Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting Information 2

I_2 catalyzed access of spiro[indoline-3,4'-pyridine] appended amine dyad: New ON-OFF chemosensors for Cu^{2+} and imaging in living cells

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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 60 °C 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). ^{1}H /^{13}C NMR spectra were recorded in a 300 MHz Bruker instrument using DMSO-d_6 solvent with TMS as reference. The absorption and emission spectra were recorded on a Hitachi UV-Vis U-3501 spectrophotometer and Perkin-Elmer LS55 fluorimeter, respectively. HRMS with an ESI resource were acquired using a Waters XEVO-G2S Q TOF mass spertrometer. 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 spiro[indoline-3,4'-pyridine] derivatives (5a-5n and 6a-6m):

In a round bottom flask equipped with a condenser, a mixture of dialkyl but-2-ynedioate (1 mmol), amine (1 mmol), isatin (1 mmol) and malononitrile (1 mmol) were added with 10 mol % of I_2 in 1:1 (v/v) aqueous ethanol (5 mL) and stirred for 8 h at 60 °C. The TLC analysis of the reaction mixture showed the completion of this reaction. After completion of the reaction, the mixture was cooled and diluted with ethyl acetate. Then the solvent was extracted with ethyl acetate for three times and followed by brine solution using separating funnel and was evaporated in a rotary evaporator. Finally, the crude residue was subjected to silicagel column chromatography using 40 % ethyl acetate in petroleum ether (60-80 °C) as eluant to afford the desired product as yellow solid. 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, ^{1}H/^{13}C NMR, melting point measurements, CHN and HRMS analysis.

Spectroscopic and Analytical characterization of compounds 5a-5n:

Diethyl 5'-cyano-2-oxo-6'-(phenylamino)-1'H-spiro[indoline-3,4'-pyridine]-2',3'-dicarboxylate: (**Scheme 2, 5a**): Yield 88 % (403 mg); yellow solid; Mp: 238-240 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.57; IR (ν_{max}, KBr, cm^{-1}): 3373, 3178, 2199, 1734, 1695, 1621, 1495, 1293, 1215, 1126, 760; ^{1}H NMR (300 MHz, DMSO-d_6) δ_H: 10.45 (s, 1H, NH), 10.19 (s, 1H, NH), 8.73 (s, 1H, NH), 7.30-7.17 (m, 4H, ArH), 7.02-6.91 (m, 4H, ArH), 6.81 (t, *J*=7.8 Hz, 1H, ArH), 4.19 (q, *J*=6.8 Hz, 2H, OCH_2), 3.78 (q, *J*=6.8 Hz, 2H, OCH_2), 1.25 (t, *J*=7.1 Hz, 3H, CH_3), 0.86 (t, *J*=6.9 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ_C: 178.7, 163.8, 162.8, 146.3, 141.3, 141.1, 139.9, 135.7, 129.2, 128.9, 124.1, 122.1, 121.4, 117.9, 117.4, 109.4, 101.9, 70.7, 62.0, 60.3, 51.0, 13.7, 13.2; Anal. calcd. for $C_{25}H_{22}N_4O_5$; C: 65.49; H: 4.84; N: 12.22. Found: C: 65.41; H: 4.85; N: 12.26%; HRMS (ESI) calcd for $C_{25}H_{22}N_4O_5$: 459.1668 $(M+H)^+$; found: 459.1679.

Diethyl 5'-cyano-2-oxo-6'-(o-tolylamino)-1'H-spiro[indoline-3,4'-pyridine]-2',3'-dicarboxylate: (**Scheme 2, 5b**): Yield 86 % (406 mg); yellow solid; Mp: 248-250 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.48; IR (ν_{max}, KBr, cm^{-1}): 3368, 3138, 2197, 1721, 1659, 1607, 1369, 1245, 1138, 1089, 812; ^{1}H NMR (300 MHz, DMSO-d_6) δ_H: 10.39 (s, 1H, NH), 9.76 (s, 1H, NH), 8.00 (s, 1H, NH), 7.22-7.11 (m, 4H, ArH), 7.01-6.92 (m, 3H, ArH), 6.78 (d, *J*=7.5 Hz, 1H, ArH), 4.18 (q, *J*=7.1 Hz, 2H, OCH_2), 3.76 (q, *J*=6.9 Hz, 2H, OCH_2), 2.20 (s, 3H, Ar-CH_3), 1.23 (t, *J*=7.1 Hz, 3H, CH_3), 0.84 (t, *J*=7.1 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ_C: 178.8, 163.9, 162.9, 147.8, 141.5, 139.6, 138.5, 135.8, 131.0, 130.8, 128.8, 126.5, 124.1, 122.2, 122.0, 117.3, 109.3, 101.9, 67.6, 62.0, 60.2, 51.2, 17.8, 13.7, 13.2; Anal. calcd. for $C_{26}H_{24}N_4O_5$; C: 66.09; H: 5.12; N: 11.86. Found: C: 66.65; H: 5.11; N: 11.91%; HRMS (ESI) calcd for $C_{26}H_{24}N_4O_5$: 473.1825 $(M+H)^+$; found: 473.1835.

Diethyl 5'-cyano-2-oxo-6'-(m-tolylamino)-1'H-spiro[indoline-3,4'-pyridine]-2',3'-dicarboxylate: (**Scheme 2, 5c**): Yield 89 % (421 mg); yellow solid; Mp: 244-246 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.43; IR (ν_{max}, KBr, cm^{-1}): 3359, 3136, 2189, 1709, 1682, 1511, 1509, 1378, 1205, 1156, 759; ^{1}H NMR (300 MHz, DMSO-d_6) δ_H: 10.45 (s, 1H, NH), 10.18 (s, 1H, NH), 8.66 (s, 1H, NH), 7.23-7.13 (m, 3H, ArH), 6.99 (t, *J*=7.5 Hz, 1H, ArH), 6.82-6.72 (m, 4H, ArH), 4.18 (q, *J*=7.1 Hz, 2H, OCH_2), 3.78 (q, *J*=7.1 Hz, 2H, OCH_2), 2.25 (s, 3H, Ar-CH_3), 1.25 (t, *J*=7.1 Hz, 3H, CH_3), 0.86 (t, *J*=7.1 Hz, 3H,

CH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ_C: 178.7, 163.8, 162.8, 146.3, 141.3, 141.0, 139.9, 138.4, 135.7, 129.1, 128.9, 124.1, 122.2, 122.1, 118.5, 117.4, 115.2, 109.4, 101.9, 70.6, 62.0, 60.3, 51.0, 21.2, 13.7, 13.2; Anal. calcd. for $C_{26}H_{24}N_4O_5$; C: 66.09; H: 5.12; N: 11.86. Found: C: 66.14; H: 5.14; N: 11.83%; HRMS (ESI) calcd for $C_{26}H_{24}N_4O_5$: 473.1825 $(M+H)^+$; found: 473.1831.

Diethyl 5'-cyano-2-oxo-6'-(p-tolylamino)-1'H-spiro[indoline-3,4'-pyridine]-2',3'-dicarboxylate: (**Scheme 2, 5d**): Yield 91 % (430 mg); greenish yellow solid; Mp: 208-210 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.50; IR (ν_{max}, KBr, cm^{-1}): 3373, 3185, 2198, 1720, 1700, 1620, 1472, 1289, 1215, 1119, 1019, 754; ^1H NMR (300 MHz, DMSO-d_6) δ_H: 10.42 (s, 1H, NH), 10.03 (s, 1H, NH), 8.60 (s, 1H, NH), 7.23-7.15 (m, 2H, ArH), 7.09 (d, *J*=8.1 Hz, 2H, ArH), 7.99 (t, *J*=7.4 Hz, 1H, ArH), 6.86-6.79 (m, 3H, ArH), 4.18 (q, *J*=6.9 Hz, 2H, OCH_2), 3.77 (q, *J*=6.9 Hz, 2H, OCH_2), 2.23 (s, 3H, Ar-CH_3), 1.25 (t, *J*=7.2 Hz, 3H, CH_3), 0.85 (t, *J*=7.1 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ_C: 178.7, 163.8, 162.8, 146.7, 141.4, 139.8, 138.1, 135.8, 130.8, 129.6, 128.8, 124.0, 122.1, 118.7, 117.6, 109.3, 102.0, 68.9, 62.0, 60.2, 51.0, 20.3, 13.7, 13.2; Anal. calcd. for $C_{26}H_{24}N_4O_5$; C: 66.09; H: 5.12; N: 11.86. Found: C: 66.01; H: 5.11; N: 11.88%; HRMS (ESI) calcd for $C_{26}H_{24}N_4O_5$: 473.1825 $(M+H)^+$; found: 473.1801.

Diethyl 5'-cyano-6'-(4-isopropylphenylamino)-2-oxo-1'H-spiro[indoline-3,4'-pyridine]-2',3'-dicarboxylate: (**Scheme 2, 5e**): Yield 90 % (450 mg); yellow solid; Mp: 232-234 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.55; IR (ν_{max}, KBr, cm^{-1}): 3307, 2959, 2192, 1740, 1714, 1623, 1533, 1471, 1372, 1219, 1015, 752; ^1H NMR (300 MHz, DMSO-d_6) δ_H: 10.43 (s, 1H, NH), 10.09 (s, 1H, NH), 8.62 (s, 1H, NH), 7.19 (q, *J*=7.5 Hz, 4H, ArH), 6.99 (t, *J*=7.4 Hz, 1H, ArH), 6.88 (d, *J*=8.1 Hz, 2H, ArH), 6.81 (d, *J*=7.8 Hz, 1H, ArH), 4.19 (q, *J*=6.9 Hz, 2H, OCH_2), 3.78 (q, *J*=6.8 Hz, 2H, OCH_2), 2.87-2.80 (m, 1H, CH), 1.25 (t, *J*=7.1 Hz, 3H, CH_3), 1.18 (d, *J*=6.6 Hz, 6H, CH_3), 0.86 (t, *J*=6.9 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ_C: 178.7, 163.8, 162.8, 146.6, 141.8, 141.3, 139.9, 138.6, 135.8, 128.8, 127.0, 124.0, 122.1, 118.4, 117.5, 109.3, 101.9, 69.6, 61.9, 60.2, 51.0, 32.8, 24.1, 13.7, 13.2; Anal. calcd. for $C_{28}H_{28}N_4O_5$; C: 67.19; H: 5.64; N: 11.19. Found: C: 67.24; H: 5.63; N: 11.16%; HRMS (ESI) calcd for $C_{28}H_{28}N_4O_5$: 501.2138 $(M+H)^+$; found: 501.2142.

Diethyl 5'-cyano-6'-(3,4-dimethylphenylamino)-2-oxo-1'H-spiro[indoline-3,4'-pyridine]-2',3'-dicarboxylate: (**Scheme 2, 5f**): Yield 91 % (443 mg); yellowish white solid; Mp: 194-196 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.48; IR (ν_{max}, KBr, cm^{-1}):

3212, 3089, 2197, 1713, 1650, 1619, 1506, 1300, 1124, 1018, 752; ^{1}H NMR (300 MHz, DMSO-d_6) δ_H: 10.42 (s, 1H, NH), 10.03 (s, 1H, NH), 8.55 (s, 1H, NH), 7.23-7.15 (m, 2H, ArH), 7.05-6.96 (m, 2H, ArH), 6.80 (d, *J*=7.5 Hz, 1H, ArH), 6.75 (s, 1H, ArH), 6.69 (d, *J*=7.8 Hz, 1H, ArH), 4.18 (q, *J*=6.8 Hz, 2H, OCH_2), 3.78 (q, *J*=6.8 Hz, 2H, OCH_2), 2.17 (s, 3H, Ar-CH_3), 2.15 (s, 3H, Ar-CH_3), 1.25 (t, *J*=6.8 Hz, 3H, CH_3), 0.86 (t, *J*=6.8 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ_C: 178.8, 163.9, 162.8, 146.7, 141.3, 139.8, 138.3, 136.8, 135.8, 130.1, 129.6, 128.8, 124.0, 122.1, 120.0, 117.7, 116.3, 109.4, 102.0, 68.7, 62.0, 60.3, 51.0, 19.7, 18.7, 13.7, 13.2; Anal. calcd. for $C_{27}H_{26}N_4O_5$; C: 66.65; H: 5.39; N: 11.52. Found: C: 66.54; H: 5.41; N: 11.46%; HRMS (ESI) calcd for $C_{27}H_{26}N_4O_5$: 487.1981 $(M+H)^+$; found: 487.1998.

Diethyl 5'-cyano-6'-(3-methoxyphenylamino)-2-oxo-1'H-spiro[indoline-3,4'-pyridine]-2',3'-dicarboxylate: (**Scheme 2, 5g**): Yield 90 % (440 mg); yellow solid; Mp: 202-204 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.45; IR (ν_{max}, KBr, cm^{-1}): 3346, 3157, 2171, 1721, 1618, 1403, 1388, 1242, 1092, 825; ^{1}H NMR (300 MHz, DMSO-d_6) δ_H: 10.46 (s, 1H, NH), 10.22 (s, 1H, NH), 8.73 (s, 1H, NH), 7.23-7.14 (m, 3H, ArH), 6.99 (t, *J*=7.5 Hz, 1H, ArH), 6.81 (d, *J*=7.8 Hz, 1H, ArH), 6.52-6.48 (m, 3H, ArH), 4.19 (q, *J*=6.8 Hz, 2H, OCH_2), 3.78 (q, *J*=7.1 Hz, 2H, OCH_2), 3.71 (s, 3H, Ar-OCH_3), 1.24 (t, *J*=7.2 Hz, 3H, CH_3), 0.86 (t, *J*=7.1 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ_C: 178.6, 163.8, 162.8, 160.1, 146.2, 142.4, 141.3, 139.8, 135.7, 130.0, 128.9, 124.0, 122.1, 117.3, 110.3, 109.4, 107.2, 103.3, 102.0, 71.0, 62.0, 60.3, 55.0, 51.0, 13.7, 13.2; Anal. calcd. for $C_{26}H_{24}N_4O_6$; C: 63.93; H: 4.95; N: 11.47. Found: C: 63.98; H: 4.94; N: 11.50%; HRMS (ESI) calcd for $C_{26}H_{24}N_4O_6$: 489.1774 $(M+H)^+$; found: 489.1883.

Diethyl 5'-cyano-6'-(4-methoxyphenylamino)-2-oxo-1'H-spiro[indoline-3,4'-pyridine]-2',3'-dicarboxylate: (**Scheme 2, 5h**): Yield 95 % (464 mg); yellow solid; Mp: 210-212 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.35; IR (ν_{max}, KBr, cm^{-1}): 3362, 3238, 2202, 1737, 1709, 1656, 1511, 1471, 1290, 1116, 752; ^{1}H NMR (300 MHz, DMSO-d_6) δ_H: 10.40 (s, 1H, NH), 9.85 (s, 1H, NH), 8.47 (s, 1H, NH), 7.22-7.15 (m, 2H, ArH), 7.00 (d, *J*=7.2 Hz, 1H, ArH), 6.96-6.87 (m, 4H, ArH), 6.80 (d, *J*=7.5 Hz, 1H, ArH), 4.18 (q, *J*=6.9 Hz, 2H, OCH_2), 3.80-3.72 (m, 5H, Ar-OCH_3, OCH_2), 1.24 (t, *J*=7.1 Hz, 3H, CH_3), 0.85 (t, *J*=7.1 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ_C: 178.8, 163.9, 162.8, 155.2, 147.3, 141.4, 139.5, 135.8, 133.1, 128.7, 124.0, 122.0, 121.5, 117.8, 114.5, 109.3, 102.3, 66.6, 62.0, 60.2, 55.4, 50.9, 13.7, 13.2; Anal. calcd. for $C_{26}H_{24}N_4O_6$; C: 63.93; H: 4.95; N: 11.47.

Found: C: 63.85; H: 4.98; N: 11.53%; HRMS (ESI) calcd for $C_{26}H_{24}N_4O_6$: 489.1774 $(M+H)^+$; found: 489.1784.

Diethyl 6'-(4-chlorophenylamino)-5'-cyano-2-oxo-1'H-spiro[indoline-3,4'-pyridine]-2',3'-dicarboxylate: (**Scheme 2, 5i**): Yield 85 % (419 mg); yellow solid; Mp: 220-222 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.55; IR (ν_{max}, KBr, cm^{-1}): 3270, 2193, 1725, 1700, 1657, 1322, 1495, 1390, 1287, 1220, 1125, 759; ^{1}H NMR (300 MHz, DMSO-d_6) δ_H: 10.46 (s, 1H, NH), 10.19 (s, 1H, NH), 8.87 (s, 1H, NH), 7.33 (d, *J*=8.7 Hz, 2H, ArH), 7.20 (d, *J*=8.7 Hz, 2H, ArH), 7.00 (t, *J*=7.4 Hz, 1H, ArH), 6.92 (d, *J*=8.7 Hz, 2H, ArH), 6.82 (d, *J*=7.8 Hz, 1H, ArH), 4.20 (q, *J*=7.1 Hz, 2H, OCH_2), 3.78 (q, *J*=7.1 Hz, 2H, OCH_2), 1.25 (t, *J*=7.2 Hz, 3H, CH_3), 0.85 (t, *J*=7.1 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ_C: 178.6, 163.7, 162.7, 146.2, 141.4, 140.1, 139.7, 135.5, 129.0, 128.9, 125.2, 124.1, 122.2, 119.5, 117.2, 109.4, 102.2, 71.2, 62.0, 60.3, 51.1, 13.7, 13.2; Anal. calcd. for $C_{25}H_{21}ClN_4O_5$; C: 60.92; H: 4.29; N: 11.37. Found: C: 60.96; H: 4.30; N: 11.33%; HRMS (ESI) calcd for $C_{25}H_{21}ClN_4O_5$: 493.1279 $(M+H)^+$; found: 493.1292.

Diethyl 2'-(4-bromophenylamino)-3'-cyano-2-oxo-1'H-spiro[indoline-3,4'-pyridine]-5',6'-dicarboxylate: (**Scheme 2, 5j**): Yield 88 % (473 mg); yellow solid; Mp: 218-220 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.46; IR (ν_{max}, KBr, cm^{-1}): 3207, 2200, 1725, 1695, 1652, 1620, 1535, 1485, 1304, 1217, 1124; ^{1}H NMR (300 MHz, DMSO-d_6) δ_H: 10.46 (s, 1H, NH), 10.20 (s, 1H, NH), 8.87 (s, 1H, NH), 7.45 (d, *J*=8.7 Hz, 2H, ArH), 7.24-7.18 (m, 2H, ArH), 7.00 (t, *J*=7.5 Hz, 1H, ArH), 6.87-6.80 (m, 3H, ArH), 4.19 (q, *J*=7.1 Hz, 2H, OCH_2), 3.78 (q, *J*=7.1 Hz, 2H, OCH_2), 1.25 (t, *J*=7.2 Hz, 3H, CH_3), 0.85 (t, *J*=7.1 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ_C: 178.6, 163.7, 162.7, 146.1, 141.3, 140.6, 139.7, 135.5, 131.9, 128.9, 124.1, 122.2, 119.8, 117.2, 112.9, 109.4, 102.1, 71.4, 62.0, 60.3, 51.0, 13.7, 13.2; Anal. calcd. for $C_{25}H_{21}BrN_4O_5$; C: 55.88; H: 3.94; N: 10.43. Found: C: 55.79; H: 3.94; N: 10.38%; HRMS (ESI) calcd for $C_{25}H_{21}BrN_4O_5$: 537.0774 $(M+H)^+$; found: 537.0781.

Diethyl 5'-cyano-6'-(4-iodophenylamino)-2-oxo-1'H-spiro[indoline-3,4'-pyridine]-2',3'-dicarboxylate: (**Scheme 2, 5k**): Yield 90 % (526 mg); yellow solid; Mp: 212-214 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.50; IR (ν_{max}, KBr, cm^{-1}): 3210, 3096, 2199, 1715, 1698, 1652, 1589, 1483, 1306, 1220, 1124, 755; ^{1}H NMR (300 MHz, DMSO-d_6) δ_H: 10.45 (s, 1H, NH), 10.20 (s, 1H, NH), 8.85 (s, 1H, NH), 7.59 (d, *J*=8.7 Hz, 2H, ArH), 7.24-7.11 (m, 2H, ArH), 6.99 (t, *J*=7.7 Hz, 1H, ArH), 6.80 (d, *J*=7.8 Hz, 1H, ArH), 6.73 (d, *J*=7.8 Hz, 2H, ArH), 4.19 (q, *J*=7.2 Hz, 2H, OCH_2), 3.77 (q, *J*=7.2 Hz, 2H,

OCH_2), 1.25 (t, *J*=7.1 Hz, 3H, CH_3), 0.85 (t, *J*=7.1 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ_C: 178.6, 163.7, 162.7, 146.0, 141.3, 141.1, 139.8, 139.1, 137.7, 135.6, 131.2, 129.0, 124.1, 122.2, 120.2, 117.2, 109.4, 102.1, 84.1, 71.5, 62.1, 60.3, 51.0, 13.7, 13.2; Anal. calcd. for $C_{25}H_{21}IN_4O_5$; C: 51.38; H: 3.62; N: 9.59. Found: C: 51.32; H: 3.62; N: 9.13%; HRMS (ESI) calcd for $C_{25}H_{21}IN_4O_5$: 585.0635 $(M+H)^+$; found: 585.0683.

Diethyl 5'-cyano-6'-(3-nitrophenylamino)-2-oxo-1'H-spiro[indoline-3,4'-pyridine]-2',3'-dicarboxylate: (**Scheme 2, 5l**): Yield 80 % (403 mg); yellow solid; Mp: 270-272 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.30; IR (ν_{max}, KBr, cm^{-1}): 3358, 3178, 1703, 1622, 1520, 1440, 1253, 1152, 1091, 755; ^{1}H NMR (300 MHz, DMSO-d_6) δ_H: 10.52 (s, 1H, NH), 10.43 (s, 1H, NH), 9.29 (s, 1H, NH), 7.77-7.69 (m, 2H, ArH), 7.57 (t, *J*=8.1 Hz, 1H, ArH), 7.32-7.21 (m, 3H, ArH), 7.02 (t, *J*=7.5 Hz, 1H, ArH), 6.83 (d, *J*=7.5 Hz, 1H, ArH), 4.21 (q, *J*=7.1 Hz, 2H, OCH_2), 3.80 (q, *J*=7.2 Hz, 2H, OCH_2), 1.25 (t, *J*=7.1 Hz, 3H, CH_3), 0.86 (t, *J*=7.1 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ_C: 178.4, 163.7, 162.6, 148.6, 145.6, 142.9, 141.3, 139.6, 135.3, 130.7, 129.1, 124.2, 123.3, 122.3, 116.8, 115.5, 111.1, 109.5, 102.5, 73.3, 62.5, 60.4, 51.1, 13.7, 13.2; Anal. calcd. for $C_{25}H_{21}N_5O_7$; C: 59.64; H: 4.20; N: 13.91. Found: C: 59.71; H: 4.21; N: 13.94%; HRMS (ESI) calcd for $C_{25}H_{21}N_5O_7$: 504.1519 $(M+H)^+$; found: 504.1531.

Diethyl 2'-(benzylamino)-3'-cyano-2-oxo-1'H-spiro[indoline-3,4'-pyridine]-5',6'-dicarboxylate (**Scheme 2, 5m**): Yield 70 % (331 mg); yellowish white solid; Mp: 234-236 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.60; IR (ν_{max}, KBr, cm^{-1}): 3313, 3107, 2187, 1727, 1685, 1514, 1484, 1309, 1044, 920, 775; ^{1}H NMR (300 MHz, DMSO-d_6) δ_H: 10.37 (s, 1H, NH), 10.13 (s, 1H, NH), 8.02 (s, 1H, NH), 7.41-7.33 (m, 5H, ArH), 7.15 (t, *J*=7.7 Hz, 1H, ArH), 6.85 (t, *J*=7.5 Hz, 1H, ArH), 6.77 (d, *J*=7.5 Hz, 1H, ArH), 6.70 (d, *J*=7.2 Hz, 1H, ArH), 4.91, 4.70 (ABq, *J*=17.3 Hz, 2H, Ar-CH_2), 4.22-4.18 (m, 2H, OCH_2), 3.75 (q, *J*=6.8 Hz, 2H, OCH_2), 1.24 (t, *J*=7.1 Hz, 3H, CH_3), 0.81 (t, *J*=7.1 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ_C: 178.6, 163.9, 163.1, 152.0, 143.7, 141.5, 136.1, 135.7, 128.5, 127.7, 127.1, 127.0, 123.5, 121.8, 118.8, 109.3, 105.5, 62.3, 61.4, 60.5, 49.7, 49.6, 13.4, 13.0; Anal. calcd. for $C_{26}H_{24}N_4O_5$; C: 66.09; H: 5.12; N: 11.86. Found: C: 66.14; H: 5.12; N: 11.88%; HRMS (ESI) calcd for $C_{26}H_{24}N_4O_5$: 473.1825 $(M+H)^+$; found: 473.1829.

Diethyl 2'-(butylamino)-3'-cyano-2-oxo-1'H-spiro[indoline-3,4'-pyridine]-5',6'-dicarboxylate (**Scheme 2, 5n**): Yield 72 % (316 mg); yellow solid; Mp: 240-242 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.65; IR (ν_{max}, KBr, cm^{-1}): 3349, 3204, 2190,

1709, 1647, 1619, 1532, 1482, 1350, 1301, 1225, 1125, 753, 705; ^{1}H NMR (300 MHz, DMSO-d_6) δ_H: 10.36 (s, 1H, NH), 9.56 (s, 1H, NH), 7.85 (s, 1H, NH), 7.20-7.15 (m, 1H, ArH), 6.97-6.94 (m, 2H, ArH), 6.78 (d, *J*=7.5 Hz, 1H, ArH), 4.28 (q, *J*=7.1 Hz, 2H, OCH_2), 3.73 (q, *J*=7.2 Hz, 2H, OCH_2), 3.59-3.51 (m, 2H, NCH_2), 1.61-1.57 (m, 2H, CH_2), 1.32-1.24 (m, 5H, CH_2, CH_3) 0.90 (t, *J*=7.2 Hz, 3H, CH_3), 0.80 (t, *J*=7.1 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ_C: 179.0, 163.9, 163.3, 152.1, 143.9, 141.5, 136.1, 128.5, 123.4, 122.0, 119.0, 109.3, 104.8, 62.4, 60.9, 60.4, 49.6, 46.8, 30.5, 19.2, 13.6, 13.1; Anal. calcd. for $C_{23}H_{26}N_4O_5$; C: 63.00; H: 5.98; N: 12.78. Found: C: 63.08; H: 5.96; N: 12.83%; HRMS (ESI) calcd for $C_{23}H_{26}N_4O_5$: 439.1981 $(M+H)^+$; found: 439.1995.

Spectroscopic and Analytical characterization of compounds 6a-6m:

Dimethyl 5'-cyano-2-oxo-6'-(p-tolylamino)-1'H-spiro[indoline-3,4'-pyridine]-2',3'-dicarboxylate (**Scheme 3, 6a**): Yield 92 % (409 mg); yellow solid; Mp: 222-224 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.50; IR (ν_{max}, KBr, cm^{-1}): 3326, 3198, 1713, 1657, 1558, 1485, 1357, 1285, 1196, 1023, 780; ^{1}H NMR (300 MHz, DMSO-d_6) δ_H: 10.44 (s, 1H, NH), 10.09 (s, 1H, NH), 8.64 (s, 1H, NH), 7.22-7.08 (m, 4H, ArH), 6.98 (t, *J*=7.4 Hz, 1H, ArH), 6.85-6.79 (m, 3H, ArH), 3.73 (s, 3H, OCH_3), 3.35 (s, 3H, OCH_3), 2.23 (s, 3H, Ar-CH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ_C: 178.6, 164.3, 163.3, 146.6, 141.2, 139.9, 138.0, 135.7, 130.9, 129.7, 128.9, 123.9, 122.1, 118.9, 117.6, 109.4, 101.9, 68.9, 53.0, 51.6, 50.9, 20.3; Anal. calcd. for $C_{24}H_{20}N_4O_5$; C: 64.86; H: 4.54; N: 12.61. Found: C: 64.90; H: 4.53; N: 11.59%; HRMS (ESI) calcd for $C_{24}H_{20}N_4O_5$: 445.1512 $(M+H)^+$; found: 445.1520.

Dimethyl 5'-cyano-6'-(4-isopropylphenylamino)-2-oxo-1'H-spiro[indoline-3,4'-pyridine]-2',3'-dicarboxylate (**Scheme 3, 6b**): Yield 93 % (439 mg); yellow solid; Mp: 214-216 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.45; IR (ν_{max}, KBr, cm^{-1}): 3322, 2927, 2195, 1722, 1658, 1470, 1305, 1288, 1120, 1026, 788; ^{1}H NMR (300 MHz, DMSO-d_6) δ_H: 10.44 (s, 1H, NH), 10.16 (s, 1H, NH), 8.65 (s, 1H, NH), 7.23-7.14 (m, 4H, ArH), 6.99 (t, *J*=7.4 Hz, 1H, ArH), 6.87 (d, *J*=8.1 Hz, 2H, ArH), 6.81 (d, *J*=7.8 Hz, 1H, ArH), 3.74 (s, 3H, OCH_3), 3.36 (s, 3H, OCH_3), 2.87-2.78 (m, 1H, CH), 1.17 (d, *J*=6.9 Hz, 6H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ_C: 178.6, 164.3, 163.4, 146.5, 141.9, 141.1, 140.0, 138.5, 135.8, 128.9, 127.0, 123.9, 122.1, 118.5, 117.5, 109.4, 101.7, 69.5, 52.9, 51.6, 50.9, 32.8, 24.1; Anal. calcd. for $C_{26}H_{24}N_4O_5$; C: 66.09; H: 5.12; N: 11.86. Found: C: 66.15; H: 5.11; N: 11.81%; HRMS (ESI) calcd for $C_{26}H_{24}N_4O_5$: 473.1825 $(M+H)^+$; found: 473.1832.

Dimethyl 5'-cyano-6'-(3,4-dimethylphenylamino)-2-oxo-1'H-spiro[indoline-3,4'-pyridine]-2',3'-dicarboxylate (**Scheme 3, 6c**): Yield 92 % (422 mg); greenish yellow solid; Mp: 188-190 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.46; IR (ν_{max}, KBr, cm^{-1}): 3312, 3139, 2195, 1723, 1655, 1535, 1472, 1371, 1091, 785; ^{1}H NMR (300 MHz, DMSO-d_6) δ_H: 10.46 (s, 1H, NH), 10.10 (s, 1H, NH), 8.60 (s, 1H, NH), 7.25-7.17 (m, 2H, ArH), 7.08-6.99 (m, 2H, ArH), 6.84 (d, *J*=7.5 Hz, 1H, ArH), 6.78 (s, 1H, ArH), 6.71 (d, *J*=8.4 Hz, 1H, ArH), 3.77 (s, 3H, OCH_3), 3.39 (s, 3H, OCH_3), 2.20 (s, 3H, Ar-CH_3), 2.18 (s, 3H, Ar-CH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ_C: 178.7, 164.3, 163.4, 146.7, 141.1, 139.9, 138.2, 136.9, 135.7, 130.1, 129.8, 128.9, 123.9, 122.1, 120.3, 117.6, 116.5, 109.4, 101.9, 68.7, 53.0, 51.6, 50.9, 19.7, 18.7; Anal. calcd. for $C_{25}H_{22}N_4O_5$; C: 65.49; H: 4.84; N: 12.22. Found: C: 65.42; H: 4.82; N: 12.25%; HRMS (ESI) calcd for $C_{25}H_{22}N_4O_5$: 459.1668 $(M+H)^+$; found: 459.1670.

Dimethyl 5'-cyano-6'-(3-methoxyphenylamino)-2-oxo-1'H-spiro[indoline-3,4'-pyridine]-2',3'-dicarboxylate (**Scheme 3, 6d**): Yield 90 % (414 mg); yellow solid; Mp: 254-256 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.44; IR (ν_{max}, KBr, cm^{-1}): 3337, 3197, 2189, 1713, 1643, 1535, 1477, 1348, 1305, 1221, 1109, 754; ^{1}H NMR (300 MHz, DMSO-d_6) δ_H: 10.46 (s, 1H, NH), 10.24 (s, 1H, NH), 8.74 (s, 1H, NH), 7.23-7.15 (m, 3H, ArH), 7.00 (d, *J*=7.5 Hz, 1H, ArH), 6.83 (t, *J*=7.5 Hz, 1H, ArH), 6.52-6.49 (m, 3H, ArH) 3.75 (s, 3H, OCH_3), 3.71 (s, 3H, Ar-OCH_3), 3.37 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ_C: 178.5, 164.2, 163.3, 160.1, 146.1, 142.2, 141.0, 139.8, 135.6, 130.0, 128.9, 123.9, 122.1, 117.2, 110.3, 109.4, 107.3, 103.3, 101.9, 70.9, 54.9, 52.9, 51.6, 50.9; Anal. calcd. for $C_{24}H_{20}N_4O_6$; C: 62.60; H: 4.38; N: 12.17. Found: C: 62.52; H: 4.38; N: 12.13%; HRMS (ESI) calcd for $C_{24}H_{20}N_4O_6$: 461.1461 $(M+H)^+$; found: 461.1478.

Dimethyl 5'-cyano-6'-(4-methoxyphenylamino)-2-oxo-1'H-spiro[indoline-3,4'-pyridine]-2',3'-dicarboxylate (**Scheme 3, 6e**): Yield 95 % (437 mg); yellowish white solid; Mp: 226-228 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.35; IR (ν_{max}, KBr, cm^{-1}): 3365, 3156, 2197, 1714, 1651, 1519, 1371, 1242, 1115, 1025, 750; ^{1}H NMR (300 MHz, DMSO-d_6) δ_H: 10.41 (s, 1H, NH), 9.90 (s, 1H, NH), 8.50 (s, 1H, NH), 7.21-7.13 (m, 2H, ArH), 7.00-6.90 (m, 5H, ArH), 6.79 (d, *J*=7.5 Hz, 1H, ArH), 3.73 (s, 3H, OCH_3), 3.71 (s, 3H, Ar-OCH_3), 3.35 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ_C: 178.7, 164.4, 163.4, 155.3, 147.2, 141.2, 139.8, 135.8, 133.0, 128.8, 123.9, 122.1, 121.7, 117.8, 114.6, 109.4, 102.0, 66.5, 55.4, 53.0, 51.6, 50.9; Anal. calcd. for $C_{24}H_{20}N_4O_6$; C: 62.60; H: 4.38; N: 12.17.

Found: C: 62.67; H: 4.37; N: 12.21%; HRMS (ESI) calcd for $C_{24}H_{20}N_4O_6$: 461.1461 $(M+H)^+$; found: 461.1473.

Dimethyl 6'-(4-chlorophenylamino)-5'-cyano-2-oxo-1'H-spiro[indoline-3,4'-pyridine]-2',3'-dicarboxylate (**Scheme 3, 6f**): Yield 85 % (395 mg); yellow solid; Mp: 204-206 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.40; IR (ν_{max}, KBr, cm^{-1}): 3229, 2199, 1718, 1689, 1621, 1589, 1534, 1470, 1300, 1215, 1119; ^{1}H NMR (300 MHz, DMSO-d_6) δ_H: 10.46 (s, 1H, NH), 10.21 (s, 1H, NH), 8.87 (s, 1H, NH), 7.33 (d, *J*=8.7 Hz, 2H, ArH), 7.23-7.17 (m, 2H, ArH), 6.99 (t, *J*=7.4 Hz, 1H, ArH), 6.91 (d, *J*=8.7 Hz, 2H, ArH), 6.82 (d, *J*=7.2 Hz, 1H, ArH), 3.75 (s, 3H, OCH_3), 3.36 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ_C: 178.5, 164.2, 163.2, 146.1, 141.2, 140.0, 139.8, 135.5, 129.1, 125.3, 124.0, 122.2, 119.7, 117.2, 109.4, 102.1, 71.1, 53.0, 51.6, 51.0; Anal. calcd. for $C_{23}H_{17}ClN_4O_5$; C: 59.43; H: 3.69; N: 12.05. Found: C: 59.49; H: 3.68; N: 12.02%; HRMS (ESI) calcd for $C_{23}H_{17}ClN_4O_5$: 465.0966 $(M+H)^+$; found: 465.0975.

Dimethyl 2'-(4-bromophenylamino)-3'-cyano-2-oxo-1'H-spiro[indoline-3,4'-pyridine]-5',6'-dicarboxylate (**Scheme 3, 6g**): Yield 87 % (443 mg); greenish yellow solid; Mp: 36-238 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.48; IR (ν_{max}, KBr, cm^{-1}): 3267, 2191, 1727, 1692, 1656, 1581, 1472, 1370, 1285, 1218, 1091, 758; ^{1}H NMR (300 MHz, DMSO-d_6) δ_H: 10.48 (s, 1H, NH), 10.25 (s, 1H, NH), 8.90 (s, 1H, NH), 7.46 (d, *J*=8.7 Hz, 2H, ArH), 7.24-7.17 (m, 2H, ArH), 7.00 (t, *J*=7.4 Hz, 1H, ArH), 6.87-6.81 (m, 3H, ArH), 3.76 (s, 3H, OCH_3), 3.36 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ_C: 178.5, 164.2, 163.2, 146.0, 141.2, 140.4, 139.8, 135.5, 131.9, 129.0, 124.0, 122.2, 120.0, 117.1, 113.1, 109.4, 102.0, 71.3, 53.0, 51.6, 51.0; Anal. calcd. for $C_{23}H_{17}BrN_4O_5$; C: 54.24; H: 3.36; N: 11.00. Found: C: 54.15; H: 3.34; N: 11.05%; HRMS (ESI) calcd for $C_{23}H_{17}BrN_4O_5$: 509.0461 $(M+H)^+$; found: 509.0465.

Dimethyl 5'-cyano-6'-(2-iodophenylamino)-2-oxo-1'H-spiro[indoline-3,4'-pyridine]-2',3'-dicarboxylate (**Scheme 3, 6h**): Yield 90 % (501 mg); yellow solid; Mp: 230-232 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.42; IR (ν_{max}, KBr, cm^{-1}): 3219, 3112, 2200, 1722, 1697, 1620, 1471, 1290, 1120, 1016, 751; ^{1}H NMR (300 MHz, DMSO-d_6) δ_H: 10.39 (s, 1H, NH), 9.78 (s, 1H, NH), 8.03 (s, 1H, NH), 7.80 (d, *J*=7.8 Hz, 1H, ArH), 7.33 (t, *J*=7.5 Hz, 1H, ArH), 7.28-7.16 (m, 2H, ArH), 7.05 (d, *J*=7.5 Hz, 1H, ArH), 6.98 (t, *J*=7.4 Hz, 1H, ArH), 6.85 (t, *J*=7.7 Hz, 1H, ArH), 6.78 (d, *J*=7.8 Hz, 1H, ArH), 3.76 (s, 3H, OCH_3), 3.34 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ_C: 178.5, 164.4, 163.2, 147.2, 141.3, 141.1,

139.4, 138.9, 135.3, 129.0, 128.9, 126.0, 124.5, 123.4, 122.1, 118.1, 116.9, 109.3, 102.5, 93.9, 68.2, 53.1, 51.6, 51.3; Anal. calcd. for $C_{23}H_{17}IN_4O_5$; C: 49.66; H: 3.08; N: 10.07. Found: C: 49.61; H: 3.09; N: 10.05%; HRMS (ESI) calcd for $C_{23}H_{17}IN_4O_5$: 557.0322 $(M+H)^+$; found: 557.0327.

Dimethyl 5'-cyano-6'-(3-nitrophenylamino)-2-oxo-1'H-spiro[indoline-3,4'-pyridine]-2',3'-dicarboxylate (**Scheme 3, 6i**): Yield 84 % (399 mg); yellow solid; Mp: 260-262 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.30; IR (ν_{max}, KBr, cm^{-1}): 3334, 3194, 2201, 1715, 1660, 1603, 1515, 1472, 1309, 1177, 1120, 756; ^{1}H NMR (300 MHz, DMSO-d_6) δ_H: 10.53 (s, 1H, NH), 10.47 (s, 1H, NH), 9.29 (s, 1H, NH), 7.76 (d, *J*=7.8 Hz, 1H, ArH), 7.70 (s, 1H, ArH), 7.57 (t, *J*=8.1 Hz, 1H, ArH), 7.31-7.21 (m, 3H, ArH), 7.01 (t, *J*=7.5 Hz, 1H, ArH), 6.83 (d, *J*=7.8 Hz, 1H, ArH), 3.77 (s, 3H, OCH_3), 3.38 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ_C: 178.3, 164.1, 163.1, 148.5, 145.5, 142.8, 141.1, 139.6, 135.2, 130.7, 129.2, 124.1, 123.4, 122.3, 116.7, 115.5, 111.2, 109.5, 102.5, 73.4, 53.1, 51.7, 51.1; Anal. calcd. for $C_{23}H_{17}N_5O_7$; C: 58.11; H: 3.60; N: 14.73. Found: C: 58.18; H: 3.61; N: 14.69%; HRMS (ESI) calcd for $C_{23}H_{17}N_5O_7$: 476.1206 $(M+H)^+$; found: 476.1217.

4-(5'-cyano-2',3'-bis(methoxycarbonyl)-2-oxo-1'H-spiro[indoline-3,4'-pyridine]-6'-ylamino)benzoic acid (**Scheme 3, 6j**): Yield 80 % (380 mg); yellow solid; Mp: 258-260 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.20; IR (ν_{max}, KBr, cm^{-1}): 3321, 3187, 2200, 1753, 1678, 1627, 1524, 1339, 1128, 988; ^{1}H NMR (300 MHz, DMSO-d_6) δ_H: 12.60 (s, 1H, COOH), 10.52 (s, 1H, NH), 10.47 (s, 1H, NH), 9.21 (s, 1H, NH), 7.86 (d, *J*=8.4 Hz, 2H, ArH), 7.23 (d, *J*=6.3 Hz, 2H, ArH), 7.03 (t, *J*=7.4 Hz, 1H, ArH), 6.94 (d, *J*=8.1 Hz, 2H, ArH), 6.85 (d, *J*=7.5 Hz, 1H, ArH), 3.78 (s, 3H, OCH_3), 3.39 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ_C: 178.4, 167.0, 164.2, 163.2, 145.9, 145.4, 141.1, 140.0, 135.4, 131.0, 129.2, 124.1, 122.8, 122.3, 116.8, 116.1, 109.5, 101.9, 74.4, 53.1, 51.7, 51.2; Anal. calcd. for $C_{24}H_{18}N_4O_7$; C: 60.76; H: 3.82; N: 11.81. Found: C: 60.68; H: 3.80; N: 11.84%; HRMS (ESI) calcd for $C_{24}H_{18}N_4O_7$: 475.1254 $(M+H)^+$; found: 475.1259.

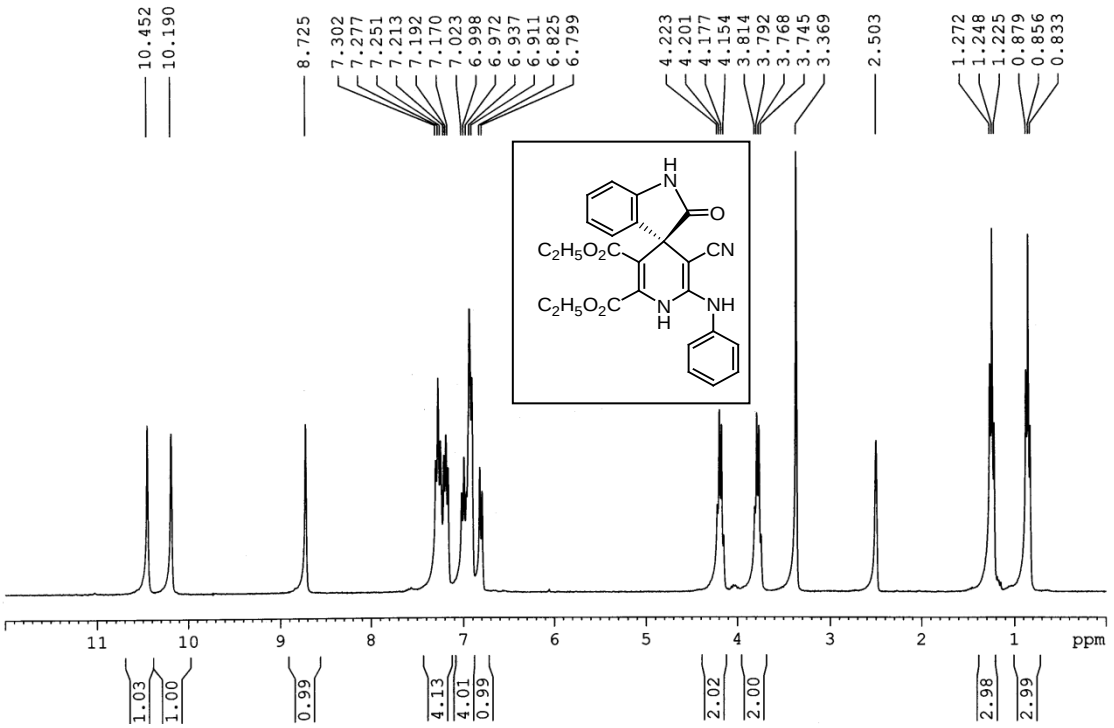
Dimethyl 5-chloro-6'-(4-chlorophenylamino)-5'-cyano-2-oxo-1'H-spiro[indoline-3,4'-pyridine]-2',3'-dicarboxylate (**Scheme 3, 6k**): Yield 88 % (439 mg); yellow solid; Mp: 268-270 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.55; IR (ν_{max}, KBr, cm^{-1}): 3329, 3104, 2189, 1734, 1703, 1616, 1473, 1295, 1099, 985, 825; ^{1}H NMR (300 MHz, DMSO-d_6) δ_H: 10.62 (s, 1H, NH), 10.27 (s, 1H, NH), 8.95 (s, 1H, NH), 7.34 (d, *J*=8.4 Hz, 2H, ArH), 7.28 (s, 2H, ArH), 6.96 (d, *J*=8.7 Hz, 2H, ArH), 6.84 (d, *J*=8.7 Hz, 1H, ArH), 3.76

(s, 3H, OCH_3), 3.39 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ_C: 178.3, 164.1, 163.1, 146.4, 140.5, 140.3, 139.6, 137.5, 129.1, 129.0, 126.1, 125.7, 124.1, 120.3, 117.1, 111.0, 101.0, 70.0, 53.1, 51.8, 51.3; Anal. calcd. for $C_{23}H_{16}Cl_2N_4O_5$; C: 55.33; H: 3.23; N: 11.22. Found: C: 55.38; H: 3.23; N: 11.20%; HRMS (ESI) calcd for $C_{23}H_{16}Cl_2N_4O_5$: 499.0576 $(M+H)^+$; found: 499.0587.

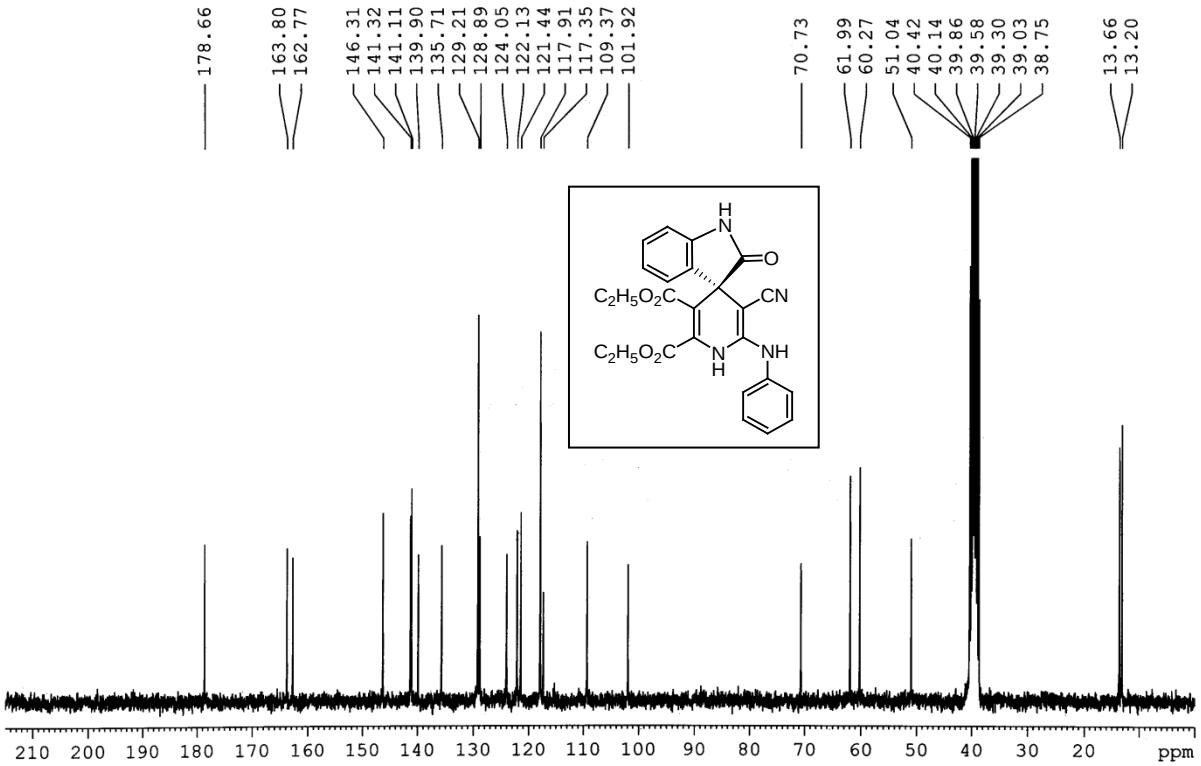
Dimethyl 5-bromo-6'-(4-chlorophenylamino)-5'-cyano-2-oxo-1'H-spiro[indoline-3,4'-pyridine]-2',3'-dicarboxylate (**Scheme 3, 6l**): Yield 86 % (468 mg); yellow solid; Mp: 224-226 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.50; IR (ν_{max}, KBr, cm^{-1}): 3330, 3105, 2179, 1757, 1717, 1651, 1491, 1313, 1217, 1132, 990, 822; ^1H NMR (300 MHz, DMSO-d_6) δ_H: 10.63 (s, 1H, NH), 10.28 (s, 1H, NH), 8.95 (s, 1H, NH), 7.45-7.33 (m, 4H, ArH), 6.97 (d, *J*=8.4 Hz, 2H, ArH), 6.80 (d, *J*=7.8 Hz, 1H, ArH), 3.76 (s, 3H, OCH_3), 3.40 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ_C: 178.2, 164.2, 163.2, 146.4, 140.7, 139.6, 137.9, 131.9, 129.1, 126.8, 125.7, 120.3, 117.1, 113.7, 111.5, 101.0, 70.1, 53.1, 51.8, 51.3; Anal. calcd. for $C_{23}H_{16}BrClN_4O_5$; C: 50.80; H: 2.97; N: 10.30. Found: C: 50.87; H: 2.96; N: 10.32%; HRMS (ESI) calcd for $C_{23}H_{16}BrClN_4O_5$: 545.0050 $(M+H)^+$; found: 545.0059.

Dimethyl 6'-(4-chlorophenylamino)-5'-cyano-5-nitro-2-oxo-1'H-spiro[indoline-3,4'-pyridine]-2',3'-dicarboxylate (**Scheme 3, 6m**): Yield 92 % (469 mg); yellow solid; Mp: 206-208 °C (EtOH); R_f [40 % EtOAc / petroleum ether (60-80°C)]: 0.30; IR (ν_{max}, KBr, cm^{-1}): 3327, 3185, 2181, 1728, 1649, 1606, 1491, 1308, 1258, 1132, 840; ^1H NMR (300 MHz, DMSO-d_6) δ_H: 11.25 (s, 1H, NH), 10.41 (s, 1H, NH), 9.03 (s, 1H, NH), 8.22 (d, *J*=8.7 Hz, 1H, ArH), 8.11 (s, 1H, ArH), 7.35 (d, *J*=8.4 Hz, 2H, ArH), 7.05 (d, *J*=8.4 Hz, 1H, ArH), 7.00 (d, *J*=8.7 Hz, 2H, ArH), 3.77 (s, 3H, OCH_3), 3.45 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ_C: 179.1, 164.1, 163.0, 147.8, 146.7, 142.7, 141.3, 139.3, 136.5, 129.1, 126.5, 126.1, 120.7, 119.6, 117.0, 109.8, 100.1, 68.8, 53.1, 51.9, 51.2; Anal. calcd. for $C_{23}H_{16}ClN_5O_7$; C: 54.18; H: 3.16; N: 13.74. Found: C: 54.12; H: 3.17; N: 13.78%; HRMS (ESI) calcd for $C_{23}H_{16}ClN_5O_7$: 510.0817 $(M+H)^+$; found: 510.0854.

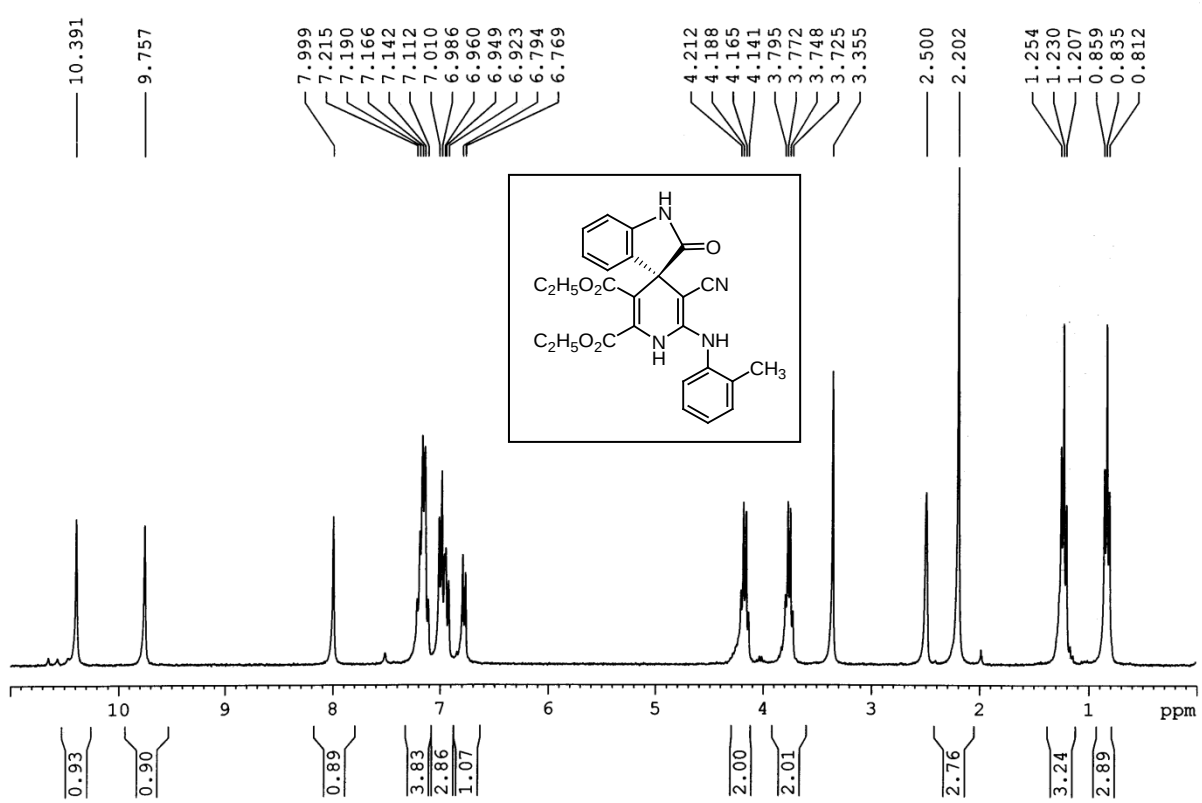
Copy of ^{1}H and ^{13}C NMR spectra of synthesized compounds (5a-5n):



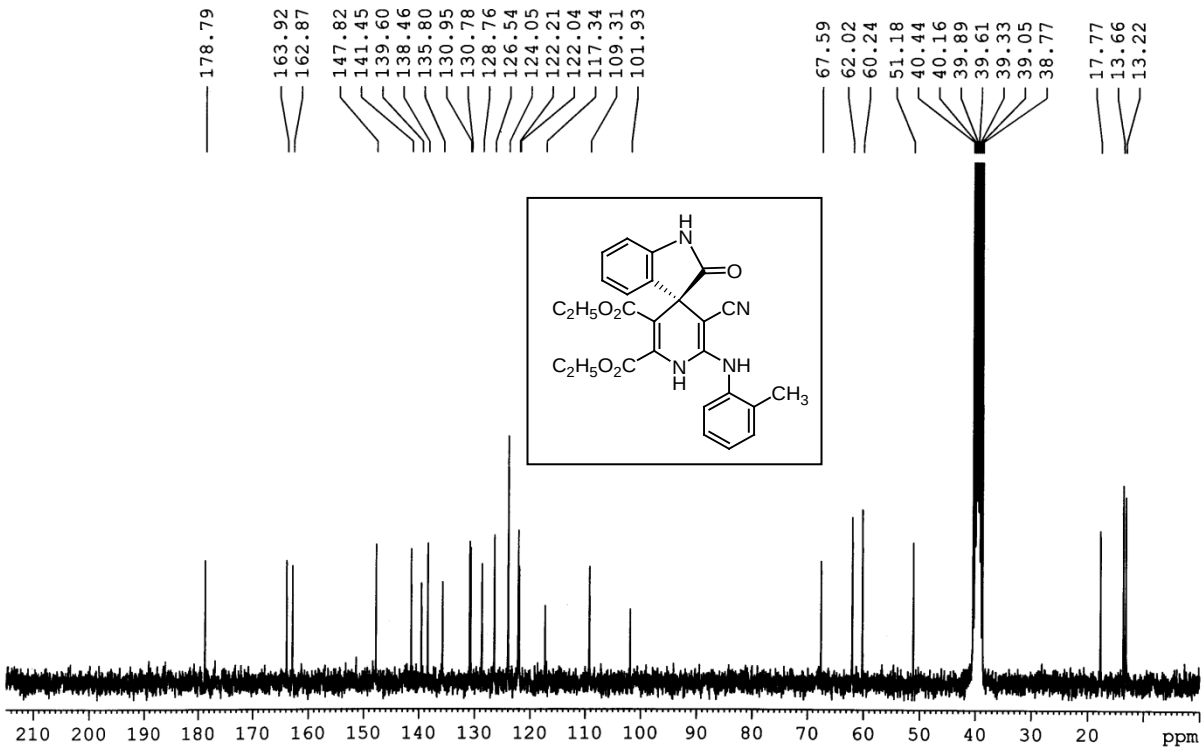
^{1}H NMR of compound **5a**



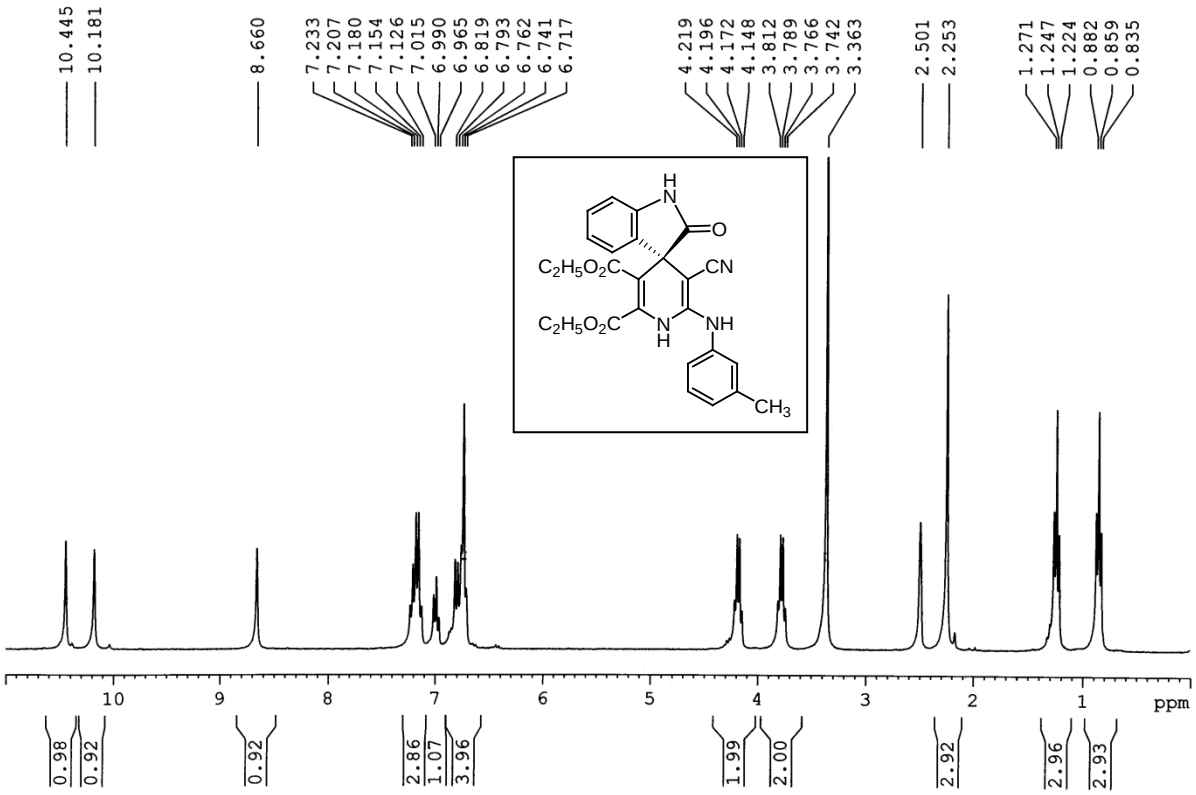
^{13}C NMR of compound **5a**



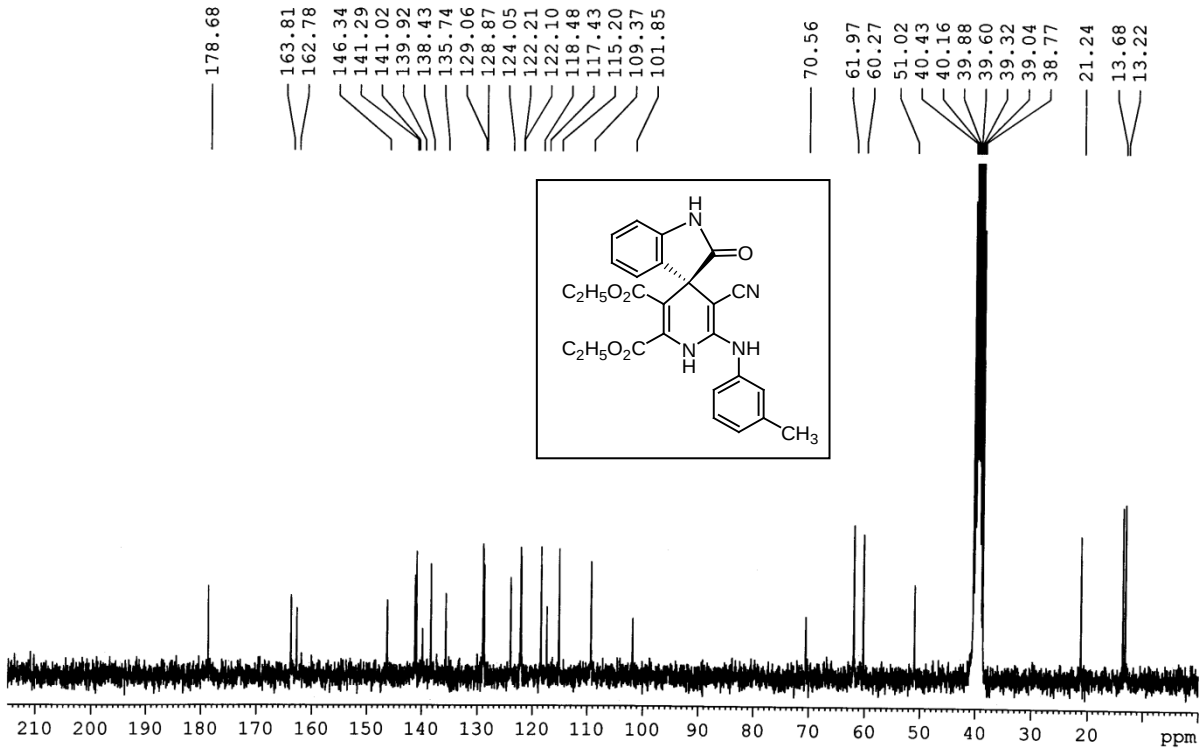
^{1}H NMR of compound **5b**



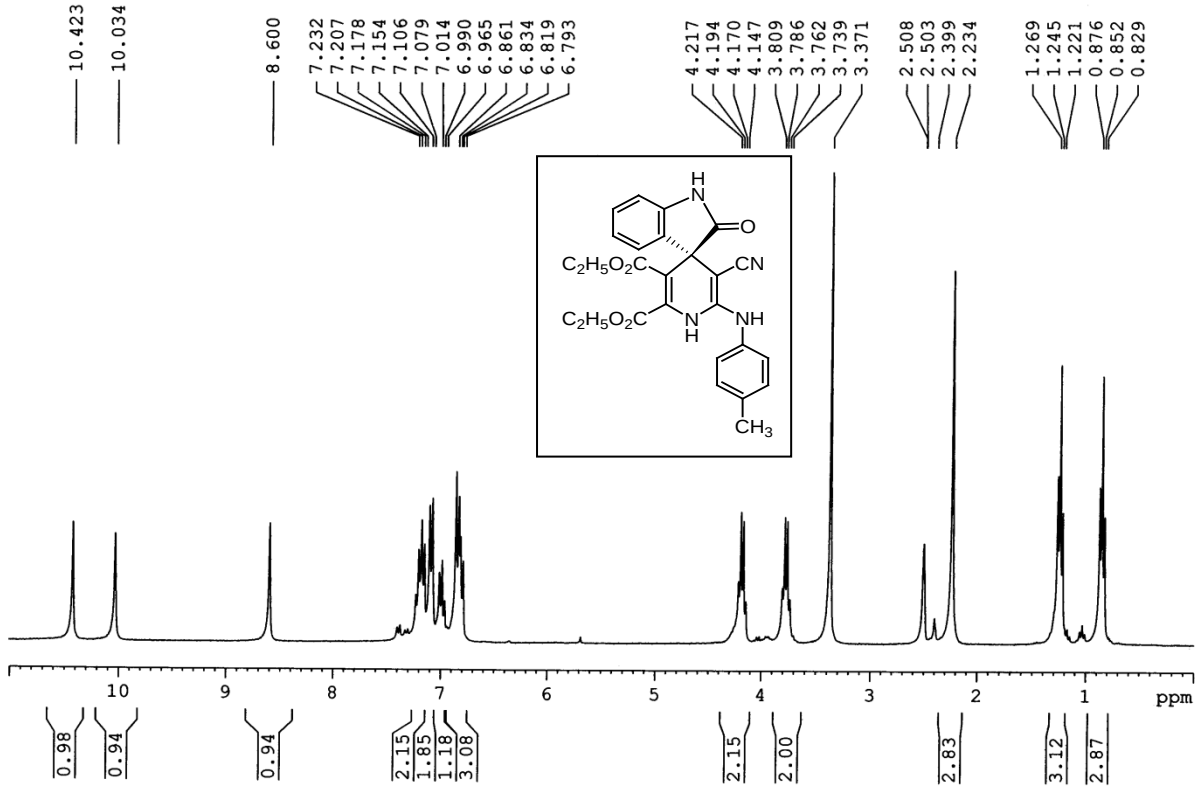
^{13}C NMR of compound **5b**



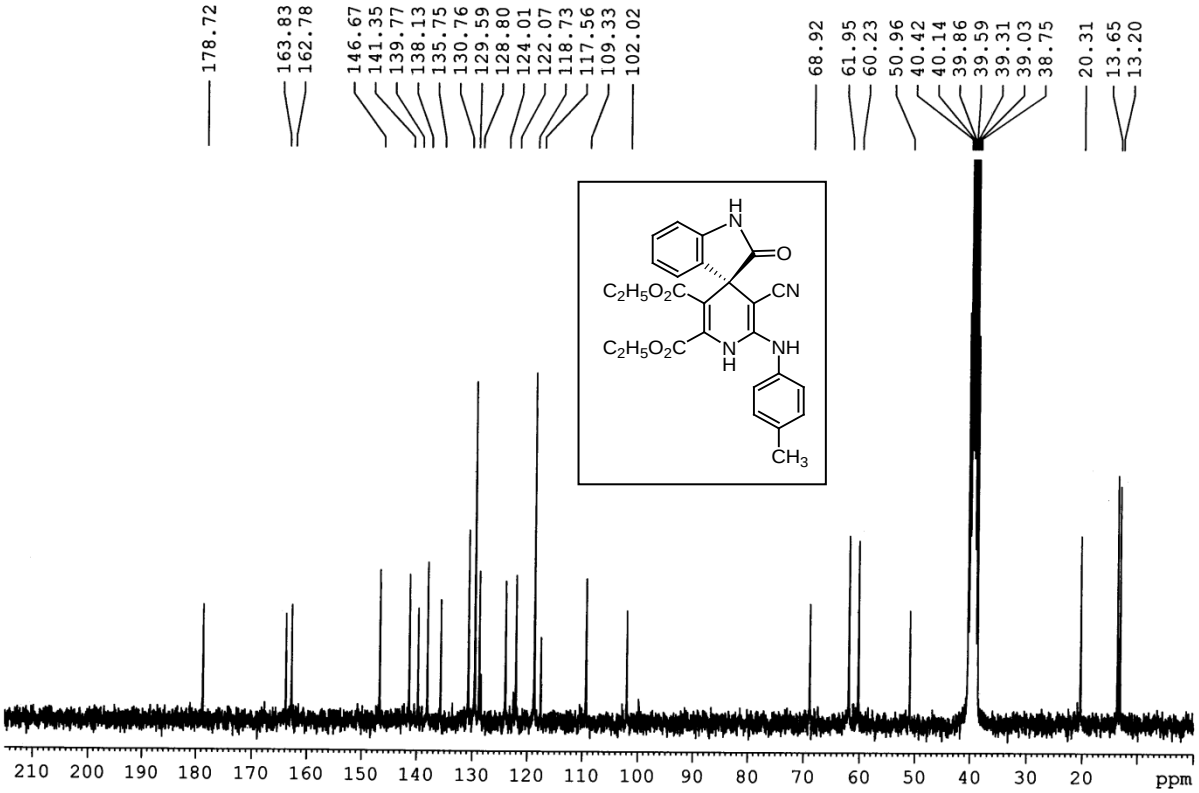
^{1}H NMR of compound **5c**



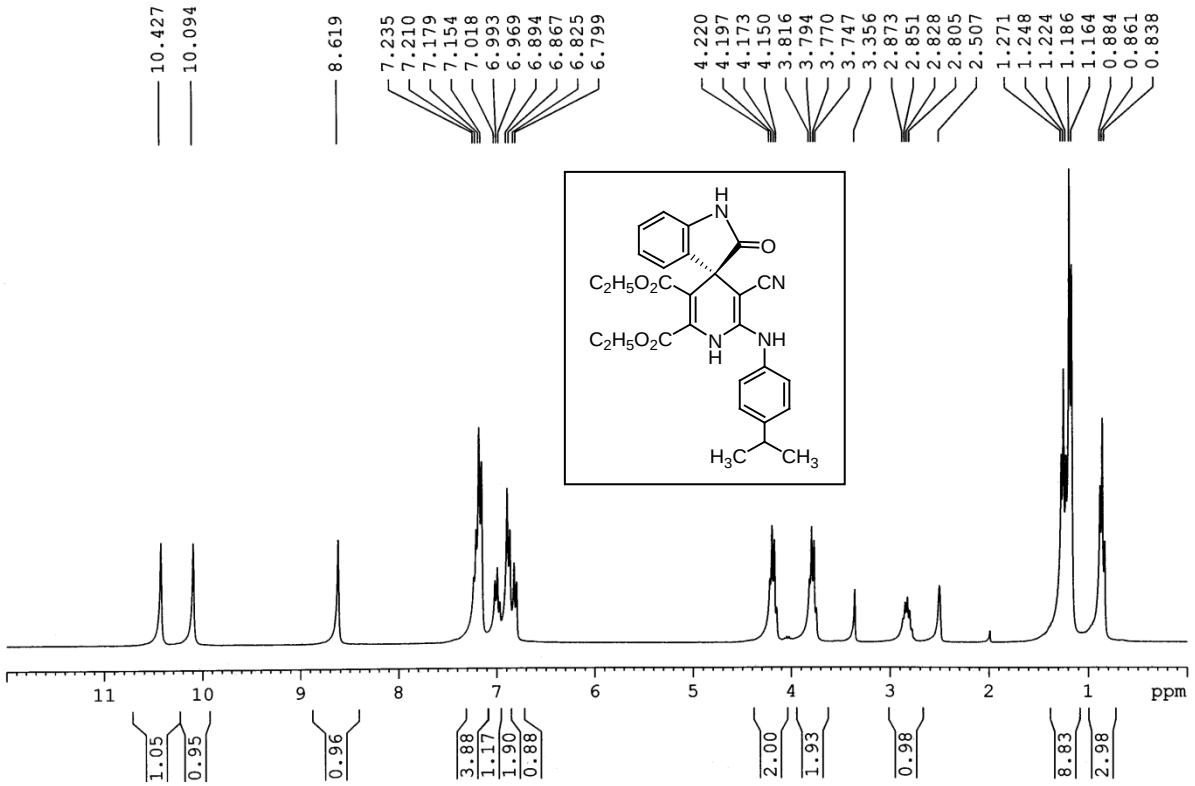
^{13}C NMR of compound **5c**



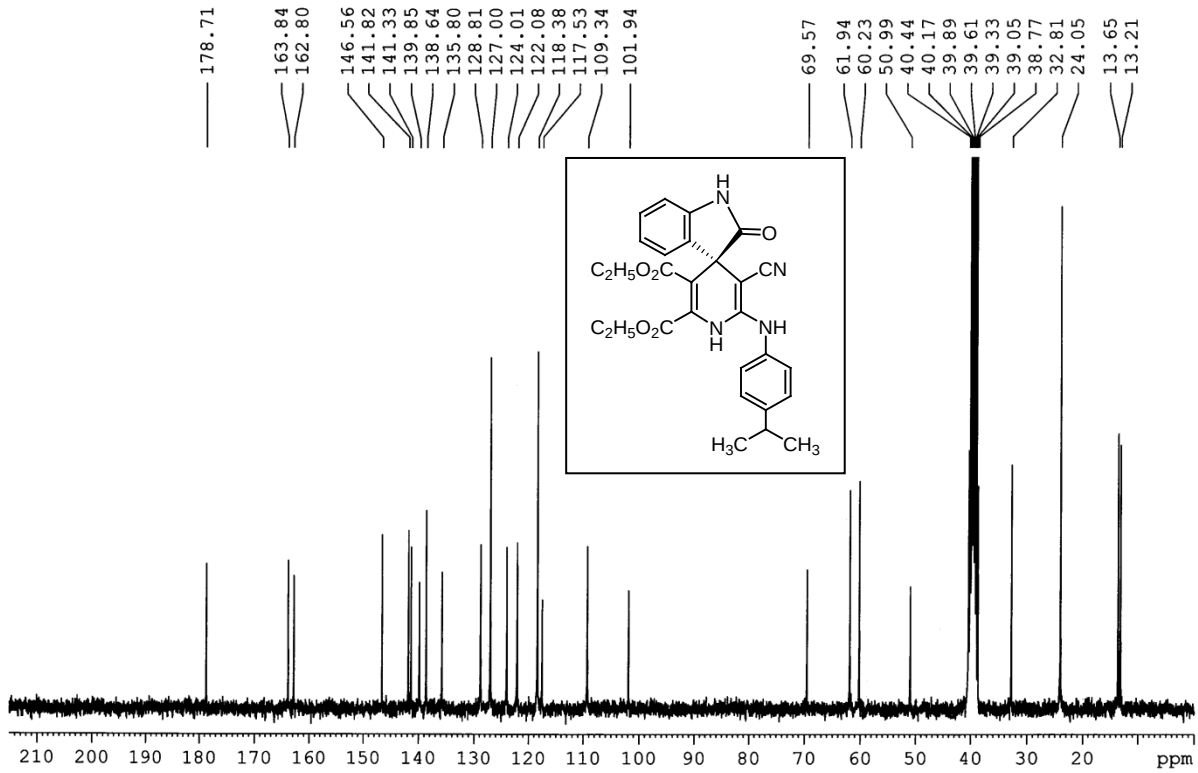
^{1}H NMR of compound **5d**



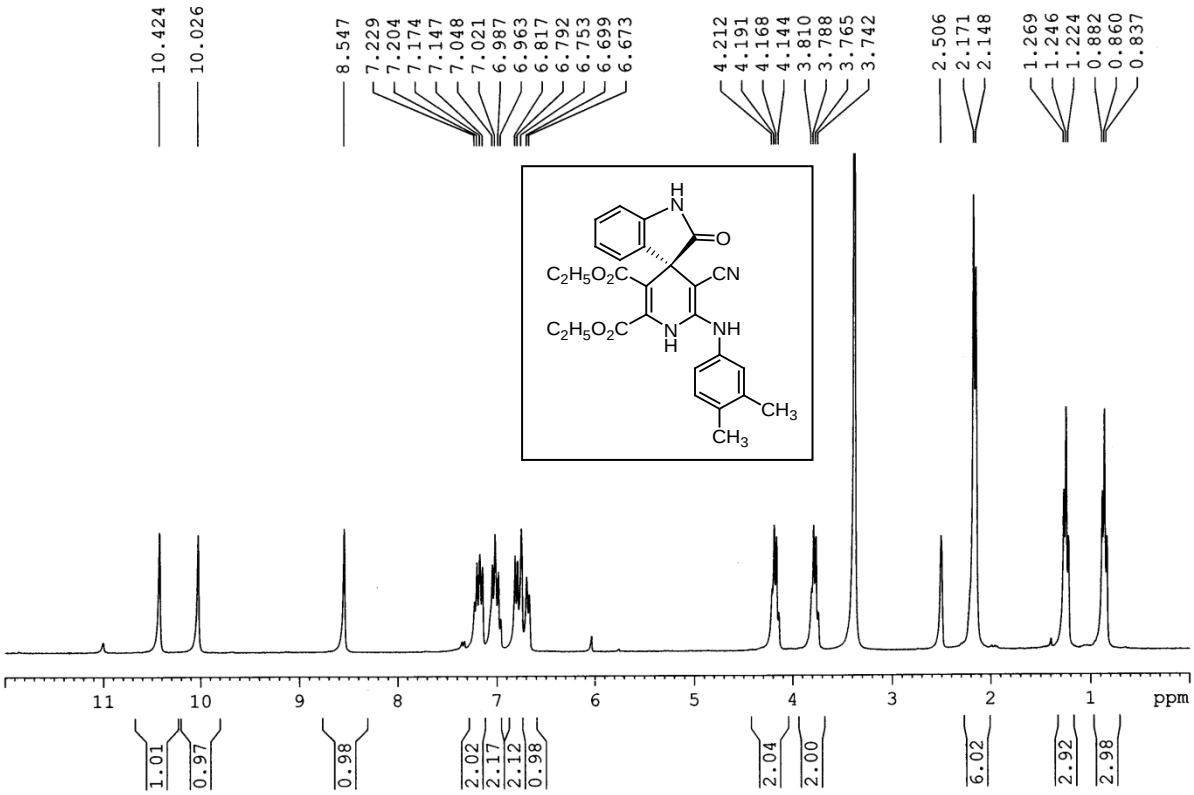
^{13}C NMR of compound **5d**



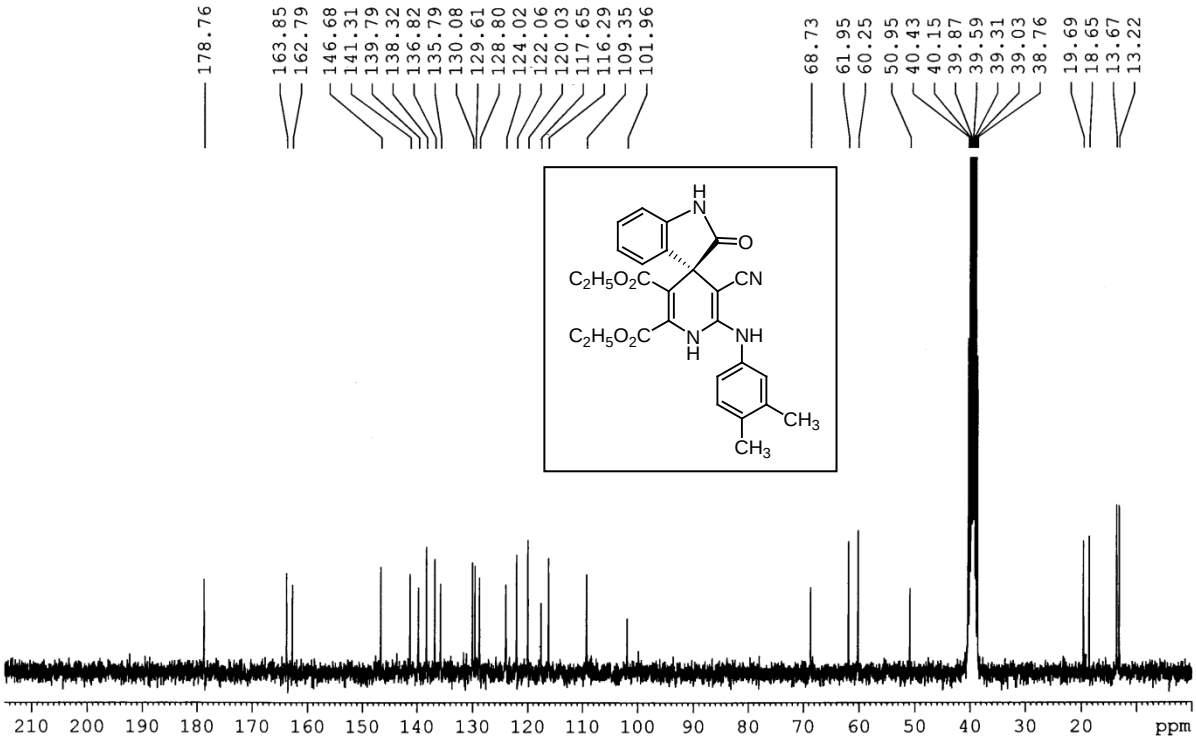
^{1}H NMR of compound **5e**



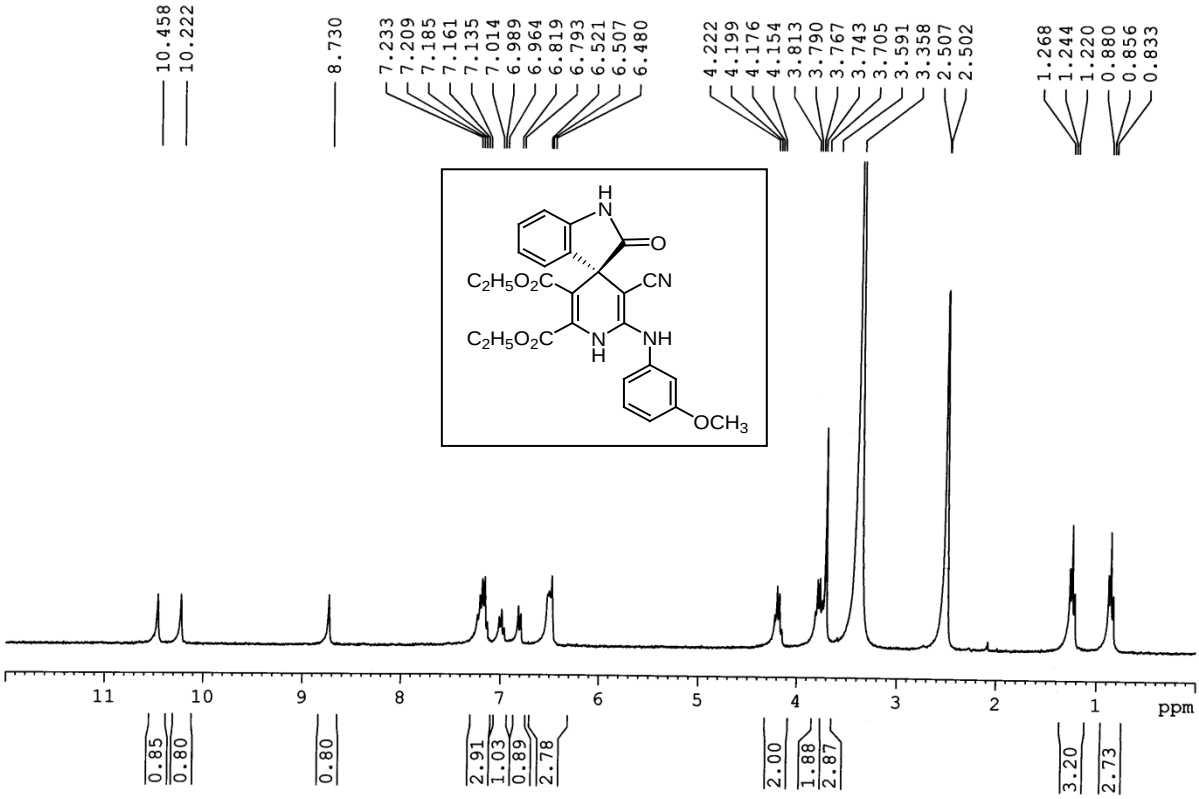
^{13}C NMR of compound **5e**



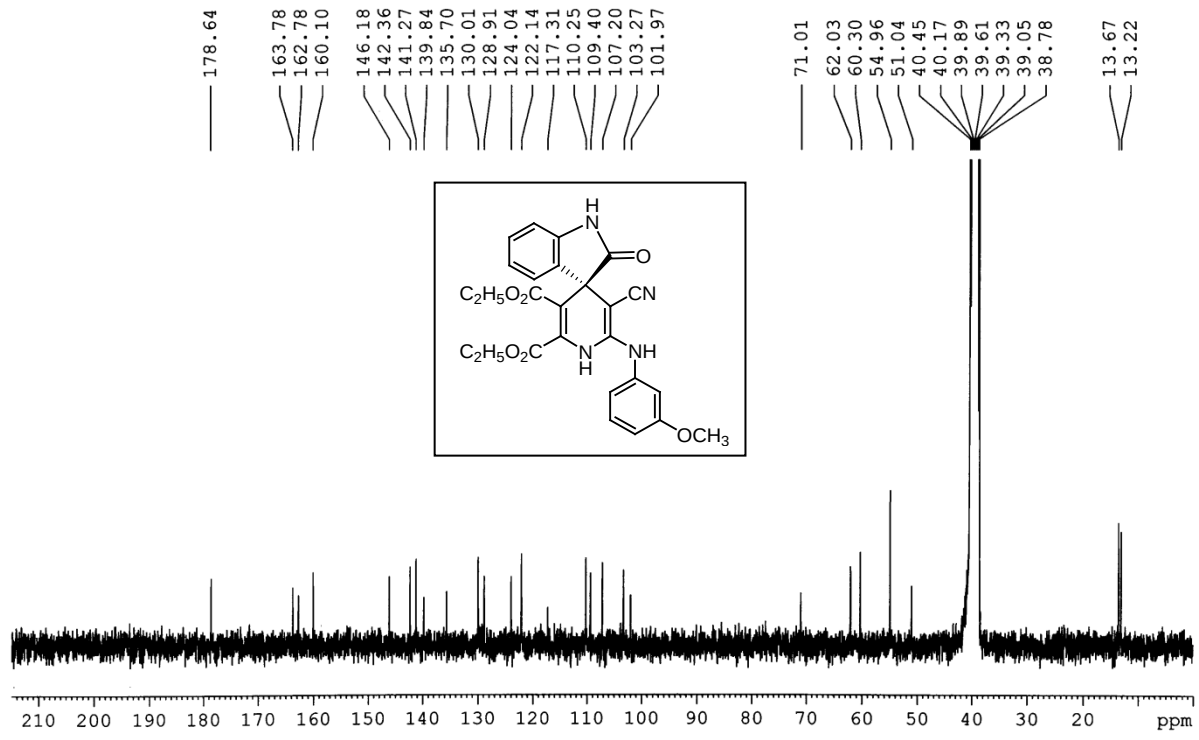
^{1}H NMR of compound **5f**



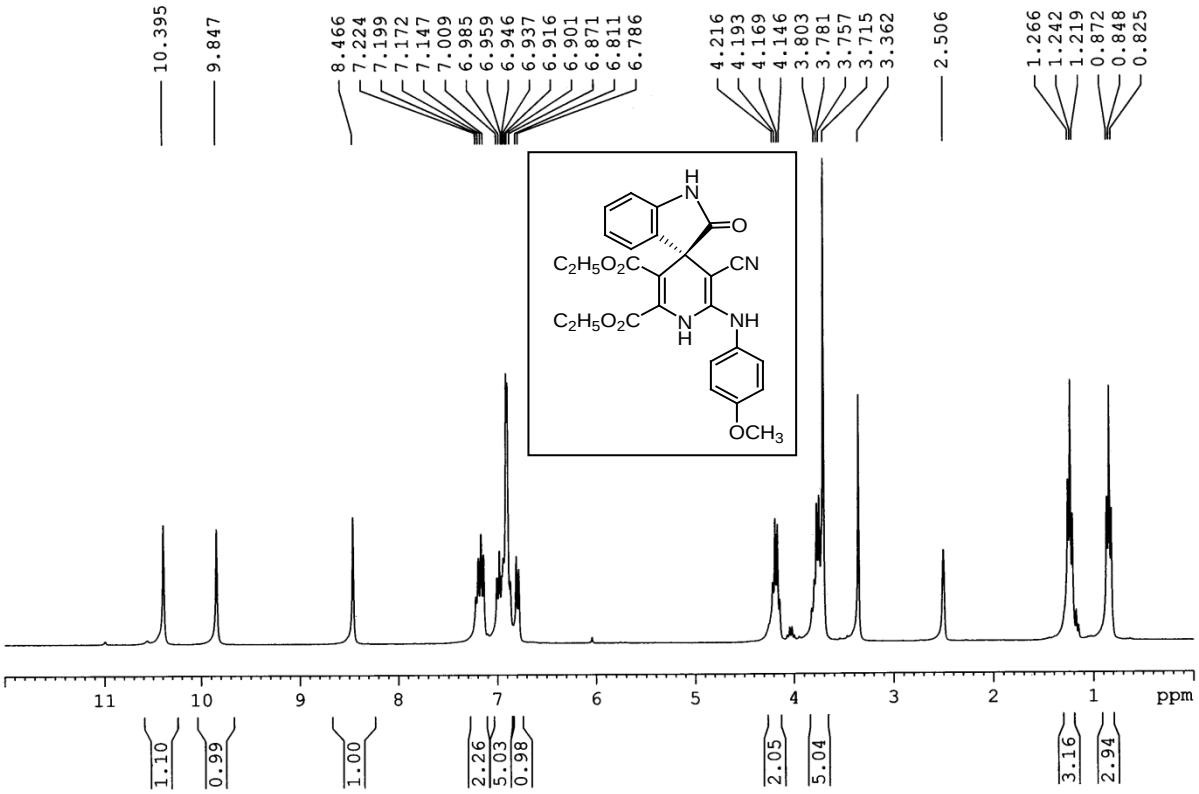
^{13}C NMR of compound **5f**



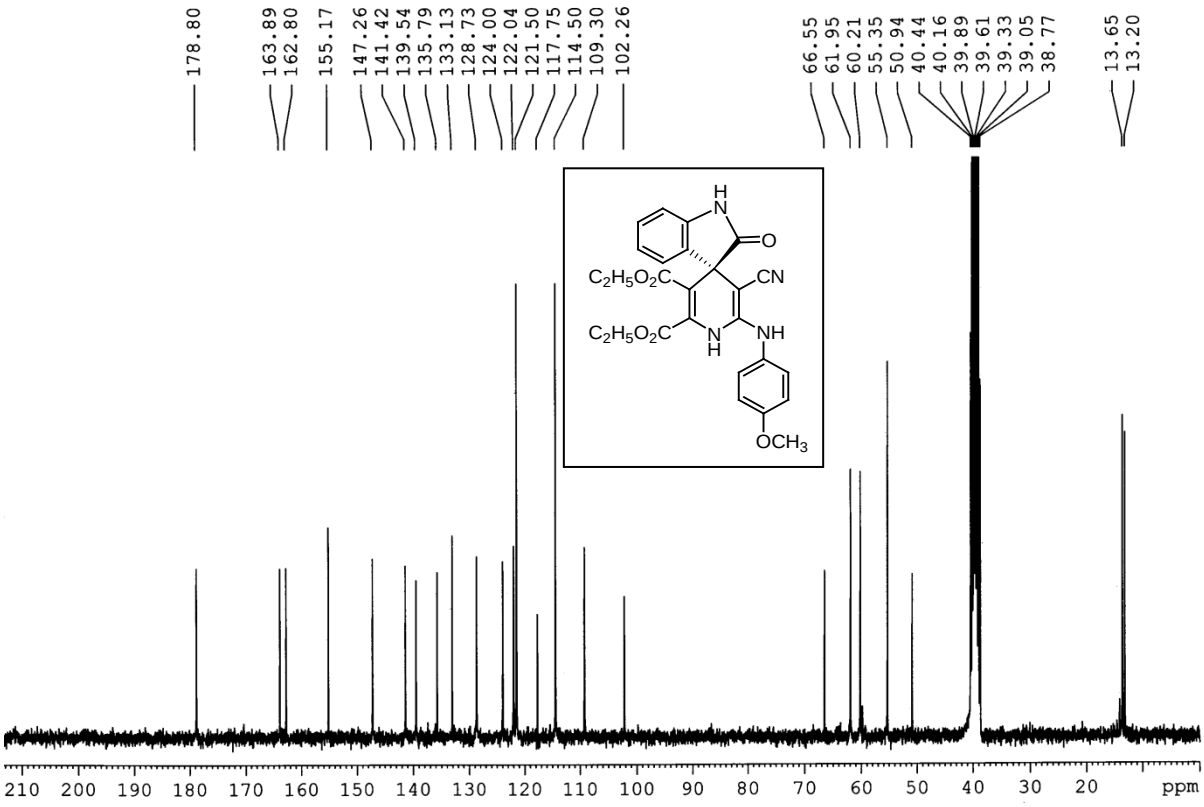
^{1}H NMR of compound **5g**



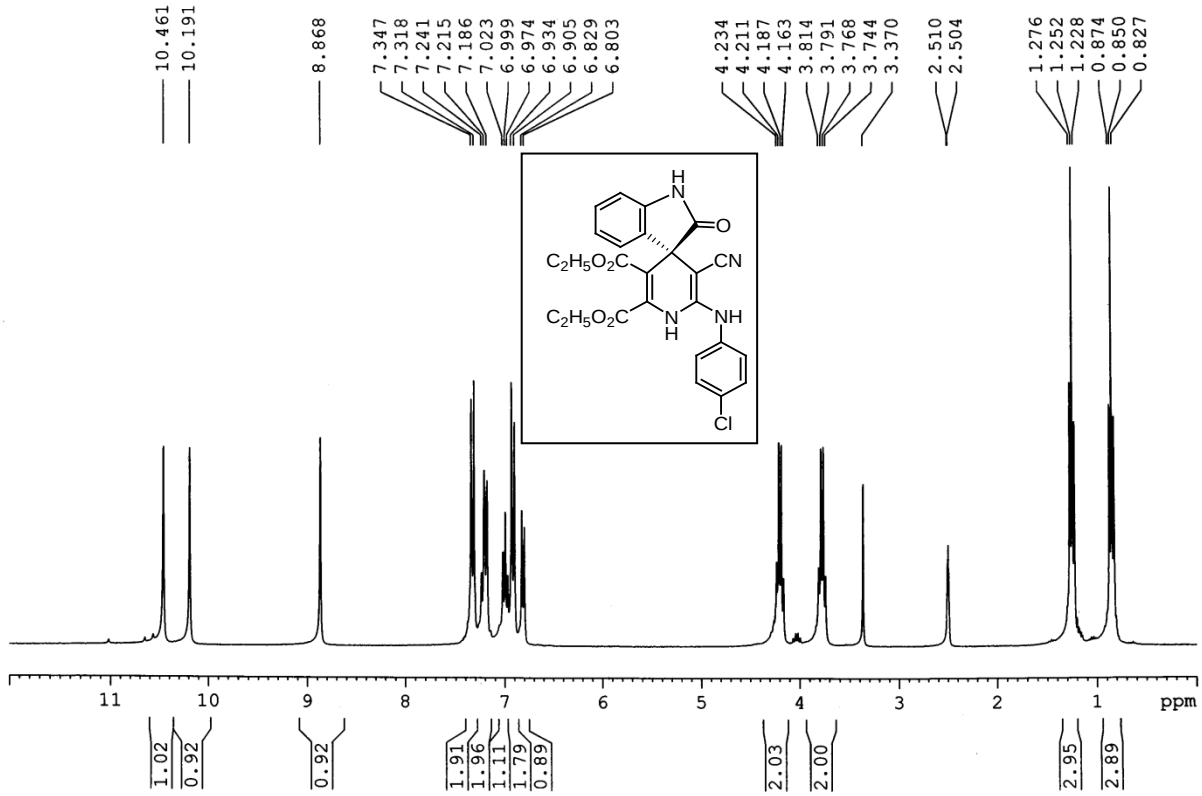
^{13}C NMR of compound **5g**



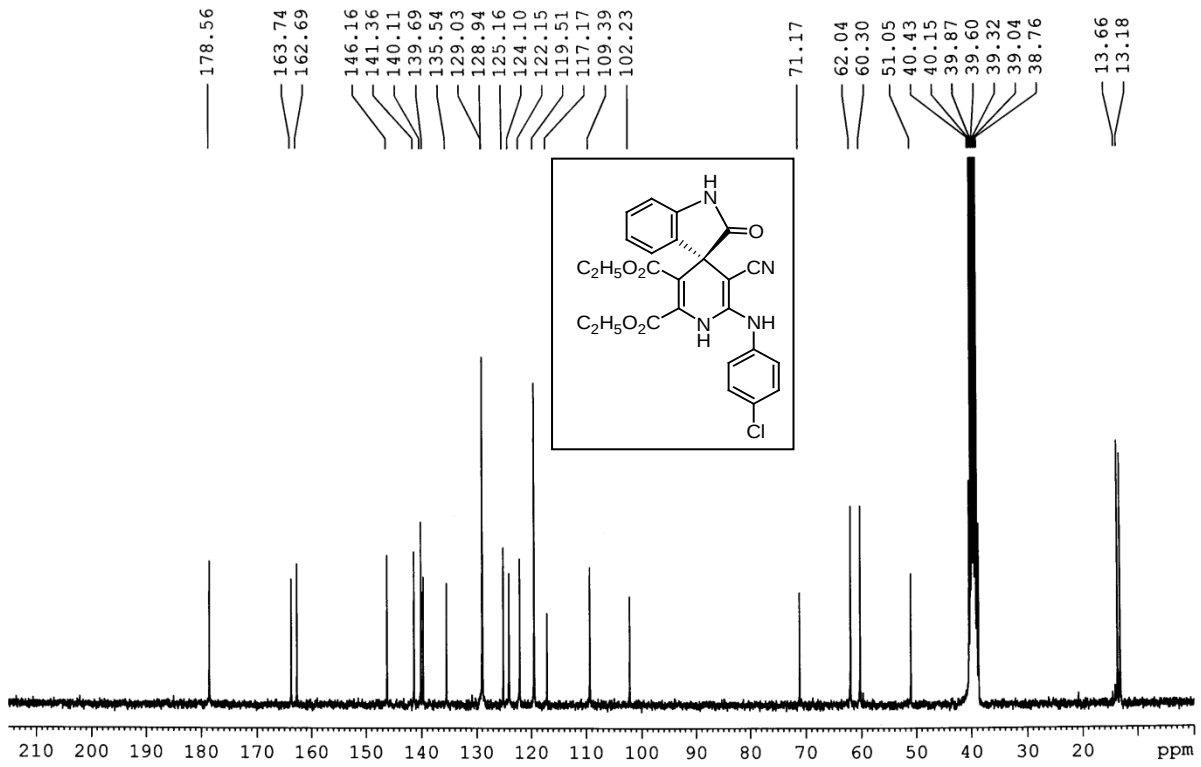
^{1}H NMR of compound **5h**



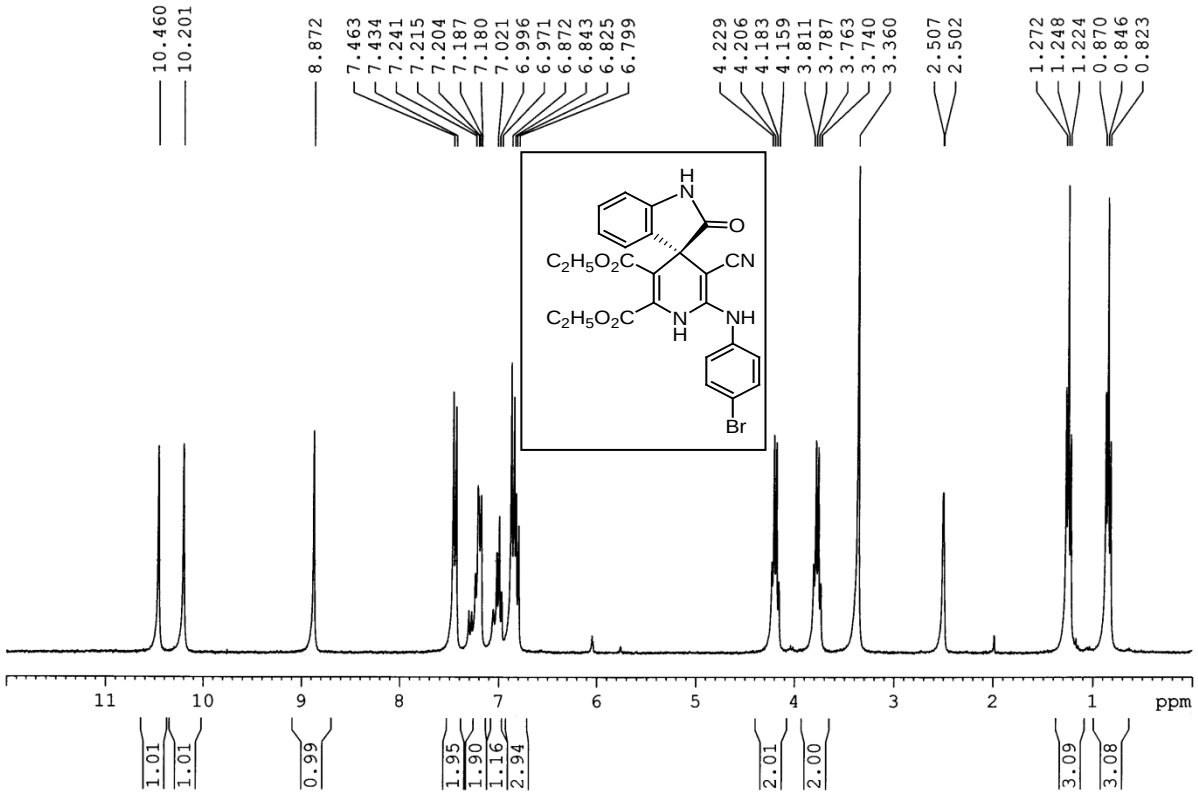
^{13}C NMR of compound **5h**



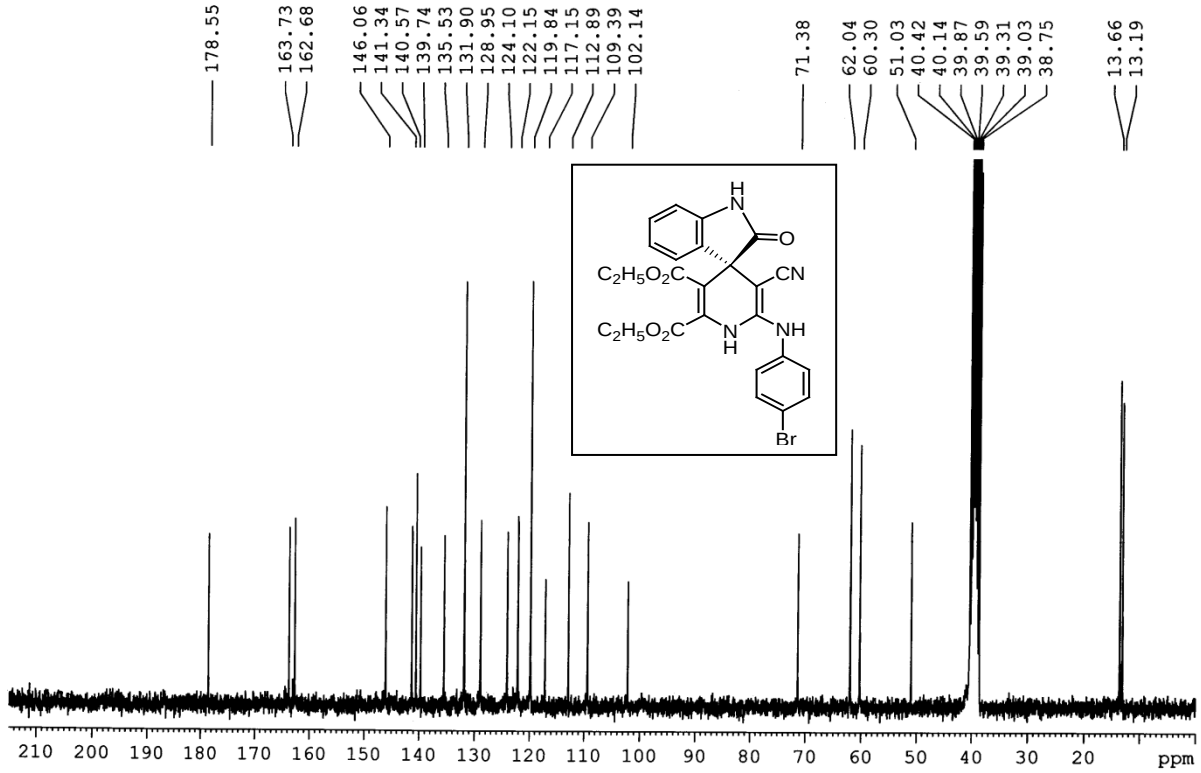
^{1}H NMR of compound **5i**



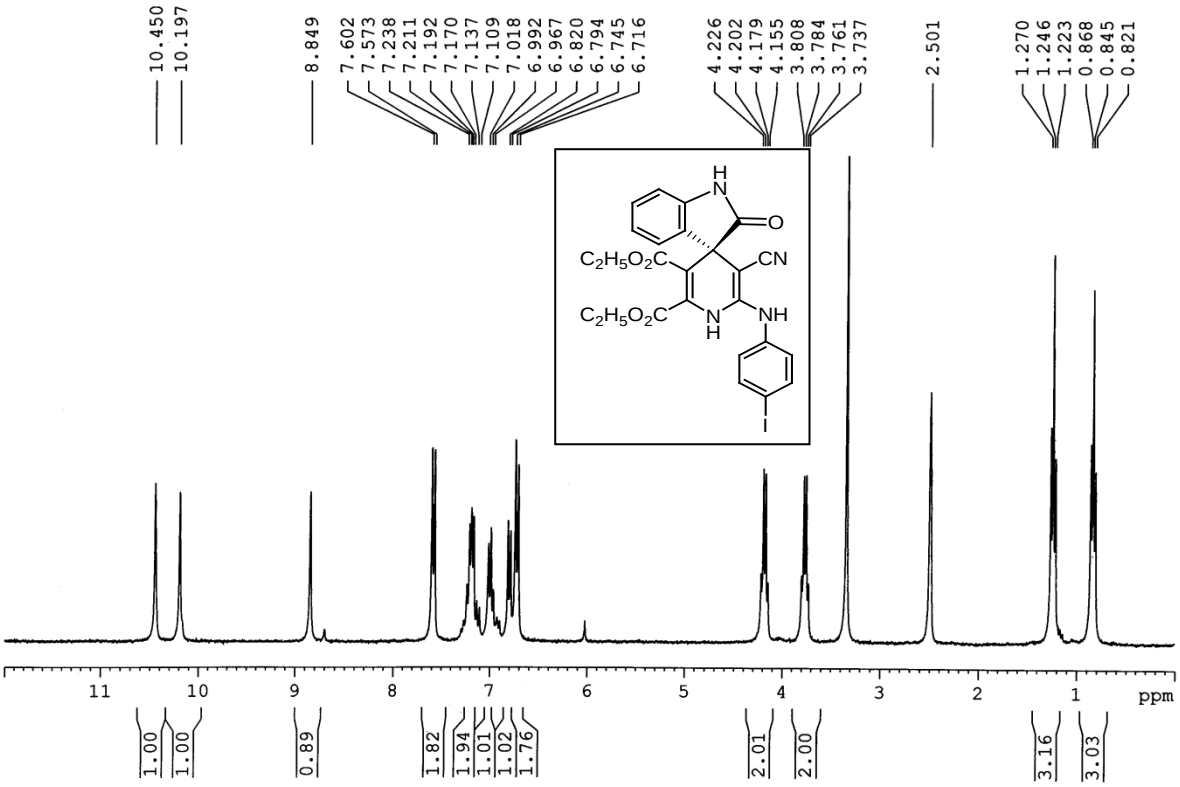
^{13}C NMR of compound **5i**



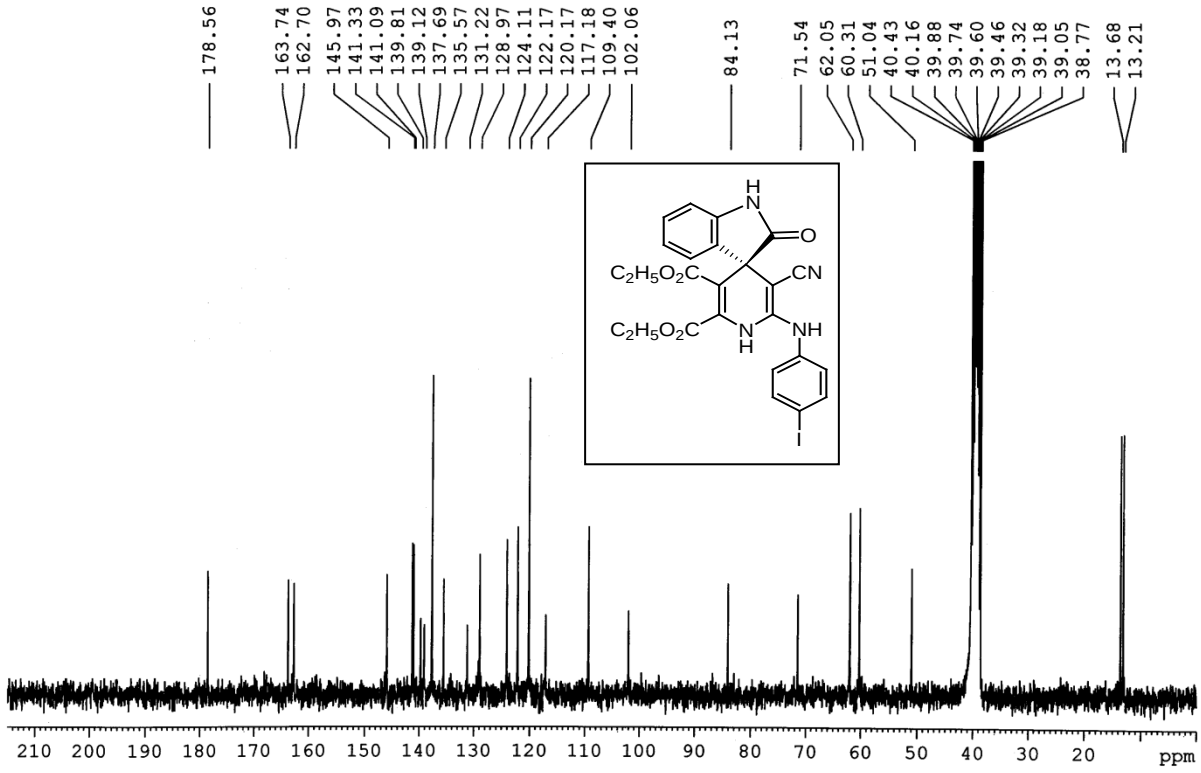
^{1}H NMR of compound **5j**



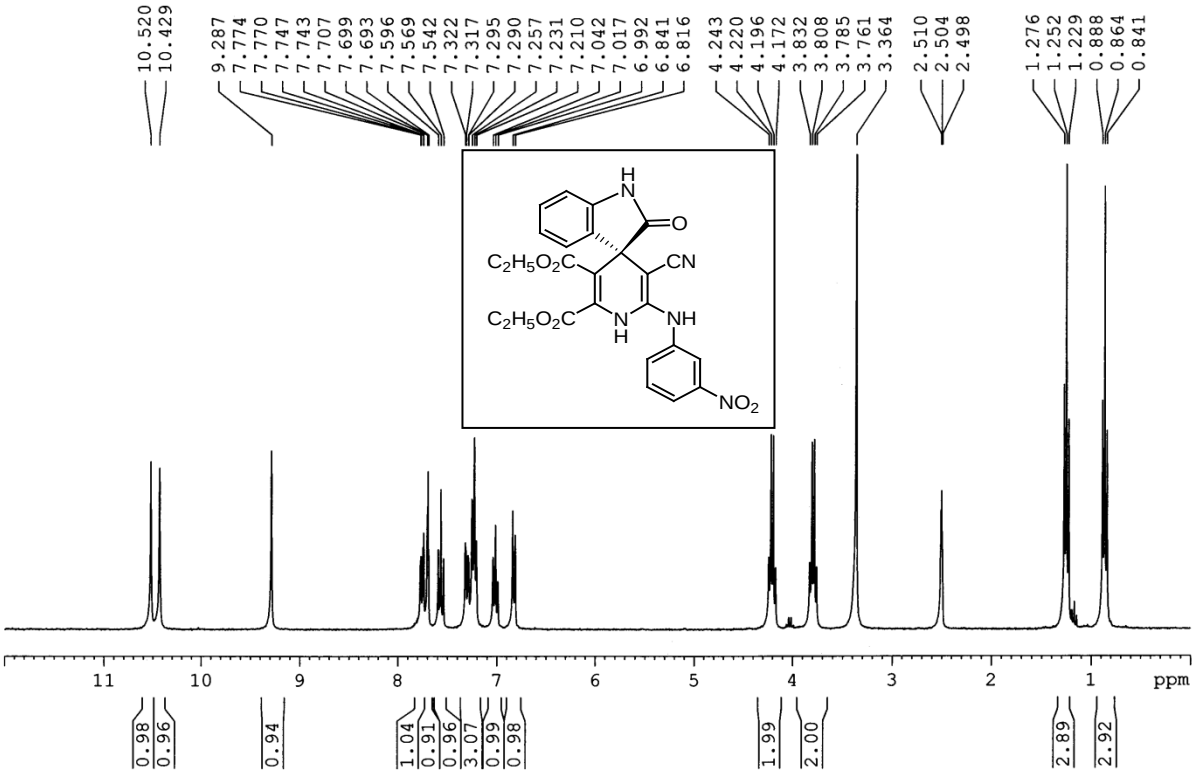
^{13}C NMR of compound **5j**



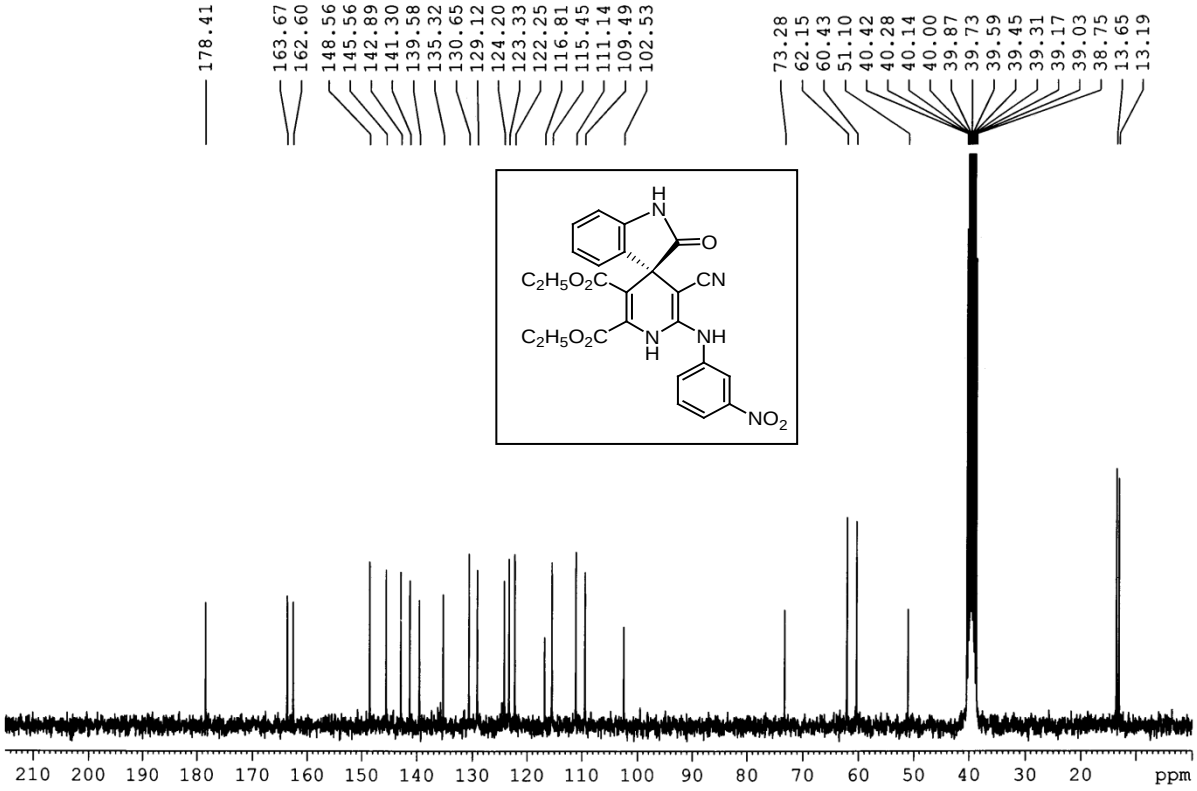
^{1}H NMR of compound **5k**



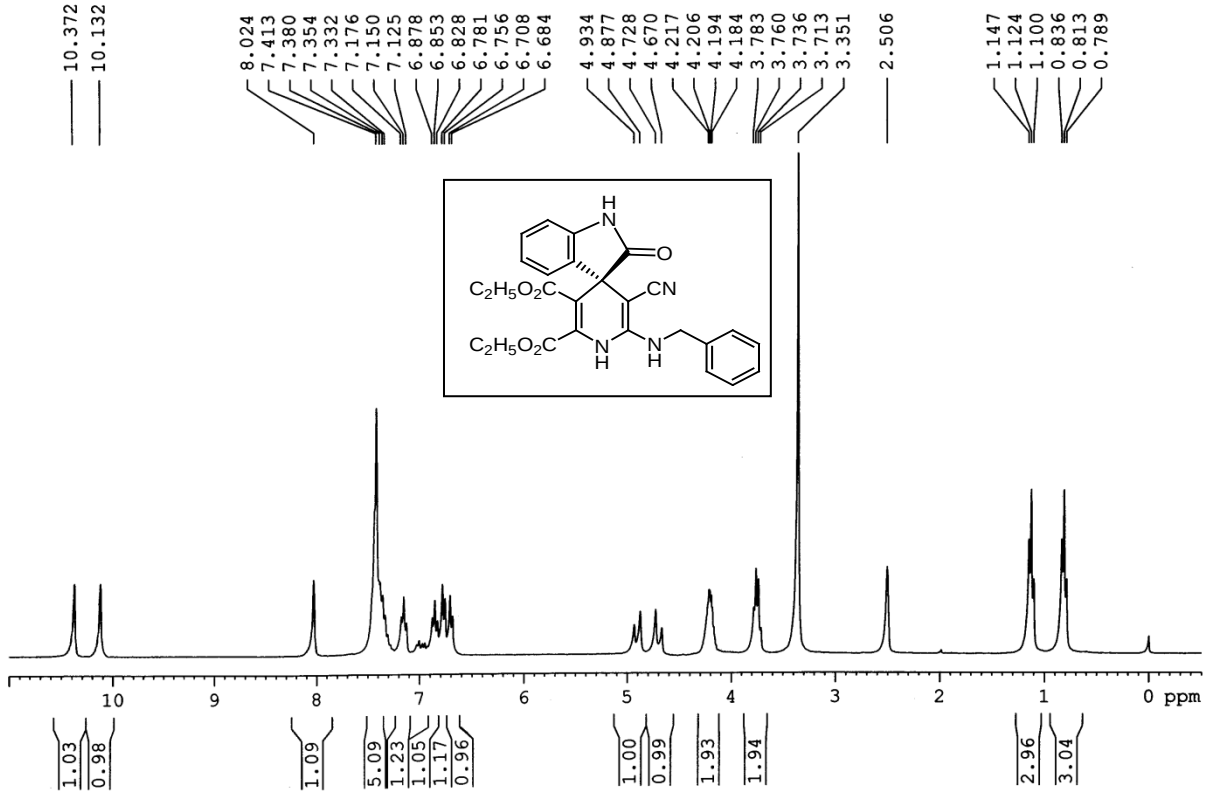
^{13}C NMR of compound **5k**



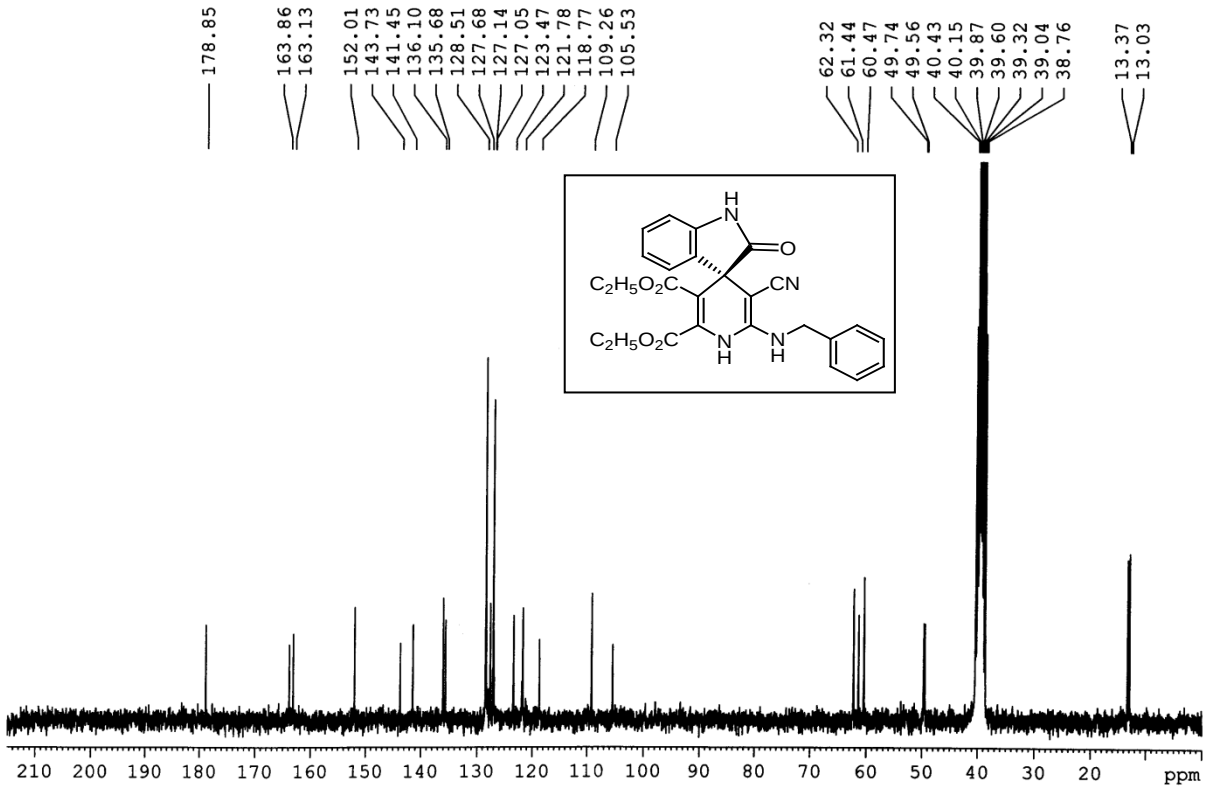
^{1}H NMR of compound **5l**



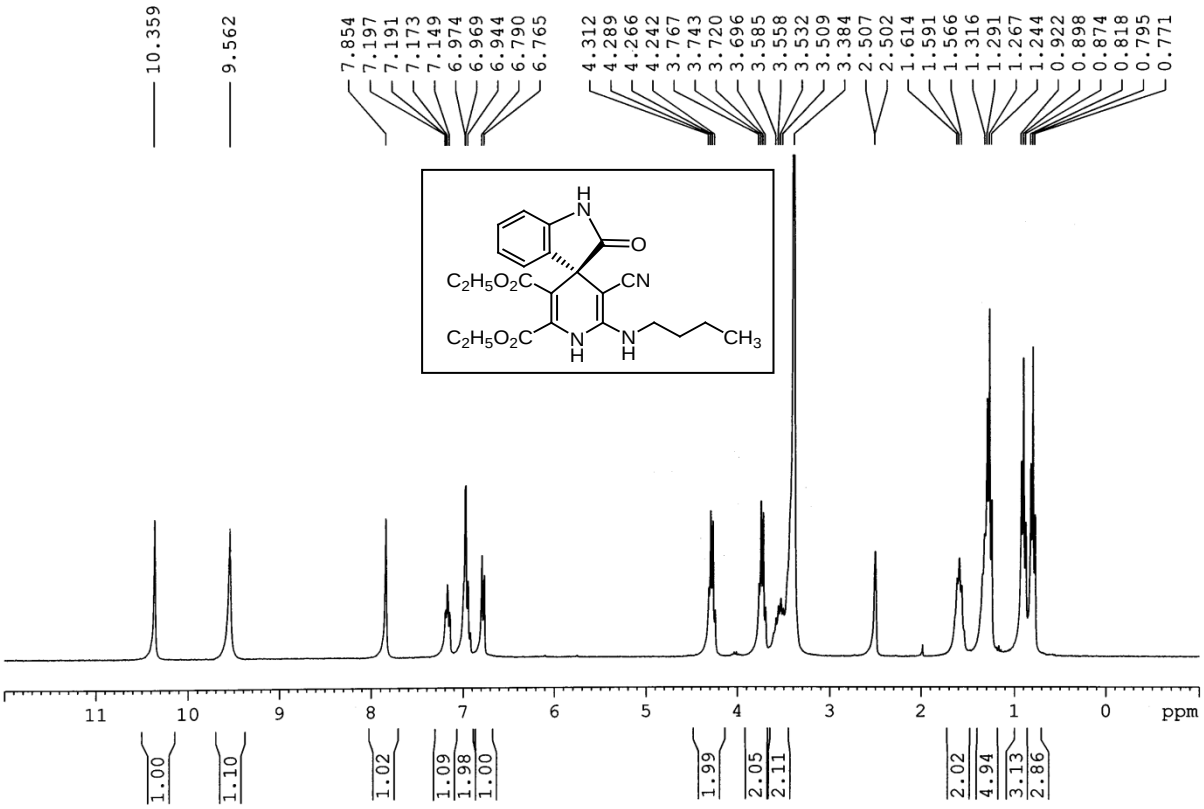
^{13}C NMR of compound **5l**



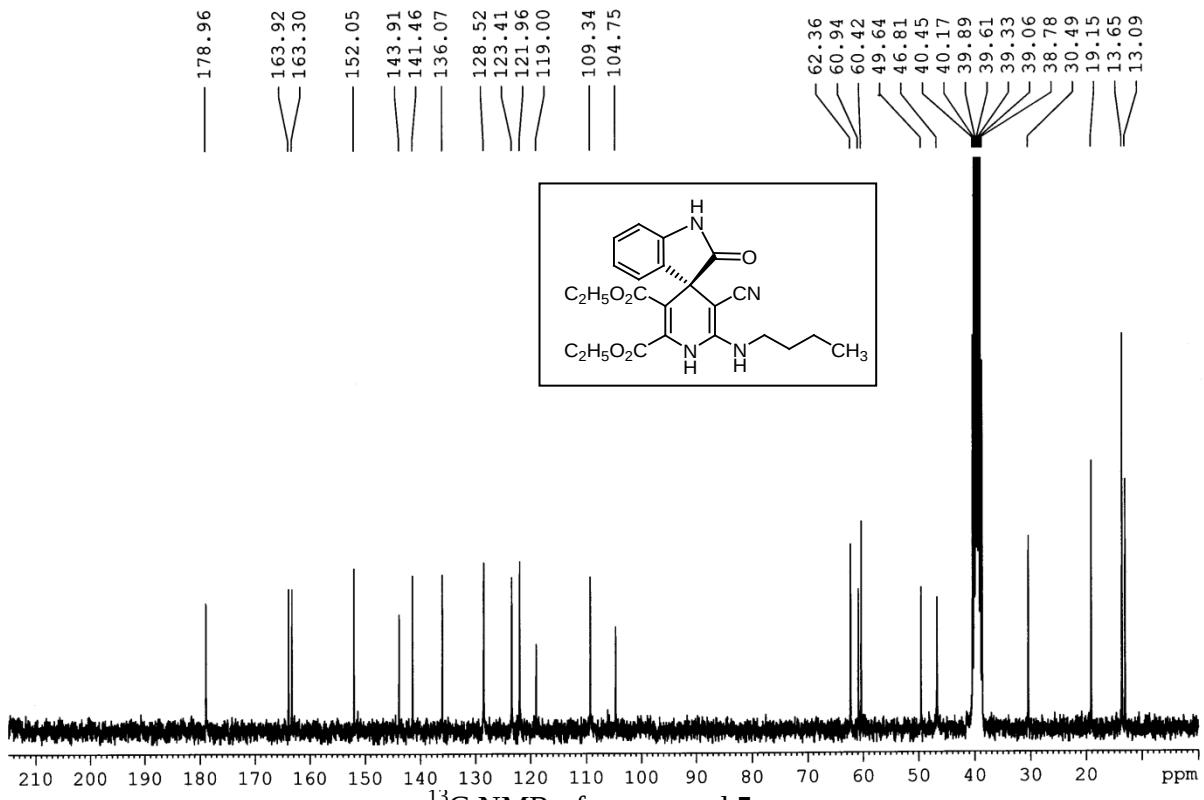
^{1}H NMR of compound **5m**



^{13}C NMR of compound **5m**

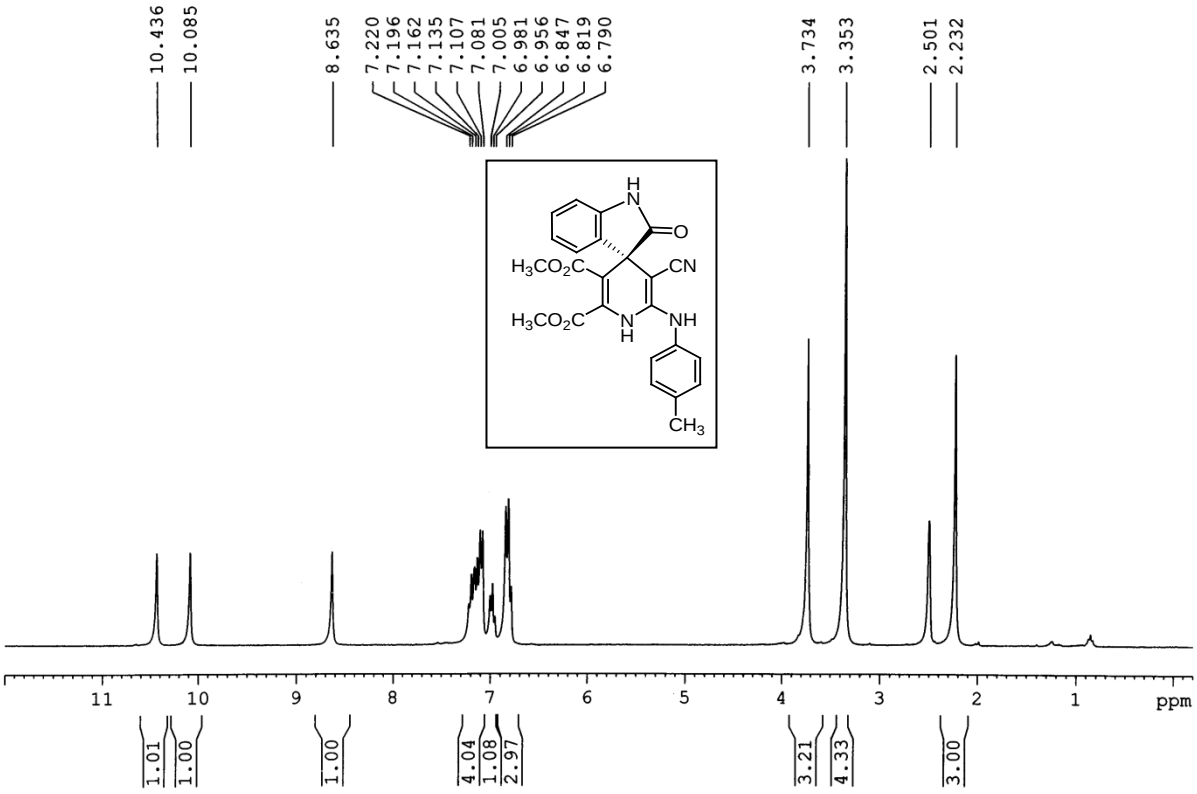


^{1}H NMR of compound **5n**

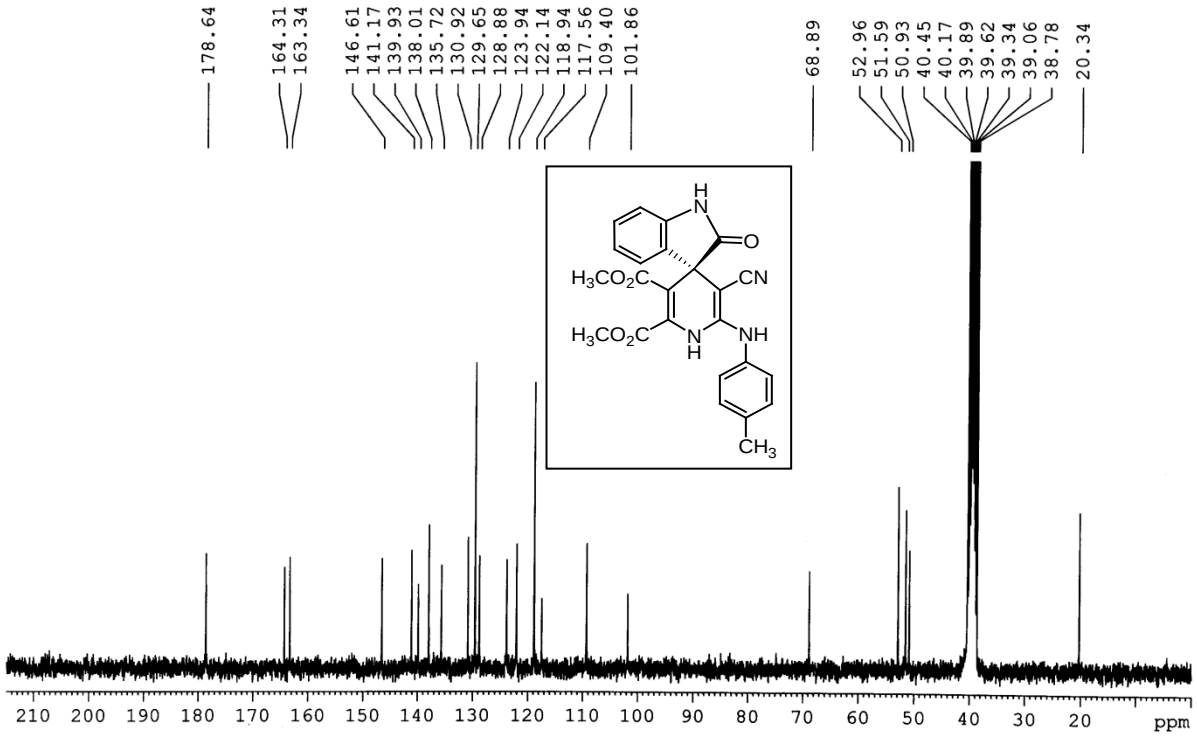


^{13}C NMR of compound **5n**

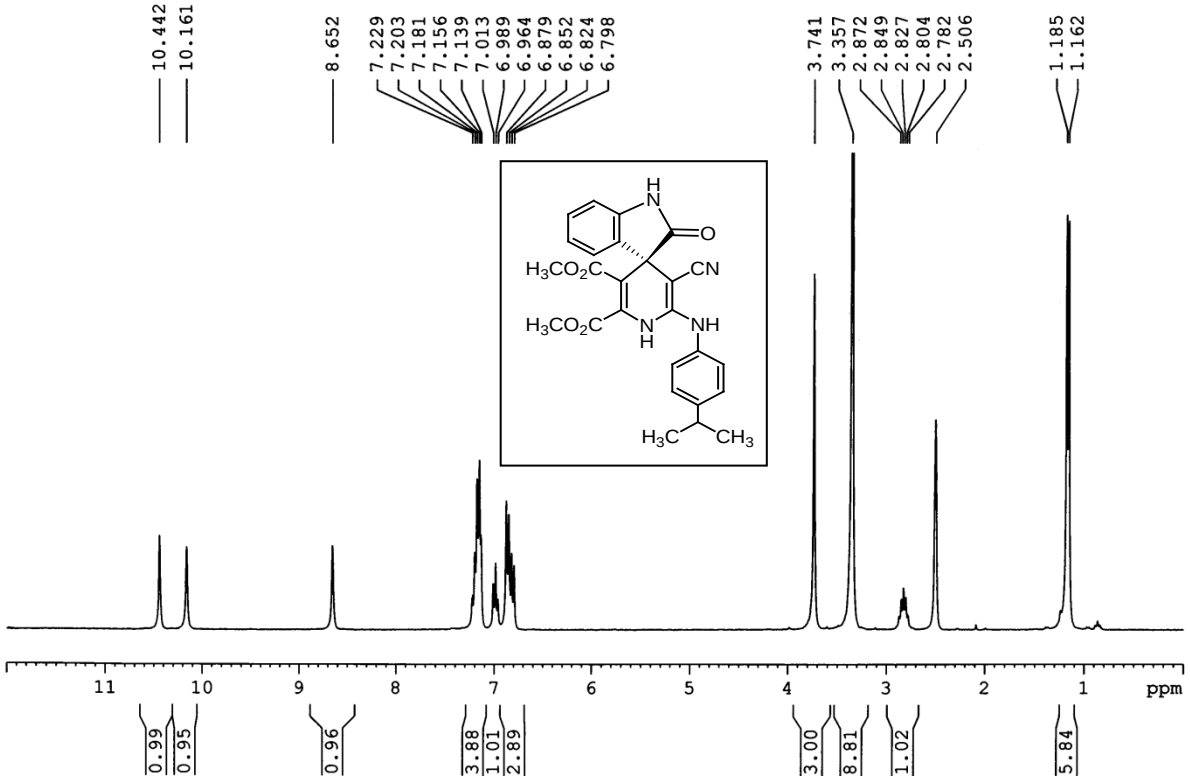
Copy of ^{1}H and ^{13}C NMR spectra of synthesized compounds (6a-6m):



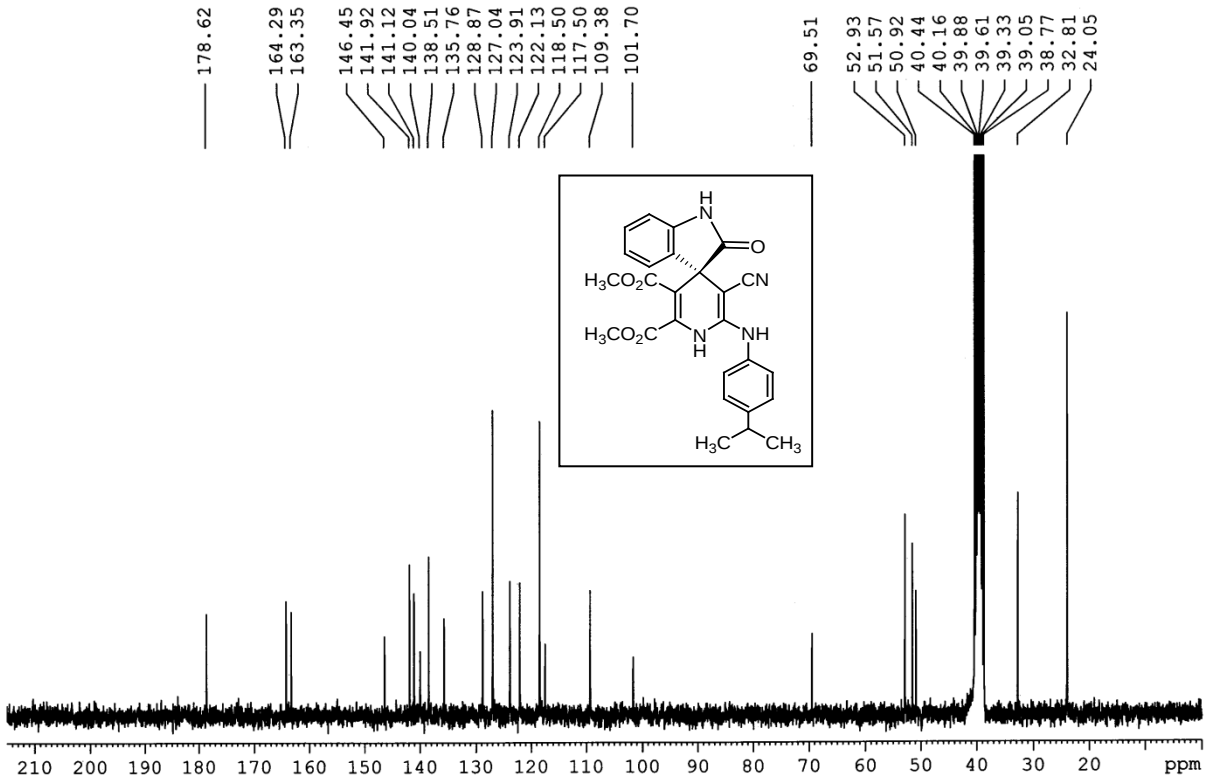
^{1}H NMR of compound **6a**



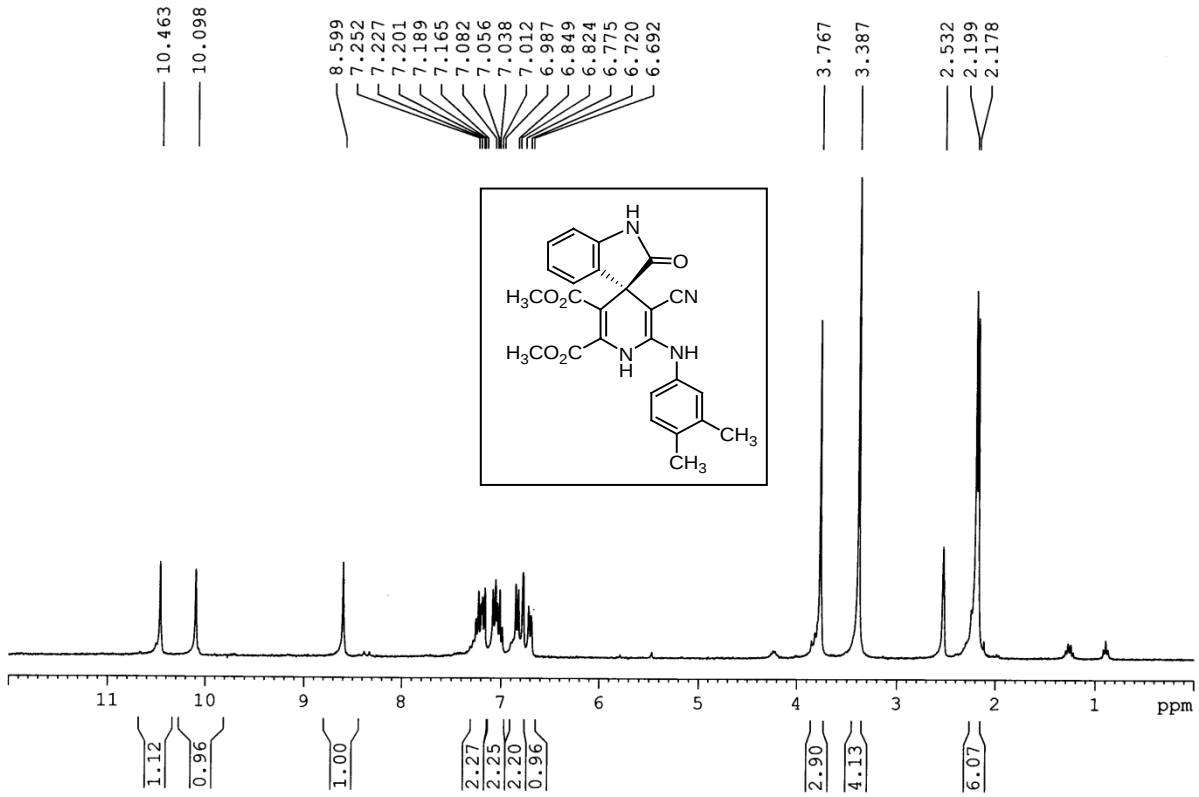
^{13}C NMR of compound **6a**



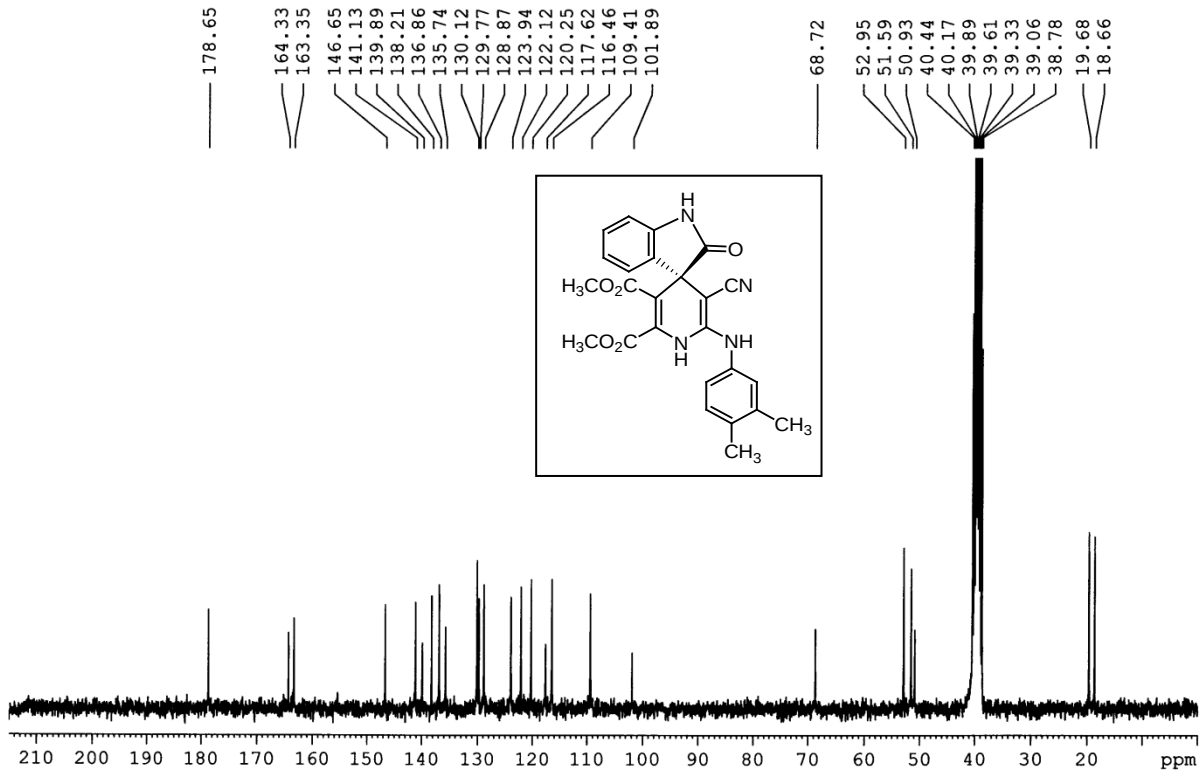
^{1}H NMR of compound **6b**



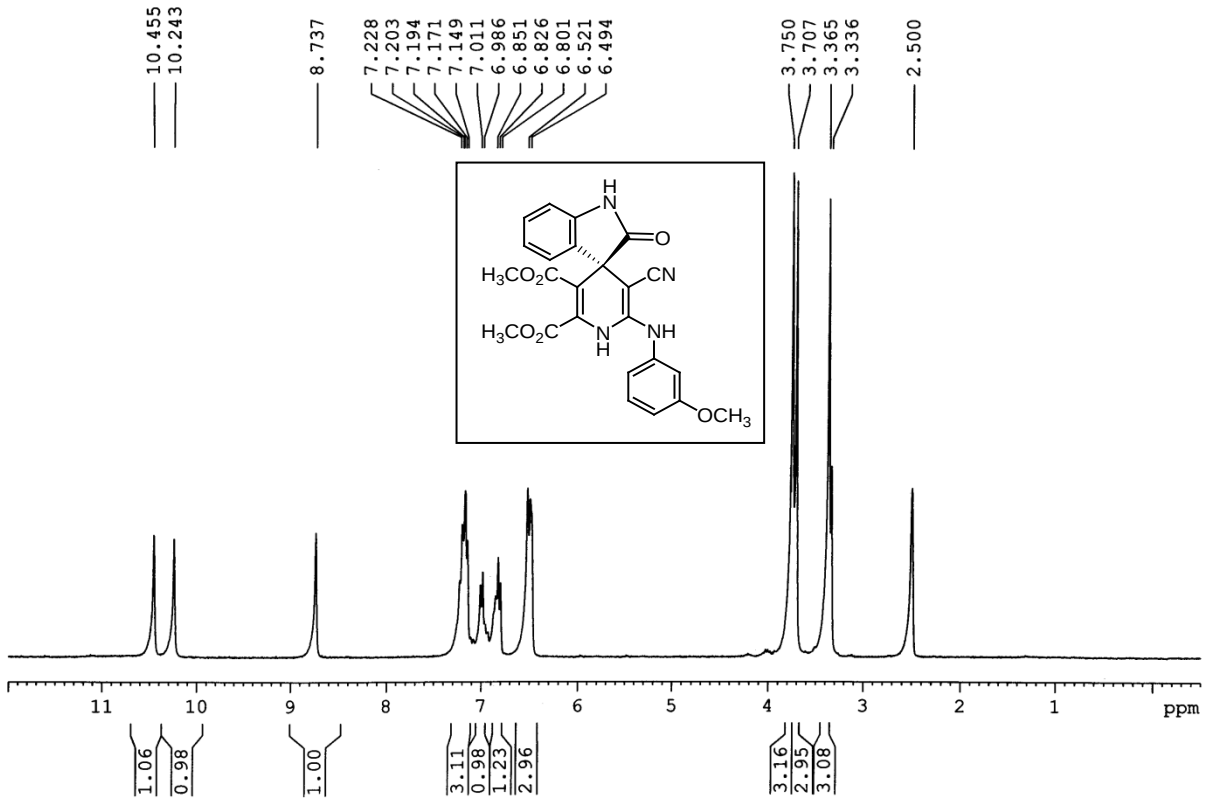
^{13}C NMR of compound **6b**



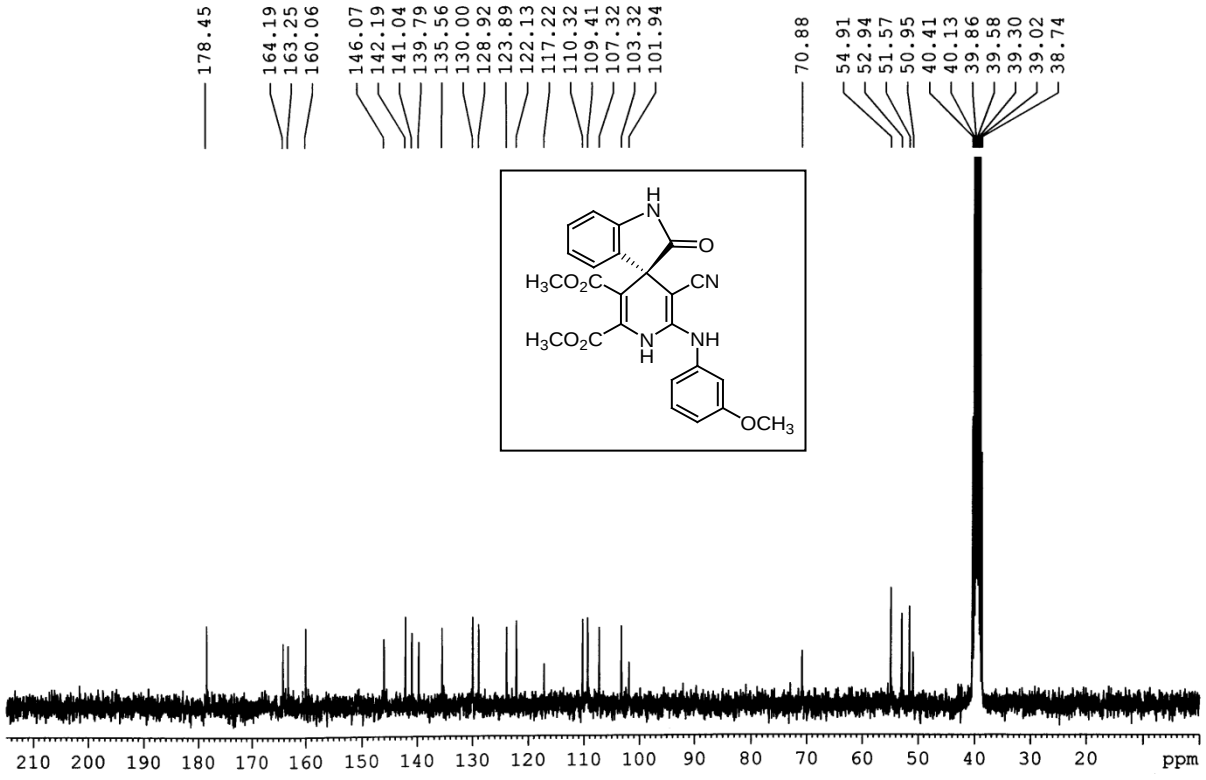
^{1}H NMR of compound **6c**



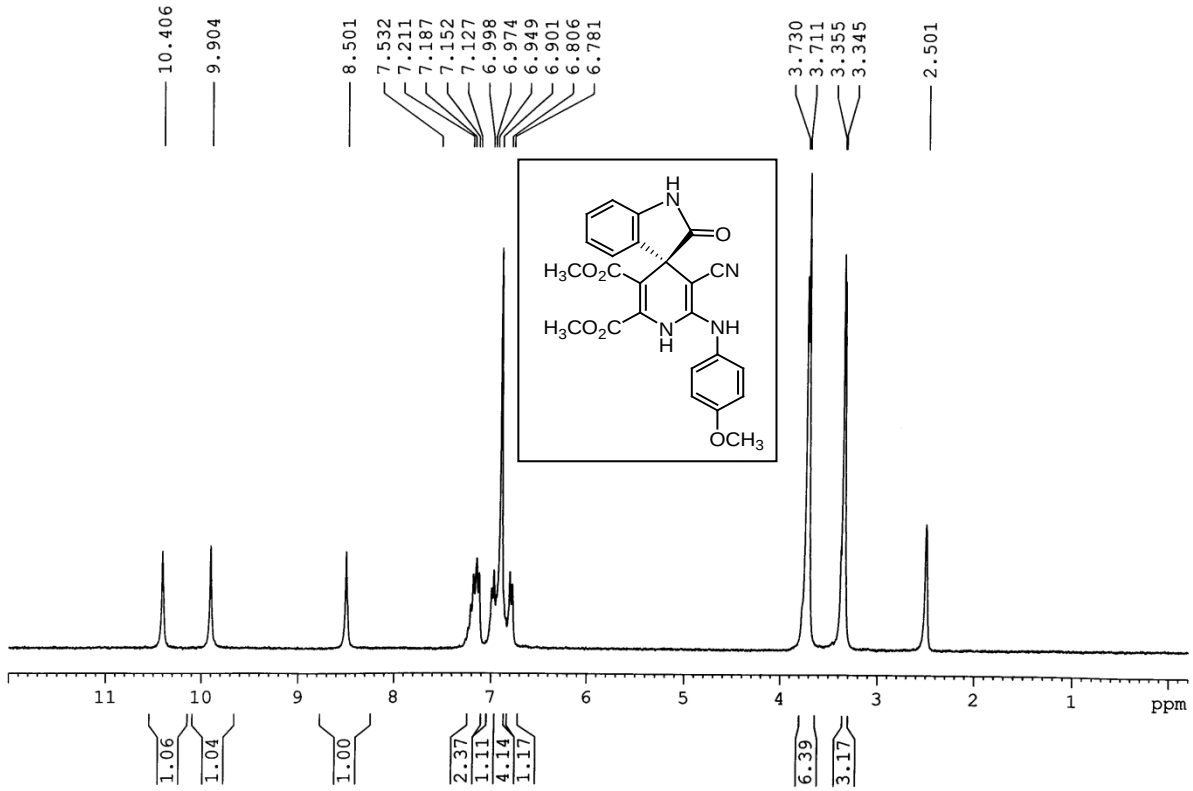
^{13}C NMR of compound **6c**



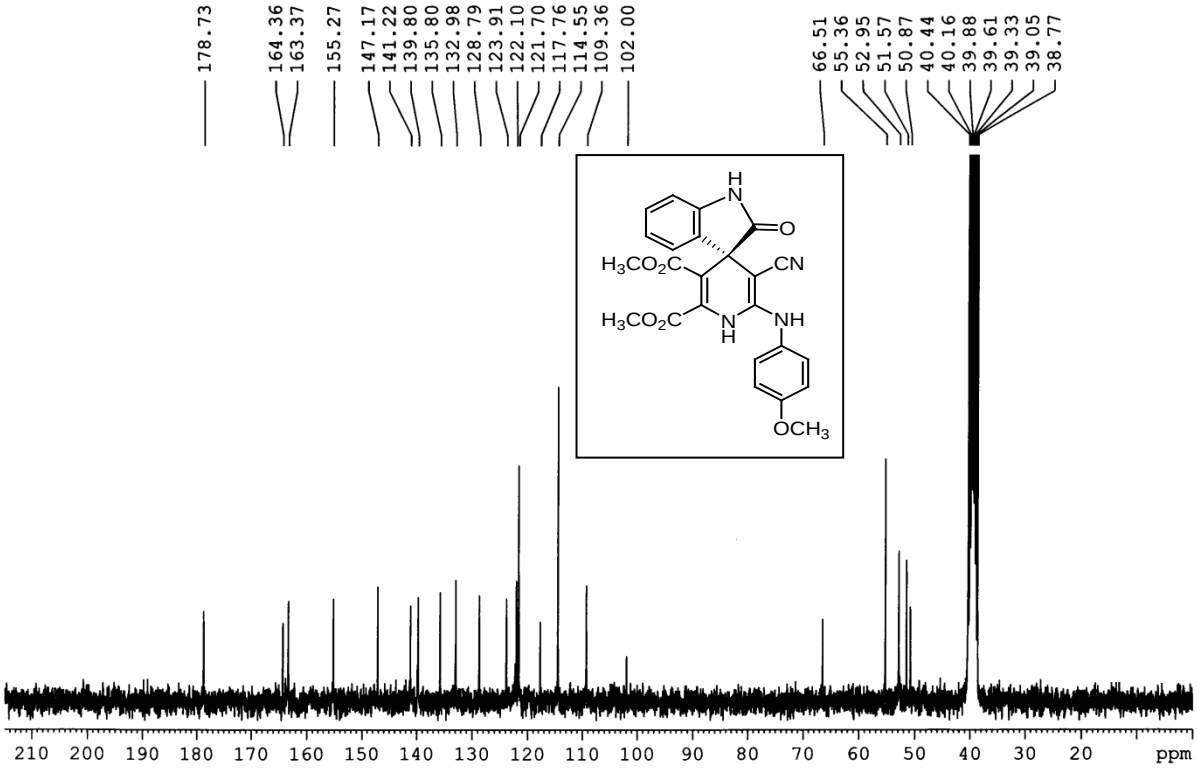
^{1}H NMR of compound **6d**



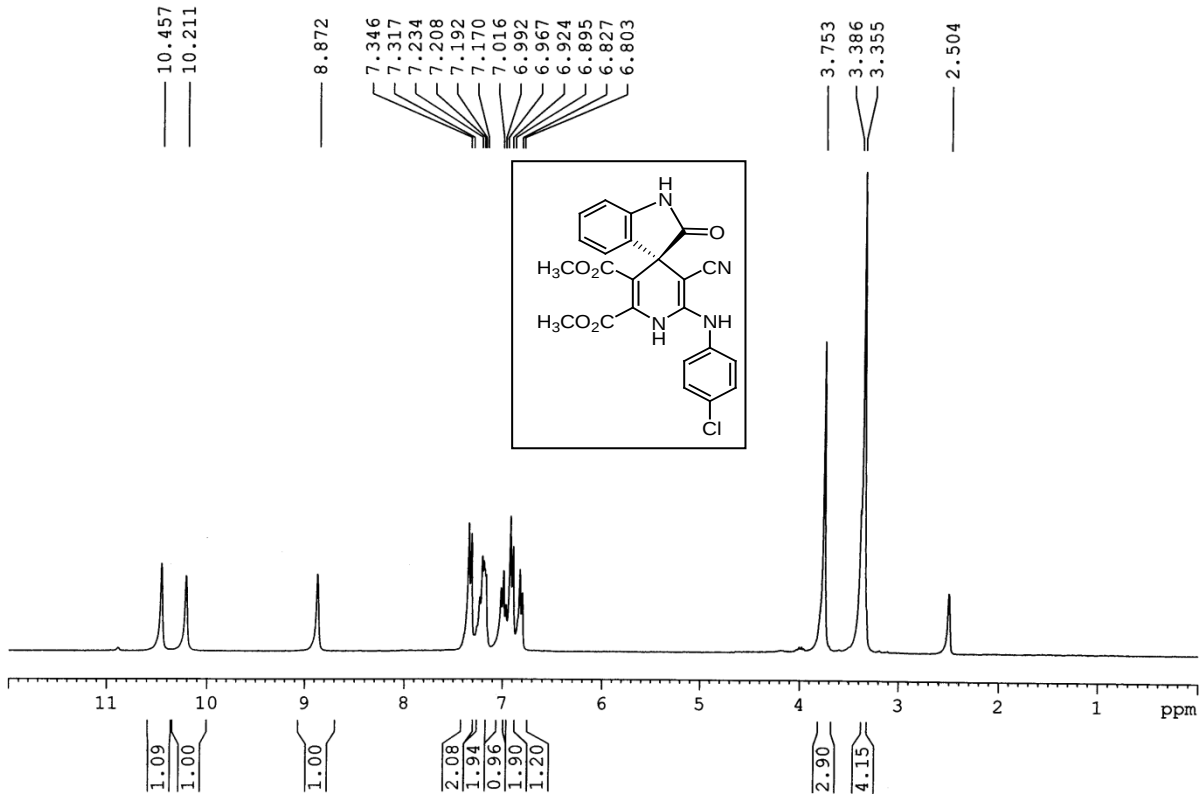
^{13}C NMR of compound **6d**



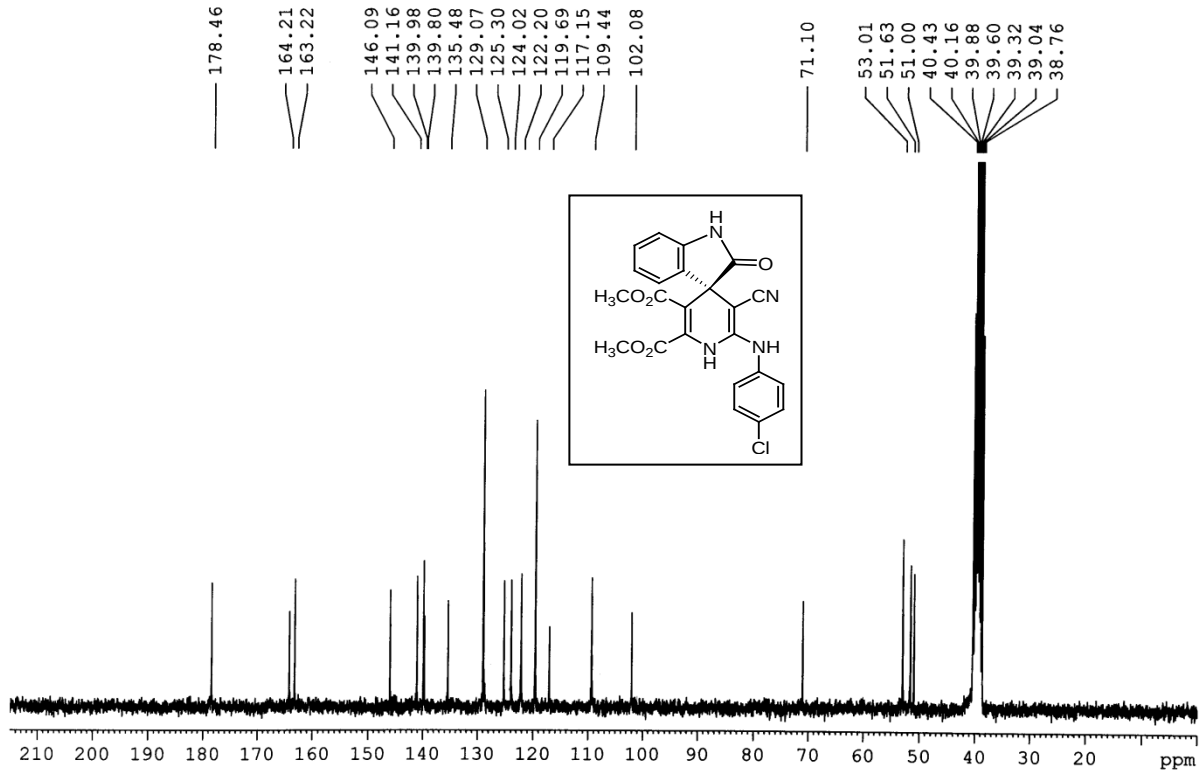
^{1}H NMR of compound **6e**



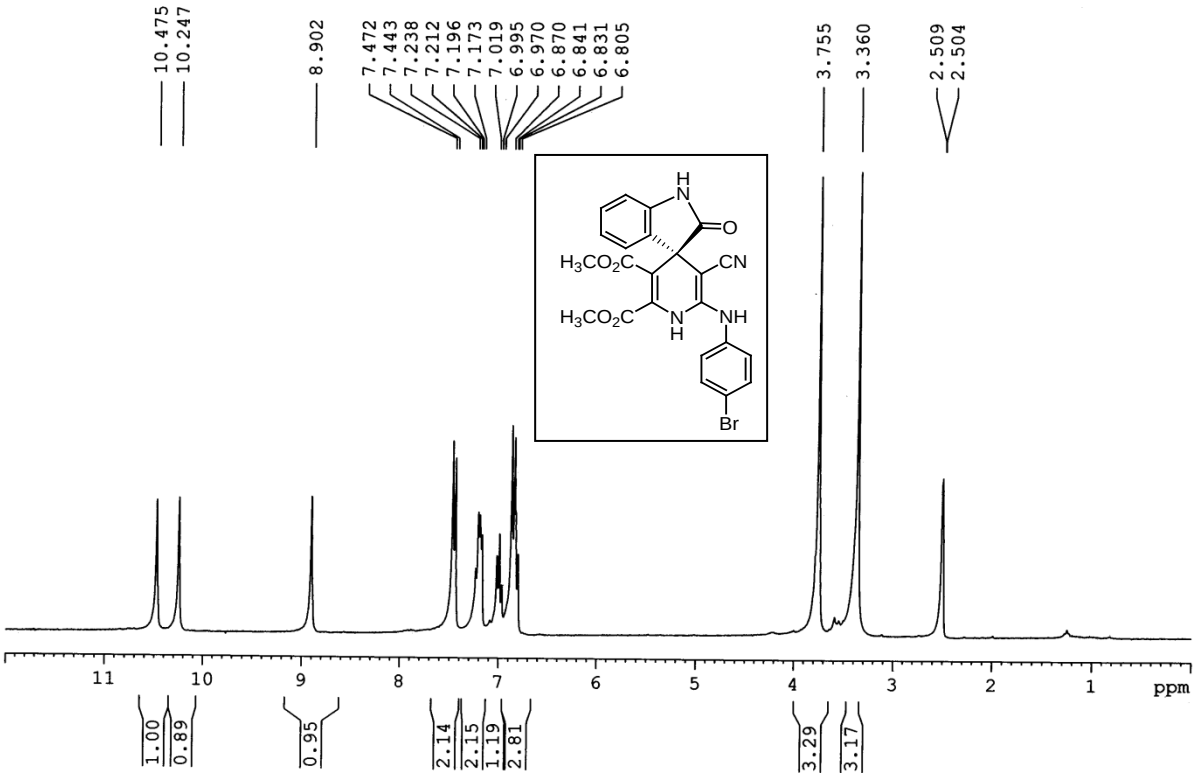
^{13}C NMR of compound **6e**



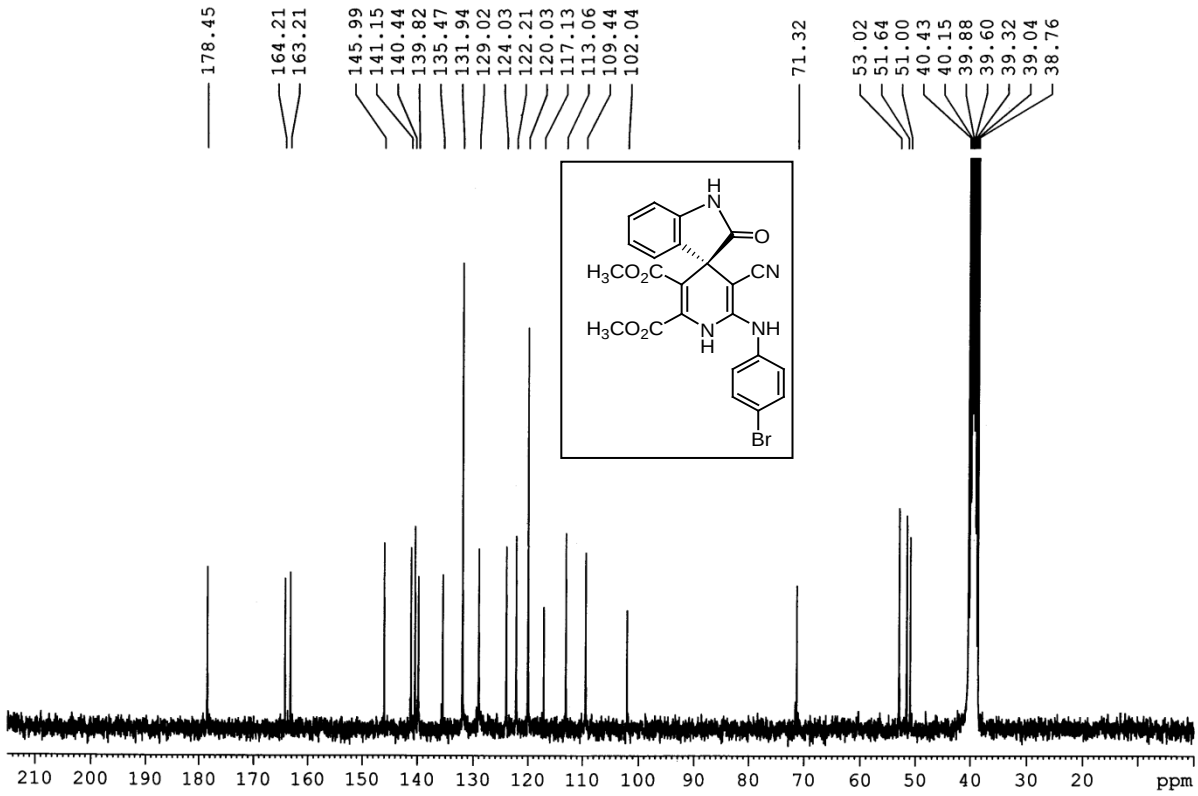
^{1}H NMR of compound **6f**



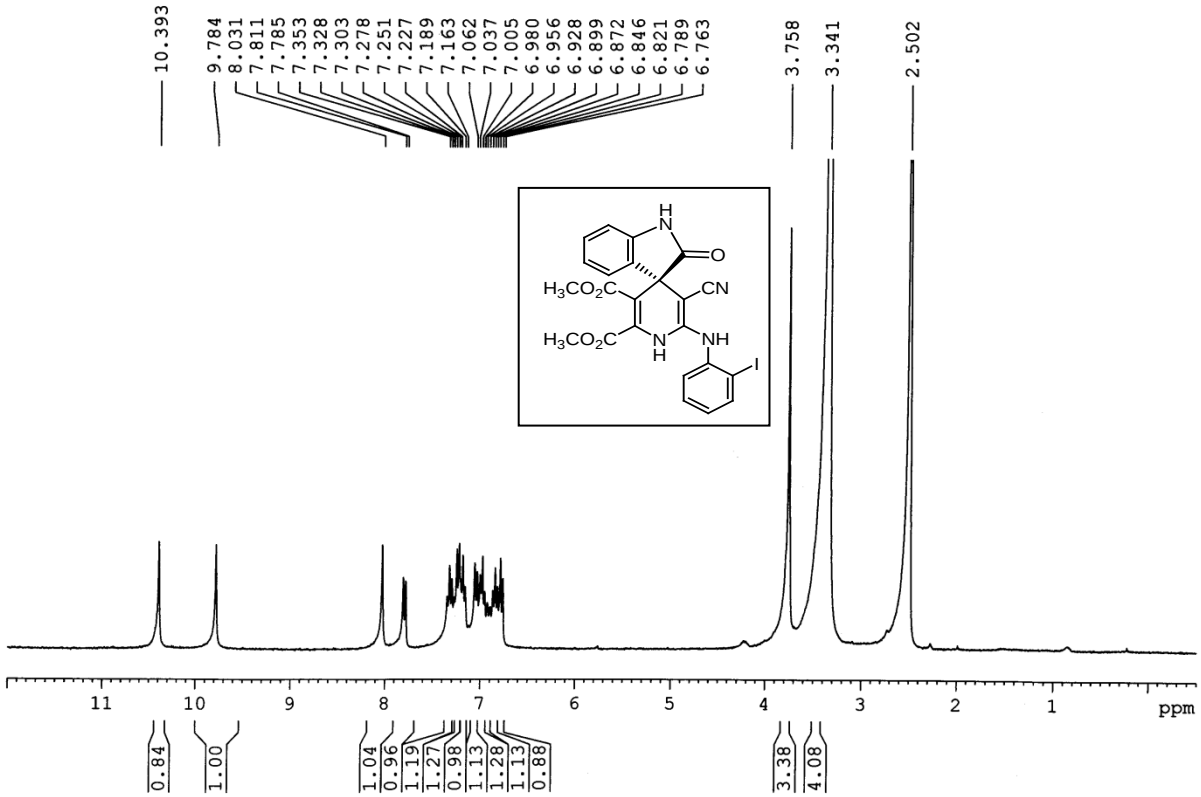
^{13}C NMR of compound **6f**



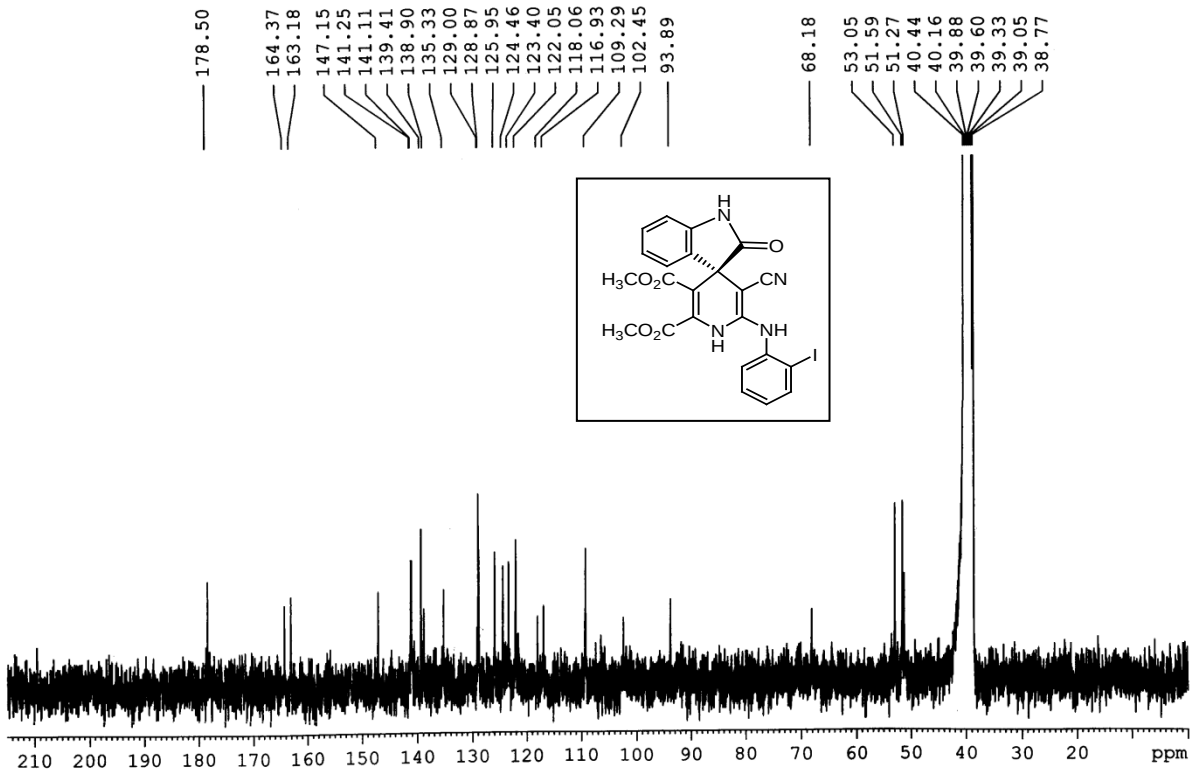
^{1}H NMR of compound **6g**



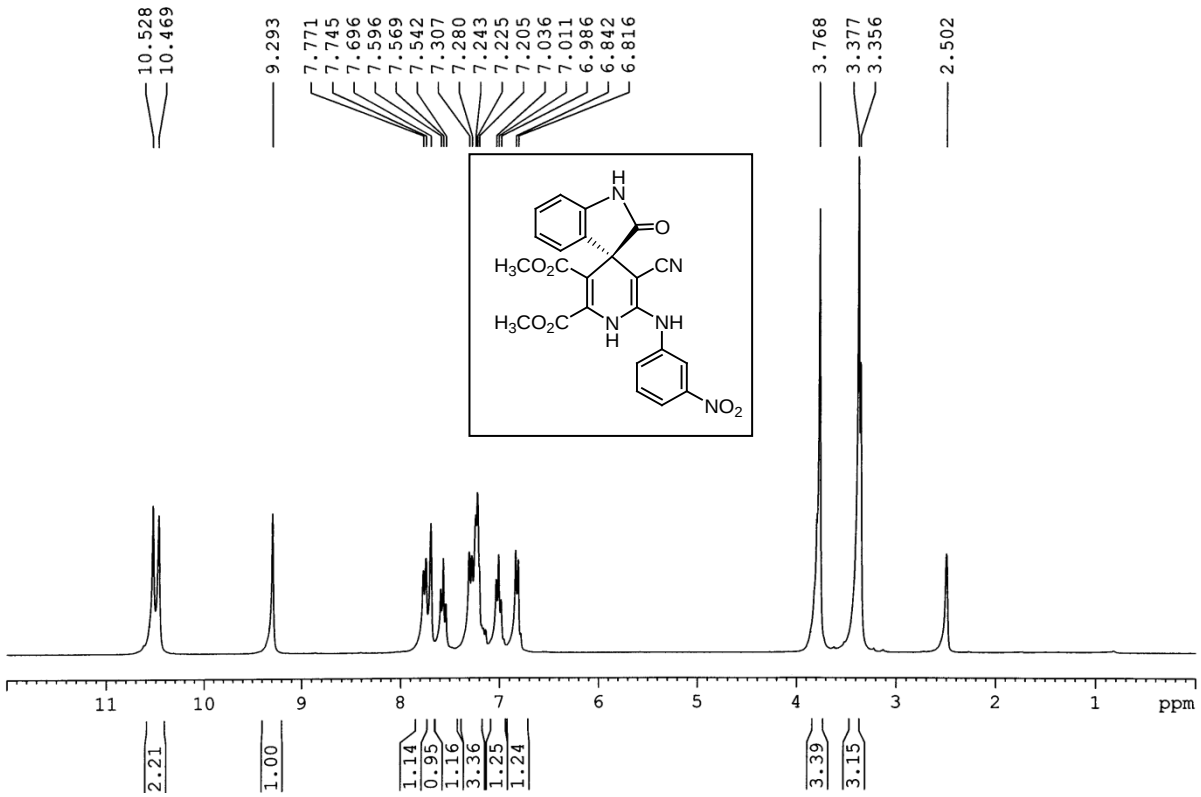
^{13}C NMR of compound **6g**



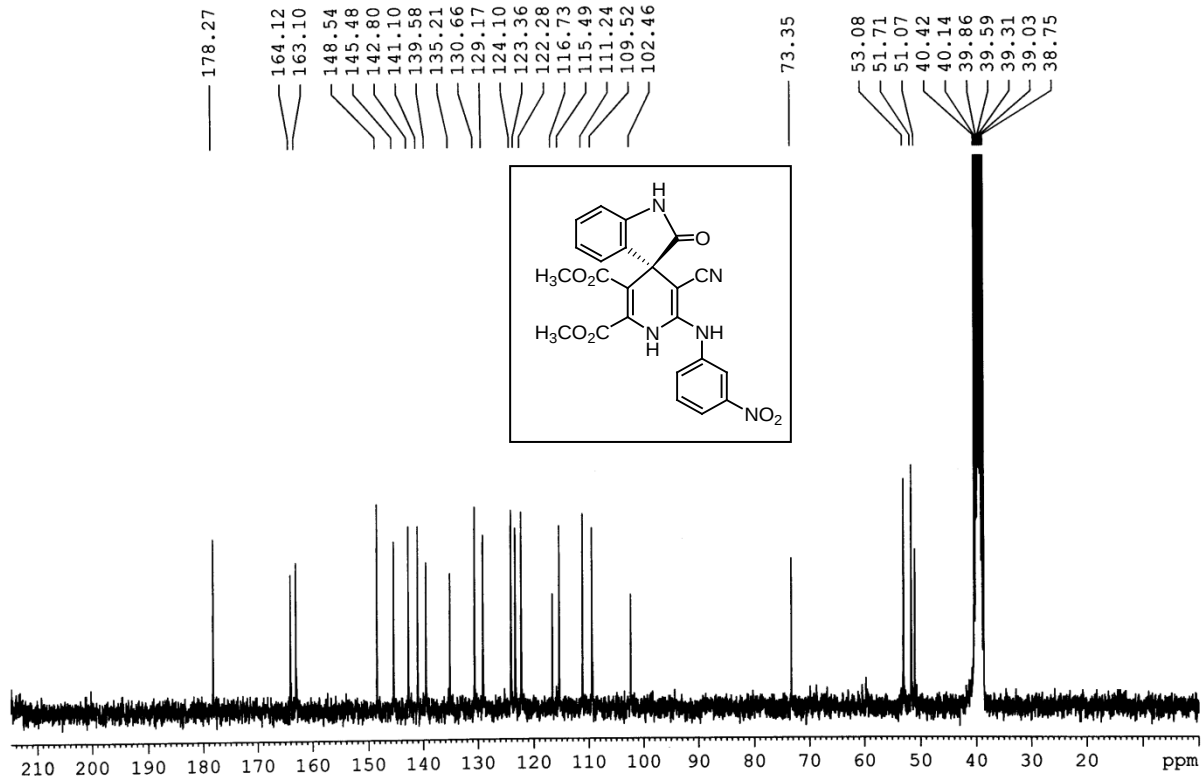
^{1}H NMR of compound **6h**



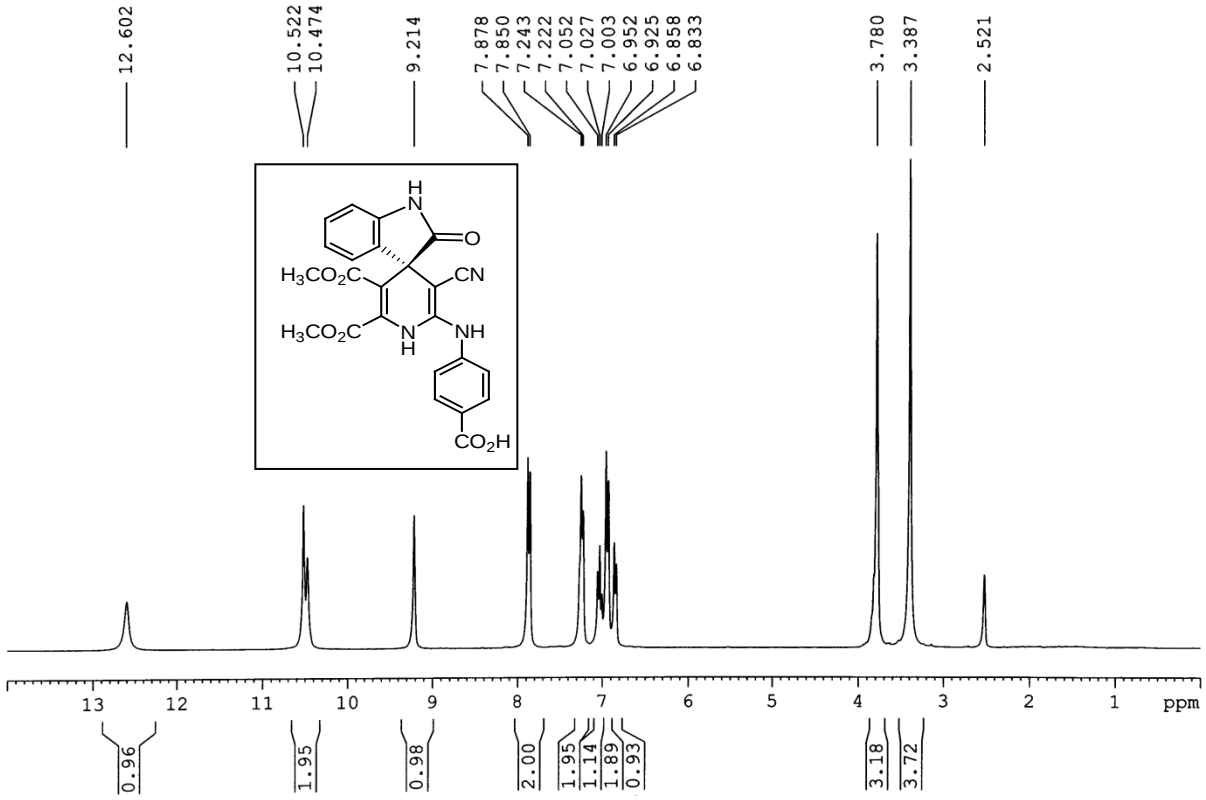
^{13}H NMR of compound **6h**



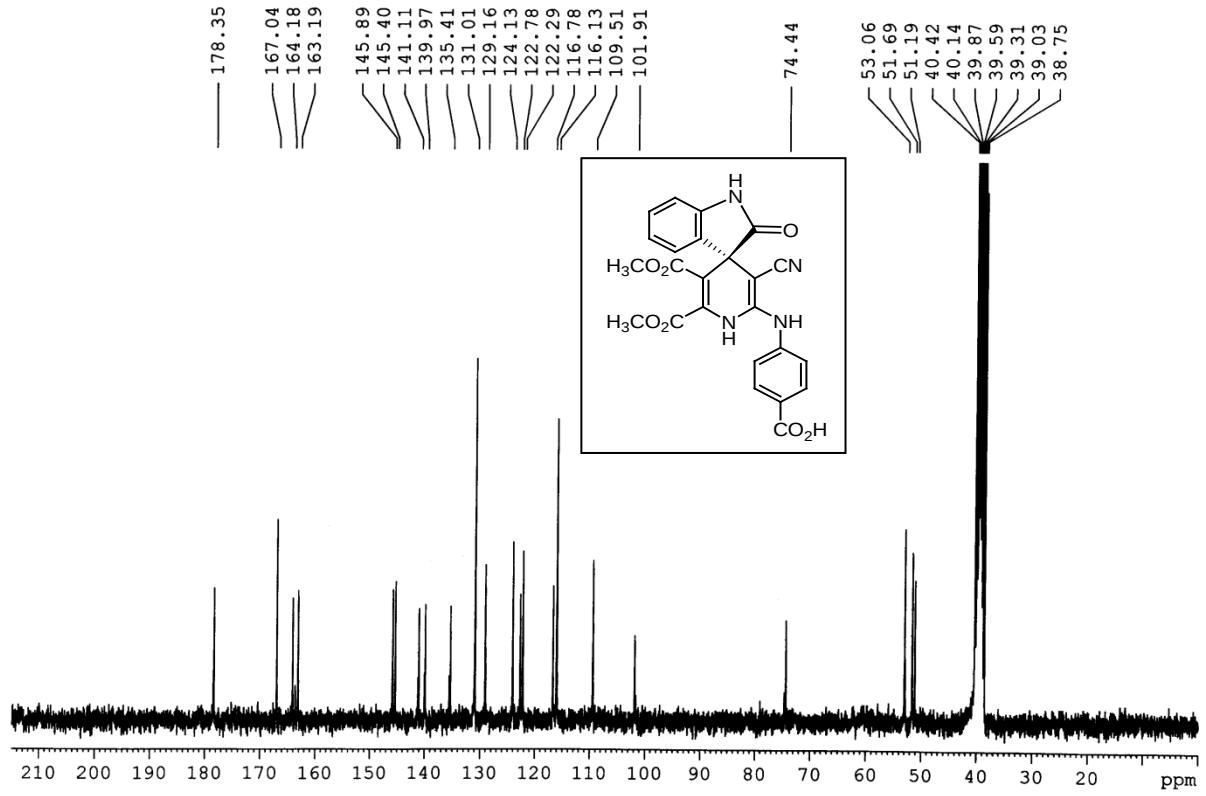
^{1}H NMR of compound **6i**



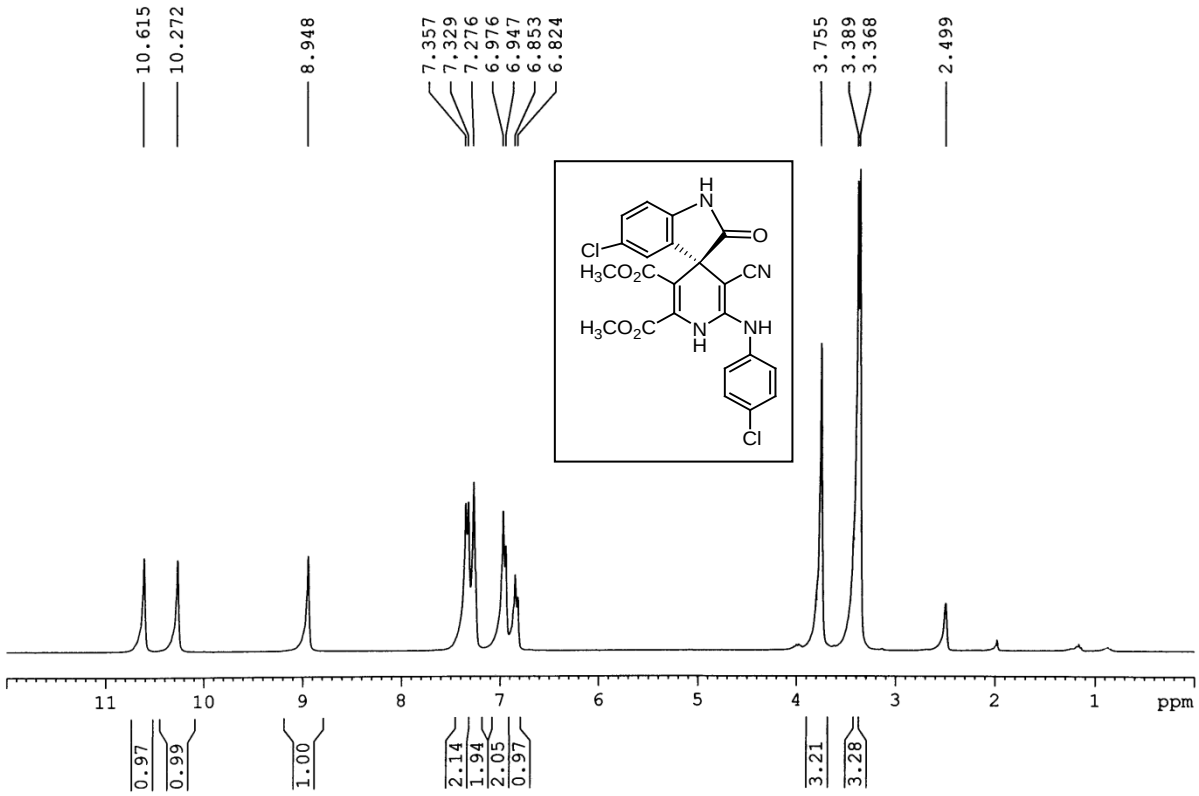
^{13}C NMR of compound **6i**



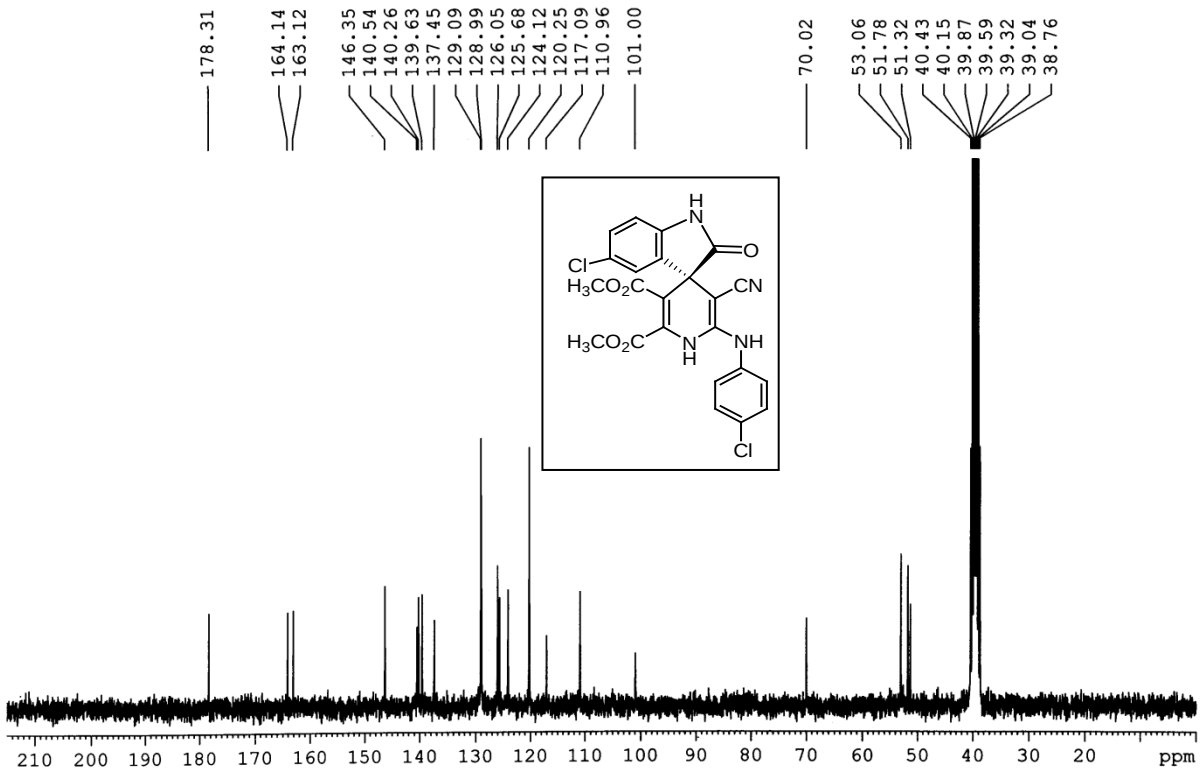
^{1}H NMR of compound **6j**



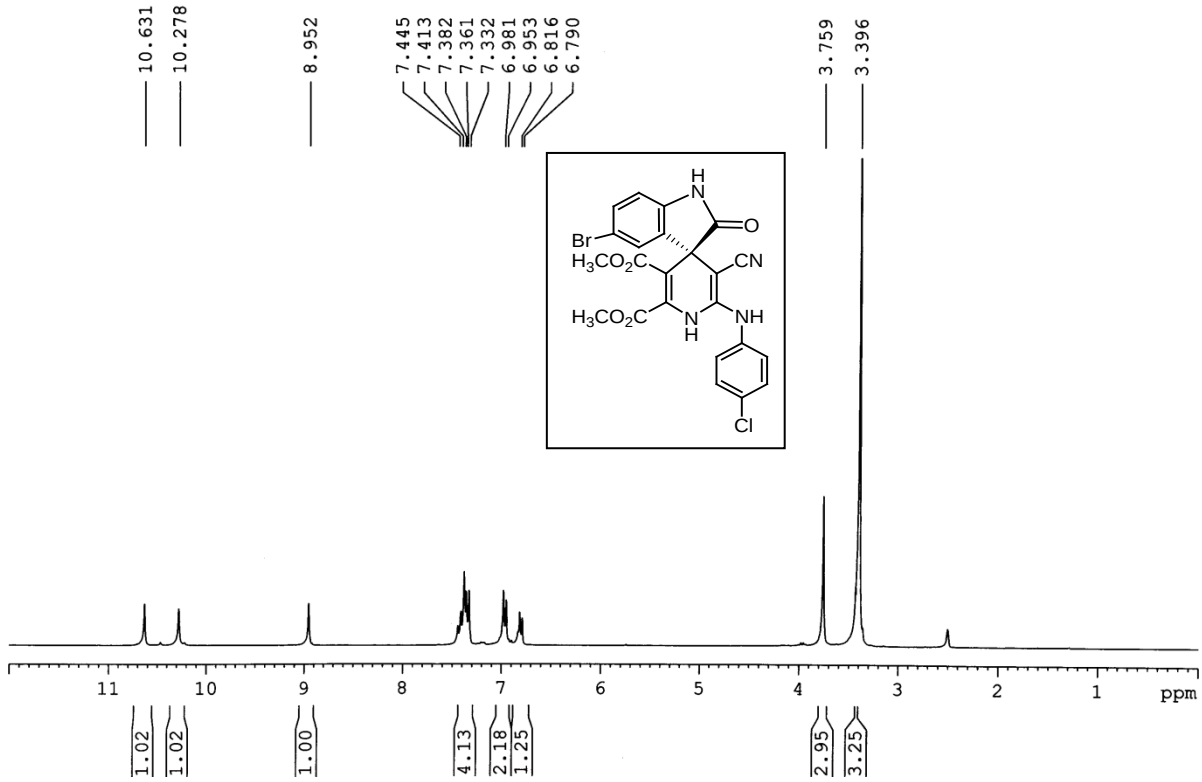
^{1}H NMR of compound **6j**



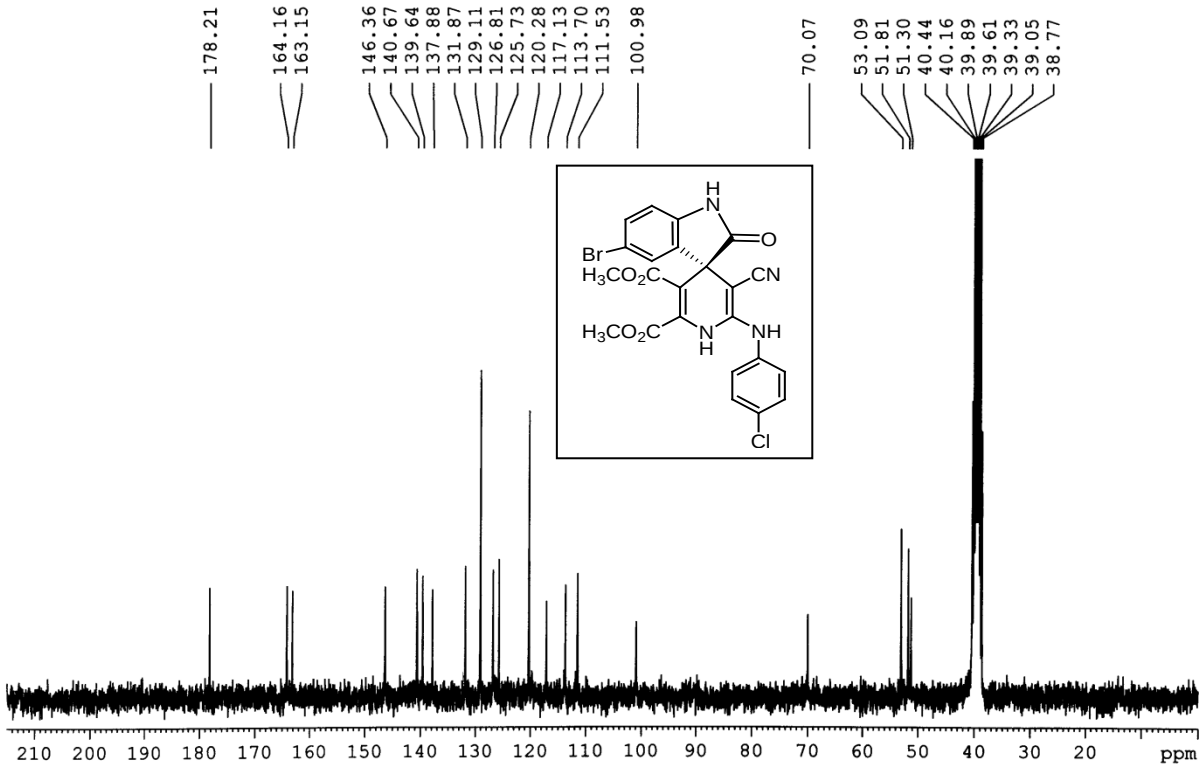
^{1}H NMR of compound **6k**



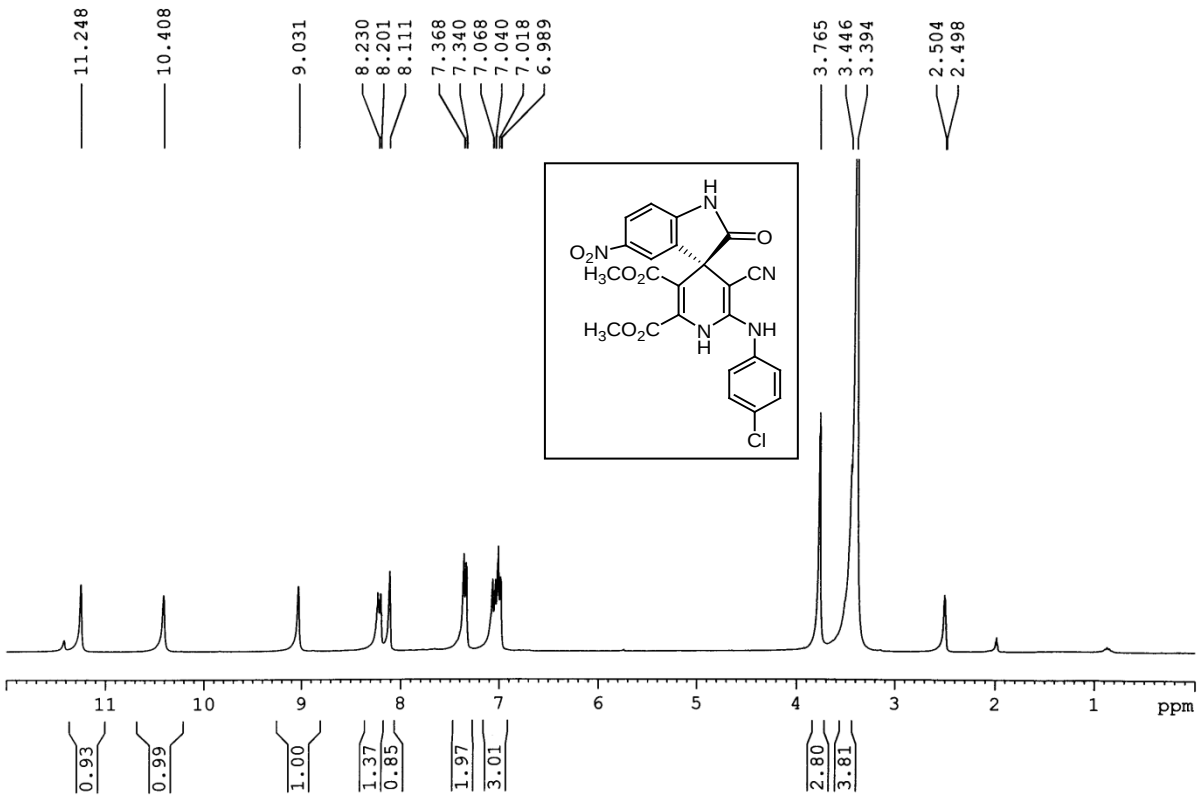
^{13}C NMR of compound **6k**



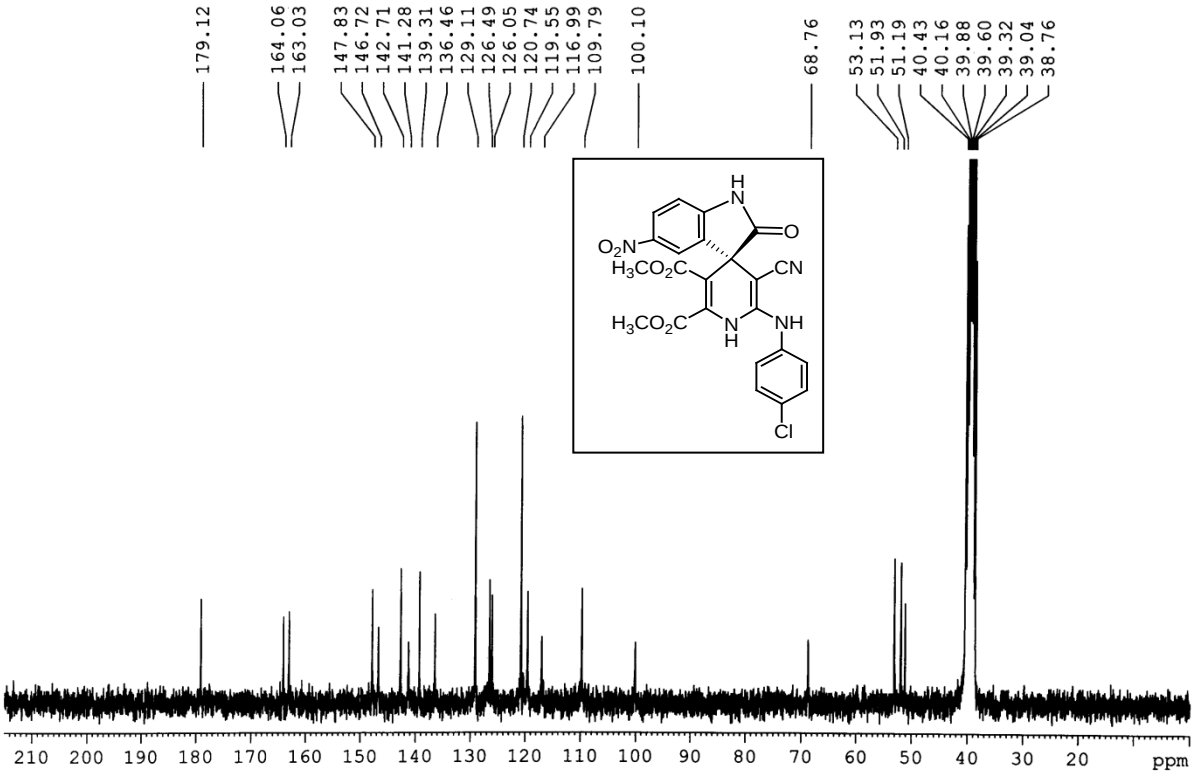
^{1}H NMR of compound **6l**



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



^{1}H NMR of compound **6m**



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