SUPPORTING INFORMATION

Reaction of Isatins with 6-Amino Uracils and Isoxazoles: Isatin Ring-Opening *vs.* Annulations and Regioselective Synthesis of Isoxazole fused Quinoline Scaffolds in Water

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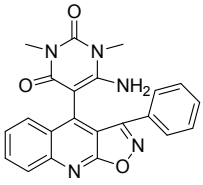
Experimental General:

All chemicals were purchased from Sigma Aldrich. All melting points are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded in DMSO-d_6 using TMS as an internal standard on a Bruker avance spectrometer at 400 Mhz amd 100 MHz respectively. Mass spectra were recorded using a JEOL GCMate-II – HR mass spectrometer. Analytical TLC was performed on precoated aluminium sheets of siliga gel G/UV-254 of 0.2 mm thickness (Merck, Germany).

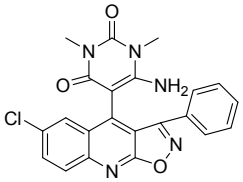
General procedure for the preparation of quinoline and spiroxindole derivatives: A mixture of isatin/N-substituted isatin **1** (1 mmol), 6-amino uracil/6-amino-1, 3-dimethyl uracil/ amino pyrazol **2** (1 mmol), isoxazole **3** (1 mmol) and *p*-TSA.H_2O (0.20 mmol) in water (3 mL) were charged in a 25 mL round bottomed flask and the mixture was heated at reflux. The resulting solution was stirred for 3-5 h. The consumption of the starting material was monitored by TLC. The precipitated solid was filtred and washed with ethanol (5-7 mL), dried under vacuum to obtain pure **4a-m**, **5a-h** and **7a-f** in good yields (78-89 %). The identities of products **4a-m, 5a-h** and **7a-f** were confirmed by NMR and EI-HRMS, giving good agreement with the assigned structures.



4a: 6-amino-1,3-dimethyl-5-(3-phenylisoxazolo[5,4-b]quinolin-4-yl)pyrimidine-2,4(1H,3H)-dione

Isolated as white solid, 89 %, m.p: 263-265^{o}C, ^{1}H NMR (400 MHz, DMSO-d_6) δ 11. 50 (s, 1H), 10.86 (s, 1H), 7.43 (t, J = 7.4 Hz, 1H), 7.35 (t, J = 7.4 Hz, 2H), 7.22 (dd, J = 13.5, 6.1 Hz, 1H), 7.09 (d, J = 7.4 Hz, 2H), 7.03 – 6.96 (m, 2H), 6.88 (t, J = 7.5 Hz, 1H), 3.13 (s, 3H), 2.95 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 180.52, 163.15, 161.53, 157.22, 152.96, 151.14, 137.58, 129.80, 129.22, 129.14, 128.56, 128.43, 128.14, 127.72, 122.81, 120.01, 117.02, 95.20, 87.49, 51.59, 31.25, 27.51 ppm.

EI-HRMS: Anal. Calcd for C_{22} H_{17} N_5 O_3: 399.1331, Found: 399. 1323

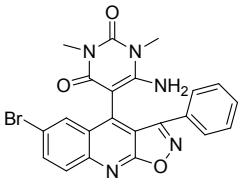


4b

4b: **6-amino-5-(6-chloro-3-phenylisoxazolo[5,4-b]quinolin-4-yl)-1,3-dimethylpyrimidine-2,4(1H,3H)-dione**

Isolated as white solid, 85 %, m.p: 260-262 ^{o}C, ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.51 (s, 1H), 11.04 (s, 1H), 7.43 (t, J = 7.3 Hz, 1H), 7.39 – 7.27 (m, 3H), 7.10 (dd, J = 12.4, 4.7 Hz, 3H), 7.03 (d, J = 8.7 Hz, 1H), 3.12 (s, 3H), 2.97 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 180.05, 162.90, 161.51, 157.28, 153.37, 151.16, 136.75, 129.85, 129.33, 128.90, 128.43, 128.15, 127.33, 126.54, 121.98, 118.62, 94.65, 87.53, 51.50, 31.27, 27.52 ppm.

EI-HRMS: Anal. Calcd for C_{22} H_{16} Cl N_5 O_3: 433.0942, Found: 433. 0942



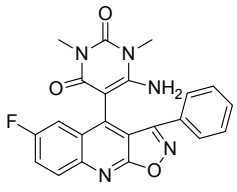
4c

4c: **6-amino-5-(6-bromo-3-phenylisoxazolo[5,4-b]quinolin-4-yl)-1,3-dimethylpyrimidine-2,4(1H,3H)-dione**

Isolated as white solid, 82 %, m.p: 275-278 ^{o}C, ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.59 (s, 1H), 11.14 (s, 1H), 7.49 (d, J = 24.2 Hz, 4H), 7.19 (t, J = 43.1 Hz, 4H), 3.21 (s, 3H), 3.07 (s, 3H) ppm. ^{13}C NMR

(100 MHz, DMSO-d_6) δ 180.06, 162.81, 161.52, 157.30, 153.38, 151.15, 137.17, 132.18, 130.06, 129.85, 128.89, 128.42, 128.15, 122.39, 119.02, 114.29, 94.67, 87.65, 51.44, 31.26, 27.53 ppm.

EI-HRMS: Anal. Calcd for C_{22} H_{16} Br N_5 O_3: 477. 0437, Found: 477. 0437

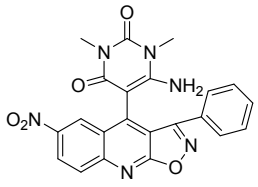


4d

4d: **6-amino-5-(6-fluoro-3-phenylisoxazolo[5,4-b]quinolin-4-yl)-1,3-dimethylpyrimidine-2,4(1H,3H)-dione**

Isolated as white solid, 81 %, m.p: 258-260 ^{o}C, ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.51 (s, 1H), 10.90 (s, 1H), 7.43 (t, J = 7.3 Hz, 1H), 7.35 (t, J = 7.5 Hz, 2H), 7.16 – 7.06 (m, 3H), 7.06 – 6.99 (m, 1H), 6.96 (dt, J = 10.1, 5.1 Hz, 1H), 3.13 (s, 3H), 2.97 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 180.11, 163.27, 161.50, 157.25, 153.32, 151.18, 134.29, 129.83, 129.02, 128.42, 128.14, 121.66, 118.34, 116.53, 116.30, 114.19, 113.96, 94.59, 86.86, 51.72, 31.27, 27.51 ppm.

EI-HRMS: Anal. Calcd for C_{22} H_{16} F N_5 O_3: 417. 1237, Found: 417. 1270

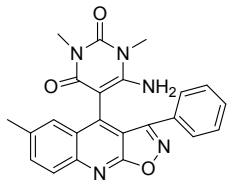


4e

4e: 6-amino-1,3-dimethyl-5-(6-nitro-3-phenylisoxazolo[5,4-b]quinolin-4-yl)pyrimidine-2,4(1H,3H)-dione

Isolated as white solid, 87 %, m.p: 258-260 ^{o}C, ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.83 (s, 1H), 11.65 (s, 1H), 8.16 (dd, J = 9.0, 2.2 Hz, 1H), 7.84 (d, J = 2.2 Hz, 1H), 7.47 (t, J = 7.3 Hz, 1H), 7.38 (t, J = 7.5 Hz, 2H), 7.21 (d, J = 9.0 Hz, 1H), 7.10 (d, J = 7.6 Hz, 2H), 3.13 (s, 3H), 2.99 (d, J = 13.5 Hz, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 179.68, 162.20, 161.54, 157.38, 153.56, 151.10, 143.50, 142.59, 130.06, 128.56, 128.44, 128.19, 125.59, 124.13, 120.88, 117.49, 94.91, 88.90, 51.43, 31.38, 27.56 ppm.

EI-HRMS: Anal. Calcd for C_{22} H_{16} N_6 O_5: 444. 1182, Found: 444. 1134

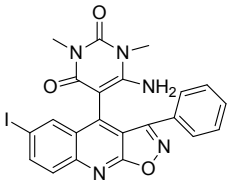


4f

4f: 6-amino-1,3-dimethyl-5-(6-methyl-3-phenylisoxazolo[5,4-b]quinolin-4-yl)pyrimidine-2,4(1H,3H)-dione

Isolated as white solid, 80 %, m.p: 256-258 ^{o}C, ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.44 (s, 1H), 10.72 (s, 1H), 7.43 (t, J = 7.3 Hz, 1H), 7.35 (t, J = 7.5 Hz, 2H), 7.06 (dd, J = 14.9, 7.9 Hz, 3H), 6.90 (d, J = 8.2 Hz, 1H), 6.79 (s, 1H), 3.13 (s, 3H), 2.96 (s, 3H), 2.14 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 180.60, 163.23, 161.52, 157.22, 152.92, 151.15, 135.25, 131.82, 129.90, 129.73, 129.23, 128.39, 128.14, 127.63, 119.81, 116.94, 95.11, 87.37, 51.58, 31.24, 27.51, 20.62 ppm.

EI-HRMS: Anal. Calcd for $C_{23}H_{19}N_5O_3$: 413. 1488, Found: 413. 1486

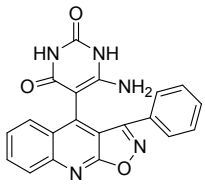


4g

4g: 6-amino-5-(6-iodo-3-phenylisoxazolo[5,4-b]quinolin-4-yl)-1,3-dimethylpyrimidine-2,4(1H,3H)-dione

Isolated as white solid, 78 %, m.p: 246-248 ^{o}C, ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.46 (s, 1H), 11.00 (s, 1H), 7.55 (d, J = 8.5 Hz, 1H), 7.43 (t, J = 7.3 Hz, 1H), 7.35 (t, J = 7.5 Hz, 2H), 7.28 (s, 1H), 7.06 (d, J = 7.6 Hz, 2H), 6.84 (d, J = 8.5 Hz, 1H), 3.10 (s, 3H), 2.97 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 180.10, 162.68, 161.51, 157.30, 153.31, 151.13, 137.92, 137.63, 135.56, 129.82, 128.91, 128.41, 128.15, 122.65, 119.32, 94.75, 87.81, 85.71, 51.24, 31.26, 27.53 ppm.

EI-HRMS: Anal. Calcd for $C_{22}H_{16}IN_5O_3$: 525. 0298, Found: 525. 0295

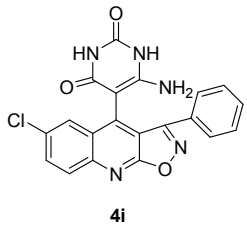


4h

4h: 6-amino-5-(3-phenylisoxazolo [5,4-b]quinolin-4-yl)pyrimidine-2,4(1H,3H)-dione

Isolated as white solid, 87 %, m.p: 268-270 ^{o}C, ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.79 (s, 1H), 10.40 (s, 1H), 7.43 (t, J = 7.3 Hz, 1H), 7.35 (t, J = 7.4 Hz, 2H), 7.18 (dd, J = 7.9, 4.1 Hz, 1H), 7.13 (d, J = 7.5 Hz, 2H), 6.96 (d, J = 8.0 Hz, 1H), 6.86 (d, J = 3.7 Hz, 2H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 185.53, 168.02, 166.33, 163.76, 158.06, 156.08, 142.17, 134.74, 133.94, 133.46, 132.73, 131.99, 127.66, 125.01, 121.76, 99.82, 91.87, and 55.38 ppm.

EI-HRMS: Anal. Calcd for $C_{20}H_{13}N_5O_3$: 371. 1013, Found: 371. 1012

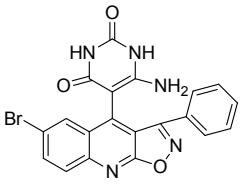


4i

4i: **6-amino-5-(6-chloro-3-phenylisoxazolo[5,4-b]quinolin-4-yl)pyrimidine-2,4(1H,3H)-dione**

Isolated as white solid, 87 %, m.p: 280-282 ^{o}C, ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.97 (s, 1H), 10.44 (s, 1H), 7.43 (t, J = 7.3 Hz, 1H), 7.35 (t, J = 7.5 Hz, 2H), 7.26 (d, J = 8.6 Hz, 1H), 7.12 (d, J = 7.7 Hz, 2H), 6.99 (d, J = 8.7 Hz, 1H), 6.95 (s, 1H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 180.33, 163.01, 161.54, 159.08, 153.56, 151.21, 136.60, 130.06, 129.28, 128.93, 128.73, 127.98, 126.90, 126.51, 122.21, 118.62, 94.45, 87.14, 50.56 ppm.

EI-HRMS: Anal. Calcd for C_{20} H_{12} Cl N_5 O_3: 405. 0629, Found: 405. 0625

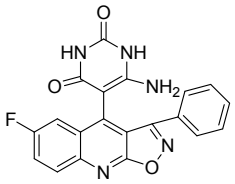


4j

4j: 6-amino-5-(6-bromo-3-phenylisoxazolo[5,4-b]quinolin-4-yl)pyrimidine-2,4(1H,3H)-dione

Isolated as white solid, 85 %, m.p: > 350 ^{o}C, ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.27 (s, 1H), 11.69 (s, 1H), 10.90 (d, J = 168.6 Hz, 1H), 10.07 (s, 1H), 7.84 – 7.55 (m, 2H), 7.23 (dd, J = 95.7, 31.5, 20.1, 7.8 Hz, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.03, 162.63, 160.49, 153.99, 149.64, 141.56, 139.66, 138.49, 133.97, 133.86, 129.27, 129.19, 128.92, 127.76, 122.87, 114.46, 112.10, 103.17, 90.46, 62.61 ppm.

EI-HRMS: Anal. Calcd for C_{20} H_{12} Br N_5 O_3: 449. 0124, Found: 449. 0123

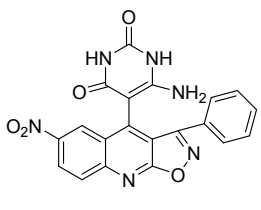


4k

4k: 6-amino-5-(6-fluoro-3-phenylisoxazolo[5,4-b]quinolin-4-yl)pyrimidine-2,4(1H,3H)-dione

Isolated as white solid, 80 %, m.p: 286-288 ^{o}C, ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.84 (s, 1H), 11.03 (s, 1H), 10.87 (s, 1H), 10.45 (s, 1H), 7.47 (t, J = 7.3 Hz, 1H), 7.38 (t, J = 7.4 Hz, 2H), 7.13 (dd, J = 14.6, 8.0 Hz, 3H), 7.02 (dd, J = 8.6, 5.1 Hz, 1H), 6.85 (d, J = 9.7 Hz, 1H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 180.36, 163.36, 161.52, 159.06, 157.08, 153.52, 151.21, 134.13, 130.01, 129.04, 128.69, 127.97, 121.90, 118.23, 116.48, 116.25, 113.83, 113.60, 94.31, 86.52, 50.76 ppm.

EI-HRMS: Anal. Calcd for C_{20} H_{12} F N_5 O_3: 389. 0924, Found: 389. 0928

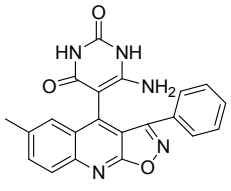


4l

4l: 6-amino-5-(6-nitro-3-phenylisoxazolo[5,4-b]quinolin-4-yl)pyrimidine-2,4(1H,3H)-dione

Isolated as white solid, 86 %, m.p: 294-296 °C, ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.03 (s, 1H), 11.82 (s, 1H), 11.29 (s, 1H), 10.59 (s, 1H), 8.15 (d, J = 8.6 Hz, 1H), 7.70 (s, 1H), 7.51 (t, J = 7.2 Hz, 1H), 7.42 (t, J = 7.3 Hz, 2H), 7.23 – 7.12 (m, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 180.00, 162.36, 161.58, 159.05, 153.62, 151.14, 143.27, 142.49, 130.30, 128.88, 128.49, 127.99, 125.51, 123.47, 121.07, 117.46, 94.95, 88.36, 50.46 ppm.

EI-HRMS: Anal. Calcd for C_{20} H_{12} N_6 O_5: 416. 0869, Found: 416. 0865

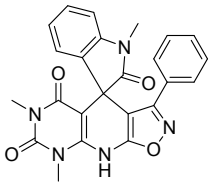


4m

4m: 6-amino-5-(6-methyl-3-phenylisoxazolo[5,4-b]quinolin-4-yl)pyrimidine-2,4(1H,3H)-dione

Isolated as white solid, 83 %, m.p: 262-264 °C, ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.51 – 10.43 (s, 4H), 7.46 (t, J = 7.4 Hz, 2H), 7.38 (t, J = 7.4 Hz, 4H), 7.15 (d, J = 5.3 Hz, 4H), 7.03 (d, J = 8.2 Hz, 2H), 6.89 (d, J = 8.1 Hz, 2H), 6.69 (s, 2H), 2.16 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 180.88, 163.33, 161.57, 159.01, 153.23, 151.33, 135.07, 131.83, 129.93, 129.85, 129.25, 128.68, 127.97, 127.16, 120.07, 116.94, 94.99, 86.96, 50.57, 20.65 ppm.

EI-HRMS: Anal. Calcd for C_{21} H_{15} N_5 O_3: 385. 1175, Found: 385. 3647

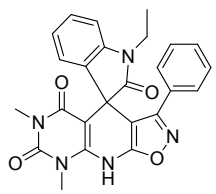


5a

5a: 1,6',8'-trimethyl-3'-phenyl-5'H-spiro[indoline-3,4'-isoxazolo[4',5':5,6]pyrido[2,3-d]pyrimidine]-2,5',7'(6'H,8'H,9'H)-trione

Isolated as white solid, 87 %, m.p: 250-252 °C, ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.57 (s, 1H), 7.47 (dd, J = 24.0, 6.8 Hz, 2H), 7.34 – 7.10 (m, 4H), 7.02 (dt, J = 14.7, 7.3 Hz, 1H), 6.69 (t, J = 7.4 Hz, 2H), 3.60 (s, 3H), 3.14 (d, J = 53.9 Hz, 3H), 2.89 (d, J = 104.1 Hz, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 180.28, 177.06, 161.50, 161.03, 160.20, 150.71, 146.74, 143.50, 135.57, 129.93, 128.39, 128.37, 128.15, 127.78, 123.85, 122.72, 108.13, 93.96, 88.58, 51.28, 40.37, 40.16, 39.95, 39.74, 39.53, 31.30, 28.06, 26.14 ppm.

EI-HRMS: Anal. Calcd for C_{24} H_{19} N_5 O_4: 441. 1437, Found: 441.1435

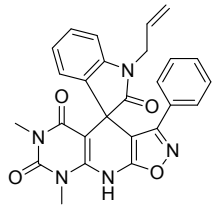


5b

5b: 1-ethyl-6',8'-dimethyl-3'-phenyl-5'H-spiro[indoline-3,4' isoxazolo[4',5':5,6]pyrido[2,3-d]pyrimidine]-2,5',7'(6'H,8'H,9'H)-trione

Isolated as white solid, 89 %, m.p: 256-258 ^{o}C, ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.56 (s, 1H), 7.35 (t, J = 7.4 Hz, 1H), 7.19 (dt, J = 14.9, 7.5 Hz, 4H), 6.97 (t, J = 7.4 Hz, 1H), 6.71 (d, J = 7.7 Hz, 1H), 6.55 (d, J = 7.5 Hz, 2H), 3.53 (s, 3H), 3.20 (dd, J = 15.5, 8.6 Hz, 2H), 3.00 (s, 3H), 0.69 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 176.57, 161.49, 161.19, 160.17, 150.70, 146.59, 143.16, 136.00, 129.98, 128.84, 128.50, 128.47, 127.99, 124.16, 122.57, 108.40, 93.68, 88.82, 48.41, 34.50, 31.28, 28.09, 12.02 ppm.

EI-HRMS: Anal. Calcd for C_{25} H_{21} N_5 O_4: 455. 1594, Found: 455.1425

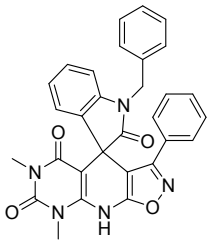


5c

5c:1-allyl-6',8'-dimethyl-3'-phenyl-5'H-spiro[indoline-3,4'-isoxazolo[4',5':5,6]pyrido[2,3-d]pyrimidine]-2,5',7'(6'H,8'H,9'H)-trione

Isolated as white solid, 86 %, m.p: 252-254 ^{o}C, ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.60 (s, 1H), 7.37 (t, J = 7.4 Hz, 1H), 7.24 – 7.12 (m, 4H), 6.96 (t, J = 7.4 Hz, 1H), 6.56 (t, J = 8.0 Hz, 3H), 5.32 (d, J = 3.5 Hz, 2H), 5.04 – 4.94 (m, 1H), 4.02 (d, J = 16.5 Hz, 1H), 3.54 (s, 3H), 3.50 (d, J = 2.8 Hz, 1H), 3.01 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 176.80, 161.49, 161.08, 160.20, 150.70, 146.76, 142.90, 135.77, 132.05, 129.97, 128.65, 128.51, 128.45, 127.83, 124.00, 122.77, 117.57, 108.93, 93.80, 88.56, 49.08, 48.46, 42.36, 31.32, 28.12 ppm.

EI-HRMS: Anal. Calcd for C_{26} H_{21} N_5 O_4: 467. 1594, Found: 467. 1534

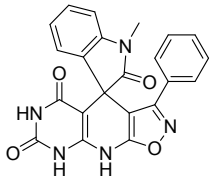


5d

5d: 1-benzyl-6',8'-dimethyl-3'-phenyl-5'H-spiro[indoline 3,4'isoxazolo[4',5':5,6]pyrido[2,3-d]pyrimidine]-2,5',7'(6'H,8'H,9'H)-trione

Isolated as white solid, 79 %, m.p: 265-267 ^{o}C, ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.66 (s, 1H), 7.41 (t, J = 7.5 Hz, 1H), 7.33 – 7.17 (m, 8H), 7.08 (t, J = 7.7 Hz, 1H), 6.95 (t, J = 7.4 Hz, 1H), 6.63 (d, J = 7.7 Hz, 2H), 6.33 (d, J = 7.8 Hz, 1H), 4.78 (d, J = 16.3 Hz, 1H), 3.94 (d, J = 16.3 Hz, 1H), 3.56 (s, 3H), 3.07 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 177.50, 161.53, 161.04, 160.28, 159.77, 150.71, 146.80, 142.93, 136.32, 135.77, 130.11, 128.77, 128.65, 128.54, 128.43, 127.82, 127.77, 127.47, 127.42, 124.08, 122.93, 108.97, 93.84, 88.58, 48.65, 43.96, 31.35, 28.15 ppm.

EI-HRMS: Anal. Calcd for C_{30} H_{23} N_5 O_4: 517. 1750, Found: 517. 1745

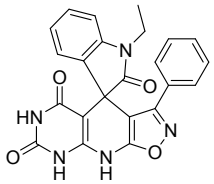


5e

5e: 1-methyl-3'-phenyl-5'H-spiro[indoline-3,4'-isoxazolo[4',5':5,6]pyrido[2,3-d]pyrimidine]-2,5',7'(6'H,8'H,9'H)-trione

Isolated as white solid, 88 %, m.p: 308-310 ^{o}C, ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.20 (s, 2H), 10.86 (s, 1H), 7.35 (t, J = 7.4 Hz, 1H), 7.25 – 7.13 (m, 3H), 7.09 (d, J = 7.2 Hz, 1H), 6.93 (t, J = 7.4 Hz, 1H), 6.61 (d, J = 7.0 Hz, 3H), 2.68 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 180.87, 163.34, 161.58, 159.02, 153.30, 151.39, 135.08, 131.84, 129.93, 129.85, 129.26, 128.68, 127.98, 127.16, 120.09, 116.95, 95.01, 86.98, 50.58, 20.65 ppm.

EI-HRMS: Anal. Calcd for C_{22} H_{15} N_5 O_4: 413. 1124, Found: 413. 1122

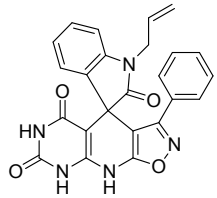


5f

5f: 1-ethyl-3'-phenyl-5'H-spiro[indoline-3,4'-isoxazolo[4',5':5,6]pyrido[2,3-d]pyrimidine]-2,5',7'(6'H,8'H,9'H)-trione

Isolated as white solid, 87 %, m.p: 298-300 ^{o}C, ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.16 (s, 2H), 10.83 (s, 1H), 7.33 (t, J = 7.4 Hz, 1H), 7.25 – 7.10 (m, 4H), 6.97 (t, J = 7.4 Hz, 1H), 6.70 (d, J = 7.7 Hz, 1H), 6.56 (d, J = 7.5 Hz, 2H), 3.18 (dd, J = 13.0, 8.0 Hz, 2H), 0.72 (t, J = 7.0 Hz, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 176.52, 162.11, 161.58, 161.02, 150.45, 146.38, 143.15, 135.71, 129.94, 128.82, 128.44, 128.02, 124.10, 122.60, 108.40, 93.61, 88.57, 47.55, 34.45, 11.92 ppm.

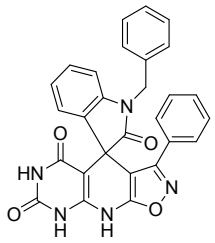
EI-HRMS: Anal. Calcd for C_{23} H_{17} N_5 O_4: 427. 1281, Found: 427. 1285



5g

5g: 1-allyl-3'-phenyl-5'H-spiro[indoline-3,4'-isoxazolo[4',5':5,6]pyrido[2,3-d]pyrimidine]-2,5',7'(6'H,8'H,9'H)-trione Isolated as white solid, 87 %, m.p: 300-302 ^{o}C, ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.21 (s, 2H), 10.89 (s, 1H), 7.35 (t, J = 7.3 Hz, 1H), 7.24 – 7.11 (m, 4H), 6.96 (t, J = 7.3 Hz, 1H), 6.54 (dd, J = 20.9, 7.5 Hz, 3H), 5.50 – 5.26 (m, 2H), 4.97 (d, J = 10.1 Hz, 1H), 4.05 (d, J = 16.1 Hz, 1H), 3.48 (s, 1H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 176.81, 162.20, 161.59, 160.89, 150.44, 146.62, 142.88, 135.46, 131.87, 129.92, 128.63, 128.46, 128.40, 127.86, 123.92, 122.81, 117.20, 108.94, 93.79, 88.24, 74.60, 47.61, 42.22 ppm.

EI-HRMS: Anal. Calcd for C_{24} H_{17} N_5 O_4: 439. 1281, Found: 439. 1280

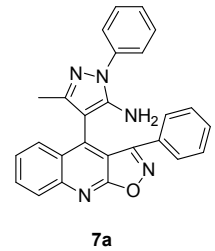


5h

5h: 1-benzyl-6',8'-dimethyl-3'-phenyl-5'H-spiro[indoline-3,4'-isoxazolo[4',5':5,6]pyrido[2,3-d]pyrimidine]-2,5',7'(6'H,8'H,9'H)-trione

Isolated as white solid, 81 %, m.p: 254-256 ^{o}C, ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.34 (s, 2H), 11.05 (s, 1H), 7.49 (t, J = 7.4 Hz, 1H), 7.44 – 7.21 (m, 8H), 7.15 (dd, J = 16.0, 7.8 Hz, 1H), 7.03 (t, J = 7.4 Hz, 1H), 6.70 (d, J = 7.4 Hz, 2H), 6.34 (d, J = 7.7 Hz, 1H), 4.95 – 4.84 (m, 1H), 3.93 (d, J = 16.4 Hz, 1H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 177.36, 162.44, 161.81, 161.60, 160.86, 150.38, 149.91, 146.79, 144.45, 142.78, 136.29, 135.47, 130.03, 128.74, 128.62, 128.50, 128.39, 127.82, 127.55, 127.42, 127.32, 124.02, 122.98, 108.97, 93.89, 88.09, 47.78, 43.79 ppm.

EI-HRMS: Anal. Calcd for C_{28} H_{19} N_5 O_4: 489. 1437, Found: 489. 1435



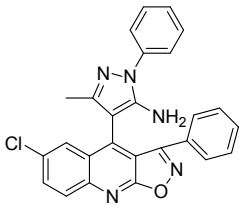
7a

7a: 3-methyl-1-phenyl-4-(3-phenylisoxazolo[5,4-b]quinolin-4-yl)-1H-pyrazol-5-amine

Isolated as white solid, 87 %, m.p: 255-257 ^{o}C, ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.17 (s, 1H), 10.54 (s, 1H), 7.65 (d, J = 7.8 Hz, 2H), 7.58 (t, J = 7.6 Hz, 2H), 7.43 (t, J = 7.2 Hz, 1H), 7.34 (t, J = 7.4 Hz, 1H), 7.20 (dd, J = 13.9, 7.0 Hz, 3H), 7.11 (d, J = 7.3 Hz, 1H), 6.97 (t, J = 7.4 Hz, 1H), 6.87 (d, J = 7.5 Hz, 2H), 6.74 (d, J = 7.7 Hz, 1H), 1.54 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 178.40,

165.11, 161.94, 145.61, 141.76, 139.44, 138.36, 135.08, 129.98, 129.94, 129.38, 128.70, 128.55, 128.30, 127.66, 125.30, 123.34, 123.03, 110.05, 101.27, 92.94, 47.49, 11.82 ppm.

EI-HRMS: Anal. Calcd for C_{26} H_{19} N_5 O: 417. 1590, Found: 417. 1544

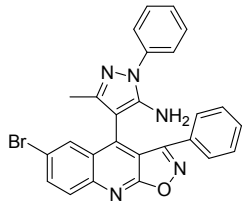


7b

7b: 4-(6-chloro-3-phenylisoxazolo[5,4-b]quinolin-4-yl)-3-methyl-1-phenyl-1H-pyrazol-5-amine

Isolated as white solid, 84 %, m.p: 220-222 ^{o}C, ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.22 (s, 1H), 10.65 (s, 1H), 7.68 – 7.54 (m, 4H), 7.44 (t, J = 7.0 Hz, 1H), 7.37 (d, J = 7.3 Hz, 1H), 7.27 – 7.18 (m, 4H), 6.90 (d, J = 7.5 Hz, 2H), 6.71 (d, J = 8.0 Hz, 1H), 1.55 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 178.21, 165.08, 161.79, 145.39, 140.56, 139.59, 138.29, 136.88, 130.02, 129.96, 129.28, 128.64, 128.57, 128.24, 127.75, 126.99, 125.47, 123.51, 111.48, 100.56, 92.39, 56.52, 19.01 ppm,

EI-HRMS: Anal. Calcd for C_{26} H_{18} Cl N_5 O: 451. 1200, Found: 451. 1234

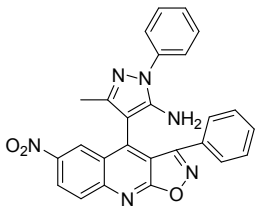


7c

7c: 4-(6-bromo-3-phenylisoxazolo[5,4-b]quinolin-4-yl)-3-methyl-1-phenyl-1H-pyrazol-5-amine

Isolated as white solid, 87 %, m.p: 230-232 ^{o}C, ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.26 (s, 1H), 10.68 (s, 1H), 7.68 – 7.56 (m, 4H), 7.49 – 7.31 (m, 4H), 7.24 (t, J = 6.9 Hz, 2H), 6.91 (d, J = 7.1 Hz, 2H), 6.68 (d, J = 7.9 Hz, 1H), 1.57 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 178.08, 165.09, 161.80, 145.41, 140.95, 139.59, 138.28, 137.27, 132.15, 130.89, 130.04, 129.95, 129.77, 128.65, 128.57, 128.24, 127.76, 124.36, 123.52, 114.62, 112.01, 100.55, 92.40, 56.54, 19.01 ppm.

EI-HRMS: Anal. Calcd for C_{26} H_{18} Br N_5 O: 495. 0695, Found: 495. 0654



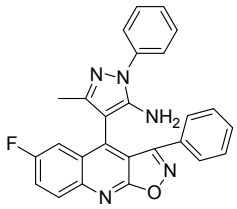
7d

7d: **3-methyl-4-(6-nitro-3-phenylisoxazolo[5,4-b]quinolin-4-yl)-1-phenyl-1H-pyrazol-5-amine**

Isolated as white solid, 83 %, m.p: 216-218 ^{o}C, ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.33 (s, 1H), 11.19 (s, 1H), 7.62 (dd, J = 18.7, 7.0 Hz, 4H), 7.47 (t, J = 7.2 Hz, 2H), 7.35 (d, J = 6.9 Hz, 1H), 7.22 (d, J = 6.7 Hz, 2H), 7.12 (d, J = 7.1 Hz, 1H), 6.86 (d, J = 5.7 Hz, 3H), 1.53 (s, 3H) ppm.

^{13}C NMR (100 MHz, DMSO-d_6) δ 178.94, 165.08, 161.79, 147.88, 145.28, 143.40, 139.86, 138.21, 135.64, 129.97, 128.70, 128.53, 128.28, 126.56, 125.97, 123.69, 121.13, 110.28, 101.00, 99.78, 93.82, 92.09, 47.43, 21.25 ppm.

EI-HRMS: Anal. Calcd for C_{26} H_{18} Br N_6 O_3: 462. 1440, Found: 462. 1432

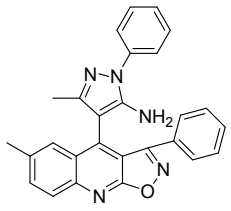


7e

7e: **4-(6-fluoro-3-phenylisoxazolo[5,4-b]quinolin-4-yl)-3-methyl-1-phenyl-1H-pyrazol-5-amine**

Isolated as white solid, 77 %, m.p: 234-236 ^{o}C, ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.23 (s, 1H), 10.57 (s, 1H), 7.67 – 7.54 (m, 4H), 7.44 (t, J = 7.1 Hz, 1H), 7.36 (t, J = 7.4 Hz, 1H), 7.23 (t, J = 7.4 Hz, 2H), 7.03 (dd, J = 20.8, 8.9 Hz, 2H), 6.91 (d, J = 7.5 Hz, 2H), 6.70 (dd, J = 8.1, 3.9 Hz, 1H), 1.55 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 178.50, 165.07, 161.85, 160.24, 157.87, 145.48, 139.53, 138.29, 137.89, 136.51, 129.99, 128.61, 128.58, 128.25, 127.74, 123.44, 115.90, 115.67, 113.15, 112.91, 110.86, 100.70, 92.49, 47.97, 11.81 ppm.

EI-HRMS: Anal. Calcd for C_{26} H_{18} F N_5 O: 435. 1495, Found: 435. 1492



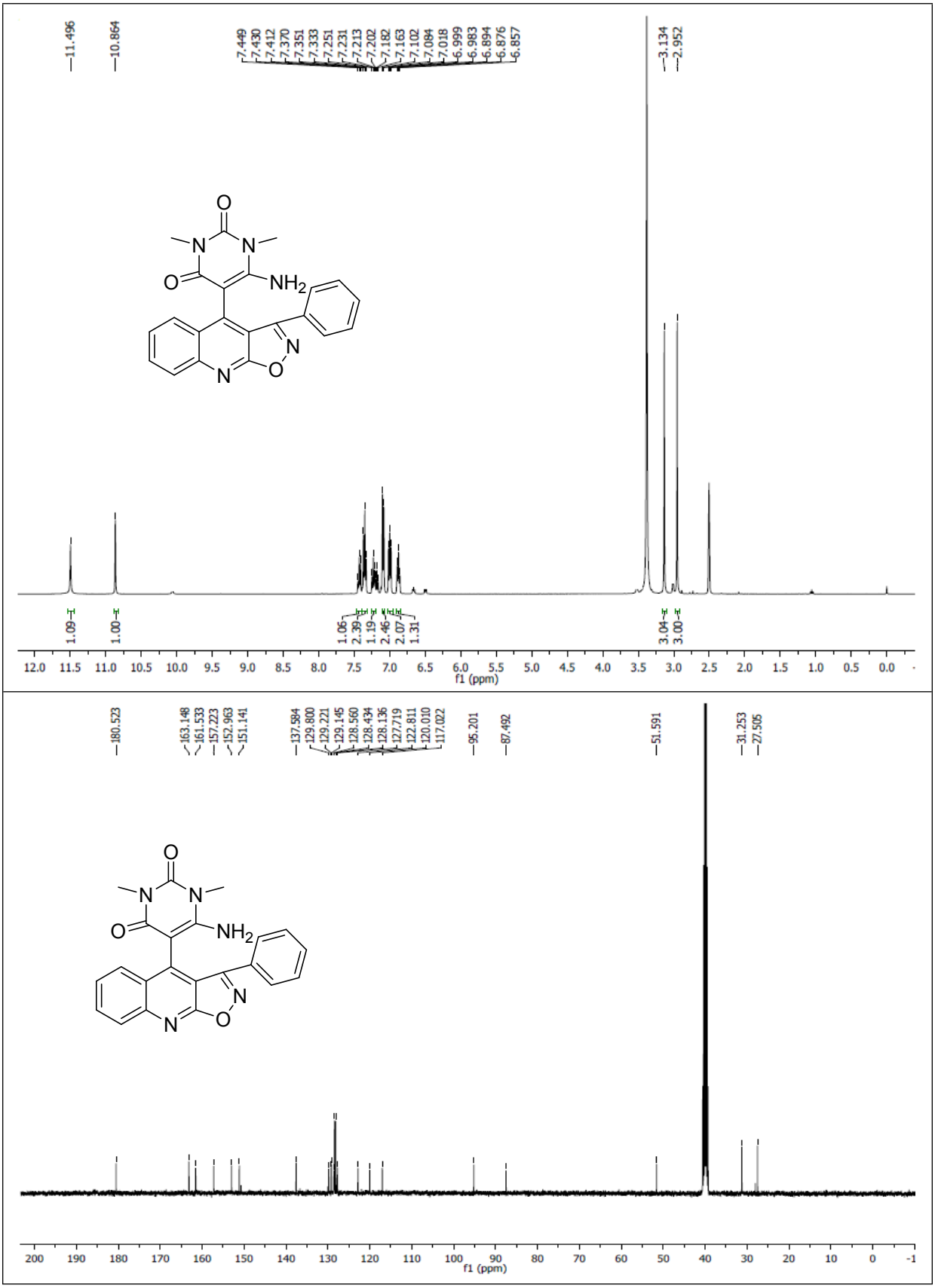
7f

7f: 3-methyl-4-(6-methyl-3-phenylisoxazolo[5,4-b]quinolin-4-yl)-1-phenyl-1H-pyrazol-5-amine

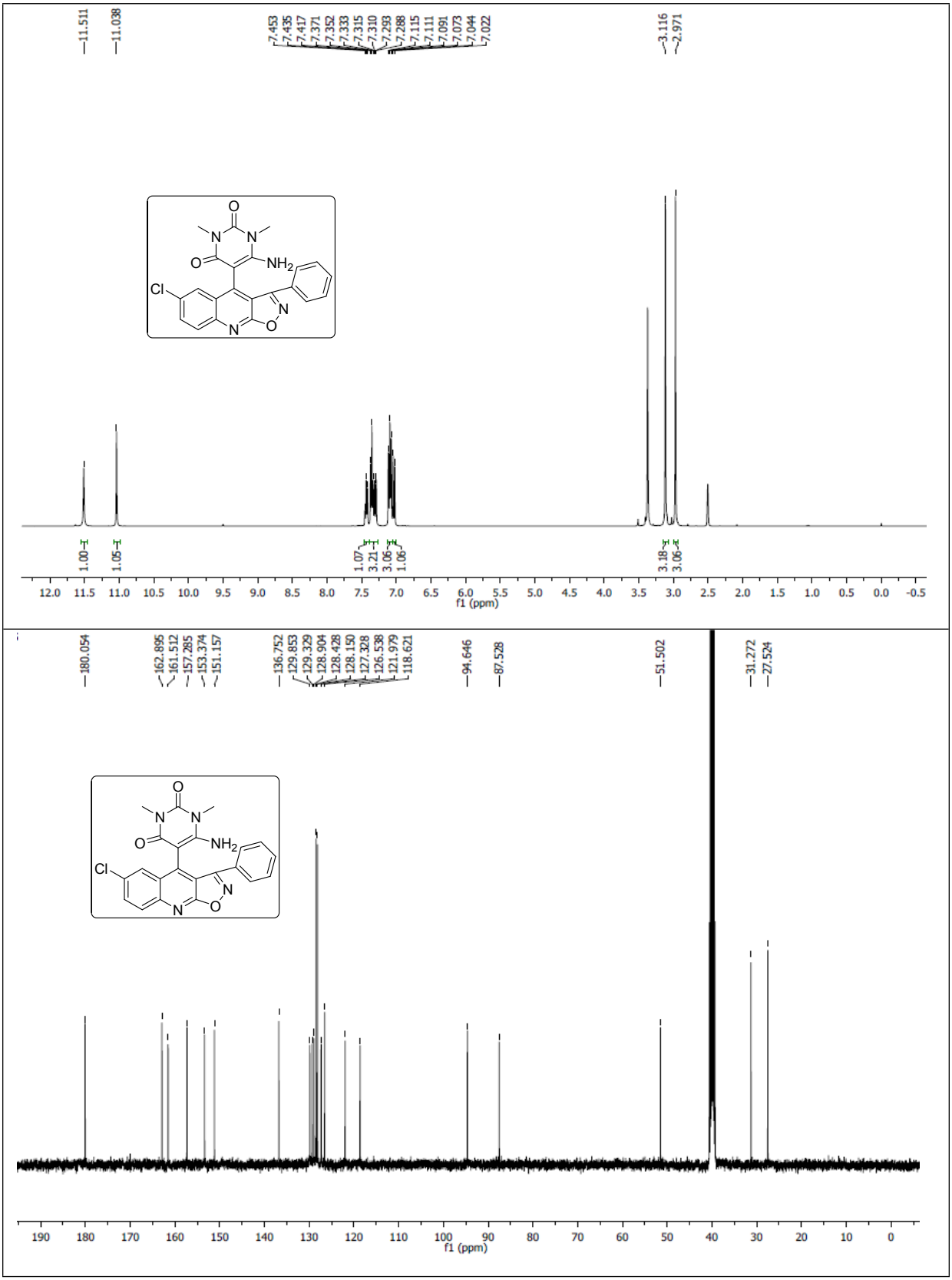
White solid, 85 %, m.p: 235-237 ^{o}C, ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.12 (s, 1H), 10.41 (s, 1H), 7.67 – 7.54 (m, 4H), 7.43 (t, J = 7.2 Hz, 1H), 7.34 (t, J = 7.4 Hz, 1H), 7.19 (t, J = 7.6 Hz, 2H), 7.02 (d, J = 7.8 Hz, 1H), 6.94 (s, 1H), 6.85 (d, J = 7.4 Hz, 2H), 6.63 (d, J = 7.8 Hz, 1H), 2.21 (s, 3H), 1.54 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 178.29, 165.07, 161.89, 145.61, 139.36, 139.29, 138.36, 135.29, 132.04, 129.98, 129.63, 128.73, 128.56, 128.31, 127.63, 125.74, 123.31, 109.80, 101.43, 93.00, 47.50, 21.03, 11.84 ppm.

EI-HRMS: Anal. Calcd for C_{27} H_{21} N_5 O: 431. 1746, Found: 431. 1734

^{1}H and ^{13}C NMR Spectra of Compound (4a)



^{1}H and ^{13}C NMR Spectra of Compound (4b)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7.417
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7.352
7.333
7.315
7.310
7.293
7.288
7.115
7.111
7.091
7.073
7.044
7.022
3.116
2.971
1.00
1.05
1.07
3.21
3.06
1.06
3.18
3.06
f1 (ppm)
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161.512
157.285
153.374
151.157
136.752
129.853
129.329
128.904
128.428
128.150
127.328
126.538
121.979
118.621
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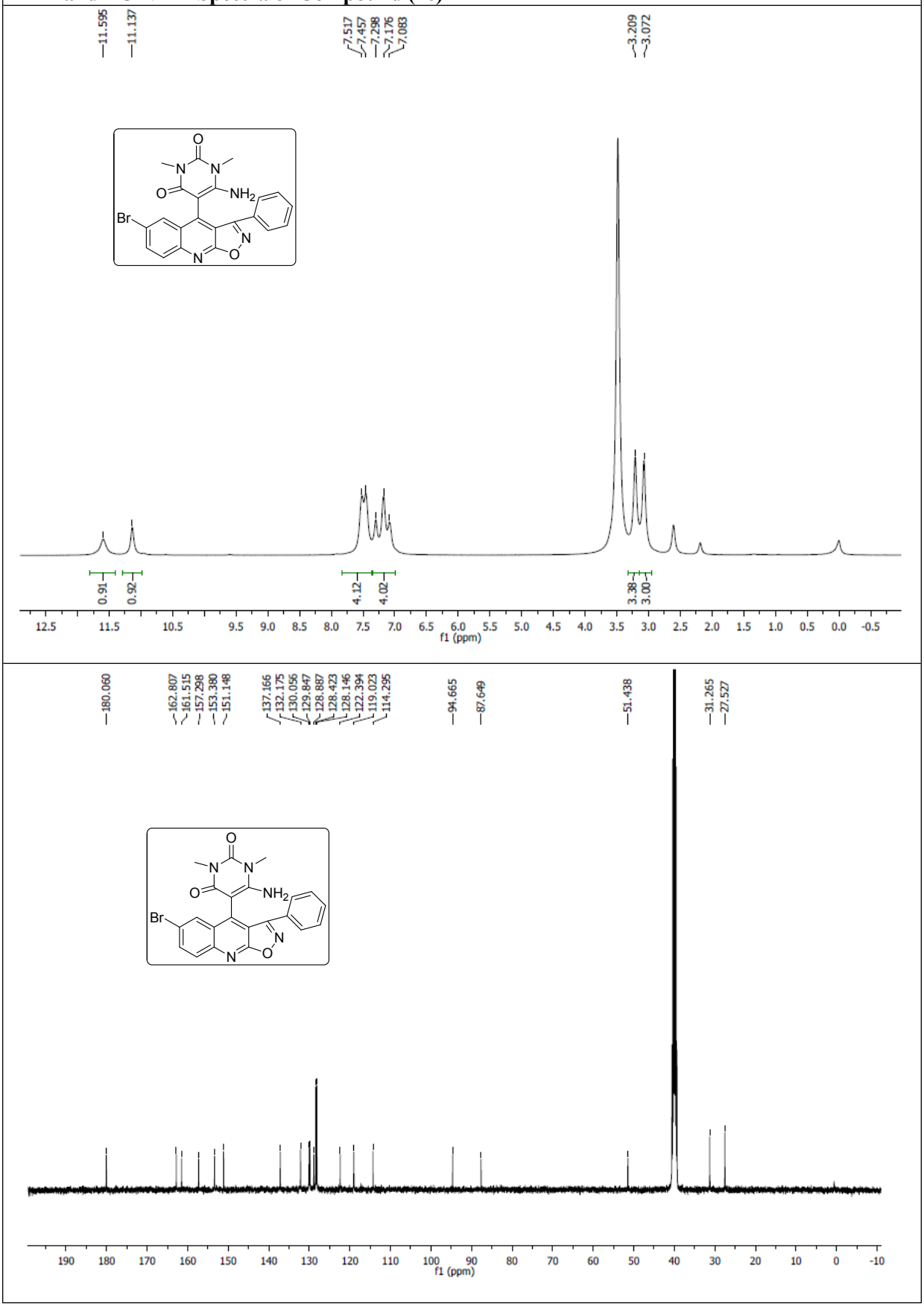
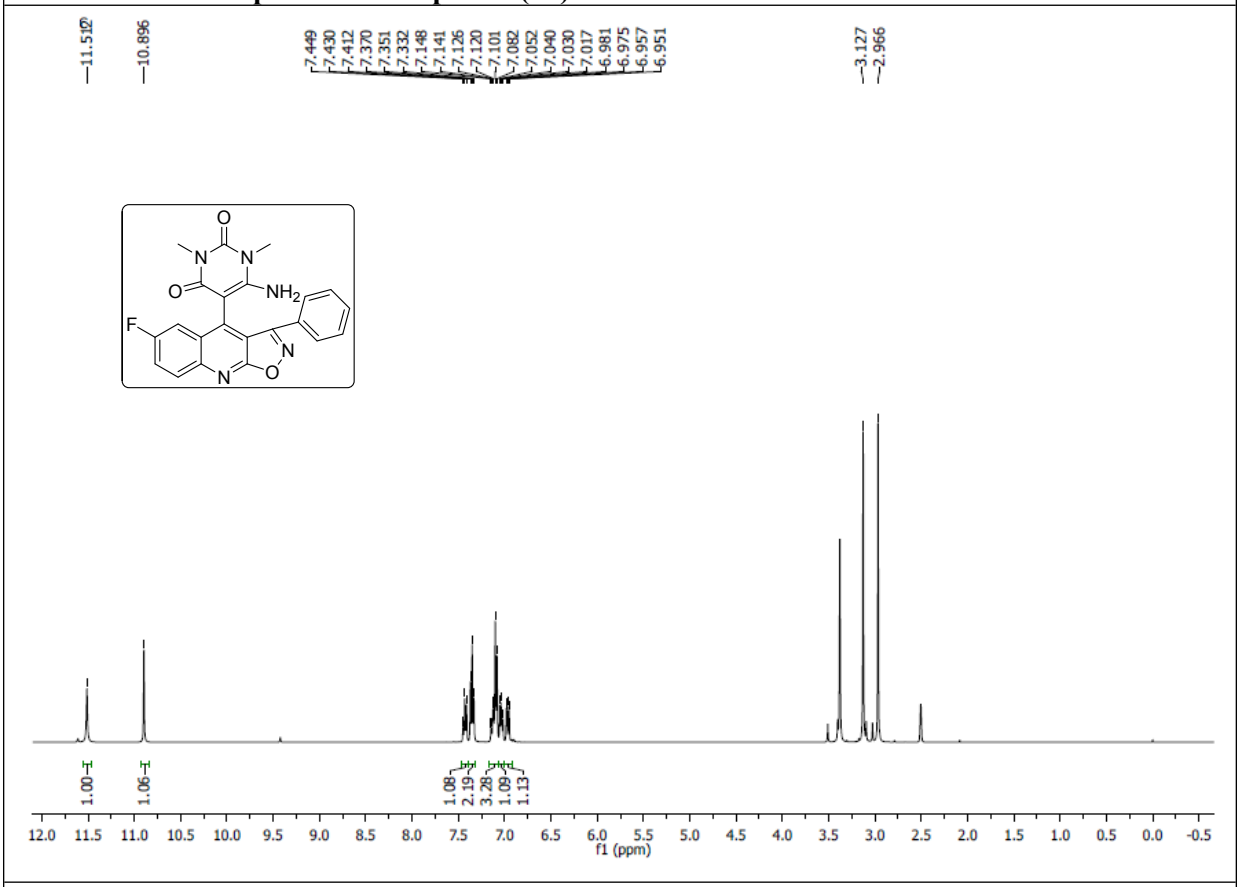
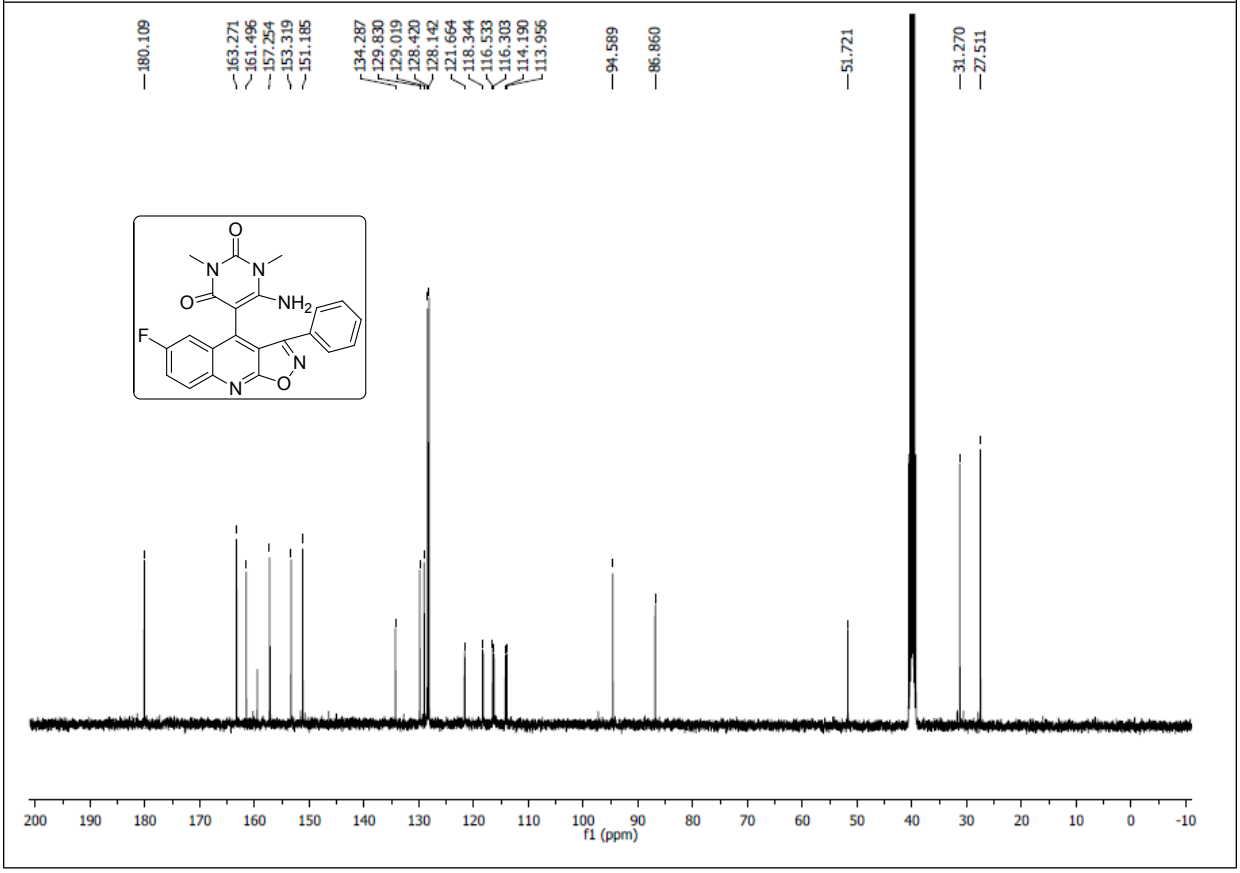
87.528
51.502
31.272
27.524
f1 (ppm)

^{1}H and ^{13}C NMR Spectra of Compound (4c)

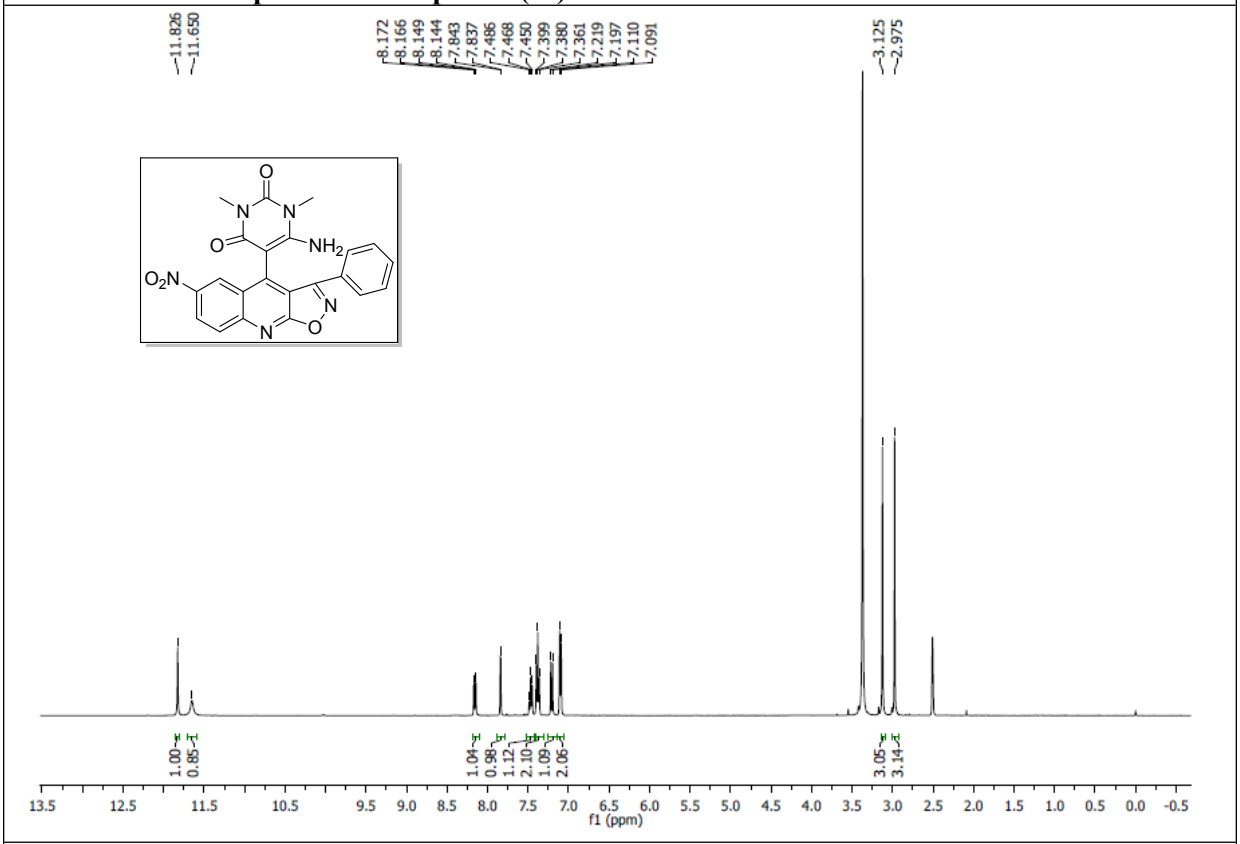


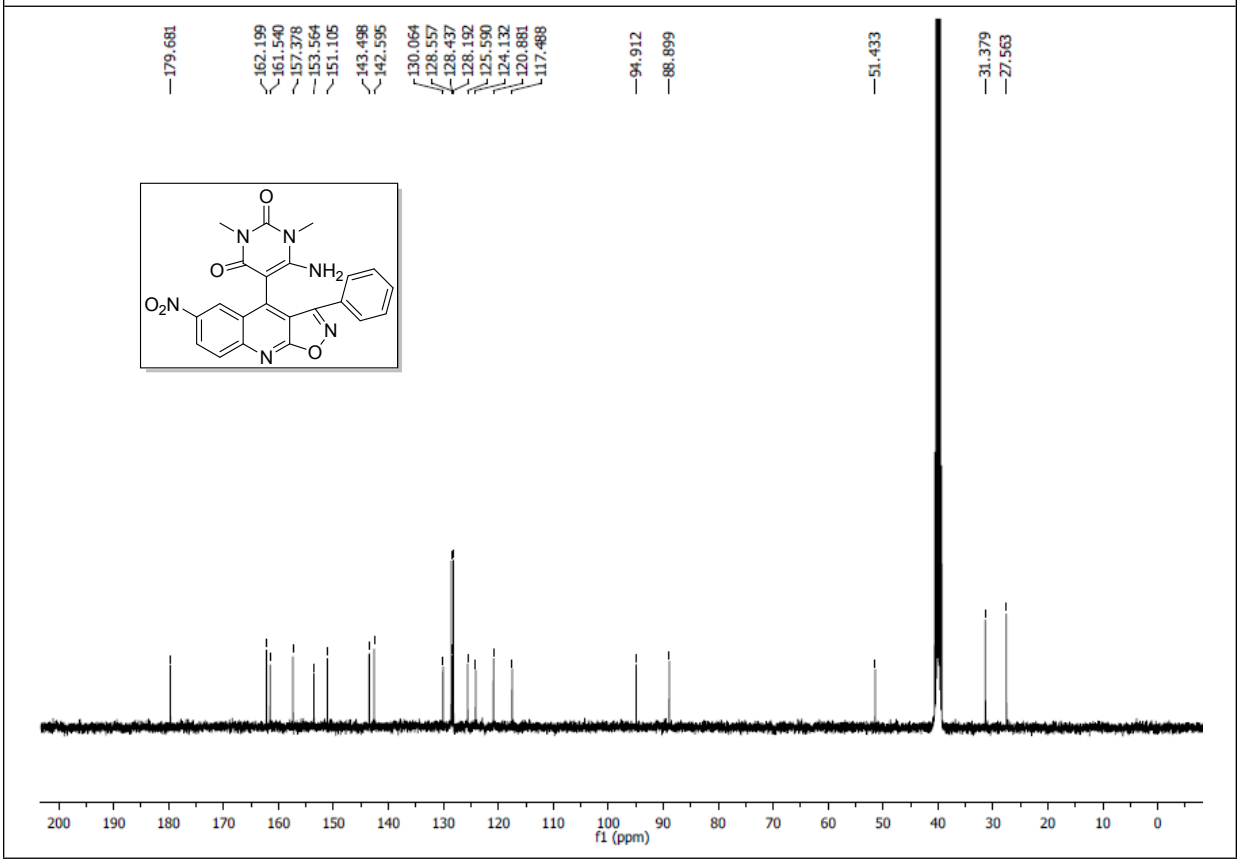
^{1}H and ^{13}C NMR Spectra of Compound (4d)



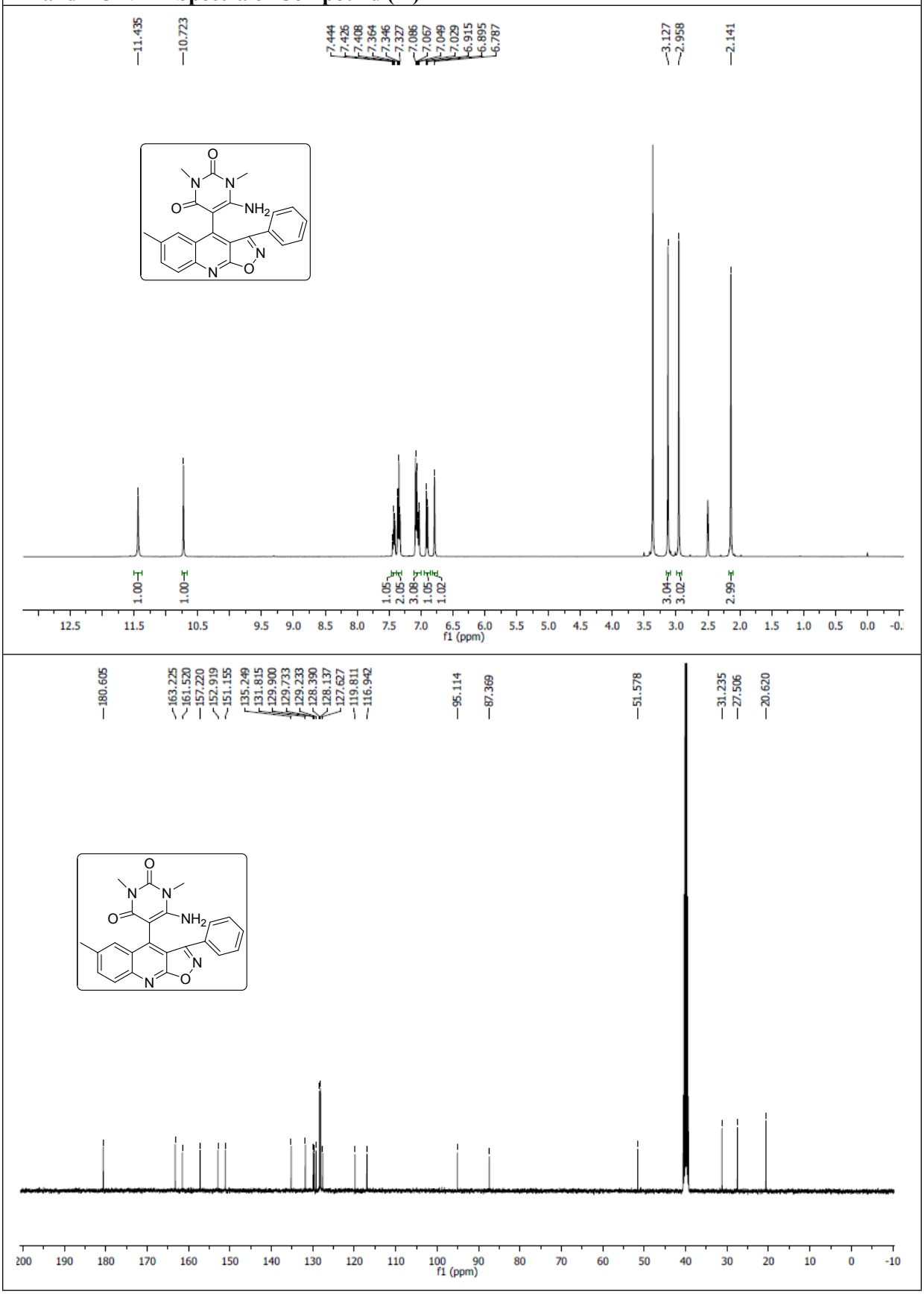


^{1}H and ^{13}C NMR Spectra of Compound (4e)

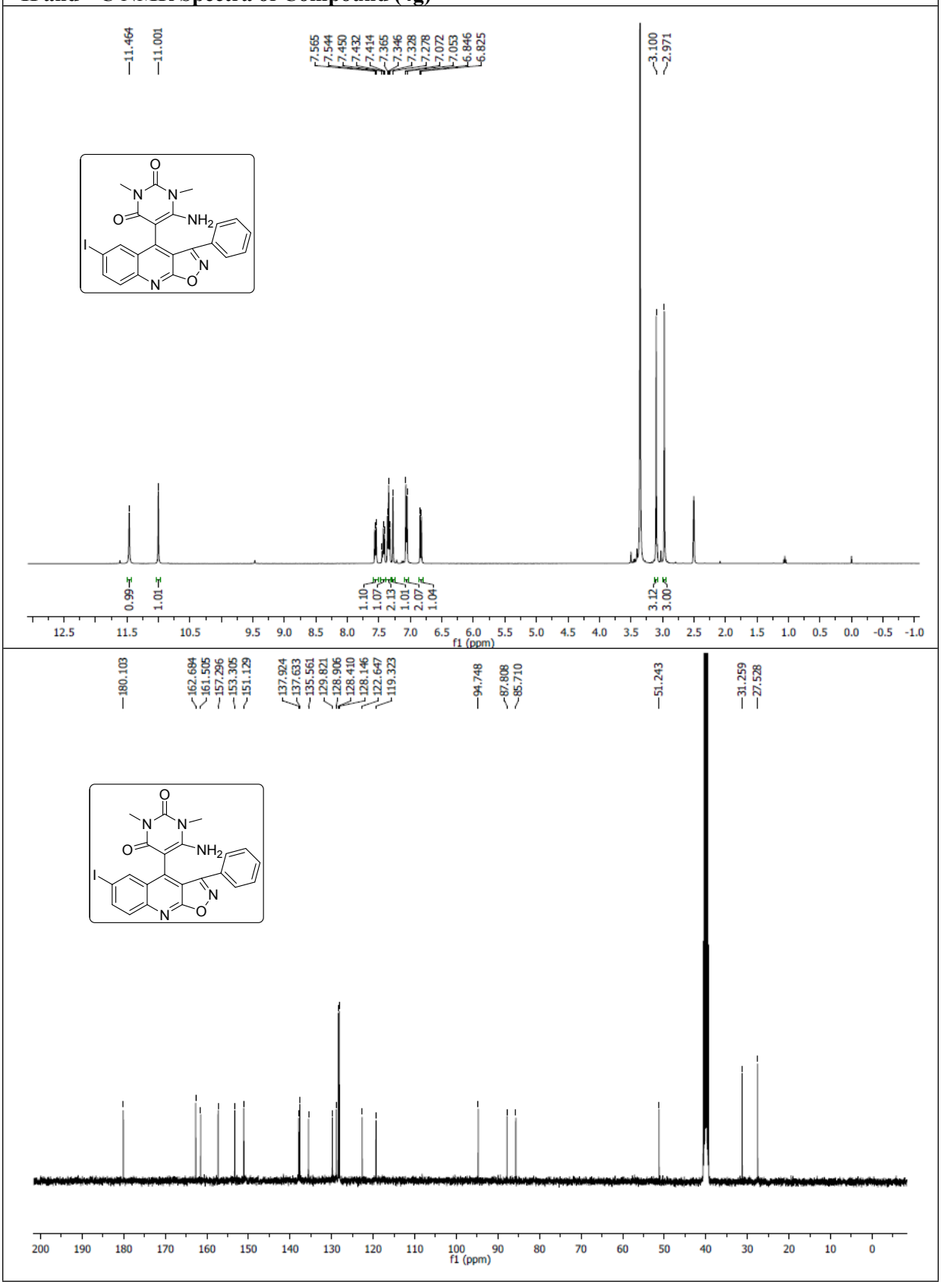




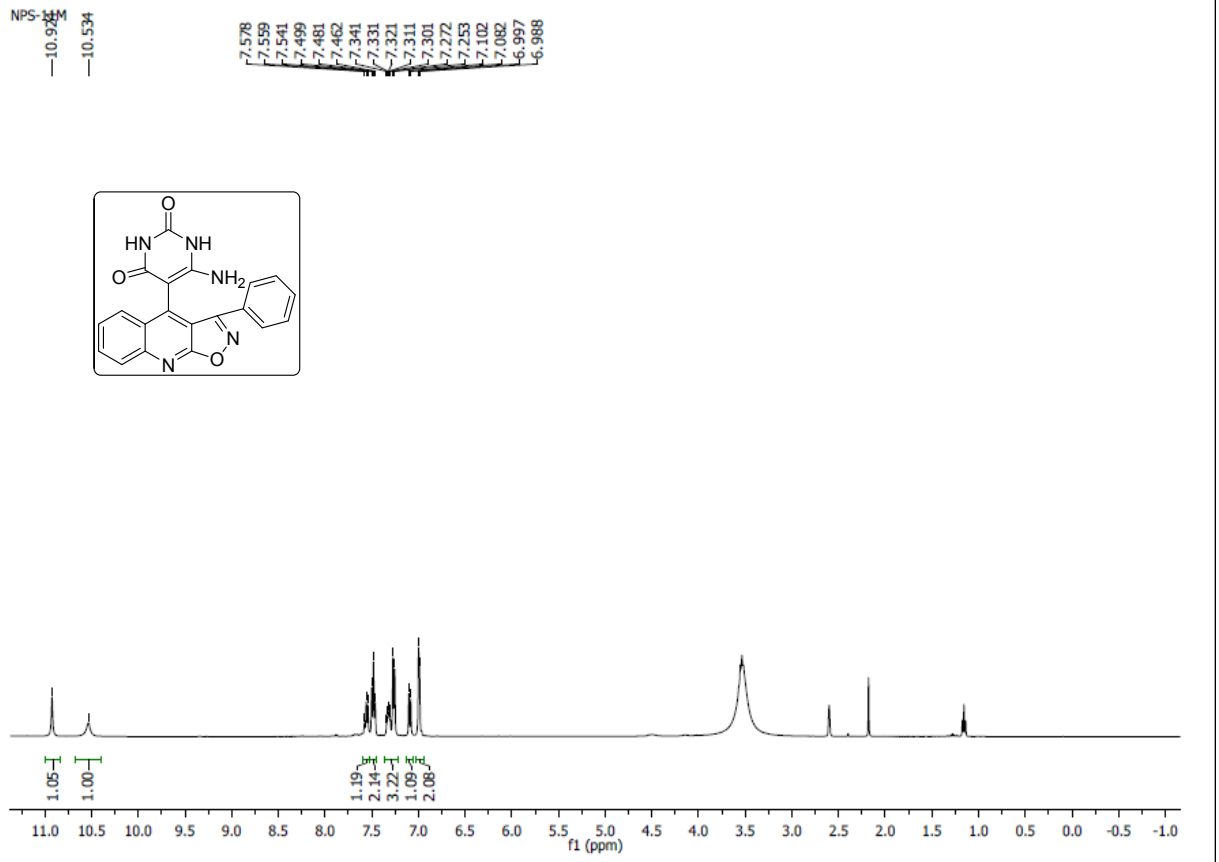
^{1}H and ^{13}C NMR Spectra of Compound (4f)

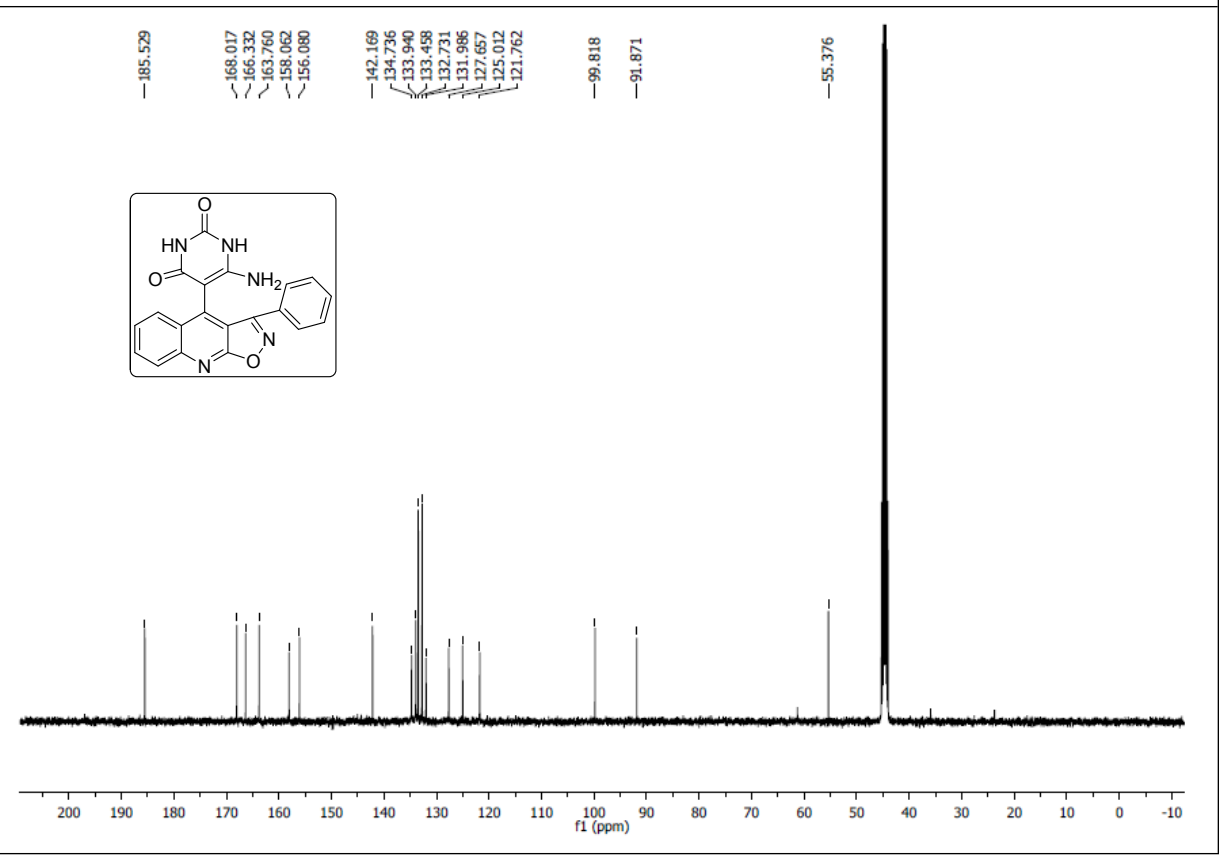


^{1}H and ^{13}C NMR Spectra of Compound (4g)

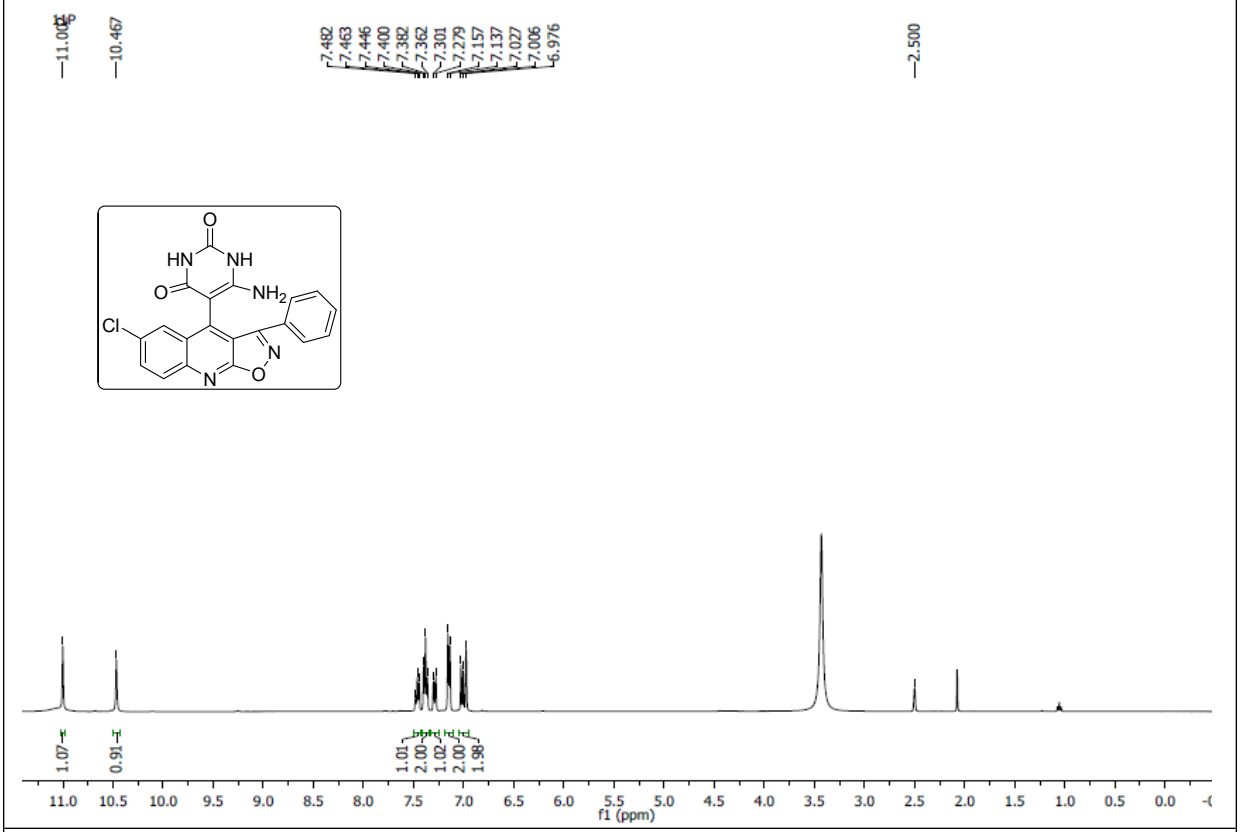


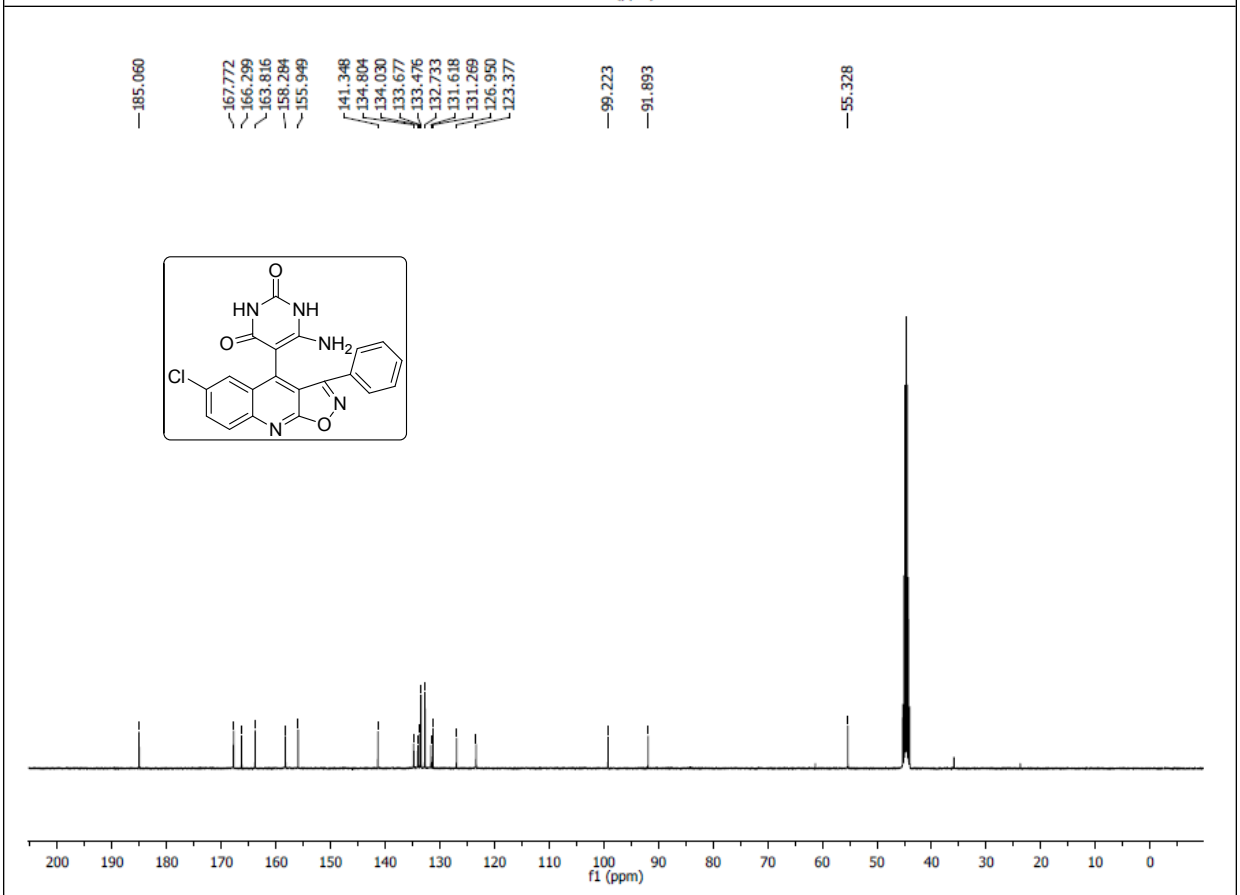
^{1}H and ^{13}C NMR Spectra of Compound (4h)



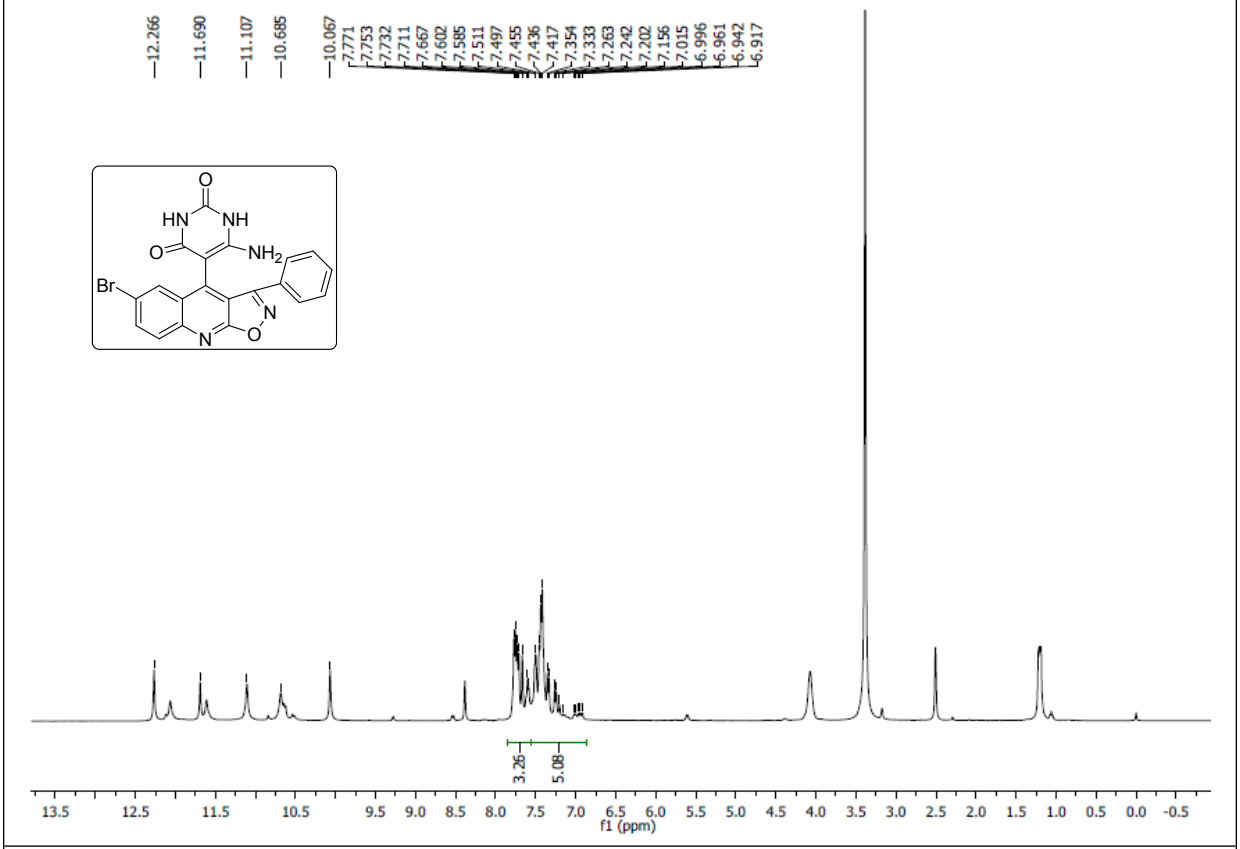


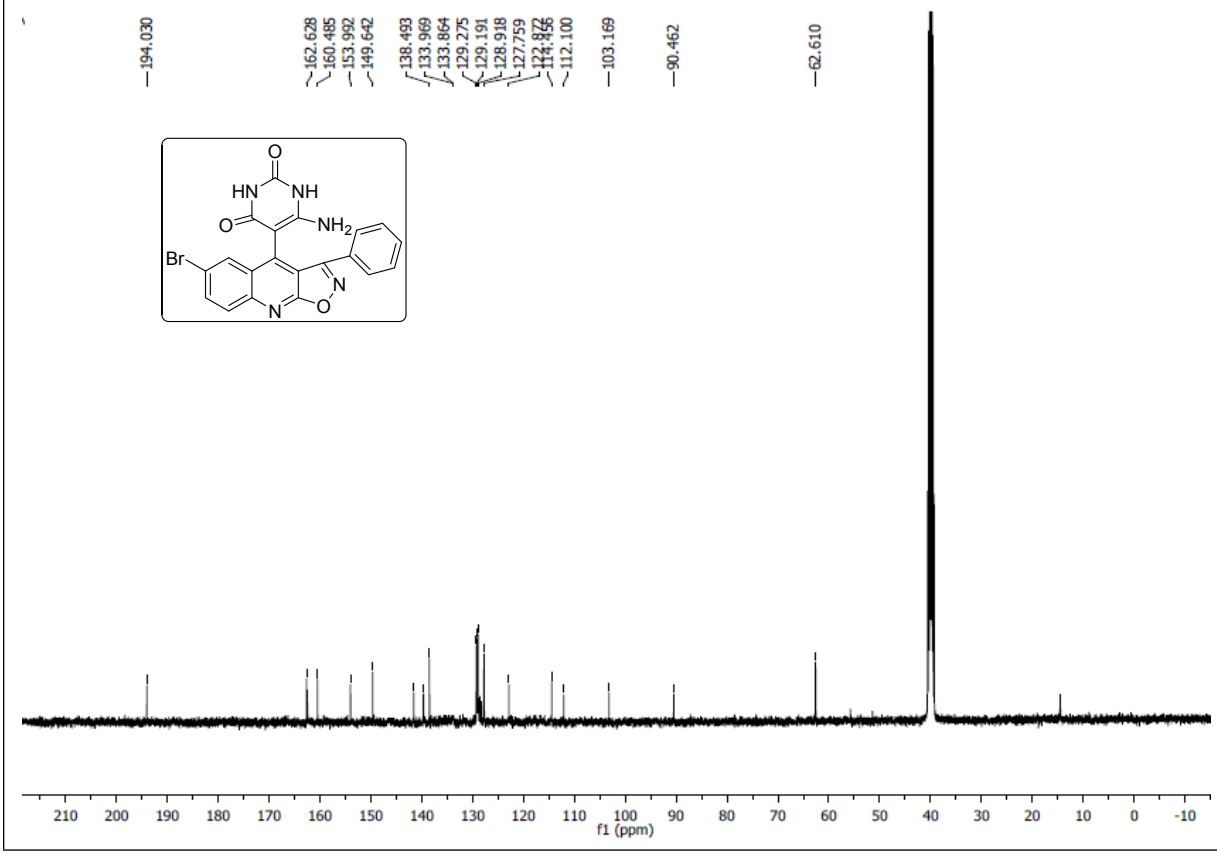
^{1}H and ^{13}C NMR Spectra of Compound (4i)



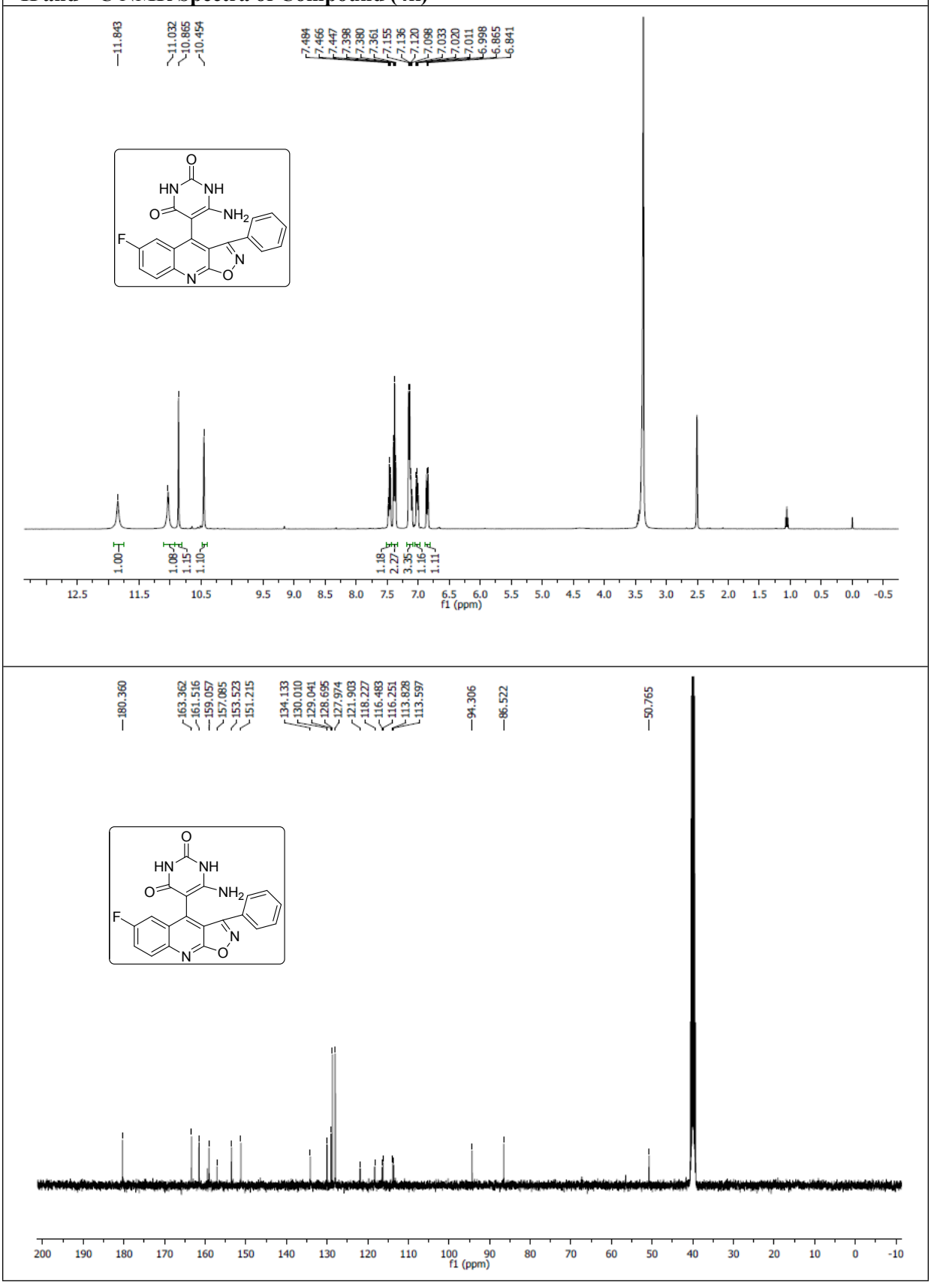


^{1}H and ^{13}C NMR Spectra of Compound (4j)

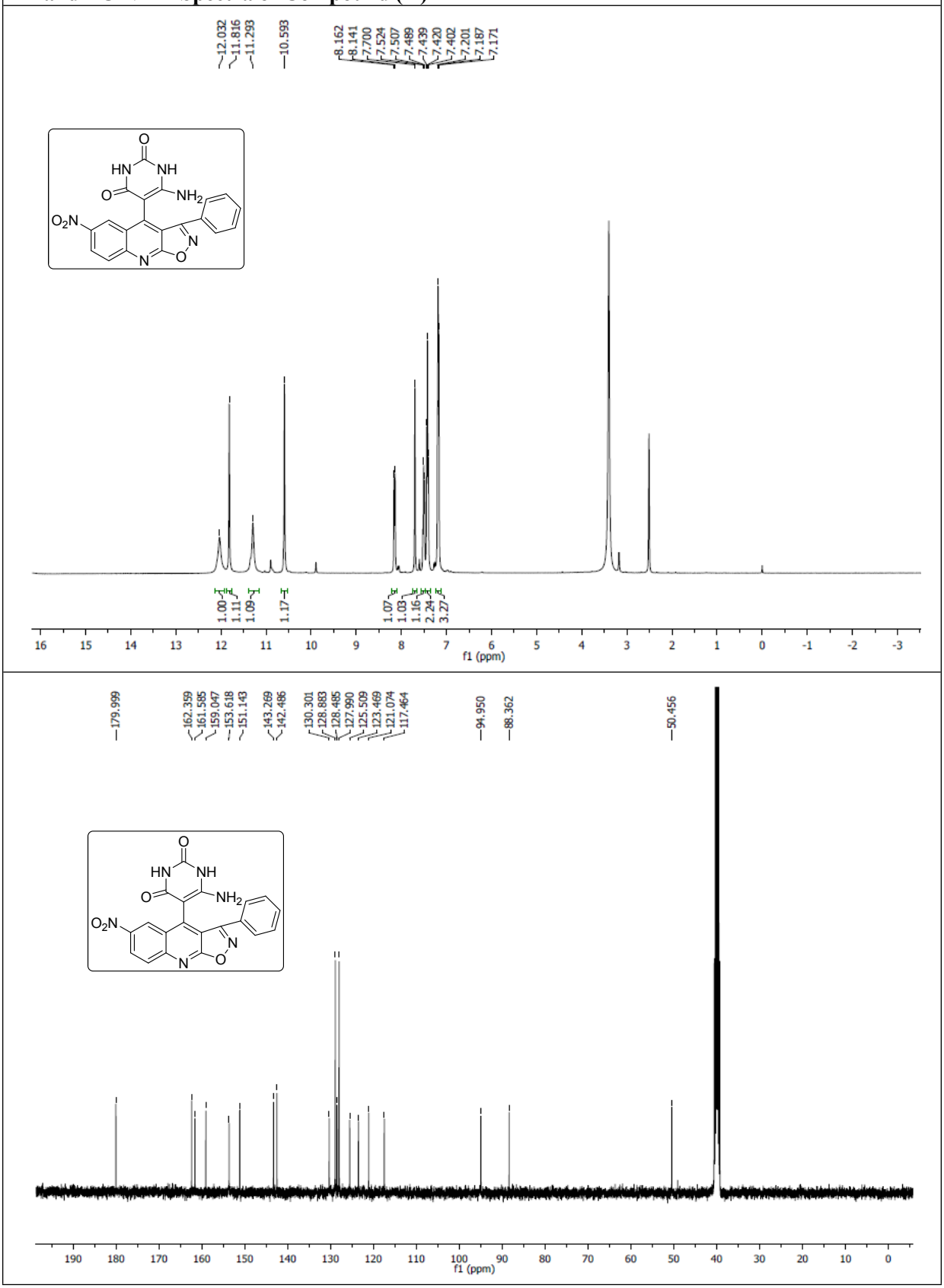




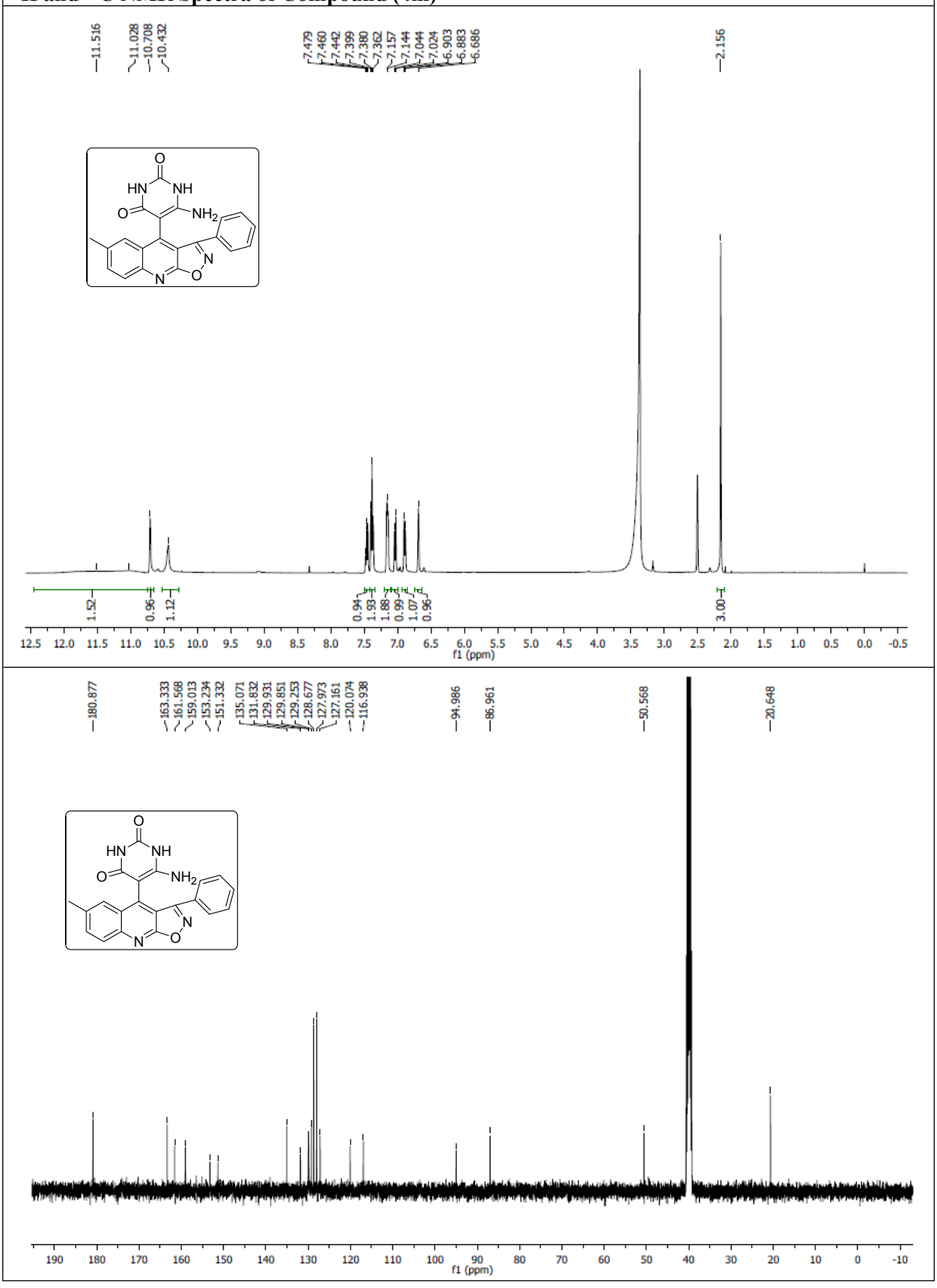
^{1}H and ^{13}C NMR Spectra of Compound (4k)



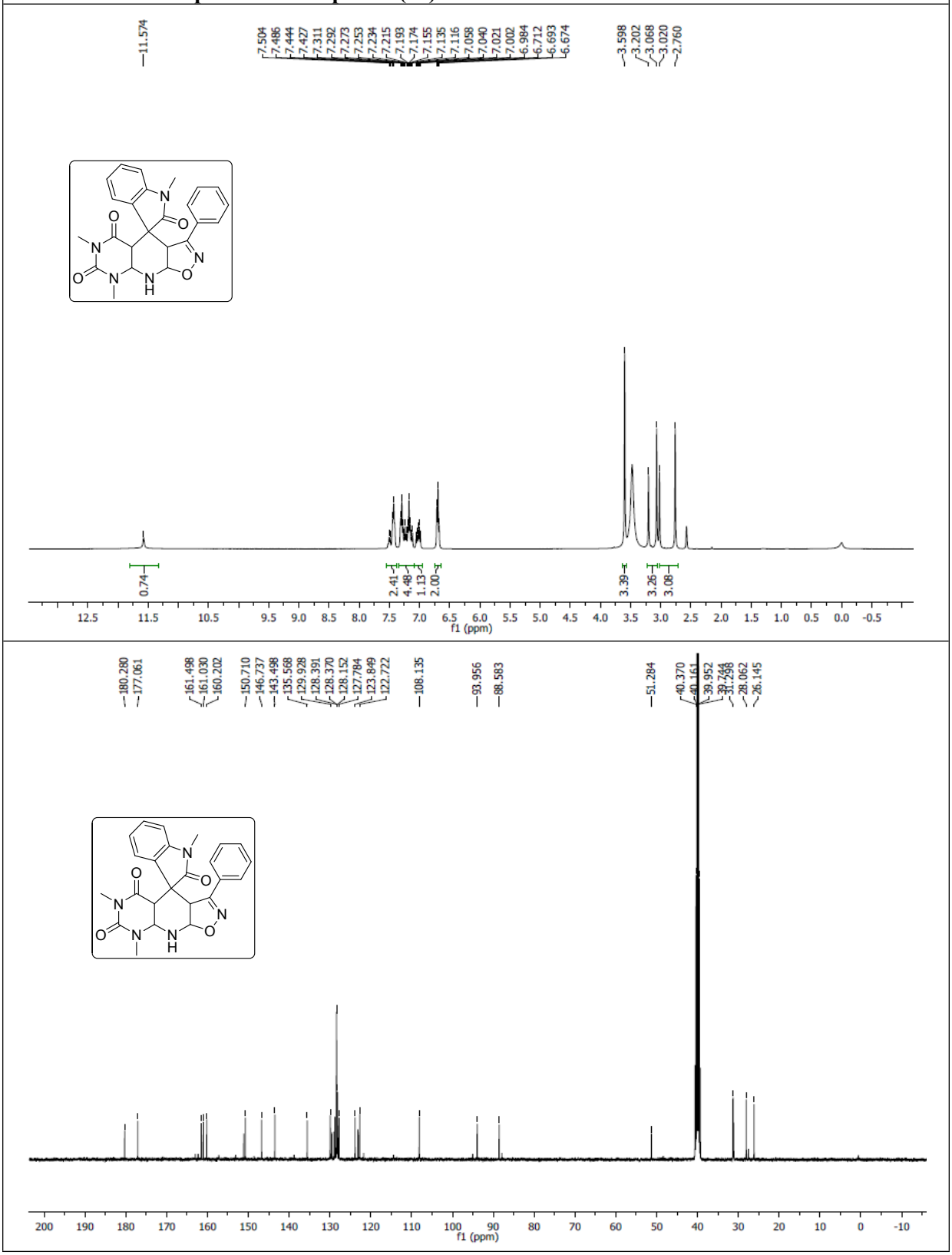
^{1}H and ^{13}C NMR Spectra of Compound (4l)



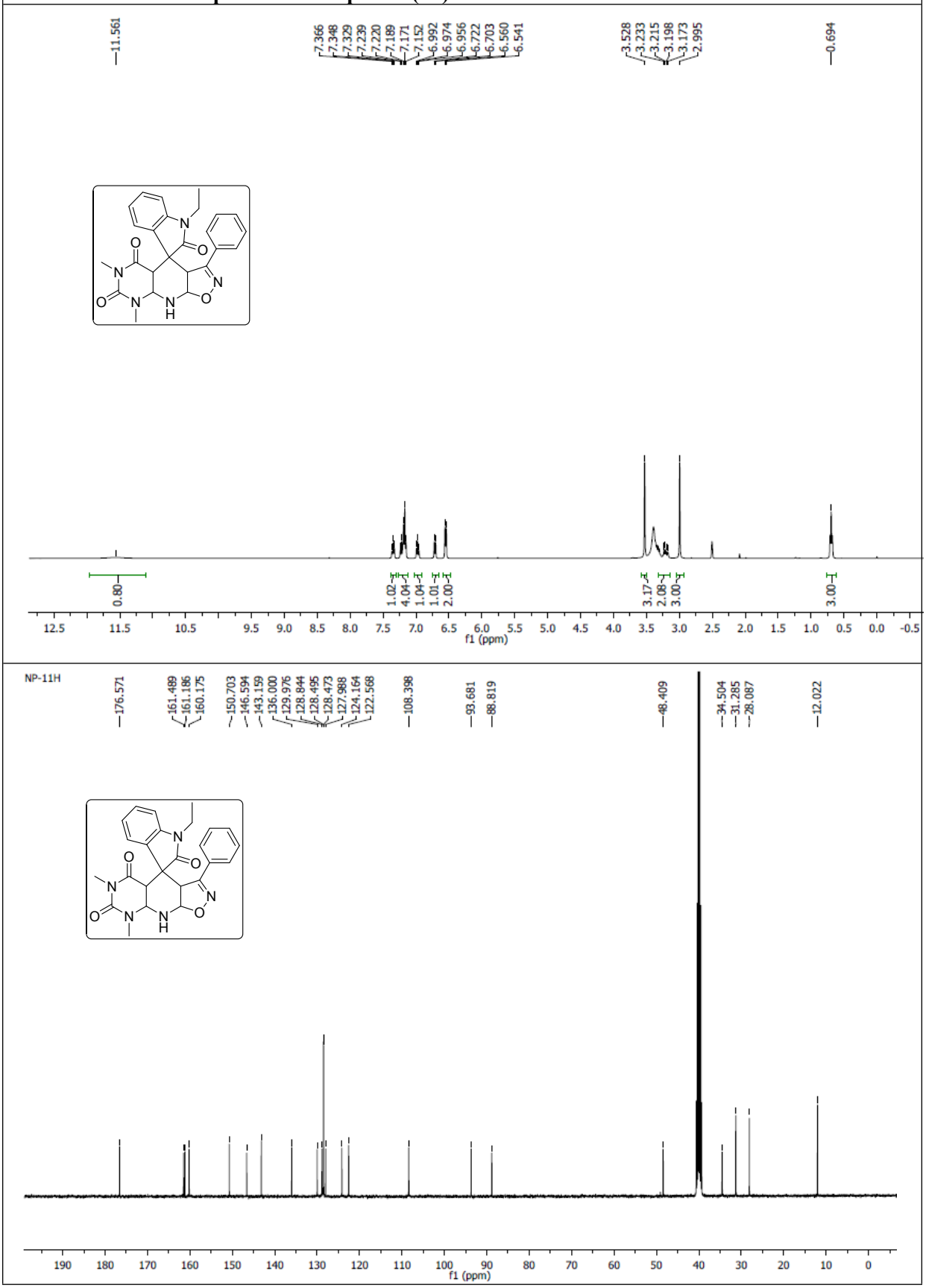
^{1}H and ^{13}C NMR Spectra of Compound (4m)



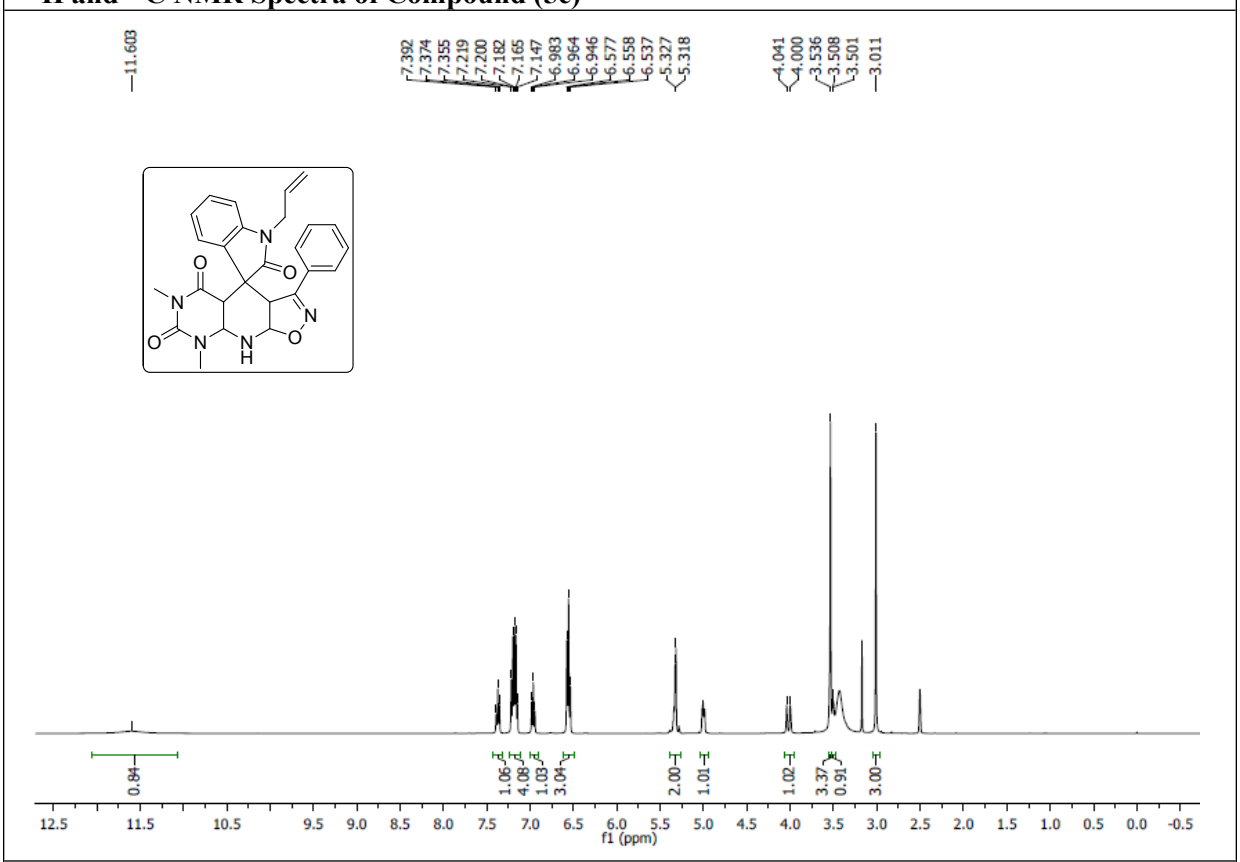
^{1}H and ^{13}C NMR Spectra of Compound (5a)

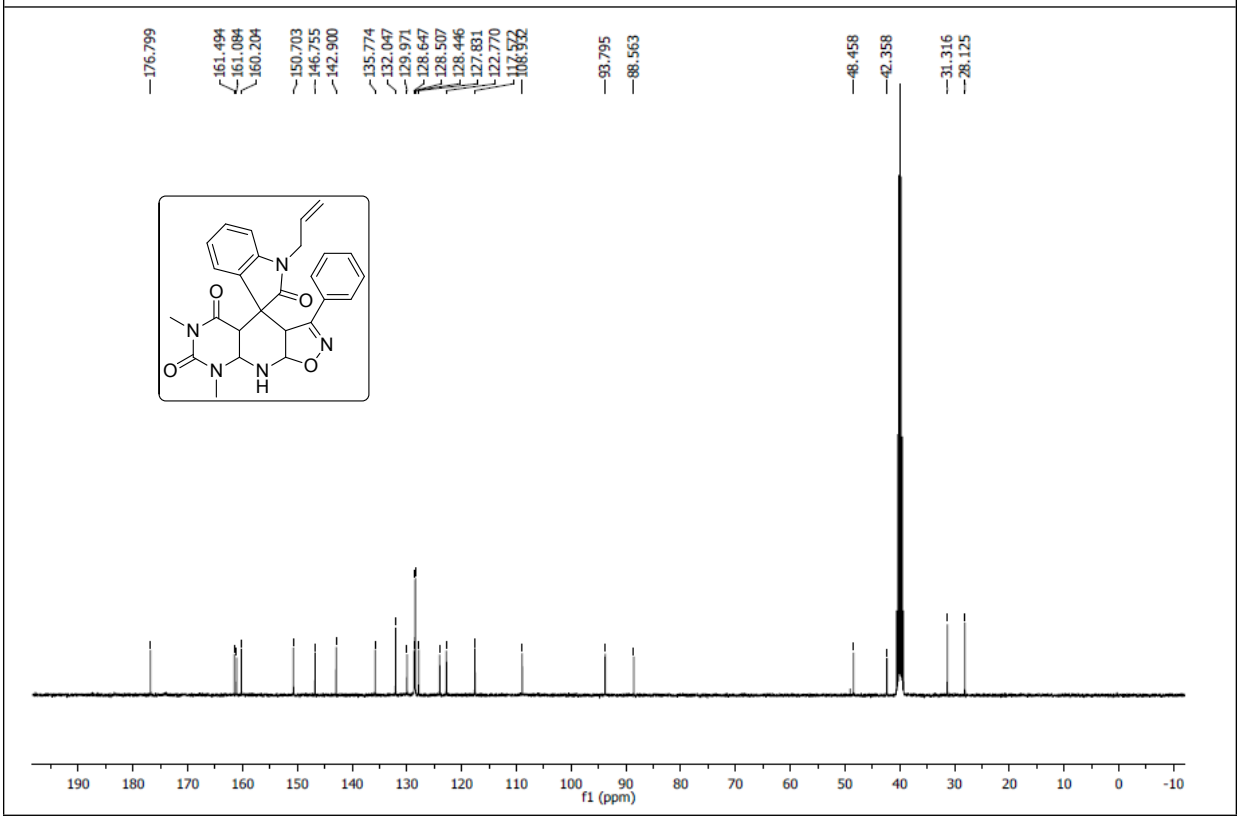


^{1}H and ^{13}C NMR Spectra of Compound (5b)

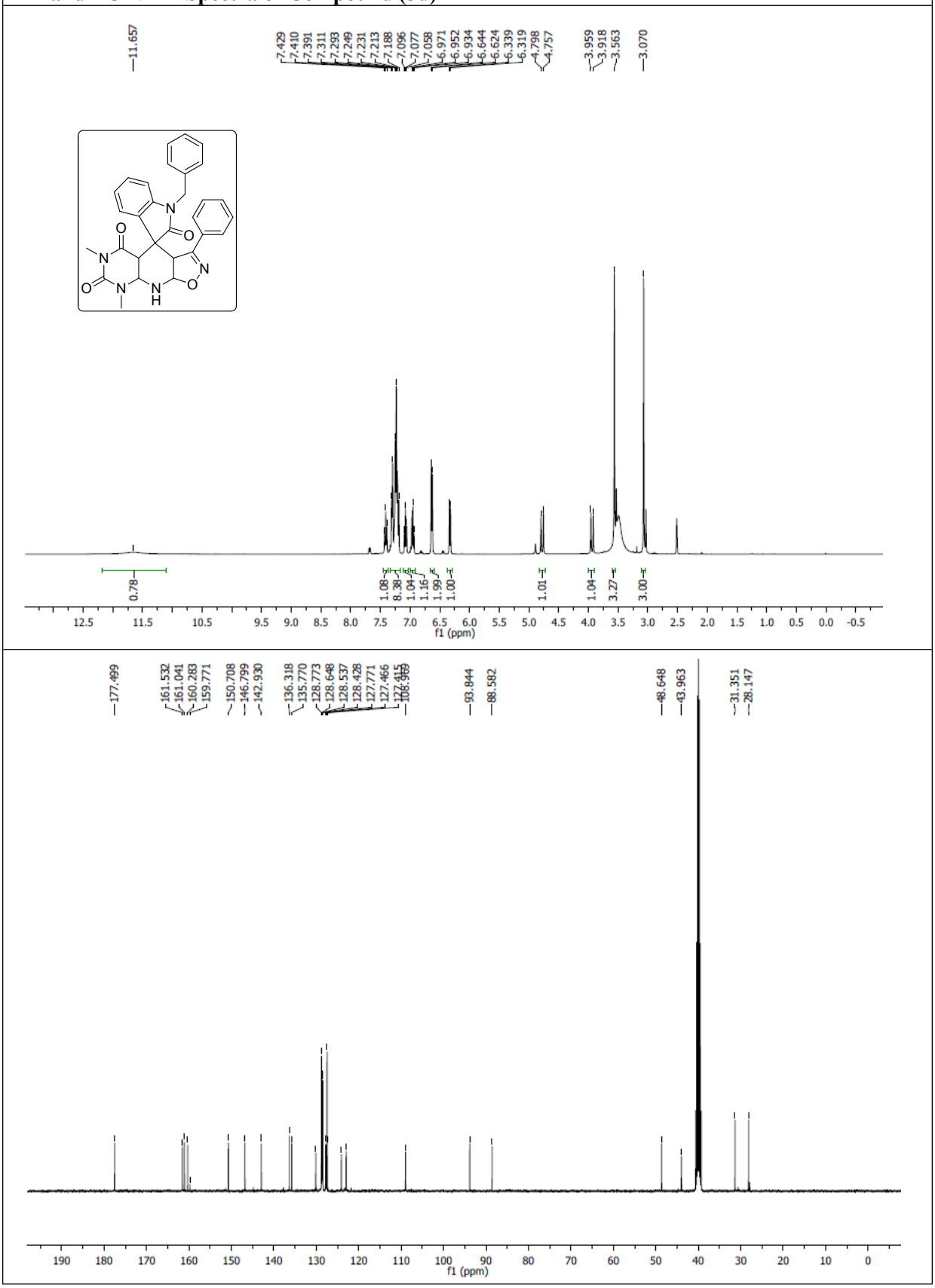


^{1}H and ^{13}C NMR Spectra of Compound (5c)

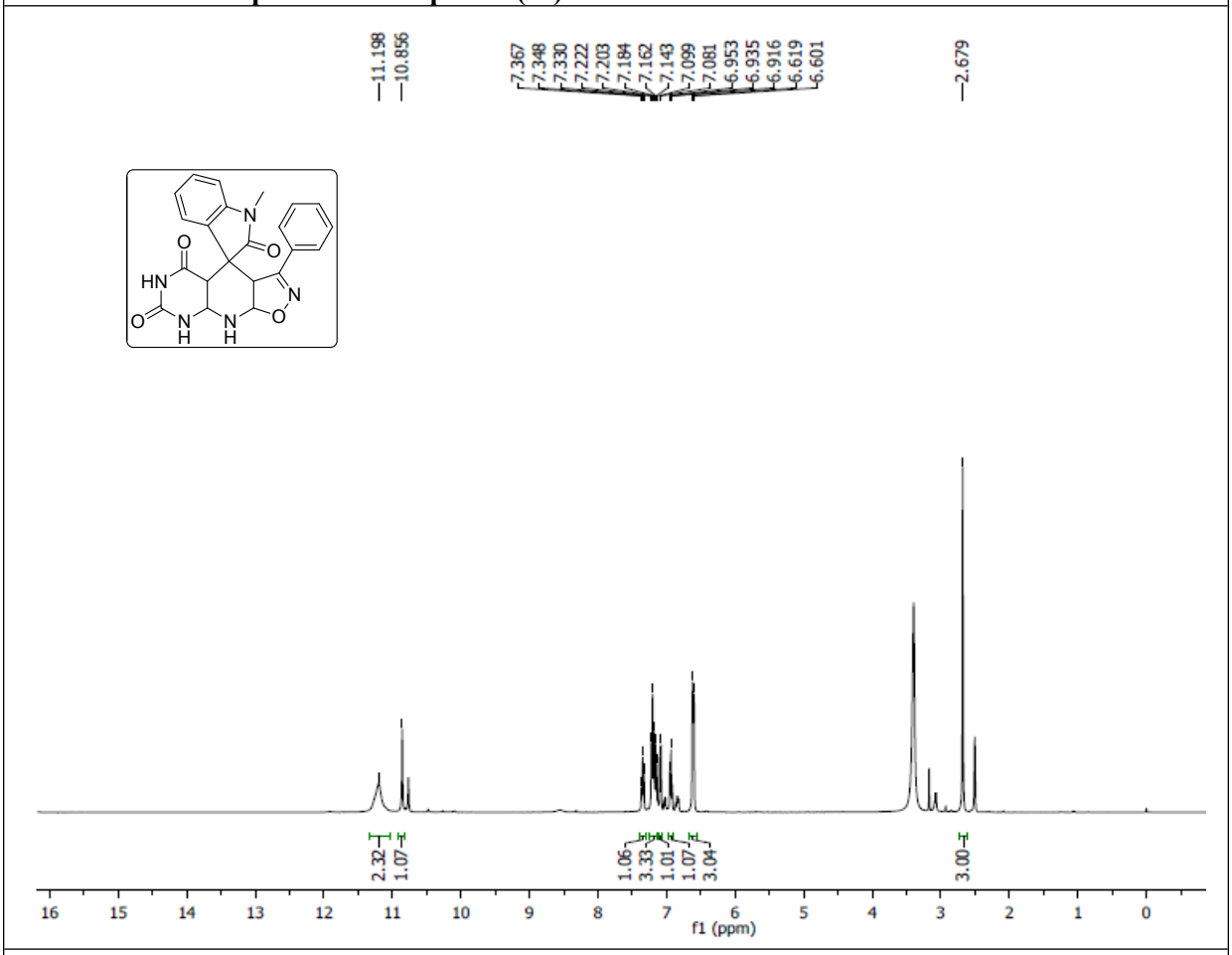


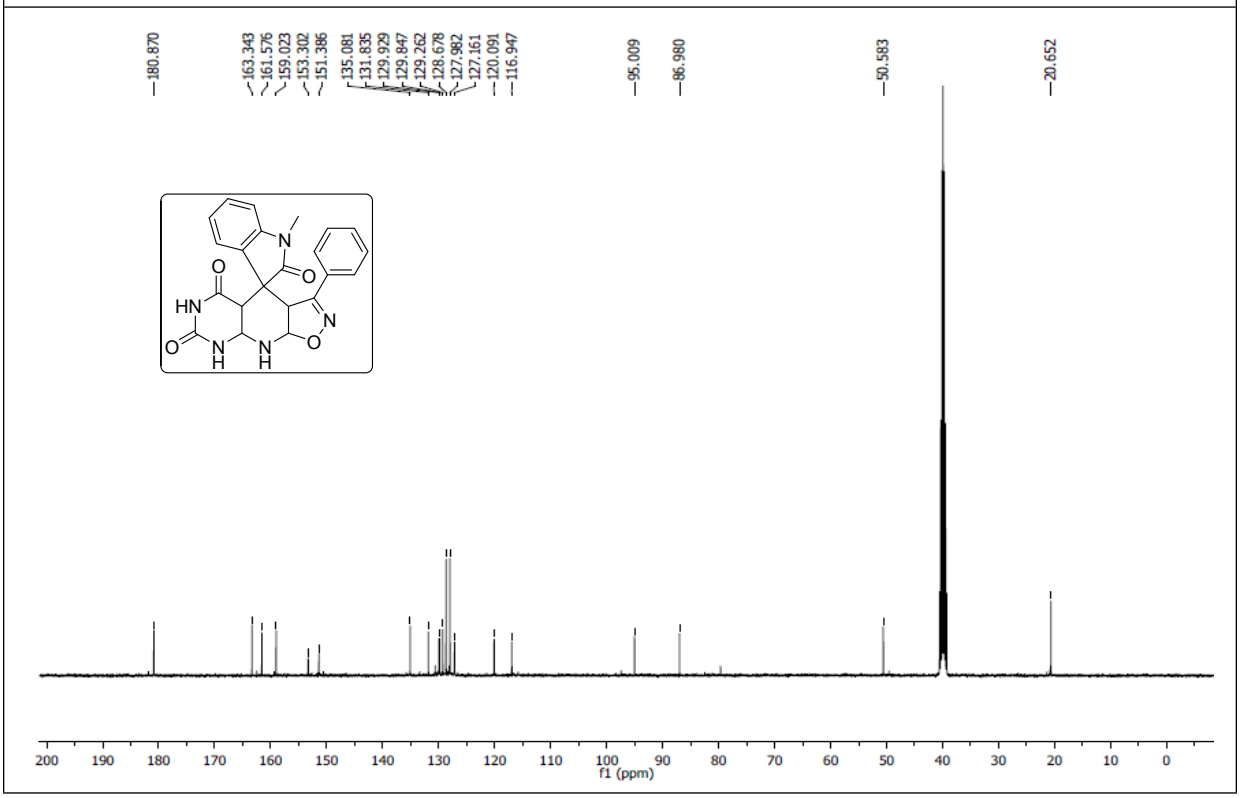


^{1}H and ^{13}C NMR Spectra of Compound (5d)

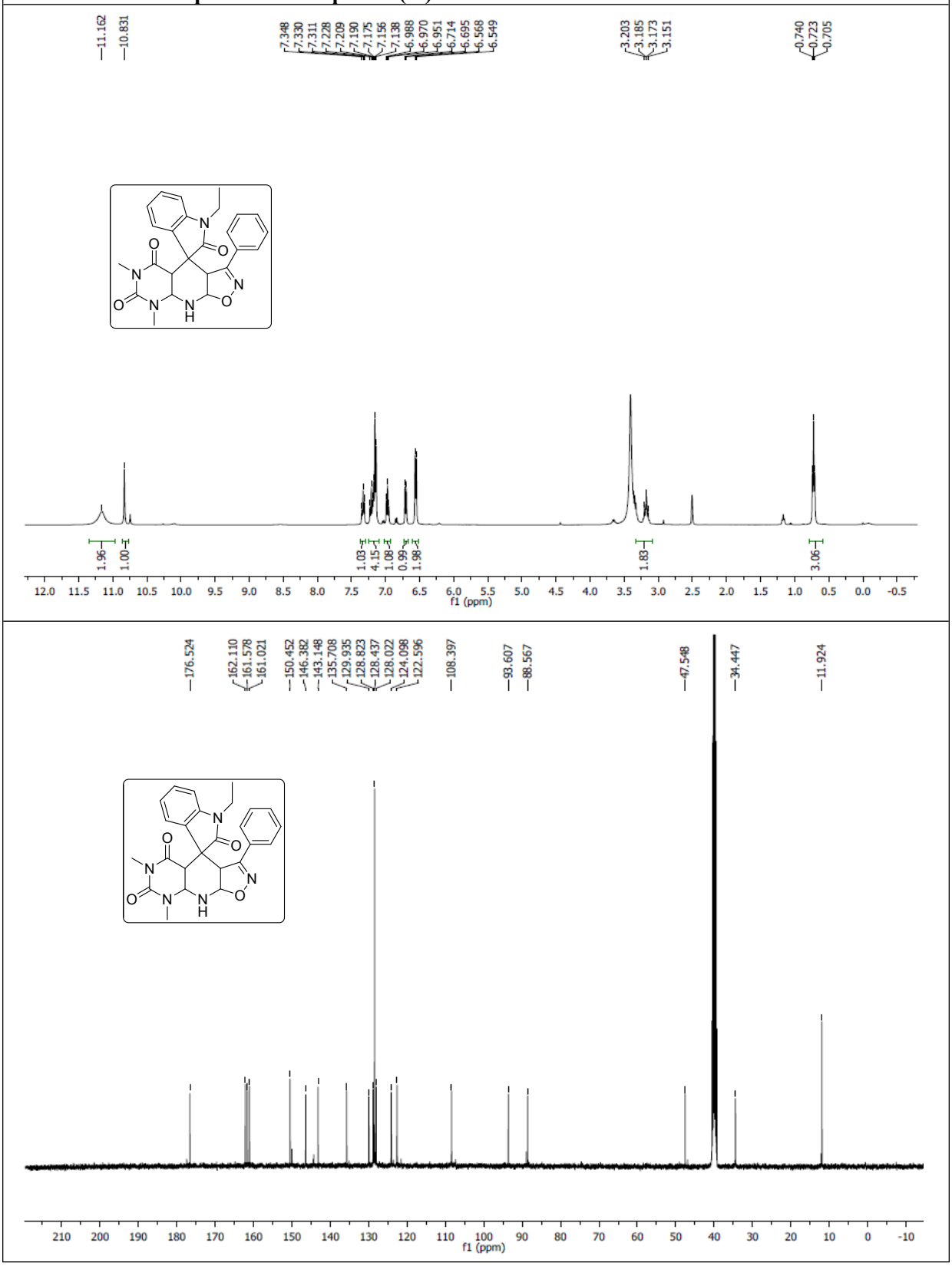


^{1}H and ^{13}C NMR Spectra of Compound (5e)

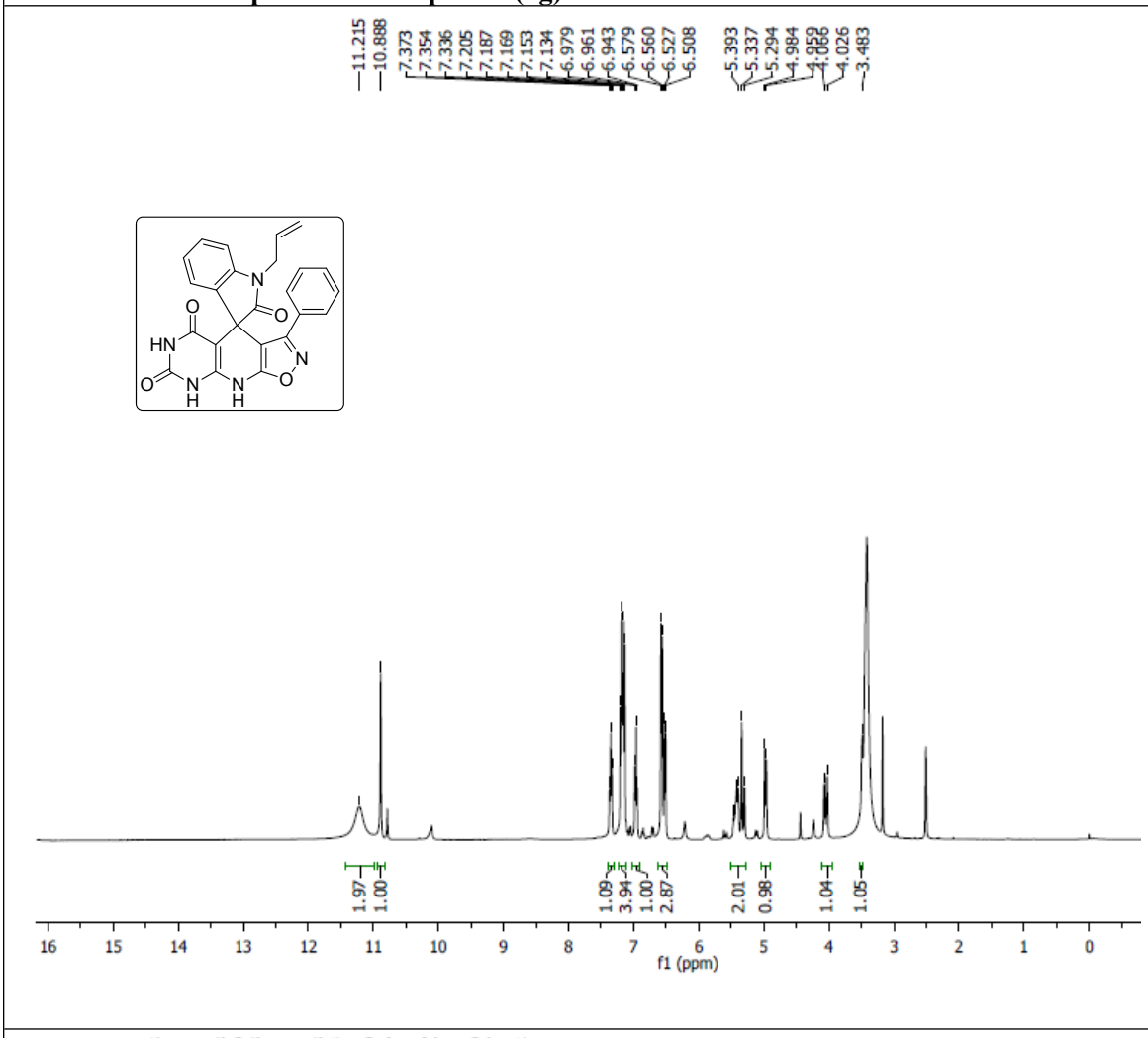


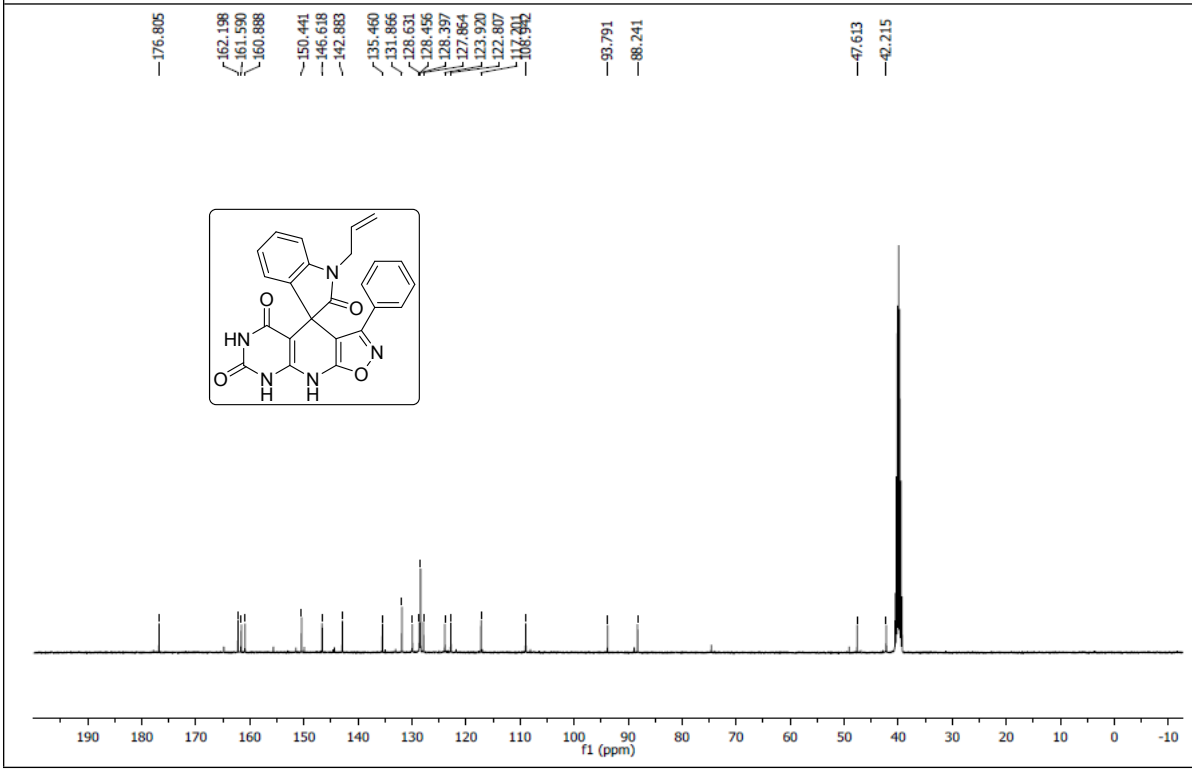


^{1}H and ^{13}C NMR Spectra of Compound (5f)

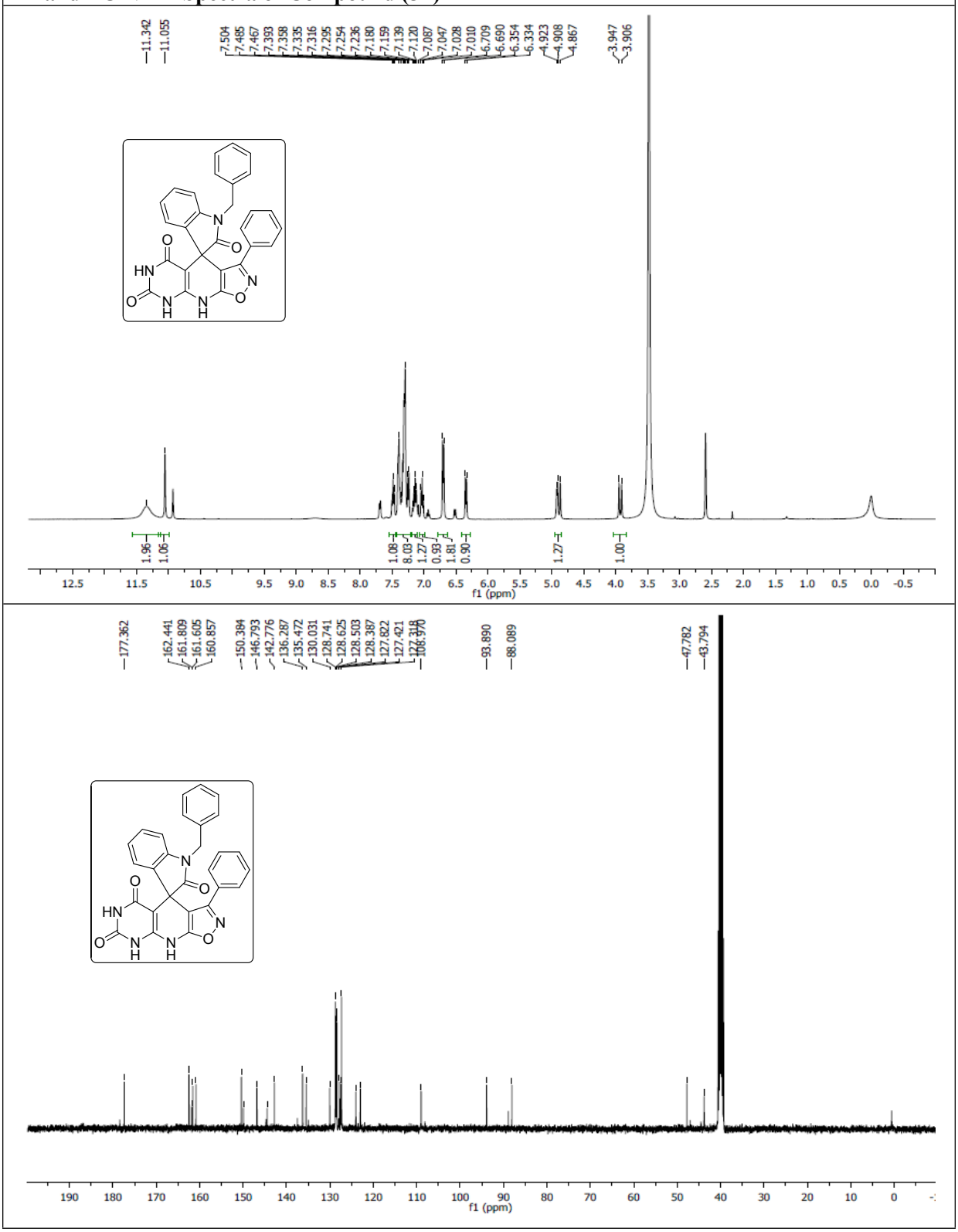


^{1}H and ^{13}C NMR Spectra of Compound (5g)

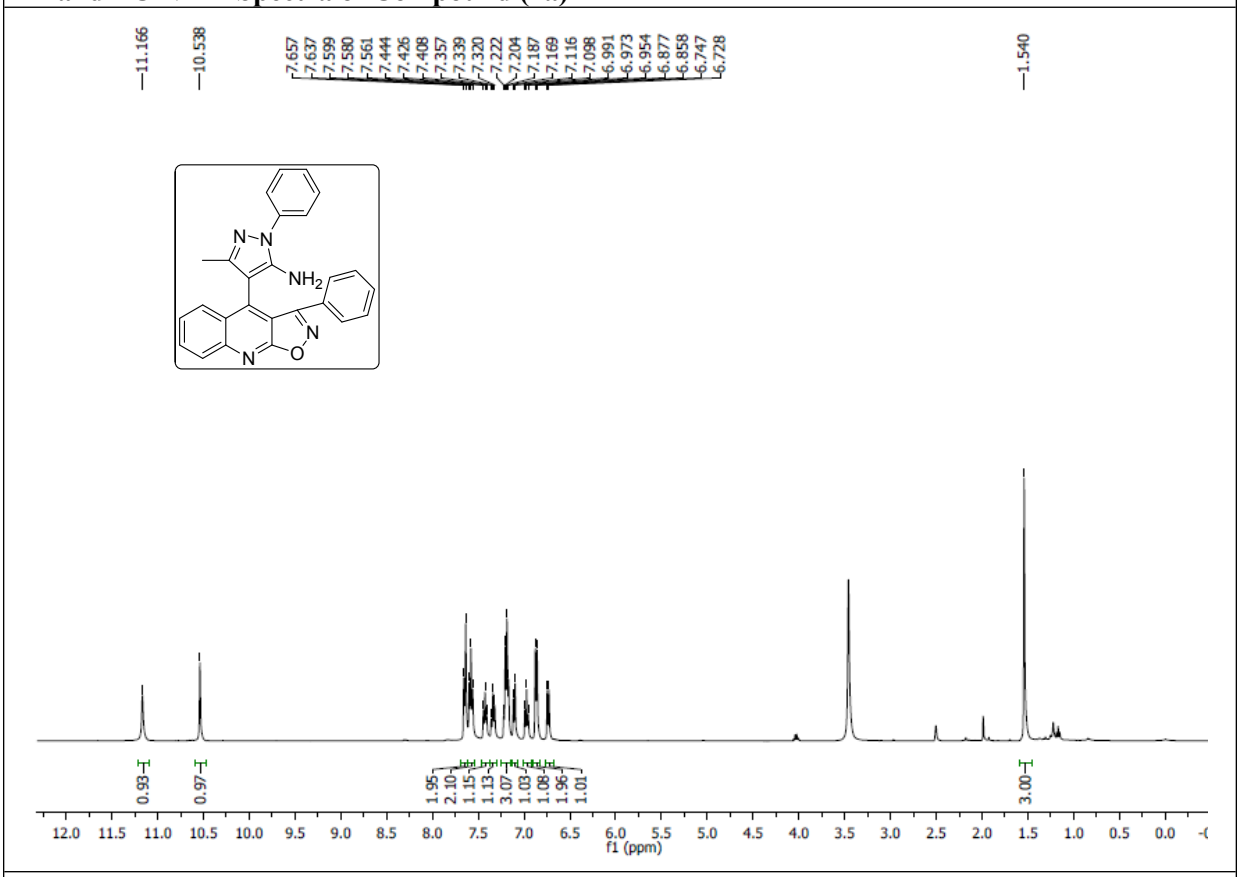


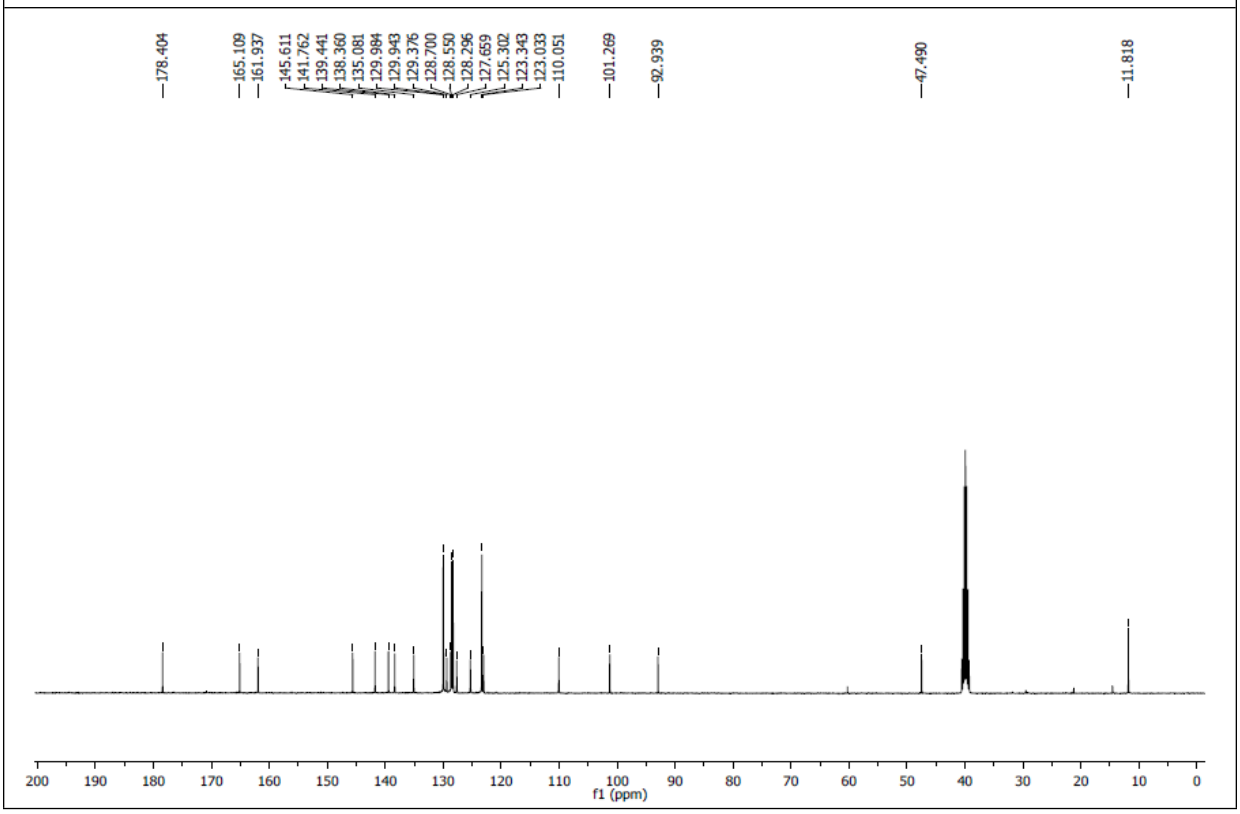


^{1}H and ^{13}C NMR Spectra of Compound (5h)

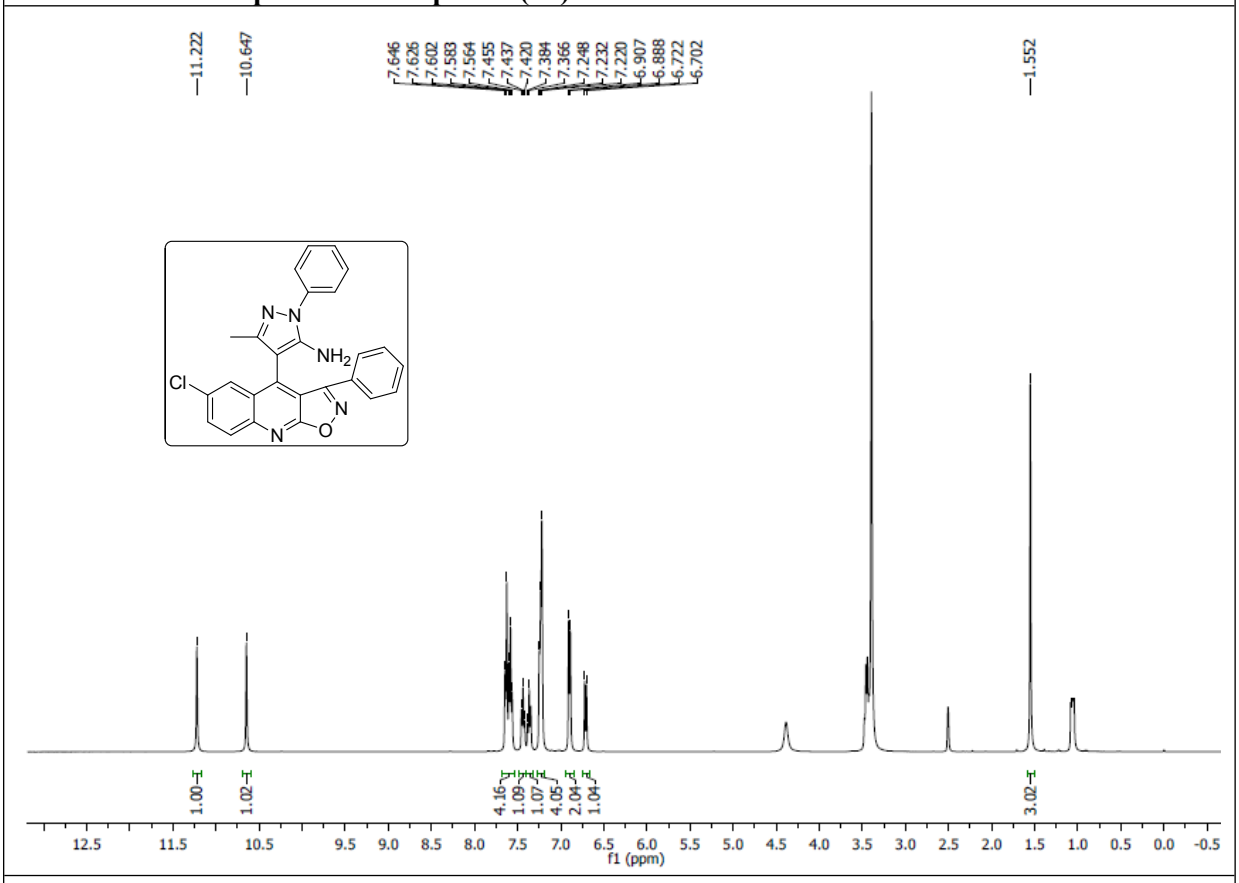


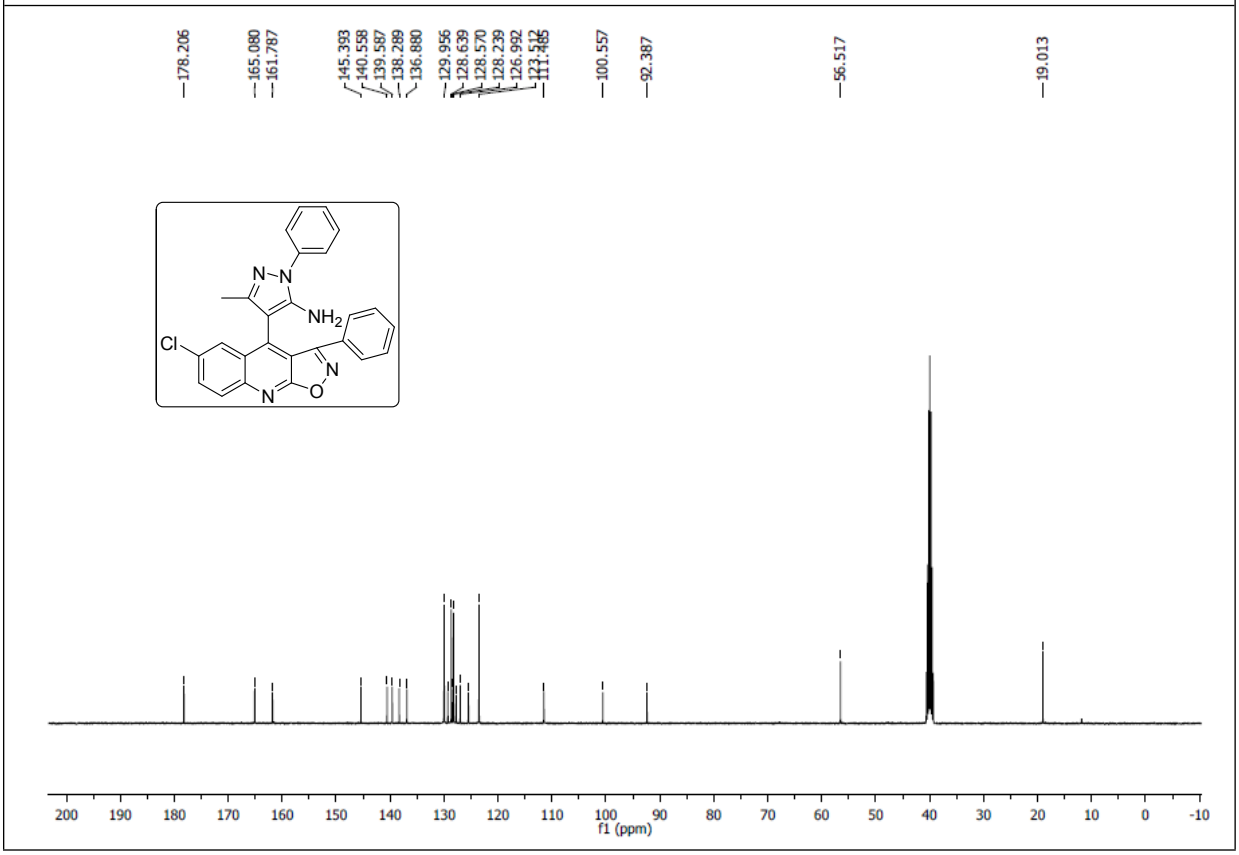
^{1}H and ^{13}C NMR Spectra of Compound (7a)



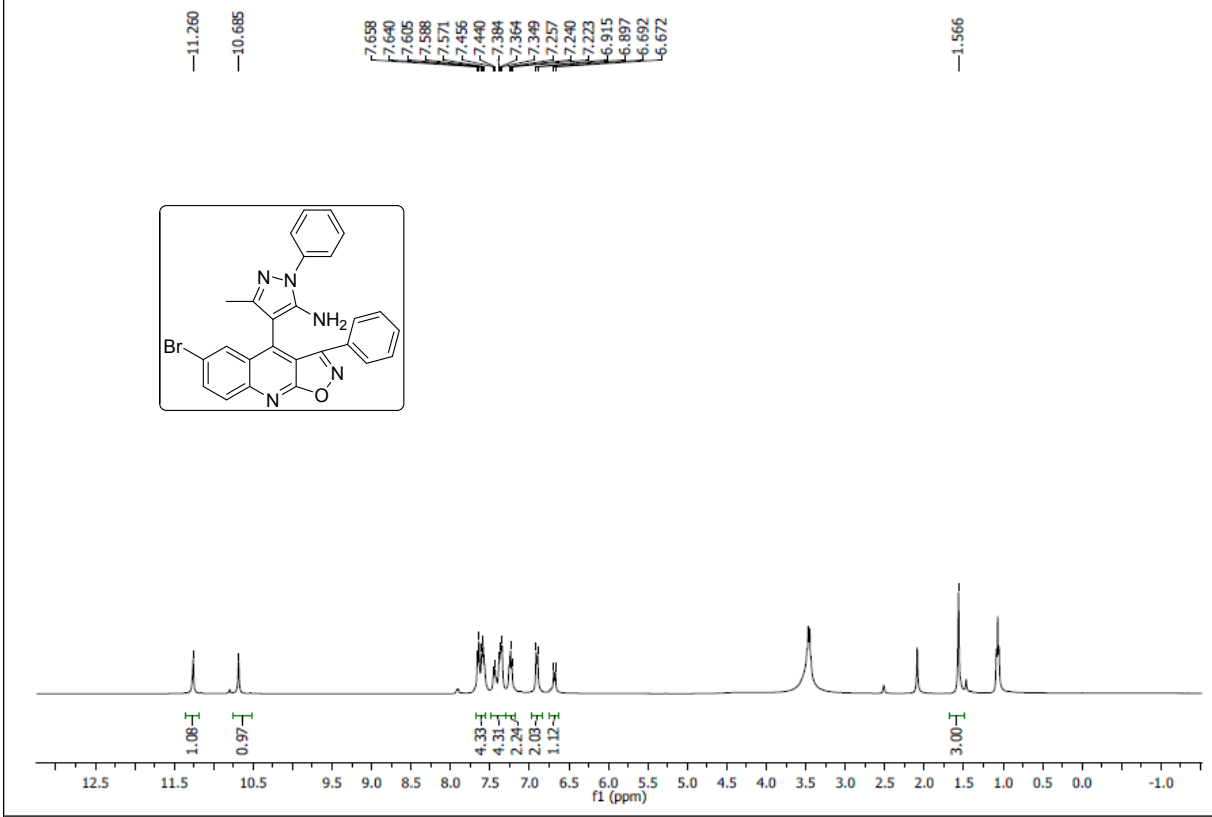


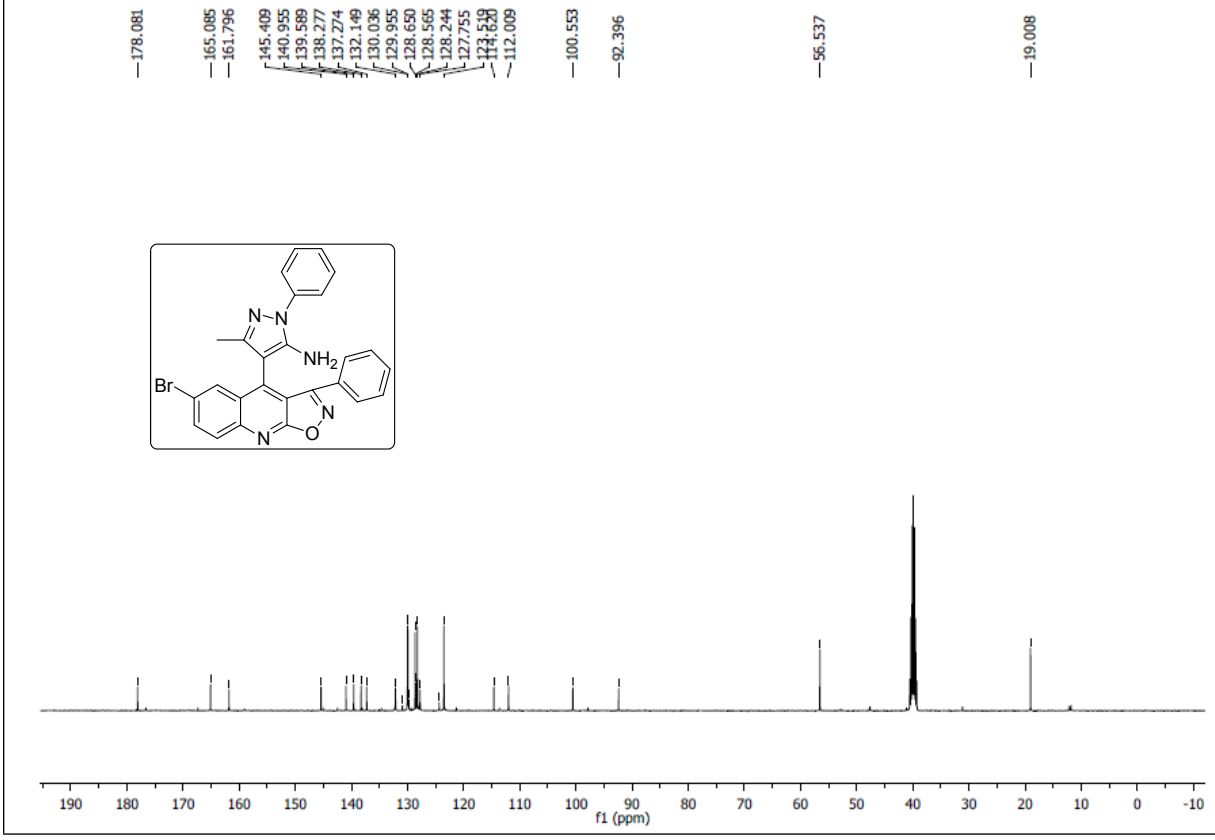
^{1}H and ^{13}C NMR Spectra of Compound (7b)



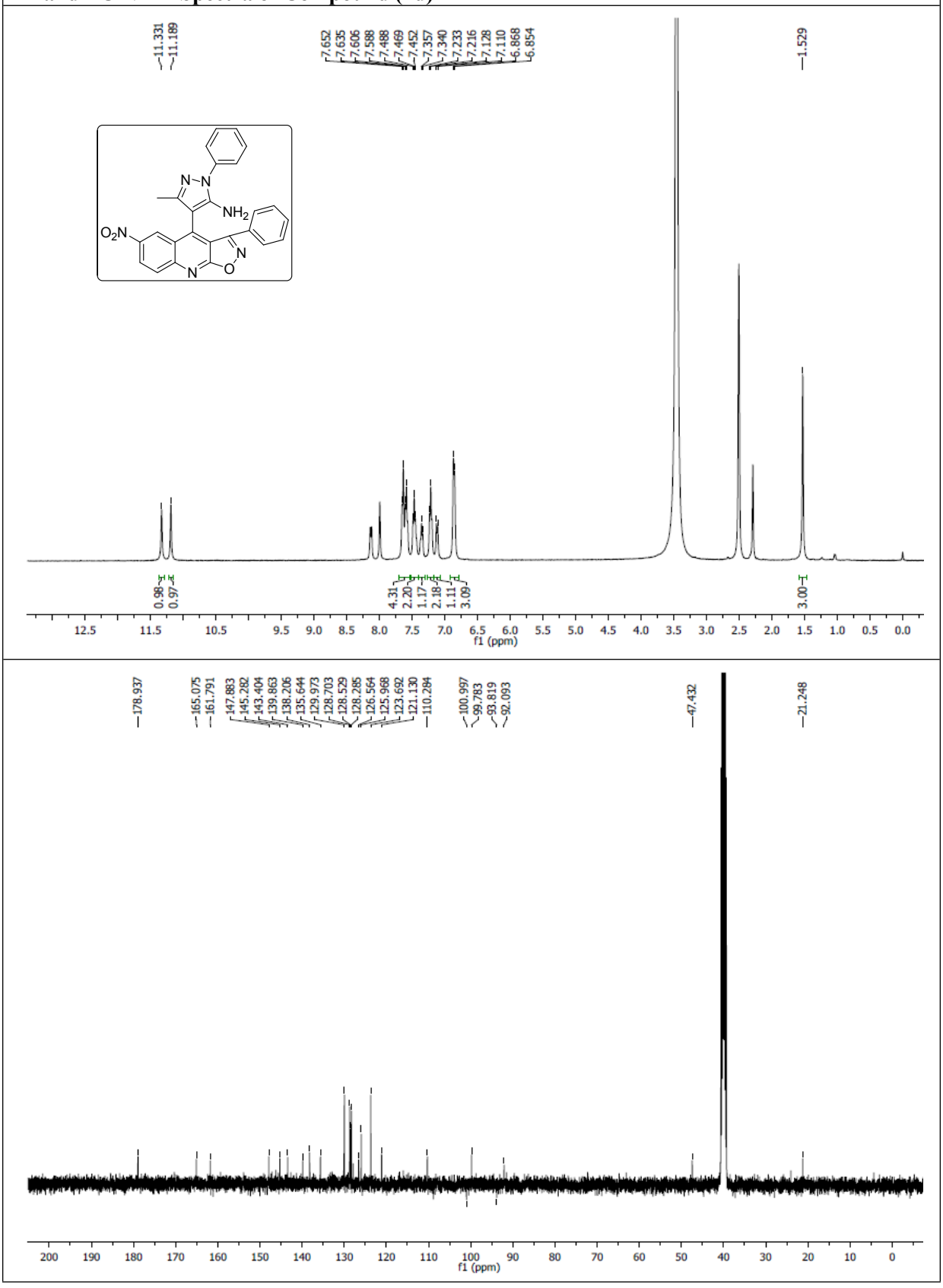


^{1}H and ^{13}C NMR Spectra of Compound (7c)





^{1}H and ^{13}C NMR Spectra of Compound (7d)



^{1}H and ^{13}C NMR Spectra of Compound (7f)