

Supplementary Material

An efficient method for the preparation of 2,2,4- trisubstituted 1,2-dihydroquinolines using catalytic amount Bi(OTf)₃ as catalyst

Zeynep Gültekin,^{a*} Wolfgang Frey^b

^aÇankırı Karatekin University, Department of Chemistry, 18100, Çankırı, Turkey

^bUniversity of Stuttgart, Institut für Organische Chemie, Pfaffenwaldring 55, D-70569 Stuttgart, Germany

E-mail: zpgul66@hotmail.com

Table of Contents

1. General Methods	S1
2. General Procedure for the synthesis of 1,2-dihydroquinolines under room temperature	S1
3. General Procedure for the synthesis of 1,2-dihydroquinolines under microwave conditions	S1
4. Characterization of products 3a-r and 4, 9	S2
5. ¹ H NMR and ¹³ C NMR Spectra of Compounds 3a-r and 4, 9	S11

General Methods. Acetonitrile, chloroform were distilled from calcium hydride immediately prior to use. DMF, toluene, nitromethane were distilled before use. All aniline derivatives, Bi(OTf)₃, methyl pyruvate are commercially available. Compounds **3a**,¹⁶ **3n**, **3o**, **3i** and **3c**¹⁷ previously reported in the literature. Column chromatography was performed using MN silica gel (particle size 0.040-0.063 mm). For thin-layer chromatography (TLC), silica gel coated aluminium plates (Merck, silica gel 60 F₂₅₄) were used and chromatography was performed using silica gel Merck 60 (particle size 0.063-0.20 mm), visualised by UV irradiation. ¹H-NMR and ¹³C-NMR were recorded on a Mercury 300 or 400 spectrometer in CDCl₃ or MeOD. Data are reported in the following order: chemical shift (δ) in ppm; multiplicities are indicated bs (broadened singlet), s (singlet), d (doublet), m (multiplet), dd (double doublet); coupling constants (*J*) are in Hertz (Hz). ¹³C NMR spectra were acquired on a broad band decoupled mode. Mass spectra was conducted on GC-MS Shimadzu QP2010 (column: Equity®-5, length × I.D. 30 m × 0.25 mm, df 0.25 μm, lot # 28089-U, Supelco). HRMS were measured on a Finnigan MAT 95 or LTQ Orbitrap XL spectrometer. IR spectra were measured in a Perkin-Elmer ATR apparatus and are reported in terms of frequency of absorption (cm⁻¹). Microwave, CEM marked, Discover SP-D With explorer 12 Hybrid was used.

General procedure for the synthesis of 1,2-dihydroquinolines under room temperature

The N-Substituted aniline (100 mg, 1 eq) was dissolved in acetonitrile (1.5 ml) in a screw-capped test tube and Bi(OTf)₃ (5 mol%, 0.05 eq) and methyl pyruvate (2.2 eq) was added to the mixture. This mixture were stirred at room temperature (For the time see: Table 3) until the starting material was completely consumed as monitored by tlc. The resultant residue was directly purified by flash chromatography on silica (EtOAc:Cyclohexane 2:98). All solid products were recrystallized over pentan and ethyl acetate.

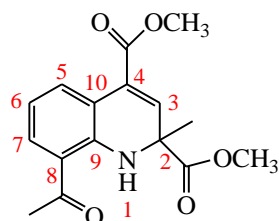
General procedure for the synthesis of 1,2-dihydroquinolines under microwave conditions

N-Substituted aniline (100 mg, 1 eq) was dissolved in acetonitrile (1.5 ml) then Bi(OTf)₃ (5 mol%, 0.05 eq) and methyl pyruvate (2.2 eq) were added to the solution. This mixture were heated by microwave irradiation (10 bar, 150 watt, 100°C, See for the time: Table 1,2 and 3).

The progress of the reaction was monitored through tlc. The resultant residue was directly purified by flash chromatography on silica (EtOAc:Cyclohexane 2:98). All solid products were recrystallized over pentan and ethyl acetate. By this method the following compounds were prepared.

Characterization of products 3a-r and 4, 9

Dimethyl 8-acetyl-2-methyl-1,2-dihydroquinoline-2,4-dicarboxylate (3a)¹⁶

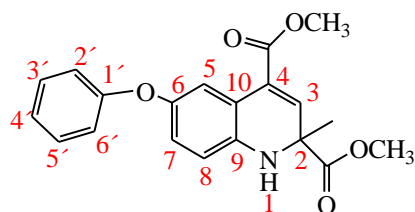


Yellow crystalline solid; yield (71%); R_f 0.5 (2:1 Cyclohexane/EtOAc); m.p: 101-102°C.

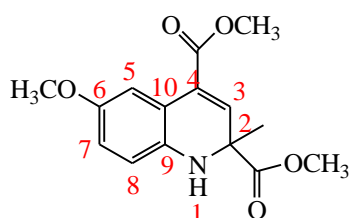
IR (KBr) 3268 (NH), 1718, 1639 (CO) cm^{-1} . $^1\text{H-NMR}$ (300 MHz, CDCl_3): δ = 1.63 (s, 3H, CH_3), 2.59 (s, 3H, COCH_3), 3.76 (s, 3H, COOCH_3), 3.85 (s, 3H, COOCH_3), 6.59-6.64 (m, 1H, Ar-H), 6.65-6.66 (d, 1H, J 1.9 Hz, $\text{C}=\text{CH}$), 7.65-7.68 (dd, 1H, J 8.1 and 1.4 Hz, Ar-H), 7.9-8.0 (m, 1H, Ar-H) 9.6 (bs, 1H, NH). $^{13}\text{C-NMR}$ (400 MHz, CDCl_3): 28.1 ($\underline{\text{C}}\text{H}_3$), 28.7 ($\text{CO}\underline{\text{C}}\text{H}_3$), 52.2, 52.9 (2x $\text{COO}\underline{\text{C}}\text{H}_3$), 58.6 (C2), 115.1 (C8), 116.7 (C6), 117.6 (C10), 127.3 (C7), 131.8 (C5). 132.0 (C3), 132.7 (C4), 146.0 (C9), 165.7 (CO), 172.9 (CO), 200.4 (CO).

Anal. Calcd for $\text{C}_{16}\text{H}_{17}\text{NO}_5$: C, 63.36; H, 5.65; N, 4.62. Found: C, 63.41; H, 5.83; N, 4.61. MS m/z (EI) 303.1 (M^+ , 3%), 245.1 (39), 244.1 (100), 228.1 (8), 226.1 (28), 185.1 (15), 167.1 (13), 142.1 (10), 115.0 (8), 59.2 (4).

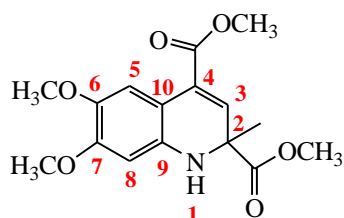
Dimethyl 6-phenoxy-2-methyl-1,2-dihydroquinoline-2,4-dicarboxylate (3b)



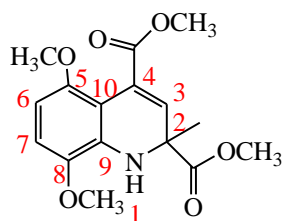
Yellow solid; yield (77%); R_f 0.43 (2:1 Cyclohexane/EtOAc); m.p: 78-79 °C. IR (KBr) 3379 (NH), 1721 (CO) cm^{-1} . $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ = 1.57 (s, 3H, CH_3), 3.76 (s, 3H, COOCH_3), 3.81 (s, 3H, COOCH_3), 4.49 (br, 1H, NH), 6.61-6.63 (d, 1H, J 8.3 Hz, Ar-H), 6.73 (bs, 1H, $\text{C}=\text{CH}$), 6.80-6.83 (dd, 1H, J 8.7 and 2.6 Hz, Ar-H), 6.92-6.94 (m, 2H, Ar-H), 6.98-7.0 (m, 1H, Ar-H), 7.25-7.29 (m, 1H, Ar-H), 7.61 (bs, 1H, Ar-H). $^{13}\text{C-NMR}$ (400 MHz, CDCl_3): 27.4 ($\underline{\text{C}}\text{H}_3$), 52.1, 52.8 (2x $\text{COO}\underline{\text{C}}\text{H}_3$), 58.7 (C2), 114.9 (C8), 117.1 (C7), 117.3 (C5), 118.6 (C10), 121.6 (C6'), 121.9 (C2'), 127.4 (C4'), 129.4 (C3' and C5'), 133.7 (C3), 138.9 (C4), 148.2 (C9), 157.0 (C6), 158.6 (C1'), 165.6 (CO), 174.2 (CO). Anal. Calcd for $\text{C}_{20}\text{H}_{19}\text{NO}_5$: C, 67.98; H, 5.42; N, 3.96. Found: C, 67.93; H, 5.54; N, 3.92; MS m/z (EI) 353.1 (M^+ , 4%), 295.1 (19), 294.1 (100), 235.1 (4), 77.2 (5), 59.3 (2).

Dimethyl 6-methoxy-2-methyl-1,2-dihydroquinoline-2,4-dicarboxylate (3c)¹⁷

Yellow oil; yield (58%); R_f 0.33 (2:1 Cyclohexane/EtOAc). IR (kapilar) 3368 (NH), 1726 (CO) cm^{-1} . $^1\text{H-NMR}$ (300MHz, CDCl_3): δ = 1.53 (s, 3H, CH_3), 3.72, 3.74, 3.85 (s, 9H, COOMe and 6-OMe), 4.34 (bs, 1H, NH), 6.57-6.59 (d, 1H, J 8.6Hz, Ar-H), 6.69-6.73 (dd, 1H, J 8.6 and 2.8 Hz, Ar-H), 6.74 (bs, 1H, $-\text{C}=\text{CH}$), 7.48-7.49 (d, 1H, J 2.8 Hz, Ar-H). $^{13}\text{C-NMR}$ (300 MHz, CDCl_3): δ = 26.9 (CH_3), 52.0, 52.7 (COOCH_3), 55.7 (OCH_3), 58.5 (C2), 111.5 (C8), 114.4 (C5), 115.1 (C10), 116.2 (C7), 127.9 (C3), 134.2 (C4), 136.6 (C9), 152.6 (C6), 166.0 (CO), 174.6 (CO). Anal. Calcd for $\text{C}_{15}\text{H}_{17}\text{NO}_5$: C, 61.85; H, 5.88; N, 4.81. Found: C, 61.62; H, 6.031; N, 5.060. MS m/z (EI) 291.2 (M^+ , 11%), 233.3 (26), 232.2 (100), 173.2 (7), 131.2 (6), 116.2 (4).

Dimethyl 6,7-dimethoxy-2-methyl-1,2-dihydroquinoline-2,4-dicarboxylate (3d)

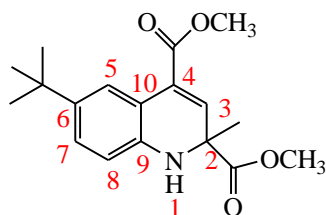
Yellow oil; yield (62%); R_f 0.16 (2:1 Cyclohexane/EtOAc). IR (kapilar) 3367 (NH), 1725 (CO) cm^{-1} . $^1\text{H-NMR}$ (300 MHz, CDCl_3): δ = 1.52 (s, 3H, CH_3), 3.72, 3.80, 3.82, 3.83 (s, 12H, COOCH_3 and 6,7- OCH_3), 4.36 (bs, 1H, NH), 6.21 (s, 1H, Ar-H), 6.57 (s, 1H, Ar-H), 7.54 (s, 1H, $-\text{C}=\text{CH}$). $^{13}\text{C-NMR}$ (300 MHz, CDCl_3): δ = 26.9 (CH_3), 51.9, 52.6 (COOCH_3), 55.6, 56.4 (OCH_3), 58.5 (C2), 98.4 (C8), 108.6 (C5), 110.5 (C9), 127.4 (C3), 130.6 (C4), 137.7 (C6), 1141.9 (C10), 150.5 (C7), 166.1 (CO), 174.9 (CO). Anal. Calcd for $\text{C}_{16}\text{H}_{19}\text{NO}_6$: C, 59.81; H, 5.96; N, 4.36. Found: C, 55.65; H, 5.810; N, 3.918. MS m/z (EI) 321.2 (M^+ , 14%), 263.2 (25), 262.2 (100), 246.1 (16), 218.2 (7), 203.2 (5), 131.1 (6).

Dimethyl 5,8-dimethoxy-2-methyl-1,2-dihydroquinoline-2,4-dicarboxylate (3e)

Yellow solid; yield (45%); R_f 0.23 (2:1 Cyclohexane/EtOAc); m.p: 100-101°C. IR (KBr) 3381 (NH), 1727 (CO) cm^{-1} . $^1\text{H-NMR}$ (300 MHz, CDCl_3): δ = 1.53 (s, 3H, CH_3), 3.70, 3.71, 3.78,

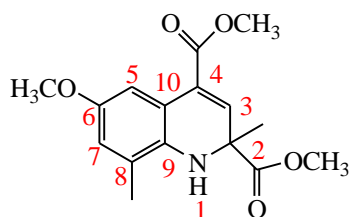
3.81 (s, 12H, COOCH₃ and 5,8-OCH₃), 4.9 (bs, 1H, NH), 6.0 (s, 1H, -C=CH), 6.14-6.16 (d, 1H, *J* 8.8 Hz, Ar-H), 6.65-6.67 (d, 1H, *J* 8.8 Hz, Ar-H). ¹³C-NMR (400 MHz, CDCl₃): δ = 26.8 (CH₃), 52.0, 52.6 (COOCH₃), 56.1, 56.2 (OCH₃), 57.6 (C2), 99.6 (C10), 107.6 (C6), 111.4 (C7), 126.4 (C8), 129.2 (C3), 134.0 (C4), 141.1 (C9), 149.8 (C5), 169.4 (CO), 174.5 (CO). Anal. Calcd for C₁₆H₁₉NO₆: C, 59.81; H, 5.96; N, 4.36. Found: C, 59.30; H, 5.61; N, 4.26. MS m/z (EI) 321.1 (M⁺, 5%), 263.1 (16), 262.1 (100), 247.1 (6), 232.1 (33), 202.1 (4), 173.1 (3).

Dimethyl 6-^tButyl-2-methyl-1,2-dihydroquinoline-2,4-dicarboxylate (3f)

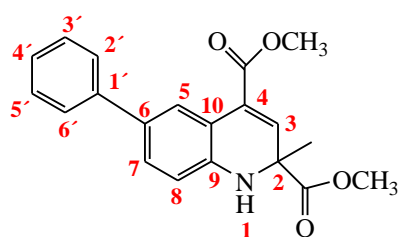


Yellow solid; yield (73%); R_f 0.66 (2:1 Cyclohexane/EtOAc); m.p: 140-141 °C. IR (KBr) 3360 (NH), 1740, 1718 (CO) cm⁻¹. ¹H-NMR (400MHz, CDCl₃): δ = 1.27 (s, 9H, ^tBu), 1.54 (s, 3H, CH₃), 3.73 (s, 3H, COOCH₃), 3.86 (s, 3H, COOCH₃), 4.43 (bs, 1H, NH), 6.56-6.58 (d, 1H, *J* 8.0, Ar-H), 6.65 (bs, 1H, -C=CH), 7.11-7.13 (d, 1H, *J* 8.0, Ar-H), 7.86 (br, 1H, Ar-H). ¹³C-NMR (400MHz, CDCl₃): 27.6 (CH₃), 31.0, 31.2, 31.3 (-C(CH₃)₃), 31.5 (-C(CH₃)₃), 52.0, 52.7 (2xCOOCH₃), 58.5 (C2), 113.6 (C8), 120.4 (C10), 123.2 (C5), 126.6 (C7), 128.3 (C3), 132.5 (C4), 140.0 (C6), 141.1 (C9), 166.1 (CO), 174.5 (CO). Anal. Calcd for C₁₈H₂₃NO₄: C, 68.12; H, 7.30; N, 4.41. Found: C, 67.73; H, 7.44; N, 4.33. MS m/z (EI) 317.2 (M⁺, 4%), 259.2 (18%), 258.2 (100), 243.2 (10), 242.2 (15), 228.1 (6), 199.1 (3).

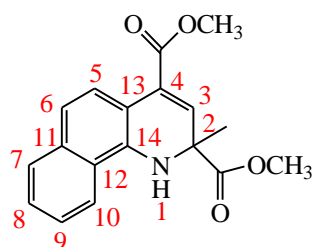
Dimethyl 6-methoxy-2,8-dimethyl-1,2-dihydroquinoline-2,4-dicarboxylate (3g)



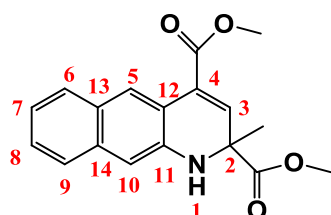
Yellow solid; yield (77%); R_f 0.5 (2:1 Cyclohexane/EtOAc); m.p: 82-83 °C. IR (KBr) 3382 (NH), 1740, 1718 (CO) cm⁻¹. ¹H-NMR (400MHz, CDCl₃): δ = 1.57 (s, 3H, CH₃), 2.2 (s, 3H, CH₃), 3.70 (s, 3H, COOCH₃), 3.73 (s, 3H, OCH₃), 3.84 (s, 3H, COOCH₃), 6.63-6.64 (d, 1H, *J* 2.6, Ar-H), 6.70 (br, 1H, -C=CH), 7.33-7.34 (d, 1H, *J* 2.6, Ar-H). ¹³C-NMR (400 MHz, CDCl₃): δ = 17.3 (CH₃), 27.2 (CH₃), 52.0, 52.8 (COOCH₃), 55.7 (OCH₃), 58.5 (C2), 109.0(C5), 117.0 (C10), 117.9 (C7), 122.7 (C8), 128.3 (C3), 133.6 (C4), 134.8 (C9), 151.7 (C6), 166.0 (CO), 174.8 (CO). Anal. Calcd for C₁₆H₁₉NO₅: C, 62.94; H, 6.27; N, 4.59. Found: C, 62.84; H, 6.42; N, 4.59. MS m/z (EI) 305.1 (M⁺, 6%), 247.2 (20), 246.1 (100), 203.1 (8), 187.1 (7), 145.1 (4).

Dimethyl 6-phenyl-2-methyl-1,2-dihydroquinoline-2,4-dicarboxylate (3h)

Yellow solid; yield (65%); R_f 0.56 (2:1 Cyclohexane/EtOAc); m.p: 109-110 °C. IR (KBr) 3364 (NH), 1712 (CO) cm^{-1} . $^1\text{H-NMR}$ (300 MHz, CDCl_3): δ = 1.59 (s, 3H, CH_3), 3.76 (s, 3H, COOCH_3), 3.88 (s, 3H, COOCH_3), 4.58 (bs, 1H, NH), 6.69-6.72 (bs, 2H, $-\text{C}=\text{CH}$ and Ar-H), 7.23-7.31 (m, 1H, Ar-H), 7.31-7.40 (m, 3H, Ar-H), 7.52-7.55 (m, 2H, Ar-H), 8.1 (br, 1H, Ar-H). $^{13}\text{C-NMR}$ (400 MHz, CDCl_3): 27.7 ($\underline{\text{C}}\text{H}_3$), 52.1, 52.9 ($2\times\text{COO}\underline{\text{C}}\text{H}_3$), 58.7 (C2), 114.4 (C8), 116.5 (C10), 125.2 (C2'), 126.1 (C7), 126.2 (C6'). 126.4 (C4'), 127.3 (C5), 128.2 (C3), 128.3 (C5'), 128.5 (C3'), 131.5 (C6), 132.9 (C4), 141.0 (C1'), 141.8 (C9), 165.9 (CO), 174.2 (CO). Anal. Calcd for $\text{C}_{20}\text{H}_{19}\text{NO}_4$: C, 71.20; H, 5.68; N, 4.15. Found: C, 70.99; H, 5.77; N, 4.11. MS m/z (EI) 337.2 (M^+ , 7%), 279.2 (21), 278.2 (100), 219.2 (7), 139.2 (4), 59.3 (2).

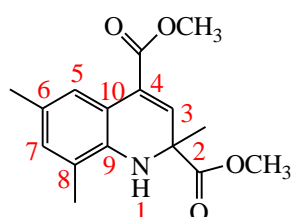
Compound (3i)^{17b}

Yellow solid; yield (53%); R_f 0.56 (2:1 Cyclohexane/EtOAc); m.p: 121-122 °C. IR (KBr) 3396 (NH), 1720 (CO) cm^{-1} . $^1\text{H-NMR}$ (300 MHz, CDCl_3): δ = 1.62 (s, 3H, CH_3), 3.77 (s, 3H, COOCH_3), 3.89 (s, 3H, COOCH_3), 5.0 (bs, 1H, NH); 6.5-6.6 (d, 1H, J 8.5 Hz, Ar-H), 6.68 (s, 1H, $\text{C}=\text{CH}$), 7.21-7.24 (d, 1H, J 8.7 Hz, Ar-H), 7.43-7.47 (m, 2H, Ar-H), 7.73-7.76 (m, 1H, Ar-H), 7.83-7.87 (m, 1H, Ar-H), 7.87-7.89 (d, 1H, J 8.7 Hz, Ar-H). $^{13}\text{C-NMR}$ (300 MHz, CDCl_3): 27.3 (CH_3), 52.0, 52.9 ($2\times\text{COO}\underline{\text{C}}\text{H}_3$), 58.6 (C2), 111.1 (C13), 117.8 (C6), 119.9 (C5), 122.2 (C12), 123.9 (C9), 125.2 (C8), 126.4 (C7), 128.5 (C3), 129.0 (C3), 130.2 (C11), 134.2 (C4), 137.9 (C14), 166.5 (CO), 174.4 (CO). Anal. Calcd for $\text{C}_{18}\text{H}_{17}\text{NO}_4$: C, 69.44; H, 5.50; N, 4.50. Found: C, 69.40; H, 5.55; N, 4.47. MS m/z (EI) 311.1 (M^+ , 16%), 253.2 (35), 252.1 (100), 192.1 (21), 59.3 (2).

Compound (3j)

Yellow solid; yield (67%); R_f 0.43 (2:1 Cyclohexane/EtOAc); m.p: 173-175 °C. IR (KBr) 3351 (NH), 1716 (CO) cm^{-1} . $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ = 1.56 (s, 3H, CH_3), 3.73 (s, 3H, COOCH_3), 3.80 (s, 3H, COOCH_3), 6.44 (s, 1H, $-\text{C}=\text{CH}$), 6.96-6.99 (d, 1H, J 8.7 Hz, Ar-H), 7.21-7.25 (m, 1H, Ar-H), 7.33-7.40 (m, 2H, Ar-H), 7.63-7.69 (m, 2H, Ar-H). $^{13}\text{C-NMR}$ (400MHz, CDCl_3): 25.5 (CH_3), 52.3, 52.8 (2x COOCH_3), 57.8 (C2), 110.4 (C10), 117.0 (C7), 122.4 (C5), 123.4 (C9), 126.1 (C8). 127.1 (C12), 128.6 (C13), 129.5 (C6), 129.9 (C3), 130.3 (C14), 130.9 (C4), 142.0 (C11), 169.4 (CO), 174.3 (CO). Anal. Calcd for $\text{C}_{18}\text{H}_{17}\text{NO}_4$: C, 69.44; H, 5.50; N, 4.50. Found: C, 69.52; H, 5.70; N, 4.45; MS m/z (EI) 311.1 (M^+ , 5%), 253.1 (19), 252.1 (100), 193.1 (10), 118.6 (4), 59.3 (3).

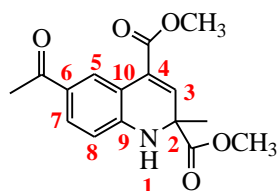
Dimethyl 2,6,8-trimethyl-1,2-dihydroquinoline-2,4-dicarboxylate (3k)



Pale yellow crystalline solid; yield (60%); R_f 0.25 (2:1 Cyclohexane/EtOAc); m.p: 147-148 °C. IR (KBr) 3352 (NH), 1740, 1709 (CO) cm^{-1} . $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ = 1.50 (s, 3H, CH_3), 2.1, 2.2 (s, 6H, 2x CH_3), 3.70, 3.80 (s, 6H, 2x COOCH_3), 6.3 (s, 1H, Ar-H), 6.42 (bs, 2H, Ar-H and $-\text{C}=\text{CH}$).

$^{13}\text{C-NMR}$ (400 MHz, CDCl_3): δ = 20.5, 21.3 (2x CH_3), 26.9 (CH_3), 52.2, 52.7 (COOCH_3), 57.7, (C2), 113.5(C10), 123.3 (C8), 130.4, 130.9 (C5 and C6), 134.7 (C7), 139.4 (C4), 143.4 (C9), 169.0 (CO), 174.3 (CO). Anal. Calcd for $\text{C}_{16}\text{H}_{19}\text{NO}_4$: C, 66.42; H, 6.62; N, 4.84. Found: C, 66.41; H, 6.69; N, 4.86. MS m/z (EI) 289.1 (M^+ , 5%), 231.2 (28), 230.1 (100), 198.1 (8), 171.1 (15), 170.1 (9), 128.1 (6).

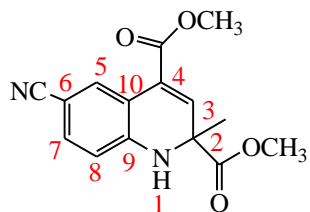
Dimethyl 6-acetyl-2-methyl-1,2-dihydroquinoline-2,4-dicarboxylate (3l)



Yellow crystalline solid; yield (91%); R_f 0.31 (2:1 Cyclohexane/EtOAc); m.p: 152-153 °C. IR (KBr) 3329 (NH), 1742, 1664 (CO) cm^{-1} . $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ = 1.57 (s, 3H, CH_3), 2.49 (s, 3H, COCH_3), 3.74 (s, 3H, COOCH_3), 3.86 (s, 3H, COOCH_3), 5.0 (br, 1H, NH); 6.5-6.6 (d, 1H, J 8.5 Hz, Ar-H), 6.69 (br, 1H, $\text{C}=\text{CH}$), 7.71-7.74 (dd, 1H, J 8.5 and 2.0 Hz, Ar-H), 8.49-8.50 (d, 1H, J 2.0 Hz, Ar-H). $^{13}\text{C-NMR}$ (400 MHz, CDCl_3): 26.1 (CH_3), 28.2 (COCH_3), 52.2, 53.0 (2x COOCH_3), 58.9 (C2), 113.5 (C8), 114.5 (C10), 127.3 (C6), 127.8 (C5), 128.1 (C3), 130.3 (C7), 132.4 (C4), 146.5 (C9), 165.5 (CO), 173.3 (CO), 196.3 (CO). Anal. Calcd for

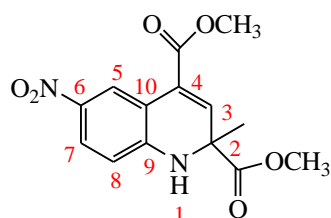
$C_{16}H_{17}NO_5$: C, 63.36; H, 5.65; N, 4.62. Found: C, 63.42; H, 5.70; N, 4.63. MS m/z (EI) 303.2 (M^+ , 3%), 245.2 (14), 244.2 (100), 201.2 (7), 186.2 (4), 114.9 (3), 59.4 (1).

Dimethyl 6-cyano-2-methyl-1,2-dihydroquinoline-2,4-dicarboxylate (3m)

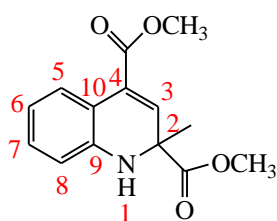


White solid; yield (71%); R_f 0.23 (2:1 Cyclohexane/EtOAc); m.p: 140-141 °C. IR (KBr) 3351 (NH), 1724, 1718 (CO) cm^{-1} . 1H -NMR (400MHz, $CDCl_3$): δ = 1.59 (s, 3H, CH_3), 3.78 (s, 3H, $COOCH_3$), 3.87 (s, 3H, $COOCH_3$), 4.9 (br, 1H, NH), 6.58-6.60 (d, 1H, J 8.3 Hz, Ar-H), 6.75 (br, 1H, $-C=CH$), 7.30-7.33 (dd, 1H, J 8.3 and 1.8 Hz, Ar-H), 8.19-8.20 (d, 1H, J 1.8, Ar-H). ^{13}C -NMR (400 MHz, $CDCl_3$): 28.4 ($\underline{C}H_3$), 52.4, 53.2 ($2xCOO\underline{C}H_3$), 58.9 (C2), 100.7 (C6), 114.0 (C8), 115.6 (C10), 119.9 (CN), 126.4 (C7). 131.0 (C3), 133.4 (C4), 133.5 (C5), 145.6 (C9), 165.0 (CO), 173.1 (CO). Anal. Calcd for $C_{15}H_{14}N_2O_4$: C, 62.93; H, 4.93; N, 9.79. Found: C, 62.96; H, 4.82; N, 9.81. MS m/z (EI) 386.1 (M^+ , 1%), 228.1 (15%), 227.1 (100), 199.1 (5), 168.0 (20), 167.1 (6), 140.1 (6), 59.2 (4).

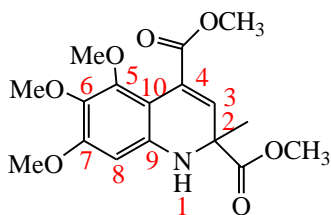
Dimethyl 6-nitro-2-methyl-1,2-dihydroquinoline-2,4-dicarboxylate (3n)¹⁷



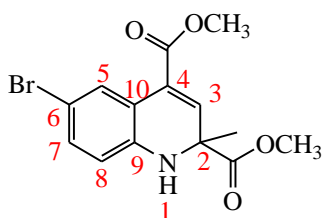
Yellow solid; yield (97%); R_f 0.23 (2:1 Cyclohexane/EtOAc); m.p: 135-136 °C. IR (KBr) 3347 (NH), 1721 (CO) cm^{-1} . 1H -NMR (300MHz, $CDCl_3$): δ = 1.62 (s, 3H, CH_3), 3.80 (s, 3H, $COOCH_3$), 3.90 (s, 3H, $COOCH_3$), 5.22 (bs, 1H, NH), 6.5-6.6 (d, 1H, J 8.9 Hz, Ar-H), 6.78 (d, 1H, J 1.54 Hz, $C=CH$), 7.9-8.0 (dd, 1H, J 8.9 and 2.5 Hz, Ar-H), 8.83-8.84 (d, 1H, J 2.5, Ar-H). ^{13}C -NMR (400 MHz, $CDCl_3$): 28.6 ($\underline{C}H_3$), 52.5, 53.3 ($2xCOO\underline{C}H_3$), 59.3 (C2), 113.3 (C8), 114.4 (C10), 123.4 (C5), 126.2 (C7), 126.4 (C3). 133.3 (C4), 139.1 (C6), 147.6 (C9), 164.9 (CO), 172.7 (CO). Anal. Calcd for $C_{14}H_{14}N_2O_6$: C, 54.90; H, 4.61; N, 9.15. Found: C, 54.84; H, 4.45; N, 9.15. MS m/z (EI) 306.1 (M^+ , 1%), 248.1 (15), 247.1 (100), 201.1 (47), 186.1 (12), 142.1 (9), 59.3 (5).

Dimethyl 2-methyl-1,2-dihydroquinoline-2,4-dicarboxylate (3o)¹⁷

Yellow solid; yield (63%); R_f 0.53 (2:1 Cyclohexane/EtOAc); m.p: 73 °C. IR (KBr) 3365 (NH), 1710 (CO) cm^{-1} . $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ = 1.55 (s, 3H, CH_3), 3.7 (s, 3H, COOMe), 3.8 (s, 3H, COOMe), 4.5 (bs, 1H, NH), 6.61-6.63 (m, 1H, Ar-H), 6.66 (s, 1H, $-\text{C}=\text{CH}$), 6.71-6.74 (m, 1H, Ar-H), 7.0-7.10 (m, 1H, Ar-H), 7.77-7.79 (m, 1H, Ar-H). $^{13}\text{C-NMR}$ (400 MHz, CDCl_3): δ = 27.6 ($\underline{\text{C}}\text{H}_3$), 52.0, 52.8 ($\text{COO}\underline{\text{C}}\text{H}_3$), 58.5 (C2), 114.1 (C5), 116.3 (C8), 118.6 (C6), 126.4 (C10), 128.1 (C7), 129.6 (C3), 132.5 (C4), 142.4 (C9), 166.0 (CO), 174.2 (CO). Anal. Calcd for $\text{C}_{14}\text{H}_{15}\text{NO}_4$: C, 64.36; H, 5.79; N, 5.36. Found: C, 64.43; H, 5.81; N, 5.41. MS m/z (EI) 261.1 (M^+ , 3%), 203.1 (15), 202.1 (100), 188.1 (4), 174.1 (5), 143.1 (18), 142.1 (7), 115.1 (7), 59.1(5).

Dimethyl 5,6,7-trimethoxy-2-methyl-1,2-dihydroquinoline-2,4-dicarboxylate (3p)

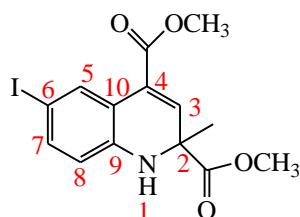
White crystalline solid; yield (83%); R_f 0.16 (2:1 Cyclohexane/EtOAc); m.p: 120-121 °C. IR (KBr) 3359 (NH), 1739 (CO) cm^{-1} . $^1\text{H-NMR}$ (300 MHz, CDCl_3): δ = 1.48 (s, 3H, CH_3), 3.69, 3.71, 3.79, 3.80 (s, 15H, $\text{COO}\underline{\text{C}}\text{H}_3$ and 5,6,7- $\text{O}\underline{\text{C}}\text{H}_3$), 4.42 (bs, 1H, NH), 5.85 (bs, 1H, Ar-H), 5.99 (s, 1H, $-\text{C}=\text{CH}$). $^{13}\text{C-NMR}$ (300 MHz, CDCl_3): δ = 26.9 ($\underline{\text{C}}\text{H}_3$), 52.1, 52.6 ($\text{COO}\underline{\text{C}}\text{H}_3$), 55.7, 58.0 (2x OCH_3), 58.0(C2), 60.9 (OCH_3), 93.7 (C8), 104.3 (C10), 123.8 (C3), 129.0 (C4), 134.2 (C9), 139.7 (C5), 149.8 (C6), 155.1 (C7), 170.3 (CO), 174.9 (CO). Anal. Calcd for $\text{C}_{17}\text{H}_{21}\text{NO}_7$: C, 58.11; H, 6.02; N, 3.99. Found: C, 57.73; H, 5.91; N, 3.93. MS m/z (EI) 351.2 (M^+ , 7%), 293.1 (19), 292.2 (100), 262.1 (6), 217.1 (7), 133.1 (3).

Dimethyl 6-bromo-2-methyl-1,2-dihydroquinoline-2,4-dicarboxylate (3q)

Yellow crystalline solid; yield (81%); R_f 0.5 (2:1 Cyclohexane/EtOAc); m.p: 106-107 °C.

IR (KBr) 3352 (NH), 1724 (CO) cm^{-1} . $^1\text{H-NMR}$ (400MHz, CDCl_3): δ = 1.54 (s, 3H, CH_3), 3.74 (s, 3H, COOCH_3), 3.85 (s, 3H, COOCH_3), 4.51 (bs, 1H, NH), 6.4-6.5 (d, 1H, J 8.5 Hz, Ar-H), 6.71 (bs, 1H, $-\text{C}=\text{CH}$), 7.14-7.17 (dd, 1H, J 8.5 and 2.1 Hz, Ar-H), 7.97-7.98 (d, 1H, J 2.1, Ar-H). $^{13}\text{C-NMR}$ (400 MHz, CDCl_3): 27.5 ($\underline{\text{C}}\text{H}_3$), 52.4, 52.9 ($2\times\text{COO}\underline{\text{C}}\text{H}_3$), 58.6 (C2), 110.4 (C6), 115.6 (C8), 117.9 (C9), 127.0 (C7), 129.0 (C3). 132.1 (C5), 133.8 (C4), 141.4 (C9), 165.4 (CO), 173.9 (CO). Anal. Calcd for $\text{C}_{14}\text{H}_{14}\text{BrNO}_4$: C, 49.43; H, 4.15; N, 4.12. Found: C, 49.38; H, 4.01; N, 4.13. MS m/z (EI) 339.0 (M^+ , 5%), 283.0 (12%), 282.0 (97), 280.0 (100%), 221.0 (7), 201.1 (11), 142.1 (6), 115.1 (6), 59.2 (6).

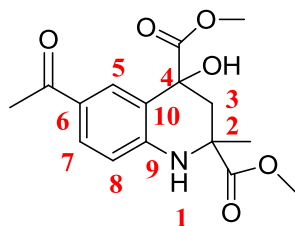
Dimethyl 6-iodo-2-methyl-1,2-dihydroquinoline-2,4-dicarboxylate (3r)



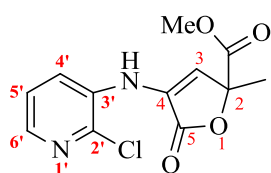
Yellow crystalline solid; yield (34%); R_f 0.56 (2:1 Cyclohexane/EtOAc); m.p: 120 $^\circ\text{C}$.

IR (KBr) 3350 (NH), 1723 (CO) cm^{-1} . $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ = 1.54 (s, 3H, CH_3), 3.74 (s, 3H, COOCH_3), 3.86 (s, 3H, COOCH_3), 4.51 (bs, 1H, NH), 6.3-6.4 (d, 1H, J 8.4 Hz, Ar-H), 6.68-6.69 (d, 1H, J 2.0 Hz, $-\text{C}=\text{CH}$), 7.32-7.35 (dd, 1H, J 8.4 and 2.0 Hz, Ar-H), 8.13-8.14 (d, 1H, J 2.0, Ar-H). $^{13}\text{C-NMR}$ (400 MHz, CDCl_3): 27.6 ($\underline{\text{C}}\text{H}_3$), 52.24, 52.97 ($2\times\text{COO}\underline{\text{C}}\text{H}_3$), 58.5 (C2), 116.15 (C8), 118.4 (C10), 126.9 (C3), 133.5 (C4), 134.8 (C5). 138.0 (C7), 142.0 (C9), 165.4 (CO), 173.9 (CO). Anal. Calcd for $\text{C}_{14}\text{H}_{14}\text{INO}_4$: C, 43.43; H, 3.64; N, 3.62. Found: C, 43.81; H, 3.58; N, 3.56. MS m/z (EI) 387.1 (M^+ , 7%), 329.0 (11), 328.0 (100), 201.2 (20), 142.2 (4), 59.3 (2).

Dimethyl 6-acetyl-4-hydroxy-2-methyl-1,2,3,4-tetrahydroquinoline-2,4-dicarboxylate (4)



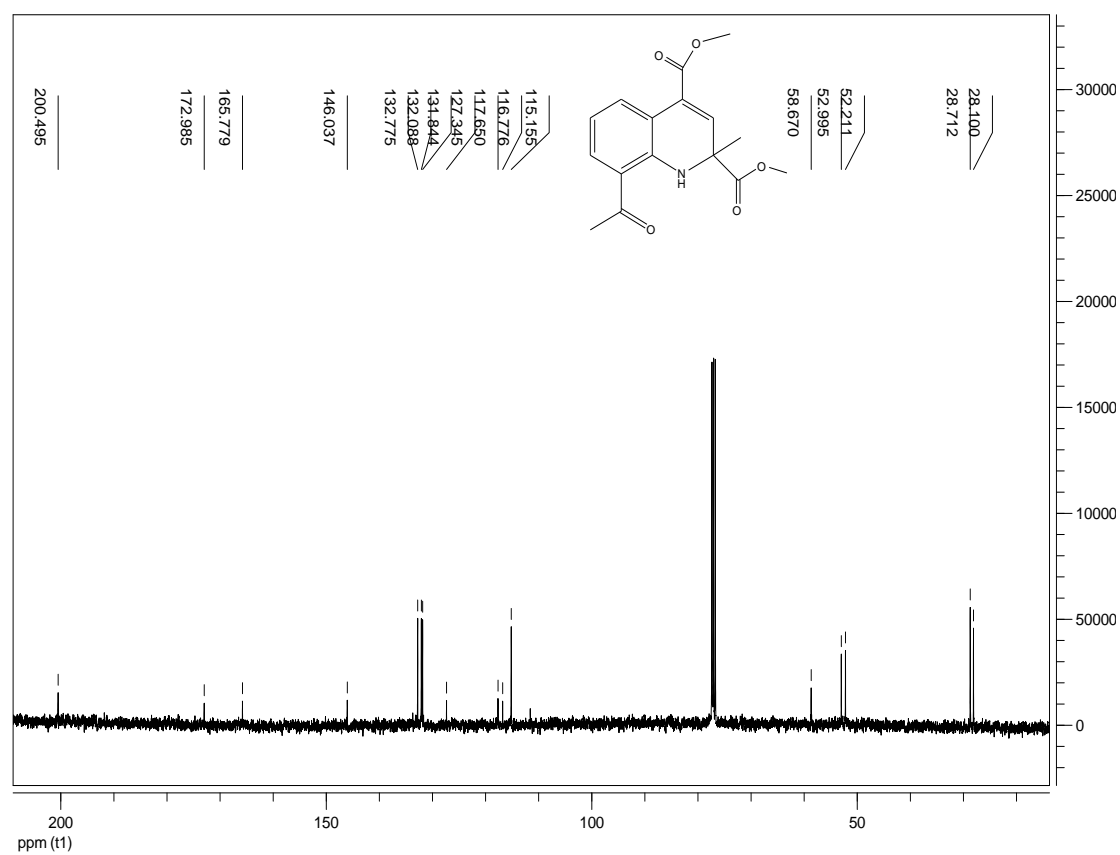
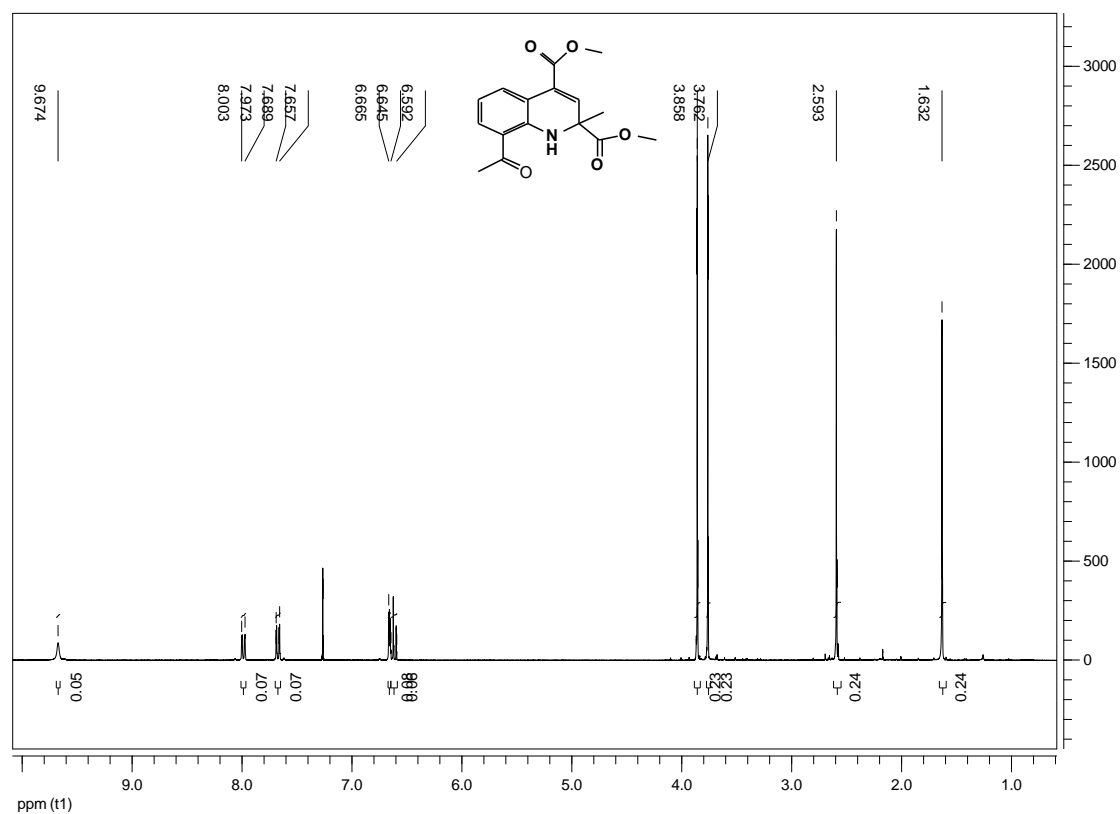
White solid; yield (54%); R_f 0.35 (1:1 Cyclohexane/EtOAc); m.p: 200-201 $^\circ\text{C}$. IR (KBr) 3325 (NH), 1743 (CO) cm^{-1} . $^1\text{H-NMR}$ (300MHz, MeOD): δ = 1.52 (s, 3H, CH_3), 2.27-2.64 (AB, 2H, J_{AB} 13.7 Hz, $-\text{CH}_2$), 2.43 (s, 3H, COCH_3), 3.6 (s, 3H, COOCH_3), 3.77 (s, 3H, COOCH_3), 6.71-6.73 (d, 1H, J 8.4 Hz, Ar-H), 7.59-7.60 (d, 1H, J 2.0 Hz, Ar-H), 7.72-7.75 (dd, 1H, J 8.6 and 2.0 Hz, Ar-H). MS m/z (EI) 321.2 (M^+ , 21%), 263.2 (5), 262.2 (28), 245.2 (20), 244.2 (100), 202.2 (29). 160.2 (7), 130.2 (4), 59.2 (4). HRMS-EI calcd. for $\text{C}_{16}\text{H}_{19}\text{NO}_6$ [M^+]: 321.12069; Found: 321.12115.

Lactone (9)

MW (10 bar, 150 watt, 100 °C, 7 h). Pale purple solid; yield (23%); R_f 0.4 (1:1 Cyclohexane/EtOAc); m.p: 98-99 °C. $^1\text{H-NMR}$ (300MHz, CDCl_3): δ = 1.79 (s, 3H, CH_3), 3.80 (s, 3H, OMe), 6.40 (s, 1H, =CH), 6.94 (1H, br, NH), 7.27-7.30 (1H, dd, J 5.0 and 8.0, Ar-H), 7.50-7.52 (1H, dd, J 1.3 and 8.0 Hz, Ar-H), 8.03-8.04 (1H, dd, J 1.4 and 4.6 Hz, Ar-H). $^{13}\text{C-NMR}$ (400 MHz, CDCl_3): 23.1 ($\underline{\text{C}}\text{H}_3$), 53.34 (OCH₃), 84.81 (C2), 115.17 (C3), 122.8 (C5'), 123.2 (C4'), 128.3 (C6'), 133.9 (C2'), 139.9 (C3'), 141,6 (C4), 168.8 (CO), 169.4 (CO).

Crystal data for **9**: $\text{C}_{12}\text{H}_{11}\text{ClN}_2\text{O}_4$, $M = 282.68$, crystallizes as colourless blocks, crystal dimensions 0.50 x 0.30 x 0.20 mm. Monoclinic, $a = 7.5735(10)$ Å, $b = 14.407(2)$ Å, $c = 11.6615(14)$ Å, $\beta = 96.641(10)^\circ$, $V = 1263.9(3)$ Å³, $z = 4$, $D_c = 1.486$ Mgm⁻³, space group $P2_1/c$ (No. 14), MoK α radiation ($\lambda = 0.71073$), $\mu = 0.314$ mm⁻¹, $F(000) = 584$.

The X-ray data were collected at 293(2) K in the range $4.5^\circ < 2\theta < 56^\circ$ on a Nicolet P3/F diffractometer by the Wyckoff scan method. The 3044 unique reflections were corrected for Lorentzian polarization effects, but not for absorption. Intensity of 1647 reflections were larger than $2\sigma(I)$. The structure was solved by Direct Methods and refined by full matrix least squares methods of F^2 with SHELXTL-97 program package. Hydrogen atoms were included in calculated positions and refined in riding mode. Refinement converged at a final $R = 0.0850$ ($wR_2 = 0.1548$, $I > 2\sigma(I)$, 179 parameters, mean and maximum δ/σ 0.000 and 0.000), with allowance of anisotropic displacement parameters for all non-hydrogen atoms. Minimum and maximum final rest-electron density is -0.255 and 0.263 eÅ⁻³.

^1H NMR and ^{13}C NMR Spectra of Compounds 3a-r and 4, 9**Figure S1.** NMR Spectrum of compound 3a.

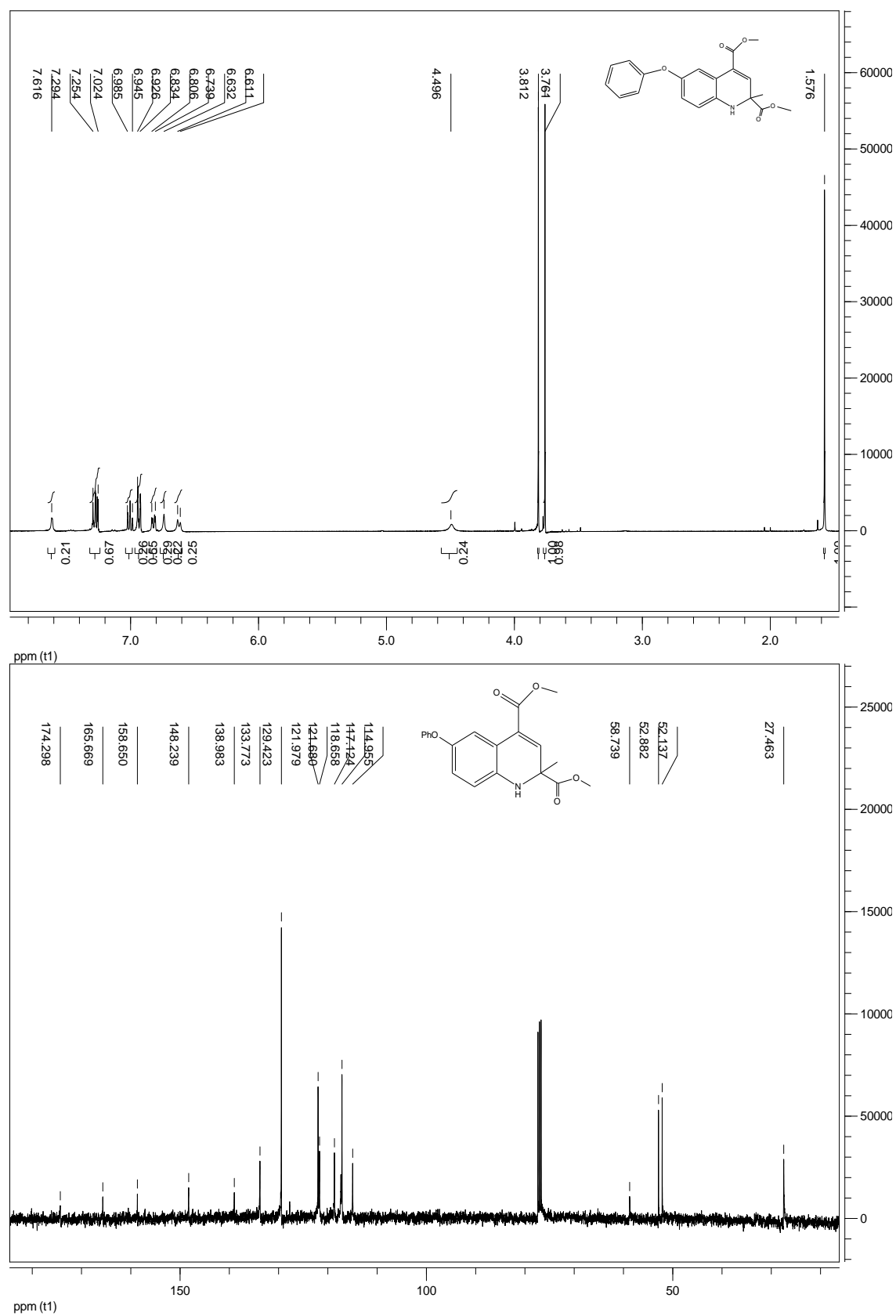


Figure S2. NMR Spectrum of compound 3b.

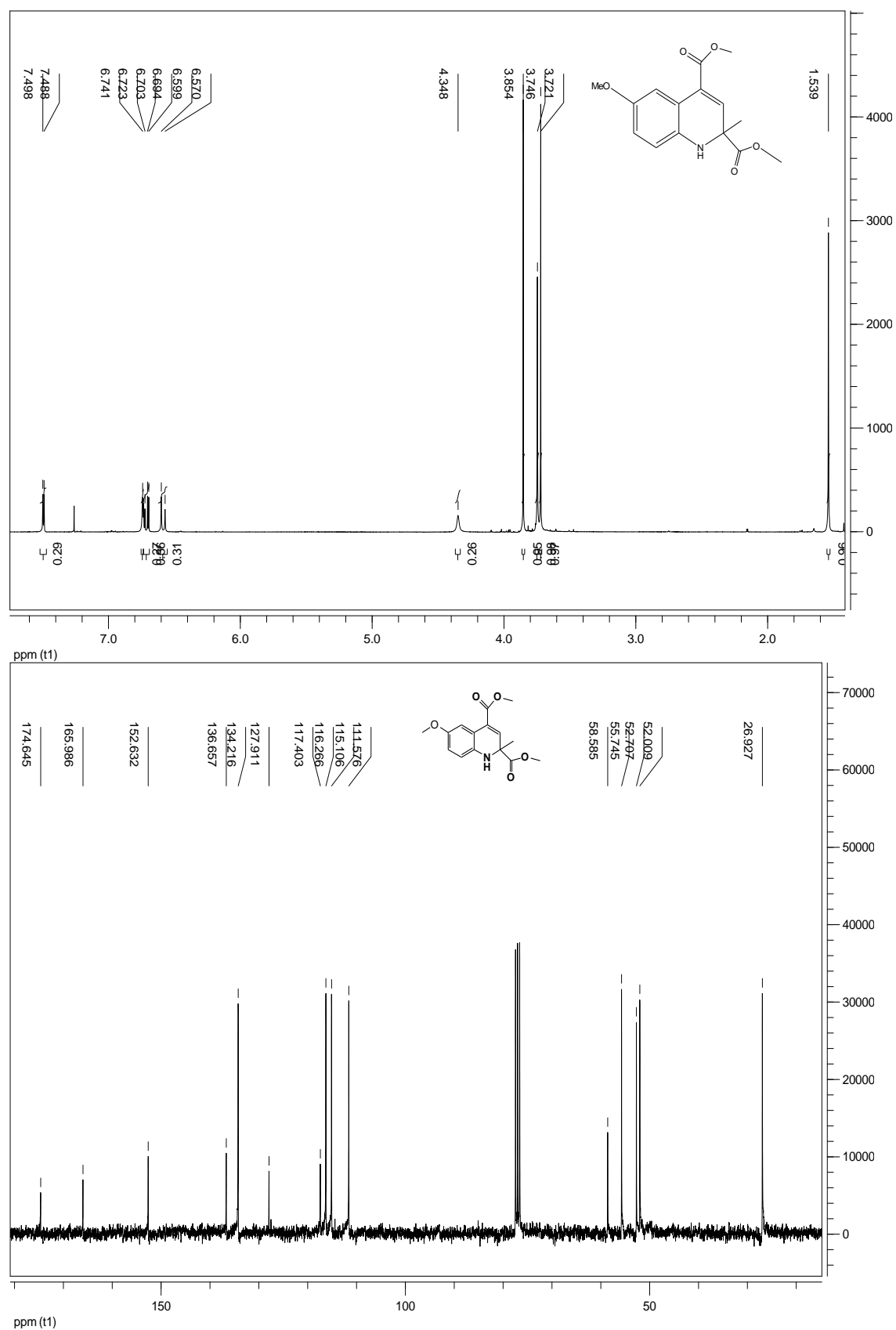


Figure S3. NMR Spectrum of compound 3c.

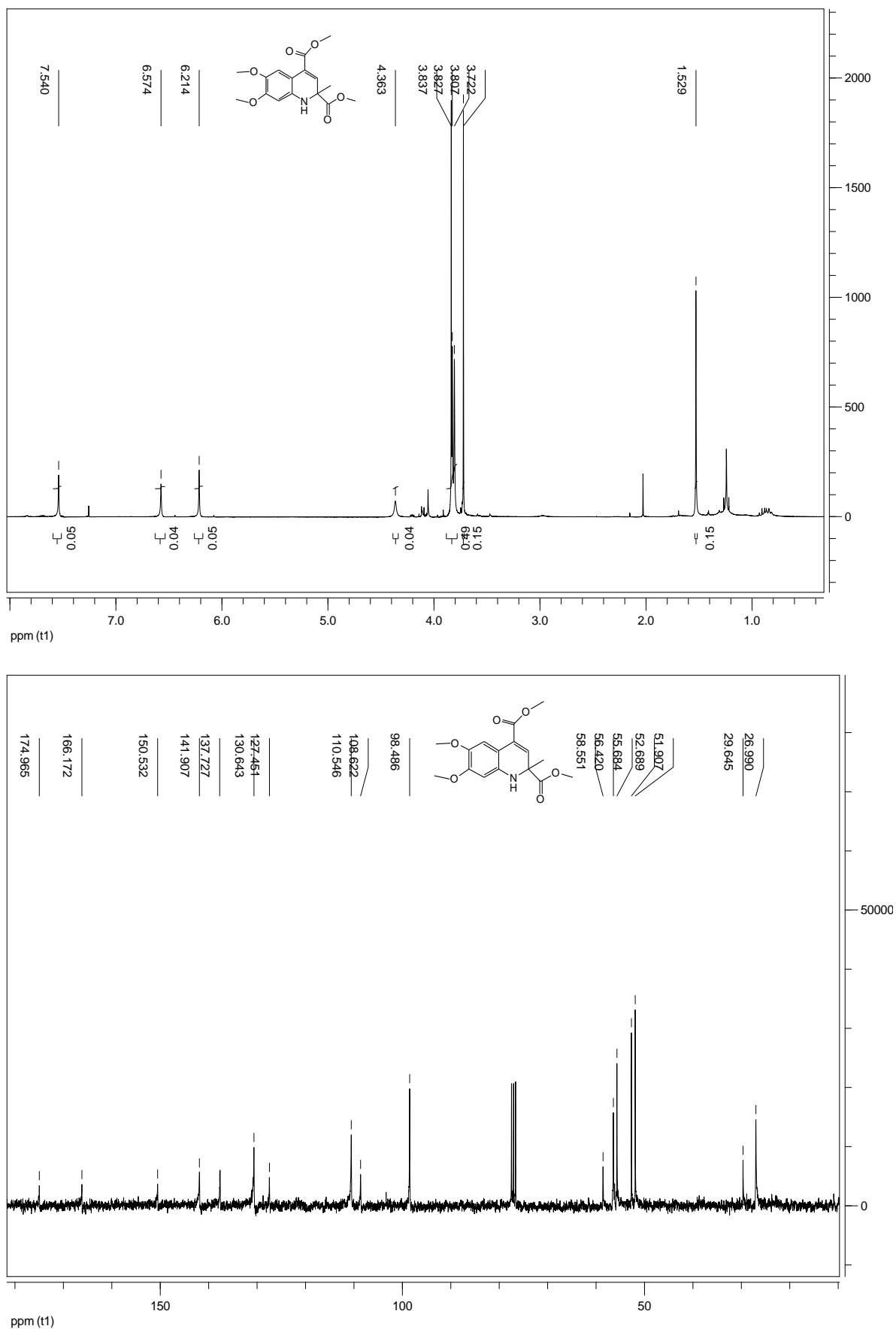


Figure S4. NMR Spectrum of compound 3d.

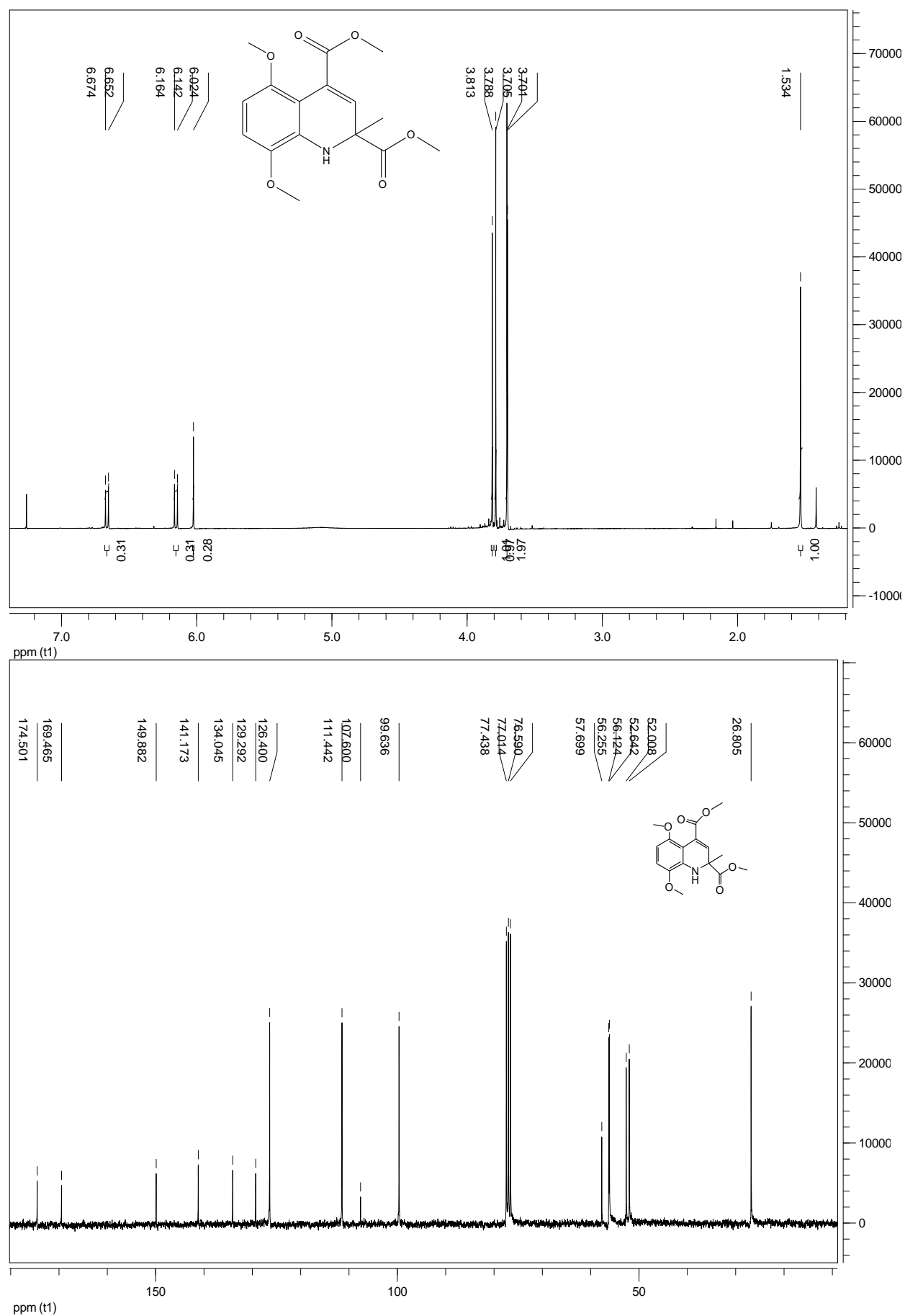


Figure S5. NMR Spectrum of compound 3e.

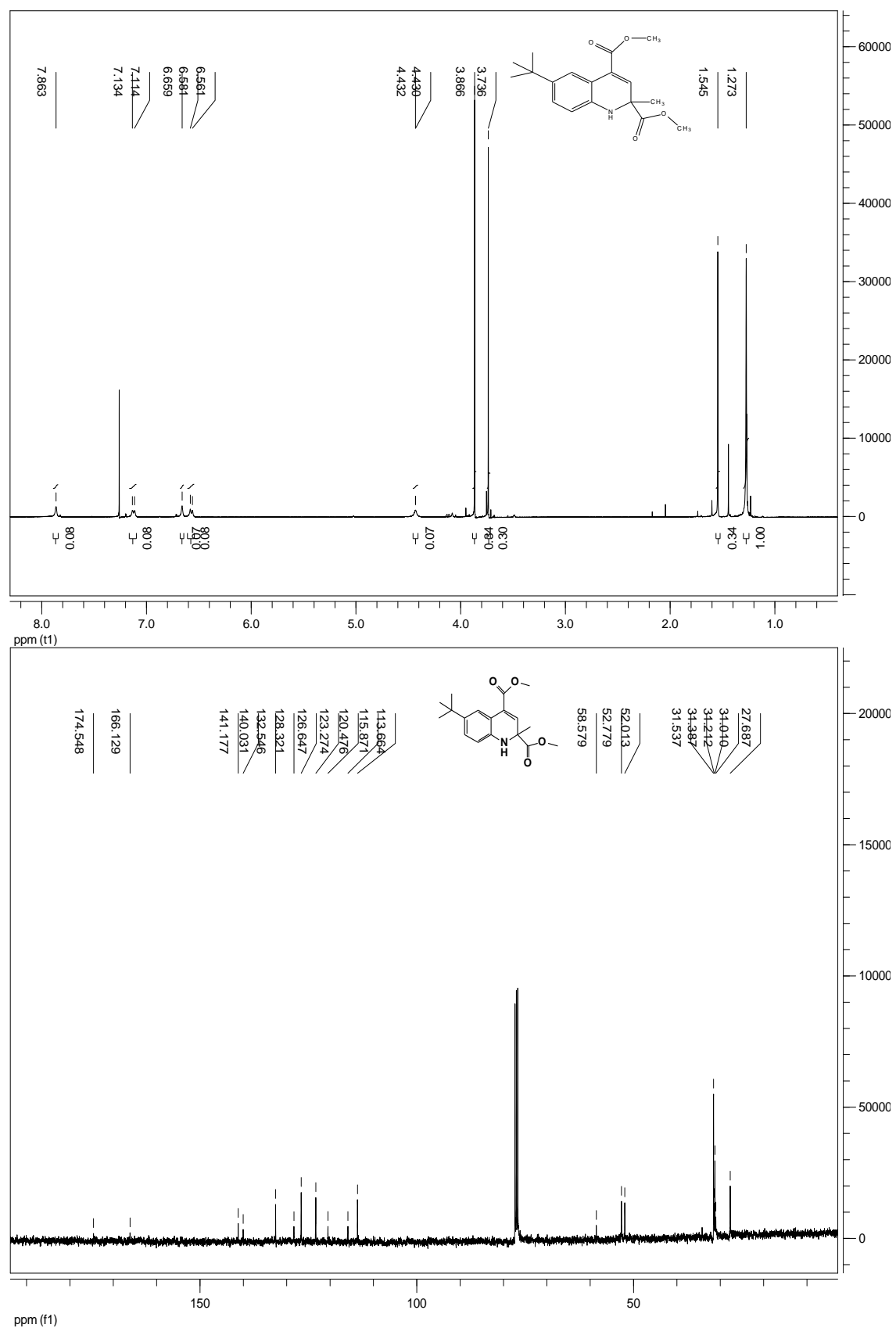


Figure S6. NMR Spectrum of compound 3f.

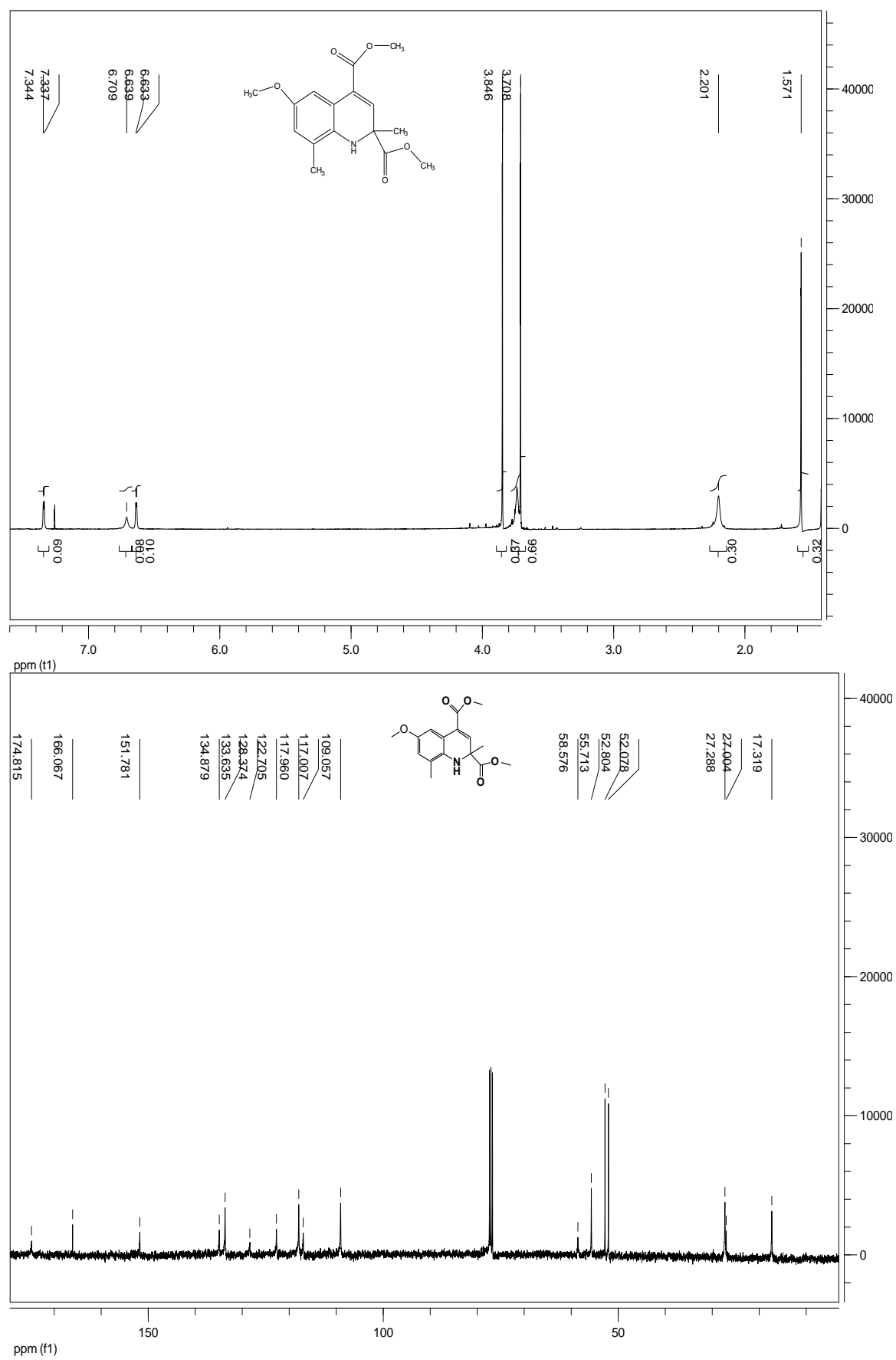


Figure S7. NMR Spectrum of compound **3g**.

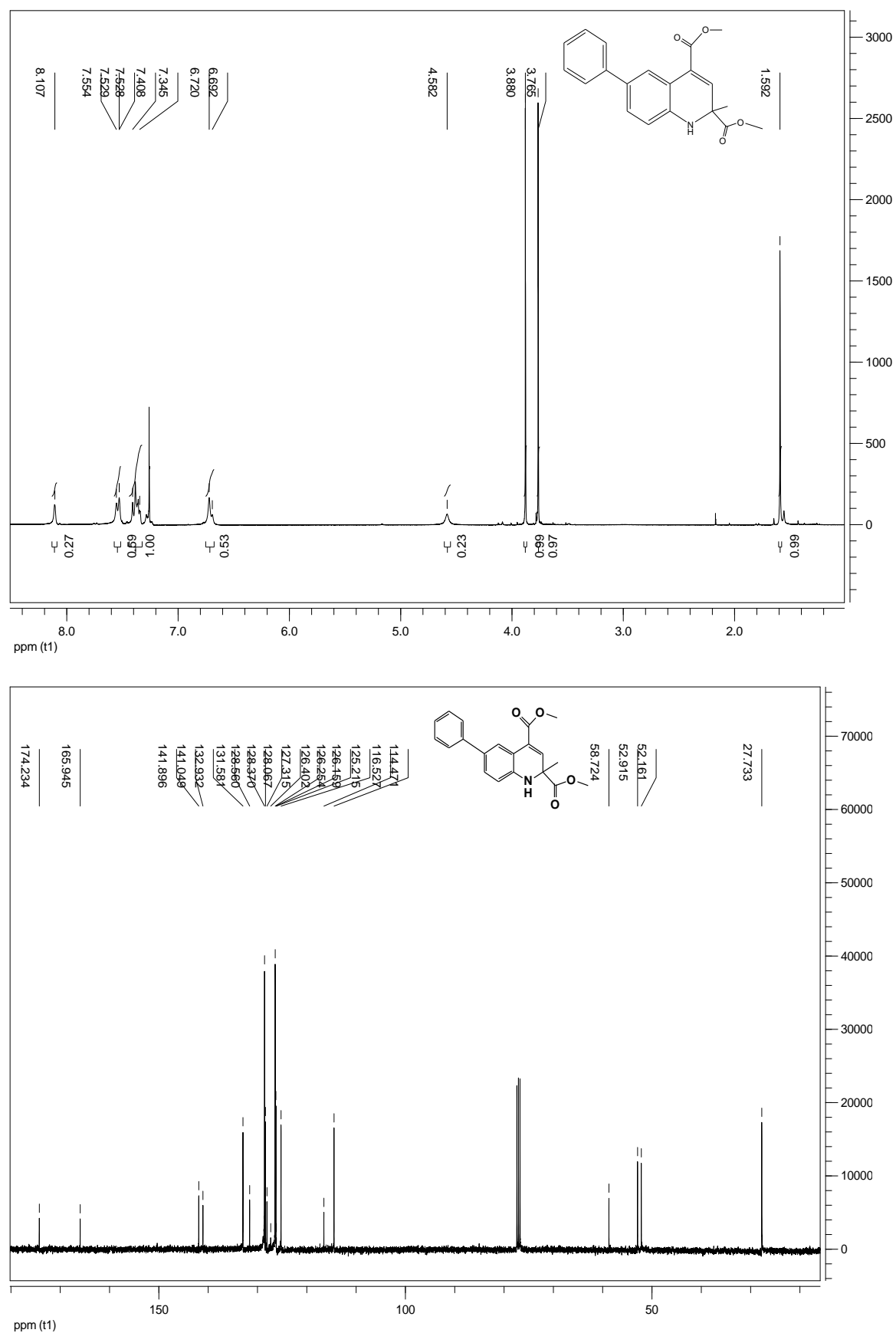
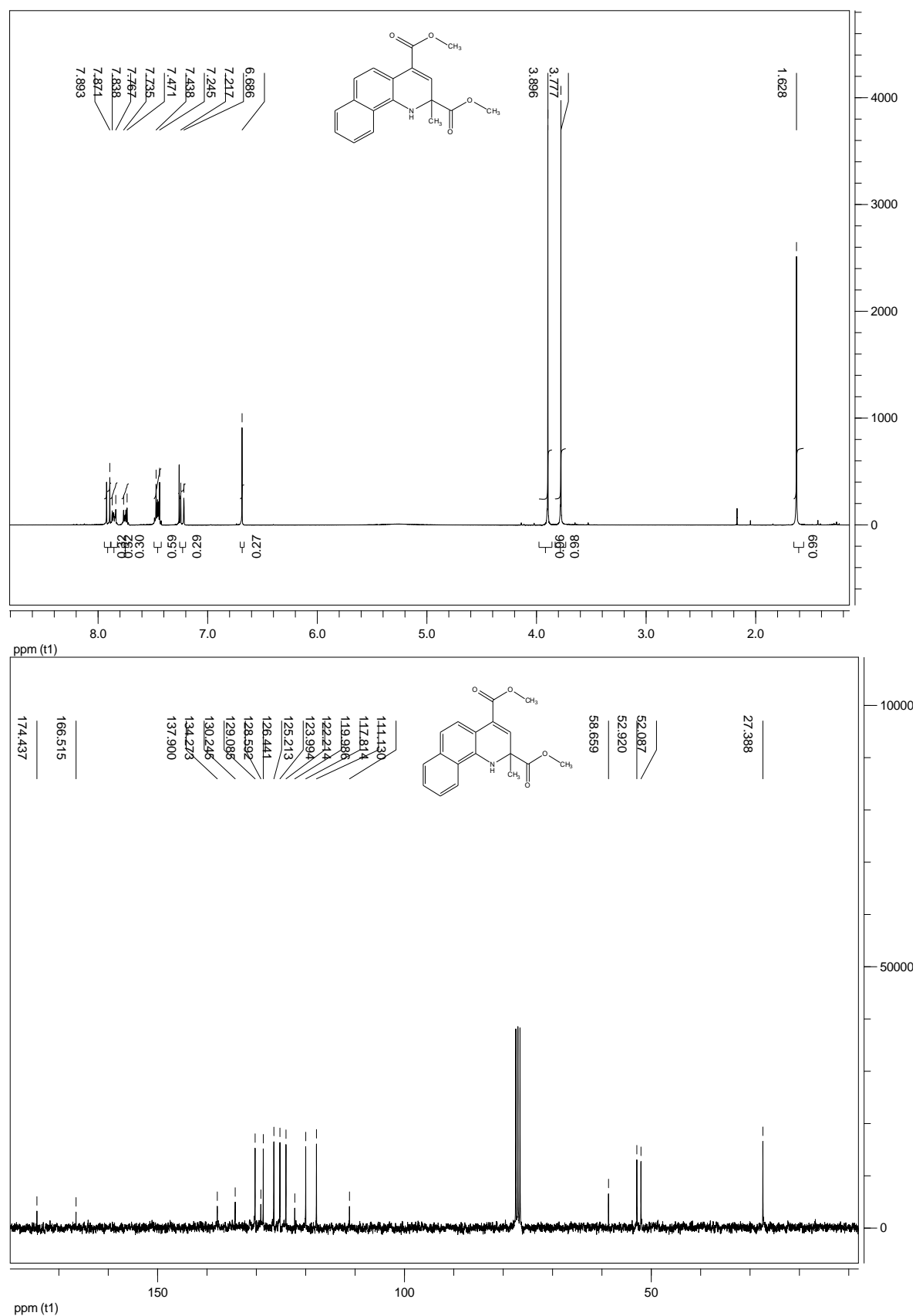


Figure S8. NMR Spectrum of compound 3h.

**Figure S9.** NMR Spectrum of compound 3i.

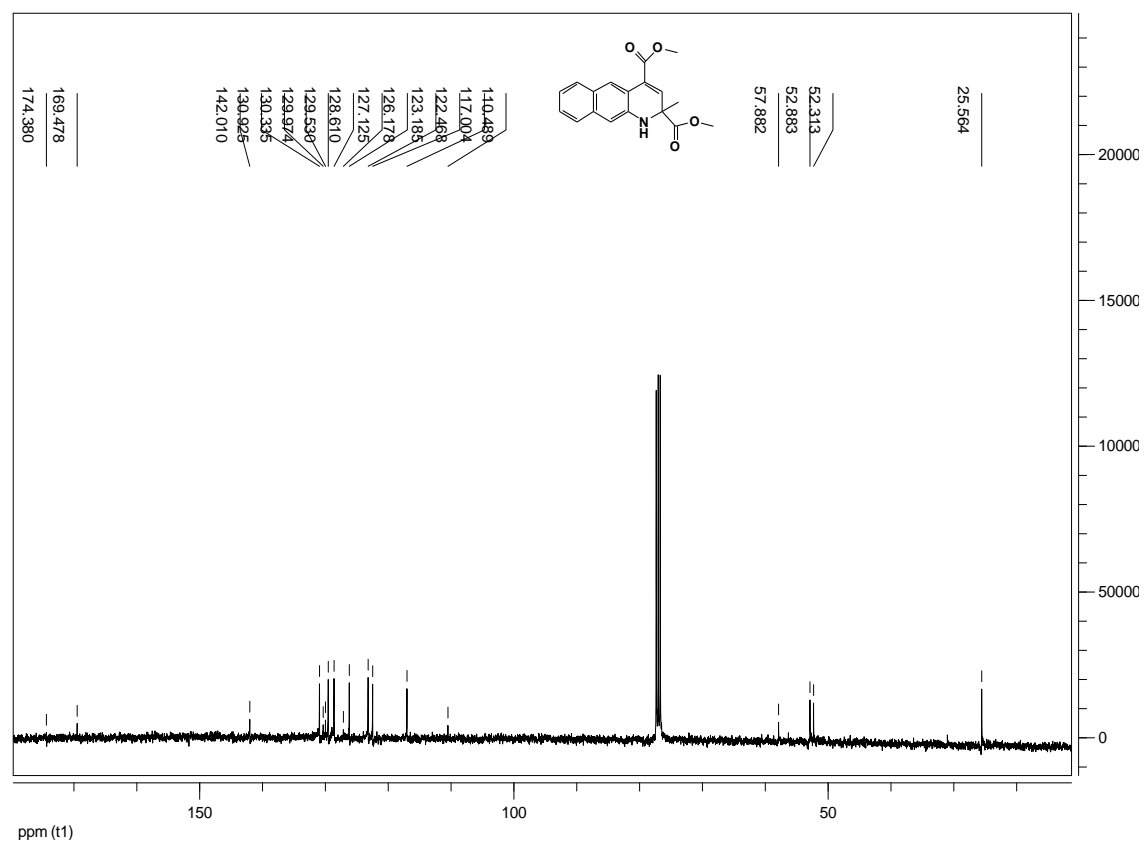
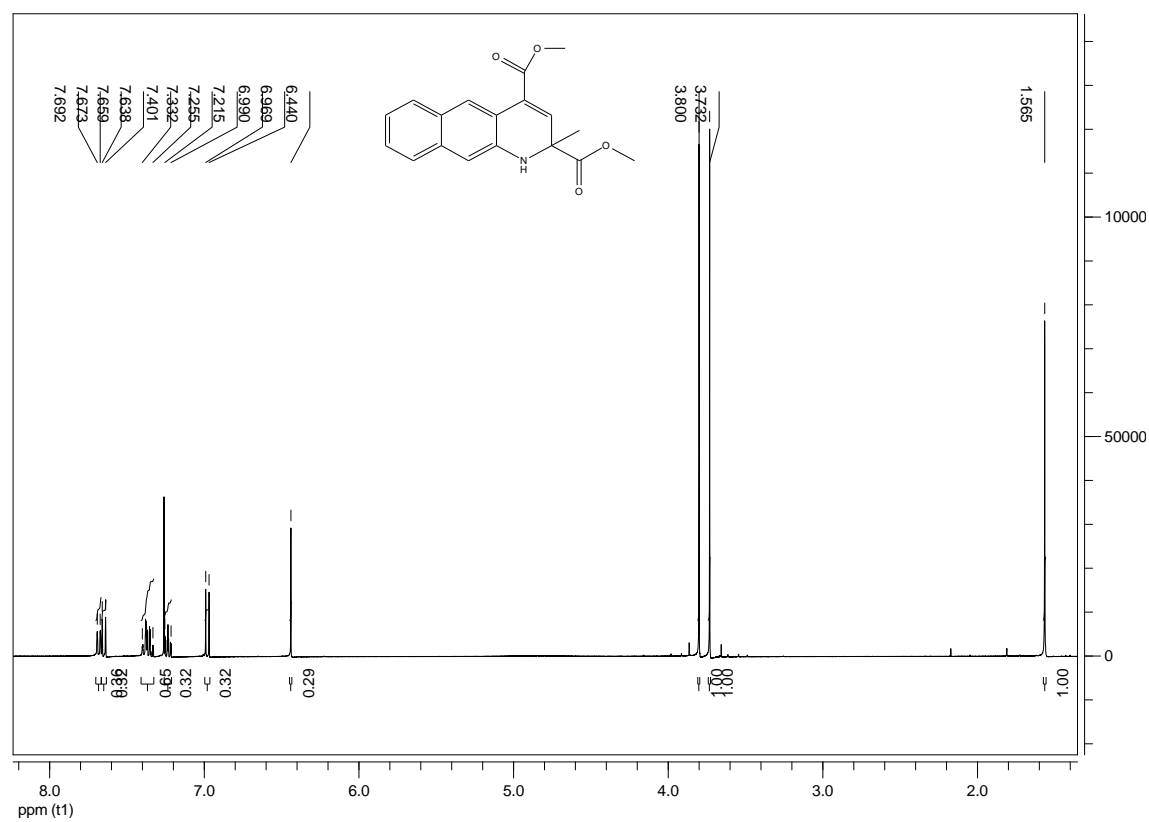


Figure S10. NMR Spectrum of compound 3j.

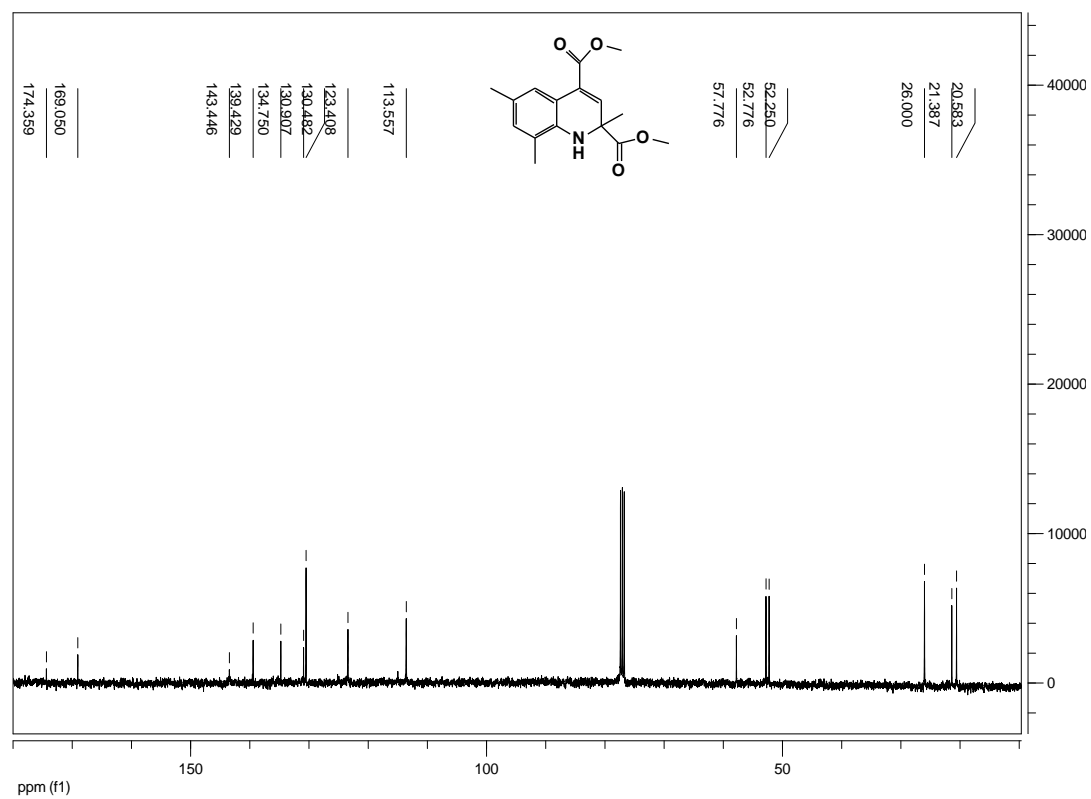
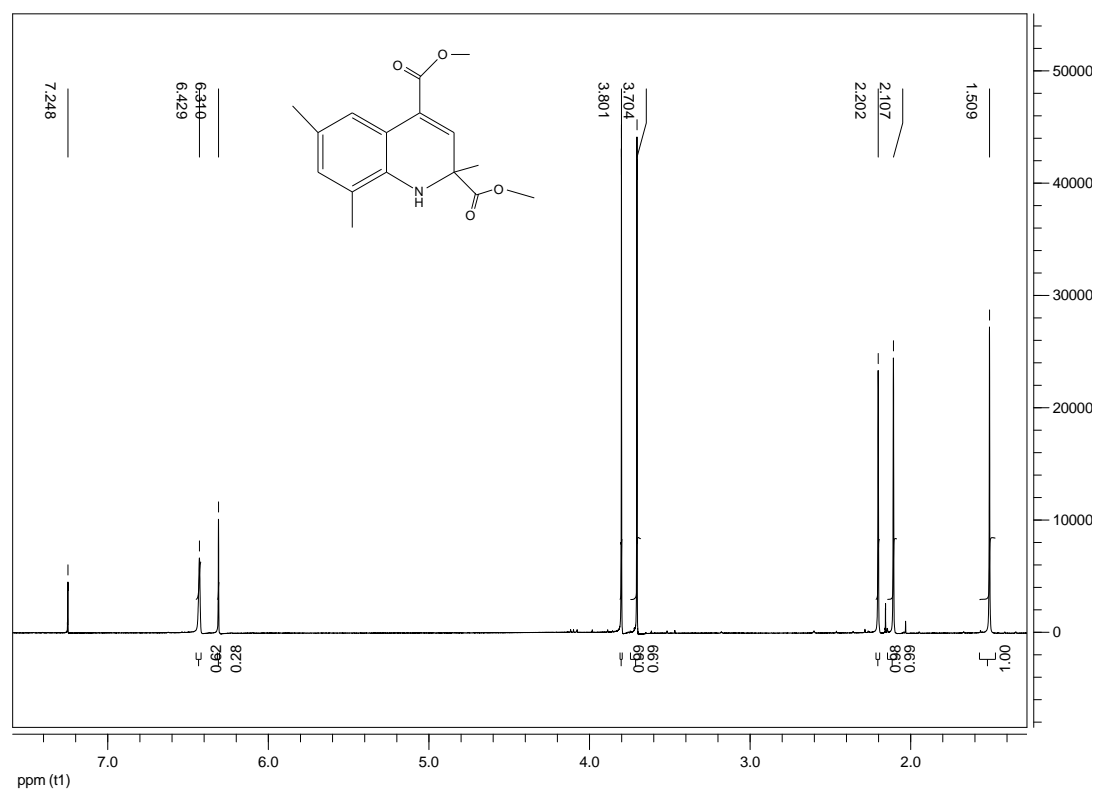


Figure S11. NMR Spectrum of compound **3k**.

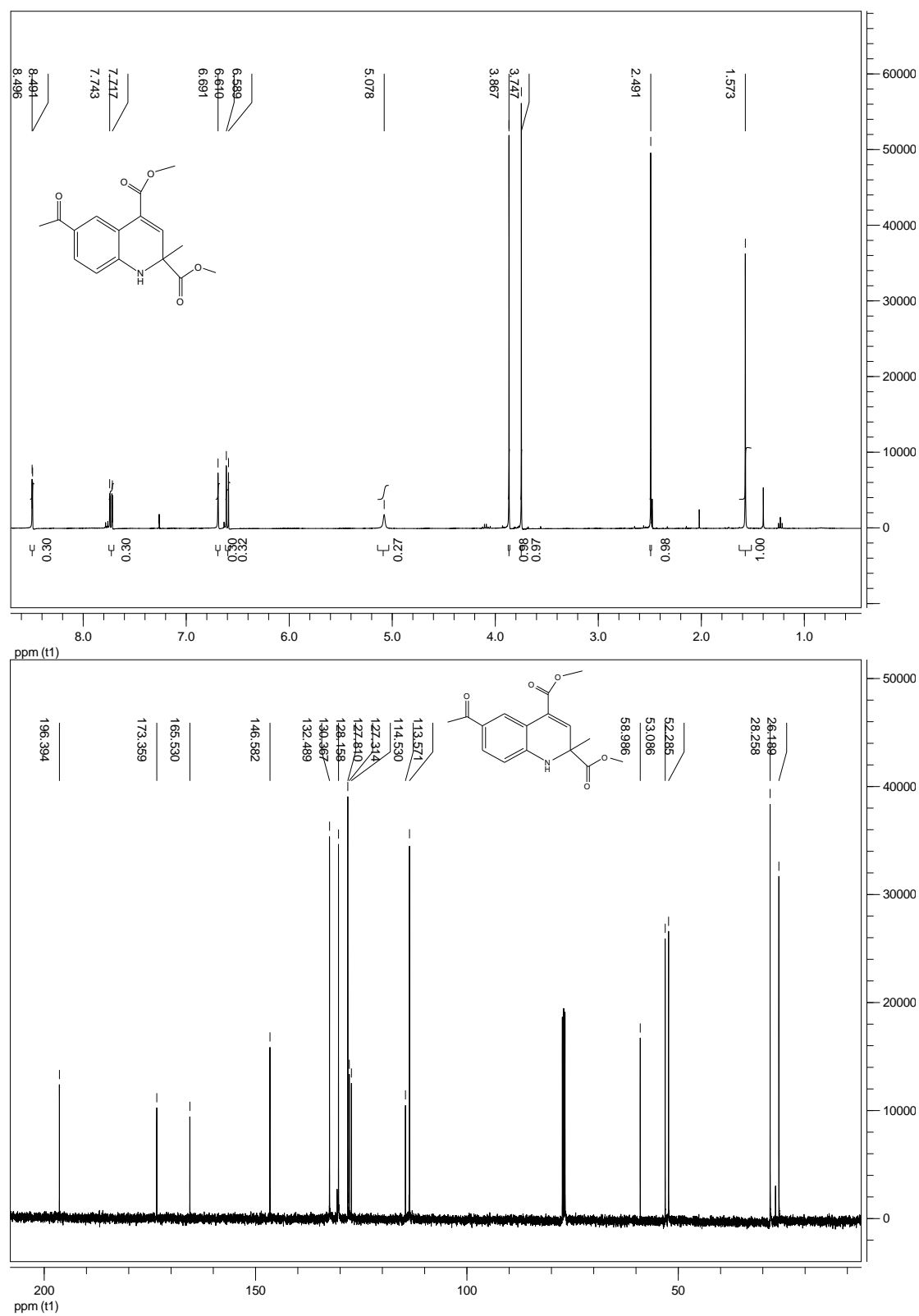


Figure S12. NMR Spectrum of compound 31.

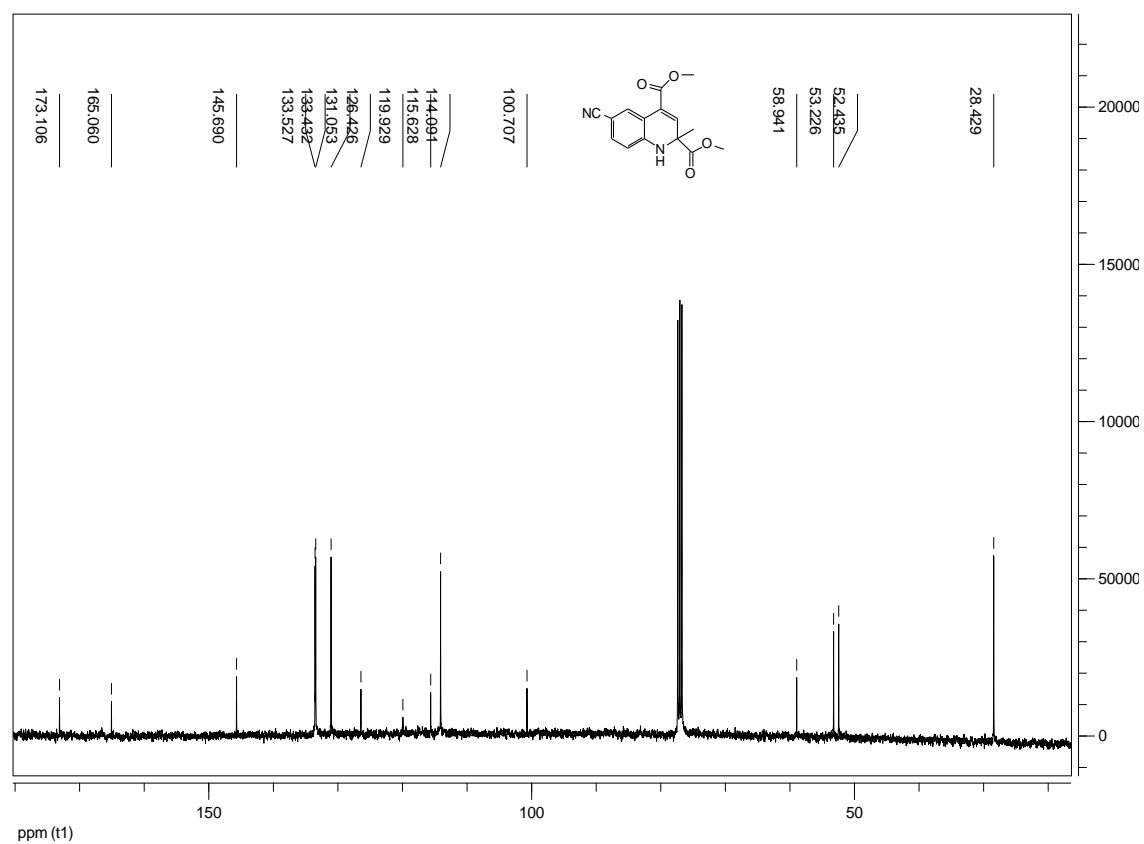
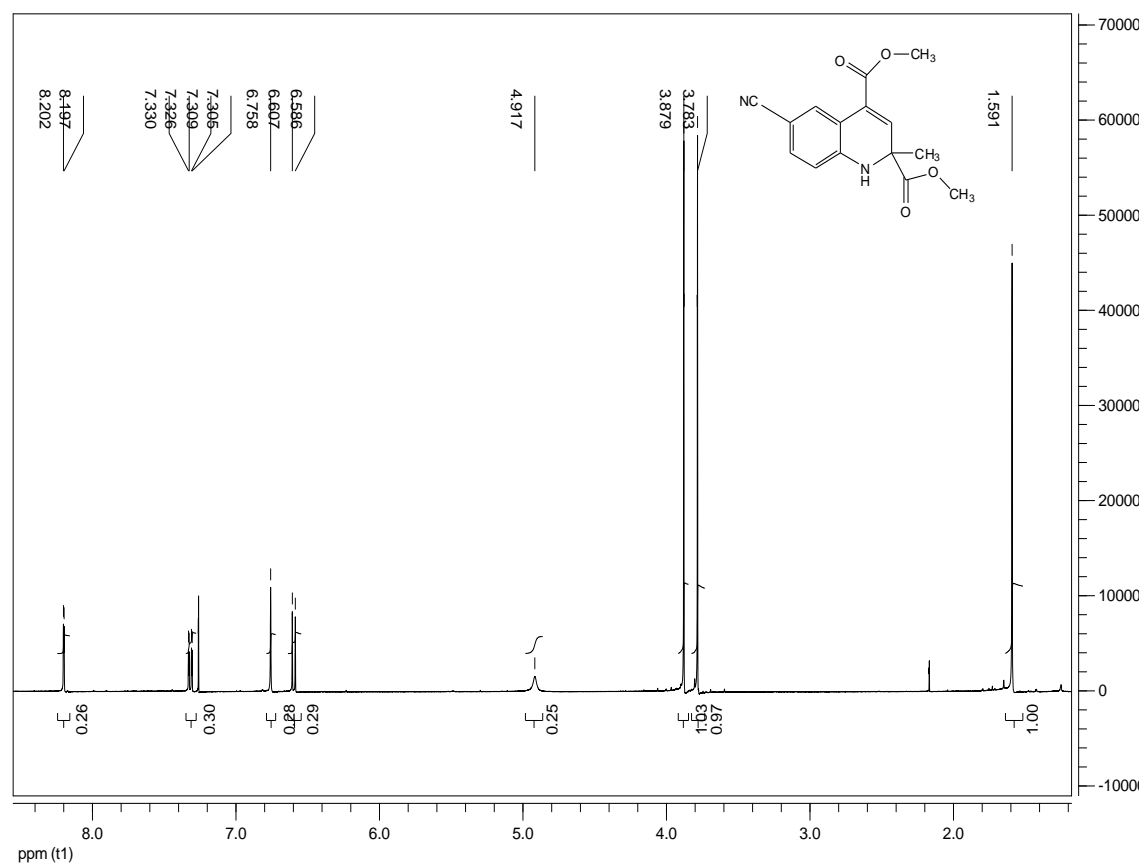


Figure S13. NMR Spectrum of compound **3m**.

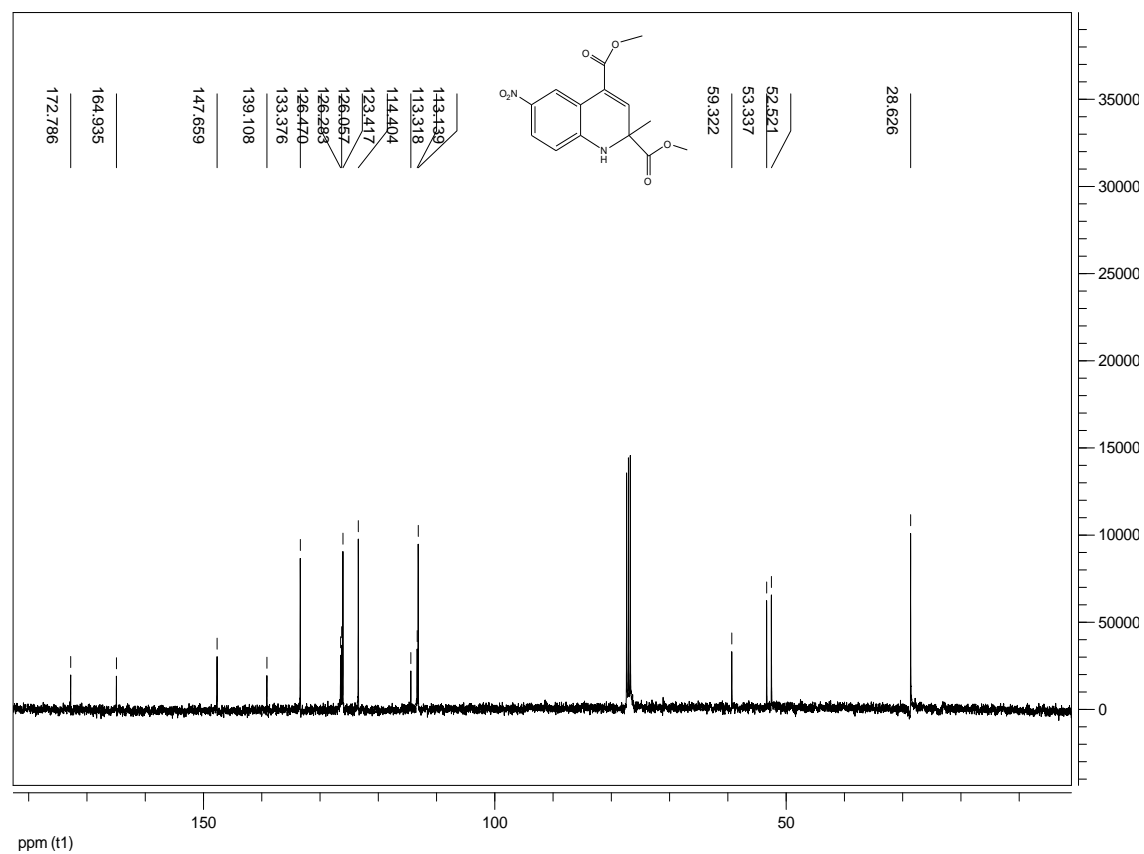
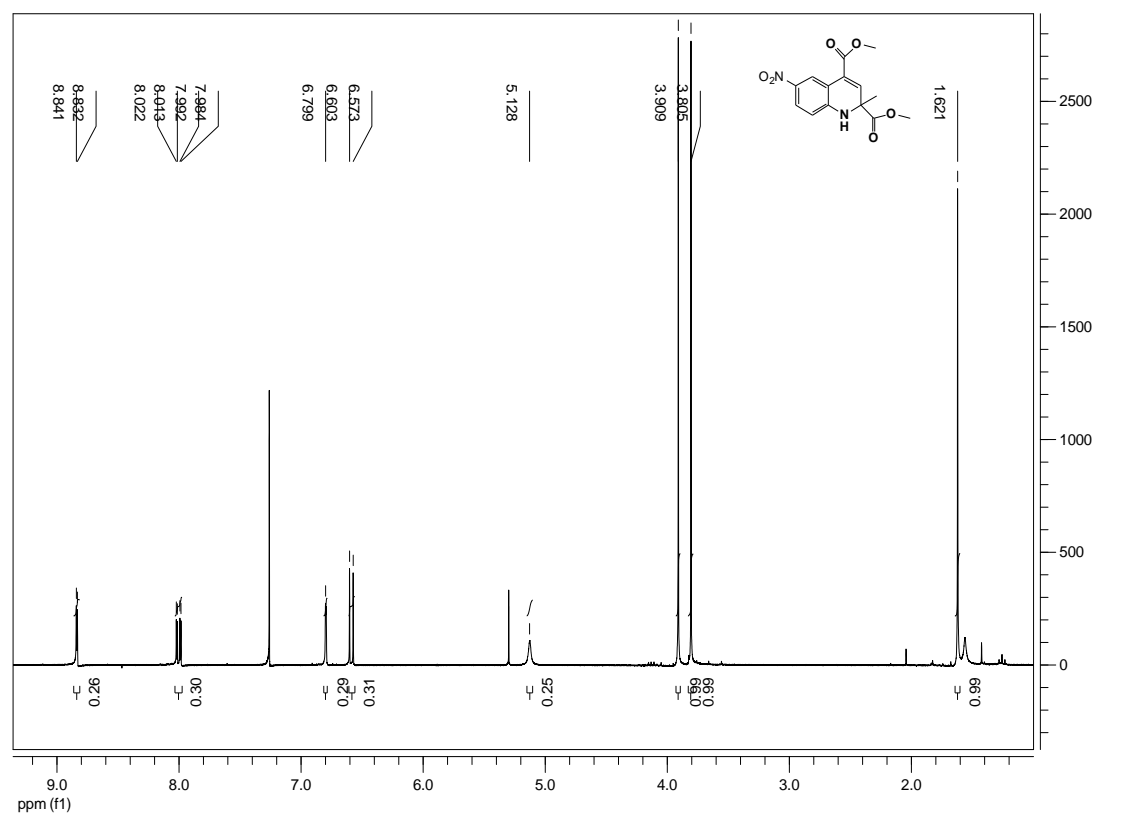


Figure S14. NMR Spectrum of compound 3n.

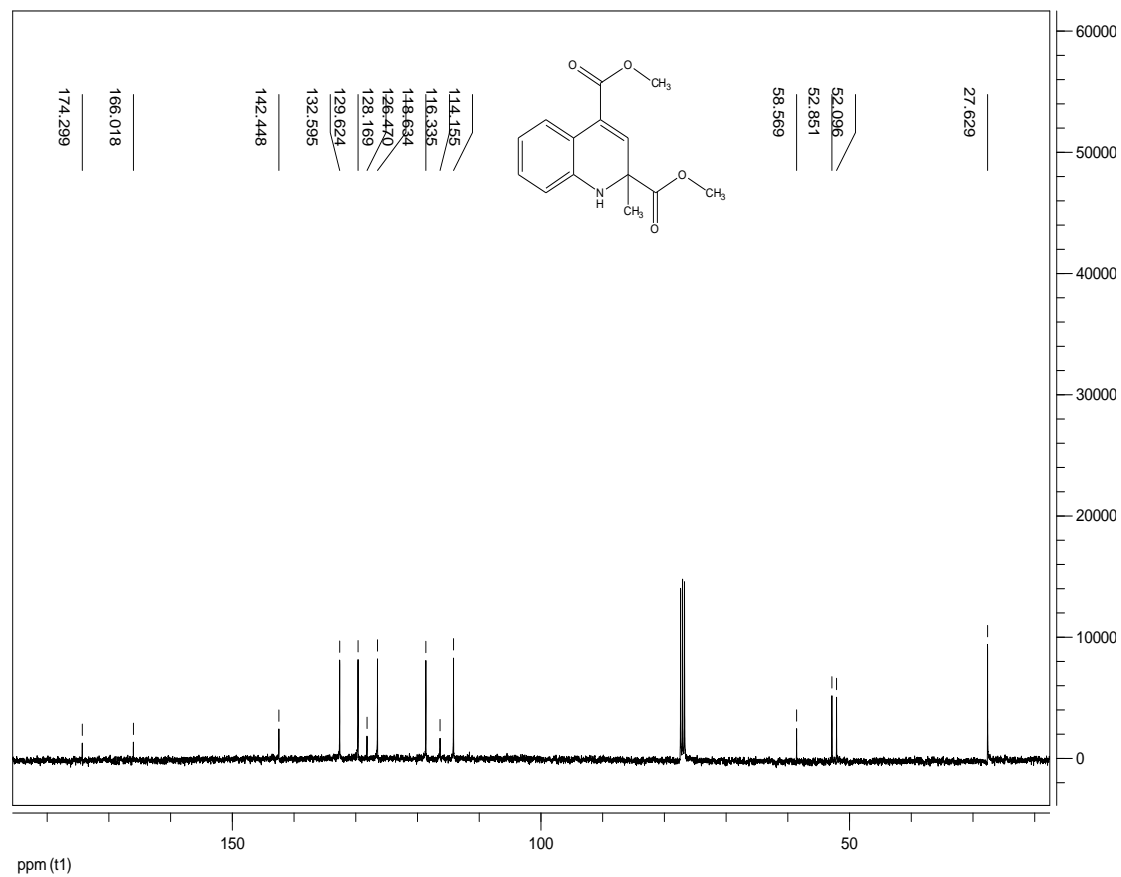
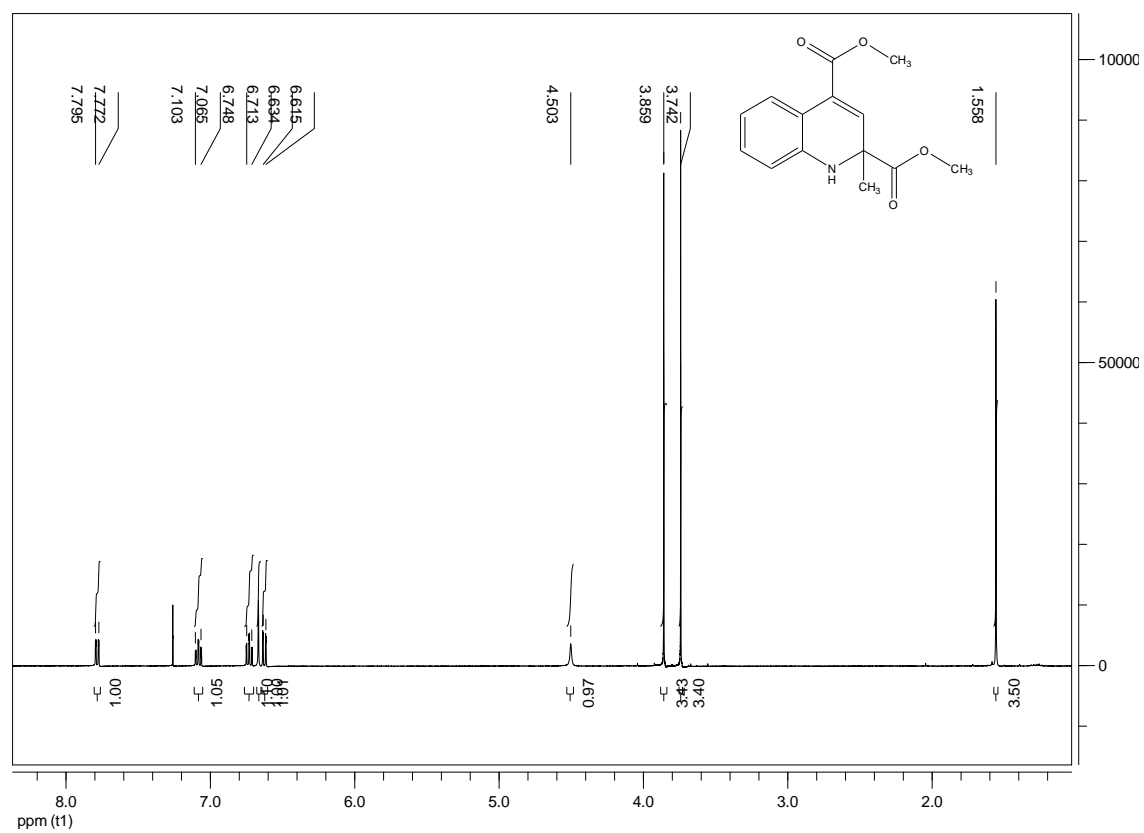


Figure S15. NMR Spectrum of compound 30.

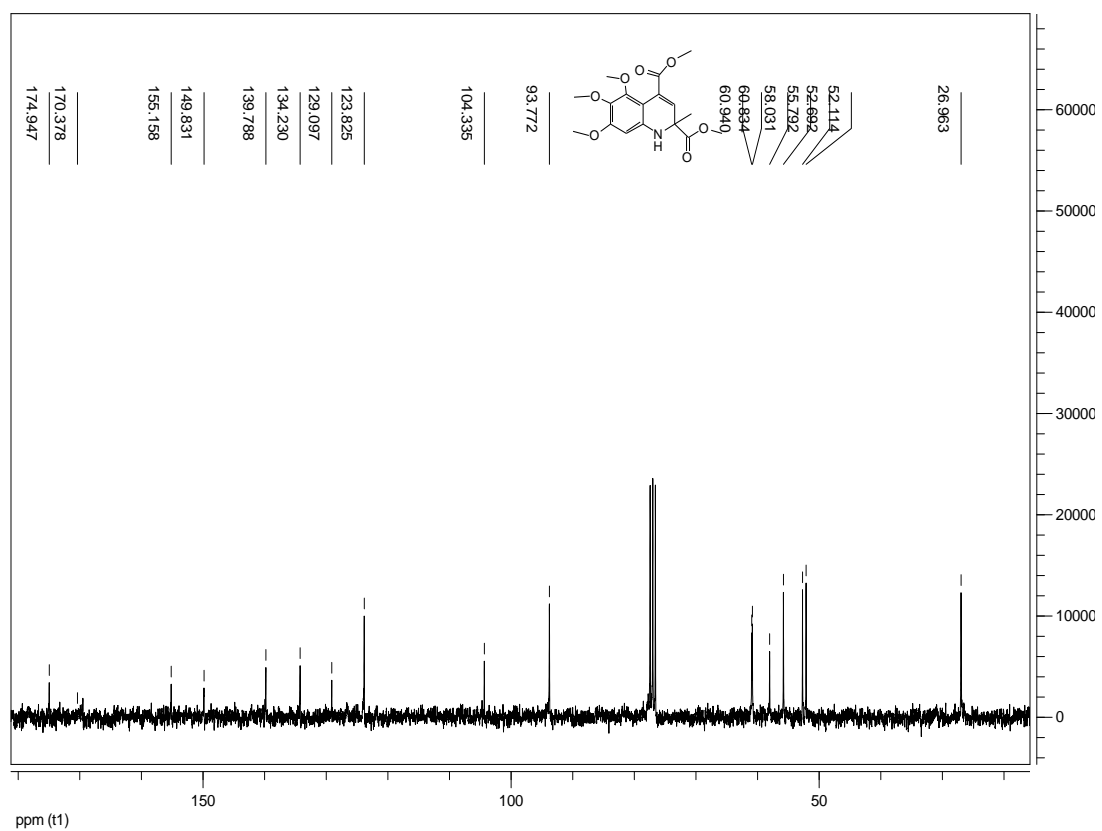
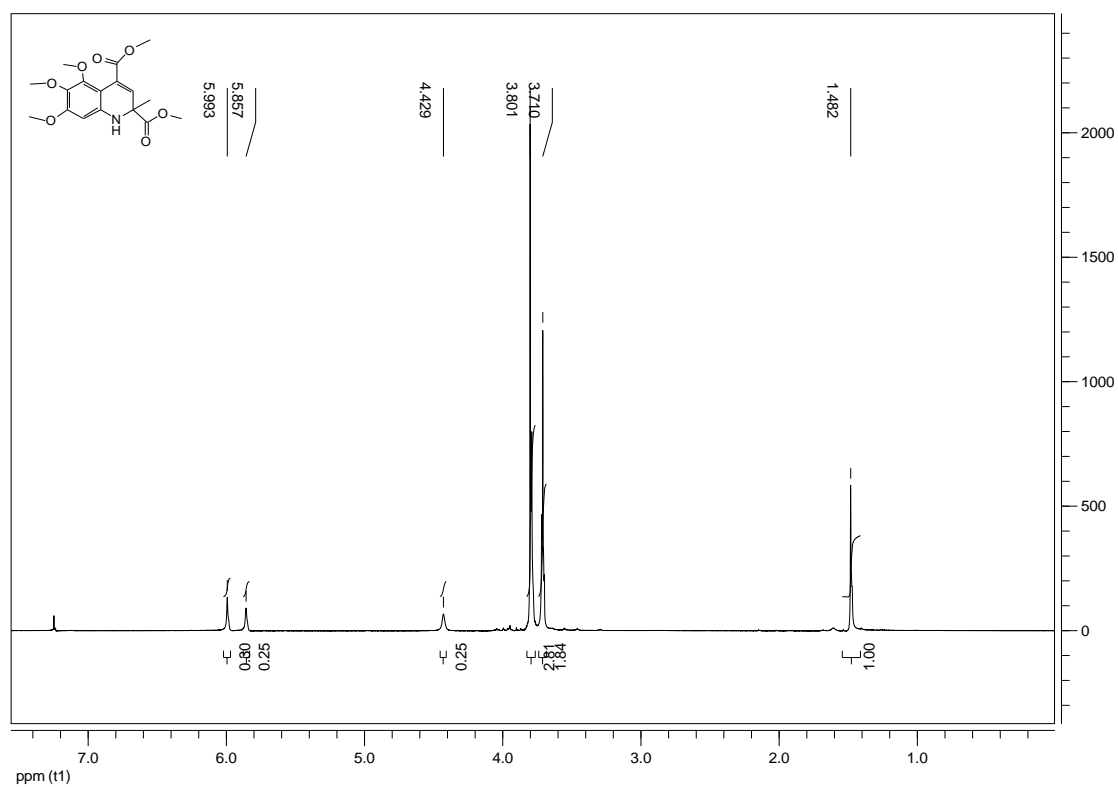


Figure S16. NMR Spectrum of compound **3p**.

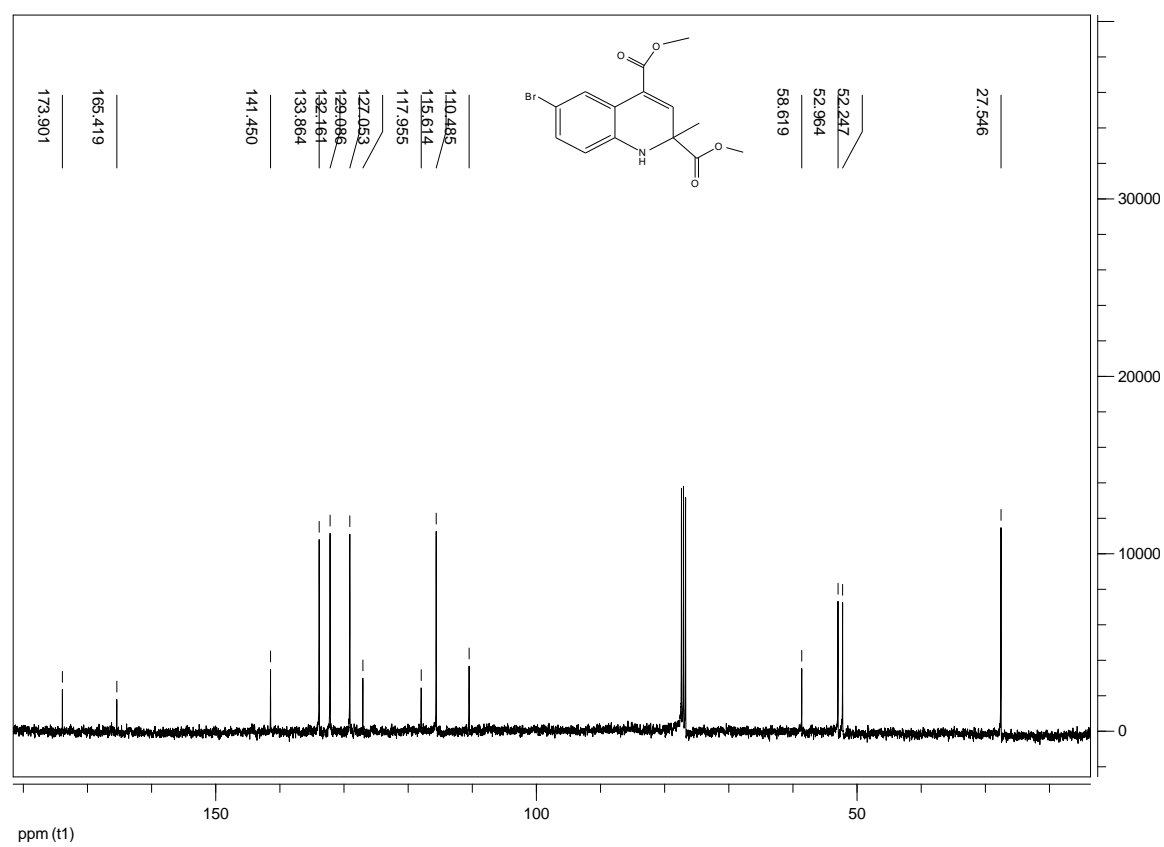
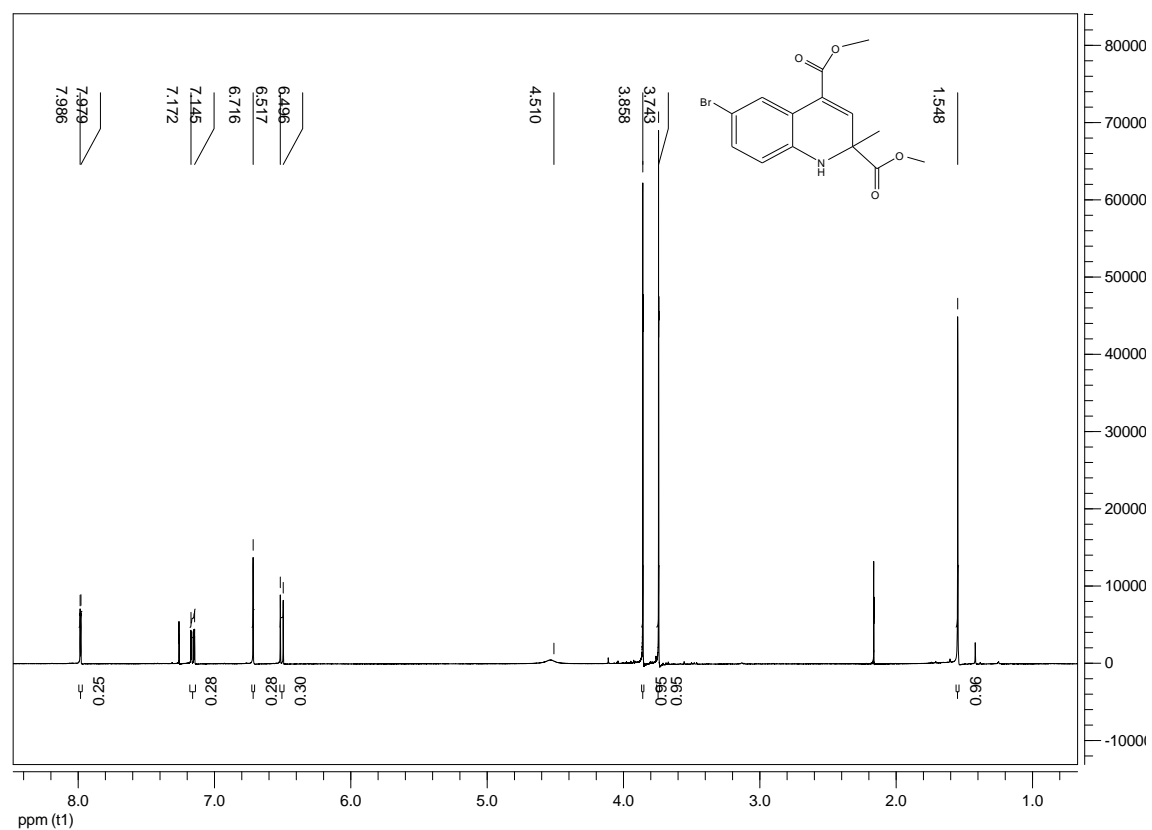


Figure S17. NMR Spectrum of compound **3q**.

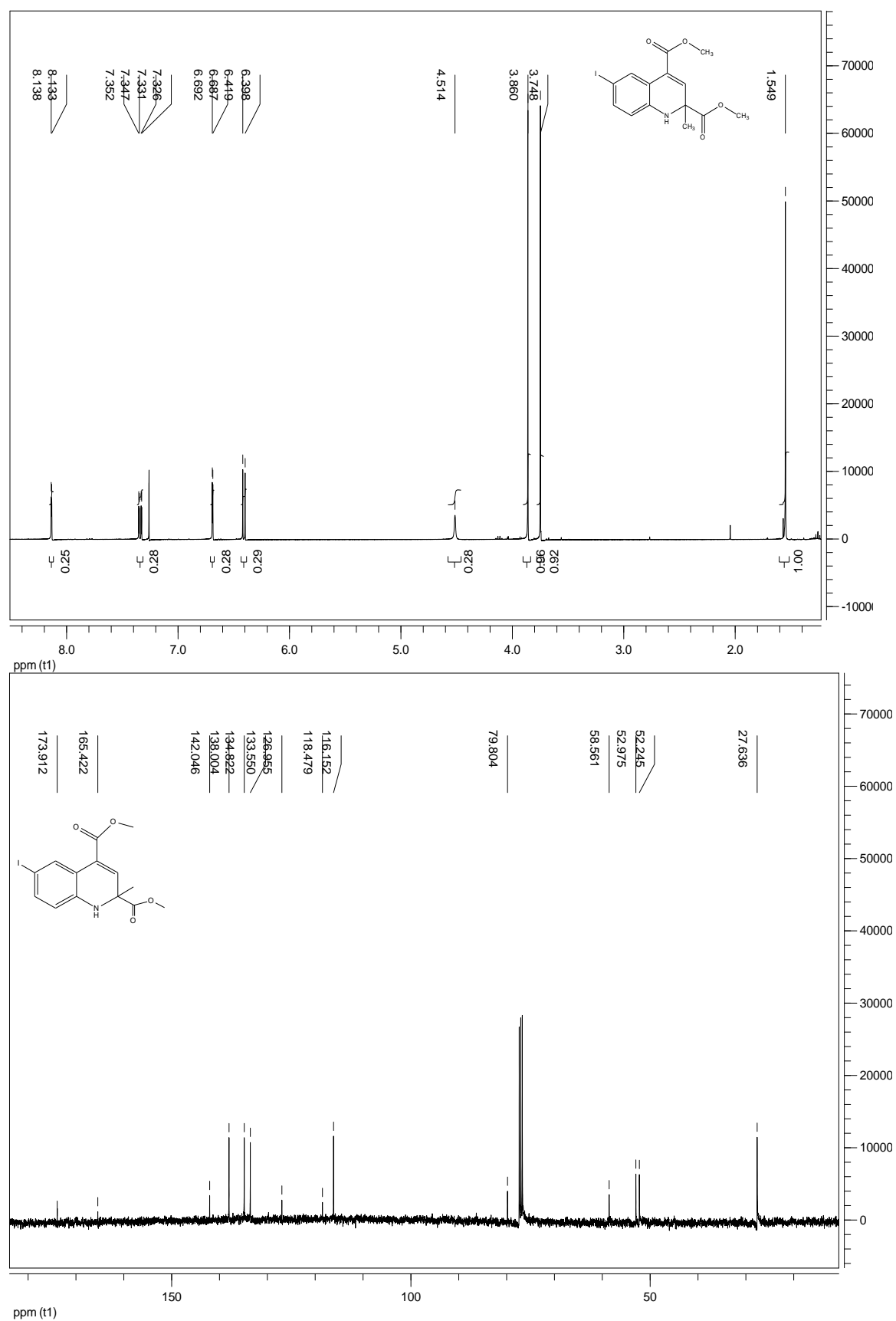


Figure S18. NMR Spectrum of compound 3r.

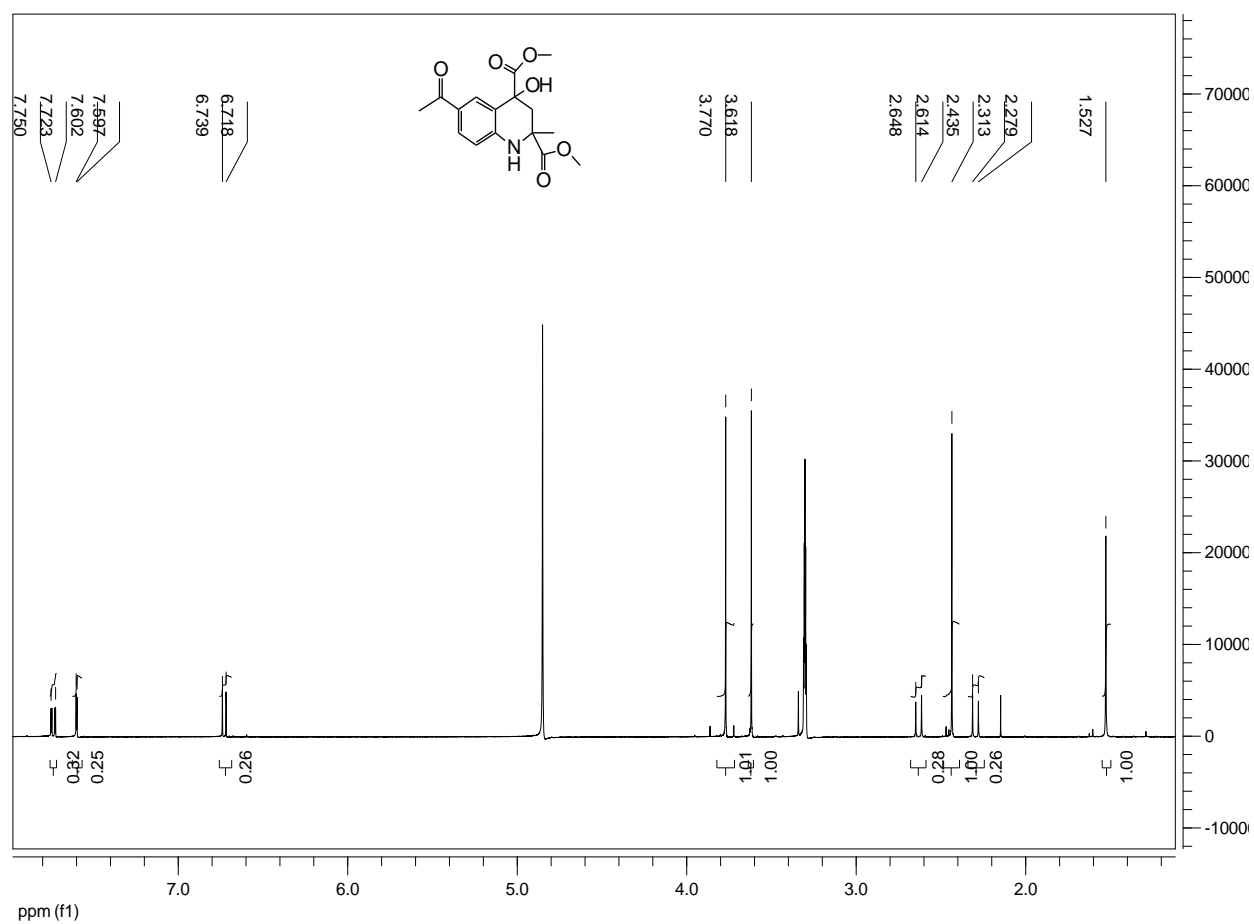


Figure S19. NMR Spectrum of compound 4.

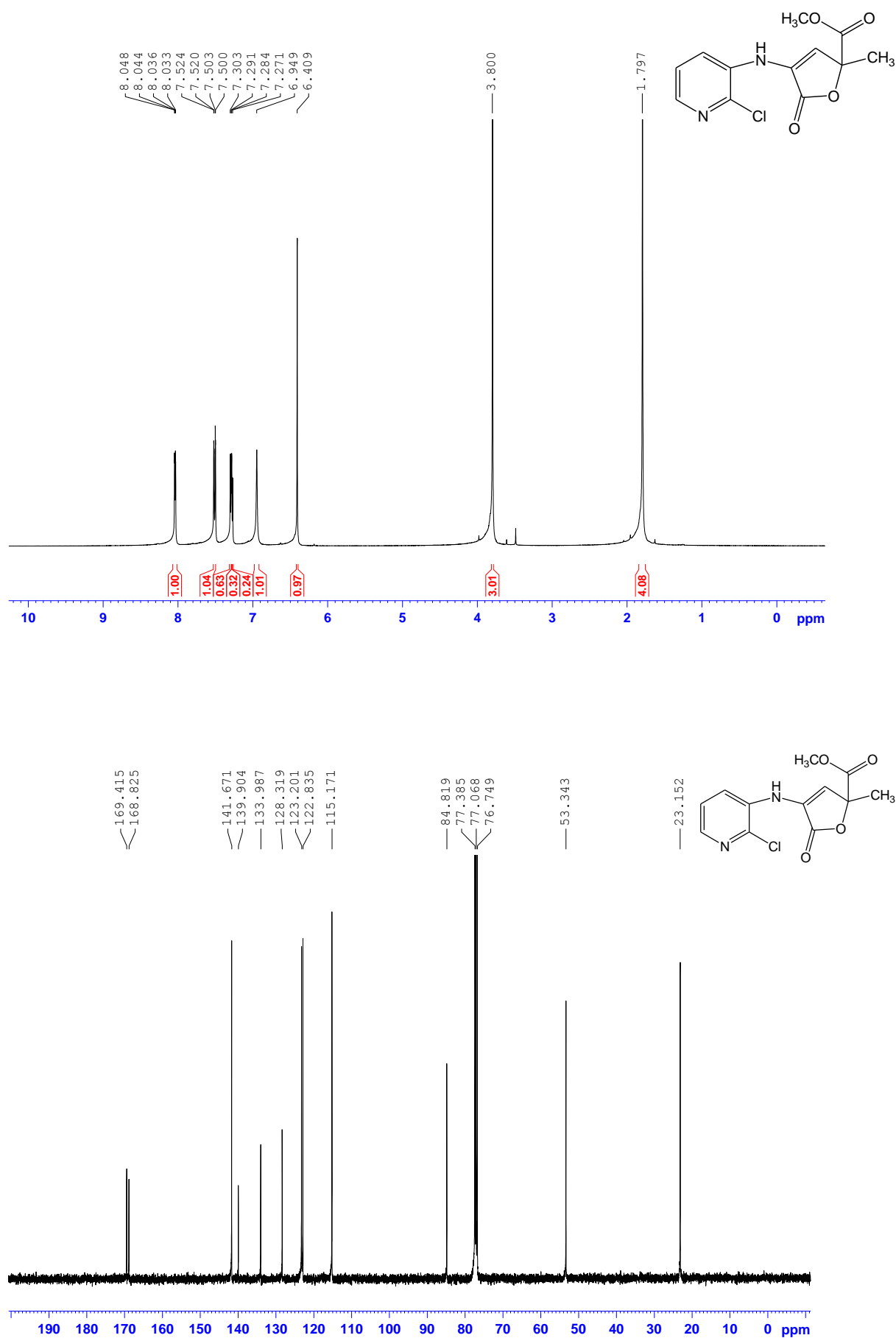


Figure S20. NMR Spectrum of compound 9.