Supporting Information

Regioselective [5+1] rearrangement-annulation: A new and efficient domino route to highly functionalized [1,6]naphthyridines

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Experimental

General information

Microwave irradiation was carried out with Initiator 2.5 Microwave Synthesizers from Biotage, Uppsala, Sweden. Melting points were determined in open capillaries and were uncorrected. IR spectra were taken on a FT-IR-Tensor 27 spectrometer in KBr pellets and reported in cm^{-1}. ^1H NMR spectra were measured on a Bruker DPX 400 MHz spectrometer in DMSO-d_6 (Or $DCCl_3$) with chemical shift (δ) given in ppm relative to TMS as internal standard [(s = singlet, d = doublet, t = triplet, brs = broad singlet, m = multiplet), coupling constant (Hz)]. HRMS (ESI) was determined by using microTOF-QⅡ HRMS/MS instrument (BRUKER). X-Ray crystallographic analysis was performed with a Siemens SMART CCD and a Siemens P4 diffractometer.

General procedure for the synthesis of 1,6-naphthyridines 3

Example for the synthesis of **3f**: 1,2,5,6-Tetrahydro-2,7-dimethyl-5-oxo-2,4-diphenyl-1,6-naphthyridine -8-carbonitrile (**3f**)

Microwave Heating: 2-(3-Cyano-6-methyl-4,6-diphenyl-5,6-dihydropyridin-2(1H)-ylidene)malononitrile (**1f**, 1.0 mmol, 0.34 g, 1.0 equiv.) was introduced in a 10-mL Initiator^{TM} reaction vial, acetic acid **2** (3.0 mL, excess) and aqueous ammonia (0.5 mL, NH_3, 25%) were then successively added. Subsequently, the reaction vial was capped and then pre-stirring for 20 second. The mixture was irradiated (Time: 50 min, Temperature: 160 ^oC; Absorption Level: High; Fixed Hold Time) until TLC (petroleum ether: acetone 4:1) revealed that conversion of the starting material **1f** was completed. The reaction mixture was then cooled to room temperature and then diluted with cold water (15 ml). The solid product was collected by Büchner filtration and was purified by recrystallization from 70% ethanol afford the desired pure 1,6-naphthyridines **3f**

General procedure for the synthesis of 5,7-diamino-1,6-naphthyridines (4a)

Example for the synthesis of **4a**: 5,7-Diamino-1,2-dihydro-2-methyl-2,4-diphenyl-1,6-naphthyridine-8-carbonitrile

Microwave Heating: 2-(3-Cyano-6-methyl-4,6-diphenyl-5,6-dihydropyridin-2(1H)-ylidene)malononitrile (**1f**, 1.0 mmol, 0.34 g, 1.0 equiv.) was introduced in a 10-mL Initiator^{TM} reaction vial, aqueous ammonia (2.0 mL, NH_3, 25%) were then successively added. Subsequently, the reaction vial was capped and then pre-stirring for 20 second. The mixture was irradiated (Time: 40 min, Temperature: 160 ^oC; Absorption Level: High; Fixed Hold Time) until TLC (petroleum ether: acetone 4:1) revealed that conversion of the starting material **1f** was completed. The reaction mixture was then cooled to room temperature, and the solid product was collected by Büchner filtration and was purified by recrystallization from 70% ethanol afford the desired pure 1,6-naphthyridines **4a**

General procedure for the synthesis of 3a under traditional heating conditions: Typically, 2-(3-cyano-6-methyl-4,6-di(4-chlorophenyl)-5,6-dihydropyridin-2(1H)-ylidene)malononitrile (**1a**, 1.0 mmol, 0.41 g, 1.0 equiv.) was introduced in a 10-mL Initiator^{TM} reaction vial, acetic acid **2** (3.0 mL, excess) and aqueous ammonia (0.5 mL, NH_3, 25%) were then successively added. Subsequently, the reaction vial was capped and stirred in oil bath at 160 ^{o}C for 50 min. Upon completion, the reaction mixture was then cooled to room temperature and then diluted with cold water (15 ml). The solid product was collected by Büchner filtration and was purified by recrystallization from 70% ethanol afford the desired pure 1,6-naphthyridines **3a** in 45% chemical yield**.**

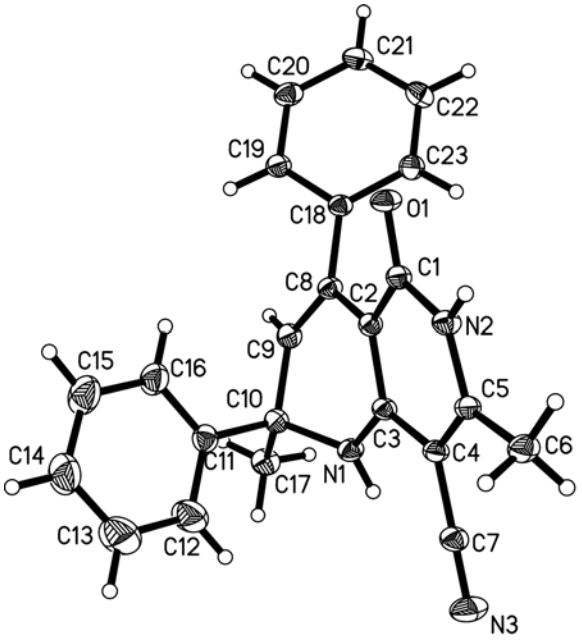
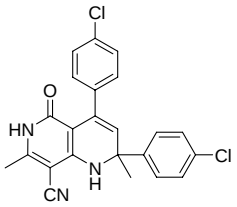


Figure 1 X-ray structure of **3f**

2,4-Bis(4-chlorophenyl)-1,2,5,6-tetrahydro-2,7-dimethyl-5-oxo-1,6-naphthyridine-8-carbonitrile (3a)



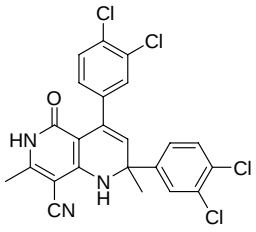
^{1}H NMR (400 MHz, DMSO-d_6) δ 11.53 (s, 1H, NH), 7.50 (s, 1H, NH), 7.48 (d, J = 8.8 Hz, 2H, Ar-H), 7.42 (d, J = 8.8 Hz, 2H, Ar-H), 7.27 (d, J = 8.0 Hz, 2H, Ar-H), 7.13 (d, J = 8.4 Hz, 2H, Ar-H), 5.47 (s, 1H, CH), 2.34 (s, 3H, CH_3), 1.72 (s, 3H, CH_3).

IR (KBr, ν, cm^{-1}): 3334,, 2217, 1638, 1556, 1455, 1096, 813.

^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 157.9, 155.3, 150.4, 147.1, 138.9, 131.3, 130.9, 129.2, 128.1, 126.9, 126.8, 125.6, 115.3, 98.5, 81.0, 56.5, 30.0, 18.3.

HRMS (ESI): m/z calcd for: $C_{23}H_{17}Cl_2N_3NaO$,444.0646[M+Na]$^+$, found: 444.0640

2,4-Bis(3,4-dichlorophenyl)-1,2,5,6-tetrahydro-2,7-dimethyl-5-oxo-1,6-naphthyridine-8-carbonitrile (3b)



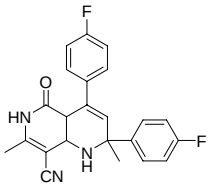
^{1}H NMR (400 MHz, DMSO-d_6) δ 11.63 (s, 1H, NH), 7.72 (s, 1H, NH), 7.64 (d, J = 8.4 Hz, 2H, Ar-H), 7.49 (d, J = 8.4 Hz, 2H, Ar-H), 7.35 (s, 1H, Ar-H), 7.13 (dd, J = 8.4 Hz, 2.0 Hz, 1H, Ar-H), 5.61 (s, 1H, CH), 2.35 (s, 3H, CH_3), 1.73 (s, 3H, CH_3).

IR (KBr, ν, cm^{-1}): 3310, 2219, 1642, 1561, 1465, 1030, 818.

^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 160.6, 158.1, 150.4, 149.0, 140.6, 130.4, 129.2, 129.1, 128.9, 127.9, 127.1, 125.9, 125.6, 116.8, 114.9, 98.3, 80.1, 56.6, 29.8, 18.5.

HRMS (ESI): m/z calcd for: $C_{23}H_{15}Cl_4N_3NaO$, 511.9867[M+Na]$^+$, found: 511.9843.

2,4-Bis(4-fluorophenyl)-1,2,4a,5,6,8a-hexahydro-2,7-dimethyl-5-oxo-1,6-naphthyridine-8-carbonitrile (3c)



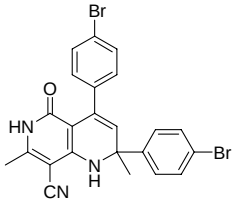
^{1}H NMR (400MHz, DMSO-d_6) δ: 11.52 (s, 1H, NH), 7.52-7.48 (m, 3H, Ar-H and NH), 7.21-7.13 (m, 4H, Ar-H), 7.04 (t, J = 8.8 Hz, 3H, Ar-H), 7.22 (t, J = 8.4 Hz, 4H, Ar-H), 7.11 (d, J = 7.6 Hz, 1H, Ar-H), 5.45 (s, 1H, CH), 2.34 (s, 3H, CH_3), 1.73 (s, 3H, CH_3).

IR (KBr, ν, cm^{-1}): 3314, 2219, 1647, 1561, 1463, 1113, 832.

^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 161.6 ($^1J_{CF}$ = 242.7 Hz), 161.3, 160.8 ($^1J_{CF}$ = 241.3 Hz), 155.8, 153.7, 144.6 ($^4J_{CF}$ = 2.8 Hz), 135.3 ($^4J_{CF}$ = 3.0 Hz), 129.9 ($^3J_{CF}$ = 8.1 Hz), 126.8 ($^3J_{CF}$ = 8.1 Hz), 125.4, 117.5, 115.0 ($^2J_{CF}$ = 21.2 Hz), 114.7 ($^2J_{CF}$ = 20.9 Hz), 89.3, 65.3, 55.9, 30.5, 18.3.

HRMS (ESI): m/z calcd for: $C_{23}H_{17}F_2N_3NaO$, 412.1237 [M+Na]$^+$, found:412.1227.

2,4-Bis(4-bromophenyl)-1,2,5,6-tetrahydro-2,7-dimethyl-5-oxo-1,6-naphthyridine-8-carbonitrile (3d)



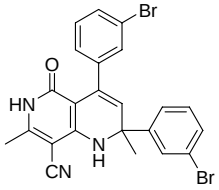
^{1}H NMR (400MHz, DMSO-d_6) δ: 11.54 (s, 1H, NH), 7.54 (t, J = 8.4 Hz, 3H, Ar-H and NH), 7.43-7.40 (m, 4H, Ar-H), 7.07 (d, J = 8.4 Hz, 3H, Ar-H), 5.48 (s, 1H, CH), 2.34 (s, 3H, CH_3), 1.72 (s, 3H, CH_3).

^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 157.9, 155.3, 150.4, 147.5, 139.3, 131.0, 129.8, 129.6, 125.6, 119.9, 119.4, 115.3, 98.4, 81.0, 56.6, 30.0, 18.3.

IR (KBr, ν, cm^{-1}): 3323, 2215, 1639, 1561, 1465, 1009,821.

HRMS (ESI): m/z calcd for: $C_{23}H_{17}Br_2N_3NaO$, 531.9636[M+Na]$^+$, found: 531.9640.

2,4-Bis(3-bromophenyl)-1,2,5,6-tetrahydro-2,7-dimethyl-5-oxo-1,6-naphthyridine-8-carbonitrile (3e)



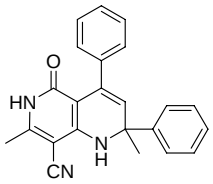
^{1}H NMR (400 MHz, DMSO-d_6) δ: 11.57 (s, 1H, NH), 7.66 (t, J = 2.0 Hz, 1H, ArH), 7.58 (s, 1H, NH), 7.48-40 (m, 3H, Ar-H), 7.34 (t, J = 8.0 Hz, 1H, Ar-H), 7.26 (t, J = 2.0 Hz, 1H, ArH), 7.21 (t, J = 8.0 Hz, 1H, Ar-H),7.14 (d, J = 8.0 Hz, 1H, Ar-H), 5.59 (s, 1H, CH), 2.35 (s, 3H, CH_3), 1.72 (s, 3H, CH_3).

^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 157.9, 155.5, 150.9, 150.4, 142.4, 130.4, 129.6, 129.2, 127.7, 126.5, 125.9, 124.1, 121.7, 120.4, 115.3, 98.3, 81.0, 56.7, 30.0, 18.3.

IR (KBr, ν, cm^{-1}): 3325, 2217, 1640, 1606, 1562, 1464, 1281, 881.

HRMS (ESI): m/z calcd for: $C_{23}H_{17}Br_2N_3NaO$, 531.9636[M+Na]$^+$, found: 531.9664.

1,2,5,6-Tetrahydro-2,7-dimethyl-5-oxo-2,4-diphenyl-1,6-naphthyridine-8-carbonitrile (3f)



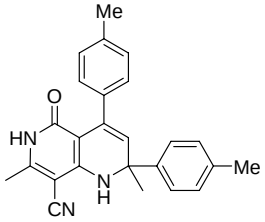
^{1}H NMR (400MHz, DMSO-d_6) δ: 11.46 (s, 1H, NH), 7.47 (d, J = 7.6 Hz, 2H, Ar-H), 7.36 (t, J = 7.6 Hz, 3H, Ar-H and NH), 7.22 (t, J = 8.4 Hz, 4H, Ar-H), 7.11 (d, J = 7.6 Hz, 1H, Ar-H), 5.45 (s, 1H, CH), 2.34 (s, 3H, CH_3), 1.73 (s, 3H, CH_3).

IR (KBr, ν, cm^{-1}): 3322, 3055, 2213, 1644, 1605, 1566, 1532, 1493, 1288, 1029, 892, 758.

^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 160.2, 155.7, 153.8, 148.7, 139.3, 132.5, 128.1, 127.7, 126.4, 125.6, 124.7, 117.5, 89.3, 65.4, 56.2, 30.6, 18.3.

HRMS (ESI): m/z calcd for: $C_{23}H_{20}N_3O$, 354.1606[M+H]$^+$, found: 354.1639.

1,2,5,6-Tetrahydro-2,7-dimethyl-5-oxo-2,4-di*p*-tolyl-1,6-naphthyridine-8-carbonitrile (3g)



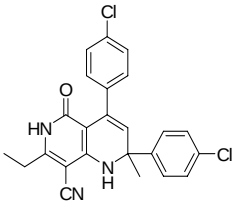
^{1}H NMR (400MHz, DMSO-d_6) δ: 11.43 (s, 1H, NH), 7.33 (d, J = 8.0 Hz, 2H, Ar-H), 7.27 (s, 1H, NH), 7.14 (d, J = 8.0 Hz, 2H, Ar-H), 7.02 (d, J = 8.0 Hz, 2H, Ar-H), 6.99 (d, J = 8.0 Hz, 2H, Ar-H), 5.39 (s, 1H, CH), 2.33 (s, 3H, CH_3), 2.28 (s, 3H, CH_3), 2.26 (s, 3H, CH_3), 1.69 (s, 3H, CH_3).

^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm):157.9, 154.9, 150.4, 145.4, 137.2, 135.7, 135.2, 133.4, 128.7, 127.6, 127.2, 125.6, 124.7, 115.5, 98.9, 80.9, 56.4, 30.3, 20.7, 20.5, 18.2.

IR (KBr, ν, cm^{-1}): 3350, 2216, 1633, 1561, 1463, 1187, 816.

HRMS (ESI): m/z calcd for: $C_{25}H_{23}N_3NaO$, 404.1739 [M+Na]$^+$,found: 404.1736.

2,4-Bis(4-chlorophenyl)-7-ethyl-1,2,5,6-tetrahydro-2-methyl-5-oxo-1,6-naphthyridine-8-carbonitrile (3h)



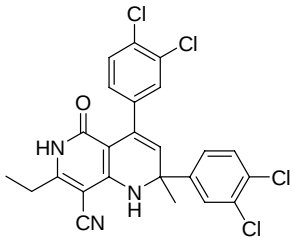
^{1}H NMR (400 MHz, DMSO-d_6) δ 11.51 (s, 1H, NH), 7.51 (s, 1H, NH), 7.48 (d, J = 8.8 Hz, 2H, Ar-H), 7.42 (d, J = 8.8 Hz, 2H, Ar-H), 7.27 (d, J = 8.4 Hz, 2H, Ar-H), 7.13 (d, J = 8.8 Hz, 2H, Ar-H), 5.47 (s, 1H, CH), 2.60 (q, J = 8.0 Hz, 2H, CH_2), 1.72 (s, 3H, CH_3), 1.21 (t, J = 7.6 Hz, 3H, CH_3).

^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm):160.2, 158.1, 150.4, 147.1, 138.9, 131.4, 130.9, 129.2, 128.1, 126.9, 125.8, 125.7, 115.0, 98.6, 80.1, 56.6, 30.0, 25.7, 13.0.

IR (KBr, ν, cm^{-1}): 3269, 2219, 1611, 1556, 1436, 1095, 828.

HRMS (ESI): m/z calcd for: $C_{24}H_{19}Cl_2N_3NaO$[M+Na]$^+$, 458.0803, found: 458.0801.

2,4-Bis(3,4-dichlorophenyl)-7-ethyl-1,2,5,6-tetrahydro-2-methyl-5-oxo-1,6-naphthyridine-8-carbonitrile (3i)



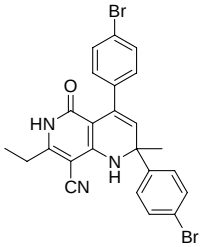
^{1}H NMR (400 MHz, DMSO) δ 11.60 (s, 1H, NH), 7.71 (d, J = 2.0 Hz, 1H, Ar-H), 7.64 (d, J = 8.4 Hz, 1H, Ar-H), 7.62 (s, 1H, NH), 7.49 (d, J = 8.8 Hz, 1H, Ar-H), 7.48-7.45 (m, 1H, ArH), 7.36 (d, J = 2.0 Hz, 1H, Ar-H), 7.27 (dd J = 8.0 Hz, 2.0, 1H, Ar-H), 5.60 (s, 1H, CH), 2.61 (q, J = 7.2 Hz, 2H, CH_2), 1.73 (s, 3H, CH_3), 1.21 (t, J = 7.6 Hz, 3H, CH_3).

^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm):160.6, 158.1, 150.4, 149.0, 140.6, 130.4, 129.7, 129.4, 129.2, 129.1, 128.9, 127.9, 127.1, 125.9, 125.6, 114.9, 98.3, 80.1, 56.6, 29.8, 25.7, 13.0.

IR (KBr, ν, cm^{-1}): 3324, 2215, 1641, 1557, 1463, 1133, 818

HRMS (ESI): m/z calcd for: $C_{24}H_{17}Cl_4N_3NaO$, 526.0023$[M+Na]^+$, found: 526.0020.

2,4-Bis(4-bromophenyl)-7-ethyl-1,2,5,6-tetrahydro-2-methyl-5-oxo-1,6-naphthyridine-8-carbonitrile (3j)



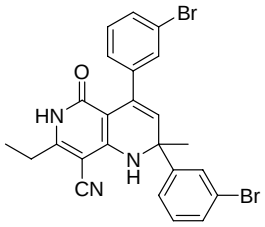
^{1}H NMR (400 MHz, DMSO-d_6) δ 11.52 (s, 1H, NH), 7.56 (d, J = 8.8 Hz, 2H, Ar-H), 7.51 (s, 1H, NH), 7.42 (d, J = 8.4 Hz, 2H, Ar-H), 7.41 (d, J = 8.4 Hz, 2H, Ar-H), 7.07 (d, J = 8.4 Hz, 2H, Ar-H), 5.47 (s, 1H, CH), 2.60 (q, J = 7.2 Hz, 2H, CH_2), 1.72 (s, 3H, CH_3), 1.21 (t, J = 7.6 Hz, 3H, CH_3).

^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm):160.3, 158.1, 150.4, 147.5, 139.3, 131.0, 129.8, 129.6, 125.7, 119.9, 119.4, 115.0, 98.5, 80.1, 56.6, 30.0, 25.7, 13.0.

IR (KBr, ν, cm^{-1}): 3320, 2219, 1638, 1557, 1463, 1139, 819.

HRMS (ESI): m/z calcd for: $C_{24}H_{19}Br_2N_3NaO[M+Na]^+$, 545.9793, found: 545.9784.

2,4-Bis(3-bromophenyl)-7-ethyl-1,2,5,6-tetrahydro-2-methyl-5-oxo-1,6-naphthyridine-8-carbonitrile (3k)



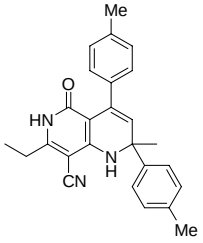
^{1}H NMR (400 MHz, DMSO-d_6) δ 11.57 (s, 1H, NH), 7.66 (t, J = 2.0 Hz, 1H, ArH), 7.56 (s, 1H, NH), 7.50-40 (m, 3H, Ar-H), 7.36-7.34 (m, 1H, Ar-H), 7.28-7.26 (m, 1H, Ar-H), 7.21 (t, J = 8.0 Hz, 1H, Ar-H), 7.15-7.13 (m, 1H, Ar-H), 5.47 (s, 1H, CH), 2.61 (q, J = 7.6 Hz, 2H, CH_2), 1.72 (s, 3H, CH_3), 1.22 (t, J = 7.6 Hz, 3H, CH_3).

^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm):160.4, 158.0, 150.9, 150.5, 142.3, 132.5, 130.5, 129.6, 129.2, 127.7, 126.0, 124.1, 124.1, 121.7, 120.4, 115.0, 98.5, 80.0, 56.8, 30.0, 25.7, 13.0.

IR (KBr, ν, cm^{-1}): 3316, 2217, 1638, 1561, 1465, 1070, 781.

HRMS (ESI): m/z calcd for: $C_{24}H_{19}Br_2N_3NaO[M+Na]^+$, 545.9793, found: 545.9791.

7-Ethyl-1,2,5,6-tetrahydro-2-methyl-5-oxo-2,4-dip-tolyl-1,6-naphthyridine-8-carbonitrile (3l)



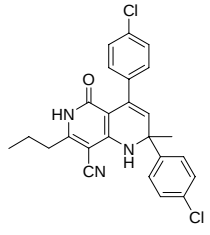
^{1}H NMR (400 MHz, DMSO-d_6) δ 11.43 (s, 1H, NH), 7.34 (d, J = 8.0 Hz, 2H, ArH), 7.25 (s, 1H, NH), 7.15 (d, J = 8.0 Hz, 2H, ArH), 7.04-7.00 (m, 4H, Ar-H), 5.38 (s, 1H, CH), 2.60 (q, J = 7.2 Hz, 2H, CH_2), 2.28 (s, 3H, CH_3), 2.26 (s, 3H, CH_3), 1.70 (s, 3H, CH_3), 1.22 (t, J = 7.6 Hz, 3H, CH_3).

^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm):159.8, 158.1, 150.4, 145.4, 137.2, 135.7, 135.2, 133.3, 128.7, 127.3, 125.7, 124.7, 115.2, 99.0, 80.0, 56.5, 30.3, 25.6, 20.7, 20.5, 13.0.

IR (KBr, ν, cm^{-1}): 3336, 2214, 1645, 1559, 1464, 1185, 813.

HRMS (ESI): m/z calcd for: $C_{26}H_{25}N_3NaO$, 418.1895$[M+Na]^+$, found: 418.1893.

2,4-Bis(4-chlorophenyl)-1,2,5,6-tetrahydro-2-methyl-5-oxo-7-propyl-1,6-naphthyridine-8-carbonitrile (3m)



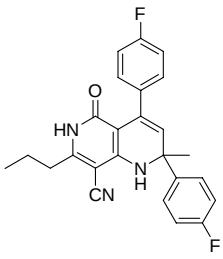
^{1}H NMR (400 MHz, DMSO) δ 11.48 (s, 1H, NH), 7.48 (d, J = 8.4 Hz, 2H, ArH), 7.47 (s, 1H, NH), 7.42 (d, J = 8.4 Hz, 2H, ArH), 7.27 (d, J = 8.4 Hz, 2H, ArH), 7.13 (d, J = 8.4 Hz, 2H, ArH), 5.47 (s, 1H, CH), 2.58 (t, J = 7.4 Hz, 2H, CH_2), 1.72 (s, 3H, CH_3), 1.66 (q, J = 7.4 Hz, 2H, CH_2), 0.93(t, J = 7.4 Hz, 3H, CH_3).

^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm):158.0, 150.3, 147.1, 138.9, 132.7, 131.3, 130.9, 129.2, 128.1, 126.9, 126.8, 125.8, 115.2, 98.6, 80.7, 56.5, 33.7, 30.0, 21.7, 13.3.

IR (KBr, ν, cm^{-1}): 3332, 2217, 1640, 1560, 1398, 1280, 814.

HRMS (ESI): m/z calcd for: $C_{25}H_{21}Cl_2N_3NaO$, 472.0959$[M+Na]^+$, found:472.0949.

2,4-Bis(4-fluorophenyl)-1,2,5,6-tetrahydro-2-methyl-5-oxo-7-propyl-1,6-naphthyridine-8-carbonitrile (3n)



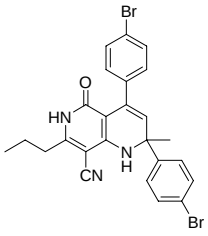
^{1}H NMR (400 MHz, DMSO-d_6) δ 11.45 (s, 1H, NH), 7.52-7.48 (m, 2H, Ar-H), 7.40 (s, 1H, NH), 7.20-7.13 (m, 4H, Ar-H), 7.03 (t, J = 8.8 Hz, 2H, Ar-H), 5.44 (s, 1H, CH), 2.58 (t, J = 7.4 Hz, 2H, CH_2), 1.73 (s, 3H, CH_3), 1.66 (q, J = 7.6 Hz, 2H, CH_2), 0.93 (t, J = 7.4 Hz, 3H, CH_3).

^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): ^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 161.1 ($^1J_{CF}$ = 240.4 Hz), 160.9 ($^1J_{CF}$ = 241.8 Hz), 158.6, 158.1, 150.2, 144.4 ($^4J_{CF}$ = 2.7 Hz), 136.3 ($^4J_{CF}$ = 3.3 Hz), 132.6, 129.2 ($^3J_{CF}$ = 7.9 Hz), 126.8 ($^3J_{CF}$ = 8.2 Hz), 125.8, 115.2, 114.8 ($^2J_{CF}$ = 21.1 Hz), 113.7 ($^2J_{CF}$ = 21.0 Hz), 112.7, 98.8, 80.7, 56.4, 33.7, 30.3, 21.7, 13.3.

IR (KBr, ν, cm^{-1}): 3331, 2217, 1638, 1556,1459, 1095, 822.

HRMS (ESI): m/z calcd for: $C_{25}H_{21}F_2N_3NaO$, 440.1550[M+Na]$^+$, found: 440.1548.

2,4-Bis(4-bromophenyl)-1,2,5,6-tetrahydro-2-methyl-5-oxo-7-propyl-1,6-naphthyridine-8-carbonitrile (3o)



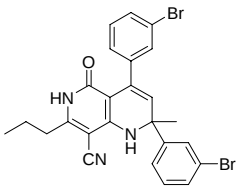
^{1}H NMR (400 MHz, DMSO-d_6) δ 11.49 (s, 1H, NH), 7.55 (d, J = 8.8 Hz, 2H, ArH), 7.46 (s, 1H, NH), 7.42 (d, J = 8.4 Hz, 2H, ArH), 7.40 (d, J = 8.0 Hz, 2H, ArH), 7.07 (d, J = 8.4 Hz, 2H, ArH), 5.47 (s, 1H, CH), 2.58 (t, J = 7.4 Hz, 2H, CH_2), 1.72 (s, 3H, CH_3), 1.66 (q, J = 7.6 Hz, 2H, CH_2), 0.93 (t, J = 7.4 Hz, 3H, CH_3).

^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm):158.7, 158.0, 150.3, 147.6, 139.3, 132.7, 131.0, 129.8, 129.6, 125.8, 119.9, 119.4, 115.2, 98.6, 80.7, 56.6, 33.7, 30. 0, 21.7, 13.3.

IR (KBr, ν, cm^{-1}): 3331, 2217, 1638, 1557, 1458, 1010, 820.

HRMS (ESI): m/z calcd for: $C_{25}H_{21}Br_2N_3NaO$, 559.9949[M+Na]$^+$, found: 559.9928..

2,4-Bis(3-bromophenyl)-1,2,5,6-tetrahydro-2-methyl-5-oxo-7-propyl-1,6-naphthyridine-8-carbonitrile (3p)



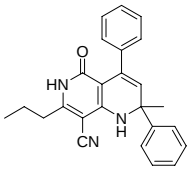
^{1}H NMR (400 MHz, DMSO-d_6) δ 11.53 (s, 1H, NH), 7.63 (s, 1H, ArH), 7.51 (s, 1H, NH), 7.49-40 (m, 3H, Ar-H), 7.36-7.32 (m, 1H, Ar-H), 7.27 (s, 1H, Ar-H), 7.20 (t, J = 7.6 Hz, 1H, Ar-H), 7.13 (d, J = 7.6 Hz, 1H, Ar-H), 5.56 (s, 1H, CH), 2.60 (t, J = 7.4 Hz, 2H, CH_2), 1.73 (s, 3H, CH_3), 1.66 (q, J = 7.6 Hz, 2H, CH_2), 0.94 (t, J = 7.2 Hz, 3H, CH_3).

^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 158.8, 158.0, 150.8, 146.7, 142.3, 139.0, 129.2, 127.6, 126.5, 126.3, 124.1, 121.6, 120.4, 112.7, 95.1, 80.7, 56.8, 33.7, 30.6, 21.7, 13.2.

IR (KBr, ν, cm^{-1}): 3306, 2218, 1642, 1462, 1160, 833.

HRMS (ESI): m/z calcd for: $C_{25}H_{21}Br_2N_3NaO$, 559.9949[M+Na]$^+$, found: 559.9928.

1,2,5,6-Tetrahydro-2-methyl-5-oxo-2,4-diphenyl-7-propyl-1,6-naphthyridine-8-carbonitrile (3q)



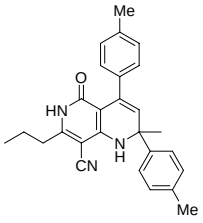
^{1}H NMR (400 MHz, DMSO-d_6) δ 11.42 (s, 1H, NH), 7.47 (d, J = 7.6 Hz, 2H, ArH), 7.36 (t, J = 7.6 Hz, 2H, ArH), 7.33 (s, 1H, NH), 7.25-7.21 (m, 4H, ArH), 7.12 (d, J = 7.6 Hz, 2H, ArH), 5.45 (s, 1H, CH), 2.59 (t, J = 7.4 Hz, 2H, CH_2), 1.73 (s, 3H, CH_3), 1.66 (q, J = 7.6 Hz, 2H, CH_2), 0.93 (t, J = 7.4 Hz, 3H, CH_3).

^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm):158.8, 158.1, 150.4, 148.4, 140.1, 133.5, 128.2, 127.4, 126.4, 126.3, 126.2, 124.7, 115.3, 112.7, 99.0, 80.8, 56.8, 33.7, 30.3, 21.7, 13.3.

IR (KBr, ν, cm^{-1}): 3333, 2218, 1638, 1556, 1448, 1077, 759.

HRMS (ESI): m/z calcd for: $C_{25}H_{23}N_3NaO$,404.1739[M+Na]$^+$, found: 404.1742.

1,2,5,6-Tetrahydro-2-methyl-5-oxo-7-propyl-2,4-dip-tolyl-1,6-naphthyridine-8-carbonitrile (3r)

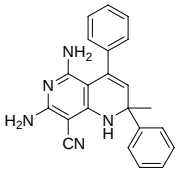


^{1}H NMR (400 MHz, DMSO-d_6) δ 11.40 (s, 1H, NH), 7.33 (d, J = 8.0 Hz, 2H, ArH), 7.23 (s, 1H, NH), 7.15 (d, J = 8.0 Hz, 2H, ArH), 7.02 (d, J = 8.4 Hz, 2H, ArH), 6.99 (d, J = 8.0 Hz, 2H, ArH), 5.39 (s, 1H, CH), 2.59 (t, J = 7.6 Hz, 2H, CH_2), 2.28 (s, 3H, CH_3), 2.26 (s, 3H, CH_3), 1.69 (s, 3H, CH_3), 1.65 (q, J = 7.6 Hz, 2H, CH_2), 0.93 (t, J = 7.4 Hz, 3H, CH_3).
^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm):158.3, 158.0, 151.7, 150.3, 145.4, 137.2, 135.7, 135.2, 133.3, 128.7, 127.2, 124.6, 115.3, 99.1, 80.7, 56.5, 33.7, 33.3, 21.7, 20.7, 20.5, 13.2.

IR (KBr, ν, cm^{-1}): 3336, 2216, 1642, 1559, 1388, 1127, 769.

HRMS (ESI): m/z calcd for: $C_{27}H_{27}N_3NaO$, 432.2052[M+Na]$^+$, found: 432.2043.

5,7-Diamino-1,2-dihydro-2-methyl-2,4-diphenyl-1,6-naphthyridine-8-carbonitrile (4a)

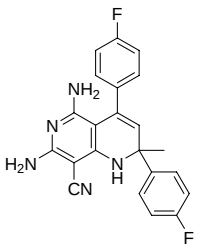


^{1}H NMR (400 MHz, DMSO-d_6) δ 7.46 (d, J = 7.6 Hz, 2H, ArH), 7.40-7.32 (m, 5H, ArH), 7.25-7.19 (m, 3H, ArH), 6.83 (s, 1H, NH), 6.13 (s, 2H, NH_2), 5.46 (s, 1H, CH), 4.79 (brs, 2H, NH_2), 1.69 (s, 3H, CH_3).
^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm):160.1, 155.7, 153.8, 148.7, 139.3, 132.5, 128.4, 128.1, 127.9, 127.7, 126.4, 125.6, 124.7, 117.5, 89.3, 65.3, 56.2, 30.5.

IR (KBr, ν, cm^{-1}):3515, 3451, 3405, 3325, 3154, 2186, 1602, 1581, 1555, 1469, 1444, 1206, 1017, 760.

HRMS (ESI): m/z calcd for: $C_{22}H_{19}N_5Na$, 376.1538[M+Na]$^+$, found: 376.1528.

5,7-Diamino-2,4-bis(4-fluorophenyl)-1,2-dihydro-2-methyl-1,6-naphthyridine-8-carbonitrile (4b)

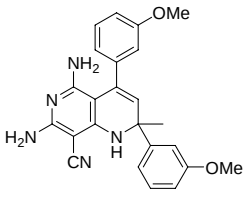


^{1}H NMR (400 MHz, DMSO-d_6) δ 7.51-7.48 (m, 2H, ArH), 7.29-7.26 (m, 2H, ArH), 7.21-7.14 (m, 4H, ArH), 6.97 (s, 1H, NH), 6.21 (s, 2H, NH_2), 5.47 (s, 1H, CH), 4.92 (brs, 2H, NH_2), 1.68 (s, 3H, CH_3).
^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm): 161.1 ($^1J_{CF}$ = 240.6 Hz), 160.9 ($^1J_{CF}$ = 241.6 Hz), 157.9, 155.2, 150.3, 144.3 ($^4J_{CF}$ = 2.8 Hz), 136.3 ($^4J_{CF}$ = 2.4 Hz), 132.7, 129.2 ($^3J_{CF}$ = 7.9 Hz), 126.9 ($^3J_{CF}$ = 8.0 Hz), 125.7, 115.4, 114.8 ($^2J_{CF}$ = 20.8 Hz), 113.7 ($^2J_{CF}$ = 21.2 Hz), 89.4, 65.4, 56.4, 30.3.

IR (KBr, ν, cm^{-1}):3515, 3477, 3408, 3323, 3173, 2191, 1602, 1556, 1506, 1439, 1220, 1014, 837

HRMS (ESI): m/z calcd for: $C_{22}H_{17}F_2N_5Na$,412.1350[M+Na]$^+$, found: 412.1356.

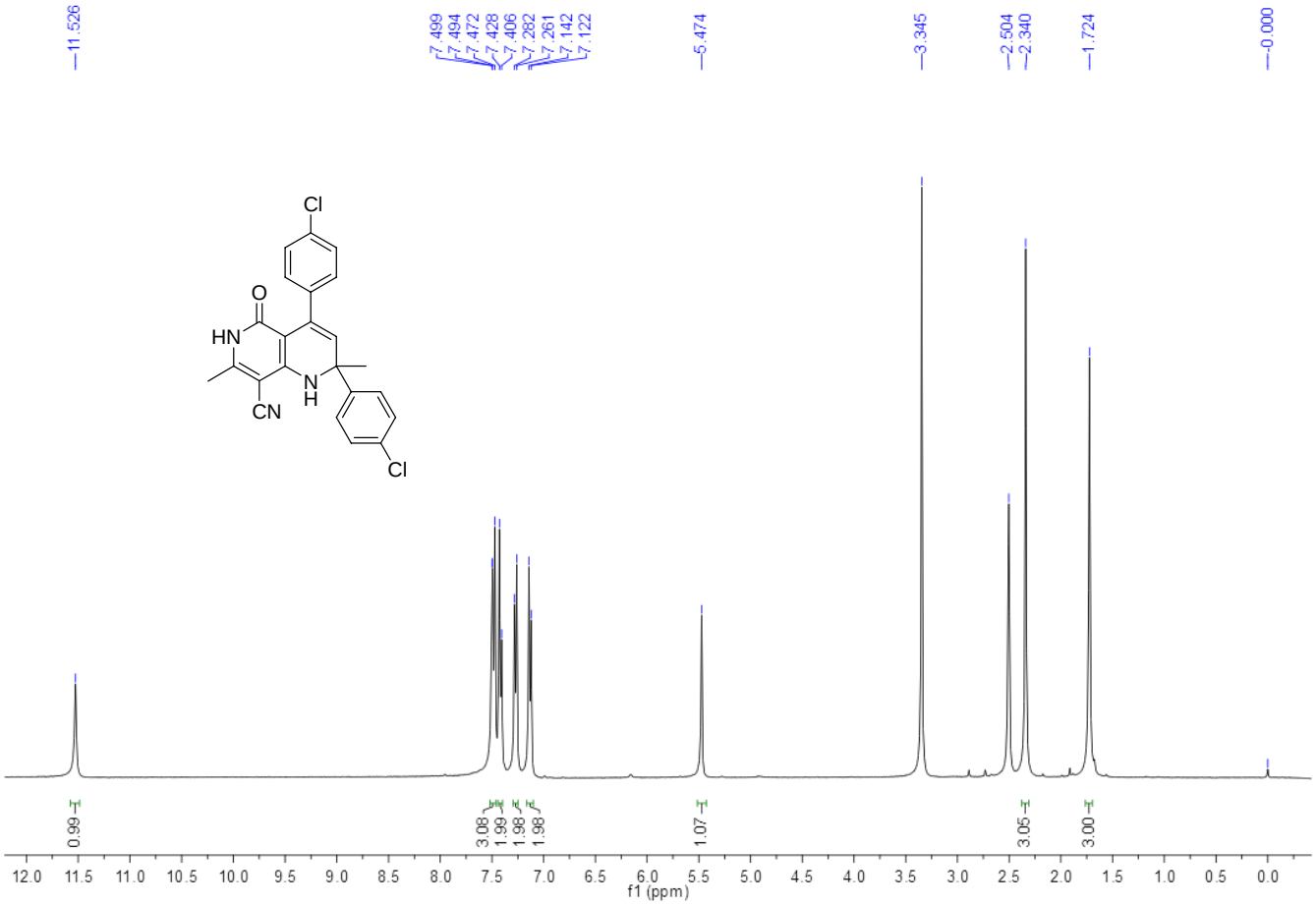
5,7-Diamino-1,2-dihydro-2,4-bis(3-methoxyphenyl)-2-methyl-1,6-naphthyridine-8-carbonitrile (4c)



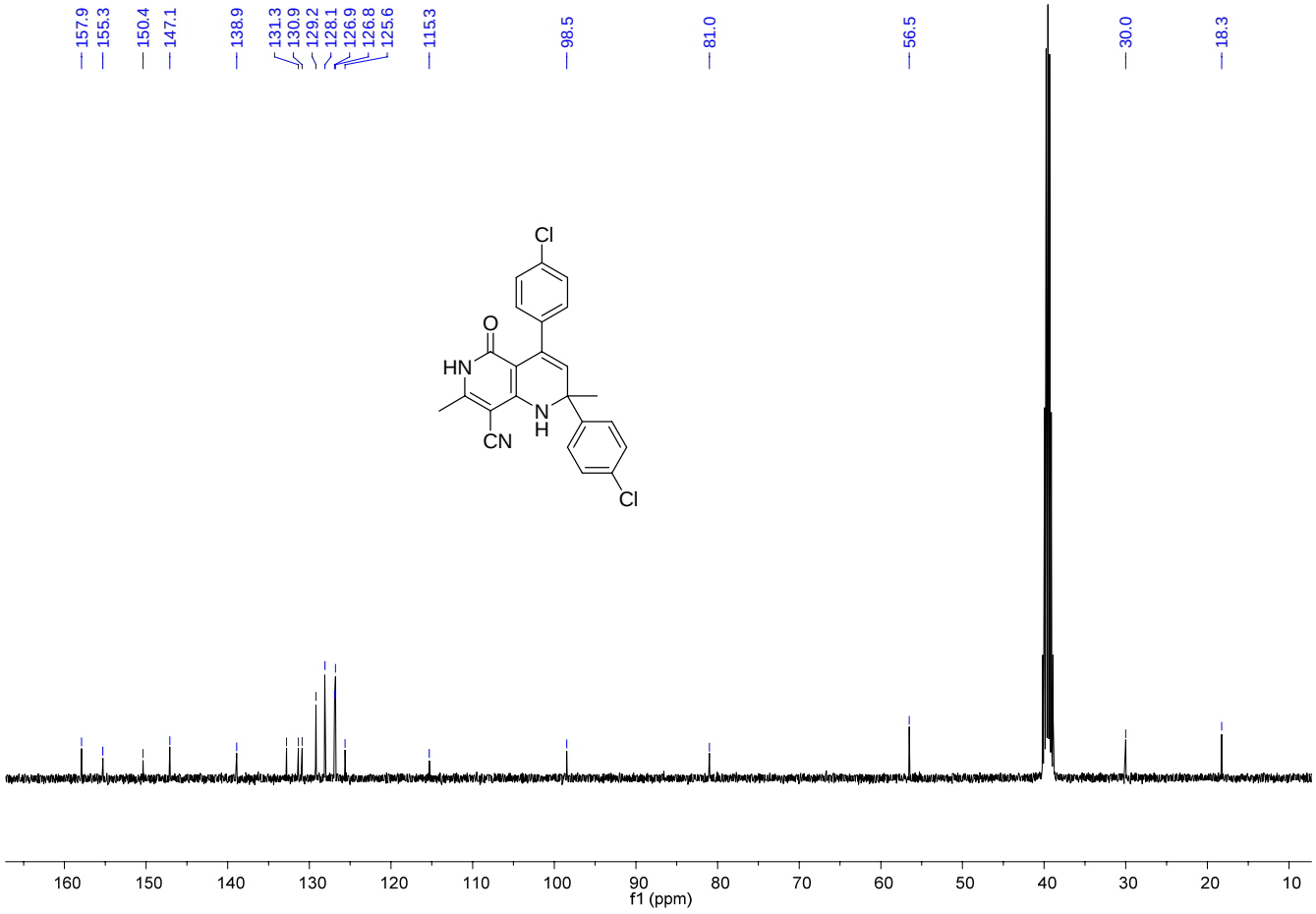
^{1}H NMR (400 MHz, DMSO-d_6) δ 7.32-7.24 (m, 2H, ArH), 7.04-7.00 (m, 2H, ArH), 6.93-6.91 (m, 1H, ArH), 6.84 (s, 1H, NH), 6.81-7.75 (m, 3H, ArH), 6.20 (s, 2H, NH_2), 5.52 (s, 1H, CH), 4.87 (brs, 2H, NH_2), 1.67 (s, 3H, CH_3).
^{13}C NMR (100 MHz, DMSO-d_6) (δ, ppm):160.1, 159.1, 159.1, 153.8, 150.4, 140.8, 132.4, 129. 2, 125.5, 120.2, 117.1, 133.3, 111.3, 111.1, 89.5, 65.5, 56.2, 55.1, 54.9, 30.5.

IR (KBr, ν, cm^{-1}):3500, 3467, 3396, 3321, 3153, 2192, 1604, 1586, 1556, 1444, 1289, 1045, 781

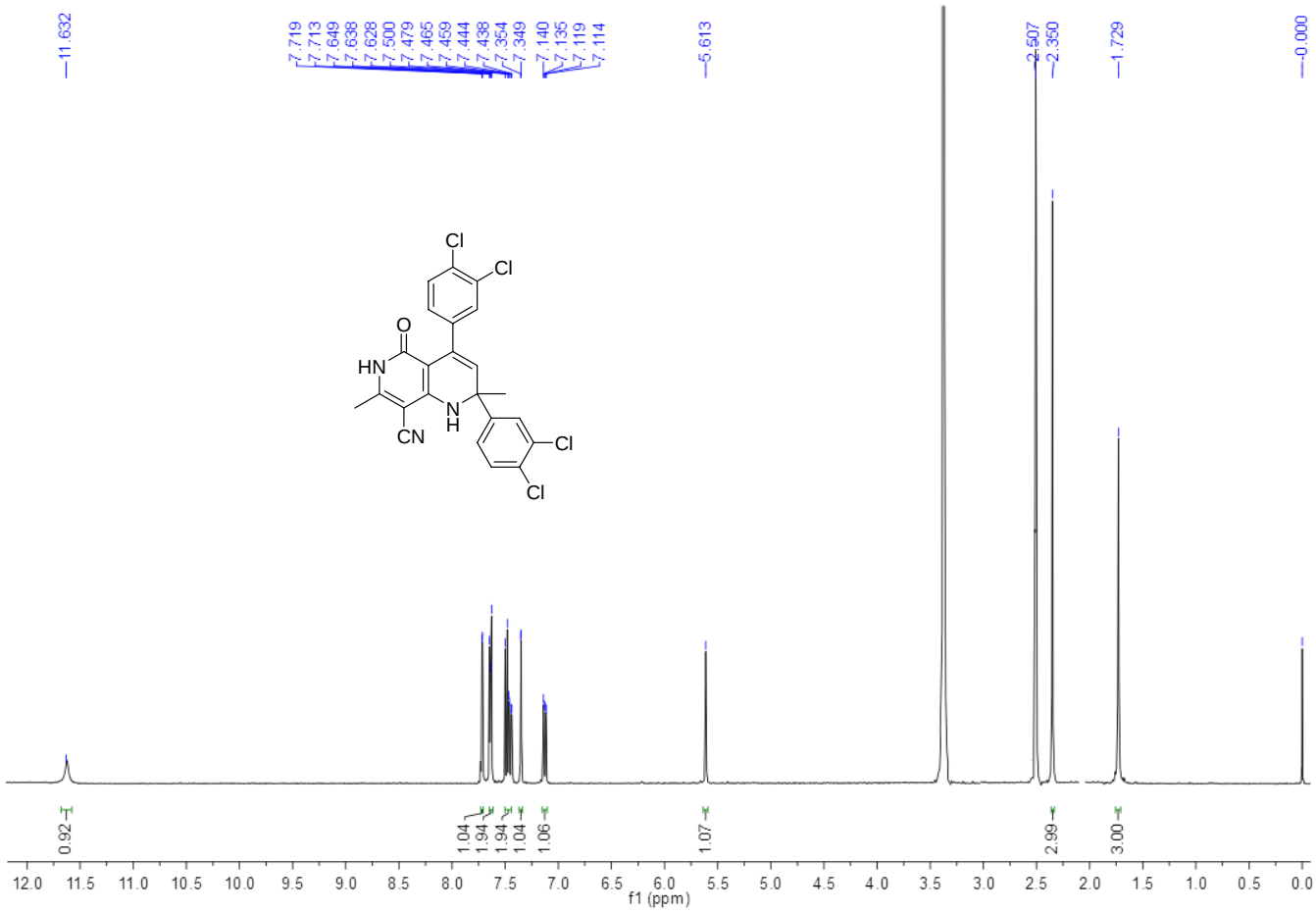
HRMS (ESI): m/z calcd for: $C_{24}H_{23}N_5NaO_2$,436.1749[M+Na]$^+$, found: 436.1730.



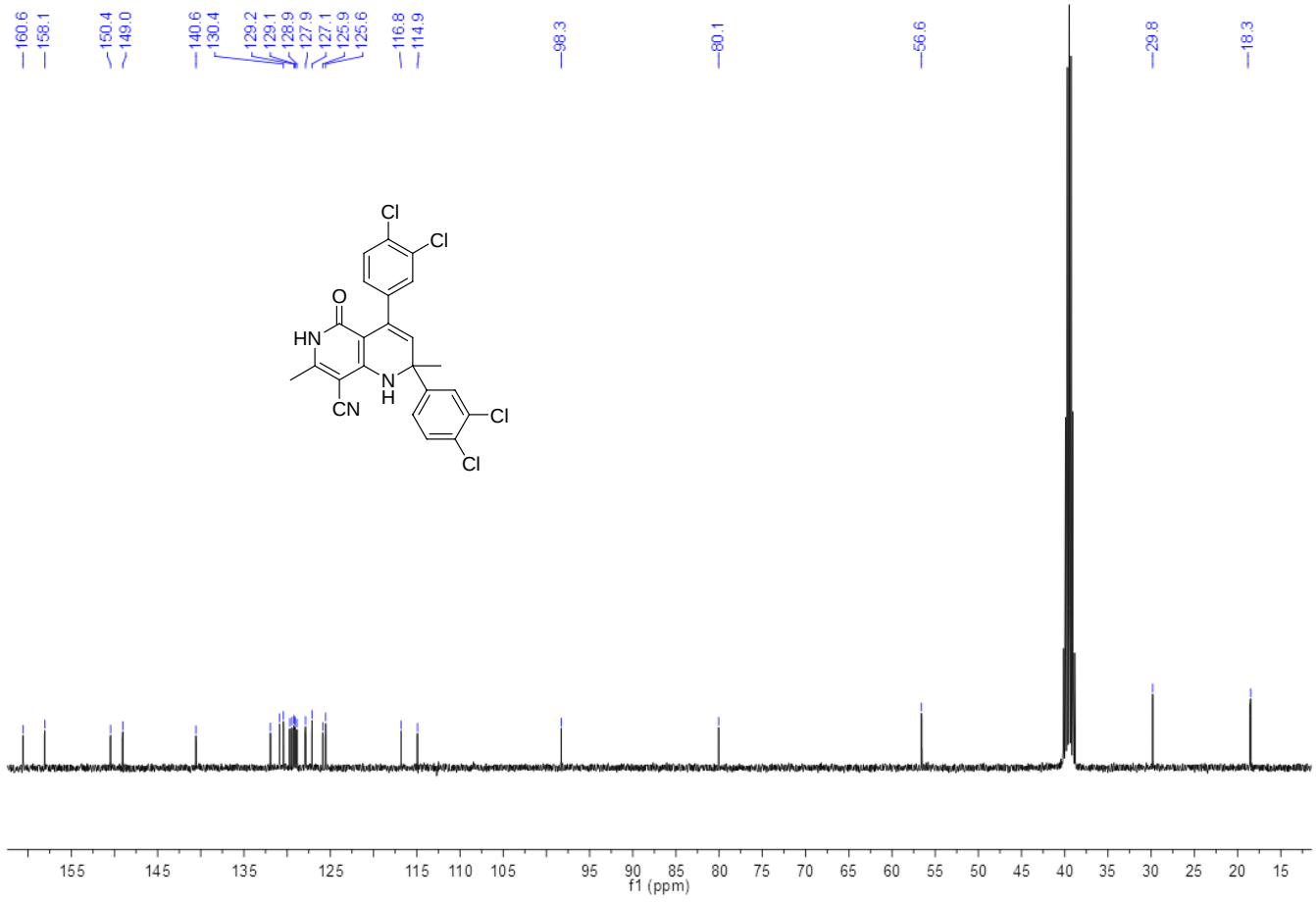
^{1}H NMR Spectrum of Compound **3a**



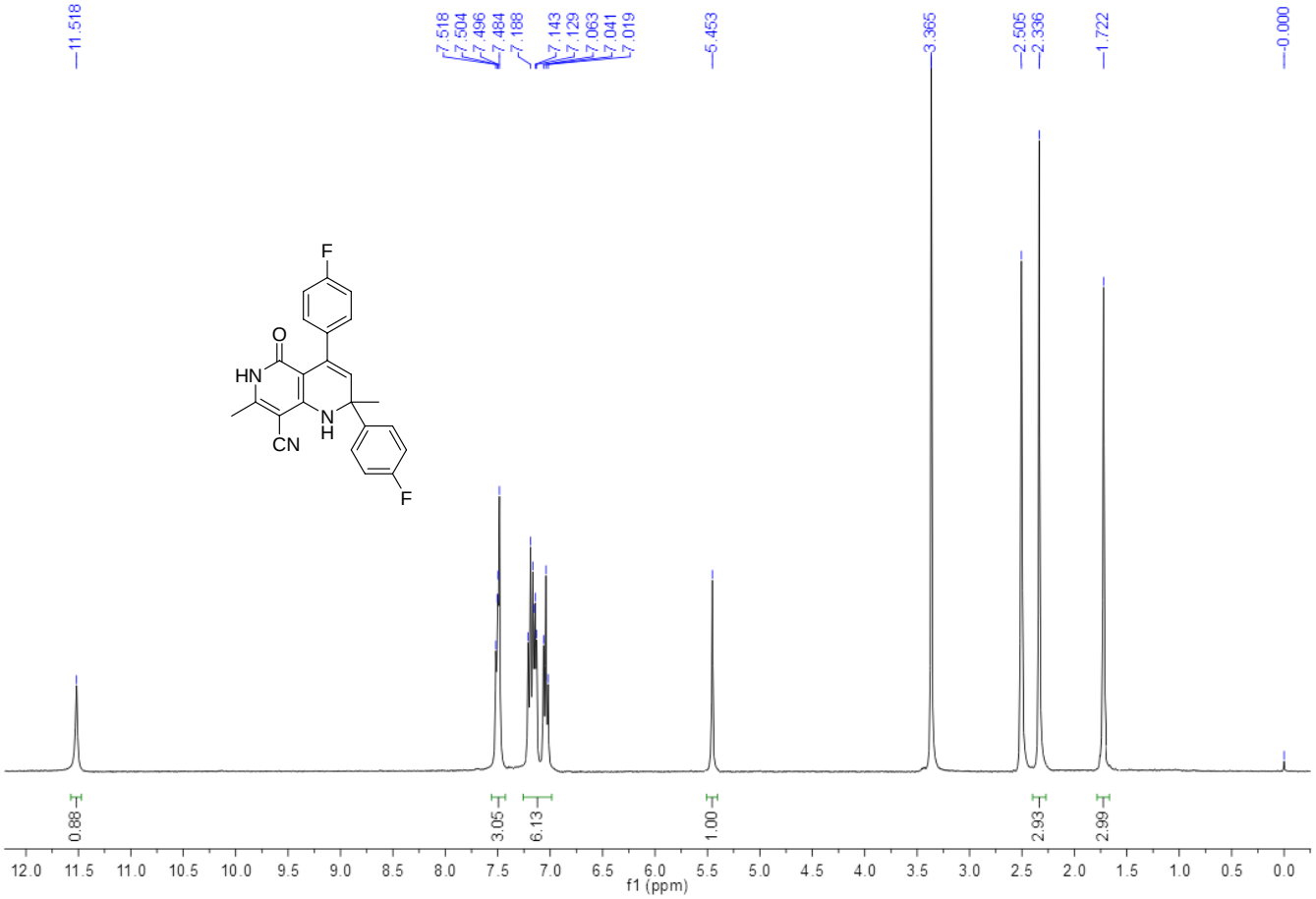
^{13}C NMR Spectrum of Compound **3a**



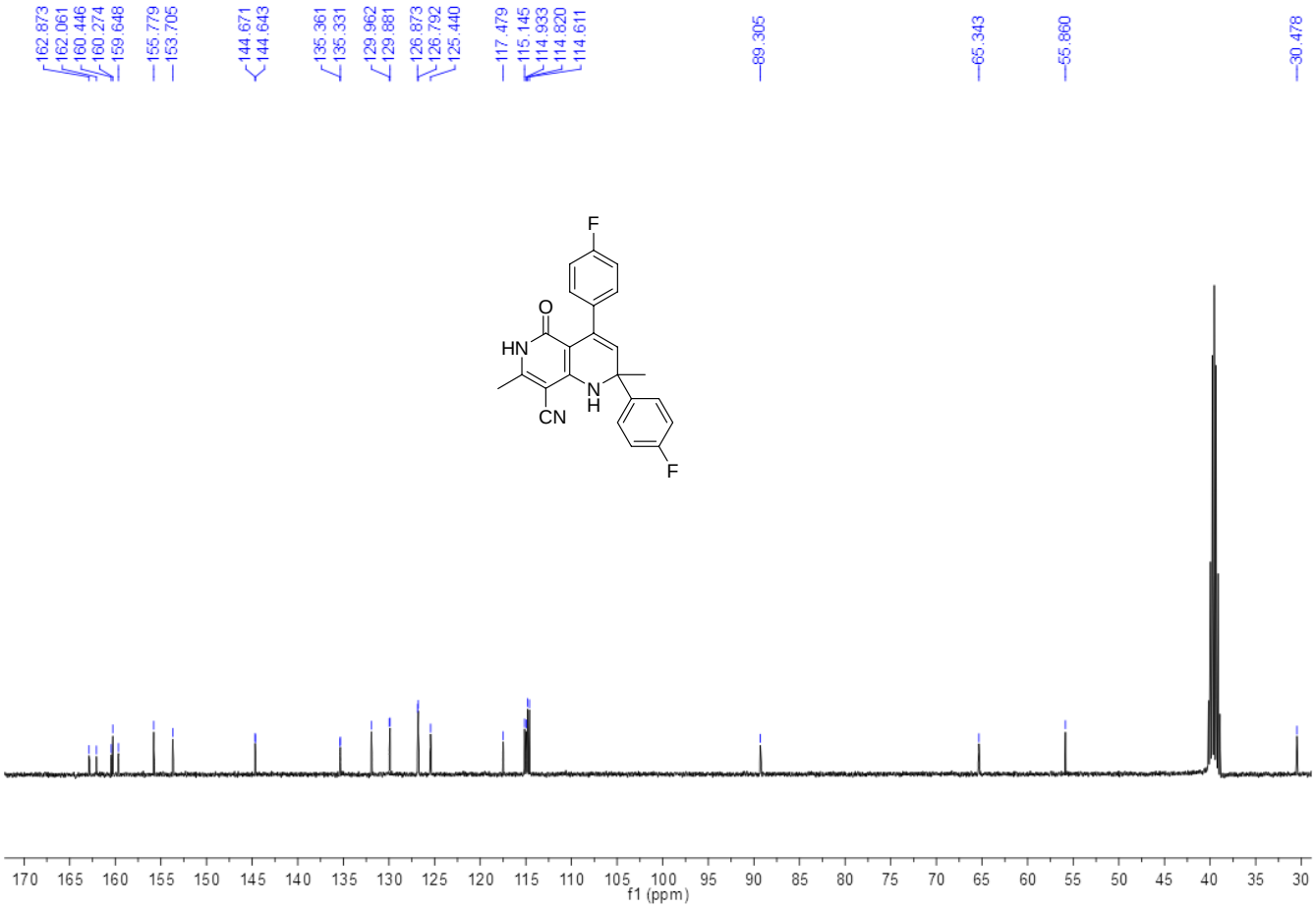
^{1}H NMR Spectrum of Compound **3b**



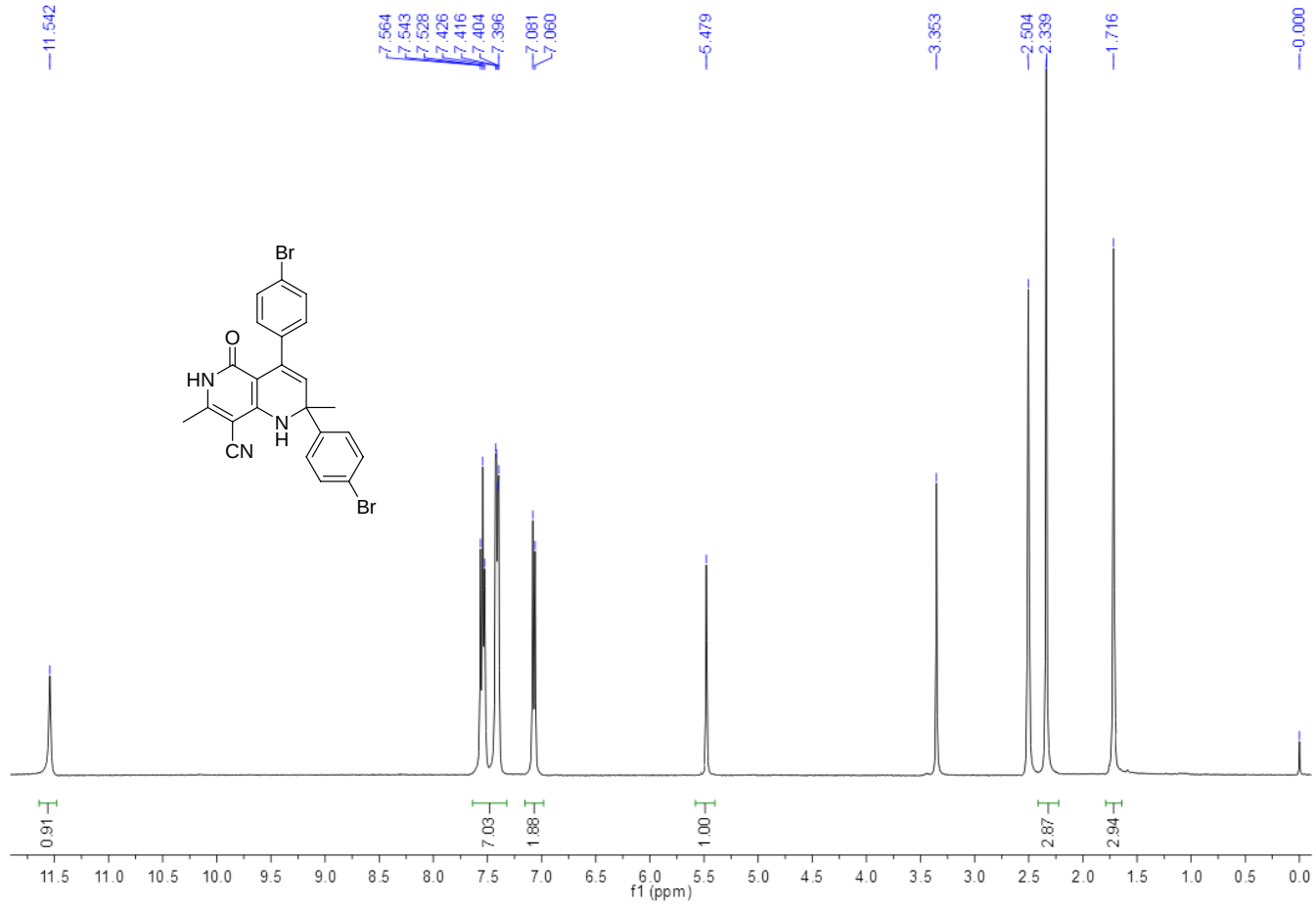
^{13}C NMR Spectrum of Compound **3b**



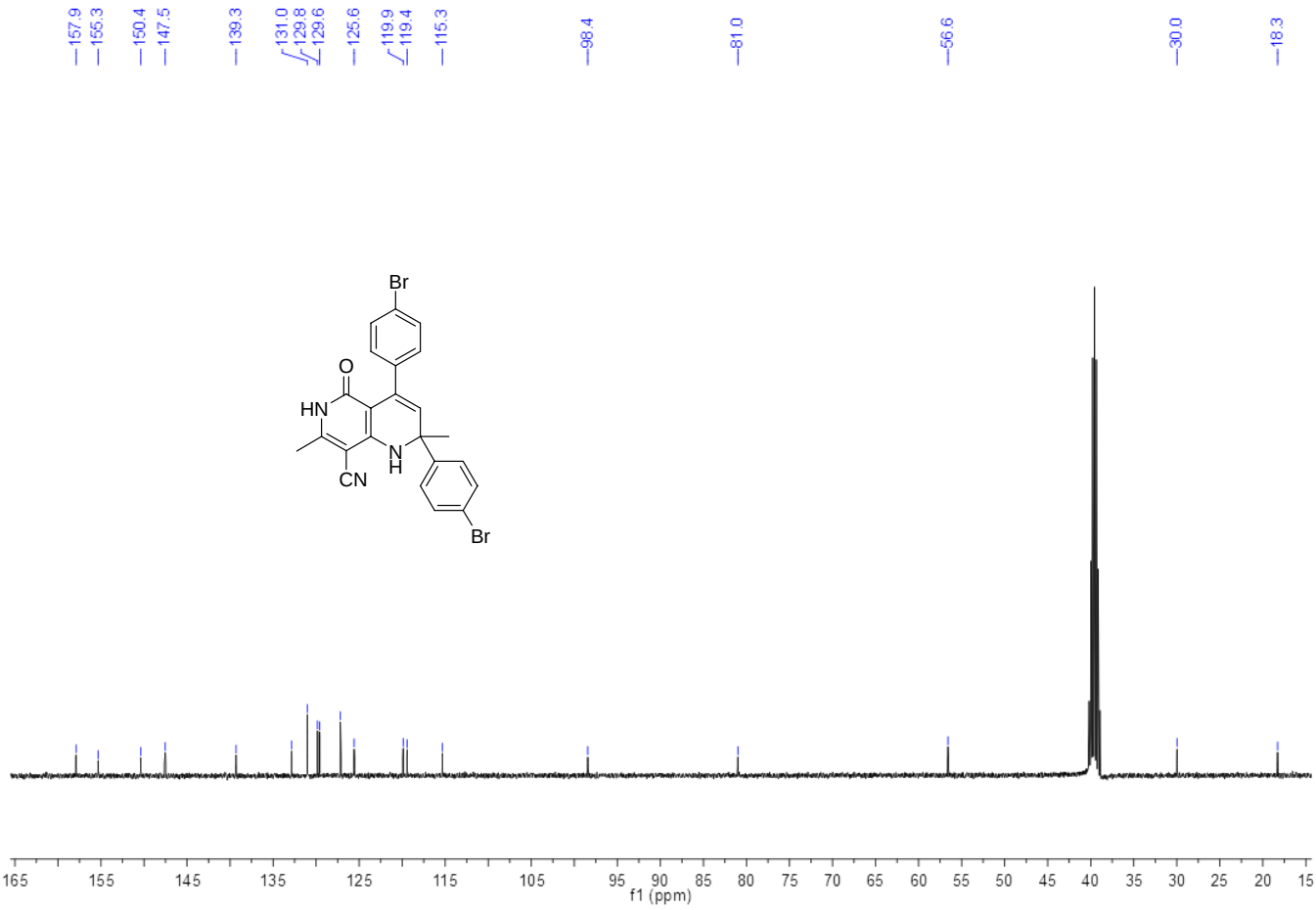
^{1}H NMR Spectrum of Compound **3c**



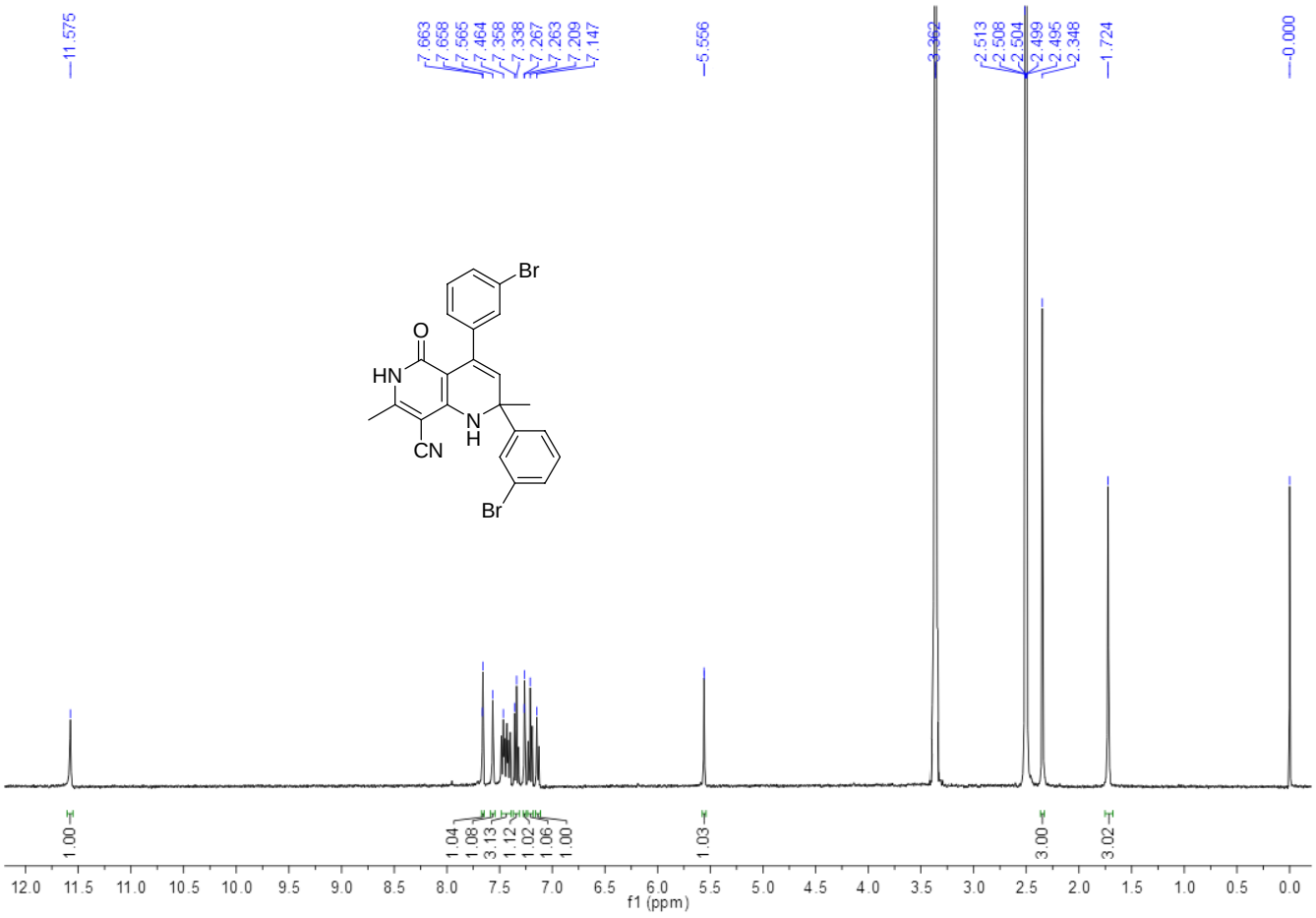
^{13}C NMR Spectrum of Compound **3c**



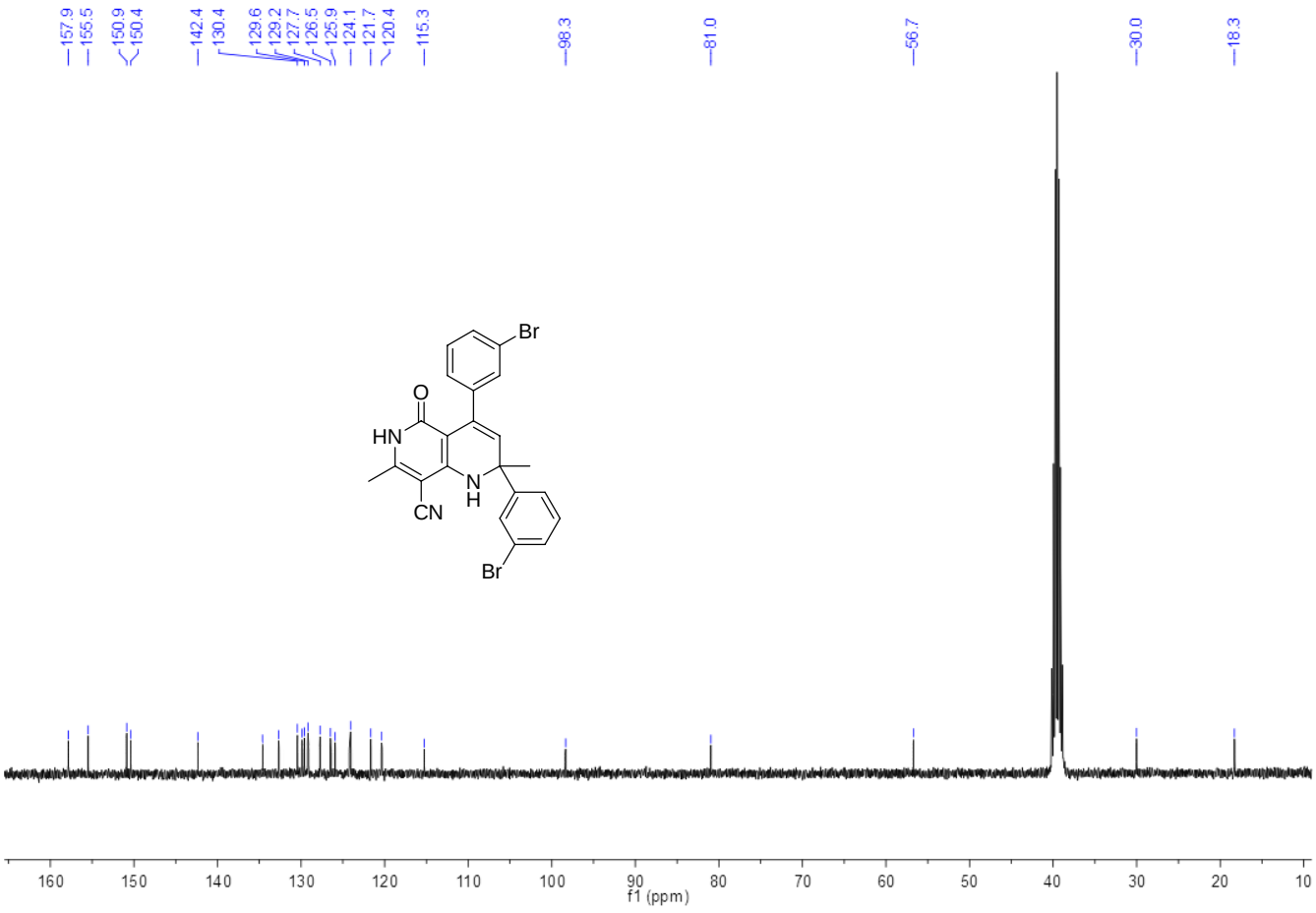
^{1}H NMR Spectrum of Compound **3d**



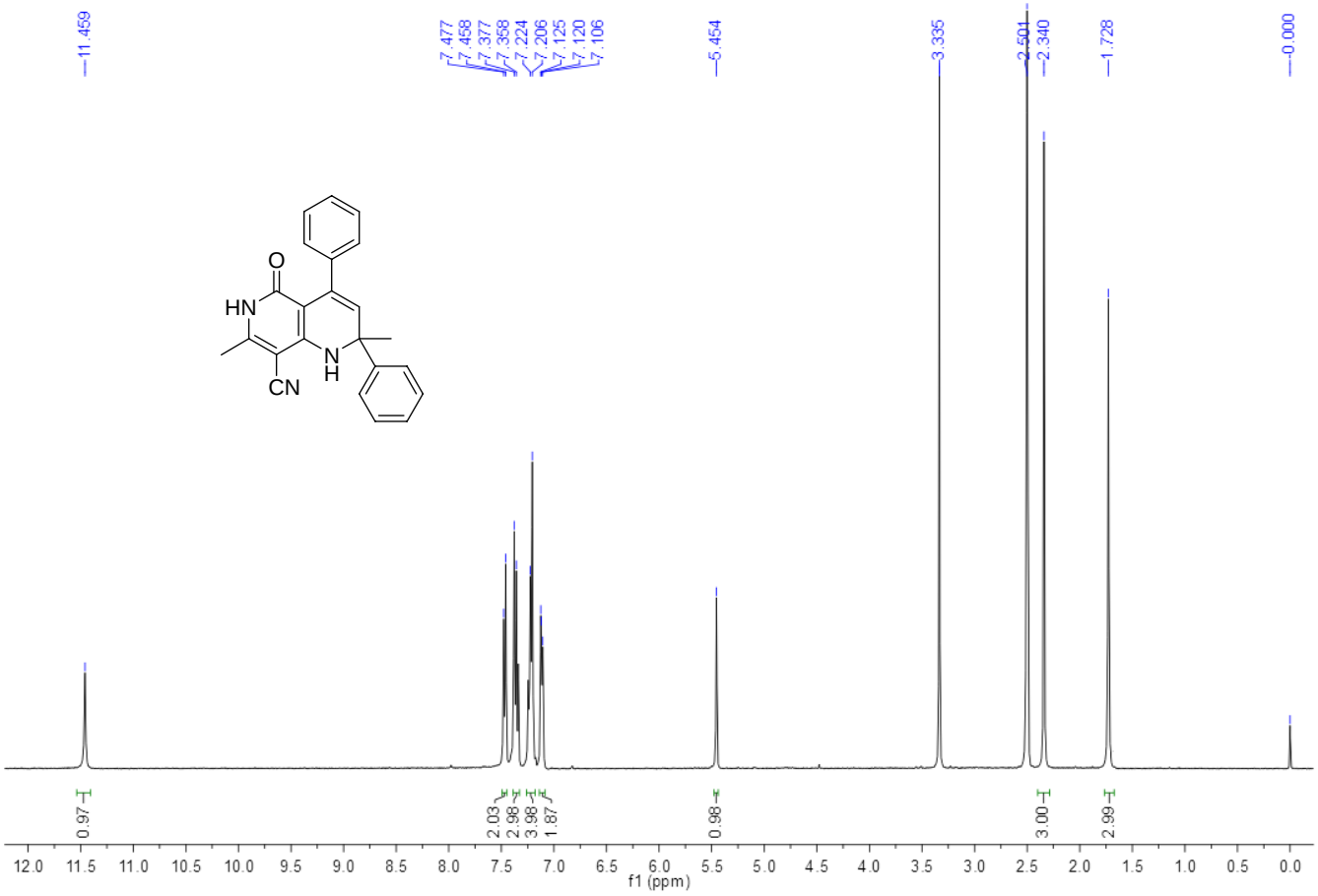
^{13}C NMR Spectrum of Compound **3d**



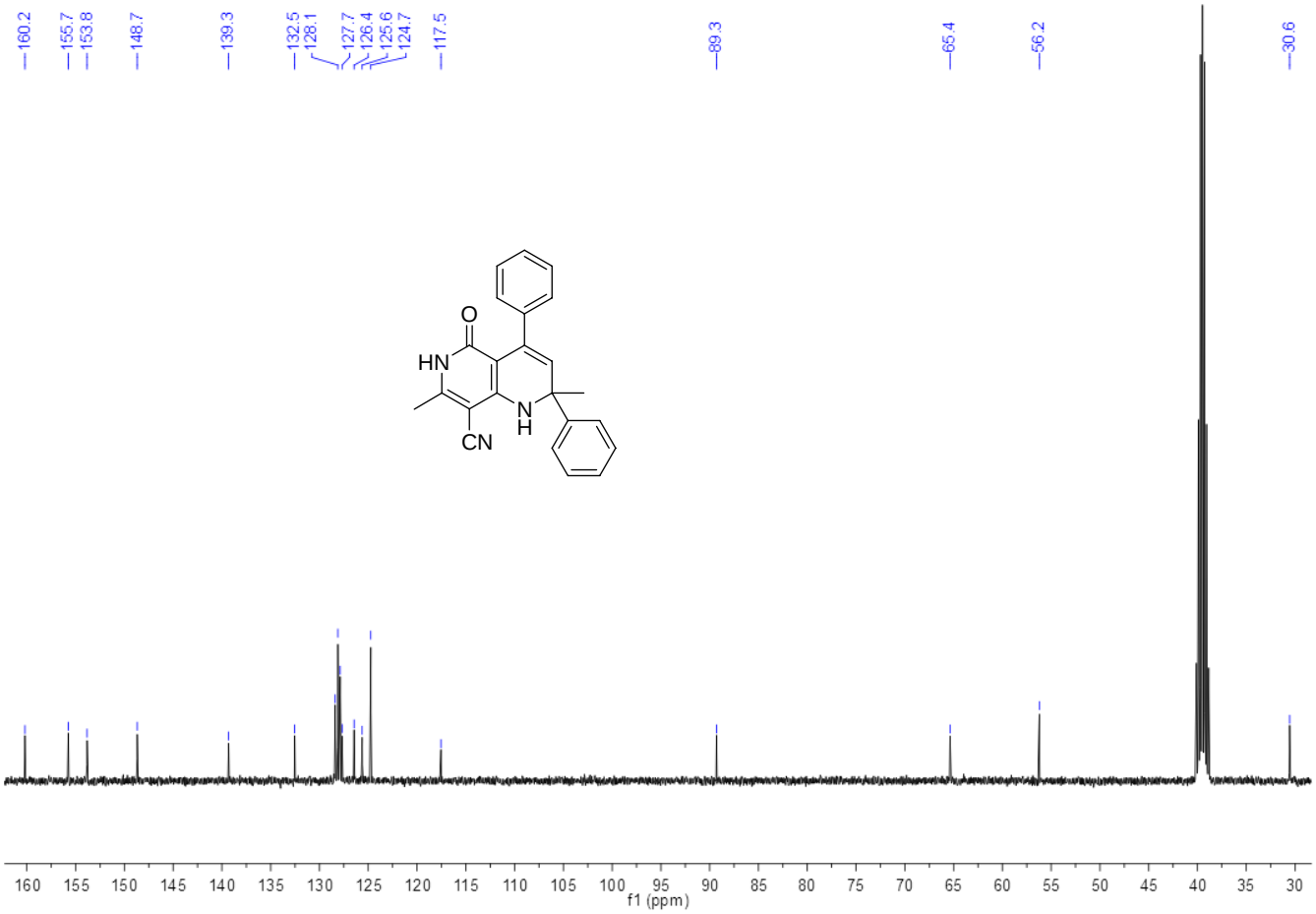
^{1}H NMR Spectrum of Compound **3e**



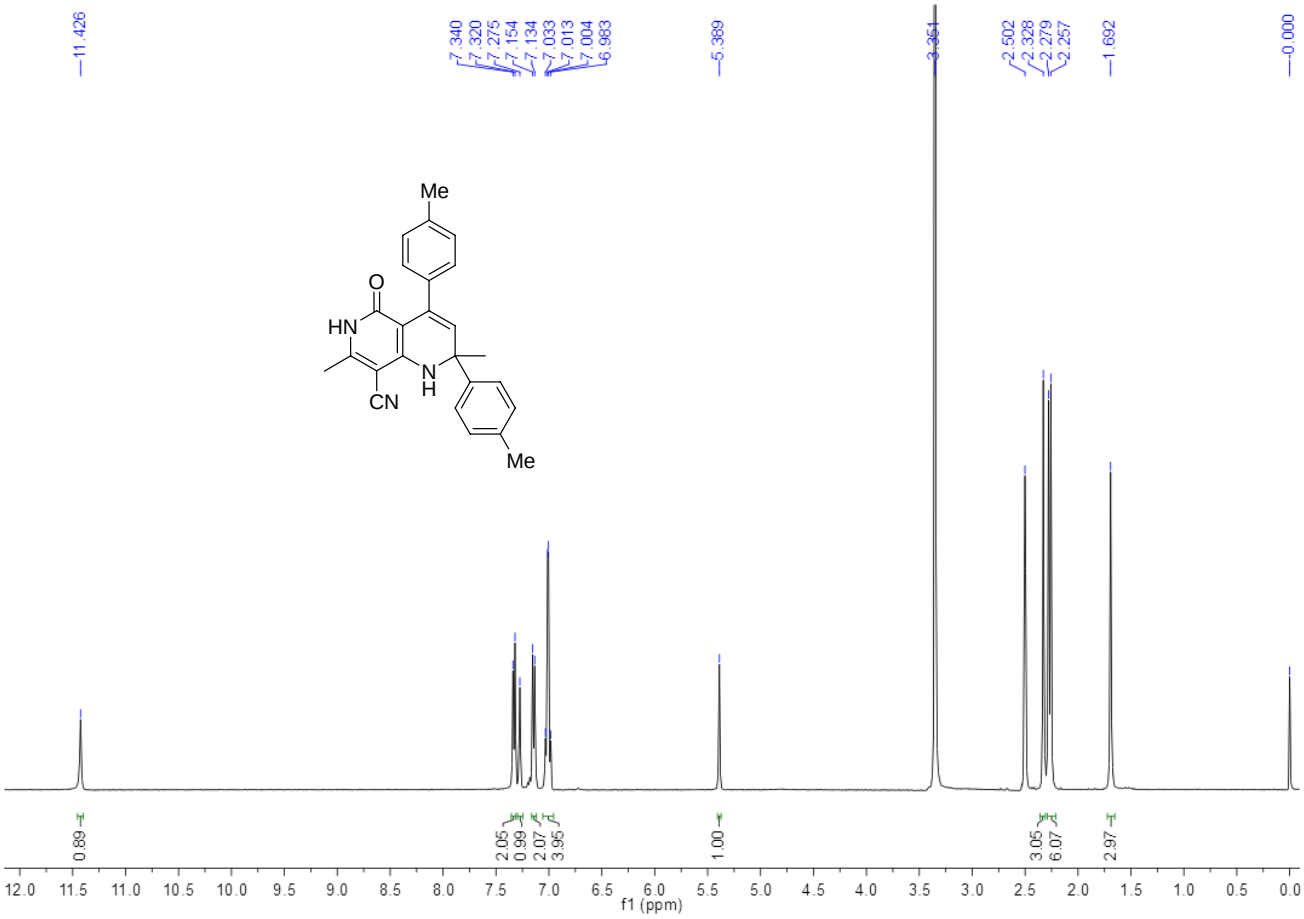
^{13}C NMR Spectrum of Compound **3e**



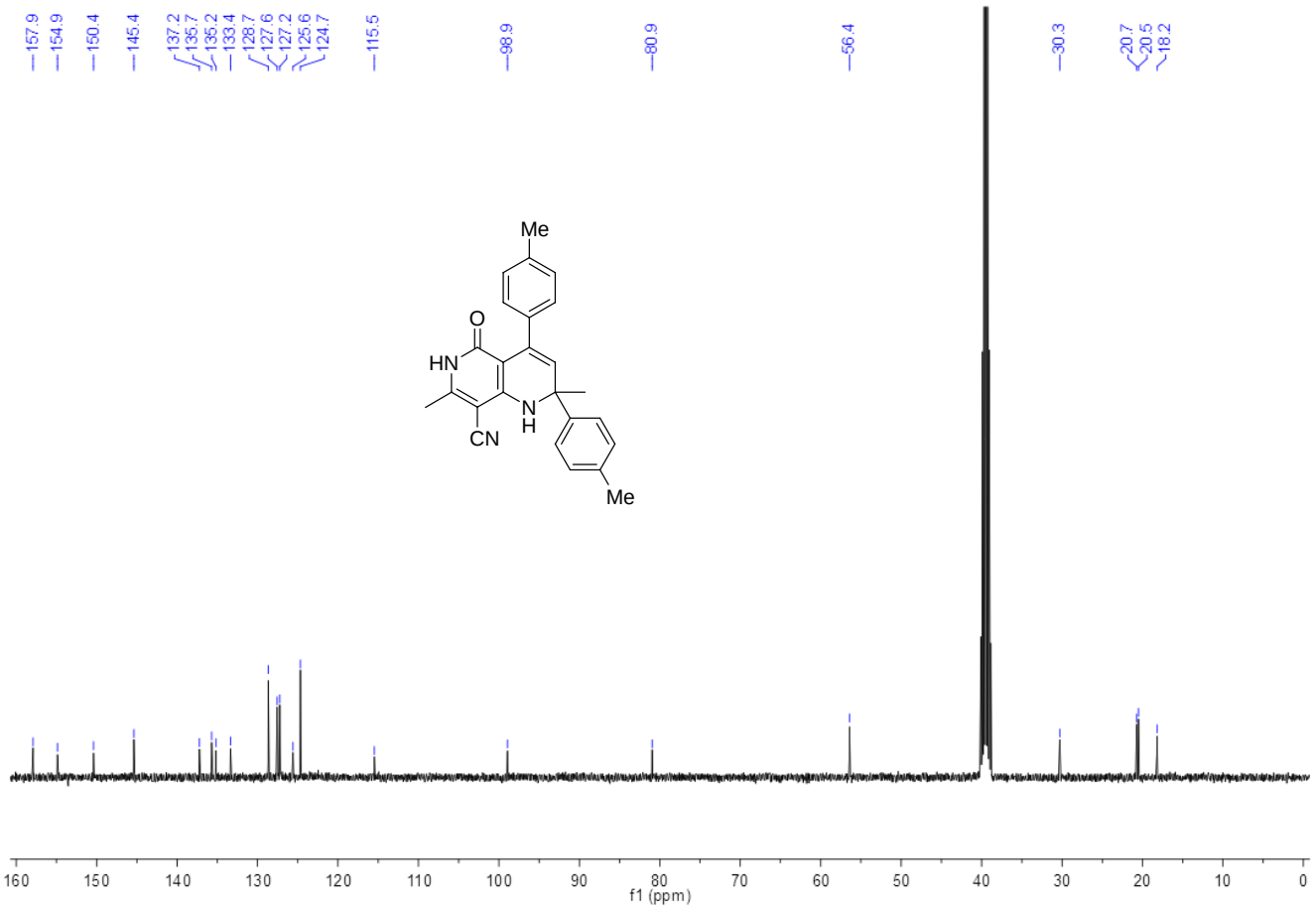
^{1}H NMR Spectrum of Compound **3f**



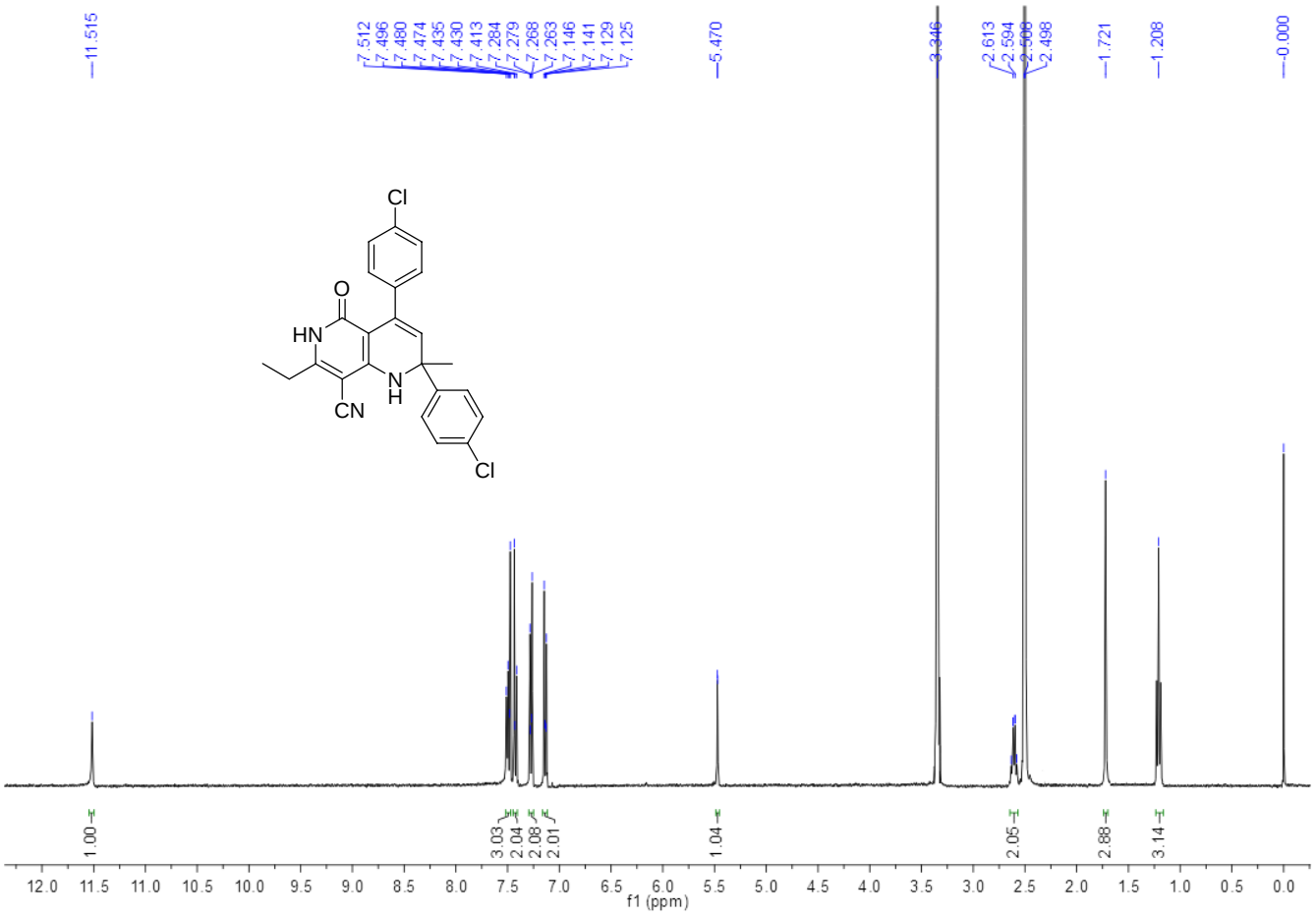
^{13}C NMR Spectrum of Compound **3f**



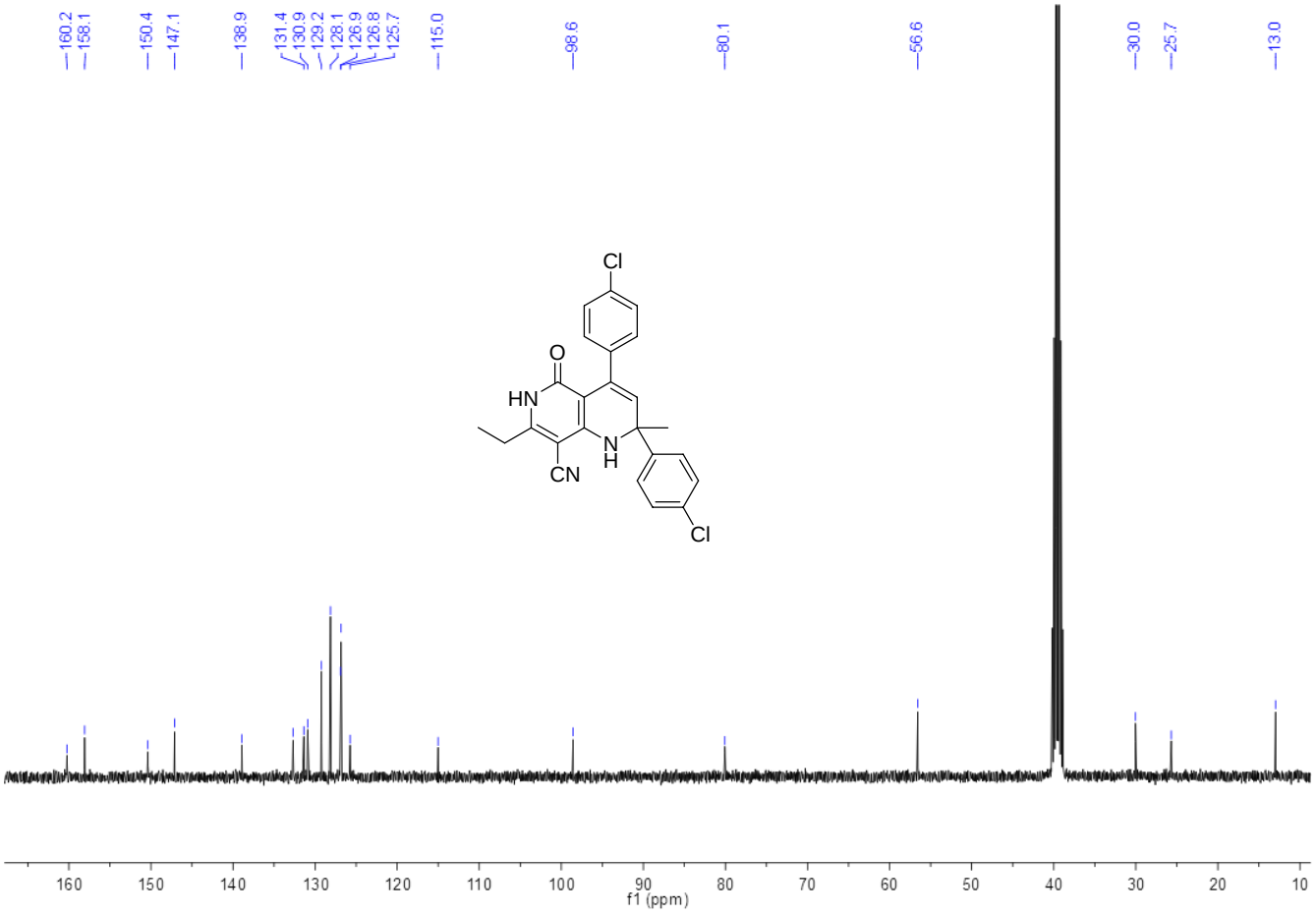
^{1}H NMR Spectrum of Compound **3g**



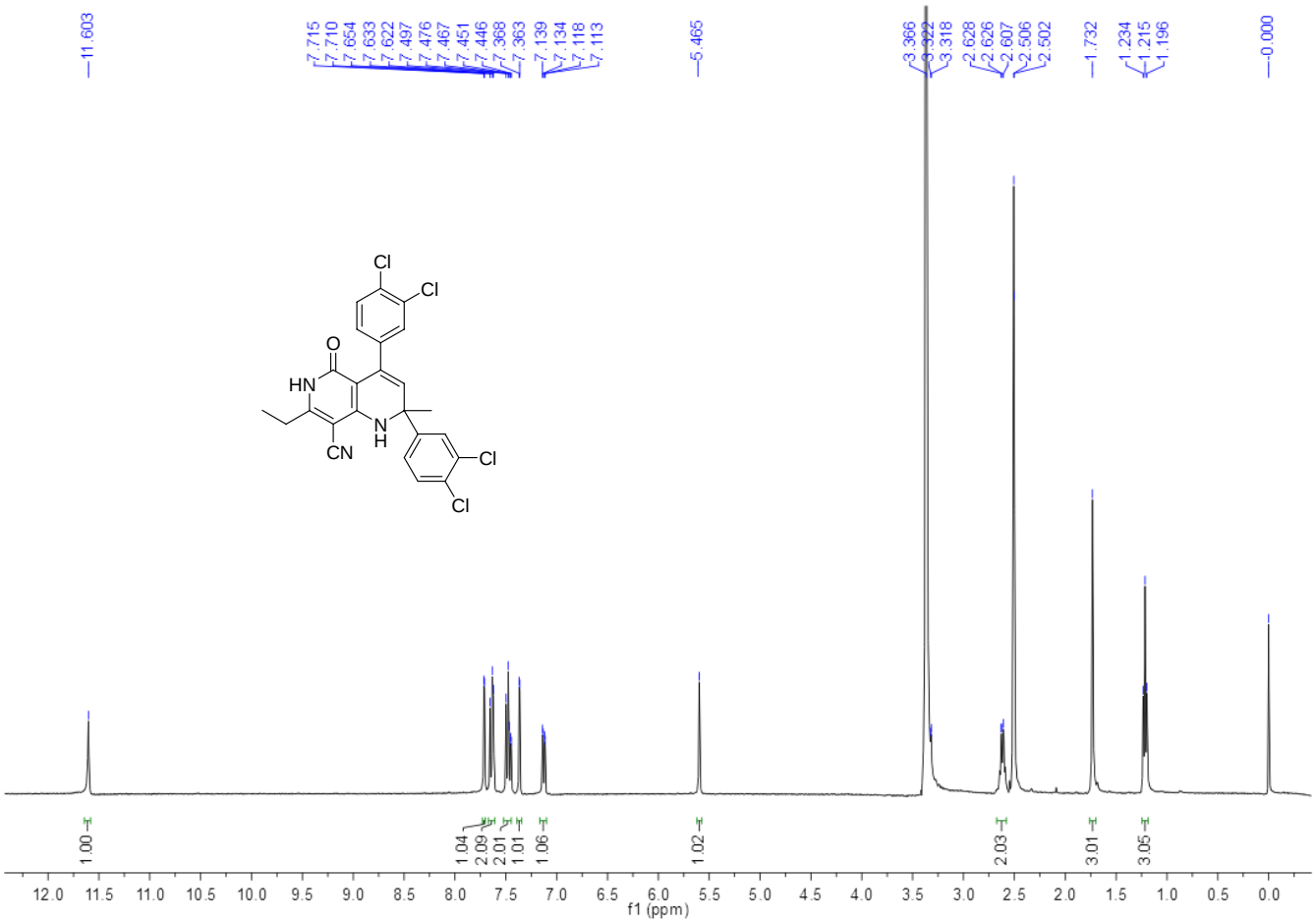
^{13}C NMR Spectrum of Compound **3g**



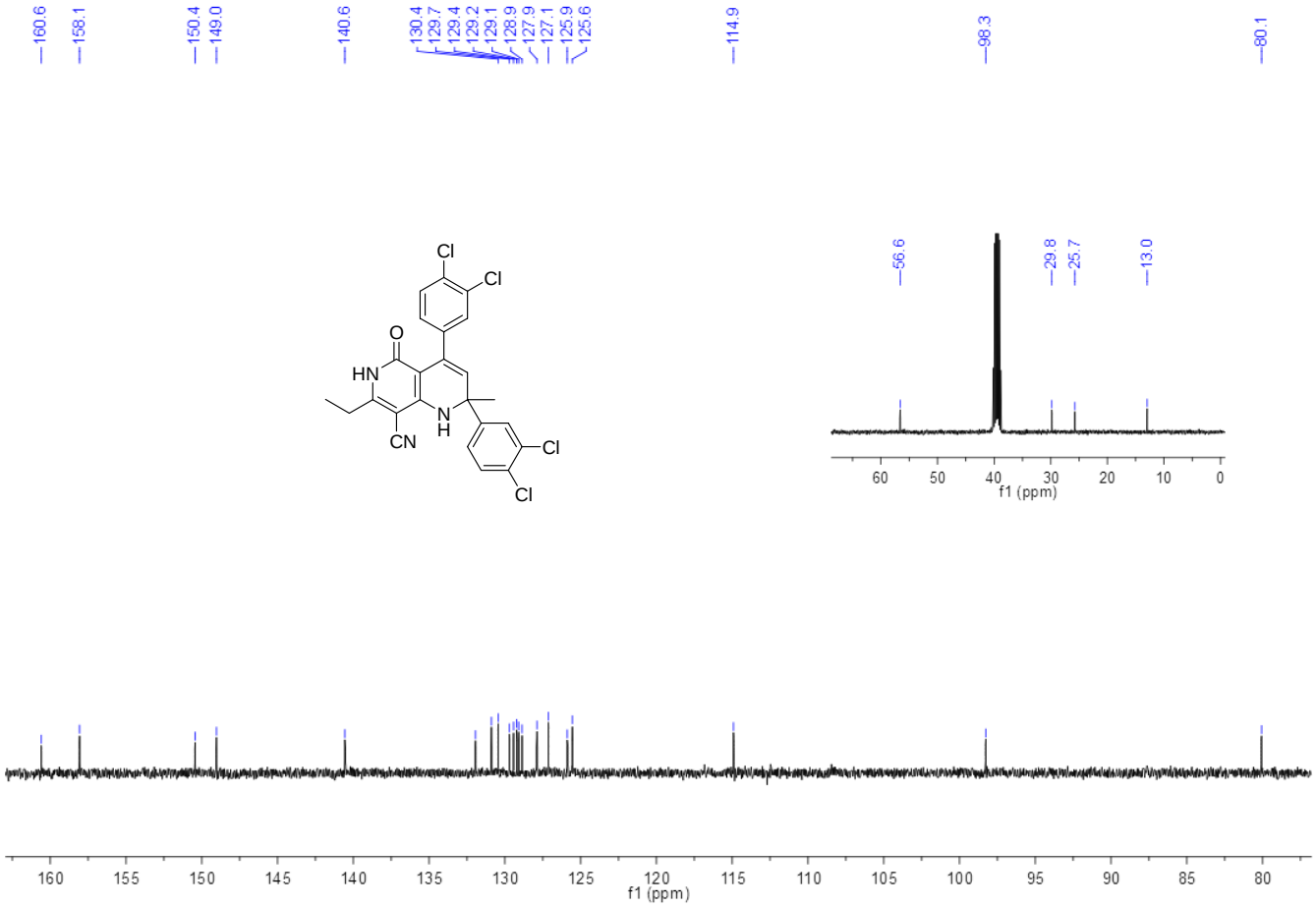
^{1}H NMR Spectrum of Compound **3h**



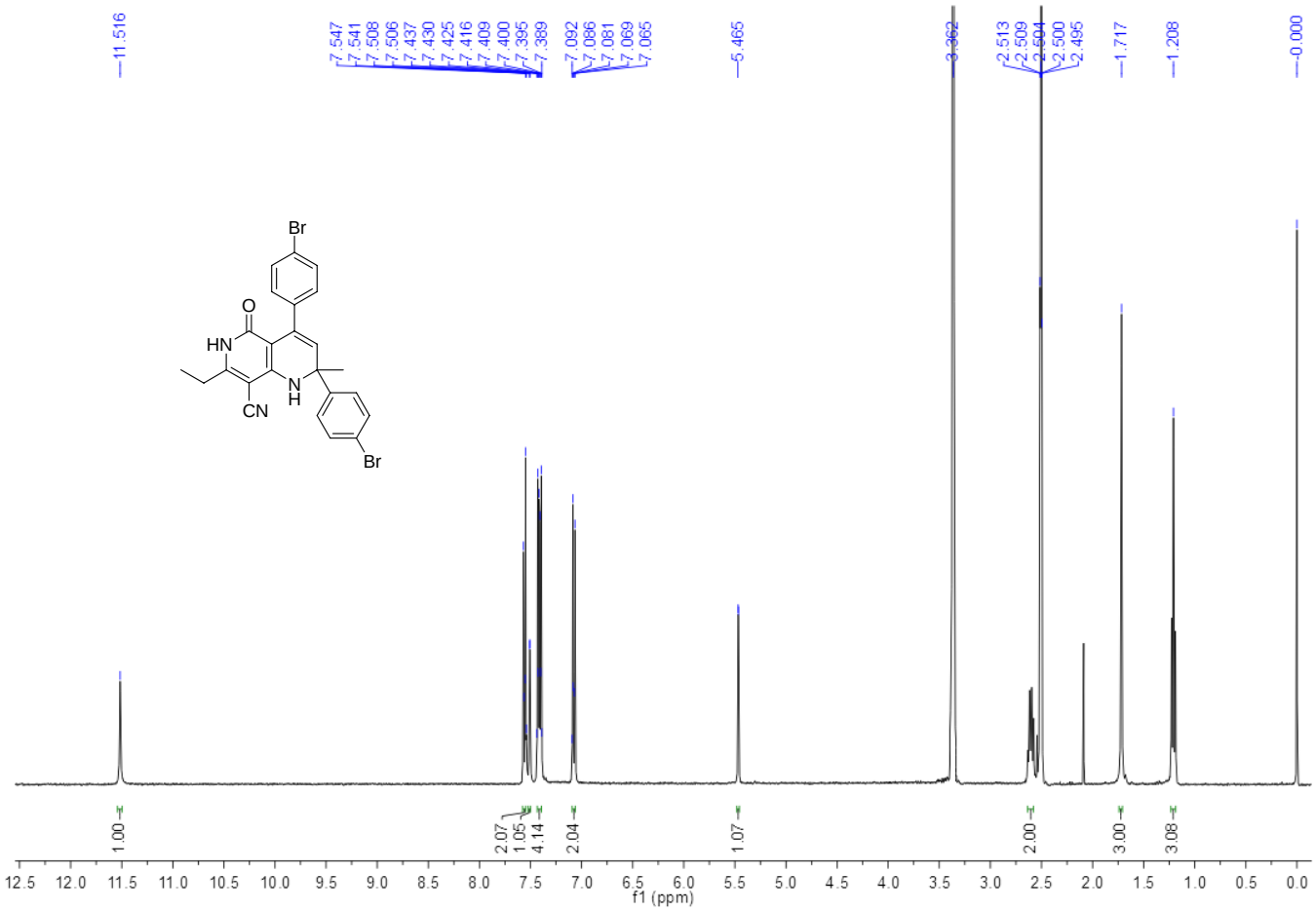
^{13}C NMR Spectrum of Compound **3h**



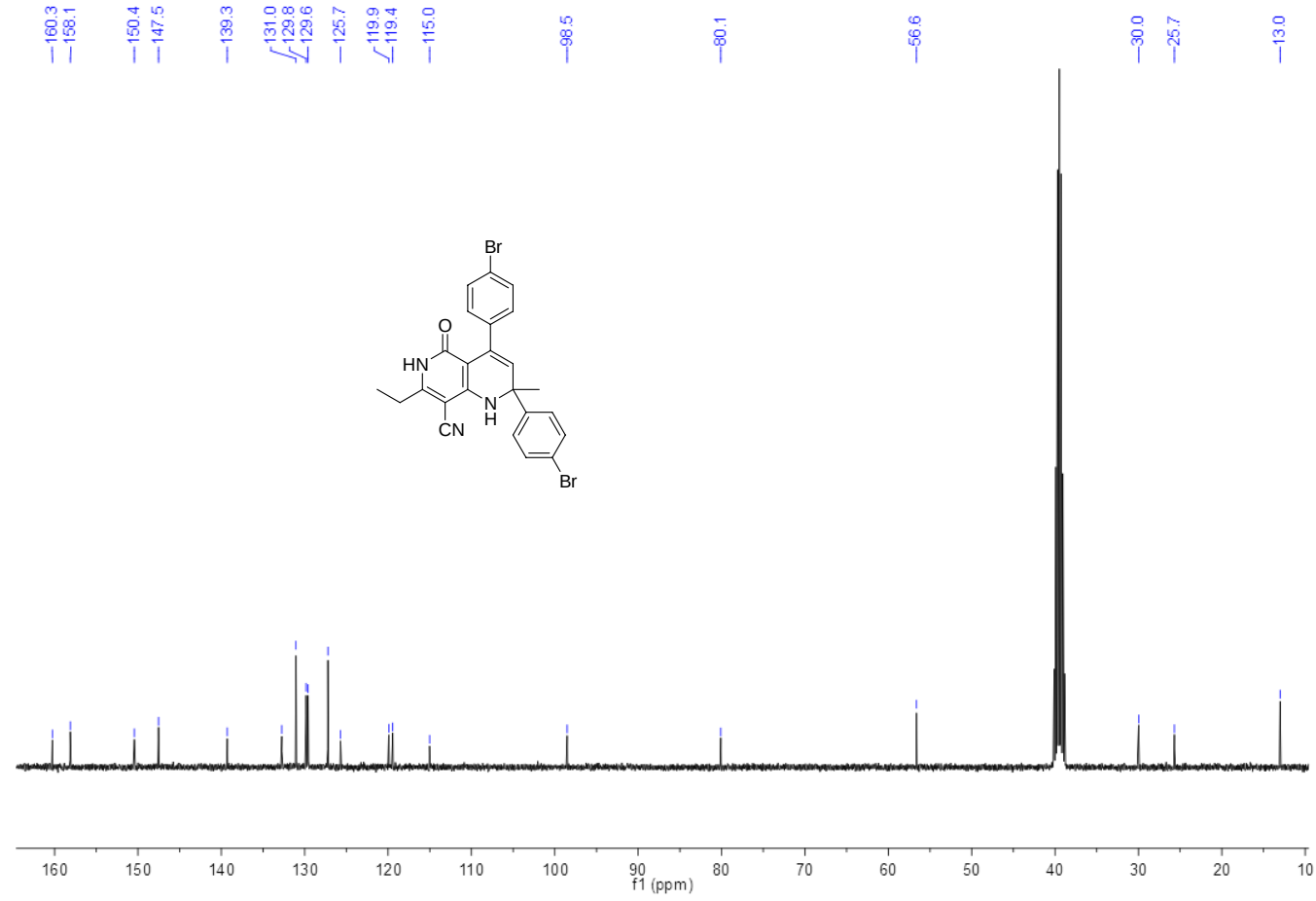
^{1}H NMR Spectrum of Compound **3i**



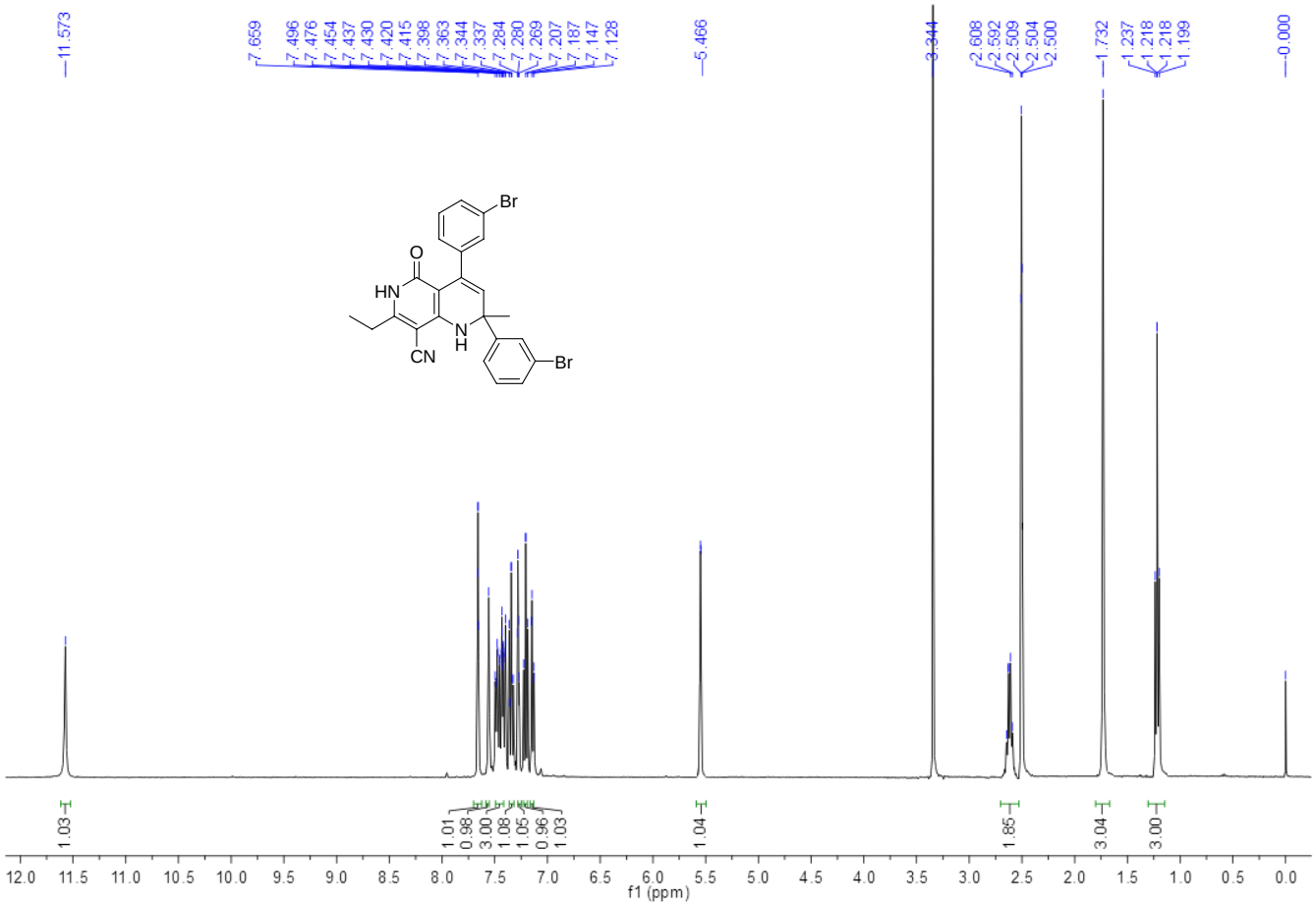
^{13}C NMR Spectrum of Compound **3i**



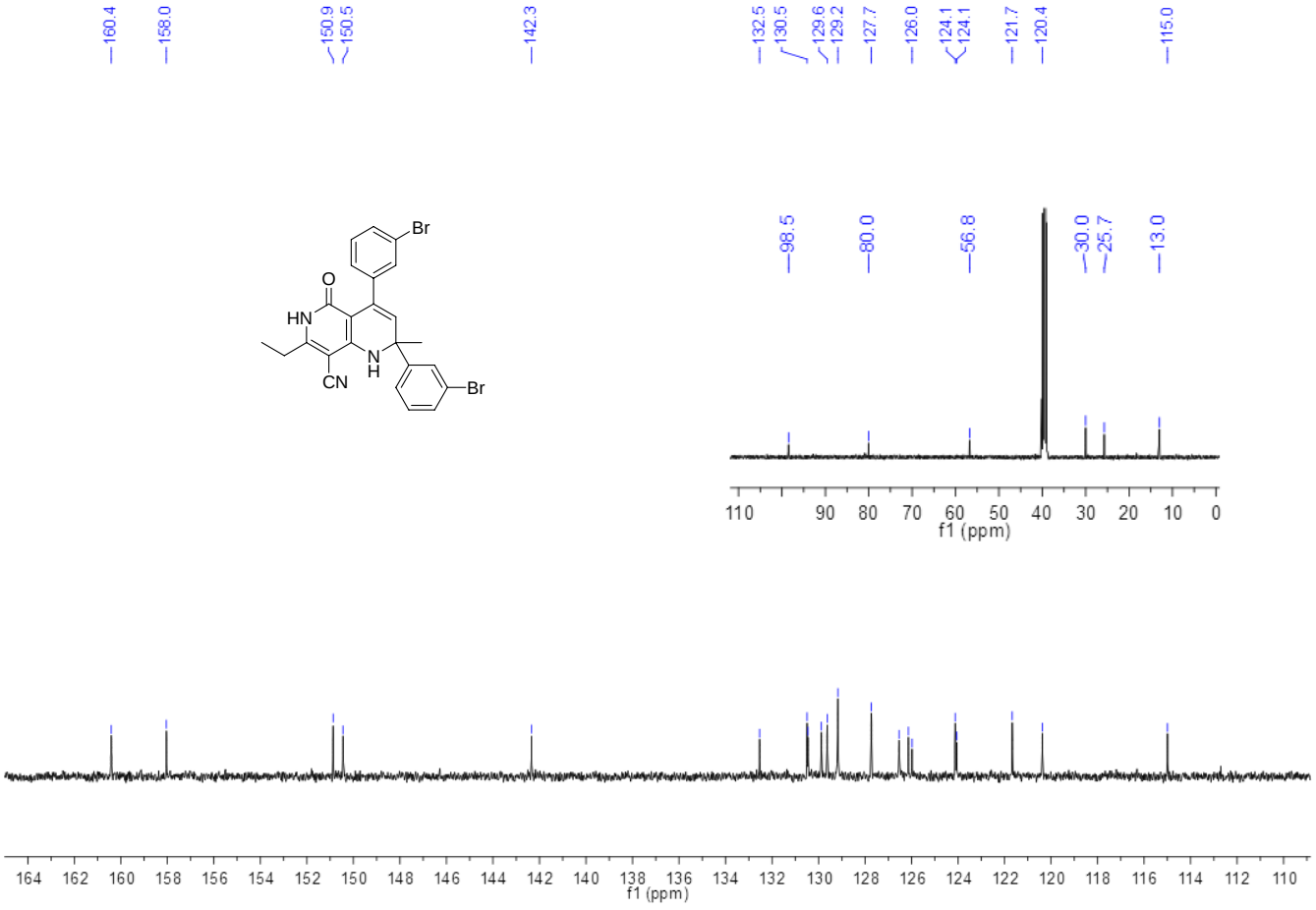
^{1}H NMR Spectrum of Compound **3j**



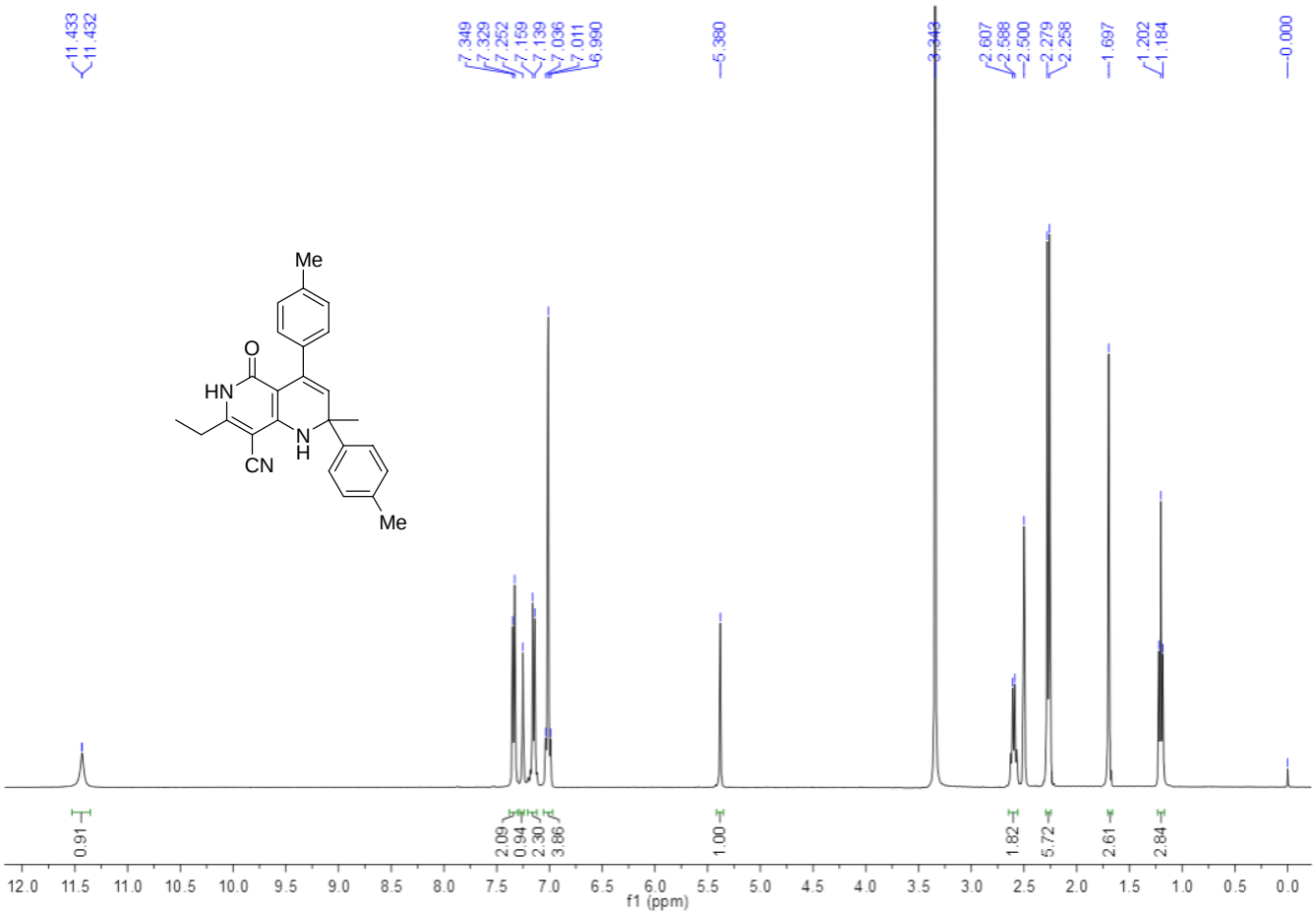
^{13}C NMR Spectrum of Compound **3j**



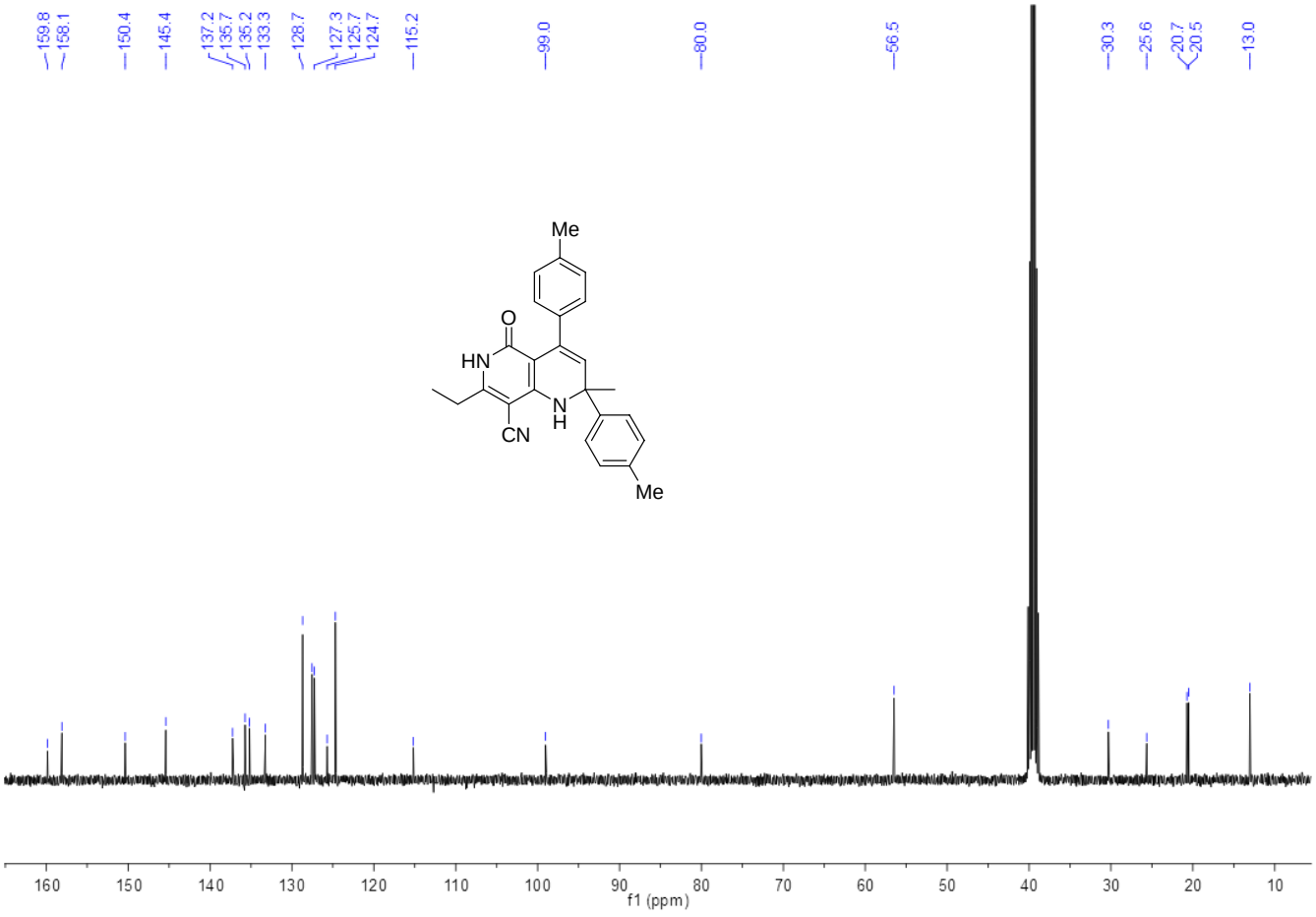
^{1}H NMR Spectrum of Compound **3k**



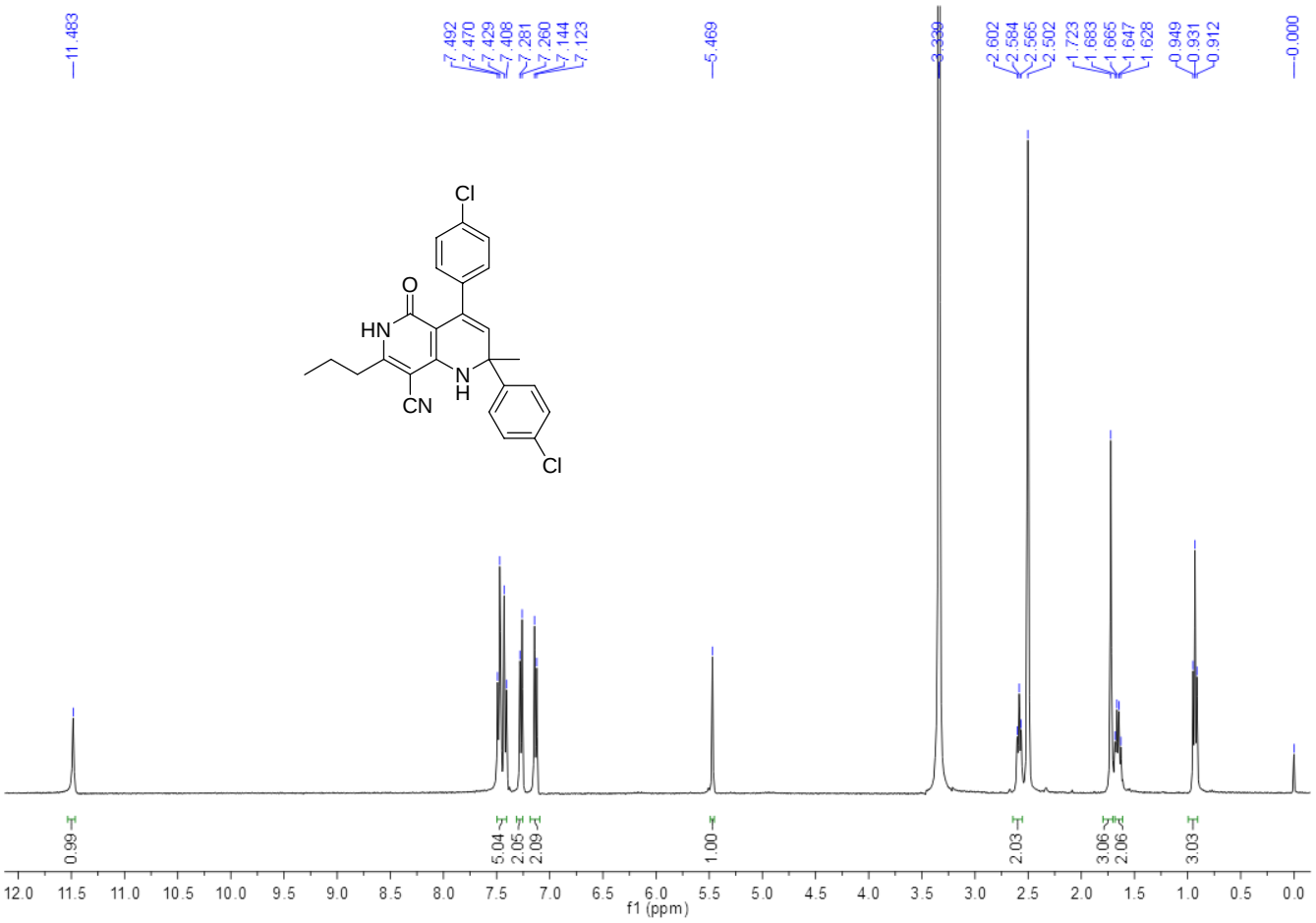
^{13}C NMR Spectrum of Compound **3k**



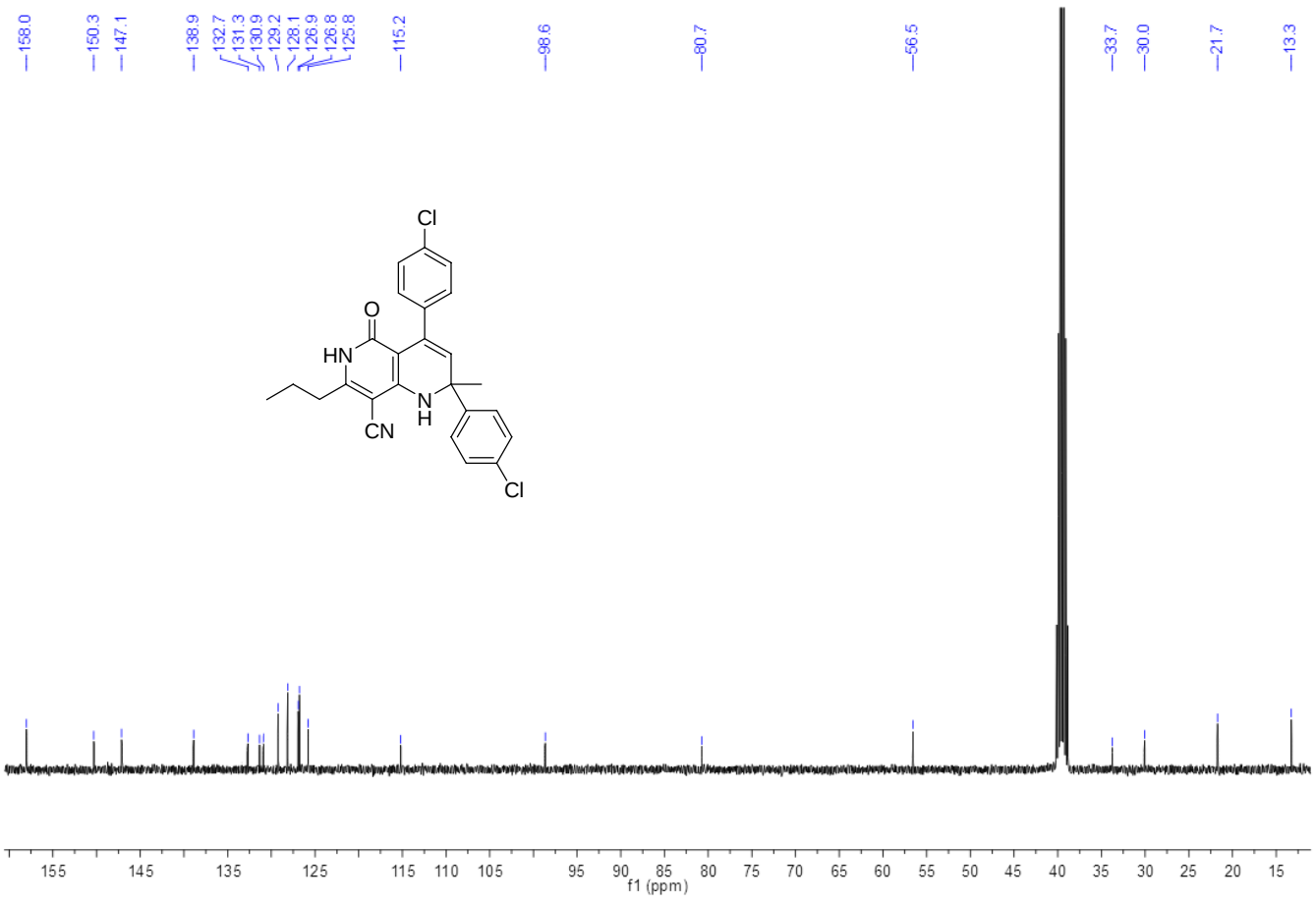
^{1}H NMR Spectrum of Compound **3l**



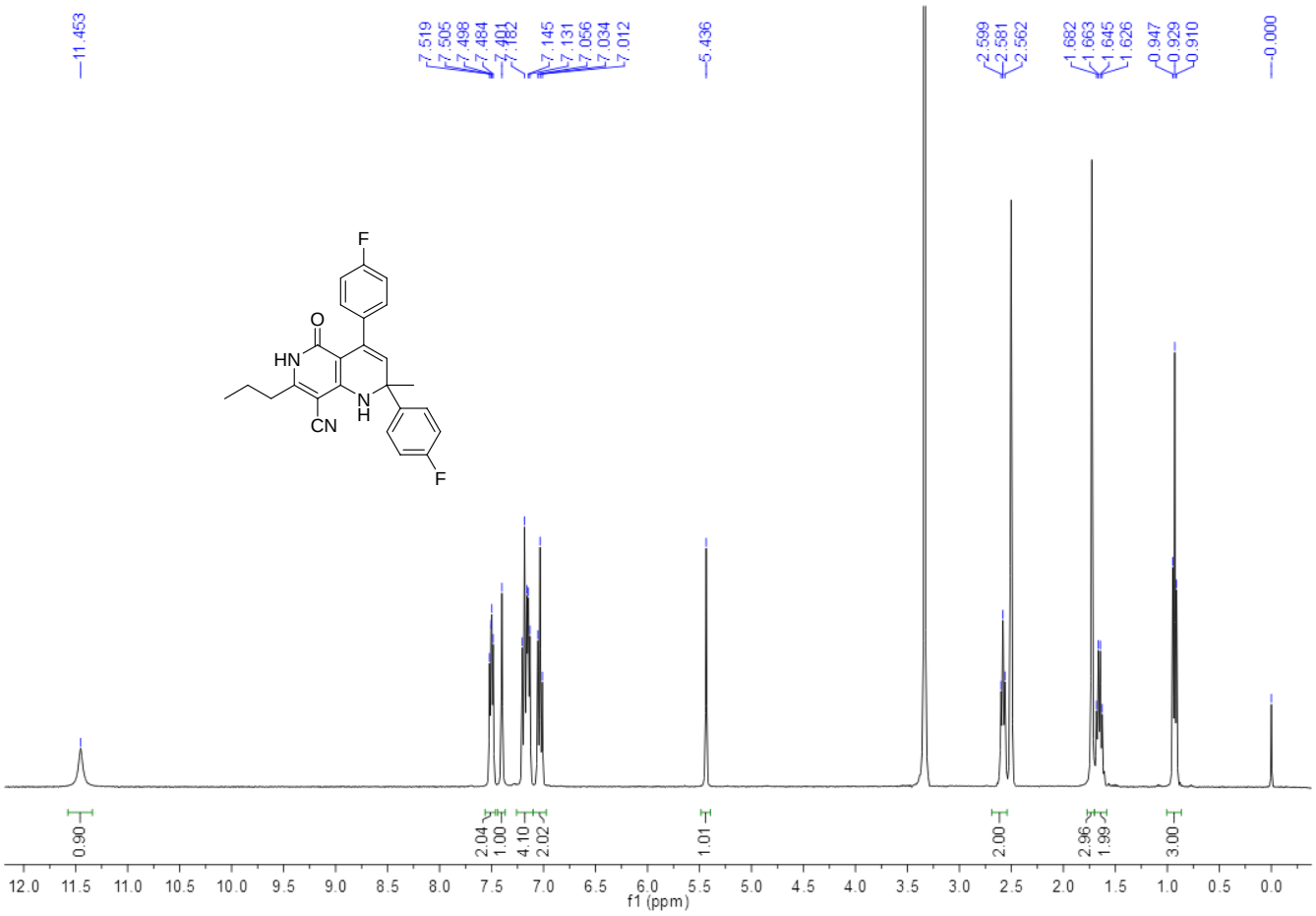
^{13}C NMR Spectrum of Compound **3l**



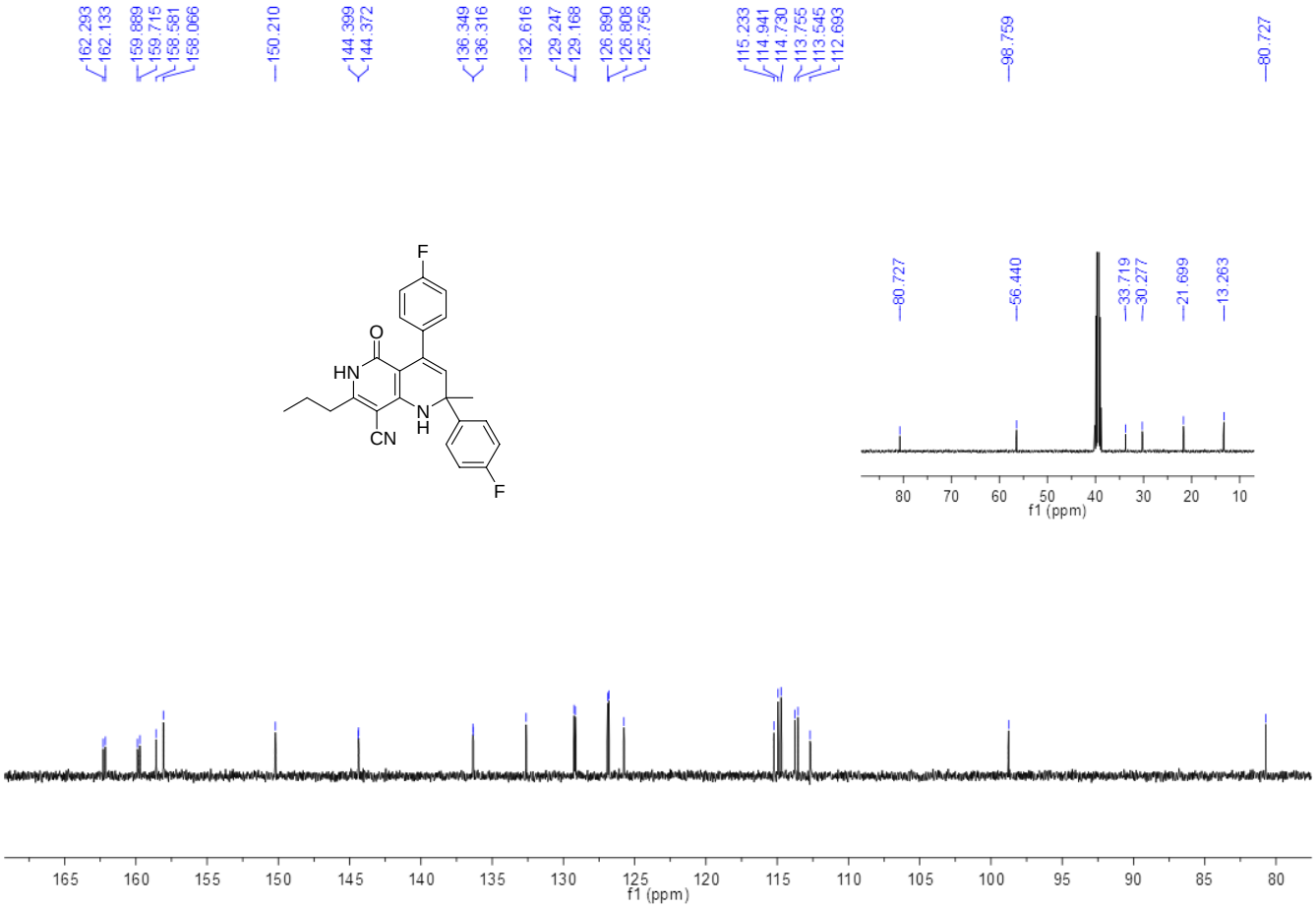
^{1}H NMR Spectrum of Compound **3m**



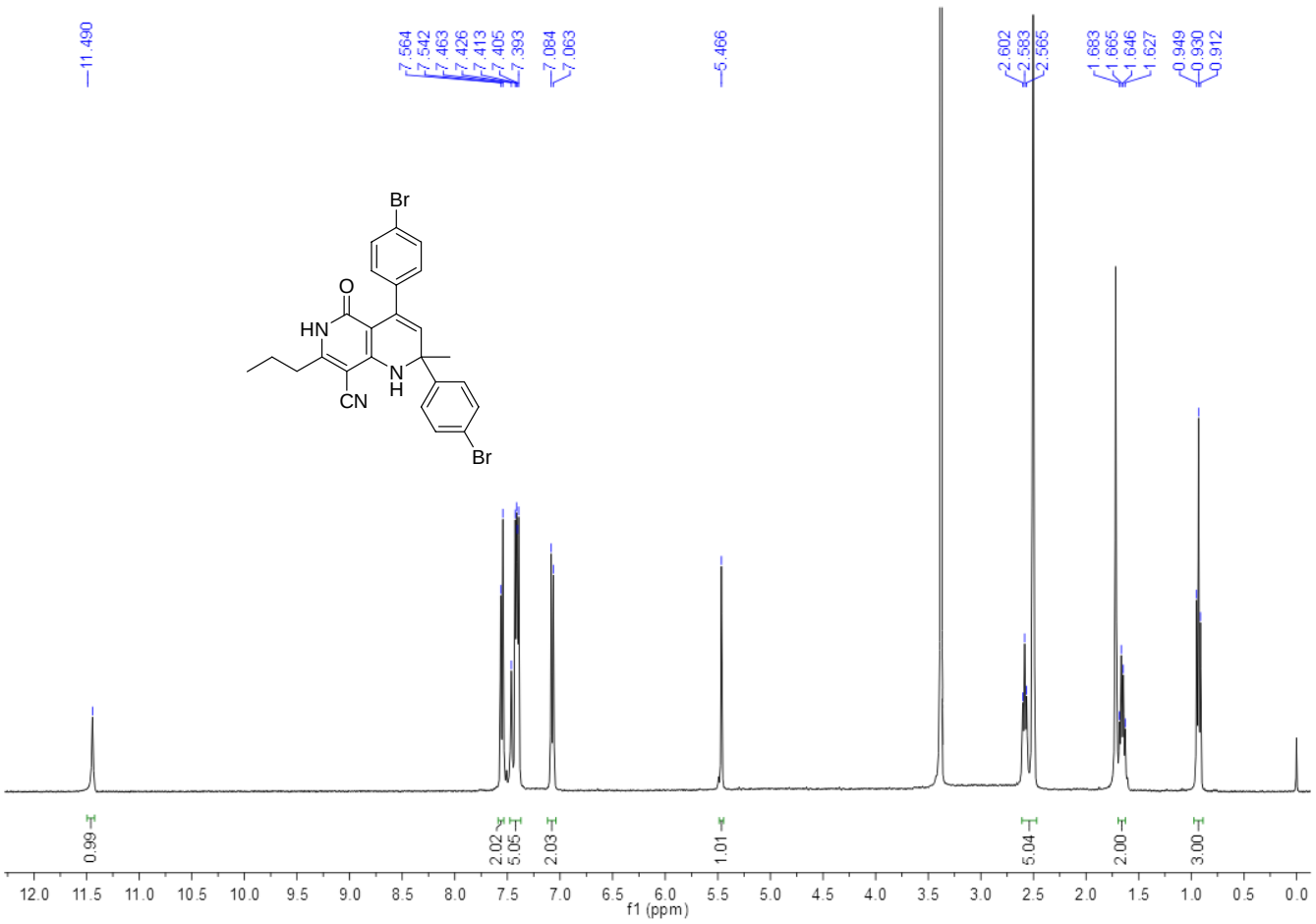
^{13}C NMR Spectrum of Compound **3m**



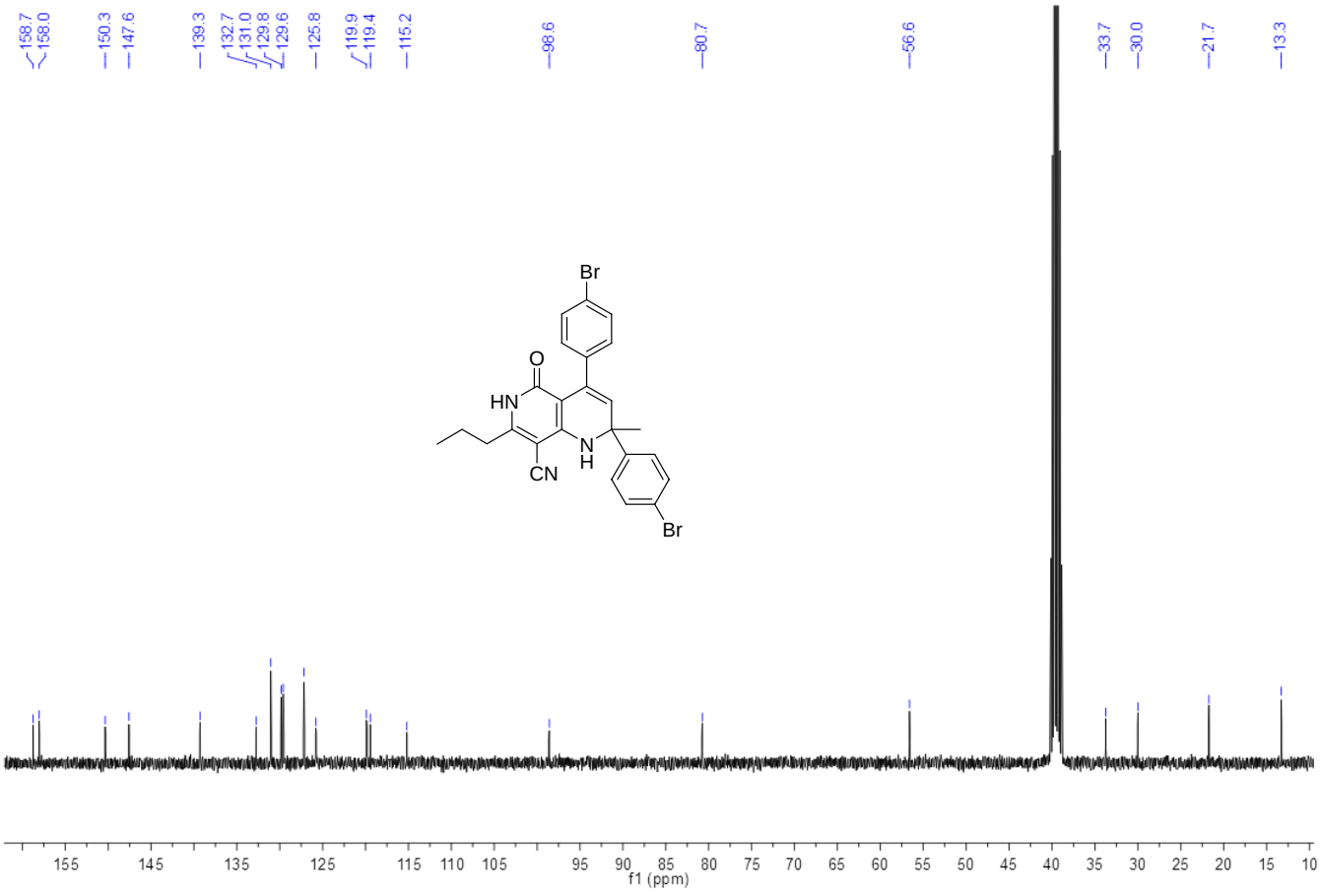
^{1}H NMR Spectrum of Compound **3n**



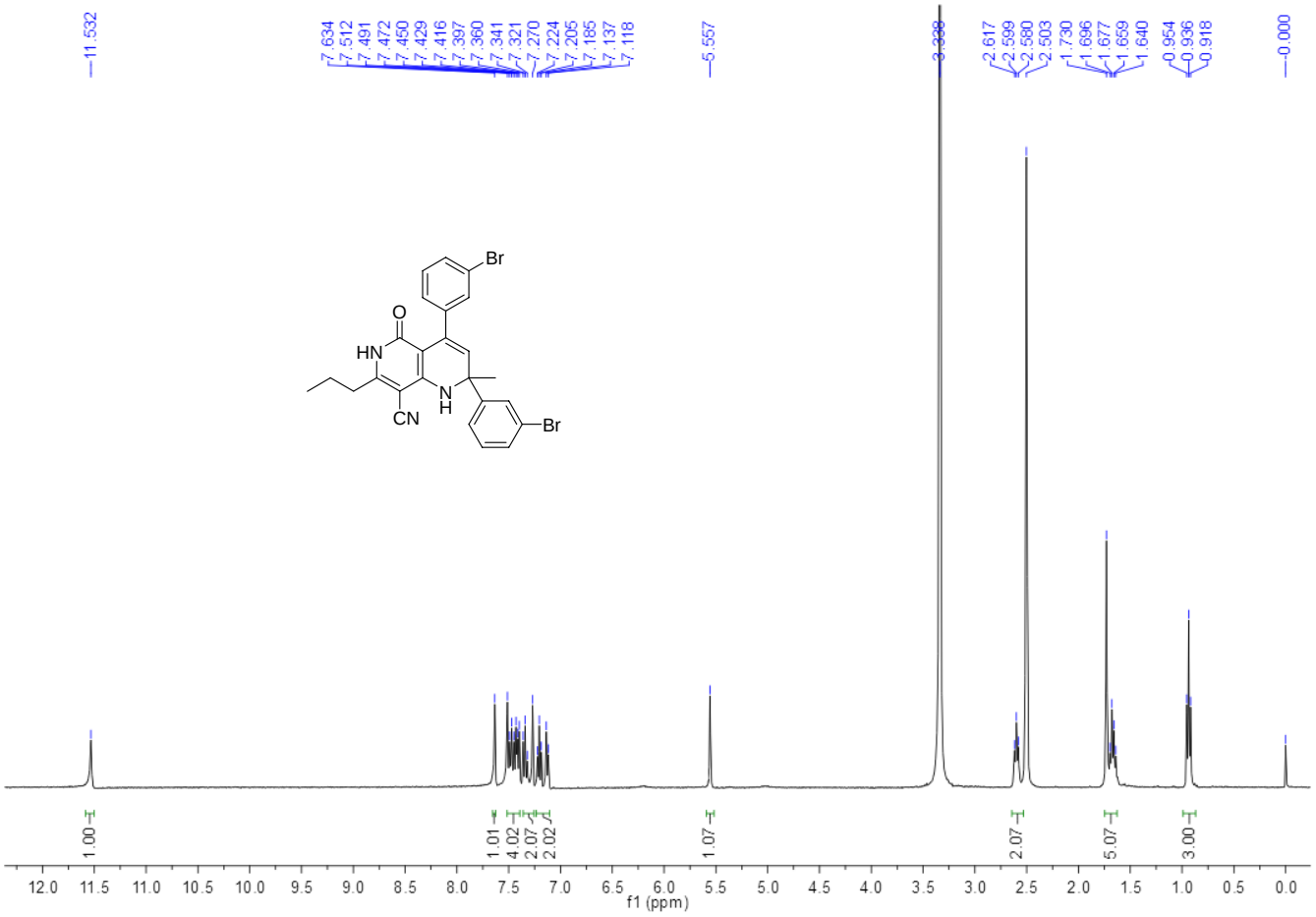
^{13}C NMR Spectrum of Compound **3n**



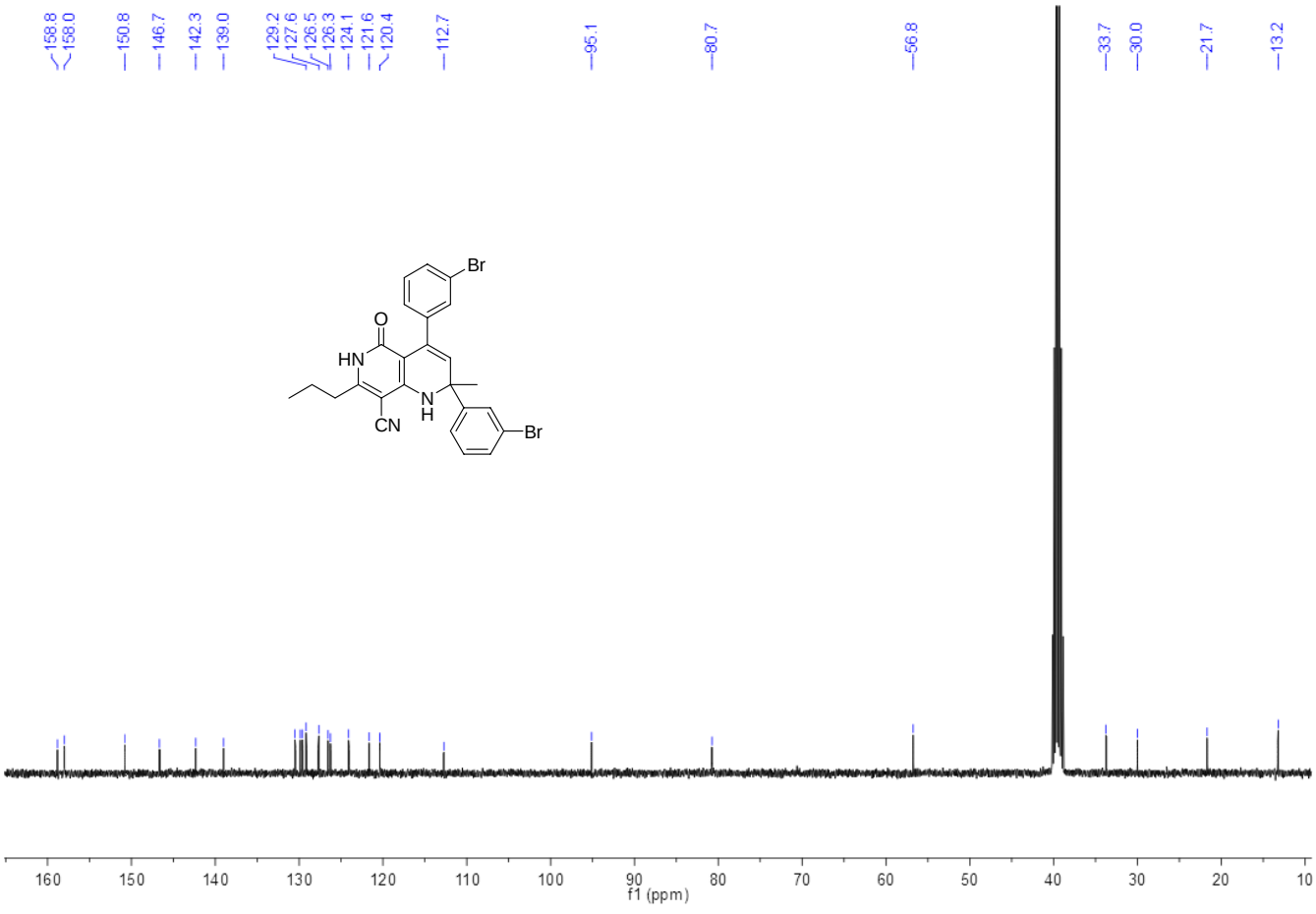
^{1}H NMR Spectrum of Compound **3o**



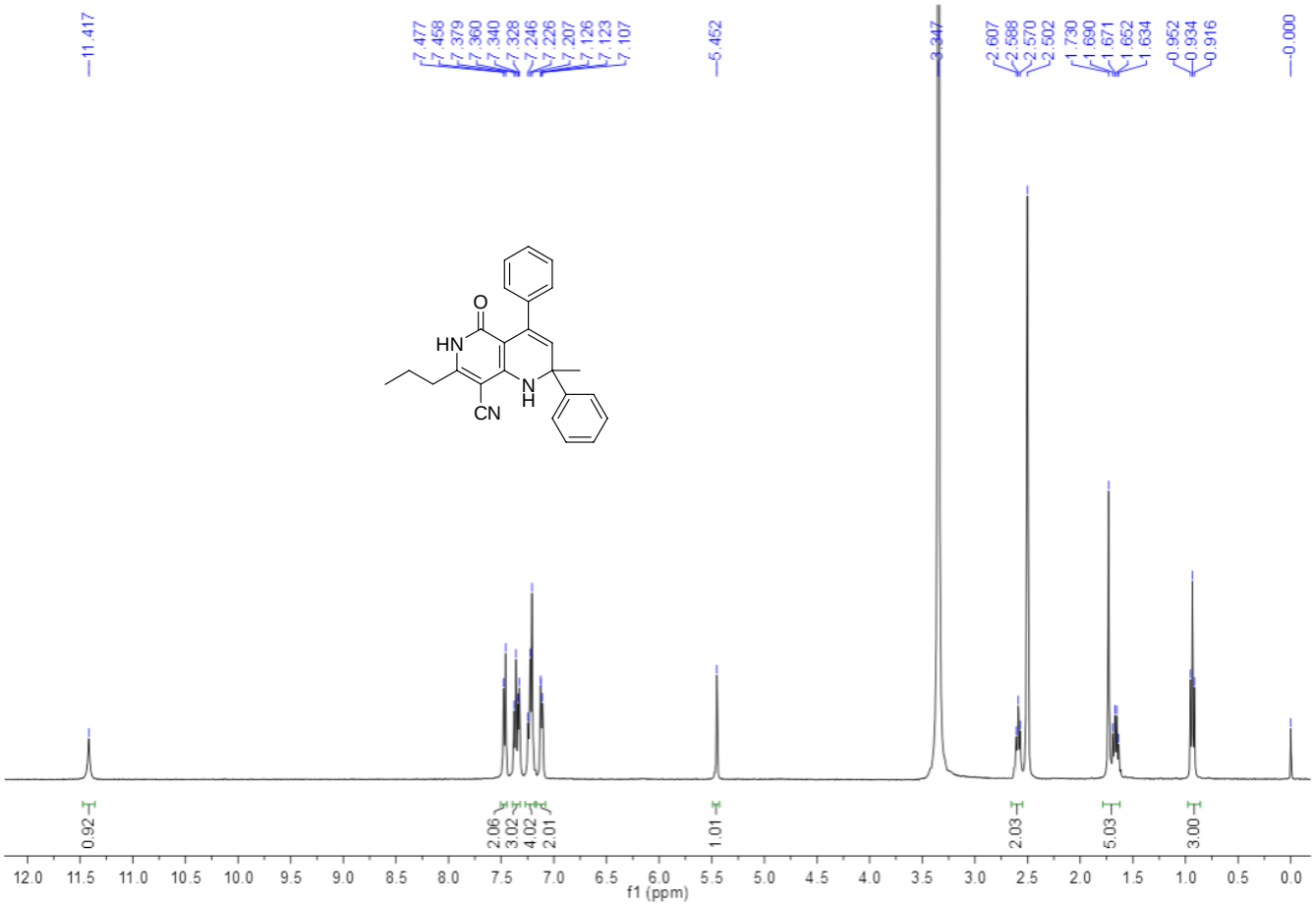
^{13}C NMR Spectrum of Compound **3o**



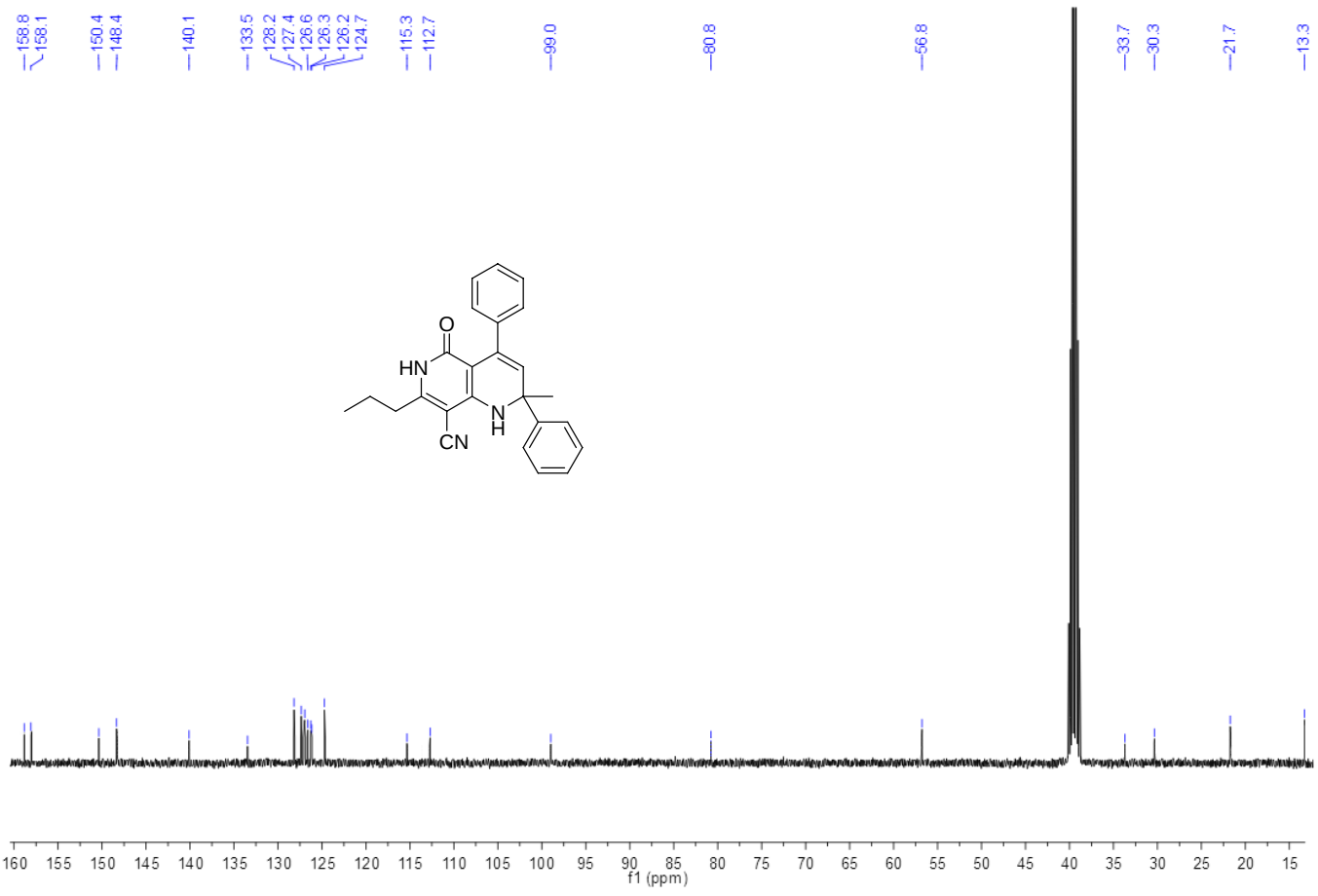
^{1}H NMR Spectrum of Compound **3p**



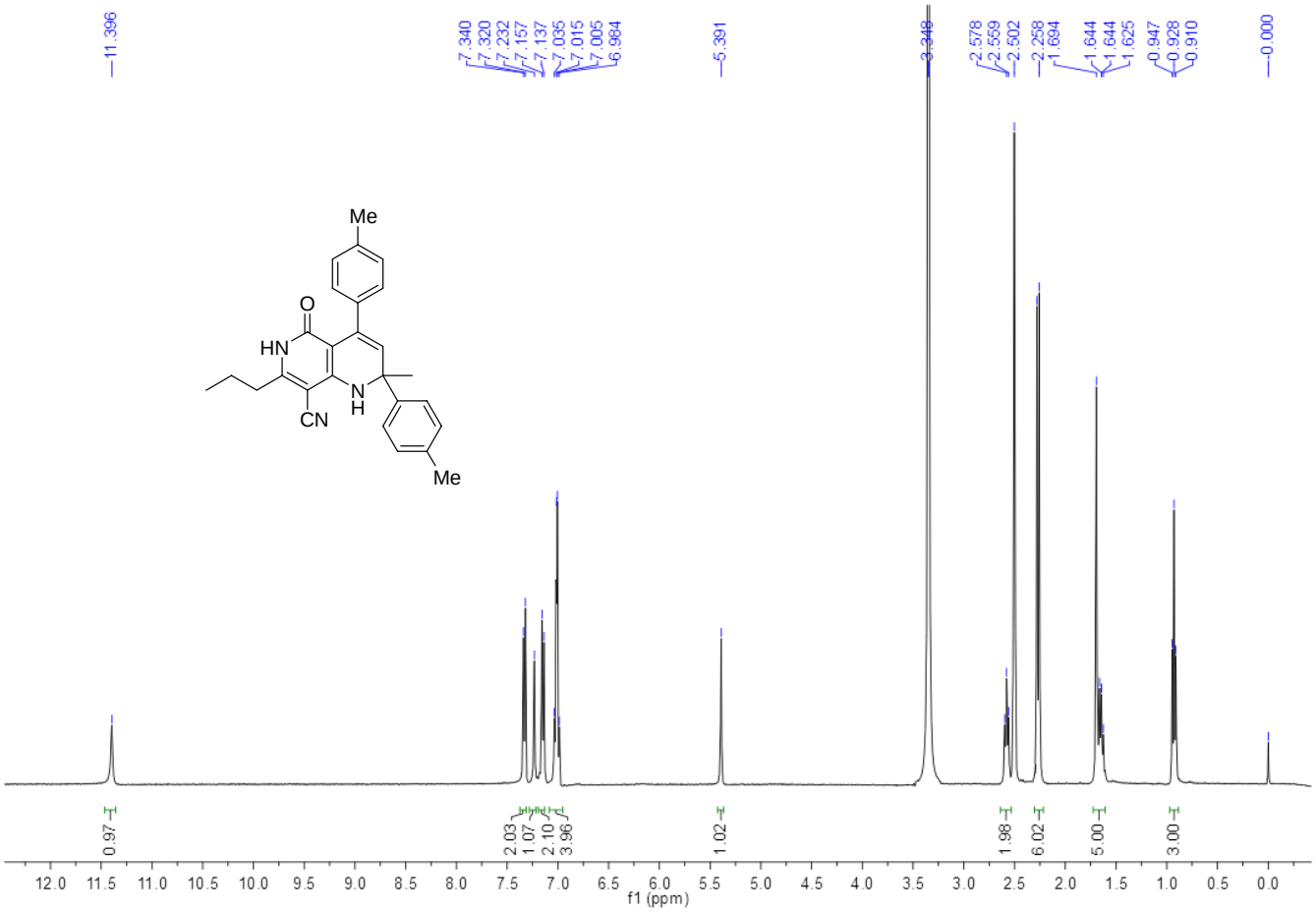
^{13}C NMR Spectrum of Compound **3p**



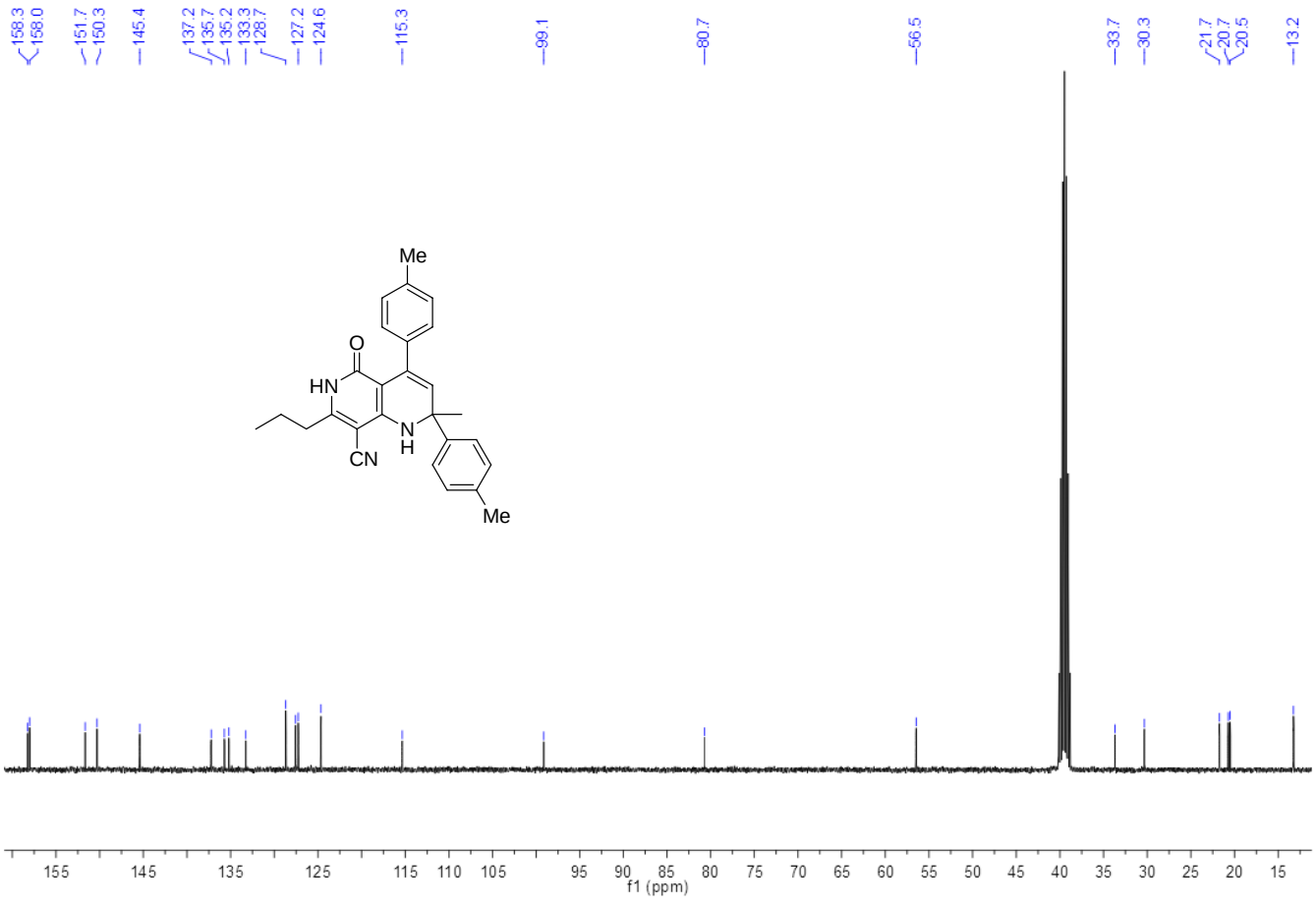
^{1}H NMR Spectrum of Compound **3q**



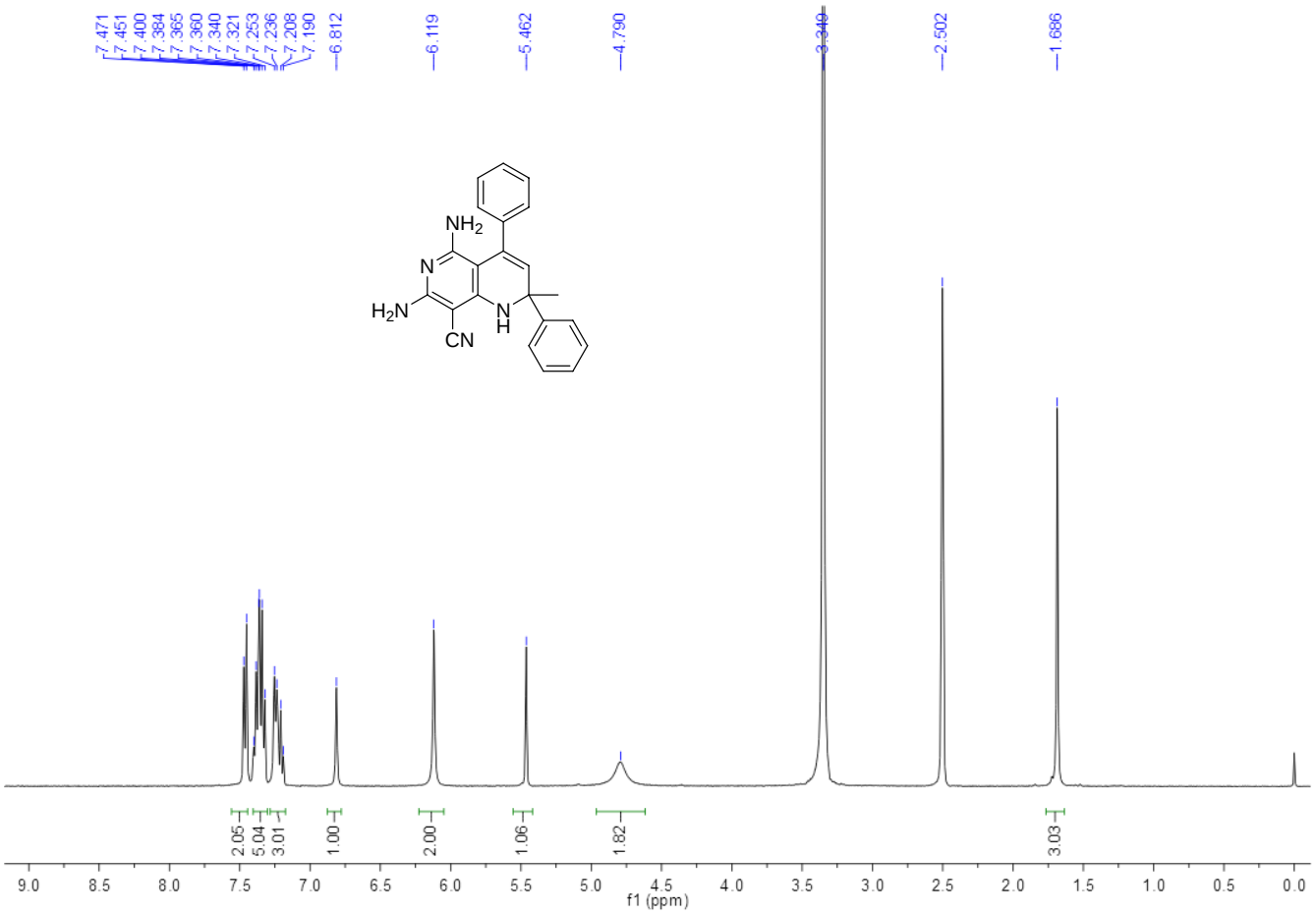
^{13}C NMR Spectrum of Compound **3q**



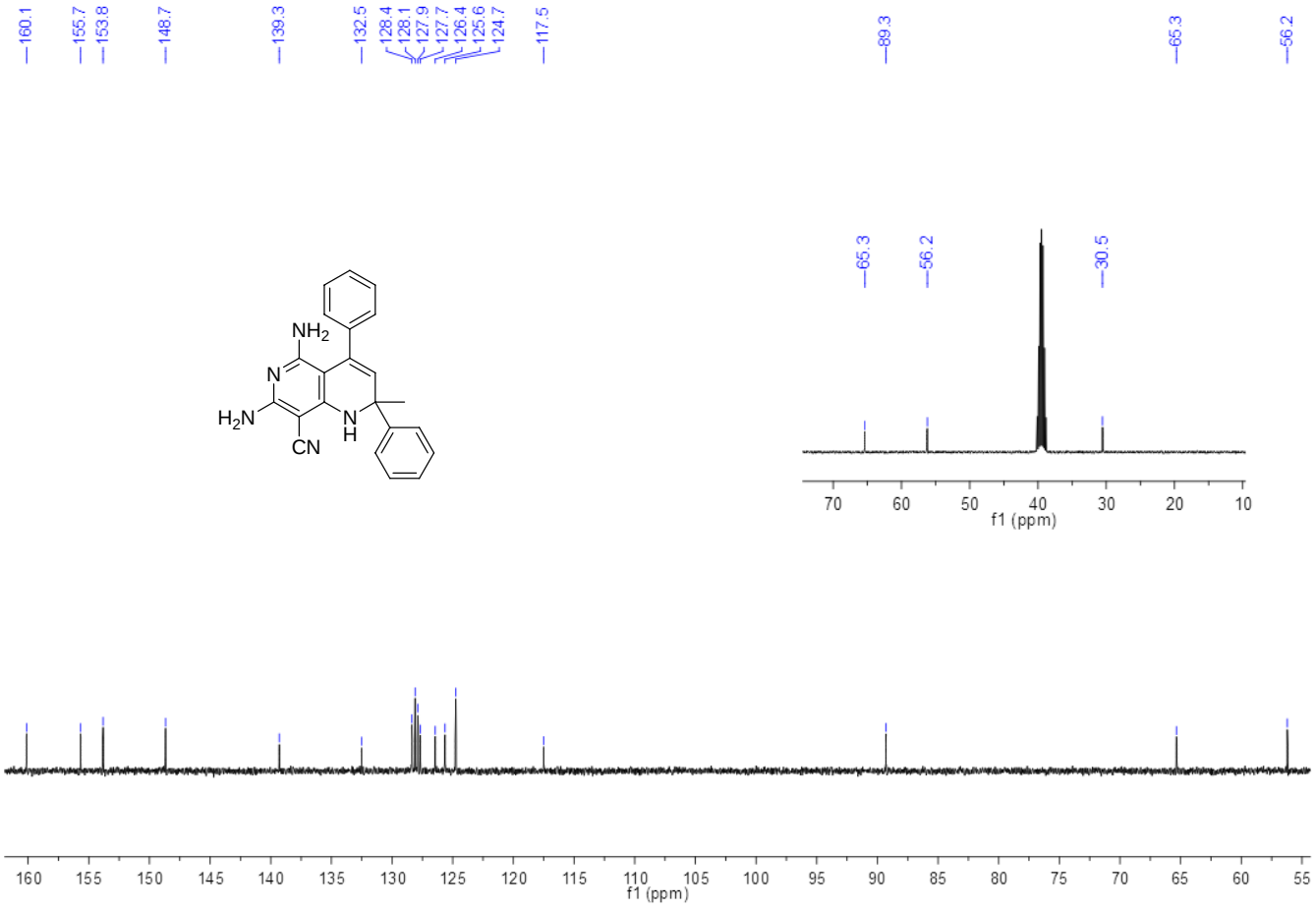
^{1}H NMR Spectrum of Compound **3r**



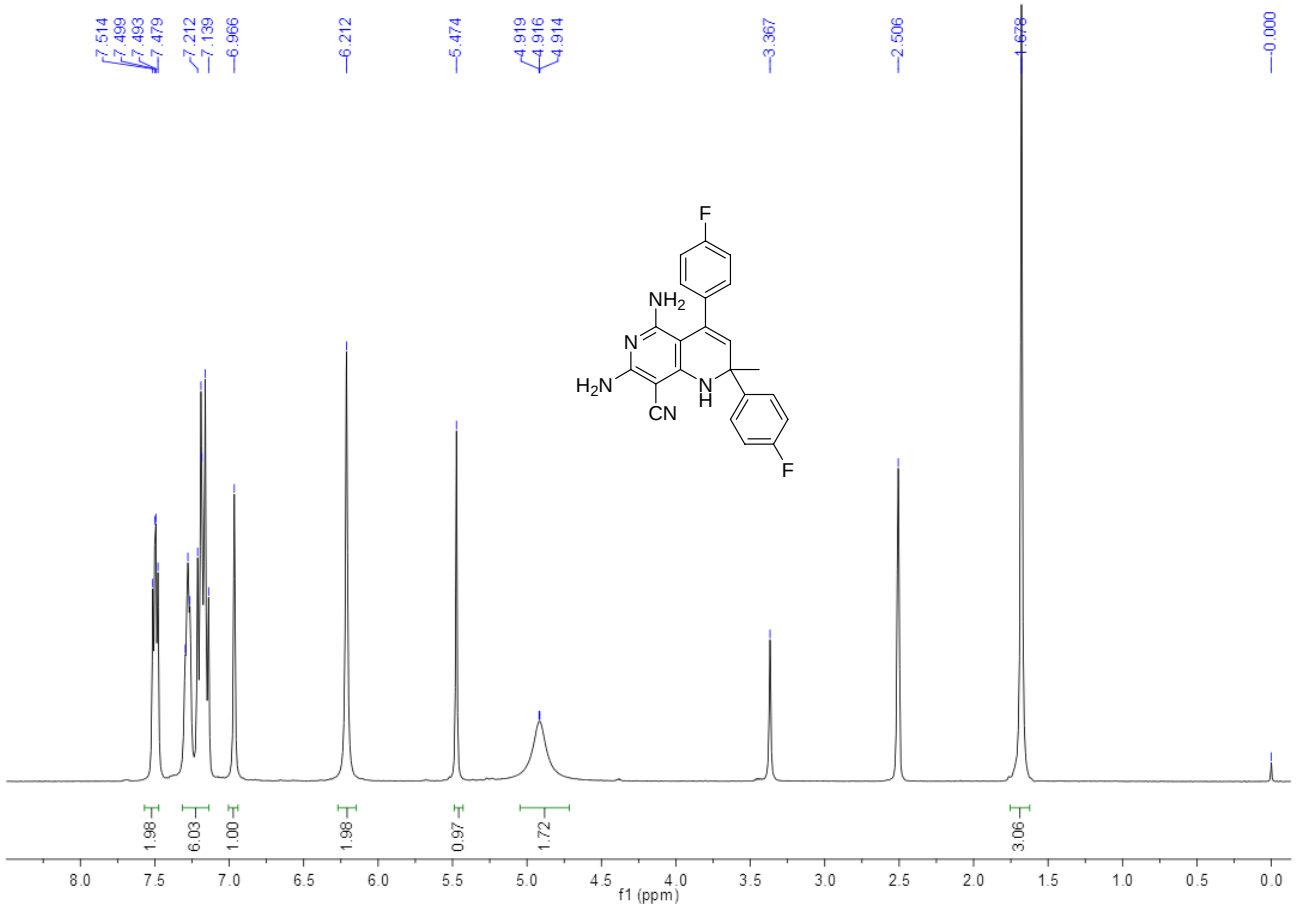
^{13}C NMR Spectrum of Compound **3r**



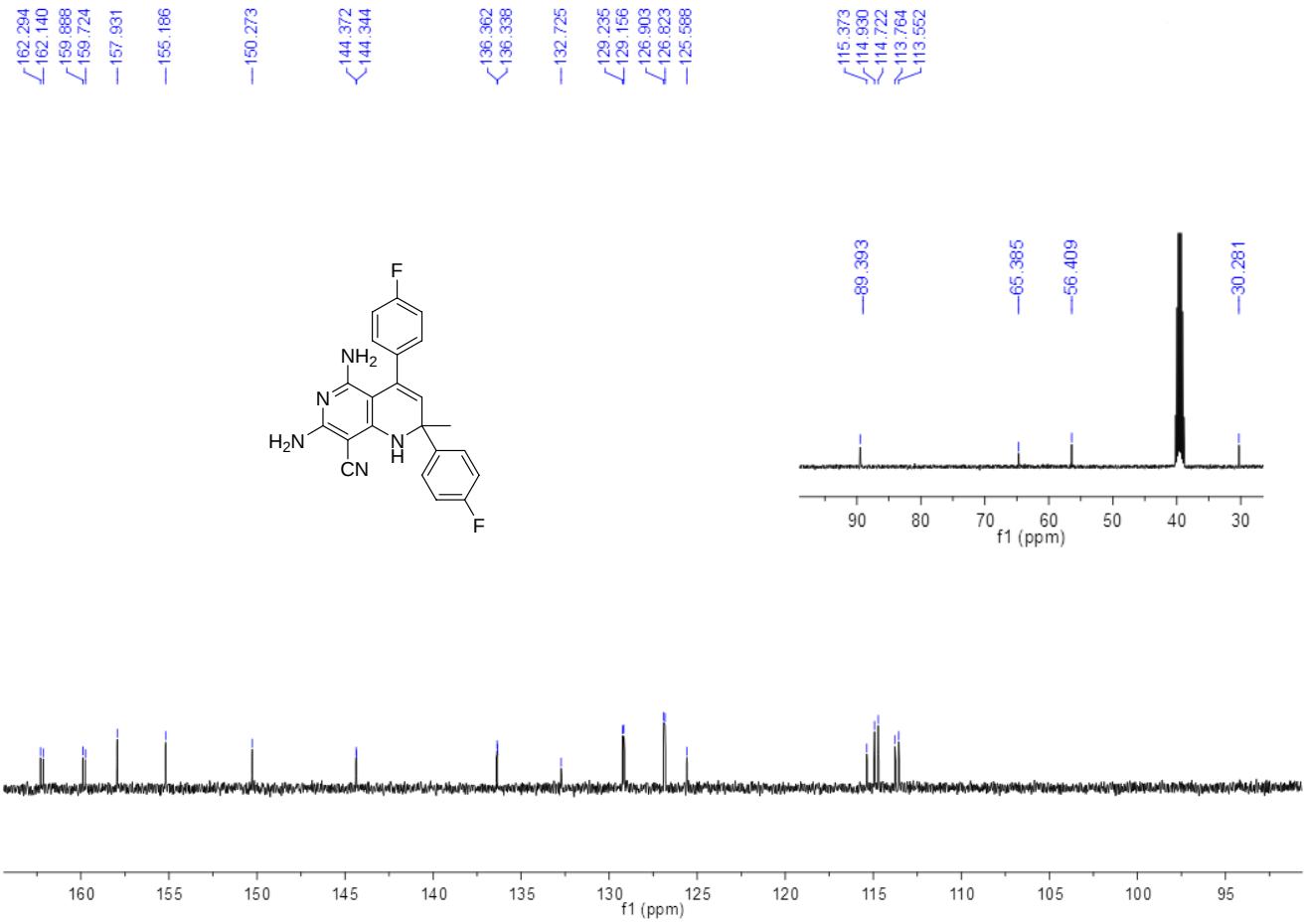
^{1}H NMR Spectrum of Compound **4a**



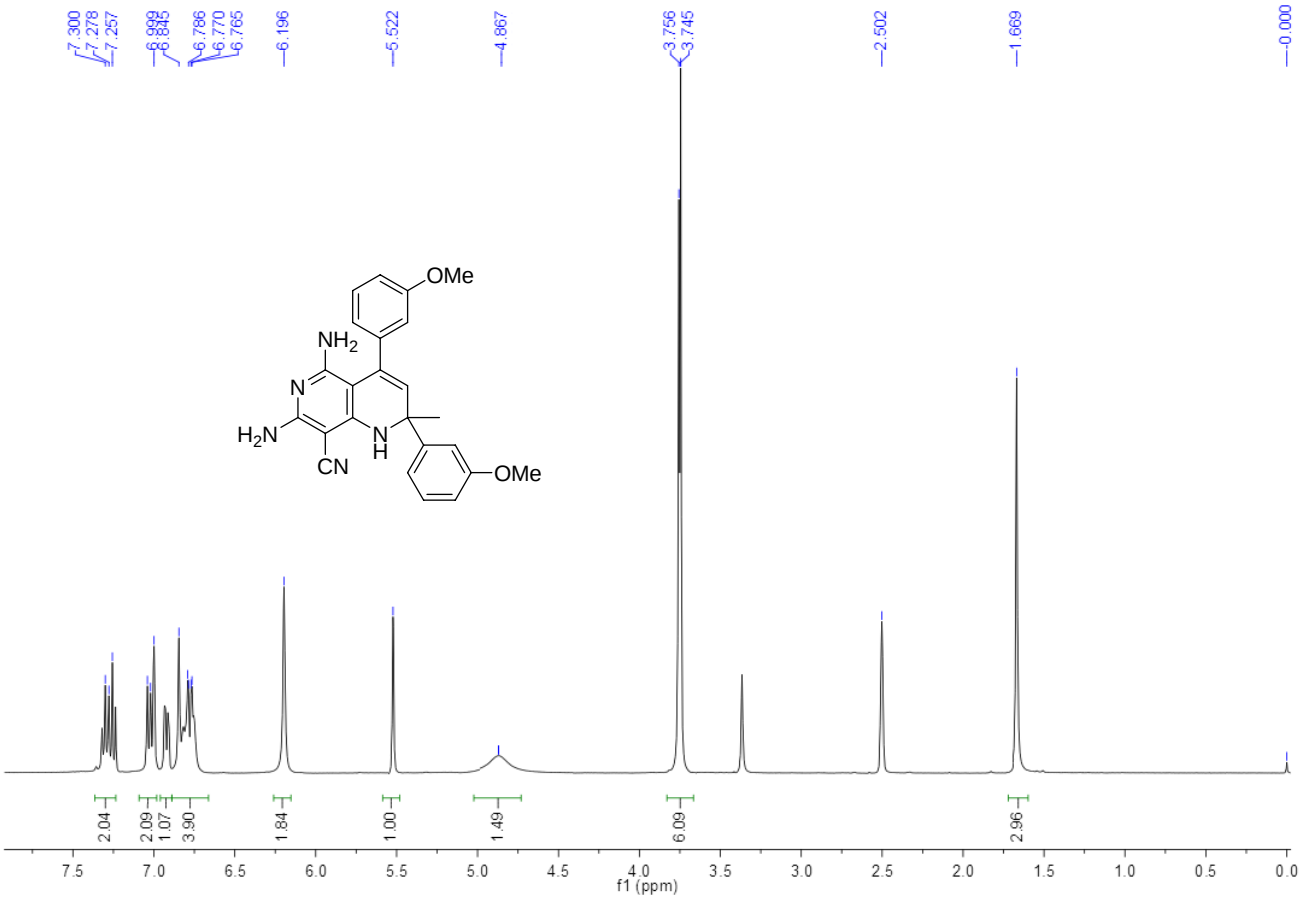
^{13}C NMR Spectrum of Compound **4a**



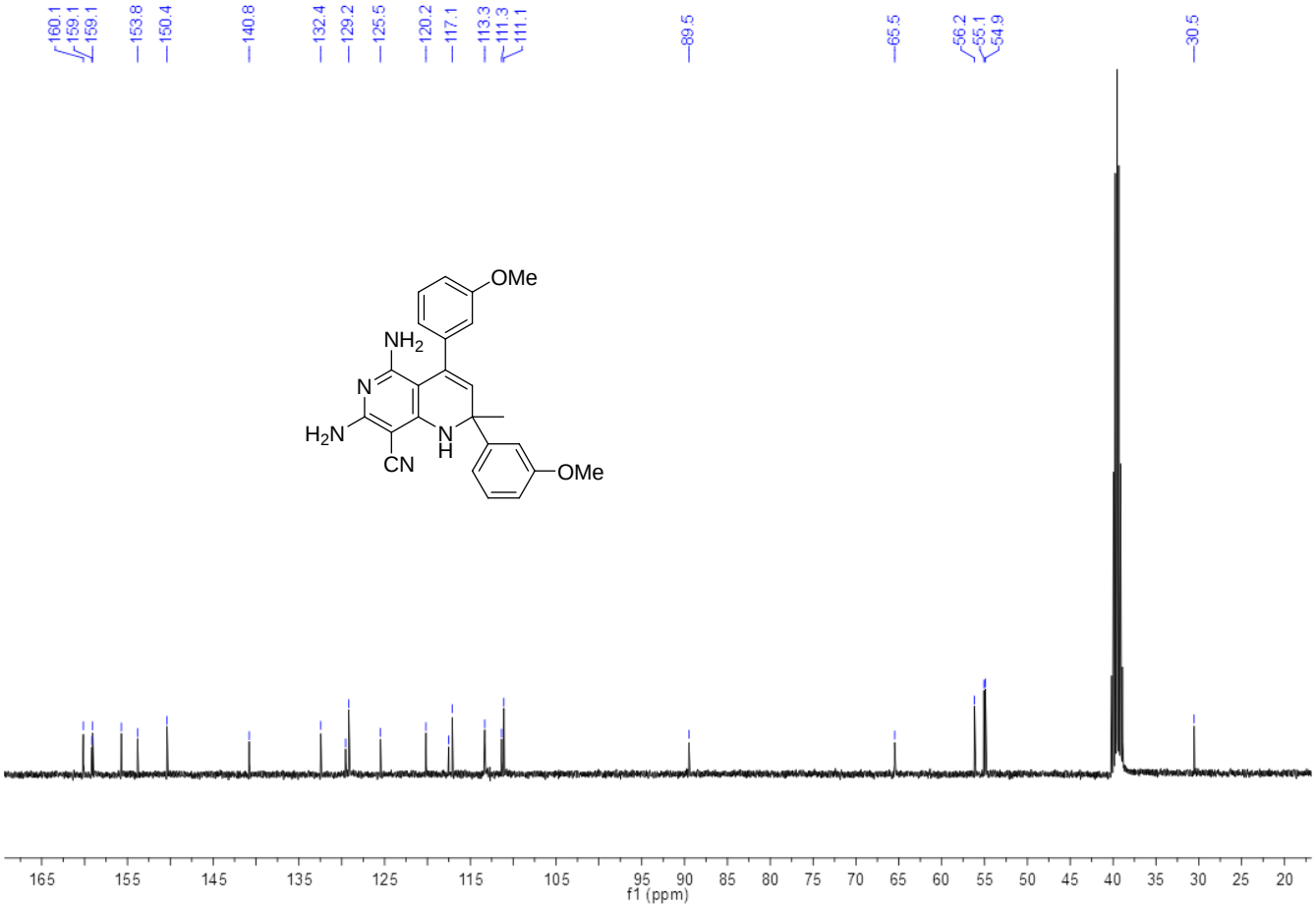
^{1}H NMR Spectrum of Compound **4b**



^{13}C NMR Spectrum of Compound **4b**



^{1}H NMR Spectrum of Compound **4c**



^{13}C NMR Spectrum of Compound **4c**