

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

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Content

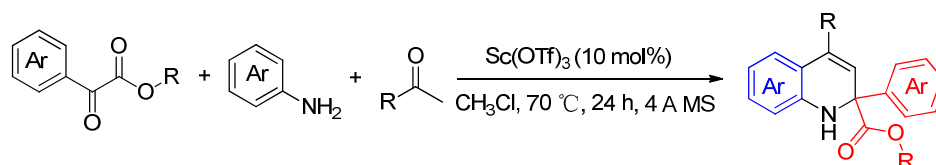
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General information

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.

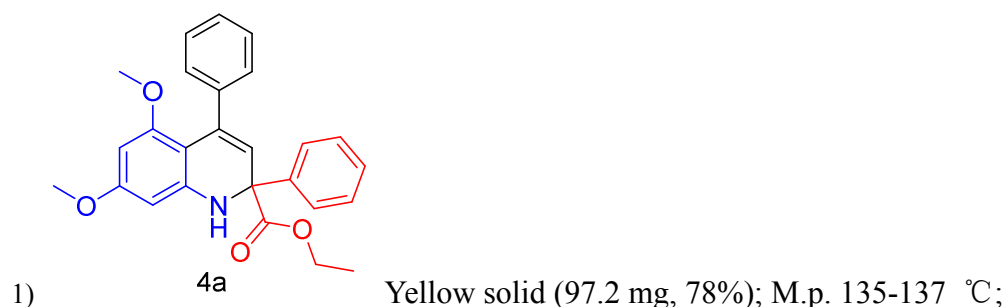
Melting points were measured on a Meltemp melting point apparatus and were not corrected. ^1H NMR spectra were recorded on commercial instruments (400 MHz). Chemical shifts were reported in ppm from tetramethylsilane with the solvent resonance as the internal standard (CDCl_3 , $\delta = 7.26$). Spectra 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.

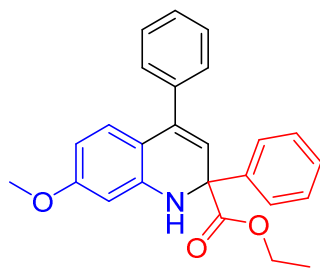


¹H NMR (400 MHz, CDCl₃) δ 7.53 (d, *J* = 7.5 Hz, 2H), 7.38 – 7.26 (m, 8H), 6.07 (s, 1H), 5.97 (s, 1H), 5.85 (s, 1H), 5.29 (s, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 3.81 (s, 3H), 3.33 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H);

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.



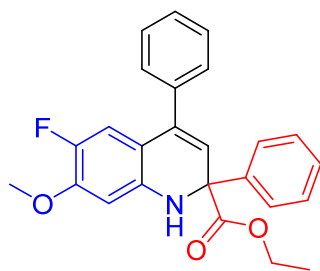
2) **4b** Yellow oil (78.6 mg, 68%);

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%);

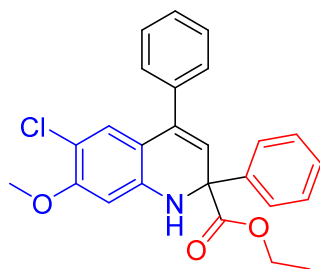
¹H NMR (400 MHz, CDCl₃) δ 7.53 (d, *J* = 7.5 Hz, 2H), 7.49 – 7.36 (m, 7H), 7.34 (d, *J* = 7.1 Hz, 1H), 6.73 (d, *J* = 12.4 Hz, 1H), 6.37 (d, *J* = 7.2 Hz, 1H), 6.03 (s, 1H), 5.06 (s, 1H), 4.30 (dd, *J* = 13.8, 6.8 Hz, 2H), 3.89 (s, 3H), 1.31 (t, *J* = 6.9 Hz, 3H);

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.



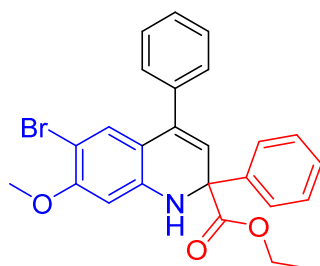
4) **4d** Yellow oil (91.8 mg, 73%);

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.



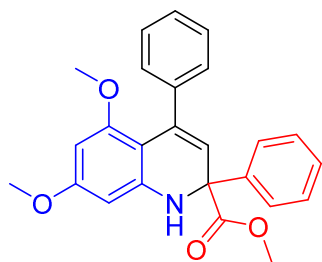
5) **4e** Yellow oil (100.0 mg, 72%);

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.



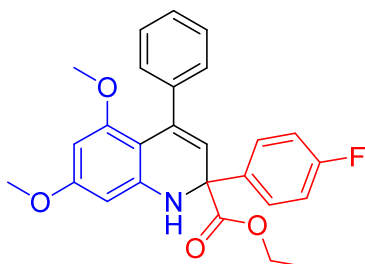
6) **4f** Yellow oil (96.3 mg, 80%);

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.



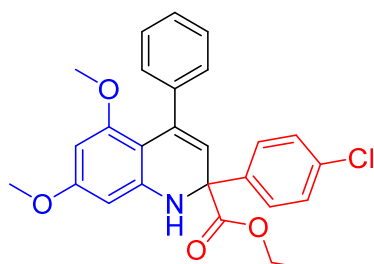
7) **4g** Yellow oil (101.4 mg, 78%);

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.



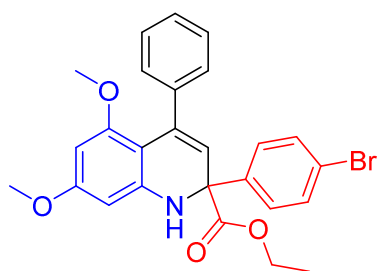
8) **4h** Yellow oil (101.0mg, 75%);

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.



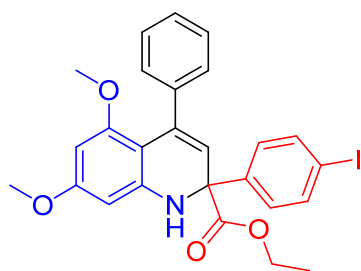
9) **4i** Yellow oil (110.9 mg, 75%);

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



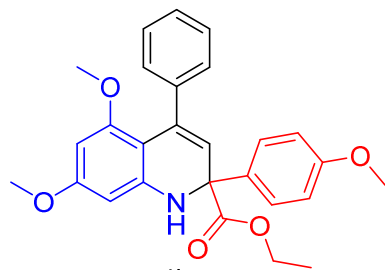
10) **4j** Yellow oil (116.9 mg, 72%);

¹H NMR (400 MHz, CDCl₃) 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.



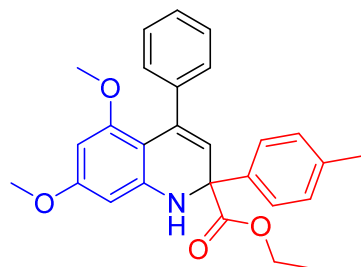
11) **4k** Yellow oil (93.5 mg, 70%);

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.



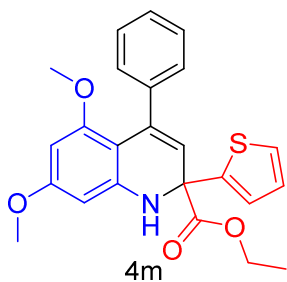
12) **4l** Yellow oil (87.5 mg, 68%);

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.



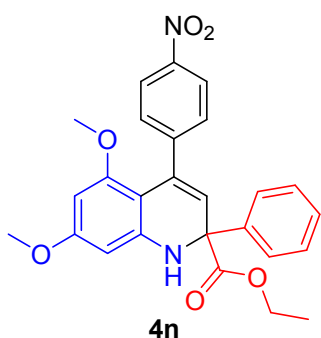
13) **4m** Yellow oil (77.1mg, 61%);

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.



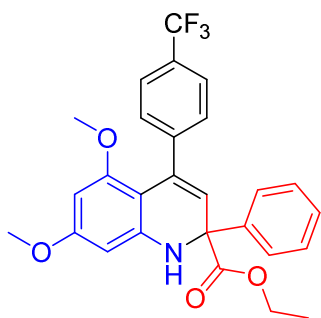
14) **4n** Green solid (110.4mg, 80%); M.p. 190-191 °C;

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);

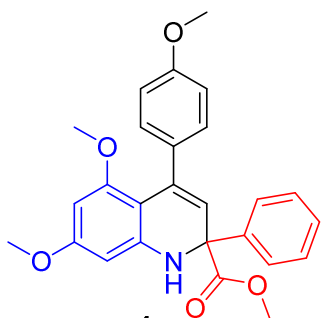
¹³C NMR (101 MHz, CDCl₃) δ 172.47, 162.04, 157.68, 149.66, 146.52, 145.14, 142.44, 135.24, 128.68, 128.26, 128.05, 125.65, 122.60, 102.65, 92.44, 90.44, 63.92, 62.16, 55.27, 54.72, 14.10;

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

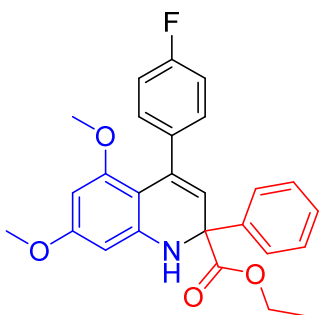
IR: 3391.22, 3078.48, 1721.51, 1615.58, 1236.22, 1092.67, 1075.74, 1198.86.



- 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.



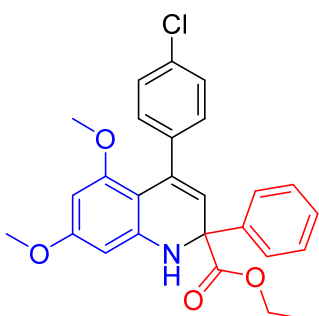
17) **4q** Yellow solid (93.6mg, 72%); M.p. 136-138 °C;

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.



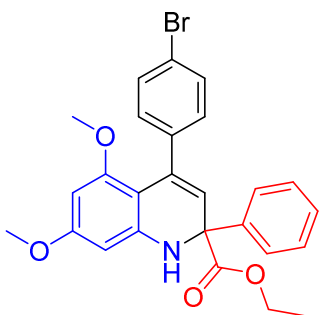
18) **4r** Yellow solid (91.6mg, 68%); M.p. 134-138 °C;

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.



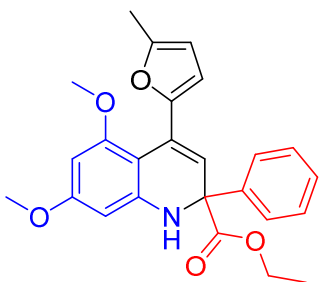
19) **4s** Yellow solid (96.2mg, 65%); M.p. 158-159 °C;

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.



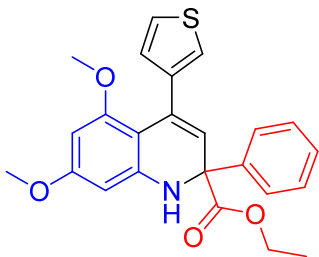
20) **4t** Yellow oil (106.9 mg, 85%);

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.



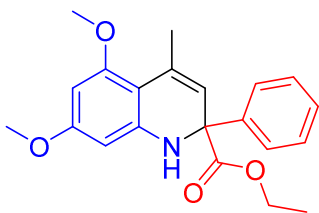
21) **4u** Yellow solid (93.5 mg, 74%); M.p. 128-130 °C;

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.



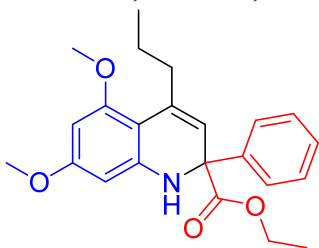
22) **4v** Yellow oil (45.6mg, 43%);

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.



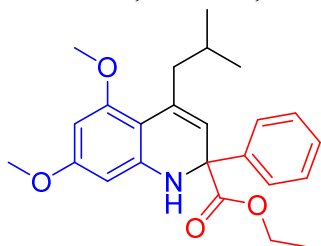
23) **4w** Yellow oil (52.6mg, 46%);

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.



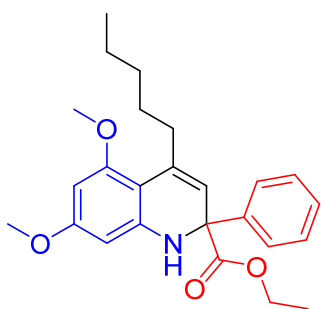
24) **4x** Yellow oil (47.4mg, 40%);

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%);

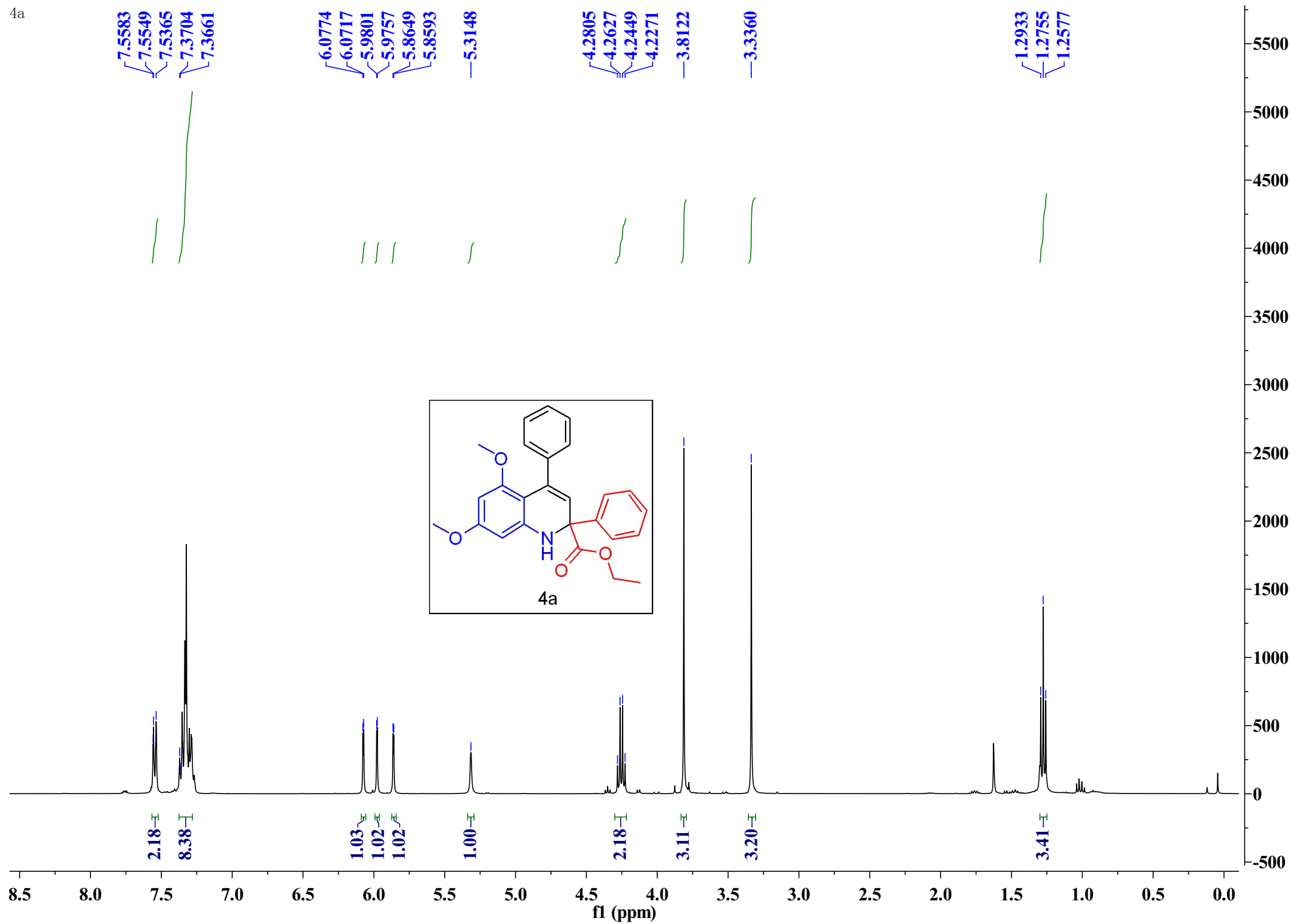
¹H NMR (400 MHz, CDCl₃) δ 7.46 (d, *J* = 7.3 Hz, 2H), 7.34 (t, *J* = 7.4 Hz, 2H), 7.28 (d, *J* = 7.1 Hz, 1H), 5.94 (d, *J* = 2.3 Hz, 1H), 5.89 (d, *J* = 2.3 Hz, 1H), 5.74 (s, 1H), 5.07 (s, 1H), 4.24 (qd, *J* = 7.1, 1.9 Hz, 2H), ¹ δ 3.77 (d, *J* = 9.4 Hz, 6H), 2.70 – 2.62 (m, 2H), 1.47 (dd, *J* = 14.2,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

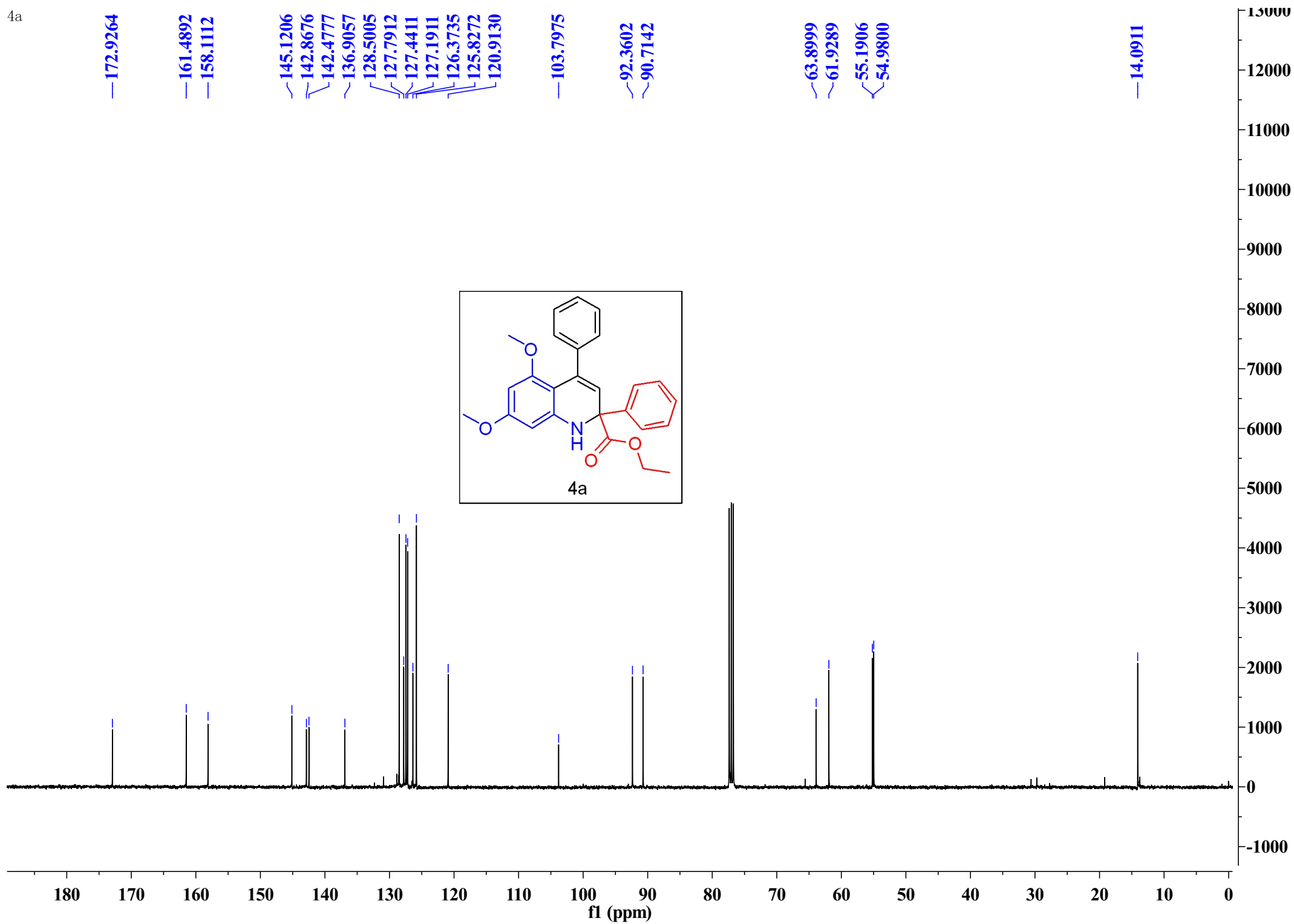
HRMS (ESI): $\text{C}_{25}\text{H}_{31}\text{NO}_4$ Neutral mass: 409.22531, Observed neutral mass: 409.2253, Observed $([\text{M}+\text{H}])^+$: 410.2326;
IR: 3378.27, 3081.58, 1720.11, 1618.58, 1246.22, 1092.19, 1075.34, 1198.86

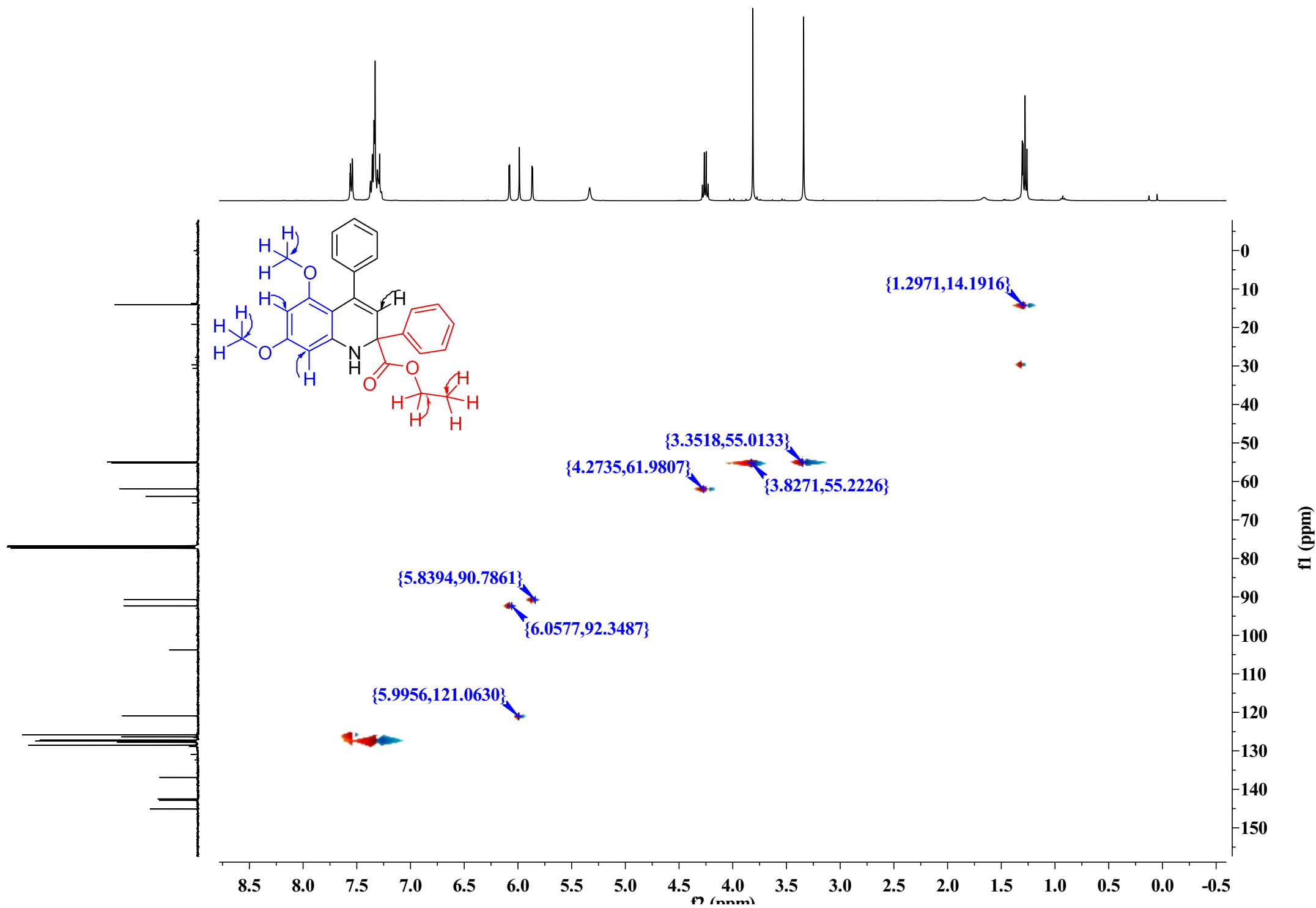
3. NMR spectrums

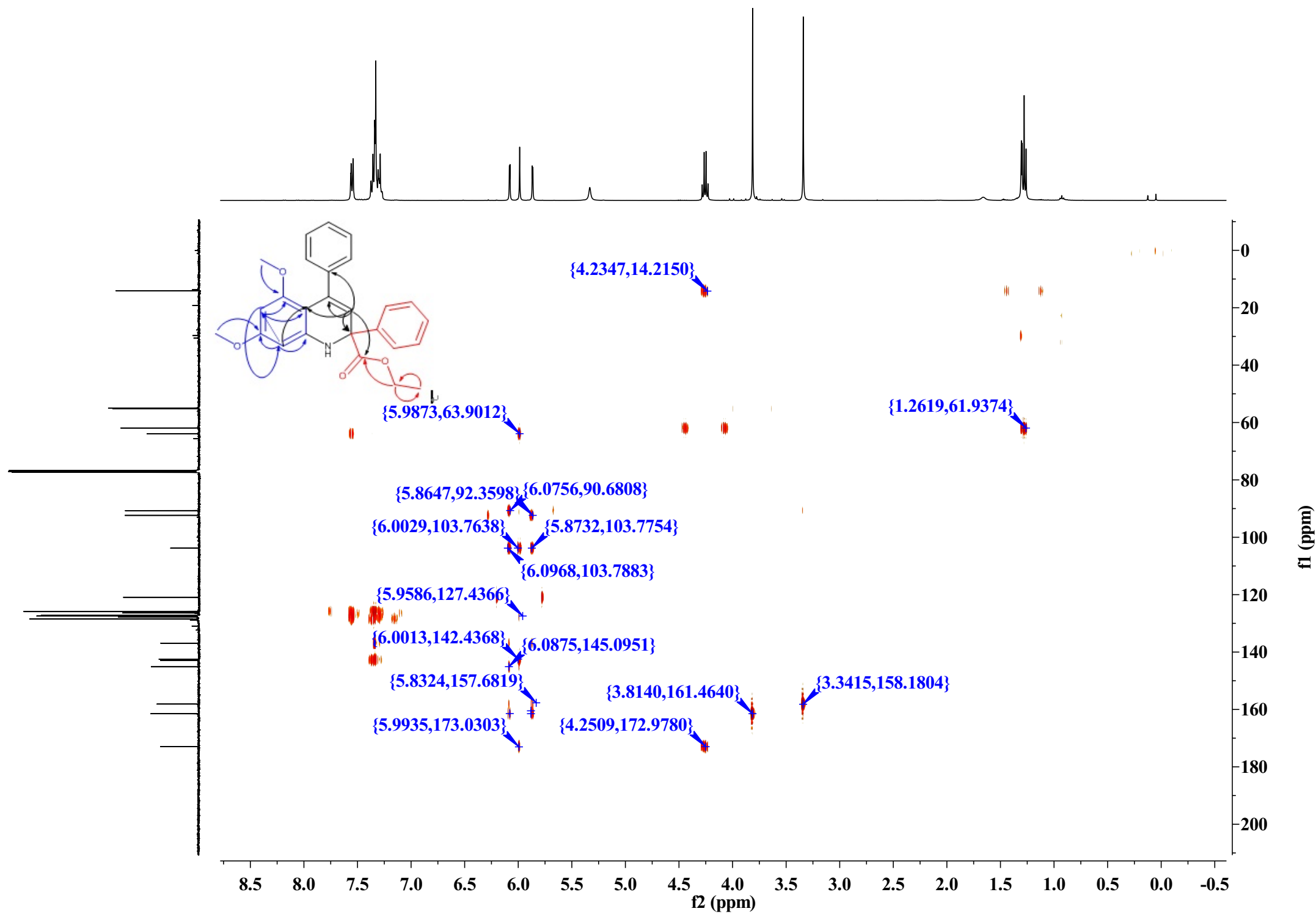
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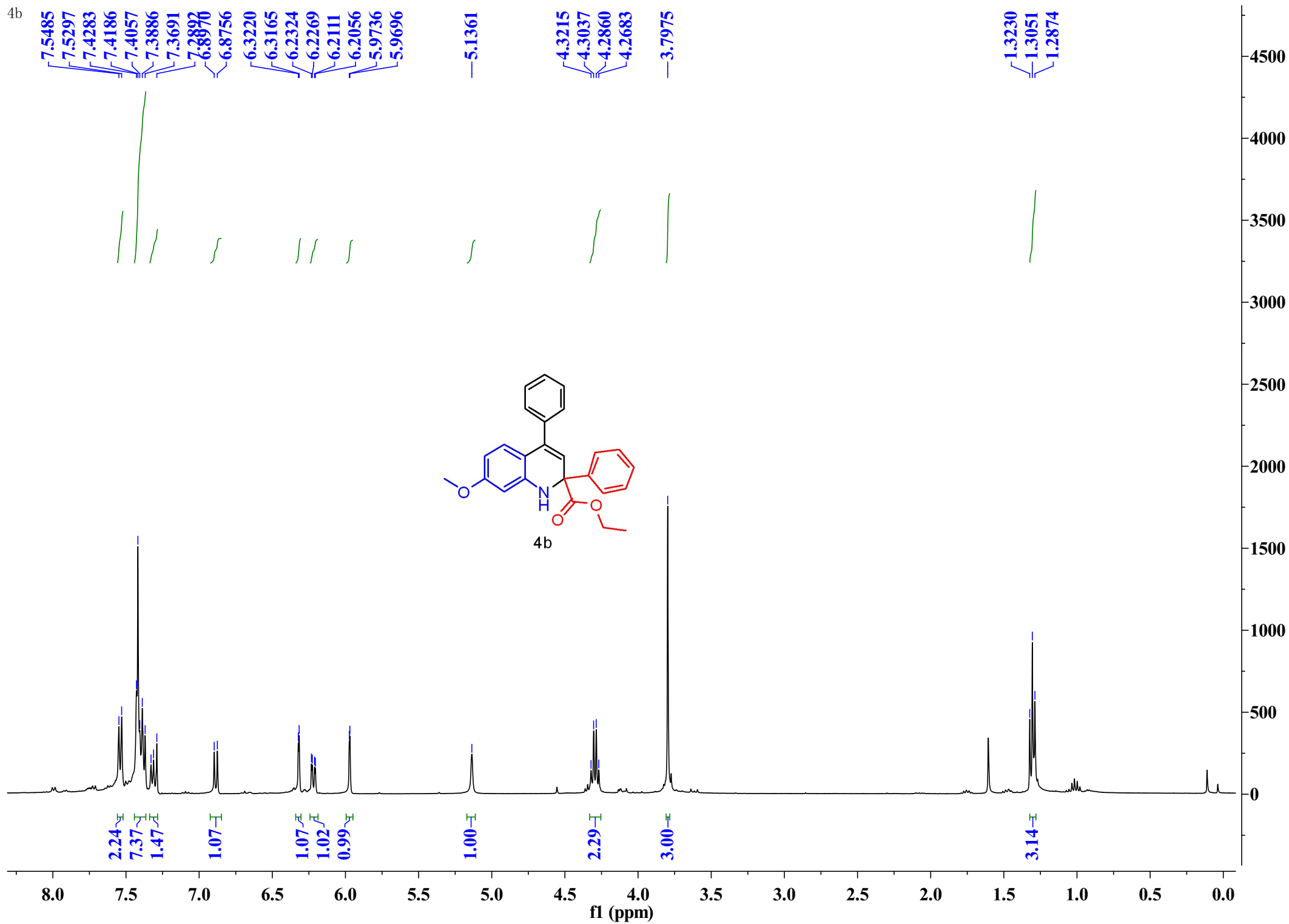
4a



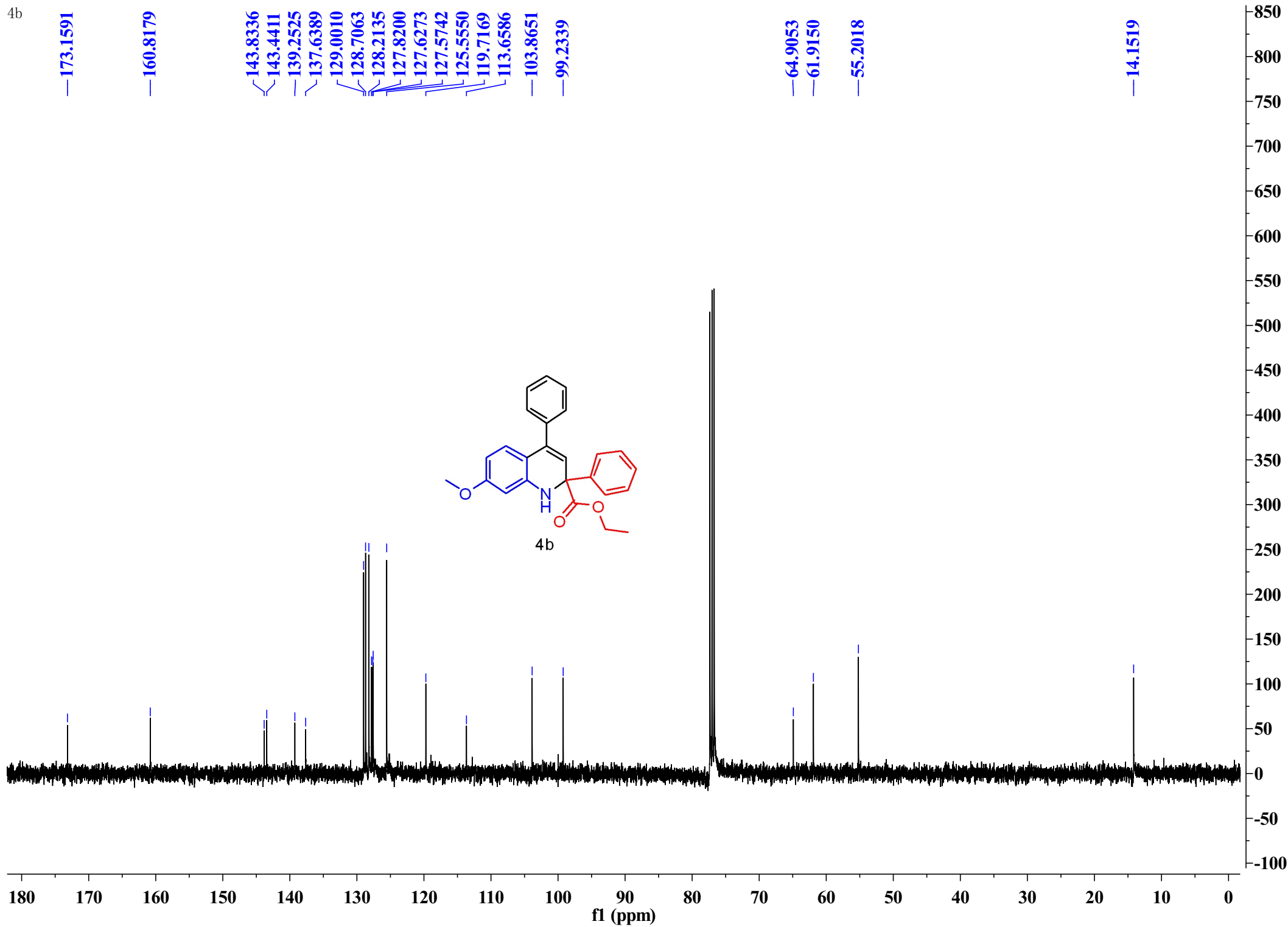




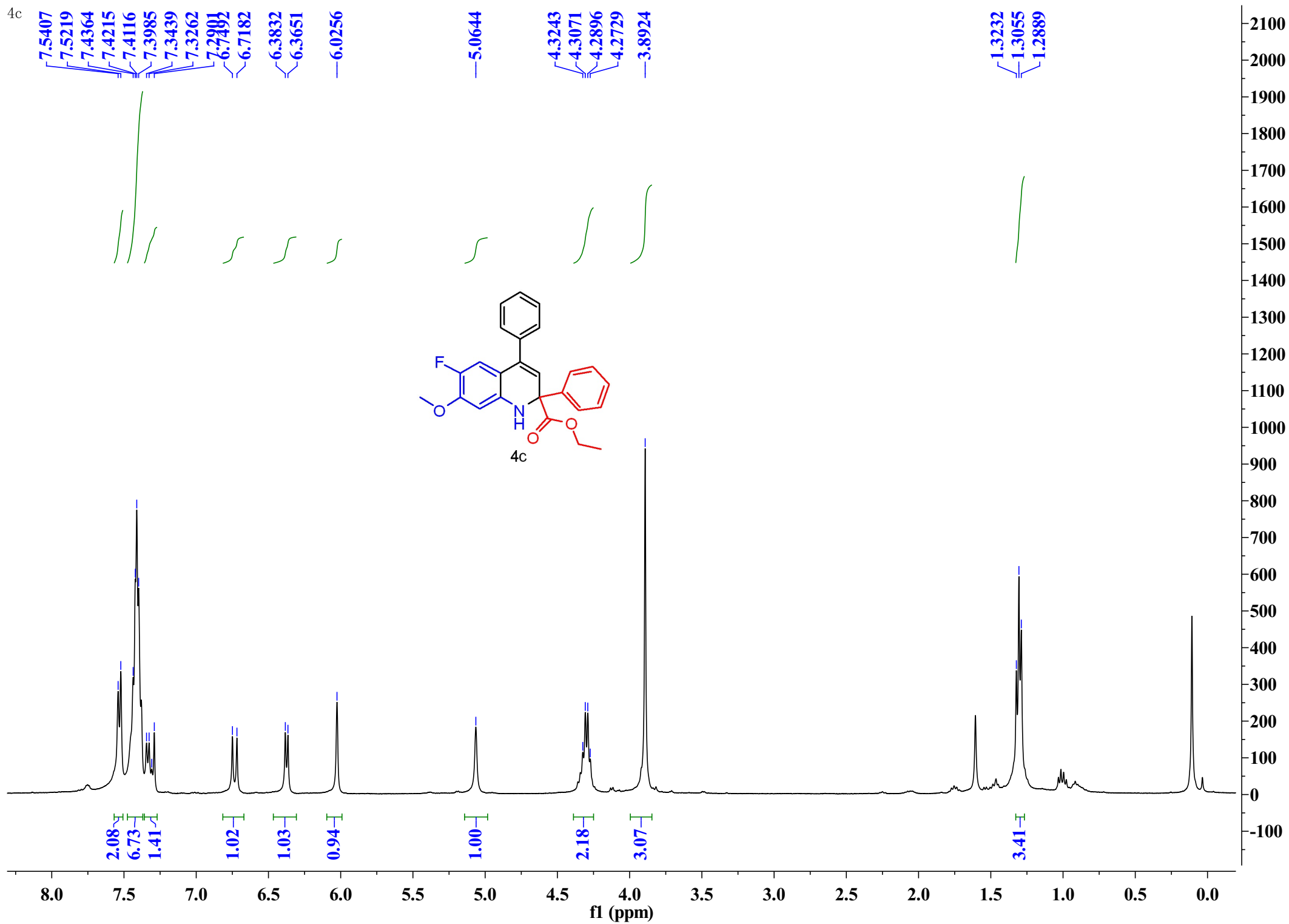
4b



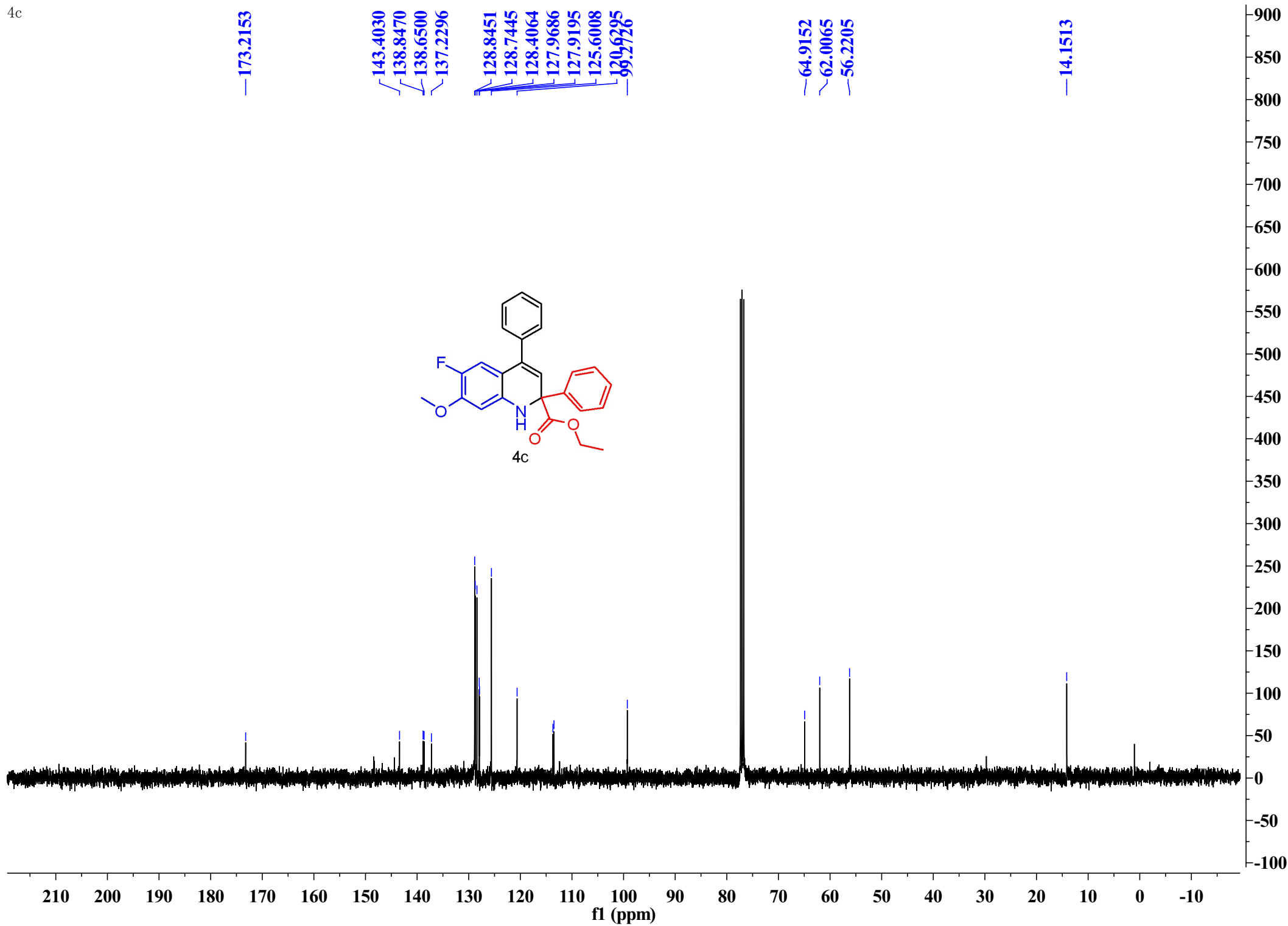
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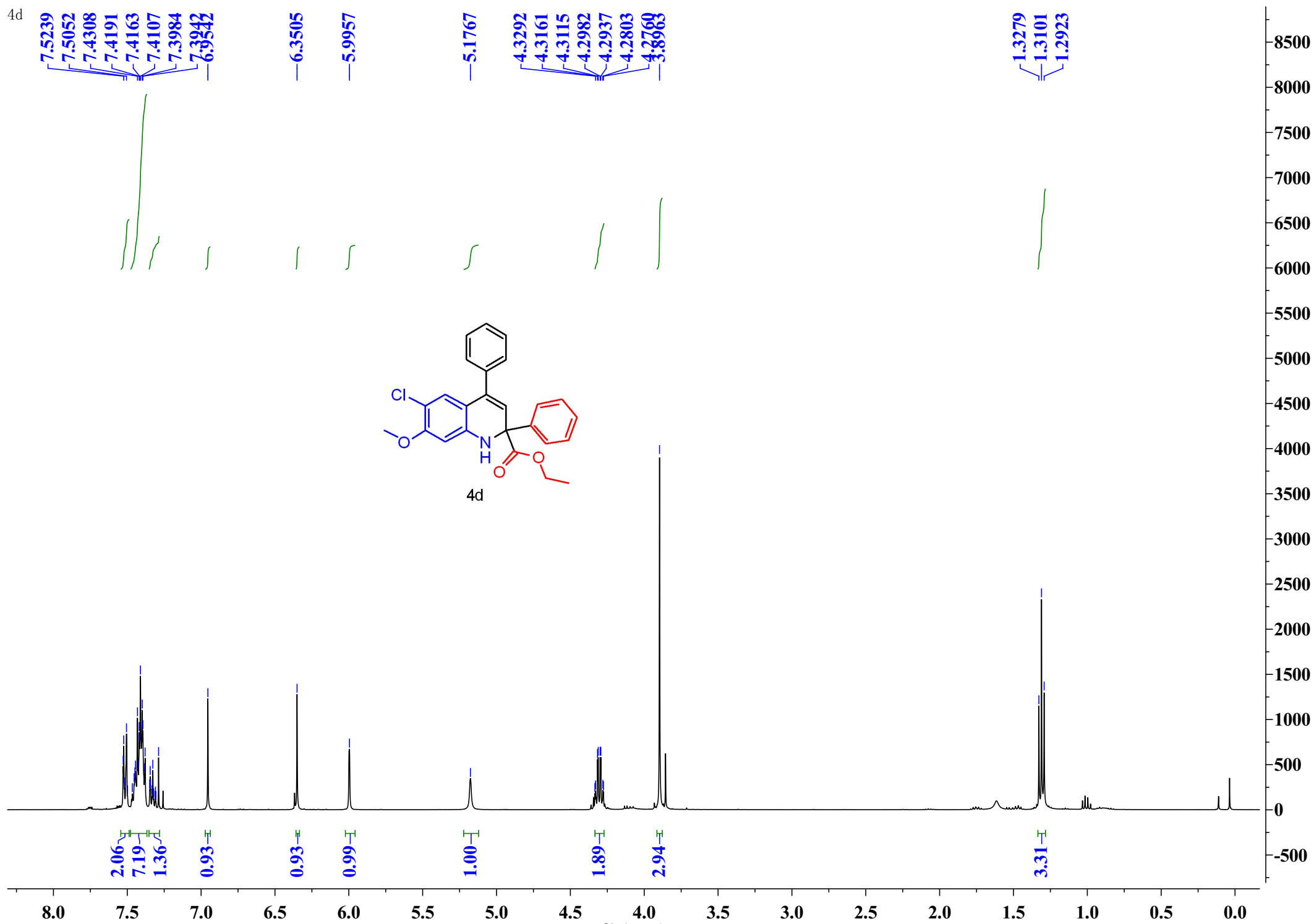
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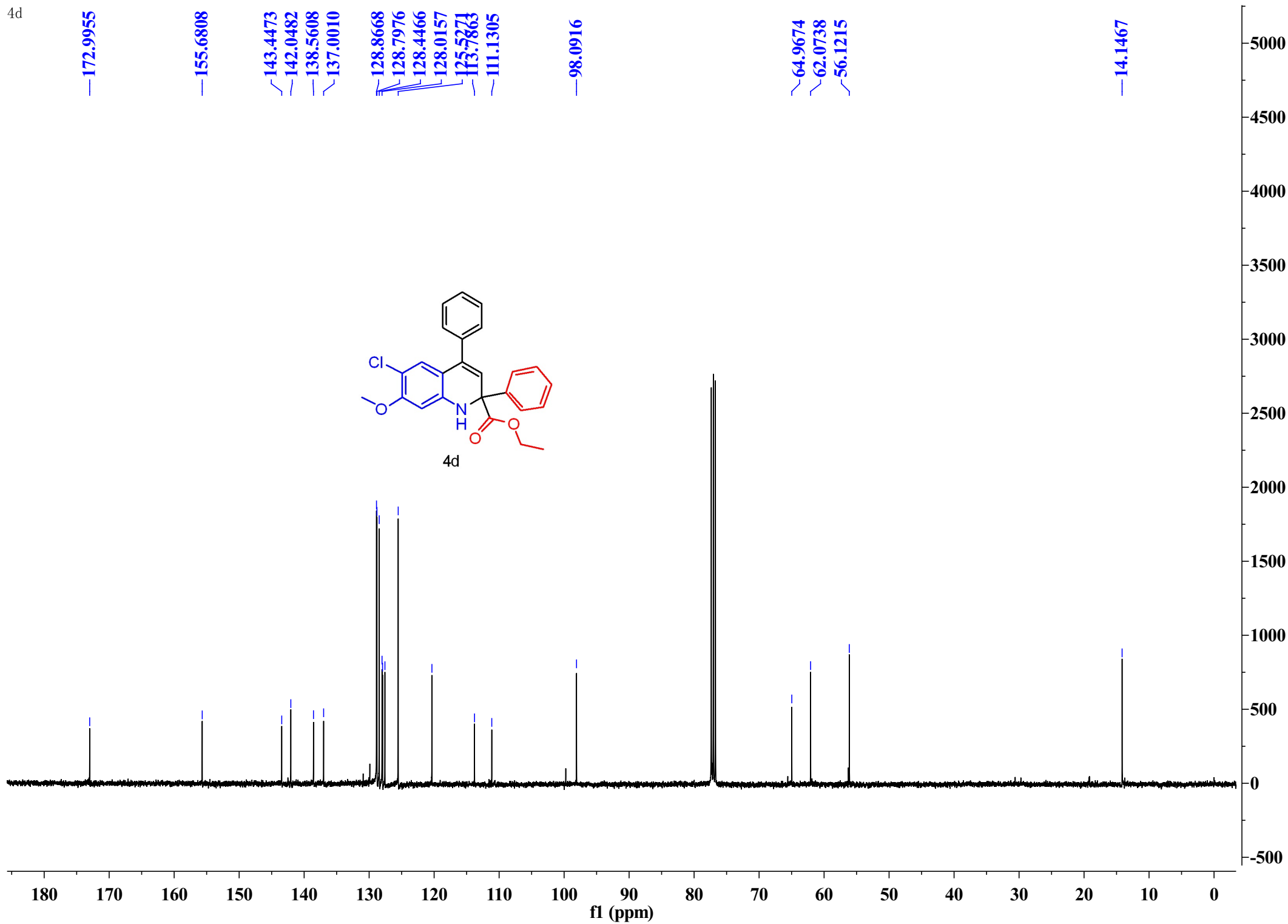
4c

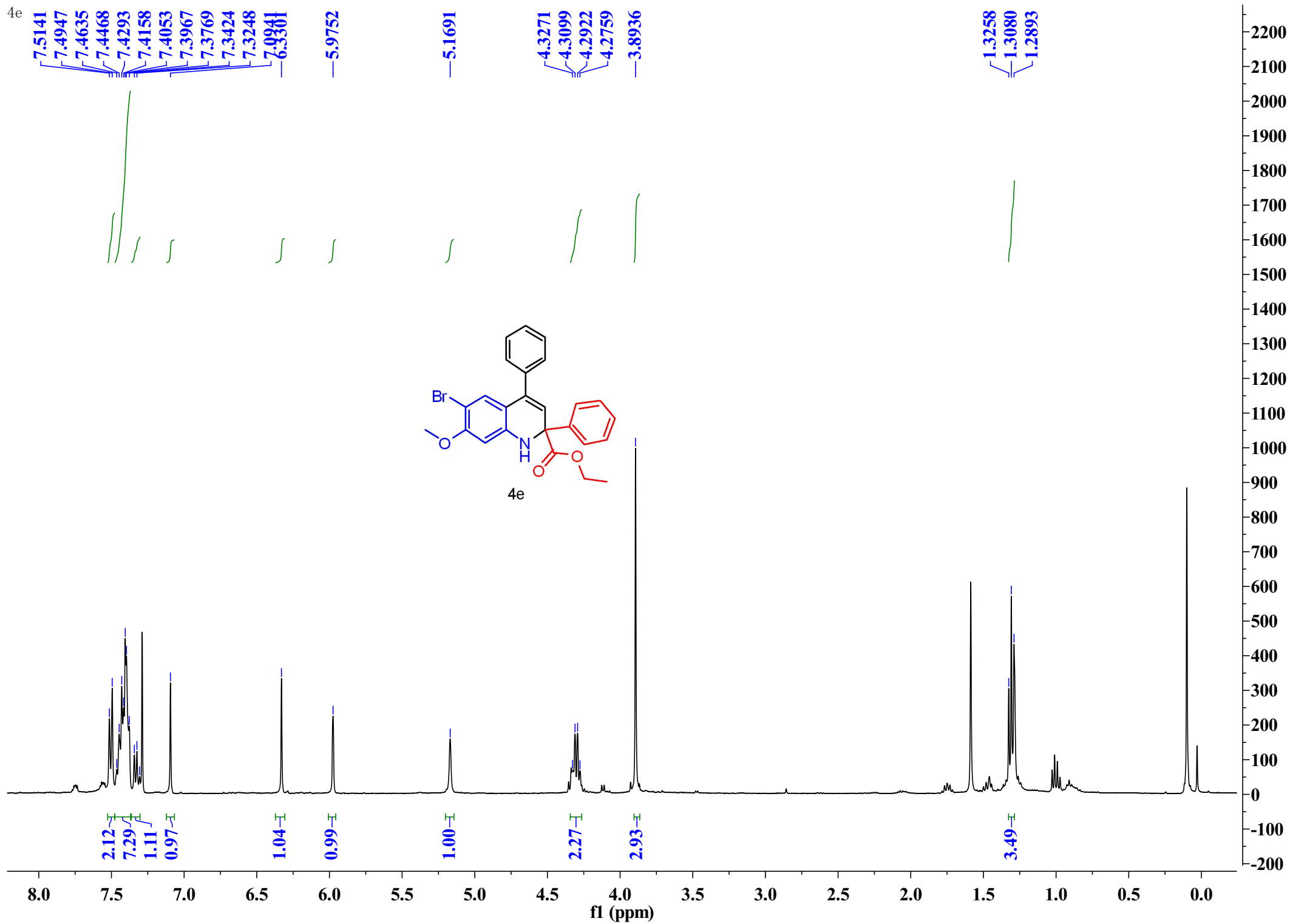


4d

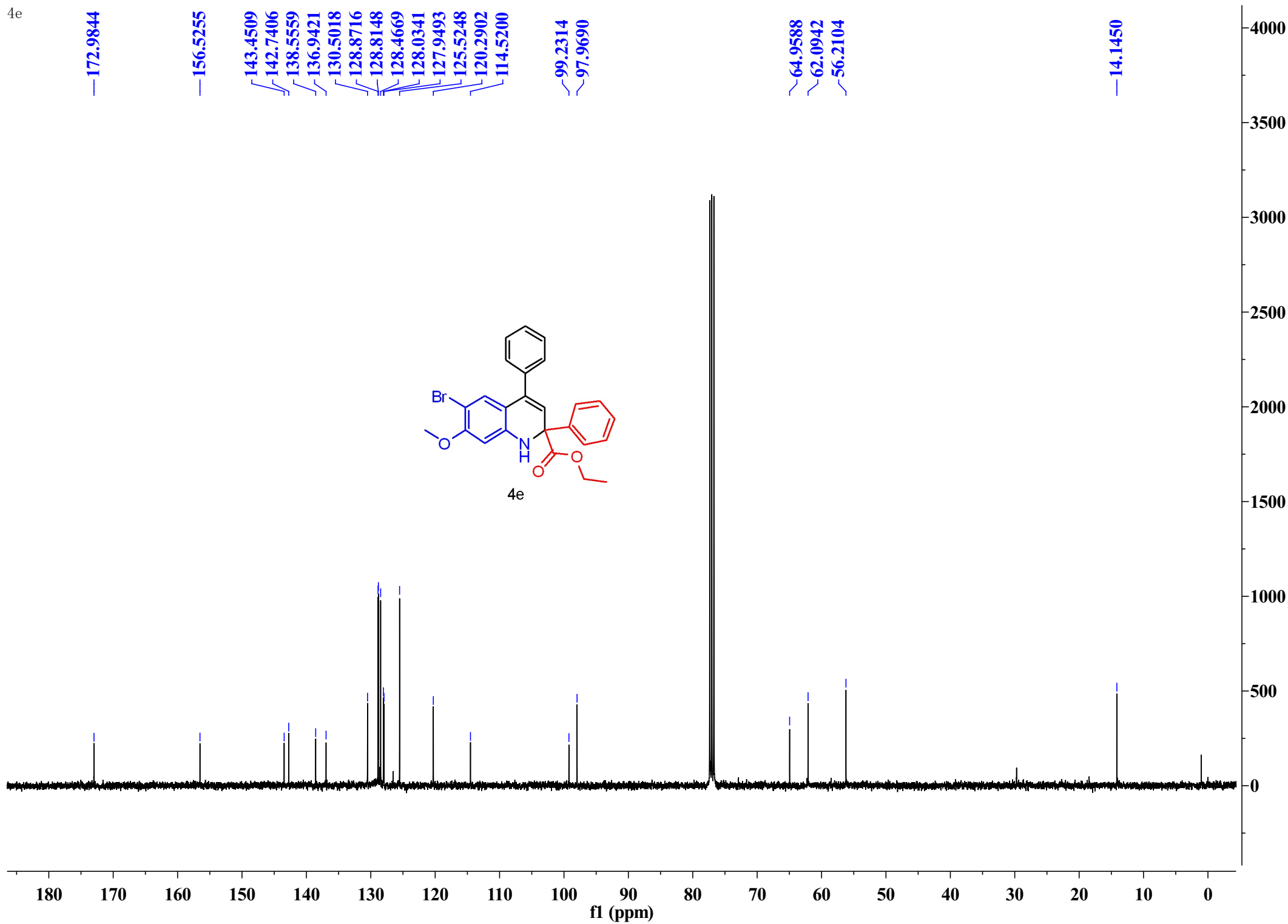


4d

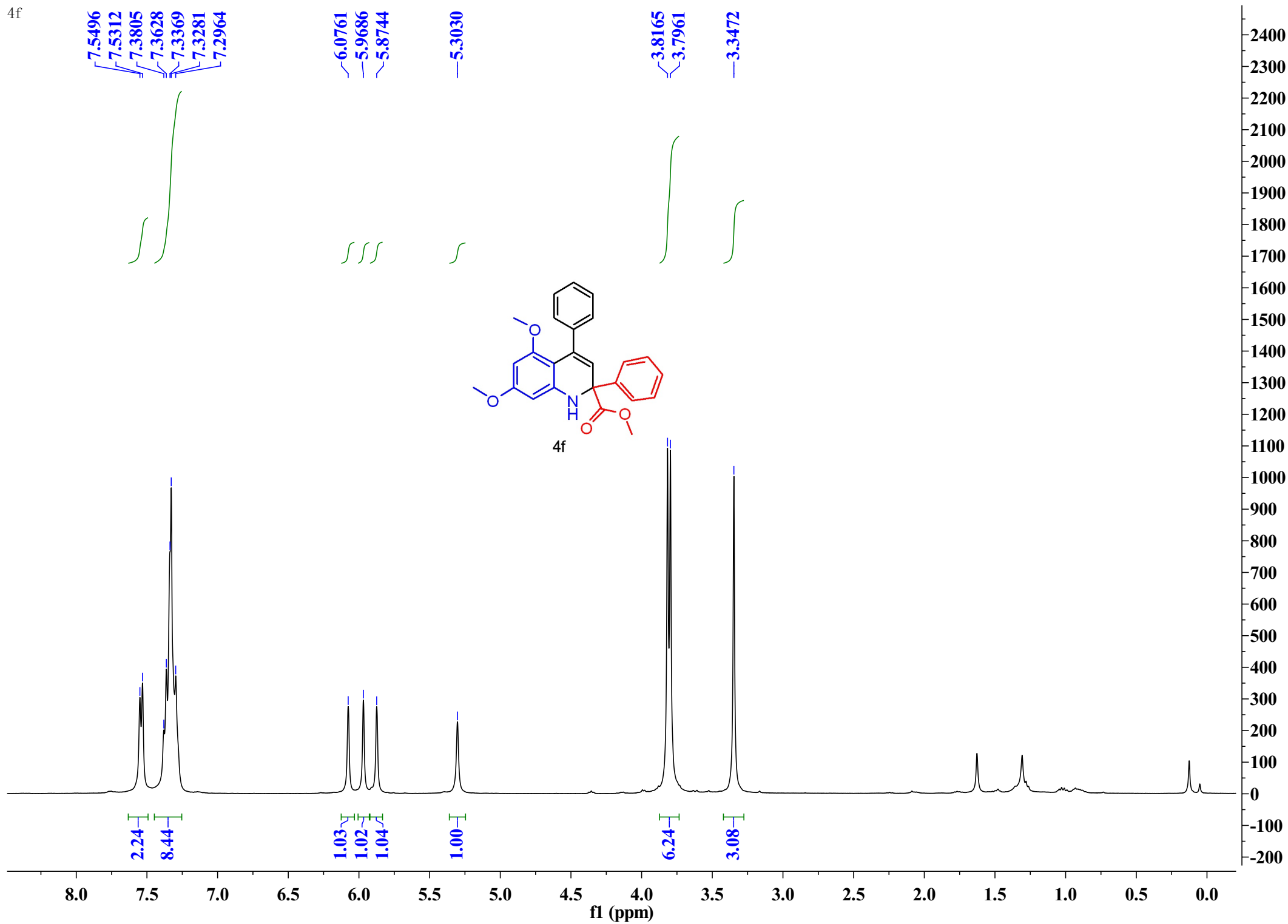




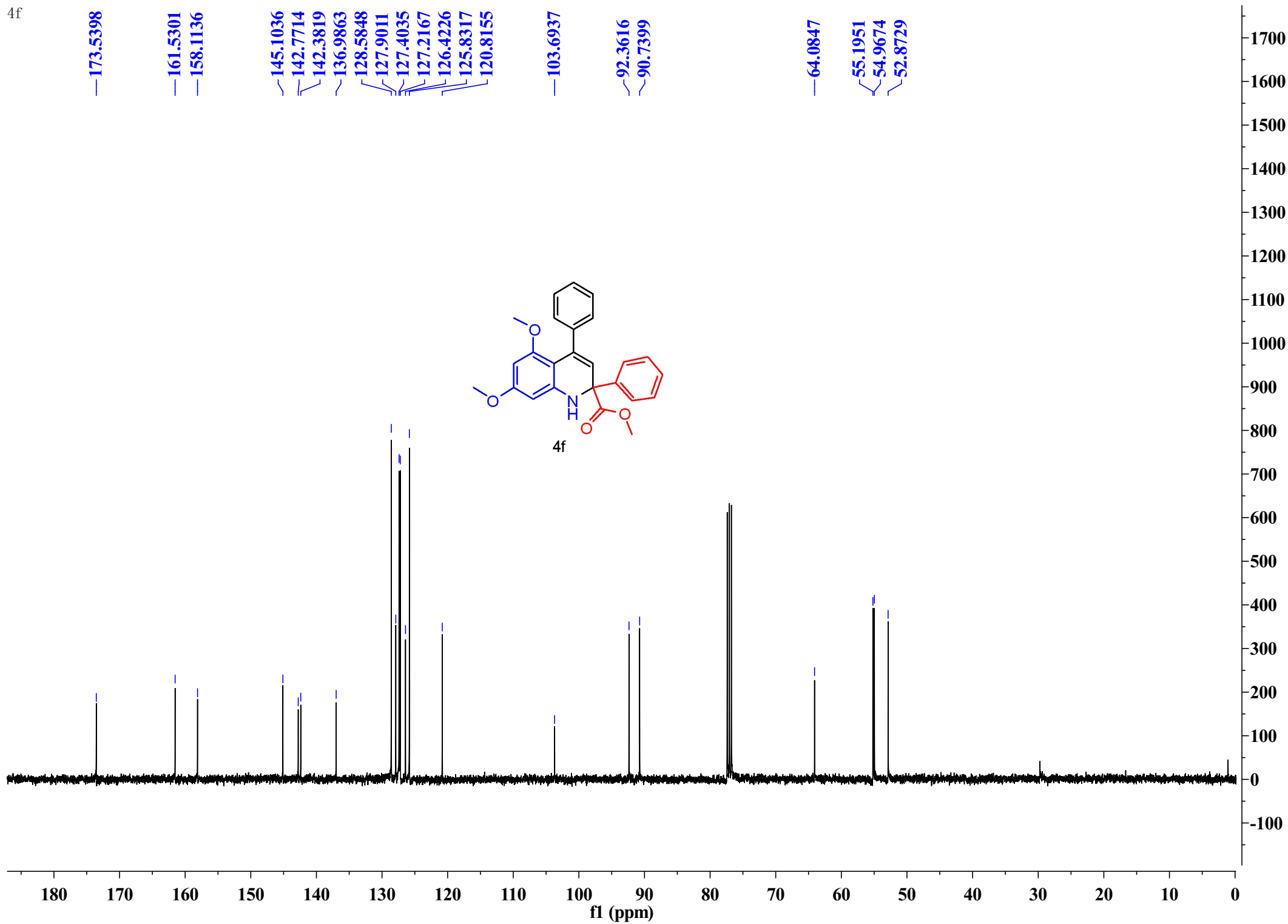
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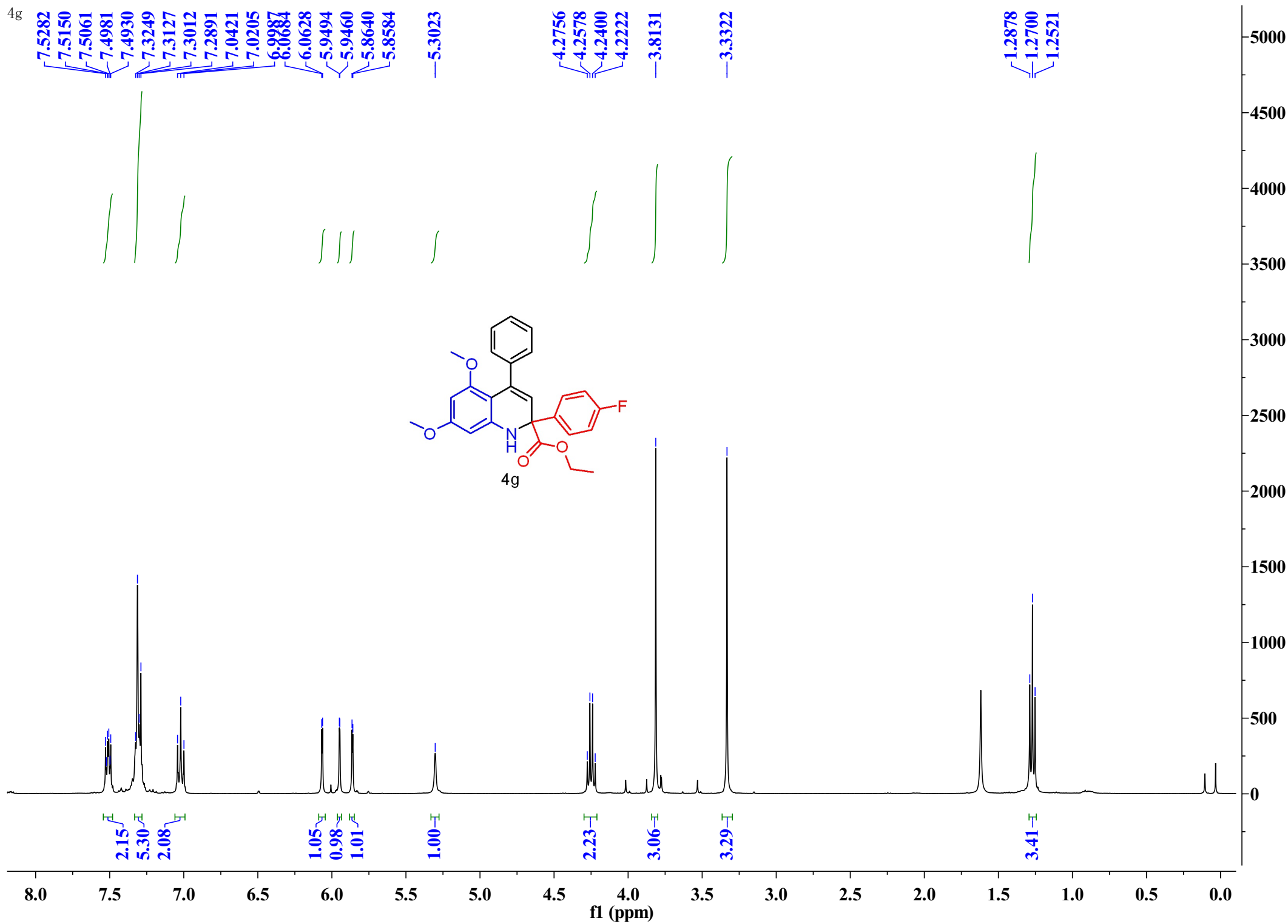


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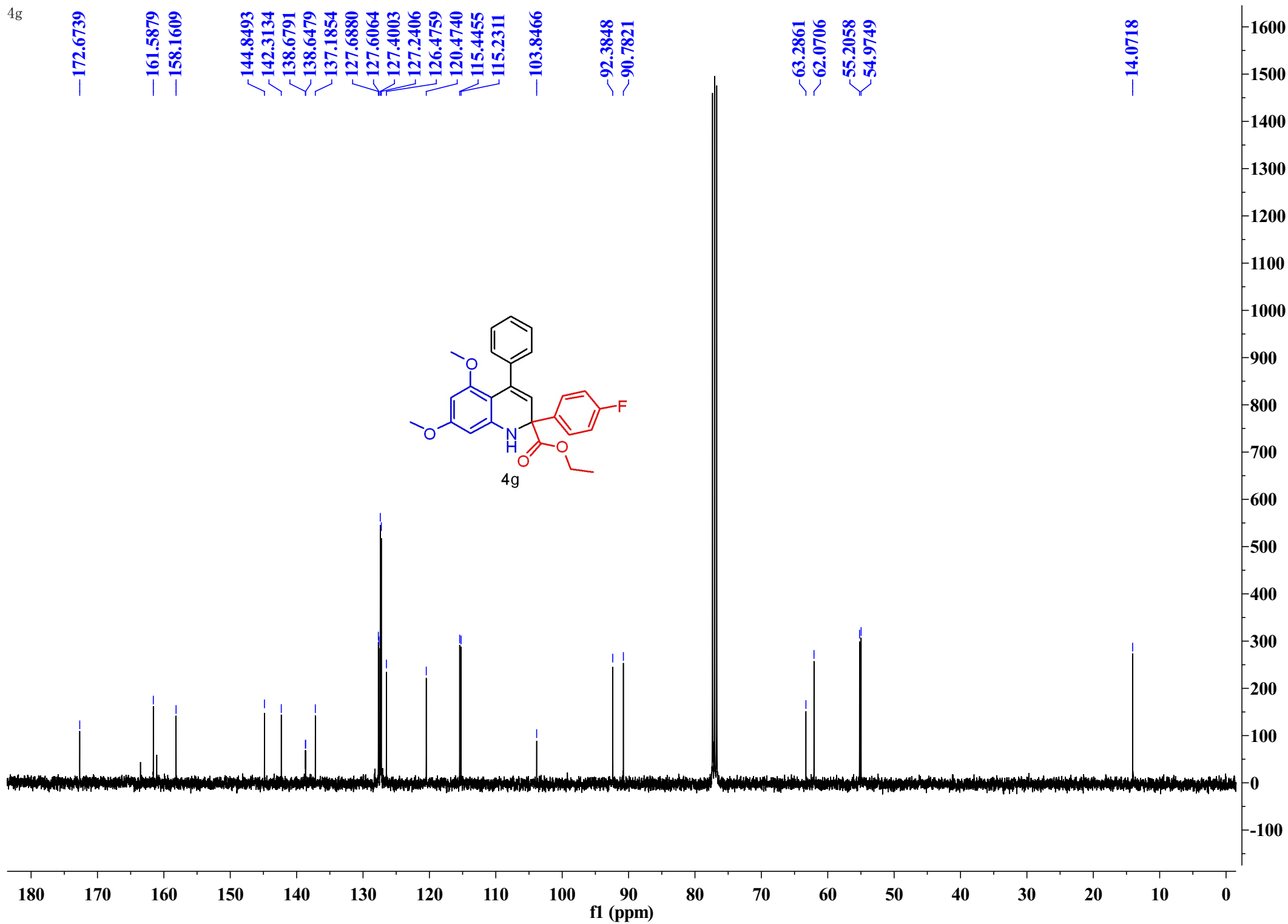


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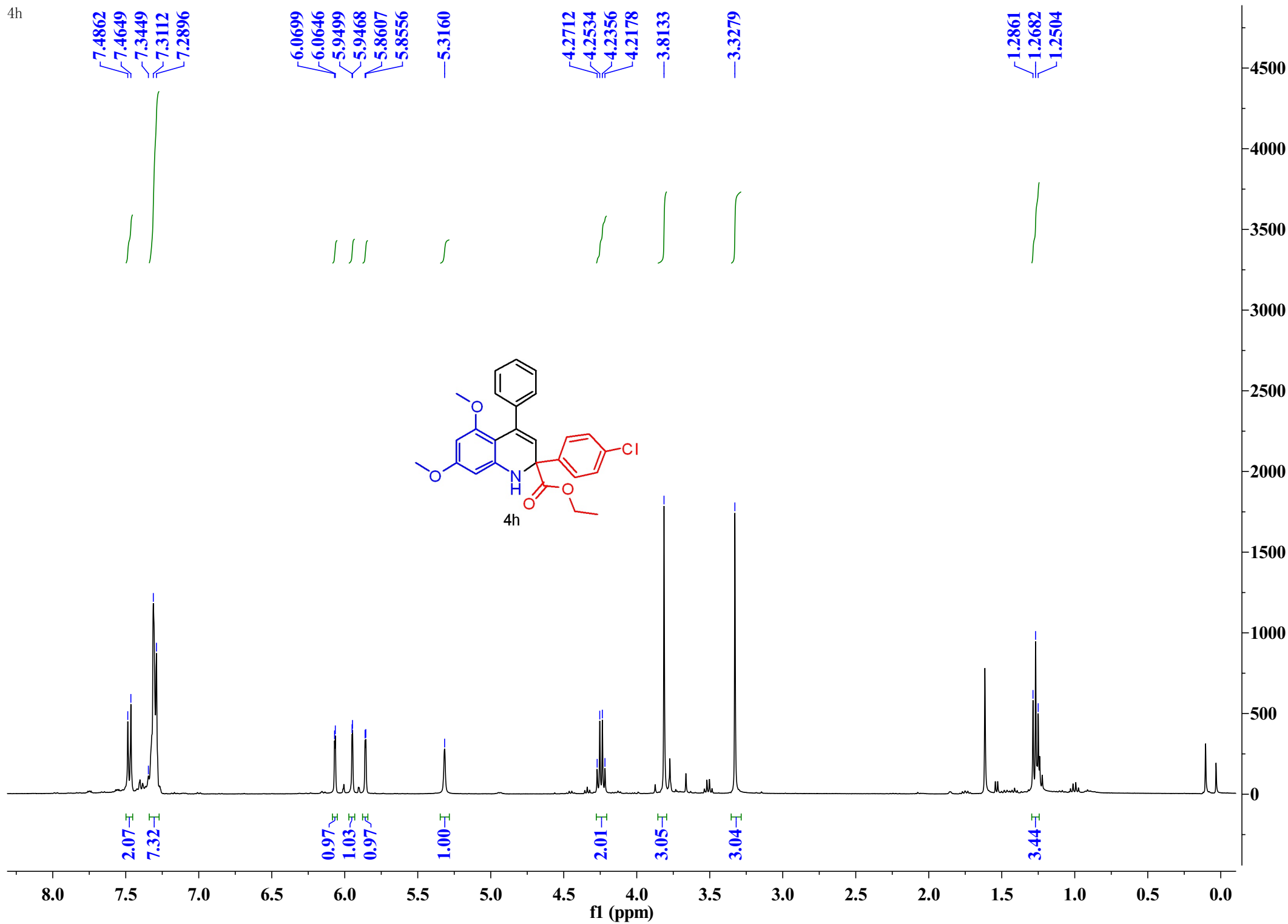




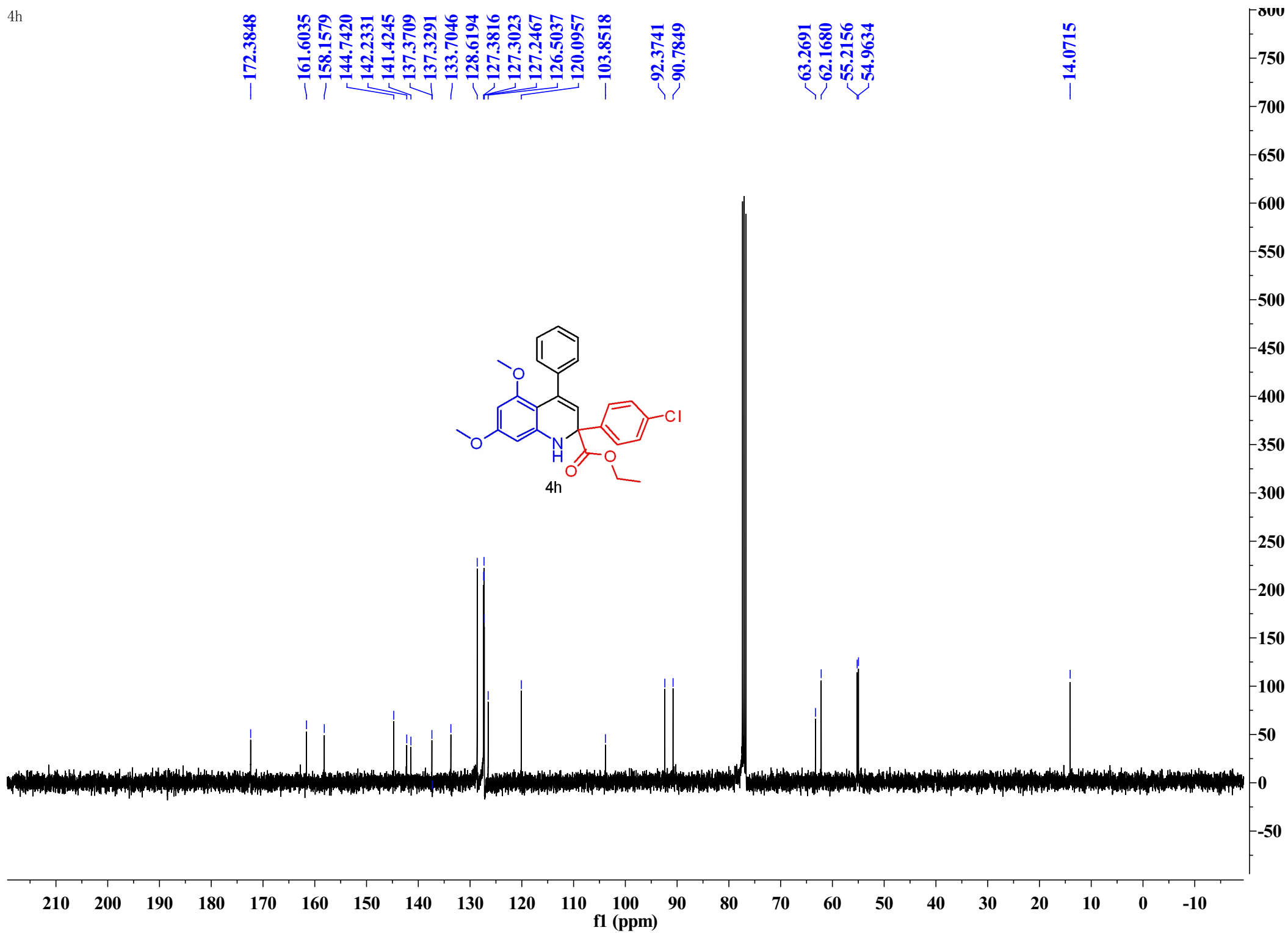
4g

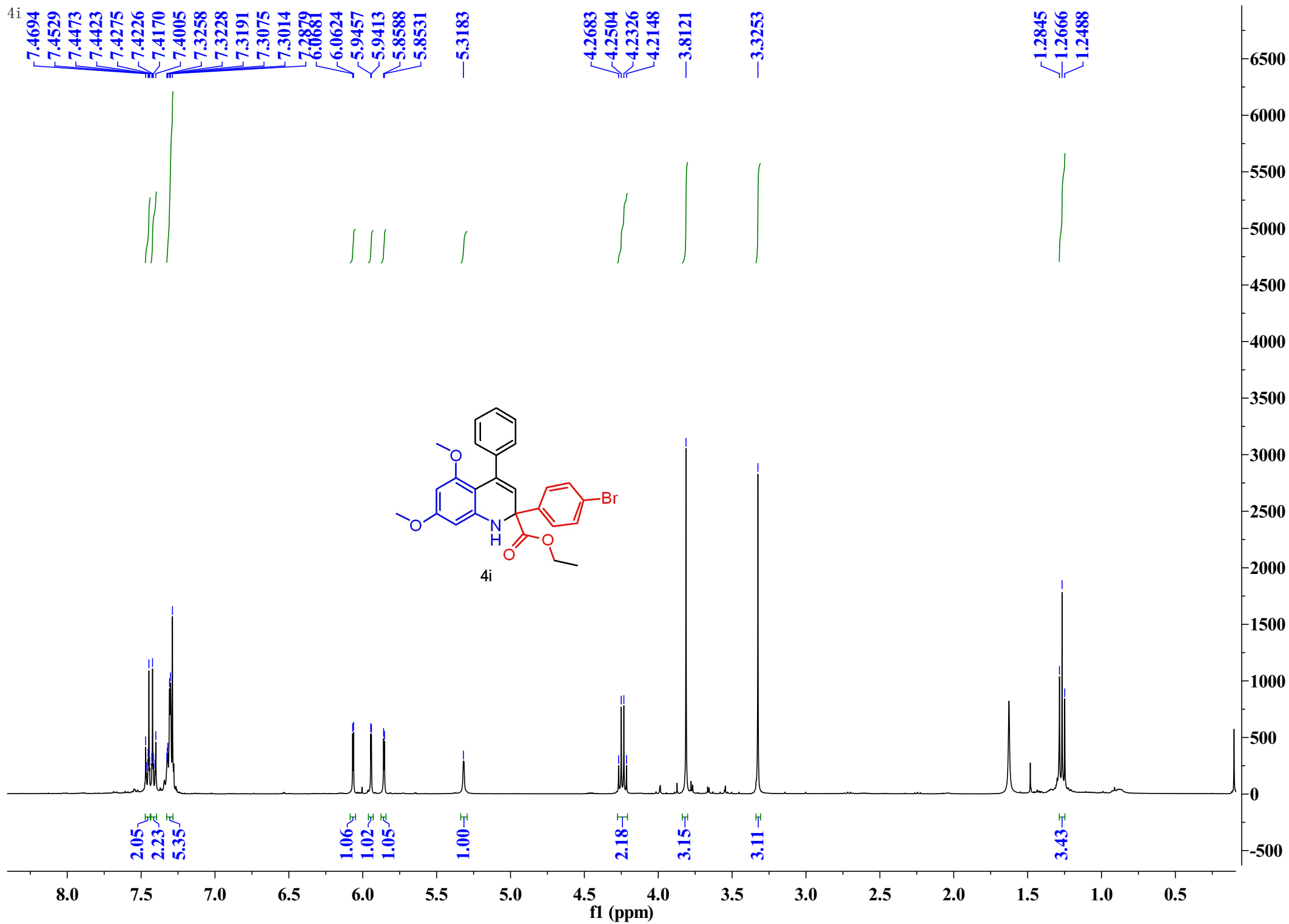


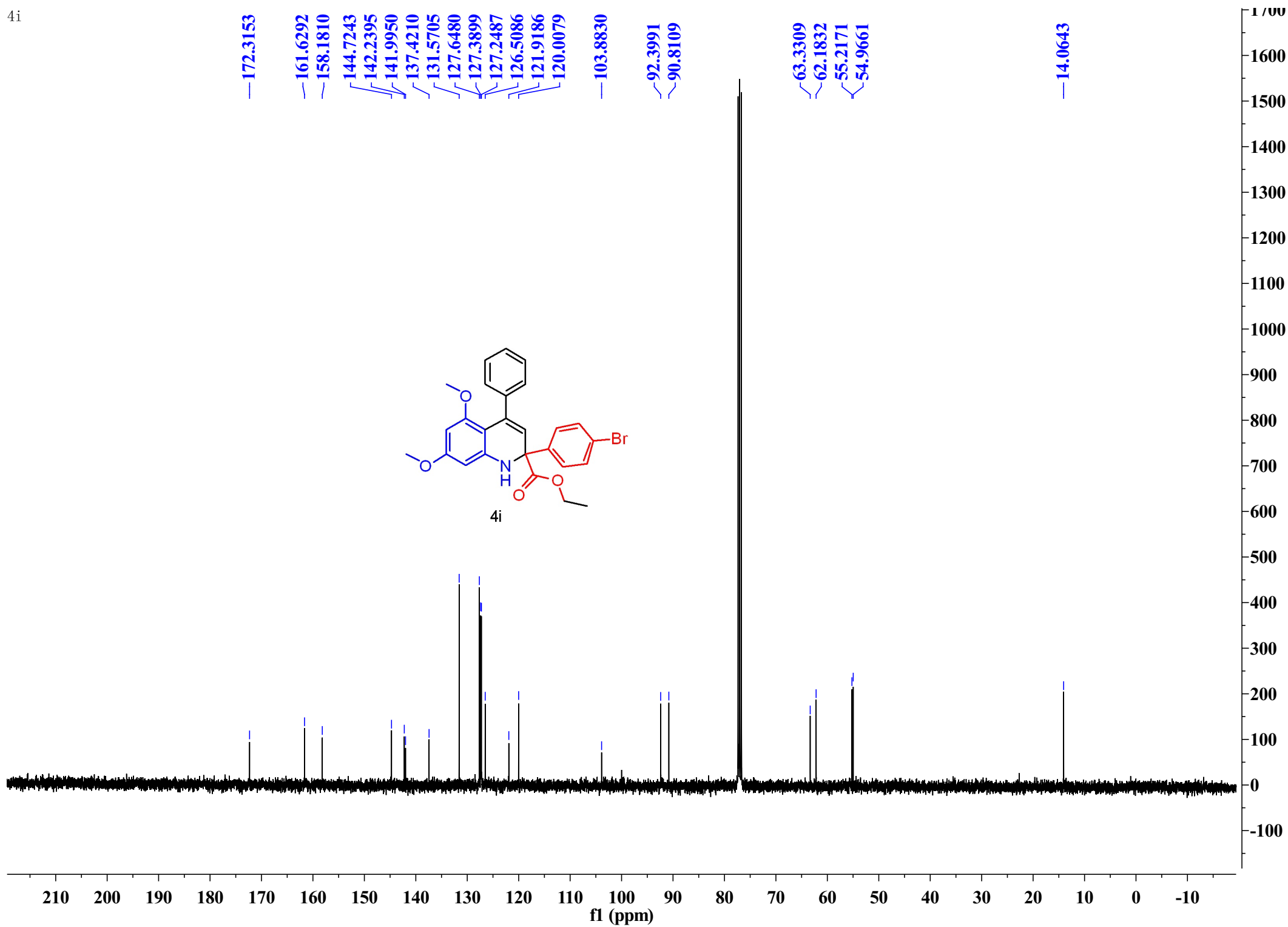
4h



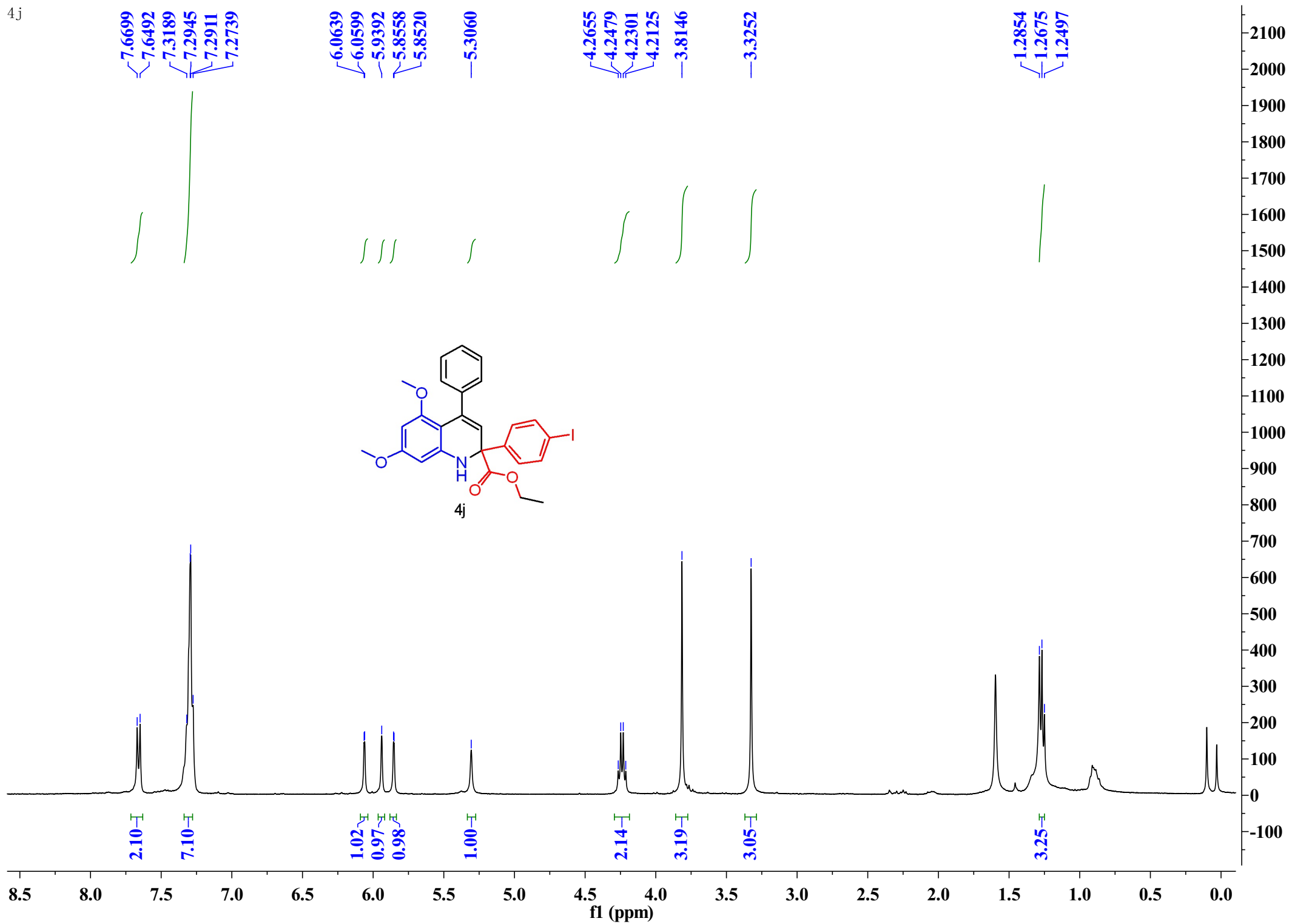
4h



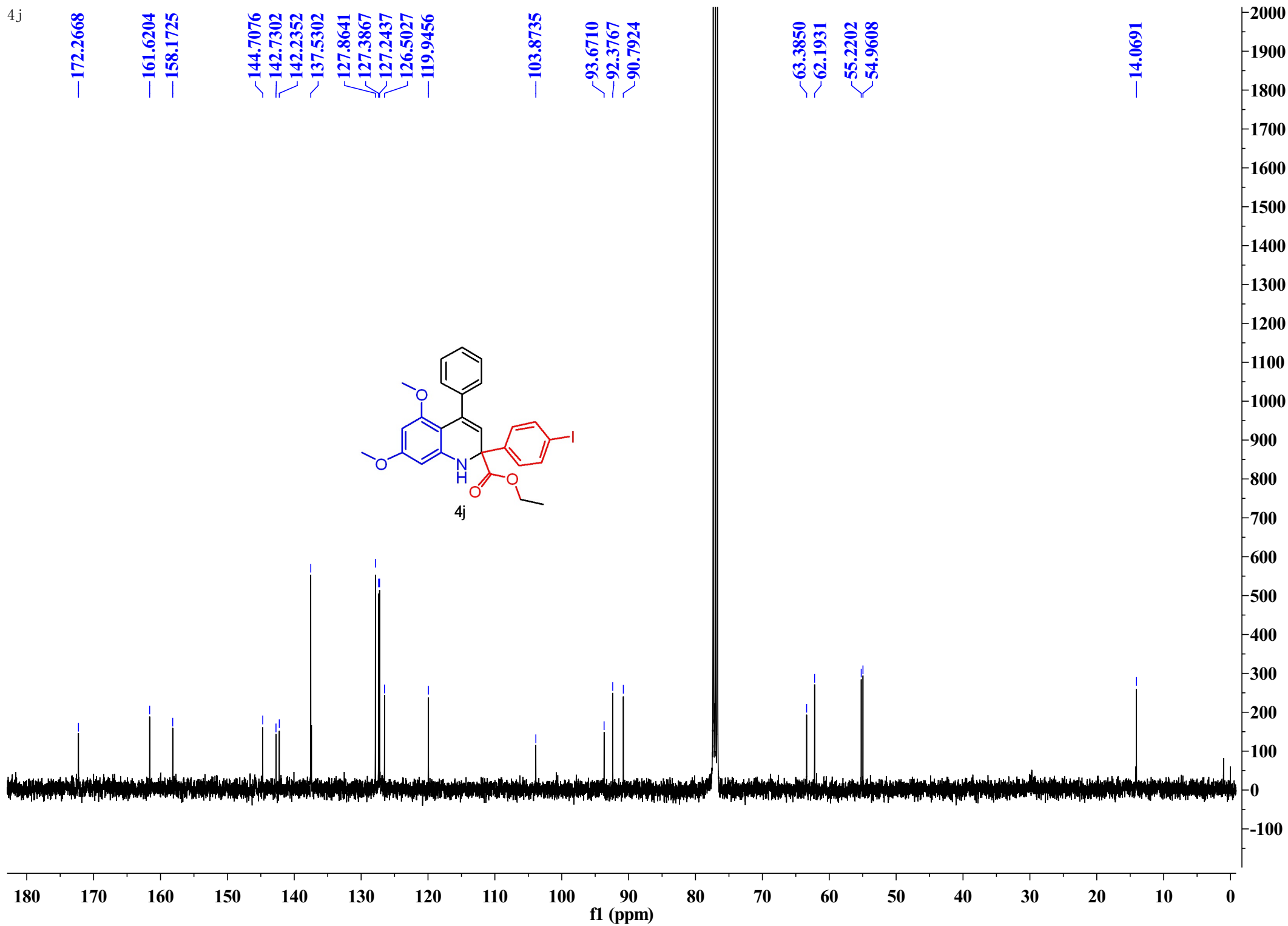


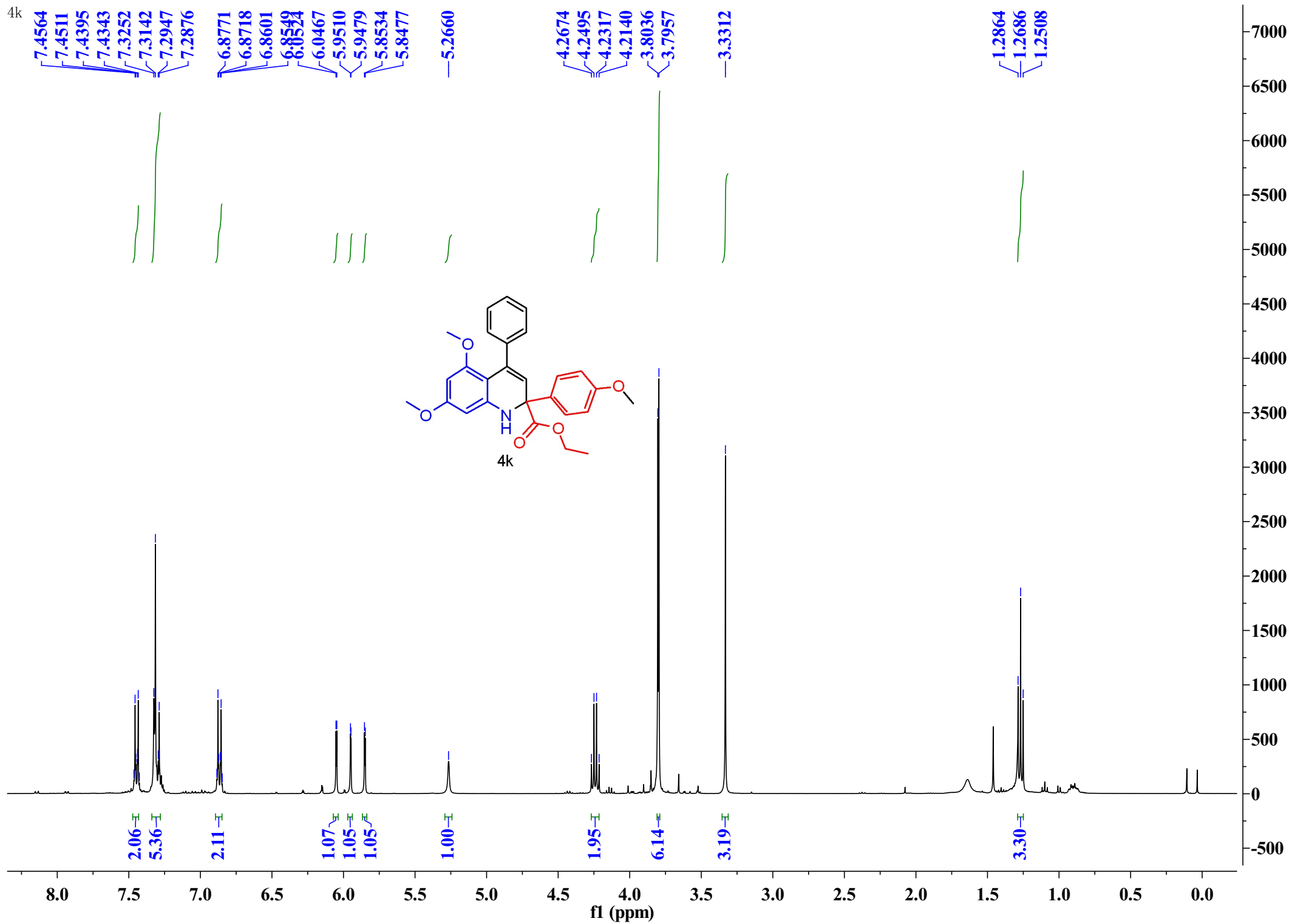


4j

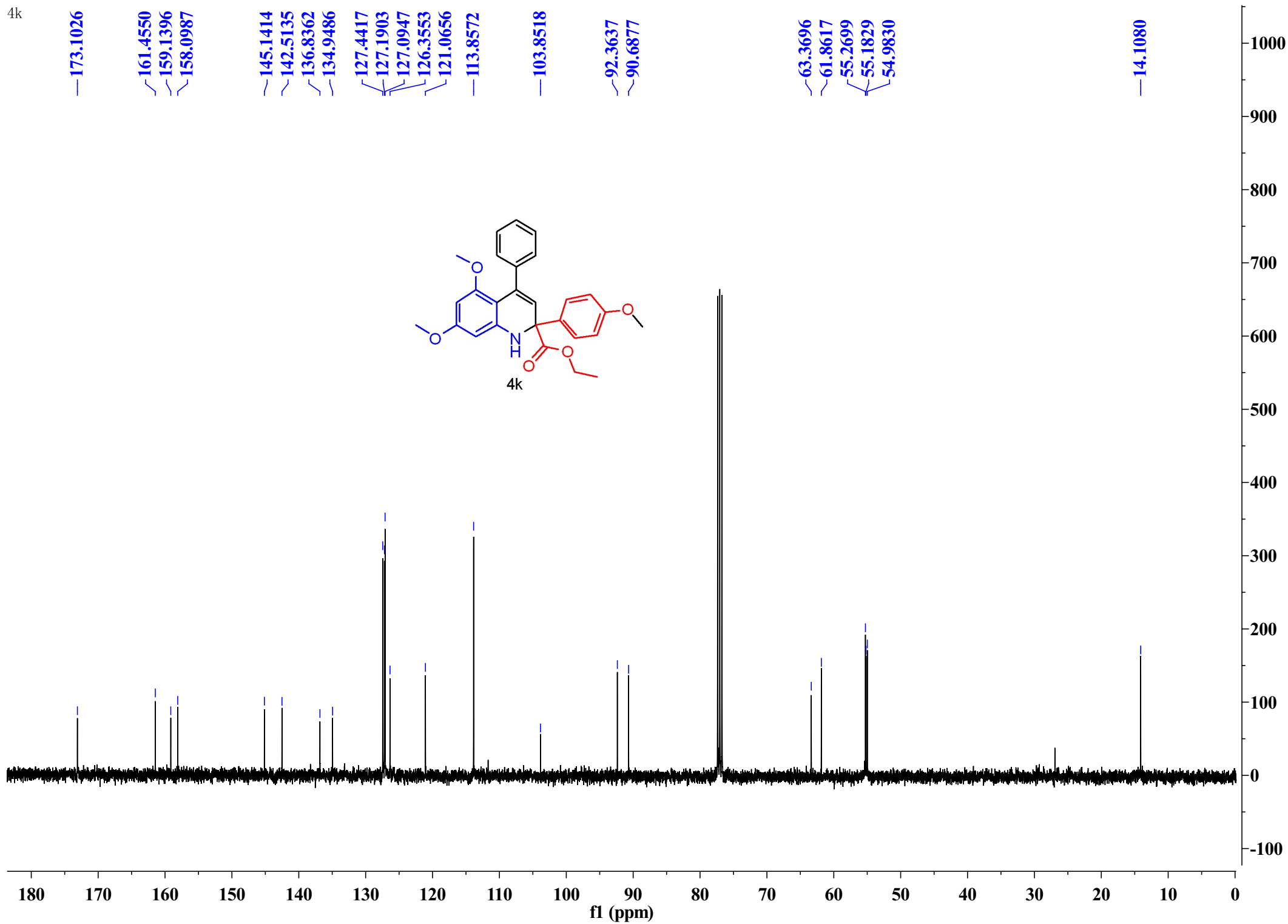


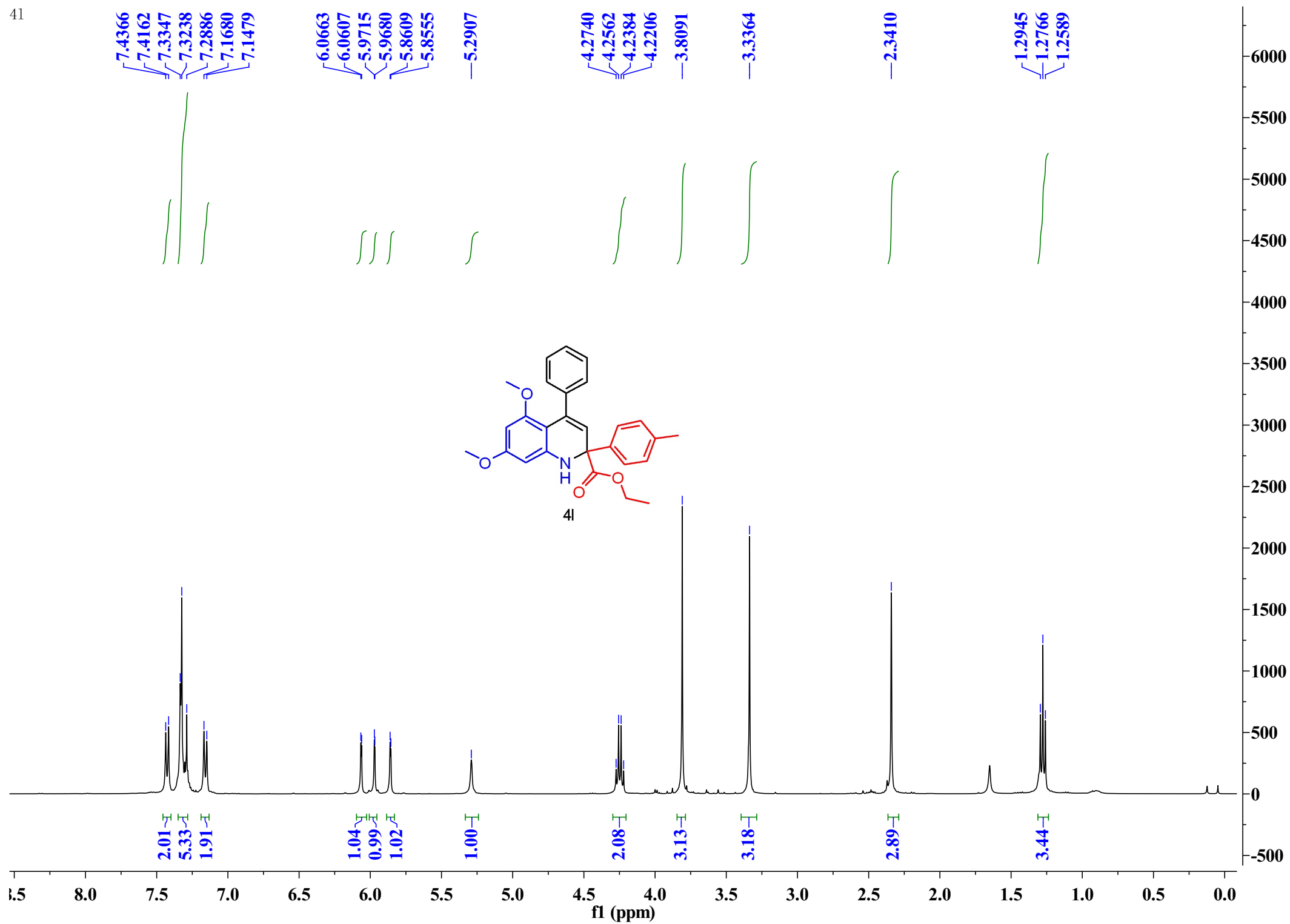
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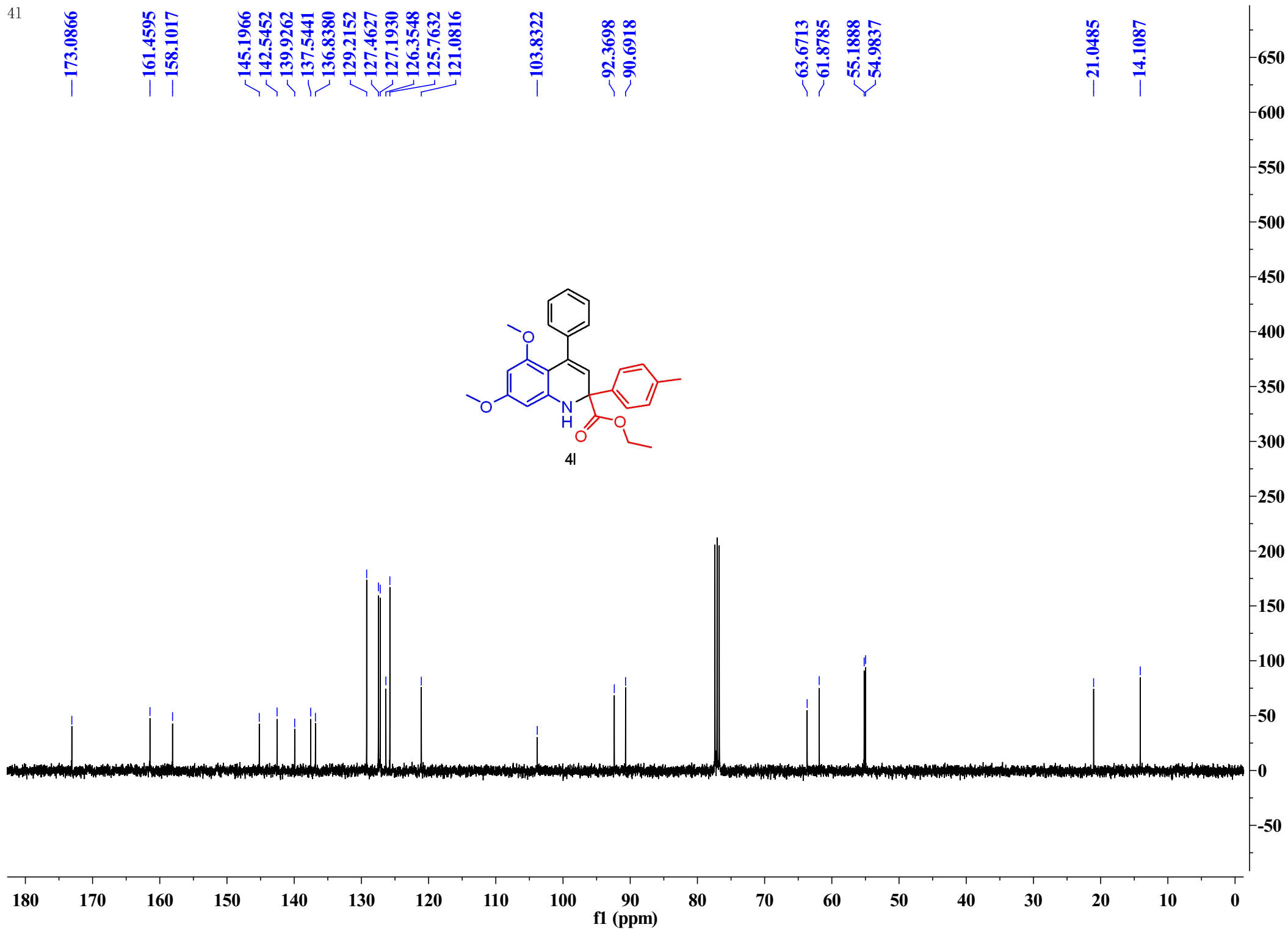


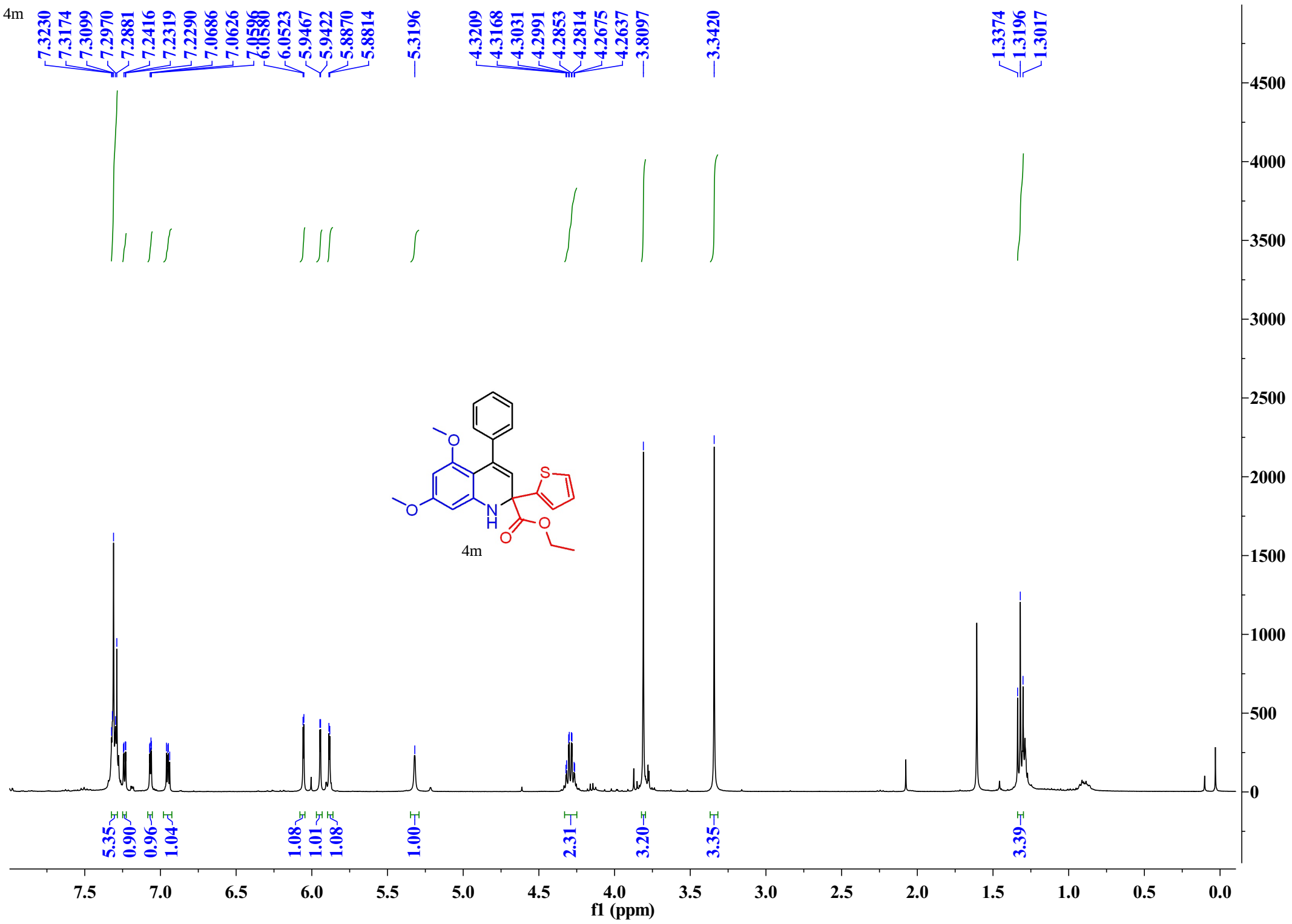


4k

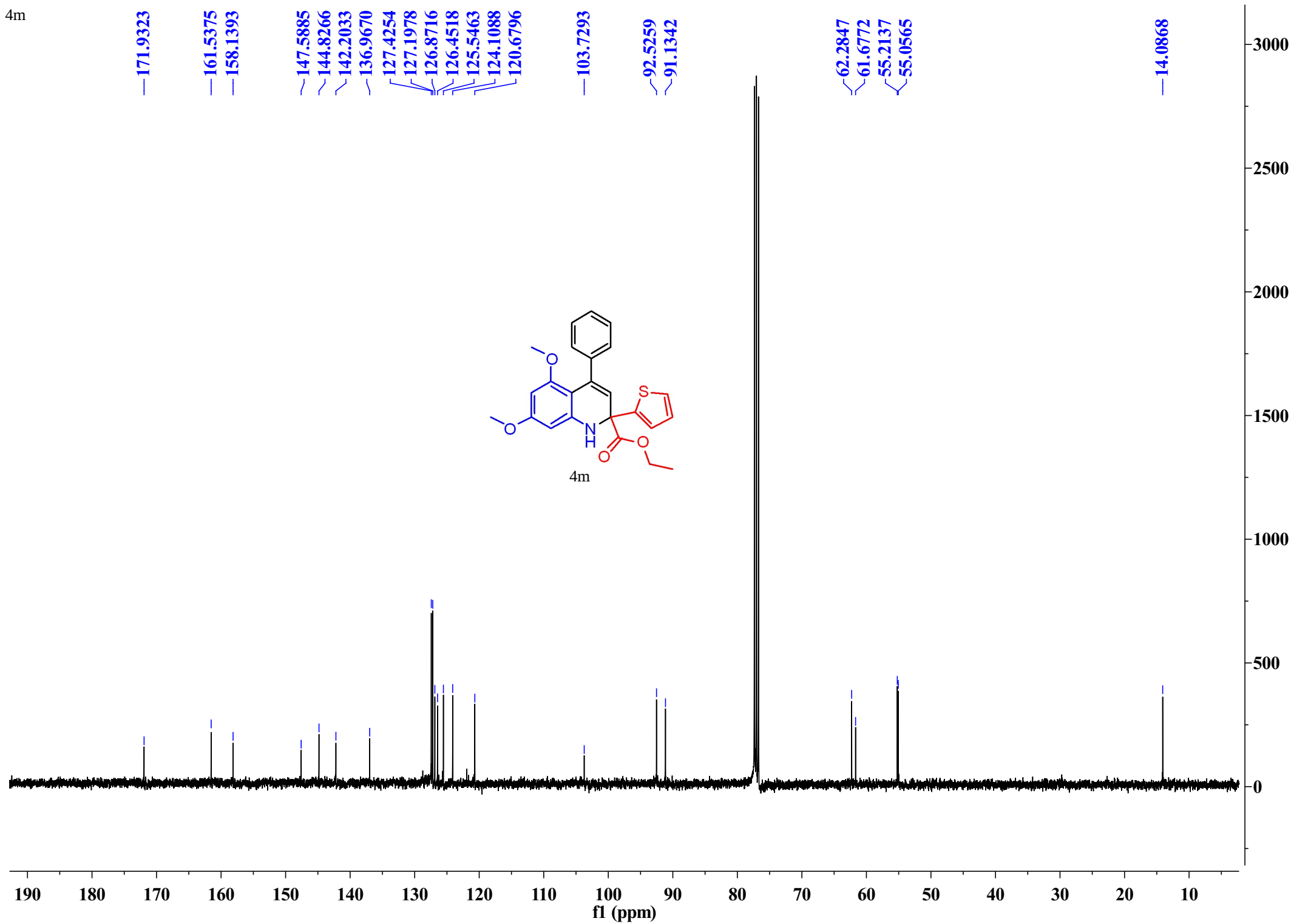




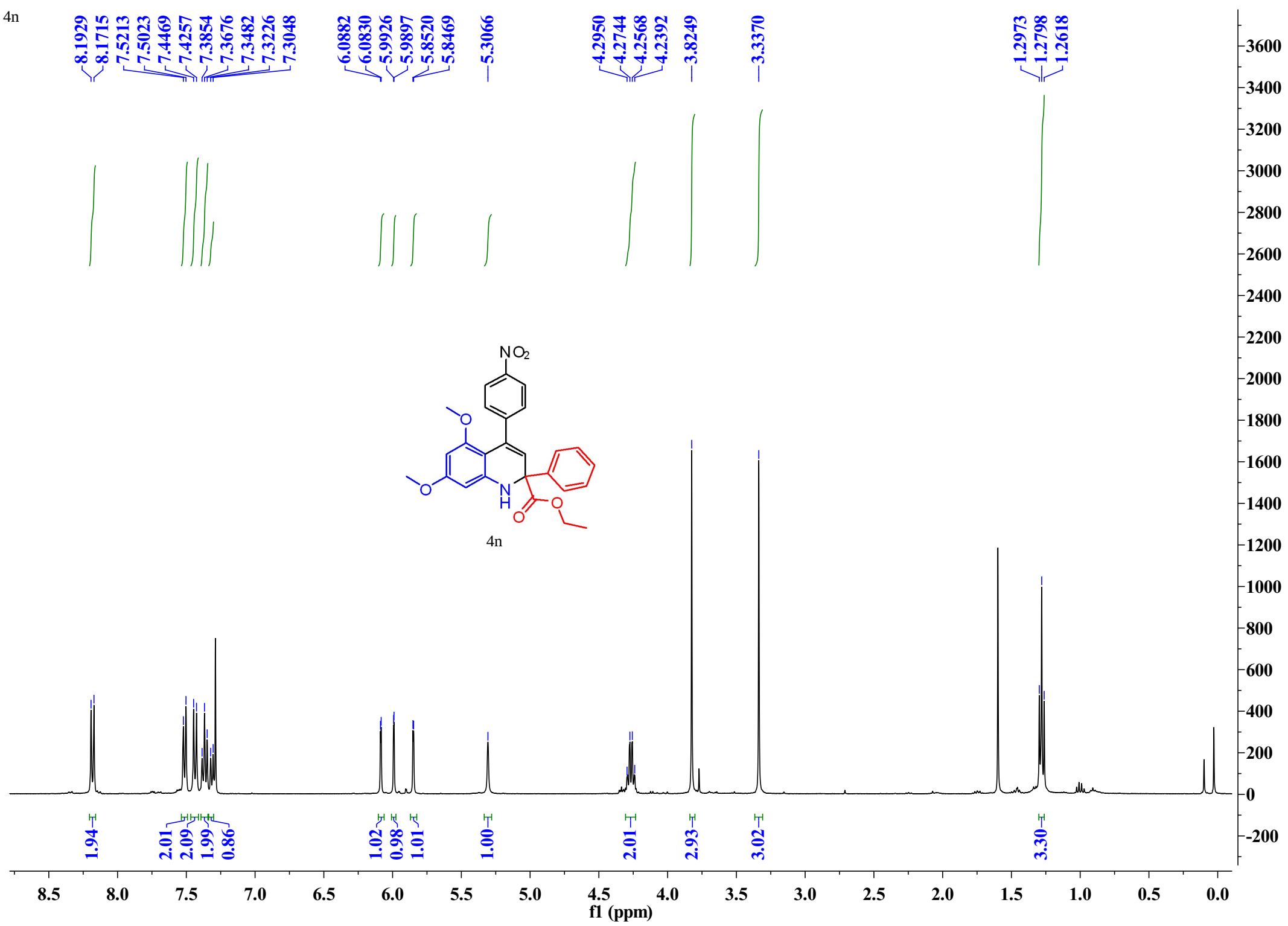




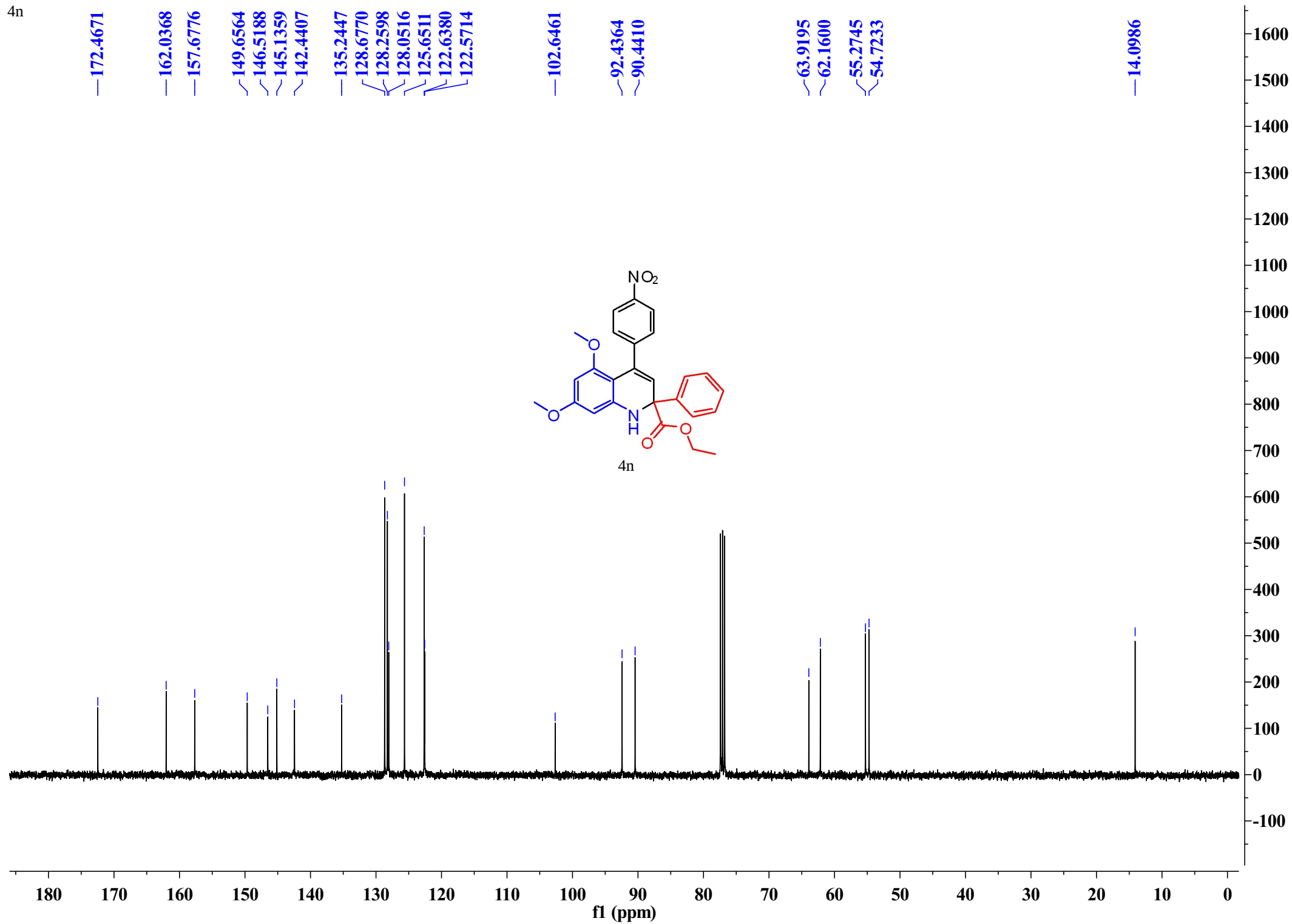
4m

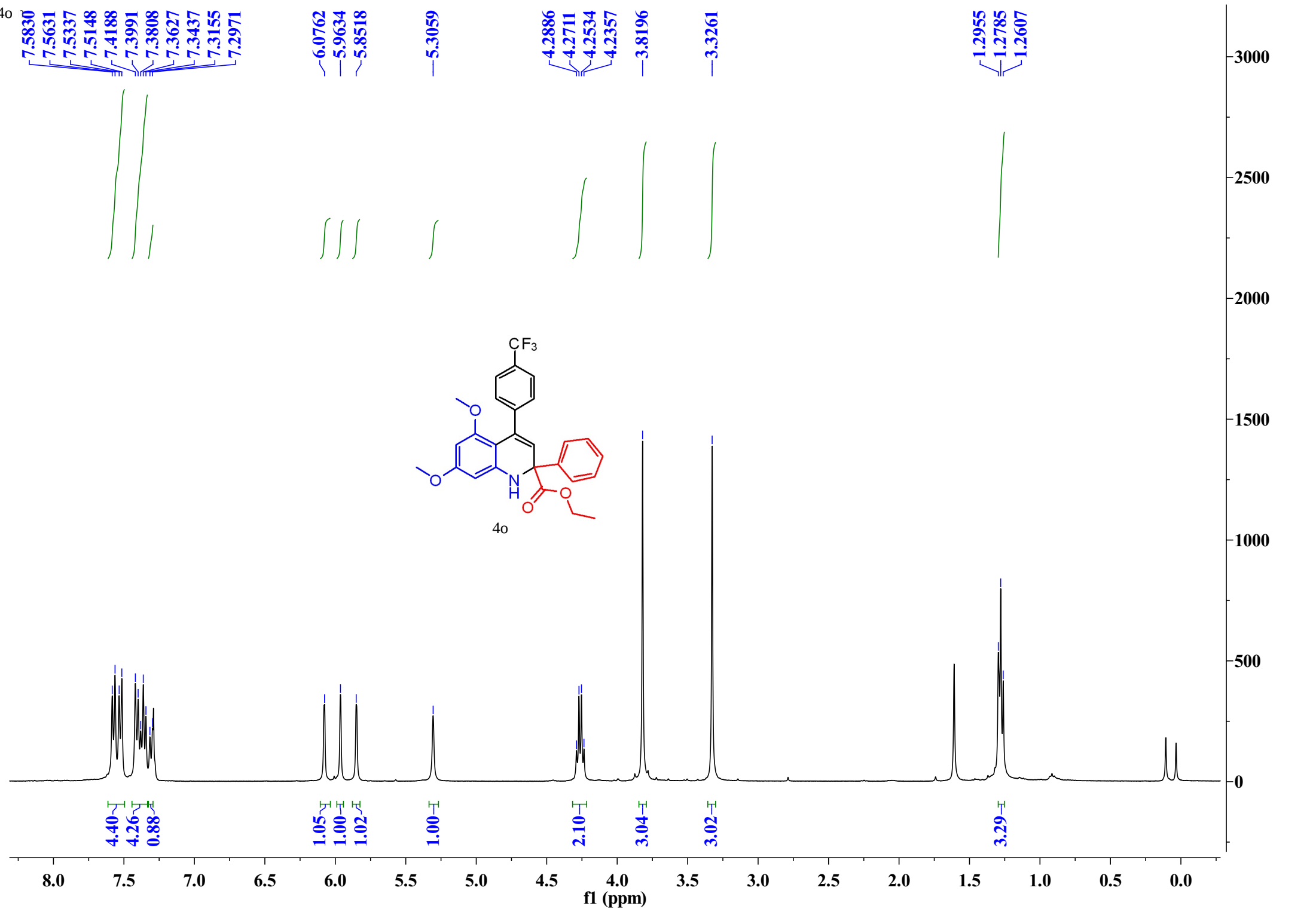


4n

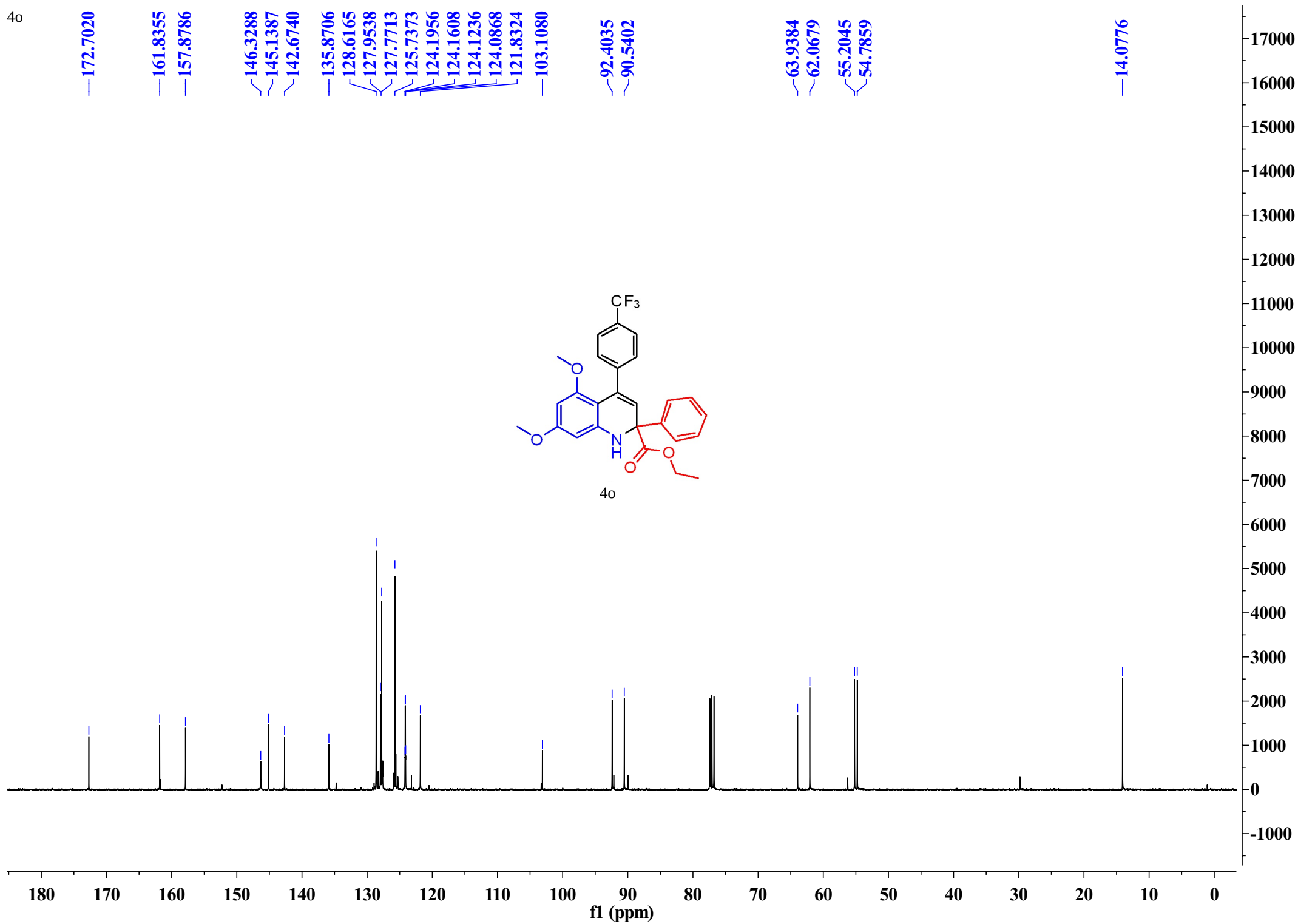


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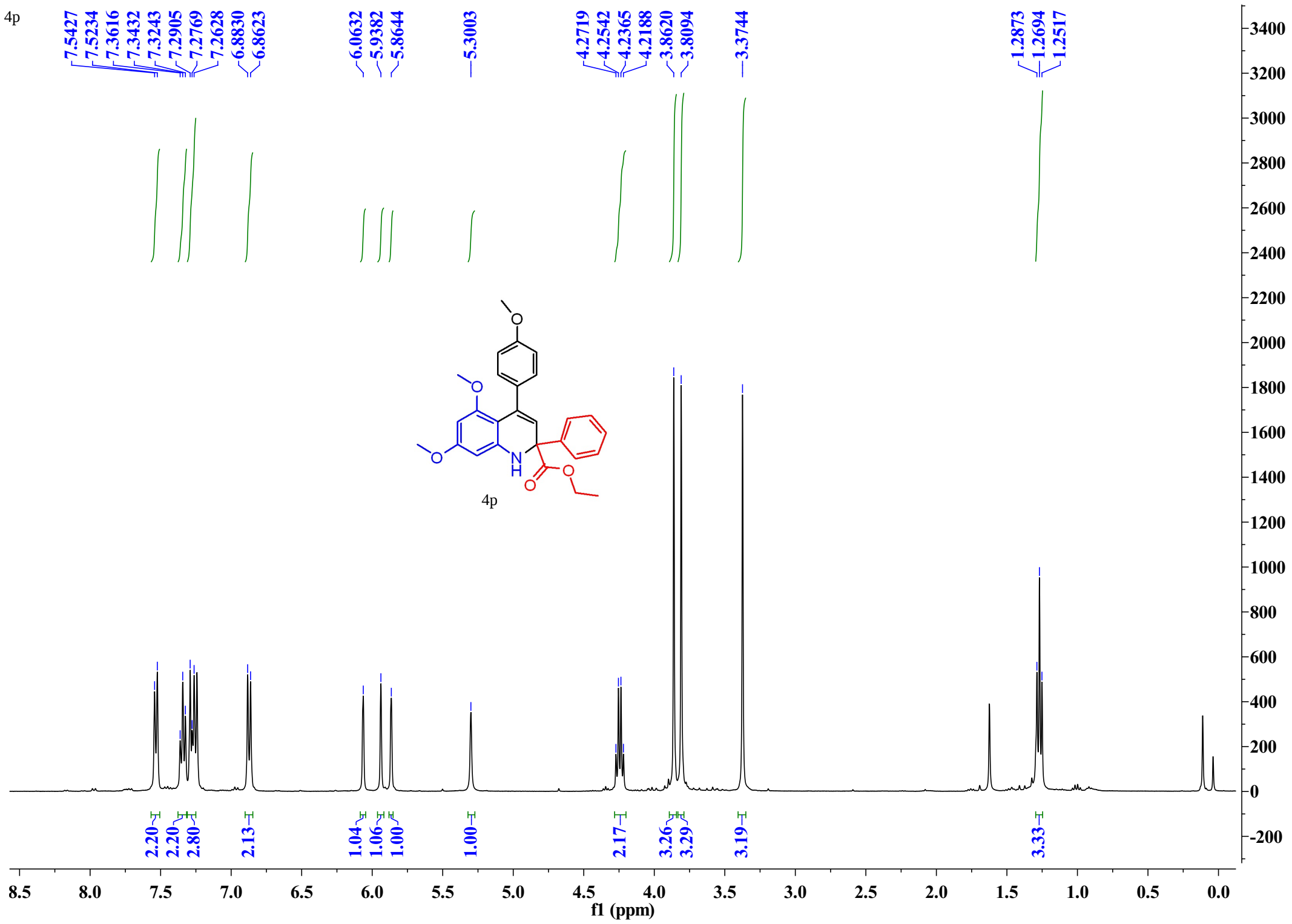




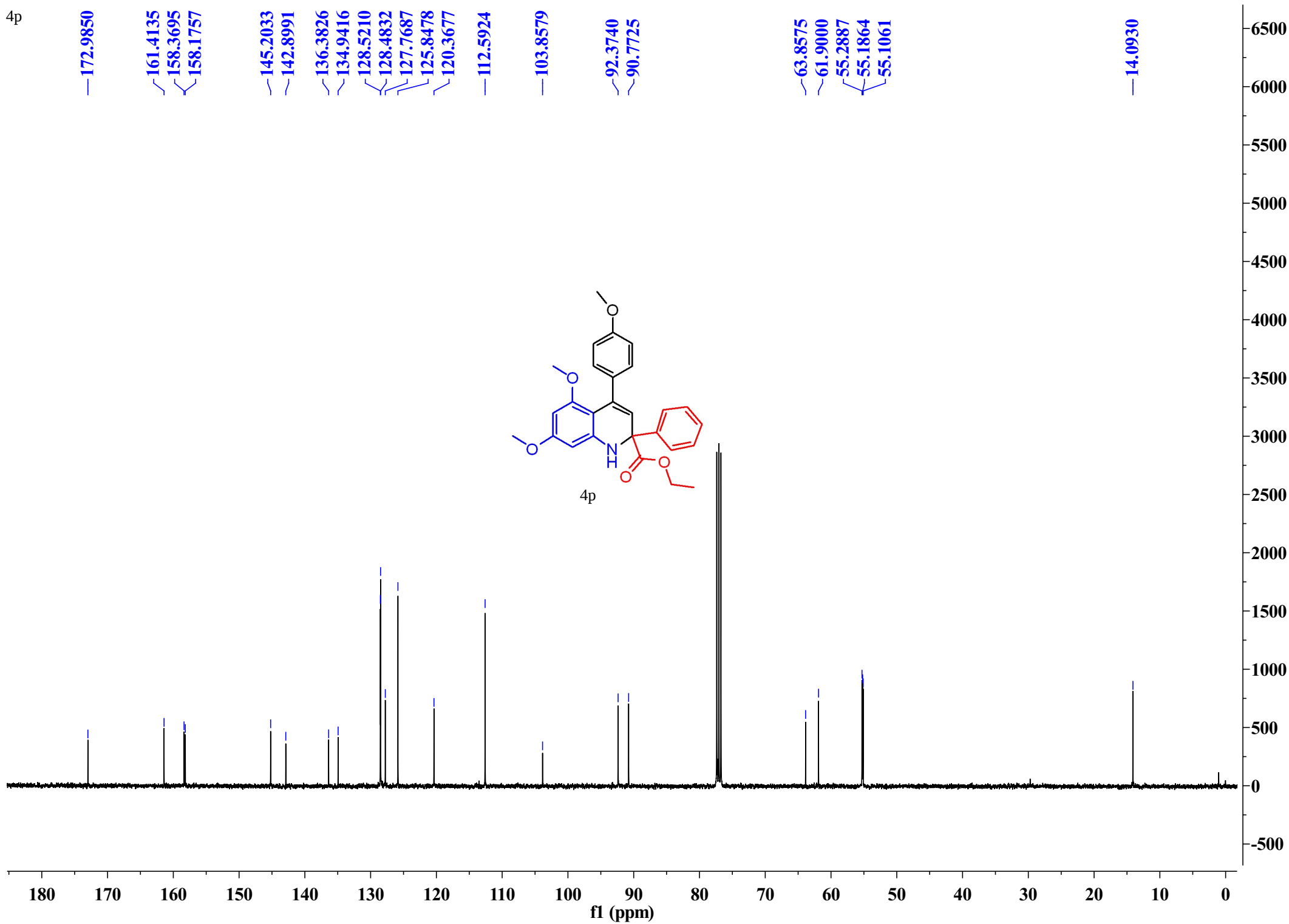
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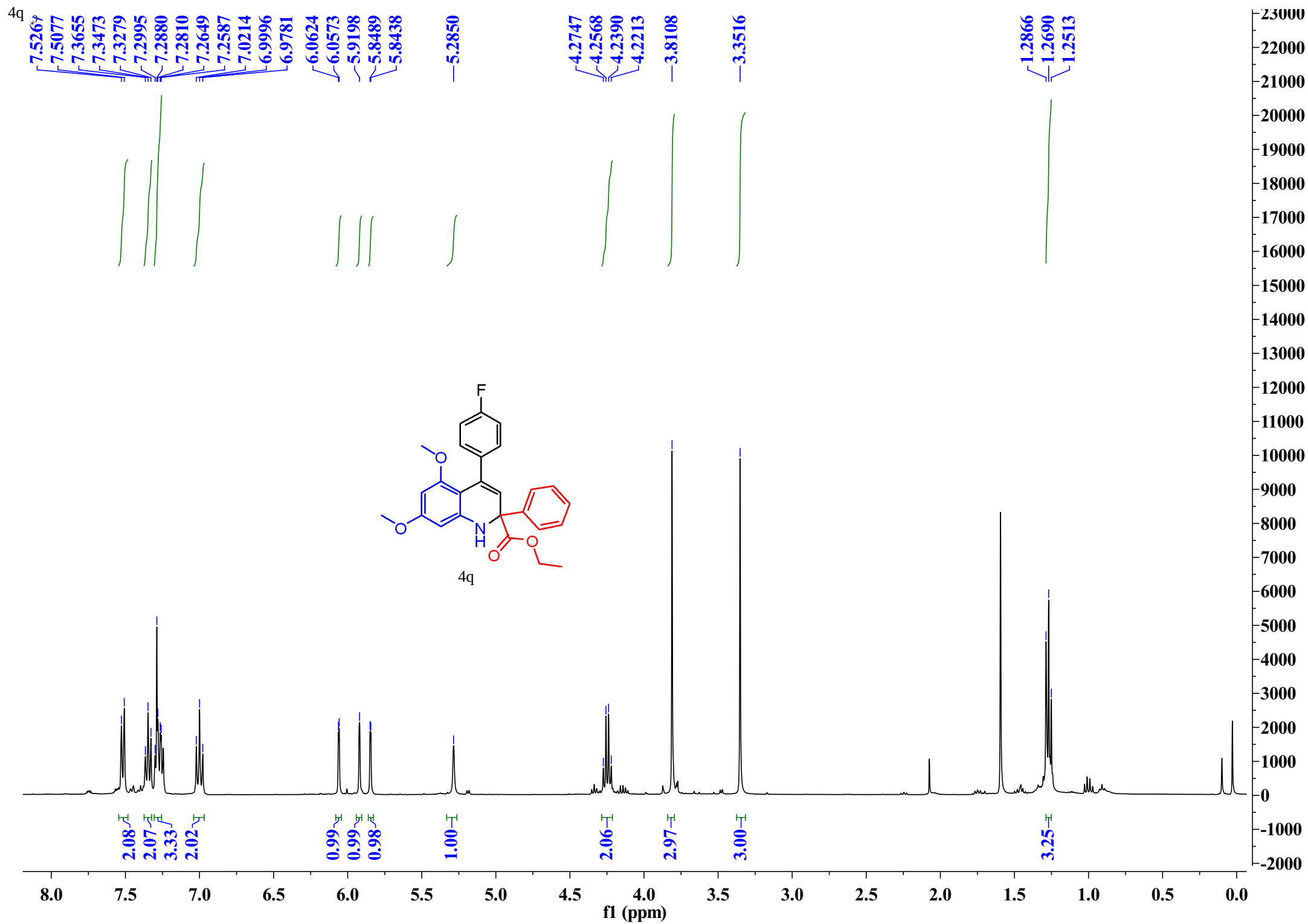


4p

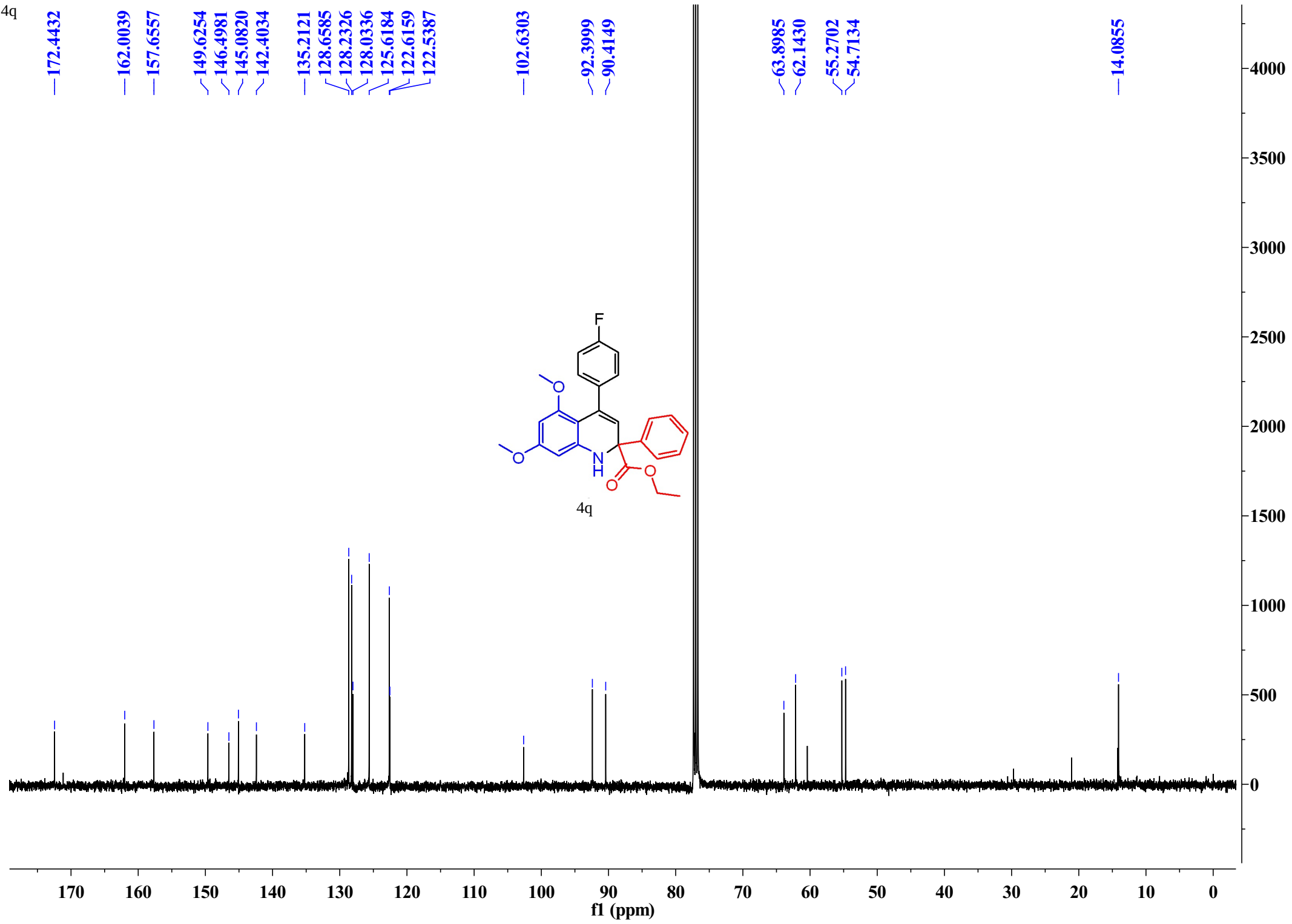


4p

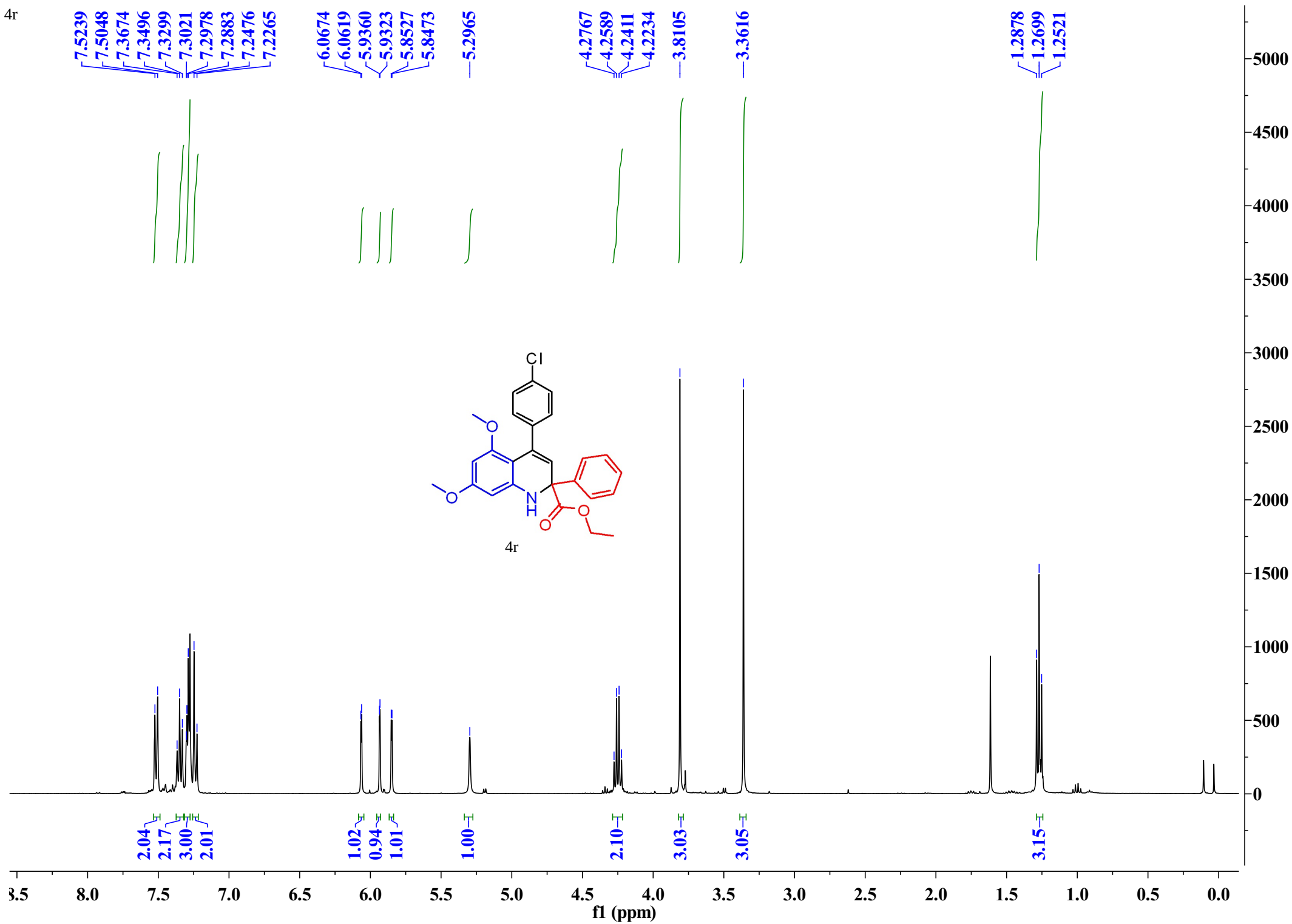




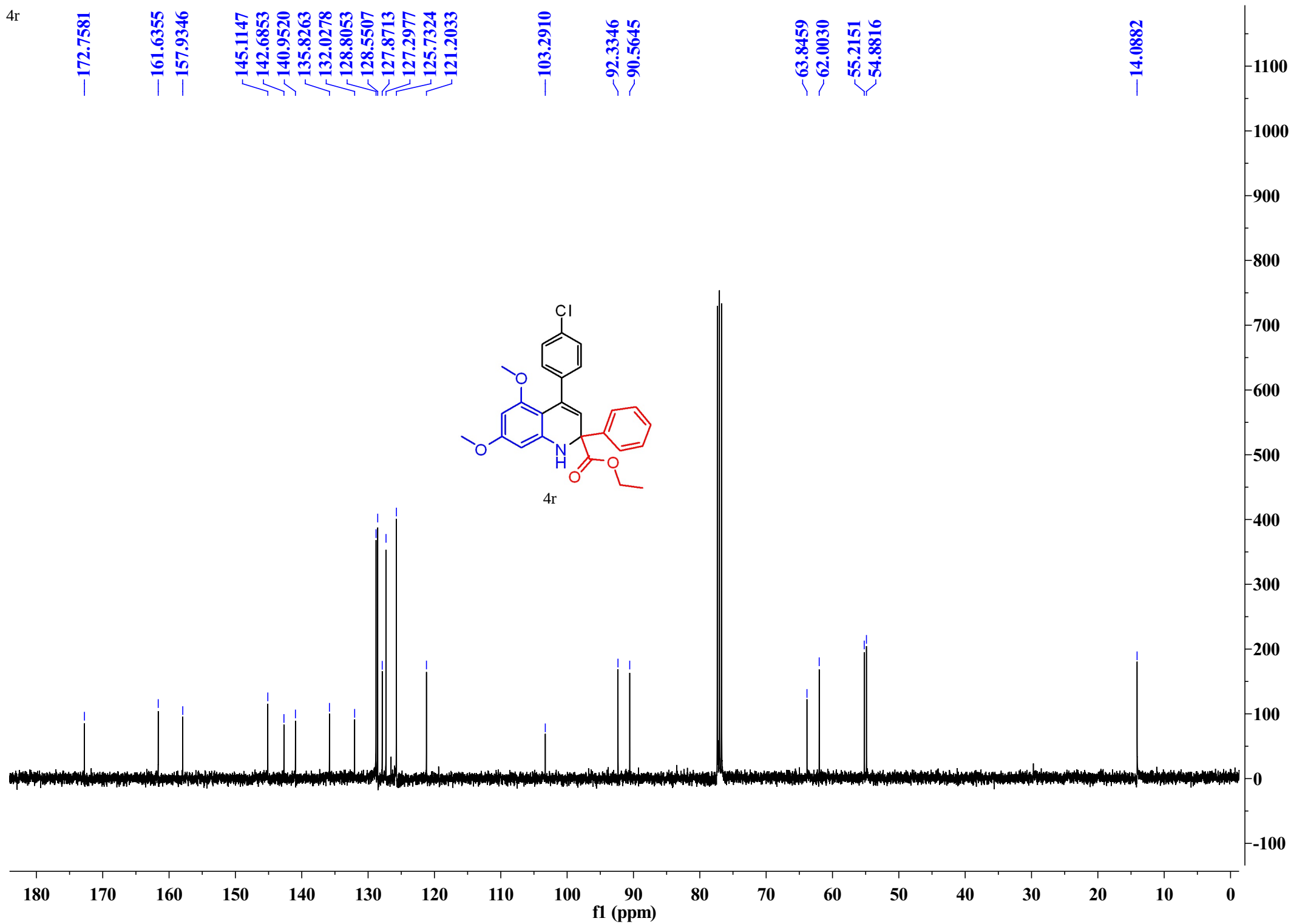
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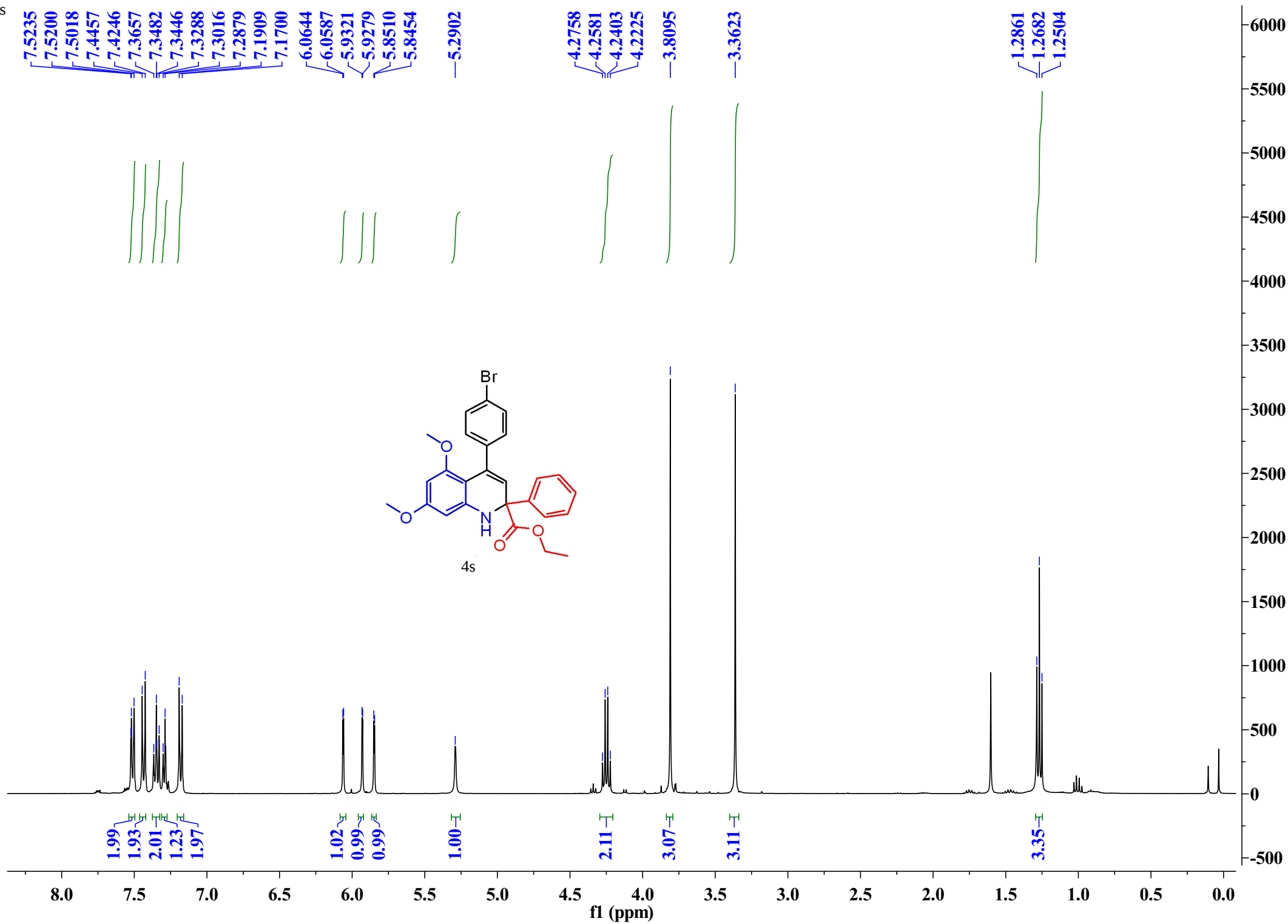
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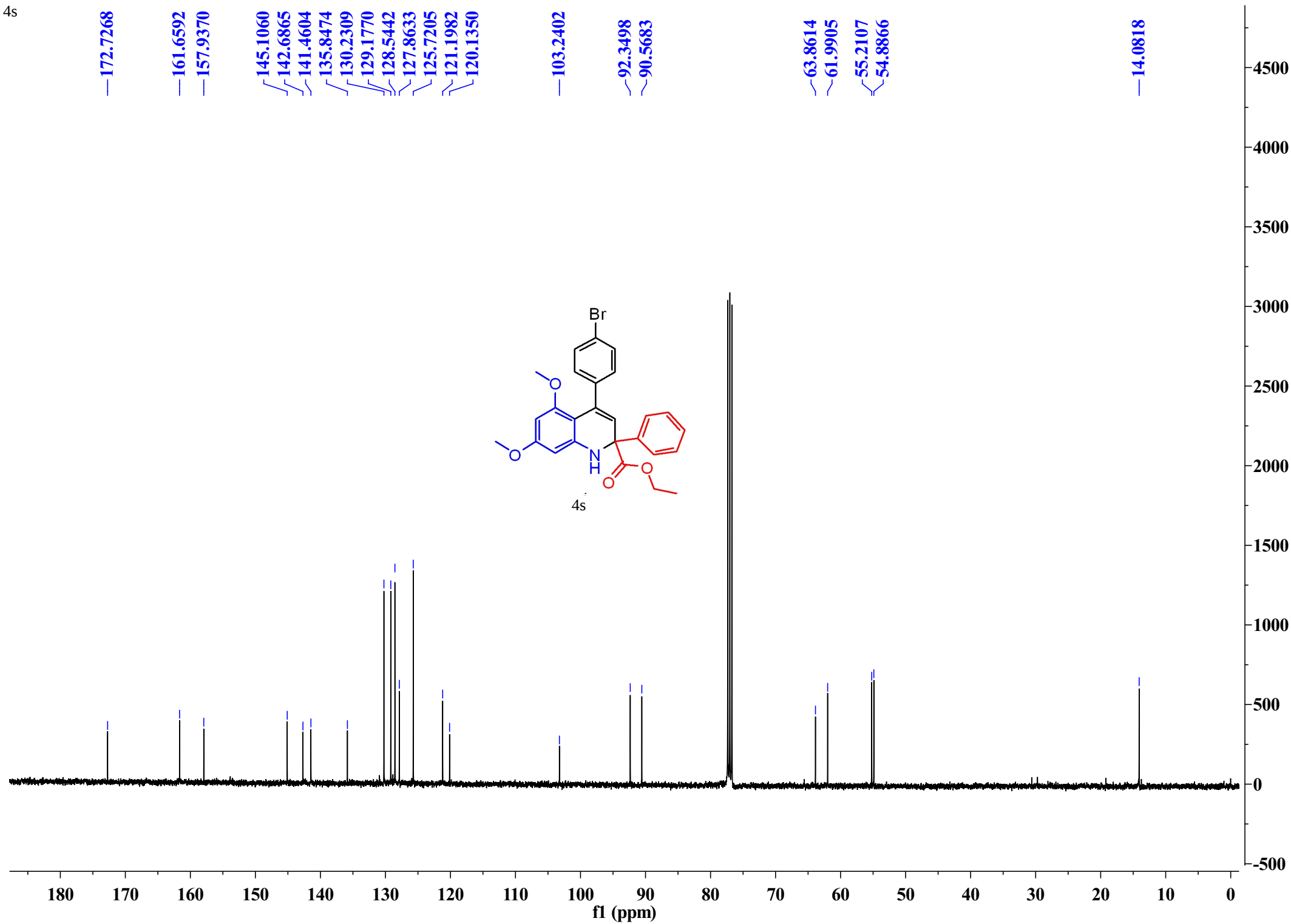
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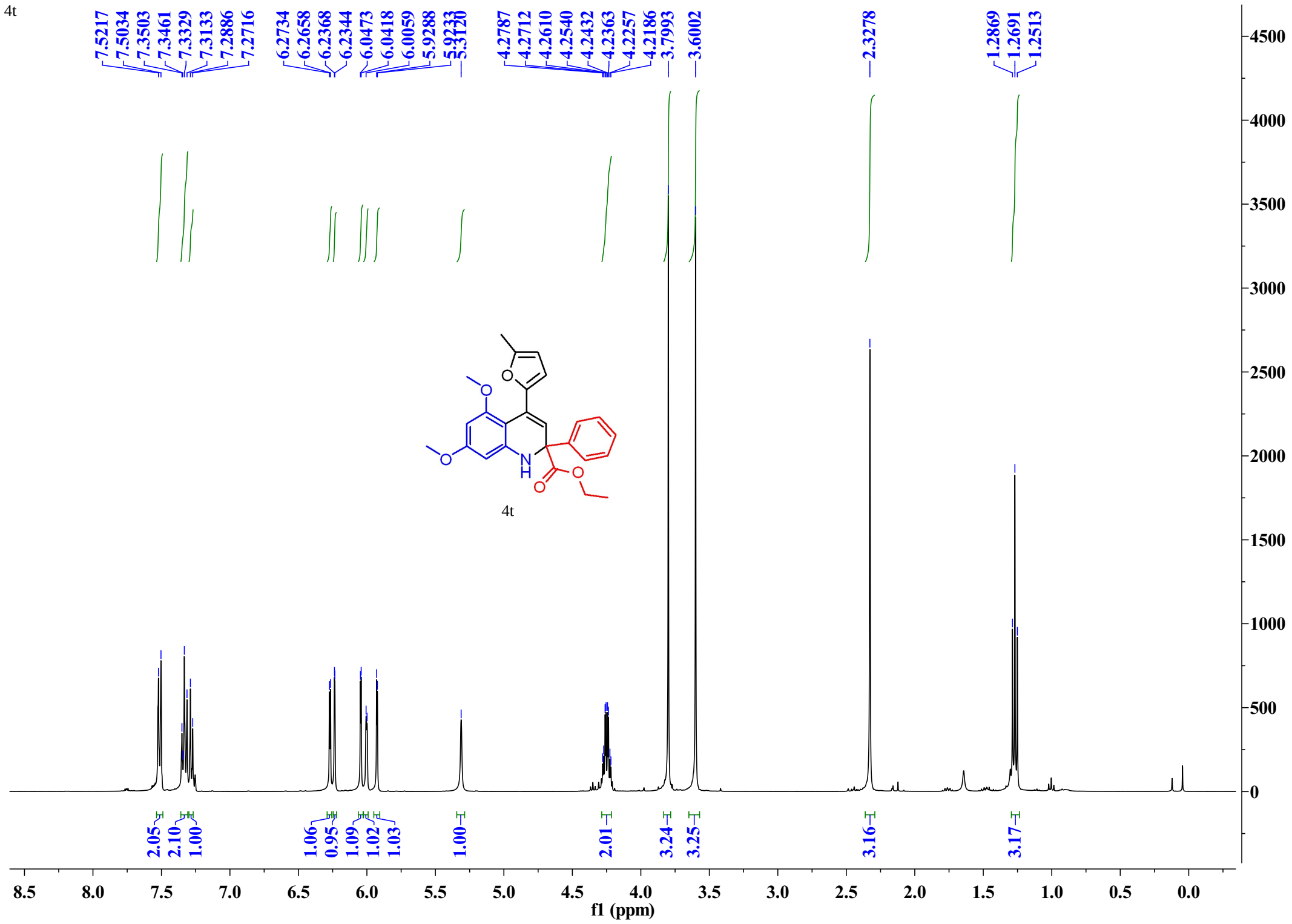
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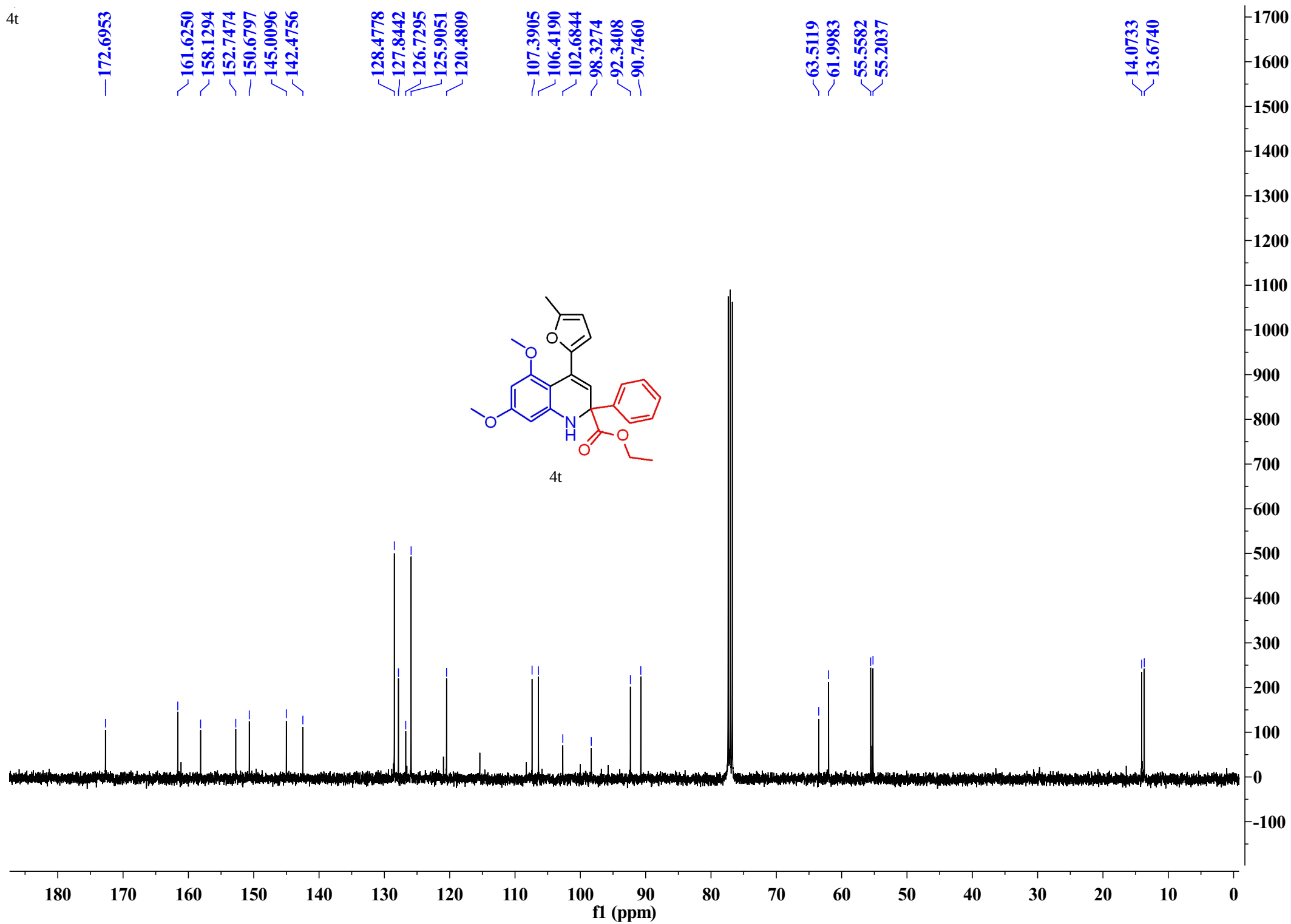
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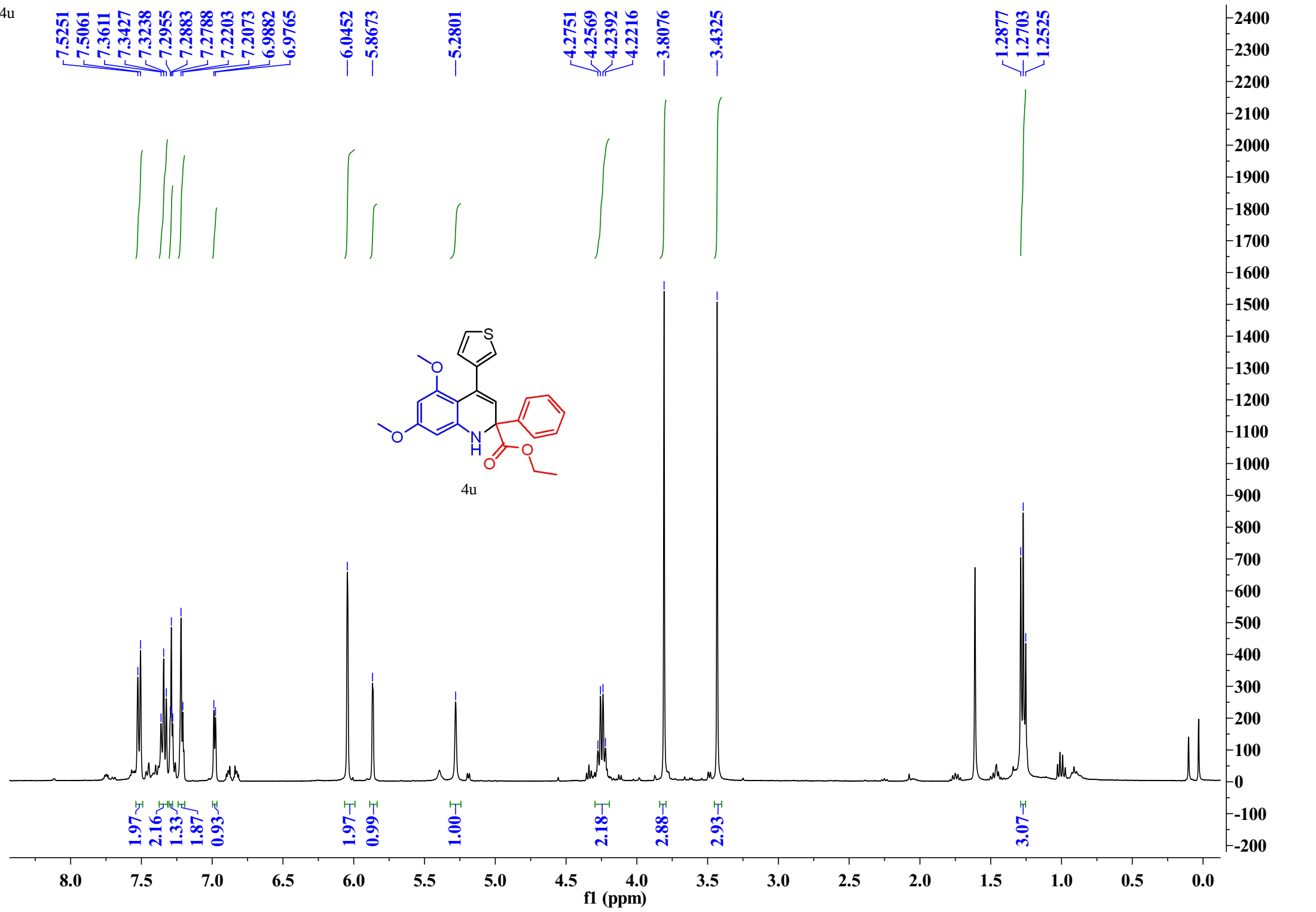


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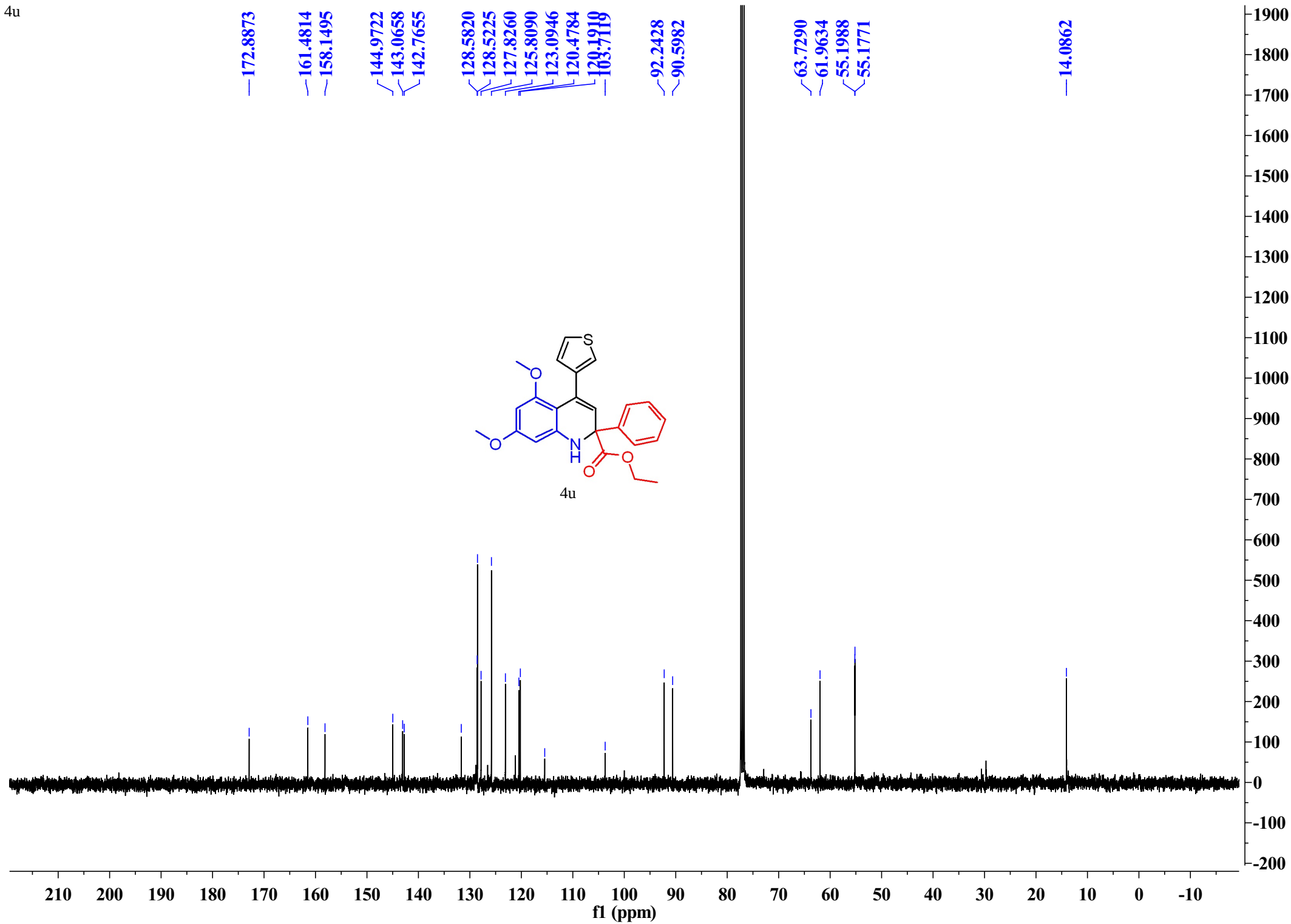


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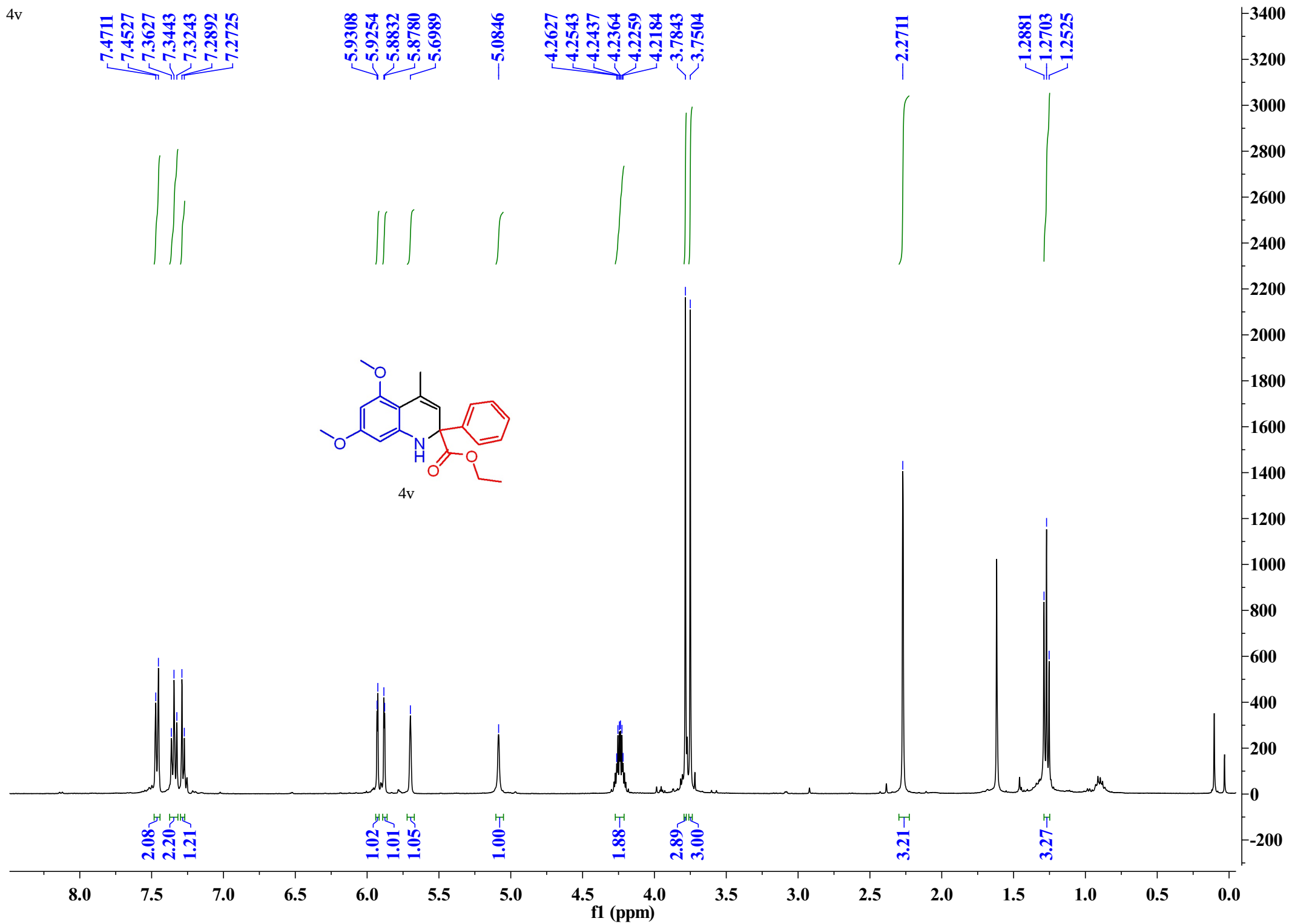




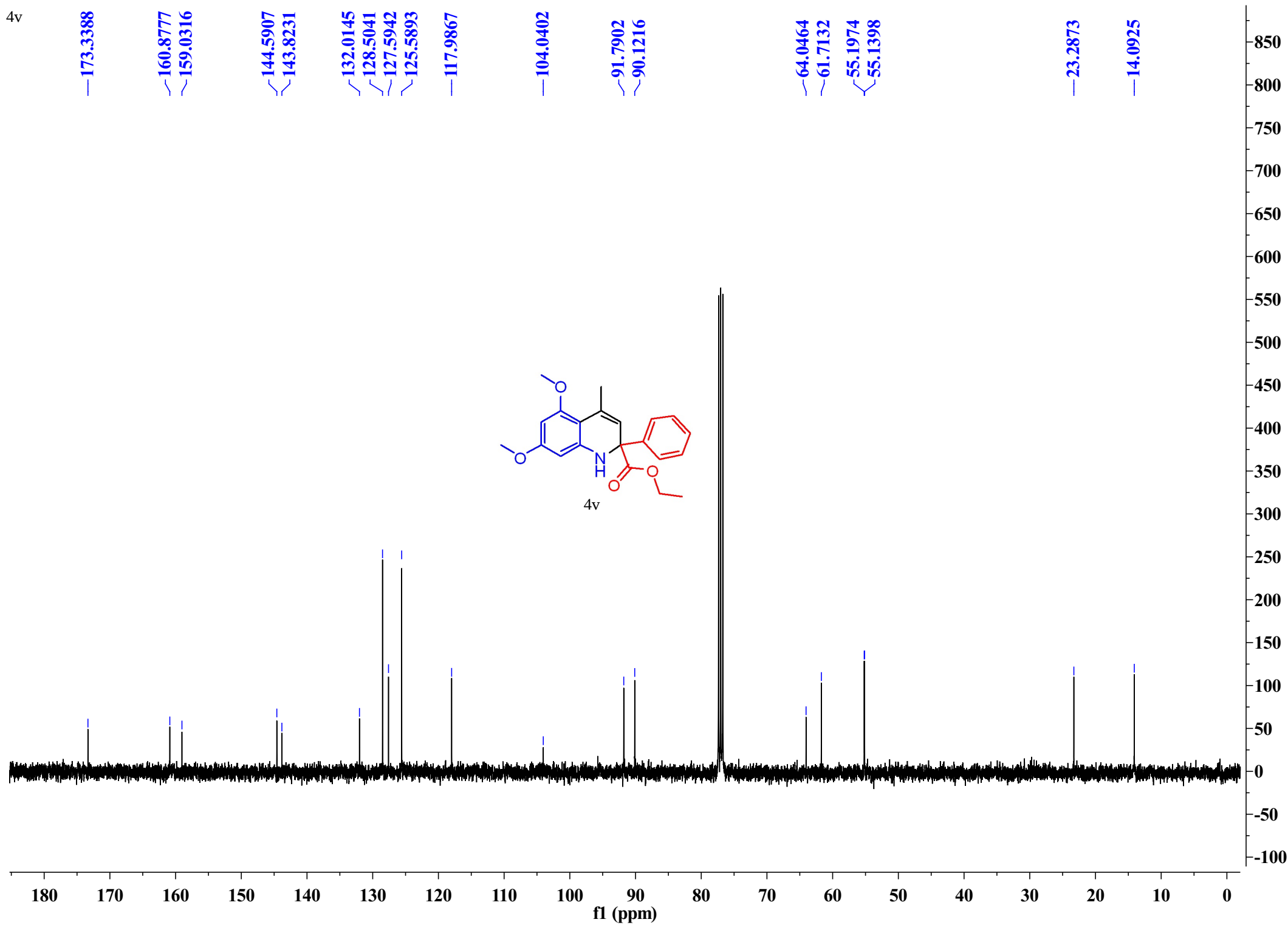
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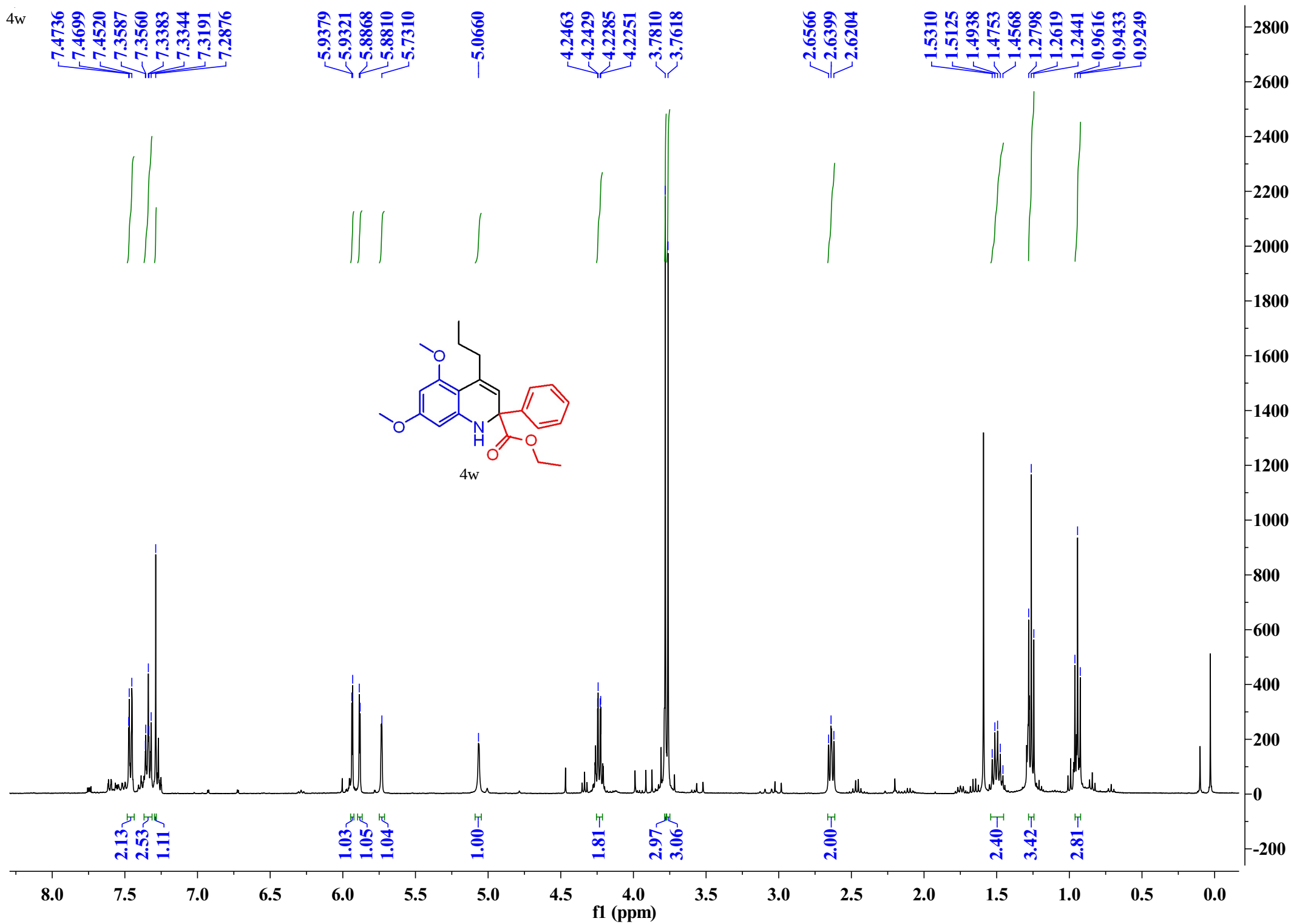
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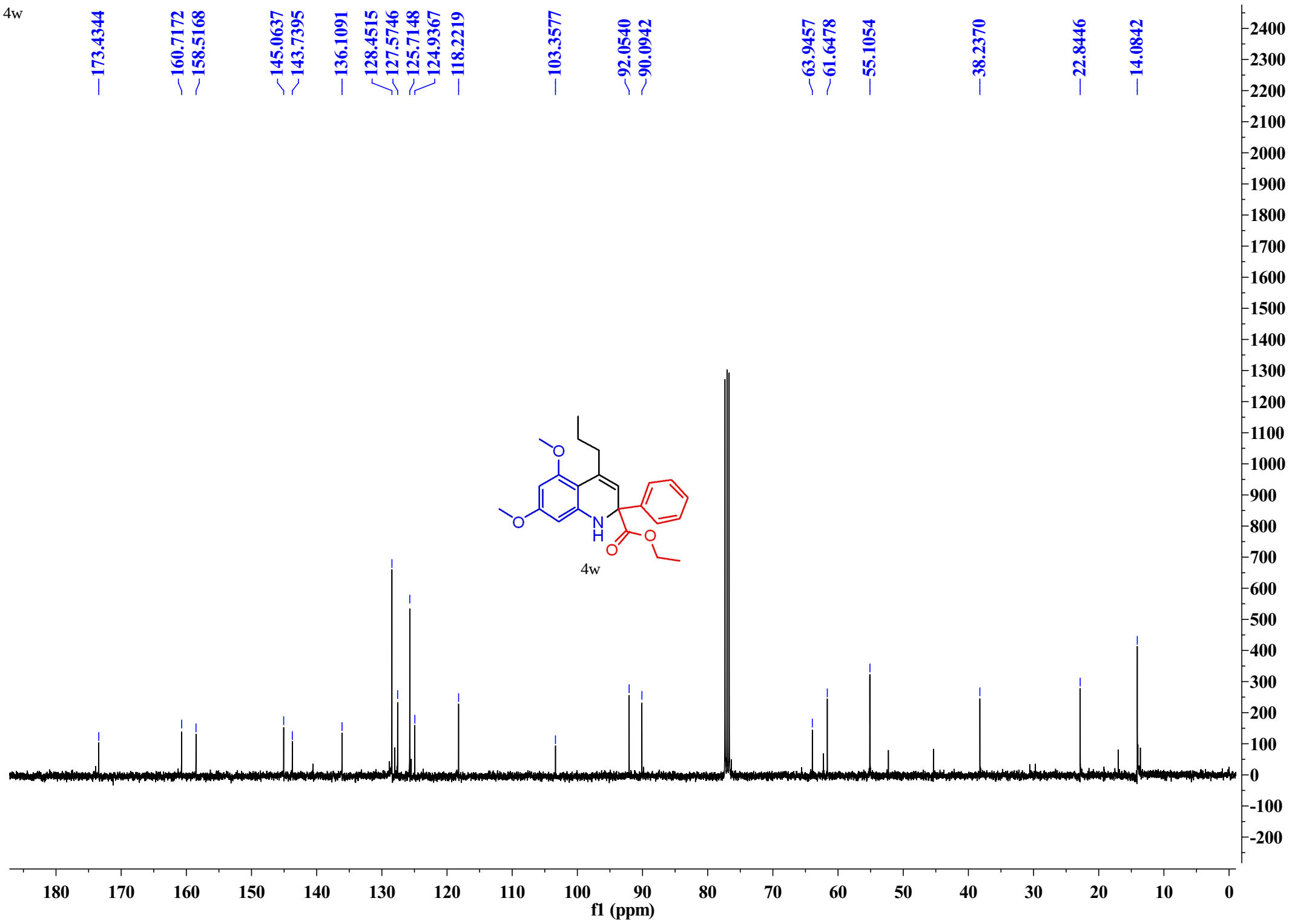


4v

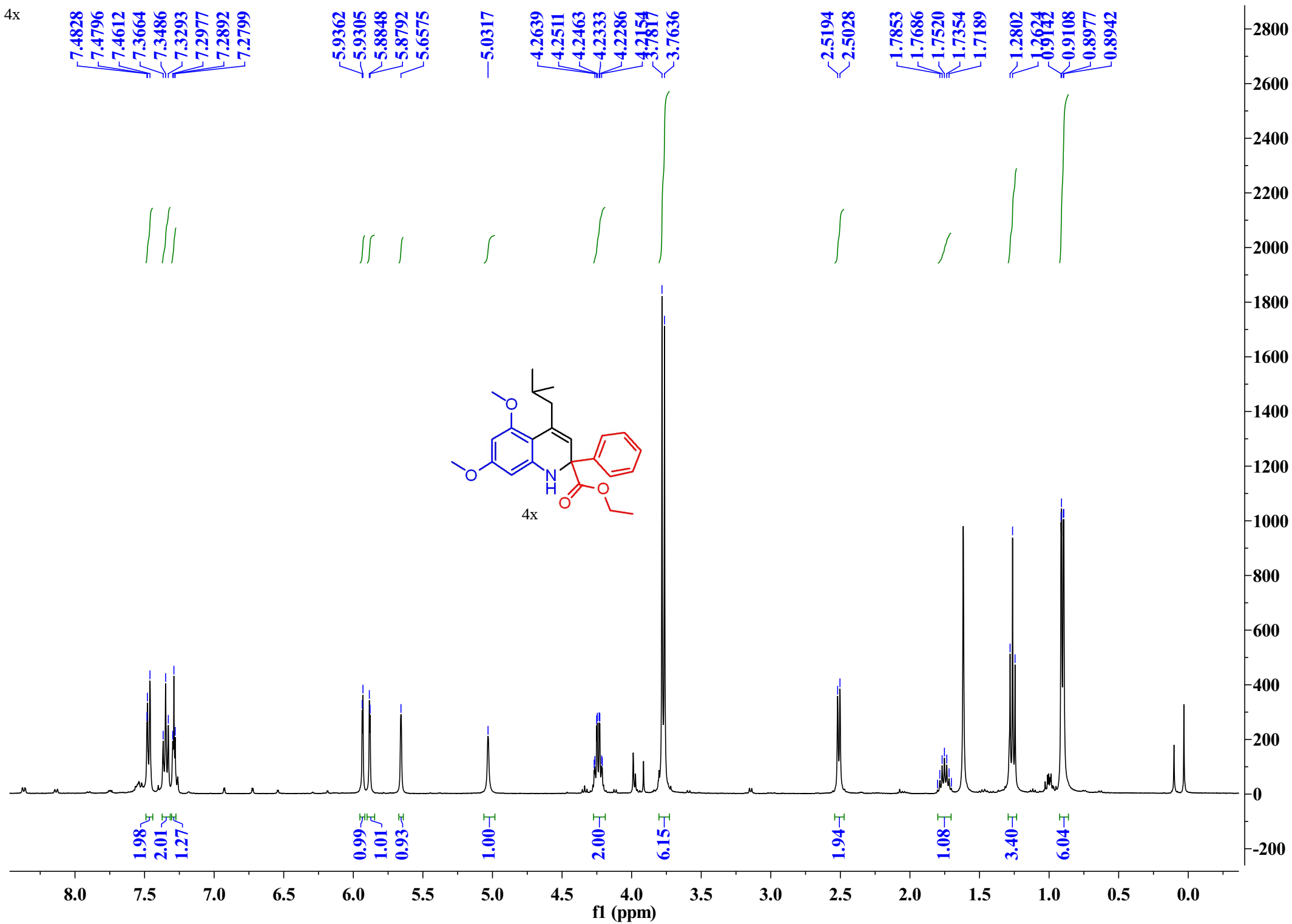


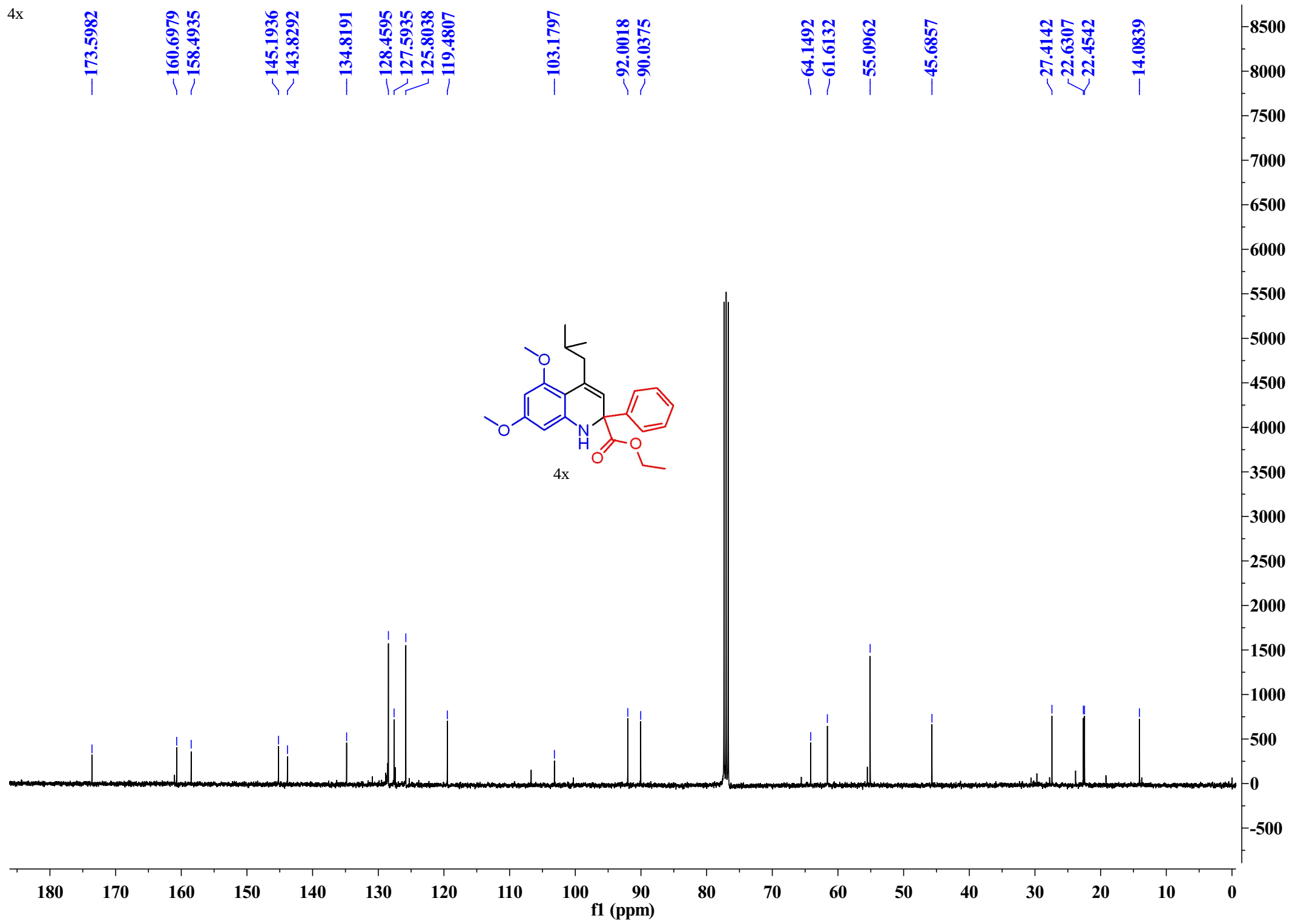
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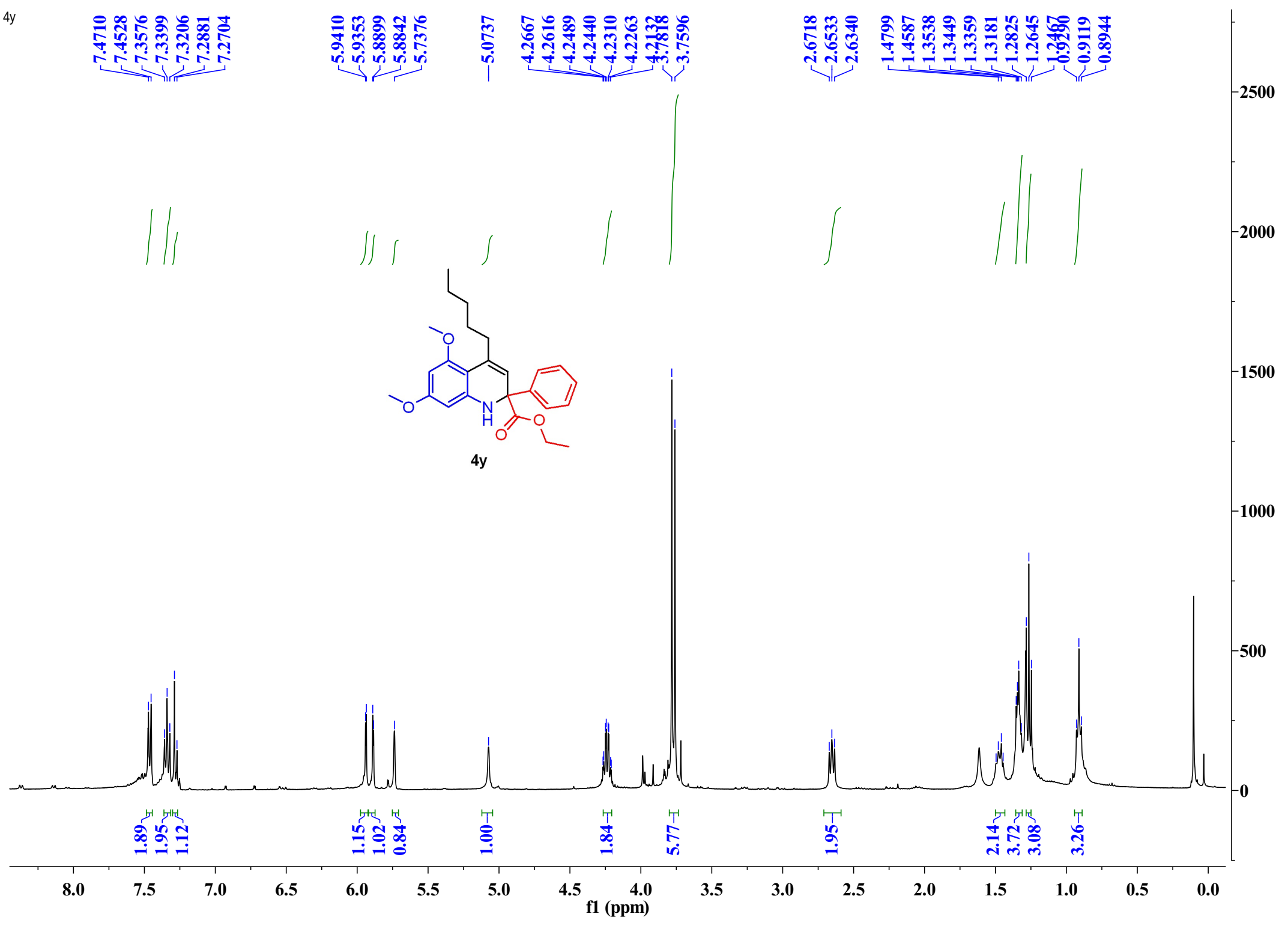


4x





4y



4y

