

Supporting Information 2

Dihydroindeno[1,2-*b*]pyrroles: New Al³⁺ selective off-on chemosensors for bio-imaging in living HepG2 cell

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Experimental Section

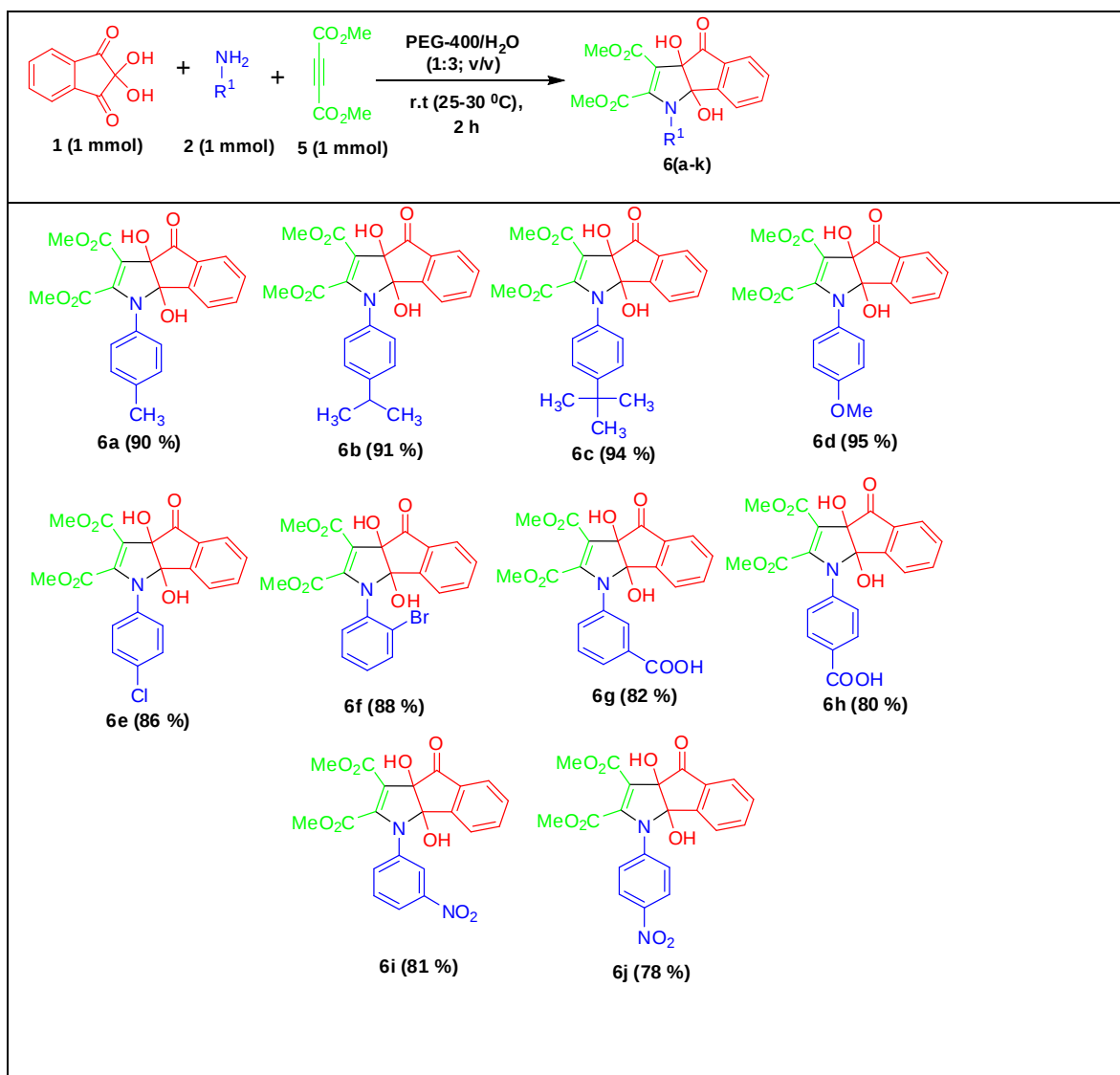
General information of materials and instruments:

All commercially available chemicals were purchased from Aldrich, USA or Spectrochem, India, and used without further purification. All solvents were used as received. All the reactions were performed in a round-bottomed flask with magnetic stir bar at room temperature (25-30⁰C) without taking precautions to exclude air and moisture. The progress of the reaction was checked by glass sheets pre-coated TLC with silica gel (with binder, 300 mesh, Spectrochem) and column chromatography was performed using silica gel (60-120 mesh). ¹H /¹³C NMR spectra were recorded in a 300 MHz Bruker instrument using CDCl₃, DMSO-d₆ solvent with TMS as reference. HRMS with an ESI resource were acquired using a Waters XEVO-G2S Q TOF mass spectrometer. 2400 Series II CHNS Analyzer, Perkin Elmer USA was used for elemental analyses. Melting points were recorded with an open capillary on an electrical melting point apparatus. IR experiment was performed using KBr pellets on Perkin Elmer RX-1 FTIR spectrophotometer and the single crystal structure of the synthesized compounds were confirmed by an X-ray crystallography experiment on a Bruker SMART diffractometer.

General procedure for synthesis of Novel Dihydroindeno[1,2-b]pyrroles derivatives:

A mixture of ninhydrin (1 mmol), acetylenedicarboxylates (1 mmol) and amines (1 mmol) were taken in PEG/H₂O in 1:3 (v/v) ratio (5 mL) and stirred for 2 hour at room temperature (25-30⁰C). The completion of the reaction indicated by thin layer chromatography (TLC) using aluminium plates coated with silica gel (Merck). After the completion of the reaction, the mixture was diluted with ethyl acetate. As a result bilayer formations take place and the organic crude product was separated from the PEG-H₂O system and comes into organic layer. The lower part (contain PEG-H₂O) of the bilayer was separated using separating funnel and it is reused for the next cycle as solvent system. Other part of the solution was evaporated in a rotary evaporator. Finally, the crude residue was subjected to column chromatography to afford the desired product as solid using 20 % ethyl acetate in petroleum ether (60-80 °C) as eluant. Some of the synthesised compounds have been purified by preparative TLC rather than the column chromatography, as it increases the green impact of the methodology. All the obtained products were characterized by IR, ¹H/¹³C NMR, melting point measurements, CHN. HRMS of some compounds are given.

Table 3. Structures of synthesized dihydroindeno[1,2-b]pyrroles 6(a-j)^a



^a**Reaction conditions:** The reaction was conducted with ninhydrin (1 mmol) and dimethylacetylenedicarboxylate (1 mmol) with different amines (1 mmol) under the optimized condition.

Spectroscopic and Analytical characterization of compounds 4a-4n:

Diethyl 3a,8b-dihydroxy-4-oxo-1-phenyl-1,3a,4,8b-tetrahydroindeno[1,2-b]pyrrole-2,3-dicarboxylate (4a): Yield 90 % (381 mg); white solid; Mp: 130°C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.56; IR ($\nu_{\max}$, KBr, cm^{-1}): 3393, 2980, 1723, 1667, 1574, 1495, 1264, 1023, 761; ^1H NMR (300 MHz, CDCl_3) δ_{H} : 7.89-7.86 (m, 1H, Ar-H), 7.49-7.47 (m, 2H, ArH), 7.39-7.34 (m, 3H, ArH), 7.30-7.29 (m, 1H, ArH), 6.80-6.77 (m, 1H, ArH), 5.15(broad-s, 2H, OH), 4.18(q, $J=7.1$ Hz, 2H, OCH_2), 4.07(q, $J=7.2$ Hz, 2H, OCH_2) 1.24 (t, $J=7.1$ Hz, 3H, CH_3), 1.00 (t, $J=7.2$ Hz, 3H, CH_3); ^{13}C NMR (75 MHz, CDCl_3) δ_{C} : 197.2, 163.8, 161.3, 151.1, 147.1, 135.9, 135.5, 135.1, 130.5, 129.4, 129.1, 129.0, 128.9, 128.6, 125.0, 124.6, 97.8, 95.6, 83.5, 62.3, 60.2, 22.6, 14.3, 13.6; Anal. calcd. for $\text{C}_{23}\text{H}_{21}\text{NO}_7$; C: 65.24; H: 5.00; N: 3.31. Found: C: 65.32 H: 5.05; N: 3.32%.

Diethyl 3a,8b-dihydroxy-4-oxo-1-m-tolyl-1,3a,4,8b-tetrahydroindeno[1,2-b]pyrrole-2,3-dicarboxylate (4b): Yield 91% (398 mg); white solid; Mp: 168°C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.54; IR ($\nu_{\max}$, KBr, cm^{-1}): 3487, 3329, 2897, 1758, 1734, 1516, 1445, 1128, 956; ^1H NMR (300 MHz, CDCl_3) δ_{H} : 7.81-7.79 (m, 1H, Ar-H), 7.43-7.40 (m, 2H, ArH), 7.20-7.07 (m, 3H, ArH), 6.99-6.96 (m, 1H, ArH), 6.76-6.73 (m, 1H, ArH), 5.03(broad-s, 2H, OH), 4.17-3.98 (m, 4H, OCH_2), 2.26 (s, 3H, Ar- CH_3), 1.17 (t, $J=7.2$ Hz, 3H, CH_3), 0.95 (t, $J=6.9$ Hz, 3H, CH_3); ^{13}C NMR (75 MHz, CDCl_3) δ_{C} : 197.3, 163.9, 161.3, 151.2, 147.1, 139.0, 135.9, 135.4, 130.4, 129.3, 129.2, 128.8, 125.8, 125.0, 124.6, 97.7, 95.6, 95.5, 83.6, 83.5, 62.2, 60.2, 21.3, 14.3, 13.6; Anal. calcd. for $\text{C}_{24}\text{H}_{23}\text{NO}_7$; C: 65.90; H: 5.30; N: 3.20. Found: C: 65.96 H: 5.32; N: 3.21%.

Diethyl 3a,8b-dihydroxy-4-oxo-1-p-tolyl-1,3a,4,8b-tetrahydroindeno[1,2-b]pyrrole-2,3-dicarboxylate (4c): Yield 93% (407 mg); white solid; Mp: 168-170 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.50; IR ($\nu_{\max}$, KBr, cm^{-1}): 3479, 3325, 2981, 1751, 1721, 1514, 1439, 1028, 963; ^1H NMR (300 MHz, CDCl_3) δ_{H} : 7.90-7.87 (m, 1H, Ar-H), 7.51-7.48 (m, 2H, ArH), 7.17-7.14 (m, 4H, ArH), 6.86-6.83 (m, 1H, ArH), 5.07(broad-s, 2H, OH), 4.28-4.20 (m, 2H, OCH_2), 4.18-4.05 (m, 2H, OCH_2), 2.39 (s, 3H, Ar- CH_3), 1.25 (t, $J=7.2$ Hz, 3H, CH_3), 1.04 (t, $J=7.2$ Hz, 3H, CH_3); ^{13}C NMR (75 MHz, CDCl_3) δ_{C} : 197.2, 163.8, 161.2, 151.3, 147.1, 138.6, 135.4, 135.1, 133.0, 130.4, 129.6, 128.7, 125.0, 124.5, 97.3, 95.4, 83.4, 62.2, 60.1, 21.1, 14.2, 13.5; Anal. calcd. for $\text{C}_{24}\text{H}_{23}\text{NO}_7$; C: 65.90; H: 5.30; N: 3.20. Found: C: 65.98 H: 5.35; N: 3.22%.

Diethyl 3a,8b-dihydroxy-1-(4-isopropylphenyl)-4-oxo-1,3a,4,8b-tetrahydroindeno[1,2-b]pyrrole-2,3-dicarboxylate (4d): Yield 92 % (428 mg); white solid; Mp: 186-188 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.59; IR ($\nu_{\max}$, KBr, cm^{-1}): 3443, 3378, 1726, 1676, 1498, 1267, 1218, 1128, 762; ^1H NMR (300 MHz, CDCl_3) δ_{H} : 7.92-7.90 (m, 1H, Ar-H), 7.56-7.51 (m, 2H, ArH), 7.28-7.18 (m, 4H, ArH), 6.88-6.85 (m, 1H, ArH), 4.93 (s, 1H, OH), 4.78 (s, 1H, OH), 4.29-4.19 (m, 2H, OCH_2), 4.17-4.08 (m, 2H, OCH_2), 2.99-2.94 (m, 1H, CH), 1.30-1.26 (m, 9H, CH_3), 1.00 (t, $J=7.2$ Hz, 3H, CH_3); ^{13}C NMR (75 MHz, CDCl_3) δ_{C} : 197.1, 163.8, 161.2, 151.4, 149.6, 147.2, 135.5, 135.2, 133.2, 130.4, 128.9, 126.9, 124.9, 124.2, 97.2, 95.4, 83.4, 62.2, 60.2, 33.8, 23.9, 23.8, 14.3, 13.5; Anal. calcd. for $\text{C}_{26}\text{H}_{27}\text{NO}_7$; C: 67.09; H: 5.85; N: 3.01. Found: C: 67.18 H: 5.90; N: 3.01%.

Diethyl 1-(4-tert-butylphenyl)-3a,8b-dihydroxy-4-oxo-1,3a,4,8b-tetrahydroindeno[1,2-b]pyrrole-2,3-dicarboxylate (4e): Yield 91 % (436 mg); white solid; Mp: 176°C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.60; IR ($\nu_{\max}$, KBr, cm^{-1}): 3392, 3180, 1728, 1695, 1492, 1269, 1218, 1138, 763; ^1H NMR (300 MHz, CDCl_3) δ_{H} : 7.94-7.71 (m, 1H, Ar-H), 7.58-7.53 (m, 2H, ArH), 7.44-7.41 (m, 2H, ArH), 7.24-7.21 (m, 2H, ArH), 6.90-6.87 (m, 1H, ArH), 4.85 (broad-s, 2H, OH), 4.29-4.20 (m, 2H, $-\text{OCH}_2$), 4.19-4.06 (m, 2H, $-\text{OCH}_2$), 1.37 (s, 9H, CH_3), 1.29 (t, $J=3.6$ Hz, 3H, CH_3), 1.00 (t, $J=7.1$ Hz, 3H, CH_3); ^{13}C NMR (75 MHz, CDCl_3) δ_{C} : 197.1, 163.9, 161.2, 151.9, 151.4, 147.2, 135.6, 135.2, 133.0, 130.4, 128.6, 125.9, 125.8, 125.0, 124.7, 97.2, 95.4, 83.4, 62.2, 60.2, 60.1, 34.7, 31.3, 31.1, 14.3, 13.6, 13.5; Anal. calcd. for $\text{C}_{27}\text{H}_{29}\text{NO}_7$; C: 67.63; H: 6.10; N: 2.92. Found: C: 67.69; H: 6.14; N: 2.93%.

Diethyl 1-(3,4-dimethylphenyl)-3a,8b-dihydroxy-4-oxo-1,3a,4,8b-tetrahydroindeno[1,2-b]pyrrole-2,3-dicarboxylate (4f): Yield 95 % (429 mg); white solid; Mp: 172 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.52; IR ($\nu_{\max}$, KBr, cm^{-1}): 3392, 3175, 1729, 1698, 1628, 1468, 1224, 1134, 765; ^1H NMR (300 MHz, CDCl_3) δ_{H} : 7.87-7.84 (m, 1H, Ar-H), 7.50-7.46 (m, 2H, ArH), 7.09 (d, $J=8.1$ Hz, 2H, ArH), 6.96-6.93 (m, 1H, ArH), 6.87-6.83 (m, 1H, Ar-H), 5.00 (broad-s, 2H, OH), 4.23-4.05 (m, 4H, OCH_2), 2.24 (d, $J=15.3$ Hz, 6H, Ar- CH_3), 1.23 (t, $J=7.2$ Hz, 3H, CH_3), 1.03 (t, $J=7.2$ Hz, 3H, CH_3); ^{13}C NMR (75 MHz, CDCl_3) δ_{C} : 197.2, 163.8, 161.2, 151.3, 147.1, 137.3, 137.1, 135.3, 135.0, 133.2, 130.3, 129.6, 126.0, 125.0, 124.4, 97.1, 95.4, 83.4, 62.1, 59.9, 19.6, 19.4, 14.2, 13.5; Anal. calcd. for $\text{C}_{25}\text{H}_{25}\text{NO}_7$; C: 66.51; H: 5.58; N: 3.10. Found: C: 66.45 H: 5.54; N: 3.09%; HRMS (ESI) calcd for $\text{C}_{25}\text{H}_{25}\text{NO}_7$: 474.1529 ($\text{M}+\text{Na}$) $^+$; found: 474.1542

Diethyl 3a,8b-dihydroxy-1-(4-methoxyphenyl)-4-oxo-1,3a,4,8b-tetrahydroindeno[1,2-b]pyrrole-2,3-dicarboxylate (4g): Yield 97 % (440 mg); white solid; Mp: 136 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.51; IR ($\nu_{\max}$, KBr, cm^{-1}): 3417, 2981, 1728, 1513, 1445, 1293, 1250, 1161, 770; ^1H NMR (300 MHz, CDCl_3) δ_{H} : 7.59-7.56 (m, 1H, Ar-H), 7.25-7.17(m, 2H, ArH), 7.03-6.90 (m, 2H, ArH), 6.62-6.59(m, 3H, ArH), 5.18(broad-s, 2H, OH), 3.96-3.75(m, 4H, OCH_2), 2.39(s, 3H, Ar- CH_3), 3.54(s, 3H, OMe), 0.93 (t, $J=7.2$ Hz, 3H, CH_3), 0.74 (t, $J=7.2$ Hz, 3H, CH_3); ^{13}C NMR (75 MHz, CDCl_3) δ_{C} : 197.2, 163.7, 161.2, 159.5, 151.4, 147.0, 135.2, 135.0, 1330.5, 130.2, 127.8, 124.9, 124.3, 113.9, 96.7, 95.4, 83.4, 62.0, 59.9, 55.2, 14.0, 13.4; Anal. calcd. for $\text{C}_{24}\text{H}_{23}\text{NO}_8$; C: 63.57; H: 5.11; N: 3.09. Found: C: 63.65 H: 5.20; N: 3.11%;

Diethyl 1-(4-chlorophenyl)-3a,8b-dihydroxy-4-oxo-1,3a,4,8b-tetrahydroindeno[1,2-b]pyrrole-2,3-dicarboxylate (4h): Yield 87 % (398 mg); white solid; Mp: 176 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.49; IR ($\nu_{\max}$, KBr, cm^{-1}): 3424, 2953, 1722, 1576, 1444, 1276, 1162, 776; ^1H NMR (300 MHz, CDCl_3) δ_{H} : 7.75 (t, $J=4.4$ Hz, 1H, Ar-H), 7.39(t, $J=3.6$ Hz, 2H, ArH), 7.25-7.13 (m, 4H, ArH), 6.73-6.70(m, 1H, ArH), 5.39-5.26(broad-s, 2H, OH), 4.10-3.94(m, 4H, OCH_2), 1.10 (t, $J=7.2$ Hz, 3H, CH_3), 0.93 (t, $J=7.2$ Hz, 3H, CH_3); ^{13}C NMR (75 MHz, CDCl_3) δ_{C} : 196.7, 163.3, 160.9, 150.3, 146.6, 135.3, 134.7, 134.2, 134.1, 130.2, 129.9, 128.9, 124.4, 98.1, 95.4, 83.2, 62.1, 60.0, 13.9, 13.3; Anal. calcd. for $\text{C}_{23}\text{H}_{20}\text{ClNO}_7$; C: 60.33; H: 4.40; N: 3.06. Found: C: 60.41 H: 4.43; N: 3.07%;

Diethyl 1-(4-bromophenyl)-3a,8b-dihydroxy-4-oxo-1,3a,4,8b-tetrahydroindeno[1,2-b]pyrrole-2,3-dicarboxylate(4i): Yield 89% (447 mg); white solid; Mp: 176-178 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.50; IR ($\nu_{\max}$, KBr, cm^{-1}): 3414, 3178, 2199, 1734, 1695, 1495, 1293, 1126, 760; ^1H NMR (300 MHz, CDCl_3) δ_{H} : 7.92-7.89 (m, 1H, Ar-H), 7.55-7.53(m, 4H, ArH), 7.28-7.19 (m, 2H, ArH), 6.87-6.83(m, 1H, ArH), 4.99(broad-s, 2H, OH), 4.28-4.09(m, 4H, OCH_2), 1.28 (t, $J=7.2$ Hz, 3H, CH_3), 1.10 (t, $J=7.2$ Hz, 3H, CH_3); ^{13}C NMR (75 MHz, CDCl_3) δ_{C} : 196.9, 163.6, 161.0, 150.5, 146.9, 135.7, 135.1, 135.0, 132.3, 130.6, 130.2, 124.8, 124.7, 122.5, 98.6, 95.5, 83.3, 62.5, 60.4, 14.2, 13.7; Anal. calcd. for $\text{C}_{23}\text{H}_{20}\text{BrNO}_7$; C: 54.99; H: 4.01; N: 2.79. Found: C: 54.96 H: 4.00; N: 2.78%; HRMS (ESI) calcd for $\text{C}_{23}\text{H}_{20}\text{BrNO}_7$: 524.0321 ($\text{M}+\text{Na}$) $^+$; found: 524.0319.

3-(2,3-bis(ethoxycarbonyl)-3a,8b-dihydroxy-4-oxo-3a,4-dihydroindeno[1,2-b]pyrrol-1(8bH)-yl)benzoic acid (4j): Yield 83 % (388 mg); white solid; Mp: 188 °C (EtOH); R_f [40

% EtOAc / petroleum ether (60-80°C)]: 0.46; IR ($\nu_{\max}$, KBr, cm^{-1}): 3393, 3168, 1738, 1696, 1495, 1298, 1217, 1123, 762; ^1H NMR (300 MHz, DMSO- d_6) δ_{H} : 13.27 (broad-s, 1H, COOH), 7.99 (d, $J=7.5\text{Hz}$, 1H, Ar-H), 7.82 (d, $J=6.0\text{Hz}$, 1H, ArH), 7.74 (s, 1H, ArH), 7.69 (s, 1H, Ar-H), 7.61-7.53 (m, 3H, Ar-H), 6.68 (d, $J=7.8\text{Hz}$, 1H, OH), 6.42 (s, 1H, OH), 4.07-3.95 (m, 4H, OCH₂), 1.17 (t, $J=6.9\text{Hz}$, 3H, CH₃), 0.96 (t, $J=7.1\text{Hz}$, 3H, CH₃); ^{13}C NMR (75 MHz, DMSO- d_6) δ_{C} : 197.1, 166.6, 162.6, 161.5, 149.9, 136.7, 135.5, 135.0, 132.7, 131.7, 130.7, 129.5, 129.1, 128.8, 125.0, 123.6, 99.9, 96.5, 84.3, 61.9, 59.1, 14.3, 13.3; Anal. calcd. for C₂₄H₂₁NO₉; C: 61.67; H: 4.53; N: 3.00. Found: C: 61.73 H: 4.58; N: 3.02%; HRMS (ESI) calcd for C₂₄H₂₁NO₉: 490.1114 (M+Na)⁺; found: 490.1117

4-(2,3-bis(ethoxycarbonyl)-3a,8b-dihydroxy-4-oxo-3a,4-dihydroindeno[1,2-b]pyrrol-1(8bH)-yl)benzoic acid (4k): Yield 80 % (374 mg); pale yellow solid; Mp: 206-208 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.44; IR ($\nu_{\max}$, KBr, cm^{-1}): 3505, 3206, 1754, 1593, 1576, 1432, 1257, 771; ^1H NMR (300 MHz, DMSO- d_6) δ_{H} : 8.03-7.90 (m, 2H, Ar-H), 7.81-7.73 (m, 2H, ArH), 7.60 (t, $J=2.4\text{Hz}$, 2H, ArH), 7.35 (q, $J=4.2\text{Hz}$, 2H, Ar-H), 6.72 (s, 1H, OH), 6.45 (s, 1H, OH), 4.07-3.97 (m, 4H, OCH₂), 1.20-1.14 (m, 3H, CH₃), 1.03-1.00 (m, 3H, CH₃); ^{13}C NMR (75 MHz, DMSO- d_6) δ_{C} : 197.1, 166.9, 162.6, 161.5, 149.5, 146.8, 140.9, 135.4, 135.7, 134.9, 130.8, 130.3, 129.9, 127.7, 123.6, 101.1, 96.9, 84.5, 62.1, 59.3, 14.3, 13.5; Anal. calcd. for C₂₄H₂₁NO₉; C: 61.67; H: 4.53; N: 3.00. Found: C: 61.72 H: 4.57; N: 3.03%; HRMS (ESI) calcd for C₂₄H₂₁NO₉: 490.1114 (M+Na)⁺; found: 490.1135.

Diethyl 3a,8b-dihydroxy-1-(3-nitrophenyl)-4-oxo-1,3a,4,8b-tetrahydroindeno[1,2-b]pyrrole-2,3-dicarboxylate (4l): Yield 81 % (379 mg); pale yellow solid; Mp: 204 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.47; IR ($\nu_{\max}$, KBr, cm^{-1}): 3413, 3176, 1738, 1692, 1621, 1492, 1293, 1219, 1126, 763; ^1H NMR (300MHz, DMSO- d_6) δ_{H} : 8.33 (d, $J=8.1\text{Hz}$, 1H, Ar-H), 8.21 (s, 1H, Ar-H), 7.87-7.77 (m, 3H, ArH), 7.64 (d, $J=5.4\text{Hz}$, 3H, ArH), 6.84-6.82 (s, 1H, OH), 6.65 (s, 1H, OH), 4.08-4.07 (m, 4H, OCH₂), 1.19 (t, $J=6.8\text{Hz}$, 3H, CH₃), 1.01 (t, $J=6.8\text{Hz}$, 3H, CH₃); ^{13}C NMR (75 MHz, DMSO- d_6) δ_{C} : 196.9, 162.5, 161.4, 149.1, 148.4, 146.6, 137.7, 135.8, 134.9, 134.6, 130.9, 130.7, 124.9, 123.6, 122.8, 122.7, 101.4, 96.9, 84.4, 62.2, 59.3, 14.2, 13.4; Anal. calcd. for C₂₃H₂₀N₂O₉; C: 58.97; H: 4.30; N: 5.98. Found: C: 58.91; H: 4.28; N: 5.97%;

Diethyl 3a,8b-dihydroxy-1-(4-nitrophenyl)-4-oxo-1,3a,4,8b-tetrahydroindeno[1,2-b]pyrrole-2,3-dicarboxylate (4m): Yield 76 % (356 mg); pale yellow solid; Mp: 206 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.46; IR ($\nu_{\max}$, KBr, cm^{-1}): 3473, 3187, 1734, 1696, 1467, 1283, 1205, 1145, 761; ^1H NMR (300 MHz, CDCl_3) δ_{H} : 8.28 (d, $J=9.6\text{Hz}$, 2H, Ar-H), 7.94-7.91 (m, 1H, ArH), 7.60-7.51 (m, 4H, ArH), 6.82 (d, $J=6.6\text{Hz}$, 1H, ArH), 5.13(s, 2H, OH), 4.27-4.12(m, 4H, OCH_2), 1.30 (t, $J=7.2\text{Hz}$, 3H, CH_3), 1.15 (t, $J=7.2\text{Hz}$, 3H, CH_3); ^{13}C NMR (75 MHz, CDCl_3) δ_{C} :196.4, 163.3, 160.9,149.3, 146.8, 146.7,142.9, 136.0, 134.9, 130.9, 127.7, 125.0, 124.7, 124.3, 101.4, 96.2, 83.4, 62.9, 60.7, 14.2, 13.7; Anal. calcd. for $\text{C}_{23}\text{H}_{20}\text{N}_2\text{O}_9$; C: 58.97; H: 4.30; N: 5.98. Found: C: 58.90;H: 4.27; N: 5.96%; HRMS (ESI) calcd for $\text{C}_{23}\text{H}_{20}\text{N}_2\text{O}_9$: 491.1066 ($\text{M}+\text{Na}$) $^+$; found: 491.1106

Diethyl 1-benzyl-3a,8b-dihydroxy-4-oxo-1,3a,4,8b-tetrahydroindeno[1,2-b]pyrrole-2,3-dicarboxylate (4n): Yield 80 % (350 mg); white solid; Mp: 124 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.58; IR ($\nu_{\max}$, KBr, cm^{-1}): 3468, 3182, 1738, 1694, 1465, 1278, 1215, 1128, 764; ^1H NMR (300 MHz, CDCl_3) δ_{H} : 7.90 (d, $J=8.1\text{Hz}$, 1H, Ar-H), 7.67 (t, $J=7.4\text{Hz}$, 1H, ArH), 7.59-7.55 (m, 2H, ArH), 7.28-7.27 (m, 3H, ArH), 7.21-7.19 (m, 2H, ArH) 4.96(d, $J=15.9\text{Hz}$, 1H, OH), 4.79(d, $J=15.9\text{Hz}$, 2H,Ar- CH_2), 4.62(s, 1H, OH),4.21-4.12(m, 2H, OCH_2), 3.93-3.86(m, 2H, OCH_2) 1.23 (t, $J=7.2\text{Hz}$, 3H, CH_3), 0.97 (t, $J=7.2\text{Hz}$, 3H, CH_3); ^{13}C NMR (75 MHz, CDCl_3) δ_{C} :197.0, 163.7, 161.7, 150.8, 147.5, 136.6, 136.0, 135.2, 130.6, 128.5, 128.3, 127.8, 127.7, 124.7, 124.4, 96.4, 95.1, 83.7, 62.3, 60.0, 46.6, 14.3, 13.3; Anal. calcd. for $\text{C}_{24}\text{H}_{23}\text{NO}_7$; C: 65.90; H: 5.30; N: 3.20. Found: C: 65.85; H: 5.26; N: 3.18%.

Spectroscopic and Analytical characterization of compounds (6a-6j & A)

Dimethyl 3a,8b-dihydroxy-4-oxo-1-p-tolyl-1,3a,4,8b-tetrahydroindeno[1,2-b]pyrrole-2,3-dicarboxylate (6a): Yield 90 % (368 mg); white solid; Mp: 168 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.51; IR ($\nu_{\max}$, KBr, cm^{-1}): 3475, 3328, 2978, 1754, 1720, 1509, 1436, 1028, 962; ^1H NMR (300 MHz, CDCl_3) δ_{H} : 7.92-7.88 (m, 1H, Ar-H), 7.53-7.50 (m, 2H, ArH), 7.21-7.14 (m, 4H, ArH), 6.84-6.81 (m, 1H, ArH), 5.30 (broad-s, 2H, OH), 3.77 (s, 3H, OMe), 3.65 (s, 3H, OMe), 2.41 (s, 3H, Ar-CH₃); ^{13}C NMR (75 MHz, CDCl_3) δ_{C} : 197.2, 164.3, 161.8, 151.5, 147.0, 138.6, 135.5, 135.1, 133.1, 130.4, 129.7, 128.4, 125.0, 124.5, 97.7, 95.6, 83.4, 52.9, 51.4, 21.1; Anal. calcd. for $\text{C}_{22}\text{H}_{19}\text{NO}_7$; C: 64.54; H: 4.68; N: 3.42. Found: C: 64.59; H: 5.38; N: 3.24%;

Dimethyl 3a,8b-dihydroxy-1-(4-isopropylphenyl)-4-oxo-1,3a,4,8b-tetrahydroindeno[1,2-b]pyrrole-2,3-dicarboxylate (6b): Yield 91 % (398 mg); grey solid; Mp: 184 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.56; IR ($\nu_{\max}$, KBr, cm^{-1}): 3477, 3334, 2978, 1754, 1726, 1524, 1445, 1027, 961; ^1H NMR (300 MHz, CDCl_3) δ_{H} : 7.93-7.90 (m, 1H, Ar-H), 7.57-7.52 (m, 2H, ArH), 7.28-7.19 (m, 4H, ArH), 6.84-6.81 (m, 1H, ArH), 4.70 (broad-s, 2H, OH), 3.79 (s, 3H, OMe), 3.67 (s, 3H, OMe), 3.00-2.96 (m, 1H, CH), 1.30 (d, $J=6.9$ Hz, 6H, CH₃); ^{13}C NMR (75 MHz, CDCl_3) δ_{C} : 197.1, 164.2, 161.8, 151.6, 149.6, 147.0, 135.6, 135.1, 133.2, 130.5, 128.4, 127.2, 125.0, 124.6, 97.5, 95.5, 83.3, 53.3, 51.5, 33.8, 23.9, 23.8, 14.3, 13.5; Anal. calcd. for $\text{C}_{24}\text{H}_{23}\text{NO}_7$; C: 65.90; H: 5.30; N: 3.20. Found: C: 65.98; H: 5.34; N: 3.21%; HRMS (ESI) calcd for $\text{C}_{24}\text{H}_{23}\text{NO}_7$: 460.1372 ($\text{M}+\text{Na}$)⁺; found: 460.1377

Dimethyl 1-(4-tert-butylphenyl)-3a,8b-dihydroxy-4-oxo-1,3a,4,8b-tetrahydroindeno[1,2-b]pyrrole-2,3-dicarboxylate (6c): Yield 94 % (424 mg); white solid; Mp: 172 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.58; IR ($\nu_{\max}$, KBr, cm^{-1}): 3393, 3178, 1736, 1696, 1495, 1296, 1225, 1132, 764; ^1H NMR (300 MHz, CDCl_3) δ_{H} : 7.92-7.89 (m, 1H, Ar-H), 7.55-7.51 (m, 2H, ArH), 7.40 (d, $J=8.4$ Hz, 2H, ArH), 7.21 (d, $J=8.4$ Hz, 2H, ArH), 6.84-6.81 (m, 1H, ArH), 4.88 (broad-s, 2H, OH), 3.77 (s, 3H, OMe), 3.66 (s, 3H, OMe), 1.36 (s, 9H, Me); ^{13}C NMR (75 MHz, CDCl_3) δ_{C} : 197.1, 164.3, 161.8, 151.9, 151.6, 147.0, 135.6, 135.1, 132.9, 130.5, 128.1, 126.0, 125.0, 124.6, 97.5, 95.6, 83.4, 53.0, 51.5, 34.7, 31.3; Anal. calcd. for $\text{C}_{25}\text{H}_{25}\text{NO}_7$; C: 66.51; H: 5.58; N: 3.10. Found: C: 66.47; H: 5.55; N: 3.09%; HRMS (ESI) calcd for $\text{C}_{25}\text{H}_{25}\text{NO}_7$: 474.1529 ($\text{M}+\text{Na}$)⁺; found: 474.1587

Dimethyl 3a,8b-dihydroxy-1-(4-methoxyphenyl)-4-oxo-1,3a,4,8b-tetrahydroindeno[1,2-b]pyrrole-2,3-dicarboxylate (6d): Yield 95 % (404 mg); pale yellow solid; Mp: 134 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.54; IR ($\nu_{\max}$, KBr, cm^{-1}): 3421, 2982, 1725, 1526, 1455, 1296, 1245, 1168, 772; ^1H NMR (300 MHz, CDCl_3) δ_{H} : 7.78-7.75 (m, 1H, Ar-H), 7.40 (t, $J=4.4\text{Hz}$, 2H, ArH), 7.08(d, $J=9.0\text{Hz}$, 2H, ArH), 6.80-6.70(m, 3H, ArH), 4.85(broad-s, 2H, OH), 3.73(m, 3H, OCH_3), 3.62(s, 3H, OMe), 3.52(s, 3H, Ar-OMe) ; ^{13}C NMR (75 MHz, CDCl_3) δ_{C} :197.2, 164.3, 161.8, 159.6, 151.7, 147.0, 135.6, 135.1, 130.4, 130.2, 128.0, 125.0, 124.6, 114.2, 97.1, 95.5, 83.3, 55.4, 55.9, 51.9; Anal. calcd. for $\text{C}_{22}\text{H}_{19}\text{NO}_8$; C: 62.12; H: 4.50; N: 3.29. Found: C: 62.18; H: 4.53; N: 3.30%;

Dimethyl 1-(4-chlorophenyl)-3a,8b-dihydroxy-4-oxo-1,3a,4,8b-tetrahydroindeno[1,2-b]pyrrole-2,3-dicarboxylate (6e): Yield 86 % (370 mg); white solid; Mp: 172 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.50; IR ($\nu_{\max}$, KBr, cm^{-1}): 3420, 2952, 1721, 1569, 1441, 1271, 1161, 775; ^1H NMR (300 MHz, CDCl_3) δ_{H} : 7.89 (t, $J=3.9\text{Hz}$, 1H, Ar-H), 7.54 (t, $J=3.9\text{Hz}$, 2H, ArH), 7.38 (d, $J=8.1\text{Hz}$, 2H, ArH), 7.26(d, $J=8.7\text{Hz}$, 2H, ArH) , 6.84-6.81 (m, 1H, ArH), 5.17(broad-s, 2H, OH), 3.74(s, 3H, OMe), 3.66(s, 3H, OMe); ^{13}C NMR (75 MHz, CDCl_3) δ_{C} :197.0, 164.0, 161.6, 150.9, 146.8, 135.8, 135.0, 134.5, 130.6, 129.7, 129.4, 124.7, 98.7, 95.8, 83.4, 53.4, 51.1, 51.5; Anal. calcd. for $\text{C}_{21}\text{H}_{16}\text{ClNO}_7$; C: 58.68; H: 3.75; N: 3.26. Found: C: 58.75 H: 3.79; N: 3.28%;

Dimethyl 1-(2-bromophenyl)-3a,8b-dihydroxy-4-oxo-1,3a,4,8b-tetrahydroindeno[1,2-b]pyrrole-2,3-dicarboxylate (6f): Yield 88 % (417 mg); white solid; Mp: 152 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.49; IR ($\nu_{\max}$, KBr, cm^{-1}): 3397, 2941, 1734, 1570, 1445, 1279, 1173, 771; ^1H NMR (300 MHz, CDCl_3) δ_{H} : 7.90-7.89 (m, 1H, Ar-H), 7.82-7.76(m, 1H, ArH), 7.64-7.46 (m, 4H, ArH), 7.42-7.28(m, 1H, ArH) , 6.87-6.84 (m, 1H, ArH), 5.36(s, 1H, OH), 5.00 (s, 1H, OH), 3.80(s, 3H, OMe), 3.63 (s, 3H, OMe); ^{13}C NMR (75 MHz, CDCl_3) δ_{C} : 196.8, 196.5, 164.0, 163.7, 160.8, 150.7, 150.1, 148.7, 146.8, 135.7, 135.5, 135.2, 134.7, 134.1, 133.8, 133.4, 133.2, 133.1, 130.9, 130.5, 130.4, 130.0, 127.9, 127.5, 127.2, 125.3, 124.7, 124.4, 98.1, 96.7, 95.7, 83.1, 82.9, 52.5, 52.4, 51.3, 51.2; Anal. calcd. for $\text{C}_{21}\text{H}_{16}\text{BrNO}_7$; C: 53.18; H: 3.40; N: 2.95. Found: C: 53.26; H: 3.45; N: 2.97%; HRMS (ESI) calcd for $\text{C}_{21}\text{H}_{16}\text{BrNO}_7$: 496.0008 ($\text{M}+\text{Na}$) $^{+}$; found: 498.0005

3-(3a,8b-dihydroxy-2,3-bis(methoxycarbonyl)-4-oxo-3a,4-dihydroindeno[1,2-b]pyrrol-1(8bH)-yl)benzoic acid (6g): Yield 82 % (360 mg); white solid; Mp: 186°C (EtOH); R_f [40

% EtOAc / petroleum ether (60-80°C): 0.43; IR ($\nu_{\max}$, KBr, cm^{-1}): 3395, 3167, 1734, 1698, 1496, 1297, 1218, 1121, 763; ^1H NMR (300 MHz, DMSO- d_6) δ_{H} : 13.25(broad-s, 1H, COOH), 8.01-7.99 (m, 2H, ArH), 7.81 (s, 3H, ArH), 7.61(s, 3H, Ar-H) , 7.51(s, 1H, ArH), 6.69 (s, 1H, OH), 6.50(s, 1H, OH), 3.62(s, 3H, OCH₃), 3.57(s, 3H, OCH₃); ^{13}C NMR (75 MHz, DMSO- d_6) δ_{C} :197.5, 167.0, 163.8, 162.4, 150.5, 147.1, 137.1, 136.0, 135.3, 132.6, 132.2, 131.1,130.0, 129.5, 129.2, 129.1, 125.3, 124.0, 100.7, 97.1, 84.6,53.2, 51.3; Anal. calcd. for C₂₂H₁₇NO₉; C: 60.14; H: 3.90; N: 3.19. Found: C: 60.21; H: 3.94; N: 3.22%; HRMS (ESI) calcd for C₂₂H₁₇NO₉: 462.0801 (M+ Na)⁺; found: 462.0844.

4-(3a,8b-dihydroxy-2,3-bis(methoxycarbonyl)-4-oxo-3a,4-dihydroindeno[1,2-b]pyrrol-1(8bH)-yl)benzoic acid (6h): Yield 80 % (351 mg); white solid; Mp: 204 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.44; IR ($\nu_{\max}$, KBr, cm^{-1}): 3503, 3207, 1753, 1591, 1575, 1434, 1257, 772; ^1H NMR (300 MHz, DMSO- d_6) δ_{H} : 13.13-13.10(broad-s, 1H, COOH), 8.02 (d, $J=7.8\text{Hz}$, 2H, Ar-H), 7.80 (s, 1H, ArH), 7.61-7.60 (m, 3H, ArH), 7.36(d, $J=7.8\text{Hz}$, 2H, Ar-H) , 6.73-6.71(s,1H,OH), 6.52(s, 1H, OH), 3.62-3.60(s, 6H, OCH₃); ^{13}C NMR (75 MHz, DMSO- d_6) δ_{C} :197.0, 166.8,163.4, 162.1, 149.6, 146.7,140.9, 135.7, 134.8, 130.7, 130.3, 129.8, 127.2, 124.9, 123.5,101.4, 97.0, 84.4, 52.9,51.0; Anal. calcd. for C₂₂H₁₇NO₉; C: 60.14; H: 3.90; N: 3.19. Found: C: 60.20; H: 3.93; N: 3.21%;

Dimethyl 3a,8b-dihydroxy-1-(3-nitrophenyl)-4-oxo-1,3a,4,8b-tetrahydroindeno[1,2-b]pyrrole-2,3-dicarboxylate (6i): Yield 81 % (357 mg); white solid; Mp: 202 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.47; IR ($\nu_{\max}$, KBr, cm^{-1}): 3438, 1767, 1724, 1576, 1492, 1339, 1277, 1172, 779; ^1H NMR (300MHz, CDCl₃) δ_{H} : 8.27-8.24 (m,2H, Ar-H), 7.95-7.92(m, 1H, Ar-H) ,7.78-7.75 (m, 1H, ArH), 7.66-7.54 (m, 3H, ArH) , 6.82-6.79 (m, 1H, Ar-H), 5.19(s, 1H, OH), 5.04(s, 1H, OH), 3.79(s, 3H, OCH₃), 3.72(s, 3H, OCH₃); ^{13}C NMR (75 MHz, CDCl₃) δ_{C} :196.5, 163.8, 161.5,149.9, 148.6, 146.7, 137.7, 136.1, 135.0, 133.8, 131.0, 130.2, 125.1, 124.3, 123.0, 122.7, , 100.6, 96.1, 83.4, 53.3, 51.8; Anal. calcd. for C₂₁H₁₆N₂O₉; C: 57.28; H: 3.66; N: 6.36. Found: C: 57.35; H: 3.68; N: 6.37%; HRMS (ESI) calcd for C₂₁H₁₆N₂O₉: 463.0753 (M+ Na)⁺; found: 463.0773

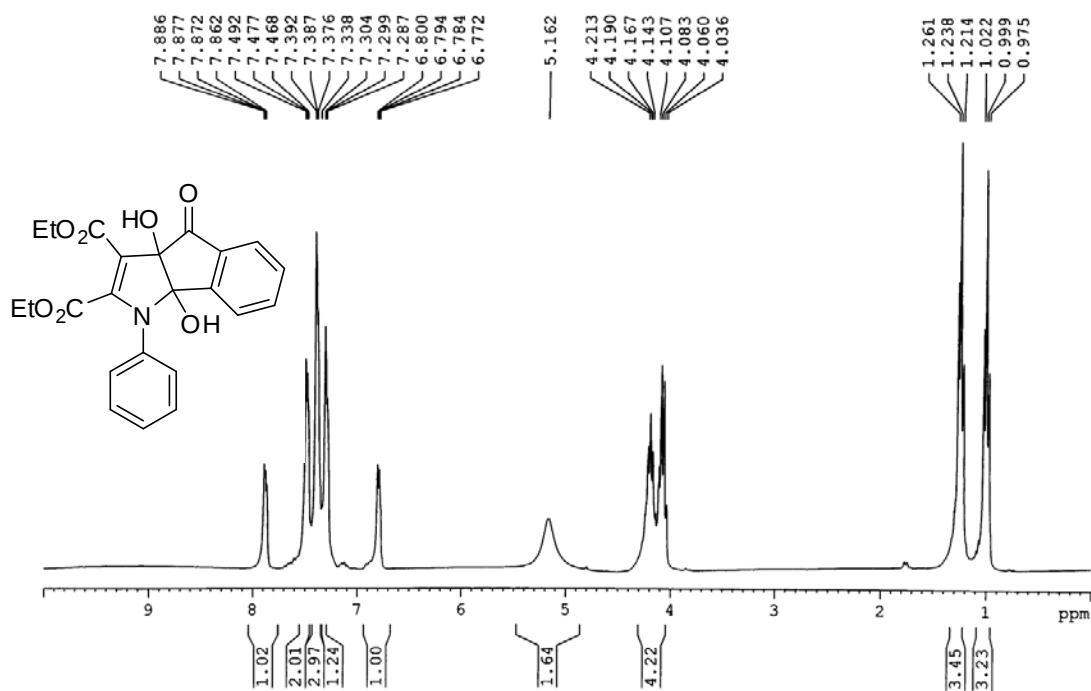
Dimethyl 3a,8b-dihydroxy-1-(4-nitrophenyl)-4-oxo-1,3a,4,8b-tetrahydroindeno[1,2-b]pyrrole-2,3-dicarboxylate (6j): Yield 78 % (344 mg); yellow solid; Mp: 198 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.46; IR ($\nu_{\max}$, KBr, cm^{-1}): 3432, 1756, 1726, 1576, 1498, 1344, 1275, 1164, 778; ^1H NMR (300MHz, CDCl₃) δ_{H} : 8.28 (d, $J=8.7\text{Hz}$, 2H,

Ar-H), 7.92-7.90(m, 1H, Ar-H), 7.59-7.54 (m, 4H, ArH), 6.84-6.82 (m, 1H, ArH) , 5.35(s, 1H, OH), 5.18(s, 1H, OH), 3.78(s, 3H, OCH₃), 3.72(s, 3H, OCH₃); ¹³C NMR (75 MHz, CDCl₃) δ_C:196.4, 163.7, 161.5,149.9, 146.7, 142.8, 136.1, 134.8, 130.9, 127.5, 125.0, 124.7, 124.6,124.3, 101.6, 96.4, 83.4, 53.4, 51.8; Anal. calcd. for C₂₁H₁₆N₂O₉; C: 57.28; H: 3.66; N: 6.36. Found: C: 57.37; H: 3.69; N: 6.38%; HRMS (ESI) calcd for C₂₁H₁₆N₂O₉: 463.0753 (M+Na)⁺; found: 463.0786

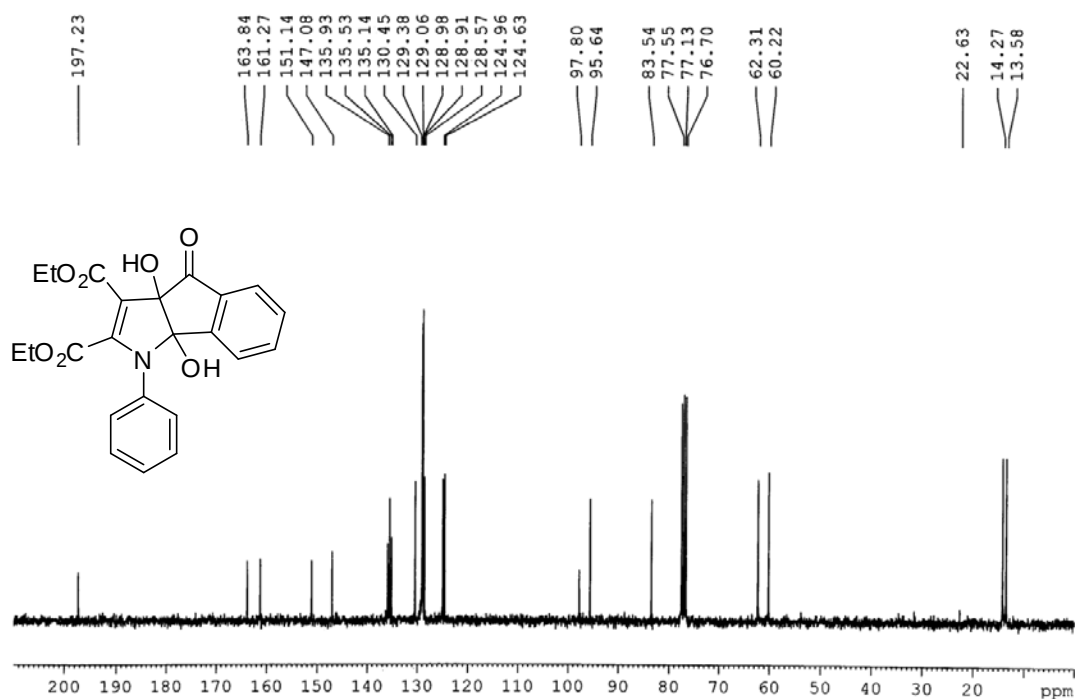
Diethyl 2-(phenylamino)fumarate (Intermediate A):

¹H NMR (300MHz, CDCl₃) δ_H: 9.75(s ,1H, NH-Ar), 8.00 (d, *J*=8.2Hz, 2H, Ar-H), 6.88 (d, *J*=8.7Hz, 2H, Ar-H), 5.57 (s, 1H, -CH), 4.24-4.16(m, 4H, OCH₂), 1.29 (t, *J*=7.1Hz, 3H, CH₃), 1.15 (t, *J*=7.1Hz, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ_C:170.8, 169.1, 164.0, 146.4, 145.3, 132.4, 131.5, 123.9, 119.2, 113.8, 97.7, 62.4, 60.4, 14.3, 13.7; HRMS (ESI) calcd for C₁₅H₁₇NO₆: 308.1125 (M+H)⁺; found: 308.1122.

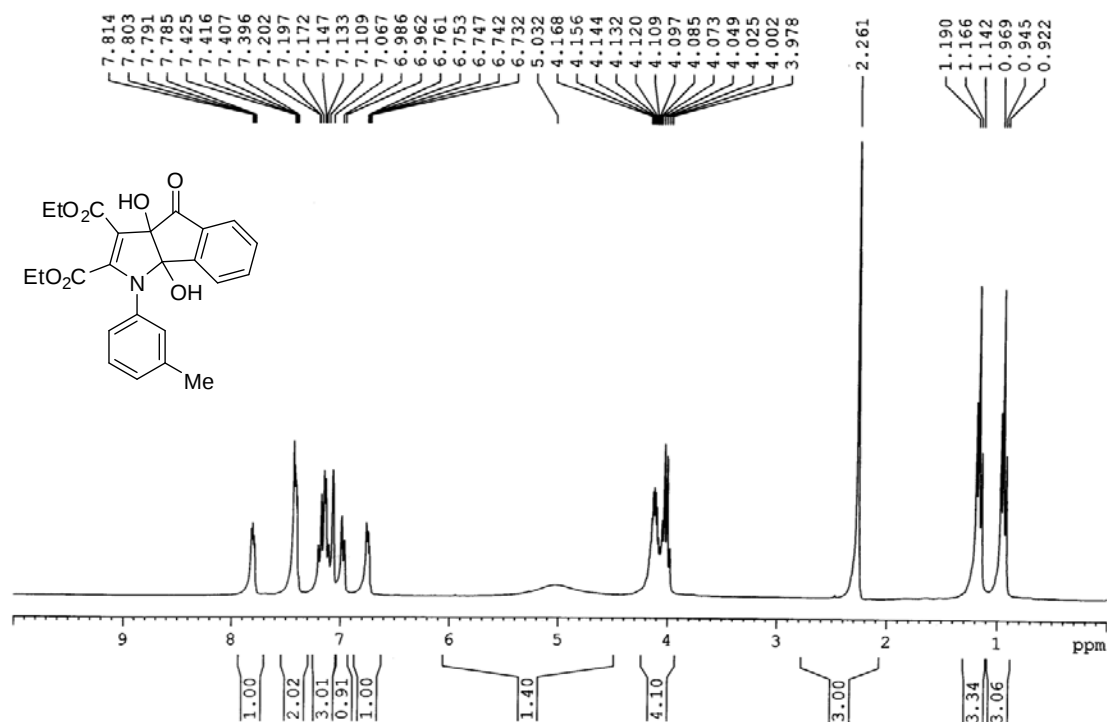
Copy of ^1H and ^{13}C NMR spectra of synthesized compounds (4a-4n):



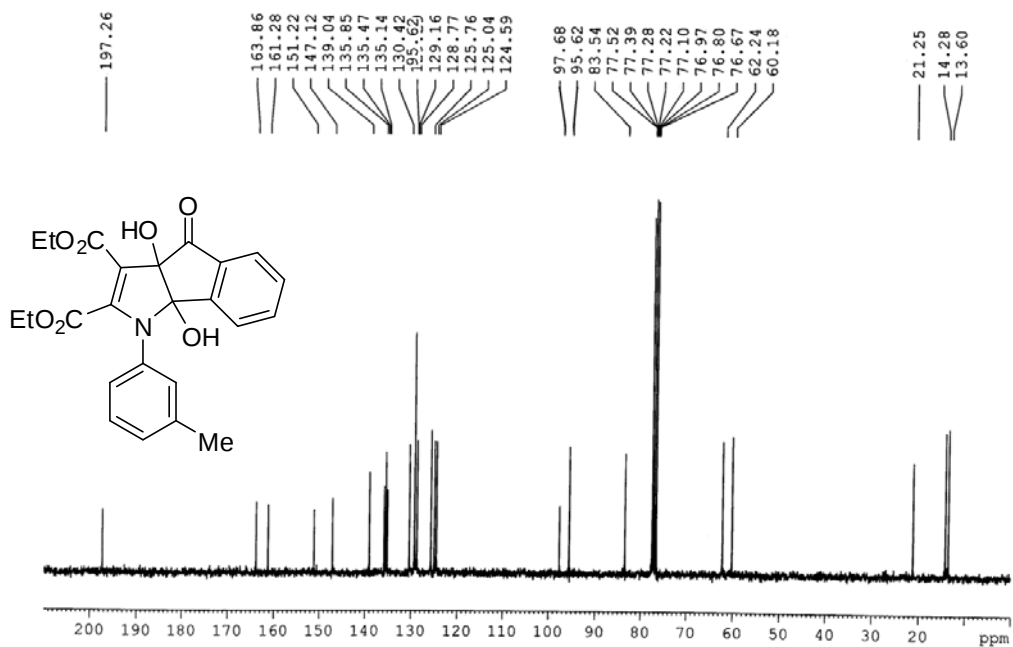
^1H NMR of compound **4a**



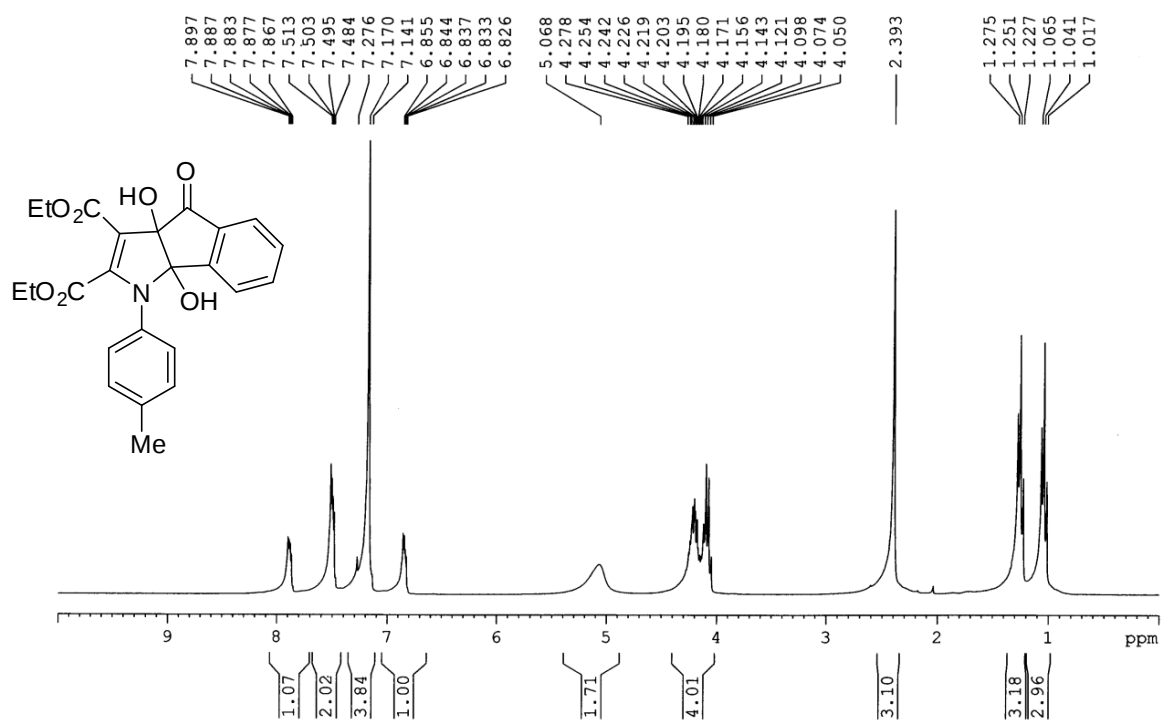
^{13}C NMR of compound **4a**



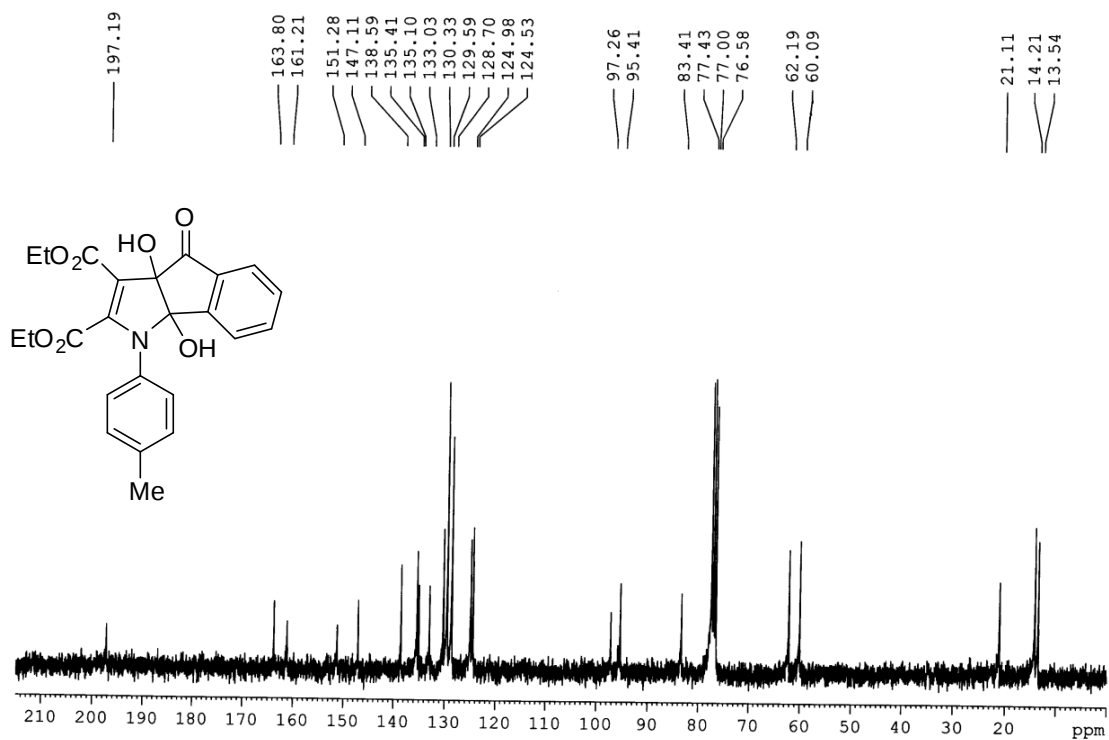
¹H NMR of compound **4b**



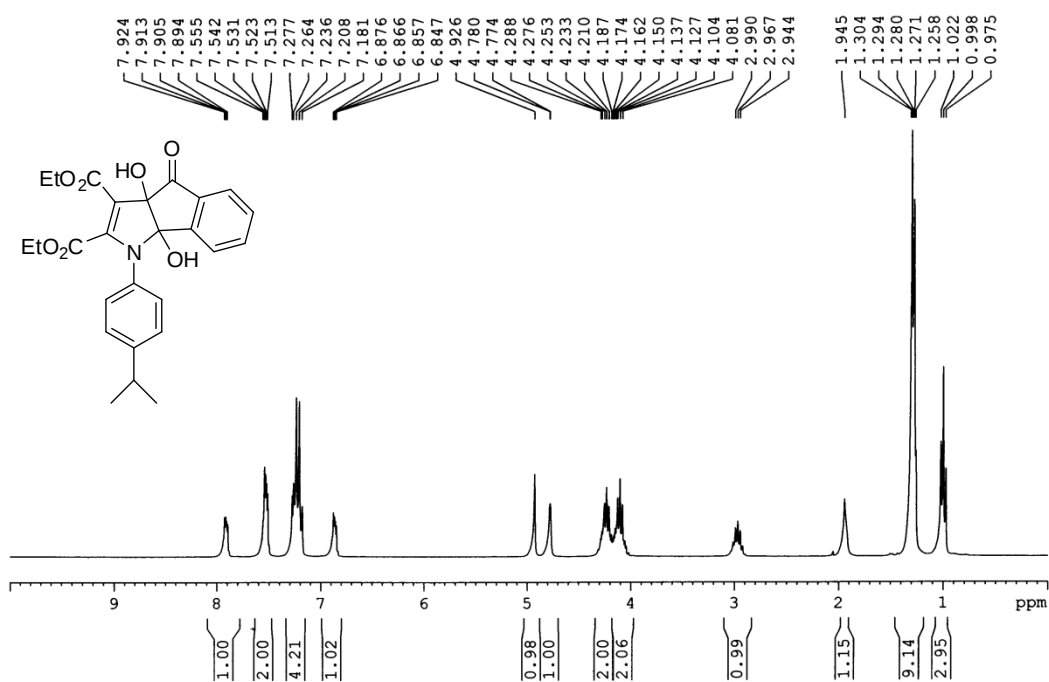
¹³C NMR of compound **4b**



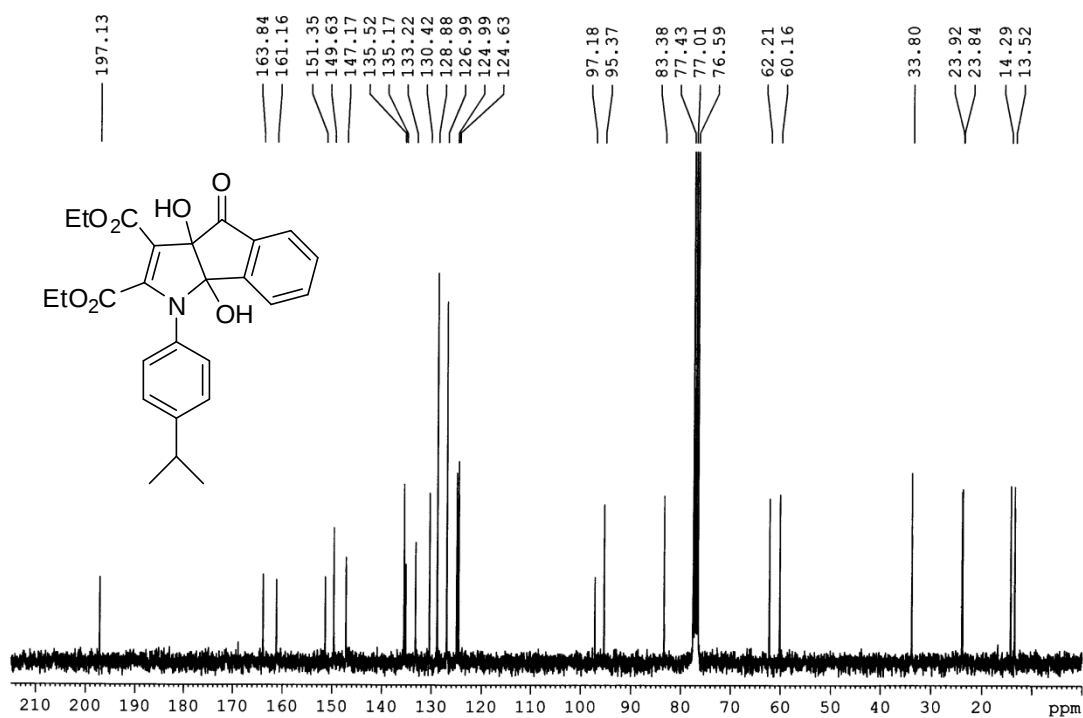
¹H NMR of compound **4c**



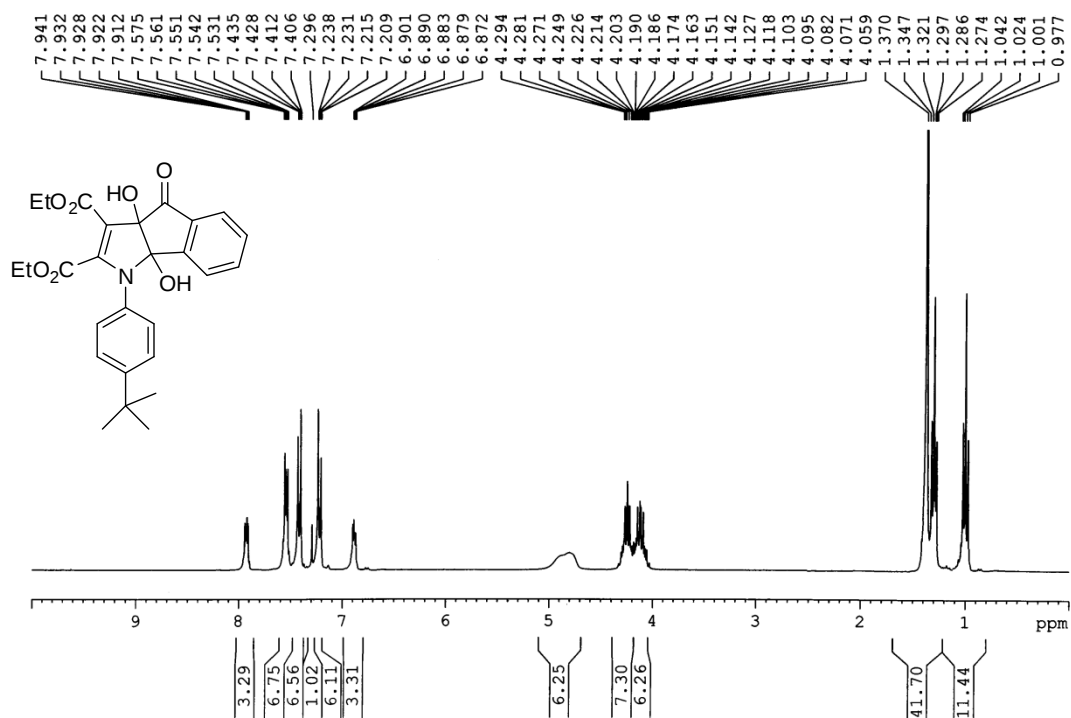
¹³C NMR of compound **4c**



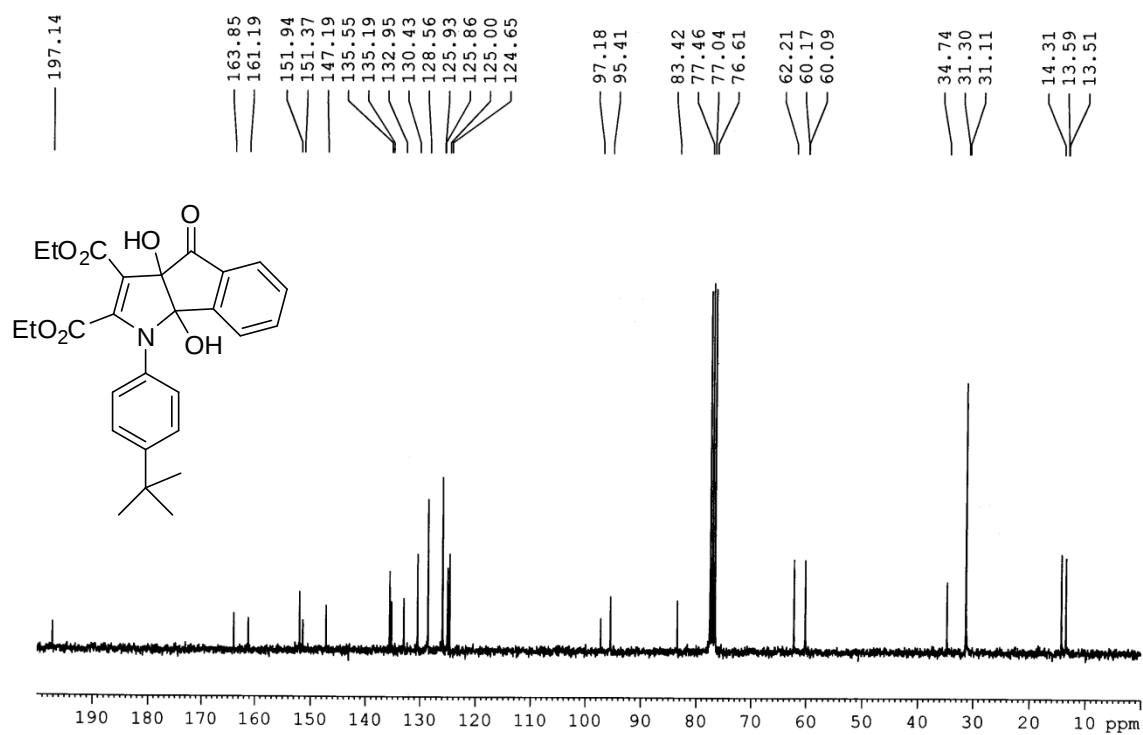
¹H NMR of compound **4d**



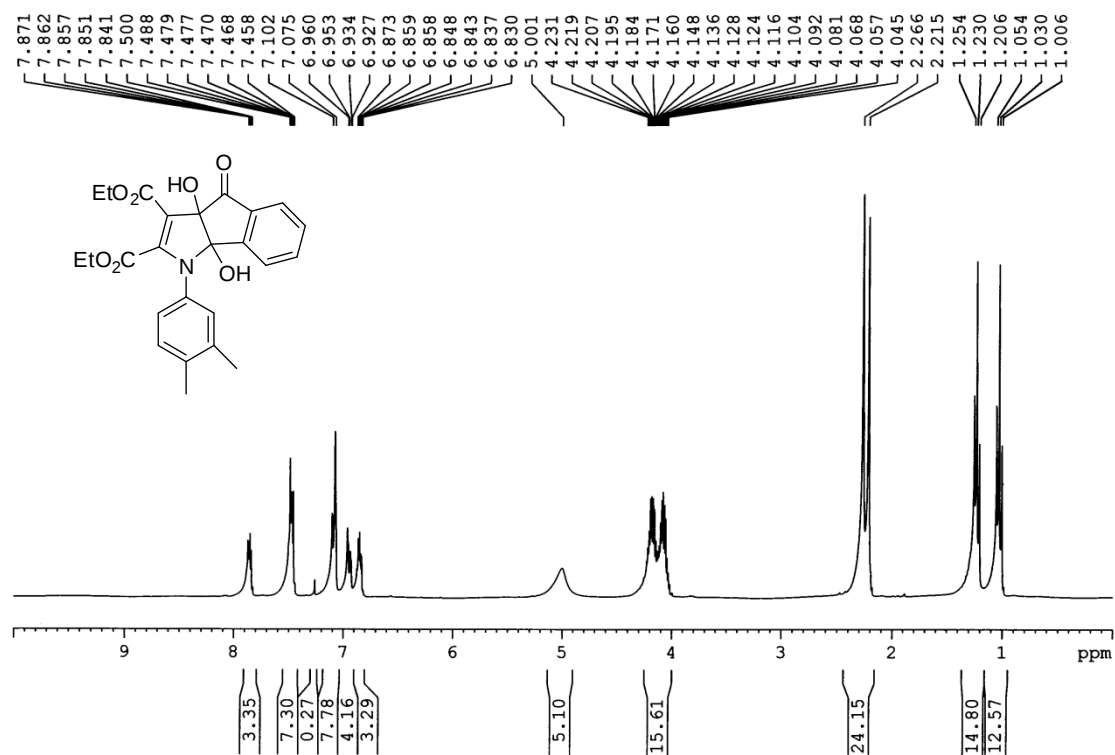
¹³C NMR of compound **4d**



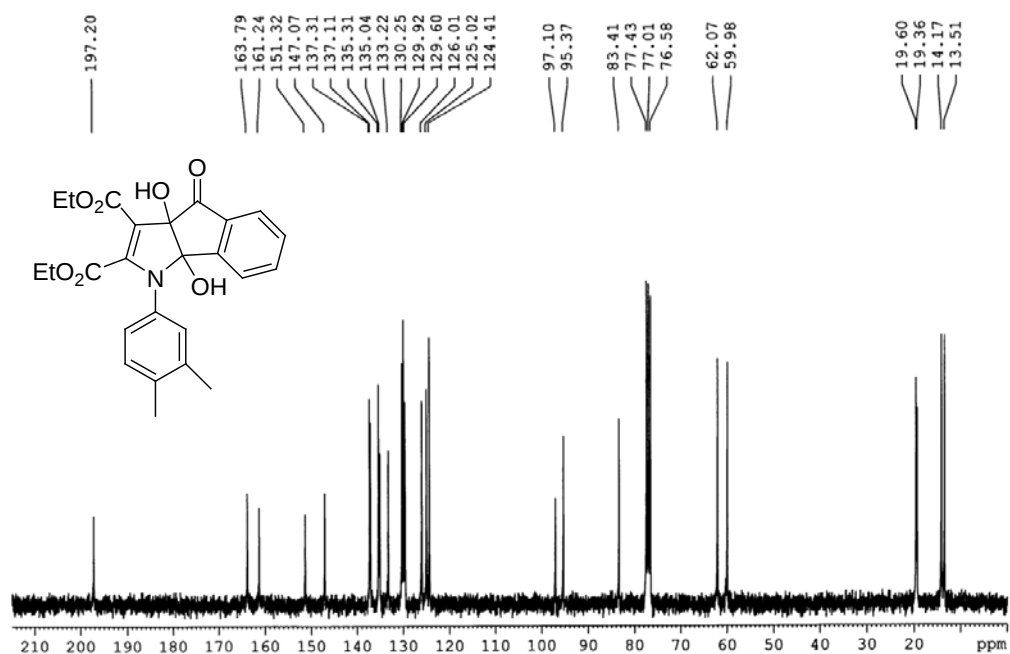
¹H NMR of compound 4e



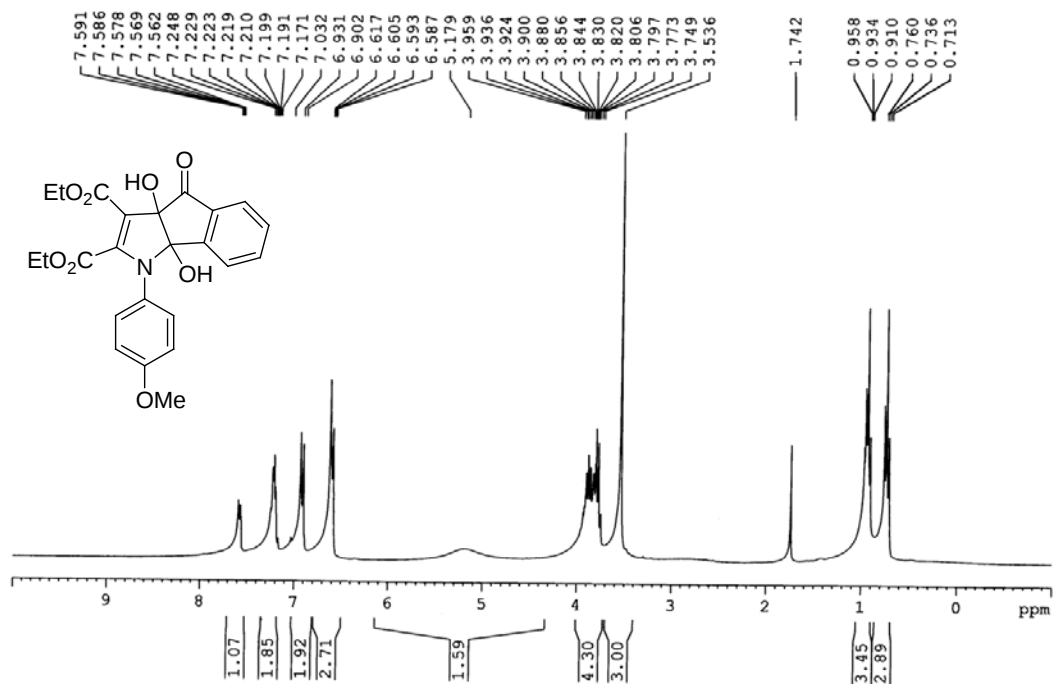
¹³C NMR of compound 4e



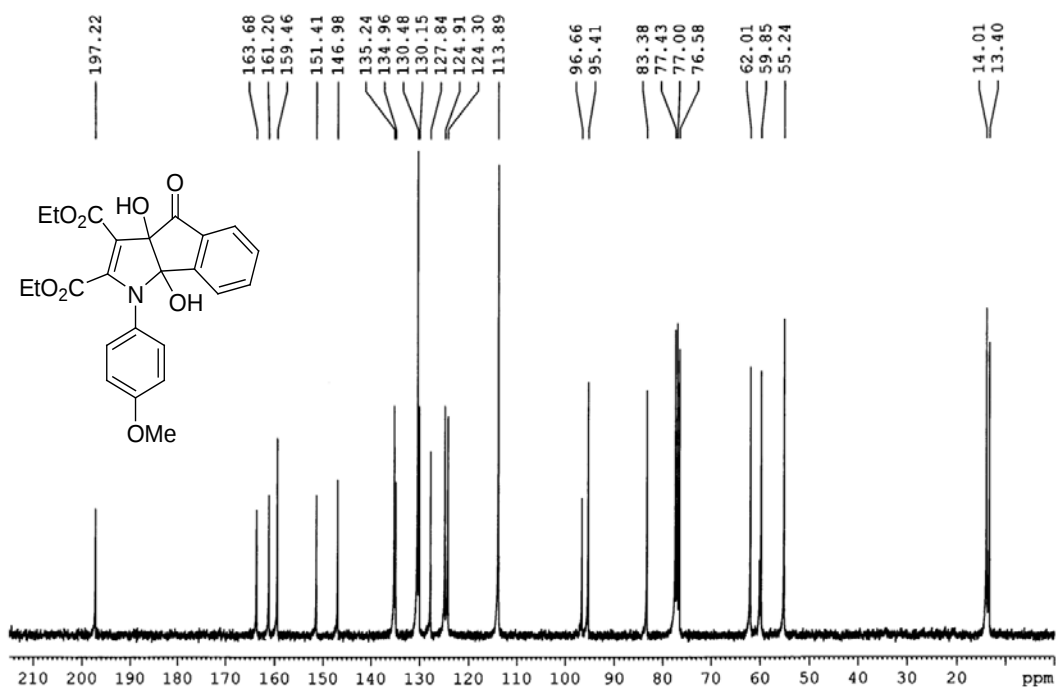
¹H NMR of compound 4f



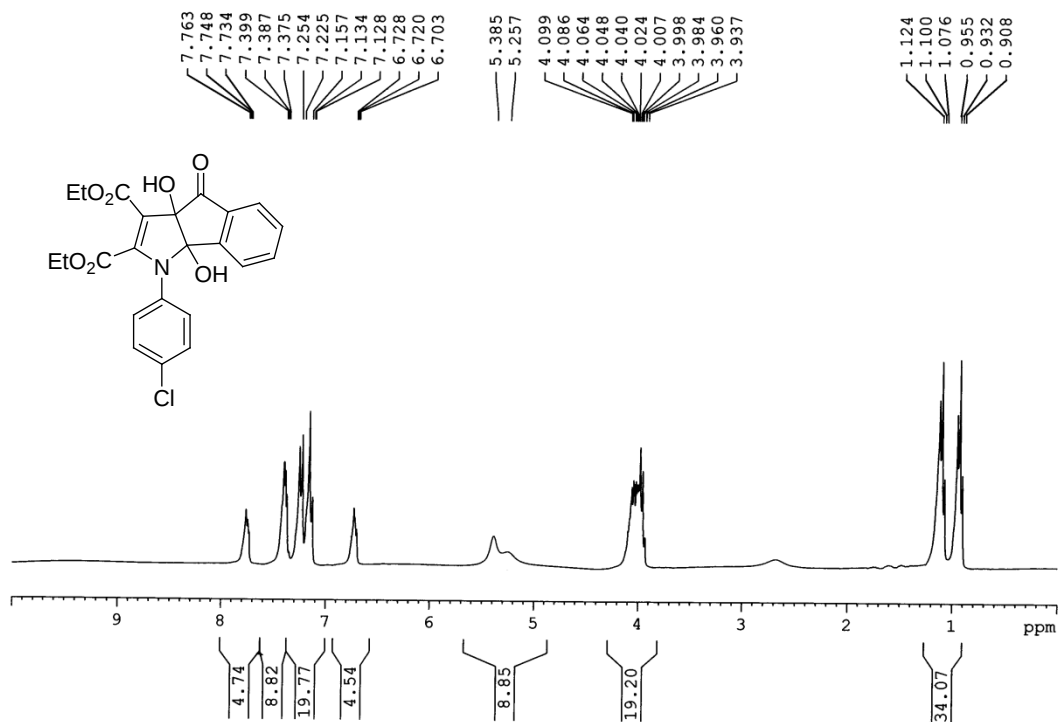
¹³C NMR of compound 4f



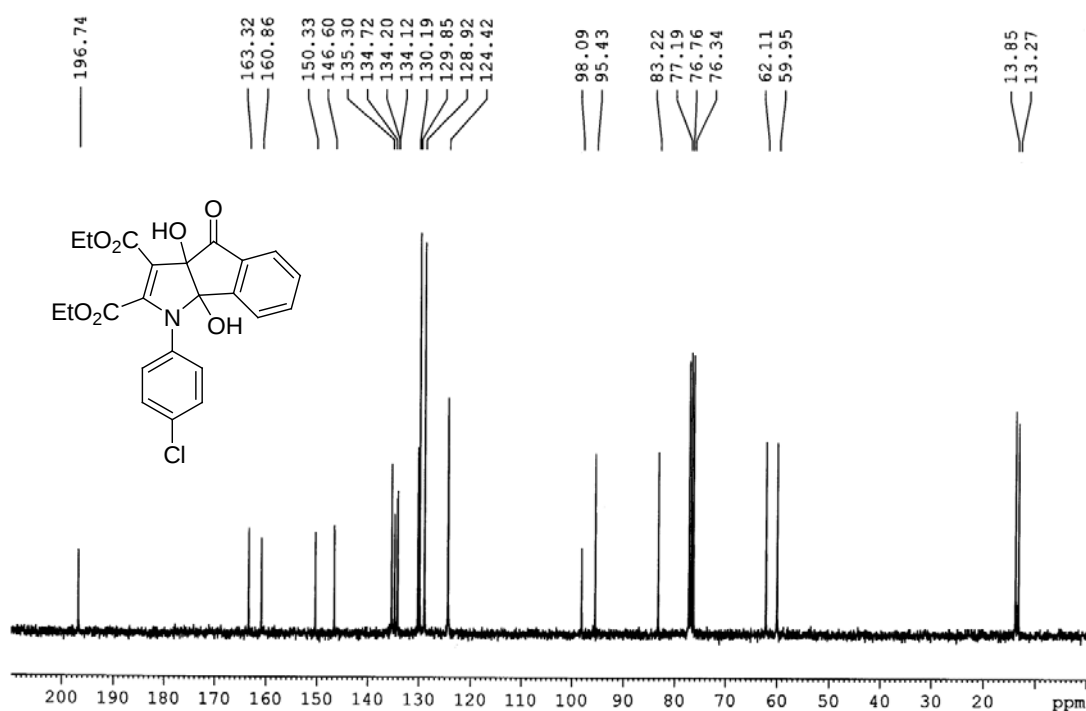
¹H NMR of compound **4g**



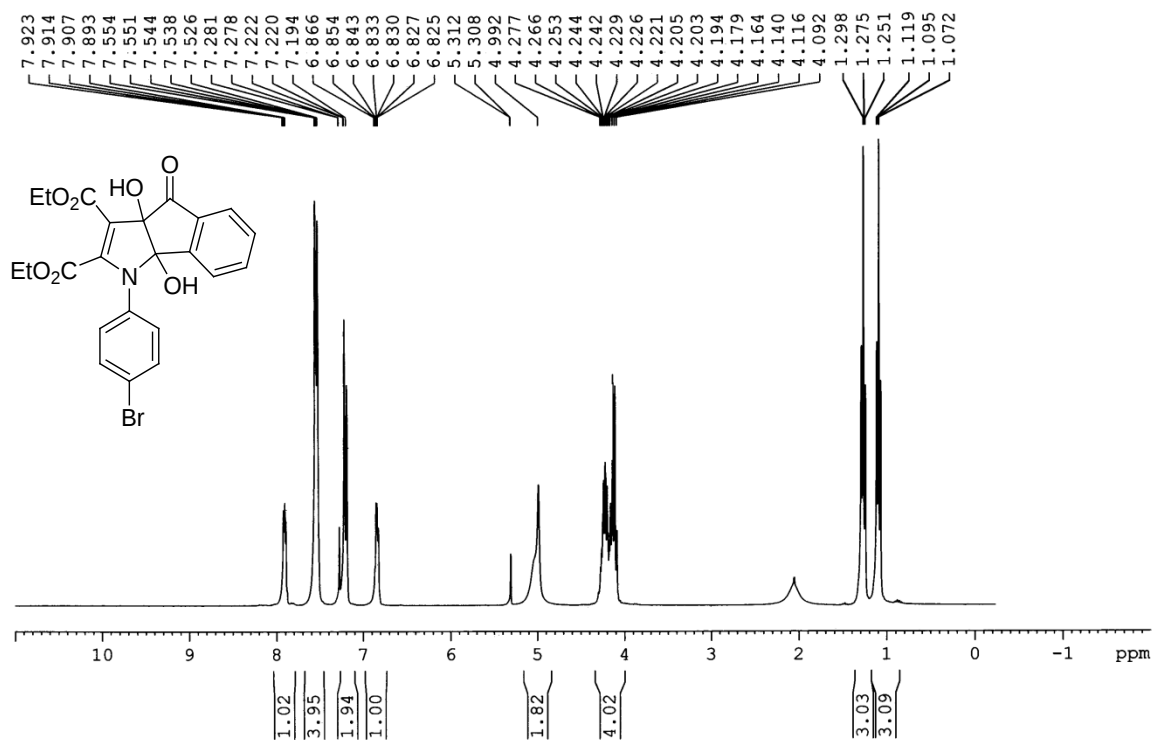
¹³C NMR of compound **4g**



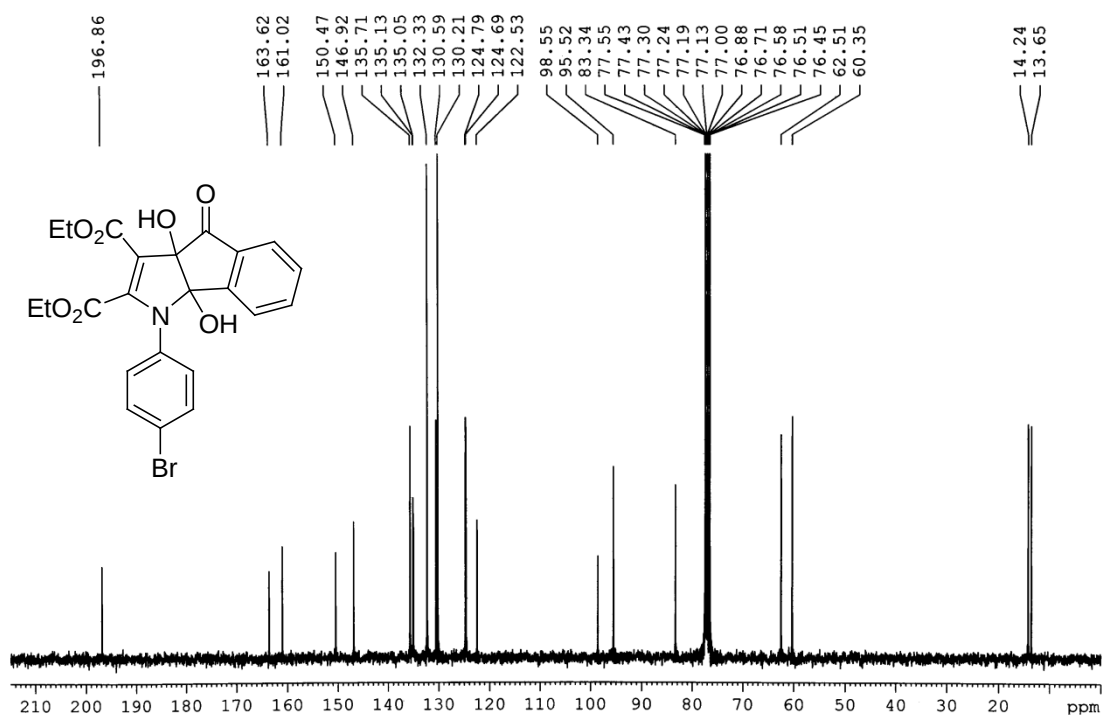
¹H NMR of compound 4h



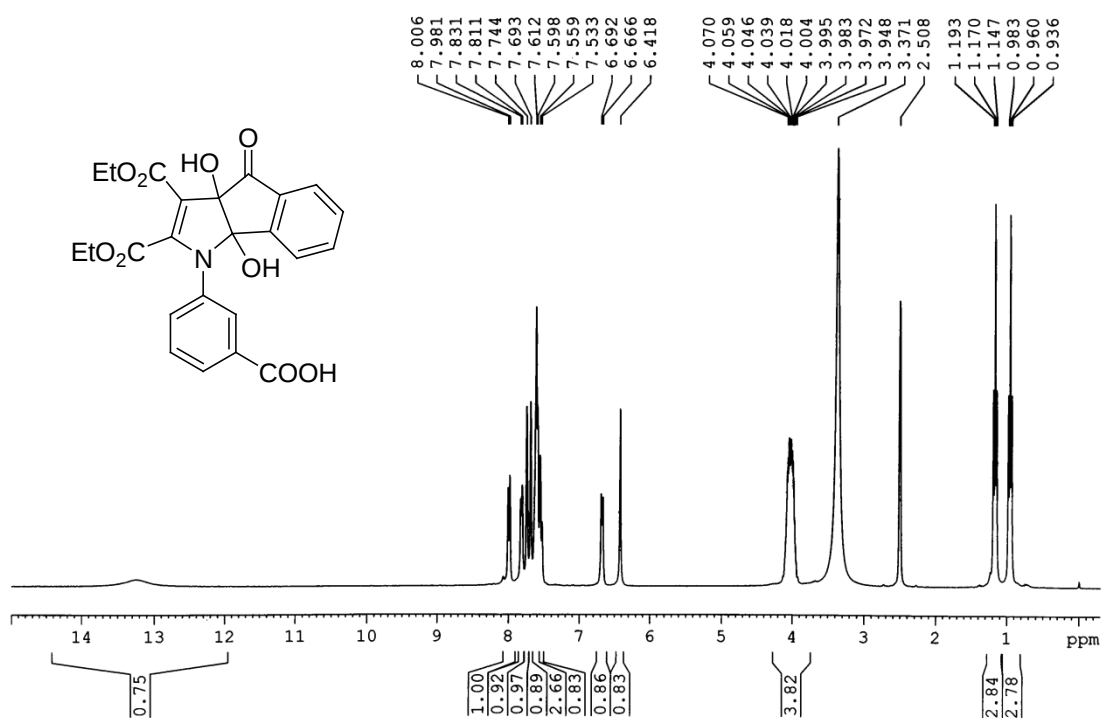
¹³C NMR of compound 4h



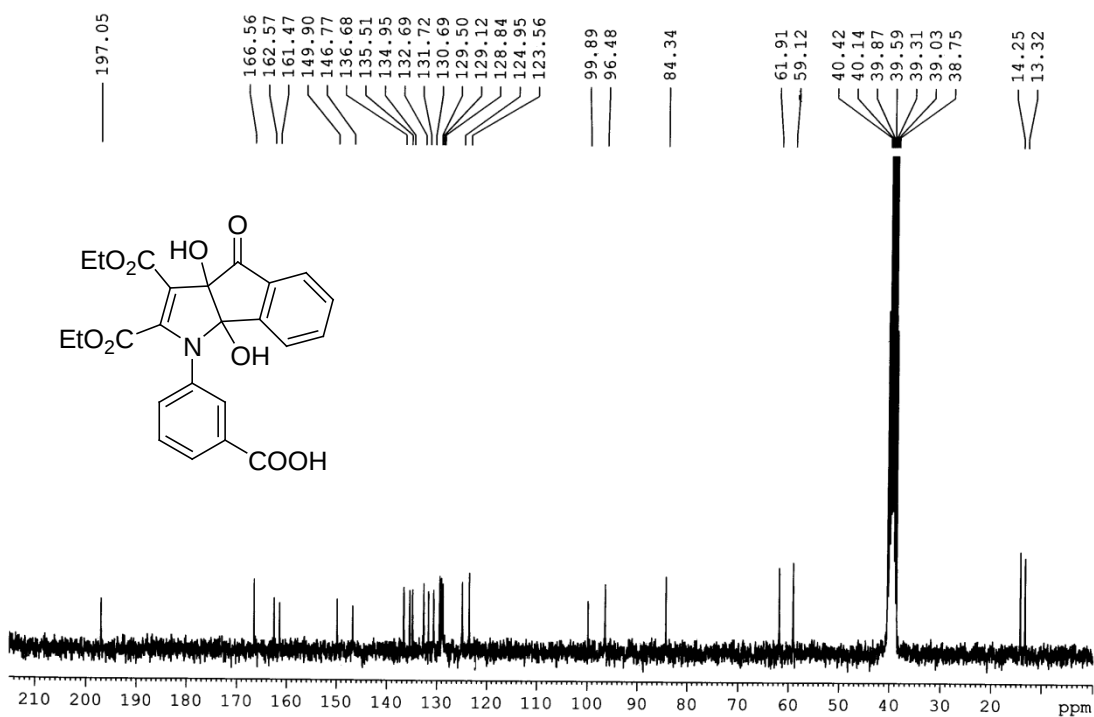
¹H NMR of compound **4i**



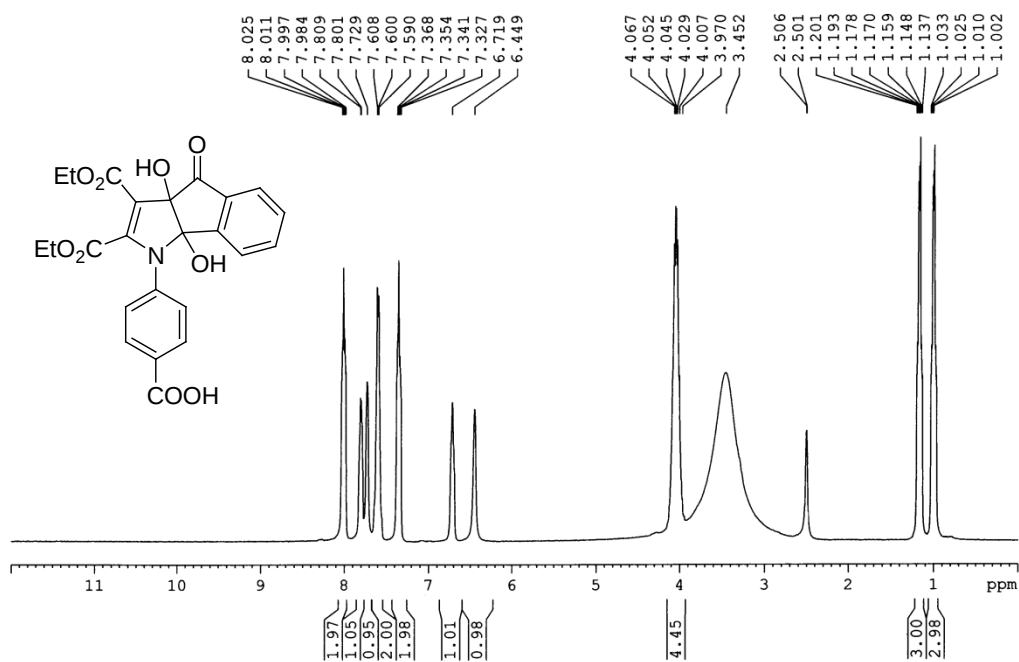
¹³C NMR of compound **4i**



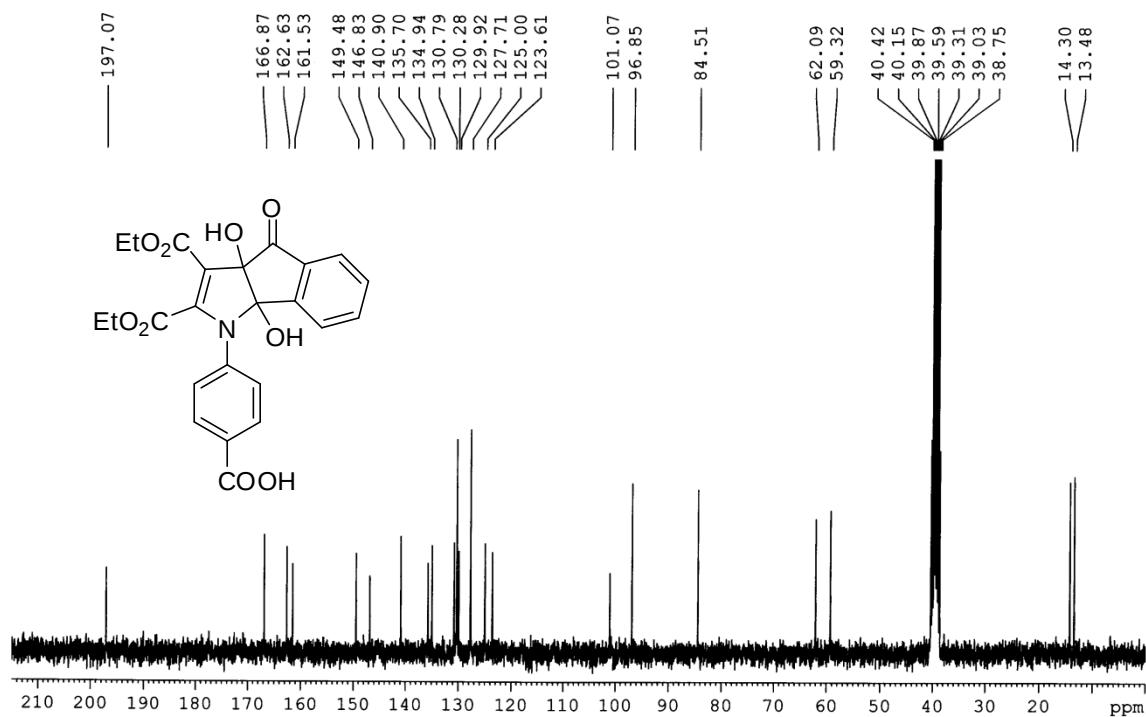
¹H NMR of compound 4j



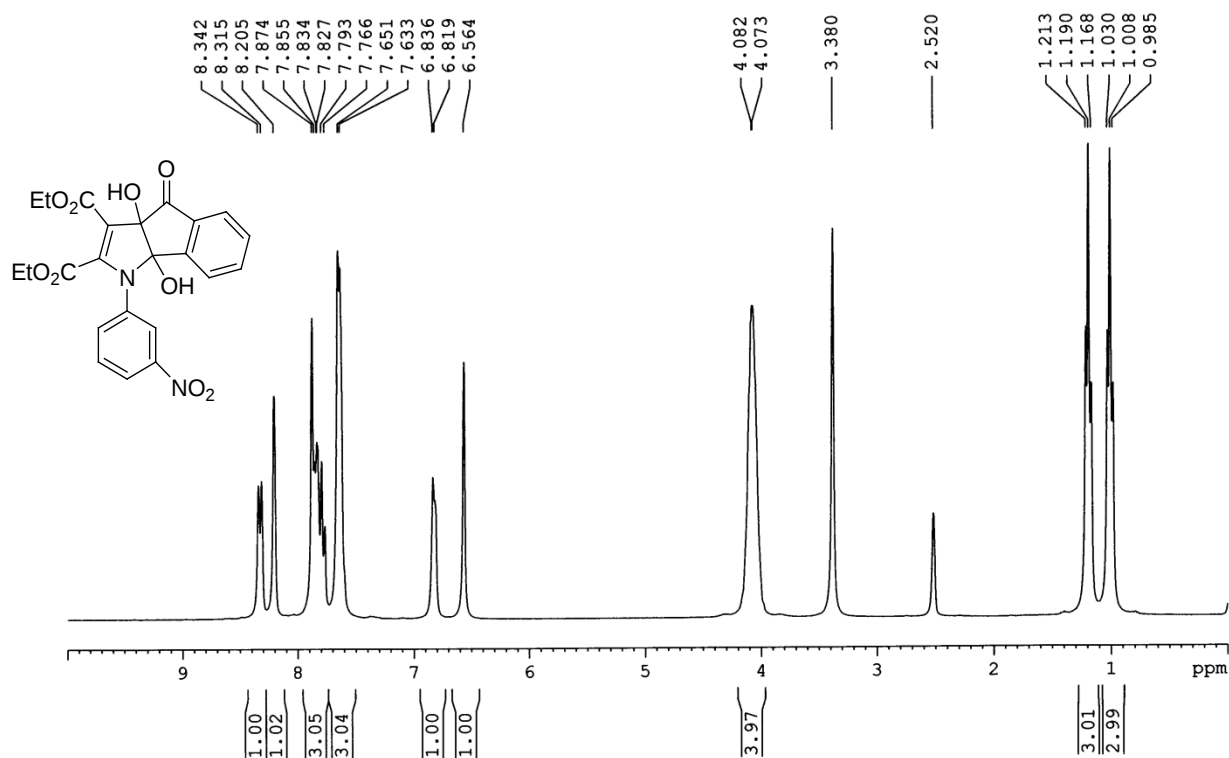
¹³C NMR of compound 4j



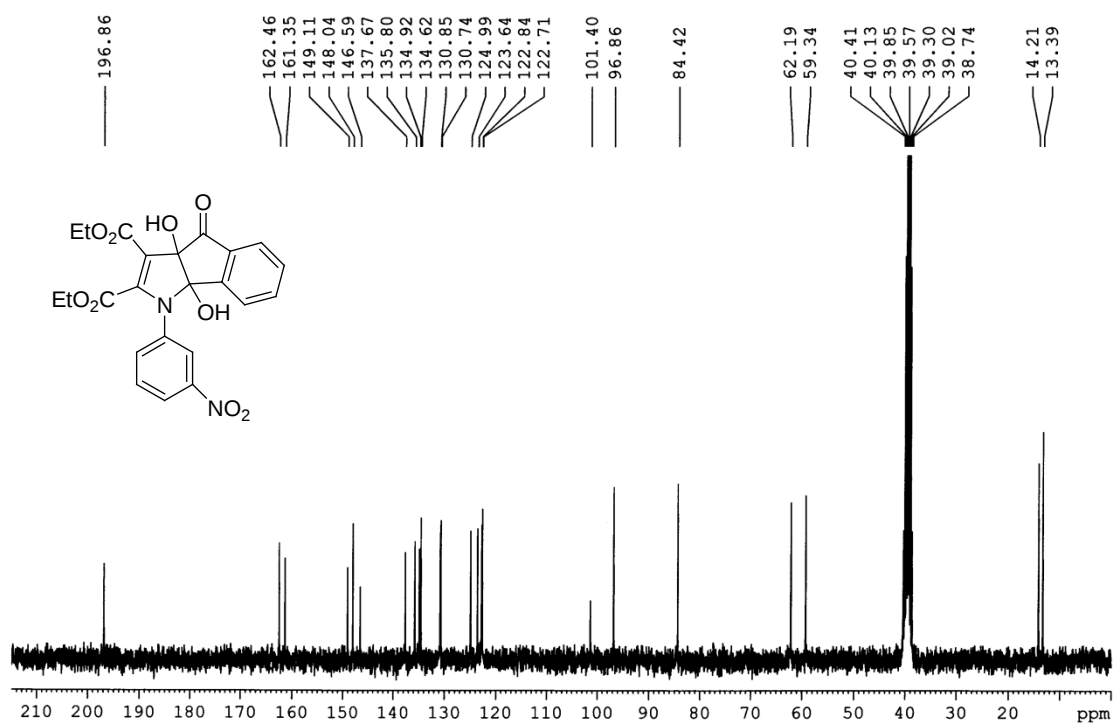
¹H NMR of compound **4k**



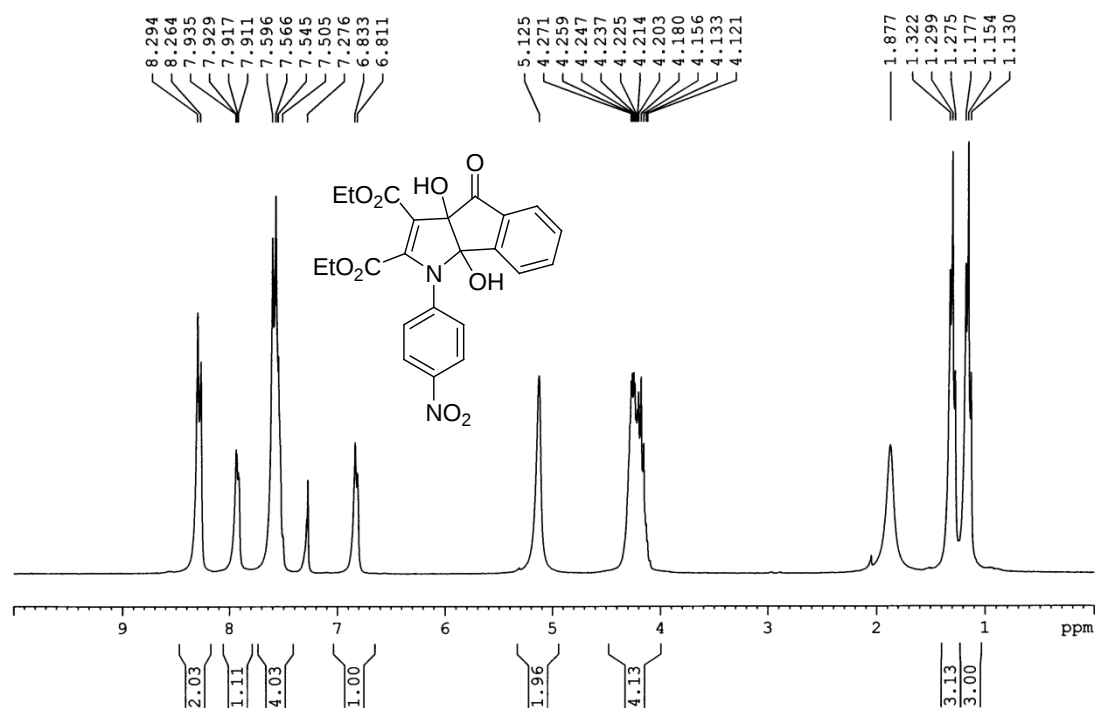
¹³C NMR of compound **4k**



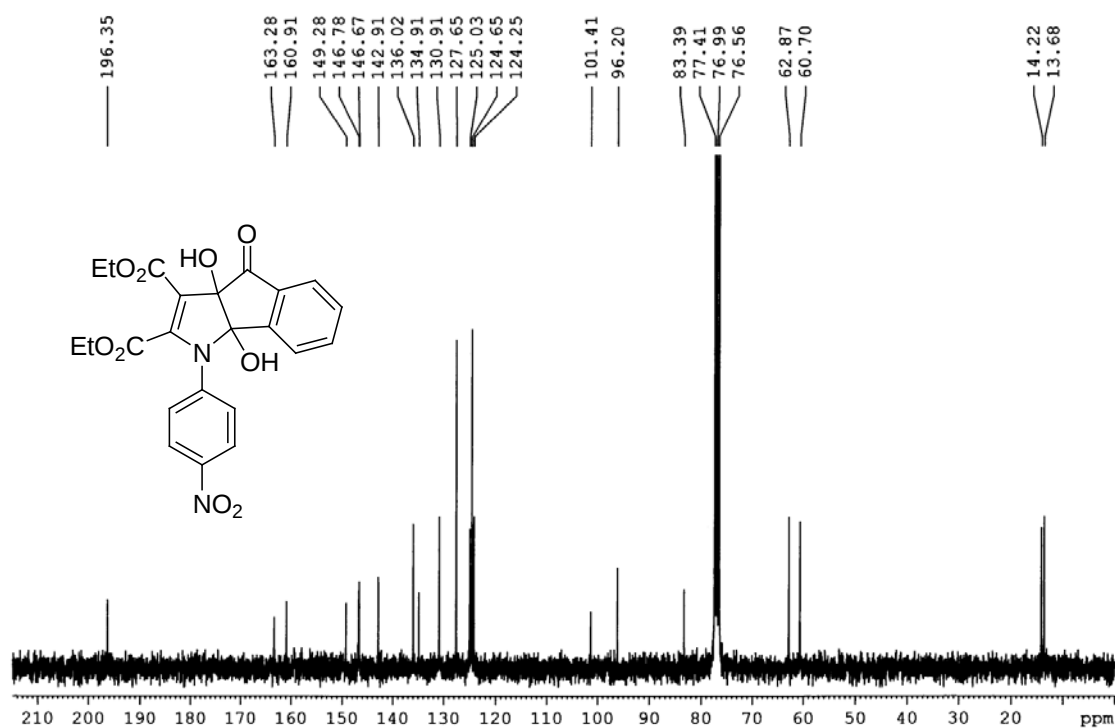
¹H NMR of compound 4I



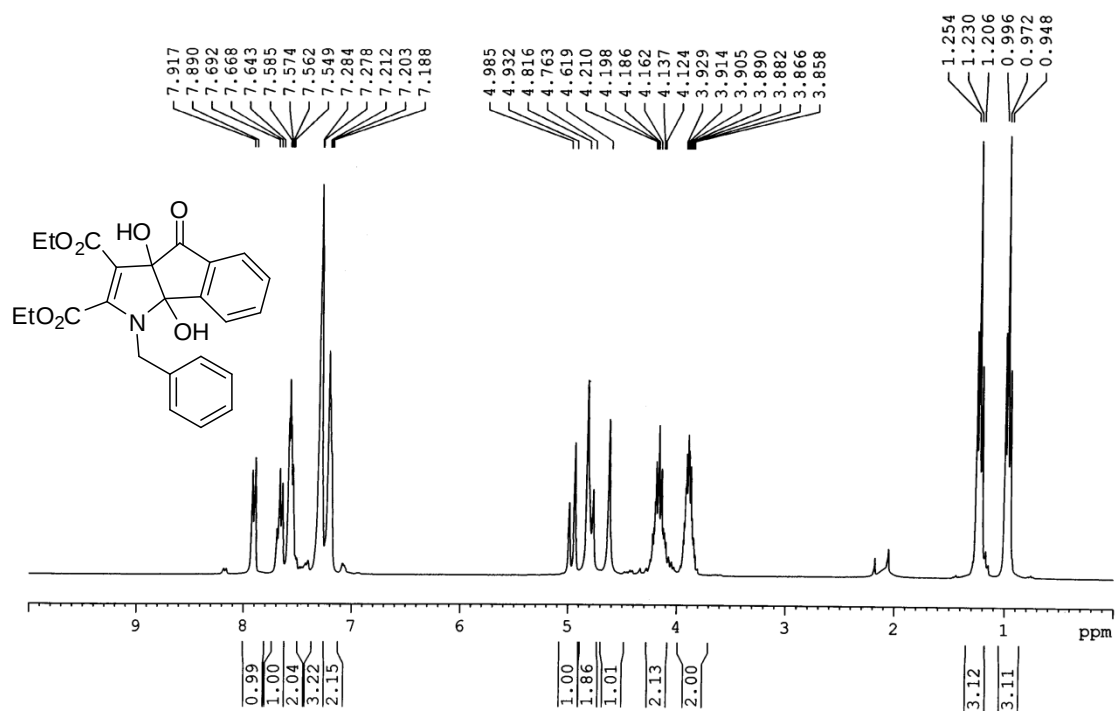
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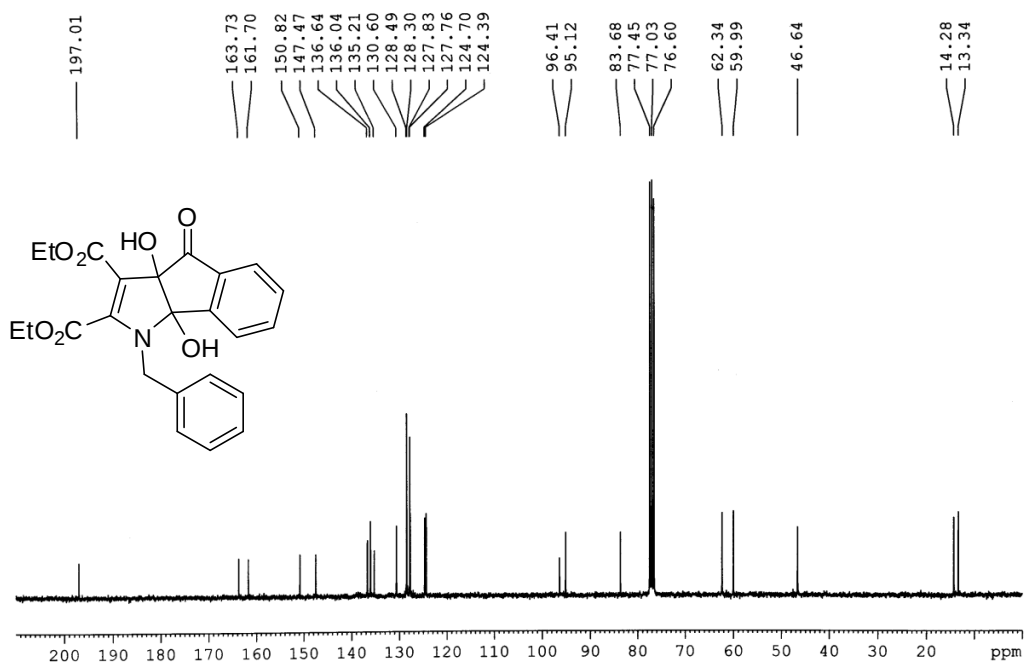
¹H NMR of compound 4m



¹³C NMR of compound 4m

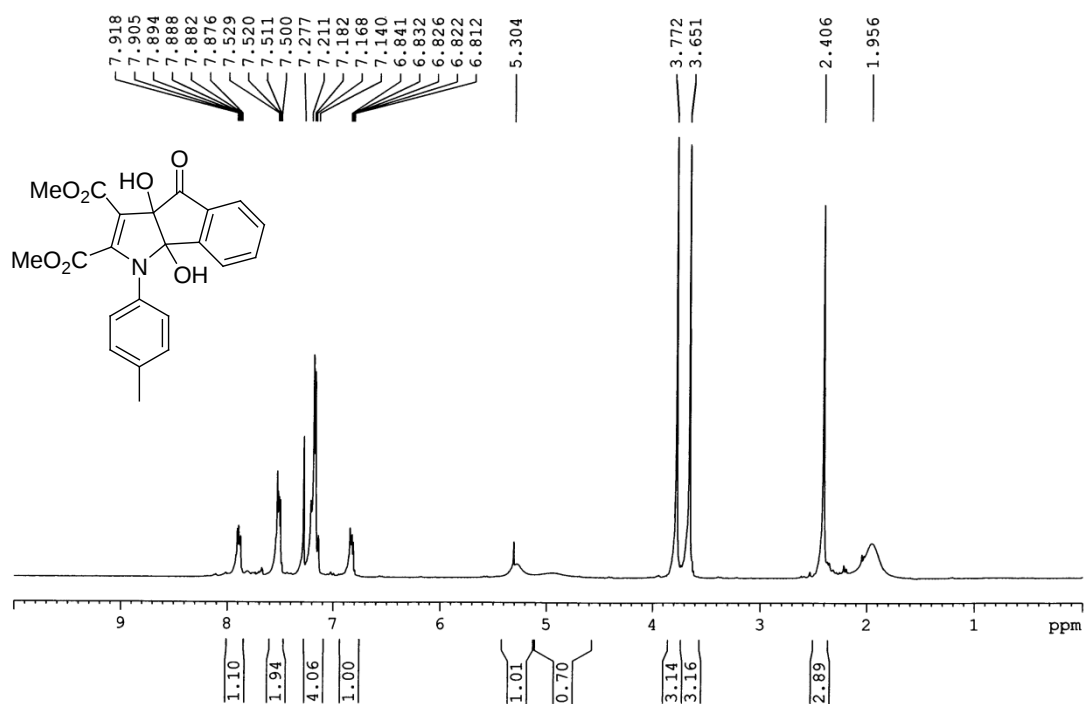


¹H NMR of compound **4n**

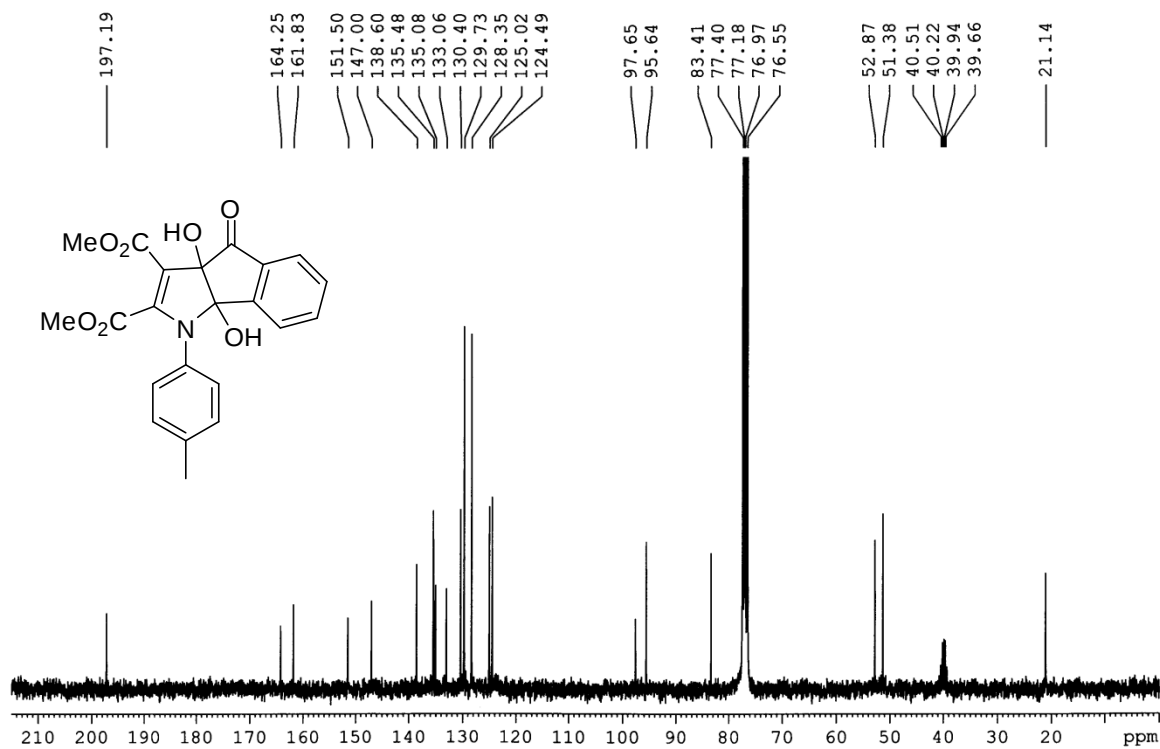


¹³C NMR of compound **4n**

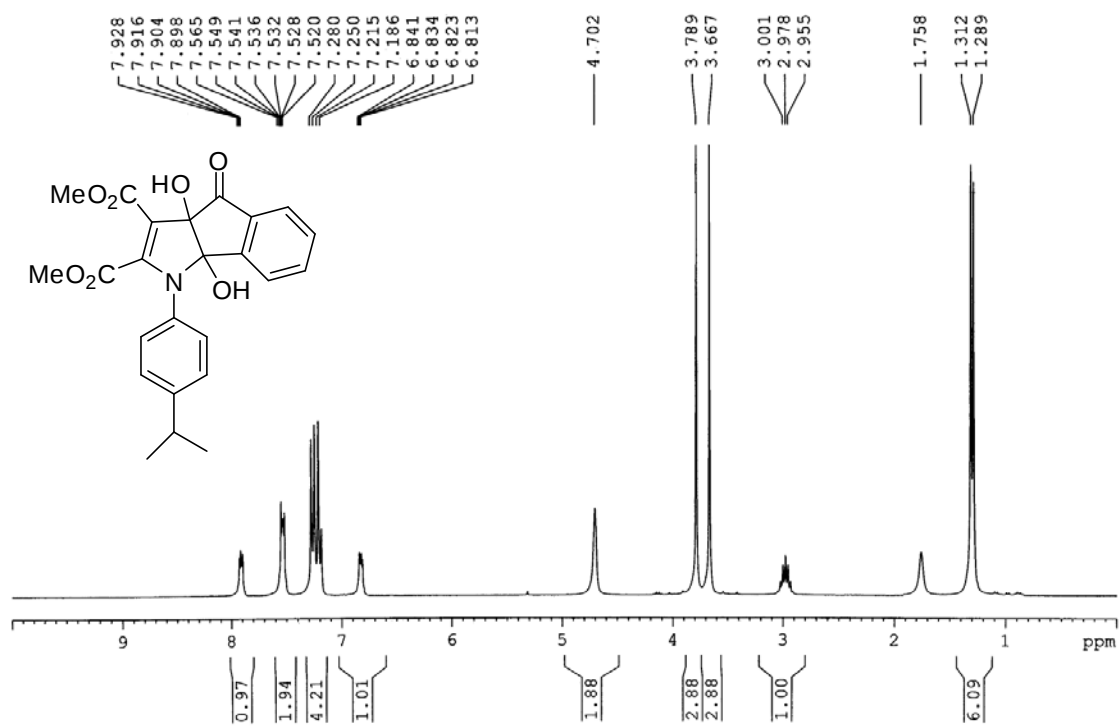
Copy of ^1H and ^{13}C NMR spectra of synthesized compounds (6a-6j):



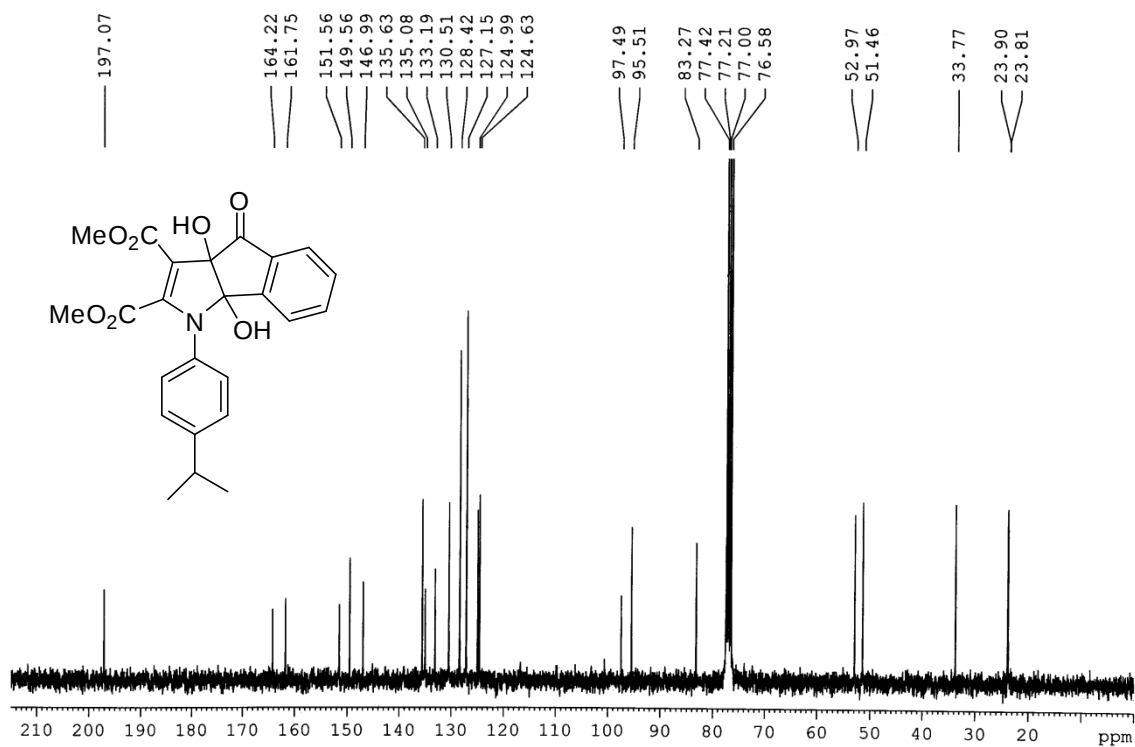
^1H NMR of compound **6a**



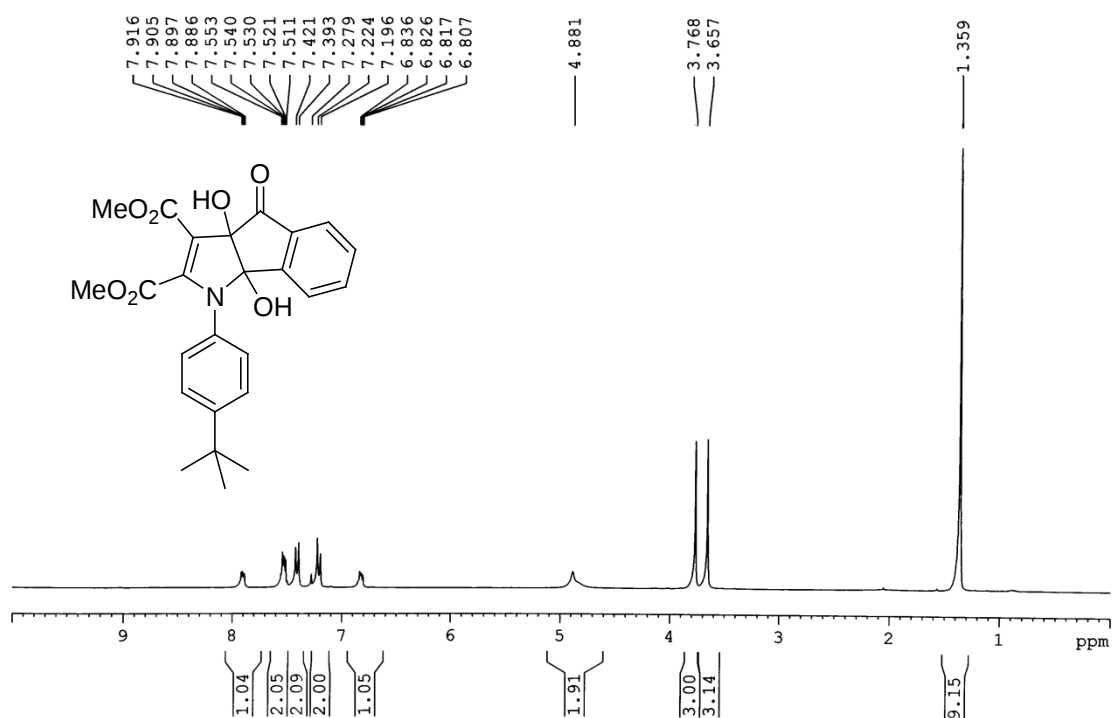
^{13}C NMR of compound **6a**



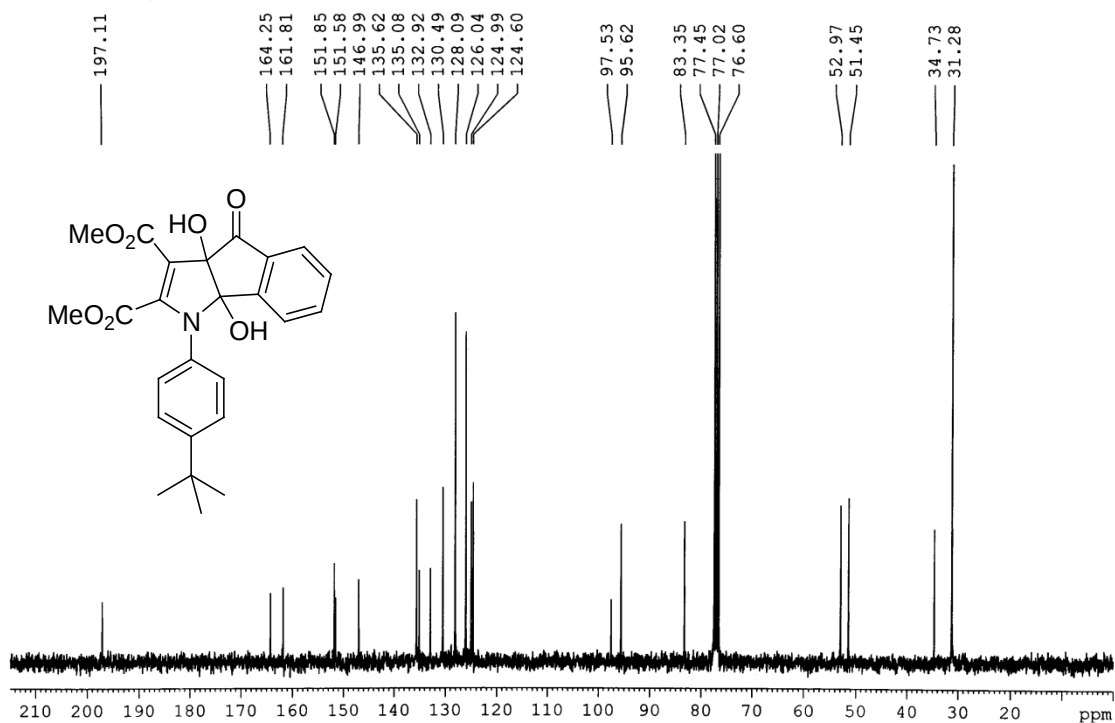
¹H NMR of compound **6b**



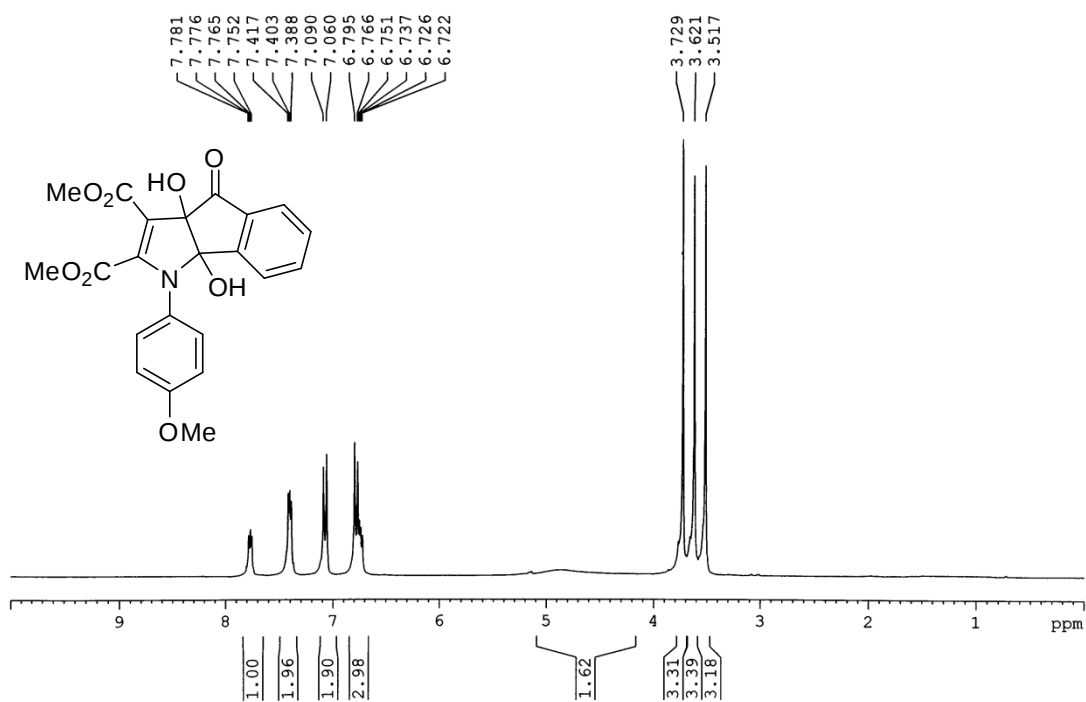
¹³C NMR of compound **6b**



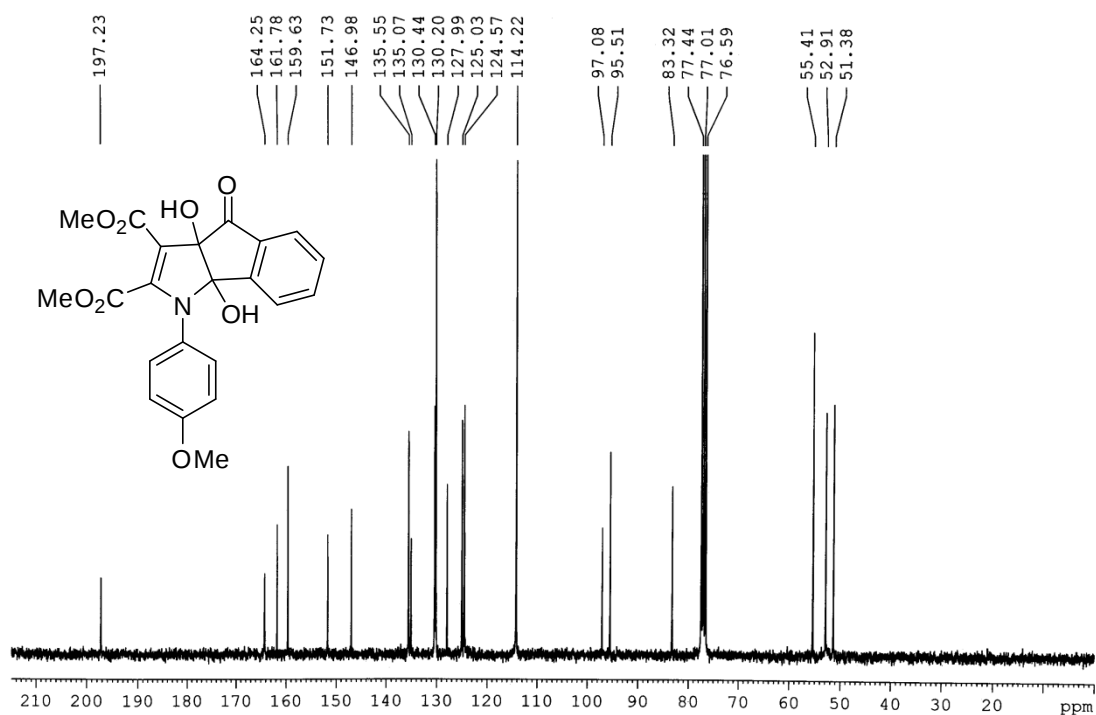
¹H NMR of compound 6c



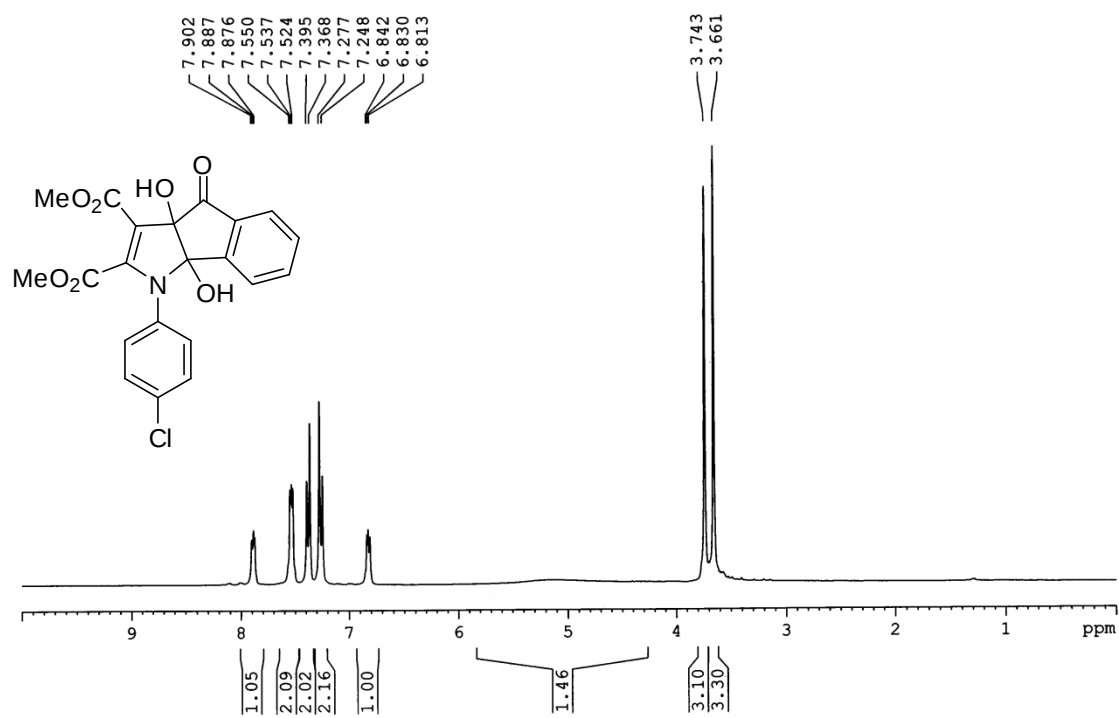
¹³C NMR of compound 6c



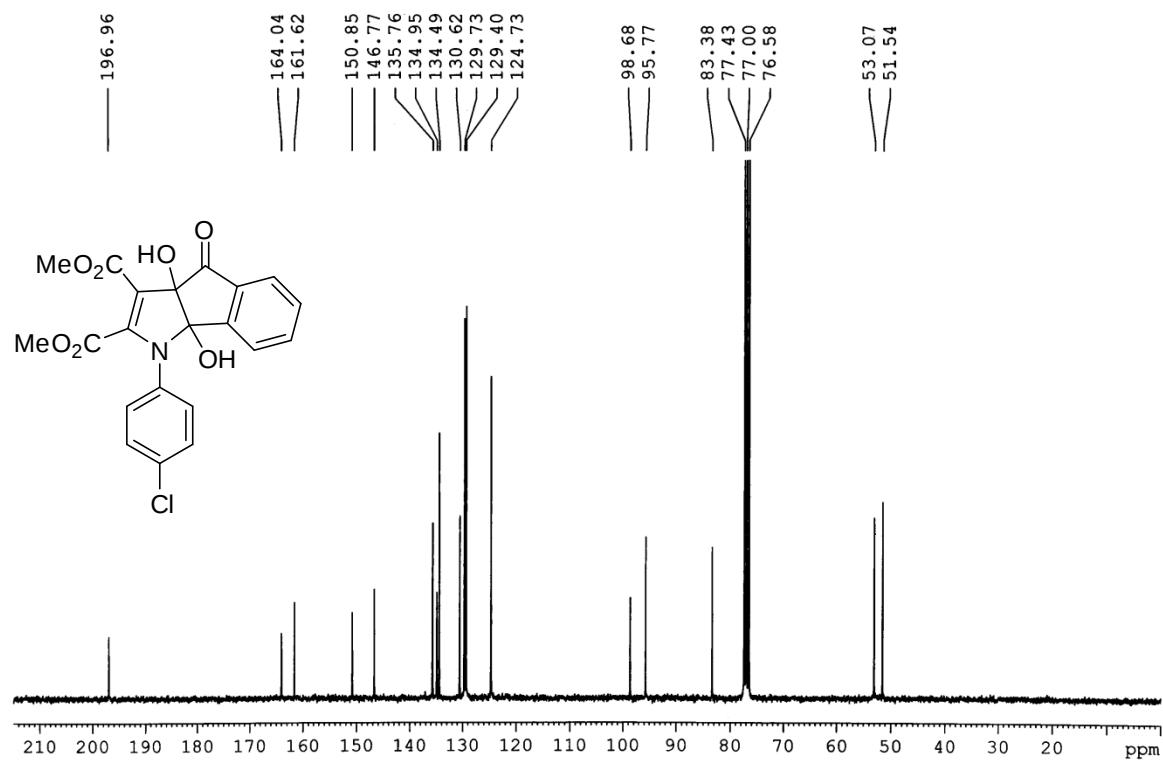
¹H NMR of compound 6d



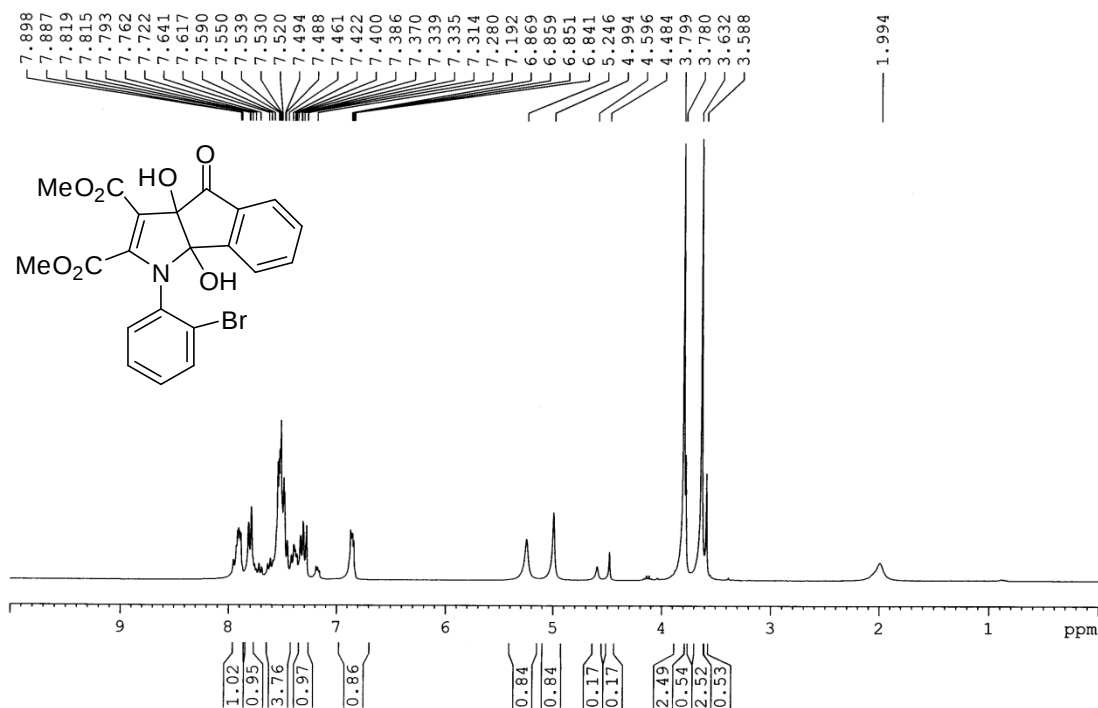
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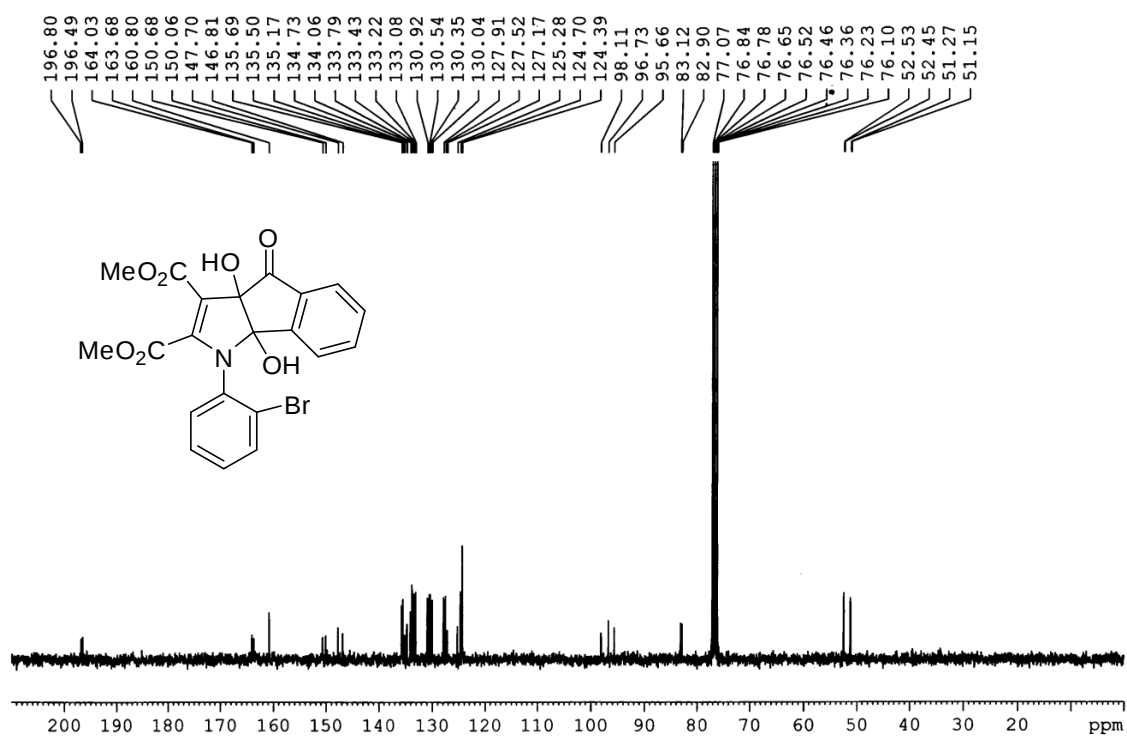
¹H NMR of compound **6e**



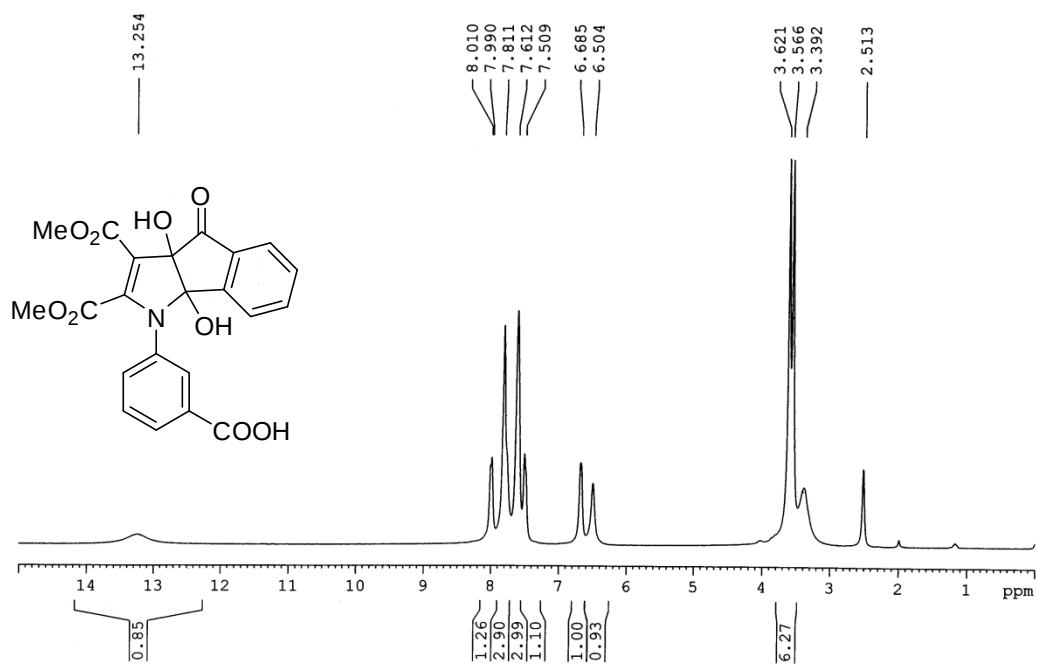
¹³C NMR of compound **6e**



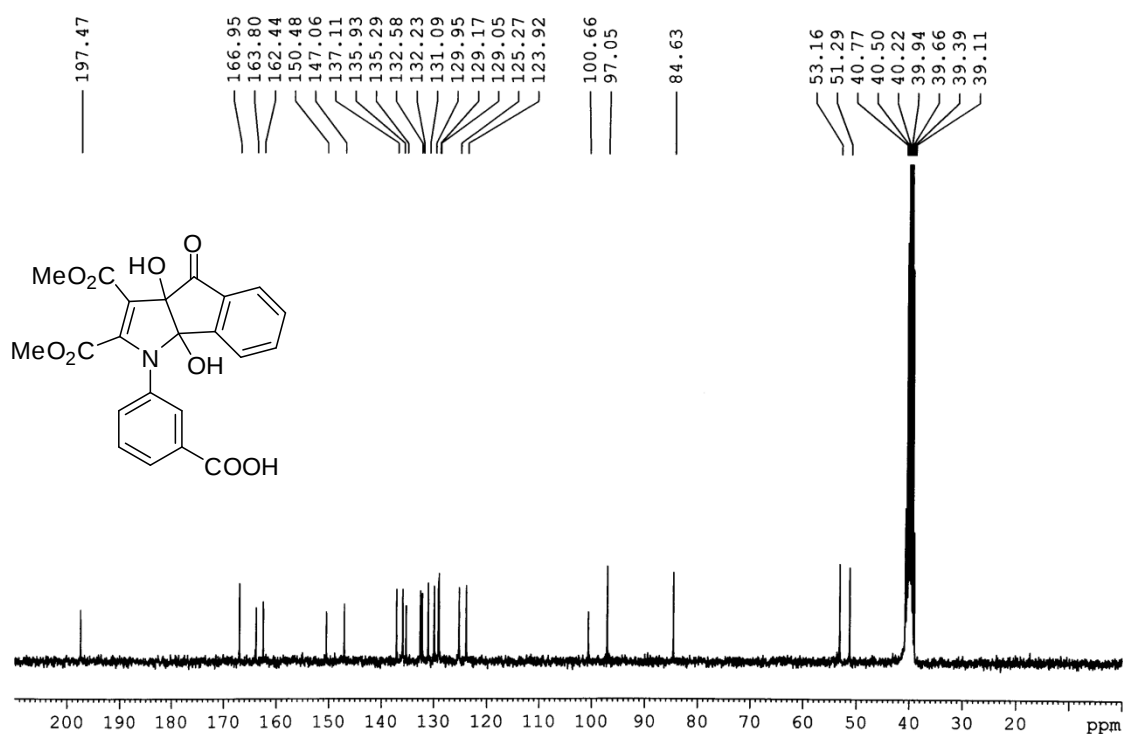
¹H NMR of compound 6f



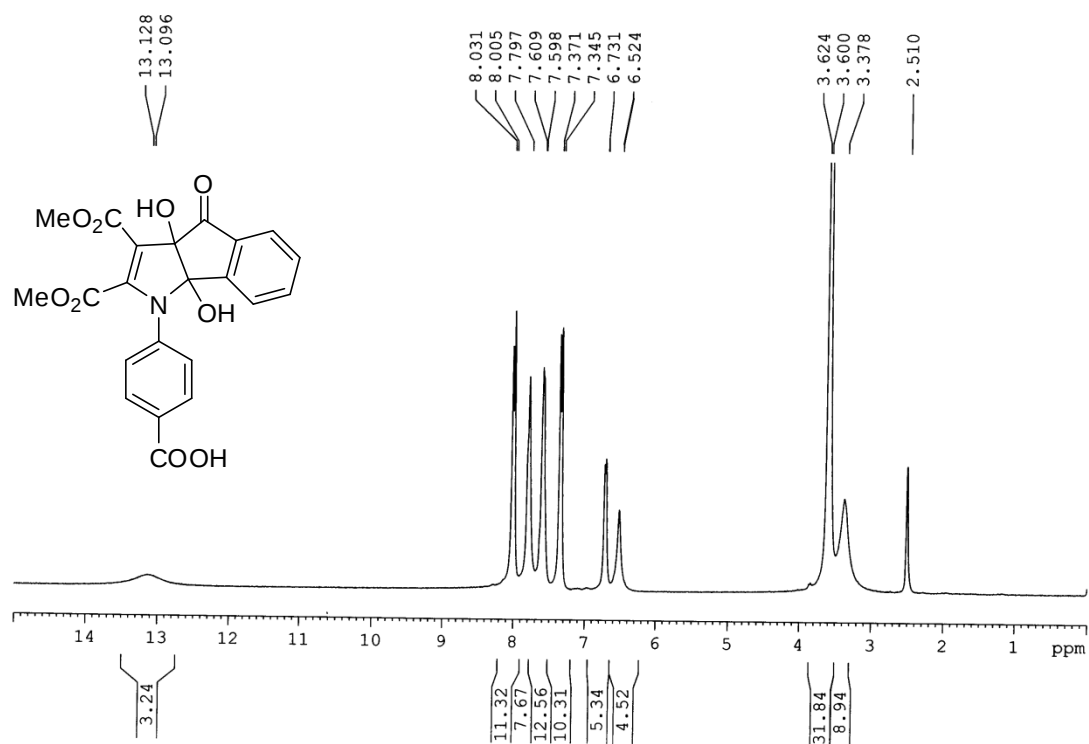
¹³C NMR of compound 6f



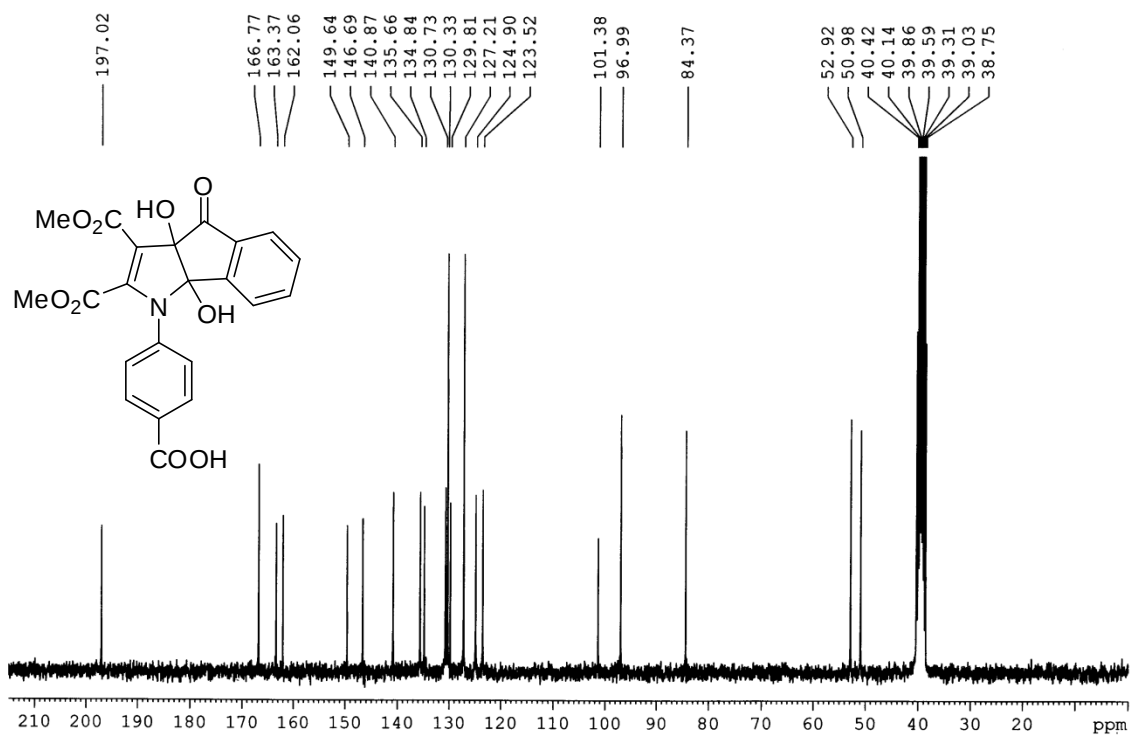
¹H NMR of compound **6g**



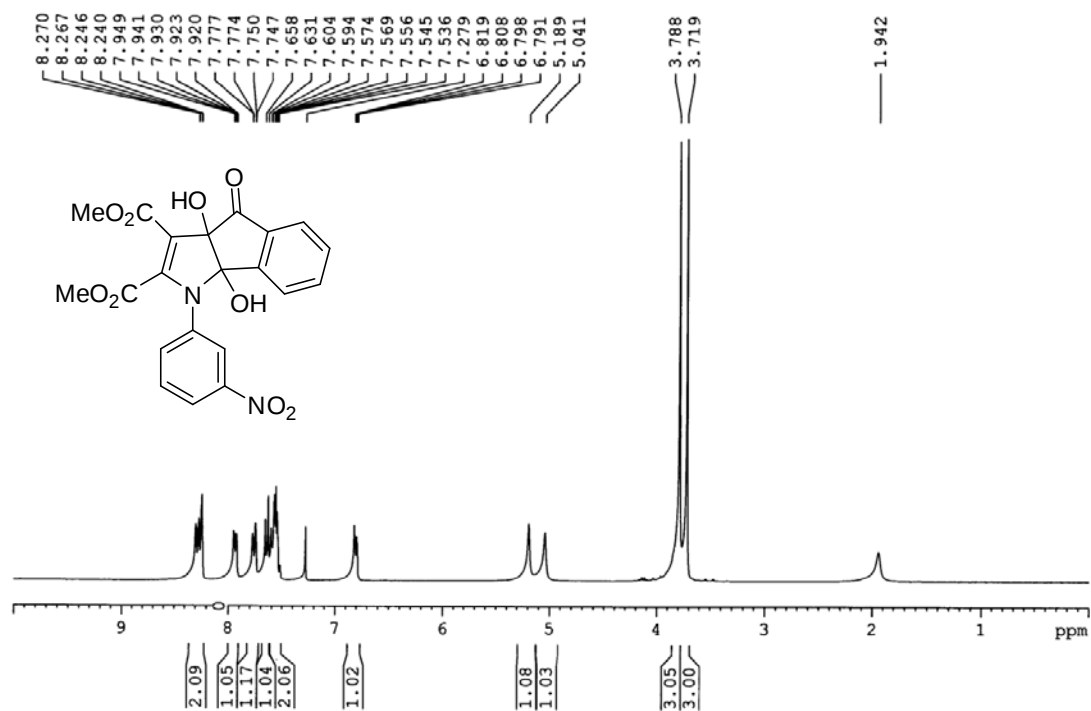
¹³C NMR of compound **6g**



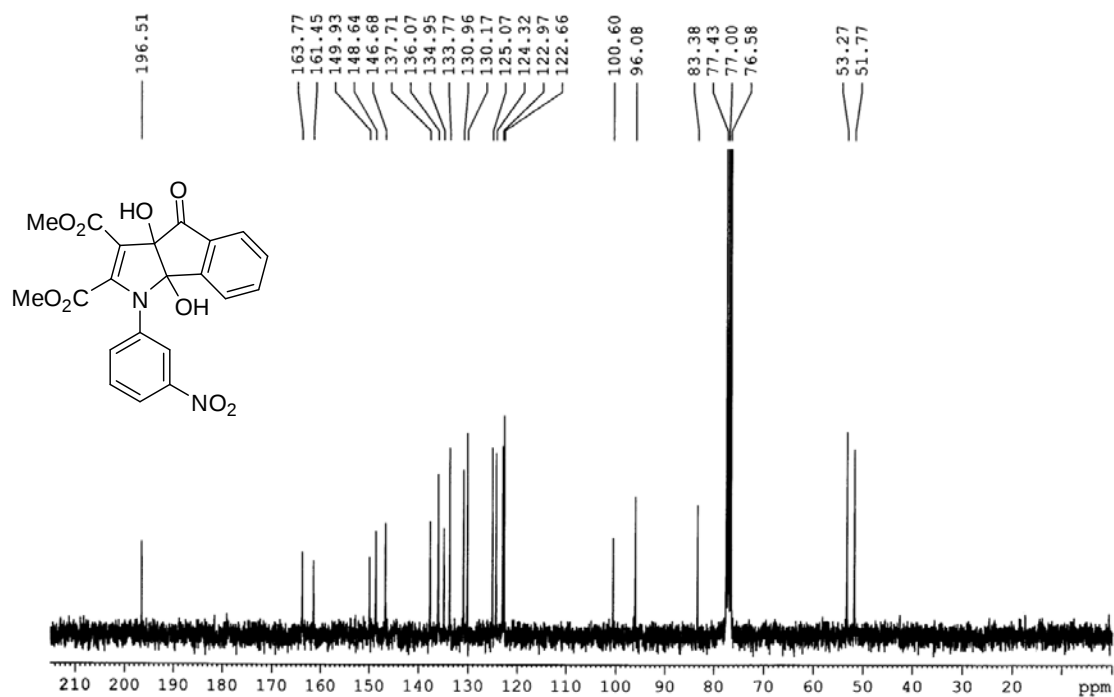
¹H NMR of compound **6h**



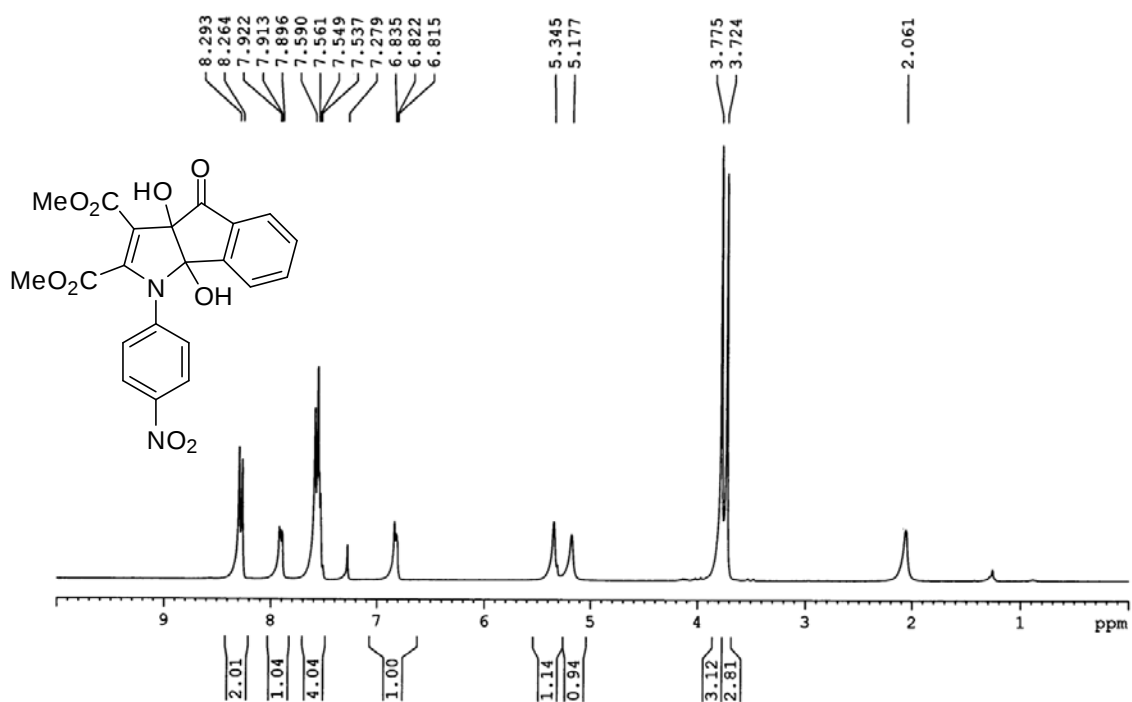
¹³C NMR of compound **6h**



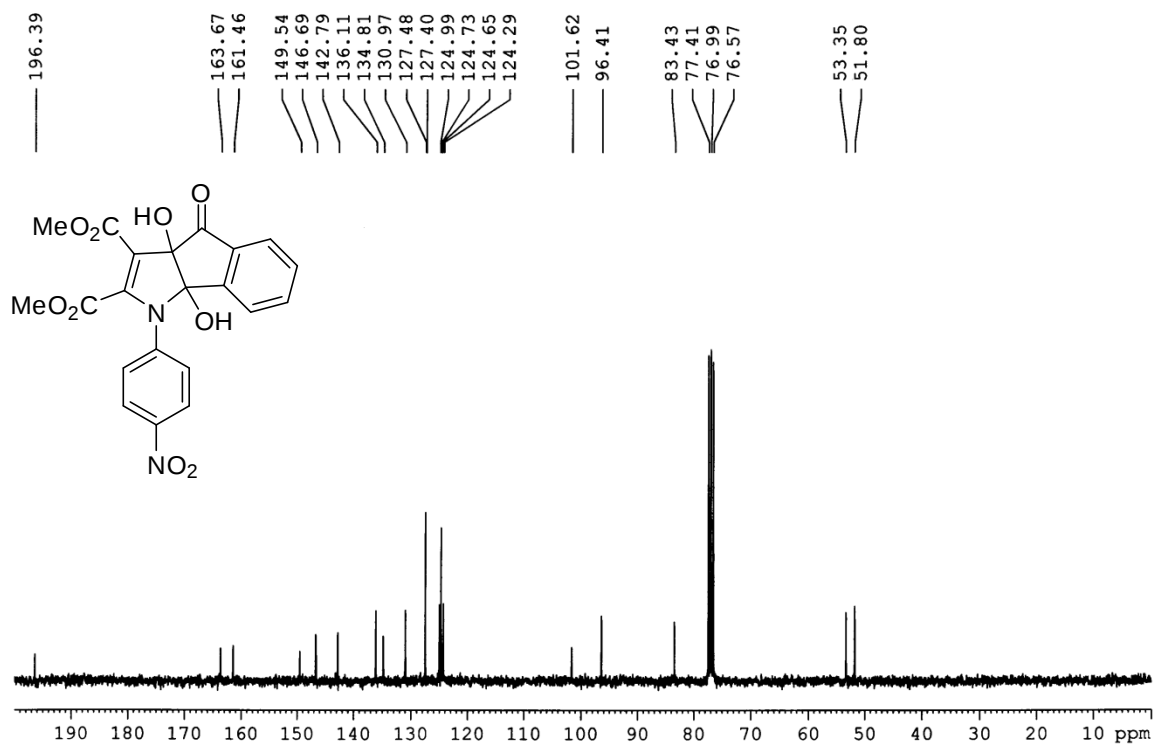
^1H NMR of compound **6i**



^{13}C NMR of compound **6i**

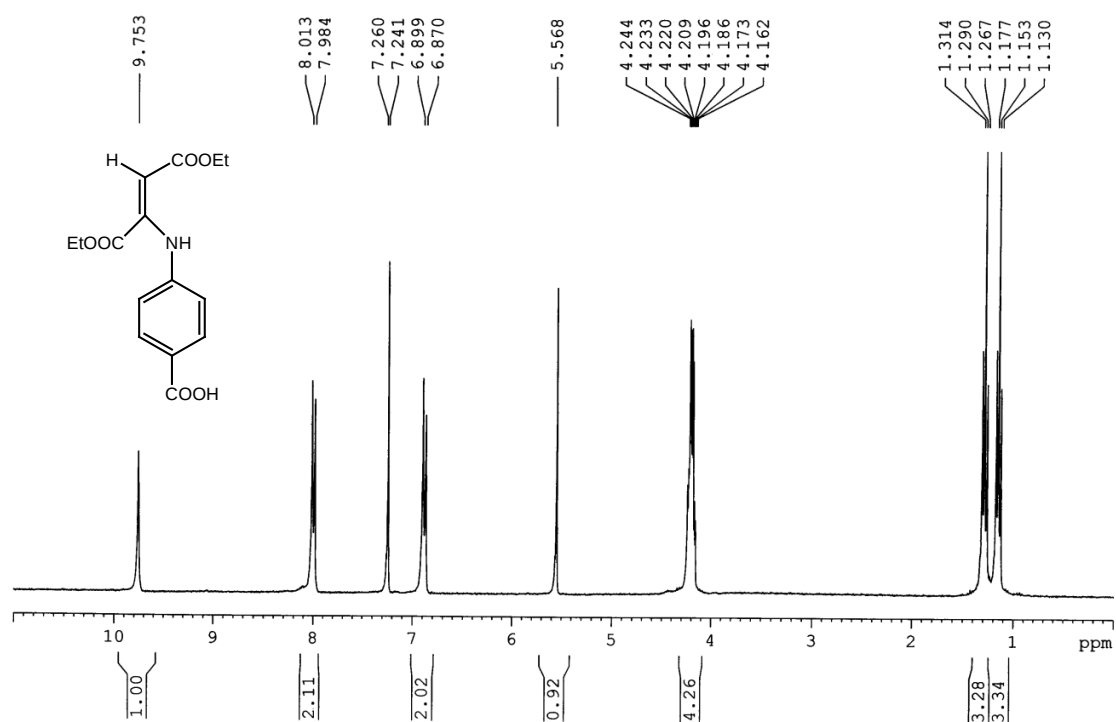


¹H NMR of compound **6j**

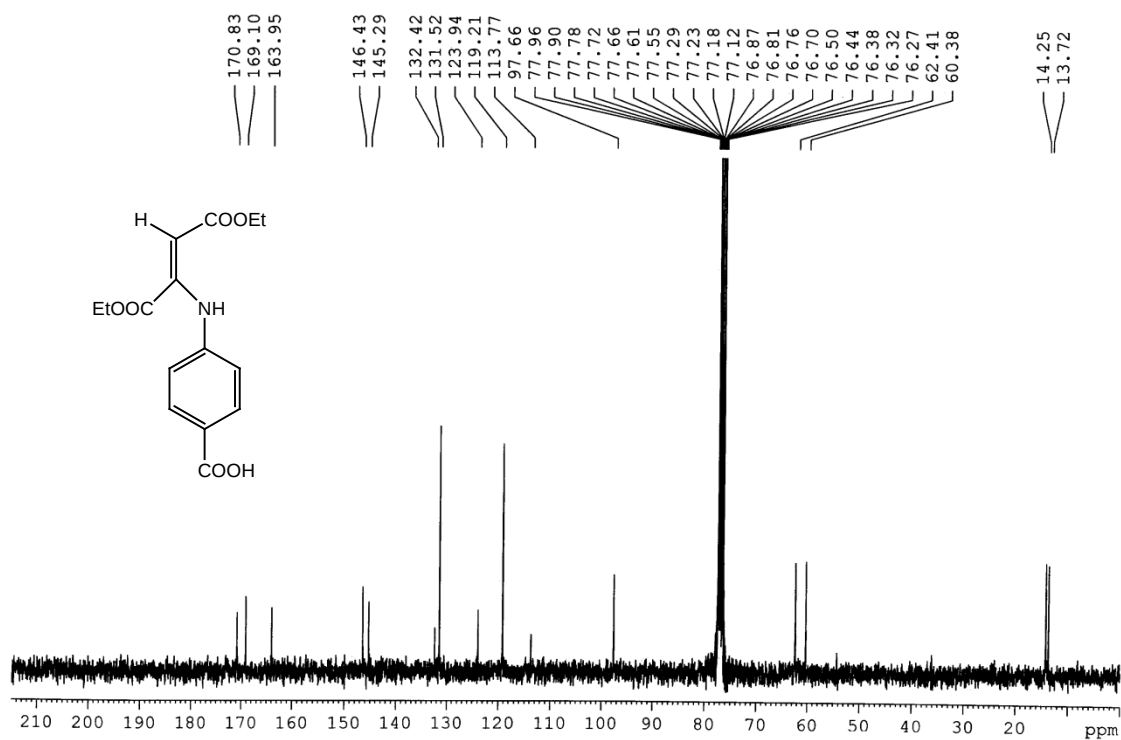


¹³C NMR of compound **6j**

Copy of ^1H and ^{13}C NMR spectra of Intermediate A:



^1H NMR of Intermediate A



^{13}C NMR of Intermediate A