmol, 98% yield).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.98 (dd, *J* = 8.2, 1.1 Hz, 1H), 7.85 (s, 1H), 7.79 (t, *J* = 7.4 Hz, 2H), 7.69 (d, *J* = 7.4 Hz, 1H), 7.60 (s, 1H), 7.52 – 7.32 (m, 5H), 5.21 (s, 1H). ^{13}C NMR (101 MHz, chloroform-*d*) δ 151.49, 140.68, 138.39, 134.74, 132.20, 130.49, 128.82, 127.87, 126.89, 126.54, 126.16, 125.17, 124.91, 124.12, 124.11, 123.29, 123.08, 110.45. HRMS (ESI$^-$) m/z: [M−H]$^-$ calcd for $C_{18}H_{12}OS$ 275.0536, found 275.0534.



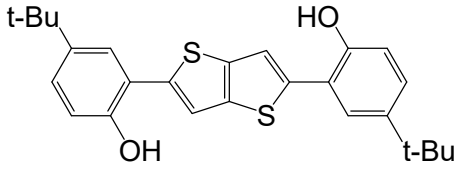
2-(thiophen-2-yl)phenol (1o)[3-4]**:** Following the general procedure, the target product was obtained after purification by column chromatography (PE/EA = 10:1) as a light yellow oil (172.3 mg, 0.978 mmol, 98% yield).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.42 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.40 (dd, *J* = 5.3, 1.2 Hz, 1H), 7.30 (dd, *J* = 3.5, 1.2 Hz, 1H), 7.24 (ddd, *J* = 8.0, 7.7, 1.5 Hz, 1H), 7.15 (dd, *J* = 5.0, 3.4 Hz, 1H), 6.99 – 6.94 (m, 2H), 5.55 (s, 1H). ^{13}C NMR (101 MHz, chloroform-*d*) δ 152.39, 138.71, 130.02, 129.30, 127.75, 126.19, 125.95, 120.93, 120.85, 116.05. HRMS (ESI$^-$) m/z: [M−H]$^-$ calcd for $C_{10}H_8OS$ 175.0223, found 175.0211.



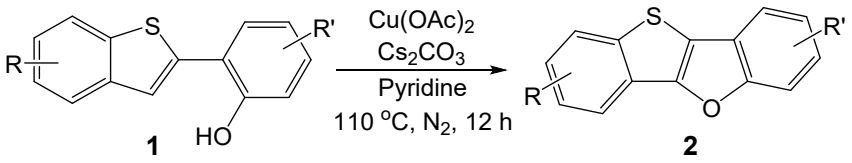
2-(thieno[3,2-*b*]thiophen-2-yl)phenol (1p): Following the general procedure, the target product was obtained after purification by column chromatography (PE/EA = 10:1) as a yellow solid (213.4 mg, 0.919 mmol, 92% yield).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.52 (d, *J* = 0.8 Hz, 1H), 7.47 (dd, *J* = 7.6, 2 Hz, 1H), 7.40 (d, *J* = 5.3 Hz, 1H), 7.29 (dd, *J* = 5.2, 0.7 Hz, 1H), 7.24 (td, *J* = 7.8, 1.6 Hz, 1H), 7.00 (td, *J* = 7.4, 0.8 Hz, 2H), 5.62 (s, 1H). ^{13}C NMR (101 MHz, chloroform-*d*) δ152.53, 140.68, 139.74, 139.39, 129.95, 129.57, 127.20, 121.33, 121.00, 119.47, 118.58, 116.23, 77.32, 77.00, 76.68. HRMS (ESI$^-$) m/z: [M−H]$^-$ calcd for $C_{12}H_8OS_2$ 230.9943, found 230.9936.

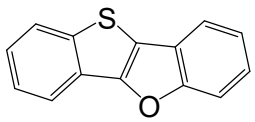


2,2'-(thieno[3,2-*b*]thiophene-2,5-diyl)bis(4-(*tert*-butyl)phenol) (1q): Following the general procedure, the target product was obtained after purification by column chromatography (PE/EA = 4:1) as a yellow solid (375.0 mg, 0.863 mmol, 86% yield).
^{1}H NMR (400 MHz, DMSO-d_6) δ 10.11 (s, 2H), 7.78 (s, 2H), 7.51 (d, *J* = 8.3 Hz, 2H), 6.92 (d, *J* = 2.1 Hz, 2H), 6.86 (dd, *J* = 8.3, 2.0 Hz, 2H), 1.21 (s, 18H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 153.72, 151.91, 141.68, 138.98, 127.72, 118.77, 117.33, 117.23, 113.72, 34.76, 31.49. HRMS (ESI$^-$) m/z: [M−H]$^-$ calcd for $C_{26}H_{28}O_2S_2$ 435.1457, found 435.1452.

3. General procedure for copper-catalyzed construction of benzothienobenzofurans

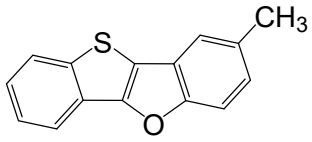


Into a 25 mL Schlenk tube with a stirring bar, substrates **1** (0.2 mmol), $Cu(OAc)_2$ (0.6 mmol, 3 equiv) and Cs_2CO_3 (0.2 mmol, 1 equiv) were sequentially added. The tube was evacuated and refilled with argon three times. Pyridine (water ≤ 50 ppm) (4 mL) was added in a stream of argon atmosphere. The tube was sealed and it was bubbled with nitrogen for 15 minutes to remove oxygen. The reaction was heated to 110 °C under nitrogen atmosphere for 12 h. After being cooled to room temperature, 1M HCl (15 mL) was added to acidify the solution. By extraction with CH_2Cl_2 (4 × 10 mL), the organic layer was separated and dried with Na_2SO_4. After evaporation under a vacuum, the residue was purified on silica gel column chromatography with hexane as the eluent to afford the target compounds **2**.



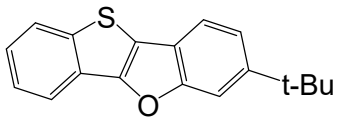
benzo[4,5]thieno[3,2-*b*]benzofuran (2a)[5-9]**:** Following the general procedure, the target product was obtained after purification by column chromatography (PE) as a white solid (38.4 mg, 0.171 mmol, 86% yield).

^{1}H NMR (400 MHz, chloroform-*d*) δ 8.02 (d, *J* = 8.1 Hz, 1H), 7.89 (d, *J* = 8.1 Hz, 1H), 7.74 (d, *J* = 8.0 Hz, 1H), 7.66 (d, *J* = 8.0 Hz, 1H), 7.53 – 7.46 (m, 1H), 7.42 – 7.32 (m, 3 H). ^{13}C NMR (101 MHz, chloroform-*d*) δ 158.90, 153.12, 142.11, 125.25, 125.07, 125.04 (one carbon was overlapped), 124.49, 124.17, 123.43, 119.82, 119.72, 118.70, 112.69. HRMS (ESI$^+$) m/z: $[M]^+$ calcd for $C_{14}H_8OS$ 224.0290, found 224.0289.



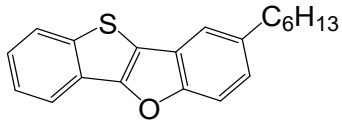
8-methylbenzo[4,5]thieno[3,2-*b*]benzofuran (2b)[10]**:** Following the general procedure, the target product was obtained after purification by column chromatography (PE) as a white solid (42.8 mg, 0.180 mmol, 90% yield).

^{1}H NMR (400 MHz, chloroform-*d*) δ 8.05 (ddd, *J* = 7.9, 1.4, 0.8 Hz, 1H), 7.83 (ddd, *J* = 8.1, 1.1, 0.8 Hz, 1H), 7.72 – 7.71 (m, 1H), 7.50 (ddd, *J* = 7.6, 7.3, 1.2 Hz, 1H), 7.48 (d, *J* = 8.5 Hz, 1H), 7.37 – 7.33 (m, 1H), 7.15 (ddd, *J* = 8.5, 1.9, 0.7 Hz, 1H), 2.54 (s, 3H). ^{13}C NMR (101 MHz, chloroform-*d*) δ 159.26, 159.20, 138.35, 133.21, 130.67, 125.42, 124.69, 124.06 (one carbon was overlapped), 123.72, 121.50, 119.83, 119.31, 111.51, 21.60. HRMS (ESI$^+$) m/z: $[M]^+$ calcd for $C_{15}H_{10}OS$ 238.0447, found 238.0442.



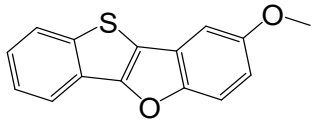
7-(tert-butyl)benzo[4,5]thieno[3,2-*b*]benzofuran (2c): Following the general procedure , the target product was obtained after purification by column chromatography (PE) as a white solid (51.0 mg, 0.182 mmol, 91% yield).

^{1}H NMR (400 MHz, chloroform-*d*) δ 8.04 (ddd, *J* = 7.9, 1.4, 0.7 Hz, 1H), 7.83 (dd, *J* = 8.2, 0.7 Hz, 1H), 7.82 (ddd, *J* = 8.2, 1.0, 0.8 Hz, 1H), 7.64 (dd, *J* = 1.7, 0.6 Hz, 1H), 7.50 (ddd, *J* = 7.8, 7.6, 1.2 Hz, 1H), 7.45 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.34 (ddd, *J* = 7.6, 7.3, 1.2 Hz, 1H), 1.42 (s, 9H). ^{13}C NMR (101 MHz, chloroform-*d*) δ 161.13, 158.68, 147.60, 138.22, 130.54, 125.26, 123.93, 123.53, 121.37, 121.32, 121.05, 119.75, 118.31, 108.85, 35.02, 31.67. HRMS (ESI$^+$) m/z: $[M]^+$ calcd for $C_{18}H_{16}OS$ 280.0916, found 280.0903.



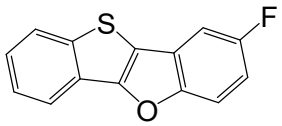
8-hexylbenzo[4,5]thieno[3,2-b]benzofuran (2d): Following the general procedure, the target product was obtained after purification by column chromatography (PE) as a white solid (55.4 mg, 0.18 mmol, 90% yield).

^{1}H NMR (400 MHz, chloroform-*d*) δ 8.07 (ddd, *J* = 7.9, 1.2, 0.7 Hz, 1H), 7.83 (dt, *J* = 8.1, 0.8 Hz, 1H), 7.71 (dd, *J* = 1.9, 0.6 Hz, 1H), 7.51 (td, *J* = 7.2, 1.0 Hz, 1H), 7.50 (d, *J* = 8.5 Hz, 1H),7.35 (ddd, *J* = 8.1, 7.3, 1.2 Hz, 1H), 7.15 (dd, *J* = 8.5, 1.9 Hz, 1H), 2.78 (t, *J* = 7.8 Hz, 2H), 1.79 – 1.64 (m, 2H), 1.44 – 1.25 (m, 6H), 0.89 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, chloroform-*d*) δ 159.16, 159.09, 138.35, 138.19, 130.54, 125.25, 124.01, 123.92, 123.89, 123.57, 121.40, 119.78, 118.54, 111.41, 36.03, 32.19, 31.76, 29.01, 22.63, 14.14. HRMS (ESI$^+$) m/z: $[M]^+$ calcd for $C_{20}H_{20}OS$ 308.1240, found 308.1219.



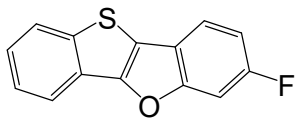
8-methoxybenzo[4,5]thieno[3,2-*b*]benzofuran (2e): Following the general procedure, the target product was obtained after purification by column chromatography (PE) as a white solid (32.5 mg, 0.128 mmol, 64% yield).

^{1}H NMR (400 MHz, chloroform-*d*) δ 8.04 (ddd, *J* = 7.9, 1.3, 0.6 Hz, 1H), 7.83 (ddd, *J* = 8.1, 1.1, 0.7 Hz, 1H), 7.58 – 7.46 (m, 2H), 7.39 (d, *J* = 2.7 Hz, 1H), 7.36 (td, *J* = 8.0, 1.3 Hz, 1H), 6.92 (dd, *J* = 9.0, 2.7 Hz, 1H), 3.95(s, 3 H). ^{13}C NMR (101 MHz, chloroform-*d*) δ 159.77, 156.33, 155.47, 138.09, 130.40, 125.30, 124.44, 123.93, 123.64, 121.24, 119.89, 112.18, 110.94, 102.75, 55.99. HRMS (ESI$^+$) m/z: $[M]^+$ calcd for $C_{15}H_{10}O_2S$ 254.0396, found 254.0390.



8-fluorobenzo[4,5]thieno[3,2-*b*]benzofuran (2f): Following the general procedure, the target product was obtained after purification by column chromatography (PE) as a white solid (41.2 mg, 0.170 mmol, 85% yield).

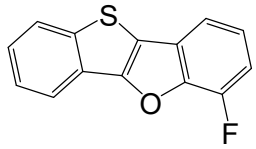
^{1}H NMR (400 MHz, chloroform-*d*) δ 8.01 (dz, *J* = 7.8 Hz, 1H), 7.89 (d, *J* = 8.2 Hz, 1H), 7.58 (dd, *J* = 9.1, 4.1 Hz, 1H), 7.49 (td, *J* = 8.7, 1.4 Hz, 1H), 7.46 – 7.36 (m, 2H), 7.10 (td, *J* = 8.9, 2.7 Hz, 1H). ^{13}C NMR (101 MHz, chloroform-*d*) δ 159.23 (d, $^1J_{C\text{-}F}$ = 239.4 Hz), 154.87, 154.57, 142.14, 125.33, 125.05, 124.89, 124.69 (d, $^3J_{C\text{-}F}$ = 10.9 Hz), 124.38, 119.86, 118.27 (d, $^4J_{C\text{-}F}$ = 3.8 Hz), 113.12 (d, $^3J_{C\text{-}F}$ = 9.6 Hz), 112.29 (d, $^2J_{C\text{-}F}$ = 26.0 Hz), 105.55 (d, $^2J_{C\text{-}F}$ = 26.5 Hz). HRMS (ESI$^+$) m/z: $[M]^+$ calcd for $C_{14}H_7FOS$ 242.0196, found 242.0196.



7-fluorobenzo[4,5]thieno[3,2-*b*]benzofuran (2g): Following the general procedure, the target product was obtained after purification by column chromatography (PE) as a white solid (37.8 mg, 0.156 mmol, 78% yield).

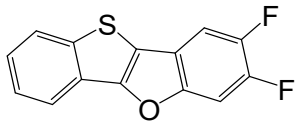
^{1}H NMR (400 MHz, chloroform-*d*) δ 8.03 (dd, *J* = 7.9, 0.7 Hz, 1H), 7.93 – 7.75 (m, 2H), 7.52 (td, *J* = 7.2, 1.0 Hz, 1H), 7.41 – 7.33 (m, 2H), 7.17 (ddd, *J* = 9.5, 8.6, 2.4 Hz, 1H). ^{13}C NMR (101 MHz, chloroform-*d*) δ 160.45 (d, $^3J_{C\text{-}F}$ = 14.0 Hz), 160.19 (d, $^1J_{C\text{-}F}$ = 242.8 Hz), 159.29 (d,

$^4J_{C\text{-}F}$ = 4 Hz) 138.35, 130.21, 125.55, 124.13, 124.02, 121.45, 120.53, 119.63, 119.17 (d, $^3J_{C\text{-}F}$ = 9.6 Hz), 111.54 (d, $^2J_{C\text{-}F}$ = 23.6 Hz), 100.48 (d, $^2J_{C\text{-}F}$ = 27.0 Hz). HRMS (ESI$^+$) m/z: $[M]^+$ calcd for $C_{14}H_7FOS$ 242.0196, found 242.0195.



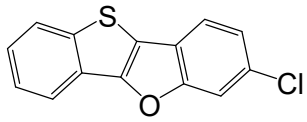
6-fluorobenzo[4,5]thieno[3,2-*b*]benzofuran (2h): Following the general procedure, the target product was obtained after purification by column chromatography (PE) as a white solid (32.9 mg, 0.136 mmol, 68% yield).

^{1}H NMR (400 MHz, chloroform-*d*) δ 8.05 (d, *J* = 7.9 Hz, 1H), 7.84 (d, *J* = 8.1 Hz, 1H), 7.68 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.52 (td, *J* = 7.6, 1.2 Hz, 1H), 7.39 (td, *J* = 8.5, 1.3 Hz, 1H), 7.33 (td, *J* = 8.0, 4.3 Hz, 1H), 7.11 (dd, *J* = 8.2, 1.1 Hz, 1H). ^{13}C NMR (101 MHz, chloroform-*d*) δ 159.88, 147.78 (d, $^1J_{C\text{-}F}$ = 250.0 Hz), 147.04 (d, $^2J_{C\text{-}F}$ = 12.6 Hz), 138.49, 129.93, 127.04 (d, $^4J_{C\text{-}F}$ = 2.6 Hz), 125.52, 124.29 (d, $^3J_{C\text{-}F}$ = 6.3 Hz), 124.16, 124.04, 121.49, 120.18, 114.71 (d, $^3J_{C\text{-}F}$ = 3.9 Hz), 110.45 (d, $^2J_{C\text{-}F}$ = 15.9 Hz). HRMS (ESI$^+$) m/z: $[M]^+$ calcd for $C_{14}H_7FOS$ 242.0196, found 242.0196.



7,8-difluorobenzo[4,5]thieno[3,2-*b*]benzofuran (2i): Following the general procedure, the target product was obtained after purification by column chromatography (PE) as a white solid (37.4 mg, 0.144 mmol, 72% yield).

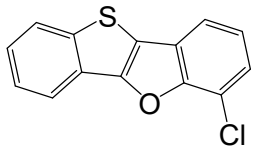
^{1}H NMR (400 MHz, chloroform-*d*) δ 7.99 (ddd, *J* = 7.3, 1.2, 0.7 Hz, 1H), 7.84 (ddd, *J* = 8.0, 1.1, 0.9 Hz, 1H), 7.67 (dd, *J* = 9.6, 7.7 Hz, 1H), 7.53 (td, *J* = 7.6, 1.1 Hz, 1H), 7.48 (dd, *J* = 9.8, 6.3 Hz, 1H), 7.39 (ddd, *J* = 8.5, 7.3, 1.4 Hz, 1H). ^{13}C NMR (101 MHz, chloroform-*d*) δ 160.20 (d, *J* = 3.7 Hz), 155.07 (d, *J* = 10.7 Hz), 147.95 (dd, *J* = 271.7, 13.9 Hz), 147.80 (dd, *J* = 215.1, 13.9 Hz), 138.15, 129.67, 125.58, 124.19, 124.06, 121.21, 119.57, 119.48, 106.18 (d, *J* = 21.2 Hz), 101.69 (d, *J* = 22.6 Hz). HRMS (ESI$^+$) m/z: $[M]^+$ calcd for $C_{14}H_6F_2OS$ 260.0102, found 260.0099.



7-chlorobenzo[4,5]thieno[3,2-*b*]benzofuran (2j): Following the general procedure, the target product was obtained after purification by column chromatography (PE) as a white solid (44.6 mg, 0.172 mmol, 86% yield).

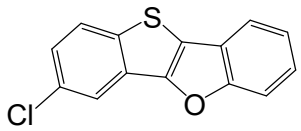
^{1}H NMR (400 MHz, chloroform-*d*) δ 8.02 (ddd, *J* = 7.9, 1.2, 0.6 Hz, 1H), 8.26 (dd, *J* = 8.2, 0.4 Hz, 1H), 7.81 (ddd, *J* = 7.9, 1.1, 0.7 Hz, 1H), 7.63 (d, *J* = 1.8 Hz, 1H), 7.51 (ddd, *J* = 7.4, 7.3, 1.1 Hz, 1H), 7.38 (d, *J* = 8.2 Hz, 1H), 7.36 (dt, *J* = 6.7, 1.2 Hz, 1H). ^{13}C NMR (101 MHz, chloroform-*d*) δ 160.53, 159.77, 138.40, 130.12, 129.50, 125.62, 124.26, 124.15 (one carbon

was overlapped), 122.71, 121.55, 119.67, 119.46, 112.78. HRMS (ESI$^+$) m/z: [M]$^+$ calcd for $C_{14}H_7ClOS$ 257.9900, found 257.9901.



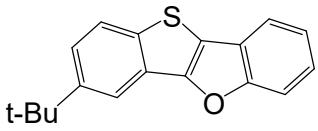
6-chlorobenzo[4,5]thieno[3,2-*b*]benzofuran (2k): Following the general procedure, the target product was obtained after purification by column chromatography (PE) as a white solid (33.6 mg, 0.130 mmol, 65% yield).

^{1}H NMR (400 MHz, chloroform-*d*) δ 8.05 (dd, *J* = 7.3, 0.7 Hz, 1H), 7.90 – 7.78 (m, 2H), 7.53 (td, *J* = 7.7, 1.5 Hz, 1H), 7.43 – 7.30 (m, 3H). ^{13}C NMR (101 MHz, chloroform-*d*) δ 159.58, 155.90, 138.39, 129.95, 125.46, 125.40, 124.38, 124.11, 123.96, 123.84, 121.42, 120.23, 117.47, 117.01. HRMS (ESI$^+$) m/z: [M]$^+$ calcd for $C_{14}H_7ClOS$ 257.9900, found 257.9894.



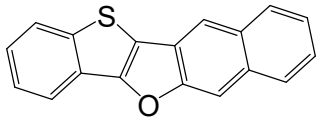
3-chlorobenzo[4,5]thieno[3,2-*b*]benzofuran (2l): Following the general procedure, the target product was obtained after purification by column chromatography (PE) as a white solid (41.7 mg, 0.161 mmol, 81% yield).

^{1}H NMR (400 MHz, chloroform-*d*) δ 8.03 (d, *J* = 2.1 Hz, 1H), 7.90 (dd, *J* = 7.3, 2.1 Hz, 1H), 7.75 (d, *J* = 8.6 Hz, 1H), 7.62 (d, *J* = 8.5 Hz, 1H), 7.47 – 7.29 (m, 3H). ^{13}C NMR (101 MHz, chloroform-*d*) δ 160.63, 160.01, 136.15, 131.58, 131.49, 124.90, 123.96 (one carbon was overlapped), 123.75, 123.50, 121.28, 119.36, 119.10, 112.06. HRMS (ESI$^+$) m/z: [M]$^+$ calcd for $C_{14}H_7ClOS$ 257.9900, found 257.9899.



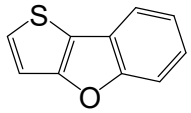
3-(tert-butyl)benzo[4,5]thieno[3,2-*b*]benzofuran (2m): Following the general procedure, the target product was obtained after purification by column chromatography (PE) as a white solid (51.0 mg, 0.182 mmol, 91% yield).

^{1}H NMR (400 MHz, chloroform-*d*) δ 8.05 (d, *J* = 2.4 Hz, 1H), 7.96 (dd, *J* = 7.1, 0.8 Hz, 1H), 7.76 (d, *J* = 8.6 Hz, 1H), 7.61 (d, *J* = 8.0, 1H), 7.48 – 7.29 (m, 3H), 1.46 (s, 9H). ^{13}C NMR (101 MHz, chloroform-*d*) δ 160.73, 159.45, 148.90, 135.40, 130.54, 126.40, 124.16, 123.54, 121.94, 120.12, 119.80, 119.20, 118.02, 112.04, 34.98, 31.75. HRMS (ESI$^+$) m/z: [M]$^+$ calcd for $C_{18}H_{16}OS$ 280.0916, found 280.0910.



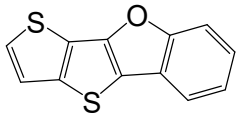
benzo[4,5]thieno[3,2-*b*]naphtho[2,3-d]furan (2n)[2,11]**:** Following the general procedure, the target product was obtained after purification by column chromatography (PE) as a white solid (34.7 mg, 0.127 mmol, 63% yield).

^{1}H NMR (400 MHz, chloroform-*d*) δ 8.32 (s, 1H), 8.18 (d, *J* = 7.3 Hz, 1H), 8.13 – 7.94 (m, 3H), 7.86 (d, *J* = 8.0 Hz, 1H), 7.66 – 7.46 (m, 3H), 7.39 (t, *J* = 8.2 Hz, 1H). ^{13}C NMR (101 MHz, chloroform-*d*) δ 162.05, 159.60, 154.96, 149.58, 138.07, 130.71, 130.54, 130.45, 128.00, 125.59, 125.12, 124.83, 124.37, 124.01, 123.80, 121.49, 116.59, 107.86. HRMS (ESI$^+$) m/z: $[M]^+$ calcd for $C_{18}H_{10}OS$ 274.0447, found 274.0457.



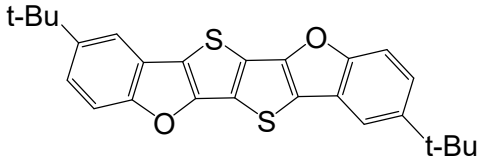
thieno[3,2-*b*]benzofuran (2o)[12]**:** Following the general procedure, the target product was obtained after purification by column chromatography (PE) as a white solid (15.7 mg, 0.0901 mmol, 45% yield).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.69 (dd, *J* = 7.1, 2.1 Hz, 1H), 7.57 (dd, *J* = 7.1, 2.3 Hz, 1H), 7.39 (d, *J* = 5.3 Hz, 1H), 7.36 – 7.28 (m, 2H), 7.17 (d, *J* = 5.3 Hz, 1H). ^{13}C NMR (101 MHz, chloroform-*d*) δ 159.28, 159.17, 127.53, 124.35, 123.75, 122.97, 119.31, 119.07, 112.44, 111.47. HRMS (ESI$^+$) m/z: $[M]^+$ calcd for $C_{10}H_6OS$ 174.0134, found 174.0132.



thieno[2',3':4,5]thieno[3,2-*b*]benzofuran (2p): Following the general procedure , the target product was obtained after purification by column chromatography (PE) as a white solid (18.6 mg, 0.0808 mmol, 40% yield).

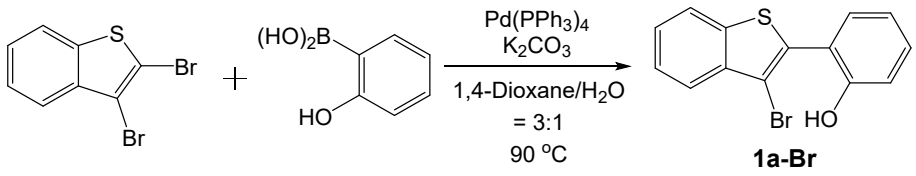
^{1}H NMR (400 MHz, chloroform-*d*) δ 7.75 – 7.63 (m, 1H), 7.61 – 7.55 (m, 1H), 7.41 (d, *J* = 5.1 Hz, 1H), 7.36 – 7.29 (m, 3H). ^{13}C NMR (101 MHz, chloroform-*d*) δ 158.26, 150.50, 141.79, 128.39, 126.63, 124.66, 124.31, 123.41, 122.60, 121.14, 118.87, 112.49. HRMS (ESI$^+$) m/z: $[M]^+$ calcd for $C_{12}H_6OS_2$ 229.9855, found 229.9855.



Thieno[4,5:4′,5′]thieno[3,2-*b*:3′,2′-*b′*]di(benzofuran) (2q): Following the general procedure, the target product was obtained after purification by column chromatography (PE) as a white solid (13.8 mg, 0.0319 mmol, 16% yield).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.63 (d, *J* = 1.6 Hz, 2H), 7.61 (d, *J* = 8.2 Hz, 2H), 7.41 (dd, *J* = 8.2, 1.7 Hz, 2H), 1.42 (s, 18H). ^{13}C NMR (101 MHz, chloroform-*d*) δ 159.05, 151.13, 148.99, 123.86, 121.90, 121.40, 120.56, 118.20, 109.46, 35.24, 31.71. HRMS (ESI$^+$) m/z: $[M]^+$ calcd for $C_{26}H_{24}O_2S_2$ 432.1212, found 432.1210.

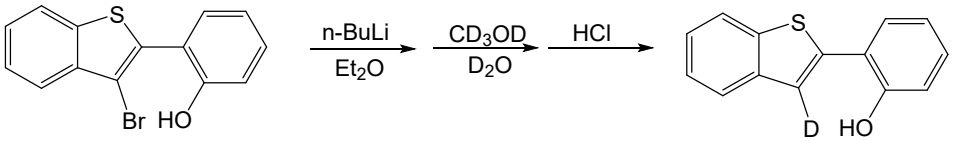
4. Kinetic isotope effect study



1a-Br

2-(3-bromobenzo[*b*]thiophen-2-yl)phenol (1a-Br) [2,6]**:** To a 100 mL two-neck flask with a stirring bar, 2,3-dibromobenzo[*b*]thiophene (5 mmol, 1 equiv), 2-hydroxyphenylboronic acid (7.5 mmol, 1.5 equiv), K_2CO_3 (10 mmol, 2 equiv) and $Pd(PPh_3)_4$ (0.25 mmol, 5 mol %) were added. The two-neck flask was evacuated and refilled with nitrogen three times. 1,4-Dioxane/H_2O (30 mL, v:v = 4:1) was added in a stream of nitrogen atmosphere. It was bubbled with nitrogen for 15 minutes to remove oxygen. The reaction was heated to 90 °C overnight. After being allowed to cool to room temperature, 1M HCl (20 mL) was added to acidify the solution. By extraction with CH_2Cl_2, the organic layer was separated and dried with Na_2SO_4. After evaporation under a vacuum, the residue was purified on silica gel column chromatography with hexane/EA (v:v = 10:1) as the eluent to afford the corresponding compound **1a-Br** (Colorless oil, 854 mg, 2.80 mmol, 56% yield).

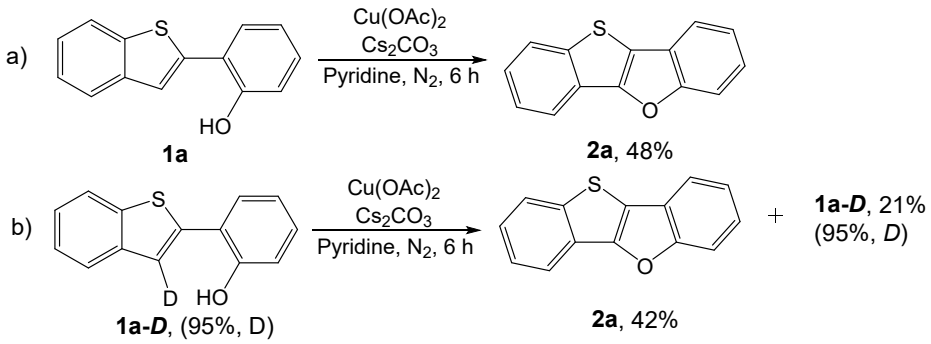
^{1}H NMR (400 MHz, chloroform-*d*) δ 7.88 (ddd, *J* = 8.1, 1.5, 0.8 Hz, 1H), 7.84 (ddd, *J* = 8.0, 1.3, 0.8 Hz, 1H), 7.55 – 7.42 (m, 2H), 7.41 – 7.32 (m, 2H), 7.09 – 7.00 (m, 2H), 5.28 (s, 1H). ^{13}C NMR (101 MHz, chloroform-*d*) δ 153.33, 138.75, 138.32, 133.40, 131.67, 131.24, 125.91, 125.47, 123.67, 122.39, 120.68, 118.96, 116.33, 108.57. HRMS (ESI$^-$) m/z: [M–H]$^-$ calcd for $C_{14}H_9BrOS$ 302.9485, found 302.9479.



1a-Br **1a-*D***

2-(benzo[*b*]thiophen-2-yl-3-d)phenol (1a-*D*): To a solution of 2-(3-bromobenzo[*b*]thiophen-2-yl)phenol (**1a-Br**, 305 mg, 1.0 mmol) in Et_2O (15 mL) was added dropwise n-BuLi (2.5 M in hexane, 2 mL, 5 mmol) at –78 °C, then the mixture was stirred for 2 h. CD_3OD (1.2 mL) was added to the reaction mixture and slowly warmed to room temperature and stirred for 1 h. D_2O (1 mL) and HCl (1 M, 10 mL) were added to the reaction mixture. By extraction with CH_2Cl_2, the organic layer was separated and dried with Na_2SO_4. After evaporation under a vacuum, the residue was purified on silica gel column chromatography with PE/EA (v:v = 10:1) as the eluent to afford the compound **1a-*D*** (209 mg, 0.919 mmol, 92% yield, 95%D).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.94 (ddd, *J* = 7.3, 2.3, 0.8 Hz, 1H), 7.64 (dd, *J* = 7.0, 1.6, 0.8 Hz, 1H), 7.47 – 7.36 (m, 2H), 7.35 – 7.28 (m, 2H), 7.09 – 6.96 (m, 2H), 5.13 (s, 1H). ^{13}C NMR (101 MHz, chloroform-*d*) δ 153.32, 140.47, 138.07, 132.10, 130.79, 129.69, 125.42 (t, *J* = 27.9 Hz), 124.92, 124.63, 123.09, 122.89, 121.56, 120.62, 115.84. HRMS (ESI$^-$) m/z: [M–H]$^-$ calcd for $C_{14}H_9DOS$ 226.0442, found 226.0433.

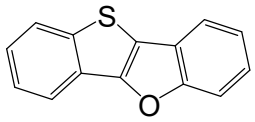


Attempt of KIE with 2a.

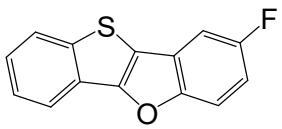
a) Into a 25 mL Schlenk tube with a stirring bar, **1a** (0.2 mmol), $Cu(OAc)_2$ (0.6 mmol, 3 equiv) and Cs_2CO_3 (0.2 mmol, 1 equiv) were sequentially added. The tube was evacuated and refilled with nitrogen three times. Pyridine (water ≤ 50 ppm) (4 mL) was added in a stream of nitrogen atmosphere. The tube was sealed and it was bubbled with nitrogen for 15 minutes to remove oxygen. The reaction was heated to 110 °C under nitrogen atmosphere for 6 h. After warmed to room temperature, 1M HCl (15 mL) was added to acidify the solution. By extraction with CH_2Cl_2 (4 × 10 mL), the organic layer was separated and dried with Na_2SO_4. After evaporation under a vacuum, the residue was purified on silica gel column chromatography with hexane as the eluent to afford the target compounds **2a** (white solid, 21.6 mg, 0.0963 mmol, 48% yield).

b) Into a 25 mL Schlenk tube with a stirring bar, **1a-*D*** (0.2 mmol), $Cu(OAc)_2$ (0.6 mmol, 3 equiv) and Cs_2CO_3 (0.2 mmol, 1 equiv) were sequentially added. The tube was evacuated and refilled with nitrogen three times. Pyridine (water ≤ 50 ppm) (4 mL) was added in a stream of nitrogen atmosphere. The tube was sealed and it was bubbled with nitrogen for 15 minutes to remove oxygen. The reaction was heated to 110 °C under nitrogen atmosphere for 6 h. After warmed to room temperature, 1M HCl (15 mL) was added to acidify the solution. By extraction with CH_2Cl_2 (4 × 10 mL), the organic layer was separated and dried with Na_2SO_4. After evaporation under a vacuum, the residue was purified on silica gel column chromatography with hexane as the eluent to afford the target compounds **2a** (white solid, 18.5 mg, 0.0824 mmol, 41% yield), **1a-*D*** (21% yield, 95%D), K_H/K_D = 1.1.

5. Gram scale synthesis.



benzo[4,5]thieno[3,2-*b*]benzofuran (2a): Into a 250 mL two-neck boiling flask with a stirring bar, substrates **1a** (1.344 g, 6 mmol), $Cu(OAc)_2$ (18 mmol, 3 equiv) and Cs_2CO_3 (6 mmol, 1 equiv) were sequentially added. The flask was evacuated and refilled with nitrogen three times. Pyridine (water ≤ 50 ppm) (100 mL) was added in a stream of nitrogen atmosphere. The flask was sealed and it was bubbled with nitrogen for 15 minutes to remove oxygen. The reaction was heated to 110 °C under nitrogen atmosphere for 16 h. After being cooled to room temperature, 1M HCl (150 mL) was added to acidify the solution. By extraction with EA (4 × 40 mL), the organic layer was separated and dried with Na_2SO_4. After evaporation under a vacuum, the residue was purified on silica gel column chromatography with hexane as the eluent to afford the target compounds **2** as a white solid (1.062 g, 4.74 mmol, 79% yield).



8-fluorobenzo[4,5]thieno[3,2-*b*]benzofuran (2f): Into a 250 mL two-neck boiling flask with a stirring bar, substrates **1f** (1.344 g, 6 mmol), $Cu(OAc)_2$ (18 mmol, 3 equiv) and Cs_2CO_3 (6 mmol, 1 equiv) were sequentially added. The flask was evacuated and refilled with nitrogen three times. Pyridine (water ≤ 50 ppm) (100 mL) was added in a stream of nitrogen atmosphere. The flask was sealed and it was bubbled with nitrogen for 15 minutes to remove oxygen. The reaction was heated to 110 °C under nitrogen atmosphere for 16 h. After being cooled to room temperature, 1M HCl (150 mL) was added to acidify the solution. By extraction with EA (4 × 40 mL), the organic layer was separated and dried with Na_2SO_4. After evaporation under a vacuum, the residue was purified on silica gel column chromatography with hexane as the eluent to afford the target compounds **2f** as a white solid (1.082 g, 4.47 mmol, 75% yield).

6. References

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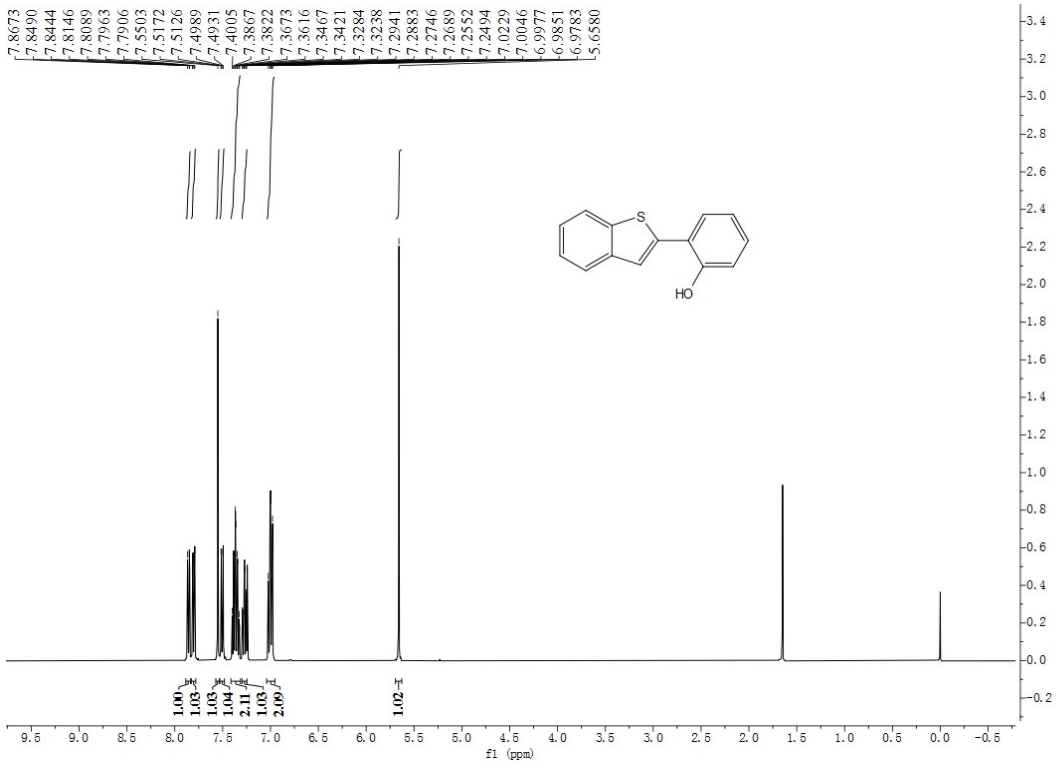
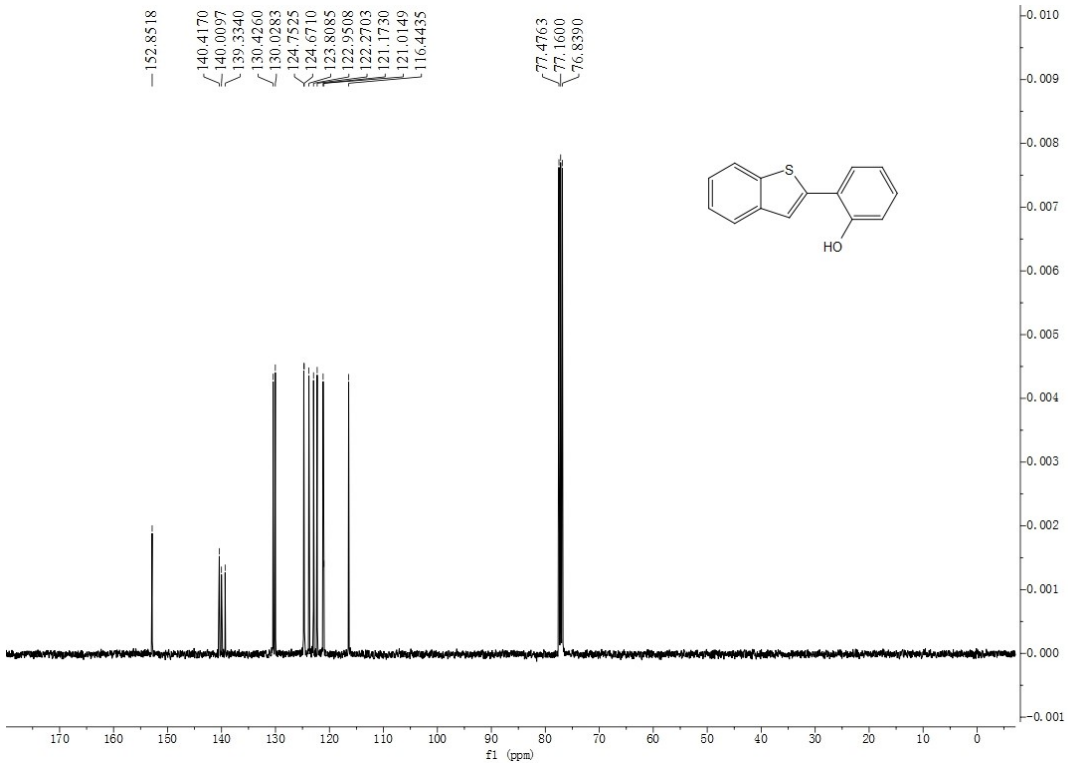
7. ^{1}H NMR and ^{13}C NMR spectra

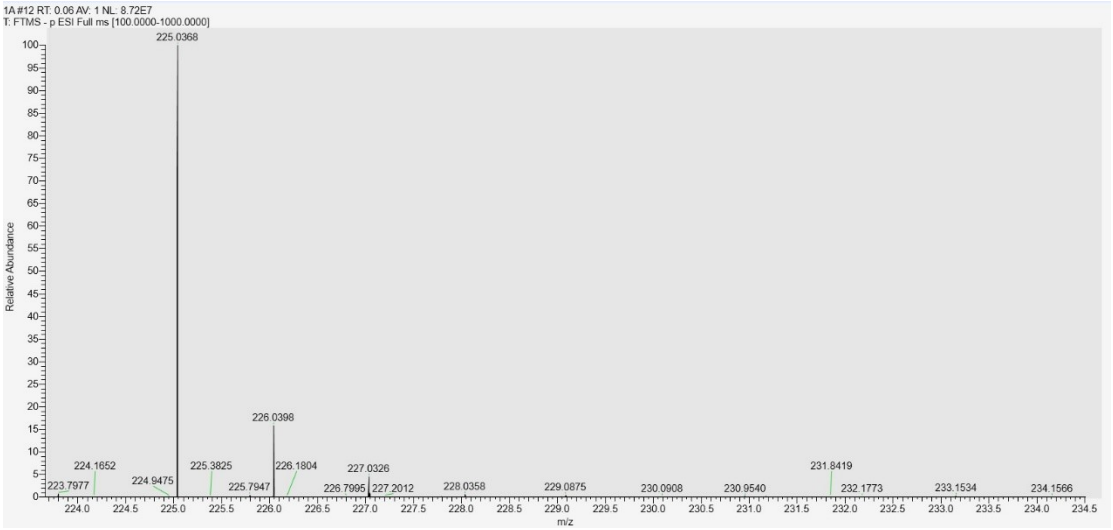
^{1}H NMR spectrum for **1a** (400 MHz, $CDCl_3$)



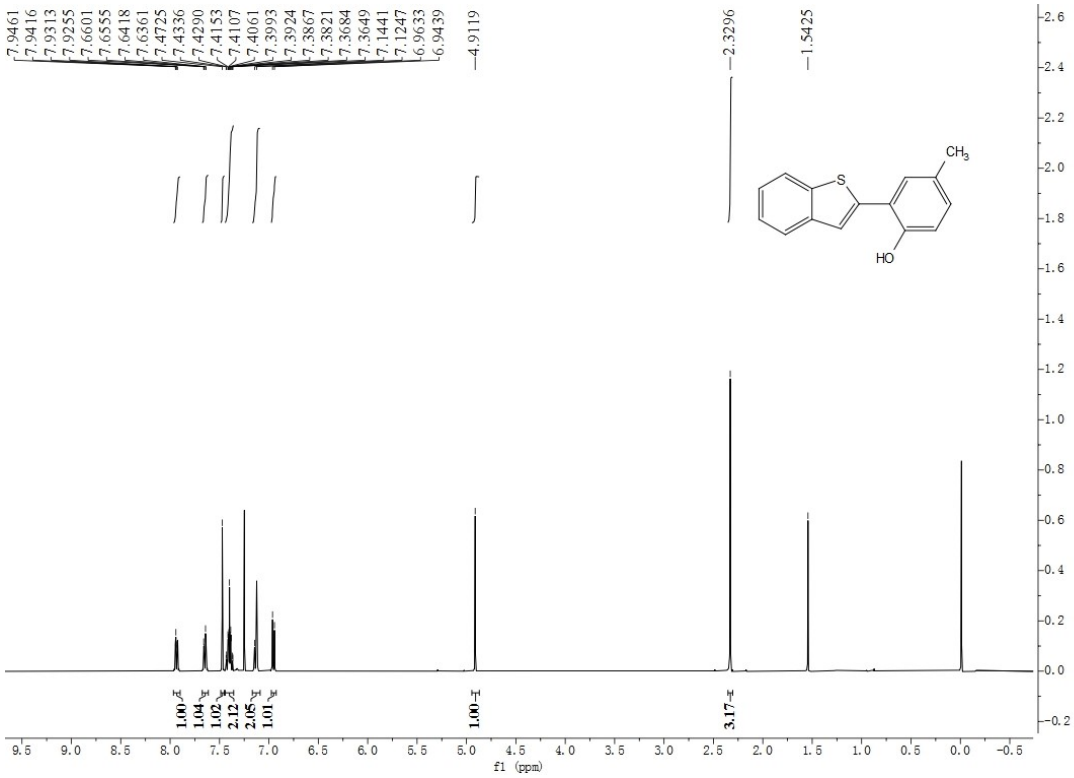
^{13}C NMR spectrum for **1a** (100 MHz,$CDCl_3$)



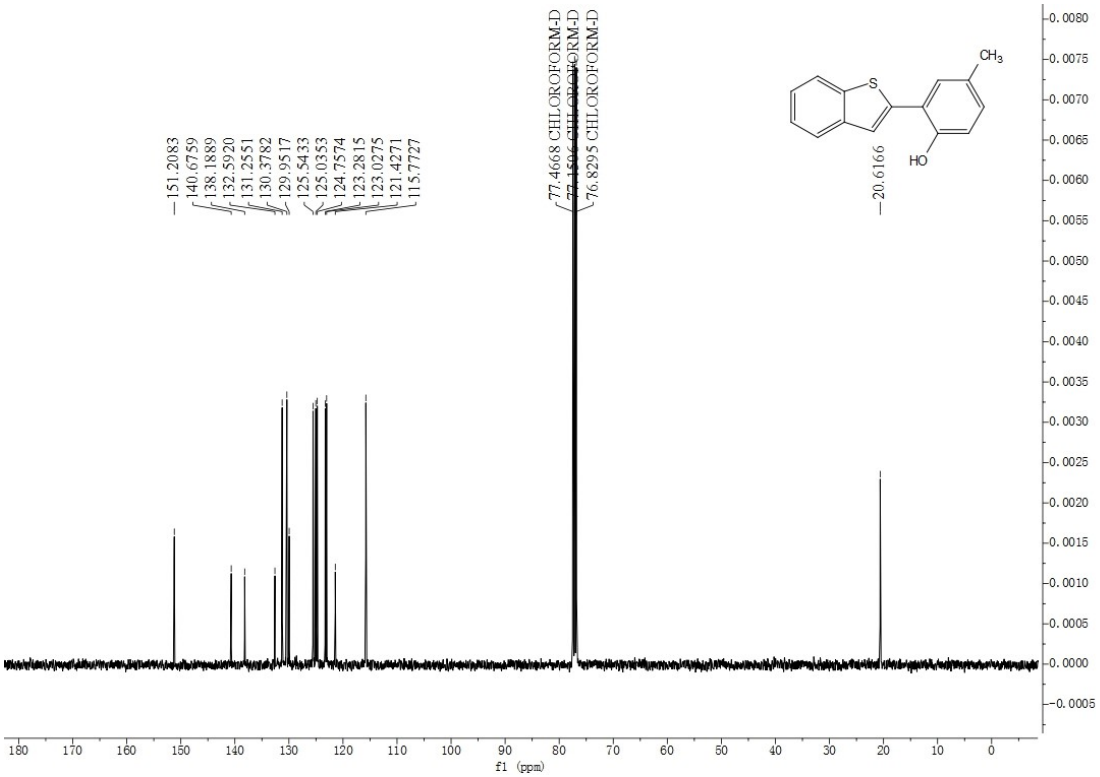
HRMS (ESI) spectrum for **1a**



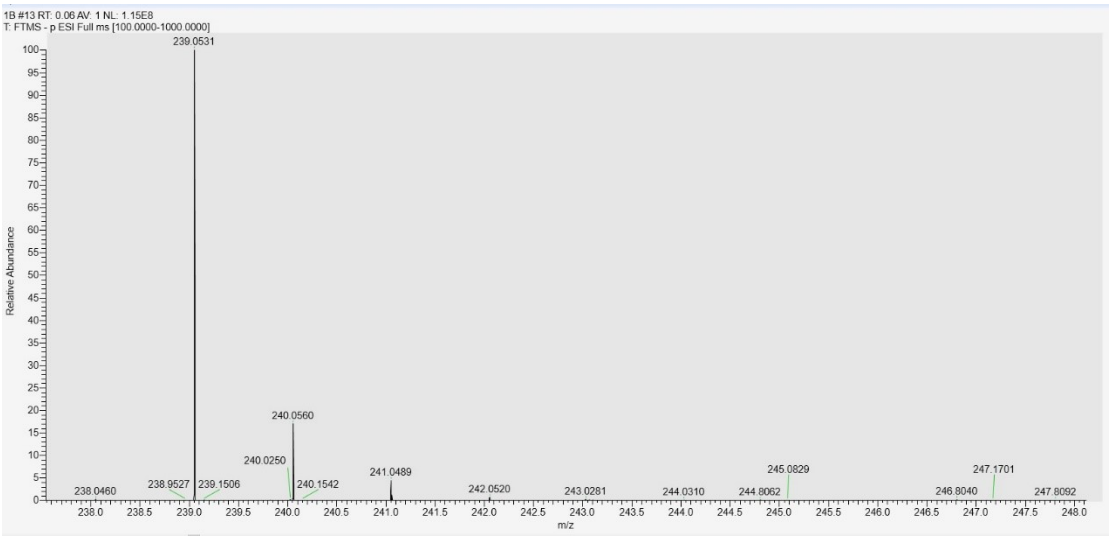
^{1}H NMR spectrum for **1b** (400 MHz,$CDCl_3$)



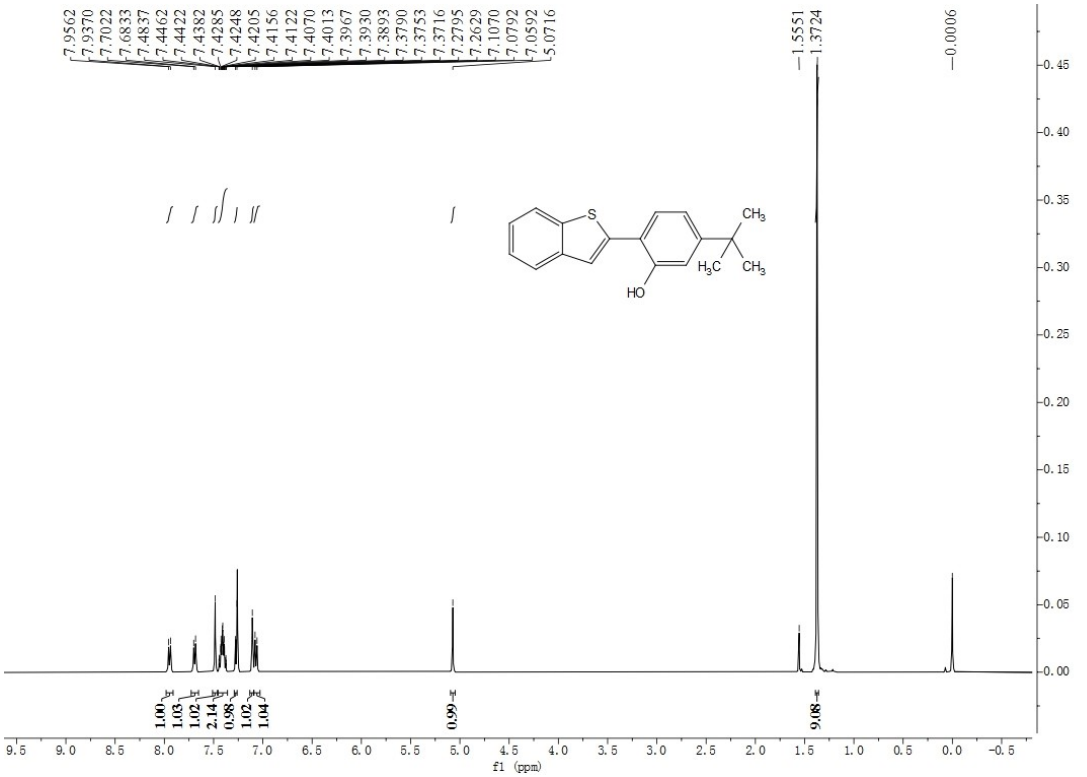
^{13}C NMR spectrum for **1b** (100 MHz,$CDCl_3$)



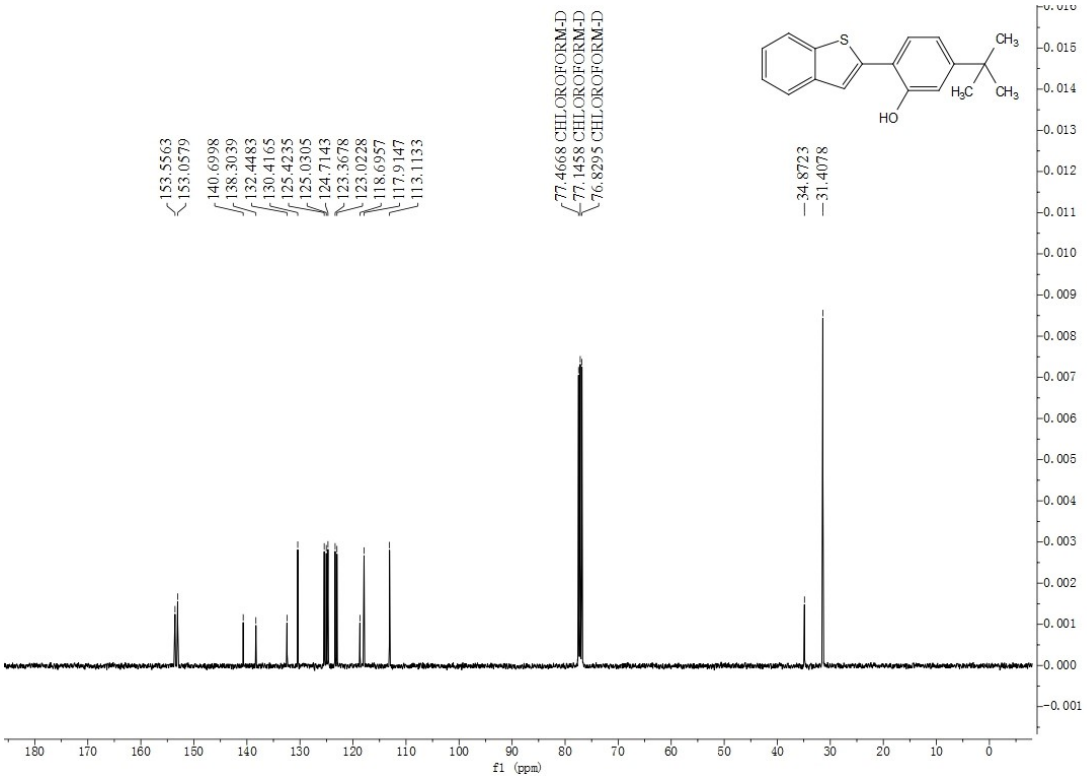
HRMS (ESI) spectrum for **1b**



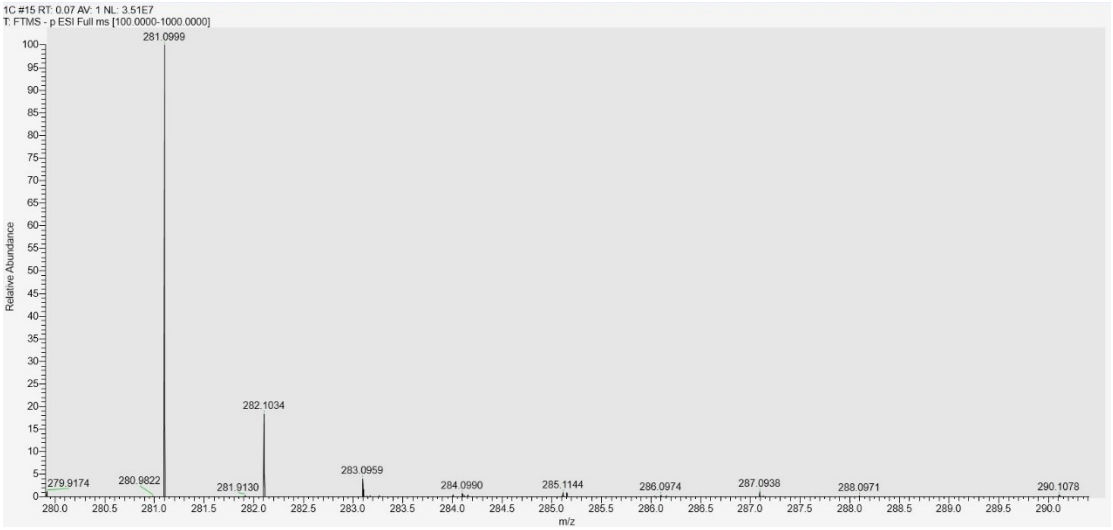
^{1}H NMR spectrum for **1c** (400 MHz,$CDCl_3$)



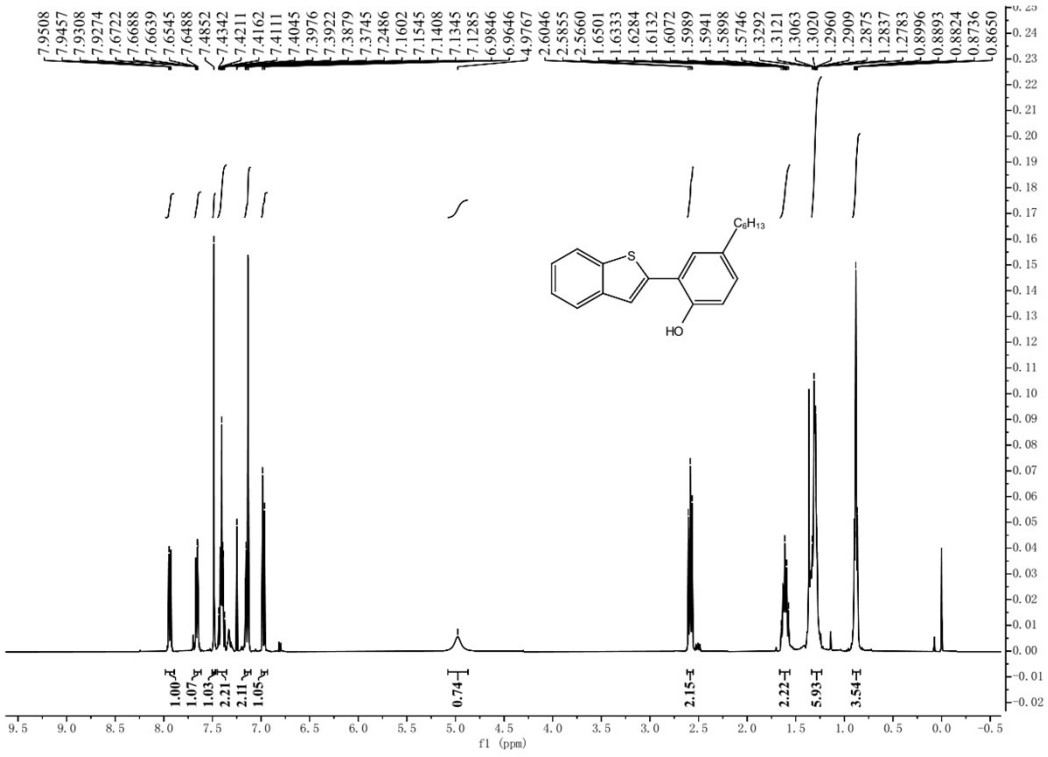
^{13}C NMR spectrum for **1c** (100 MHz,$CDCl_3$)



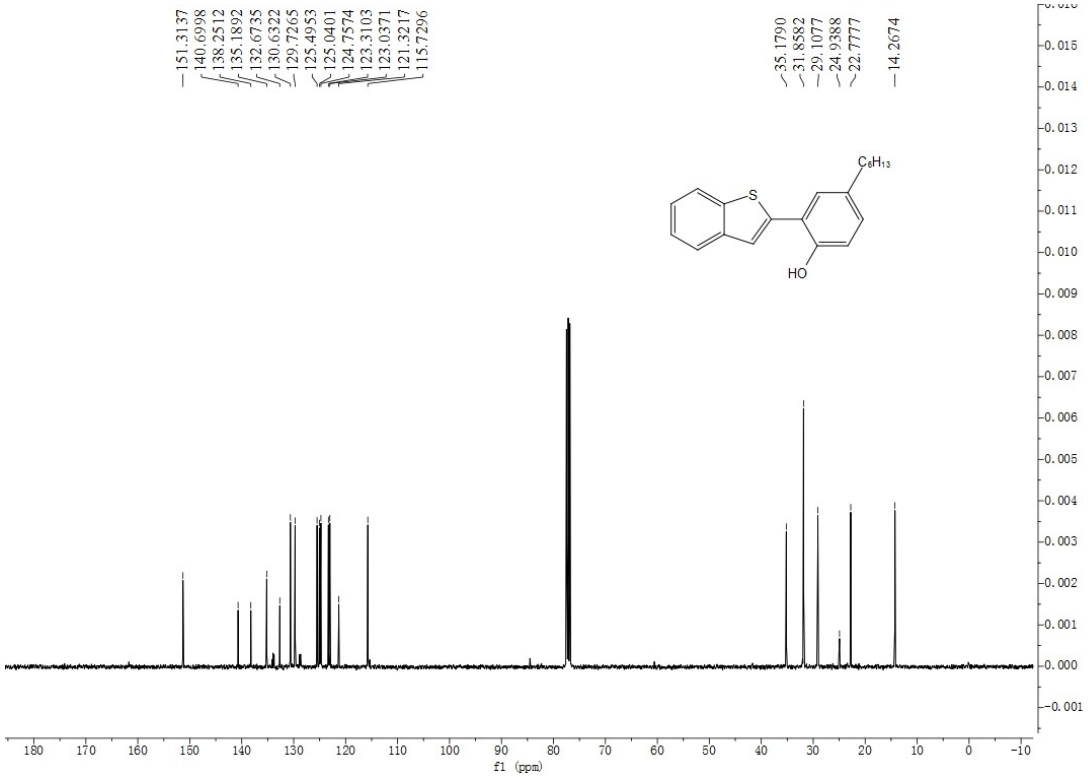
HRMS (ESI) spectrum for **1c**



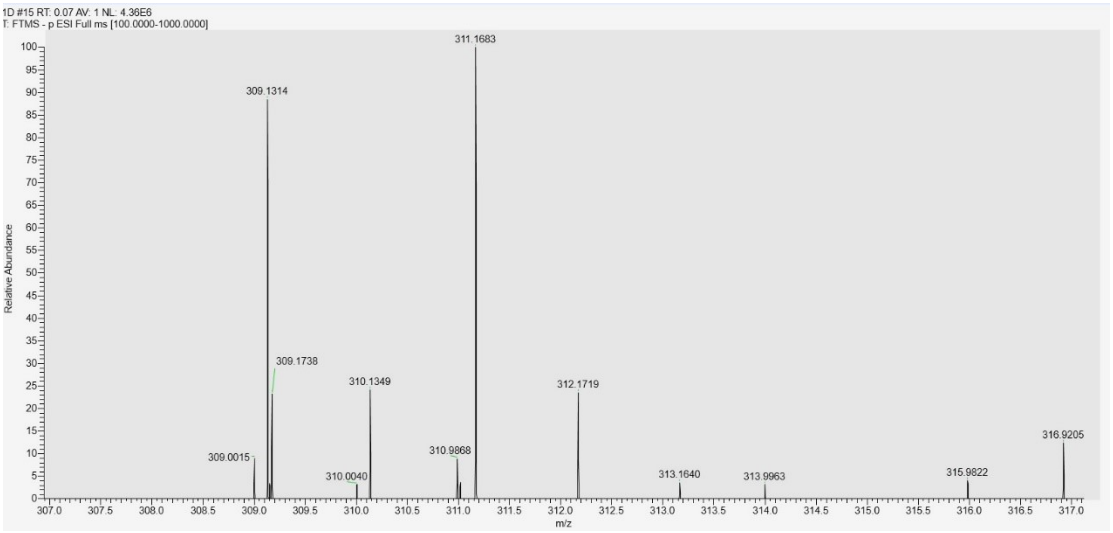
^{1}H NMR spectrum for **1d** (400 MHz,$CDCl_3$)



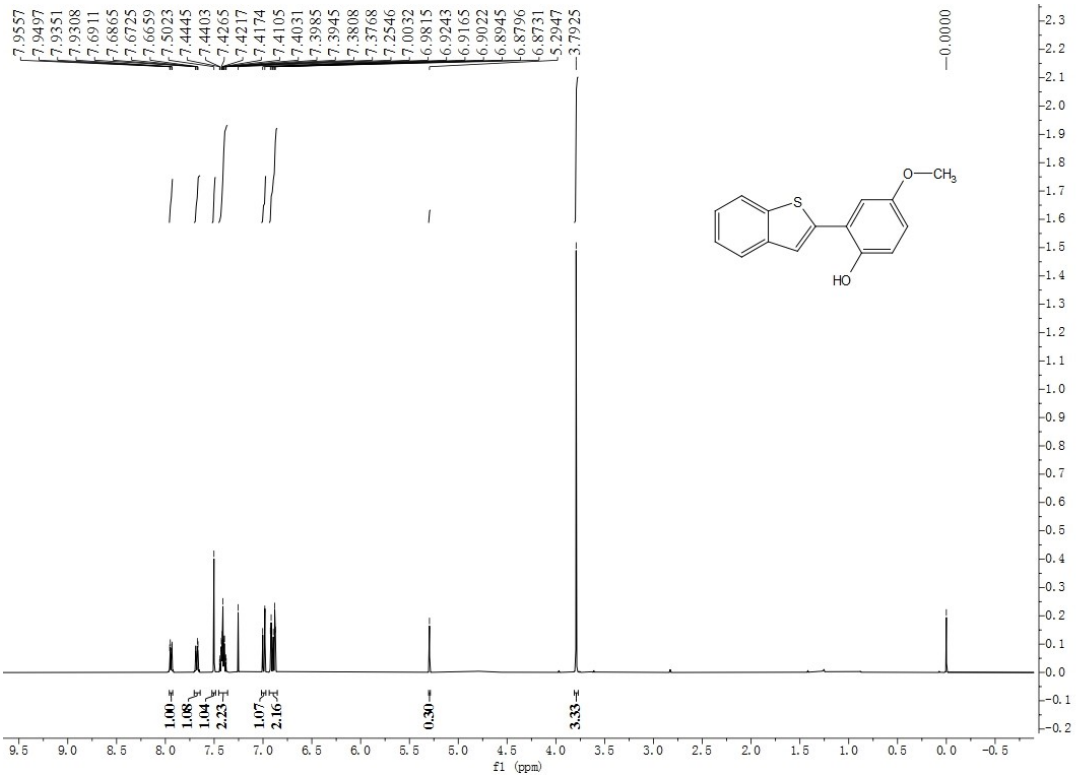
^{13}C NMR spectrum for **1d** (100 MHz,$CDCl_3$)



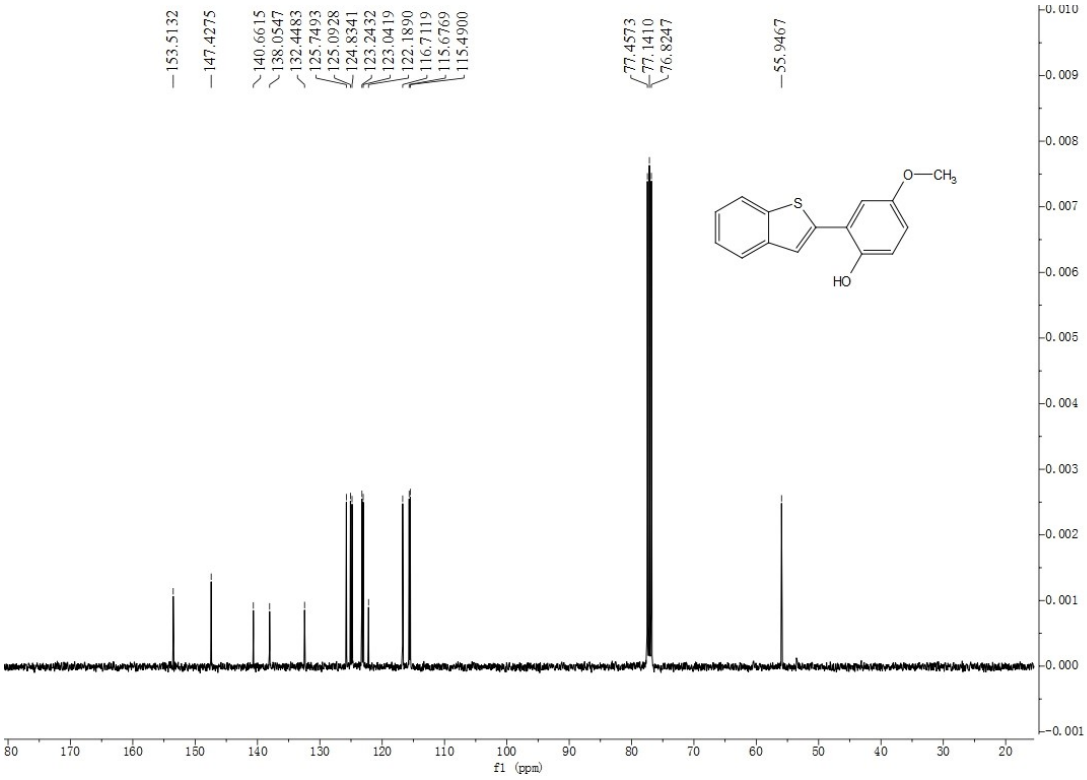
HRMS (ESI) spectrum for **1d**



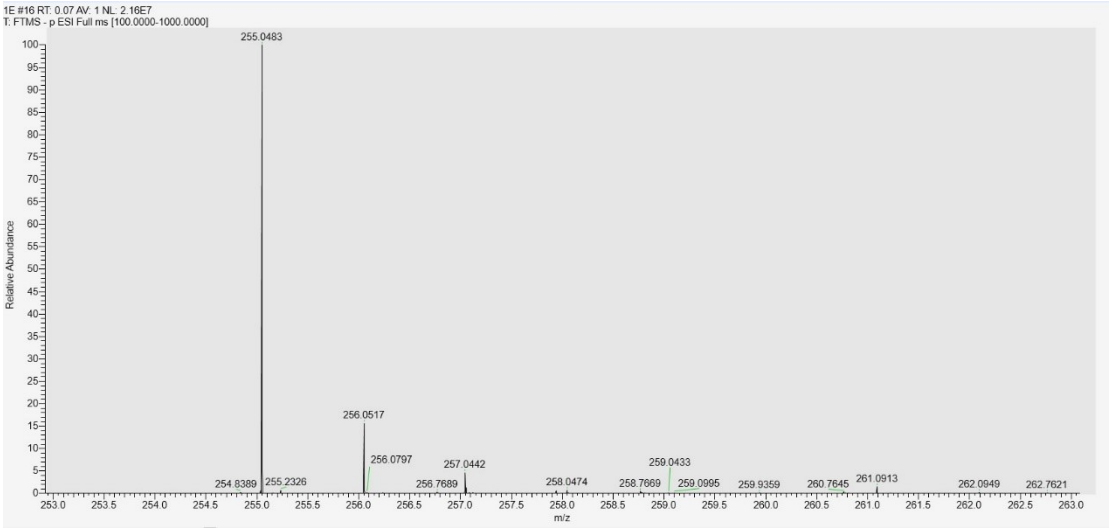
^{1}H NMR spectrum for **1e** (400 MHz,$CDCl_3$)



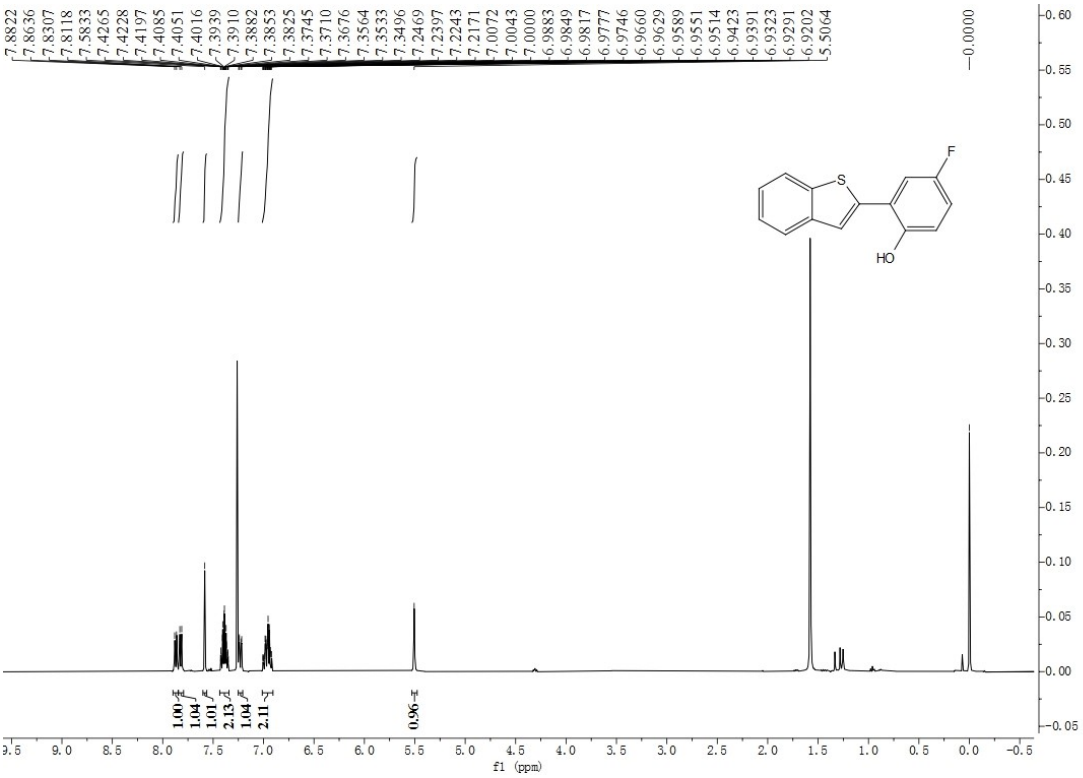
^{13}C NMR spectrum for **1e** (100 MHz,$CDCl_3$)



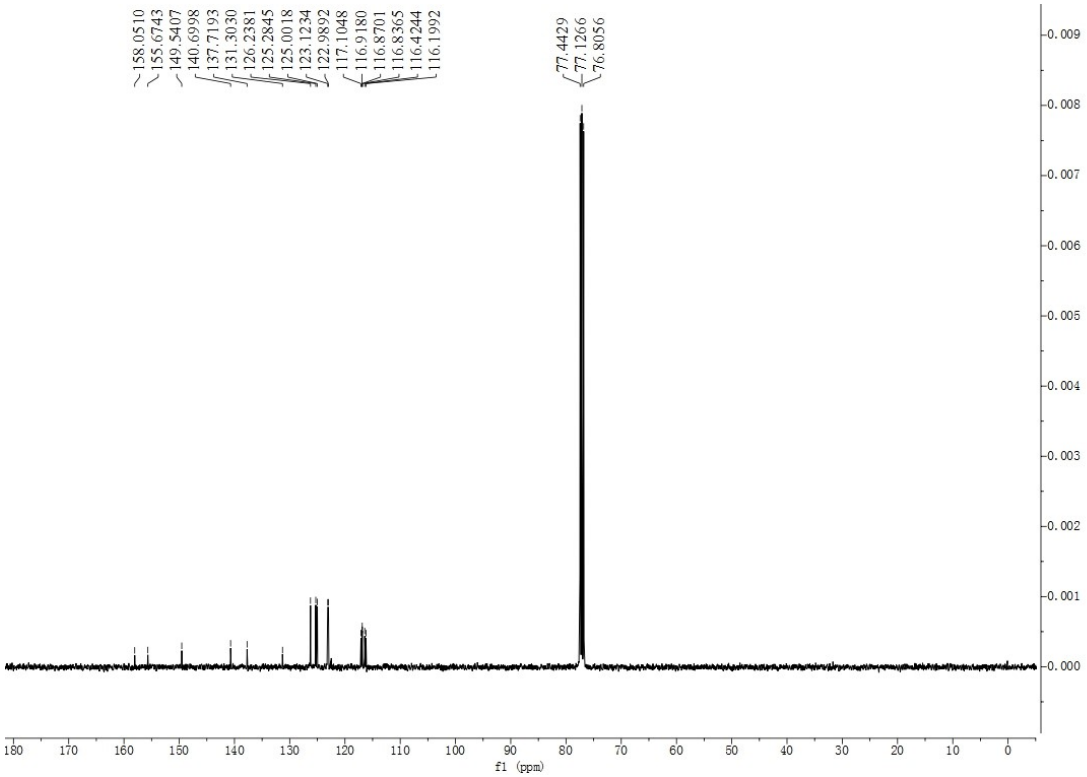
HRMS (ESI) spectrum for **1e**



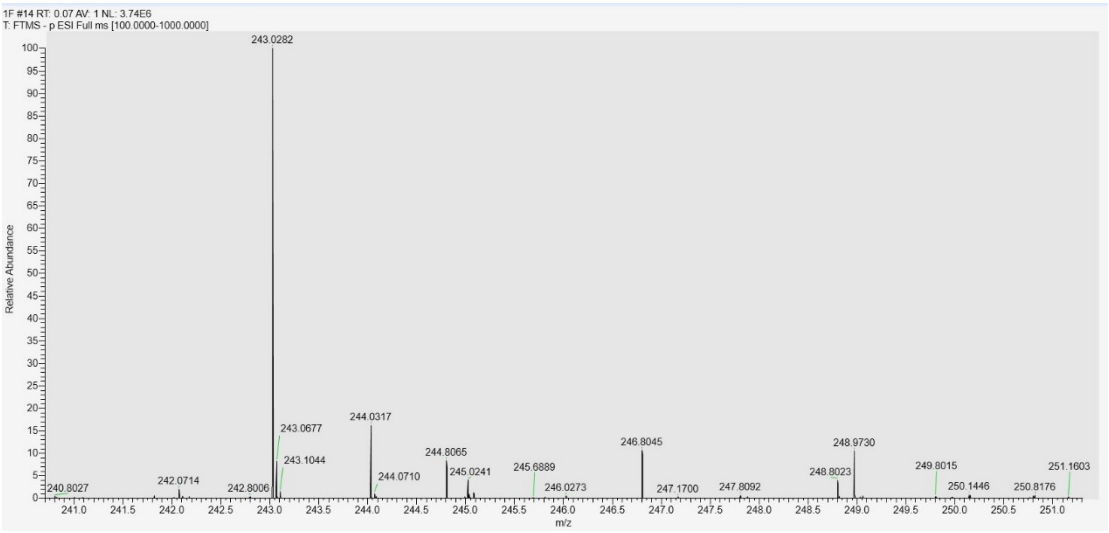
^{1}H NMR spectrum for **1f** (400 MHz, $CDCl_3$)



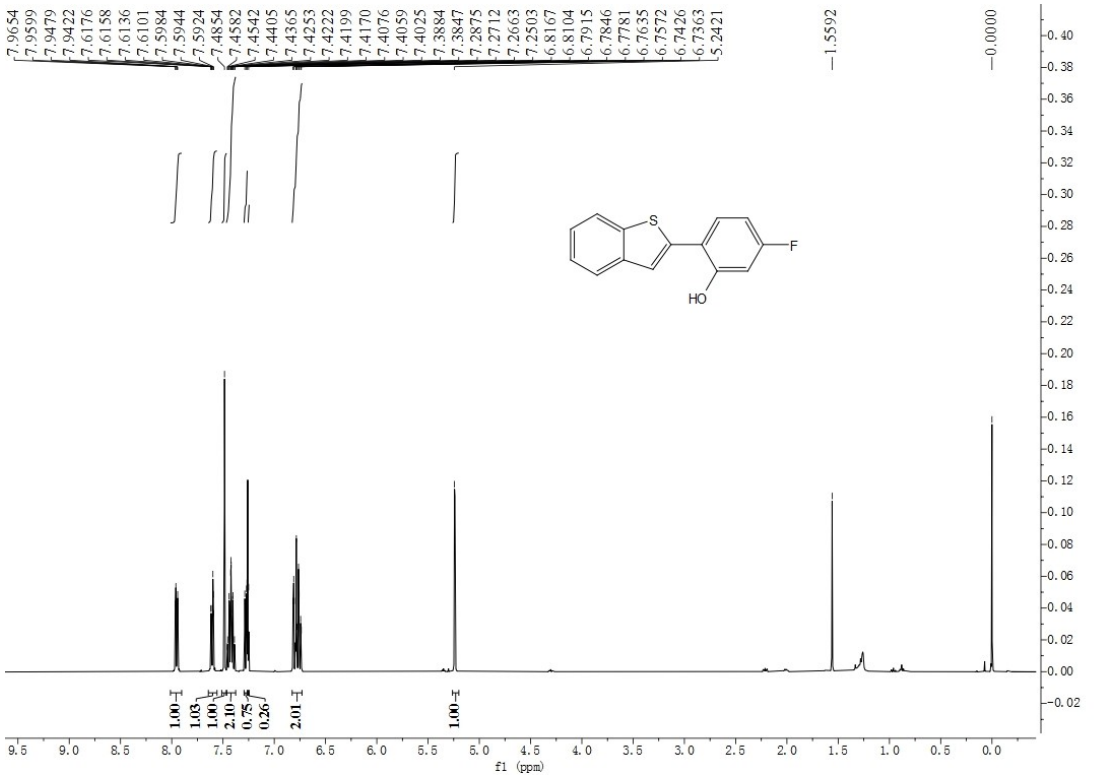
^{13}C NMR spectrum for **1f** (100 MHz,$CDCl_3$)



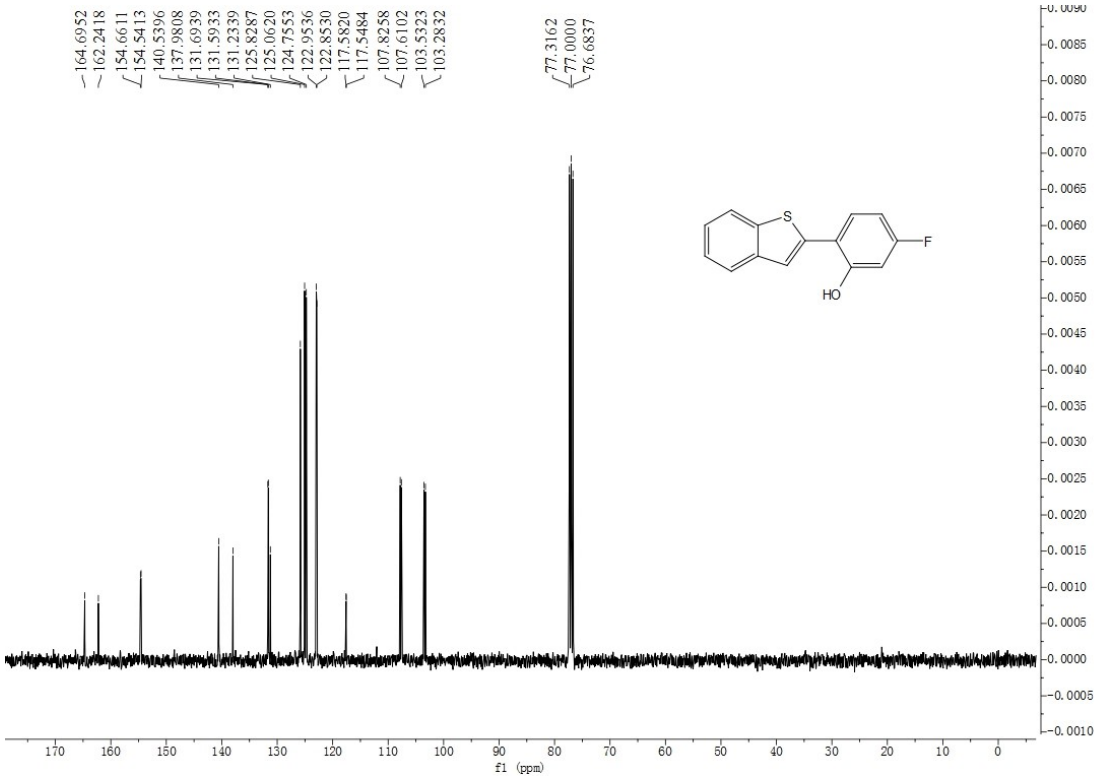
HRMS (ESI) spectrum for **1f**



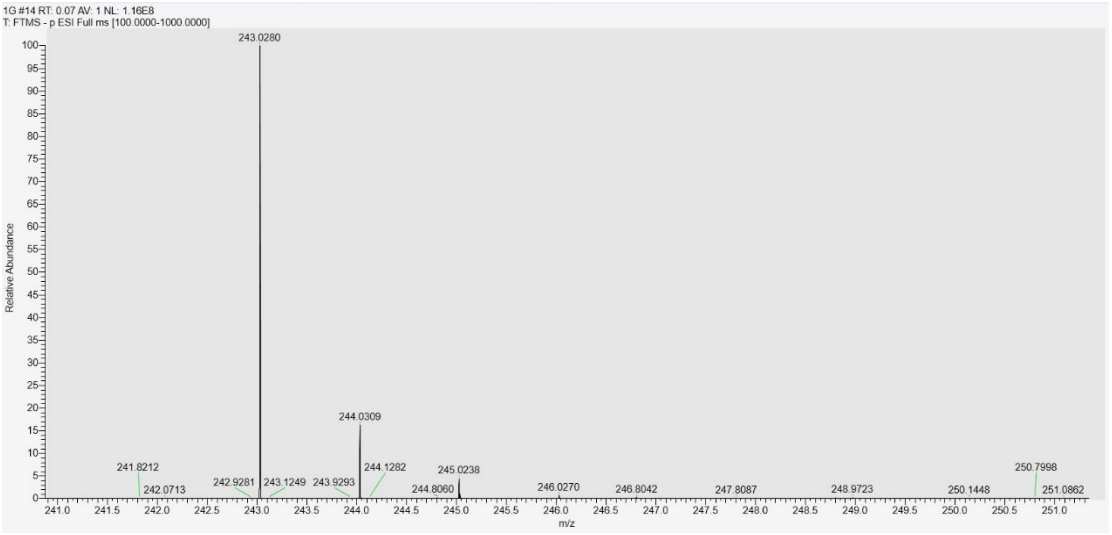
^{1}H NMR spectrum for **1g** (400 MHz,$CDCl_3$)



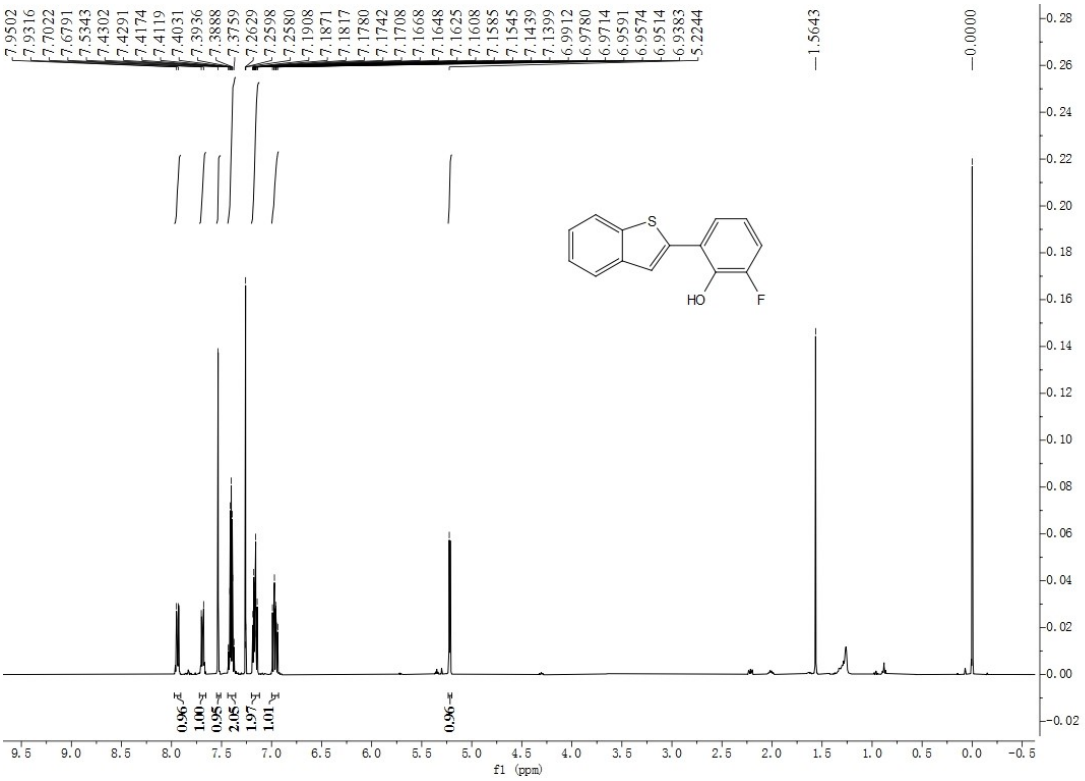
^{13}C NMR spectrum for **1g** (100 MHz,$CDCl_3$)



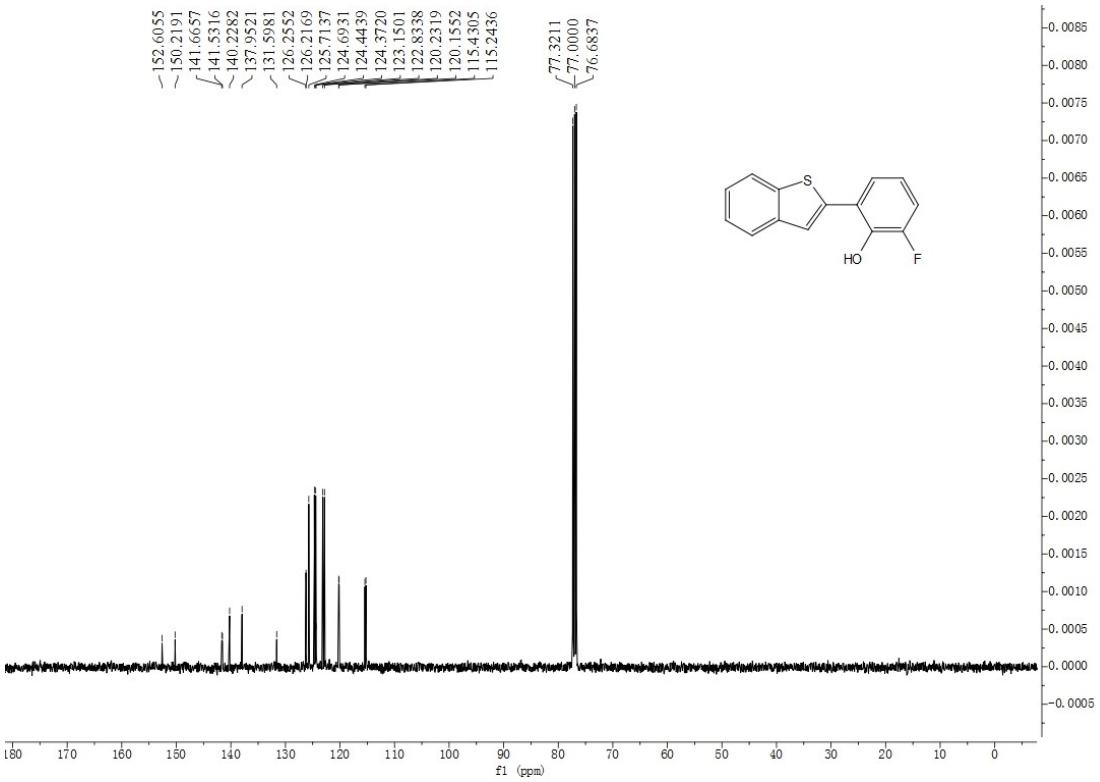
HRMS (ESI) spectrum for **1g**



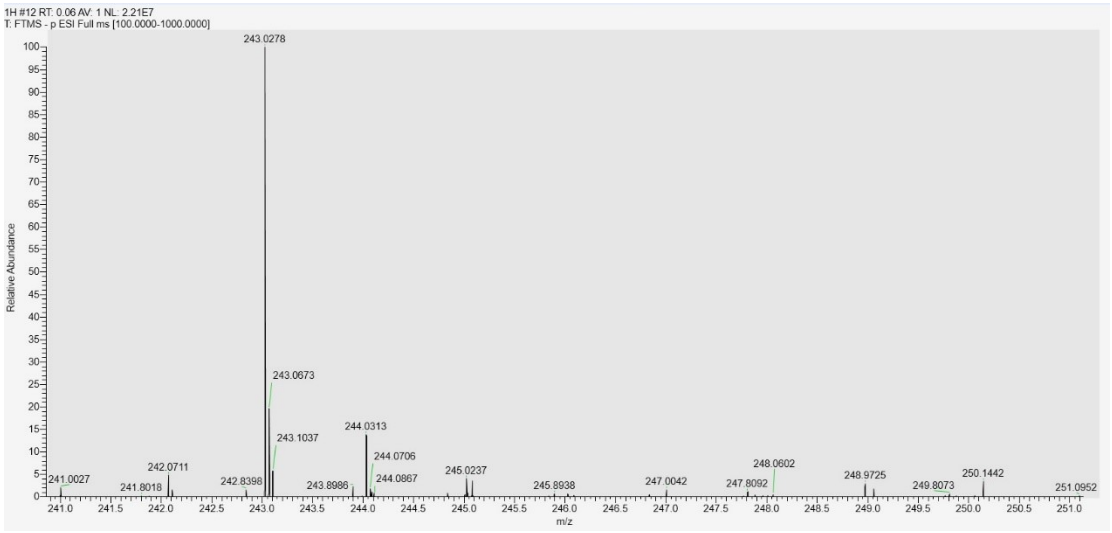
^{1}H NMR spectrum for **1h** (400 MHz,$CDCl_3$)



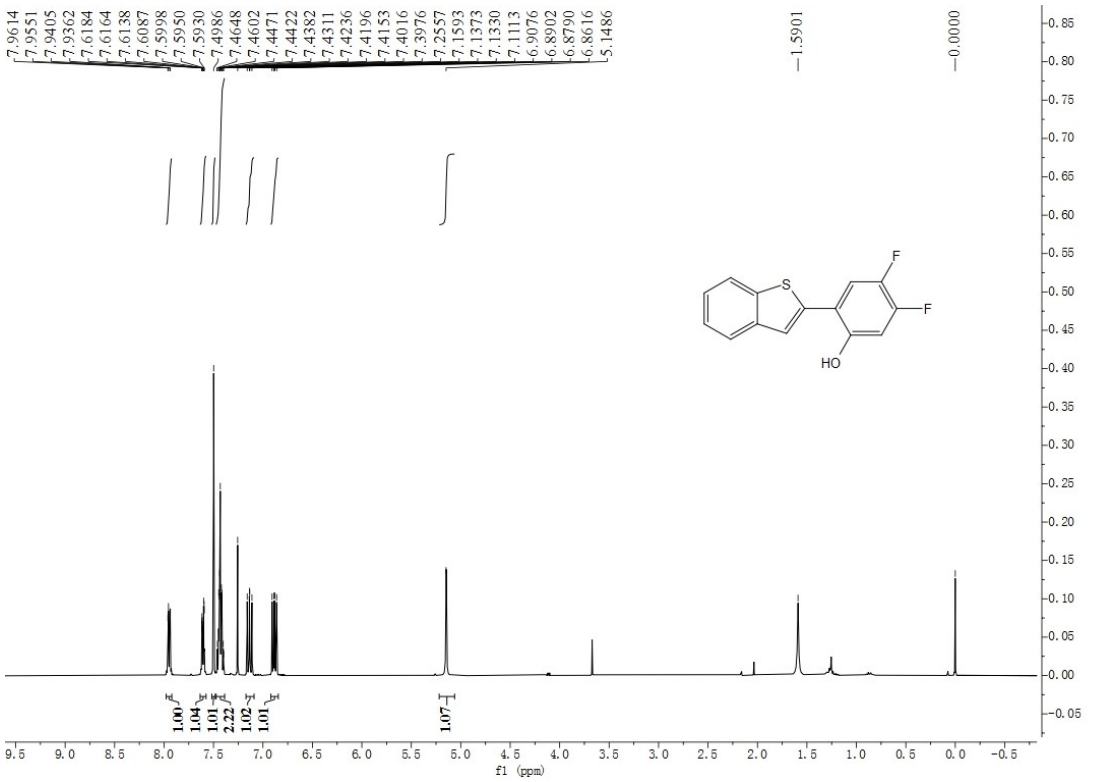
^{13}C NMR spectrum for **1h** (100 MHz,$CDCl_3$)



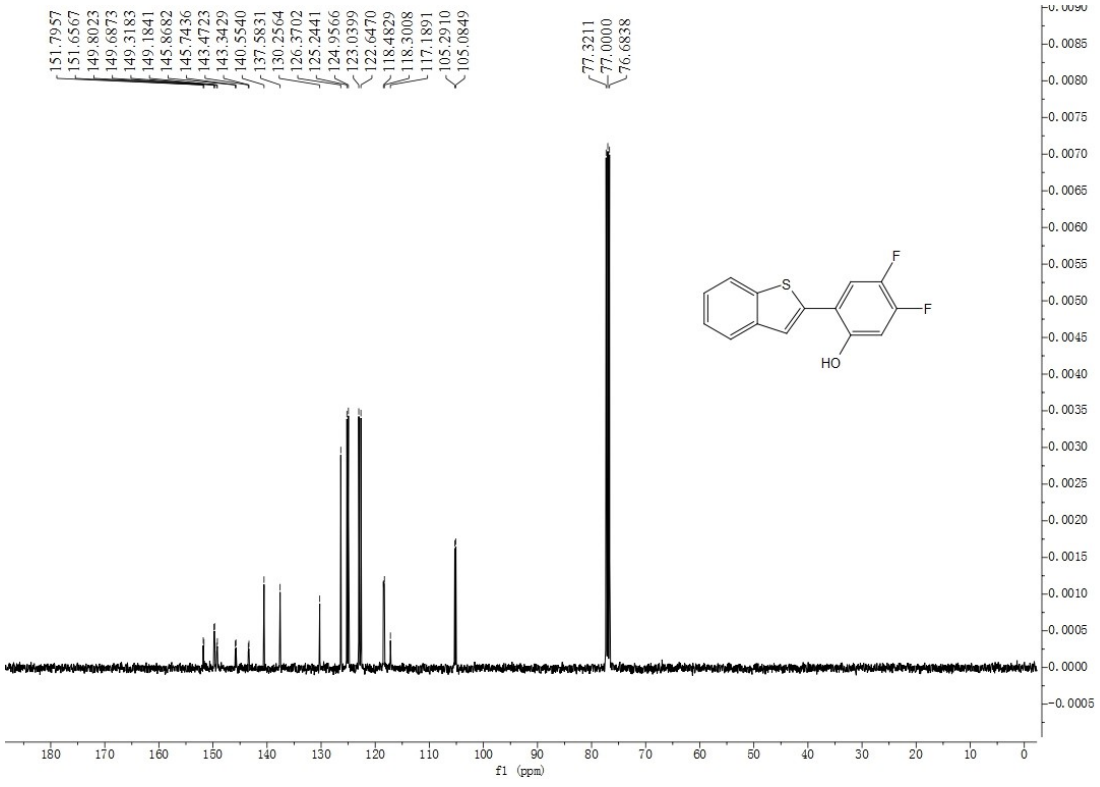
HRMS (ESI) spectrum for **1h**



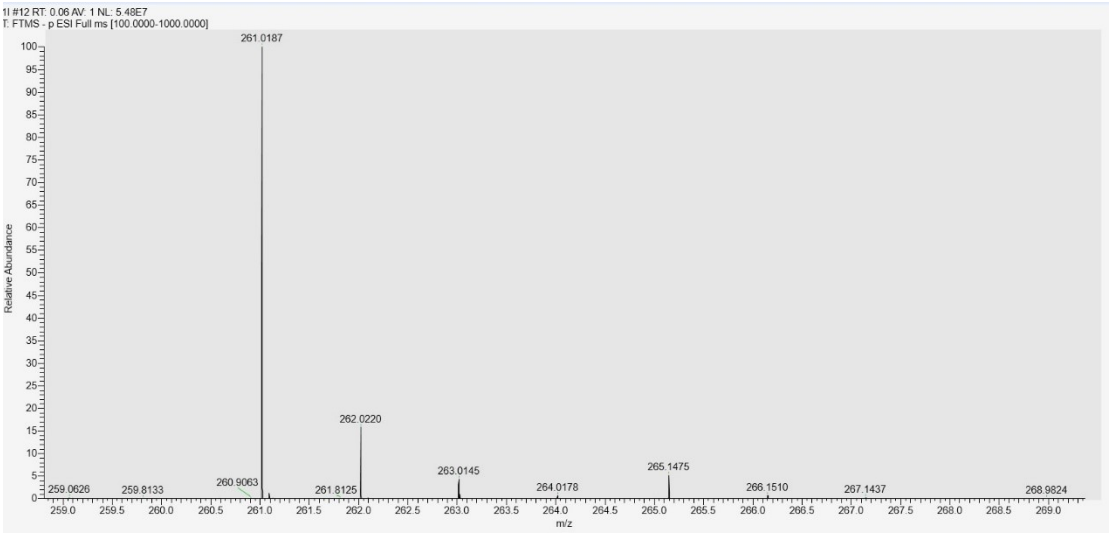
^{1}H NMR spectrum for **1i** (400 MHz,$CDCl_3$)



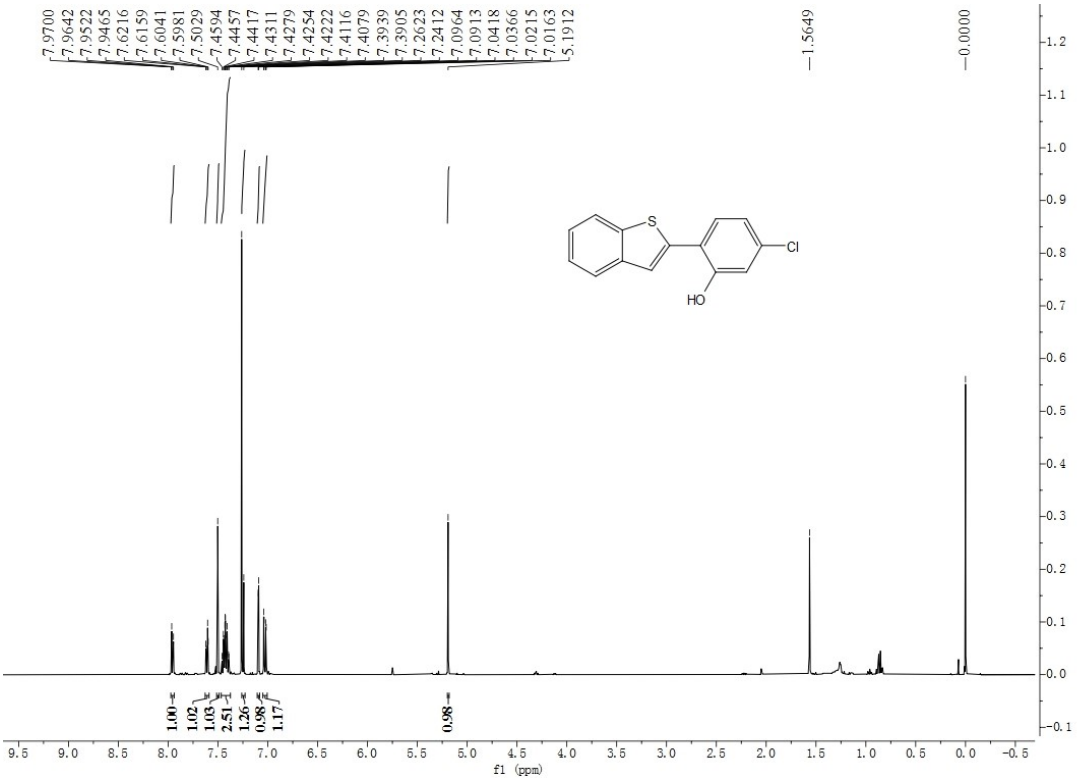
^{13}C NMR spectrum for **1i** (100 MHz,$CDCl_3$)



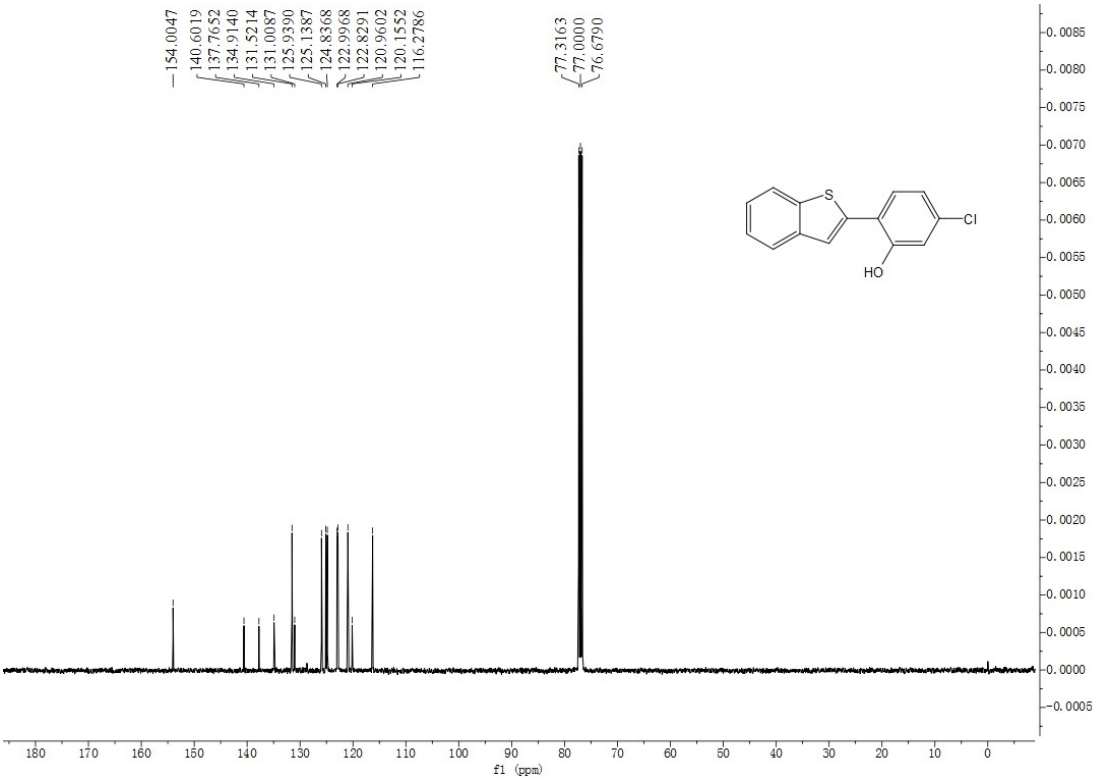
HRMS (ESI) spectrum for **1i**



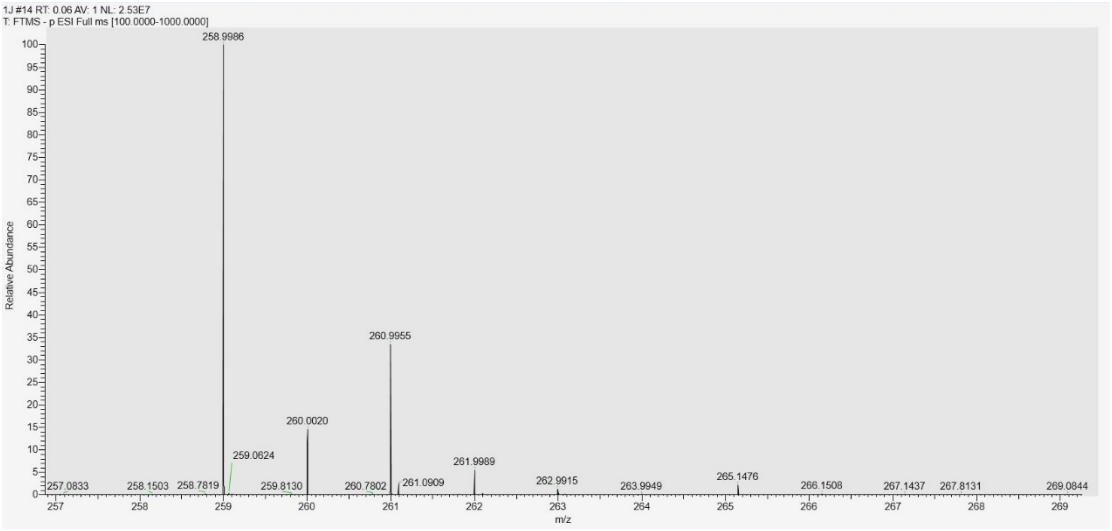
^{1}H NMR spectrum for **1j** (400 MHz,$CDCl_3$)



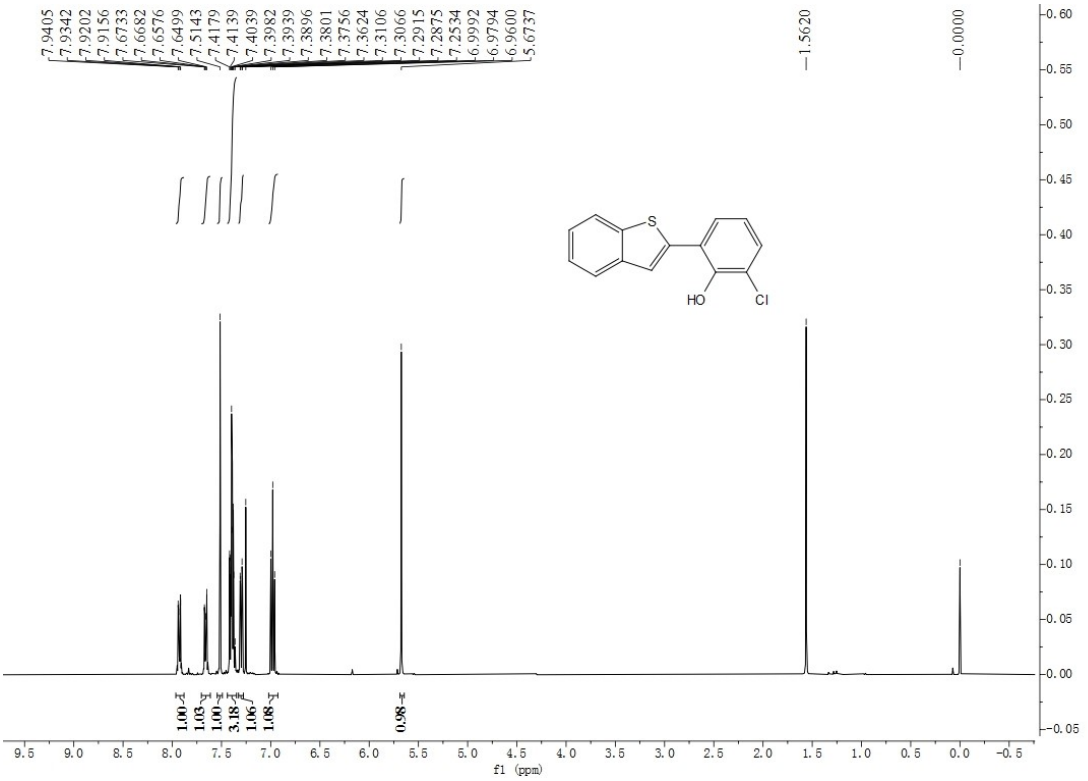
^{13}C NMR spectrum for **1j** (100 MHz,$CDCl_3$)



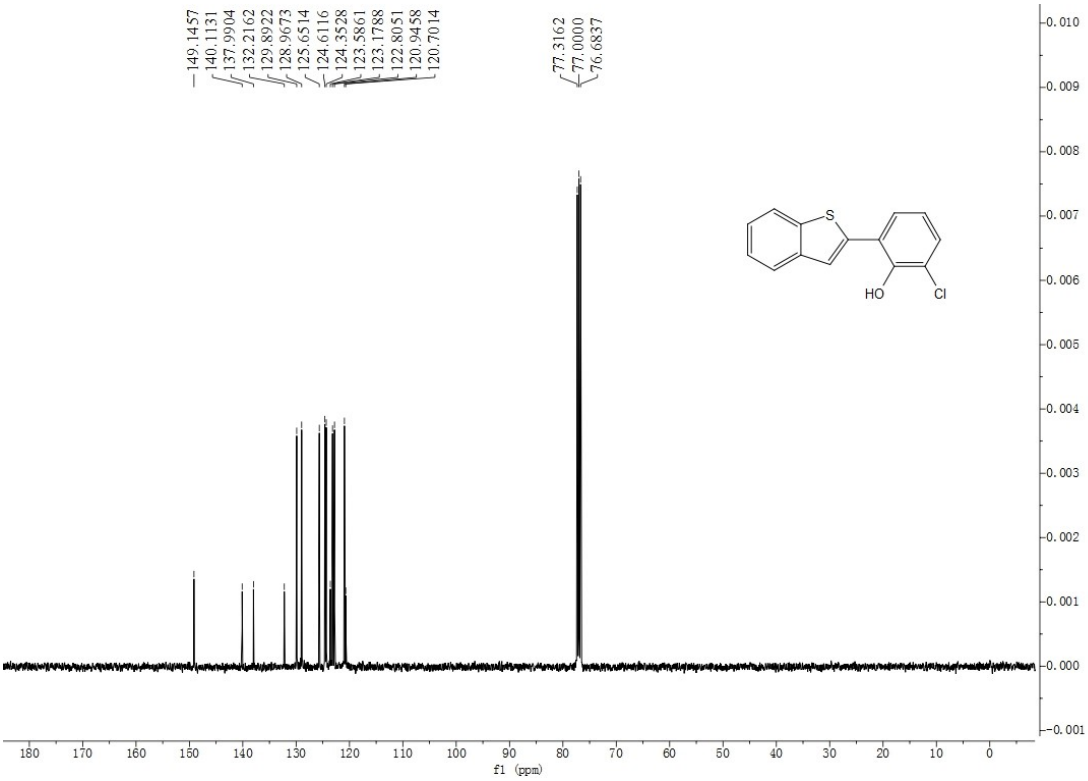
HRMS (ESI) spectrum for **1j**



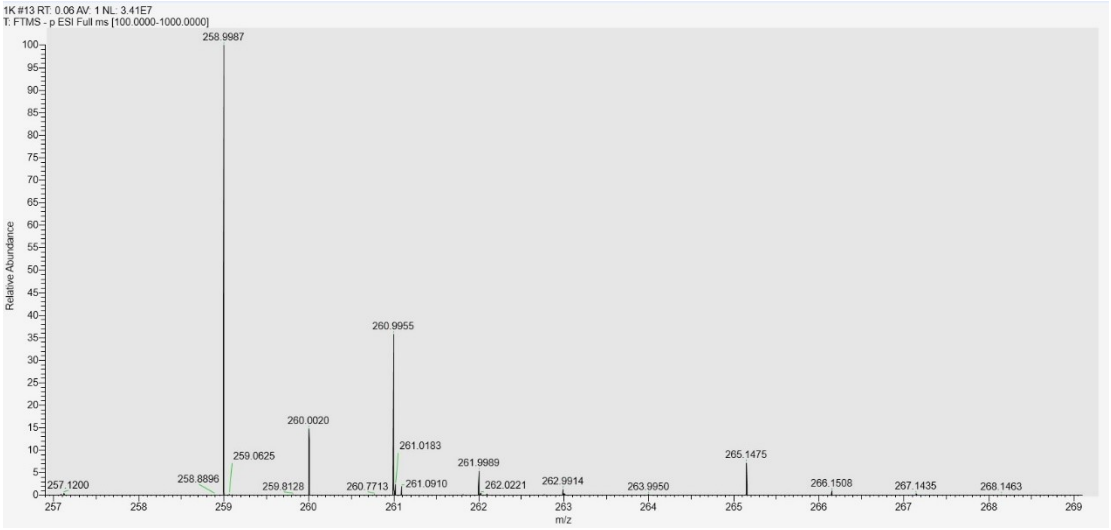
^{1}H NMR spectrum for **1k** (400 MHz,$CDCl_3$)



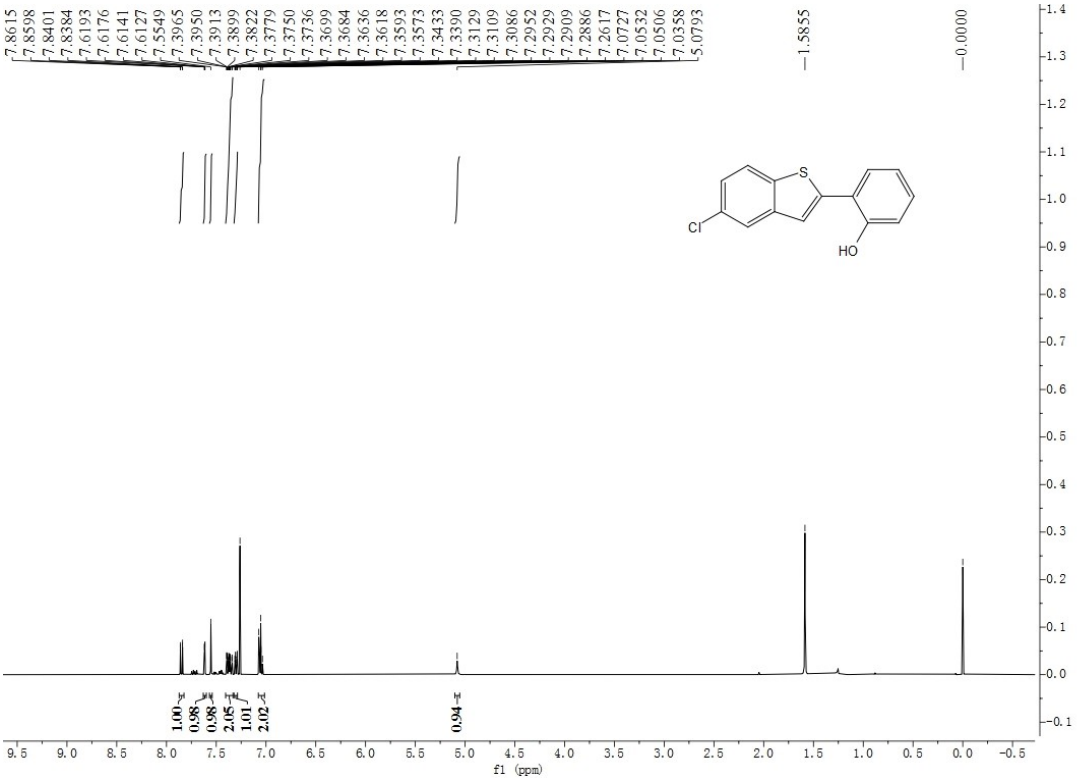
^{13}C NMR spectrum for **1k** (100 MHz,$CDCl_3$)



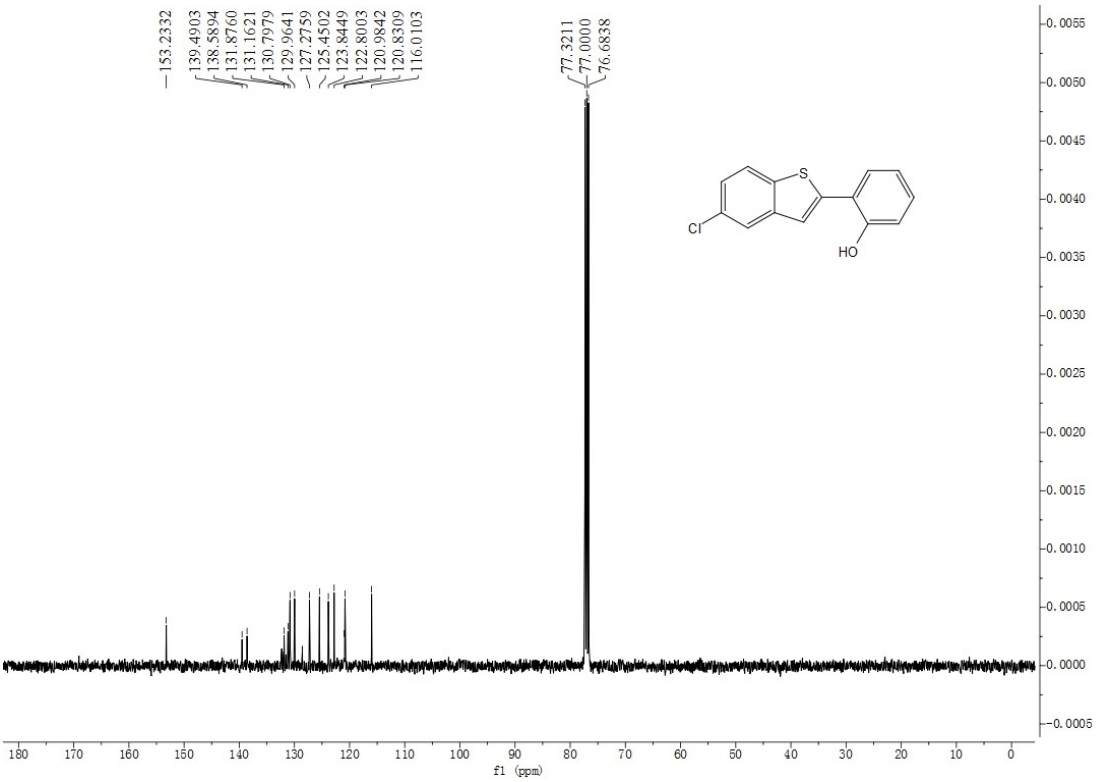
HRMS (ESI) spectrum for **1k**



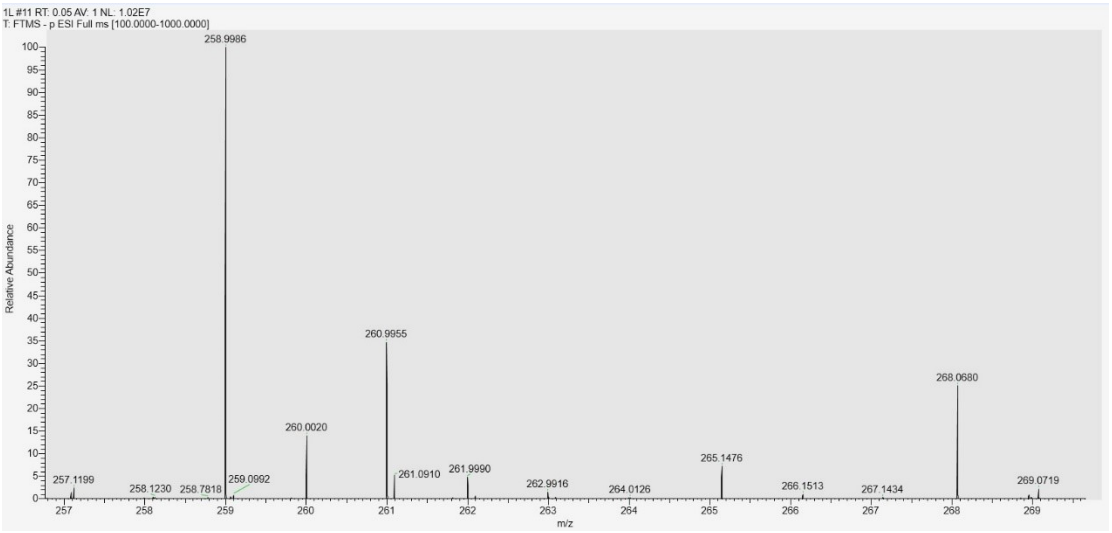
^{1}H NMR spectrum for **1l** (400 MHz,$CDCl_3$)



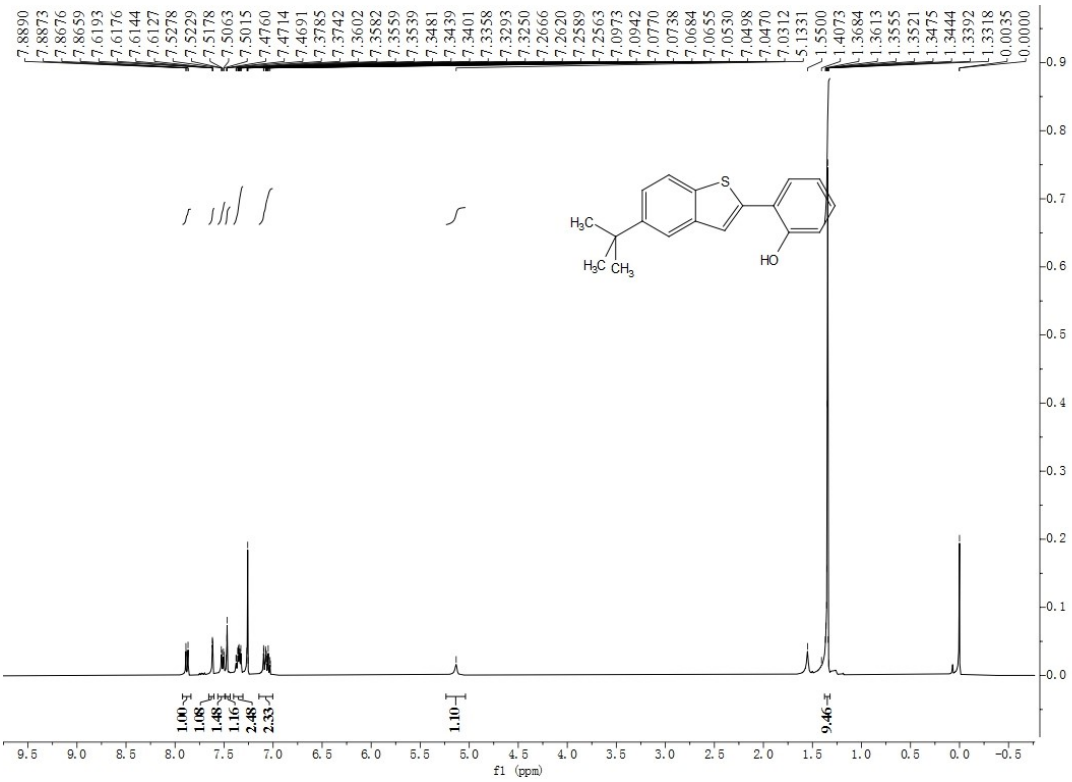
^{13}C NMR spectrum for **1l** (100 MHz,$CDCl_3$)



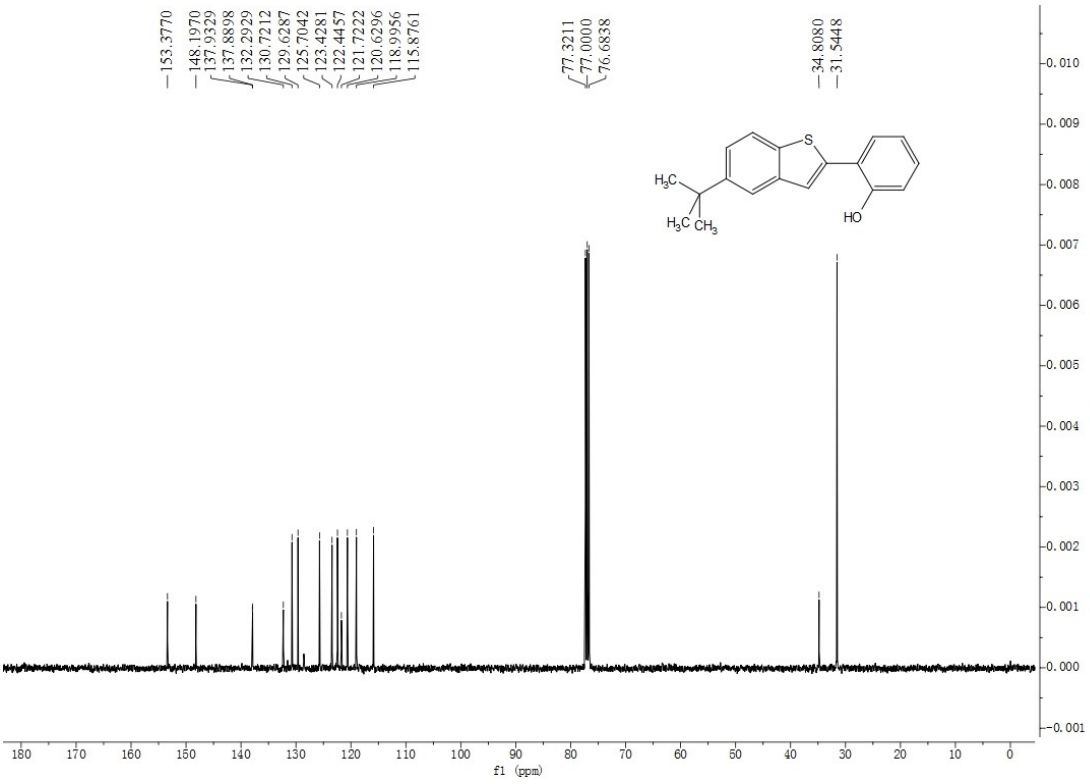
HRMS (ESI) spectrum for **1l**



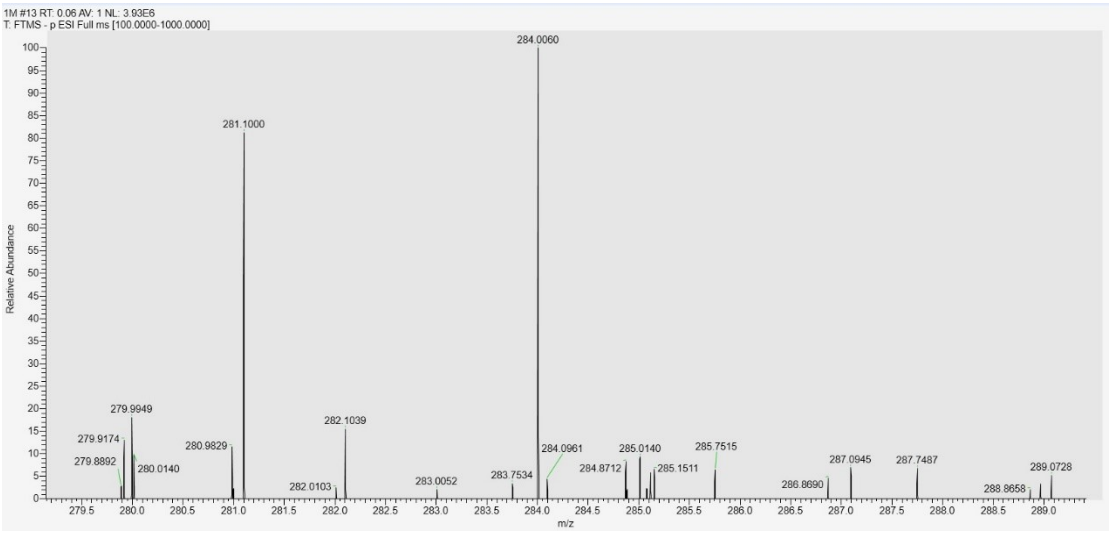
^{1}H NMR spectrum for **1m** (400 MHz,$CDCl_3$)



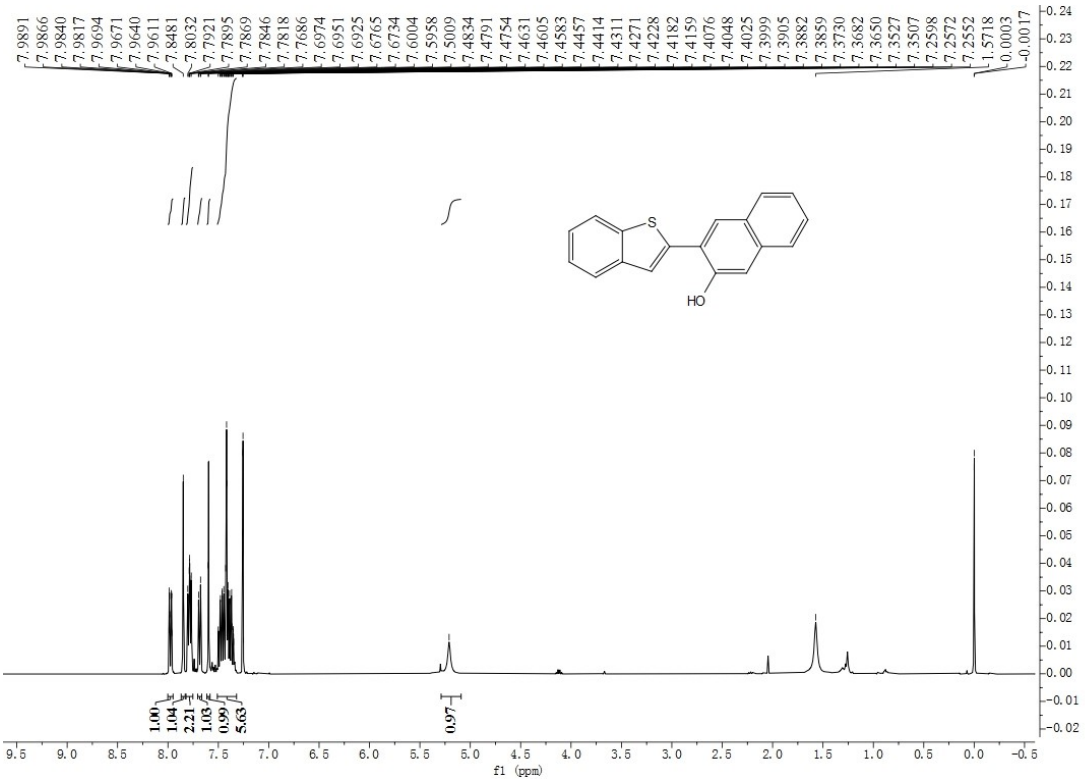
^{13}C NMR spectrum for **1m** (100 MHz,$CDCl_3$)



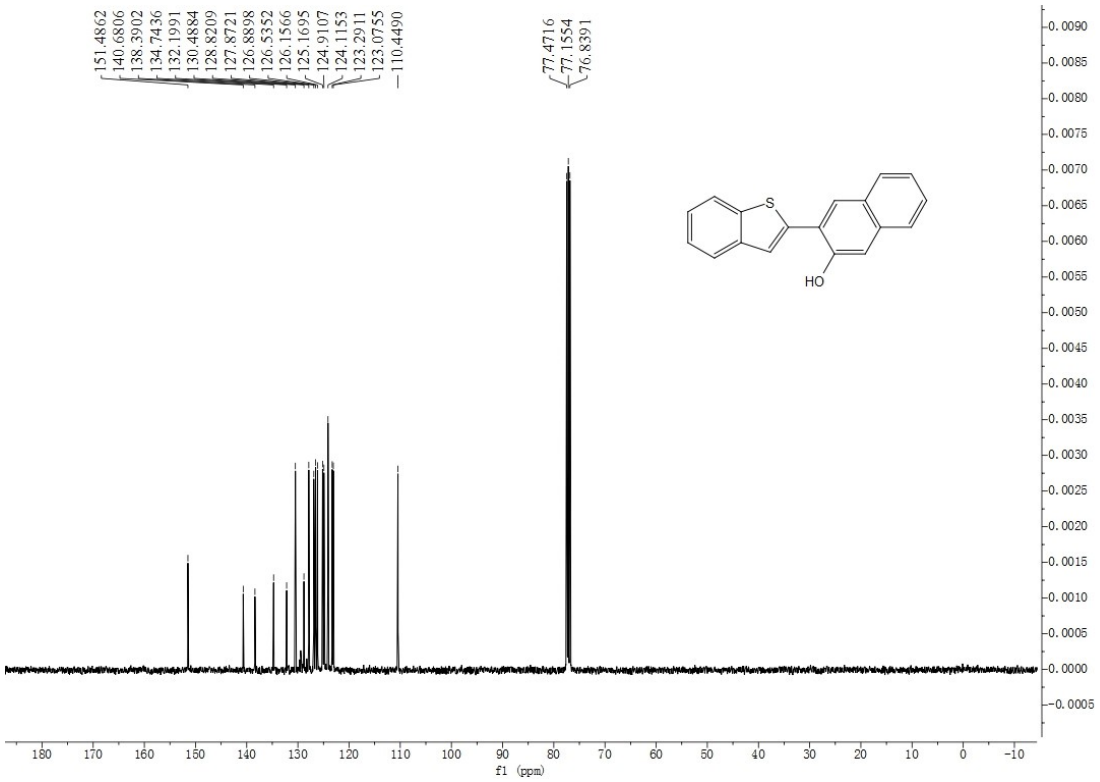
HRMS (ESI) spectrum for **1m**



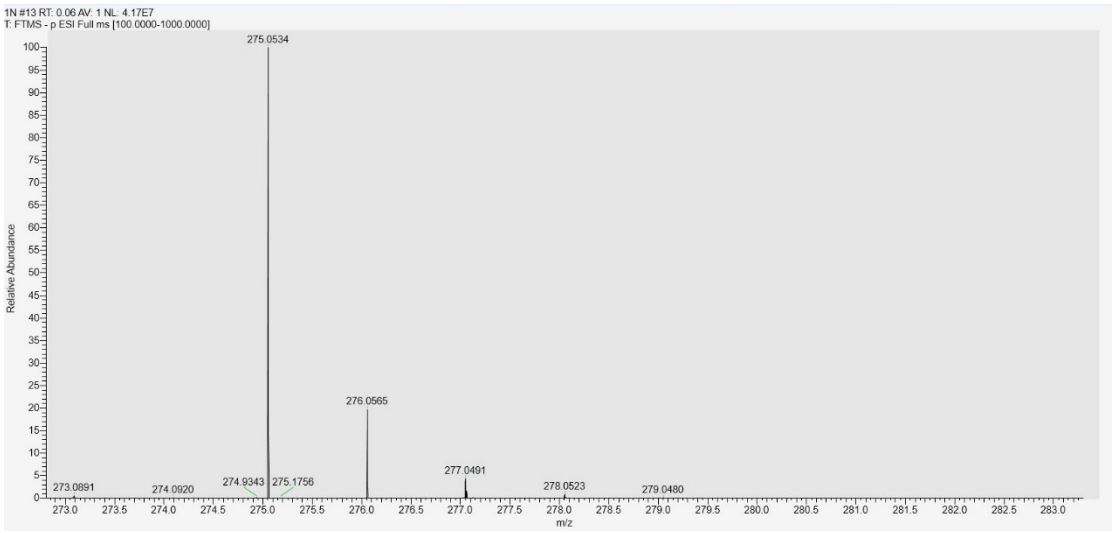
^{1}H NMR spectrum for **1n** (400 MHz,$CDCl_3$)



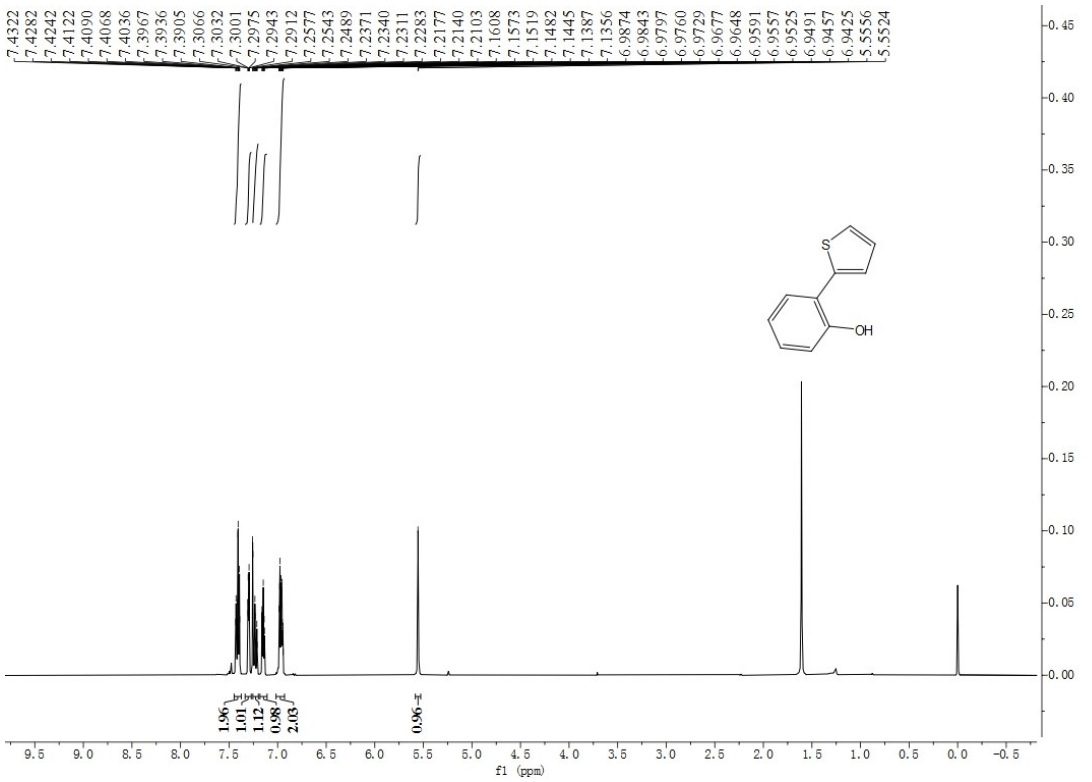
^{13}C NMR spectrum for **1n** (100 MHz,$CDCl_3$)



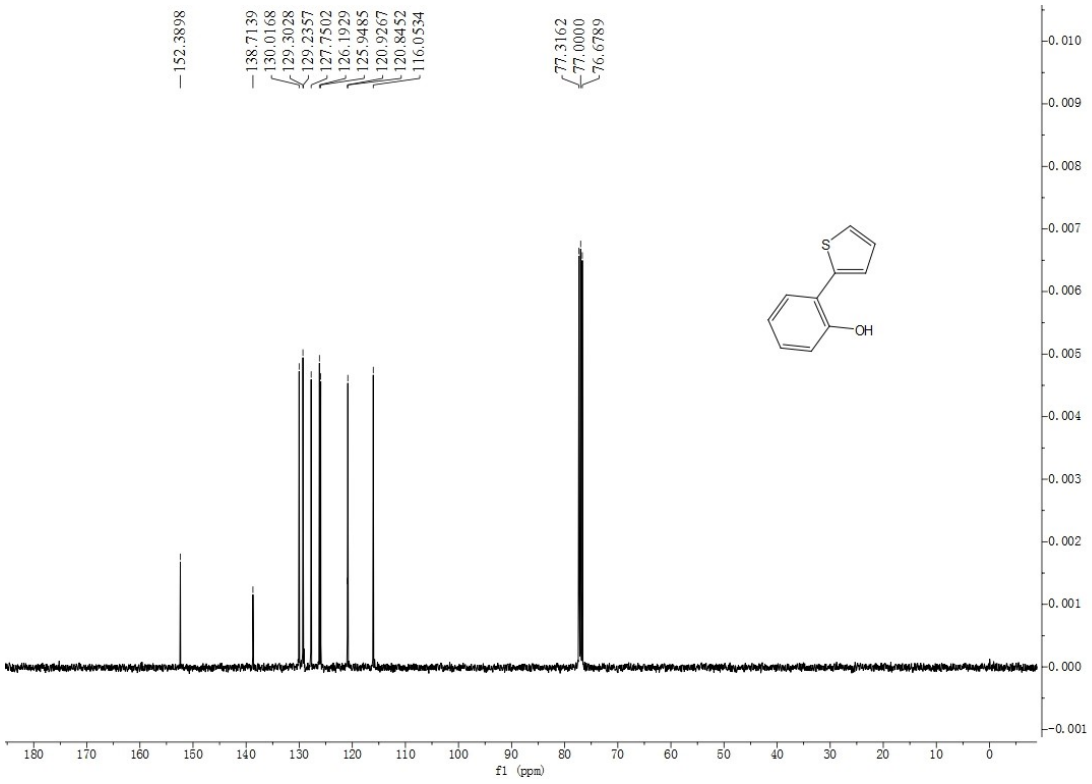
HRMS (ESI) spectrum for **1n**



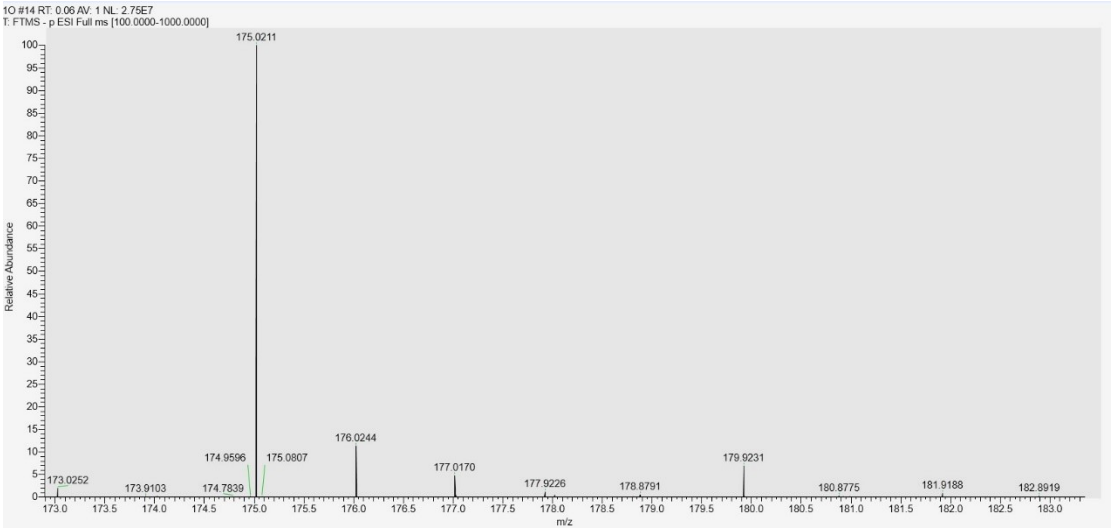
^{1}H NMR spectrum for **1o** (400 MHz,$CDCl_3$)



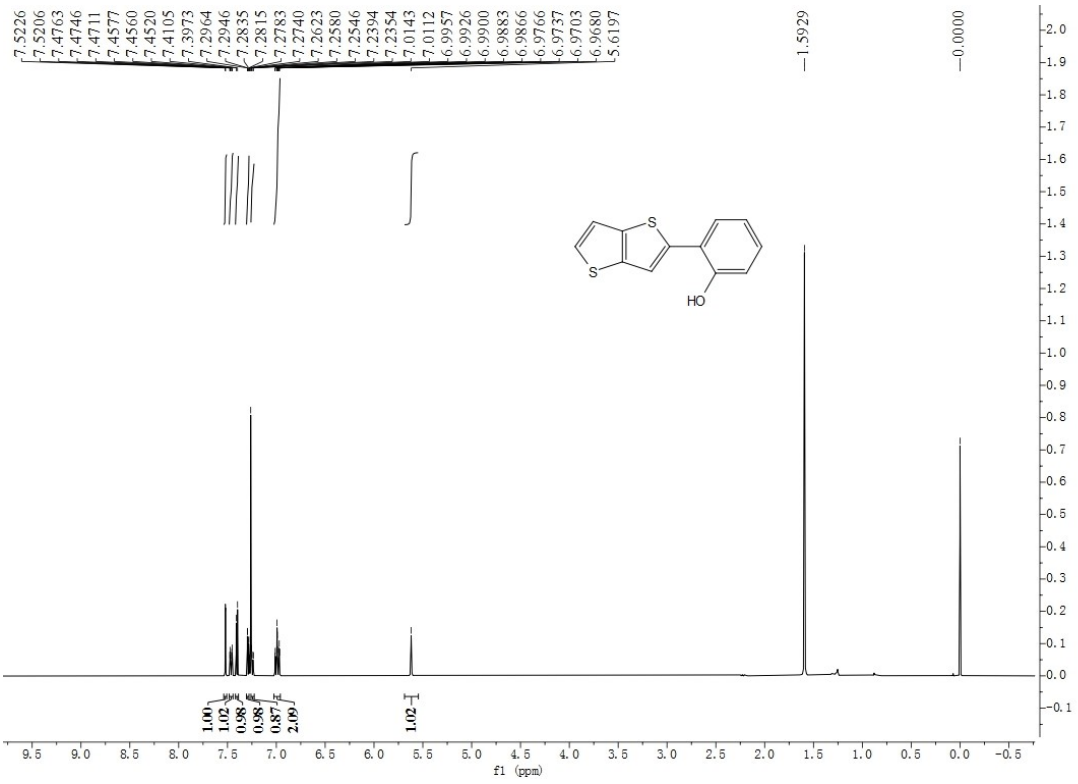
^{13}C NMR spectrum for **1o** (100 MHz,$CDCl_3$)



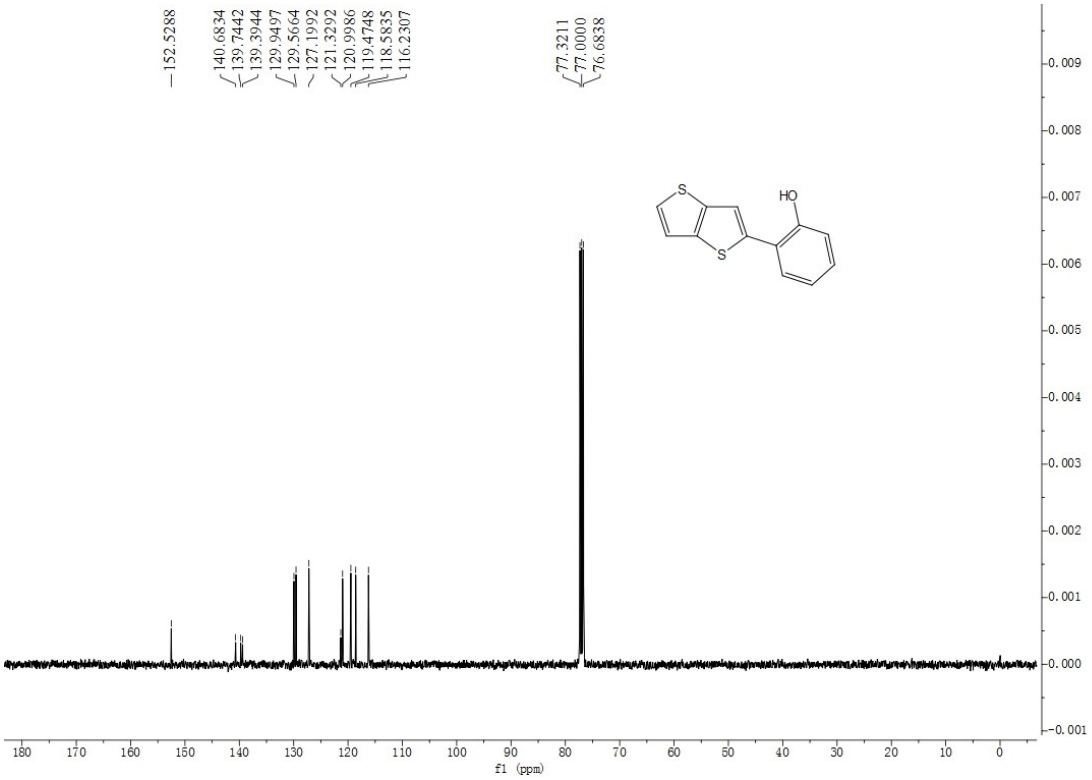
HRMS (ESI) spectrum for **1o**



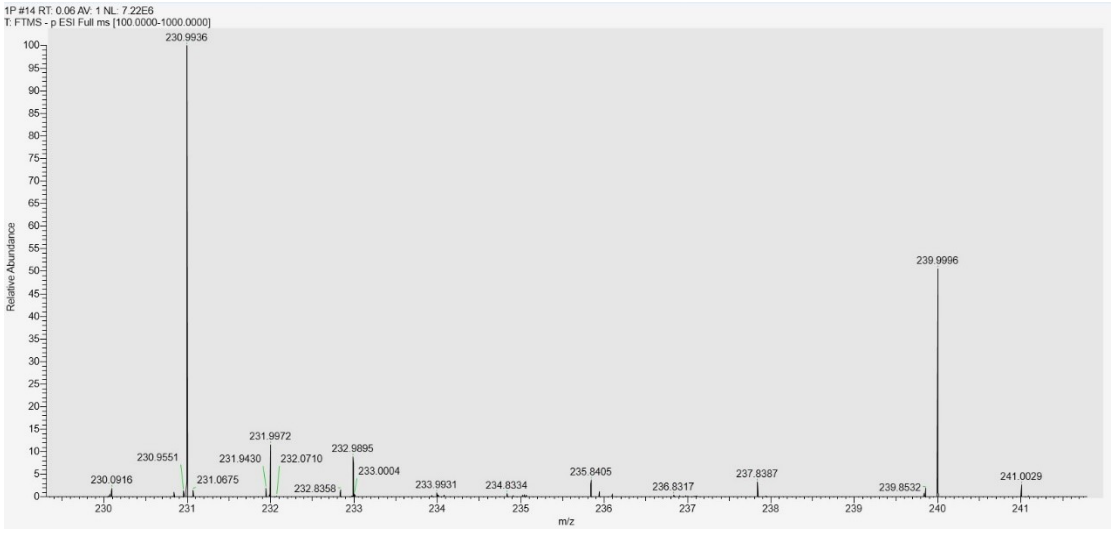
^{1}H NMR spectrum for **1p** (400 MHz,$CDCl_3$)



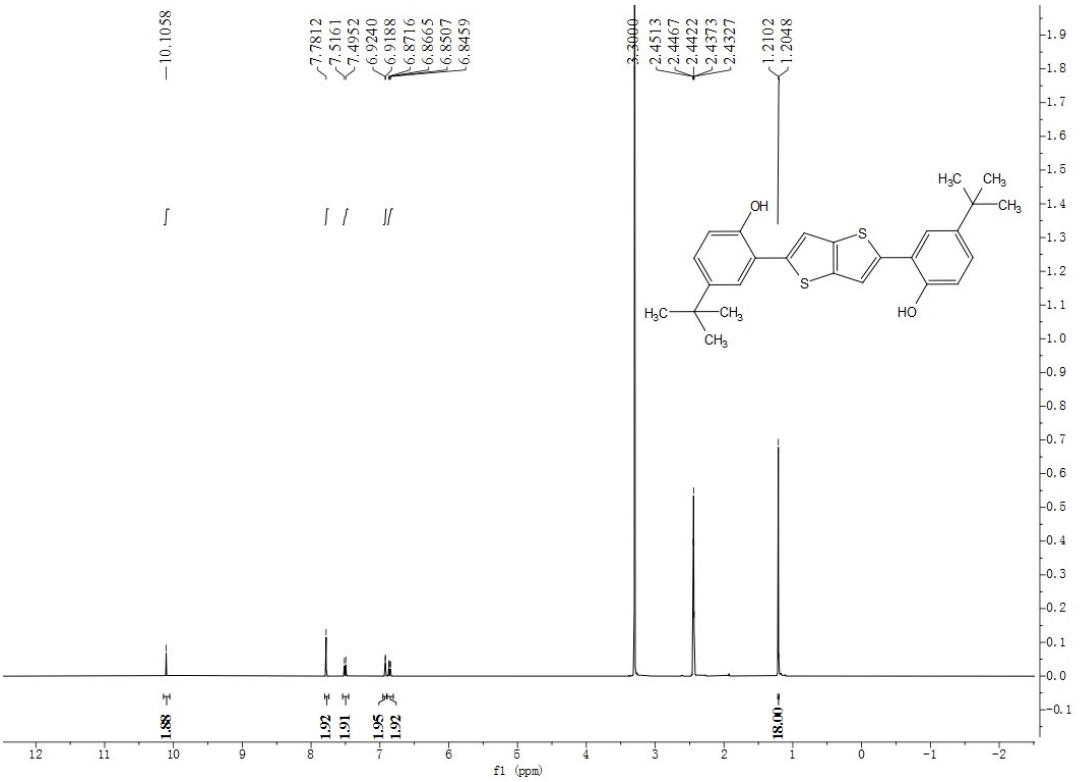
^{13}C NMR spectrum for **1p** (100 MHz,$CDCl_3$)



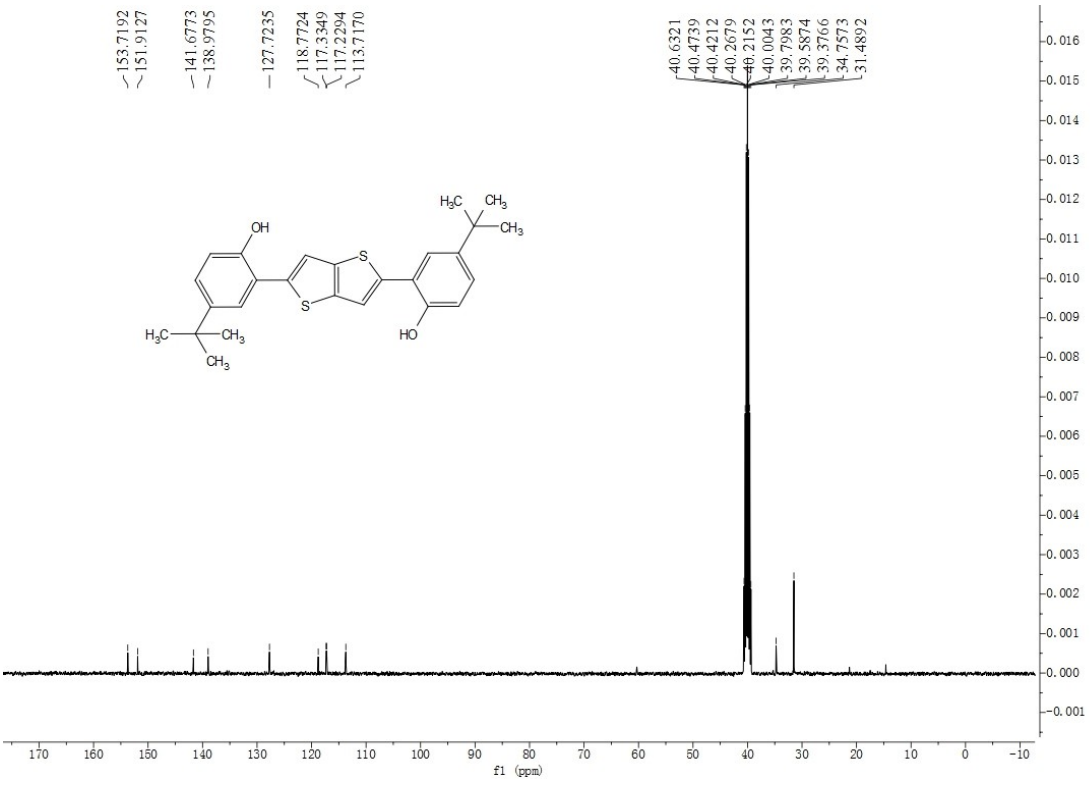
HRMS (ESI) spectrum for **1p**



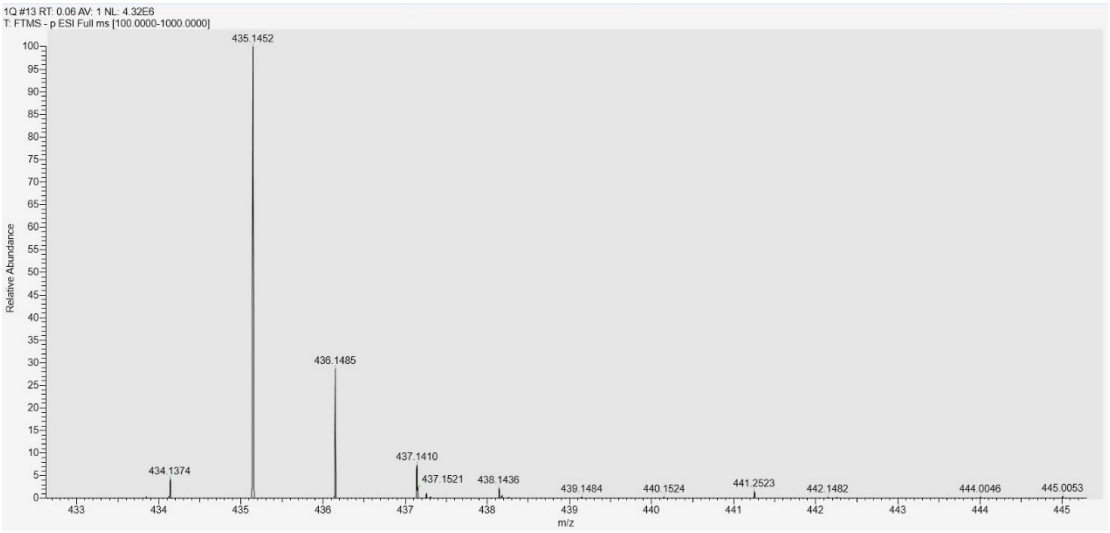
^{1}H NMR spectrum for **1q** (400 MHz,$CDCl_3$)



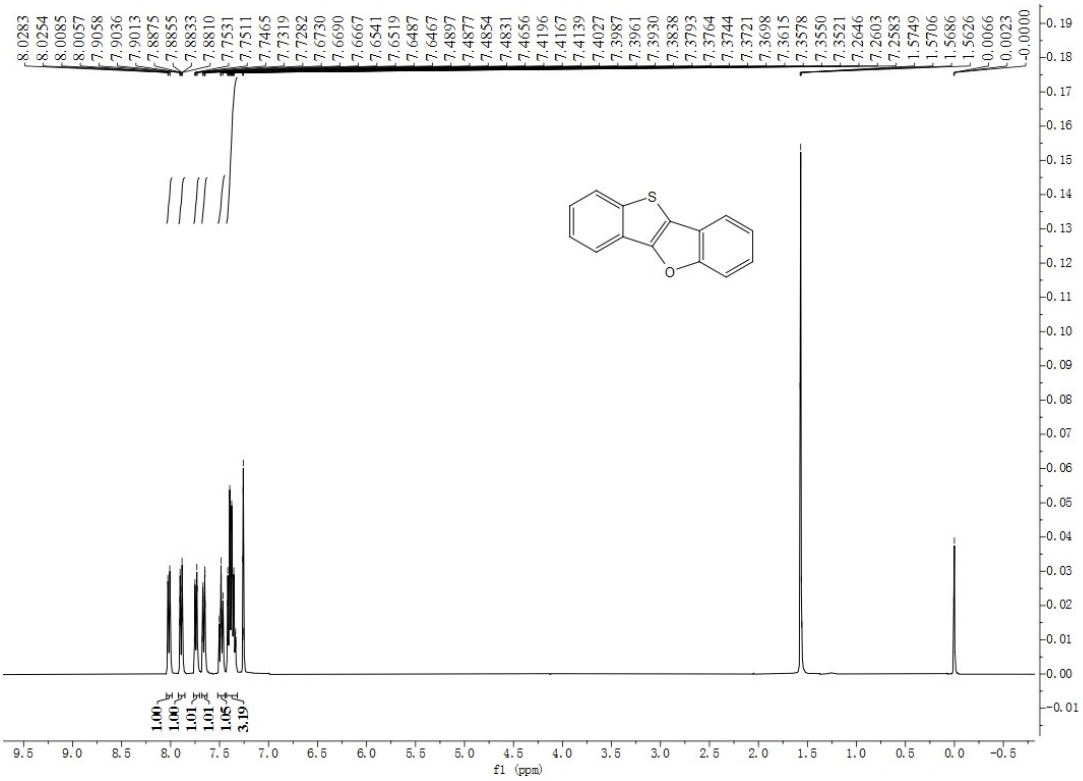
^{13}C NMR spectrum for **1q** (100 MHz,$CDCl_3$)



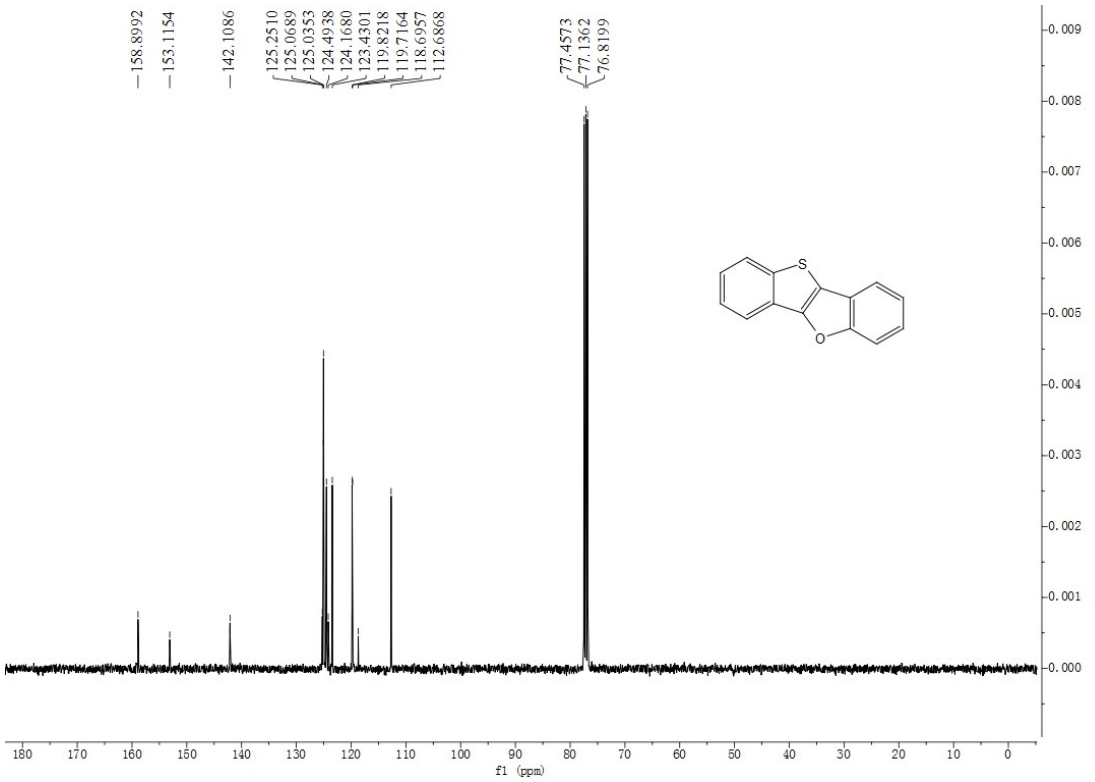
HRMS (ESI) spectrum for **1q**



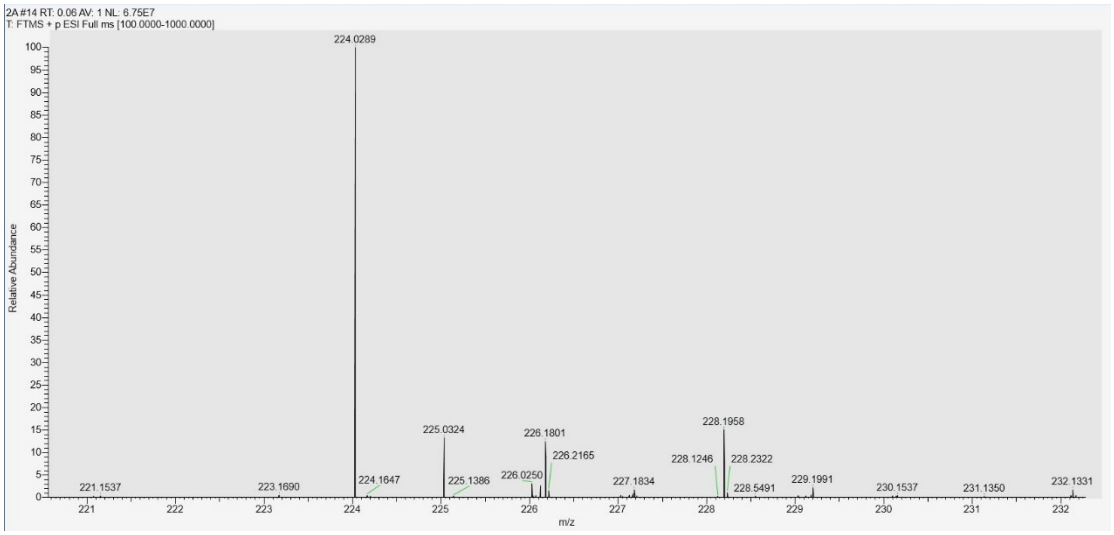
^{1}H NMR spectrum for **2a** (400 MHz,$CDCl_3$)



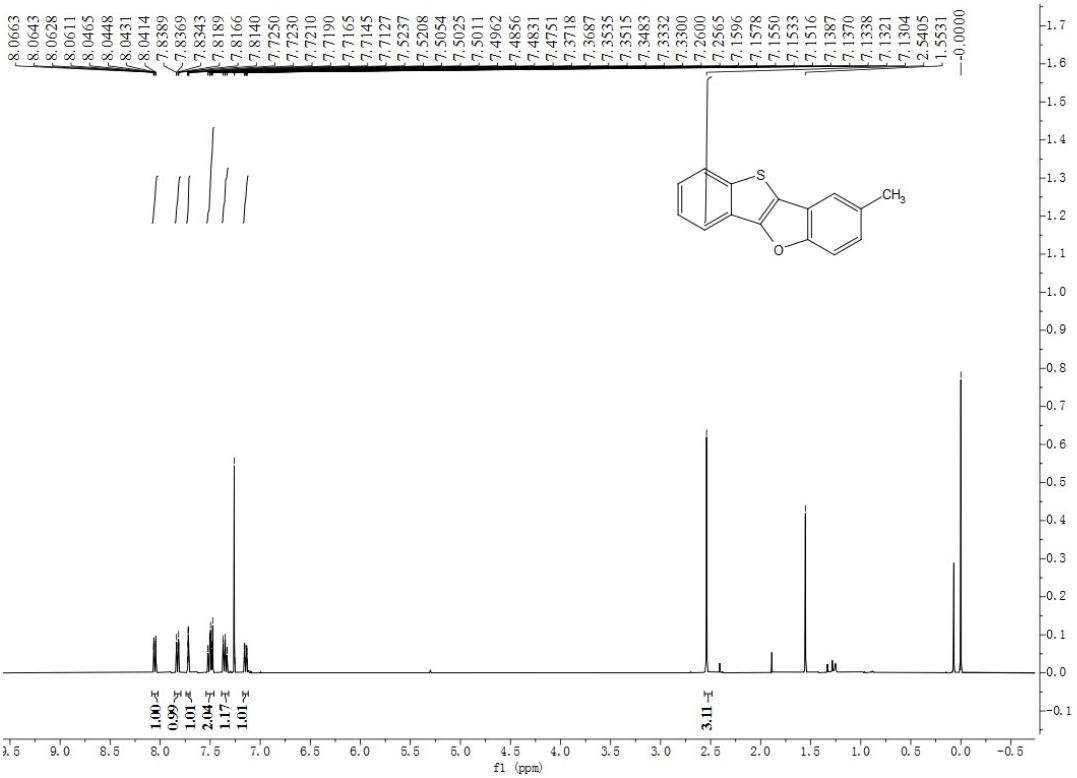
^{13}C NMR spectrum for **2a** (100 MHz,$CDCl_3$)



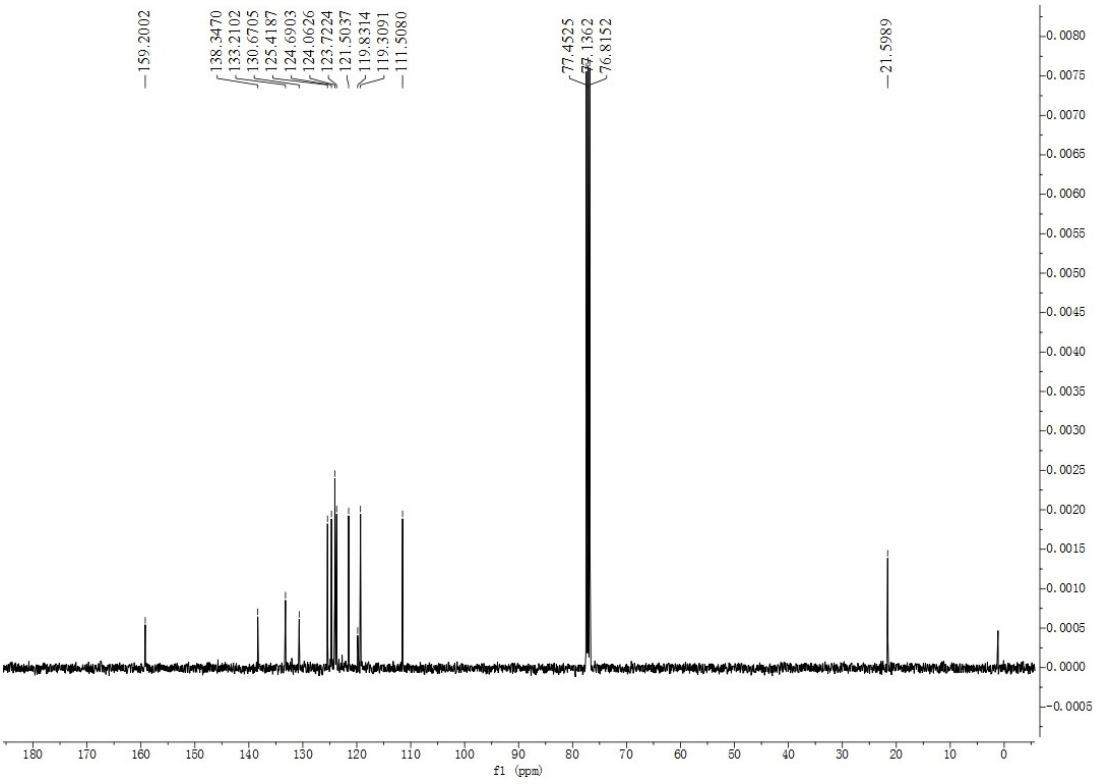
HRMS (ESI) spectrum for **2a**



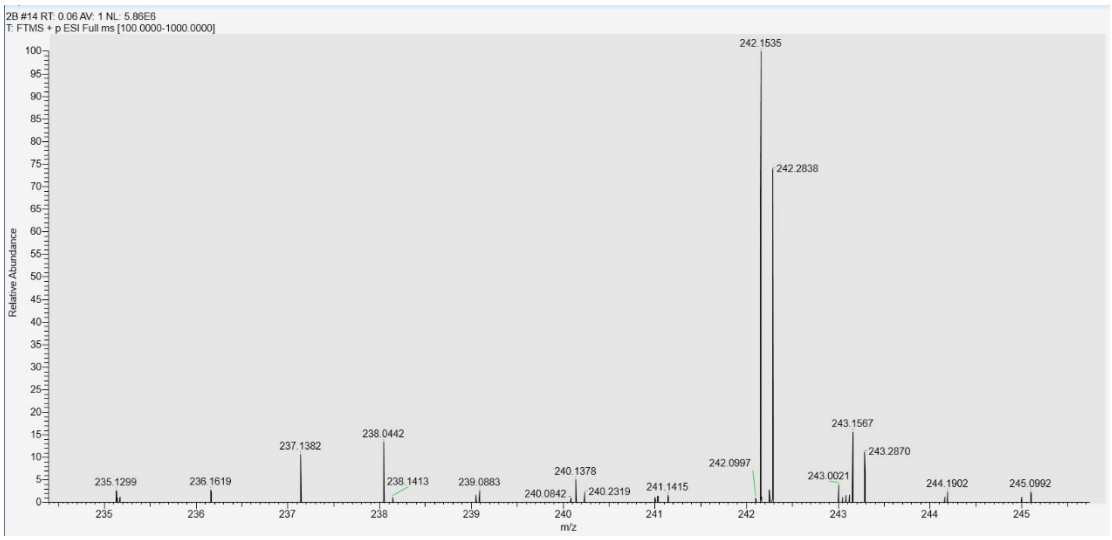
^{1}H NMR spectrum for **2b** (400 MHz,$CDCl_3$)



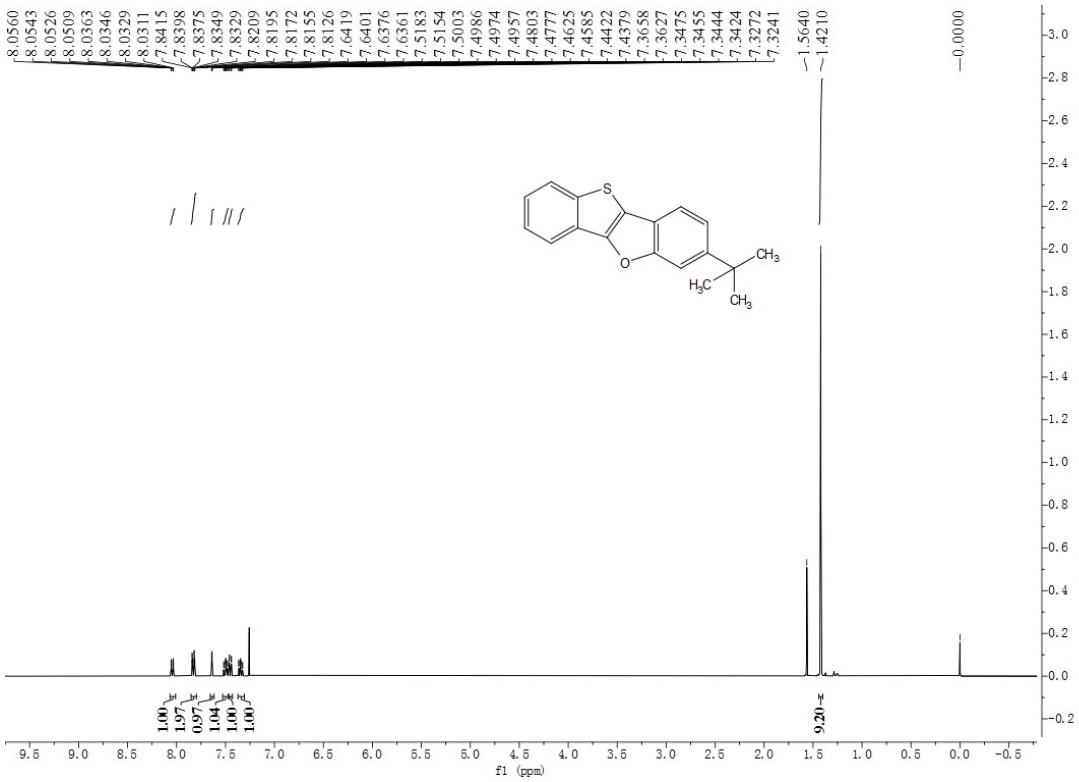
^{13}C NMR spectrum for **2b** (100 MHz,$CDCl_3$)



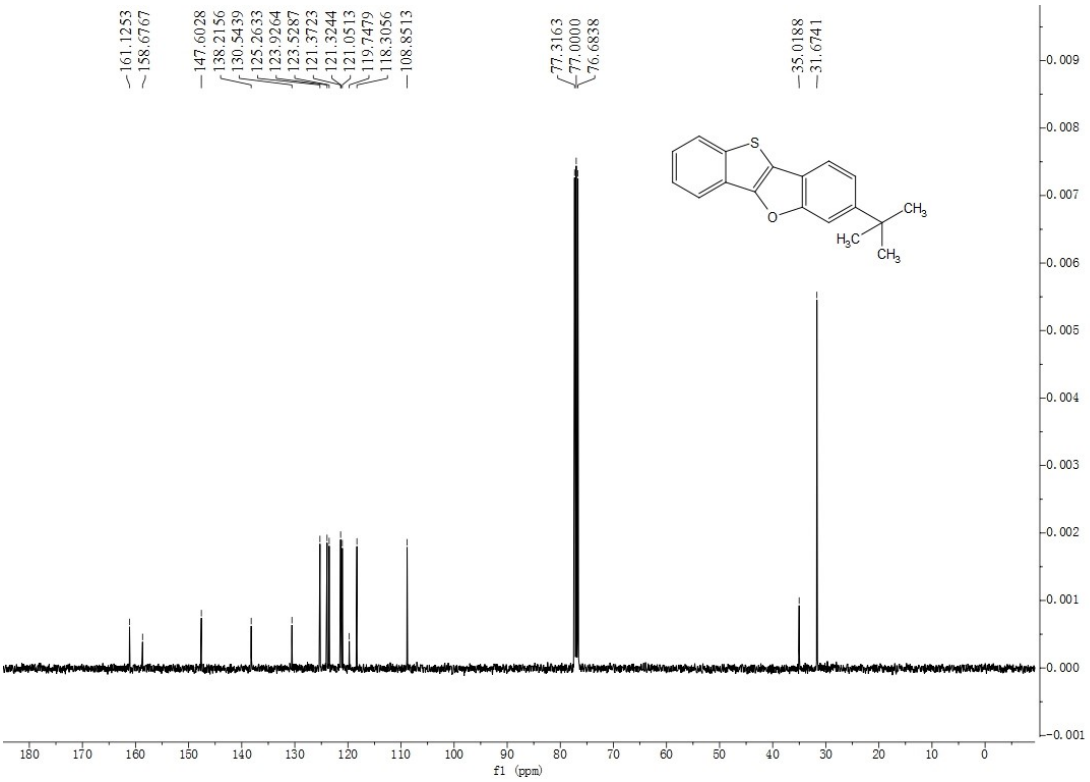
HRMS (ESI) spectrum for **2b**



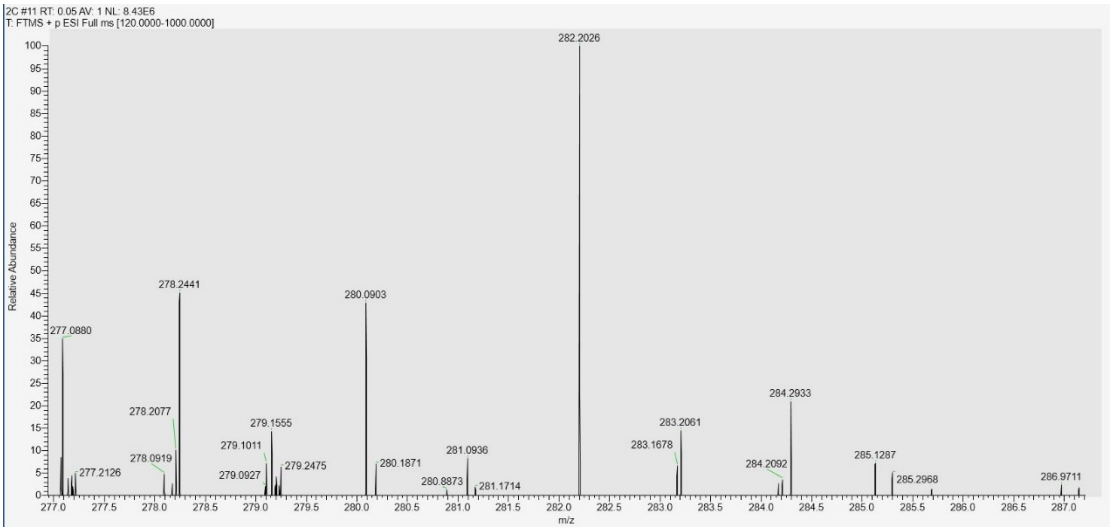
^{1}H NMR spectrum for **2c** (400 MHz,$CDCl_3$)



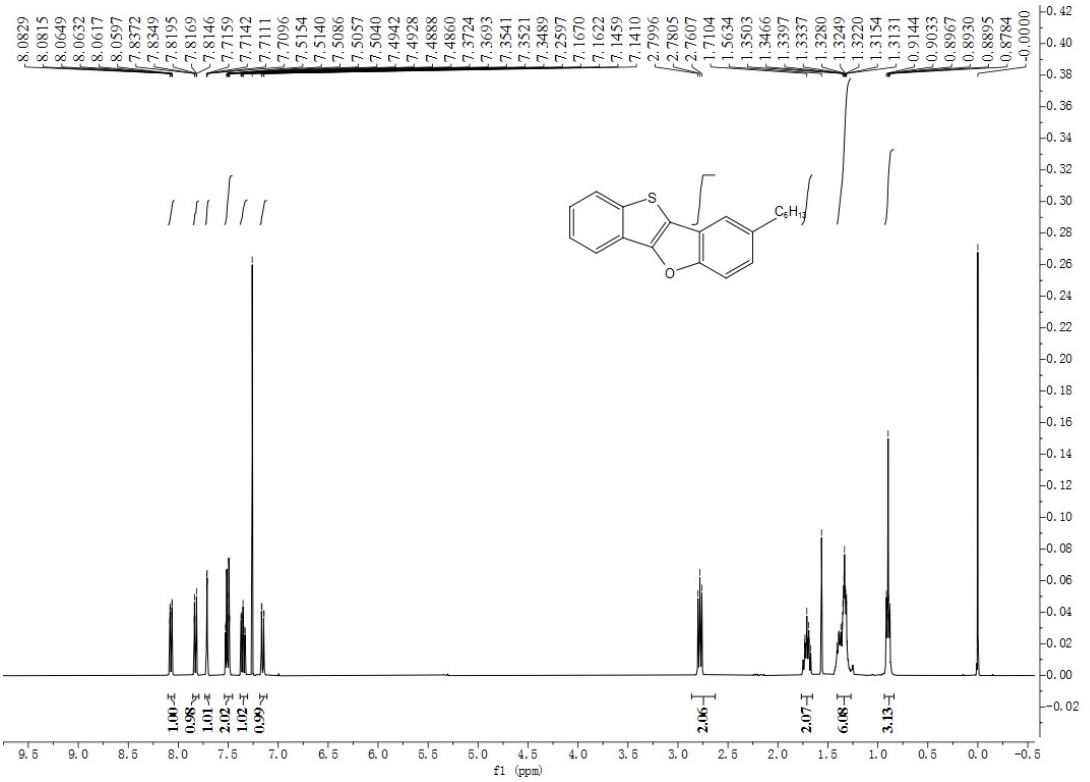
^{13}C NMR spectrum for **2c** (100 MHz,$CDCl_3$)



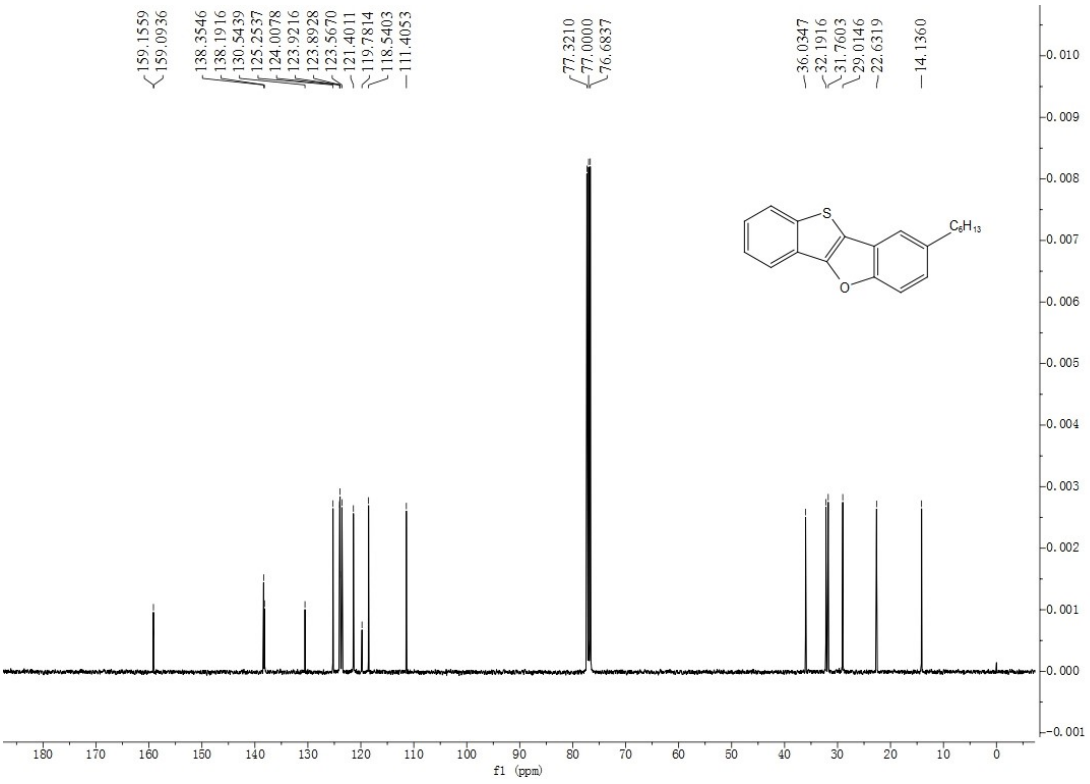
HRMS (ESI) spectrum for **2c**



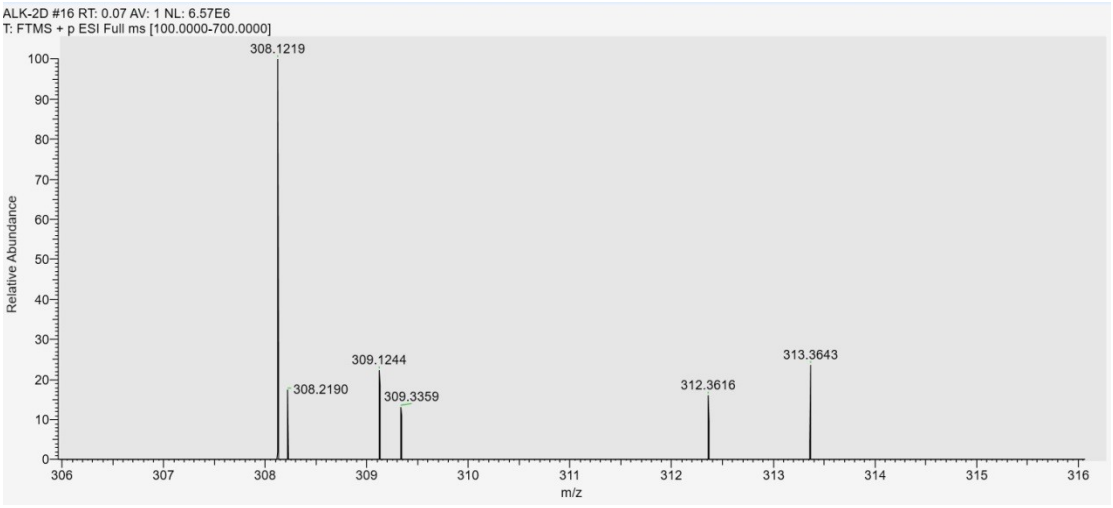
^{1}H NMR spectrum for **2d** (400 MHz,$CDCl_3$)



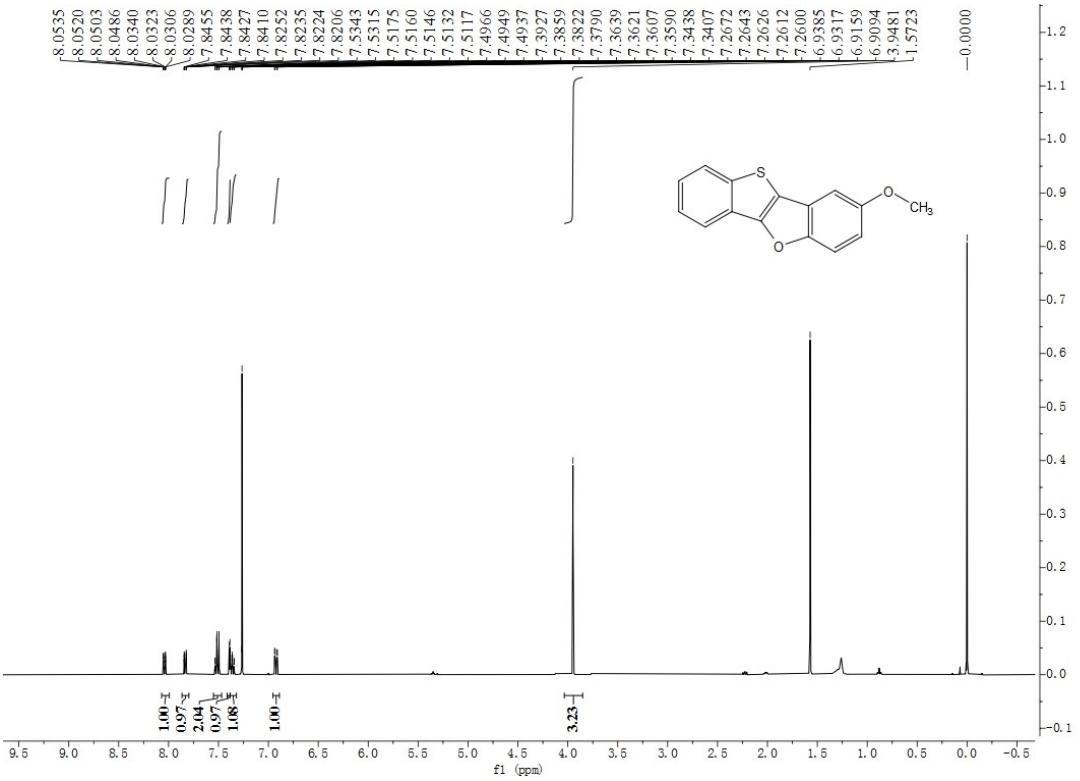
^{13}C NMR spectrum for **2d** (100 MHz,$CDCl_3$)



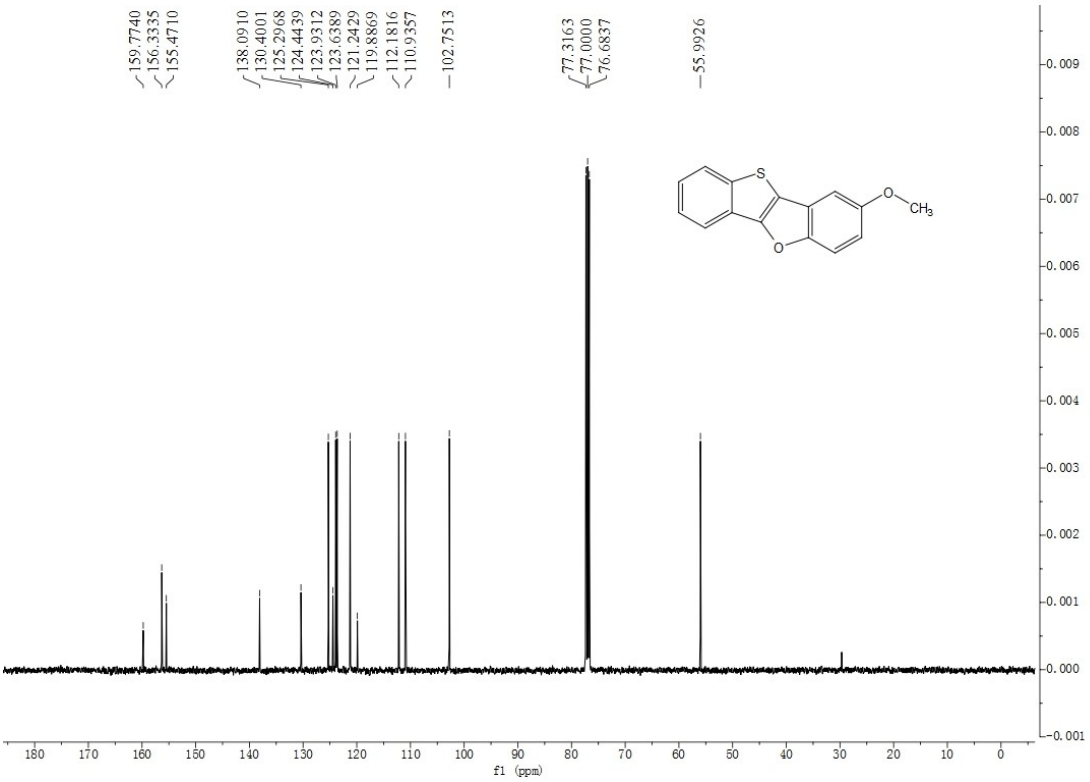
HRMS (ESI) spectrum for **2d**



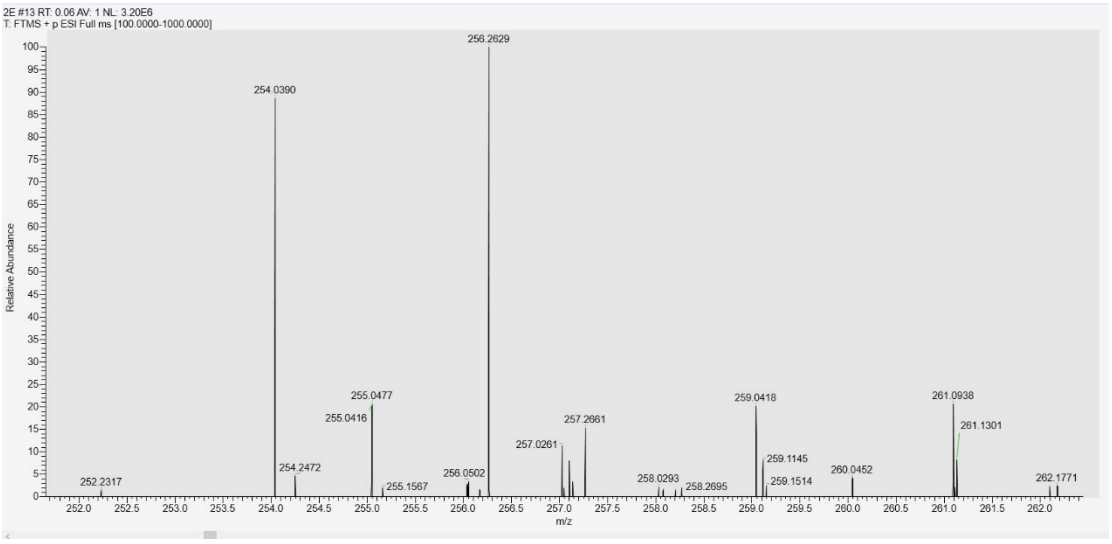
^{1}H NMR spectrum for **2e** (400 MHz,$CDCl_3$)



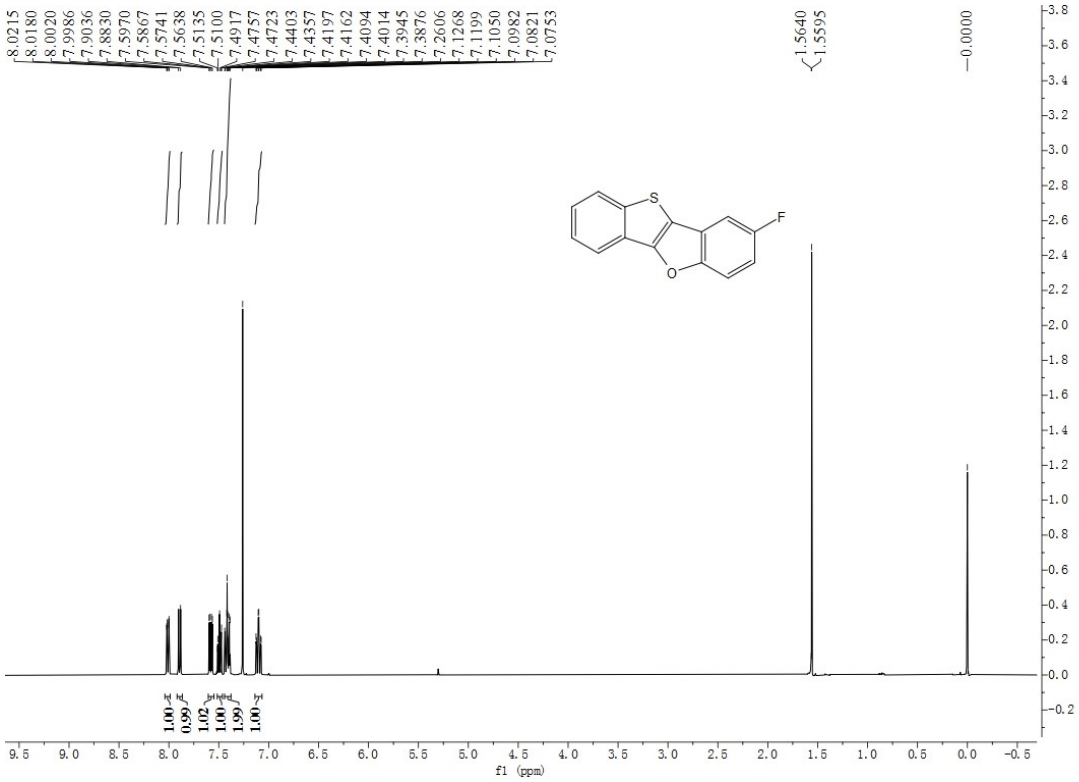
^{13}C NMR spectrum for **2e** (100 MHz,$CDCl_3$)



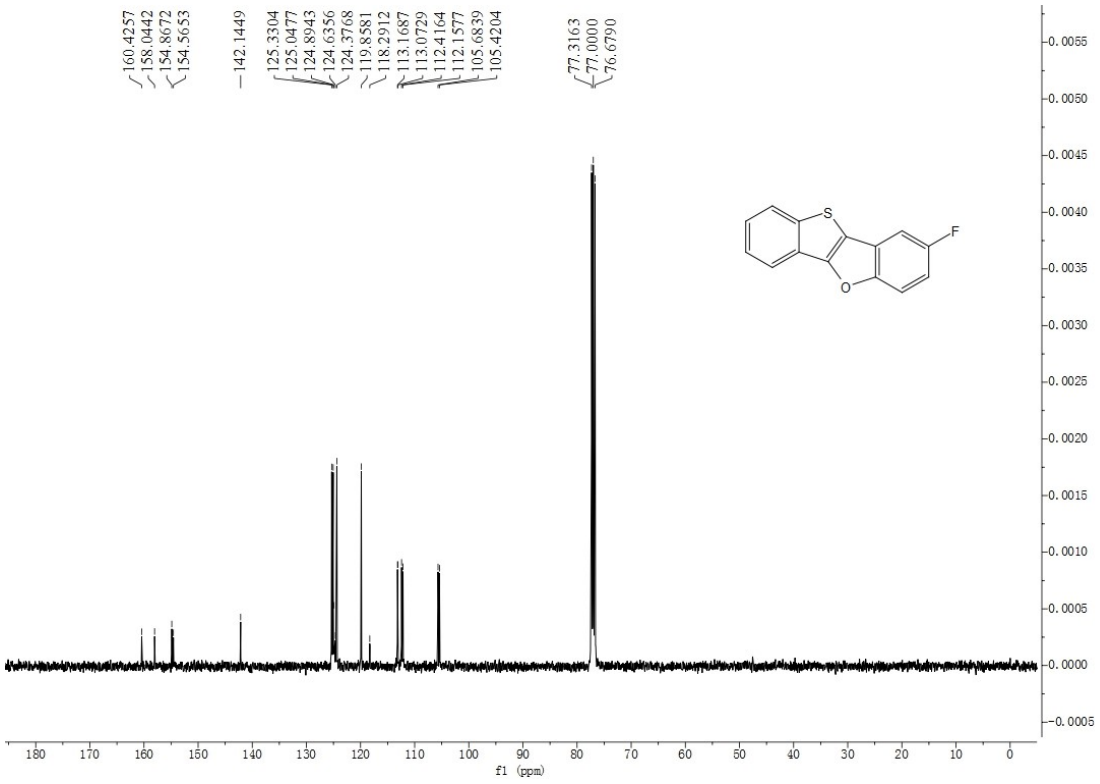
HRMS (ESI) spectrum for **2e**



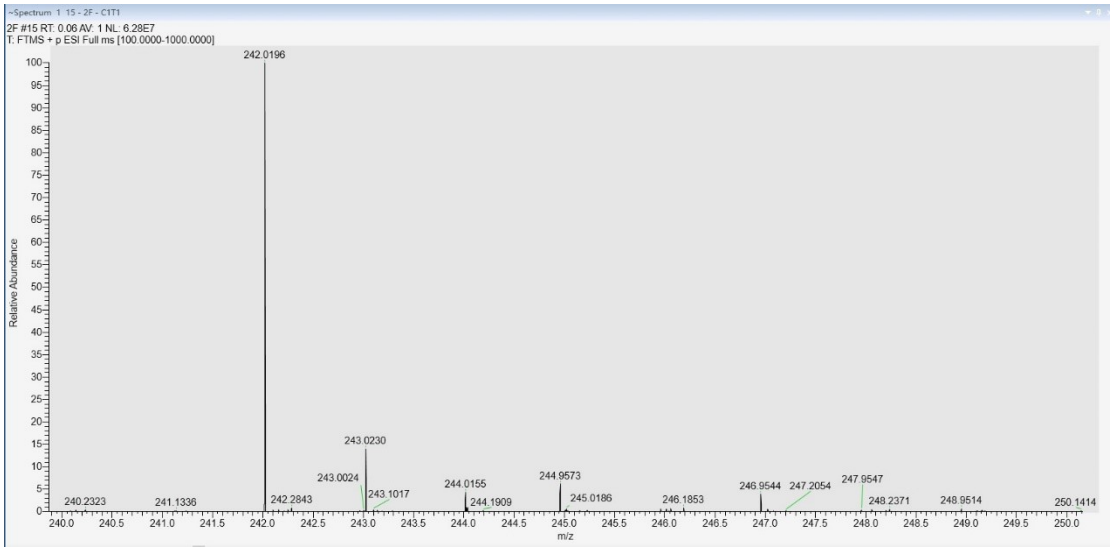
^{1}H NMR spectrum for **2f** (400 MHz,$CDCl_3$)



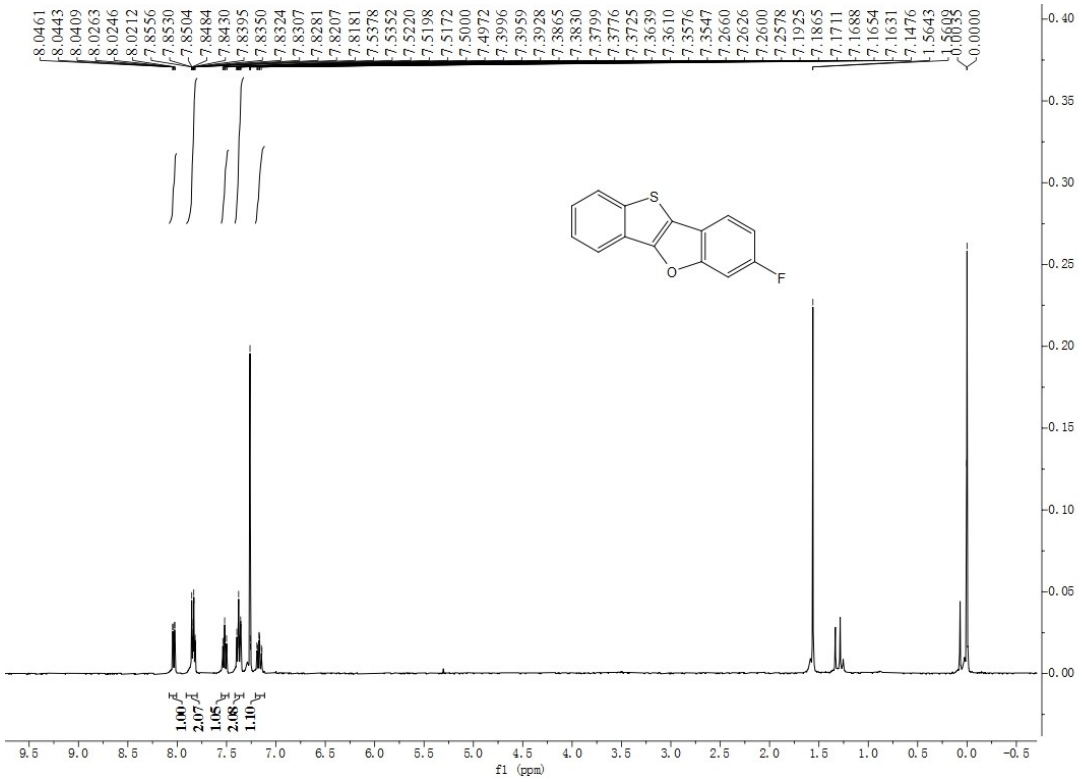
^{13}C NMR spectrum for **2f** (100 MHz,$CDCl_3$)



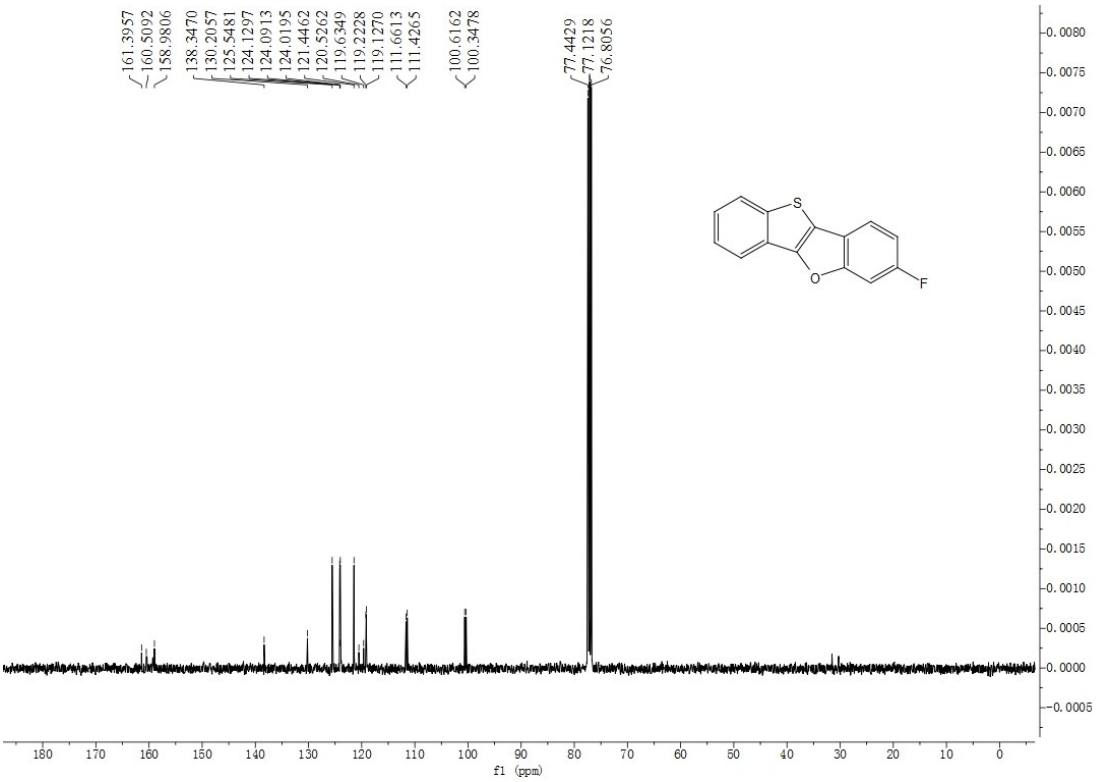
HRMS (ESI) spectrum for **2f**



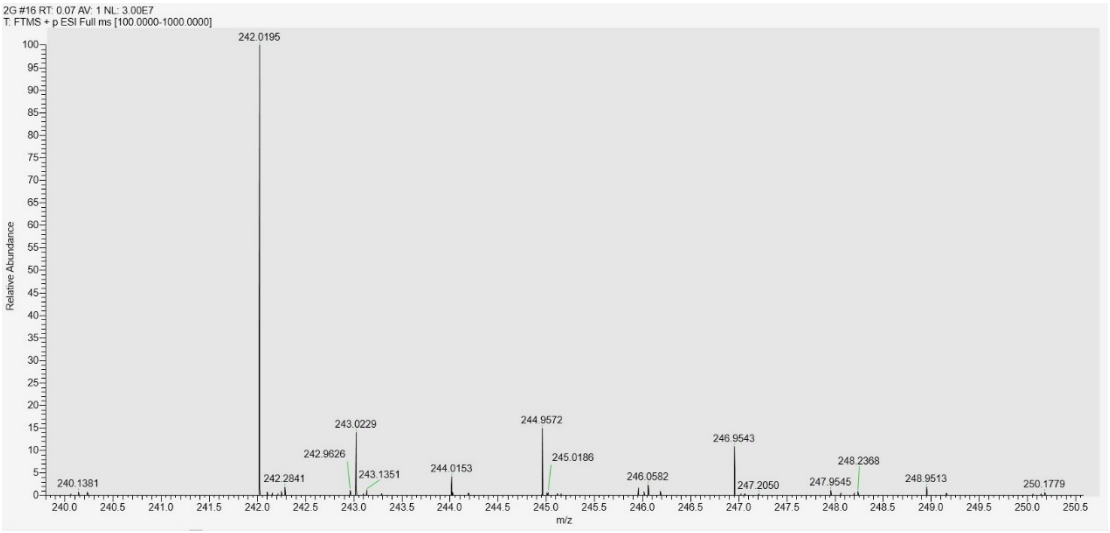
^{1}H NMR spectrum for **2g** (400 MHz,$CDCl_3$)



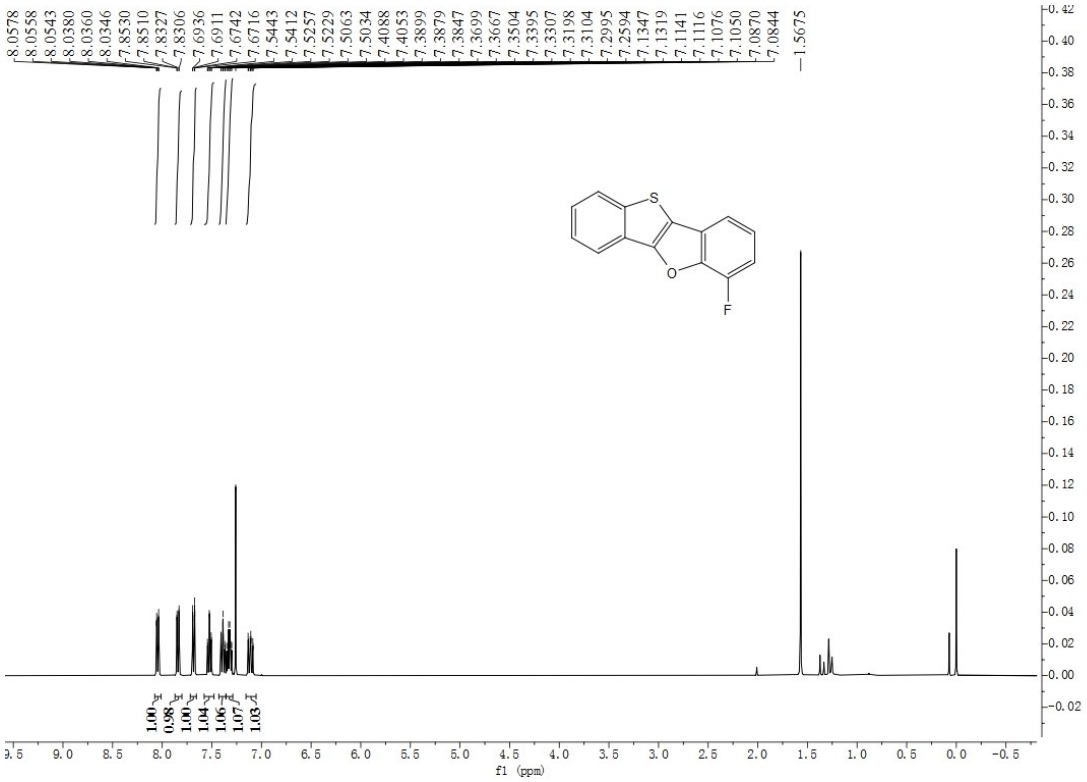
^{13}C NMR spectrum for **2g** (100 MHz,$CDCl_3$)



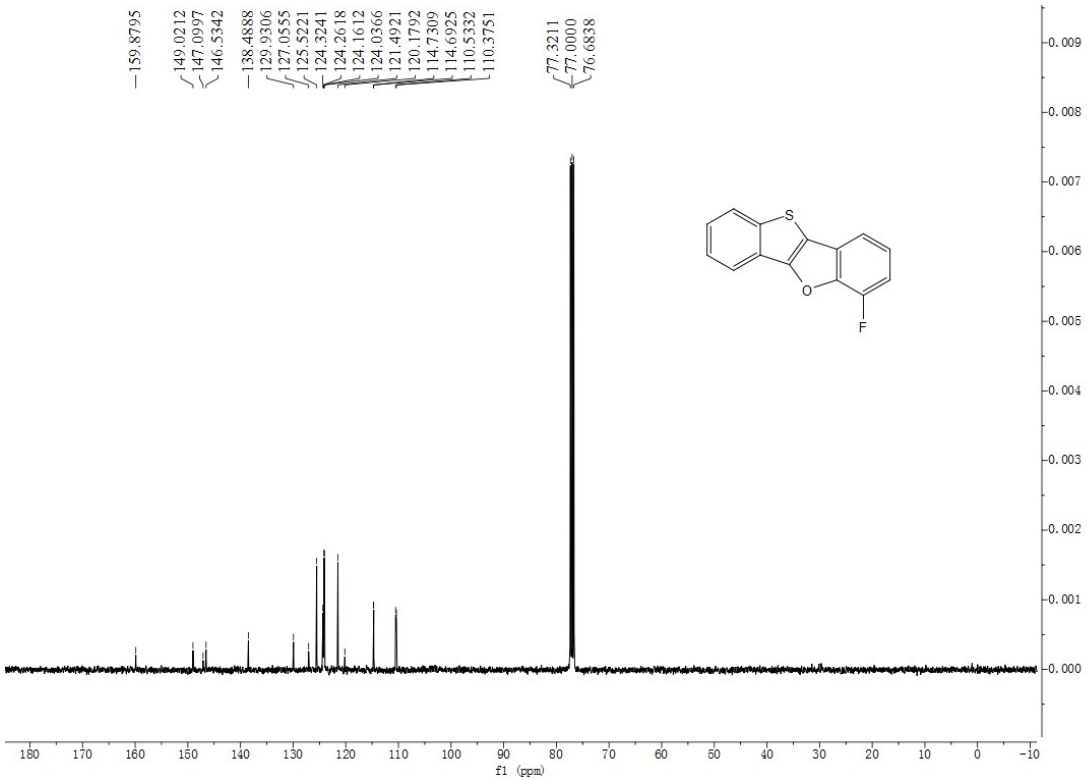
HRMS (ESI) spectrum for **2g**



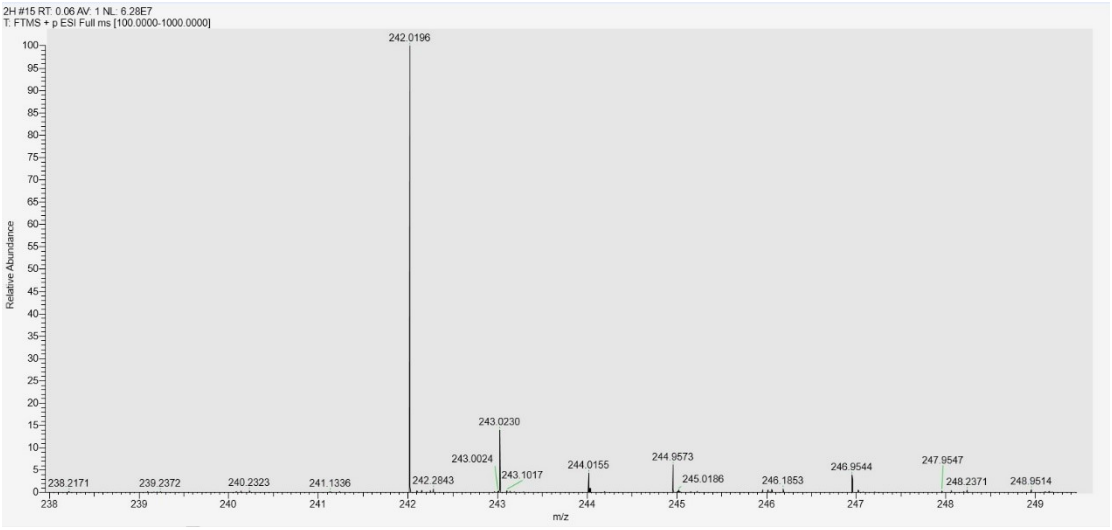
^{1}H NMR spectrum for **2h** (400 MHz,$CDCl_3$)



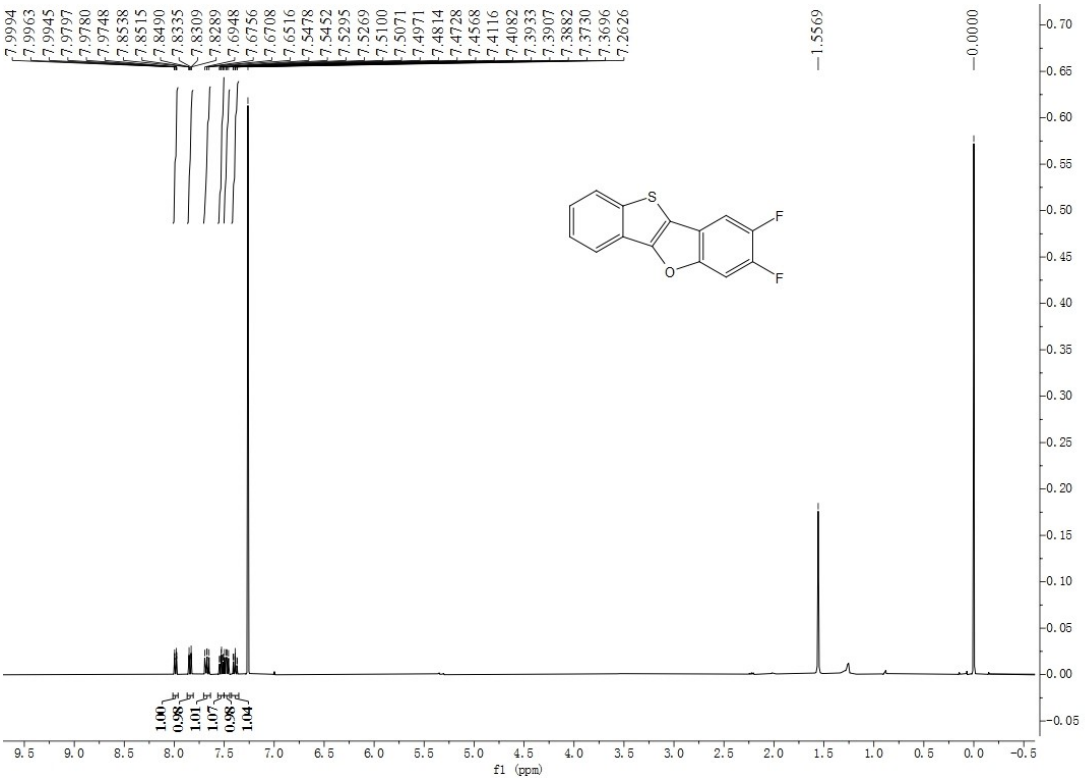
^{13}C NMR spectrum for **2h** (100 MHz,$CDCl_3$)



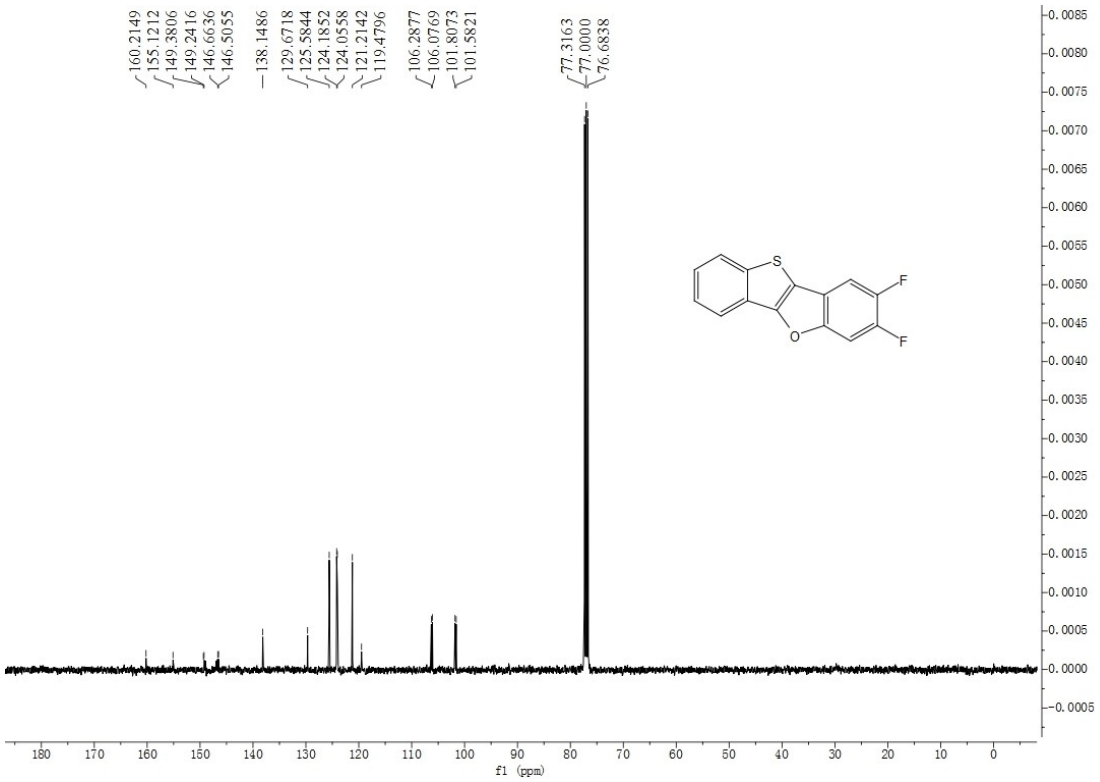
HRMS (ESI) spectrum for **2h**



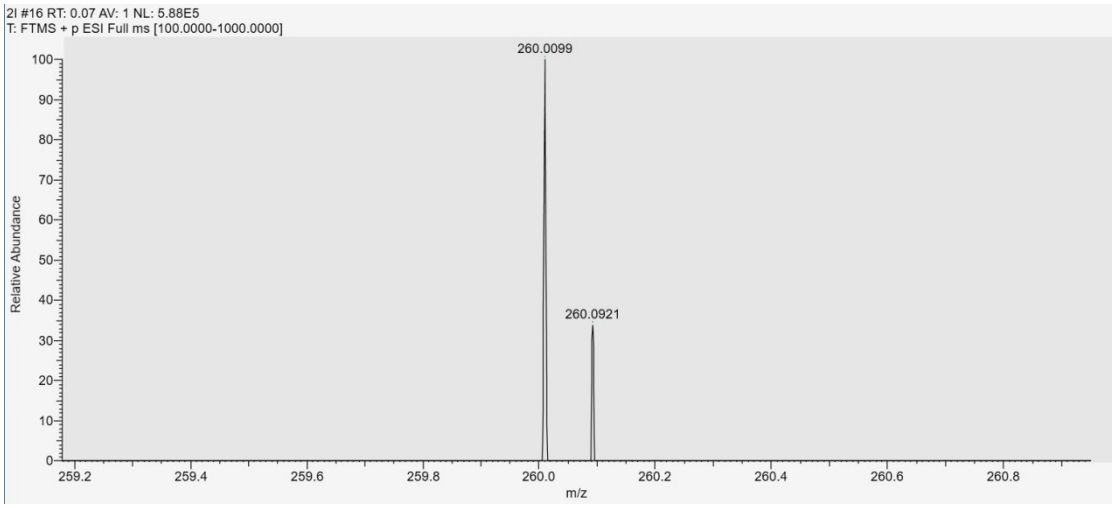
^{1}H NMR spectrum for **2i** (400 MHz,$CDCl_3$)



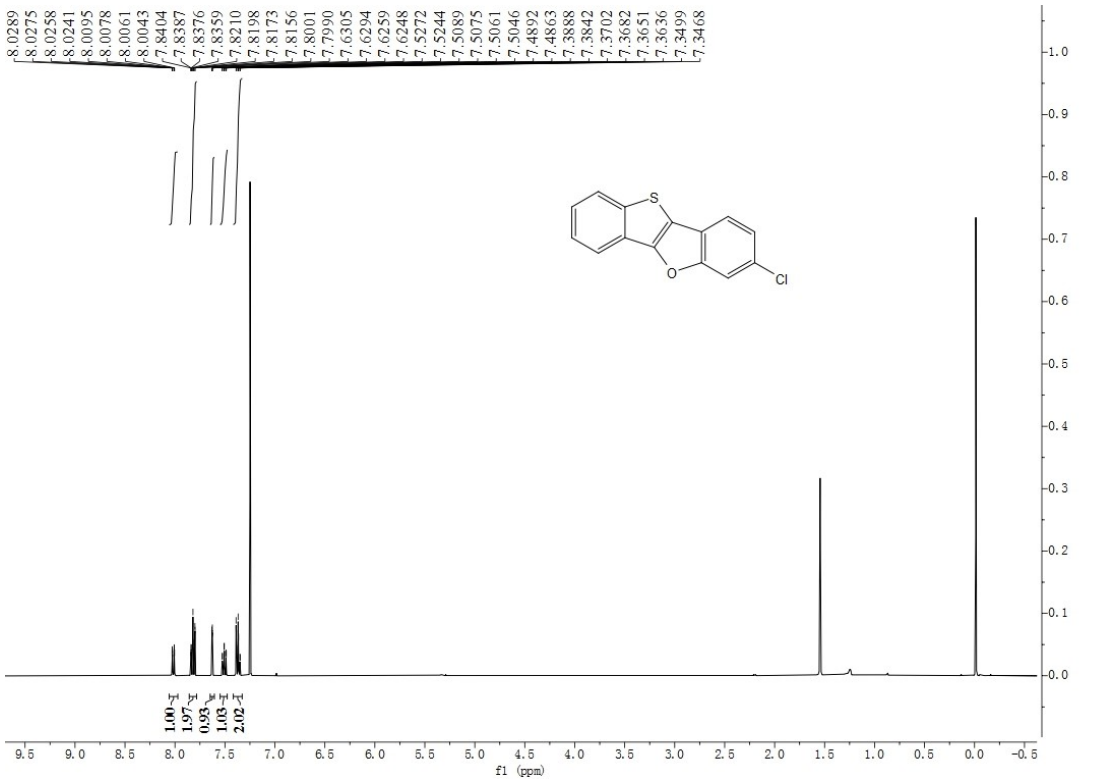
^{13}C NMR spectrum for **2i** (100 MHz,$CDCl_3$)



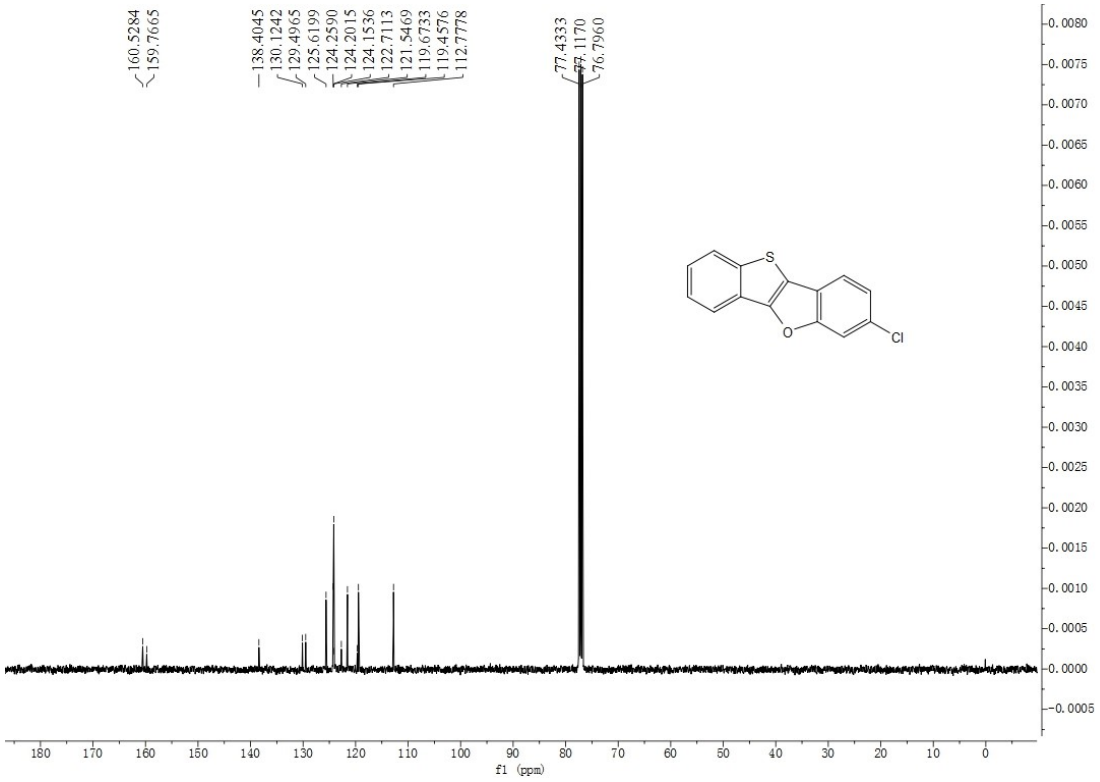
HRMS (ESI) spectrum for **2i**



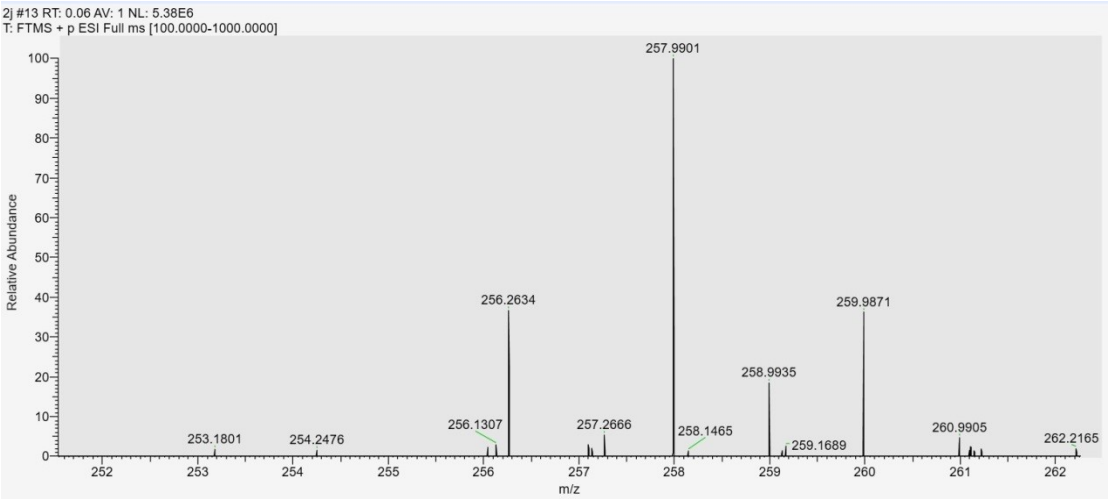
^{1}H NMR spectrum for **2j** (400 MHz,$CDCl_3$)



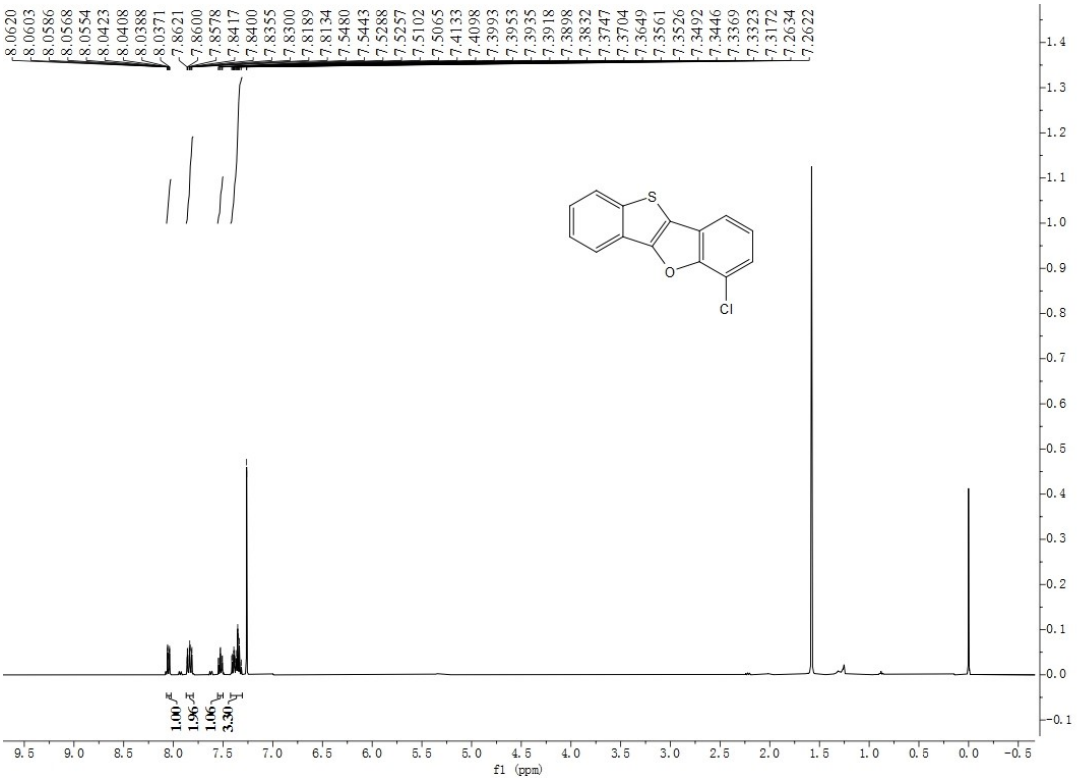
^{13}C NMR spectrum for **2j** (100 MHz,$CDCl_3$)



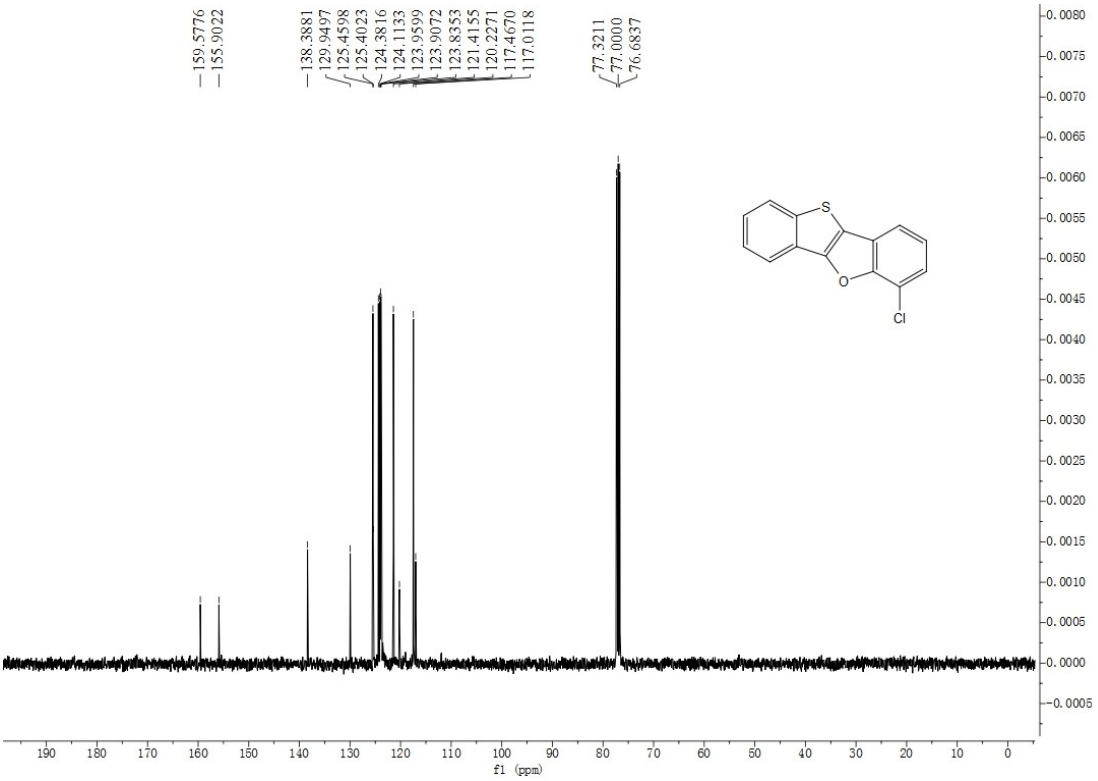
HRMS (ESI) spectrum for **2j**



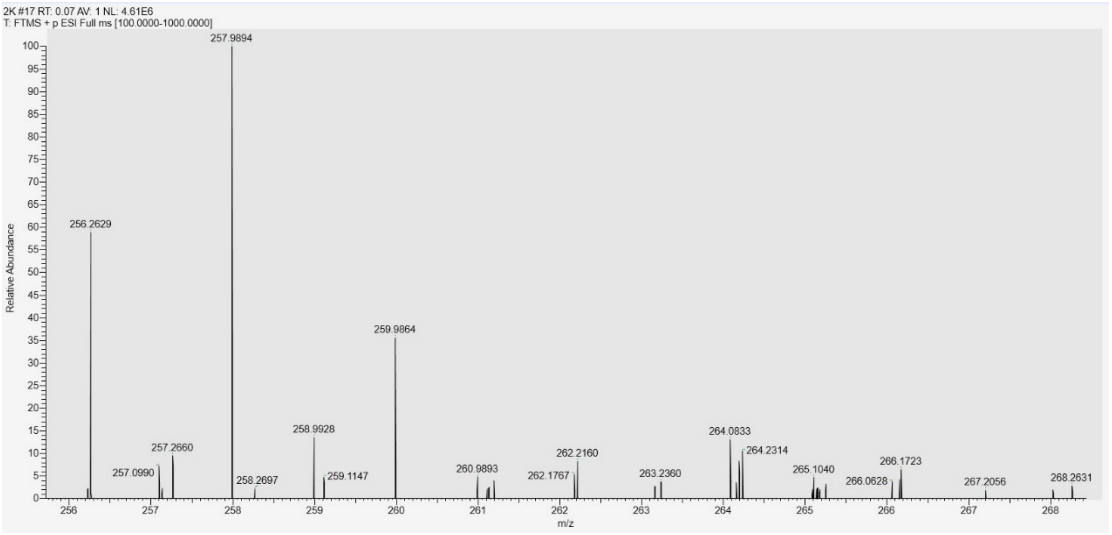
^{1}H NMR spectrum for **2k** (400 MHz,$CDCl_3$)



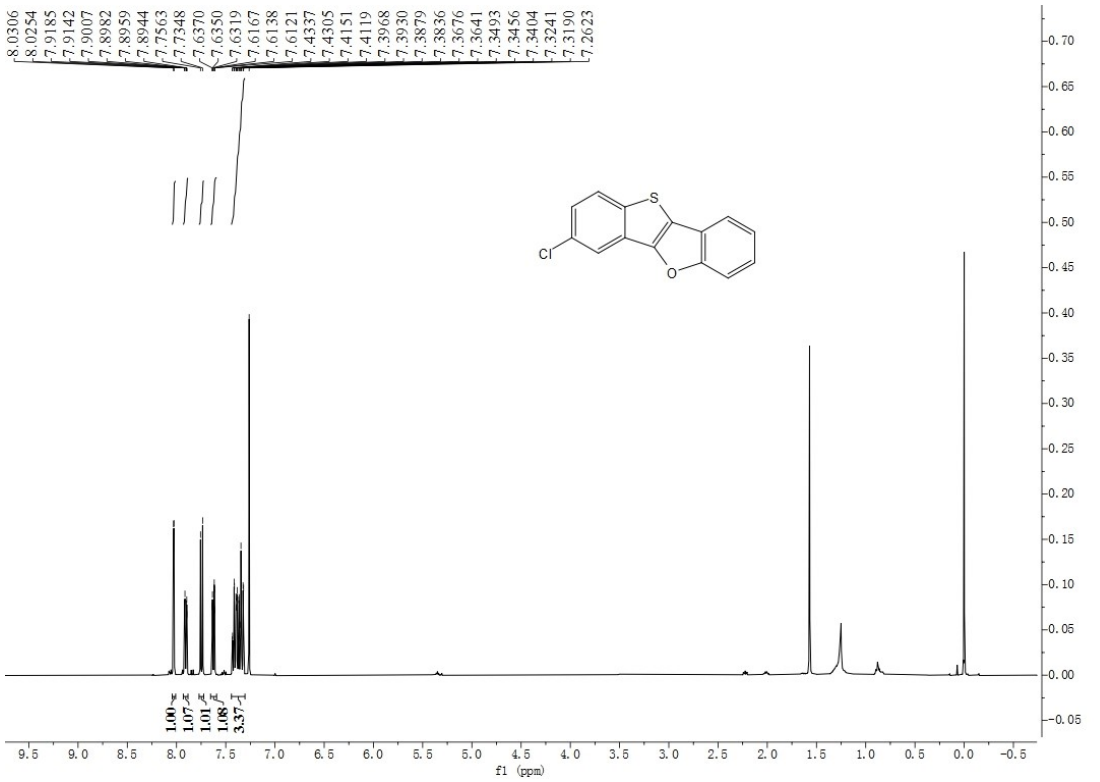
^{13}C NMR spectrum for **2k** (100 MHz,$CDCl_3$)



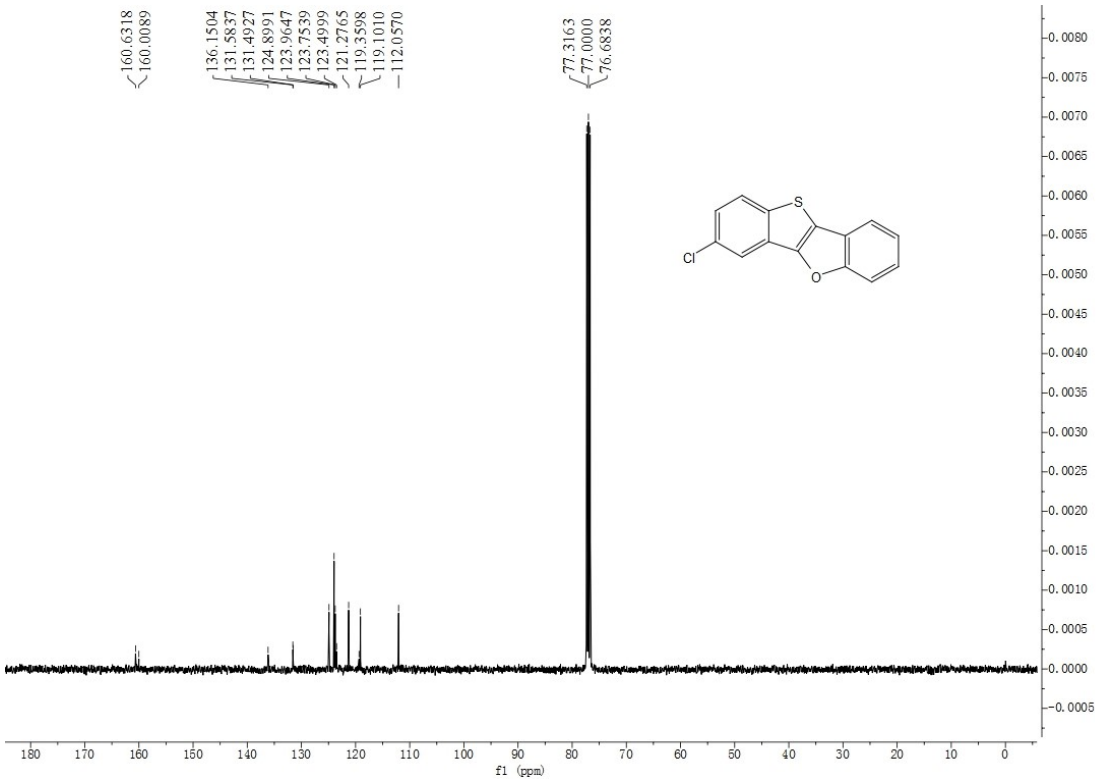
HRMS (ESI) spectrum for **2k**



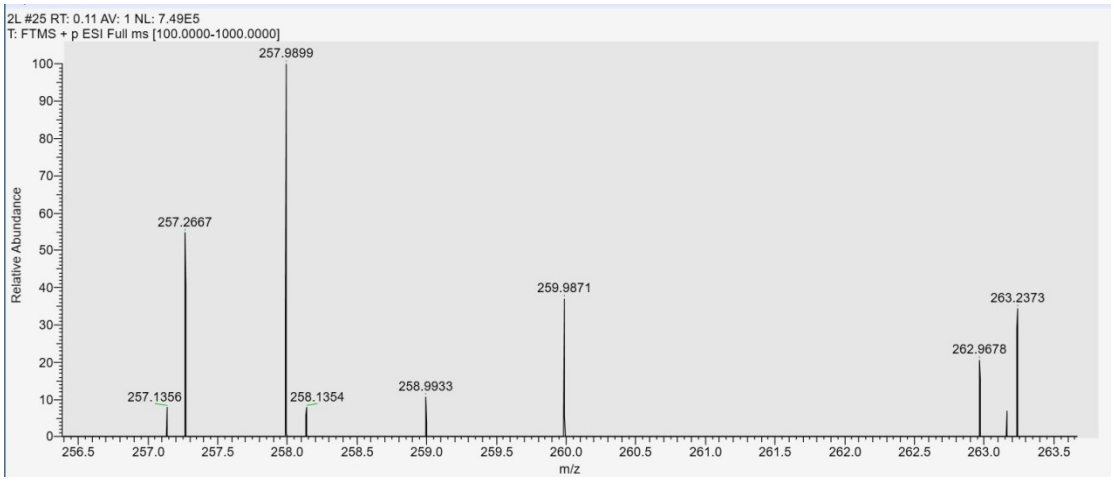
^{1}H NMR spectrum for **2l** (400 MHz,$CDCl_3$)



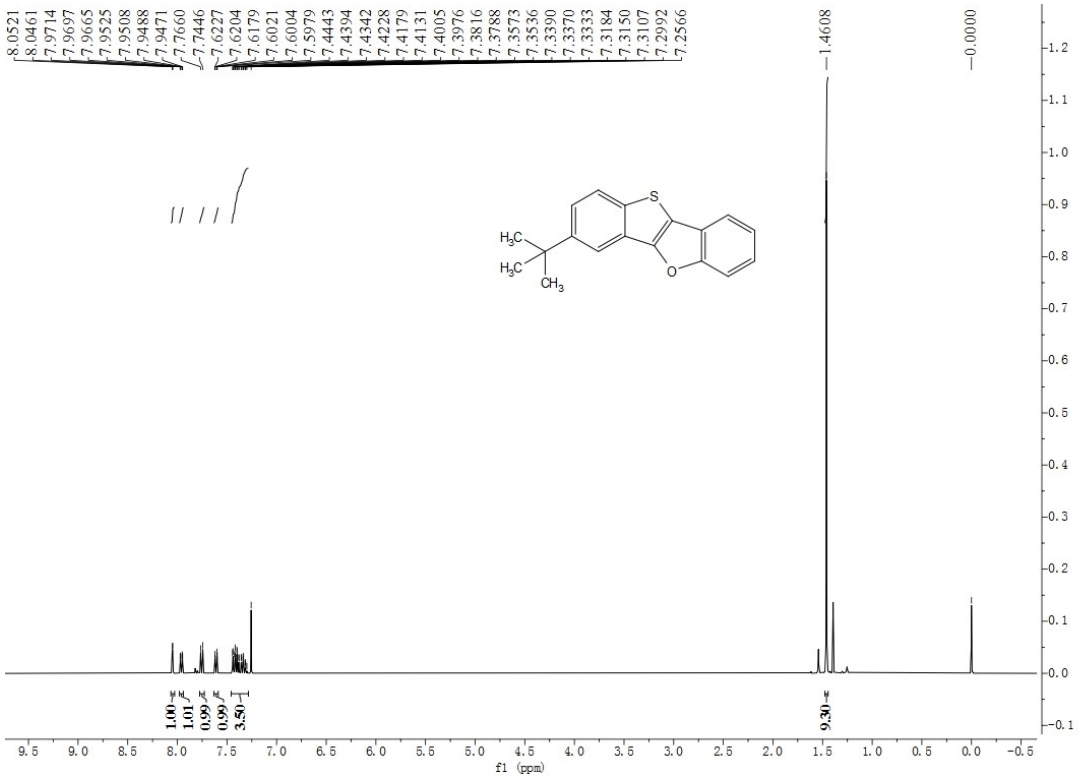
^{13}C NMR spectrum for **2l** (100 MHz,$CDCl_3$)



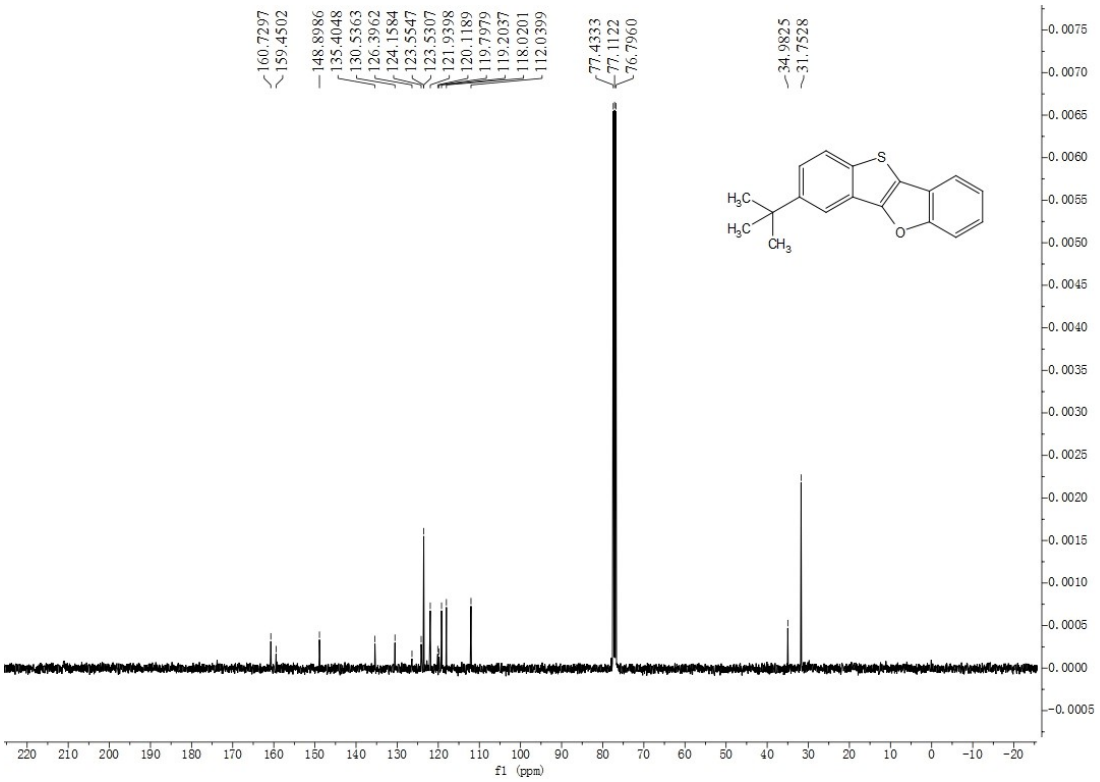
HRMS (ESI) spectrum for **2l**



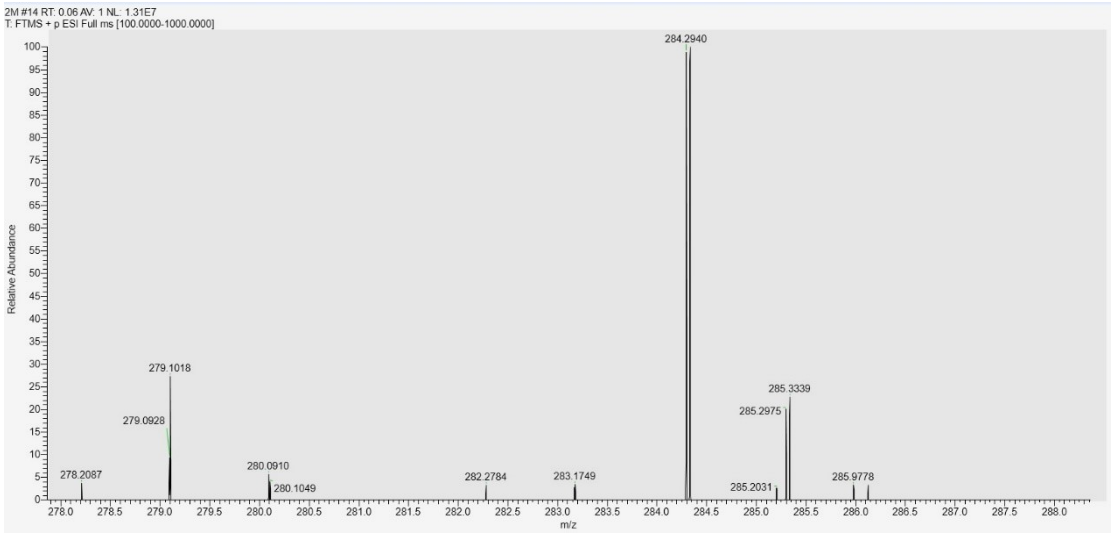
^{1}H NMR spectrum for **2m** (400 MHz,$CDCl_3$)



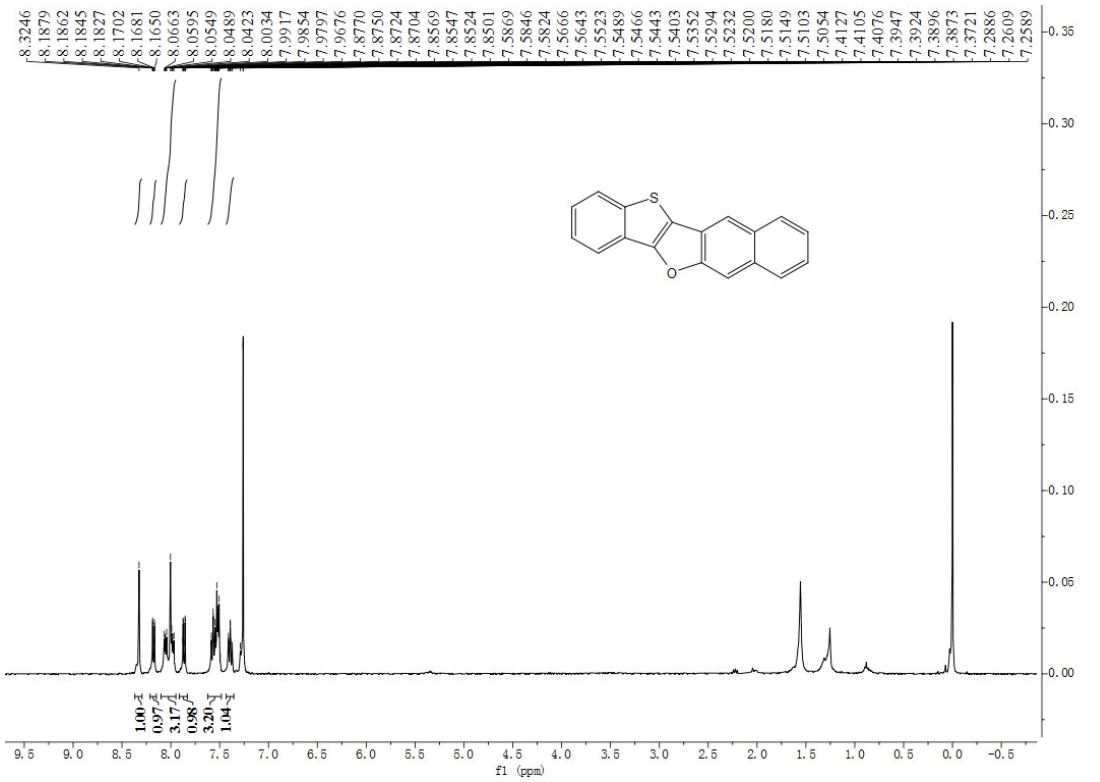
^{13}C NMR spectrum for **2m** (100 MHz,$CDCl_3$)



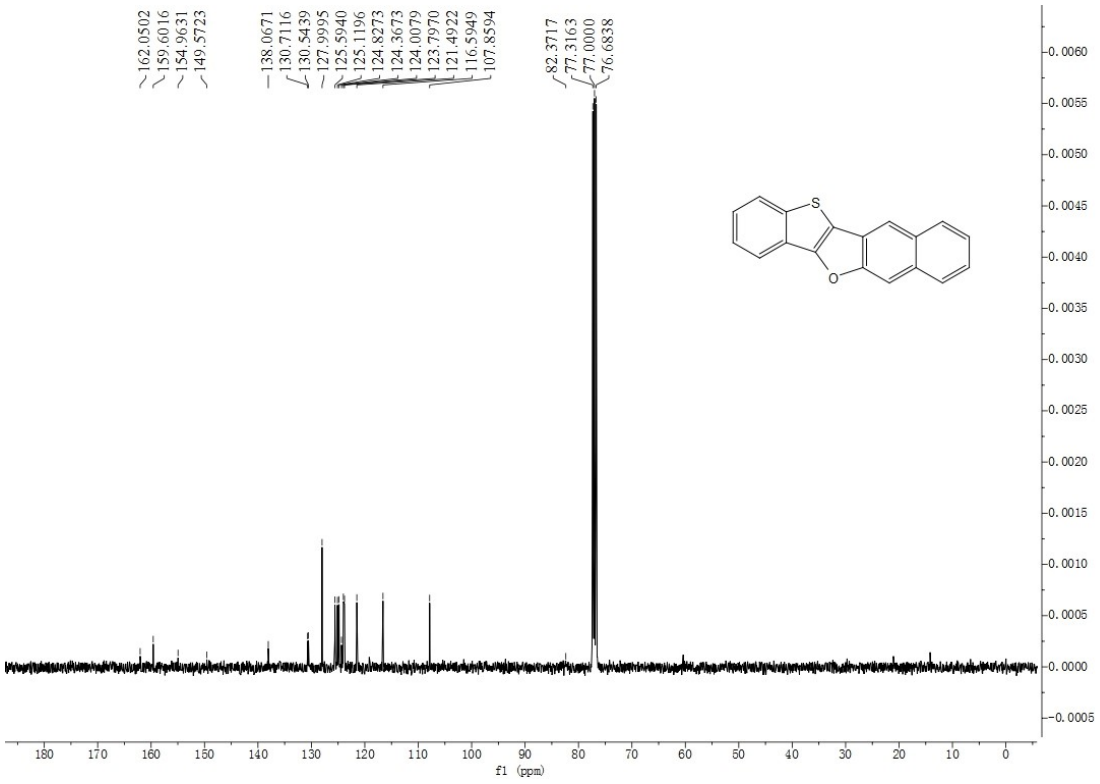
HRMS (ESI) spectrum for **2m**



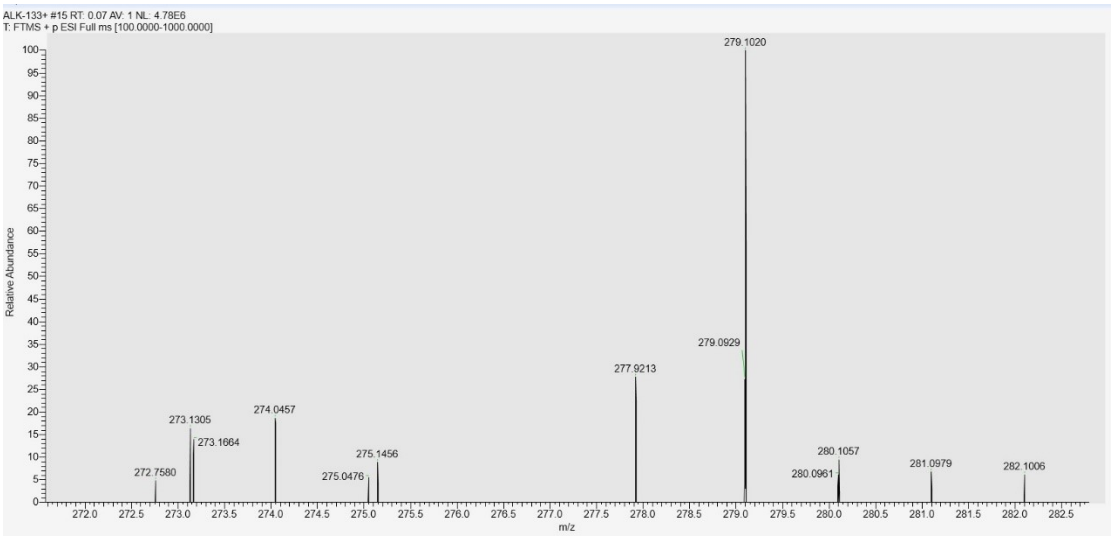
^{1}H NMR spectrum for **2n** (400 MHz,$CDCl_3$)



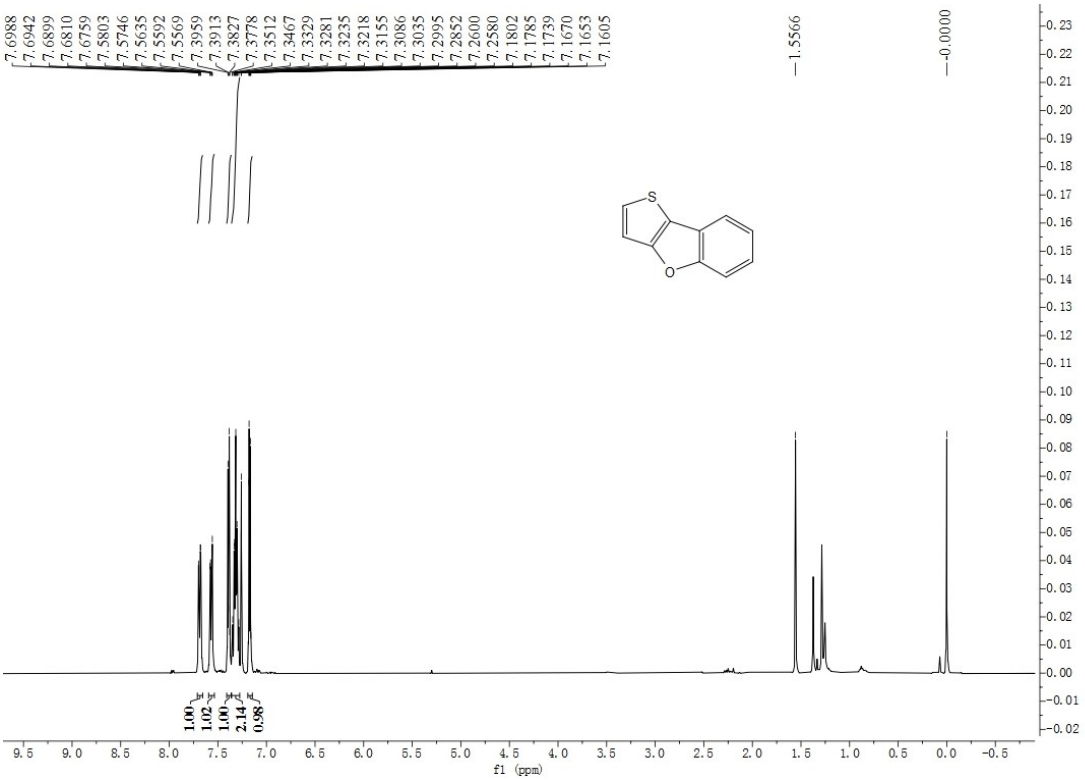
^{13}C NMR spectrum for **2n** (100 MHz,$CDCl_3$)



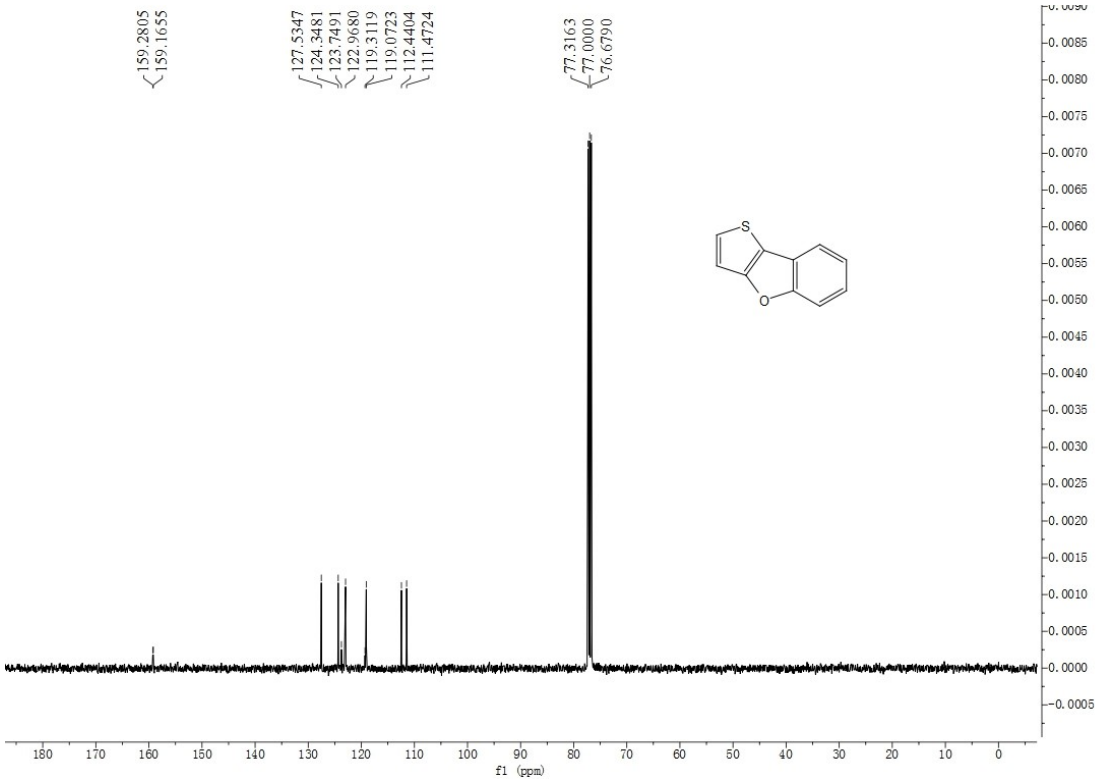
HRMS (ESI) spectrum for **2n**



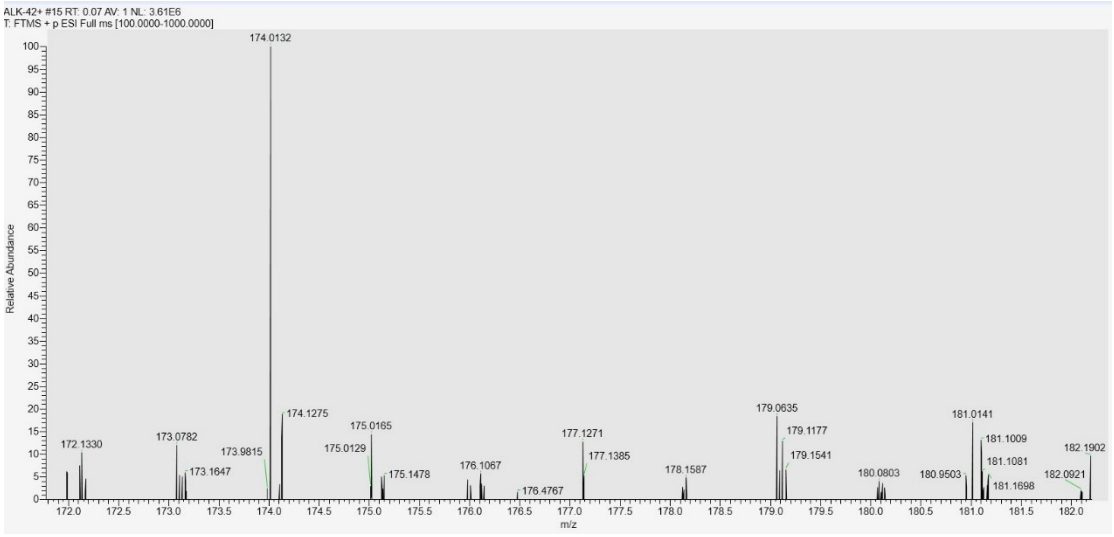
^{1}H NMR spectrum for **2o** (400 MHz,$CDCl_3$)



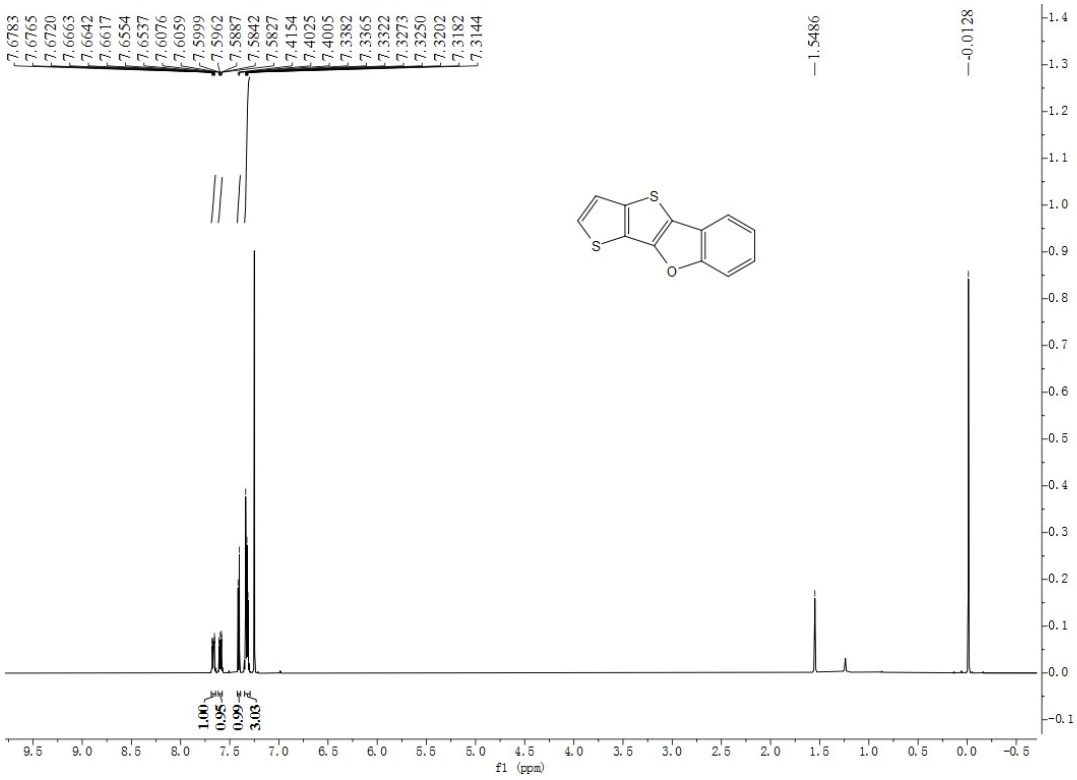
^{13}C NMR spectrum for **2o** (100 MHz,$CDCl_3$)



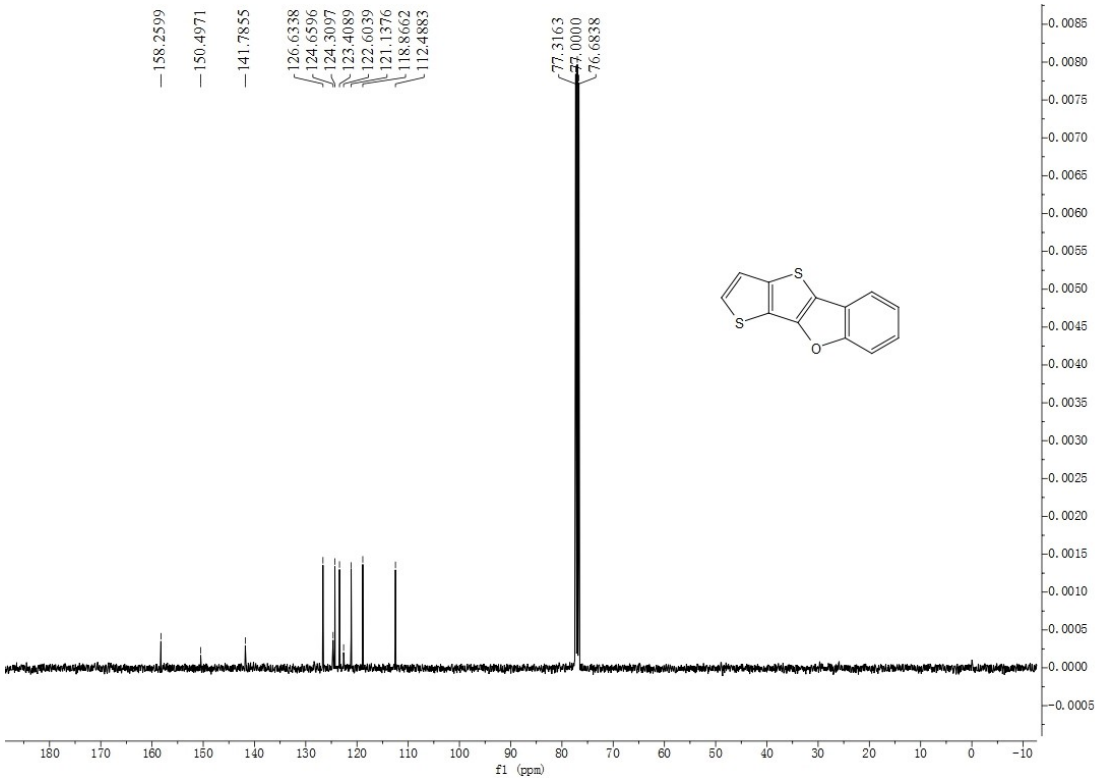
HRMS (ESI) spectrum for **2o**



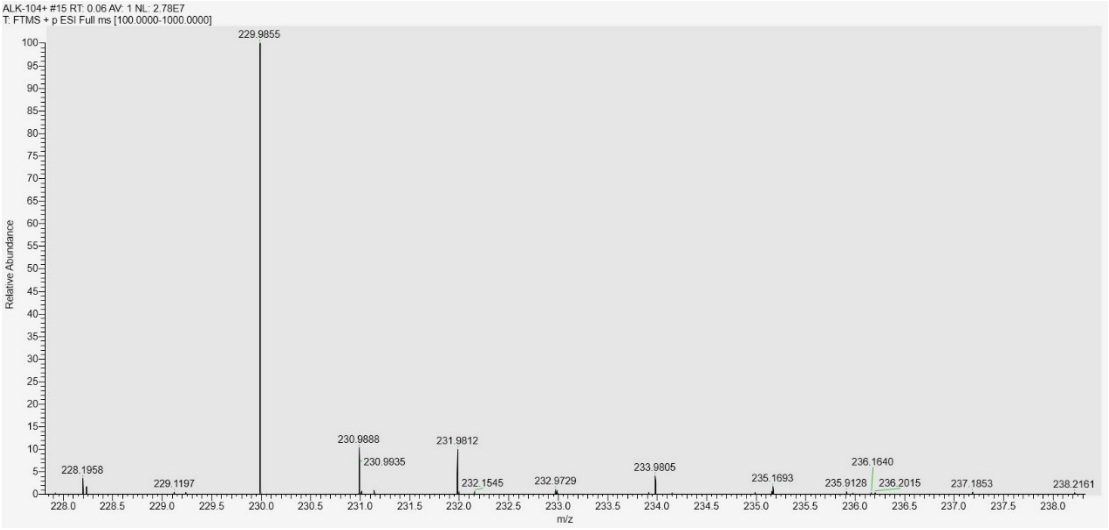
^{1}H NMR spectrum for **2p** (400 MHz,$CDCl_3$)



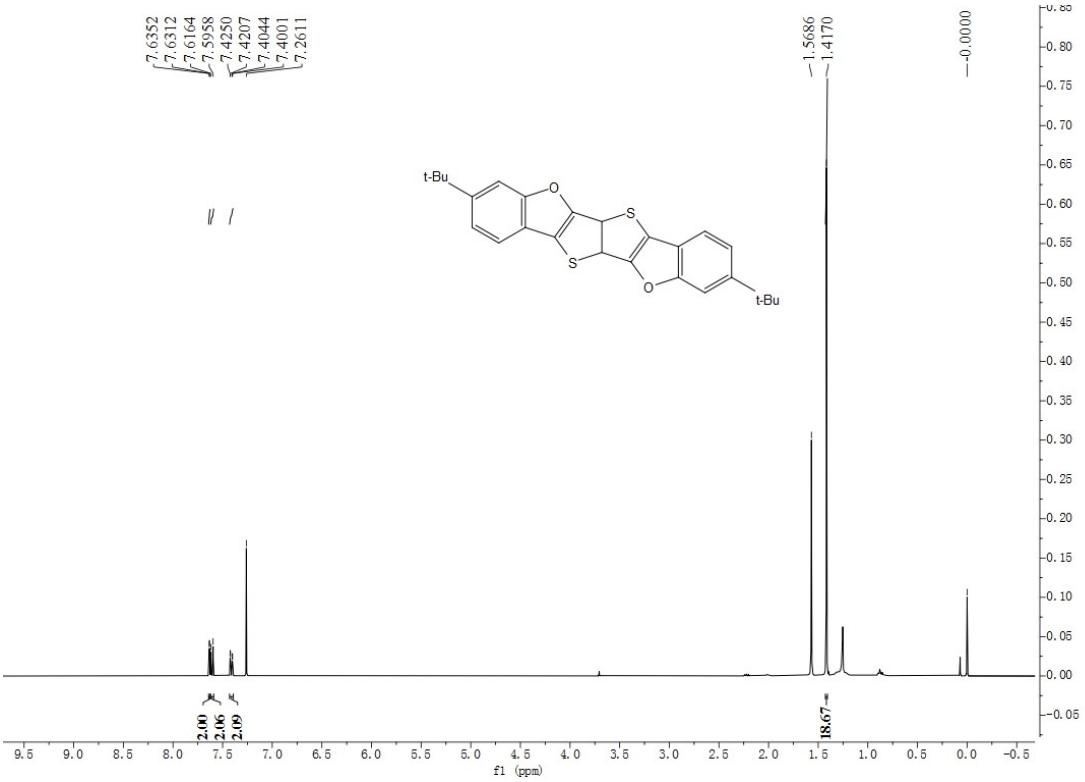
^{13}C NMR spectrum for **2p** (100 MHz,$CDCl_3$)



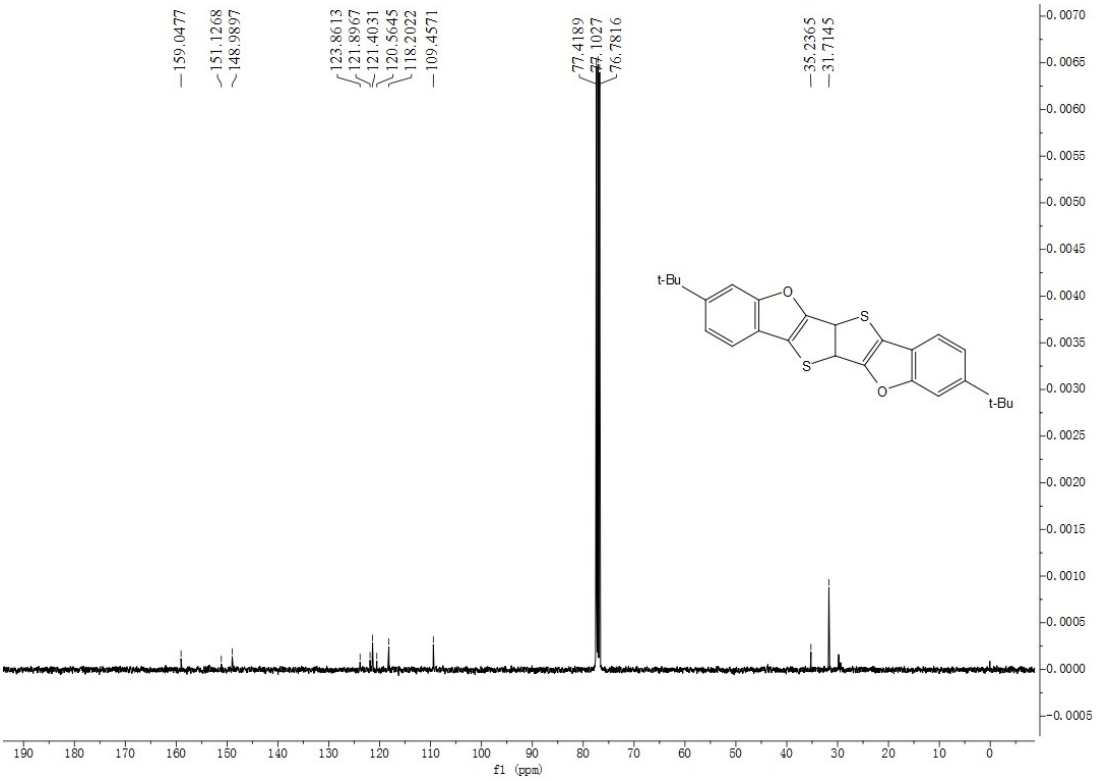
HRMS (ESI) spectrum for **2p**



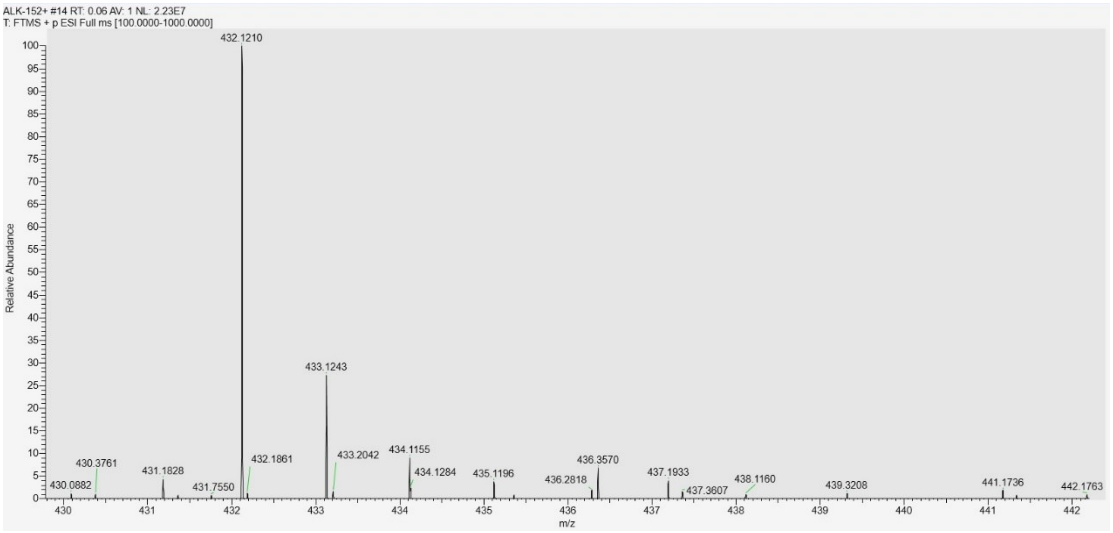
^{1}H NMR spectrum for **2q** (400 MHz,$CDCl_3$)



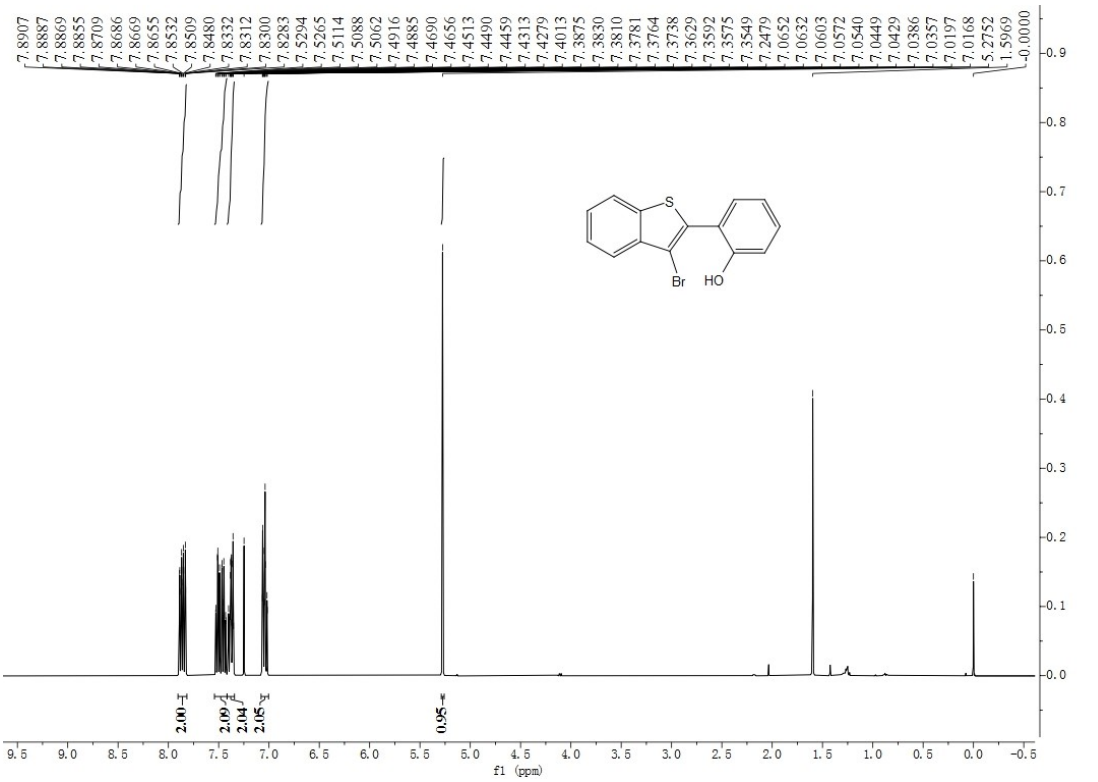
^{13}C NMR spectrum for **2q** (100 MHz,$CDCl_3$)



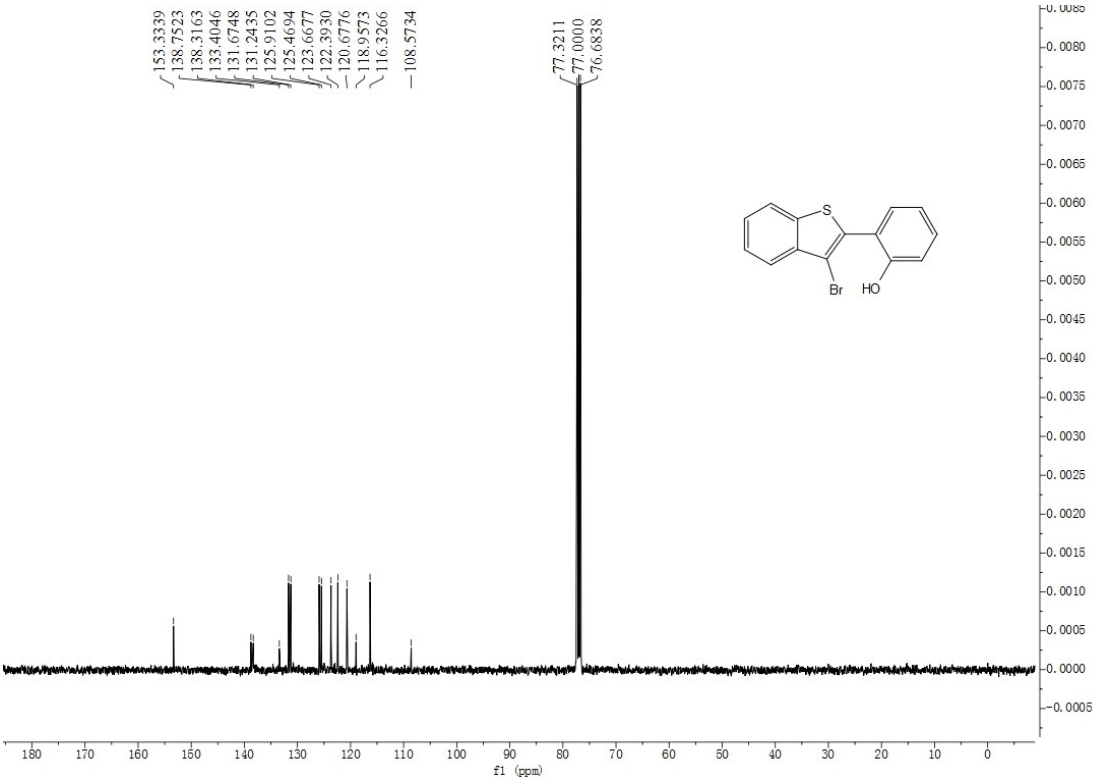
HRMS (ESI) spectrum for **2q**



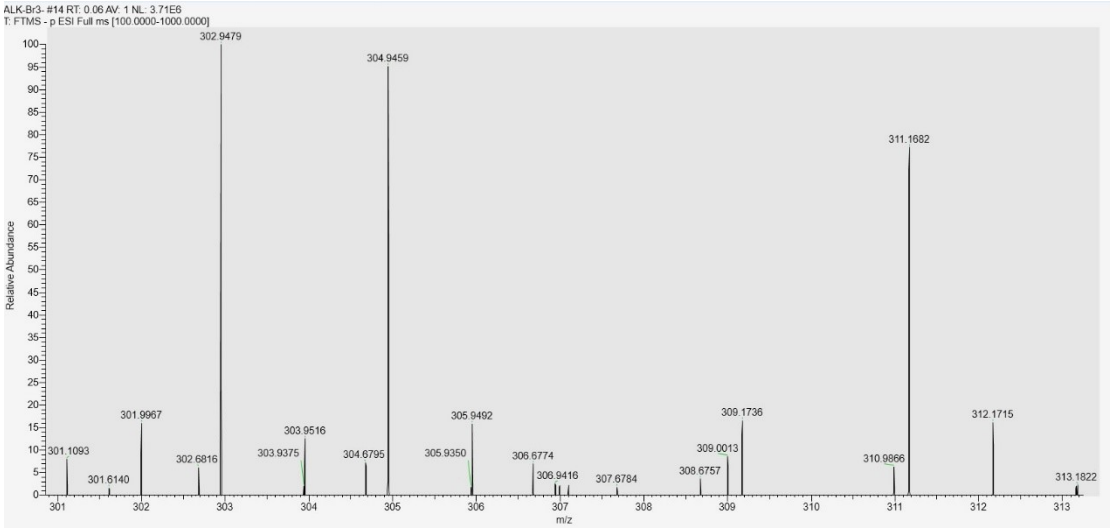
^{1}H NMR spectrum for **1a-Br** (400 MHz,$CDCl_3$)



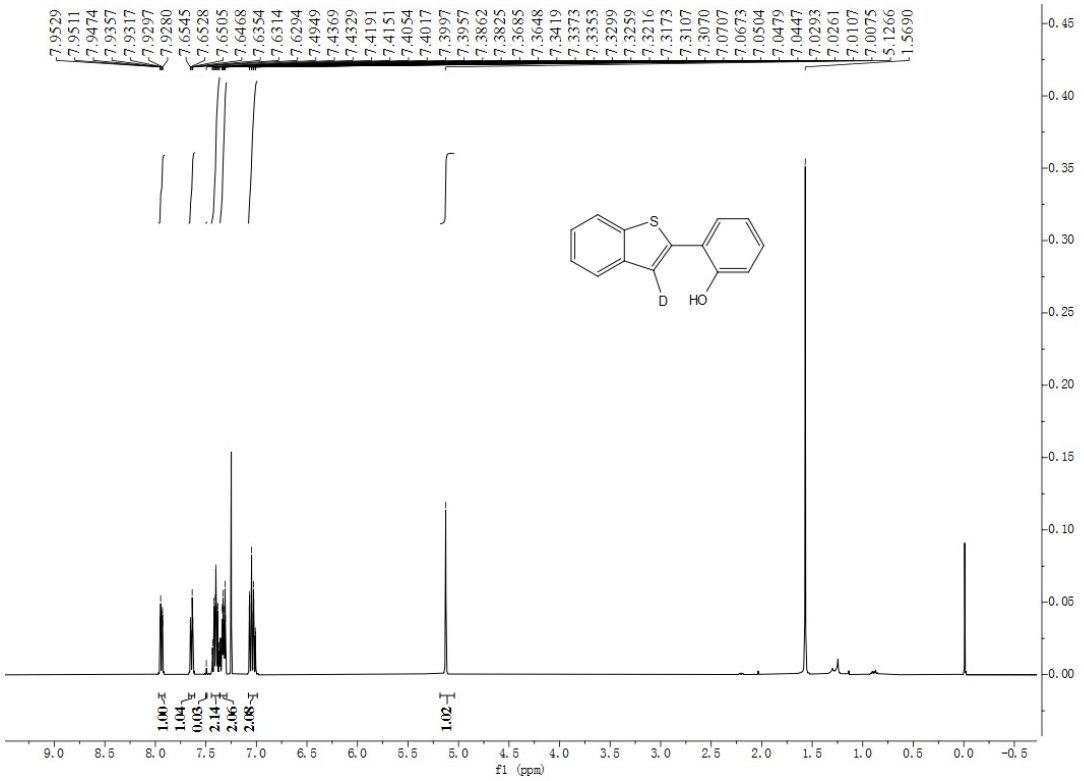
^{13}C NMR spectrum for **1a-Br** (100 MHz,$CDCl_3$)



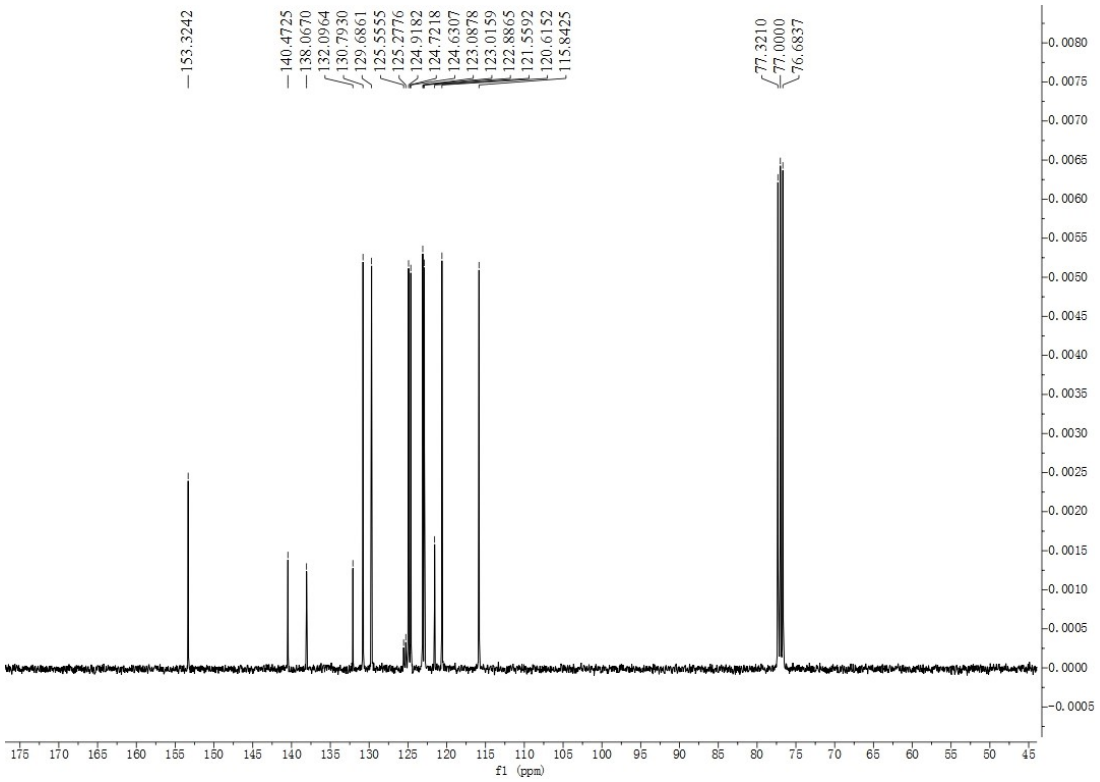
HRMS (ESI) spectrum for **1a-Br**



^{1}H NMR spectrum for **1a-*D*** (400 MHz,$CDCl_3$)



^{13}C NMR spectrum for **1a-*D*** (100 MHz,$CDCl_3$)



HRMS (ESI) spectrum for **1a-*D***