

## Supporting Information

### **Synergistic silver/scandium catalytic spiroketalization of $\beta$ -alkynyl ketones for the atom-economic synthesis of skeletally diverse spirocyclic isochromenes**

Cheng-Long Ji,<sup>a</sup> Yao Pan,<sup>a</sup> Fang-Zhou Geng,<sup>a</sup> Wen-Juan Hao,<sup>a,\*</sup> Shu-Jiang Tu,<sup>a,\*</sup> and Bo Jianga,<sup>\*</sup>

<sup>a</sup>School of Chemistry & Materials Science, Jiangsu Key Laboratory of Green Synthetic Chemistry for Functional Materials, Jiangsu Normal University, Xuzhou 221116, P. R. China; email [jiangchem@jsnu.edu.cn](mailto:jiangchem@jsnu.edu.cn) (B.J.); [wjhao@jsnu.edu.cn](mailto:wjhao@jsnu.edu.cn) (W.J.H.), [laotu@jsnu.edu.cn](mailto:laotu@jsnu.edu.cn) (S.J.T.)

#### Context

General Information.....	S2
General Procedure for the Synthesis of Compounds <b>3</b> .....	S2
Characterization Data of Compounds <b>3a-3q</b> .....	S2-S7
General Procedure for the Synthesis of Compounds <b>5</b> .....	S7
Characterization Data of Compounds <b>5a-5z</b> .....	S7-S16
Copies of <sup>1</sup> H and <sup>13</sup> C NMR Spectra for Compounds <b>3a-3q</b> .....	S17-S50
Copies of <sup>1</sup> H and <sup>13</sup> C NMR Spectra for Compounds <b>5a-5z</b> .....	S51-S102

## General Information

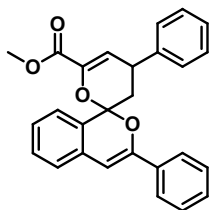
$^1\text{H}$  NMR ( $^{13}\text{C}$  NMR) spectra were measured on a Bruker DPX 400 MHz spectrometer in  $\text{CDCl}_3$  ( $\text{DMSO-}d_6$ ) with chemical shift ( $\delta$ ) given in ppm relative to TMS as internal standard [(s = singlet, d = doublet, t = triplet, brs = broad singlet, m = multiplet), coupling constant (Hz)]. HRMS (ESI) was determined by using microTOF-QII HRMS/MS instrument (BRUKER). X-Ray crystallographic analysis was performed with a Siemens SMART CCD and a Siemens P4 diffractometer.

### General procedure for the synthesis of compounds 3

Example for the synthesis of **3a**:

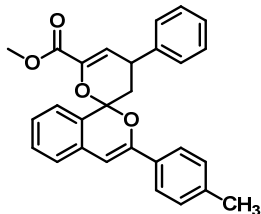
A mixture of 1-(2-(phenylethynyl)phenyl)ethanone (**1a**, 0.45 mmol, 99 mg), (*E*)-methyl 2-oxo-4-phenylbut-3-enoate (**2a**, 0.3 mmol, 57 mg), AgTFA (10 mol%, 6 mg) and  $\text{Sc}(\text{OTf})_3$  (10 mol%, 15mg) were sequentially added in a 10-mL reaction vial. Then, toluene (3.0 mL) was added into this reaction system. The reaction vial was sealed and stirred at room temperature until TLC (petroleum ether: ethyl acetate= 12:1) revealed that conversion of the starting material **1a** was completed. Next, the reaction mixture was concentrated by vacuum distillation and was purified by flash column chromatography (silica gel, petroleum ether) to afford the desired pure product **3a**.

#### Methyl 3,4'-diphenyl-3',4'-dihydrospiro[isochromene-1,2'-pyran]-6'-carboxylate (**3a**)



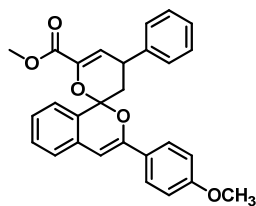
White solid; 86.1 mg, 70% yield; mp: 157-158 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ) ( $\delta$ , ppm): 7.76 – 7.70 (m, 2H), 7.44 – 7.37 (m, 9H), 7.33 – 7.26 (m, 3H), 6.66 (s, 1H), 6.50 (d,  $J$  = 1.6 Hz, 1H), 4.34 – 4.28 (m, 1H), 3.71 (s, 3H), 2.78 – 2.71 (m, 1H), 2.60 – 2.52 (m, 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ) ( $\delta$ , ppm): 163.0, 149.01, 142.7, 141.6, 134.4, 130.8, 129.7, 129.0, 128.9, 128.6, 128.5, 127.7, 127.2, 127.2, 125.2, 125.1, 123.9, 115.1, 101.2, 99.2, 52.2, 38.2, 36.0. IR (KBr,  $\nu$ ,  $\text{cm}^{-1}$ ): 3031, 2955, 1733, 1645, 1454, 839, 756; HRMS (ESI -TOF)  $m/z$  calcd for  $\text{C}_{27}\text{H}_{22}\text{O}_4\text{Na}$  [ $\text{M}+\text{Na}$ ] $^+$  443.1416, found 443.1419;

#### Methyl 4'-phenyl-3-(*p*-tolyl)-3',4'-dihydrospiro[isochromene-1,2'-pyran]-6'-carboxylate (**3b**)



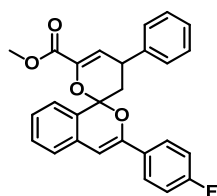
White solid; 105.6 mg, 83% yield; mp: 150-151 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ) ( $\delta$ , ppm): 7.62 (d,  $J$  = 8.4 Hz, 2H), 7.42 – 7.36 (m, 7H), 7.28 (s, 1H), 7.26 – 7.20 (m, 3H), 6.60 (s, 1H), 6.52 – 6.48 (m, 1H), 4.33 – 4.27 (m, 1H), 3.71 (s, 3H), 2.78 – 2.68 (m, 1H), 2.57 (d,  $J$  = 12.4 Hz, 1H), 2.40 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ) ( $\delta$ , ppm): 163.0, 149.2, 142.8, 141.6, 139.0, 131.6, 131.0, 129.6, 129.3, 128.9, 128.3, 127.7, 127.1, 127.0, 125.1, 125.0, 123.8, 115.1, 100.5, 99.2, 52.2, 38.2, 36.0, 21.4. IR (KBr,  $\nu$ ,  $\text{cm}^{-1}$ ): 3054, 2961, 1730, 1559, 1457, 839, 760; HRMS (ESI -TOF)  $m/z$  calcd for  $\text{C}_{28}\text{H}_{24}\text{O}_4\text{Na}$  [ $\text{M}+\text{Na}$ ] $^+$  447.1572, found 447.1583;

**Methyl 3-(4-methoxyphenyl)-4'-phenyl-3',4'-dihydrospiro[isochromene-1,2'-pyran]-6'-carboxylate (3c)**



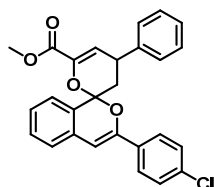
White solid; 66.0 mg, 50% yield; mp: 145-146 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) (δ, ppm): 7.65 (d, *J* = 8.8 Hz, 2H), 7.40 – 7.35 (m, 7H), 7.32 (d, *J* = 6.4 Hz, 1H), 7.23 (d, *J* = 8.0 Hz, 1H), 6.94 (d, *J* = 8.8 Hz, 2H), 6.53 (s, 1H), 6.48 (s, 1H), 4.31 – 4.27 (m, 1H), 3.85 (s, 3H), 3.71 (s, 3H), 2.76 – 2.70 (m, 1H), 2.56 (d, *J* = 12.8 Hz, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) (δ, ppm): 163.0, 160.3, 149.0, 142.8, 141.6, 131.1, 129.6, 128.9, 128.2, 127.7, 127.1, 127.1, 126.7, 126.6, 124.9, 123.8, 115.0, 114.0, 99.6, 99.2, 55.4, 52.2, 38.2, 36.0. IR (KBr, ν, cm<sup>-1</sup>): 3052, 2961, 1728, 1539, 1454, 843, 760; HRMS (ESI -TOF) *m/z* calcd for C<sub>28</sub>H<sub>24</sub>O<sub>5</sub>Na [M+Na]<sup>+</sup>463.1521, found 463.1527;

**Methyl 3-(4-fluorophenyl)-4'-phenyl-3',4'-dihydrospiro[isochromene-1,2'-pyran]-6'-carboxylate (3d)**



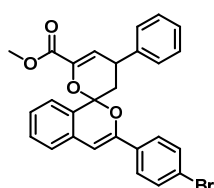
Yellow solid; 111.7 mg, 87% yield; mp: 148-149 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) (δ, ppm): 7.71 – 7.67 (m, 2H), 7.43 – 7.35 (m, 7H), 7.33 (d, *J* = 6.8 Hz, 1H), 7.28 (d, *J* = 2.0 Hz, 1H), 7.13 – 7.08 (m, 2H), 6.58 (s, 1H), 6.49 (s, 1H), 4.30 – 4.25 (m, 1H), 3.72 (s, 3H), 2.76 – 2.71 (m, 1H), 2.60 – 2.53 (m, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) (δ, ppm): 164.4 (<sup>1</sup>*J*<sub>CF</sub> = 247.5 Hz), 163.0, 162.0, 148.2, 142.6, 141.6, 130.7 (<sup>3</sup>*J*<sub>CF</sub> = 7.3 Hz), 130.6, 130.6, 129.7, 129.0, 128.3, 127.7, 127.2 (<sup>4</sup>*J*<sub>CF</sub> = 4.4 Hz), 127.2, 127.0, 126.9, 125.1, 123.9, 115.7 (<sup>2</sup>*J*<sub>CF</sub> = 21.7 Hz), 115.5, 115.1, 101.0, 99.2, 52.3, 38.1, 36.0. IR (KBr, ν, cm<sup>-1</sup>): 3063, 2956, 1724, 1652, 1456, 854, 768; HRMS (ESI -TOF) *m/z* calcd for C<sub>27</sub>H<sub>21</sub>FO<sub>4</sub>Na [M+Na]<sup>+</sup>451.1322, found 451.1318;

**Methyl 3-(4-chlorophenyl)-4'-phenyl-3',4'-dihydrospiro[isochromene-1,2'-pyran]-6'-carboxylate (3e)**



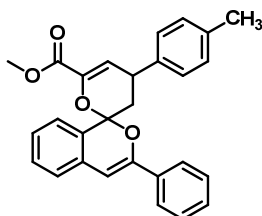
Yellow solid; 103.9 mg, 87% yield; mp: 154-155 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) (δ, ppm): 7.64 (d, *J* = 8.4 Hz, 2H), 7.42 – 7.36 (m, 9H), 7.31 (d, *J* = 7.6 Hz, 2H), 6.63 (s, 1H), 6.49 (s, 1H), 4.30 – 4.24 (m, 1H), 3.72 (s, 3H), 2.76 – 2.71 (m, 1H), 2.59 – 2.53 (m, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) (δ, ppm): 162.9, 148.0, 142.6, 141.5, 134.7, 132.9, 130.5, 129.7, 129.0, 128.8, 128.5, 127.7, 127.4, 127.2, 126.3, 125.3, 123.9, 115.1, 101.7, 99.2, 52.3, 38.1, 36.0. IR (KBr, ν, cm<sup>-1</sup>): 3066, 2950, 1733, 1646, 1455, 809, 760; HRMS (ESI -TOF) *m/z* calcd for C<sub>27</sub>H<sub>21</sub>ClO<sub>4</sub>Na [M+Na]<sup>+</sup>467.1026, found 467.1043;

**Methyl 3-(4-bromophenyl)-4'-phenyl-3',4'-dihydrospiro[isochromene-1,2'-pyran]-6'-carboxylate (3f)**



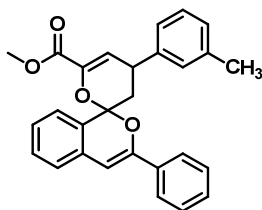
Yellow solid; 101.0 mg, 69% yield; mp: 152-153 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) (δ, ppm): 7.58 (d, *J* = 8.4 Hz, 2H), 7.53 (d, *J* = 8.4 Hz, 2H), 7.43 – 7.35 (m, 7H), 7.33 – 7.28 (m, 2H), 6.65 (s, 1H), 6.48 (s, 1H), 4.29 – 4.24 (m, 1H), 3.72 (s, 3H), 2.76 – 2.71 (m, 1H), 2.59 – 2.53 (m, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) (δ, ppm): 162.9, 148.0, 142.6, 141.5, 133.3, 131.8, 130.5, 129.7, 129.0, 128.5, 127.7, 127.5, 127.2, 126.5, 125.3, 123.9, 123.0, 115.1, 101.8, 99.2, 52.2, 38.1, 35.9. IR (KBr, ν, cm<sup>-1</sup>): 3054, 2957, 1732, 1644, 1452, 852, 758; HRMS (ESI -TOF) *m/z* calcd for C<sub>27</sub>H<sub>21</sub>BrO<sub>4</sub>Na [M+Na]<sup>+</sup>511.0521, found 511.0513;

**Methyl 3-phenyl-4'-(*p*-tolyl)-3',4'-dihydrospiro[isochromene-1,2'-pyran]-6'-carboxylate (3g)**



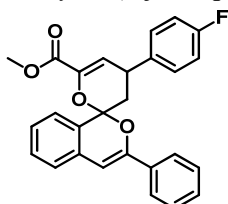
White solid; 108.1 mg, 85% yield; mp: 146-147 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) (δ, ppm): 7.75 – 7.70 (m, 2H), 7.44 – 7.36 (m, 6H), 7.29 (d, *J* = 1.4 Hz, 1H), 7.27 (d, *J* = 2.0 Hz, 1H), 7.26 (s, 1H), 7.21 (d, *J* = 8.0 Hz, 2H), 6.65 (s, 1H), 6.50 – 6.46 (m, 1H), 4.30 – 4.25 (m, 1H), 3.71 (s, 3H), 2.74 – 2.69 (m, 1H), 2.60 – 2.51 (m, 1H), 2.38 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) (δ, ppm): 162.9, 149.1, 142.3, 141.8, 134.3, 133.1, 130.9, 129.7, 128.9, 128.8, 128.7, 128.5, 128.4, 128.2, 127.1, 125.1, 125.0, 124.4, 123.8, 114.3, 101.1, 99.4, 52.3, 36.0, 35.6. IR (KBr, ν, cm<sup>-1</sup>): 3031, 2963, 1731, 1559, 1456, 839 762; HRMS (ESI -TOF) *m/z* calcd for C<sub>28</sub>H<sub>24</sub>O<sub>4</sub>Na [M+Na]<sup>+</sup>447.1572, found 447.1580;

**Methyl 3-phenyl-4'-(*m*-tolyl)-3',4'-dihydrospiro[isochromene-1,2'-pyran]-6'-carboxylate (3h)**



White solid; 101.7 mg, 80% yield; mp: 144-145 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) (δ, ppm): 7.72 (d, *J* = 7.2 Hz, 2H), 7.44 – 7.36 (m, 6H), 7.30 – 7.27 (m, 3H), 7.19 – 7.11 (m, 3H), 6.65 (s, 1H), 6.49 (s, 1H), 4.30 – 4.23 (m, 1H), 3.71 (s, 3H), 2.76 – 2.68 (m, 1H), 2.60 – 2.52 (m, 1H), 2.39 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) (δ, ppm): 163.0, 149.0, 142.7, 141.5, 138.6, 134.4, 130.8, 129.6, 128.9, 128.8, 128.7, 128.7, 128.6, 128.5, 128.4, 128.4, 127.9, 127.7, 127.2, 125.2, 125.1, 124.8, 123.9, 115.3, 101.2, 99.2, 52.2, 38.2, 35.9, 21.5. IR (KBr, ν, cm<sup>-1</sup>): 3065, 2951, 1725, 1653, 1455, 854 764; HRMS (ESI -TOF) *m/z* calcd for C<sub>28</sub>H<sub>24</sub>O<sub>4</sub>Na [M+Na]<sup>+</sup>447.1572, found 447.1577;

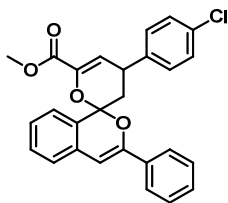
**Methyl 4'-(4-fluorophenyl)-3-phenyl-3',4'-dihydrospiro[isochromene-1,2'-pyran]-6'-carboxylate (3i)**



White solid; 101.4 mg, 79% yield; mp: 170-171 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) (δ, ppm): 7.76 – 7.68 (m, 2H), 7.44 – 7.36 (m, 5H), 7.36 – 7.31 (m, 2H), 7.29 (d, *J* = 7.2 Hz, 2H), 7.12 – 7.04 (m, 2H), 6.65 (s, 1H), 6.50 – 6.37 (m, 1H), 4.33 – 4.25 (m, 1H), 3.71 (s, 3H), 2.77 – 2.67 (m, 1H), 2.60 – 2.45 (m, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) (δ, ppm): 163.2 (<sup>1</sup>*J*<sub>CF</sub> = 243.9 Hz), 162.9, 160.7, 149.0, 141.7, 138.4 (<sup>4</sup>*J*<sub>CF</sub> = 3.2 Hz), 138.4, 134.3, 132.7, 130.8, 129.7, 129.2, 129.2

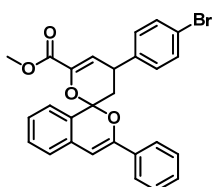
( $^3J_{\text{CF}} = 8.0$  Hz), 129.0, 128.7, 128.6, 128.3, 128.1, 127.7, 127.2, 126.4, 126.1, 125.2, 125.1, 123.8, 115.8 ( $^2J_{\text{CF}} = 21.3$  Hz), 115.6, 114.8, 101.2, 99.2, 52.3, 38.4, 35.3. IR (KBr,  $\nu$ ,  $\text{cm}^{-1}$ ): 3034, 2955, 1734, 1646, 1455, 832, 766; HRMS (ESI -TOF)  $m/z$  calcd for  $\text{C}_{27}\text{H}_{21}\text{FO}_4\text{Na}$   $[\text{M}+\text{Na}]^+451.1322$ , found 451.1338;

**Methyl 4'-(4-chlorophenyl)-3-phenyl-3',4'-dihydrospiro[isochromene-1,2'-pyran]-6'-carboxylate (3j)**



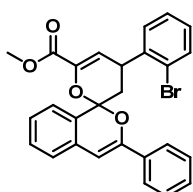
White solid; 119.9 mg, 90% yield; mp: 168-169 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ) ( $\delta$ , ppm): 7.78 – 7.74 (m, 2H), 7.50 – 7.41 (m, 7H), 7.37 – 7.32 (m, 4H), 6.70 (s, 1H), 6.49 (s, 1H), 4.37 – 4.31 (m, 1H), 3.76 (s, 3H), 2.80 – 2.70 (m, 1H), 2.63 – 2.50 (m, 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ) ( $\delta$ , ppm): 162.9, 149.0, 141.9, 141.2, 134.3, 132.9, 130.8, 129.7, 129.1, 129.1, 129.0, 128.7, 128.7, 128.6, 128.4, 128.3, 128.1, 127.2, 125.2, 125.1, 123.8, 114.4, 101.3, 99.1, 52.3, 38.2, 35.4. IR (KBr,  $\nu$ ,  $\text{cm}^{-1}$ ): 3032, 2953, 1737, 1644, 1454, 856, 767; HRMS (ESI -TOF)  $m/z$  calcd for  $\text{C}_{27}\text{H}_{21}\text{ClO}_4\text{Na}$   $[\text{M}+\text{Na}]^+467.1026$ , found 467.1058;

**Methyl 4'-(4-bromophenyl)-3-phenyl-3',4'-dihydrospiro[isochromene-1,2'-pyran]-6'-carboxylate (3k)**



White solid; 127.4 mg, 87% yield; mp: 162-163 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ) ( $\delta$ , ppm): 7.73 – 7.68 (m, 2H), 7.52 (d,  $J = 8.0$  Hz, 2H), 7.44 – 7.36 (m, 5H), 7.29 (d,  $J = 7.2$  Hz, 2H), 7.24 (s, 2H), 6.65 (s, 1H), 6.43 (s, 1H), 4.31 – 4.23 (m, 1H), 3.71 (s, 3H), 2.77 – 2.65 (m, 1H), 2.57 – 2.44 (m, 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ) ( $\delta$ , ppm): 162.9, 149.0, 141.9, 141.8, 134.3, 132.0, 130.8, 129.7, 129.5, 129.0, 128.6, 128.2, 128.1, 127.7, 127.2, 125.2, 125.1, 123.8, 120.9, 114.2, 101.3, 99.1, 52.3, 38.1, 35.5. IR (KBr,  $\nu$ ,  $\text{cm}^{-1}$ ): 3038, 2956, 1737, 1644, 1455, 856, 766; HRMS (ESI -TOF)  $m/z$  calcd for  $\text{C}_{27}\text{H}_{21}\text{BrO}_4\text{Na}$   $[\text{M}+\text{Na}]^+511.0521$ , found 511.0529;

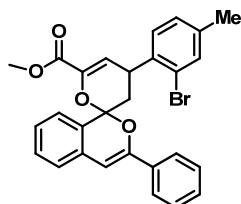
**Methyl 4'-(2-bromophenyl)-3-phenyl-3',4'-dihydrospiro[isochromene-1,2'-pyran]-6'-carboxylate (3l)**



White solid; 66.0 mg, 45% yield; mp: 193-194 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ) ( $\delta$ , ppm): 7.75 (d,  $J = 7.6$  Hz, 2H), 7.60 (d,  $J = 8.0$  Hz, 1H), 7.43 – 7.34 (m, 6H), 7.29 (s, 1H), 7.20 – 7.12 (m, 1H), 6.65 (s, 1H), 6.47 (s, 1H), 4.87 – 4.74 (m, 1H), 3.73 (s, 3H), 3.07 – 2.83 (m, 1H), 2.37 – 2.27 (m, 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ) ( $\delta$ , ppm): 162.9, 149.1, 142.3, 141.8, 134.3, 133.1, 130.9, 129.7, 128.9, 128.8, 128.7, 128.5, 128.4, 128.2, 127.1, 125.1, 125.0, 124.4, 123.8, 114.3, 101.1, 99.4, 52.3, 36.0, 35.6.

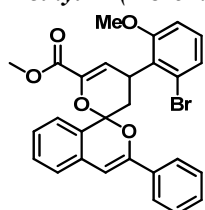
IR (KBr,  $\nu$ ,  $\text{cm}^{-1}$ ): 3060, 2952, 1731, 1652, 1455, 855, 759; HRMS (ESI -TOF)  $m/z$  calcd for  $\text{C}_{27}\text{H}_{21}\text{BrO}_4\text{Na}$   $[\text{M}+\text{Na}]^+511.0521$ , found 511.0524;

**Methyl 4'-(2-bromo-4-methylphenyl)-3-phenyl-3',4'-dihydrospiro[isochromene-1,2'-pyran]-6'-carboxylate (3m)**



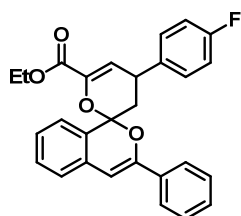
White solid; 93.7 mg, 62% yield; mp: 178-179 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) (δ, ppm): 7.77 – 7.71 (m, 2H), 7.45 – 7.34 (m, 7H), 7.28 (d, *J* = 2.8 Hz, 2H), 7.17 (d, *J* = 7.2 Hz, 1H), 6.65 (s, 1H), 6.46 (s, 1H), 4.80 – 4.72 (m, 1H), 3.72 (s, 3H), 2.93 – 2.88 (m, 1H), 2.35 (s, 3H), 2.29 (d, *J* = 12.8 Hz, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) (δ, ppm): 162.9, 149.1, 142.1, 138.8, 138.7, 134.3, 133.5, 130.9, 129.6, 129.0, 128.9, 128.5, 128.5, 128.4, 127.1, 125.1, 125.1, 124.1, 123.8, 114.7, 101.1, 99.4, 52.3, 36.1, 35.2. IR (KBr, ν, cm<sup>-1</sup>): 3063, 2951, 1731, 1651, 1455, 855, 767; HRMS (ESI -TOF) *m/z* calcd for C<sub>28</sub>H<sub>23</sub>BrO<sub>4</sub>Na [M+Na]<sup>+</sup>525.0677, found 525.0667;

**Methyl 4'-(2-bromo-6-methoxyphenyl)-3-phenyl-3',4'-dihydrospiro[isochromene-1,2'-pyran]-6'-carboxylate (3n)**



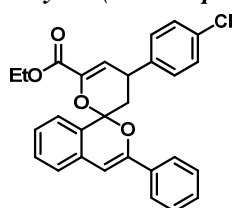
Yellow solid; 93.2 mg, 60% yield; mp: 132-133 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) (δ, ppm): 7.75 (d, *J* = 7.2 Hz, 2H), 7.48 (d, *J* = 8.4 Hz, 1H), 7.44 – 7.36 (m, 5H), 7.29 (s, 1H), 6.95 (d, *J* = 2.8 Hz, 1H), 6.75 – 6.71 (m, 1H), 6.65 (s, 1H), 6.46 (s, 1H), 4.79 – 4.74 (m, 1H), 3.83 (s, 3H), 3.73 (s, 3H), 2.95 – 2.89 (m, 1H), 2.35 – 2.28 (m, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) (δ, ppm): 162.8, 159.5, 149.1, 142.9, 142.3, 134.3, 133.6, 130.9, 129.7, 128.9, 128.5, 128.3, 127.1, 125.1, 125.0, 123.8, 114.8, 114.7, 114.2, 114.0, 101.1, 99.4, 55.6, 52.3, 35.9, 35.7. IR (KBr, ν, cm<sup>-1</sup>): 3057, 2954, 1737, 1645, 1455, 856, 756; HRMS (ESI -TOF) *m/z* calcd for C<sub>28</sub>H<sub>23</sub>BrO<sub>5</sub>Na [M+Na]<sup>+</sup>541.0627, found 541.0632;

**Ethyl 4'-(4-fluorophenyl)-3-phenyl-3',4'-dihydrospiro[isochromene-1,2'-pyran]-6'-carboxylate (3o)**



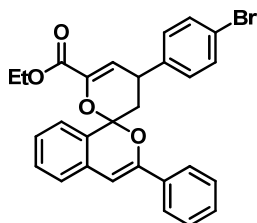
White solid; 99.5 mg, 75% yield; mp: 150-151 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) (δ, ppm): 7.72 (d, *J* = 7.2 Hz, 2H), 7.43 – 7.32 (m, 7H), 7.28 (d, *J* = 6.8 Hz, 2H), 7.11 – 7.06 (m, 2H), 6.65 (s, 1H), 6.43 (s, 1H), 4.32 – 4.26 (m, 1H), 4.22 – 4.16 (m, 2H), 2.74 – 2.68 (m, 1H), 2.55 – 2.47 (m, 1H), 1.26 – 1.21 (m, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) (δ, ppm): 162.4 (<sup>1</sup>*J*<sub>CF</sub> = 243.8 Hz), 160.7, 149.0, 141.9, 138.5, 134.4, 130.8, 129.6, 129.3 (<sup>3</sup>*J*<sub>CF</sub> = 8.5 Hz), 129.2, 128.9, 128.6 (<sup>4</sup>*J*<sub>CF</sub> = 4.3 Hz), 128.5, 128.4, 127.1, 125.2, 125.1, 123.9, 115.8 (<sup>2</sup>*J*<sub>CF</sub> = 21.5 Hz), 115.6, 114.4, 101.3, 99.2, 61.2, 38.4, 35.3, 14.1. IR (KBr, ν, cm<sup>-1</sup>): 3042, 2957, 1718, 1644, 1457, 862, 762; HRMS (ESI -TOF) *m/z* calcd for C<sub>28</sub>H<sub>23</sub>FO<sub>4</sub>Na [M+Na]<sup>+</sup>465.1478, found 465.1516;

**Ethyl 4'-(4-chlorophenyl)-3-phenyl-3',4'-dihydrospiro[isochromene-1,2'-pyran]-6'-carboxylate (3p)**



White solid; 112.7 mg, 82% yield; mp: 175-176 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) (δ, ppm): 7.71 (d, *J* = 7.6 Hz, 2H), 7.44 – 7.35 (m, 7H), 7.32 (s, 1H), 7.29 (d, *J* = 3.2 Hz, 1H), 7.27 (s, 1H), 7.26 (d, *J* = 3.2 Hz, 1H), 6.64 (s, 1H), 6.41 (s, 1H), 4.31 – 4.25 (m, 1H), 4.22 – 4.16 (m, 2H), 2.74 – 2.67 (m, 1H), 2.53 – 2.46 (m, 1H), 1.26 – 1.21 (m, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) (δ, ppm): 162.3, 149.0, 142.0, 141.3, 134.4, 132.9, 130.8, 129.7, 129.1, 129.0, 128.9, 128.5, 128.4, 127.2, 125.2, 125.1, 123.9, 114.0, 101.3, 99.1, 61.3, 38.2, 35.4, 14.1. IR (KBr, ν, cm<sup>-1</sup>): 3051, 2960, 1726, 1642, 1455, 861, 761; HRMS (ESI -TOF) *m/z* calcd for C<sub>28</sub>H<sub>23</sub>ClO<sub>4</sub>Na [M+Na]<sup>+</sup>481.1183, found 481.1194;

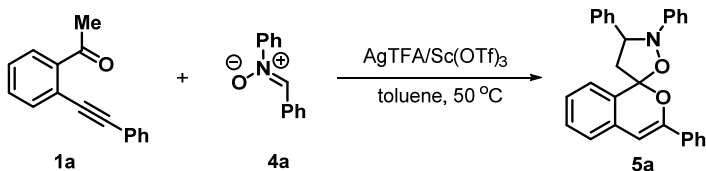
**Ethyl 4'-(4-bromophenyl)-3-phenyl-3',4'-dihydrospiro[isochromene-1,2'-pyran]-6'-carboxylate (3q)**



White solid; 117.5 mg, 78% yield; mp: 172-173 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) (δ, ppm): 7.71 (d, *J* = 7.2 Hz, 2H), 7.52 (d, *J* = 8.4 Hz, 2H), 7.44 – 7.36 (m, 5H), 7.29 (s, 2H), 7.24 (s, 2H), 6.64 (s, 1H), 6.40 (s, 1H), 4.29 – 4.24 (m, 1H), 4.22 – 4.16 (m, 2H), 2.73 – 2.67 (m, 1H), 2.53 – 2.46 (m, 1H), 1.25 – 1.20 (m, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) (δ, ppm): 162.3, 149.0, 142.1, 141.9, 134.4, 132.0, 130.8, 129.7, 129.5, 128.9, 128.6, 128.3, 127.2, 125.2, 125.1, 123.9, 120.9, 113.9, 101.3, 99.1, 61.3, 38.1, 35.5, 14.1. IR (KBr, ν, cm<sup>-1</sup>): 3035, 2962, 1726, 1643, 1455, 861, 761; HRMS (ESI -TOF) *m/z* calcd for C<sub>28</sub>H<sub>23</sub>BrO<sub>4</sub>Na [M+Na]<sup>+</sup>525.0677, found 525.0692;

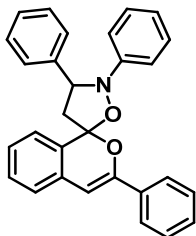
**General procedure for the synthesis of compounds 5**

Example for the synthesis of **5a**:



In a reaction vial, 1-(2-(phenylethynyl)phenyl)ethanone (**1a**, 0.45 mmol, 99 mg), (*Z*)-*N*-benzylideneaniline oxide (**4a**, 0.3 mmol, 59 mg), AgTFA (10 mol%, 6 mg) and Sc(OTf)<sub>3</sub> (10 mol%, 15mg) were mixed in toluene (3.0 mL). Then the vial was stirred and heated at 50 °C for 8 hours until complete consumption of starting material as monitored by TLC (petroleum ether: ethyl acetate 10:1) analysis. Then the solvent was evaporated under reduced pressure, and the crude products were purified through preparative thin layer chromatography to get chiral desired products **5a**.

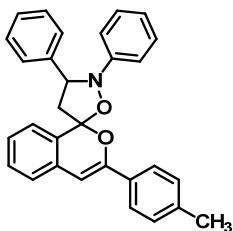
**2',3,3'-Triphenylspiro[isochromene-1,5'-isoxazolidine] (5a)**



White solid; 85.0 mg, 68% yield; mp: 179-180 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) (δ, ppm): 7.73 (d, *J* = 7.2 Hz, 2H), 7.56 – 7.47 (m, 4H), 7.42 (d, *J* = 7.2 Hz, 1H), 7.37 – 7.33 (m, 2H), 7.24 – 7.20 (m, 1H), 7.19 – 7.12 (m, 4H), 7.08 – 7.03 (m, 2H), 6.97 – 6.90 (m, 2H), 6.81 – 6.76 (m, 1H), 6.66 (s, 1H), 5.45 – 5.38 (m, 1H), 3.38 – 3.27 (m, 2H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) (δ, ppm): 153.8, 150.0, 142.0, 133.6, 132.6, 130.2, 129.2, 128.7, 128.67, 128.6, 128.6, 128.6, 128.0,

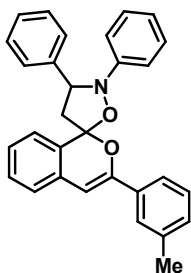
128.0, 127.9, 127.0, 126.6, 125.3, 125.1, 124.5, 123.7, 121.2, 113.6, 107.0, 100.5, 69.9, 50.0. IR (KBr,  $\nu$ ,  $\text{cm}^{-1}$ ): 3035, 2965, 1749, 1540, 1457, 852, 703; HRMS (ESI -TOF)  $m/z$  calcd for  $\text{C}_{29}\text{H}_{23}\text{NO}_2\text{Na}$   $[\text{M}+\text{Na}]^+$  45.1626, found 44.1617;

**2',3'-Diphenyl-3-(p-tolyl)spiro[isochromene-1,5'-isoxazolidine] (5b)**



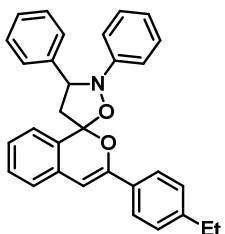
Yellow solid; 77.6 mg, 60% yield; mp: 177-178 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ) ( $\delta$ , ppm): 7.69 (d,  $J = 7.2\text{Hz}$ , 2H), 7.53 – 7.43 (m, 4H), 7.38 (d,  $J = 7.2\text{ Hz}$ , 1H), 7.32 – 7.28 (m, 2H), 7.06 – 6.99 (m, 4H), 6.92 – 6.85 (m, 4H), 6.80 – 6.74 (m, 1H), 6.56 (s, 1H), 5.39 – 5.33 (m, 1H), 3.33 – 3.24 (m, 2H), 2.29 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ) ( $\delta$ , ppm): 153.7, 150.1, 141.9, 138.5, 132.7, 130.8, 130.0, 129.1, 128.7, 128.5, 128.4, 127.8, 126.7, 126.5, 125.2, 124.9, 124.3, 123.5, 121.0, 113.5, 106.9, 99.6, 69.7, 50.0, 29.7, 21.3 IR (KBr,  $\nu$ ,  $\text{cm}^{-1}$ ): 3034, 2962, 1635, 1540, 1452, 836, 701; HRMS (ESI -TOF)  $m/z$  calcd for  $\text{C}_{30}\text{H}_{25}\text{NO}_2\text{Na}$   $[\text{M}+\text{Na}]^+$  45.1783, found 45.1784;

**2',3'-Diphenyl-3-(m-tolyl)spiro[isochromene-1,5'-isoxazolidine] (5c)**



Yellow solid; 81.5 mg, 63% yield; mp: 139-140 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ) ( $\delta$ , ppm): 7.70 (d,  $J = 7.2\text{ Hz}$ , 2H), 7.54 – 7.42 (m, 5H), 7.39 (d,  $J = 7.2\text{ Hz}$ , 1H), 7.33 – 7.29 (m, 2H), 7.07 – 7.01 (m, 5H), 6.89 (d,  $J = 7.6\text{ Hz}$ , 2H), 6.79 (s, 1H), 6.60 (s, 1H), 5.42 – 5.37 (m, 1H), 3.35 – 3.26 (m, 2H), 2.13 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ) ( $\delta$ , ppm): 153.8, 152.7, 141.9, 137.6, 133.5, 132.6, 130.1, 129.4, 129.1, 128.6, 127.8, 126.8, 126.5, 126.4, 126.2, 124.9, 124.4, 123.5, 122.5, 1223, 121.0, 117.2, 113.4, 109.8, 106.9, 100.2, 99.1, 69.7, 49.9, 30.6, 21.3, 11.4. IR (KBr,  $\nu$ ,  $\text{cm}^{-1}$ ): 2927, 2854, 1598, 1507, 1454, 875, 700; HRMS (ESI -TOF)  $m/z$  calcd for  $\text{C}_{30}\text{H}_{25}\text{NO}_2\text{Na}$   $[\text{M}+\text{Na}]^+$  45.1783, found 45.1787;

**3-(4-Ethylphenyl)-2',3'-diphenylspiro[isochromene-1,5'-isoxazolidine] (5d)**

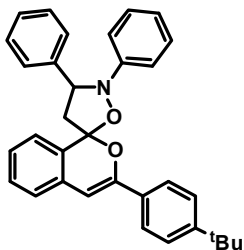


Yellow solid; 86.8 mg, 65% yield; mp: 153-154 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ) ( $\delta$ , ppm): 7.68 (d,  $J = 7.6\text{ Hz}$ , 2H), 7.53 – 7.37 (m, 5H), 7.31 – 7.28 (m, 2H), 7.07 – 6.99 (m, 4H), 6.93 (d,  $J = 8.4\text{ Hz}$ , 2H), 6.88 (d,  $J = 8.0\text{ Hz}$ , 2H), 6.79 – 6.74 (m, 1H), 6.55 (d,  $J = 7.6\text{ Hz}$ , 1H), 5.39 – 5.33 (m, 1H), 3.34 – 3.21 (m, 2H), 2.62 – 2.54 (m, 2H), 1.23 – 1.15 (m, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ) ( $\delta$ , ppm): 153.7, 150.1, 144.9, 141.9, 132.7, 131.1, 130.0, 129.1, 128.5, 128.4, 127.8, 127.5, 126.7, 126.5, 125.6, 125.3, 124.9, 124.3, 123.5, 121.0, 117.5, 113.6, 106.9, 99.7, 69.7, 50.0, 28.6, 15.5. IR (KBr,



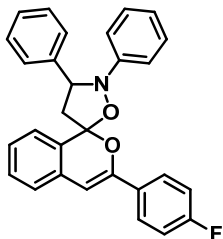
$\nu$ ,  $\text{cm}^{-1}$ ): 3034, 2962, 1633, 1515, 1451, 842, 700; HRMS (ESI -TOF)  $m/z$  calcd for  $\text{C}_{31}\text{H}_{27}\text{NO}_2\text{Na}$   $[\text{M}+\text{Na}]^+$  468.1939, found 468.1920;

**3-(4-(tert-Butyl)phenyl)-2',3'-diphenylspiro[isochromene-1,5'-isoxazolidine] (5e)**



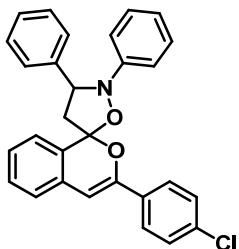
White solid; 76.6 mg, 54% yield; mp: 174-175 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ) ( $\delta$ , ppm): 7.68 (d,  $J = 7.2$  Hz, 2H), 7.51 – 7.39 (m, 5H), 7.31 – 7.28 (m, 2H), 7.13 – 7.10 (m, 2H), 7.08 – 7.00 (m, 4H), 6.89 – 6.85 (m, 2H), 6.77 – 6.72 (m, 1H), 6.57 (s, 1H), 5.38 – 5.33 (m, 1H), 3.33 – 3.23 (m, 2H), 1.28 (s, 9H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ) ( $\delta$ , ppm): 153.8, 150.2, 144.9, 138.8, 137.5, 132.7, 131.1, 130.0, 129.8, 128.5, 127.5, 126.7, 126.4, 125.4, 124.9, 124.4, 123.6, 121.0, 113.61 106.9, 99.7, 69.6, 50.1, 28.7, 21.2, 15.6. IR (KBr,  $\nu$ ,  $\text{cm}^{-1}$ ): 3033, 2970, 1631, 1598, 1452, 876, 701; HRMS (ESI -TOF)  $m/z$  calcd for  $\text{C}_{33}\text{H}_{31}\text{NO}_2\text{Na}$   $[\text{M}+\text{Na}]^+$  496.2252, found 496.2265;

**3-(4-Fluorophenyl)-2',3'-diphenylspiro[isochromene-1,5'-isoxazolidine] (5f)**



White solid; 94.0 mg, 72% yield; mp: 160-161 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ) ( $\delta$ , ppm): 7.72 – 7.68 (m, 2H), 7.54 – 7.44 (m, 4H), 7.42 – 7.38 (m, 1H), 7.36 – 7.30 (m, 2H), 7.13 – 7.01 (m, 4H), 6.90 – 6.85 (m, 2H), 6.82 – 6.76 (m, 3H), 6.58 (s, 1H), 5.40 – 5.35 (m, 1H), 3.37 – 3.25 (m, 2H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ) ( $\delta$ , ppm): 164.1 ( $^1J_{\text{CF}} = 247$  Hz), 161.6, 153.7, 149.0, 141.8, 132.4, 130.2, 129.7 ( $^4J_{\text{CF}} = 3.3$  Hz), 129.7, 129.1, 129.0, 128.6, 127.8, 127.3, 127.1, 127.0 ( $^3J_{\text{CF}} = 8.3$  Hz), 126.4, 125.0, 124.3, 123.3, 121.1, 115.0 ( $^2J_{\text{CF}} = 21.6$  Hz), 114.8, 113.3, 106.9, 100.3, 69.7, 49.7, 29.7, 29.3, 14.1. IR (KBr,  $\nu$ ,  $\text{cm}^{-1}$ ): 3025, 2927, 1634, 1593, 1453, 874, 700; HRMS (ESI -TOF)  $m/z$  calcd for  $\text{C}_{29}\text{H}_{22}\text{FNO}_2\text{Na}$   $[\text{M}+\text{Na}]^+$  458.1532, found 458.1526;

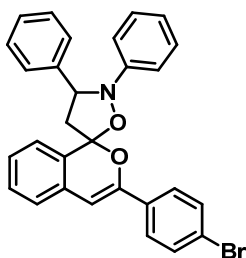
**3-(4-Chlorophenyl)-2',3'-diphenylspiro[isochromene-1,5'-isoxazolidine] (5g)**



Yellow solid; 83.8 mg, 62% yield; mp: 158-159 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ) ( $\delta$ , ppm): 7.69 (d,  $J = 7.6$  Hz, 2H), 7.54 – 7.44 (m, 4H), 7.41 – 7.36 (m, 1H), 7.35 – 7.29 (m, 2H), 7.07 – 6.98 (m, 6H), 6.85 (d,  $J = 8.4$  Hz, 2H), 6.77 (d,  $J = 7.1$  Hz, 1H), 6.61 (s, 1H), 5.38 – 5.32 (m, 1H), 3.35 – 3.20 (m, 2H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ) ( $\delta$ , ppm): 162.3, 149.0, 142.1, 141.9, 134.4, 132.0, 130.8, 129.7, 129.5, 129.9, 128.6, 128.3, 127.2, 125.2, 125.1, 123.9, 120.9, 113.9,

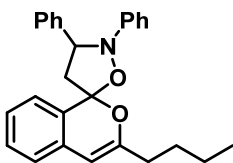
101.3, 99.1, 61.3, 38.1, 35.5. IR (KBr,  $\nu$ ,  $\text{cm}^{-1}$ ): 3062, 2960, 1630, 1596, 1452, 876, 697; HRMS (ESI -TOF)  $m/z$  calcd for  $\text{C}_{29}\text{H}_{22}\text{ClNO}_2\text{Na}$   $[\text{M}+\text{Na}]^+$  474.1237, found 474.1242;

**3-(4-Bromophenyl)-2',3'-diphenylspiro[isochromene-1,5'-isoxazolidine] (5h)**



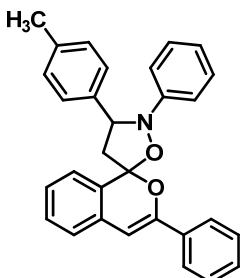
Yellow solid; 93.6 mg, 63% yield; mp: 198-199 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ) ( $\delta$ , ppm): 7.69 (d,  $J = 7.6$  Hz, 2H), 7.52 – 7.45 (m, 4H), 7.39 (d,  $J = 7.2$  Hz, 1H), 7.35 – 7.30 (m, 2H), 7.21 (d,  $J = 8.8$  Hz, 2H), 7.05 – 7.00 (m, 2H), 6.96 (d,  $J = 8.8$  Hz, 2H), 6.86 (d,  $J = 8.0$  Hz, 2H), 6.81 – 6.77 (m, 1H), 6.62 (s, 1H), 5.39 – 5.33 (m, 1H), 3.34 – 3.25 (m, 2H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ) ( $\delta$ , ppm): 153.7, 148.8, 141.7, 132.5, 132.2, 131.5, 131.0, 130.2, 129.1, 128.6, 127.8, 127.2, 126.6, 126.4, 125.1, 124.4, 123.5, 122.6, 121.1, 117.3, 113.3, 106.9, 100.9, 69.7, 49.7. IR (KBr,  $\nu$ ,  $\text{cm}^{-1}$ ): 3024, 2359, 1633, 1595, 1455, 876, 726; HRMS (ESI -TOF)  $m/z$  calcd for  $\text{C}_{29}\text{H}_{22}\text{BrNO}_2\text{Na}$   $[\text{M}+\text{Na}]^+$  518.0732, found 518.0726;

**3-Pentyl-2',3'-diphenylspiro[isochromene-1,5'-isoxazolidine] (5i)**



Yellow oil; 62.0 mg, 52% yield;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ) ( $\delta$ , ppm): 7.65 (d,  $J = 7.2$  Hz, 2H), 7.47 – 7.43 (m, 3H), 7.38 – 7.34 (m, 2H), 7.25 – 7.12 (m, 4H), 6.91 – 6.87 (m, 3H), 5.84 (s, 1H), 5.23 – 5.18 (m, 1H), 3.19 – 3.09 (m, 2H), 1.85 – 1.77 (m, 2H), 1.37 – 1.12 (m, 4H), 0.82 – 0.76 (m, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ) ( $\delta$ , ppm): 154.6, 153.8, 142.0, 132.8, 130.0, 129.1, 128.6, 128.5, 128.5, 127.8, 126.6, 126.2, 124.3, 124.0, 122.9, 120.9, 113.6, 106.4, 100.2, 69.3, 49.8, 32.9, 28.2, 22.4, 13.9. IR (KBr,  $\nu$ ,  $\text{cm}^{-1}$ ): 3061, 2857, 1659, 1598, 1489, 875, 695; HRMS (ESI -TOF)  $m/z$  calcd for  $\text{C}_{28}\text{H}_{29}\text{NO}_2\text{Na}$   $[\text{M}+\text{Na}]^+$  420.1939, found 420.1928;

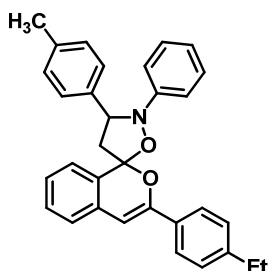
**2',3-Diphenyl-3'-(p-tolyl)spiro[isochromene-1,5'-isoxazolidine] (5j)**



Yellow solid; 90.5 mg, 70% yield; mp: 181-182 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ) ( $\delta$ , ppm): 7.58 (d,  $J = 8.0$  Hz, 2H), 7.53 (d,  $J = 8.0$  Hz, 1H), 7.46 – 7.42 (m, 1H), 7.33 – 7.27 (m, 4H), 7.21 – 7.17 (m, 1H), 7.15 – 7.10 (m, 4H), 7.03 – 6.99 (m, 2H), 6.87 (d,  $J = 8.0$  Hz, 2H), 6.77 – 6.73 (m, 1H), 6.62 (s, 1H), 5.37 – 5.33 (m, 1H), 3.31 – 3.24 (m, 2H), 2.42 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ) ( $\delta$ , ppm): 153.7, 150.1, 141.9, 138.5, 132.7, 130.8, 130.0, 129.1, 128.7, 128.5, 128.5, 127.8, 126.7, 126.5, 125.2, 124.9, 124.3, 123.4, 121.0, 113.5, 106.9, 99.6, 69.7, 50.0, 29.7, 21.3. IR (KBr,  $\nu$ ,  $\text{cm}^{-1}$ )

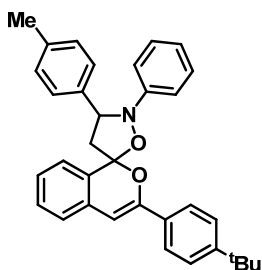
<sup>1</sup>): 3057, 2917, 1595, 1510, 1455, 876, 726; HRMS (ESI -TOF) m/z calcd for C<sub>30</sub>H<sub>25</sub>NO<sub>2</sub>Na [M+Na]<sup>+</sup>454.1783, found 454.1789;

**3-(4-Ethylphenyl)-2'-phenyl-3'-(p-tolyl)spiro[isochromene-1,5'-isoxazolidine] (5k)**



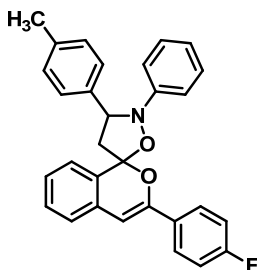
Yellow solid; 92.3 mg, 67% yield; mp: 177-178 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) (δ, ppm): 7.59 (d, *J* = 8.0 Hz, 2H), 7.53 (d, *J* = 7.6 Hz, 1H), 7.46 – 7.42 (m, 1H), 7.29 (d, *J* = 7.6 Hz, 4H), 7.07 – 7.02 (m, 4H), 6.94 (d, *J* = 8.0 Hz, 2H), 6.89 (d, *J* = 8.0 Hz, 2H), 6.80 – 6.75 (m, 1H), 6.57 (s, 1H), 5.37 – 5.32 (m, 1H), 3.33 – 3.23 (m, 2H), 2.62 – 2.56 (m, 2H), 2.43 (s, 3H), 1.23 – 1.18 (m, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) (δ, ppm): 153.8, 149.9, 138.8, 137.5, 133.5, 132.5, 130.1, 129.8, 129.7, 128.5, 128.4, 128.3, 127.9, 126.9, 126.4, 125.2, 125.0, 124.3, 123.6, 121.0, 113.5, 106.8, 100.4, 69.6, 49.9, 21.2. IR (KBr, ν, cm<sup>-1</sup>): 3034, 2962, 1596, 1511, 1454, 876, 686; HRMS (ESI -TOF) m/z calcd for C<sub>32</sub>H<sub>29</sub>NO<sub>2</sub>Na [M+Na]<sup>+</sup>482.2096, found 482.2113;

**3-(4-(tert-Butyl)phenyl)-2'-phenyl-3'-(p-tolyl)spiro[isochromene-1,5'-isoxazolidine] (5l)**



White solid; 80.4 mg, 55% yield; mp: 182-183 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) (δ, ppm): 7.57 (d, *J* = 7.6 Hz, 2H), 7.52 (d, *J* = 7.6 Hz, 1H), 7.42 (d, *J* = 7.6 Hz, 1H), 7.32 – 7.27 (m, 5H), 7.12 (d, *J* = 8.4 Hz, 2H), 7.07 (d, *J* = 8.4 Hz, 2H), 7.04 – 7.00 (m, 2H), 6.87 (d, *J* = 8.0 Hz, 2H), 6.77 – 6.73 (m, 1H), 6.57 (s, 1H), 5.36 – 5.30 (m, 1H), 3.31 – 3.19 (m, 2H), 2.43 (d, *J* = 4.4 Hz, 3H), 1.28 (s, 9H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) (δ, ppm): 153.8, 151.7, 150.1, 138.8, 137.5, 132.7, 130.8, 130.0, 129.8, 129.7, 128.5, 128.4, 127.3, 126.7, 126.4, 125.4, 125.3, 125.0, 124.9, 124.3, 123.6, 121.0, 117.6, 113.6, 106.9, 99.8, 69.7, 50.1, 34.6, 31.3, 31.2 21.2. IR (KBr, ν, cm<sup>-1</sup>): 2964, 2359, 1631, 1596, 1451, 845, 695; HRMS (ESI -TOF) m/z calcd for C<sub>34</sub>H<sub>33</sub>NO<sub>2</sub>Na [M+Na]<sup>+</sup>510.2409, found 510.2415;

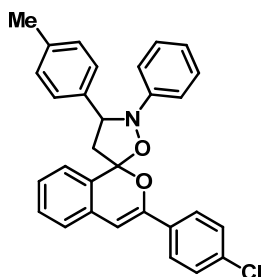
**3-(4-Fluorophenyl)-2'-phenyl-3'-(p-tolyl)spiro[isochromene-1,5'-isoxazolidine] (5m)**



White solid; 98.3 mg, 73% yield; mp: 201-202 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) (δ, ppm): 7.58 (d, *J* = 8.0 Hz, 2H), 7.52 (d, *J* = 7.6 Hz, 1H), 7.47 – 7.42 (m, 1H), 7.34 – 7.27 (m, 4H), 7.10 – 7.05 (m, 2H), 7.04 – 6.99 (m, 2H), 6.88 – 6.84 (m,

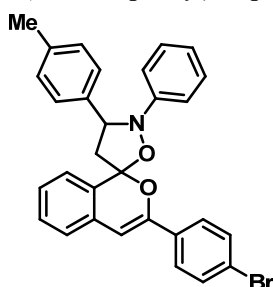
2H), 6.81 – 6.74 (m, 3H), 6.53 (d,  $J = 19.9$  Hz, 1H), 5.36 – 5.30 (m, 1H), 3.32 – 3.22 (m, 2H), 2.43 (d,  $J = 3.6$  Hz, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ) ( $\delta$ , ppm): 164.0 ( $^1J_{\text{CF}} = 246.9$  Hz), 161.6, 153.8, 149.0, 138.7, 137.5, 132.4, 130.1 ( $^3J_{\text{CF}} = 7.3$  Hz), 129.8, 129.7, 129.7, 128.5, 128.5, 127.2, 127.1, 127.0 ( $^4J_{\text{CF}} = 4.1$  Hz), 126.9, 125.0, 124.3, 123.4, 121.0, 117.4, 115.0 ( $^2J_{\text{CF}} = 21.6$  Hz), 114.8, 113.4, 106.9, 100.3, 69.6, 49.7, 21.2. IR (KBr,  $\nu$ ,  $\text{cm}^{-1}$ ): 3029, 2359, 1634, 1597, 1454, 880, 692; HRMS (ESI -TOF)  $m/z$  calcd for  $\text{C}_{30}\text{H}_{24}\text{FNO}_2\text{Na}$  [ $\text{M}+\text{Na}$ ] $^+$ 472.1689, found 472.1679;

**3-(4-Chlorophenyl)-2'-phenyl-3'-(p-tolyl)spiro[isochromene-1,5'-isoxazolidine] (5n)**



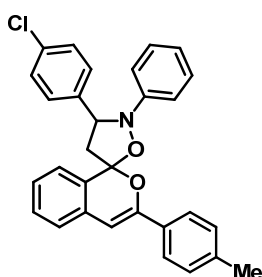
Yellow solid; 108.8 mg, 78% yield; mp: 181-182 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ) ( $\delta$ , ppm): 7.57 (d,  $J = 8.0$  Hz, 2H), 7.52 (d,  $J = 7.6$  Hz, 1H), 7.45 – 7.42 (m, 1H), 7.34 – 7.27 (m, 5H), 7.05 – 7.01 (m, 5H), 6.87 – 6.84 (m, 2H), 6.79 – 6.75 (m, 1H), 6.60 (s, 1H), 5.34 – 5.30 (m, 1H), 3.29 – 3.24 (m, 2H), 2.42 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ) ( $\delta$ , ppm): 153.7, 148.8, 138.7, 137.5, 134.2, 132.3, 132.1, 130.1, 129.8, 129.7, 128.5, 128.1, 127.1, 126.8, 126.4, 125.1, 124.4, 123.6, 121.1, 117.4, 113.4, 106.9, 100.9, 77.34, 77.2, 77.0, 76.7, 69.6, 49.8, 21.2. IR (KBr,  $\nu$ ,  $\text{cm}^{-1}$ ): 3027, 2915, 1625, 1595, 1454, 876, 686; HRMS (ESI -TOF)  $m/z$  calcd for  $\text{C}_{30}\text{H}_{24}\text{ClNO}_2\text{Na}$  [ $\text{M}+\text{Na}$ ] $^+$ 488.1393, found 488.1395;

**3-(4-Bromophenyl)-2'-phenyl-3'-(p-tolyl)spiro[isochromene-1,5'-isoxazolidine] (5o)**



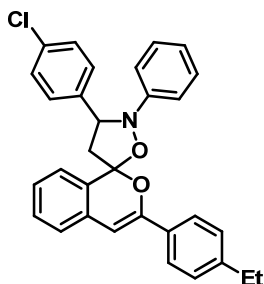
Yellow solid; 105.3 mg, 69% yield; mp: 188-189 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ) ( $\delta$ , ppm): 7.58 (d,  $J = 8.0$  Hz, 2H), 7.52 (d,  $J = 7.6$  Hz, 1H), 7.47 – 7.42 (m, 1H), 7.35 – 7.28 (m, 4H), 7.22 (d,  $J = 8.8$  Hz, 2H), 7.05 – 7.00 (m, 2H), 6.97 (d,  $J = 8.4$  Hz, 2H), 6.88 – 6.84 (m, 2H), 6.81 – 6.76 (m, 1H), 6.62 (s, 1H), 5.35 – 5.30 (m, 1H), 3.32 – 3.22 (m, 2H), 2.43 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ) ( $\delta$ , ppm): 153.7, 148.8, 138.7, 137.5, 132.5, 132.2, 131.1, 130.2, 129.8, 128.6, 127.2, 126.6, 126.4, 125.1, 124.4, 123.6, 122.6, 121.1, 113.4, 106.9, 100.9, 69.6, 49.8, 21.2. IR (KBr,  $\nu$ ,  $\text{cm}^{-1}$ ): 3091, 2960, 1633, 1596, 1453, 880, 691; HRMS (ESI -TOF)  $m/z$  calcd for  $\text{C}_{30}\text{H}_{24}\text{BrNO}_2\text{Na}$  [ $\text{M}+\text{Na}$ ] $^+$ 532.0888, found 532.0892;

**3'-(4-Chlorophenyl)-2'-phenyl-3-(p-tolyl)spiro[isochromene-1,5'-isoxazolidine] (5p)**



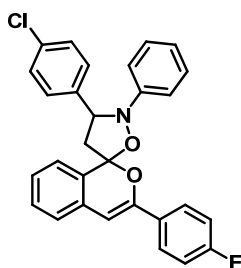
White solid; 90.7 mg, 65% yield; mp: 191-192 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) (δ, ppm): 7.63 (d, *J* = 8.4 Hz, 2H), 7.50 (d, *J* = 8.0 Hz, 1H), 7.46 – 7.42 (m, 3H), 7.32 – 7.28 (m, 2H), 7.08 – 6.99 (m, 4H), 6.92 (d, *J* = 8.4 Hz, 2H), 6.86 (d, *J* = 8.4 Hz, 2H), 6.82 – 6.78 (m, 1H), 6.57 (s, 1H), 5.37 – 5.32 (m, 1H), 3.33 – 3.27 (m, 1H), 3.24 – 3.16 (m, 1H), 2.30 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) (δ, ppm): 153.4, 150.0, 140.4, 139.6, 138.6, 133.5, 132.7, 130.8, 130.1, 129.7, 129.3, 129.1, 129.1, 128.7, 128.6, 128.6, 127.9, 126.7, 126.6, 125.4, 125.2, 124.9, 124.8, 124.5, 124.3, 123.3, 123.1, 121.3, 117.2, 113.5, 107.0, 105.6, 99.9, 99.7, 69.6, 69.1, 50.7, 49.8, 21.4, 21.3. IR (KBr, ν, cm<sup>-1</sup>): 3026, 2958, 1634, 1558, 1453, 877, 690; HRMS (ESI -TOF) *m/z* calcd for C<sub>30</sub>H<sub>24</sub>ClNO<sub>2</sub>Na [M+Na]<sup>+</sup>488.1393, found 488.1386;

**3'-(4-Chlorophenyl)-3-(4-ethylphenyl)-2'-phenylspiro[isochromene-1,5'-isoxazolidine] (5q)**



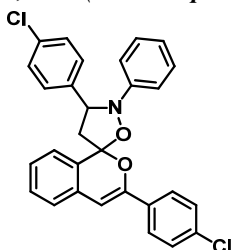
White solid; 100.8 mg, 70% yield; mp: 182-183 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) (δ, ppm): 7.65 (d, *J* = 8.4 Hz, 2H), 7.52 (d, *J* = 7.6 Hz, 1H), 7.48 – 7.44 (m, 3H), 7.34 – 7.30 (m, 2H), 7.09 – 7.04 (m, 4H), 6.96 (d, *J* = 8.0 Hz, 2H), 6.88 (d, *J* = 8.8 Hz, 2H), 6.83 – 6.79 (m, 1H), 6.59 (s, 1H), 5.39 – 5.34 (m, 1H), 3.35 – 3.29 (m, 1H), 3.25 – 3.18 (m, 1H), 2.65 – 2.58 (m, 2H), 1.25 – 1.20 (m, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) (δ, ppm): 153.4, 150.1, 145.0, 140.4, 133.5, 132.7, 131.0, 130.1, 129.6, 129.3, 129.2, 128.7, 128.6, 128.6, 127.9, 127.5, 126.7, 125.5, 125.3, 124.9, 124.3, 123.3, 121.2, 117.2, 113.5, 107.0, 99.7, 69.1, 49.9, 28.6, 15.5. IR (KBr, ν, cm<sup>-1</sup>): 3026, 2961, 1635, 1597, 1453, 877, 690; HRMS (ESI -TOF) *m/z* calcd for C<sub>31</sub>H<sub>26</sub>ClNO<sub>2</sub>Na [M+Na]<sup>+</sup>502.1550, found 502.1547;

**3'-(4-Chlorophenyl)-3-(4-fluorophenyl)-2'-phenylspiro[isochromene-1,5'-isoxazolidine] (5r)**



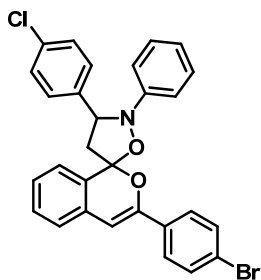
White solid; 106.9 mg, 76% yield; mp: 224-225 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) (δ, ppm): 7.62 (d, *J* = 8.4 Hz, 2H), 7.51 – 7.43 (m, 4H), 7.34 – 7.29 (m, 2H), 7.09 – 7.01 (m, 4H), 6.86 – 6.74 (m, 5H), 6.56 (s, 1H), 5.37 – 5.30 (m, 1H), 3.33 – 3.18 (m, 2H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) (δ, ppm): 164.1 (<sup>1</sup>*J*<sub>CF</sub> = 247.2 Hz), 161.6, 153.5, 148.9, 140.3, 133.6, 132.4, 130.2, 129.7, 129.6 (<sup>4</sup>*J*<sub>CF</sub> = 3. Hz), 129.3, 129.2, 128.6, 127.8, 127.0 (<sup>3</sup>*J*<sub>CF</sub> = 8.2 Hz), 126.9, 125.1, 124.3, 123.2, 121.3, 117.2, 115.0 (<sup>2</sup>*J*<sub>CF</sub> = 21.6 Hz), 114.8, 113.3, 107.0, 100.3, 69.1, 49.5. IR (KBr, ν, cm<sup>-1</sup>): 3021, 2359, 1598, 1507, 1489, 877, 757; HRMS (ESI -TOF) *m/z* calcd for C<sub>29</sub>H<sub>21</sub>ClFNO<sub>2</sub>Na [M+Na]<sup>+</sup>479.1064, found 479.1068;

**3,3'-bis(4-Chlorophenyl)-2'-phenylspiro[isochromene-1,5'-isoxazolidine] (5s)**



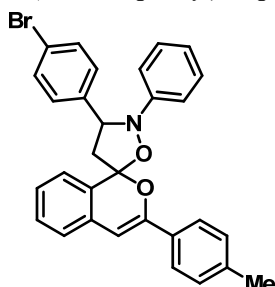
White solid; 116.4 mg, 80% yield; mp: 212-213 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) (δ, ppm): 7.62 (d, *J* = 8.4 Hz, 2H), 7.49 (d, *J* = 8.0 Hz, 1H), 7.47 – 7.42 (m, 3H), 7.35 – 7.30 (m, 2H), 7.08 – 6.99 (m, 6H), 6.84 – 6.77 (m, 3H), 6.61 (s, 1H), 5.36 – 5.29 (m, 1H), 3.33 – 3.26 (m, 1H), 3.25 – 3.18 (m, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) (δ, ppm): 153.4, 148.7, 140.3, 134.3, 133.6, 132.2, 132.0, 130.3, 129.3, 128.6, 128.1, 127.8, 127.2, 126.3, 125.2, 124.3, 123.3, 121.3, 1133, 107.0, 100.9, 69.1, 49.6. IR (KBr, ν, cm<sup>-1</sup>): 3026, 2962, 1633, 1597, 1453, 877, 689; HRMS (ESI -TOF) *m/z* calcd for C<sub>29</sub>H<sub>21</sub>Cl<sub>2</sub>NO<sub>2</sub> [M+Na]<sup>+</sup>508.0847, found 508.0862;

**3-(4-Bromophenyl)-3'-(4-chlorophenyl)-2'-phenylspiro[isochromene-1,5'-isoxazolidine] (5t)**



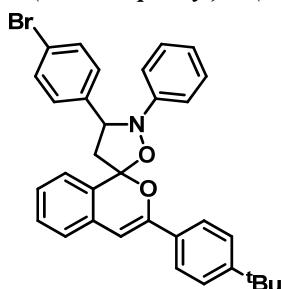
Yellow solid; 107.9 mg, 68% yield; mp: 207-208 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) (δ, ppm): 7.62 (d, *J* = 8.4 Hz, 2H), 7.50 – 7.43 (m, 4H), 7.35 – 7.29 (m, 2H), 7.25 – 7.19 (m, 2H), 7.05 – 7.00 (m, 2H), 6.96 – 6.90 (m, 2H), 6.85 – 6.75 (m, 3H), 6.61 (s, 1H), 5.36 – 5.28 (m, 1H), 3.33 – 3.26 (m, 1H), 3.25 – 3.18 (m, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) (δ, ppm): 153.4, 148.7, 140.3, 133.6, 132.4, 132.2, 131.5, 131.1, 130.3, 129.3, 129.2, 128.7, 128.6, 128.6, 127.8, 127.2, 126.9, 126.6, 125.2, 124.3, 123.3, 122.6, 121.4, 117.2, 113.3, 107.0, 101.0, 69.1, 49.6. IR (KBr, ν, cm<sup>-1</sup>): 3026, 2915, 1596, 1584, 1453, 876, 686; HRMS (ESI -TOF) *m/z* calcd for C<sub>29</sub>H<sub>21</sub>BrClNO<sub>2</sub>Na [M+Na]<sup>+</sup>552.0342, found 552.0339;

**3'-(4-Bromophenyl)-2'-phenyl-3-(*p*-tolyl)spiro[isochromene-1,5'-isoxazolidine] (5u)**



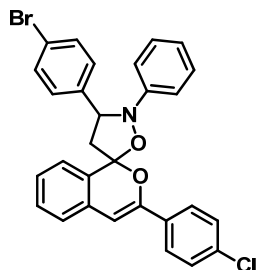
White solid; 96.4 mg, 63% yield; mp: 202-203 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) (δ, ppm): 7.60 – 7.55 (m, 4H), 7.49 (d, *J* = 8.0 Hz, 1H), 7.46 – 7.42 (m, 1H), 7.32 – 7.28 (m, 2H), 7.07 – 7.03 (m, 2H), 7.00 (d, *J* = 8.0 Hz, 2H), 6.91 (d, *J* = 8.0 Hz, 2H), 6.85 (d, *J* = 8.0 Hz, 2H), 6.82 – 6.78 (m, 1H), 6.56 (s, 1H), 5.35 – 5.30 (m, 1H), 3.32 – 3.27 (m, 1H), 3.22 – 3.16 (m, 1H), 2.30 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) (δ, ppm): 153.4, 150.0, 140.9, 138.6, 132.7, 132.2, 132.1, 131.7, 130.7, 130.1, 129.7, 129.1, 129.0, 128.7, 128.6, 1283, 126.7, 126.6, 125.4, 125.2, 124.9, 124.5, 124.3, 123.2, 123.0, 121.6, 121.3, 117.1, 113.5, 107.0, 105.7, 99.8, 99.7, 69.6, 69.1, 50.6, 49.8, 21.4, 21.3. IR (KBr, ν, cm<sup>-1</sup>): 3026, 2359, 1634, 1596, 1453, 878, 693; HRMS (ESI -TOF) *m/z* calcd for C<sub>30</sub>H<sub>24</sub>BrNO<sub>2</sub>Na [M+Na]<sup>+</sup>532.0888, found 532.0893;

**3'-(4-Bromophenyl)-3-(4-(*tert*-butyl)phenyl)-2'-phenylspiro[isochromene-1,5'-isoxazolidine] (5v)**



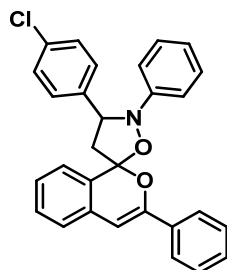
Yellow solid; 86.0 mg, 50% yield; mp: 189-190 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) (δ, ppm): 7.60 – 7.54 (m, 4H), 7.51 – 7.48 (m, 1H), 7.43 (d, *J* = 8.4 Hz, 1H), 7.32 – 7.28 (m, 2H), 7.11 (d, *J* = 8.8 Hz, 2H), 7.07 – 7.00 (m, 4H), 6.84 (d, *J* = 7.9 Hz, 2H), 6.79 – 6.74 (m, 1H), 6.57 (s, 1H), 5.34 – 5.29 (m, 1H), 3.32 – 3.26 (m, 1H), 3.21 – 3.14 (m, 1H), 1.28 (s, 9H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) (δ, ppm): 153.4, 151.7, 150.0, 140.9, 132.7, 132.2, 132.1, 130.7, 130.1, 129.0, 128.6, 128.3, 126.7, 125.3, 125.2, 124.9, 124.9, 124.3, 123.3, 121.6, 121.2, 117.1, 113.5, 106.9, 99.8, 69.2, 49.8, 34.6, 31.3, 31.2. IR (KBr, ν, cm<sup>-1</sup>): 3025, 2359, 1595, 1488, 1454, 876, 689; HRMS (ESI -TOF) *m/z* calcd for C<sub>33</sub>H<sub>30</sub>BrNO<sub>2</sub>Na [M+Na]<sup>+</sup>574.1358, found 574.340;

**3'-(4-Bromophenyl)-3-(4-chlorophenyl)-2'-phenylspiro[isochromene-1,5'-isoxazolidine] (5w)**



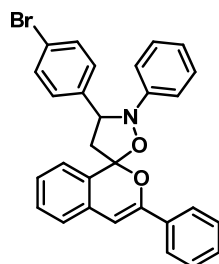
White solid; 95.4 mg, 60% yield; mp: 227-228 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) (δ, ppm): 7.61 – 7.55 (m, 4H), 7.50 – 7.44 (m, 2H), 7.35 – 7.30 (m, 2H), 7.07 – 6.99 (m, 6H), 6.84 – 6.76 (m, 3H), 6.61 (s, 1H), 5.34 – 5.28 (m, 1H), 3.32 – 3.18 (m, 2H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) (δ, ppm): 153.4, 148.7, 140.8, 134.3, 132.3, 132.2, 132.1, 131.9, 130.3, 128.9, 128.7, 128.5, 128.2, 128.1, 127.2, 126.6, 126.3, 125.2, 124.3, 123.3, 121.6, 121.3, 117.1, 113.3, 106.9, 100.9, 69.1, 49.5. IR (KBr, ν, cm<sup>-1</sup>): 3026, 2962, 1633, 1597, 1453, 877, 689; HRMS (ESI -TOF) *m/z* calcd for C<sub>29</sub>H<sub>21</sub>BrClNO<sub>2</sub>Na [M+Na]<sup>+</sup>552.0342, found 552.0345;

**3-(4-Chlorophenyl)-2',3'-diphenylspiro[isochromene-1,5'-isoxazolidine] (5x)**



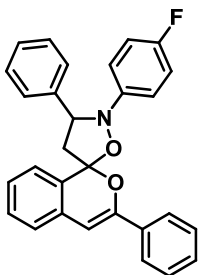
Yellow solid; 105.5 mg, 78% yield; mp: 161-162 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) (δ, ppm): 7.62 (d, *J* = 8.4 Hz, 2H), 7.50 (d, *J* = 8.0 Hz, 1H), 7.47 – 7.42 (m, 3H), 7.37 – 7.28 (m, 3H), 7.18 (d, *J* = 6.4 Hz, 1H), 7.14 – 7.07 (m, 4H), 7.04 – 6.99 (m, 2H), 6.83 (d, *J* = 8.4 Hz, 2H), 6.79 – 6.74 (m, 1H), 6.62 (s, 1H), 5.38 – 5.32 (m, 1H), 3.33 – 3.27 (m, 1H), 3.24 – 3.17 (m, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) (δ, ppm): 153.7, 151.7, 150.0, 141.9, 132.7, 130.8, 130.0, 129.1, 128.5, 127.8, 126.7, 126.5, 125.0, 124.9, 124.3, 123.5, 121.0, 113.6, 106.9, 99.8, 69.8, 50.0, 34.6, 31.3, 31.2. IR (KBr, ν, cm<sup>-1</sup>): 3024, 2359, 1596, 1507, 1455, 839, 692; HRMS (ESI -TOF) *m/z* calcd for C<sub>29</sub>H<sub>22</sub>ClNO<sub>2</sub>Na [M+Na]<sup>+</sup>474.1237, found 474.1246;

**3'-(4-Bromophenyl)-2',3'-diphenylspiro[isochromene-1,5'-isoxazolidine] (5y)**



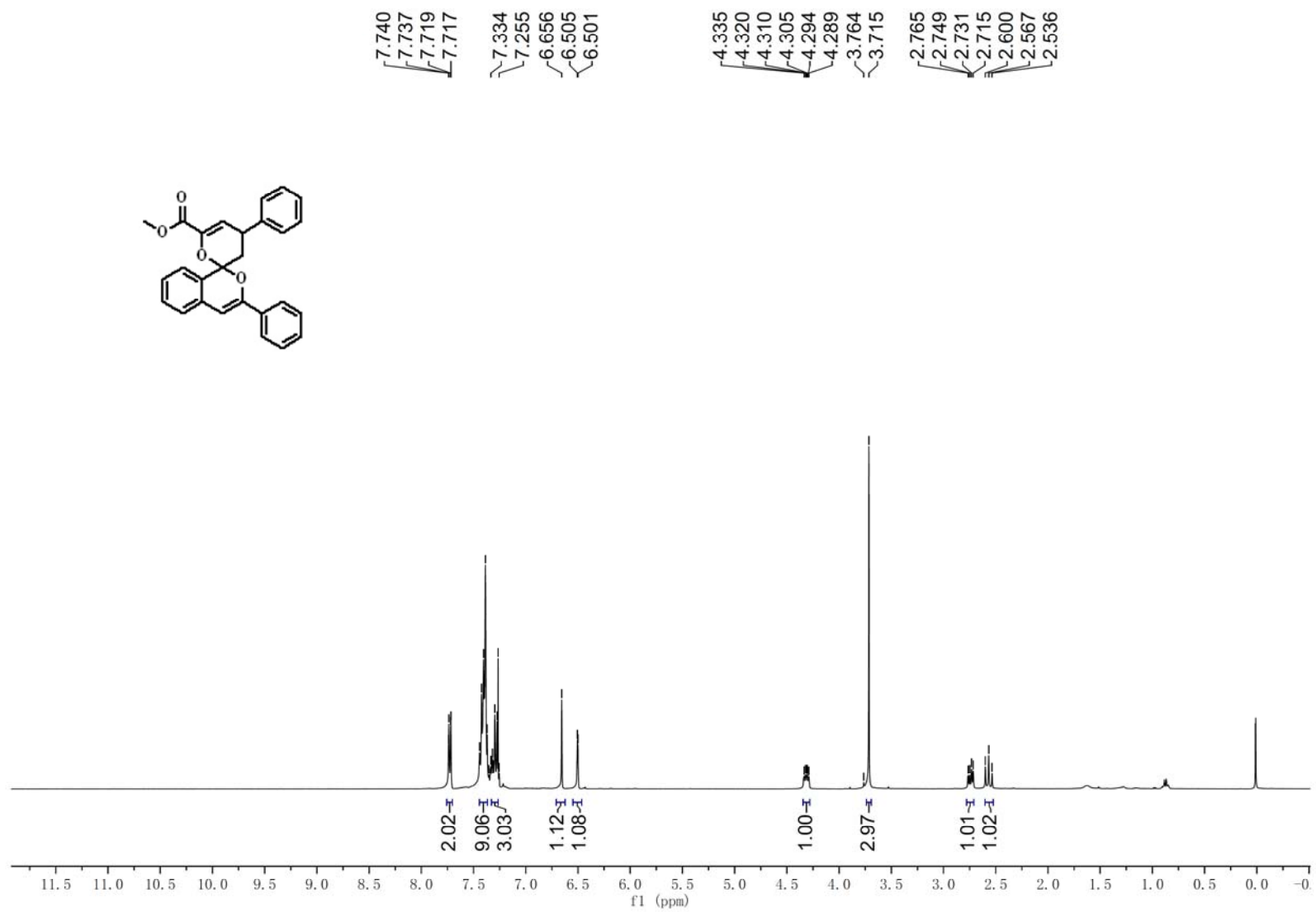
Yellow solid; 101.0 mg, 68% yield; mp: 200-201 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ) ( $\delta$ , ppm): 7.61 – 7.56 (m, 4H), 7.51 – 7.43 (m, 2H), 7.34 – 7.26 (m, 3H), 7.15 – 7.08 (m, 4H), 7.05 – 6.98 (m, 2H), 6.84 (d,  $J$  = 8.0 Hz, 2H), 6.80 – 6.73 (m, 1H), 6.60 (d,  $J$  = 20.0 Hz, 1H), 5.37 – 5.30 (m, 1H), 3.34 – 3.27 (m, 1H), 3.24 – 3.17 (m, 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ) ( $\delta$ , ppm): 153.4, 149.8, 140.9, 133.4, 132.5, 132.2, 132.1, 130.2, 129.0, 128.6, 128.5, 128.3, 128.2, 128.0, 127.0, 125.4, 125.1, 125.1, 124.3, 123.3, 121.6, 121.3, 117.1, 113.5, 106.9, 100.4, 69.2, 49.7. IR (KBr,  $\nu$ ,  $\text{cm}^{-1}$ ): 3058, 2360, 1595, 1488, 1455, 874, 693; HRMS (ESI -TOF)  $m/z$  calcd for  $\text{C}_{29}\text{H}_{22}\text{BrNO}_2\text{Na}$  [ $\text{M}+\text{Na}$ ] $^{+}$ 518.0732, found 58.0720;

**2'-(4-Fluorophenyl)-3,3'-diphenylspiro[isochromene-1,5'-isoxazolidine] (5z)**

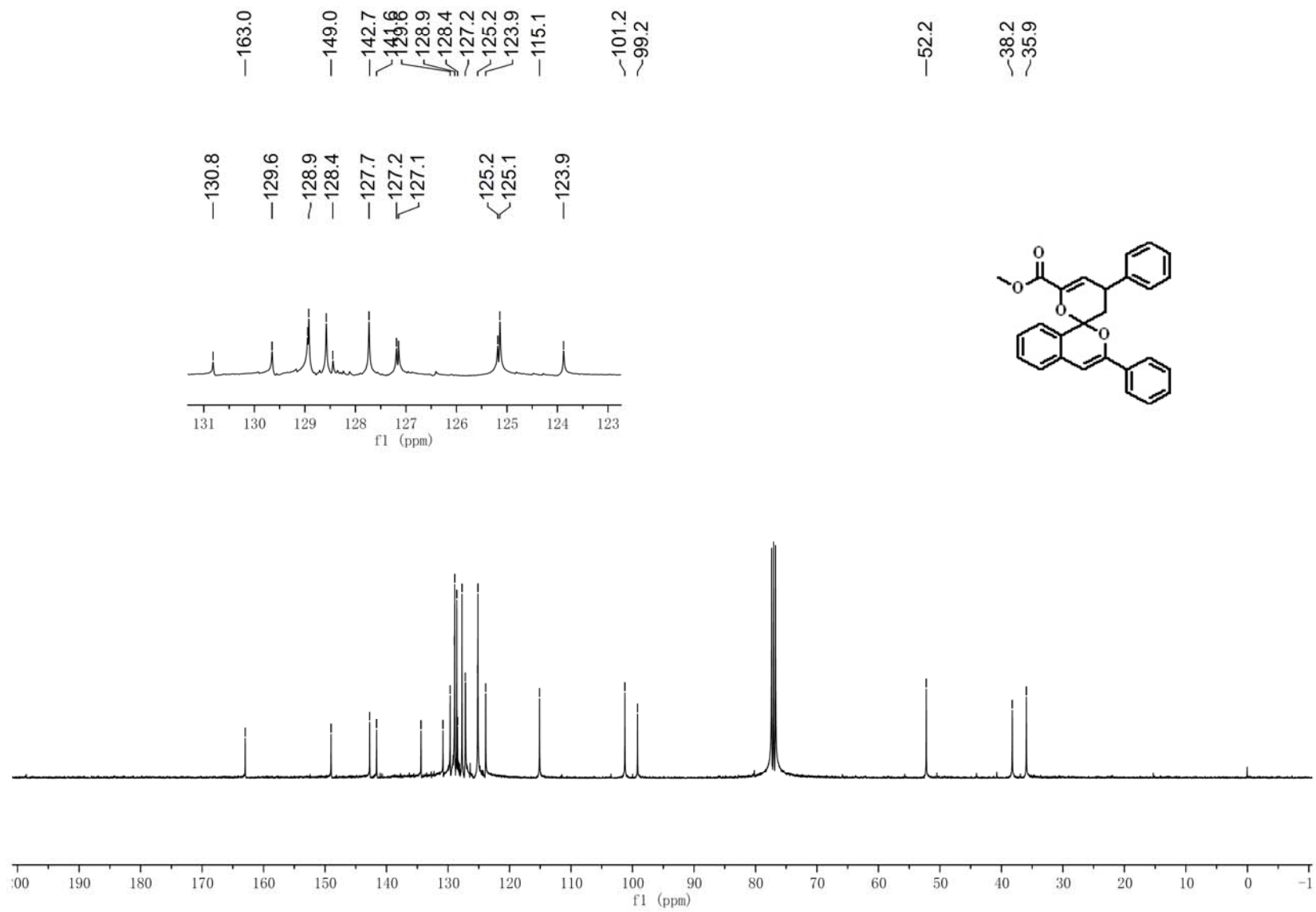


Yellow solid; 84.8 mg, 65% yield; mp: 171-172 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ) ( $\delta$ , ppm): 7.68 (d,  $J$  = 7.6 Hz, 2H), 7.53 – 7.44 (m, 4H), 7.40 – 7.37 (m, 1H), 7.34 – 7.30 (m, 2H), 7.25 – 7.13 (m, 5H), 6.83 – 6.79 (m, 2H), 6.72 – 6.63 (m, 3H), 5.34 – 5.28 (m, 1H), 3.35 – 3.24 (m, 2H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ) ( $\delta$ , ppm): 159.2 ( $^1J_{\text{CF}}$  = 237.5 Hz), 156.8, 150.0, 149.6, 141.4, 133.4, 132.4, 130.1, 129.2, 129.0, 128.7, 128.4, 128.0 ( $^4J_{\text{CF}}$  = 6.3 Hz), 127.9, 127.6, 127.0, 126.6, 125.6, 125.1 ( $^2J_{\text{CF}}$  = 17.7 Hz), 124.9, 124.3, 123.6, 120.1, 115.1, 115.0, 114.9 ( $^3J_{\text{CF}}$  = 8.0 Hz), 114.8, 106.9, 100.5, 70.4, 52.0, 49.9. IR (KBr,  $\nu$ ,  $\text{cm}^{-1}$ ): 3031, 2359, 1558, 1504, 1455, 876, 702; HRMS (ESI -TOF)  $m/z$  calcd for  $\text{C}_{29}\text{H}_{22}\text{FNO}_2\text{Na}$  [ $\text{M}+\text{Na}$ ] $^{+}$ 458.1532, found 458.1542;

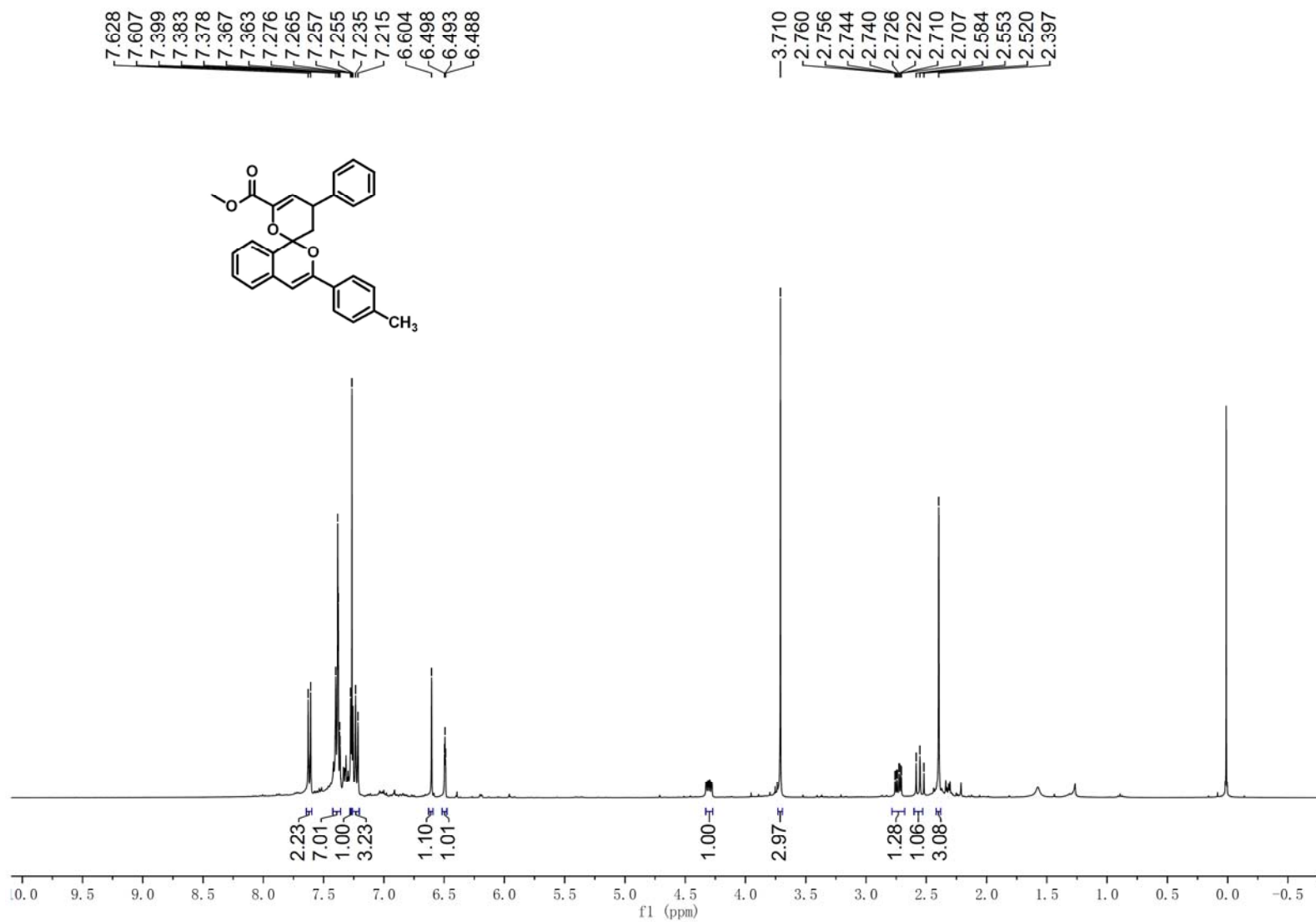




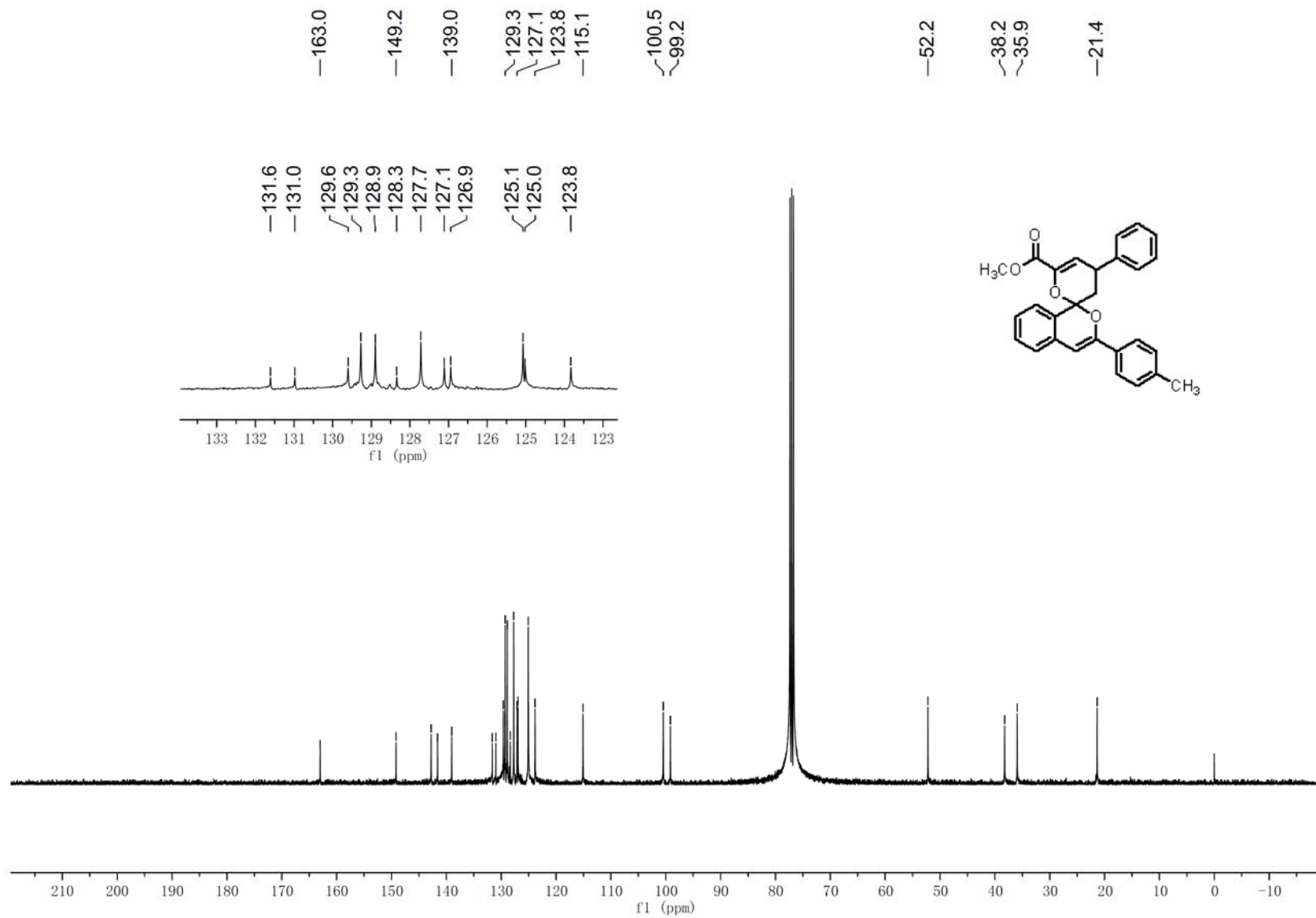
<sup>1</sup>H NMR Spectrum of Compound 3a



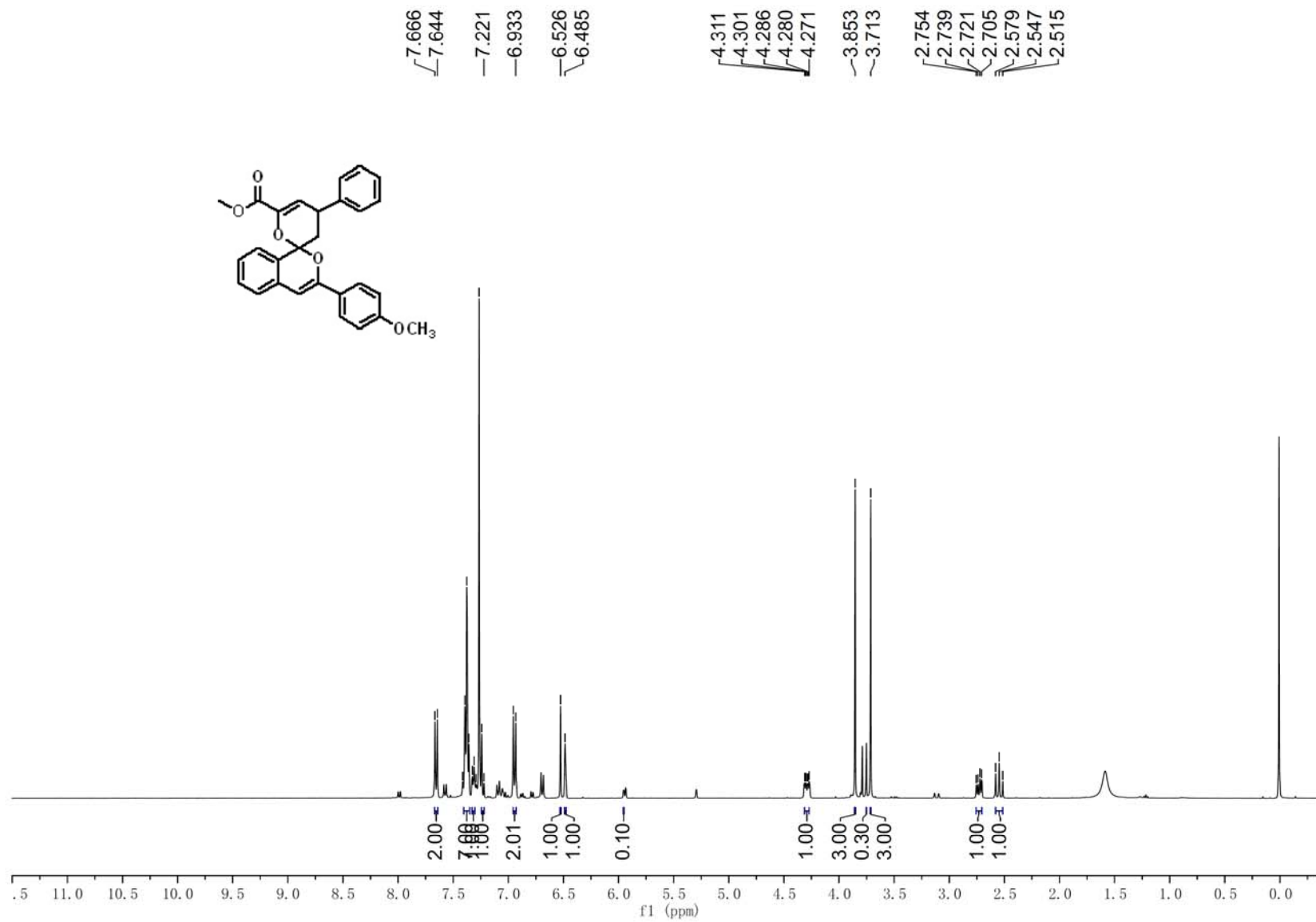
**<sup>13</sup>C NMR Spectrum of Compound 3a**



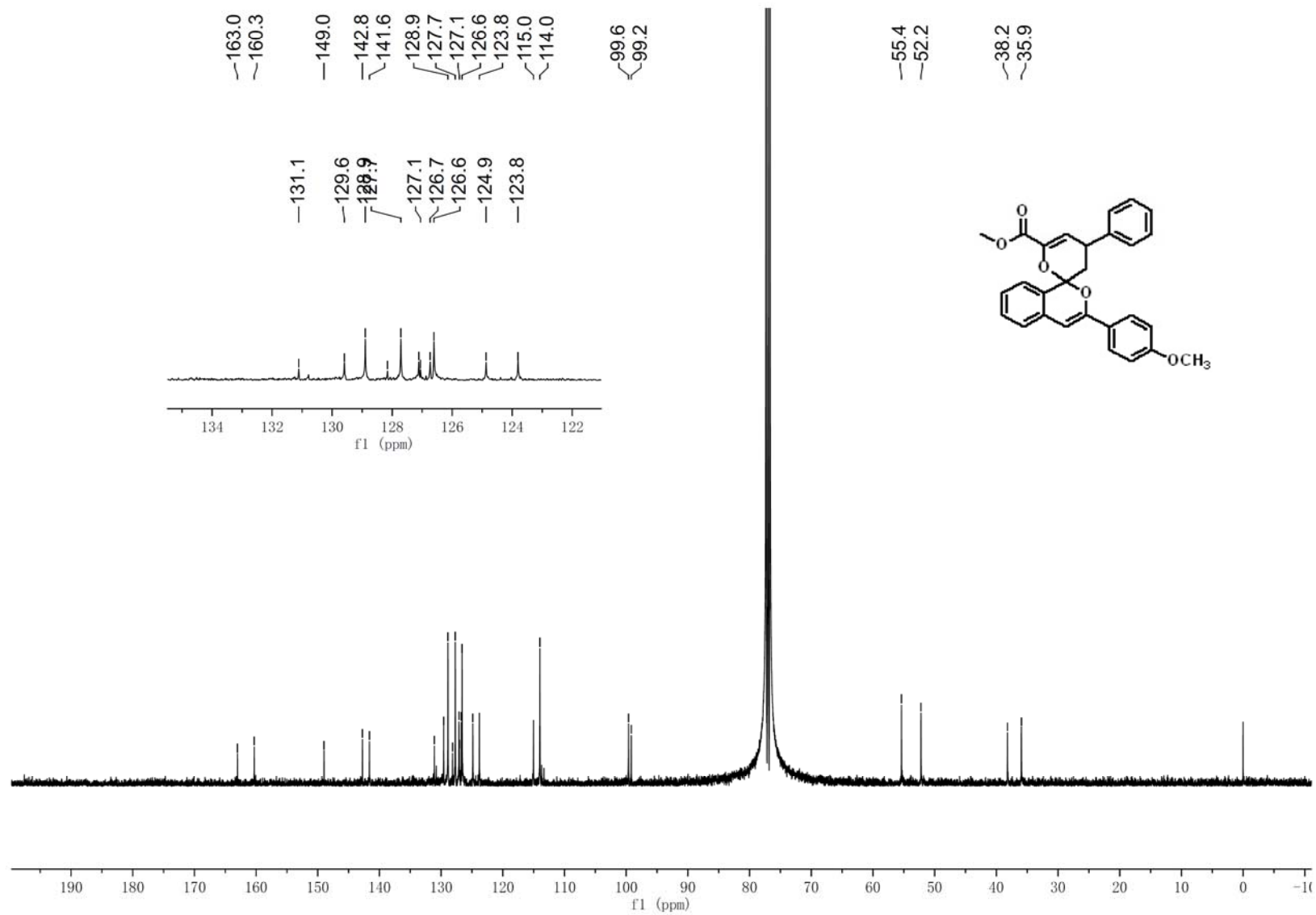
**<sup>1</sup>H NMR Spectrum of Compound 3b**



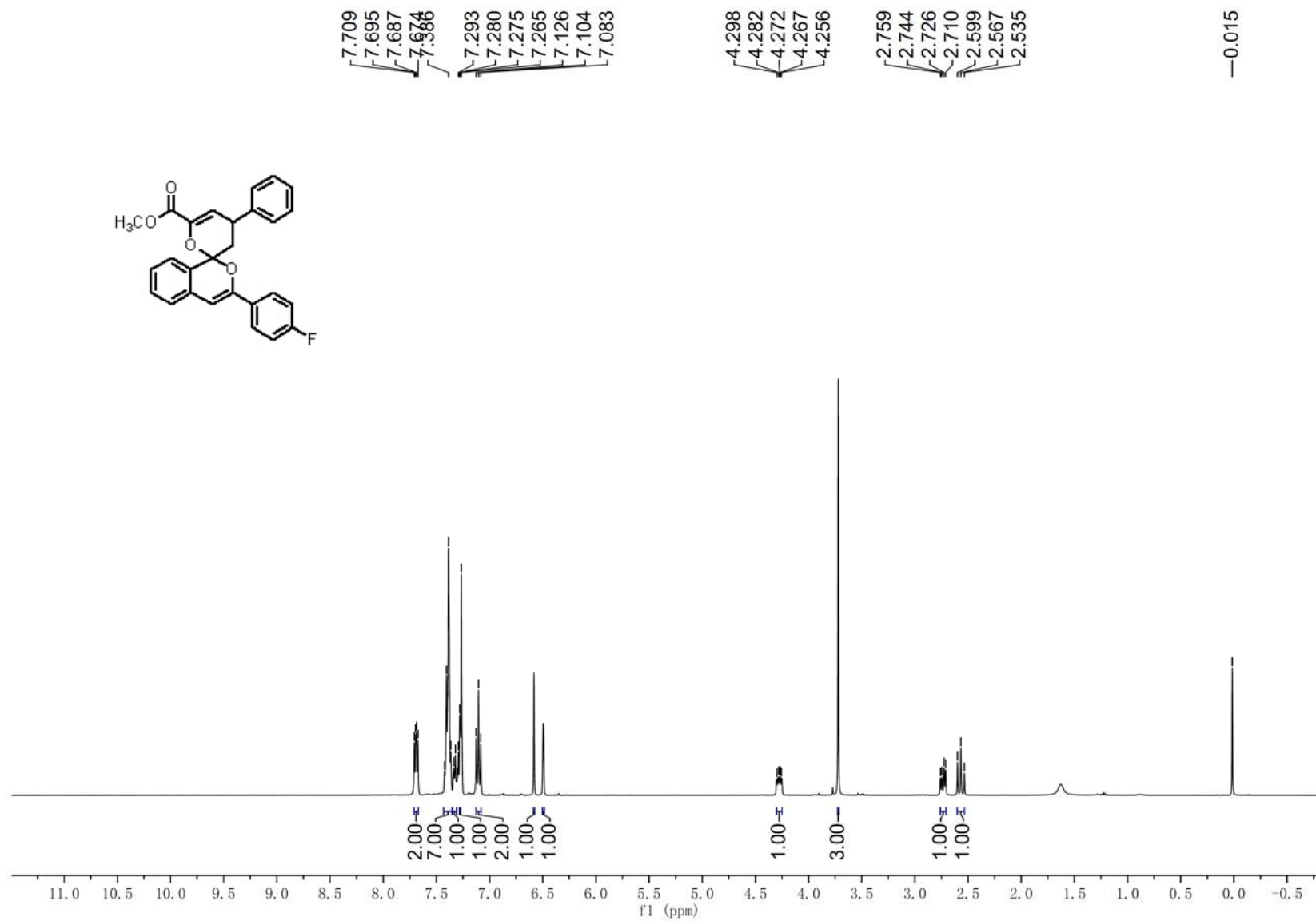
**<sup>13</sup>C NMR Spectrum of Compound 3b**



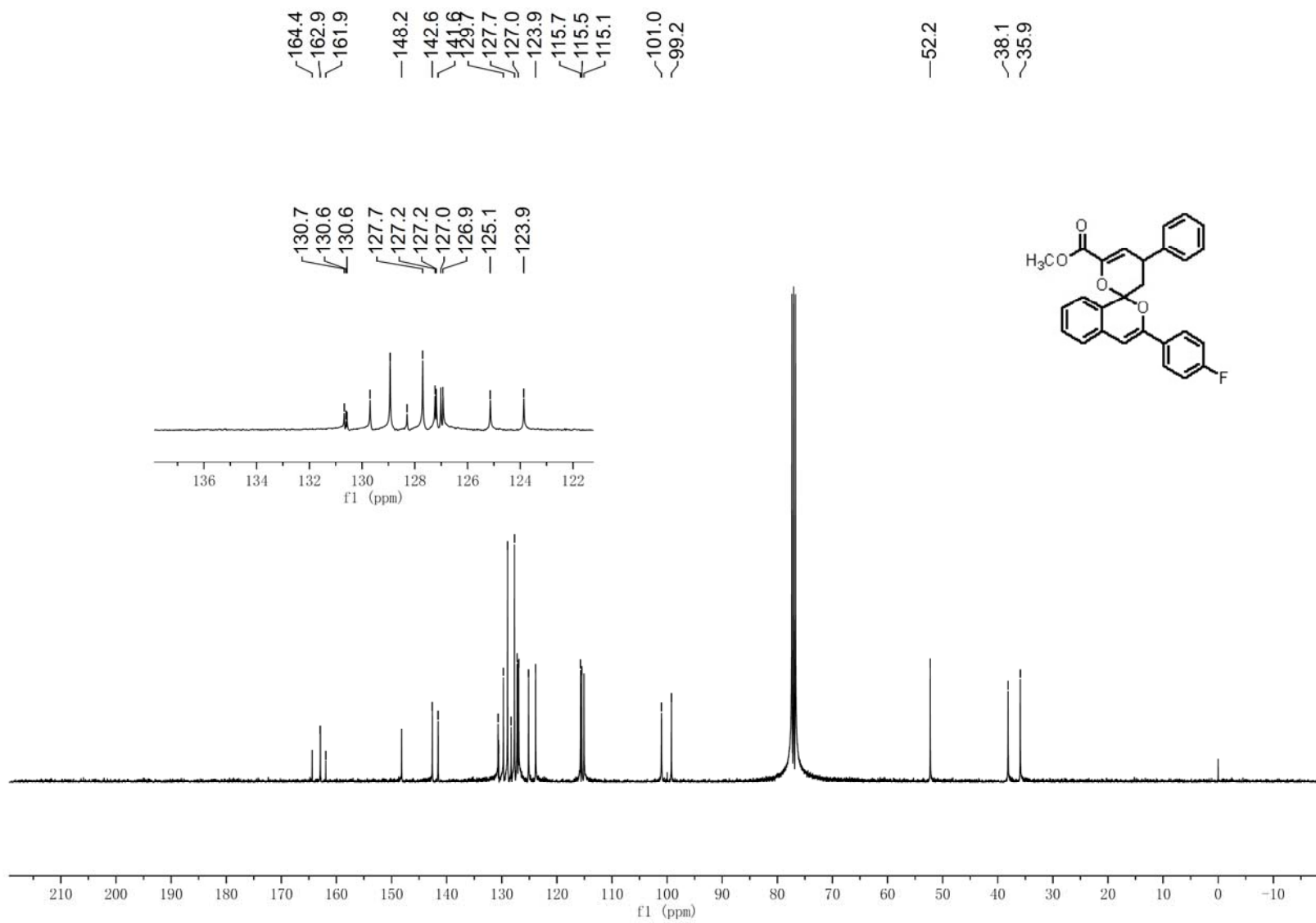
<sup>1</sup>H NMR Spectrum of Compound 3c



**<sup>13</sup>C NMR Spectrum of Compound 3c**

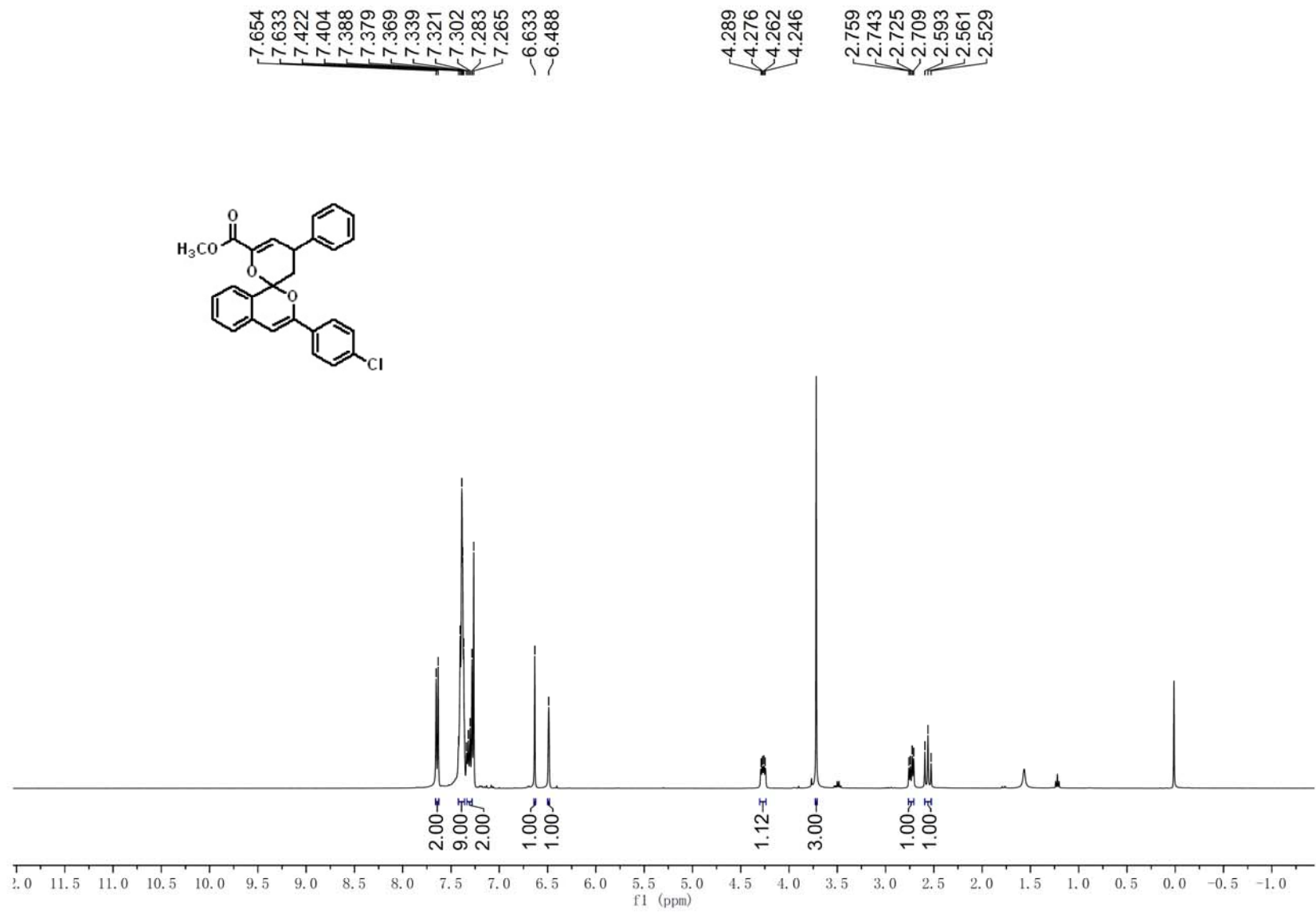


<sup>1</sup>H NMR Spectrum of Compound 3d

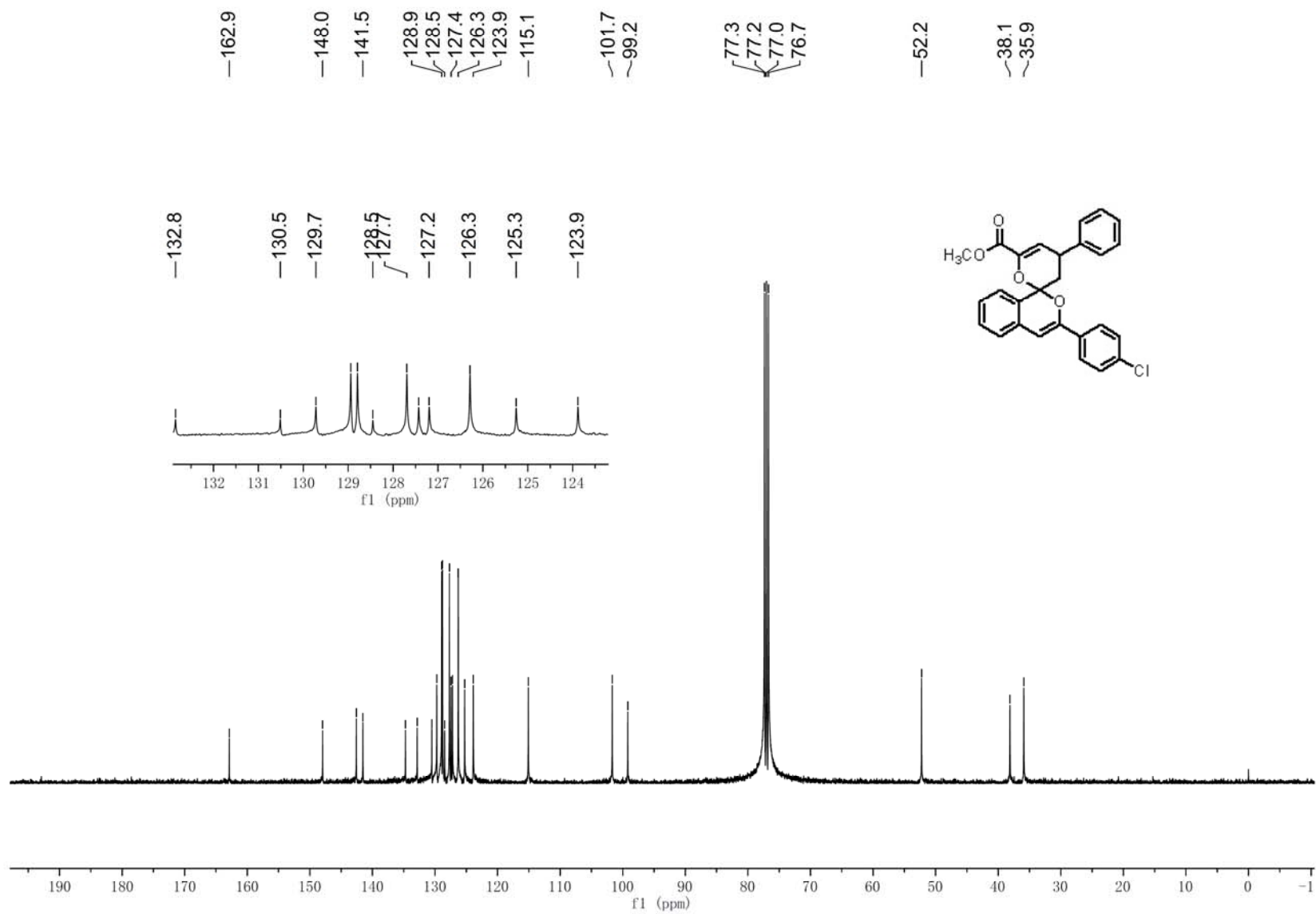


$^{13}\text{C}$  NMR Spectrum of Compound 3d

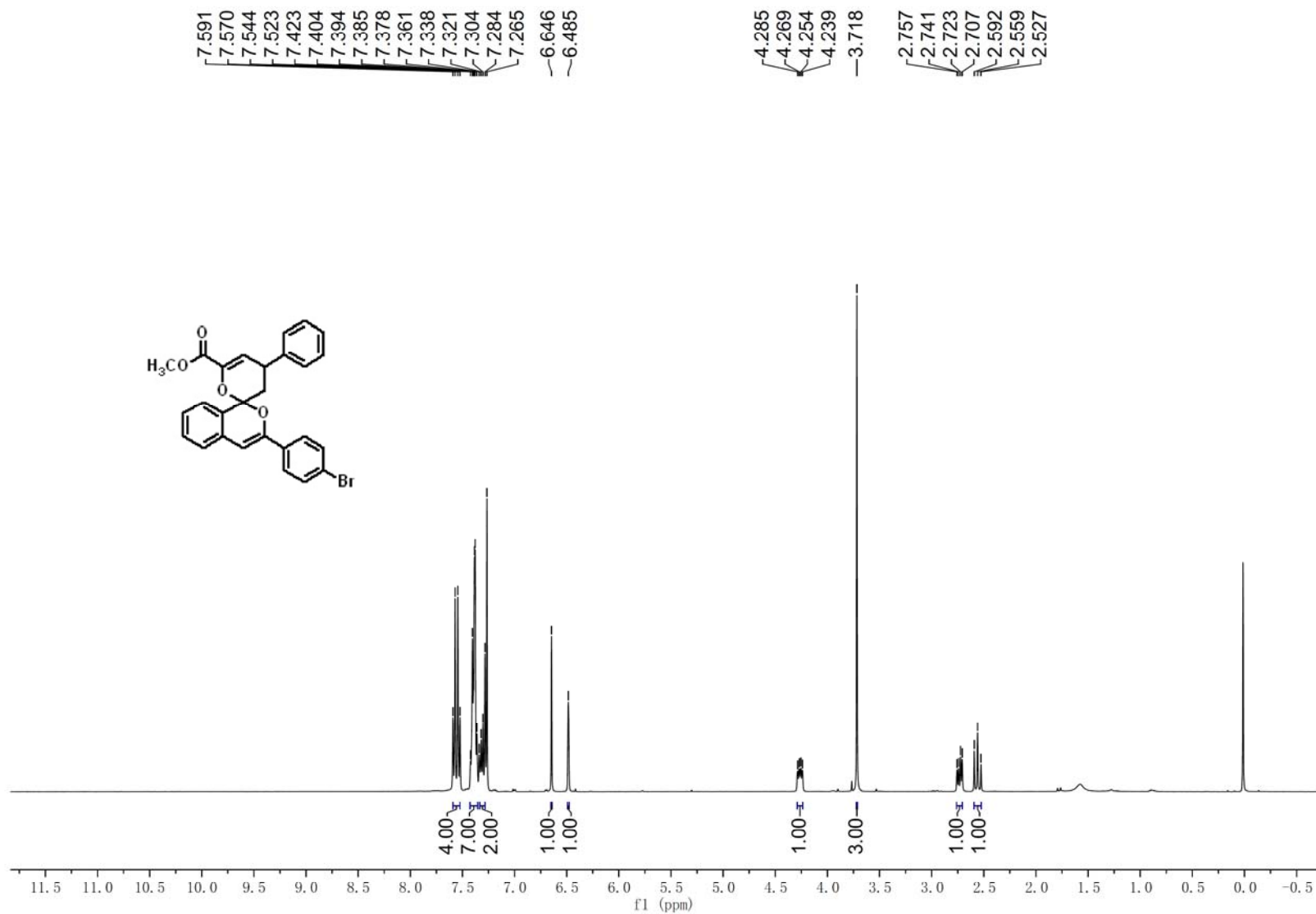




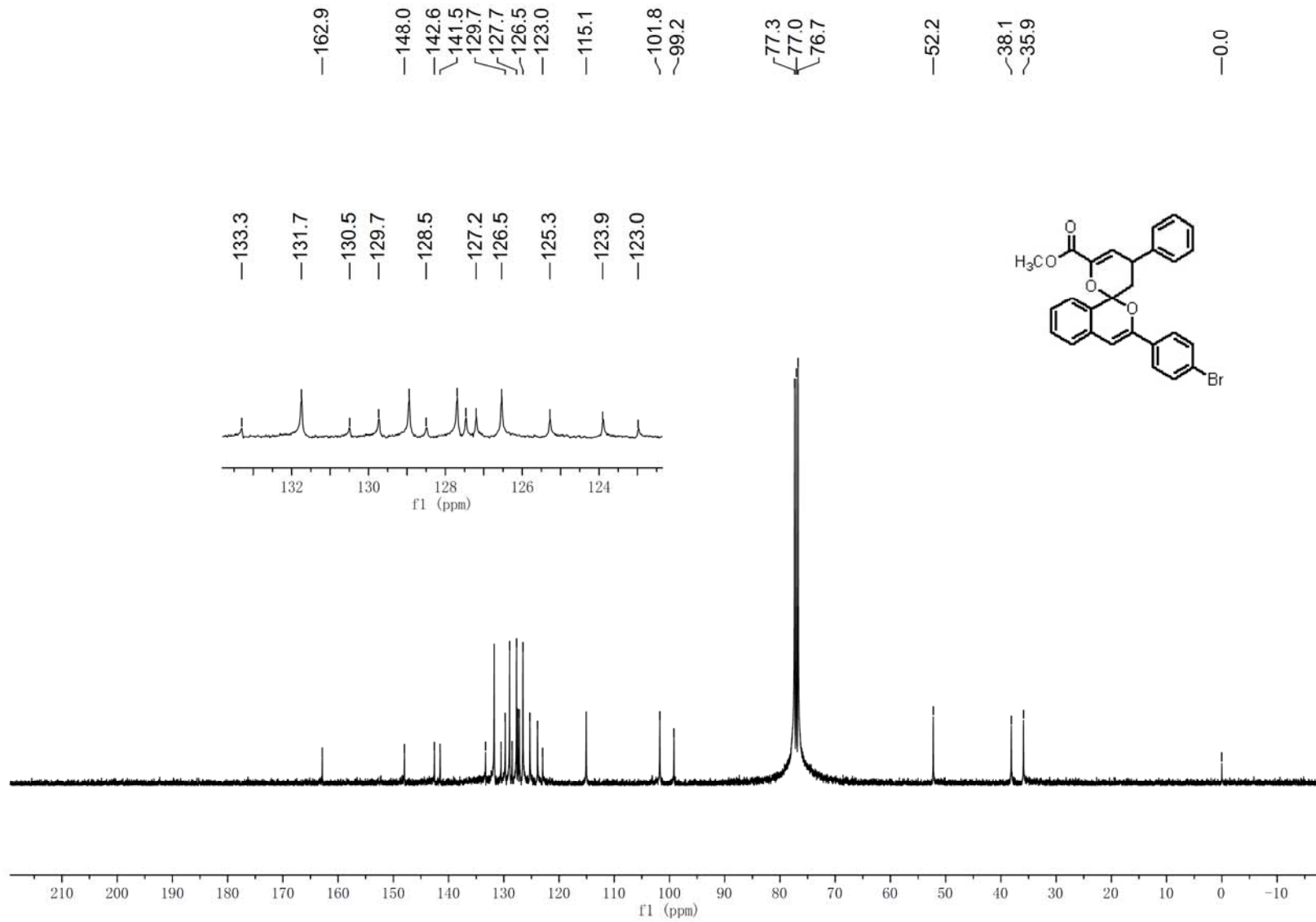
<sup>1</sup>H NMR Spectrum of Compound 3e



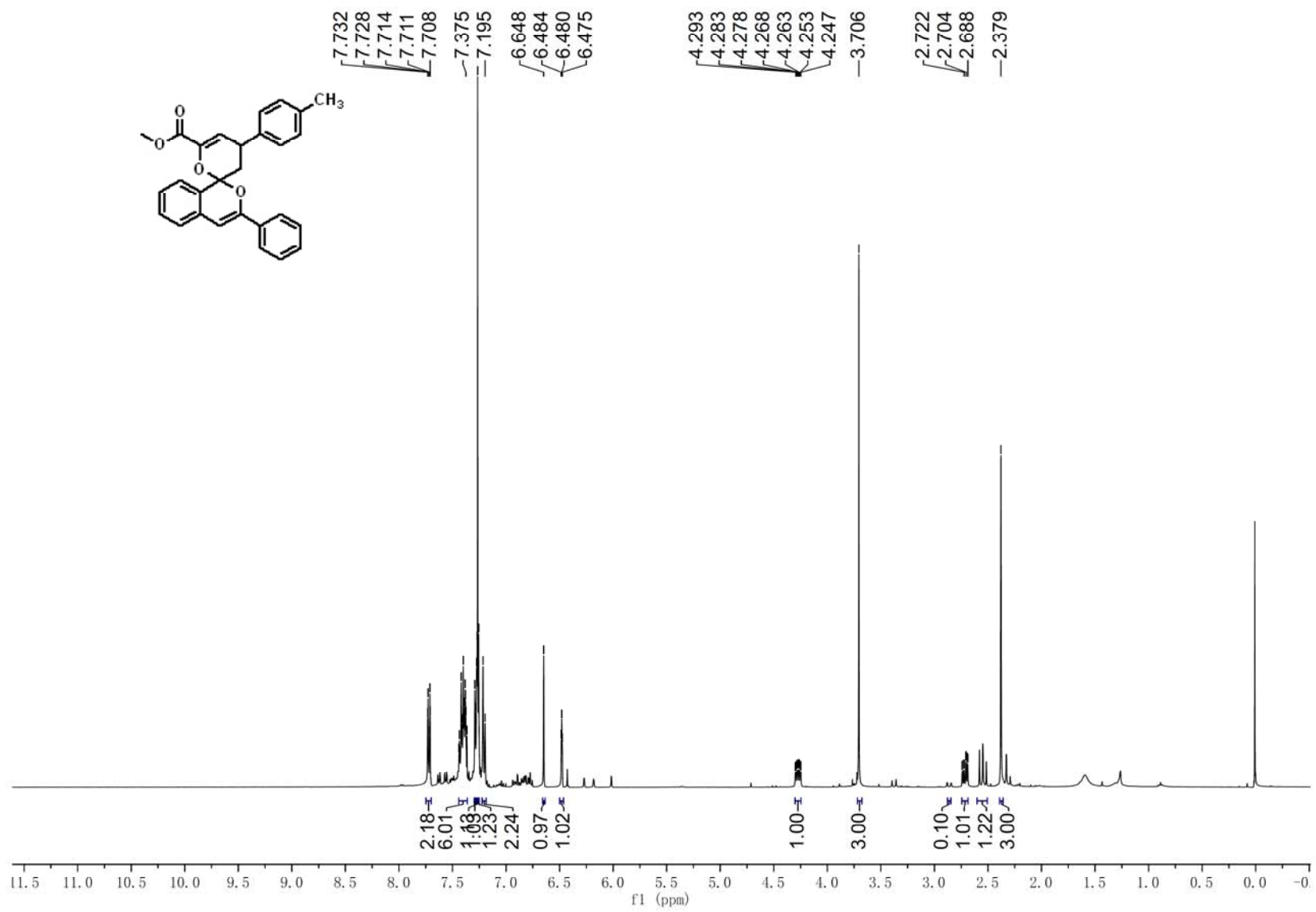
$^{13}\text{C}$  NMR Spectrum of Compound 3e



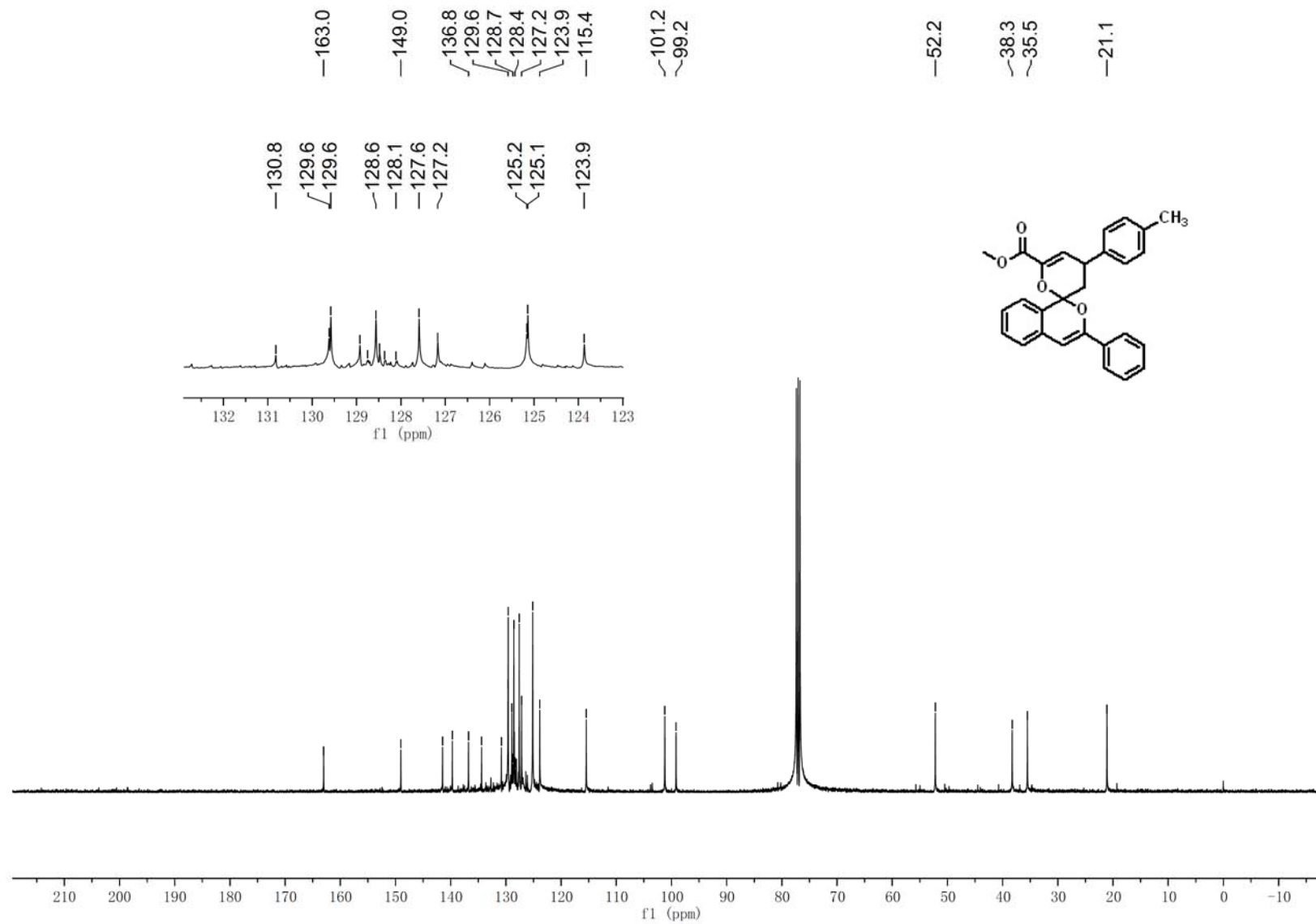
**<sup>1</sup>H NMR Spectrum of Compound 3f**



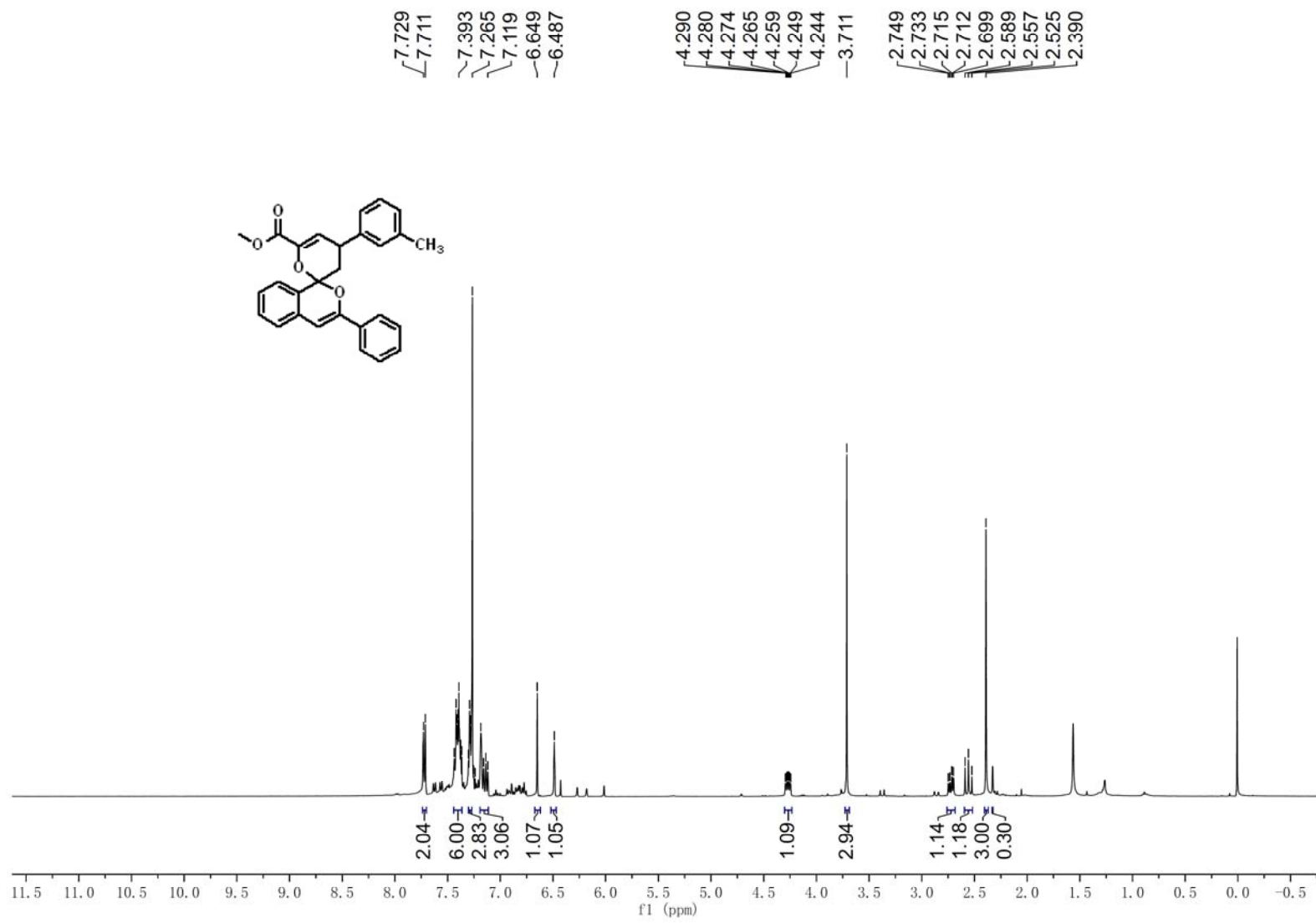
**<sup>13</sup>C NMR Spectrum of Compound 3f**



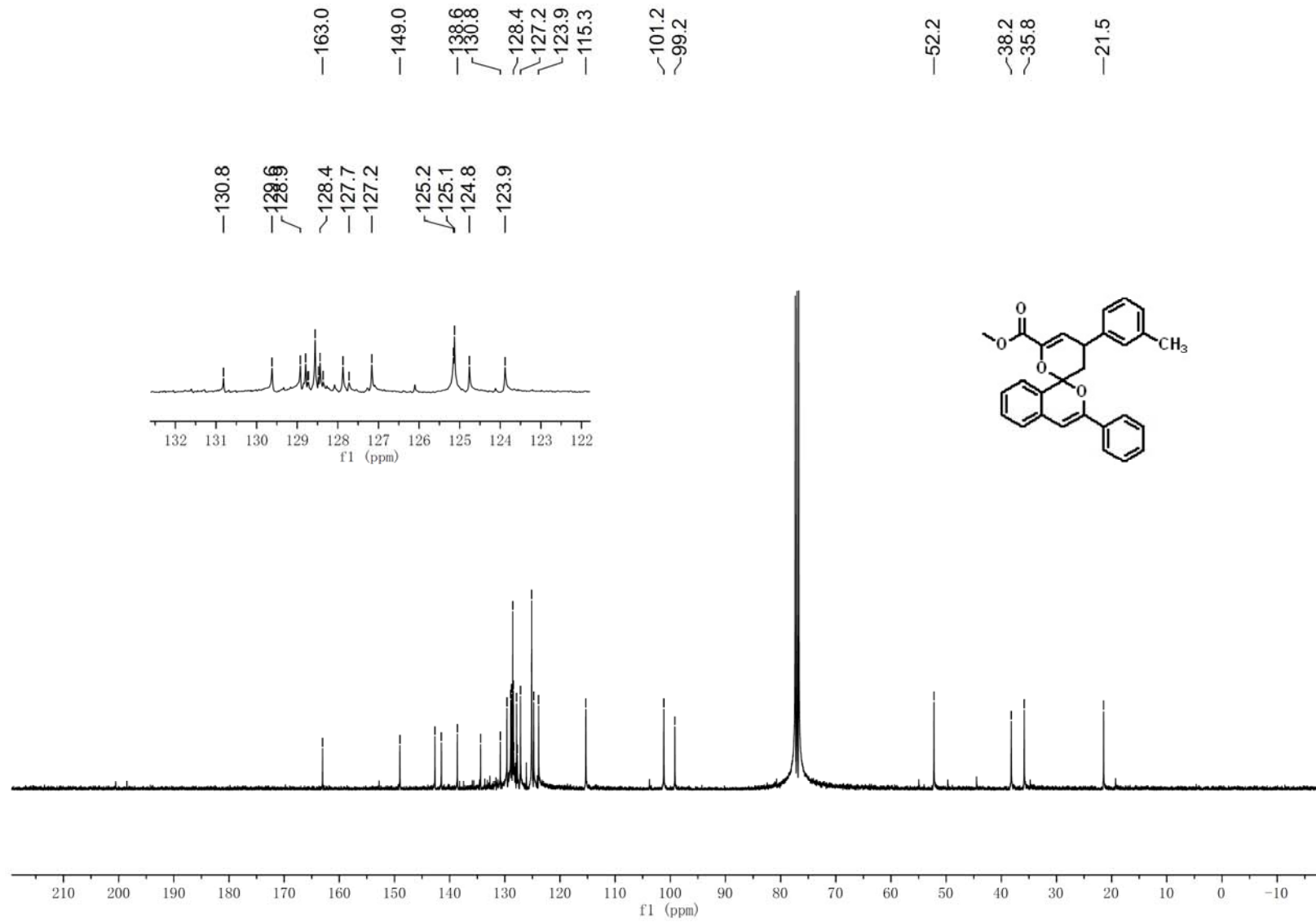
**<sup>1</sup>H NMR Spectrum of Compound 3g**



**<sup>13</sup>C NMR Spectrum of Compound 3g**

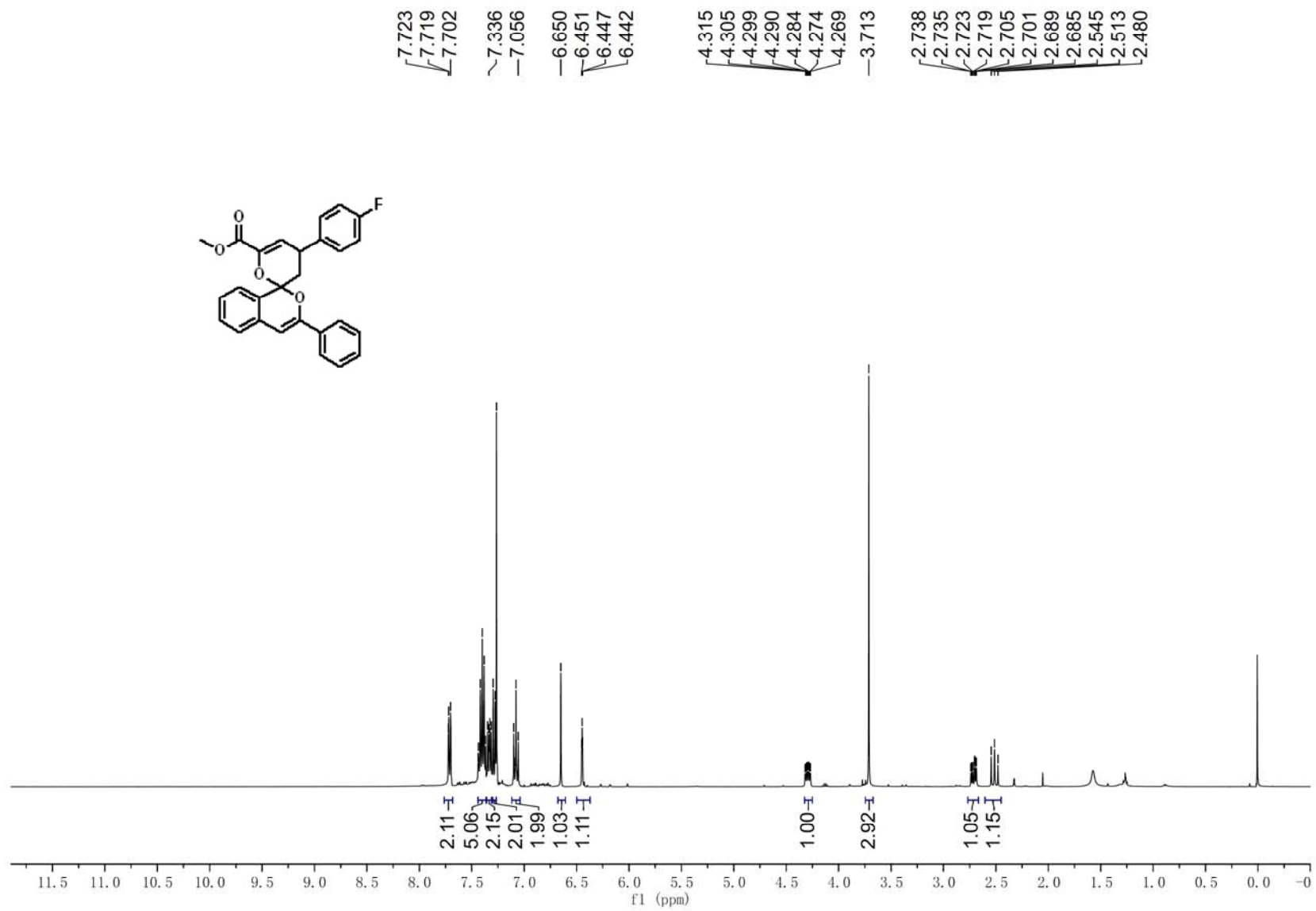


**<sup>1</sup>H NMR Spectrum of Compound 3h**

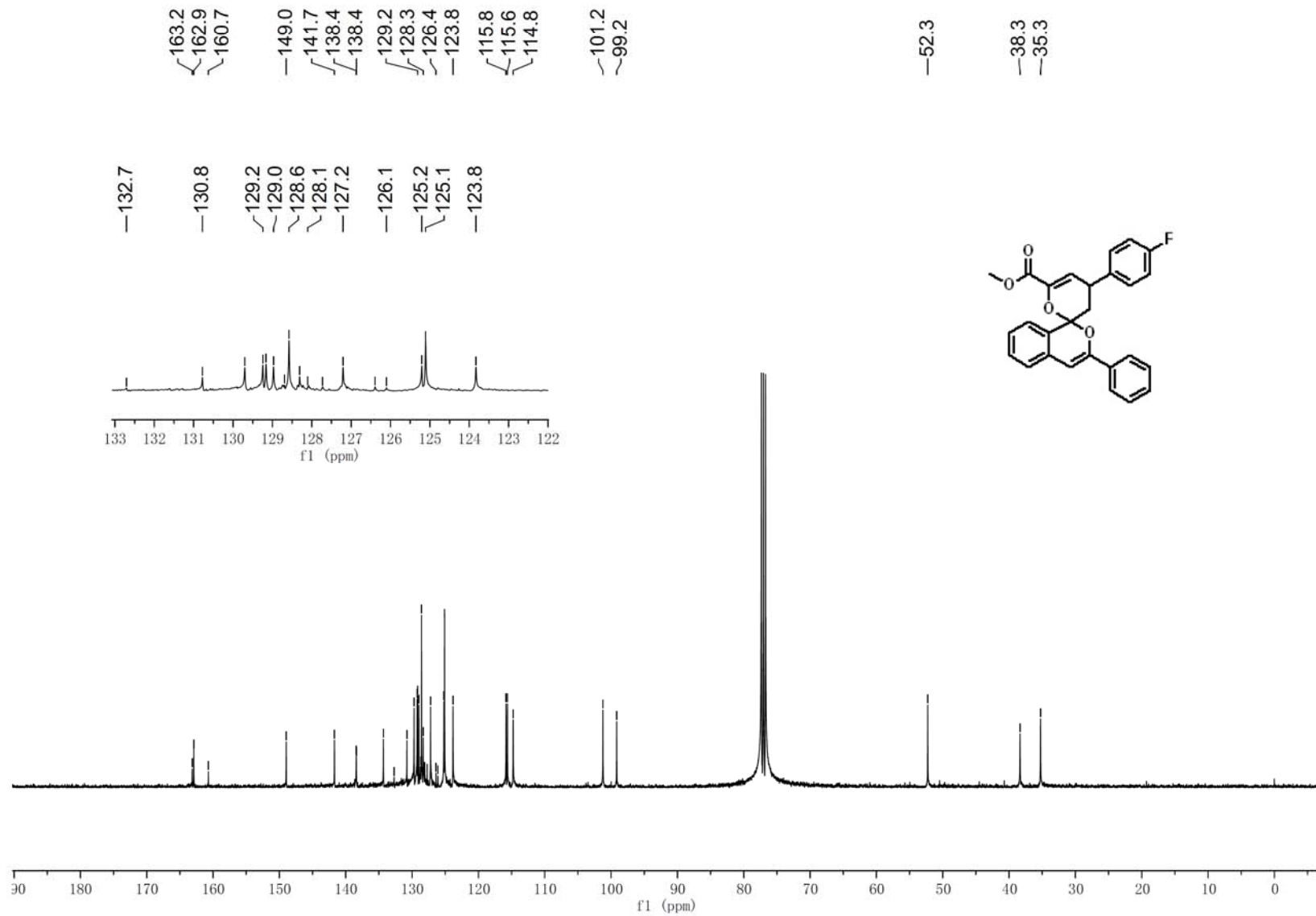


$^{13}\text{C}$  NMR Spectrum of Compound 3h

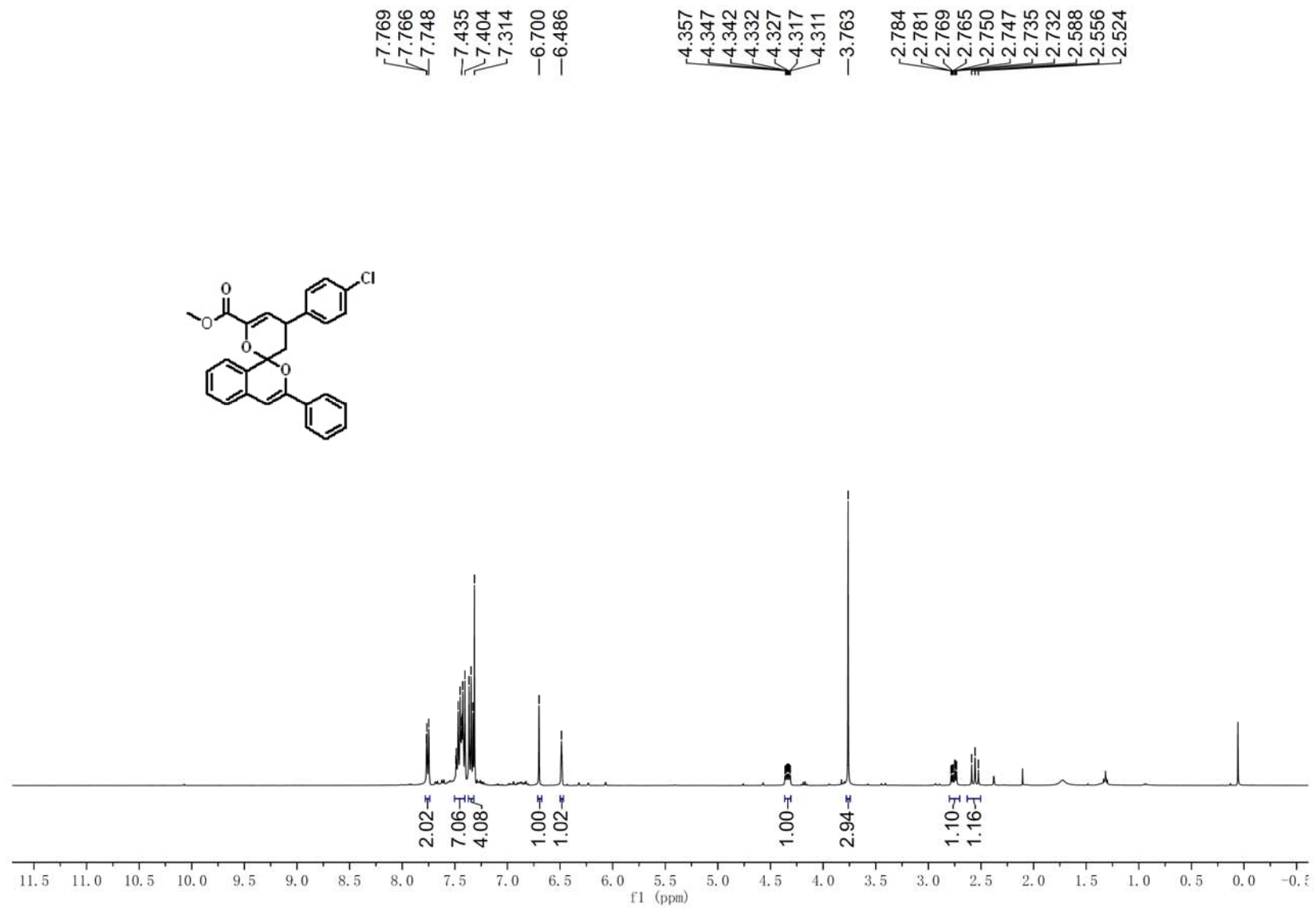




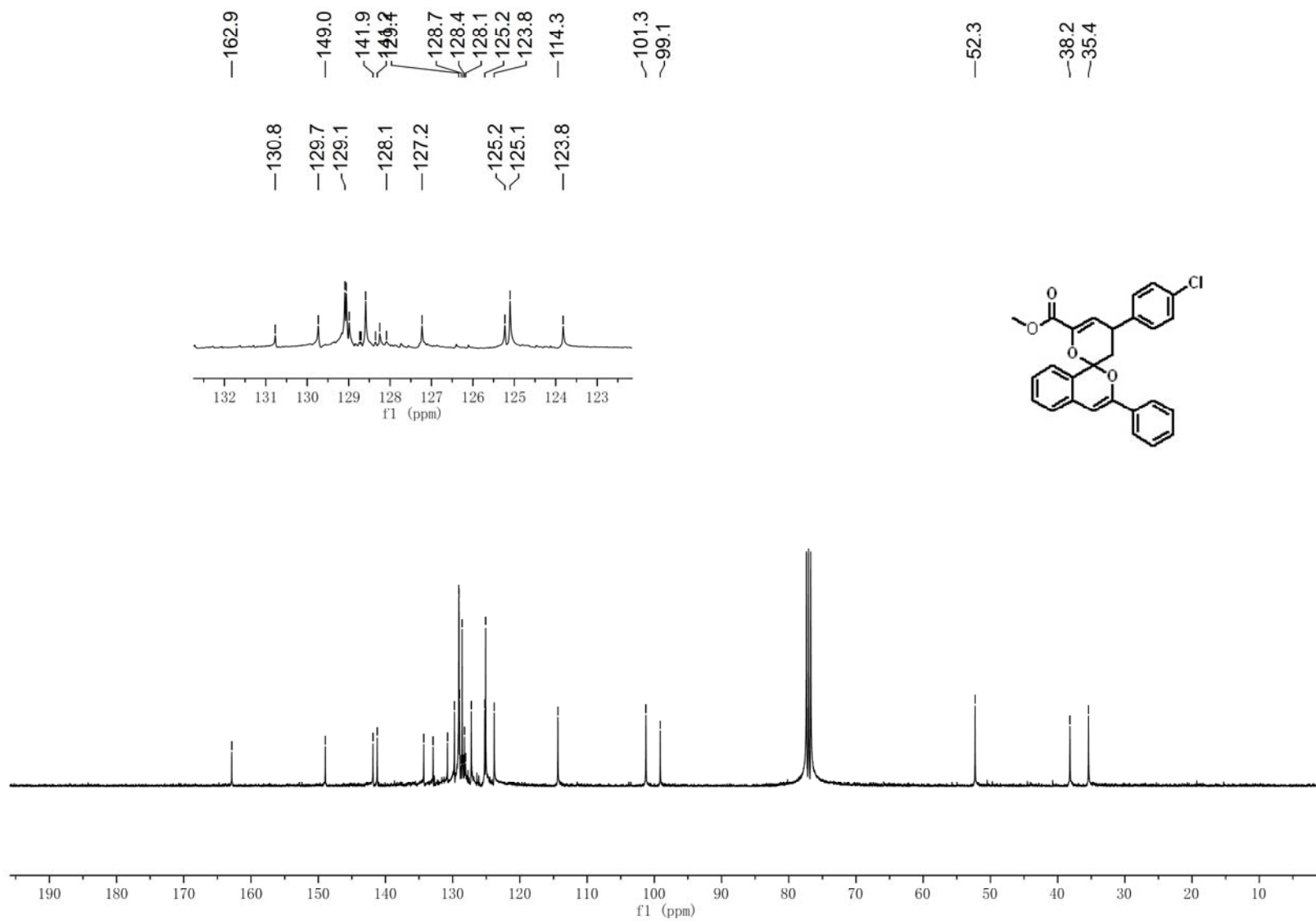
<sup>1</sup>H NMR Spectrum of Compound 3i



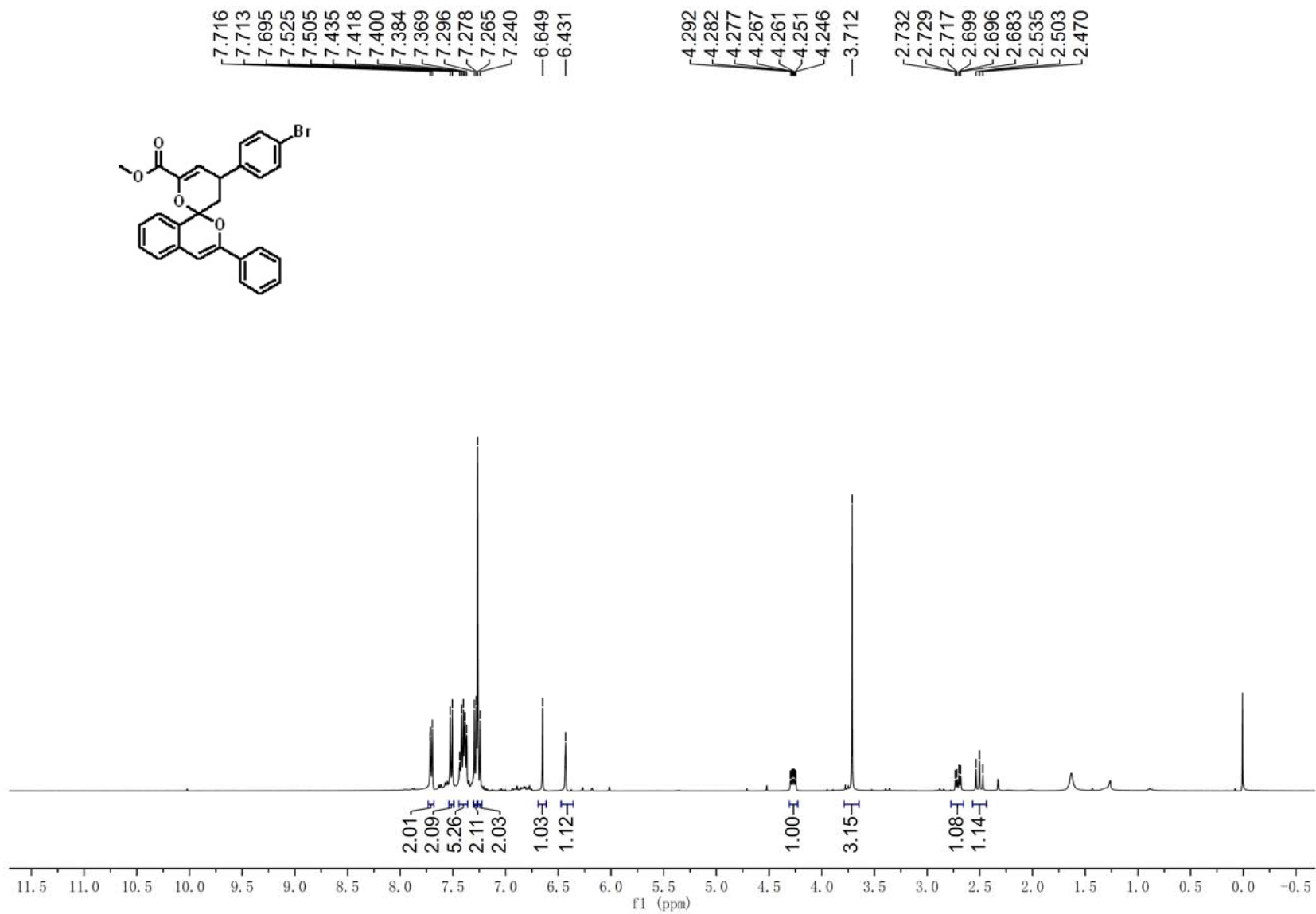
$^{13}\text{C}$  NMR Spectrum of Compound 3i



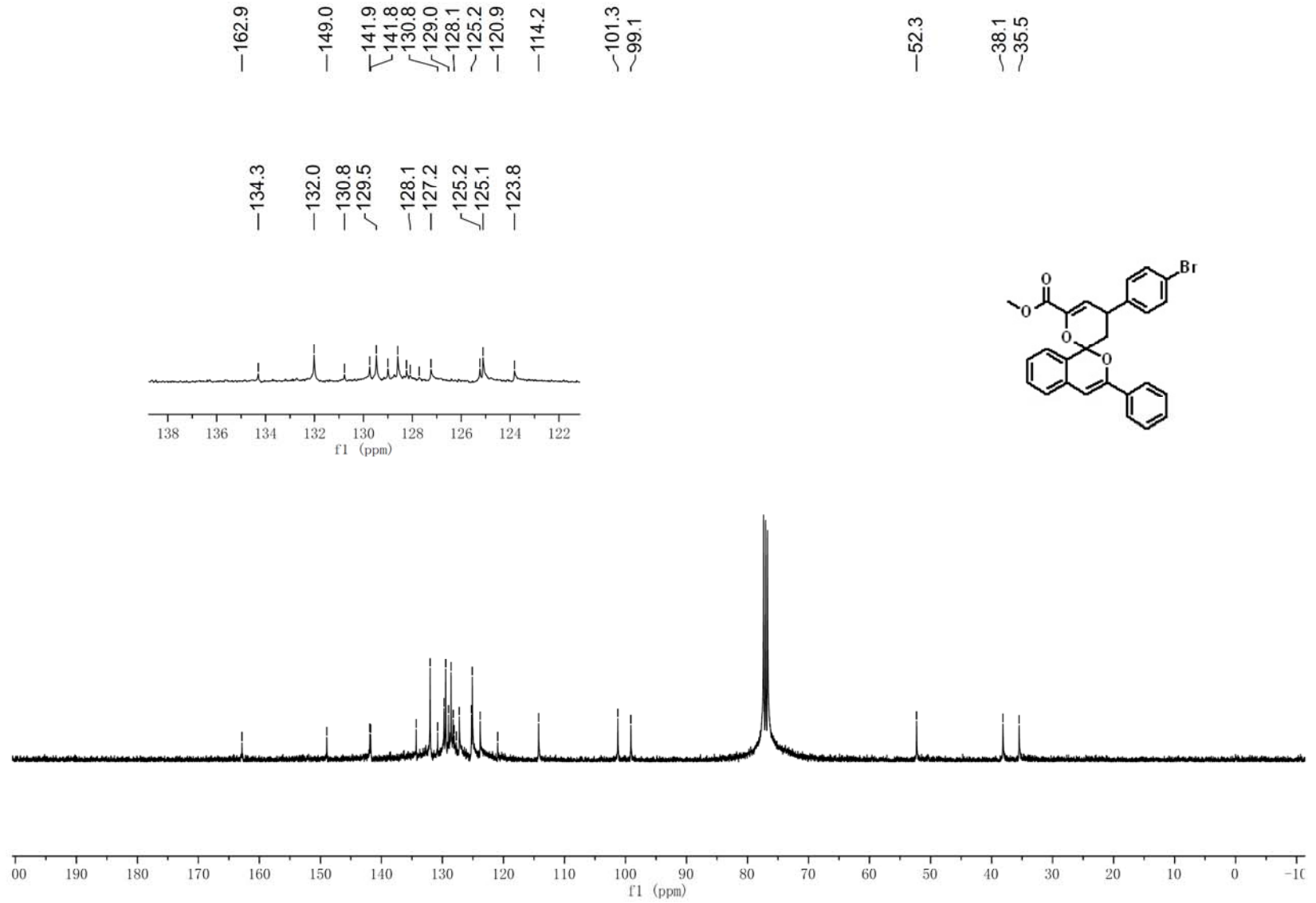
**<sup>1</sup>H NMR Spectrum of Compound 3j**



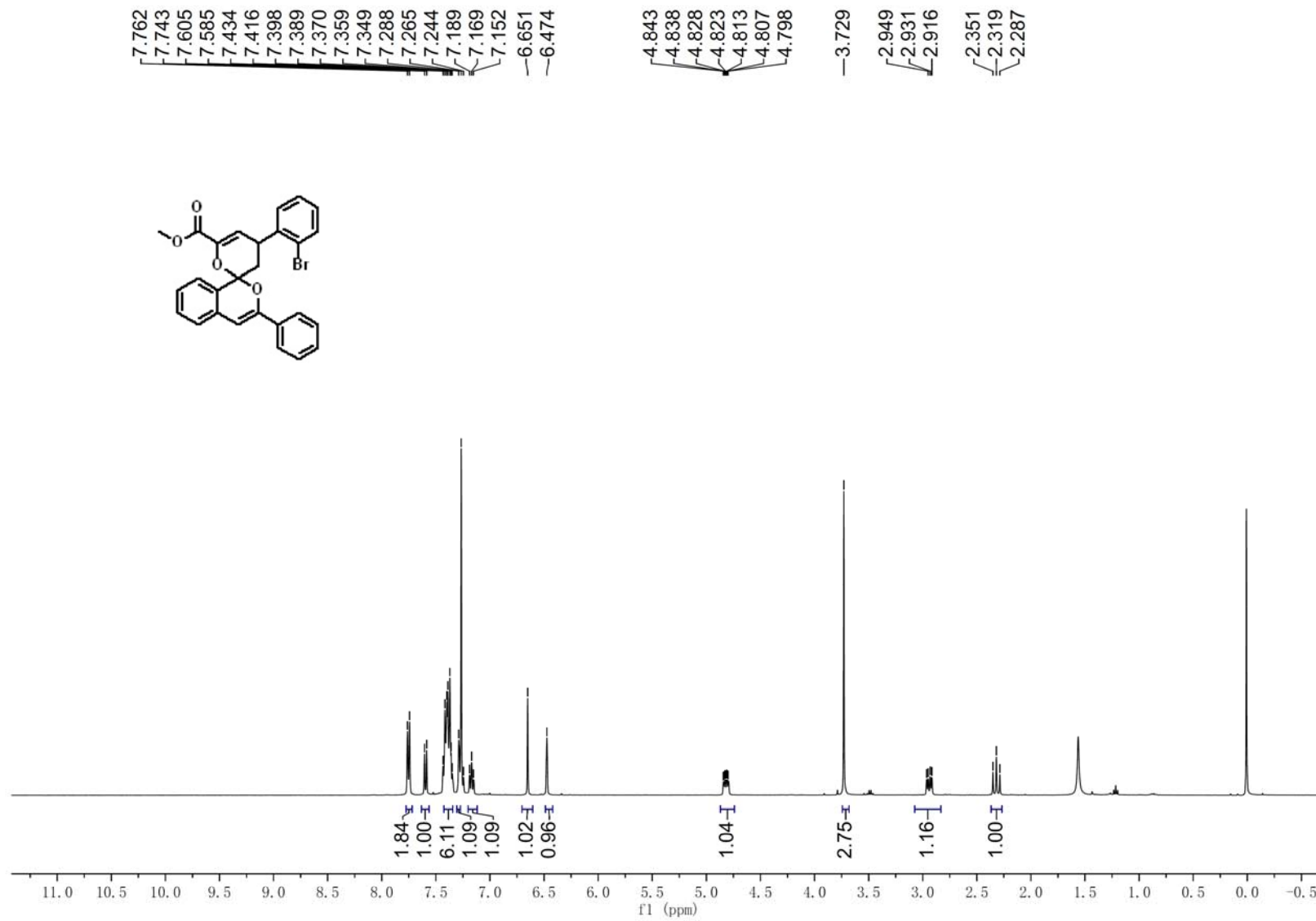
<sup>13</sup>C NMR Spectrum of Compound 3j



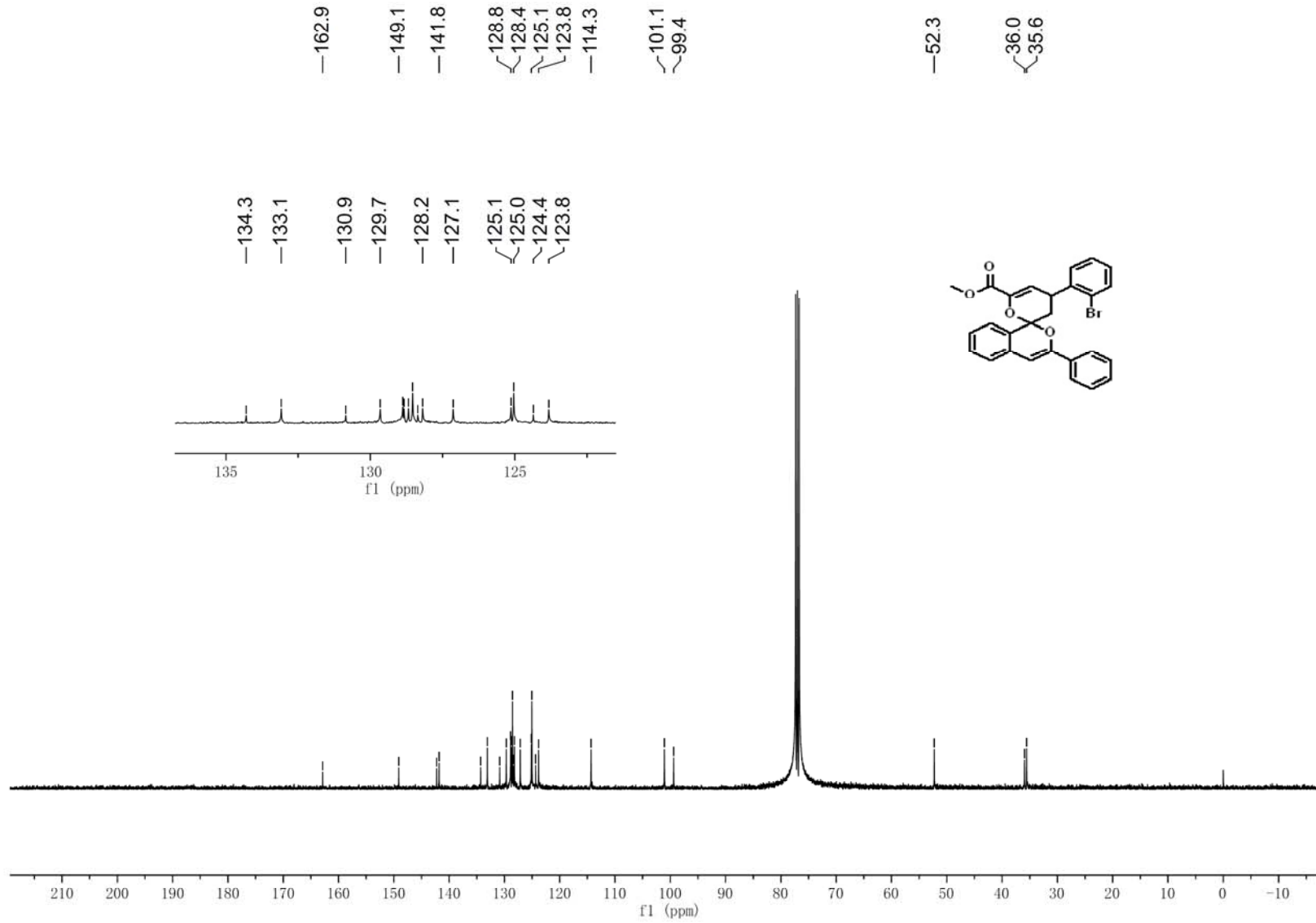
<sup>1</sup>H NMR Spectrum of Compound 3k



$^{13}\text{C}$  NMR Spectrum of Compound 3k

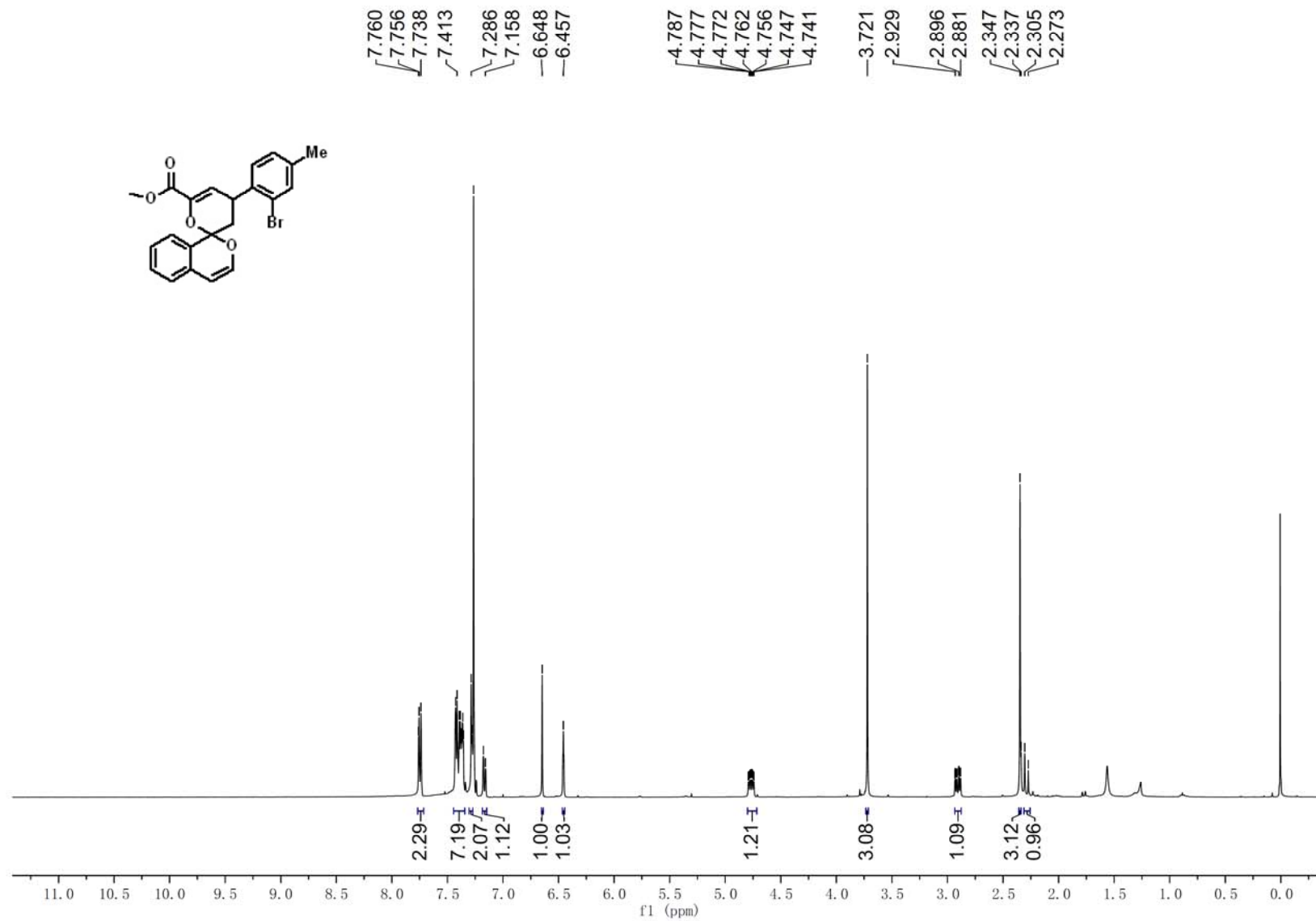


<sup>1</sup>H NMR Spectrum of Compound 31

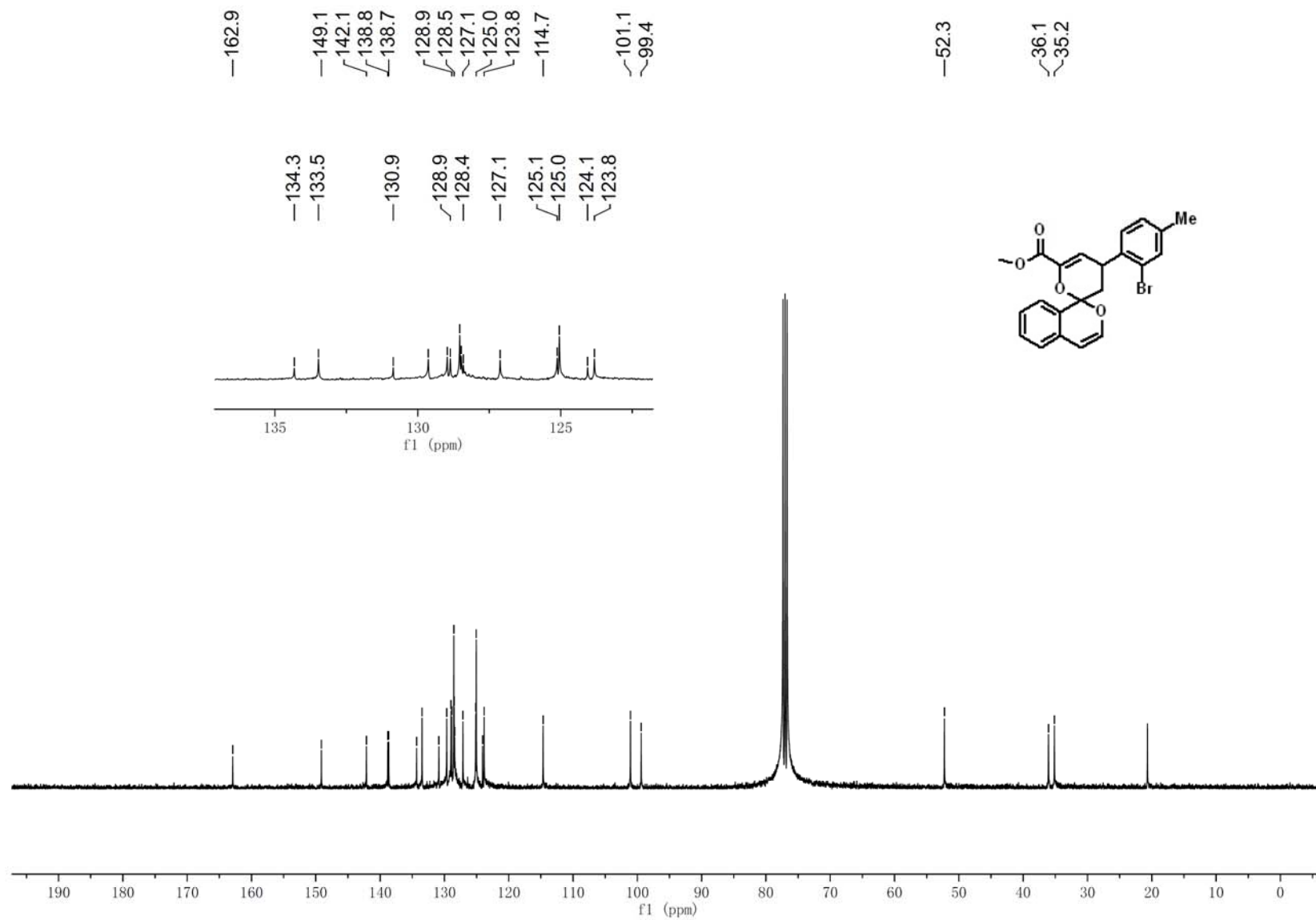


$^{13}\text{C}$  NMR Spectrum of Compound 31

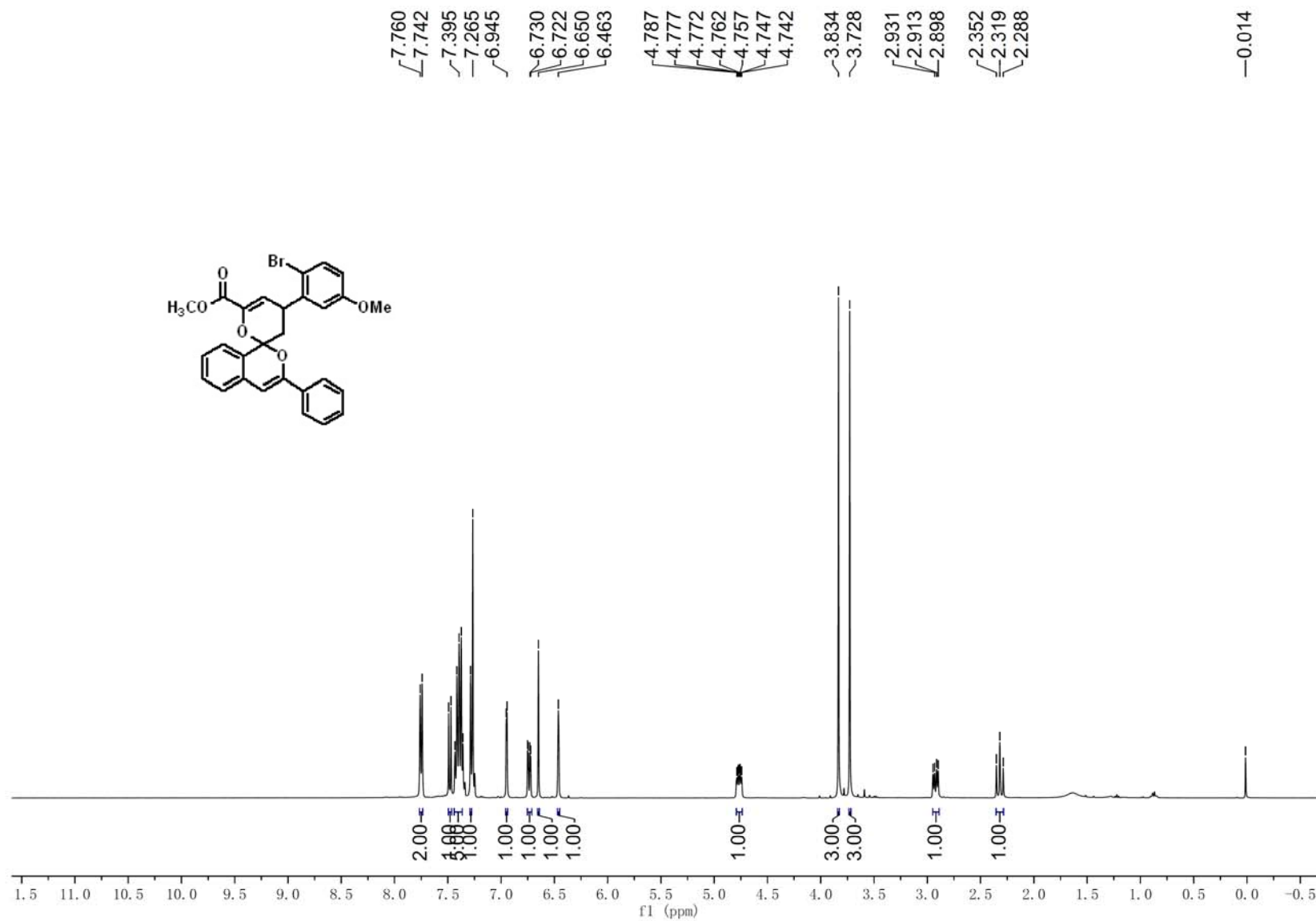




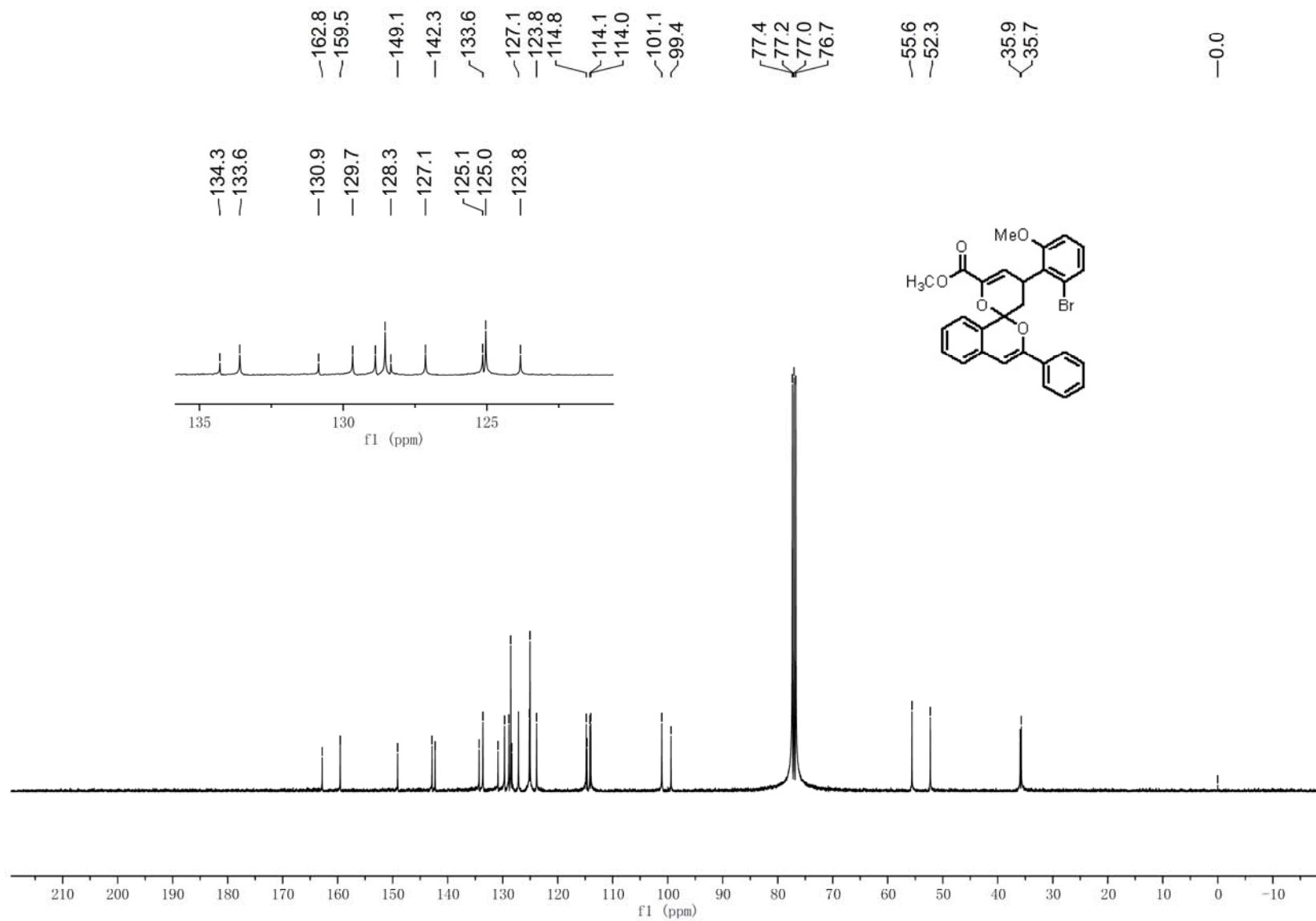
<sup>1</sup>H NMR Spectrum of Compound 3m



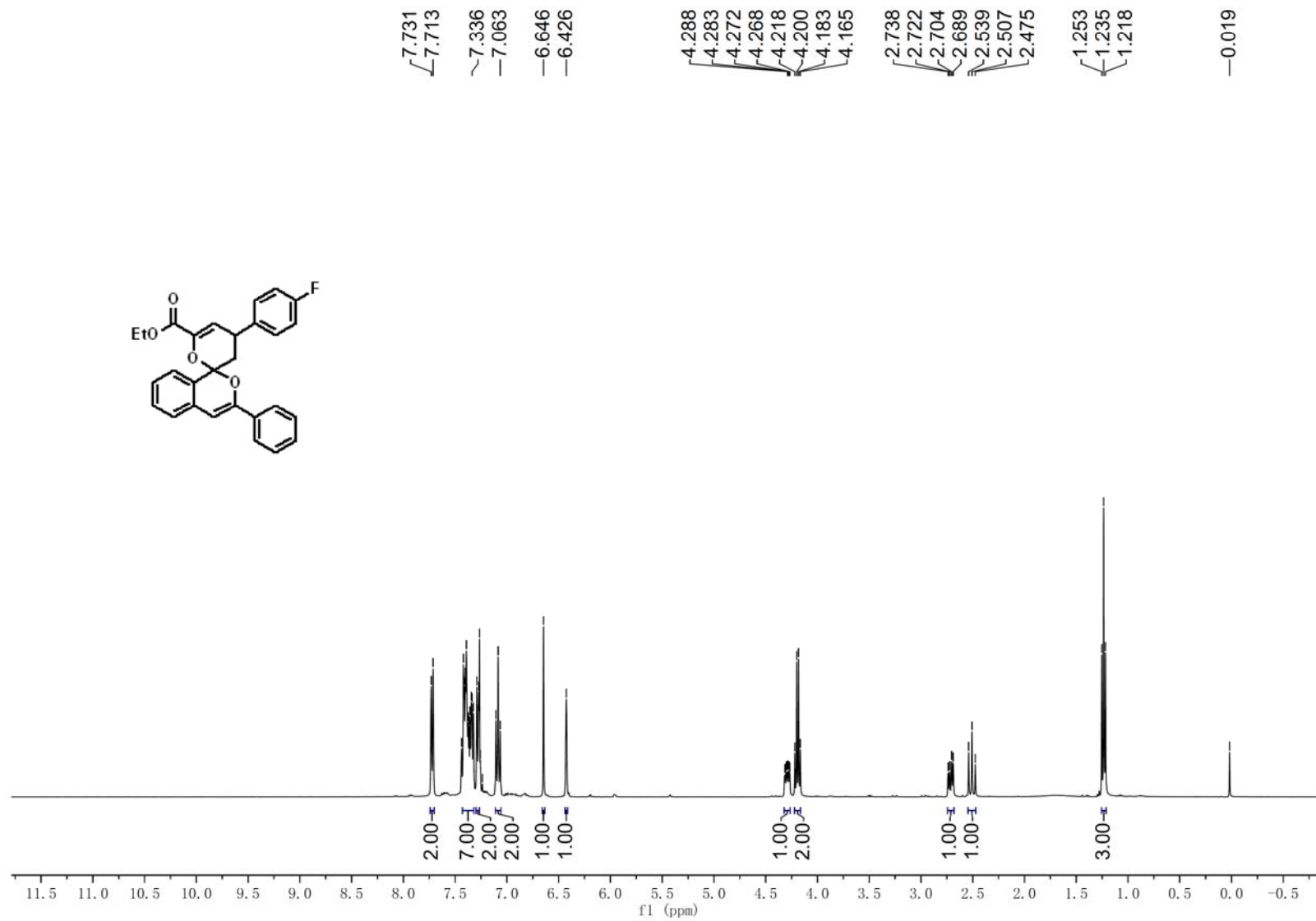
**<sup>13</sup>C NMR Spectrum of Compound 3m**



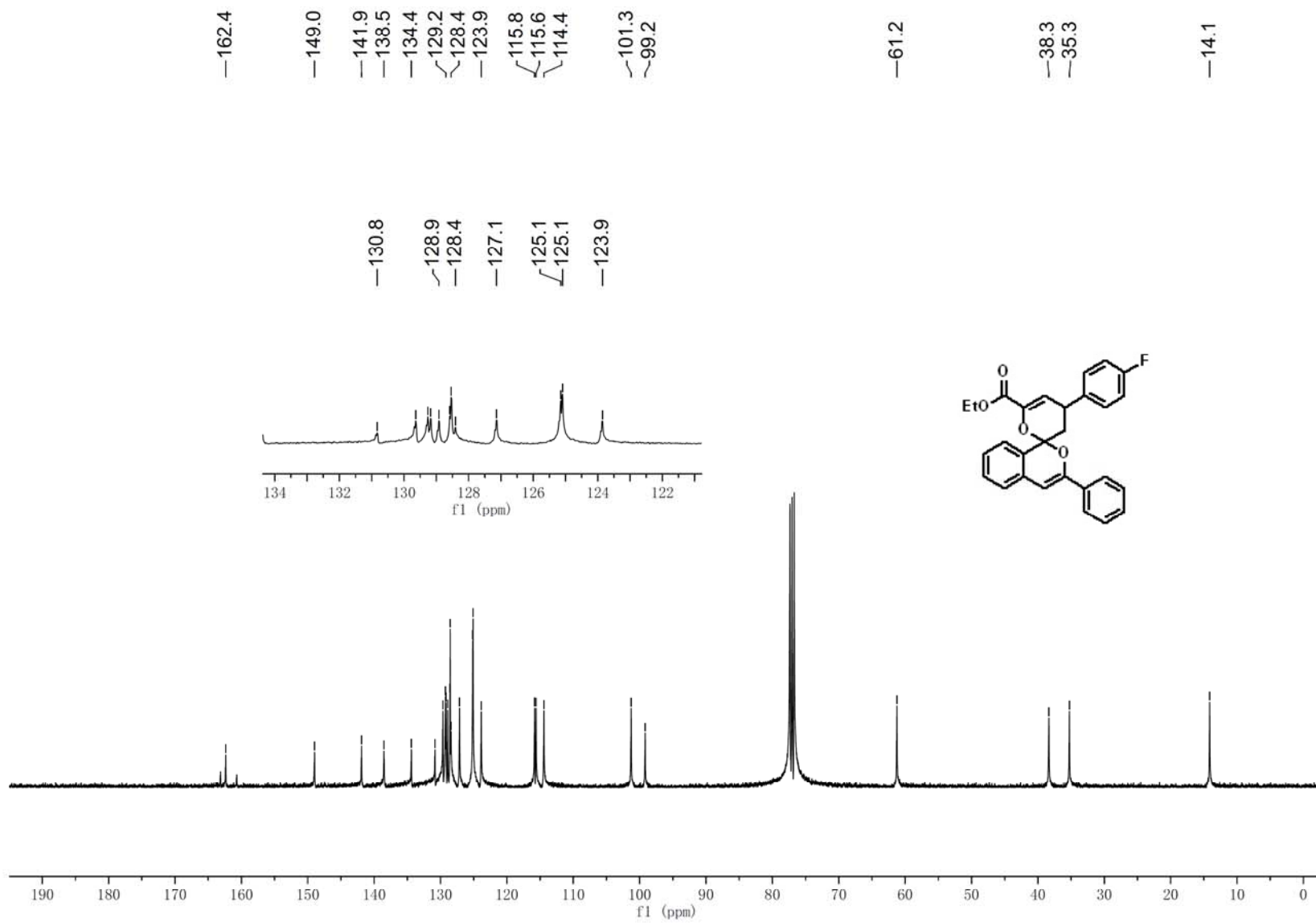
<sup>1</sup>H NMR Spectrum of Compound 3n



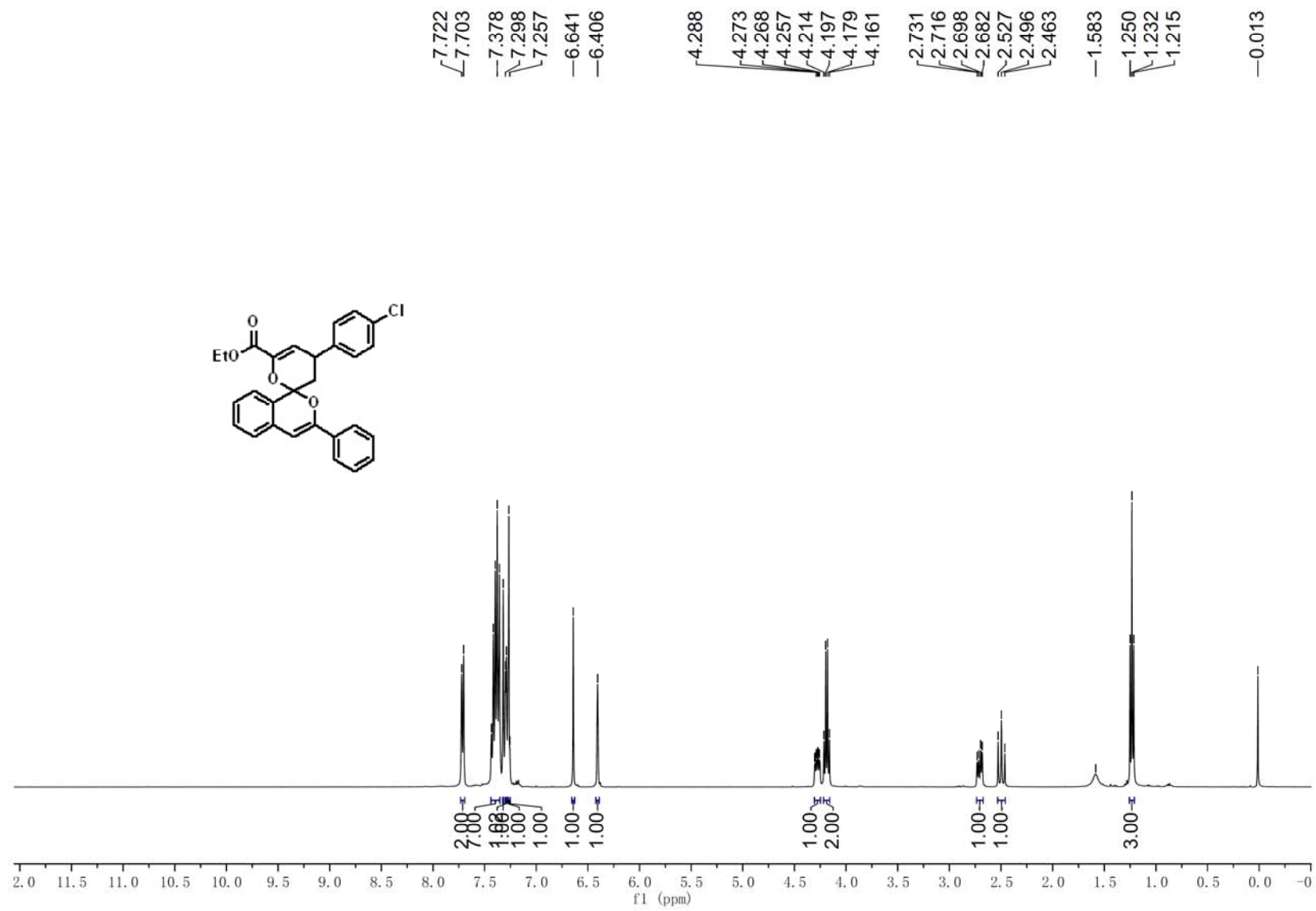
**<sup>13</sup>C NMR Spectrum of Compound 3n**



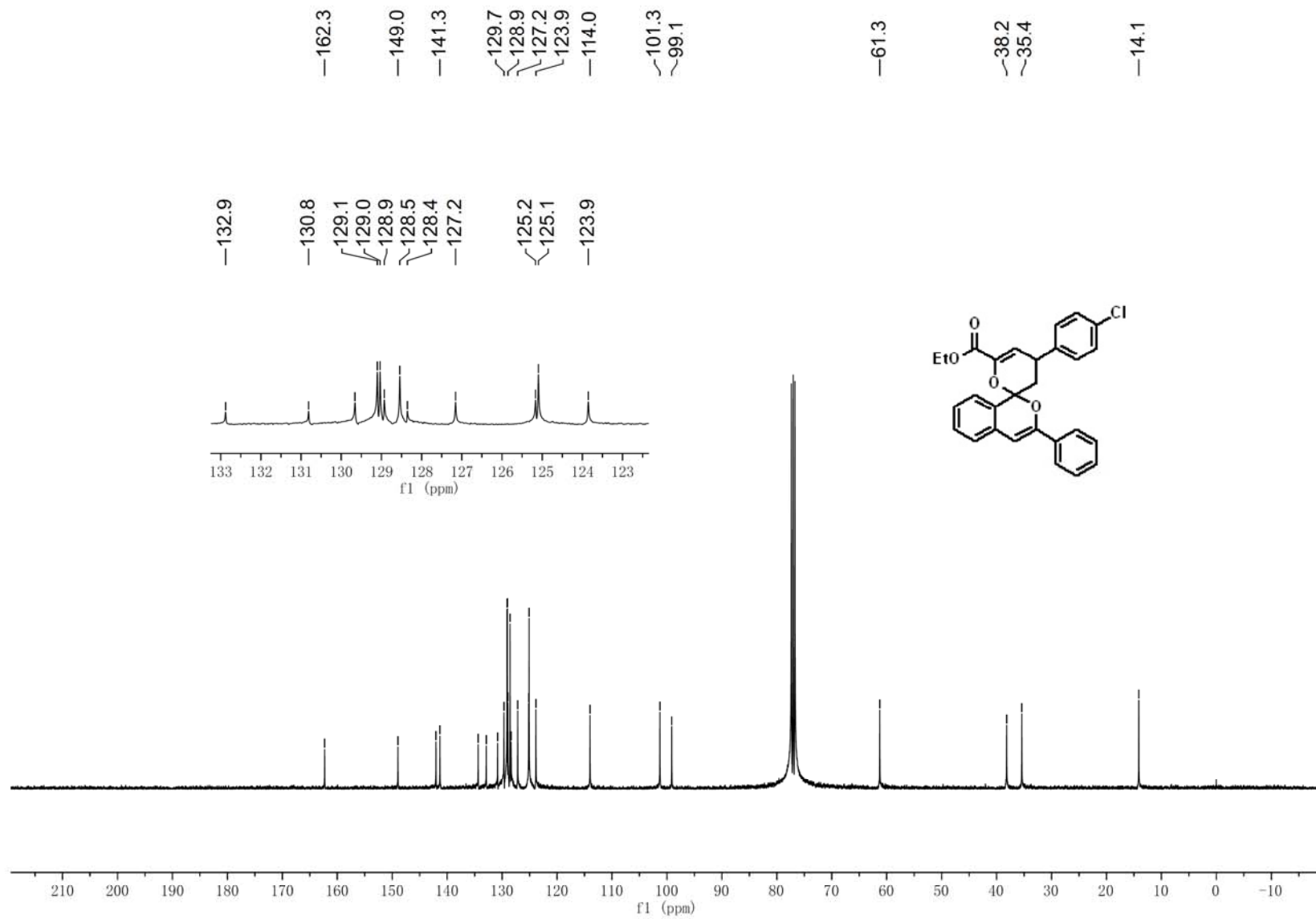
<sup>1</sup>H NMR Spectrum of Compound 3o



**<sup>13</sup>C NMR Spectrum of Compound 3o**

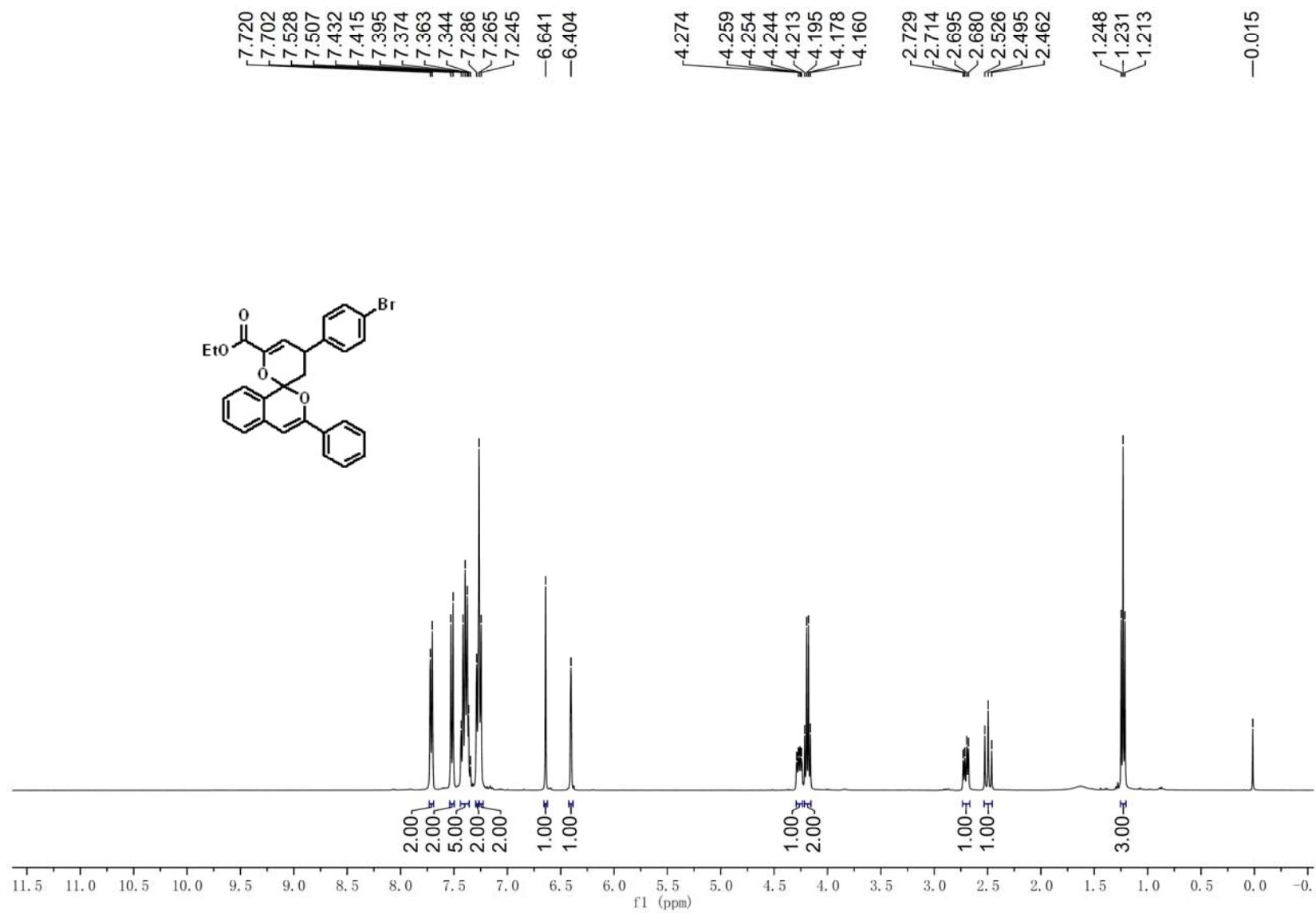


<sup>1</sup>H NMR Spectrum of Compound 3p

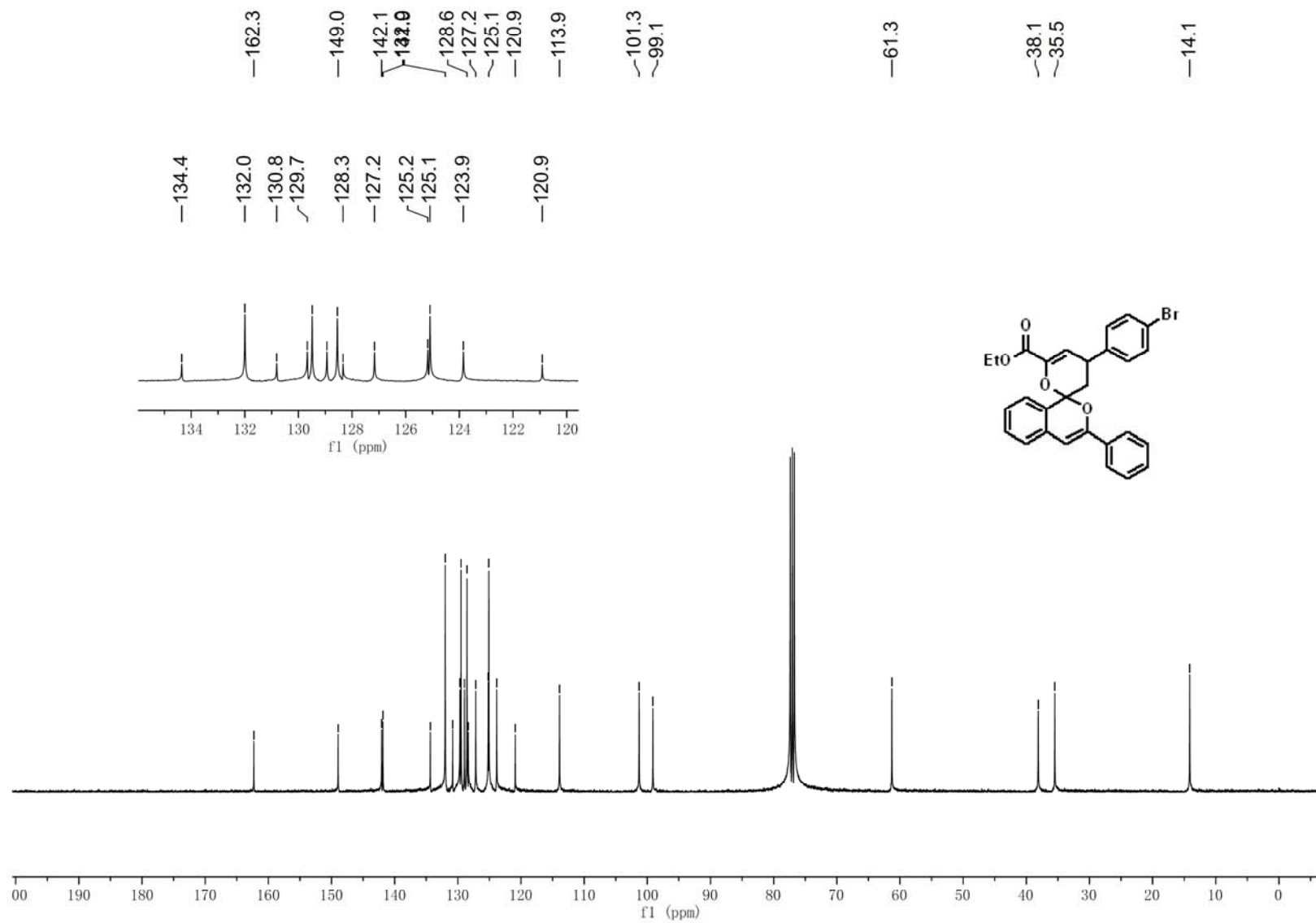


$^{13}\text{C}$  NMR Spectrum of Compound 3p



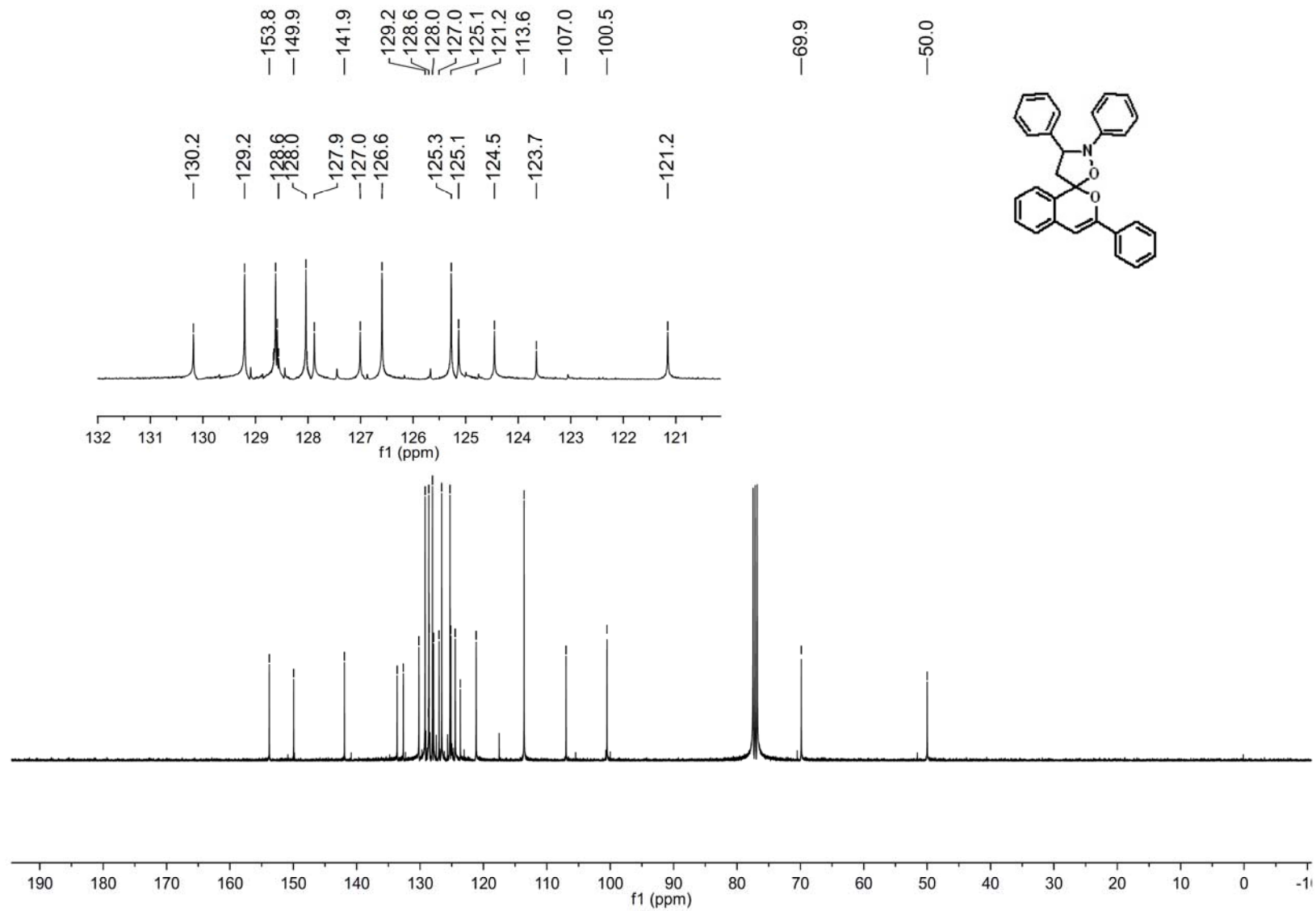


<sup>1</sup>H NMR Spectrum of Compound 3q

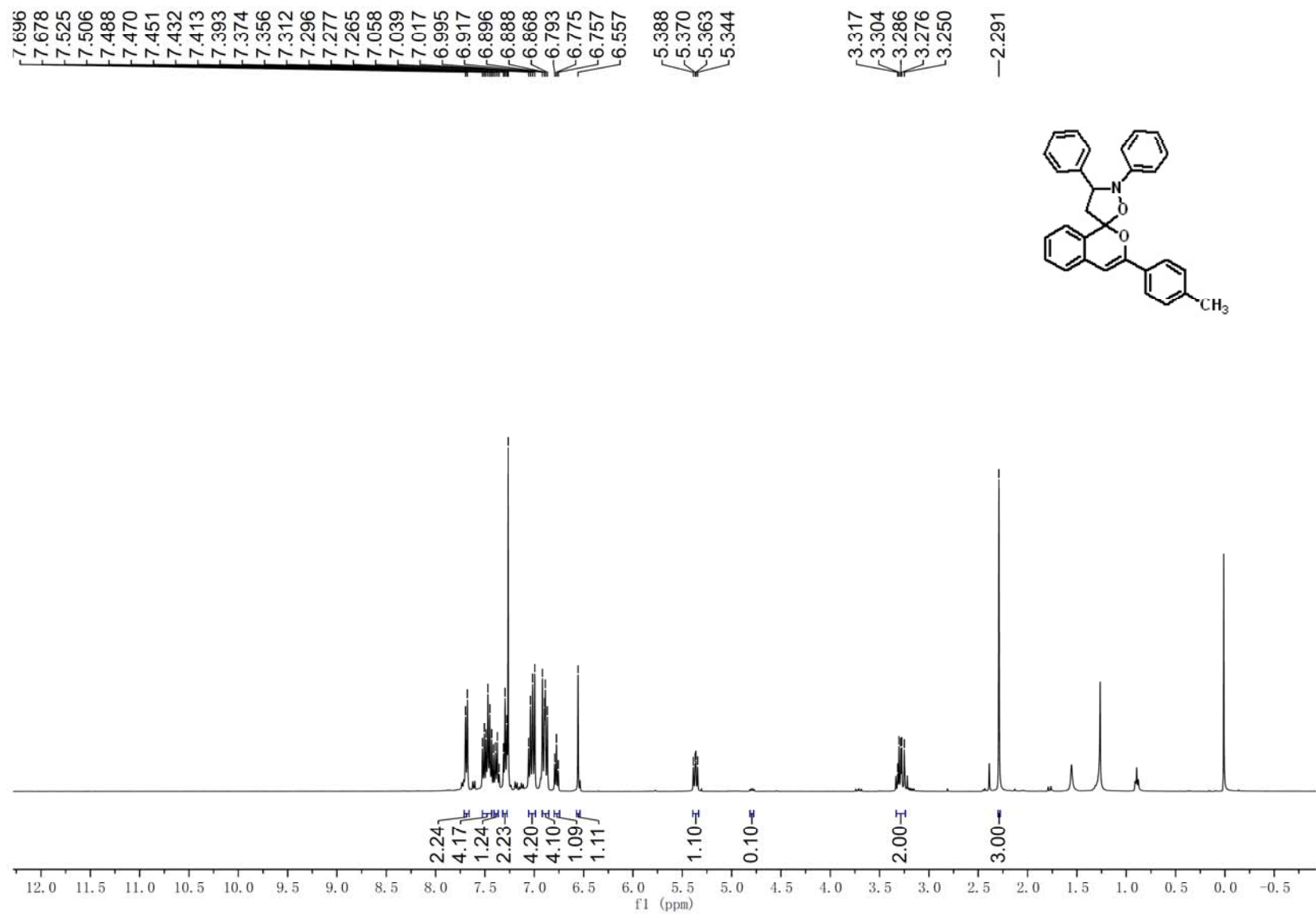


$^{13}\text{C}$  NMR Spectrum of Compound 3q

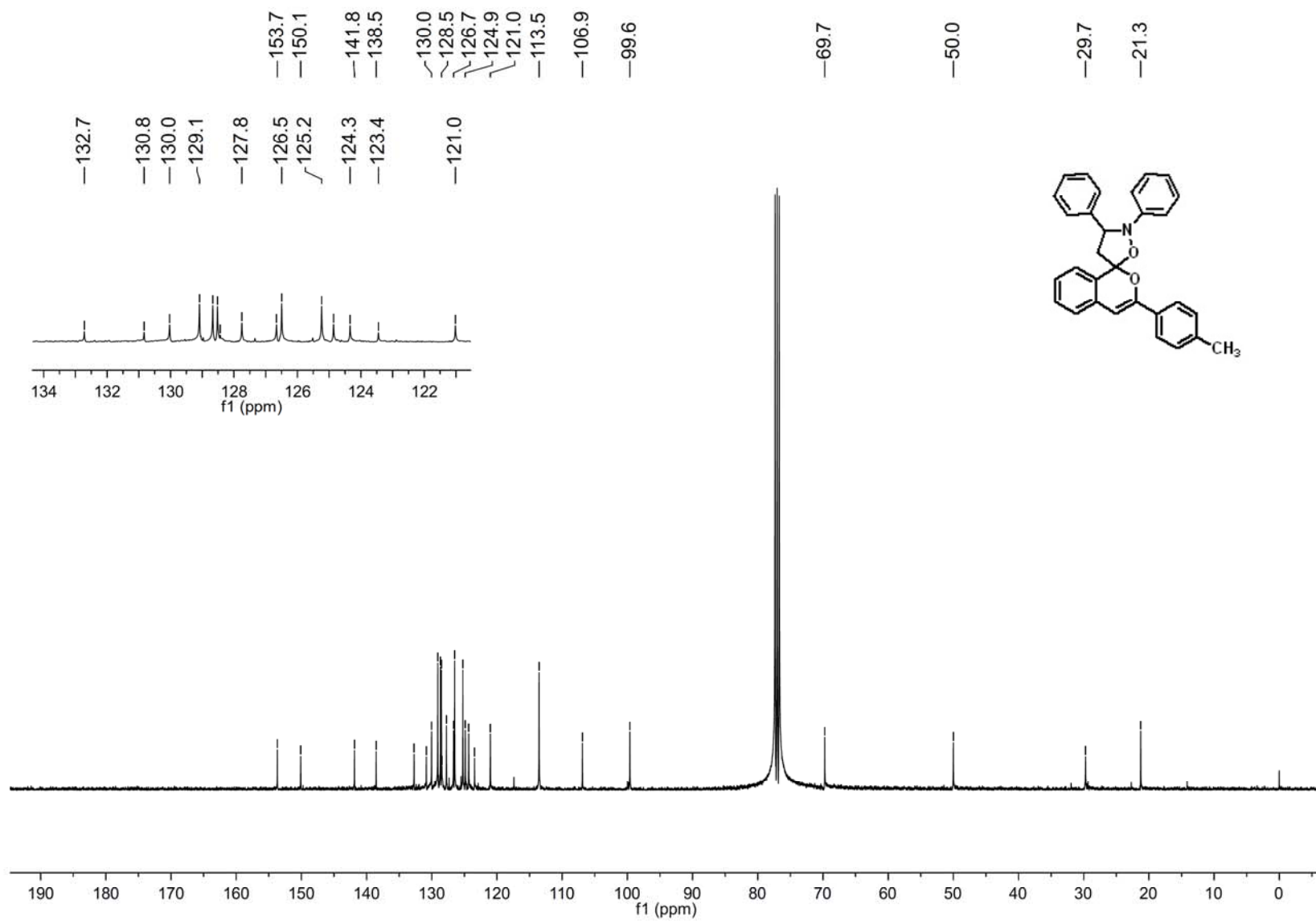




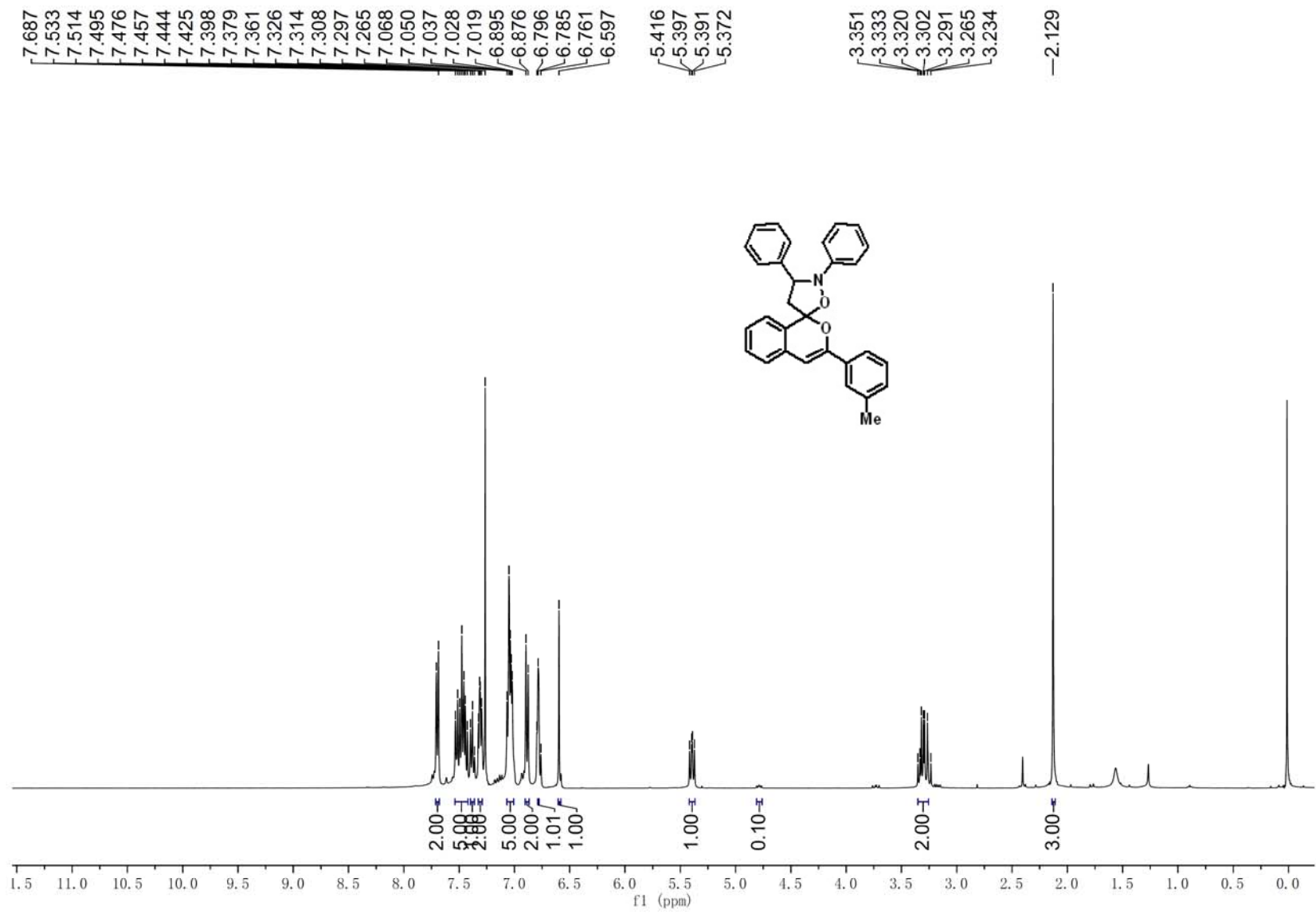
<sup>13</sup>C NMR Spectrum of Compound 5a



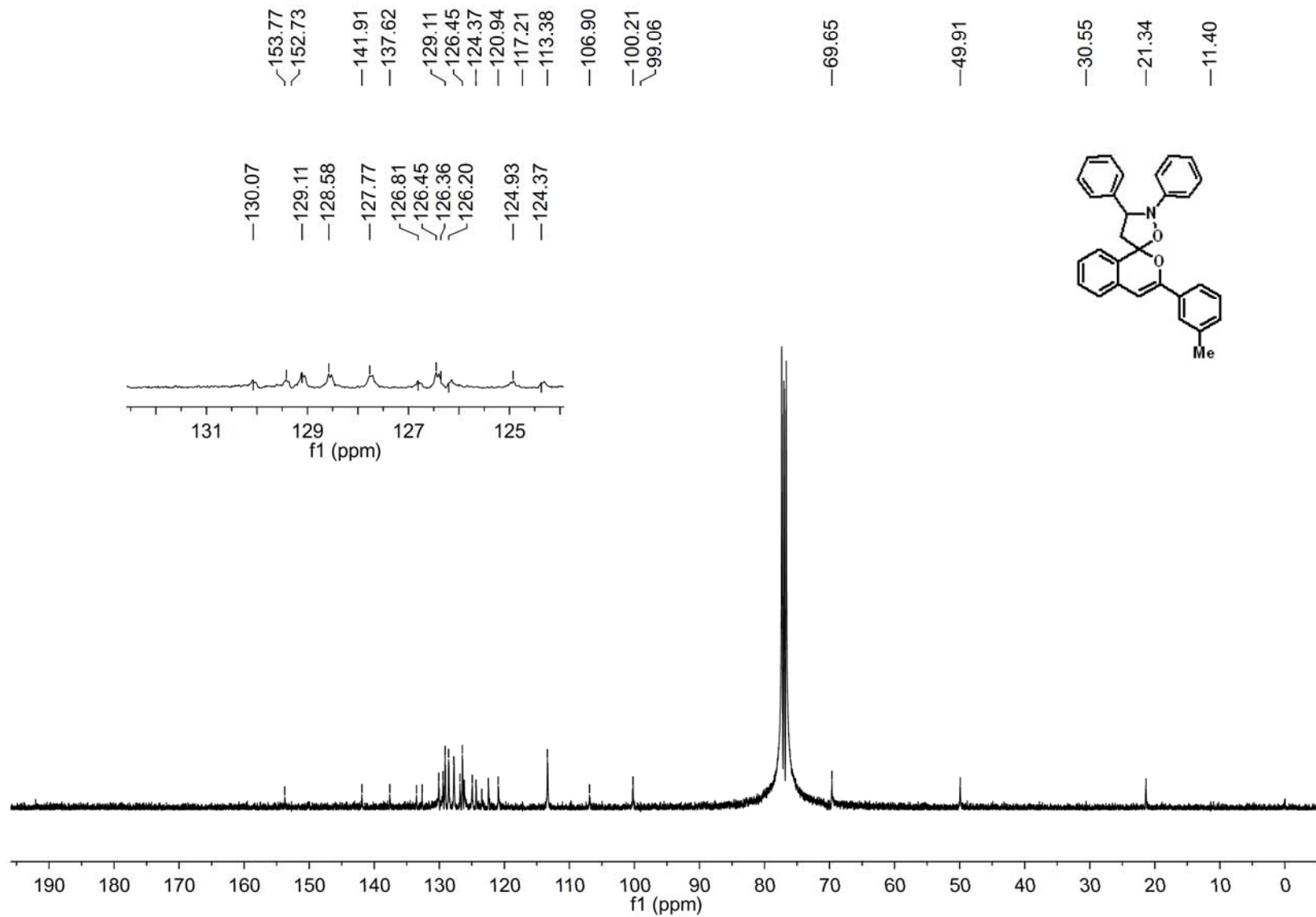
**<sup>1</sup>H NMR Spectrum of Compound 5b**



$^{13}\text{C}$  NMR Spectrum of Compound 5b

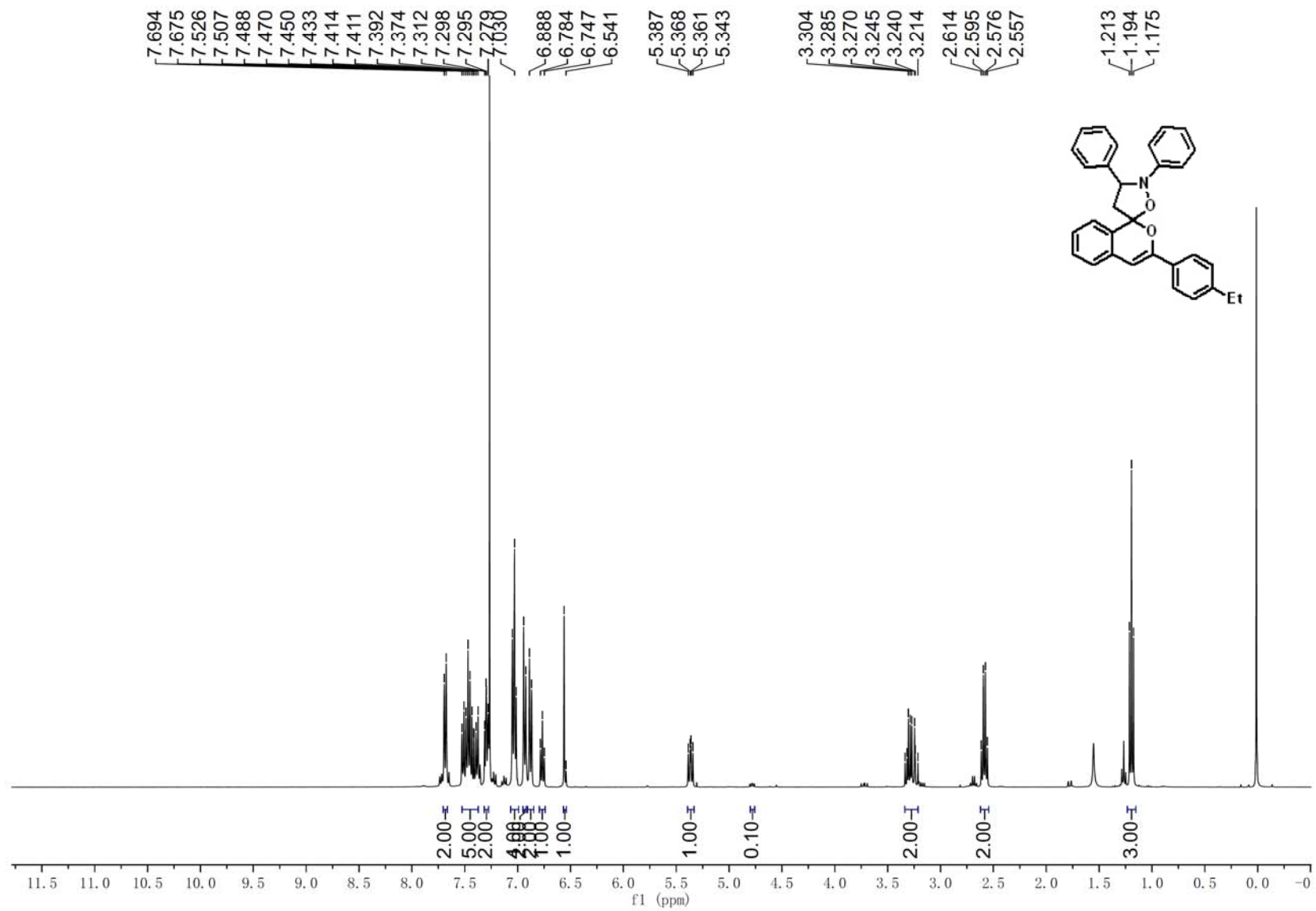


**<sup>1</sup>H NMR Spectrum of Compound 5c**

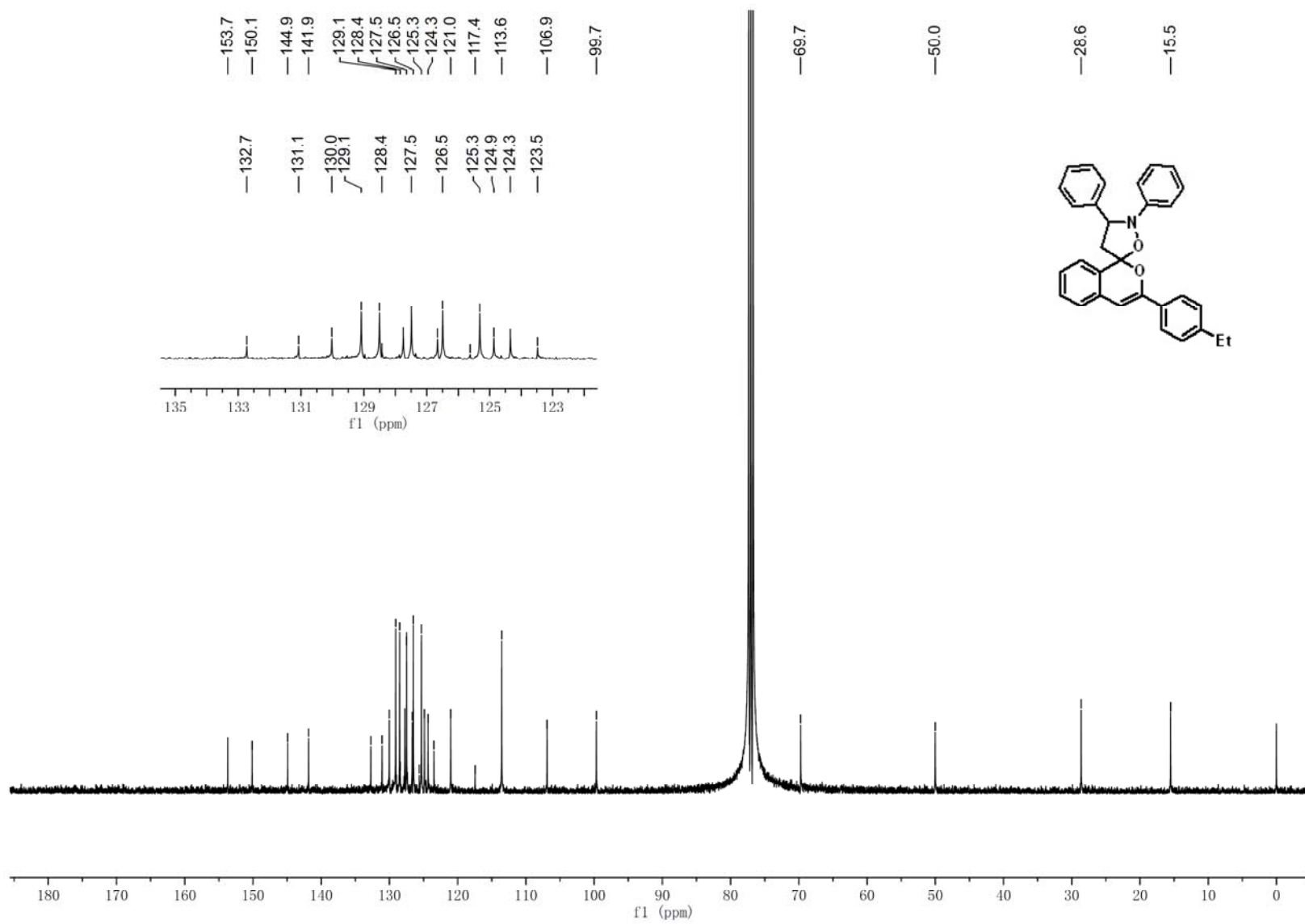


<sup>13</sup>C NMR Spectrum of Compound 5c

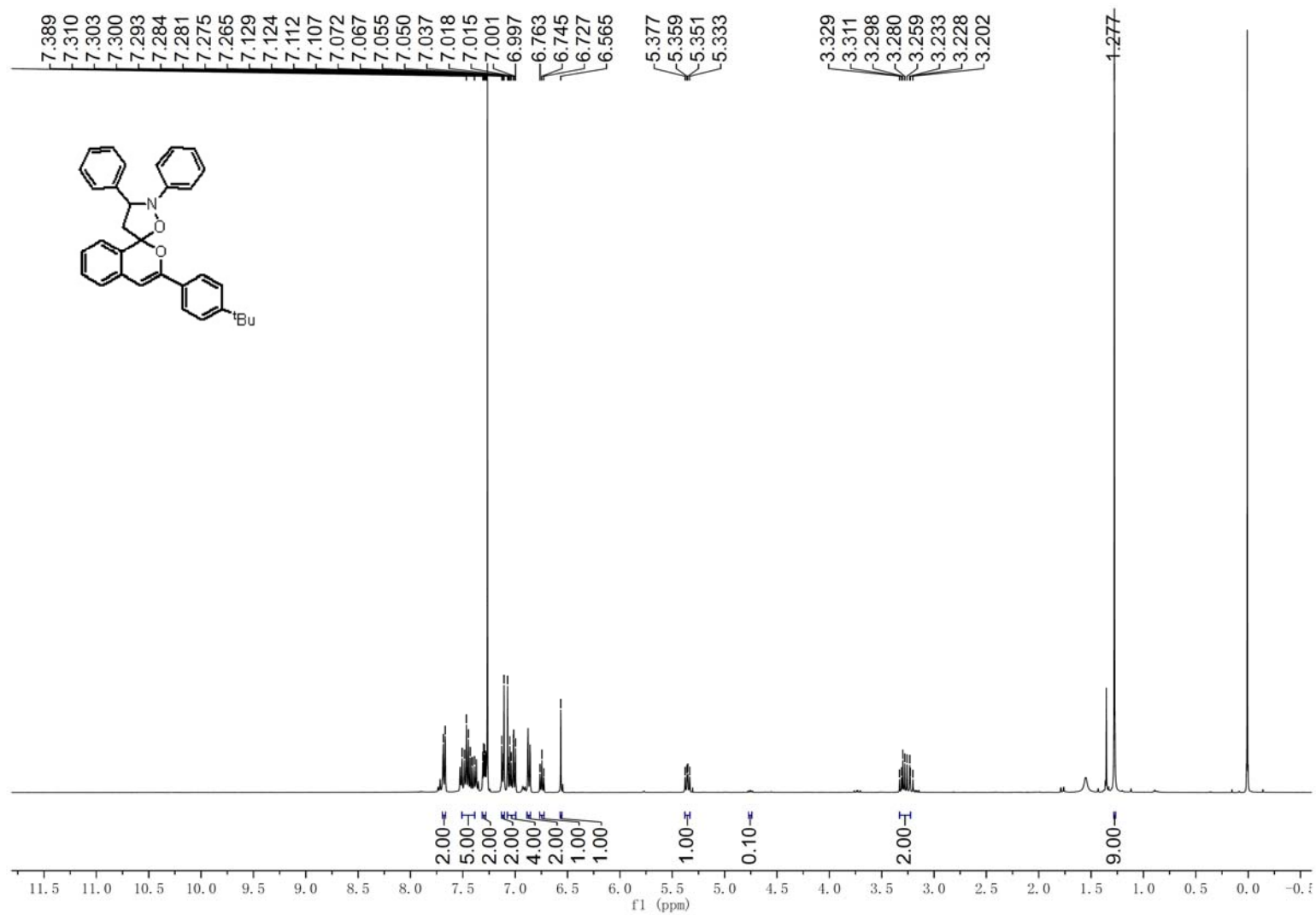




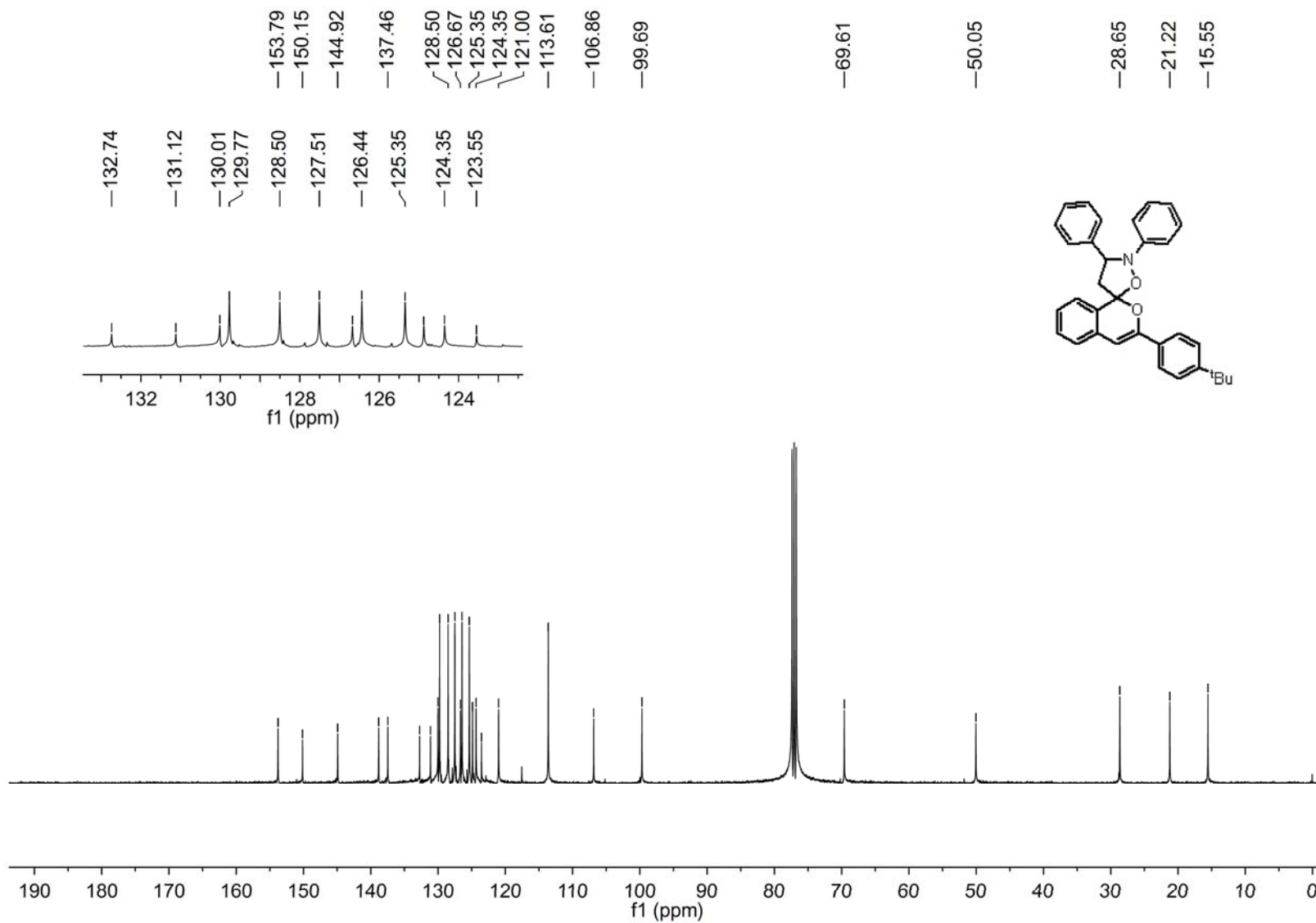
**<sup>1</sup>H NMR Spectrum of Compound 5d**



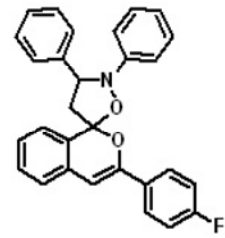
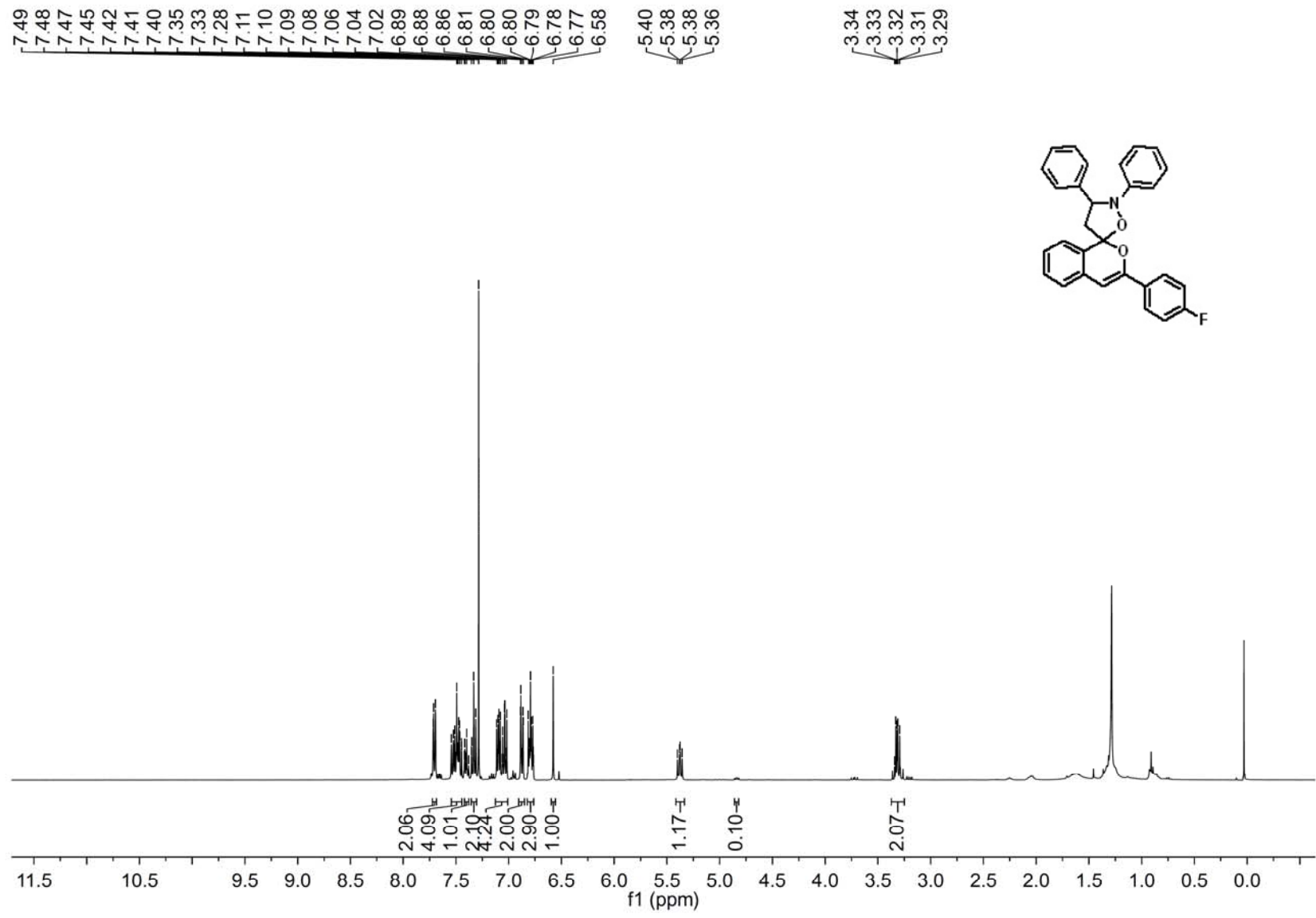
$^{13}\text{C}$  NMR Spectrum of Compound 5d



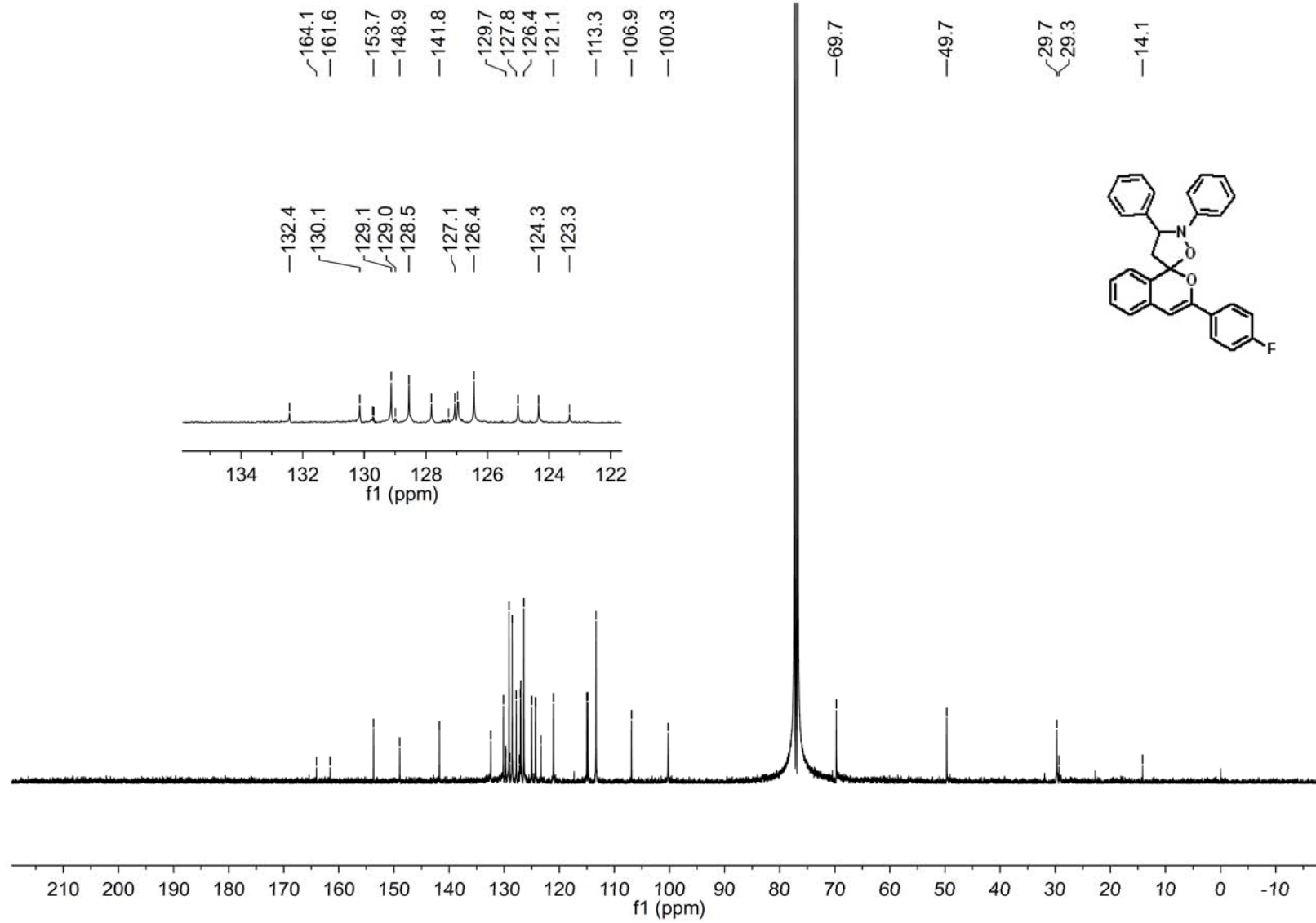
**<sup>1</sup>H NMR Spectrum of Compound 5e**



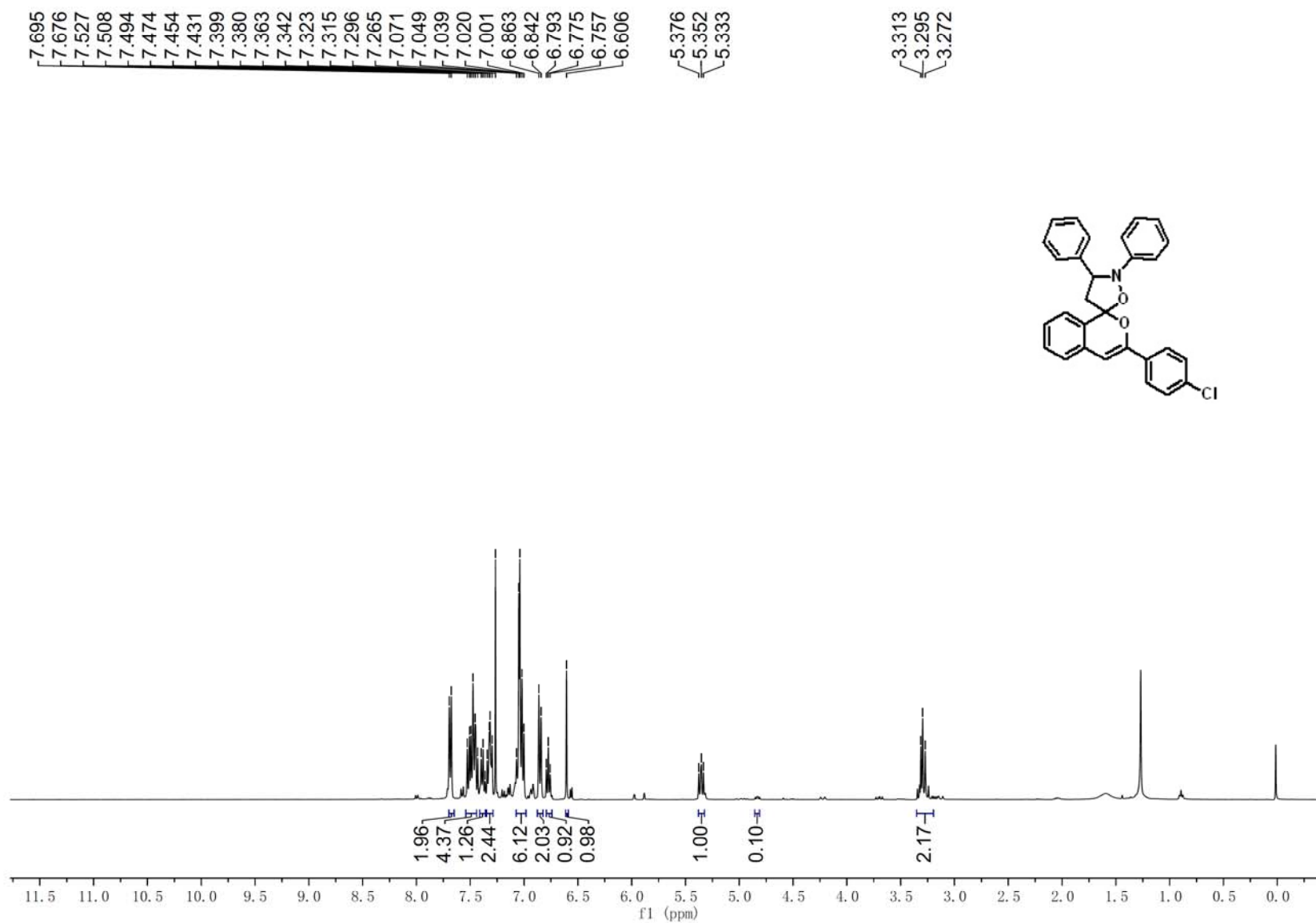
$^{13}\text{C}$  NMR Spectrum of Compound 5e



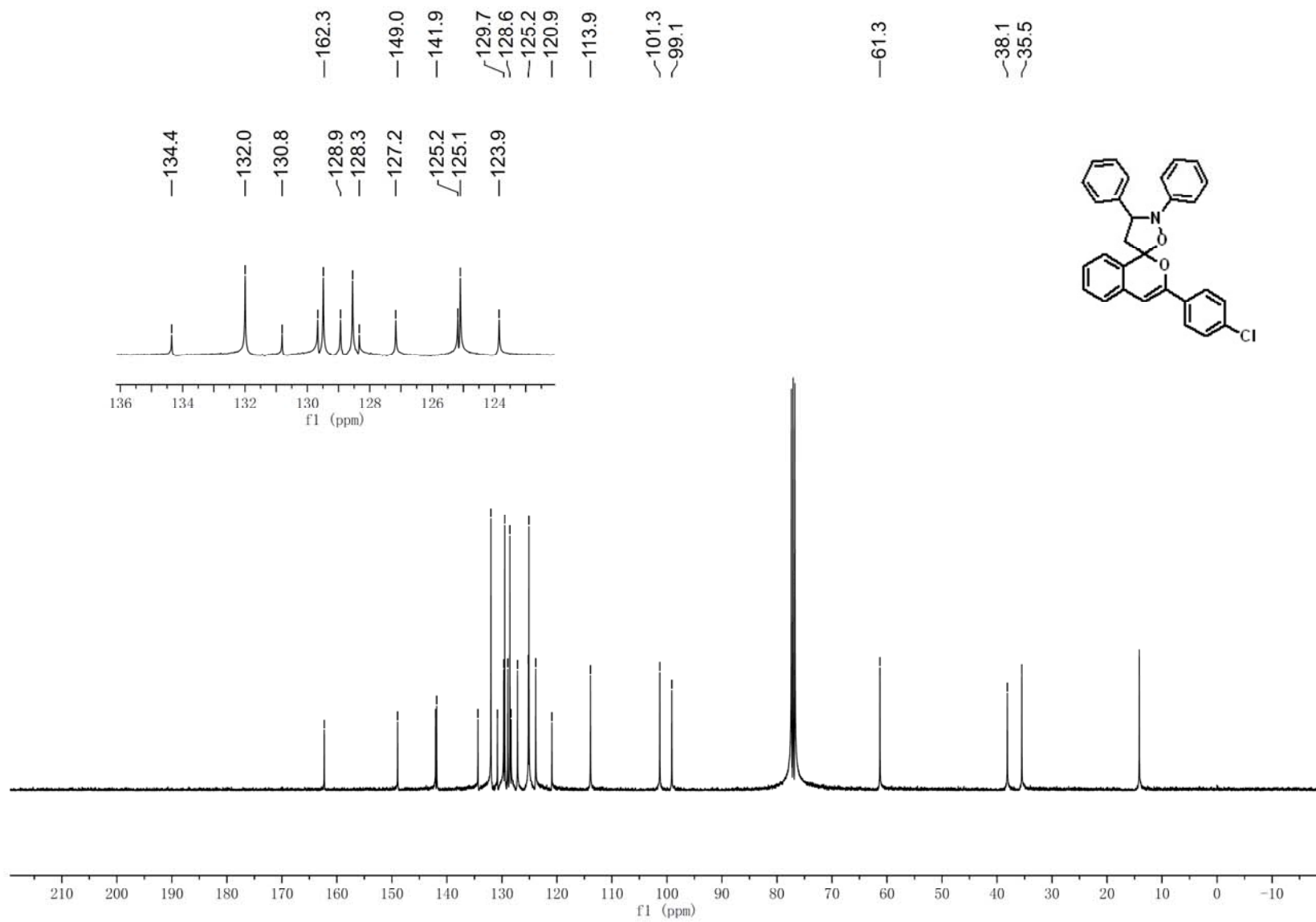
**<sup>1</sup>H NMR Spectrum of Compound 5f**



$^{13}\text{C}$  NMR Spectrum of Compound 5f



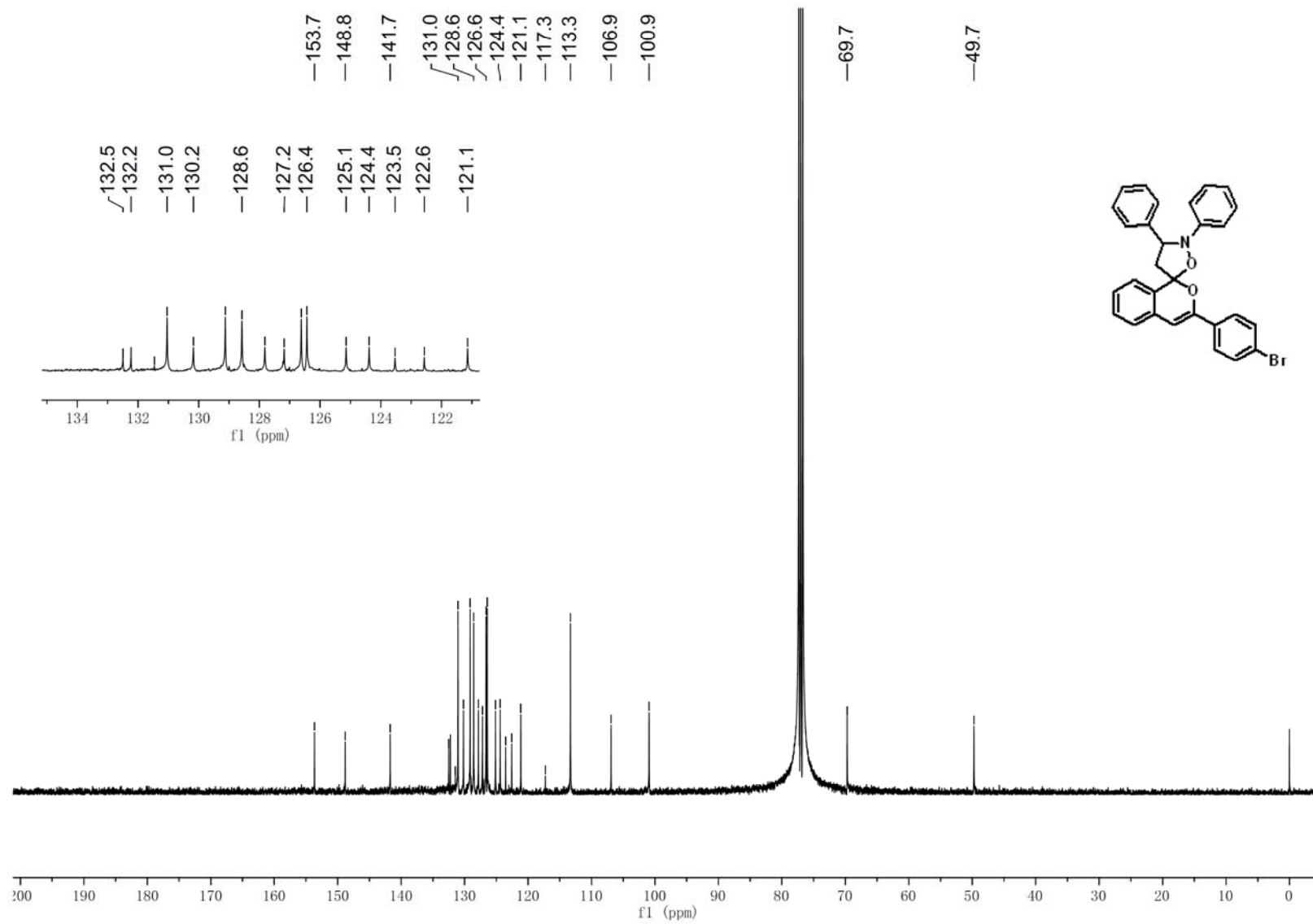
**<sup>1</sup>H NMR Spectrum of Compound 5g**



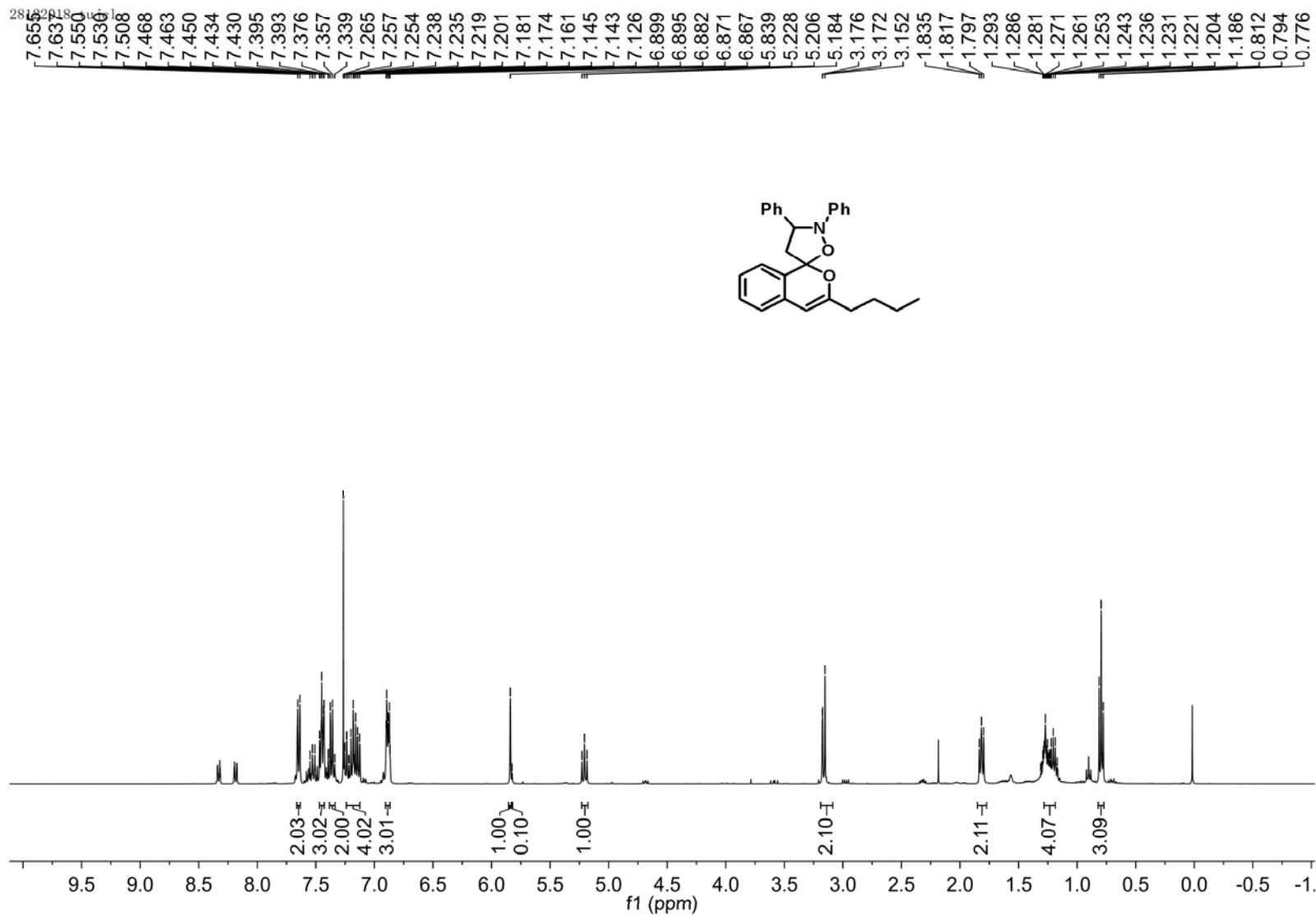
**<sup>13</sup>C NMR Spectrum of Compound 5g**



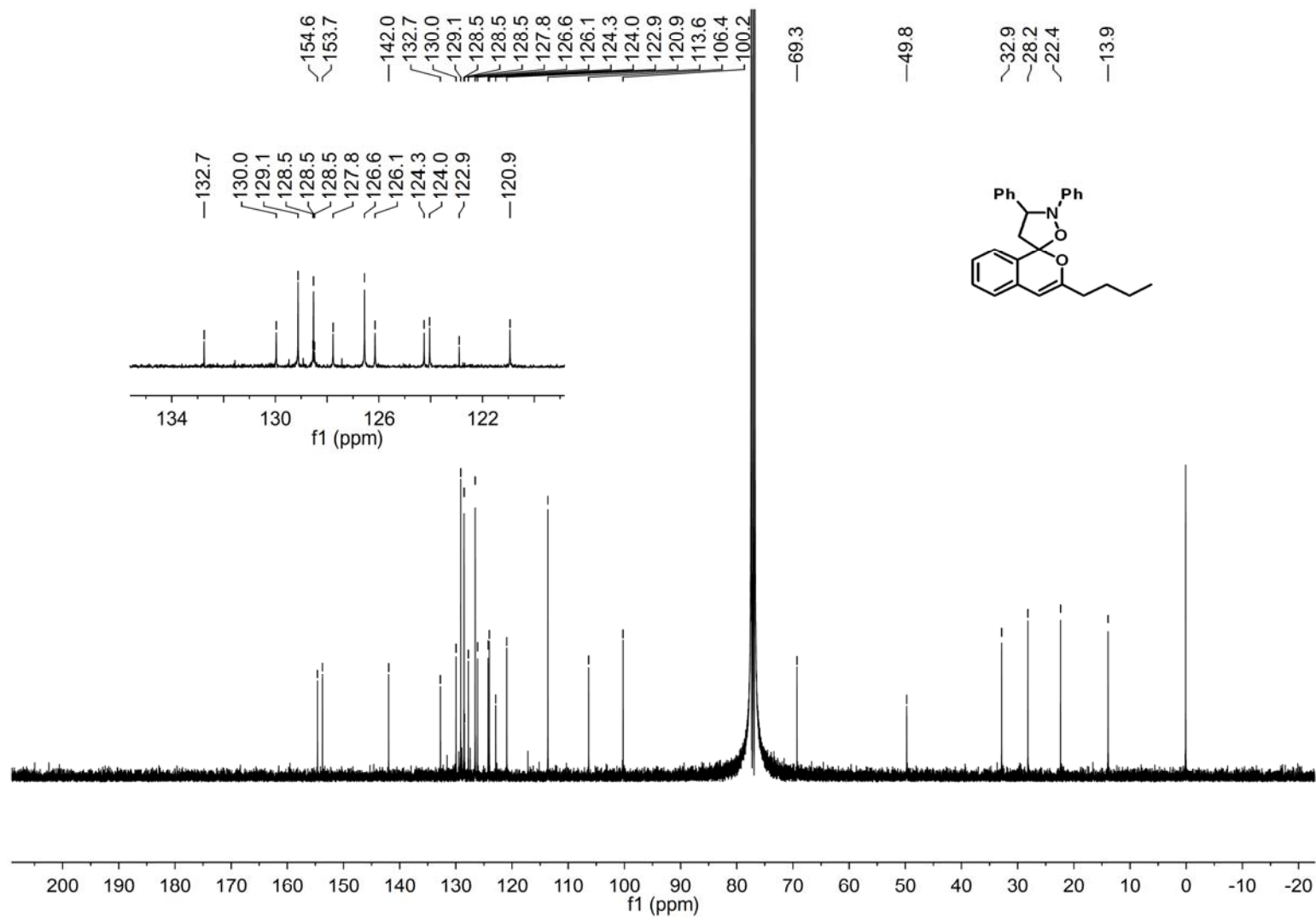




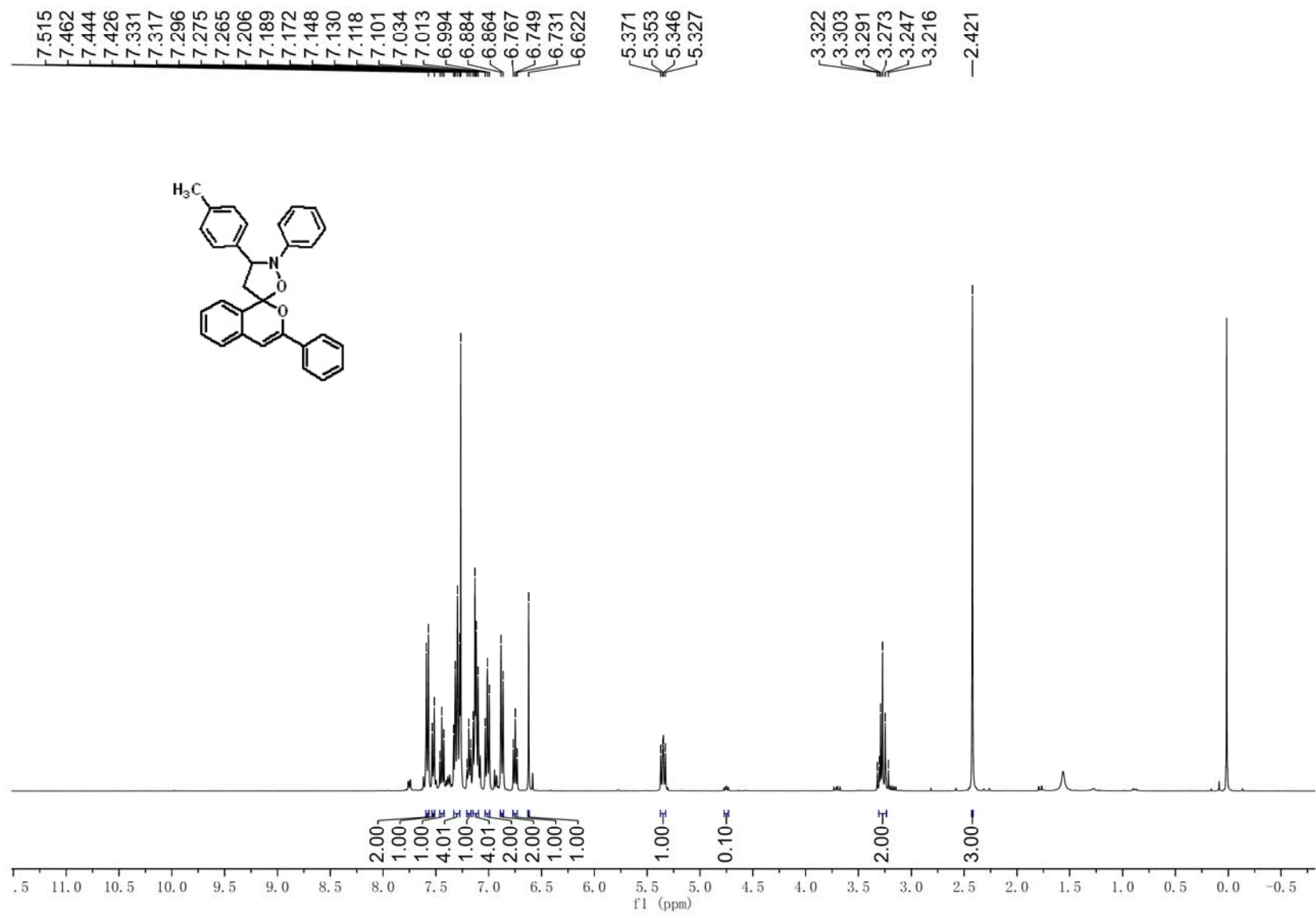
$^{13}\text{C}$  NMR Spectrum of Compound 5h



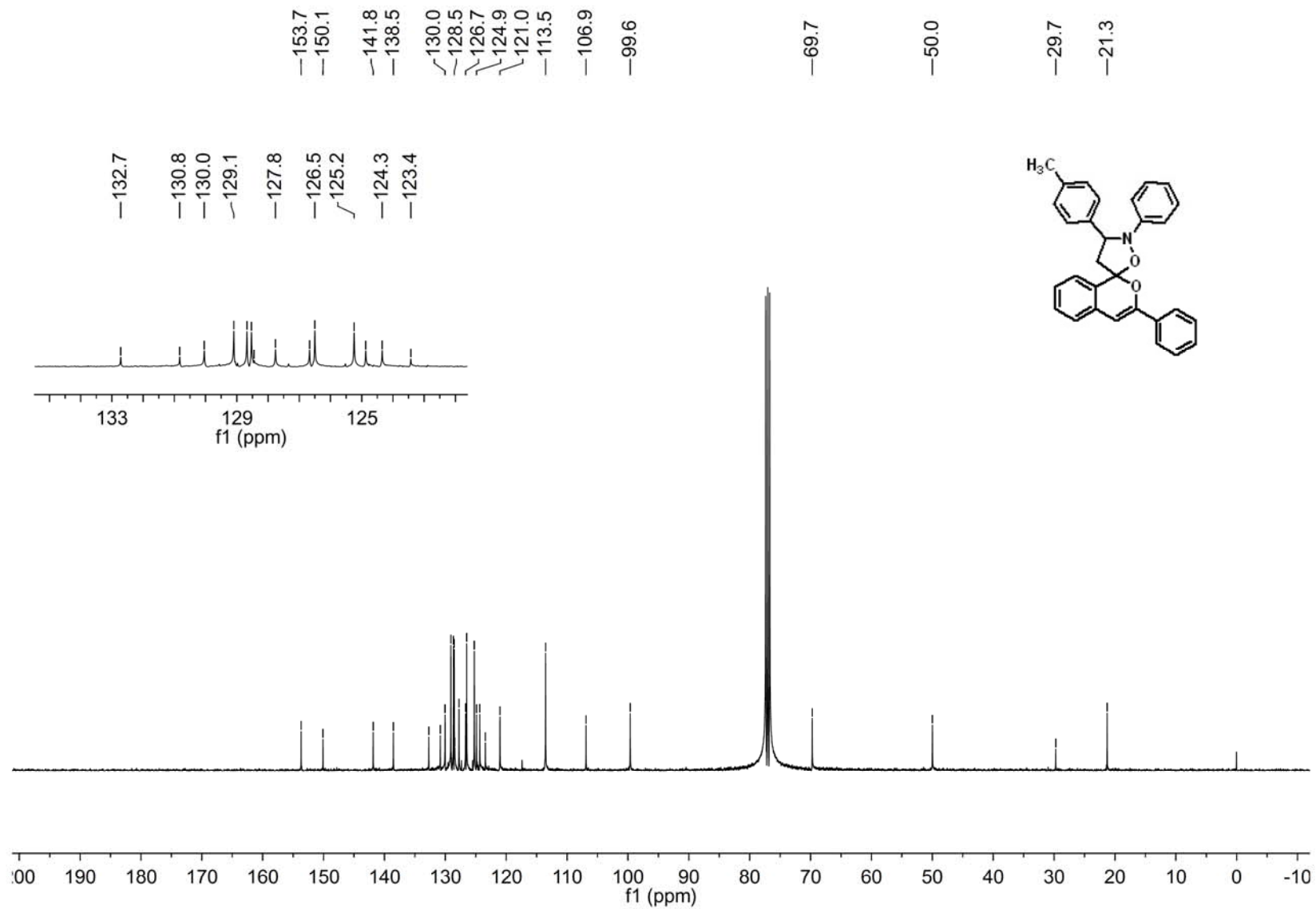
<sup>1</sup>H NMR Spectrum of Compound 5i



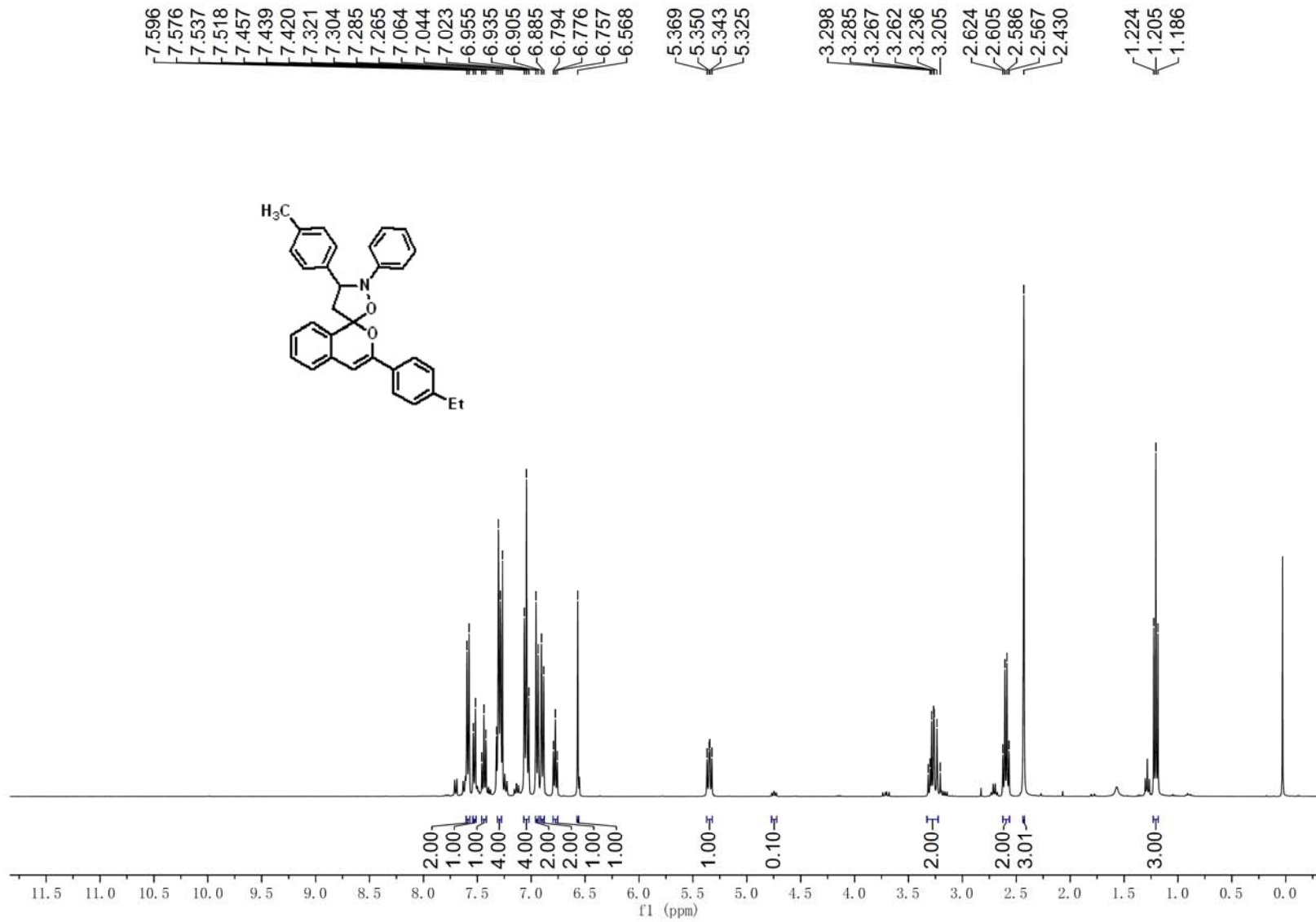
**<sup>13</sup>C NMR Spectrum of Compound 5i**



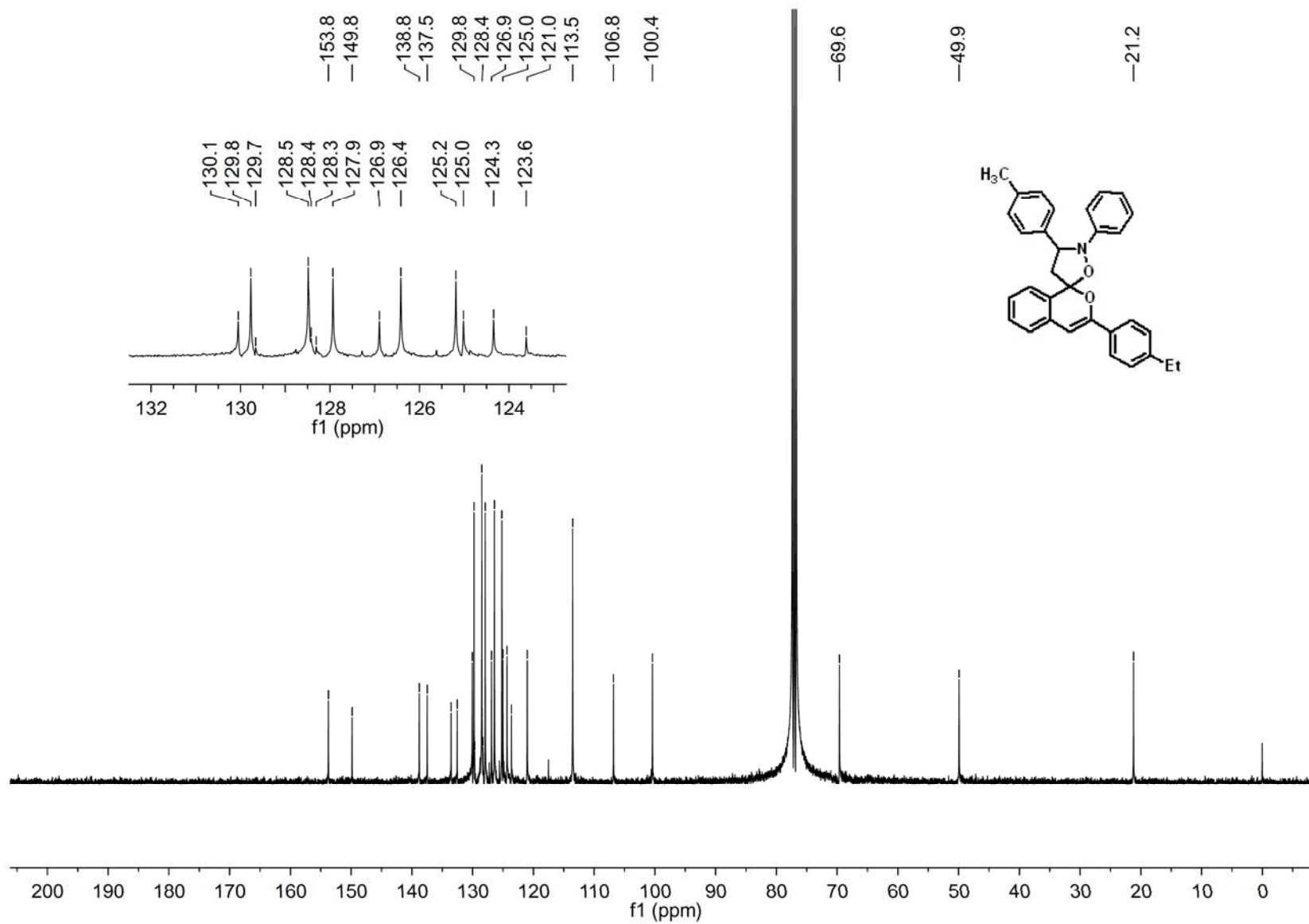
<sup>1</sup>H NMR Spectrum of Compound 5j



$^{13}\text{C}$  NMR Spectrum of Compound 5j

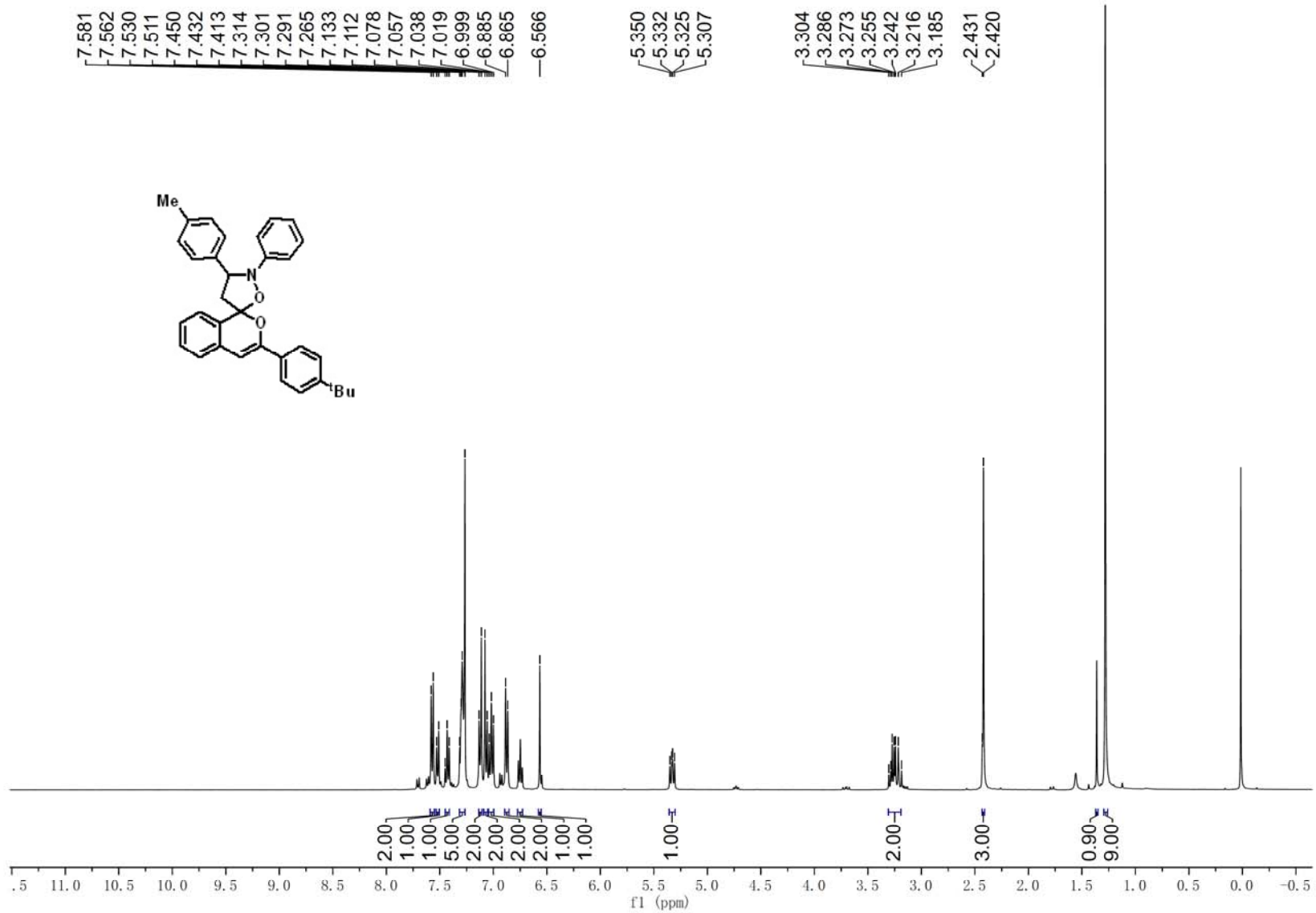


**<sup>1</sup>H NMR Spectrum of Compound 5k**

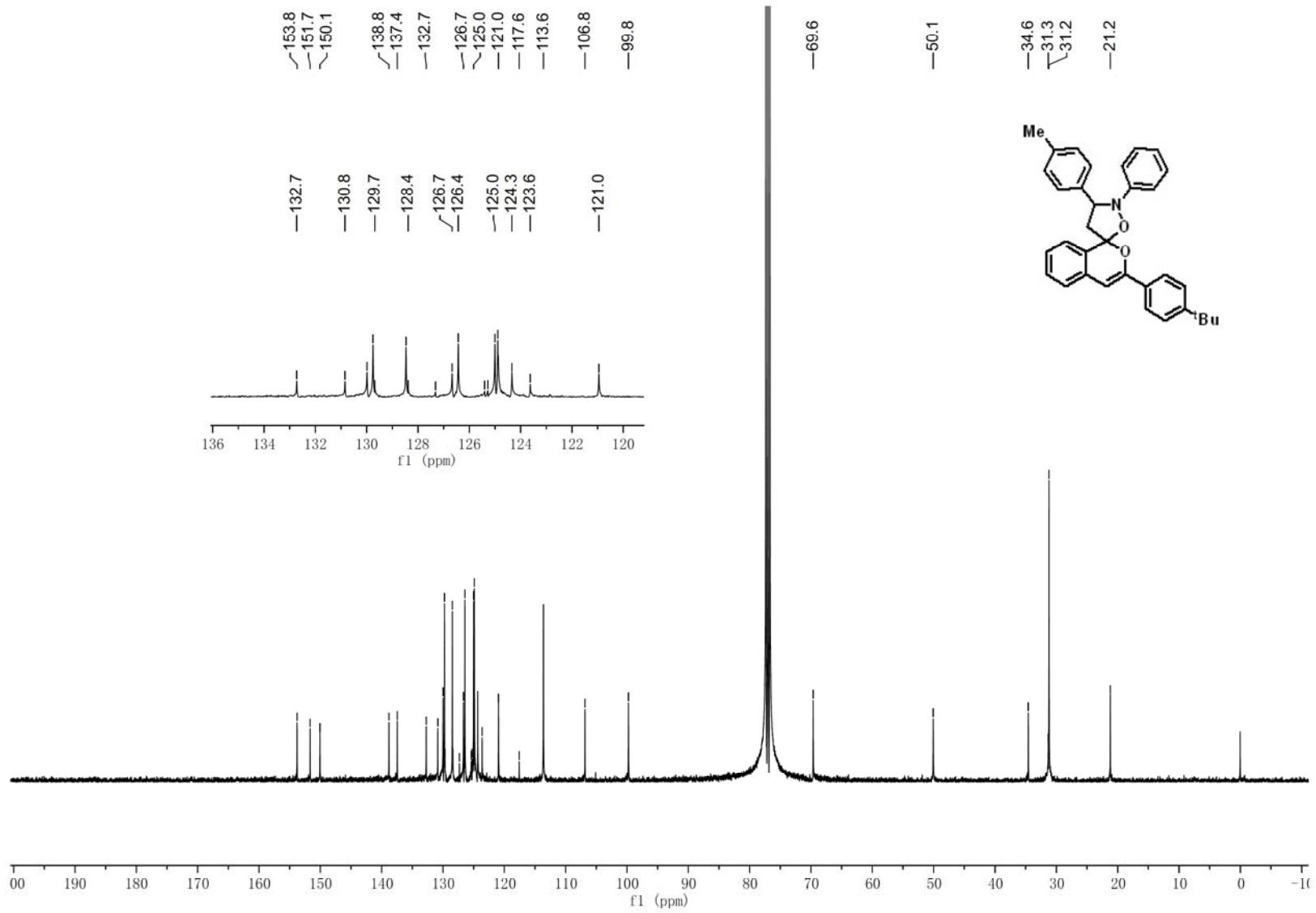


**<sup>13</sup>C NMR Spectrum of Compound 5k**

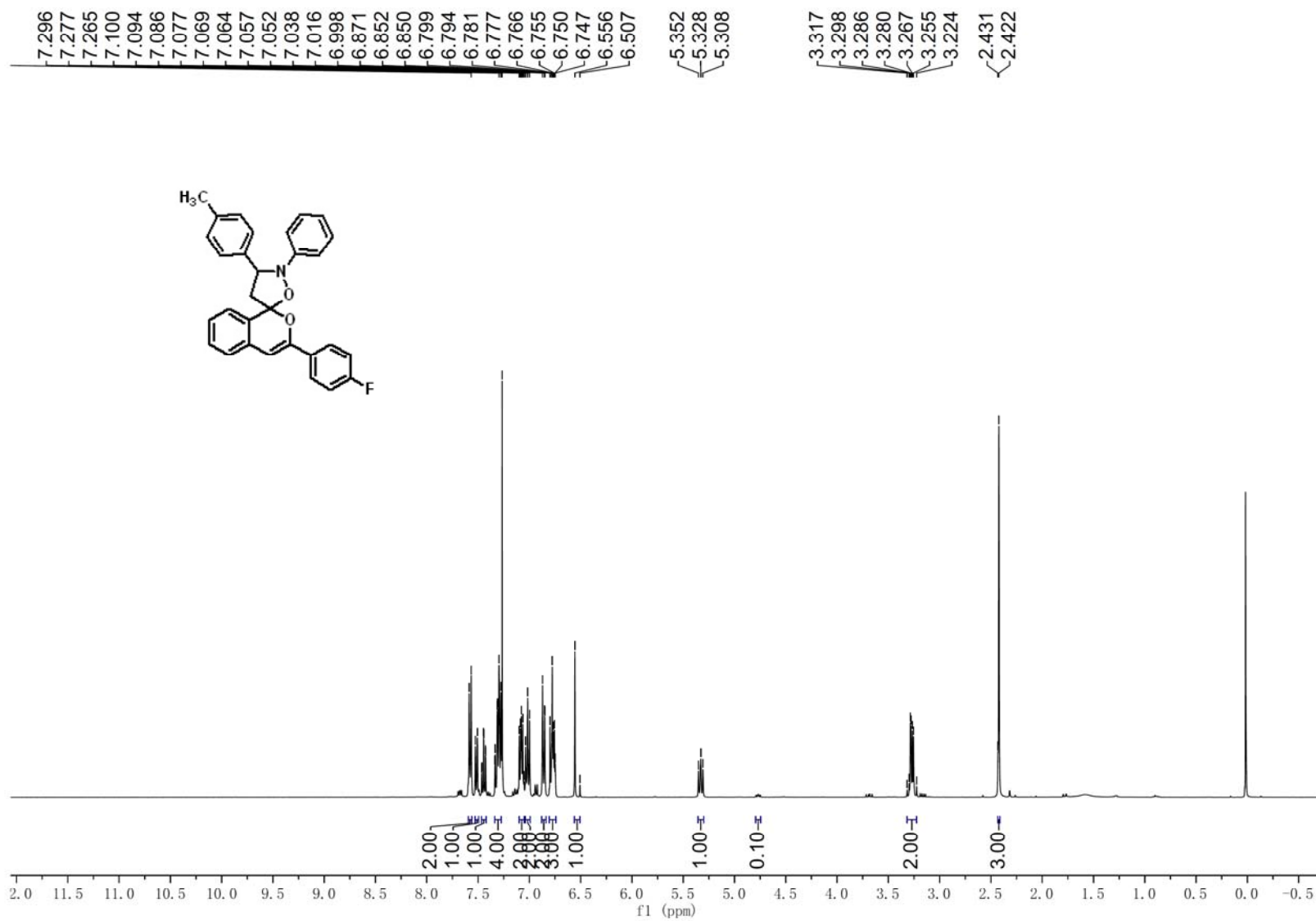




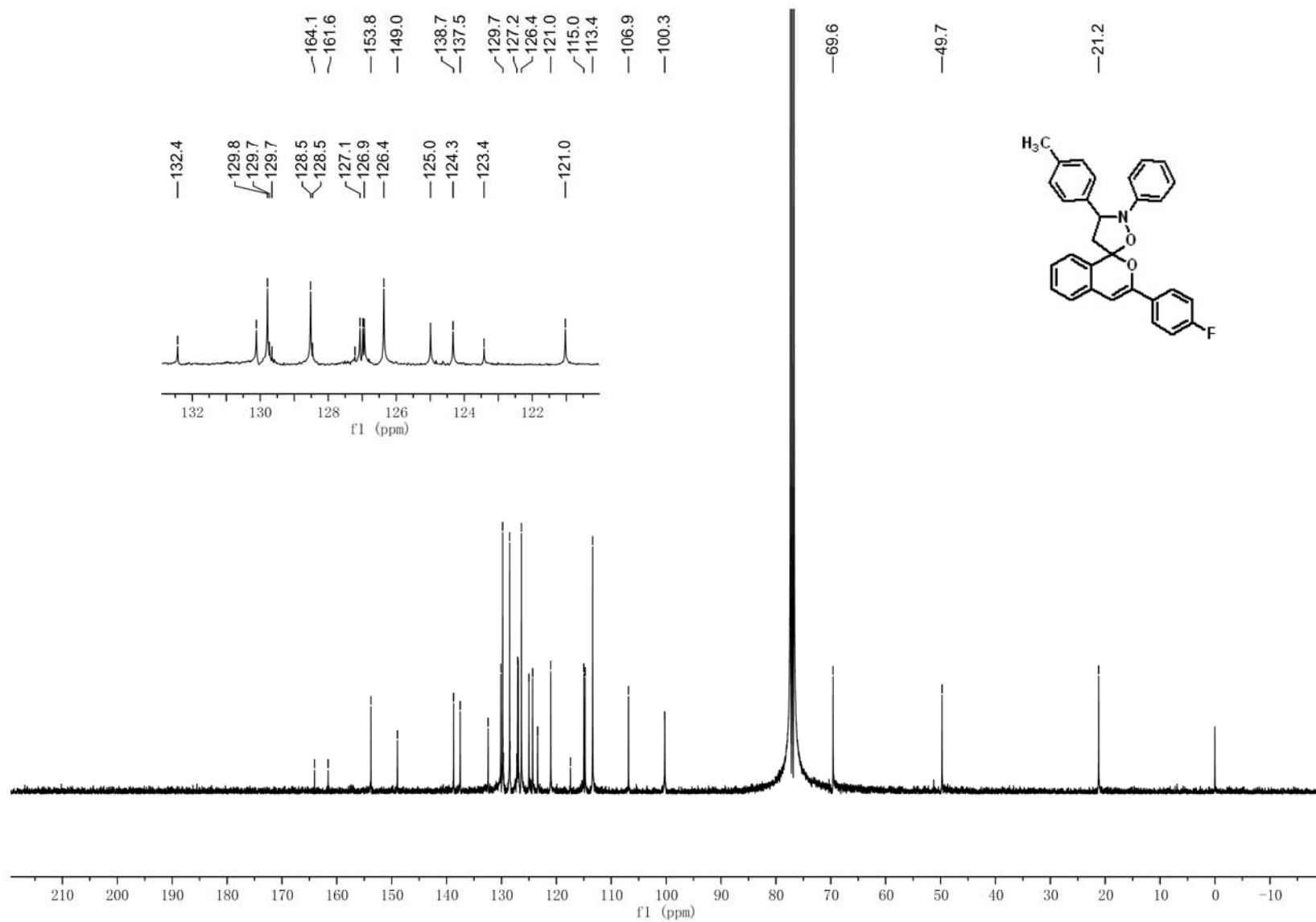
**<sup>1</sup>H NMR Spectrum of Compound 51**



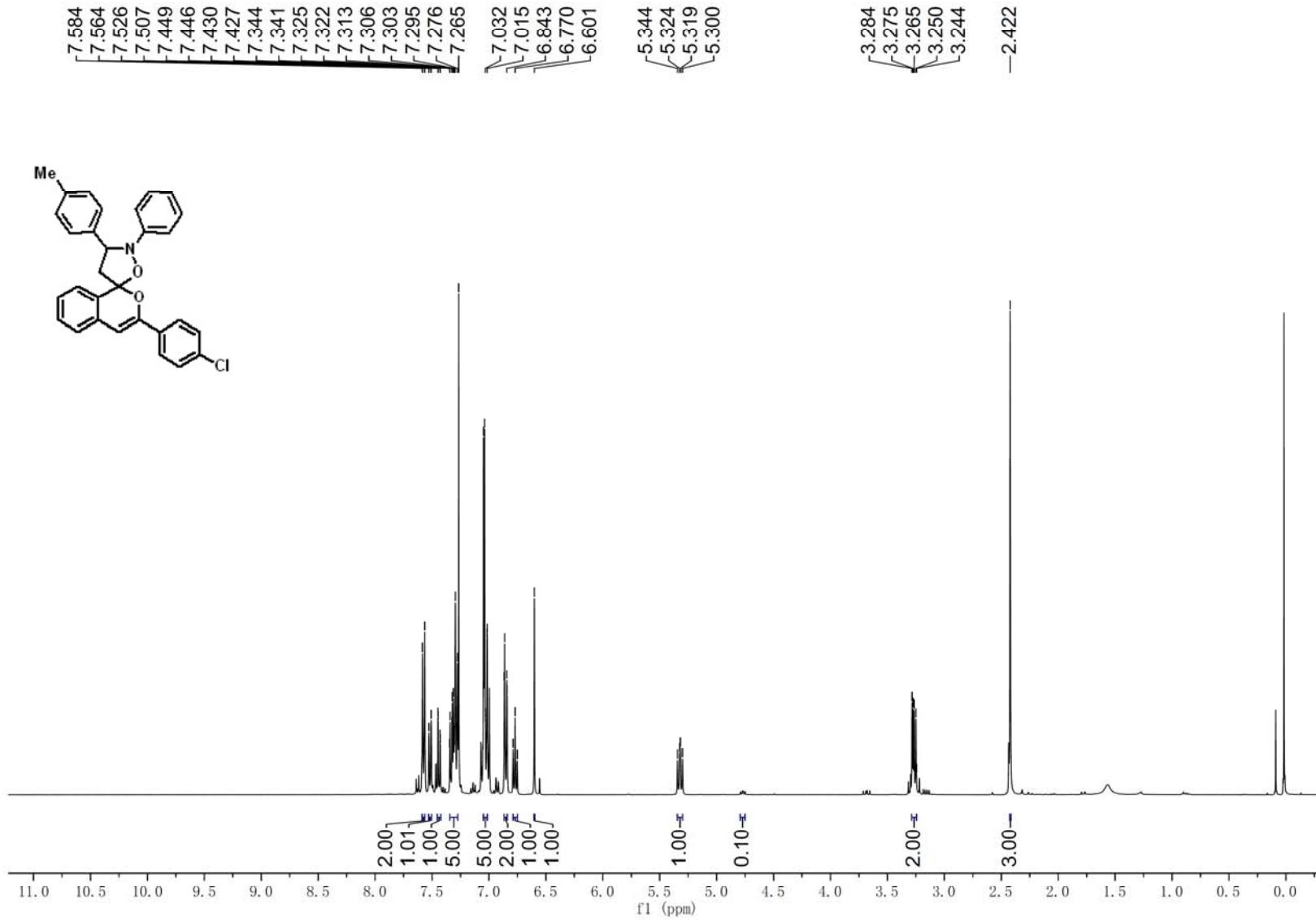
**<sup>13</sup>C NMR Spectrum of Compound 51**



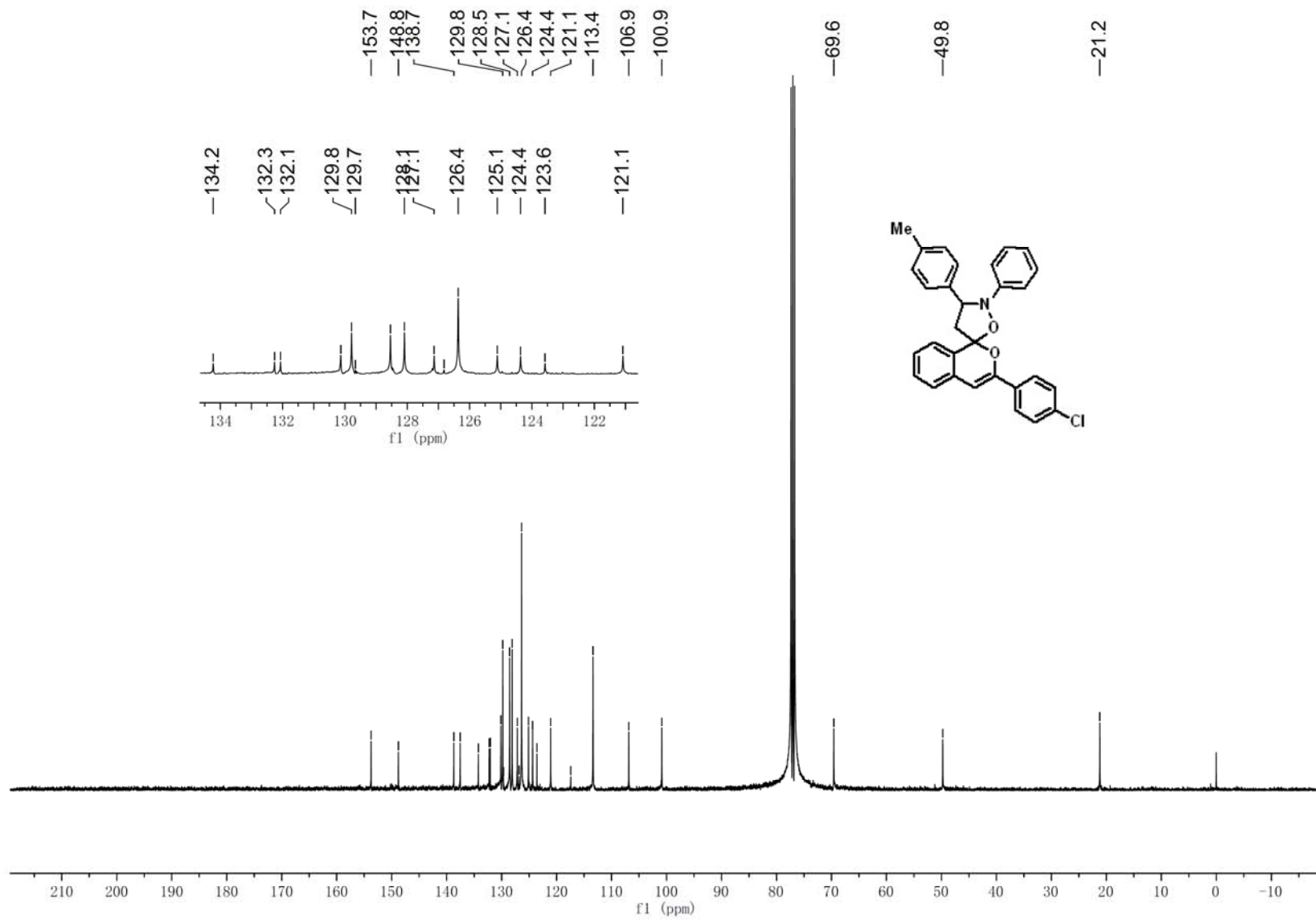
<sup>1</sup>H NMR Spectrum of Compound 5m



$^{13}\text{C}$  NMR Spectrum of Compound 5m

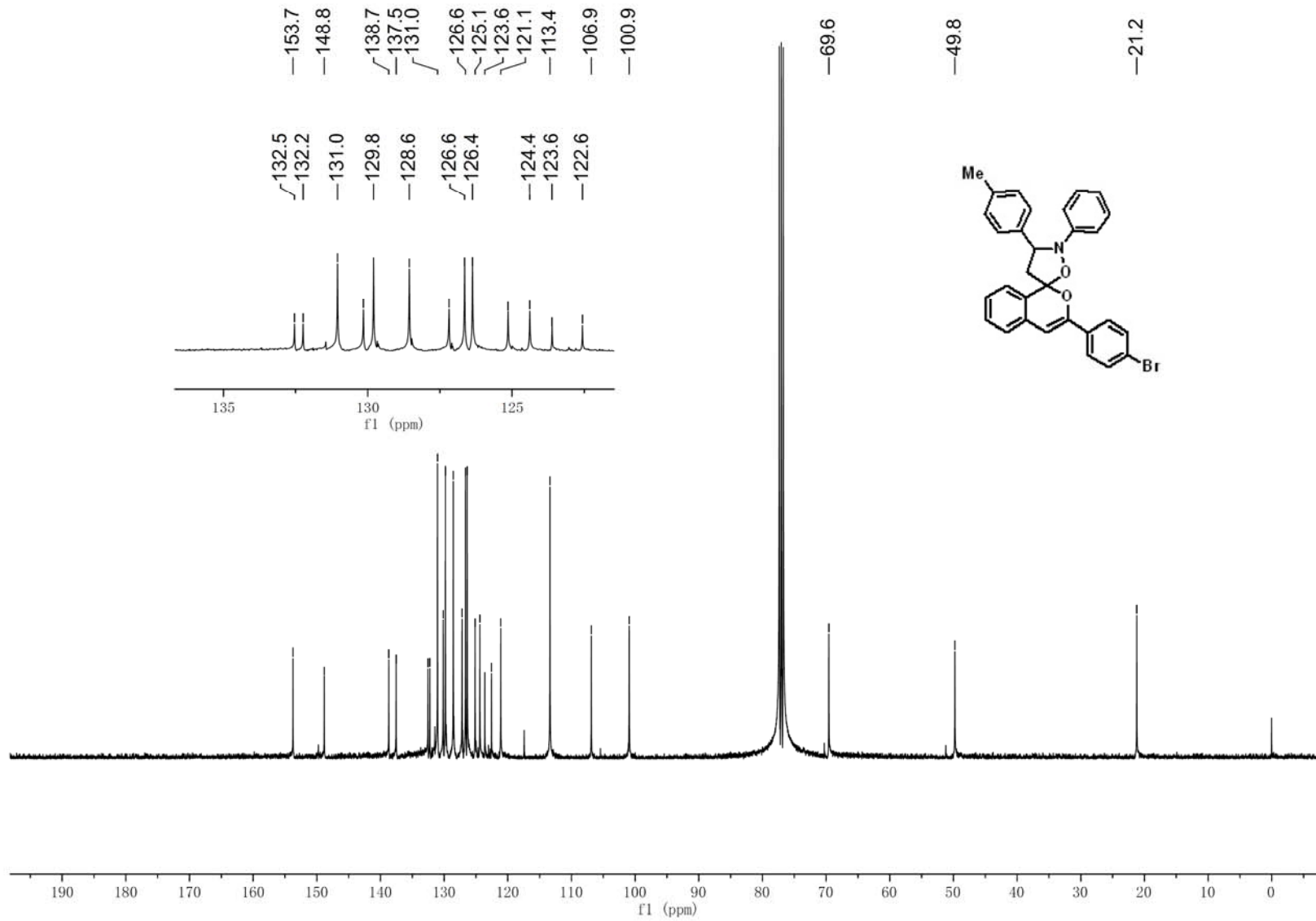


**<sup>1</sup>H NMR Spectrum of Compound 5n**



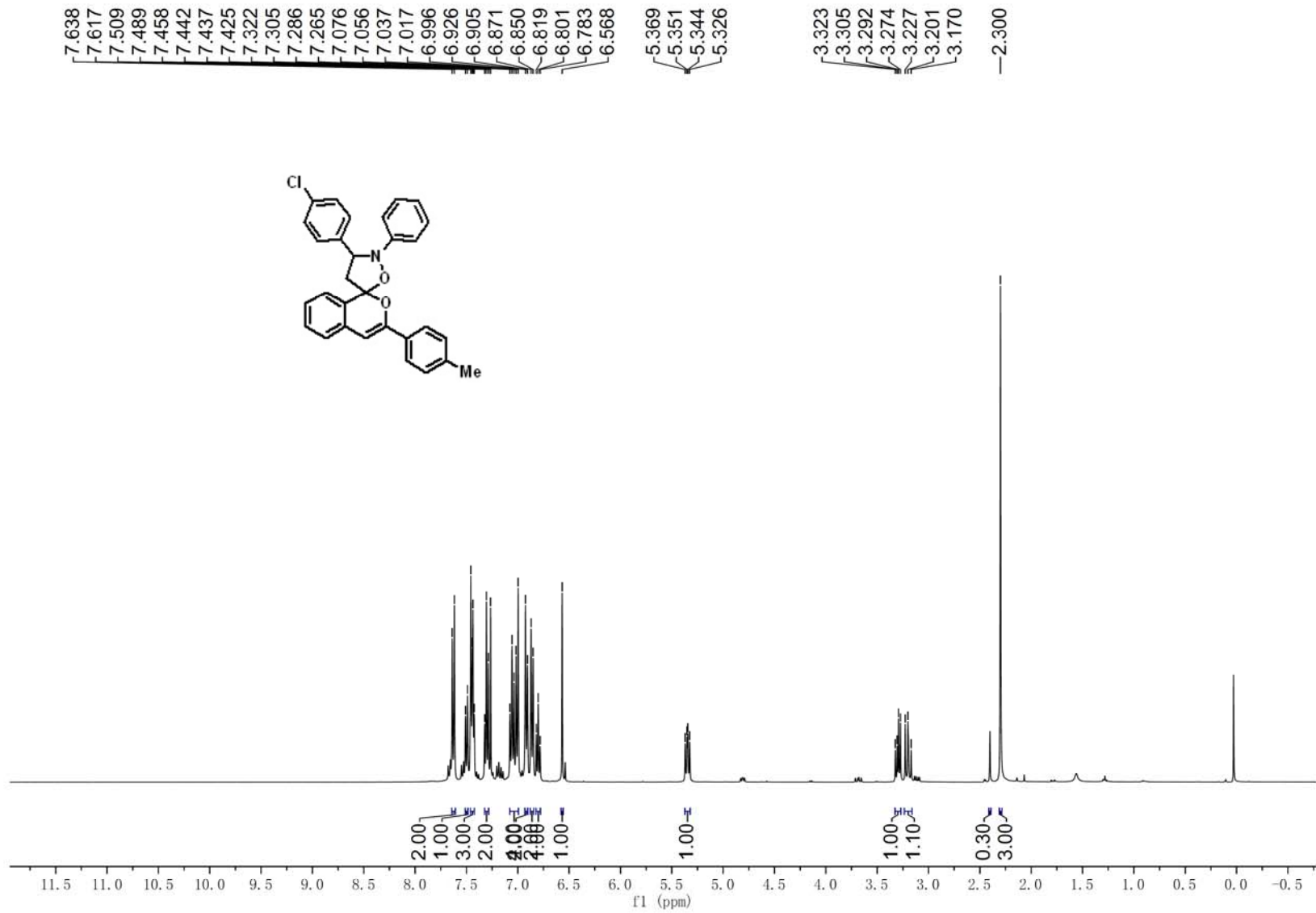
**<sup>13</sup>C NMR Spectrum of Compound 5n**



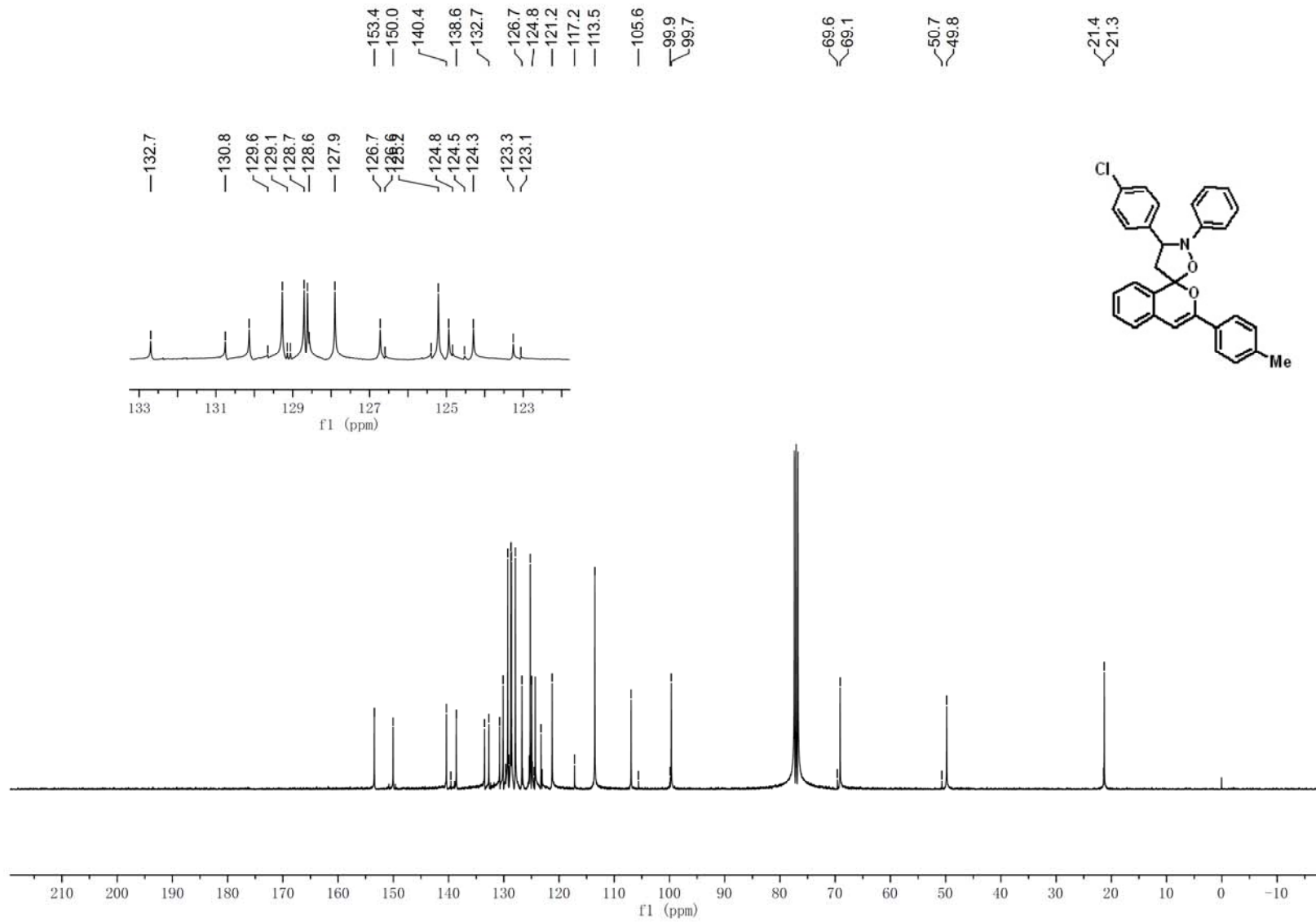


<sup>13</sup>C NMR Spectrum of Compound 5o

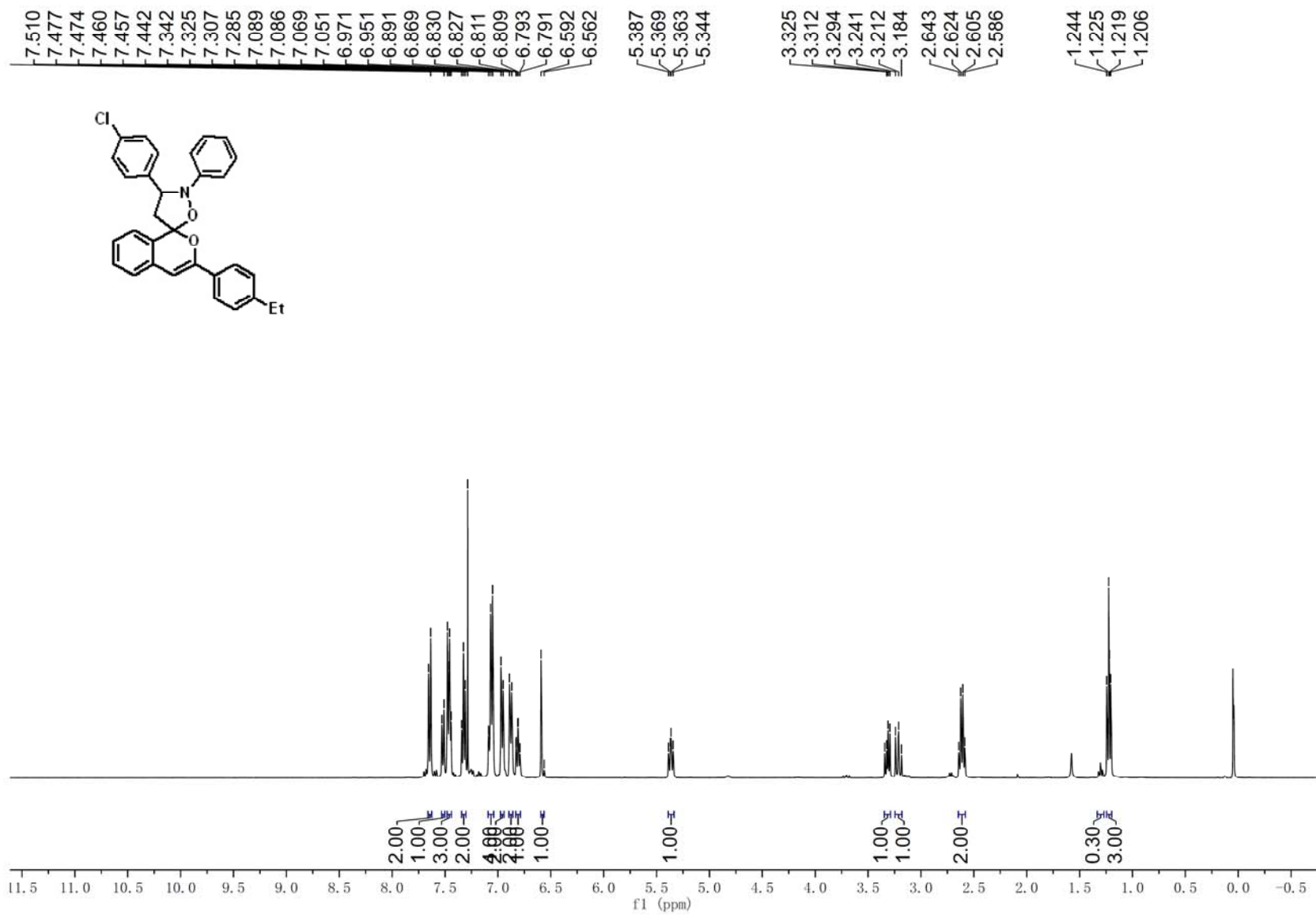




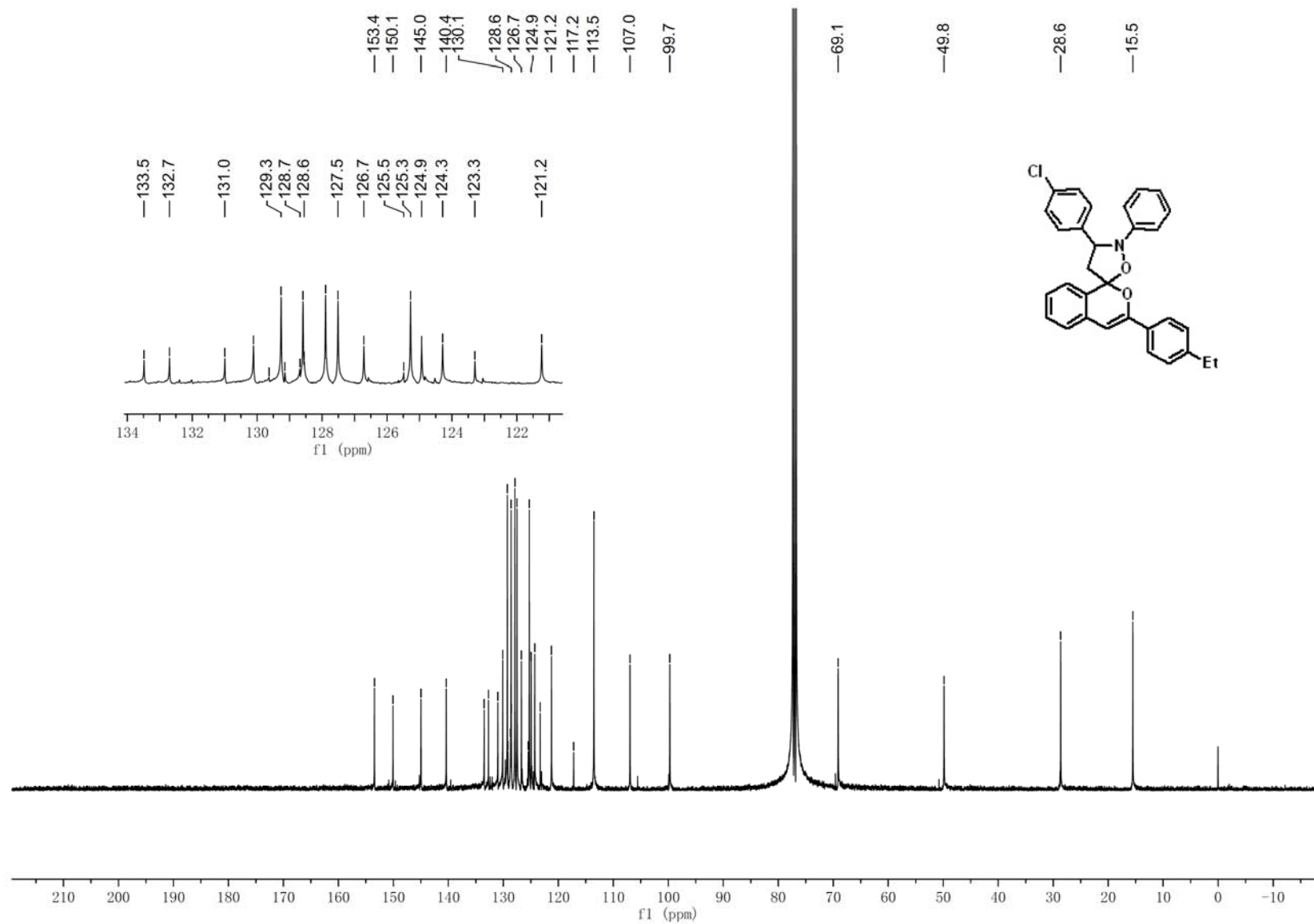
<sup>1</sup>H NMR Spectrum of Compound 5p



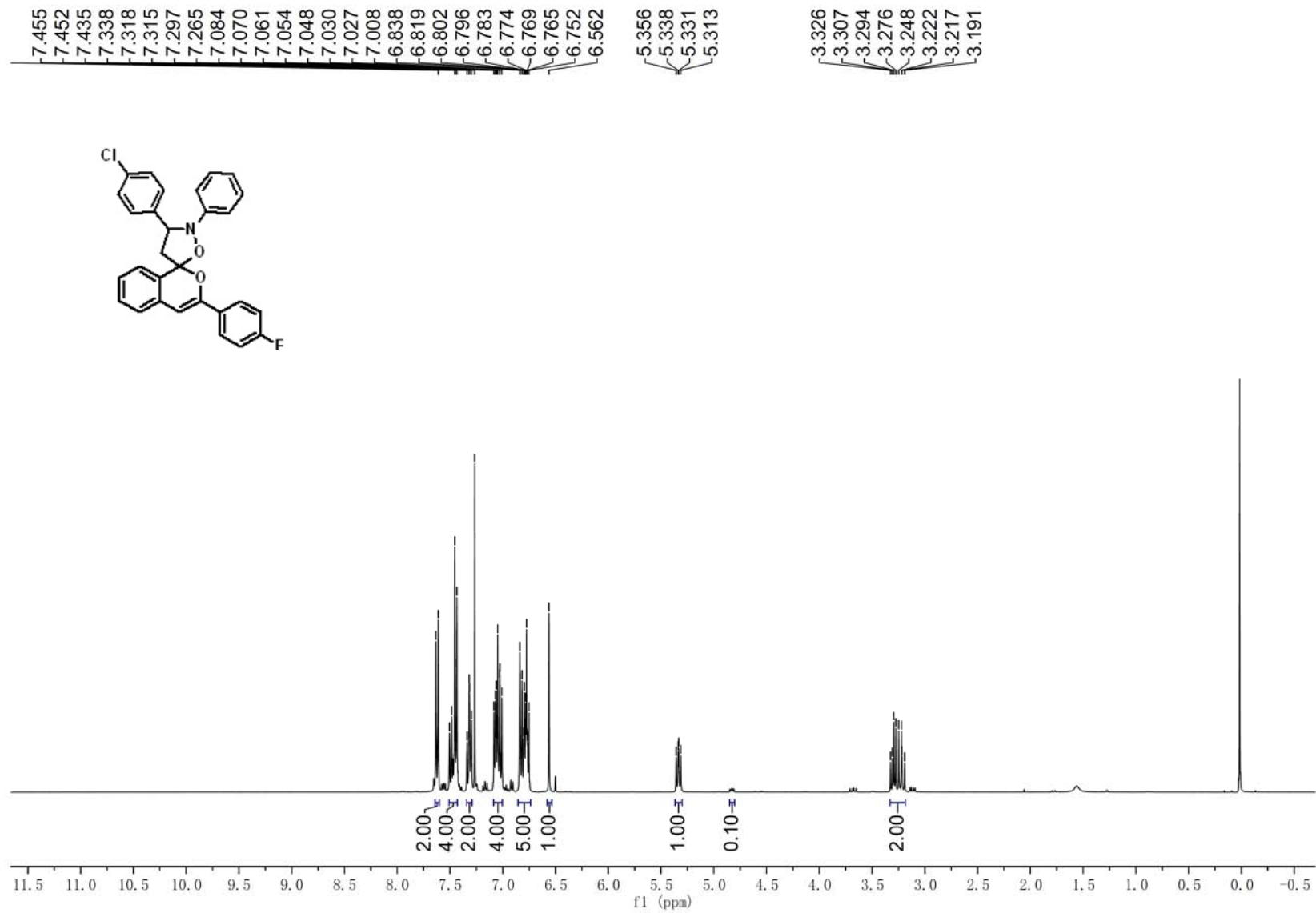
$^{13}\text{C}$  NMR Spectrum of Compound 5p



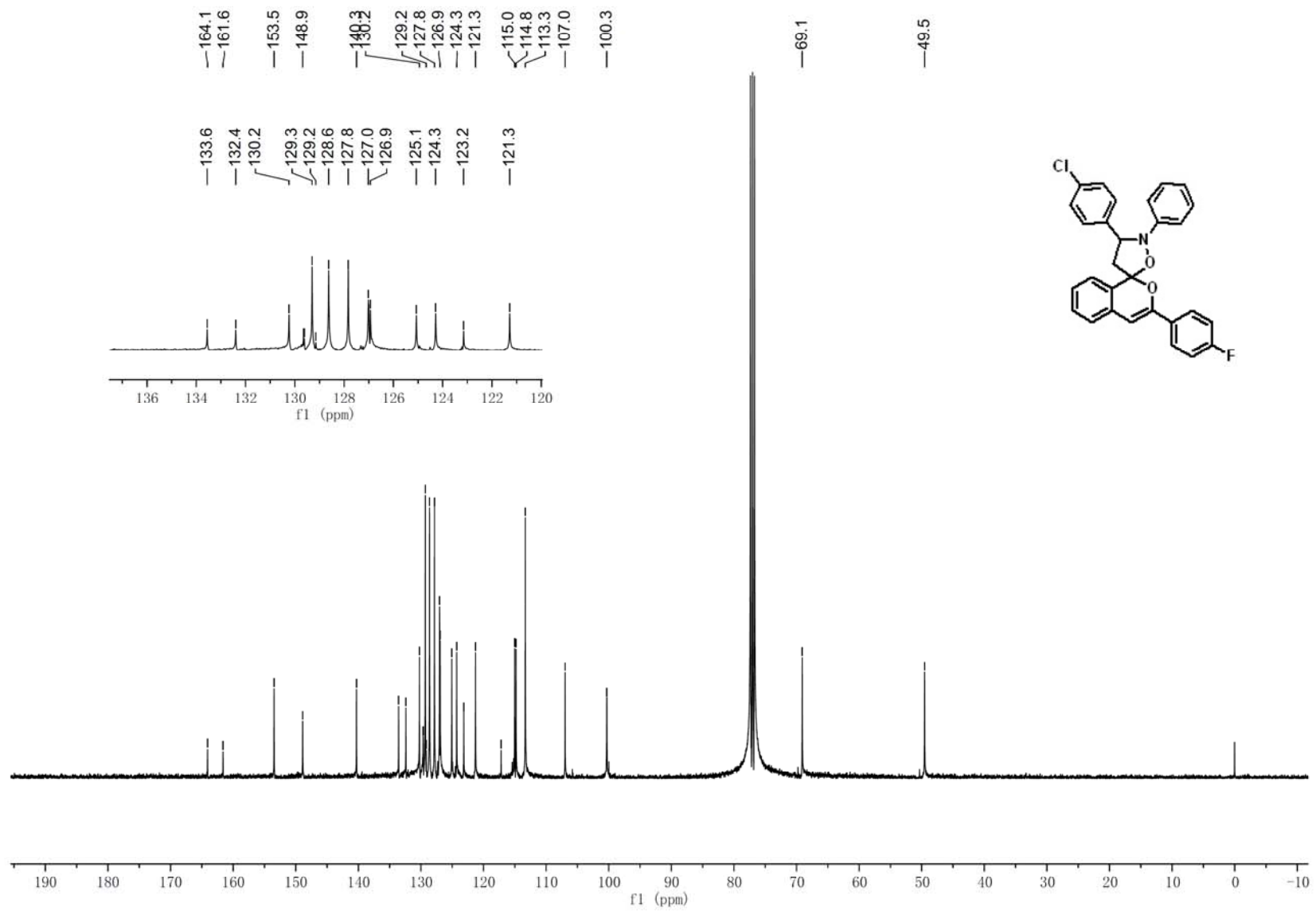
<sup>1</sup>H NMR Spectrum of Compound 5q



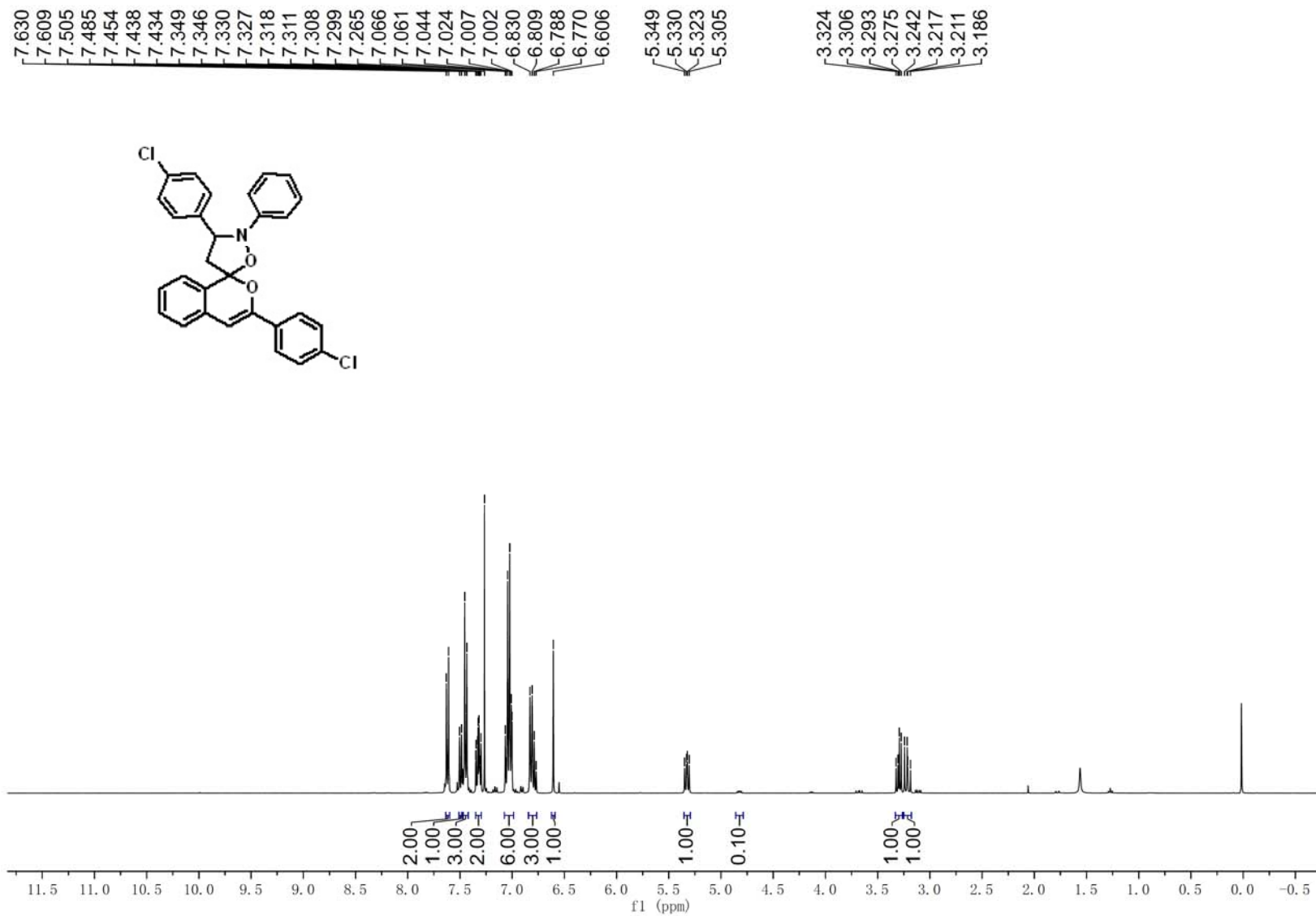
**<sup>13</sup>C NMR Spectrum of Compound 5q**



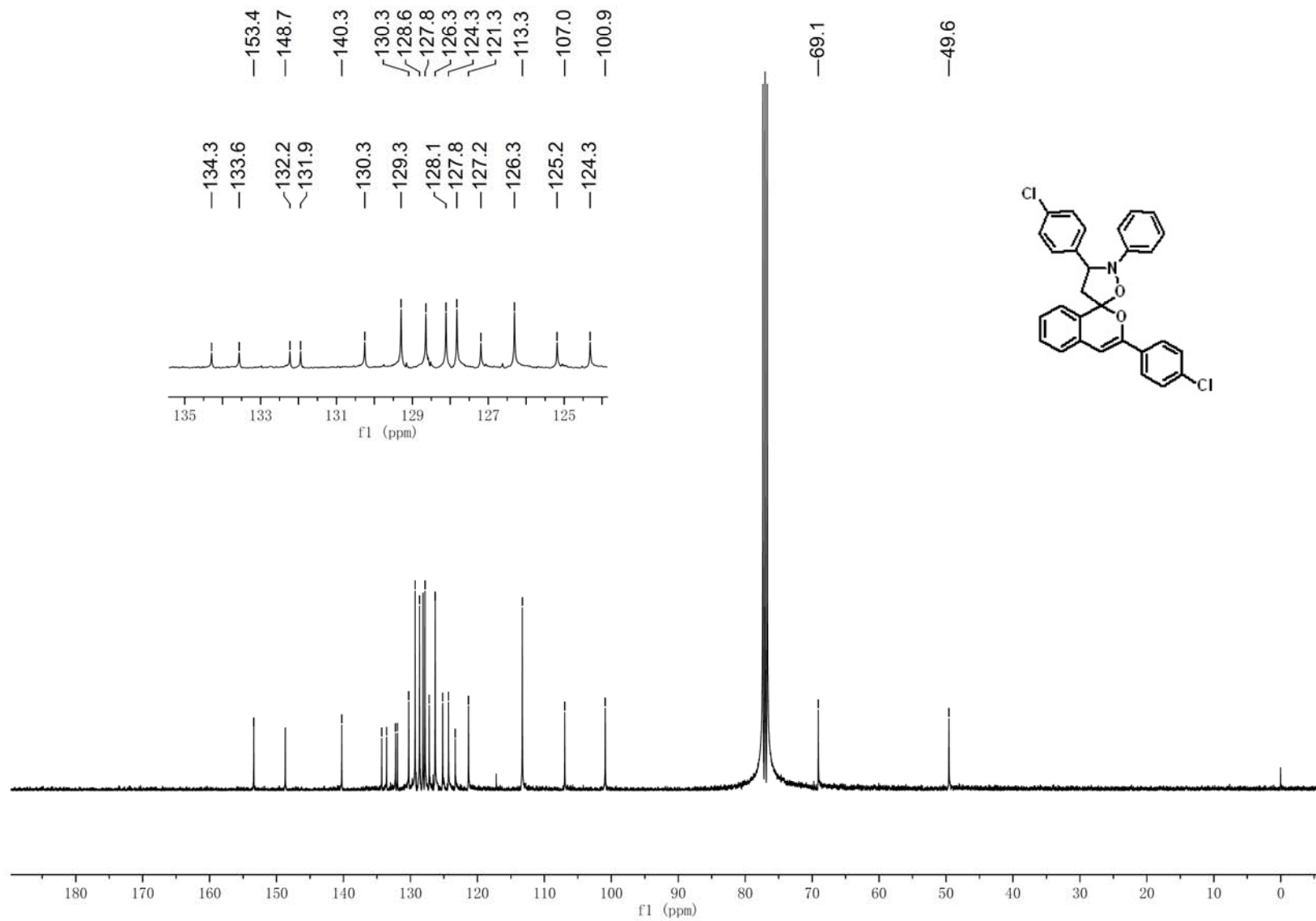
<sup>1</sup>H NMR Spectrum of Compound 5r



$^{13}\text{C}$  NMR Spectrum of Compound 5r

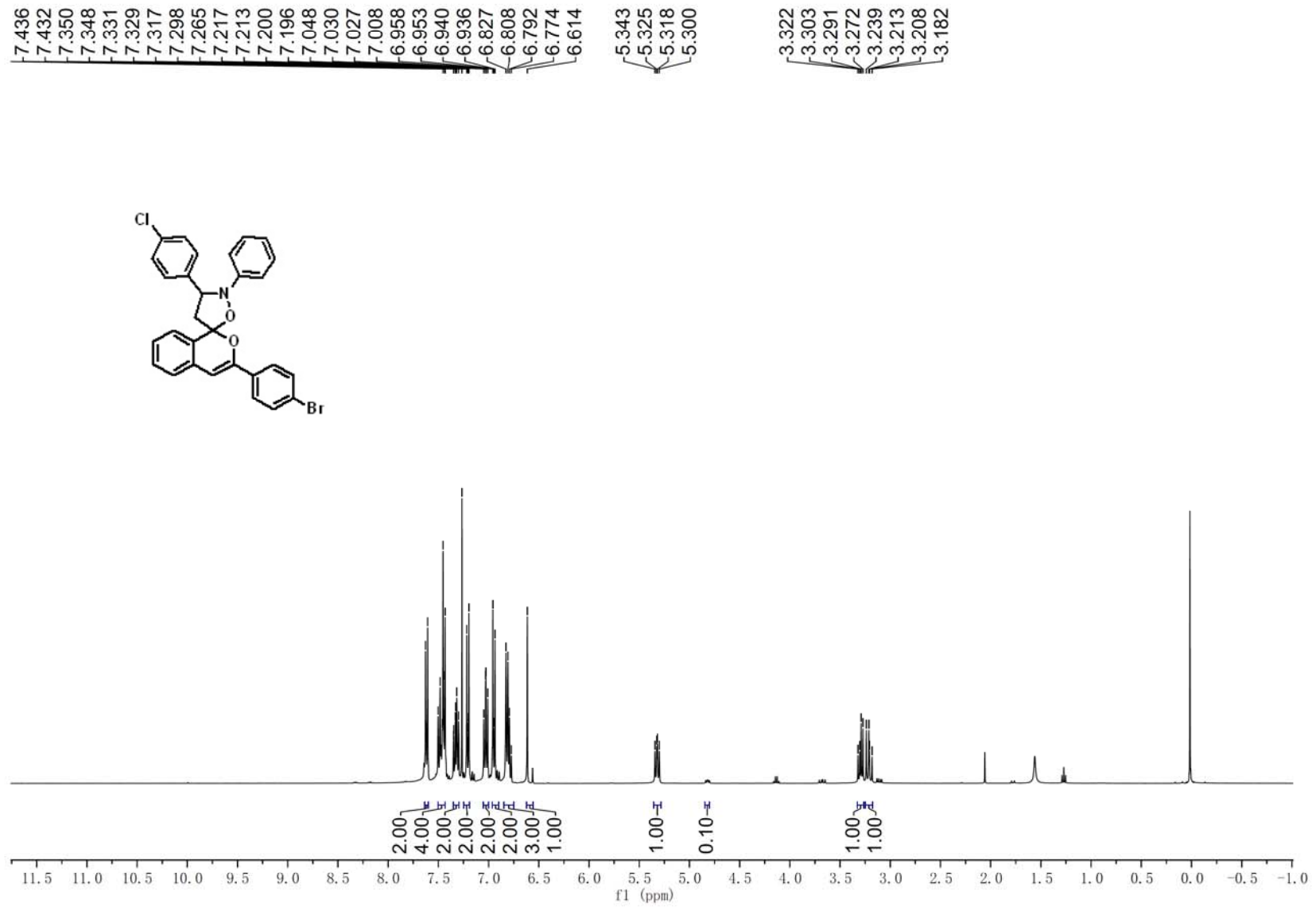


<sup>1</sup>H NMR Spectrum of Compound 5s

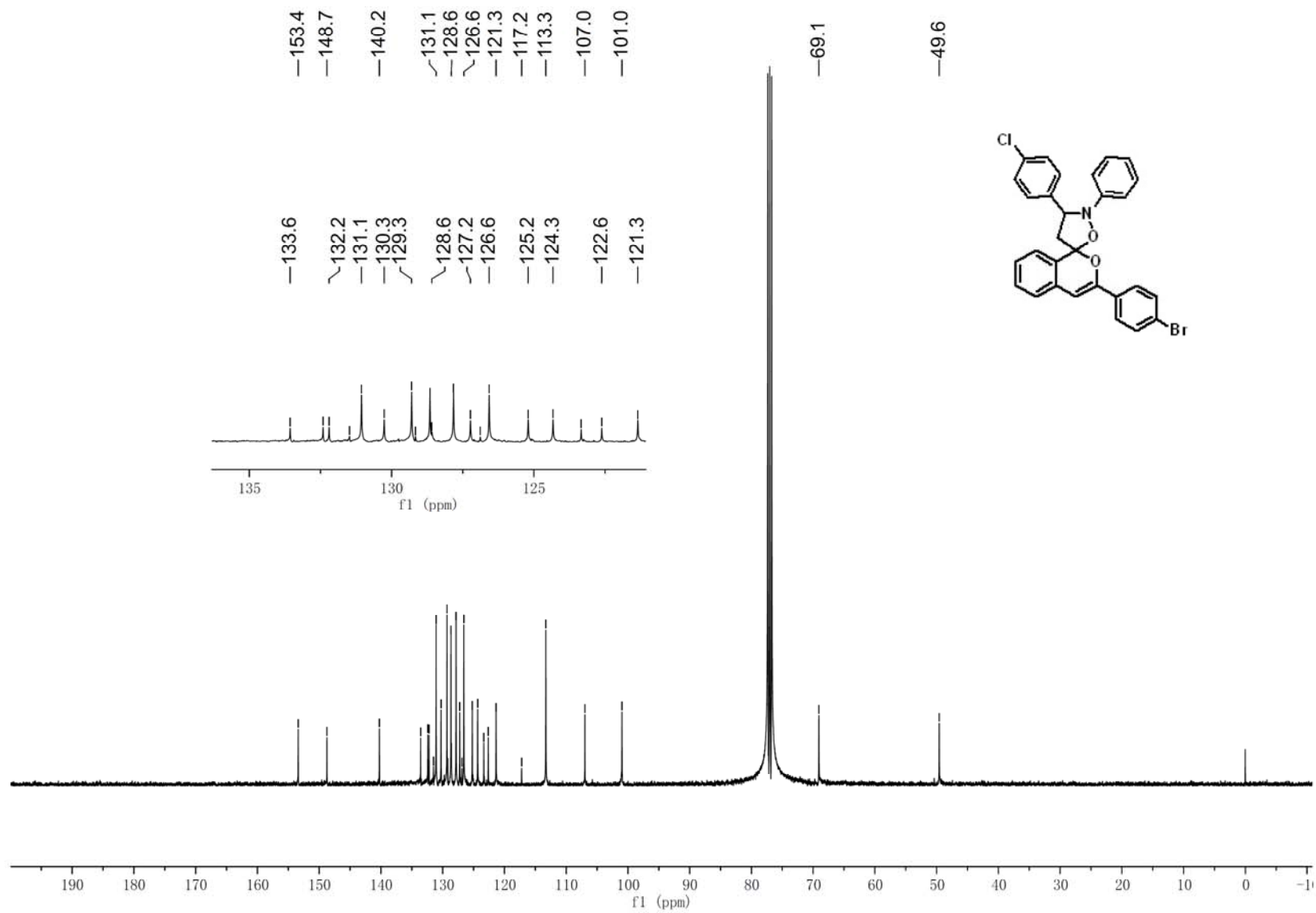


$^{13}\text{C}$  NMR Spectrum of Compound 5s

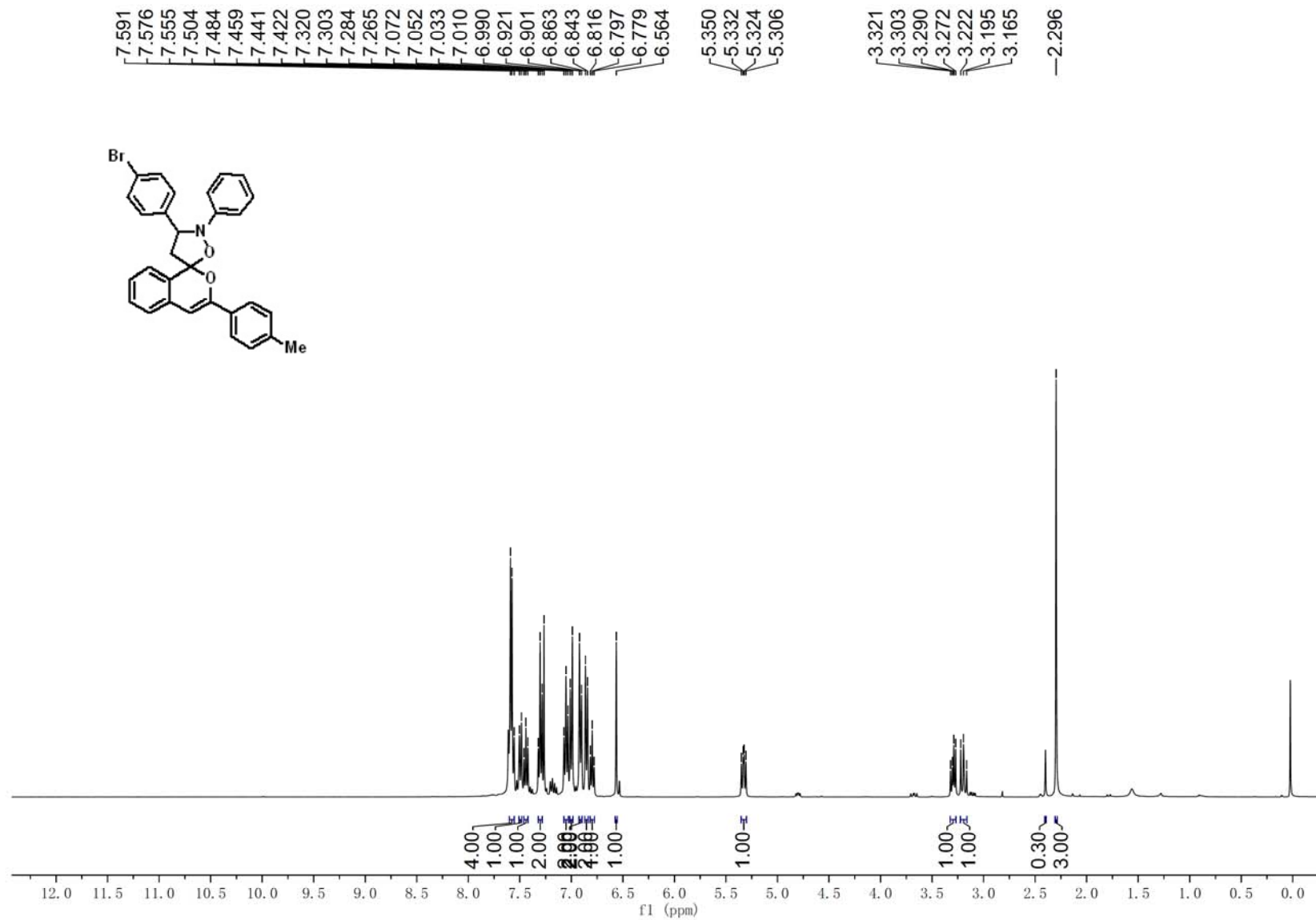




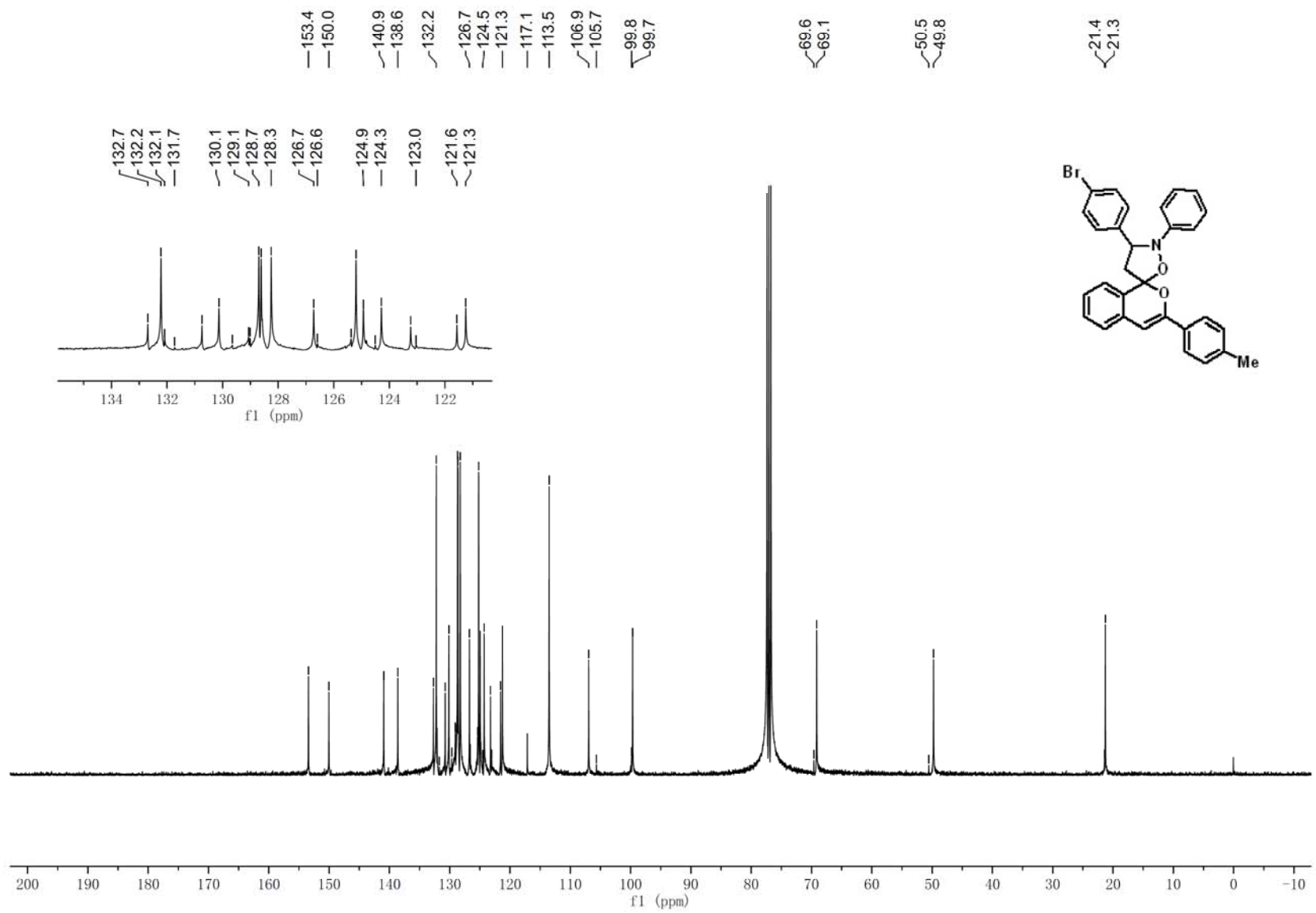
<sup>1</sup>H NMR Spectrum of Compound 5t



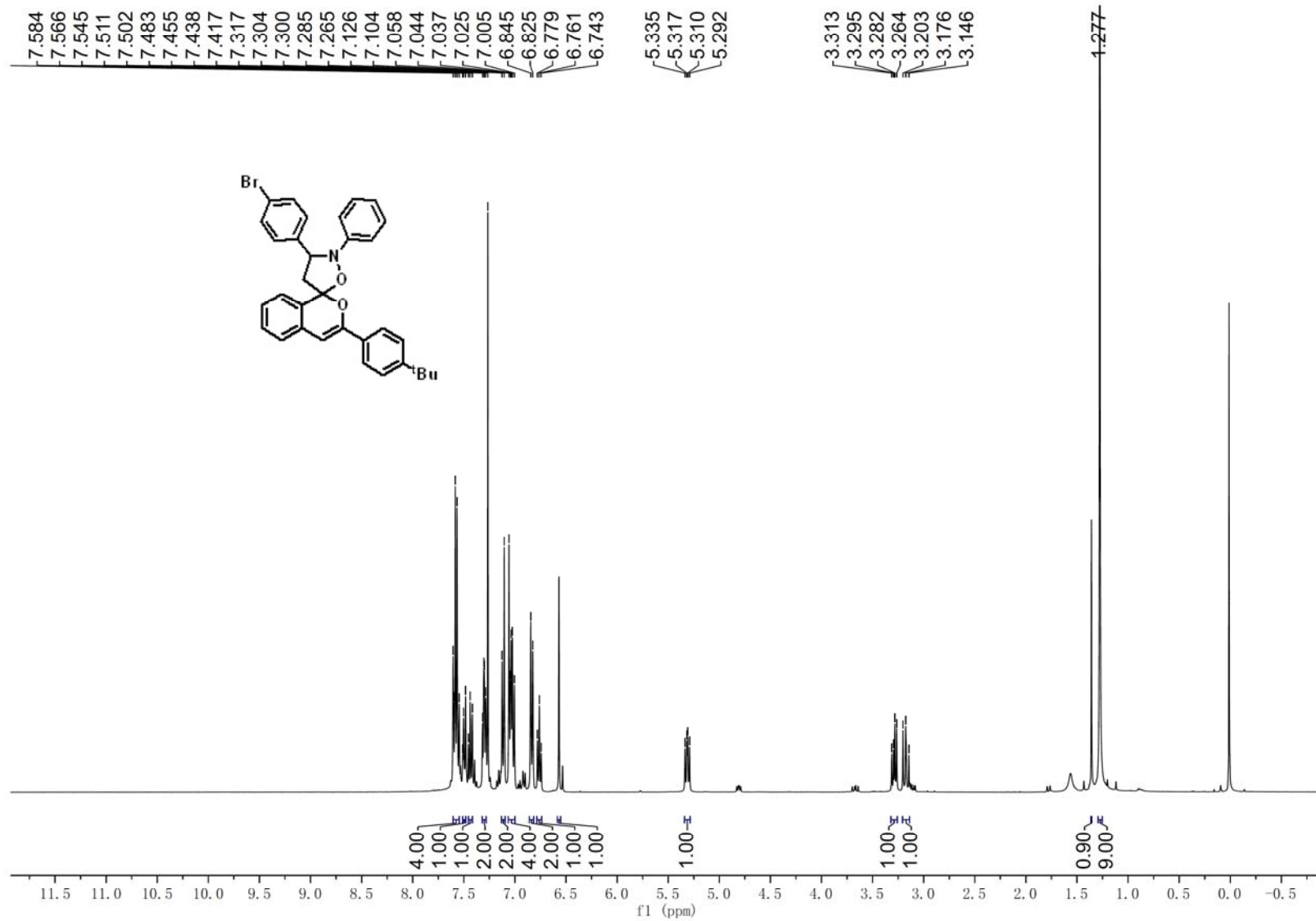
**<sup>13</sup>C NMR Spectrum of Compound 5t**



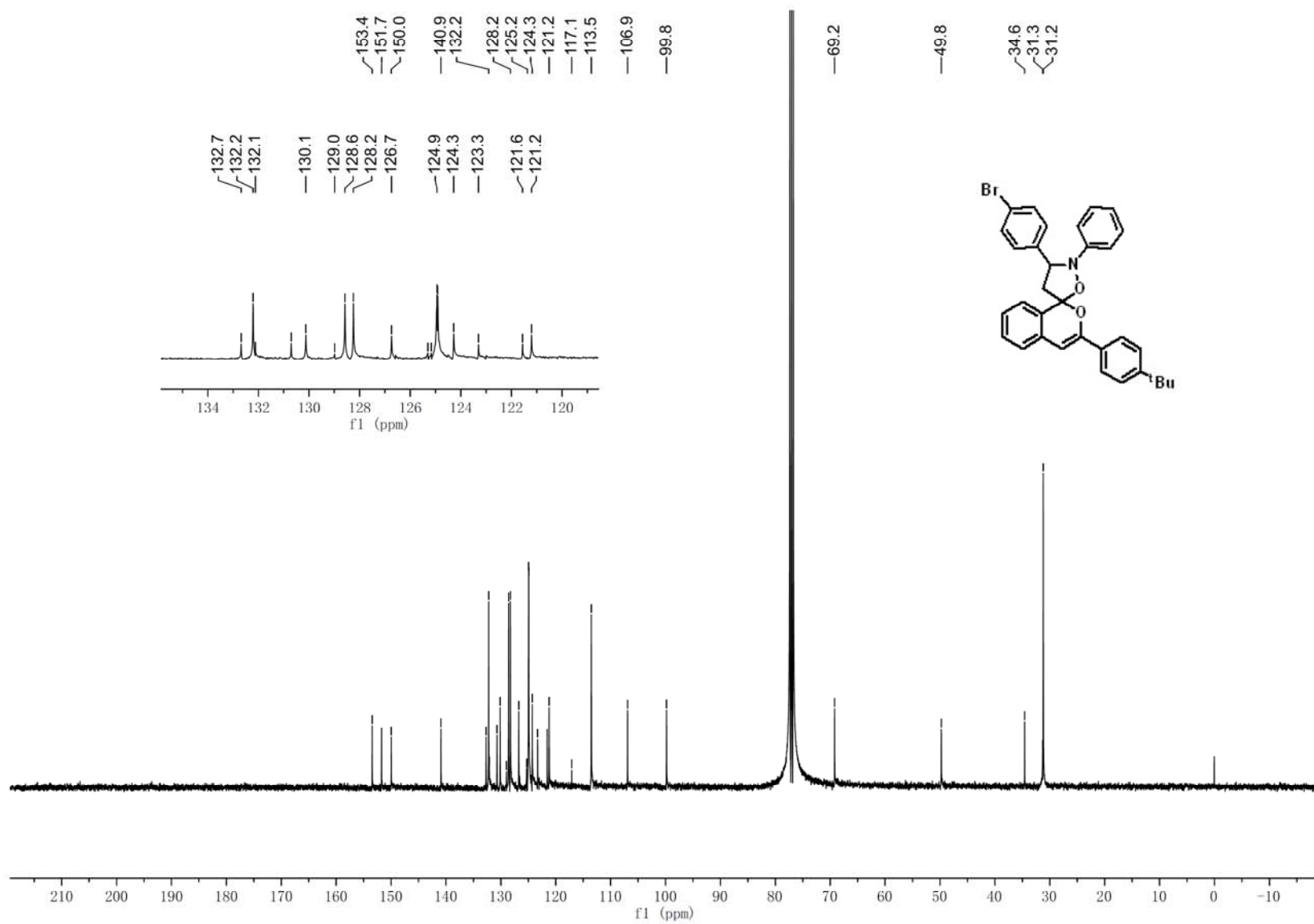
<sup>1</sup>H NMR Spectrum of Compound 5u



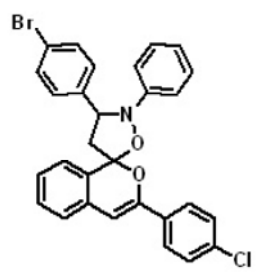
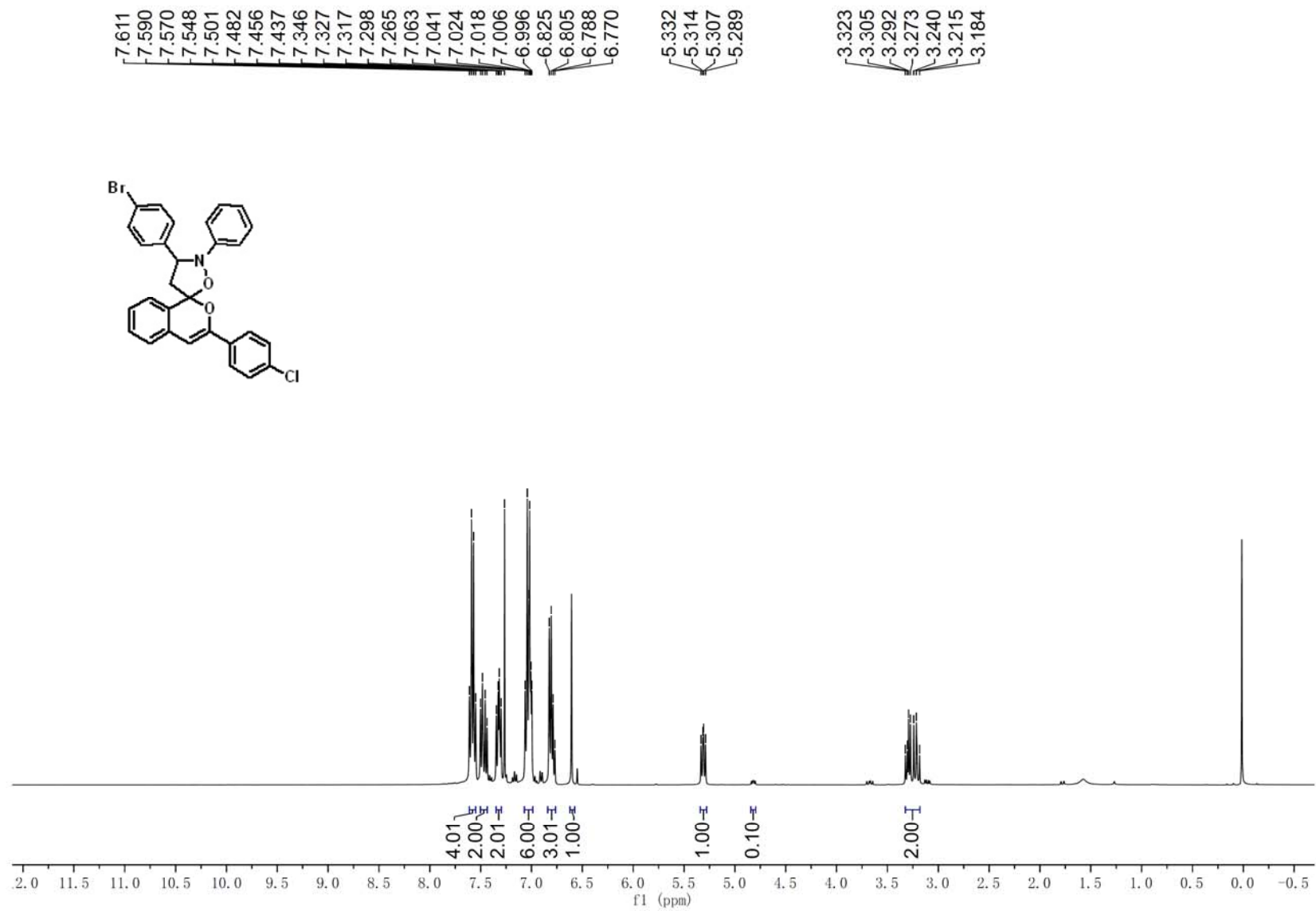
$^{13}\text{C}$  NMR Spectrum of Compound 5u



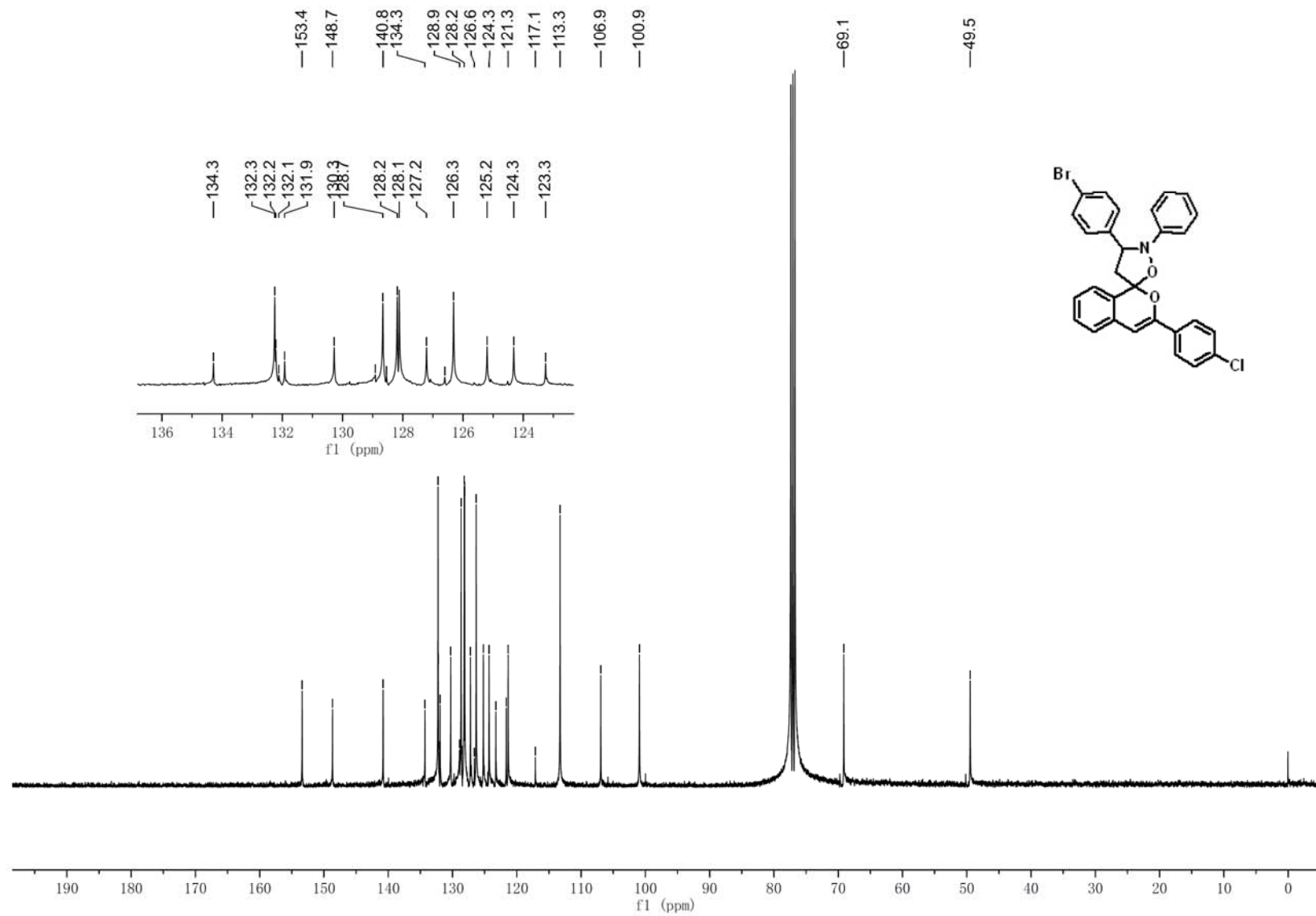
<sup>1</sup>H NMR Spectrum of Compound 5v



**<sup>13</sup>C NMR Spectrum of Compound 5v**

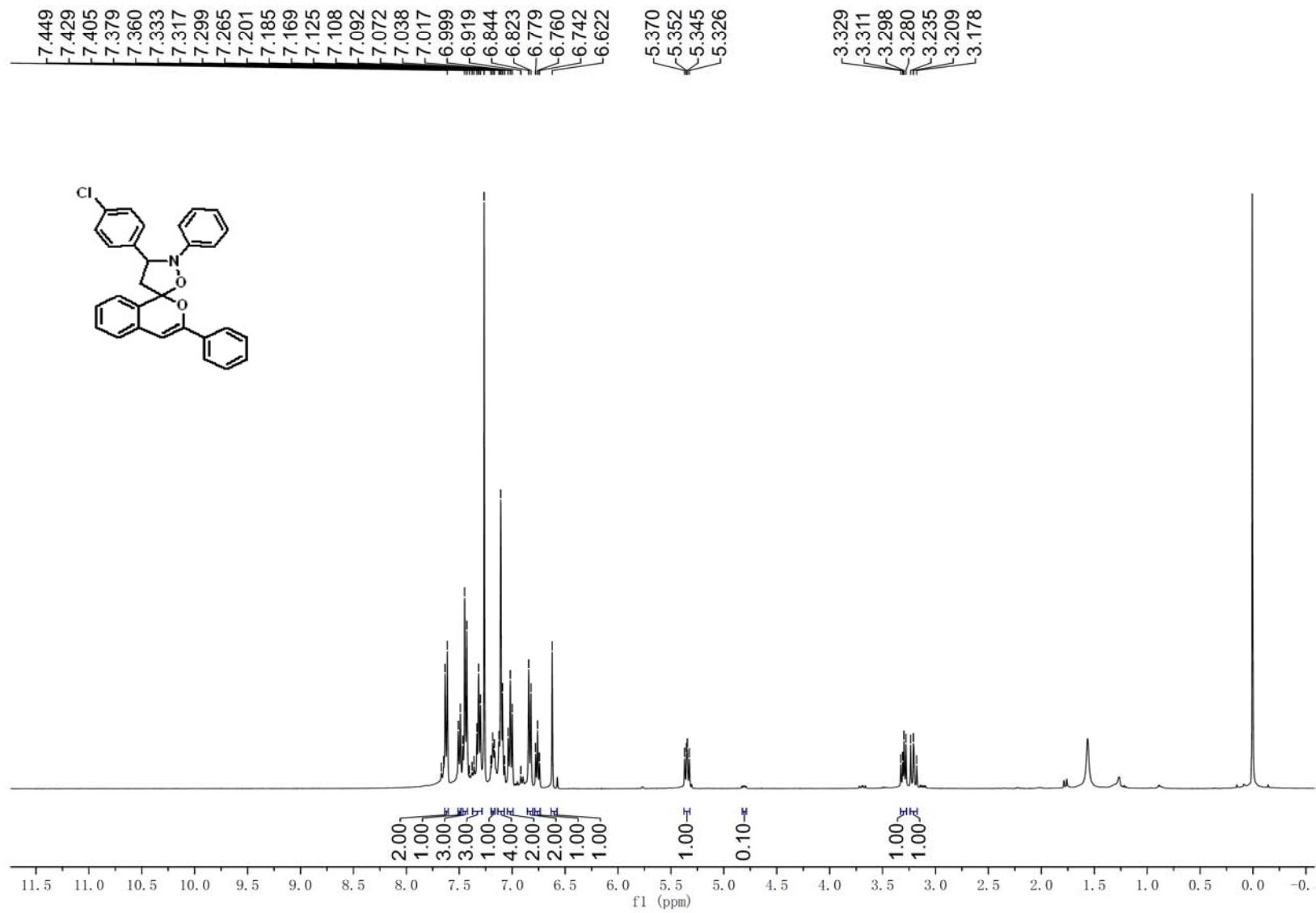


**<sup>1</sup>H NMR Spectrum of Compound 5w**

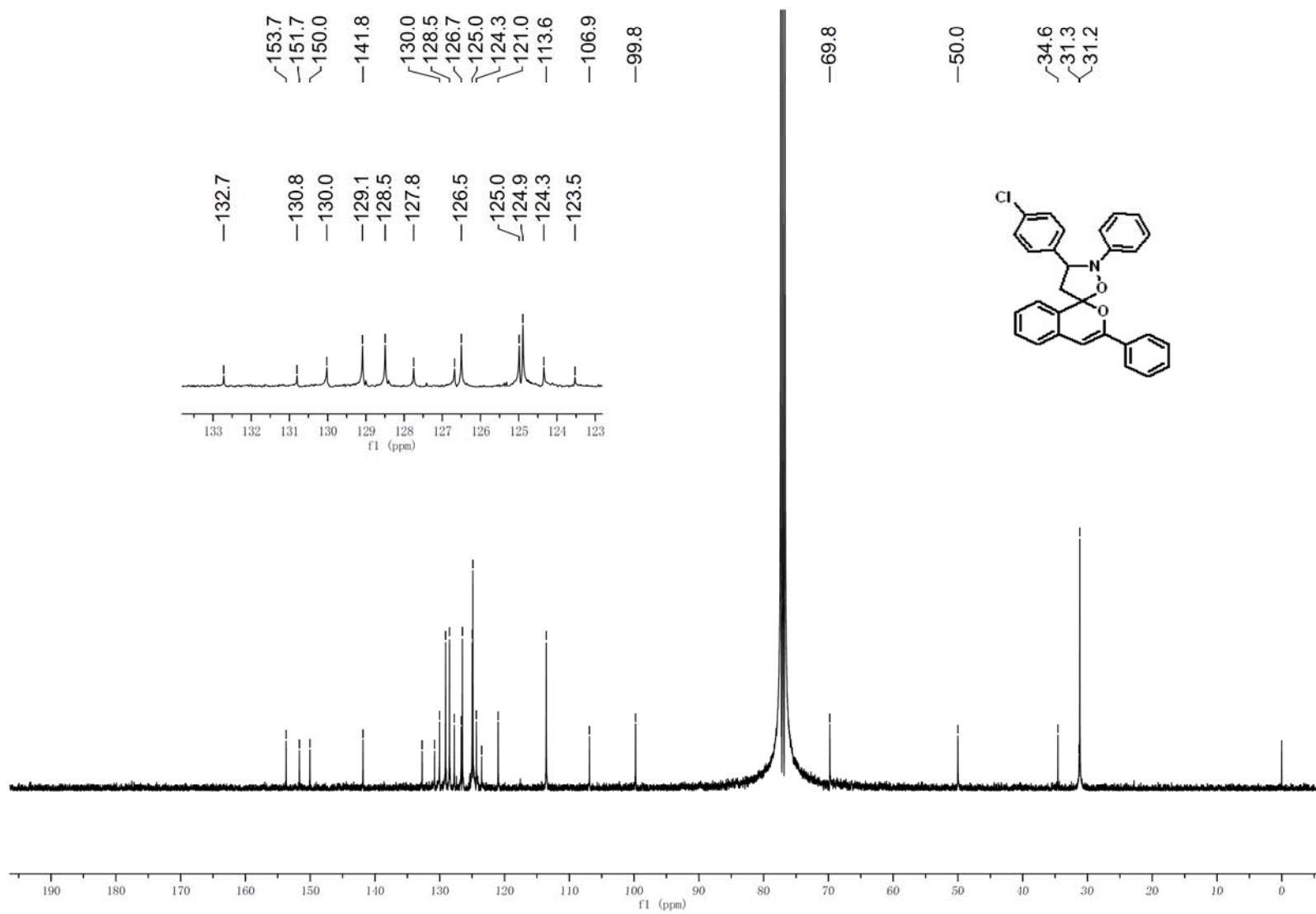


$^{13}\text{C}$  NMR Spectrum of Compound 5w

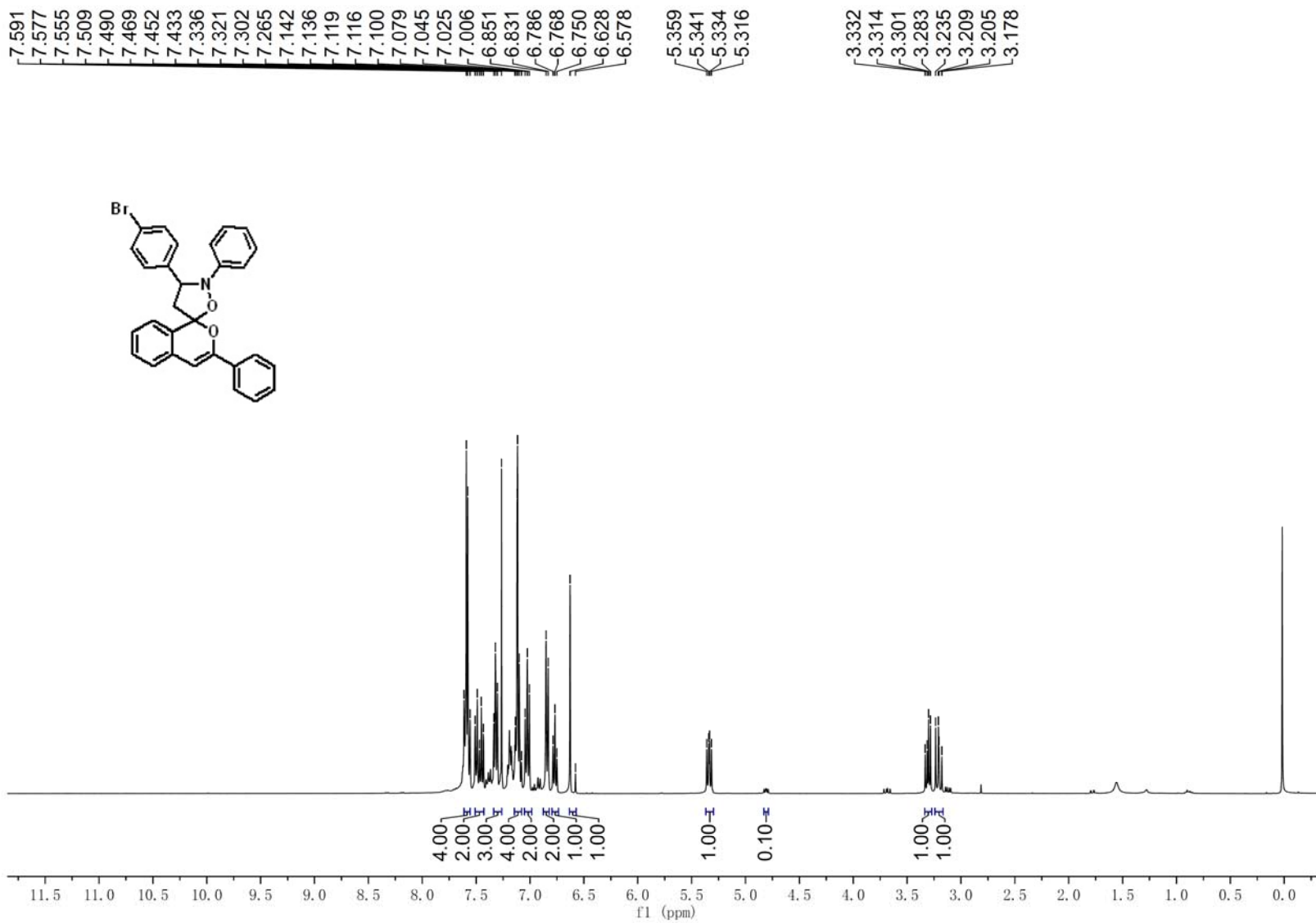




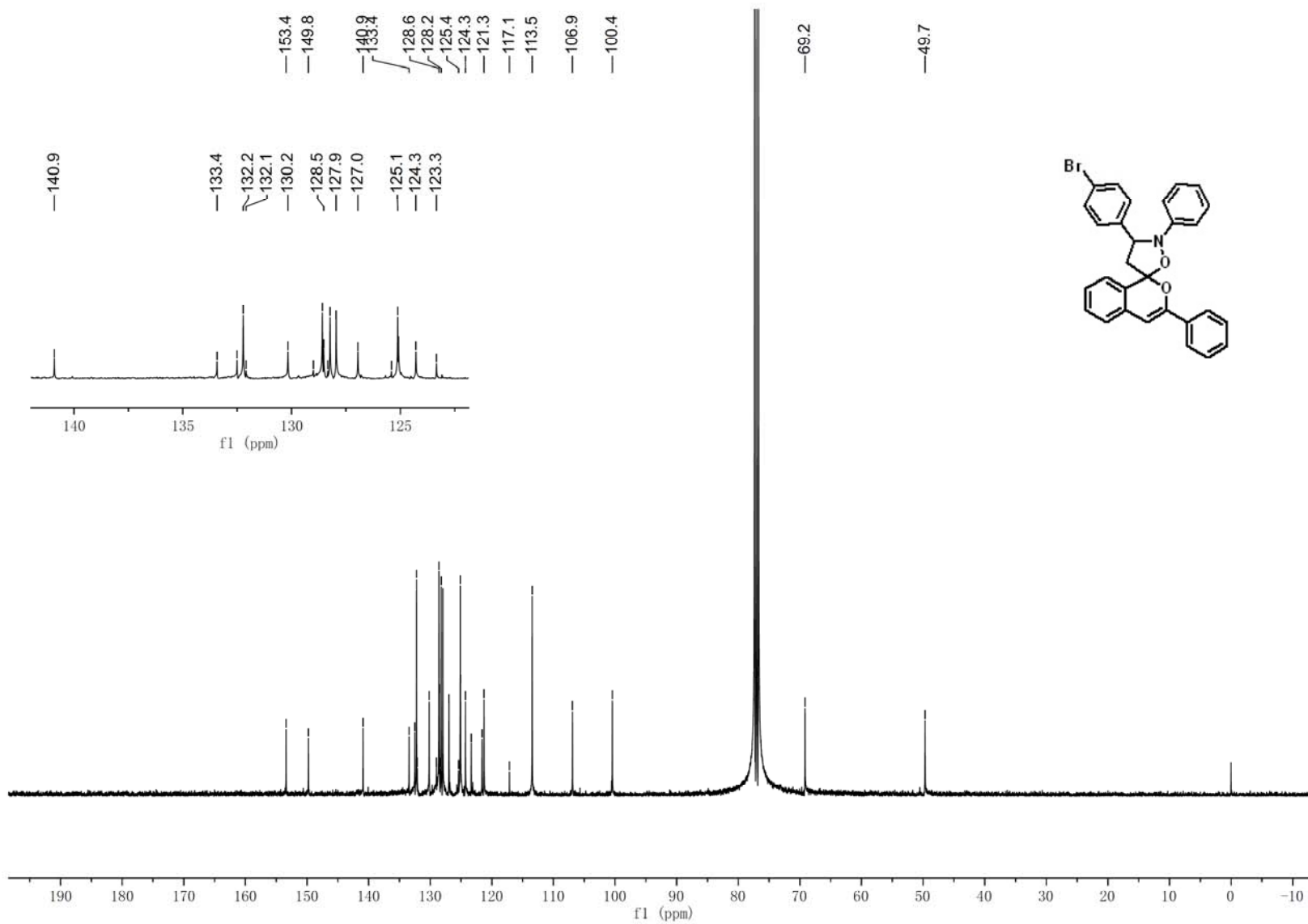
<sup>1</sup>H NMR Spectrum of Compound 5x



**<sup>13</sup>C NMR Spectrum of Compound 5x**

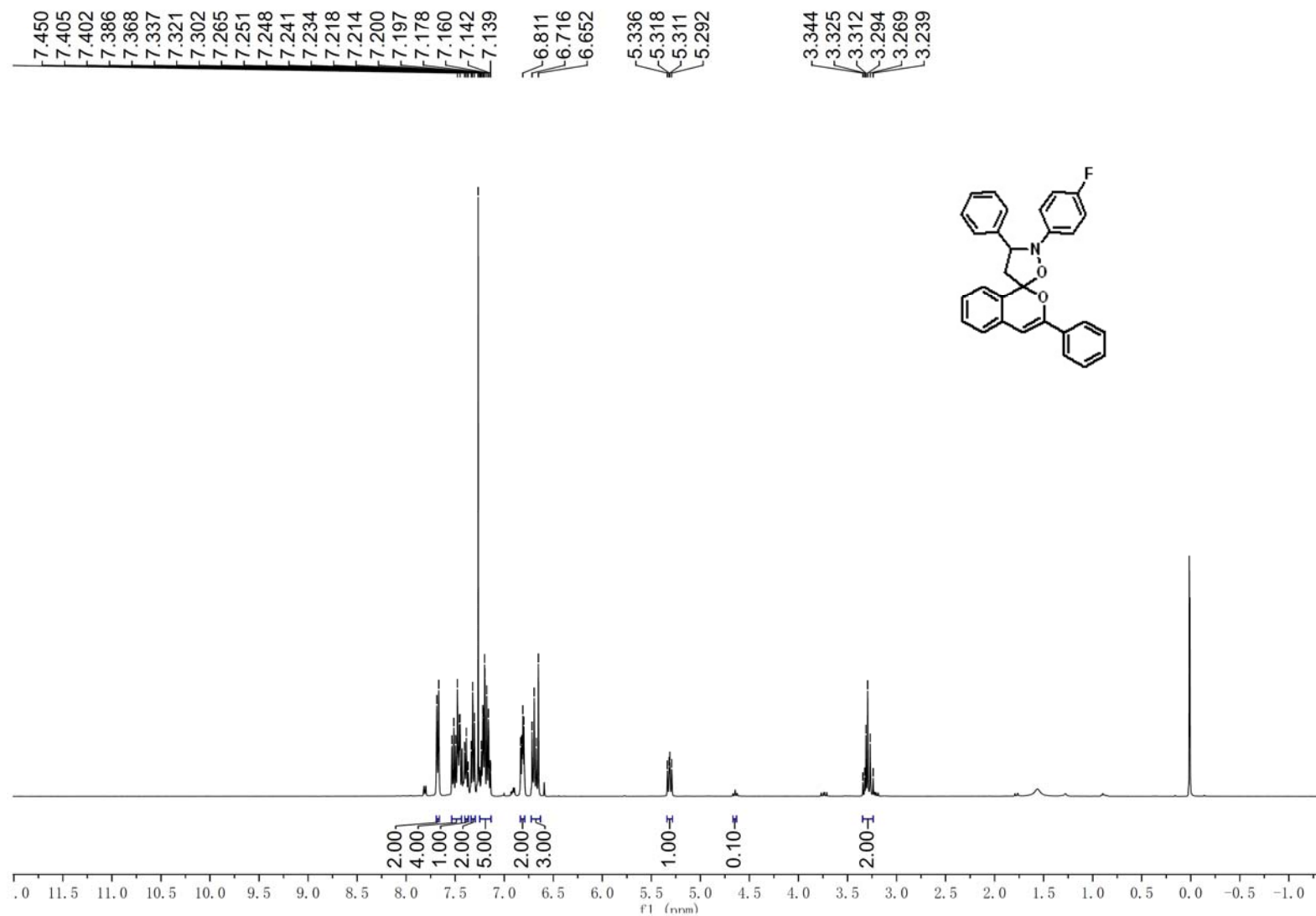


<sup>1</sup>H NMR Spectrum of Compound 5y

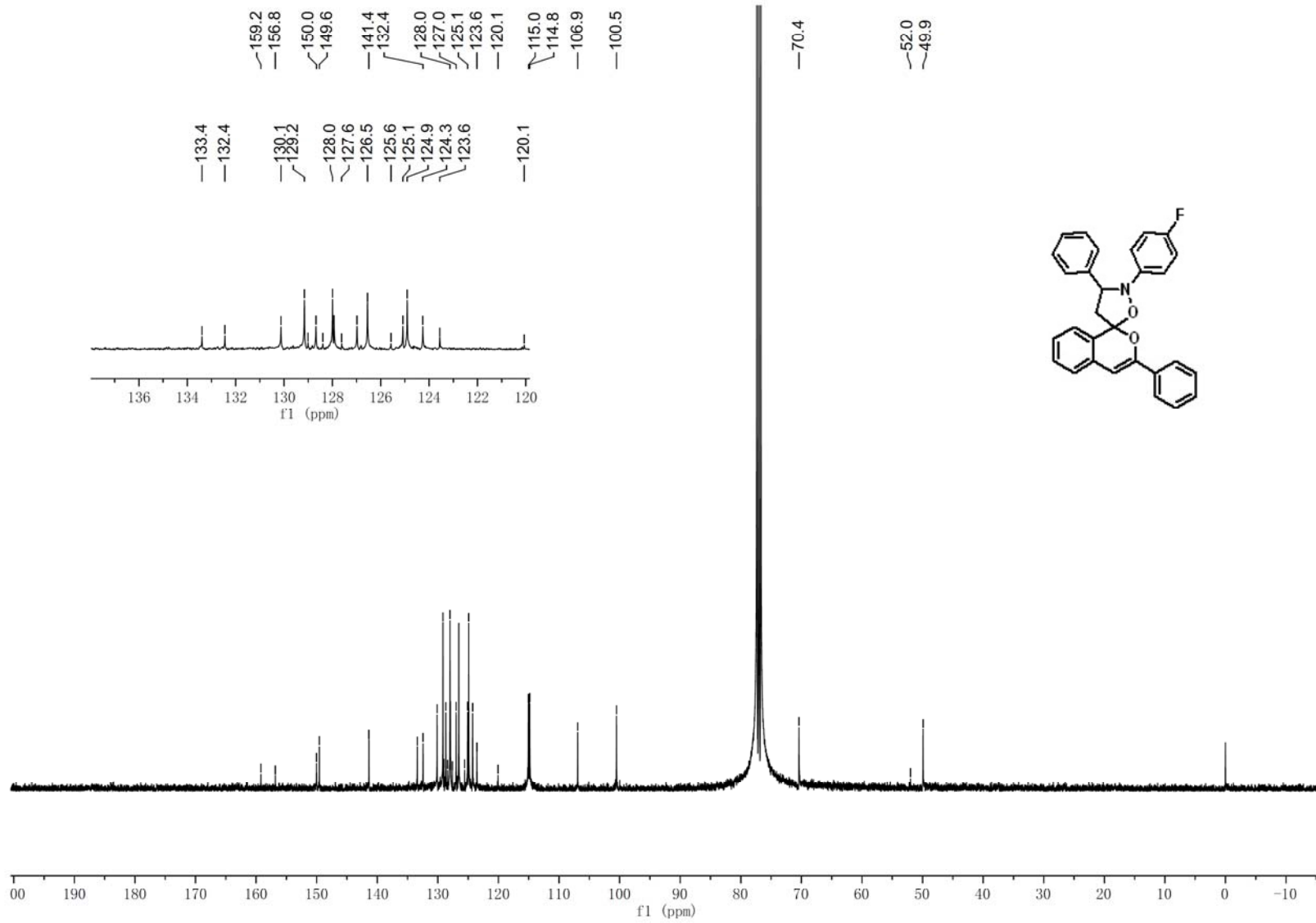


**<sup>13</sup>C NMR Spectrum of Compound 5y**

S100



<sup>1</sup>H NMR Spectrum of Compound 5z



$^{13}\text{C}$  NMR Spectrum of Compound 5z