Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Chiral-at-metal Rh(III) Complex Catalyzed Enantioselective Synthesis of C2-Substituted Benzofuran Derivatives

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Table of Contents

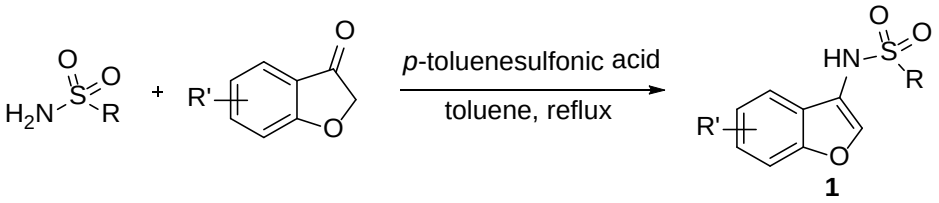
1. General Information

All reactions were performed in Schlenk tubes at room temperature using oven-dried glassware. Commercially obtained reagents were used without further purification, unless otherwise noted. Dry 1,2-dichloroethane (DCE) were obtained from solvent distillation machine (Vigor VSPS-5) and stored under argon over 4 Å type molecular sieves. THF and toluene were distilled freshly before use over sodium and benzophenone. Dichloromethane (DCM) was distilled from CaH_2. Methanol was used without further purification. Reactions were checked by TLC analysis and plates were visualized with short-wave UV light (254 nm). The ^{1}H, ^{13}C NMR and ^{19}F spectra were obtained in $CDCl_3$, DMSO-D_6 or Acetone-D_6 using a Bruker-BioSpin AVANCE III HD NMR spectrometer at 400, 100 and 376.4 MHz, respectively. Chemical shifts are reported in parts per million (δ value) calibrated against the residual solvent peak. Signal patterns are indicated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Coupling constants (*J*) are given in hertz (Hz). HPLC analyses of the compounds were done using chiralcel IA-IF columns and chiralcel AD-H, AS-H, OJ-H and OD-H columns using hexane and isopropanol as eluent. The infrared spectra were recorded on a Bruker VERTEX 70 IR spectrometer as KBr pellets, with absorption reported in cm^{-1}. High-resolution mass spectra were recorded on a Bruker Impact II UHR TOF LC/MS Mass Spectrometry. Crystal structure data were collected on a SuperNova, Dual, Cu at zero, Atlas diffractometer.

2. Experimental Section

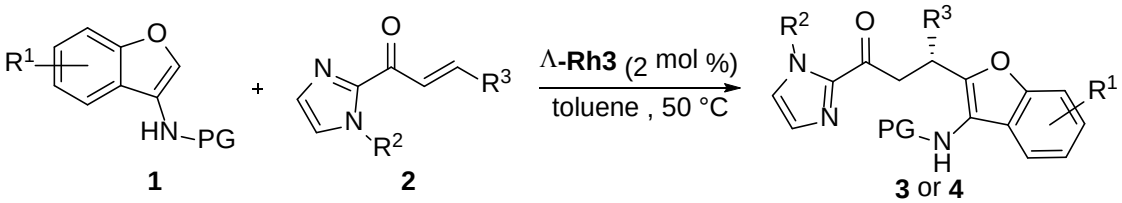
Chiral-at-metal complexes **Λ-Rh1, Λ-Rh2** and **Λ-Rh3** were prepared according to reported procedure.[1] *α,β*-Unsaturated 2-acyl imidazoles[2] and most of 3-aminobenzofurans[3] were synthesized according to reported procedures.

General procedure for the synthesis of 3-aminobenzofuran 1.



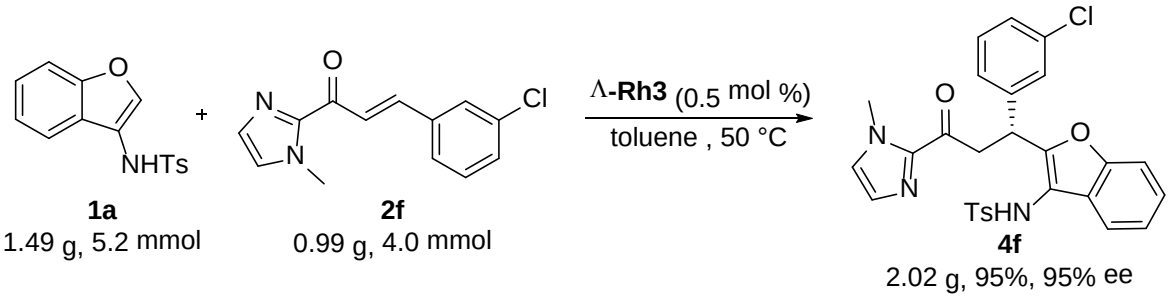
Sulfonamide (1.05 mmol), 2*H*-bezofuran-3-one (1 mmol) and *p*-toluenesulfonic acid (9.5 mg, 0.05 mmol) were dissolved in toluene (20 mL) in a round Schlenk flask. The flask was equipped with a Dean-Stark trap and reflux condenser. The mixture was heated to reflux until the 2*H*-bezofuran-3-one was completed consumed, monitored by TLC. After removing the solvent in vacuo, the residue was purified by column chromatography on silica gel (with ethyl acetate and petroleum ether as the eluent) to get corresponding products **1a**–**1k** in 40–65% yield.

General procedure for asymmetric alkylation at the C2-position of 3-aminobenzofurans with *α,β*-unsaturated 2-acyl imidazoles via chiral-at-metal Rh(III) complex-catalyzed.



To an over-dried 25 mL Schlenk tube equipped with a magnetic stir bar, **Λ-Rh3** (2 mol %) was added along with 3-aminobenzofuran **1** (1.3 equiv., 0.26 mmol), *α,β*-unsaturated 2-acyl imidazole **2** (1 equiv., 0.2 mmol) and toluene (1 mL). The reaction was stirred at 50 °C for about 24 hours until the *α,β*-unsaturated 2-acyl imidazole was completely consumed (monitored by TLC). The reaction mixture was concentrated and directly purified by column chromatography on silica gel (with ethyl acetate and petroleum ether as the eluent) to afford the desired products **3** or **4**.

Gram-scale experiment with low catalyst loading.



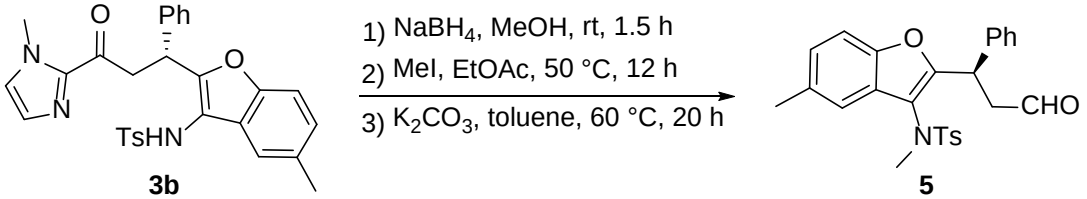
1a
1.49 g, 5.2 mmol

2f
0.99 g, 4.0 mmol

4f
2.02 g, 95%, 95% ee

To an over-dried 50 mL Schlenk tube equipped with a magnetic stir bar, **Λ-Rh3** (12.5 mg, 0.5 mol %) was added along with 3-aminobenzofuran **1a** (1.49 g, 5.2 mmol, 1.3 equiv.), *α,β*-unsaturated 2-acyl imidazole **2f** (0.99 g, 4.0 mmol, 1 equiv.) and toluene (10 mL). The reaction was stirred at 50 °C for about 24 hours until **2f** was completely consumed. The reaction mixture was concentrated and directly purified by column chromatography on silica gel (EtOAc/Petroleum ether = 1:1) to afford the corresponding product **4f** (light yellow solid, 2.02 g, 95% yield, 95% ee).

Procedures for synthetic transformations.

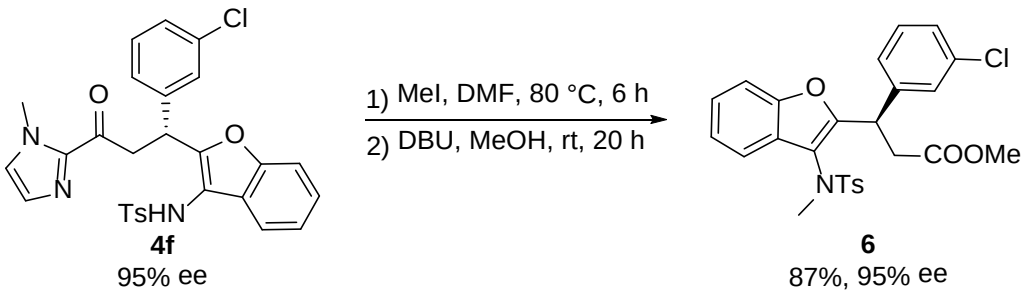


3b
98% ee

5
57%, 98% ee

To a solution of **3b** (250 mg, 0.5 mmol) in MeOH (5.0 mL) was added $NaBH_4$ (48 mg, 1.25 mmol). The mixture was stirred at room temperature for 1.5 hours (monitored by TLC) under argon atmosphere. Afterwards, the mixture was quenched with H_2O (2 mL). The result solution was diluted with EtOAc (25 mL) and H_2O (25 mL). The aqueous layer was separated and extracted with EtOAc (2 × 25 mL). The combined organic layers were washed with brine (10 mL), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to afford a white solid. The solid was dissolved in EtOAc (2.0 mL) before MeI (355 mg, 2.5 mmol, 5.0 equiv.) was added. After stirring at 50 °C for 12 hours, MeI and EtOAc were removed under reduced pressure, followed by addition of toluene (2.0 mL) and an aqueous solution of 10% K_2CO_3 (2.5 mmol, 5.0 equiv.). After stirring at 60 °C for 20 hours, the reaction mixture was cooled down to room temperature and diluted with EtOAc (30 mL). The organic layer was separated, washed with brine (5 mL), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (20%

EtOAc in petroleum ether) to provide the compound **5** as colorless oil (126 mg, 57% yield).

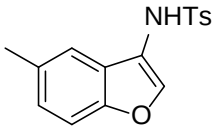


4f
95% ee

6
87%, 95% ee

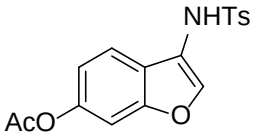
To a solution of **4f** (266 mg, 0.5 mmol) in DMF (5.0 mL) was added MeI (355 mg, 2.5 mmol, 5.0 equiv.). The mixture was stirred at 80 °C for 6 hours (monitored by TLC) under argon atmosphere, followed by addition of MeOH (2.0 mL) and DBU (76 mg, 2.5 mmol, 5.0 equiv.). After stirring at room temperature for 20 hours, the reaction mixture was diluted with EtOAc (25 mL) and H_2O (25 mL). The aqueous layer was separated and extracted with EtOAc (2 × 25 mL). The combined organic layers were washed with brine (10 mL), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (20% EtOAc in petroleum ether) to provide the compound **6** as light yellow oil (216 mg, 87% yield).

3. Characterization of Compounds



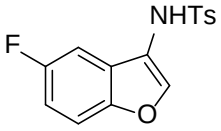
1b

Brown solid, m.p. 120-122 °C, 182 mg, 57% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.72 (d, *J* = 8.1 Hz, 2H), 7.53 (s, 1H), 7.27 (d, *J* = 8.8 Hz, 1H), 7.21 (d, *J* = 8.1 Hz, 2H), 7.07 (d, *J* = 6.4 Hz, 2H), 6.84 (s, 1H), 2.37 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 152.5, 144.1, 139.0, 135.8, 132.6, 129.6, 127.4, 126.4, 123.8, 118.2, 118.1, 111.3, 21.5, 21.2. IR (KBr): ν (cm^{-1}) 3138, 2921, 2858, 1743, 1700, 1596, 1462, 1337, 1159, 1090, 891, 815, 798, 770, 670. HRMS (ESI, *m/z*) calcd for $C_{16}H_{15}NNaO_3S$ $[M+Na]^+$: 324.0665, found: 324.0666.



1c

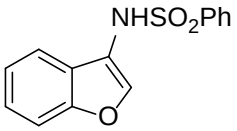
Yellow solid, m.p. 167-169 °C, 190 mg, 55% yield. ^{1}H NMR (400 MHz, DMSO-d6) δ = 10.40 (s, 1H), 7.82 (s, 1H), 7.69 (d, *J* = 8.2 Hz, 2H), 7.60 (d, *J* = 8.5 Hz, 1H), 7.36 (d, *J* = 1.6 Hz, 1H), 7.32 (d, *J* = 8.2 Hz, 2H), 6.99 (dd, *J* = 8.5, 1.6 Hz, 1H), 2.31 (s, 3H), 2.26 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ = 169.8, 153.5, 148.7, 143.9, 137.5, 136.7, 130.1, 127.3, 121.3, 120.0, 119.9, 117.9, 106.2, 21.4, 21.3. IR (KBr): ν (cm^{-1}) 2854, 2742, 2256, 2128, 1760, 1653, 1473, 1331, 1209, 1163, 1129, 1025, 1002, 825, 764, 663. HRMS (ESI, *m/z*) calcd for $C_{17}H_{15}NNaO_5S$ $[M+Na]^+$: 368.0563, found: 368.0561.



1g

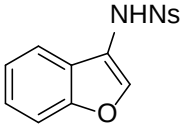
Light yellow solid, m.p. 125-127 °C, 199 mg, 65% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.73 (d, *J* = 8.2 Hz, 2H), 7.63 (s, 1H), 7.61 (s, 1H), 7.31 (dd, *J* = 9.0, 3.9 Hz, 1H), 7.21 (d, *J* = 8.2 Hz, 2H), 7.07 (dd, *J* = 8.3, 2.5 Hz, 1H), 6.96 (td, *J* = 9.0, 2.5 Hz, 1H), 2.36 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 159.1 (d, *J* = 238.0 Hz), 150.1, 144.2, 140.5, 135.6, 129.7, 127.3, 124.6 (d, *J* = 11.1 Hz), 118.8 (d, *J* = 4.0 Hz), 112.9 (d, *J* = 27.0 Hz), 112.5 (d, *J* = 9.5 Hz), 104.6 (d, *J* = 26.0 Hz), 21.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -119.83. IR (KBr): ν (cm^{-1}) 3108, 3034, 2917, 1736, 1597, 1478, 1452,1399, 1334, 1158, 871, 870, 681. HRMS (ESI, *m/z*) calcd for

$C_{15}H_{12}FNNaO_3S$ [M+Na]$^+$: 328.0414, found: 328.0414.



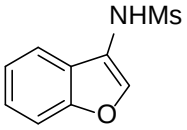
1h

Yellow solid, m.p. 101-103 °C, 139 mg, 51% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.87 (d, *J* = 7.7 Hz, 2H), 7.62 (s, 1H), 7.51 (t, *J* = 7.4 Hz, 1H), 7.40-7.34 (m, 5H), 7.25 (t, *J* = 7.7 Hz, 1H), 7.13 (t, *J* = 7.5 Hz, 1H).^{13}C NMR (100 MHz, $CDCl_3$) δ = 153.9, 138.5, 133.2, 129.1, 127.3, 125.1, 123.5, 123.0, 118.5, 118.3, 111.7. IR (KBr): ν (cm^{-1}) 2812, 2733, 1718, 1579, 1451, 1421, 1357, 1324, 1196, 1157, 1091, 905, 851, 750, 720, 685, 638. HRMS (ESI, *m/z*) calcd for $C_{14}H_{11}NNaO_3S$ [M+Na]$^+$: 296.0352, found: 296.0353.



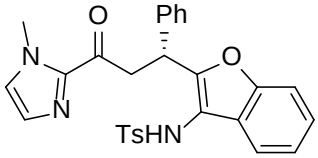
1i

Yellow solid, m.p. 133-135 °C, 127 mg, 40% yield. ^{1}H NMR (400 MHz, Acetone-d6) δ = 9.39 (s, 1H), 8.36 (d, *J* = 8.7 Hz, 2H), 8.11 (d, *J* = 8.7 Hz, 2H), 7.82 (s, 1H), 7.55 (d, *J* = 7.8 Hz, 1H), 7.47 (d, *J* = 8.3 Hz, 1H), 7.32 (t, *J* = 7.7 Hz, 1H), 7.20 (t, *J* = 7.5 Hz, 1H). ^{13}C NMR (100 MHz, Acetone-d6) δ = 154.9, 151.3, 146.1, 139.5, 129.6, 126.1, 125.2, 124.5, 123.9, 120.0, 119.8, 112.5. IR (KBr): ν (cm^{-1}) 2920, 2850, 1716, 1524, 1450, 1351, 1309, 1162, 1114, 853, 741, 682, 620. HRMS (ESI, *m/z*) calcd for $C_{14}H_{10}N_2NaO_5S$ [M+Na]$^+$: 341.0203, found: 341.0201.



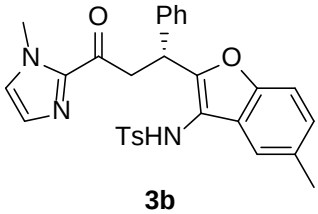
1j

Yellow solid, m.p. 93-95 °C, 99 mg, 47% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.79 (s, 1H), 7.62 (d, *J* = 7.7 Hz, 1H), 7.49 (d, *J* = 8.2 Hz, 1H), 7.36 (t, *J* = 6.8 Hz, 1H), 7.29 (t, *J* = 8.0 Hz, 1H), 6.97 (s, 1H), 3.04 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 154.1, 138.2, 125.4, 123.4, 123.3, 118.4, 118.3, 112.1, 39.1. IR (KBr): ν (cm^{-1}) 3111, 3020, 3009, 2931, 2812, 1733, 1607, 1452, 1410, 1353, 1310, 1148, 980, 854, 743, 634. HRMS (ESI, *m/z*) calcd for $C_9H_9NNaO_3S$ [M+Na]$^+$: 234.0201, found: 234.0202.



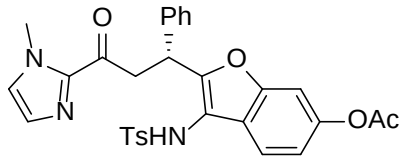
3a

Light yellow solid, m.p. 76-78 °C, 92 mg, 92% yield, 96% ee (HPLC: chiralpak IC column, 254 nm, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, 40 °C, tr (major) = 12.39 min, tr (minor) = 15.57 min). $[\alpha]_D^{25}$ = +8.18 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.94 (s, 1H), 7.73-7.63 (m, 3H), 7.31-7.27 (m, 1H), 7.24-7.12 (m, 8H), 7.02 (s, 1H), 6.89-6.81 (m, 2H), 4.40 (dd, *J* = 9.3, 4.9 Hz, 1H), 4.03 (dd, *J* = 18.0, 9.3 Hz, 1H), 3.92 (s, 3H), 3.58 (dd, *J* = 18.0, 4.9 Hz, 1H), 2.35 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 190.1, 153.4, 153.0, 143.6, 141.9, 138.6, 136.3, 129.7, 129.2, 128.2, 128.1, 127.5, 127.4, 126.9, 125.9, 124.3, 123.0, 120.6, 113.7, 111.2, 43.9, 36.5, 36.3, 21.5. IR (KBr): ν (cm^{-1}) 3030, 2971, 1676, 1618, 1452, 1408, 1326, 1163, 1091, 751, 704, 666. HRMS (ESI, *m/z*) calcd for $C_{28}H_{25}N_3NaO_4S$ $[M+Na]^+$: 522.1458, found: 522.1460.



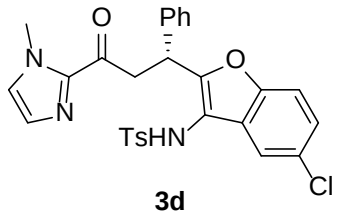
3b

Light yellow solid, m.p. 79-81 °C, 98 mg, 96% yield, 98% ee (HPLC: chiralpak IC column, 254 nm, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, 40 °C, tr (major) = 11.60 min, tr (minor) = 13.96 min). $[\alpha]_D^{25}$ = +8.33 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.84 (s, 1H), 7.68 (d, *J* = 8.2 Hz, 2H), 7.43 (s, 1H), 7.19-7.13 (m, 7H), 7.00 (d, *J* = 7.6 Hz, 2H), 6.86 (dd, *J* = 6.4, 2.7 Hz, 2H), 4.37 (dd, *J* = 9.4, 4.9 Hz, 1H), 4.01 (dd, *J* = 18.0, 9.4 Hz, 1H), 3.92 (s, 3H), 3.56 (dd, *J* = 18.0, 4.9 Hz, 1H), 2.38 (s, 3H), 2.35 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 190.2, 153.3, 151.9, 143.6, 142.0, 138.7, 136.3, 132.5, 129.7, 129.4, 128.1, 128.05, 127.5, 127.4, 126.9, 125.9, 125.5, 120.2, 113.3, 110.7, 43.9, 36.5, 36.3, 21.5, 21.3. IR (KBr): ν (cm^{-1}) 3026, 2821, 2751, 1681, 1598, 1414, 1328, 1260, 1159, 1090, 985, 787, 695, 663. HRMS (ESI, *m/z*) calcd for $C_{29}H_{27}N_3NaO_4S$ $[M+Na]^+$: 536.1614, found: 536.1611.



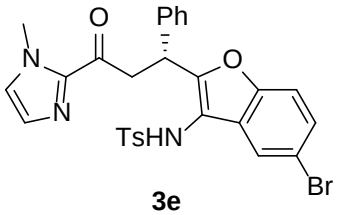
3c

Light yellow oil, 108 mg, 97% yield, 98% ee (HPLC: chiralpak IC column, 254 nm, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, 40 °C, tr (major) = 21.76 min, tr (minor) = 27.25 min). $[\alpha]_D^{25}$ = +9.19 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.01 (s, 1H), 7.74 (d, *J* = 8.5 Hz, 1H), 7.68 (d, *J* = 8.2 Hz, 2H), 7.19-7.12 (m, 6H), 7.06 (d, *J* = 1.8 Hz, 1H), 7.03 (s, 1H), 6.93 (dd, *J* = 8.5, 1.9 Hz, 1H), 6.81-6.76 (m, 2H), 4.33 (dd, *J* = 9.7, 4.6 Hz, 1H), 4.03 (dd, *J* = 18.0, 9.7 Hz, 1H), 3.93 (s, 3H), 3.53 (dd, *J* = 18.0, 4.6 Hz, 1H), 2.36 (s, 3H), 2.29 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 190.1, 169.7, 153.6, 153.2, 147.8, 143.7, 141.9, 138.3, 136.1, 129.8, 129.4, 128.1, 128.0, 127.4, 127.0, 123.8, 121.0, 117.2, 113.7, 105.2, 43.7, 36.5, 36.3, 21.5, 21.1. IR (KBr): ν (cm^{-1}) 3029, 2924, 1763, 1678, 1597, 1410, 1207, 963, 913, 814, 704, 670. HRMS (ESI, *m/z*) calcd for $C_{30}H_{27}N_3NaO_6S$ $[M+Na]^+$: 580.1513, found: 580.1513.



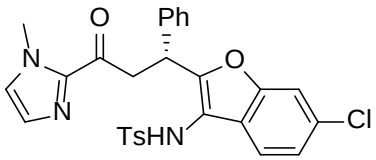
3d

Light yellow solid, m.p. 96-98 °C, 103 mg, 97% yield, 87% ee (HPLC: chiralpak IC column, 254 nm, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, 40 °C, tr (major) = 9.25 min, tr (minor) = 11.67 min). $[\alpha]_D^{25}$ = +8.83 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.94 (s, 1H), 7.67 (d, *J* = 8.2 Hz, 2H), 7.51 (d, *J* = 1.9 Hz, 1H), 7.22-7.10 (m, 8H), 7.04 (s, 1H), 6.91-6.86 (m, 2H), 4.43 (dd, *J* = 9.2, 5.0 Hz, 1H), 4.02 (dd, *J* = 18.0, 9.2 Hz, 1H), 3.93 (s, 3H), 3.61 (dd, *J* = 18.0, 5.0 Hz, 1H), 2.37 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 189.8, 154.8, 151.8, 143.9, 141.8, 138.2, 136.2, 129.8, 129.1, 128.7, 128.3, 128.1, 127.5, 127.45, 127.2, 127.1, 124.6, 120.1, 113.3, 112.3, 43.8, 36.7, 36.4, 21.5. IR (KBr): ν (cm^{-1}) 3030, 2923, 1678, 1598, 1448, 1409, 1333, 1163, 1091, 985, 812, 705, 665. HRMS (ESI, *m/z*) calcd for $C_{28}H_{24}ClN_3NaO_4S$ $[M+Na]^+$: 556.1068, found: 556.1068.



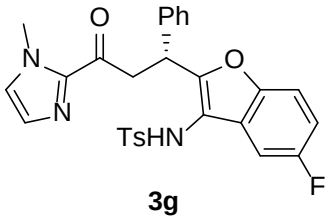
3e

Light yellow solid, m.p. 99-101 °C, 101 mg, 88% yield, 88% ee (HPLC: chiralpak IC column, 254 nm, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, 40 °C, tr (major) = 9.54 min, tr (minor) = 12.20 min). $[\alpha]_D^{25}$ = +11.63 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.92 (s, 1H), 7.67 (d, *J* = 8.2 Hz, 2H), 7.62 (d, *J* = 1.8 Hz, 1H), 7.27 (dd, *J* = 8.6, 2.0 Hz, 1H), 7.21-7.13 (m, 7H), 7.03 (s, 1H), 6.92-6.87 (m, 2H), 4.45 (dd, *J* = 9.2, 5.1 Hz, 1H), 4.01 (dd, *J* = 18.0, 9.2 Hz, 1H), 3.93 (s, 3H), 3.61 (dd, *J* = 18.0, 5.1 Hz, 1H), 2.38 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 189.9, 154.8, 152.1, 143.9, 141.9, 138.3, 136.1, 129.8, 129.3, 128.2, 128.1, 127.8, 127.5, 127.45, 127.2, 127.1, 123.1, 116.2, 113.1, 112.7, 43.7, 36.6, 36.3, 21.5. IR (KBr): ν (cm^{-1}) 2955, 2923, 2853, 1664, 1610, 1447, 1404, 1336, 1163, 1093, 991, 913, 772, 703, 678. HRMS (ESI, *m/z*) calcd for $C_{28}H_{24}BrN_3NaO_4S$ $[M+Na]^+$: 600.0563, found: 600.0562.



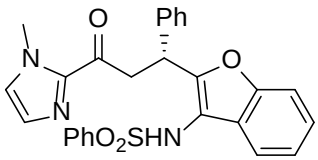
3f

Light yellow solid, m.p. 64-66 °C, 94 mg, 88% yield, 95% ee (HPLC: chiralpak IC column, 254 nm, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, 40 °C, tr (major) = 9.50 min, tr (minor) = 11.06 min). $[\alpha]_D^{25}$ = +9.00 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.02 (s, 1H), 7.66 (d, *J* = 8.4 Hz, 2H), 7.63 (d, *J* = 9.2 Hz, 1H), 7.30 (d, *J* = 1.4 Hz, 1H), 7.22-7.12 (m, 7H), 7.04 (s, 1H), 6.85-6.75 (m, 2H), 4.36 (dd, *J* = 9.3, 4.8 Hz, 1H), 4.02 (dd, *J* = 18.0, 9.3 Hz, 1H), 3.94 (s, 3H), 3.57 (dd, *J* = 18.0, 4.8 Hz, 1H), 2.37 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 189.9, 153.6, 153.4, 143.8, 141.7, 138.2, 136.2, 130.2, 129.8, 129.2, 128.2, 128.0, 127.5, 127.1, 124.6, 123.8, 121.4, 113.7, 111.8, 43.9, 36.7, 36.4, 21.5. IR (KBr): ν (cm^{-1}) 3028, 2744, 1684, 1600, 1473, 1454, 1411, 1327, 1156, 1094, 902, 817, 706, 678. HRMS (ESI, *m/z*) calcd for $C_{28}H_{24}ClN_3NaO_4S$ $[M+Na]^+$: 556.1068, found: 556.1063.



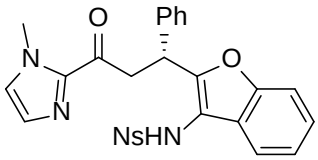
3g

Light yellow solid, m.p. 78-80 °C, 102 mg, 99% yield, 92% ee (HPLC: chiralpak IC column, 254 nm, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, 40 °C, tr (major) = 9.72 min, tr (minor) = 11.66 min). $[\alpha]_D^{25}$ = +10.94 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.01 (s, 1H), 7.67 (d, *J* = 8.2 Hz, 2H), 7.34 (dd, *J* = 8.6, 2.5 Hz, 1H), 7.23-7.13 (m, 7H), 7.04 (s, 1H), 6.91 (td, *J* = 9.0, 2.6 Hz, 1H), 6.87-6.80 (m, 2H), 4.38 (dd, *J* = 9.2, 4.9 Hz, 1H), 4.00 (dd, *J* = 18.0, 9.2 Hz, 1H), 3.94 (s, 3H), 3.58 (dd, *J* = 18.0, 4.9 Hz, 1H), 2.36 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 190.0, 159.2 (d, *J* = 238.0 Hz), 155.0, 149.6, 143.8, 141.9, 138.3, 136.2, 129.8, 129.4, 128.2, 128.0, 127.5, 127.1, 126.8 (d, *J* = 11.0 Hz), 113.9 (d, *J* = 3.8 Hz), 112.2, 112.0 (d, *J* = 3.0 Hz), 111.9, 106.4 (d, *J* = 26.0 Hz), 43.8, 36.7, 36.3, 21.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -119.96 (s). IR (KBr): ν (cm^{-1}) 3030, 2783, 2729, 1678, 1600, 1475, 1450, 1408, 1329, 1159, 1093, 990, 815, 759, 687, 659. HRMS (ESI, *m/z*) calcd for $C_{28}H_{24}FN_3NaO_4S$ $[M+Na]^+$: 540.1364, found: 540.1363.



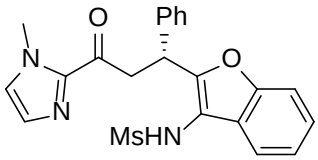
3h

Light yellow solid, m.p. 154-156 °C, 94 mg, 97% yield, 98% ee (HPLC: chiralpak IC column, 254 nm, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, 40 °C, tr (major) = 10.44 min, tr (minor) = 12.61 min). $[\alpha]_D^{25}$ = +9.95 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.98 (s, 1H), 7.81 (d, *J* = 7.4 Hz, 2H), 7.67-7.59 (m, 1H), 7.51 (t, *J* = 7.5 Hz, 1H), 7.38 (t, *J* = 7.8 Hz, 2H), 7.28 (d, *J* = 7.3 Hz, 1H), 7.22-7.13 (m, 6H), 7.01 (s, 1H), 6.86 (dd, *J* = 5.9, 3.3 Hz, 2H), 4.44 (dd, *J* = 9.4, 4.9 Hz, 1H), 4.04 (dd, *J* = 18.0, 9.4 Hz, 1H), 3.91 (s, 3H), 3.59 (dd, *J* = 18.0, 4.9 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 190.2, 153.4, 153.3, 142.0, 139.4, 138.6, 132.8, 129.4, 129.1, 128.2, 128.0, 127.4, 127.38, 127.0, 125.8, 124.3, 123.0, 120.4, 113.4, 111.2, 43.7, 36.6, 36.3. IR (KBr): ν (cm^{-1}) 3028, 2733, 1685, 1476, 1453, 1416, 1324, 1155, 1090, 988, 906, 746, 705. HRMS (ESI, m/z) calcd for $C_{27}H_{23}N_3NaO_4S$ $[M+Na]^+$: 508.1301, found: 508.1300.



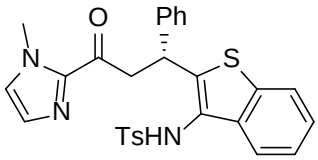
3i

Light yellow solid, m.p. 86-88 °C, 103 mg, 97% yield, 96% ee (HPLC: chiralpak IC column, 254 nm, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, 40 °C, tr (major) = 10.76 min, tr (minor) = 13.76 min). $[\alpha]_D^{25}$ = +6.53 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.11-8.04 (m, 3H), 7.88 (d, *J* = 8.7 Hz, 2H), 7.73-7.69 (m, 1H), 7.38 (d, *J* = 7.4 Hz, 1H), 7.31-7.20 (m, 2H), 7.17-7.07 (m, 4H), 7.01 (s, 1H), 6.91-6.86 (m, 2H), 4.31 (dd, *J* = 9.2, 5.0 Hz, 1H), 3.96 (dd, *J* = 18.1, 9.2 Hz, 1H), 3.89 (s, 3H), 3.53 (dd, *J* = 18.1, 5.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 189.8, 153.5, 149.9, 144.4, 141.9, 138.6, 129.4, 128.8, 128.7, 128.5, 128.3, 127.5, 127.3, 125.5, 124.7, 124.2, 123.4, 120.3, 113.1, 111.5, 44.6, 36.6, 36.2. IR (KBr): ν (cm^{-1}) 3103, 2959, 2854, 1680, 1605, 1530, 1453, 1408, 1347, 1168, 1090, 914, 853, 745, 607. HRMS (ESI, *m/z*) calcd for $C_{27}H_{22}N_4NaO_6S$ $[M+Na]^+$: 553.1152, found: 553.1152.



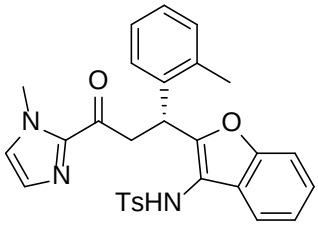
3j

Light yellow solid, m.p. 77-79 °C, 75 mg, 90% yield, 98% ee (HPLC: chiralpak IC column, 254 nm, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, 40 °C, tr (major) = 14.59 min, tr (minor) = 16.68 min). $[\alpha]_D^{25}$ = +0.95 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.67 (dd, *J* = 6.0, 2.7 Hz, 1H), 7.48 (d, *J* = 7.5 Hz, 2H), 7.42 (s, 1H), 7.37 (dd, *J* = 6.4, 2.4 Hz, 1H), 7.29 (t, *J* = 7.5 Hz, 2H), 7.24-7.17 (m, 3H), 7.13 (s, 1H), 6.97 (s, 1H), 5.03 (dd, *J* = 9.1, 5.4 Hz, 1H), 4.20 (dd, *J* = 18.2, 9.1 Hz, 1H), 3.84 (s ,3H), 3.80 (dd, *J* = 18.2, 5.4 Hz , 1H), 3.02 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 189.6, 154.4, 153.3, 142.0, 139.5, 128.9, 128.7, 128.1, 127.2, 126.0, 124.4, 123.2, 119.7, 113.2, 111.5, 43.7, 39.8, 37.1, 36.1. IR (KBr): ν (cm^{-1}) 2925, 2854, 1733, 1677, 1454, 1409, 1321, 1155, 1130, 982, 750, 703. HRMS (ESI, *m/z*) calcd for $C_{22}H_{21}N_3NaO_4S$ $[M+Na]^+$: 446.1145, found: 446.1144.



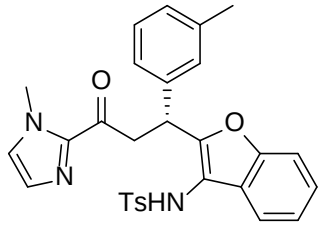
3k

Colorless oil, 78 mg, 76% yield, 76% ee (HPLC: chiralpak IC column, 254 nm, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, 40 °C, tr (minor) = 11.82 min, tr (major) = 13.76 min). $[\alpha]_D^{25}$ = +11.29 (c = 1.0, $CHCl_3$). 1H NMR (400 MHz, CDCl3) δ = 9.40 (s, 1H), 8.08 (d, J = 8.1 Hz, 1H), 7.63 (d, J = 8.2 Hz, 2H), 7.58 (d, J = 8.0 Hz, 1H), 7.41 (s, 1H), 7.34 (t, J = 7.5 Hz, 1H), 7.25 (t, J = 7.5 Hz, 1H), 7.21-7.15 (m, 5H), 7.07 (s, 1H), 6.78-6.69 (m, 2H), 4.71 (t, J = 6.8 Hz, 1H), 3.95 (s, 3H), 3.88 (dd, J = 15.9, 6.2 Hz, 1H), 3.49 (dd, J = 15.9, 7.5 Hz, 1H), 2.37 (s, 3H). 13C NMR (100 MHz, CDCl3) δ = 189.9, 143.9, 143.7, 141.9, 140.4, 137.0, 136.9, 136.7, 129.8, 129.6, 128.4, 127.8, 127.7, 127.4, 127.3, 124.64, 124.59, 124.4, 123.9, 122.2, 46.9, 39.6, 36.4, 21.5. IR (KBr): ν (cm-1) 2920, 2851, 1642,01, 1159, 1095, 815, 756, 665. HRMS (ESI, m/z) calcd for $C_{28}H_{25}N_3NaO_3S_2$ $[M+Na]^+$: 538.1230, found: 538.1230.



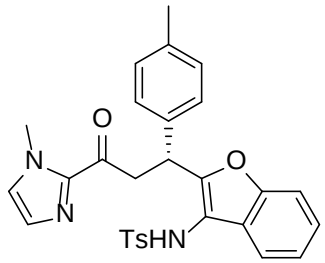
4a

Light yellow solid, m.p. 80-82 °C, 84 mg, 82% yield, 91% ee (HPLC: chiralpak IA column, 254 nm, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, 40 °C, tr (major) = 10.89 min, tr (minor) = 13.29 min). $[\alpha]_D^{25}$ = +8.67 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.58 (d, *J* = 8.2 Hz, 2H), 7.48-7.42 (m, 2H), 7.36 (d, *J* = 8.2 Hz, 1H), 7.21 (t, *J* = 7.2 Hz, 1H), 7.16-7.07 (m, 5H), 7.06-6.98 (m, 4H), 4.85 (dd, *J* = 7.1, 7.1 Hz, 1H), 3.90 (s, 3H), 3.80 (dd, *J* = 18.1, 7.1 Hz, 1H), 3.71 (dd, *J* = 18.1, 7.1 Hz, 1H), 2.24 (s, 3H), 2.12 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 189.6, 154.0, 153.3, 143.6, 142.2, 137.7, 136.3, 135.6, 130.4, 129.5, 129.2, 127.5, 127.2, 126.8, 126.2, 125.8, 124.2, 123.0, 120.0, 113.5, 111.3, 43.6, 36.1, 33.1, 21.4, 19.5. IR (KBr): ν (cm^{-1}) 2923, 2852, 1699, 1617, 1541, 1508, 1455, 1406, 1321, 1161, 1091, 750, 668. HRMS (ESI, *m/z*) calcd for $C_{29}H_{27}N_3NaO_4S$ $[M+Na]^+$: 536.1614, found: 536.1612.



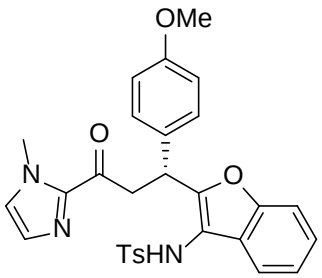
4b

Light yellow solid, m.p. 77-79 °C, 98 mg, 96% yield, 92% ee (HPLC: chiralpak IA column, 254 nm, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, 40 °C, tr (minor) = 10.50 min, tr (major) = 11.99 min). $[\alpha]_D^{25}$ = +10.96 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.98 (s, 1H), 7.74-7.64 (m, 3H), 7.32-7.26 (m, 1H), 7.22-7.14 (m, 5H), 7.07-6.96 (m, 3H), 6.84 (s, 1H), 6.55 (d, *J* = 7.5 Hz, 1H), 4.40 (dd, *J* = 9.2, 5.0 Hz, 1H), 4.00 (dd, *J* = 18.0, 9.2 Hz, 1H), 3.92 (s, 3H), 3.57 (dd, *J* = 18.0, 5.0 Hz, 1H), 2.33 (s, 3H), 2.28 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 190.3, 153.4, 153.2, 143.5, 142.0, 138.5, 137.8, 136.4, 129.7, 129.4, 128.6, 128.0, 127.7, 127.5, 127.4, 125.9, 125.1, 124.2, 122.9, 120.6, 113.6, 111.2, 43.8, 36.4, 36.3, 21.5, 21.4. IR (KBr): ν (cm^{-1}) 2959, 2922, 1682, 1616, 1541, 1508, 1454, 1408, 1326, 1163, 1092, 751, 667. HRMS (ESI, *m/z*) calcd for $C_{29}H_{27}N_3NaO_4S$ $[M+Na]^+$: 536.1614, found: 536.1614.



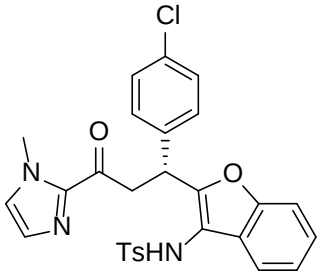
4c

Light yellow solid, m.p. 77-79 °C, 91 mg, 89% yield, 96% ee (HPLC: chiralpak IC column, 254 nm, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, 40 °C, tr (major) = 13.14 min, tr (minor) = 15.42 min). $[\alpha]_D^{25}$ = +12.41 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.98 (s, 1H), 7.72 (dd, *J* = 6.2, 2.9 Hz, 1H), 7.67 (d, *J* = 8.2 Hz, 2H), 7.30-7.26 (m, 1H), 7.21-7.14 (m, 5H), 7.01 (s, 1H), 6.97 (d, *J* = 8.0 Hz, 2H), 6.73 (d, *J* = 8.0 Hz, 2H), 4.35 (dd, *J* = 9.2, 5.0 Hz, 1H), 3.99 (dd, *J* = 17.9, 9.2 Hz, 1H), 3.92 (s, 3H), 3.54 (dd, *J* = 17.9, 5.0 Hz, 1H), 2.36 (s, 3H), 2.28 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 190.3, 153.4, 153.2, 143.6, 142.0, 136.5, 136.3, 135.5, 129.7, 129.4, 128.8, 127.9, 127.5, 127.3, 125.9, 124.2, 122.9, 120.6, 113.5, 111.2, 43.9, 36.3, 36.2, 21.5, 21.0. IR (KBr): ν (cm^{-1}) 2955, 2923, 2854, 1680, 1454, 1409, 1371, 1328, 1163, 1092, 745, 667. HRMS (ESI, *m/z*) calcd for $C_{29}H_{27}N_3NaO_4S$ $[M+Na]^+$: 536.1614, found: 536.1612.



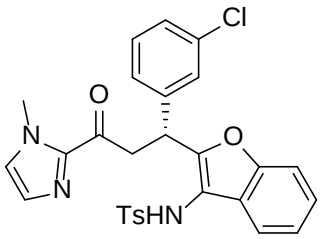
4d

Light yellow solid, m.p. 88-90 °C, 92 mg, 87% yield, 94% ee (HPLC: chiralpak IA column, 254 nm, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, 40 °C, tr (minor) = 16.43 min, tr (major) = 20.04 min). $[\alpha]_D^{25}$ = +7.19 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.96 (s, 1H), 7.74-7.63 (m, 3H), 7.32-7.27 (m, 1H), 7.23-7.14 (m, 5H), 7.02 (s, 1H), 6.78 (d, *J* = 8.8 Hz, 2H), 6.70 (d, *J* = 8.8 Hz, 2H), 4.35 (dd, *J* = 9.2, 5.1 Hz, 1H), 3.98 (dd, *J* = 17.9, 9.2 Hz, 1H), 3.93 (s, 3H), 3.76 (s, 3H), 3.53 (dd, *J* = 17.9, 5.1 Hz, 1H), 2.36 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 190.3, 158.4, 153.41, 153.39, 143.6, 142.0, 136.3, 130.7, 129.7, 129.4, 129.1, 127.5, 127.4, 125.9, 124.2, 123.0, 120.6, 113.5, 113.4, 111.2, 55.1, 44.1, 36.3, 35.8, 21.5. IR (KBr): ν (cm^{-1}) 2924, 2854, 1636, 1510, 1456, 1409, 1377, 1248, 1162, 753, 695, 667. HRMS (ESI, *m/z*) calcd for $C_{29}H_{27}N_3NaO_5S$ $[M+Na]^+$: 552.1564, found: 552.1567.



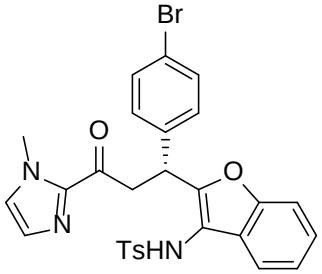
4e

Light yellow solid, m.p. 90-92 °C, 105 mg, 99% yield, 93% ee (HPLC: chiralpak IA column, 254 nm, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, 40 °C, tr (minor) = 13.43 min, tr (major) = 18.08 min). $[\alpha]_D^{25}$ = +10.00 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.97 (s, 1H), 7.69-7.57 (m, 3H), 7.29 (d, *J* = 7.6 Hz, 1H), 7.23-7.09 (m, 7H), 7.01 (s, 1H), 6.84 (d, *J* = 8.4 Hz, 2H), 4.43 (dd, *J* = 9.1, 5.3 Hz, 1H), 3.92 (dd, *J* = 18.0, 9.1 Hz, 1H), 3.90 (s, 3H), 3.58 (dd, *J* = 18.0, 5.3 Hz, 1H), 2.33 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 189.7, 153.4, 152.8, 143.7, 141.9, 137.3, 136.2, 132.6, 129.6, 129.4, 128.2, 127.44, 127.39, 125.7, 124.4, 123.0, 120.4, 113.7, 111.2, 43.7, 36.2, 35.9, 21.4. IR (KBr): ν (cm^{-1}) 2923, 2853, 1677, 1596, 1491, 1454, 1411, 1327, 1163, 1131, 1091, 1014, 985, 814, 750, 666. HRMS (ESI, *m/z*) calcd for $C_{28}H_{24}ClN_3NaO_4S$ $[M+Na]^+$: 556.1068, found: 556.1067.



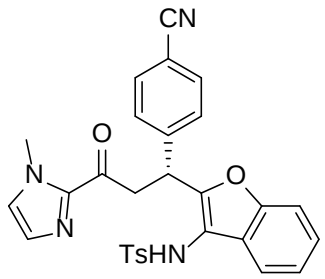
4f

Light yellow solid, m.p. 94-96 °C, 105 mg, 99% yield, 95% ee (HPLC: chiralpak IA column, 254 nm, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, 40 °C, tr (minor) = 11.61 min, tr (major) = 13.24 min). $[\alpha]_D^{25}$ = +10.93 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.00 (s, 1H), 7.72-7.65 (m, 3H), 7.31 (dd, *J* = 6.7, 2.1 Hz, 1H), 7.25-7.09 (m, 7H), 7.03 (s, 1H), 6.89 (d, *J* = 7.4 Hz, 1H), 6.83 (s, 1H), 4.40 (dd, *J* = 9.3, 4.9 Hz, 1H), 3.98 (dd, *J* = 18.0, 9.3 Hz, 1H), 3.93 (s, 3H), 3.56 (dd, *J* = 18.0, 4.9 Hz, 1H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 189.7, 153.5, 152.2, 143.8, 141.9, 140.6, 136.2, 133.9, 129.7, 129.5, 129.4, 128.1, 127.5, 127.3, 127.2, 126.2, 125.8, 124.5, 123.1, 120.6, 114.0, 111.2, 43.8, 36.2 (2C), 21.5. IR (KBr): ν (cm^{-1}) 3024, 2811, 2737, 1683, 1597, 1573, 1475, 1412, 1290, 1158, 1094, 984, 904, 749, 680. HRMS (ESI, m/z) calcd for $C_{28}H_{24}ClN_3NaO_4S$ $[M+Na]^+$: 556.1068, found: 556.1065.



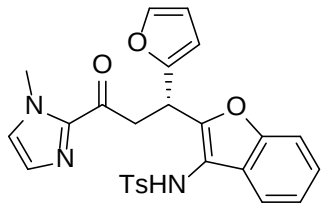
4g

Light yellow solid, m.p. 93-95 °C, 111 mg, 97% yield, 92% ee (HPLC: chiralpak IA column, 254 nm, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, 40 °C, tr (minor) = 13.91 min, tr (major) = 19.16 min). $[\alpha]_D^{25}$ = +8.44 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.95 (s, 1H), 7.67-7.58 (m, 3H), 7.33-7.24 (m, 3H), 7.23-7.09 (m, 5H), 7.01 (s, 1H), 6.78 (d, *J* = 8.5 Hz, 2H), 4.41 (dd, *J* = 9.1, 5.3 Hz, 1H), 3.91 (dd, *J* = 18.0, 9.1 Hz, 1H), 3.90 (s, 3H), 3.57 (dd, *J* = 18.0, 5.3 Hz, 1H), 2.33 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 189.6, 153.4, 152.7, 143.7, 141.9, 137.8, 136.2, 131.2, 129.7, 129.6, 129.4, 127.44, 127.39, 125.7, 124.4, 123.0, 120.8, 120.4, 113.7, 111.2, 43.6, 36.2, 36.0, 21.4. IR (KBr): ν (cm^{-1}) 2995, 2853, 1681, 1489, 1454, 1411, 1328, 1163, 750, 667. HRMS (ESI, m/z) calcd for $C_{28}H_{24}BrN_3NaO_4S$ $[M+Na]^+$: 600.0563, found: 600.0565.



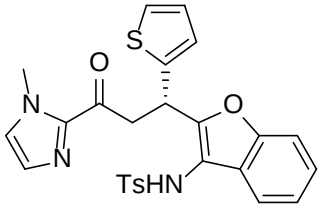
4h

Light yellow solid, m.p. 96-98 °C, 101 mg, 97% yield, 91% ee (HPLC: chiralpak IA column, 254 nm, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, 40 °C, tr (minor) = 22.24 min, tr (major) = 29.10 min). $[\alpha]_D^{25}$ = +8.82 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.92 (s, 1H), 7.65 (d, *J* = 8.2 Hz, 2H), 7.49-7.43 (m, 3H), 7.30 (d, *J* = 8.2 Hz, 1H), 7.21 (t, *J* = 7.3 Hz, 1H), 7.17-7.09 (m, 6H), 7.04 (s, 1H), 4.64 (dd, *J* = 8.0, 6.0 Hz, 1H), 3.91 (s, 3H), 3.90 (dd, *J* = 18.0, 8.0 Hz, 1H), 3.73 (dd, *J* = 18.0, 6.0 Hz, 1H), 2.33 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 189.0, 153.3, 152.3, 144.4, 143.7, 141.8, 136.3, 131.9, 129.6, 129.4, 128.9, 127.5, 127.4, 125.5, 124.6, 123.1, 120.1, 118.6, 113.9, 111.2, 110.6, 43.1, 36.6, 36.1, 21.4. IR (KBr): ν (cm^{-1}) 2924, 2854, 2227, 1733, 1677, 1606, 1505, 1453, 1411, 1328, 1163, 1091, 985, 814, 745, 667. HRMS (ESI, *m/z*) calcd for $C_{29}H_{24}N_4NaO_4S$ $[M+Na]^+$: 547.1410, found: 547.1411.



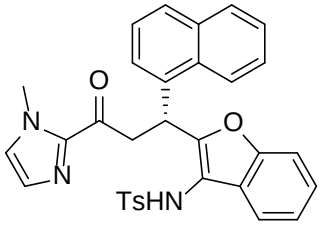
4i

Light yellow solid, m.p. 60-62 °C, 80 mg, 82% yield, 95% ee (HPLC: chiralpak IC column, 254 nm, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, 40 °C, tr (major) = 13.00 min, tr (minor) = 19.54 min). $[\alpha]_D^{25}$ = +12.04 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.81-7.75 (m, 2H), 7.63 (d, *J* = 8.2 Hz, 2H), 7.36-7.30 (m, 1H), 7.27-7.21 (m, 2H), 7.19 (s, 1H), 7.15 (s, 1H), 7.09 (d, *J* = 8.2 Hz, 2H), 7.02 (s, 1H), 6.23 (dd, *J* = 3.1, 1.9 Hz, 1H), 5.96 (d, *J* = 3.2 Hz, 1H), 4.27 (dd, *J* = 9.3, 4.8 Hz, 1H), 3.93 (s, 3H), 3.82 (dd, *J* = 18.3, 9.3 Hz, 1H), 3.63 (dd, *J* = 18.3, 4.8 Hz, 1H), 2.28 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 189.7, 153.5, 151.5, 150.8, 143.5, 141.9, 141.3, 135.8, 129.6, 129.5, 127.4, 127.2, 126.0, 124.5, 123.1, 120.6, 114.6, 111.2, 110.2, 106.7, 42.2, 36.2, 30.9, 21.4. IR (KBr): ν (cm^{-1}) 2923, 2853, 1679, 1596, 1454, 1410, 1329, 1164, 1091, 1012, 914, 814, 746, 669. HRMS (ESI, m/z) calcd for $C_{26}H_{23}N_3NaO_5S$ $[M+Na]^+$: 512.1251, found: 512.1251.



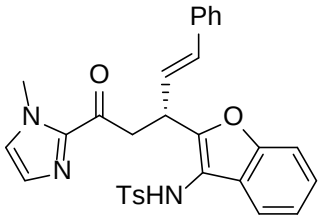
4j

Light yellow solid, m.p. 65-67 °C, 81 mg, 80% yield, 96% ee (HPLC: chiralpak IC column, 254 nm, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, 40 °C, tr (major) = 13.44 min, tr (minor) = 18.02 min). $[\alpha]_D^{25}$ = +10.70 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.77 (s, 1H), 7.74-7.68 (m, 1H), 7.64 (d, *J* = 8.2 Hz, 2H), 7.37-7.31 (m, 1H), 7.25-7.21 (m, 2H), 7.18 (s, 1H), 7.14-7.08 (m, 3H), 7.03 (s, 1H), 6.83 (dd, *J* = 5.0, 3.7 Hz, 1H), 6.54 (d, *J* = 3.4 Hz, 1H), 4.63 (dd, *J* = 9.2, 5.0 Hz, 1H), 4.00 (dd, *J* = 18.0, 9.2 Hz, 1H), 3.95 (s, 3H), 3.60 (dd, *J* = 18.0, 5.0 Hz, 1H), 2.30 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 189.5, 153.4, 152.1, 143.7, 141.8, 141.4, 136.0, 129.7, 129.4, 127.5, 127.3, 126.3, 125.9, 125.5, 124.6, 124.3, 123.2, 120.6, 113.8, 111.3, 45.5, 36.3, 32.3, 21.5. IR (KBr): ν (cm^{-1}) 2923, 2852, 1699, 1636, 1617, 1541, 1508, 1455, 1163, 1091, 753, 668. HRMS (ESI, *m/z*) calcd for $C_{26}H_{23}N_3NaO_4S_2$ $[M+Na]^+$: 528.1022, found: 528.1021.



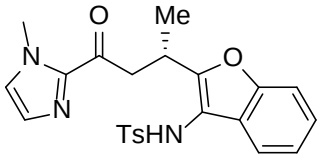
4k

Light yellow solid, m.p. 97-99 °C, 91 mg, 93% yield, 96% ee (HPLC: chiralpak IC column, 254 nm, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, 40 °C, tr (major) = 13.42 min, tr (minor) = 16.66 min). $[\alpha]_D^{25}$ = -4.92 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.80 (dd, *J* = 12.3, 7.7 Hz, 2H), 7.67 (dd, *J* = 17.9, 7.7 Hz, 2H), 7.55 (d, *J* = 7.2 Hz, 1H), 7.49-7.36 (m, 5H), 7.30 (t, *J* = 7.7 Hz, 2H), 7.25-7.15 (m, 2H), 7.09 (s, 1H), 6.96 (s, 1H), 6.55 (d, *J* = 8.1 Hz, 2H), 5.38 (dd, *J* = 9.3, 4.7 Hz, 1H), 4.01 (dd, *J* = 18.3, 9.3 Hz, 1H), 3.86 (s, 3H), 3.72 (dd, *J* = 18.3, 4.7 Hz, 1H), 1.84 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 189.7, 153.54, 153.52, 143.2, 142.1, 135.6, 135.3, 133.8, 130.5, 129.3, 129.1, 129.0, 127.5, 127.3, 126.8, 126.2, 126.1, 125.4, 125.3, 125.1, 124.3, 123.1, 122.7, 120.4, 114.2, 111.3, 44.2, 36.1, 32.4, 21.1. IR (KBr): ν (cm^{-1}) 3047, 2922, 2852, 1676, 1596, 1509, 1453, 1409, 1326, 1162, 1091, 778, 748, 668. HRMS (ESI, *m/z*) calcd for $C_{32}H_{27}N_3NaO_4S$ $[M+Na]^+$: 572.1614, found: 572.1614.



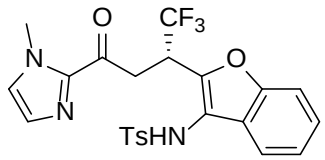
4l

Light yellow solid, m.p. 103-105 °C, 80 mg, 76% yield, 85% ee (HPLC: chiralpak IA column, 254 nm, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, 40 °C, tr (minor) = 11.77 min, tr (major) = 14.54 min). $[\alpha]_D^{25}$ = +9.23 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.96 (s, 1H), 7.80-7.76 (m, 1H), 7.67 (d, *J* = 8.2 Hz, 2H), 7.36-7.16 (m, 11H), 7.02 (s, 1H), 6.02-5.90 (m, 2H), 3.92 (s, 3H), 3.85-3.71 (m, 2H), 3.39-3.26 (m, 1H), 2.19 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 190.1, 153.5, 152.8, 143.6, 142.0, 136.5, 136.0, 131.3, 129.6, 129.4, 128.5, 127.6, 127.5, 127.4, 126.3, 126.2, 126.0, 124.3, 123.1, 120.6, 113.8, 111.1, 43.4, 36.3, 34.4, 21.3. IR (KBr): ν (cm^{-1}) 2955, 2923, 2853, 1672, 1454, 1408, 1329, 1164, 1091, 748, 694, 665. HRMS (ESI, *m/z*) calcd for $C_{30}H_{27}N_3NaO_4S$ $[M+Na]^+$: 548.1614, found: 548.1614.



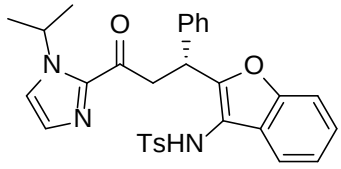
4m

Light yellow oil, 87 mg, 99% yield, 96% ee (HPLC: chiralpak IC column, 254 nm, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, 40 °C, tr (major) = 12.20 min, tr (minor) = 14.54 min). $[\alpha]_D^{25}$ = +14.50 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.00 (s, 1H), 7.75-7.69 (m, 1H), 7.63 (d, *J* = 8.2 Hz, 2H), 7.35-7.28 (m, 1H), 7.25-7.18 (m, 4H), 7.14 (s, 1H), 7.01 (s, 1H), 3.92 (s, 3H), 3.55 (dd, *J* = 17.9, 9.4 Hz, 1H), 3.03 (dd, *J* = 17.9, 4.4 Hz, 1H), 2.90-2.80 (m, 1H), 2.37 (s, 3H), 0.91 (d, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 191.0, 155.3, 153.1, 143.5, 141.9, 135.9, 129.4, 129.2, 127.4, 127.3, 126.2, 124.0, 122.9, 120.3, 113.1, 110.9, 45.3, 36.2, 25.8, 21.4, 17.0. IR (KBr): ν (cm^{-1}) 2971, 2927, 1676, 1579, 1454, 1410, 1329, 1164, 1092, 985, 914, 815, 749, 665. HRMS (ESI, *m/z*) calcd for $C_{23}H_{23}N_3NaO_4S$ $[M+Na]^+$: 460.1301, found: 460.1301.



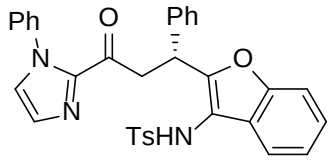
4n

Light yellow oil, 96 mg, 98% yield, 91% ee (HPLC: chiralpak IA column, 254 nm, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, 40 °C, tr (major) = 7.78 min, tr (minor) = 9.95 min). $[\alpha]_D^{25}$ = +10.14 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.71 (m, 4H), 7.38 (d, *J* = 8.1 Hz, 1H), 7.31-7.21 (m, 4H), 7.16 (s, 1H), 7.06 (s, 1H), 3.94 (s, 3H), 3.89-3.71 (m, 2H), 3.57 (dd, *J* = 17.6, 2.1 Hz, 1H), 2.37 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 188.0, 153.8, 145.0, 144.1, 141.5, 135.8, 129.8, 129.7, 128.2, 127.9, 127.1, 125.3, 124.9 (q, *J* = 276.7 Hz), 123.4, 120.7, 117.4, 111.5, 37.5, 36.3 (q, *J* = 30.0 Hz), 36.2, 21.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -67.72 (s). IR (KBr): ν (cm^{-1}) 2957, 2924, 2853, 1683, 1597, 1454, 1415, 1347, 1255, 1165, 1092, 989, 749, 668. HRMS (ESI, *m/z*) calcd for $C_{23}H_{20}F_3N_3NaO_4S$ $[M+Na]^+$: 514.1019, found: 514.1019.



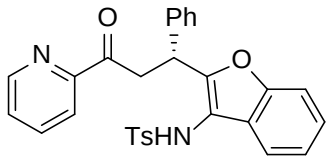
4o

Light yellow solid, m.p. 73-75 °C, 101 mg, 96% yield, 96% ee (HPLC: chiralpak IC column, 254 nm, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, 40 °C, tr (major) = 9.92 min, tr (minor) = 12.70 min). $[\alpha]_D^{25}$ = +7.95 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.89 (s, 1H), 7.78-7.71 (m, 1H), 7.68 (d, *J* = 8.2 Hz, 2H), 7.34-7.27 (m, 1H), 7.25 (s, 1H), 7.22-7.15 (m, 8H), 6.85 (dd, *J* = 6.4, 2.9 Hz, 2H), 5.44 (m, 1H), 4.38 (dd, *J* = 9.6, 4.8 Hz, 1H), 4.05 (dd, *J* = 18.0, 9.6 Hz, 1H), 3.58 (dd, *J* = 18.0, 4.8 Hz, 1H), 2.36 (s, 3H), 1.40 (d, *J* = 7.2 Hz, 3H), 1.38 (d, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 190.3, 153.4, 153.0, 143.6, 141.3, 138.7, 136.3, 129.9, 129.7, 128.1, 128.07, 127.5, 126.9, 125.9, 124.3, 123.0, 121.6, 120.7, 113.7, 111.2, 49.3, 44.4, 36.6, 23.7, 23.3, 21.5. IR (KBr): ν (cm^{-1}) 3253, 2980, 2924, 2851, 1677, 1597, 1494, 1396, 1255, 1164, 1091, 978, 750, 704, 666. HRMS (ESI, *m/z*) calcd for $C_{30}H_{29}N_3NaO_4S$ $[M+Na]^+$: 550.1771, found: 550.1771.



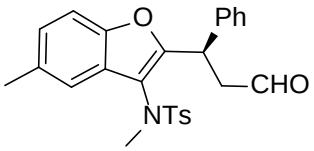
4p

Light yellow oil, 101 mg, 90% yield, 98% ee (HPLC: chiralpak IC column, 254 nm, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, 40 °C, tr (major) = 13.25 min, tr (minor) = 17.72 min). $[\alpha]_D^{25}$ = +5.21 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.62 (d, *J* = 7.5 Hz, 1H), 7.57 (d, *J* = 8.2 Hz, 2H), 7.49-7.35 (m, 4H), 7.30 (d, *J* = 7.5 Hz, 1H), 7.21-7.04 (m, 11H), 6.92-6.83 (m, 2H), 4.41 (dt, *J* = 9.1, 4.7 Hz, 1H), 4.00 (ddd, *J* = 17.5, 9.1, 2.6 Hz, 1H), 3.59 (dt, *J* = 17.5, 4.7 Hz, 1H), 2.29 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 188.6, 153.32, 153.25, 143.5, 142.1, 138.7, 137.6, 136.1, 129.8, 129.6, 129.0, 128.9, 128.1, 128.0, 127.4, 127.3, 126.8, 125.9, 125.5, 124.2, 122.9, 120.4, 113.5, 111.2, 43.9, 36.7, 21.4. IR (KBr): ν (cm^{-1}) 3029, 2923, 2854, 1693, 1596, 1493, 1452, 1409, 1328, 1159, 1091, 965, 814, 756, 704, 666. HRMS (ESI, *m/z*) calcd for $C_{33}H_{27}N_3NaO_4S$ $[M+Na]^+$: 584.1614, found: 584.1614.



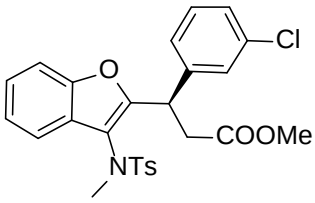
4q

Yellow solid, m.p. 116-118 °C, 96 mg, 96% yield, 95% ee (HPLC: chiralpak IC column, 254 nm, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, 40 °C, tr (major) = 11.82 min, tr (minor) = 17.08 min). $[\alpha]_D^{25}$ = +6.29 (c = 1.0, $CHCl_3$). 1H NMR (400 MHz, CDCl3) δ = 8.65 (d, J = 4.3 Hz, 1H), 7.96 (d, J = 7.8 Hz, 1H), 7.79 (td, J = 7.7, 1.2 Hz, 1H), 7.70 (d, J = 8.2 Hz, 2H), 7.67-7.62 (m, 1H), 7.54 (s, 1H), 7.45 (dd, J = 6.9, 4.9 Hz, 1H), 7.30-7.14 (m, 8H), 6.95 (dd, J = 6.5, 2.8 Hz, 2H), 4.42 (dd, J = 9.8, 4.2 Hz, 1H), 4.12 (dd, J = 19.1, 9.9 Hz, 1H), 3.72 (dd, J = 19.1, 4.3 Hz, 1H), 2.32 (s, 3H). 13C NMR (100 MHz, CDCl3) δ = 199.9, 153.48, 153.42, 152.5, 149.0, 143.7, 139.3, 137.1, 136.5, 129.8, 128.3, 128.2, 127.7, 127.6, 127.0, 126.1, 124.3, 123.1, 122.1, 120.6, 113.7, 111.2, 42.9, 36.5, 21.5. IR (KBr): ν (cm-1) 2992, 2852, 1697, 1598, 1494, 1453, 1325, 1164, 1091, 994, 749, 701, 665. HRMS (ESI, m/z) calcd for $C_{29}H_{24}N_2NaO_4S$ $[M+Na]^+$: 519.1349, found: 519.1349.



5

ee = 98% (HPLC: Chiralpak column IC, λ = 254 nm, *n*-hexane/*i*-PrOH = 90:10, flow rate: 1.0 mL/min, 40 °C, tr (major) = 13.79 min, tr (minor) = 18.66 min). $[\alpha]_D^{25}$ = +7.66 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.77 (s, 1H), 7.60 (s, 2H), 7.46-7.16 (m, 8H), 6.95 (d, *J* = 8.3 Hz, 1H), 5.95 (s, 1H), 5.02 (t, *J* = 6.9 Hz, 1H), 3.43-3.05 (m, 5H), 2.44 (s, 3H), 2.13 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 200.4, 157.0, 151.7, 143.9, 139.9, 135.2, 132.1, 129.6, 128.8, 128.0, 127.2, 125.3, 124.2, 118.9, 111.2, 46.6, 37.9, 36.9, 21.5, 20.9. IR (KBr): ν (cm^{-1}) 2961, 2922, 2851, 2360, 1725, 1599, 1494, 1455, 1350, 1261, 1156, 1089, 1036, 802, 699, 670. HRMS (ESI, *m*/*z*) calcd for $C_{26}H_{25}NNaO_4S$ $[M+Na]^+$: 470.1397, found: 470.1395.



6

ee = 95% (HPLC: Chiralpak column IC, λ = 254 nm, *n*-hexane/*i*-PrOH = 90:10, flow rate: 1.0 mL/min, 40 °C, tr (major) = 21.14 min, tr (minor) = 24.80 min). $[\alpha]_D^{25}$ = +11.11 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, DMSO-d6): δ = 7.65-7.50 (m, 3H), 7.47 (s, 1H), 7.42-7.28 (m, 5H), 7.21 (t, *J* = 7.7 Hz, 1H), 6.97 (t, *J* = 7.4 Hz, 1H), 6.42 (d, *J* = 7.2 Hz, 1H), 4.77 (s, 1H), 3.55 (s, 3H), 3.31-3.03 (m, 5H), 2.39 (s, 3H). ^{13}C NMR (100 MHz, Acetone-d6): δ = 170.7, 156.2, 153.3, 144.2, 142.4, 135.6, 133.7, 130.2, 129.8, 128.2, 127.8, 127.2, 126.8, 124.5, 124.4, 122.8, 119.4, 111.6, 51.1, 41.4, 37.5, 26.8, 20.6. IR (KBr): ν (cm^{-1}) 2921, 2850, 1738, 1654, 1453, 1350, 1165, 1026, 999, 826, 764, 675, 583. HRMS (ESI, *m*/*z*) calcd for $C_{26}H_{24}ClNNaO_5S$ $[M+Na]^+$: 520.0956, found: 520.0955.

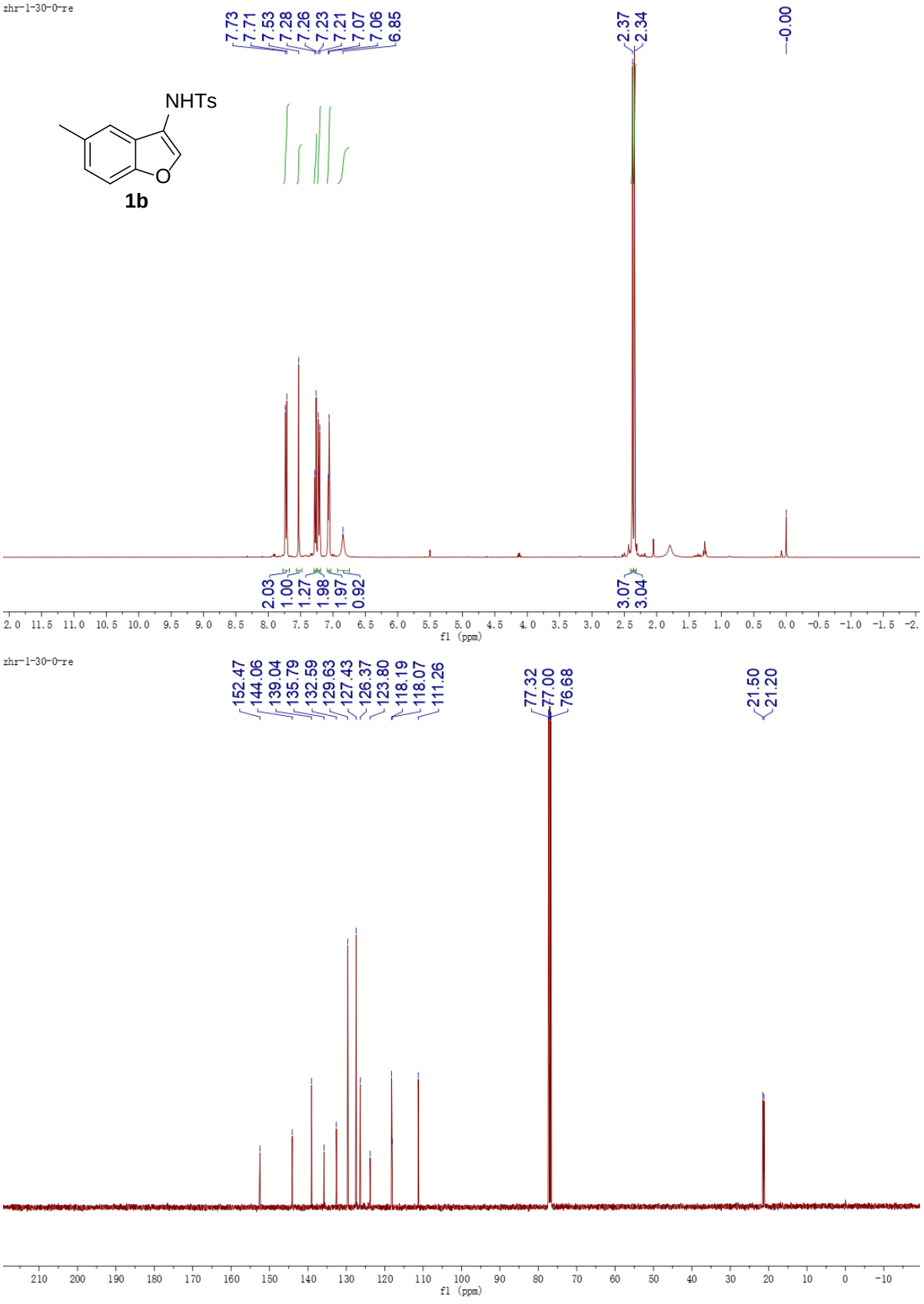
4. References

(1) (a) C. Wang, L.-A. Chen, H. Huo, X. Shen, K. Harms, L. Gong and E. Meggers, *Chem. Sci.*, 2015, **6**, 1094; (b) G.-J. Sun, J. Gong and Q. Kang, *J. Org. Chem.*, 2017, **82**, 796; (c) S.-W. Li, J. Gong and Q. Kang, *Org. Lett*., 2017, **19**, 1350; (d) K. Li, Q. Wan and Q. Kang, *Org. Lett*., 2017, **19**, 3299; (e) S.-X. Lin, G.-J. Sun and Q. Kang, *Chem. Commun.*, 2017, **53**, 7665.

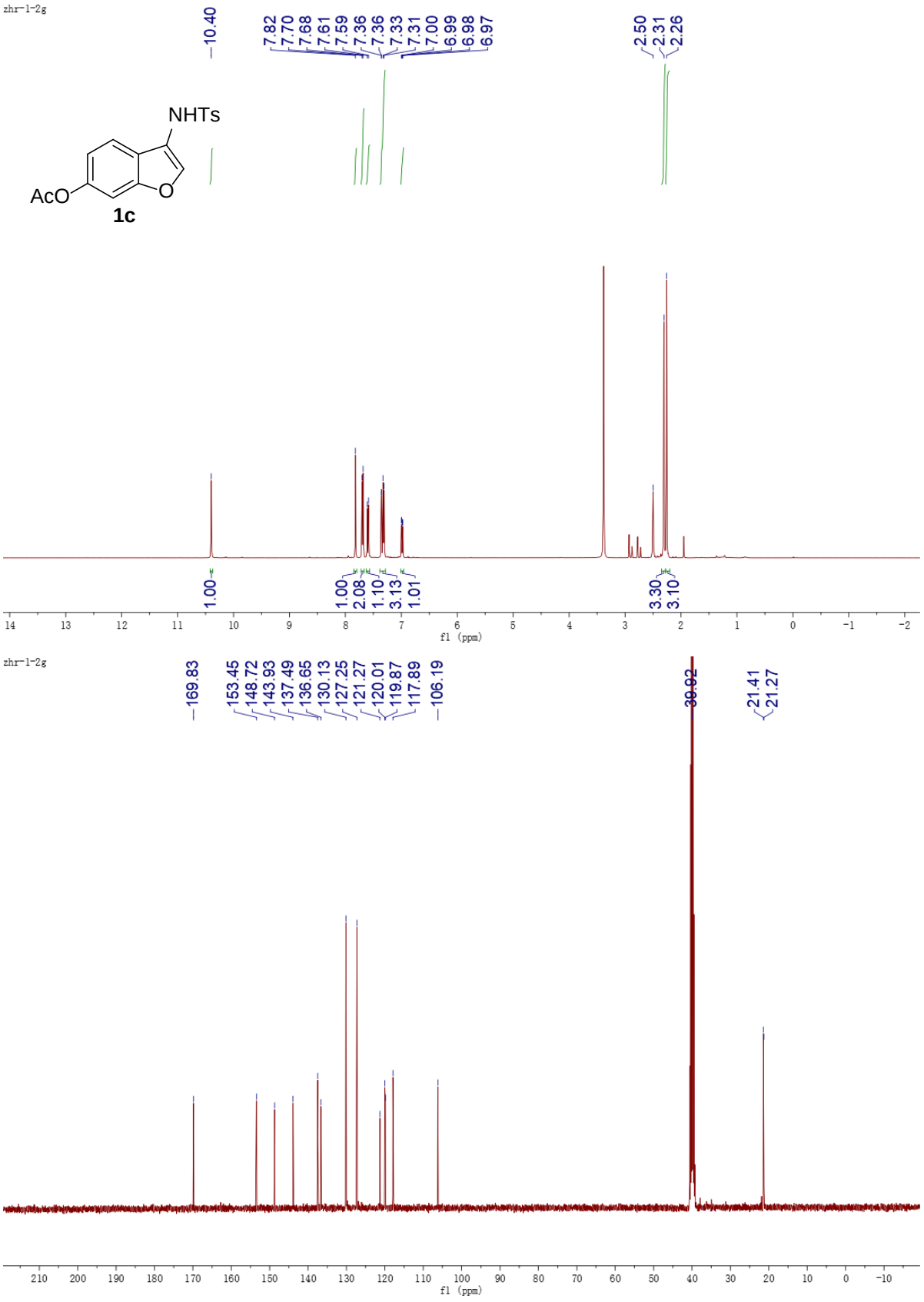
(2) H. Huo, C. Fu, K. Harms and E. Meggers, *J. Am. Chem. Soc*., 2014, **136**, 2990.

(3) X.-F. Ding, R.-H. Su, W.-L. Yang and W.-P. Deng, *Adv. Synth. Catal.*, 2018, **360**, 4168.

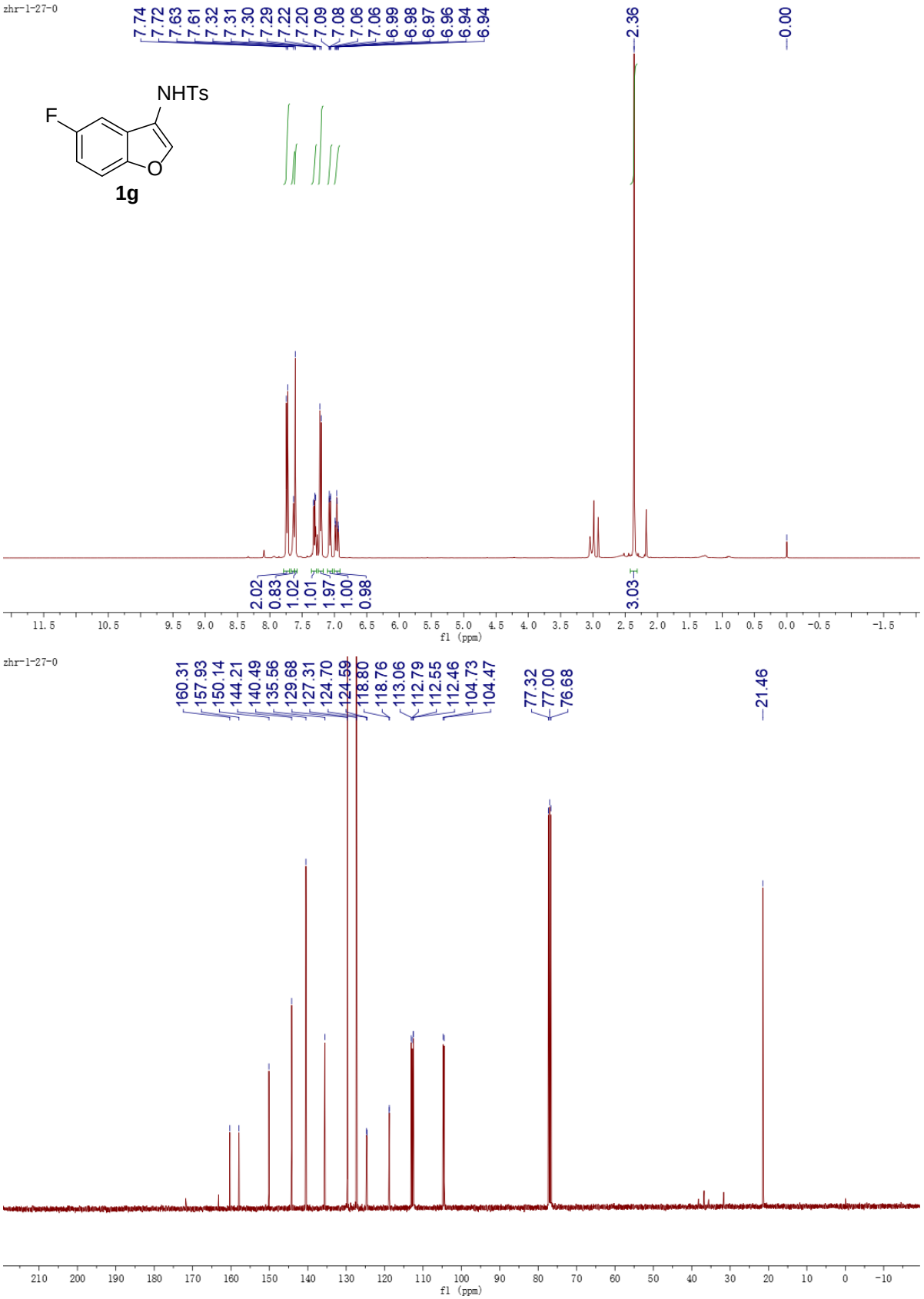
5. NMR Spectra



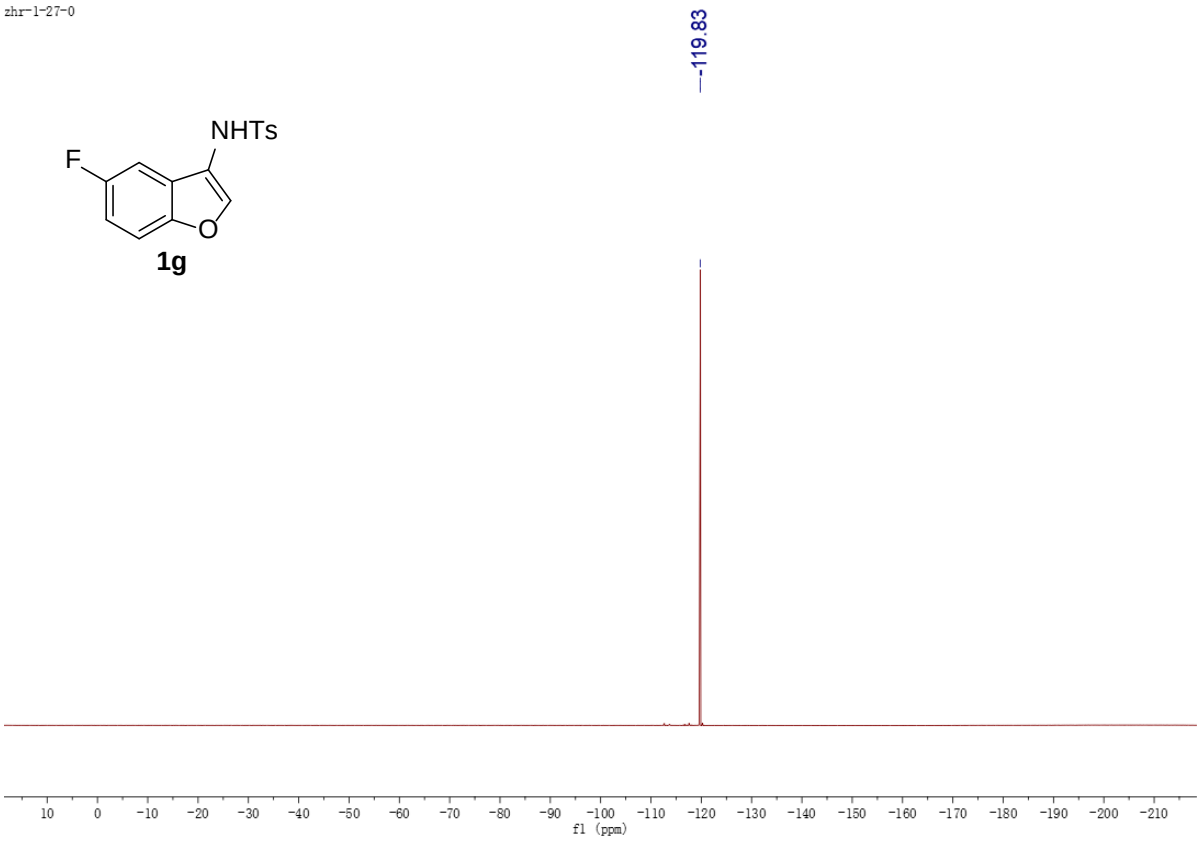
^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **1b**



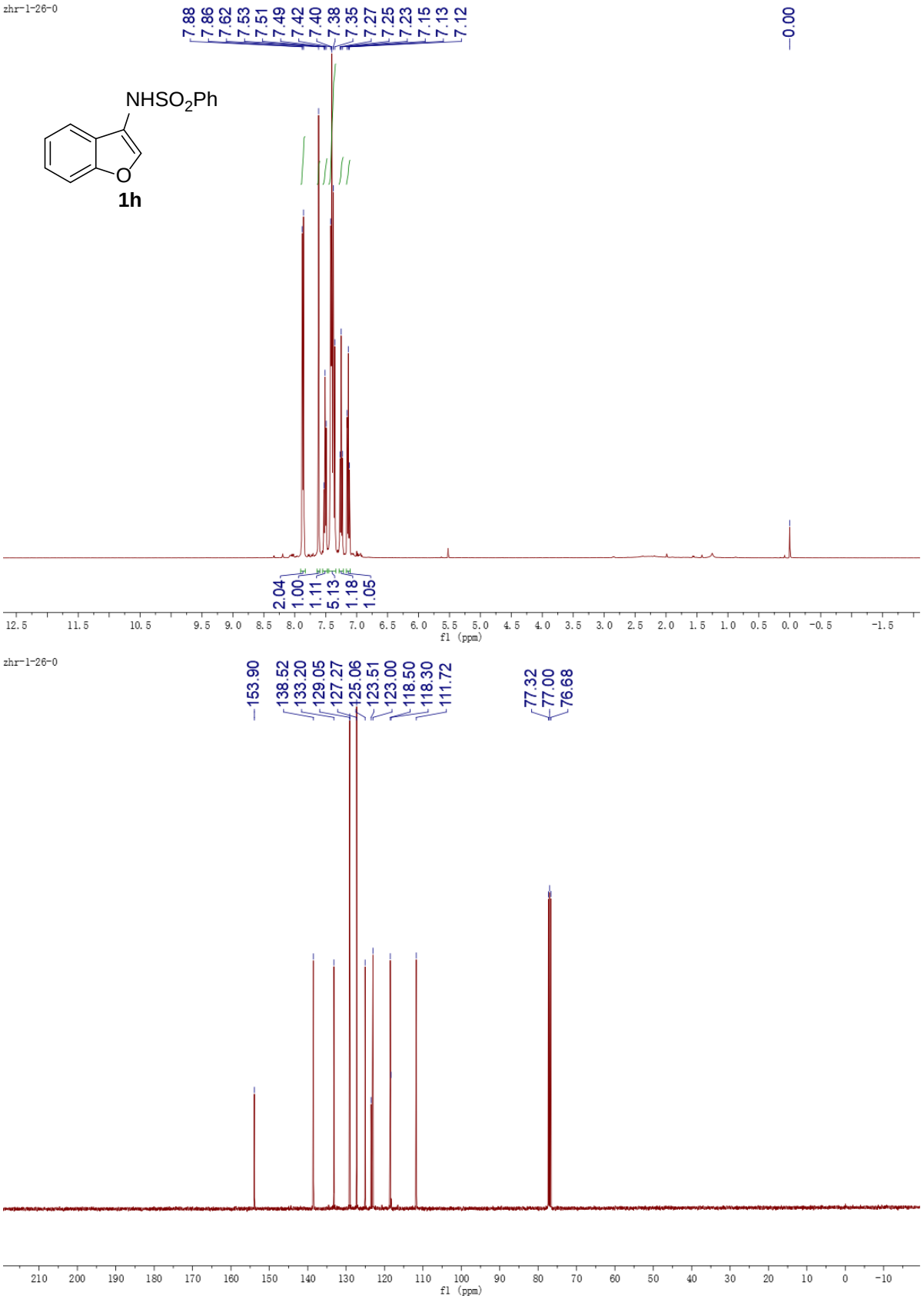
^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **1c**



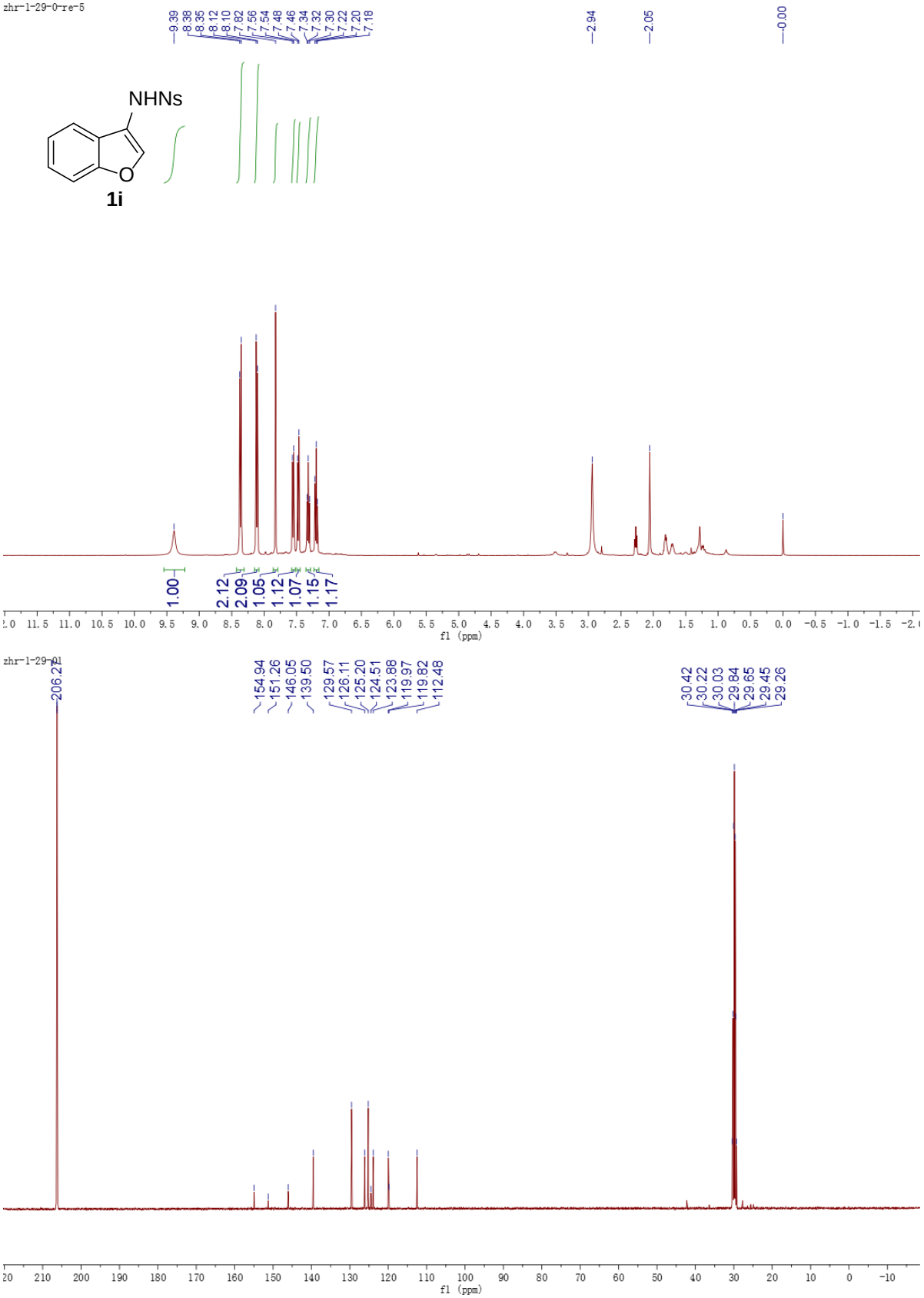
^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **1g**



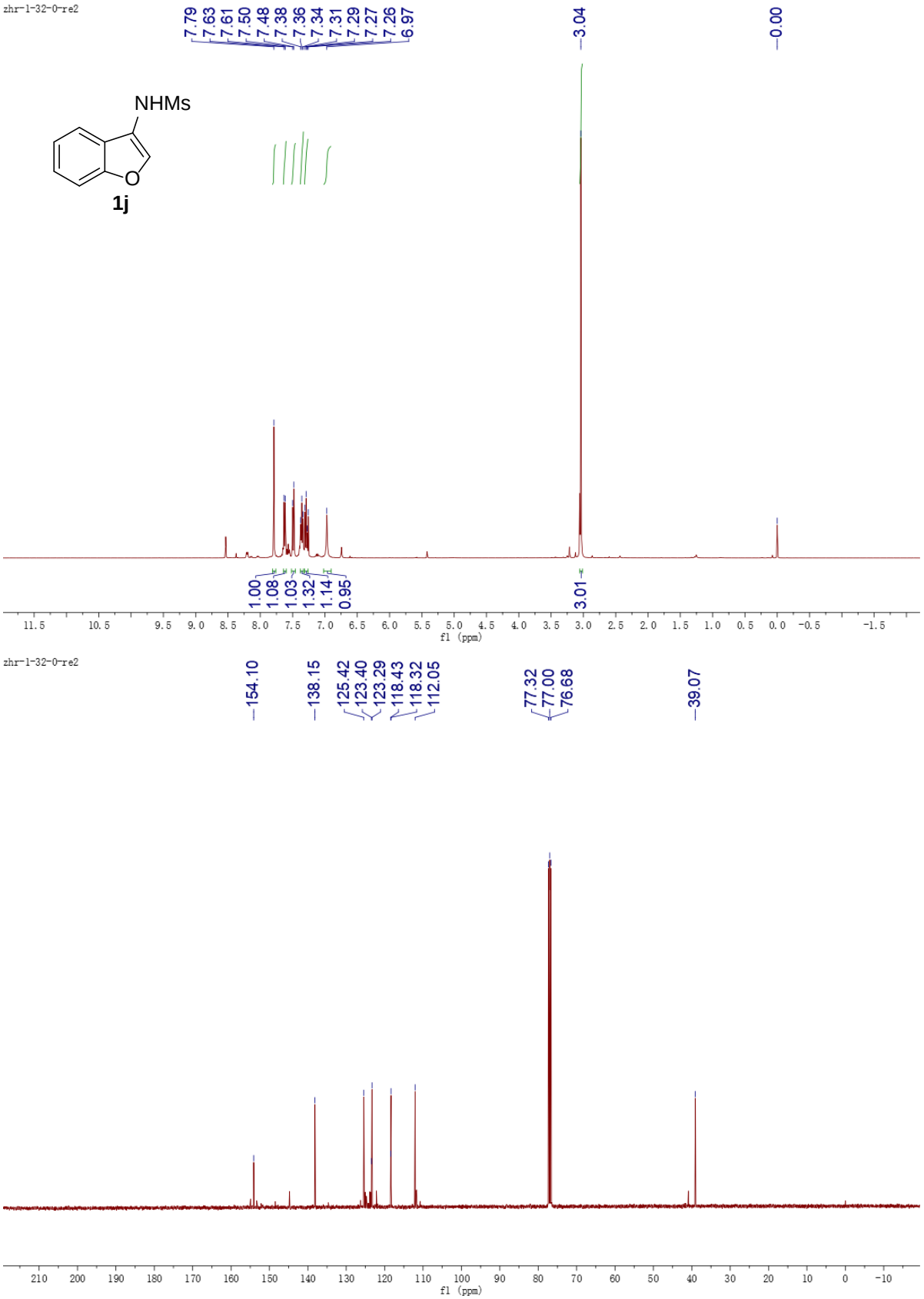
^{19}F NMR (376 MHz) spectrum of **1g**



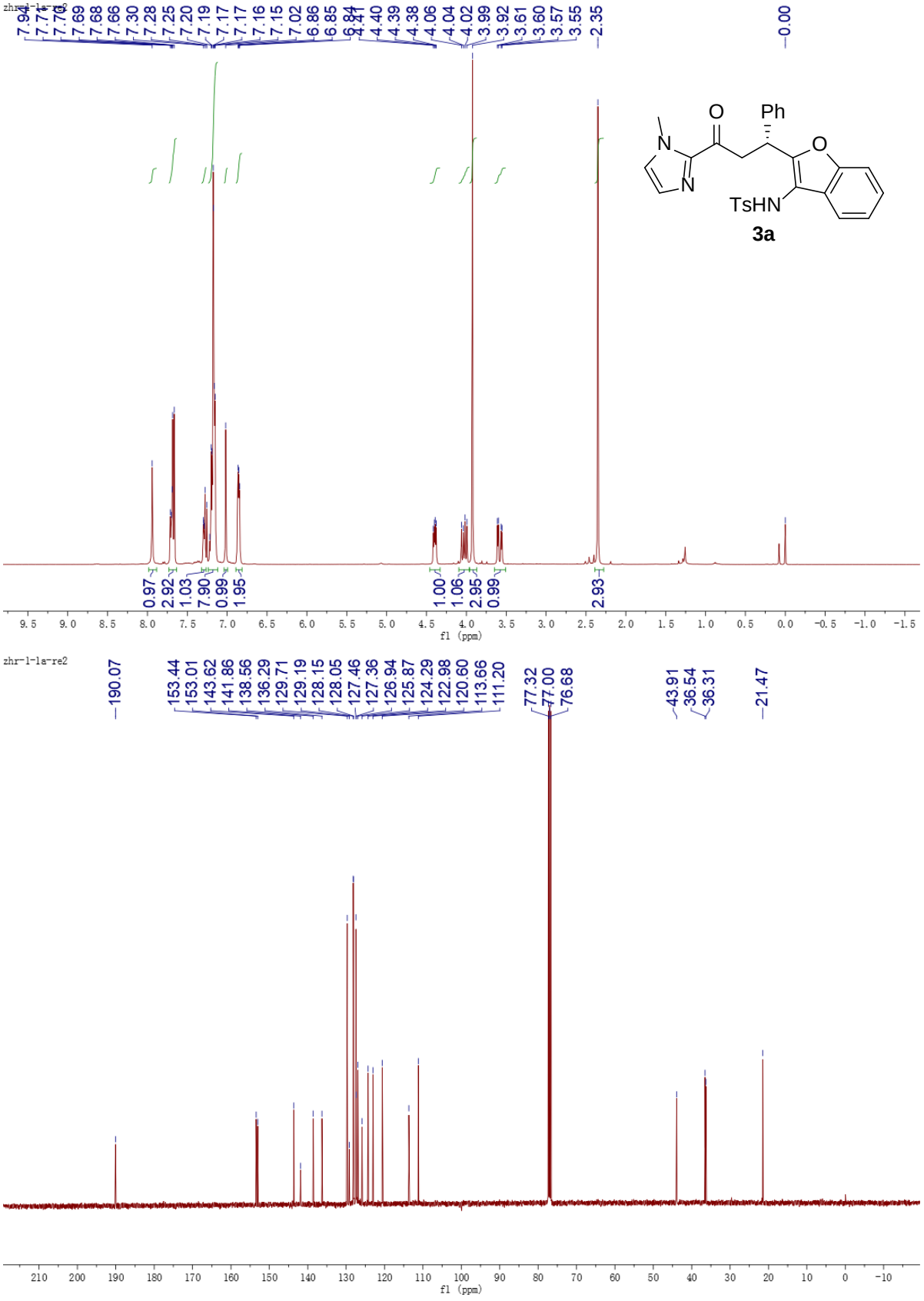
^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **1h**



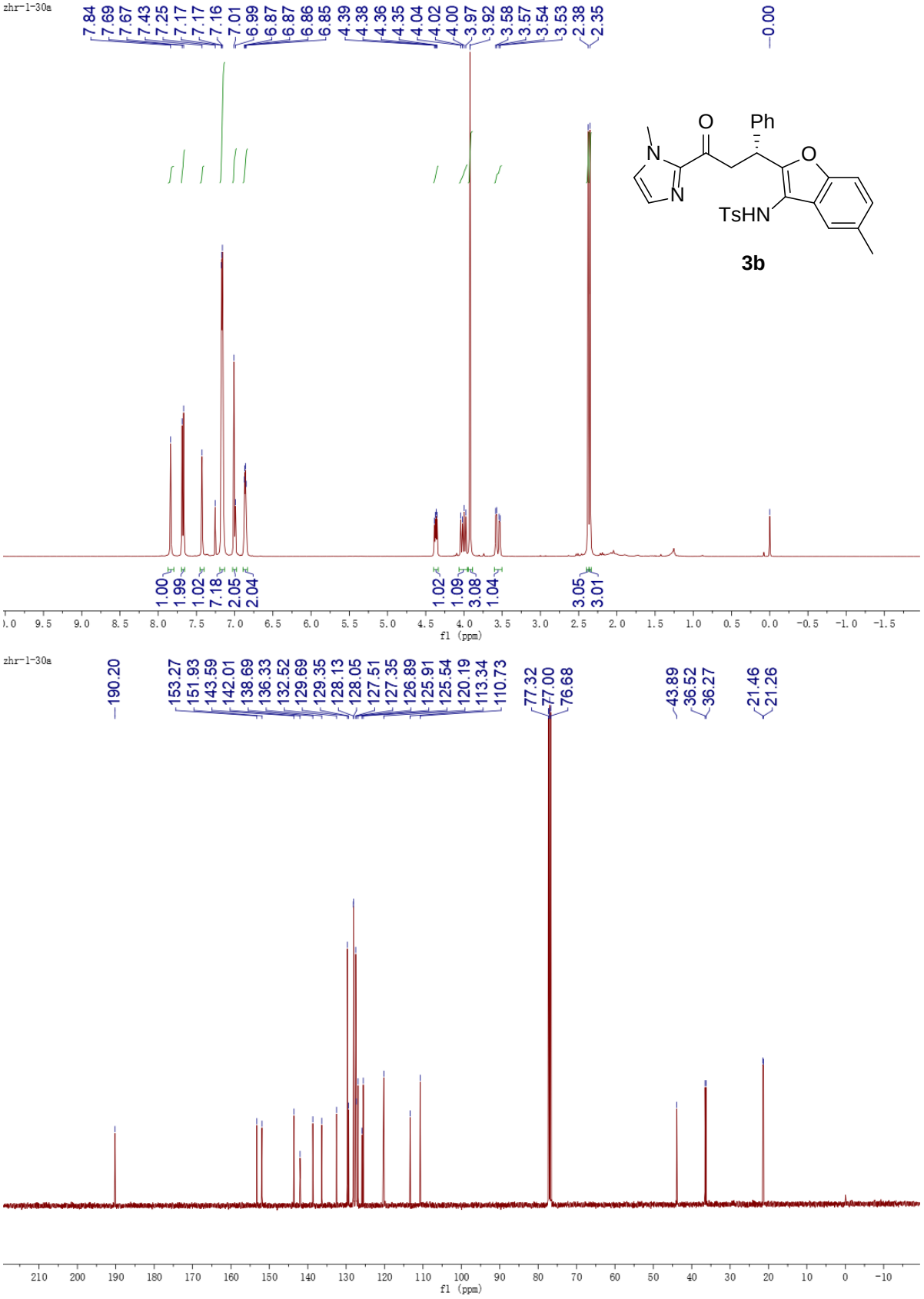
^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **1i**



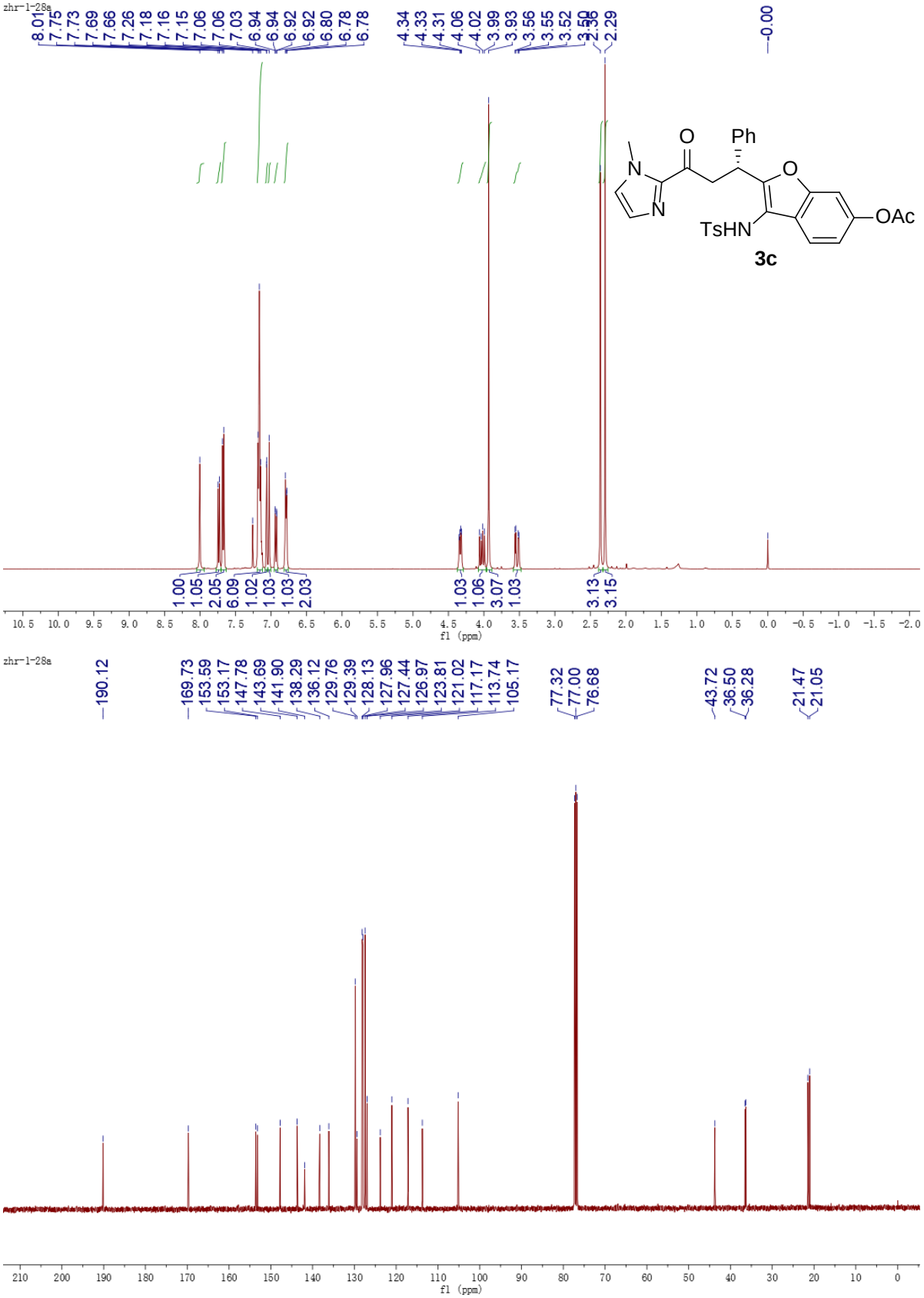
^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **1j**



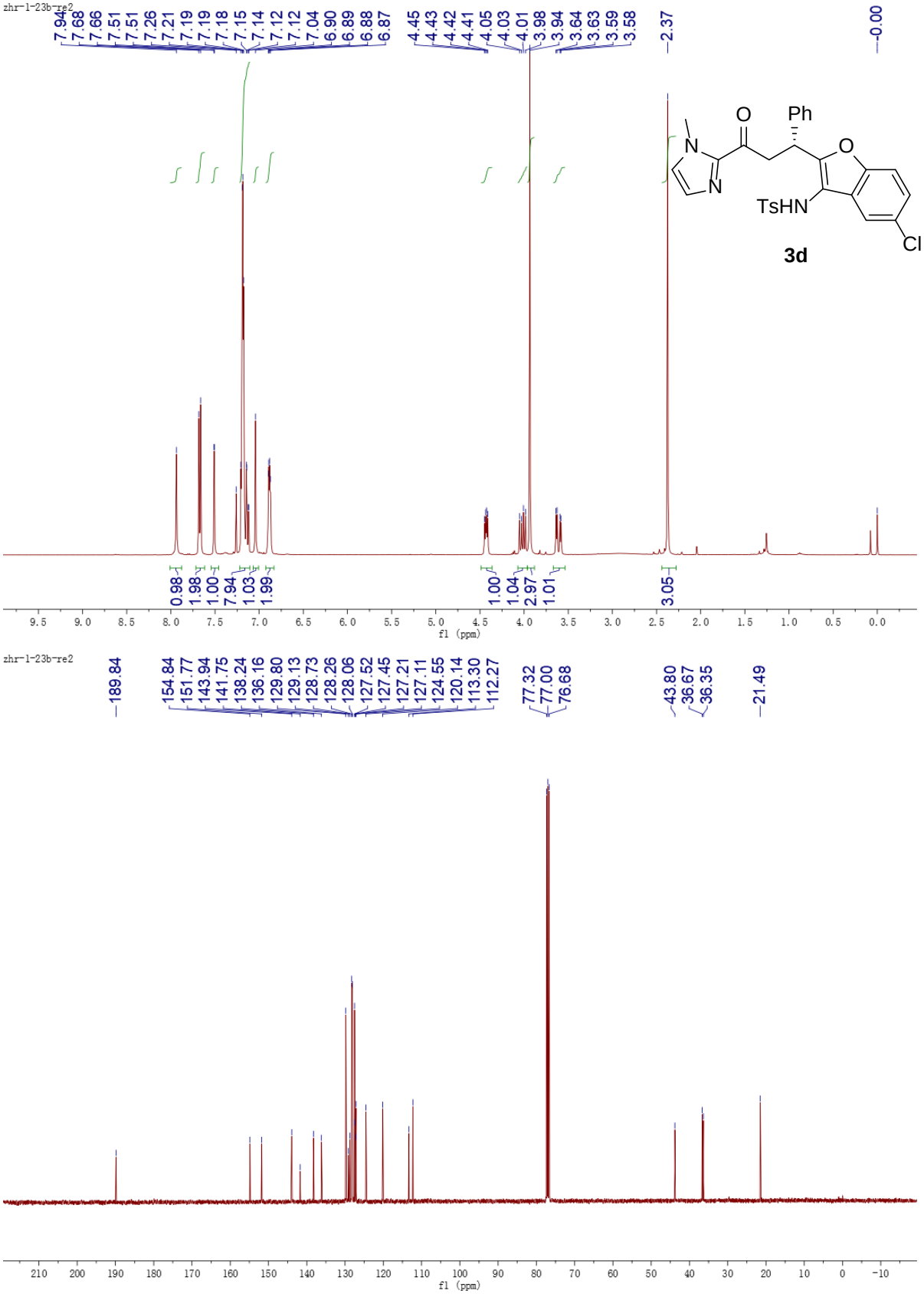
^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **3a**



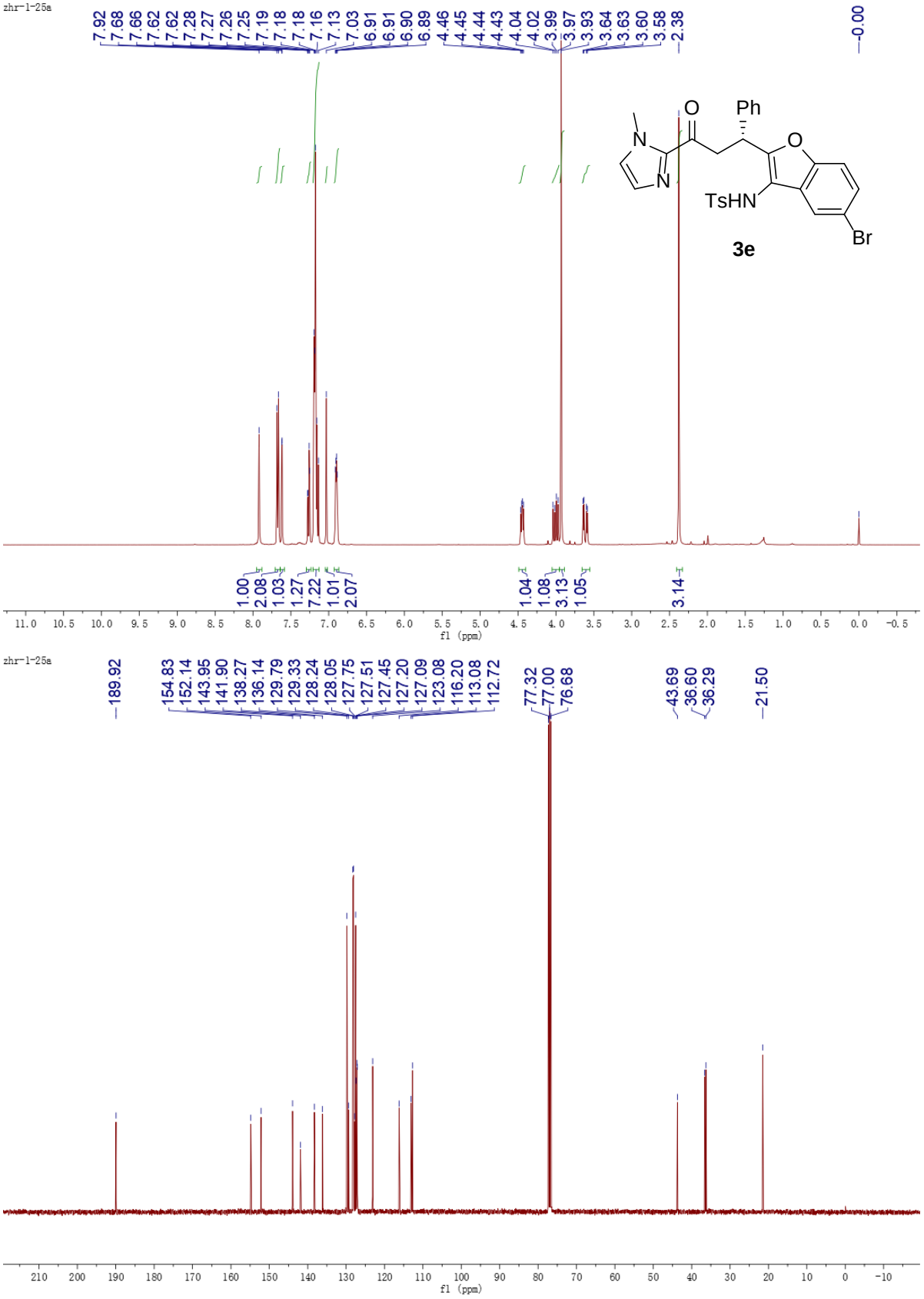
^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **3b**



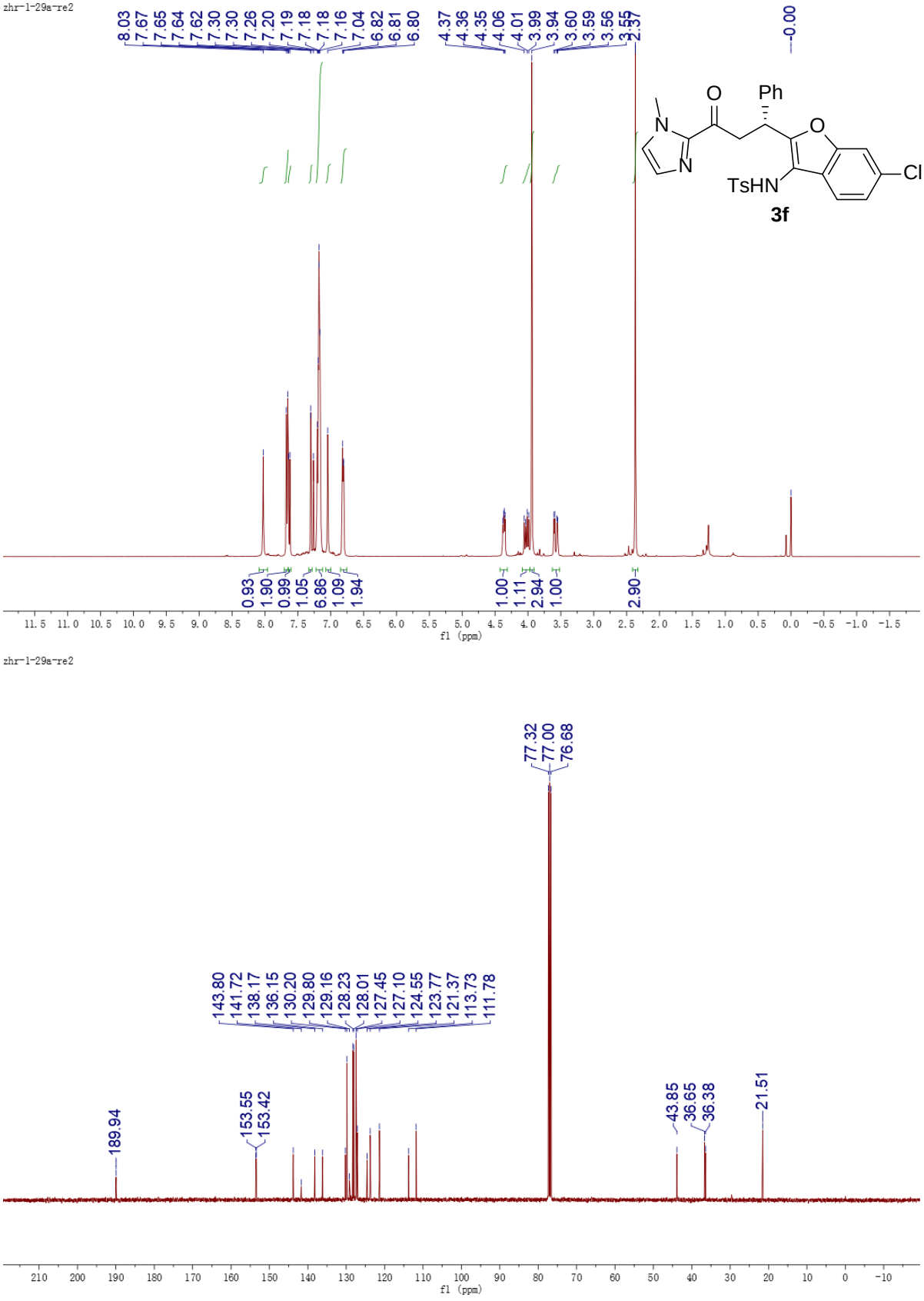
^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **3c**



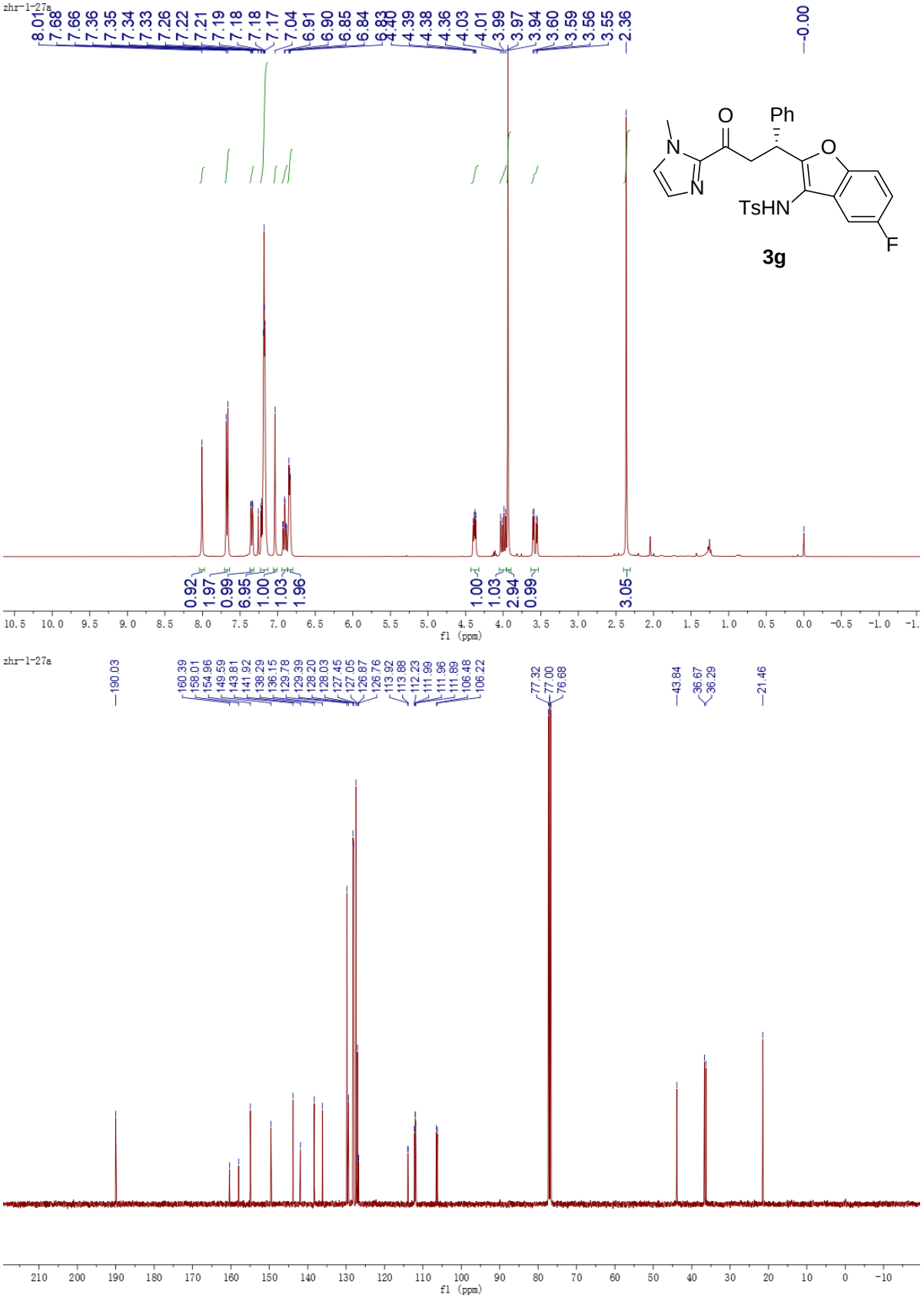
^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **3d**



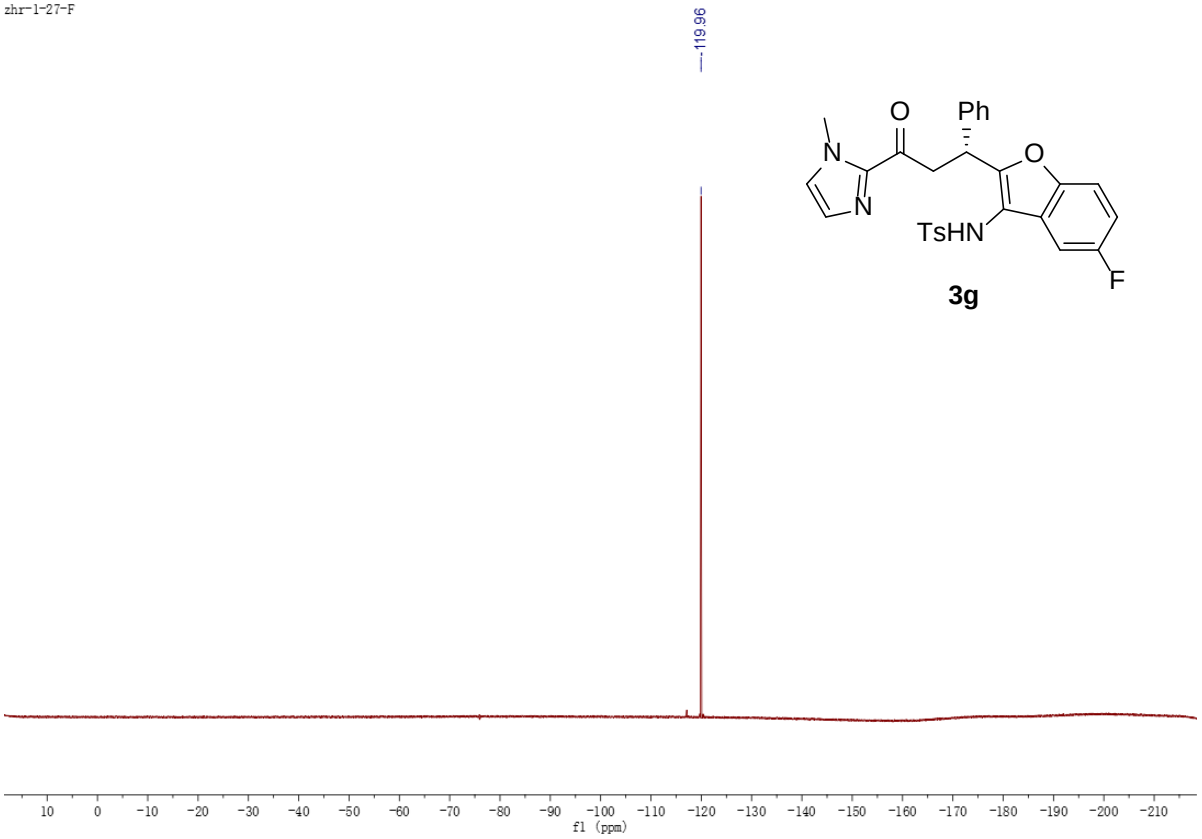
^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **3e**



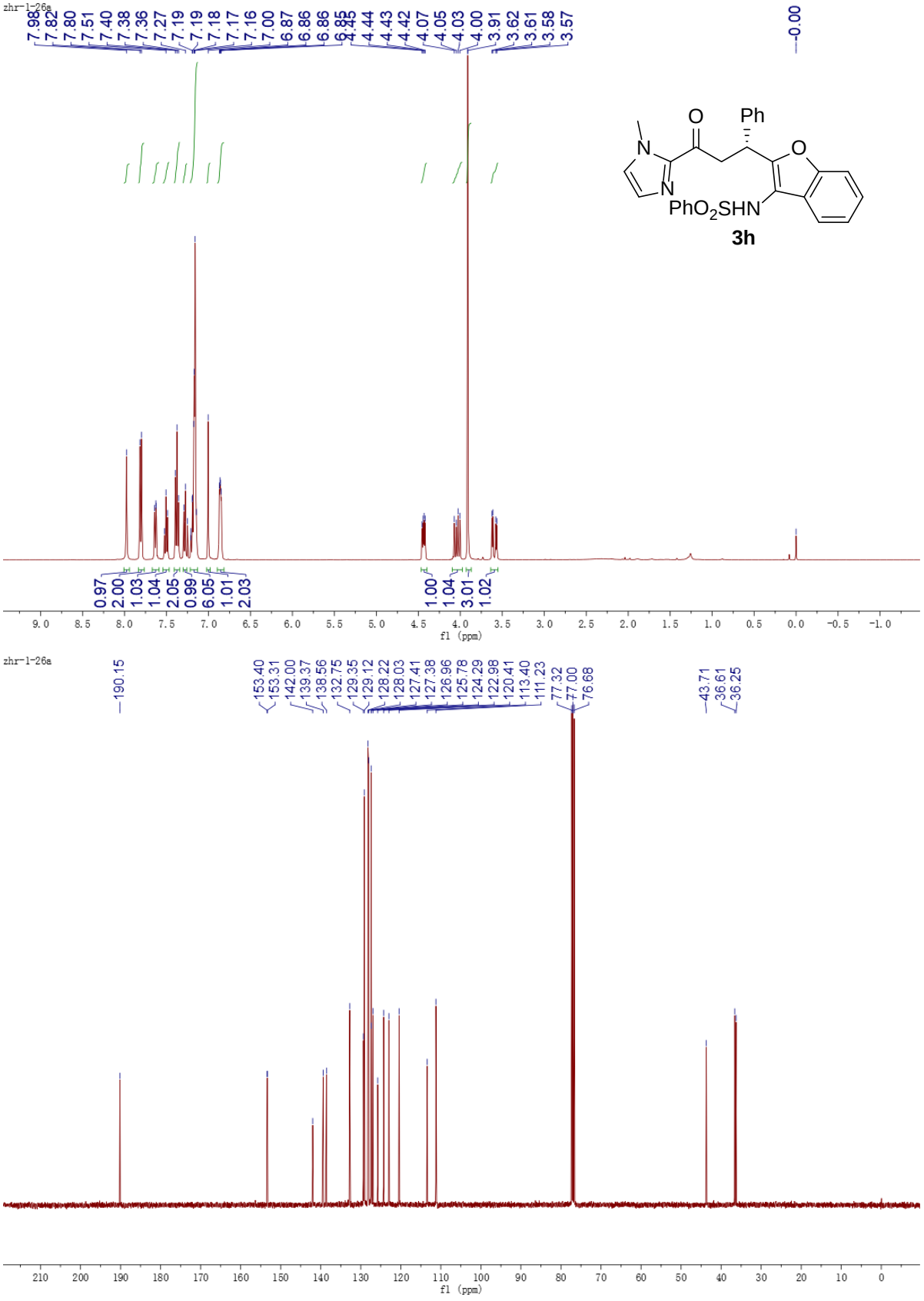
^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **3f**



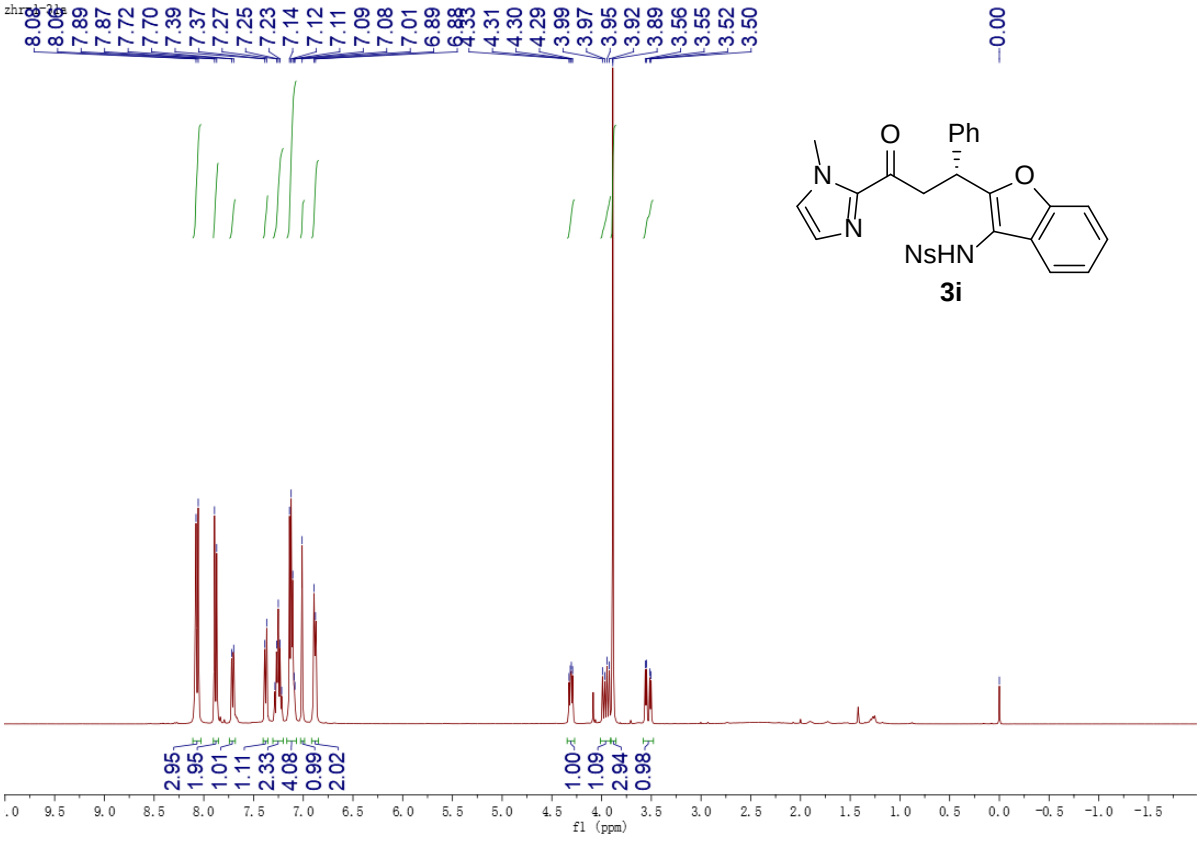
^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **3g**

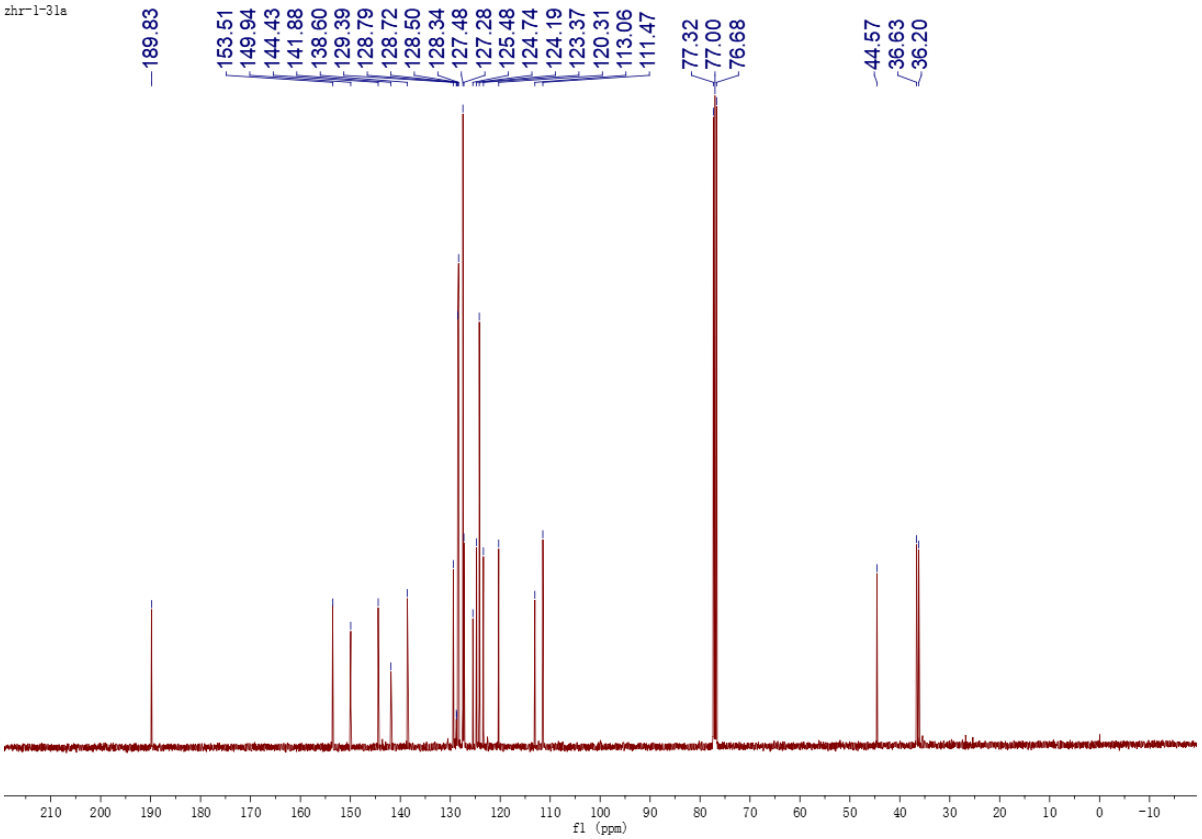


^{19}F NMR (376 MHz) spectrum of **3g**

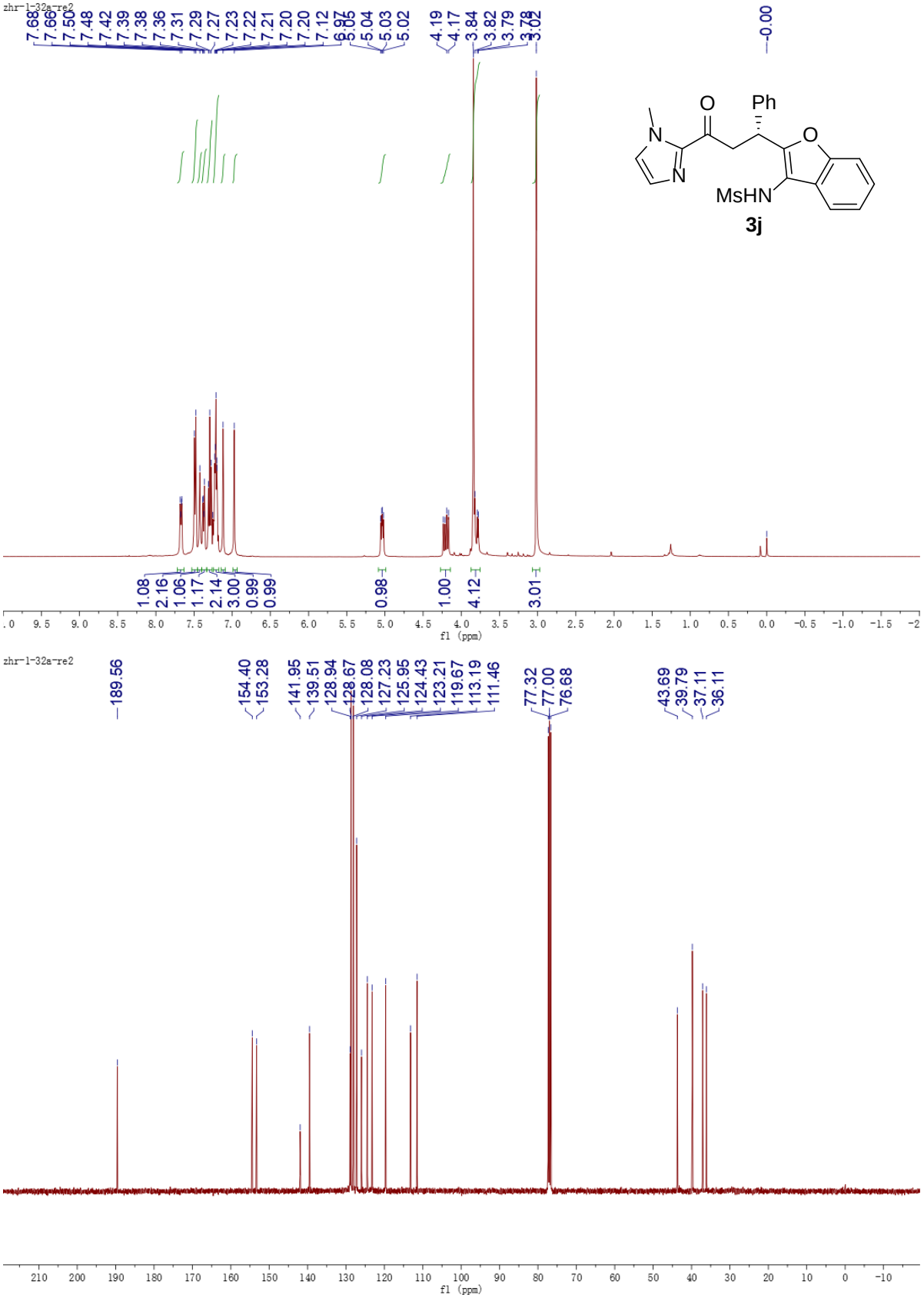


^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **3h**

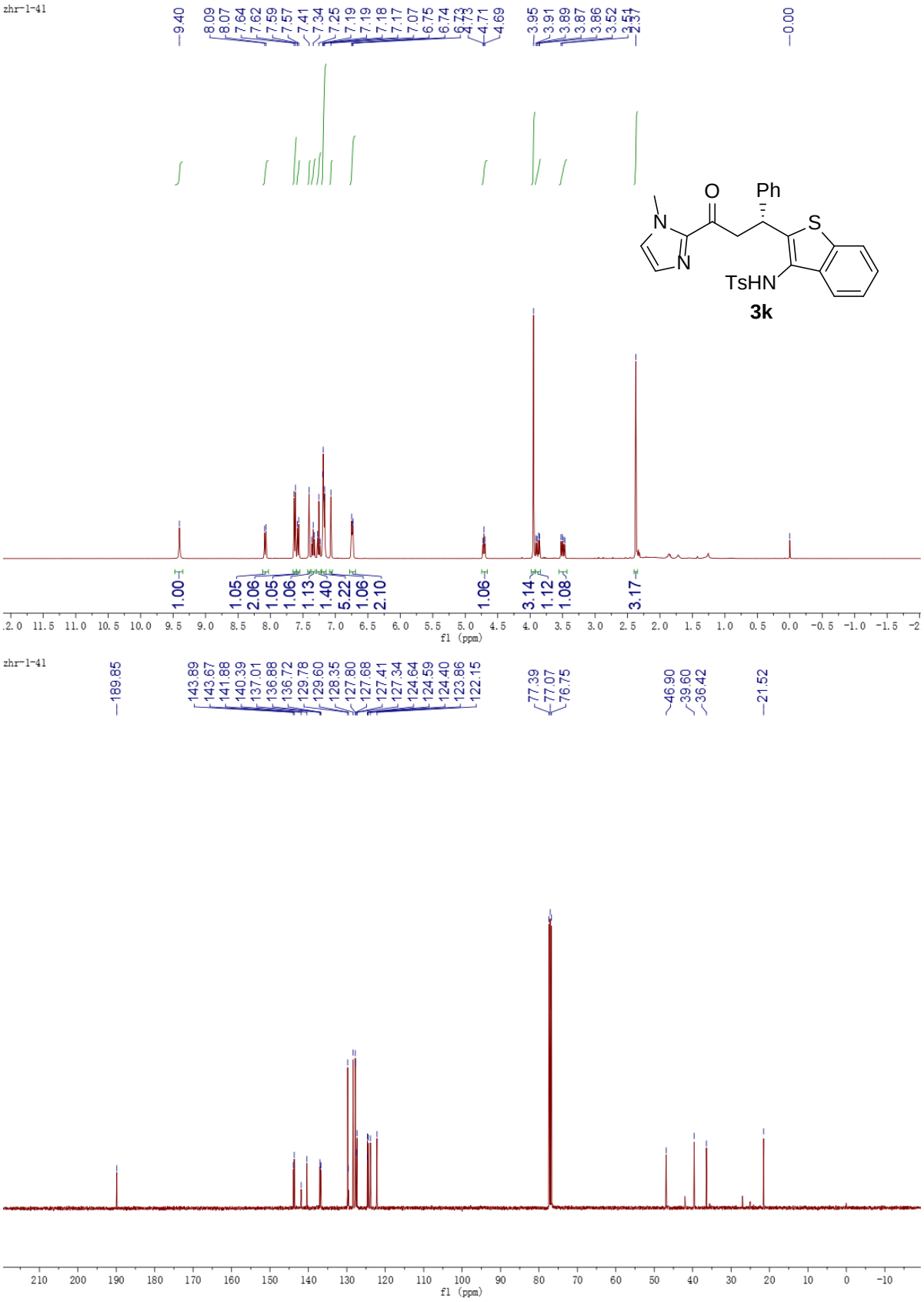




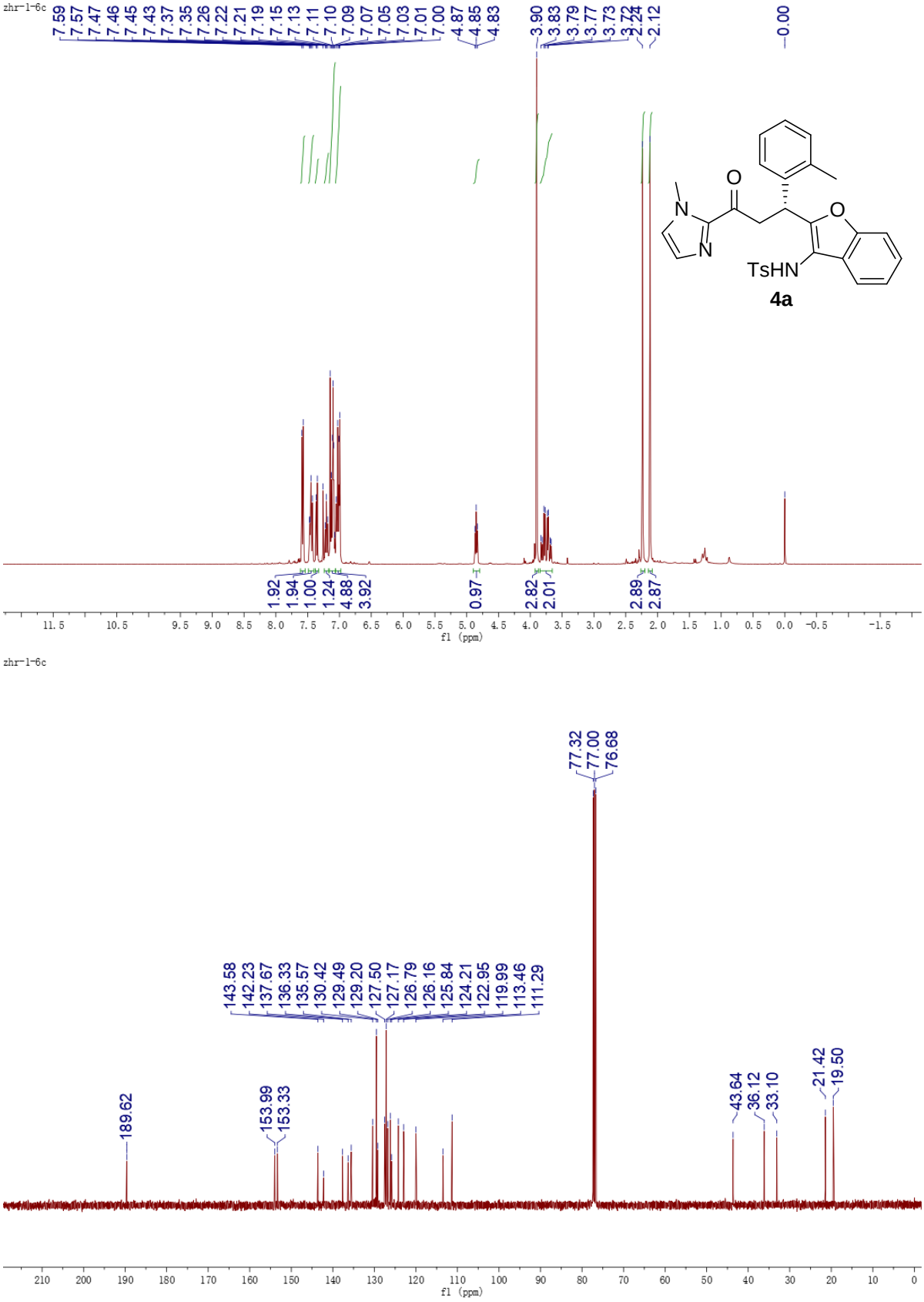
^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **3i**



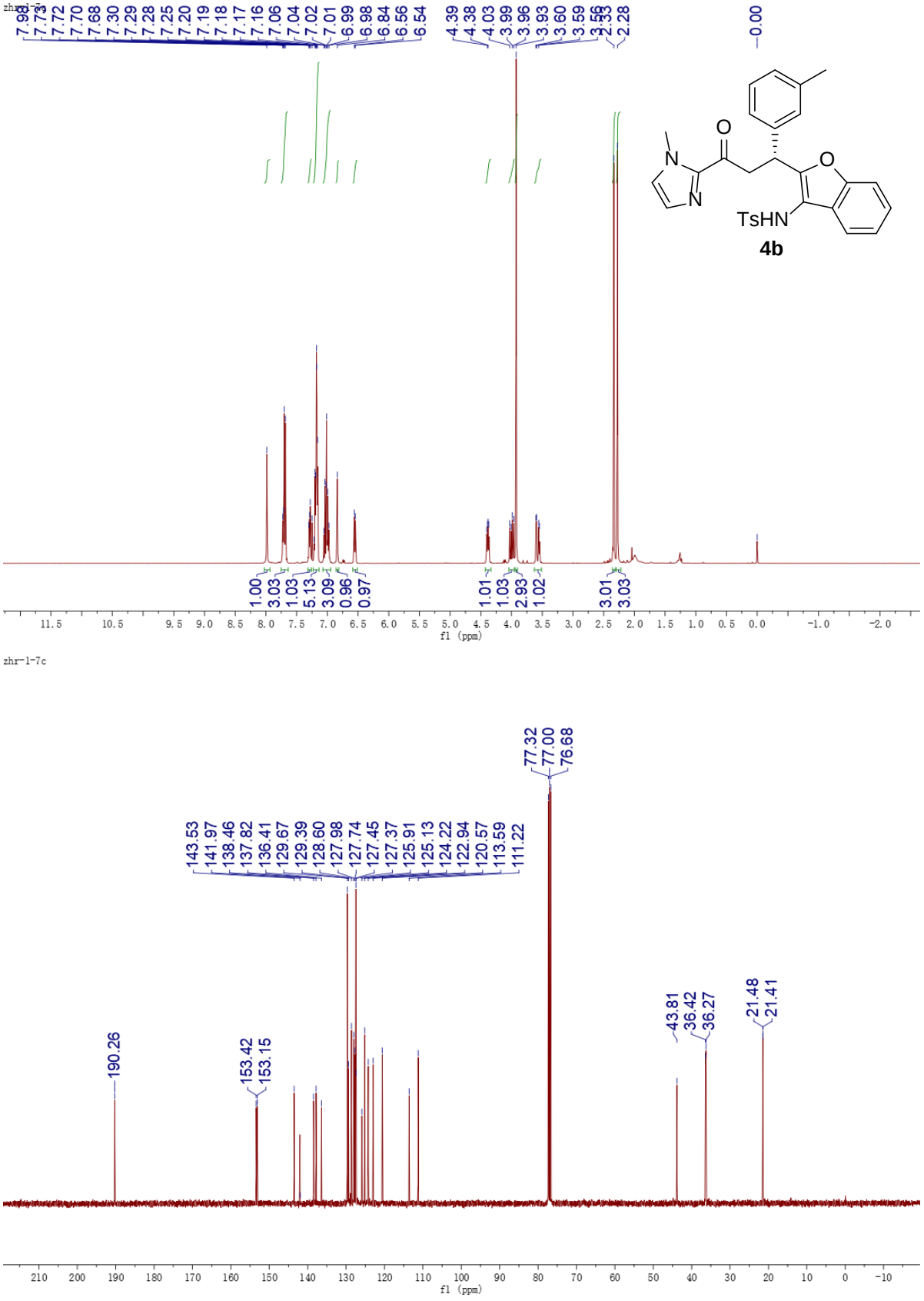
^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **3j**



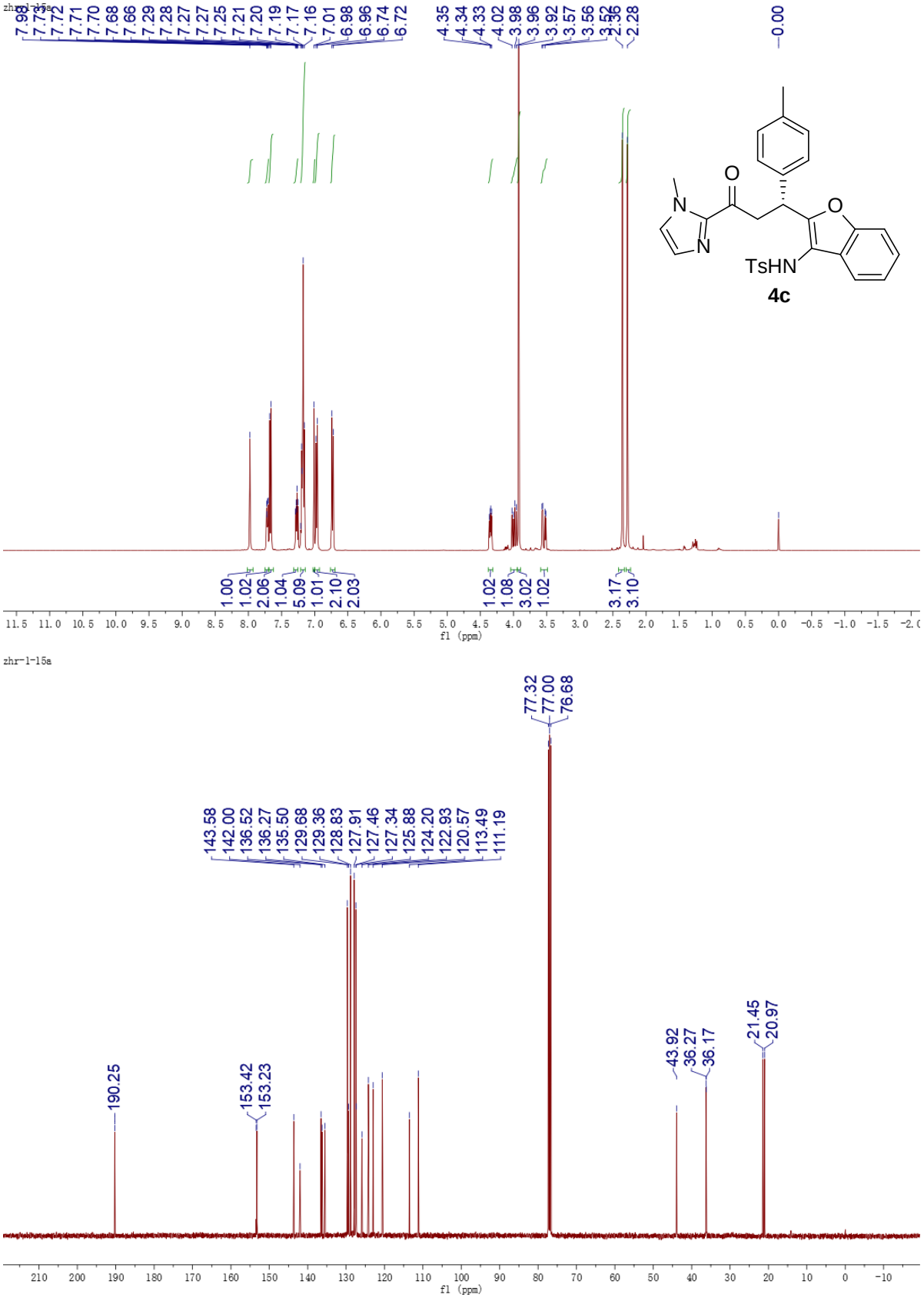
^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **3k**



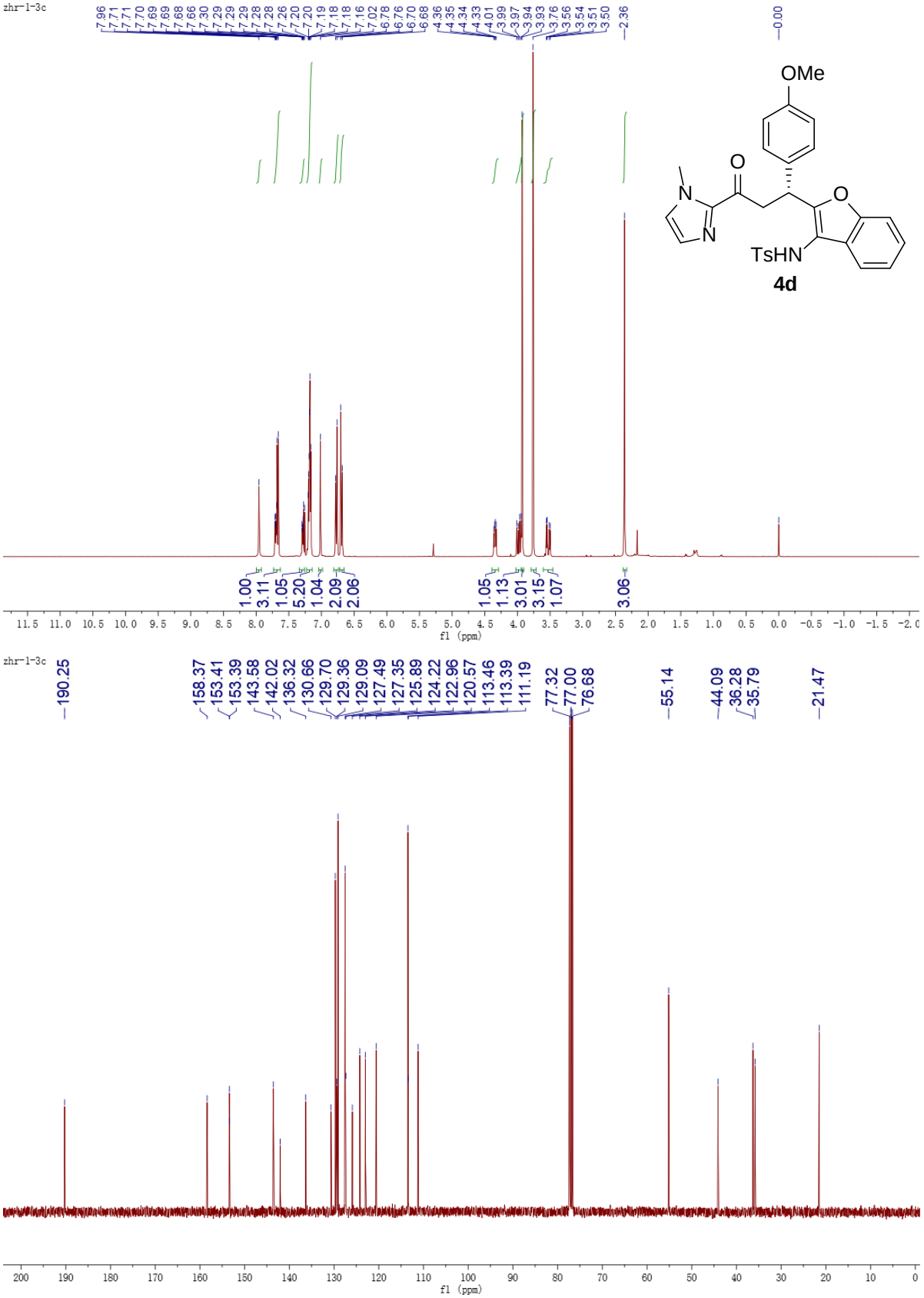
^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **4a**



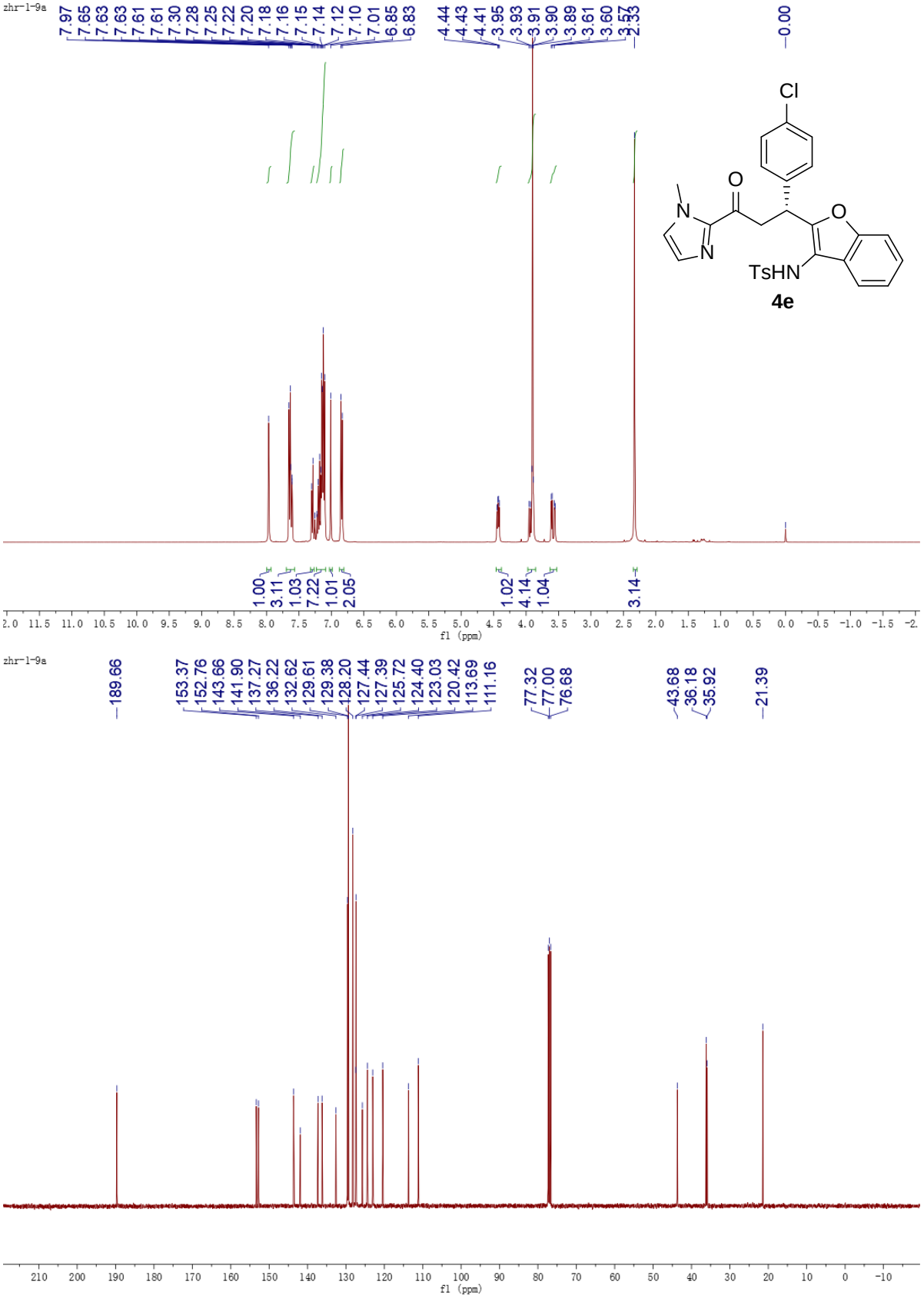
^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **4b**



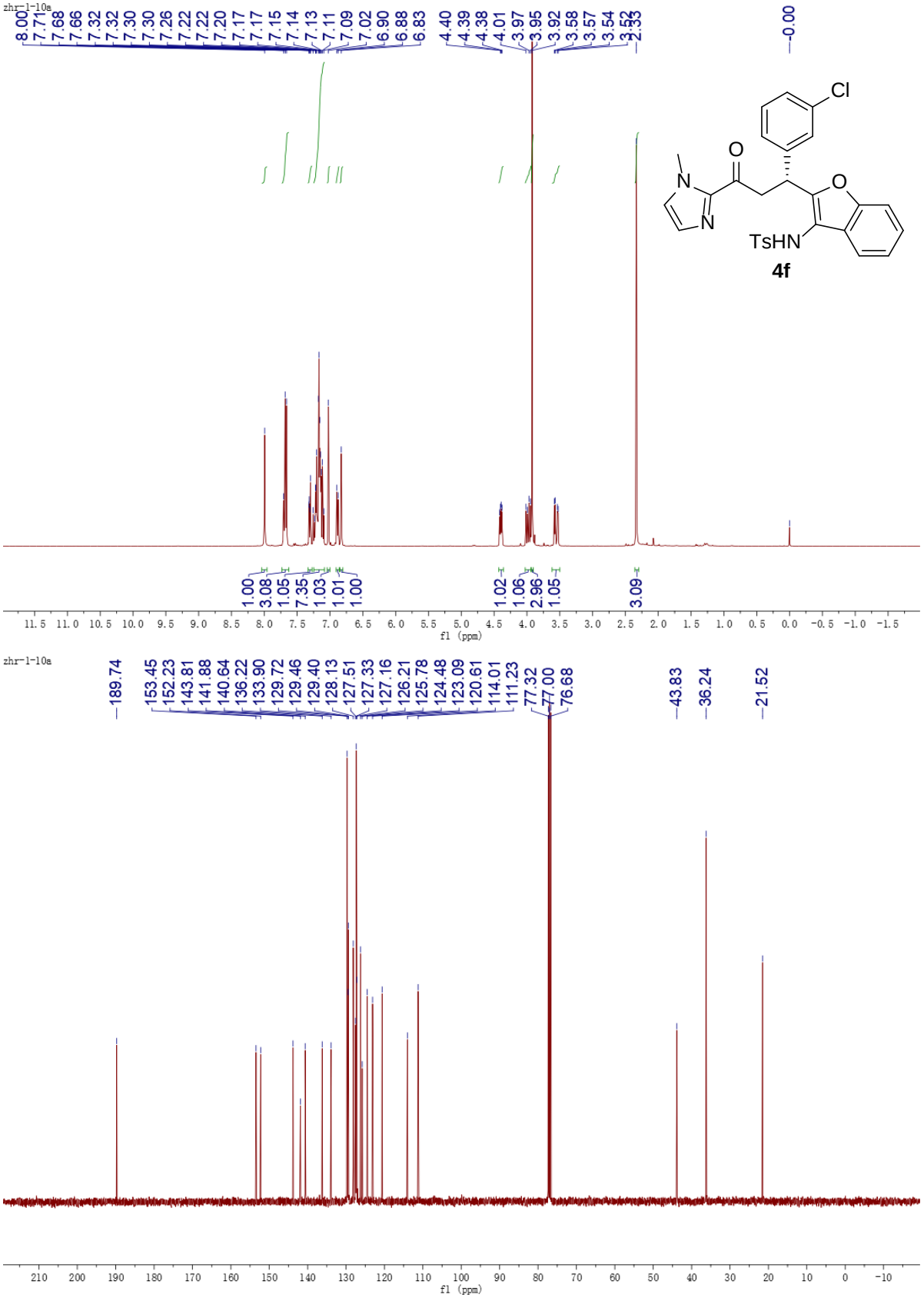
^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **4c**



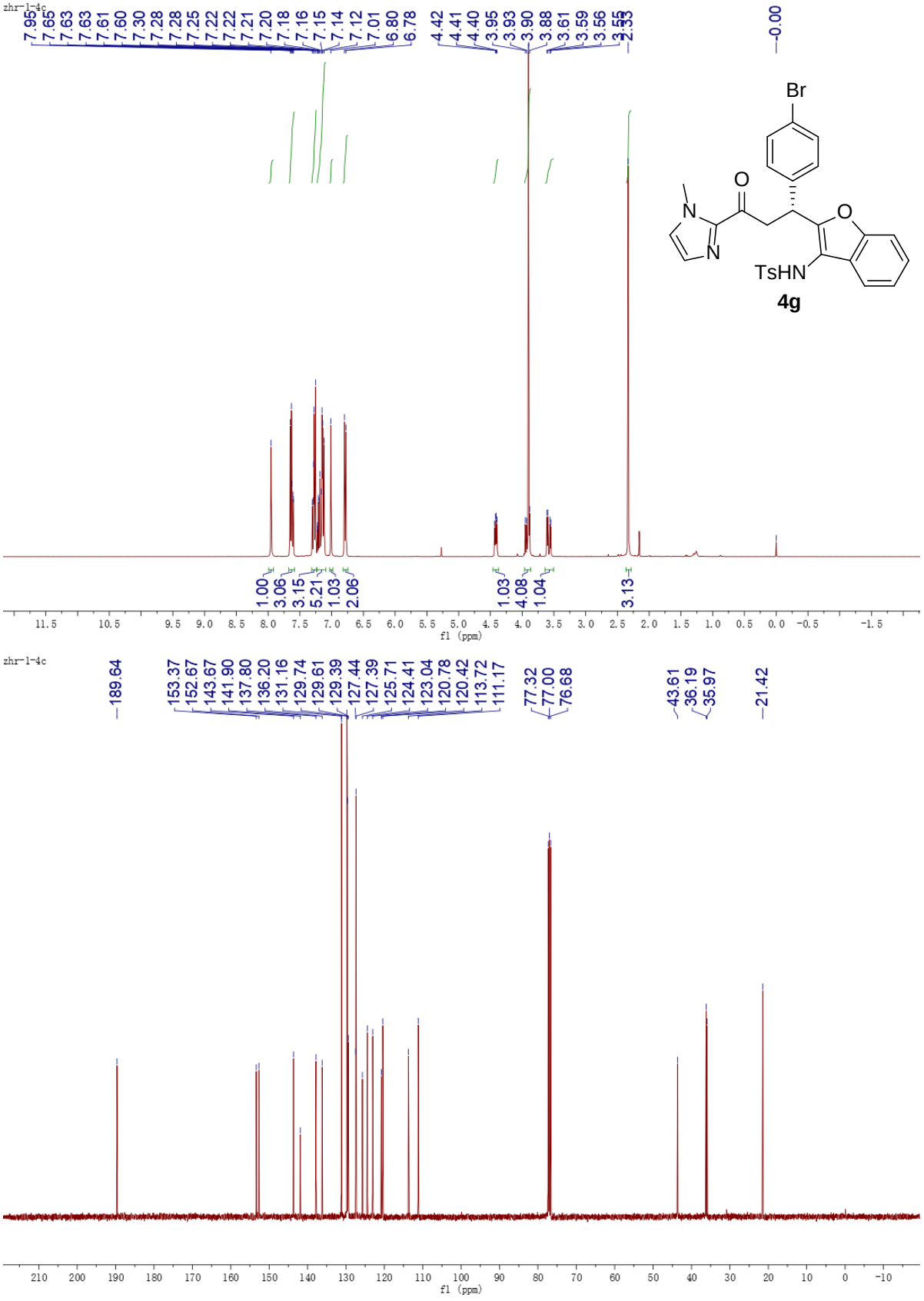
^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **4d**



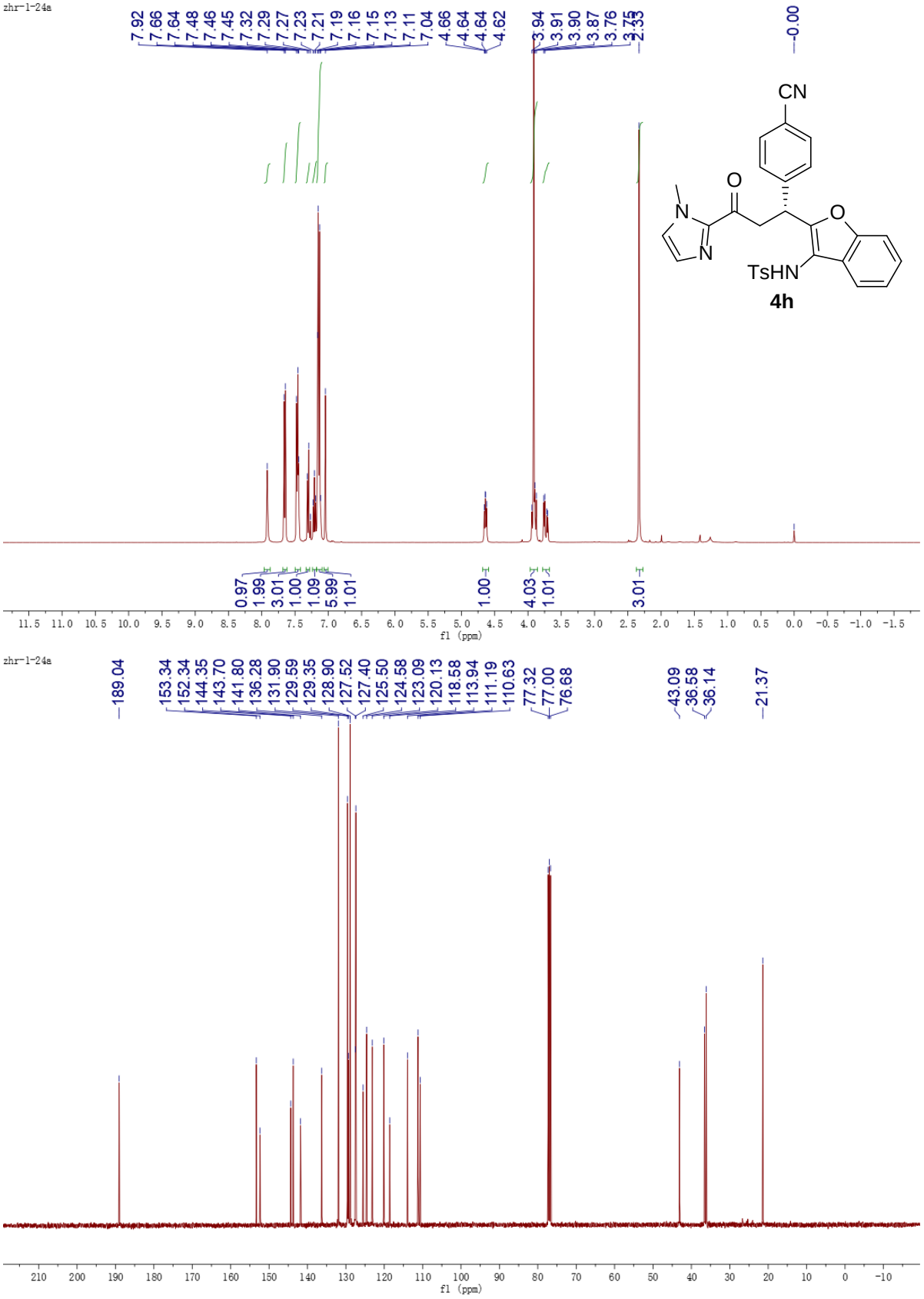
^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **4e**



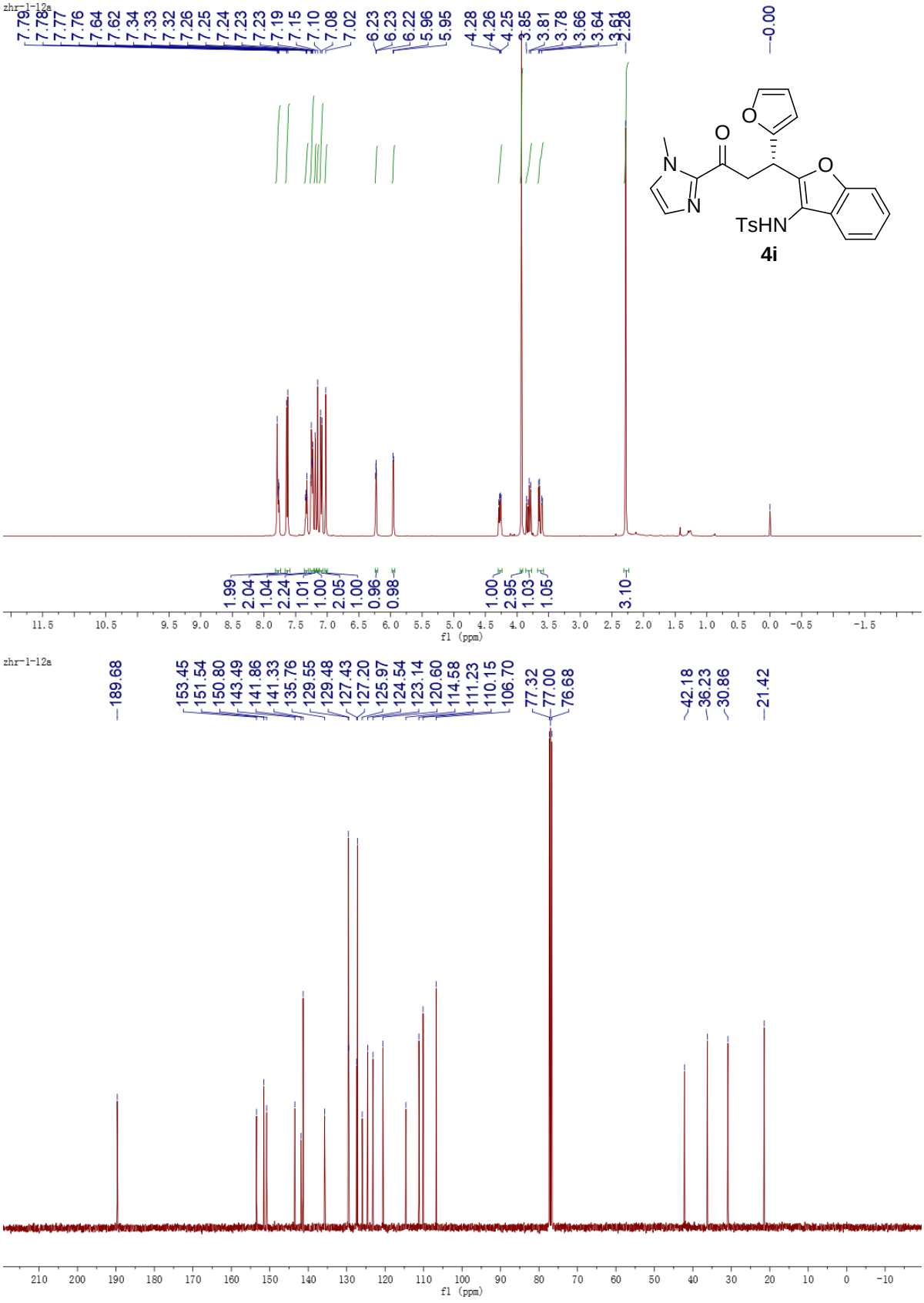
^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **4f**



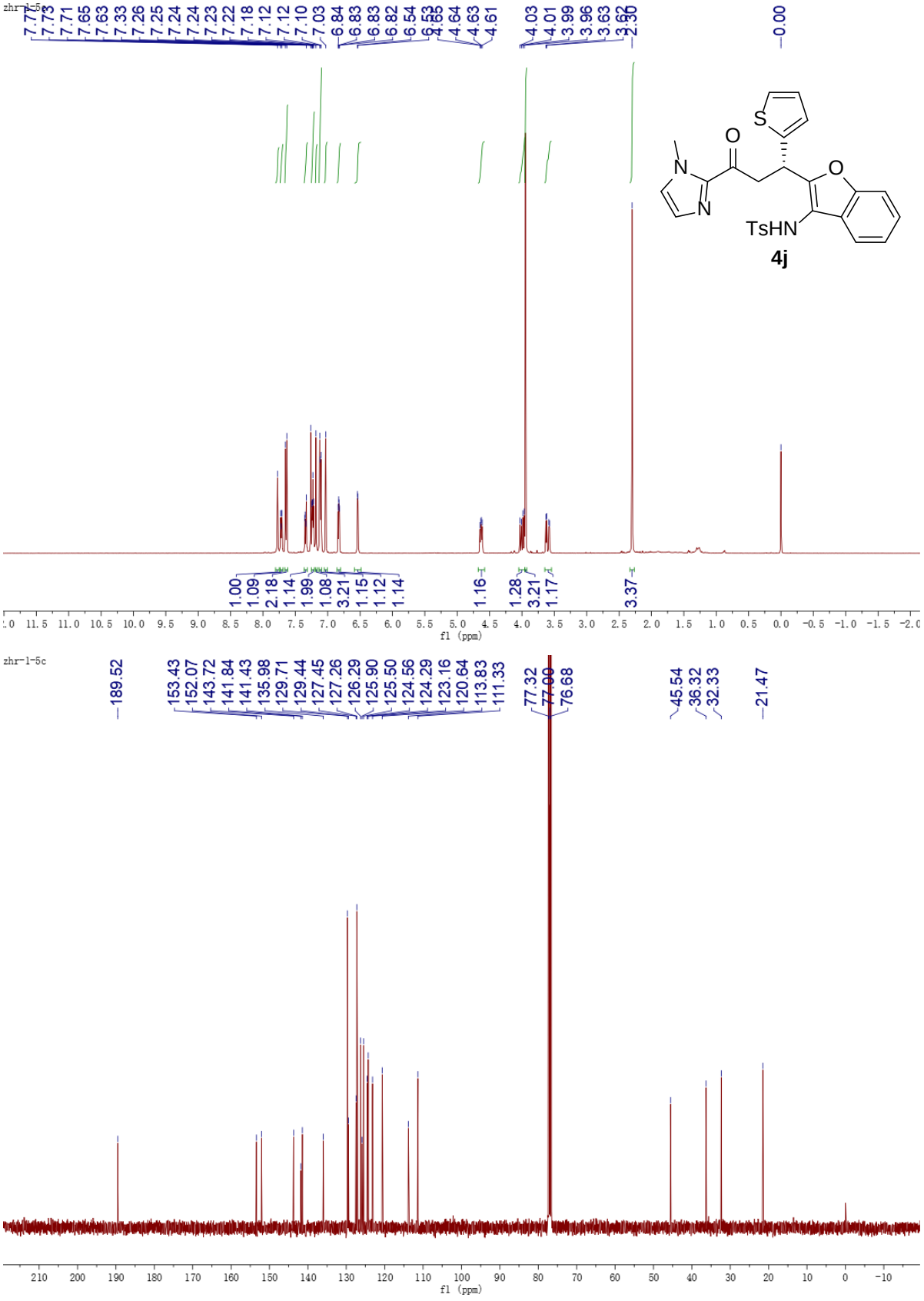
^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **4g**



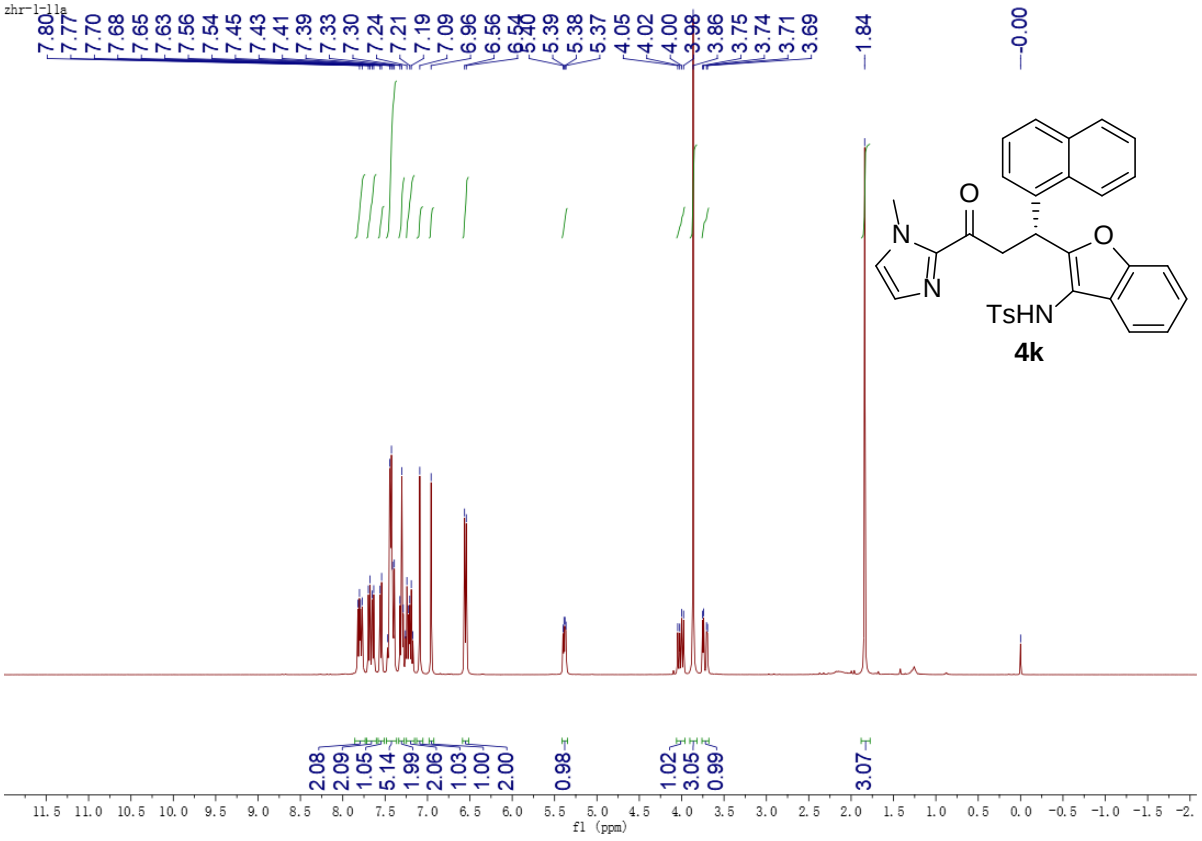
^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **4h**

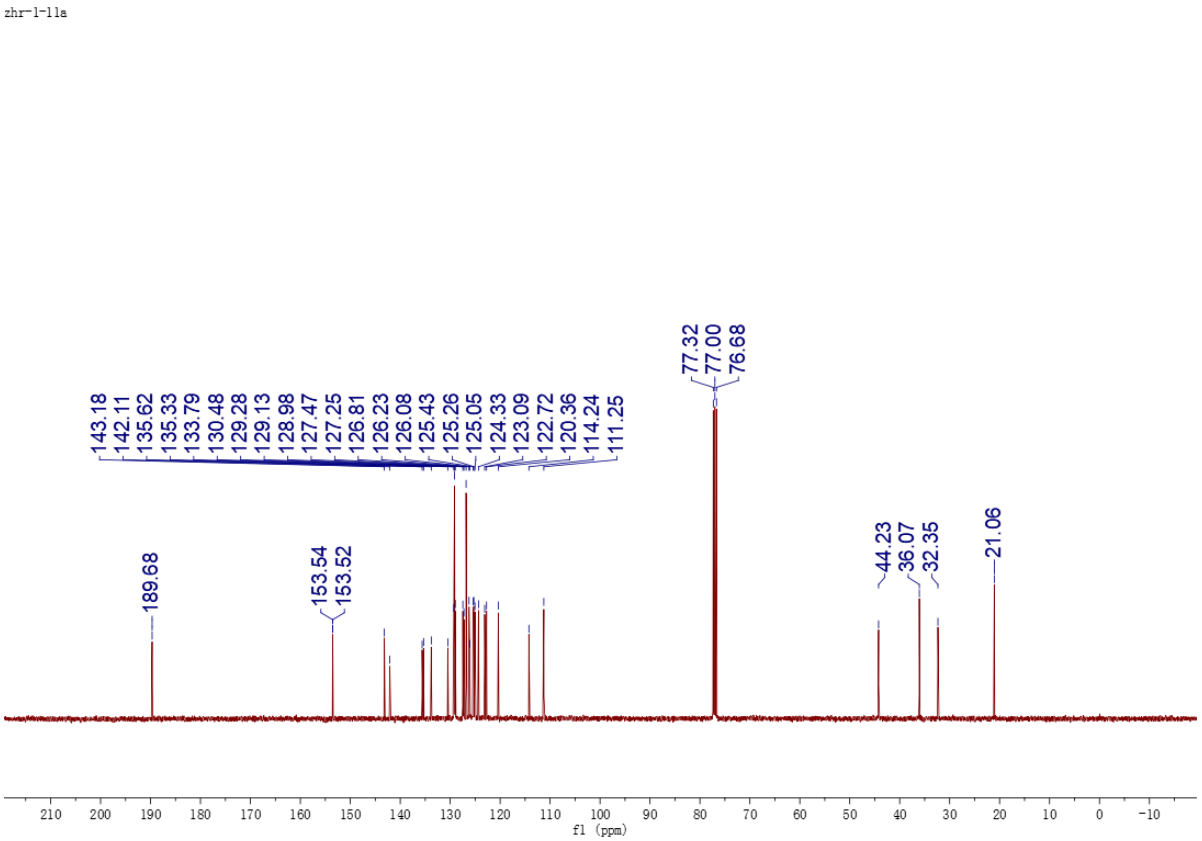


^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **4i**

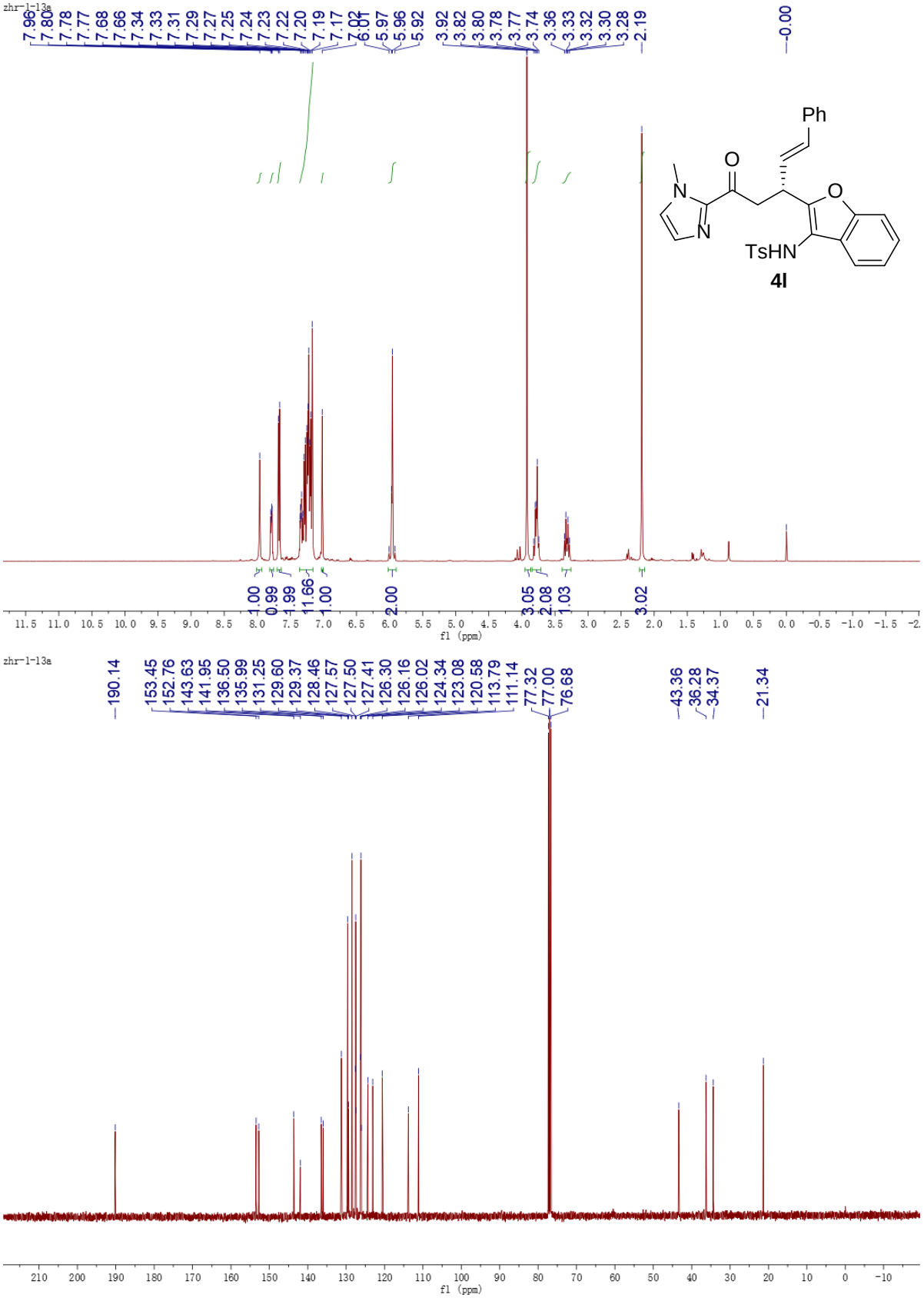


^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **4j**





^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **4k**



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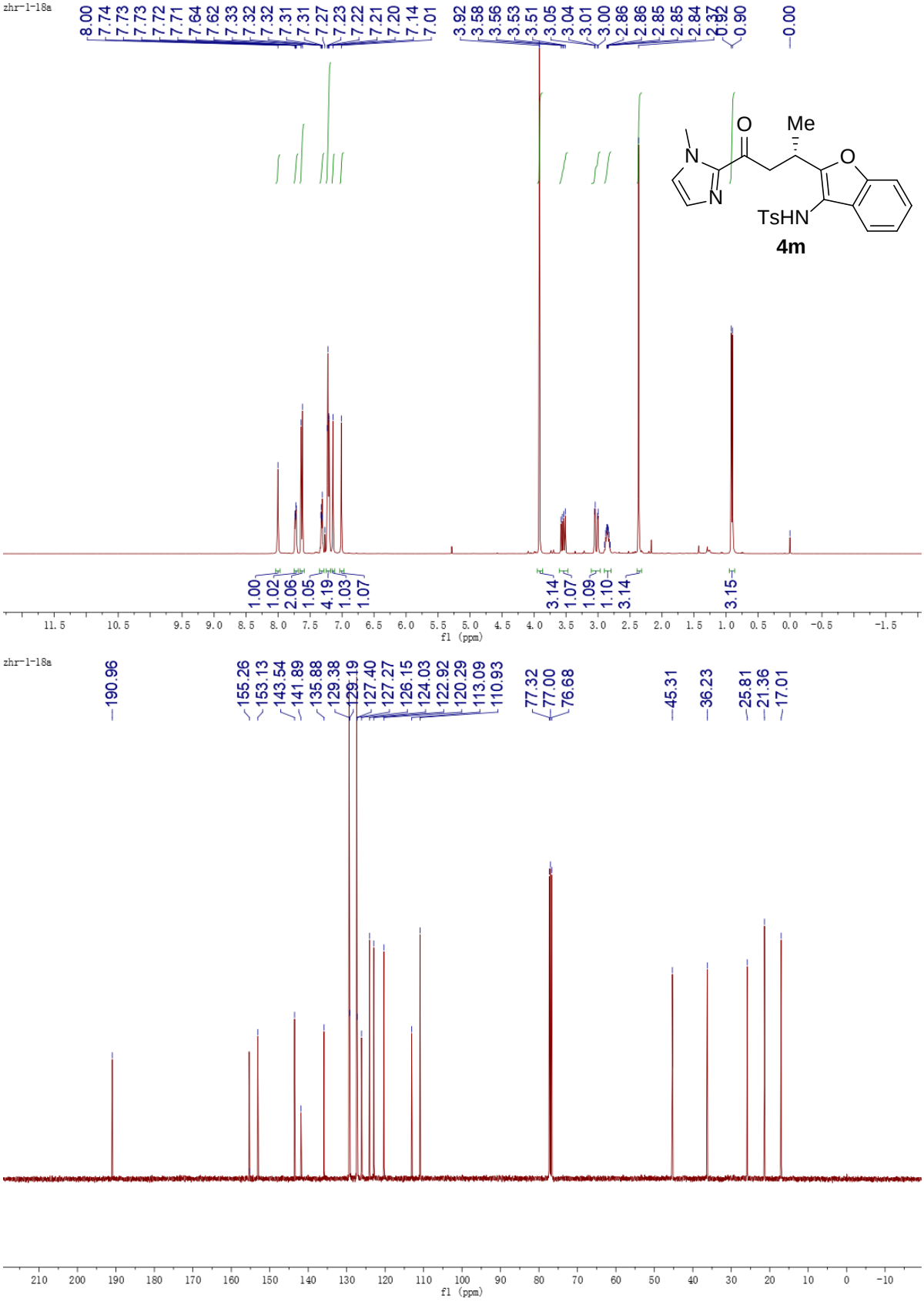
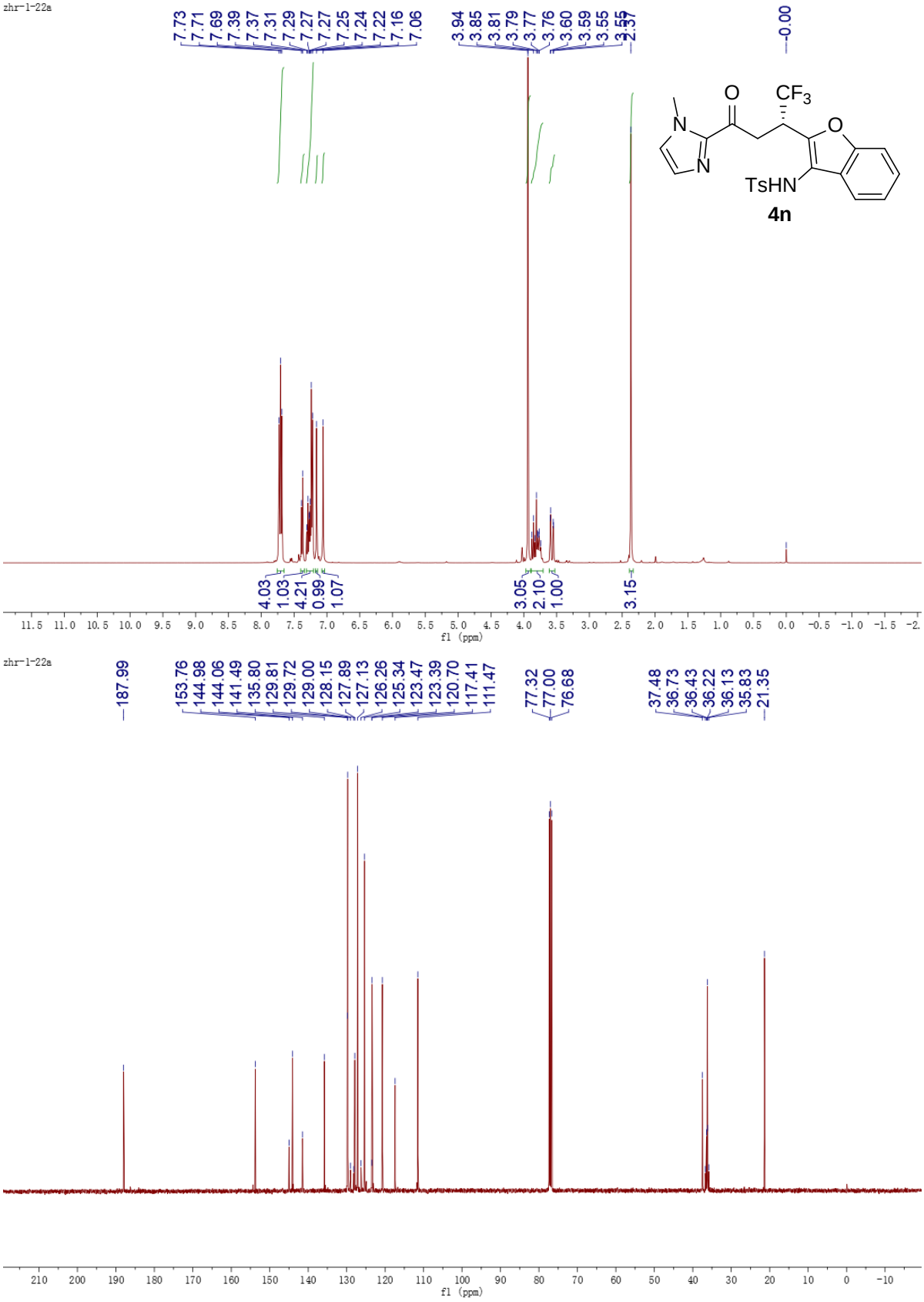


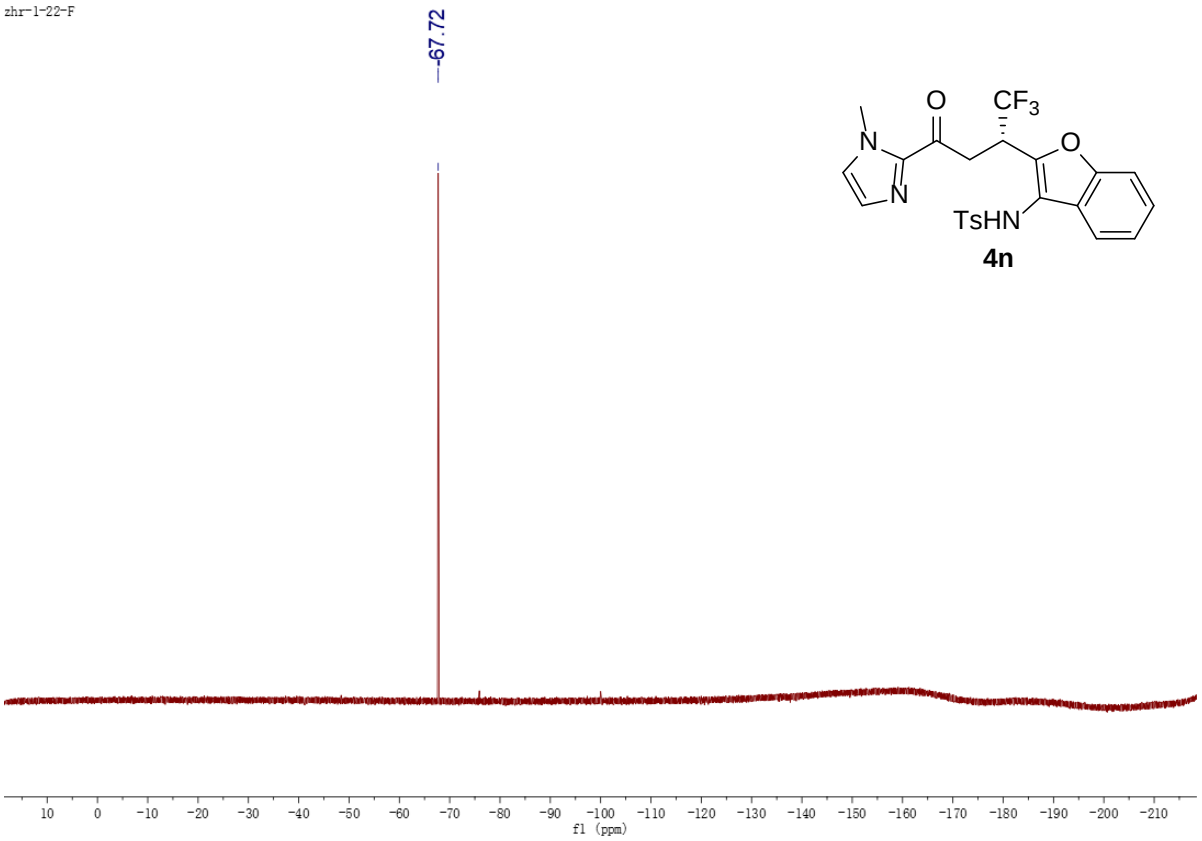
O
Me
N
N
O
TsHN

4m

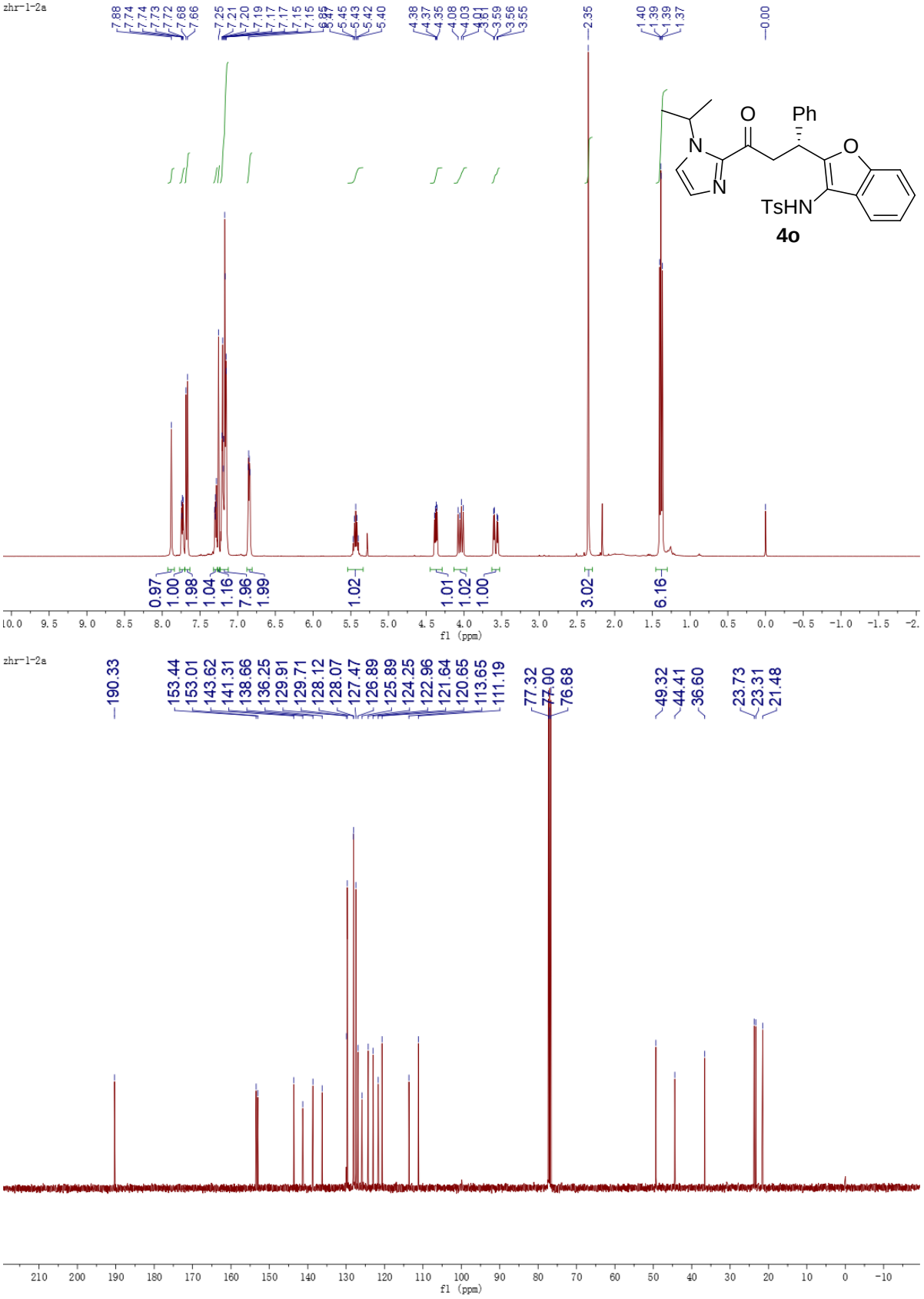
^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **4m**



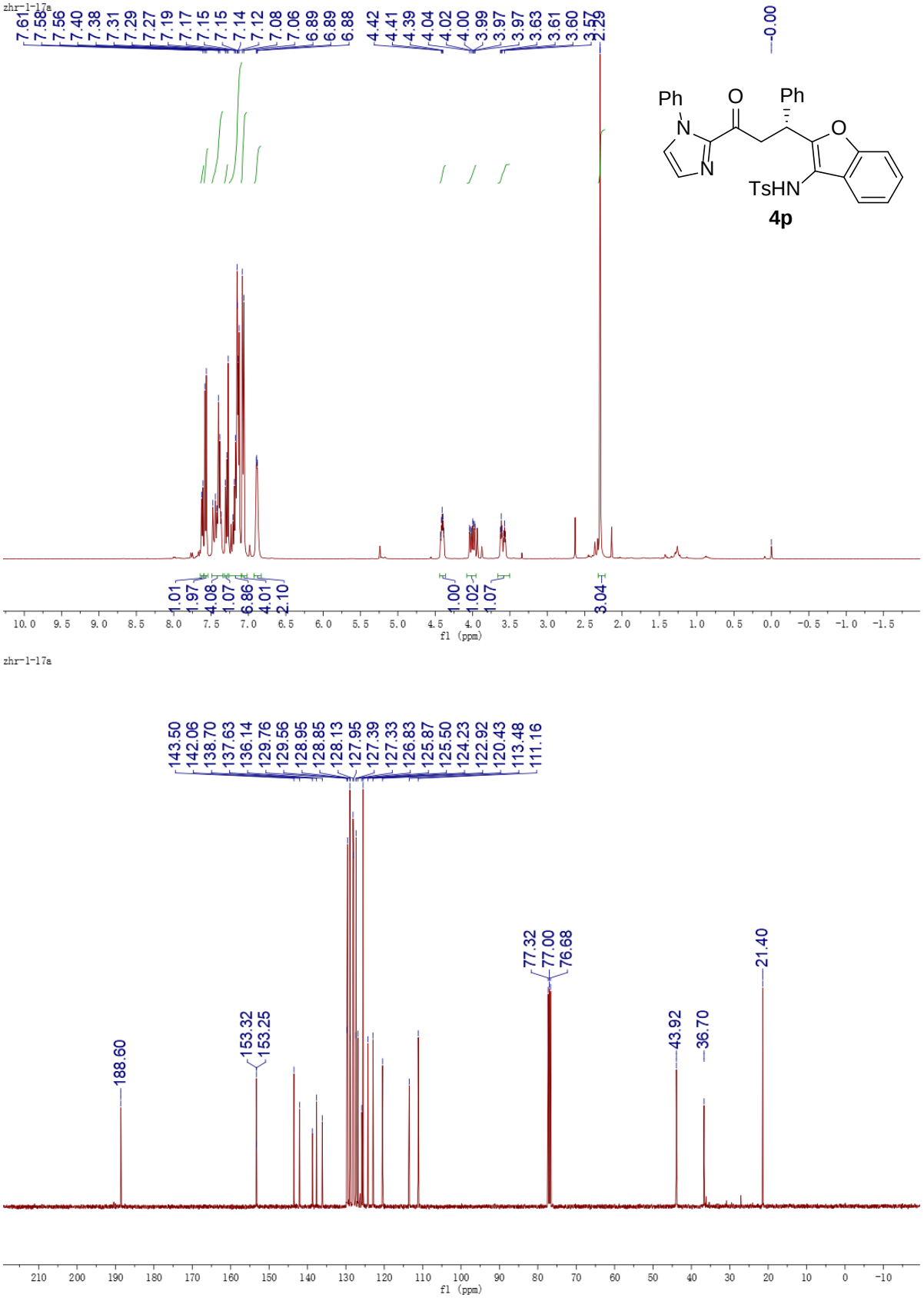
^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **4n**



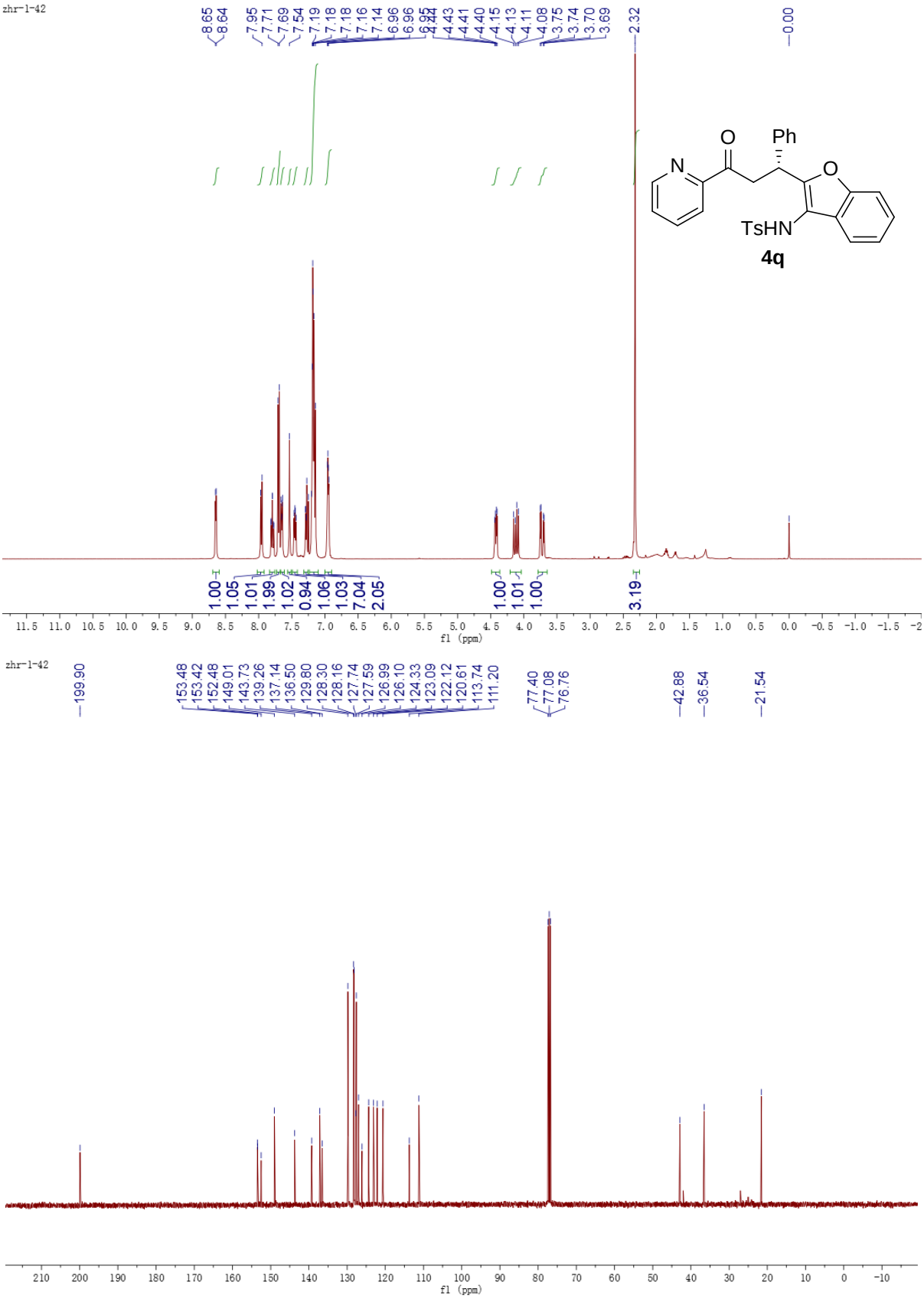
^{19}F NMR (376 MHz) spectrum of **4n**



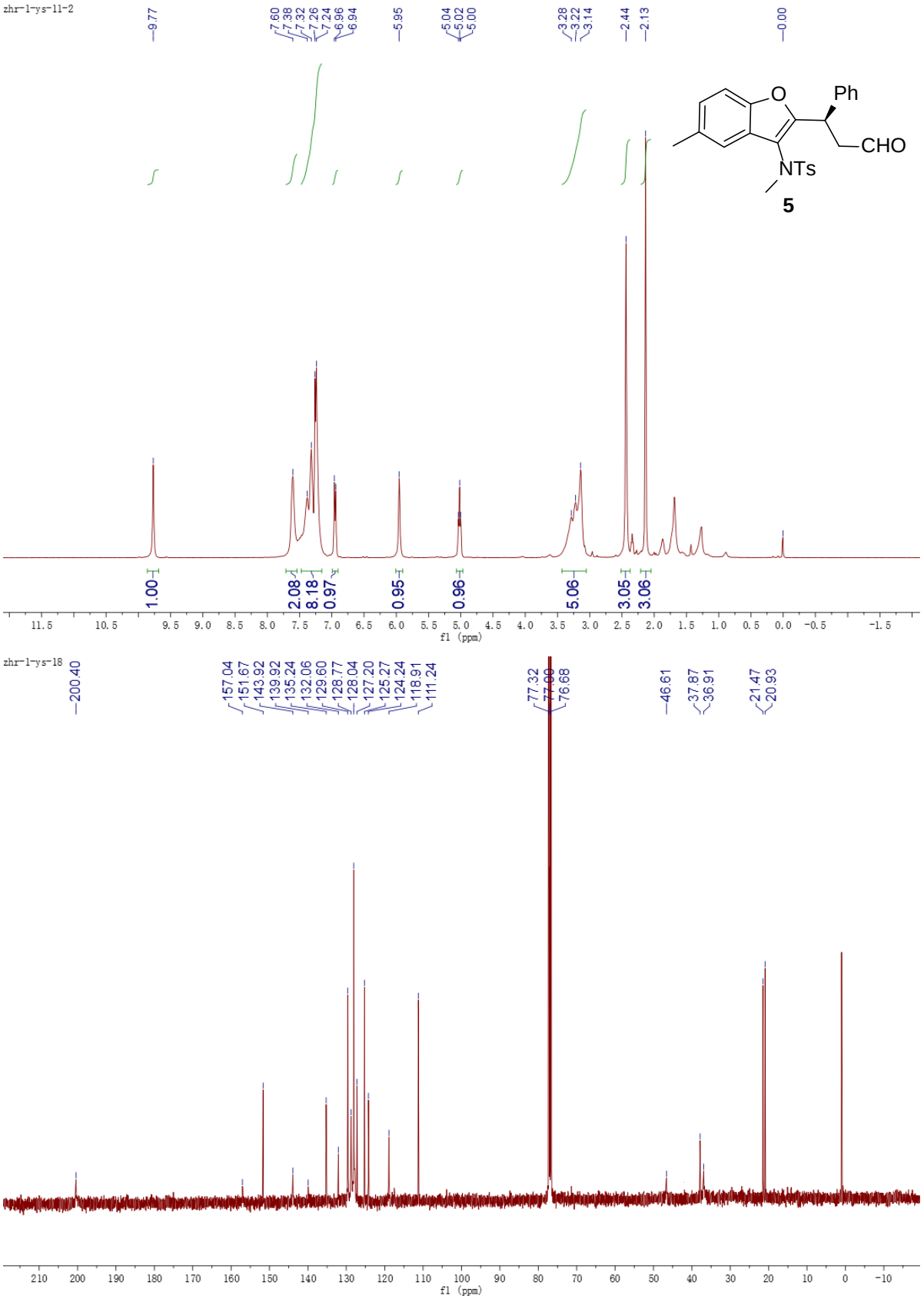
^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **4o**



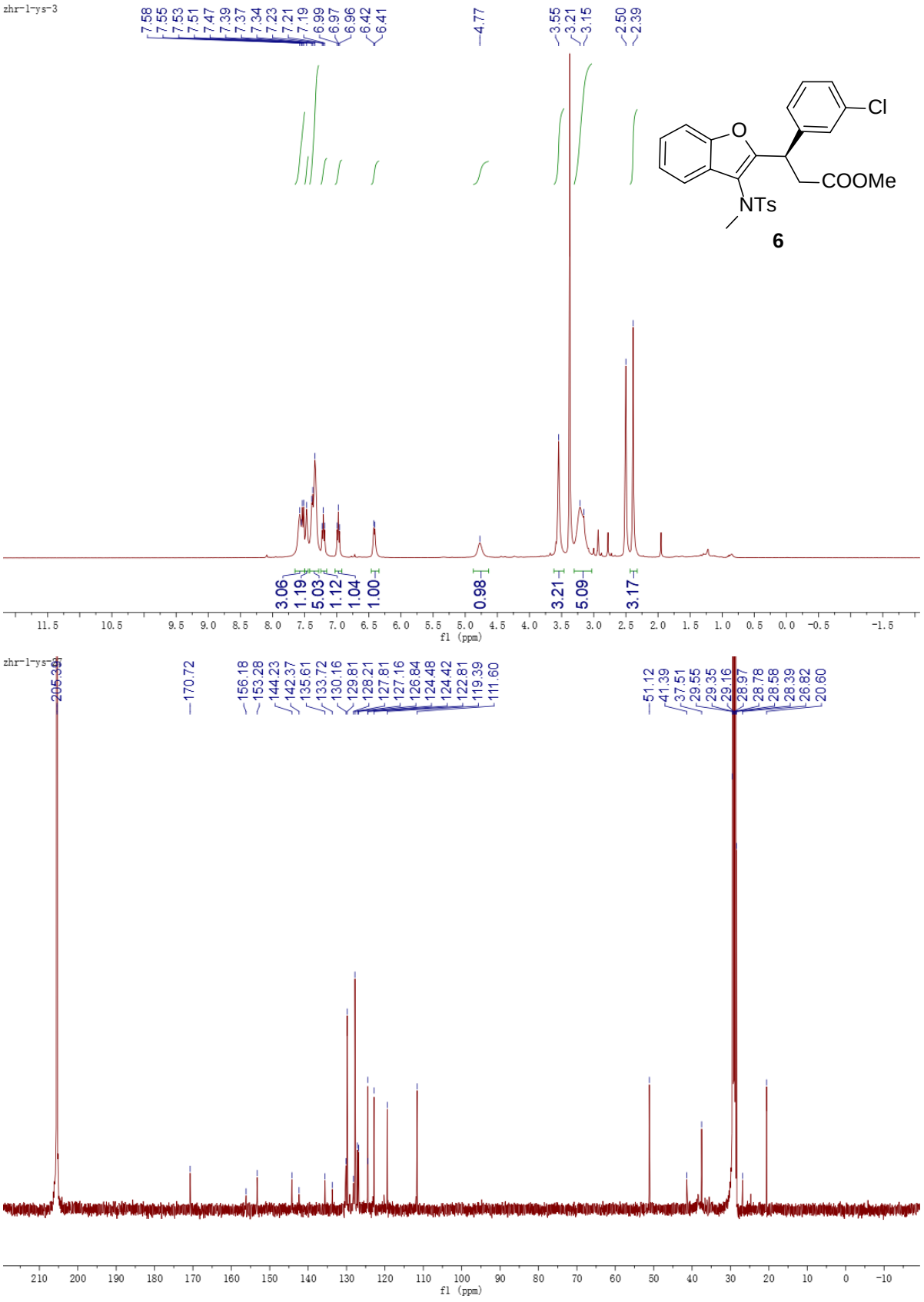
^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **4p**



^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **4q**



^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **5**

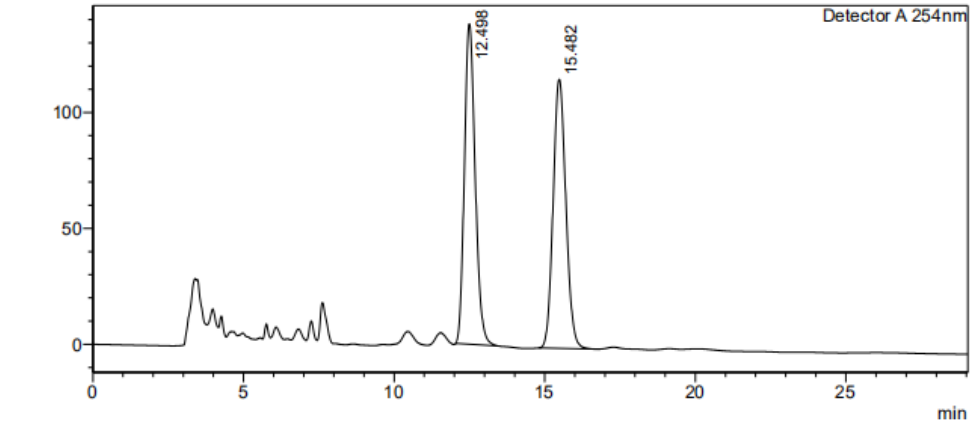


^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of **6**

6. Chiral HPLC Analysis

Racemic **3a**:

<Chromatogram>



<Peak Table>

Detector A 254nm

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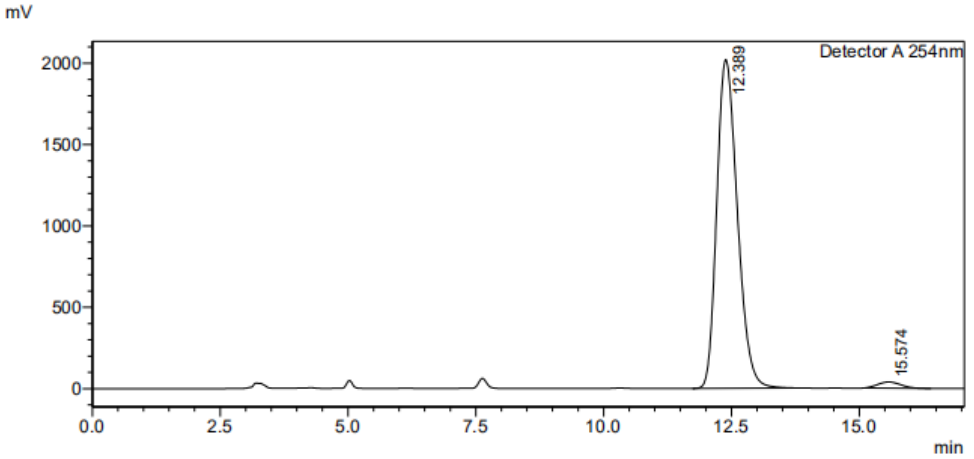
2	15.482	3401117	115996	49.746		M	
Total		6836954	254091				

Chiral **3a**:

<Chromatogram>



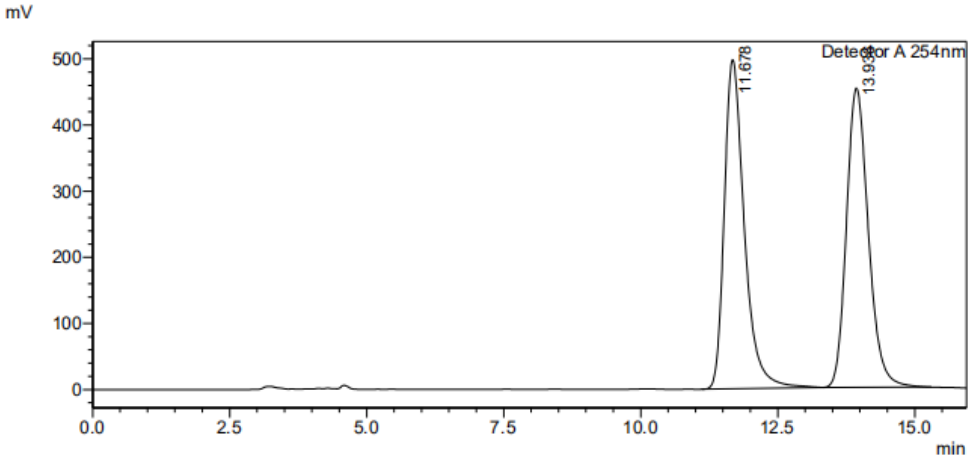
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	12.389	56655992	2019195	97.893		M	
2	15.574	1219144	38502	2.107		M	
Total		57875136	2057698				

Racemic **3b**:

<Chromatogram>



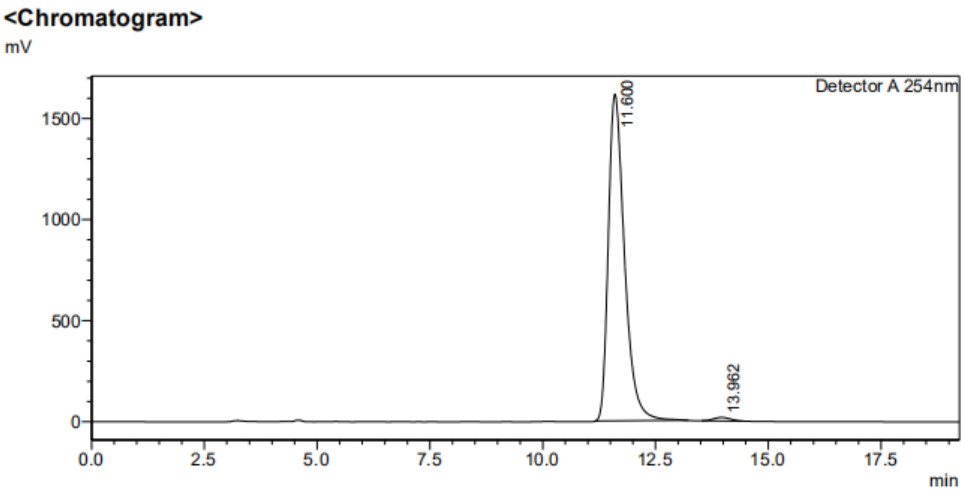
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	11.678	12636085	497313	50.134		M	
2	13.936	12568501	452317	49.866		M	
Total		25204586	949630				

Chiral **3b**:

<Chromatogram>

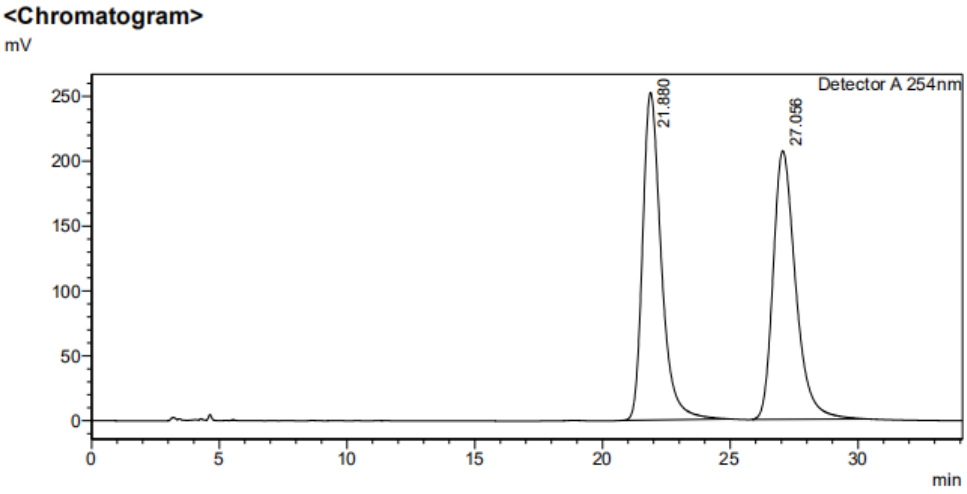


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	11.600	40253768	1615396	98.868		M	
2	13.962	460891	17446	1.132		M	
Total		40714658	1632842				

Racemic **3c**:

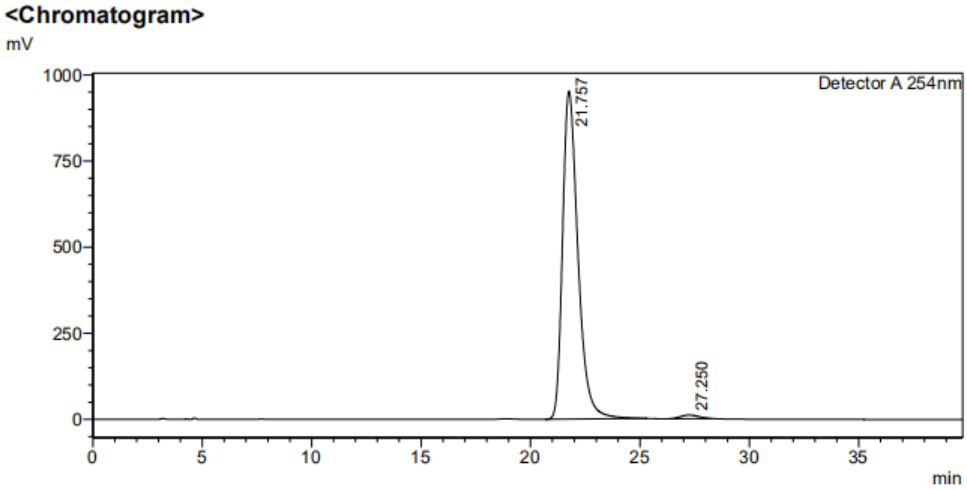


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	21.880	12769106	252404	50.160		M	
2	27.056	12687424	206878	49.840		M	
Total		25456530	459282				

Chiral **3c**:



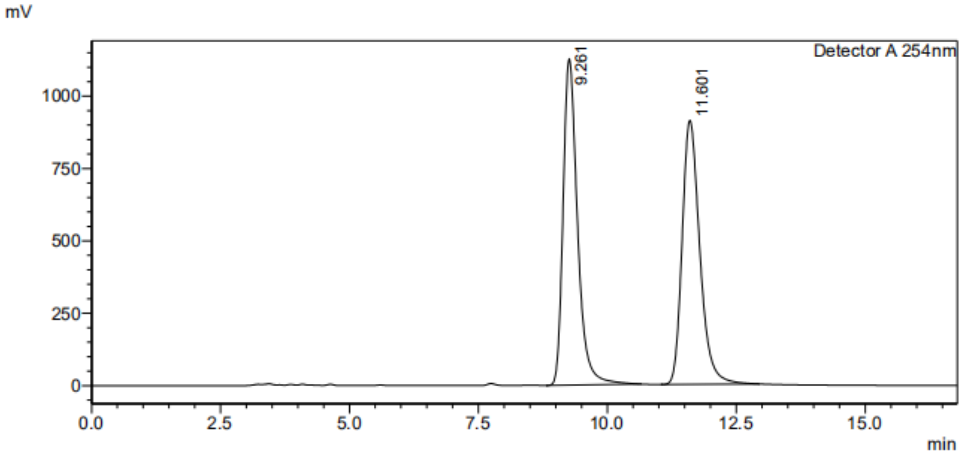
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	21.757	46597034	951235	98.766		M	
2	27.250	581999	10418	1.234		M	
Total		47179033	961653				

Racemic **3d**:

<Chromatogram>



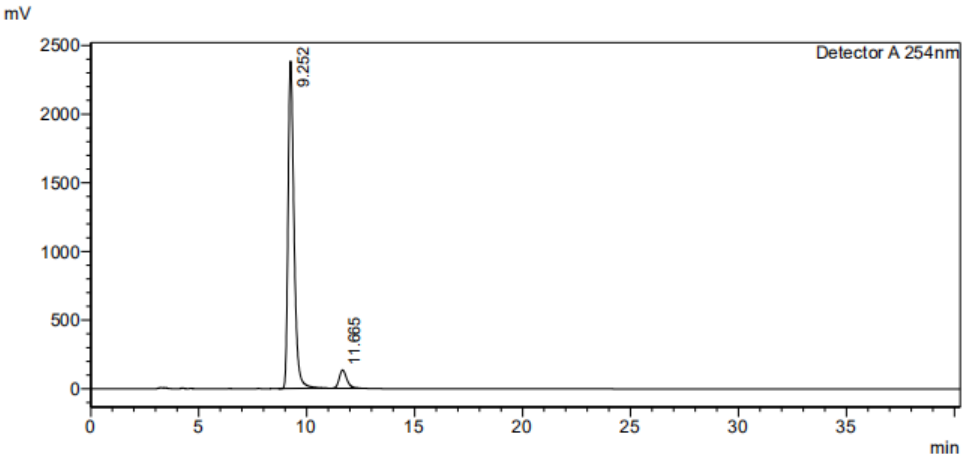
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.261	21952946	1126590	50.225		M	
2	11.601	21756043	912283	49.775		M	
Total		43708989	2038873				

Chiral **3d**:

<Chromatogram>

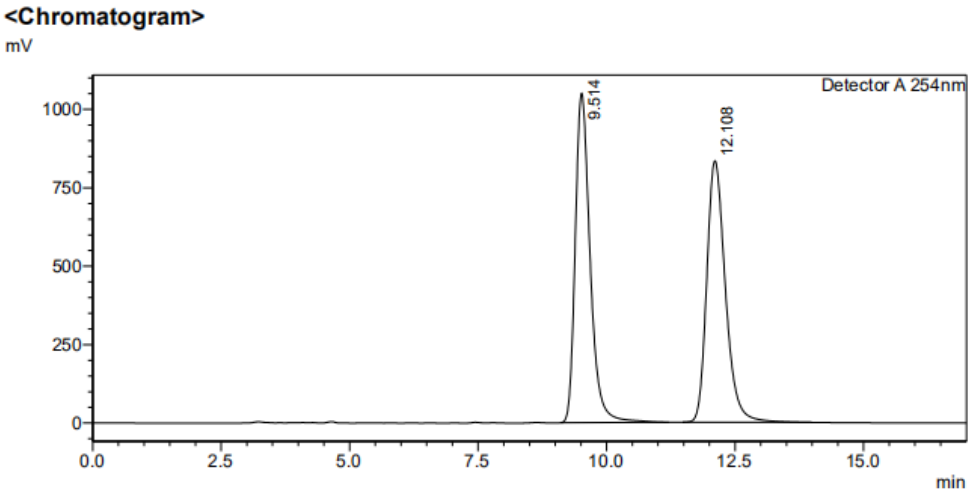


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.252	45582439	2385694	93.371		M	
2	11.665	3236051	132951	6.629		M	
Total		48818490	2518645				

Racemic **3e**:

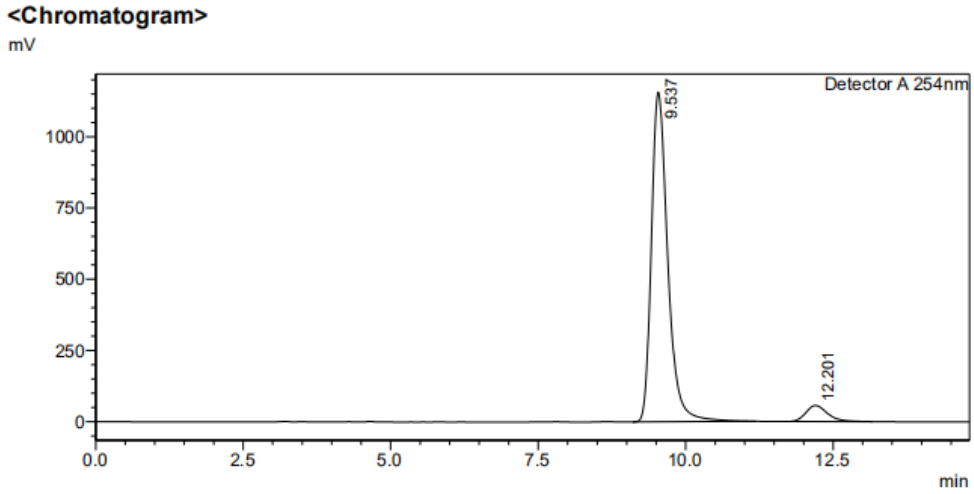


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.514	21118696	1049263	50.072		M	
2	12.108	21057955	833667	49.928		M	
Total		42176651	1882929				

Chiral **3e**:

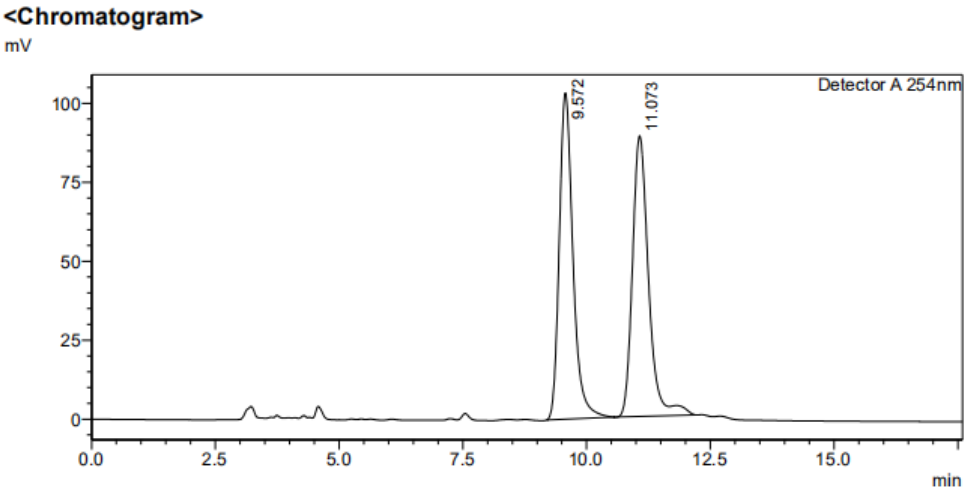


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.537	22330021	1155757	93.960		M	
2	12.201	1435421	56337	6.040		M	
Total		23765442	1212094				

Racemic **3f**:

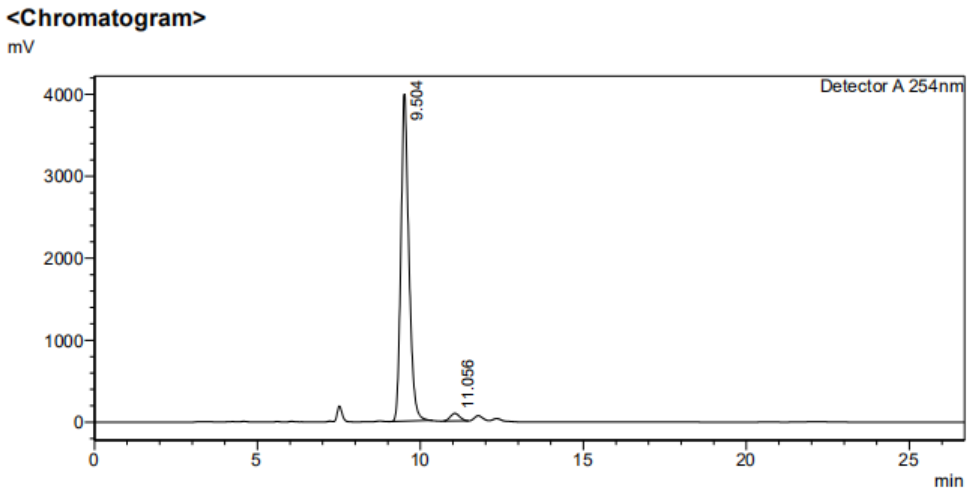


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.572	1982808	103216	49.681		M	
2	11.073	2008275	88825	50.319		M	
Total		3991083	192041				

Chiral **3f**:

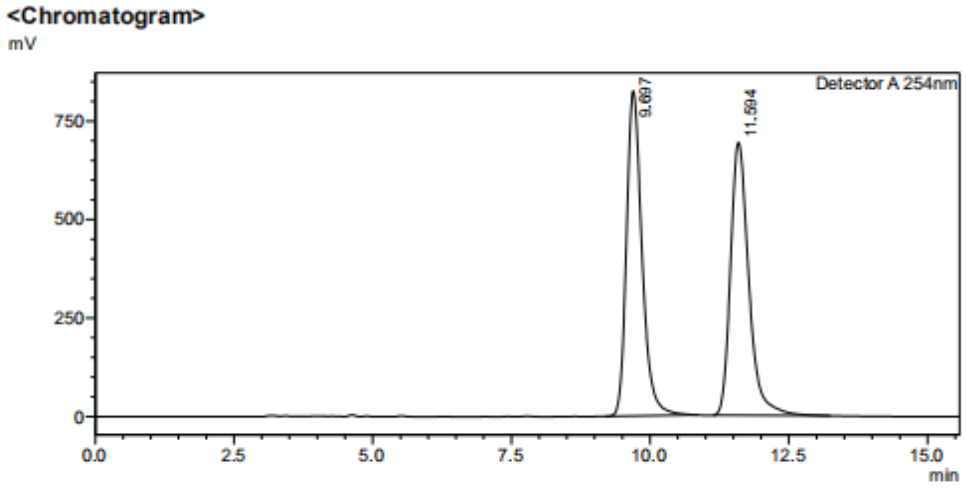


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.504	67789008	3988319	97.389		M	
2	11.056	1817149	91833	2.611		M	
Total		69606157	4080152				

Racemic **3g**:

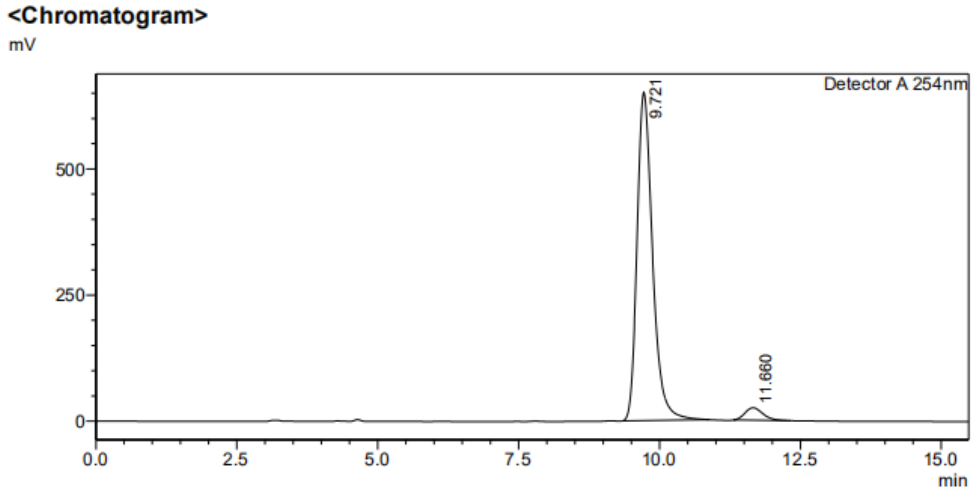


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.697	16029644	824594	50.212		M	
2	11.594	15894369	692504	49.788		M	
Total		31924013	1517098				

Chiral **3g**:

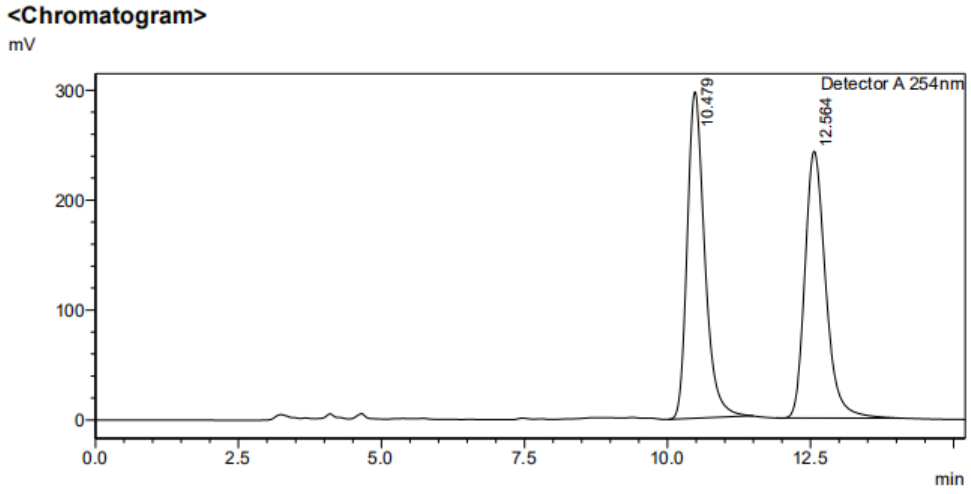


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.721	12466216	650724	95.795		M	
2	11.660	547260	24724	4.205		M	
Total		13013476	675448				

Racemic **3h**:

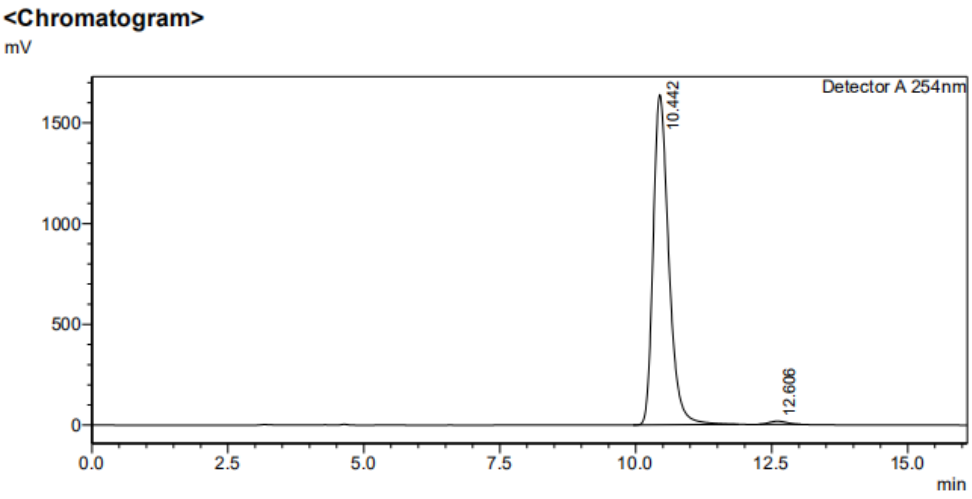


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	10.479	6335609	296778	50.922		M	
2	12.564	6106275	242701	49.078		M	
Total		12441885	539479				

Chiral **3h**:



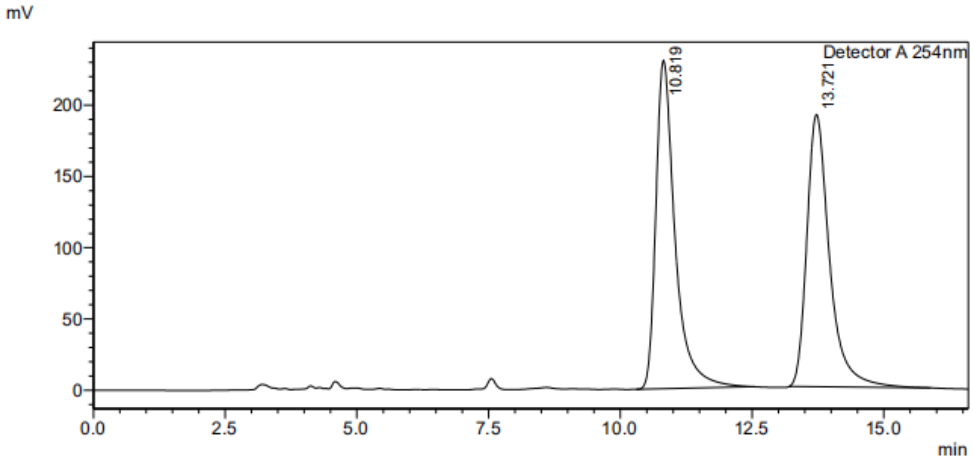
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	10.442	32661156	1636508	98.977		M	
2	12.606	337525	15645	1.023		M	
Total		32998681	1652153				

Racemic **3i**:

<Chromatogram>



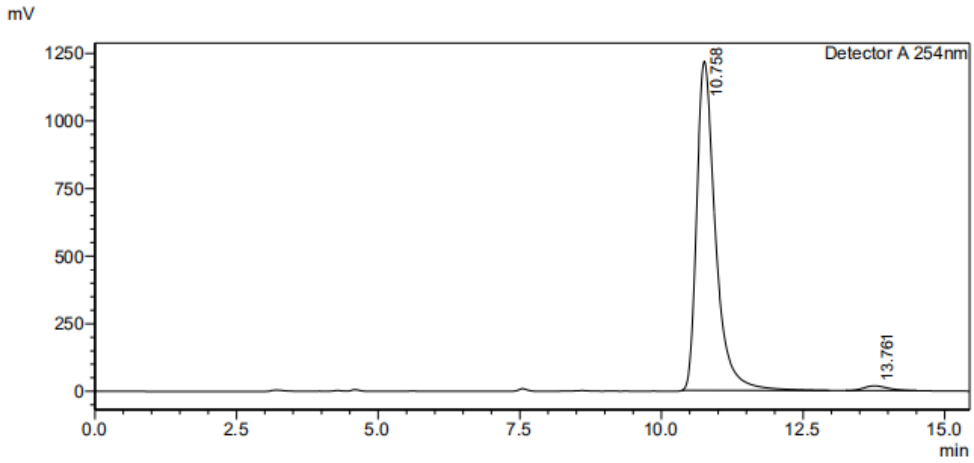
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	10.819	5848963	230236	50.589		M	
2	13.721	5712692	190866	49.411		M	
Total		11561655	421103				

Chiral **3i**:

<Chromatogram>



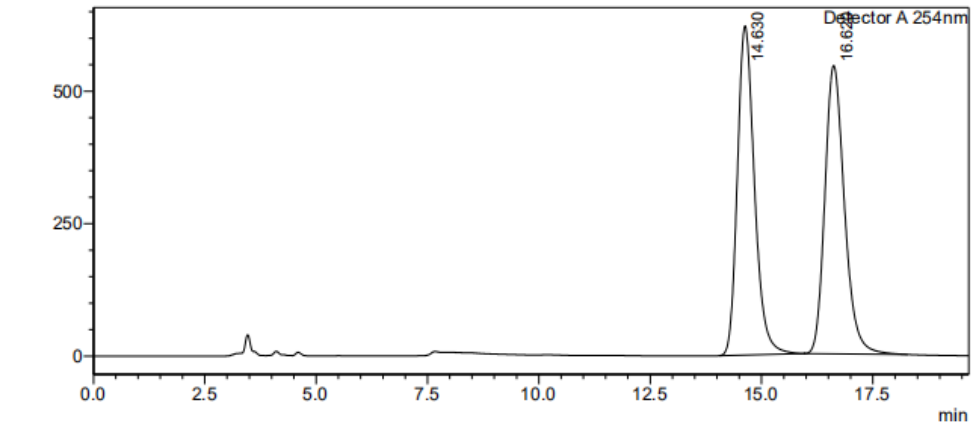
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	10.758	28054325	1216618	98.179		M	
2	13.761	520227	17718	1.821		M	
Total		28574551	1234335				

Racemic **3j**:

<Chromatogram>



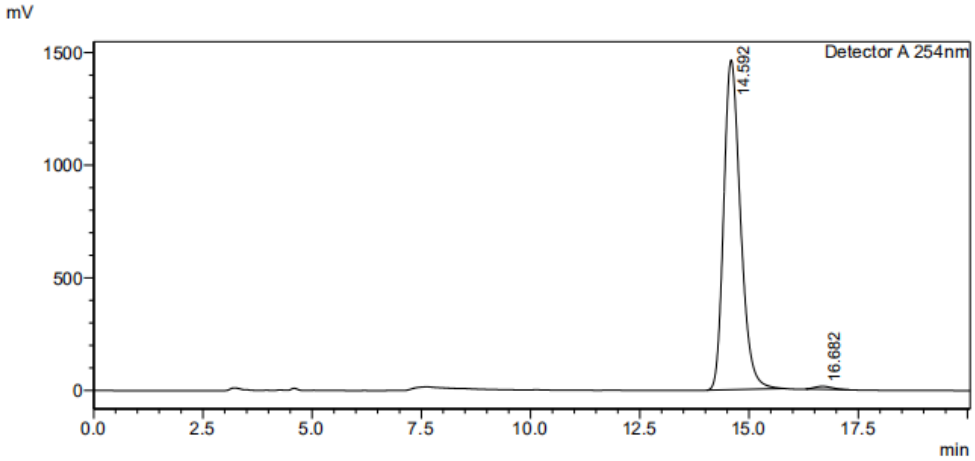
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	14.630	16606051	620983	49.917		M	
2	16.620	16661571	544161	50.083		M	
Total		33267622	1165144				

Chiral **3j**:

<Chromatogram>

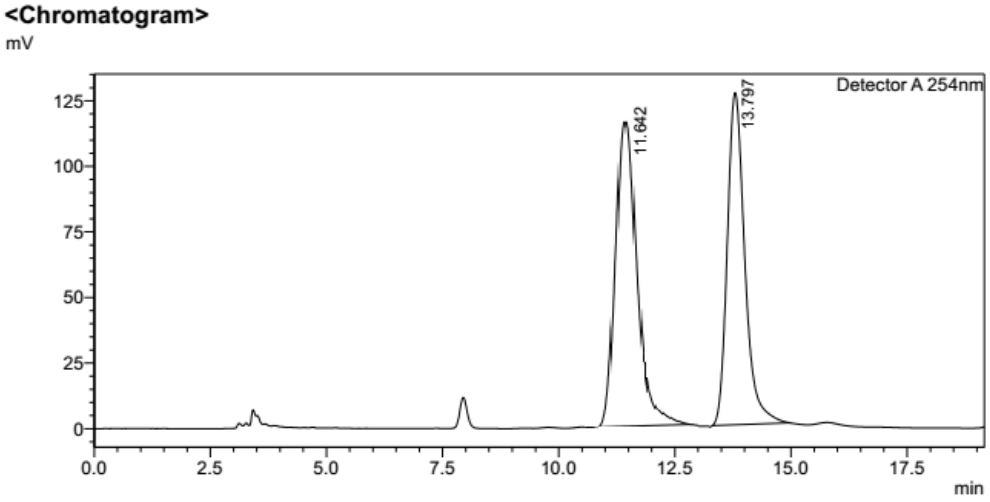


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	14.592	39100482	1462859	99.055		M	
2	16.682	372827	13419	0.945		M	
Total		39473310	1476278				

Racemic **3k**:

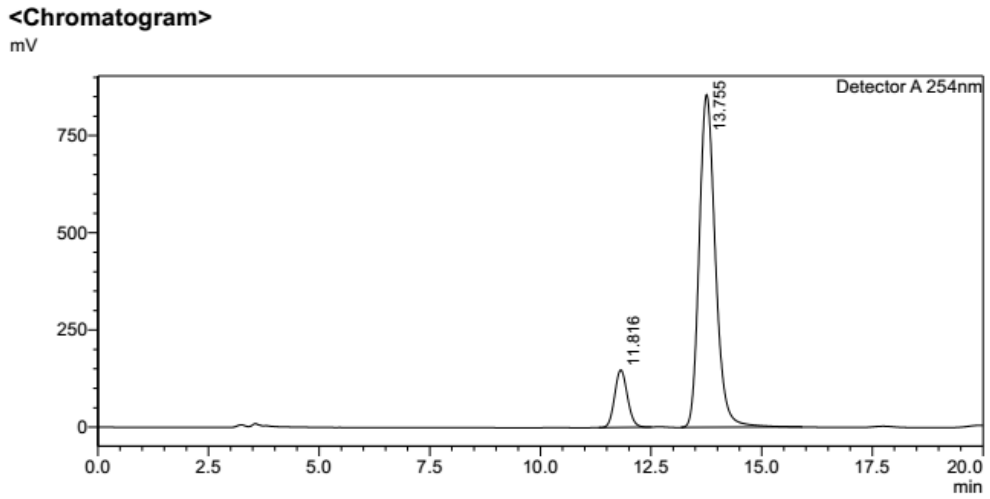


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	11.642	3325854	121820	50.079		M	
2	13.797	3315425	126580	49.921		M	
Total		6641279	248400				

Chiral **3k**:



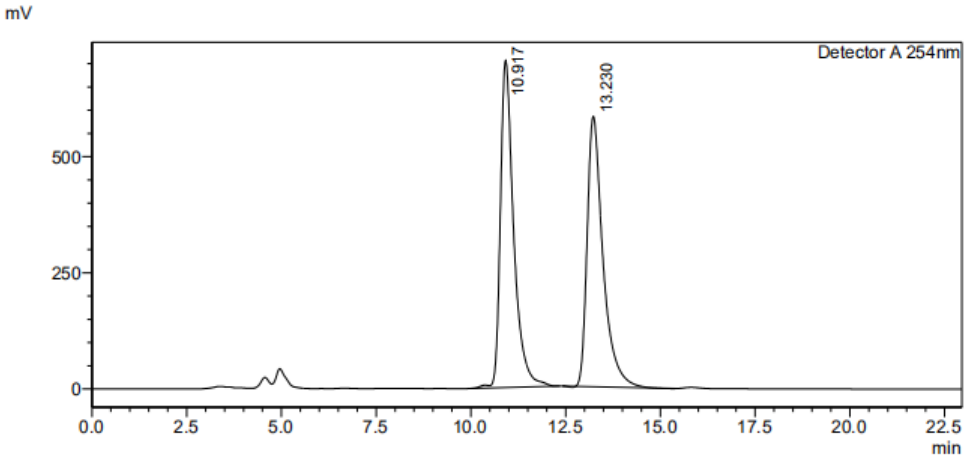
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	11.816	2961114	147531	11.974		M	
2	13.755	21769385	856007	88.026		M	
Total		24730499	1003538				

Racemic **4a**:

<Chromatogram>



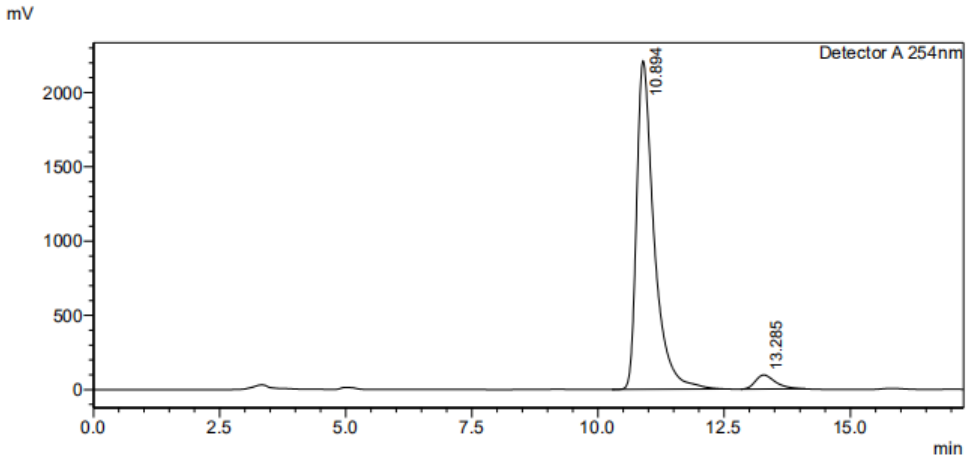
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	10.917	17155637	703540	50.431		M	
2	13.230	16862414	581630	49.569		M	
Total		34018051	1285170				

Chiral **4a**:

<Chromatogram>

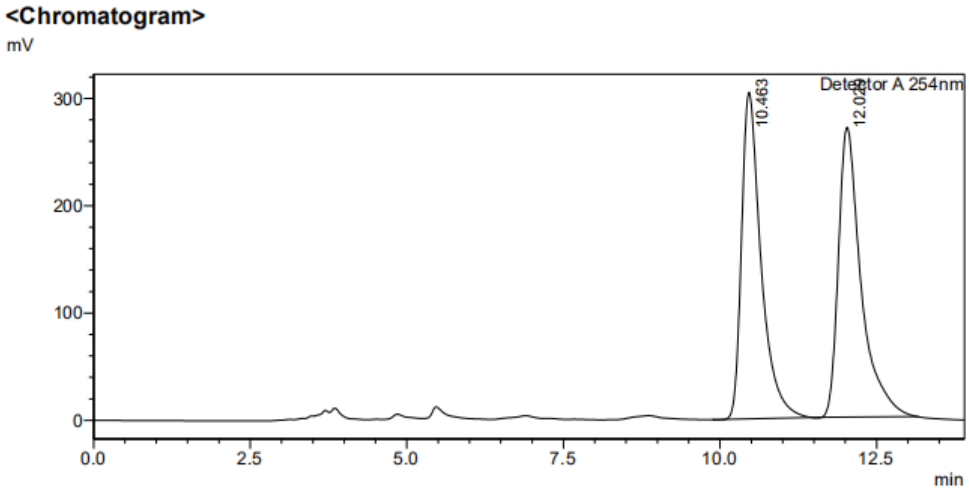


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	10.894	53242431	2209778	95.342		M	
2	13.285	2601254	94596	4.658		M	
Total		55843685	2304374				

Racemic **4b**:

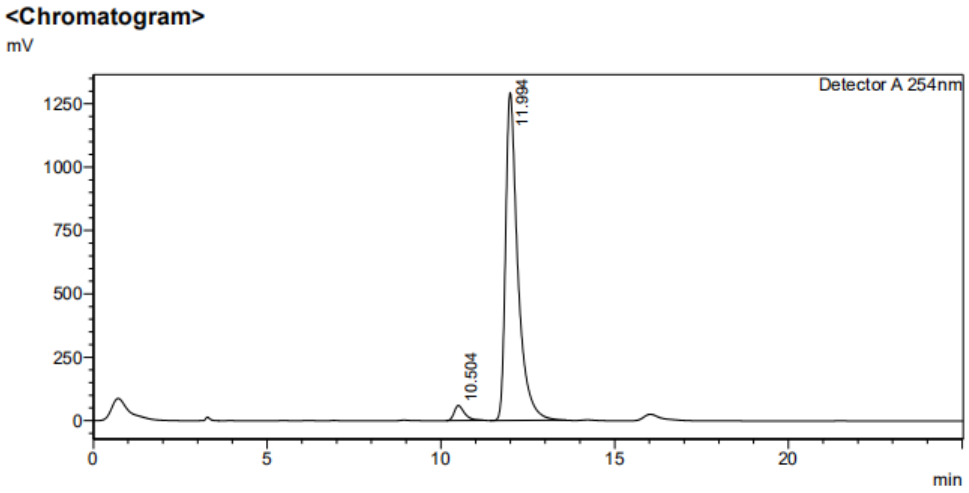


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	10.463	6580348	304172	49.136		M	
2	12.029	6811836	270043	50.864		M	
Total		13392184	574214				

Chiral **4b**:



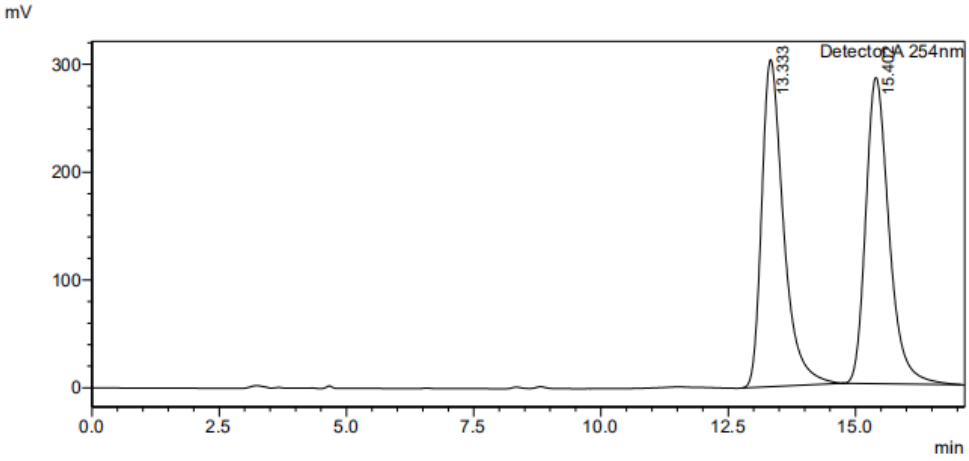
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	10.504	1243675	59313	3.775		M	
2	11.994	31697925	1292248	96.225		M	
Total		32941600	1351562				

Racemic **4c**:

<Chromatogram>



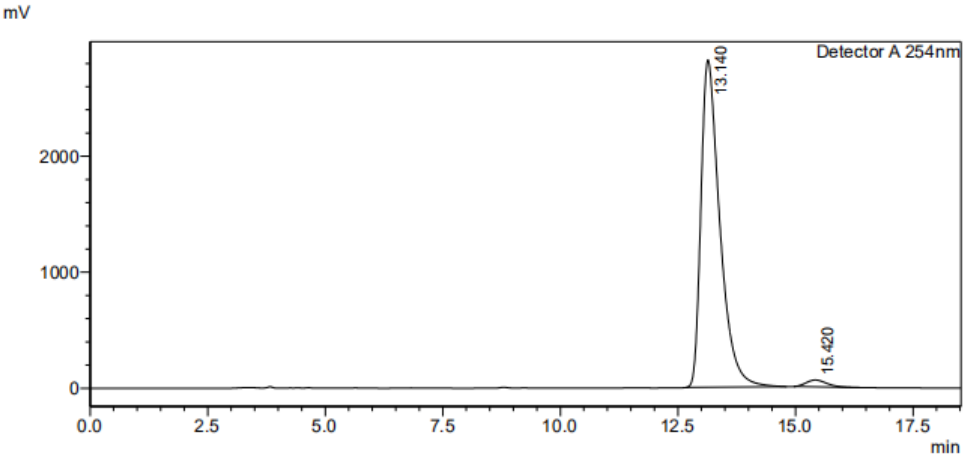
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	13.333	9076841	303238	50.062		M	
2	15.402	9054485	284046	49.938		M	
Total		18131327	587283				

Chiral **4c**:

<Chromatogram>



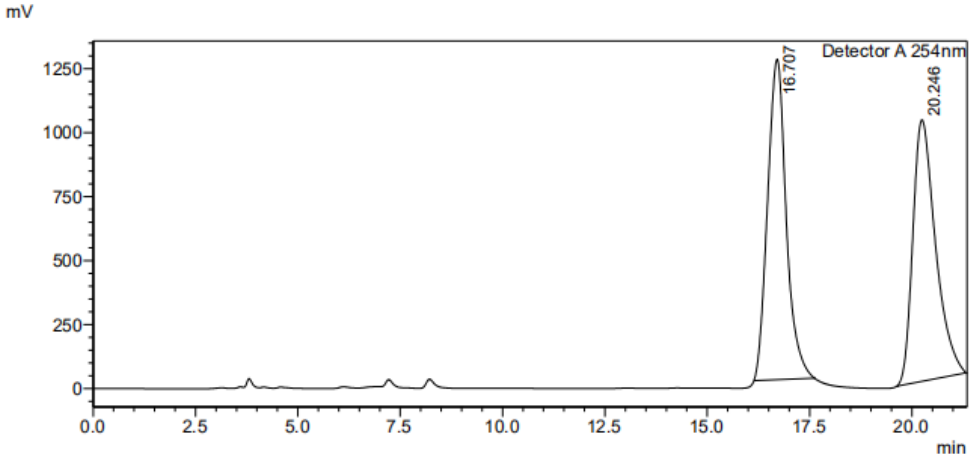
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	13.140	78760350	2821101	97.757		M	
2	15.420	1807226	59005	2.243		M	
Total		80567576	2880106				

Racemic **4d**:

<Chromatogram>



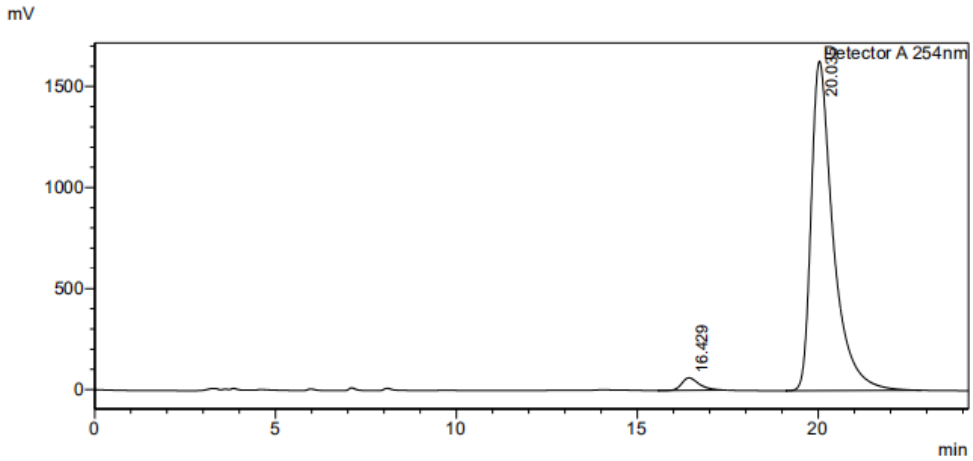
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	16.707	39709612	1251502	50.233		M	
2	20.246	39341561	1021520	49.767		M	
Total		79051173	2273022				

Chiral **4d**:

<Chromatogram>

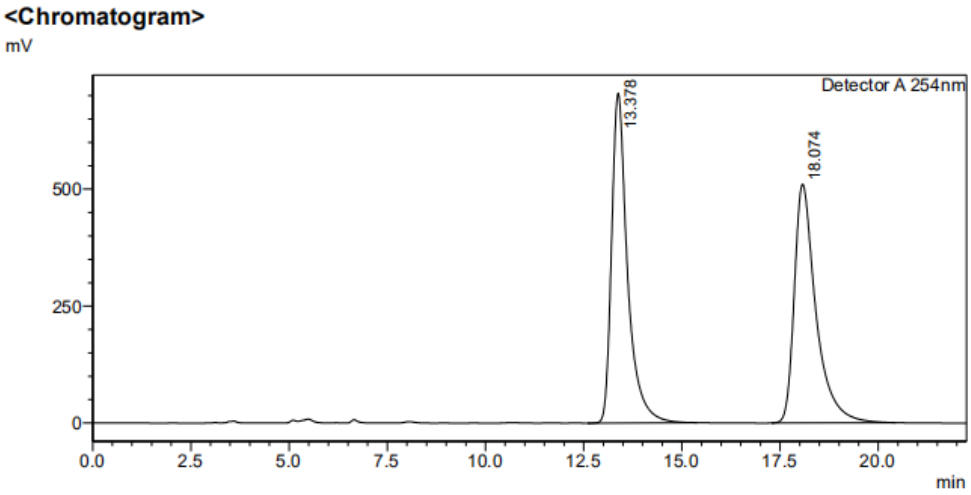


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	16.429	2043789	61736	2.875		M	
2	20.035	69037423	1629022	97.125		M	
Total		71081212	1690758				

Racemic **4e**:

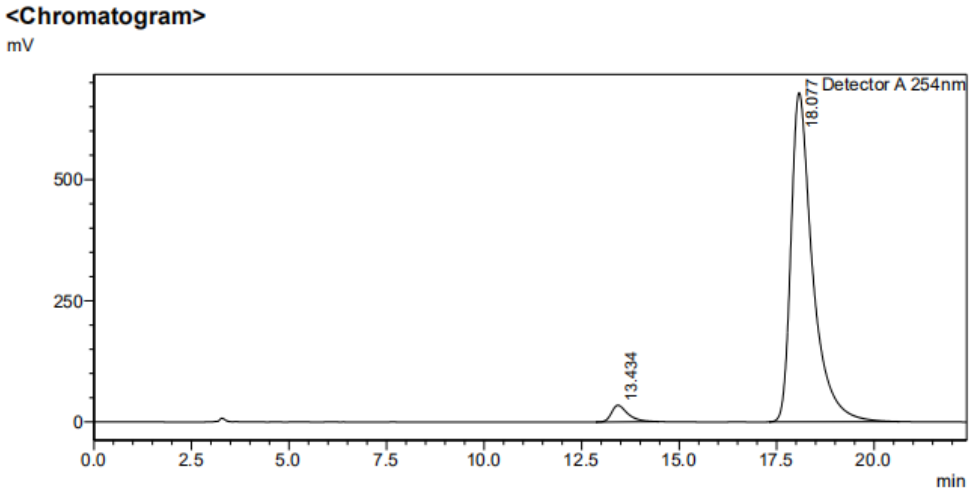


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	13.378	19875766	704552	50.377		M	
2	18.074	19578245	510411	49.623		M	
Total		39454011	1214963				

Chiral **4e**:



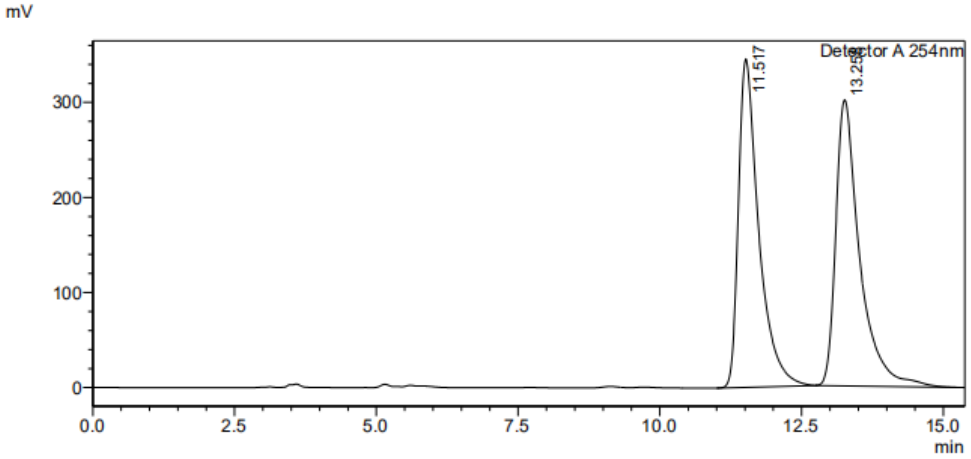
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	13.434	994030	34269	3.660		M	
2	18.077	26164316	678624	96.340		M	
Total		27158346	712893				

Racemic **4f**:

<Chromatogram>



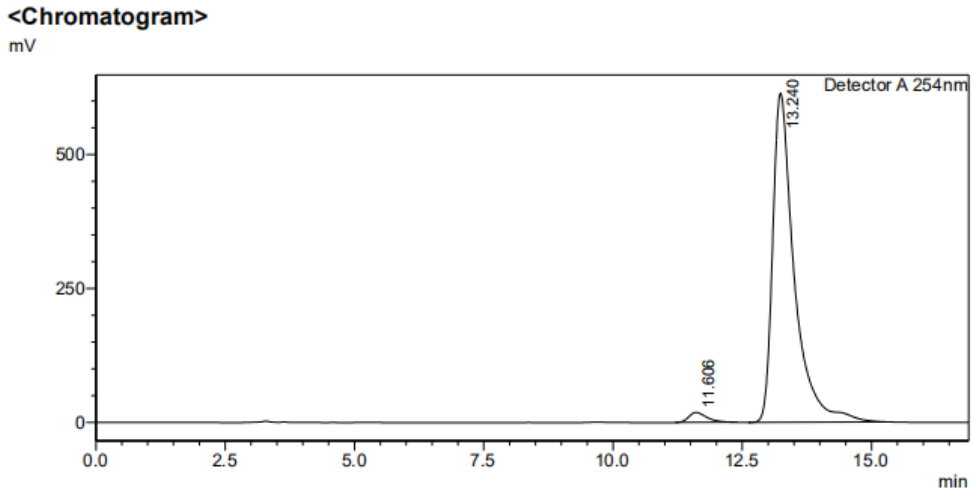
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	11.517	8592286	345152	49.364		M	
2	13.258	8813739	300819	50.636		M	
Total		17406026	645971				

Chiral **4f**:

<Chromatogram>

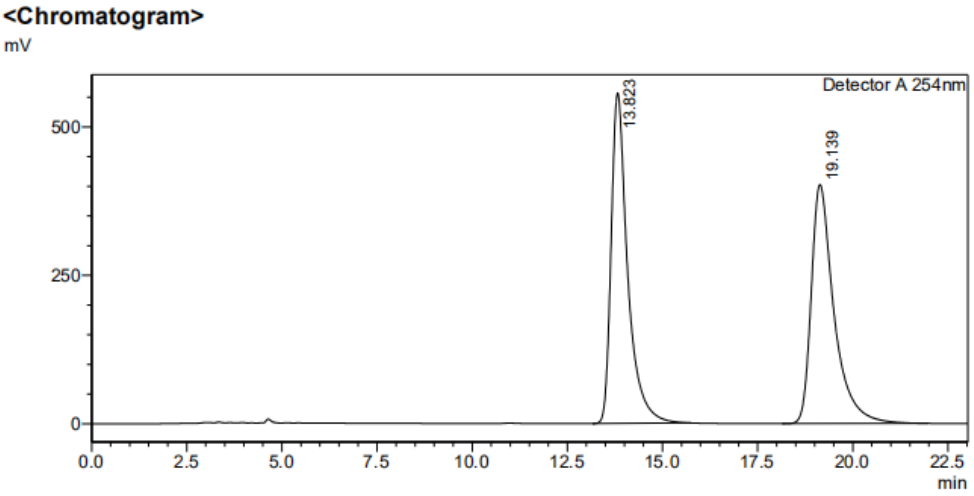


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	11.606	454216	18554	2.475		M	
2	13.240	17899410	613766	97.525		M	
Total		18353626	632320				

Racemic **4g**:

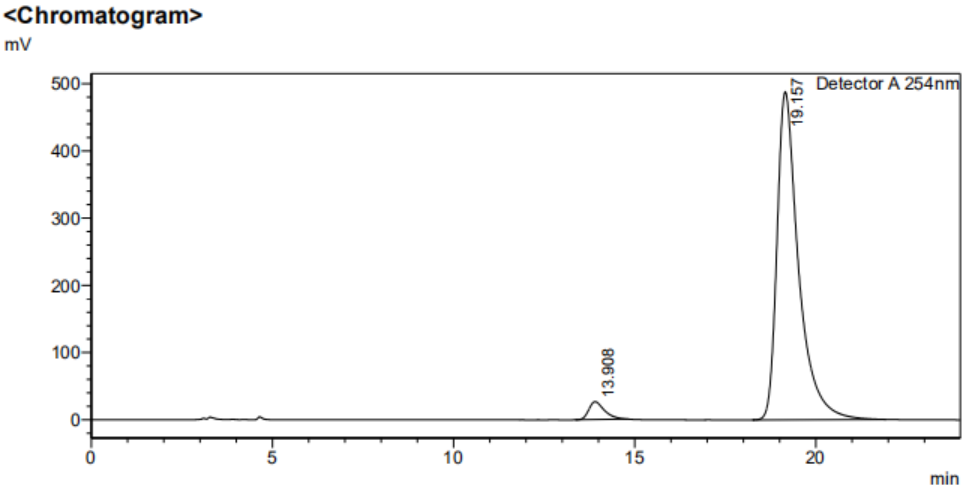


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	13.823	16771275	556485	50.034		M	
2	19.139	16748485	402683	49.966		M	
Total		33519760	959168				

Chiral **4g**:



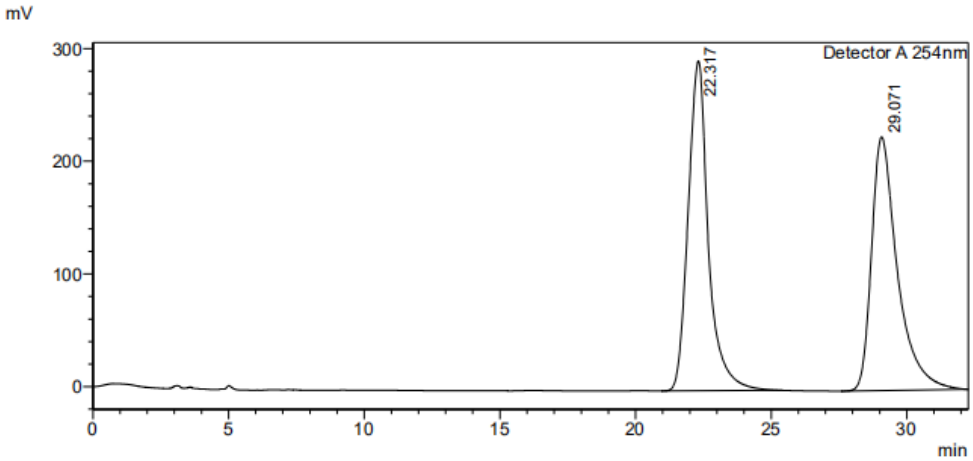
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	13.908	803472	26614	3.824		M	
2	19.157	20205777	487841	96.176		M	
Total		21009249	514455				

Racemic **4h**:

<Chromatogram>



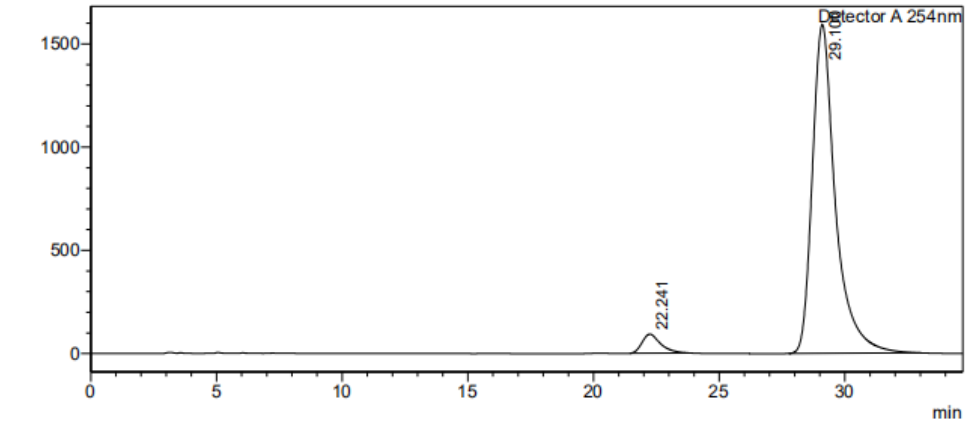
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	22.317	15135423	292581	50.336		M	
2	29.071	14933178	224972	49.664		M	
Total		30068601	517553				

Chiral **4h**:

<Chromatogram>

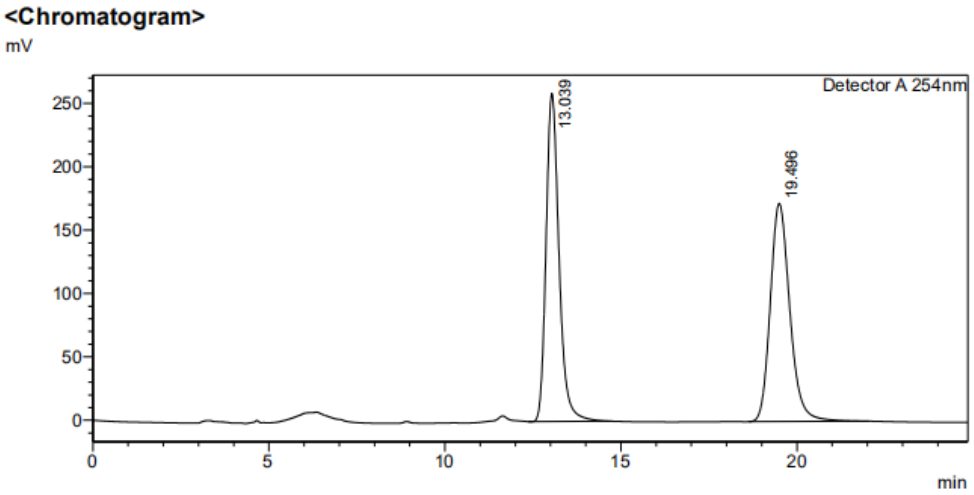


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	22.241	4757238	92283	4.458		M	
2	29.100	101955035	1591897	95.542		M	
Total		106712273	1684180				

Racemic **4i**:

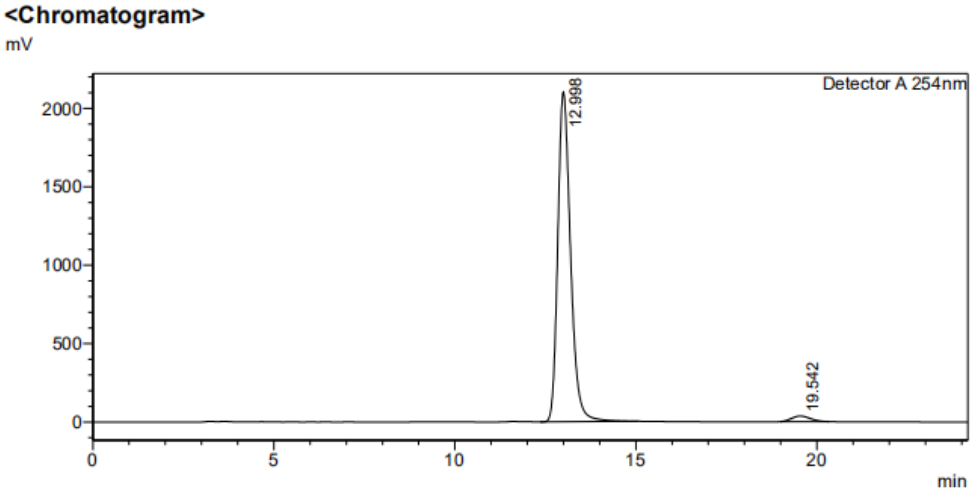


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	13.039	6632747	258739	49.985		M	
2	19.496	6636824	171989	50.015		M	
Total		13269571	430727				

Chiral **4i**:



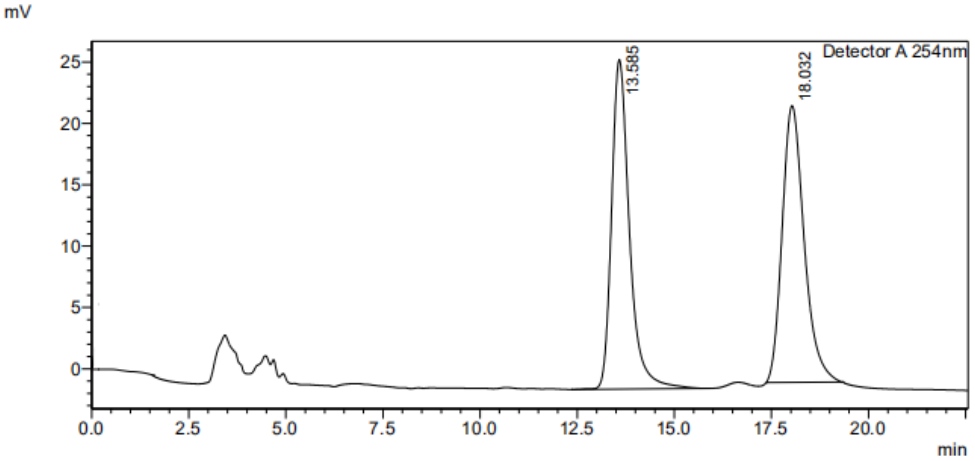
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	12.998	51512522	2102186	97.603		M	
2	19.542	1265087	35496	2.397		M	
Total		52777609	2137682				

Racemic **4j**:

<Chromatogram>



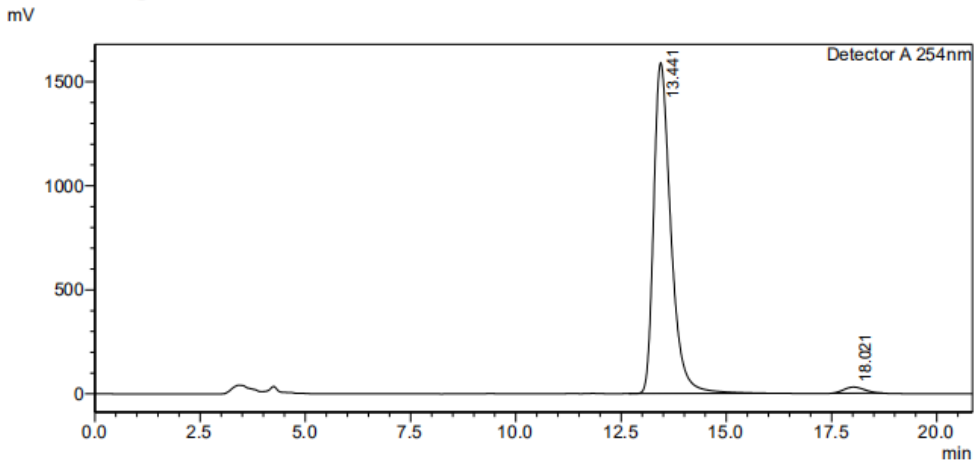
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	13.585	858846	26836	49.206		M	
2	18.032	886557	22530	50.794		M	
Total		1745403	49366				

Chiral **4j**:

<Chromatogram>

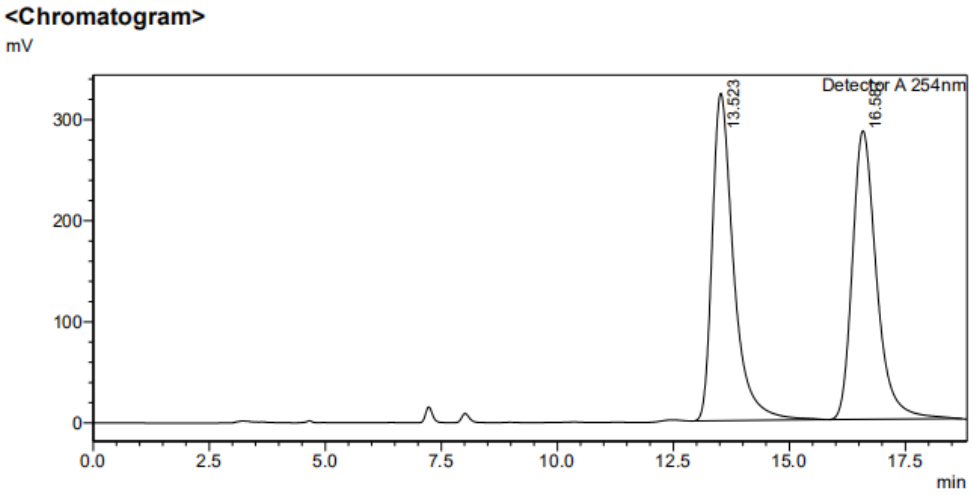


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	13.441	45010824	1588971	97.804		M	
2	18.021	1010600	29661	2.196		M	
Total		46021424	1618632				

Racemic **4k**:

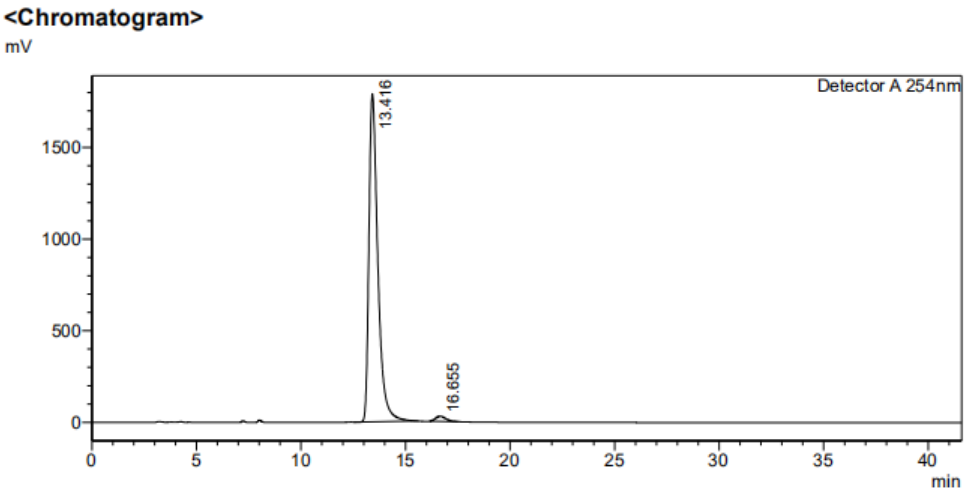


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	13.523	10378532	323694	50.104		M	
2	16.587	10335260	285412	49.896		M	
Total		20713792	609106				

Chiral **4k**:

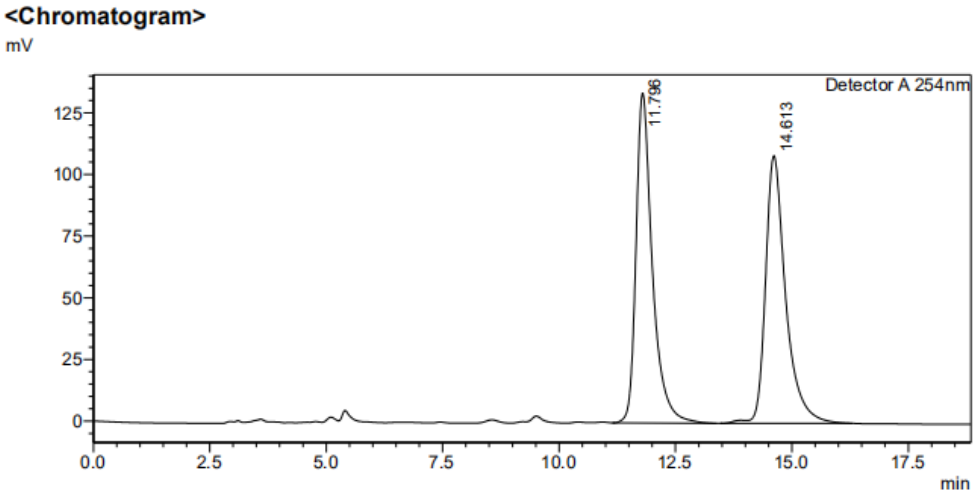


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	13.416	53073071	1788719	98.239		M	
2	16.655	951507	28009	1.761		M	
Total		54024578	1816728				

Racemic **4l**:

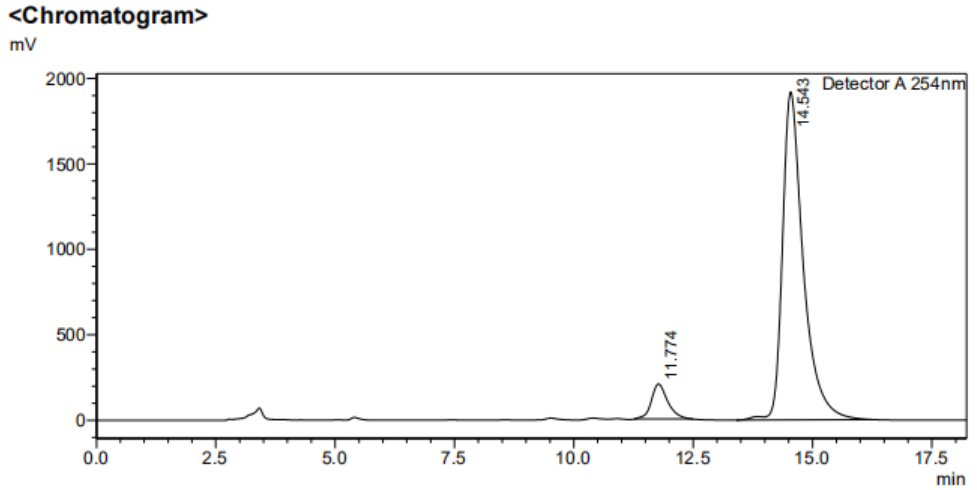


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	11.796	3270373	133735	50.010		M	
2	14.613	3269021	108490	49.990		M	
Total		6539394	242224				

Chiral **4l**:



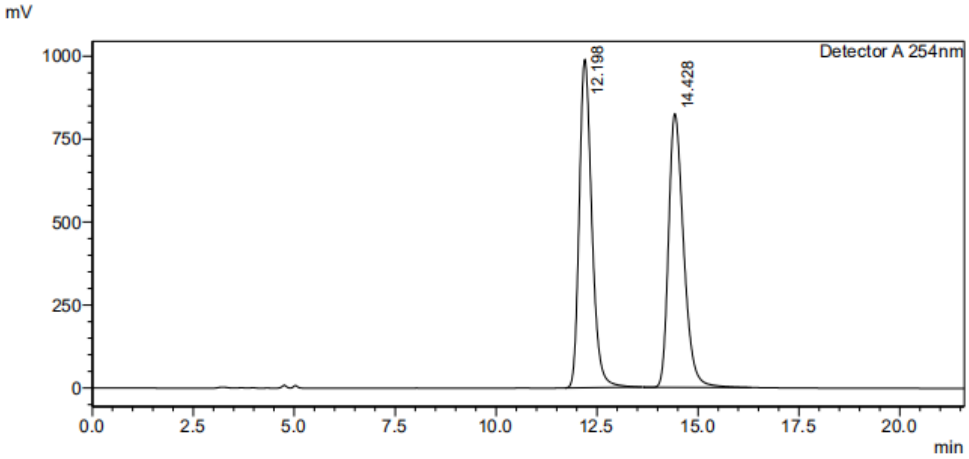
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	11.774	4867780	203610	7.706		M	
2	14.543	58297711	1918338	92.294		M	
Total		63165491	2121948				

Racemic **4m**:

<Chromatogram>



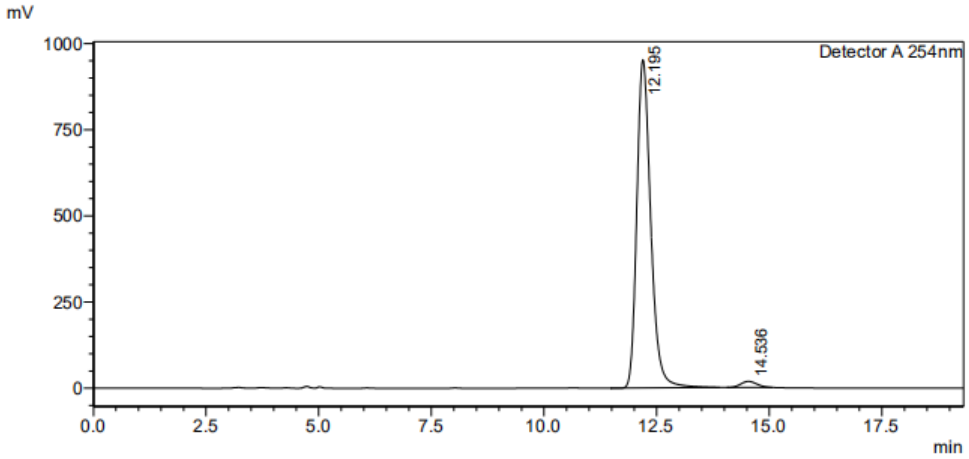
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	12.198	21347584	988628	49.906		M	
2	14.428	21428353	824070	50.094		M	
Total		42775937	1812698				

Chiral **4m**:

<Chromatogram>



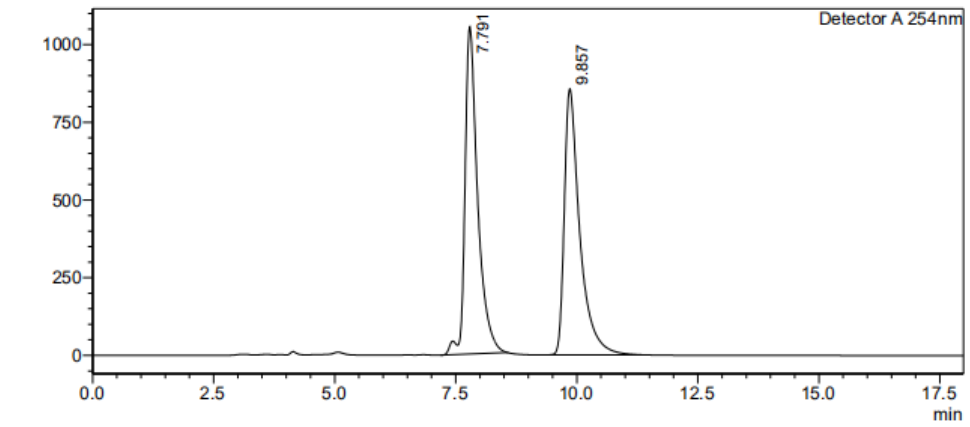
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	12.195	20479577	951554	97.935		M	
2	14.536	431885	17514	2.065		M	
Total		20911461	969068				

Racemic **4n**:

<Chromatogram>



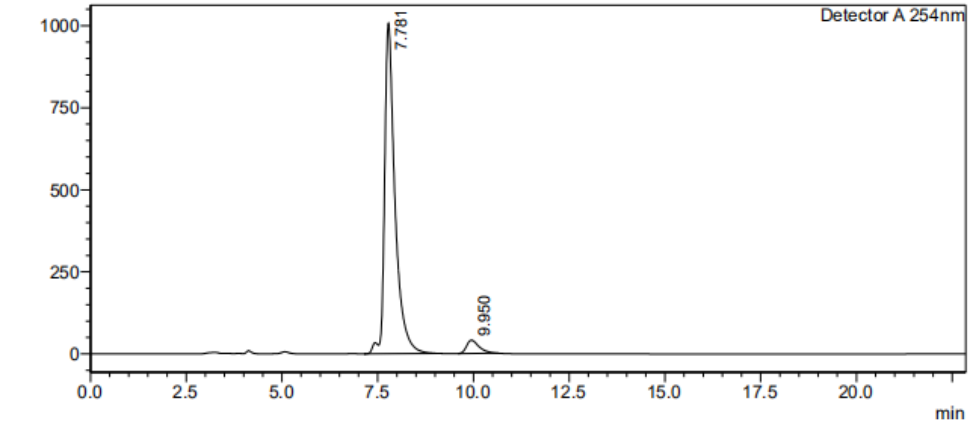
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.791	19173767	1051664	50.245		M	
2	9.857	18986508	855752	49.755		M	
Total		38160275	1907416				

Chiral **4n**:

<Chromatogram>



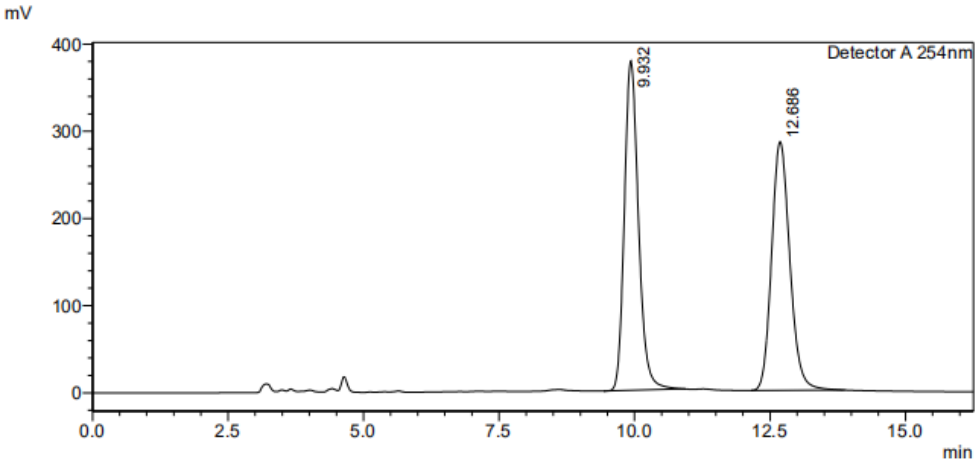
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.781	19031443	1005713	95.390		M	
2	9.950	919734	40451	4.610		M	
Total		19951177	1046164				

Racemic **4o**:

<Chromatogram>



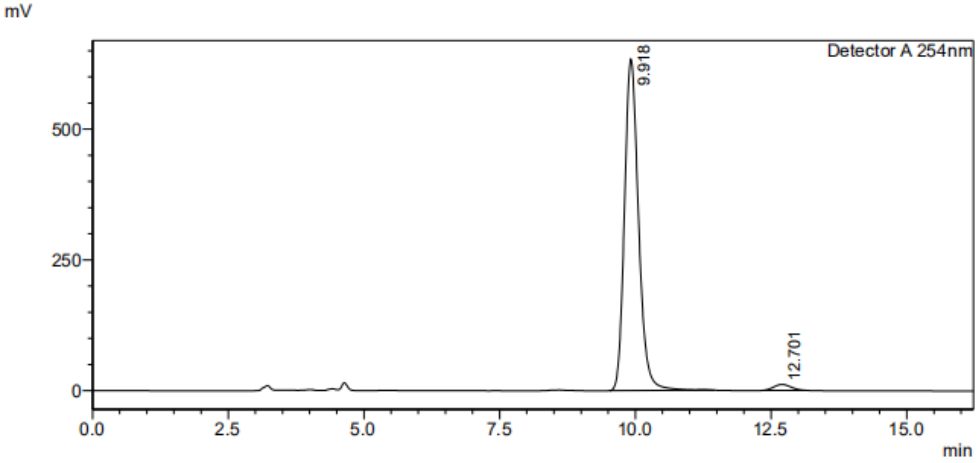
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.932	6845677	377652	50.641		M	
2	12.686	6672355	285189	49.359		M	
Total		13518032	662841				

Chiral **4o**:

<Chromatogram>



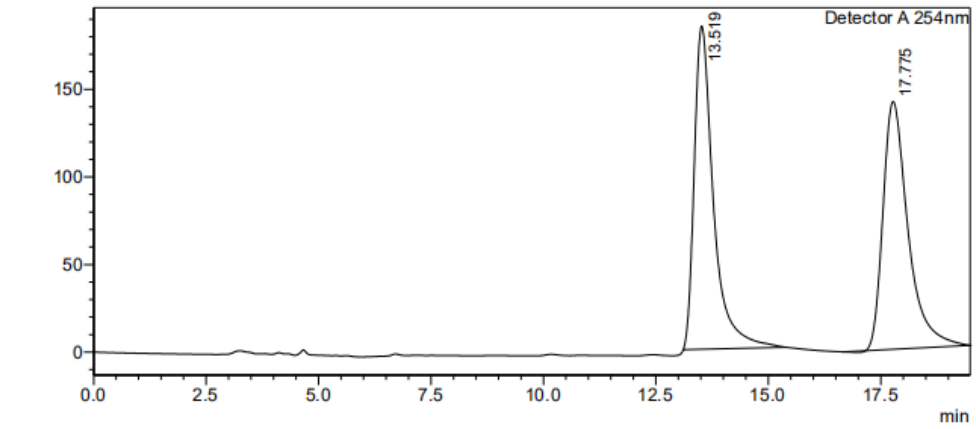
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.918	11420370	633450	97.813		M	
2	12.701	255358	11486	2.187		M	
Total		11675729	644936				

Racemic **4p**:

<Chromatogram>



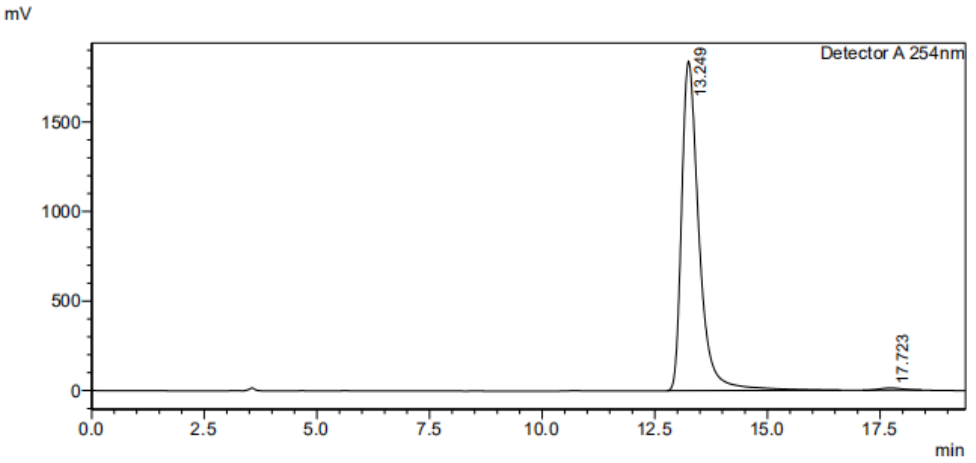
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	13.519	5497035	184428	50.094		M	
2	17.775	5476490	141390	49.906		M	
Total		10973526	325817				

Chiral **4p**:

<Chromatogram>

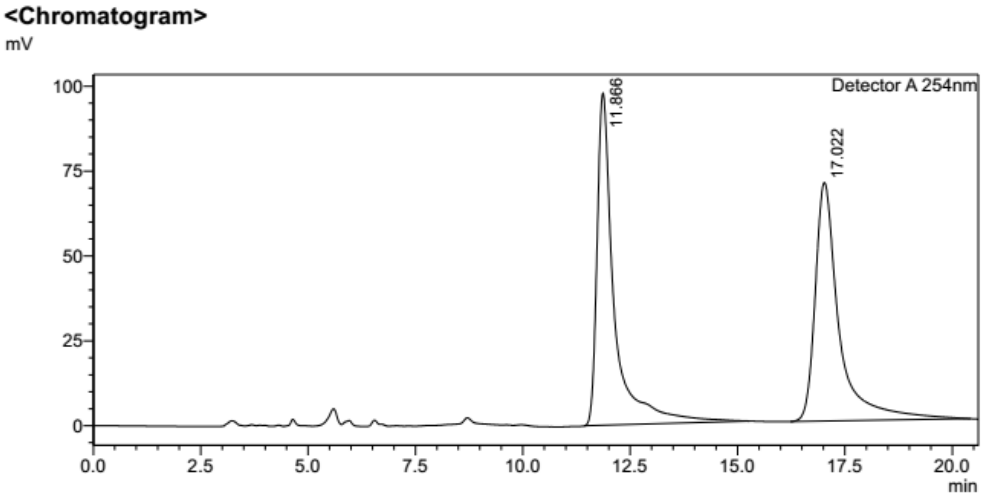


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	13.249	49411443	1838299	99.142		M	
2	17.723	427735	12149	0.858		M	
Total		49839178	1850447				

Racemic **4q**:

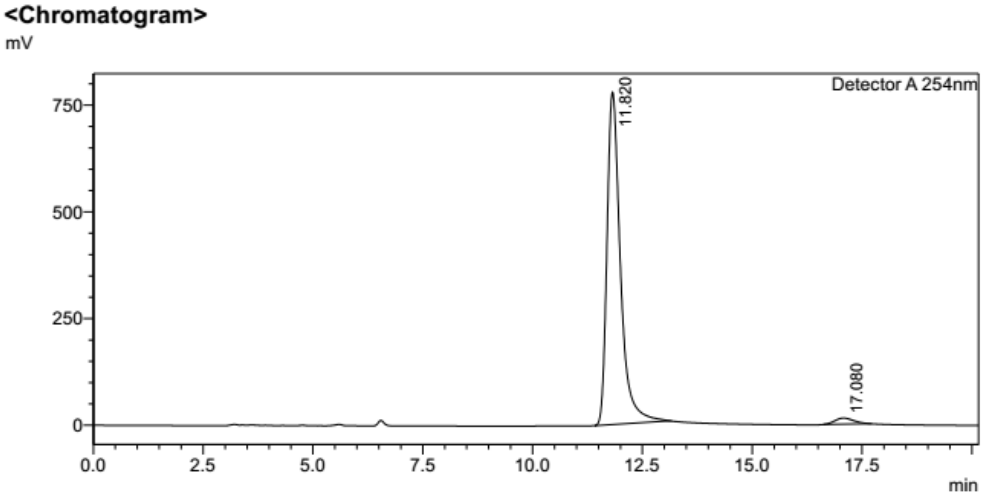


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	11.866	2737593	97806	50.020		M	
2	17.022	2735396	70212	49.980		M	
Total		5472989	168018				

Chiral **4q**:

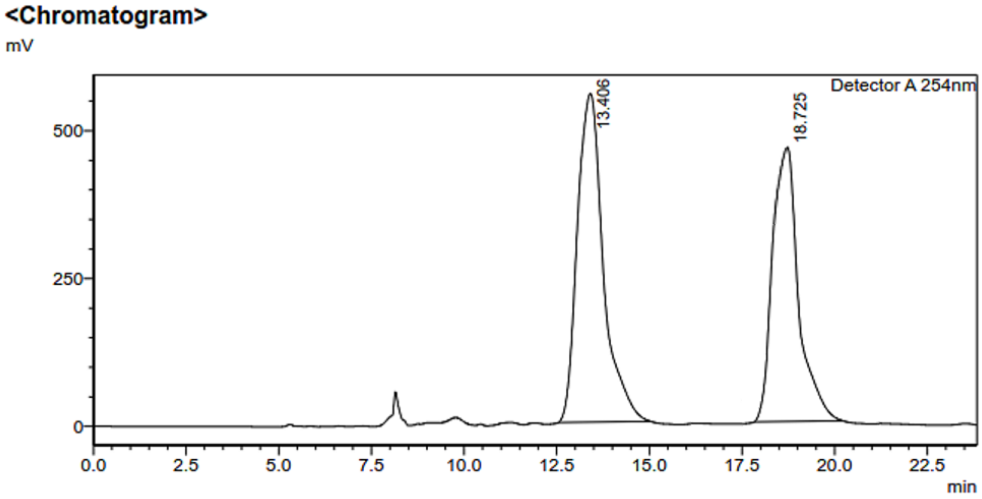


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	11.820	16566274	778512	97.500		M	
2	17.080	424793	14197	2.500		M	
Total		16991067	792709				

Racemic **5**:

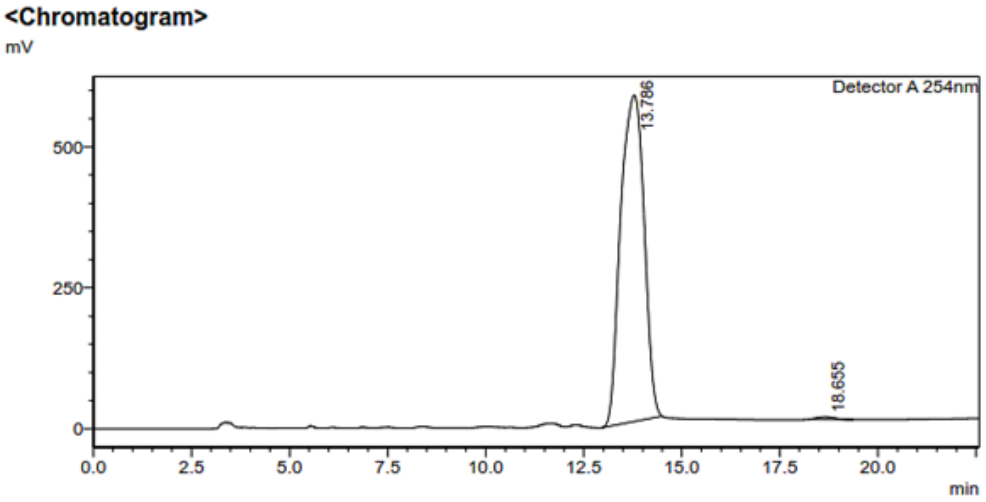


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	13.406	27147153	555958	50.409		M	
2	18.725	26681903	444755	49.591		M	
Total		53829057	1000713				

Chiral **5**:

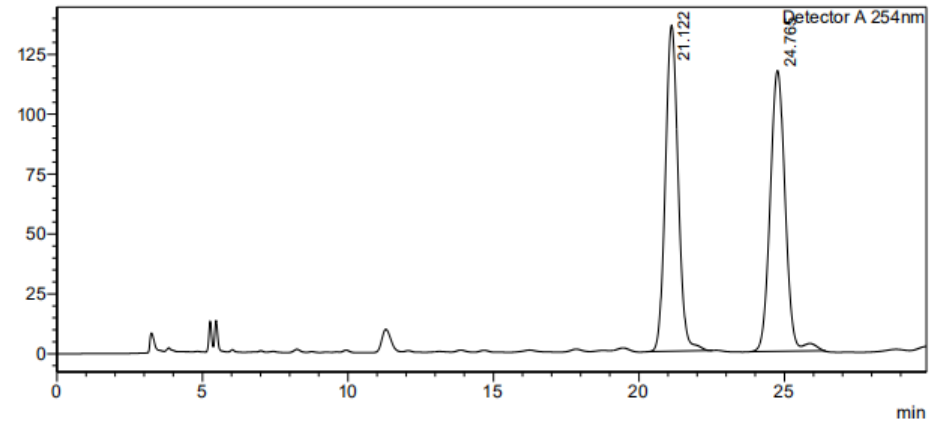


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	13.786	24089891	578911	99.173		M	
2	18.655	200809	4474	0.827		M	
Total		24290701	583385				

Racemic **6**:

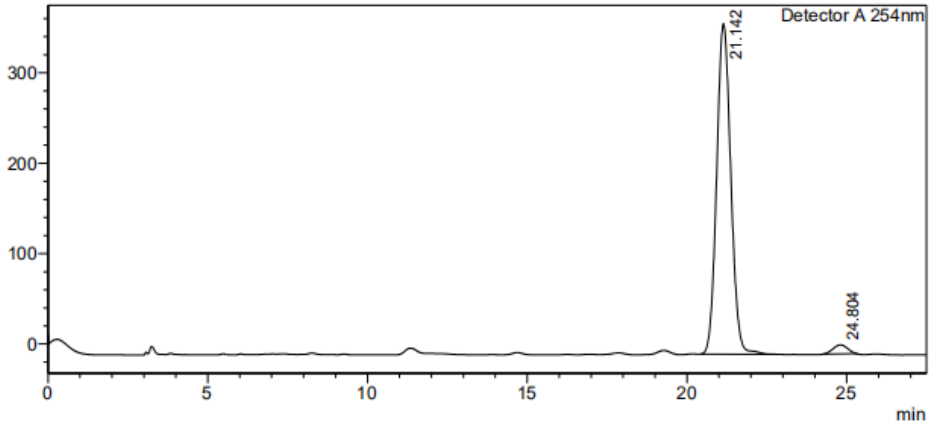


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	21.122	4177889	136077	49.780		M	
2	24.765	4214822	117245	50.220		M	
Total		8392711	253322				

Chiral **6**:



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	21.142	11230051	365377	97.334		M	
2	24.804	307550	9871	2.666		M	
Total		11537601	375248				

7. Single Crystal X-Ray Diffraction Studies

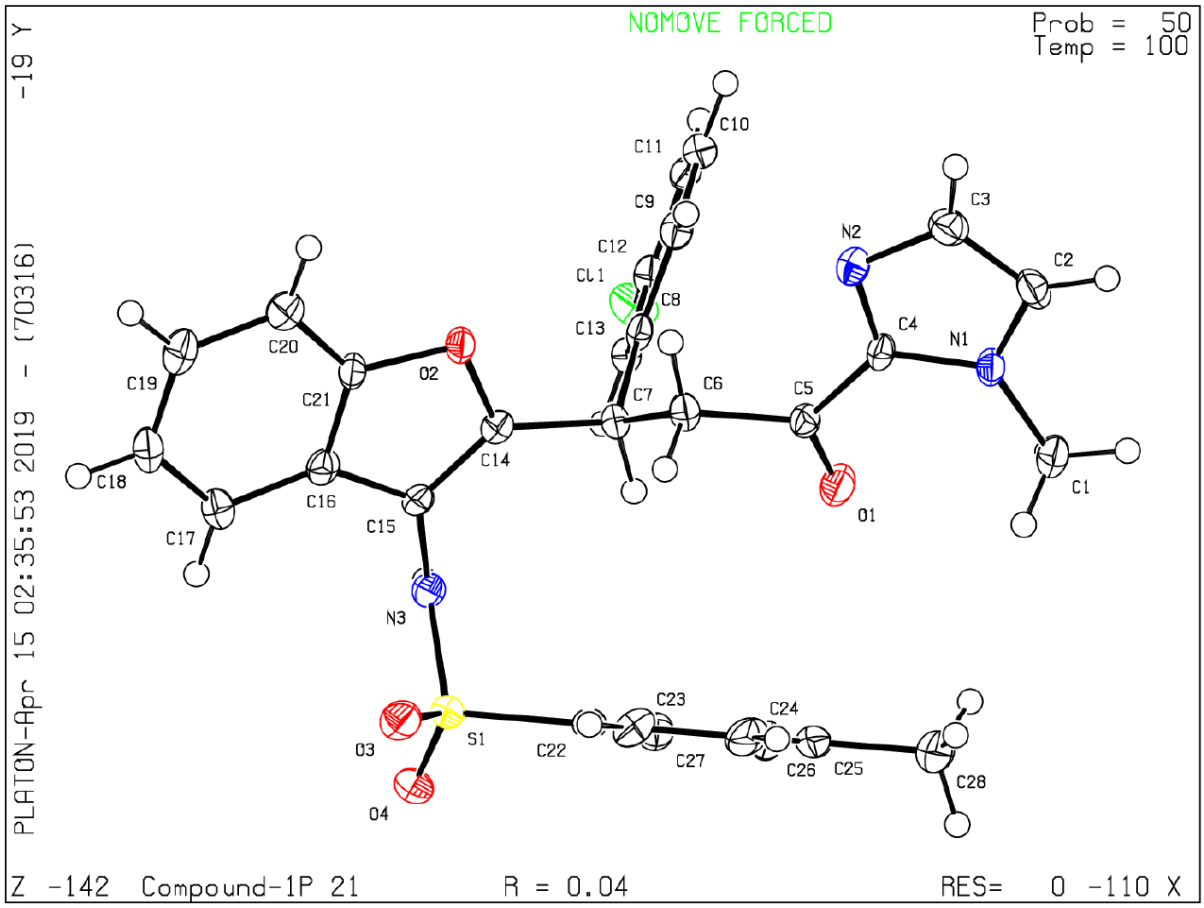


Figure S1. The X-ray structure of **4f** with thermal ellipsoids shown at the 50% probability level.

Table 1. Crystal data and structure refinement for data.

Identification code	Compound-1	
Empirical formula	C28 H24 Cl N3 O4 S	
Formula weight	534.01	
Temperature	100.0(3) K	
Wavelength	1.54184 Å	
Crystal system	Monoclinic	
Space group	P 21	
Unit cell dimensions	a = 9.5954(4) Å	α= 90°.
	b = 12.6894(4) Å	β= 112.927(4)°.
	c = 11.2412(4) Å	γ= 90°.
Volume	1260.60(9) $Å^3$	
Z	2	
Density (calculated)	1.407 Mg/m^3	
Absorption coefficient	2.456 mm^{-1}	
F(000)	556	
Crystal size	0.21 × 0.17 × 0.14 mm^3	
Theta range for data collection	4.270 to 73.351°.	
Index ranges	-11<=h<=11, -15<=k<=15, -11<=l<=13	

Reflections collected	9033
Independent reflections	4900 [R(int) = 0.0532]
Completeness to theta = 67.684°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.00000 and 0.60035
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4900 / 1 / 336
Goodness-of-fit on F^2	1.031
Final R indices [I>2sigma(I)]	R1 = 0.0402, wR2 = 0.0890
R indices (all data)	R1 = 0.0477, wR2 = 0.0936
Absolute structure parameter	-0.014(13)
Extinction coefficient	n/a
Largest diff. peak and hole	0.212 and -0.345 e.$Å^{-3}$