Supporting Information

A Novel One pot four-component reaction for the efficient synthesis of spiro[indoline-3,4'-pyrano[2,3-*c*]pyrazole]-3'-carboxylate and trifluoromethylated spiro[indole-3,4'-pyrano[2,3-*c*]pyrazole] derivatives using recyclable PEG-400

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Contents

General Information:

All chemical were purchased from Sigma Aldrich with purity not less than 99.9%. Analytical Thin Layer Chromatography (TLC) was carried out by using silica gel 60 F_{254} pre-coated plates. Visualization was accomplished with UV lamp of I_2 stain. All products were characterized by their NMR and Mass spectra.^{1}H NMR and ^{13}C NMR recorded on 300 or 500 MHz, in DMSO-d_6 and Acetone-d_6 using TMS as the internal standard, chemical shifts were reported in parts per million (ppm, δ) downfield from the tetramethylsilane.

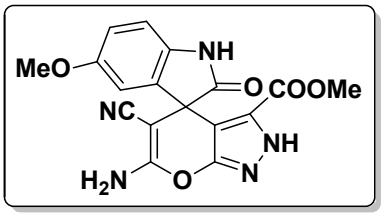
General procedure for the synthesis of spiro[indoline-3,4'-pyrano[2,3-*c*]pyrazole]-3'-carboxylate and trifluoromethylated spiro[indole-3,4'-pyrano[2,3-*c*]pyrazole] derivatives:

To a stirred solution of polyethylene glycol (PEG)-400 (5 mL), isatin (1.0 mmol), and malononitrile (1.0 mmol) were added and stirred at 100 - 110 °C for 20 min. Then a solution of hydrazine hydrate (1.0 mmol) and dialkyl acetylenedicrboxylate / ethyl 4,4,4-trifluoroacetoacetate (1.0 mmol) in PEG-400 was added to it. The whole reaction mixture was stirred until the reaction was complete as indicated by TLC. After completion of the reaction, ether (5mL) was added and stirred for a 5-10 mins and cooled to -50 ^{o} C. At this temperature PEG became solid and the ether layer saturated with product was separated and evaporated. The crude product was purified by column chromatography, using hexane and EtOAc as eluent to provide the title compound. The recovered PEG was reused for further cycles. For the NMR spectroscopic analysis the title compound was dissolved in the ratio of solvents Acetone-d_6 and DMSO-d_6 is 4:1.

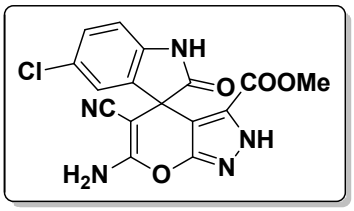
Crystal data collection and refinement: X-ray data for the compound were collected at room temperature using a Bruker Smart Apex CCD diffractometer with graphite monochromated Mo-Kα radiation (λ=0.71073Å) with ω-scan method.[1] Preliminary lattice parameters and orientation matrices were obtained from four sets of frames. Unit cell dimensions were determined using 4356 reflections. Integration and scaling of intensity data were accomplished using SAINT program.[1] The structures were solved by Direct Methods using SHELXS97[2] and refinement was carried out by full-matrix least-squares technique using SHELXL2014/7.[2] Anisotropic displacement parameters were included for all non-hydrogen atoms. All H atoms were positioned geometrically and treated as riding on their parent C atoms, with C-H distances of 0.93--0.97 Å, and with U_{iso}(H) = 1.2U_{eq} (C) or 1.5U_{eq} for methyl atoms. The bromine atom on the phenyl ring was disordered over two sites with equal site occupancy (i.e. 50% each for Br1 and Br1D, respectively). The C24, C25 and O5 atoms of acetone solvent were also disordered over two sites, with the major component refining to 74% site occupancy (C24/C25/O5) and minor component to 26% site occupancy (C24D/C25D/O5D). PART and FVAR instructions were used for disorder treatment. The anisotropic displacement parameters of the disordered atoms were restrained to be similar (SIMU instruction) and the direction of motion along the axis between these atoms was also restrained (DELU instruction).[3] Similar treatment was employed for disordered bromine atoms on the phenyl ring. The bond distances of disordered atoms were restrained, where distances C12-Br1, C23-O5, C23-C24 and C23-C25 were set to expected values of 1.89, 1.20, 1.50 and 1.50Å, respectively.

1. SMART & SAINT. Software Reference manuals. Versions 6.28a & 5.625, Bruker Analytical X-ray Systems Inc., Madison, Wisconsin, U.S.A., 2001.
2. Sheldrick, G. M. SHELXS97 and SHELXL Version 2014/7, http://shelx.uni-ac.gwdg.de/SHELX/index.php
3. Muller, P, Herbst-Imer, R, Spek, A. L, Schneider, T. R, and Sawaya, M. R. Crystal Structure Refinement: A Crystallographer's Guide to SHELXL. Muller, P. Ed. 2006 Oxford University Press: Oxford, New York, pp. 57–91.

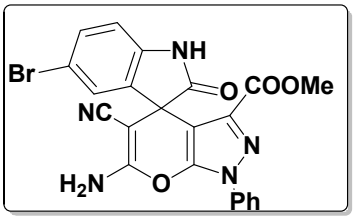
Spectroscopic Data:



Methyl 6'-amino-5'-cyano-5-methoxy-2-oxo-2'H-spiro[indoline-3,4'-pyrano[2,3-c]pyrazole]-3'-carboxylate (Table 1, Entry 1): IR (KBr) 3445, 3275, 3185, 2933, 2192, 1710, 1635, 1494, 1222, 1089 cm^{-1}; ^1H NMR (300 MHz, Acetone-d_6+DMSO-d_6) δ 9.83 (s, 1H), 6.89 (d, *J* = 8.4 Hz, 1H), 6.80-6.76 (m, 1H), 6.74 – 6.70 (m, 1H), 6.67 (s, 2H), 3.69 (s, 3H), 3.52 (s, 3H) ppm. ^{13}C NMR (75 MHz, Acetone-d_6+DMSO-d_6) δ 177.3, 161.3, 158.0, 155.9, 135.8, 135.3, 129.2, 128.7, 117.5, 113.4, 110.6, 109.7, 101.1, 58.7, 55.0, 51.0, 48.3 ppm. ESI-MS: 368 $(M+H)^{+;}$ $C_{17}H_{14}N_5O_5$.

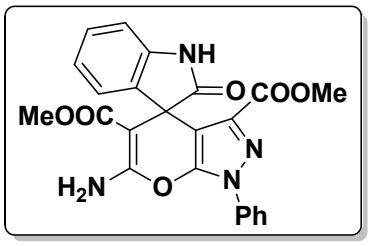


Methyl 6'-amino-5-chloro-5'-cyano-2-oxo-2'H-spiro[indoline-3,4'-pyrano[2,3-c]pyrazole]-3'-carboxylate (Table 1, Entry 2): IR (KBr) 3442, 3275, 3180, 2933, 2185, 1710, 1622, 1494, 1222, 1089 cm^{-1}; ^1H NMR (300 MHz, Acetone-d_6+DMSO-d_6) δ 10.60 (s, 1H), 7.26-7.23 (m, 1H), 7.10-7.14 (m, 3H), 6.97 (d, *J* = 8.3 Hz, 1H), 3.55 (s, 3H) ppm. ^{13}C NMR (75 MHz, Acetone-d_6+DMSO-d_6) δ 177.2, 161.2, 157.9, 156.3, 141.5, 136.1, 128.9, 128.4, 126.3, 124.1, 117.6, 110.7, 100.3, 57.1, 51.2, 48.0 ppm. ESI-MS: 372 $(M+H)^{+;}$ $C_{16}H_{11}ClN_5O_4$.

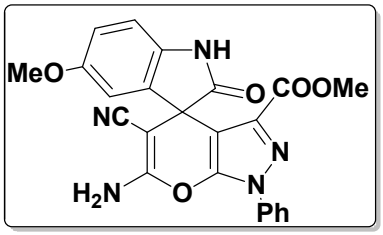


Methyl 6'-amino-5-bromo-5'-cyano-2-oxo-1'-phenyl-1'H-spiro[indoline-3,4'-pyrano[2,3-c]pyrazole]-3'-carboxylate (Table 1, Entry 3): IR (KBr) 3444, 3273, 3180, 2930, 2182, 1715, 1622, 1494, 1220, 1085 cm^{-1}; ^1H NMR (300 MHz, Acetone-

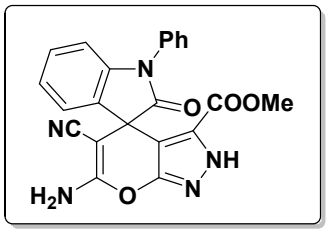
d_6+DMSO-d_6) δ 10.34 (s, 1H), 7.89 (d, *J* = 8.1 Hz, 2H), 7.64 (t, *J* = 8.1 Hz, 1H), 7.34 (t, *J* = 7.5 Hz, 1H), 7.19-7.16 (m, 3H), 7.10 (d, *J* = 7.1 Hz, 1H), 6.98-6.92 (m, 2H), 3.48 (s, 3H) ppm. ^{13}C NMR (75 MHz, Acetone-d_6+DMSO-d_6) δ 177.8, 160.6, 159.0, 142.4, 138.3, 137.5, 134.0, 129.5, 128.7, 128.1, 125.4, 124.0, 122.4, 122.0, 121.8, 117.2, 109.5, 59.2, 51.0, 48.5 ppm. ESI-MS: 492 $(M+H)^{+;}$ $C_{22}H_{15}BrN_5O_4$.



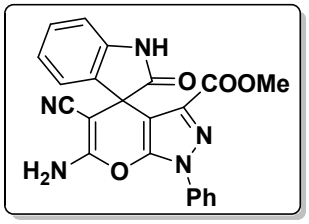
Dimethyl 6'-amino-2-oxo-1'-phenyl-1'H-spiro[indoline-3,4'-pyrano[2,3-c]pyrazole]-3',5'-dicarboxylate (Table 1, Entry 4): IR (KBr) 3442, 3275, 3180, 2935, 2185, 1715, 1622, 1494, 1222, 1089 cm^{-1}; ^{1}H NMR (300 MHz, Acetone-d_6+DMSO-d_6) δ 10.10 (s, 1H), 8.10 (s, 2H), 7.94 (d, *J* = 7.9 Hz, 2H), 7.59 (t, *J* = 7.9 Hz, 2H), 7.47 (t, *J* = 7.3 Hz, 1H), 7.12 (t, *J* = 7.5 Hz, 1H), 6.96 (d, *J* = 7.1 Hz, 1H), 6.89 (d, *J* = 7.7 Hz, 1H), 6.81 (t, *J* = 7.5 Hz, 1H), 3.55 (s, 3H), 3.34 (s, 3H).ppm. ^{13}C NMR (75 MHz, Acetone-d_6+DMSO-d_6) δ 176.4, 161.6, 158.7, 144.4, 139.3, 138.6, 135.2, 130.2, 129.2, 128.0, 125.4, 123.8, 122.4, 121.8, 115.6, 108.4, 73.5, 58.6, 51.4, 46.3 ppm. ESI-MS: 447 $(M+H)^{+}$; $C_{23}H_{19}N_4O_6$.



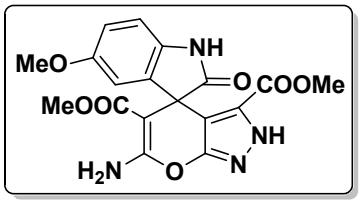
Methyl 6'-amino-5'-cyano-5-methoxy-2-oxo-1'-phenyl-1'H-spiro[indoline-3,4'-pyrano[2,3-c]pyrazole]-3'-carboxylate (Table 1, Entry 5): IR (KBr) 3440, 3278, 3180, 2933, 2185, 1710, 1622, 1494, 1222, 1089 cm^{-1}; ^{1}H NMR (300 MHz, Acetone-d_6+DMSO-d_6) δ 9.93 (s, 1H), 7.43 (m, 3H), 7.28 (m, 2H), 6.91 (d, *J* = 8.4 Hz, 1H), 6.82-6.79 (m, 1H), 6.74 – 6.70 (m, 1H), 6.64 (s, 2H), 3.71 (s, 3H), 3.52 (s, 3H) ppm. ^{13}C NMR (75 MHz, Acetone-d_6+DMSO-d_6) δ 177.2, 160.4, 159.9, 155.5, 146.3, 138.0, 137.0, 135.8, 135.0, 129.3, 127.9, 121.6, 117.1, 113.2, 110.7, 109.6, 99.1, 59.0, 55.0, 50.6, 48.6 ppm. ESI-MS: 444 $(M+H)^{+}$; $C_{23}H_{18}N_5O_5$.



Methyl 6'-amino-5'-cyano-2-oxo-1-phenyl-2'H-spiro[indoline-3,4'-pyrano[2,3-c]pyrazole]-3'-carboxylate (Table 1, Entry 6): IR (KBr) 3468, 3374, 3074, 2195, 1732, 1643, 1596, 1443, 1335, 1220, 1058 cm^{-1}; ^1H NMR (300 MHz, Acetone-d_6+DMSO-d_6) δ=10.08 (s, 1H), 7.62-7.59 (m, 2H), 7.51-7.49 (m, 3H), 7.30-7.28 (m, 1H), 7.17 (s, 2H), 7.07-7.04 (m, 2H), 6.90 (d, *J* = 7.8 Hz, 1H), 3.48 (s, 3H) ppm. ^{13}C NMR (75MHz, Acetone-d_6+DMSO-d_6) δ 177.2, 162.2, 158.1, 156.3, 143.4, 134.7, 133.0, 129.8, 129.4, 128.9, 128.3, 126.9, 124.2, 124.0, 118.4, 110.0, 100.5, 58.3, 52.0, 48.0 ppm. ESI-MS: 414 $(M+H)^+$; $C_{22}H_{16}N_5O_4$.

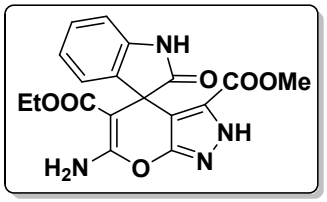


Methyl 6'-amino-5'-cyano-2-oxo-1'-phenyl-1'H-spiro[indoline-3,4'-pyrano[2,3-c]pyrazole]-3'-carboxylate (Table 1, Entry 7): IR (KBr) 3460, 3342, 2192, 1746, 1711, 1645, 1578, 1470, 1394, 1210, 1060 cm^{-1}; ^1H NMR (300 MHz, Acetone-d_6+DMSO-d_6) δ=10.38 (s, 1H), 7.94 (d, *J* = 8.1 Hz, 2H), 7.61 (t, *J* = 8.1 Hz, 2H), 7.48 (t, *J* = 7.5 Hz, 1H), 7.25-7.20 (m, 3H), 7.12 (d, *J* = 7.1 Hz, 1H), 6.98-6.92 (m, 2H), 3.50 (s, 3H) ppm. ^{13}C NMR (75 MHz, Acetone-d_6+DMSO-d_6) δ 177.3, 160.0, 160.4, 146.4, 142.6, 138.1, 137.1, 133.9, 129.4, 128.5, 128.0, 123.9, 121.9, 121.7, 117.0, 109.4, 59.4, 50.7, 48.2 ppm. ESI-MS: 414 $(M+H)^+$; $C_{22}H_{16}N_5O_4$

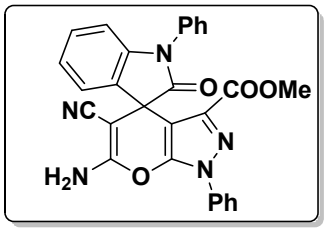


Dimethyl 6'-amino-5-methoxy-2-oxo-2'H-spiro[indoline-3,4'-pyrano[2,3-c]pyrazole]-3',5'-dicarboxylate (Table 1, Entry 8): IR (KBr) 3440, 3275, 3180,

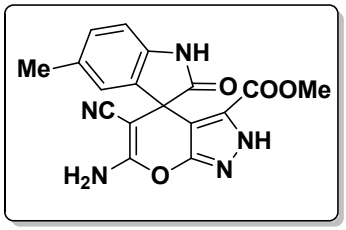
2935, 2185, 1710, 1630, 1494, 1222, 1089 cm^{-1}; ^1H NMR (300 MHz, Acetone-d_6+DMSO-d_6) δ 13.55 (s, 1H), 9.83 (s, 1H), 7.92 (s, 2H), 6.79 (d, *J* = 8.3 Hz, 1H), 6.69-6.65 (m, 1H), 6.53 – 6.52 (m, 1H), 3.63 (s, 3H), 3.58 (s, 3H), 3.32 (s, 3H) ppm. ^{13}C NMR (75 MHz, Acetone-d_6+DMSO-d_6) δ 170.5, 159.9, 153.4, 149.6, 146.6, 146.2, 129.1, 128.7, 122.7, 120.0, 103.2, 101.1, 99.8, 94.1, 58.7, 46.3, 42.5, 41.2 ppm. ESI-MS: 401 $(M+H)^+$; $C_{18}H_{17}N_4O_7$.



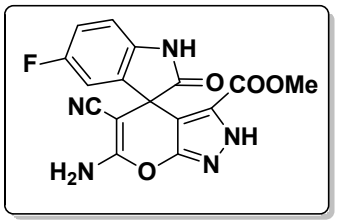
5'-Ethyl 3'-methyl 6'-amino-2-oxo-2'H-spiro[indoline-3,4'-pyrano[2,3-c]pyrazole]-3',5'-dicarboxylate (Table 1, Entry 9): IR (KBr) 3460, 3338, 2192, 1744, 1717, 1640, 1578, 1472, 1394, 1212, 1060 cm^{-1}; ^1H NMR (300 MHz, Acetone-d_6+DMSO-d_6) δ 13.50 (s, 1H), 10.23 (s, 1H) , 7.46 (s, 2H), 7.13-7.10 (m, 1H), 6.86-6.82 (m, 3H), 3.82 (q, *J* = 7.1 Hz, 2H), 3.50 (s, 3H), 0.82 (t, *J* = 7.1 Hz, 3H) ppm. ^{13}C NMR (75 MHz, Acetone-d_6+DMSO-d_6) δ 177.8, 168.4, 162.0, 159.0, 155.6, 143.2, 136.6, 129.0, 127.6, 123.3, 121.6, 108.9, 102.5, 74.8, 59.0, 50.8, 48.1, 12.8 ppm. ESI-MS: 385 $(M+H)^+$; $C_{18}H_{17}N_4O_6$.



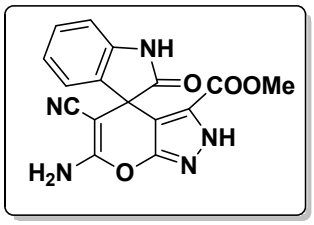
Methyl 6'-amino-5'-cyano-2-oxo-1,1'-diphenyl-1'H-spiro[indoline-3,4'-pyrano[2,3-c]pyrazole]-3'-carboxylate (Table 1, Entry 10): IR (KBr) 3445, 3246, 3110, 2930, 1708, 1647, 1223, 1090 cm^{-1}; ^1H NMR (300MHz, Acetone-d_6+DMSO-d_6) δ= 7.61-7.58 (m, 3H), 7.50-7.47 (m, 4H), 7.40-7.38 (m, 2H), 7.24-7.21 (m, 2H), 7.20 (s, 2H), 7.07-7.05 (m, 2H), 6.76 (d, *J* = 7.8 Hz, 1H), 3.50 (s, 3H) ppm. ^{13}C NMR (75MHz, Acetone-d_6+DMSO-d_6) δ 175.2, 160.7, 159.9, 146.5, 143.7, 137.7, 136.9, 134.8, 132.6, 131.2, 129.4, 128.7, 128.6, 128.0, 126.8, 124.1, 123.1, 121.7, 117.1, 108.6, 98.9, 58.6, 51.3, 47.8 ppm. ESI-MS: 490 $(M+H)^+$; $C_{29}H_{20}N_5O_4$.



Methyl 6'-amino-5'-cyano-5-methyl-2-oxo-2'H-spiro[indoline-3,4'-pyrano[2,3-c]pyrazole]-3'-carboxylate (Table 1, Entry 11): IR (KBr) 3440, 3320, 3176, 2960, 2214, 1734, 1710, 1610, 1490, 1222, 1061 cm^{-1}; ^1H NMR (300MHz, Acetone-d_6+DMSO-d_6) δ= 13.52 (s, 1H), 10.20 (s, 1H) , 7.24 (s, 2H), 7.19 (s, 1H), 6.98-6.96 (m, 1H), 6.90 (d, *J* = 8.3 Hz, 1H), 3.48 (s, 3H), 2.36 (s, 3H) ppm. ^{13}C NMR (75MHz, Acetone-d_6+DMSO-d_6) δ 177.7, 163.0, 161.8, 158.2, 156.2, 141.1, 135.9, 130.1, 127.0, 124.2, 118.4, 111.2, 102.0, 57.0, 51.9, 48.1, 21.0 ppm. ESI-MS: 352 $(M+H)^+$; $C_{17}H_{14}N_5O_4$.

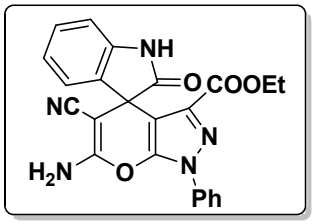


Methyl 6'-amino-5'-cyano-5-fluoro-2-oxo-2'H-spiro[indoline-3,4'-pyrano[2,3-c]pyrazole]-3'-carboxylate (Table 1, Entry 12): IR (KBr) 3445, 3240, 3111, 2928, 1699, 1645, 1219, 1085 cm^{-1}; ^1H NMR (300 MHz, Acetone-d_6+DMSO-d_6) δ 10.40 (s, 1H), 7.07-6.98 (m, 3H), 6.97-6.92 (m, 2H), 3.54 (s, 3H) ppm. ^{13}C NMR (75 MHz, Acetone-d_6+DMSO-d_6) δ 177.5, 161.5, 160.3, 157.9, 157.2, 156.4, 138.8, 135.7, 129.0, 117.6, 114.8, 114.5, 111.7, 111.3, 110.0, 109.9, 100.4, 57.4, 51.1, 48.2 ppm. ESI-MS: 356 $(M+H)^+$; $C_{16}H_{11}FN_5O_4$.

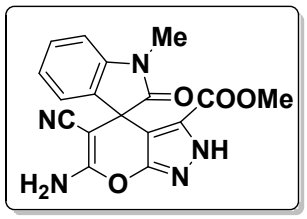


Methyl 6'-amino-5'-cyano-2-oxo-2'H-spiro[indoline-3,4'-pyrano[2,3-c]pyrazole]-3'-carboxylate (Table 1, Entry 13): IR (KBr) 3242, 3114, 2926, 1713, 1650, 1227, 1092 cm^{-1}; ^1H NMR (300MHz, Acetone-d_6+DMSO-d_6) δ= 13.51 (s, 1H), 10.52 (s, 1H) , 7.20-

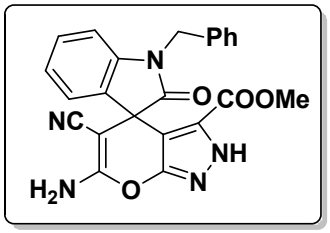
7.16 (m, 1H), 7.02 (s, 2H), 6.89-6.87 (m, 2H), 6.78 (d, *J* = 7.6 Hz, 1H), 3.50 (s, 3H) ppm. ^{13}C NMR (75MHz, Acetone-d_6+DMSO-d_6) δ 177.7, 161.0, 157.5, 155.9, 141.8, 134.0, 128.9, 128.1, 123.5, 121.9, 117.9, 109.2, 99.7, 57.1, 55.6, 47.4 ppm. ESI-MS: 338 $(M+H)^+$; $C_{16}H_{12}N_5O_4$.



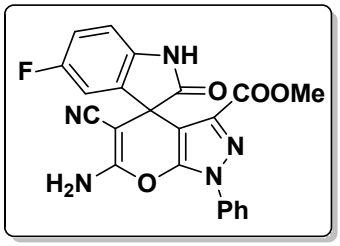
Ethyl 6'-amino-5'-cyano-2-oxo-1'-phenyl-1'H-spiro[indoline-3,4'-pyrano[2,3-c]pyrazole]-3'-carboxylate (Table 1, Entry 14): IR (KBr) 3310, 3245, 3108, 2932, 1709, 1651, 1222, 1091 cm^{-1}; ^{1}H NMR (300MHz, Acetone-d_6+DMSO-d_6) δ= 10.51 (s, 1H), 7.87 (d, *J* = 7.6 Hz, 2H), 7.58-7.54 (m, 2H), 7.45 (t, *J* = 7.4 Hz, 1H), 7.35 (s, 2H), 7.20 (t, *J* = 7.6 Hz, 1H), 7.03 (d, *J* = 7.0 Hz, 1H), 6.93-6.90 (m, 2H), 3.97 (q, *J* = 7.0 Hz, 2H), 1.01 (t, *J* = 7.0 Hz, 3H) ppm. ^{13}C NMR (75MHz, Acetone-d_6+DMSO-d_6) δ 177.5, 159.8, 159.7, 146.0, 142.0, 138.0, 136.5, 133.6, 129.2, 128.4, 127.9, 123.6, 121.8, 121.6, 117.3, 109.3, 98.3, 60.2, 58.2, 47.9, 13.6 ppm. ESI-MS: 428 $(M+H)^+$; $C_{23}H_{18}N_5O_4$.



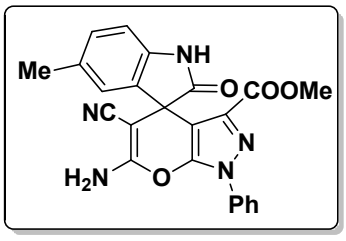
Methyl 6'-amino-5'-cyano-1-methyl-2-oxo-2'H-spiro[indoline-3,4'-pyrano[2,3-c]pyrazole]-3'-carboxylate (Table 1, Entry 15): IR (KBr) 3240, 3114, 2930, 1715, 1650, 1222, 1092 cm^{-1}; ^{1}H NMR (300MHz, Acetone-d_6+DMSO-d_6) δ= 13.50 (s, 1H), 7.25-7.20 (m, 1H), 7.05 (s, 2H), 6.94-6.89 (m, 2H), 6.76 (d, *J* = 7.6 Hz, 1H), 3.50 (s, 3H) 3.36 (s, 3H) ppm. ^{13}C NMR (75MHz, Acetone-d_6+DMSO-d_6) δ 177.6, 161.0, 156.8, 156.0, 141.8, 134.2, 128.9, 127.5, 123.5, 122.2, 117.9, 110.0, 99.7, 62.0, 57.1, 55.8, 47.4 ppm. ESI-MS: 352 $(M+H)^+$; $C_{17}H_{14}N_5O_4$.



Methyl 6'-amino-1-benzyl-5'-cyano-2-oxo-2'H-spiro[indoline-3,4'-pyrano[2,3-c]pyrazole]-3'-carboxylate (Table 1, Entry 16): IR (KBr) 3243, 3112, 2926, 1710, 1651, 1227, 1090 cm^{-1}; ^1H NMR (300MHz, Acetone-d_6+DMSO-d_6) δ= 7.58 (d, *J* = 7.1 Hz, 2H), 7.37-7.28 (m, 3H), 7.21 (t, *J* = 7.5 Hz, 1H), 7.11 (d, *J* = 6.6 Hz, 1H), 7.03-6.89 (m, 4H), 5.22 (d, *J* = 15.8 Hz, 1H), 4.86 (d, *J* = 15.8 Hz, 1H), 3.32 (s, 3H) ppm. ^{13}C NMR (75MHz, Acetone-d_6+DMSO-d_6) δ 177.7, 163.0, 159.3, 144.6, 137.7, 134.7, 130.0, 129.9, 129.0, 128.7, 125.1, 124.3, 119.5, 110.2, 58.4, 52.9, 48.8, 45.1 ppm. ESI-MS: 428 $(M+H)^+$; $C_{23}H_{18}N_5O_4$.

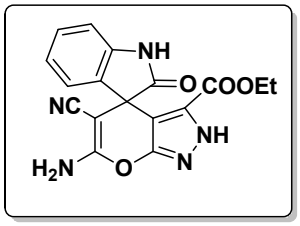


Methyl 6'-amino-5'-cyano-5-fluoro-2-oxo-1'-phenyl-1'H-spiro[indoline-3,4'-pyrano[2,3-c]pyrazole]-3'-carboxylate (Table 1, Entry 17): IR (KBr) 3241, 3113, 2924, 1709, 1652, 1227, 1085 cm^{-1}; ^1H NMR (300MHz, Acetone-d_6) δ= 9.66 (s, 1H), 7.91 (d, *J* = 8.1 Hz, 2H), 7.58 (t, *J* = 8.1 Hz, 2H), 7.51-7.45 (m, 1H), 7.09-7.00 (m, 3H), 6.88 (s, 2H), 3.55 (s, 3H) ppm. ^{13}C NMR (75MHz, Acetone-d_6) δ 179.0, 161.9, 162.4, 159.2, 148.2, 140.2, 139.9, 138.8, 131.1, 129.9, 123.6, 118.3, 116.9, 116.6, 113.8, 113.5, 100.4, 73.0, 61.4, 52.5 ppm. ESI-MS: 432 $(M+H)^+$; $C_{22}H_{15}FN_5O_4$.

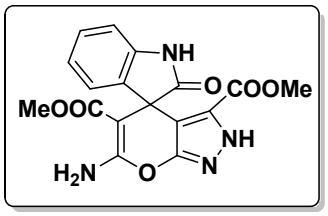


Methyl 6'-amino-5'-cyano-5-methyl-2-oxo-1'-phenyl-1'H-spiro[indoline-3,4'-pyrano[2,3-c]pyrazole]-3'-carboxylate (Table 1, Entry 18): IR (KBr) 3241, 3113,

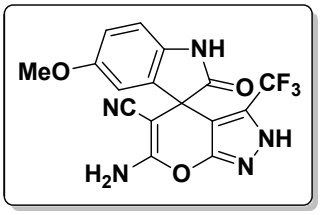
2924, 1709, 1652, 1227, 1085 cm^{-1}; ^1H NMR (300MHz, Acetone-d_6) δ= 10.27 (s, 1H), 7.02 (d, *J* = 7.5 Hz, 2H), 6.95 (s, 3H), 6.85-6.81 (m, 3H), 3.51 (s, 3H), 2.21 (s, 3H) ppm. ^{13}C NMR (75MHz, Acetone-d_6) δ 177.1, 161.2, 158.0, 156.4, 140.1, 138.4, 137.0, 134.7, 130.2, 128.5, 122.2, 117.8, 115.8, 114.6, 112.0, 109.5, 98.6, 71.5, 59.7, 51.2, 29.6 ppm. ESI-MS: 428 $(M+H)^+$; $C_{23}H_{18}N_5O_4$.



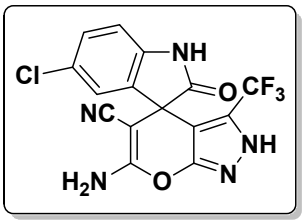
Ethyl 6'-amino-5'-cyano-2-oxo-2'H-spiro[indoline-3,4'-pyrano[2,3-c]pyrazole]-3'-carboxylate (Table 1, Entry 19): IR (KBr) 3310, 3245, 3108, 2932, 1709, 1651, 1222, 1091 cm^{-1}; ^1H NMR (300MHz, Acetone-d_6+DMSO-d_6) δ= 13.57 (s, 1H), 10.39 (s, 1H), 7.20 (t, *J* = 7.5 Hz, 1H), 6.99-6.91 (m, 3H), 6.87 (s, 2H), 3.99 (q, *J* = 7.1 Hz, 2H), 0.99 (t, *J* = 7.1 Hz, 3H) ppm. ^{13}C NMR (75MHz, Acetone-d_6+DMSO-d_6) δ 177.5, 160.2, 159.7, 146.0, 142.0, 136.5, 128.6, 126.5, 123.6, 121.8, 120.8, 117.3, 109.8, 98.6, 60.2, 58.7, 47.9, 13.6 ppm. ESI-MS: 352 $(M+H)^+$; $C_{17}H_{14}N_5O_4$.



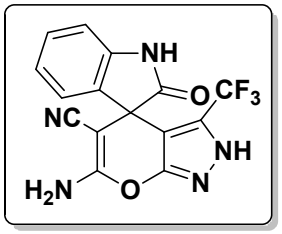
Dimethyl 6'-amino-2-oxo-2'H-spiro[indoline-3,4'-pyrano[2,3-c]pyrazole]-3',5'-dicarboxylate (Table 1, Entry 20): IR (KBr) 3242, 3112, 2928, 1715, 1650, 1222, 1092 cm^{-1}; ^1H NMR (300MHz, Acetone-d_6+DMSO-d_6) δ= 13.51 (s, 1H), 10.50 (s, 1H) , 7.24-7.19 (m, 1H), 7.12 (s, 2H), 6.92-6.89 (m, 2H), 6.80 (d, *J* = 7.6 Hz, 1H), 3.50 (s, 3H) 3.32 (s, 3H) ppm. ^{13}C NMR (75MHz, Acetone-d_6+DMSO-d_6) δ 177.7, 161.0, 157.5, 156.0, 141.6, 134.0, 129.2, 128.1, 123.5, 121.9, 109.2, 99.7, 94.1, 57.1, 55.6, 51.2, 47.4 ppm. ESI-MS: 371 $(M+H)^+$; $C_{17}H_{15}N_4O_6$.



6'-Amino-5-methoxy-2-oxo-3'-(trifluoromethyl)-2'H-spiro[indoline-3,4'-pyrano[2,3-c]pyrazole]-5'-carbonitrile (Table 2, Entry 1): IR (KBr) 3470, 3311, 3175, 3105, 2205, 1711, 1648, 1501, 1402, 1336, 1146, 1018 cm^{-1}. ^{1}H NMR (300 MHz, acetone-d_6) δ= 9.51 (s, 1H), 6.94-6.83 (m, 3H), 6.66 (s, 2H), 3.72 (s, 3H) ppm. ^{13}C NMR (75 MHz, acetone-d_6): δ 49.6, 56.9, 60.6, 112.1, 113.2, 116.3, 118.6, 123.2, 130.5, 135.6, 136.7, 136.8, 158.1, 163.0, 178.7 ppm. ESI-MS: 378 $(M+H)^{+}$; $C_{16}H_{11}F_3N_5O_3$.

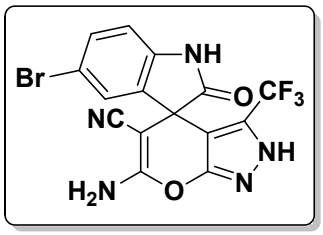


6'-Amino-5-chloro-2-oxo-3'-(trifluoromethyl)-2'H-spiro[indoline-3,4'-pyrano[2,3-c]pyrazole]-5'-carbonitrile (Table 2, Entry 2): IR (KBr) 3472, 3313, 3175, 3100, 2210, 1715, 1645, 1501, 1405, 1333, 1146, 1016 cm^{-1}. ^{1}H NMR (300 MHz, acetone-d_6) δ= 9.84 (s, 1H), 7.54-7.50 (m, 2H), 7.05-7.00 (m, 1H), 6.82 (s, 2H) ppm. ^{13}C NMR (75 MHz, acetone-d_6): δ 50.2, 59.8, 112.7, 113.3, 114.6, 115.0, 117.2, 117.9, 118.7, 136.0, 136.4, 140.5, 160.0, 162.8, 163.4, 177.9 ppm. ESI-MS: 382 $(M+H)^{+}$; $C_{15}H_8ClF_3N_5O_2$.

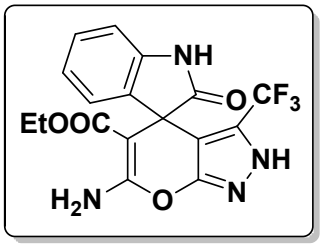


6'-Amino-2-oxo-3'-(trifluoromethyl)-2'H-spiro[indoline-3,4'-pyrano[2,3-c]pyrazole]-5'-carbonitrile (Table 2, Entry 3): IR (KBr) 3470, 3310, 3175, 3104, 2205, 1712, 1650, 1504, 1402, 1332, 1142, 1018 cm^{-1}. ^{1}H NMR (300 MHz, acetone-d_6) δ= 13.23 (s, 1H), 9.65 (s, 1H), 7.28 (t, J = 7.7 Hz, 1H), 7.20 (d, J = 7.1 Hz, 1H), 7.07-6.96 (m, 4H), 6.67 (s, 2H) ppm. ^{13}C NMR (75 MHz, acetone-d_6): δ 49.8, 59.8, 112.0, 114.9, 117.5, 122.7,

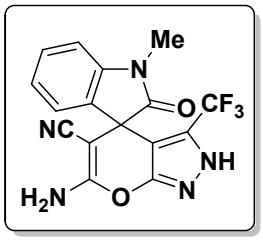
123.8, 126.0, 129.8, 136.0, 142.8, 159.2, 162.4, 163.1, 178.5 ppm. ESI-MS: 348 $(M+H)^+$; $C_{15}H_9F_3N_5O_2$.



6'-Amino-5-bromo-2-oxo-3'-(trifluoromethyl)-2'H-spiro[indoline-3,4'-pyrano[2,3-c]pyrazole]-5'-carbonitrile (Table 2, Entry 4): IR (KBr) 3472, 3311, 3170, 3105, 2210, 1711, 1652, 1496, 1402, 1332, 1146, 1016 cm^{-1}. ^1H NMR (300 MHz, acetone-d_6) δ= 9.81 (s, 1H), 7.50-7.45 (m, 2H), 7.01-6.96 (m, 1H), 6.77 (s, 2H) ppm. ^{13}C NMR (75 MHz, acetone-d_6): δ 49.8, 59.8, 112.5, 113.0, 114.6, 114.8, 117.2, 118.0, 118.7, 136.0, 136.2, 140.2, 159.4, 162.8, 163.1, 178.6 ppm. ESI-MS: 425 $(M+H)^+$; $C_{15}H_8BrF_3N_5O_2$.

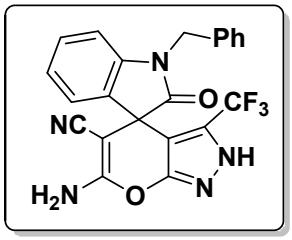


Ethyl 6'-amino-2-oxo-3'-(trifluoromethyl)-2'H-spiro[indoline-3,4'-pyrano[2,3-c]pyrazole]-5'-carboxylate (Table 2, Entry 5): IR (KBr) 3468, 3310, 2192, 1717, 1650, 1472, 1334, 1148, 1060 cm^{-1}; ^1H NMR (300 MHz, Acetone-d_6) δ 13.50 (s, 1H), 10.03 (s, 1H) , 7.50 (s, 2H), 7.18-7.15 (m, 1H), 6.90-6.86 (m, 3H), 3.80 (q, J = 7.1 Hz, 2H), 0.90 (t, J = 7.1 Hz, 3H) ppm. ^{13}C NMR (75 MHz, Acetone-d_6) δ 176.5, 162.5, 160.2, 155.8, 142.9, 136.6, 128.4, 127.4, 123.3, 121.8, 109.6, 75.2, 58.9, 48.2, 12.6 ppm. ESI-MS: 395 $(M+H)^+$; $C_{17}H_{14}F_3N_4O_4$.

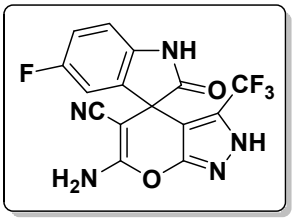


6'-Amino-1-methyl-2-oxo-3'-(trifluoromethyl)-2'H-spiro[indoline-3,4'-pyrano[2,3-c]pyrazole]-5'-carbonitrile (Table 2, Entry 6): IR (KBr) 3470, 3310, 3175, 3104, 2210,

1712, 1650, 1504, 1402, 1332, 1142, 1018 cm^{-1}; ^1H NMR (300MHz, Acetone-d_6) δ= 13.48 (s, 1H), 7.27-7.22 (m, 1H), 7.08 (s, 2H), 7.02-6.98 (m, 2H), 6.76 (d, *J* = 7.6 Hz, 1H), 3.38 (s, 3H) ppm. ^{13}C NMR (75MHz, Acetone-d_6) δ 177.4, 157.8, 156.4, 141.8, 135.0, 128.9, 128.0, 123.2, 122.0, 117.9, 112.2, 109.7, 57.5, 54.6, 42.4 ppm. ESI-MS: 362 $(M+H)^+$; $C_{16}H_{11}F_3N_5O_2$.



6'-Amino-1-benzyl-2-oxo-3'-(trifluoromethyl)-2'H-spiro[indoline-3,4'-pyrano[2,3-c]pyrazole]-5'-carbonitrile (Table 2, Entry 7)*[1]*: IR (KBr) 3470, 3313, 3175, 3098, 2212, 1715, 1645, 1502, 1405, 1333, 1148, 1010 cm^{-1}; ^1H NMR (300MHz, Acetone-d_6) δ= 7.60 (d, *J* = 7.1 Hz, 2H), 7.42-7.35 (m, 3H), 7.28 (t, *J* = 7.5 Hz, 1H), 7.18 (d, *J* = 6.6 Hz, 1H), 7.10-7.05 (m, 4H), 5.12 (d, *J* = 15.8 Hz, 1H), 5.08 (d, *J* = 15.8 Hz, 1H) ppm. ^{13}C NMR (75MHz, Acetone-d_6) δ 177.7, 163.5, 160.5, 144.6, 137.5, 134.2, 130.0, 129.8, 129.2, 128.7, 125.1, 124.8, 119.2, 110.2, 58.8, 52.9, 45.7 ppm. ESI-MS: 438 $(M+H)^+$; $C_{22}H_{15}F_3N_5O_2$.



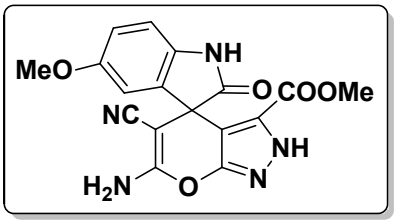
6'-Amino-5-fluoro-2-oxo-3'-(trifluoromethyl)-2'H-spiro[indoline-3,4'-pyrano[2,3-c]pyrazole]-5'-carbonitrile (Table 2, Entry 8): IR (KBr) 3470, 3313, 3172, 3108, 2205, 1715, 1648, 1502, 1405, 1336, 1148, 1018 cm^{-1}. ^1H NMR (300 MHz, acetone-d_6) δ= 13.35 (s, 1H), 9.74 (s, 1H), 7.16-6.99 (m, 3H), 6.76 (s, 2H) ppm. ^{13}C NMR (75 MHz, acetone-d_6): δ 49.6, 59.8, 112.6, 112.7, 114.2, 114.5, 117.4, 117.7, 118.5, 136.0, 136.1, 139.7, 159.4, 162.6, 163.1, 178.9 ppm. ESI-MS: 366 $(M+H)^+$; $C_{15}H_8F_4N_5O_2$.

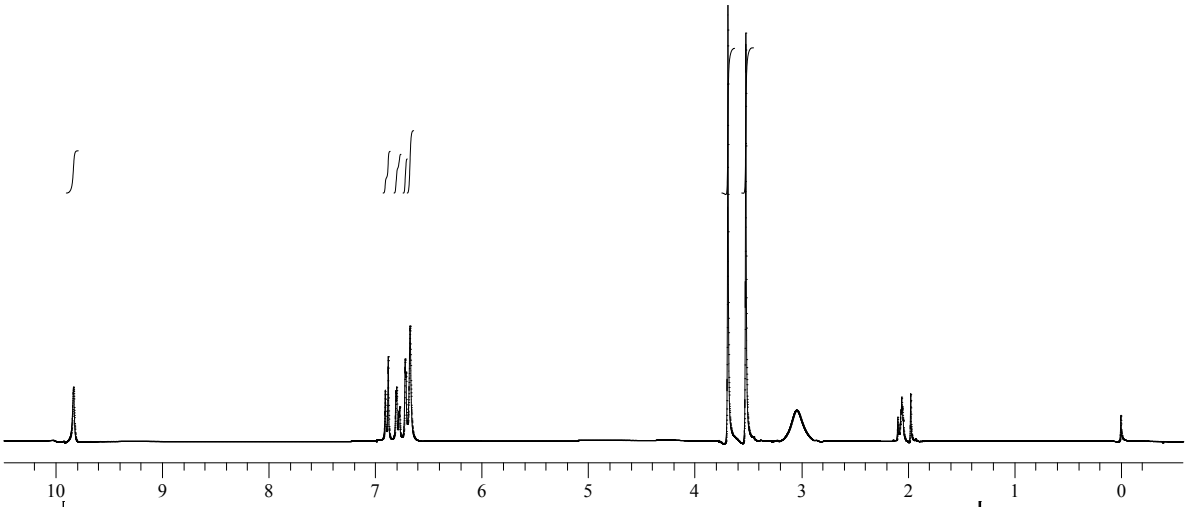
Reference:

1. MolPort-000-925-373.

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

Table 1, Entry 1





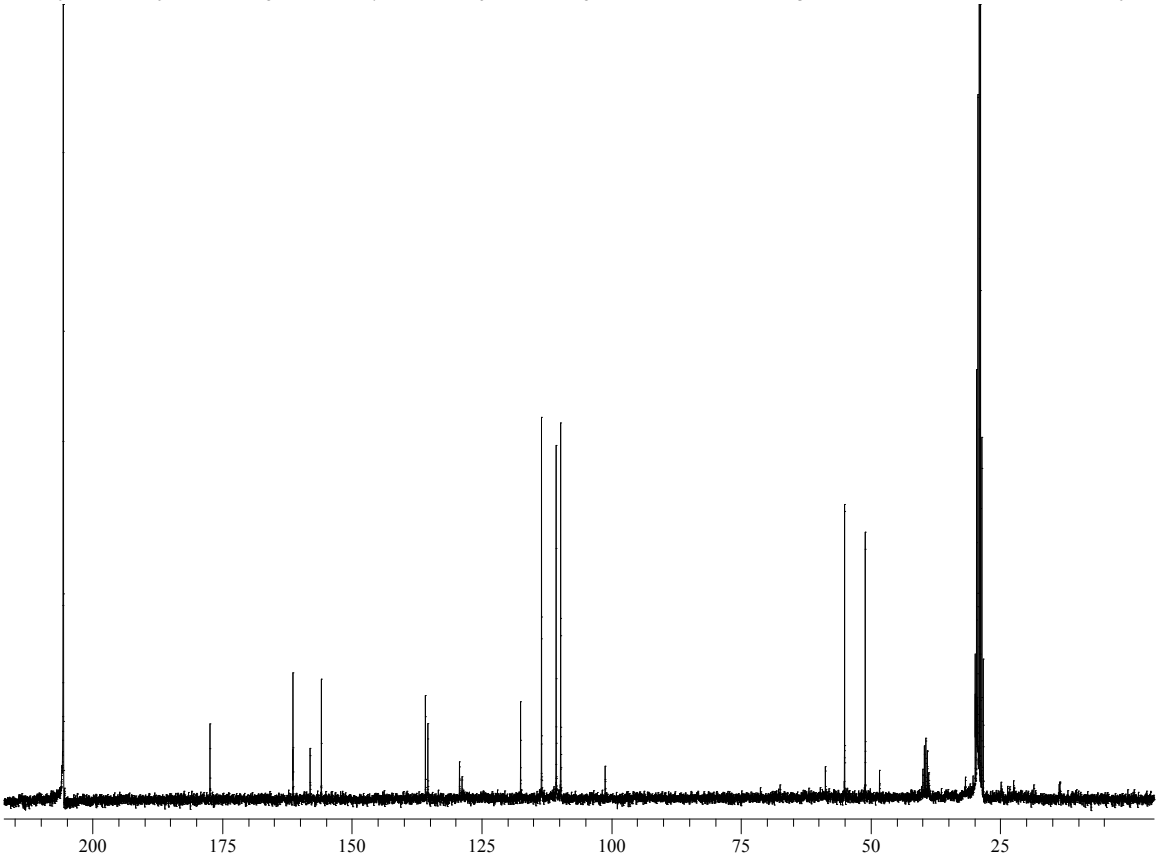


Table 1, Entry 2

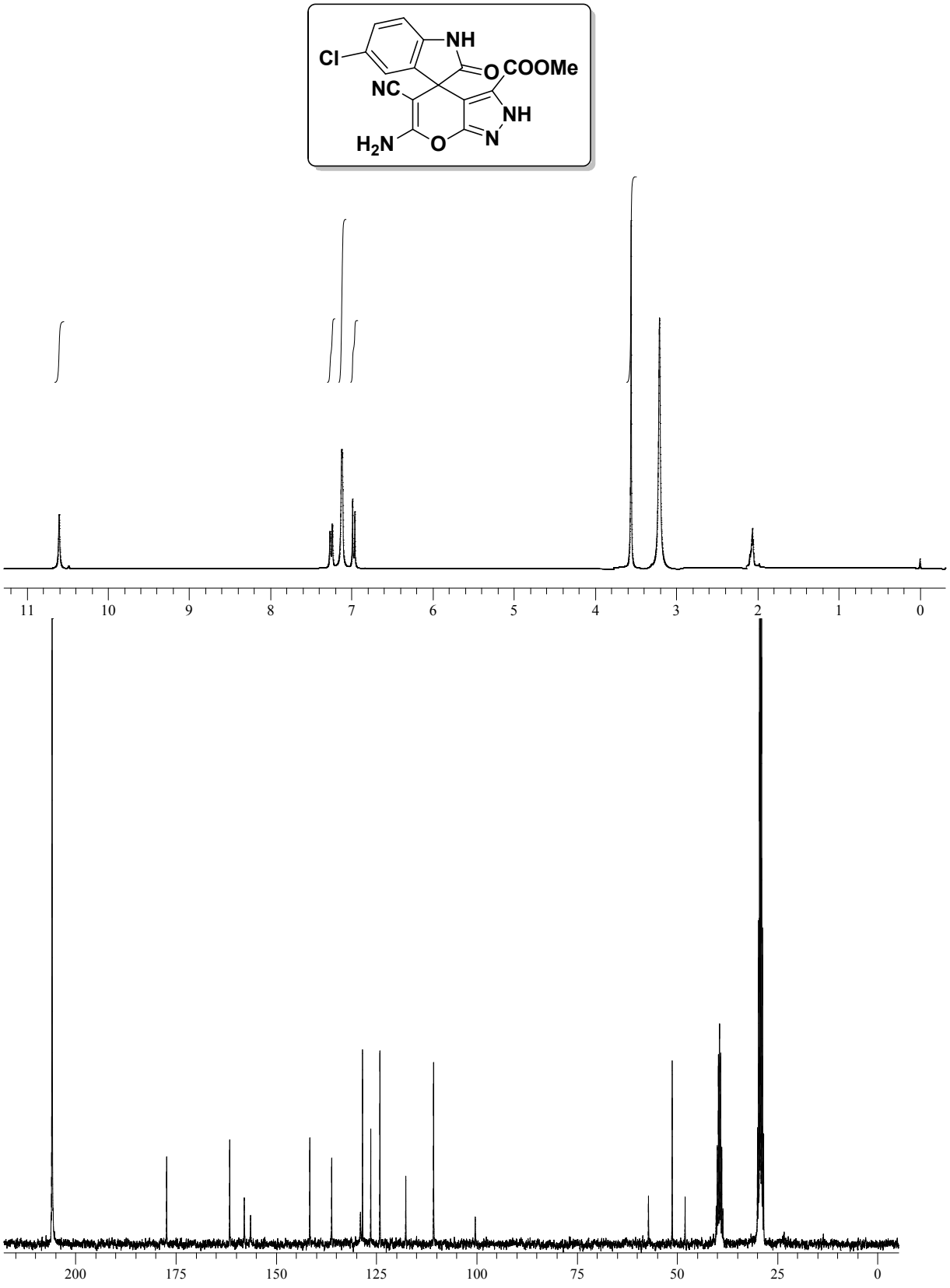
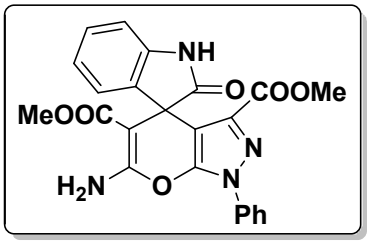
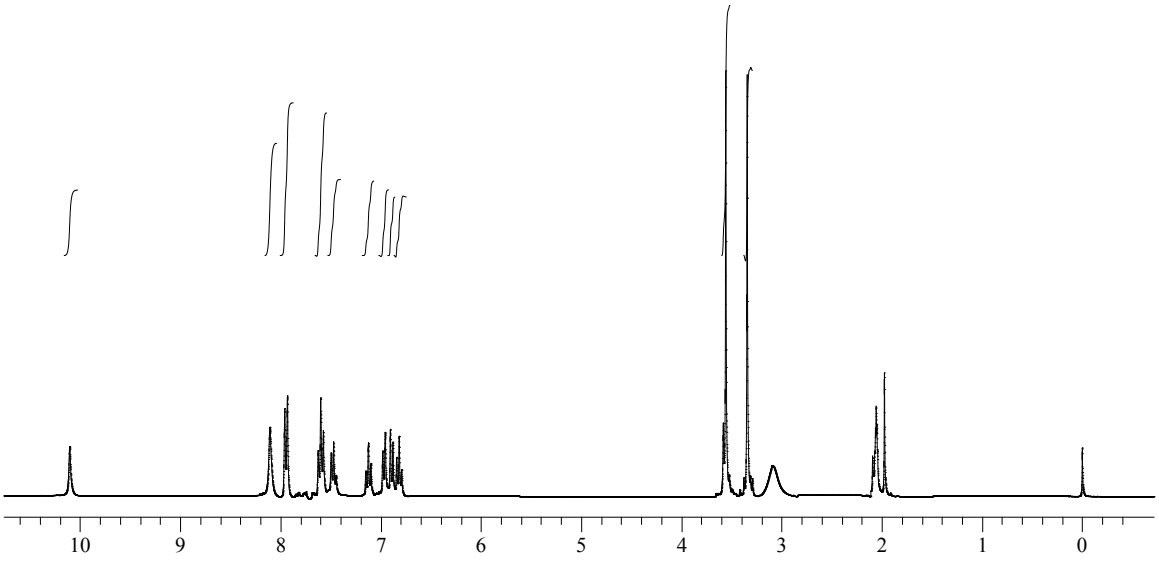


Table 1, Entry 4





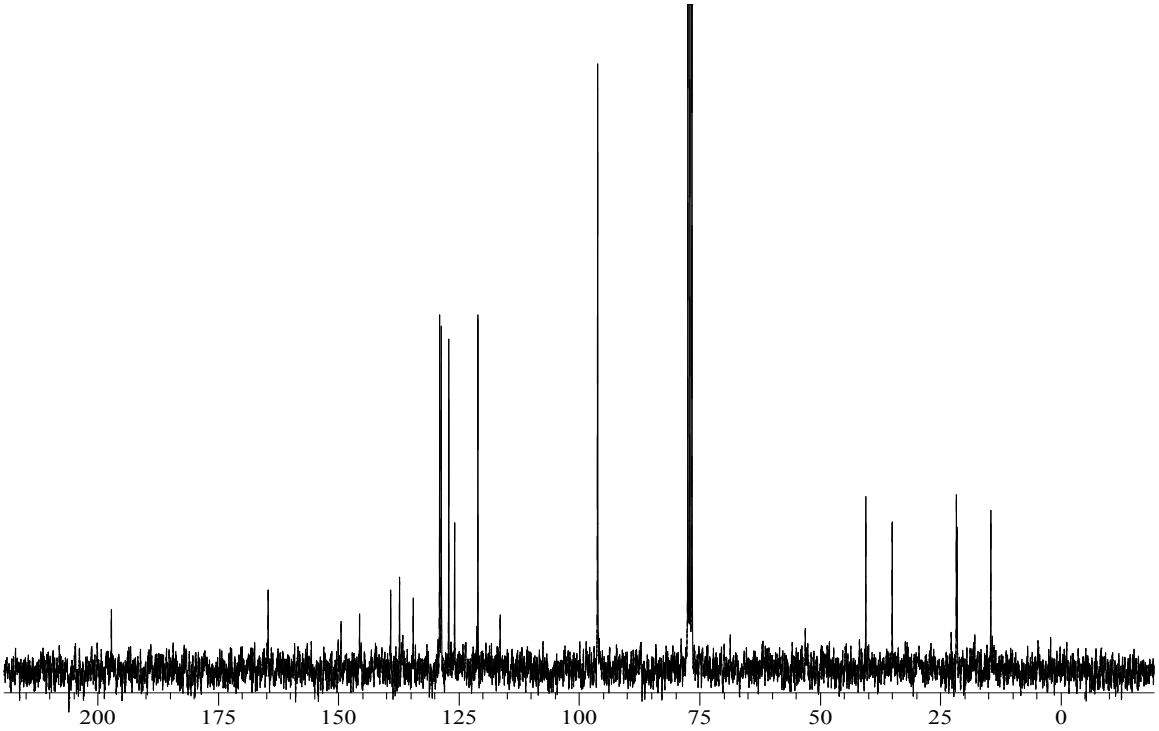


Table 1, Entry 5

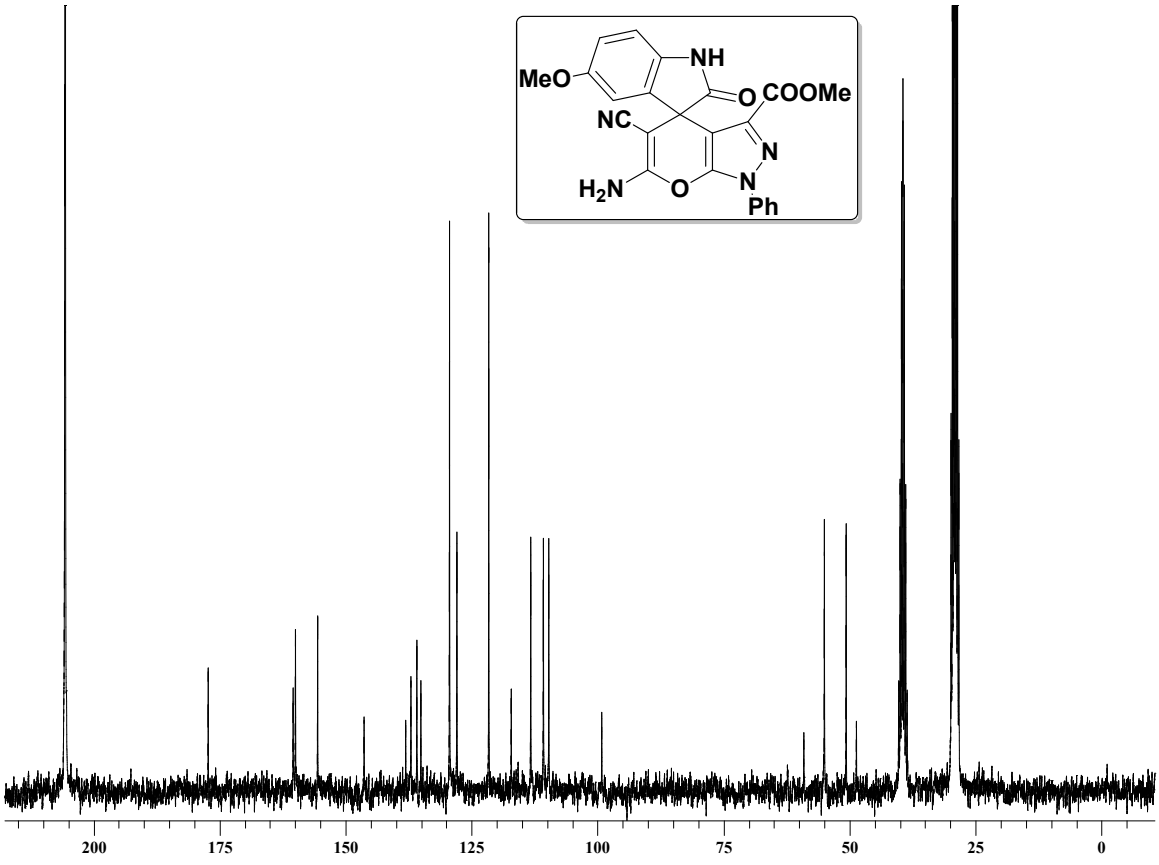
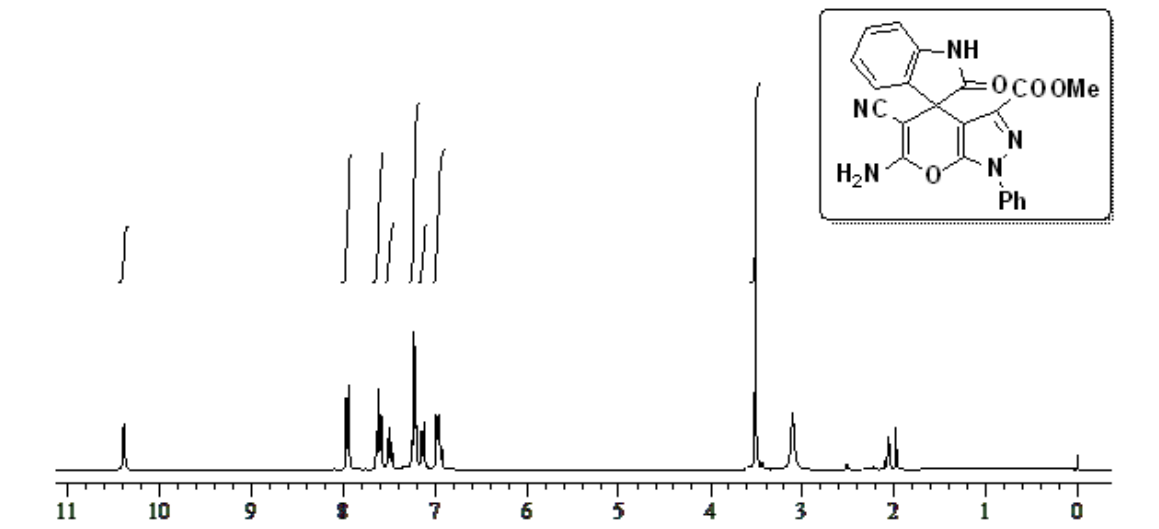


Table 1, Entry 7



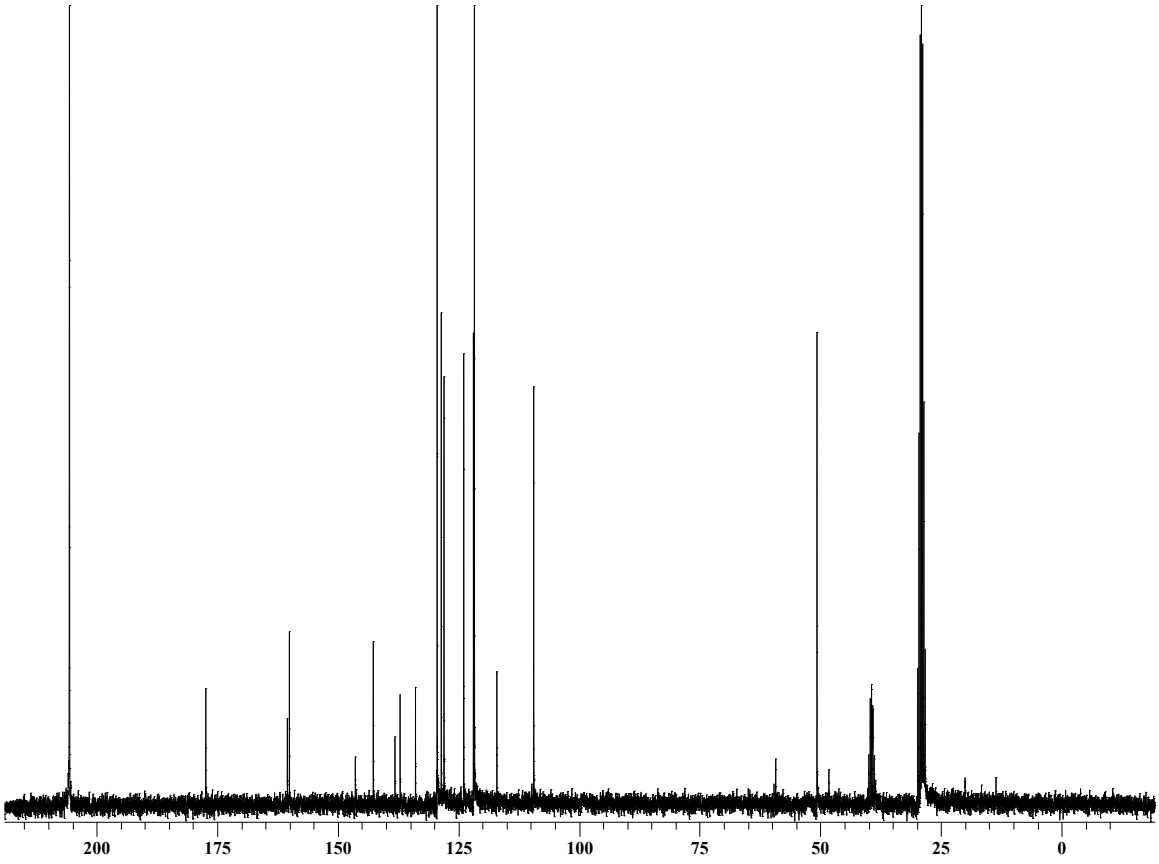


Table 1, Entry 8

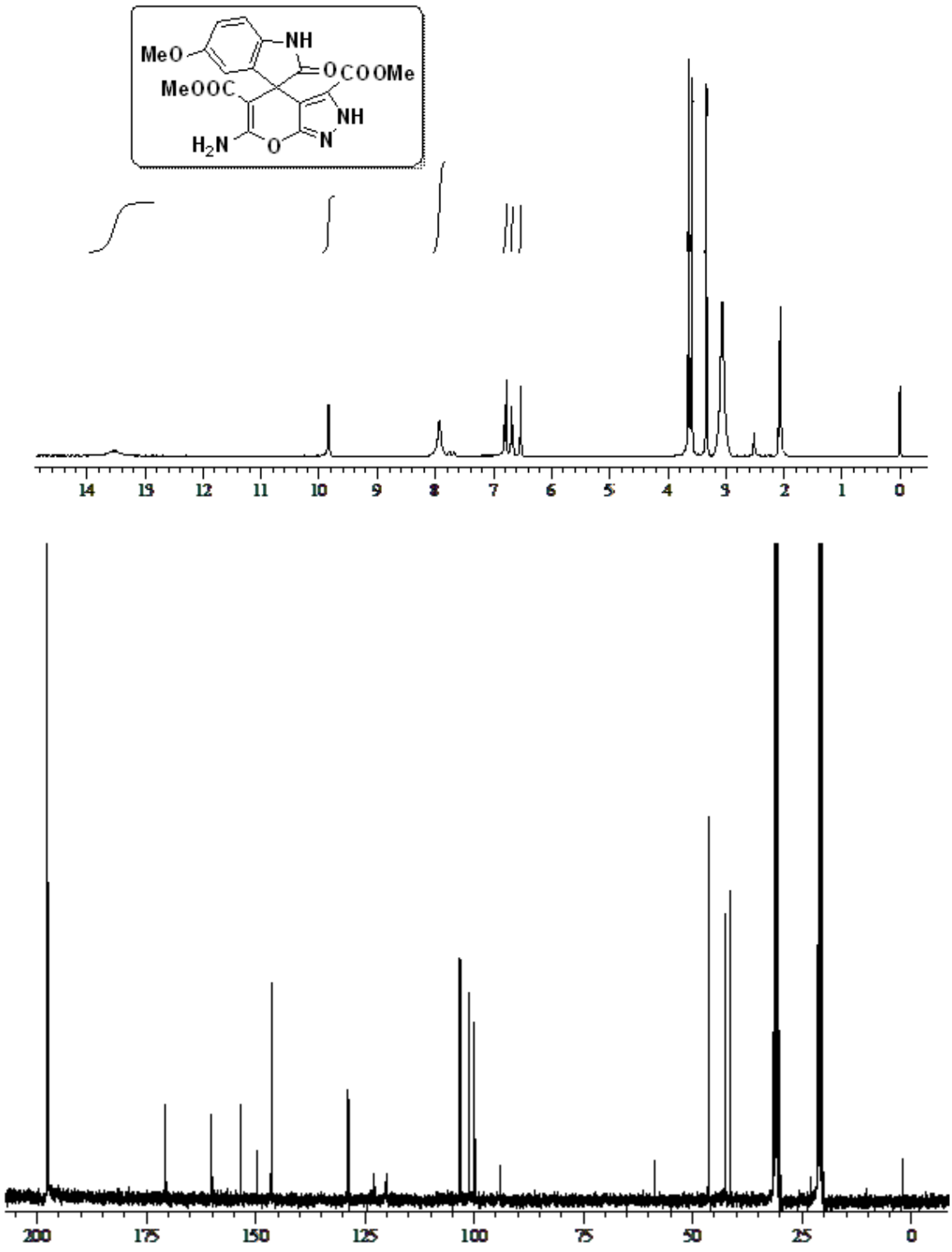


Table 1, Entry 10

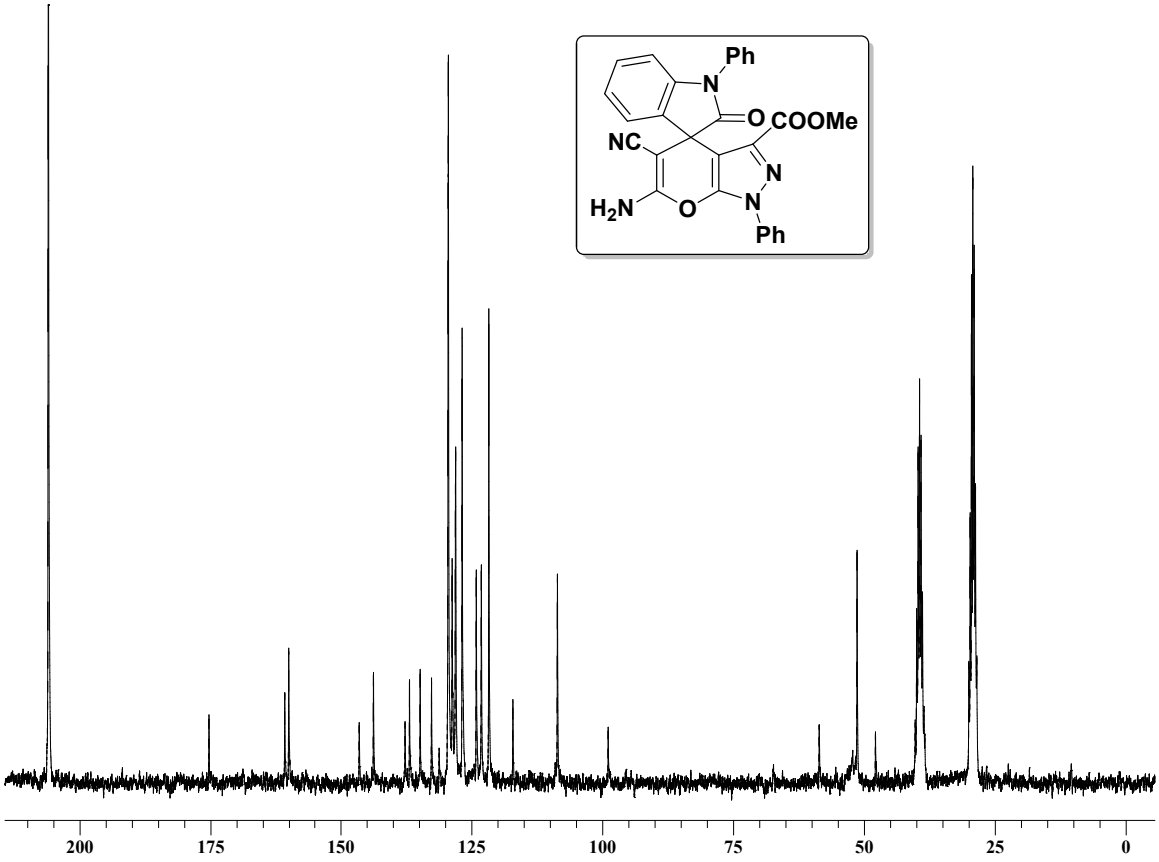


Table 1, Entry 12

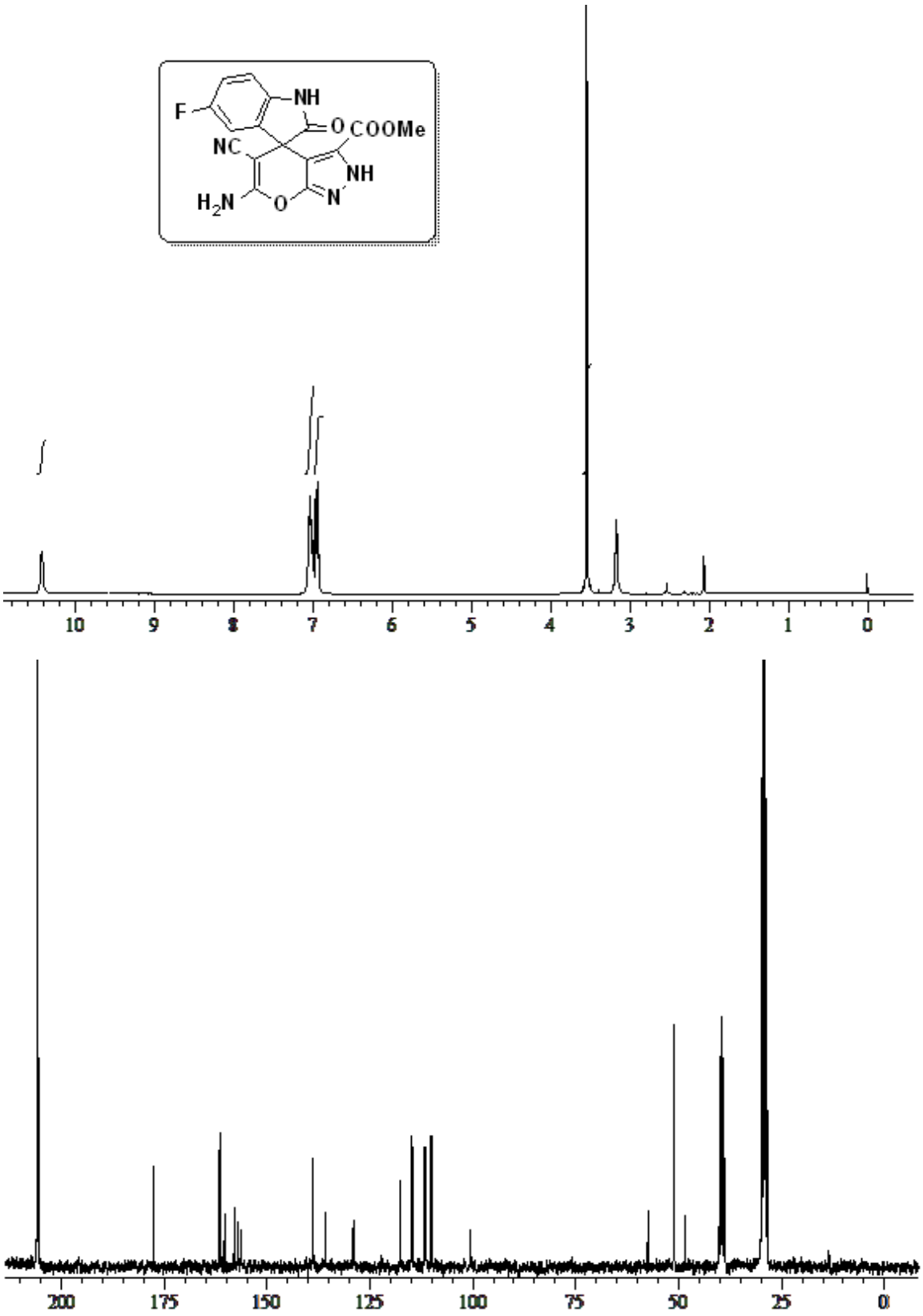
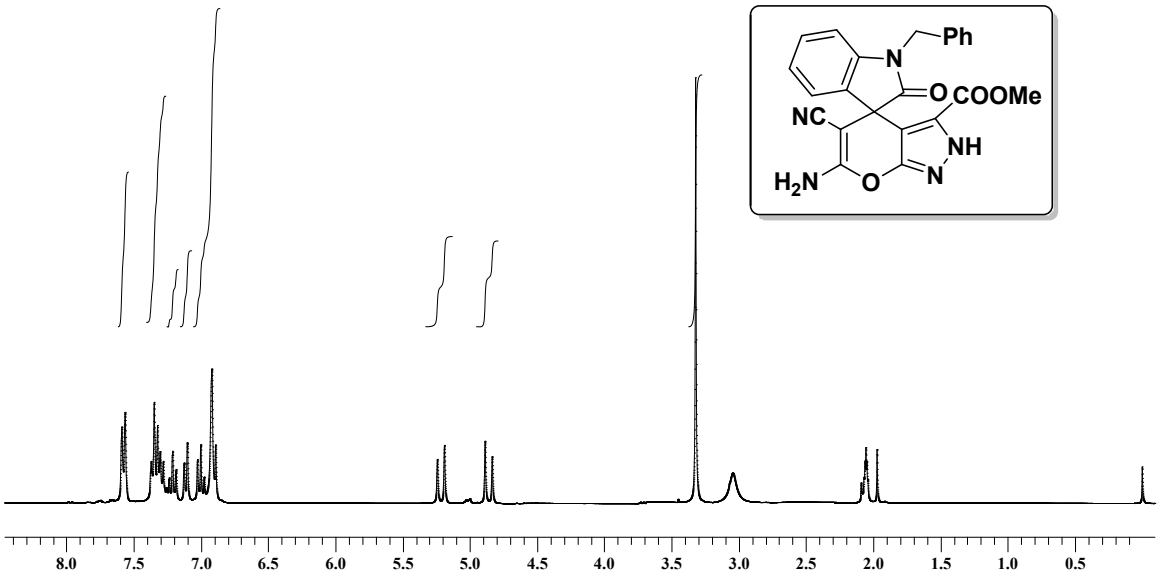


Table 1, Entry 16



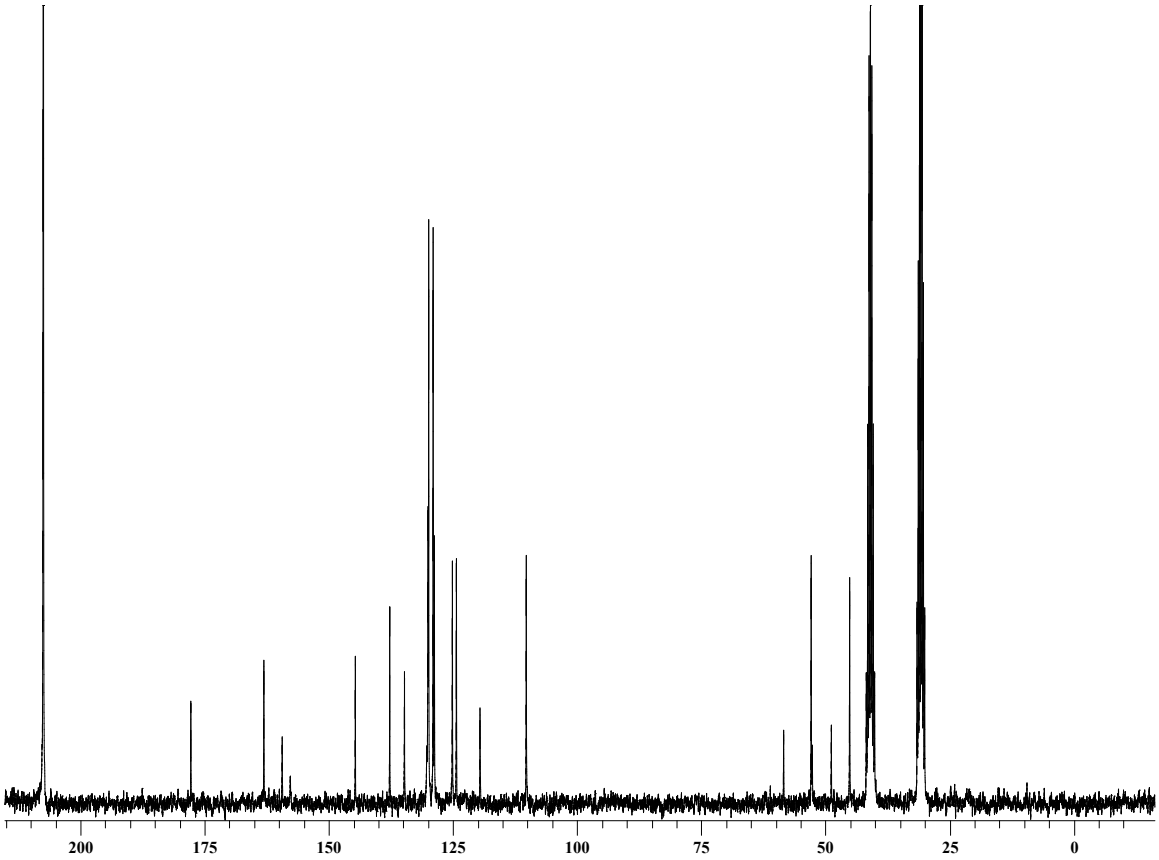


Table 1, Entry 17