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Polyethylene glycol (PEG-400) promoted as an efficient and recyclable reaction medium for one-pot eco-friendly synthesis of functionalized isoxazole substituted spirooxindole derivatives

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Supporting Information

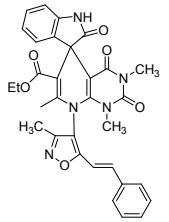
Contents

General information: All the melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected. Analytical TLC was performed on Merck precoated 60 F_{254} silica gel plates. Visualization was done by exposing to iodine vapour. IR spectra (KBr pellet) were recorded on a Perkin-Elmer BX series FT-IR spectrometer. ^{1}H NMR spectra were recorded on a Varian Gemini 300 MHz spectrometer. ^{13}C NMR spectra were recorded on a Bruker 75 MHz spectrometer. Chemical shift values are given in ppm (δ) with tetramethyl silane as internal standard. High-resolution mass spectra (HRMS) were recorded on Q-TOF Micro mass spectrometer.

General procedure for the synthesis of ethyl-(*E*)-3-(3-methyl-5-[(E)-2-aryl-1-ethenyl]-4-isoxazolylamino)-2-butenoates 1: A mixture of 4-amino-3-methyl-5-styrylisoxazole (1 mmol), and β-keto ester (1 mmol) in PEG-400 (10 mL) were stirred at ambient temperature for 4 h. After completion of the reaction (monitored by TLC), the reaction mixture was quenched by water, and extracted with diethyl ether (3 × 15 mL), washed with brine, dried by $MgSO_4$, filtered, and concentrated under vacuum. The residue was purified by column chromatography on silica gel using ethyl acetate/petroleum ether (1:2) as eluent to give the pure product **1**.

General procedure for the synthesis of isoxazole substituted spirooxindole derivatives: A mixture of isoxazolyl enamino ester **1** (0.600 g, 1.0 mmol), isatin **2** (0.282 g, 1.0 mmol) and 1,3-dimethylbarbituric acid **3** (0.300 g, 1.0 mmol) in PEG-400 (5 mL) was refluxed at 100 ^{o}C for 2 h. After completion of the reaction (monitored by TLC), the mixture was cooled to room temperature and poured into ice-cold water. The precipitate that formed was filtered off, washed with ice cold water and the crude product was purified by recrystallization from methanol to get the pure product **4**.

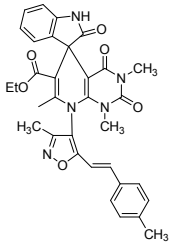
(*E*)-Ethyl-1',3',7'-trimethyl-8'-(3-methyl-5-styrylisoxazol-4-yl)-2,2',4'-trioxo-2',3',4',8'-tetrahydro-1'*H*-spiro[indoline-3,5'-pyrido[2,3-*d*]pyrimidine]-6'-carboxylate (4a):



Yield: 90%, mp 265-267 ^{o}C. IR (KBr): 3421, 3223, 2950, 2845, 1684, 1660, 1540, 1068 cm^{-1}, ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.35 (t, J = 6.2 Hz, 3H), 1.93 (s, 3H), 2.27 (s, 3H), 2.95 (s, 3H), 3.31 (s, 3H), 4.25 (q, J = 6.2 Hz, 2H), 6.65 (d, J = 12 Hz, 1H), 6.73 (d, J = 12 Hz, 1H), 6.98-7.66 (m, 9H), 10.42 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.3, 13.4, 15.9, 28.8, 31.6, 49.6, 61.3, 88.3, 100.3, 109.2, 112.3, 122.6, 125.1, 127.2, 127.7, 128.3, 128.4, 129.1, 129.9,

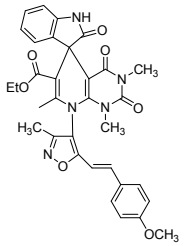
134.4, 136.6, 140.8, 144.2, 149.4, 152.8, 156.4, 158.8, 160.6, 165.6, 176.3. HRMS (ESI-MS) calcd for $C_{32}H_{29}N_5NaO_6$ $(M+Na)^+$ 602.2016, found 602.2023.

(*E*)-Ethyl-1',3',7'-trimethyl-8'-(3-methyl-5-(4-methylstyryl)isoxazol-4-yl)-2,2',4'-trioxo-2',3',4',8'-tetrahydro-1'*H*-spiro[indoline-3,5'-pyrido[2,3-*d*]pyrimidine]-6'-carboxylate (4b):



Yield: 84%, mp 271-273 ^oC. IR (KBr): 3435, 3242, 2955, 2848, 1680, 1663, 1546, 1060 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 1.32 (t, J = 6.2 Hz, 3H), 1.98 (s, 3H), 2.23 (s, 3H), 2.46 (s, 3H), 2.98 (s, 3H), 3.33 (s, 3H), 4.24 (q, J = 6.2 Hz, 2H), 6.64 (d, J = 12 Hz, 1H), 6.70 (d, J = 12 Hz, 1H), 7.04-7.69 (m, 8H), 10.53 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.2, 13.7, 16.3, 25.3, 28.6, 31.0, 48.2, 61.6, 88.6, 100.3, 109.8, 112.5, 122.2, 125.5, 126.8, 127.8, 128.8, 128.9, 129.4, 129.9, 134.2, 136.3, 140.1, 144.9, 149.8, 152.3, 156.7, 158.8, 160.9, 165.6, 176.1. HRMS (ESI-MS) calcd for $C_{33}H_{31}N_5NaO_6$ $(M+Na)^+$ 616.2172, found 616.2183.

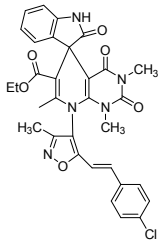
(*E*)-Ethyl-8'-(5-(4-methoxystyryl)-3-methylisoxazol-4-yl)-1',3',7'-trimethyl-2,2',4'-trioxo-2',3',4',8'-tetrahydro-1'*H*-spiro[indoline-3,5'-pyrido[2,3-*d*]pyrimidine]-6'-carboxylate (4c):



Yield: 86%, mp 260-262 ^oC. IR (KBr): 3430, 3229, 2950, 2844, 1683, 1661, 1542, 1065 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 1.34 (t, J = 6.2 Hz, 3H), 1.93 (s, 3H), 2.22 (s, 3H), 2.93 (s, 3H), 3.32 (s, 3H), 3.53 (s, 3H), 4.25 (q, J = 6.2 Hz, 2H), 6.64 (d, J = 12 Hz, 1H), 6.72 (d, J = 12 Hz, 1H), 6.96-7.68 (m, 8H), 10.44 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.5, 13.6, 16.3, 28.3, 30.9, 48.5, 59.6, 61.5, 88.5, 100.2, 109.5, 112.6, 122.5, 125.5, 127.2, 127.7, 128.3, 128.8, 129.6, 129.7, 134.4, 136.8, 140.2,

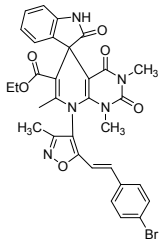
144.4, 149.2, 152.4, 156.3, 158.8, 160.4, 165.6, 176.2. HRMS (ESI-MS) calcd for $C_{33}H_{31}N_5NaO_7$ $(M+Na)^+$ 632.2121, found 632.2121.

(*E*)-Ethyl-8'-(5-(4-chlorostyryl)-3-methylisoxazol-4-yl)-1',3',7'-trimethyl-2,2',4'-trioxo-2',3',4',8'-tetrahydro-1'*H*-spiro[indoline-3,5'-pyrido[2,3-*d*]pyrimidine]-6'-carboxylate (4d):



Yield: 90%, mp 277-279 ^oC. IR (KBr): 3426, 3237, 2954, 2840, 1680, 1659, 1547, 1062 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 1.36 (t, J = 6.2 Hz, 3H), 1.99 (s, 3H), 2.24 (s, 3H), 2.95 (s, 3H), 3.34 (s, 3H), 4.28 (q, J = 6.2 Hz, 2H), 6.62 (d, J = 12 Hz, 1H), 6.70 (d, J = 12 Hz, 1H), 6.96-7.69 (m, 8H), 10.48 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.1, 13.4, 16.6, 28.3, 30.8, 48.6, 60.8, 88.6, 100.4, 109.6, 113.8, 122.6, 125.6, 127.3, 127.8, 128.3, 128.8, 129.1, 129.2, 134.4, 136.5, 140.6, 144.8, 149.8, 152.6, 156.3, 158.8, 160.7, 165.3, 176.6. HRMS (ESI-MS) calcd for $C_{32}H_{28}ClN_5NaO_6$ $(M+Na)^+$ 636.1626, found 636.1635.

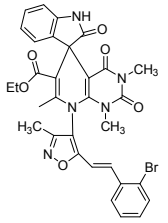
(*E*)-Ethyl-8'-(5-(4-bromostyryl)-3-methylisoxazol-4-yl)-1',3',7'-trimethyl-2,2',4'-trioxo-2',3',4',8'-tetrahydro-1'*H*-spiro[indoline-3,5'-pyrido[2,3-*d*]pyrimidine]-6'-carboxylate (4e):



Yield: 92%, mp 285-287 ^oC. IR (KBr): 3435, 3243, 2950, 2846, 1682, 1658, 1542, 1060 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 1.39 (t, J = 6.2 Hz, 3H), 1.96 (s, 3H), 2.27 (s, 3H), 2.95 (s, 3H), 3.36 (s, 3H), 4.22 (q, J = 6.2 Hz, 2H), 6.61 (d, J = 12 Hz, 1H), 6.71 (d, J = 12 Hz, 1H), 6.95-7.65 (m, 8H), 10.54 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 10.9, 13.5, 16.7, 28.5, 31.3, 48.6, 61.4, 87.6, 100.2, 109.6, 112.6, 122.5, 125.6, 127.3, 127.7, 128.4, 128.9, 129.2, 129.6, 134.7, 136.3, 140.2, 144.1, 149.3,

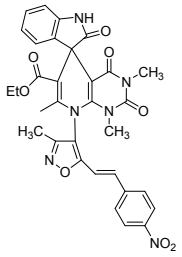
152.7, 156.3, 158.6, 160.6, 165.5, 176.7. HRMS (ESI-MS) calcd for $C_{32}H_{28}BrN_5NaO_6$ $(M+Na)^+$ 680.1121, found 680.1129.

(*E*)-Ethyl-8'-(5-(2-bromostyryl)-3-methylisoxazol-4-yl)-1',3',7'-trimethyl-2,2',4'-trioxo-2',3',4',8'-tetrahydro-1'*H*-spiro[indoline-3,5'-pyrido[2,3-*d*]pyrimidine]-6'-carboxylate (4f):



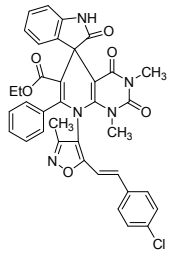
Yield: 80%, mp 281-283 °C. IR (KBr): 3441, 3253, 2958, 2840, 1680, 1655, 1546, 1067 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 1.32 (t, J = 6.2 Hz, 3H), 1.93 (s, 3H), 2.24 (s, 3H), 2.96 (s, 3H), 3.33 (s, 3H), 4.27 (q, J = 6.2 Hz, 2H), 6.62 (d, J = 12 Hz, 1H), 6.69 (d, J = 12 Hz, 1H), 6.93-7.67 (m, 8H), 10.48 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.3, 13.7, 16.4, 28.3, 31.5, 48.3, 60.5, 88.2, 100.3, 110.4, 112.4, 122.3, 125.4, 127.1, 127.8, 128.2, 128.8, 129.3, 129.8, 134.4, 136.6, 140.3, 144.4, 149.6, 152.4, 156.2, 158.5, 160.3, 165.2, 176.3. HRMS (ESI-MS) calcd for $C_{32}H_{28}BrN_5NaO_6$ $(M+Na)^+$ 680.1121, found 680.1129.

(*E*)-Ethyl-1',3',7'-trimethyl-8'-(3-methyl-5-(4-nitrostyryl)isoxazol-4-yl)-2,2',4'-trioxo-2',3',4',8'-tetrahydro-1'*H*-spiro[indoline-3,5'-pyrido[2,3-*d*]pyrimidine]-6'-carboxylate (4g):



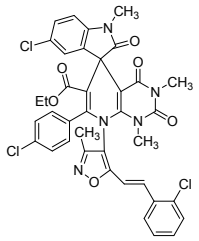
Yield: 90%, mp 268-270 °C. IR (KBr): 3429, 3250, 2952, 2846, 1684, 1661, 1540, 1060 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 1.35 (t, J = 6.2 Hz, 3H), 1.98 (s, 3H), 2.28 (s, 3H), 2.97 (s, 3H), 3.31 (s, 3H), 4.25 (q, J = 6.2 Hz, 2H), 6.64 (d, J = 12 Hz, 1H), 6.71 (d, J = 12 Hz, 1H), 6.96-7.68 (m, 8H), 10.51 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.3, 13.8, 16.8, 28.2, 32.4, 48.7, 61.3, 88.7, 100.3, 109.2, 112.1, 122.3, 125.6, 127.1, 127.9, 128.2, 128.8, 129.5, 129.8, 134.5, 136.4, 140.3, 144.4, 149.7, 152.2, 156.4, 158.6, 160.4, 165.2, 176.6. HRMS (ESI-MS) calcd for $C_{32}H_{28}N_6NaO_8$ $(M+Na)^+$ 647.1866, found 647.1866.

(*E*)-Ethyl-8'-(5-(4-chlorostyryl)-3-methylisoxazol-4-yl)-1',3'-dimethyl-2,2',4'-trioxo-7'-phenyl-2',3',4',8'-tetrahydro-1'*H*-spiro[indoline-3,5'-pyrido[2,3-*d*]pyrimidine]-6'-carboxylate (4h):



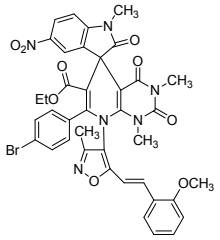
Yield: 89%, mp 268-270 °C. IR (KBr): 3425, 3256, 2950, 2848, 1680, 1659, 1543, 1062 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 1.32 (t, J = 6.2 Hz, 3H), 2.27 (s, 3H), 2.96 (s, 3H), 3.28 (s, 3H), 4.23 (q, J = 6.2 Hz, 2H), 6.62 (d, J = 12 Hz, 1H), 6.70 (d, J = 12 Hz, 1H), 7.12-7.70 (m, 13H), 10.47 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.1, 13.2, 28.7, 32.4, 48.5, 61.7, 88.6, 100.2, 103.2, 107.5, 122.5, 125.4, 127.3, 127.5, 127.6, 128.0, 128.3, 128.5, 129.1, 129.9, 131.3, 132.0, 134.5, 137.2, 139.9, 145.6, 149.3, 152.7, 156.6, 158.6, 160.8, 165.3, 176.6. HRMS (ESI-MS) calcd for $C_{37}H_{30}ClN_5NaO_6$ $(M+Na)^+$ 698.1782, found 698.1782.

(*E*)-Ethyl-5-chloro-7'-(4-chlorophenyl)-8'-(5-(2-chlorostyryl)-3-methylisoxazol-4-yl)-1,1',3'-trimethyl-2,2',4'-trioxo-2',3',4',8'-tetrahydro-1'*H*-spiro[indoline-3,5'-pyrido[2,3-*d*]pyrimidine]-6'-carboxylate (4i):



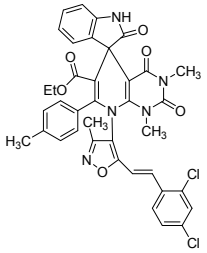
Yield: 79%, mp >300 °C. IR (KBr): 3439, 3250, 2952, 2846, 1684, 1661, 1540, 1060 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 1.35 (t, J = 6.2 Hz, 3H), 2.25 (s, 3H), 2.95 (s, 3H), 3.27 (s, 3H), 3.43 (s, 3H), 4.25 (q, J = 6.2 Hz, 2H), 6.63 (d, J = 12 Hz, 1H), 6.72 (d, J = 12 Hz, 1H), 7.10-7.69 (m, 11H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.2, 13.3, 28.7, 31.6, 34.3, 48.5, 61.6, 88.2, 100.1, 109.4, 112.6, 122.3, 125.5, 127.3, 127.7, 128.1, 128.4, 128.6, 129.2, 129.4, 129.8, 130.2, 131.3, 132.4, 134.8, 136.4, 140.5, 144.3, 149.2, 152.7, 156.3, 158.5, 160.3, 165.7, 176.2. HRMS (ESI-MS) calcd for $C_{38}H_{30}Cl_3N_5NaO_6$ $(M+Na)^+$ 780.1159, found 780.1160.

(*E*)-Ethyl-7'-(4-bromophenyl)-8'-(5-(2-methoxystyryl)-3-methylisoxazol-4-yl)-1,1',3'-trimethyl-5-nitro-2,2',4'-trioxo-2',3',4',8'-tetrahydro-1'*H*-spiro[indoline-3,5'-pyrido[2,3-*d*]pyrimidine]-6'-carboxylate (4j):



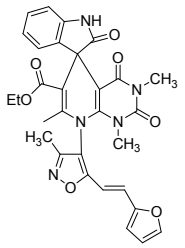
Yield: 75%, mp >300 °C. IR (KBr): 3425, 3254, 2958, 2857, 1680, 1666, 1545, 1059 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 1.33 (t, J = 6.2 Hz, 3H), 2.22 (s, 3H), 2.94 (s, 3H), 3.19 (s, 3H), 3.42 (s, 3H), 3.62 (s, 3H), 4.27 (q, J = 6.2 Hz, 2H), 6.62 (d, J = 12 Hz), 6.70 (d, J = 12 Hz, 1H), 7.02-7.70 (m, 11H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.5, 13.9, 27.5, 30.3, 34.3, 48.9, 58.6, 61.4, 88.0, 100.2, 109.4, 112.0, 122.1, 123.9, 127.7, 127.8, 128.5, 128.6, 128.9, 129.3, 129.5, 129.6, 130.3, 133.7, 136.9, 141.0, 142.7, 144.8, 149.9, 152.7, 154.9, 156.8, 158.9, 160.6, 165.7, 176.4. HRMS (ESI-MS) calcd for $C_{39}H_{33}BrN_6NaO_9$ $(M+Na)^+$ 831.1390, found 831.1398.

(*E*)-Ethyl-8'-(5-(2,4-dichlorostyryl)-3-methylisoxazol-4-yl)-1',3'-dimethyl-2,2',4'-trioxo-7'-(p-tolyl)-2',3',4',8'-tetrahydro-1'*H*-spiro[indoline-3,5'-pyrido[2,3-*d*]pyrimidine]-6'-carboxylate (4k):



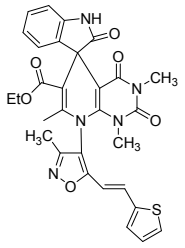
Yield: 80%, mp >300 °C. IR (KBr): 3429, 3250, 2950, 2853, 1684, 1660, 1543, 1061 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 1.35 (t, J = 6.2 Hz, 3H), 2.26 (s, 3H), 2.42 (s, 3H), 2.96 (s, 3H), 3.12 (s, 3H), 4.22 (q, J = 6.2 Hz, 2H), 6.64 (d, J = 12 Hz, 1H), 6.72 (d, J = 12 Hz, 1H), 7.18-7.68 (m, 11H), 10.52 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.8, 13.4, 24.3, 28.6, 32.3, 48.5, 60.4, 88.6, 100.1, 109.3, 112.6, 122.5, 125.4, 127.1, 127.4, 127.8, 128.1, 128.5, 128.9, 129.3, 129.5, 129.9, 130.3, 132.6, 134.8, 136.5, 138.4, 140.3, 144.6, 149.5, 152.3, 156.4, 158.5, 160.3, 165.4, 176.2. HRMS (ESI-MS) calcd for $C_{38}H_{31}Cl_2N_5NaO_6$ $(M+Na)^+$ 746.1549, found 746.1558.

(*E*)-Ethyl-8'-(5-(2-(furan-2-yl)vinyl)-3-methylisoxazol-4-yl)-1',3',7'-trimethyl-2,2',4'-trioxo-2',3',4',8'-tetrahydro-1'*H*-spiro[indoline-3,5'-pyrido[2,3-*d*]pyrimidine]-6'-carboxylate (4l):



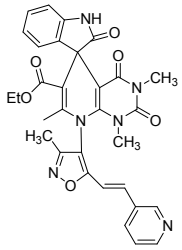
Yield: 85%, mp 254-256 °C. IR (KBr): 3445, 3257, 2958, 2850, 1680, 1660, 1542, 1060 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 1.42 (t, J = 6.2 Hz, 3H), 1.95 (s, 3H), 2.22 (s, 3H), 2.93 (s, 3H), 3.18 (s, 3H), 4.41 (q, J = 6.2 Hz, 2H), 6.62 (d, J = 12 Hz, 1H), 6.71 (d, J = 12 Hz, 1H), 6.97-7.68 (m, 7H), 10.50 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.1, 13.6, 15.6, 27.6, 31.2, 49.2, 61.9, 88.6, 100.4, 107.2, 109.9, 112.3, 114.6, 122.7, 125.3, 127.6, 128.5, 129.4, 134.5, 140.4, 142.7, 144.3, 146.6, 149.7, 152.5, 156.5, 158.5, 161.7, 165.9, 176.5. HRMS (ESI-MS) calcd for $C_{30}H_{27}N_5NaO_7$ $(M+Na)^+$ 592.1808, found 592.1808.

(*E*)-Ethyl-1',3',7'-trimethyl-8'-(3-methyl-5-(2-(thiophen-2-yl)vinyl)isoxazol-4-yl)-2,2',4'-trioxo-2',3',4',8'-tetrahydro-1'*H*-spiro[indoline-3,5'-pyrido[2,3-*d*]pyrimidine]-6'-carboxylate (4m):



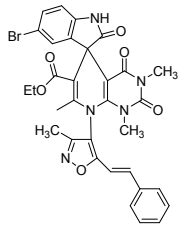
Yield: 82%, mp 267-269 °C. IR (KBr): 3432, 3251, 2950, 2855, 1684, 1663, 1540, 1064 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 1.34 (t, J = 6.2 Hz, 3H), 1.95 (s, 3H), 2.27 (s, 3H), 2.96 (s, 3H), 3.15 (s, 3H), 4.24 (q, J = 6.2 Hz, 2H), 6.63 (d, J = 12 Hz, 1H), 6.72 (d, J = 12 Hz, 1H), 7.06-7.66 (m, 7H), 10.35 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.2, 13.4, 15.9, 27.8, 31.2, 49.7, 61.2, 88.4, 100.2, 109.3, 111.3, 122.3, 125.5, 127.4, 128.3, 128.9, 129.4, 129.5, 130.3, 133.8, 140.4, 142.7, 144.6, 148.6, 152.7, 156.9, 158.6, 161.5, 165.6, 176.8. HRMS (ESI-MS) calcd for $C_{30}H_{27}N_5NaO_6S$ $(M+Na)^+$ 608.1580, found 608.1592.

(*E*)-Ethyl-1',3',7'-trimethyl-8'-(3-methyl-5-(2-(pyridin-3-yl)vinyl)isoxazol-4-yl)-2,2',4'-trioxo-2',3',4',8'-tetrahydro-1'*H*-spiro[indoline-3,5'-pyrido[2,3-*d*]pyrimidine]-6'-carboxylate (4n):



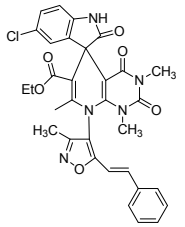
Yield: 80%, mp 273-275 °C. IR (KBr): 3446, 3250, 2959, 2850, 1680, 1662, 1545, 1061 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 1.36 (t, J = 6.2 Hz, 3H), 1.98 (s, 3H), 2.27 (s, 3H), 2.94 (s, 3H), 3.18 (s, 3H), 4.27 (q, J = 6.2 Hz, 2H), 6.62 (d, J = 12 Hz, 1H), 6.71 (d, J = 12 Hz, 1H), 7.10-7.68 (m, 6H), 8.25 (d, J = 8.2 Hz, 1H), 9.13 (s, 1H), 10.48 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.1, 13.6, 15.5, 28.2, 31.2, 49.4, 61.6, 88.5, 100.3, 109.6, 112.3, 122.6, 124.3, 127.1, 127.9, 128.2, 129.3, 129.4, 130.4, 135.3, 140.2, 143.2, 144.9, 145.6, 149.7, 152.5, 156.4, 158.3, 162.2, 165.9, 176.8. HRMS (ESI-MS) calcd for $C_{31}H_{28}N_6NaO_6$ $(M+Na)^+$ 603.1968, found 603.1978.

(*E*)-Ethyl-5-bromo-1',3',7'-trimethyl-8'-(3-methyl-5-styrylisoxazol-4-yl)-2,2',4'-trioxo-2',3',4',8'-tetrahydro-1'*H*-spiro[indoline-3,5'-pyrido[2,3-*d*]pyrimidine]-6'-carboxylate (4o):



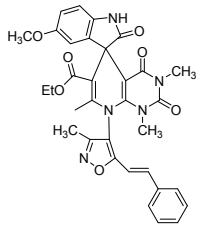
Yield: 90%, mp 295-297 °C. IR (KBr): 3434, 3236, 2954, 2840, 1680, 1662, 1546, 1060 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 1.32 (t, J = 6.2 Hz, 3H), 1.97 (s, 3H), 2.27 (s, 3H), 2.96 (s, 3H), 3.28 (s, 3H), 4.22 (q, J = 6.2 Hz, 2H), 6.61 (d, J = 12 Hz, 1H), 6.83 (d, J = 12 Hz, 1H), 7.12-7.72 (m, 8H), 10.47 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.2, 13.9, 16.7, 28.8, 32.6, 49.5, 61.2, 88.4, 100.2, 109.5, 114.5, 122.2, 126.1, 127.3, 127.7, 128.8, 128.9, 129.1, 129.3, 134.2, 137.1, 140.3, 144.4, 149.7, 152.4, 156.8, 158.3, 160.8, 165.9, 176.4. HRMS (ESI-MS) calcd for $C_{32}H_{28}BrN_5NaO_6$ $(M+Na)^+$ 680.1121, found 680.1127.

(*E*)-Ethyl-5-chloro-1',3',7'-trimethyl-8'-(3-methyl-5-styrylisoxazol-4-yl)-2,2',4'-trioxo-2',3',4',8'-tetrahydro-1'*H*-spiro[indoline-3,5'-pyrido[2,3-*d*]pyrimidine]-6'-carboxylate (4p):



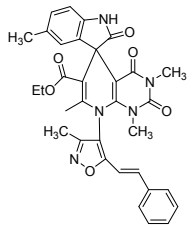
Yield: 92%, mp 276-278 °C. IR (KBr): 3428, 3230, 2952, 2848, 1684, 1660, 1545, 1067 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 1.38 (t, J = 6.2 Hz, 3H), 1.95 (s, 3H), 2.27 (s, 3H), 2.97 (s, 3H), 3.16 (s, 3H), 4.23 (q, J = 6.2 Hz, 2H), 6.59 (d, J = 12 Hz, 1H), 6.69 (d, J = 12 Hz, 1H), 7.19-7.62 (m, 8H), 10.44 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.3, 13.6, 16.5, 28.1, 32.3, 49.9, 61.3, 88.6, 100.1, 109.4, 112.8, 122.6, 126.1, 127.2, 127.7, 128.2, 128.9, 129.1, 129.9, 134.5, 138.0, 140.2, 144.4, 149.1, 152.6, 156.9, 158.4, 161.7, 166.2, 177.0. HRMS (ESI-MS) calcd for $C_{32}H_{28}ClN_5NaO_6$ $(M+Na)^+$ 636.1626, found 636.1626.

(*E*)-Ethyl-5-methoxy-1',3',7'-trimethyl-8'-(3-methyl-5-styrylisoxazol-4-yl)-2,2',4'-trioxo-2',3',4',8'-tetrahydro-1'*H*-spiro[indoline-3,5'-pyrido[2,3-*d*]pyrimidine]-6'-carboxylate (4q):



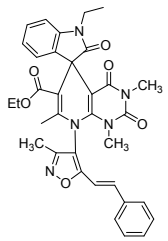
Yield: 82%, mp 262-264 °C. IR (KBr): 3432, 3241, 2950, 2844, 1681, 1658, 1540, 1062 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 1.34 (t, J = 6.2 Hz, 3H), 1.96 (s, 3H), 2.26 (s, 3H), 2.98 (s, 3H), 3.18 (s, 3H), 3.56 (s, 3H), 4.28 (q, J = 6.2 Hz, 2H), 6.63 (d, J = 12 Hz, 1H), 6.72 (d, J = 12 Hz, 1H), 7.16-7.65 (m, 8H), 10.48 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.5, 13.4, 16.1, 28.4, 32.7, 49.7, 56.0, 61.6, 88.2, 100.2, 109.7, 113.6, 122.2, 124.6, 127.0, 127.9, 128.2, 128.8, 129.1, 129.9, 134.4, 135.2, 139.9, 144.6, 149.9, 152.2, 156.4, 158.4, 161.7, 165.9, 176.3. HRMS (ESI-MS) calcd for $C_{33}H_{31}N_5NaO_7$ $(M+Na)^+$ 632.2121, found 632.2121.

(*E*)-Ethyl-1',3',5,7'-tetramethyl-8'-(3-methyl-5-styrylisoxazol-4-yl)-2,2',4'-trioxo-2',3',4',8'-tetrahydro-1'*H*-spiro[indoline-3,5'-pyrido[2,3-*d*]pyrimidine]-6'-carboxylate (4r):



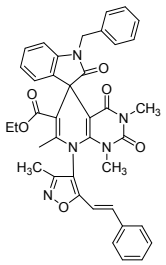
Yield: 80%, mp 259-261 °C. IR (KBr): 3421, 3240, 2948, 2852, 1680, 1662, 1544, 1060 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 1.32 (t, J = 6.2 Hz, 3H), 1.95 (s, 3H), 2.23 (s, 3H), 2.38 (s, 3H), 2.96 (s, 3H), 3.15 (s, 3H), 4.25 (q, J = 6.2 Hz, 2H), 6.62 (d, J = 12 Hz), 6.70 (d, J = 12 Hz, 1H), 7.12-7.67 (m, 8H), 10.42 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.1, 13.5, 16.7, 24.3, 28.3, 32.9, 49.6, 61.8, 88.1, 100.1, 109.9, 112.5, 122.3, 125.1, 127.2, 127.8, 128.3, 128.8, 129.4, 129.7, 134.3, 136.5, 140.2, 144.7, 149.3, 152.5, 156.3, 158.6, 160.4, 165.3, 176.6. HRMS (ESI-MS) calcd for $C_{33}H_{31}N_5NaO_6$ $(M+Na)^+$ 616.2172, found 616.2179.

(*E*)-Ethyl-1-ethyl-1',3',7'-trimethyl-8'-(3-methyl-5-styrylisoxazol-4-yl)-2,2',4'-trioxo-2',3',4',8'-tetrahydro-1'*H*-spiro[indoline-3,5'-pyrido[2,3-*d*]pyrimidine]-6'-carboxylate (4s):



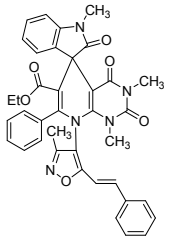
Yield: 84%, mp 266-268 °C. IR (KBr): 3436, 3239, 2945, 2850, 1683, 1660, 1548, 1059 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 1.19 (t, J = 6.6 Hz, 3H), 1.38 (t, J = 6.2 Hz, 3H), 1.93 (s, 3H), 2.25 (s, 3H), 2.95 (s, 3H), 3.17 (s, 3H), 3.53-3.61 (m, 2H), 4.28 (q, J = 6.2 Hz, 2H), 6.63 (d, J = 12 Hz, 1H), 6.72 (d, J = 12 Hz, 1H), 7.10-7.65 (m, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.4, 12.5, 13.8, 16.9, 28.2, 32.7, 36.4, 49.3, 61.5, 88.4, 100.3, 109.6, 112.2, 122.6, 125.5, 127.4, 128.2, 128.7, 129.9, 134.5, 136.2, 140.4, 144.5, 149.7, 152.2, 156.1, 158.5, 160.6, 165.9, 176.5. HRMS (ESI-MS) calcd for $C_{34}H_{33}N_5NaO_6$ $(M+Na)^+$ 630.2329, found 630.2338.

(*E*)-Ethyl-1-benzyl-1',3',7'-trimethyl-8'-(3-methyl-5-styrylisoxazol-4-yl)-2,2',4'-trioxo-2',3',4',8'-tetrahydro-1'*H*-spiro[indoline-3,5'-pyrido[2,3-*d*]pyrimidine]-6'-carboxylate (4t):



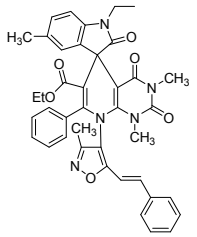
Yield: 80%, mp 282-284 °C. IR (KBr): 3442, 3230, 2951, 2857, 1680, 1663, 1546, 1060 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 1.34 (t, J = 6.2 Hz, 3H), 1.98 (s, 3H), 2.27 (s, 3H), 2.93 (s, 3H), 3.15 (s, 3H), 4.25 (q, J = 6.2 Hz, 2H), 5.04 (s, 2H), 6.61 (d, J = 12 Hz, 1H), 6.70 (d, J = 12 Hz, 1H), 7.05-7.68 (m, 14H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.2, 13.6, 16.9, 28.3, 32.4, 49.5, 55.8, 61.7, 88.5, 100.2, 109.8, 112.5, 122.0, 125.3, 126.4, 127.4, 128.1, 128.6, 128.8, 129.2, 130.7, 131.6, 132.9, 136.8, 139.1, 142.1, 144.8, 149.5, 152.8, 156.5, 158.7, 161.2, 165.9, 176.9. HRMS (ESI-MS) calcd for $C_{39}H_{35}N_5NaO_6$ $(M+Na)^+$ 692.2485, found 692.2485.

(*E*)-Ethyl-1,1',3'-trimethyl-8'-(3-methyl-5-styrylisoxazol-4-yl)-2,2',4'-trioxo-7'-phenyl-2',3',4',8'-tetrahydro-1'*H*-spiro[indoline-3,5'-pyrido[2,3-*d*]pyrimidine]-6'-carboxylate (4u):



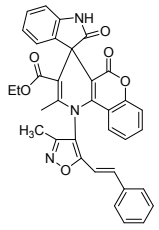
Yield: 82%, mp 289-291 °C. IR (KBr): 3436, 3258, 2950, 2841, 1680, 1660, 1547, 1063 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 1.35 (t, J = 6.2 Hz, 3H), 2.24 (s, 3H), 2.93 (s, 3H), 3.15 (s, 3H), 3.43 (s, 3H), 4.25 (q, J = 6.2 Hz, 2H), 6.63 (d, J = 12 Hz, 1H), 6.74 (d, J = 12 Hz, 1H), 7.11-7.68 (m, 14H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.3, 13.6, 28.3, 32.7, 36.3, 48.3, 61.0, 88.6, 100.3, 109.1, 113.8, 122.1, 125.6, 126.6, 127.2, 127.8, 128.3, 128.4, 128.8, 129.1, 129.2, 129.8, 134.4, 136.6, 140.8, 144.8, 149.3, 152.2, 156.9, 158.6, 161.8, 166.9, 176.7. HRMS (ESI-MS) calcd for $C_{38}H_{33}N_5NaO_6$ $(M+Na)^+$ 678.2329, found 678.2339.

(*E*)-Ethyl-1-ethyl-1',3',5-trimethyl-8'-(3-methyl-5-styrylisoxazol-4-yl)-2,2',4'-trioxo-7'-phenyl-2',3',4',8'-tetrahydro-1'*H*-spiro[indoline-3,5'-pyrido[2,3-*d*]pyrimidine]-6'-carboxylate (4v):



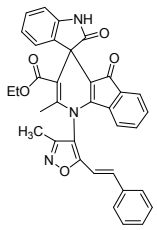
Yield: 79%, mp >300 °C. IR (KBr): 3450, 3245, 2948, 2852, 1682, 1665, 1544, 1060 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 1.19 (t, J = 6.4 Hz, 3H), 1.39 (t, J = 6.2 Hz, 3H), 2.22 (s, 3H), 2.38 (s, 3H), 2.96 (s, 3H), 3.13 (s, 3H), 3.50-3.59 (m, 2H), 4.27 (q, J = 6.2 Hz, 2H), 6.61 (d, J = 12 Hz, 1H), 6.71 (d, J = 12 Hz, 1H), 7.09-7.66 (m, 13H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.1, 12.4, 13.7, 28.4, 30.9, 36.4, 48.7, 61.8, 88.4, 100.4, 109.6, 112.2, 123.2, 126.1, 127.1, 127.9, 128.3, 128.8, 128.9, 129.1, 129.3, 129.9, 131.1, 134.2, 137.1, 138.7, 140.9, 144.7, 149.6, 152.4, 156.8, 158.9, 160.9, 165.6, 176.7. HRMS (ESI-MS) calcd for $C_{40}H_{37}N_5NaO_6$ $(M+Na)^+$ 706.2642, found 706.2651.

(*E*)-Ethyl-2-methyl-1-(3-methyl-5-styrylisoxazol-4-yl)-2',5-dioxo-1,5-dihydrospiro[chromeno[4,3-*b*]pyridine-4,3'-indoline]-3-carboxylate (6a):



Yield: 82%, mp 255-257 °C. IR (KBr): 3442, 3250, 2956, 2842, 1680, 1658, 1546, 1061 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 1.29 (t, J = 6.2 Hz, 3H), 1.97 (s, 3H), 2.26 (s, 3H), 4.22 (q, J = 6.2 Hz, 2H), 6.64 (d, J = 12 Hz, 1H), 6.71 (d, J = 12 Hz, 1H), 7.08-7.67 (m, 13H), 10.56 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.3, 13.6, 16.5, 50.9, 61.4, 88.7, 100.2, 110.4, 112.3, 115.6, 118.2, 121.3, 122.7, 125.7, 126.3, 127.7, 128.3, 128.5, 129.0, 129.8, 134.3, 136.7, 140.5, 144.7, 148.4, 150.8, 152.6, 156.6, 157.4, 160.6, 165.8, 172.4. HRMS (ESI-MS) calcd for $C_{35}H_{27}N_3NaO_6$ $(M+Na)^+$ 608.1798, found 608.1806.

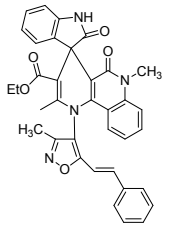
(*E*)-Ethyl-2-methyl-1-(3-methyl-5-styrylisoxazol-4-yl)-2',5-dioxo-1,5-dihydrospiro[indeno[1,2-*b*]pyridine-4,3'-indoline]-3-carboxylate (6b):



Yield: 75%, mp >300 °C. IR (KBr): 3421, 3255, 2950, 2851, 1683, 1655, 1540, 1060 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 1.27 (t, J = 6.2 Hz, 3H), 1.98 (s, 3H), 2.26 (s, 3H), 4.25 (q, J = 6.2 Hz, 2H), 6.60 (d, J = 12 Hz, 1H), 6.70 (d, J = 12 Hz, 1H), 7.04-7.68 (m, 13H), 10.37 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.2, 13.6, 16.6, 50.4, 61.1, 95.4, 100.3, 109.6, 113.2, 122.5, 123.9, 125.5, 127.2, 127.5, 128.3, 128.5, 129.4, 129.9, 130.3, 132.2, 134.8, 136.9, 139.0, 140.5, 142.2, 149.3, 152.3, 156.5, 158.9, 160.7, 165.5, 172.9. HRMS (ESI-MS) calcd for $C_{35}H_{27}N_3NaO_5$ $(M+Na)^+$ 592.1848, found 592.1848.

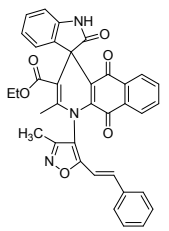
(*E*)-Ethyl-2,6-dimethyl-1-(3-methyl-5-styrylisoxazol-4-yl)-2',5-dioxo-5,6-dihydro-1*H*-spiro[benzo[*h*][1,6]naphthyridine-4,3'-indoline]-3-carboxylate (6c):

3.36 (s, 3H, N-CH_3),



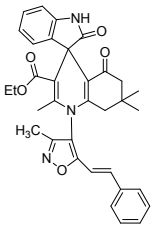
Yield: 75%, mp 294-296 °C. IR (KBr): 3445, 3250, 2952, 2848, 1680, 1658, 1543, 1058 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 1.31 (t, J = 6.2 Hz, 3H), 1.92 (s, 3H), 2.25 (s, 3H), 3.31 (s, 3H), 4.28 (q, J = 6.2 Hz, 2H), 6.61 (d, J = 12 Hz, 1H), 6.70 (d, J = 12 Hz, 1H), 7.12-7.66 (m, 13H), 10.52 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.5, 13.6, 16.6, 33.3, 50.8, 61.2, 90.5, 100.3, 109.6, 112.2, 115.4, 118.7, 121.8, 122.7, 125.9, 126.8, 127.8, 128.2, 128.8, 129.7, 129.9, 132.6, 134.4, 136.8, 140.4, 144.3, 148.7, 152.1, 156.5, 158.1, 160.6, 165.3, 174.4. HRMS (ESI-MS) calcd for $C_{36}H_{30}N_4NaO_5$ $(M+Na)^+$ 621.2114, found 621.2123.

(*E*)-Ethyl-2-methyl-1-(3-methyl-5-styrylisoxazol-4-yl)-2',5,10-trioxo-5,10-dihydro-1*H*-spiro[benzo[*g*]quinoline-4,3'-indoline]-3-carboxylate (6d):



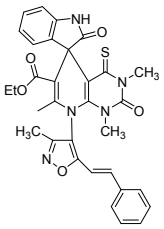
Yield: 70%, mp 291-293 °C. IR (KBr): 3435, 3250, 2958, 2850, 1680, 1652, 1549, 1059 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 1.34 (t, J = 6.2 Hz, 3H), 1.98 (s, 3H), 2.27 (s, 3H), 4.25 (q, J = 6.2 Hz, 2H), 6.61 (d, J = 12 Hz, 1H), 6.72 (d, J = 12 Hz, 1H), 7.07-7.65 (m, 13H), 10.48 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.3, 13.6, 16.3, 50.6, 61.9, 97.6, 100.1, 110.6, 113.7, 122.7, 125.9, 127.2, 127.5, 128.3, 128.5, 129.2 129.9, 130.2, 132.7, 134.4, 136.3, 138.5, 140.7, 144.5, 148.2, 152.2, 156.6, 158.4, 160.7, 165.7, 175.5, 188.3. HRMS (ESI-MS) calcd for $C_{36}H_{27}N_3NaO_6$ $(M+Na)^+$ 620.1798, found 620.1798.

(*E*)-Ethyl-2',7',7'-trimethyl-1'-(3-methyl-5-styrylisoxazol-4-yl)-2,5'-dioxo-5',6',7',8'-tetrahydro-1'*H*-spiro[indoline-3,4'-quinoline]-3'-carboxylate (6e):



Yield: 80%, mp 257-259 °C. IR (KBr): 3435, 3250, 2949, 2840, 1680, 1658, 1547, 1060 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 1.03 (s, 6H), 1.34 (t, J = 6.2 Hz, 3H), 1.98 (s, 3H), 2.24 (s, 3H), 2.42 (s, 2H), 2.74 (s, 2H), 4.25 (q, J = 6.2 Hz, 2H), 6.62 (d, J = 12 Hz, 1H), 6.70 (d, J = 12 Hz, 1H), 7.06-7.66 (m, 9H), 10.45 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.1, 13.6, 16.7, 27.3, 34.7, 36.4, 49.2, 52.5, 61.6, 94.8, 100.4, 109.3, 112.6, 122.3, 125.8, 127.9, 128.2, 128.8, 129.2, 134.4, 136.6, 140.5, 144.4, 149.4, 152.8, 156.3, 158.6, 160.4, 165.6, 192.4. HRMS (ESI-MS) calcd for $C_{34}H_{33}N_3NaO_5$ $(M+Na)^+$ 586.2318, found 586.2330.

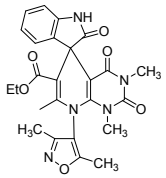
(*E*)-Ethyl-1',3',7'-trimethyl-8'-(3-methyl-5-styrylisoxazol-4-yl)-2,2'-dioxo-4'-thioxo-2',3',4',8'-tetrahydro-1'*H*-spiro[indoline-3,5'-pyrido[2,3-*d*]pyrimidine]-6'-carboxylate (6f):



Yield: 78%, mp 274-276 °C. IR (KBr): 3445, 3256, 2957, 2849, 1680, 1659, 1548, 1060 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 1.25 (t, J = 6.2 Hz, 3H), 1.97 (s, 3H), 2.25 (s, 3H), 2.94 (s, 3H), 3.27 (s, 3H), 4.23 (q, J = 6.2 Hz, 2H), 6.63 (d, J = 12 Hz, 1H),

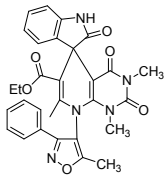
6.72 (d, J = 12 Hz, 1H), 7.04-7.64 (m, 9H), 10.53 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.5, 13.3, 16.5, 28.6, 31.5, 49.4, 60.6, 90.4, 100.4, 109.3, 112.8, 122.3, 125.6, 127.1, 127.2, 128.4, 128.8, 129.7, 129.9, 133.3, 135.4, 140.7, 144.8, 149.7, 152.2, 156.7, 158.5, 161.5, 165.6, 187.3. HRMS (ESI-MS) calcd for $C_{32}H_{29}N_5NaO_5S$ $(M+Na)^+$ 618.1787, found 618.1787.

Ethyl-8'-(3,5-dimethylisoxazol-4-yl)-1',3',7'-trimethyl-2,2',4'-trioxo-2',3',4',8'-tetrahydro-1'*H*-spiro[indoline-3,5'-pyrido[2,3-*d*]pyrimidine]-6'-carboxylate (8a):



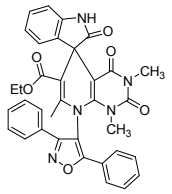
Yield: 82%, mp 235-237 ^{o}C. IR (KBr): 3445, 3236, 2955, 2849, 1682, 1660, 1542, 1061 cm^{-1}, ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.35 (t, J = 6.2 Hz, 3H), 1.97 (s, 3H), 2.10 (s, 3H), 2.30 (s, 3H), 2.97 (s, 3H), 3.19 (s, 3H), 4.23 (q, J = 6.2 Hz, 2H), 7.20-7.51 (m, 4H), 10.52 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 10.4, 12.4, 13.6, 16.4, 28.7, 31.7, 49.3, 61.3, 90.4, 100.5, 109.6, 112.2, 125.2, 127.9, 128.3, 129.3, 140.1, 144.1, 149.6, 152.4, 156.5, 158.6, 161.6, 165.4, 176.2. HRMS (ESI-MS) calcd for $C_{25}H_{25}N_5NaO_6$ $(M+Na)^+$ 514.1703, found 514.1711.

Ethyl-1',3',7'-trimethyl-8'-(5-methyl-3-phenylisoxazol-4-yl)-2,2',4'-trioxo-2',3',4',8'-tetrahydro-1'*H*-spiro[indoline-3,5'-pyrido[2,3-*d*]pyrimidine]-6'-carboxylate (8b):



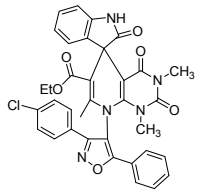
Yield: 75%, mp 243-245 ^{o}C. IR (KBr): 3440, 3252, 2950, 2845, 1680, 1659, 1540, 1060 cm^{-1}, ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.35 (t, J = 6.2 Hz, 3H), 1.95 (s, 3H), 2.13 (s, 3H), 2.94 (s, 3H), 3.21 (s, 3H), 4.24 (q, J = 6.2 Hz, 2H), 7.08-7.68 (m, 9H), 10.49 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 10.9, 13.3, 16.6, 28.7, 31.5, 49.3, 61.4, 90.5, 100.3, 109.2, 112.5, 125.5, 127.0, 127.6, 128.4, 128.6, 129.8, 129.9, 130.3, 140.9, 144.5, 149.7, 152.3, 156.3, 158.3, 160.4, 165.6, 176.6. HRMS (ESI-MS) calcd for $C_{30}H_{27}N_5NaO_6$ $(M+Na)^+$ 576.1859, found 576.1859.

Ethyl-8'-(3,5-diphenylisoxazol-4-yl)-1',3',7'-trimethyl-2,2',4'-trioxo-2',3',4',8'-tetrahydro-1'*H*-spiro[indoline-3,5'-pyrido[2,3-*d*]pyrimidine]-6'-carboxylate (8c):

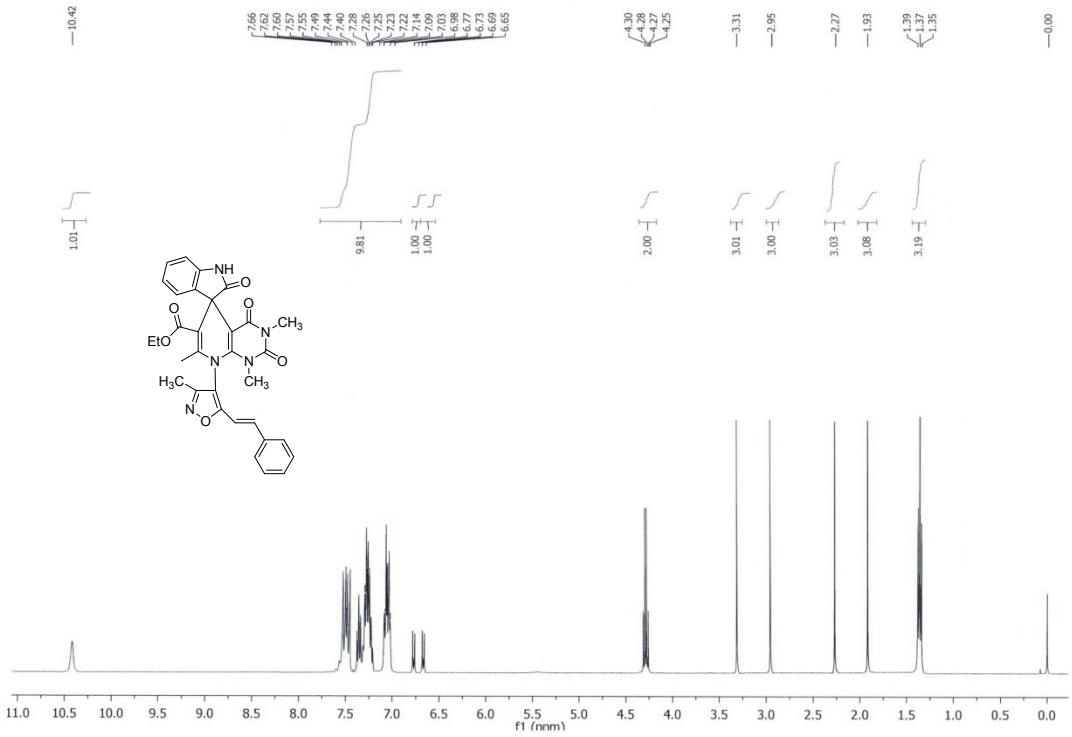


Yield: 70%, mp 286-288 ^{o}C. IR (KBr): 3436, 3247, 2955, 2840, 1678, 1660, 1548, 1059 cm^{-1}, ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.38 (t, J = 6.2 Hz, 3H), 1.94 (s, 3H), 2.96 (s, 3H), 3.18 (s, 3H), 4.28 (q, J = 6.2 Hz, 2H), 7.12-7.71 (m, 14H), 10.37 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.6, 16.3, 28.5, 31.2, 49.7, 61.5, 90.6, 100.1, 109.4, 112.3, 125.5, 126.7, 127.3, 127.8, 128.2, 128.4, 128.8, 129.1, 129.5, 129.8, 130.4, 132.4, 140.6, 144.2, 149.5, 152.4, 156.2, 158.6, 160.8, 165.4, 176.8. HRMS (ESI-MS) calcd for $C_{35}H_{29}N_5NaO_6$ $(M+Na)^+$ 638.2016, found 638.2022.

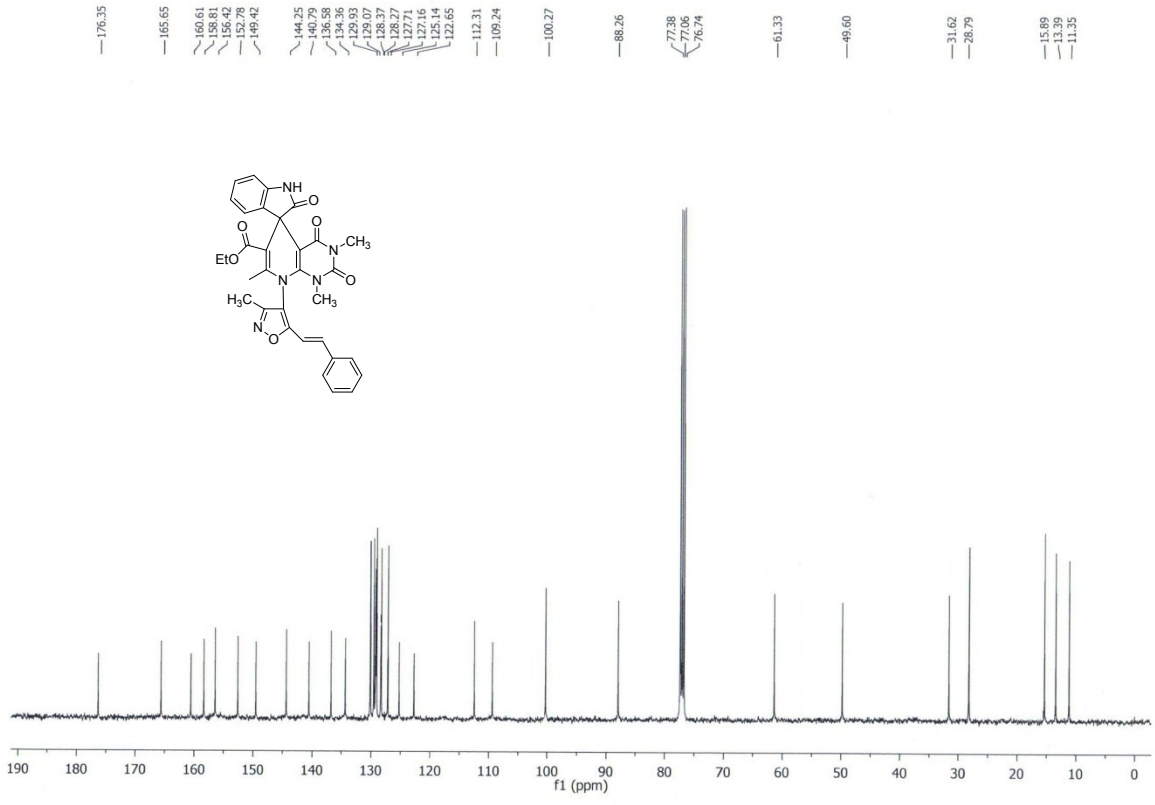
Ethyl-8'-(3-(4-chlorophenyl)-5-phenylisoxazol-4-yl)-1',3',7'-trimethyl-2,2',4'-trioxo-2',3',4',8'-tetrahydro-1'*H*-spiro[indoline-3,5'-pyrido[2,3-*d*]pyrimidine]-6'-carboxylate (8d):



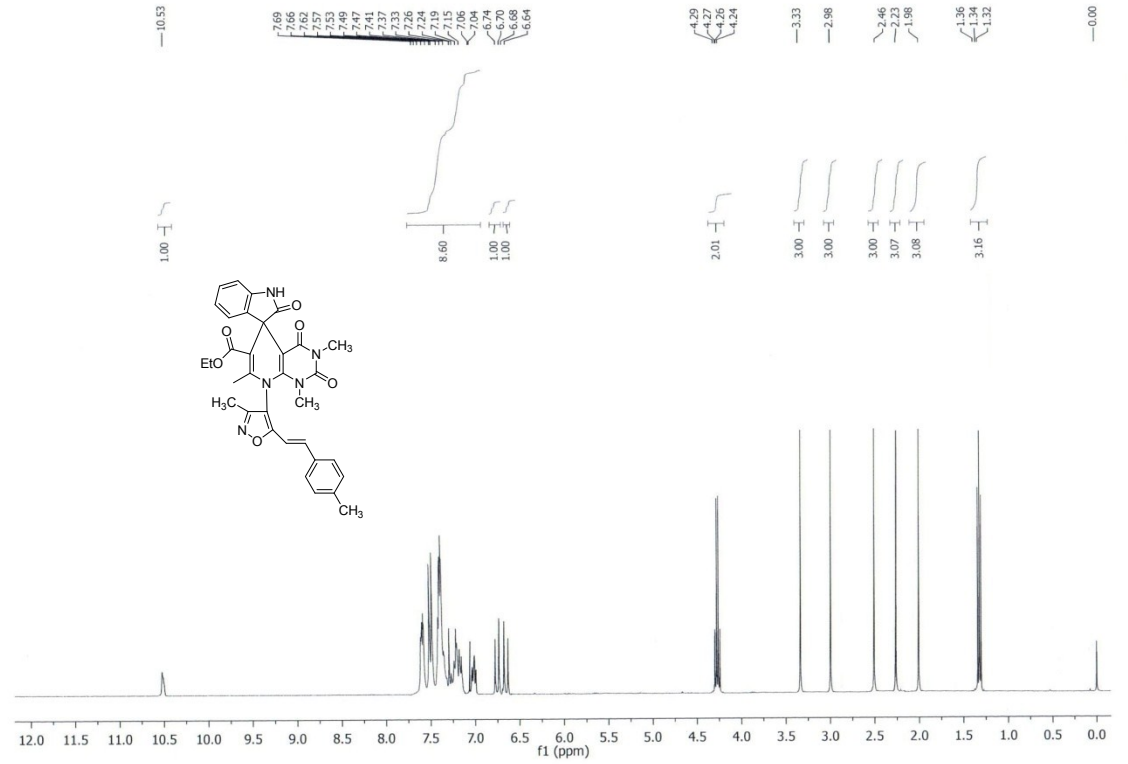
Yield: 80%, mp >300 ^{o}C. IR (KBr): 3449, 3252, 2950, 2849, 1680, 1658, 1540, 1063 cm^{-1}, ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.34 (t, J = 6.2 Hz, 3H), 1.99 (s, 3H), 2.98 (s, 3H), 3.22 (s, 3H), 4.27 (q, J = 6.2 Hz, 2H), 7.10-7.68 (m, 13H), 9.70 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.4, 16.4, 28.8, 31.6, 49.4, 61.3, 90.4, 100.3, 109.7, 112.6, 125.4, 126.5, 127.3, 127.8, 128.2, 128.3, 128.5, 129.3, 129.8, 129.9, 131.3, 134.4, 140.8, 144.4, 149.7, 152.6, 156.6, 158.4, 160.6, 165.5, 176.5. HRMS (ESI-MS) calcd for $C_{35}H_{28}ClN_5NaO_6$ $(M+Na)^+$ 672.1626, found 672.1635.



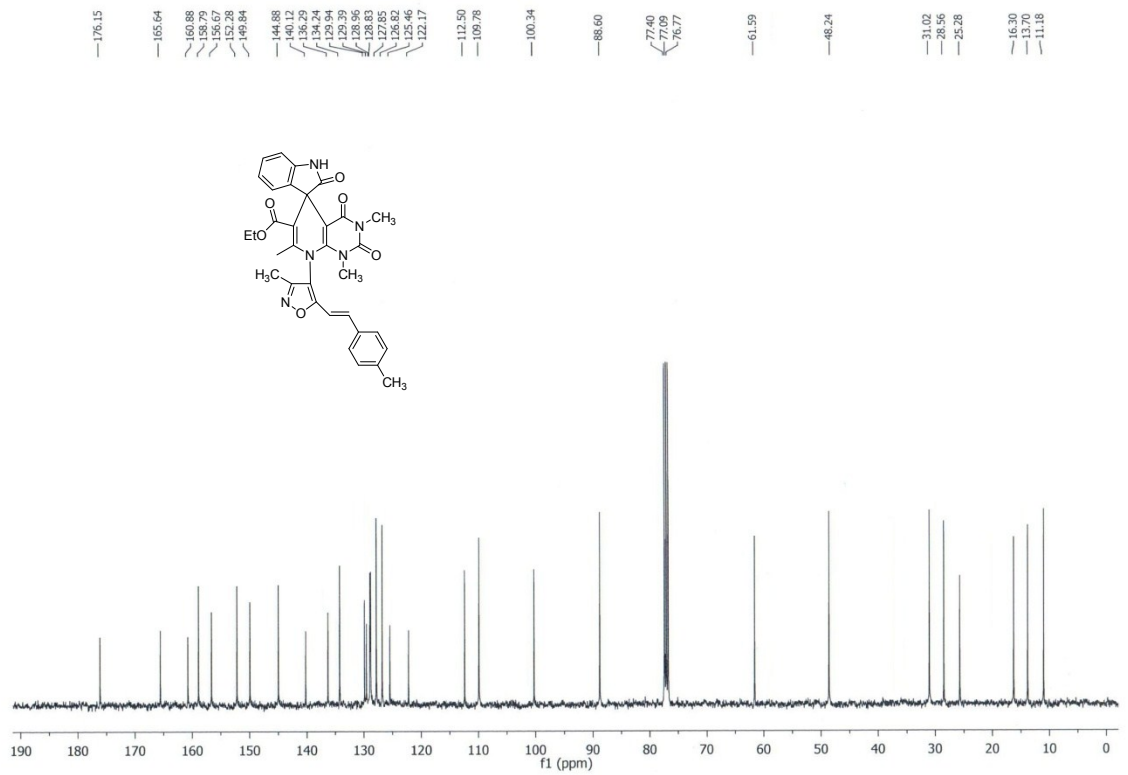
^{1}H NMR of compound 4a



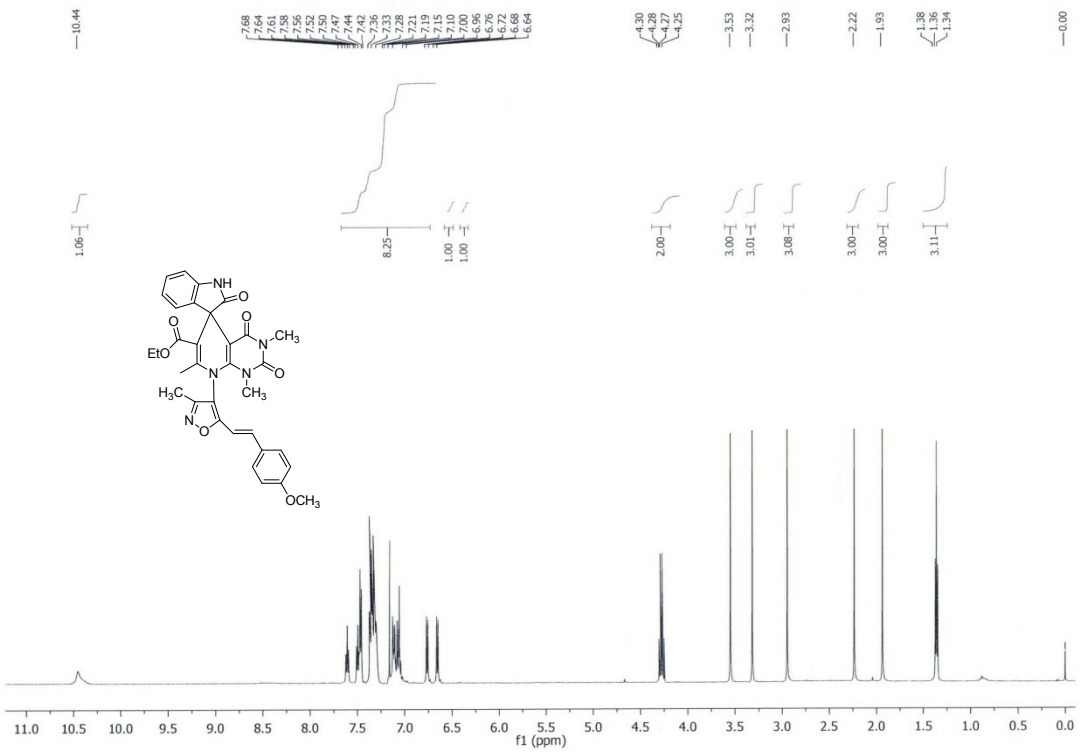
^{13}C NMR of compound 4a



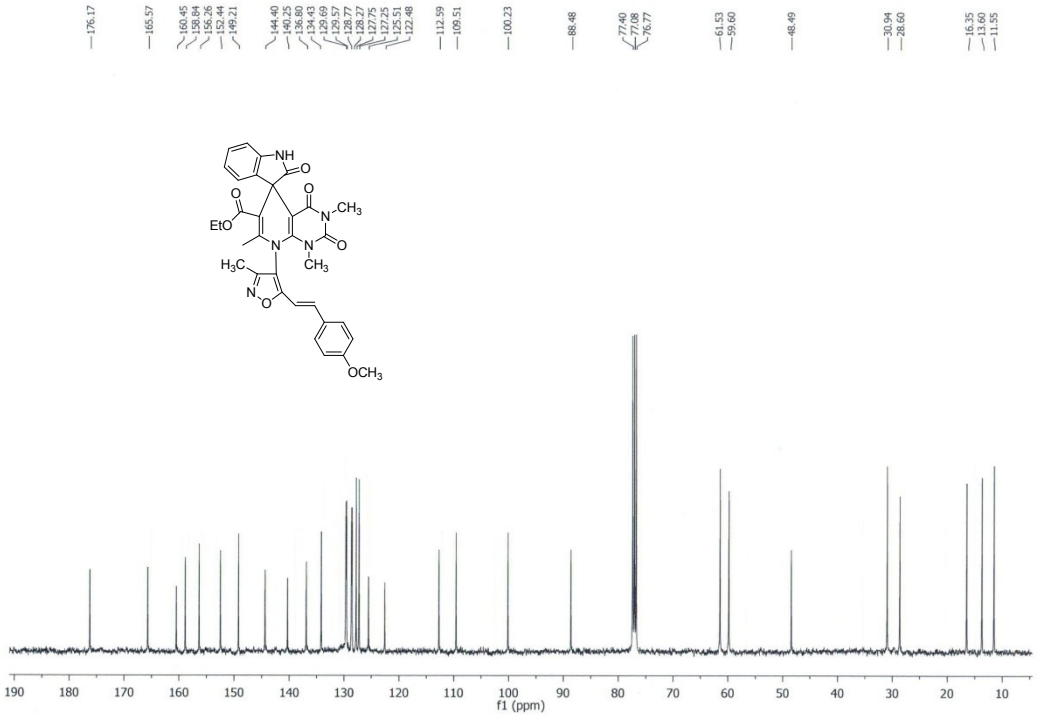
^{1}H NMR of compound 4b



^{13}C NMR of compound 4b

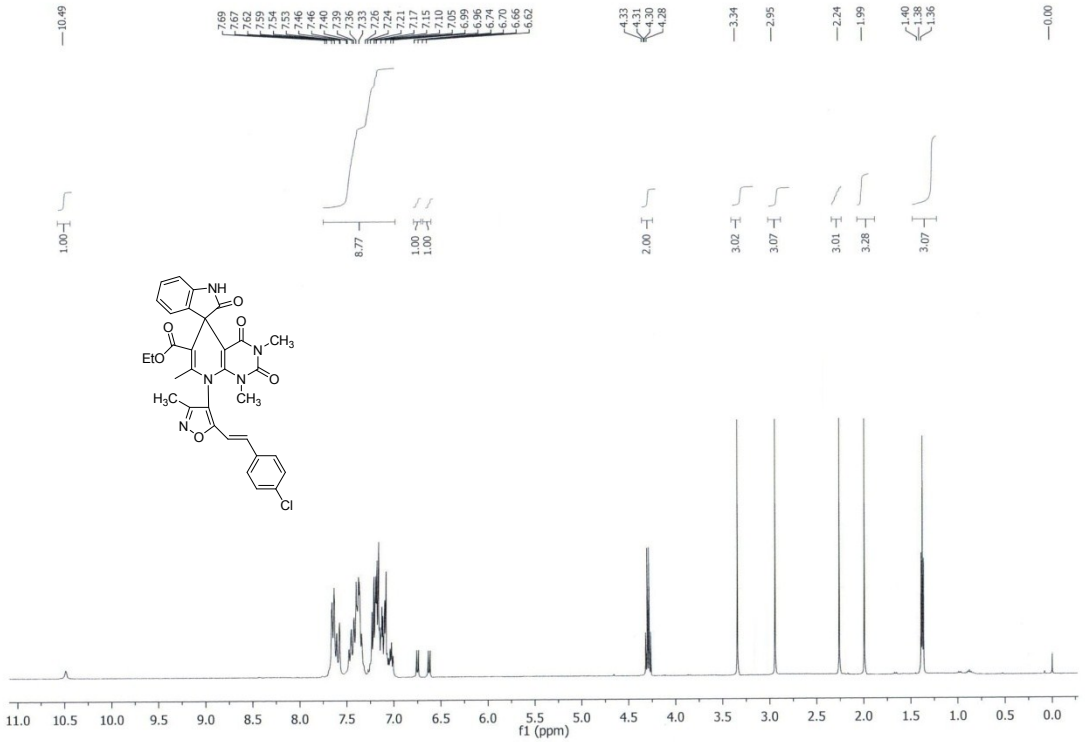


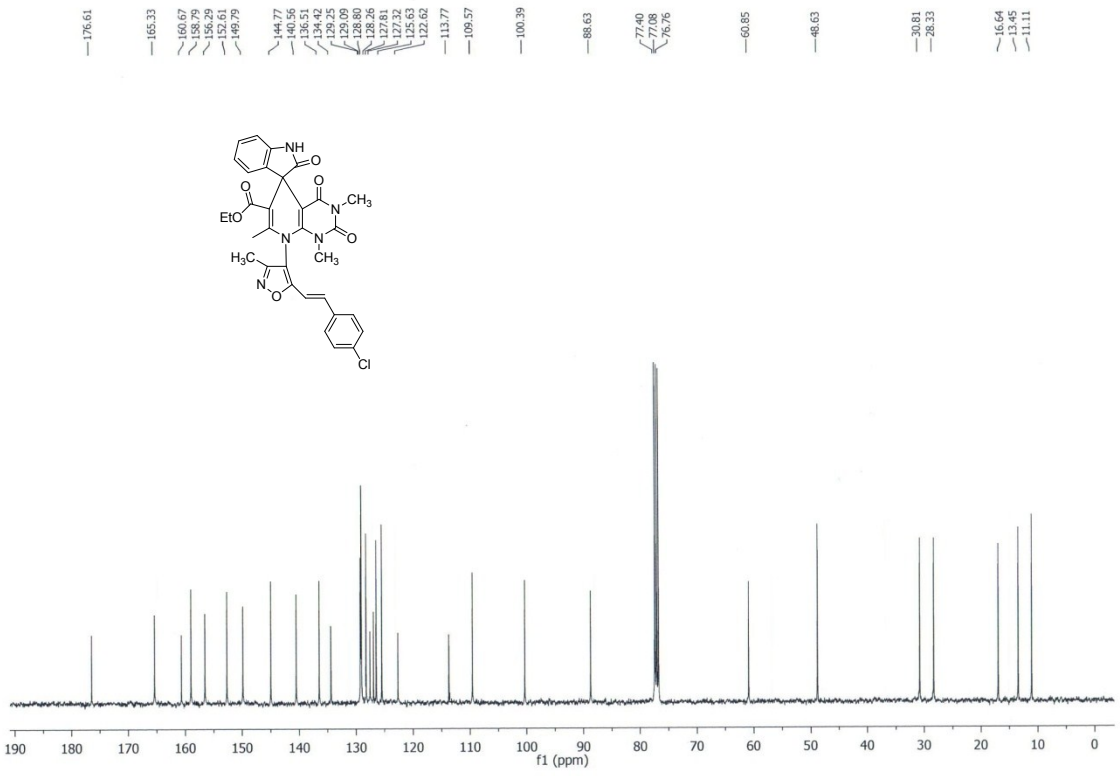
[1]H NMR of compound 4c



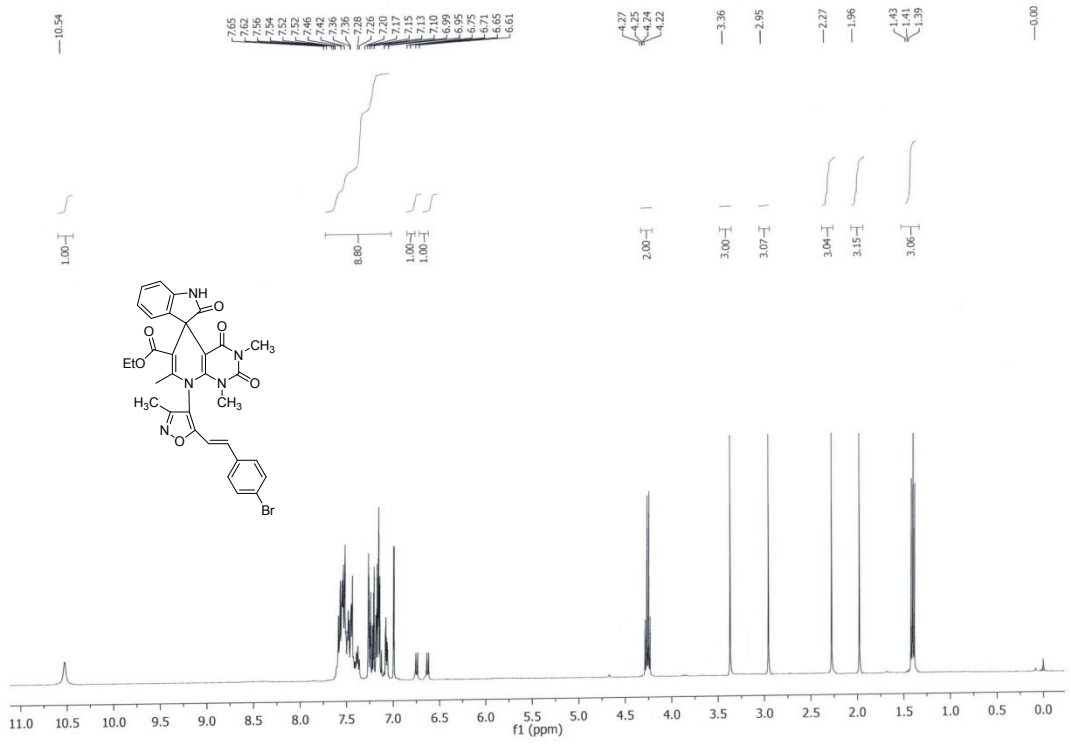
[13]C NMR of compound 4c

^{1}H NMR of compound 4d

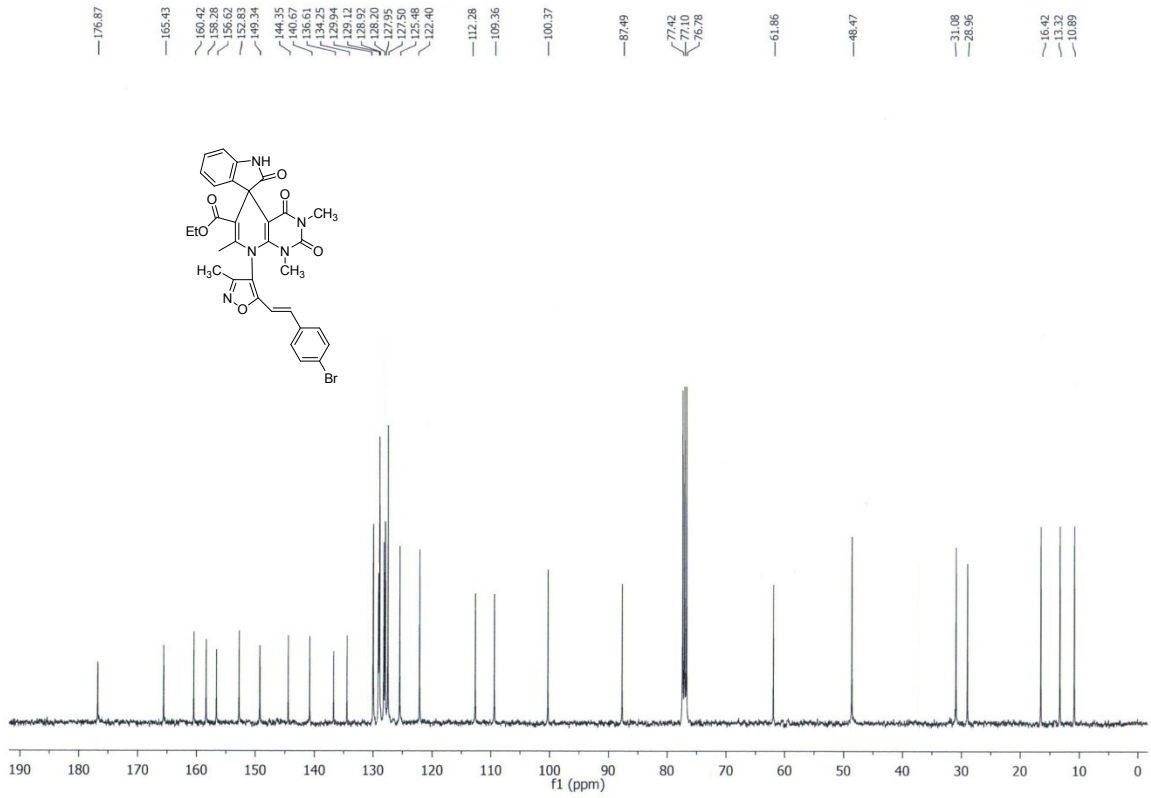




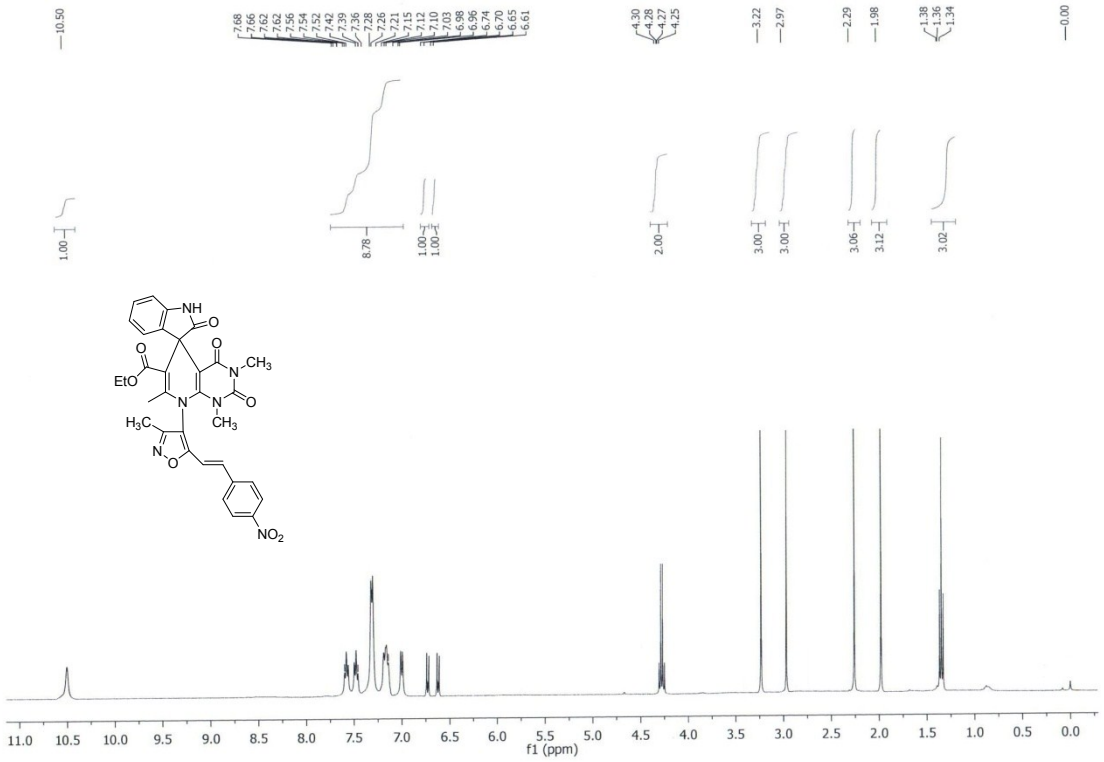
^{13}C NMR of compound 4d



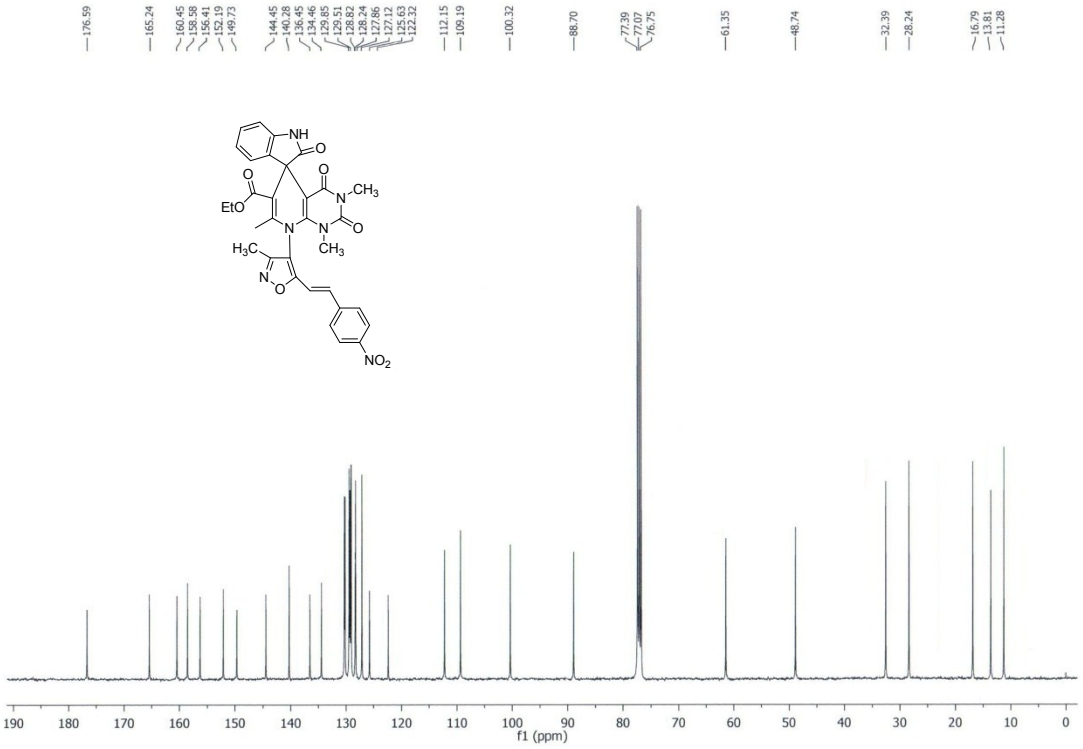
[1]H NMR of compound 4e



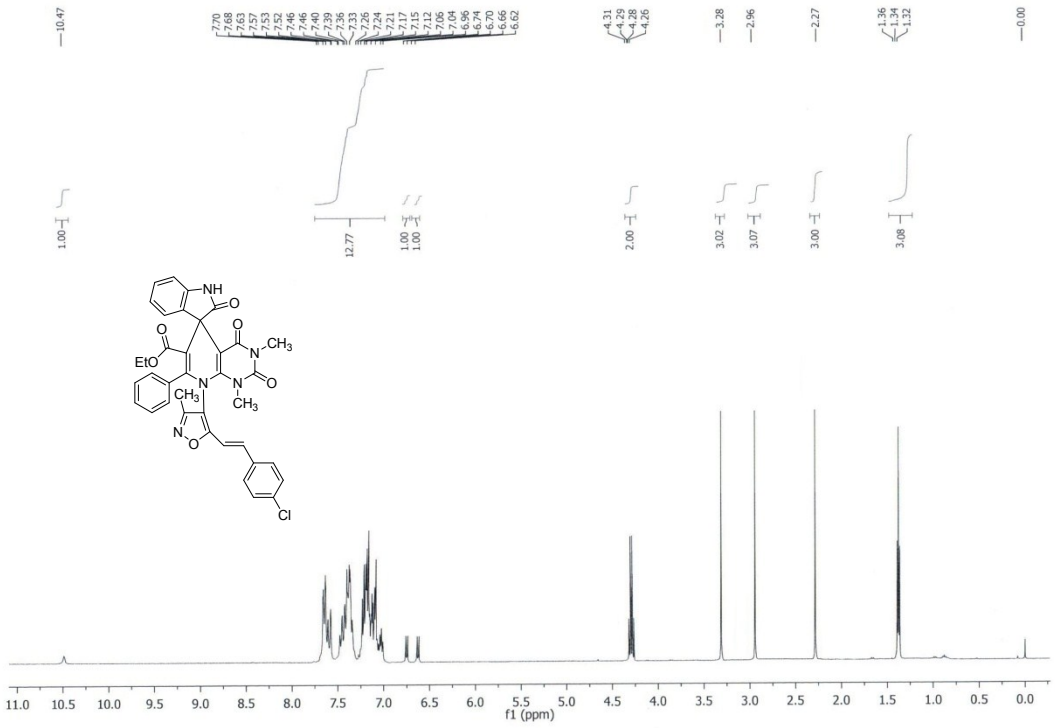
[13]C NMR of compound 4e



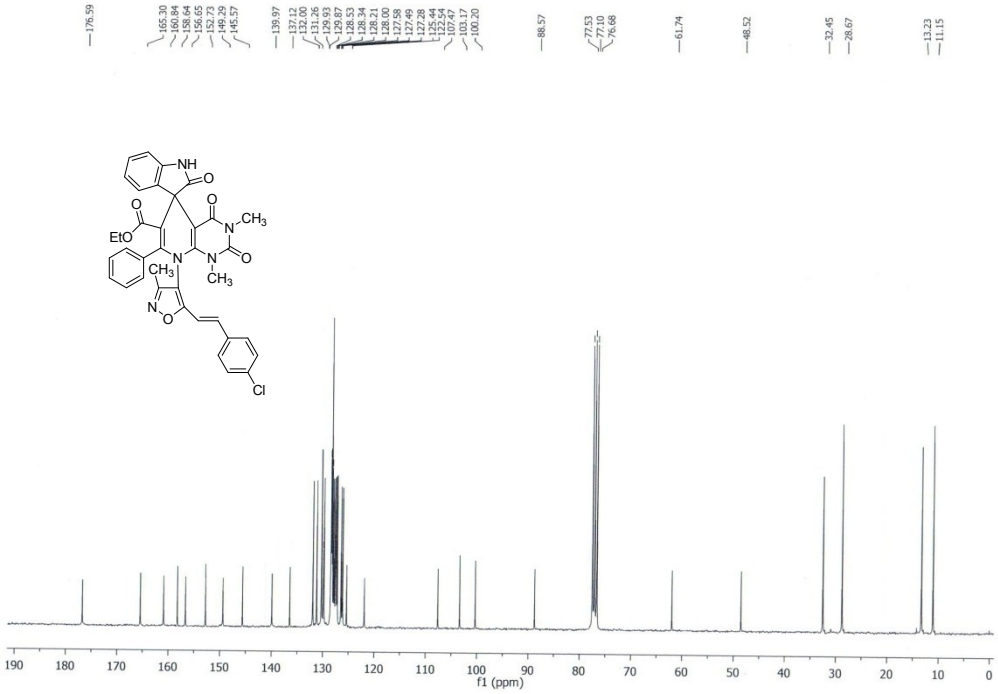
^{1}H NMR of compound 4g



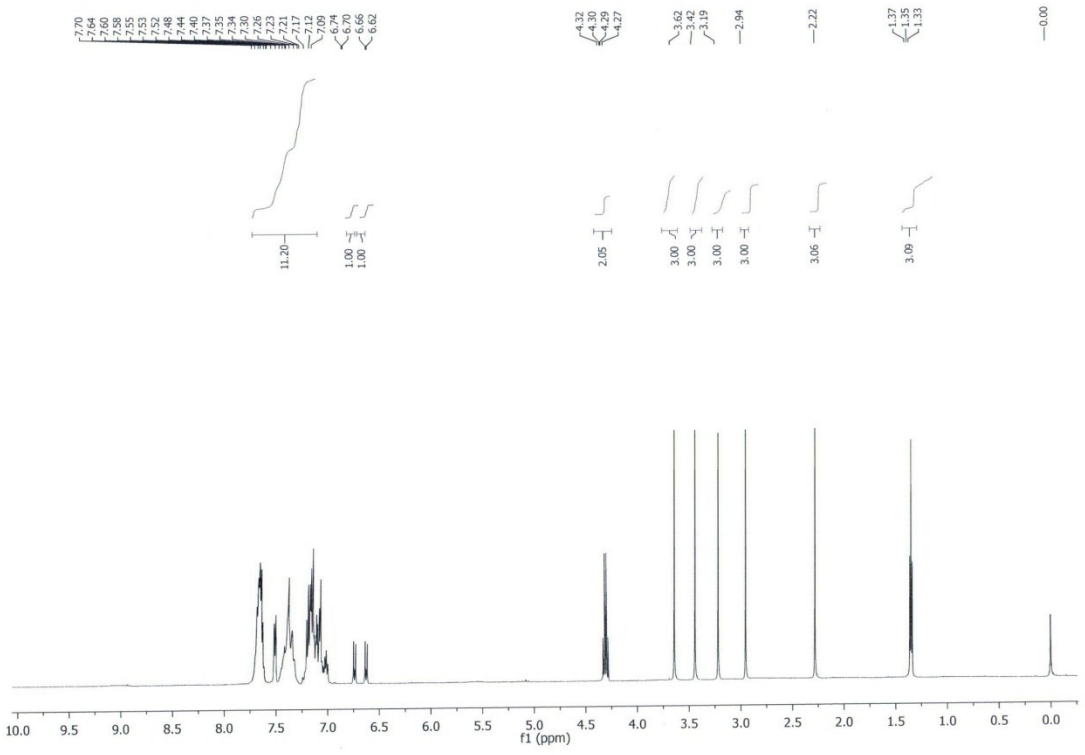
^{13}C NMR of compound 4g



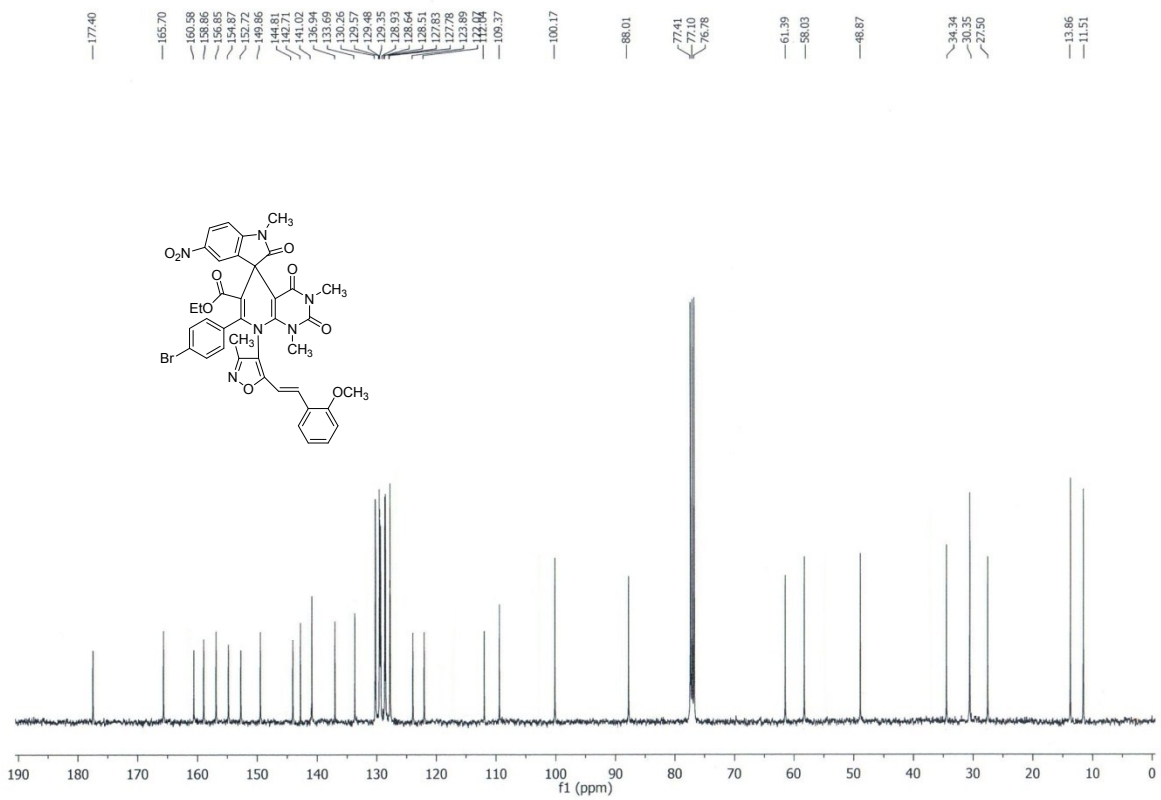
[1]H NMR of compound 4h



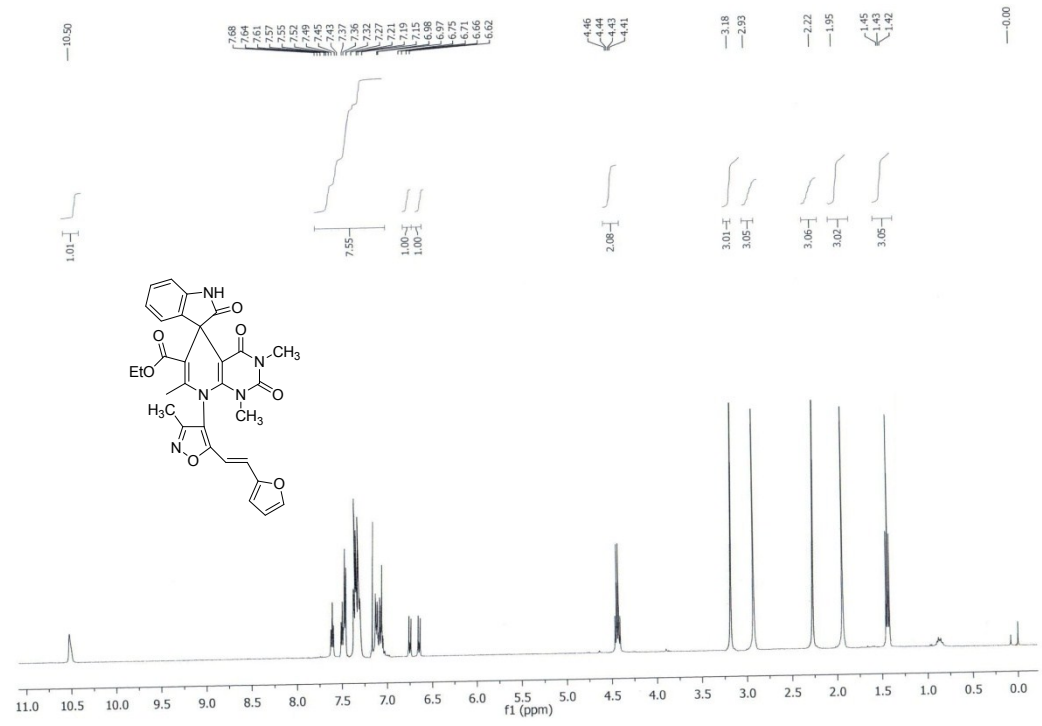
[13]C NMR of compound 4h



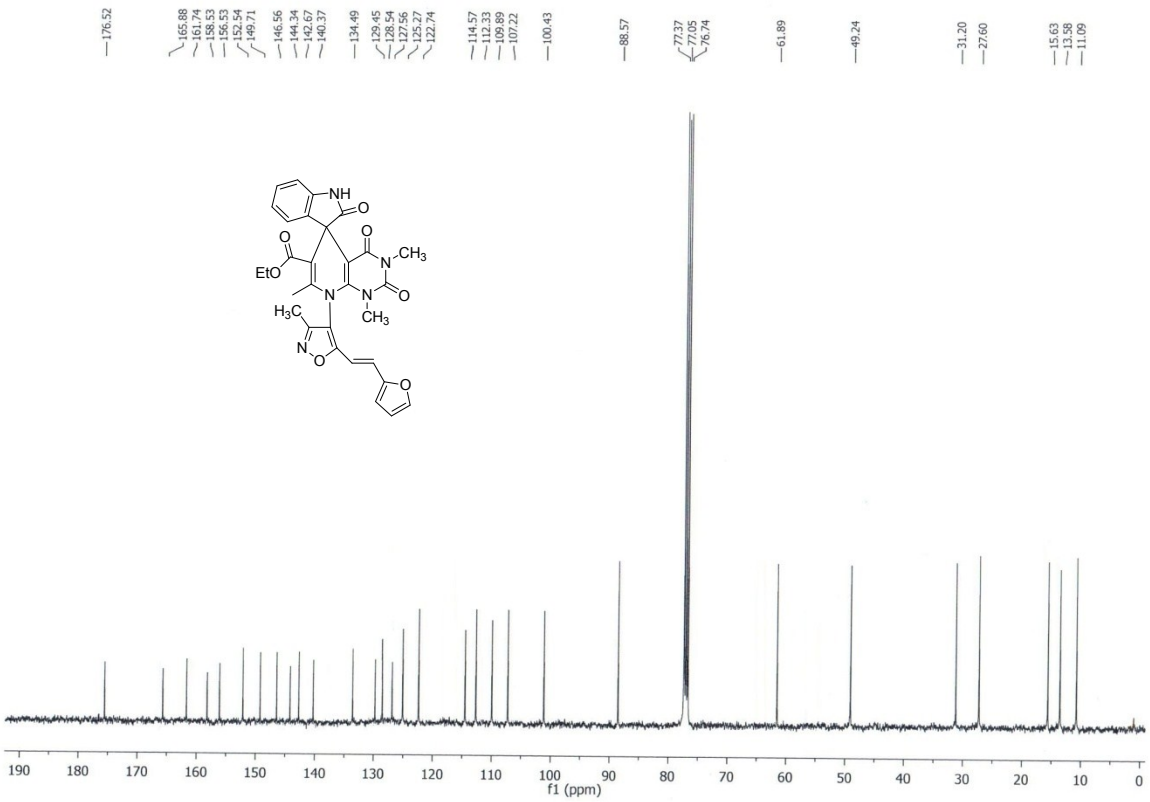
^{1}H NMR of compound 4j



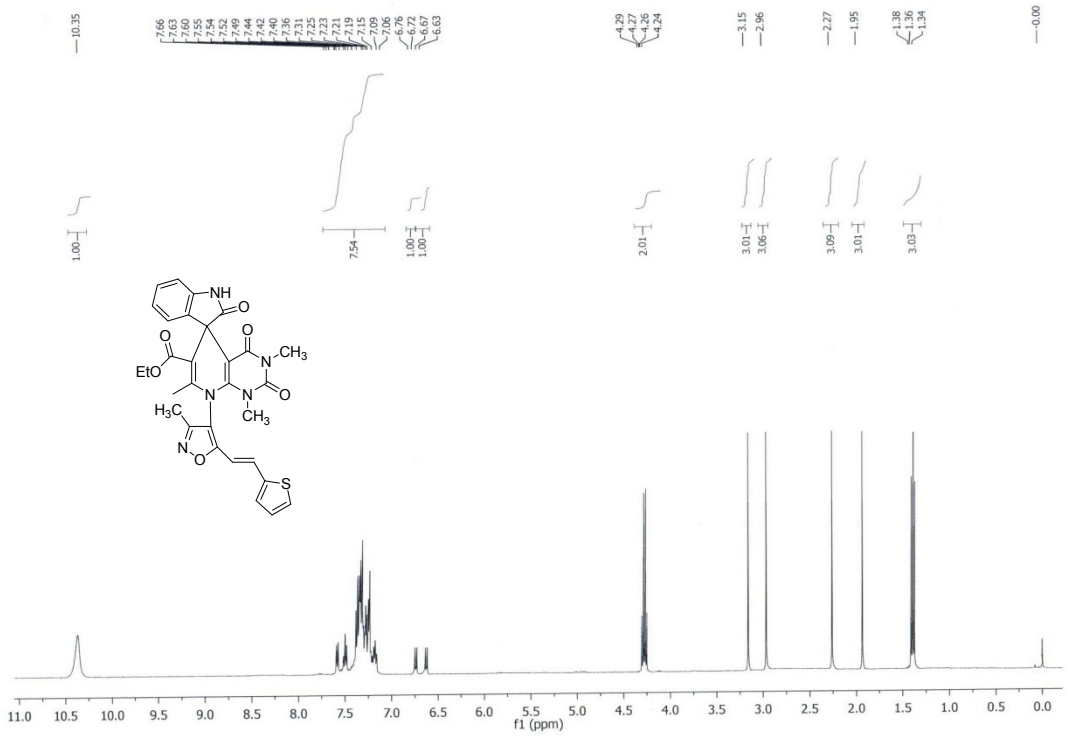
^{13}C NMR of compound 4j



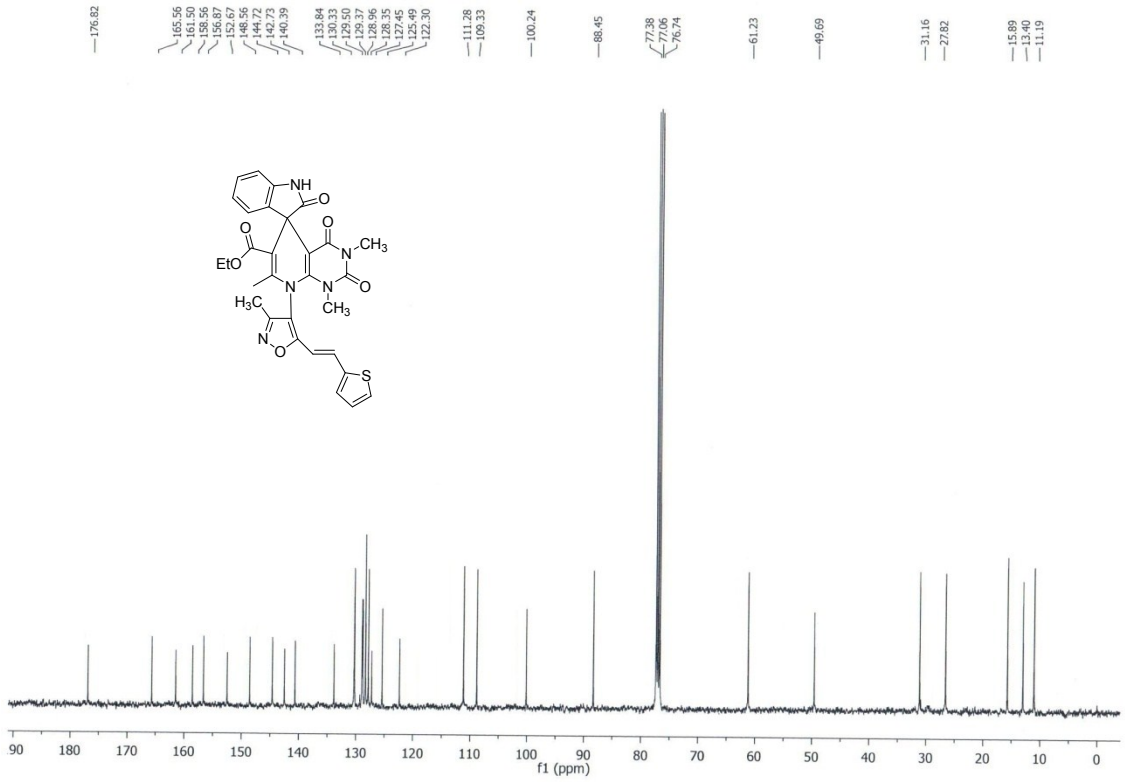
^{1}H NMR of compound 4l



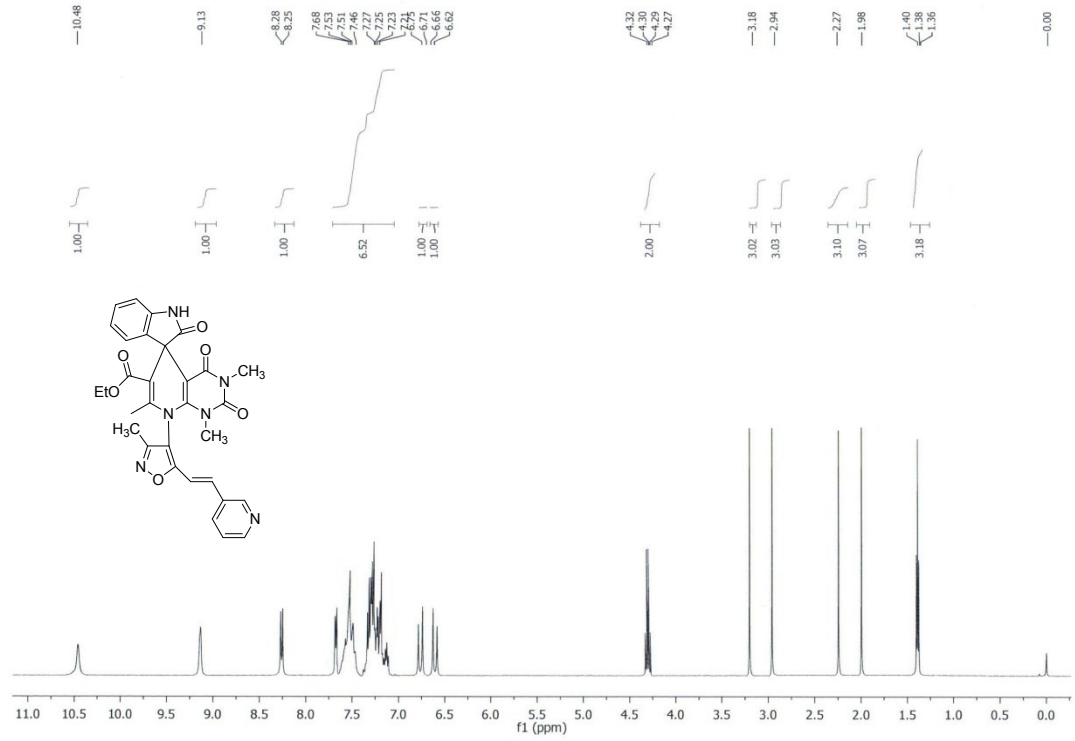
^{13}C NMR of compound 4l



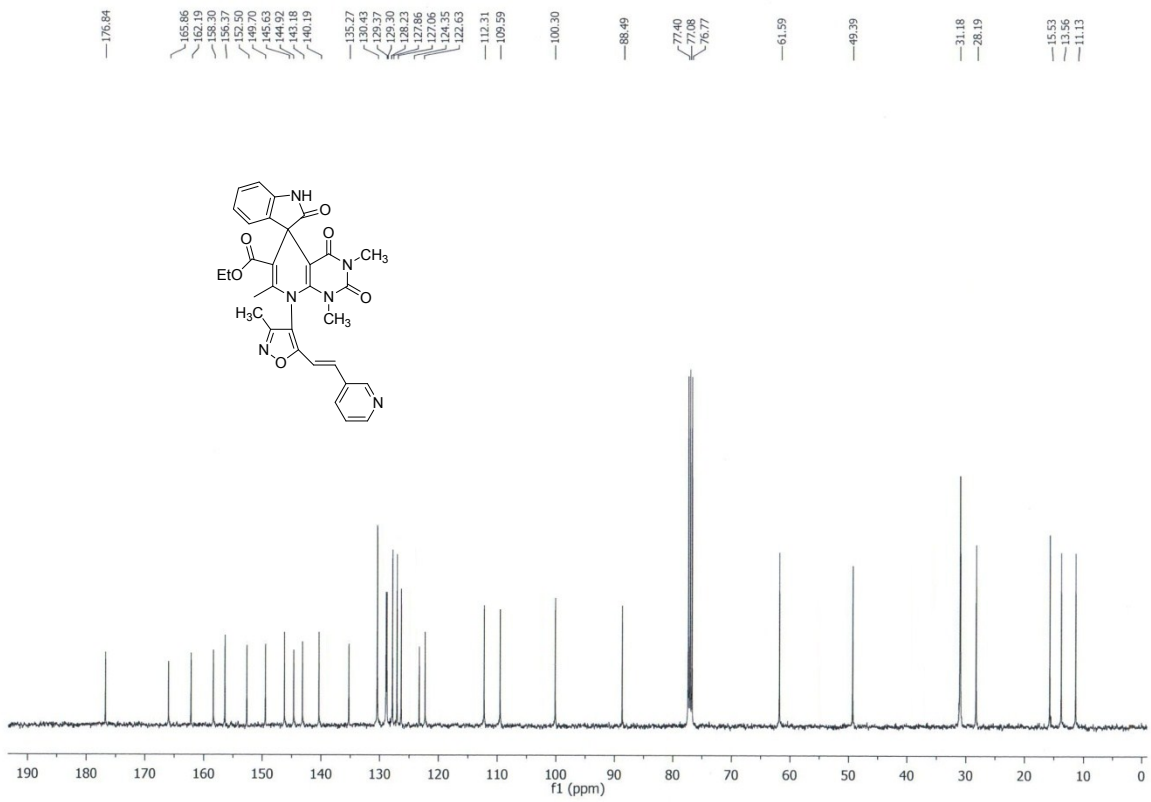
^{1}H NMR of compound 4m



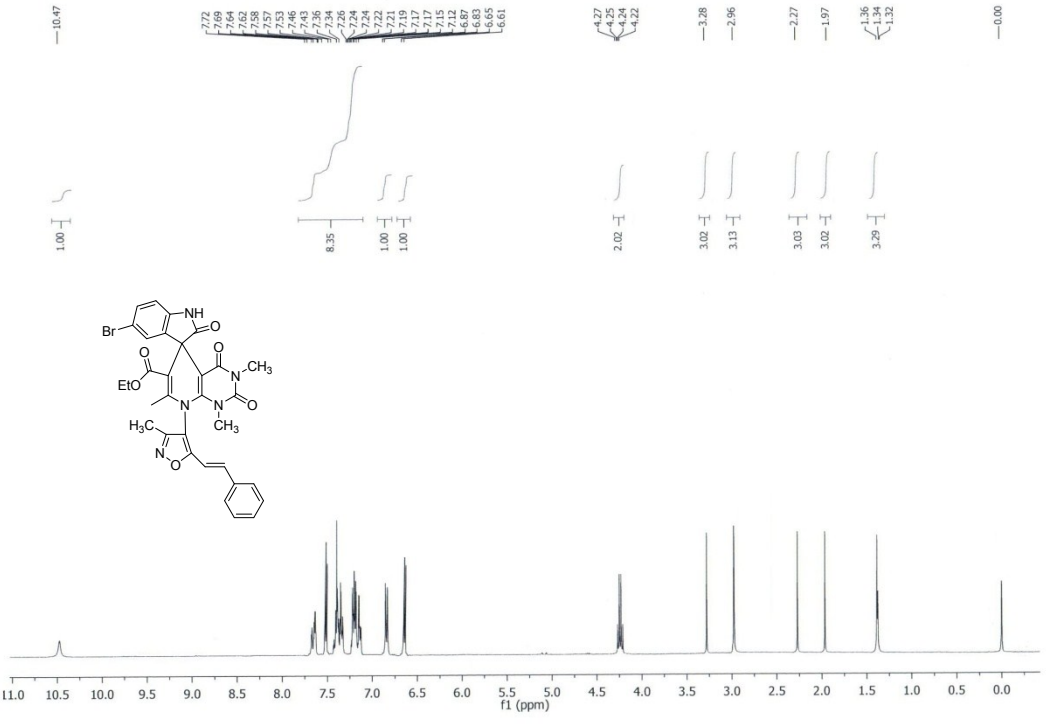
^{13}C NMR of compound 4m



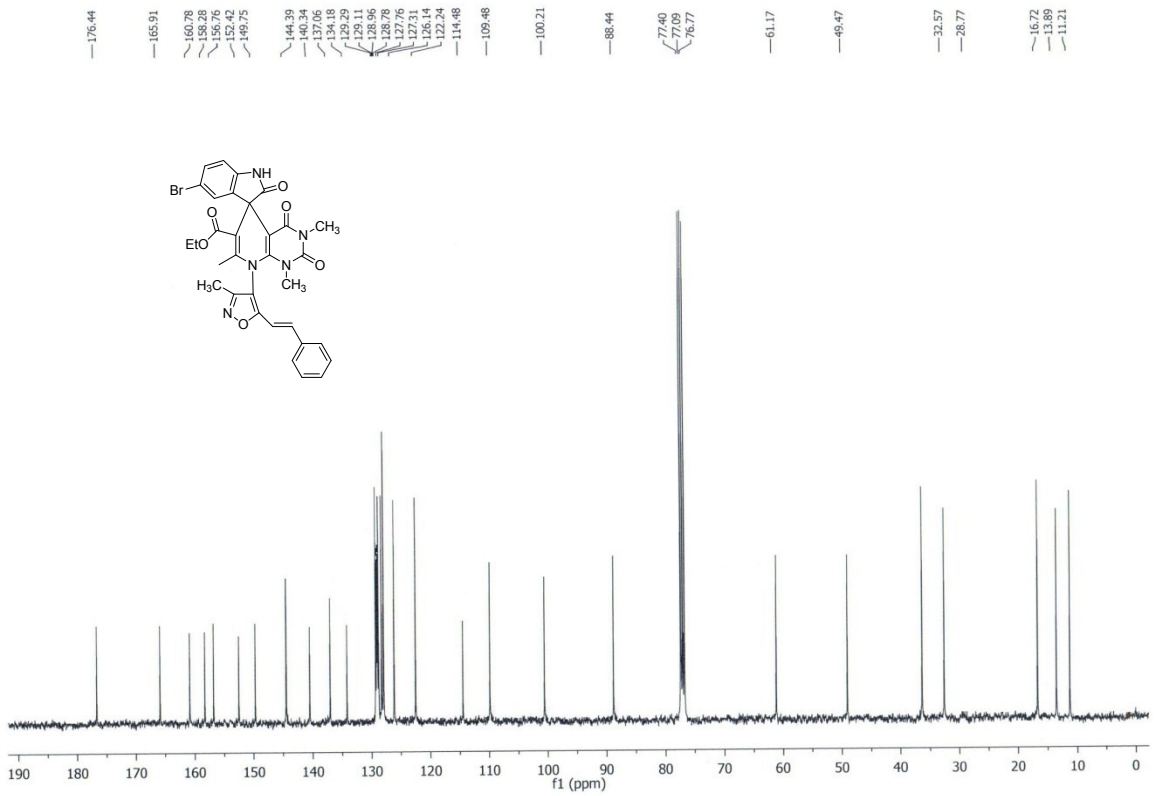
^{1}H NMR of compound 4n



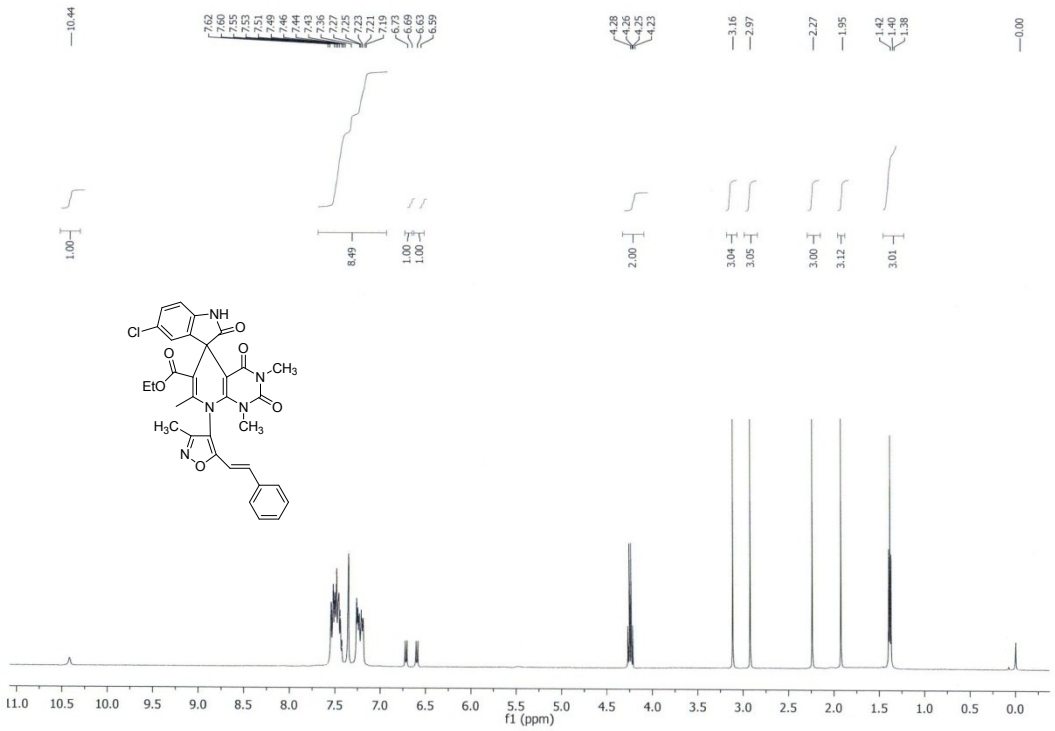
^{13}C NMR of compound 4n



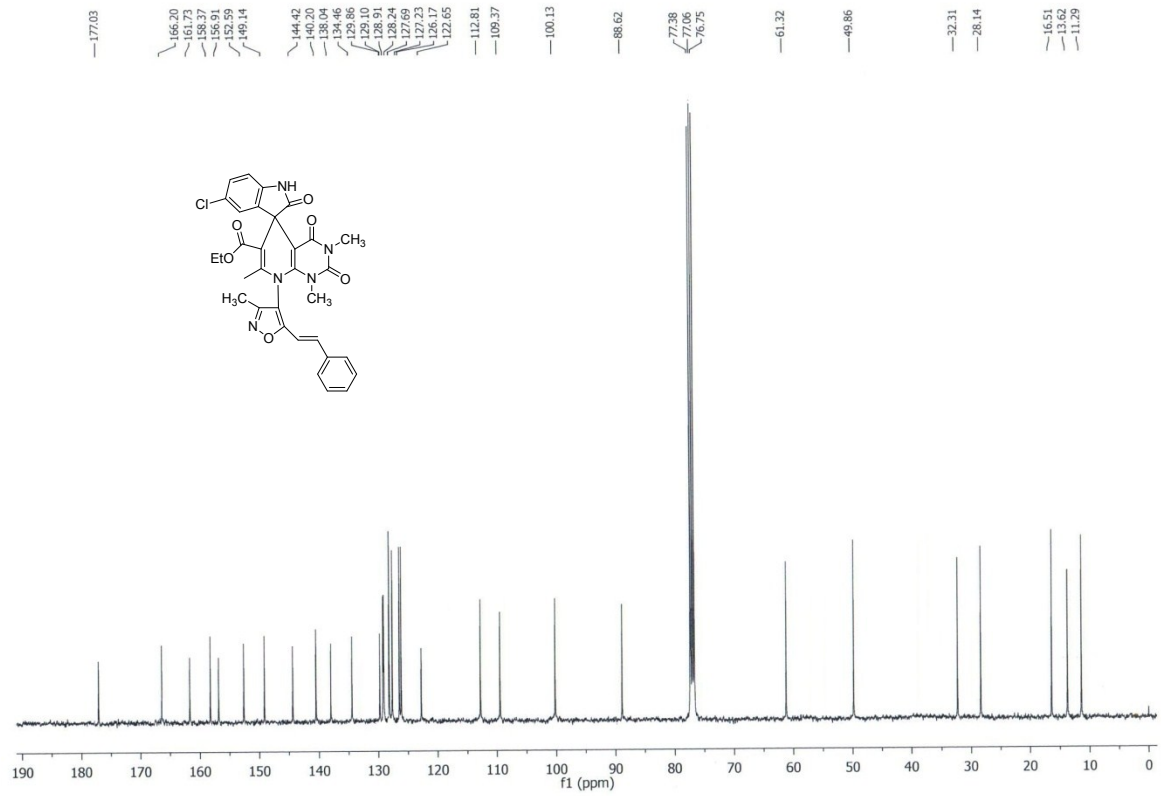
^{1}H NMR of compound 4o



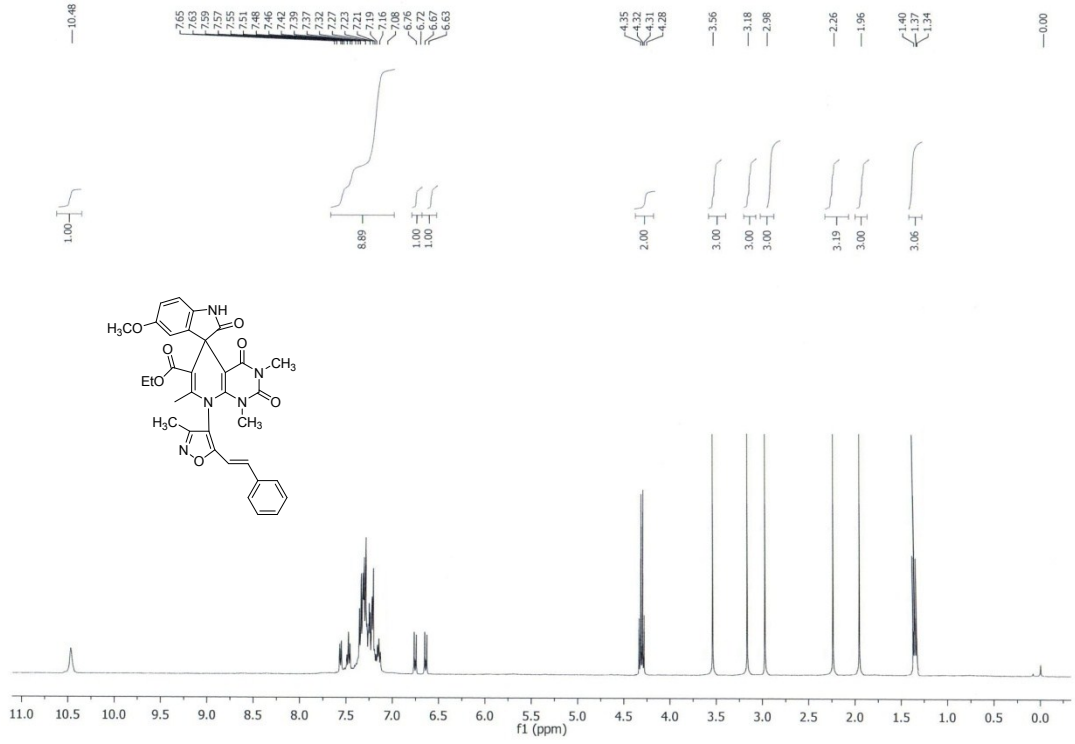
^{13}C NMR of compound 4o



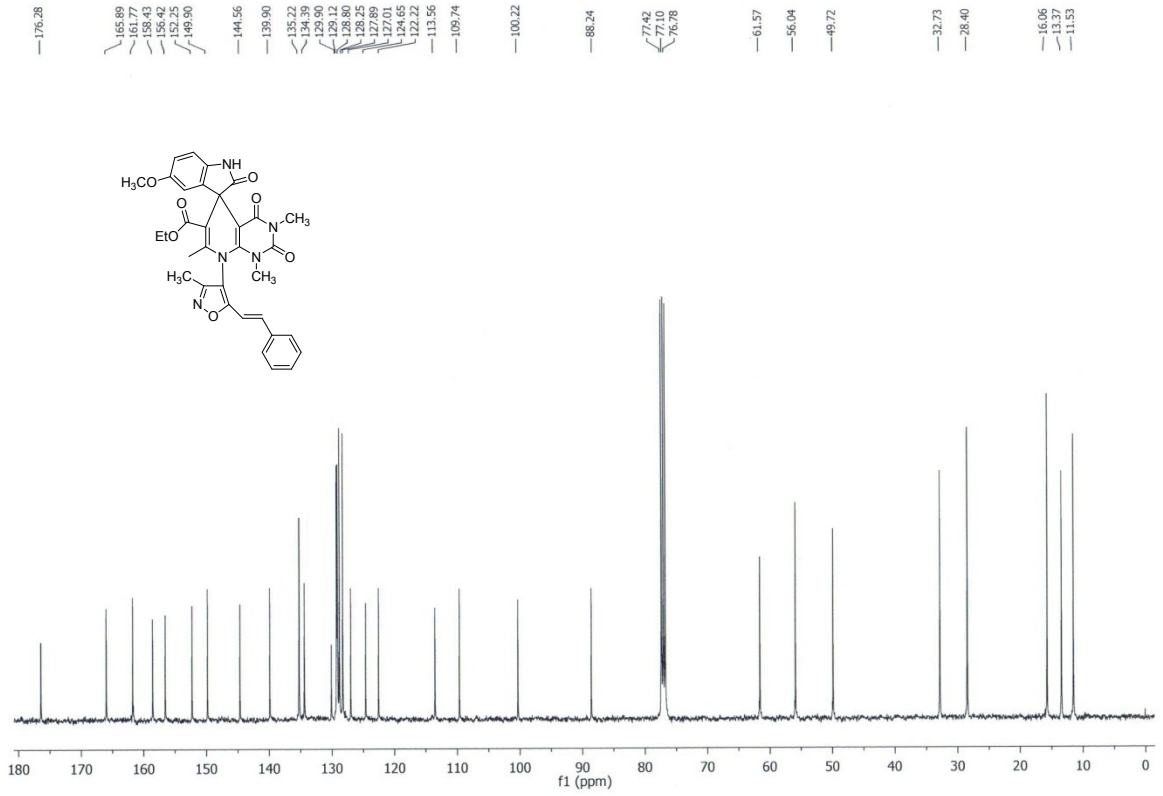
^{1}H NMR of compound 4p



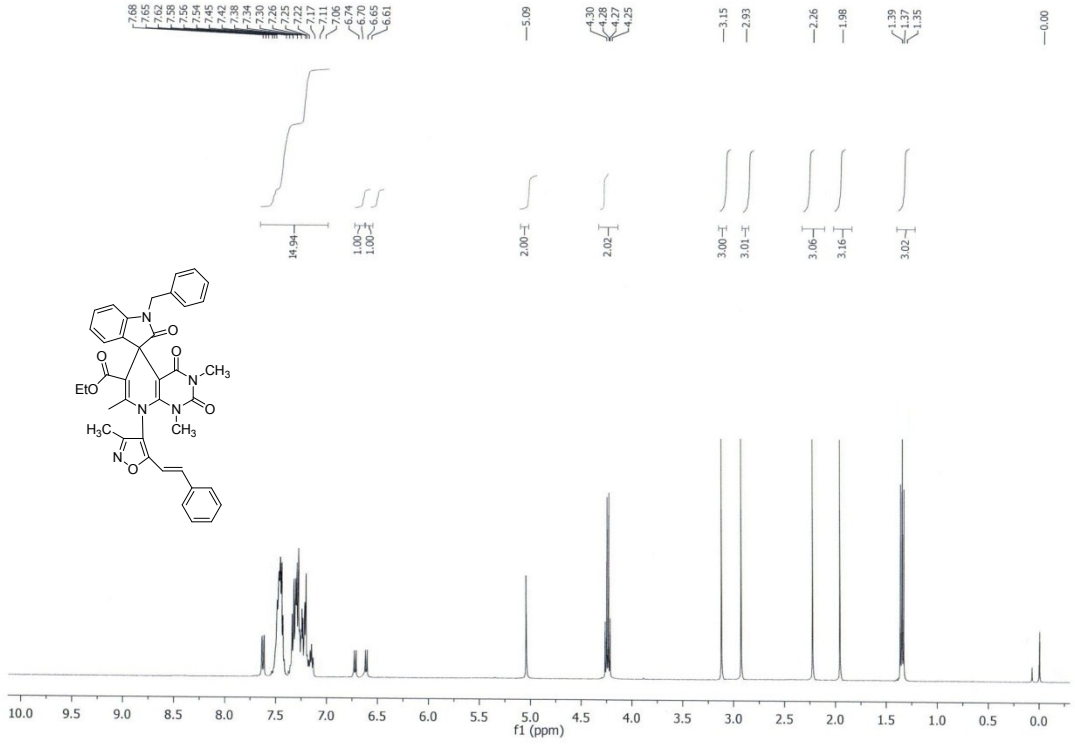
^{13}C NMR of compound 4p



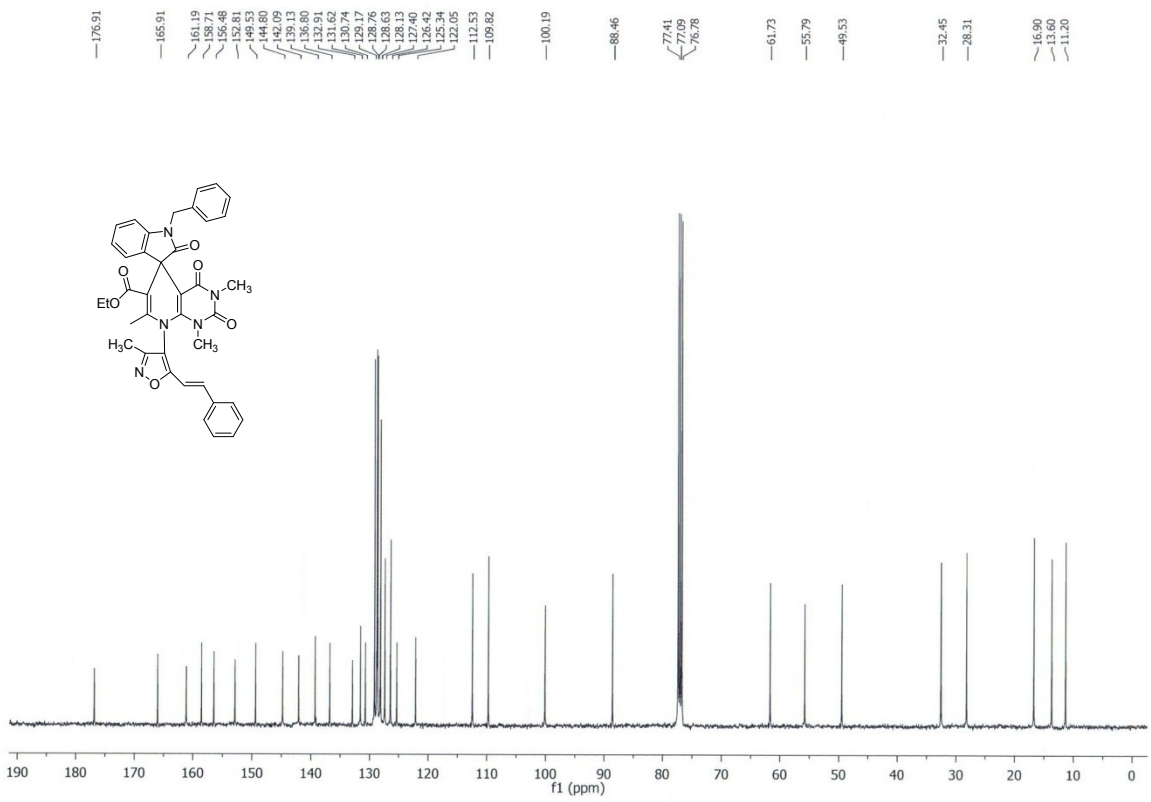
^{1}H NMR of compound 4q



^{13}C NMR of compound 4q

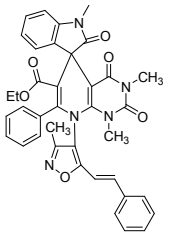


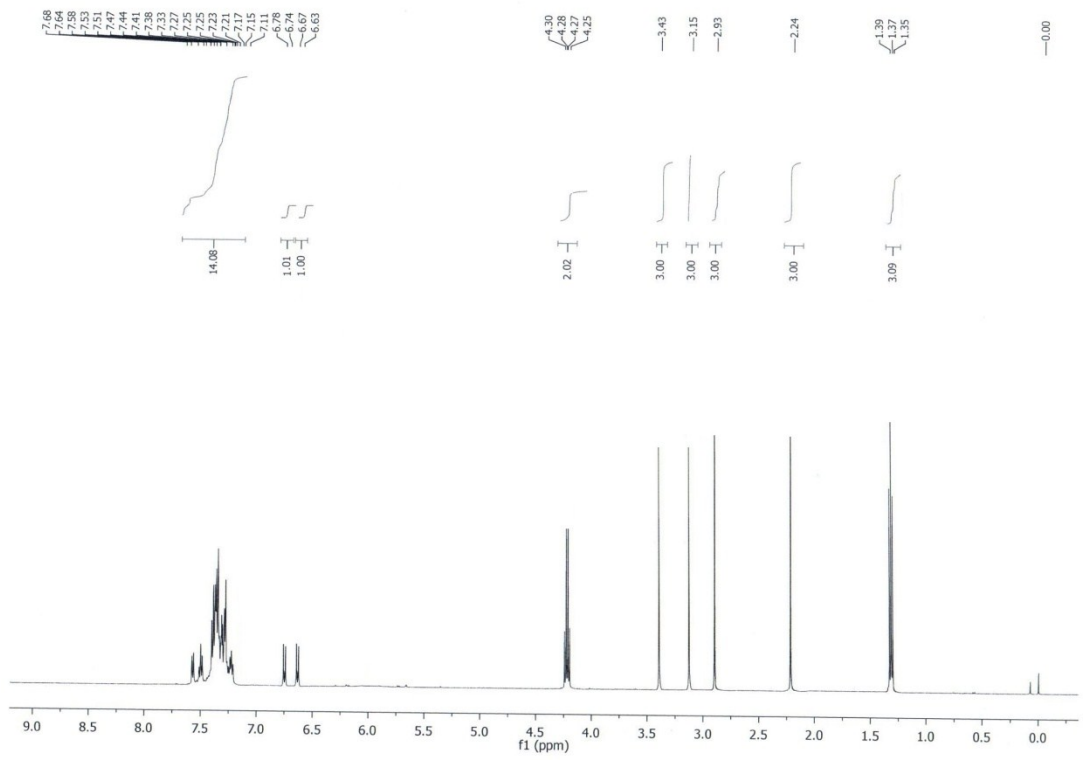
^{1}H NMR of compound 4t

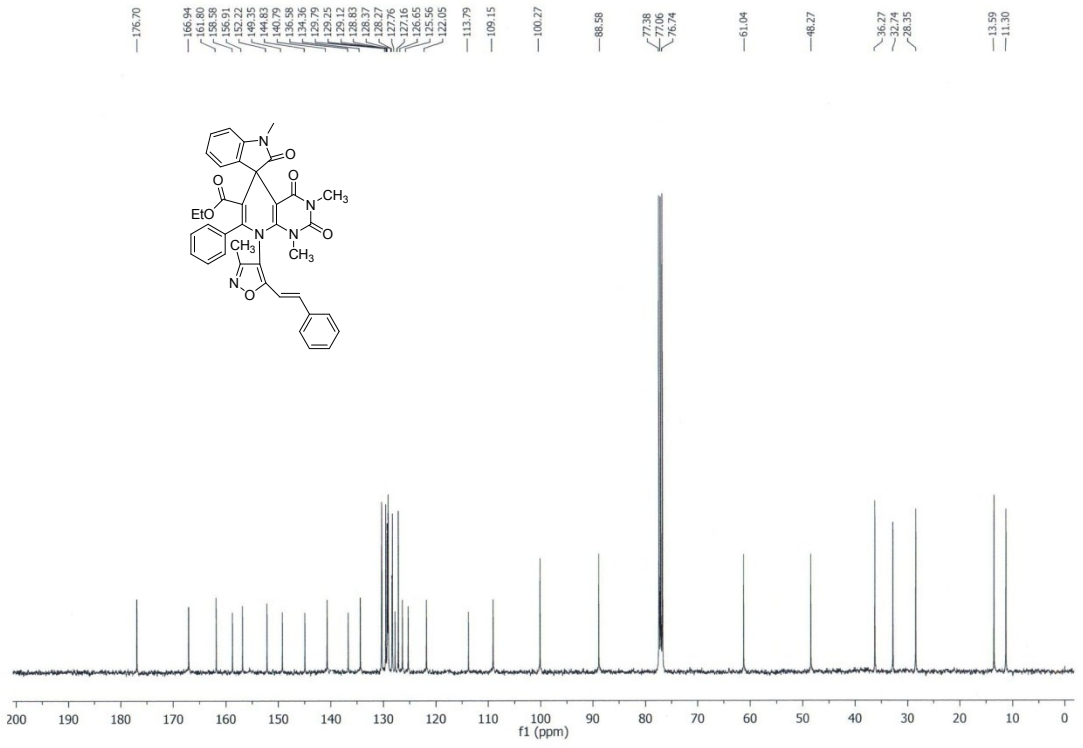


^{13}C NMR of compound 4t

^{1}H NMR of compound 4u



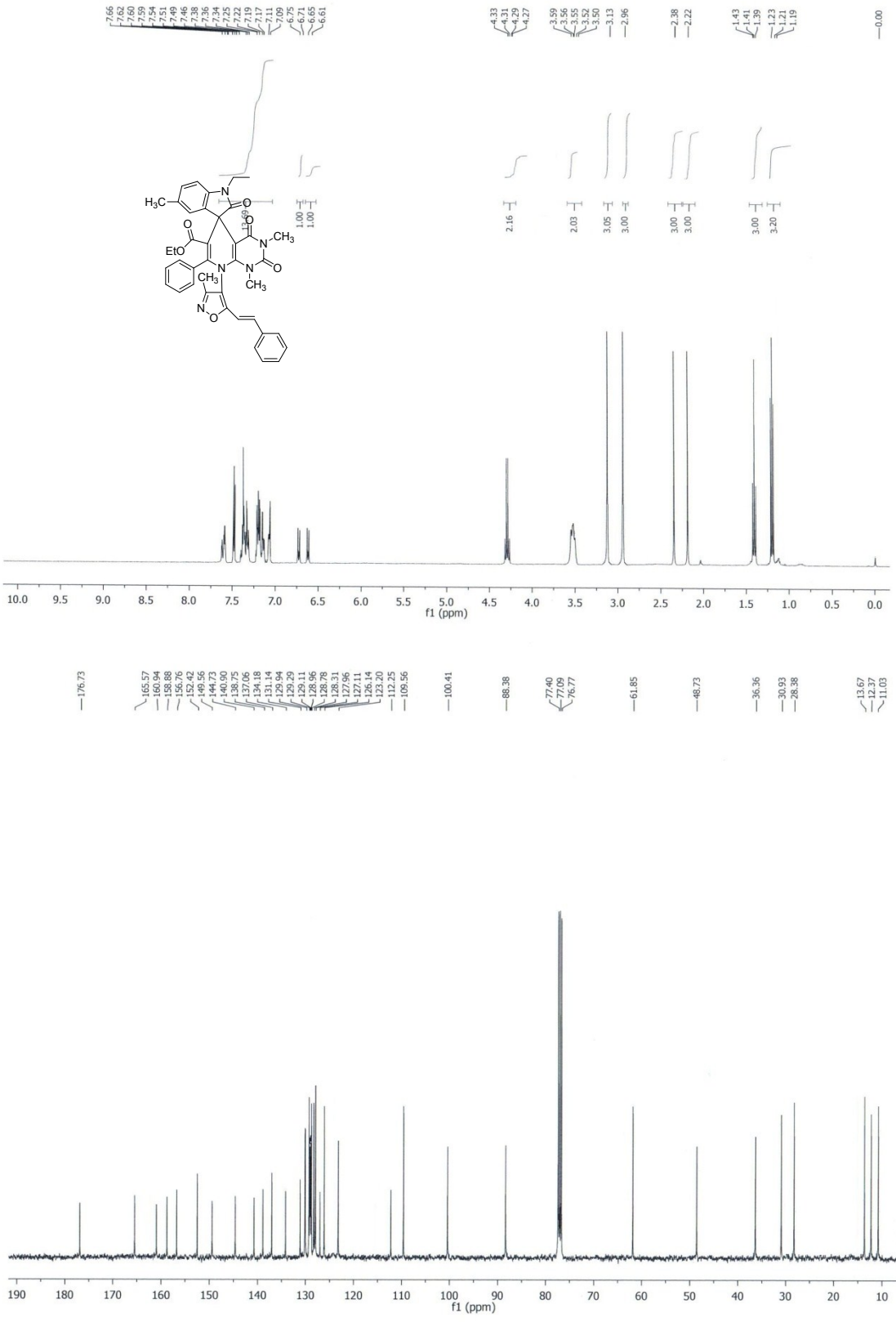




^{13}C

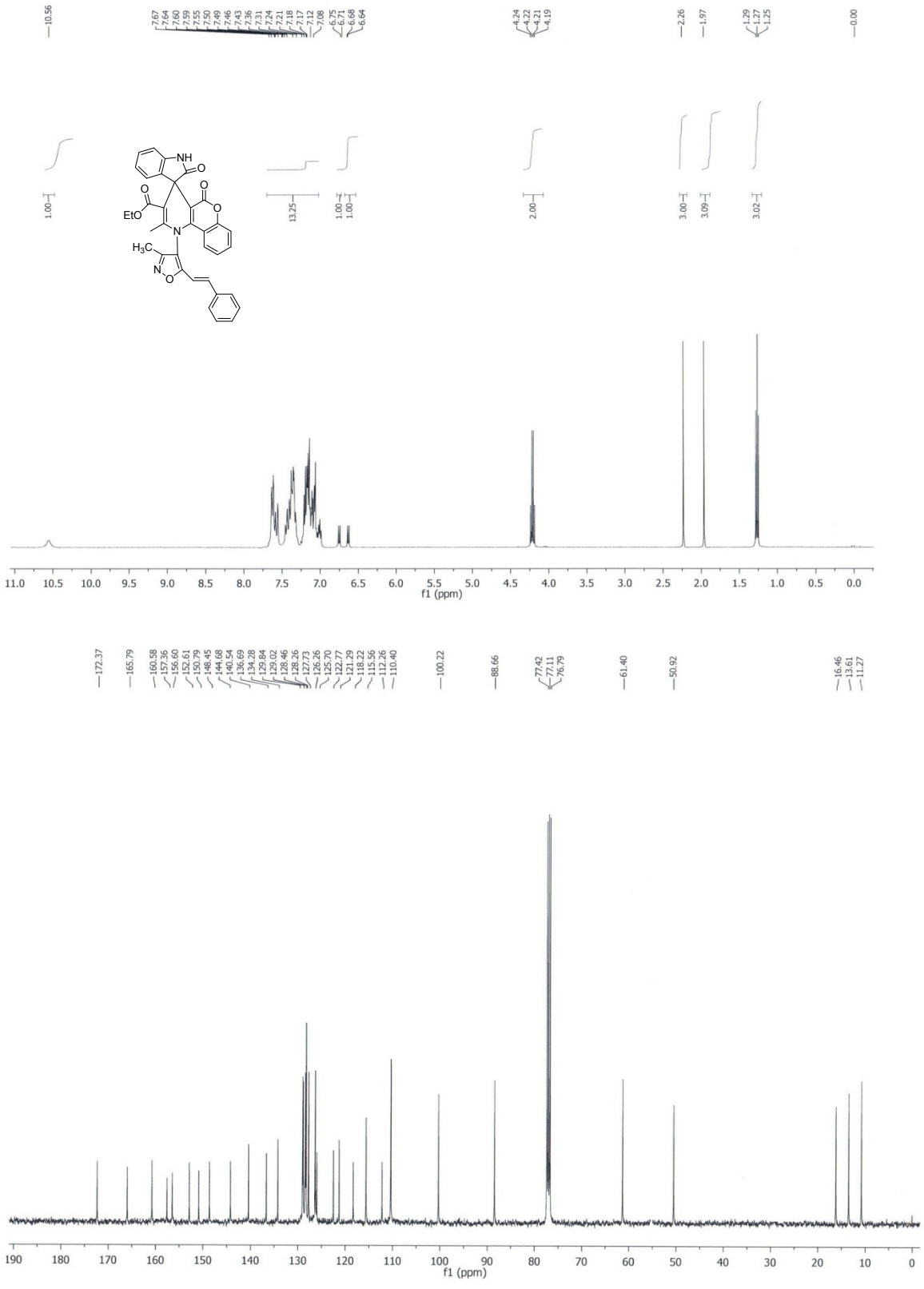
NMR of compound 4u

^{1}H NMR of compound 4v

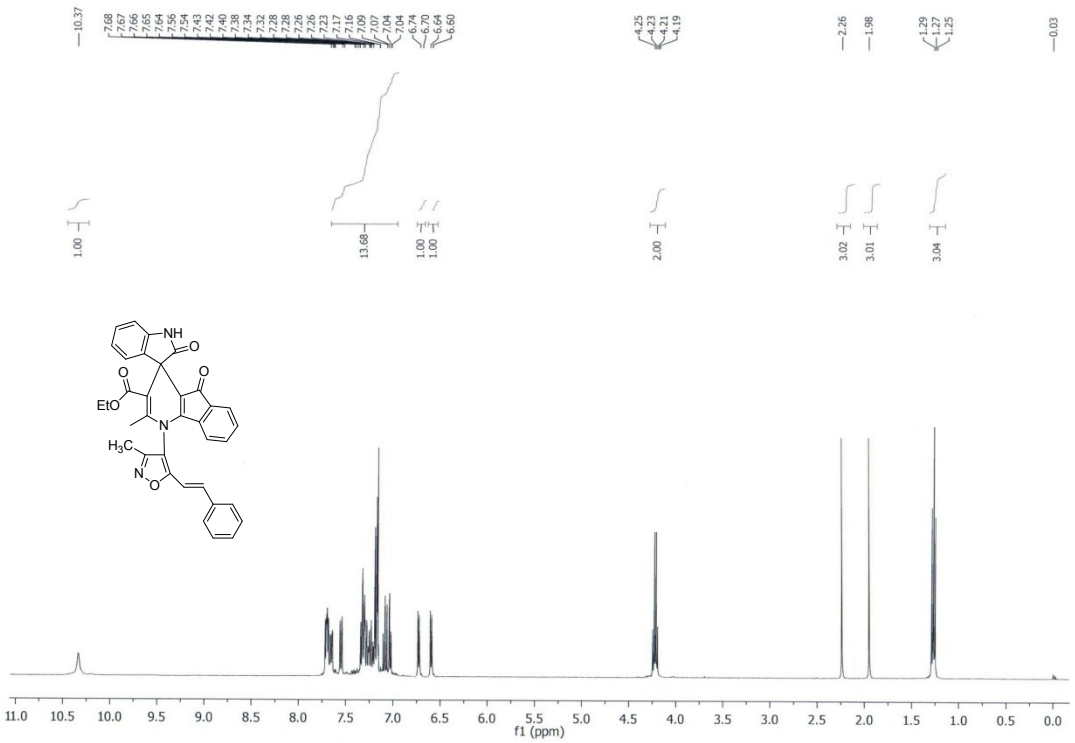


^{13}C NMR of compound 4v

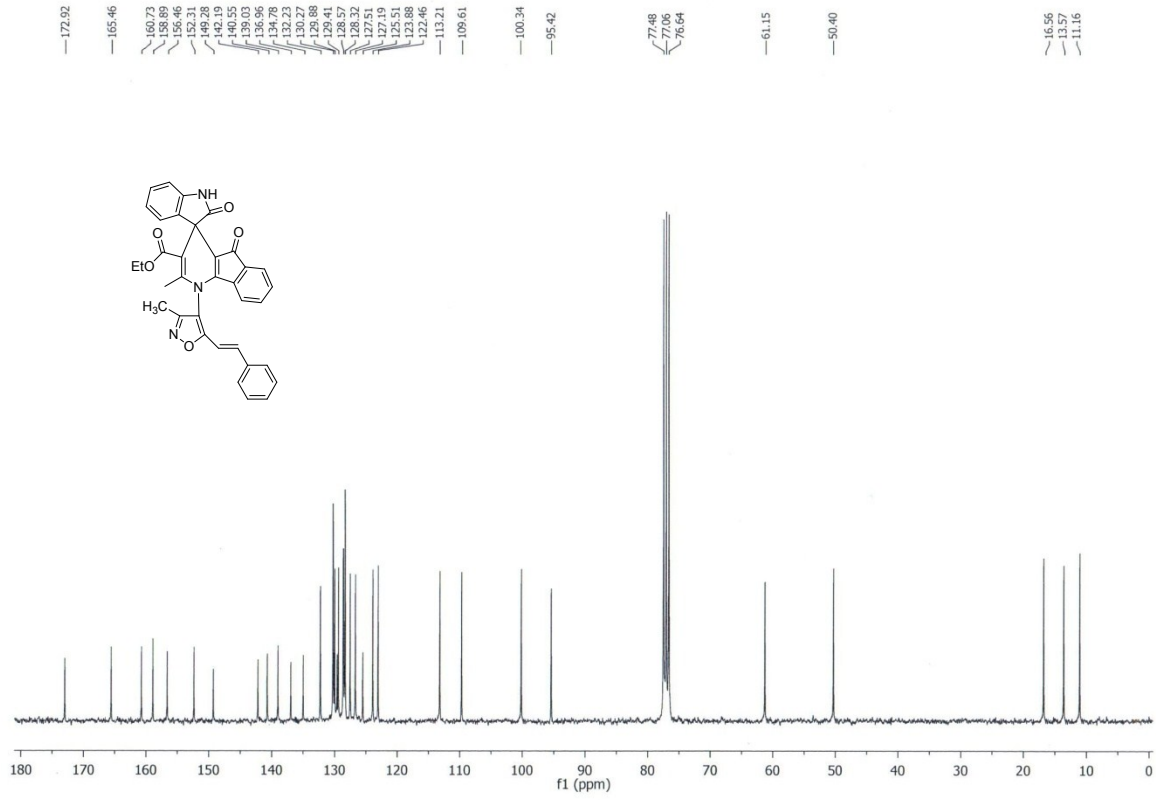
^{1}H NMR of compound 6a



^{13}C NMR of compound 6a

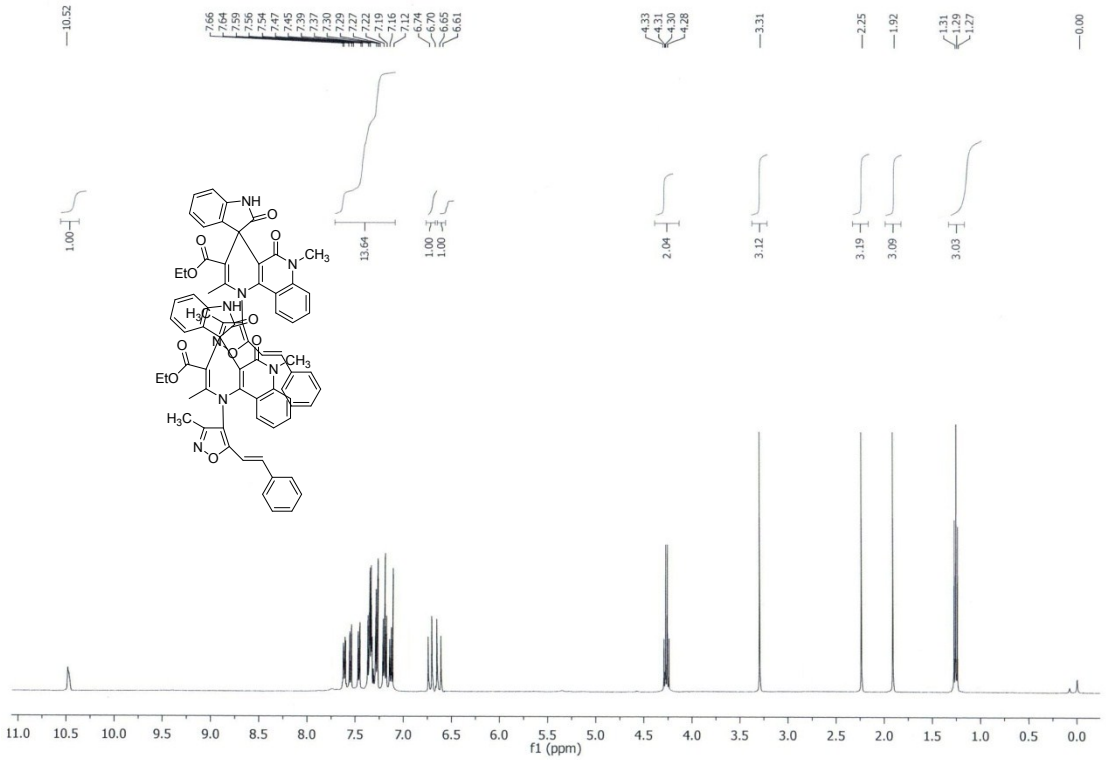


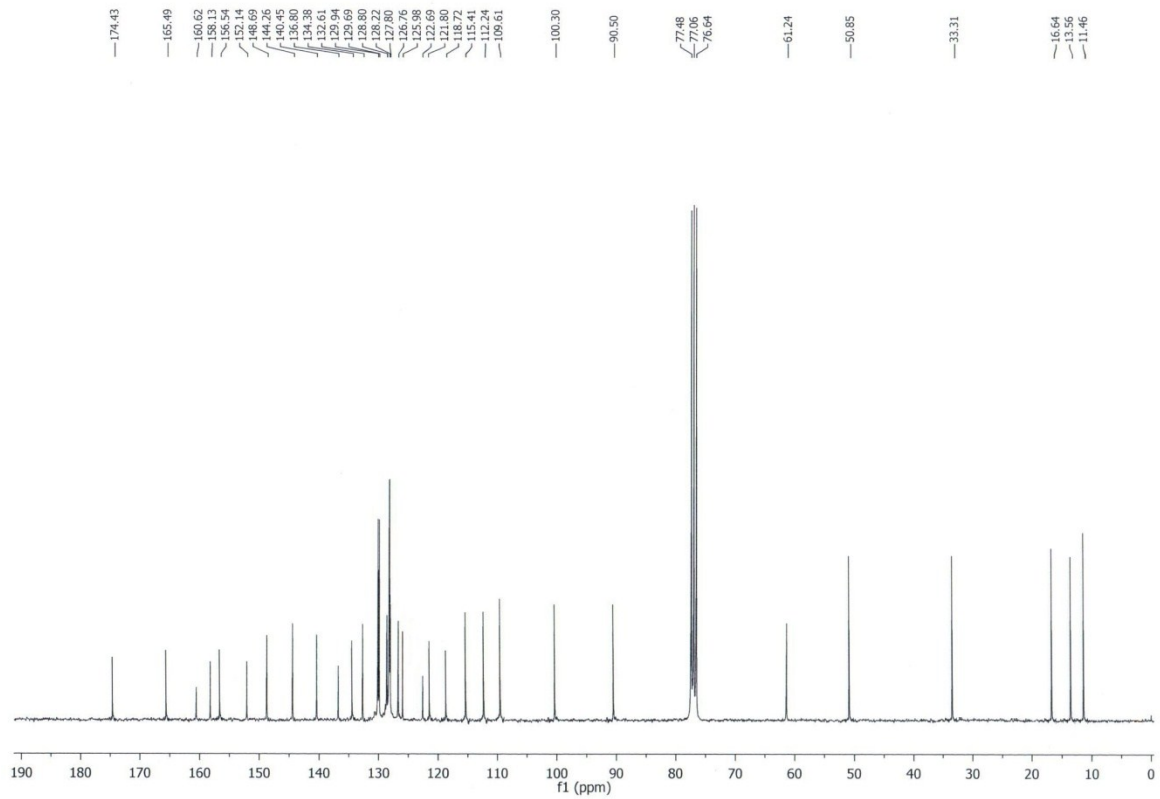
[1]H NMR of compound 6b



[13]C NMR of compound 6b

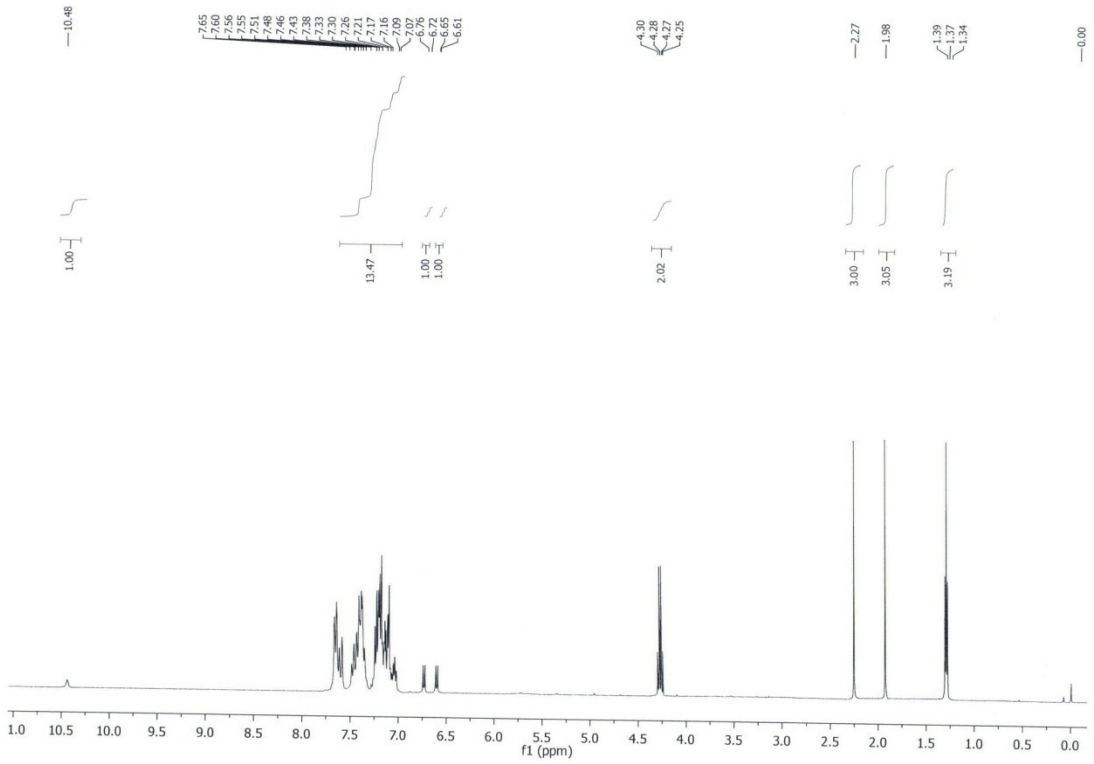
[1]H NMR of compound 6c

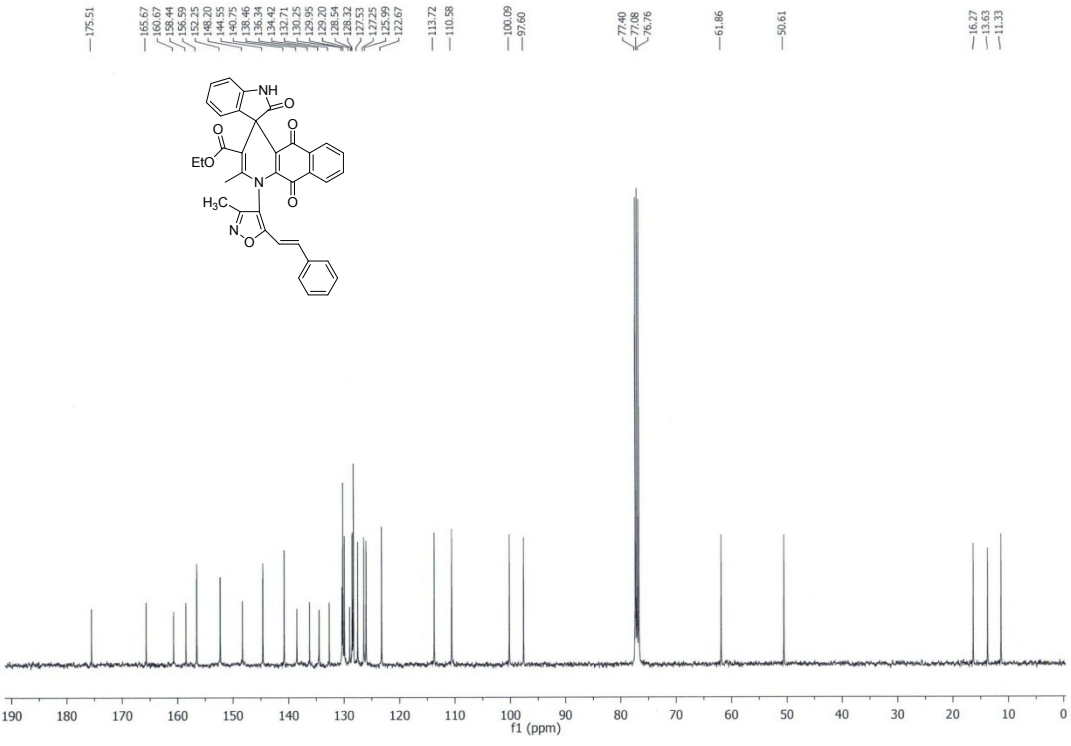




[13]C NMR of compound 6c

[1]H NMR of compound 6d

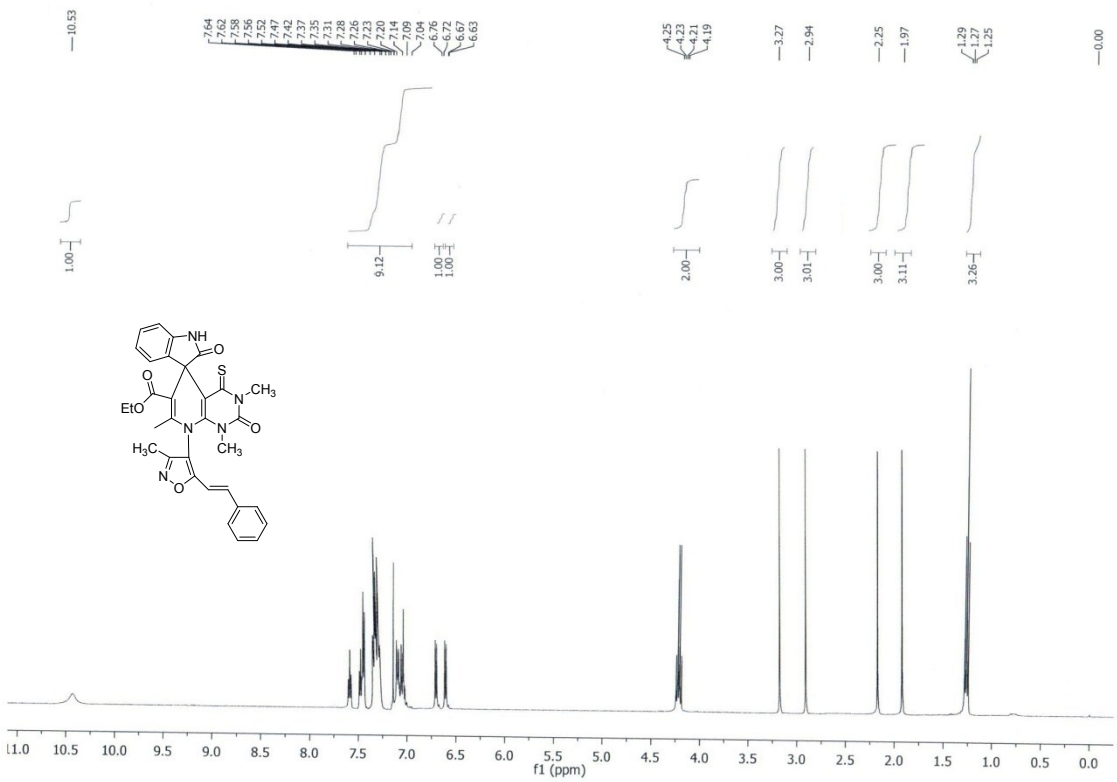


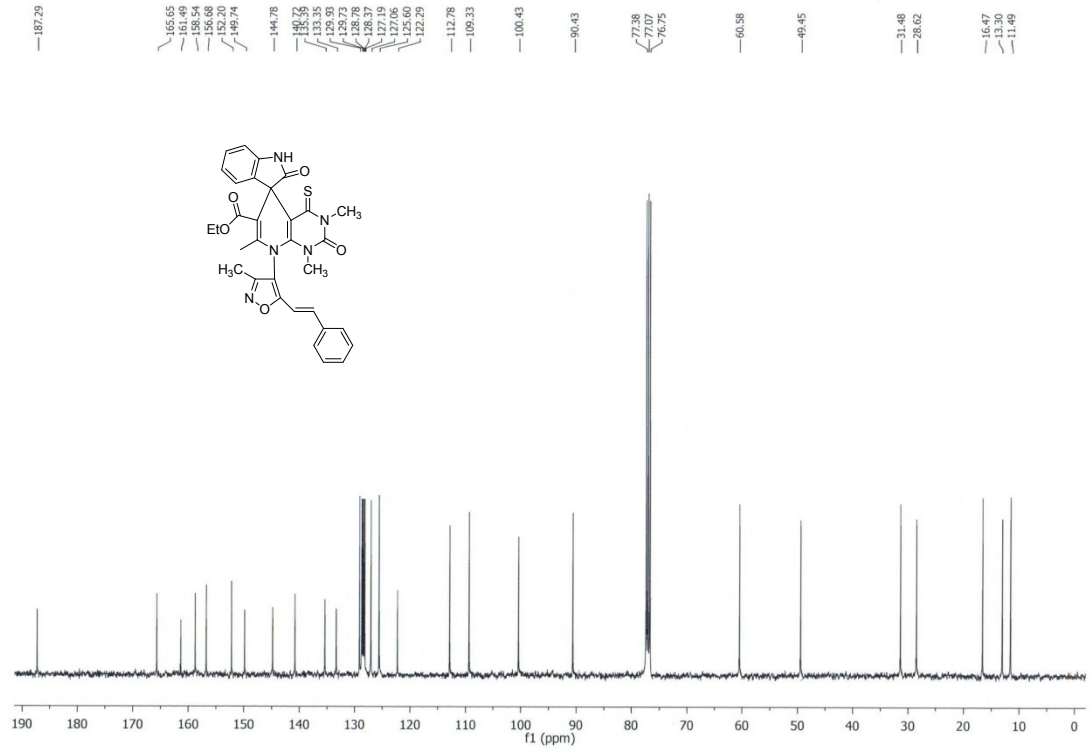


^{13}C

NMR of compound 6d

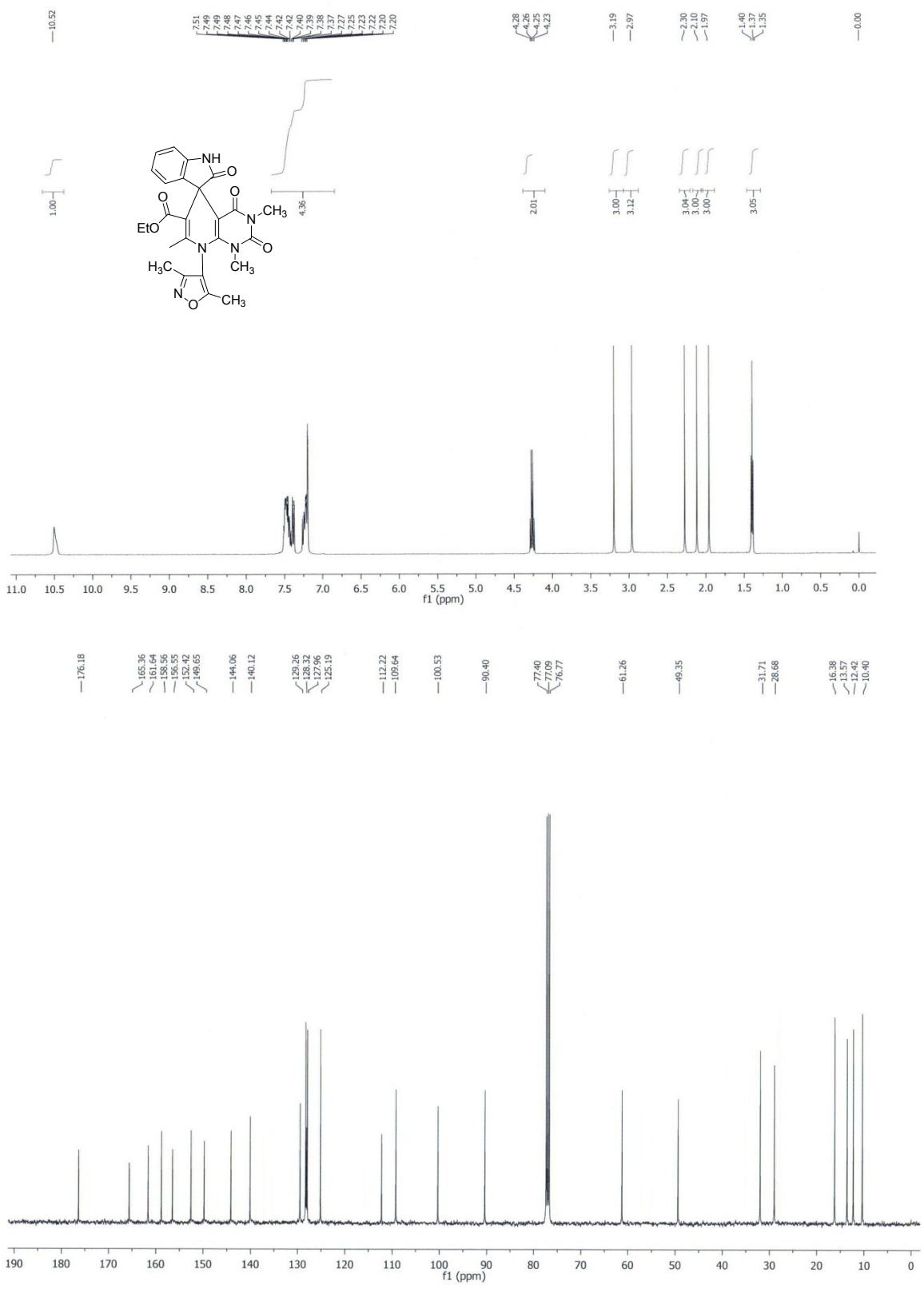
[1]H NMR of compound 6f



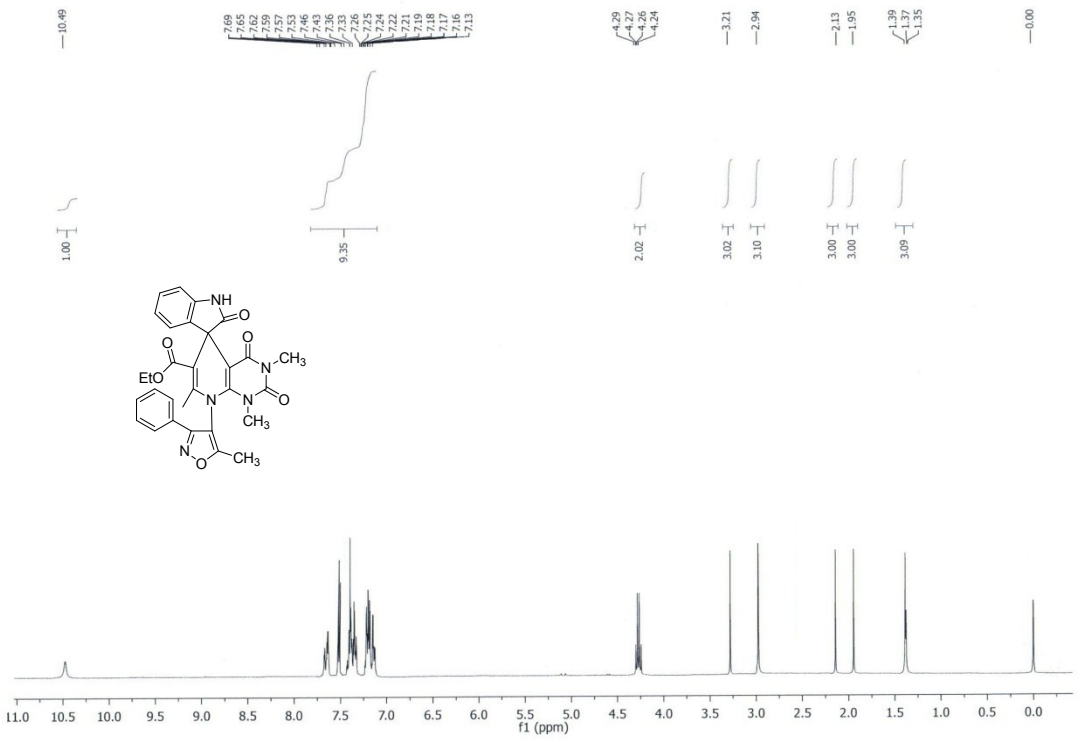


[13]C NMR of compound 6f

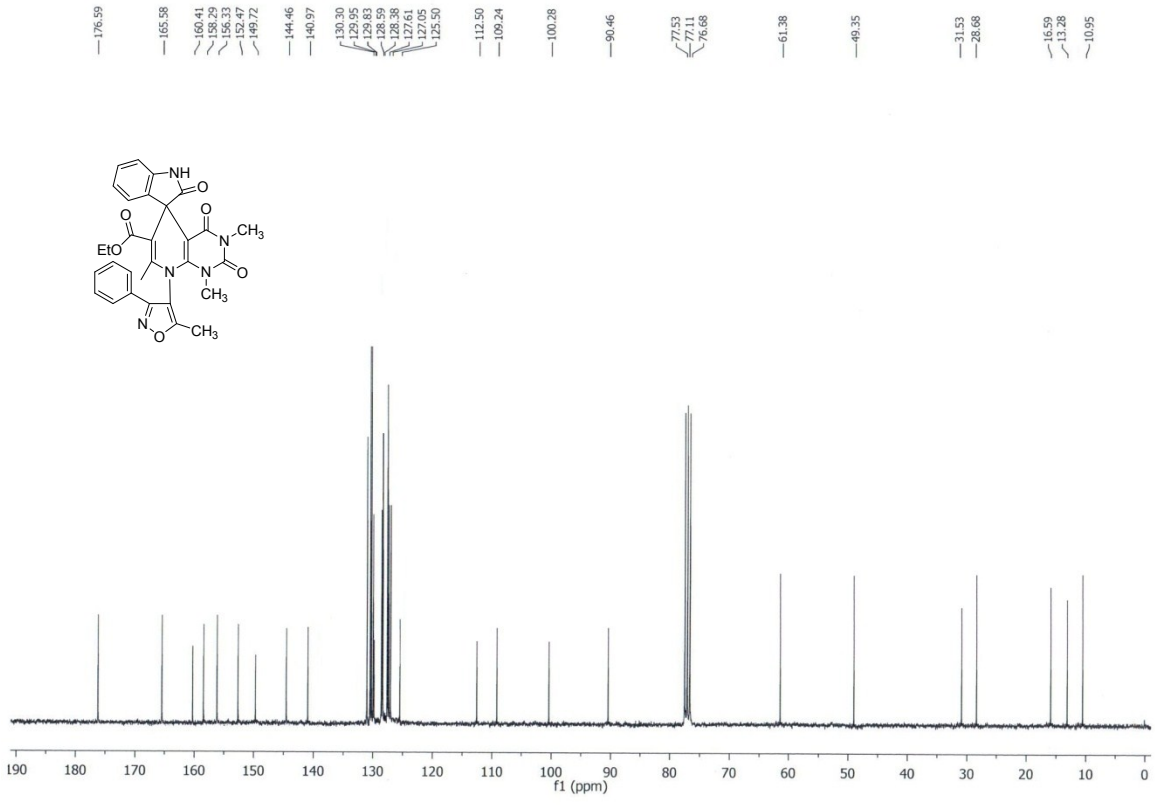
[1]H NMR of compound 8a



^{13}C NMR of compound 8a

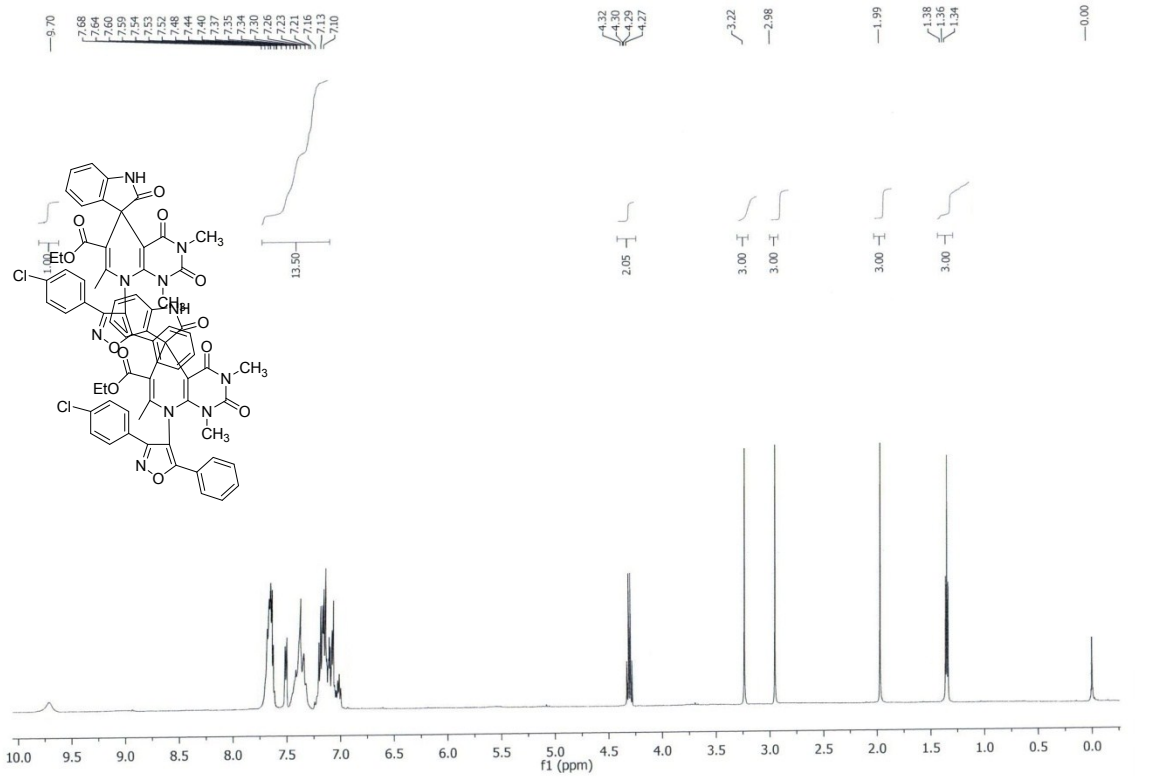


^{1}H NMR of compound 8b



^{13}C NMR of compound 8b

^{1}H NMR of compound 8d



^{13}C NMR of compound 8d