Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.


# Copper-catalyzed [3+2+1] annulation for functionalized pyridines as potent and dynamic UV absorbers

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# Supporting Information

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## General information

All experiments were carried out under open air without inert gas protection. The starting materials, benzochromenone carbaldehydes **1a**–**1j**, and β-enamino esters **2a**–**2e** were synthesized in the laboratory, while other enamino substrates **7a**–**7c** were purchased from Alfa aesar and used as received. Ammonium acetate and copper(II) trifluoromethanesulfonate were purchased from Sigma-Aldrich. Merck pre-coated silica gel plates (Art. 5554) with a fluorescent indicator were used for analytical TLC. Flash column chromatography was performed using silica gel 9385 (Merck). Melting points were determined with micro-cover glasses on a Fisher-Johns apparatus and are uncorrected. $^{1}$H NMR spectra were recorded on a Varian-VNS (600 MHz) or DPX (300 MHz) spectrometer in $CDCl_3$ with 7.24 ppm as the internal standard solvent chemical shift. $^{13}$C NMR spectra were recorded on a Varian-VNS (150 MHz) or DPX (75 MHz) spectrometer in $CDCl_3$ with 77.0 ppm as the internal standard solvent chemical shift. All chemical shifts ($\delta$) are expressed in units of ppm, and $J$ values are given in Hz. Multiplicities are abbreviated as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet or overlap of non-equivalent resonances, and dd = doublet of doublets. Infrared (IR) spectra were recorded on a PerkinElmer Spectrum Two™ IR spectrometer with frequencies expressed in $cm^{-1}$. High-resolution mass spectrometry (HRMS) spectra were obtained at the Korea Basic Science Institute using a JEOL JMS-700 spectrometer.

### General procedure for the synthesis of functionalized pyridines 4

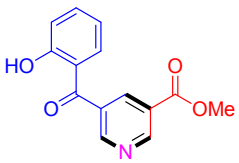
To a magnetically stirred solution of benzochromenone carbaldehyde (**1a**–**1h**, 1.0 mmol) in 1,2-DCE (5 mL), β-enamino ester (**2a**–**2e**, 1.0 mmol) and ammonium acetate **3** (231 mg, 3.0 equiv.) were added. This was followed by the addition of $Cu(OTf)_2$ (10 mol%) to the solution, which was mixed well. The reaction mixture was refluxed for 7 h. The reaction was monitored using a TLC (hexane/ethyl acetate = 6:1) until it was complete. Then, the reaction mixture was subjected to flash column chromatography using hexane/ethyl acetate (20:1) as the solvent system.

### Gram scale synthesis of 4b

To a magnetically stirred solution of 3-formyl-4*H*-chromen-4-one (**1a**), (1.742 g, 10 mmol) in 1,2-DCE (50 mL), ethyl (*E*)-3-(dimethylamino)acrylate (**2b**), (1.432 g, 10 mmol) and ammonium acetate **3** (2.313 g, 30 mmol) were added. This was followed by the addition of $Cu(OTf)_2$ (362 mg, 10 mol%) to the solution, which was mixed well. The reaction mixture was refluxed for 7 h. The reaction was monitored using a TLC (hexane/ethyl acetate = 6:1) until it was complete. Then, the reaction mixture was subjected to flash column chromatography using hexane/ethyl acetate (20:1) as the solvent system. Compound **4b** was isolated in 78% yield (2.005 g).

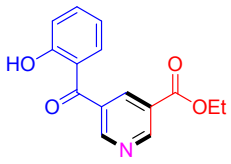
## Characterization data of compounds 4

### Methyl 5-(2-hydroxybenzoyl) nicotinate (4a)



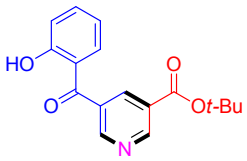

The product **4a** was obtained as a yellow solid, mp 94-96 °C. Yield: 85% (219 mg); $^{1}$H NMR (600 MHz, $CDCl_3$) $\delta$ 11.71 (1H, s), 9.38 (1H, d, $J$ = 1.8 Hz), 9.04 (1H, d, $J$ = 2.4 Hz), 8.58 (1H, t, $J$ = 2.4 Hz), 7.54 (1H, td, $J$ = 9.0, 1.8 Hz), 7.45 (1H, dd, $J$ = 7.8, 1.2 Hz), 7.10 (1H, d, $J$ = 8.4 Hz), 6.91 (1H, t, $J$ = 7.2 Hz), 3.98 (3H, s); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 198.3, 164.8, 163.4, 153.1, 152.9, 137.4, 137.4, 133.4, 132.8, 125.9, 119.3, 118.9, 118.7, 52.80; IR (ATR) 3069, 2957, 1732, 1619, 1590, 1464, 1289, 1204, 829 $cm^{-1}$; HRMS $m/z$ ($M^+$) calcd for $C_{14}H_{11}NO_4$: 257.0688, Found: 257.0686.

**Ethyl 5-(2-hydroxybenzoyl) nicotinate (4b)**



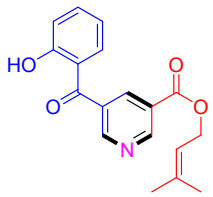
The product **4b** was obtained as a yellow solid, mp 72-74 °C. Yield: 83% (225 mg); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 11.74 (1H, s), 9.38 (1H, s), 9.02 (1H, s), 8.56 (1H, s), 7.55 (1H, t, $J$ = 7.2 Hz), 7.46 (1H, d, $J$ = 8.1 Hz), 7.09 (1H, d, $J$ = 8.1 Hz), 6.91 (1H, t, $J$ = 7.2 Hz), 4.44 (2H, q, $J$ = 7.2 Hz), 1.41 (3H, t, $J$ = 6.9 Hz); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 198.3, 164.3, 163.3, 153.1, 152.7, 137.4, 137.4, 133.4, 132.8, 126.2, 119.3, 118.8, 118.7, 62.0, 14.2; IR (ATR) 3064, 2991, 1726, 1623, 1487, 1444, 1277, 1233, 1106, 756 cm$^{-1}$; HRMS *m/z* ($M^+$) calcd for $C_{15}H_{13}NO_4$: 271.0845, Found: 271.0847.

**tert-Butyl 5-(2-hydroxybenzoyl) nicotinate (4c)**



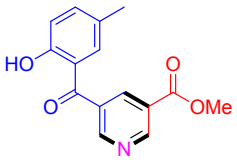
The product **4c** was obtained as a brown liquid. Yield: 79% (236 mg); $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 11.70 (1H, s), 9.27 (1H, s), 8.94 (1H, s), 8.45 (1H, s), 7.49 (1H, t, $J$ = 7.2 Hz), 7.42 (1H, d, $J$ = 7.8 Hz), 7.02 (1H, d, $J$ = 8.4 Hz), 6.86 (1H, t, $J$ = 7.8 Hz), 1.57 (9H, s); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 198.2, 163.1, 163.0, 152.8, 152.2, 137.0, 133.0, 132.6, 127.3, 119.0, 118.5, 118.5, 82.5, 27.8; IR (ATR) 2979, 1716, 1626, 1284, 1240, 1153, 1110, 757, 709 cm$^{-1}$; HRMS *m/z* ($M^+$) calcd for $C_{17}H_{17}NO_4$: 299.1158, Found: 299.1156.

**3-Methylbut-2-en-1-yl 5-(2-hydroxybenzoyl) nicotinate (4d)**



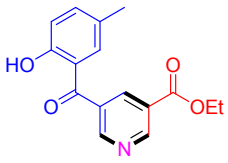
The product **4d** was obtained as a yellow solid, mp 44-46 °C. Yield: 73% (227 mg); $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 11.66 (1H, s), 9.31 (1H, s), 8.96 (1H, s), 8.49 (1H, s), 7.47 (1H, t, $J$ = 9.0 Hz), 7.40 (1H, d, $J$ = 7.8 Hz), 7.00 (1H, d, $J$ = 8.4 Hz), 6.83 (1H, t, $J$ = 7.2 Hz), 5.40 (1H, t, $J$ = 6.6 Hz), 4.81 (2H, d, $J$ = 7.2 Hz), 1.71 (6H, d, 1.8 Hz); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 198.1, 164.1, 163.3, 153.0, 152.6, 140.0, 137.2, 137.1, 132.7, 119.1, 118.6, 118.6, 117.8, 62.5, 25.6, 17.9; IR (ATR) 2977, 1718, 1623, 1445, 1269, 1232, 1019, 904, 755, 707 cm$^{-1}$; HRMS *m/z* ($M^+$) calcd for $C_{18}H_{17}NO_4$: 311.1158, Found: 311.1158.

**Methyl 5-(2-hydroxy-5-methylbenzoyl) nicotinate (4e)**



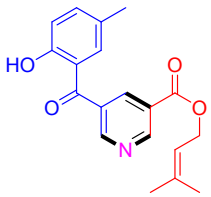
The product **4e** was obtained as a yellow solid, mp 152-154 °C. Yield: 74% (201 mg); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 11.54 (1H, s), 9.36 (1H, s), 9.00 (1H, s), 8.54 (1H, s), 7.35 (1H, d, $J$ = 8.4 Hz), 7.19 (1H, s), 6.97 (1H, d, $J$ = 8.4 Hz), 3.97 (3H, s), 2.24 (3H, s); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 198.1, 164.8, 161.3, 152.9, 152.7, 138.5, 137.4, 133.6, 132.3, 128.5, 125.9, 118.6, 118.4, 52.8, 20.4; IR (ATR) 3055, 1717, 1632, 1488, 1428, 1343, 1282, 1216, 712 cm$^{-1}$; HRMS *m/z* ($M^+$) calcd for $C_{15}H_{13}NO_4$: 271.0845, Found: 271.0847.

**Ethyl 5-(2-hydroxy-5-methylbenzoyl) nicotinate (4f)**



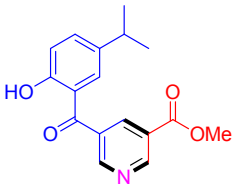
The product **4f** was obtained as a yellow solid, mp 79-80 °C. Yield: 69% (197 mg); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 11.55 (1H, s), 9.36 (1H, s), 9.00 (1H, s), 8.54 (1H, s), 7.34 (1H, d, $J$ = 8.4 Hz), 7.20 (1H, s), 6.97 (1H, d, $J$ = 8.7 Hz), 4.43 (2H, q, $J$ = 7.2 Hz), 2.22 (3H, s), 1.40 (3H, t, $J$ = 7.2 Hz); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 198.1, 164.3, 161.3, 152.9, 152.6, 138.5, 137.4, 133.5, 132.3, 128.5, 126.2, 118.5, 118.4, 61.9, 20.4, 14.9; IR (ATR) 2980, 1713, 1627, 1484, 1342, 1278, 1247, 1206, 1119, 767 cm$^{-1}$; HRMS *m/z* ($M^+$) calcd for $C_{16}H_{15}NO_4$: 285.1001, Found: 285.1000.

**3-Methylbut-2-en-1-yl 5-(2-hydroxy-5-methylbenzoyl) nicotinate (4g)**



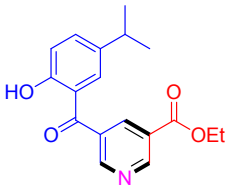
The product **4g** was obtained as a yellow liquid. Yield: 79% (257 mg); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$–11.60 (1H, s), 9.41 (1H, s), 9.04 (1H, s), 8.60 (1H, s), 7.40 (1H, d, $J$ = 8.4 Hz), 7.28 (1H, s), 7.02 (1H, d, $J$ = 8.4 Hz), 5.49 (1H, t, $J$ = 7.2 Hz), 4.90 (2H, d, $J$ = 7.5 Hz), 2.27 (3H, s), 1.81 (6H, d, $J$ = 3.3 Hz); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 198.1, 164.3, 161.3, 152.9, 152.5, 140.4, 138.5, 137.5, 133.6, 132.4, 128.5, 126.4, 118.6, 118.4, 117.8, 62.7, 25.8, 20.4, 18.1; IR (ATR) 2923, 1723, 1630, 1481, 1339, 1273, 1207, 1103, 929, 760 cm$^{-1}$; HRMS $m/z$ ($M^+$) calcd for $C_{19}H_{19}NO_4$: 325.1314, Found: 325.1314.

**Methyl 5-(2-hydroxy-5-isopropylbenzoyl) nicotinate (4h)**



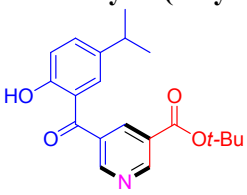
The product **4h** was obtained as a yellow solid, mp 102-104 $^o$C. Yield: 77% (230 mg); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 11.55 (1H, s), 9.37 (1H, s), 9.03 (1H, s), 8.57 (1H, s), 7.43 (1H, d, $J$ = 8.4 Hz), 7.25 (1H, s), 7.01 (1H, d, $J$ = 8.7 Hz), 3.97 (3H, s), 2.84-2.75 (1H, m), 1.15 (6H, d, $J$ = 6.9 Hz); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 198.0, 164.7, 162.3, 161.5, 153.0, 152.9, 139.7, 137.7, 135.9, 133.5, 129.9, 125.9, 118.7, 118.3, 52.8, 33.1, 23.9; IR (ATR) 2961, 1719, 1627, 1479, 1274, 1213, 1110, 764, 729 cm$^{-1}$; HRMS $m/z$ ($M^+$) calcd for $C_{17}H_{17}NO_4$: 299.1158, Found: 299.1156.

**Ethyl 5-(2-hydroxy-5-isopropylbenzoyl) nicotinate (4i)**



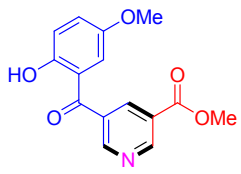
The product **4i** was obtained as a yellow solid, mp 83-85 $^o$C. Yield: 63% (197 mg); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 11.56 (1H, s), 9.38 (1H, s), 9.03 (1H, s), 8.58 (1H, s), 7.43 (1H, d, $J$ = 8.7 Hz), 7.26 (1H, s), 7.01 (1H, d, $J$ = 8.4 Hz), 4.43 (2H, q, $J$ = 7.2 Hz), 2.84-2.75 (1H, m), 1.40 (3H, t, $J$ = 7.2 Hz), 1.15 (6H, d, $J$ = 6.6 Hz); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 198.1, 164.2, 162.3, 161.5, 153.0, 152.8, 139.7, 137.6, 135.9, 133.5, 129.9, 126.2, 118.7, 118.3, 61.9, 33.1, 23.9, 14.2; IR (ATR) 2968, 1723, 1629, 1584, 1486, 1321, 1271, 1216, 1101, 762, 727 cm$^{-1}$; HRMS $m/z$ ($M^+$) calcd for $C_{18}H_{19}NO_4$: 313.1314, Found: 313.1315.

**tert-Butyl 5-(2-hydroxy-5-isopropylbenzoyl) nicotinate (4j)**



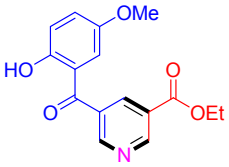
The product **4j** was obtained as a yellow solid, mp 86-88 $^o$C. Yield: 74% (253 mg); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 11.59 (1H, s), 9.33 (1H, s), 9.01 (1H, s), 8.51 (1H, s), 7.44 (1H, d, $J$ = 9.0 Hz), 7.27 (1H, s), 7.02 (1H, d, $J$ = 8.7 Hz), 2.85-2.76 (1H, m), 1.60 (9H, s), 1.16 (6H, d, $J$ = 6.9 Hz); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 198.3, 164.3, 162.3, 161.5, 153.0, 152.3, 139.6, 137.5, 135.9, 133.5, 130.0, 126.7, 118.7, 118.4, 82.9, 33.2, 28.1, 23.9; IR (ATR) 2974, 1716, 1630, 1585, 1486, 1369, 1321, 1283, 1252, 1221, 1160, 842, 762 cm$^{-1}$; HRMS $m/z$ ($M^+$) calcd for $C_{20}H_{23}NO_4$: 341.1627, Found: 341.1624.

**Methyl 5-(2-hydroxy-5-methoxybenzoyl) nicotinate (4k)**



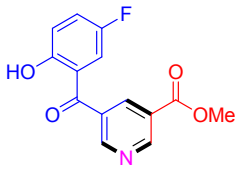
The product **4k** was obtained as an orange solid, mp 158-160 $^o$C. Yield: 74% (212 mg); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 11.32 (1H, s), 9.39 (1H, s), 9.06 (1H, s), 8.58 (1H, s), 7.18 (1H, d, $J$ = 9.0 Hz), 7.03 (1H, d, $J$ = 9.0 Hz), 6.81 (1H, s), 3.97 (3H, s), 3.68 (3H, s); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 197.7, 164.7, 162.3, 157.7, 153.1, 152.8, 151.8, 137.5, 125.4, 120.0, 119.8, 118.1, 115.0, 55.9, 52.8; IR (ATR) 2960, 1735, 1634, 1571, 1488, 1270, 1228, 1110, 687 cm$^{-1}$; HRMS $m/z$ ($M^+$) calcd for $C_{15}H_{13}NO_5$: 287.0794, Found: 287.0795.

**Ethyl 5-(2-hydroxy-5-methoxybenzoyl) nicotinate (4l)**



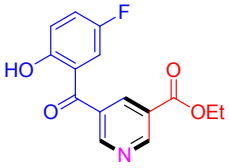

The product **4l** was obtained as a yellow solid, mp 138-140 °C. Yield: 76% (229 mg); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 11.35 (1H, s), 9.40 (1H, s), 9.06 (1H, s), 8.59 (1H, s), 7.19 (1H, d, $J$ = 9.0 Hz), 7.04 (1H, d, $J$ = 9.3 Hz), 6.88 (1H, s), 4.44 (2H, q, $J$ = 6.9 Hz), 3.69 (3H, s), 1.41 (3H, t, $J$ = 7.2 Hz); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 197.8, 164.3, 157.8, 153.1, 152.7, 151.8, 137.3, 133.4, 126.3, 125.4, 119.8, 118.2, 115.0, 62.0, 55.9, 14.2; IR (ATR) 2916, 1727, 1578, 1485, 1266, 1221, 1106, 688 cm$^{-1}$; HRMS $m/z$ ($M^+$) calcd for $C_{16}H_{15}NO_5$: 301.0950, Found: 301.0951.

**Methyl 5-(5-fluoro-2-hydroxybenzoyl) nicotinate (4m)**



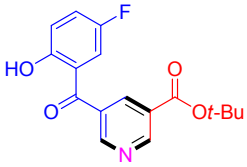

The product **4m** was obtained as a white solid, mp 151-153 °C. Yield: 83% (228 mg); $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 11.45 (1H, s), 9.46 (1H, s), 9.10 (1H, s), 8.55 (1H, s), 7.31-7.29 (1H, m), 7.13-7.12 (1H, m), 7.07-7.05 (1H, m), 3.98 (3H, s); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 197.4, 164.7, 159.5, 156.3, 153.2 (d, $J$ = 17.2 Hz), 152.6, 137.2, 125.2, 124.9, 120.3 (d, $J$ = 7.5 Hz), 118.1 (d, $J$ = 6.0 Hz), 117.5, 117.2, 52.8; IR (ATR) 3067, 1733, 1639, 1608, 1480, 1298, 1204, 829 cm$^{-1}$; HRMS $m/z$ ($M^+$) calcd for $C_{14}H_{10}FNO_4$: 275.0594, Found: 275.0594.

**Ethyl 5-(5-fluoro-2-hydroxybenzoyl) nicotinate (4n)**



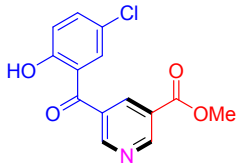

The product **4n** was obtained as a yellow solid, mp 70-71 °C. Yield: 80% (231 mg); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 11.45 (1H, s), 9.39 (1H, s), 9.03 (1H, s), 8.55 (1H, s), 7.33-7.27 (1H, m), 7.15-7.11 (1H, m), 7.09-7.04 (1H, m), 4.44 (2H, d, $J$ = 7.2 Hz), 1.41 (3H, t, $J$ = 7.2 Hz); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 197.5, 164.1, 162.3, 159.5, 156.3, 153.0 (d, $J$ = 124.5 Hz), 137.3, 132.9, 126.3, 125.1 (d, $J$ = 46.5 Hz), 120.3 (d, $J$ = 7.5 Hz), 118.1 (d, $J$ = 6.0 Hz), 117.4 (d, $J$ = 48.0 Hz), 62.1, 14.2; IR (ATR) 3064, 2999, 1727, 1592, 1481, 1286, 1215, 758, 740 cm$^{-1}$; HRMS $m/z$ ($M^+$) calcd for $C_{15}H_{12}FNO_4$: 289.0750, Found: 289.0753.

**tert-Butyl 5-(5-fluoro-2-hydroxybenzoyl) nicotinate (4o)**



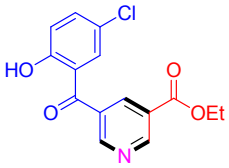

The product **4o** was obtained as a yellow solid, mp 68-70 °C. Yield: 53% (168 mg); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 11.47 (1H, s), 9.31 (1H, s), 8.98 (1H, s), 8.48 (1H, s), 7.31-7.25 (1H, m), 7.15-7.12 (1H, m), 7.06-7.02 (1H, m), 1.59 (9H, s); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 197.6 (d, $J$ = 4.5 Hz), 163.1, 159.4, 156.3, 153.4, 152.2, 137.1, 132.7, 127.7, 124.9 (d, $J$ = 23.3 Hz), 120.3 (d, $J$ = 7.5 Hz), 118.2 (d, $J$ = 6.0 Hz), 117.4 (d, $J$ = 24.0 Hz), 83.0, 28.1; IR (ATR) 2980, 1717, 1624, 1478, 1278, 1218, 1158, 1113, 841, 762, 729 cm$^{-1}$; HRMS $m/z$ ($M^+$) calcd for $C_{17}H_{16}FNO_4$: 317.1063, Found: 317.1060.

**Methyl 5-(5-chloro-2-hydroxybenzoyl) nicotinate (4p)**



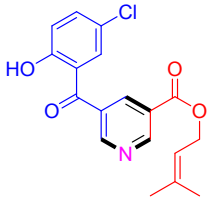

The product **4p** was obtained as a yellow solid, mp 177-179 °C. Yield: 72% (210 mg); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 11.62 (1H, s), 9.41 (1H, s), 9.03 (1H, s), 8.56 (1H, s), 7.50 (1H, d, $J$ = 8.7 Hz), 7.41 (1H, s), 7.06 (1H, d, $J$ = 9.0 Hz), 3.99 (3H, s); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 197.4, 164.6, 162.3, 161.8, 153.4, 152.7, 137.4, 137.3, 132.9, 131.5, 124.1, 120.6, 119.3, 52.9; IR (ATR) 3053, 1717, 1634, 1475, 1278, 1210, 761, 709 cm$^{-1}$; HRMS $m/z$ ($M^+$) calcd for $C_{14}H_{10}ClNO_4$: 291.0298, Found: 291.0296.

**Ethyl 5-(5-chloro-2-hydroxybenzoyl) nicotinate (4q)**



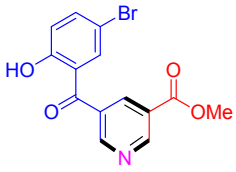
The product **4q** was obtained as a yellow solid, mp 102-103 °C. Yield: 81% (247 mg); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 11.57 (1H, s), 9.36 (1H, s), 8.98 (1H, s), 8.52 (1H, s), 7.44 (1H, d, $J$ = 9.0 Hz), 7.38 (1H, s), 7.00 (1H, d, $J$ = 9.0 Hz), 4.41 (2H, q, $J$ = 7.2 Hz), 1.38 (3H, t, $J$ = 6.9 Hz); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 197.4, 164.0, 161.6, 153.4, 152.5, 137.2, 137.1, 132.7, 131.5, 126.3, 123.9, 120.4, 119.2, 61.9, 14.1; IR (ATR) 2982, 1713, 1626, 1467, 1337, 1279, 1209, 762, 710 cm$^{-1}$; HRMS *m/z* ($M^+$) calcd for $C_{15}H_{12}ClNO_4$: 305.0455, Found: 305.0456.

**3-Methylbut-2-en-1-yl 5-(5-chloro-2-hydroxybenzoyl) nicotinate (4r)**



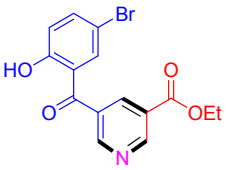
The product **4r** was obtained as a white solid, mp 83-85 °C. Yield: 55% (190 mg); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 11.62 (1H, s), 9.39 (1H, s), 9.01 (1H, s), 8.55 (1H, s), 7.49 (1H, d, $J$ = 9.0 Hz), 7.41 (1H, s), 7.05 (1H, d, $J$ = 8.7 Hz), 5.45 (1H, t, $J$ = 6.9 Hz), 4.87 (2H, d, $J$ = 7.2 Hz), 1.77 (6H, d, $J$ = 2.7 Hz); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 197.4, 164.1, 161.7, 153.4, 152.4, 140.5, 137.4, 137.3, 132.8, 131.5, 126.5, 124.1, 120.5, 119.3, 117.8, 62.8, 25.8, 18.1; IR (ATR) 2907, 2695, 1727, 1661, 1597, 1420, 1379, 1276, 1215, 920, 808, 749, 655 cm$^{-1}$; HRMS *m/z* ($M^+$) calcd for $C_{18}H_{16}ClNO_4$: 345.0768, Found: 345.0766.

**Methyl 5-(5-bromo-2-hydroxybenzoyl) nicotinate (4s)**



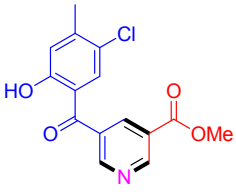
The product **4s** was obtained as a yellow solid, mp 177-179 °C. Yield: 71% 238 mg); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 11.62 (1H, s), 9.39 (1H, s), 9.01 (1H, s), 8.54 (1H, s), 7.61 (1H, d, $J$ = 8.7 Hz), 7.54 (1H, s), 6.99 (1H, d, $J$ = 9.0 Hz), 3.98 (3H, s); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 197.3, 164.6, 162.2, 153.5, 152.7, 140.0, 137.3, 134.5, 132.8, 126.1, 120.9, 119.9, 110.9, 52.9; IR (ATR) 3052, 1718, 1633, 1471, 277, 1208, 758, 701 cm$^{-1}$; HRMS *m/z* ($M^+$) calcd for $C_{14}H_{10}BrNO_4$: 334.9793, Found: 334.9789.

**Ethyl 5-(5-bromo-2-hydroxybenzoyl) nicotinate (4t)**



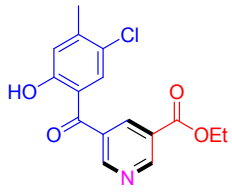
The product **4t** was obtained as a yellow solid, mp 93-95°C. Yield: 75% (262 mg); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 11.64 (1H, s), 9.40 (1H, s), 9.02 (1H, s), 8.55 (1H, s), 7.62 (1H, d, $J$ = 8.7 Hz), 7.55 (1H, s), 7.00 (1H, d, $J$ = 9.0 Hz), 4.45 (2H, q, $J$ = 7.2 Hz), 1.42 (3H, t, $J$ = 6.9 Hz); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 197.4, 164.1, 162.2, 153.5, 152.5, 140.0, 137.4, 134.6, 132.8, 126.4, 120.9, 119.9, 110.9, 62.1, 14.2; IR (ATR) 2981, 1713, 1624, 1233, 1207, 755, 704 cm$^{-1}$; HRMS *m/z* ($M^+$) calcd for $C_{15}H_{12}BrNO_4$: 348.9950, Found: 348.9948.

**Methyl 5-(5-chloro-2-hydroxy-4-methylbenzoyl) nicotinate (4u)**



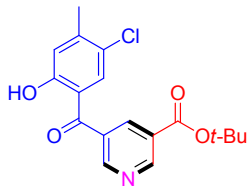
The product **4u** was obtained as a white solid, mp 124-126 °C. Yield: 68% (207 mg); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 11.62 (1H, s), 9.39 (1H, s), 9.01 (1H, s), 8.54 (1H, s), 7.39 (1H, s), 6.98 (1H, s), 3.98 (3H, s), 2.40 (3H, s); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 196.9, 164.7, 161.7, 153.3, 152.6, 147.1, 137.3, 133.1, 131.9, 126.0, 124.8, 120.8, 117.6, 52.9, 21.0; IR (ATR) 3183, 1723, 1627, 1450, 1232, 1163, 732, 705 cm$^{-1}$; HRMS *m/z* ($M^+$) calcd for $C_{15}H_{12}ClNO_4$: 305.0455, Found: 305.0452.

**Ethyl 5-(5-chloro-2-hydroxy-4-methylbenzoyl) nicotinate (4v)**



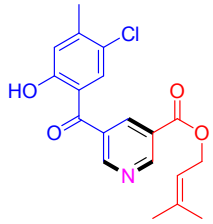

The product **4v** was obtained as a yellow solid, mp 109-110 °C. Yield: 74% (236 mg); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 11.64 (1H, s), 9.41 (1H, s), 9.02 (1H, s), 8.54 (1H, s), 7.40 (1H, s), 6.99 (1H, s), 4.45 (2H, q, $J$ = 7.2 Hz), 2.40 (3H, s), 1.42 (3H, t, $J$ = 6.9 Hz); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 197.0, 164.2, 161.7, 153.3, 152.5, 147.1, 137.3, 132.0, 124.8, 120.9, 117.7, 62.0, 21.0, 14.2; IR (ATR) 2991, 1714, 1633, 1236, 765, 708 cm$^{-1}$; HRMS *m/z* ($M^+$) calcd for $C_{16}H_{14}ClNO_4$: 319.0611, Found: 319.0614.

***tert*-Butyl 5-(5-chloro-2-hydroxy-4-methylbenzoyl) nicotinate (4w)**



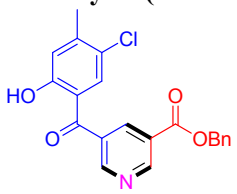

The product **4w** was obtained as a yellow solid, mp 105-107 °C. Yield: 62% (215 mg); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 11.64 (1H, s), 9.34 (1H, s), 8.99 (1H, s), 8.48 (1H, s), 7.40 (1H, s), 6.97 (1H, s), 2.39 (3H, s), 1.60 (9H, s); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 197.1, 163.1, 161.7, 156.2, 153.1, 152.0, 147.0, 137.2, 132.0, 124.7, 120.8, 117.7, 83.0, 28.1, 21.0; IR (ATR) 2978, 1720, 1625, 1476, 1240, 1164, 1107, 1026, 851, 759, 703 cm$^{-1}$; HRMS *m/z* ($M^+$) calcd for $C_{18}H_{18}ClNO_4$: 347.0924, Found: 347.0927.

**3-Methylbut-2-en-1-yl 5-(5-chloro-2-hydroxy-4-methylbenzoyl) nicotinate (4x)**




The product **4x** was obtained as a yellow solid, mp 98-99 °C. Yield: 50% (180 mg); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 11.62 (1H, s), 9.39 (1H, s), 9.00 (1H, s), 8.55 (1H, s), 7.39 (1H, s), 6.98 (1H, s), 5.45 (1H, t, $J$ = 7.5 Hz), 4.87 (2H, d, $J$ = 7.2 Hz), 2.39 (3H, s), 1.78 (3H, s), 1.77 (3H, s); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 196.9, 164.1, 161.7, 153.1, 152.3, 147.0, 140.5, 137.4, 133.1, 131.9, 126.6, 124.7, 120.8, 117.8, 117.7, 62.8, 25.8, 20.9, 18.1; IR (ATR) 2915, 1791, 1655, 1447, 1399, 1220, 1172, 1126, 746 cm$^{-1}$; HRMS *m/z* ($M^+$) calcd for $C_{19}H_{18}ClNO_4$: 359.0924, Found: 359.0924.

**Benzyl 5-(5-chloro-2-hydroxy-4-methylbenzoyl) nicotinate (4y)**



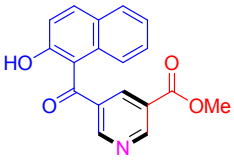

The product **4y** was obtained as a yellow solid, mp 110-112 °C. Yield: 53% (202 mg); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 11.62 (1H, s), 9.42 (1H, s), 9.01 (1H, s), 8.57 (1H, s), 7.45-7.32 (6H, m), 6.98 (1H, s), 5.42 (2H, s), 2.39 (3H, s); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 196.8, 164.0, 161.7, 153.3, 152.6, 147.1, 137.5, 135.0, 133.1, 131.9, 128.7, 128.7, 128.5, 126.1, 124.8, 120.9, 117.6, 67.7, 21.0; IR (ATR) 3045, 1723, 1631, 1588, 1477, 1346, 1294, 1245, 1225, 1174, 728, 689 cm$^{-1}$; HRMS *m/z* ($M^+$) calcd for $C_{21}H_{16}ClNO_4$: 381.0768, Found: 381.0769.

**General procedure for the synthesis of functionalized pyridines 5 and 6**

To a magnetically stirred solution of benzochromenone carbaldehyde **1i** and **1j** (1.0 mmol) in 1,2-DCE (5mL), β-enamino esters **2a-2e** (1.0 mmol), and ammonium acetate **3** (231 mg, 3.0 equiv.) were added. This was followed by the addition of $Cu(OTf)_2$ (10 mol%) to the solution, which was mixed well. The reaction mixture was refluxed for 7 hours. The reaction was monitored using a TLC (hexane/ethyl acetate = 6:1) until it was complete. Then, the reaction mixture was subjected to flash column chromatography using hexane/ethyl acetate (20:1) as the solvent system.

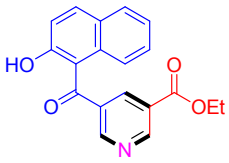
## Characterization data of compounds 5 and 6

### Methyl 5-(2-hydroxy-1-naphthoyl) nicotinate (5a)



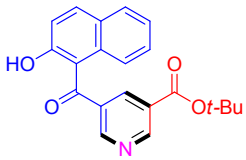
The product **5a** was obtained as a yellow solid, mp 207-208 °C. Yield: 57% (175 mg); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 11.23 (1H, s), 9.32 (1H, s), 8.86 (1H, s), 8.56 (1H, s), 7.96 (1H, d, $J$ = 9.0 Hz), 7.77 (1H, d, $J$ = 8.1 Hz), 7.32-7.27 (1H, m), 7.21-7.19 (3H, m), 3.93 (3H, s); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 196.7, 164.7, 161.9, 153.5, 153.2, 137.6, 137.4, 135.7, 131.8, 129.1, 128.5, 127.6, 126.3, 125.5, 124.2, 119.1, 113.7, 52.8; IR (ATR) 2955, 1725, 1661, 1434, 1283, 1216, 1146, 807, 751 cm$^{-1}$; HRMS *m/z* ($M^+$) calcd for $C_{18}H_{13}NO_4$: 307.0845, Found: 307.0847.

### Ethyl 5-(2-hydroxy-1-naphthoyl) nicotinate (5b)



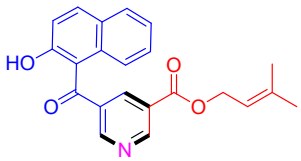
The product **5b** was obtained as a yellow solid, mp 189-191 °C. Yield: 56% (180 mg); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 11.25 (1H, s), 9.34 (1H, s), 8.84 (1H, s), 8.61 (1H, s), 7.97 (1H, d, $J$ = 9.3 Hz), 7.77 (1H, d, $J$ = 8.1 Hz), 7.33-7.26 (2H, m), 7.23-7.18 (2H, m), 4.41 (2H, q, $J$ = 7.2 Hz), 1.38 (3H, t, $J$ = 7.2 Hz); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 196.5, 164.1, 162.0, 153.1, 152.8, 137.9, 137.5, 135.9, 131.8, 129.1, 128.6, 127.6, 126.8, 125.5, 124.3, 119.2, 113.7, 62.0, 14.2; IR (ATR) 2925, 1718, 1665, 1509, 1282, 1215, 1108, 806, 745 cm$^{-1}$; ; HRMS *m/z* ($M^+$) calcd for $C_{19}H_{15}O_4$: 321.1001, Found: 321.0009.

### tert-Butyl 5-(2-hydroxy-1-naphthoyl) nicotinate (5c)



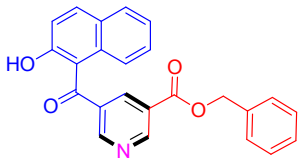
The product **5c** was obtained as a yellow solid, mp 200-201 °C. Yield: 53% (185 mg); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 11.25 (1H, s), 9.27 (1H, s), 8.79 (1H, s), 8.57 (1H, s), 7.96 (1H, d, $J$ = 9.0 Hz), 7.77 (1H, d, $J$ = 8.1 Hz), 7.30 (2H, t, $J$ = 7.8 Hz), 7.23-7.18 (2H, m), 1.58 (9H, s); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 196.8, 163.3, 161.6, 153.1, 153.1, 137.6, 137.2, 135.5, 131.8, 129.0, 128.5, 128.1, 127.5, 125.5, 124.2, 119.1, 113.9, 82.9, 28.1; IR (ATR) 3333, 2972, 1712, 1645, 1588, 1514, 1441, 1364, 1313, 1277, 1223, 1150, 824, 753, 631 cm$^{-1}$; HRMS *m/z* ($M^+$) calcd for $C_{21}H_{19}NO_4$: 349.1314, Found: 349.1310.

### 3-Methylbut-2-en-1-yl 5-(2-hydroxy-1-naphthoyl) nicotinate (5d)



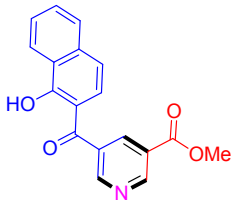
The product **5d** was obtained as a yellow solid, mp 125-127 °C. Yield: 45% (163 mg); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 11.30 (1H, s), 9.39 (1H, s), 9.90 (1H, s), 8.67 (1H, s), 8.02 (1H, d, $J$ = 9.0 Hz), 7.84 (1H, d, $J$ = 7.8 Hz), 7.37 (2H, t, $J$ = 8.1 Hz), 7.31-7.29 (2H, m), 5.50 (1H, t, $J$ = 6.8 Hz), 4.91 (2H, d, $J$ = 7.2 Hz), 1.83 (6H, d, $J$ = 8.7 Hz); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 196.7, 164.3, 161.6, 153.4, 153.2, 140.3, 137.7, 137.2, 135.6, 131.8, 129.0, 128.5, 127.6, 126.7, 125.4, 124.2, 119.1, 117.8, 113.9, 62.7, 25.8, 18.1; IR (ATR) 2920, 2596, 1716, 1656, 1509, 1441, 1348, 1283, 1215, 1093, 915, 804, 740 cm$^{-1}$; HRMS *m/z* ($M^+$) calcd for $C_{22}H_{19}NO_4$: 361.1314, Found 361.1310.

### Benzyl 5-(2-hydroxy-1-naphthoyl) nicotinate (5e)



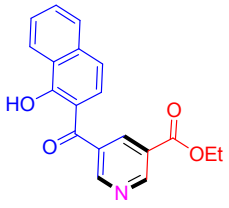
The product **5e** was obtained as a yellow solid, mp 152-154 °C. Yield: 86% (330 mg); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 11.25 (1H, s), 9.35 (1H, s), 8.86 (1H, s), 8.61 (1H, s), 7.95 (1H, d, $J$ = 9.0 Hz), 7.77 (1H, d, $J$ = 8.1 Hz), 7.38 (5H, m), 7.33-7.27 (1H, m), 7.24-7.21 (3H, m), 5.37 (2H, s); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 196.5, 164.1, 161.8, 153.6, 153.3, 137.8, 137.3, 135.6, 135.1, 131.8, 129.1, 128.7, 128.6, 128.5, 128.4, 127.6, 126.3, 125.5, 124.2, 119.1, 113.7, 67.5; IR (ATR) 2991, 2606, 1724, 1656, 1509, 1440, 1352, 1284, 1218, 1161, 1000, 802, 738 cm$^{-1}$; HRMS *m/z* ($M^+$) calcd for $C_{24}H_{17}NO_4$: 383.1158, Found: 383.1157.

**Methyl 5-(1-hydroxy-2-naphthoyl) nicotinate (6a)**



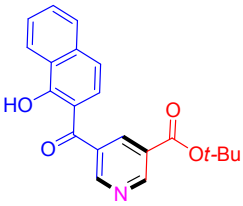
The product **6a** was obtained as a brown solid, mp 61-63 °C. Yield: 83% (255 mg); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 13.66 (1H, s), 9.38 (1H, s), 9.08 (1H, s), 8.60 (1H, s), 8.49 (1H, d, $J$ = 8.4 Hz), 7.75 (1H, d, $J$ = 8.1 Hz), 7.66 (1H, t, $J$ = 6.9 Hz), 7.55 (1H, t, $J$ = 8.1 Hz), 7.36 (1H, d, $J$ = 9.0 Hz), 7.26-7.21 (1H, m), 3.98 (3H, s); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 197.6, 164.8, 164.3, 152.8, 152.8, 137.5, 137.4, 133.6, 130.9, 127.5, 126.3, 125.9, 125.8, 125.0, 124.5, 118.7, 112.1, 52.7; IR (ATR) 2926, 1733, 1585, 1279, 1252, 808, 748 cm$^{-1}$; HRMS *m/z* ($M^+$) calcd for $C_{18}H_{13}NO_4$: 307.0845, Found: 307.0843.

**Ethyl 5-(1-hydroxy-2-naphthoyl) nicotinate (6b)**



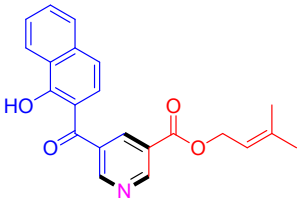
The product **6b** was obtained as a yellow solid, mp 79-81 °C. Yield: 87% (279 mg); $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 13.64 (1H, s), 9.36 (1H, s), 9.04 (1H, s), 8.57 (1H, s), 8.47 (1H, d, $J$ = 8.4 Hz), 7.73 (1H, d, $J$ = 8.4 Hz), 7.64 (1H, t, $J$ = 7.2 Hz), 7.53 (1H, t, $J$ = 7.8 Hz), 7.34 (1H, d, $J$ = 9.6 Hz), 7.21 (1H, d, $J$ = 9.0 Hz), 4.41 (2H, q, $J$ = 7.2 Hz), 1.38 (3H, t, $J$ = 7.2 Hz); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 197.8, 164.4, 164.4, 152.8, 152.7, 137.6, 137.3, 133.7, 131.0, 127.5, 126.4, 126.2, 126.0, 125.1, 124.6, 118.8, 112.2, 61.9, 14.2; IR (ATR) 2986, 1730, 1588, 1275, 1247, 1186, 1018, 811, 744 cm$^{-1}$; HRMS *m/z* ($M^+$) calcd for $C_{19}H_{15}O_4$: 321.1001, Found: 321.1002.

***tert*-Butyl 5-(1-hydroxy-2-naphthoyl) nicotinate (6c)**



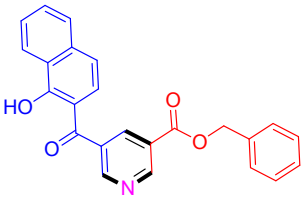
The product **6c** was obtained as a yellow solid, mp 169-170 °C. Yield: 49% (171 mg); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 13.70 (1H, s), 9.33 (1H, s), 9.04 (1H, s), 8.56 (1H, s), 8.51 (1H, d, $J$ = 8.1 Hz), 7.77 (1H, d, $J$ = 8.1 Hz), 7.67 (1H, t, $J$ = 6.9 Hz), 7.56 (1H, t, $J$ = 8.1 Hz), 7.39 (1H, d, $J$ = 9.0 Hz), 7.25 (1H, d, $J$ = 8.4 Hz), 1.61 (9H, s); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 197.9, 164.4, 163.3, 152.6, 152.2, 137.6, 137.4, 133.7, 131.0, 127.7, 127.6, 126.4, 126.1, 125.2, 124.6, 118.8, 112.3, 82.9, 28.1; IR (ATR) 2978, 1718, 598, 1345, 1275, 1249, 1163, 818, 755 cm$^{-1}$; HRMS *m/z* ($M^+$) calcd for $C_{21}H_{19}NO_4$: 349.1314, Found: 349.1316.

**3-Methylbut-2-en-1-yl 5-(1-hydroxy-2-naphthoyl) nicotinate (6d)**



The product **6d** was obtained as a yellow solid, mp 119-121 °C. Yield: 48% (173 mg); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 13.68 (1H, s), 9.41 (1H, s), 9.09 (1H, s), 8.63 (1H, s), 8.52 (1H, d, $J$ = 8.1 Hz), 7.78 (1H, d, $J$ = 8.1 Hz), 7.58 (1H, t, $J$ = 6.9 Hz), 7.57 (1H, t, $J$ = 8.1 Hz), 7.38 (1H, d, $J$ = 8.7 Hz), 7.26 (1H, d, $J$ = 7.8 Hz), 7.47 (1H, t, $J$ = 6.0 Hz), 4.88 (2H, d, $J$ = 7.2 Hz), 1.79 (6H, s); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 197.7, 197.7, 164.5, 164.3, 152.6, 152.4, 140.4, 137.6, 133.8, 131.0, 127.6, 126.4, 126.0, 125.2, 124.6, 118.8, 117.9, 112.2, 62.8, 25.8, 18.1; IR (ATR) 3057, 2977, 2909, 1726, 1567, 1456, 1389, 1332, 1279, 1254, 1196, 1026, 937, 812, 748 cm$^{-1}$; HRMS *m/z* ($M^+$) calcd for $C_{22}H_{19}NO_4$: 361.1314, Found 361.1313.

**Benzyl 5-(1-hydroxy-2-naphthoyl) nicotinate (6e)**



The product **6e** was obtained as a yellow solid, mp 126-127 °C. Yield: 78% (299 mg); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 13.67 (1H, s), 9.42 (1H, s), 9.08 (1H, s), 8.63 (1H, s), 8.51 (1H, d, $J$ = 8.1 Hz), 7.76 (1H, d, $J$ = 8.1 Hz), 7.67 (1H, t, $J$ = 6.9 Hz), 7.56 (1H, t, $J$ = 7.8 Hz), 7.46-7.35 (6H, m), 7.24 (1H, d, $J$ = 8.7 Hz), 5.38 (2H, s); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 197.6, 164.4, 164.2, 152.8, 137.6, 135.1, 133.7, 131.0, 128.7, 128.7, 128.5, 127.5, 126.4, 126.0, 125.1, 124.6, 118.8, 112.2, 67.6; IR (ATR) 3061, 1724, 1567, 1459, 1388,

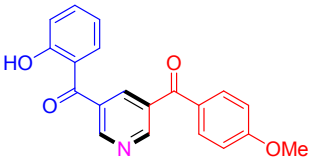
1279, 1253, 1200, 1024, 798, 736, 693 $cm^{-1}$; HRMS *m/z* ($M^+$) calcd for $C_{24}H_{17}NO_4$: 383.1158, Found: 383.1159.

**General procedure for the synthesis of functionalized pyridines 8**

To a magnetically stirred solution of 3-formyl-4*H*-chromen-4-one (**1a**), (174 mg, 1.0 mmol) in 1,2-DCE (5 mL), β-enamino ketones (**7a**–**7b**, 1.0 mmol) or (*E*)-3-(dimethylamino)acrylonitrile (**7c**), (96 mg, 1.0 mmol), and ammonium acetate **3** (231 mg, 3.0 equiv.) were added. This was followed by the addition of $Cu(OTf)_2$ (10 mol%) to the solution, which was mixed well. The reaction mixture was refluxed for 7 h. The reaction was monitored using a TLC (hexane/ethyl acetate = 6:1) until it was complete. Then, the reaction mixture was subjected to flash column chromatography using hexane/ethyl acetate (20:1) as the solvent system.

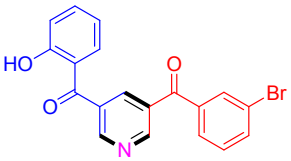
**Characterization data of compounds 8**

**(5-(2-Hydroxybenzoyl)pyridin-3-yl)(4-methoxyphenyl)methanone (8a)**



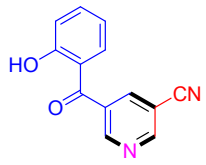

The product **8a** was obtained as a bright yellow orange liquid. Yield: 83% (276 mg); $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 11.70 (1H, s), 9.07 (1H, s), 9.01 (1H, s), 8.28 (1H, t, $J$ = 1.8 Hz), 7.79 (2H, d, $J$ = 9.0 Hz), 7.52-7.49 (2H, m), 7.04 (1H, d, $J$ = 8.4 Hz), 6.95 (2H, d, $J$ = 9.0 Hz), 6.88 (1H, t, $J$ = 7.2 Hz), 3.85 (3H, s); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 198.3, 192.0, 164.0, 163.2, 152.5, 151.6, 137.2, 137.1, 133.5, 133.2, 132.8, 132.4, 128.7, 119.2, 118.7, 118.6, 114.0, 55.5; IR (ATR) 3051, 2841, 1624, 1593, 1243, 1166, 1024, 911, 842, 756, 714, 645, 605 $cm^{-1}$; HRMS *m/z* ($M^+$) calcd for $C_{20}H_{15}NO_4$: 333.1001, Found: 333.1000.

**(5-(3-Bromobenzoyl)pyridin-3-yl)(2-hydroxyphenyl)methanone (8b)**




The product **8b** was obtained as a light yellow liquid. Yield: 77% (293 mg); $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 11.68 (1H, s), 9.14 (1H, s), 9.09 (1H, s), 8.36 (1H, t, $J$ = 2.4 Hz), 7.97 (1H, t, $J$ = 1.8 Hz), 7.77 (1H, d, $J$ = 7.8 Hz), 7.72 (1H, d, $J$ = 7.2 Hz), 7.56 (1H, d, $J$ = 7.8 Hz), 7.50 (1H, dd, $J$ = 7.8, 1.8 Hz), 7.41 (1H, d, $J$ = 7.8 Hz), 7.10 (1H, d, $J$ = 8.4 Hz), 6.94 (1H, d, $J$ = 7.8 Hz); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 197.9, 192.1, 163.4, 160.5, 156.8, 152.5, 152.3, 137.8, 137.6, 137.5, 136.5, 132.7, 132.7, 130.4, 128.5, 123.2, 119.4, 119.0, 118.6; IR (ATR) 3056, 2921, 1659, 1623, 1567, 1237, 1001, 911, 714, 668 $cm^{-1}$; HRMS *m/z* ($M^+$) calcd for $C_{19}H_{12}BrNO_3$: 381.0001, Found: 380.9999.

**5-(2-Hydroxybenzoyl)nicotinonitrile (8c)**



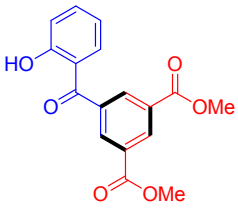

The product **8c** was obtained as a yellow solid, mp 107-109 °C. Yield: 78% (175 mg); $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 11.54 (1H, s), 9.06 (1H, d, $J$ = 1.8 Hz), 9.04 (1H, d, $J$ = 1.8 Hz), 8.24 (1H, t, $J$ = 1.8 Hz), 7.57 (1H, t, $J$ = 7.8 Hz), 7.41 (1H, dd, $J$ = 8.4, 1.8 Hz), 7.09 (1H, dd, $J$ = 8.4, 1.2 Hz), 6.93 (1H, dd, $J$ = 7.2, 1.2 Hz); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 196.6, 163.4, 154.4, 152.4, 139.5, 137.8, 133.5, 132.5, 119.5, 119.1, 118.3, 115.5, 110.2; IR (ATR) 3062, 2236, 1618, 1483, 1449, 1417, 1037, 1251, 1186, 688 $cm^{-1}$; HRMS *m/z* ($M^+$) calcd for $C_{13}H_8N_2O_2$: 224.0586, Found: 224.0583.

**General procedure for the synthesis of 9**

To a magnetically stirred solution of 3-formyl-4*H*-chromen-4-one (**1a**, 1.0 mmol) in 1,2-DCE (5 mL), methyl (*E*)-3-(dimethylamino)acrylate (**2a**, 1.0 mmol) was added. This was followed by the addition of $Cu(OTf)_2$ (10 mol%) to the solution, which was mixed well. The reaction mixture was refluxed for 7 h. The reaction was monitored using a TLC (hexane/ethyl acetate = 6:1) until it was complete. Then, the reaction mixture was subjected to flash column chromatography using hexane/ethyl acetate (20:1) as the solvent system.

**Characterization data of compound 9**

**Dimethyl 5-(2-hydroxybenzoyl)isophthalate (9)**




The product **9** was obtained as a yellow solid, mp 99-101 °C. Yield: 45% (141 mg); $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 11.79 (1H, s), 8.85 (1H, t, $J$ = 1.2 Hz), 8.48 (1H, s), 8.47 (1H, s), 7.53 (1H, t, $J$ = 8.4 Hz), 7.46 (1H, dd, $J$ = 8.4, 1.8 Hz), 7.08 (1H, dd, $J$ = 8.4, 1.2 Hz), 6.88 (1H, d, $J$ = 7.8 Hz), 3.96 (6H, s); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 199.5, 165.3, 163.4, 138.6, 137.0, 133.8, 133.4, 133.0, 131.1, 119.1, 118.7, ,118.6, 52.7; IR (ATR) 2922, 2852, 1716, 1629, 1442, 1294, 1235, 1167, 746 cm$^{-1}$; HRMS *m/z* ($M^+$) calcd for $C_{17}H_{14}O_6$: 314.0790, Found: 314.0792.

**General procedure for the synthesis of 12**

To a magnetically stirred solution of 3-formyl-4*H*-chromen-4-one (**1a**) (174 mg, 1.0 mmol) in 1,2-DCE (5 mL), methyl (*E*)-3-(dimethylamino)acrylate (**2a**) (143mg, 1.0 mmol) and aniline hydrochloride (**11)** (130 mg, 1.0 equiv.) were added. This was followed by the addition of $Cu(OTf)_2$ (10 mol%) to the solution, which was mixed well. The reaction mixture was refluxed for 7 h. The reaction was monitored using a TLC (hexane/ethyl acetate = 6:1) until it was complete. Then, the reaction mixture was subjected to flash column chromatography using hexane/ethyl acetate (20:1) as the solvent system. Compound **12** was isolated in 58 mg.

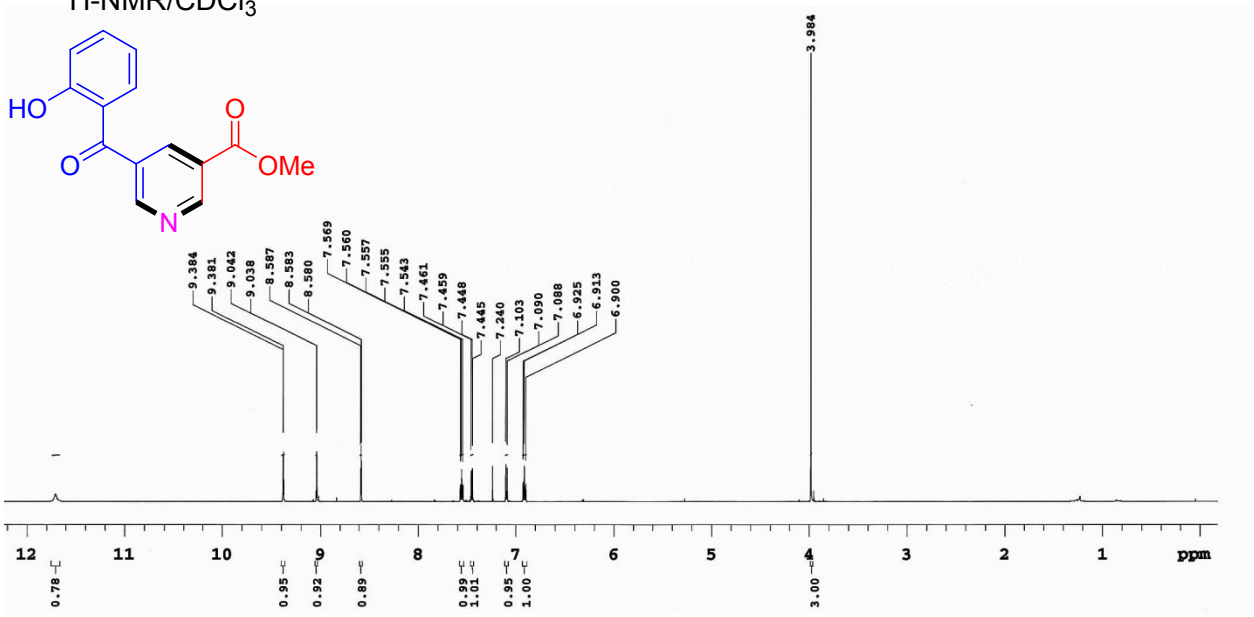
**General procedure for the synthesis of 13**

To a magnetically stirred solution of 6-chloro-4-oxo-4*H*-chromene-3-carbaldehyde (**1f**), (208 mg, 1.0 mmol) in 1,2-DCE (5 mL), ammonium acetate **3** (231 mg, 3.0 equiv.) was added. This was followed by the addition of $Cu(OTf)_2$ (10 mol%) to the solution, which was mixed well. The reaction mixture was kept at room temperature for 12 h. The reaction was monitored using a TLC (hexane/ethyl acetate = 1:1) until it was complete. Then, the reaction mixture was subjected to flash column chromatography using hexane/ethyl acetate (2:1) as the solvent system to isolate compound **13** in 102 mg.

## $^{1}$H NMR and $^{13}$C NMR Spectra of compounds 4- 6, 8- 9, 12 and 13☐

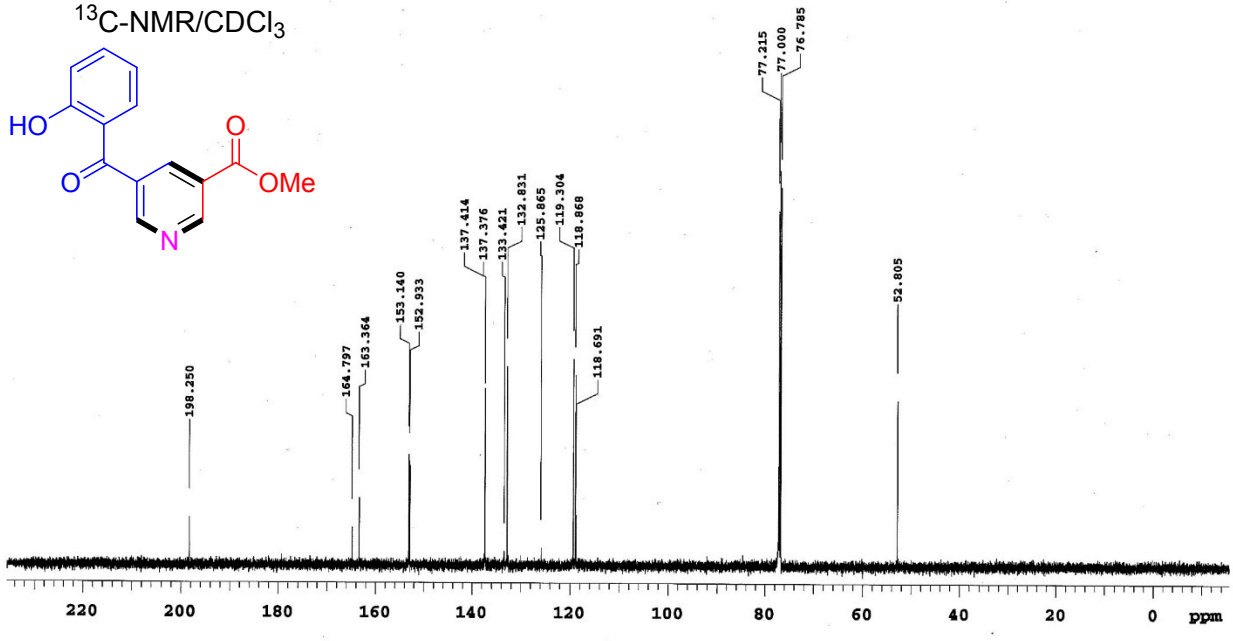
Compound-**4a**

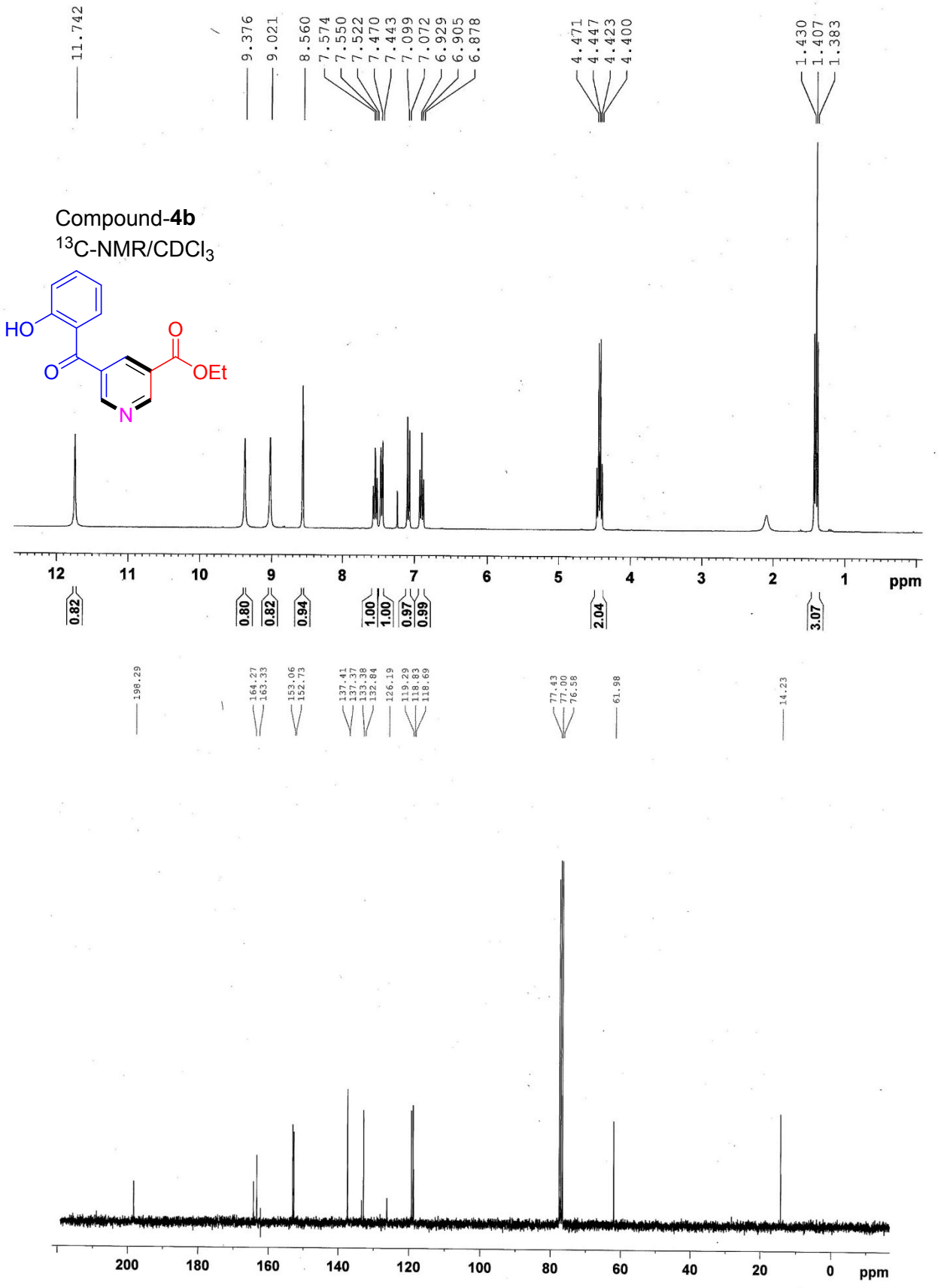
$^{1}$H-NMR/$CDCl_3$




Compound-**4a**

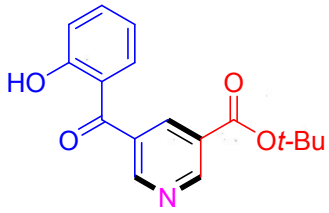
$^{13}$C-NMR/$CDCl_3$




Compound-4b
13C-NMR/CDCl3
HO
O
O
OEt
N
11.742
9.376
9.021
8.560
7.574
7.550
7.522
7.470
7.443
7.099
7.072
6.929
6.905
6.878
4.471
4.447
4.423
4.400
1.430
1.407
1.383
ppm
0.82
0.80
0.82
0.94
1.00
1.00
0.97
0.99
2.04
3.07
198.29
164.27
163.33
153.06
152.73
137.41
137.37
133.38
132.84
126.19
119.29
118.83
118.69
77.43
77.00
76.58
61.98
14.23
ppm

Compound-**4c**

$^{1}$H-NMR/$CDCl_3$

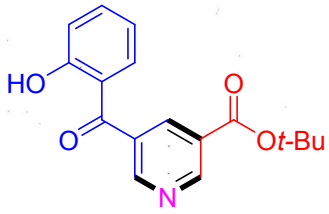


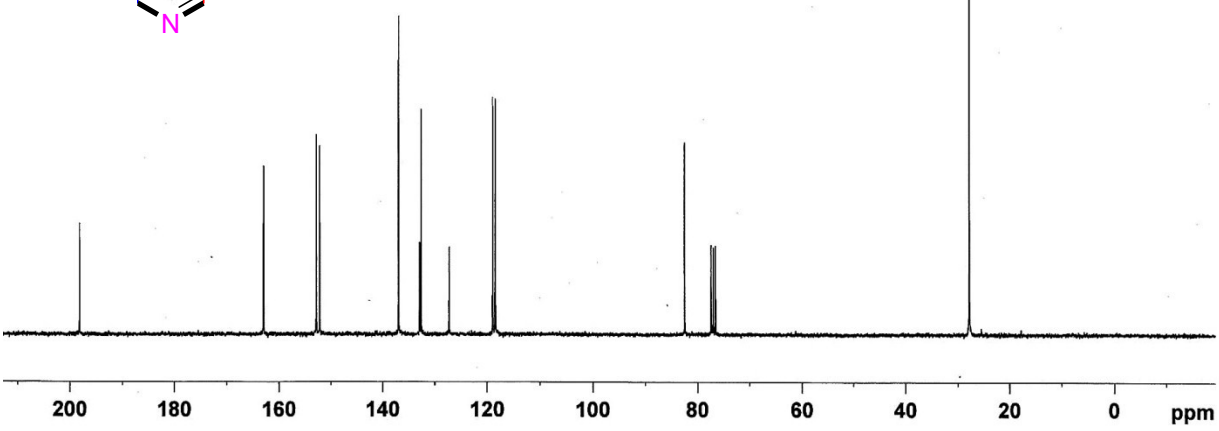





Compound-**4c**

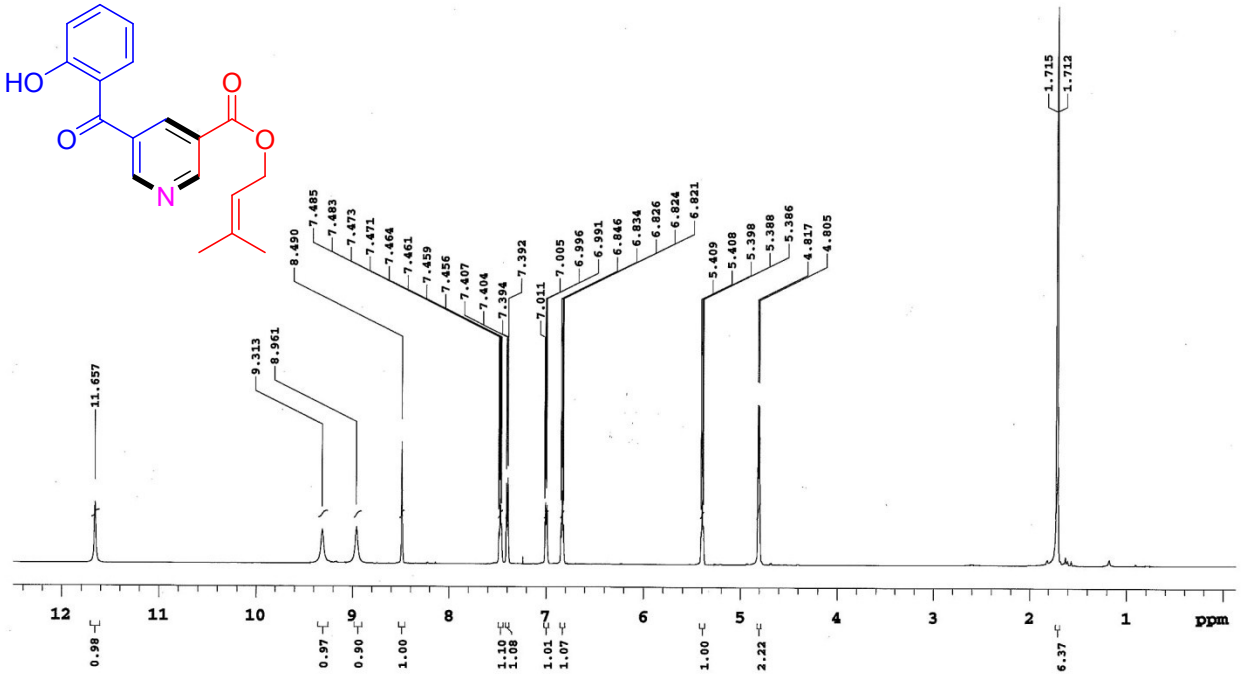
$^{13}$C-NMR/$CDCl_3$



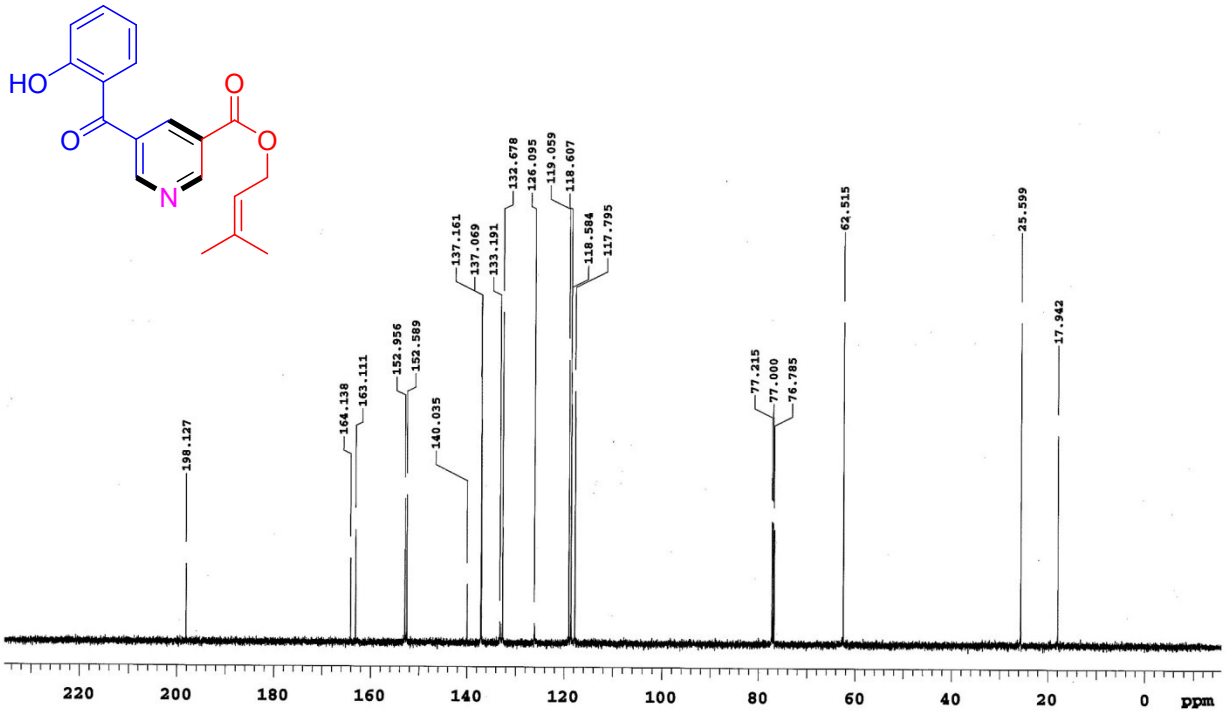
Compound-**4d**

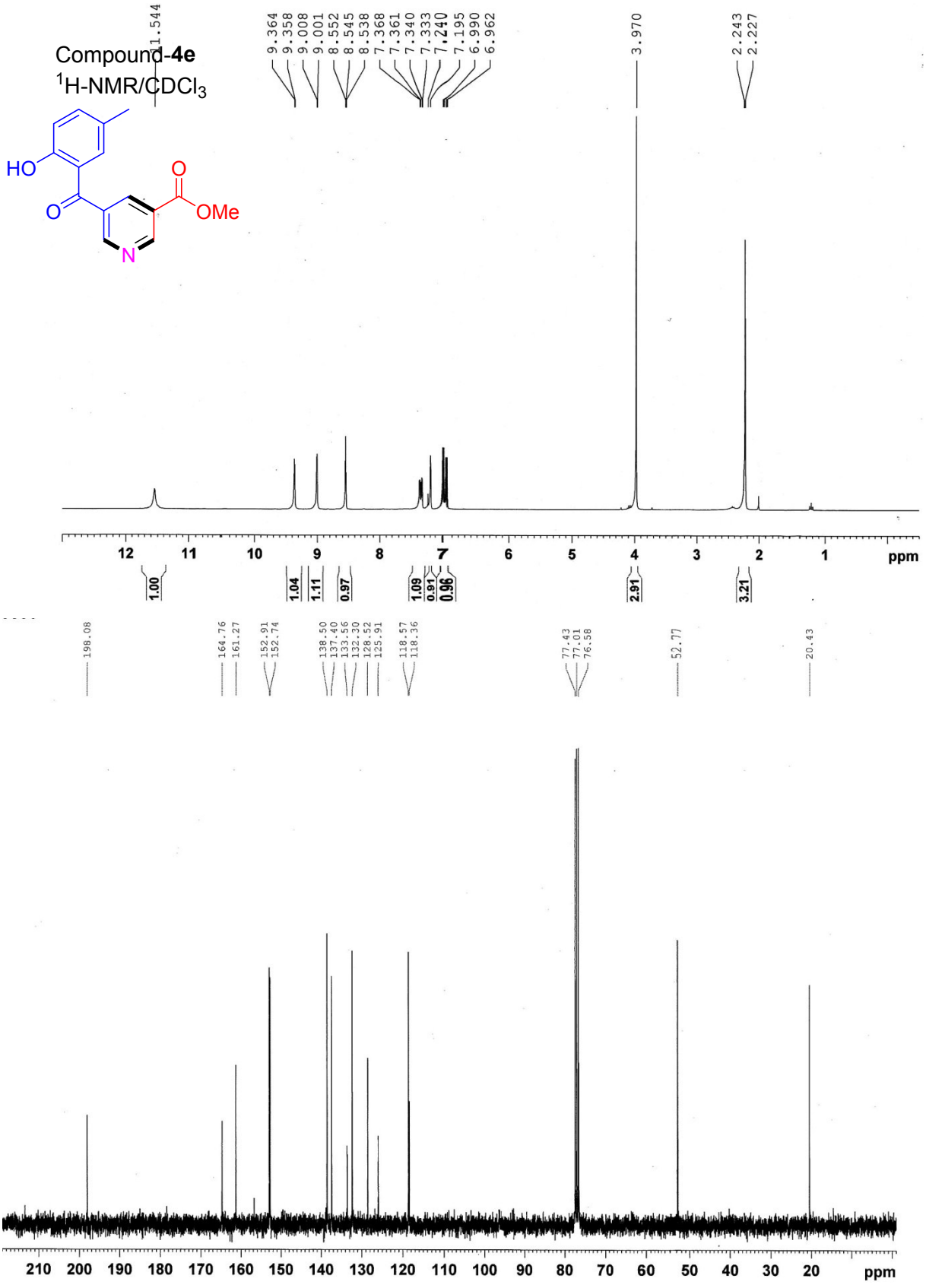
$^{1}$H-NMR/$CDCl_3$




Compound-**4d**

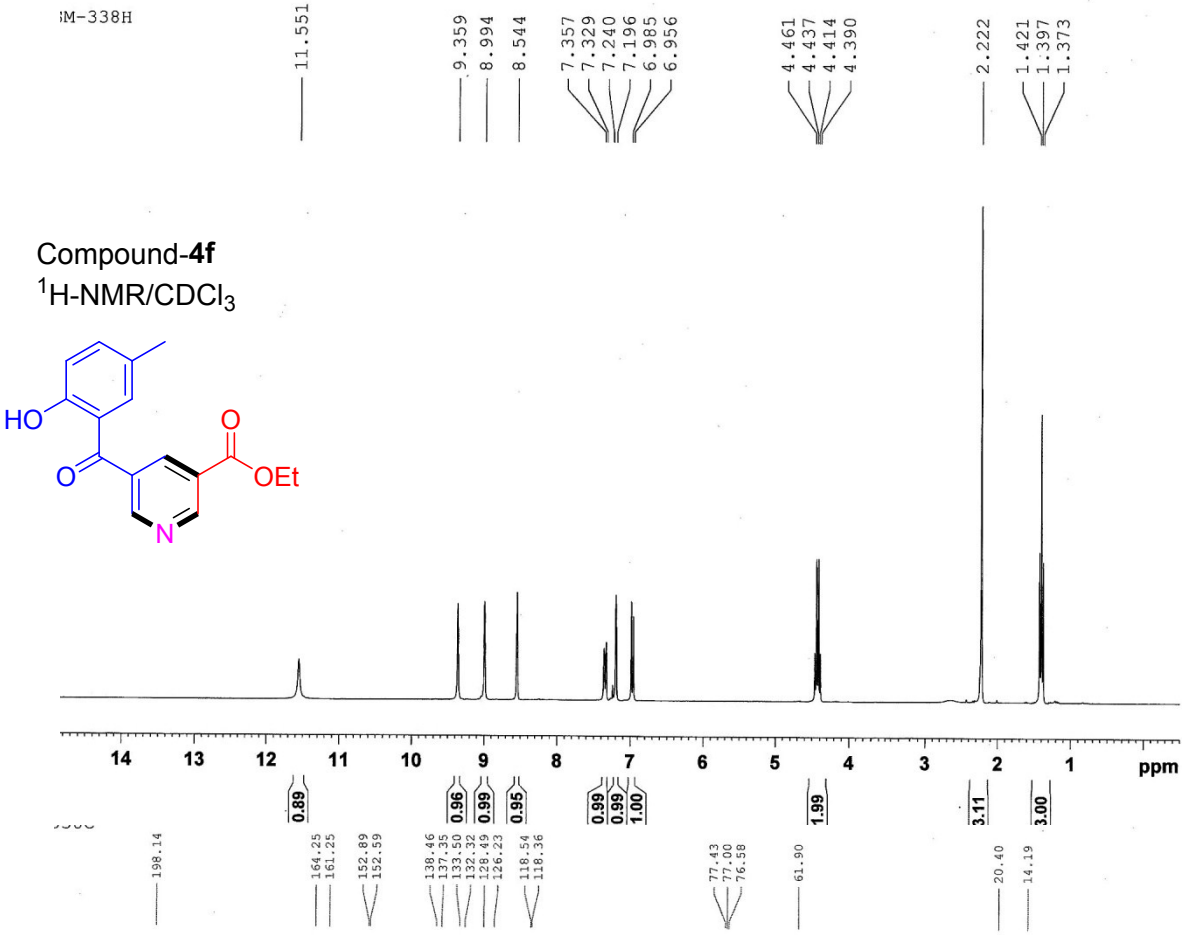
$^{13}$C-NMR/$CDCl_3$




Compound-4e
1H-NMR/CDCl3
HO
O
O
OMe
N
11.544
9.364
9.358
9.008
9.001
8.552
8.545
8.538
7.368
7.361
7.340
7.333
7.240
7.195
6.990
6.962
3.970
2.243
2.227
ppm
198.08
164.76
161.27
152.91
152.74
138.50
137.40
133.56
132.30
128.52
125.91
118.57
118.36
77.43
77.01
76.58
52.77
20.43
ppm

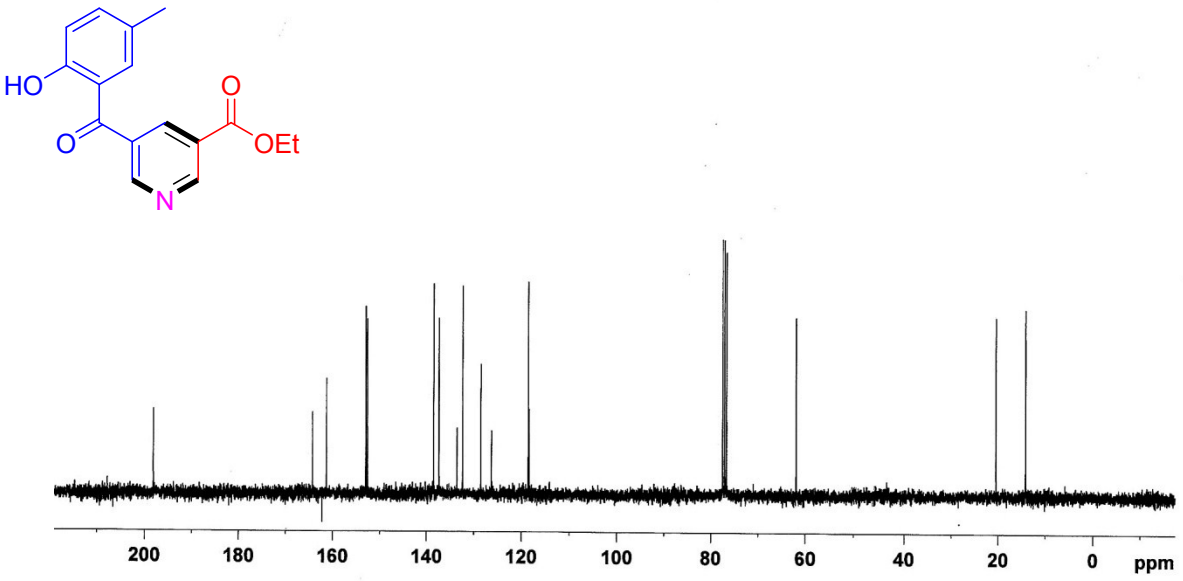
Compound-**4f**

$^{1}$H-NMR/$CDCl_3$



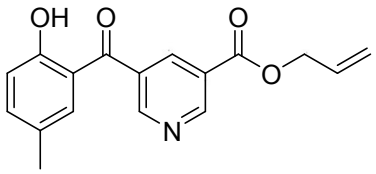

Compound-**4f**

$^{13}$C-NMR/$CDCl_3$



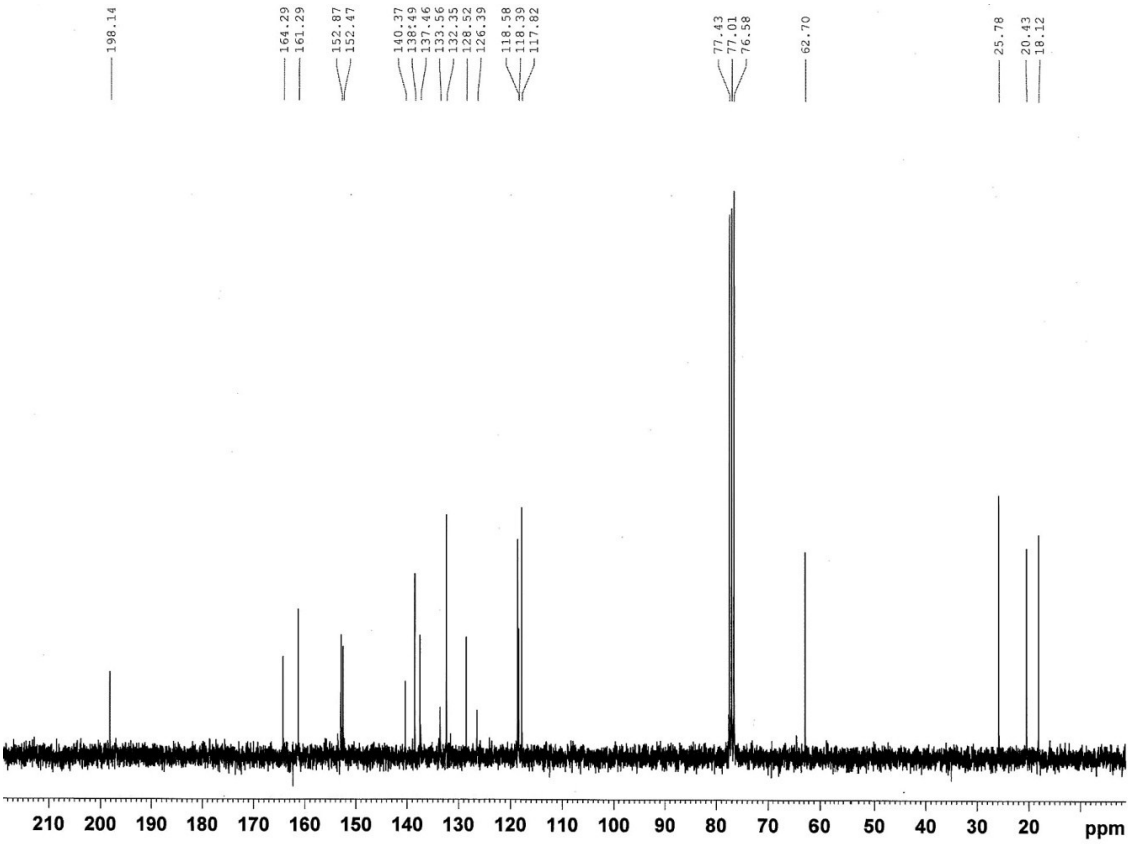
Compound-**4g**

$^1$H-NMR/$CDCl_3$



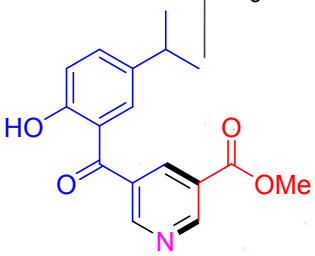






Compound-**4h**

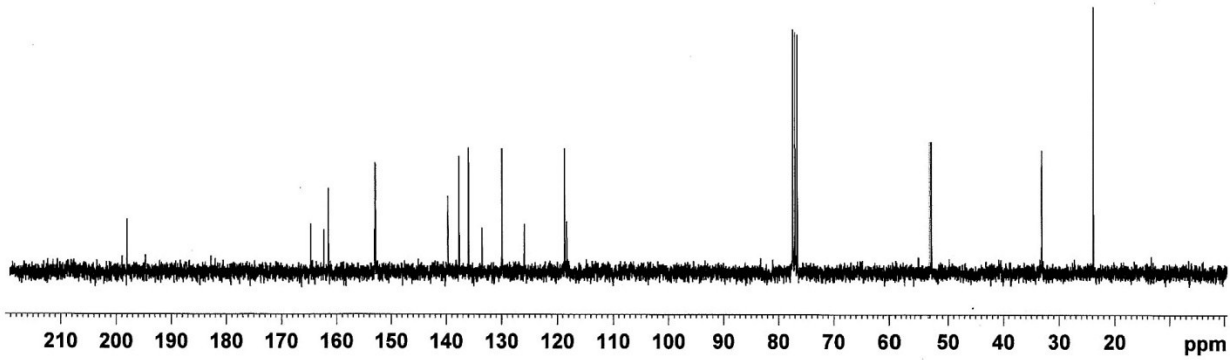
$^{13}$C-NMR/$CDCl_3$

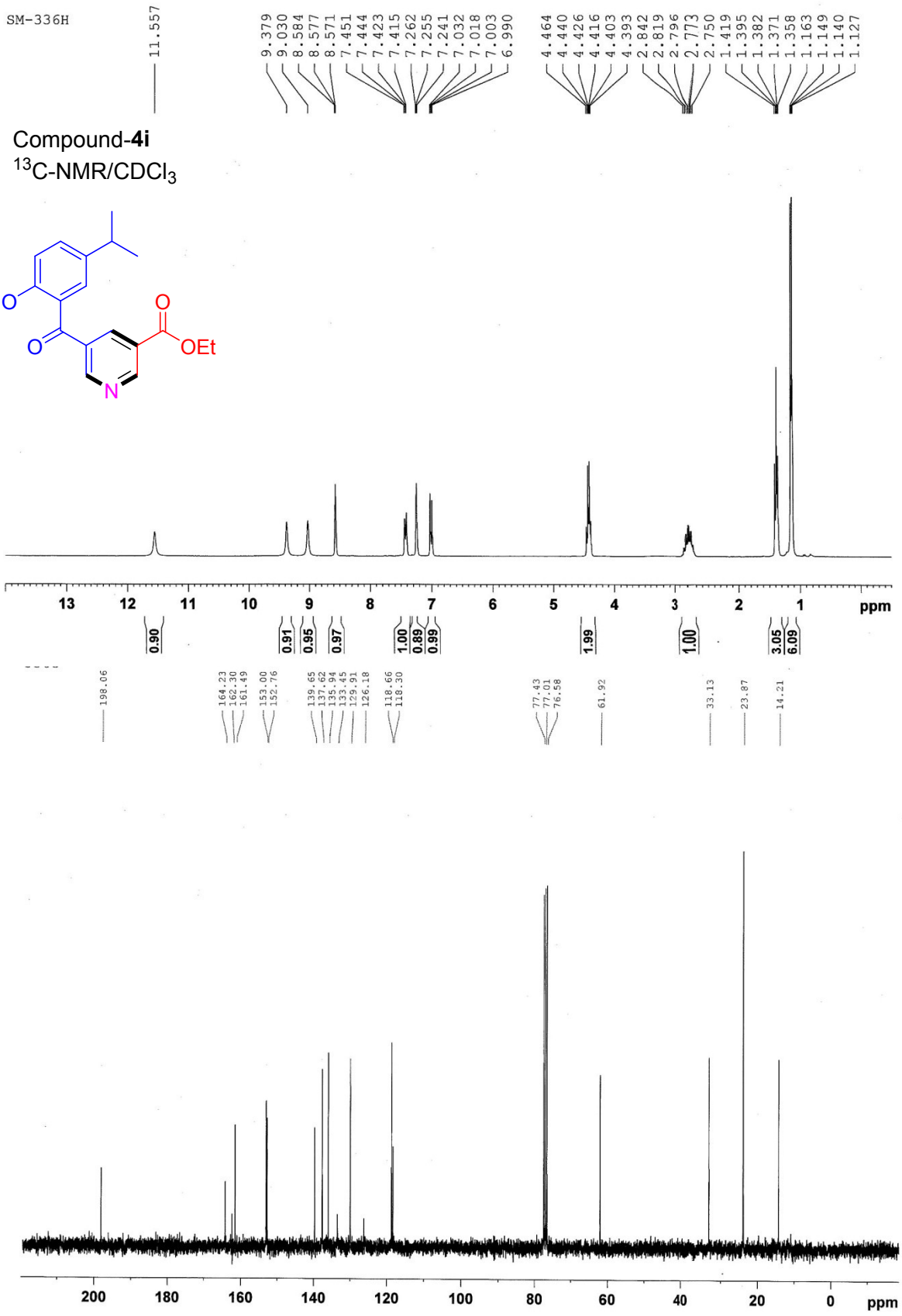


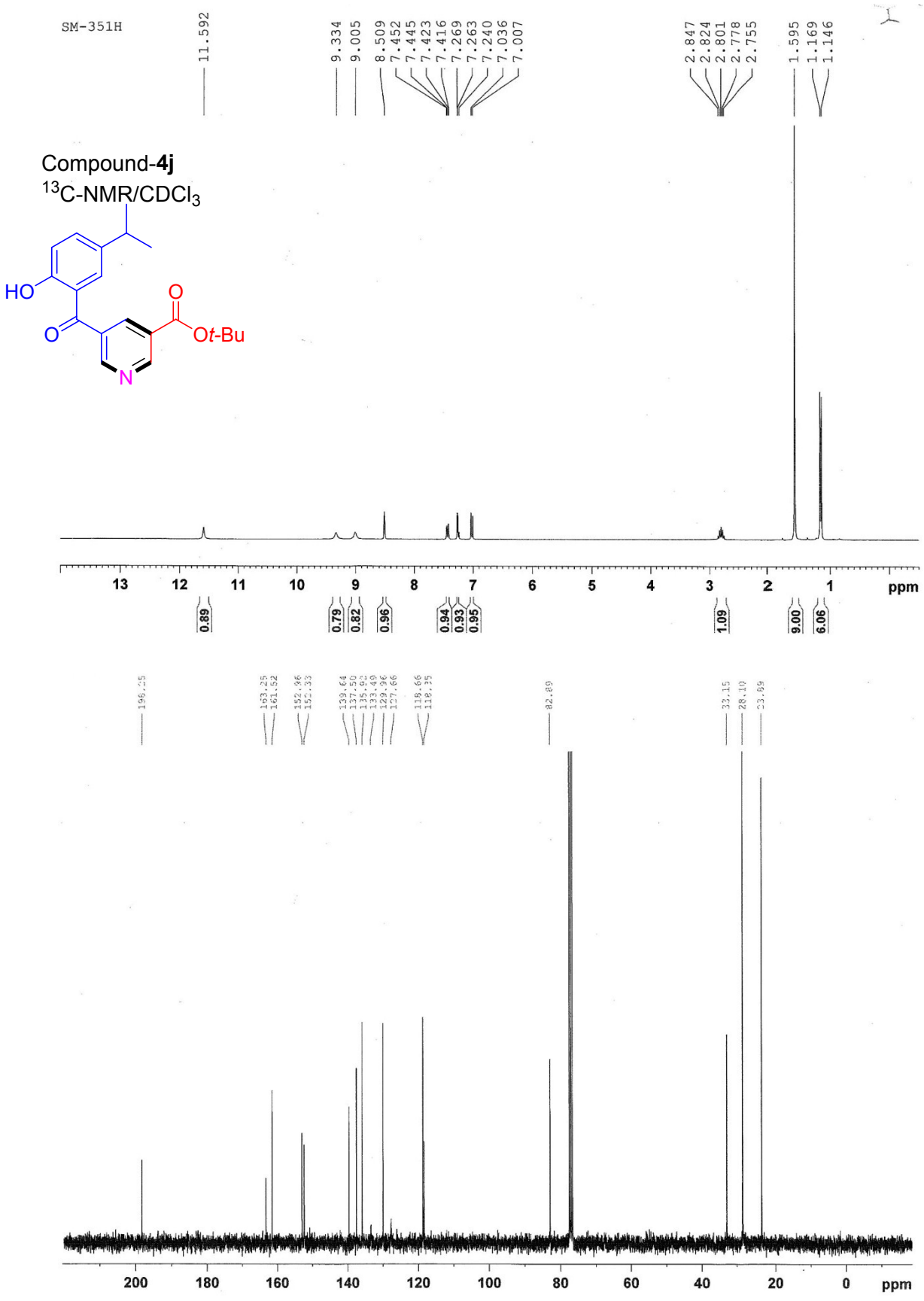


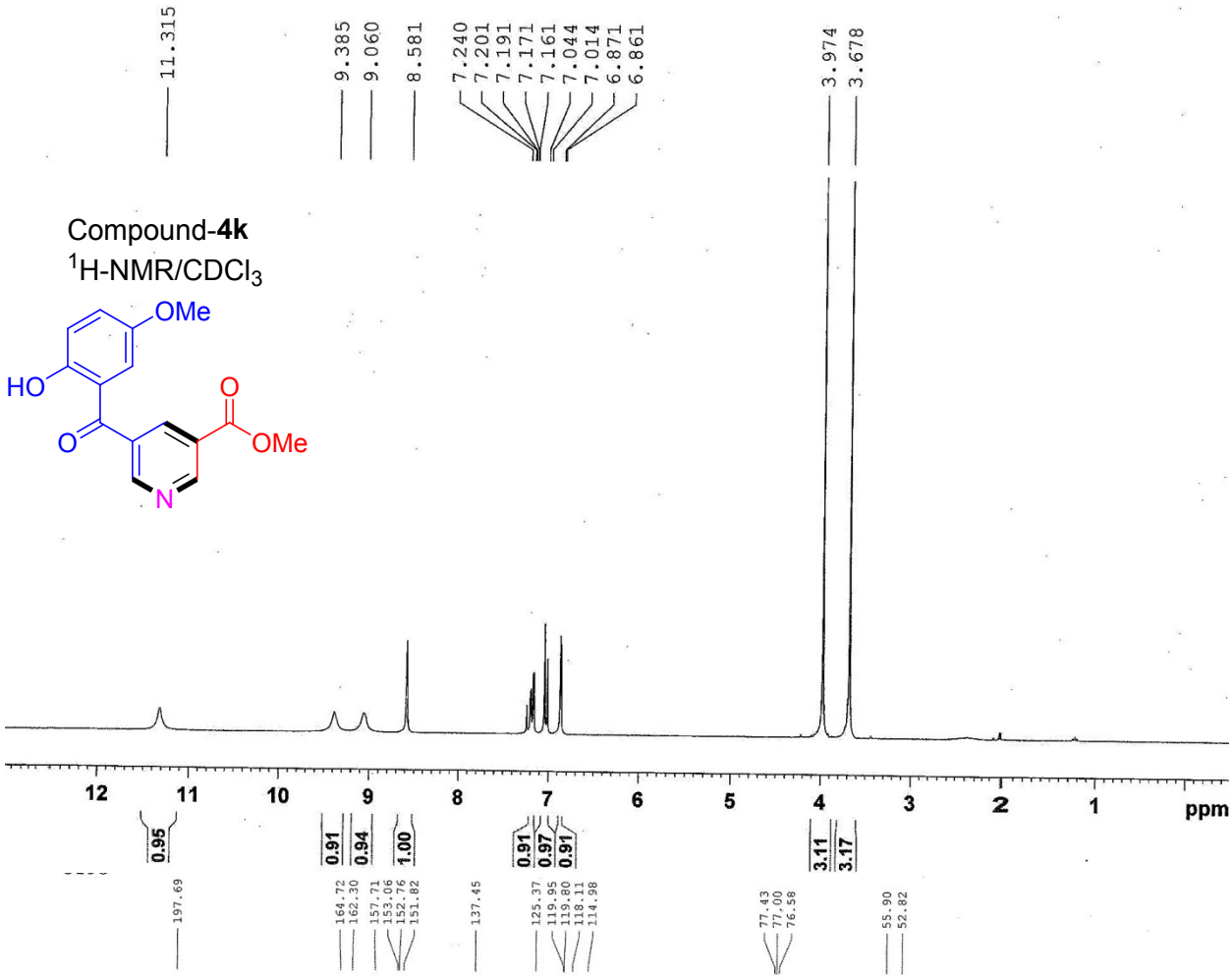


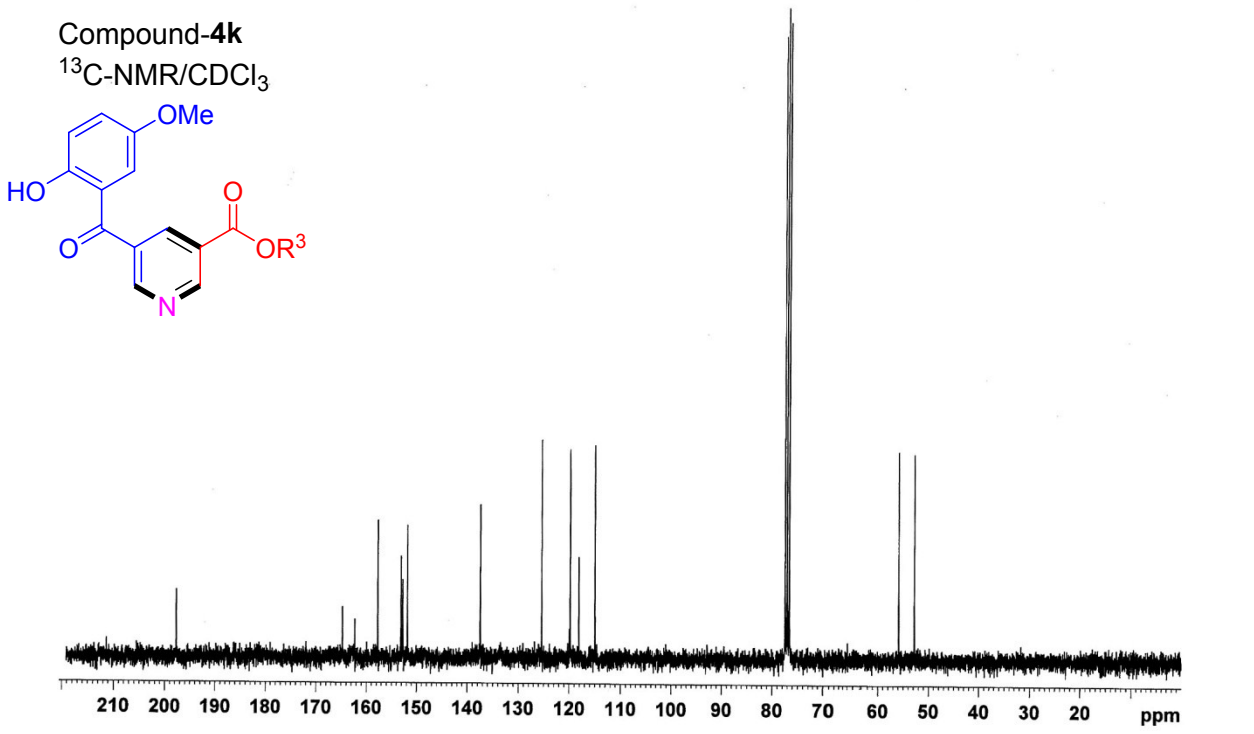



SM-336H
11.557
9.379
9.030
8.584
8.577
8.571
7.451
7.444
7.423
7.415
7.262
7.255
7.241
7.032
7.018
7.003
6.990
4.464
4.440
4.426
4.416
4.403
4.393
2.842
2.819
2.796
2.773
2.750
1.419
1.395
1.382
1.371
1.358
1.163
1.149
1.140
1.127
Compound-4i
13C-NMR/CDCl3
HO
O
O
OEt
N
ppm
0.90
0.91
0.95
0.97
1.00
0.89
0.99
1.99
1.00
3.05
6.09
198.06
164.23
162.30
161.49
153.00
152.76
139.65
137.62
135.94
133.45
129.91
126.18
118.66
118.30
77.43
77.01
76.58
61.92
33.13
23.87
14.21
ppm

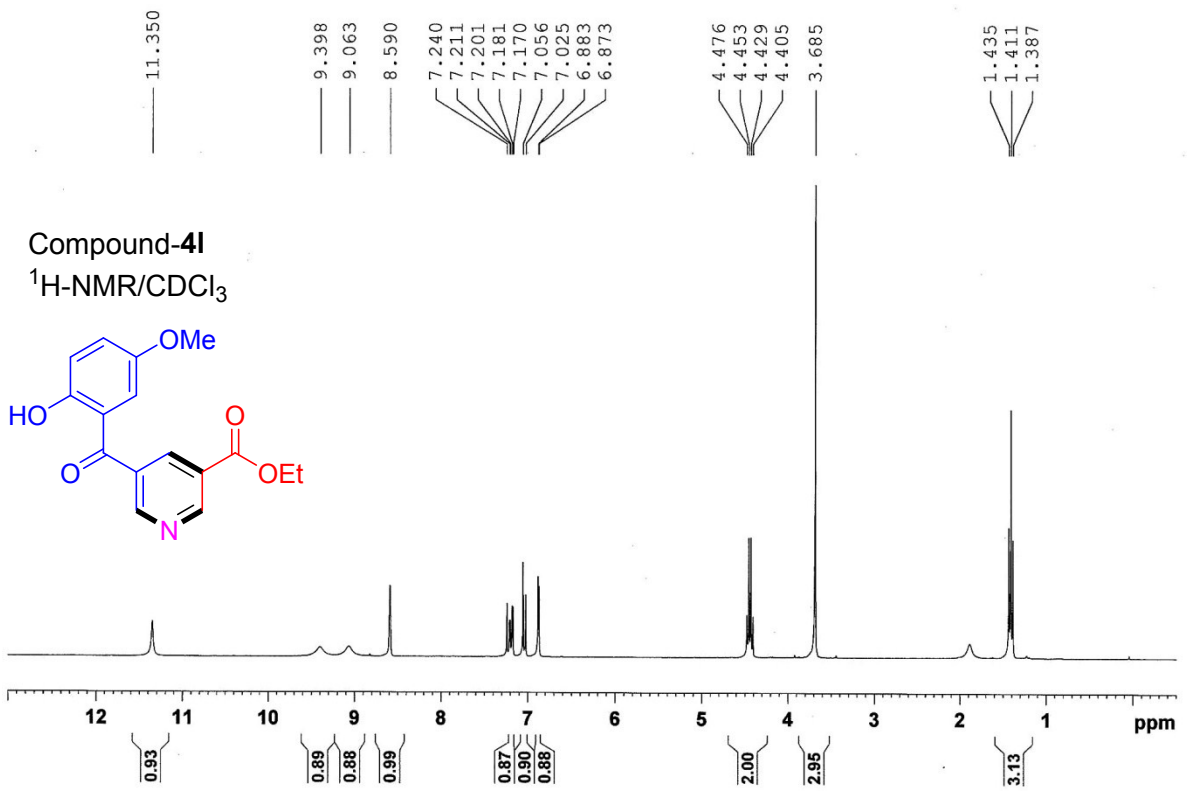

SM-351H
Compound-4j
13C-NMR/CDCl3
HO
O
O
Ot-Bu
N
ppm


11.315
9.385
9.060
8.581
7.240
7.201
7.191
7.171
7.161
7.044
7.014
6.871
6.861
3.974
3.678
Compound-4k
1H-NMR/CDCl3
OMe
HO
O
O
OMe
N
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.95
0.91
0.94
1.00
0.91
0.97
0.91
3.11
3.17


197.69
164.72
162.30
157.71
153.06
152.76
151.82
137.45
125.37
119.95
119.80
118.11
114.98
77.43
77.00
76.58
55.90
52.82
Compound-4k
13C-NMR/CDCl3
OMe
HO
O
O
OR3
N
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

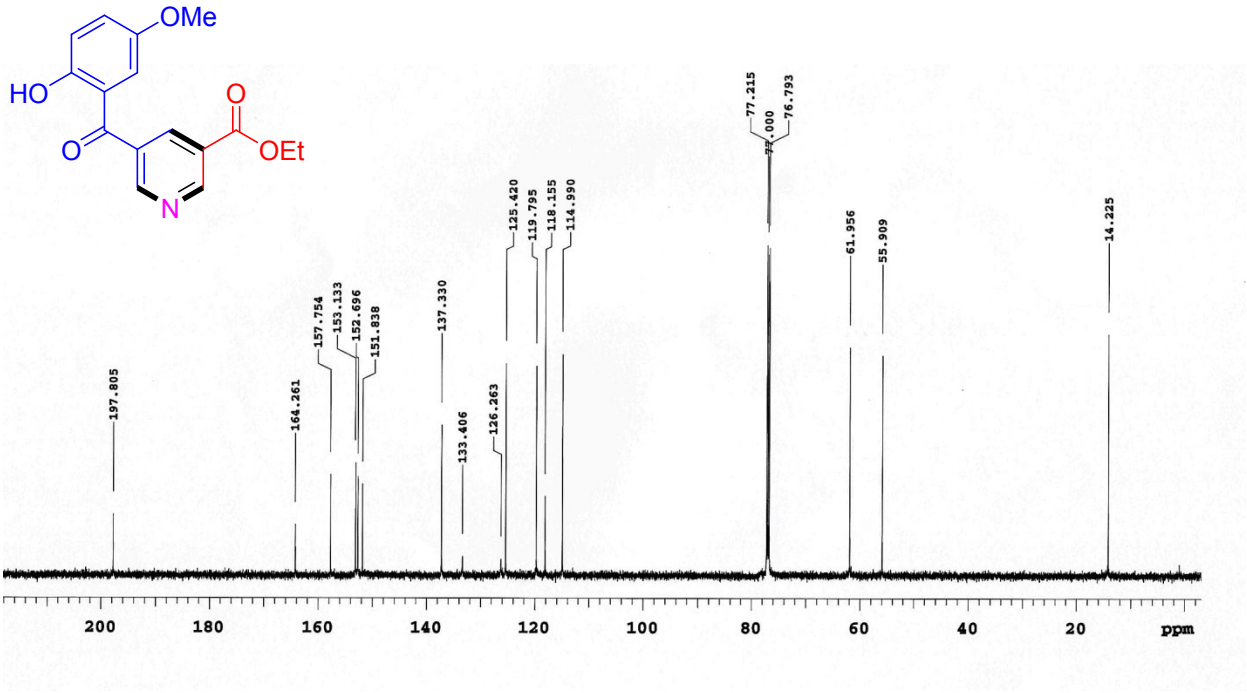
Compound-**4l**

$^{1}$H-NMR/$CDCl_3$



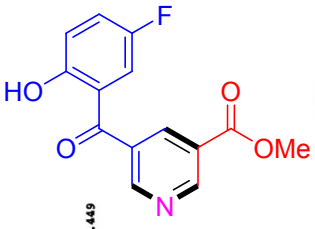

Compound-**4l**

$^{13}$C-NMR/$CDCl_3$



Compound-**4m**

$^{1}$H-NMR/$CDCl_3$

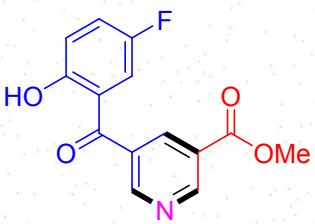






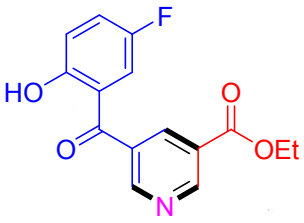
Compound-**4m**

$^{13}$C-NMR/$CDCl_3$



Compound-**4n**

$^{1}$H-NMR/$CDCl_3$

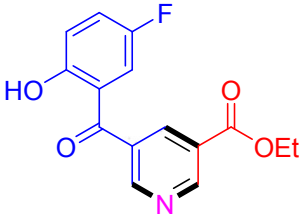






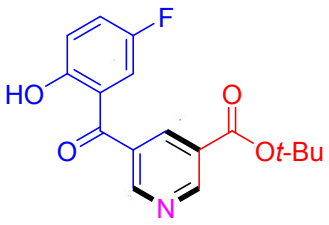
Compound-**4n**

$^{13}$C-NMR/$CDCl_3$



Compound-**4o**

$^{1}$H-NMR/$CDCl_3$

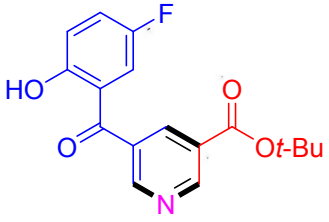


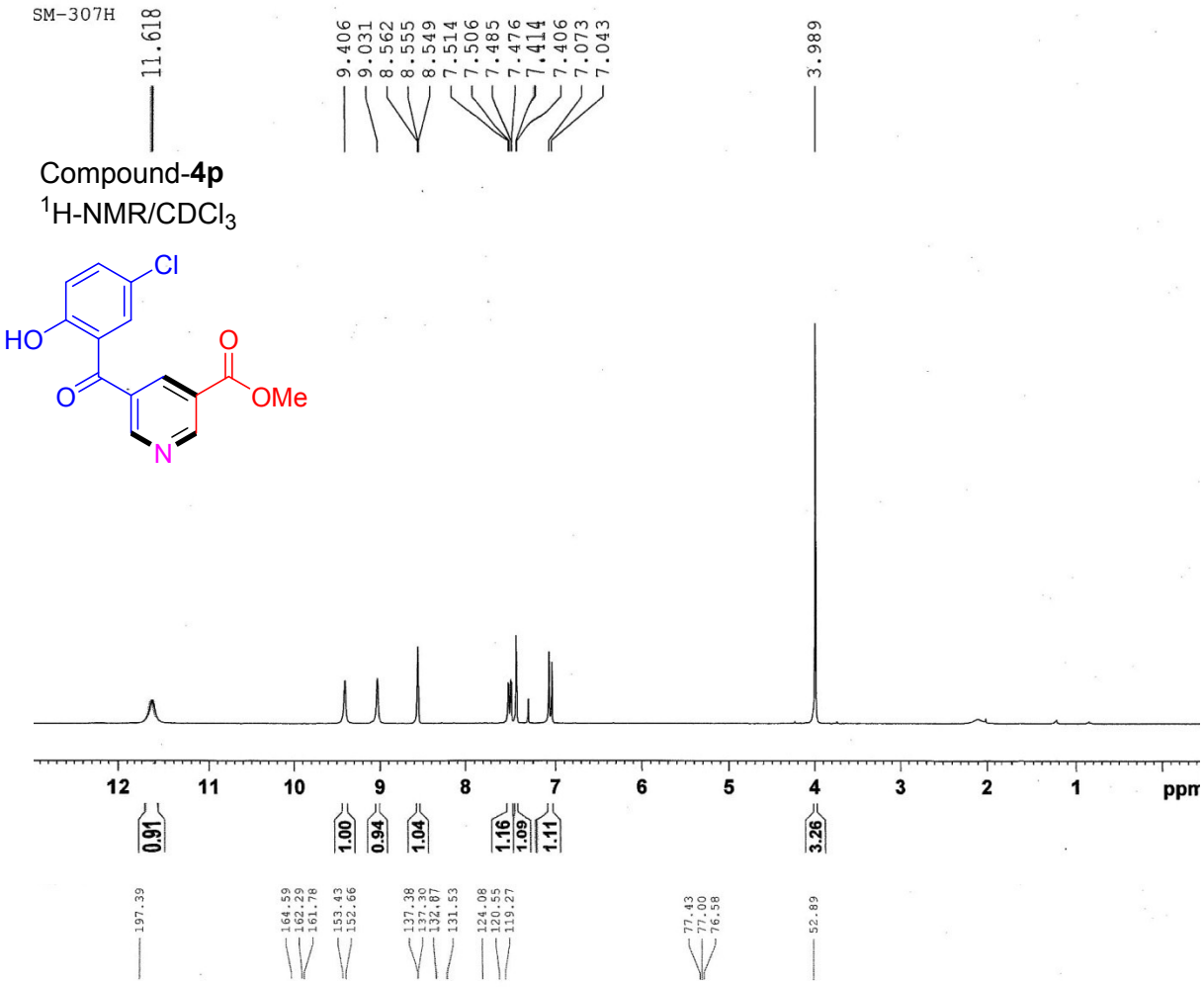




Compound-**4o**

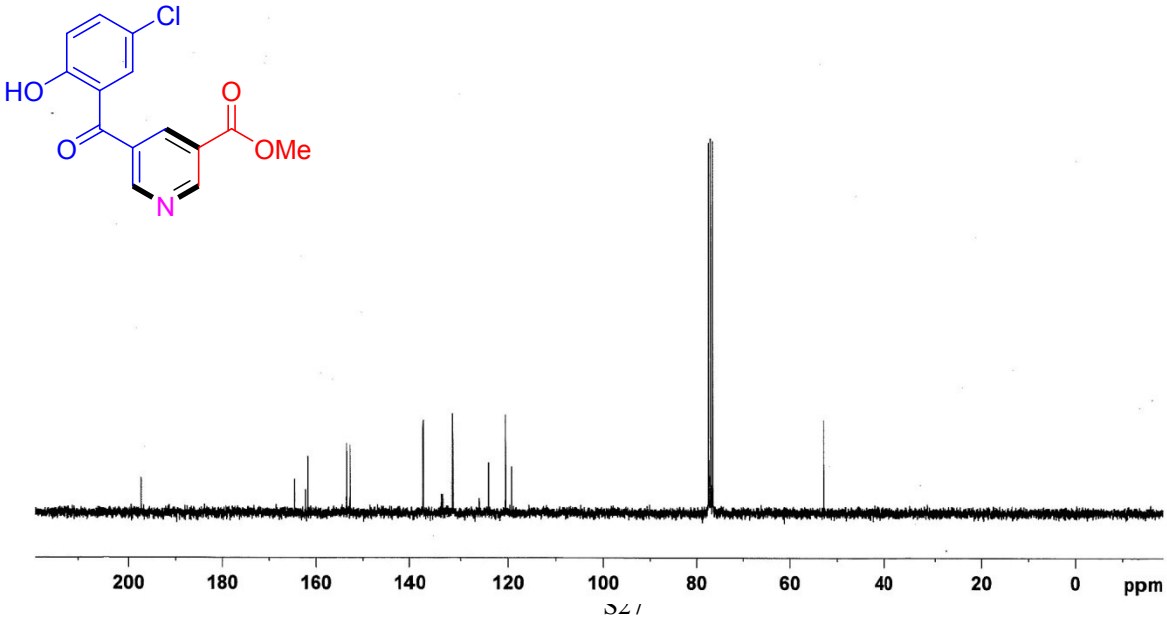
$^{13}$C-NMR/$CDCl_3$






Compound-**4p**

$^{1}$H-NMR/$CDCl_3$

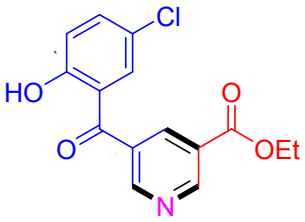



Compound-**4p**

$^{13}$C-NMR/$CDCl_3$

Compound-**4q**

$^{1}$H-NMR/$CDCl_3$

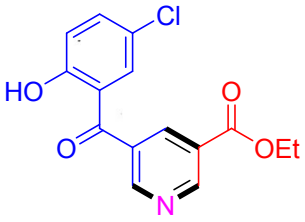






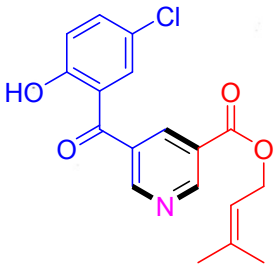
Compound-**4q**

$^{13}$C-NMR/$CDCl_3$



Compound-**4r**

$^{1}$H-NMR/$CDCl_3$

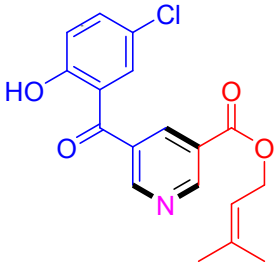






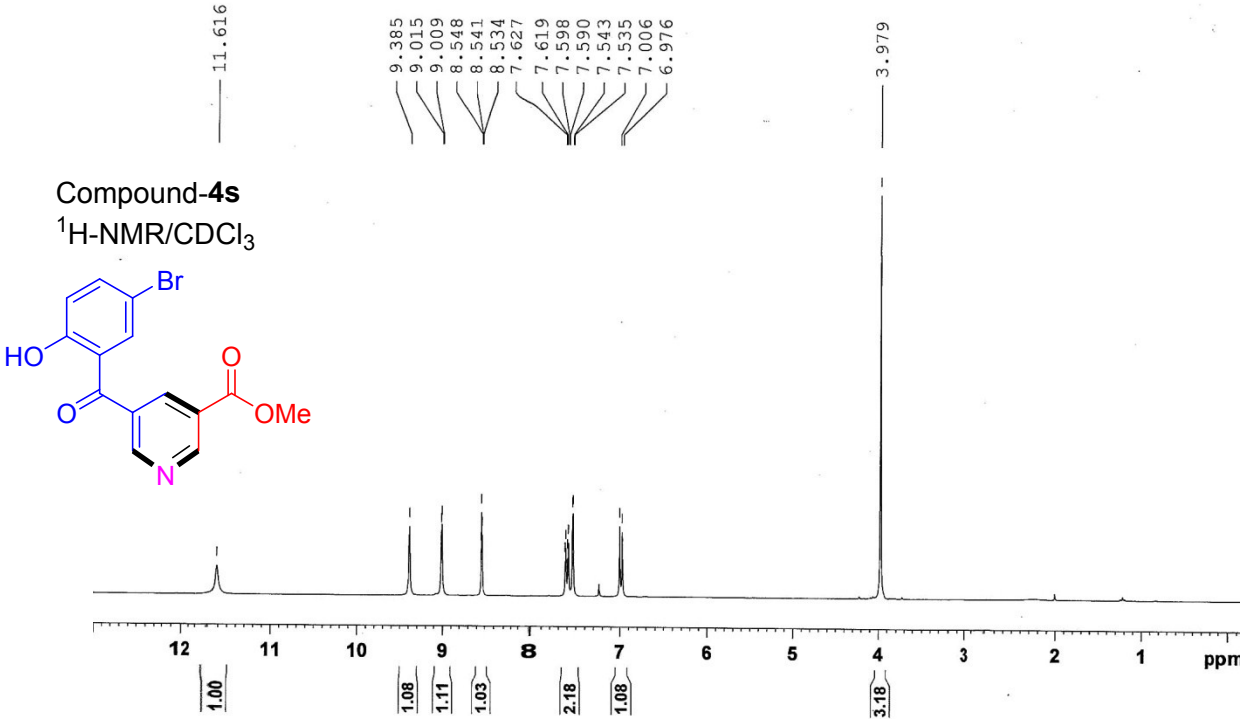
Compound-**4r**

$^{13}$C-NMR/$CDCl_3$



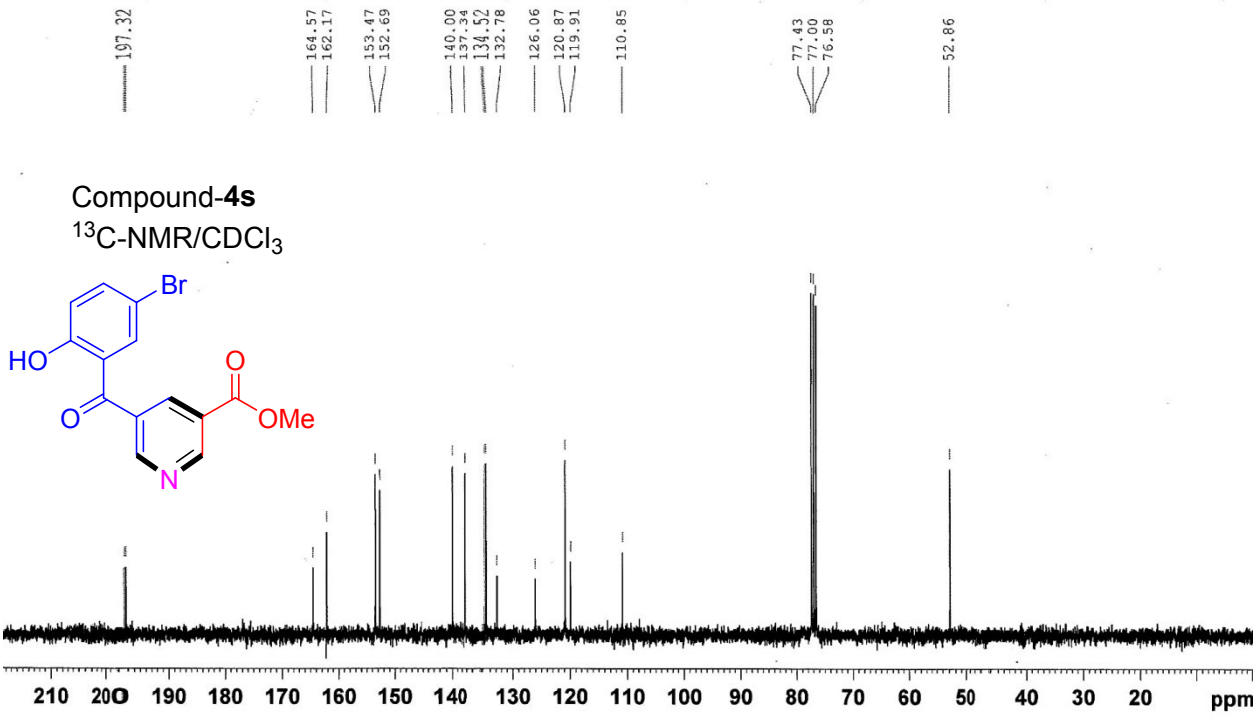
Compound-**4s**

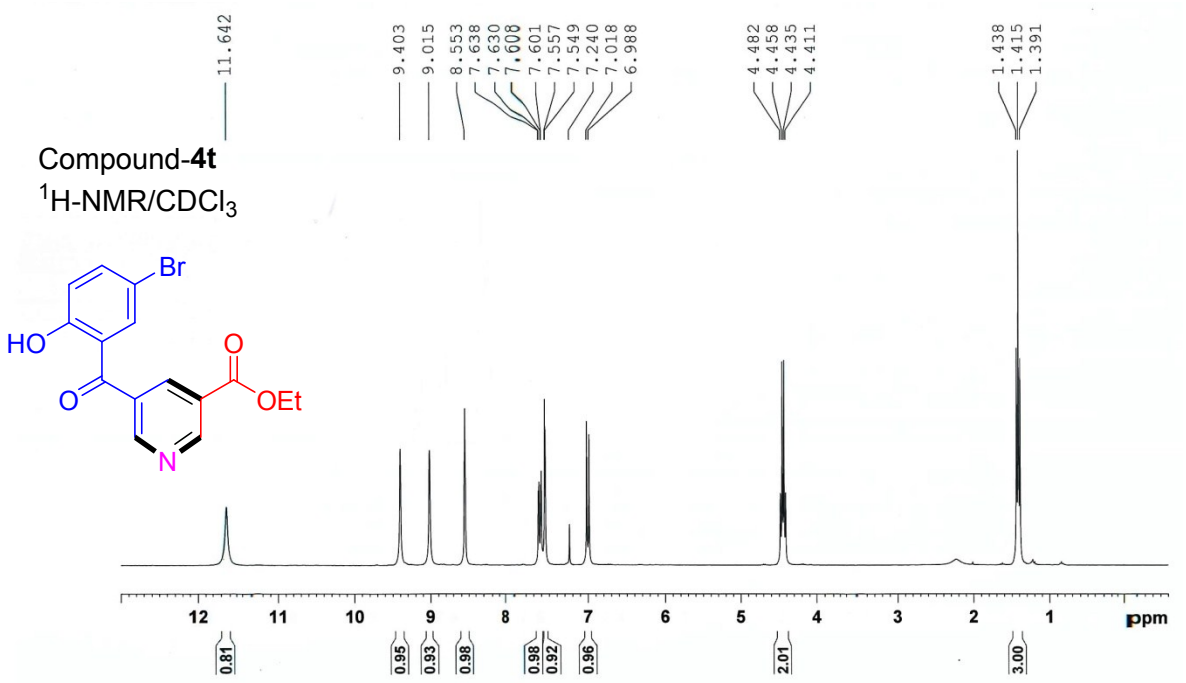
$^{1}$H-NMR/$CDCl_3$

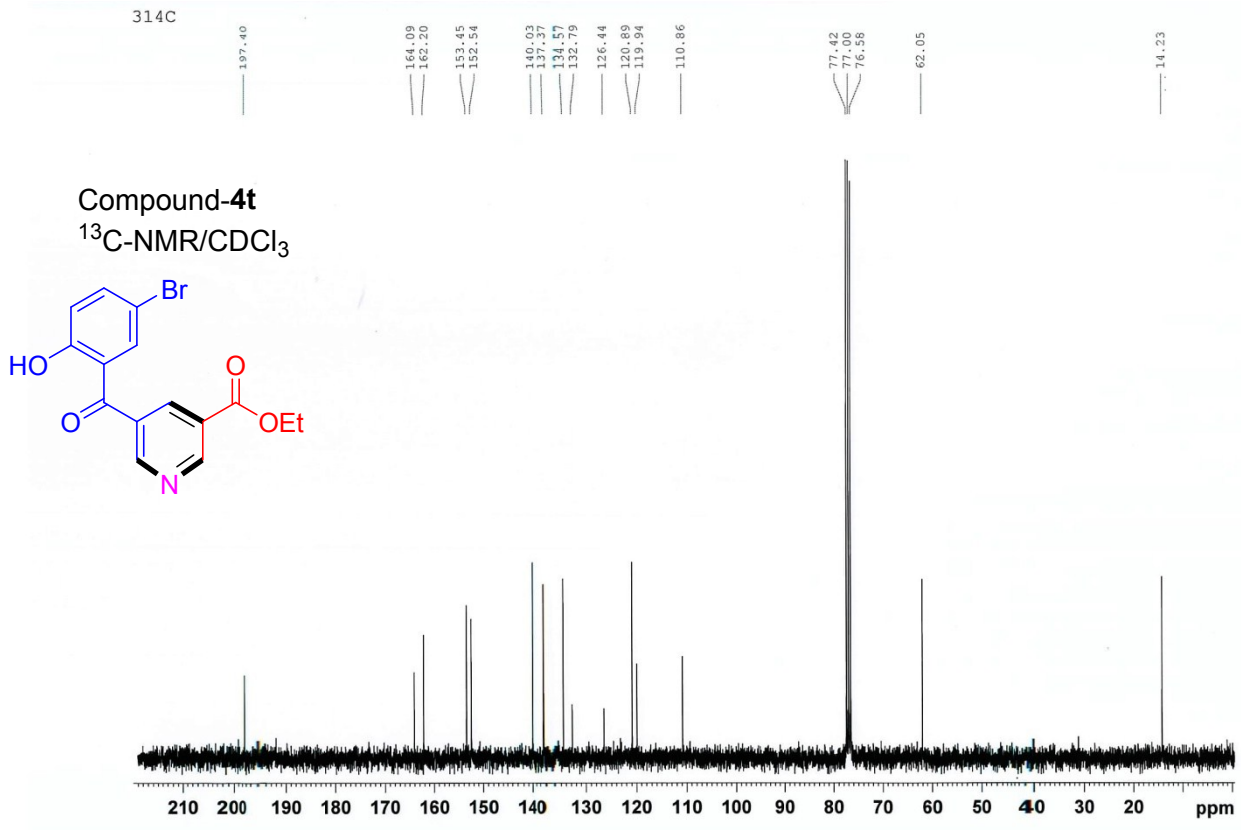



Compound-**4s**

$^{13}$C-NMR/$CDCl_3$

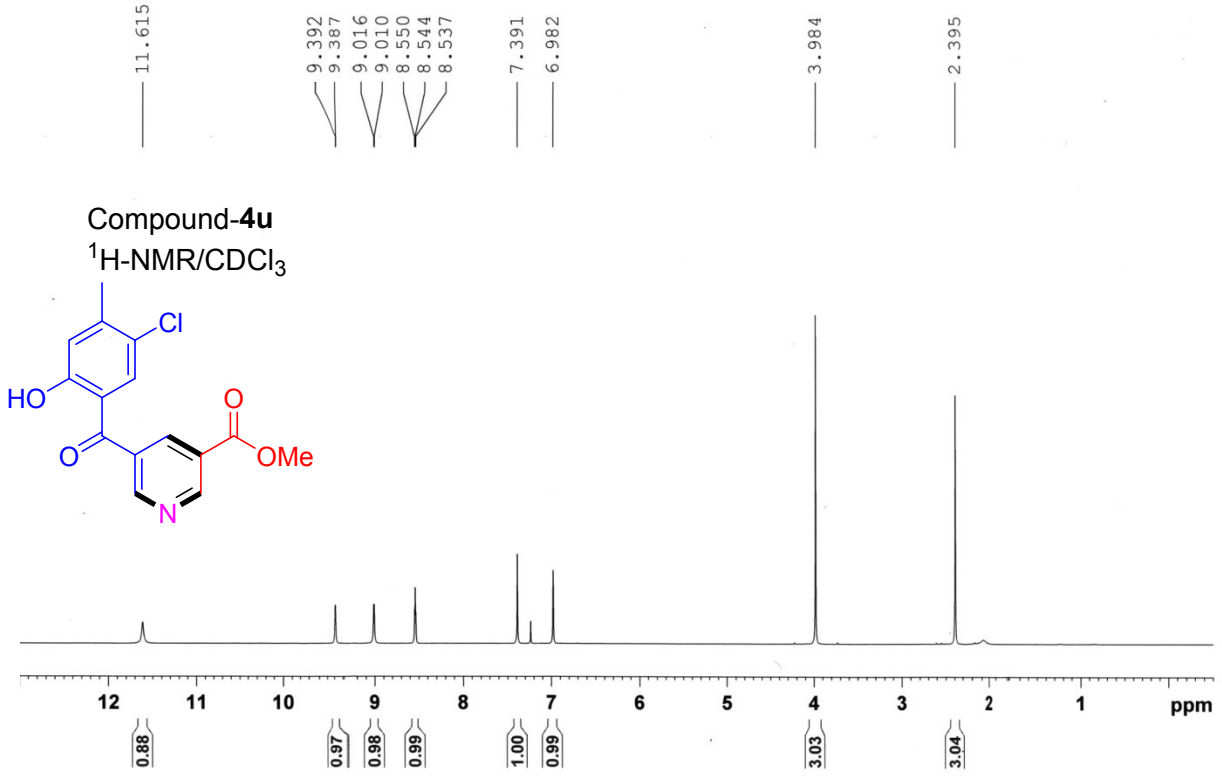



Compound-4t
1H-NMR/CDCl3
Br
HO
O
O
OEt
N
11.642
9.403
9.015
8.553
7.638
7.630
7.608
7.601
7.557
7.549
7.240
7.018
6.988
4.482
4.458
4.435
4.411
1.438
1.415
1.391
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.81
0.95
0.93
0.98
0.98
0.92
0.96
2.01
3.00


314C
Compound-4t
13C-NMR/CDCl3
Br
HO
O
O
OEt
N
197.40
164.09
162.20
153.45
152.54
140.03
137.37
134.57
132.79
126.44
120.89
119.94
110.86
77.42
77.00
76.58
62.05
14.23
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

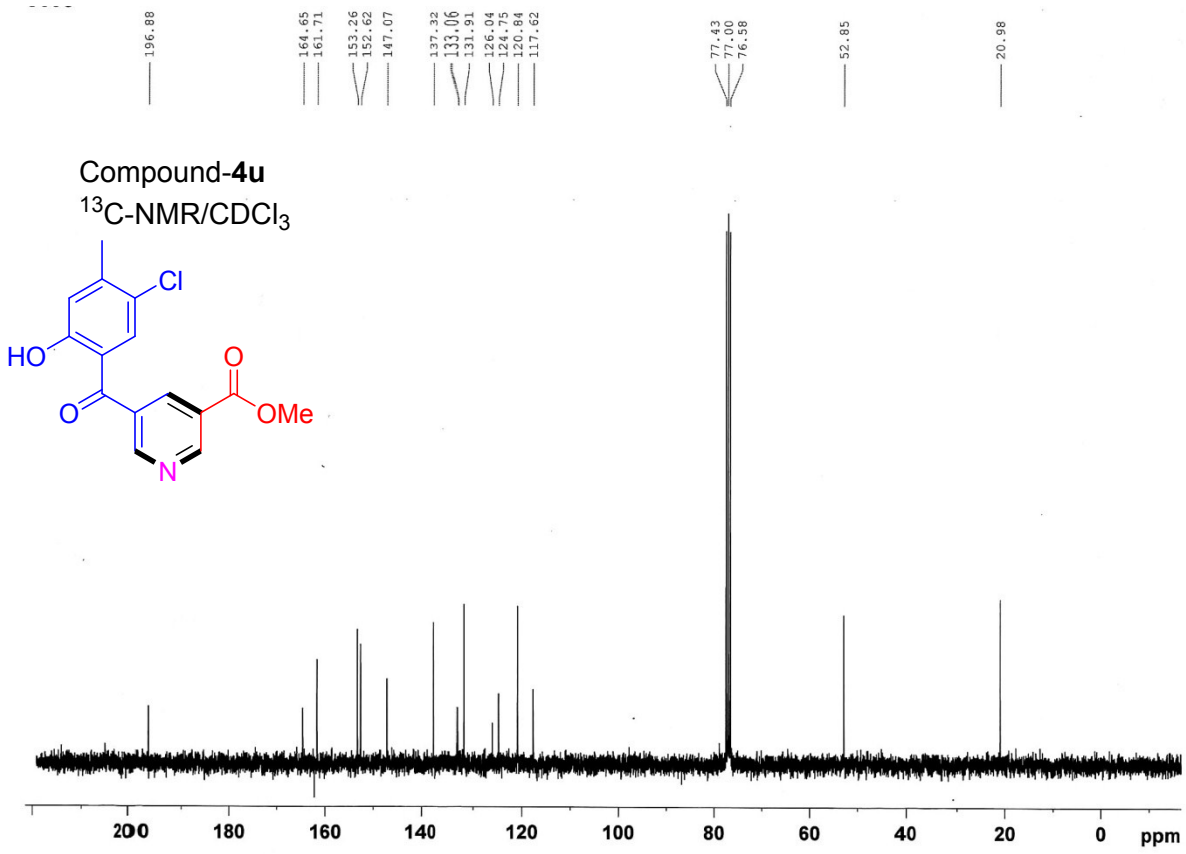
Compound-**4u**

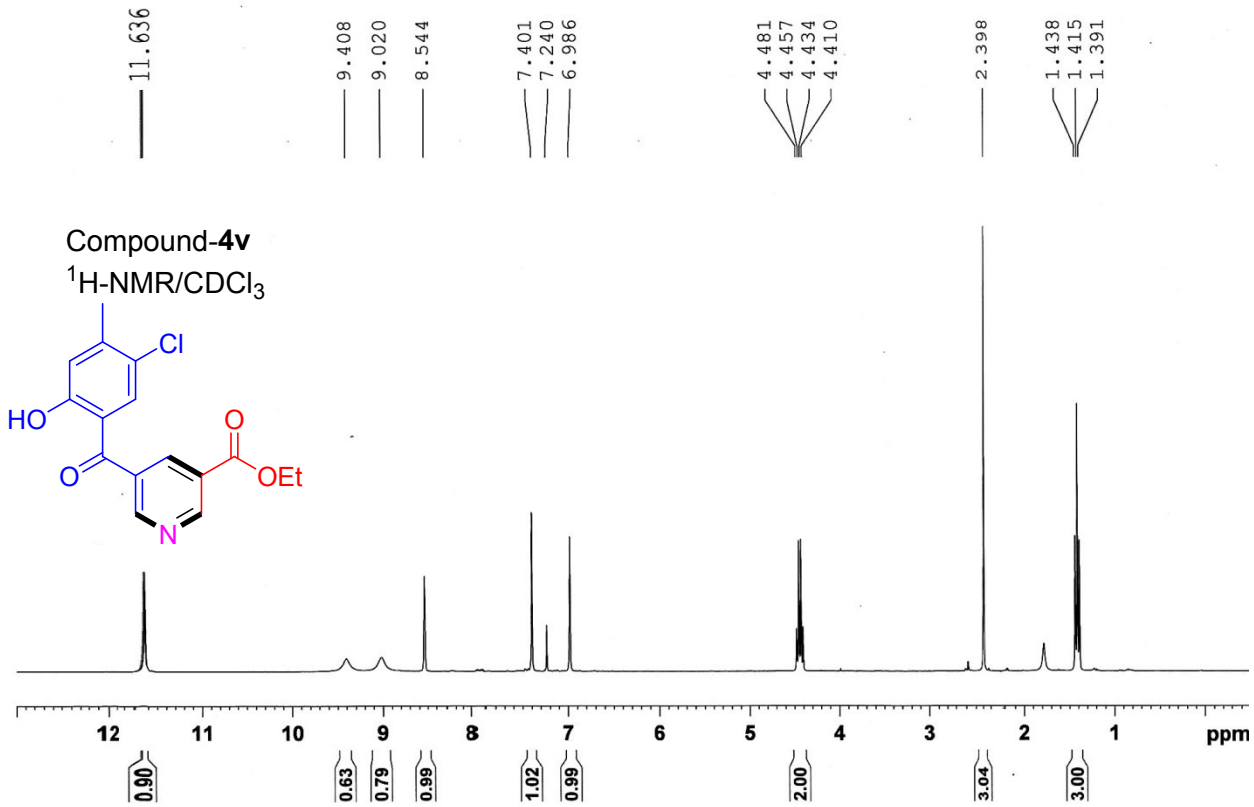
$^{1}$H-NMR/$CDCl_3$

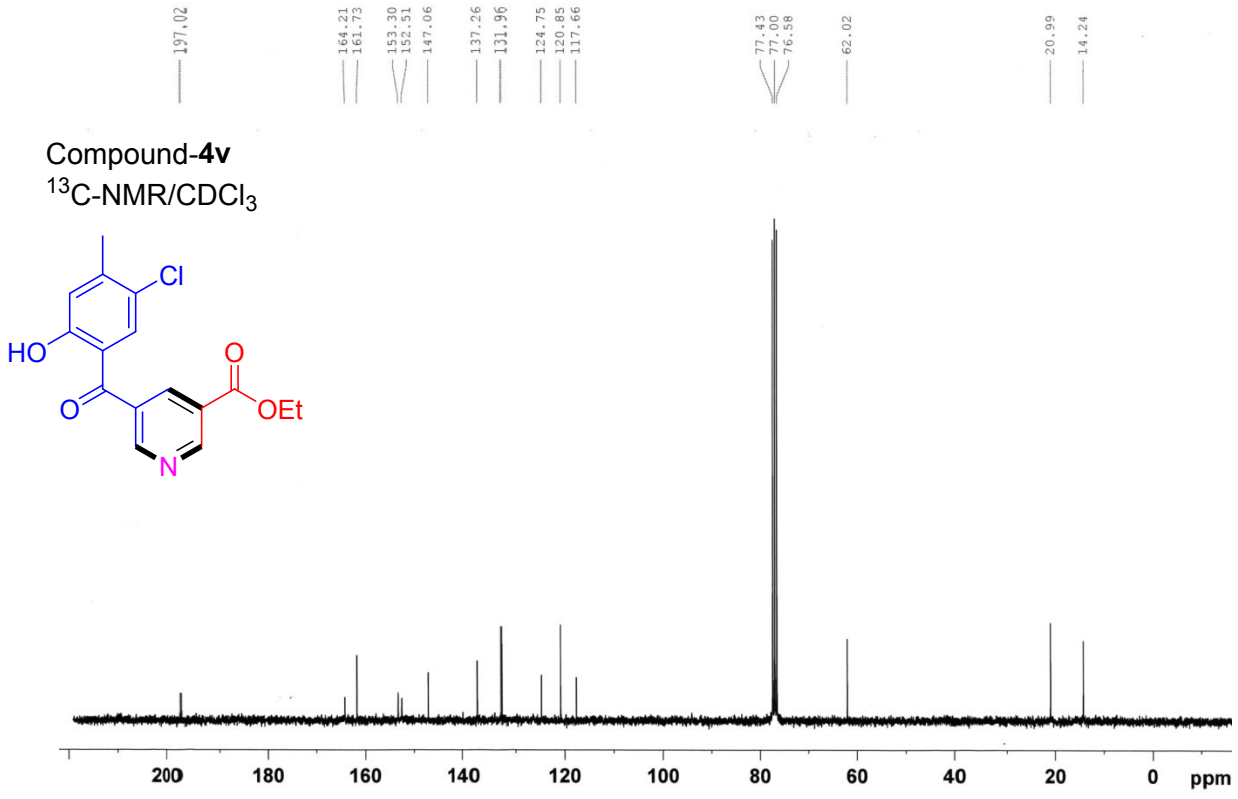


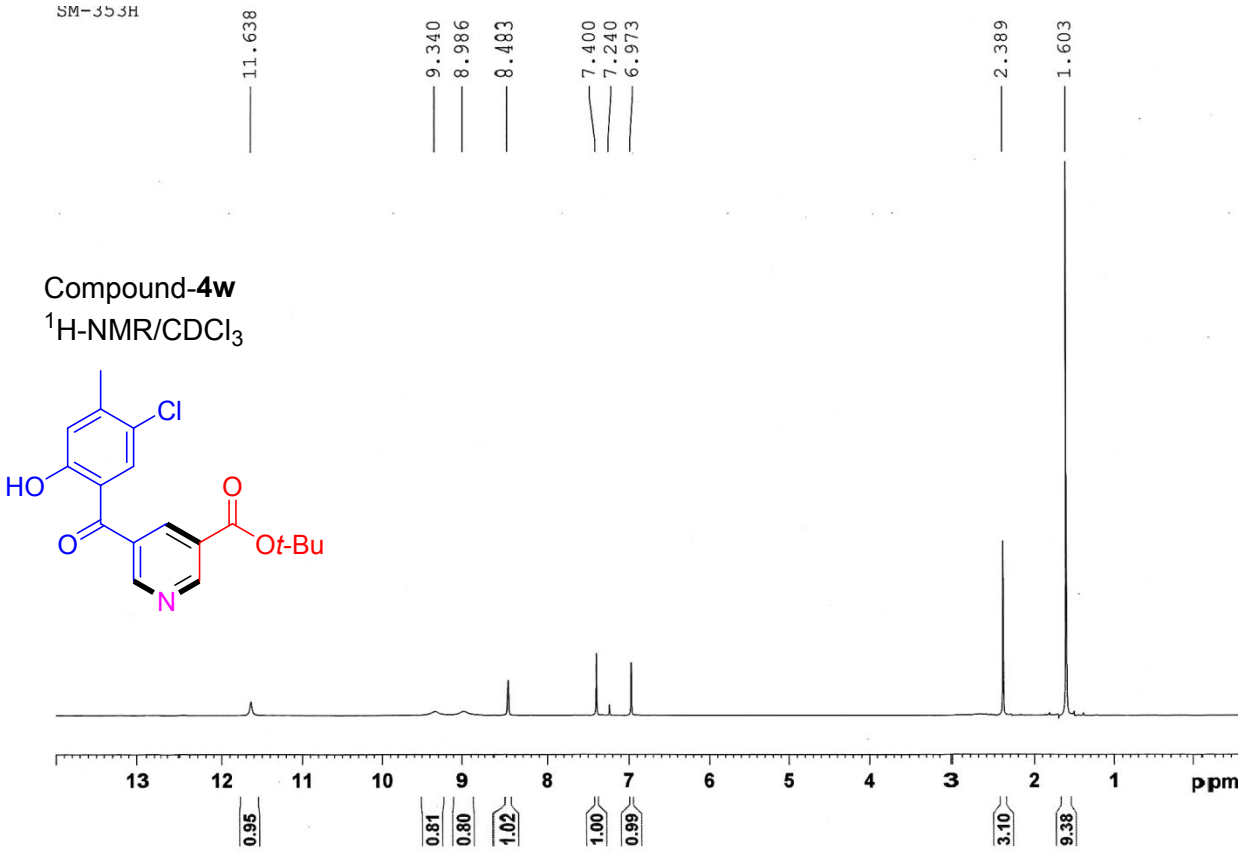

Compound-**4u**

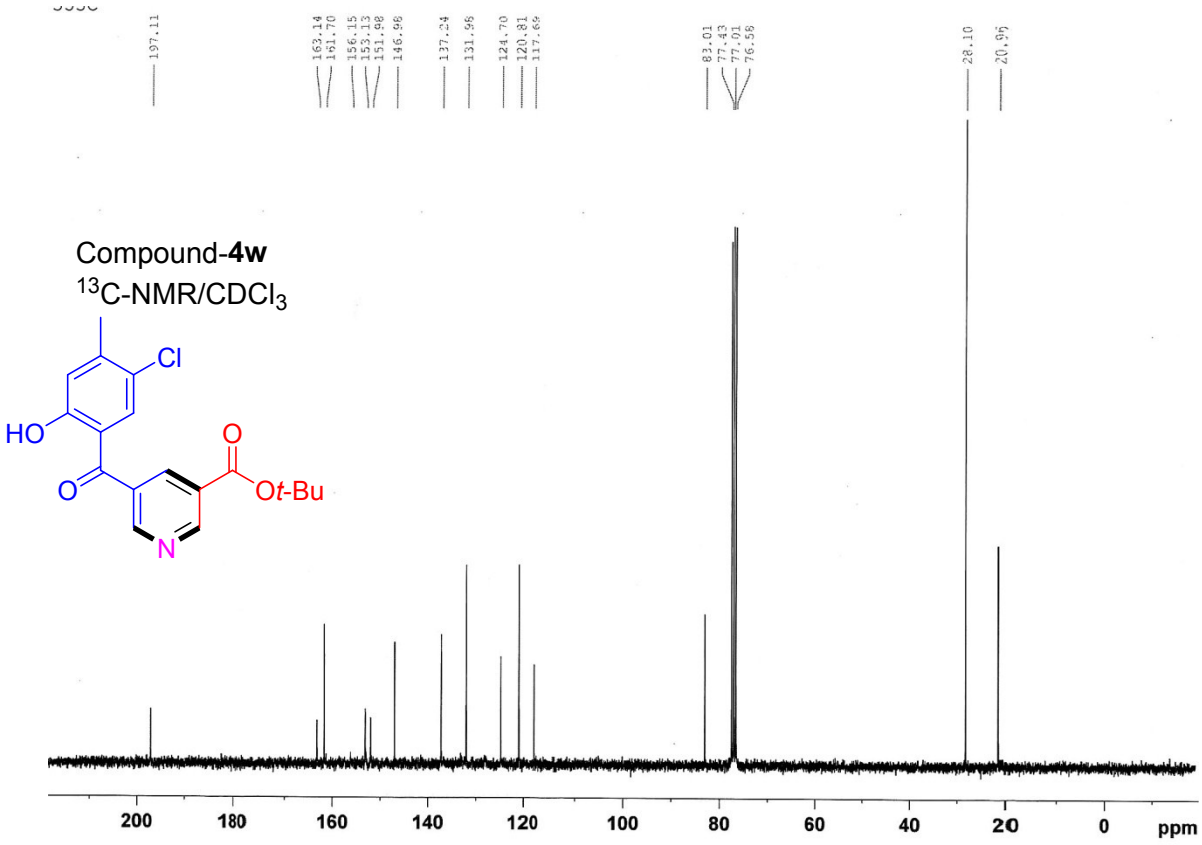
$^{13}$C-NMR/$CDCl_3$




11.636
9.408
9.020
8.544
7.401
7.240
6.986
4.481
4.457
4.434
4.410
2.398
1.438
1.415
1.391
Compound-4v
1H-NMR/CDCl3
Cl
HO
O
O
OEt
N
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.90
0.63
0.79
0.99
1.02
0.99
2.00
3.04
3.00

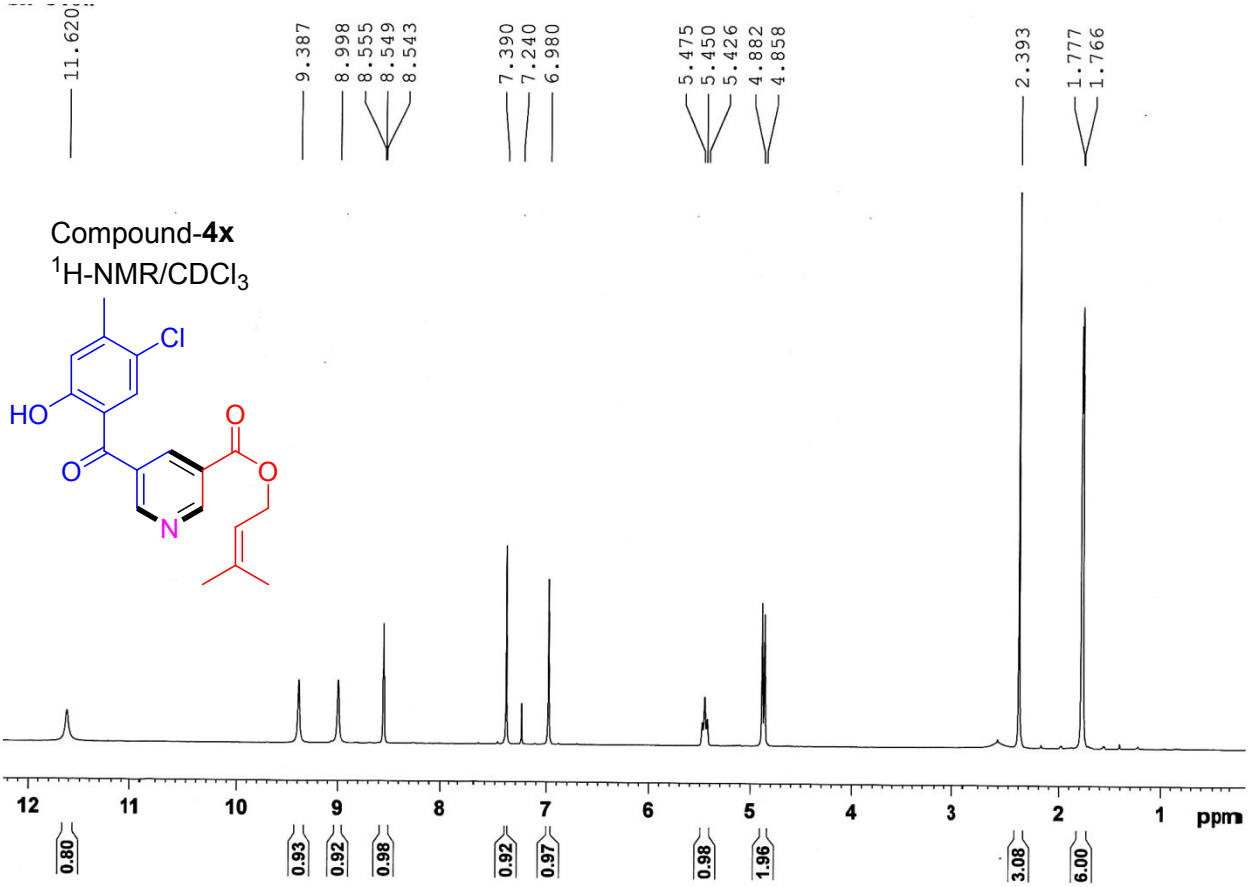

197.02
164.21
161.73
153.30
152.51
147.06
137.26
131.96
124.75
120.85
117.66
77.43
77.00
76.58
62.02
20.99
14.24
Compound-4v
13C-NMR/CDCl3
Cl
HO
O
O
OEt
N
200
180
160
140
120
100
80
60
40
20
0
ppm


SM-353H
11.638
9.340
8.986
8.483
7.400
7.240
6.973
2.389
1.603
Compound-4w
1H-NMR/CDCl3
Cl
HO
O
O
Ot-Bu
N
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.95
0.81
0.80
1.02
1.00
0.99
3.10
9.38


197.11
163.14
161.70
156.15
153.13
151.98
146.96
137.24
131.96
124.70
120.81
117.64
83.01
77.43
77.01
76.56
28.10
20.96
Compound-4w
13C-NMR/CDCl3
Cl
HO
O
O
Ot-Bu
N
200
180
160
140
120
100
80
60
40
20
0
ppm

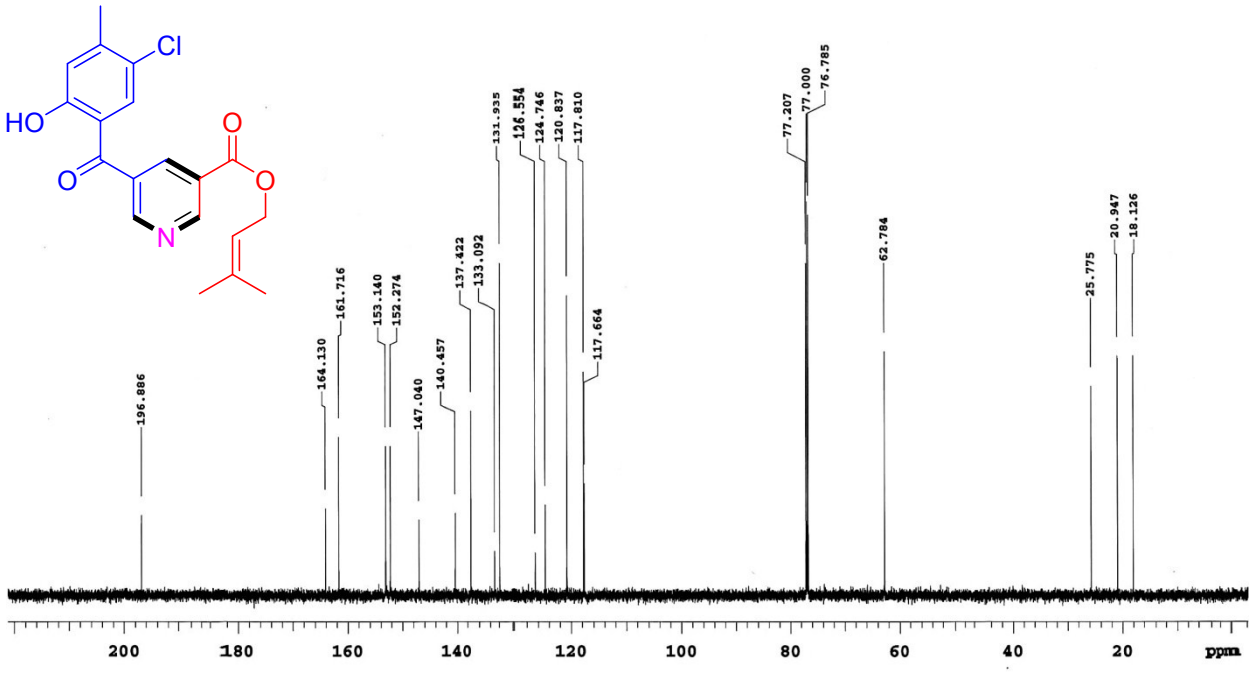
Compound-**4x**

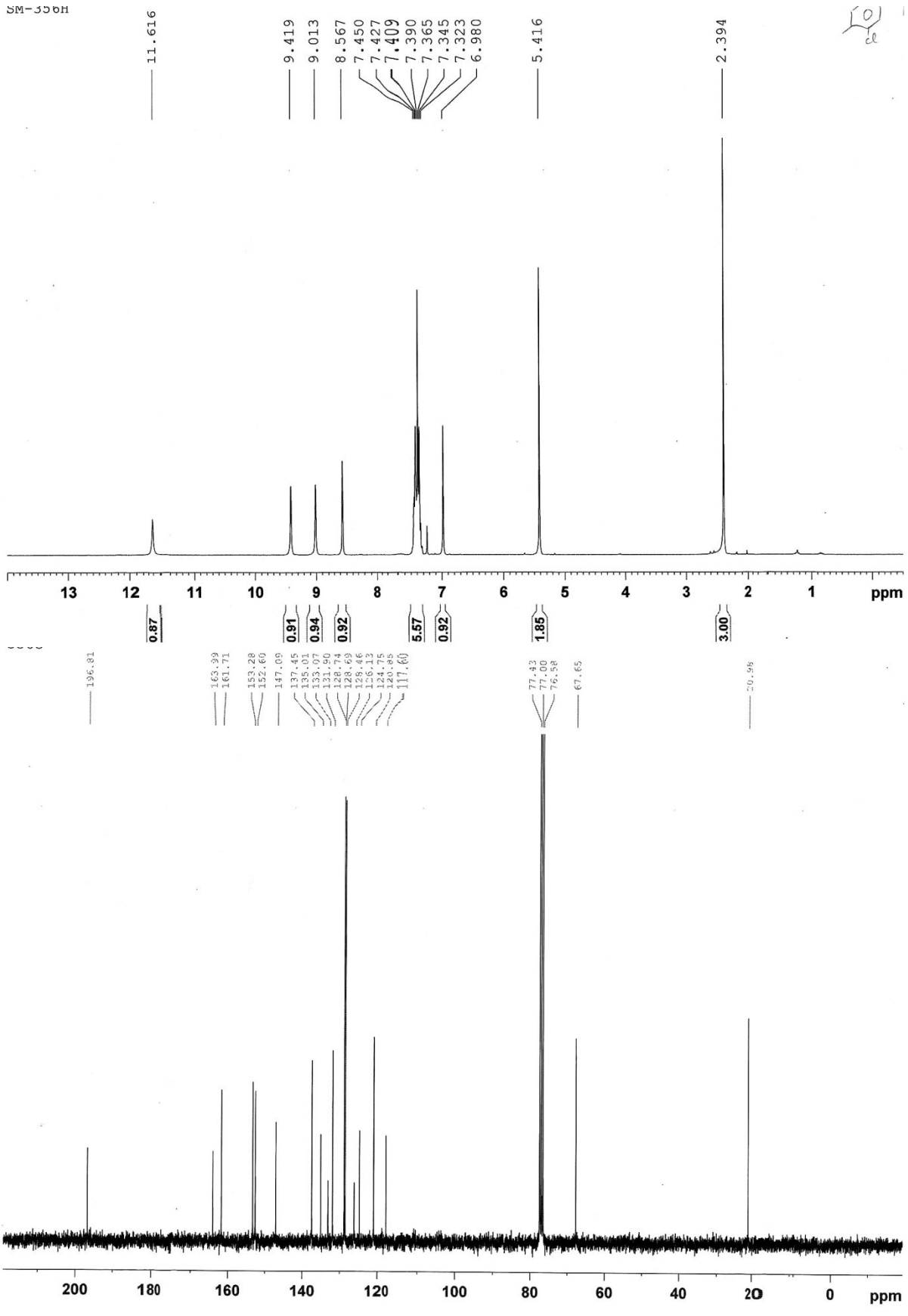
$^{1}$H-NMR/$CDCl_3$

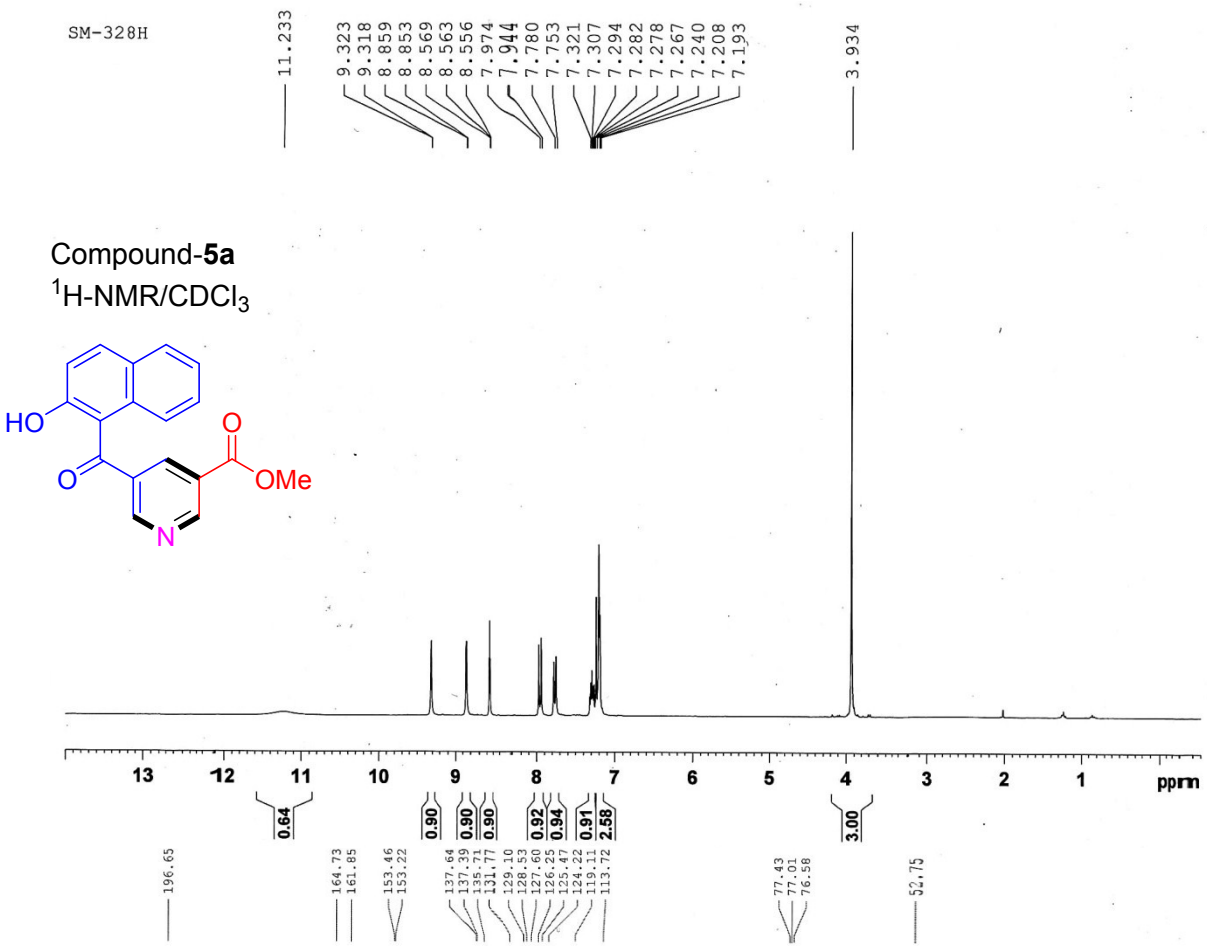


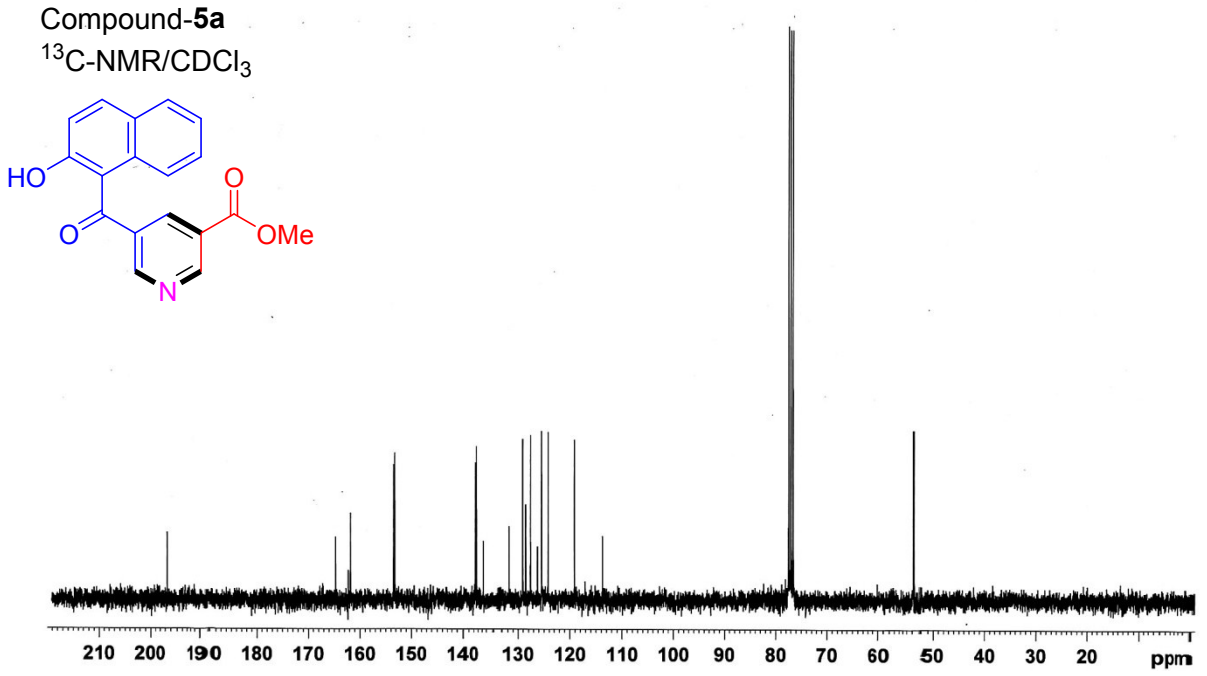

Compound-**4x**

$^{13}$C-NMR/$CDCl_3$



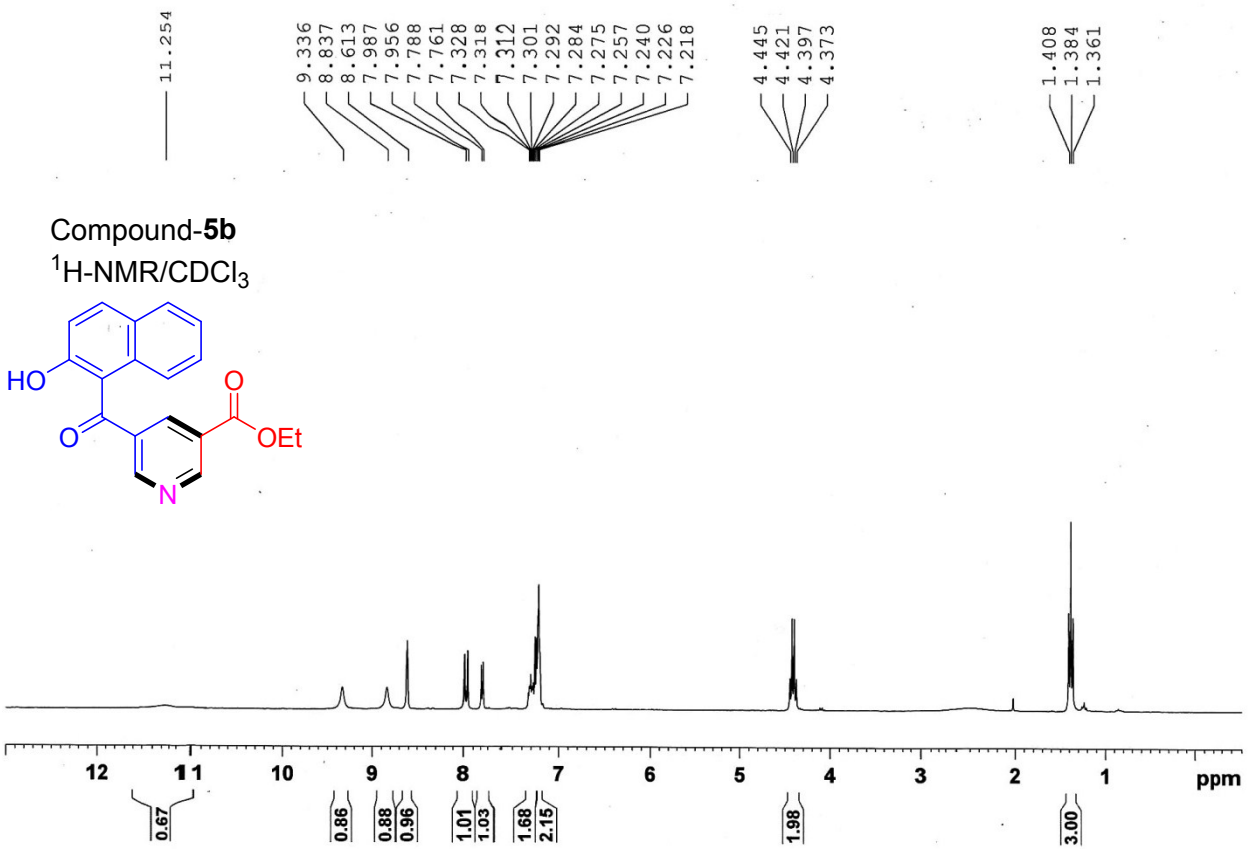

11.616
9.419
9.013
8.567
7.450
7.427
7.409
7.390
7.365
7.345
7.323
6.980
5.416
2.394
ppm
0.87
0.91
0.94
0.92
5.57
0.92
1.85
3.00
196.81
163.99
161.71
153.28
152.60
147.09
137.45
135.01
133.07
131.90
128.74
128.69
128.46
126.13
124.75
120.85
117.60
77.43
77.00
76.58
67.65
20.96
ppm


SM-328H
11.233
9.323
9.318
8.859
8.853
8.569
8.563
8.556
7.974
7.944
7.780
7.753
7.321
7.307
7.294
7.282
7.278
7.267
7.240
7.208
7.193
3.934
Compound-5a
1H-NMR/CDCl3
HO
O
O
OMe
N
13 12 11 10 9 8 7 6 5 4 3 2 1 ppm
0.64
0.90
0.90
0.90
0.92
0.94
0.91
2.58
3.00
196.65
164.73
161.85
153.46
153.22
137.64
137.39
135.71
131.77
129.10
128.53
127.60
126.25
125.47
124.22
119.11
113.72
77.43
77.01
76.58
52.75


Compound-5a
13C-NMR/CDCl3
HO
O
O
OMe
N
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

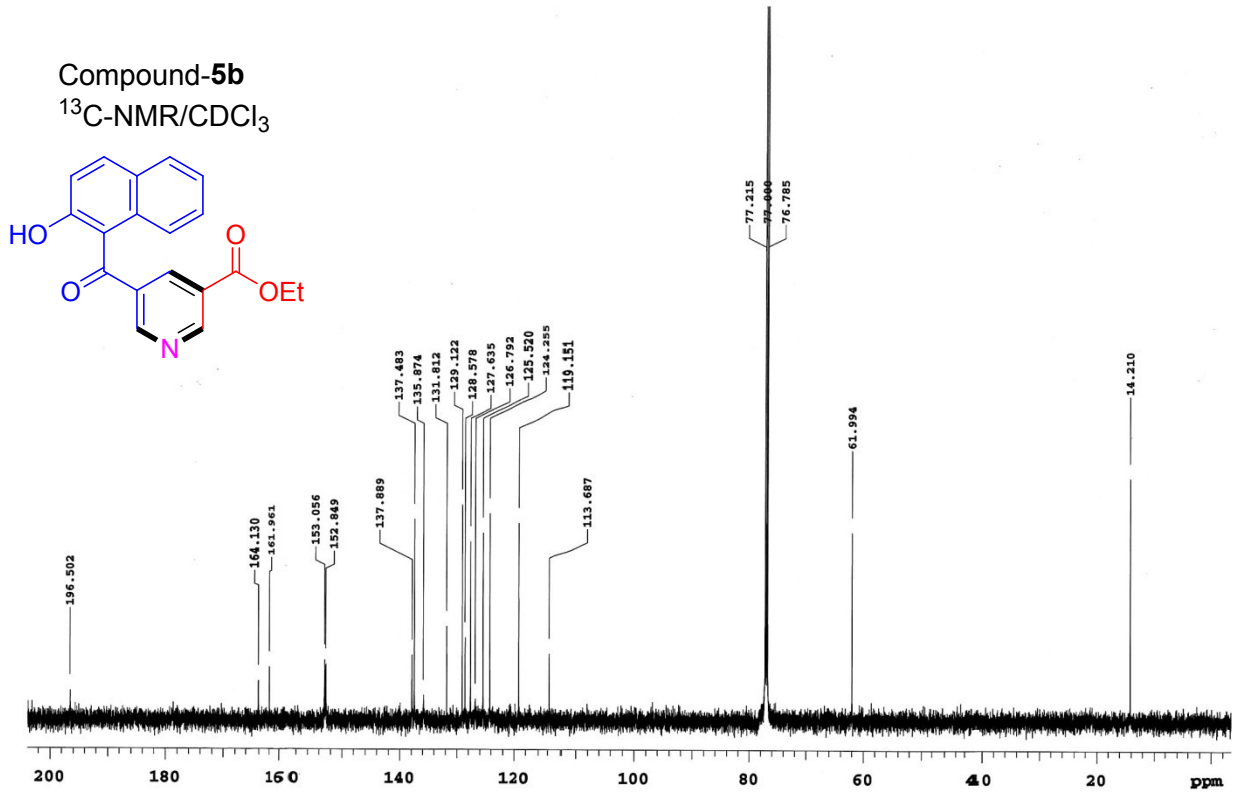
Compound-**5b**

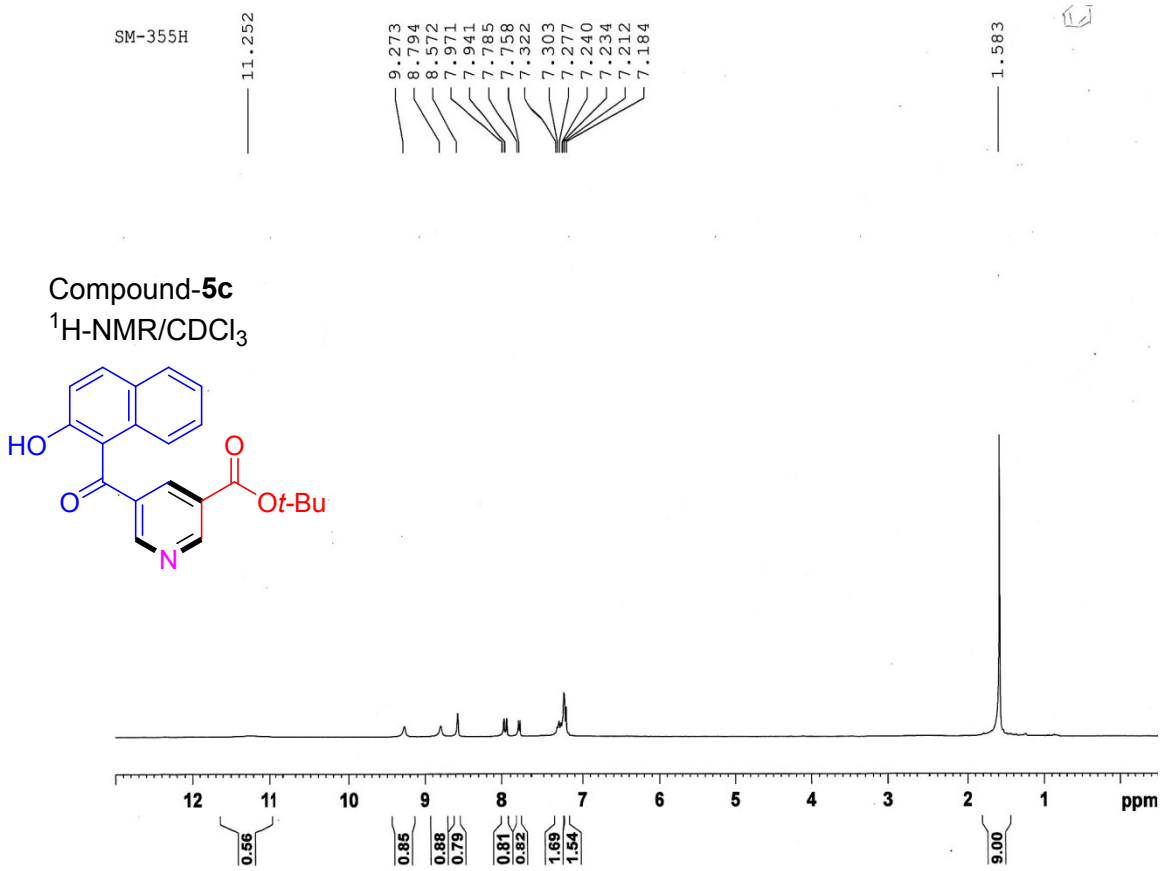
$^{1}$H-NMR/$CDCl_3$



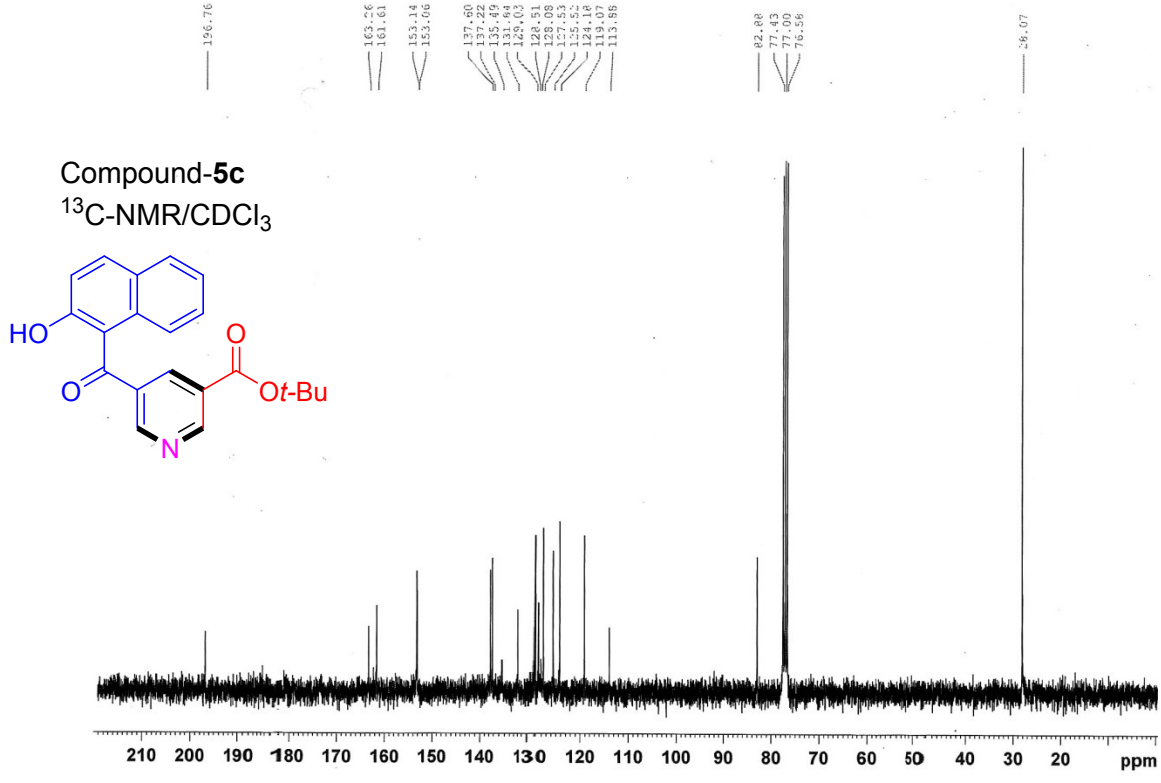

Compound-**5b**

$^{13}$C-NMR/$CDCl_3$

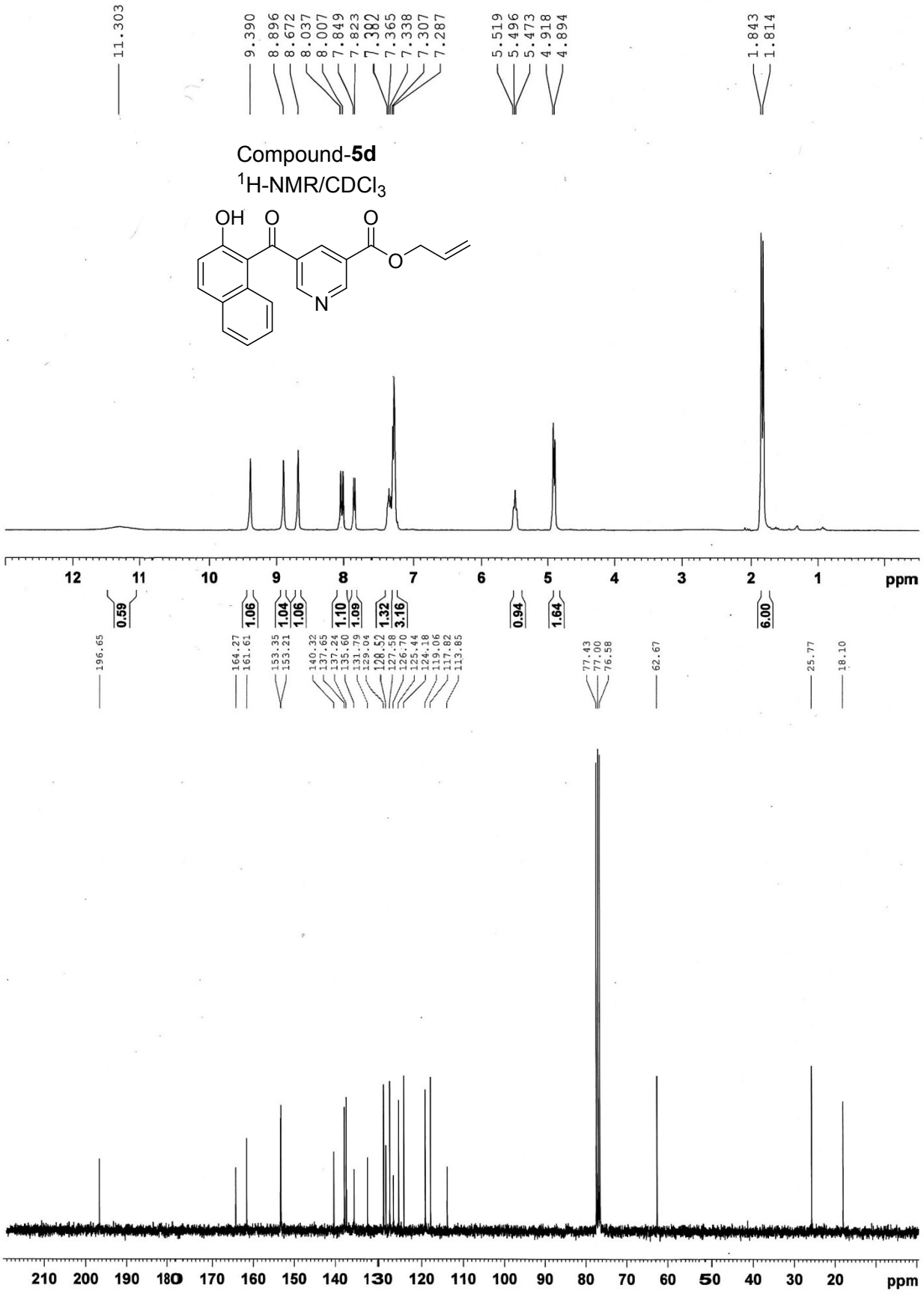


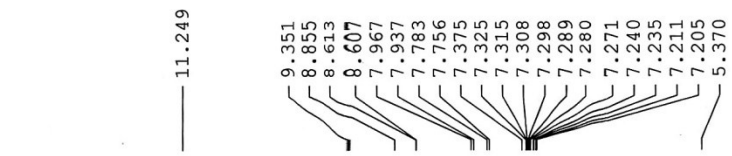



Compound-**5c**
$^{1}$H-NMR/$CDCl_3$



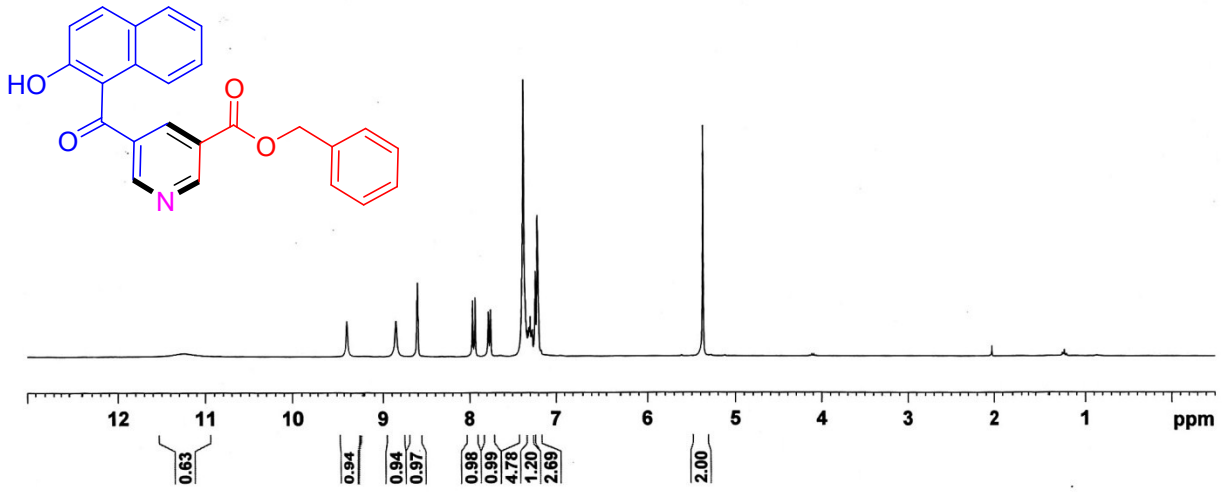

Compound-**5c**
$^{13}$C-NMR/$CDCl_3$

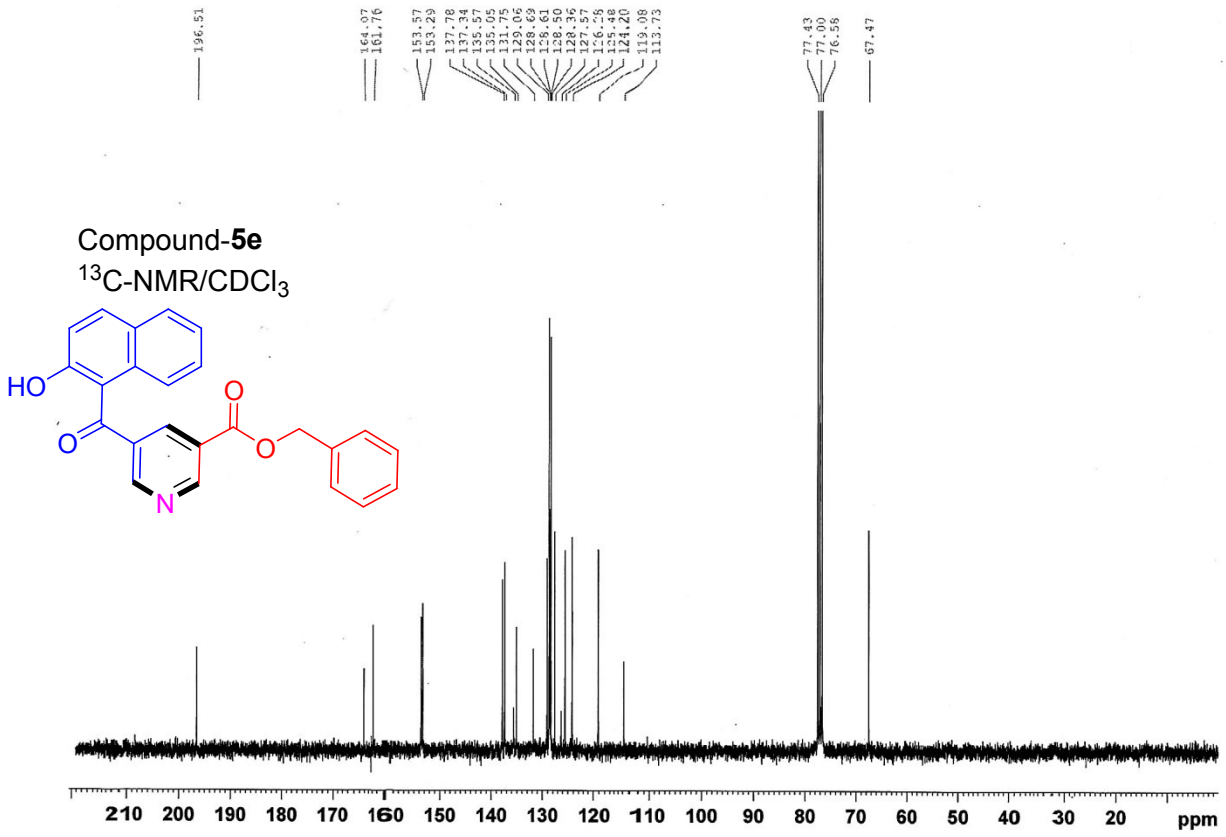

11.303
9.390
8.896
8.672
8.037
8.007
7.849
7.823
7.382
7.365
7.338
7.307
7.287
5.519
5.496
5.473
4.918
4.894
1.843
1.814
Compound-5d
1H-NMR/CDCl3
OH
O
O
O
N
ppm
0.59
1.06
1.04
1.06
1.10
1.09
1.32
3.16
0.94
1.64
6.00
196.65
164.27
161.61
153.35
153.21
140.32
137.65
137.24
135.60
131.79
129.04
128.52
127.58
126.70
125.44
124.18
119.06
117.82
113.85
77.43
77.00
76.58
62.67
25.77
18.10
ppm




Compound-**5e**

$^{1}$H-NMR/$CDCl_3$



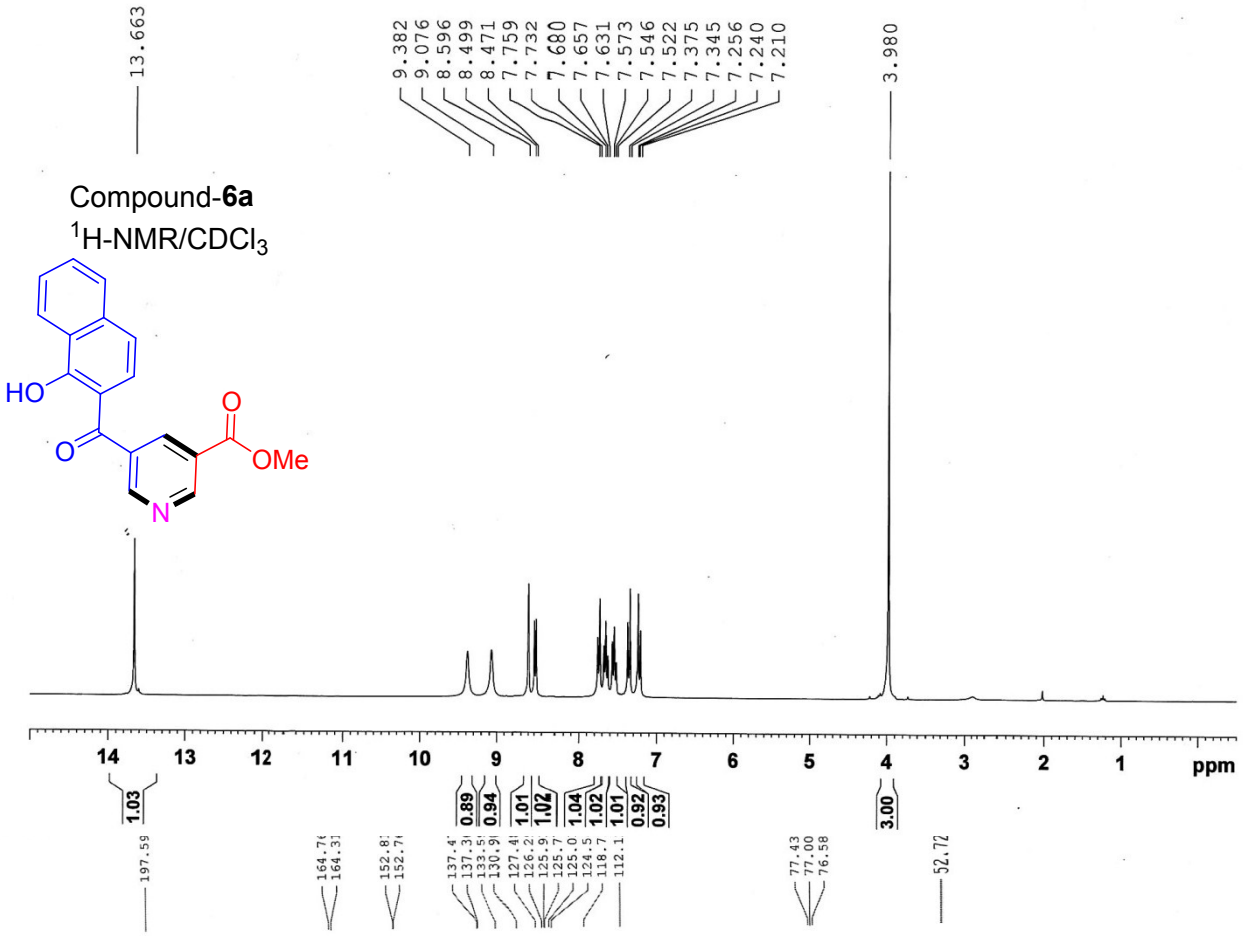




Compound-**5e**

$^{13}$C-NMR/$CDCl_3$

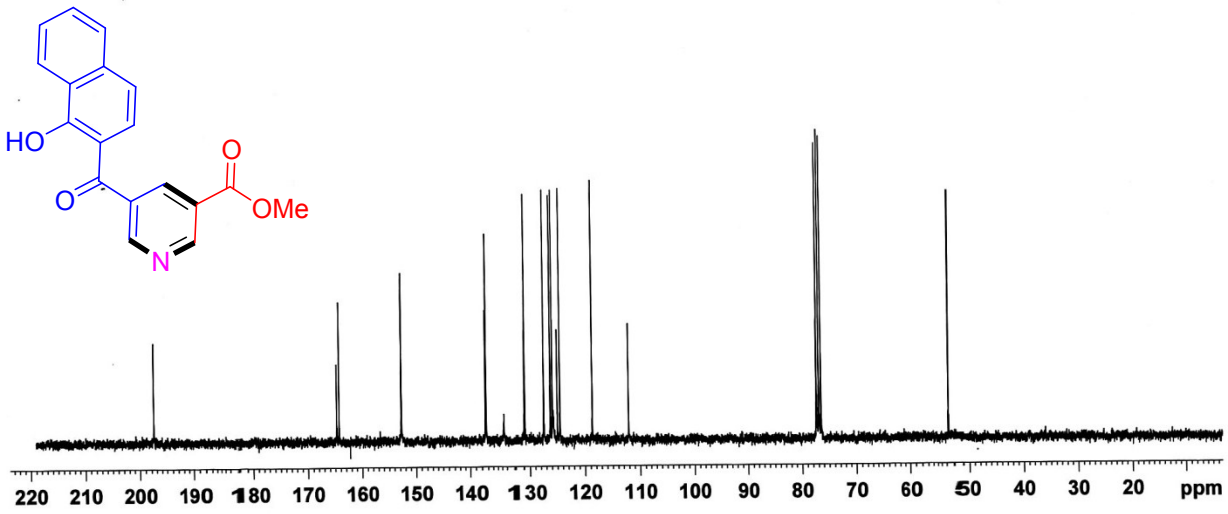
Compound-**6a**

$^{1}$H-NMR/$CDCl_3$



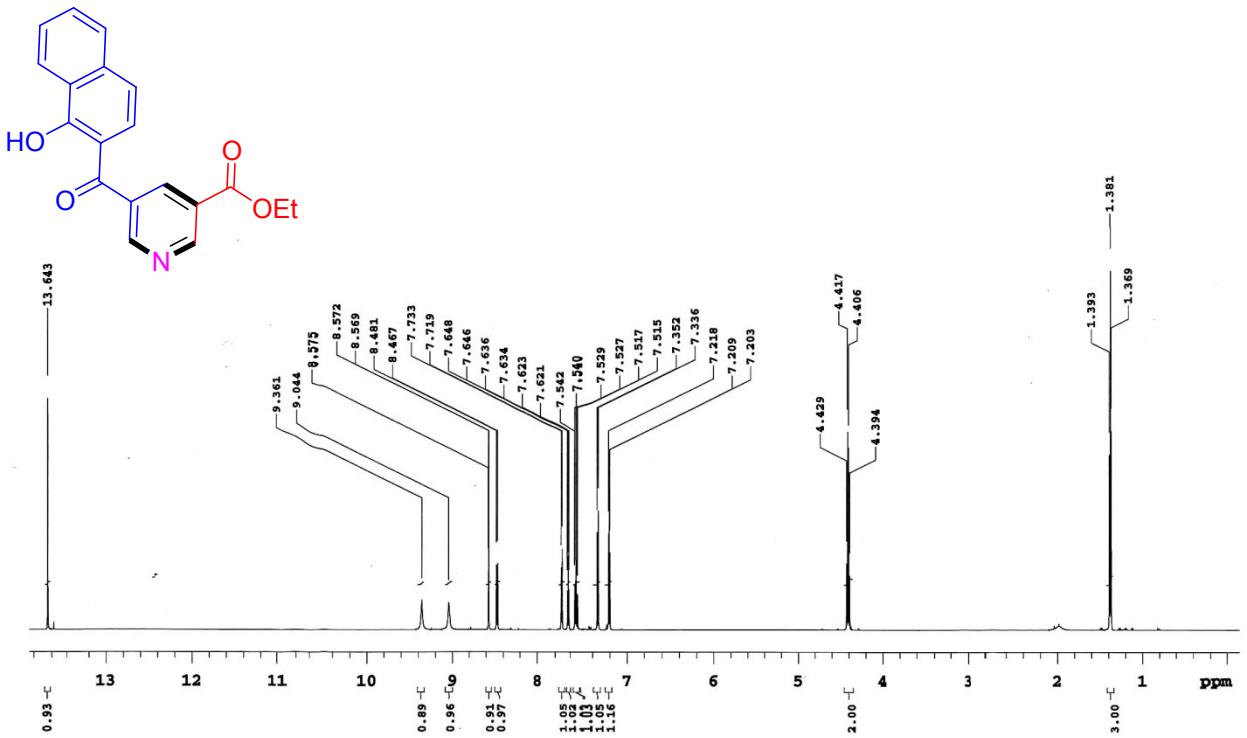

Compound-**6a**

$^{13}$C-NMR/$CDCl_3$



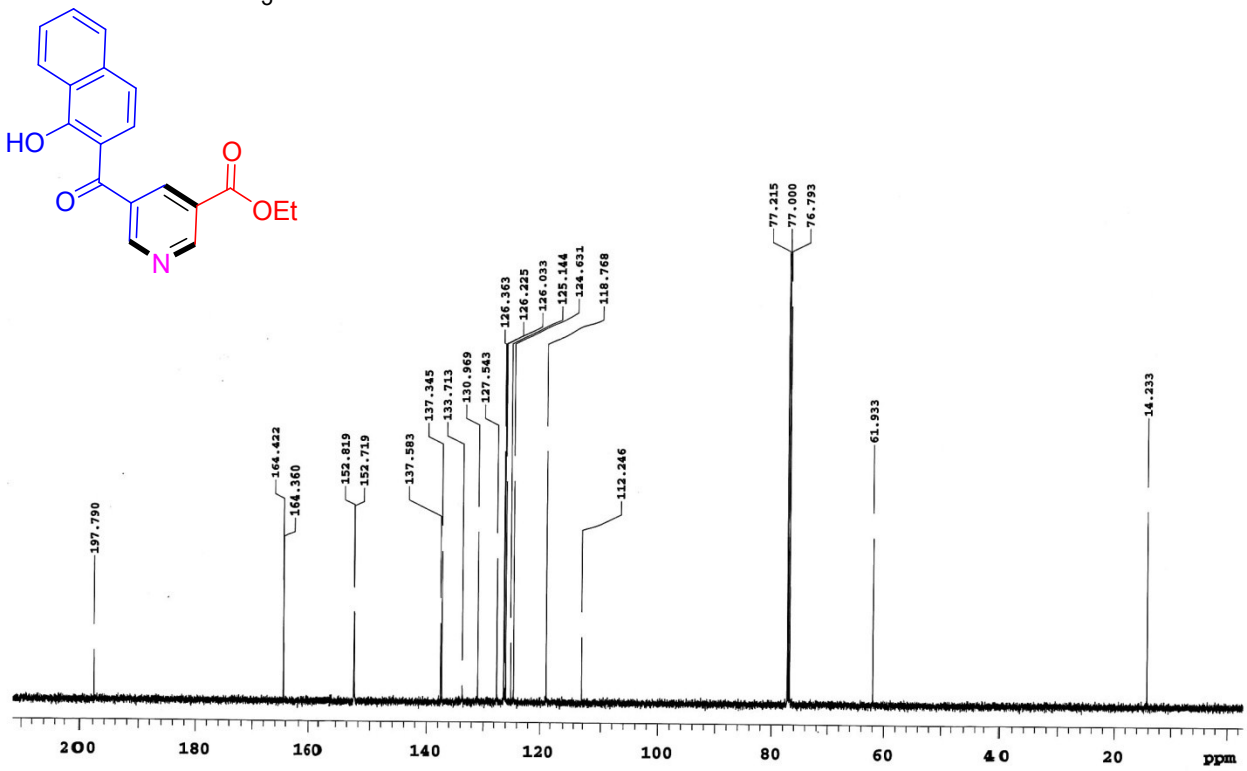
Compound-**6b**

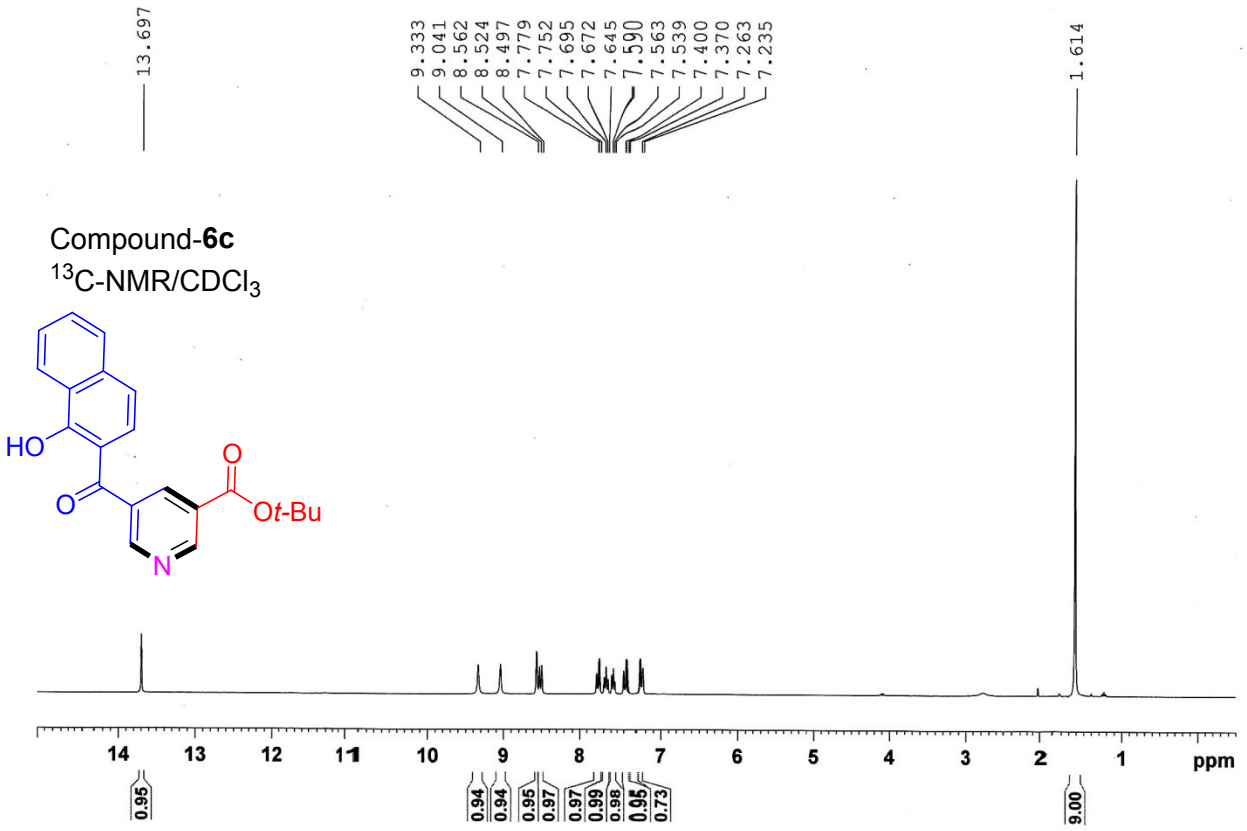
$^{1}$H-NMR/$CDCl_3$

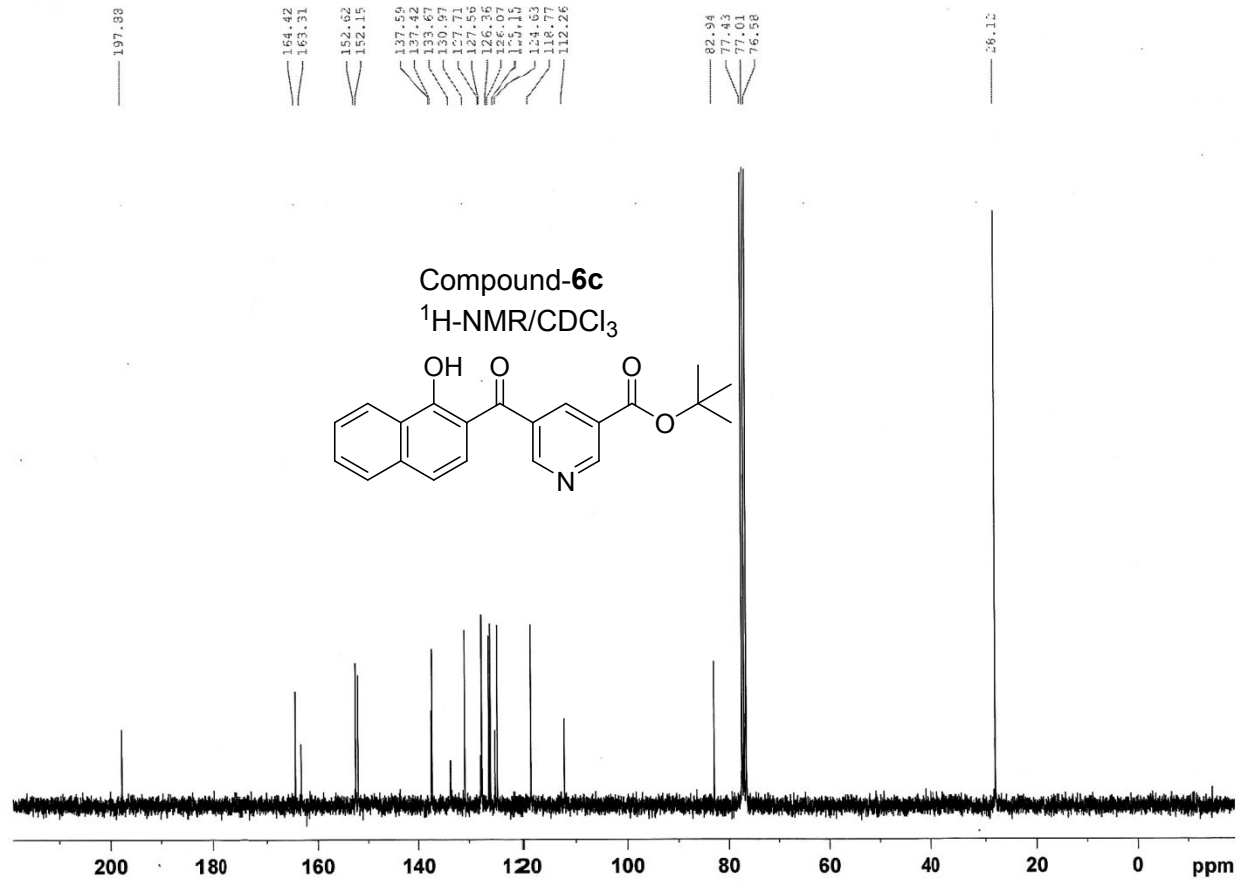



Compound-**6b**

$^{13}$C-NMR/$CDCl_3$

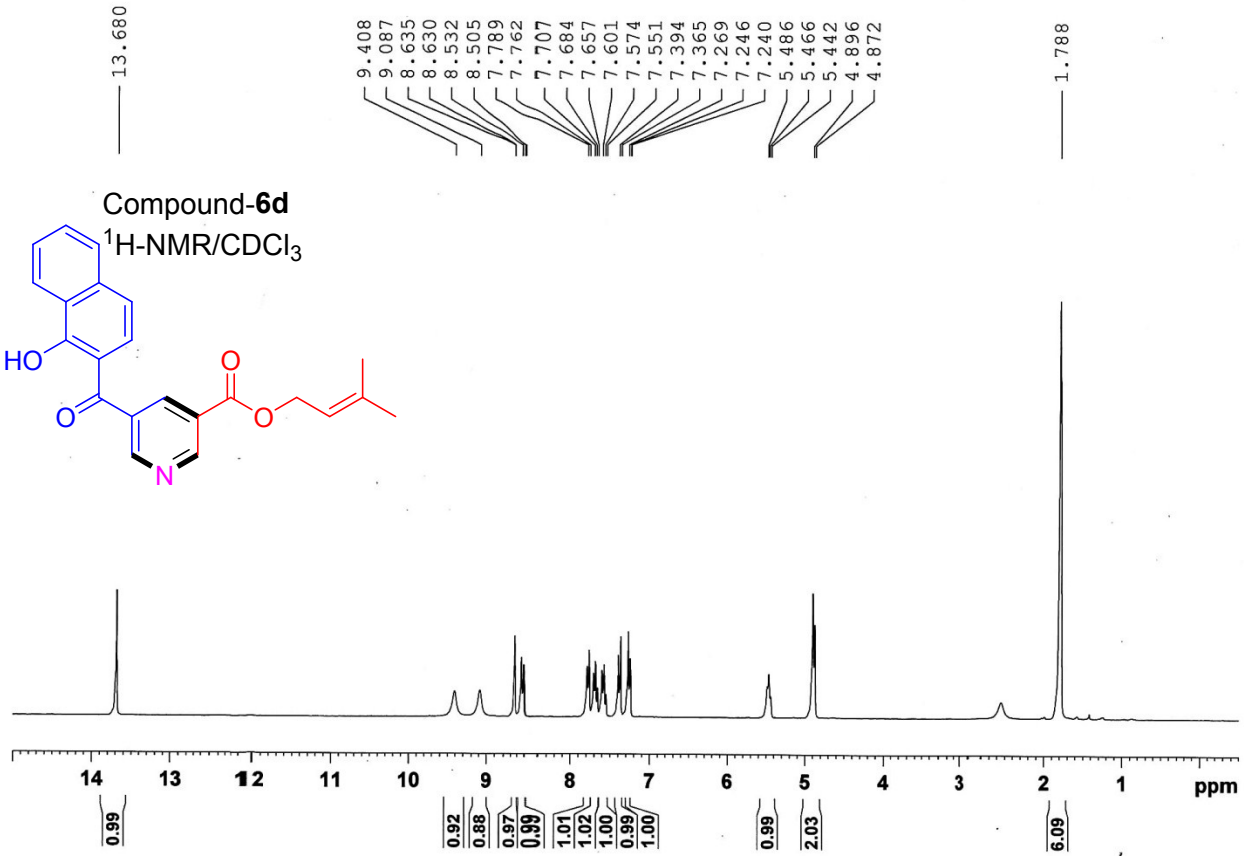



13.697
9.333
9.041
8.562
8.524
8.497
7.779
7.752
7.695
7.672
7.645
7.590
7.563
7.539
7.400
7.370
7.263
7.235
1.614
Compound-6c
13C-NMR/CDCl3
HO
O
O
Ot-Bu
N
14
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.95
0.94
0.94
0.95
0.97
0.97
0.99
0.98
0.95
0.73
9.00


197.38
164.42
163.31
152.62
152.15
137.59
137.42
133.67
130.97
127.71
127.56
126.36
126.07
124.63
118.77
112.26
82.94
77.43
77.01
76.58
Compound-6c
1H-NMR/CDCl3
OH
O
O
O
N
200
180
160
140
120
100
80
60
40
20
0
ppm

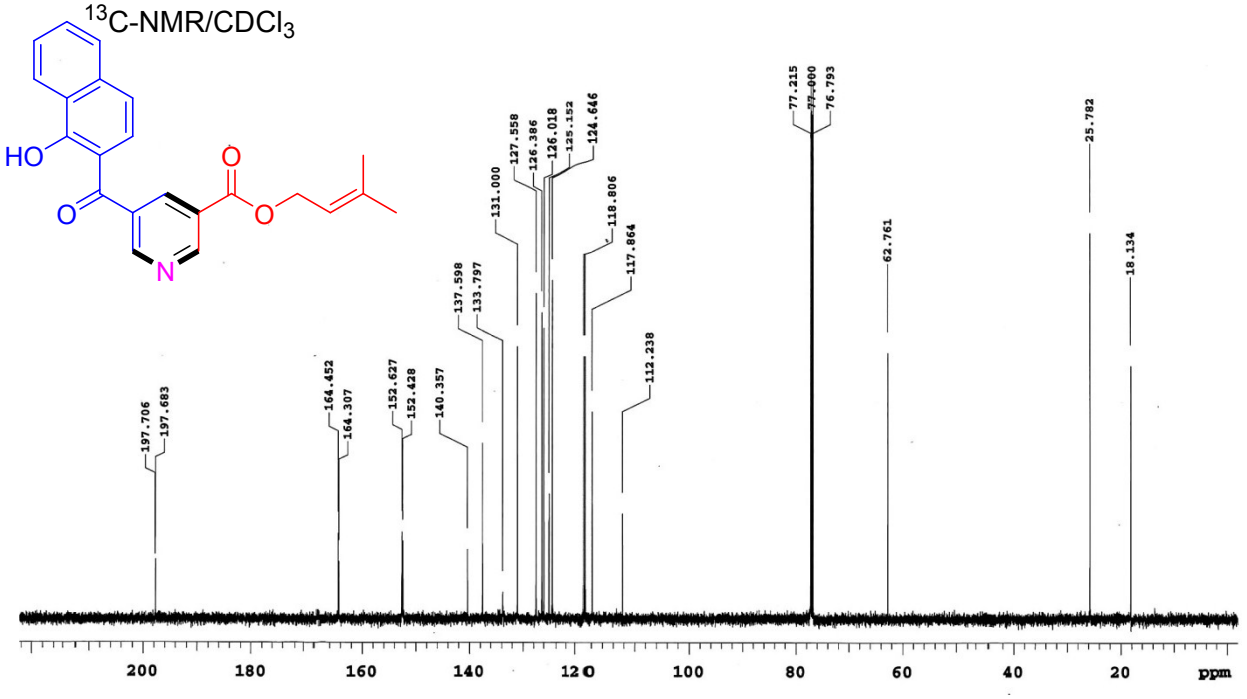
Compound-**6d**

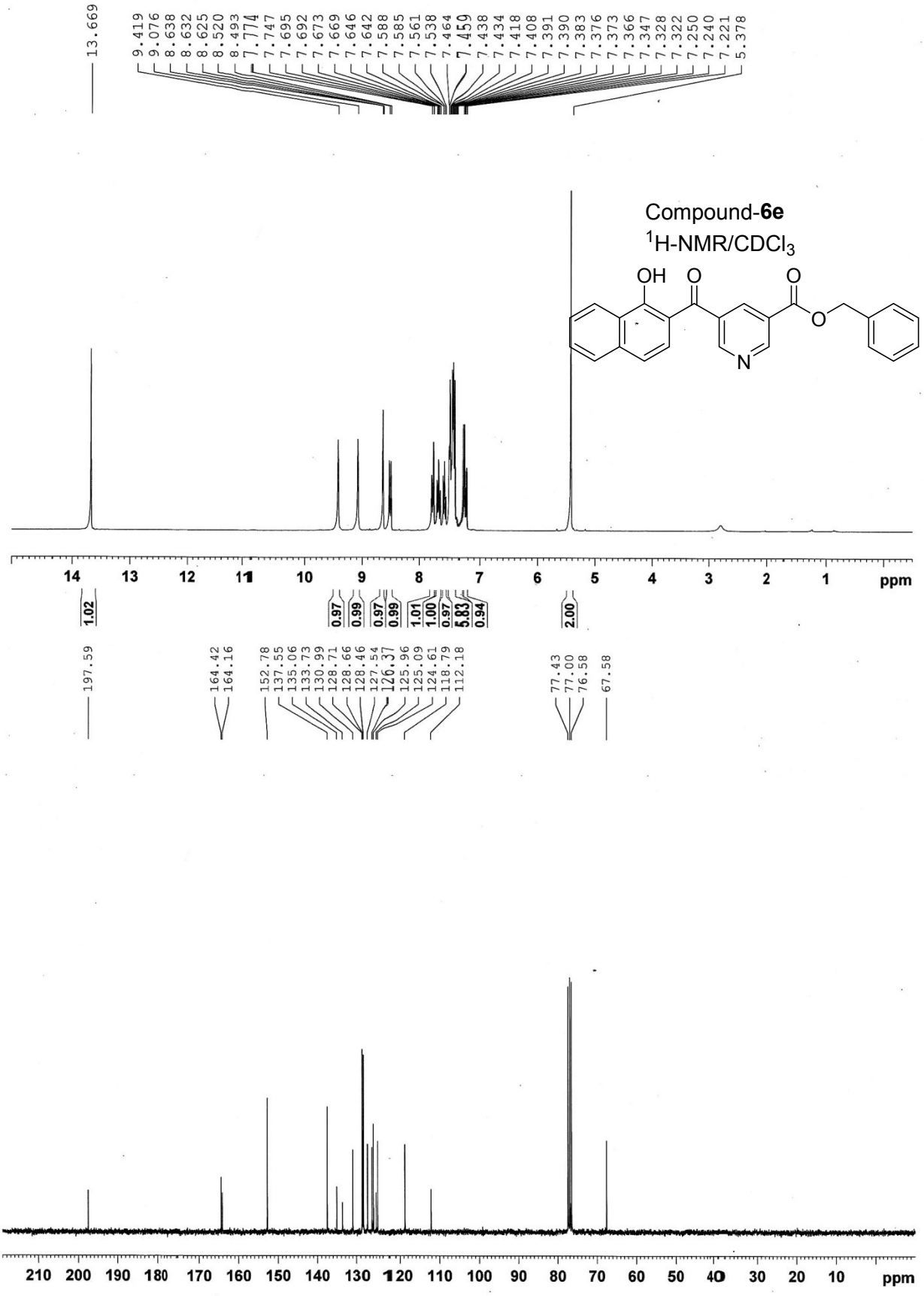
$^{1}$H-NMR/CDCl$_3$




Compound-**6d**

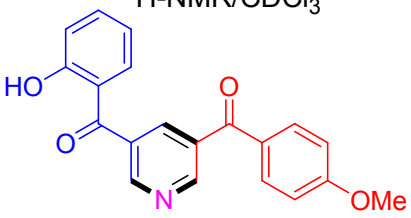
$^{13}$C-NMR/CDCl$_3$

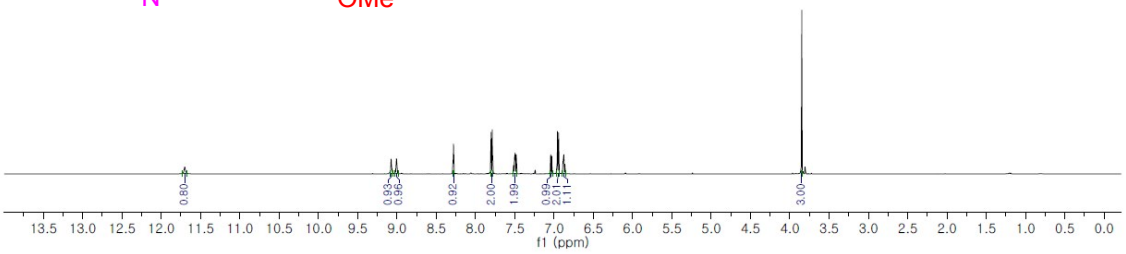


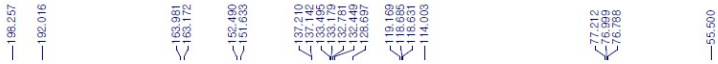

13.669
9.419
9.076
8.638
8.632
8.625
8.520
8.493
7.774
7.747
7.695
7.692
7.673
7.669
7.646
7.642
7.588
7.585
7.561
7.538
7.464
7.459
7.438
7.434
7.418
7.408
7.391
7.390
7.383
7.376
7.373
7.366
7.347
7.328
7.322
7.250
7.240
7.221
5.378
Compound-6e
1H-NMR/CDCl3
OH
O
O
O
N
14
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
1.02
0.97
0.99
0.97
0.99
1.01
1.00
0.97
5.83
0.94
2.00
197.59
164.42
164.16
152.78
137.55
135.06
133.73
130.99
128.71
128.66
128.46
127.54
126.37
125.96
125.09
124.61
118.79
112.18
77.43
77.00
76.58
67.58
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


Compound-**8a**

$^{1}$H-NMR/$CDCl_3$

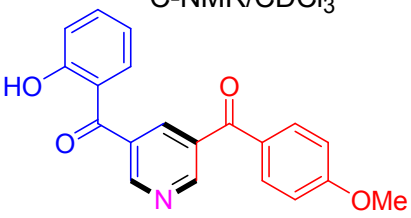


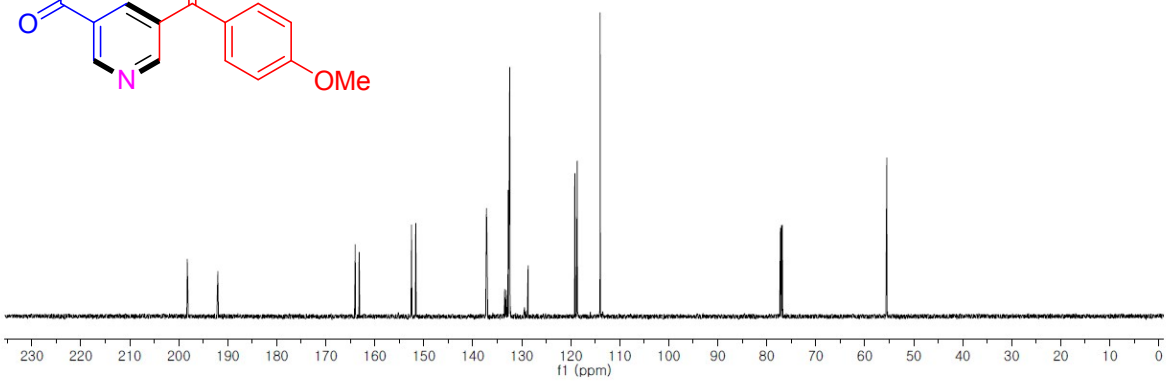




Compound-**8a**

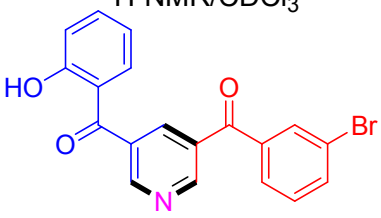
$^{13}$C-NMR/$CDCl_3$

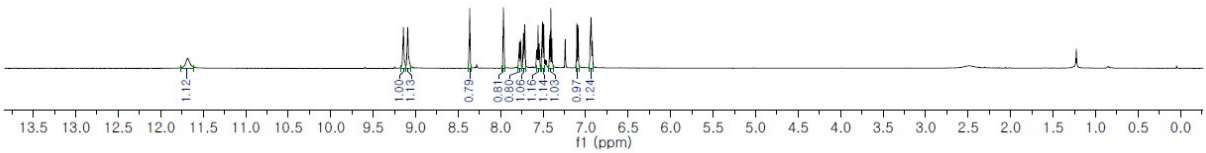



Compound-**8b**

$^{1}$H-NMR/$CDCl_3$

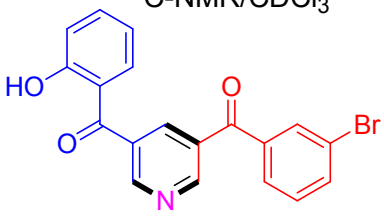


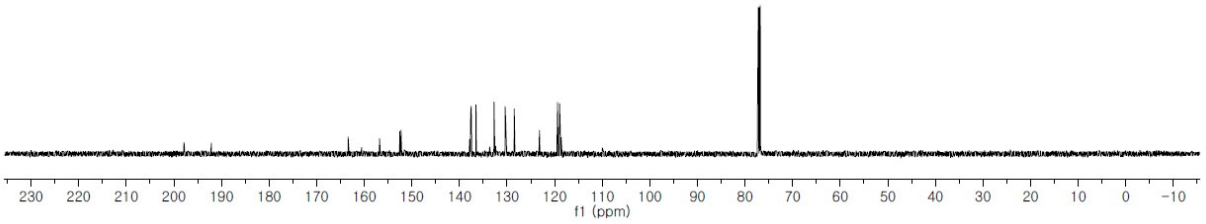





Compound-**8b**

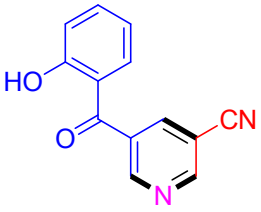
$^{13}$C-NMR/$CDCl_3$

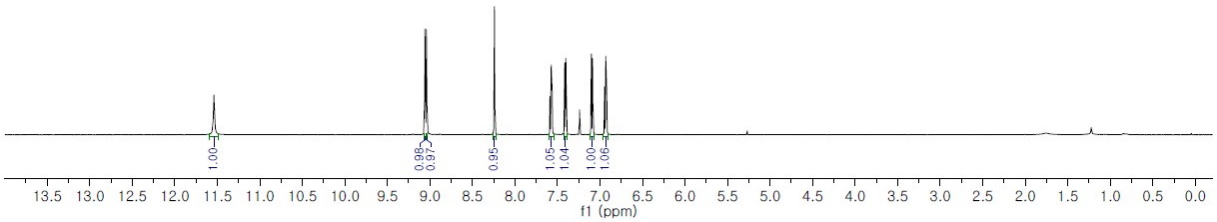


Compound-**8c**

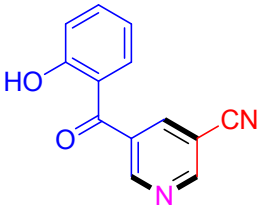
$^{1}$H-NMR/$CDCl_3$

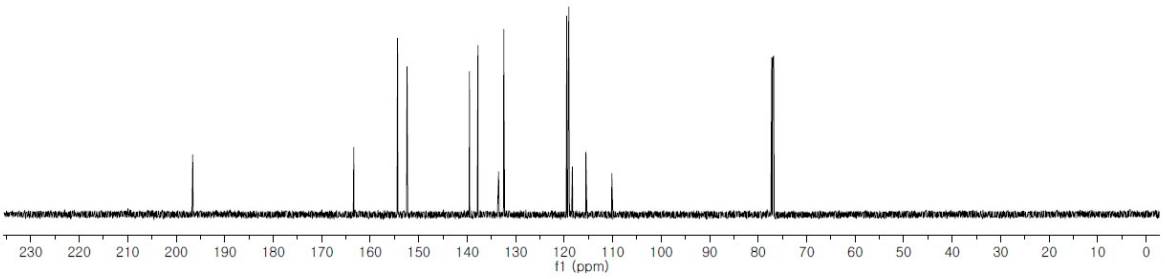



Compound-**8c**

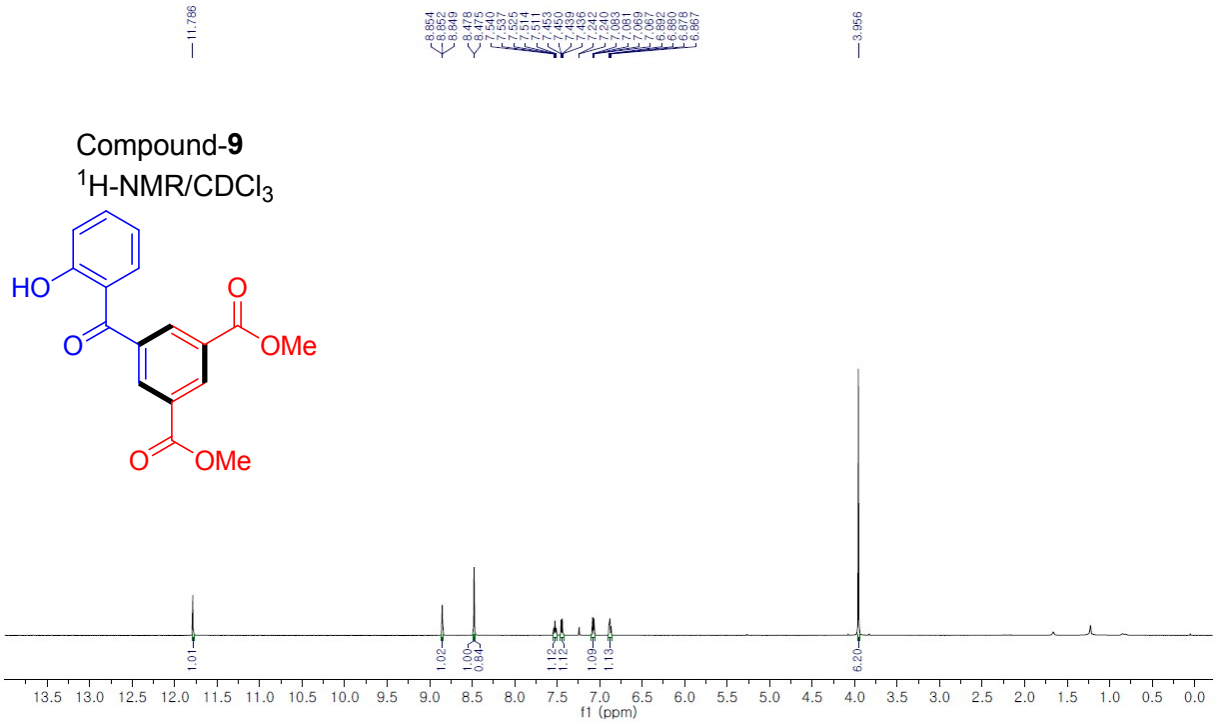
$^{13}$C-NMR/$CDCl_3$



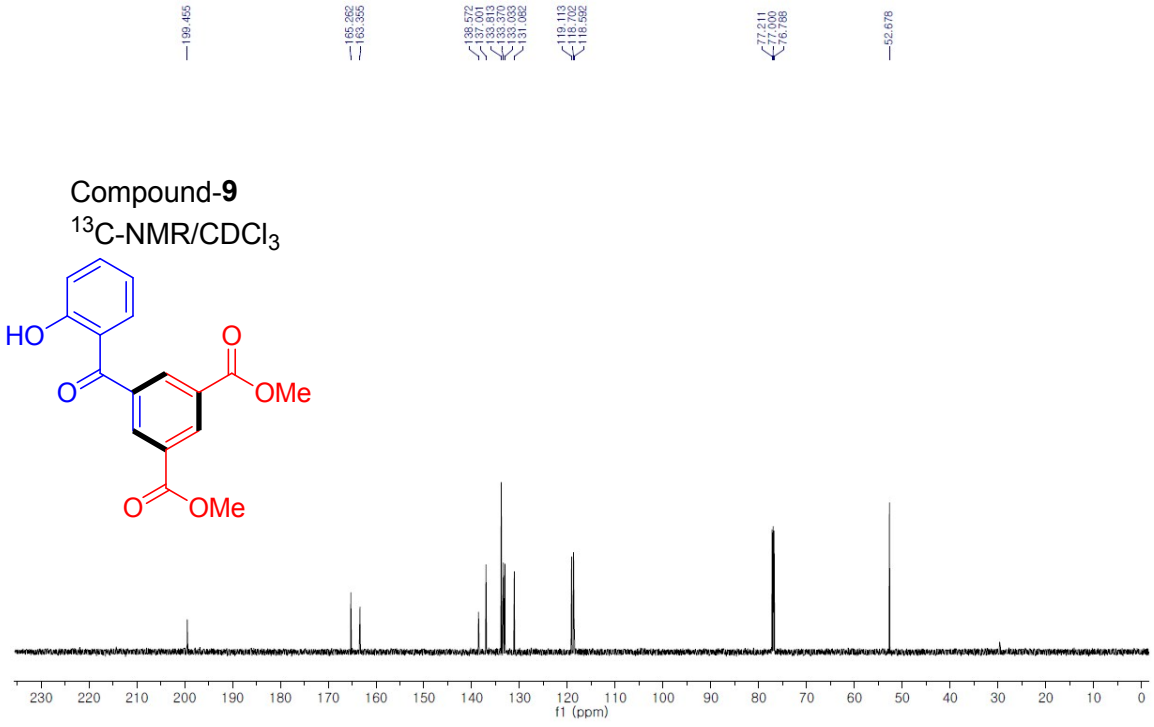
Compound-**9**

$^{1}$H-NMR/$CDCl_3$



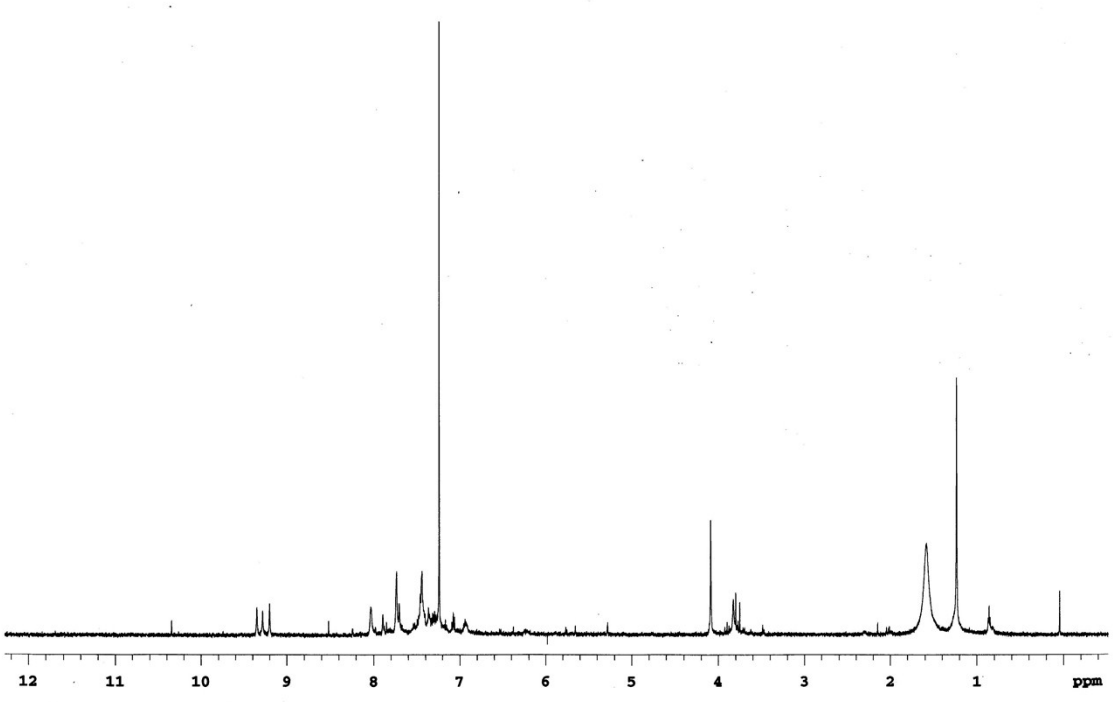

Compound-**9**

$^{13}$C-NMR/$CDCl_3$

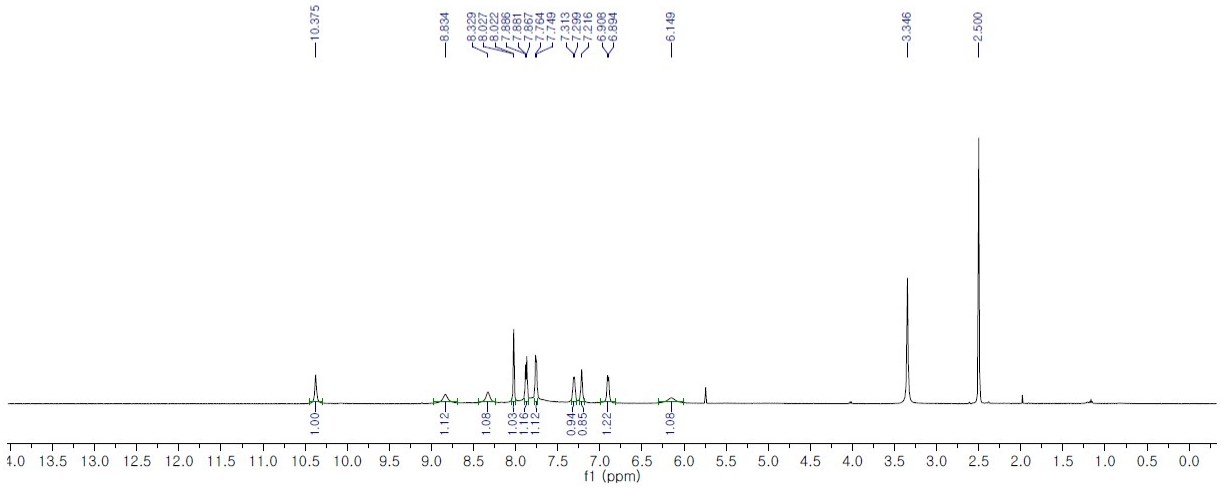


Compound-**12**

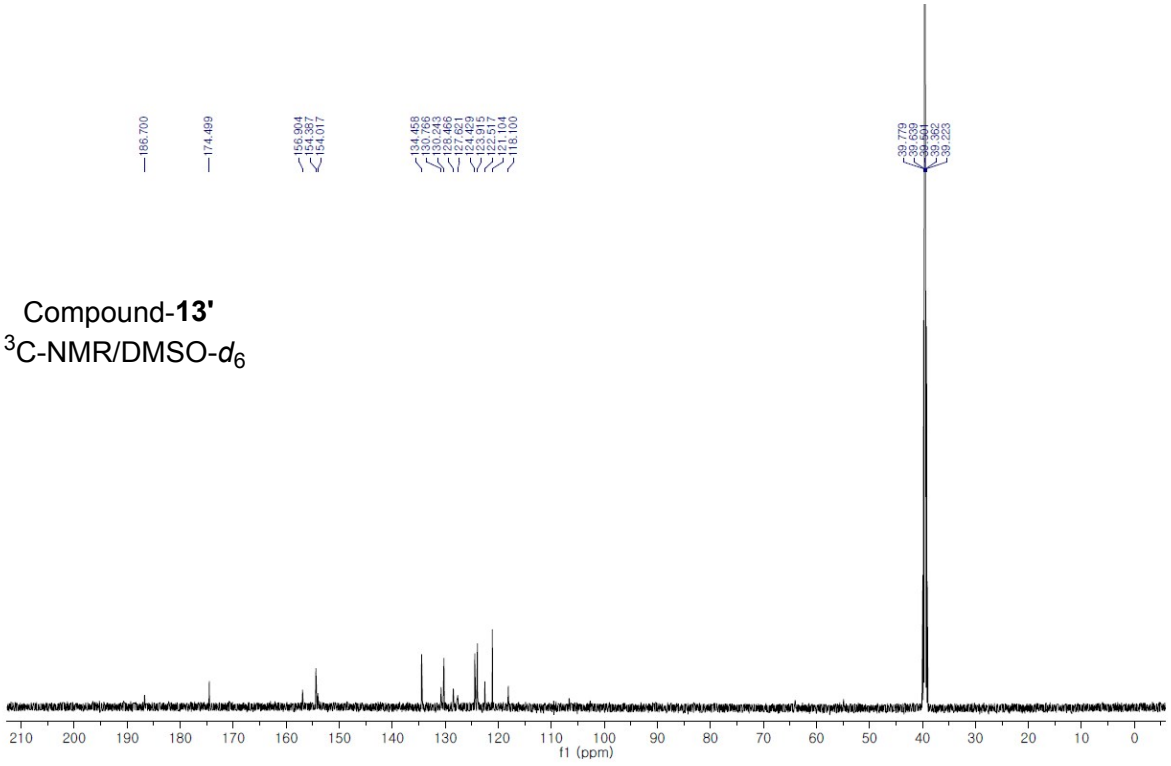
$^{1}$H-NMR/$CDCl_3$



Compound-**13'**
$^{1}$H-NMR/DMSO-$d_6$




Compound-**13'**
$^{13}$C-NMR/DMSO-$d_6$



**Application as UV absorbers *in vitro* procedure**

***Spectrophotometric Measurements***

Optizen UV-3200, a UV-vis spectrophotometer, was used to acquire the absorbance spectra of the tested compounds at room temperature (298K). All samples **4a**, **4m**, **4p**, **4s**, **4u**, **5a-5e**, **6a-6e** and Oxybenzone (OBZ) were prepared in methanol solvent (Sigma-Aldrich, ≥99.8% pure) at a quantified concentration of 50 μM. The data were corrected for solvent background by the instrument's calibration, setting the solvent as blank. As the absorption spectra for the determination of the typical parameter for UV protecting materials (UVA/UVB) is in the range of 290-400nm, the samples absorption spectra were observed in the range of 200-550/290-400 nm. Samples were prepared in 1 cm quartz cell, and readings were taken at an interval of 1nm, evaluated by the data analysis. Crucial parameters used for this sun-protection analysis are UVA/UVB ratio and Critical wavelength ($\lambda_c$). UVA/UVB ratio is a reduction of the complete spectral information to one number, characterizing in some way the shape of the spectrum in terms of the amount of UVA-coverage to that of the amount of UVB-coverage (eq. 1). Critical wavelength ($\lambda_c$) is described as the wavelength at which 90% of the area under the absorbance (290 nm- the approximate lower wavelength limit of terrestrial sunlight to $\lambda_c$) curve resides from 290 to 400 nm (eq. 2).

Eq.1

$$\frac{\int_{320}^{400} A(\lambda)d\lambda / \int_{320}^{400} d\lambda}{\int_{290}^{320} A(\lambda)d\lambda / \int_{290}^{320} d\lambda}$$

Eq.2

$$\int_{290}^{\lambda_c} A(\lambda)d\lambda = 0.90 \int_{290}^{400} A(\lambda)d\lambda$$

**X-Ray crystallographic structure and data of compound 4s:** Empirical Formula- $C_{14}H_{10}BrNO_4$, M = 336.14, Orthorhombic, Space group $P_{bca}$, a = 7.5983(3) Å, b = 16.4240(7) Å, c = 20.8458(8) Å, V = 2601.44(18) Å3, Z = 8, T = 223(2) K, $\rho_{calcd}$ = 1.717 $Mg/m^3$, $2\Theta_{max.}$ = 28.322°, Refinement of 183 parameters on 3232 independent reflections out of 80416 collected reflections ($R_{int}$ = 0.0581) led to $R_1$ = 0.0252 [I >2σ(I)], $wR_2$ = 0.0658 (all data) and S = 1.055 with the largest difference peak and hole of 0.616 and -0.474 e. $Å^{-3}$ respectively. The crystal structure has been deposited at the Cambridge Crystallographic Data Centre (CCDC 1858926). The data can be obtained free of charge via the Internet at www.ccdc.cam.ac.uk/data_request/cif.

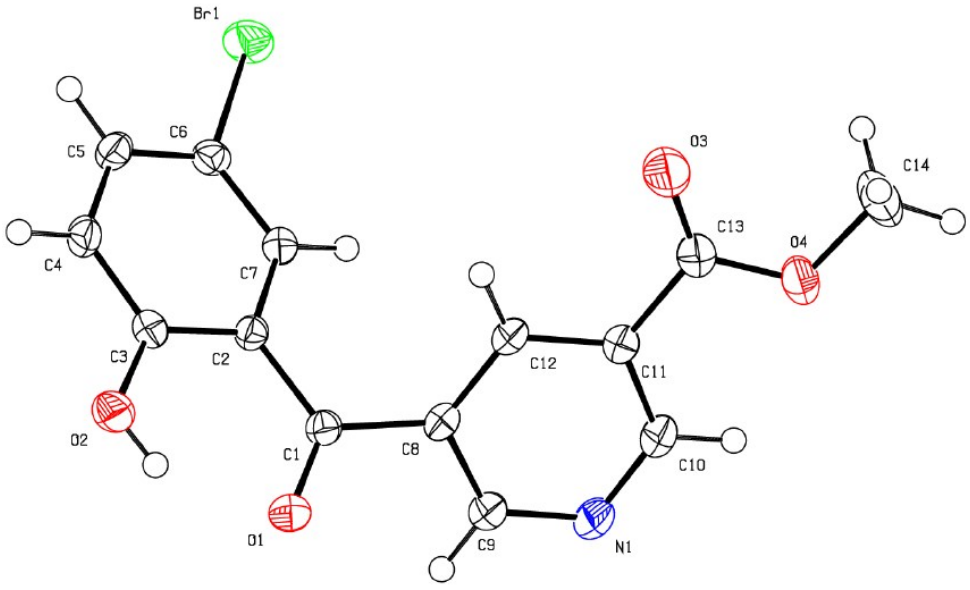



Fig. S1 X-Ray Structure of Compound **4s**.

Table 1. Crystal data and structure refinement for **4s**.

| | | |
|---|---|---|
| Identification code | **4s** | |
| Empirical formula | $C_{14}\ H_{10}\ Br\ N\ O_4$ | |
| Formula weight | 336.14 | |
| Temperature | 223(2) K | |
| Wavelength | 0.71073 Å | |
| Crystal system | Orthorhombic | |
| Space group | Pbca | |
| Unit cell dimensions | a = 7.5983(3) Å | α= 90°. |
| | b = 16.4240(7) Å | β= 90°. |
| | c = 20.8458(8) Å | γ = 90°. |
| Volume | 2601.44(18) $Å^3$ | |
| Z | 8 | |
| Density (calculated) | 1.717 $Mg/m^3$ | |
| Absorption coefficient | 3.173 $mm^{-1}$ | |
| F(000) | 1344 | |
| Crystal size | 0.230 x 0.200 x 0.100 $mm^3$ | |
| Theta range for data collection | 2.480 to 28.322°. | |
| Index ranges | -10<=h<=10, -21<=k<=21, -27<=l<=27 | |
| Reflections collected | 80416 | |
| Independent reflections | 3232 [R(int) = 0.0581] | |
| Completeness to theta = 25.242° | 100.0 % | |
| Absorption correction | Semi-empirical from equivalents | |
| Refinement method | Full-matrix least-squares on $F^2$ | |
| Data / restraints / parameters | 3232 / 0 / 183 | |
| Goodness-of-fit on $F^2$ | 1.055 | |
| Final R indices [I>2sigma(I)] | R1 = 0.0252, wR2 = 0.0607 | |
| R indices (all data) | R1 = 0.0345, wR2 = 0.0658 | |
| Extinction coefficient | n/a | |
| Largest diff. peak and hole | 0.616 and -0.474 $e.Å^{-3}$ | |

Table 2. Atomic coordinates ( x $10^4$) and equivalent isotropic displacement parameters ($Å^2$x $10^3$) for **4s**. U(eq) is defined as one third of the trace of the orthogonalized $U^{ij}$ tensor.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| C(1) | 2742(2) | -92(1) | 4159(1) | 21(1) |
| O(1) | 3349(2) | -780(1) | 4221(1) | 31(1) |
| C(2) | 2118(2) | 376(1) | 4715(1) | 19(1) |
| C(3) | 2588(2) | 126(1) | 5338(1) | 21(1) |
| C(4) | 2093(2) | 594(1) | 5865(1) | 25(1) |
| C(5) | 1052(2) | 1273(1) | 5785(1) | 26(1) |
| C(6) | 498(2) | 1494(1) | 5174(1) | 22(1) |
| C(7) | 1036(2) | 1063(1) | 4643(1) | 21(1) |
| O(2) | 3539(2) | -553(1) | 5453(1) | 29(1) |
| Br(1) | -997(1) | 2405(1) | 5077(1) | 34(1) |
| C(8) | 2683(2) | 268(1) | 3500(1) | 23(1) |
| C(9) | 2113(2) | -222(1) | 2996(1) | 28(1) |
| N(1) | 2119(2) | 12(1) | 2382(1) | 32(1) |
| C(10) | 2754(2) | 753(1) | 2254(1) | 29(1) |
| C(11) | 3376(2) | 1284(1) | 2722(1) | 24(1) |
| C(12) | 3315(2) | 1039(1) | 3359(1) | 24(1) |
| C(13) | 4123(3) | 2097(1) | 2558(1) | 29(1) |
| O(3) | 4564(3) | 2590(1) | 2947(1) | 53(1) |
| O(4) | 4265(2) | 2203(1) | 1930(1) | 39(1) |
| C(14) | 4982(3) | 2978(1) | 1723(1) | 48(1) |

Table 3. Bond lengths [Å] and angles [°] for **4s**.

| | |
|---|---|
| C(1)-O(1)#1 | 1.2260(19) |
| C(1)-O(1) | 1.2260(19) |
| C(1)-C(2) | 1.470(2) |
| C(1)-C(8) | 1.497(2) |
| O(1)-O(1)#1 | 0.000(4) |
| C(2)-C(7) | 1.403(2) |

| | |
|---|---|
| C(2)-C(3) | 1.407(2) |
| C(3)-O(2) | 1.3509(19) |
| C(3)-C(4) | 1.393(2) |
| C(4)-C(5) | 1.377(2) |
| C(4)-H(4) | 0.9400 |
| C(5)-C(6) | 1.391(2) |
| C(5)-H(5) | 0.9400 |
| C(6)-C(7) | 1.376(2) |
| C(6)-Br(1) | 1.8890(16) |
| C(7)-H(7) | 0.9400 |
| O(2)-H(2) | 0.8300 |
| C(8)-C(12) | 1.386(2) |
| C(8)-C(9) | 1.393(2) |
| C(9)-N(1) | 1.336(2) |
| C(9)-H(9) | 0.9400 |
| N(1)-C(10) | 1.336(2) |
| C(10)-C(11) | 1.391(2) |
| C(10)-H(10) | 0.9400 |
| C(11)-C(12) | 1.389(2) |
| C(11)-C(13) | 1.491(2) |
| C(12)-H(12) | 0.9400 |
| C(13)-O(3) | 1.195(2) |
| C(13)-O(4) | 1.326(2) |
| O(4)-C(14) | 1.449(2) |
| C(14)-H(14A) | 0.9700 |
| C(14)-H(14B) | 0.9700 |
| C(14)-H(14C) | 0.9700 |

| | |
|---|---|
| O(1)#1-C(1)-C(2) | 121.40(14) |
| O(1)-C(1)-C(2) | 121.40(14) |
| O(1)#1-C(1)-C(8) | 118.11(14) |
| O(1)-C(1)-C(8) | 118.11(14) |
| C(2)-C(1)-C(8) | 120.48(14) |
| C(7)-C(2)-C(3) | 118.84(14) |
| C(7)-C(2)-C(1) | 121.66(14) |
| C(3)-C(2)-C(1) | 119.49(14) |

| | |
|---|---|
| O(2)-C(3)-C(4) | 117.34(14) |
| O(2)-C(3)-C(2) | 122.78(14) |
| C(4)-C(3)-C(2) | 119.86(14) |
| C(5)-C(4)-C(3) | 120.45(15) |
| C(5)-C(4)-H(4) | 119.8 |
| C(3)-C(4)-H(4) | 119.8 |
| C(4)-C(5)-C(6) | 119.71(15) |
| C(4)-C(5)-H(5) | 120.1 |
| C(6)-C(5)-H(5) | 120.1 |
| C(7)-C(6)-C(5) | 120.86(15) |
| C(7)-C(6)-Br(1) | 120.04(12) |
| C(5)-C(6)-Br(1) | 119.10(12) |
| C(6)-C(7)-C(2) | 120.08(14) |
| C(6)-C(7)-H(7) | 120.0 |
| C(2)-C(7)-H(7) | 120.0 |
| C(3)-O(2)-H(2) | 109.5 |
| C(12)-C(8)-C(9) | 118.42(15) |
| C(12)-C(8)-C(1) | 123.03(14) |
| C(9)-C(8)-C(1) | 118.28(15) |
| N(1)-C(9)-C(8) | 123.74(16) |
| N(1)-C(9)-H(9) | 118.1 |
| C(8)-C(9)-H(9) | 118.1 |
| C(10)-N(1)-C(9) | 116.99(15) |
| N(1)-C(10)-C(11) | 123.70(16) |
| N(1)-C(10)-H(10) | 118.2 |
| C(11)-C(10)-H(10) | 118.2 |
| C(12)-C(11)-C(10) | 118.51(15) |
| C(12)-C(11)-C(13) | 119.44(15) |
| C(10)-C(11)-C(13) | 122.04(15) |
| C(8)-C(12)-C(11) | 118.61(15) |
| C(8)-C(12)-H(12) | 120.7 |
| C(11)-C(12)-H(12) | 120.7 |
| O(3)-C(13)-O(4) | 124.00(17) |
| O(3)-C(13)-C(11) | 123.93(17) |
| O(4)-C(13)-C(11) | 112.06(15) |
| C(13)-O(4)-C(14) | 116.06(15) |

| | |
|---|---|
| O(4)-C(14)-H(14A) | 109.5 |
| O(4)-C(14)-H(14B) | 109.5 |
| H(14A)-C(14)-H(14B) | 109.5 |
| O(4)-C(14)-H(14C) | 109.5 |
| H(14A)-C(14)-H(14C) | 109.5 |
| H(14B)-C(14)-H(14C) | 109.5 |

Symmetry transformations used to generate equivalent atoms:

#1 x,y,z

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for **4s**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

| | $U^{11}$ | $U^{22}$ | $U^{33}$ | $U^{23}$ | $U^{13}$ | $U^{12}$ |
|---|---|---|---|---|---|---|
| C(1) | 22(1) | 21(1) | 21(1) | -1(1) | 2(1) | -2(1) |
| O(1) | 41(1) | 23(1) | 28(1) | -1(1) | 6(1) | 6(1) |
| C(2) | 20(1) | 20(1) | 18(1) | -1(1) | 2(1) | -1(1) |
| C(3) | 21(1) | 21(1) | 22(1) | 3(1) | -1(1) | -2(1) |
| C(4) | 32(1) | 27(1) | 17(1) | 1(1) | -1(1) | -4(1) |
| C(5) | 30(1) | 26(1) | 21(1) | -4(1) | 6(1) | -3(1) |
| C(6) | 21(1) | 19(1) | 26(1) | 0(1) | 4(1) | 1(1) |
| C(7) | 21(1) | 21(1) | 20(1) | 1(1) | 0(1) | -1(1) |
| O(2) | 36(1) | 24(1) | 28(1) | 3(1) | -5(1) | 7(1) |
| Br(1) | 34(1) | 27(1) | 43(1) | 0(1) | 5(1) | 11(1) |
| C(8) | 26(1) | 25(1) | 19(1) | -3(1) | 4(1) | 2(1) |
| C(9) | 35(1) | 24(1) | 23(1) | -3(1) | 4(1) | -4(1) |
| N(1) | 45(1) | 31(1) | 21(1) | -6(1) | 0(1) | -6(1) |
| C(10) | 38(1) | 31(1) | 19(1) | -2(1) | 2(1) | -2(1) |
| C(11) | 28(1) | 24(1) | 22(1) | -1(1) | 4(1) | -1(1) |
| C(12) | 30(1) | 25(1) | 18(1) | -4(1) | 2(1) | -1(1) |
| C(13) | 33(1) | 28(1) | 25(1) | 2(1) | 1(1) | -1(1) |
| O(3) | 91(1) | 37(1) | 31(1) | -2(1) | -5(1) | -25(1) |
| O(4) | 58(1) | 32(1) | 26(1) | 6(1) | 2(1) | -11(1) |
| C(14) | 65(2) | 36(1) | 42(1) | 16(1) | -4(1) | -12(1) |

Table 5. Hydrogen coordinates ( x $10^4$) and isotropic displacement parameters (Å$^2$x $10^3$) for **4s**.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| H(4) | 2471 | 445 | 6278 | 30 |
| H(5) | 718 | 1586 | 6143 | 31 |
| H(7) | 677 | 1228 | 4231 | 25 |
| H(2) | 3672 | -810 | 5114 | 44 |
| H(9) | 1701 | -748 | 3093 | 33 |
| H(10) | 2781 | 925 | 1824 | 35 |
| H(12) | 3696 | 1388 | 3688 | 29 |
| H(14A) | 4308 | 3417 | 1914 | 72 |
| H(14B) | 4918 | 3016 | 1260 | 72 |
| H(14C) | 6200 | 3019 | 1858 | 72 |

Table 6. Torsion angles [°] for **4s**.

| | |
|---|---|
| C(2)-C(1)-O(1)-O(1)#1 | 0.00(6) |
| C(8)-C(1)-O(1)-O(1)#1 | 0.00(4) |
| O(1)#1-C(1)-C(2)-C(7) | -163.79(16) |
| O(1)-C(1)-C(2)-C(7) | -163.79(16) |
| C(8)-C(1)-C(2)-C(7) | 17.5(2) |
| O(1)#1-C(1)-C(2)-C(3) | 15.1(2) |
| O(1)-C(1)-C(2)-C(3) | 15.1(2) |
| C(8)-C(1)-C(2)-C(3) | -163.68(15) |
| C(7)-C(2)-C(3)-O(2) | 176.04(15) |
| C(1)-C(2)-C(3)-O(2) | -2.8(2) |
| C(7)-C(2)-C(3)-C(4) | -5.0(2) |
| C(1)-C(2)-C(3)-C(4) | 176.14(15) |
| O(2)-C(3)-C(4)-C(5) | -176.89(15) |
| C(2)-C(3)-C(4)-C(5) | 4.1(2) |
| C(3)-C(4)-C(5)-C(6) | -0.2(3) |

| | |
|---|---|
| C(4)-C(5)-C(6)-C(7) | -2.7(3) |
| C(4)-C(5)-C(6)-Br(1) | 177.75(13) |
| C(5)-C(6)-C(7)-C(2) | 1.7(2) |
| Br(1)-C(6)-C(7)-C(2) | -178.74(12) |
| C(3)-C(2)-C(7)-C(6) | 2.1(2) |
| C(1)-C(2)-C(7)-C(6) | -179.04(15) |
| O(1)#1-C(1)-C(8)-C(12) | -130.04(18) |
| O(1)-C(1)-C(8)-C(12) | -130.04(18) |
| C(2)-C(1)-C(8)-C(12) | 48.7(2) |
| O(1)#1-C(1)-C(8)-C(9) | 44.0(2) |
| O(1)-C(1)-C(8)-C(9) | 44.0(2) |
| C(2)-C(1)-C(8)-C(9) | -137.26(16) |
| C(12)-C(8)-C(9)-N(1) | -0.9(3) |
| C(1)-C(8)-C(9)-N(1) | -175.18(17) |
| C(8)-C(9)-N(1)-C(10) | 1.7(3) |
| C(9)-N(1)-C(10)-C(11) | -0.8(3) |
| N(1)-C(10)-C(11)-C(12) | -0.9(3) |
| N(1)-C(10)-C(11)-C(13) | 178.17(18) |
| C(9)-C(8)-C(12)-C(11) | -0.9(2) |
| C(1)-C(8)-C(12)-C(11) | 173.12(15) |
| C(10)-C(11)-C(12)-C(8) | 1.7(3) |
| C(13)-C(11)-C(12)-C(8) | -177.40(16) |
| C(12)-C(11)-C(13)-O(3) | -6.0(3) |
| C(10)-C(11)-C(13)-O(3) | 174.9(2) |
| C(12)-C(11)-C(13)-O(4) | 173.11(16) |
| C(10)-C(11)-C(13)-O(4) | -6.0(3) |
| O(3)-C(13)-O(4)-C(14) | -0.8(3) |
| C(11)-C(13)-O(4)-C(14) | -179.94(17) |

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Symmetry transformations used to generate equivalent atoms:

#1 x,y,z

Table 7. Hydrogen bonds for **4s** [Å and °].

| D-H...A | d(D-H) | d(H...A) | d(D...A) | <(DHA) |
|---|---|---|---|---|
| O(2)-H(2)...O(1)#1 | 0.83 | 1.88 | 2.6002(17) | 144.6 |

Symmetry transformations used to generate equivalent atoms:

#1 x,y,z