

**One Pot Three-Component Reaction for Preparation of Dihydroquinolines with
Two Different Ketones and Aromatic Amines**

Guobing Yang,^a Guangxun Li^{b*} Jin Huang^b Zhuo Tang^{b*} and Jinzhong Zhao ^{a*}

Content

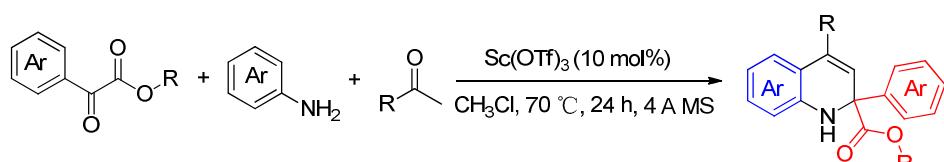
General information	2
1. General procedural for synthesis of Substituted 1,2-dihydroquinoline.....	2
2.Characterization of selected substrates and products.....	2
3. NMR spectrums	14

General information

All reactions that required anhydrous conditions were carried by standard procedures under a nitrogen atmosphere. Commercially available reagents from Alfa Aesar and Adamas-beta were used as received. The solvents were dried by distillation over the appropriate drying reagents.

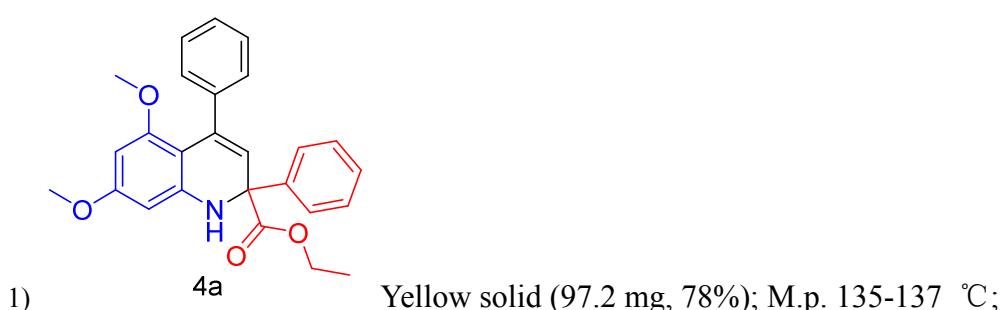
Melting points were measured on a Meltemp melting point apparatus and were not corrected. ^1H NMR spectra were recorded on commercial instruments (400 MHz). Chemical shifts were reported in ppm from tetramethylsilane with the solvent resonance as the internal standard (CDCl_3 , $\delta = 7.26$). Spectra were reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz), integration and assignment. ^{13}C NMR spectra were collected on commercial instruments (101 Hz) with complete proton decoupling. Chemical shifts are reported in ppm from the tetramethylsilane with the solvent resonance as internal standard (CDCl_3 , $\delta = 77.0$).

1. General procedural for synthesis of Substituted 1,2-dihydroquinoline.



A reaction tube was charged with the Aromatic keto ester **1** (0.3 mmol, 1 eq.), Aromatic amines **2** (0.3 mmol, 1 eq.), ketones **3** (0.3 mmol, 1 eq.), CH_3Cl (1.5 mL), $\text{Sc}(\text{OTf})_3$ (10% mol), and 4 Å molecular sieves (100 mg). The system was stirred under nitrogen atmosphere at 70 °C for 24 h. Then the products were obtained by purification with flash column chromatography over silica gel eluted with petroleum: ethyl acetate (10/1-1/5).

2. Characterization of selected substrates and products.

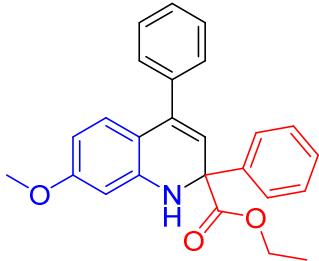


¹H NMR (400 MHz, CDCl₃) δ 7.53 (d, *J* = 7.5 Hz, 2H), 7.38 – 7.26 (m, 8H), 6.07 (s, 1H), 5.97 (s, 1H), 5.85 (s, 1H), 5.29 (s, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 3.81 (s, 3H), 3.33 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H);

¹³C NMR (101 MHz, CDCl₃) δ 172.93, 161.49, 158.11, 145.12, 142.87, 142.48, 136.91, 128.50, 127.79, 127.44, 127.19, 126.37, 125.83, 120.91, 103.80, 92.36, 90.71, 63.90, 61.93, 55.19, 54.98, 14.09;

HRMS (ESI): C₂₆H₂₅NO₄ Neutral mass: 415.17836, Observed neutral mass: 415.1784, Observed ([M+H]⁺): 416.1857;

IR: 3381.27, 3081.58, 1720.51, 1618.58, 1246.22, 1092.14, 1075.34, 1198.86.



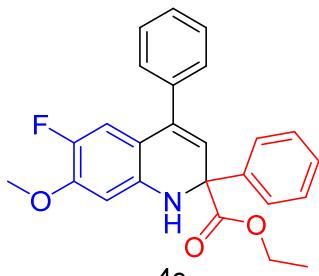
2) **4b** Yellow oil (78.6 mg, 68%);

¹H NMR (400 MHz, CDCl₃) δ 7.54 (d, *J* = 7.5 Hz, 2H), 7.45 – 7.36 (m, 7H), 7.34 – 7.28 (m, 1H), 6.89 (d, *J* = 8.5 Hz, 1H), 6.32 (d, *J* = 2.2 Hz, 1H), 6.22 (dd, *J* = 8.5, 2.2 Hz, 1H), 5.97 (d, *J* = 1.6 Hz, 1H), 5.14 (s, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 3.80 (s, 3H), 1.31 (t, *J* = 7.1 Hz, 3H);

¹³C NMR (101 MHz, CDCl₃) δ 173.16, 160.82, 143.83, 143.44, 139.25, 137.64, 129.00, 128.71, 128.21, 127.82, 127.60, 125.55, 119.72, 113.66, 103.87, 99.23, 64.91, 61.91, 55.20, 14.15;

HRMS (ESI): C₂₅H₂₃NO₃ Neutral mass: 385.16779, Observed neutral mass: 385.1674, Observed ([M+H]⁺): 386.1747;

IR: 3382.31, 3081.54, 1719.23, 1618.55, 1250.22, 1093.14, 1075.34, 1877.96.



3) **4c** Yellow oil (90.7 mg, 75%);

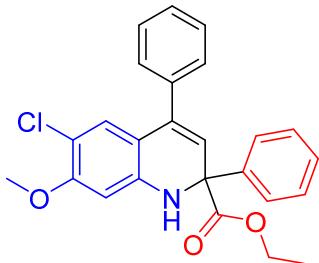
¹H NMR (400 MHz, CDCl₃) δ 7.53 (d, *J* = 7.5 Hz, 2H), 7.49 – 7.36 (m, 7H), 7.34 (d, *J* = 7.1 Hz, 1H), 6.73 (d, *J* = 12.4 Hz, 1H), 6.37 (d, *J* = 7.2 Hz, 1H), 6.03 (s, 1H), 5.06 (s, 1H), 4.30 (dd, *J* = 13.8, 6.8 Hz, 2H), 3.89 (s, 3H), 1.31 (t, *J* = 6.9 Hz, 3H);

¹³C NMR (101 MHz, CDCl₃) δ 173.22, 144.42, 143.40, 138.85, 138.65, 137.23, 128.85, 128.74, 128.41, 127.94, 120.63, 113.69, 113.48, 99.27, 64.92, 62.01, 56.22, 14.15;

HRMS (ESI): C₂₅H₂₂FNO₃ Neutral mass: 403.15837, Observed neutral mass: 403.1581, Observed ([M+H]⁺): 404.1654;

IR: 3381.98, 3082.34, 1723.49, 1629.35, 1239.42, 1166.32, 1093.14, 1195.34,

989.56.



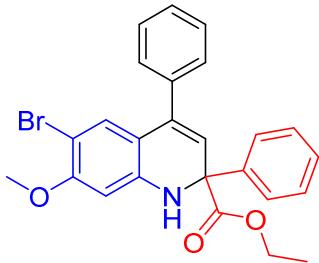
4) 4d Yellow oil (91.8 mg, 73%);

¹H NMR (400 MHz, CDCl₃) δ 7.52 (d, *J* = 7.4 Hz, 2H), 7.43 (dd, *J* = 12.8, 5.1 Hz, 7H), 7.34 (d, *J* = 7.0 Hz, 1H), 6.96 (s, 1H), 6.36 (s, 1H), 6.00 (s, 1H), 5.19 (s, 1H), 4.31 (dd, *J* = 13.0, 6.1 Hz, 2H), 3.90 (s, 3H), 1.31 (t, 3H);

¹³C NMR (101 MHz, CDCl₃) δ 173.00, 155.68, 143.45, 142.05, 138.56, 137.00, 128.83, 128.45, 127.98, 127.57, 125.53, 120.34, 113.79, 111.13, 98.09, 64.97, 62.07, 56.12, 14.15;

HRMS (ESI): C₂₅H₂₂ClNO₃ Neutral mass: 419.12882, Observed neutral mass: 419.1273, Observed ([M+H]⁺: 420.1346;

IR: 3381.47, 3082.32, 1721.51, 1630.15, 1251.44, 1087.31, 1064.34, 1211.31, 732.37.



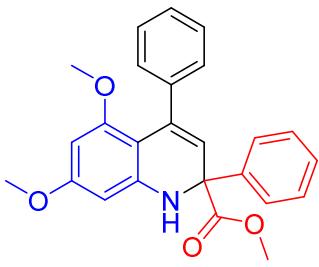
5) 4e Yellow oil (100.0 mg, 72%);

¹H NMR (400 MHz, CDCl₃) δ 7.50 (d, *J* = 7.7 Hz, 2H), 7.47 – 7.36 (m, 7H), 7.33 (d, *J* = 7.0 Hz, 1H), 7.09 (s, 1H), 6.33 (s, 1H), 5.98 (s, 1H), 5.17 (s, 1H), 4.30 (dd, *J* = 15.7, 8.7 Hz, 2H), 3.89 (s, 3H), 1.31 (t, *J* = 7.3 Hz, 3H);

¹³C NMR (101 MHz, CDCl₃) δ 172.98, 156.53, 143.45, 142.74, 138.56, 136.94, 130.50, 128.84, 128.47, 128.03, 127.95, 125.52, 120.29, 114.52, 99.23, 97.97, 64.96, 62.09, 56.21, 14.15;

HRMS (ESI): C₂₅H₂₂BrNO₃ Neutral mass: 463.07831, Observed neutral mass: 463.0776, Observed ([M+Na]⁺: 486.0668;

IR: 3381.36, 3083.25, 1724.52, 1632.15, 1248.41, 1081.31, 1044.43, 1213.31, 582.37.



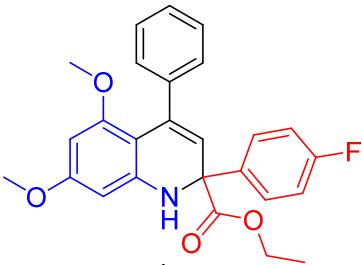
6) **4f** Yellow oil (96.3 mg, 80%);

¹H NMR (400 MHz, CDCl₃) δ 7.54 (d, *J* = 7.4 Hz, 2H), 7.40 – 7.24 (m, 8H), 6.08 (s, 1H), 5.97 (s, 1H), 5.87 (s, 1H), 5.30 (s, 1H), 3.81 (d, *J* = 8.2 Hz, 6H), 3.35 (s, 3H);

¹³C NMR (101 MHz, CDCl₃) δ 173.54, 161.53, 158.11, 145.10, 142.77, 142.38, 136.99, 128.58, 127.90, 127.40, 127.22, 126.42, 125.83, 120.82, 103.69, 92.36, 90.74, 64.08, 55.20, 54.97, 52.87;

HRMS (ESI): C₂₅H₂₃NO₄ Neutral mass: 401.16271, Observed neutral mass: 401.1626, Observed ([M+H]⁺): 402.1698;

IR: 3381.27, 3081.58, 1720.51, 1618.58, 1246.22, 1092.14, 1075.34, 1059.86.



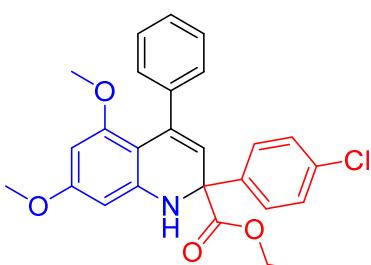
7) **4g** Yellow oil (101.4 mg, 78%);

¹H NMR (400 MHz, CDCl₃) δ 7.55 – 7.47 (m, 2H), 7.36 – 7.29 (m, 5H), 7.07 – 6.97 (m, 2H), 6.07 (d, *J* = 2.3 Hz, 1H), 5.95 (d, *J* = 1.3 Hz, 1H), 5.86 (d, *J* = 2.2 Hz, 1H), 5.30 (s, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 3.81 (s, 3H), 3.33 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H);

¹³C NMR (101 MHz, CDCl₃) δ 172.67, 161.59, 158.16, 144.85, 142.31, 138.65, 137.19, 127.69, 127.61, 127.40, 127.24, 126.48, 120.47, 115.45, 115.23, 103.85, 92.38, 90.78, 63.29, 62.07, 55.21, 54.97, 14.07;

HRMS (ESI): C₂₆H₂₄FNO₄ Neutral mass: 433.16894, Observed neutral mass: 433.1694, Observed ([M+H]⁺): 434.1767;

IR: 3384.27, 3082.58, 1723.11, 1618.79, 1245.22, 1093.14, 1065.34, 1198.81, 995.43.



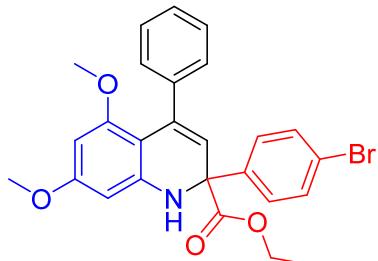
8) **4h** Yellow oil (101.0mg, 75%);

¹H NMR (400 MHz, CDCl₃) δ 7.48 (d, *J* = 8.5 Hz, 2H), 7.35 – 7.27 (m, 7H), 6.07 (d, *J* = 2.1 Hz, 1H), 5.95 (d, *J* = 1.2 Hz, 1H), 5.86 (d, *J* = 2.0 Hz, 1H), 5.32 (s, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 3.81 (s, 3H), 3.33 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H);

¹³C NMR (101 MHz, CDCl₃) δ 172.38, 161.60, 158.16, 144.74, 142.23, 141.42, 137.37, 133.70, 128.62, 127.45 – 127.13, 126.50, 120.10, 103.85, 92.37, 90.78, 63.27, 62.17, 55.22, 54.96, 14.07;

HRMS (ESI): C₂₆H₂₄ClNO₄ Neutral mass: 449.13939, Observed neutral mass: 449.1389, Observed ([M+H]⁺: 450.1462;

IR: 3381.27, 3080.58, 1723.51, 1628.58, 1246.42, 1095.34, 1073.34, 1198.54
745.35.



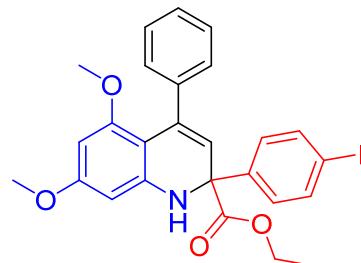
9) 4i Yellow oil (110.9 mg, 75%);

¹H NMR (400 MHz, CDCl₃) δ 7.48 – 7.44 (m, 2H), 7.43 – 7.39 (m, 2H), 7.33 – 7.28 (m, 5H), 6.07 (d, *J* = 2.3 Hz, 1H), 5.94 (d, *J* = 1.8 Hz, 1H), 5.86 (d, *J* = 2.3 Hz, 1H), 5.32 (s, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 3.81 (s, 3H), 3.33 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H);

¹³C NMR (101 MHz, CDCl₃) δ 172.32, 161.63, 158.18, 144.72, 142.24, 142.00, 137.42, 131.57, 127.65, 127.39, 127.25, 126.51, 121.92, 120.01, 103.88, 92.40, 90.81, 63.33, 62.18, 55.22, 54.97, 14.06;

HRMS (ESI): C₂₆H₂₄BrNO₄ Neutral mass: 493.08887, Observed neutral mass: 493.0895, Observed ([M+H]⁺: 494.09033;

IR: 3382.27, 3071.54, 1721.51, 1617.58, 1245.22, 1092.17, 1076.34, 1188.86, 543.35



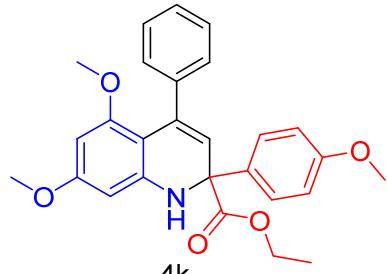
10) 4j Yellow oil (116.9 mg, 72%);

¹H NMR (400 MHz, CDCl₃) 1H NMR (400 MHz, CDCl₃) δ 7.66 (d, *J* = 8.3 Hz, 2H), 7.42 – 7.21 (m, 7H), 6.06 (d, *J* = 1.6 Hz, 1H), 5.94 (s, 1H), 5.85 (d, *J* = 1.6 Hz, 1H), 5.31 (s, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 3.81 (s, 3H), 3.33 (s, 3H), 1.51 – 1.02 (t, *J* = 7.1 Hz, 3H);

¹³C NMR (101 MHz, CDCl₃) δ 172.27, 161.62, 158.17, 144.71, 142.73, 142.24, 137.53, 127.86, 127.39, 127.24, 126.50, 119.95, 103.87, 93.67, 92.38, 90.79, 63.39, 62.19, 55.22, 54.96, 14.07;

HRMS (ESI): C₂₆H₂₄INO₄ Neutral mass: 541.07500, Observed neutral mass: 541.07540, Observed ([M+H]⁺): 542.0824;

IR: 3382.56, 3079.34, 1721.32, 1618.58, 1246.22, 1092.16, 1078.34, 1188.86.



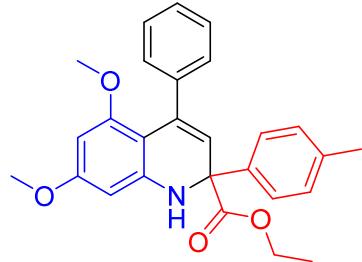
11) 4k Yellow oil (93.5 mg, 70%);

¹H NMR (400 MHz, CDCl₃) δ 7.49 – 7.39 (m, 2H), 7.34 – 7.28 (m, 5H), 6.92 – 6.74 (m, 2H), 6.05 (d, J = 2.3 Hz, 1H), 5.95 (d, J = 1.2 Hz, 1H), 5.85 (d, J = 2.3 Hz, 1H), 5.27 (s, 1H), 4.24 (q, J = 7.1 Hz, 2H), 3.80 (d, J = 3.2 Hz, 6H), 3.33 (s, 3H), 1.27 (t, J = 7.1 Hz, 3H);

¹³C NMR (101 MHz, CDCl₃) δ 173.10, 161.46, 159.14, 158.10, 145.14, 142.51, 136.84, 134.95, 127.44, 127.19, 127.09, 126.36, 121.07, 113.86, 103.85, 92.36, 90.69, 63.37, 61.86, 55.27, 55.18, 54.98, 14.11;

HRMS (ESI): C₂₇H₂₇NO₅ Neutral mass: 445.18892, Observed neutral mass: 445.1893, Observed ([M+H]⁺): 446.4437;

IR: 3381.27, 3081.58, 1720.51, 1618.58, 1246.22, 1092.14, 1075.34, 1198.86.



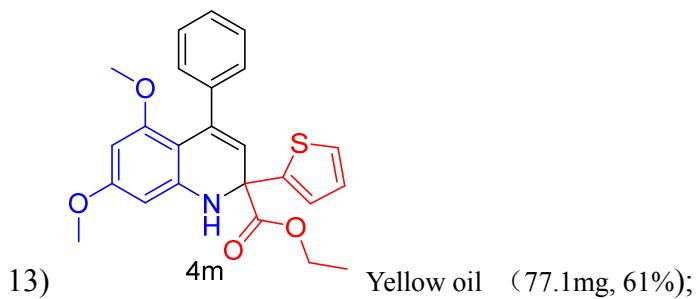
12) 4l Yellow oil (87.5 mg, 68%);

¹H NMR (400 MHz, CDCl₃) δ 7.43 (d, J = 8.2 Hz, 2H), 7.32 (t, J = 6.4 Hz, 5H), 7.16 (d, J = 8.0 Hz, 2H), 6.06 (d, J = 2.2 Hz, 1H), 5.97 (d, J = 1.4 Hz, 1H), 5.86 (d, J = 2.2 Hz, 1H), 5.29 (s, 1H), 4.25 (q, J = 7.1 Hz, 2H), 3.81 (s, 3H), 3.34 (s, 3H), 2.34 (s, 3H), 1.28 (t, J = 7.1 Hz, 3H);

¹³C NMR (101 MHz, CDCl₃) δ 173.09, 161.46, 158.10, 145.20, 142.55, 139.93, 137.54, 136.84, 129.22, 127.46, 127.19, 126.35, 125.76, 121.08, 103.83, 92.37, 90.69, 63.67, 61.88, 55.19, 54.98, 21.05, 14.11;

HRMS (ESI): C₂₇H₂₇NO₄ Neutral mass: 429.19401, Observed neutral mass: 429.1944, Observed ([M+H]⁺): 430.2026;

IR: 3380.27, 3079.58, 1721.53, 1618.58, 1246.22, 1092.24, 1075.34, 1188.32.

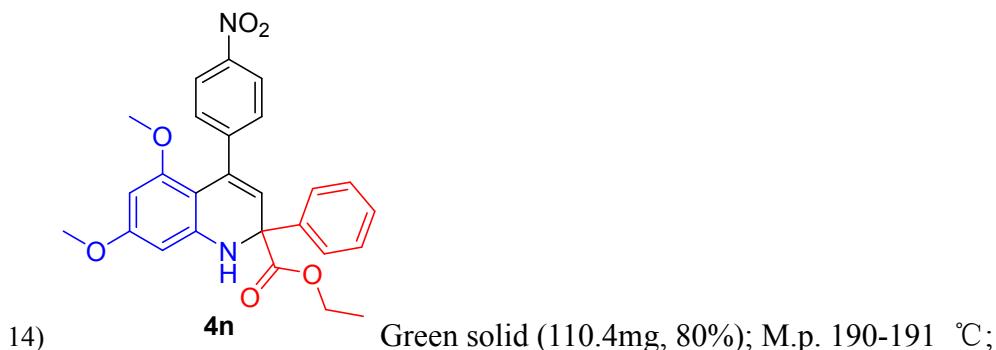


¹H NMR (400 MHz, CDCl₃) δ 7.33 – 7.28 (m, 5H), 7.24 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.07 (dd, *J* = 3.6, 1.2 Hz, 1H), 6.95 (dd, *J* = 5.0, 3.6 Hz, 1H), 6.06 (d, *J* = 2.3 Hz, 1H), 5.94 (d, *J* = 1.8 Hz, 1H), 5.88 (d, *J* = 2.3 Hz, 1H), 5.32 (s, 1H), 4.29 (qd, *J* = 7.1, 1.6 Hz, 2H), 3.81 (s, 3H), 3.34 (s, 3H), 1.32 (t, *J* = 7.1 Hz, 3H);

¹³C NMR (101 MHz, CDCl₃) δ 171.93, 161.54, 158.14, 147.59, 144.83, 142.20, 136.97, 127.43, 127.20, 126.87, 126.45, 125.55, 124.11, 120.68, 103.73, 92.53, 91.13, 62.28, 61.68, 55.21, 55.06, 14.09;

HRMS (ESI): C₂₄H₂₃NO₄S Neutral mass: 421.13478, Observed neutral mass: 421.13484, Observed ([M+H]⁺): 422.14212;

IR: 3379.27, 3083.58, 1718.25, 1608.28, 1223.12, 1068.07, 1078.04, 1188.86, 702.43.

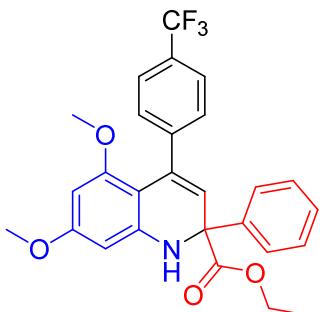


¹H NMR (400 MHz, CDCl₃) δ 8.18 (d, *J* = 8.6 Hz, 2H), 7.51 (d, *J* = 7.6 Hz, 2H), 7.44 (d, *J* = 8.5 Hz, 2H), 7.37 (t, *J* = 7.5 Hz, 2H), 7.31 (d, *J* = 7.1 Hz, 1H), 6.09 (d, *J* = 2.1 Hz, 1H), 5.99 (d, *J* = 1.2 Hz, 1H), 5.85 (d, *J* = 2.0 Hz, 1H), 5.31 (s, 1H), 4.27 (dd, *J* = 7.1 Hz, 2H), 3.82 (s, 3H), 3.34 (s, 3H), 1.28 (t, *J* = 7.1 Hz, 3H);

¹³C NMR (101 MHz, CDCl₃) δ 172.47, 162.04, 157.68, 149.66, 146.52, 145.14, 142.44, 135.24, 128.68, 128.26, 128.05, 125.65, 122.60, 102.65, 92.44, 90.44, 63.92, 62.16, 55.27, 54.72, 14.10;

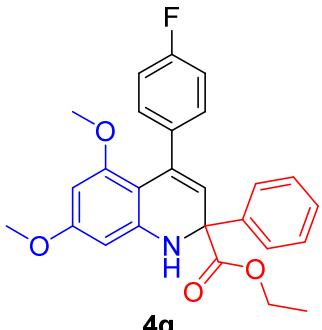
HRMS (ESI): C₂₆H₂₄N₂O₆ Neutral mass: 460.16344, Observed neutral mass: 460.1634, Observed ([M+H]⁺): 461.1707;

IR: 3391.22, 3078.48, 1721.51, 1615.58, 1236.22, 1092.67, 1075.74, 1198.86.



15) **4o** Yellow solid (120.3mg, 83%); M.p. 176-179 °C;
¹H NMR (400 MHz, CDCl₃) δ 7.57 (d, *J* = 8.0 Hz, 2H), 7.52 (d, *J* = 7.6 Hz, 2H), 7.44 – 7.33 (m, 4H), 7.30 (d, *J* = 10.1 Hz, 1H), 6.08 (s, 1H), 5.96 (s, 1H), 5.85 (s, 1H), 5.31 (s, 1H), 4.26 (q, *J* = 7.0 Hz, 2H), 3.82 (s, 3H), 3.33 (s, 3H), 1.28 (t, *J* = 7.0 Hz, 3H);
¹³C NMR (101 MHz, CDCl₃) δ 172.70, 161.84, 157.88, 146.33, 145.14, 142.67, 135.87, 128.62, 127.95, 127.77, 125.74, 103.11, 92.40, 90.54, 63.94, 62.07, 55.20, 54.79, 14.08;
HRMS (ESI): C₂₇H₂₄F₃NO₄ Neutral mass: 483.16574, Observed neutral mass: 483.1659, Observed ([M+H]⁺: 484.1732;
IR: 3371.27, 3051.58, 1721.51, 1609.58, 1245.22, 1032.14, 1055.34, 1198.86, 994.21.

16) **4p** Yellow solid (86.8mg, 65%); M.p. 132-133 °C;
¹H NMR (400 MHz, CDCl₃) δ 7.53 (d, *J* = 7.7 Hz, 2H), 7.34 (t, *J* = 7.5 Hz, 2H), 7.27 (dd, *J* = 12.5, 6.8 Hz, 3H), 6.87 (d, *J* = 8.3 Hz, 2H), 6.06 (s, 1H), 5.94 (s, 1H), 5.86 (s, 1H), 5.30 (s, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 3.84 (d, *J* = 21.0 Hz, 3H), 3.37 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H);
¹³C NMR (101 MHz, CDCl₃) δ 172.98, 161.41, 158.37, 158.18, 145.20, 142.90, 136.38, 134.94, 128.50, 127.77, 125.85, 120.37, 112.59, 103.86, 92.37, 90.77, 63.86, 61.90, 55.29, 55.19, 55.11, 14.09;
HRMS (ESI): C₂₇H₂₇NO₅ Neutral mass: 445.18892, Observed neutral mass: 445.1889, Observed ([M+H]⁺: 446.1962;
IR: 3381.27, 3121.58, 1720.51, 1658.58, 1246.22, 1092.14, 1075.34, 1198.86.



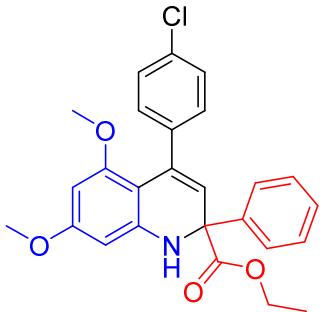
17) **4q** Yellow solid (93.6mg, 72%); M.p. 136-138 °C;

¹H NMR (400 MHz, CDCl₃) δ 7.52 (d, *J* = 7.6 Hz, 2H), 7.35 (t, *J* = 7.5 Hz, 2H), 7.31 – 7.25 (m, 3H), 7.00 (t, *J* = 8.7 Hz, 2H), 6.06 (d, *J* = 2.1 Hz, 1H), 5.92 (s, 1H), 5.85 (d, *J* = 2.0 Hz, 1H), 5.29 (s, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 3.81 (s, 3H), 3.35 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H);

¹³C NMR (101 MHz, CDCl₃) δ 172.44, 162.00, 157.66, 149.63, 146.50, 145.08, 142.40, 135.21, 128.66, 128.23, 128.03, 125.62, 122.62, 102.63, 92.40, 90.41, 63.90, 62.14, 55.27, 54.71, 14.09;

HRMS (ESI): C₂₆H₂₄FNO₄ Neutral mass: 433.16894, Observed neutral mass: 433.1686, Observed ([M+H]⁺: 434.1759;

IR: 3381.27, 3081.58, 1720.51, 1578.58, 1246.22, 1092.14, 1075.34, 1198.86, 994.34.



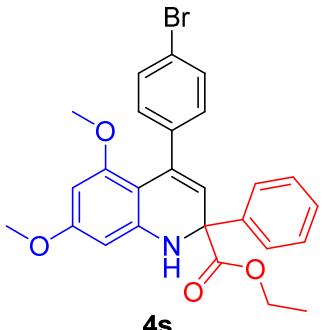
18) **4r** Yellow solid (91.6mg, 68%); M.p. 134-138 °C;

¹H NMR (400 MHz, CDCl₃) δ 7.51 (d, *J* = 7.7 Hz, 2H), 7.35 (t, *J* = 7.5 Hz, 2H), 7.29 (dd, *J* = 7.1, 3.3 Hz, 4H), 7.24 (d, *J* = 8.4 Hz, 1H), 6.06 (d, *J* = 2.2 Hz, 1H), 5.93 (d, *J* = 1.5 Hz, 1H), 5.85 (d, *J* = 2.2 Hz, 1H), 5.30 (s, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 3.81 (s, 3H), 3.36 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H);

¹³C NMR (101 MHz, CDCl₃) δ 172.76, 161.64, 157.93, 145.11, 142.69, 140.95, 135.83, 132.03, 128.81, 128.55, 127.87, 127.30, 125.73, 121.20, 103.29, 92.33, 90.56, 63.85, 62.00, 55.22, 54.88, 14.09;

HRMS (ESI): C₂₆H₂₄ClNO₄ Neutral mass: 449.13939, Observed neutral mass: 449.1389, Observed ([M+H]⁺: 450.1462;

IR: 3381.27, 3081.58, 1720.51, 1590.58, 1246.22, 1092.14, 1075.34, 1198.86, 744.21.



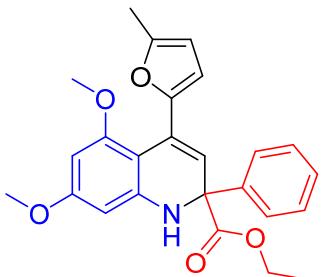
19) **4s** Yellow solid (96.2mg, 65%); M.p. 158-159 °C;

1H NMR (400 MHz, CDCl₃) δ 7.51 (d, *J* = 7.3 Hz, 2H), 7.44 (d, *J* = 8.5 Hz, 2H), 7.35 (dd, *J* = 8.1, 6.7 Hz, 2H), 7.29 (d, *J* = 5.5 Hz, 1H), 7.18 (d, *J* = 8.4 Hz, 2H), 6.06 (d, *J* = 2.3 Hz, 1H), 5.93 (d, *J* = 1.6 Hz, 1H), 5.85 (d, *J* = 2.2 Hz, 1H), 5.29 (s, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 3.81 (s, 3H), 3.36 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H);

13C NMR (101 MHz, CDCl₃) δ 172.73, 161.66, 157.94, 145.11, 142.69, 141.46, 135.85, 130.23, 129.18, 128.54, 127.86, 125.72, 121.20, 120.14, 103.24, 92.35, 90.57, 63.86, 61.99, 55.21, 54.89, 14.08;

HRMS (ESI): C₂₆H₂₄BrNO₄ Neutral mass: 493.08887, Observed neutral mass: 493.0894, Observed ([M+Na]⁺): 516.0787;

IR: 3381.27, 3081.58, 1720.51, 1618.58, 1246.22, 1092.14, 1075.34, 1198.86, 538.27.



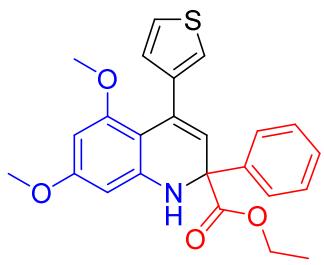
20) **4t** Yellow oil (106.9 mg, 85%);

1H NMR (400 MHz, CDCl₃) δ 7.51 (d, *J* = 7.4 Hz, 2H), 7.33 (t, *J* = 7.4 Hz, 2H), 7.28 (d, *J* = 6.8 Hz, 1H), 6.27 (d, *J* = 3.0 Hz, 1H), 6.23 (s, 1H), 6.04 (d, *J* = 2.2 Hz, 1H), 6.00 (d, *J* = 2.8 Hz, 1H), 5.93 (d, *J* = 2.2 Hz, 1H), 5.31 (s, 1H), 4.25 (qd, *J* = 7.1, 2.9 Hz, 2H), 3.80 (s, 3H), 3.60 (s, 3H), 2.33 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H);

13C NMR (101 MHz, CDCl₃) δ 172.70, 161.63, 158.13, 152.75, 150.68, 145.01, 142.48, 128.48, 127.84, 126.73, 125.91, 120.48, 107.39, 106.42, 102.68, 98.33, 92.34, 90.75, 63.51, 62.00, 55.56, 55.20, 14.07, 13.67;

HRMS (ESI): C₂₅H₂₅NO₅ Neutral mass: 419.17327, Observed neutral mass: 419.1732, Observed ([M+H]⁺): 420.1805;

IR: 3384.27, 3142.61, 3081.58, 1722.11, 1618.58, 1246.22, 1092.14, 1078.04, 1173.86.



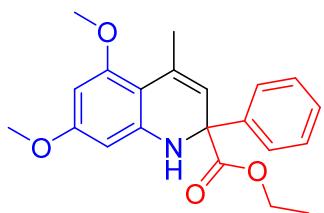
21) **4u** Yellow solid (93.5 mg, 74%); M.p. 128-130 °C;

1H NMR (400 MHz, CDCl₃) δ 7.52 (d, J = 7.6 Hz, 2H), 7.34 (t, J = 7.5 Hz, 2H), 7.28 (d, J = 3.8 Hz, 1H), 7.21 (d, J = 5.2 Hz, 2H), 6.98 (d, J = 4.7 Hz, 1H), 6.05 (s, 2H), 5.87 (s, 1H), 5.28 (s, 1H), 4.25 (q, J = 7.2 Hz, 2H), 3.81 (s, 3H), 3.43 (s, 3H), 1.27 (t, J = 5.4 Hz, 3H);

13C NMR (101 MHz, CDCl₃) δ 172.89, 161.48, 158.15, 144.97, 143.07, 142.77, 131.67, 128.58, 128.52, 127.83, 125.81, 123.09, 121.15, 120.48, 120.19, 115.46, 103.71, 92.24, 90.60, 55.19, 14.09;

HRMS (ESI): C₂₄H₂₃NO₄S Neutral mass: 421.13478, Observed neutral mass: 421.1349, Observed ([M+H]⁺): 422.1422;

IR: 3381.27, 3081.58, 3071.33, 1720.51, 1618.58, 1246.22, 1092.14, 1075.34, 1198.86.



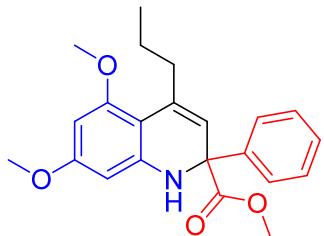
22) **4v** Yellow oil (45.6mg, 43%);

1H NMR (400 MHz, CDCl₃) δ 7.46 (d, J = 7.3 Hz, 2H), 7.34 (t, J = 7.7 Hz, 2H), 7.28 (d, J = 6.7 Hz, 1H), 5.93 (d, J = 2.2 Hz, 1H), 5.88 (d, J = 2.1 Hz, 1H), 5.70 (s, 1H), 5.08 (s, 1H), 4.24 (pd, J = 7.6, 3.7 Hz, 2H), 3.78 (s, 3H), 3.75 (s, 3H), 2.27 (s, 3H), 1.27 (t, J = 7.1 Hz, 3H);

13C NMR (101 MHz, CDCl₃) δ 173.34, 160.88, 159.03, 144.59, 143.82, 132.01, 128.50, 127.59, 125.59, 117.99, 104.04, 91.79, 90.12, 64.05, 61.71, 55.20, 55.14, 23.29, 14.09;

HRMS (ESI): C₂₁H₂₃NO₄ Neutral mass: 353.16271, Observed neutral mass: 353.1626, Observed ([M+H]⁺): 354.1699;

IR: 3381.27, 3081.58, 1720.51, 1618.58, 1246.22, 1092.14, 1075.34, 1198.86.



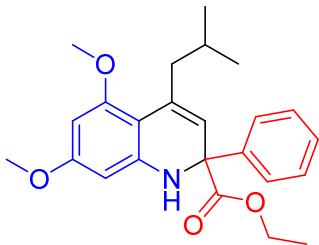
23) **4w** Yellow oil (52.6mg, 46%);

¹H NMR (400 MHz, CDCl₃) δ 7.46 (d, *J* = 7.2 Hz, 2H), 7.34 (t, *J* = 7.4 Hz, 2H), 7.29 (s, 1H), 5.93 (d, *J* = 2.3 Hz, 1H), 5.88 (d, *J* = 2.3 Hz, 1H), 5.73 (s, 1H), 5.07 (s, 1H), 4.24 (dt, *J* = 7.1, 5.8 Hz, 2H), 3.77 (d, *J* = 7.7 Hz, 7H), 2.67 – 2.60 (m, 2H), 1.57 – 1.41 (m, 3H), 1.26 (t, *J* = 7.1 Hz, 4H), 0.94 (t, *J* = 7.4 Hz, 3H);

¹³C NMR (101 MHz, CDCl₃) δ 173.43, 160.71, 158.51, 145.05, 143.73, 136.11, 128.45, 127.57, 125.71, 118.22, 92.05, 90.09, 63.94, 61.65, 55.12, 38.23, 22.84, 14.08;

HRMS (ESI): C₂₃H₂₇NO₄ Neutral mass: 381.19401, Observed neutral mass: 381.1944, Observed ([M+H]⁺): 382.2016;

IR: 3381.17, 3071.58, 1721.51, 1618.58, 1246.22, 1092.14, 1075.34, 1198.86.



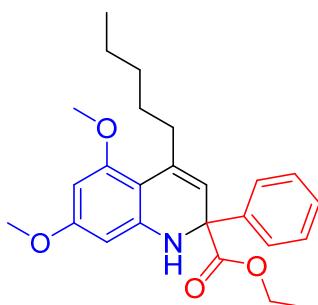
24) **4x** Yellow oil (47.4mg, 40%);

¹H NMR (400 MHz, CDCl₃) δ 7.47 (d, *J* = 7.4 Hz, 2H), 7.35 (t, *J* = 7.5 Hz, 2H), 7.29 (t, *J* = 3.5 Hz, 1H), 5.93 (d, *J* = 2.2 Hz, 1H), 5.88 (d, *J* = 2.2 Hz, 1H), 5.66 (s, 1H), 5.04 (s, 1H), 4.24 (qd, *J* = 7.1, 1.9 Hz, 2H), 3.77 (d, *J* = 7.0 Hz, 6H), 2.51 (d, *J* = 6.6 Hz, 2H), 1.84 – 1.69 (m, 1H), 1.26 (t, *J* = 7.2 Hz, 3H), 0.90 (d, *J* = 6.6 Hz, 6H);

¹³C NMR (101 MHz, CDCl₃) δ 173.60, 160.70, 158.49, 145.19, 143.83, 134.82, 128.46, 127.59, 125.80, 119.48, 106.72, 103.18, 92.00, 90.04, 64.15, 61.61, 55.10, 45.69, 27.41, 22.63, 22.45, 14.08;

HRMS (ESI): C₂₄H₂₉NO₄ Neutral mass: 395.20966, Observed neutral mass: 395.2101, Observed ([M+Na]⁺): 418.1993;

IR: 3381.27, 3081.58, 1730.51, 1628.53, 1246.22, 1092.14, 1075.44, 1198.87.



25) **4y** Yellow oil (41.7mg, 34%);

¹H NMR (400 MHz, CDCl₃) δ 7.46 (d, *J* = 7.3 Hz, 2H), 7.34 (t, *J* = 7.4 Hz, 2H), 7.28 (d, *J* = 7.1 Hz, 1H), 5.94 (d, *J* = 2.3 Hz, 1H), 5.89 (d, *J* = 2.3 Hz, 1H), 5.74 (s, 1H), 5.07 (s, 1H), 4.24 (qd, *J* = 7.1, 1.9 Hz, 2H), ¹δ 3.77 (d, *J* = 9.4 Hz, 6H), 2.70 – 2.62 (m, 2H), 1.47 (dd, *J* = 14.2, 5.7 Hz, 2H), 1.34 (dd, *J* = 9.0, 5.3 Hz, 4H), 1.26 (t, *J* = 7.2 Hz, 3H), 0.91 (t, *J* = 6.9 Hz, 3H);

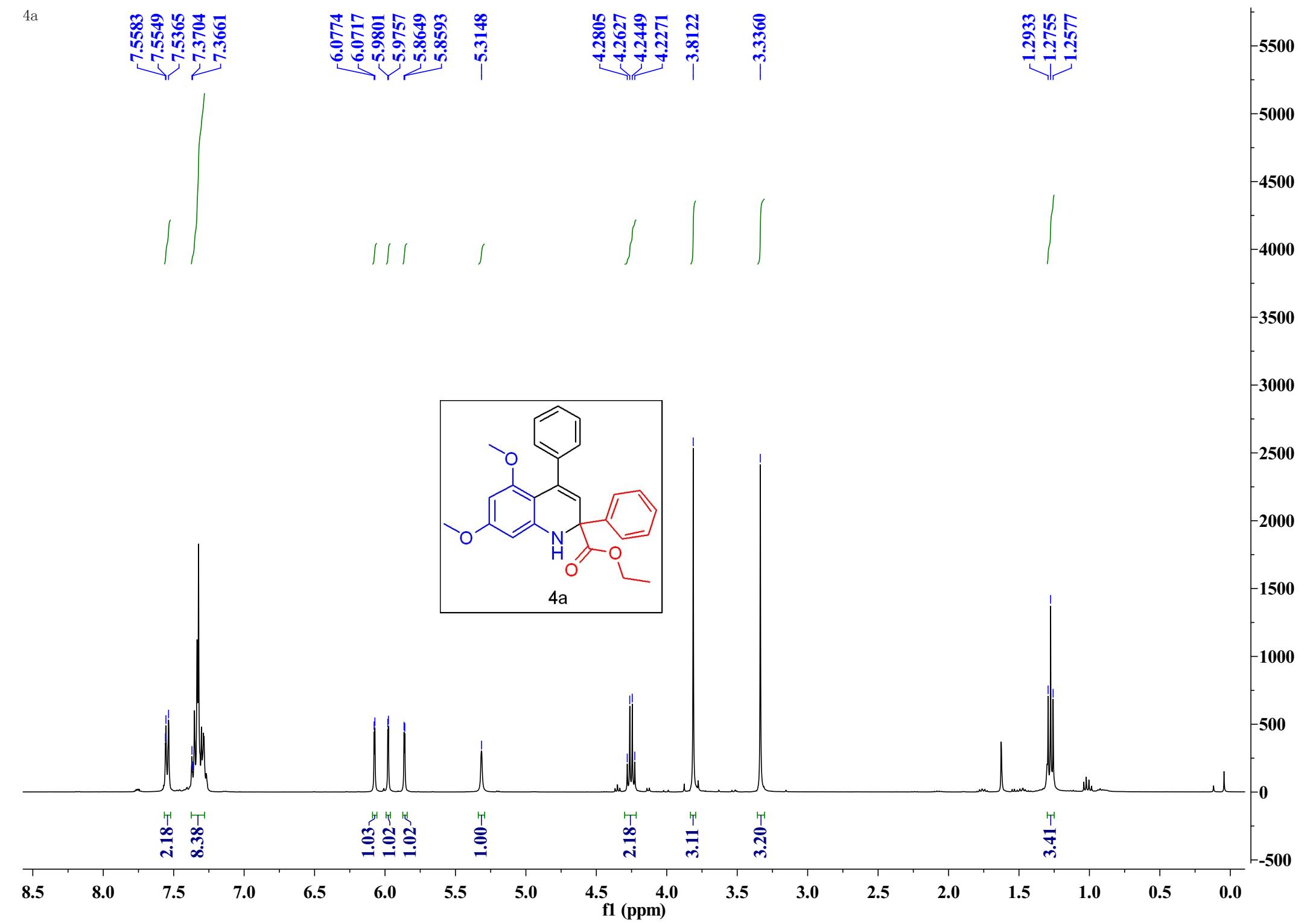
¹³C NMR (101 MHz, CDCl₃) δ 173.42, 160.71, 158.49, 145.05, 143.74, 136.45, 128.45, 127.57, 125.71, 118.03, 103.37, 63.93, 61.65, 55.10, 36.20, 32.01, 29.53, 22.60, 14.19, 14.08;

HRMS (ESI): C₂₅H₃₁NO₄ Neutral mass: 409.22531, Observed neutral mass: 409.2253, Observed ([M+H])⁺: 410.2326;

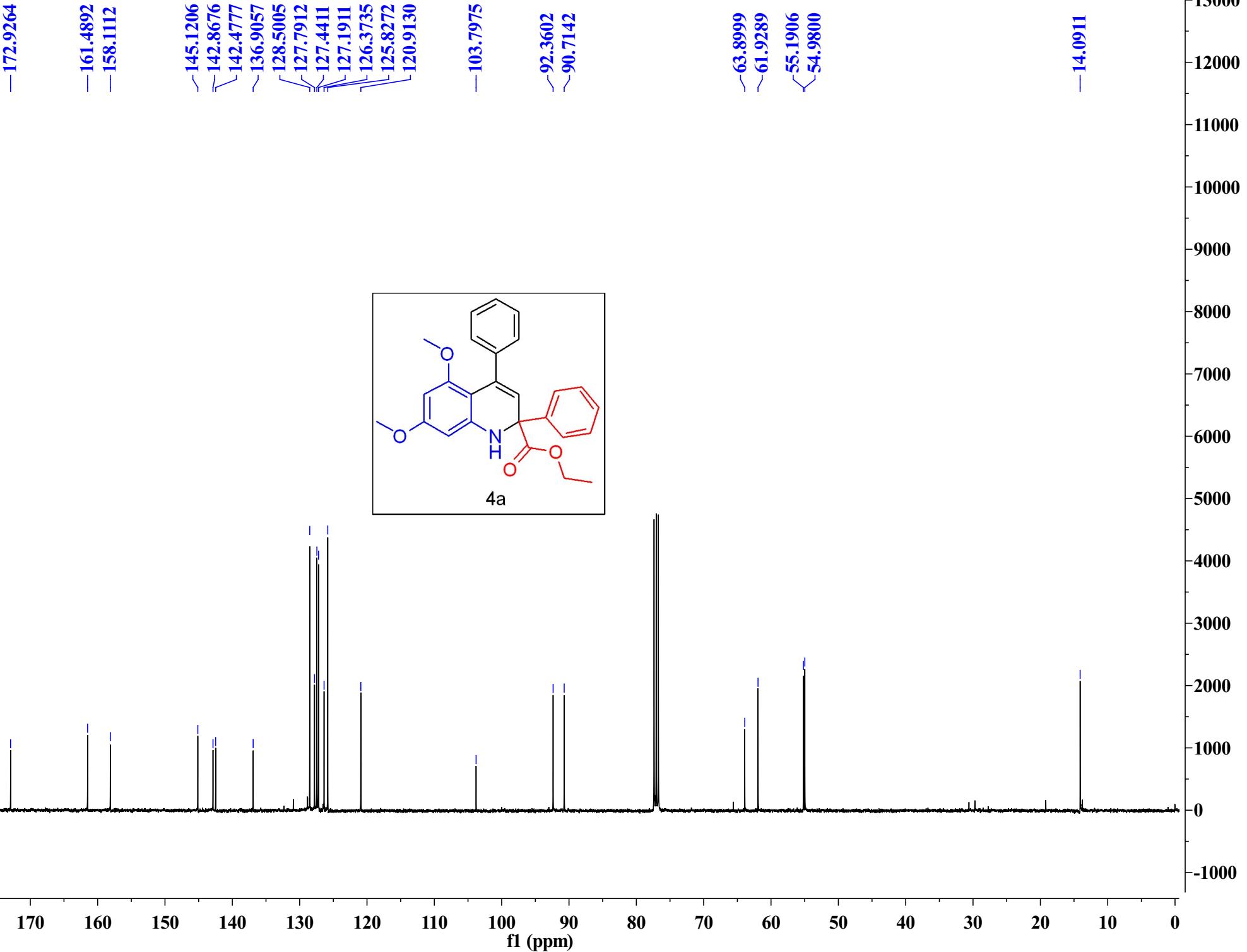
IR: 3378.27, 3081.58, 1720.11, 1618.58, 1246.22, 1092.19, 1075.34, 1198.86

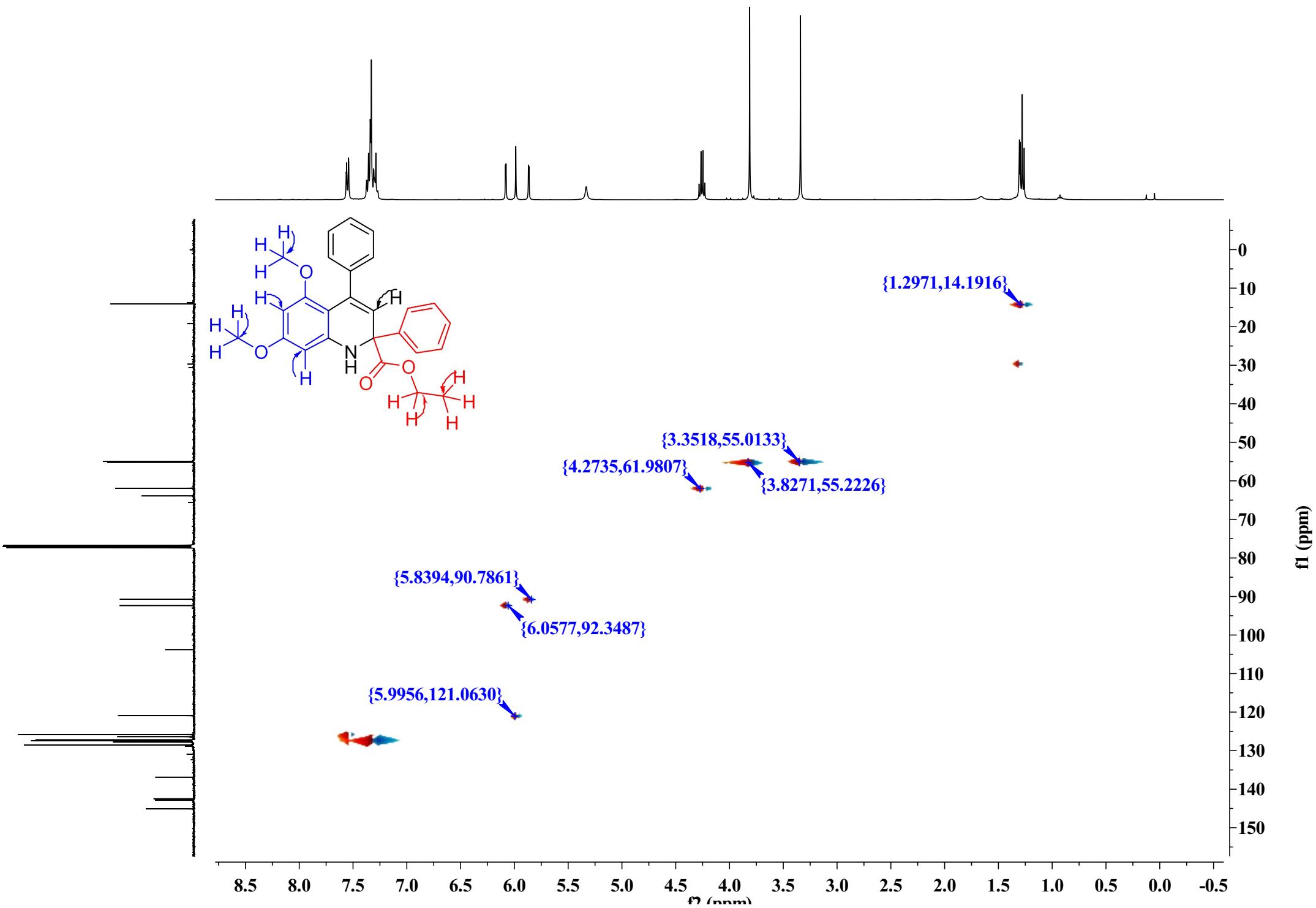
3. NMR spectrums

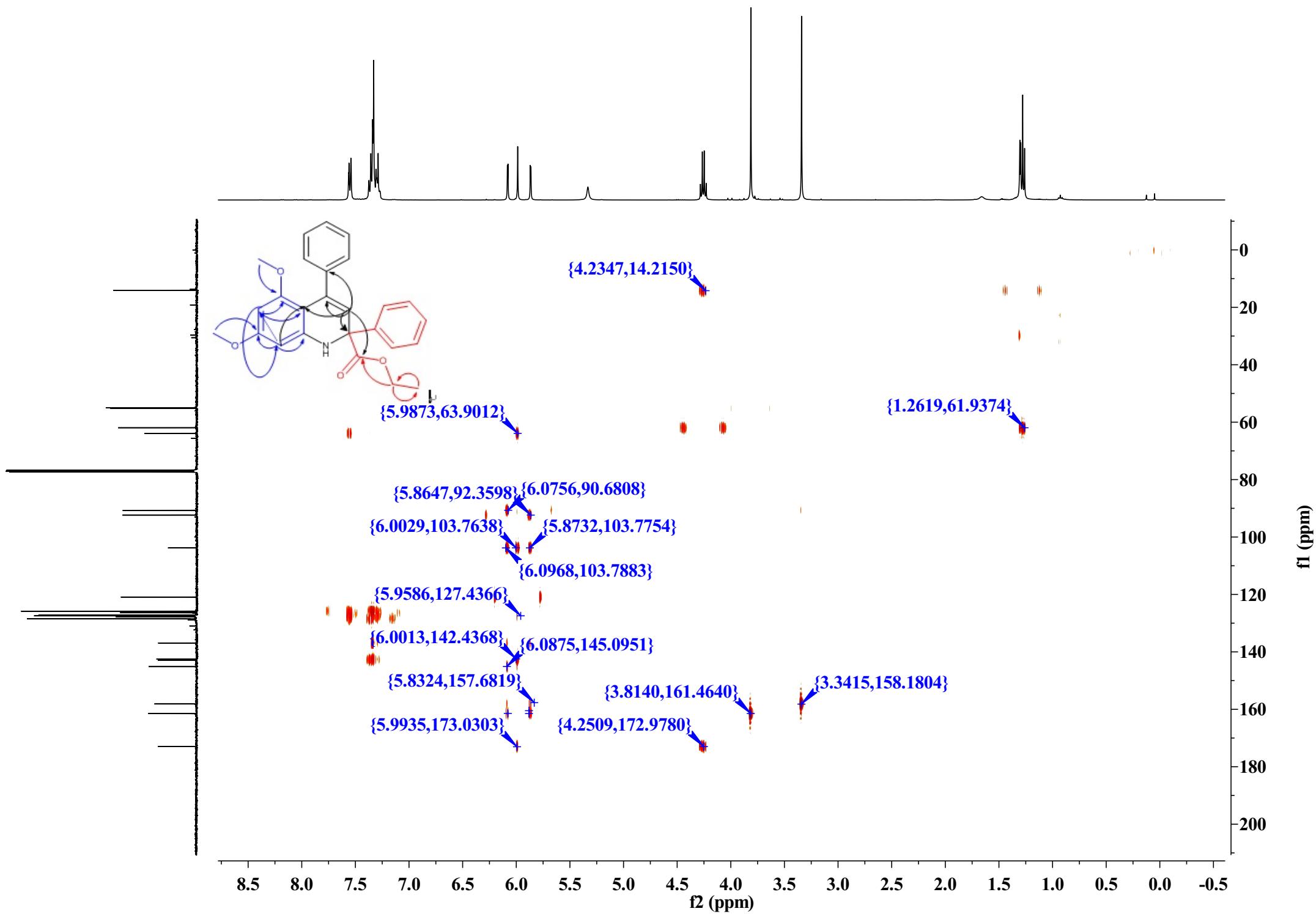
4a

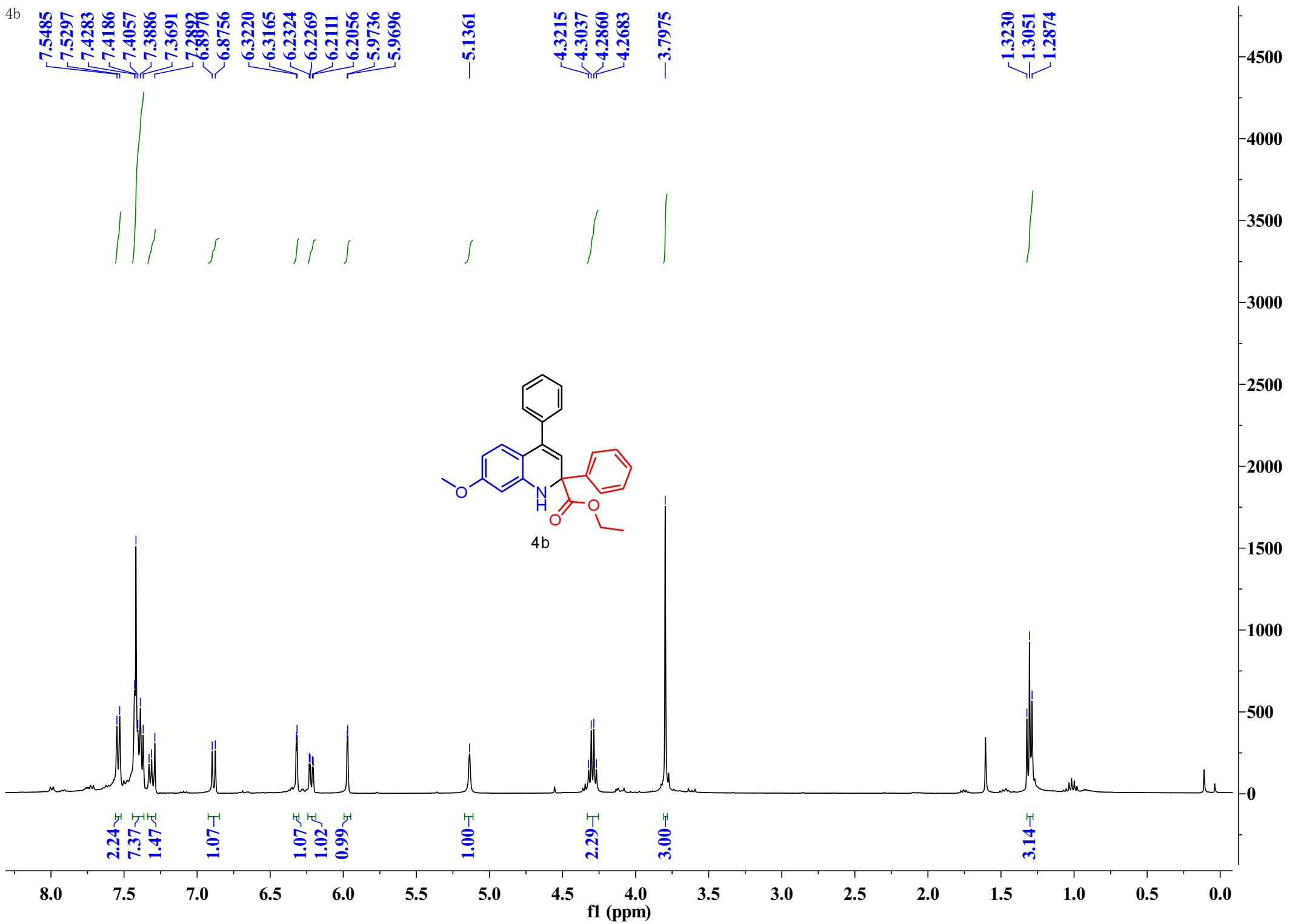


4a









4b

—173.1591

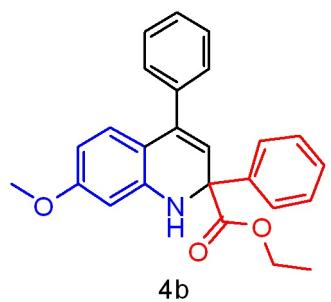
—160.8179

143.8336
143.4411
139.2525
137.6389
129.0010
128.7063
128.2135
127.8200
127.6273
127.5742
125.5550
119.7169
113.6586
—103.8651
—99.2339

—64.9053
—61.9150
—55.2018

—14.1519

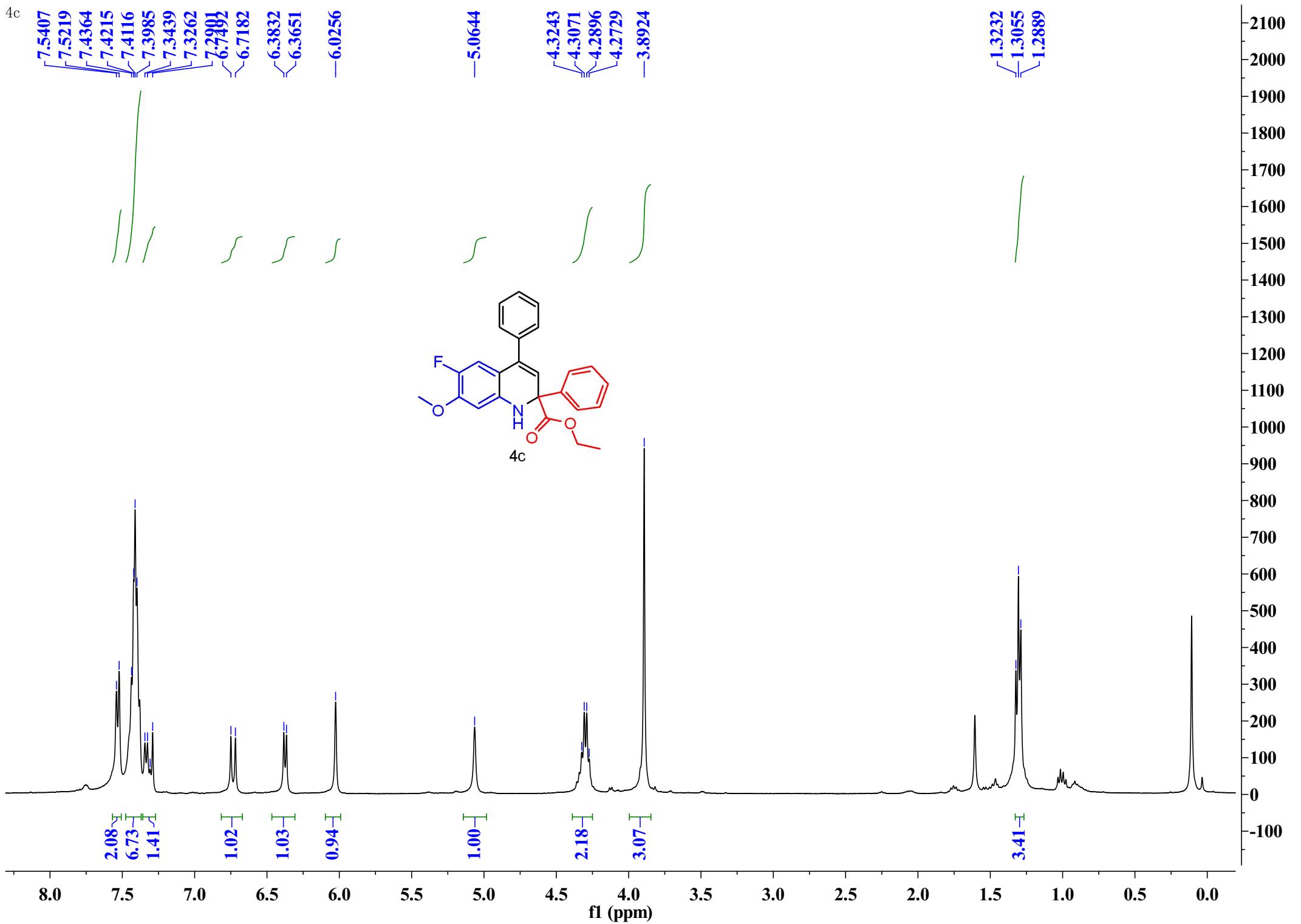
850
800
750
700
650
600
550
500
450
400
350
300
250
200
150
100
50
0
-50
-100



4b

180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

f1 (ppm)



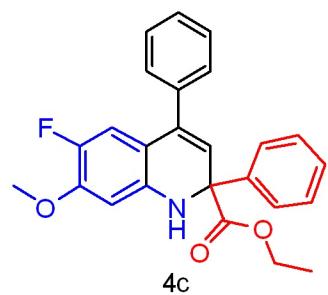
4c

—173.2153

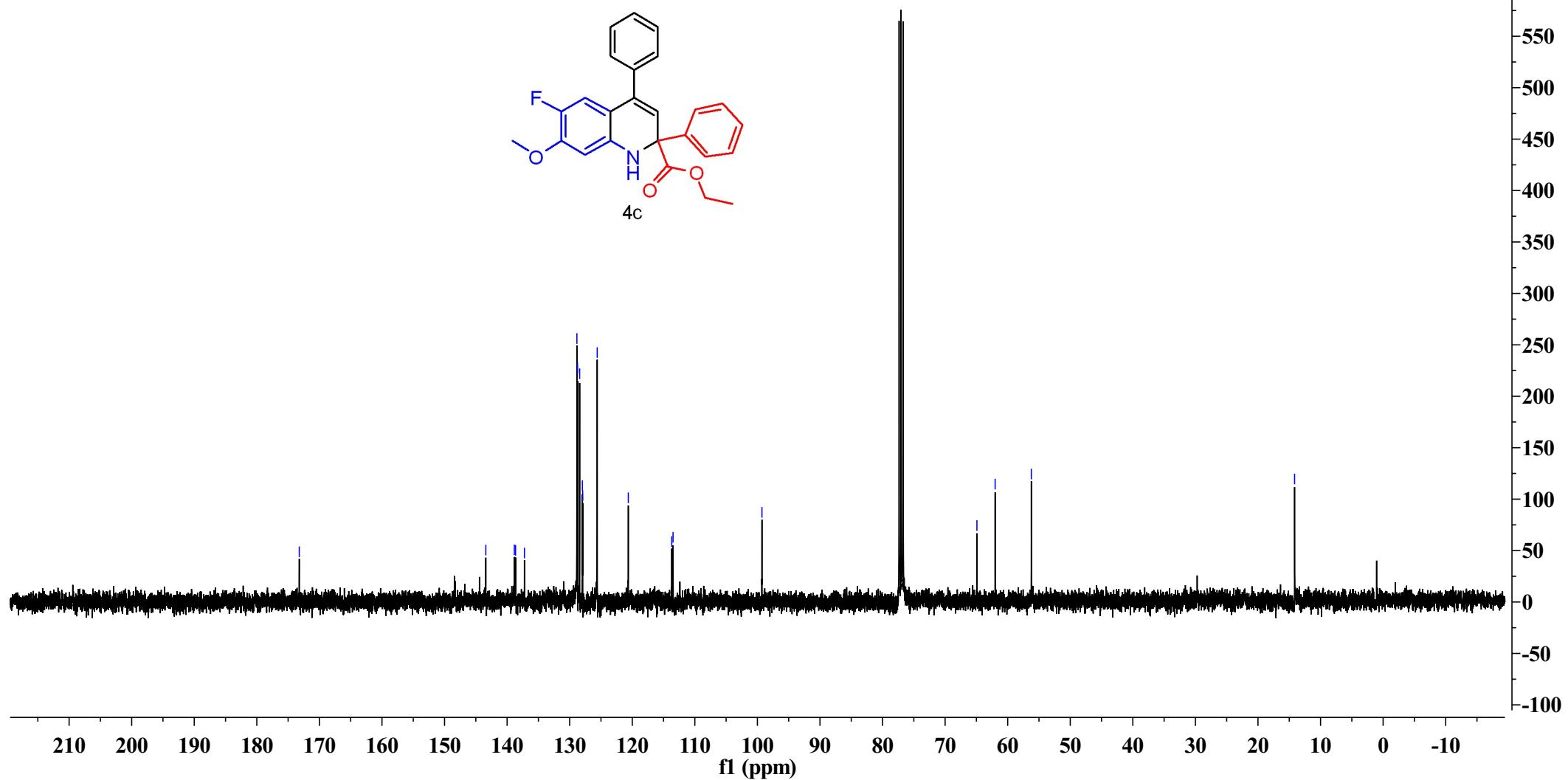
143.4030
138.8470
138.6500
137.2296

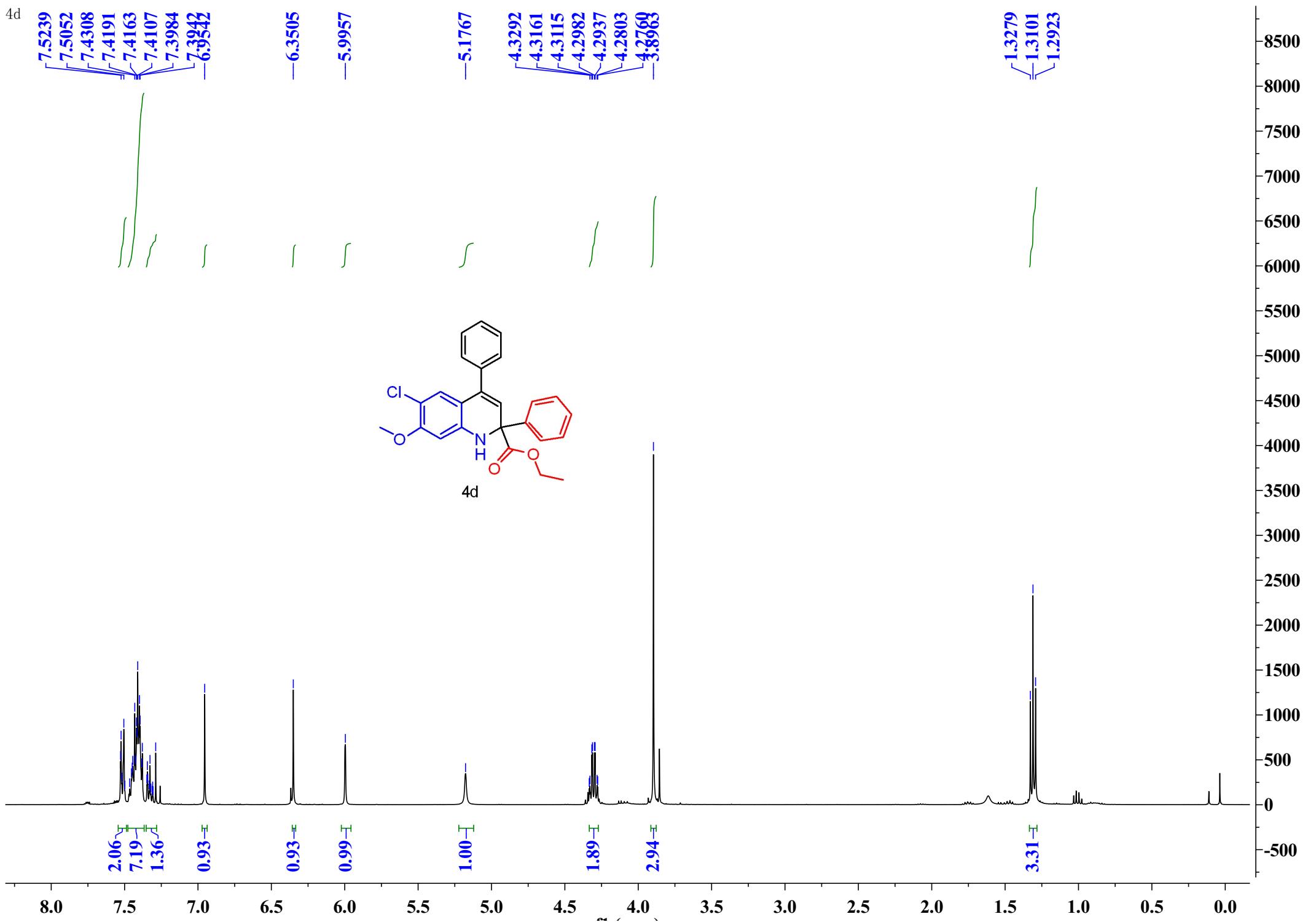
128.8451
128.7445
128.4064
127.9686
127.9195
125.6008
120.9395

—14.1513



4c





4d

-172.9955

-155.6808

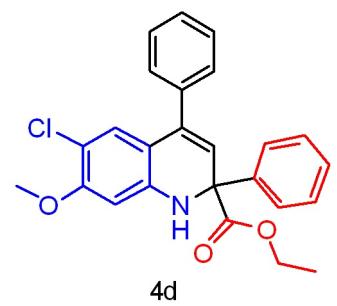
✓143.4473
—142.0482
—138.5608
~137.0010

128.8668
✓128.7976
—128.4466
—128.0157
—125.5871
~111.1305

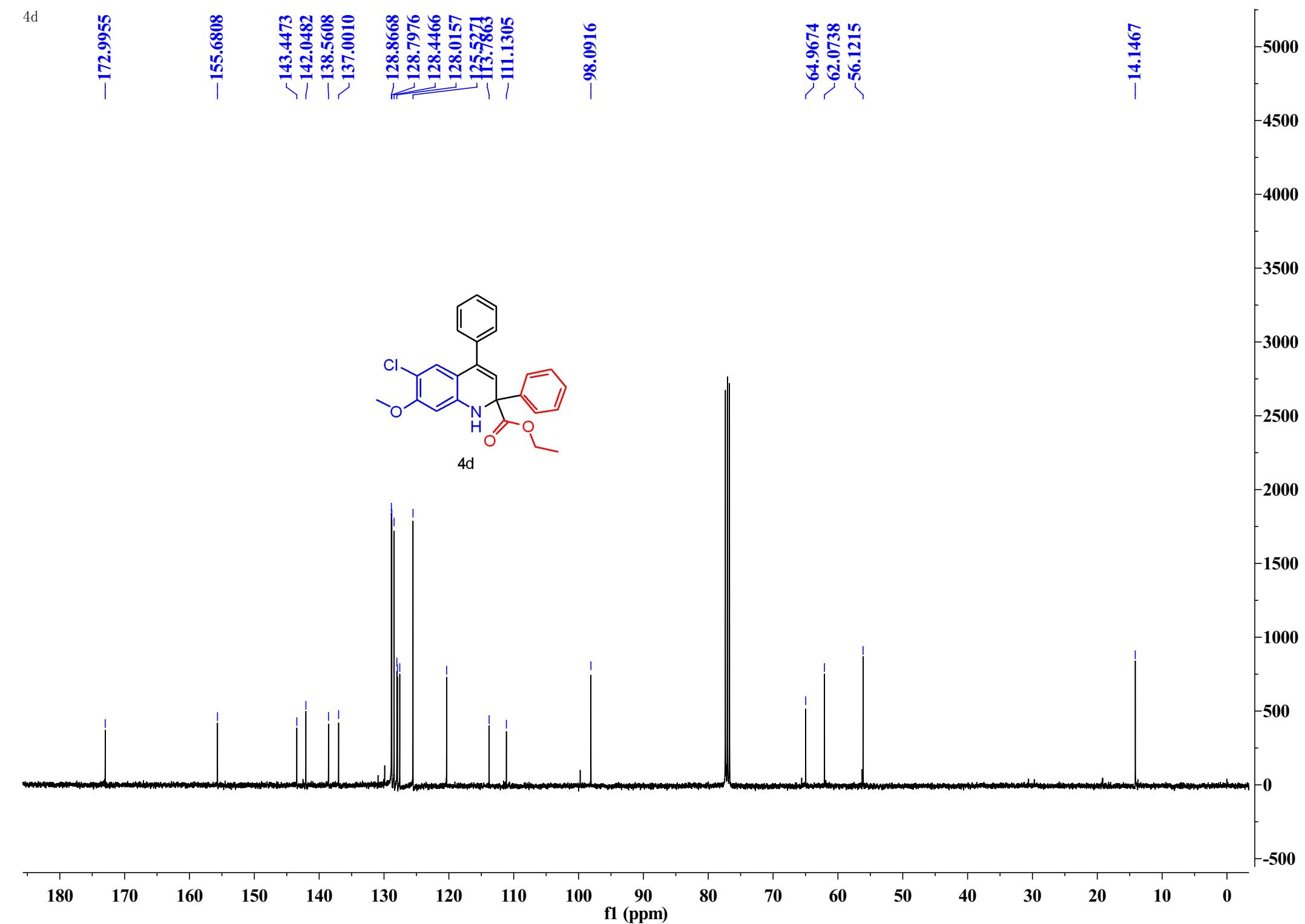
-98.0916

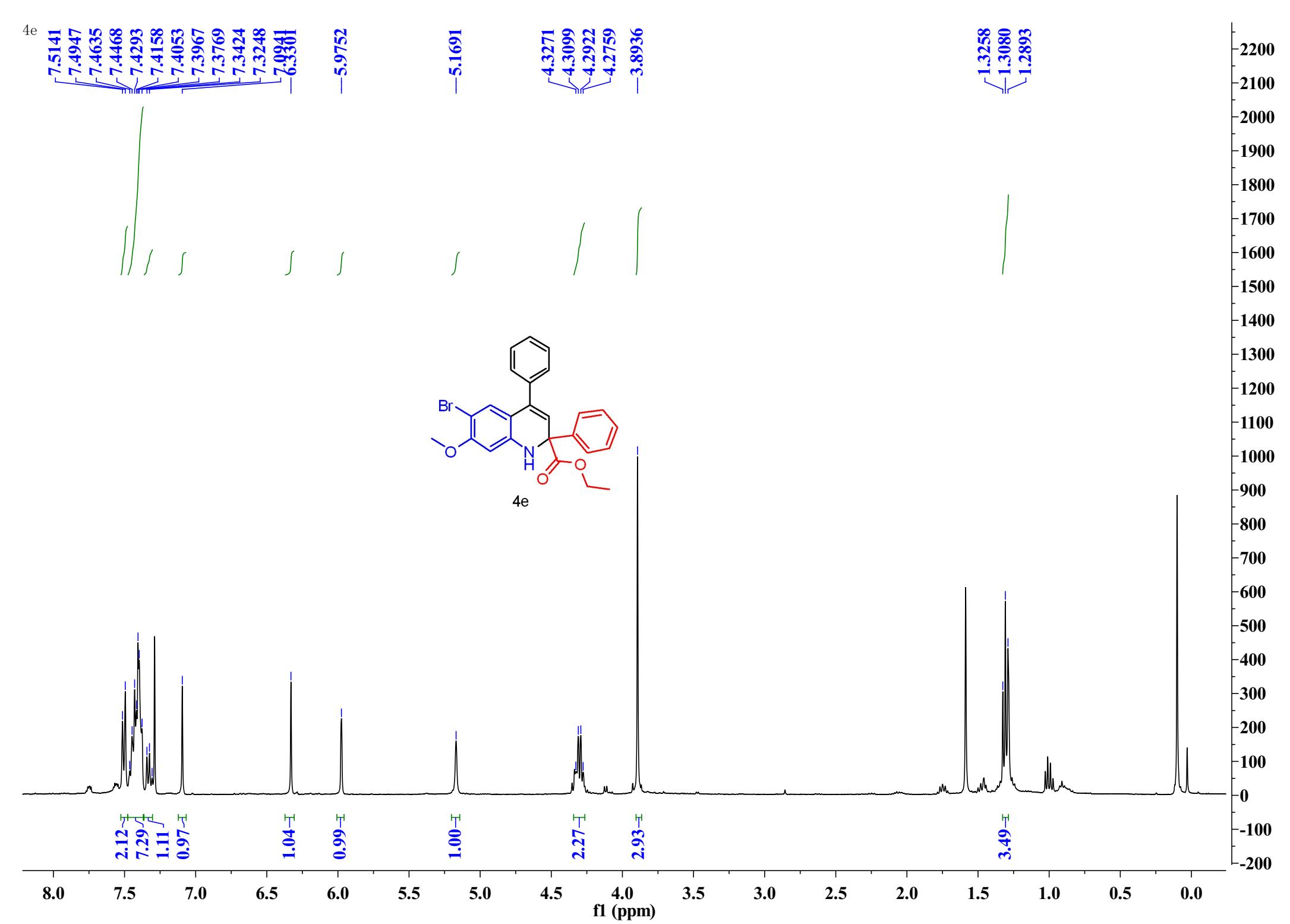
~64.9674
~62.0738
~56.1215

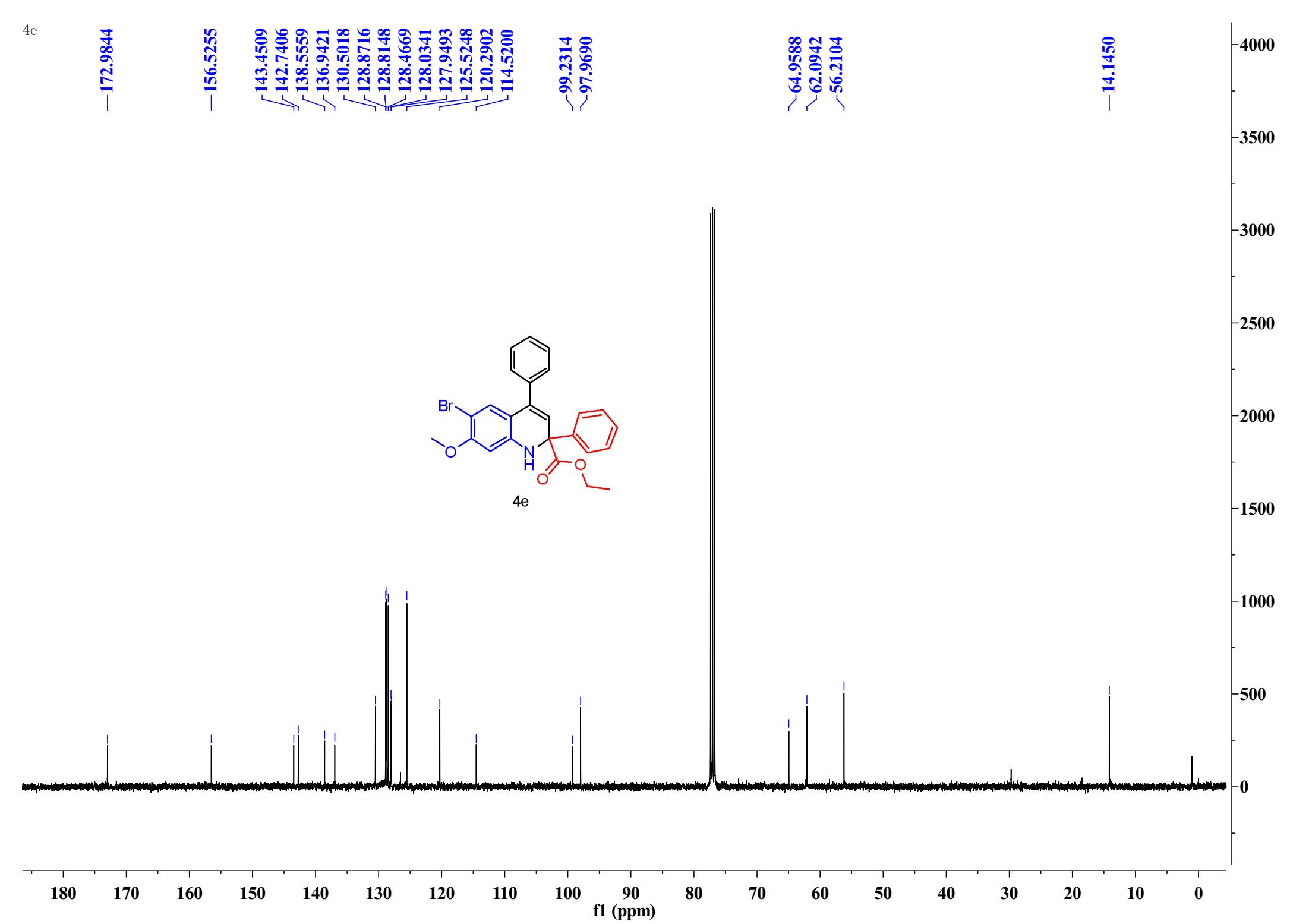
-14.1467



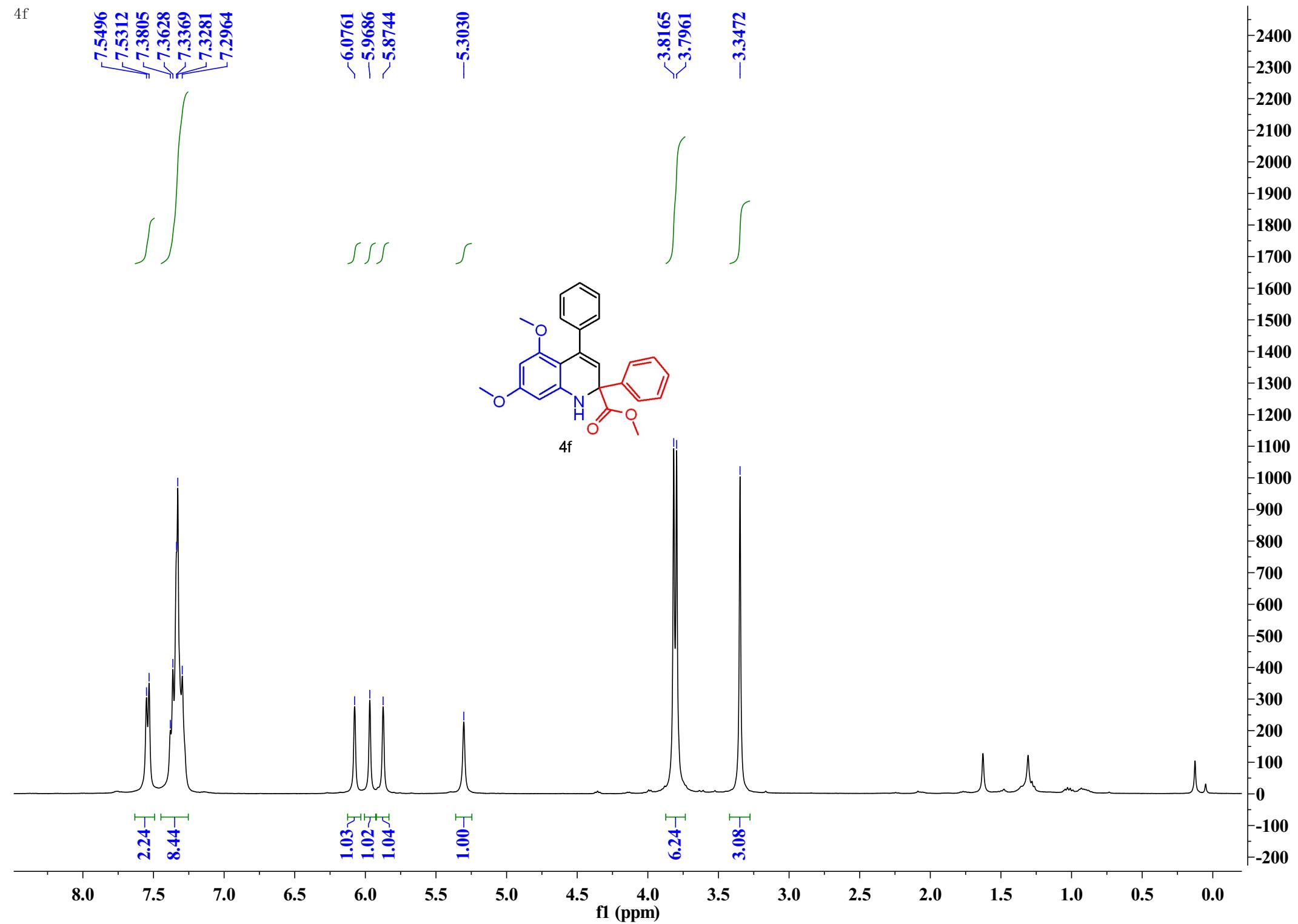
4d



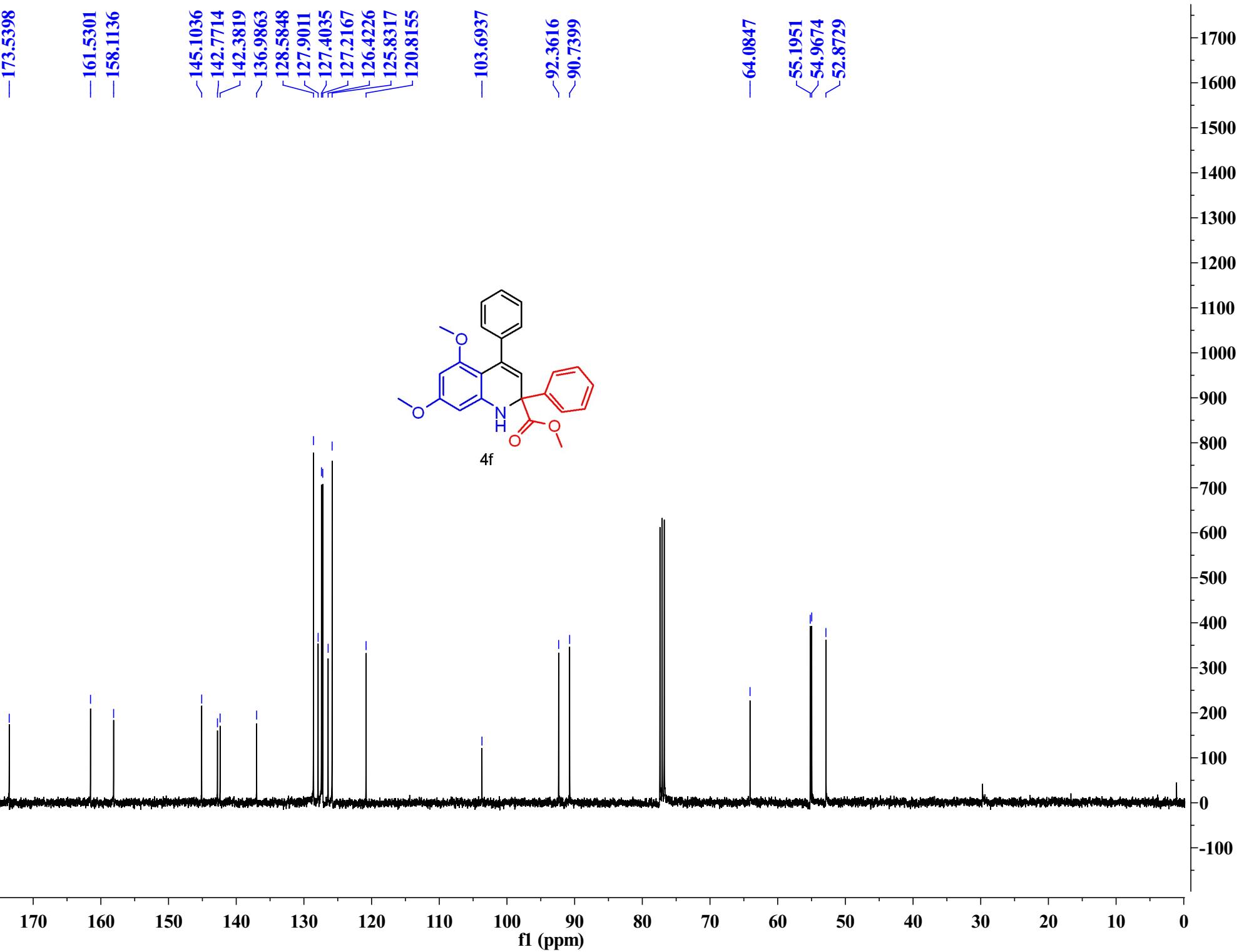


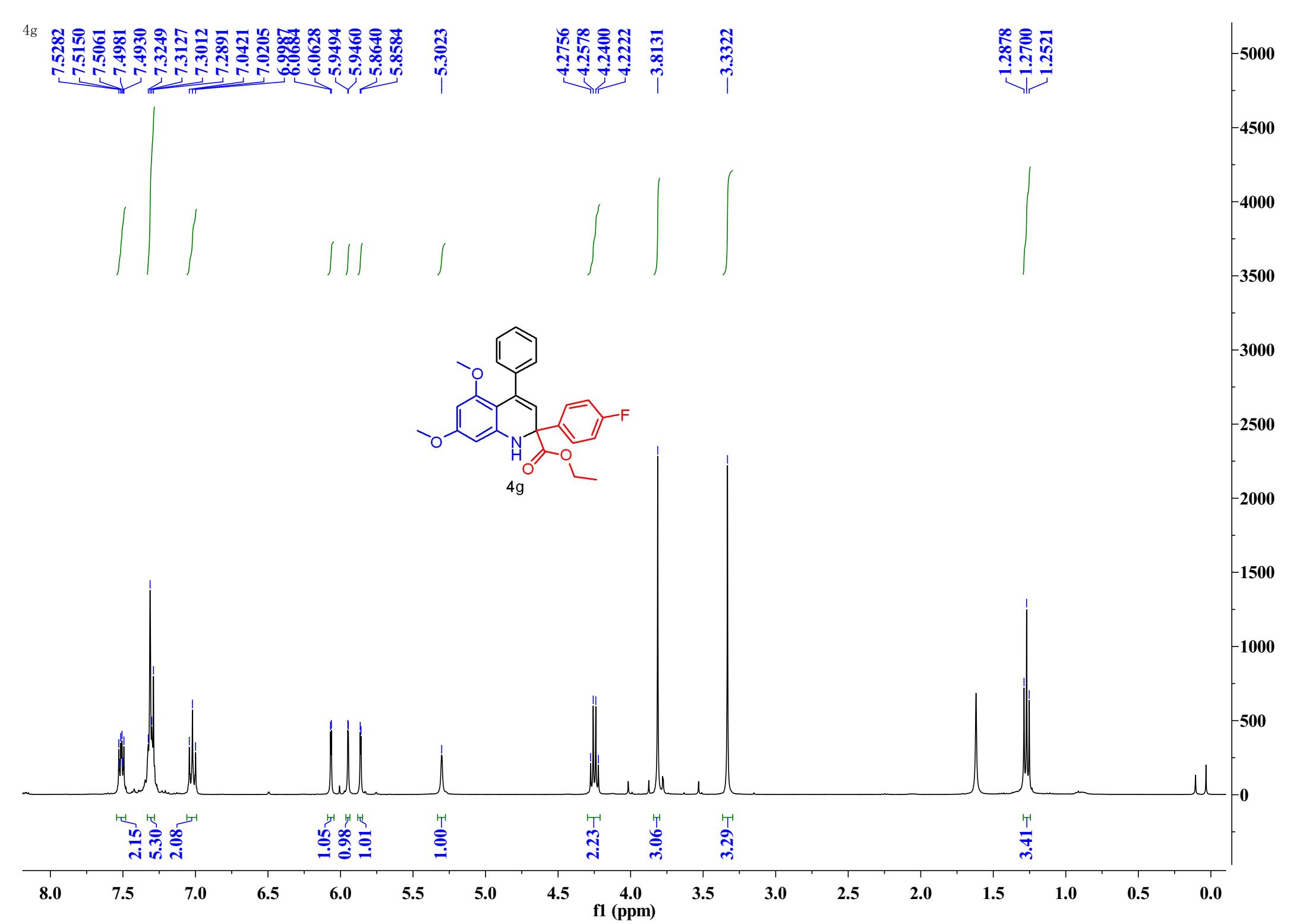


4f



4f





4g

—172.6739

—161.5879

—158.1609

144.8493

142.3134

138.6791

138.6479

137.1854

127.6880

127.6064

127.4003

127.2406

126.4759

120.4740

115.4455

115.2311

—103.8466

92.3848

~90.7821

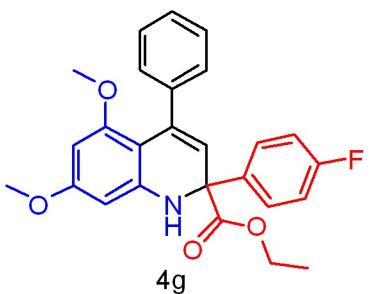
63.2861

~62.0706

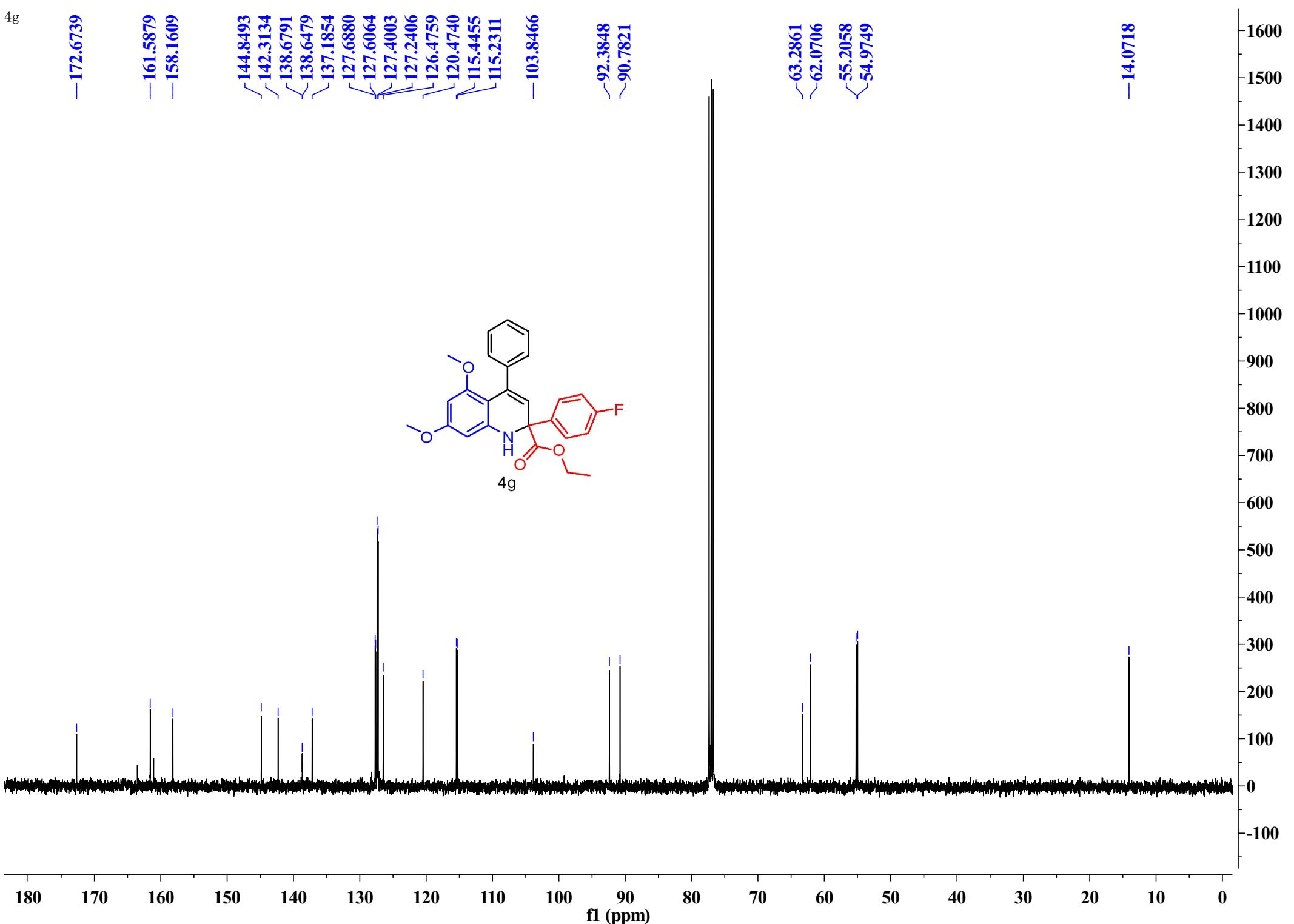
55.2058

~54.9749

—14.0718



4g



4h

7.4862
7.4649
7.3449
7.3112
7.2896

6.0699
6.0646
5.9499
5.9468
5.8607
5.8556

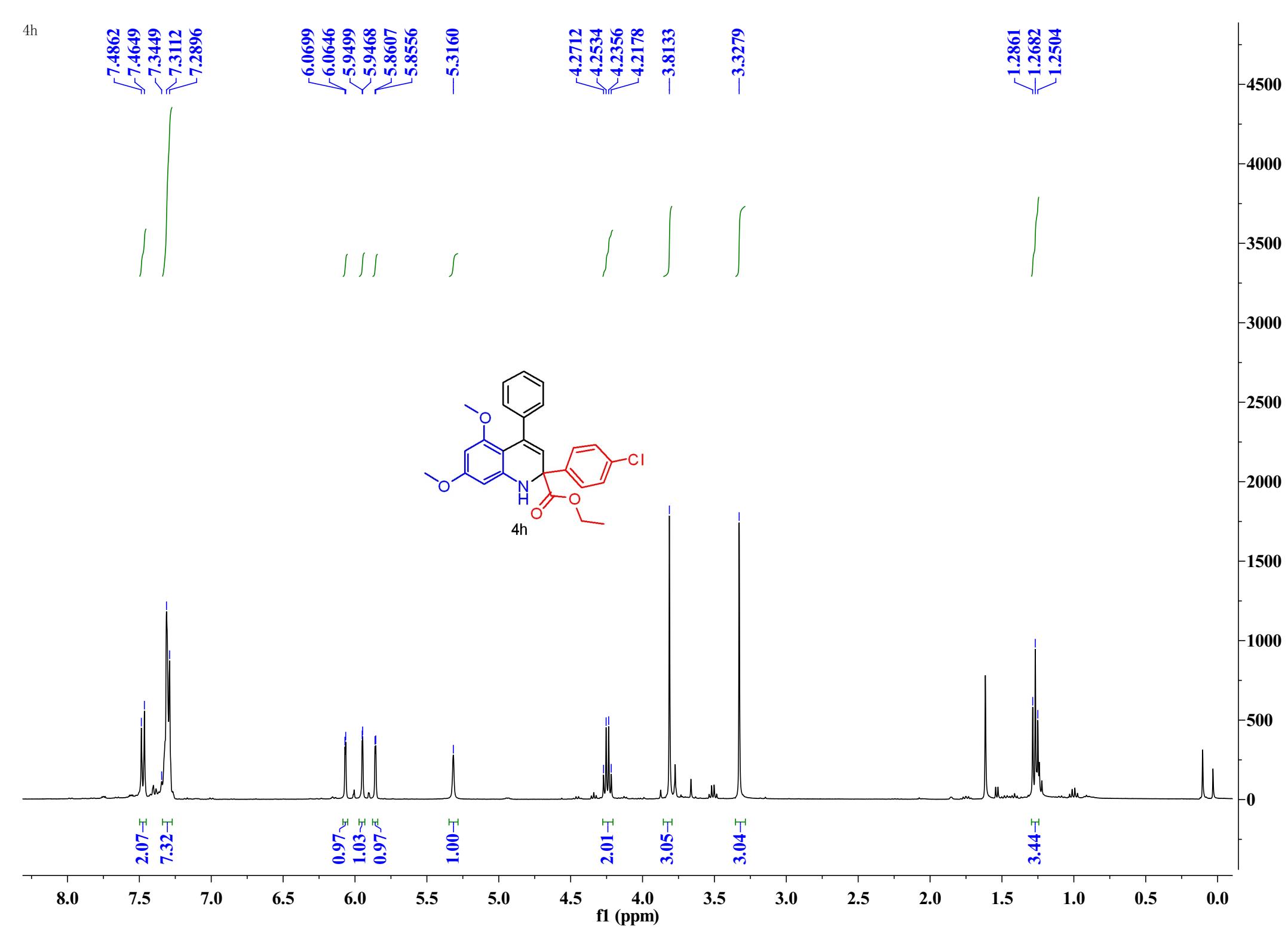
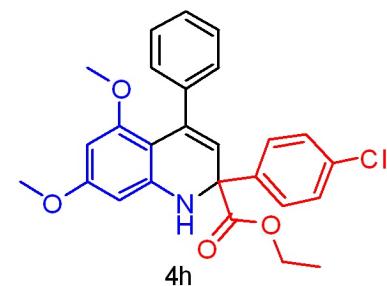
-5.3160

4.22712
4.2534
4.2356
4.2178

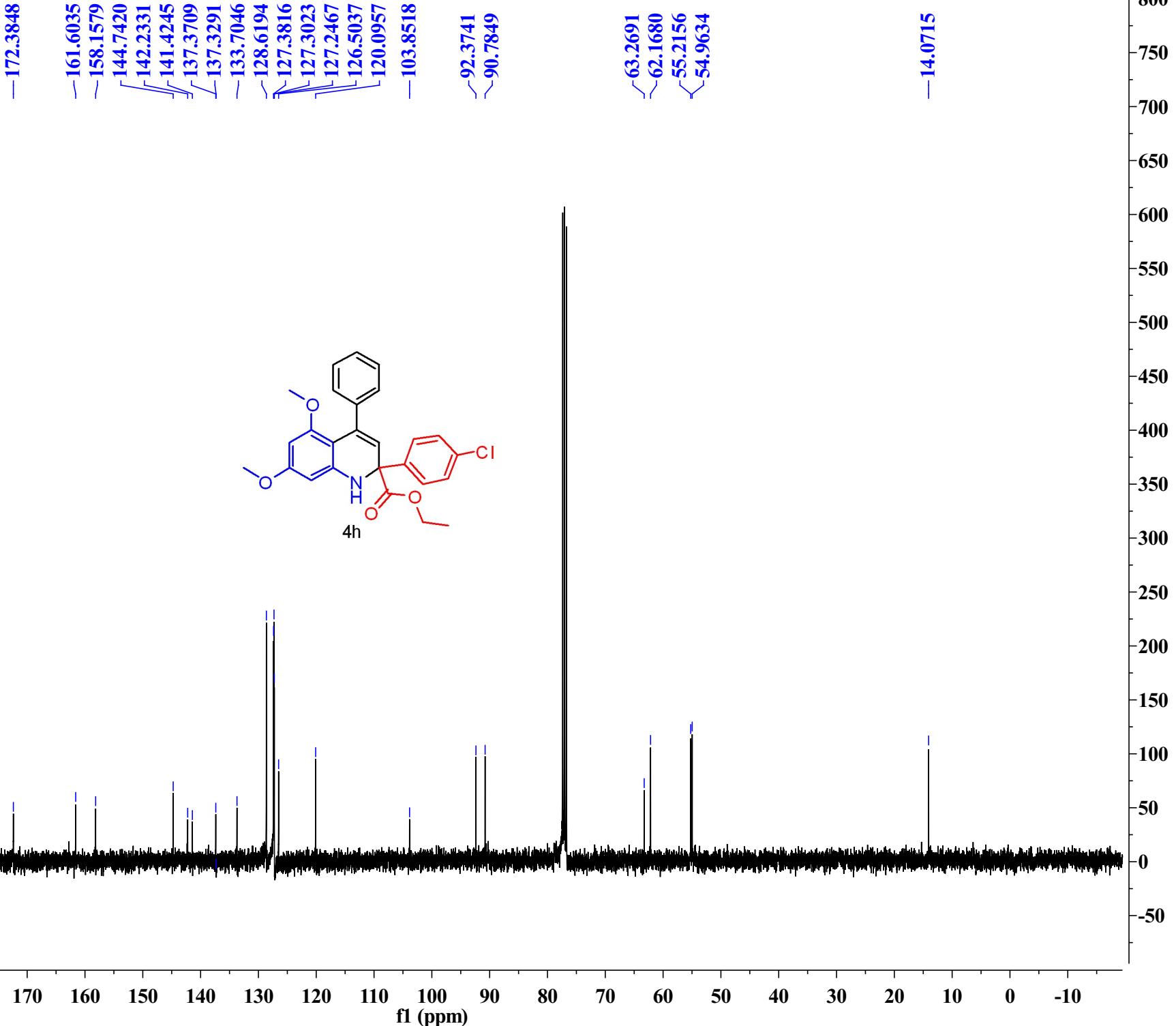
-3.8133

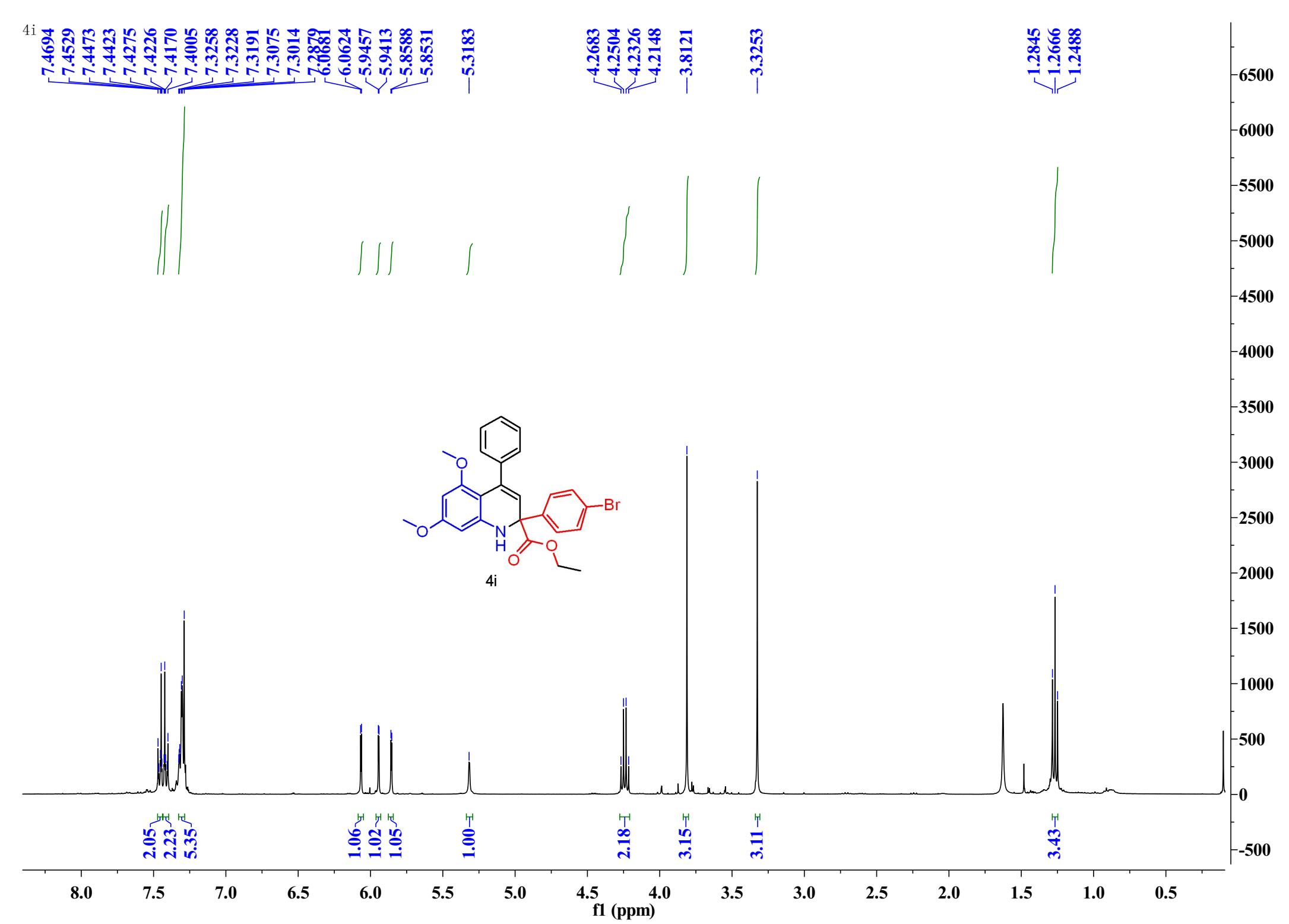
-3.3279

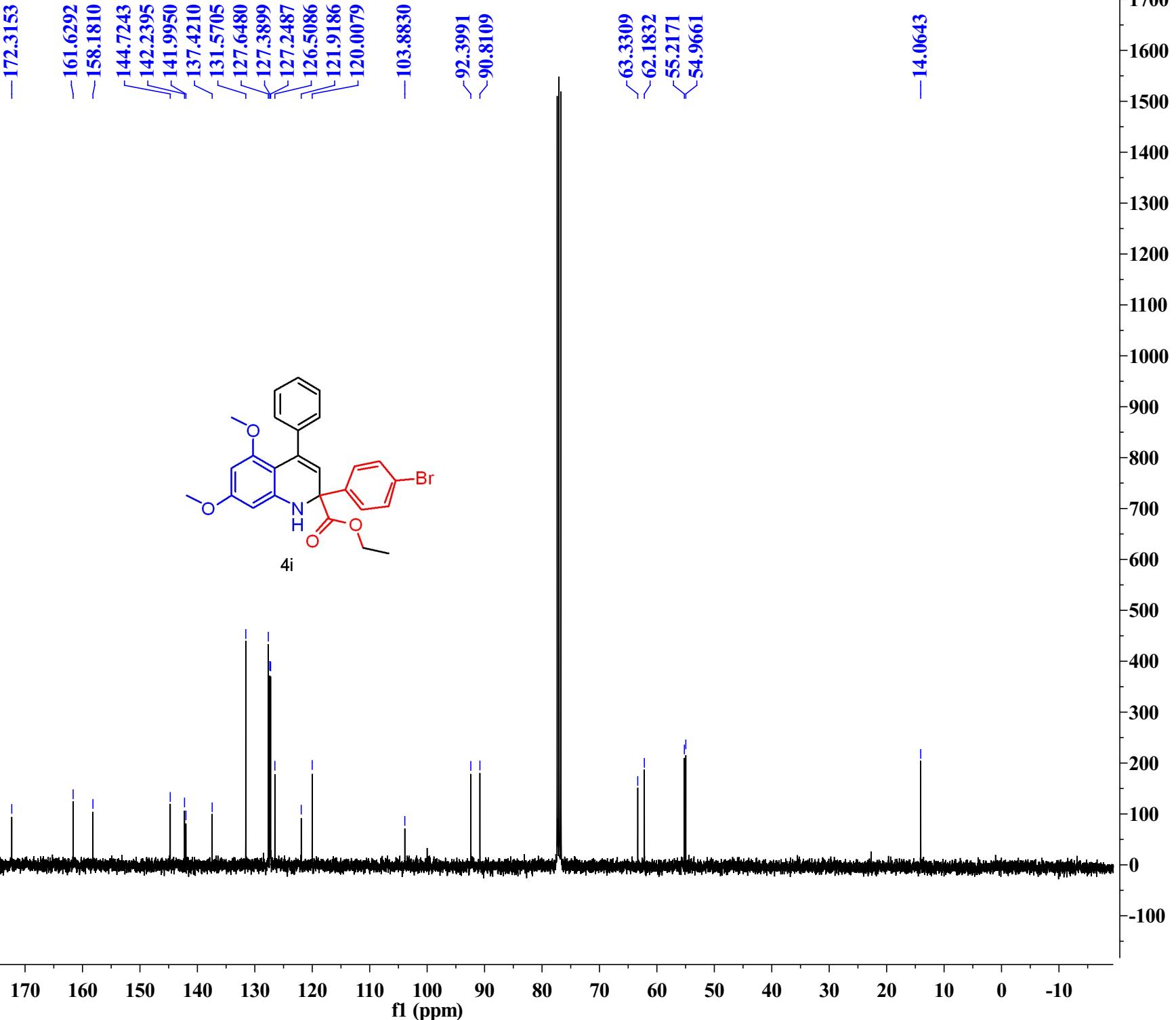
1.2861
1.2682
1.2504



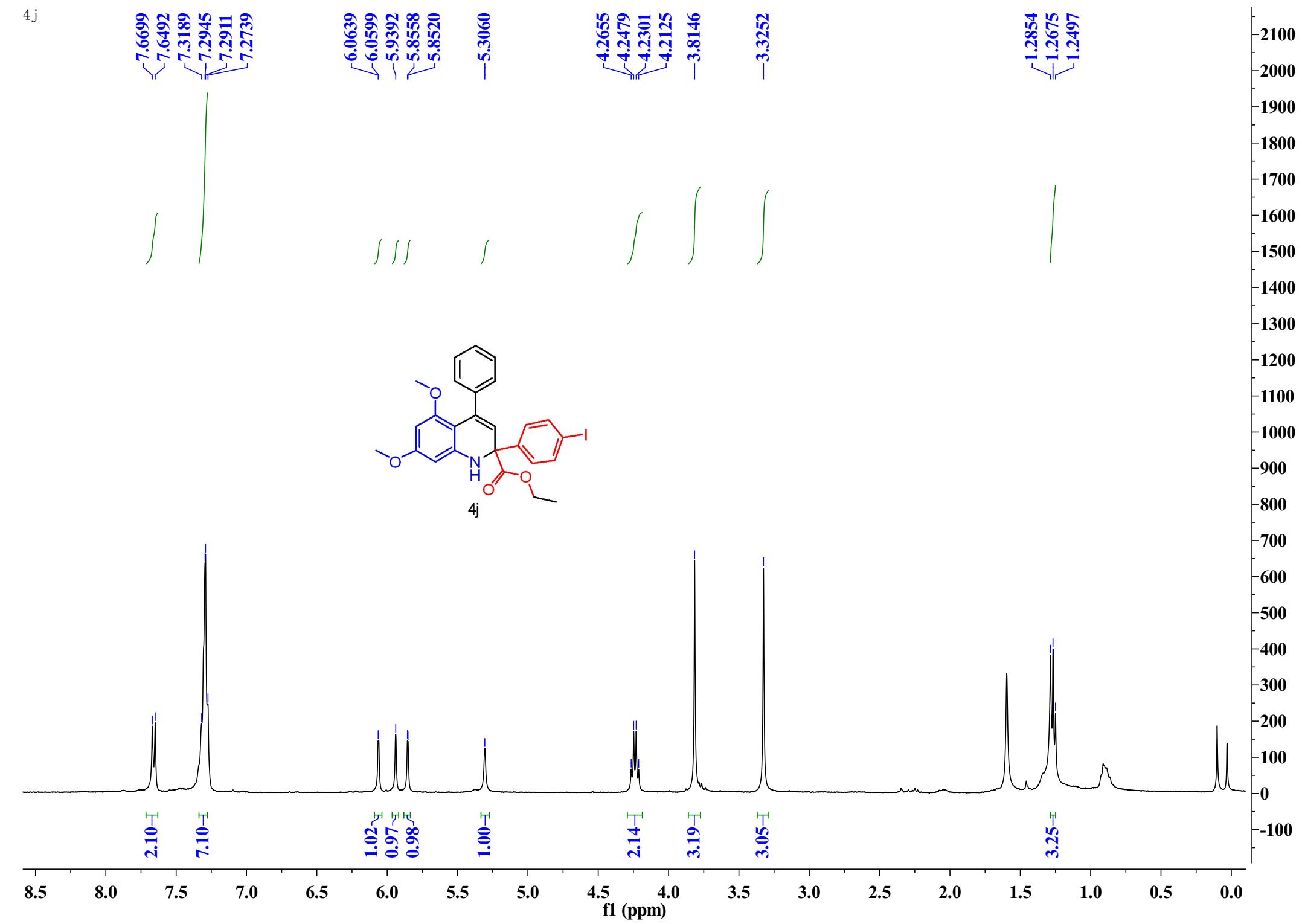
4h



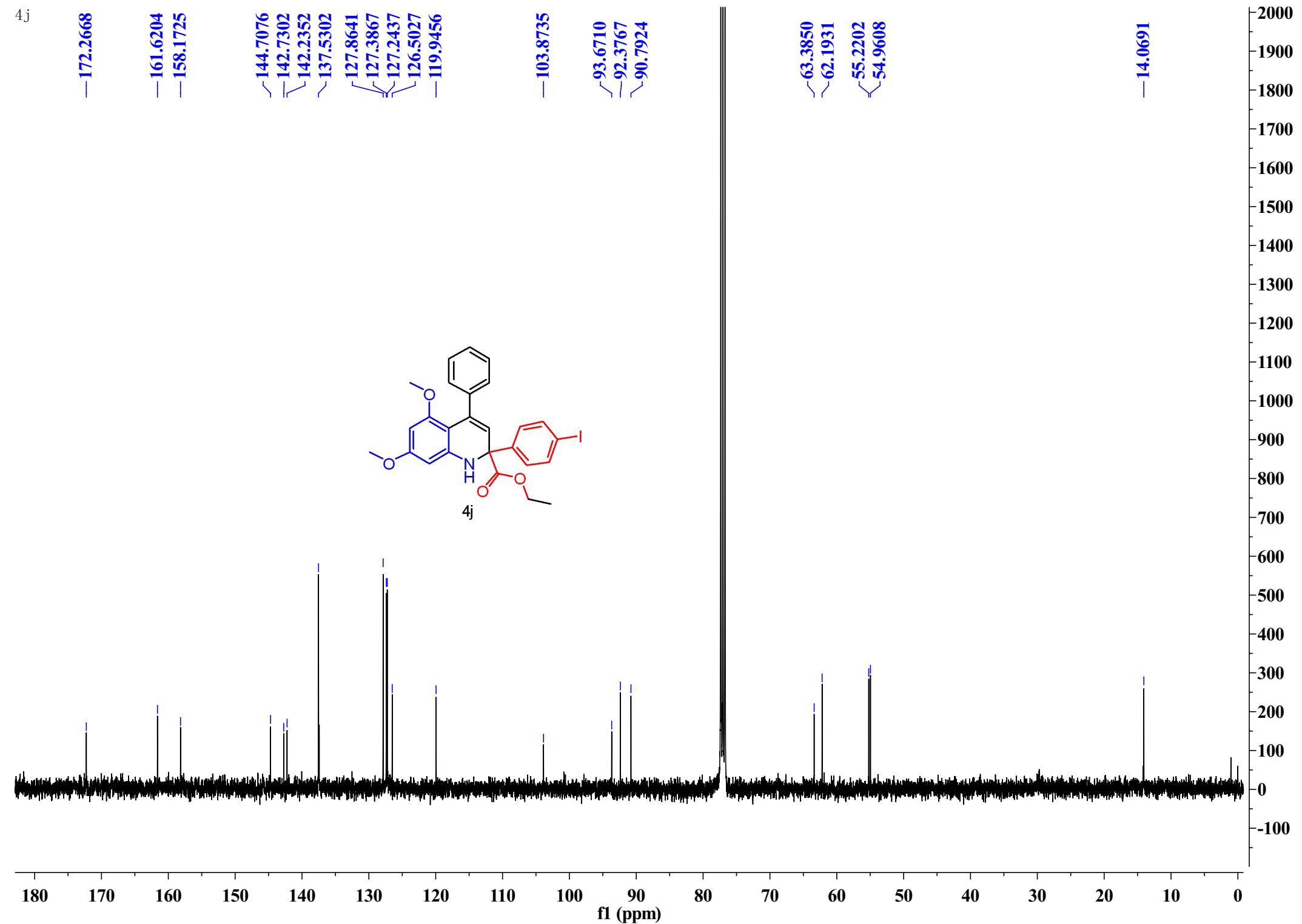


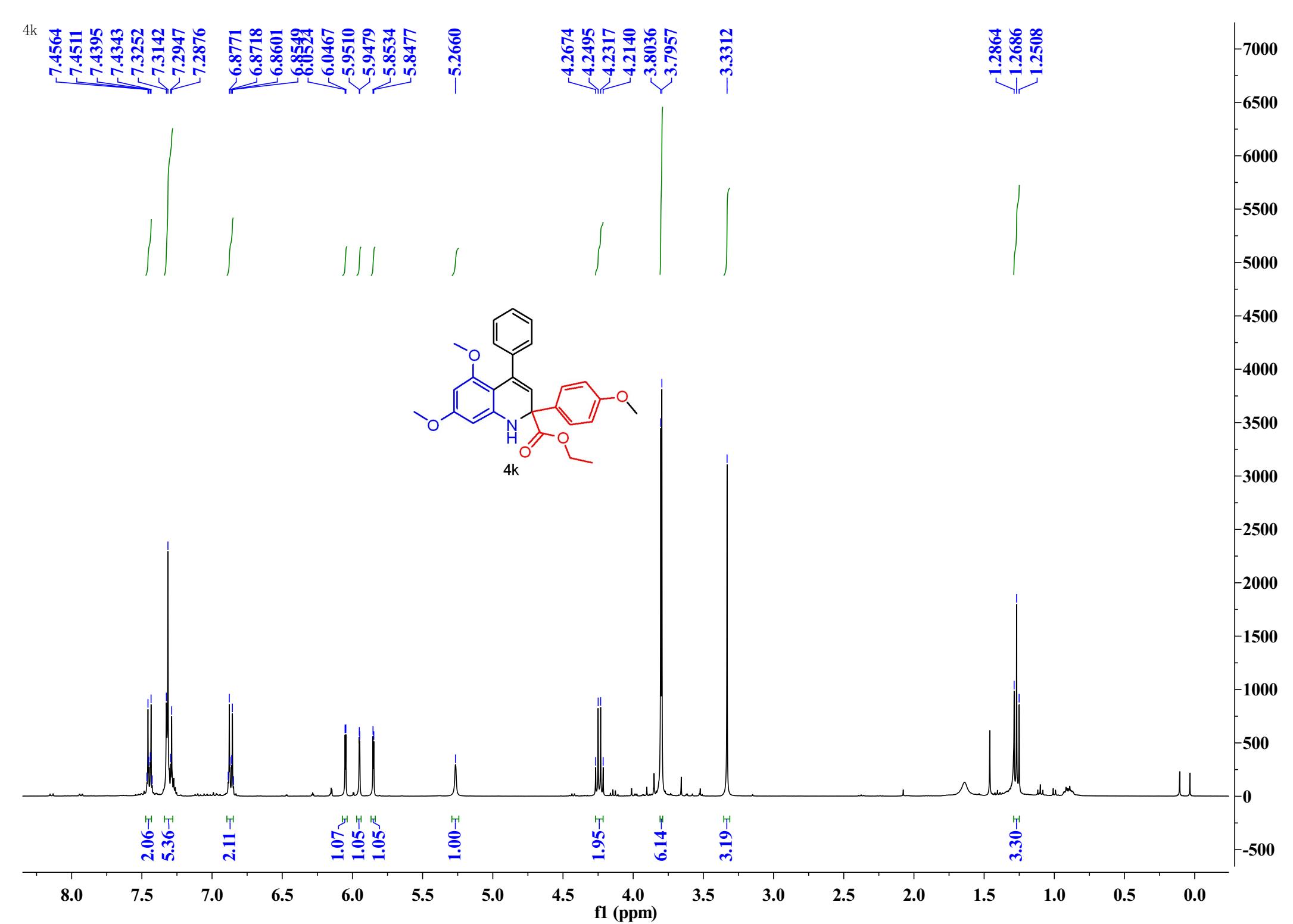


4j



4j





4k

—173.1026

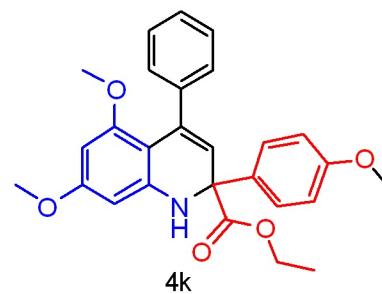
 \swarrow 161.4550
 \searrow 159.1396
 \swarrow 158.0987 \sim 145.1414
 \sim 142.5135
 \swarrow 136.8362
 \sim 134.9486 \swarrow 127.4417
 \swarrow 127.1903
 \swarrow 127.0947
 \swarrow 126.3553
 \swarrow 121.0656

—113.8572

—103.8518

 \sim 92.3637
 \sim 90.6877 \swarrow 63.3696
 \sim 61.8617
 \swarrow 55.2699
 \swarrow 55.1829
 \swarrow 54.9830

—14.1080



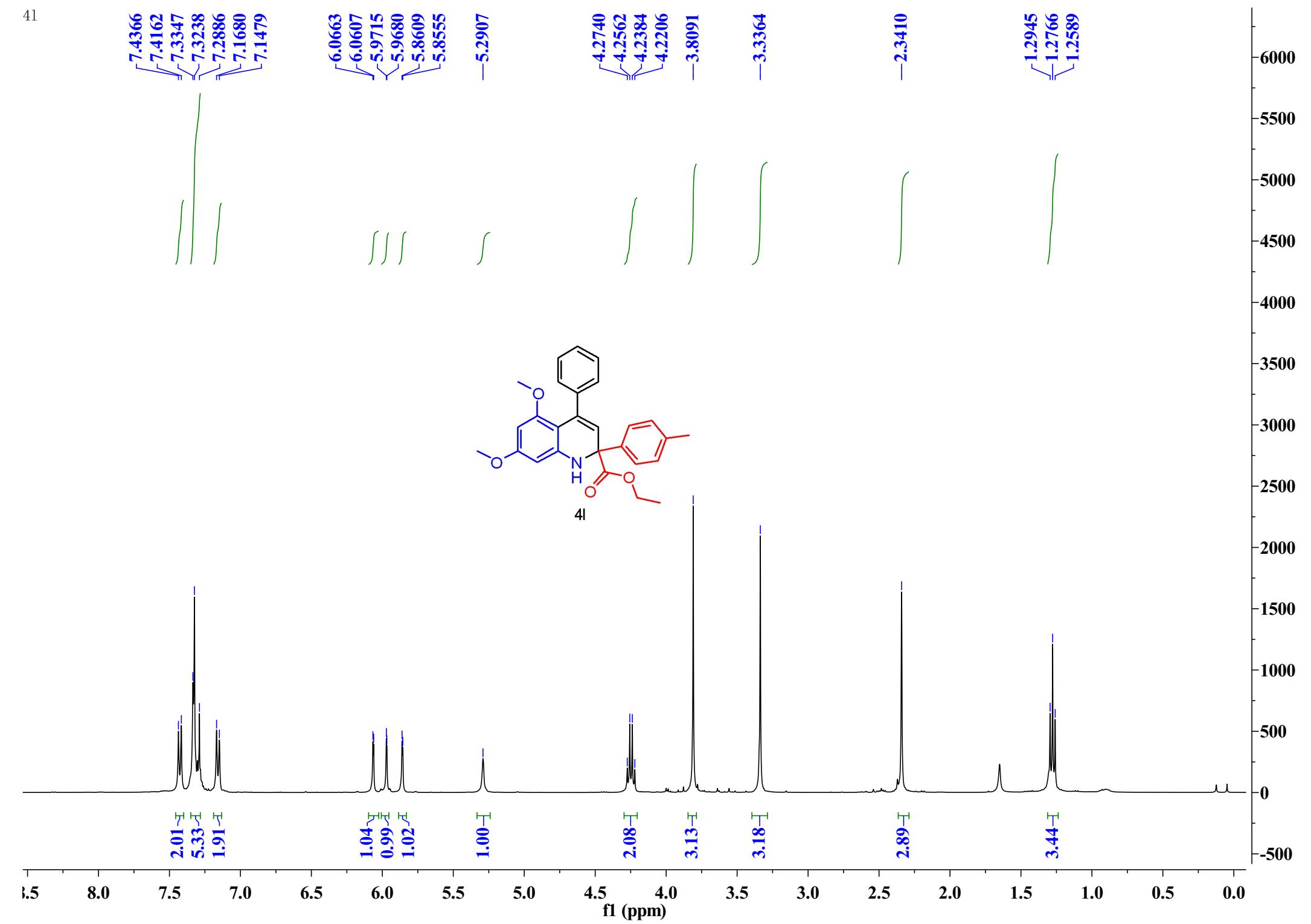
4k

4k

180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

f1 (ppm)

1000
900
800
700
600
500
400
300
200
100
0
-100



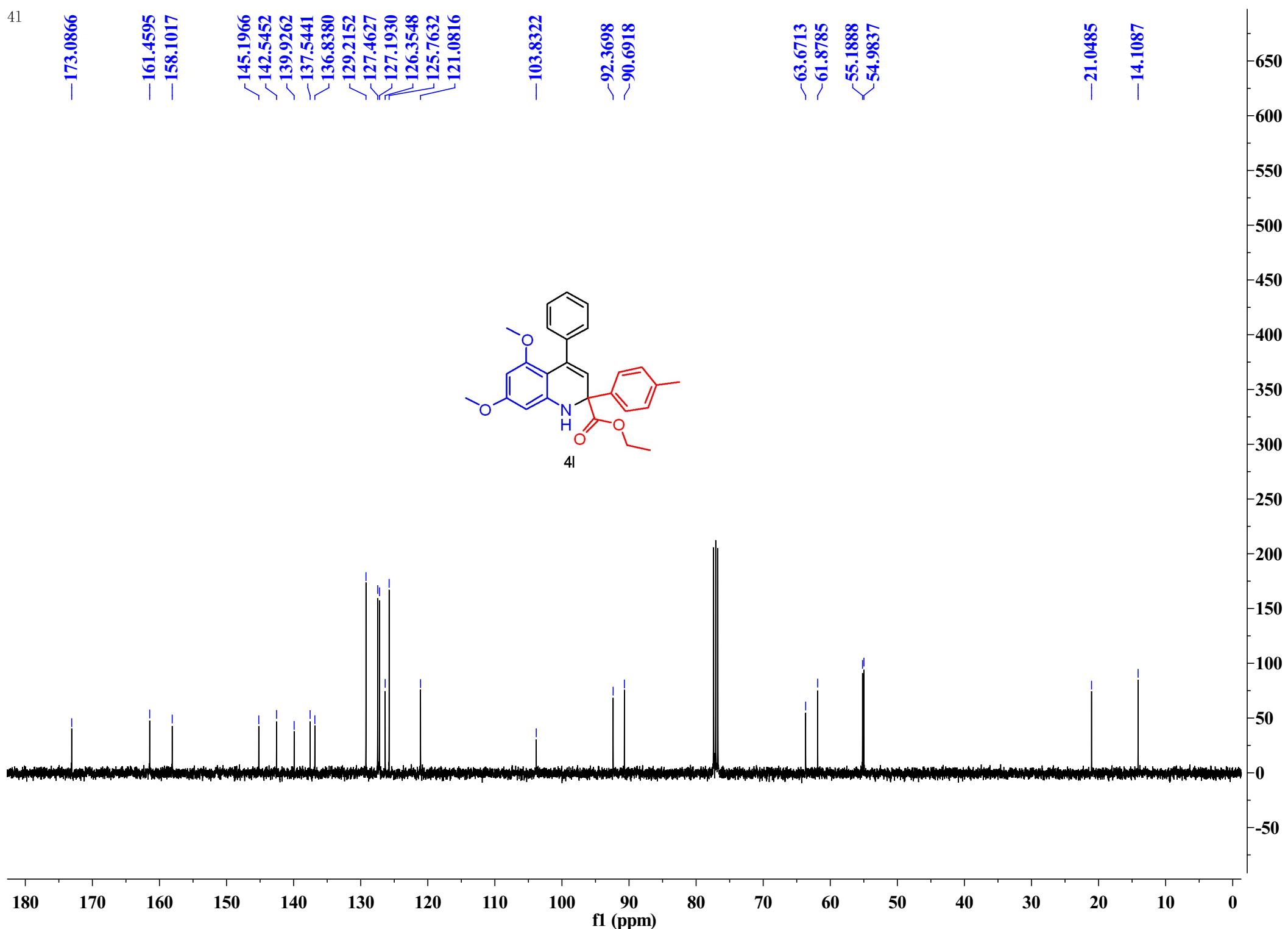
-173.0866**-161.4595****-158.1017**

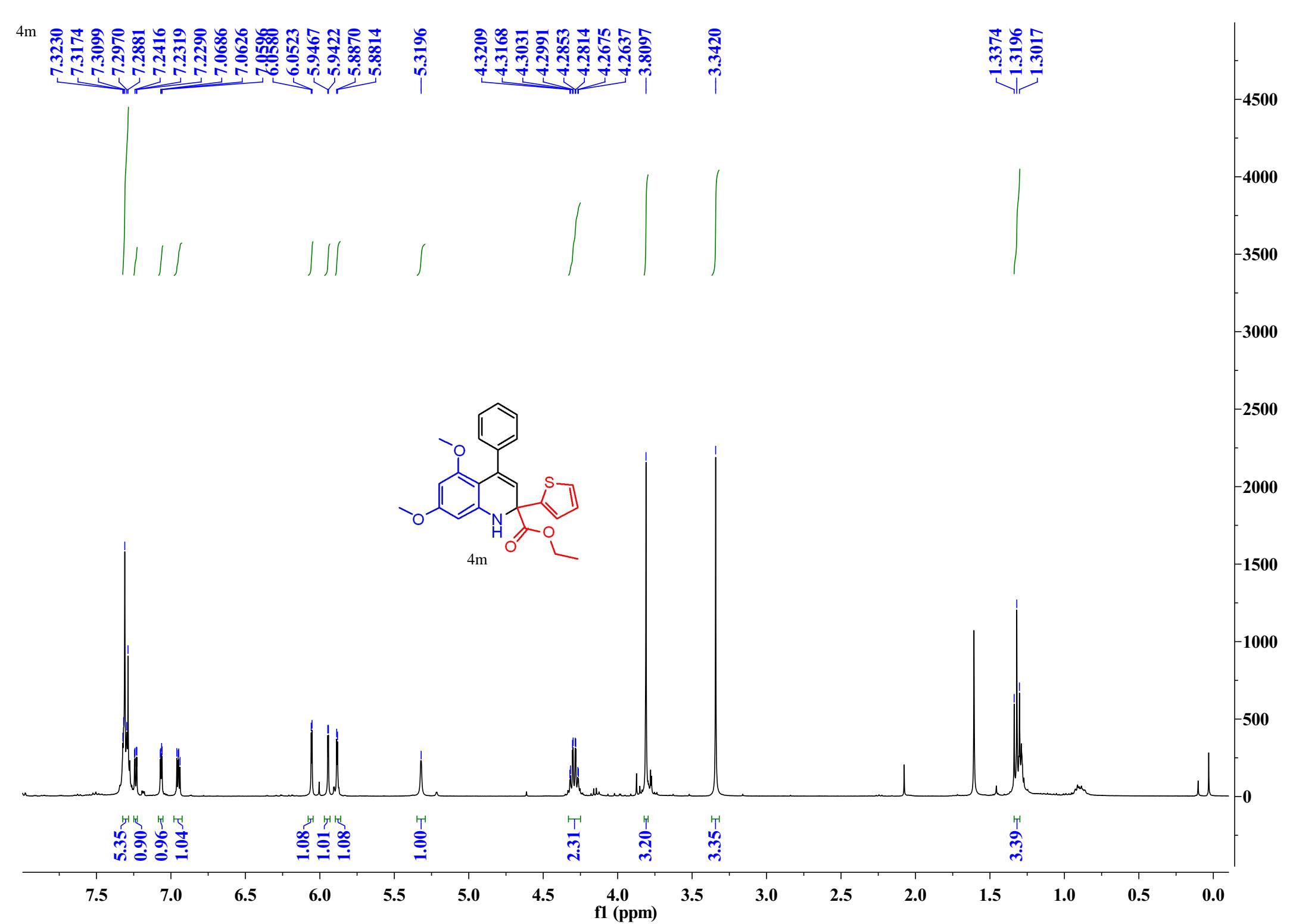
↗145.1966
 ↗142.5452
 ↘139.9262
 ↖137.5441
 ↖136.8380
 ↗129.2152
 ↗127.4627
 ↘127.1930
 ↘126.3548
 ↗125.7632
 ↗121.0816

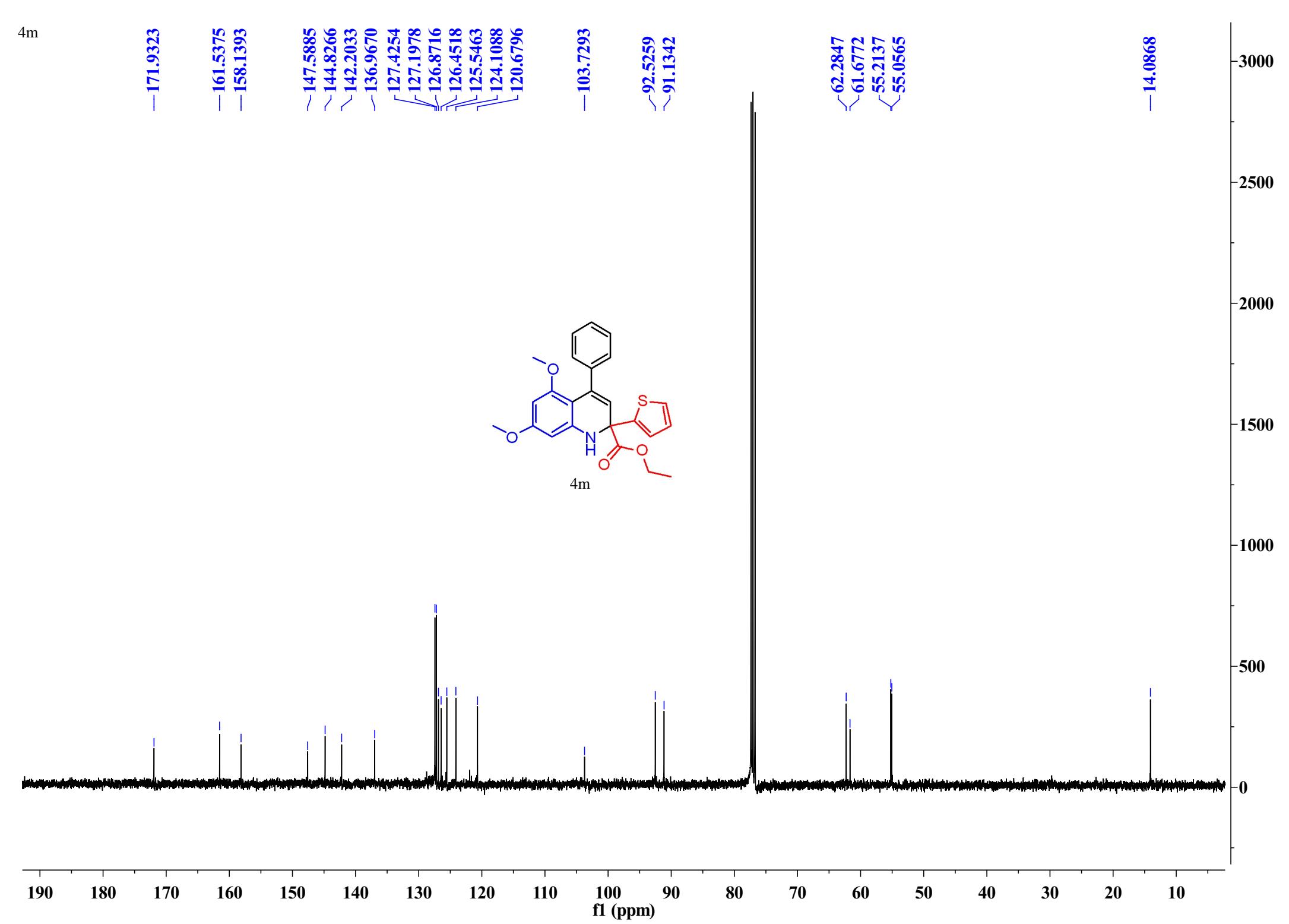
-103.8322

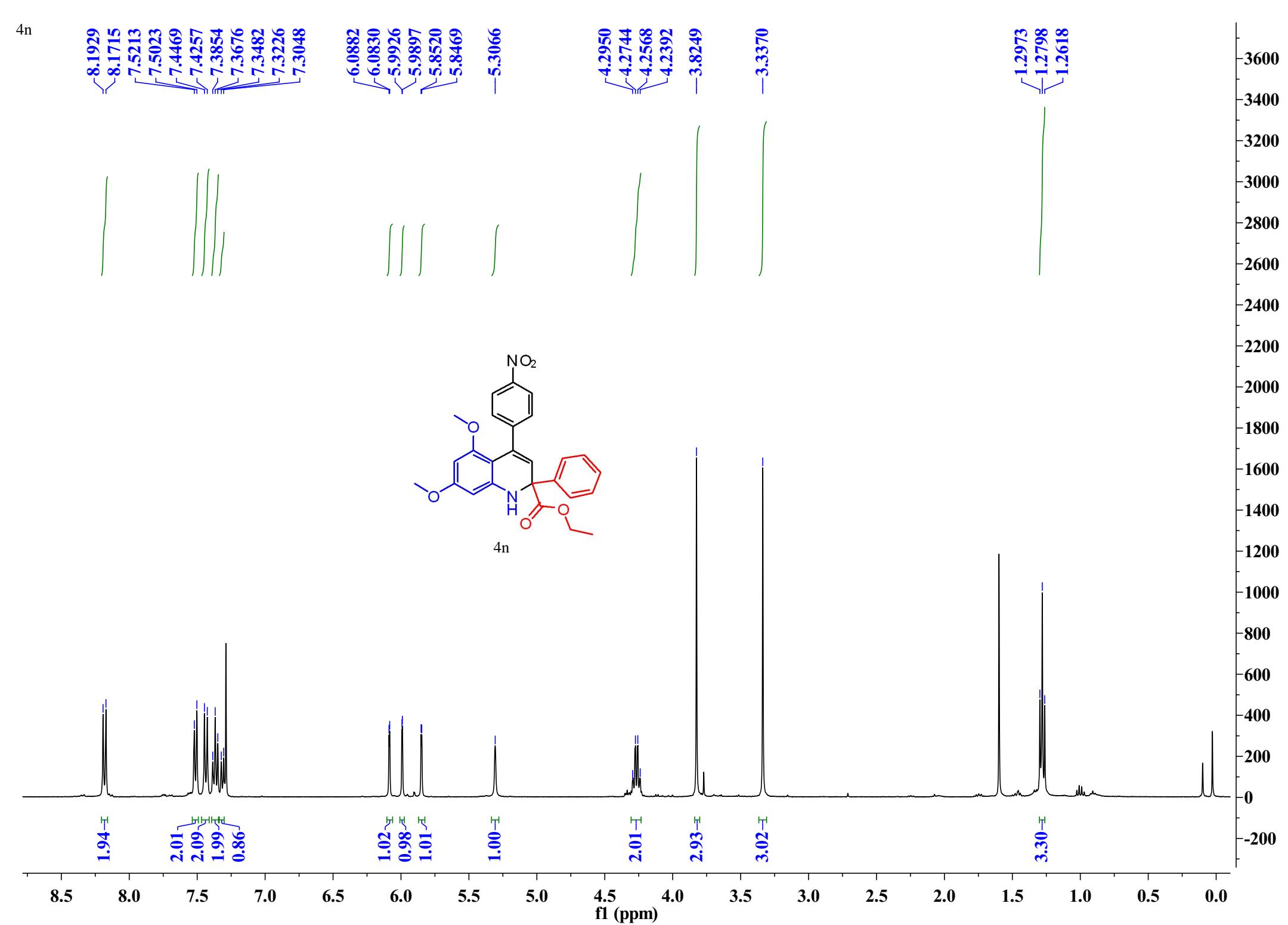
↗92.3698
 ↗90.6918

↗63.6713
 ↗61.8785
 ↖55.1888
 ↖54.9837

-21.0485**-14.1087**







4n

—172.4671

—162.0368

—157.6776

~149.6564

~146.5188

~145.1359

~142.4407

—135.2447

128.6770

~128.2598

~128.0516

~125.6511

~122.6380

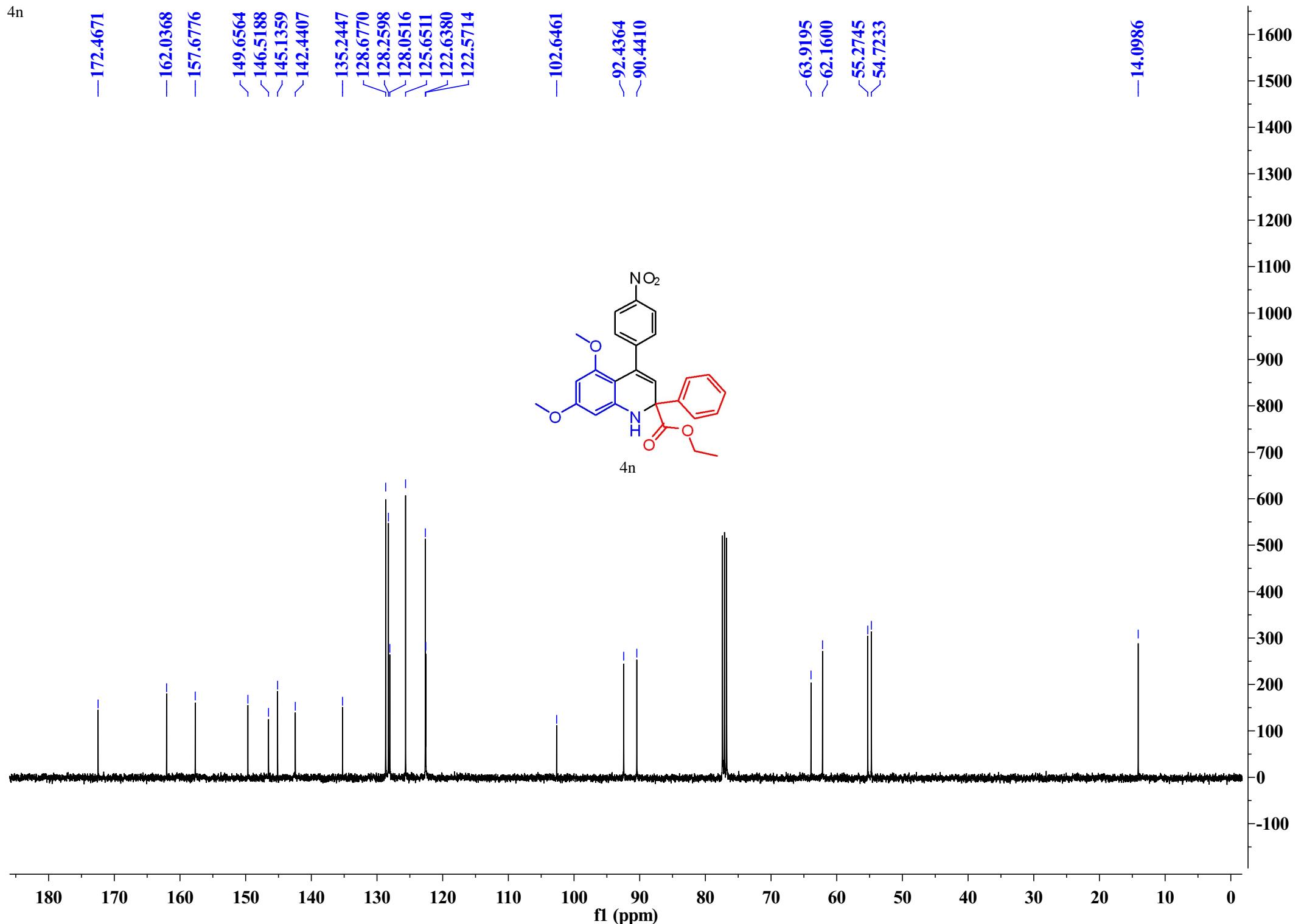
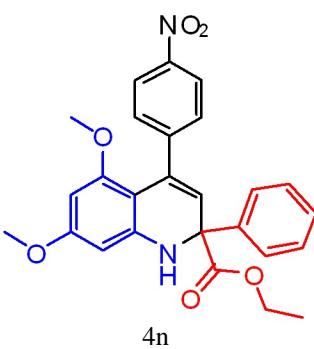
~122.5714

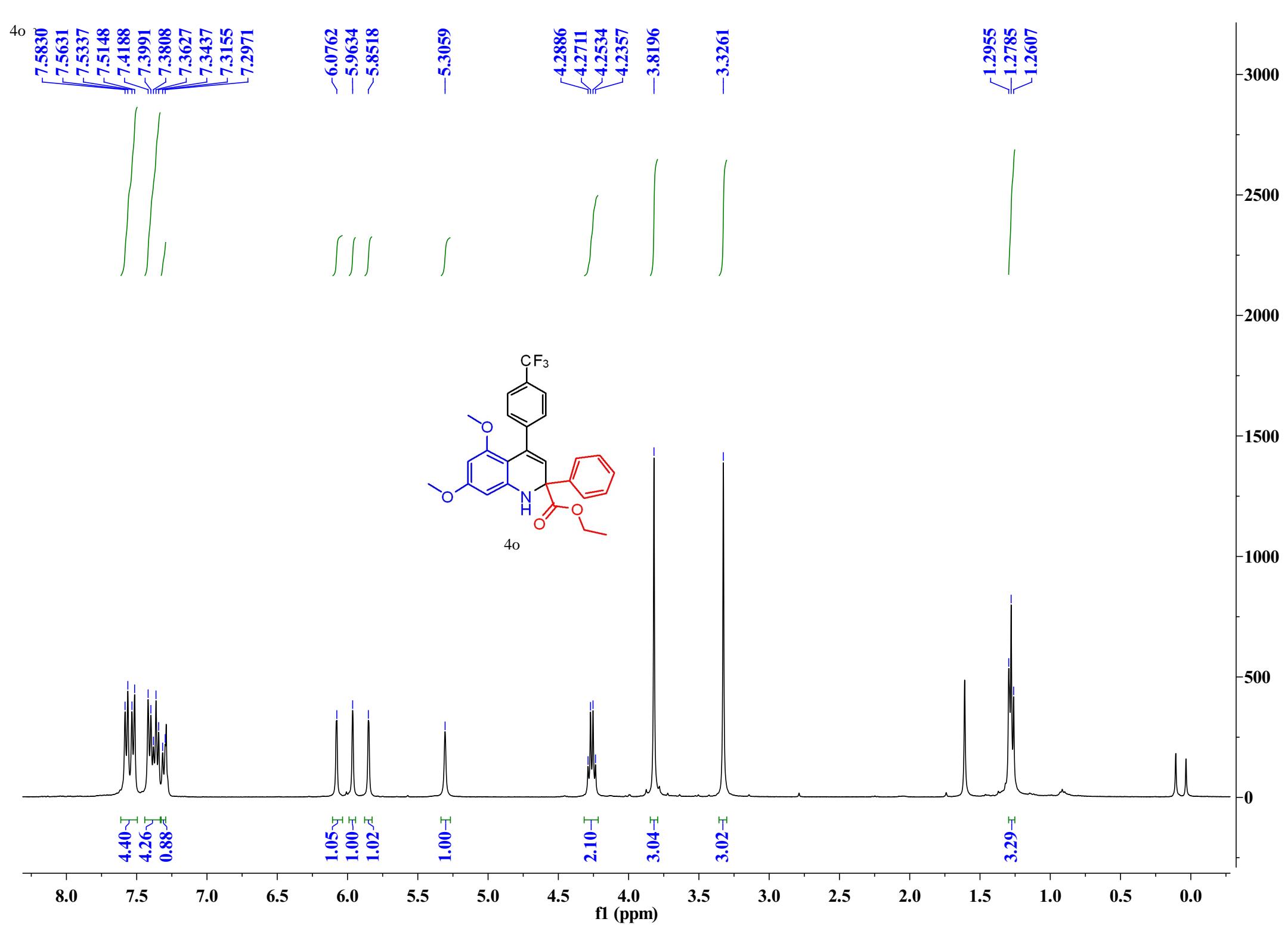
—102.6461

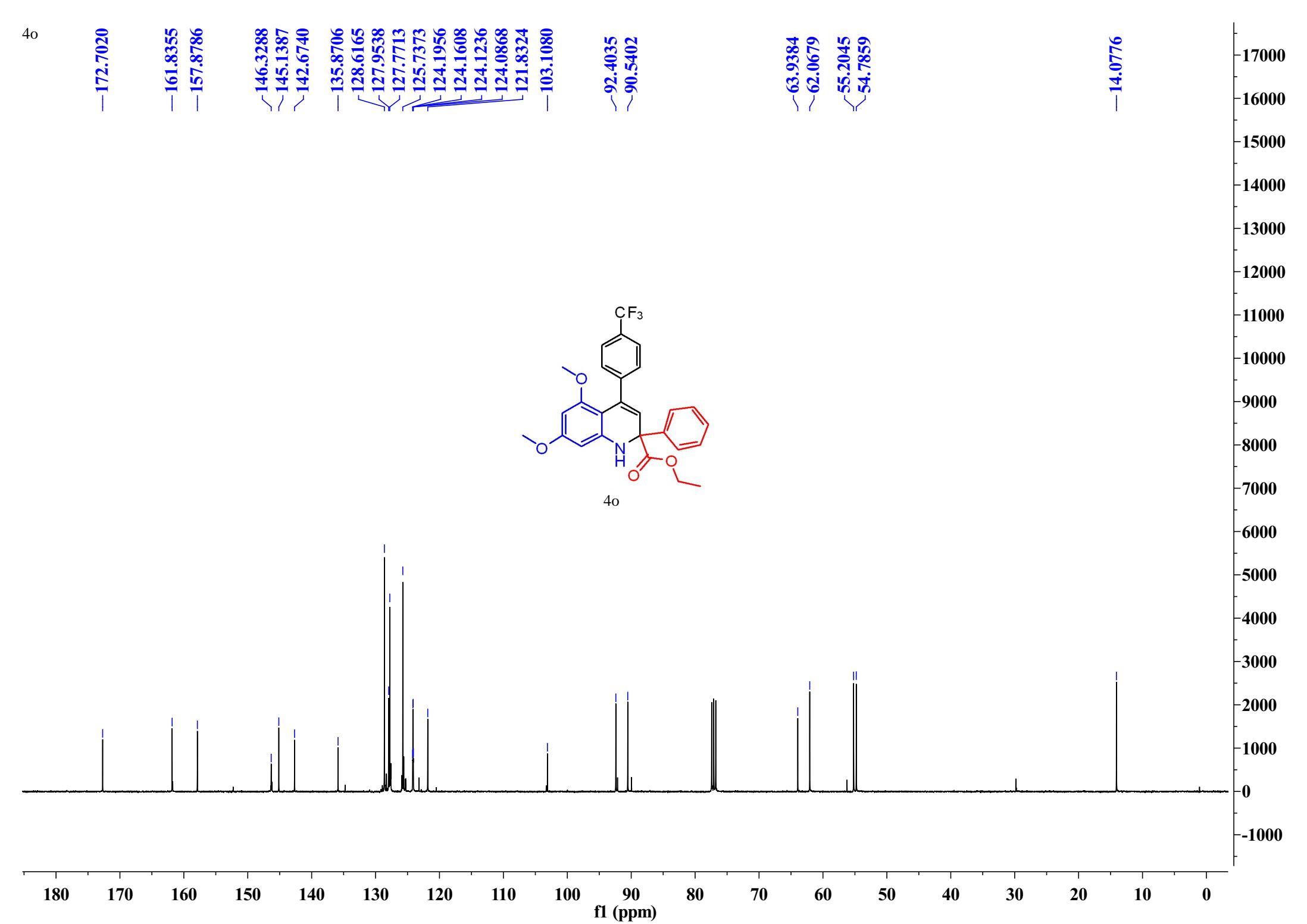
~92.4364

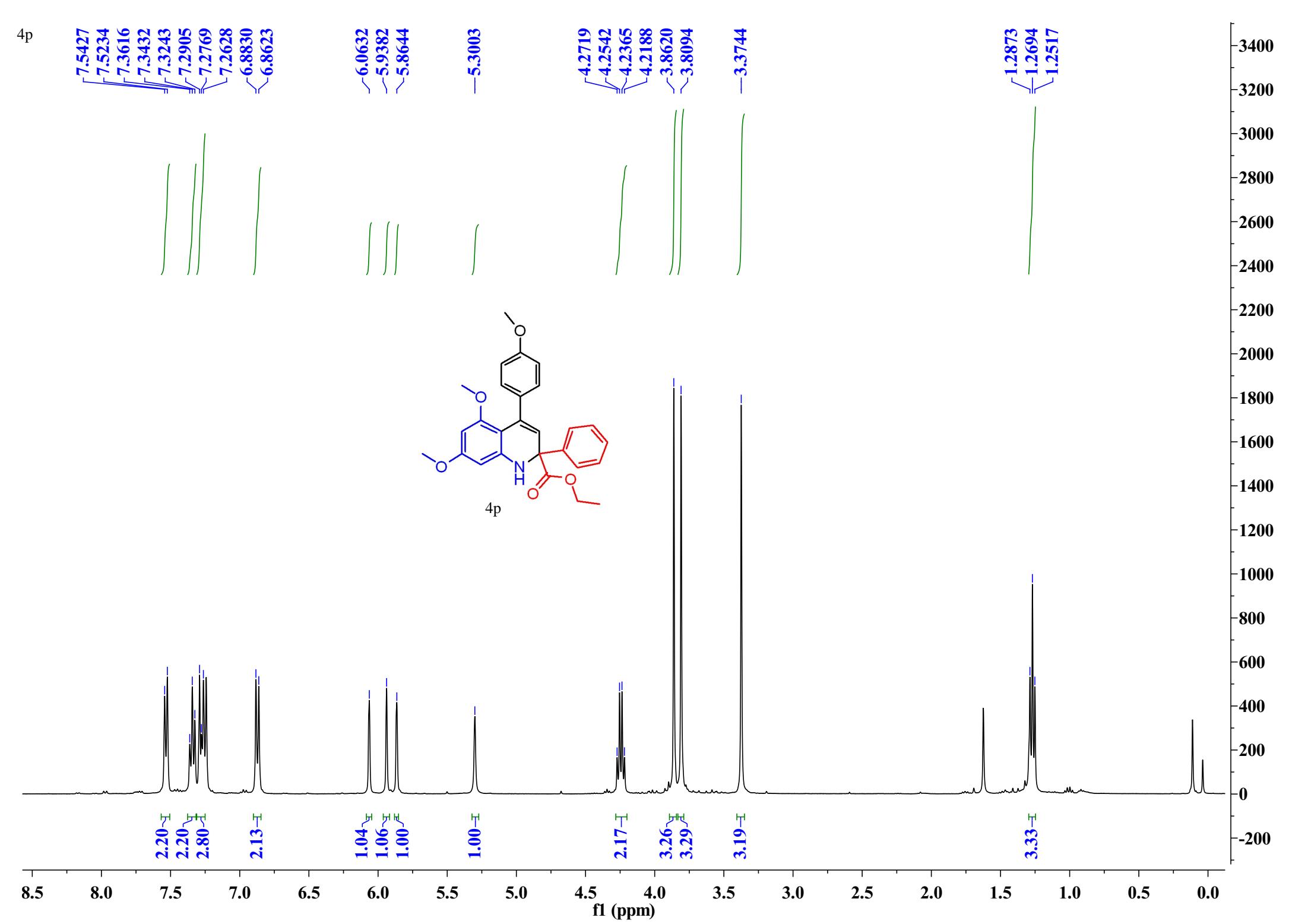
~90.4410

—14.0986









4p

-172.9850

✓ 161.4135
✓ 158.3695
✓ 158.1757

✓ 145.2033
✓ 142.8991

✓ 136.3826
✓ 134.9416
✓ 128.5210
✓ 128.4832
✓ 127.7687
✓ 125.8478
✓ 120.3677

-112.5924

-103.8579

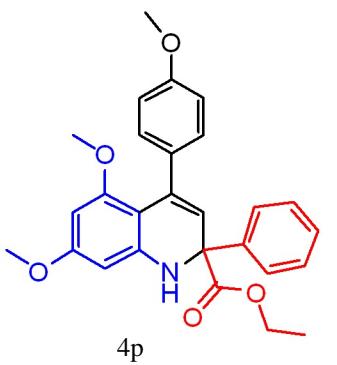
✓ 92.3740
✓ 90.7725

✓ 63.8575
✓ 61.9000
✓ 55.2887
✓ 55.1864
✓ 55.1061

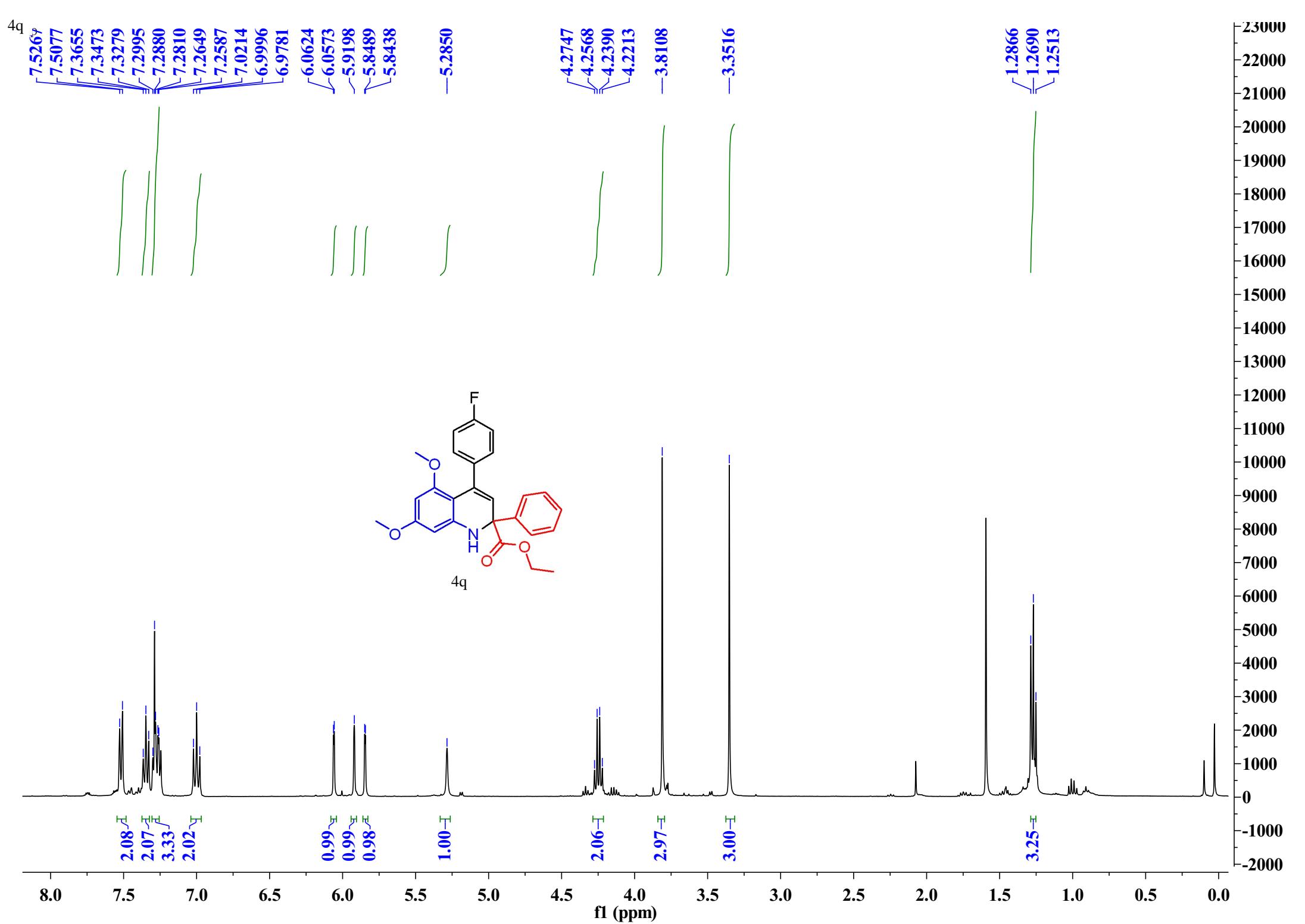
-14.0930

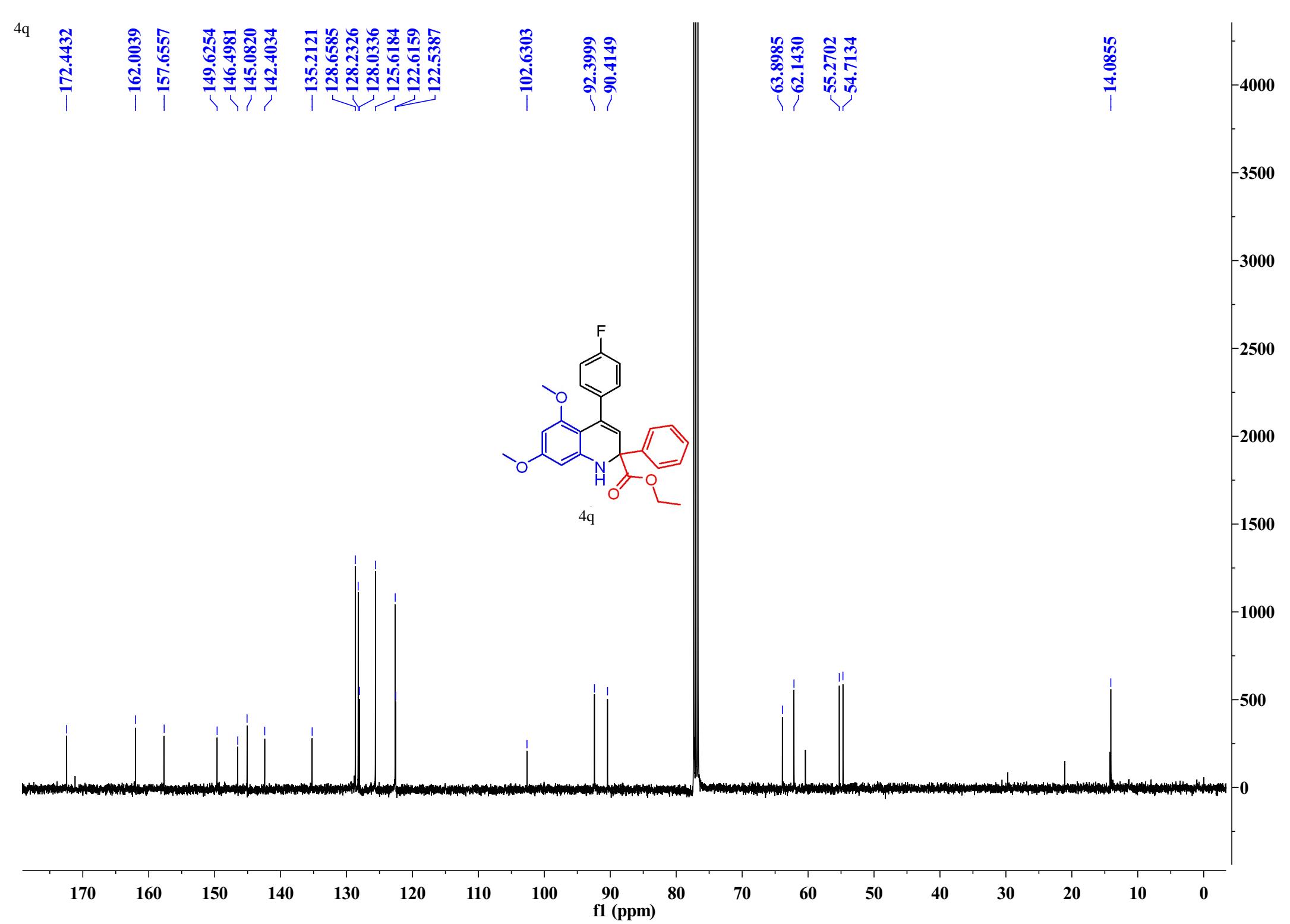
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500

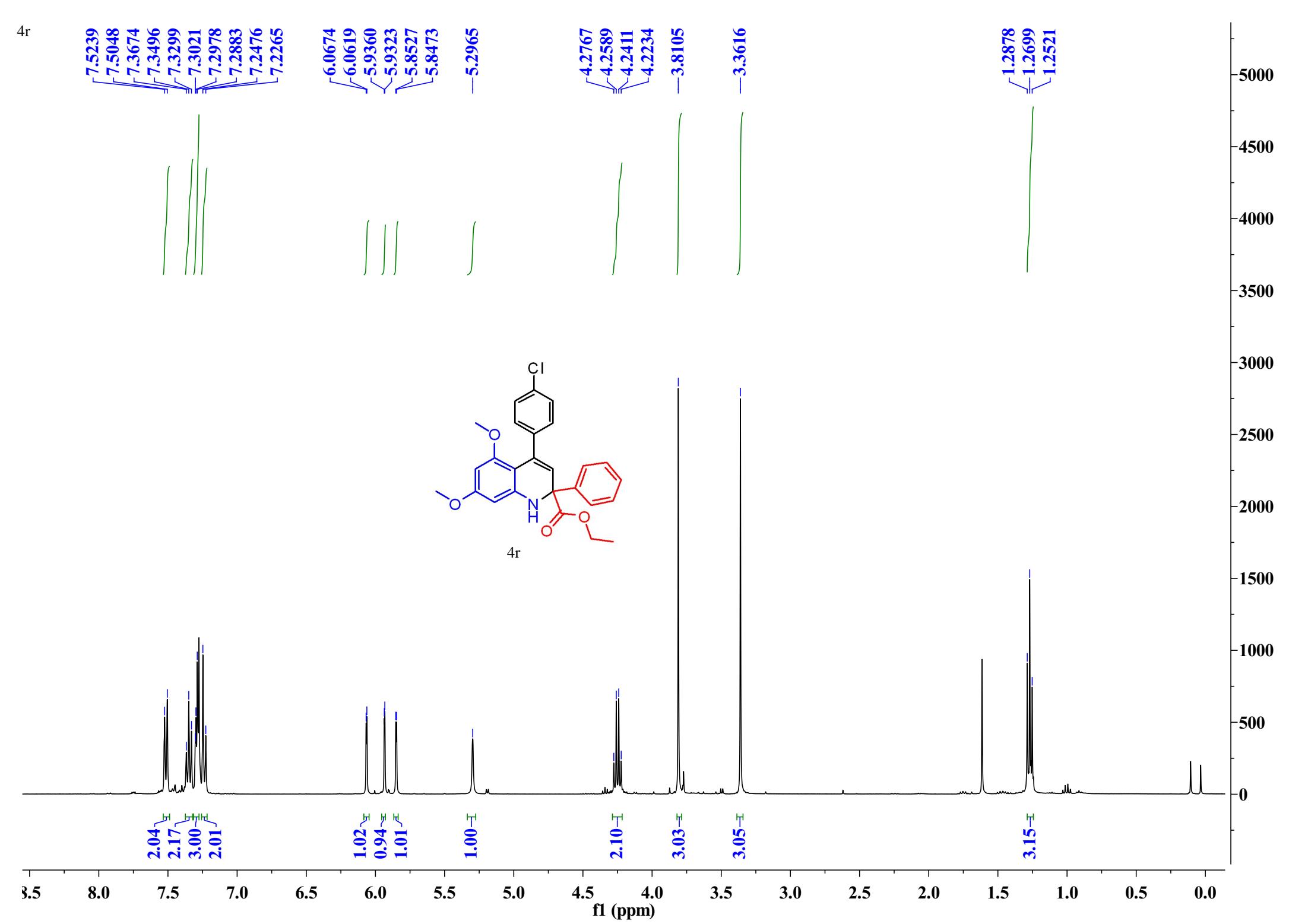
f1 (ppm)



180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0







4r

—172.7581

—161.6355

—157.9346

145.1147

142.6853

140.9520

135.8263

132.0278

128.8053

128.5507

127.8713

127.2977

125.7324

121.2033

—103.2910

—92.3346

~90.5645

~63.8459

~62.0030

55.2151

54.8816

—14.0882

1100

1000

900

800

700

600

500

400

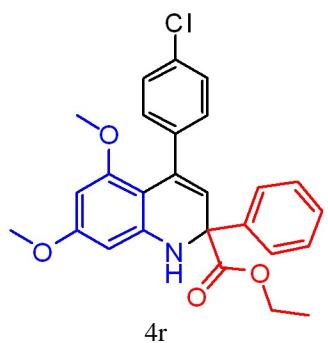
300

200

100

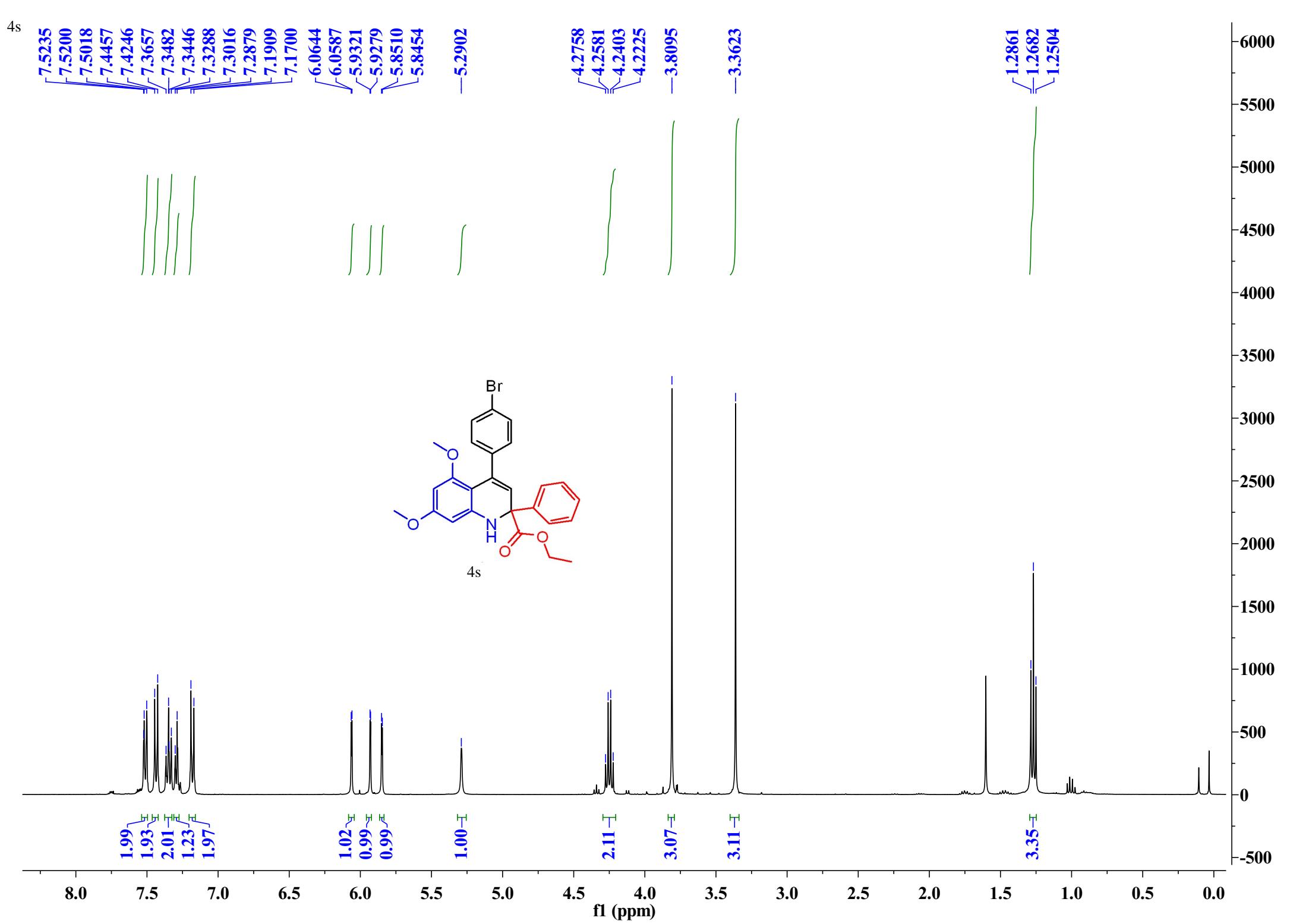
0

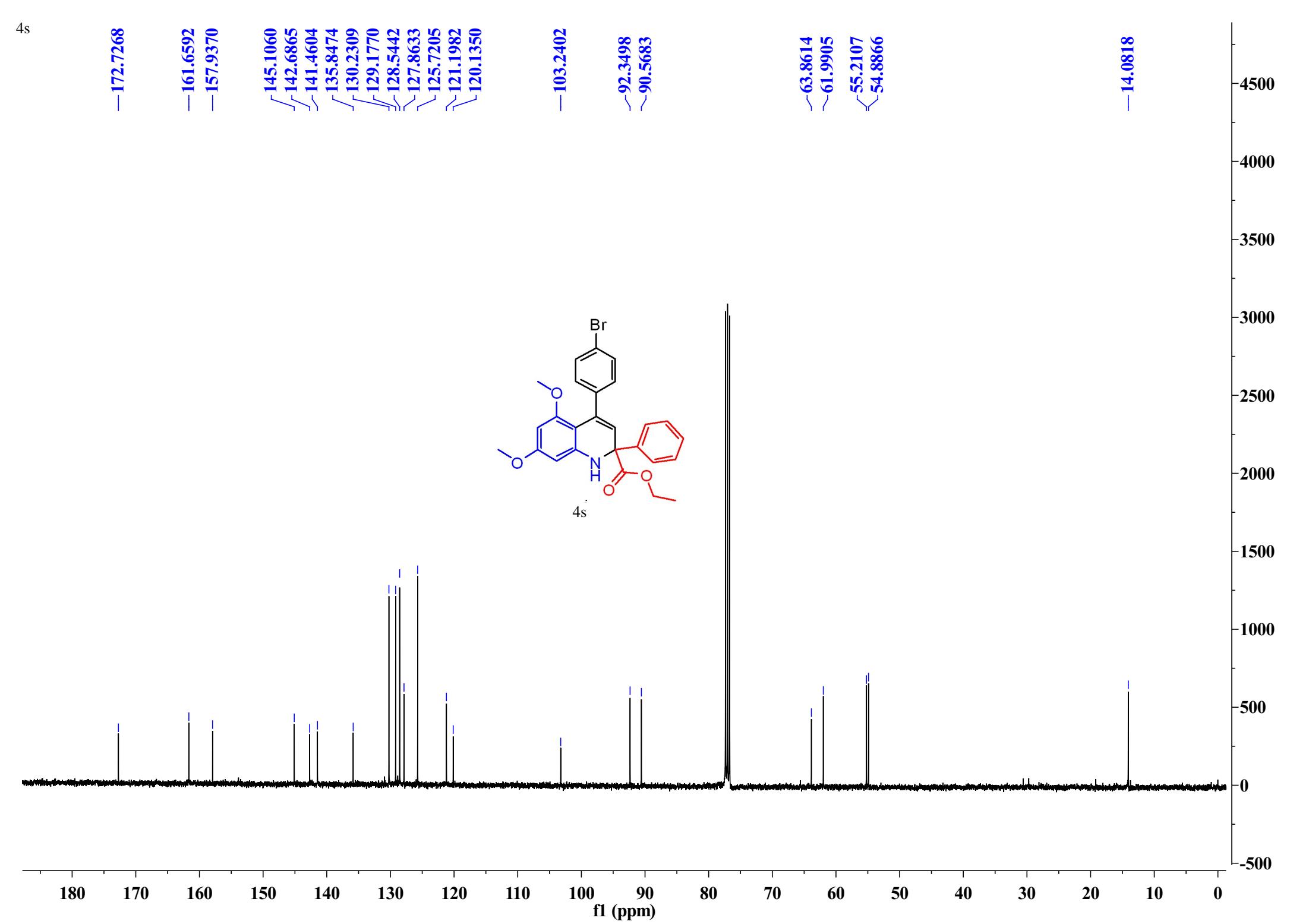
-100

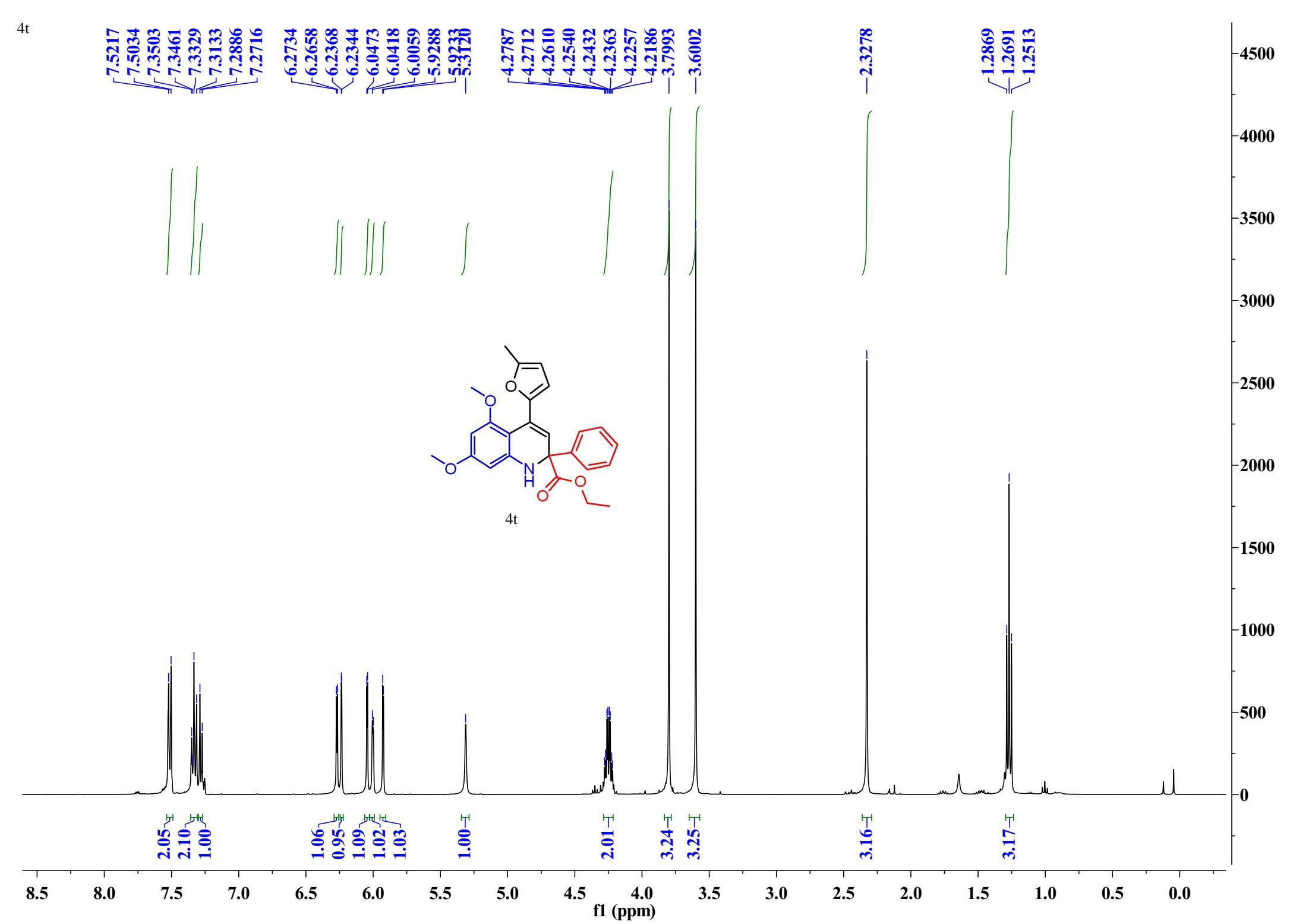


180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

f1 (ppm)







4t

— 172.6953

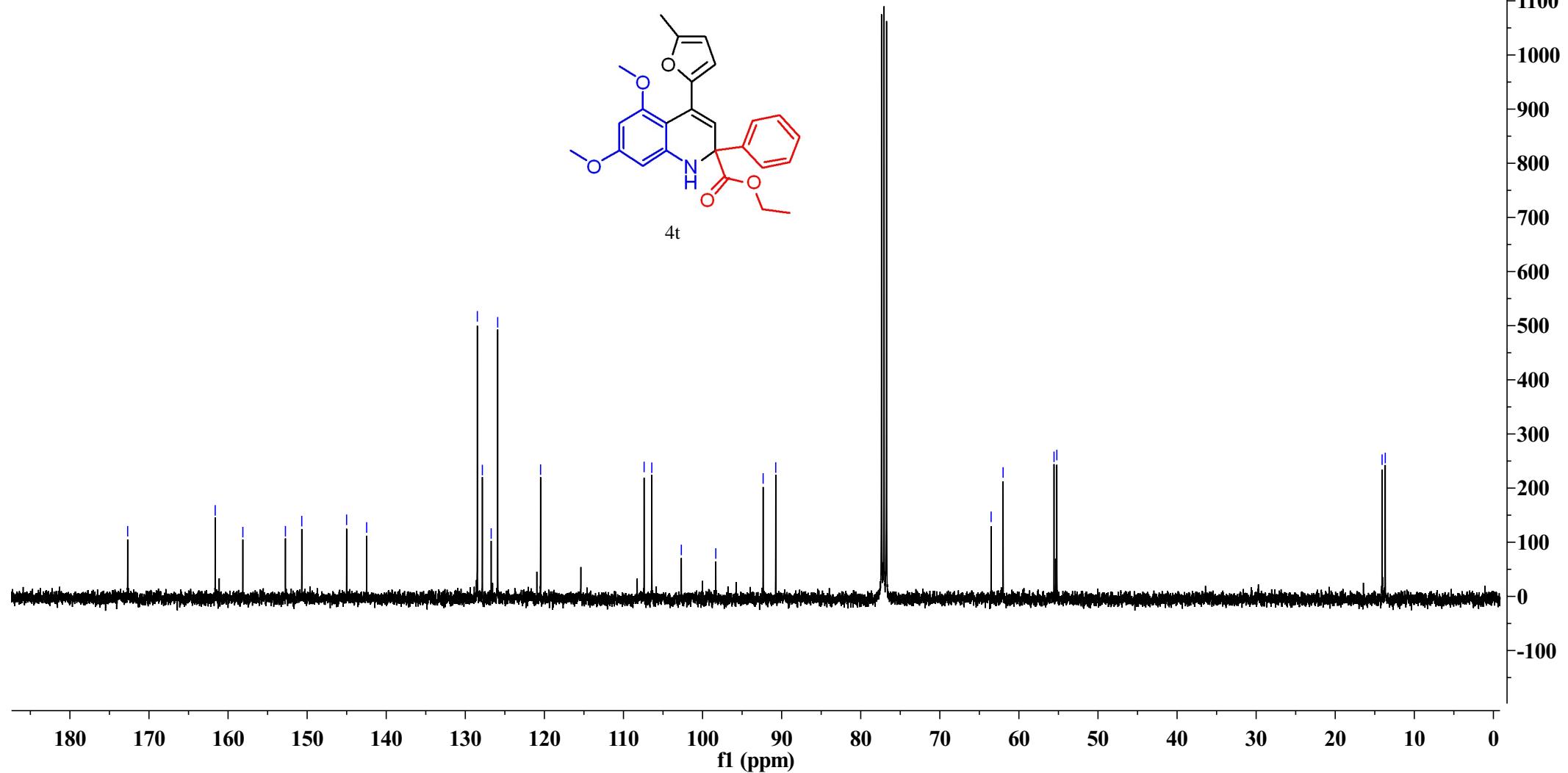
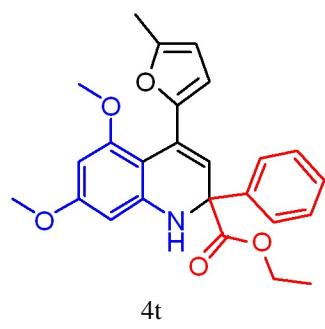
~161.6250
~158.1294
~152.7474
— 150.6797
~145.0096
/ 142.4756

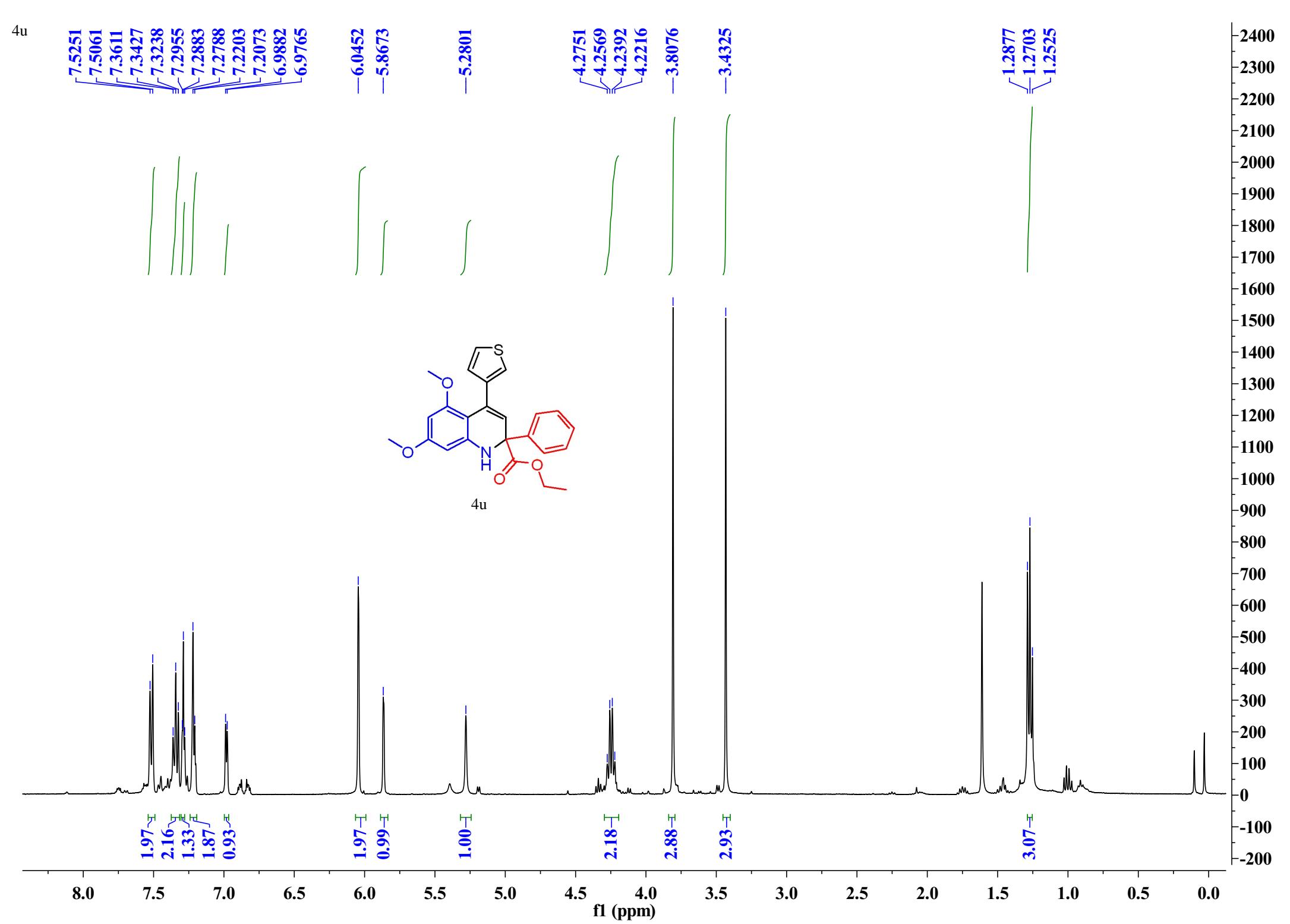
/ 128.4778
/ 127.8442
/ \ 126.7295
/ \ 125.9051
/ \ 120.4809

\ 107.3905
/ \ 106.4190
/ \ 102.6844
~ 98.3274
/ \ 92.3408
/ \ 90.7460

\ 63.5119
~ 61.9983
/ \ 55.5582
/ \ 55.2037

/ \ 14.0733
/ \ 13.6740





4u

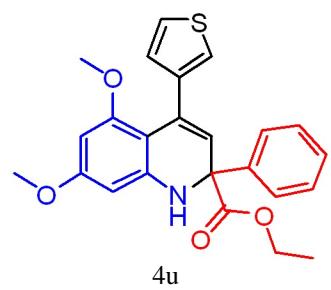
-172.8873

-161.4814

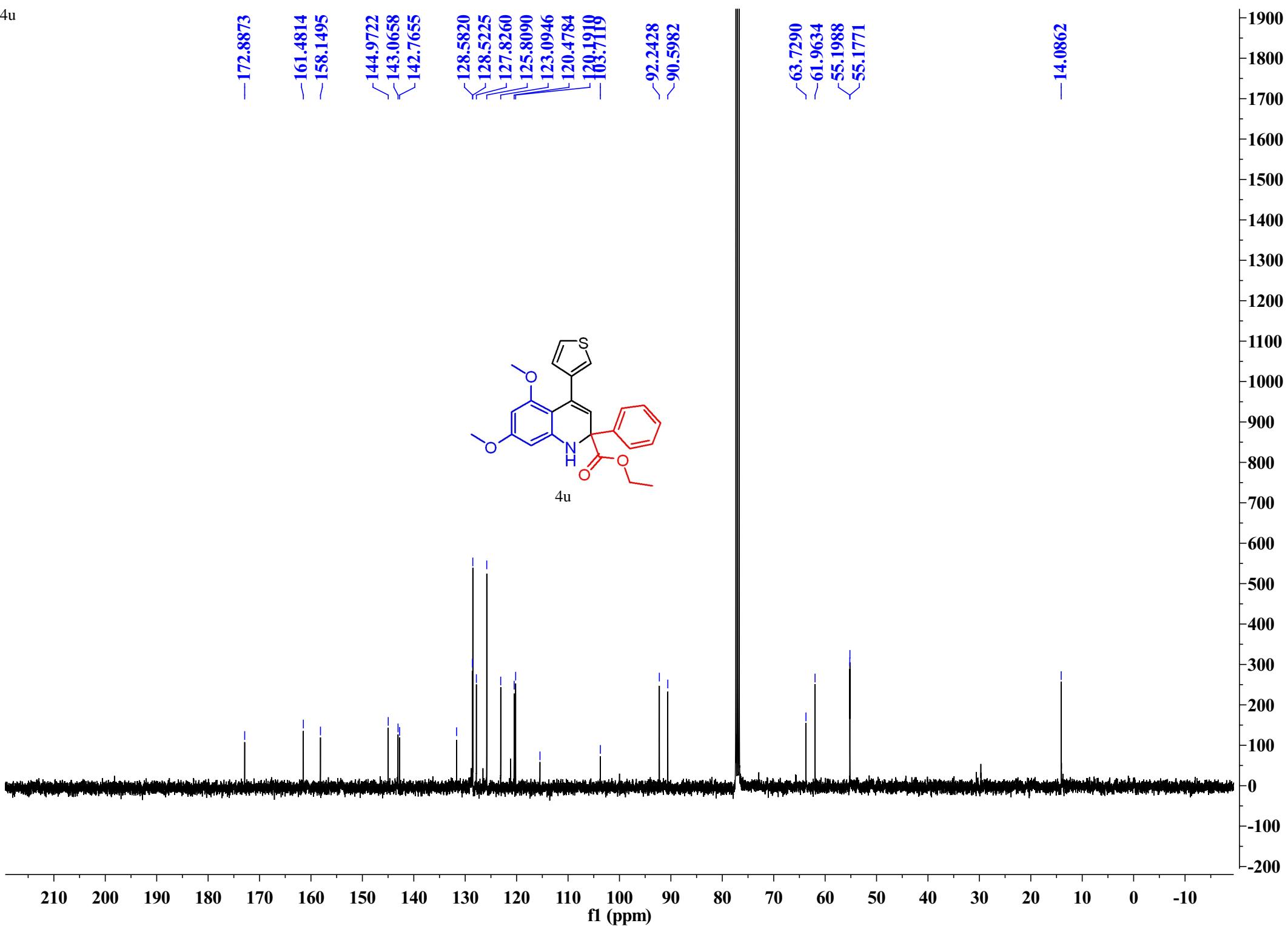
-158.1495

144.9722
143.0658
142.7655128.5820
128.5225
127.8260
125.8090
123.0946
120.4784
103.1919-92.2428
-90.5982-63.7290
-61.9634
-55.1988
-55.1771

-14.0862



4u



4v

7.4711
 7.4527
 7.3627
 7.3443
 7.3243
 7.2892
 7.2725

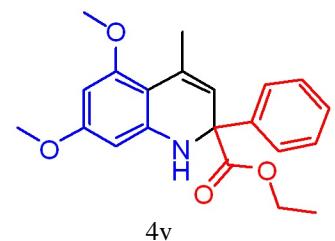
5.9308
 5.9254
 5.8832
 5.8780
 5.6989

-5.0846

4.2627
 4.2543
 4.2437
 4.2364
 4.2259
 4.2184
 3.7843
 3.7504

-2.2271

1.2881
 1.2703
 1.2525



2.08^H
 2.20^H
 1.21^H

1.02^{HH}
 1.01^{HH}
 1.05^H

1.00^H

1.88^H
 2.89^{HH}
 3.00^H

3.21^H3.27^H

8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

f1 (ppm)

3400
 3200
 3000
 2800
 2600
 2400
 2200
 2000
 1800
 1600
 1400
 1200
 1000
 800
 600
 400
 200
 0
 -200

4v

—173.3388

 \sim 160.8777
 \sim 159.0316144.5907
143.8231132.0145
128.5041
127.5942
125.5893

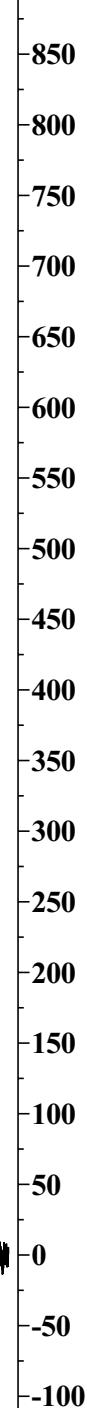
—117.9867

—104.0402

 \sim 91.7902
 \sim 90.1216—64.0464
—61.7132
55.1974
55.1398

—23.2873

—14.0925



180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

f1 (ppm)

-100

-50

0

50

100

150

200

250

300

350

400

450

500

550

600

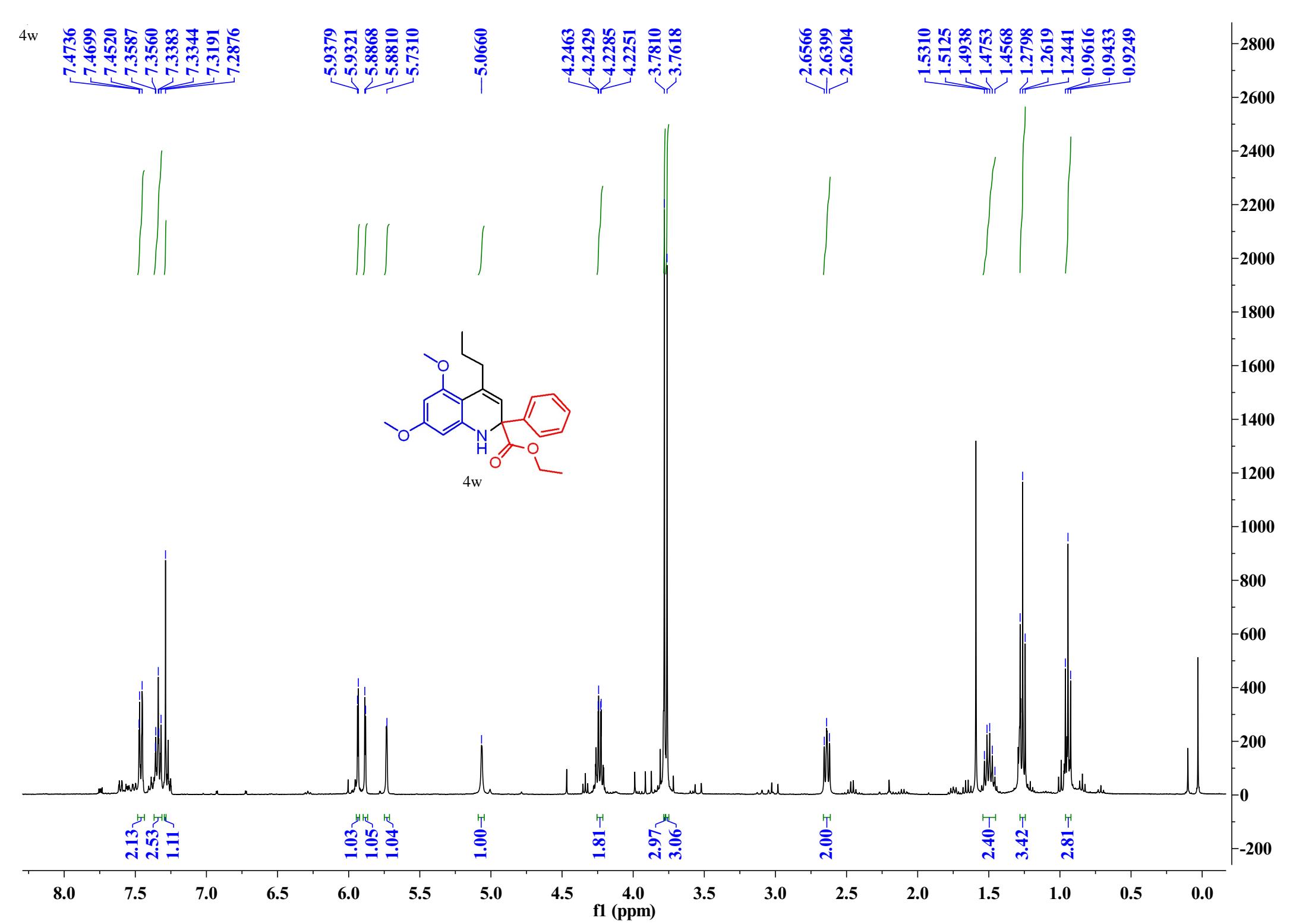
650

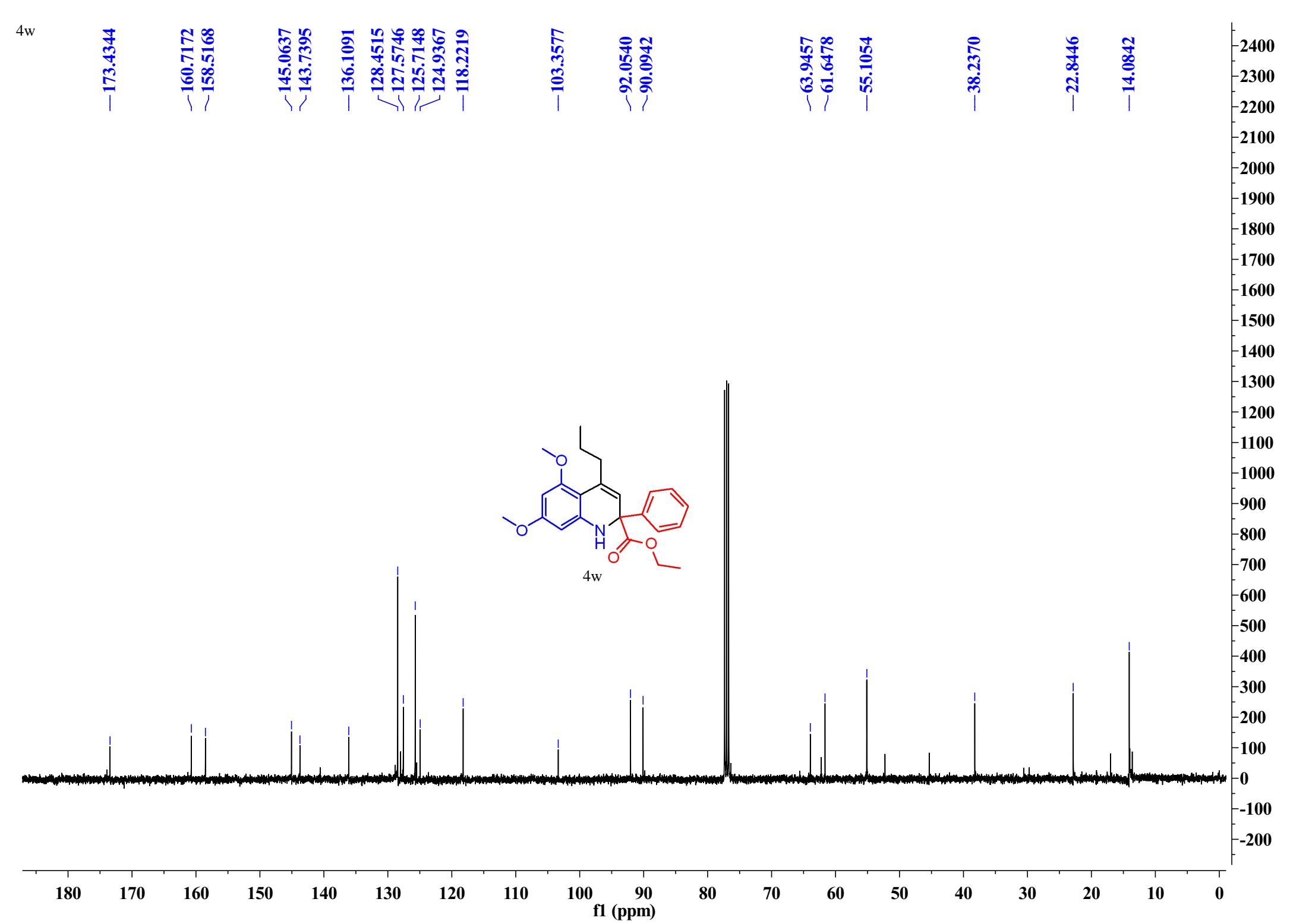
700

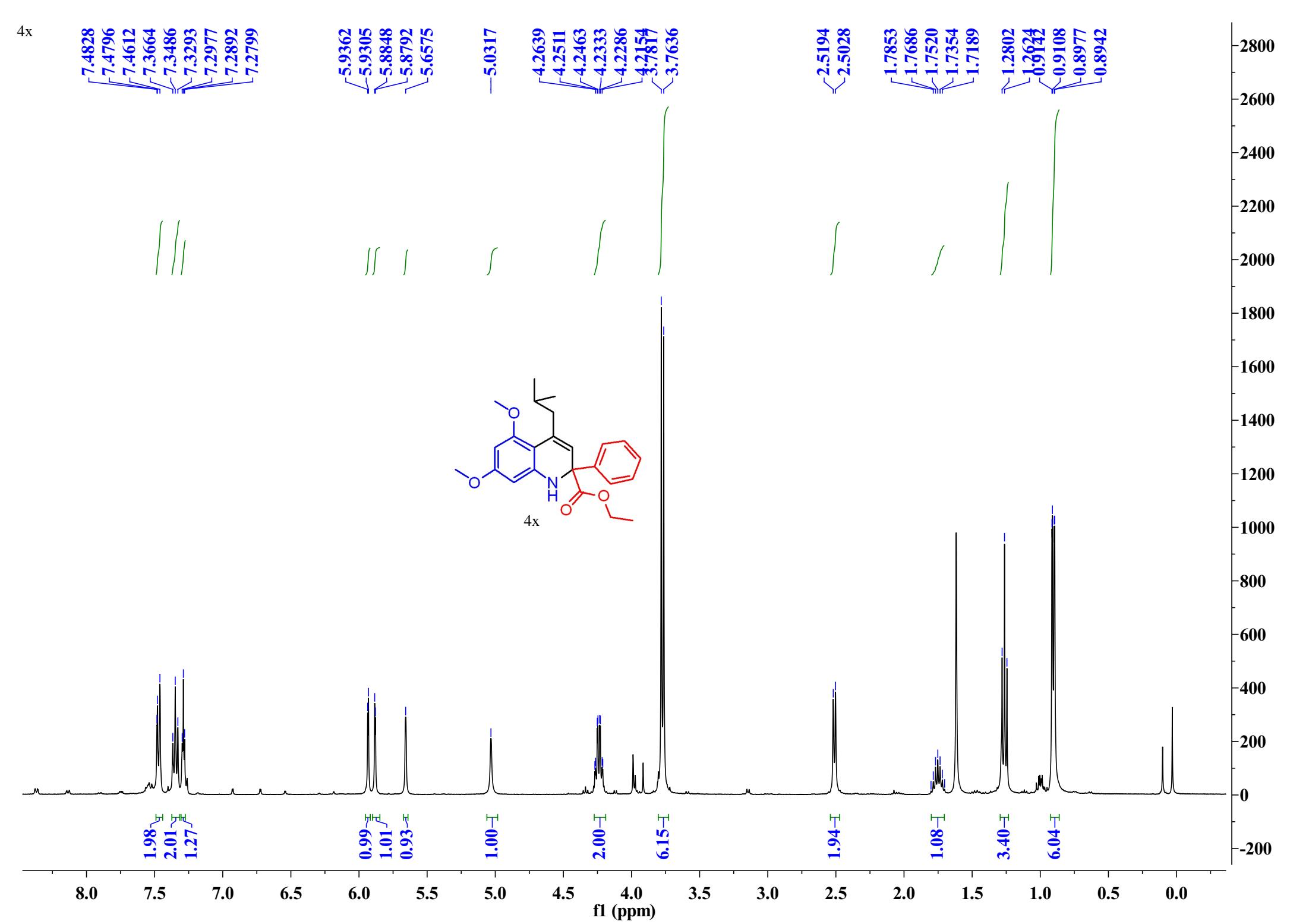
750

800

850







4x

 -173.5982 -160.6979
 ~ 158.4935 ~ 145.1936
 ~ 143.8292 -134.8191 -128.4595
 $\swarrow 127.5935$
 $\searrow 125.8038$
 ~ 119.4807 -103.1797 ~ 92.0018
 ~ 90.0375 -64.1492
 ~ 61.6132 -55.0962 -45.6857 ~ 27.4142
 $\swarrow 22.6307$
 $\searrow 22.4542$ -14.0839

8500

8000

7500

7000

6500

6000

5500

5000

4500

4000

3500

3000

2500

2000

1500

1000

500

0

-500

