Solid-state synthesis of polyfunctionalized 2-pyridones and conjugated dienes

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Supplementary Information

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Experimental Part

General Information

All materials were purchased from commercial suppliers and were used without further purification. All solvents were distilled before use. Solid state reactions were performed with silica gel 60 (0.063-0.200 mm, Merck) in Thermo Scientific™ Reacti-Vials™ Small Glass Reaction Vials.[1] For gram-scale reactions PYREX® 11 mL Screw Cap Culture Tubes with Phenolic Caps, 16x100 mm were used.[2] Silica gel containing 15% of Cs_2CO_3 was prepared by mixing silica gel (4.25 g) with powdered Cs_2CO_3 (0.75 g) in boiling EtOH (20 mL). After 10 min stirring, the solvent was evaporated under reduced pressure and the residue was heated in a laboratory drier at 120 °C for 2 h. Silica gel containing 1% of H_2SO_4 was obtained by mixing silica gel (9.9 g) with conc. H_2SO_4 (54 μL, 0.1 g) and acetone (10 mL). The suspension was stirred overnight in a closed round-bottom flask, at room temperature. Then, acetone was evaporated under reduced pressure and the residue was heated in a laboratory drier at 120 °C for 2 h. Both solid phases were stored in a dessicator over anh. $CaCl_2$. Course of reactions was monitored by thin layer chromatography (TLC) which was performed on precoated silica gel 60 F_{254} (Merck). TLC spots were visualized by UV light and iodine vapour. Preparative TLC was carried out on TLC plates 20×20 cm, with 0.5 mm layer of silica gel 60 GF254 (Merck). The quoted reaction temperatures refer to the temperature of a laboratory drier, or room temperature (rt). Melting points were determined on Stuart SMP10 apparatus. IR spectra were recorded on Thermo Scientific Nicolet 6700 FT-IR spectrometer using ATR technique. NMR spectra were recorded in $CDCl_3$ and DMSO-d_6 on Bruker Avance III spectrometer, operating at 500.3 MHz for ^{1}H and 125.8 MHz for ^{13}C, or on Bruker Ascend 400 spectrometer, operating at 400.1 MHz for ^{1}H and 100.6 MHz for ^{13}C. Chemical shifts are given as δ values in ppm and are referenced to tetramethylsilane (TMS) proton signal ($\delta = 0$ ppm) for ^{1}H NMR spectra and to the solvent carbon resonance ($\delta = 77.0$ ppm $CDCl_3$, $\delta = 39.5$ ppm DMSO-d_6) for ^{13}C NMR spectra. Coupling constants J are given in Hz. HRMS was recorded for new compounds on Orbitrap Exploris 240 mass spectrometer.

General Procedure for Solid-State Reactions

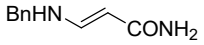
Reactants were dissolved in a small volume of DCM and mixed with silica gel. The solvent was evaporated and the solid residue was transferred to the reaction vial. After completion of the reaction, monitored by TLC, crude mixture was exctracted with ethyl acetate and purified by preparative TLC using toulene:ethyl acetate (T:EA) as eluent, unless otherwise stated. Other details are provided in experimental procedures that follow.

Isolation of amines 1i and 1l from commercially available hydrochlorides

Amines **1i** and **1l** are commercially available as hydrochlorides, which were neutralized with K_2CO_3 (2 equiv.) in MeCN in the presence of 1 mole of **2a**. After filtration, another mole of **2a** and SiO_2 were added and solvent was evaporated.

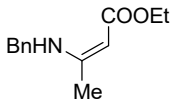
Synthesis of enamino amide 3d and enamino esters 3e,f

(*E*) 3-(benzylamino)acrylamide (**3d**)



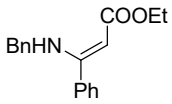
A solution of **1e** (42.0 mg, 0.39 mmol) and **2d** (28.1 mg, 0.40 mmol) in EtOH (2.0 mL) was heated under reflux for 3 h yielding **3d** (68.0 mg, 100%) as a pale yellow solid, mp 105-106 °C, containing a mixture of isomers, *Z/E* 4:1; compound is unstable and should be used after preparation; IR (ATR, mixture of isomers): 3464, 3325, 3203, 1651, 1573, 1495, 1306, 1233 cm^{-1}; ^1H NMR (500.3 MHz, DMSO-d_6): 7.34 (t, 2H, J = 7.0 Hz), 7.24-7.29 (m, 4H), 6.89 (m, 1H), 4.68 (d, 1H, J = 13.5 Hz), 4.12 (d, 2H, J = 6.0 Hz); $^{13}C\{^1H\}$ NMR (125.8 MHz, DMSO-d_6): *Z* isomer, 169.9, 146.2, 138.8, 128.4, 127.2, 126.9, 88.4, 47.4; HRMS (HESI) m/z: $[M+Na]^+$ Calcd. for $C_{10}H_{12}N_2NaO$ 199.08418; Found 199.08446.

(*Z*) ethyl 3-(benzylamino)but-2-enoate (**3e**)[3]



From **1e** (60.0 mg, 0.56 mmol) and **2e** (62.8 mg, 0.56 mmol) on silica gel (500.0 mg). Reaction temperature: 60 °C; reaction time: 3 h; eluent: toluene; white amorphous substance; 64.5 mg, 52% yield; Alternatively, **1e** (60.0 mg, 0.56 mmol) and **2e** (62.8 mg, 0.56 mmol) were dissolved in DMSO (0.3 mL) and stirred at rt for 3 days. Reaction mixture was directly applied to a silica gel plate and purified as described above giving **3e** (86.83 mg; 70%); IR (ATR): 3292, 1651, 1608, 1289, 1236, 1172; ^1H NMR (500.3 MHz, $CDCl_3$): 8.95 (broad s, 1H), 7.34 (t, 2H, J = 7.5 Hz), 7.25-7.27 (m, 3H), 4.53 (s, 1H), 4.43 (d, 2H, J = 6.5 Hz), 4.10 (q, 2H, J = 7.0 Hz), 1.91 (s, 3H), 1.25 (t, 3H, J = 7.0 Hz); $^{13}C\{^1H\}$ NMR (125.8 MHz, $CDCl_3$): 170.6, 161.8, 138.7, 128.8, 127.3, 126.7, 83.2, 58.4, 46.8, 19.4, 14.6.

(*Z*) ethyl 3-(benzylamino)-3-phenylacrylate (**3f**)[4]

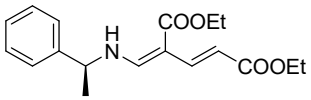


From **1e** (60.0 mg, 0.56 mmol) and **2f** (97.6 mg, 0.56 mmol) on silica gel (500.0 mg). Reaction temperature: 60 °C; reaction time: 3 h; eluent: toluene; white crystals; mp 70-72 °C; 55.0 mg, 35% yield; Alternatively, **1e** (60.0 mg, 0.56 mmol) and **2f** (97.6 mg, 0.56 mmol) were dissolved in DMSO (0.3 mL) and stirred at rt for 3 days. Reaction mixture was directly applied to a silica gel plate and purified as described above giving **3f** (119.7.0 mg; 76%); IR (ATR): 3285, 1652, 1612, 1595, 1302, 1173, 1143 cm^{-1}; ^{1}H NMR (500.3 MHz, $CDCl_3$): 8.90 (broad s, 1H), 7.32-7.38 (m, 5H), 7.29 (t, 2H, *J* = 7.0 Hz), 7.22 (t, 1H, *J* = 7.0 Hz), 7.17 (d, 1H, *J* = 7.0 Hz), 4.67 (s, 1H), 4.26 (d, 2H, *J* = 6.5 Hz), 4.15 (q, 2H, *J* = 7.0 Hz), Hz), 1.27 (t, 3H, *J* = 7.0 Hz); $^{13}C\{^{1}H\}$ NMR (125.8 MHz, $CDCl_3$): 170.4, 164.7, 139.2, 135.9, 129.2, 128.6, 128.3, 127.9, 127.2, 126.8, 86.2, 58.8, 48.3, 14.6.

Synthesis of dienes 4

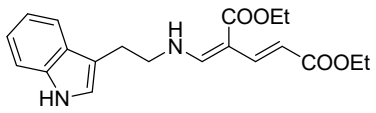
Dienes **4a-e**, **4g** and **4m-r** were synthesized as described previuosly.[5]

(*2E,4Z*)-diethyl 4-((((*S*)-1-phenylethyl)amino)methylene)pent-2-enedioate (**4f**)



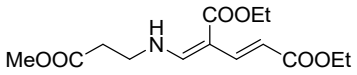
From **1f** (50.3 mg, 0.41 mmol) and **2a** (80.5 mg, 0.82 mmol) on silica gel (350.0 mg). Reaction temperature: 60 °C; reaction time: 3 h; eluent: T:EA 9:1 v/v; colourless oil; 89.4 mg, 69 % yield; IR (ATR): 3279, 1697, 1661, 1597, 1274, 1225, 1157 cm^{-1}; ^{1}H NMR (500.3 MHz, $CDCl_3$): 9.25 (dd, 1H, *J* = 6.0, 13.5 Hz), 7.28-7.38 (m, 4H), 7.26 (d, 2H, *J* = 7.0 Hz), 7.21 (d, 1H, *J* = 13.5 Hz), 6.01 (d, 1H, *J* = 16.0 Hz), 4.53 (quintet, 1H, *J* = 6.5 Hz), 4.26 (q, 2H, *J* = 7.0 Hz), 4.17 (q, 2H, *J* = 7.0 Hz), 1.60 (d, 3H, *J* = 7.0 Hz), 1.36 (t, 3H, *J* = 7.0 Hz), 1.27 (t, 3H, *J* = 7.0 Hz); $^{13}C\{^{1}H\}$ NMR (125.8 MHz, $CDCl_3$): 169.1, 168.8, 155.6, 143.2, 142.2, 129.0, 127.9, 126.0, 108.2, 95.2, 59.5, 57.9, 23.2, 14.4; HRMS (HESI) m/z: $[M+Na]^+$ Calcd. for $C_{18}H_{23}NNaO_4$ 340.15193; Found 340.15069.

Diethyl (*2E,4Z*)-4-(((2-(1*H*-indol-2-yl)ethyl)amino)methylene)pent-2-enedioate (**4h**)[6]



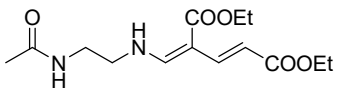
From **1h** (200.0 mg, 1.24 mmol) and **2a** (269.0 mg, 2.75 mmol) on silica gel (938.0 mg). Reaction temperature: 60 °C; reaction time: 3 h; T:EA 6:4 v/v; white solid; mp 99-100 °C; 306.0 mg, 68% yield; IR (ATR): 3320, 1660, 1594, 1296, 1232, 1112 cm^{-1}; ^1H NMR (400.1 MHz, $CDCl_3$): 8.97 (t, 1H, *J* = 6.4 Hz), 8.17 (s, 1H), 7.55 (d, 1H, *J* = 8.0 Hz), 7.38 (d, 1H, *J* = 8.0 Hz), 7.30 (d, 1H, *J* = 15.6 Hz), 7.22 (t, 1H, *J* = 7.2 Hz), 7.14 (t, 1H, *J* = 7.2 Hz), 7.04 (d, 1H, *J* = 14.0 Hz), 7.02 (s, 1H), 5.93 (d, 1H, *J* = 15.6 Hz), 4.22 (q, 2H, *J* = 7.2 Hz), 4.17 (q, 2H, *J* = 7.2 Hz), 3.58 (q, 2H, *J* = 6.4 Hz), 3.04 (t, 2H, *J* = 6.4 Hz), 1.32 (t, 3H, *J* = 7.2 Hz), 1.28 (t, 3H, *J* = 7.2 Hz); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): 169.1, 169.0, 157.2, 143.4, 136.3, 126.8, 122.5, 122.3, 119.6, 118.3, 111.5, 111.4, 107.5, 94.4, 59.8, 59.6, 49.8, 27.1, 14.5, 14.4.

Diethyl (*2E*,*4Z*)-4-(((3-methoxy-3-oxopropyl)amino)methylene)pent-2-enedioate (**4i**)



From **1i**×HCl (56.0 mg, 0.40 mmol), **2a** (39.7 mg, 0.40 mmol) and K_2CO_3 (110.2 mg, 0.80 mmol) in MeCN (2 mL). After stirring at 80 °C for 1 h and filtration, another mole of **2a** and SiO_2 (300.0 mg) were added, solvent was evaporated under reduced pressure and the reaction mixture was transferred to the reaction vial. Reaction temperature: 30 °C; reaction time: 15 h; T:EA 5:5 v/v; pale yellow solid; mp 64 °C; 50.1 mg, 42% yield (based on **1i**×HCl); IR (ATR): 3302, 1727, 1700, 1654, 1621, 1597, 1289, 1226, 1159 cm^{-1}; ^1H NMR (400.1 MHz, $CDCl_3$): 9.04 (broad t, 1H, *J* = 10.4 Hz), 7.37 (d, 1H, *J* = 15.6 Hz), 7.24 (d, 1H, *J* = 13.2 Hz), 6.04 (d, 1H, *J* = 15.6 Hz), 4.25 (q, 2H, *J* = 7.2 Hz), 4.18 (q, 2H, *J* = 7.2 Hz), 3.72 (s, 3H), 3.58 (q, 2H, *J* = 6.0 Hz), 2.62 (t, 2H, *J* = 6.0 Hz), 1.35 (t, 3H, *J* = 7.2 Hz), 1.29 (t, 3H, *J* = 7.2 Hz); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): 171.3, 168.9, 168.7, 157.0, 143.1, 108.2, 95.2, 59.8, 59.5, 52.0, 44.8, 35.1, 14.39, 14.36; HRMS (HESI) m/z: $[M+Na]^+$ Calcd. for $C_{14}H_{21}NNaO_6$ 322.12611; Found 322.12475.

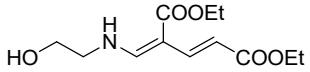
Diethyl (*2E,4Z*)-4-(((2-acetamidoethyl)amino)methylene)pent-2-enedioate (**4j**)



From **1j**[7] (51.0 mg, 0.50 mmol) and **2a** (98.0 mg, 1.00 mmol) on silica gel (298.0 mg). Reaction temperature: 50 °C; reaction time: 8 h; EA:MeOH 9:1 v/v; pale yellow solid; mp 95-96 °C; 53.0 mg, 36% yield; IR (ATR): 3294, 1670, 1618, 1583, 1226, 1178 cm^{-1}; ^1H NMR (400.1 MHz,

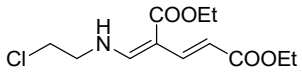
$CDCl_3$): 8.92 (broad t, 1H, *J* = 6.8 Hz), 7.35 (d, 1H, *J* = 15.8 Hz), 7.18 (d, 1H, *J* = 13.2 Hz), 6.24 (broad s, 1H), 6.02 (d, 1H, *J* = 15.8 Hz), 4.25 (q, 2H, *J* = 7.2 Hz), 4.18 (q, 2H, *J* = 7.2 Hz), 3.43 (m, 4H), 2.00 (s, 3H), 1.35 (t, 3H, *J* = 7.2 Hz), 1.29 (t, 3H, *J* = 7.2 Hz); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): 170.8, 169.1, 168.8, 157.2, 143.0, 108.3, 95.3, 59.9, 59.7, 48.7, 40.4, 23.1, 14.4; HRMS (HESI) m/z: $[M+Na]^+$ Calcd. for $C_{14}H_{22}N_2NaO_5$ 321.14209; Found 321.14134.

Diethyl (*2E*,*4Z*)-4-(((2-hydroxyethyl)amino)methylene)pent-2-enedioate (**4k**)



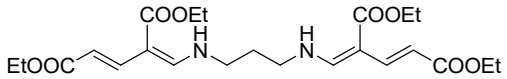
From **1k** (80.0 mg, 1.31 mmol) and **2a** (257.0 mg, 2.62 mmol) on silica gel (674.0 mg). Reaction temperature: 50 °C; reaction time: 3.5 h; T:EA 3:7 v/v; pale yellow solid; mp 103-104 °C; 150.0 mg, 44% yield; IR (ATR): 3440, 3300, 1663, 1596, 1287, 1226, 1182 cm^{-1}; ^1H NMR (400.1 MHz, $CDCl_3$): 9.02 (s, 1H), 7.39 (d, 1H, *J* = 15.6 Hz), 7.26 (d, 1H, *J* = 13.6 Hz), 6.04 (d, 1H, *J* = 15.6 Hz), 4.26 (q, 2H, *J* = 7.2 Hz), 4.19 (q, 2H, *J* = 7.2 Hz), 3.78 (q, 2H, *J* = 5.6 Hz), 3.44 (q, 2H, *J* = 5.6 Hz), 1.80 (t, 1H, *J* = 5.6 Hz), 1.36 (t, 3H, *J* = 7.2 Hz), 1.29 (t, 3H, *J* = 7.2 Hz); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): 169.3, 168.9, 157.6, 143.2, 108.3, 95.2, 62.1, 59.9, 59.7, 51.2, 14.5; HRMS (HESI) m/z: $[M+Na]^+$ Calcd. for $C_{12}H_{19}NNaO_5$ 280.11554; Found 280.11639.

Diethyl (*2E,4Z*)-4-(((2-chloroethyl)amino)methylene)pent-2-enedioate (**4l**)



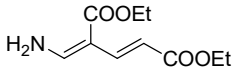
From **1l**×HCl (177.2 mg, 1.01 mmol), **2a** (100.1 mg, 1.01 mmol) and K_2CO_3 (278.8 mg, 2.02 mmol) in MeCN (2 mL). After stirring at rt for 6 h and filtration, another mole of **2a** and SiO_2 (700.0 mg) were added, solvent was evaporated under reduced pressure and the reaction mixture was transferred to the reaction vial. Reaction temperature: 60 °C; reaction time: 1.5 h; T:EA 9:1 v/v; pale yellow solid; mp 77-78 °C; 107.9 mg, 39% yield (based on **1l**×HCl); IR (ATR): 3311, 1680, 1649, 1603, 1374, 1271, 1218, 1143 cm^{-1}; ^1H NMR (400.1 MHz, $CDCl_3$): 9.12 (d, 1H, *J* = 13.2 Hz), 7.37 (d, 1H, *J* = 15.6 Hz), 7.22 (d, 1H, *J* = 13.2 Hz), 6.07 (d, 1H, *J* = 15.6 Hz), 4.27 (q, 2H, *J* = 7.2 Hz), 4.19 (q, 2H, *J* = 7.2 Hz), 3.63 (s, 4H) 1.36 (t, 3H, *J* = 7.2 Hz), 1.29 (t, 3H, *J* = 7.2 Hz); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): 169.1, 168.7, 156.8, 142.8, 109.1, 95.9, 60.0, 59.7, 50.7, 43.9, 14.43, 14.40; HRMS (HESI) m/z: $[M+Na]^+$ Calcd. for $C_{12}H_{18}ClNNaO_4$ 298.08166; Found 298.08166.

(*2E,2'E,4Z,4'Z*)-tetraethyl 4,4'-((propane-1,3-diylbis(azanediyl))bis(methanylylidene))bis(pent-2-enedioate) (**4s**)



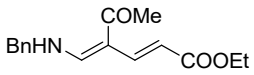
From **1s** (58.1 mg, 0.78 mmol) and **2a** (307.6 mg, 3.14 mmol) on silica gel (800.0 mg). Reaction temperature: 100 °C; reaction time: 4 h; not isolated, 29% yield (based on NMR integrals); ^{1}H NMR (500.3 MHz, $CDCl_3$): signals indicating a diene 9.01 (broad s, 2H), 7.45 (d, 2H, *J* = 15.5 Hz), 7.29 (d, 2H, *J* = 13.0 Hz), 6.13 (d, 2H, *J* = 15.5 Hz), 3.48 (q, 4H, *J* = 6.5 Hz), 2.00 (quintet, 2H, *J* = 6.5 Hz); ^{13}C{^{1}H} NMR (125.8 MHz, $CDCl_3$): signals indicating a diene 169.2, 168.6, 156.5, 142.7, 108.6, 95.5, 59.9, 59.6, 46.0, 31.7, 14.44, 14.38.

Diethyl (*2E,4Z*)-4-(aminomethylene)pent-2-enedioate (**4t**)



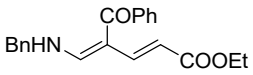
From **1t** (79.0 mg, 0.92 mmol, as a 20% aq. solution) and **2a** (181.2 mg, 1.85 mmol) on silica gel (500.0 mg). Reaction temperature: 60 °C; reaction time: 1.5 h; T:EA 5:5 v/v; white solid; mp 104-105 °C; 40.2 mg, 20% yield; IR (ATR): 3412, 3319, 1667, 1603, 1214, 1163 cm^{-1}; ^{1}H NMR (400.1 MHz, $CDCl_3$): 8.44 (broad s, 1H), 7.35 (d, 1H, *J* = 16.0 Hz), 7.33 (t, 1H, *J* = 11.6 Hz), 6.10 (d, 1H, *J* = 16.0 Hz), 5.69 (broad s, 1H), 4.27 (q, 2H, *J* = 7.2 Hz), 4.19 (q, 2H, *J* = 7.2 Hz), 1.36 (t, 3H, *J* = 7.2 Hz), 1.29 (t, 3H, *J* = 7.2 Hz); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): 168.9, 168.7, 154.5, 143.3, 109.6, 97.1, 59.9, 59.8, 14.42, 14.40; HRMS (HESI) m/z: $[M+Na]^+$ Calcd. for $C_{10}H_{15}NNaO_4$ 236.08933; Found 236.09001.

(*2E,4Z*)-ethyl 4-((benzylamino)methylene)-5-oxohex-2-enoate (**4u**)



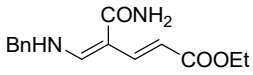
From **3b** (55.8 mg, 0.32 mmol), obtained by mixing **1e** and **2b**, and **2a** (31.5 mg, 0.32 mmol) on silica gel (250.0 mg). Reaction temperature: 60 °C; reaction time: 1.5 h; T:EA 7:3 v/v; yellow oil; 16.1 mg, 18% yield; IR (ATR): 3195, 1697, 1644, 1599, 1223, 1170 cm^{-1}; ^{1}H NMR (400.1 MHz, $CDCl_3$): 11.15 (broad s, 1H), 7.69 (d, 1H, *J* = 15.6 Hz), 7.46 (d, 1H, *J* = 12.8 Hz), 7.32-7.39 (m, 3H), 7.24 (d, 2H, *J* = 7.2 Hz), 5.66 (d, 1H, *J* = 15.6 Hz), 4.50 (d, 2H, *J* = 6.0 Hz), 4.20 (q, 2H, *J* = 7.2 Hz), 2.32 (s, 3H), 1.29 (t, 3H, *J* = 7.2 Hz); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): 197.4, 167.9, 154.2, 143.5, 136.2, 129.0, 128.2, 127.3, 106.3, 104.5, 59.8, 53.4, 27.9, 14.4; HRMS (HESI) m/z: $[M+Na]^+$ Calcd. for $C_{16}H_{19}NNaO_3$ 296.12571; Found 296.12538.

(*2E,4Z*)-ethyl 4-benzoyl-5-(benzylamino)penta-2,4-dienoate (**4v**)



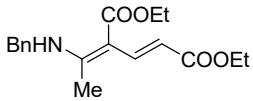
From **3c** (73.5 mg, 0.31 mmol), obtained by mixing **1e** and **2c**, and **2a** (30.5 mg, 0.31 mmol) on silica gel (250.0 mg). Reaction temperature: 80 °C; reaction time: 4 h; T:EA 8:2 v/v; pale yellow solid; mp 128-130 °C; 27.3 mg, 26% yield; IR (ATR): 3208, 1692, 1632, 1600, 1273, 1239, 1165 cm^{-1}; ^1H NMR (500.3 MHz, $CDCl_3$): 11.33 (broad s, 1H), 7.66 (d, 1H, *J* = 13.0 Hz), 7.61 (d, 1H, *J* = 15.5 Hz), 7.48-7.50 (m, 2H), 7.39-7.45 (m, 5H), 7.35 (t, 1H, *J* = 7.0 Hz), 7.30 (d, 2H, *J* = 7.0 Hz), 5.60 (d, 1H, *J* = 15.5 Hz), 4.58 (d, 2H, *J* = 6.0 Hz), 4.13 (q, 2H, *J* = 7.0 Hz), 1.23 (t, 3H, *J* = 7.0 Hz); $^{13}C\{^1H\}$ NMR (125.8 MHz, $CDCl_3$): 195.1, 167.7, 155.6, 144.8, 140.1, 136.0, 130.5, 129.1, 128.4, 128.2, 128.0, 127.5, 106.4, 103.7, 59.8, 53.6, 14.4; HRMS (HESI) m/z: $[M+Na]^+$ Calcd. for $C_{21}H_{21}NNaO_3$ 358.14136; Found 358.14040.

Ethyl (*2E,4Z*)-5-(benzylamino)-4-carbamoylpenta-2,4-dienoate (**4w**)



From **3d** (43.0 mg, 0.44 mmol) and **2a** (43.2 mg, 0.44 mmol) in EtOH (2 mL). Reaction temperature: reflux; reaction time: 2 h; EA; light brown solid; mp 144-146 °C; 23.3 mg, 19% yield; IR (ATR): 3403, 3185, 1734, 1687, 1646, 1599, 1266, 1175 cm^{-1}; ^1H NMR (400.1 MHz, $CDCl_3$): 9.71 (broad s, 1H), 7.23-7.39 (m, 5H), 7.18 (d, 1H, *J* = 13.2 Hz), 5.70 (d, 1H, *J* = 15.6 Hz), 5.62 (broad s, 2H), 4.43 (d, 2H, *J* = 6.0 Hz), 4.18 (q, 2H, *J* = 7.2 Hz), 1.28 (t, 3H, *J* = 7.2 Hz); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): 171.1, 168.2, 155.5, 144.0, 137.0, 128.9, 128.0, 127.2, 106.6, 96.7, 59.8, 52.8, 14.4; HRMS (HESI) m/z: $[M+Na]^+$ Calcd. for $C_{15}H_{18}N_2NaO_3$ 297.12096; Found 297.12201.

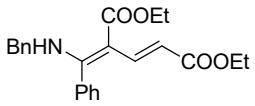
(*2E,4Z*)-diethyl 4-(1-(benzylamino)ethylidene)pent-2-enedioate (**4x**)



From **3e** (30.0 mg, 0.14 mmol) and **2a** (13.7 mg, 0.14 mmol) on silica gel (350.0 mg). Reaction temperature: rt; reaction time: 2.5 h; T:EA 9:1 v/v; yellow oil; 29.8 mg, 67% yield; IR (ATR): 3065, 1732, 1693, 1643, 1572, 1281, 1201, 1156 cm^{-1}; ^1H NMR (500.3 MHz, $CDCl_3$): 10.96 (broad s, 1H), 7.76 (d, 1H, *J* = 15.5 Hz), 7.36 (t, 2H, *J* = 7.5 Hz), 7.30 (t, 1H, *J* = 7.5 Hz), 7.25 (d, 2H, *J* = 7.5 Hz), 6.11 (d, 1H, *J* = 15.5 Hz), 4.56 (d, 2H, *J* = 6.0 Hz), 4.25 (q, 2H, *J* = 7.0 Hz), 4.19 (q, 2H, *J*

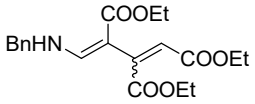
= 7.0 Hz), 2.25 (s, 3H), 1.36 (t, 3H, *J* = 7.0 Hz), 1.29 (t, 3H, *J* = 7.0 Hz); $^{13}C\{^{1}H\}$ NMR (125.8 MHz, $CDCl_3$): 170.5, 169.6, 166.5, 140.6, 137.1, 129.0, 127.8, 126.8, 110.6, 94.0, 59.8, 59.6, 47.8, 16.0, 14.5, 14.4; HRMS (HESI) m/z: $[M+Na]^+$ Calcd. for $C_{18}H_{23}NNaO_4$ 340.15193; Found 340.15121.

(*2E,4Z*)-diethyl 4-((benzylamino)(phenyl)methylene)pent-2-enedioate (**4y**)



From **3f** (30.0 mg, 0.11 mmol) and **2a** (10.8 mg, 0.11 mmol) on silica gel (350.0 mg). Reaction temperature: rt; reaction time: 21 h; T:EA 9:1 v/v; pale yellow solid; mp 89-91 °C; 30.0 mg, 72% yield; IR (ATR): 3180, 1697, 1645, 1608, 1560, 1289, 1267, 1152 cm^{-1}; ^{1}H NMR (400.1 MHz, $CDCl_3$): 10.71 (broad s, 1H), 7.46-7.47 (m, 3H), 7.25-7.32 (m, 3H), 7.17-7.19 (m, 2H), 7.11 (d, 2H, *J* = 7.6 Hz), 7.05 (d, 1H, *J* = 15.6 Hz), 6.05 (d, 1H, *J* = 15.6 Hz), 4.32 (q, 2H, *J* = 7.2 Hz), 4.15 (d, 2H, *J* = 6.0 Hz), 4.03 (q, 2H, *J* = 7.2 Hz), 1.40 (t, 3H, *J* = 7.2 Hz), 1.15 (t, 3H, *J* = 7.2 Hz); $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): 170.6, 169.2, 169.1, 142.4, 137.6, 133.2, 129.6, 129.0, 128.8, 128.0, 127.6, 127.0, 109.9, 95.4, 60.1, 59.3, 49.1, 14.5, 14.3; HRMS (HESI) m/z: $[M+Na]^+$ Calcd. for $C_{23}H_{25}NNaO_4$ 402.16758; Found 402.16583.

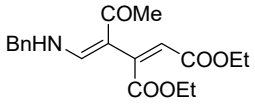
Triethyl (*1Z,3Z*)- and (*1E,3Z*) 4-(benzylamino)buta-1,3-diene-1,2,3-tricarboxylate (**4za**)



From **3a** (75.6 mg, 0.37 mmol), obtained by mixing **1e** and **2a**, and **2g** (62.6 mg, 0.37 mmol) on silica gel (300.0 mg). Reaction temperature: rt; reaction time: 1.5 h; T:EA 9:1 v/v; colourless oil; 84.2 mg, 61% yield (31% *1E,3Z* and 30% *1Z,3Z*); IR (ATR): *1Z,3Z* isomer, 3292, 1727, 1666, 1579, 1267, 1215, 1182, *1E,3Z* isomer, 3306, 1716, 1672, 1615, 1251, 1214, 1188 cm^{-1}; ^{1}H NMR (400.1 MHz, $CDCl_3$): *1Z,3Z* isomer, 9.20 (broad s, 1H), 7.30-7.39 (m, 3H), 7.24 (d, 2H, *J* = 7.6 Hz), 7.15 (d, 1H, *J* = 13.6 Hz), 6.01 (s, 1H), 4.44 (d, 2H, *J* = 6.0 Hz), 4.28 (q, 2H, *J* = 7.2 Hz), 4.13-4.22 (m, 4H), 1.25-1.34 (m, 9H), *1E,3Z* isomer, 8.80 (broad s, 1H), 7.26-7.38 (m, 5H), 7.16 (d, 1H, *J* = 13.2 Hz), 6.41 (s, 1H), 4.45 (d, 2H, *J* = 6.0 Hz), 4.22 (q, 2H, *J* = 7.2 Hz), 4.13 (q, 2H, *J* = 7.2 Hz), 4.09 (q, 2H, *J* = 7.2 Hz), 1.30 (t, 3H, *J* = 7.2 Hz), 1.25 (t, 3H, *J* = 7.2 Hz), 1.19 (t, 3H, *J* = 7.2 Hz); $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): *1Z,3Z* isomer, 169.0, 168.2, 165.9, 154.8, 146.9, 136.7, 128.9, 128.0, 127.3, 111.9, 94.4, 61.4, 60.2, 60.0, 53.0, 14.22, 14.17, 13.8, *1E,3Z* isomer, 168.6, 168.4,

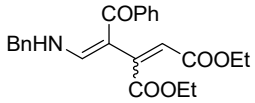
166.0, 155.8, 143.9, 137.5, 128.8, 127.8, 127.4, 121.5, 90.3, 61.5, 60.4, 59.4, 52.8, 14.22, 14.18, 14.1; HRMS (HESI) m/z: $[M+Na]^+$ Calcd. for $C_{20}H_{25}NNaO_6$ 398.15741; Found 398.15617.

Diethyl 2-((*Z*)-1-(benzylamino)-3-oxobut-1-en-2-yl)maleate (**4zb**)



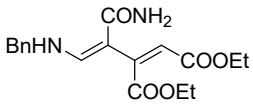
From **3b** (80.0 mg, 0.46 mmol), obtained by mixing **1e** and **2b**, and **2g** (78.3 mg, 0.46 mmol) on silica gel (500.0 mg). Reaction temperature: rt; reaction time: 48 h; T:EA 6:4 v/v; redish oil; 46.1 mg, 29% yield; IR (ATR): 1730, 1640, 1592, 1259, 1211, 1178 cm^{-1}; ^1H NMR (500.3 MHz, $CDCl_3$): 10.80 (broad s, 1H), 7.29-7.37 (m, 3H), 7.23 (d, 2H, J = 7.0 Hz), 7.08 (d, 1H, J = 13.0 Hz), 5.76 (s, 1H), 4.43 (d, 2H, J = 6.0 Hz), 4.29 (q, 2H, J = 7.0 Hz), 4.18 (q, 2H, J = 7.0 Hz), 2.22 (s, 3H), 1.31 (t, 3H, J = 7.0 Hz), 1.28 (t, 3H, J = 7.0 Hz); $^{13}C\{^1H\}$ NMR (125.8 MHz, $CDCl_3$): 196.3, 168.8, 165.2, 154.4, 147.4, 136.5, 128.9, 128.0, 127.2, 117.6, 105.1, 61.6, 60.5, 53.0, 28.6, 14.1, 13.8; HRMS (HESI) m/z: $[M+Na]^+$ Calcd. for $C_{19}H_{23}NNaO_5$ 368.14684; Found 368.14706.

Diethyl 2-((*Z*)-1-(benzylamino)-3-oxo-3-phenylprop-1-en-2-yl)maleate and diethyl 2-((Z)-1-(benzylamino)-3-oxo-3-phenylprop-1-en-2-yl)fumarate (**4zc**)



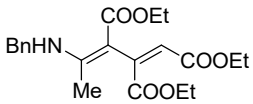
From **3c** (30.0 mg, 0.13 mmol), obtained by mixing **1e** and **2c**, and **2g** (22.1 mg, 0.13 mmol) on silica gel (350.0 mg). Reaction temperature: rt; reaction time: 22 h; T:EA 8:2 v/v; yellow solid; mp 100-102 °C; 31.2 mg, 59% yield; maleate/fumarate 1 : 0.8; IR (ATR): 3246, 1714, 1634, 1368, 1250, 1188 cm^{-1}; ^1H NMR (500.3 MHz, $CDCl_3$): maleate 10.69 (broad s, 1H), 7.58-7.59 (m, 2H), 7.26-7.41 (m, 9H), 5.49 (s, 1H), 4.50 (d, 2H, J = 6.0 Hz), 4.07 (q, 2H, J = 7.0 Hz), 4.02 (q, 2H, J = 7.0 Hz), 1.19 (t, 3H, J = 7.0 Hz), 1.15 (t, 3H, J = 7.0 Hz), fumarate 10.92 (broad s, 1H), 7.49-7.50 (m, 2H), 7.26-7.41 (m, 8H), 7.22 (d, 1H, J = 13.0 Hz), 6.49 (s, 1H), 4.52 (d, 2H, J = 6.0 Hz), 4.15 (q, 2H, J = 7.0 Hz), 3.81 (q, 2H, J = 7.0 Hz), 1.24 (t, 3H, J = 7.0 Hz), 0.98 (t, 3H, J = 7.0 Hz); $^{13}C\{^1H\}$ NMR (125.8 MHz, $CDCl_3$): 194.1, 193.1, 168.3, 167.6, 166.1, 165.3, 158.0, 155.6, 147.2, 145.5, 141.6, 140.2, 136.8, 136.3, 130.5, 130.1, 129.0, 128.8, 128.3, 128.2, 127.9, 127.8, 127.6, 127.5, 127.4, 122.5, 117.4, 104.3, 101.2, 61.6, 61.4, 60.6, 60.4, 53.2, 53.1, 14.1, 14.0, 13.7; HRMS (HESI) m/z: $[M+Na]^+$ Calcd. for $C_{24}H_{25}NNaO_5$ 430.16249; Found 430.16181.

Diethyl 2-((*Z*)-3-amino-1-(benzylamino)-3-oxoprop-1-en-2-yl)maleate (**4zd**)



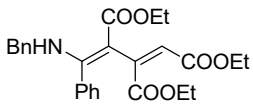
From **3d** (120.0 mg, 0.59 mmol) and **2g** (111.8 mg, 0.66 mmol) in MeCN (2 ml). Reaction temperature: reflux; reaction time: 1 h; EA:MeOH 9:1 v/v; yellow solid; mp 105-106 °C; 92.0 mg, 44% yield; IR (ATR): 3414, 3185, 1716, 1695, 1650, 1573, 1271, 1171 cm^{-1}; ^{1}H NMR (500.3 MHz, $CDCl_3$): 9.57 (broad s, 1H), 7.36 (t, 2H, *J* = 7.5 Hz), 7.30 (t, 1H, *J* = 7.5 Hz), 7.25 (t, 2H, *J* = 7.5 Hz), 6.96 (d, 1H, *J* = 13.0 Hz), 5.80 (s, 1H), 4.40 (d, 2H, *J* = 6.0 Hz), 4.32 (q, 2H, *J* = 7.0 Hz), 4.17 (q, 2H, *J* = 7.0 Hz), 1.32 (t, 3H, *J* = 7.0 Hz), 1.27 (t, 3H, *J* = 7.0 Hz); $^{13}C\{^{1}H\}$ NMR (125.8 MHz, $CDCl_3$): 170.3, 169.3, 165.3, 153.0, 148.4, 137.3, 128.8, 127.8, 127.2, 114.2, 95.6, 62.0, 64.0, 52.7, 14.2, 13.9; HRMS (HESI) m/z: $[M+Na]^+$ Calcd. for $C_{18}H_{22}N_2NaO_5$ 369.14209; Found 369.14120.

Triethyl (*1Z,3Z*)-4-(benzylamino)penta-1,3-diene-1,2,3-tricarboxylate (**4ze**)



From **3e** (30.0 mg, 0.14 mmol) and **2g** (23.8 mg, 0.14 mmol) on silica gel (350.0 mg). Reaction temperature: rt; reaction time: 3 h; T:EA 9:1 v/v; yellow oil; 32.2 mg, 59% yield; IR (ATR): 3259, 1720, 1653, 1597, 1244, 1096, 1035 cm^{-1}; ^{1}H NMR (400.1 MHz, $CDCl_3$): 9.95 (broad s, 1H), 7.25-7.37 (m, 5H), 6.77 (s, 1H), 4.50 (d, 2H, *J* = 6.4 Hz), 4.23 (q, 2H, *J* = 7.2 Hz), 4.14 (q, 2H, *J* = 7.2 Hz), 4.01-4.12 (2 × q, 2H, *J* = 7.2 Hz), 1.87 (s, 3H), 1.29 (t, 3H, *J* = 7.2 Hz), 1.24 (t, 3H, *J* = 7.2 Hz), 1.16 (t, 3H, *J* = 7.2 Hz); $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): 168.5, 168.2, 165.4, 161.9, 142.9, 138.2, 128.8, 127.4, 127.1, 126.8, 89.9, 61.4, 60.4, 59.0, 47.2, 16.4, 14.3, 14.2; HRMS (HESI) m/z: $[M+Na]^+$ Calcd. for $C_{21}H_{27}NNaO_6$ 412.17306; Found 412.17356.

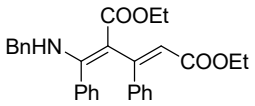
Triethyl (*3Z*)-4-(benzylamino)-4-phenylbuta-1,3-diene-1,2,3-tricarboxylate (**4zf)**



From **3f** (40.0 mg, 0.14 mmol) and **2g** (23.8 mg, 0.14 mmol) on silica gel (350.0 mg). Reaction temperature: rt; reaction time: 3 h; T:EA 9:1 v/v; yellow oil; 27.8 mg, 44% yield; the stereochemistry of the C1C2 double bond has not been unequivocally established; IR (ATR): 3424, 3306, 1720, 1656, 1608, 1589, 1573, 1248, 1164, 1131, 1037 cm^{-1}; ^{1}H NMR (400.1 MHz, $CDCl_3$):

9.79 (broad s, 1H), 7.15-7.37 (m, 10H), 6.34 (s, 1H), 4.02-4.15 (m, 8H), 1.15-1.24 (m, 9H); $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): 168.6, 168.0, 165.4, 163.3, 142.8, 138.8, 133.7, 129.1, 128.5, 127.7, 127.1, 126.8, 92.0, 61.2, 60.2, 59.3, 48.4, 14.3, 14.14, 14.08; HRMS (HESI) m/z: $[M+Na]^+$ Calcd. for $C_{26}H_{29}NNaO_6$ 490.18362; Found 490.18237.

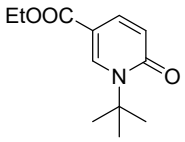
(*2E,4Z*)-Diethyl 4-((benzylamino)(phenyl)methylene)-3-phenylpent-2-enedioate (**4ff**)



From **3f** (60.0 mg, 0.21 mmol) and **2f** (36.6 mg, 0.21 mmol) on 1%H_2SO_4/SiO_2 (500.0 mg). Reaction temperature: 100 °C; reaction time: 24 h; T:EA 9:1 v/v; yellow oil; 19.1 mg, 20% yield; IR (ATR): 3264, 1711, 1648, 1608, 1585, 1571, 1266, 1159 cm^{-1}; ^{1}H NMR (400.1 MHz, $CDCl_3$): 9.85 (broad t, 1H, *J* = 6.0 Hz), 7.05-7.30 (m, 13H), 6.82 (broad t, 1H, *J* = 7.2 Hz), 6.49 (broad d, 1H, *J* = 6.4 Hz), 5.93 (s, 1H), 4.08-4.21 (m, 6H), 1.29 (t, 3H, *J* = 7.2 Hz), 1.11 (t, 3H, *J* = 7.2 Hz); $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): 169.4, 166.4, 162.5, 153.5, 143.3, 139.1, 134.0, 128.8, 128.5, 128.3, 128.0, 127.8, 127.7, 127.2, 127.1, 126.9, 119.6, 96.6, 59.6, 59.1, 48.3, 14.4, 14.3; HRMS (HESI) m/z: $[M+Na]^+$ Calcd. for $C_{29}H_{29}NNaO_4$ 478.19888; Found 478.19841.

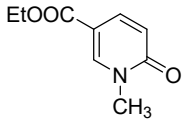
Synthesis of 2-pyridones 5

Ethyl 1-(*ter*t-butyl)-6-oxo-1,6-dihydropyridine-3-carboxylate (**5a**)



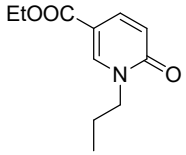
From **4a** (74.0 mg, 0.27 mmol) on 15%$CsCO_3/SiO_2$ (894.0 mg). Reaction temperature: 110 °C; reaction time: 7 h; T:EA 8:2 v/v; yellow oil; 48.5 mg, 79% yield; IR (ATR): 1714, 1666, 1281, 1196, 1104 cm^{-1}; ^{1}H NMR (400.1 MHz, $CDCl_3$): 8.44 (s, 1H), 7.77 (d, 1H, *J* = 9.4 Hz), 6.44 (d, 1H, *J* = 9.4 Hz), 4.32 (q, 2H, *J* = 7.2 Hz), 1.71 (s, 9H),1.36 (t, 3H, *J* = 7.2 Hz); $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): 164.8, 163.7, 139.6, 137.2, 121.3, 109.0, 62.5, 60.8, 28.2, 14.3; HRMS (HESI) m/z: $[M+Na]^+$ Calcd. for $C_{12}H_{17}NNaO_3$ 246.11006; Found 246.10968.

Ethyl 1-methyl-6-oxo-1,6-dihydropyridine-3-carboxylate (**5b**)[8]



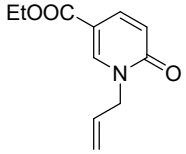
From **4b** (32.4 mg, 0.14 mmol) on 15%$CsCO_3/SiO_2$ (456.0 mg). Reaction temperature: 110 °C; reaction time: 1 h; T:EA 6:4 v/v; colourless amorphous substance; 14.6 mg, 58% yield; IR (ATR): 1715, 1668, 1296, 1111, 1052 cm^{-1}; ^1H NMR (400.1 MHz, $CDCl_3$): 8.21 (d, 1H, J = 1.6 Hz), 7.87 (dd, 1H, J = 1.6, 9.6 Hz), 6.54 (d, 1H, J = 9.6 Hz), 4.33 (q, 2H, J = 7.2 Hz), 3.61 (s, 3H), 1.36 (t, 3H, J = 7.2 Hz); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): 164.1, 162.9, 143.4, 138.6, 119.2, 109.8, 60.9, 38.2, 14.2.

Ethyl 6-oxo-1-propyl-1,6-dihydropyridine-3-carboxylate (**5c**)[9]



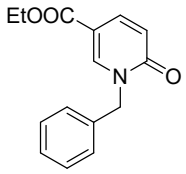
From **4c** (50.0 mg, 0.20 mmol) on 15%$CsCO_3/SiO_2$ (651.6 mg). Reaction temperature: 110 °C; reaction time: 2 h; T:EA 8:2 v/v; yellow oil; 33.0 mg, 79% yield; IR (ATR): 1716, 1667, 1297, 1239, 1110 cm^{-1}; ^1H NMR (500.3 MHz, $CDCl_3$): 8.16 (s, 1H), 7.84 (d, 1H, J = 9.5 Hz), 6.53 (d, 1H, J = 9.5 Hz), 4.33 (q, 2H, J = 7.0 Hz), 3.95 (t, 2H, J = 7.0 Hz), 1.81 (sext, 2H, J = 7.0 Hz), 1.36 (t, 3H, J = 7.0 Hz), 0.98 (t, 3H, J = 7.0 Hz); $^{13}C\{^1H\}$ NMR (125.8 MHz, $CDCl_3$): 164.2, 162.4, 142.7, 138.3, 119.6, 109.7, 60.9, 51.9, 22.4, 14.2, 10.9.

Ethyl 1-allyl-6-oxo-1,6-dihydropyridine-3-carboxylate (**5d**)



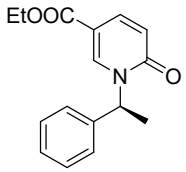
From **4d** (47.8 mg, 0.19 mmol) on 15%$CsCO_3/SiO_2$ (620.0 mg). Reaction temperature: 110 °C; reaction time: 1 h; T:EA 9:1 v/v; colourless amorphous substance; 26.3 mg, 67% yield; IR (ATR): 1717, 1668, 1296, 1236, 1112 cm^{-1}; ^1H NMR (400.1 MHz, $CDCl_3$): 8.16 (s, 1H), 7.86 (d, 1H, J = 9.4 Hz), 6.55 (d, 1H, J = 9.4 Hz), 5.92-6.02 (m, 1H), 5.32 (d, 1H, J = 10.4 Hz), 5.26 (d, 1H, J = 17.2 Hz), 4.61 (d, 2H, J = 5.6 Hz), 4.32 (q, 2H, J = 7.2 Hz), 1.36 (t, 3H, J = 7.2 Hz); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): 164.1, 162.1, 142.3, 138.5, 131.6, 119.6, 119.3, 110.0, 60.9, 51.5, 14.2; HRMS (HESI) m/z: $[M+Na]^+$ Calcd. for $C_{11}H_{13}NNaO_3$ 230.07876; Found 230.07825.

Ethyl 1-benzyl-6-oxo-1,6-dihydropyridine-3-carboxylate (**5e**)[10]



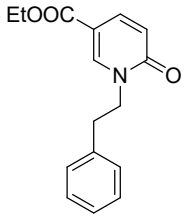
From **4e** (33.0 mg, 0.11 mmol) on 15%$CsCO_3/SiO_2$ (355.0 mg). Reaction temperature: 110 °C; reaction time: 45 min; T:EA 4:1 v/v; white solid; mp 56-57 °C; 25.1 mg, 89% yield; IR (ATR): 1715, 1668, 1296, 1232, 1112 cm^{-1}; ^1H NMR (400.1 MHz, $CDCl_3$): 8.18 (s, 1H), 7.84 (dd, 1H, J = 1.2, 9.6 Hz), 7.31-7.37 (m, 5H), 6.57 (d, 1H, J = 9.6 Hz), 5.17 (s, 2H), 4.29 (q, 2H, J = 7.2 Hz), 1.33 (t, 3H, J = 7.2 Hz); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): 164.2, 162.4, 142.5, 138.5, 135.5, 129.0, 128.3, 128.1, 119.9, 110.3, 61.0, 52.7, 14.3.

Ethyl (*S*)-6-oxo-1-(1-phenylethyl)-1,6-dihydropyridine-3-carboxylate (**5f**)



From **4f** (27.0 mg, 0.08 mmol) on 15%$CsCO_3/SiO_2$ (277.0 mg). Reaction temperature: 110 °C; reaction time: 1 h; T:EA 8:2 v/v; colourless amorphous substance; 15.4 mg, 67% yield; IR (ATR): 1716, 1667, 1295, 1240, 1110 cm^{-1}; ^1H NMR (400.1 MHz, $CDCl_3$): 8.05 (d, 1H, J = 2.4 Hz), 7.81 (dd, 1H, J = 2.4, 9.6 Hz), 7.30-7.40 (m, 5H), 6.57 (d, 1H, J = 9.6 Hz), 6.40 (q, 1H, J = 7.2 Hz), 4.26 (q, 2H, J = 7.2 Hz), 1.76 (d, 3H, J = 7.2 Hz), 1.30 (t, 3H, J = 7.2 Hz); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): 164.2, 162.3, 139.7, 139.4, 137.9, 129.0, 128.3, 127.3, 119.4, 110.4, 60.9, 53.4, 19.3, 14.2; HRMS (HESI) m/z: $[M+Na]^+$ Calcd. for $C_{16}H_{17}NO_3$ 294.11006; Found 294.10922.

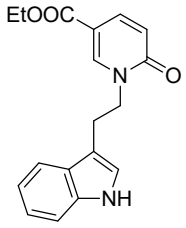
Ethyl 6-oxo-1-phenethyl-1,6-dihydropyridine-3-carboxylate (**5g**)



From **4g** (60.0 mg, 0.19 mmol) on 15%$CsCO_3/SiO_2$ (490.0 mg). Reaction temperature: 110 °C; reaction time: 2 h; T:EA 8:2 v/v; yellow oil; 49.0 mg, 96% yield; IR (ATR): 1716, 1668, 1297, 1112 cm^{-1}; ^1H NMR (400.1 MHz, $CDCl_3$): 7.79-7.84 (m, 2H), 7.29 (t, 2H, J = 7.2 Hz), 7.23 (t, 1H, J = 7.2 Hz), 7.16 (d, 2H, J = 7.2 Hz), 6.54 (d, 1H, J = 9.6 Hz), 4.26 (q, 2H, J = 7.2 Hz), 4.19 (t, 2H,

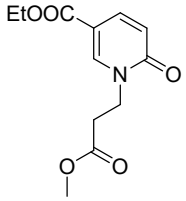
J = 7.2 Hz), 3.06 (t, 2H, *J* = 7.2 Hz), 1.31 (t, 3H, *J* = 7.2 Hz); $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): 164.1, 162.3, 142.9, 138.6, 137.2, 128.8, 128.7, 126.9, 119.6, 109.5, 60.8, 52.3, 35.0, 14.2; HRMS (HESI) m/z: $[M+Na]^+$ Calcd. for $C_{16}H_{17}NNaO_3$ 294.11006; Found 294.10941.

Ethyl 1-(2-(1*H*-indol-3-yl)ethyl)-6-oxo-1,6-dihydropyridine-3-carboxylate (**5h**)[6]



From **4h** (58.0 mg, 0.16 mmol) on 15%$CsCO_3/SiO_2$ (530.0 mg). Reaction temperature: 110 °C; reaction time: 1 h; T:EA 7:3 v/v; pale yellow solid; mp 99-100 °C; 39.2 mg, 78% yield; Gram-scale synthesis; from **1h** (1 g, 6.26 mmol) and **2a** (1.23 g, 12.58 mmol) on SiO_2 (4.6 g); after 1.5 h at 60 °C, Cs_2CO_3 (3.06 g) in EtOH (50 mL) was added together with SiO_2 (12.2 g) and the solvent was evaporated; in this way 15%$CsCO_3/SiO_2$ was obtained; reaction temperature: 110 °C; reaction time: 2 h; column chromatography, gradient petrol ether (40-60 °C):EA 100:0 to 60:40 v/v; 1.03 g, 53% yield (based on **1h**); IR (ATR): 3325, 1716, 1661, 1298, 1114 cm^{-1}; ^{1}H NMR (400.1 MHz, $CDCl_3$): 8.33 (broad s, 1H), 7.80 (d, 1H, *J* = 9.6 Hz), 7.74 (s, 1H), 7.63 (d, 1H, *J* = 8.0 Hz), 7.35 (d, 1H, *J* = 8.4 Hz), 7.20 (t, 1H, *J* = 7.4 Hz), 7.13 (t, 1H, *J* = 7.4 Hz), 6.91 (s, 1H), 6.54 (d, 1H, *J* = 9.6 Hz), 4.26 (t, 2H, *J* = 6.8 Hz), 4.19 (q, 2H, *J* = 7.2 Hz), 3.22 (t, 2H, *J* = 6.8 Hz), 1.24 (t, 3H, *J* = 7.2 Hz); $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): 164.2, 162.5, 143.1, 140.2, 138.6, 136.4, 126.9, 122.6, 122.2, 119.6, 119.4, 118.4, 111.3, 111.2, 109.3, 60.8, 51.1, 24.8, 14.2.

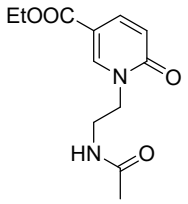
Ethyl 1-(3-methoxy-3-oxopropyl)-6-oxo-1,6-dihydropyridine-3-carboxylate (**5i**)



From **4i** (54.3 mg, 0.18 mmol) on 15%$CsCO_3/SiO_2$ (585.0 mg). Reaction temperature: 110 °C; reaction time: 0.5 h; T:EA 9:1 v/v; pale yellow solid; mp 145-146 °C; 18.7 mg, 40% yield; IR (ATR): 1737, 1717, 1667, 1298, 1174 cm^{-1}; ^{1}H NMR (400.1 MHz, $CDCl_3$): 8.31 (d, 1H, *J* = 2.0 Hz), 7.86 (dd, 1H, *J* = 2.0, 9.6 Hz), 6.52 (d, 1H, *J* = 9.6 Hz), 4.33 (q, 2H, *J* = 7.2 Hz), 4.23 (t, 2H, *J* = 6.4 Hz), 3.69 (s, 3H), 2.88 (t, 2H, *J* = 6.4 Hz), 1.36 (t, 3H, *J* = 7.2 Hz); $^{13}C\{^{1}H\}$ NMR (100.6

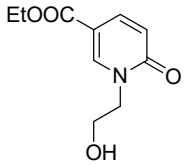
MHz, $CDCl_3$): 171.5, 164.2, 162.4, 143.8, 139.0, 119.6, 110.0, 61.0, 52.0, 47.0, 32.6, 14.3; HRMS (HESI) m/z: $[M+Na]^+$ Calcd. for $C_{12}H_{15}NNaO_5$ 276.08424; Found 276.08513.

Ethyl 1-(2-acetamidoethyl)-6-oxo-1,6-dihydropyridine-3-carboxylate (**5j**)



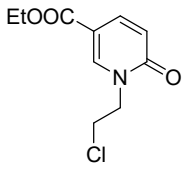
From **4j** (29.4 mg, 0.1 mmol) on 15%$CsCO_3/SiO_2$ (320.0 mg). Reaction temperature: 110 °C; reaction time: 0.5 h; T:EA 9:1 v/v; pale yellow solid; mp 144-145 °C; 15.2 mg, 61% yield; IR (ATR): 3333, 1702, 1677, 1654, 1299, 1112 cm^{-1}; ^1H NMR (400.1 MHz, $CDCl_3$): 8.15 (d, 1H, J = 2.0 Hz), 7.89 (dd, 1H, J = 2.0, 9.6 Hz), 6.53 (d, 1H, J = 9.6 Hz), 6.48 (broad s, 1H), 4.33 (q, 2H, J = 7.2 Hz), 4.16 (t, 2H, J = 6.0 Hz), 3.60 (dt, 2H, J = 5.6, 6.0 Hz), 1.97 (s, 3H), 1.36 (t, 3H, J = 7.2 Hz); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): 170.9, 163.9, 163.1, 143.0, 139.2, 119.5, 110.5, 61.1, 49.6, 39.2, 23.0, 14.3; HRMS (HESI) m/z: $[M+Na]^+$ Calcd. for $C_{12}H_{16}N_2NaO_4$ 275.10023; Found 275.10051.

Ethyl 1-(2-hydroxyethyl)-6-oxo-1,6-dihydropyridine-3-carboxylate (**5k**)



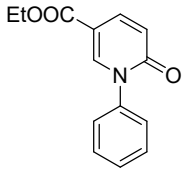
From **4k** (165.1 mg, 0.64 mmol) on 15%$CsCO_3/SiO_2$ (1.387 g). Reaction temperature: 100 °C; reaction time: 4 h; T:EA 3:7 v/v; white solid; mp 89-90 °C; 37.3 mg, 36% yield; IR (ATR): 3257, 1703, 1664, 1593, 1295, 1238, 1162 cm^{-1}; ^1H NMR (400.1 MHz, $CDCl_3$): 8.24 (d, 1H, J = 2.0 Hz), 7.88 (dd, 1H, J = 2.0, 9.6 Hz), 6.53 (d, 1H, J = 9.6 Hz), 4.31 (q, 2H, J = 7.2 Hz), 4.15 (t, 2H, J = 4.8 Hz), 3.95 (t, 2H, J = 4.8 Hz), 3.07 (broad s, 1H), 1.35 (t, 3H, J = 7.2 Hz); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): 164.2, 163.2, 143.8, 139.1, 119.4, 110.2, 61.1, 60.8, 53.4, 14.3; HRMS (HESI) m/z: $[M+Na]^+$ Calcd. for $C_{10}H_{13}NNaO_4$ 234.07368; Found 234.07416.

Ethyl 1-(2-chloroethyl)-6-oxo-1,6-dihydropyridine-3-carboxylate (**5l**)



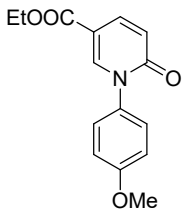
From **4l** (23.1 mg, 0.08 mmol) on 15%$CsCO_3/SiO_2$ (275.0 mg). Reaction temperature: 110 °C; reaction time: 1 h; T:EA 3:7 v/v; white solid; mp 94-95 °C; 19.3 mg, 65% yield; IR (ATR): 3253, 1705, 1662, 1593, 1294, 1239, 1165 cm^{-1}; ^1H NMR (500.3 MHz, $CDCl_3$): 8.23 (d, 1H, J = 2.5 Hz), 7.88 (dd, 1H, J = 2.5, 9.5 Hz), 6.55 (d, 1H, J = 9.5 Hz), 4.32 (q, 2H, J = 7.0 Hz), 4.16 (t, 2H, J = 5.0 Hz), 3.97 (t, 2H, J = 5.0 Hz), 1.36 (t, 3H, J = 7.0 Hz); $^{13}C\{^1H\}$ NMR (125.8 MHz, $CDCl_3$): 164.2, 163.3, 143.8, 139.2, 119.5, 110.2, 61.1, 61.0, 53.5, 14.3; HRMS (HESI) m/z: $[M+Na]^+$ Calcd. for $C_{10}H_{13}NNaO_4$ 234.07368; Found 234.07345 (Cl is substituted by OH[11]).

Ethyl 6-oxo-1-phenyl-1,6-dihydropyridine-3-carboxylate (**5m**)



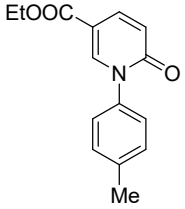
From **4m** (30.0 mg, 0.10 mmol) on 15%$CsCO_3/SiO_2$ (325.8 mg). Reaction temperature: 100 °C; reaction time: 2.5 h; T:EA 8:2 v/v; white solid; mp 80-82 °C; 15.3 mg, 63% yield; Gram-scale synthesis: from **4m** (1 g, 3.45 mmol) on 15%$CsCO_3/SiO_2$ (11.27 g). Reaction temperature: 100 °C; reaction time: 6 h; column chromatography, gradient petrol ether (40-60 °C):EA 100:0 to 90:10; 0.438 g, 52% yield; IR (ATR): 1717, 1676, 1309, 1261, 1104 cm^{-1}; ^1H NMR (400.1 MHz, $CDCl_3$): 8.22 (d, 1H, J = 2.4 Hz), 7.93 (dd, 1H, J = 2.4, 9.6 Hz), 7.53 (t, 2H, J = 7.2 Hz), 7.47 (t, 1H, J = 7.2 Hz), 7.39 (d, 2H, J = 7.6 Hz), 6.64 (d, 1H, J = 9.6 Hz), 4.33 (q, 2H, J = 7.2 Hz), 1.35 (t, 3H, J = 7.2 Hz); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): 164.2, 162.2, 143.1, 140.2, 139.0, 129.5, 129.1, 126.4, 120.6, 110.2, 61.1, 14.3; HRMS (HESI) m/z: $[M+Na]^+$ Calcd. for $C_{14}H_{13}NNaO_3$ 266.07876; Found 266.07813.

Ethyl 1-(4-methoxyphenyl)-6-oxo-1,6-dihydropyridine-3-carboxylate (**5n**)



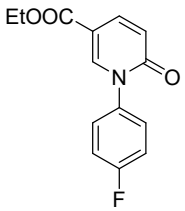
From **4n** (32.0 mg, 0.10 mmol) on 15%$CsCO_3/SiO_2$ (325.8 mg). Reaction temperature: 100 °C; reaction time: 3 h; T:EA 8:2 v/v; colourless oil; 19.9 mg, 73% yield; IR (ATR): 1715, 1675, 1512, 1310, 1262, 1106 cm^{-1}; ^1H NMR (400.1 MHz, $CDCl_3$): 8.20 (d, 1H, J = 2.4 Hz), 7.91 (dd, 1H, J = 2.4, 9.6 Hz), 7.30 (d, 2H, J = 9.2 Hz), 7.01 (d, 2H, J = 9.2 Hz), 6.62 (d, 1H, J = 9.6 Hz), 4.32 (q, 2H, J = 7.2 Hz), 3.86 (s, 3H), 1.35 (t, 3H, J = 7.2 Hz); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): 164.2, 162.5, 159.8, 143.5, 138.8, 133.0, 127.5, 120.4, 114.7, 110.0, 61.1, 55.6, 14.3; HRMS (HESI) m/z: $[M+Na]^+$ Calcd. for $C_{15}H_{15}NNaO_4$ 296.08933; Found 296.08859.

Ethyl 6-oxo-1-(*p*-tolyl)-1,6-dihydropyridine-3-carboxylate (**5o**)



From **4o** (30.3 mg, 0.10 mmol) on 15%$CsCO_3/SiO_2$ (325.8 mg). Reaction temperature: 100 °C; reaction time: 3 h; T:EA 8:2 v/v; white crystals; mp 141-143 °C; 15.7 mg, 61% yield; IR (ATR): 1711, 1671, 1512, 1311, 1276, 1104 cm^{-1}; ^1H NMR (400.1 MHz, $CDCl_3$): 8.21 (d, 1H, J = 2.4 Hz), 7.92 (dd, 1H, J = 2.4, 9.6 Hz), 7.32 (d, 2H, J = 8.0 Hz), 7.26 (d, 2H, J = 8.0 Hz), 6.62 (d, 1H, J = 9.6 Hz), 4.32 (q, 2H, J = 7.2 Hz), 2.42 (s, 3H), 1.34 (t, 3H, J = 7.2 Hz); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): 164.2, 162.3, 143.3, 139.2, 138.8, 137.7, 130.1, 126.1, 120.5, 110.0, 61.1, 21.2, 14.3; HRMS (HESI) m/z: $[M+Na]^+$ Calcd. for $C_{15}H_{15}NNaO_3$ 280.09441; Found 280.09360.

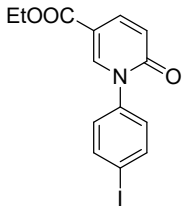
Ethyl 1-(4-fluorophenyl)-6-oxo-1,6-dihydropyridine-3-carboxylate (**5p**)



From **4p** (30.7 mg, 0.10 mmol) on 15%$CsCO_3/SiO_2$ (325.8 mg). Reaction temperature: 100 °C; reaction time: 3 h; T:EA 8:2 v/v; white crystals; mp 104-106 °C; 16.7 mg, 64% yield; IR (ATR): 1720, 1661, 1506, 1264, 1125, 1106 cm^{-1}; ^1H NMR (400.1 MHz, $CDCl_3$): 8.19 (d, 1H, J = 2.4 Hz), 7.93 (dd, 1H, J = 2.4, 9.6 Hz), 7.36-7.39 (m, 2H), 7.20 (t, 2H, J = 8.4 Hz), 6.63 (d, 1H, J = 9.6 Hz), 4.33 (q, 2H, J = 7.2 Hz), 1.35 (t, 3H, J = 7.2 Hz); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): 164.2, 162.5 (d, J_{CF} = 249.5 Hz), 162.1, 143.0, 139.0, 136.0, 128.3 (d, J_{CF} = 8.0 Hz), 120.5, 116.5 (d, J_{CF} = 23.1

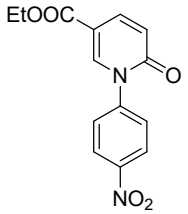
Hz), 110.3, 61.2, 14.3; HRMS (HESI) m/z: $[M+Na]^+$ Calcd. for $C_{14}H_{12}FNNaO_3$ 284.06934; Found 284.06851.

Ethyl 1-(4-iodophenyl)-6-oxo-1,6-dihydropyridine-3-carboxylate (**5q**)



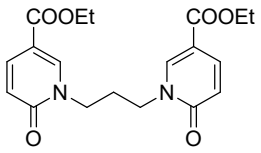
From **4q** (41.5 mg, 0.10 mmol) on 15%$CsCO_3/SiO_2$ (325.8 mg). Reaction temperature: 100 °C; reaction time: 3 h; T:EA 8:2 v/v; white crystals; mp 154-156 °C; 25.5 mg, 69% yield; IR (ATR): 1720, 1670, 1539, 1264, 1118, 1106 cm^{-1}; ^1H NMR (400.1 MHz, $CDCl_3$): 8.17 (d, 1H, J = 2.4 Hz), 7.92 (dd, 1H, J = 2.4, 9.6 Hz), 7.85 (d, 2H, J = 8.4 Hz), 7.15 (d, 2H, J = 8.0 Hz), 6.62 (d, 1H, J = 9.6 Hz), 4.33 (q, 2H, J = 7.2 Hz), 1.35 (t, 3H, J = 7.2 Hz); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): 164.0, 161.8, 142.6, 139.8, 139.1, 138.7, 128.2, 120.6, 110.5, 94.6, 61.2, 14.3; HRMS (HESI) m/z: $[M+Na]^+$ Calcd. for $C_{14}H_{12}INNaO_3$ 391.97541; Found 391.97469.

Ethyl 1-(4-nitrophenyl)-6-oxo-1,6-dihydropyridine-3-carboxylate (**5r**)



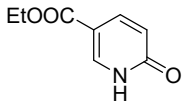
From **4n** (33.4 mg, 0.10 mmol) on 15%$CsCO_3/SiO_2$ (325.8 mg). Reaction temperature: 100 °C; reaction time: 3 h; T:EA 8:2 v/v; white solid; mp 204-206 °C; 15.0 mg, 52% yield; IR (ATR): 1712, 1655, 1523, 1260, 1128, 1111 cm^{-1}; ^1H NMR (400.1 MHz, $CDCl_3$): 8.40 (d, 2H, J = 8.8 Hz), 8.20 (d, 1H, J = 2.4 Hz), 7.96 (dd, 1H, J = 2.4, 9.6 Hz), 7.63 (d, 2H, J = 8.8 Hz), 6.66 (d, 1H, J = 9.6 Hz), 4.35 (q, 2H, J = 7.2 Hz), 1.36 (t, 3H, J = 7.2 Hz); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): 163.8, 161.5, 147.9, 145.1, 141.8, 139.4, 127.7, 124.9, 121.0, 111.1, 61.4, 14.3; HRMS (HESI) m/z: $[M+Na]^+$ Calcd. for $C_{14}H_{12}N_2NaO_5$ 311.06384; Found 311.06309.

Diethyl 1,1'-(propane-1,3-diyl)bis(6-oxo-1,6-dihydropyridine-3-carboxylate) (**5s**)



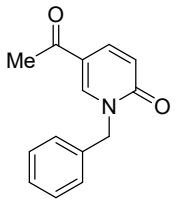
From **4s** (120.0 mg, 0.26 mmol) on 15%$CsCO_3/SiO_2$ (1.680 g). Reaction temperature: 100 °C; reaction time: 4 h; T:EA 3:7 v/v; white solid; mp 123-124 °C; 21.0 mg, 22% yield; IR (ATR): 1716, 1668, 1338, 1298, 1110 cm^{-1}; ^1H NMR (500.3 MHz, $CDCl_3$): 8.22 (d, 2H, J = 2.5 Hz), 7.86 (dd, 2H, J = 2.5, 9.5 Hz), 6.54 (d, 2H, J = 9.5 Hz), 4.33 (q, 4H, J = 7.2 Hz), 4.07 (t, 4H, J = 7.2 Hz), 2.27 (quint, 2H, J = 7.2 Hz), 1.37 (t, 3H, J = 7.2 Hz); $^{13}C\{^1H\}$ NMR (125.8 MHz, $CDCl_3$): 164.0, 162.4, 142.6, 138.8, 119.8, 110.4, 61.1, 47.9, 29.0, 14.3; HRMS (HESI) m/z: $[M+Na]^+$ Calcd. for $C_{19}H_{22}N_2NaO_6$ 397.13701; Found 397.13617.

Ethyl 6-oxo-1,6-dihydropyridine-3-carboxylate (**5t**)[12]



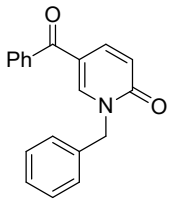
From **4t** (38.5 mg, 0.18 mmol) on 15%$CsCO_3/SiO_2$ (590.0 mg). Reaction temperature: 110 °C; reaction time: 1.25 h; EA; white solid; mp 139-140 °C; 24.2 mg, 80% yield; IR (ATR): 3118, 3041, 1708, 1603, 1298, 1269, 1228, 1118, 1107 cm^{-1}; ^1H NMR (400.1 MHz, $CDCl_3$): 13.3 (broad s, 1H), 8.23 (d, 1H, J = 2.4 Hz), 8.03 (dd, 1H, J = 2.4, 9.6 Hz), 6.58 (d, 1H, J = 9.6 Hz), 4.33 (q, 2H, J = 7.2 Hz), 1.36 (t, 3H, J = 7.2 Hz); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): 165.6, 164.0, 141.0, 139.7, 119.4, 111.4, 61.1, 14.2.

5-Acetyl-1-benzylpyridin-2(1H)-one (**5u**)[13]



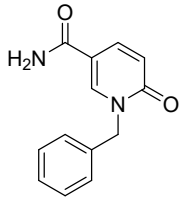
From **4u** (27.3 mg, 0.10 mmol) on 15%$CsCO_3/SiO_2$ (325.0 mg). Reaction temperature: 110 °C; reaction time: 1 h; T:EA 7:3 v/v; colourless oil; 15.0 mg, 67% yield; IR (ATR): 1660, 1295, 1188, 1146 cm^{-1}; ^1H NMR (400.1 MHz, $CDCl_3$): 8.10 (d, 1H, J = 2.4 Hz), 7.86 (dd, 1H, J = 2.4, 9.6 Hz), 7.31-7.39 (m, 5H), 6.61 (d, 1H, J = 9.6 Hz), 5.19 (s, 2H), 2.39 (s, 3H); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): 193.0, 162.3, 142.0, 137.6, 135.3, 129.1, 128.5, 128.2, 120.2, 118.0, 52.8, 25.7.

5-Benzoyl-1-benzylpyridin-2(1H)-one (**5v**)[14]



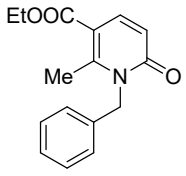
From **1e** (30.5 mg, 0.28 mmol), **2c** (36.5 mg, 0.28 mmol) and **2a** (28.0 mg, 0.28 mmol) on silica gel (200.0 mg). Crude **4v** was extracted with ethyl acetate, 15%$CsCO_3/SiO_2$ (910.0 mg) was added and solvent was evaporated under reduced pressure. Reaction temperature: 110 °C; reaction time: 1 h; T:EA 8:2 v/v; white solid; mp 104-105 °C; 24.4 mg, 30% yield based on **1e**; IR (ATR): 1731, 1673, 1644, 1295, 1266, 1180 cm^{-1}; ^1H NMR (400.1 MHz, $CDCl_3$): 7.97 (s, 1H), 7.87 (d, 1H, J = 9.6 Hz), 7.54-7.60 (m, 3H), 7.44 (t, 2H, J = 7.2 Hz), 7.30-7.38 (m, 5H), 6.64 (d, 1H, J = 9.6 Hz), 5.16 (s, 2H); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): 191.6, 162.2, 144.1, 139.0, 135.4, 132.3, 129.1, 129.0, 128.50, 128.47, 128.3, 120.1, 117.4, 52.6.

1-Benzyl-6-oxo-1,6-dihydropyridine-3-carboxamide (**5w**)[15]



From **4w** (34.3 mg, 0.12 mmol) on 15%$CsCO_3/SiO_2$ (405.0 mg). Reaction temperature: 110 °C; reaction time: 2 h; EA:MeOH 9:1 v/v; white solid; m.p. 161-163 °C; 19.1 mg, 68% yield; IR (ATR): 3350, 3174, 1733, 1674, 1602, 1265, 1178 cm^{-1}; ^1H NMR (400.1 MHz, DMSO-d_6): 8.44 (s, 1H), 7.85 (d, 1H, J = 9.6 Hz), 7.76 (broad s, 1H), 7.24-7.34 (m, 6H), 6.41 (d, 1H, J = 9.6 Hz), 5.11 (s, 2H); $^{13}C\{^1H\}$ NMR (100.6 MHz, DMSO-d_6): 165.1, 161.4, 141.7, 138.3, 137.0, 128.7, 127.82, 127.75, 118.6, 112.8, 51.8.

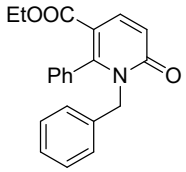
Ethyl 1-benzyl-2-methyl-6-oxo-1,6-dihydropyridine-3-carboxylate (**5x**)[14]



From **4x** (32.0 mg, 0.1 mmol) on 15%$CsCO_3/SiO_2$ (325.8 mg). Reaction temperature: 110 °C; reaction time: 2 h; T:EA 9:1 v/v; pale yellow oil; 18.1 mg, 67% yield; IR (ATR): 1713, 1667, 1538, 1268, 1148, 1121 cm^{-1}; ^1H NMR (400.1 MHz, $CDCl_3$): 7.91 (d, 1H, J = 9.6 Hz), 7.22-7.31 (m, 3H),

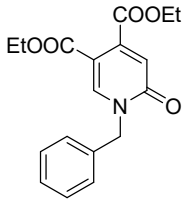
7.10 (d, 2H, *J* = 7.6 Hz), 6.53 (d, 1H, *J* = 9.6 Hz), 5.42 (broad s, 2H), 4.26 (q, 2H, *J* = 7.2 Hz), 2.69 (s, 3H), 1.33 (t, 3H, *J* = 7.2 Hz); $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): 165.6, 163.2, 153.9, 140.0, 135.6, 128.9, 127.5, 126.2, 116.6, 109.8, 61.0, 47.5, 17.6, 14.2.

Ethyl 1-benzyl-6-oxo-2-phenyl-1,6-dihydropyridine-3-carboxylate (**5y**)



From **4y** (30.0 mg, 0.08 mmol) on 15%$CsCO_3/SiO_2$ (263.1 mg). Reaction temperature: 100 °C; reaction time: 2 h; T:EA 9:1 v/v; white solid; mp 119-121 °C; 16.3 mg, 61% yield; IR (ATR): 1727, 1701, 1671, 1302, 1286, 1112 cm^{-1}; ^{1}H NMR (400.1 MHz, $CDCl_3$): 8.00 (d, 1H, *J* = 9.6 Hz), 7.41 (t, 1H, *J* = 7.6 Hz), 7.30 (t, 2H, *J* = 7.6 Hz), 7.17-7.18 (m, 3H), 6.98 (d, 2H, *J* = 7.6 Hz), 6.79-6.80 (m, 2H), 6.72 (d, 1H, *J* = 9.6 Hz), 5.08 (s, 2H), 3.93 (q, 2H, *J* = 7.2 Hz), 0.91 (t, 3H, *J* = 7.2 Hz); $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): 164.9, 162.9, 139.9, 136.6, 134.0, 129.1, 128.3, 128.2, 128.0, 127.2, 126.6, 118.9, 110.9, 60.7, 49.0, 13.6; HRMS (HESI) m/z: $[M+Na]^+$ Calcd. for $C_{21}H_{19}NNaO_3$ 356.12571; Found 356.12414.

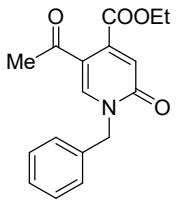
Diethyl 1-benzyl-6-oxo-1,6-dihydropyridine-3,4-dicarboxylate (**5za**)[16]



5za

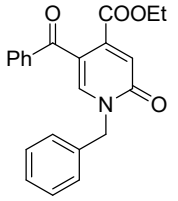
From **4za** (30.0 mg, 0.08 mmol) on 15%$CsCO_3/SiO_2$ (260.0 mg). Reaction temperature: rt; reaction time: 1 h; T:EA 8:2 v/v; white solid; mp 115-116 °C; 13.4 mg, 51% yield; IR (ATR): 1736, 1673, 1313, 1265, 1113 cm^{-1}; ^{1}H NMR (400.1 MHz, $CDCl_3$): 8.12 (s, 1H), 7.30-7.40 (m, 5H), 6.60 (s, 1H), 5.16 (s, 2H), 4.37 (q, 2H, *J* = 7.2 Hz), 4.26 (q, 2H, *J* = 7.2 Hz), 1.36 (t, 3H, *J* = 7.2 Hz), 1.30 (t, 3H, *J* = 7.2 Hz); $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): 166.2, 163.1, 161.5, 144.1, 143.2, 135.0, 129.1, 128.6, 128.2, 118.9, 107.8, 62.2, 61.5, 52.8, 14.1, 14.0.

Ethyl 5-acetyl-1-benzyl-2-oxo-1,2-dihydropyridine-4-carboxylate (**5zb**)



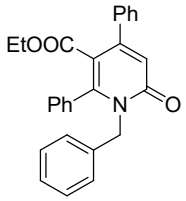
From **4zb** (31.0 mg, 0.09 mmol) on 15%$CsCO_3/SiO_2$ (293.2 mg). Reaction temperature: 110 °C; reaction time: 0.5 h; T:EA 6:4 v/v; pale brown solid; mp 123-125 °C; 14.6 mg, 54% yield; IR (ATR): 1736, 1668, 1318, 1262, 1034 cm^{-1}; ^1H NMR (500.3 MHz, $CDCl_3$): 7.91 (s, 1H), 7.34-7.41 (m, 3H), 7.30-7.32 (m, 2H), 6.62 (s, 1H), 5.17 (s, 2H), 4.38 (q, 2H, J = 7.0 Hz), 2.32 (s, 3H), 1.36 (t, 3H, J = 7.0 Hz); $^{13}C\{^1H\}$ NMR (125.8 MHz, $CDCl_3$): 192.1, 166.6, 161.4, 143.4, 142.4, 134.8, 129.2, 128.7, 128.2, 119.6, 116.7, 62.2, 52.6, 25.9, 13.9; HRMS (HESI) m/z: $[M+Na]^+$ Calcd. for $C_{17}H_{17}NNaO_4$ 322.10498; Found 322.10577.

Ethyl 5-benzoyl-1-benzyl-2-oxo-1,2-dihydropyridine-4-carboxylate (**5zc**)



From **4zc** (30.0 mg, 0.07 mmol) on 15%$CsCO_3/SiO_2$ (228.1 mg). Reaction temperature: 110 °C; reaction time: 15 min; T:EA 8:2 v/v; yellow oil; 12.2 mg, 48% yield; IR (ATR): 1734, 1678, 1652, 1324, 1261, 1050 cm^{-1}; ^1H NMR (500.3 MHz, $CDCl_3$): 7.69 (s, 1H), 7.68 (d, 2H, J = 7.5 Hz), 7.56 (t, 1H, J = 7.5 Hz), 7.43 (t, 2H, J = 7.5 Hz), 7.33-7.37 (m, 3H), 7.29-7.31 (m, 2H), 6.93 (s, 1H), 5.15 (s, 2H), 4.07 (q, 2H, J = 7.0 Hz), 1.14 (t, 3H, J = 7.0 Hz); $^{13}C\{^1H\}$ NMR (125.8 MHz, $CDCl_3$): 191.1, 165.3, 161.4, 143.0, 142.2, 137.1, 135.0, 133.0, 129.2, 129.1, 128.6, 128.4, 121.3, 117.0, 62.2, 52.6, 13.6; HRMS (HESI) m/z: $[M+Na]^+$ Calcd. for $C_{22}H_{19}NNaO_4$ 384.12063; Found 384.12024.

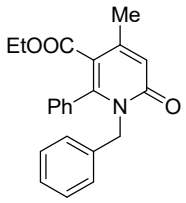
Ethyl 1-benzyl-6-oxo-2,4-diphenyl-1,6-dihydropyridine-3-carboxylate (**5ff**)



From **4ff** (16.0 mg, 0.04 mmol) on 15%$CsCO_3/SiO_2$ (114.0 mg). Reaction temperature: 110 °C; reaction time: 1 h; T:EA 9:1 v/v; colourless oil; 10.4 mg, 74% yield; IR (ATR): 1726, 1663, 1289,

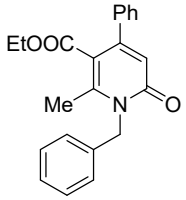
1211, 1104 cm^{-1}; ^1H NMR (400.1 MHz, $CDCl_3$): 7.40 (broad s, 6H), 7.31 (t, 1H, J = 7.6 Hz), 7.20 (m, 3H), 7.11 (d, 2H, J = 7.2 Hz), 6.88 (m, 2H), 6.71 (s, 1H), 5.13 (s, 2H), 3.62 (q, 2H, J = 7.2 Hz), 0.65 (t, 3H, J = 7.2 Hz); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): 166.5, 162.3, 150.9, 148.9, 137.9, 136.6, 132.7, 129.6, 129.1, 128.8, 128.5, 128.3, 128.1, 127.3, 127.2, 127.0, 119.2, 115.7, 61.0, 48.8, 13.2; HRMS (HESI) m/z: $[M+Na]^+$ Calcd. for $C_{27}H_{23}NNaO_3$ 432.15701; Found 432.15542.

Ethyl 1-benzyl-4-methyl-6-oxo-2-phenyl-1,6-dihydropyridine-3-carboxylate (**5fe**)



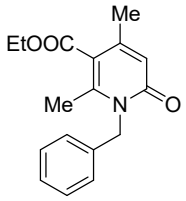
From **3f** (28.1 mg, 0.10 mmol) and **2a** (11.2 mg, 0.10 mmol) on 15%$CsCO_3/SiO_2$ (325.8 mg). Reaction temperature: 120 °C; reaction time: 7 h; T:EA 8:2 v/v; pale yellow oil; 4.5 mg, 13% yield; IR (ATR): 1720, 1666, 1289, 1133, 1064 cm^{-1}; ^1H NMR (500.3 MHz, $CDCl_3$): 7.38 (t, 1H, J = 7.5 Hz), 7.28 (t, 2H, J = 7.5 Hz), 7.16-7.17 (m, 3H), 7.04 (d, 2H, J = 7.5 Hz), 6.80-6.82 (m, 2H), 6.55 (s, 1H), 5.07 (s, 2H), 3.81 (q, 2H, J = 7.0 Hz), 2.62 (s, 3H), 0.79 (t, 3H, J = 7.0 Hz); $^{13}C\{^1H\}$ NMR (125.8 MHz, $CDCl_3$): 166.5, 162.3, 148.5, 148.0, 136.8, 133.2, 129.4, 129.0, 128.3, 128.1, 127.1, 126.8, 119.2, 116.3, 61.0, 48.6, 20.2, 13.4; HRMS (HESI) m/z: $[M+Na]^+$ Calcd. for $C_{22}H_{21}NNaO_3$ 370.14136; Found 370.14135.

Ethyl 1-benzyl-4-methyl-6-oxo-2-phenyl-1,6-dihydropyridine-3-carboxylate (**5ef**)



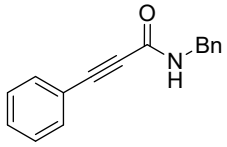
From **3e** (22.0 mg, 0.10 mmol) and **2f** (17.4 mg, 0.10 mmol) on 15%$CsCO_3/SiO_2$ (325.8 mg). Reaction temperature: 120 °C; reaction time: 7 h; T:EA 8:2 v/v; pale yellow oil; 4.8 mg, 14% yield; IR (ATR): 1719, 1661, 1283, 1116, 1045 cm^{-1}; ^1H NMR (400.1 MHz, $CDCl_3$): 7.39-7.40 (m, 3H), 7.33-7.34 (m, 4H), 7.29 (d, 1H, J = 7.2 Hz), 7.22 (d, 2H, J = 7.6 Hz), 6.56 (s, 1H), 5.43 (s, 2H), 3.90 (q, 2H, J = 7.2 Hz), 2.42 (s, 3H), 0.382 (t, 3H, J = 7.2 Hz); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): 167.8, 162.6, 151.4, 147.0, 138.8, 135.8, 128.9, 128.6, 128.5, 127.6, 127.0, 126.6, 117.5, 114.2, 61.4, 47.6, 17.9, 13.4; HRMS (HESI) m/z: $[M+Na]^+$ Calcd. for $C_{22}H_{21}NNaO_3$ 370.14136; Found 370.14127.

Ethyl 1-benzyl-2,4-dimethyl-6-oxo-1,6-dihydropyridine-3-carboxylate (**5ee**)



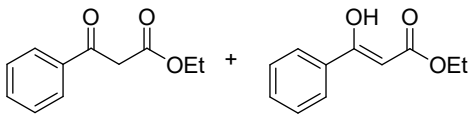
From **3e** (22.0 mg, 0.10 mmol) and **2e** (11.2 mg, 0.10 mmol) on 15%$CsCO_3/SiO_2$ (325.8 mg). Reaction temperature: 120 °C; reaction time: 7 h; T:EA 8:2 v/v; pale yellow oil; 8.5 mg, 20% yield; IR (ATR): 1720, 1666, 1284, 1173, 1136 cm^{-1}; ^1H NMR (400.1 MHz, $CDCl_3$): 7.40 (broad s, 6H), 7.31 (t, 1H, J = 7.6 Hz), 7.25 (t, 1H, J = 7.6 Hz), 7.14 (d, 2H, J = 7.6 Hz), 6.41 (s, 1H), 5.36 (s, 2H), 4.32 (q, 2H, J = 7.2 Hz), 2.31 (s, 3H), 2.20 (s, 3H), 1.35 (t, 3H, J = 7.2 Hz); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): 167.7, 162.7, 147.8, 145.8, 136.0, 128.8, 127.4, 126.4, 117.6, 115.2, 61.4, 47.2, 20.5, 18.0, 14.2; HRMS (HESI) m/z: $[M+Na]^+$ Calcd. for $C_{17}H_{19}NNaO_3$ 308.12571; Found 308.12556.

N-benzyl-3-phenylpropiolamide (**6**)[17]



From **1e** (50.0 mg, 0.47 mmol) and **2f** (81.9 mg, 0.47 mmol) on silica gel (500.0 mg). Reaction temperature: 60 °C; reaction time: 3 h; white solid; mp 109-111 °C; 44.2 mg, 40% yield; IR (ATR): 3273, 1726, 2220, 1635, 1548, 1312 cm^{-1}; ^1H NMR (400.1 MHz, $CDCl_3$): 7.50 (d, 2H, J = 8.4 Hz), 7.29-7.42 (m, 8H), 6.23 (broad s, 1H), 4.53 (d, 2H, J = 6.0 Hz); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): 153.2, 137.2, 132.5, 130.1, 128.8, 128.5, 128.0, 127.8, 120.1, 85.1, 82.8, 44.0.

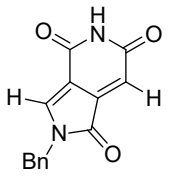
Ethyl 3-oxo-3-phenylpropanoate (**7**)[18]



From **1e** (50.0 mg, 0.47 mmol) and **2f** (81.9 mg, 0.47 mmol) on silica gel (500.0 mg). Reaction temperature: 60 °C; reaction time: 3 h; toluene; pale yellow oil; 9.0 mg, 10% yield; IR (ATR): 3063, 1741, 1688, 1268, 1198, 1148 cm^{-1}; ^1H NMR (400.1 MHz, $CDCl_3$): keto form 7.95 (d, 2H, J = 7.2 Hz), 7.60 (t, 1H, J = 7.2 Hz), 7.49 (t, 1H, J = 7.2 Hz), 4.22 (q, 2H, J = 7.2 Hz), 4.00 (s, 2H), 1.26 (t, 3H, J = 7.2 Hz), enol form 12.59 (s, 1H), 7.78 (d, 2H, J = 7.2 Hz), 7.40-7.45 (m, 3H), 5.67 (s, 1H), 4.27 (q, 2H, J = 7.2 Hz), 1.34 (t, 3H, J = 7.2 Hz); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): keto

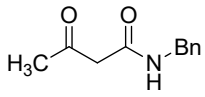
+ enol form 192.5, 167.5, 136.0, 133.7, 131.2, 128.7, 128.50, 128.47, 126.0, 87.4, 61.5, 60.3, 46.0, 14.3, 14.0.

2-Benzyl-1H-pyrrolo[3,4-c]pyridine-1,4,6(2H,5H)-trione (**8**)



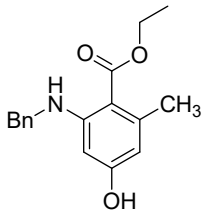
From **4zd** (31.0 mg, 0.09 mmol) in EtOH (2 mL) containing Cs_2CO_3 (44.0 mg, 0.13 mmol). Reaction temperature (of an oil bath): 50 °C; reaction time: 15 min; after completion of the reaction, water (3 mL) and few drops of 36% HCl were added and the mixture was extracted with DCM (3×3mL). Organic layer was dried with anh. Na_2SO_4 and solvent was evaporated under reduced pressure to give **8**; dark greenish oil; 21.1 mg, 93% yield; IR (ATR): 3380, 1732, 1673, 1027, 1007 cm^{-1}; ^1H NMR (500.3 MHz, DMSO-d_6): 11.53 (s, 1H), 8.75 (s, 1H), 7.29-7.35 (m, 5H), 6.76 (s, 1H), 5.19 (s, 2H); $^{13}C\{^1H\}$ NMR (125.8 MHz, DMSO-d_6): 166.6, 166.3, 162.0, 142.4, 138.5, 136.4, 128.6, 127.87, 127.82, 113.3, 109.1, 42.4; HRMS (HESI) m/z: $[M–H]^-$ Calcd. for $C_{14}H_9N_2O_3$ 253.06187; Found 253.06198.

N-benzyl-3-oxobutanamide (**10**)



From **1e** (30.0 mg, 0.28 mmol) and **2e** (62.8 mg, 0.56 mmol) on silica gel (500.0 mg). Reaction temperature: 60 °C (3 h), 100 °C (22 h); T:EA 3:7 v/v; white solid; m.p. 101-103 °C; 13.9 mg, 26% yield; IR (ATR): 3302, 1720, 1651, 1551, 1360, 1160, 1030 cm^{-1}; ^1H NMR (500.3 MHz, $CDCl_3$): 7.27-7.34 (m, 5H, overlapped with $CDCl_3$ residual peak), 7.23-7.26 (m, 1H), 4.46 (d, 1H, J = 5.5 Hz), 3.44 (s, 2H), 2.26 (s, 3H); $^{13}C\{^1H\}$ NMR (125.8 MHz, $CDCl_3$): 204.5, 165.4, 137.9, 128.7, 127.7, 127.5, 49.5, 43.5, 31.0.

Ethyl 2-(benzylamino)-4-hydroxy-6-methylbenzoate (**11**)



From **3e** (44.0 mg, 0.20 mmol) and **2e** (22.4 mg, 0.20 mmol) on silica gel containing 1% of H_2SO_4 (500.0 mg). Reaction temperature: 100 °C; reaction time: 24 h; T:EA 9:1 v/v; pale brown solid; m.p. 102-104 °C; 29.7 mg, 52% yield; IR (ATR): 3360, 1664, 1594, 1249, 1182, 1124, 1096 cm^{-1}; ^1H NMR (400.1 MHz, $CDCl_3$): 7.81 (s, 1H), 7.29-7.32 (m, 4H), 7.23-7.26 (m, 1H), 5.97 (m, 1H), 5.92 (d, 1H, J = 1.6 Hz), 4.28-4.33 (m, 4H), 2.44 (s, 3H), 1.35 (t, 3H, J = 7.2 Hz); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): 169.7, 159.0, 153.0, 144.0, 138.8, 128.6, 127.08, 127.07, 107.5, 105.8, 95.6, 60.2, 47.4, 24.4, 14.3; HRMS (HESI) m/z: $[M+Na]^+$ Calcd. for $C_{17}H_{19}NNaO_3$ 308.12571; Found 308.12547.

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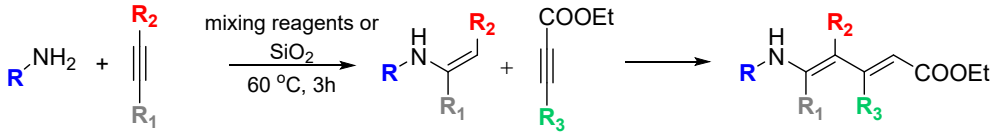
Table S1. Optimization of reaction conditions for the synthesis of enaminones **3** and dienes **4**.[a]



1e **2** **3** **2'** **4**

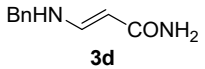
Entry	Compound	Synthesis of enaminone **3**.						
		R	R_1	R_2	Solid phase or solvent	Reaction temperature (°C)	Reaction time (h)	Yield (%)[b]
1	**3e**	Bn	Me	CO_2Et	SiO_2	60	3	52
2					DMSO	rt	72	70
3	**3f**	Bn	Ph	CO_2Et	SiO_2	60	3	35
4					DMSO	rt	72	76
	Compound	Synthesis of dienes **4**.						
		R	R_1	R_2	R_3	Solid phase or solvent	Reaction temperature (°C)	Reaction time (h)	Yield (%)[b]
5	**4i**	$(CH_2)_2CO_2Me$	H	CO_2Et	H	SiO_2	rt	18	27
6						SiO_2	30	15	42
7						SiO_2	60	2	33
8						SiO_2	100	2	0
9	**4j**	$(CH_2)_2CONH_2$	H	CO_2Et	H	SiO_2	60	3	12
10						SiO_2	50	8	36
11	**4k**	$(CH_2)_2OH$	H	CO_2Et	H	SiO_2	50	0.75	44
12						EtOH	reflux	0.5	0
13	**4l**	$(CH_2)_2Cl$	H	CO_2Et	H	SiO_2	50	2	36
14						SiO_2	60	1.5	39
15	**4t**[c]	H	H	CO_2Et	H	SiO_2	25	18	0
16						SiO_2	50	3	19
17						SiO_2	60	1.5	20
18						H_2O	60	1	0
19						MeOH	30	18	16
20						MeOH	reflux	1	0
21						EtOH	reflux	1	0
22						THF	reflux	1	0
23	**4u**	Bn	H	COMe	H	SiO_2	60	1	0
24						SiO_2	70	1.5	18
25						MeOH	reflux	2	0
26	**4v**	Bn	H	COPh	H	SiO_2	60	1	0

27						SiO_2	70	1	0
28						SiO_2	80	4	26
29	**4w**	Bn	H	$CONH_2$	H	SiO_2	60	1	0
30						MeCN	reflux	3	25
31						EtOH	reflux	2	19
32	**4x**	Bn	Me	CO_2Et	H	SiO_2	60	2.5	48
33						SiO_2	rt	2.5	67
34	**4y**	Bn	Ph	CO_2Et	H	SiO_2	60	7	15
35						SiO_2	rt	21	72
36						EtOH	reflux	14	30
37	**4za**	Bn	H	CO_2Et	CO_2Et	SiO_2	60	1	0
38						SiO_2	rt	1.5	61
39	**4zd**	Bn	H	$CONH_2$	CO_2Et	SiO_2	25	0.5	0
40						EtOH	reflux	1	0
41						MeCN	reflux	1	44
42	**4ee**	Bn	Me	CO_2Et	Me	SiO_2	rt	22	0
43						SiO_2	60	22	0
44						SiO_2	100	22	0
45						EtOH	reflux	22	0
46						$1\%H_2SO_4/SiO_2$	100	24	0
47	**4ff**	Bn	Ph	CO_2Et	Ph	SiO_2	rt	22	0
48						SiO_2	60	22	0
49						SiO_2	100	22	0
50						EtOH	reflux	22	0
51						$1\%H_2SO_4/SiO_2$	100	24	20
52	**4fe**	Bn	Ph	COOEt	Me	$1\%H_2SO_4/SiO_2$	100	24	0
53	**4ef**	Bn	Me	COOEt	Ph	$1\%H_2SO_4/SiO_2$	100	24	0

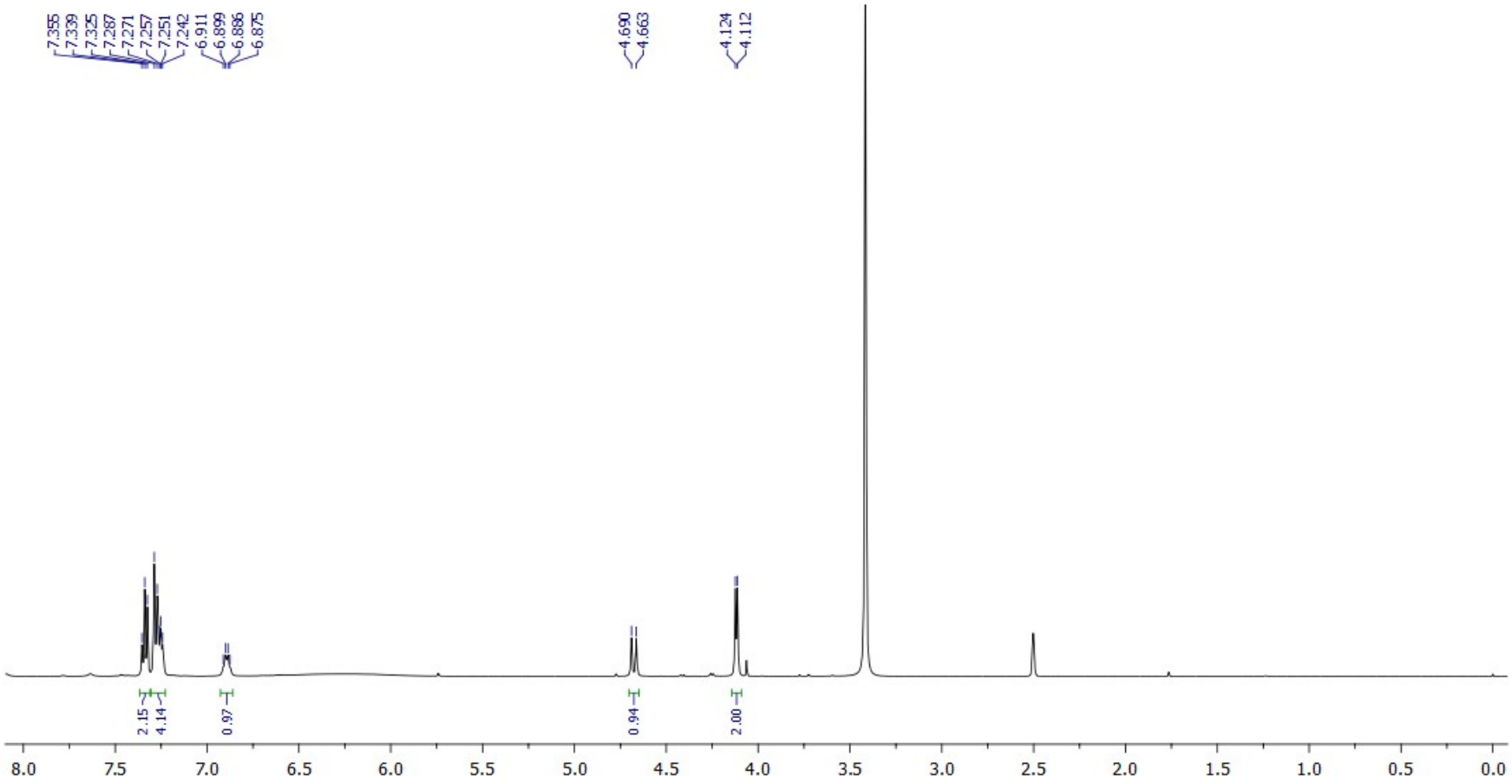
[a] The best conditions are shaded grey. [b] Yield of isolated product. [c] From 20% NH_3/H_2O.

Copies of ^{1}H NMR and ^{13}C NMR spectra of synthesized compounds

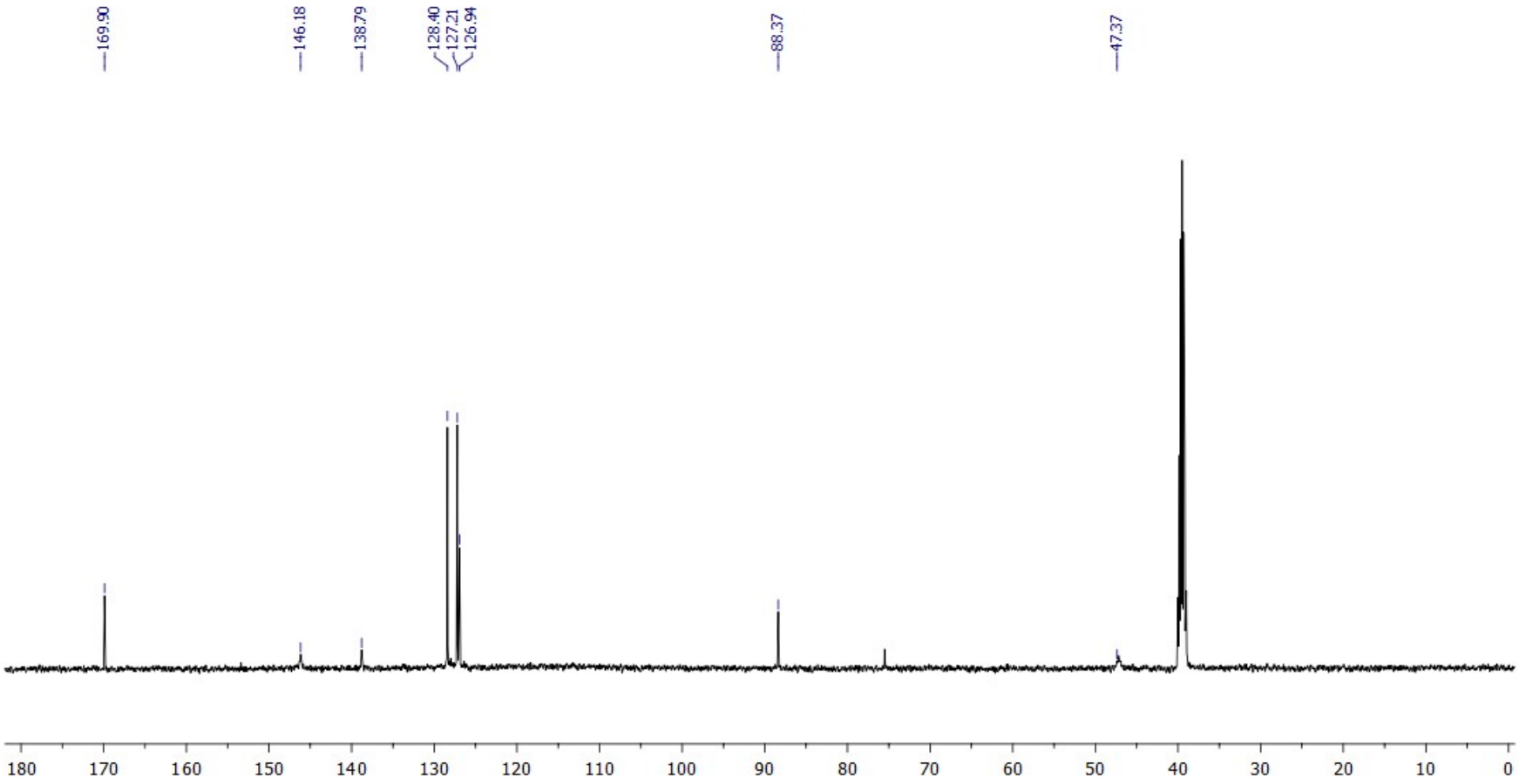
Enaminones 3



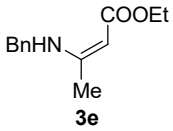
3d



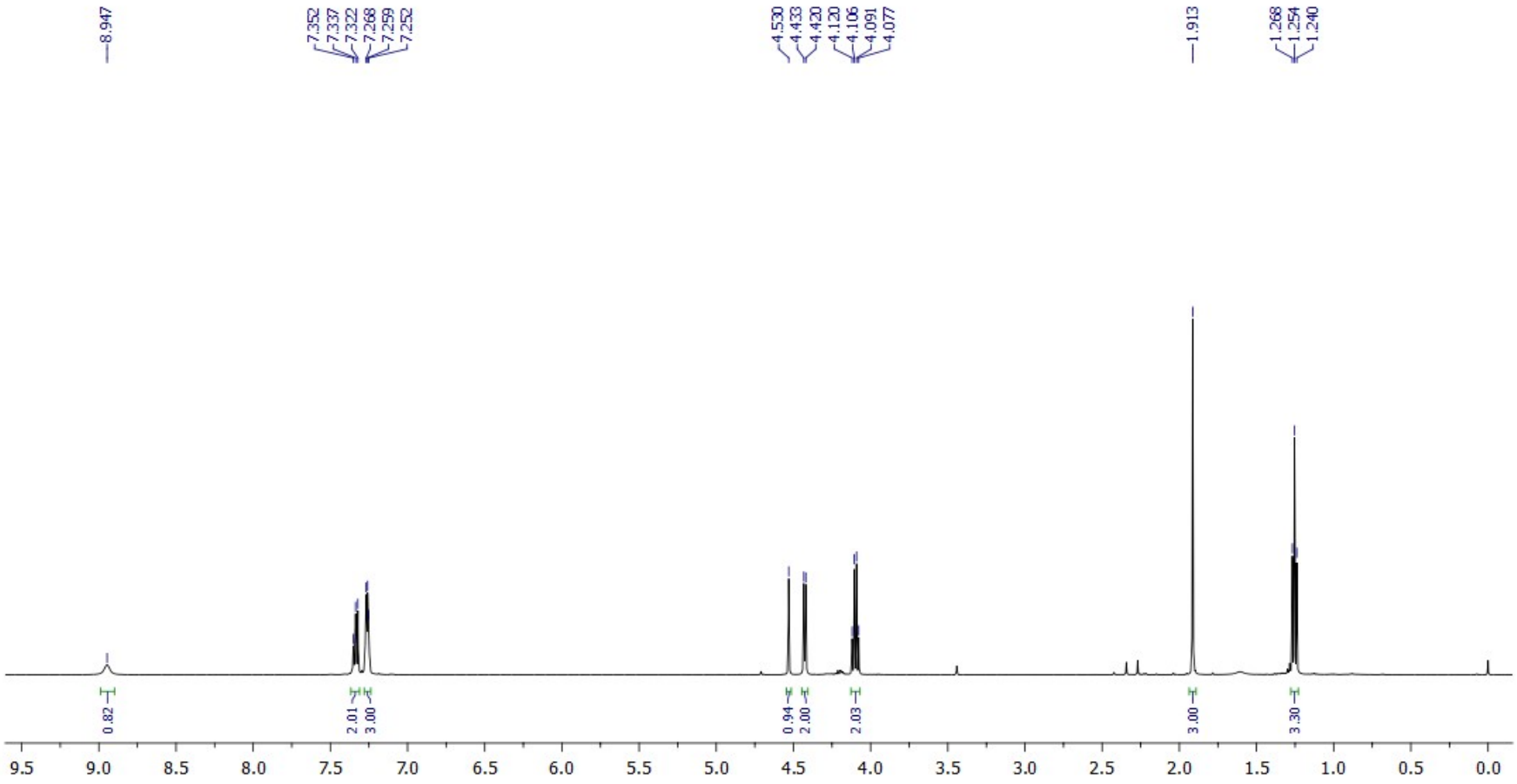
^{1}H NMR (500.3 MHz, DMSO-d_6)



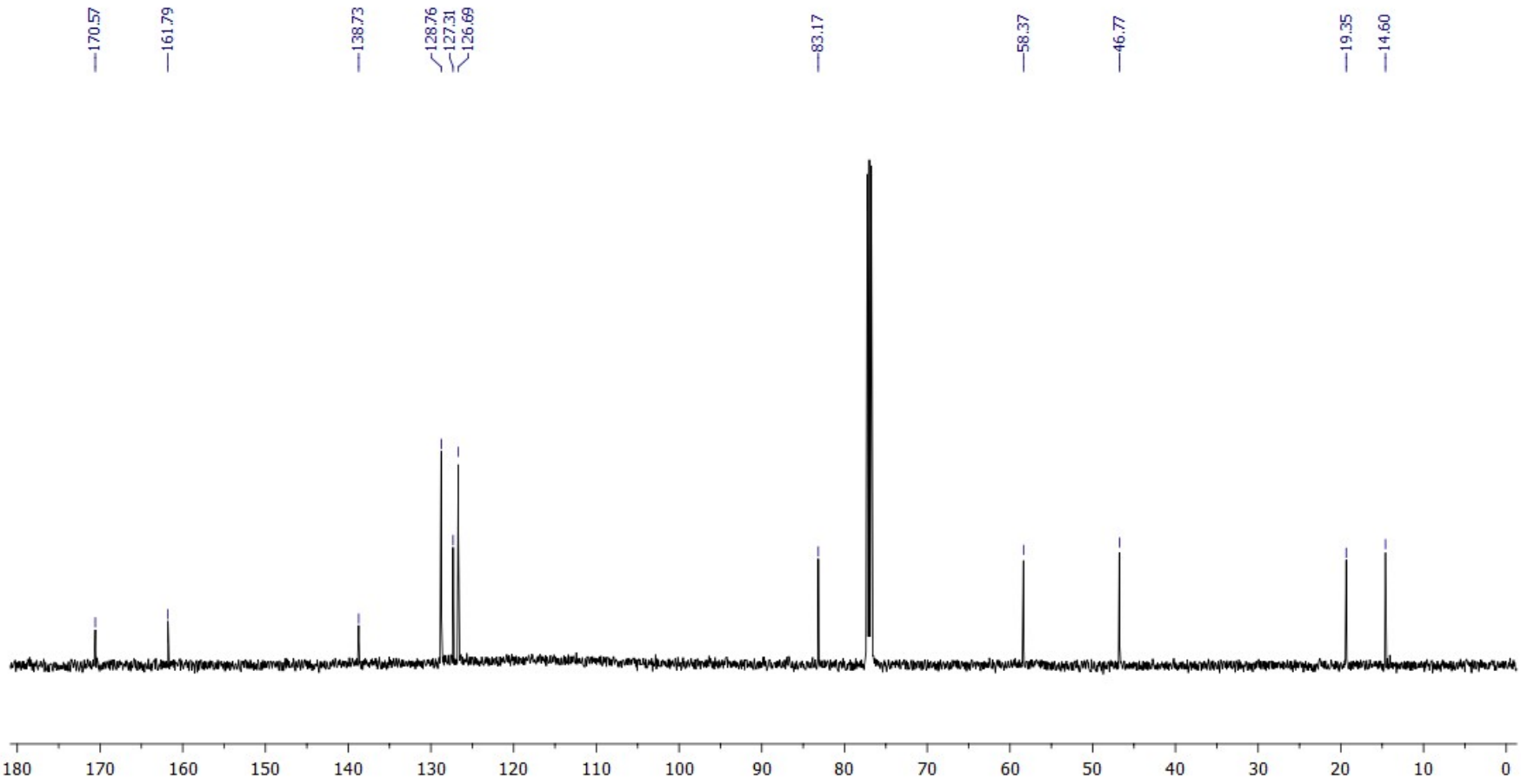
$^{13}C\{^{1}H\}$ NMR (125.8 MHz, DMSO-d_6)



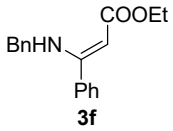
3e



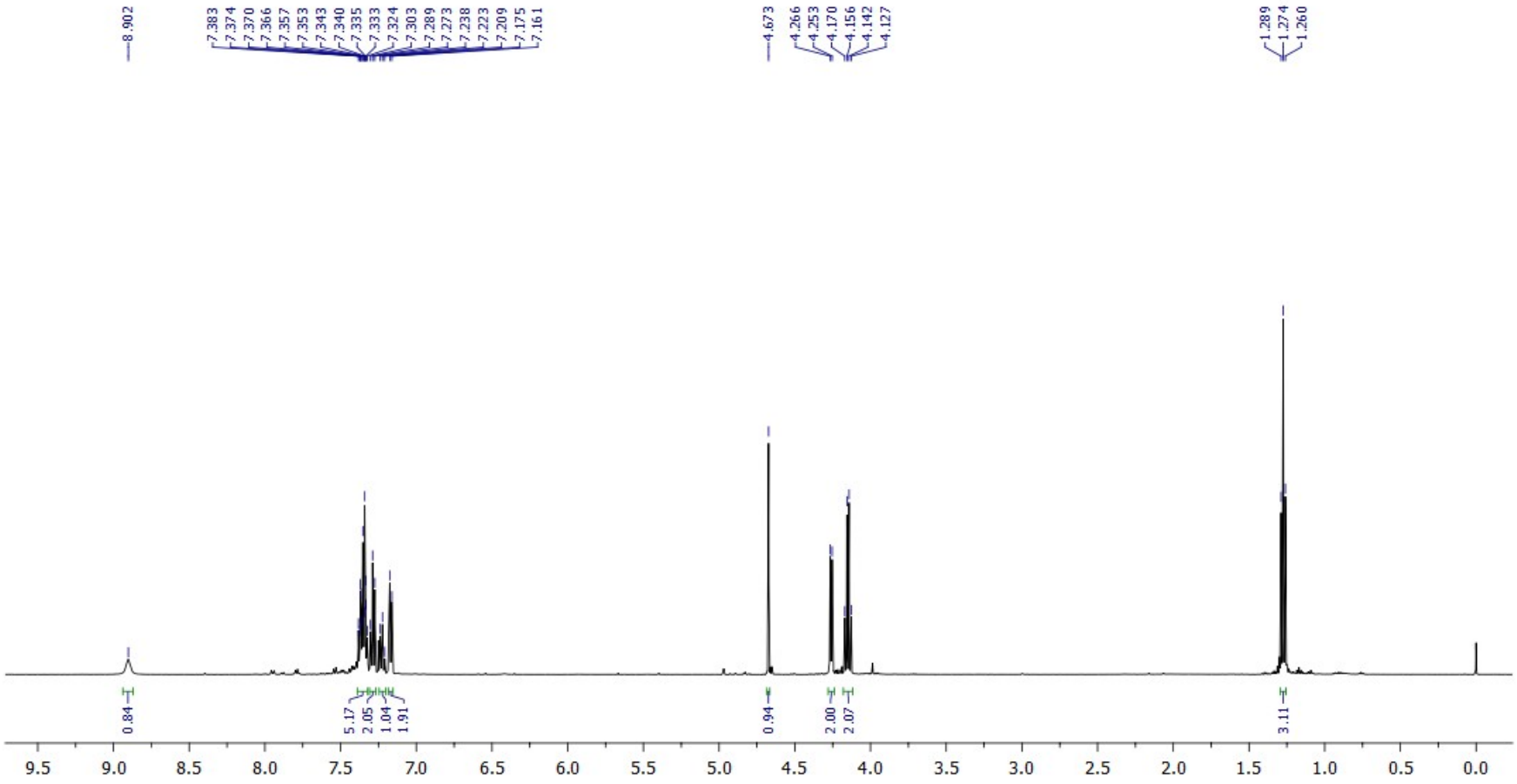
^{1}H NMR (500.3 MHz, $CDCl_3$)



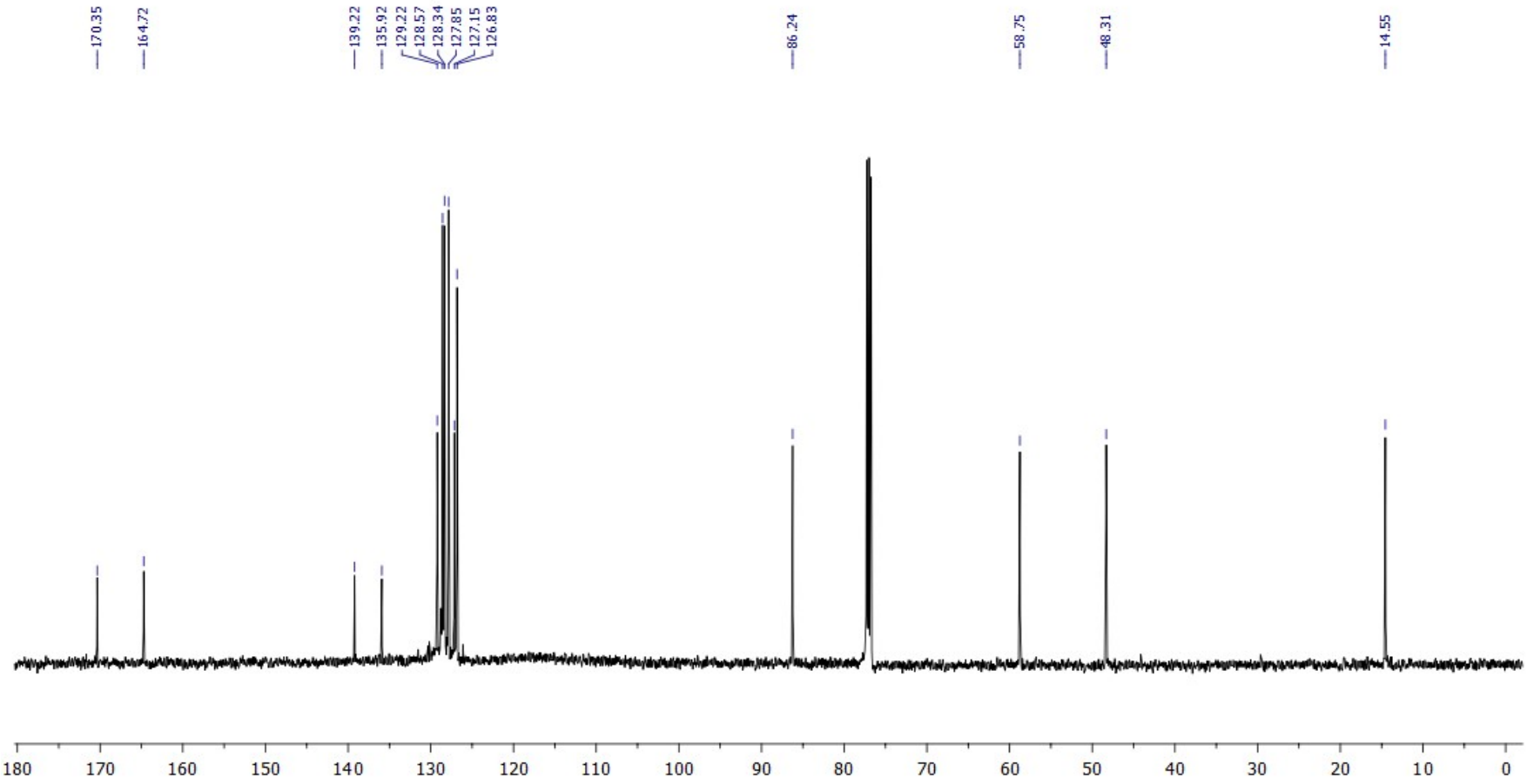
$^{13}C\{^{1}H\}$ NMR (125.8 MHz, $CDCl_3$)



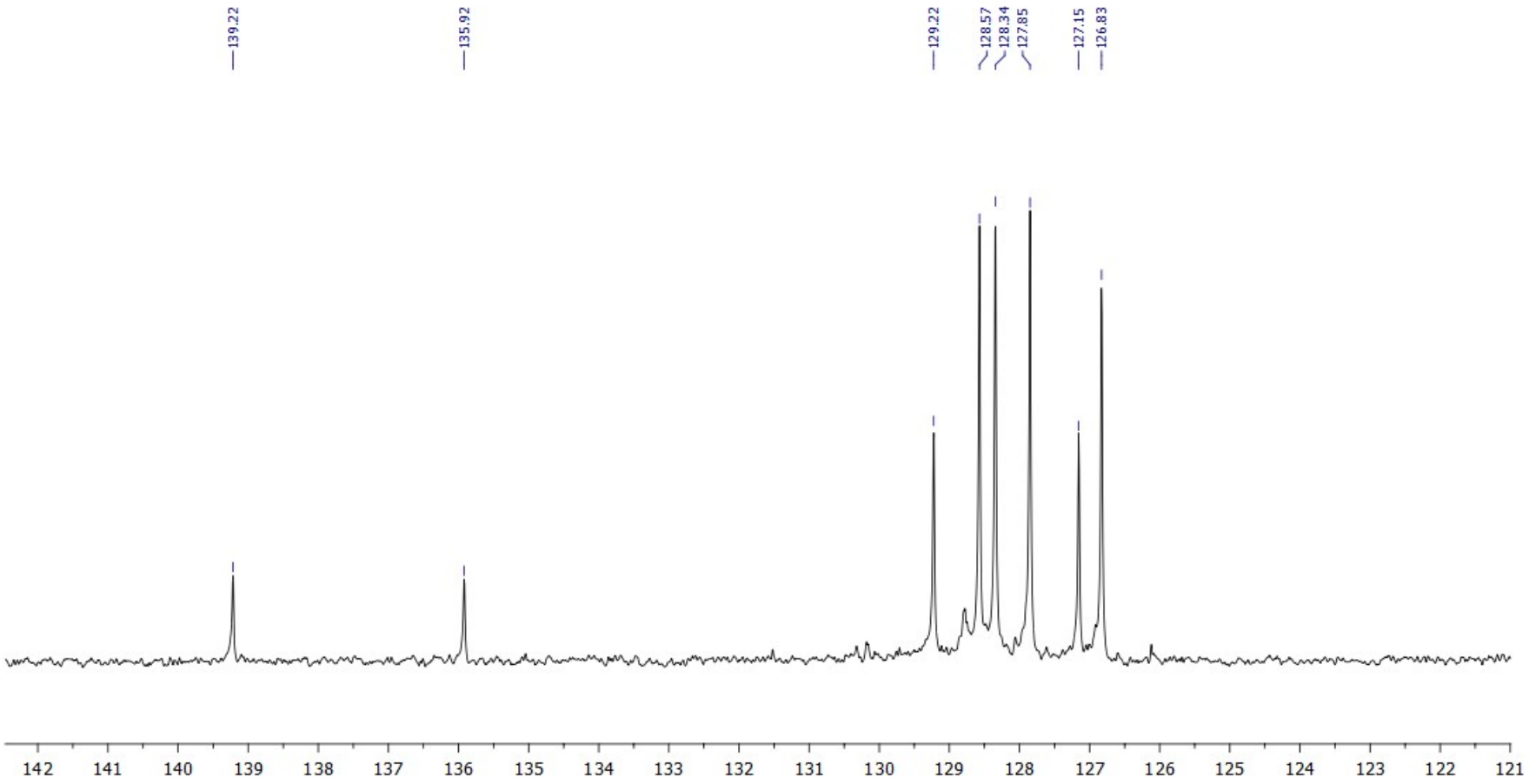
3f



^{1}H NMR (500.3 MHz, $CDCl_3$)

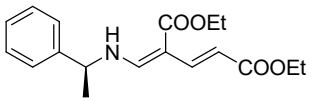


$^{13}C\{^{1}H\}$ NMR (125.8 MHz, $CDCl_3$)

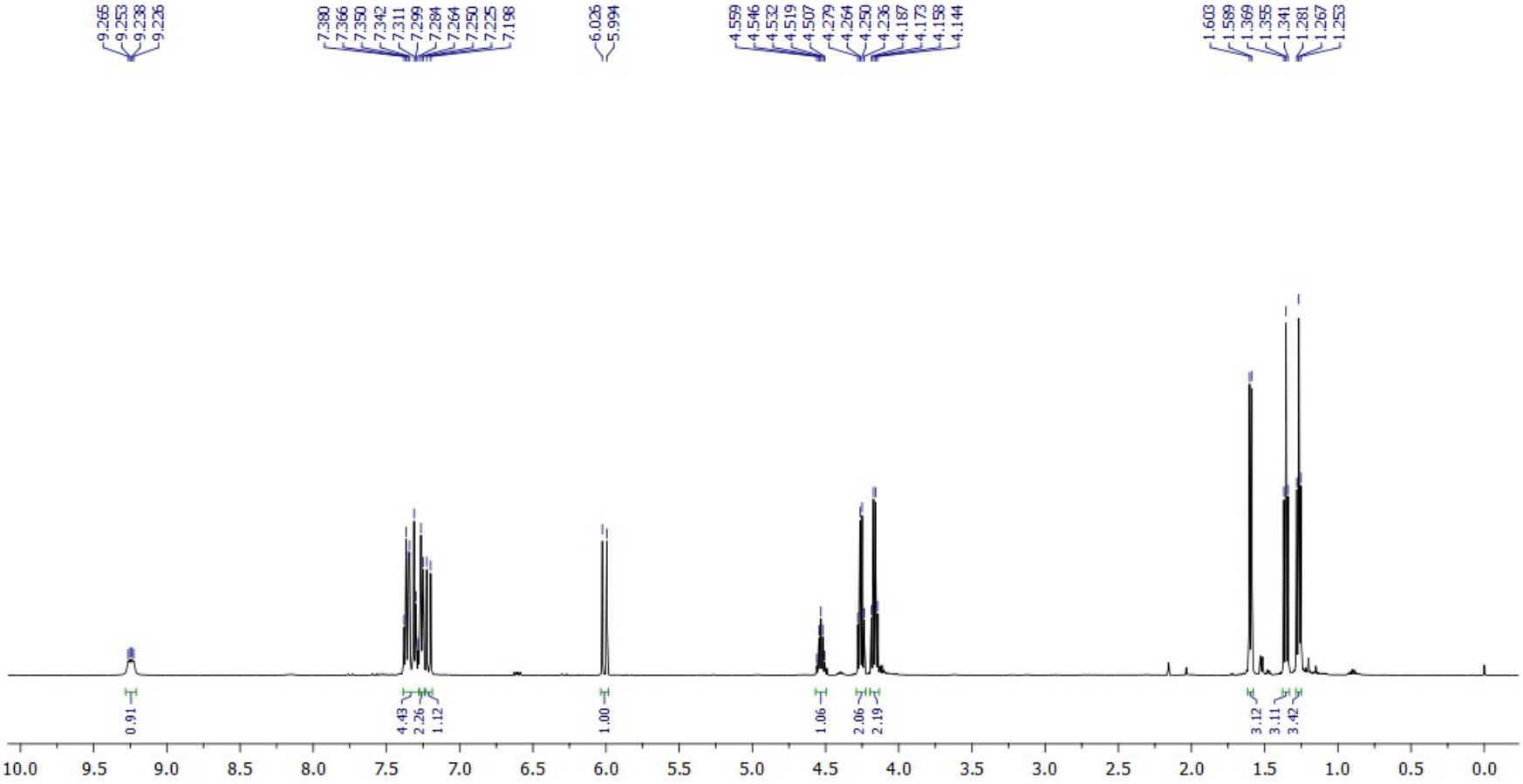


$^{13}C\{^{1}H\}$ NMR (125.8 MHz, $CDCl_3$), expanded aromatic region

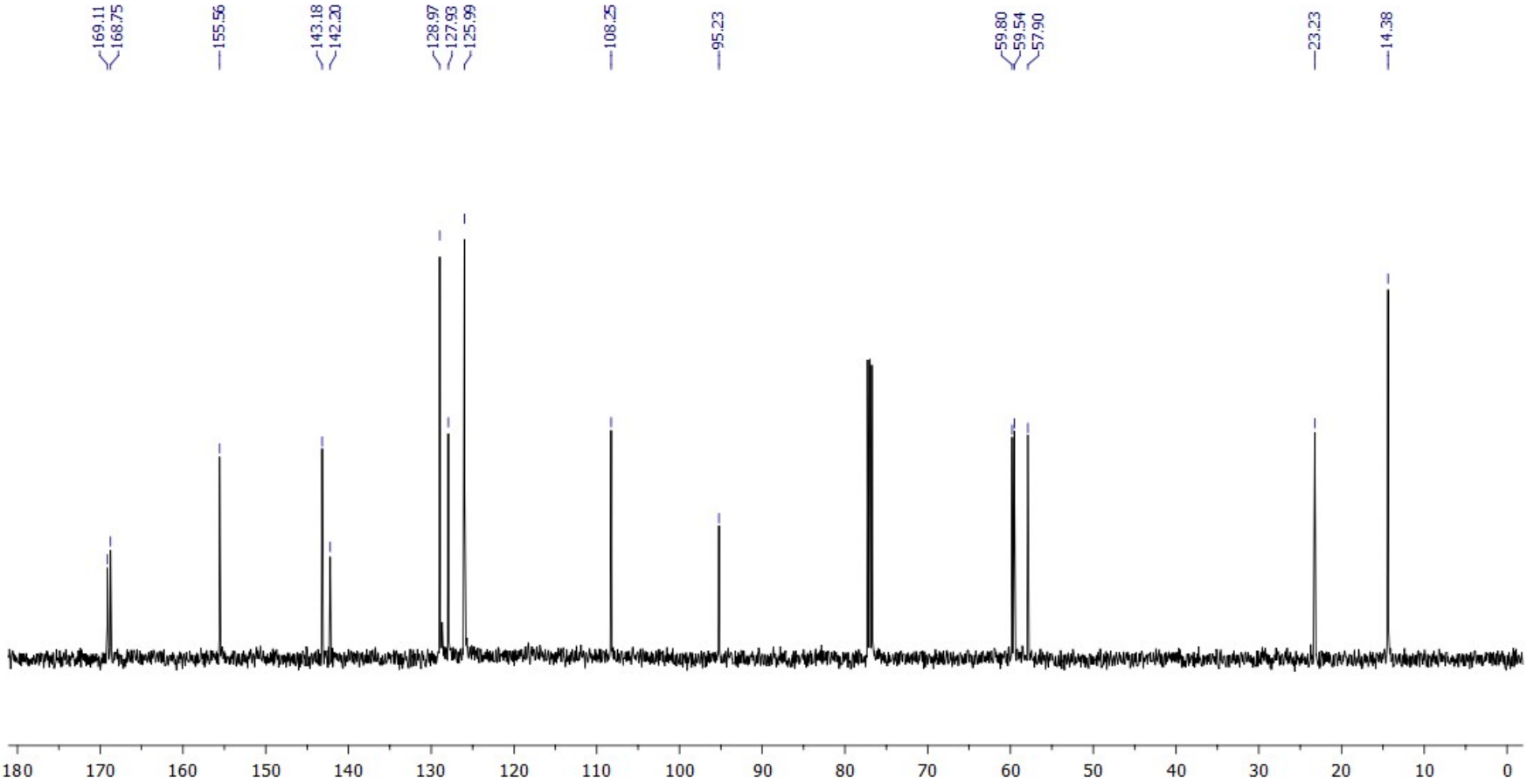
Dienes 4



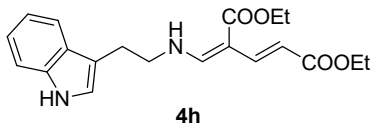
4f



^{1}H NMR (500.3 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (125.8 MHz, $CDCl_3$)



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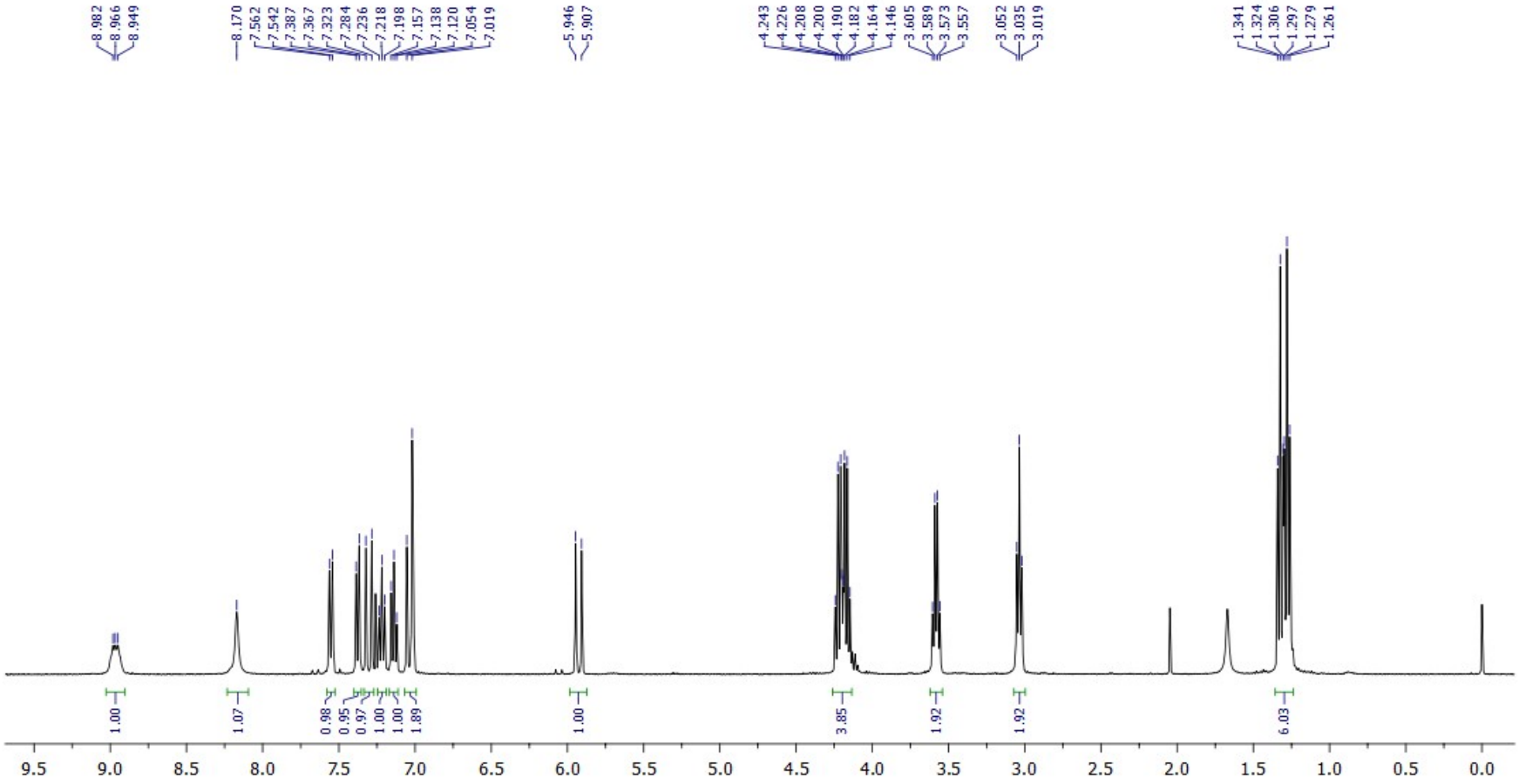
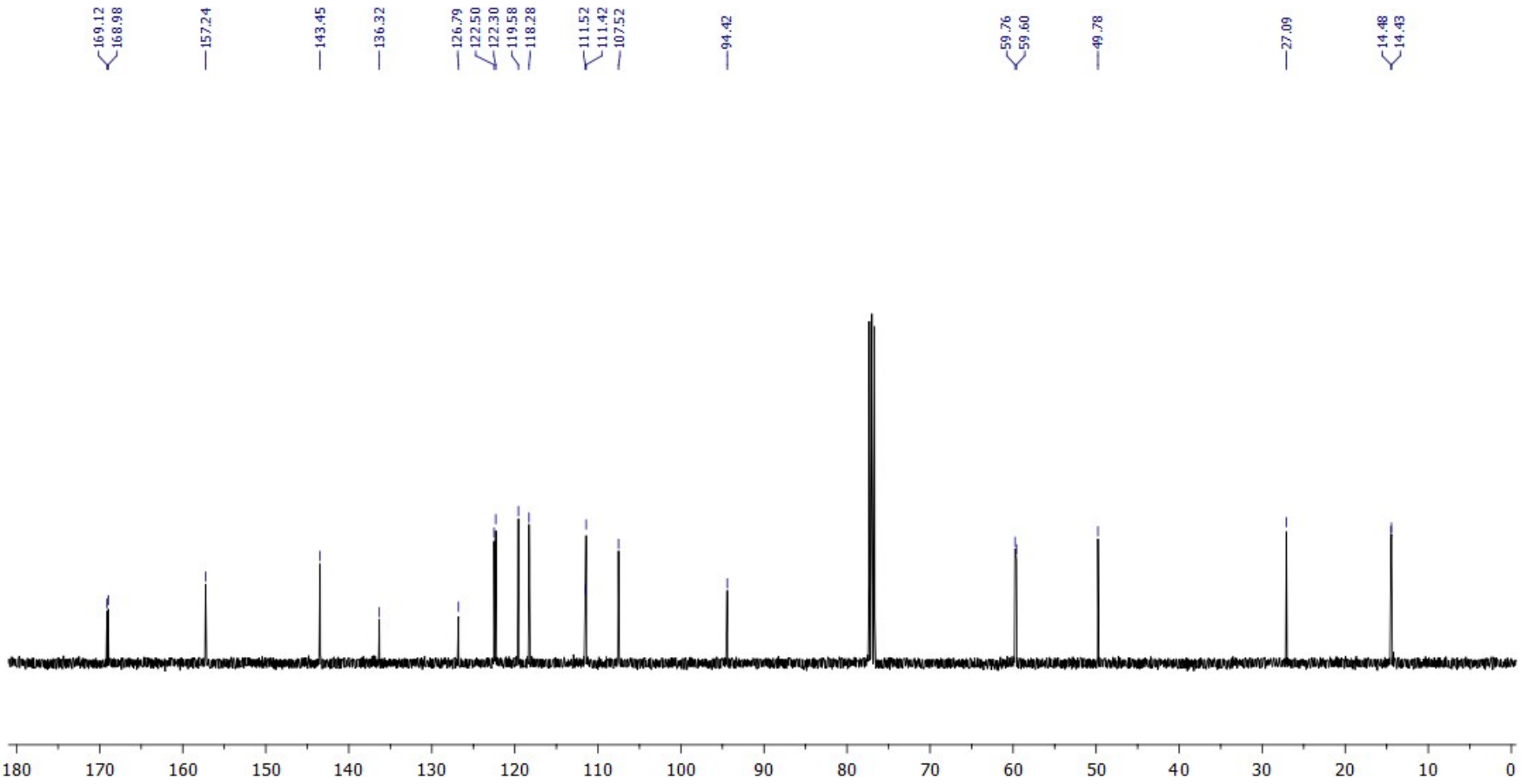
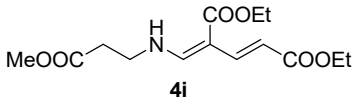


^{1}H NMR (400.1 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$)



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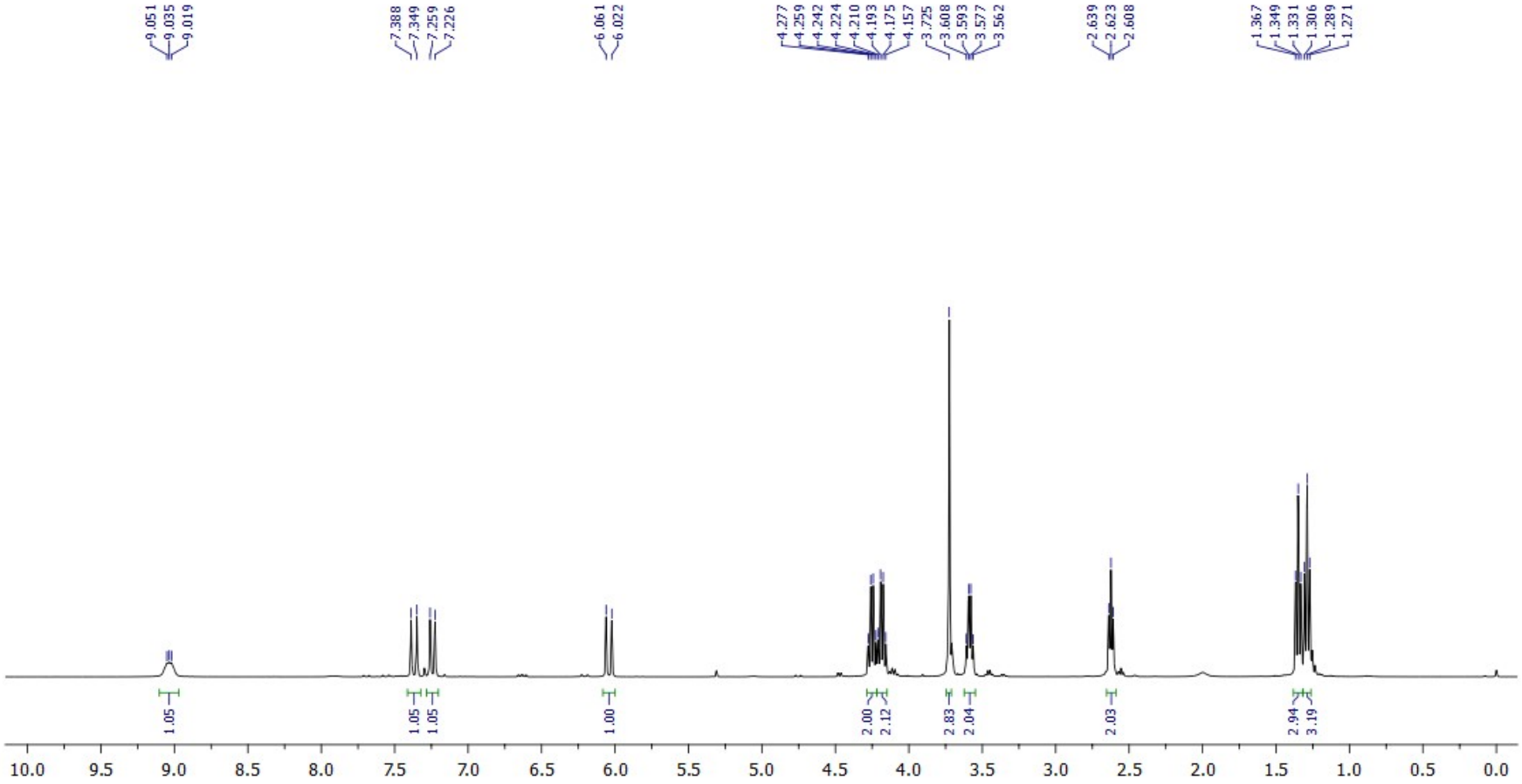
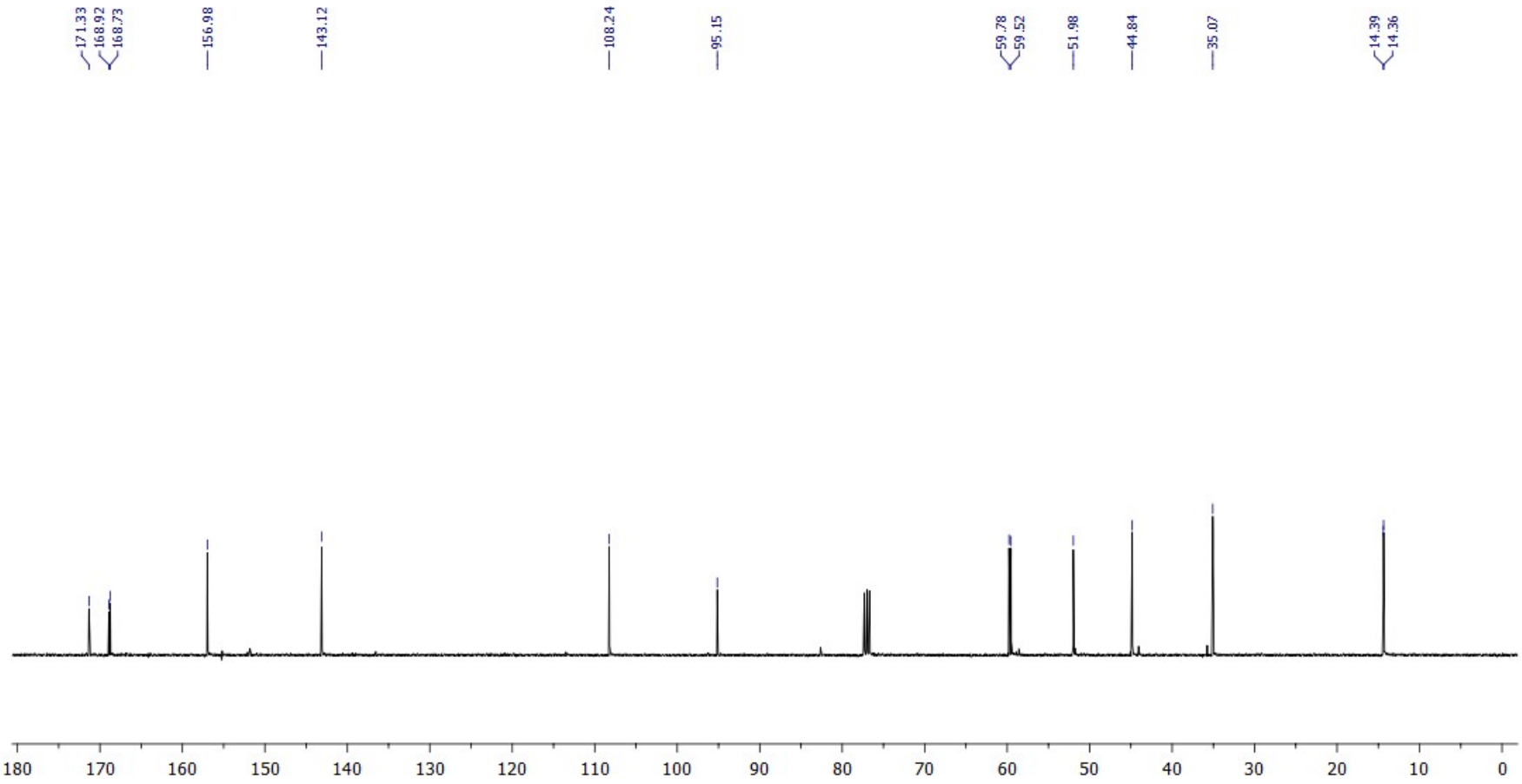
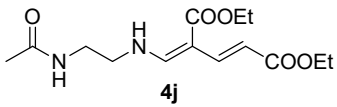


^{1}H NMR (400.1 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$)



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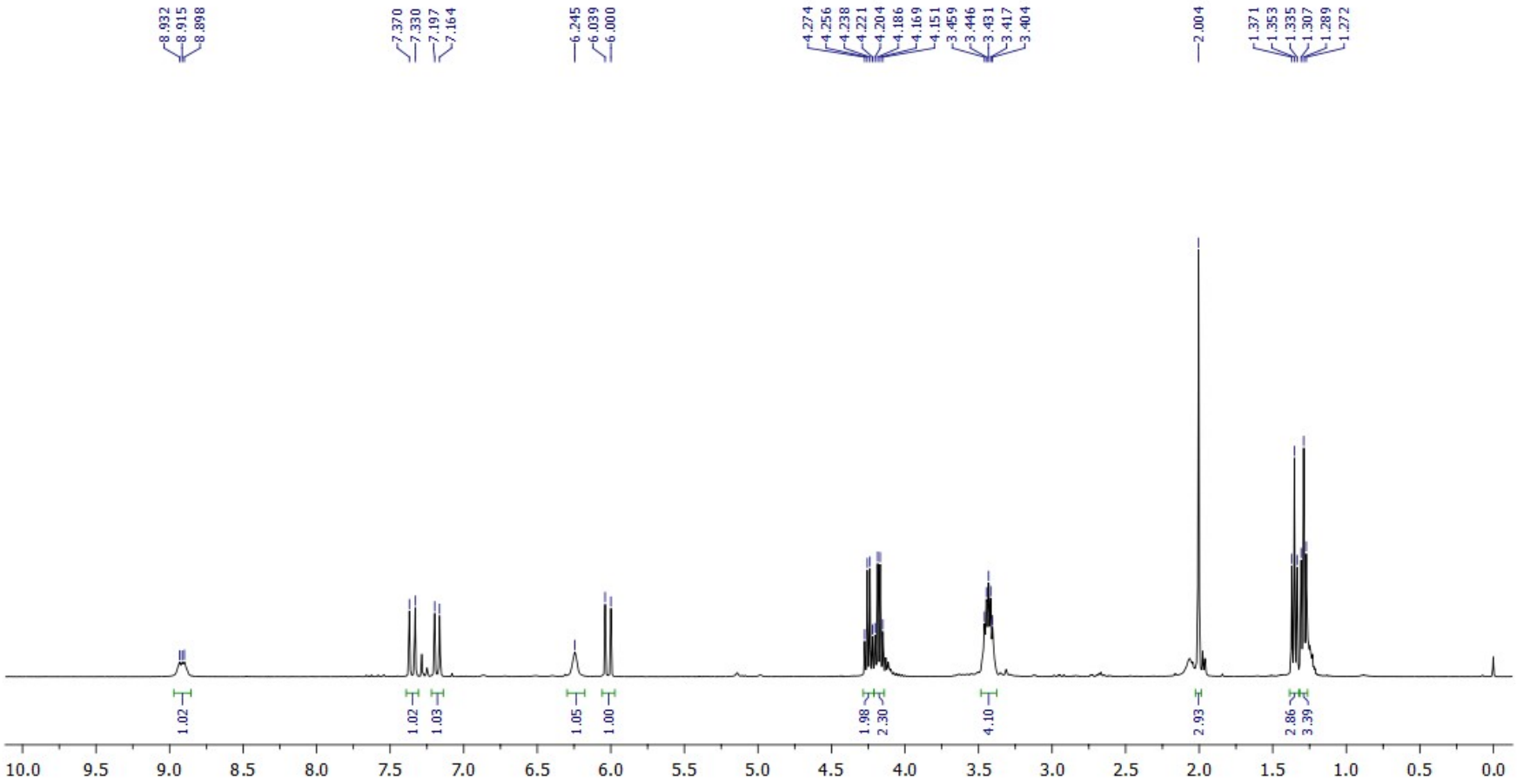
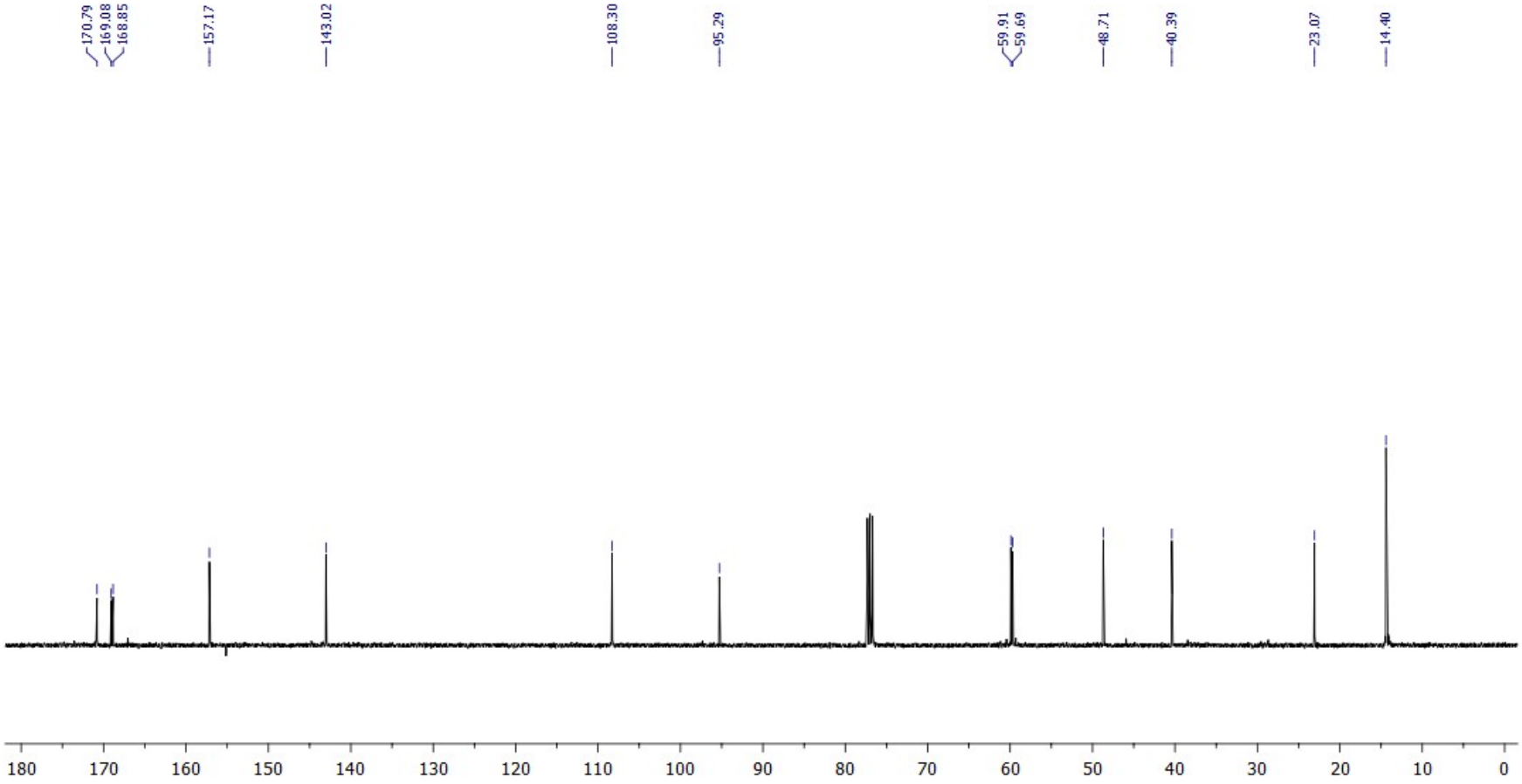
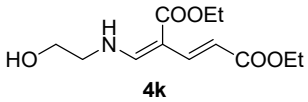


^{1}H NMR (400.1 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$)



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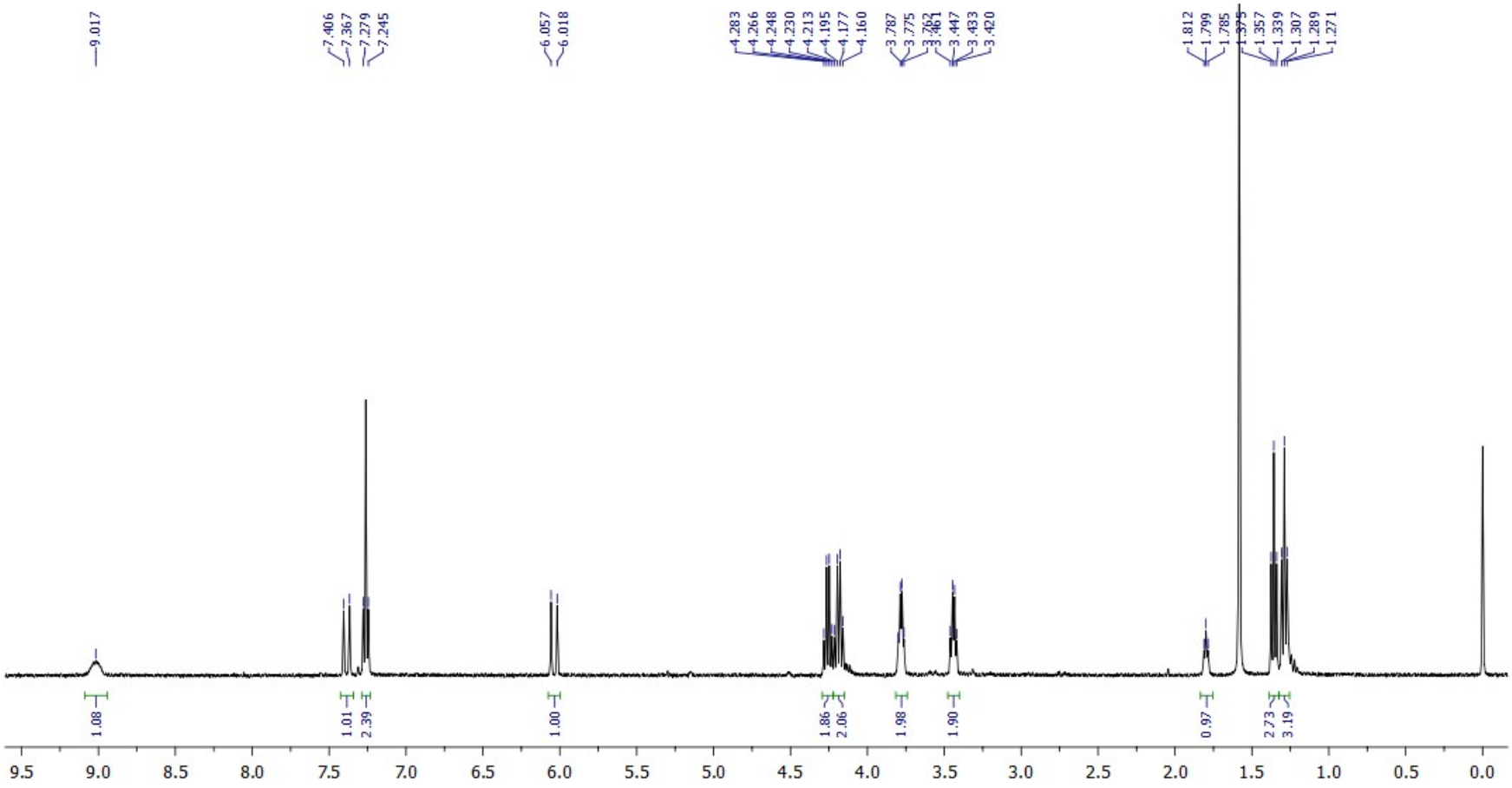
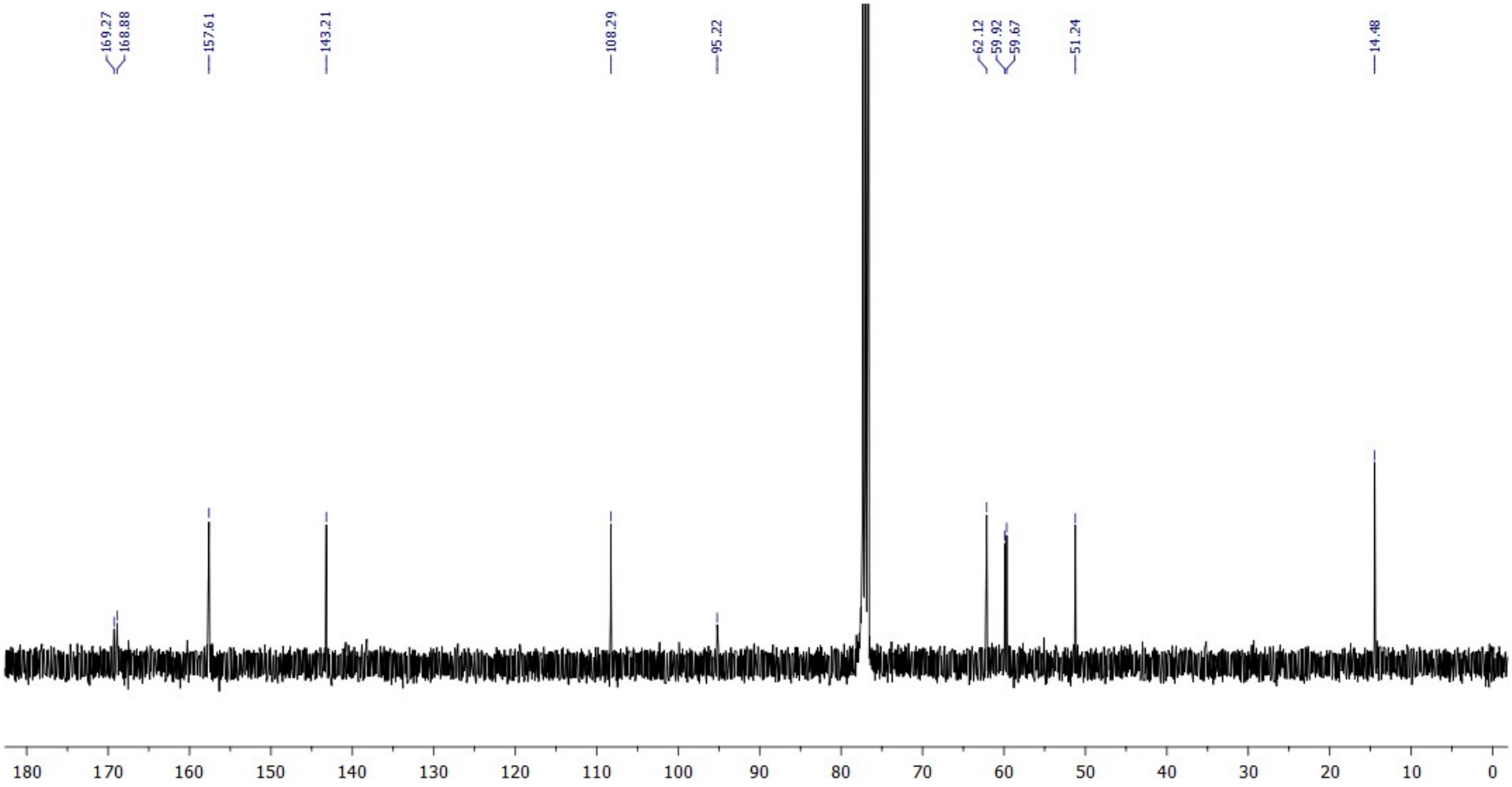
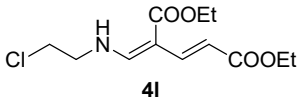


^{1}H NMR (400.1 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$)



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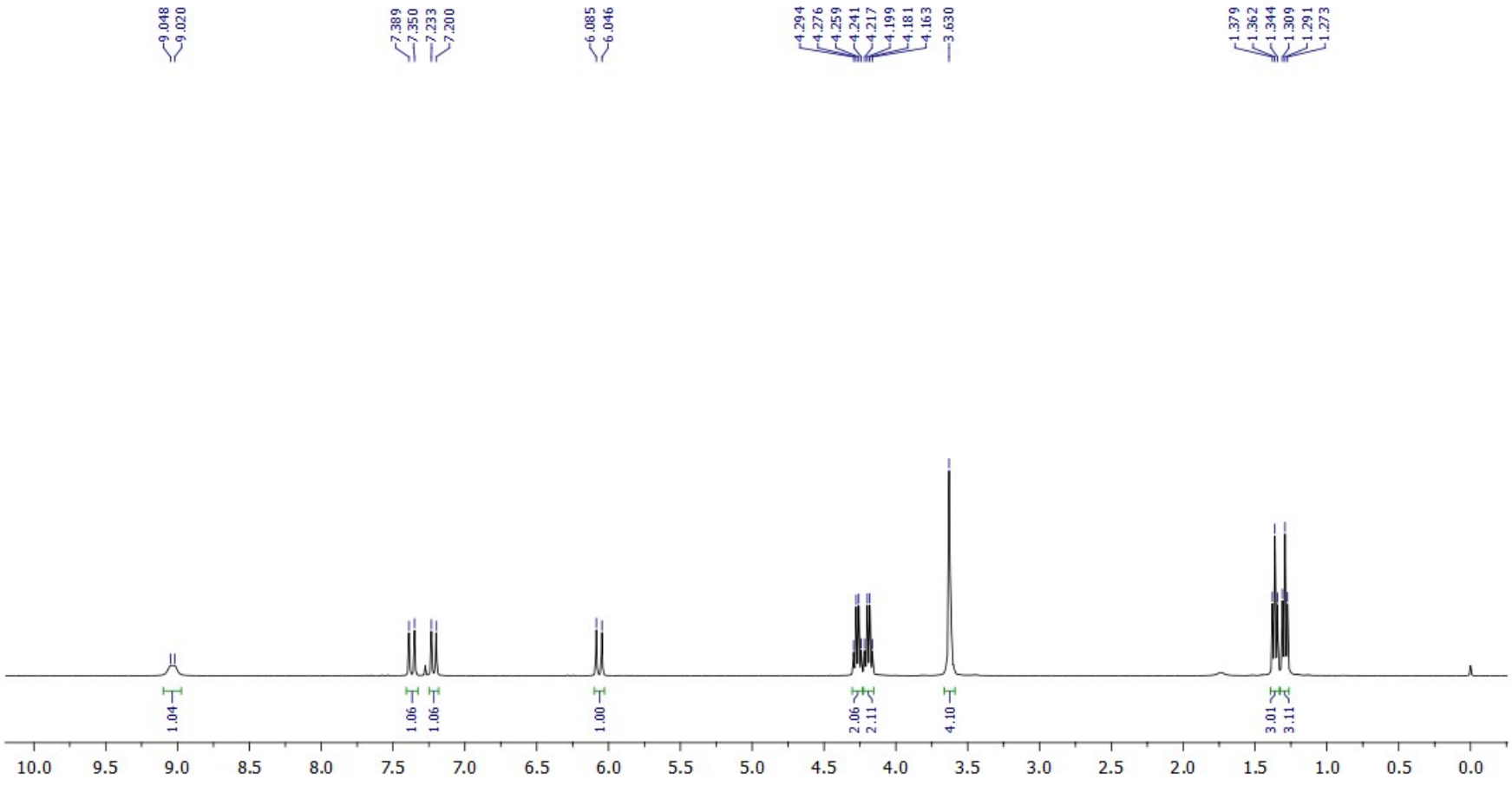
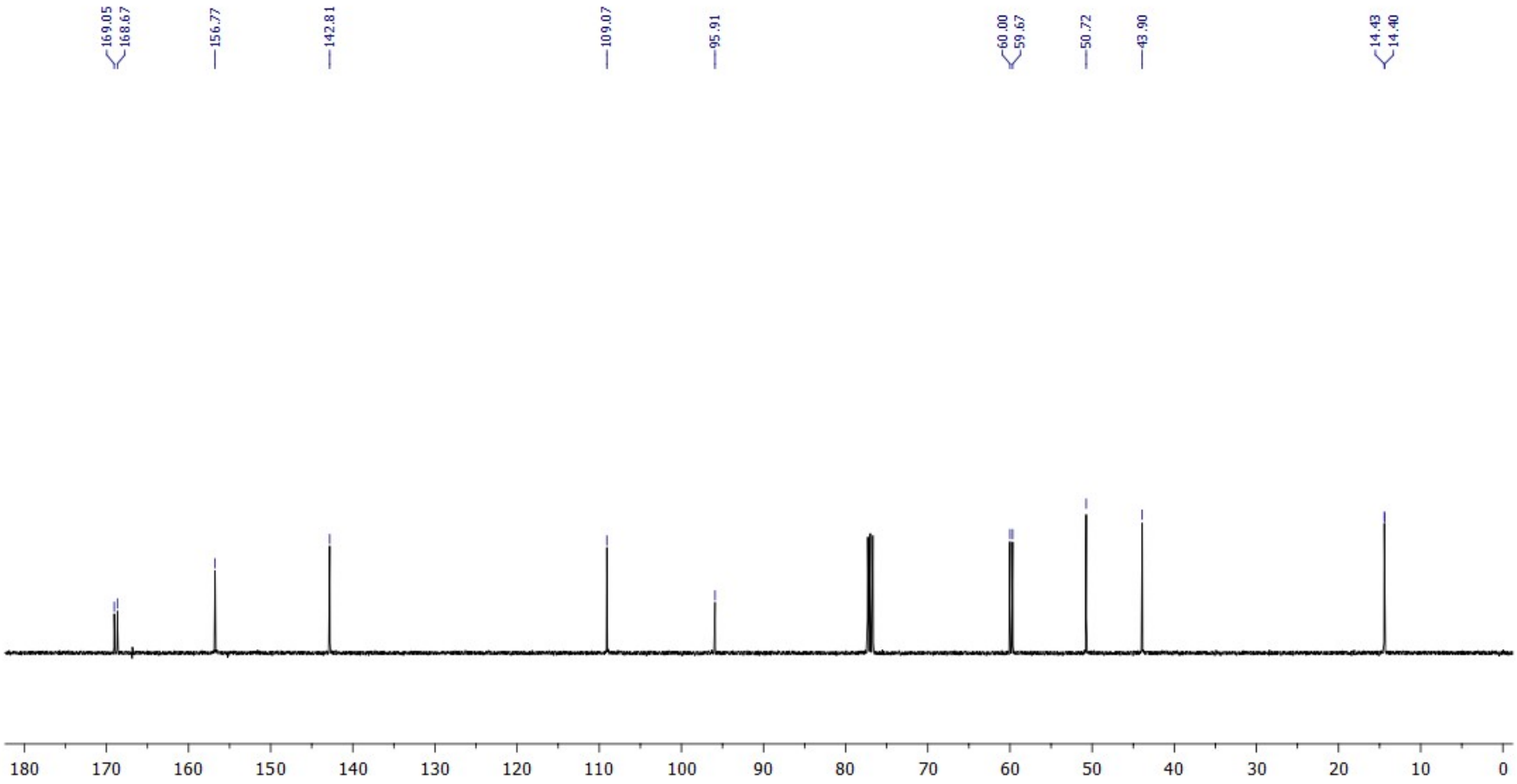
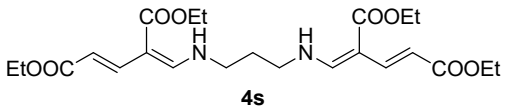


^{1}H NMR (400.1 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$)



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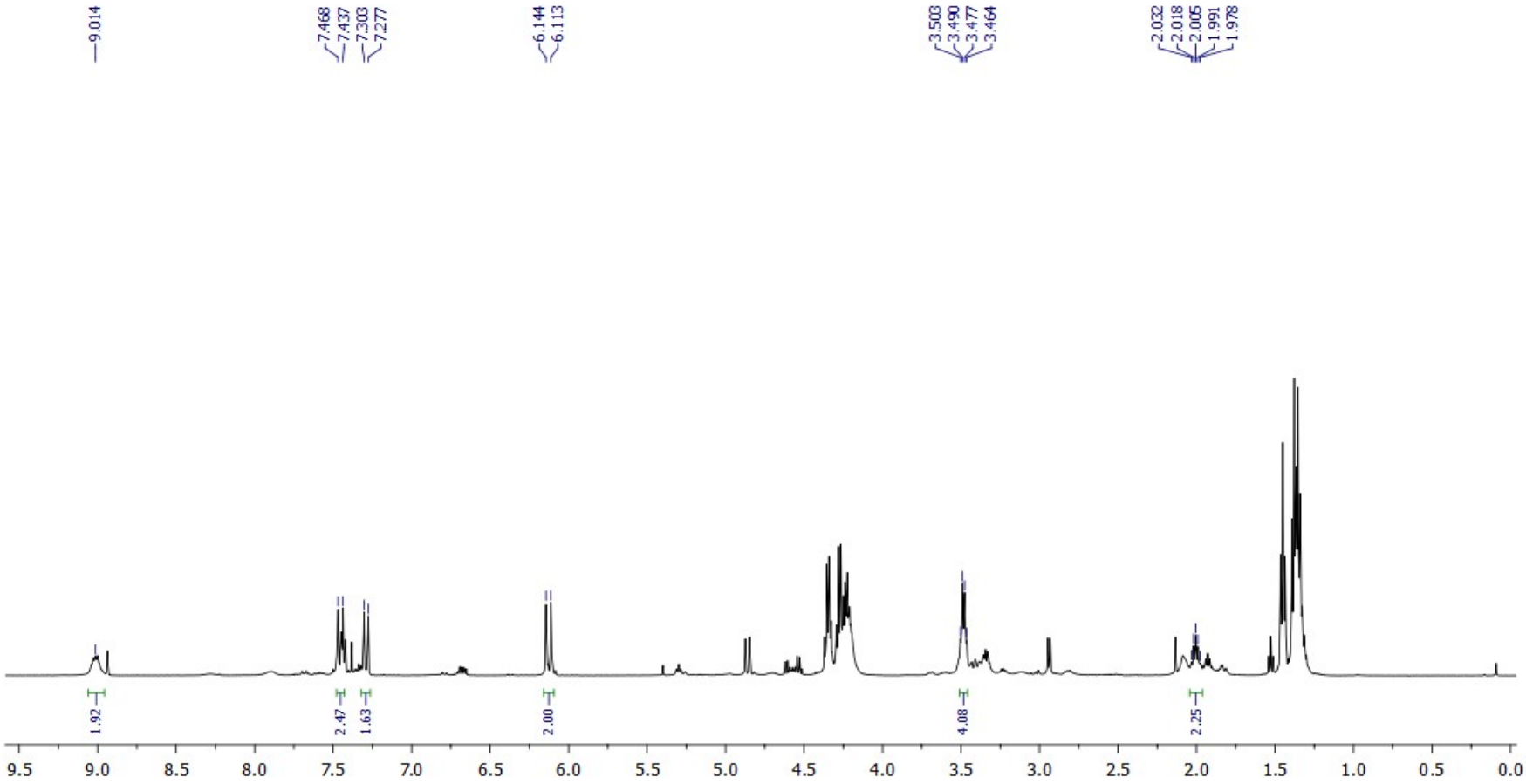
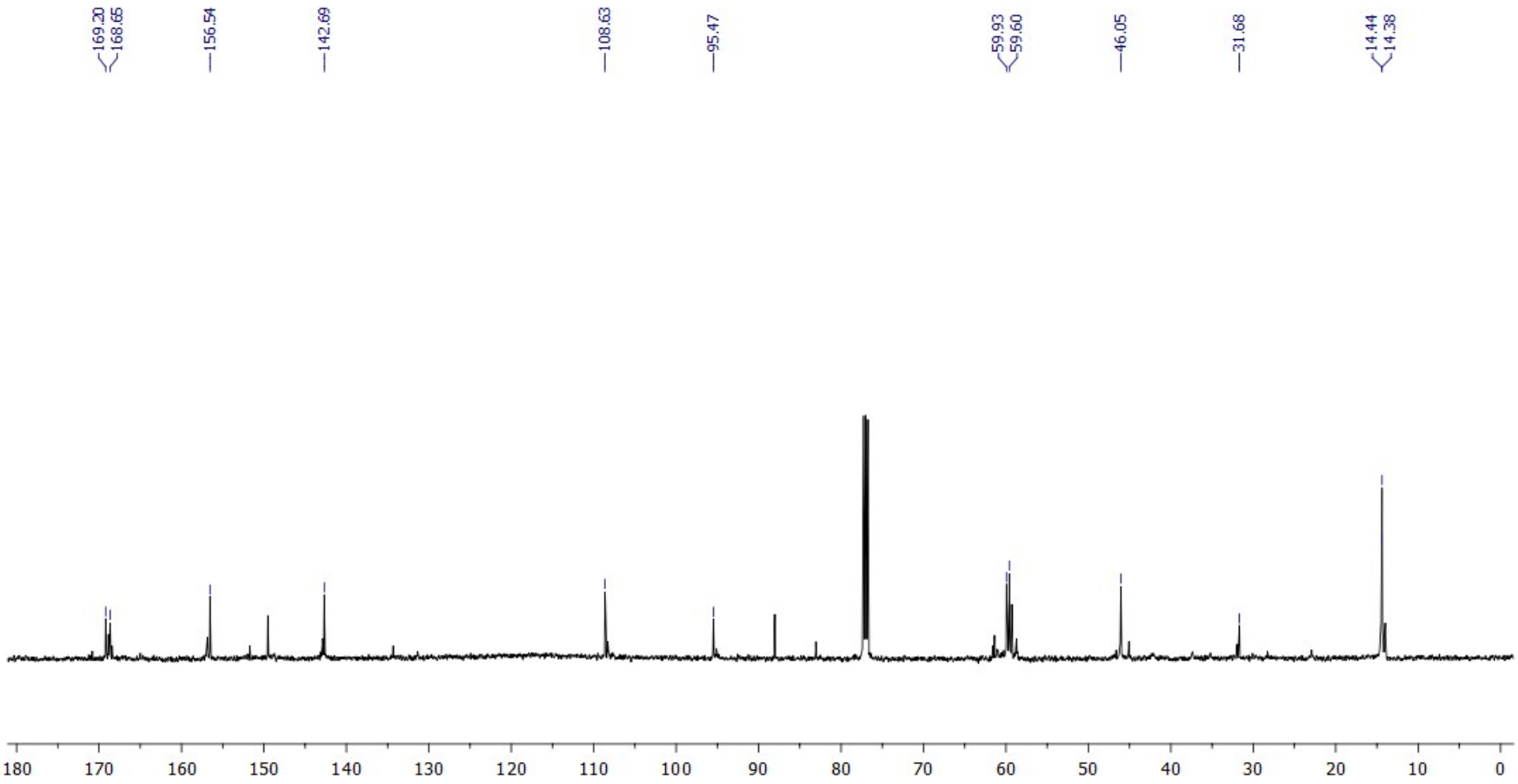
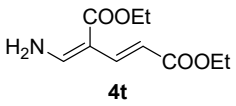


^{1}H NMR (500.3 MHz, $CDCl_3$, reaction mixture, signals indicating a diene are marked)



$^{13}C\{^{1}H\}$ NMR (125.8 MHz, $CDCl_3$, reaction mixture, signals indicating a diene are marked)



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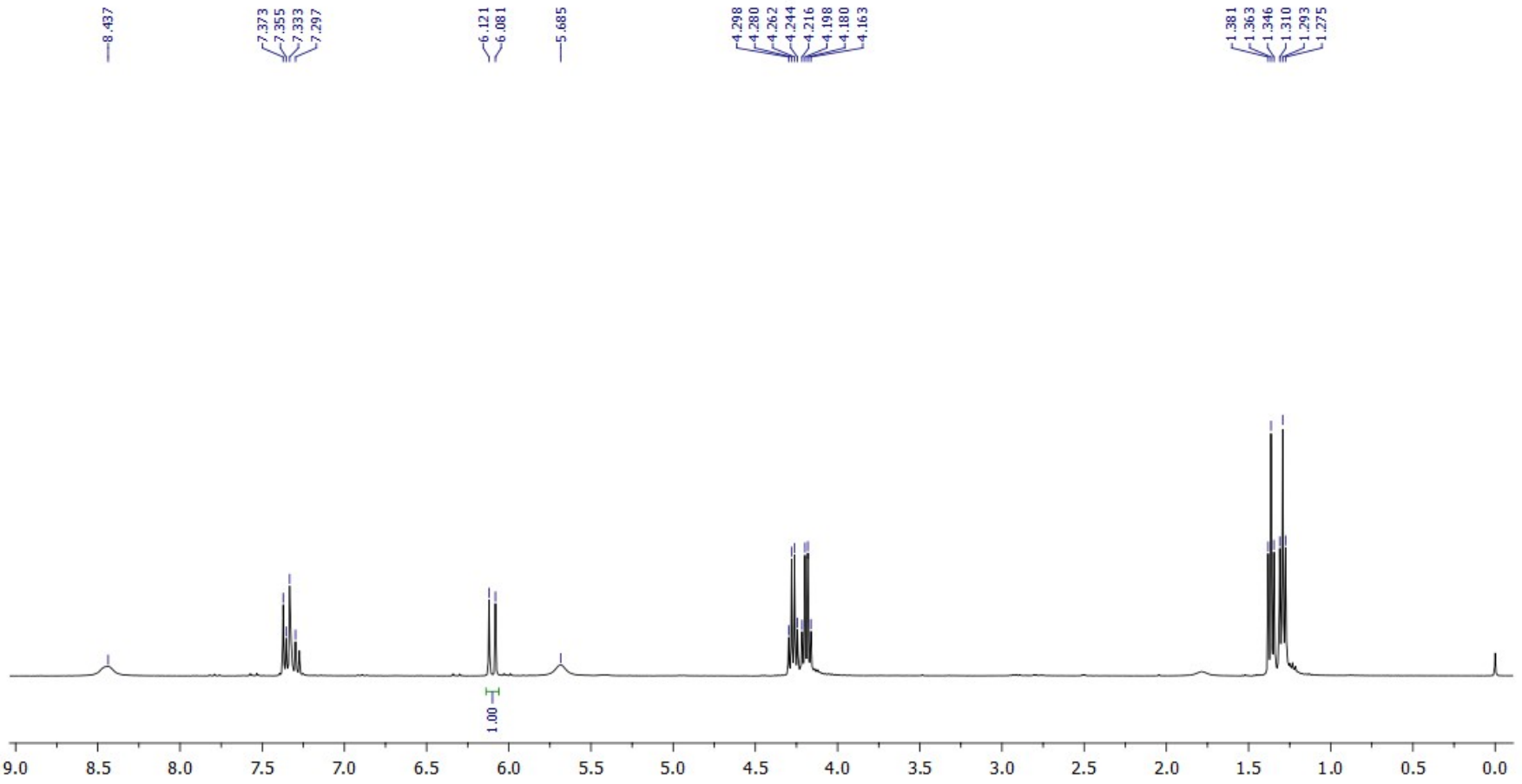
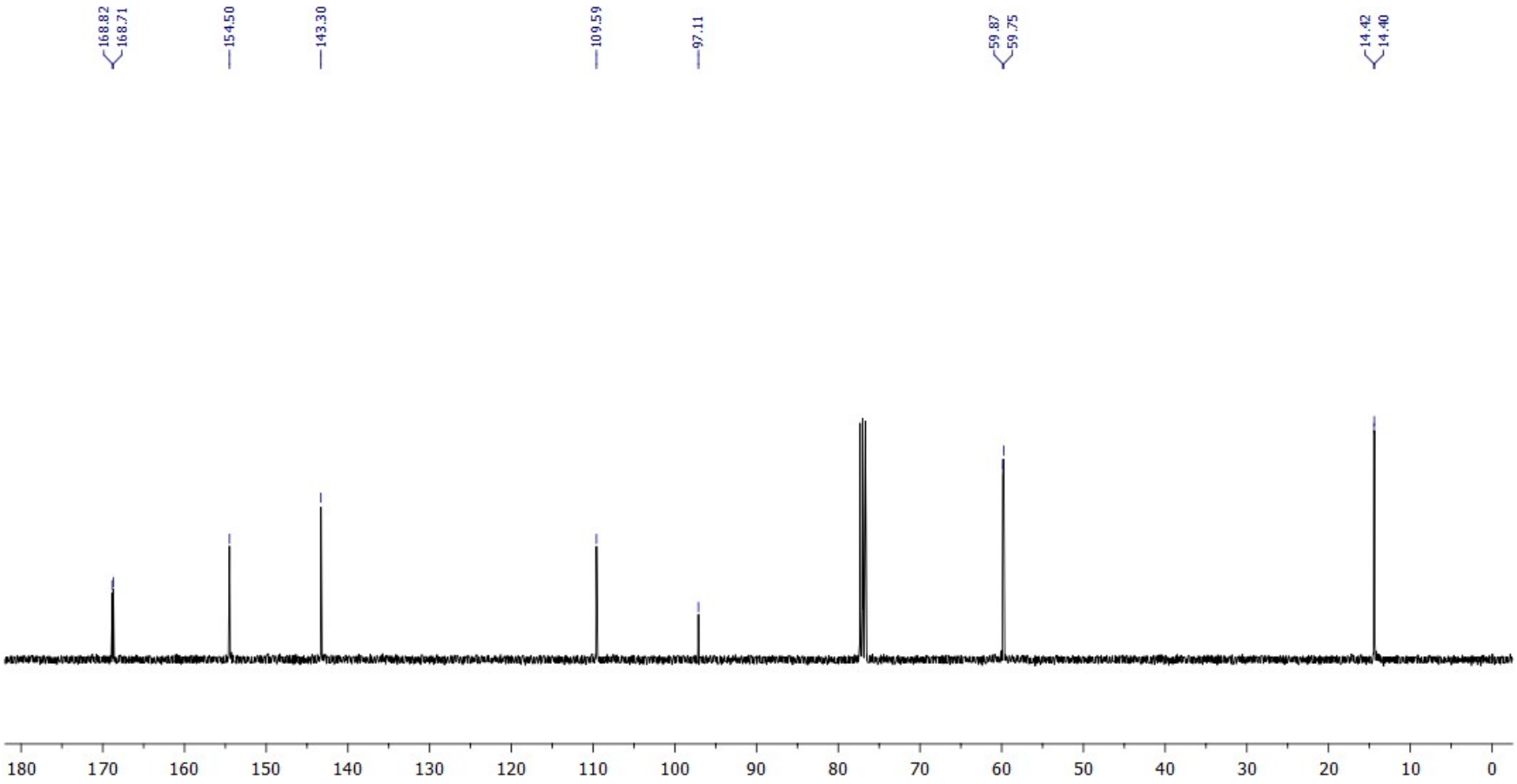
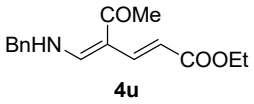


^{1}H NMR (400.1 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$)



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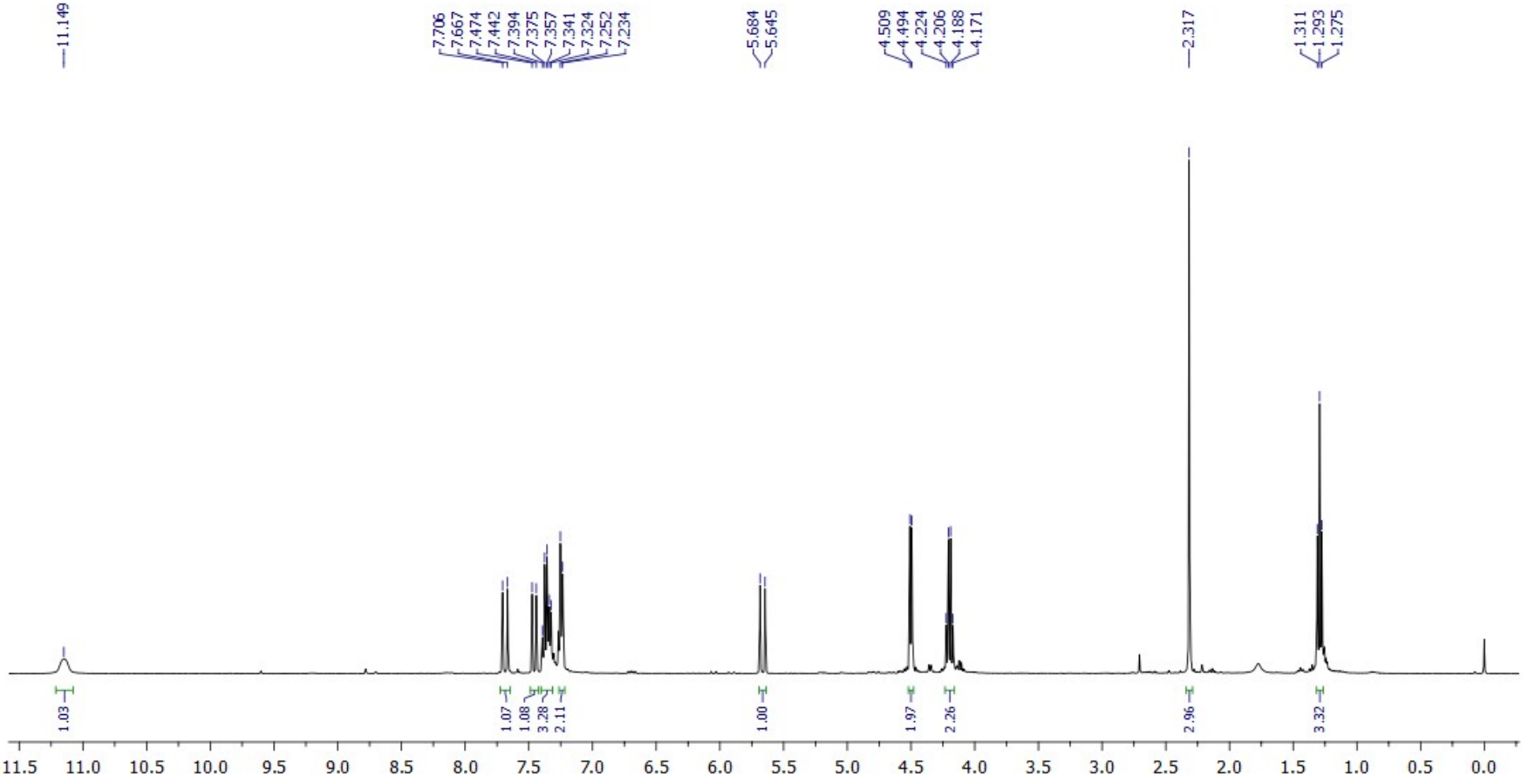
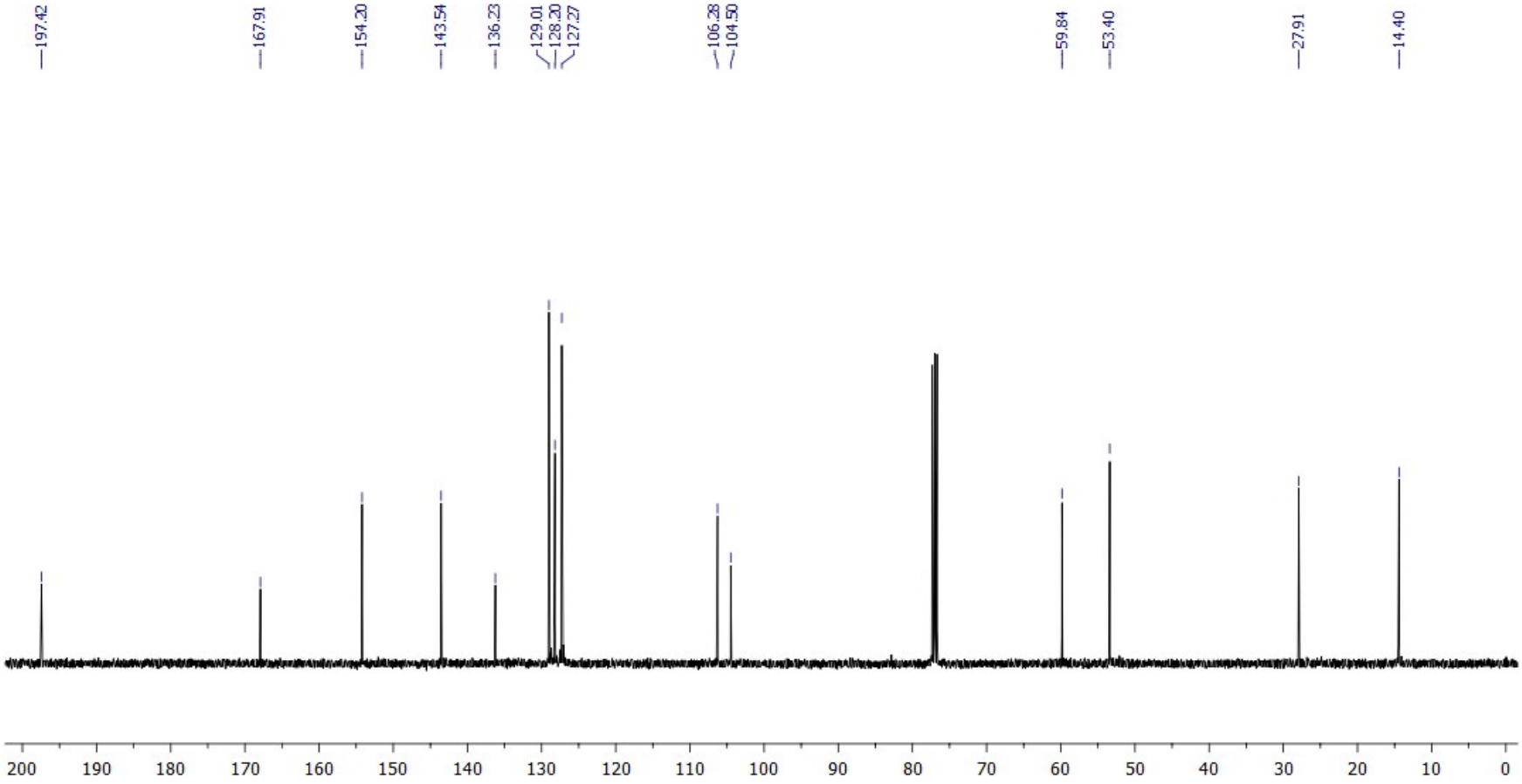
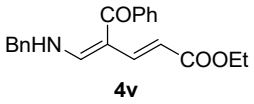


^{1}H NMR (400.1 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$)



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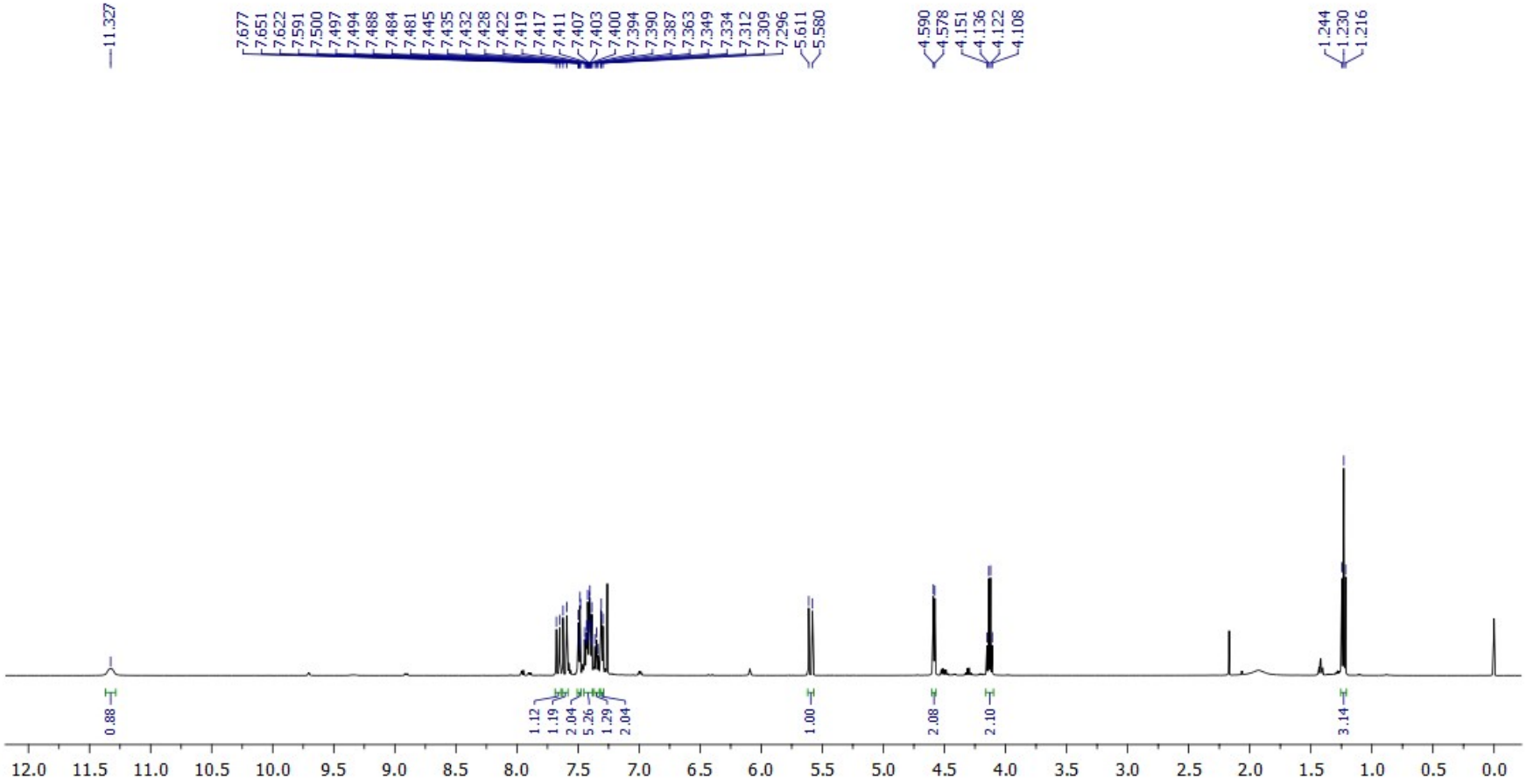
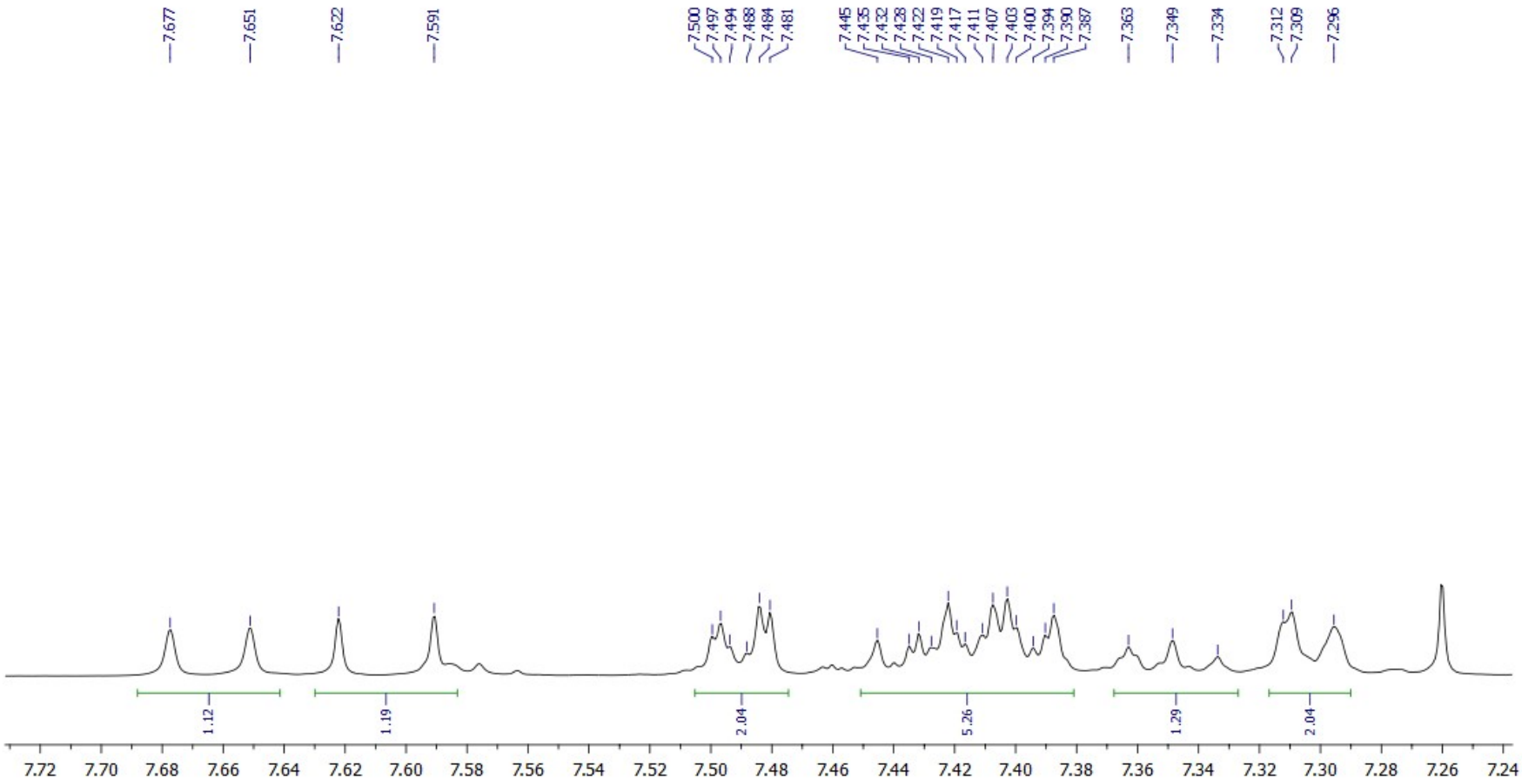
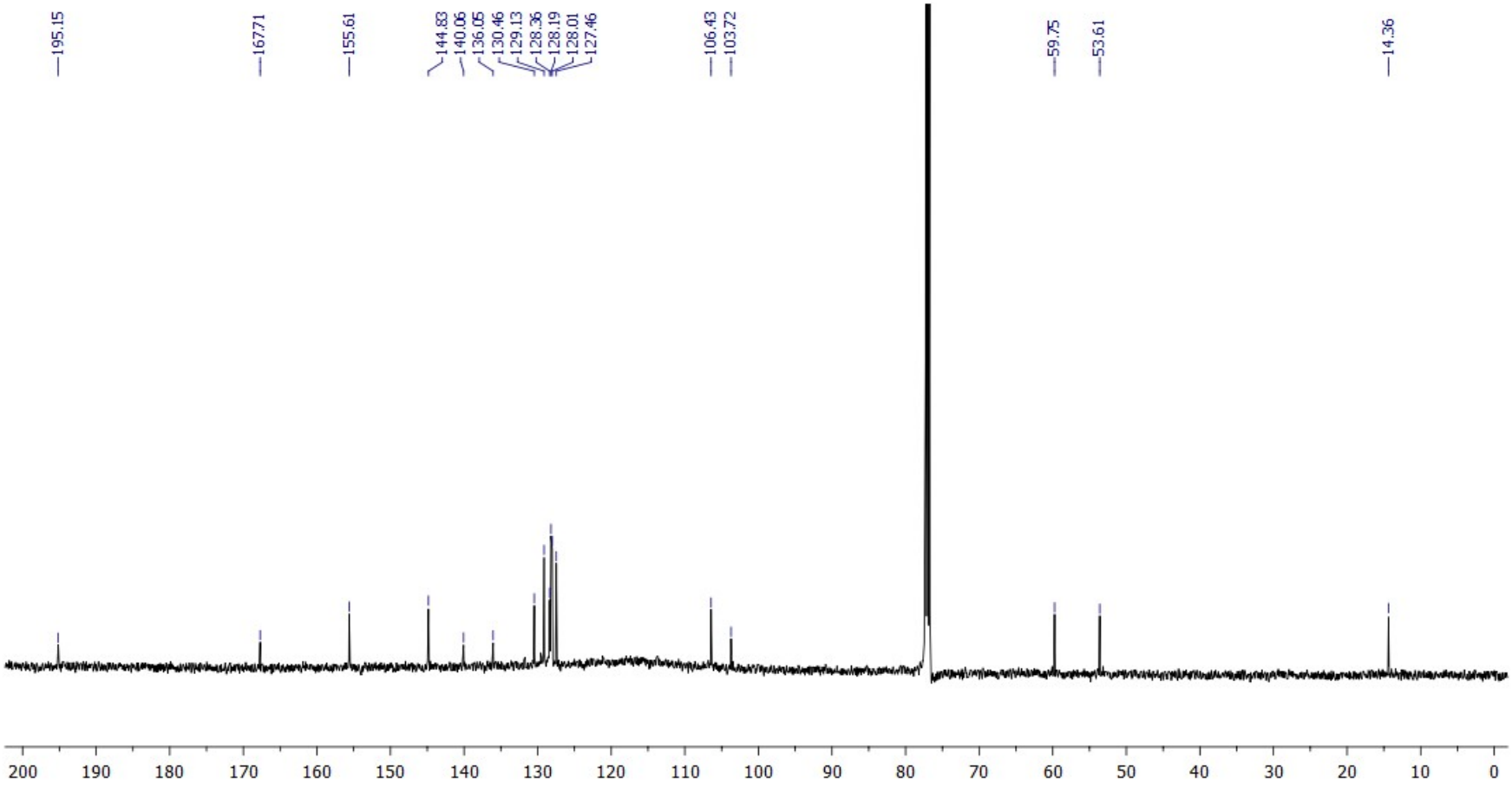


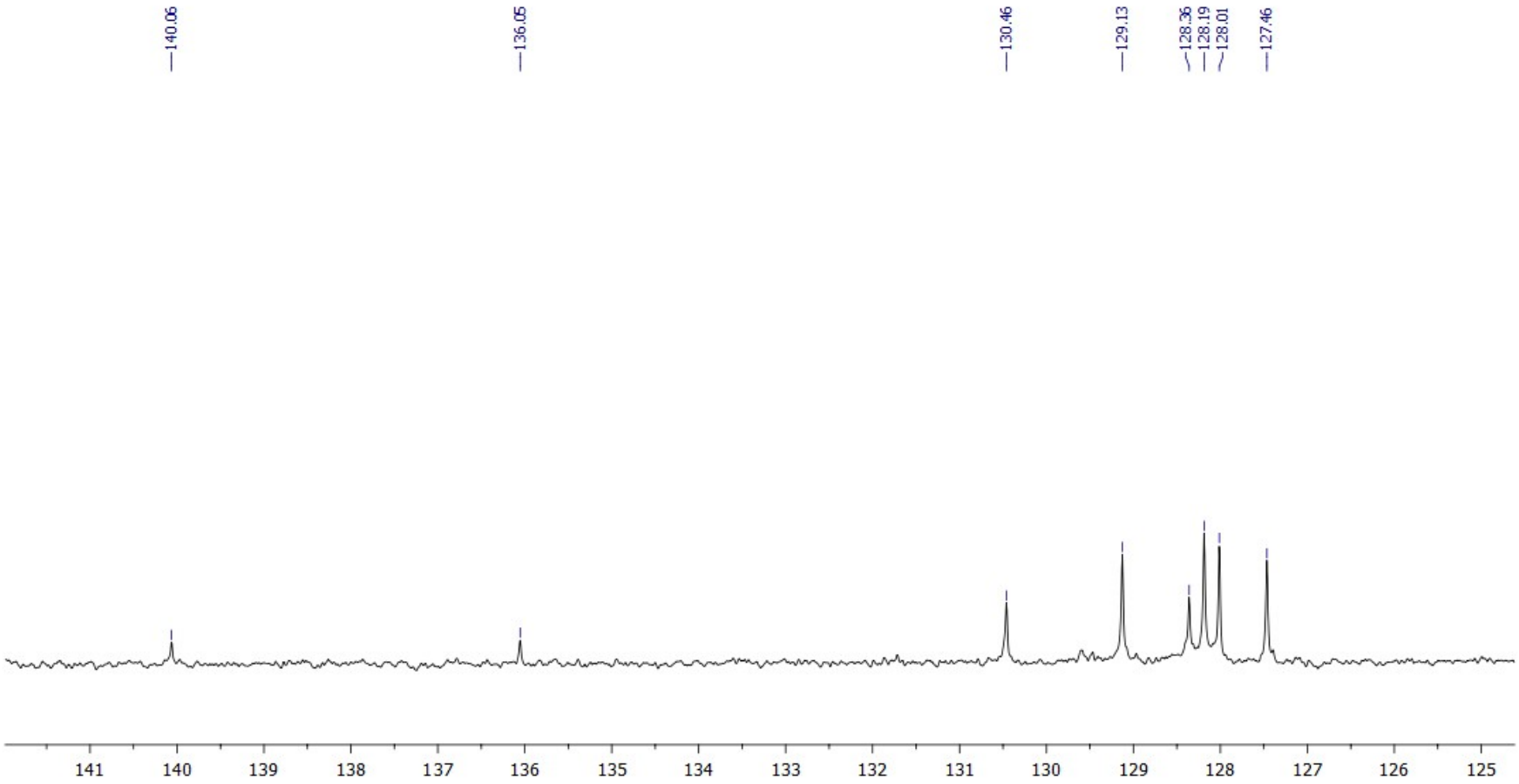
^{1}H NMR (500.3 MHz, $CDCl_3$)



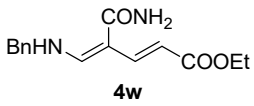
^{1}H NMR (500.3 MHz, $CDCl_3$) expanded aromatic region



$^{13}C\{^{1}H\}$ NMR (125.8 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (125.8 MHz, $CDCl_3$) expanded aromatic region



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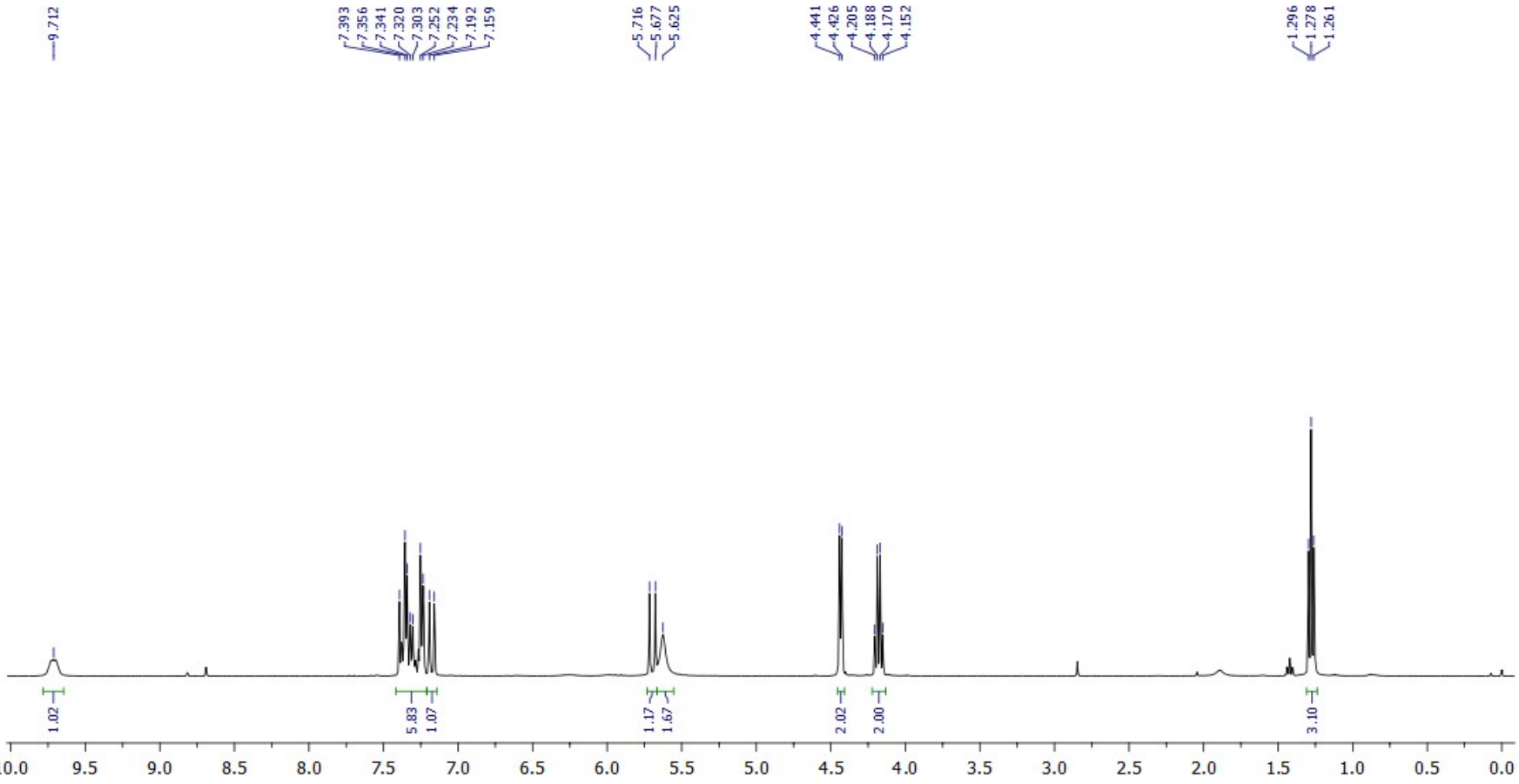
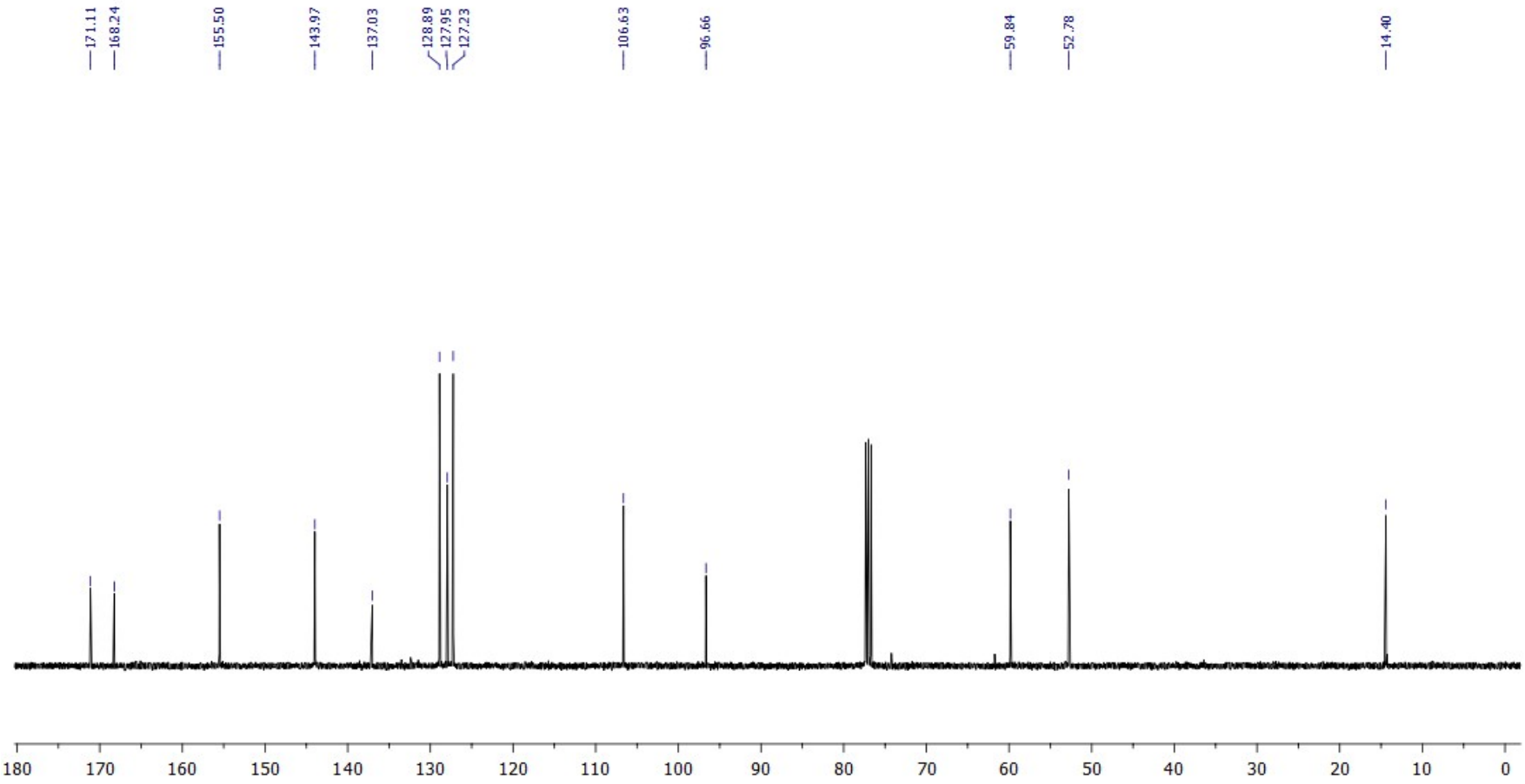
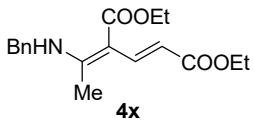


^{1}H NMR (400.1 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$)



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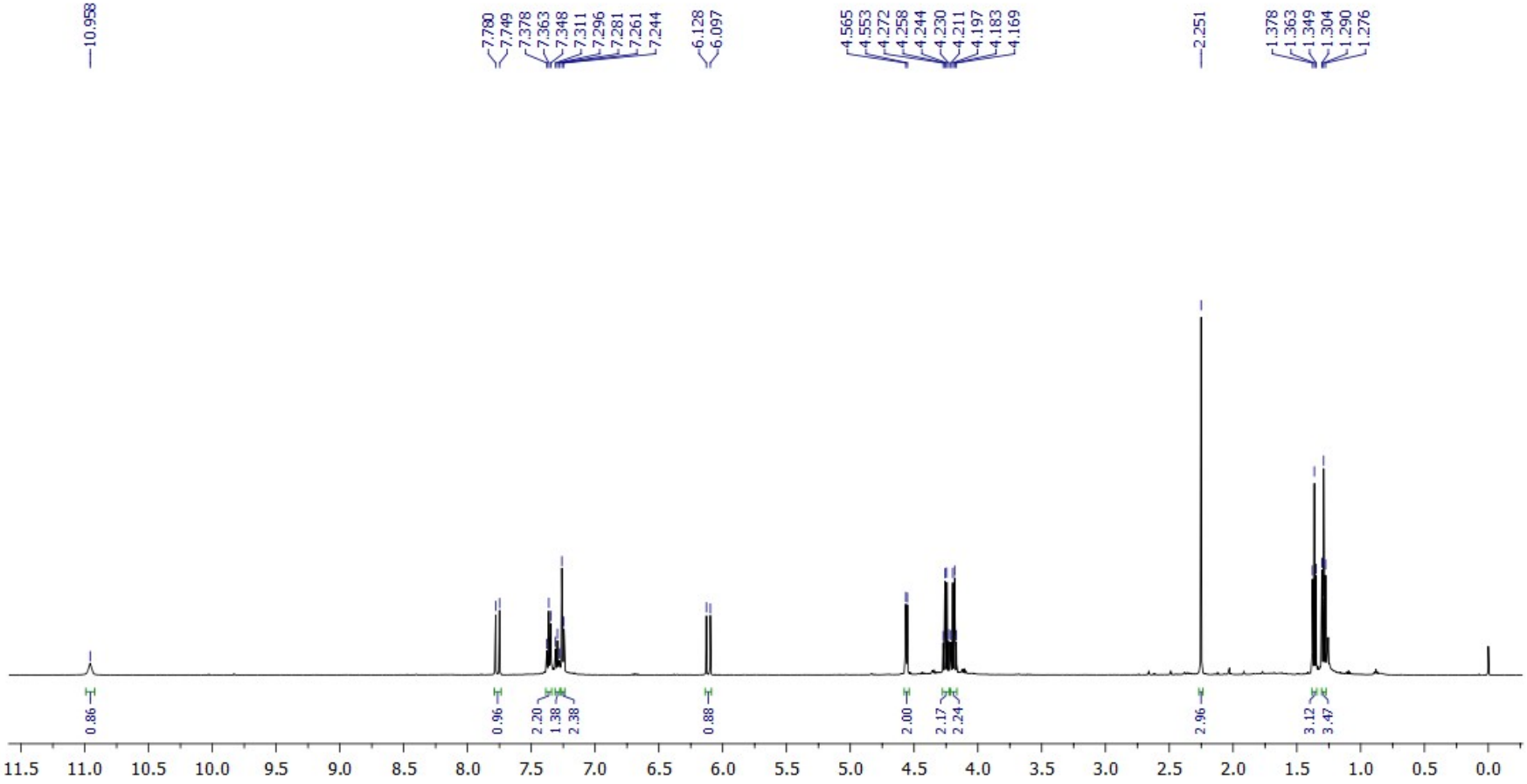
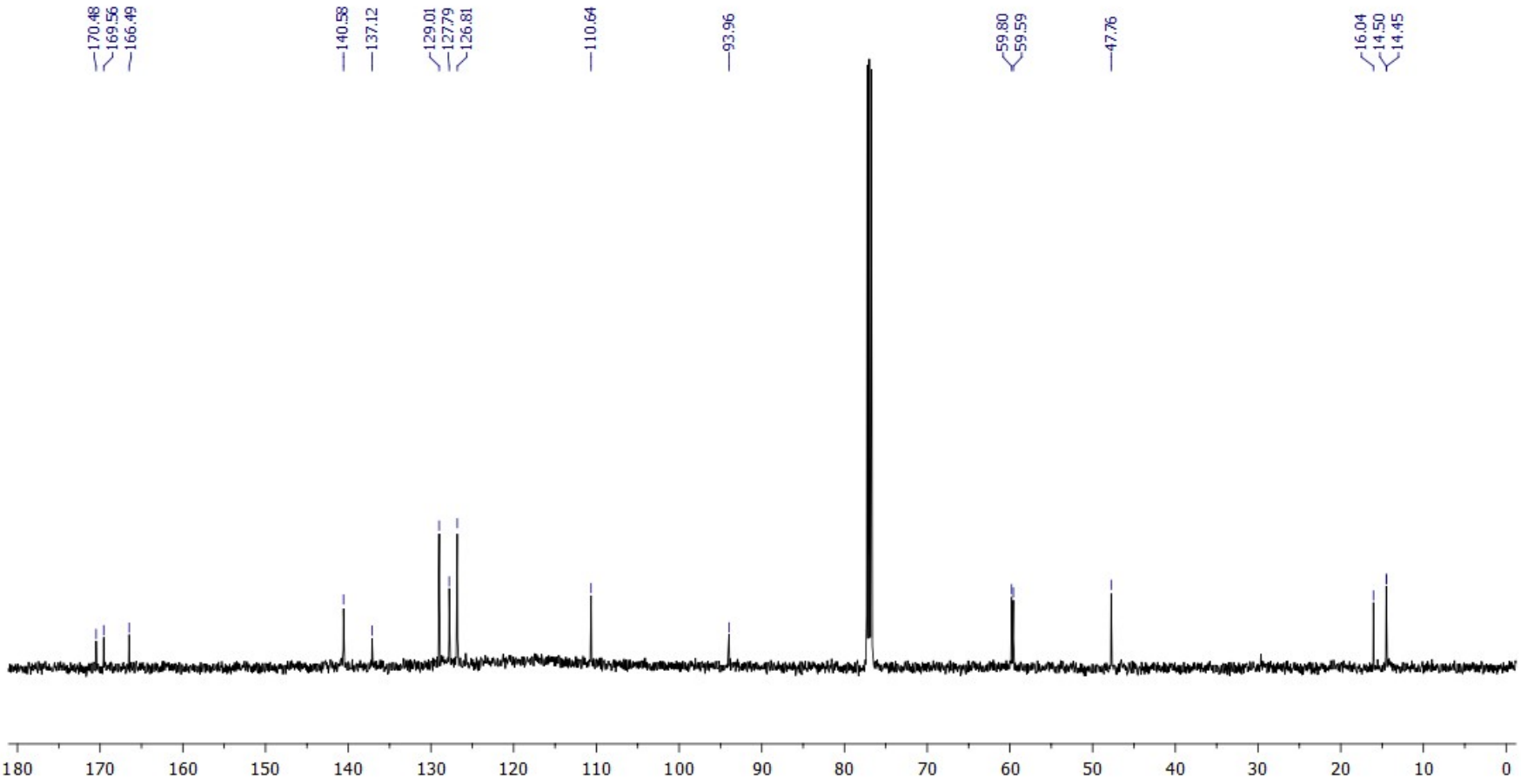
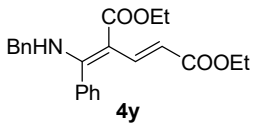


^{1}H NMR (500.3 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (125.8 MHz, $CDCl_3$)



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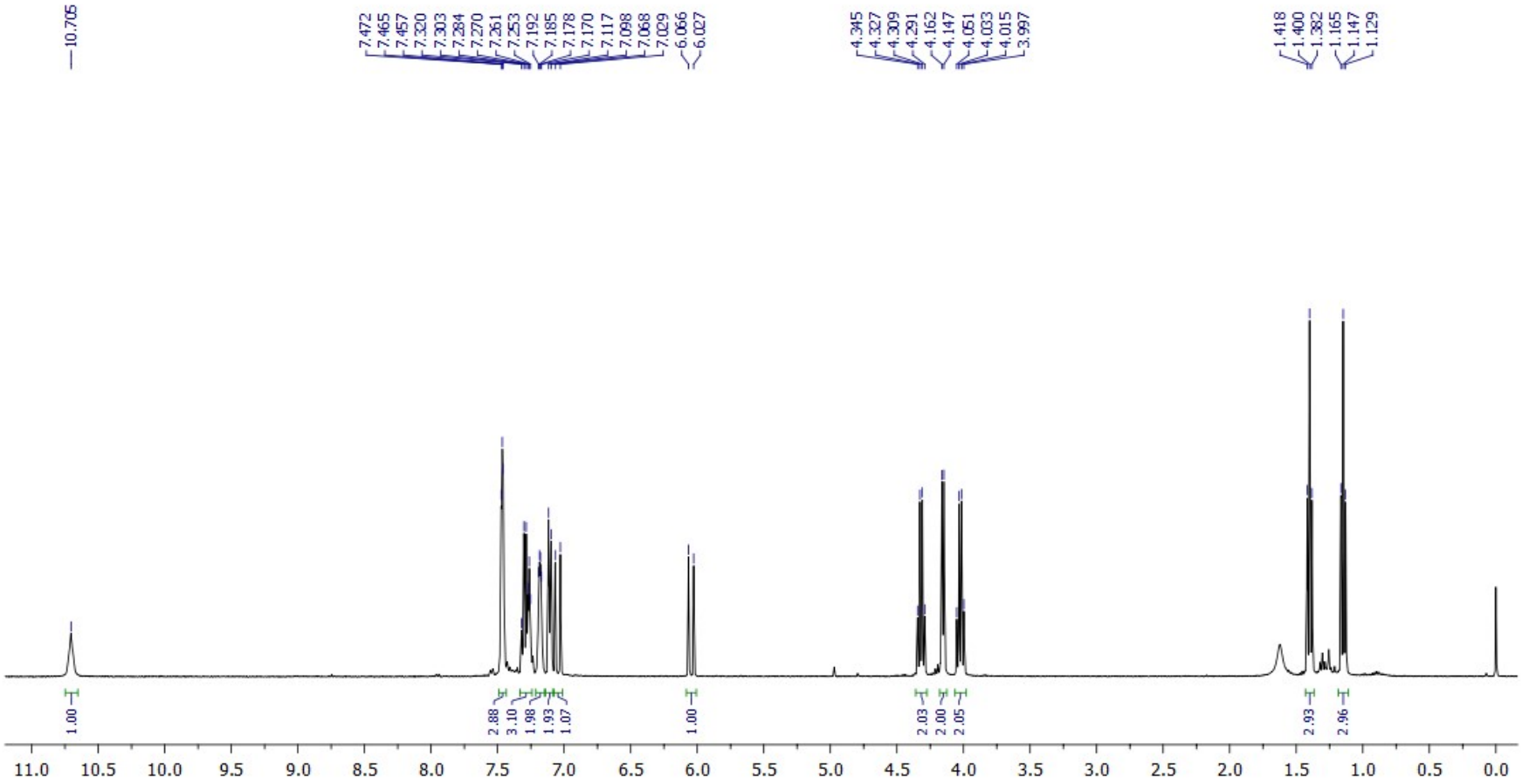
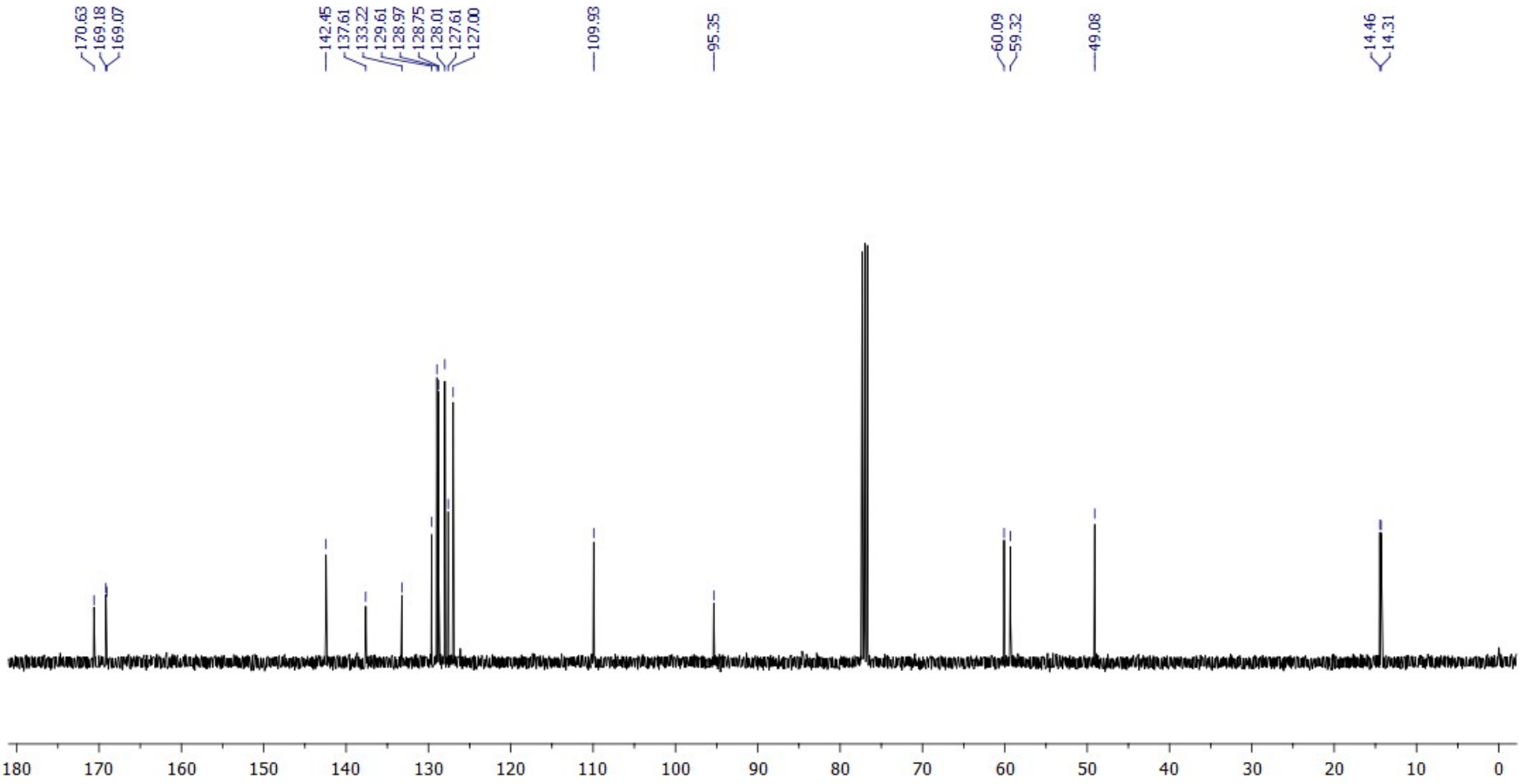
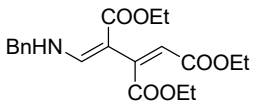


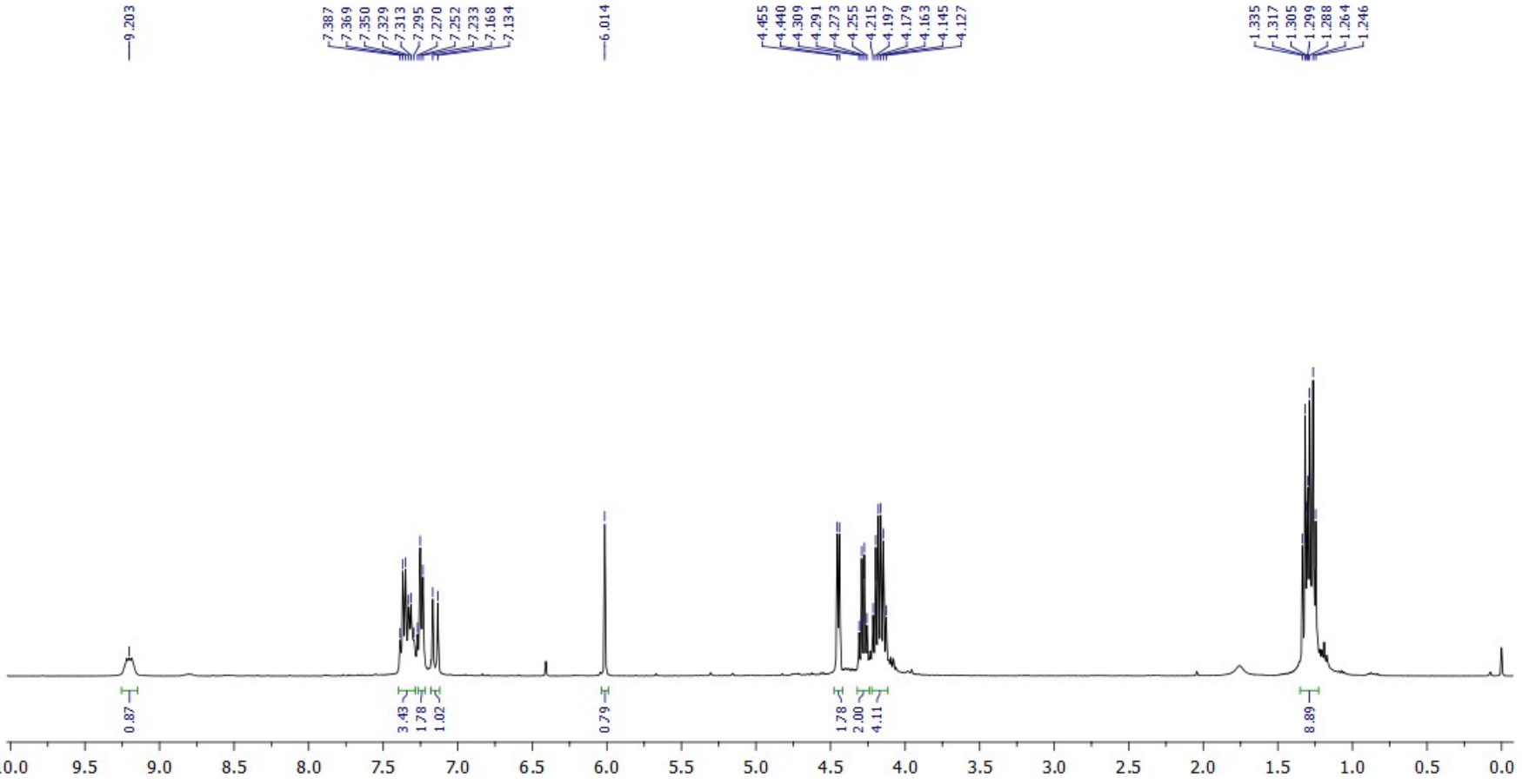
^{1}H NMR (400.1 MHz, $CDCl_3$)



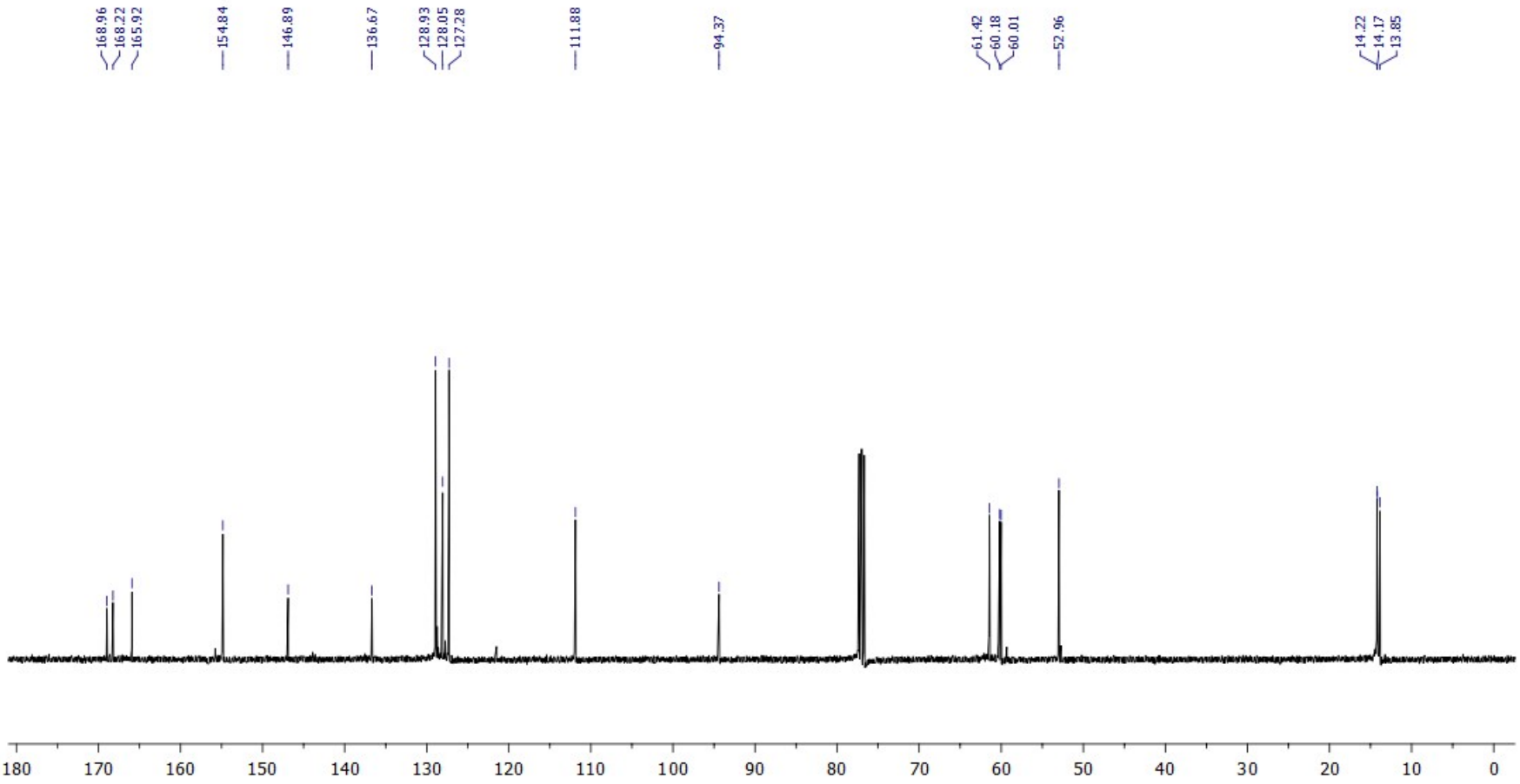
$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$)



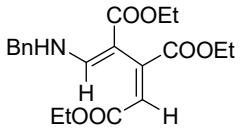
4za-*1Z,3Z*



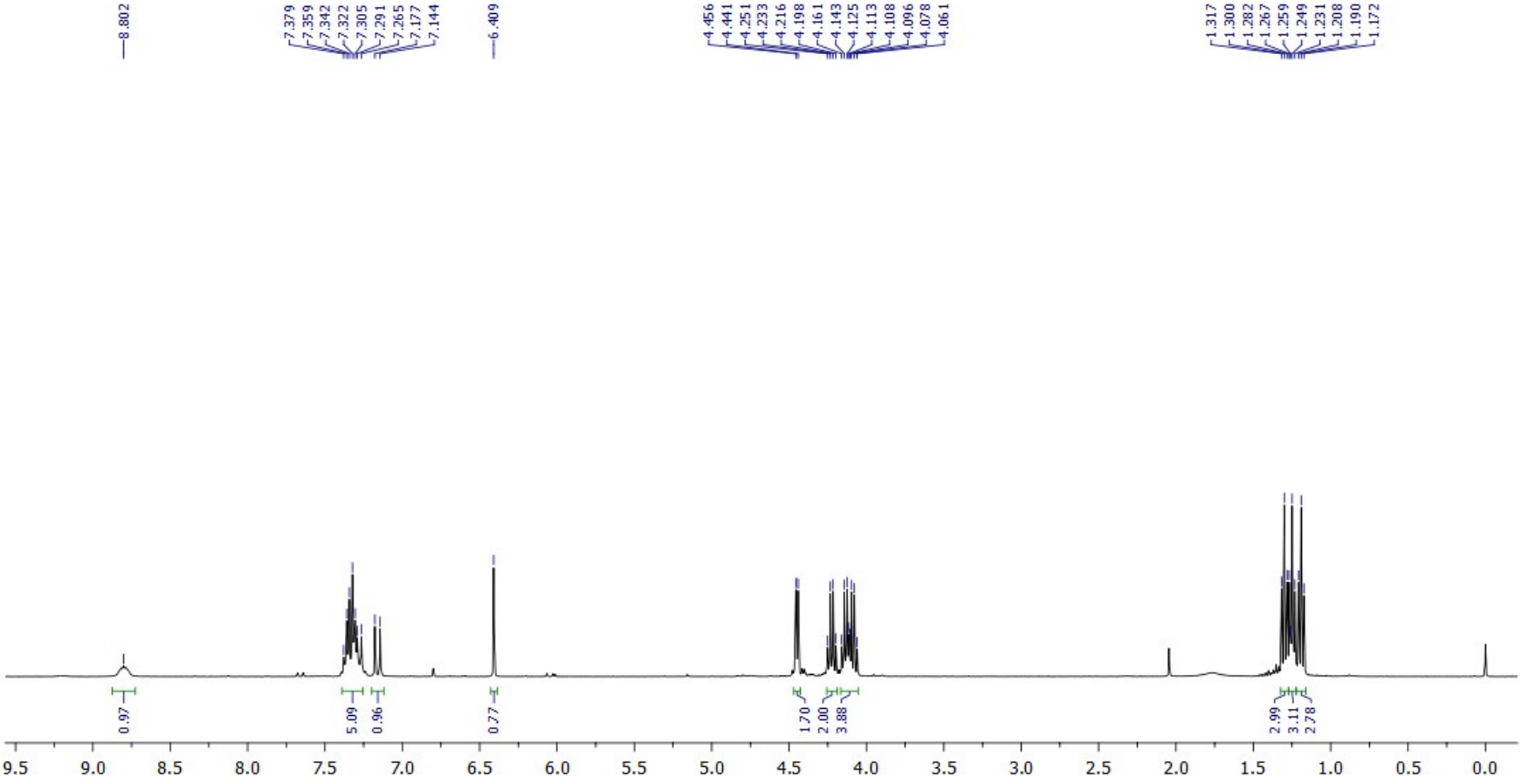
^{1}H NMR (400.1 MHz, $CDCl_3$)



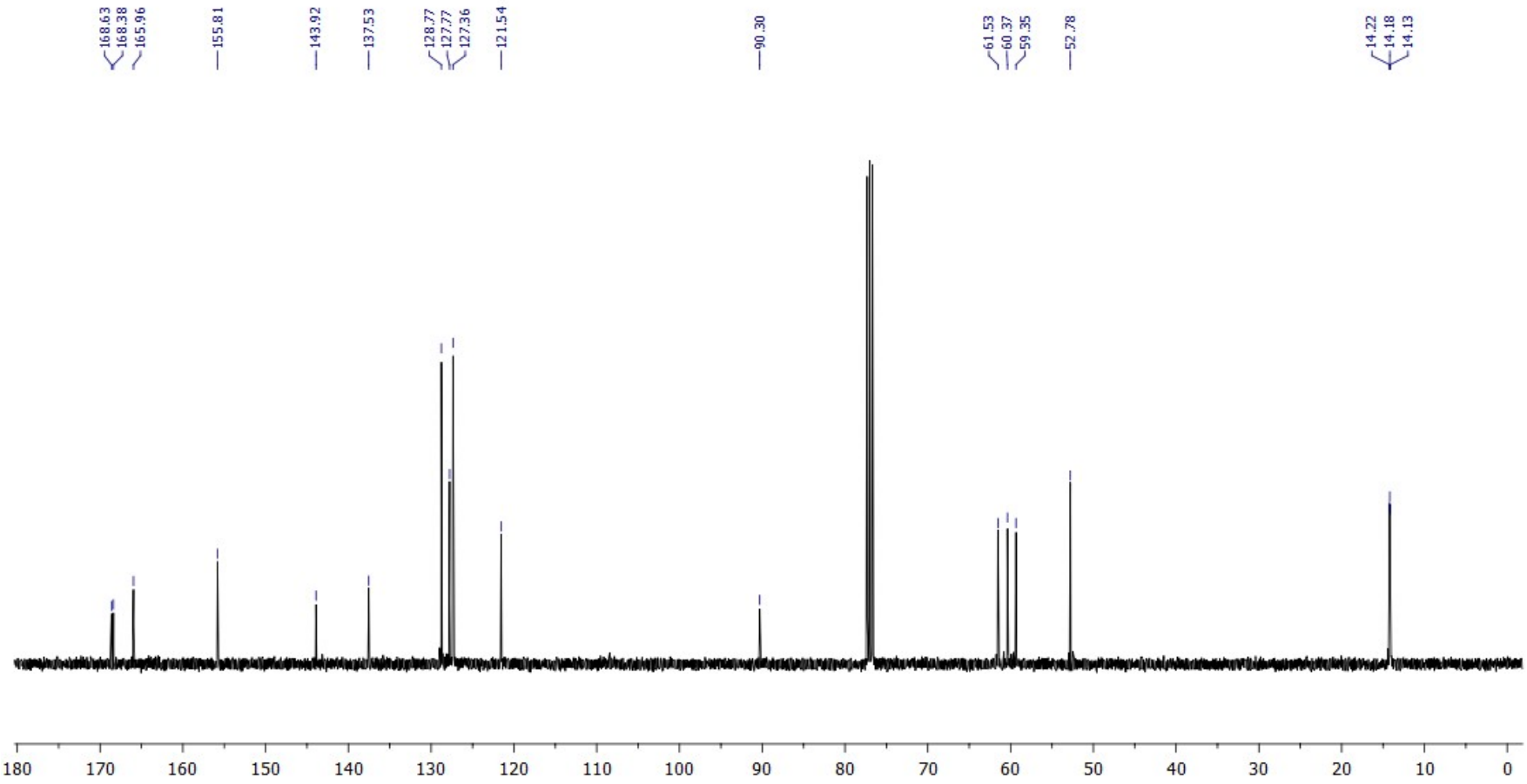
$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$)



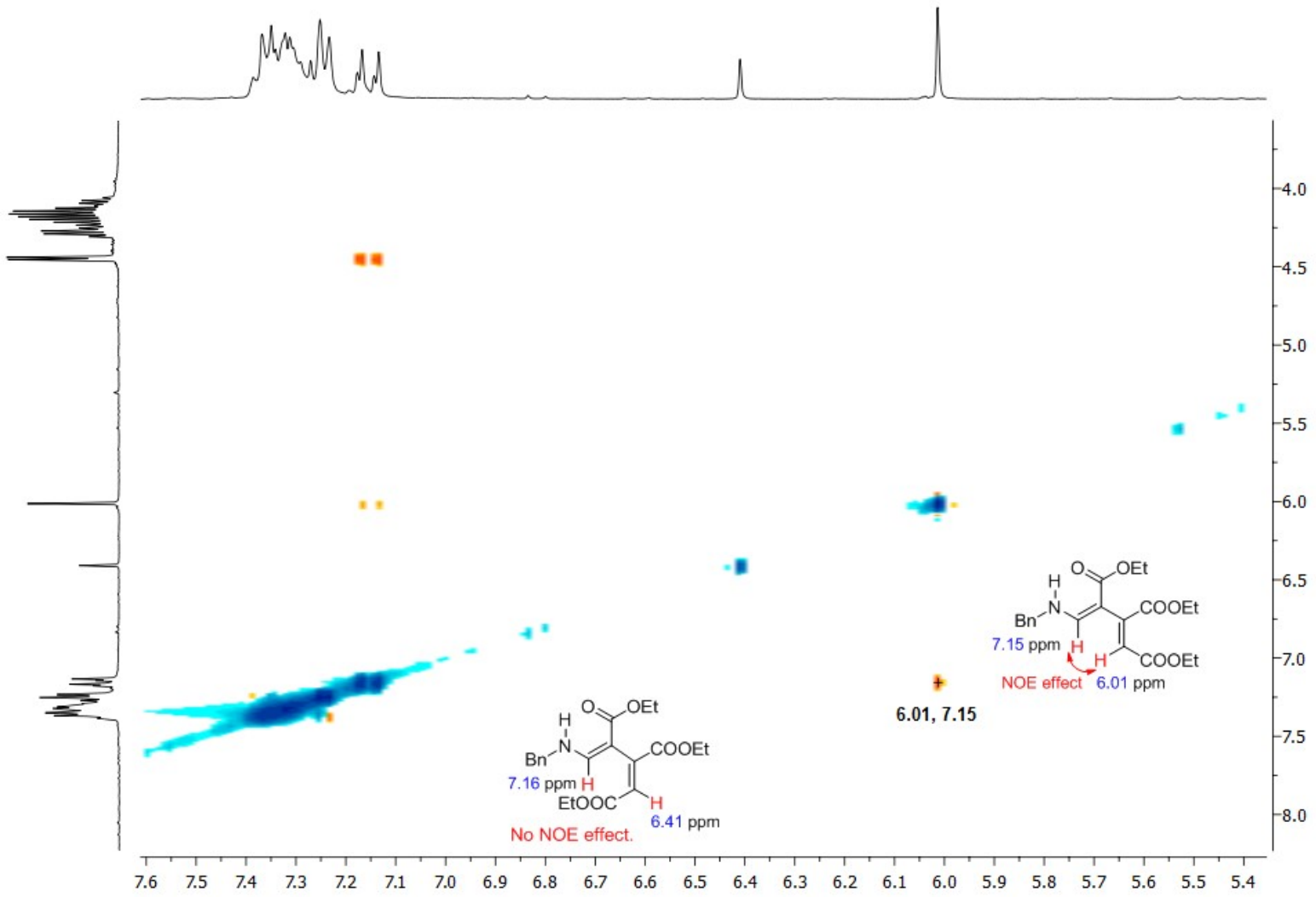
4za-*1E,3Z*



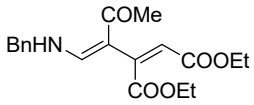
^{1}H NMR (400.1 MHz, $CDCl_3$)



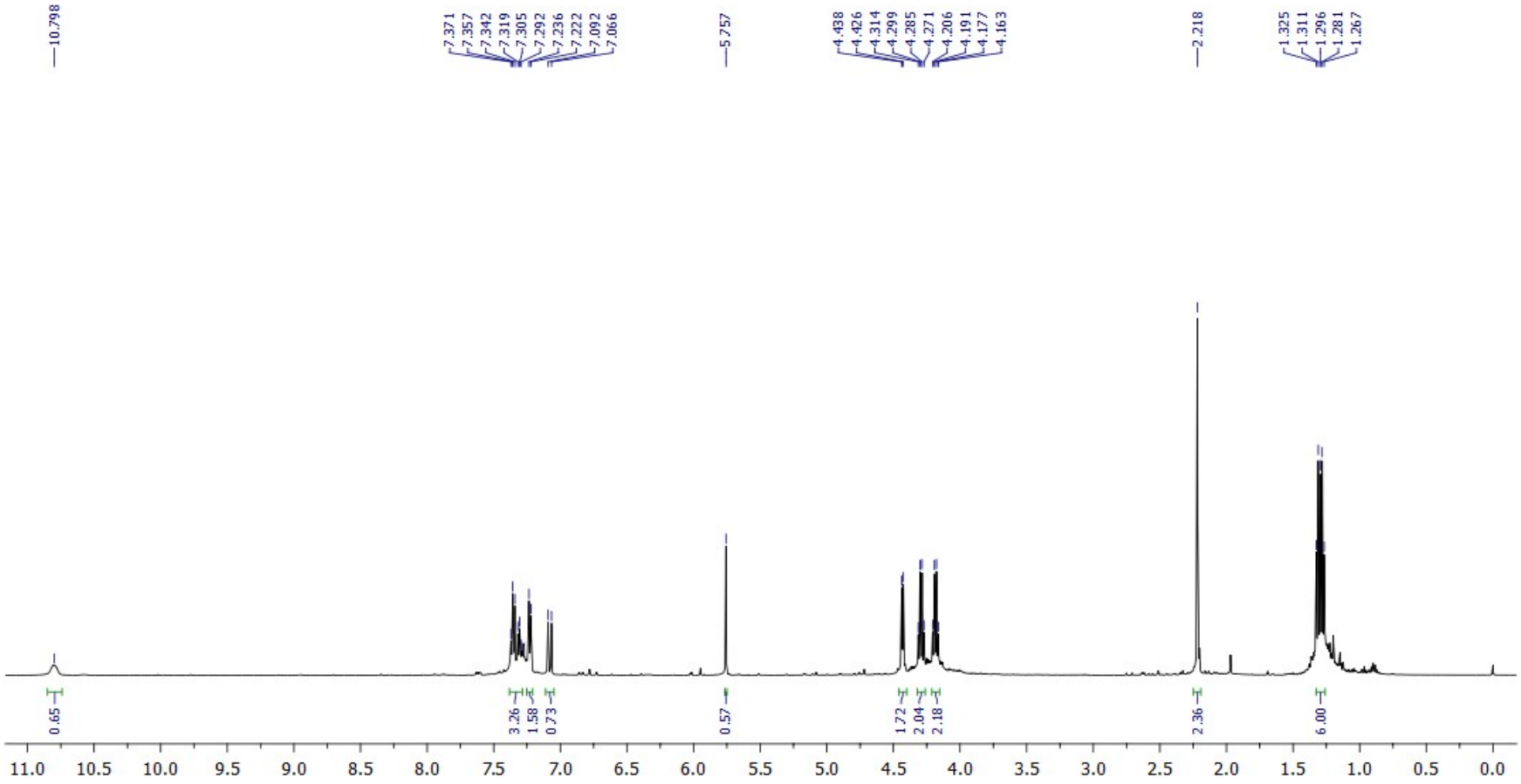
$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$)



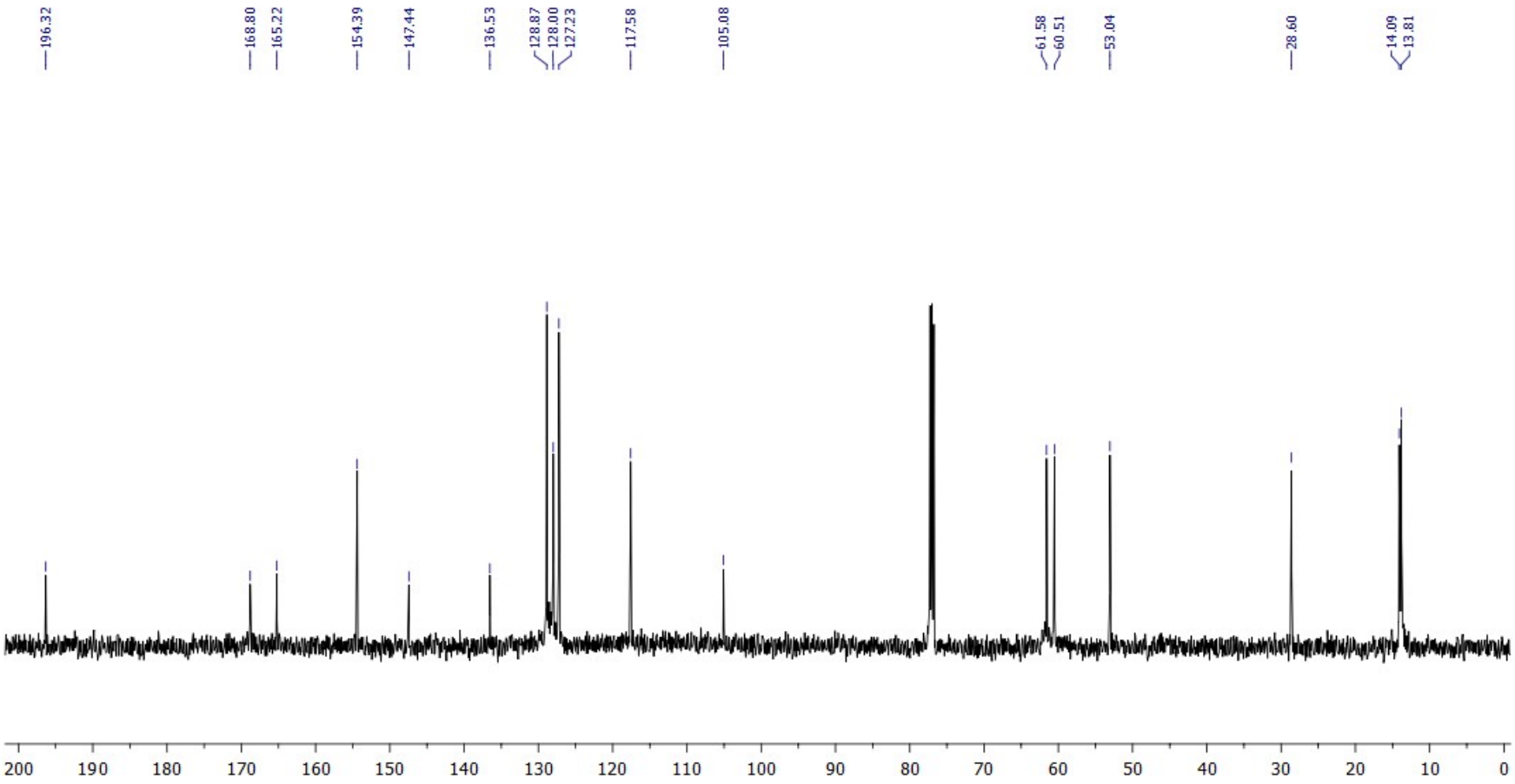
A part of **NOESY** spectrum of **4za** (mixture of *1Z,3Z* and *1E,3Z* isomers) used to distinguish between the isomers.



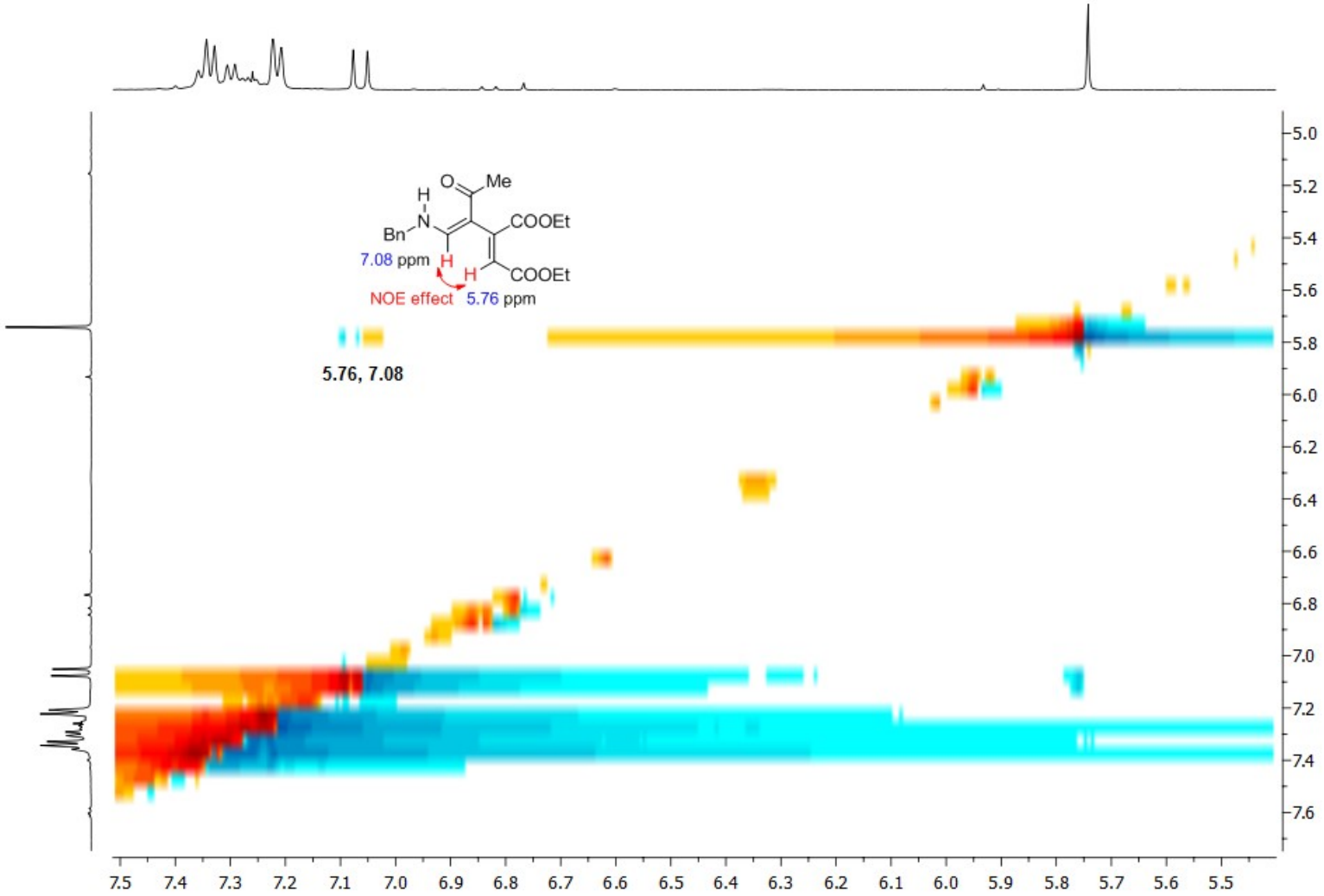
4zb



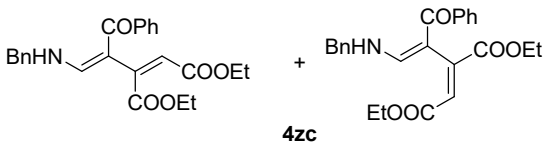
^{1}H NMR (500.3 MHz, $CDCl_3$)



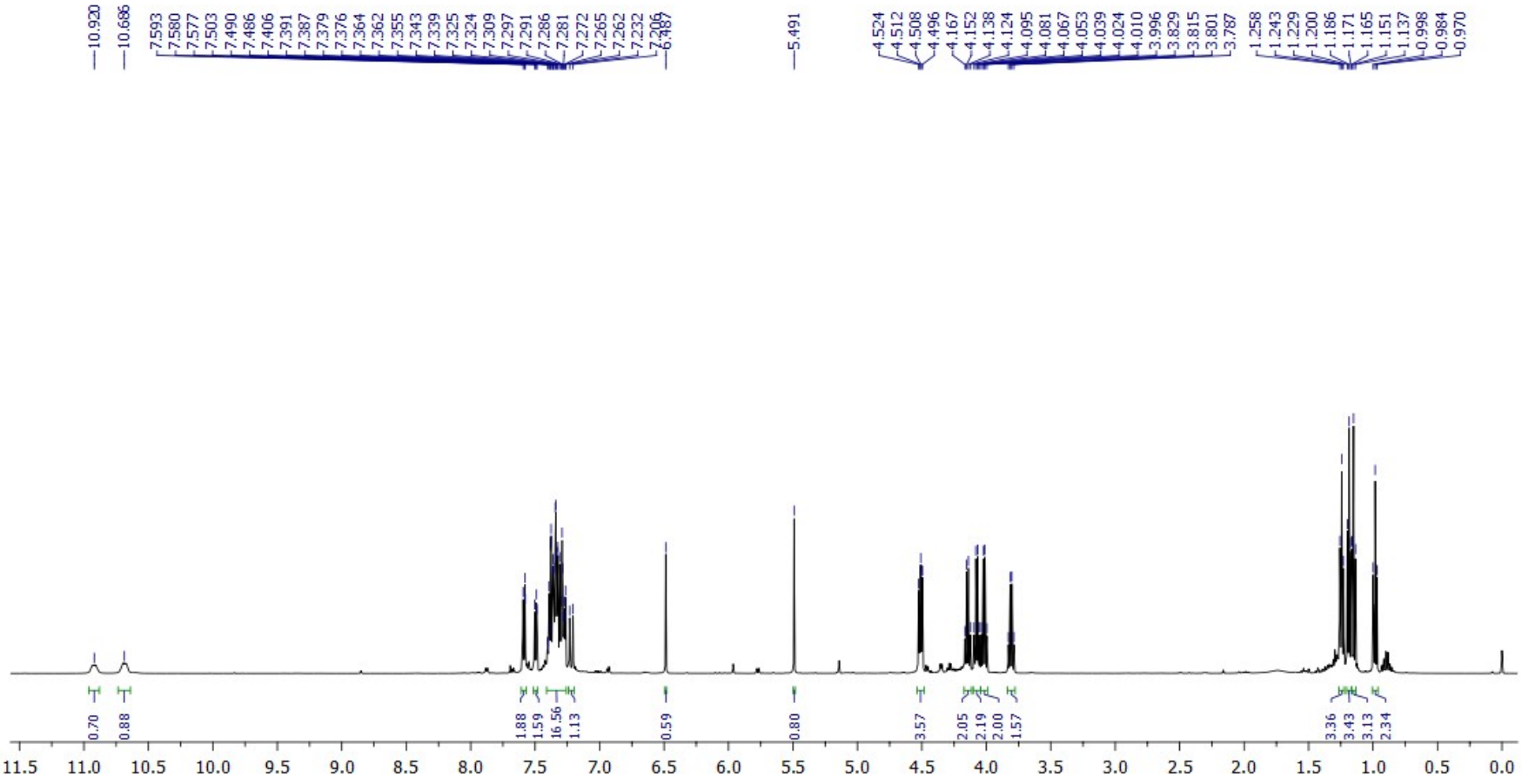
$^{13}C\{^{1}H\}$ NMR (125.8 MHz, $CDCl_3$)



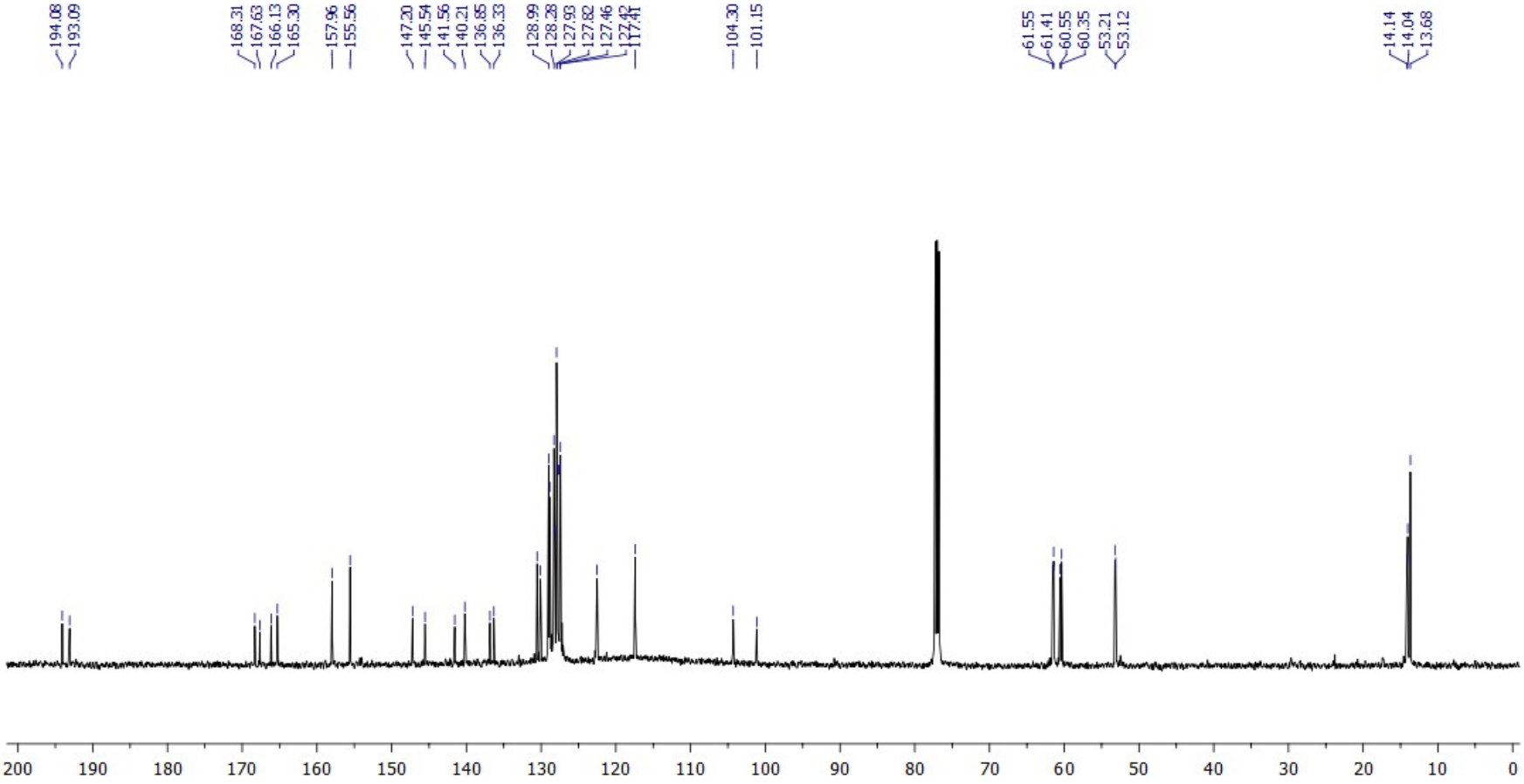
A part of **NOESY** spectrum of **4zb** showing cross-peak between the two vinyl hydrogen atoms and *Z* stereochemistry of the C1C2 double bond (maleic acid fragment).



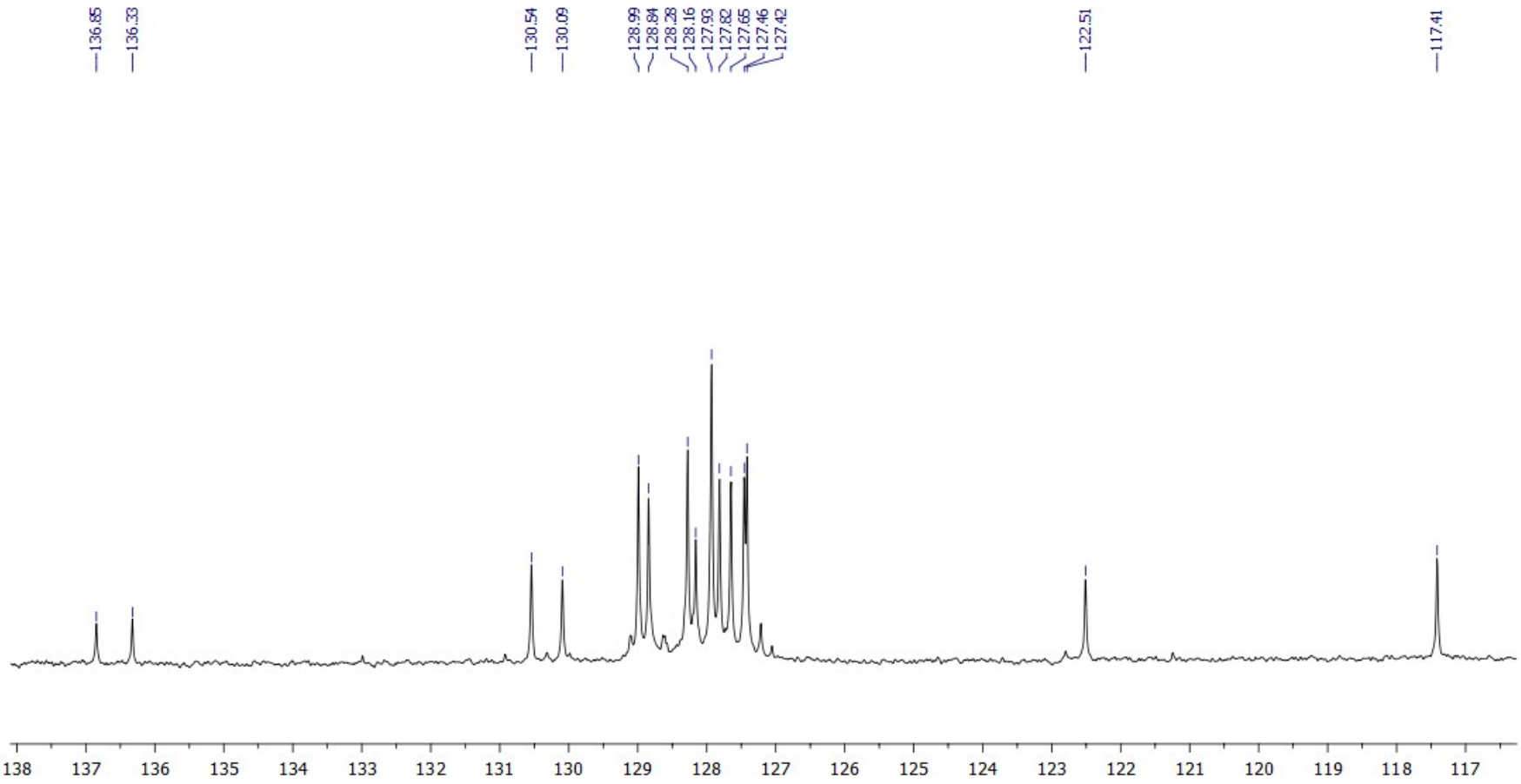
4zc



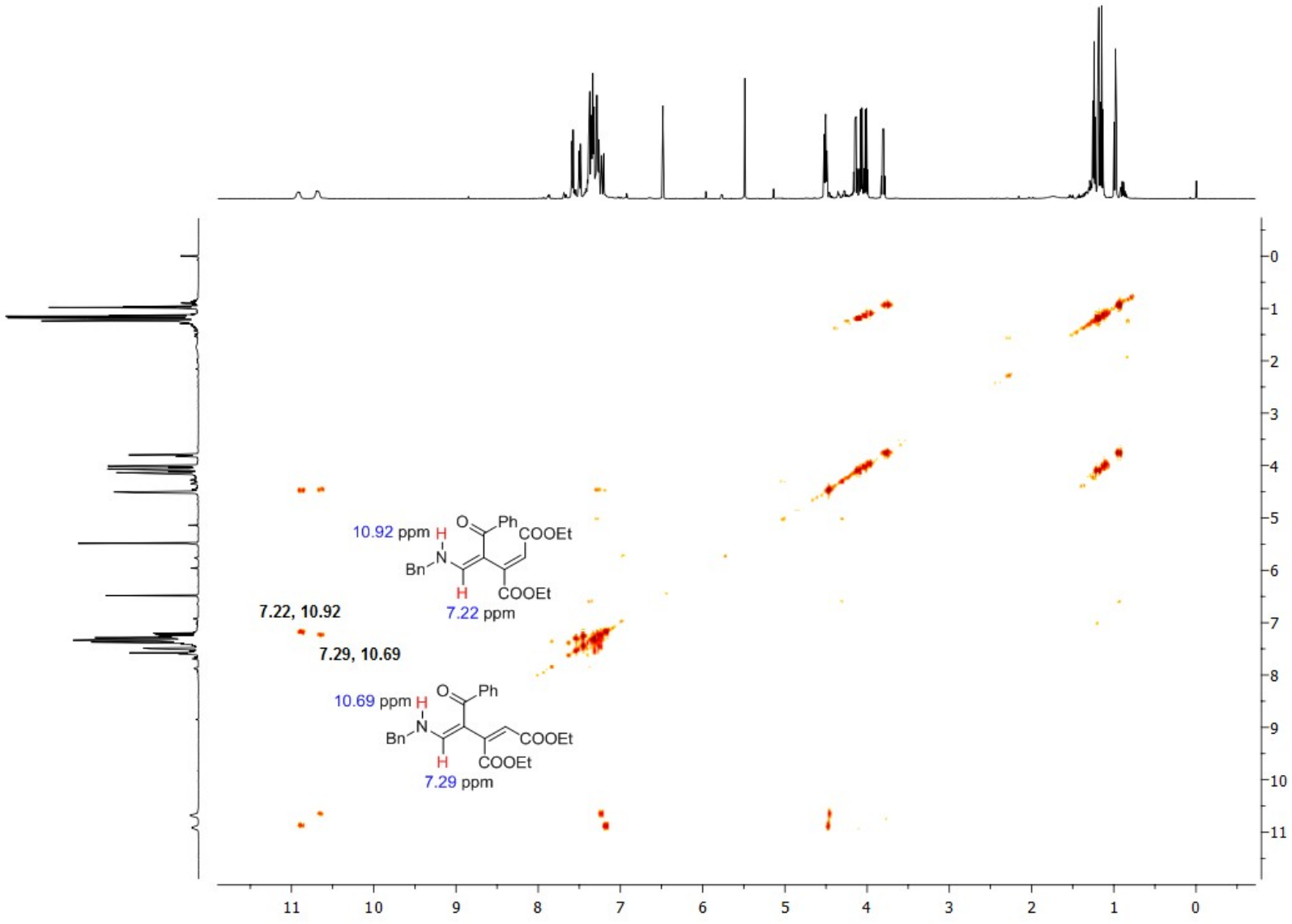
^{1}H NMR (500.3 MHz, $CDCl_3$) maleate/fumarate 1 : 0.8



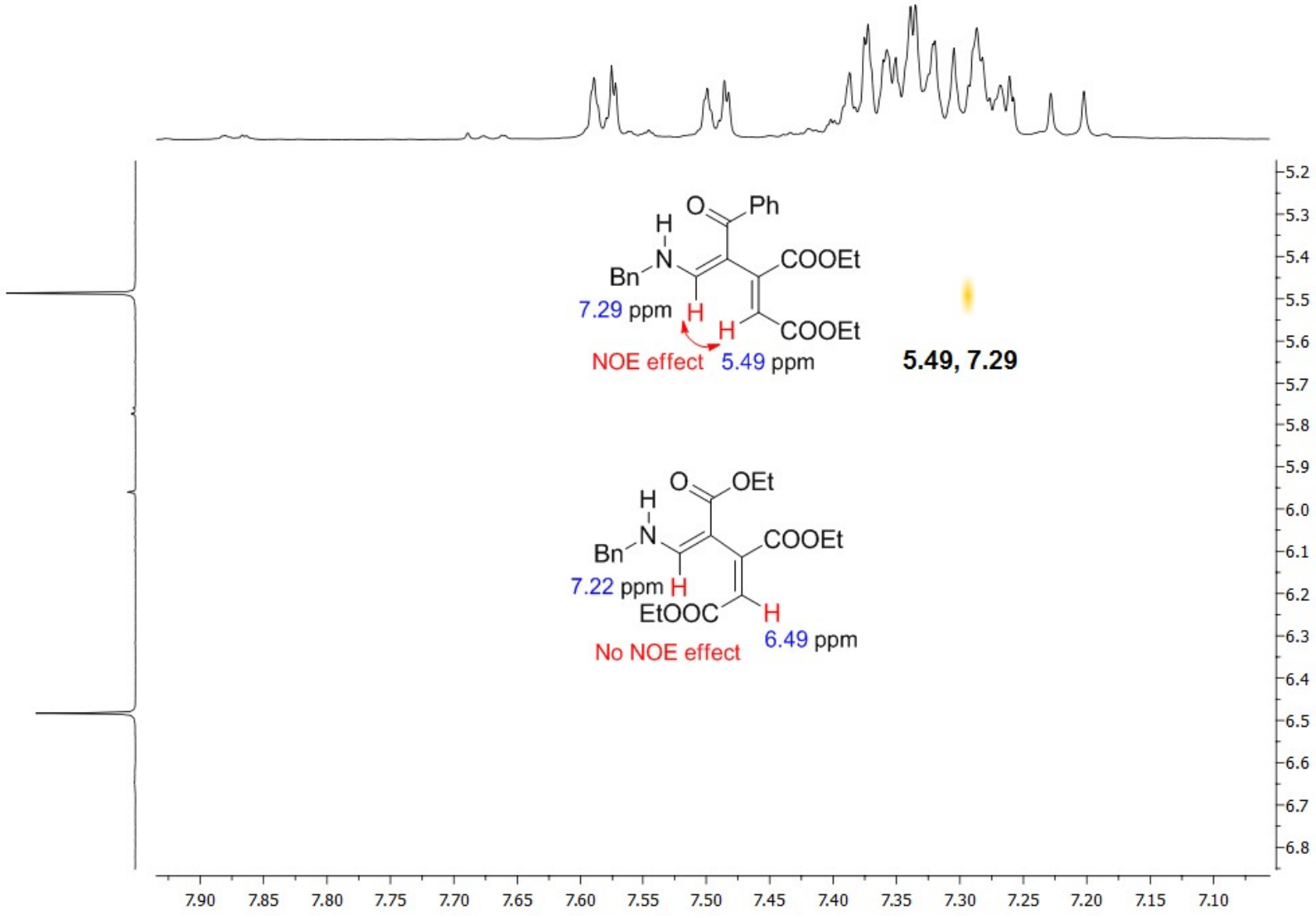
$^{13}C\{^{1}H\}$ NMR (125.8 MHz, $CDCl_3$) maleate/fumarate 1 : 0.8



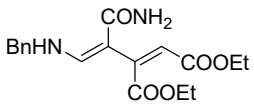
$^{13}C\{^{1}H\}$ NMR (125.8 MHz, $CDCl_3$) expanded



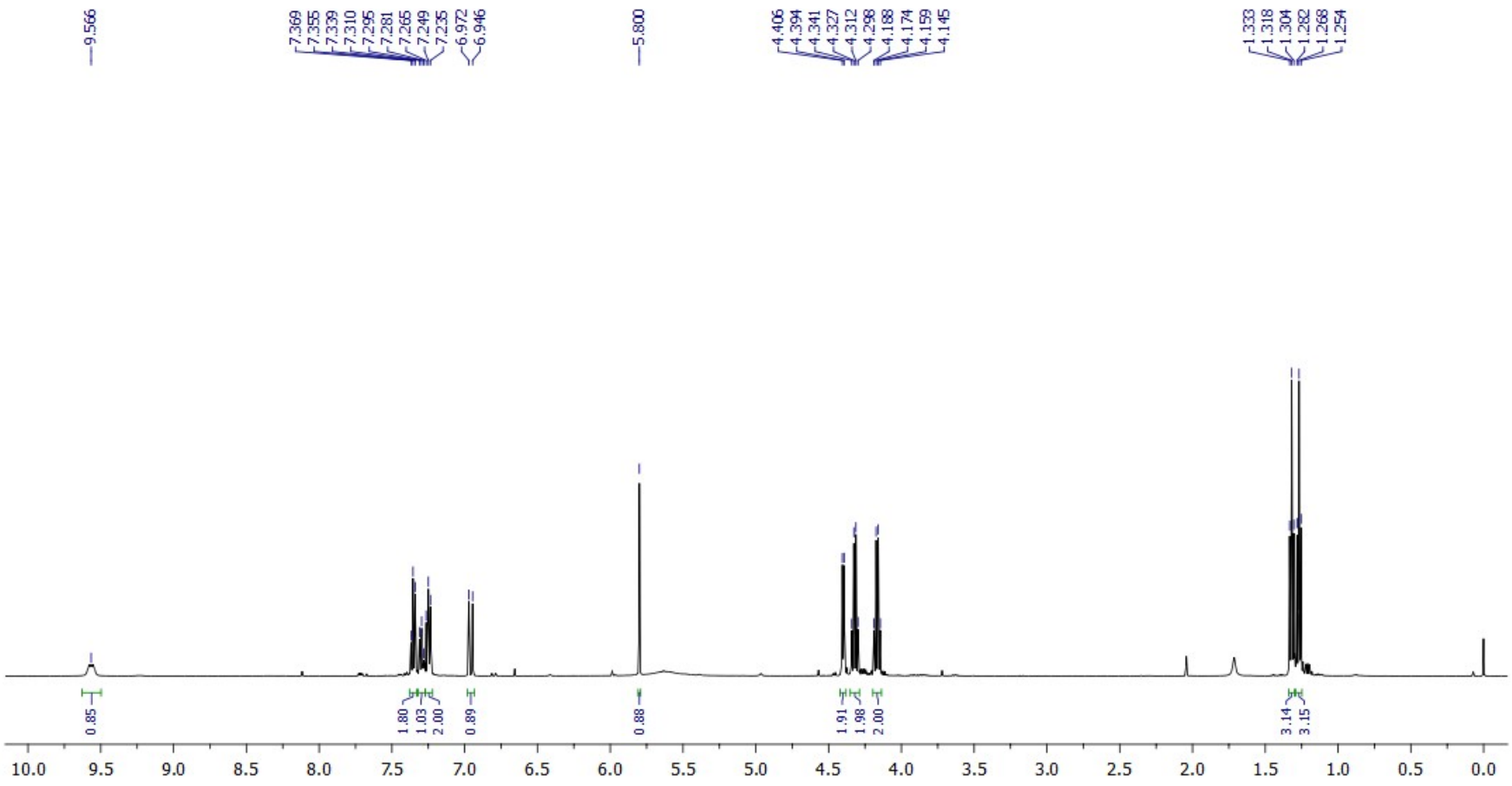
COSY spectrum of **4zc** used to unequivocally determine the position of the C4-**H** atoms of the two isomers. They couple with the adjacent N**H** proton.



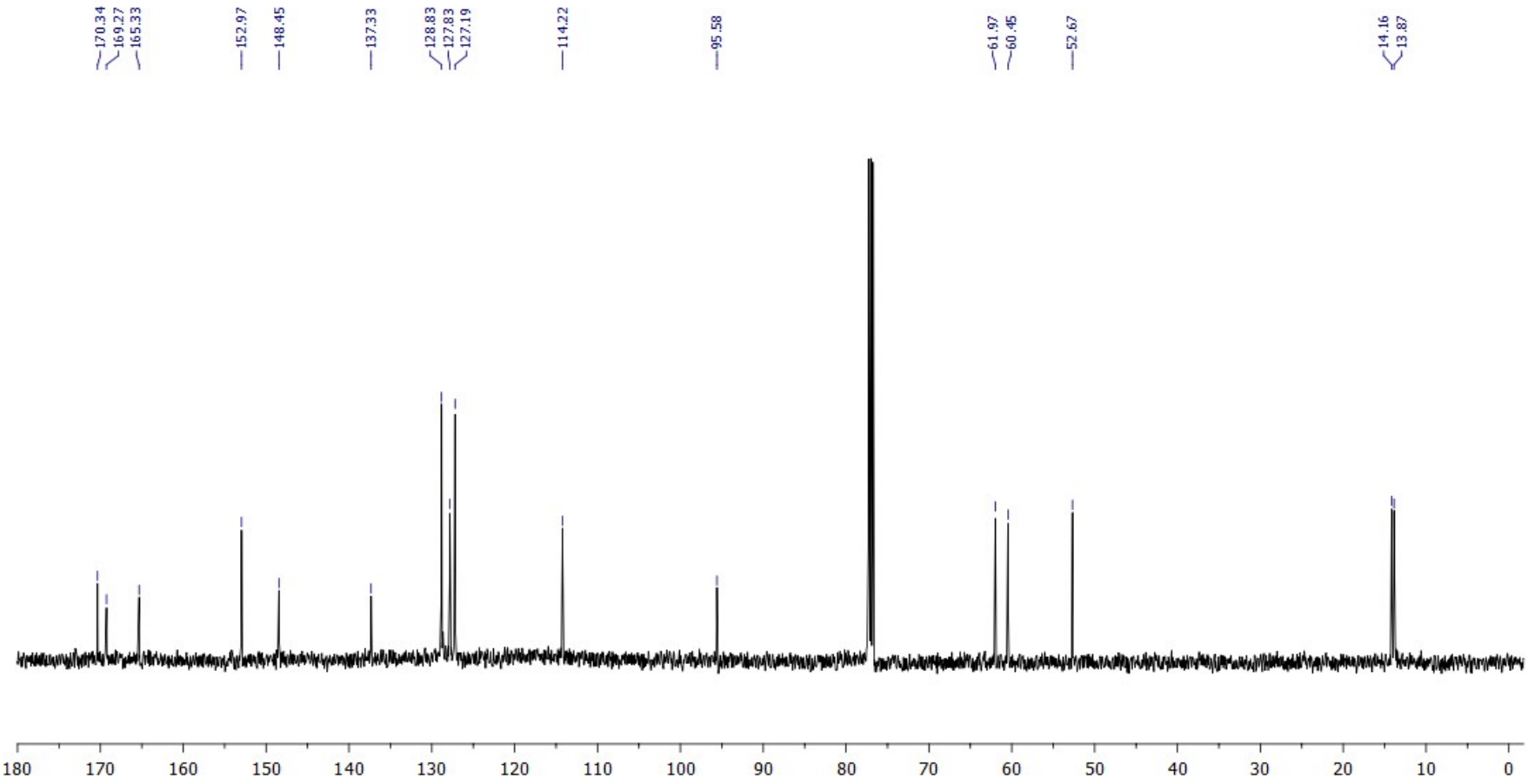
A part of **NOESY** spectrum of **4zc** used to distinguish the two isomers around the C1C2 double bond.



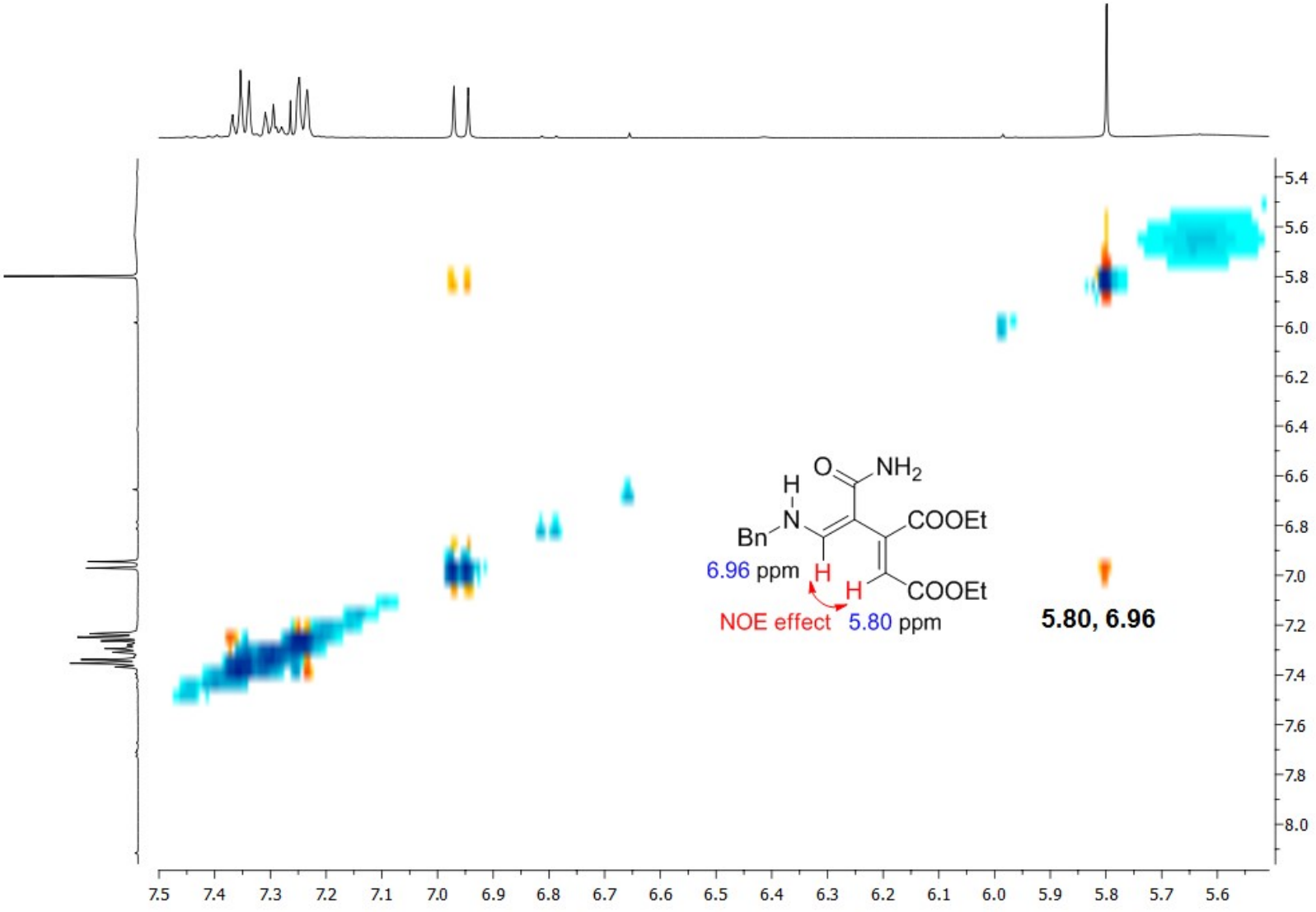
4zd



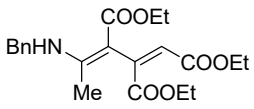
^{1}H NMR (500.3 MHz, $CDCl_3$)



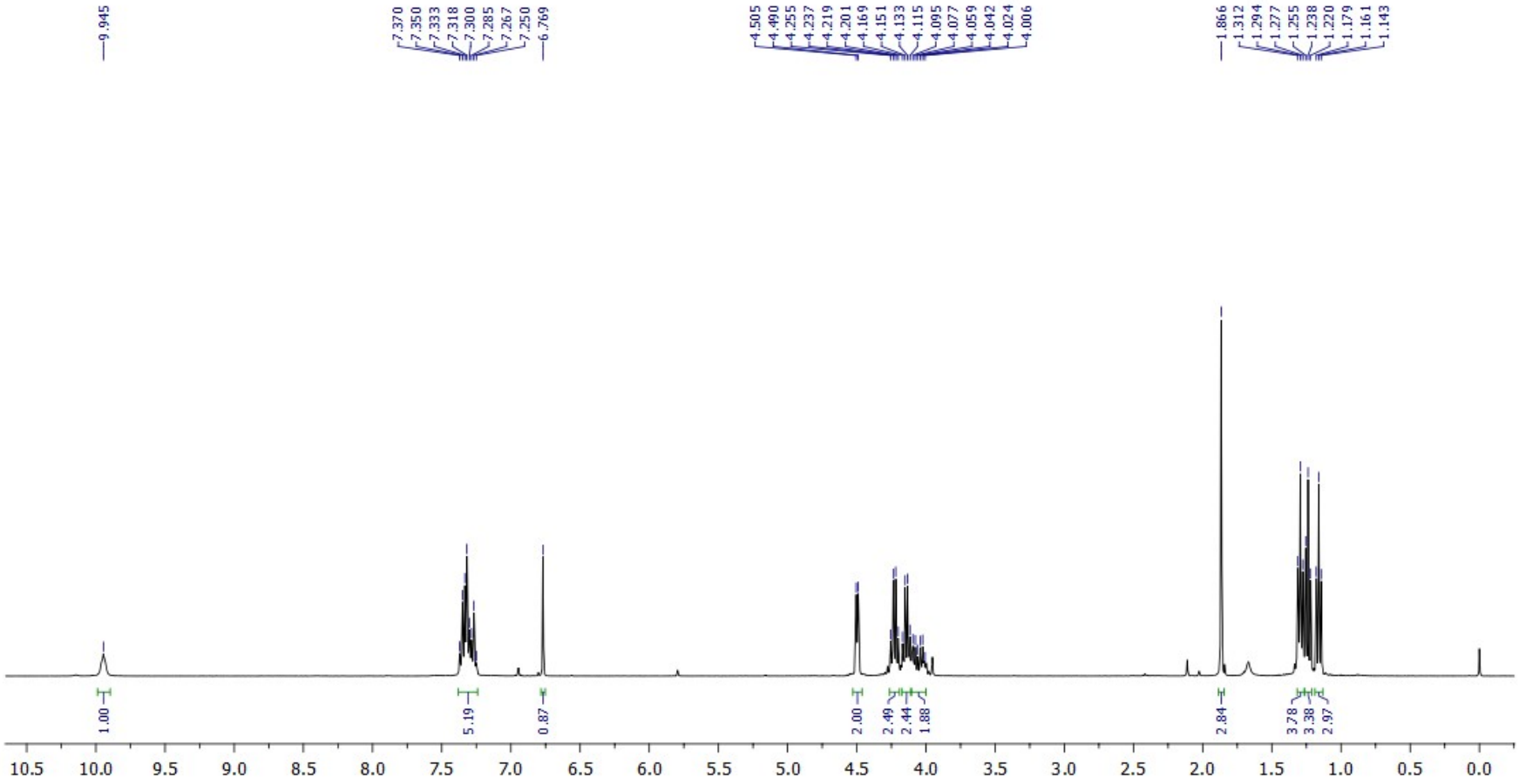
$^{13}C\{^{1}H\}$ NMR (125.8 MHz, $CDCl_3$)



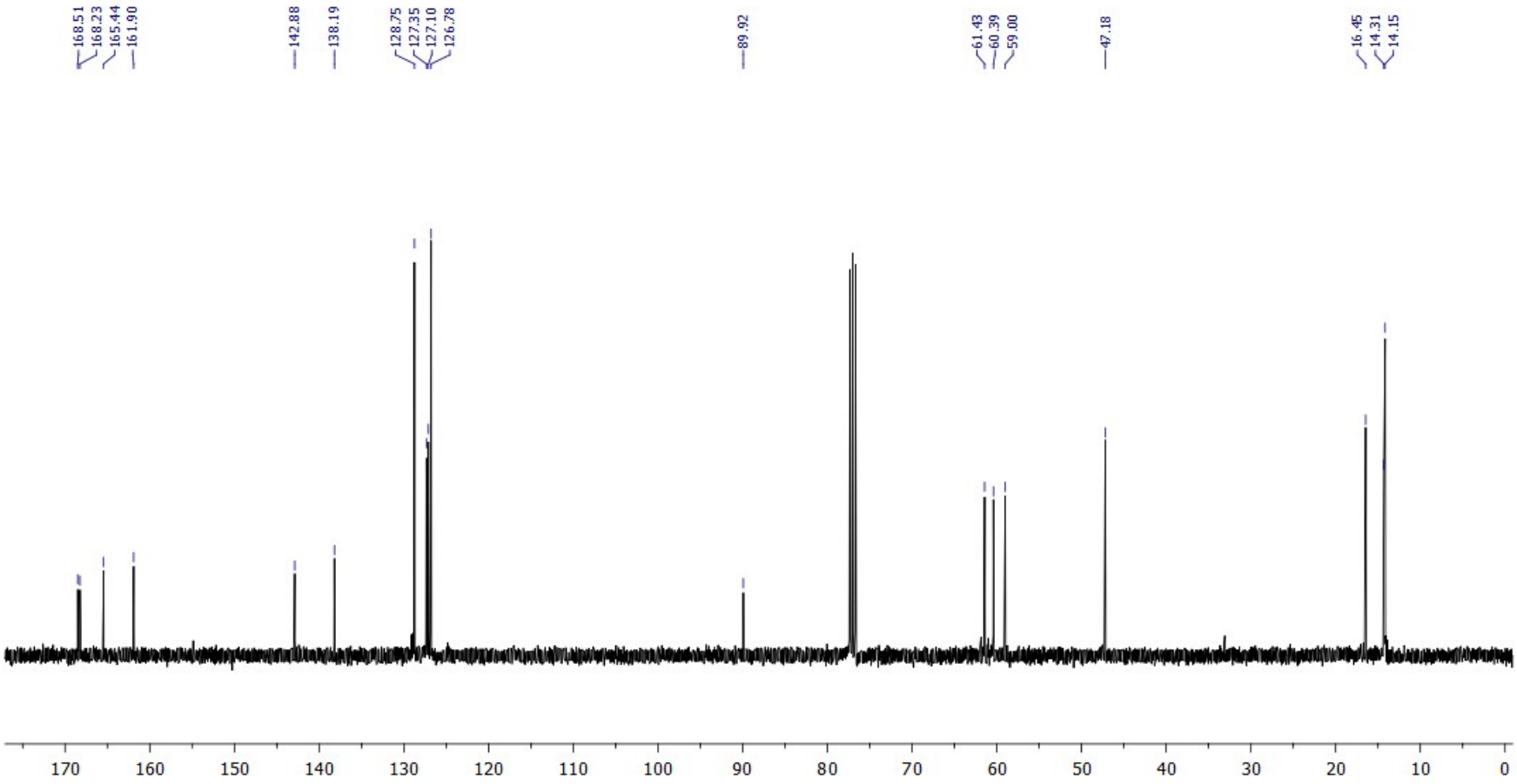
A part of **NOESY** spectrum of **4zd** showing cross-peak between the two vinyl hydrogen atoms and *Z* stereochemistry of the C1C2 double bond (maleic acid fragment).



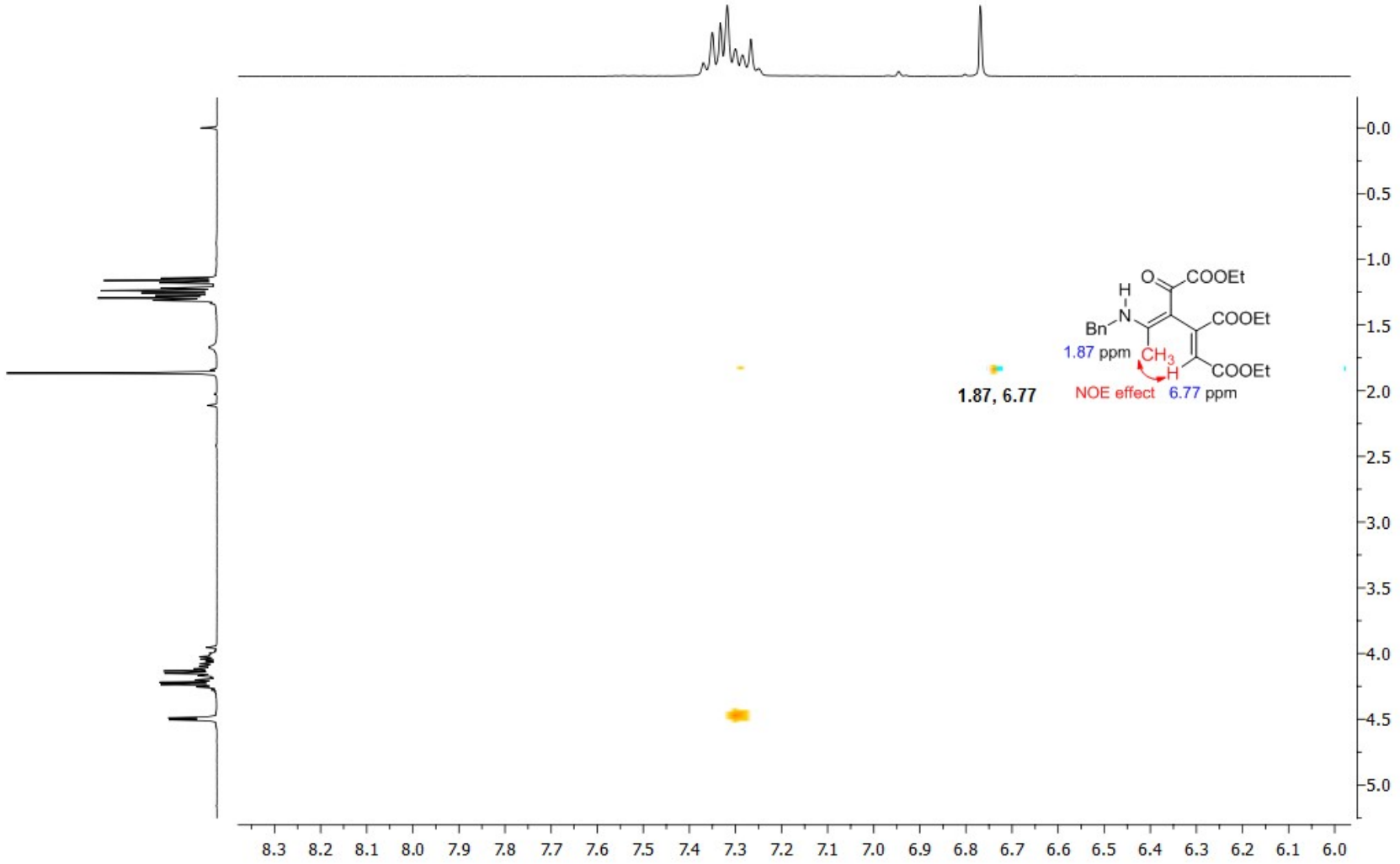
4ze



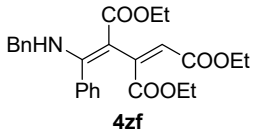
^{1}H NMR (400.1 MHz, $CDCl_3$)



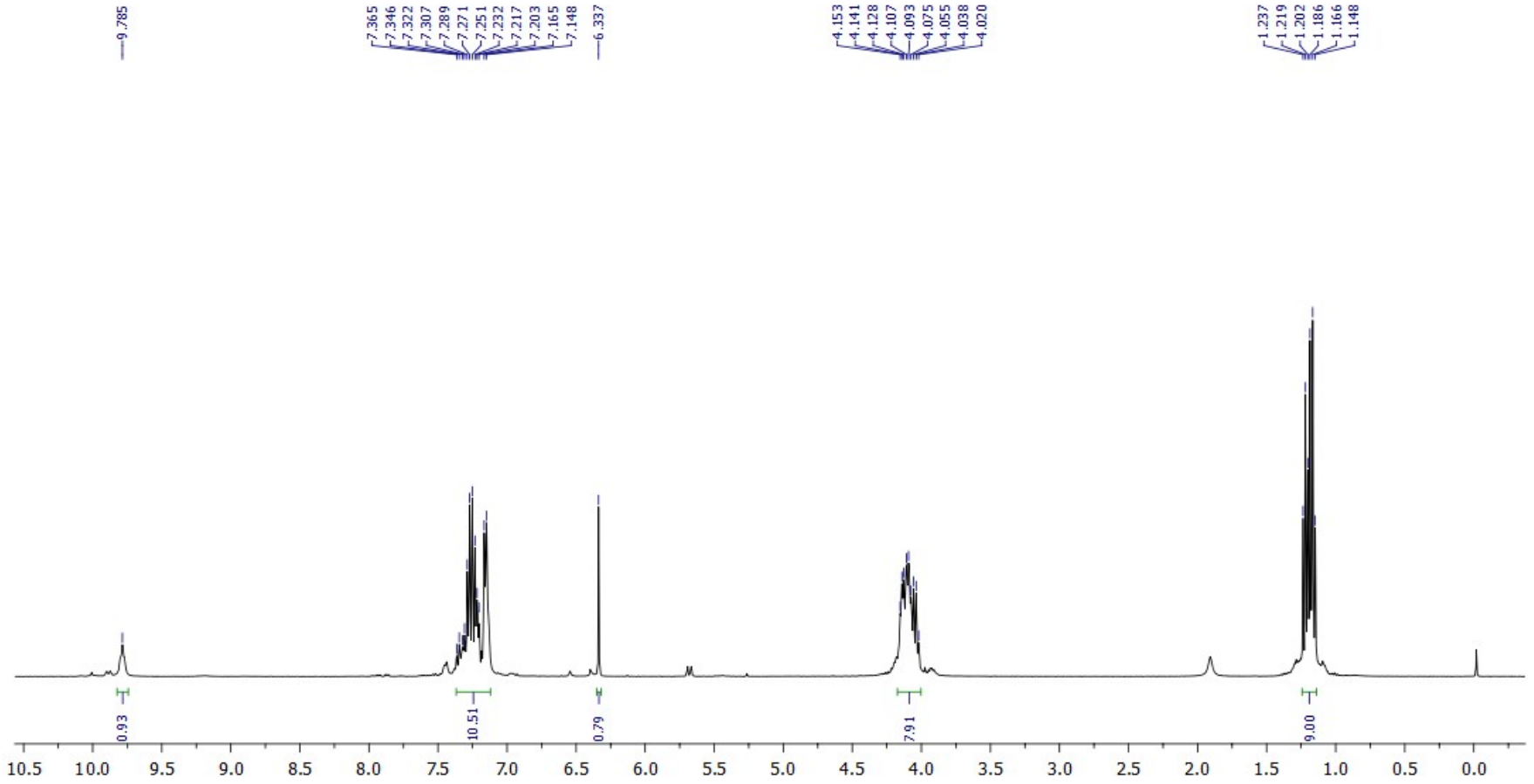
$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$)



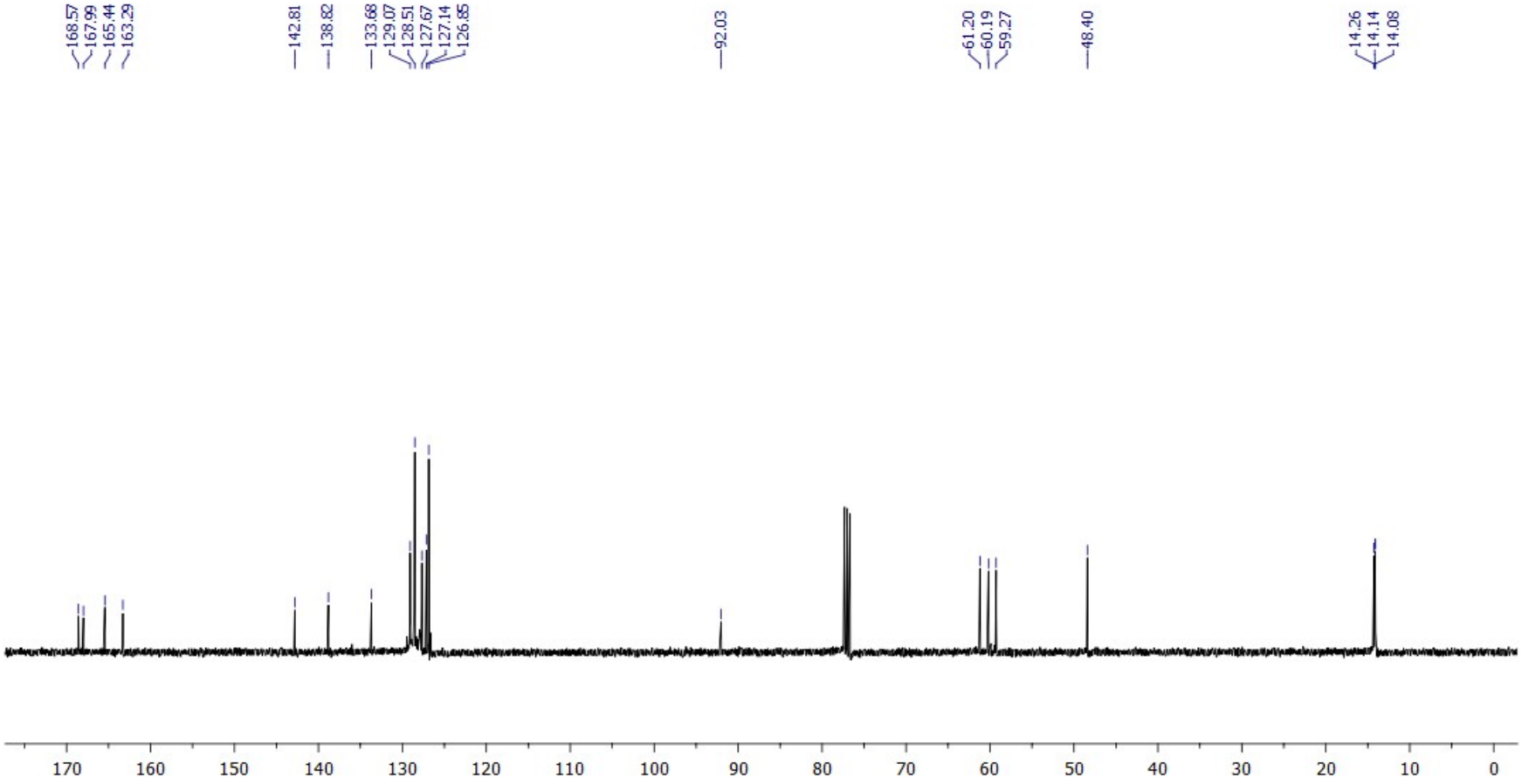
A part of **NOESY** spectrum of **4ze** showing the *Z* stereochemistry at the C1 double bond.



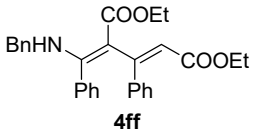
4zf



^{1}H NMR (400.1 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$)



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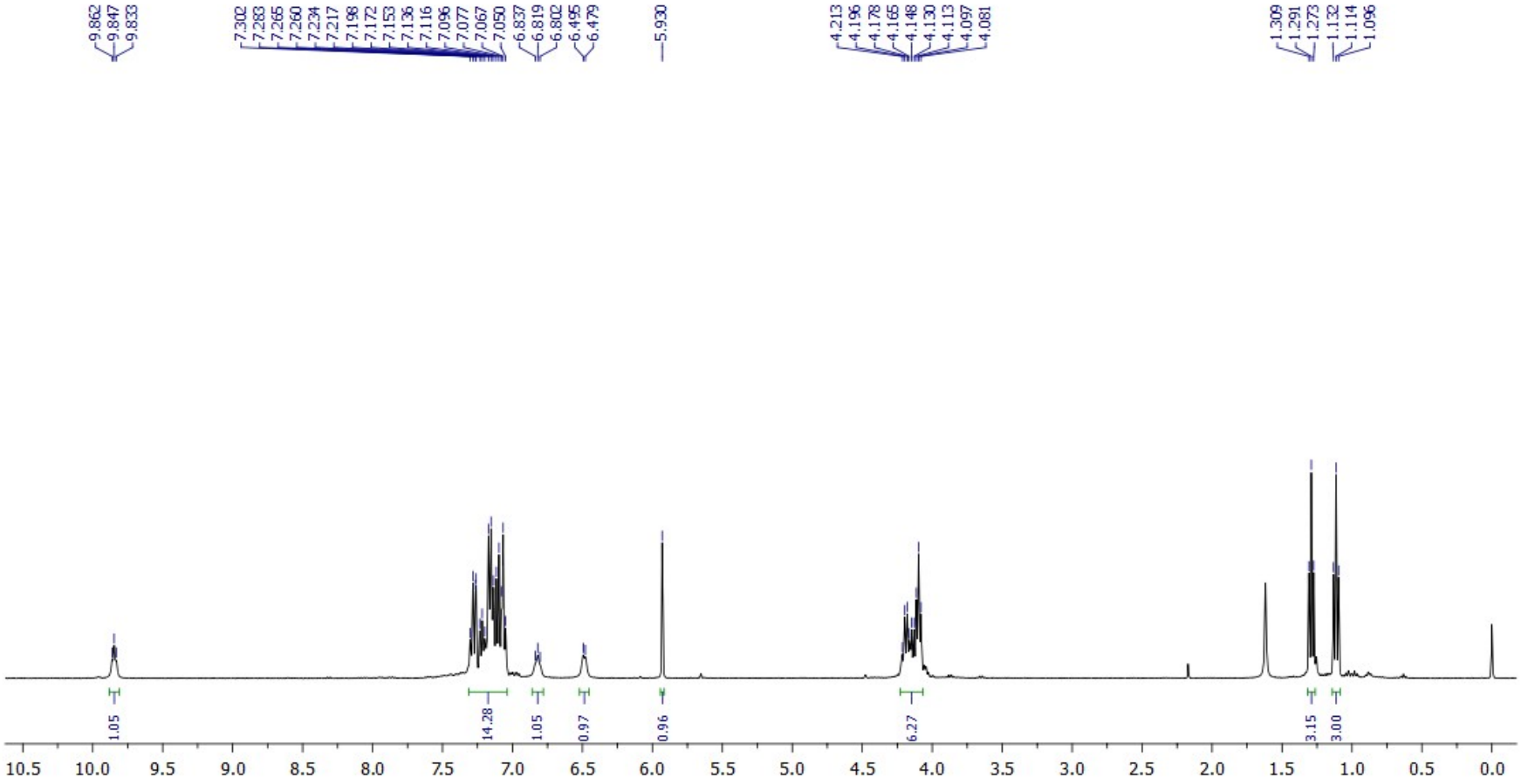
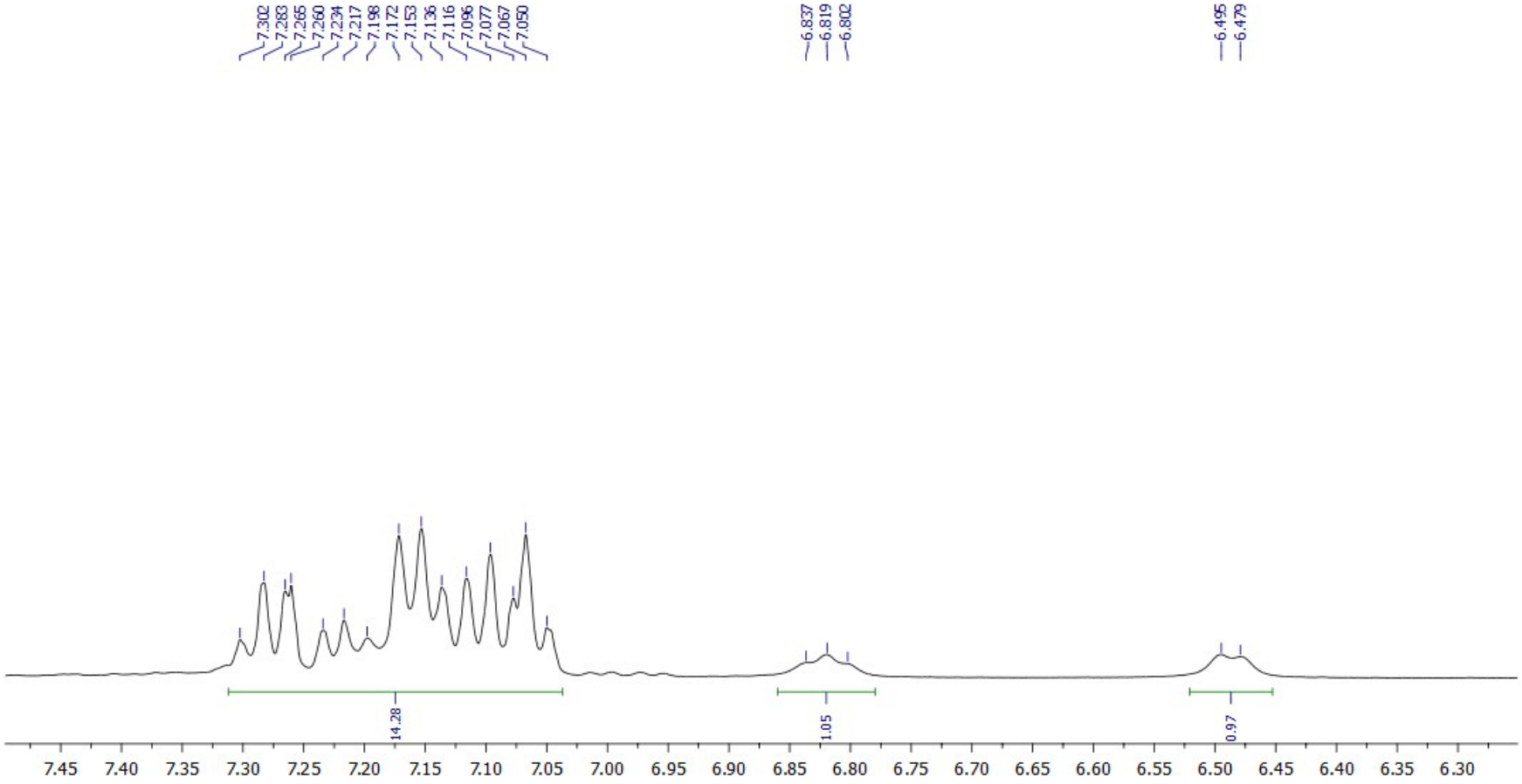
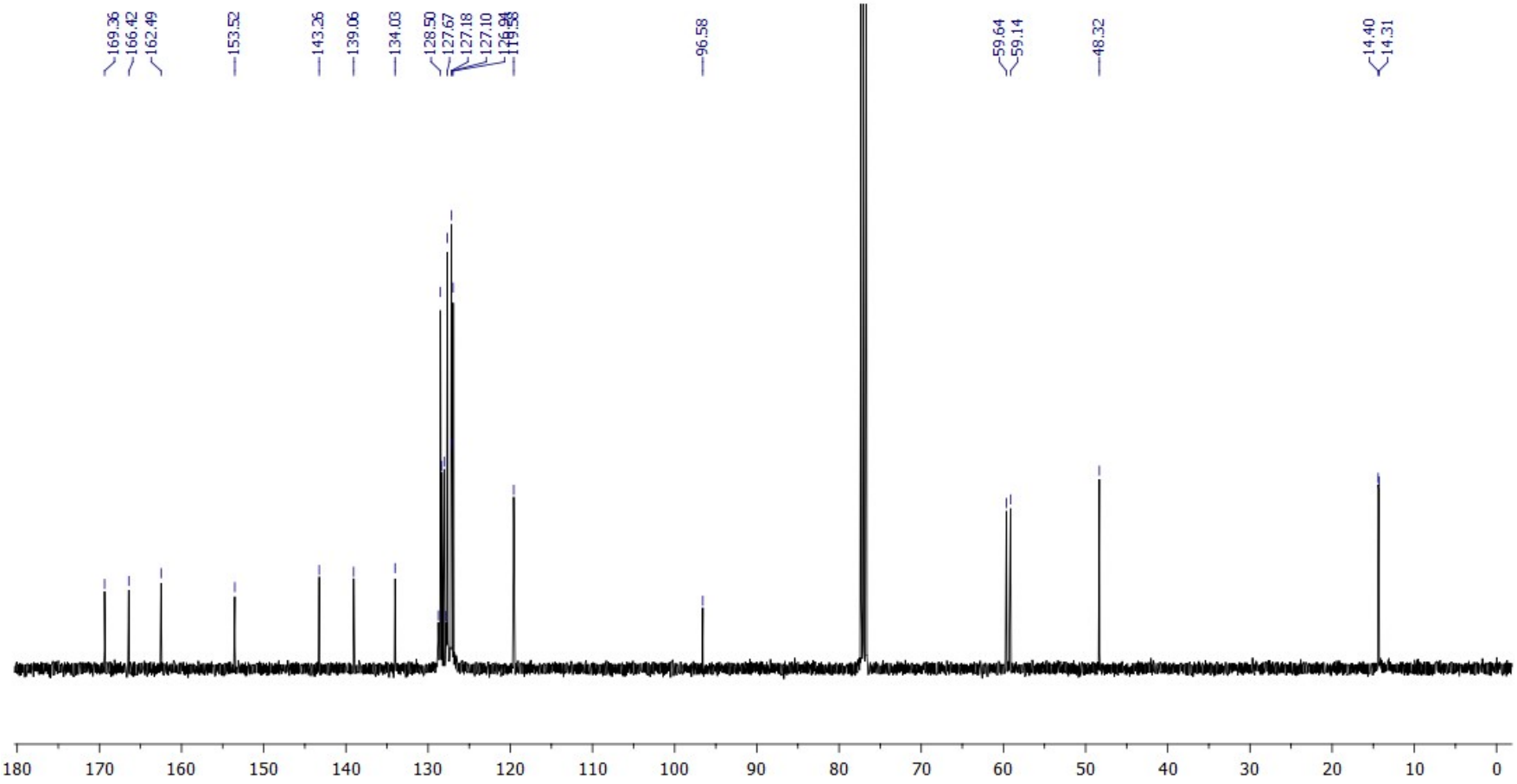


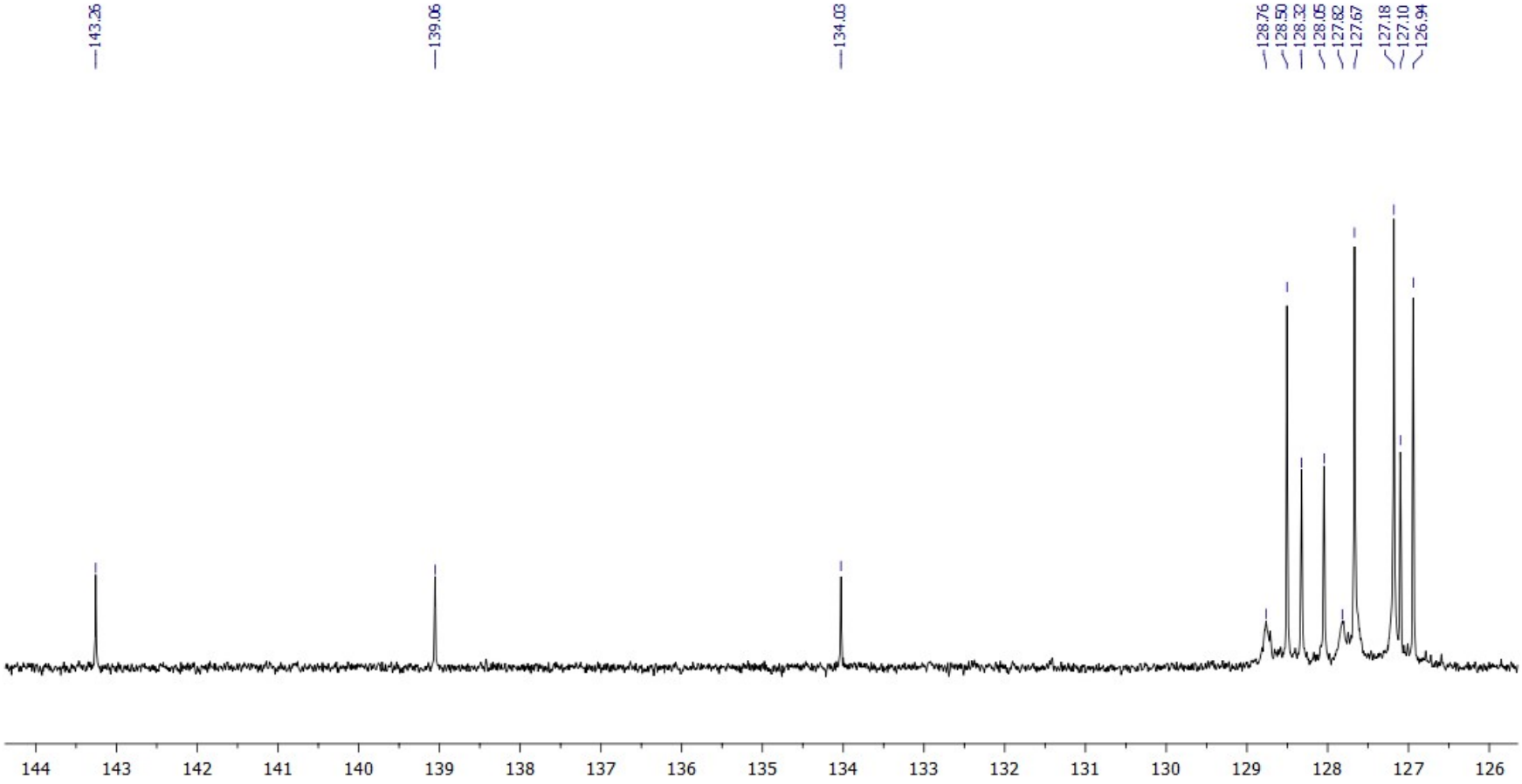
^{1}H NMR (400.1 MHz, $CDCl_3$)



^{1}H NMR (400.1 MHz, $CDCl_3$) expanded aromatic region

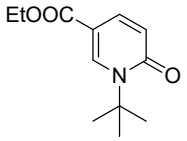


$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$), expanded aromatic region

2-Pyridones 5



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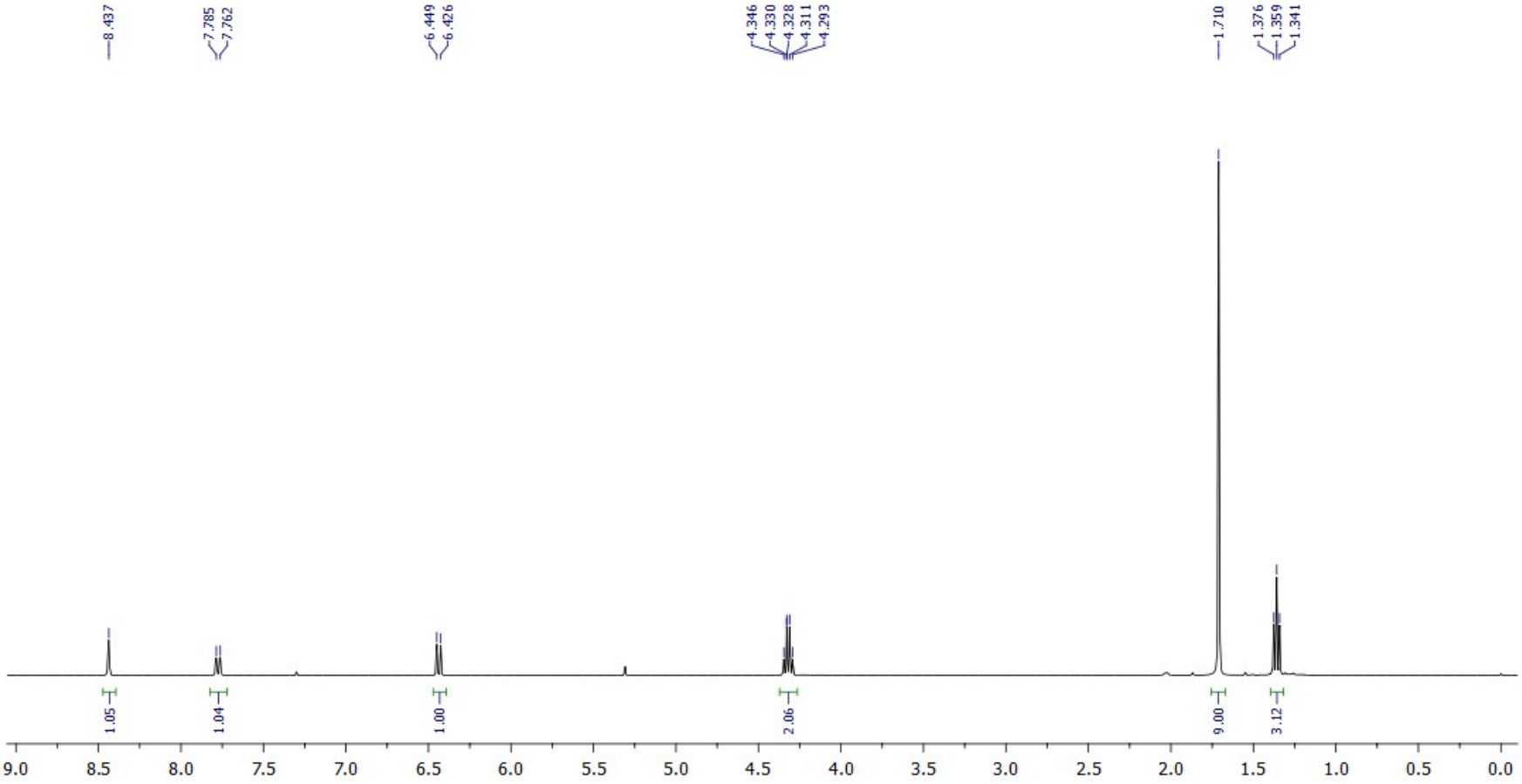
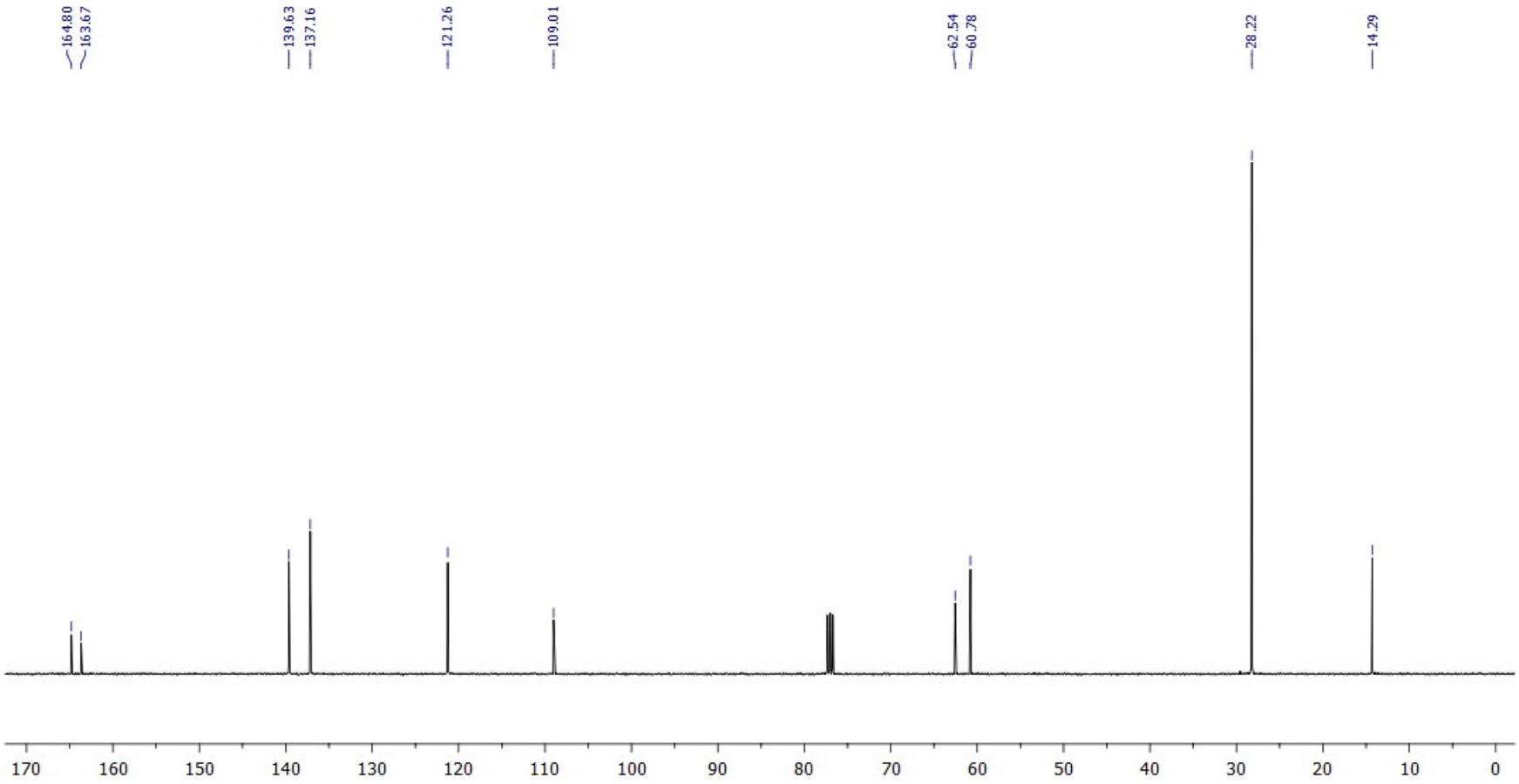
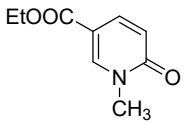


^{1}H NMR (400.1 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$)



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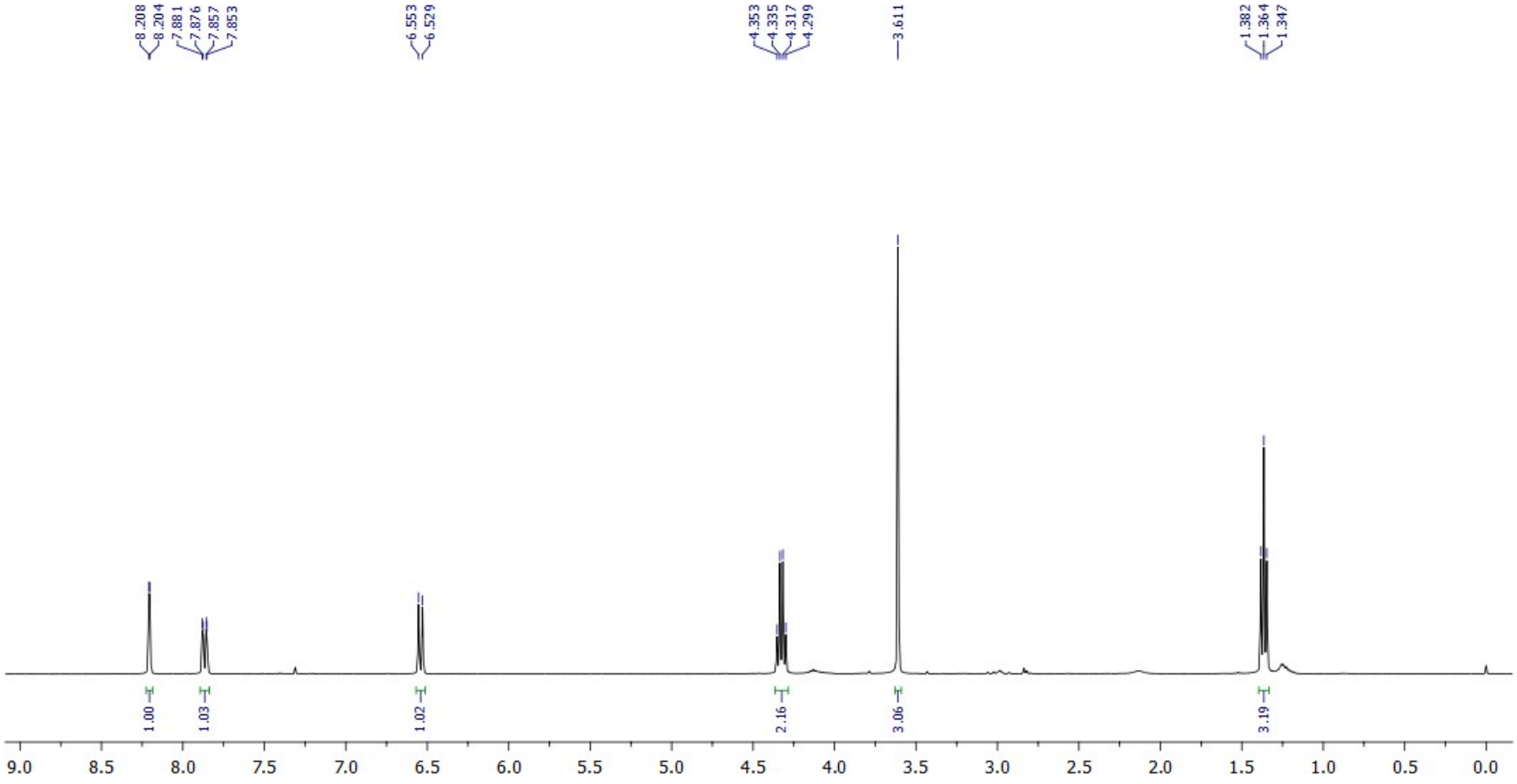
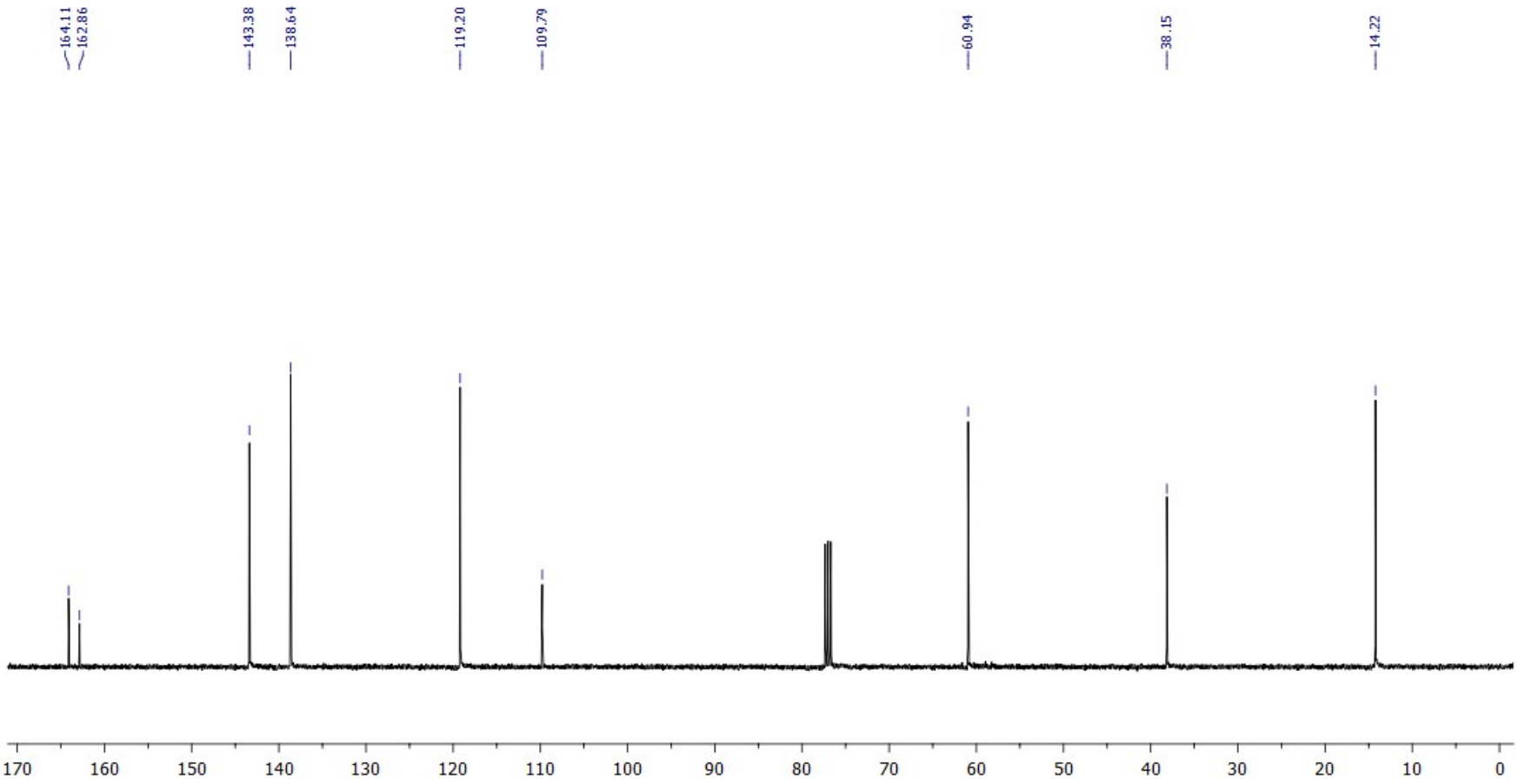
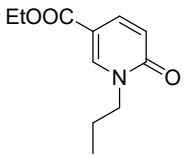


^{1}H NMR (400.1 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$)



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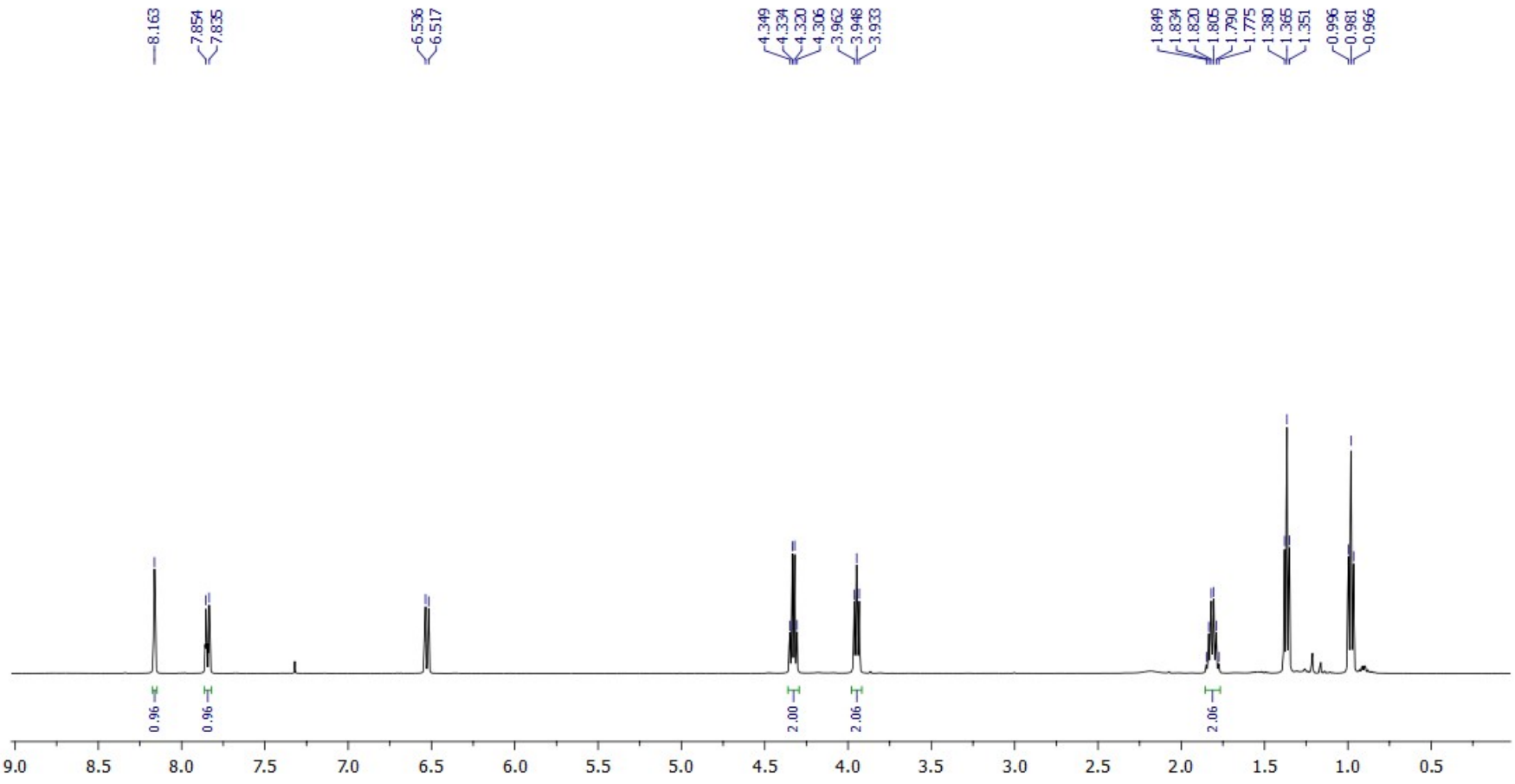
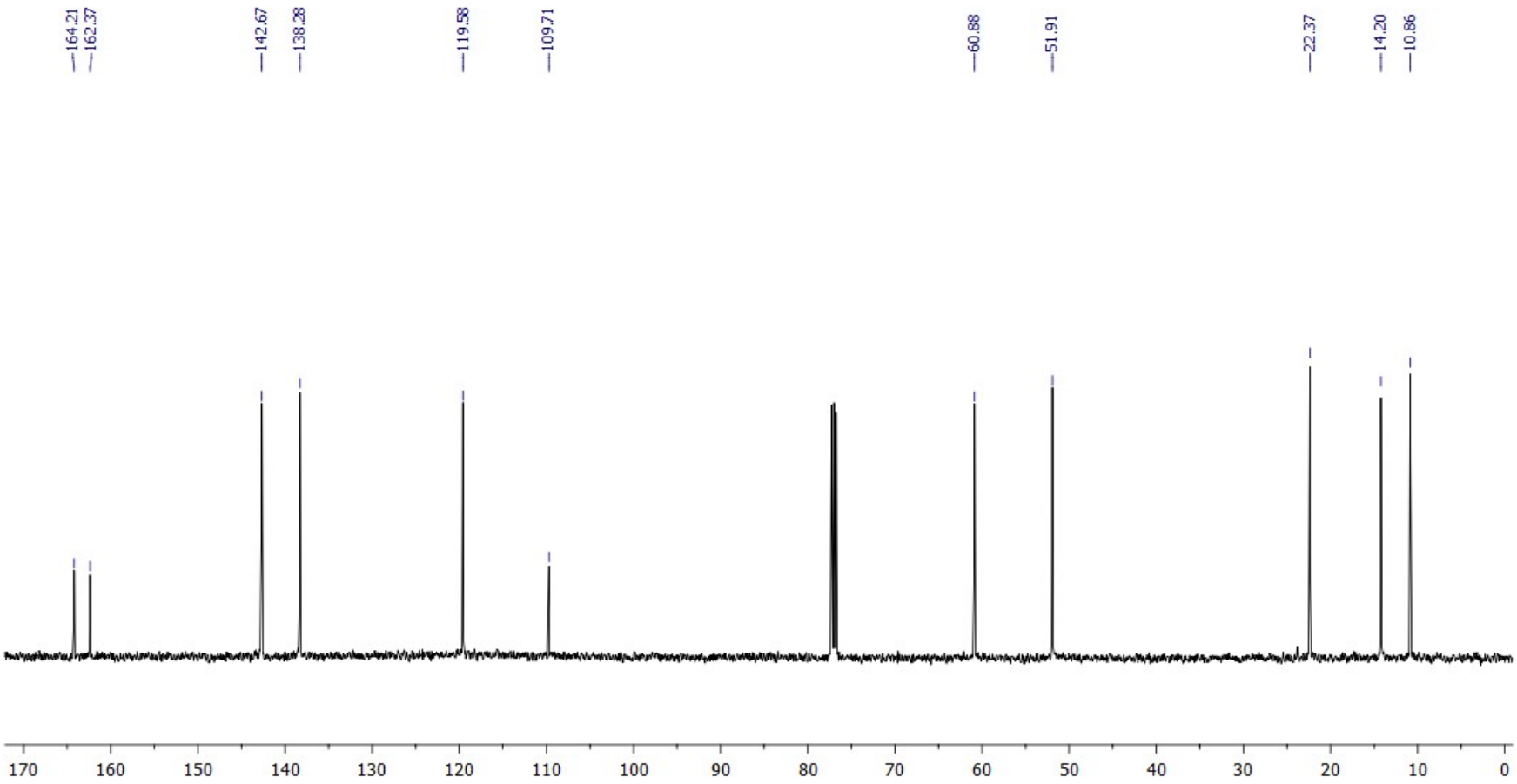
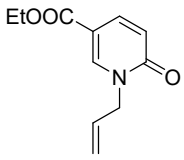


^{1}H NMR (500.3 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (125.8 MHz, $CDCl_3$)



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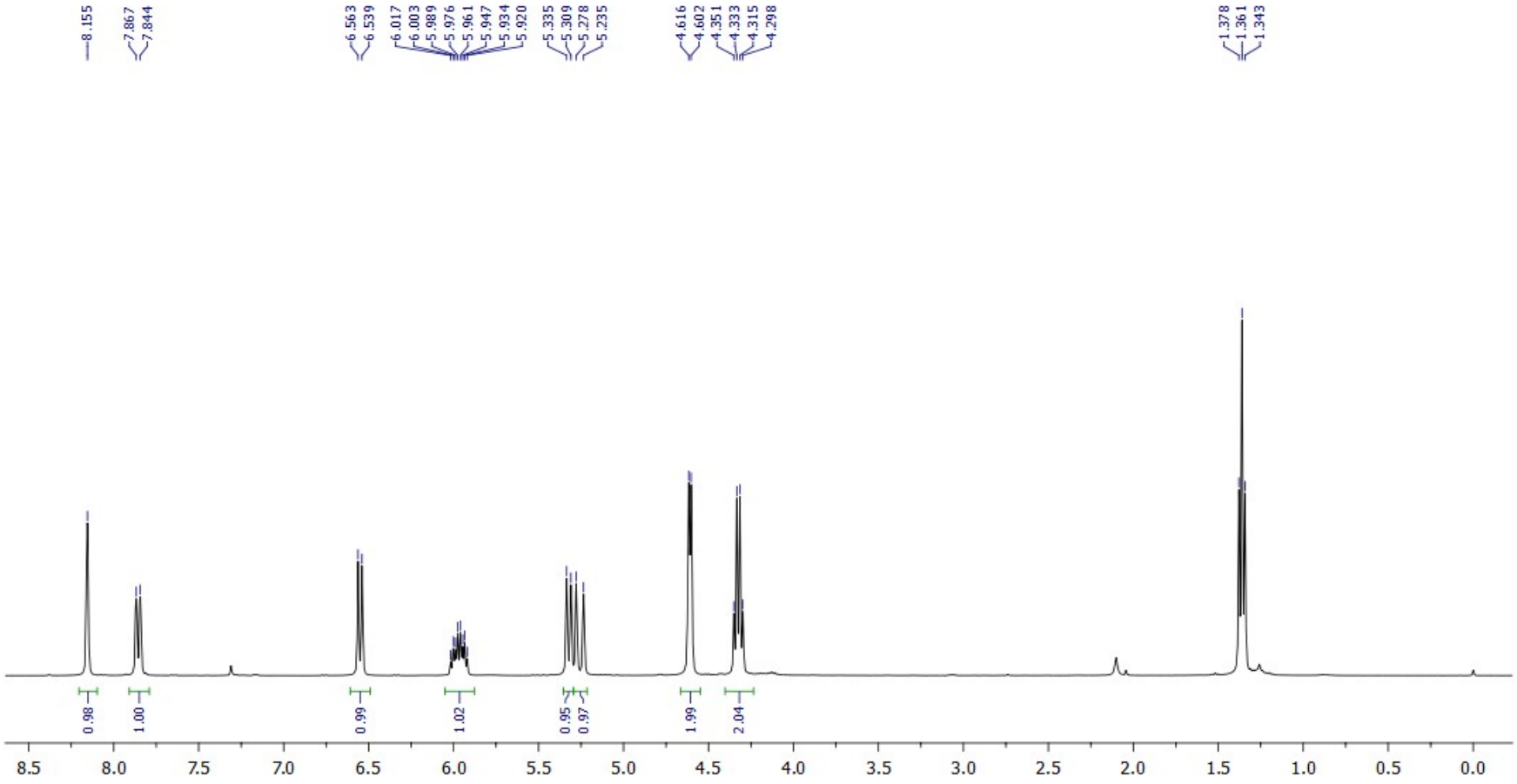
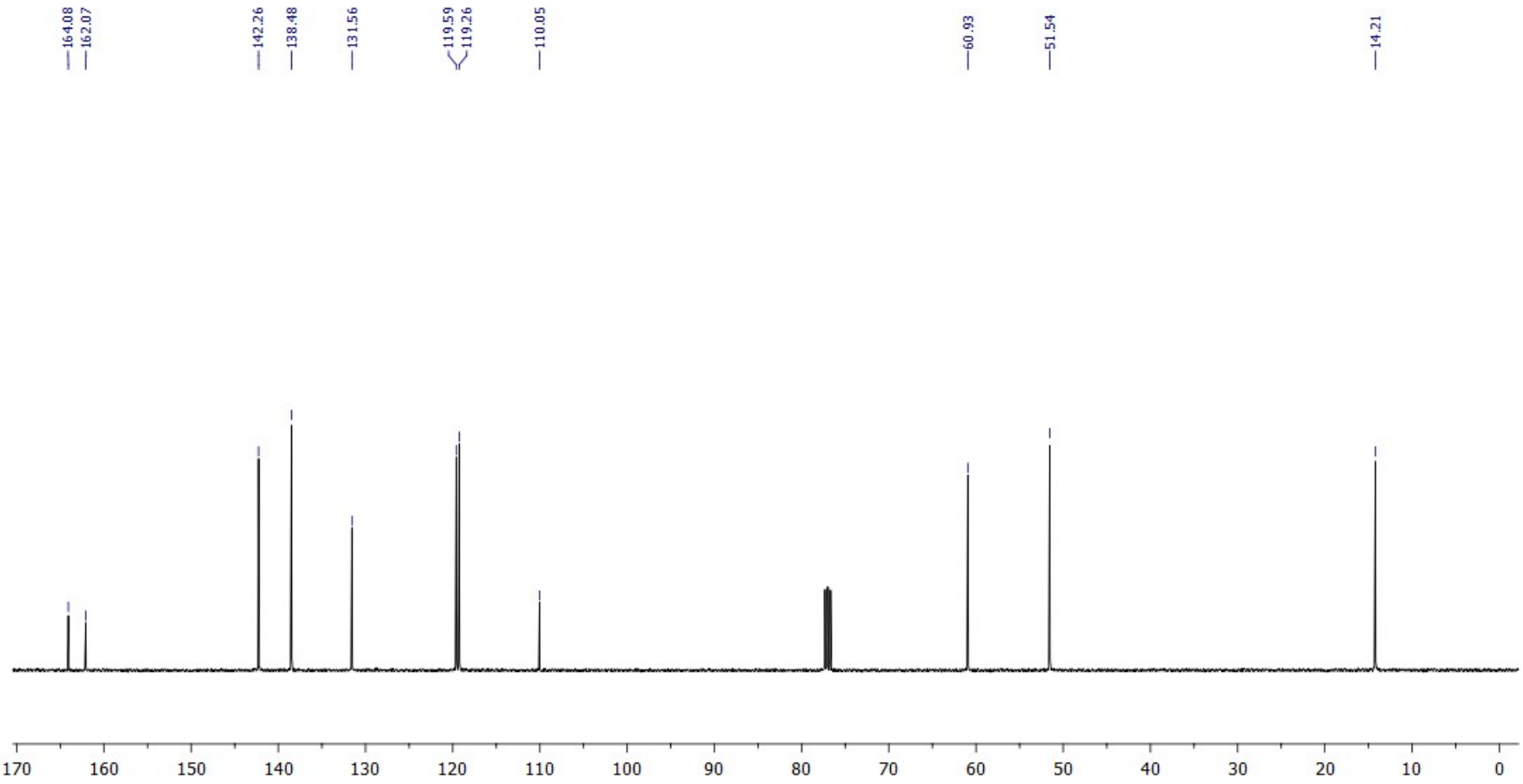
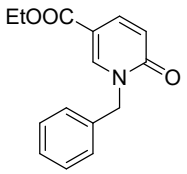


^{1}H NMR (400.1 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$)



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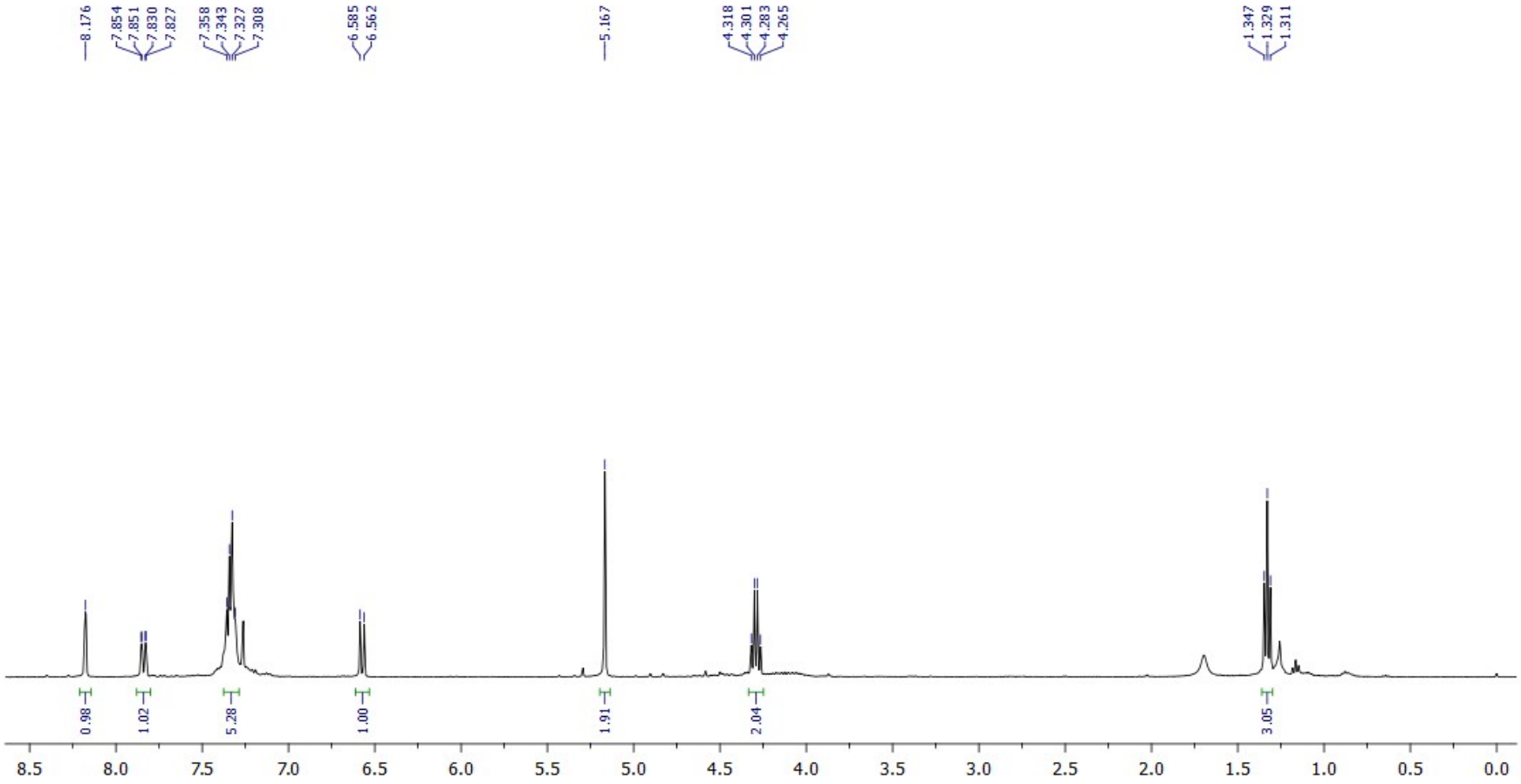
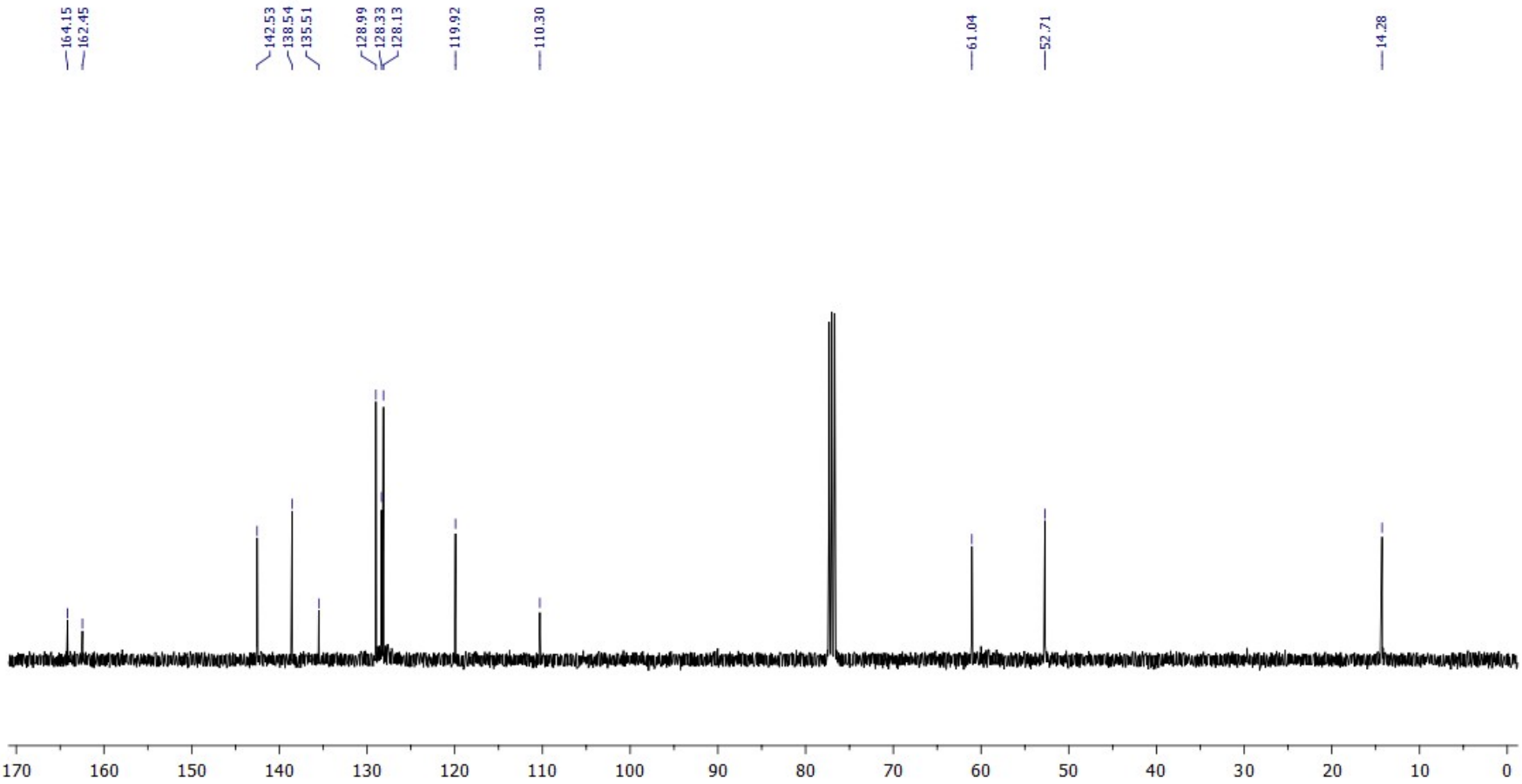
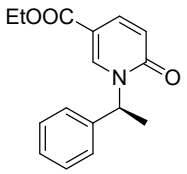


^{1}H NMR (400.1 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$)



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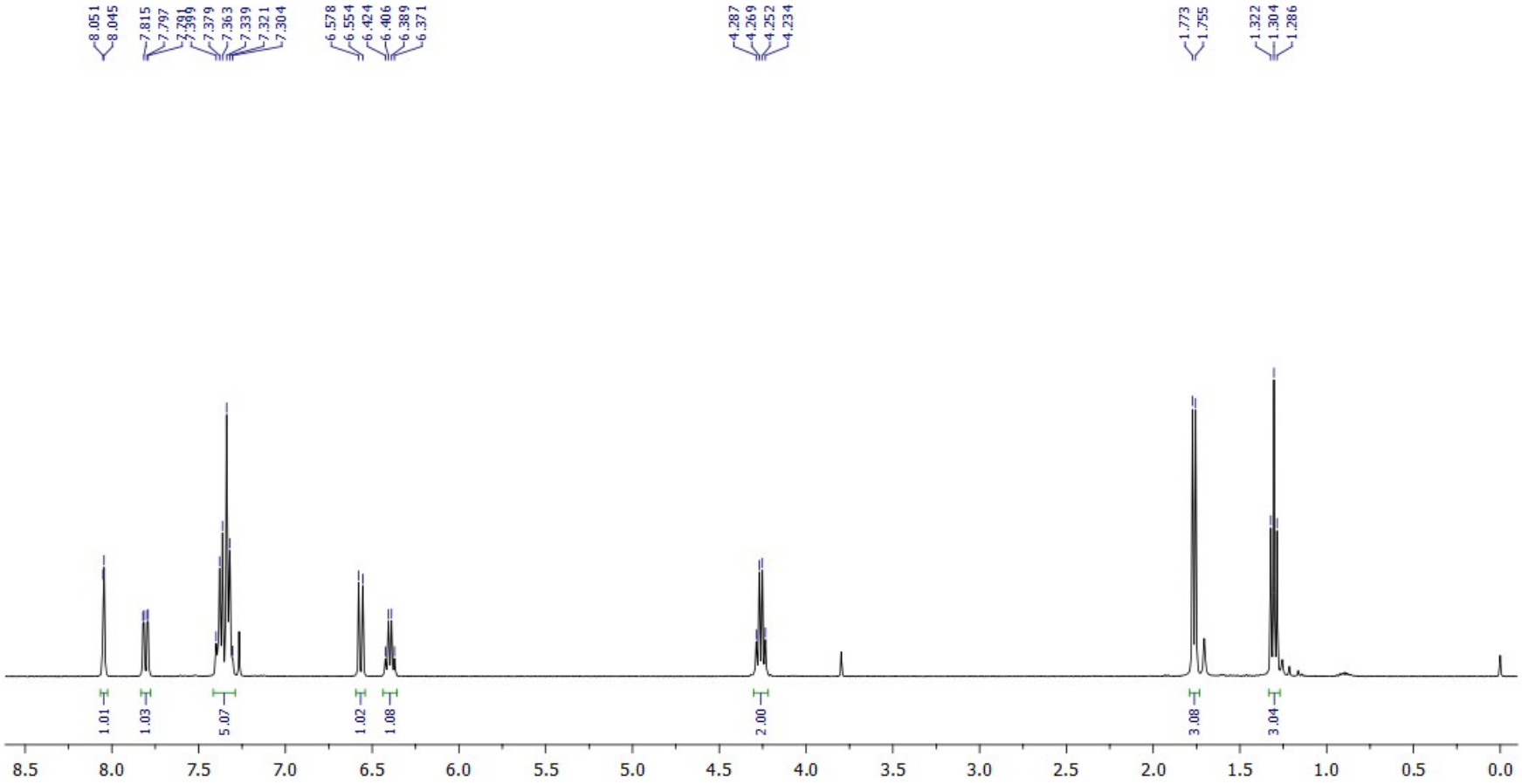
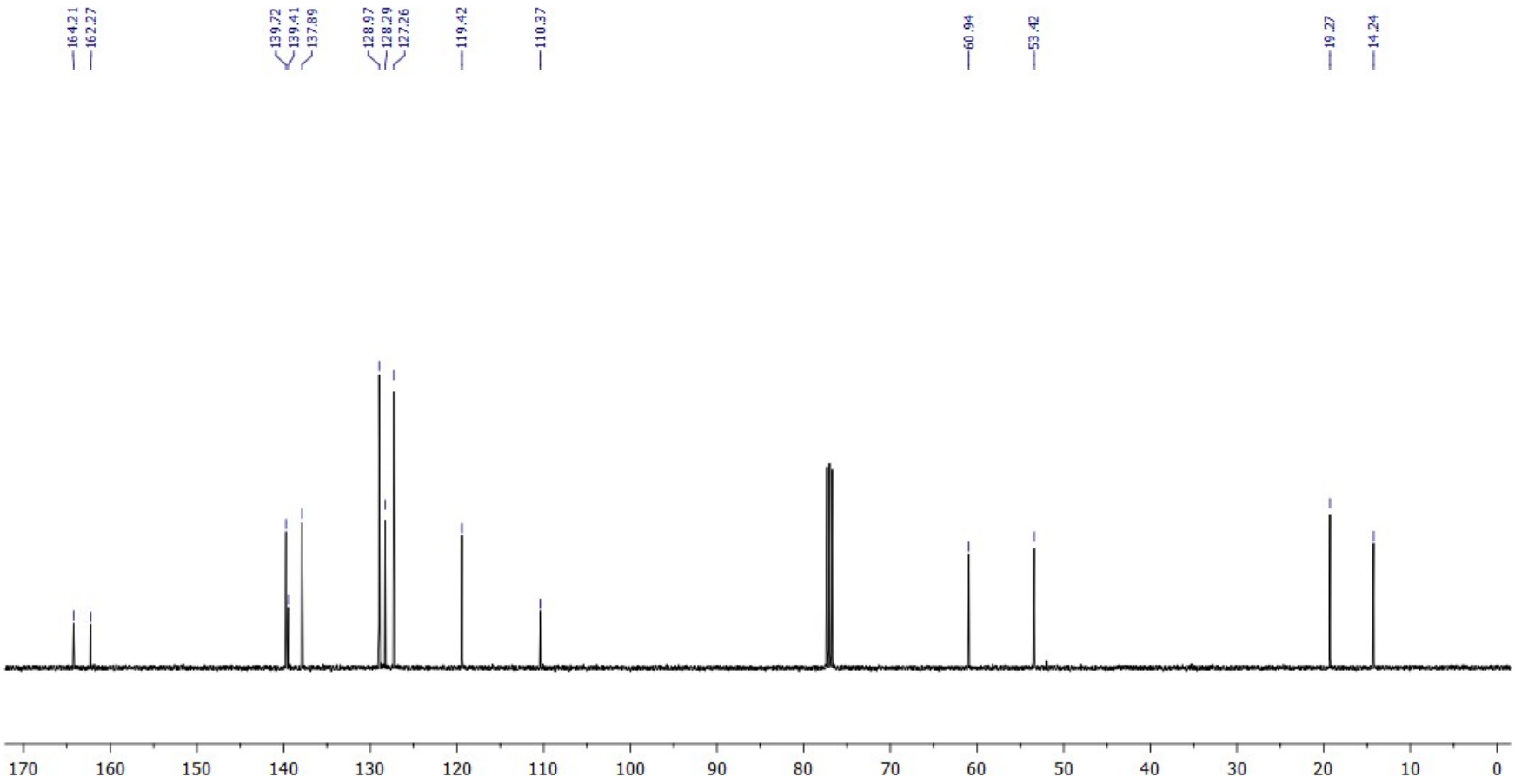
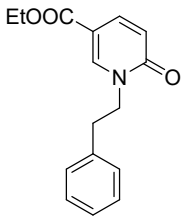


^{1}H NMR (400.1 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$)



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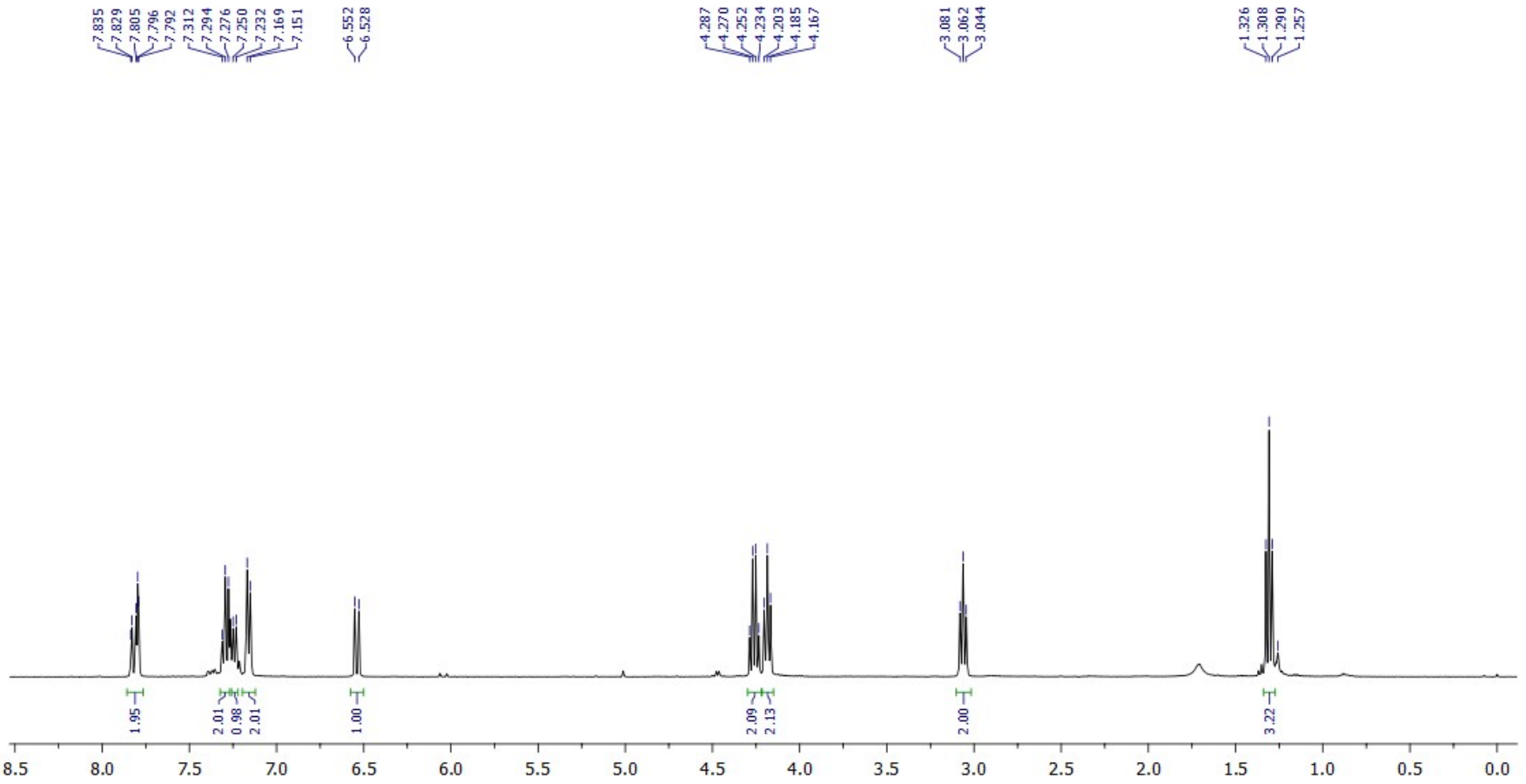
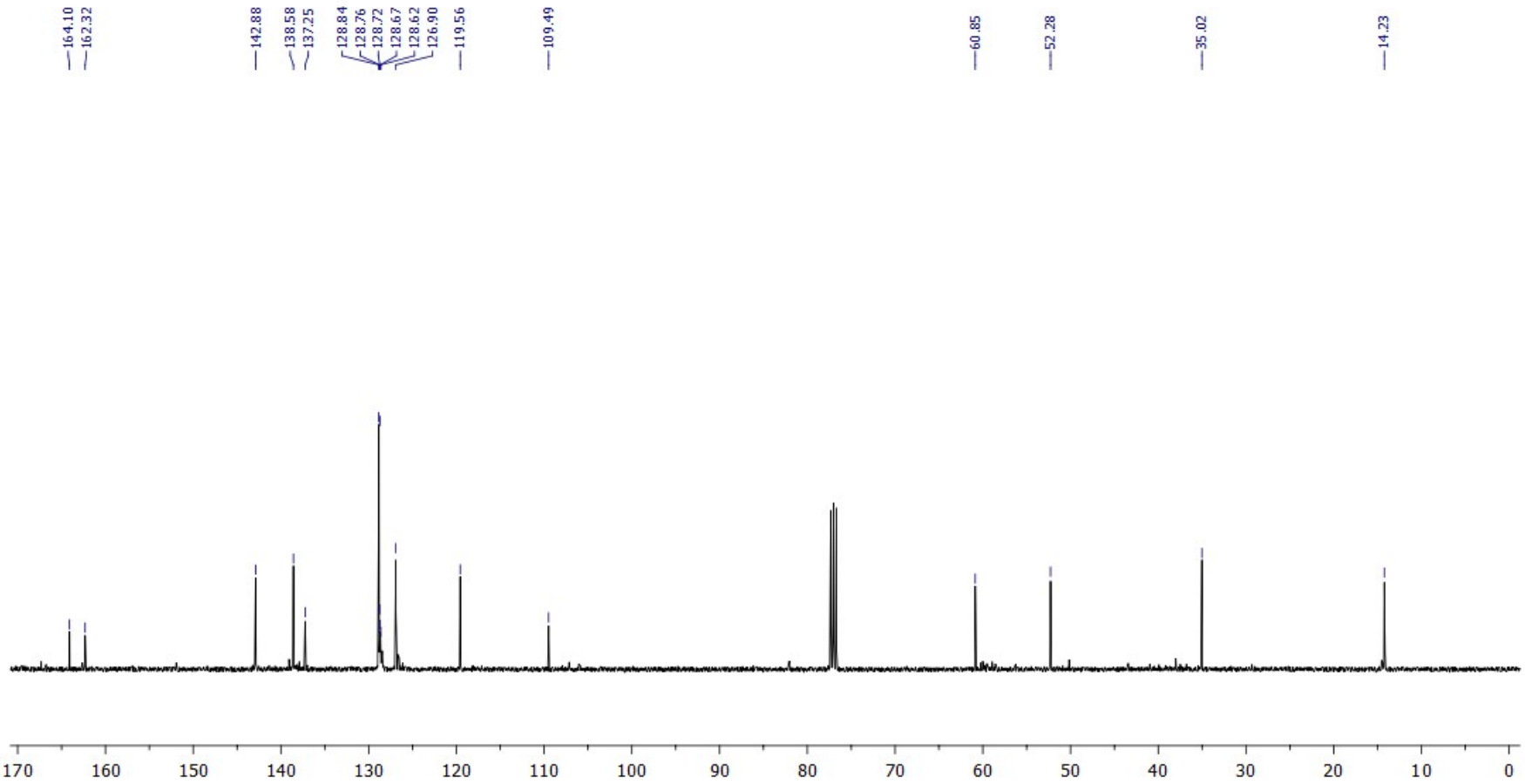
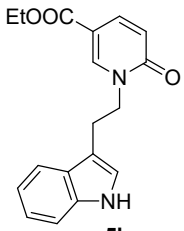


^{1}H NMR (400.1 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$)



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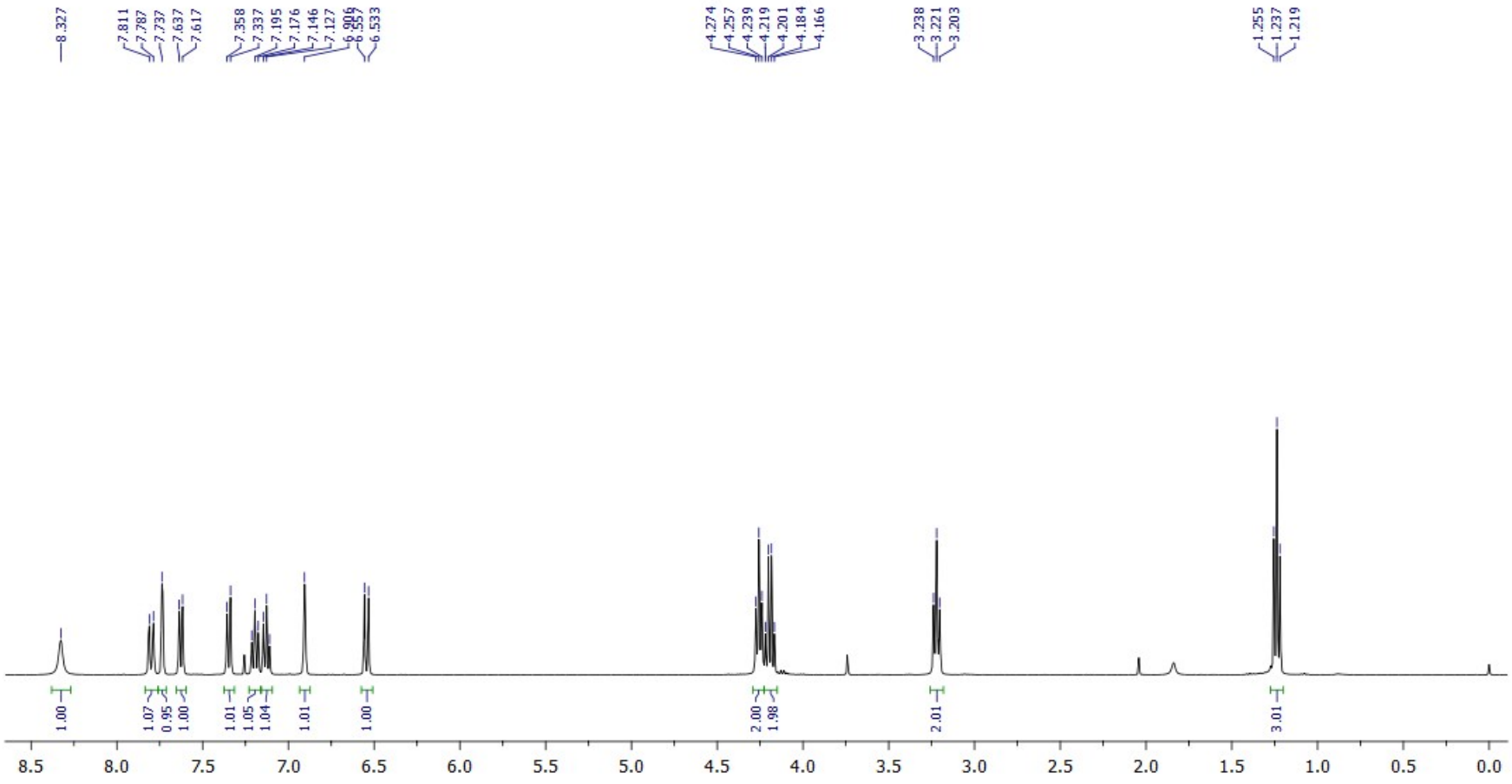
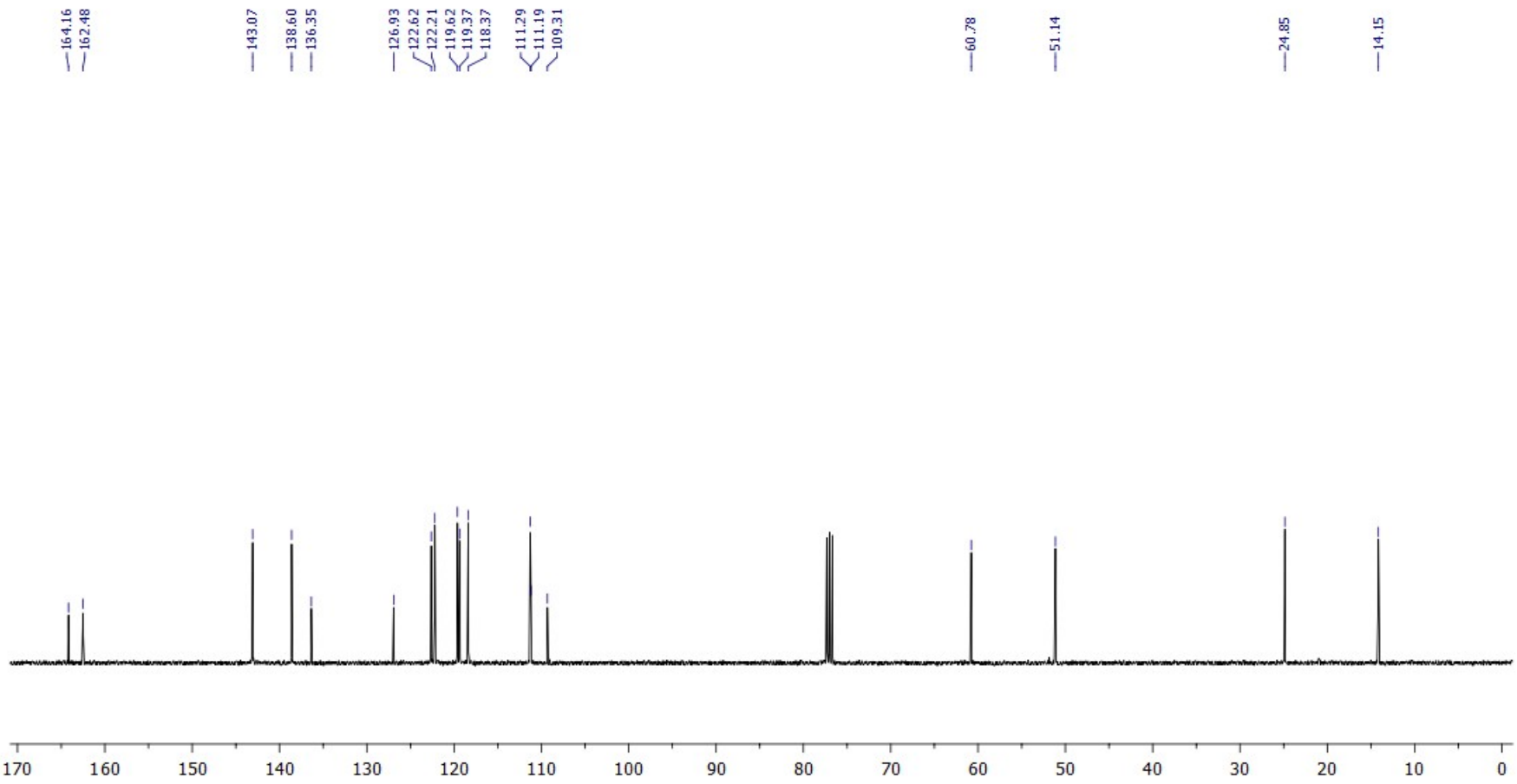
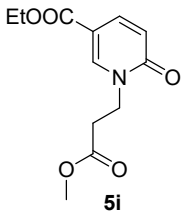


^{1}H NMR (400.1 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$)



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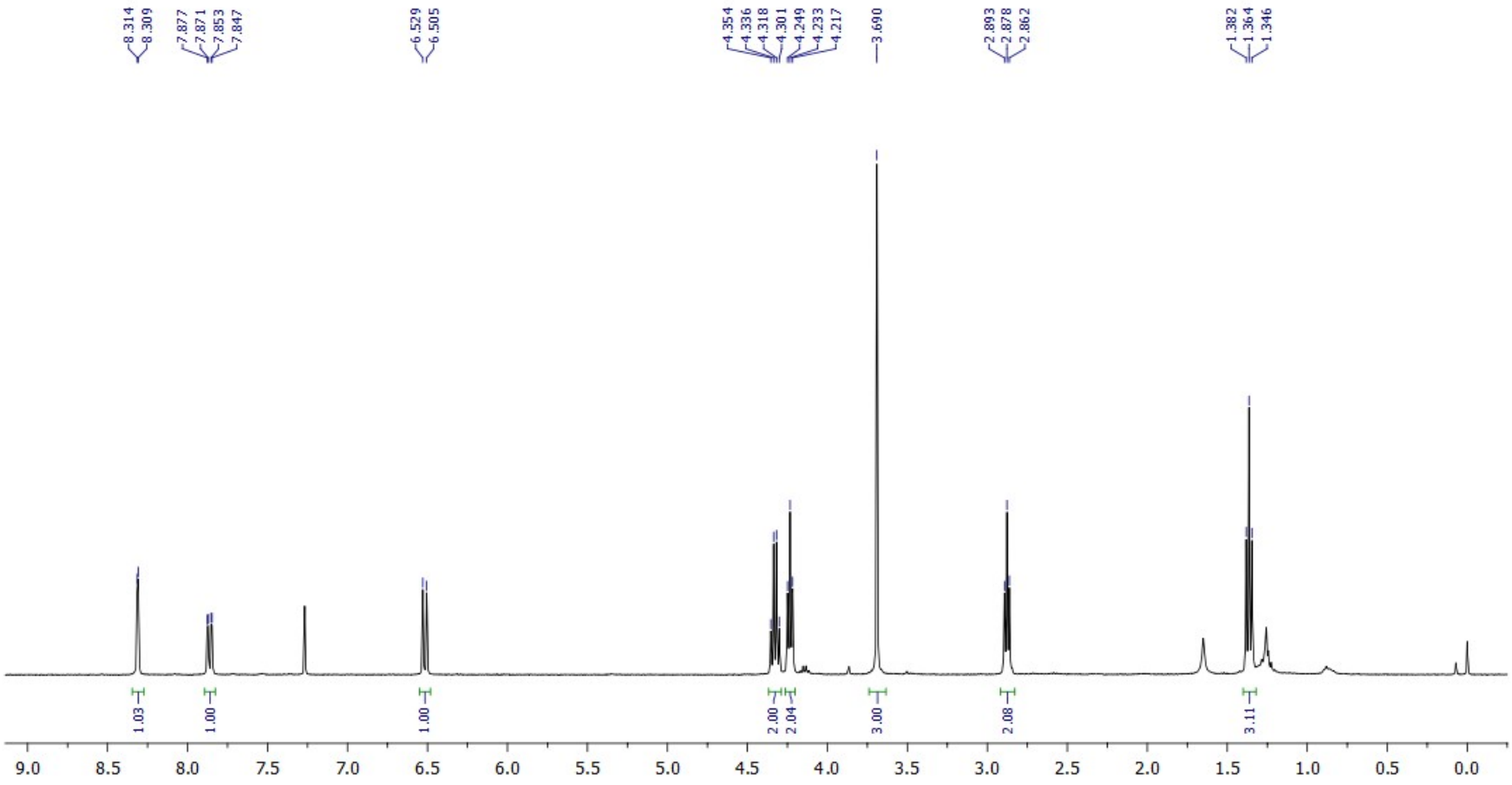
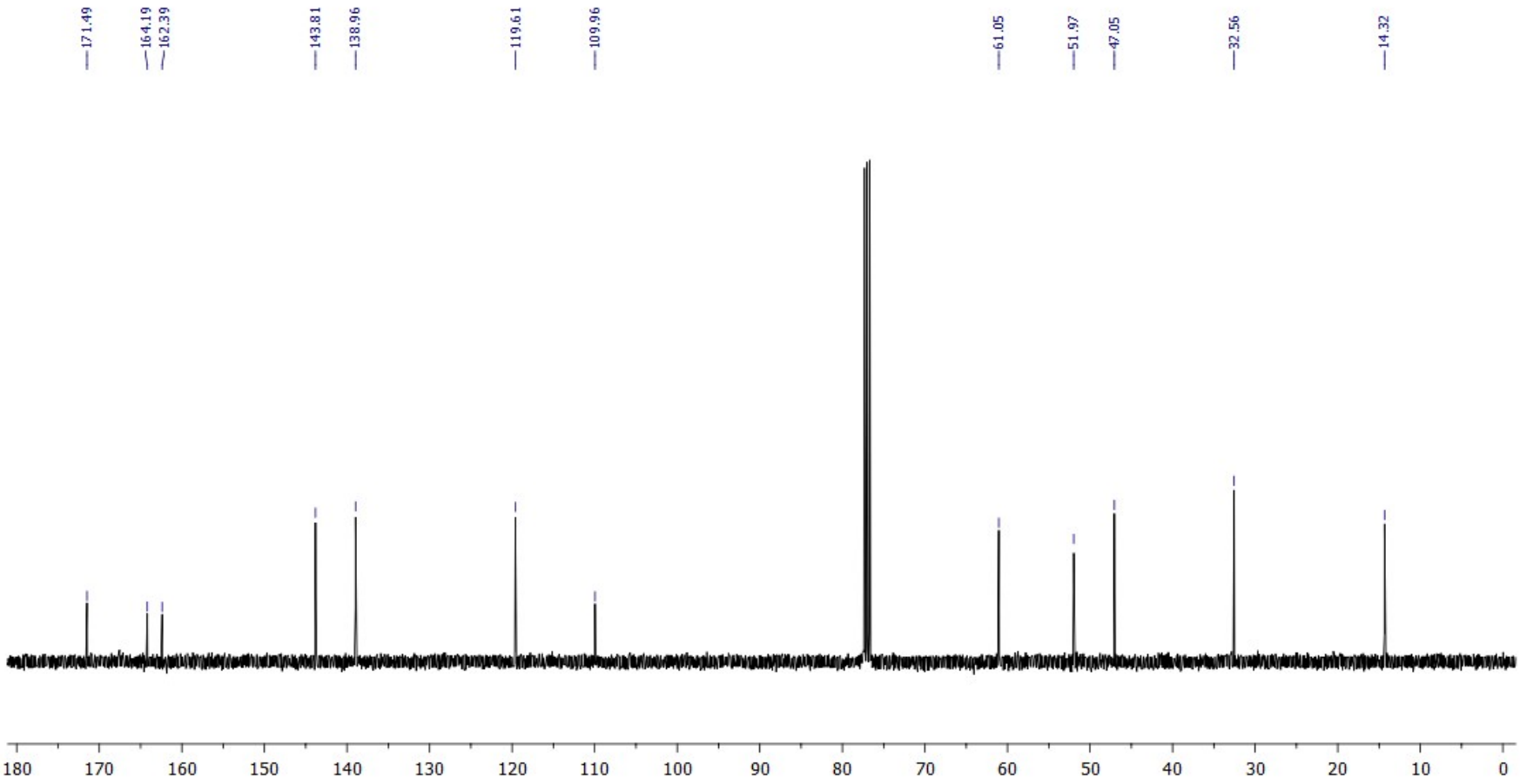
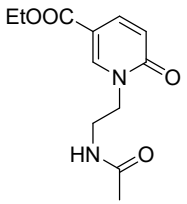


^{1}H NMR (400.1 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$)



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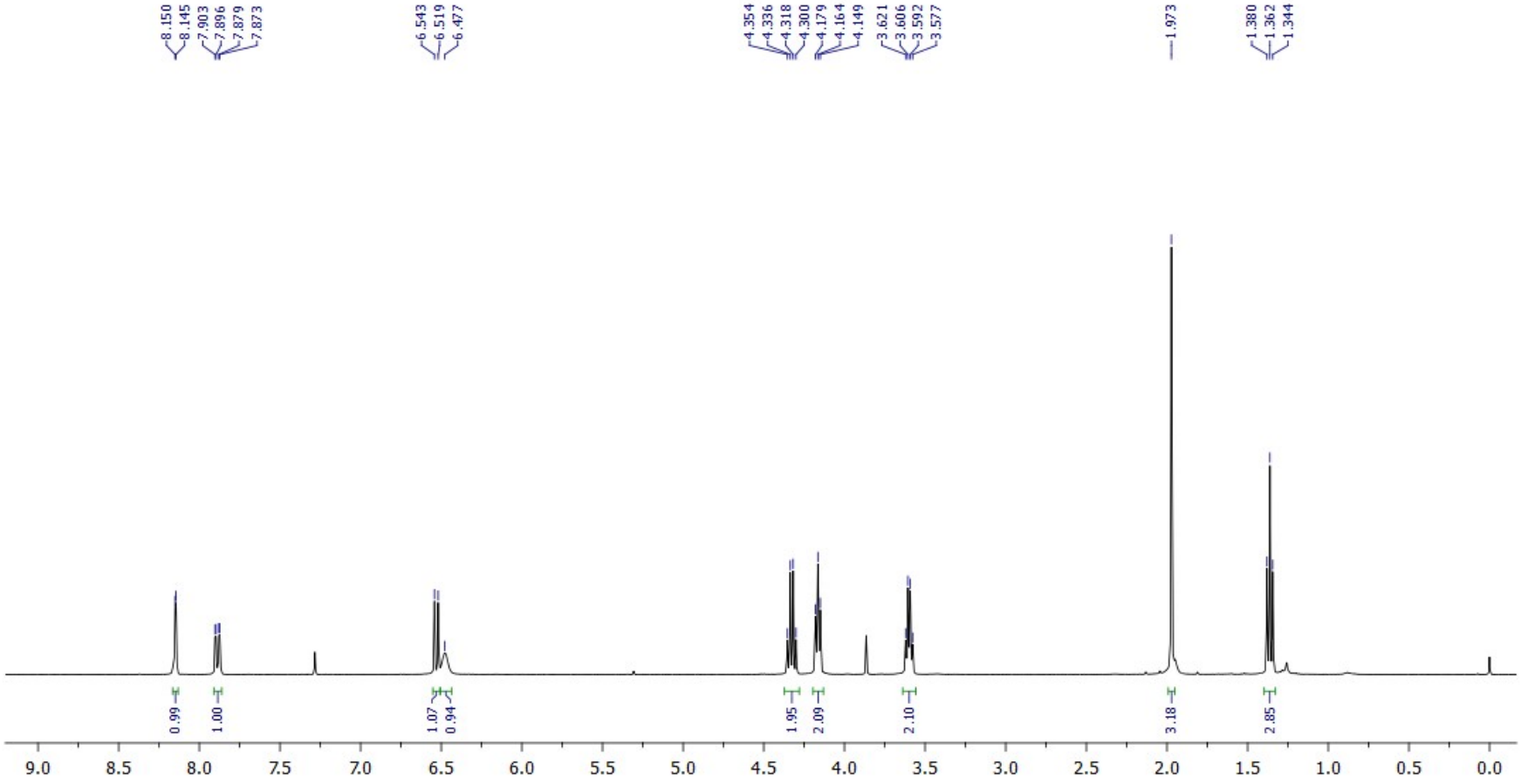
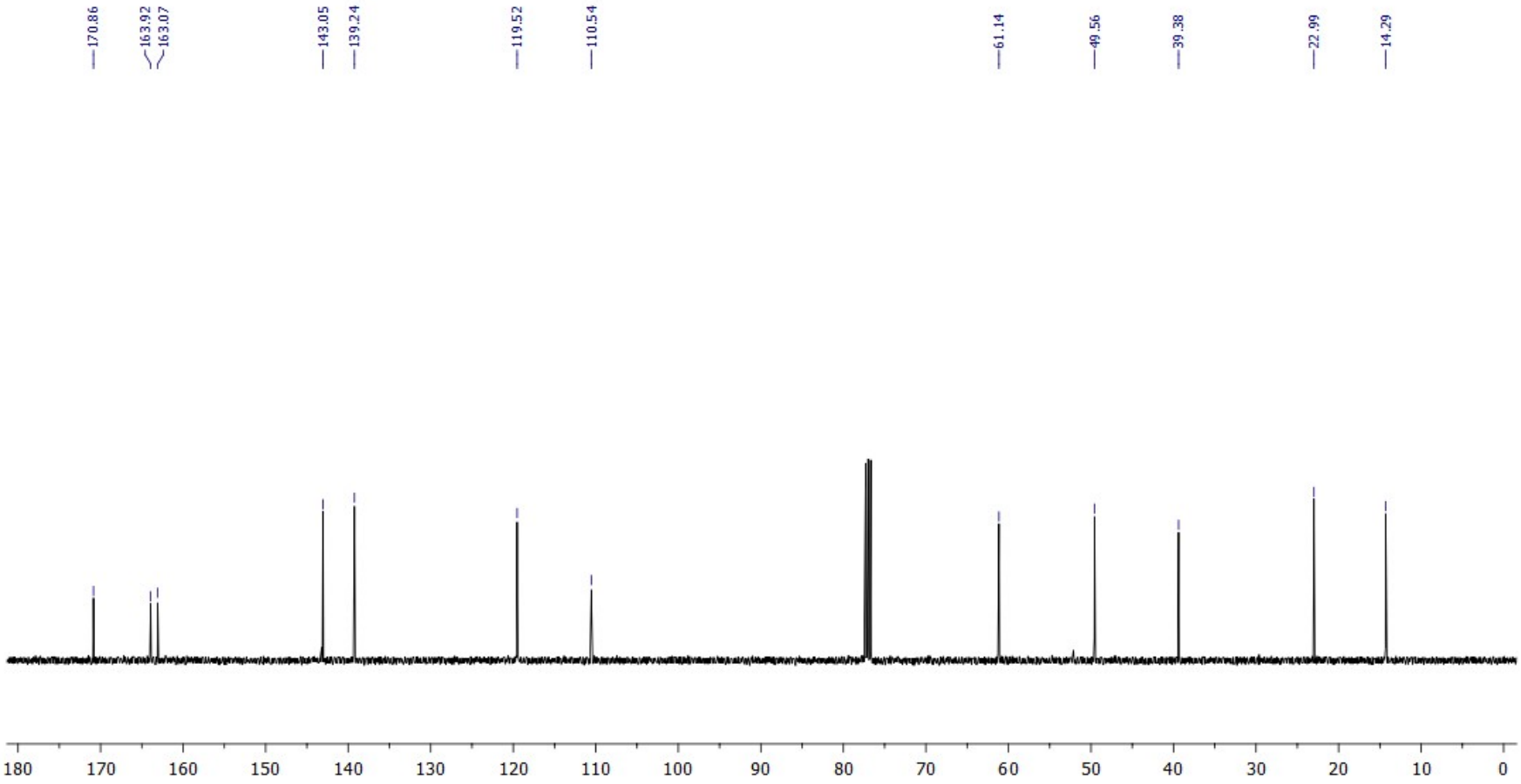
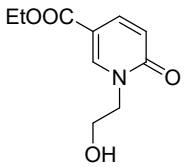


^{1}H NMR (400.1 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$)



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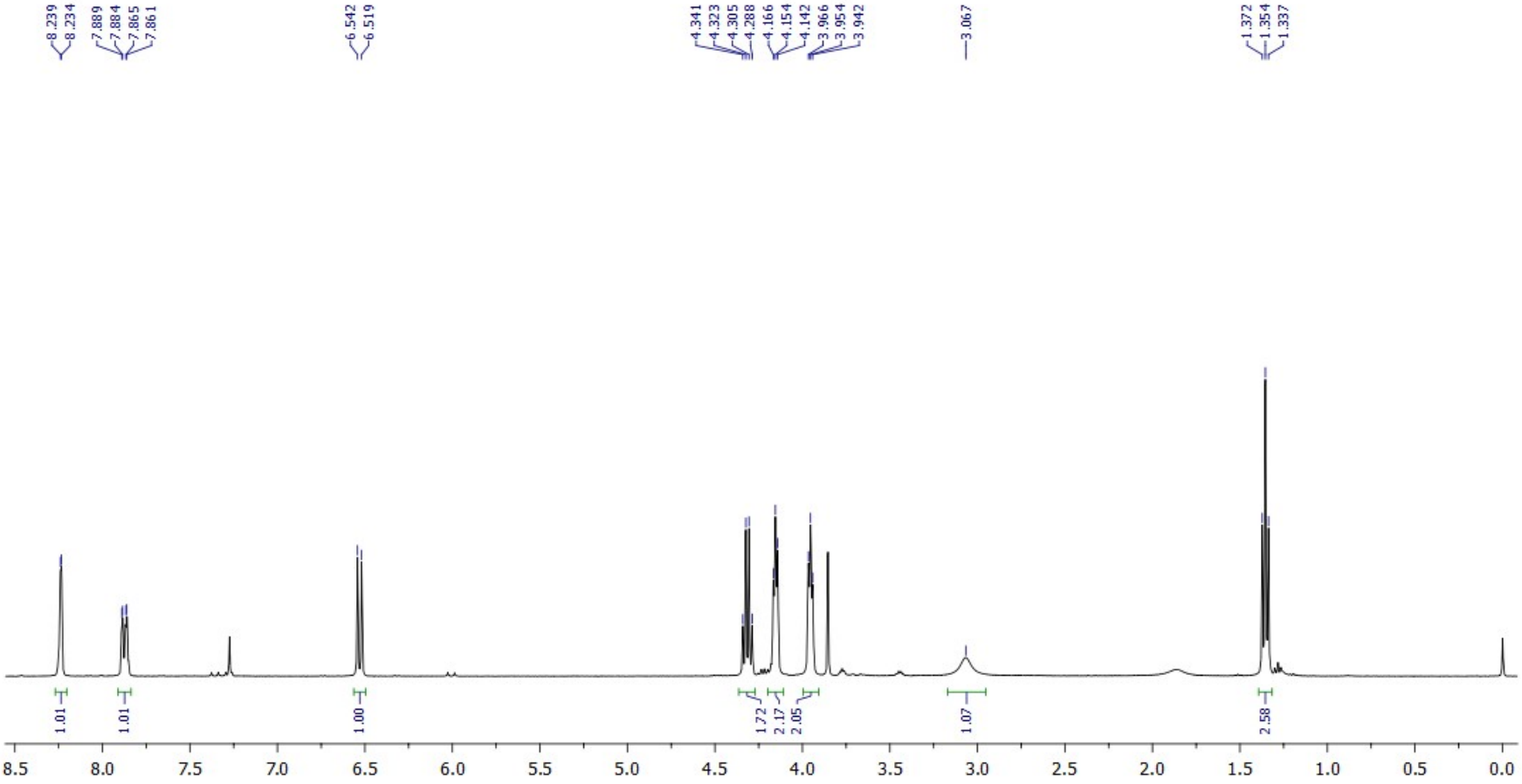
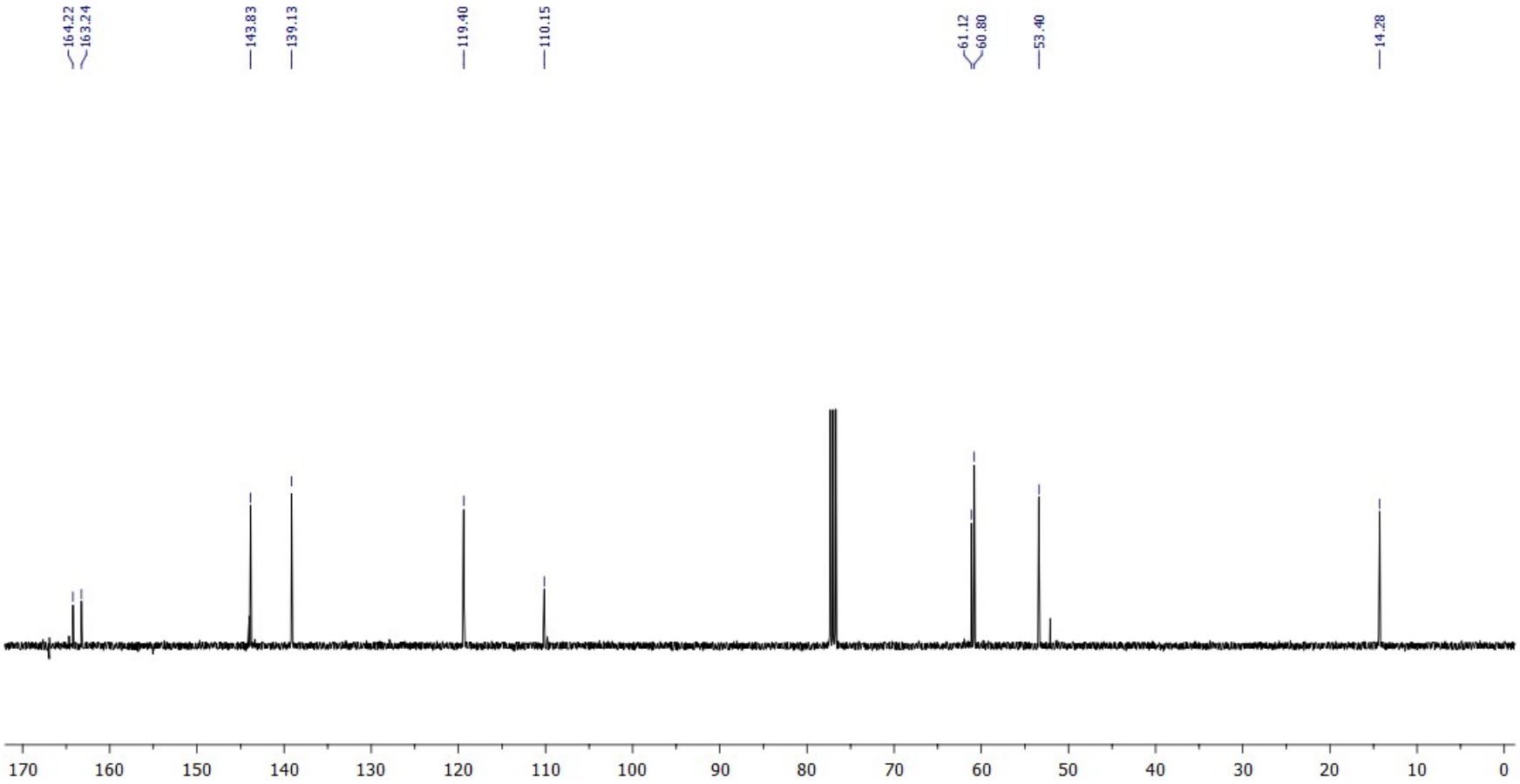
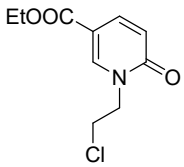


^{1}H NMR (400.1 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$)



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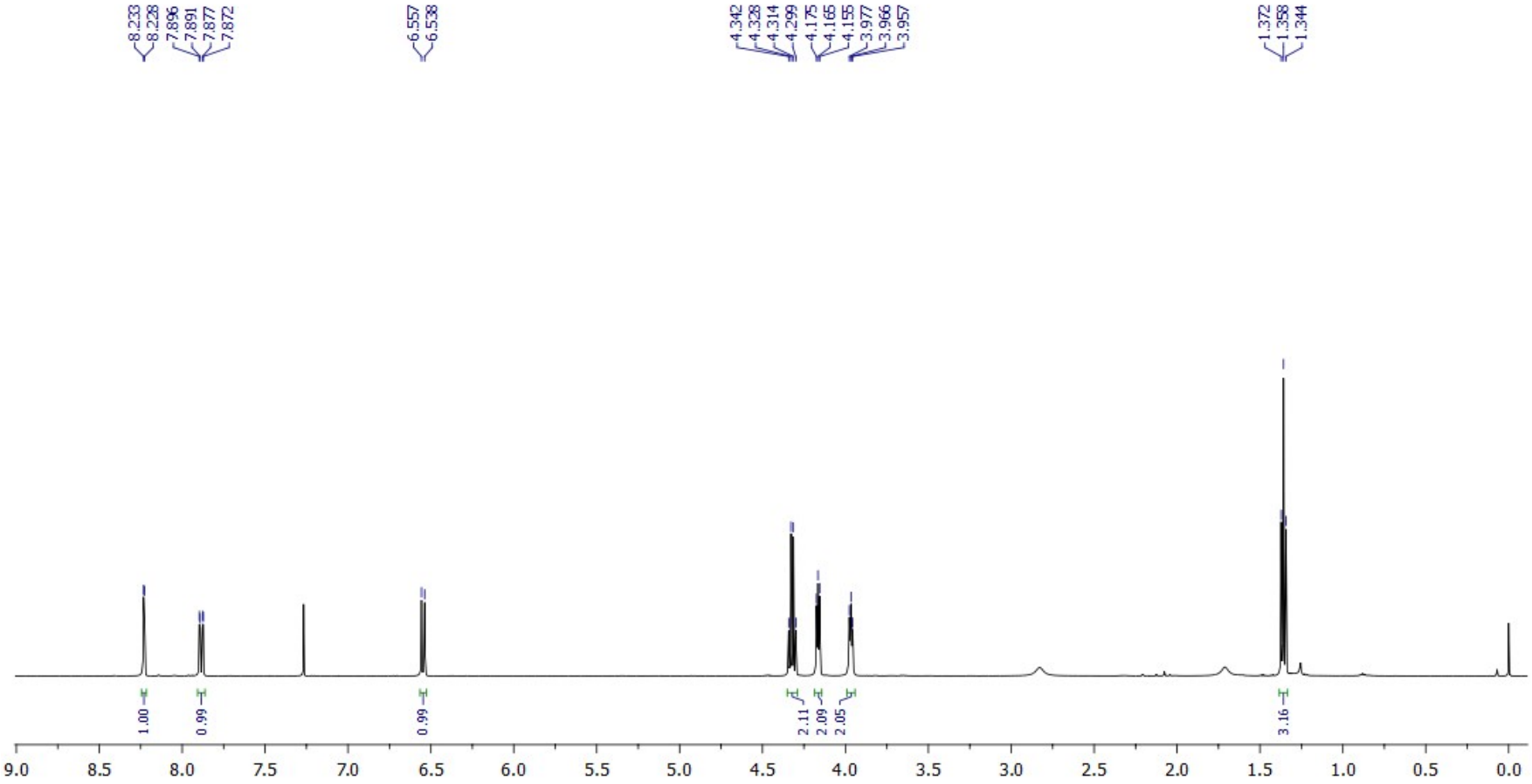
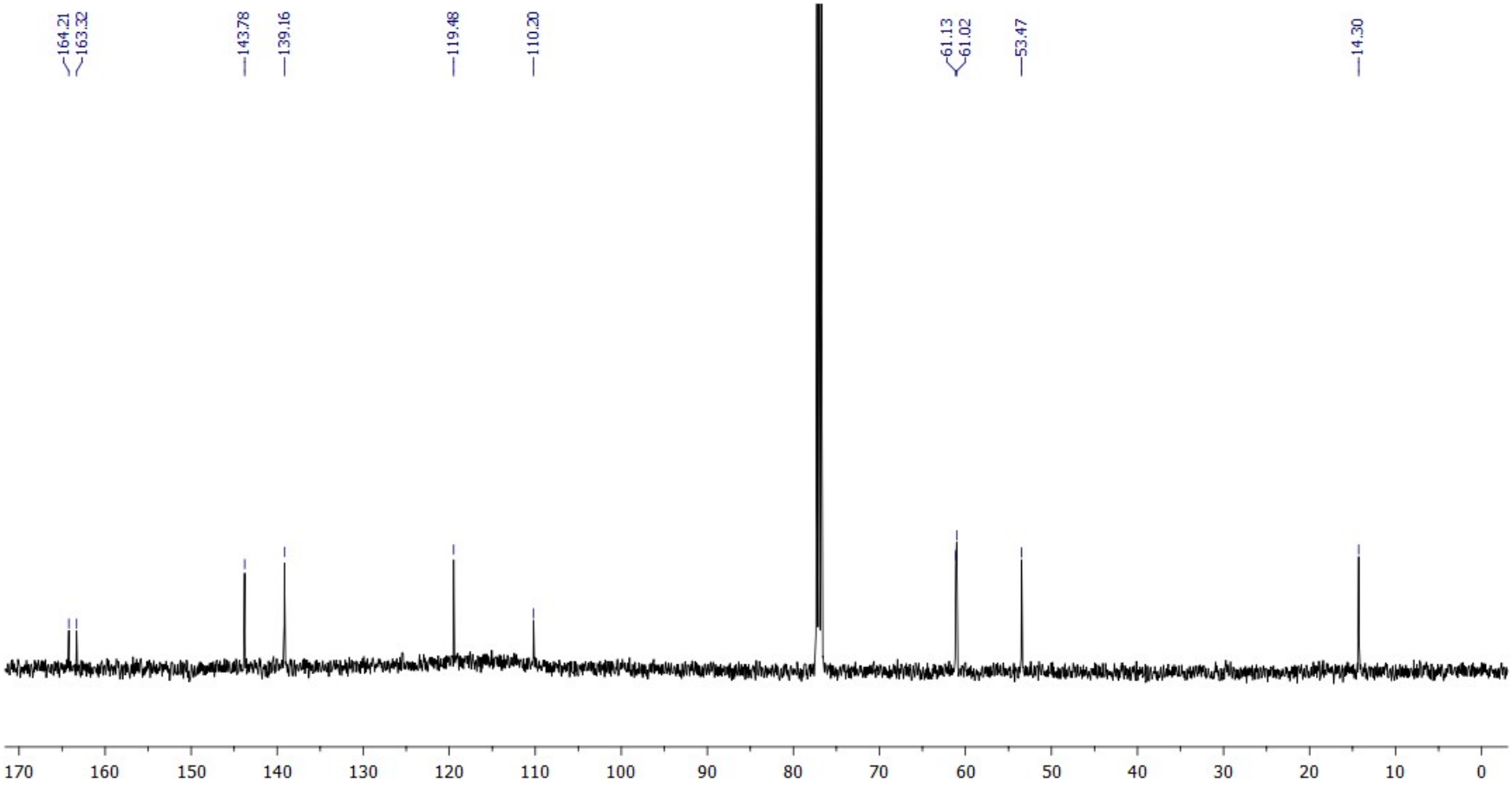
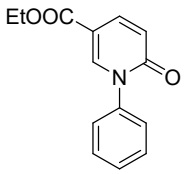


^{1}H NMR (500.3 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (125.8 MHz, $CDCl_3$)



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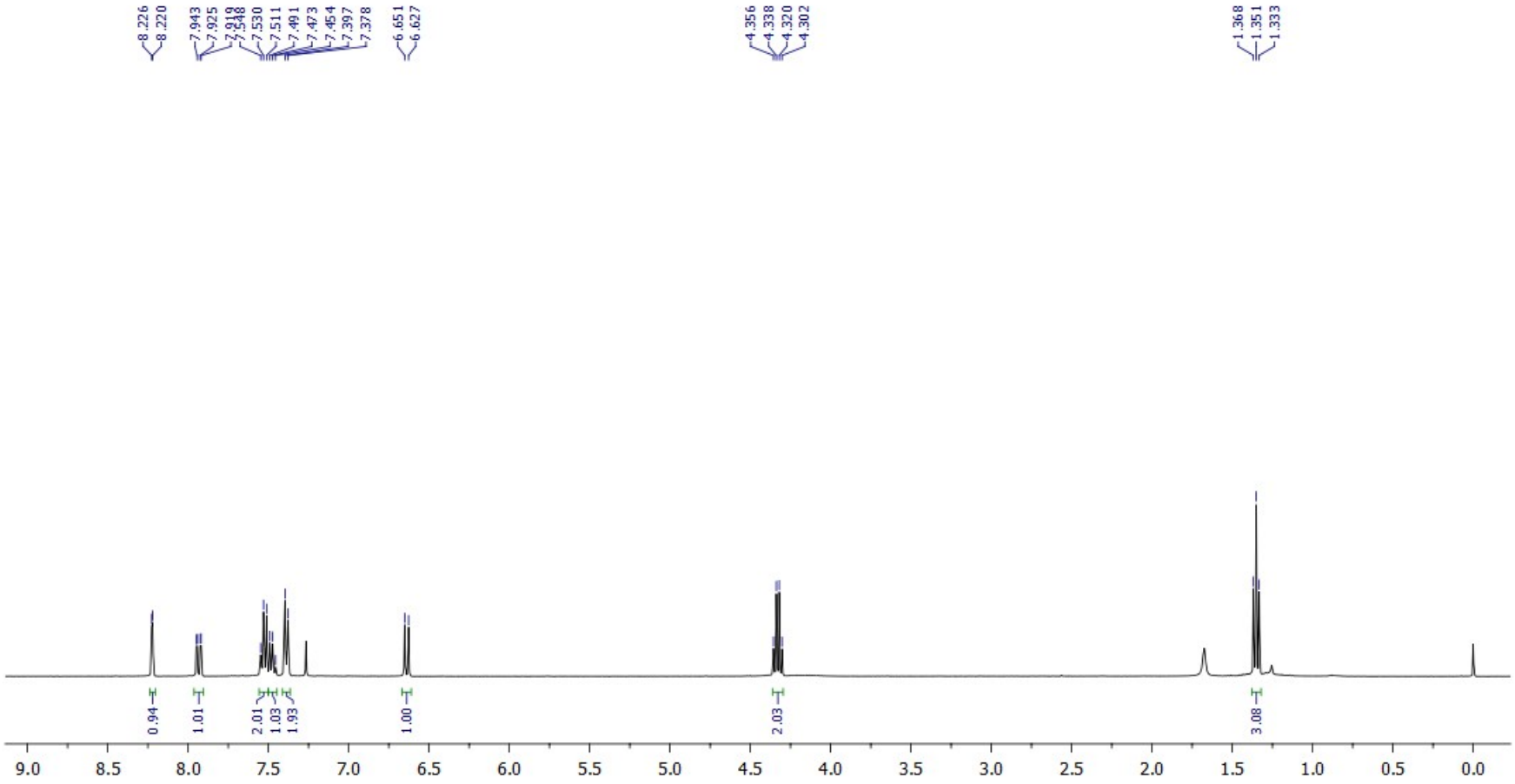
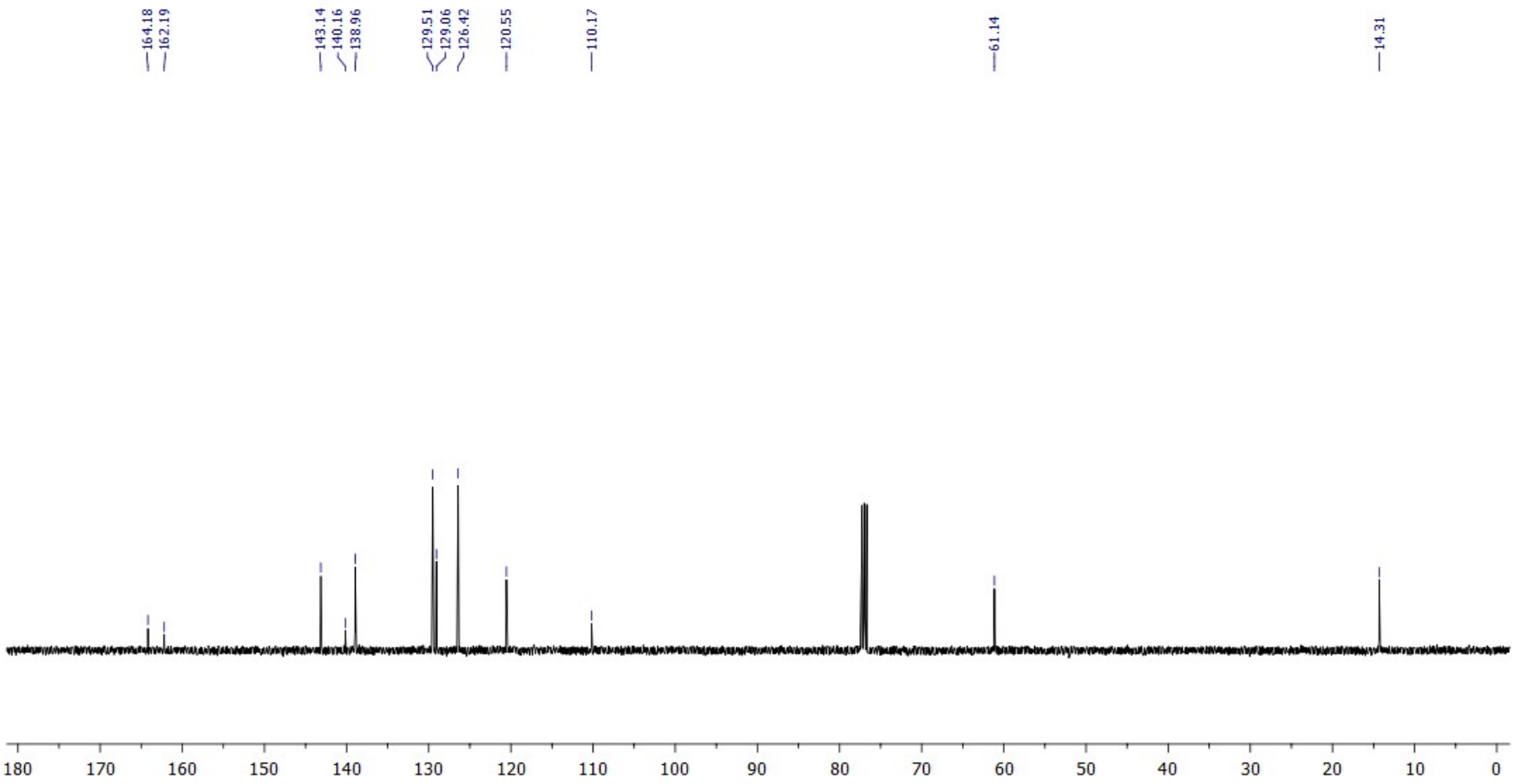
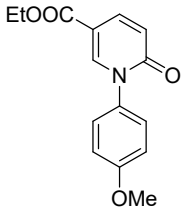


^{1}H NMR (400.1 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$)



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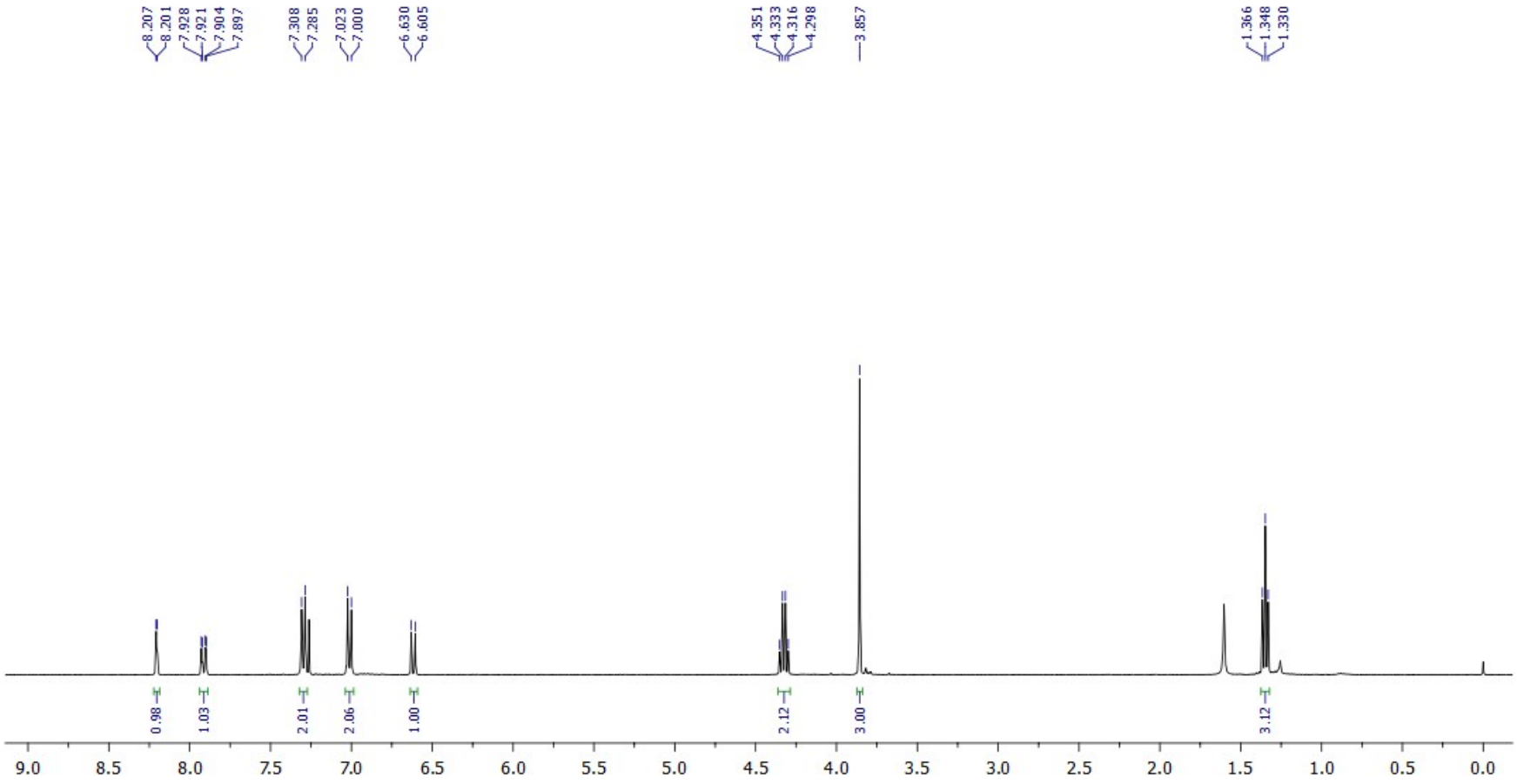
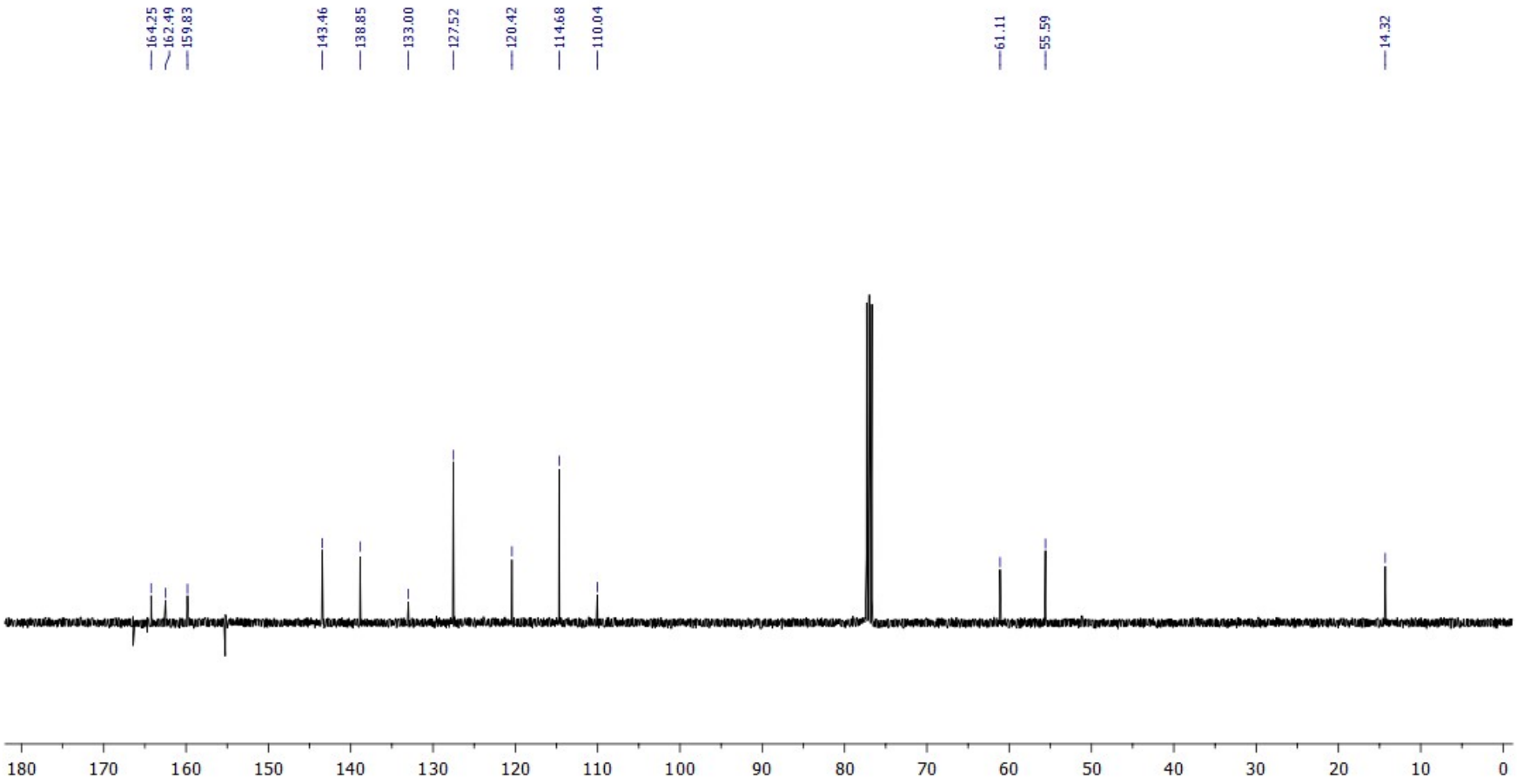
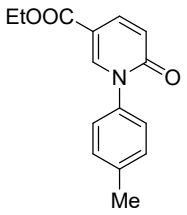


^{1}H NMR (400.1 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$)



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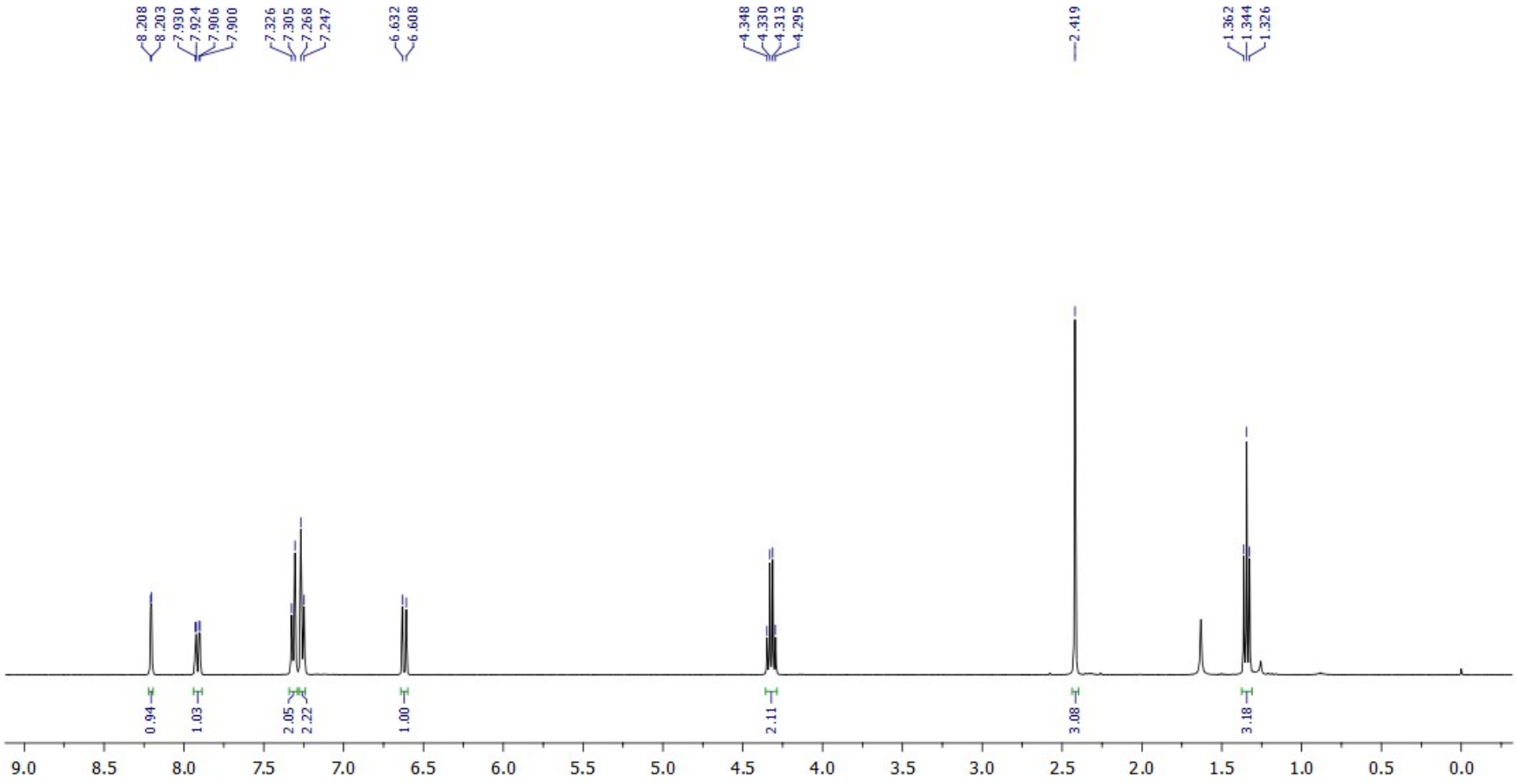
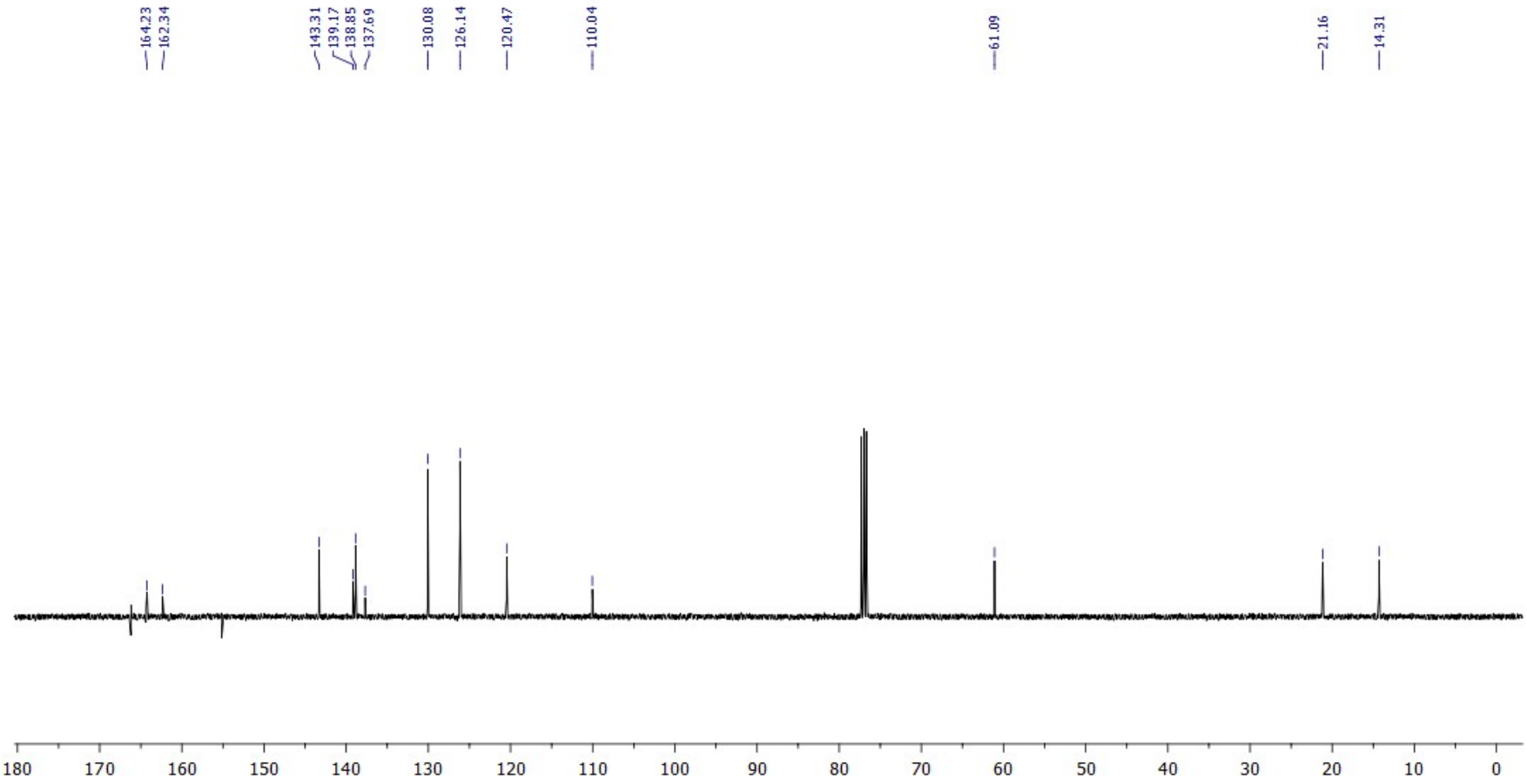
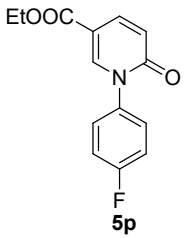


^{1}H NMR (400.1 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$)



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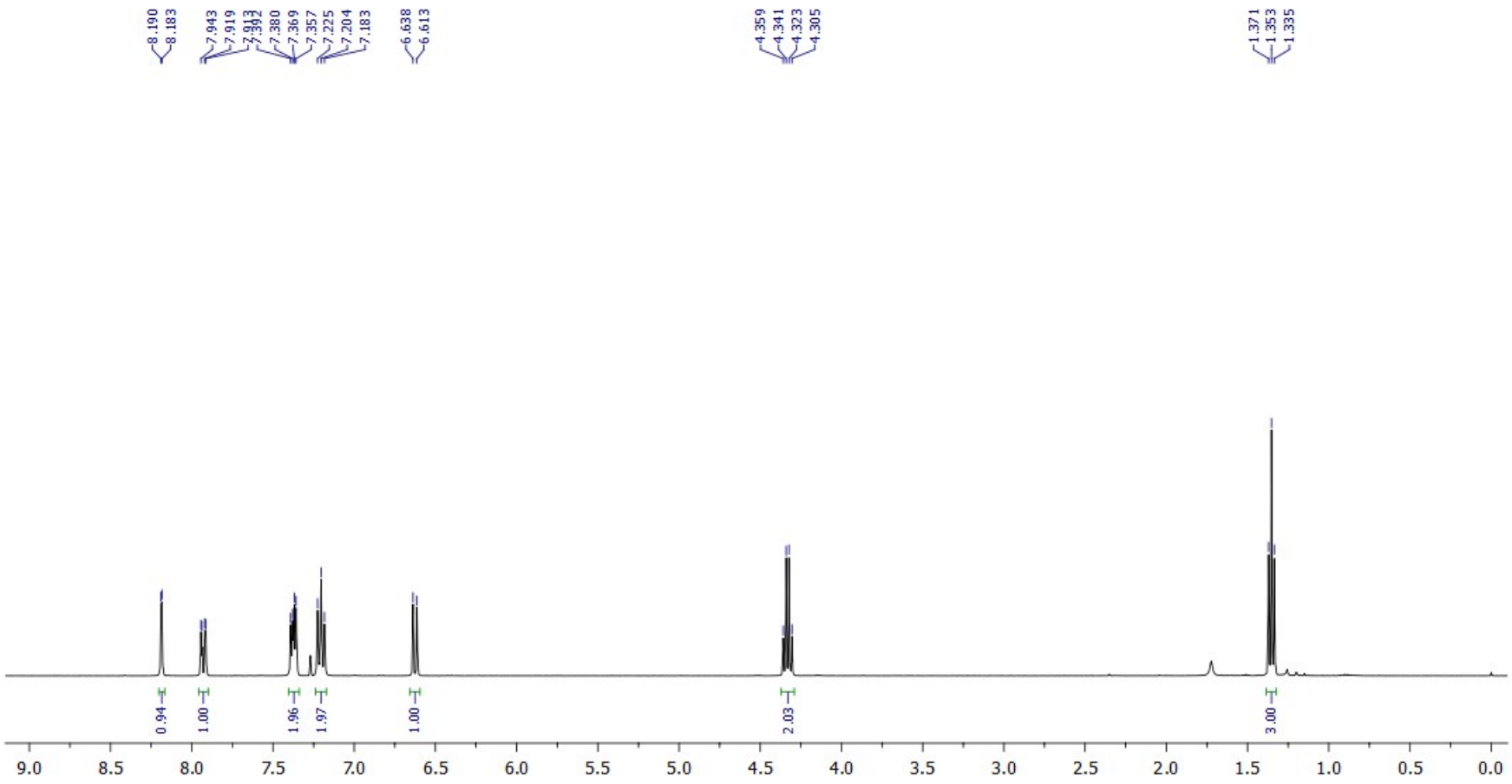
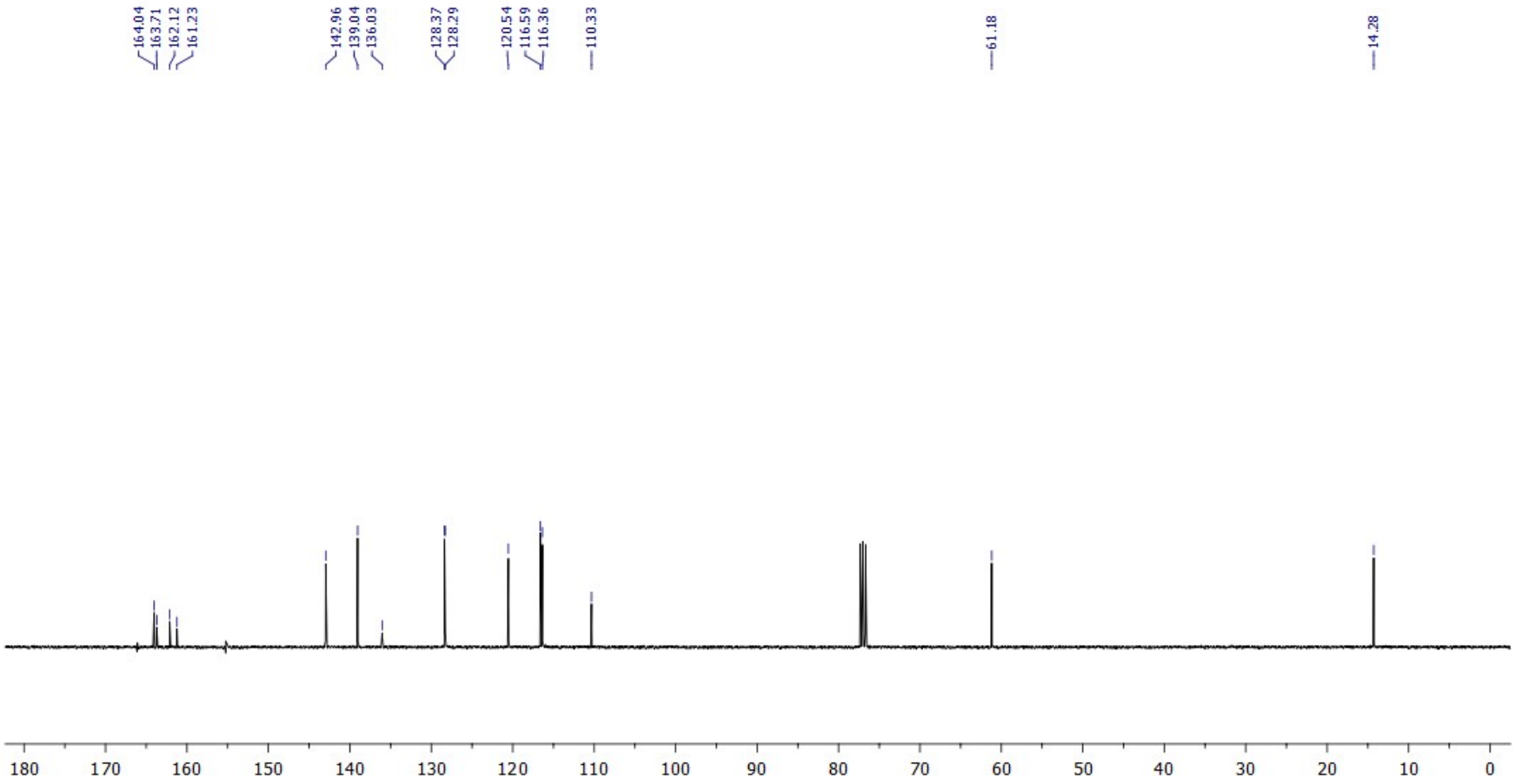
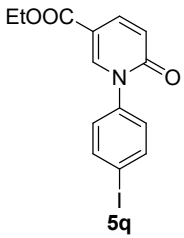


^{1}H NMR (400.1 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$)



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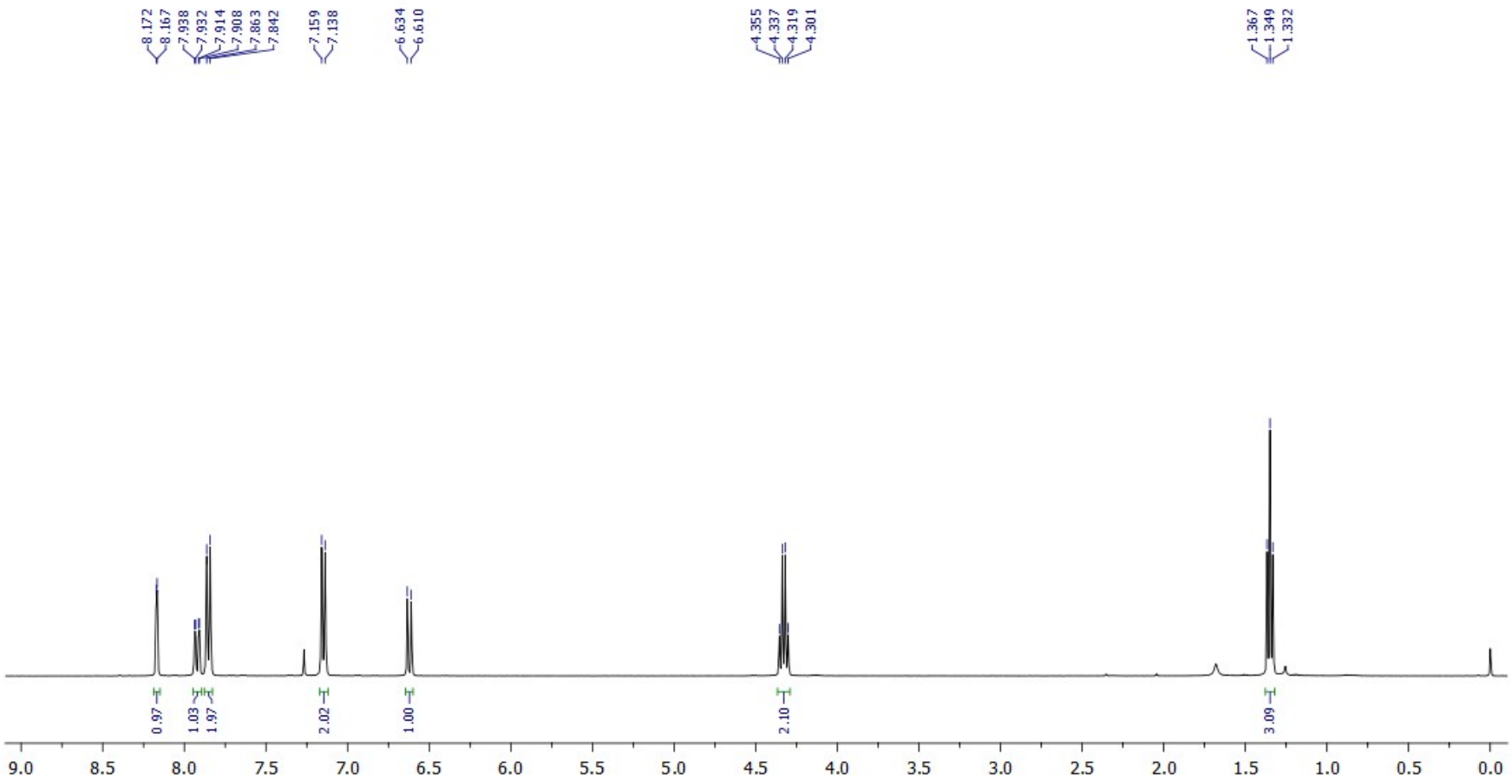
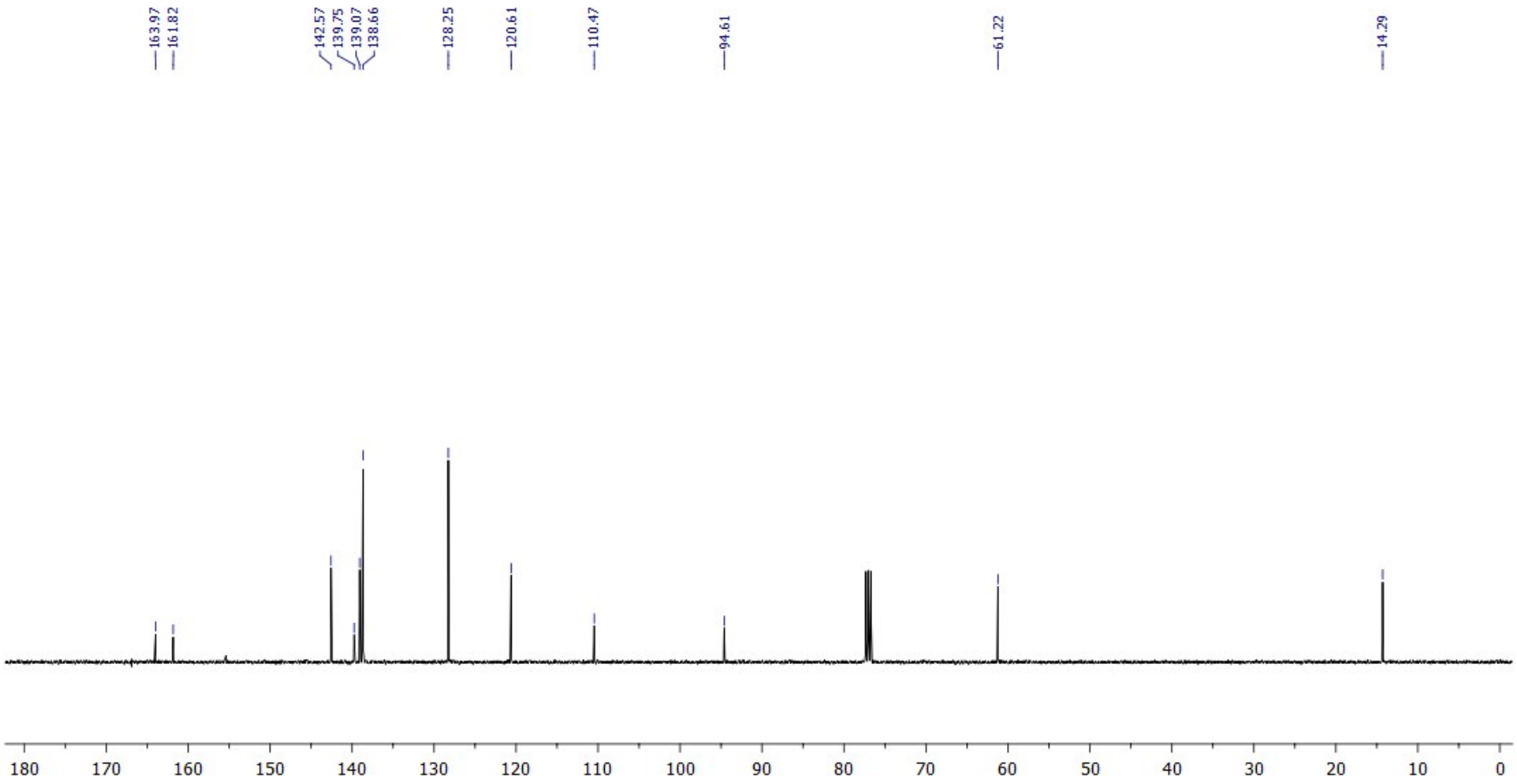
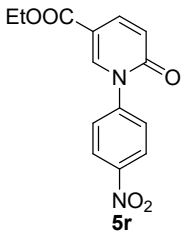


^{1}H NMR (400.1 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$)



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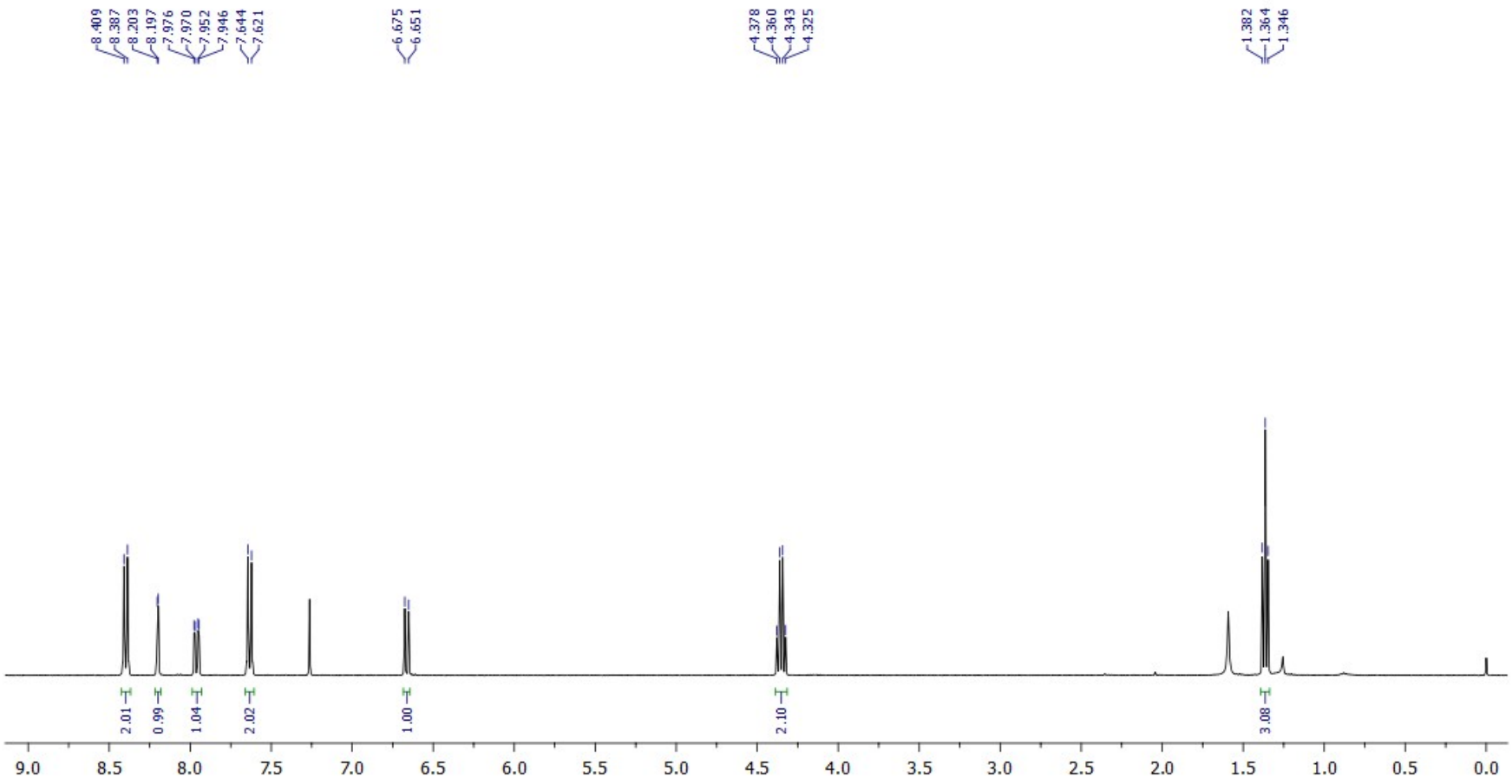
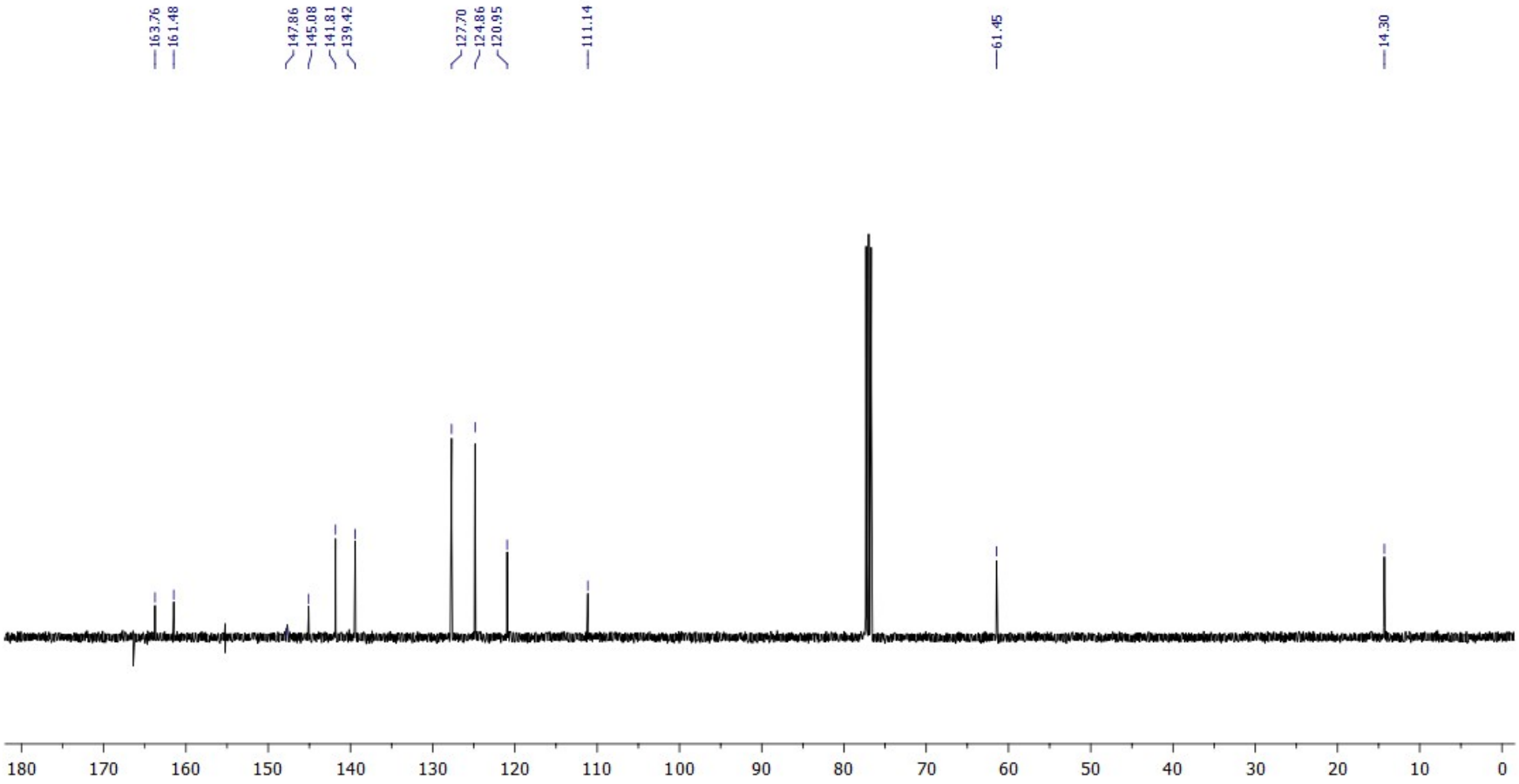
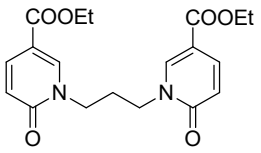


^{1}H NMR (400.1 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$)



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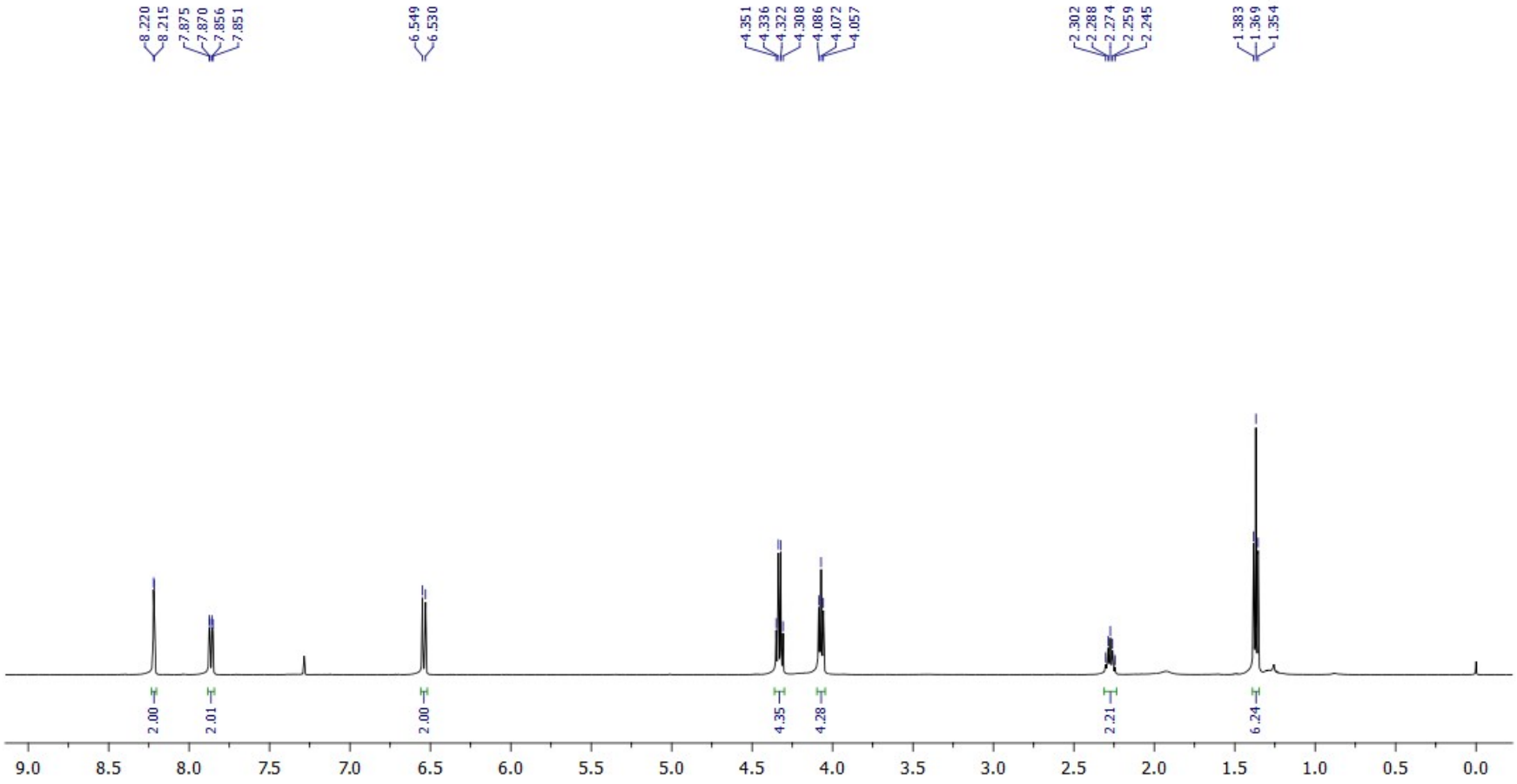
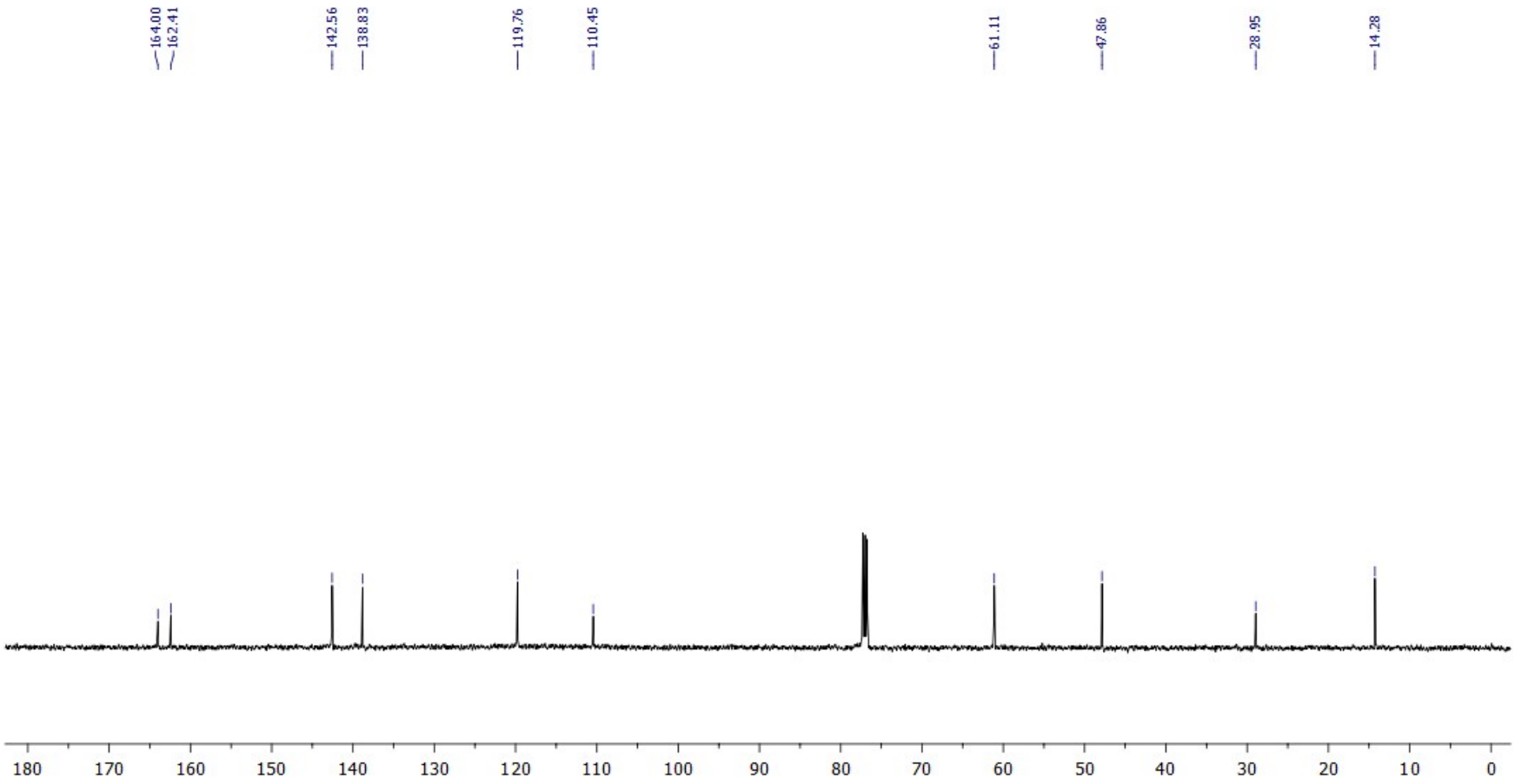
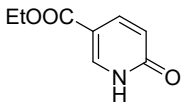


^{1}H NMR (500.3 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (125.8 MHz, $CDCl_3$)



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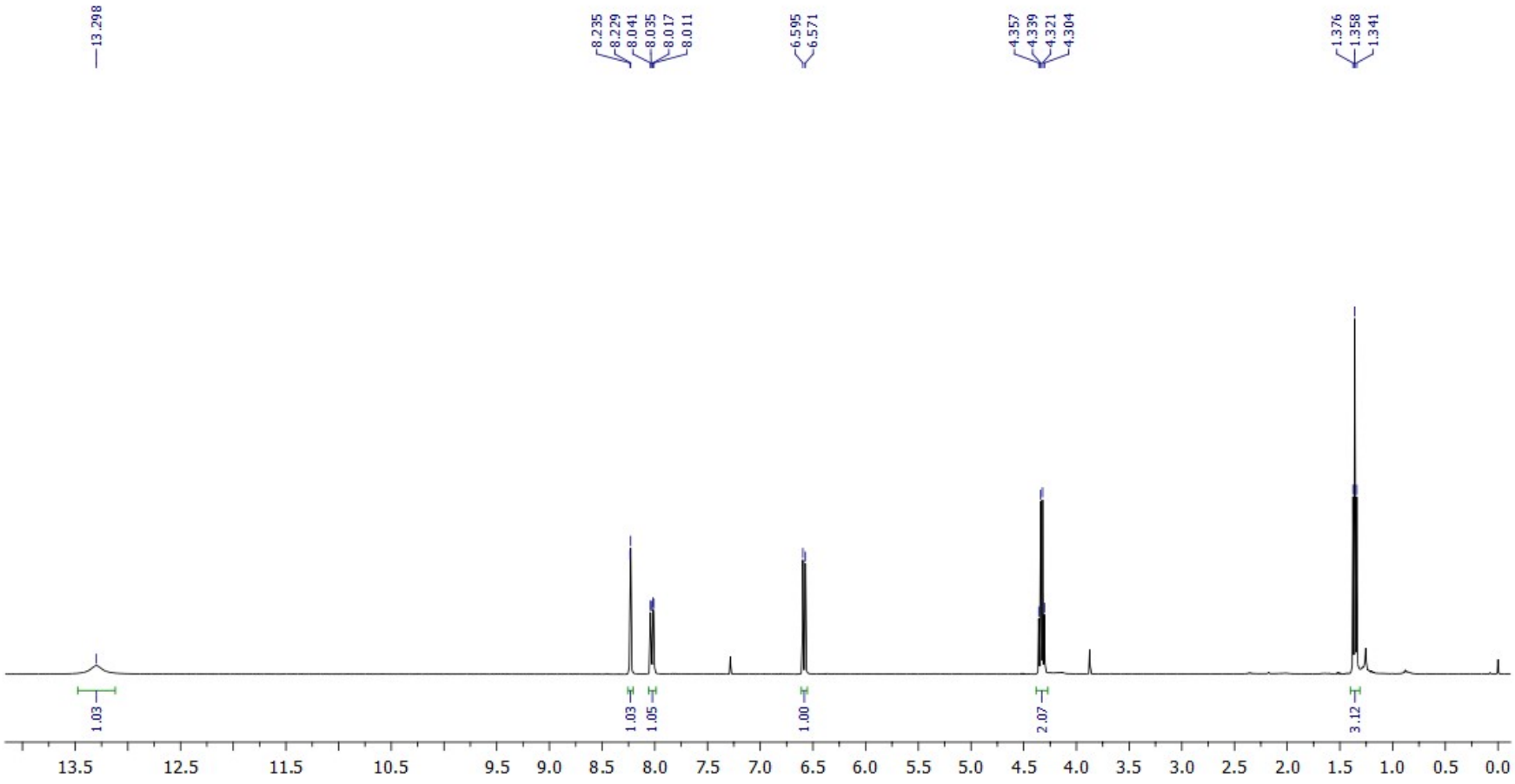
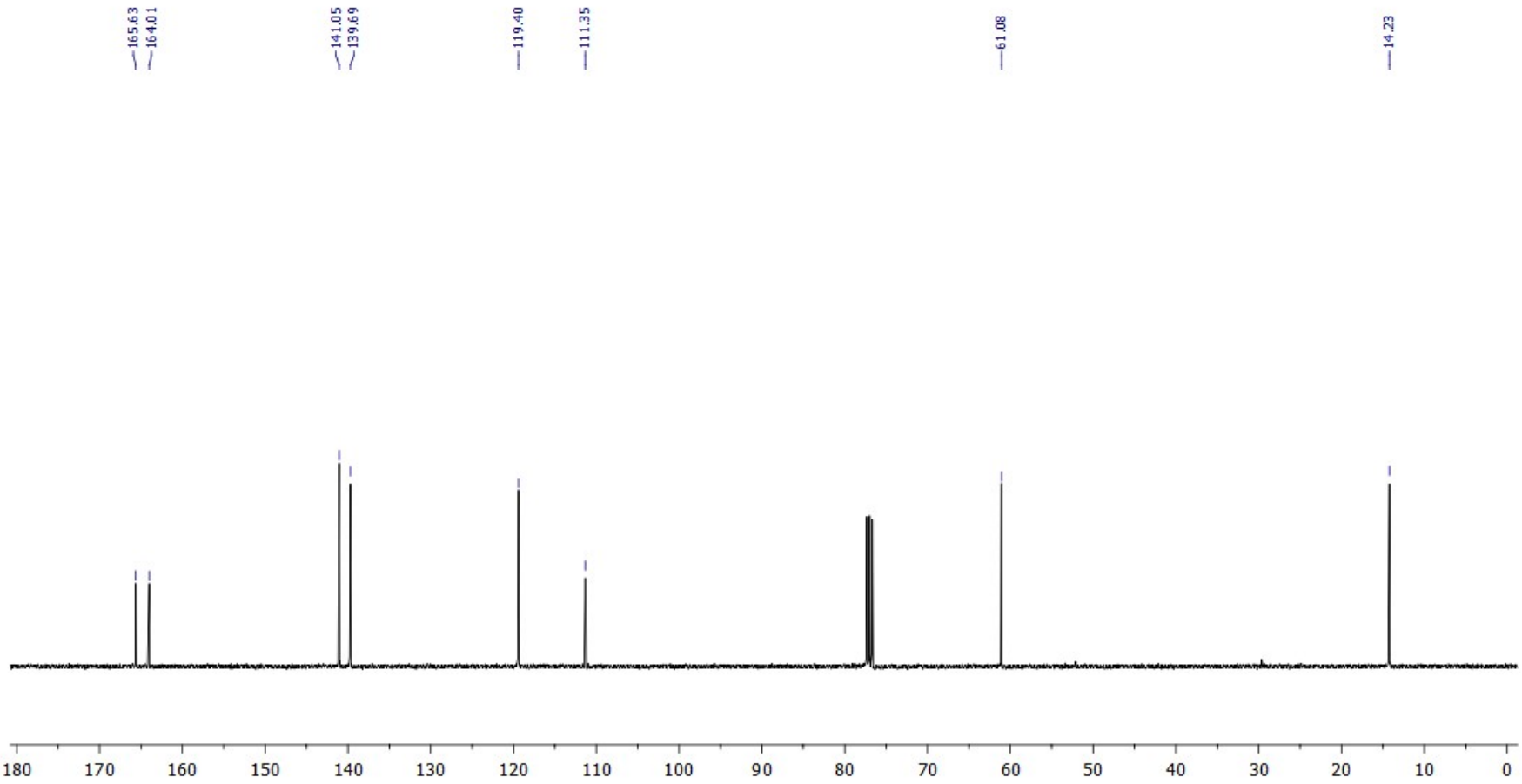
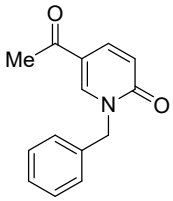


^{1}H NMR (400.1 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$)



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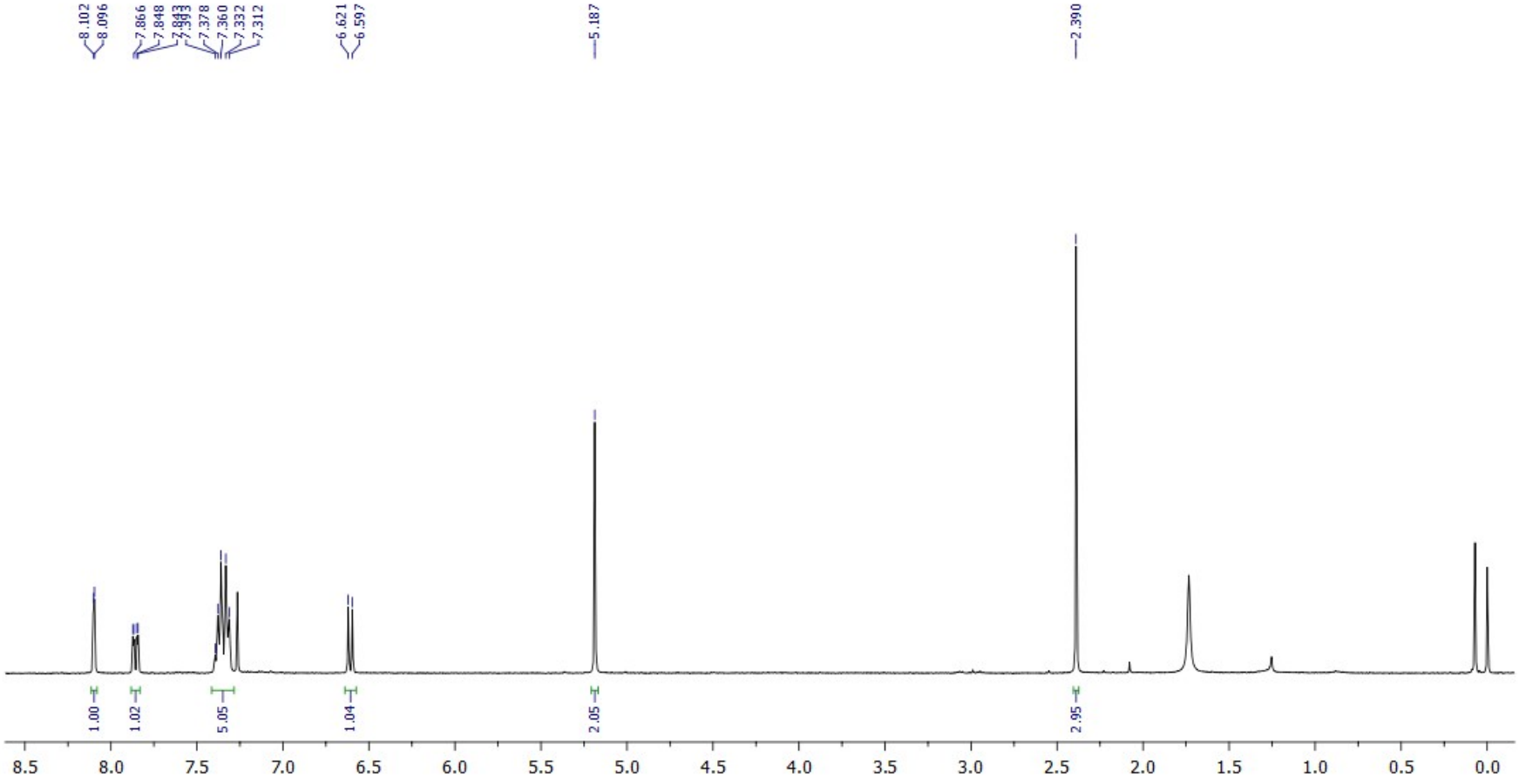
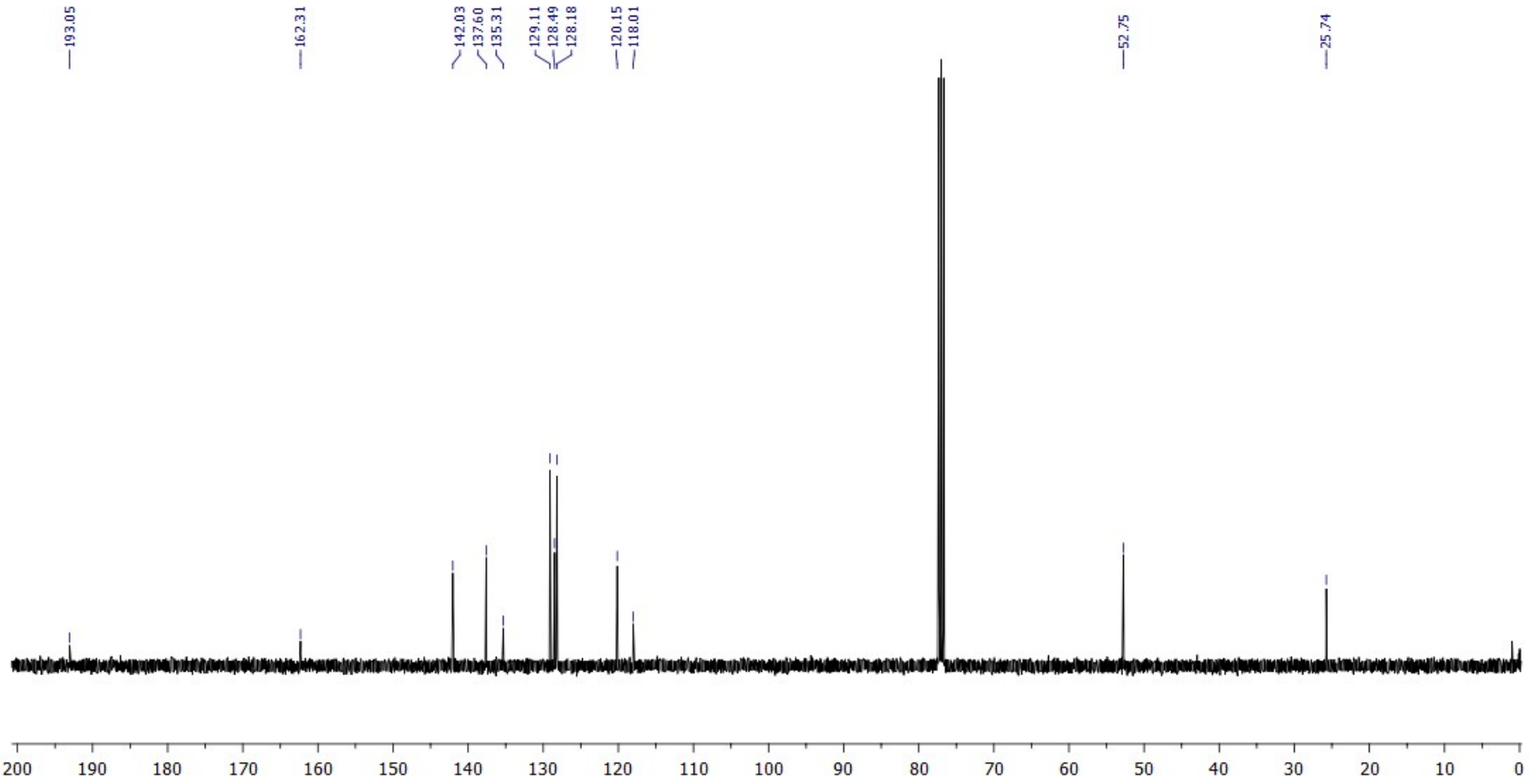
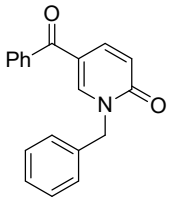


^{1}H NMR (400.1 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$)



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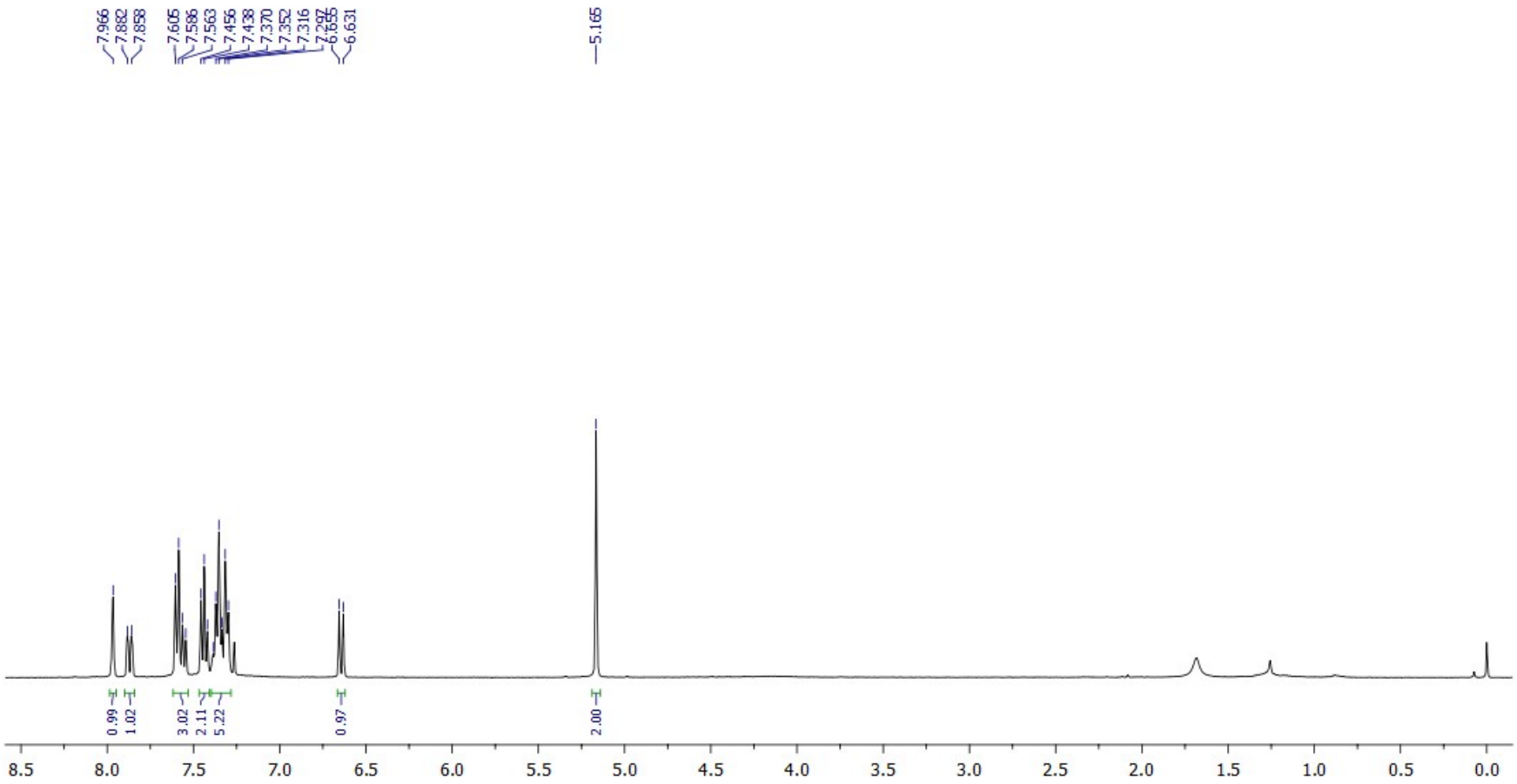
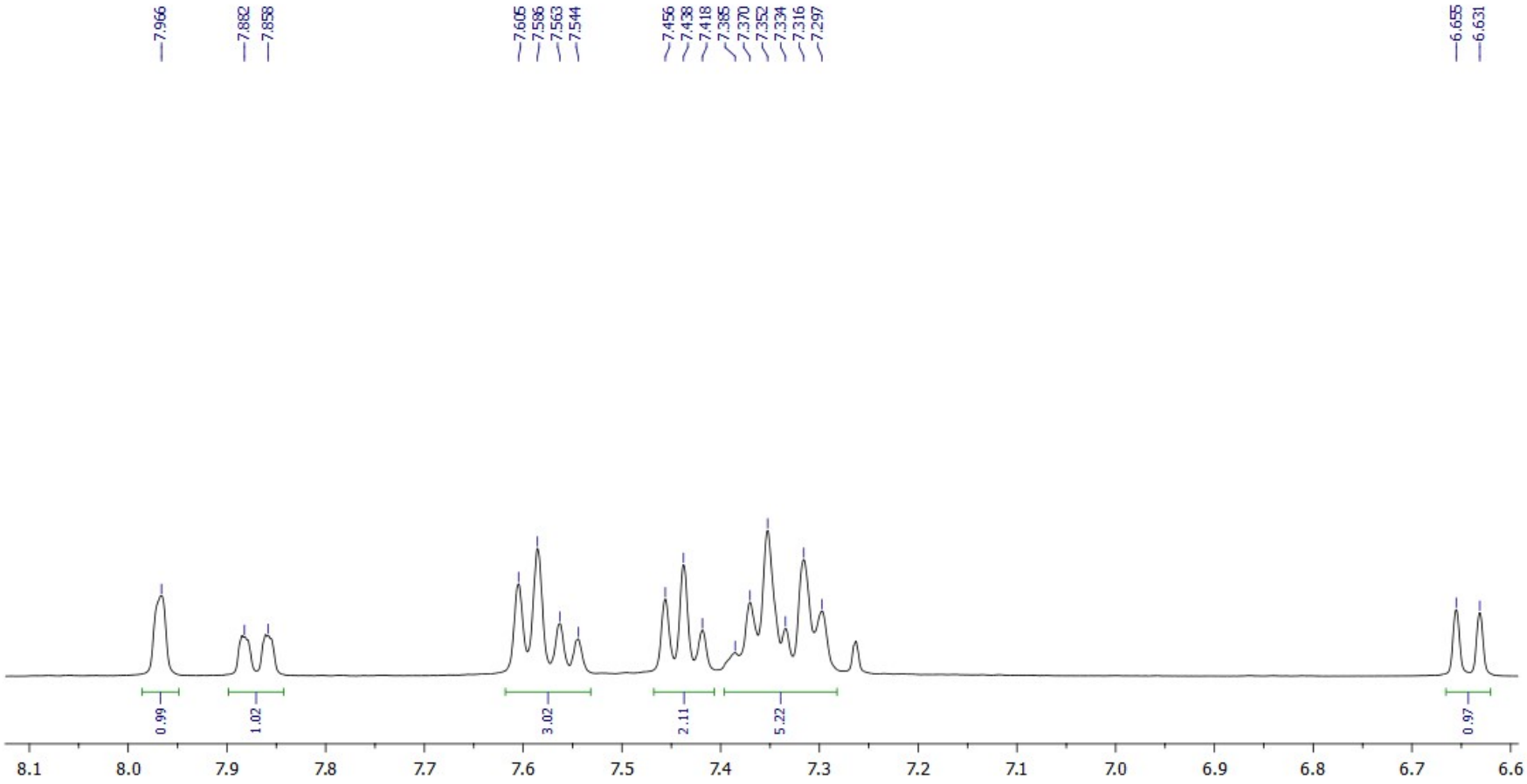
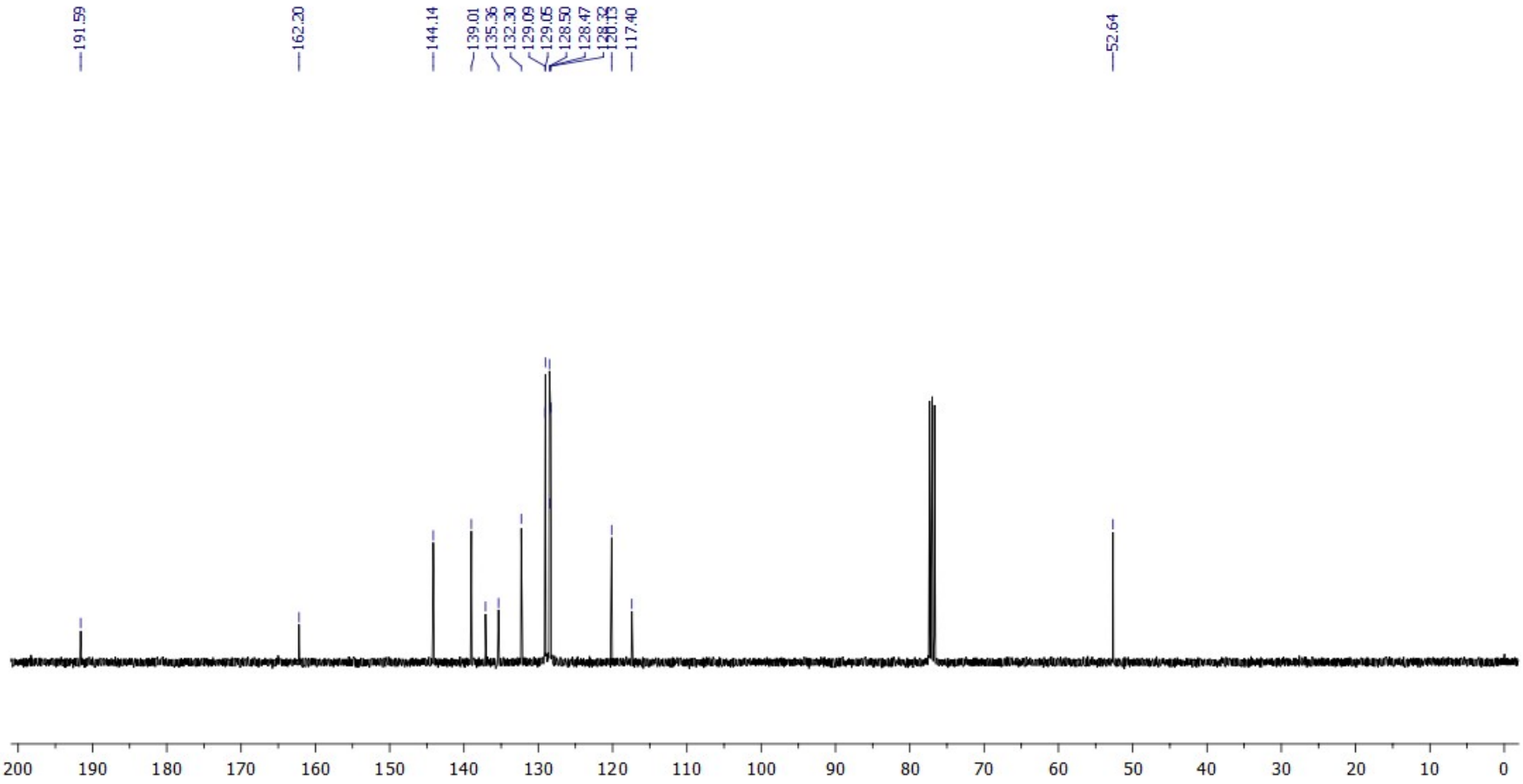


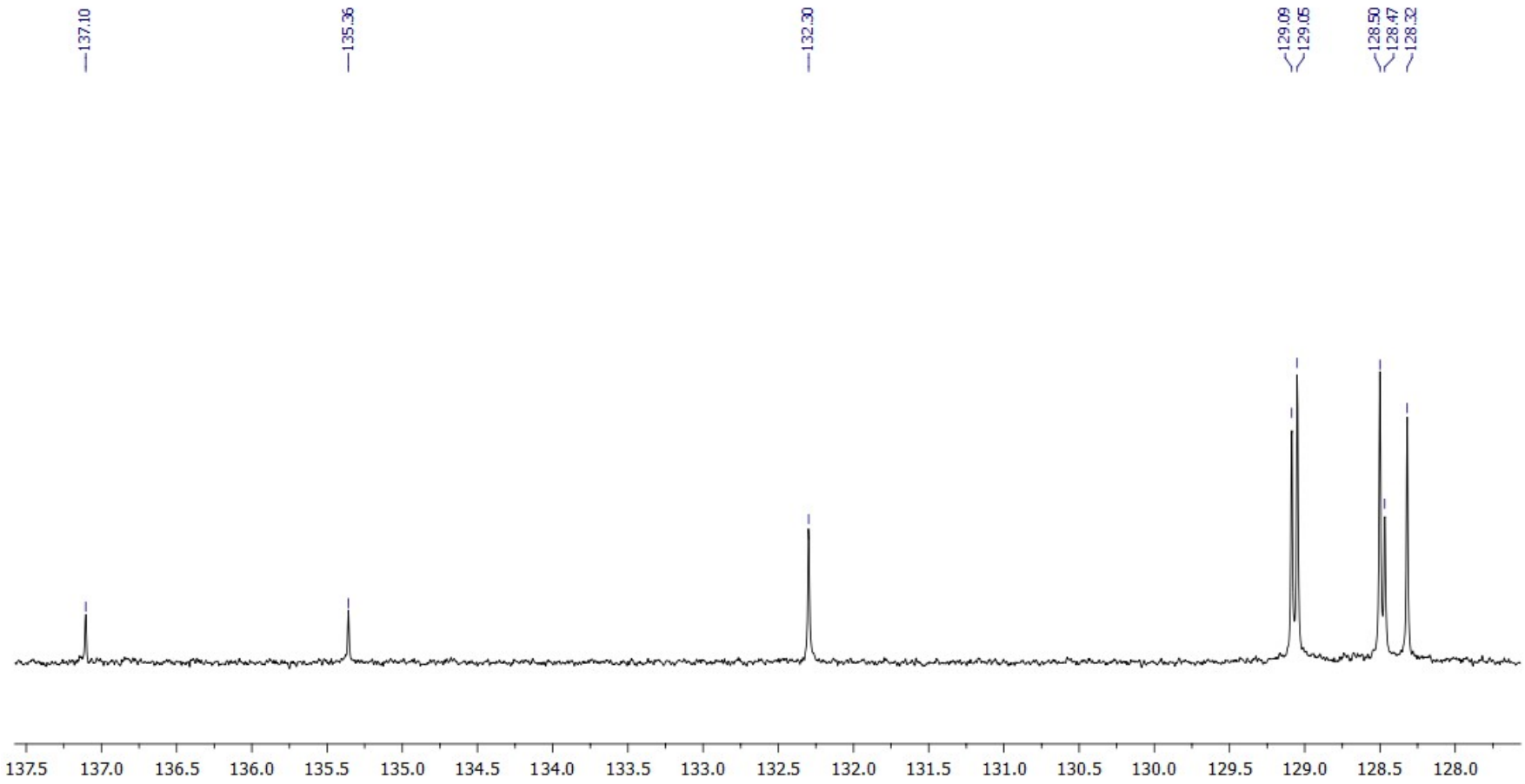
^{1}H NMR (400.1 MHz, $CDCl_3$)



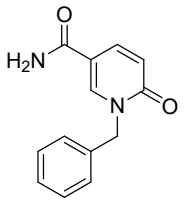
^{1}H NMR (400.1 MHz, $CDCl_3$) expanded aromatic region



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$) expanded aromatic region



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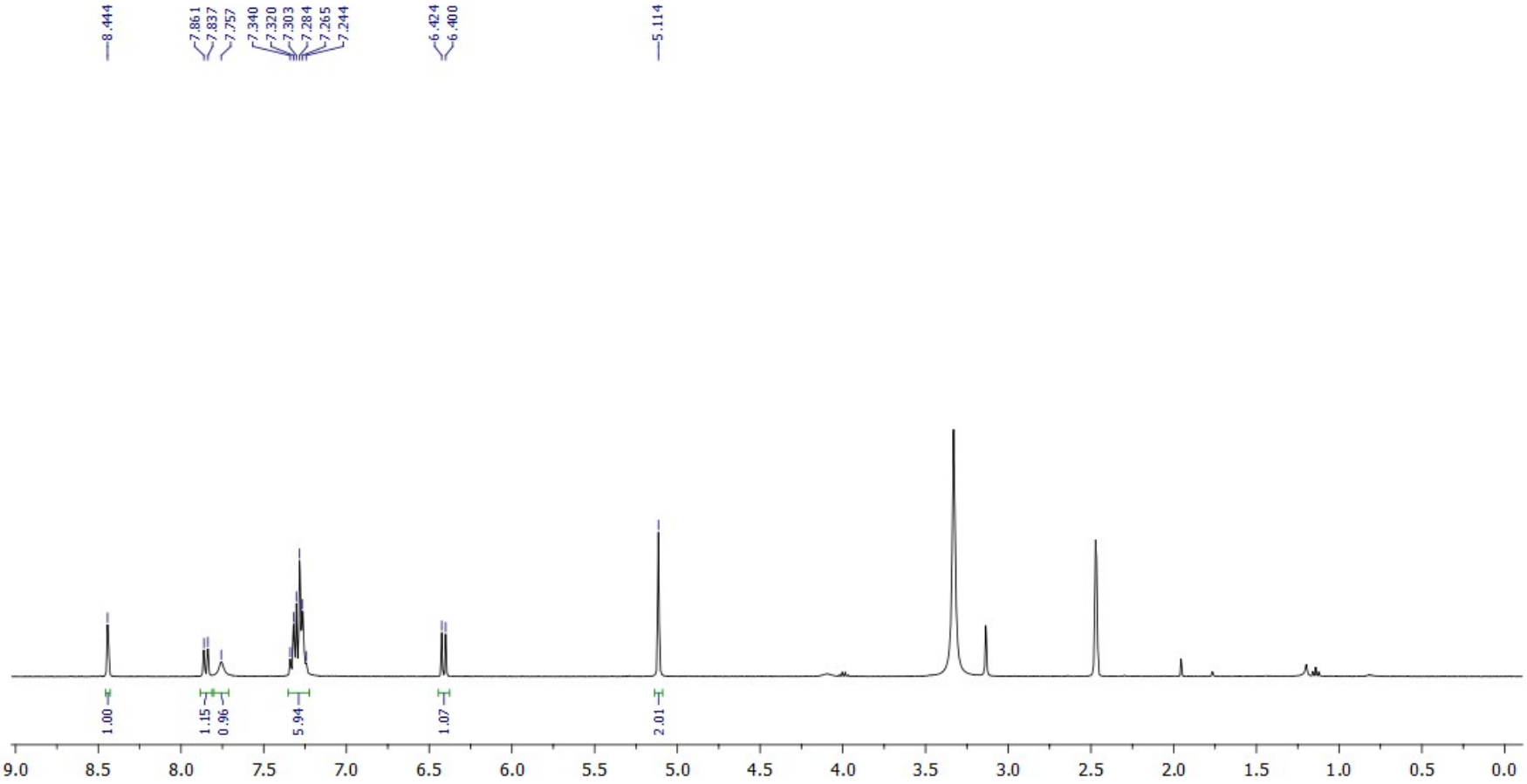
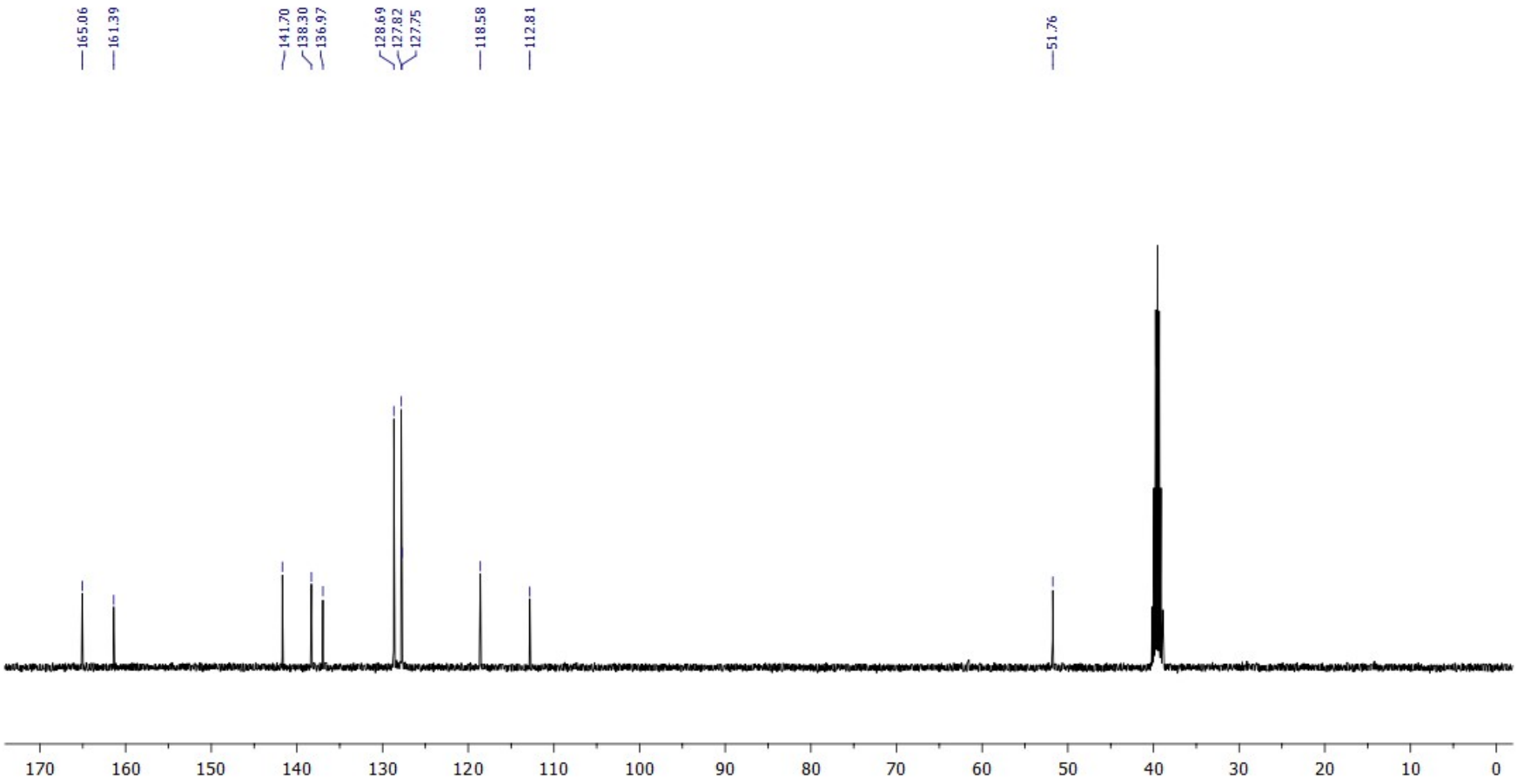
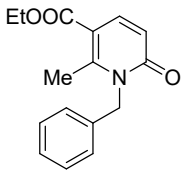


^{1}H NMR (400.1 MHz, DMSO-d_6)



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, DMSO-d_6)



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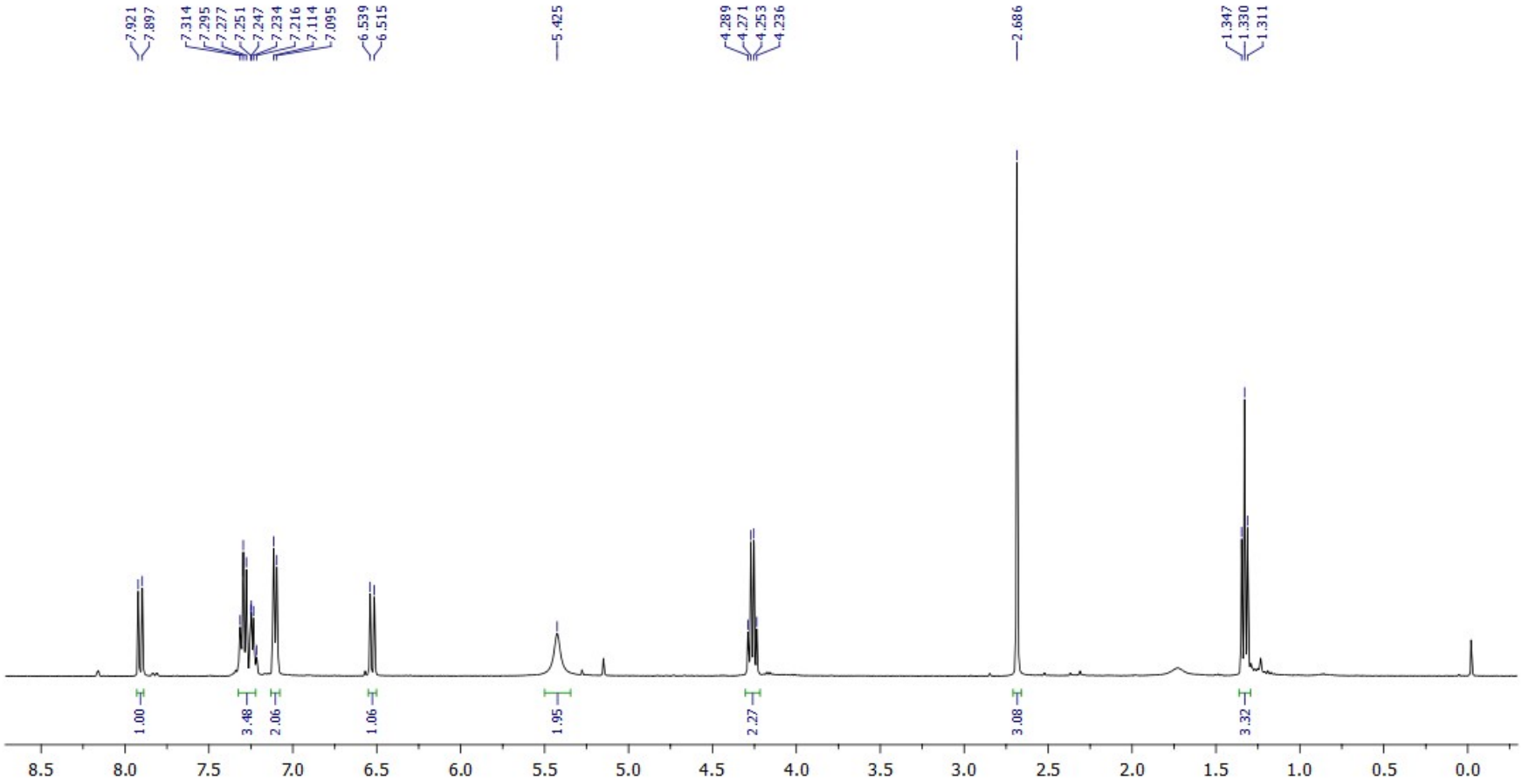
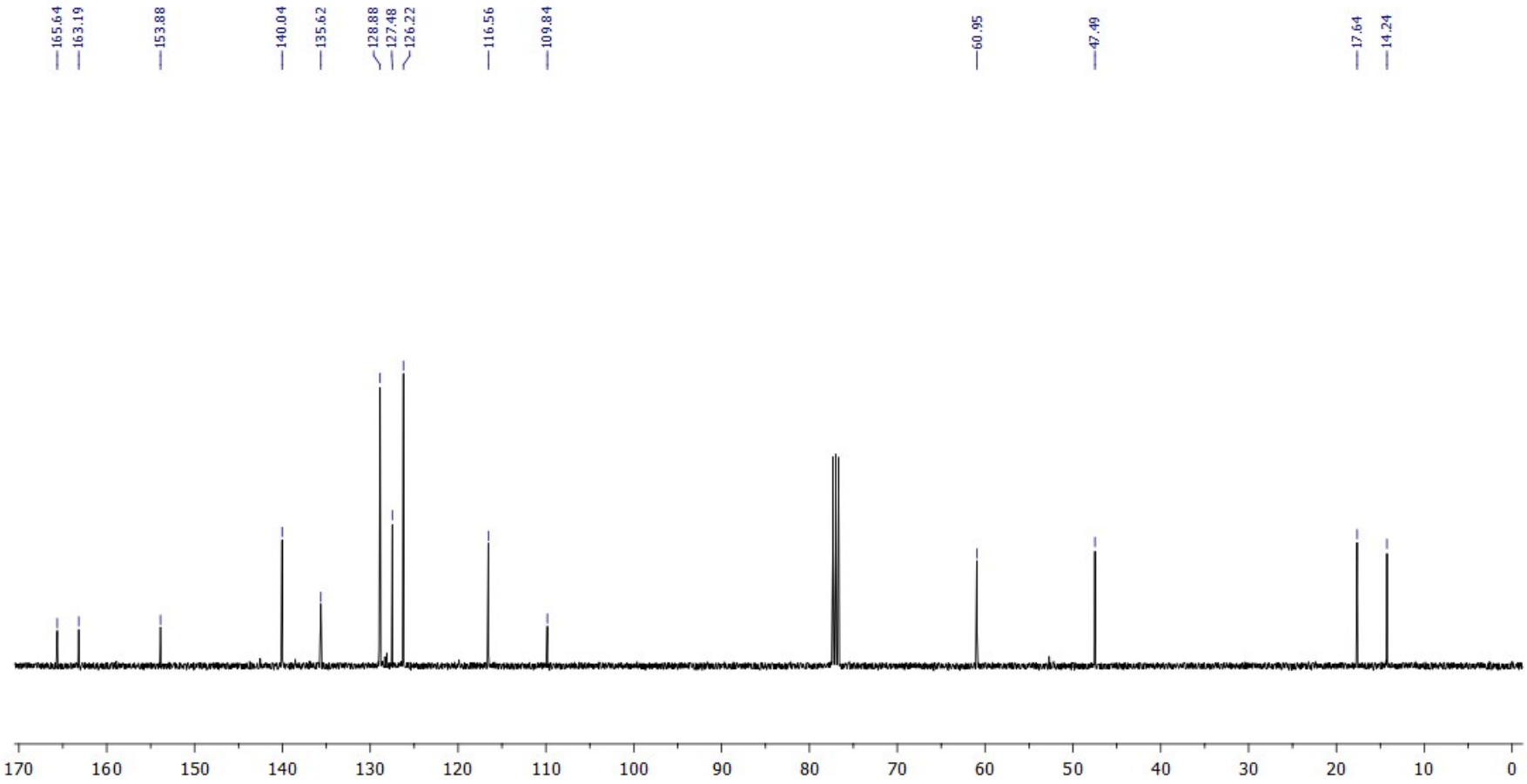
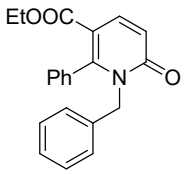


^{1}H NMR (400.1 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$)



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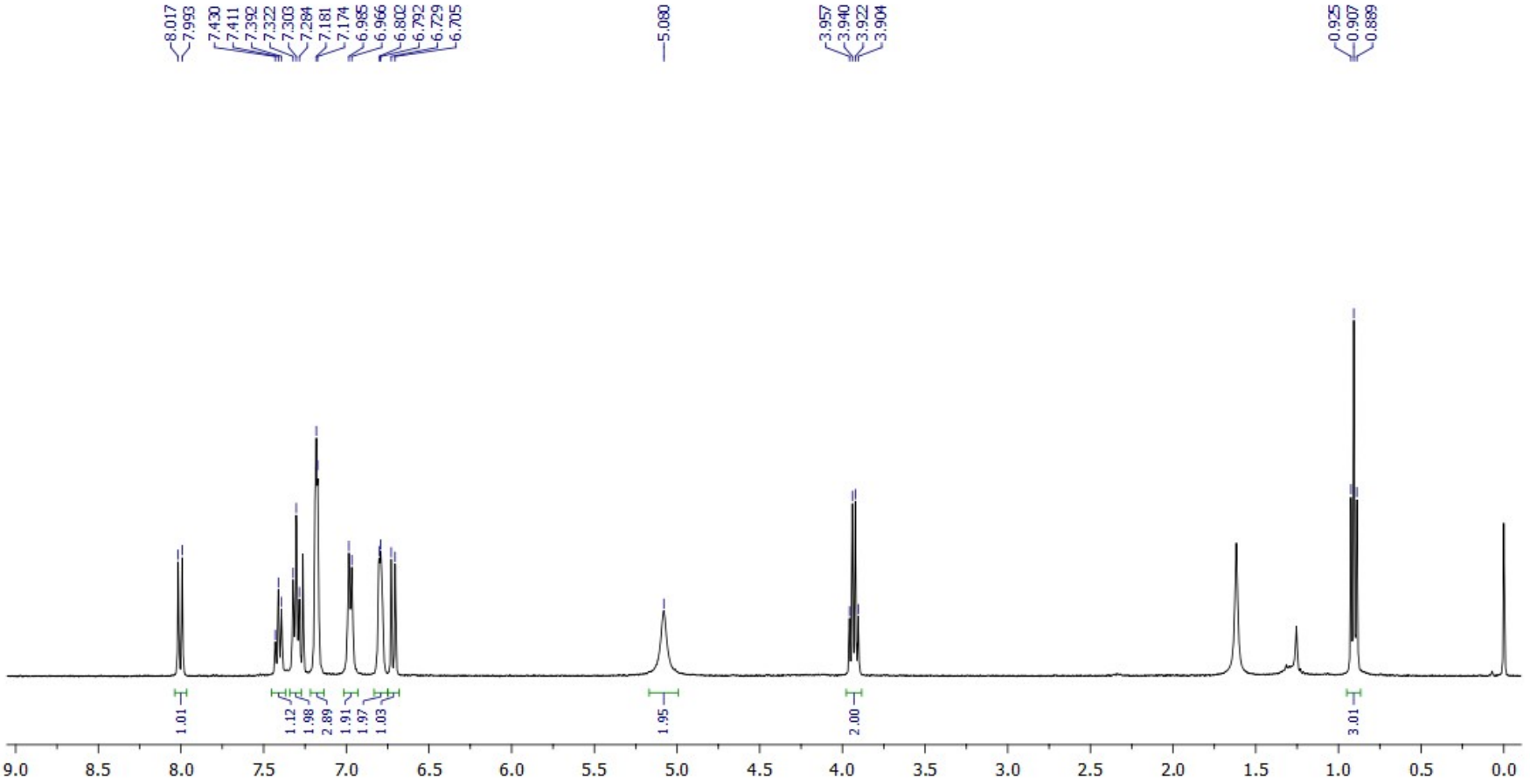
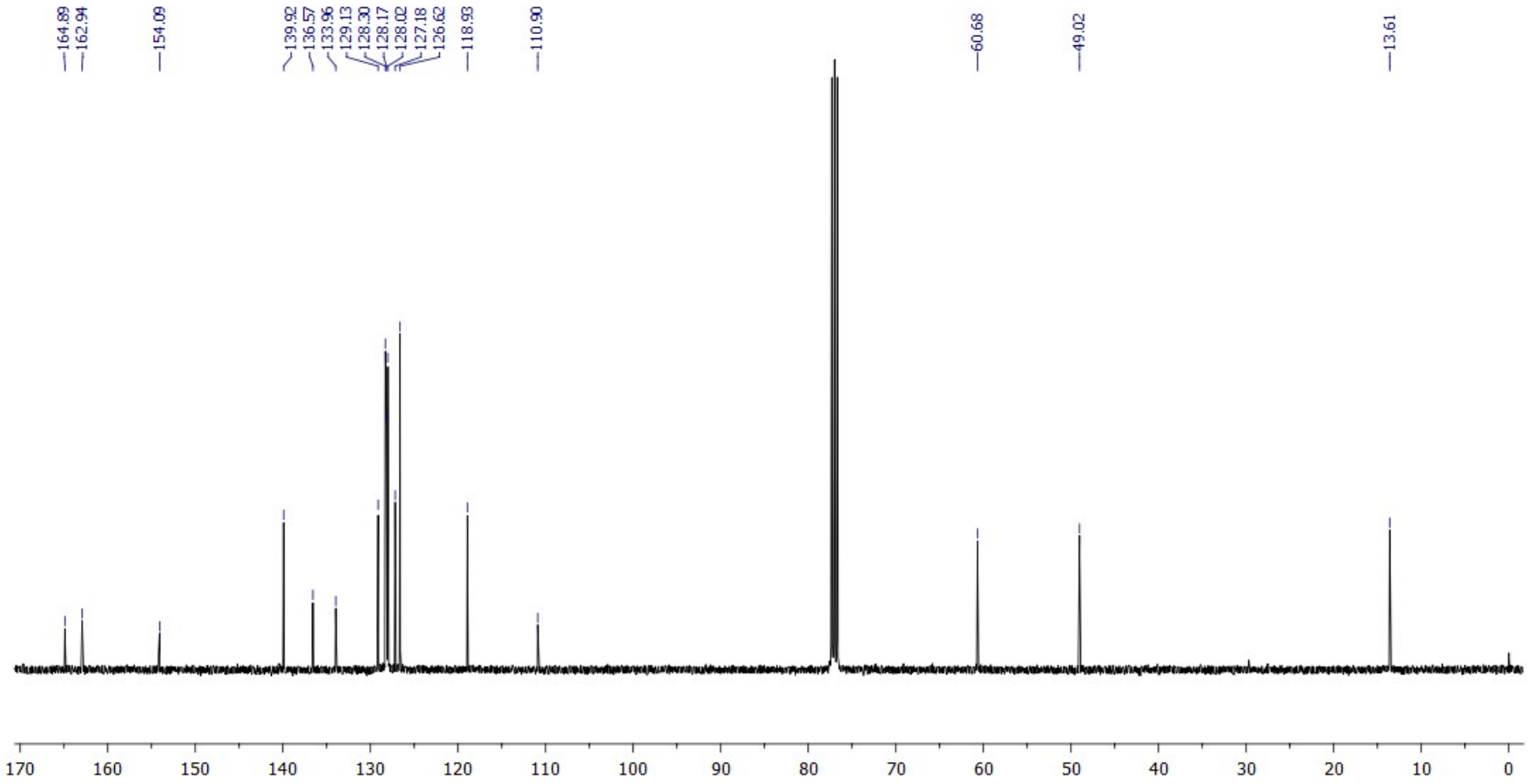
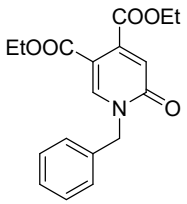


^{1}H NMR (400.1 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$)



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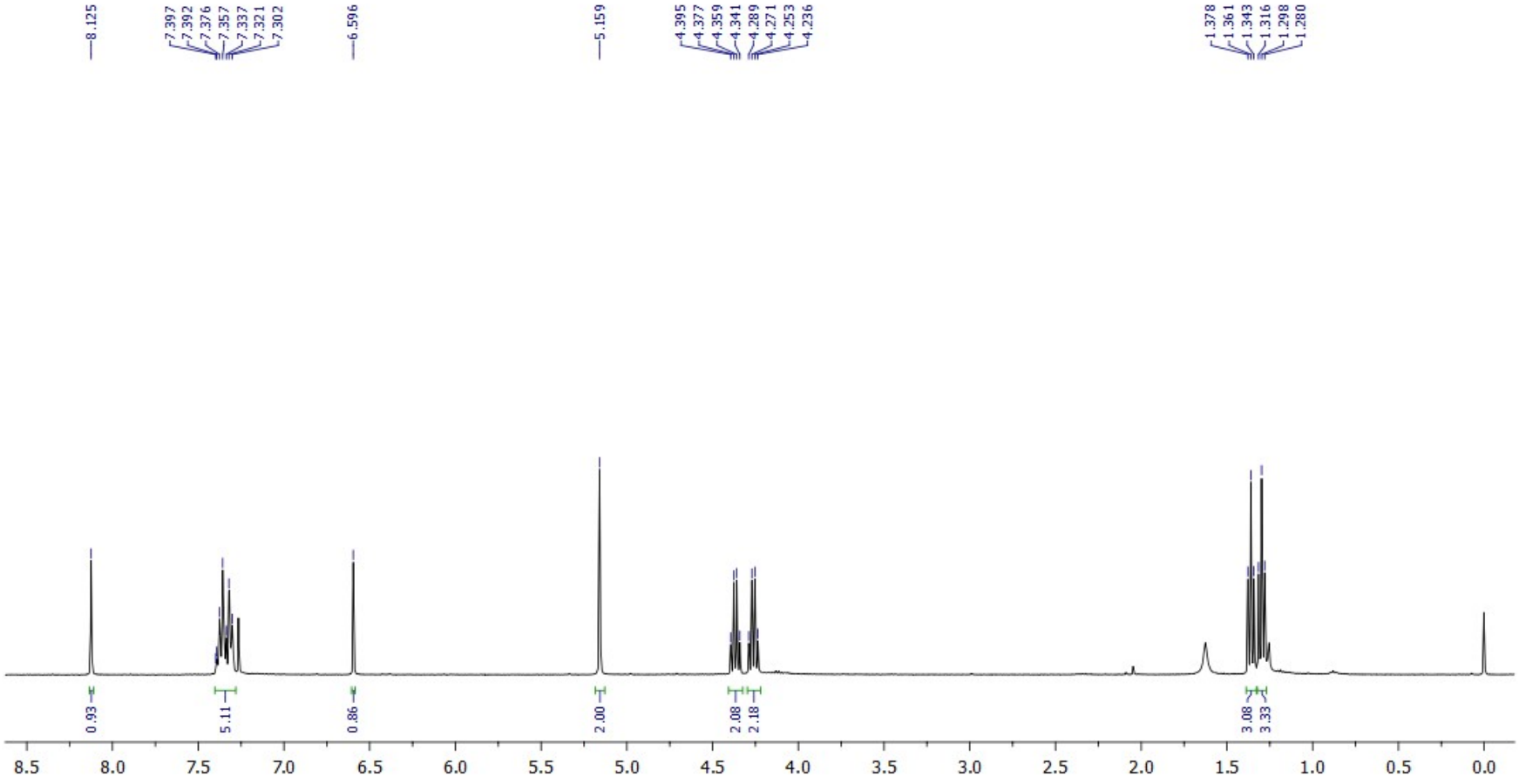
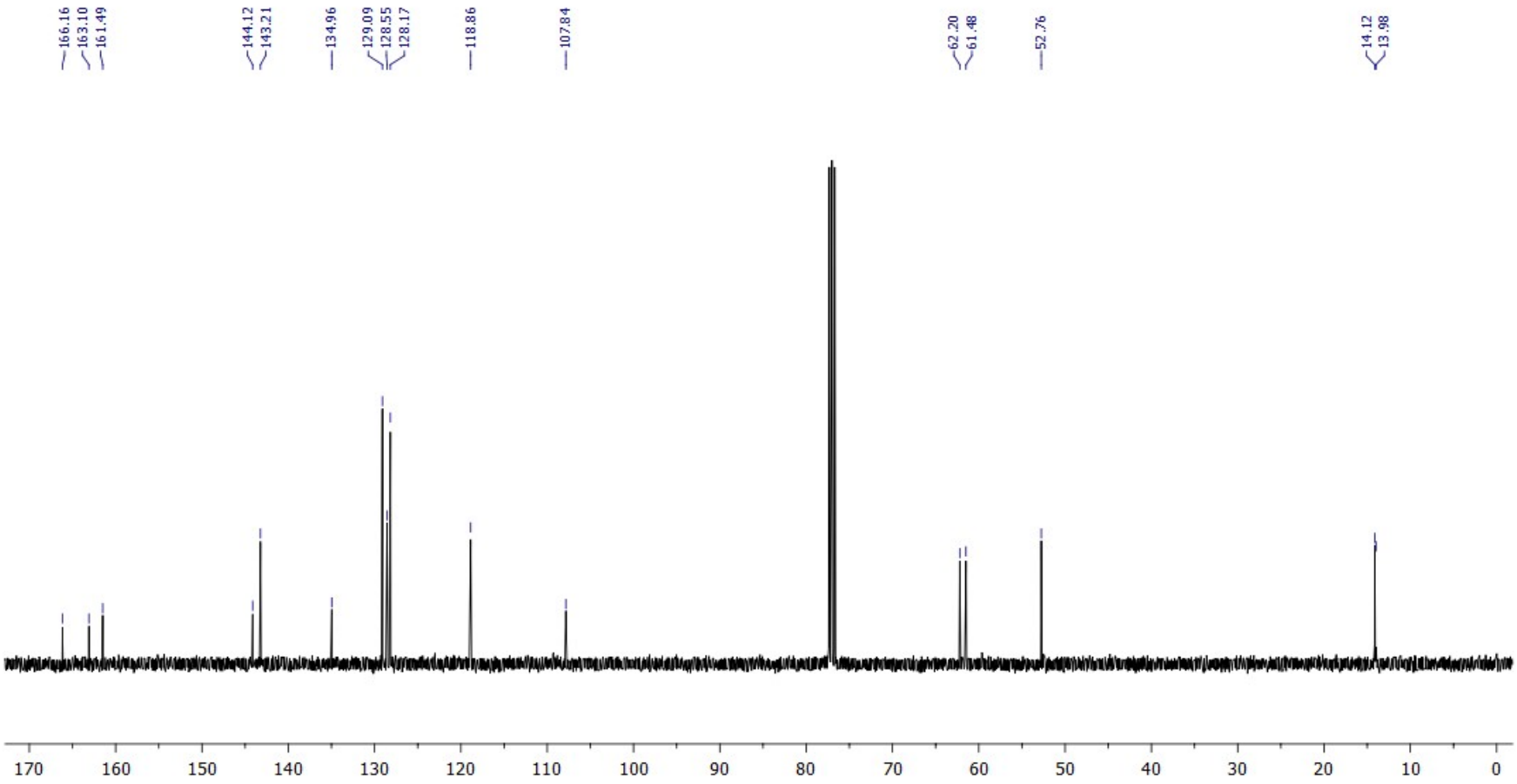
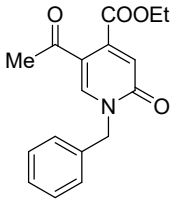


^{1}H NMR (400.1 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$)



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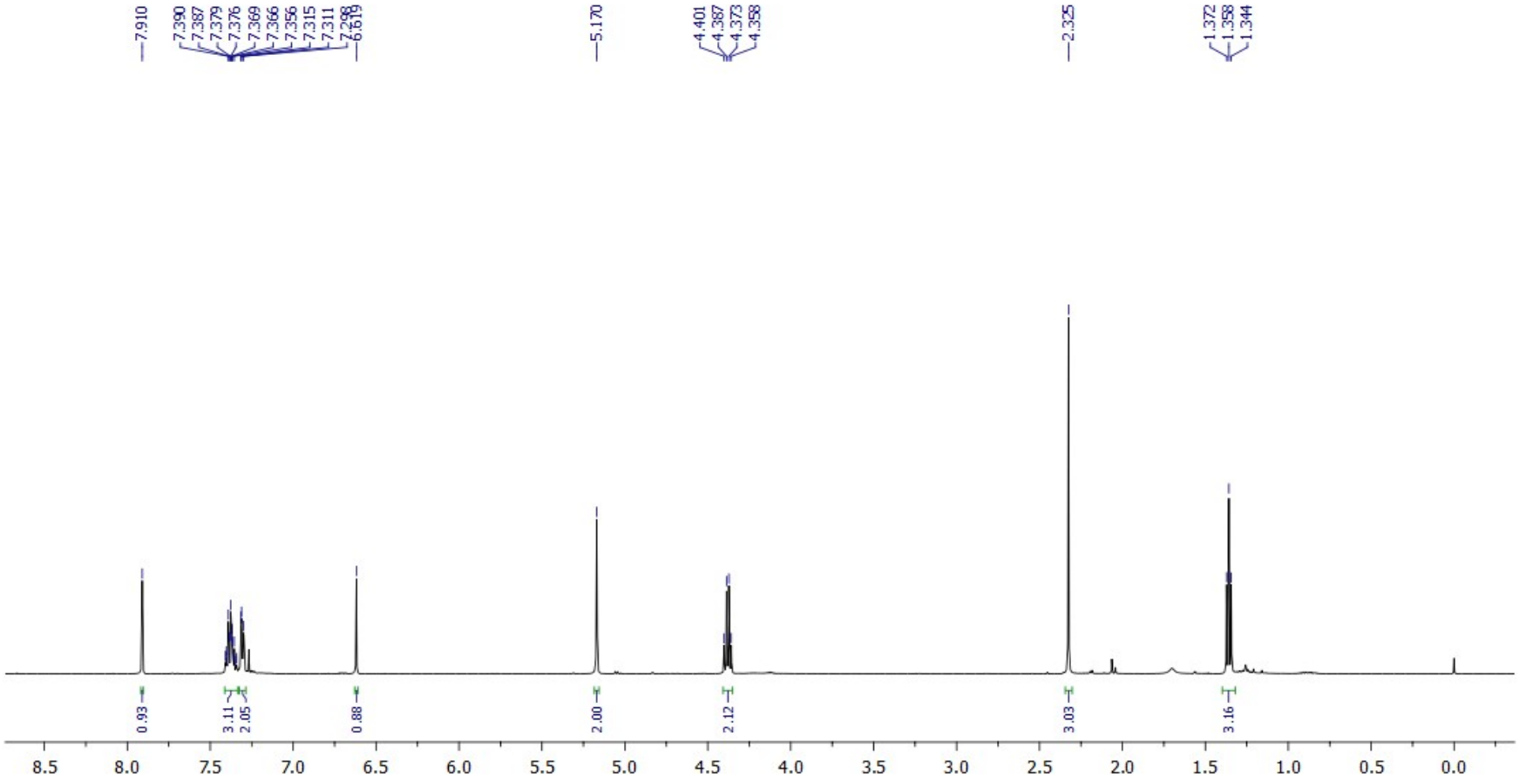
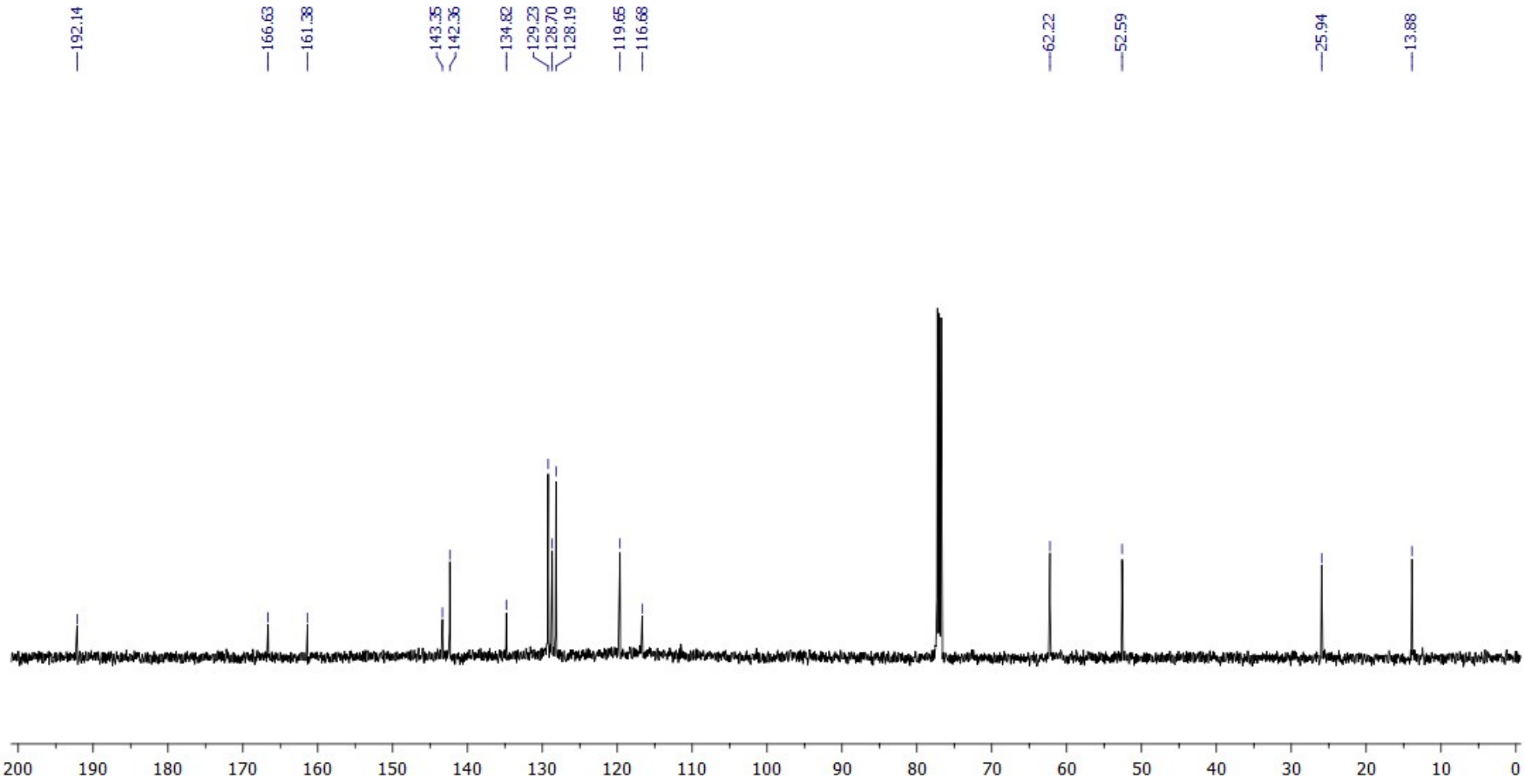
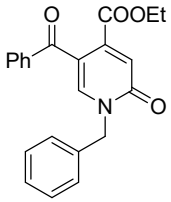


^{1}H NMR (500.3 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (125.8 MHz, $CDCl_3$)



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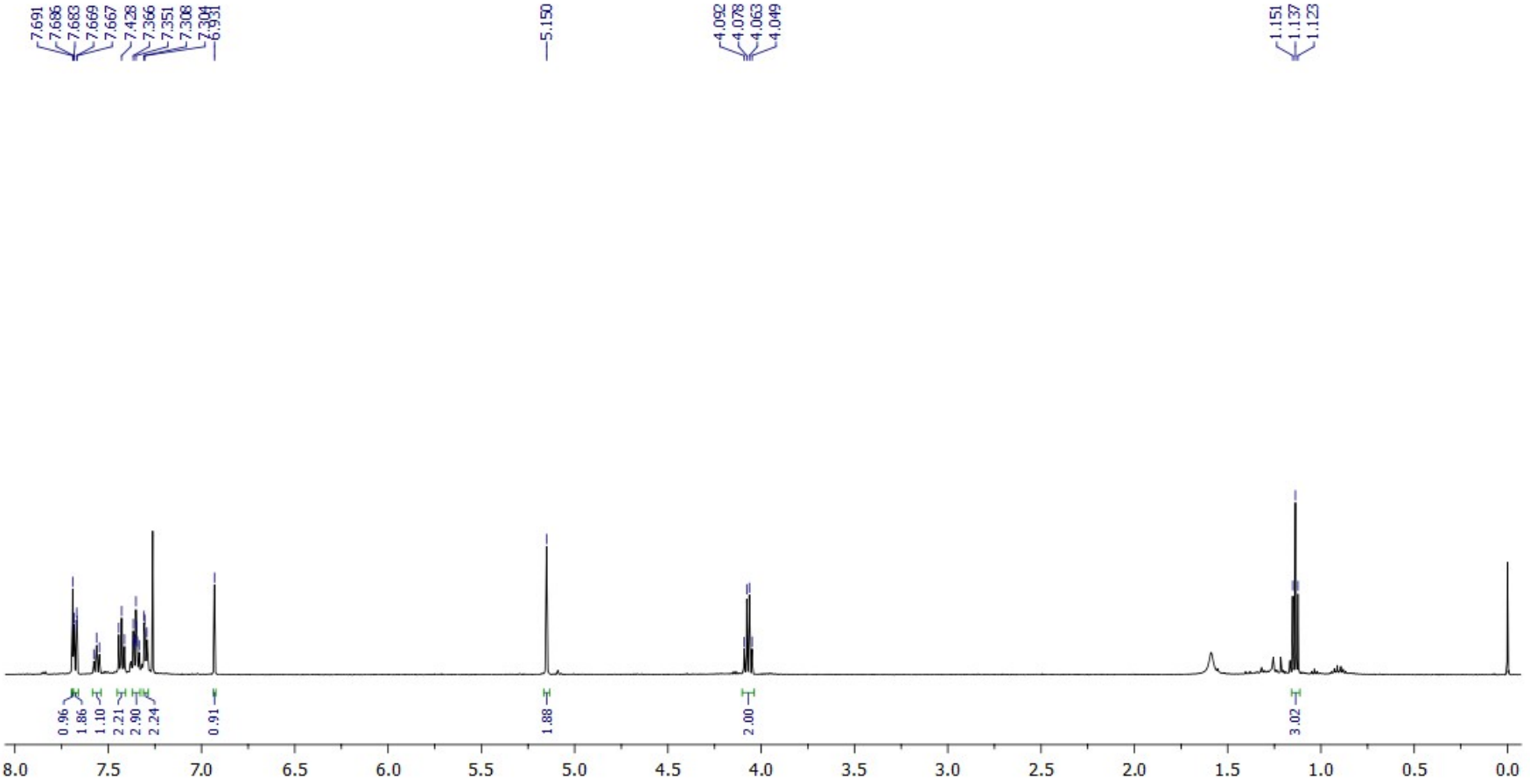
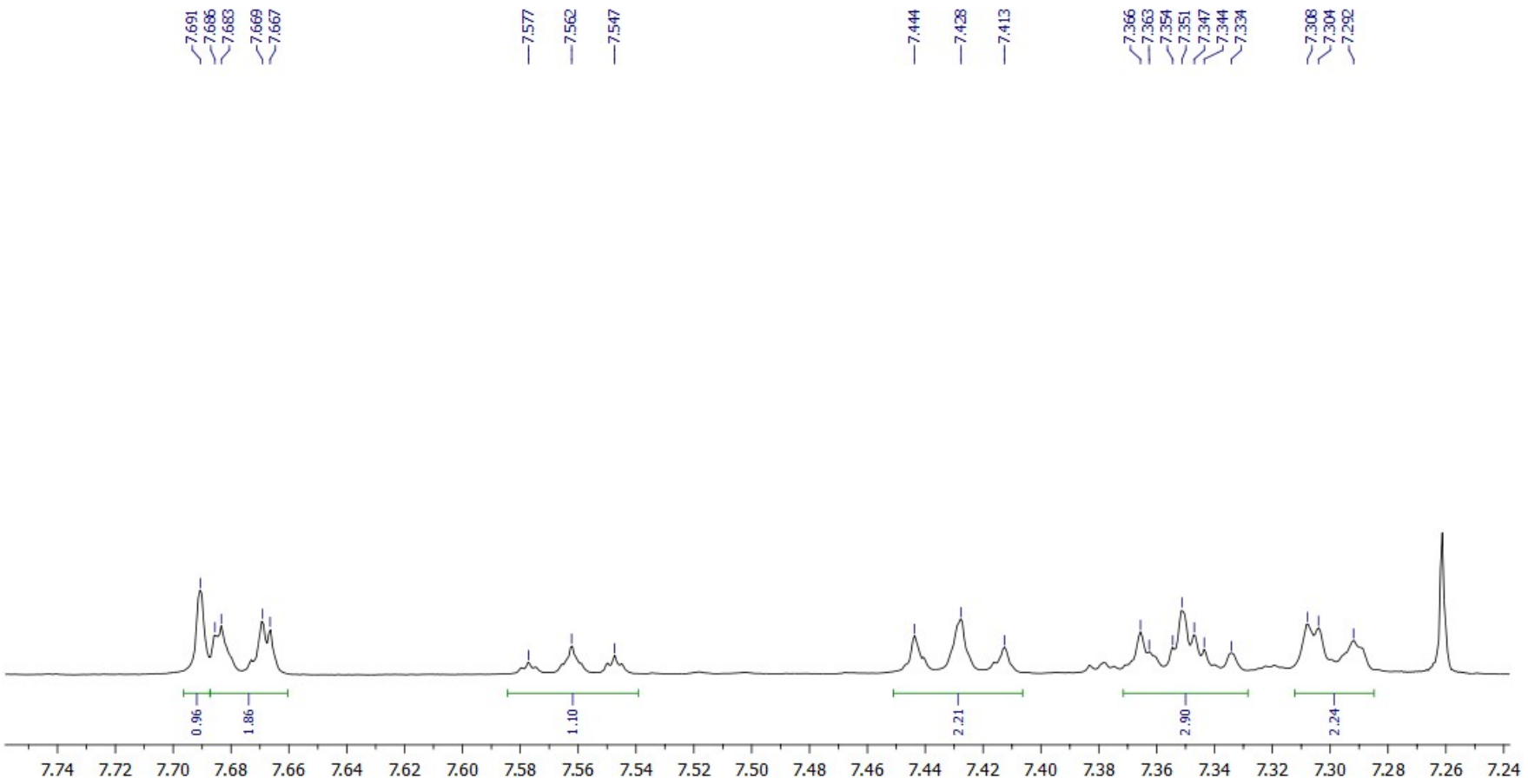
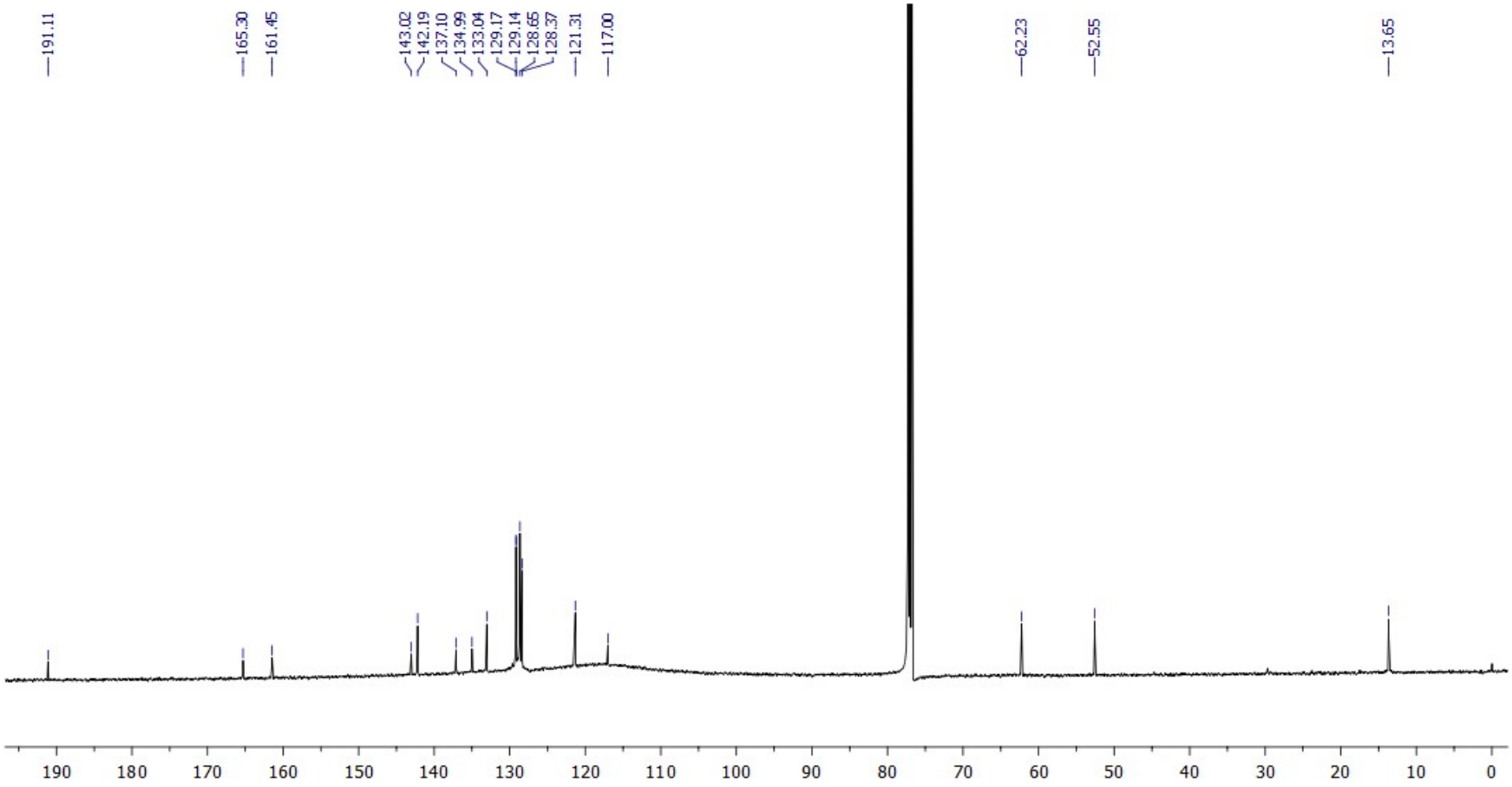


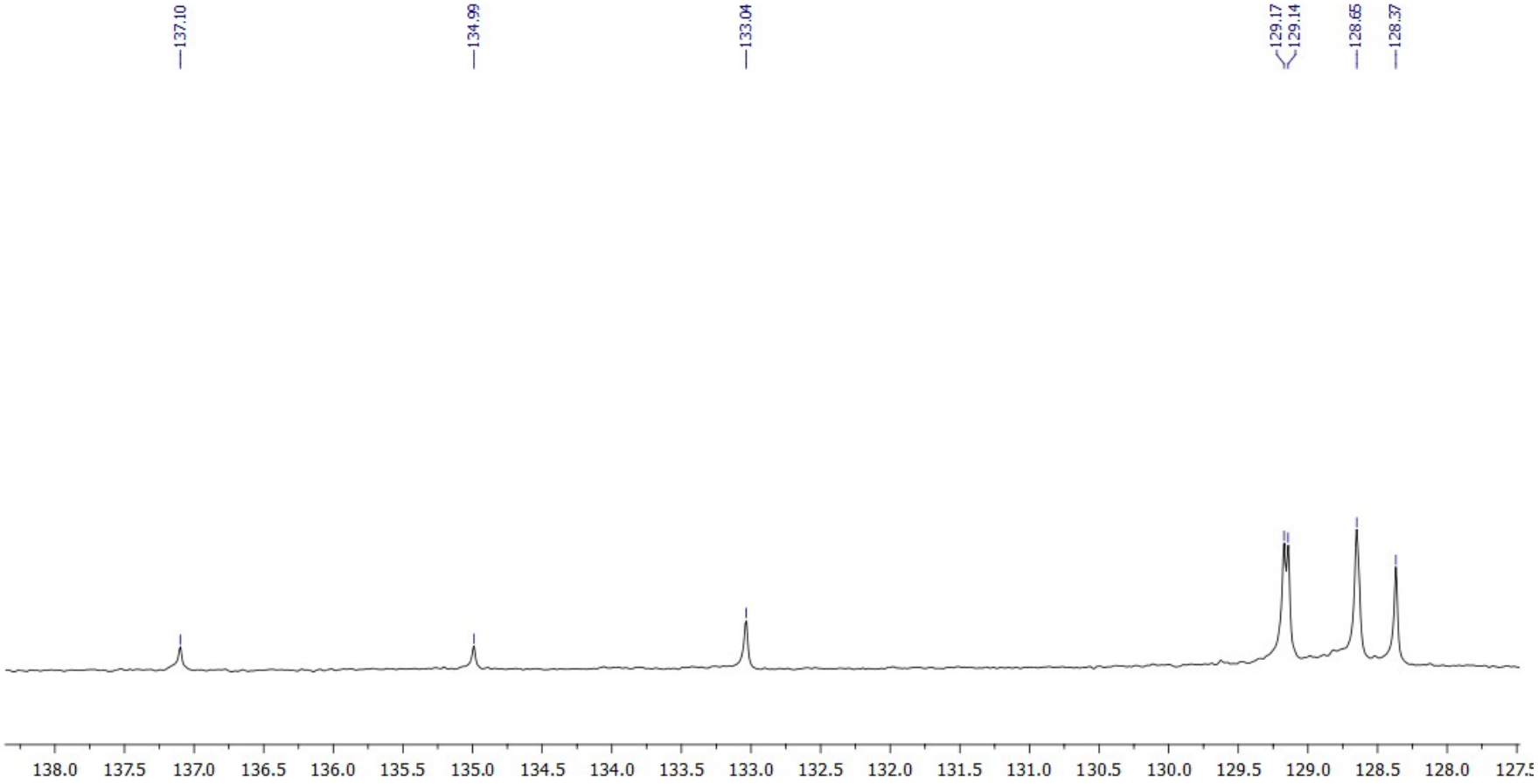
^{1}H NMR (500.3 MHz, $CDCl_3$)



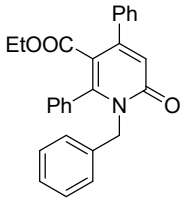
^{1}H NMR (500.3 MHz, $CDCl_3$), expanded aromatic region



$^{13}C\{^{1}H\}$ NMR (125.8 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (125.8 MHz, $CDCl_3$) expanded aromatic region



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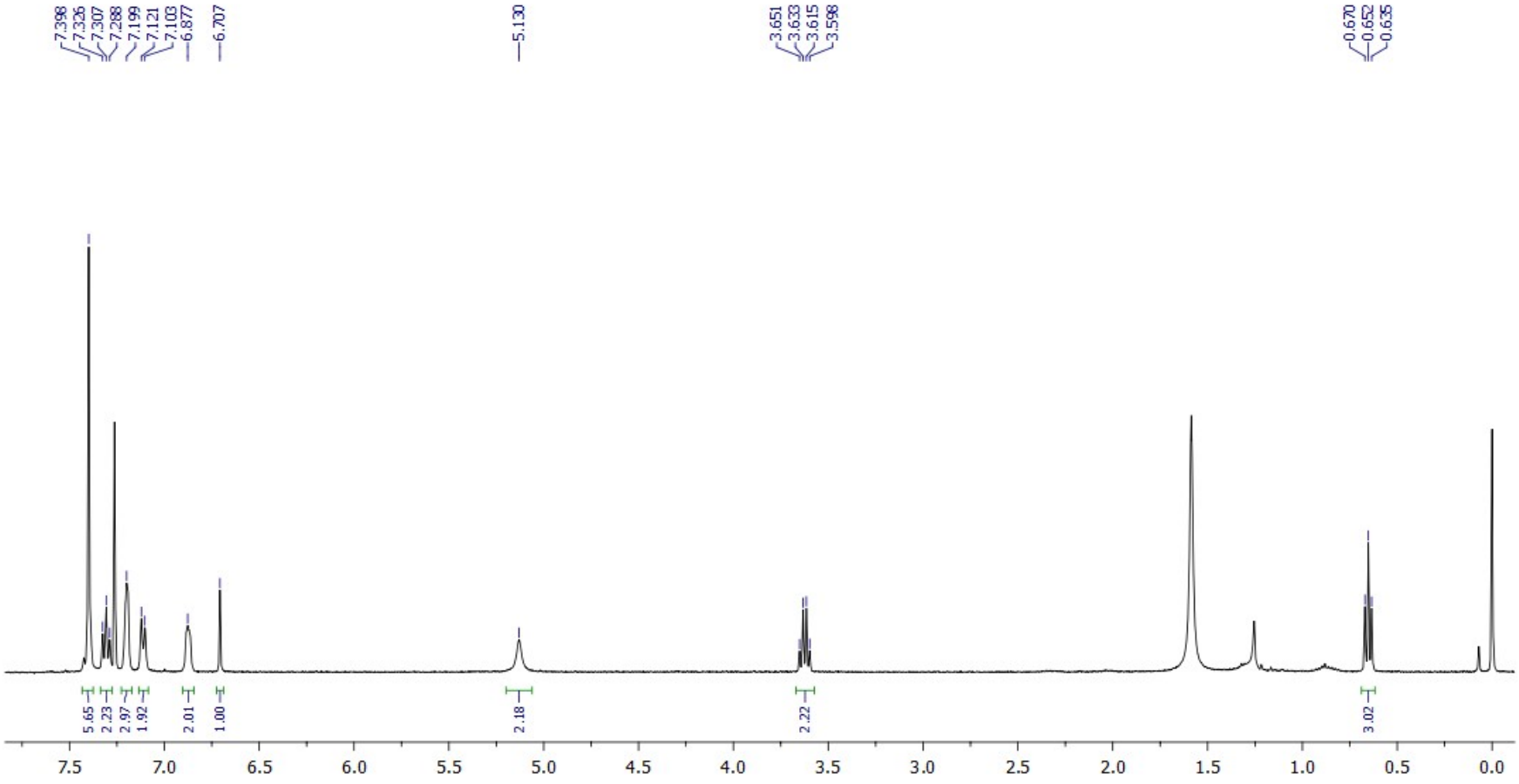
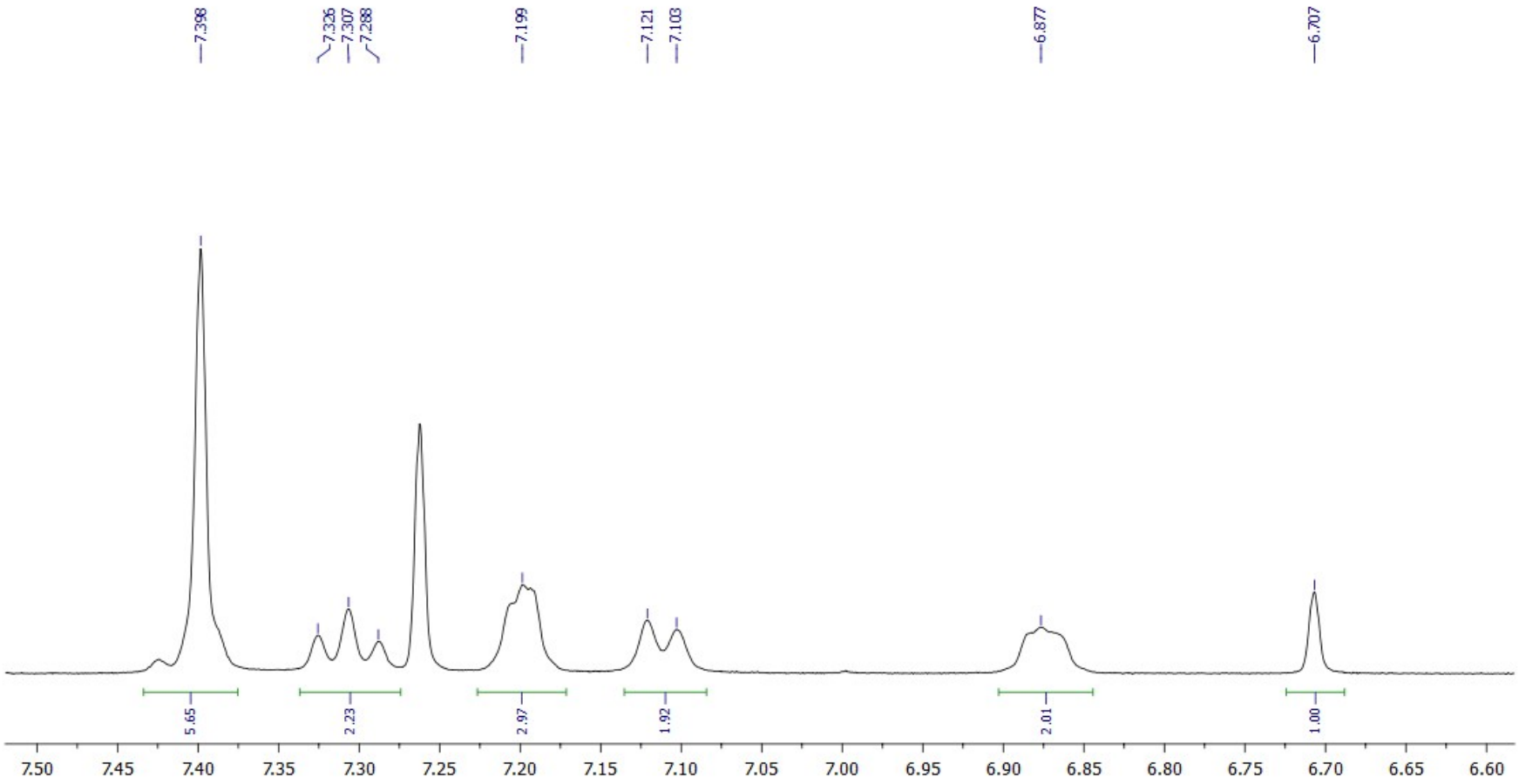
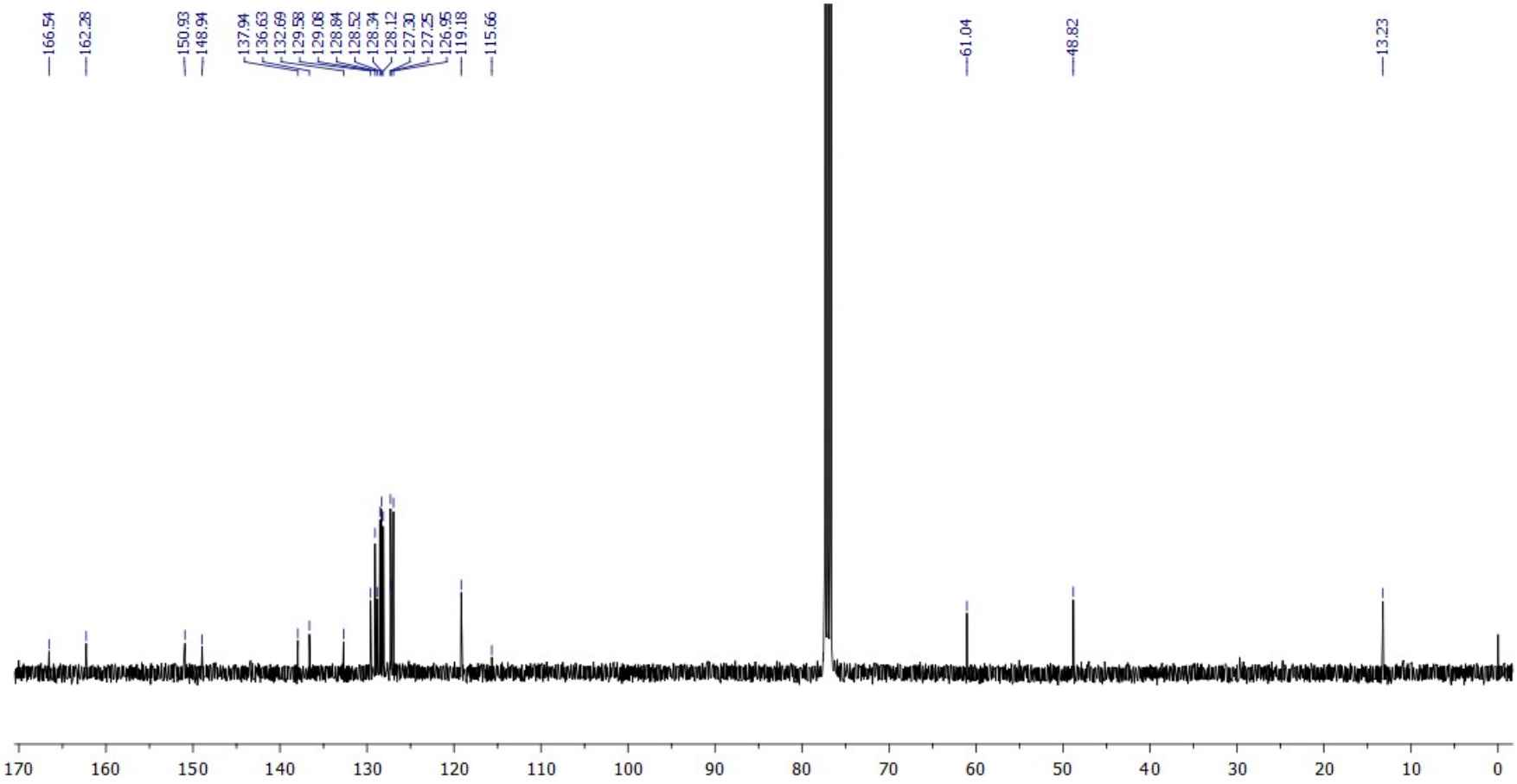


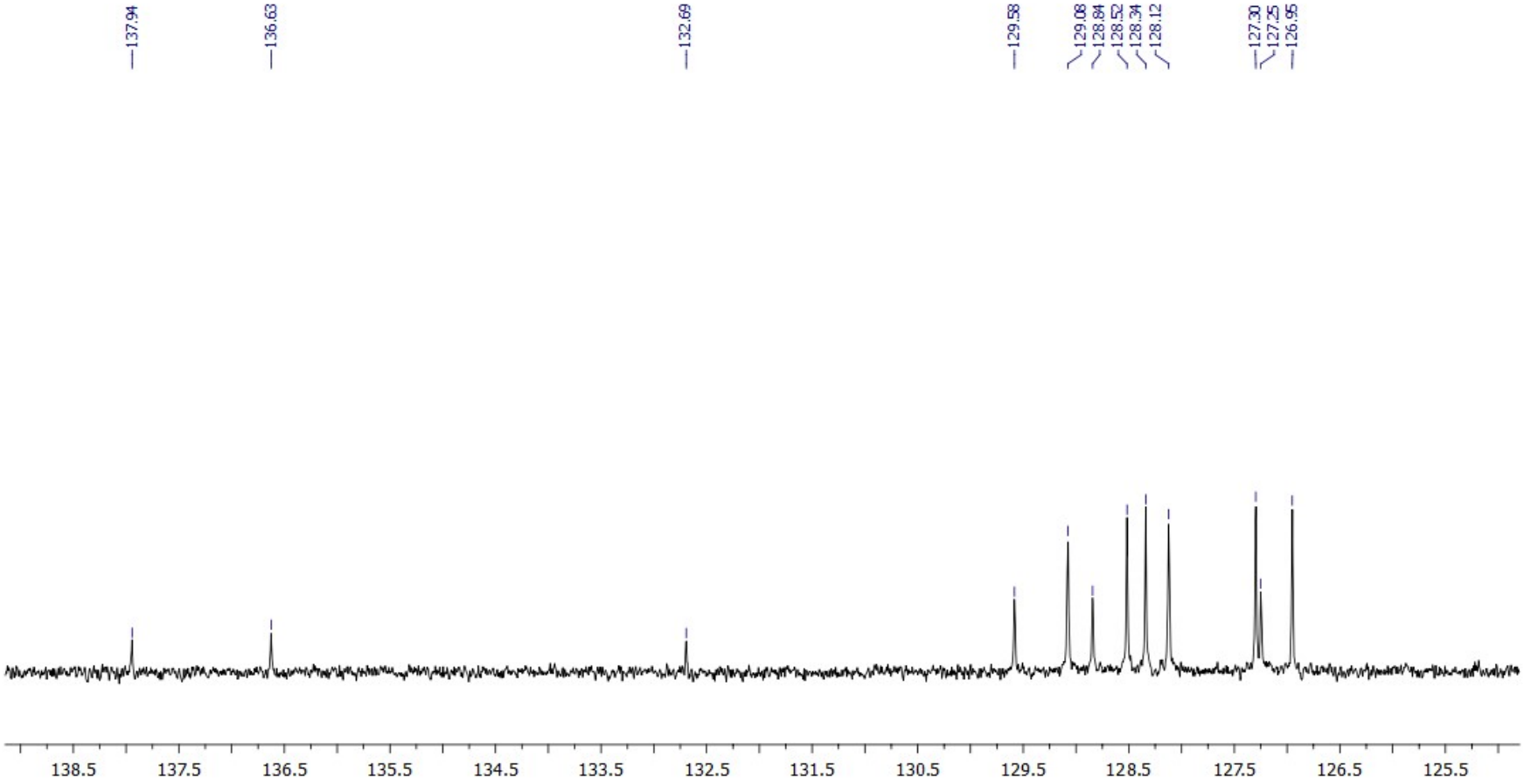
^{1}H NMR (400.1 MHz, $CDCl_3$)



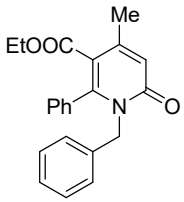
^{1}H NMR (400.1 MHz, $CDCl_3$), expanded aromatic region



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$), expanded aromatic region



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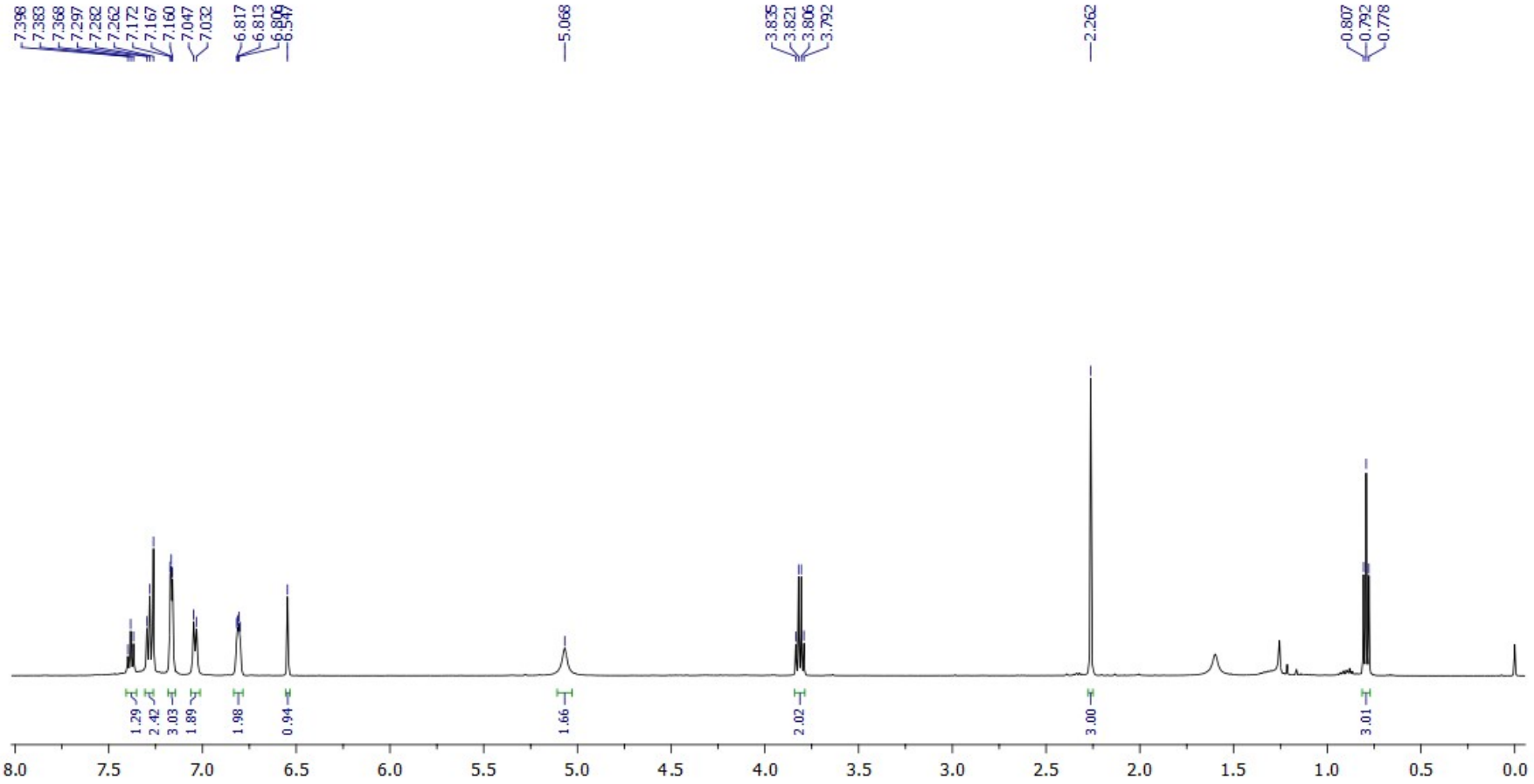
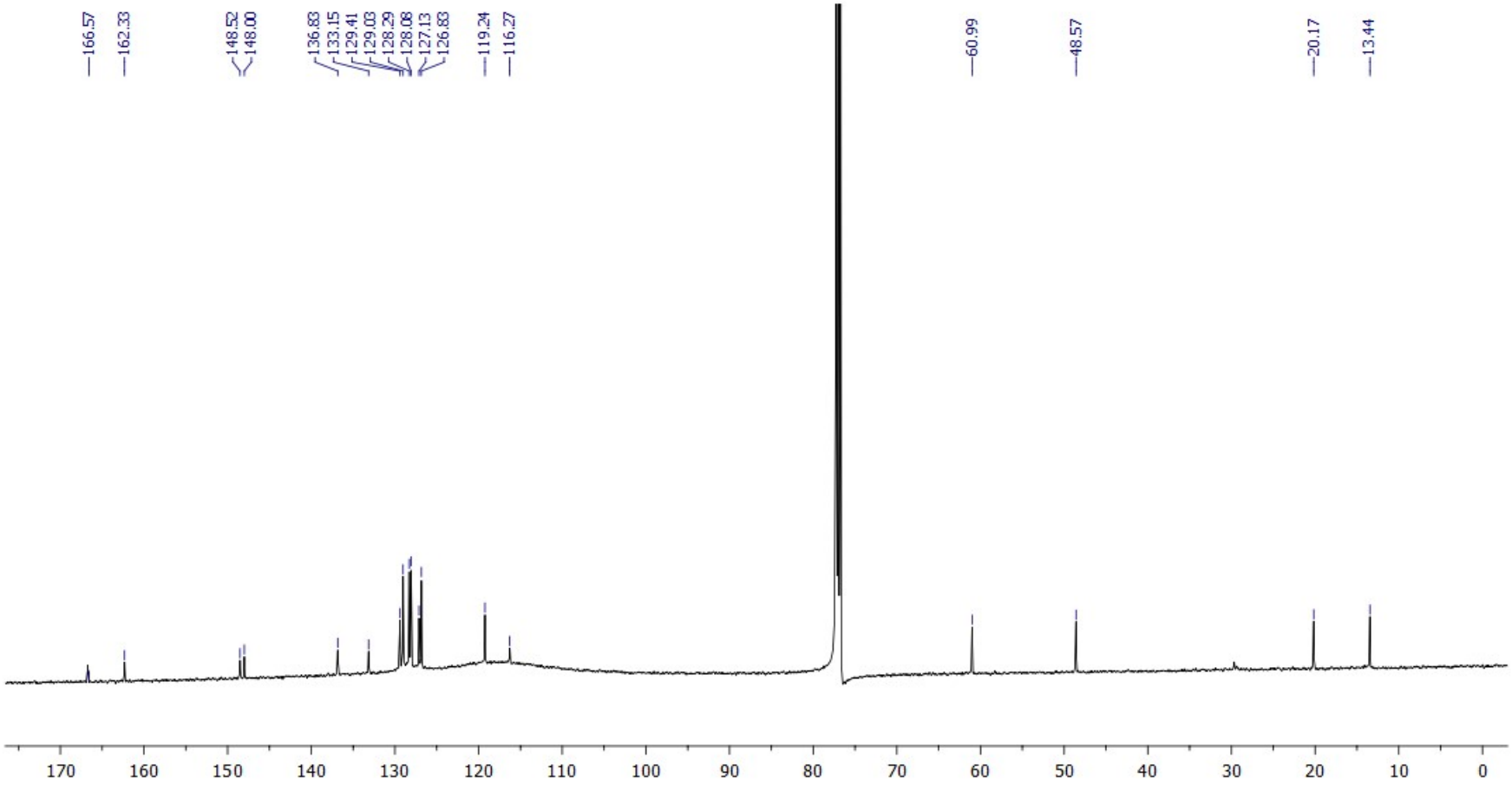
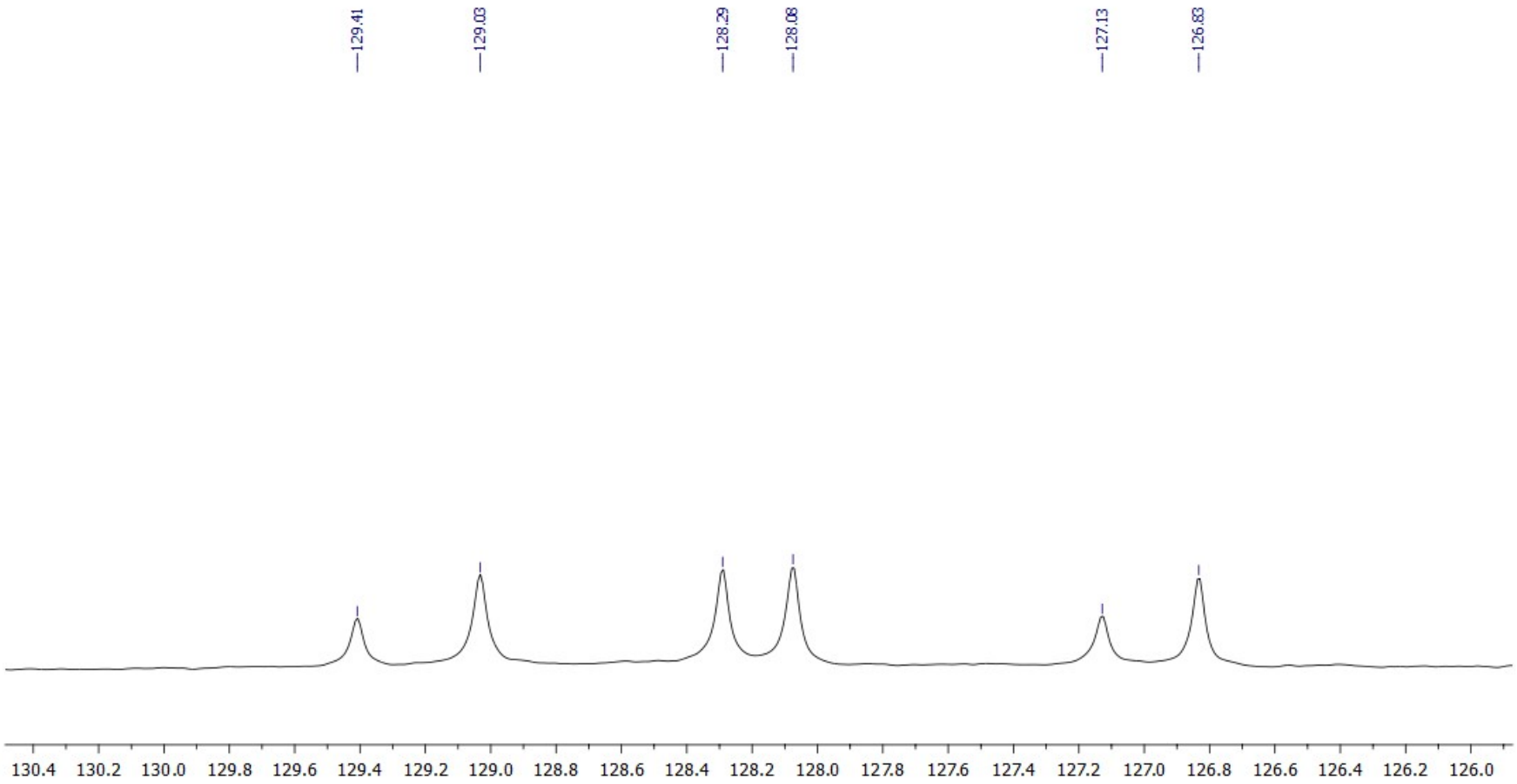


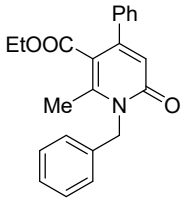
^{1}H NMR (500.3 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (125.8 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (125.8 MHz, $CDCl_3$), expanded aromatic region



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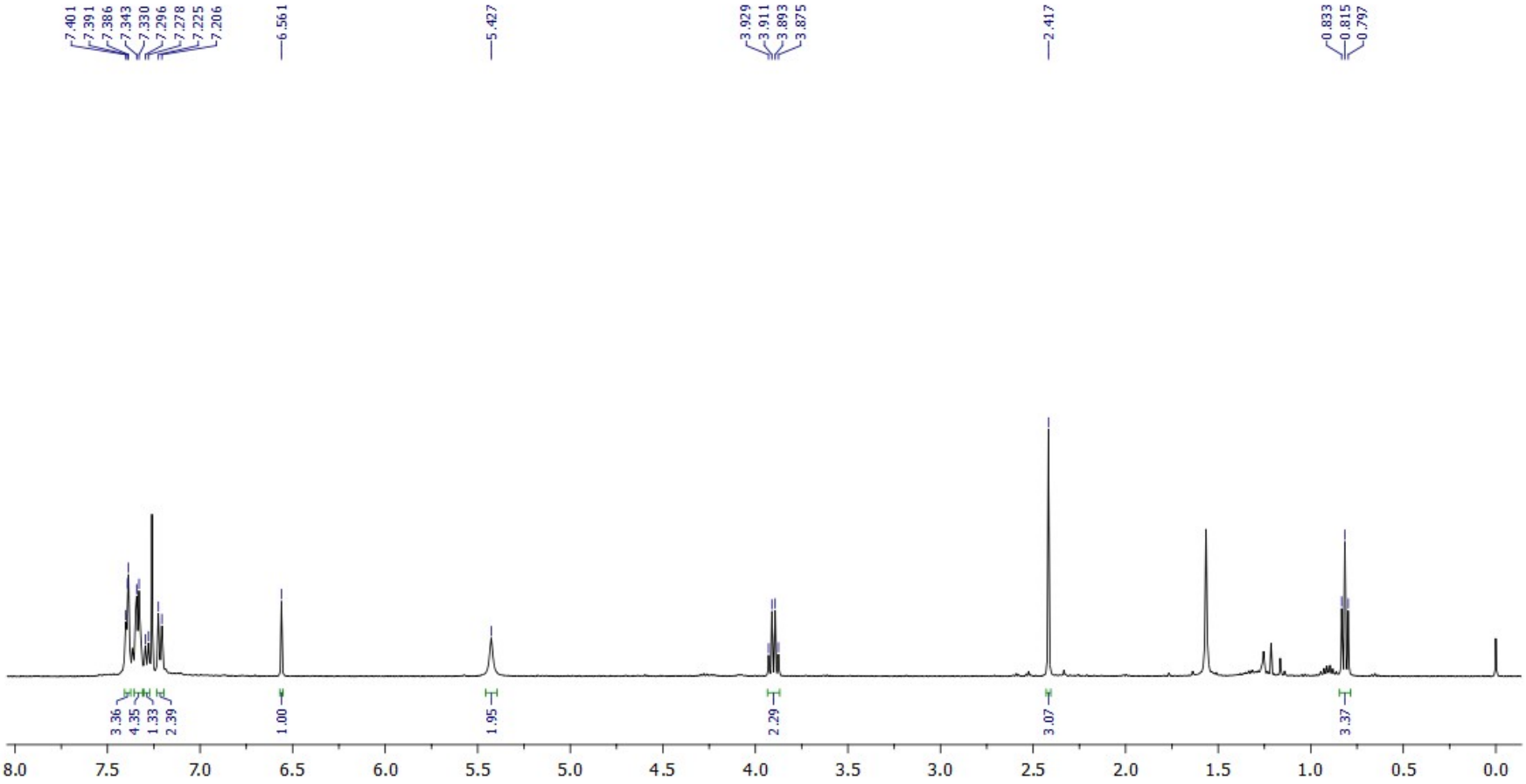
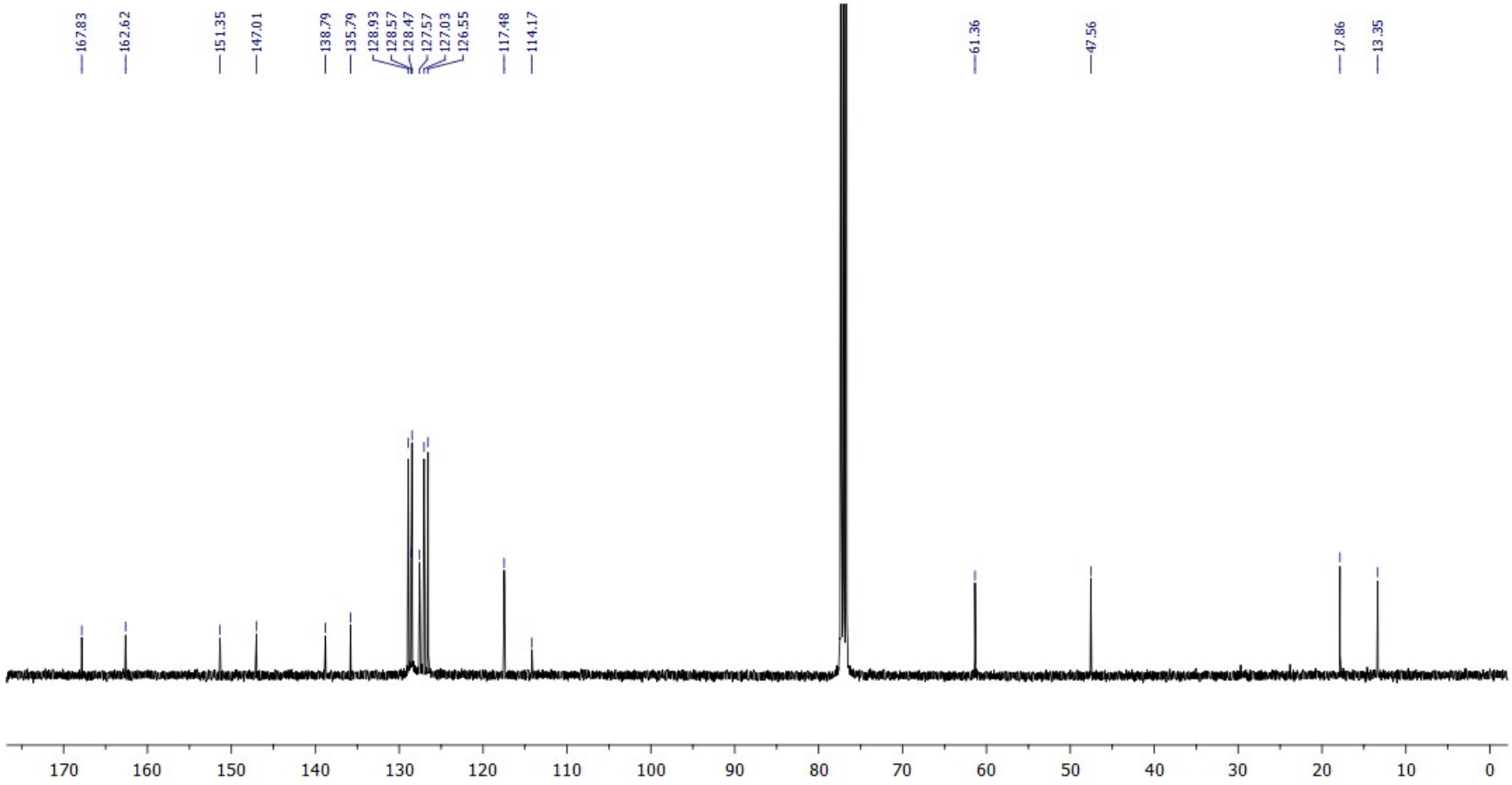
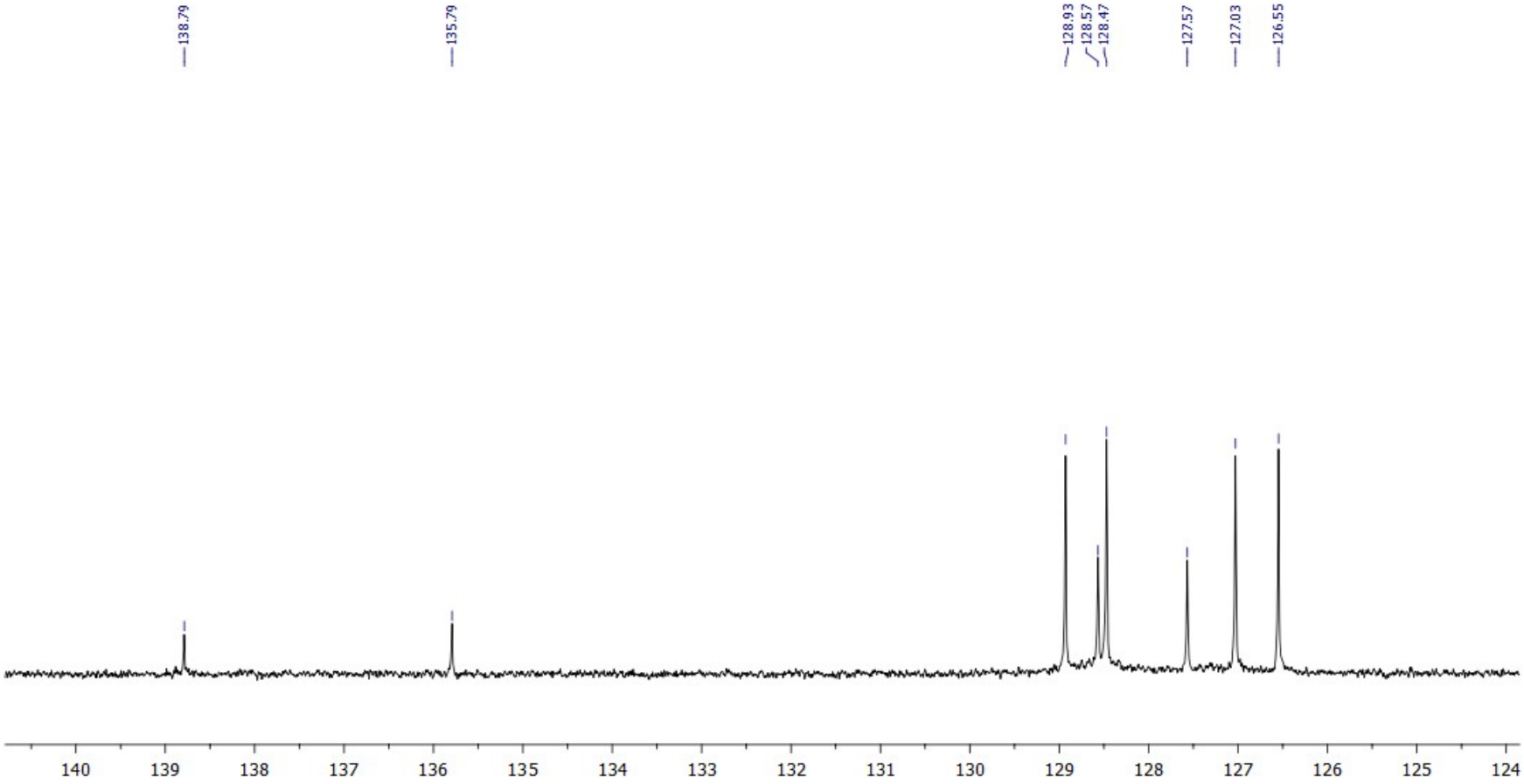


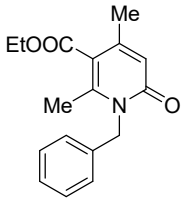
^{1}H NMR (400.1 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$) expanded aromatic region



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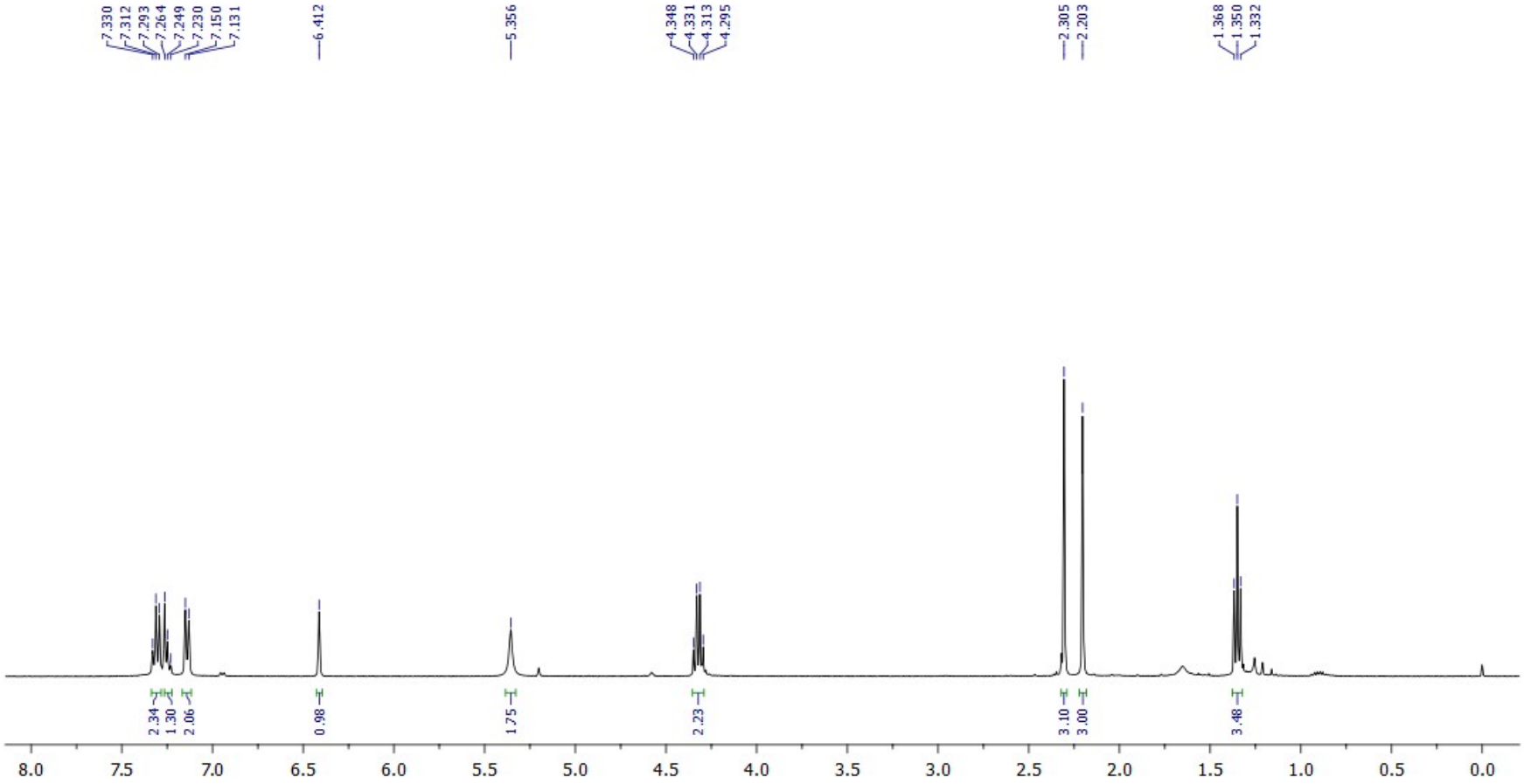
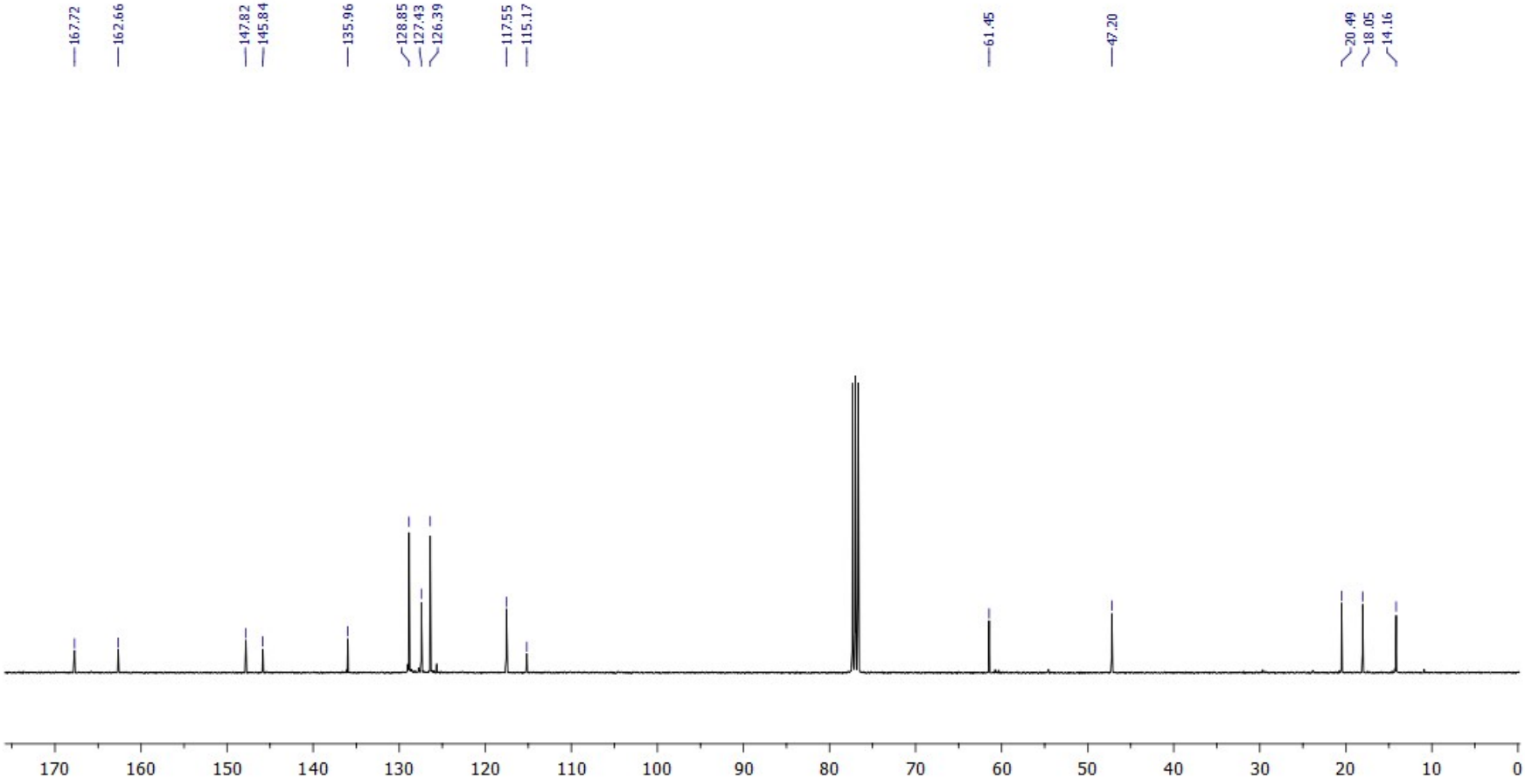
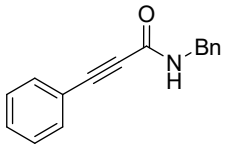


^{1}H NMR (400.1 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$)



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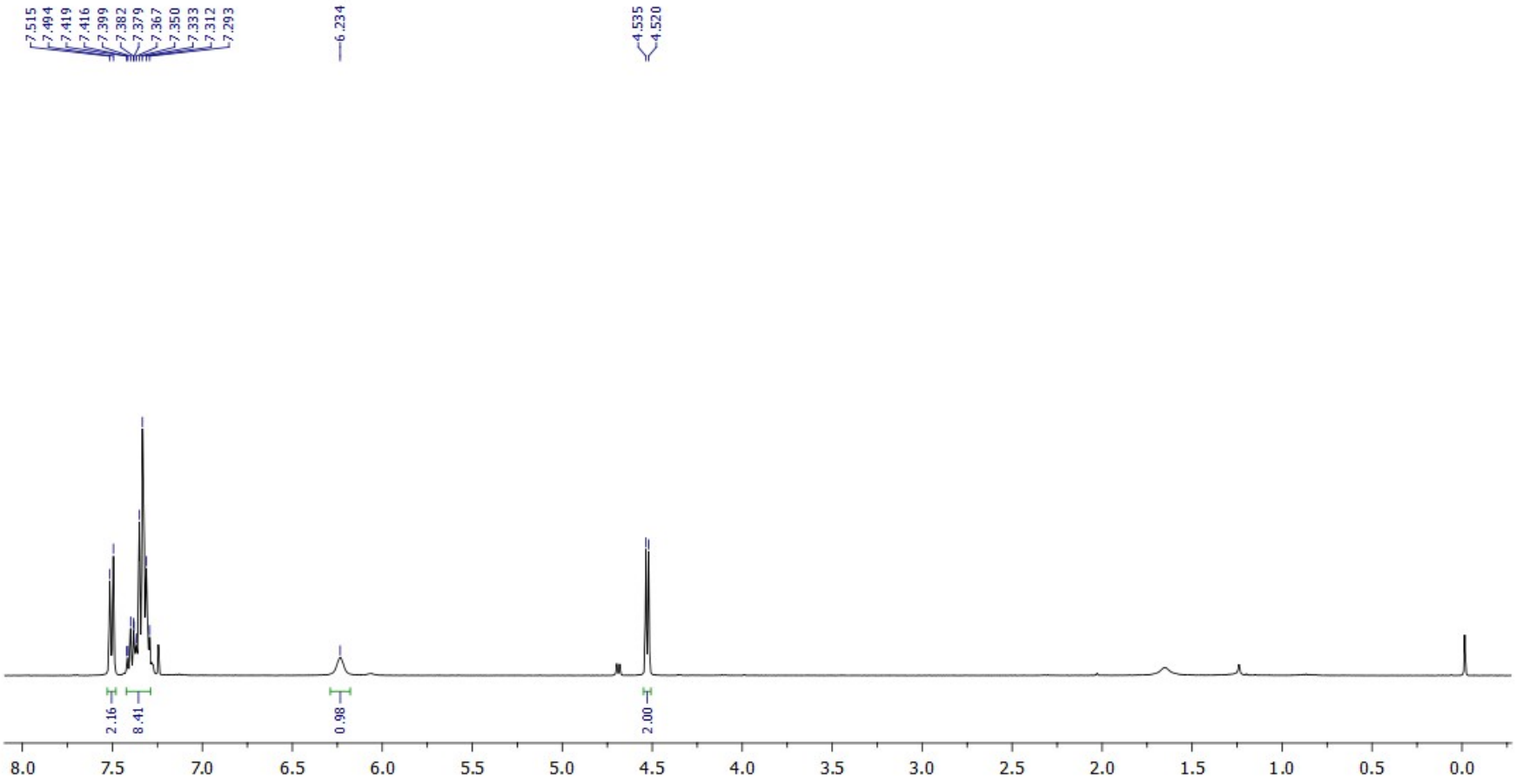
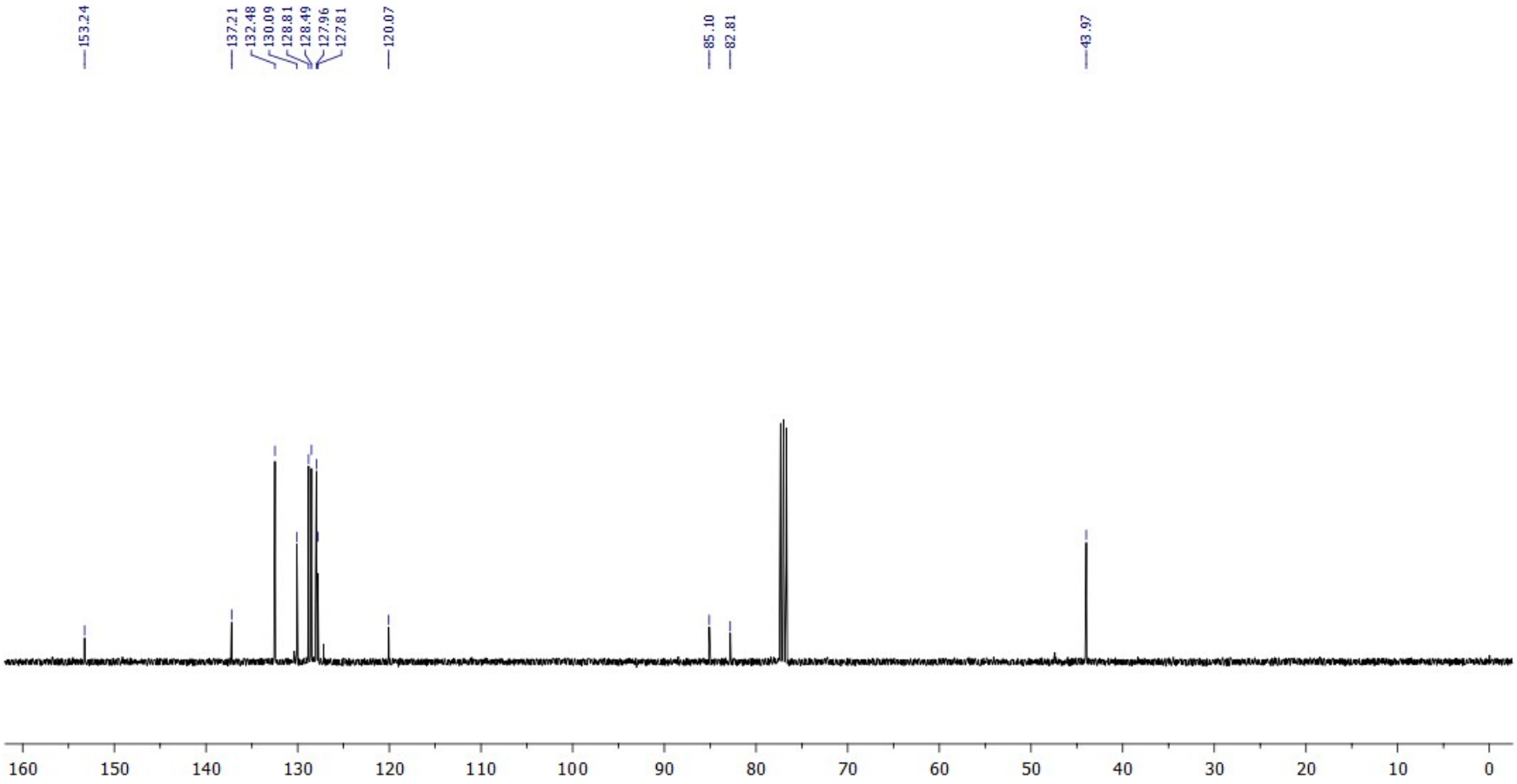
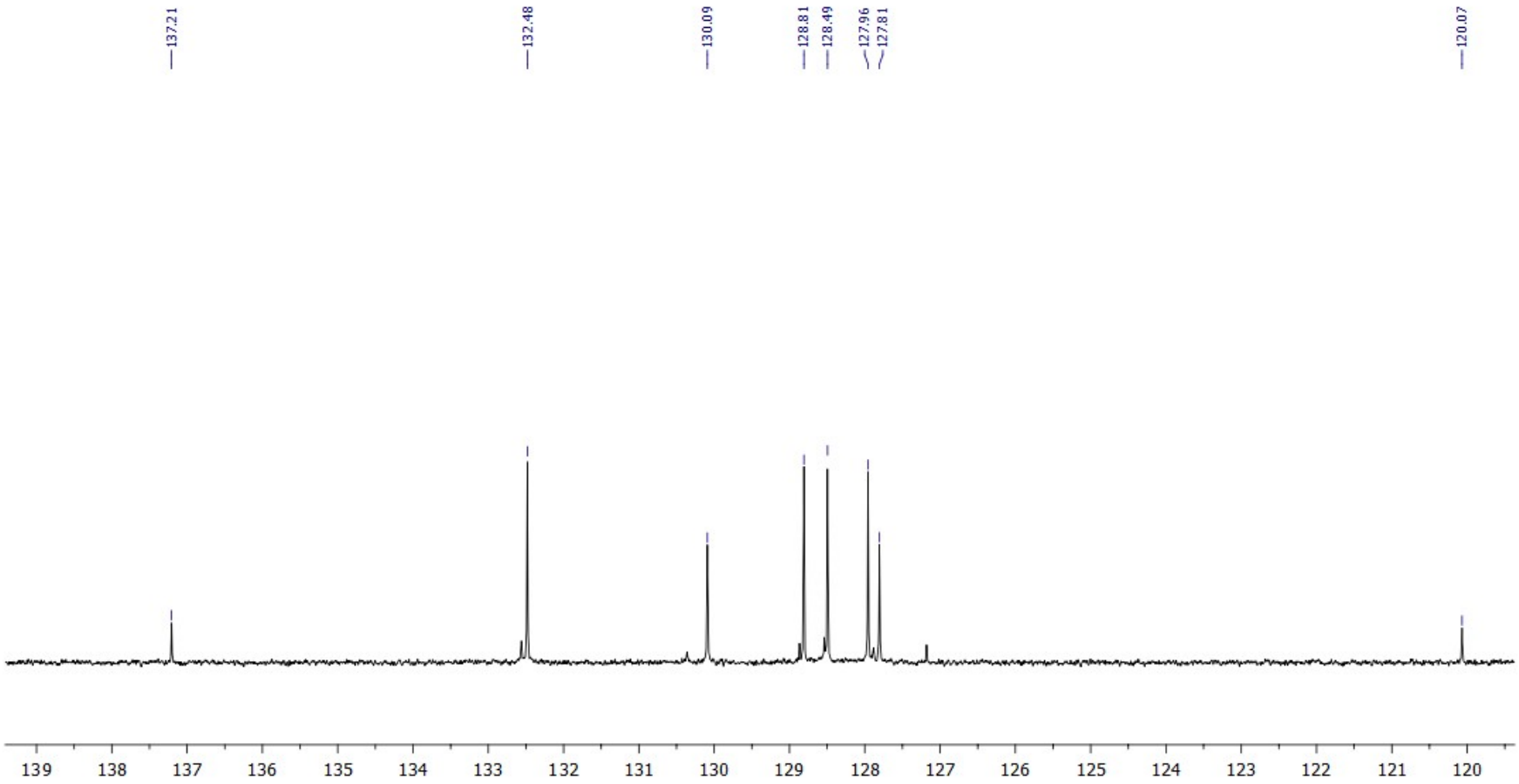


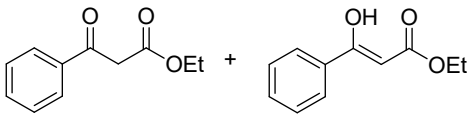
^{1}H NMR (400.1 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$) expanded aromatic region



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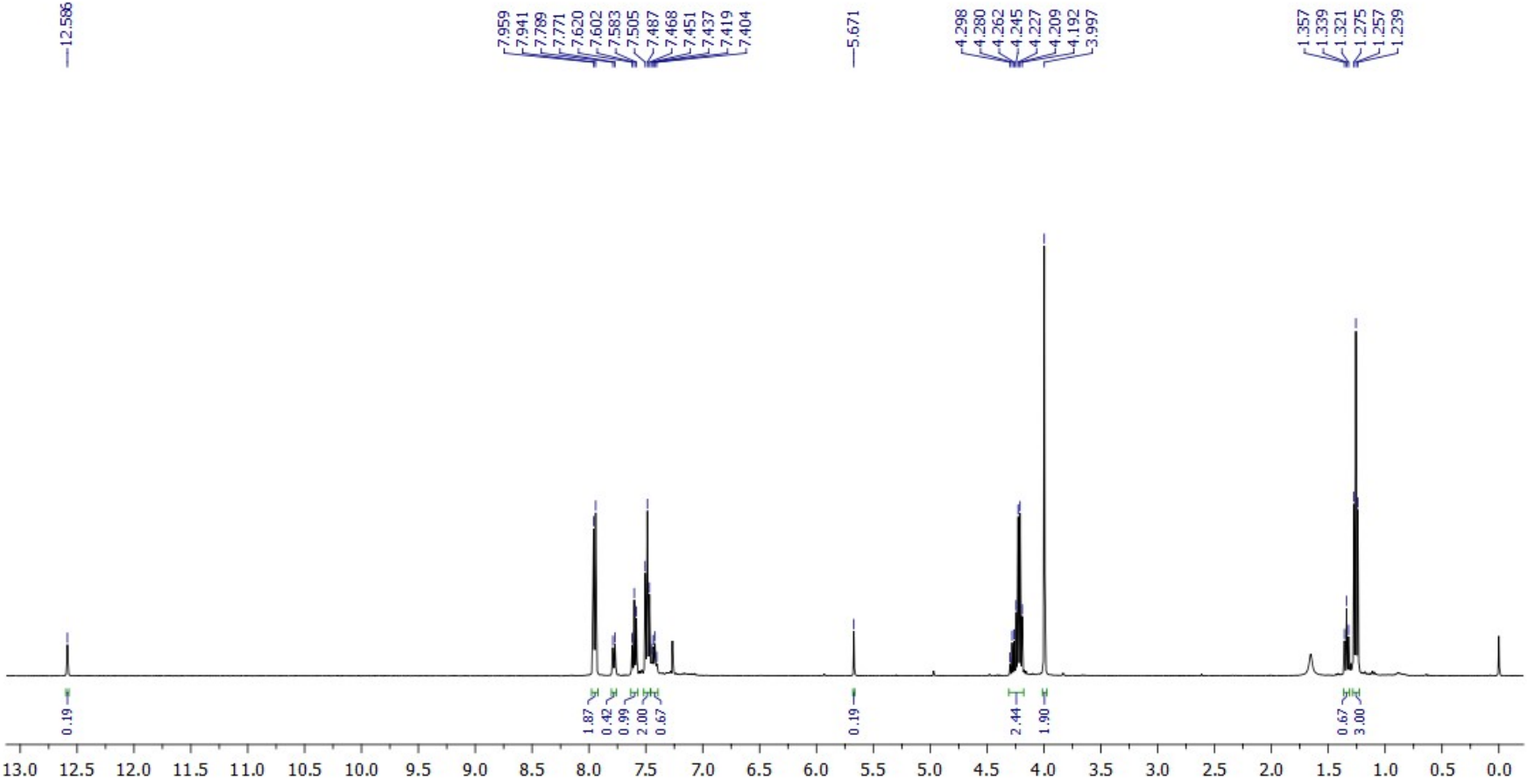
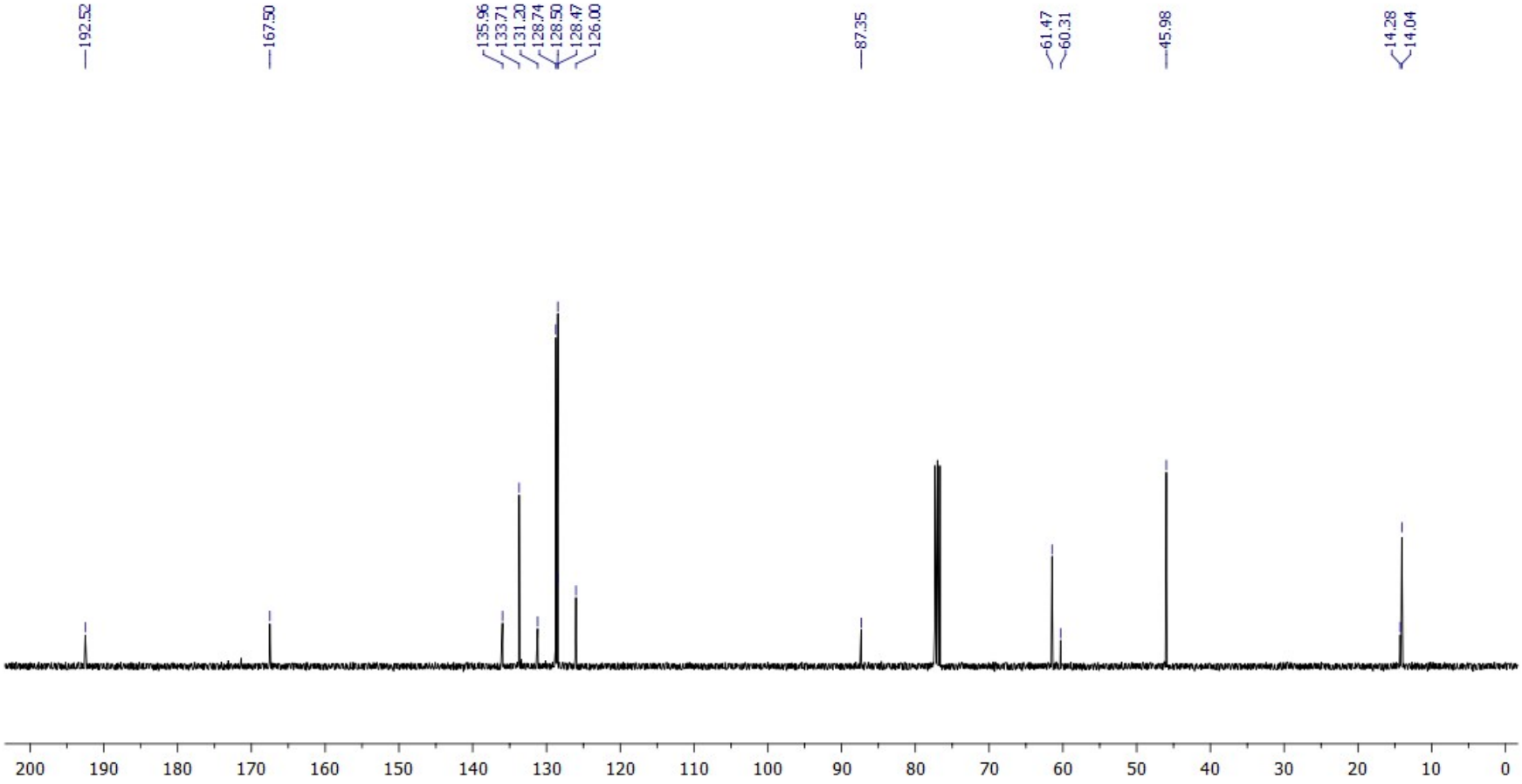
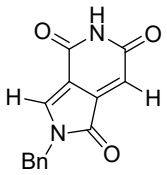


^{1}H NMR (400.1 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$)



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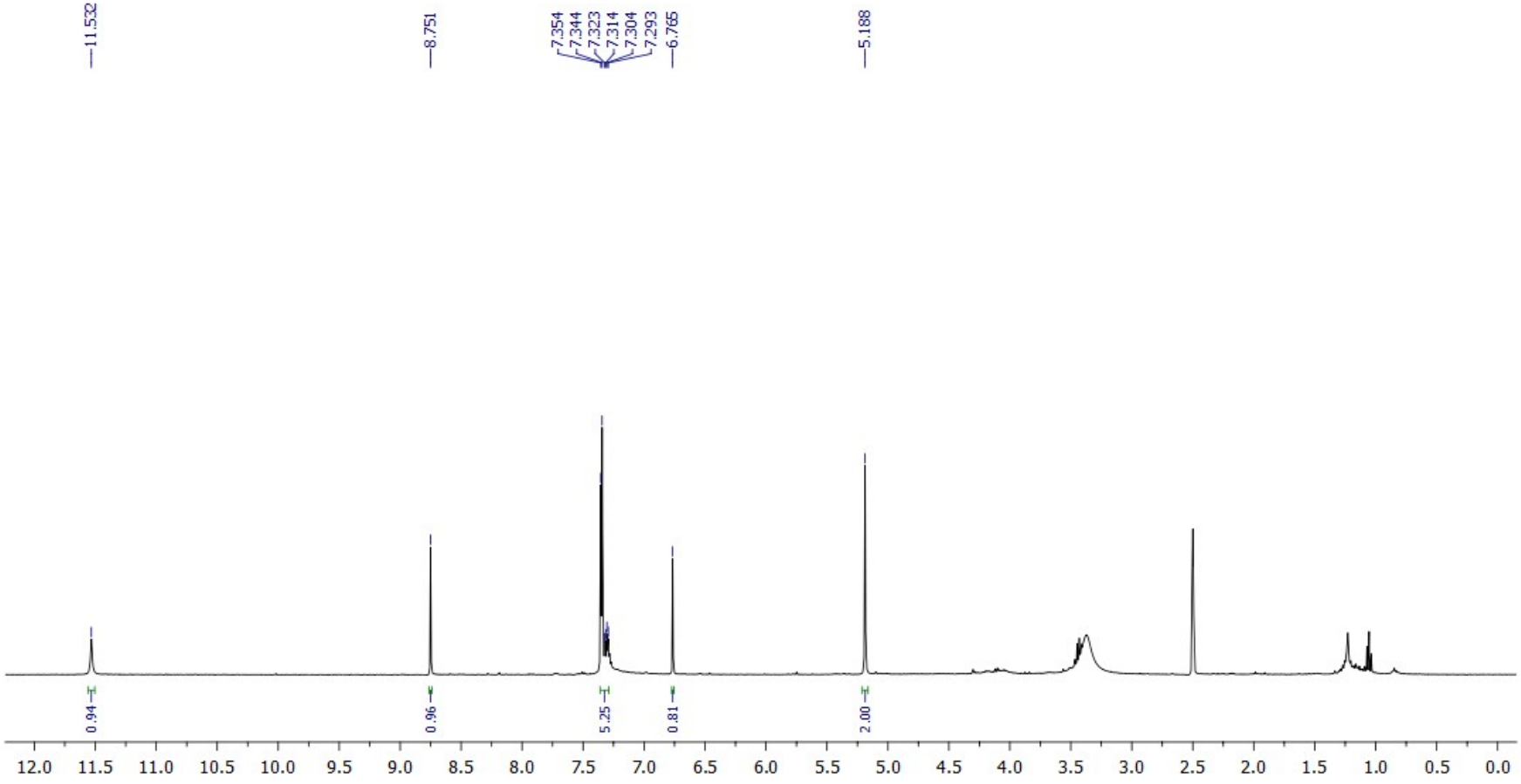
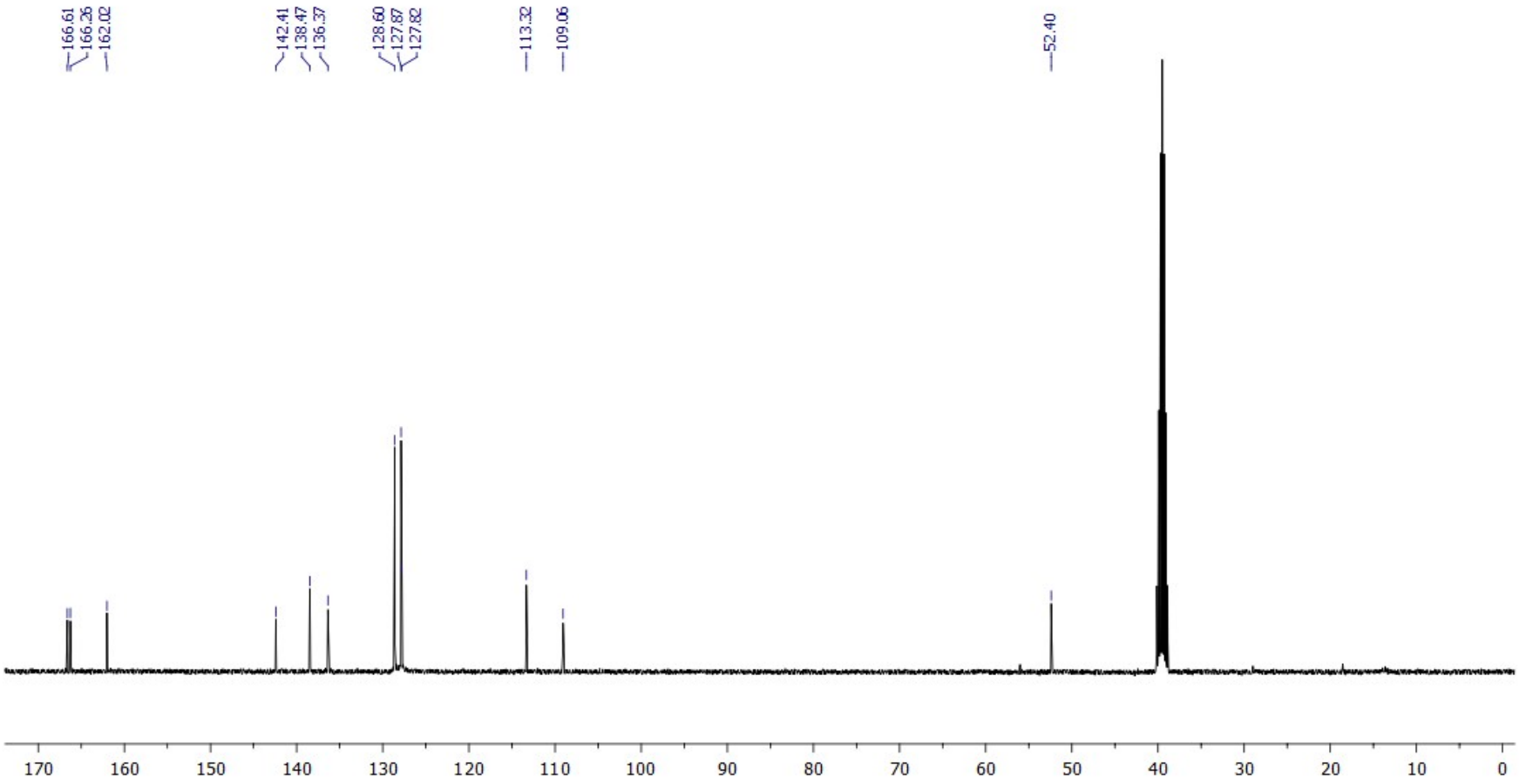


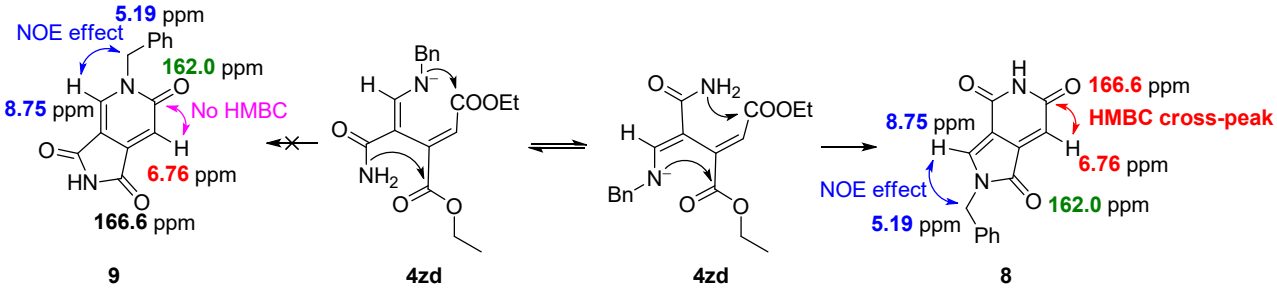
^{1}H NMR (500.3 MHz, DMSO-d_6)

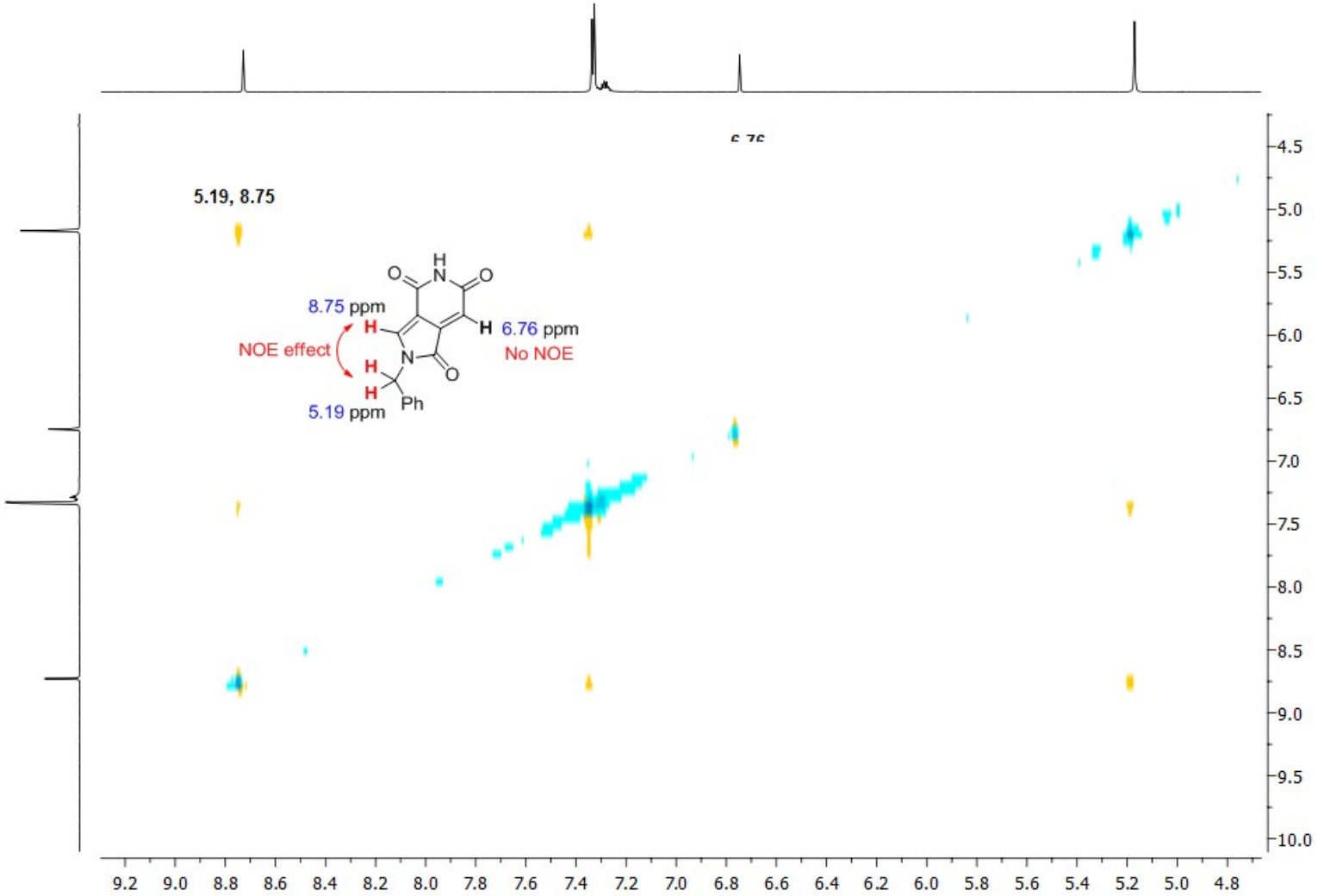


$^{13}C\{^{1}H\}$ NMR (125.8 MHz, DMSO-d_6)

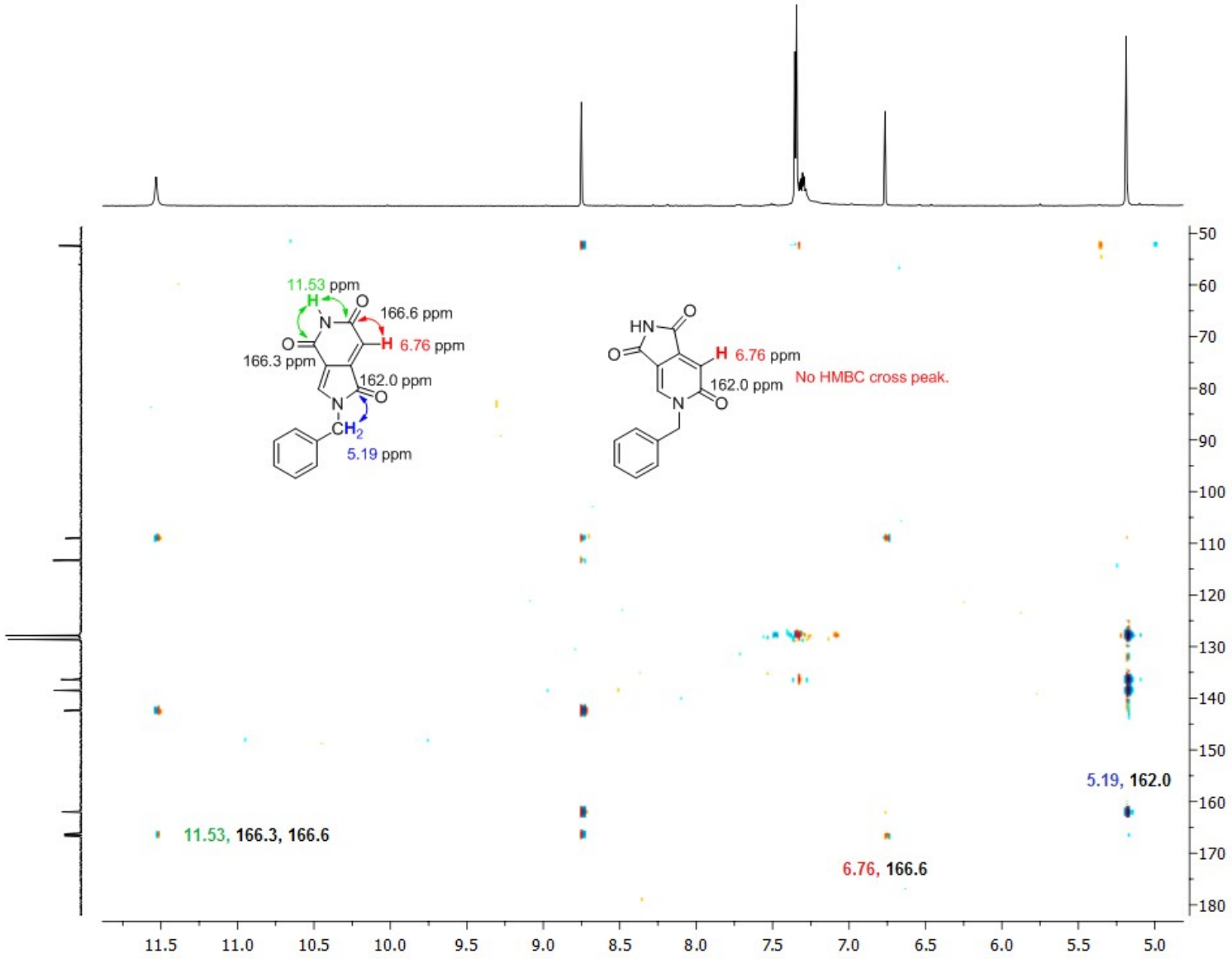
Determination of structure of compound 8

Product of cyclization of diene **4zd** shows four singlets in ^{1}H NMR spectrum: δ 11.53 ppm (s, 1H, NH), 5.19 ppm (s, 2H, Bn), 8.75 ppm and 6.76 ppm, belonging to two vinyl hydrogen atoms (NMR spectrum on p. S168). The position of the =C**H** atom (8.75 ppm) within the structure was unequivocally determined by the NOESY cross-peak between 5.19 ppm (Bn) and 8.75 ppm (=CH) (see, NOESY spectrum below). The assignment of signals belonging to carbonyl groups was made on the basis of the HMBC cross-peak: the signal at 162.0 ppm was assigned to carbonyl group near the Bn group due to the presence of the cross-peak, visible in HMBC spectrum on p. S172. Therefore, the other two carbonyl groups show very close signals at 166.3 ppm and 166.6 ppm. Additional evidence for this is the HMBC cross-peak between the carbonyl signals at 166.3/166.6 ppm and signal of the NH hydrogen atom (p. S172). Finally, the evidence for structure **8** came from the HMBC cross-peak between the =C**H** (6.76 ppm) and C=O (166.6 ppm), but not between the 6.76 ppm and 162.0 ppm signals, thus ruling out the structure **9**.

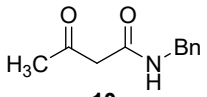




A part of **NOESY** spectrum of **8** used to distinguish between the two vinyl hydrogen atoms.



A part of **HMBC** spectrum of **8** used to distinguish between the two isomeric structures.



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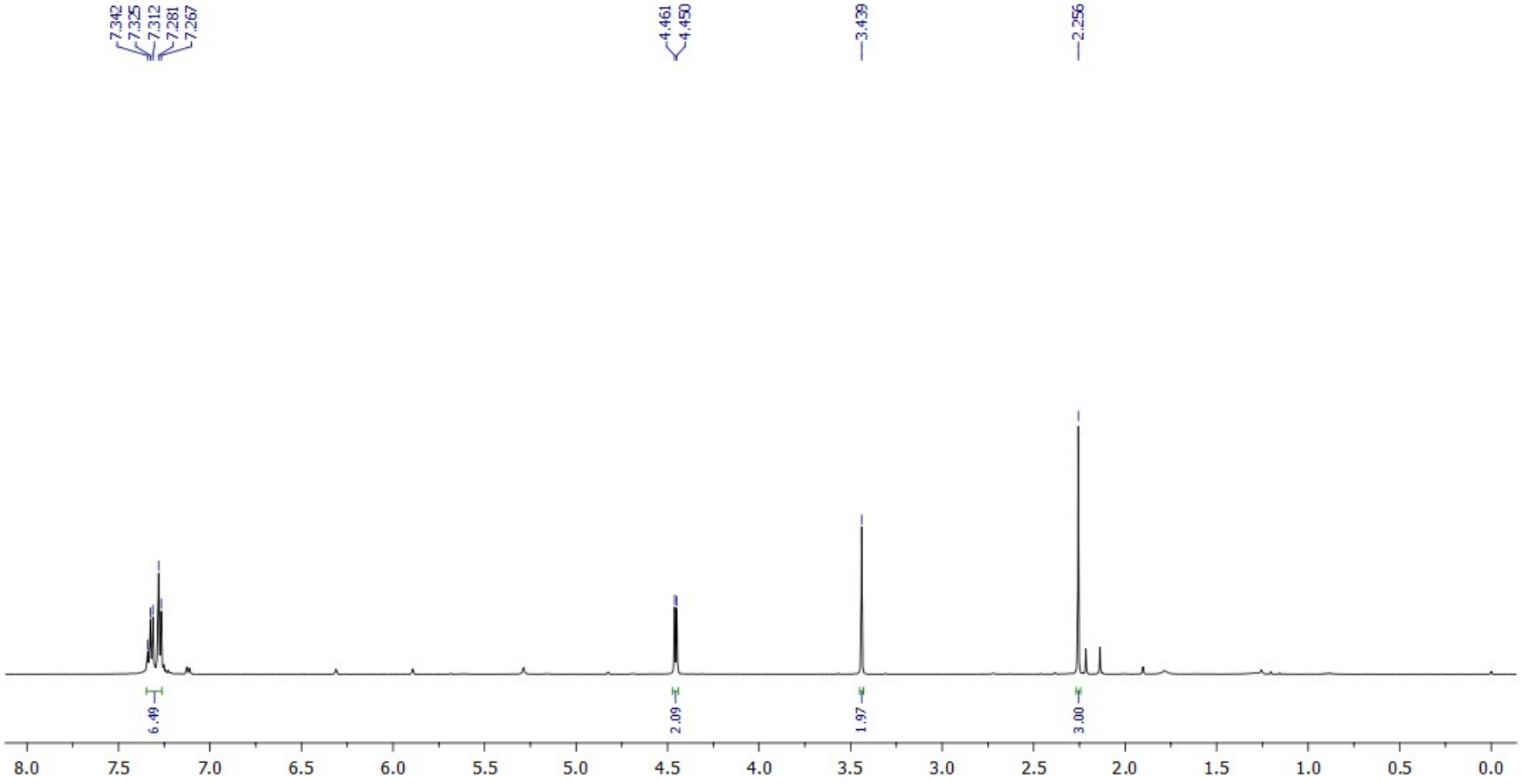
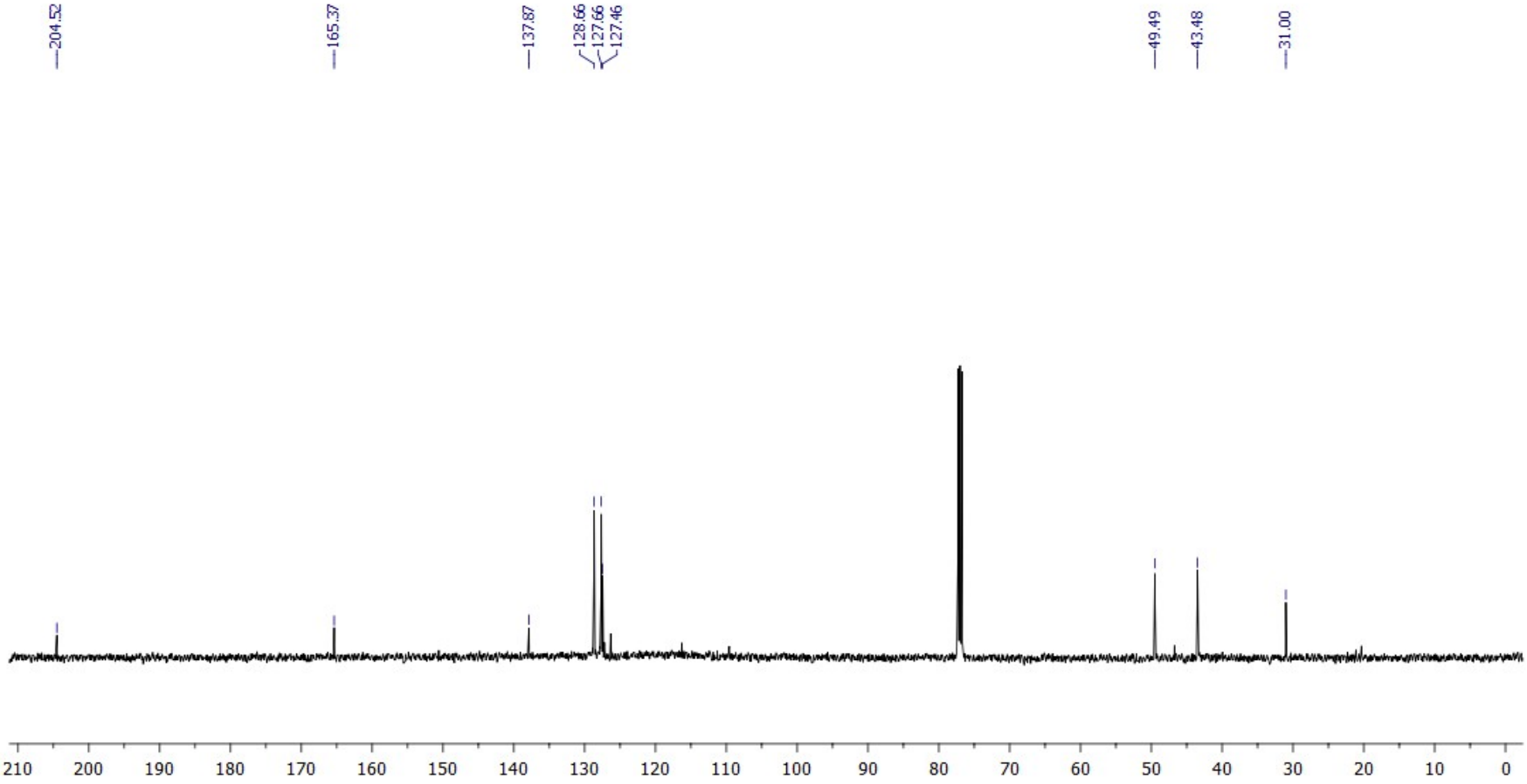
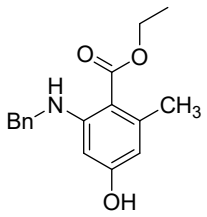


^{1}H NMR (500.3 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (125.8 MHz, $CDCl_3$)



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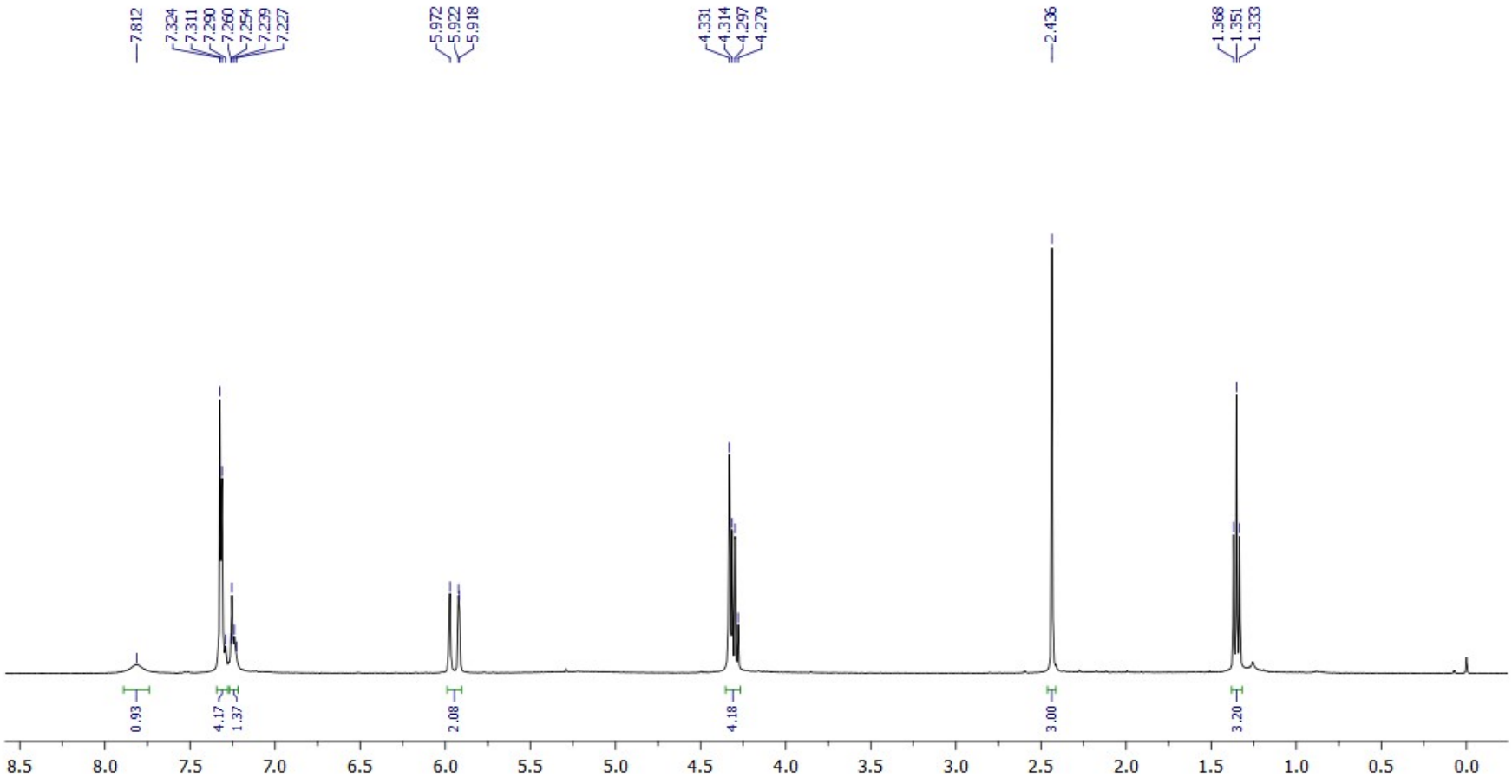
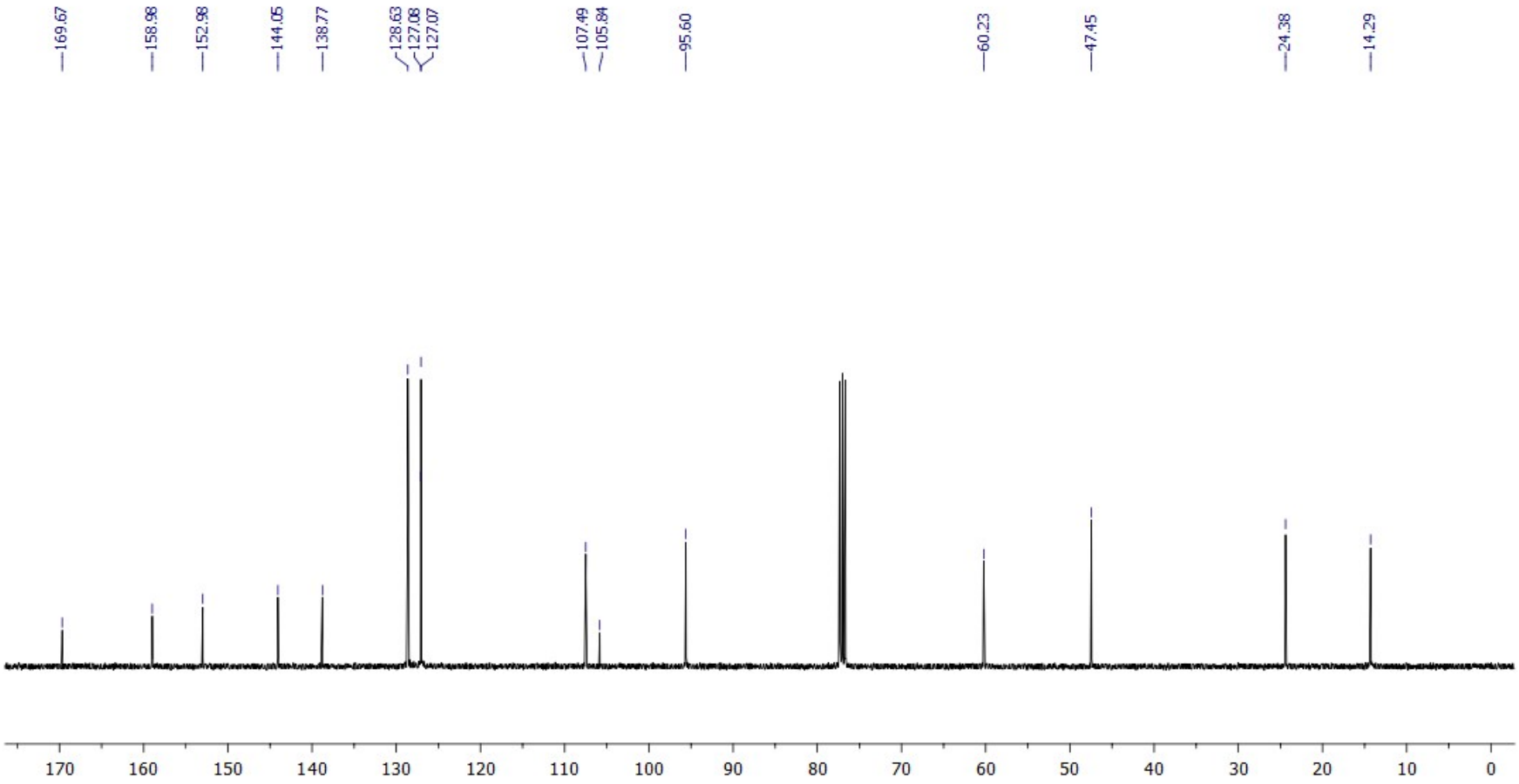


^{1}H NMR (400.1 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$)