Regioselective synthesis of functionalized [1,8]naphthyridine derivatives via three-component domino reaction under catalyst-free conditions

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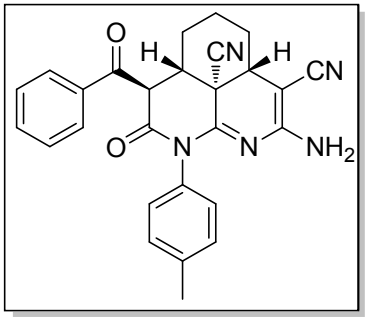
1. General methods

Melting points were measured using a XT-4 micro melting point apparatus and were uncorrected. IR spectra were recorded with a Varian F-1000 spectrometer using KBr disks; absorptions are reported as cm^{-1}. ^{1}H NMR and ^{13}C NMR spectra were obtained in DMSO-d_6 solution, using a Varian Inova 400 MHz or 300 MHz spectrometer. *J* values are reported in hertz and chemical shifts are expressed in parts per million downfield from TMS as the internal standard. HRMS analyses were carried out using a Bruker micrOTOF-Q instrument or TOF-MS instrument.

2. General procedure for the Synthesis of 4.

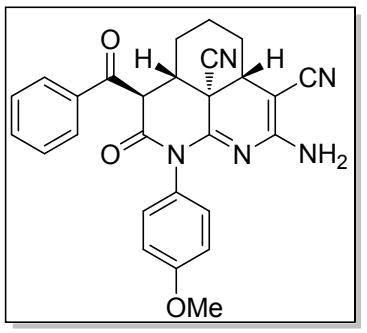
Glutaraldehyde (**1**) (1 mmol), malononitrile (**2**) (2 mmol) and *β*-ketoamides (**3**) (1 mmol) were placed in a 10 mL Initiator reactor vial, followed by EtOH (5 mL). The reaction vial was then sealed and prestirred for 10 s before being irradiated in the microwave (time, 20 min; temperature, 100 °C; absorption level, high; fixed hold time) until TLC (4:1 mixture of petroleum ether and acetone) revealed the complete consumption of the starting materials. The reaction mixture was then cooled to room temperature and diluted with cold water (20 mL) to give a precipitate, which was collected by Büchner filtration. The solid material was then purified by recrystallization from 95% EtOH to afford the desired product **4aa**.

3. Characterizations for all compounds



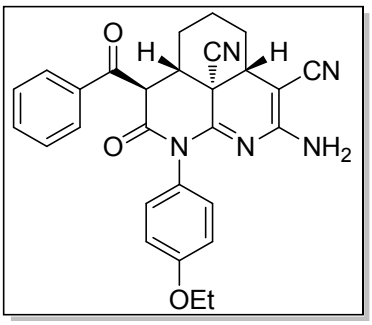
8-Amino-3-benzoyl-2-oxo-1-(*p*-tolyl)-2,3,3a,3a^1,4,5,6,6a-octahydro-1*H*-benzo[*de*][1,8]naphthyridine-3a^1,7-dicarbonitrile (4aa)

Isolated as a yellow solid; mp > 300°C; IR (KBr, ν, cm^{-1}): 3345, 2933, 2189, 1623, 1584, 1511, 1436, 1406, 1236, 1158, 1098, 897, 822, 736; 1H NMR (400 MHz, DMSO-d_6) δ_H: 8.12 (d, J = 7.6 Hz, 2H, ArH), 7.74–7.70 (m, 1H, ArH), 7.61–7.58 (m, 2H, ArH), 7.27–7.20 (m, 4H, ArH), 6.55 (s, 2H, NH_2), 5.01 (d, J = 12.8 Hz, 1H, CH), 3.19–3.13 (m, 1H, CH), 3.03–3.00 (m, 1H, CH), 2.32 (s, 3H, CH_3), 2.06–2.01 (m, 1H, CH_2), 1.87–1.84 (m, 1H, CH_2), 1.64–1.36 (m, 4H, 2 × CH_2); 13C NMR (100 MHz, DMSO-d_6) δ_C: 195.6, 168.4, 158.4, 157.1, 138.2, 137.6, 134.7, 133.5, 129.9, 129.4, 129.3, 129.0, 119.8, 115.5, 58.7, 52.8, 43.8, 38.1, 37.6, 27.3, 26.3, 23.7, 21.2; HRMS calcd for $C_{27}H_{22}N_5O_2$ [M-H]$^-$: 448.1773, found: 448.1777.



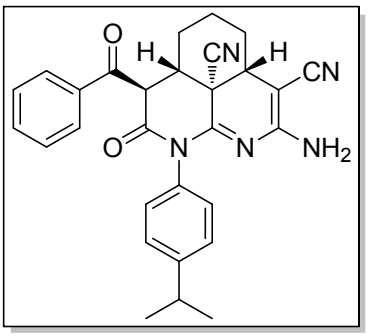
8-Amino-3-benzoyl-1-(4-methoxyphenyl)-2-oxo-2,3,3a,3a^1,4,5,6,6a-octahydro-1*H*-benzo[*de*][1,8]naphthyridine-3a^1,7-dicarbonitrile (4ab)

Isolated as a yellow solid; mp 244–246°C; IR (KBr, ν, cm^{-1}): 3323, 2958, 2184, 1628, 1547, 1503, 1421, 1338, 1332, 1253, 1203, 1050, 997, 845, 748, 731; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 8.11 (d, J = 6.6 Hz, 2H, ArH), 7.76–7.70 (m, 1H, ArH), 7.60–7.54 (m, 2H, ArH), 7.24–7.22 (m, 2H, ArH), 7.01–6.99 (m, 2H, ArH), 6.52 (s, 2H, NH_2), 4.99 (d, J = 12.4 Hz, 1H, CH), 3.77 (s, 3H, CH_3O), 3.18–3.12 (m, 1H, CH), 3.02–3.00 (m, 1H, CH), 2.06–2.03 (m, 1H, CH_2), 1.87–1.84 (m, 1H, CH_2), 1.64–1.36 (m, 4H, 2 × CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 195.6, 168.5, 159.4, 158.5, 157.3, 137.6, 134.7, 130.3, 129.4, 128.6, 119.8, 115.8, 114.6, 58.6, 55.8, 52.8, 43.8, 38.0, 37.6, 27.3, 26.3, 23.7; HRMS calcd for $C_{26}H_{22}N_5O_3$ [M-H]$^-$: 464.1723, found: 464.1739.



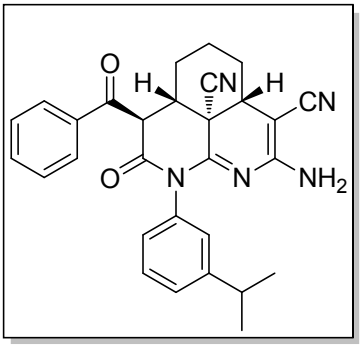
8-Amino-3-benzoyl-1-(4-ethoxyphenyl)-2-oxo-2,3,3a,3a^1,4,5,6,6a-octahydro-1*H*-benzo[*de*][1,8]naphthyridine-3a^1,7-dicarbonitrile (4ac)

Isolated as a yellow solid; mp 266–268°C; IR (KBr, ν, cm^{-1}): 3332, 2949, 2177, 1639, 1564, 1504, 1460, 1334, 1330, 1252, 1201, 1054, 996, 835, 738, 721; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 8.12–8.11 (m, 2H, ArH), 7.71 (s, 1H, ArH), 7.61–7.59 (m, 2H, ArH), 7.23–7.21 (m, 2H, ArH), 6.99–6.97 (m, 2H, ArH), 6.52 (s, 2H, NH_2), 5.00 (m, J = 12.4 Hz, 1H, CH), 4.03–4.02 (m, 2H, CH_2), 3.18–3.13 (m, 1H,CH), 3.03–3.01 (m, 1H,CH), 2.06–2.03 (m, 1H, CH_2), 1.87–1.85 (m, 1H, CH_2), 1.64–1.33 (m, 7H, 2 × CH_2 + CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 195.6, 168.5, 158.7, 158.5, 157.3, 137.6, 134.6, 130.2, 129.4, 129.3, 128.4, 119.8, 115.5, 114.9, 63.7, 58.7, 52.8, 43.8, 38.0, 37.6, 27.3, 26.3, 23.7, 15.1; HRMS calcd for $C_{28}H_{24}N_5O_3$ [M-H]$^-$: 478.1879, found: 478.1879.



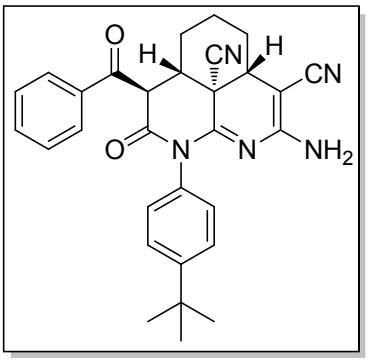
8-Amino-3-benzoyl-1-(4-isopropylphenyl)-2-oxo-2,3,3a,3a^1,4,5,6,6a-octahydro-1*H*-benzo[*de*][1,8]naphthyridine-3a^1,7-dicarbonitrile (4ad)

Isolated as a yellow solid; mp >300 °C; IR (KBr, ν, cm^{-1}): 3336, 2954, 2167, 1662, 1639, 1589, 1561, 1382, 1336, 1248, 1125, 1009, 879, 742; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 8.12–8.10 (m, 2H, ArH), 7.72–7.69 (m, 1H, ArH), 7.60–7.57 (m, 2H, ArH), 7.34–7.32 (m, 2H, ArH), 7.24–7.23 (m, 2H, ArH), 6.53 (s, 2H, NH_2), 5.00 (d, J = 12.8 Hz, 1H, CH), 3.19–3.13 (m, 1H, CH), 3.04–3.02 (m, 1H, CH), 2.94–2.90 (m, 1H, CH_2), 2.06–2.04 (m, 1H, CH_2), 1.87–1.85 (m, 1H, CH_2), 1.65–1.37 (m, 4H, 2 × CH_2), 1.21 (d, J = 6.4 Hz, 6H, 2 × CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 195.6, 168.5, 158.5, 157.2, 148.7, 137.6, 134.6, 133.8, 129.4, 129.3, 129.0, 127.2, 119.8, 115.5, 58.7, 52.9, 43.8, 38.0, 37.5, 33.5, 27.3, 26.3, 24.3, 24.2, 23.7; HRMS calcd for $C_{29}H_{26}N_5O_2$ [M-H]$^-$: 476.2087, found: 476.2069.



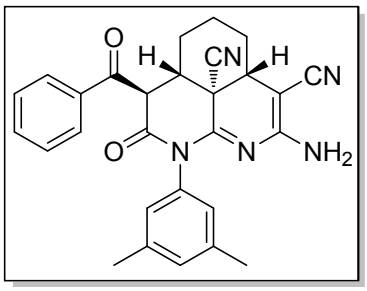
8-Amino-3-benzoyl-1-(3-isopropylphenyl)-2-oxo-2,3,3a,3a^1,4,5,6,6a-octahydro-1*H*-benzo[*de*][1,8]naphthyridine-3a^1,7-dicarbonitrile (4ae)

Isolated as a yellow solid; mp 240–242°C; IR (KBr, ν, cm^{-1}): 3332, 2941, 2130, 1651, 1637, 1557, 1505, 1463, 1385, 1335, 1252, 1204, 1103, 1044, 1015, 994, 742, 725; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 8.11 (d, J = 7.2 Hz, 2H, ArH), 7.74–7.70 (m, 1H, ArH), 7.62–7.58 (m, 2H, ArH), 7.39–7.36(m, 1H, ArH), 7.27–7.25 (m, 1H, ArH), 7.19 (s, 1H, ArH), 7.14–7.12 (m, 1H, ArH), 6.52 (s, 2H, NH_2), 5.02 (d, J = 12.8 Hz, 1H, CH), 3.21–3.14 (m, 1H, CH), 3.05–3.01 (m, 1H, CH), 2.94–2.87 (m, 1H, CH_2), 2.06–2.04 (m, 1H, CH_2), 1.88–1.85 (m, 1H, CH_2), 1.65–1.37 (m, 4H, 2 × CH_2), 1.22–1.20 (m, 6H, 2 × CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 195.6, 168.4, 158.5, 157.1, 149.6, 137.6, 136.1, 134.7, 129.4, 129.2, 126.8, 119.8, 115.5, 58.7, 52.8, 43.8, 38.0, 37.5, 33.7, 27.3, 26.3, 24.3, 24.1, 23.7; HRMS calcd for $C_{29}H_{26}N_5O_2$ [M-H]$^-$: 476.2087, found: 476.2070.



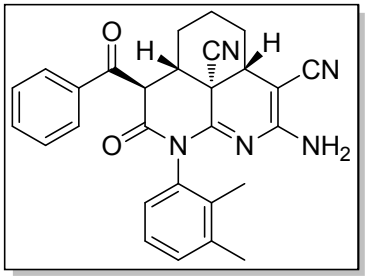
8-Amino-3-benzoyl-1-(4-(tert-butyl)phenyl)-2-oxo-2,3,3a,3a^1,4,5,6,6a-octahydro-1*H*-benzo[*de*][1,8]naphthyridine-3a^1,7-dicarbonitrile(4af)

Isolated as a yellow solid; mp > 300°C; IR (KBr, ν, cm^{-1}): 3333, 2958, 2137, 1619, 1467, 1528, 1451, 1348, 1342, 1243, 1223, 1058, 994, 843, 743, 734; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 8.12 (d, J = 7.6 Hz, 2H, ArH), 7.71 (t, J = 7.2 Hz, 1H, ArH), 7.61–7.57 (m, 2H, ArH), 7.48 (d, J = 8.7 Hz, 2H, ArH), 7.25 (d, J = 8.2 Hz, 2H, ArH), 6.54 (s, 2H, NH_2), 5.01 (d, J = 12.8 Hz, 1H, CH), 3.21–3.14 (m, 1H, CH), 3.06–3.02 (m, 1H, CH), 2.09–2.04(m, 1H, CH_2), 1.88–1.85 (m, 1H, CH_2), 1.66–1.38 (m, 4H, 2 × CH_2), 1.30 (s, 9H, 3 × CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 195.5, 168.5, 158.5, 157.2, 151.0, 137.6, 134.6, 133.5, 129.4, 129.3, 128.7, 126.2, 119.8, 115.5, 58.8, 52.9, 43.8, 38.0, 37.5, 34.9, 31.6, 27.4, 26.3, 23.7; HRMS calcd for $C_{30}H_{28}N_5O_2$ [M-H]$^-$: 490.2243, found: 490.2253.



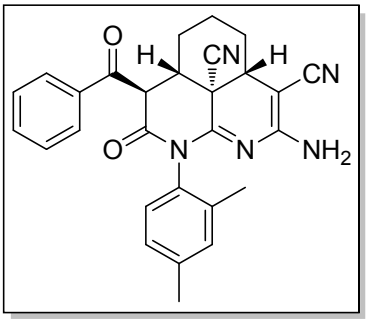
8-Amino-3-benzoyl-1-(3,5-dimethylphenyl)-2-oxo-2,3,3a,3a^1,4,5,6,6a-octahydro-1*H*-benzo[*de*][1,8]naphthyridine-3a^1,7-dicarbonitrile (4ag)

Isolated as a yellow solid; mp 228–230°C; IR (KBr, ν, cm^{-1}): 3329, 2939, 2185, 1639, 1557, 1518, 1441, 1328, 1322, 1243, 1213, 1056, 994, 843, 744, 730; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 8.11 (d, J = 6.8 Hz, 2H, ArH), 7.76–7.70 (m, 1H, ArH), 7.61–7.54 (m, 2H, ArH), 7.00 (s, 1H, ArH), 6.94 (s, 2H, ArH), 6.56 (s, 2H, NH_2), 5.01 (d, J = 12.8 Hz, 1H), 3.17–3.11(m, 1H, CH), 3.02–3.00 (m, 1H, CH), 2.28 (s, 6H, 2 × CH_3), 2.05–2.03 (m, 1H, CH_2), 1.87–1.84 (m, 1H, CH_2), 1.64–1.36 (m, 4H, 2 × CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 195.6, 168.3, 158.4, 157.1, 138.5, 137.6, 136.0, 134.7, 130.4, 129.4, 126.6, 119.8, 115.4, 58.7, 52.7, 40.4, 40.2, 40.0, 39.7, 39.5, 27.3, 26.4, 23.7, 21.20; HRMS calcd for $C_{28}H_{24}N_5O_2$ [M-H]$^-$: 462.1930, found: 462.1948.



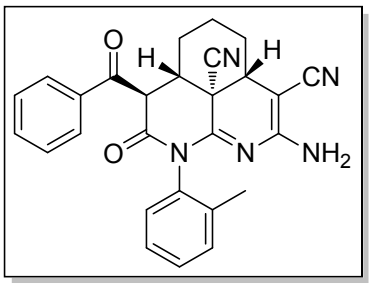
8-Amino-3-benzoyl-1-(2,3-dimethylphenyl)-2-oxo-2,3,3a,3a^1,4,5,6,6a-octahydro-1*H*-benzo[*de*][1,8]naphthyridine-3a^1,7-dicarbonitrile (4ah)

Isolated as a yellow solid; mp > 300°C; IR (KBr, ν, cm^{-1}): 3413, 3327, 2958, 2175, 1632, 1605, 1565, 1470, 1380, 1336, 1283, 1257, 1221, 1106, 933, 925, 849, 737; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 8.14 (d, J = 7.2 Hz, 2H, ArH), 7.72–7.70 (m, 1H, ArH), 7.60 (s, 2H, ArH), 7.19–7.02 (m, 3H, ArH), 6.61 (s, 2H, NH_2), 5.03–5.01 (m, 1H, CH), 3.38–3.01 (m, 2H, 2 × CH), 2.2–2.21 (m, 3H, CH_3), 2.05 (s, 1H, CH_2), 1.99–1.94 (m, 3H, CH_3), 1.84 (s, 1H, CH_2), 1.62–1.42 (m, 4H, 2 × CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 195.7, 195.5, 168.2, 167.8, 158.4, 158.3, 156.5, 156.3, 138.0, 137.9, 137.5, 137.3, 135.0, 134.9, 134.8, 133.9, 130.5, 129.6, 129.5, 129.4, 126.9, 126.6, 126.4, 119.7, 119.7, 115.4, 115.1, 58.9, 58.6, 52.9, 52.8, 43.5, 43.3, 38.7, 38.1, 27.4, 26.7, 23.7, 23.3, 20.4, 20.4, 14.0, 13.9; HRMS calcd for $C_{28}H_{24}N_5O_2$ [M-H]$^-$: 462.1930, found: 462.1958.



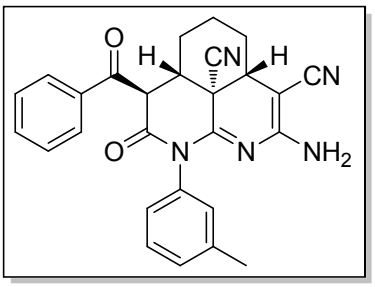
8-Amino-3-benzoyl-1-(2,4-dimethylphenyl)-2-oxo-2,3,3a,3a^1,4,5,6,6a-octahydro-1*H*-benzo[*de*][1,8]naphthyridine-3a^1,7-dicarbonitrile (4ai)

Isolated as a yellow solid; mp 296–298°C; IR (KBr, ν, cm^{-1}): 3423, 3317, 2968, 2275, 1642, 1615, 1545, 1460, 1386, 1346, 1293, 1267, 1231, 1116, 943, 925, 859, 747; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 8.13 (d, J = 6.4 Hz, 2H, ArH), 7.72–7.70 (m, 1H, ArH), 7.59 (s, 2H, ArH), 7.13–7.11 (m, 3H, ArH), 6.58 (s, 2H, NH_2), 5.11–4.98 (m, 1H, CH), 3.37–3.01 (m, 2H, 2 × CH), 2.29 (s, 3H, CH_3), 2.07 (s, 3H, CH_3), 2.00 (s, 1H, CH_2), 1.84 (s, 1H, CH_2), 1.60–1.42 (m, 4H, 2 × CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 195.8, 195.5, 168.2, 167.7, 158.3, 156.4, 156.3, 138.6, 138.5, 137.5, 137.3, 135.9, 134.9, 134.8, 132.4, 132.3, 131.8, 129.6, 129.5, 129.4, 129.1, 128.6, 127.9, 127.7, 119.7, 115.4, 115.1, 58.9, 58.6, 52.9, 52.8, 43.3, 38.2, 37.6, 27.4, 26.8, 23.6, 23.6, 21.1, 17.4, 17.2; HRMS calcd for $C_{28}H_{24}N_5O$ [M-H]$^-$: 462.1930, found: 462.1946.



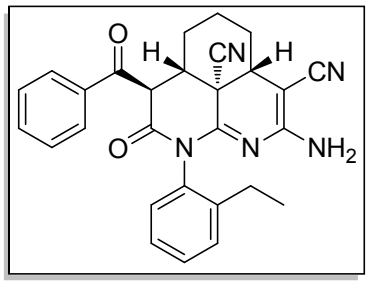
8-Amino-3-benzoyl-2-oxo-1-(*o*-tolyl)-2,3,3a,3a^1,4,5,6,6a-octahydro-1*H*-benzo[*de*][1,8]naphthyridine-3a^1,7-dicarbonitrile (4aj)

Isolated as a yellow solid; mp > 300°C; IR (KBr, ν, cm^{-1}): 3324, 2953, 2186, 1643, 1632, 1533, 1529, 1451, 1362, 1343, 1273, 1261, 1223, 1141, 994, 903, 830, 757; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 8.14-8.13 (m, 2H, ArH), 7.72–7.60 (m, 3H, ArH), 7.31–7.21 (m, 4H, ArH), 6.58 (s, 2H, NH_2), 5.13–5.00 (m, 1H, CH), 3.36–3.04 (m, 2H, 2 × CH), 2.12–2.05 (m, 4H, CH_2 + CH_3), 1.85 (s, 1H, CH_2), 1.61–1.45 (m, 4H, 2 × CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 195.7, 195.5, 168.2, 167.7, 158.3, 156.2, 137.5, 137.3, 136.3, 135.3, 135.1, 134.9, 134.8, 131.1, 131.0, 129.6, 129.5, 129.3, 128.9, 127.3, 127.1, 119.6, 115.4, 115.1, 58.9, 58.7, 52.8, 40.4, 43.2, 40.0, 39.8, 27.3, 26.7, 26.6, 23.7, 23.4, 17.4, 17.2; HRMS calcd for $C_{27}H_{222}N_5O_2$ [M-H]$^-$: 448.1773, found: 448.1771.



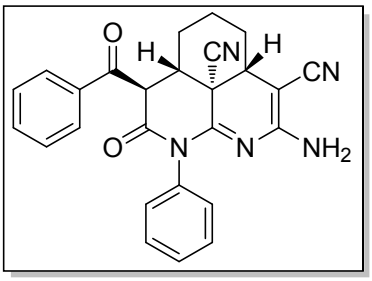
8-Amino-3-benzoyl-2-oxo-1-(*m*-tolyl)-2,3,3a,3a^1,4,5,6,6a-octahydro-1*H*-benzo[*de*][1,8]naphthyridine-3a^1,7-dicarbonitrile (4ak)

Isolated as a yellow solid; mp 256–258°C; IR (KBr, ν, cm^{-1}): 3330, 2961, 2180, 1661, 1627, 1567, 1509, 1461, 1381, 1332, 1253, 1204, 1108, 1049, 1019, 995, 742, 726; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 8.12 (d, J = 7.6 Hz, 2H, ArH), 7.74–7.70 (m, 1H, ArH), 7.62–7.56 (m, 2H, ArH), 7.37–7.33 (m, 1H, ArH), 7.20–7.12 (m, 3H, ArH), 6.53 (s, 2H, NH_2), 5.02 (d, J = 12.8 Hz, 1H), 3.19–3.14 (m, 1H, CH), 3.04–3.01 (m, 1H, CH), 2.33 (s, 3H, CH_3), 2.06–2.05 (m, 1H, CH_2), 1.88–1.85 (m, 1H, CH_2), 1.65–1.37 (m, 4H, 2 × CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 195.6, 168.3, 158.4, 157.1, 138.7, 137.6, 136.1, 134.7, 129.5, 129.4, 129.2, 126.3, 119.8, 115.4, 58.7, 52.8, 43.8, 38.1, 37.6, 27.3, 26.3, 23.7, 21.3; HRMS calcd for $C_{27}H_{22}N_5O_2$ [M-H]$^-$: 448.1773, found: 448.1767.



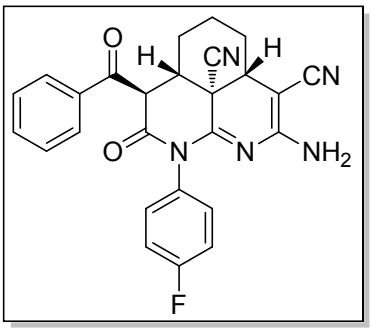
8-Amino-3-benzoyl-1-(2-ethylphenyl)-2-oxo-2,3,3a,3a^1,4,5,6,6a-octahydro-1*H*-benzo[*de*][1,8]naphthyridine-3a^1,7-dicarbonitrile (4al)

Isolated as a yellow solid; mp 293–295°C; IR (KBr, ν, cm^{-1}): 3331, 2958, 2175, 1654, 1631, 1600, 1564, 1469, 1381, 1338, 1258, 1212, 1160, 735; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 8.15–8.11 (m, 2H, ArH), 7.72–7.70 (m, 1H, ArH), 7.62–7.60 (m, 2H, ArH), 7.38–7.21 (m, 4H, ArH), 6.58–6.55 (m, 2H, NH_2), 5.15–5.00 (m, 1H, CH), 3.30–2.99 (m, 2H, 2 × CH), 2.40–2.35 (m, 1H, CH_2), 2.08 (s, 2H, CH_2), 1.85 (s, 1H, CH_2), 1.63–1.44 (m, 4H, 2 × CH_2), 1.21–1.04 (m, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 195.7, 195.4, 168.4, 167.9, 158.2, 158.1, 156.7, 141.4, 140.7, 137.5, 137.3, 134.8, 134.5, 134.3, 129.5, 129.4, 129.0, 127.3, 127.1, 119.7, 115.3, 115.1, 58.9, 58.7, 52.8, 43.5, 43.4, 38.8, 38.2, 38.0, 37.6, 31.1, 27.4, 26.8, 26.6, 23.7, 23.3, 14.5, 14.0; HRMS calcd for $C_{28}H_{23}N_5O_2$ [M-H]$^-$: 462.1930, found: 462.1955.



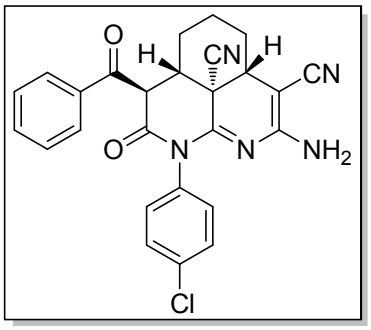
8-Amino-3-benzoyl-2-oxo-1-phenyl-2,3,3a,3a^1,4,5,6,6a-octahydro-1*H*-benzo[*de*][1,8]naphthyridine-3a^1,7-dicarbonitrile (4am)

Isolated as a yellow solid; mp > 300°C; IR (KBr, ν, cm^{-1}): 3328, 2956, 2180, 1633, 1612, 1563, 1509, 1461, 1382, 1333, 1283, 1251, 1203, 1161, 997, 908, 835, 767, 734; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 8.12 (d, J = 7.6 Hz, 2H, ArH), 7.74–7.70 (m, 1H, ArH), 7.61–7.58 (m, 2H, ArH), 7.49–7.75 (m, 2H, ArH), 7.40–7.32 (m, 3H, ArH), 6.52 (s, 2H, NH_2), 5.02 (d, J = 12.8 Hz, 1H, CH), 3.21–3.15 (m, 1H, CH), 3.04–3.02 (m, 1H, CH), 2.06–2.03 (m, 1H, CH_2), 1.88–1.85 (m, 1H, CH_2), 1.65–1.37 (m, 4H, 2 × CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 195.6, 168.4, 158.4, 157.1, 137.6, 136.2, 134.7, 129.4, 119.8, 115.5, 58.8, 52.8, 43.8, 38.1, 37.6, 27.4, 26.4, 23.8; HRMS calcd for $C_{26}H_{20}N_5O_2$ [M-H]$^-$: 434.1617, found: 434.1623.



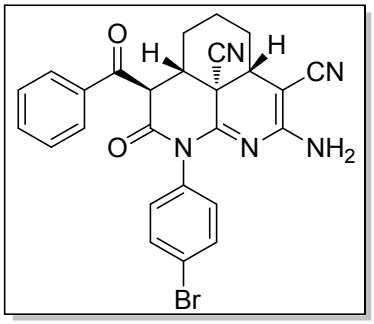
8-Amino-3-benzoyl-1-(4-fluorophenyl)-2-oxo-2,3,3a,3a^1,4,5,6,6a-octahydro-1*H*-benzo[*de*][1,8]naphthyridine-3a^1,7-dicarbonitrile (4an)

Isolated as a yellow solid; mp 279–280°C; IR (KBr, ν, cm^{-1}): 3335, 2963, 2176, 1659, 1629, 1561, 1504, 1379, 1246, 1218, 1189, 1152, 991, 842, 739; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 8.13–8.11 (m, 2H, ArH), 7.74–7.70 (m, 1H, ArH), 7.62–7.58 (m, 2H, ArH), 7.41–7.40 (m, 2H, ArH), 7.33–7.29 (m, 2H, ArH), 6.56 (s, 2H, NH_2), 5.03 (d, J = 12.8 Hz, 1H, CH), 3.22–3.16 (m, 1H, CH), 3.04–3.01 (m, 1H, CH), 2.07–2.04 (m, 1H, CH_2), 1.88–1.86 (m, 1H, CH_2), 1.66–1.37 (m, 4H, 2 × CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 195.5, 168.4, 162.1 (^1J = 243 Hz) 158.3, 157.1, 137.6, 134.7, 132.3, 131.4 (^3J = 9 Hz), 129.4, 119.7, 116.2 (^2J = 23 Hz), 115.4, 58.7, 52.8, 43.8, 38.0, 37.6, 27.3, 26.3, 23.8; HRMS calcd for $C_{26}H_{19}FN_5O_2$ [M-H]$^-$: 452.1523, found: 452.1530.



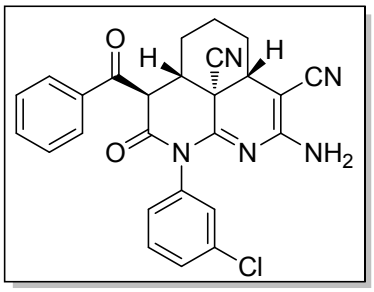
8-Amino-3-benzoyl-1-(4-chlorophenyl)-2-oxo-2,3,3a,3a^1,4,5,6,6a-octahydro-1*H*-benzo[*de*][1,8]naphthyridine-3a^1,7-dicarbonitrile (4ao)

Isolated as a yellow solid; mp 294–296°C; IR (KBr, ν, cm^{-1}): 3332, 2955, 2182, 1630, 1568, 1509, 1509, 1454, 1379, 1252, 1191, 1026, 911, 889, 755; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 8.13–8.11 (m, 2H, ArH), 7.74–7.70 (m, 1H, ArH), 7.62–7.58 (m, 2H, ArH), 7.41–7.40 (m, 2H, ArH), 7.33–7.29 (m, 2H, ArH), 6.56 (s, 2H, NH_2), 5.03 (d, J = 12.8 Hz, 1H, CH), 3.22–3.16 (m, 1H, CH), 3.04–3.01 (m, 1H, CH), 2.07–2.04 (m, 1H, CH_2), 1.88–1.86 (m, 1H, CH_2), 1.66–1.37 (m, 4H, 2 × CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 195.5, 168.3, 158.3, 156.9, 137.6, 135.1, 134.7, 133.5, 131.3, 129.4, 129.3, 119.7, 115.4, 58.7, 52.7, 43.8, 38.0, 37.7, 27.3, 26.3, 23.8; HRMS calcd for $C_{26}H_{19}ClN_5O_2$ [M-H]$^-$: 468.1227, found: 468.1227.



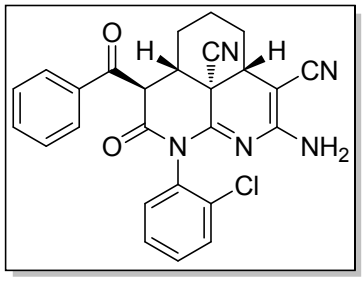
8-Amino-3-benzoyl-1-(4-bromophenyl)-2-oxo-2,3,3a,3a^1,4,5,6,6a-octahydro-1*H*-benzo[*de*][1,8]naphthyridine-3a^1,7-dicarbonitrile (4ap)

Isolated as a yellow solid; mp 288–290°C; IR (KBr, ν, cm^{-1}): 3334, 2956, 2184, 1634, 1567, 1508, 1506, 1464, 1389, 1262, 1181, 1036, 911, 886, 785; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 8.11 (d, J = 7.6 Hz, 2H, ArH), 7.73–7.67 (m, 3H, ArH), 7.61–7.57 (m, 2H, ArH), 7.34 (d, J = 8.4 Hz, 2H, ArH), 6.57 (s, 2H, NH_2), 5.02 (d, J = 12.8 Hz, 1H, CH), 3.22–3.16 (m, 1H, CH), 3.04–3.00 (m, 1H, CH), 2.08–2.04 (m, 1H, CH_2), 1.88–1.85 (m, 1H, CH_2), 1.66–1.34 (m, 4H, 2 × CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 195.5, 168.3, 158.3, 156.9, 137.6, 135.6, 134.7, 132.4, 131.6, 129.4, 122.1, 119.7, 115.4, 58.7, 52.8, 43.8, 38.0, 37.6, 27.3, 26.3, 23.8; HRMS calcd for $C_{26}H_{19}BrN_5O_2$ [M-H]$^-$: 512.0722, found: 512.0707.



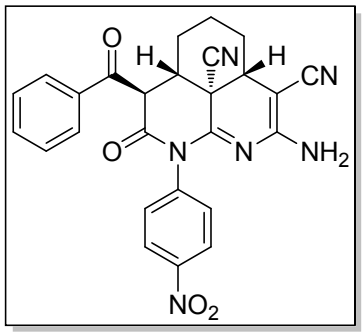
8-Amino-3-benzoyl-1-(3-chlorophenyl)-2-oxo-2,3,3a,3a^1,4,5,6,6a-octahydro-1*H*-benzo[*de*][1,8]naphthyridine-3a^1,7-dicarbonitrile (4aq)

Isolated as a yellow solid; mp 228–230°C; IR (KBr, ν, cm^{-1}): 3337, 2939, 2147, 1653, 1668, 1579, 1541, 1557, 1363, 1279, 1180, 1093, 941, 869; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 8.12 (d, J = 7.2 Hz, 2H, ArH), 7.74–7.70 (m, 1H, ArH), 7.62–7.58 (m, 3H, ArH), 7.55–7.45 (m, 2H, ArH), 7.37 (d, J = 7.4 Hz, 1H, ArH), 6.60 (s, 2H, NH_2), 5.03 (d, J = 12.8 Hz, 1H, CH), 3.20–3.19 (m, 1H, CH), 3.05–3.01 (m, 1H, CH), 2.08–2.05 (m, 1H, CH_2), 1.89–1.86 (m, 1H, CH_2), 1.67–1.38 (m, 4H, 2 × CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 195.4, 168.3, 158.3, 156.9, 137.6, 134.7, 133.4, 131.0, 129.4, 129.0, 128.4, 119.7, 115.4, 58.9, 52.7, 43.8, 38.0, 37.6, 27.3, 26.2, 23.8; HRMS calcd for $C_{26}H_{19}ClN_5O_2$ [M-H]$^-$: 468.1227, found: 468.1227.



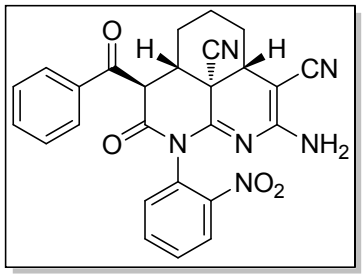
8-Amino-3-benzoyl-1-(2-chlorophenyl)-2-oxo-2,3,3a,3a^1,4,5,6,6a-octahydro-1*H*-benzo[*de*][1,8]naphthyridine-3a^1,7-dicarbonitrile (4ar)

Isolated as a yellow solid; mp > 300°C; IR (KBr, ν, cm^{-1}): 3334, 2968, 2195, 1644, 1641, 1630, 1544, 1459, 1371, 1348, 1268, 1242, 1166, 739; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 8.13–8.05 (m, 2H, ArH), 7.74–7.71 (m, 1H, ArH), 7.62–7.48 (m, 6H, ArH), 6.67–6.62 (m, 2H, NH_2), 5.31–4.88 (m, 1H, CH), 3.33–2.89 (m, 2H, 2 × CH), 2.07 (s, 1H, CH_2), 1.86 (s, 1H, CH_2), 1.69–1.48 (m, 4H, 2 × CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 195.1, 194.9, 167.9, 167.2, 158.1, 158.0, 156.1, 156.0, 132.1, 131.2, 131.1, 129.6, 129.4, 129.3, 119.6, 115.1, 115.0, 59.0, 58.9, 52.8, 52.7, 43.6, 43.4, 37.6, 27.3, 26.6, 26.3, 23.7, 23.4; HRMS calcd for $C_{26}H_{19}ClN_5O_2$ [M-H]$^-$: 468.1227, found: 468.1226.



8-Amino-3-benzoyl-1-(4-nitrophenyl)-2-oxo-2,3,3a,3a^1,4,5,6,6a-octahydro-1*H*-benzo[*de*][1,8]naphthyridine-3a^1,7-dicarbonitrile (4as)

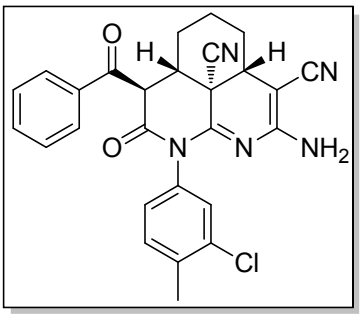
Isolated as a yellow solid; mp > 300°C; IR (KBr, ν, cm^{-1}): 3327, 2929, 2167, 1663, 1638, 1589, 1561, 1507, 1383, 1249, 1110, 1043, 921, 879; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 8.39 (d, J = 9.2 Hz, 2H, ArH), 8.14 (d, J = 7.6 Hz, 2H, ArH), 7.75–7.72 (m, 3H, ArH), 7.62–7.59 (m, 2H, ArH), 6.59 (s, 2H, NH_2), 5.10 (d, J = 12.8 Hz, 1H, CH), 3.30–3.23 (m, 1H, CH), 3.08–3.04 (m, 1H, CH), 2.09–2.07 (m, 1H, CH_2), 1.91–1.88 (m, 1H, CH_2), 1.69–1.40 (m, 4H, 2 × CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 195.3, 168.3, 158.1, 156.8, 147.7, 142.3, 137.6, 134.7, 131.2, 129.4, 124.7, 119.7, 115.3, 59.0, 52.8, 43.8, 38.0, 37.6, 27.2, 26.2, 23.9; HRMS calcd for $C_{26}H_{19}N_6O_4$ [M-H]$^-$: 479.1468, found: 479.1475.



8-Amino-3-benzoyl-1-(2-nitrophenyl)-2-oxo-2,3,3a,3a^1,4,5,6,6a-octahydro-1*H*-benzo[*de*][1,8]naphthyridine-3a^1,7-dicarbonitrile (4at)

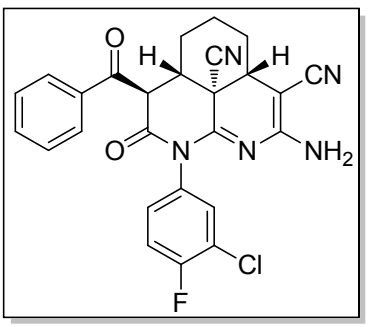
Isolated as a yellow solid; mp > 300°C; IR (KBr, ν, cm^{-1}): 3349, 2960, 2172, 1657, 1628, 1558, 1490, 1457, 1378, 1334, 1278, 1247, 1202, 1188, 1045, 764, 732, 696; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 8.34–8.23 (m, 1H, ArH), 8.11 (d, J = 7.3 Hz, 1H, ArH), 8.01–7.95 (m, 2H, ArH), 7.76–7.69 (m, 3H, ArH), 7.63–7.59 (m, 2H, ArH), 6.68–6.60 (m, 2H, NH_2), 5.16–4.80 (m, 1H, CH), 3.17–2.79 (m, 2H, 2 × CH), 2.07–2.06 (m, 1H, CH_2), 1.88 (s, 1H, CH_2), 1.70–1.46 (m, 4H, 2 × CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 194.8, 194.7, 168.0, 167.8, 157.8, 156.3, 145.4, 144.8, 137.4, 137.0, 136.0, 135.8, 135.0, 132.5, 132.3, 131.3, 131.1,

129.7, 129.5, 129.5, 129.4, 126.3, 126.0, 119.5, 119.4, 114.8, 114.6, 59.0, 58.9, 53.1, 43.5, 43.4, 37.7, 37.5, 27.1, 26.4, 23.7, 23.5; HRMS calcd for $C_{26}H_{19}N_6O_4$ [M-H]$^-$: 479.1468, found: 479.1450.



8-Amino-3-benzoyl-1-(3-chloro-4-methylphenyl)-2-oxo-2,3,3a,3a^1,4,5,6,6a-octahydro-1*H*-benzo[*de*][1,8]naphthyridine-3a^1,7-dicarbonitrile (4au)

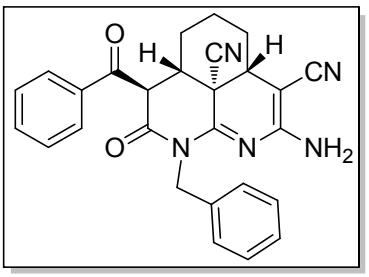
Isolated as a yellow solid; mp 278–280°C; IR (KBr, ν, cm^{-1}): 3333, 2853, 2267, 1561, 1436, 1397, 1241, 1183, 1035, 949, 739, 690; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 8.12 (d, J = 7.6 Hz, 2H, ArH), 7.74–7.71 (m, 1H, ArH), 7.63–7.59 (m, 2H, ArH), 7.54 (s, 1H, ArH), 7.46 (d, J = 8.1 Hz, 1H, ArH), 7.26 (d, J = 7.7 Hz, 1H, ArH), 6.59 (s, 2H, NH_2), 5.01 (d, J = 12.8 Hz, 1H, CH), 3.21–3.18 (m, 1H, CH), 3.03–3.00 (m, 1H, CH), 2.35 (s, 3H, CH_3), 2.07–2.04(m, 1H, CH_2), 1.89–1.86 (m, 1H, CH_2), 1.66–1.37 (m, 4H, 2 × CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 195.4, 168.3, 158.3, 157.0, 137.6, 136.2, 135.1, 134.7, 133.4, 131.8, 129.5, 129.4, 129.3, 119.7, 115.4, 58.8, 52.7, 40.6, 40.4, 40.2, 40.0, 39.8, 27.3 26.2, 23.8, 19.8; HRMS calcd for $C_{27}H_{21}ClN_5O_2$ [M-H]$^-$: 482.1384, found: 482.1377.



8-Amino-3-benzoyl-1-(3-chloro-4-fluorophenyl)-2-oxo-2,3,3a,3a^1,4,5,6,6a-octahydro-1*H*-benzo[*de*][1,8]naphthyridine-3a^1,7-dicarbonitrile (4av)

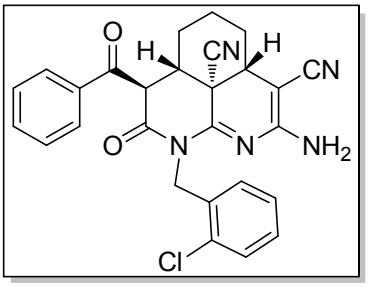
Isolated as a yellow solid; mp 264–266°C; IR (KBr, ν, cm^{-1}): 3323, 2954, 2165, 1666, 1635, 1604, 1563, 1382, 1331, 1245, 1124, 1072, 1016, 875, 734; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 8.11 (d, J = 7.6 Hz, 2H, ArH), 7.76–7.70 (m, 2H, ArH), 7.62–7.41 (m, 4H, ArH), 6.62 (s, 2H, NH_2), 5.01 (d, J = 12.8 Hz, 1H, CH), 3.21–3.16 (m, 1H, CH), 3.02–2.99 (m, 1H, CH), 2.08–2.05 (m, 1H, CH_2), 1.90–1.87 (m, 1H, CH_2), 1.67–1.38 (m, 4H, 2 ×

CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 195.3, 168.3, 158.2, 157.2 (^1J = 246 Hz), 156.9, 137.6, 134.7, 133.1, 133.0, 131.6, 130.5 (^3J = 8 Hz), 129.4, 129.3, 120.0 (^2J = 19 Hz), 119.7, 117.6 (^2J = 22 Hz), 115.3, 58.8, 52.7, 43.8, 37.9, 37.6, 27.2, 26.2, 23.9; HRMS calcd for $C_{26}H_{18}ClFN_5O_2$ [M-H]$^-$: 486.1133, found: 486.1126.



8-Amino-3-benzoyl-1-benzyl-2-oxo-2,3,3a,3a^1,4,5,6,6a-octahydro-1*H*-benzo[*de*][1,8]naphthyridine-3a^1,7-dicarbonitrile (4aw)

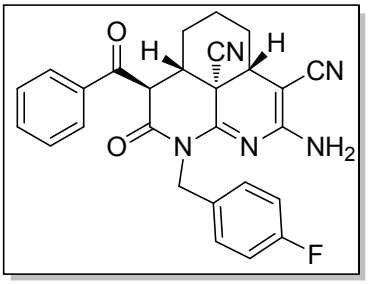
Isolated as a yellow solid; mp > 300°C; IR (KBr, ν, cm^{-1}): 3338, 2962, 2179, 1680, 1647, 1622, 1553, 1361, 1345, 1259, 1136, 1063, 1027, 868, 734; ^1H NMR (400 MHz, DMSO-d_6) δ_H: 8.08 (d, J = 7.6 Hz, 2H), 7.74–7.70 (m, 1H), 7.60–7.56 (m, 2H), 7.33–7.20 (m, 5H), 6.87 (s, 2H, NH_2), 5.17–5.07 (m, 2H, CH_2), 4.89 (d, J = 12.8 Hz, 1H), 2.97–2.90 (m Hz, 2H, 2 × CH), 2.02–1.99 (m, 1H, CH_2), 1.80–1.77 (m, 1H, CH_2), 1.54–1.34 (m, 4H, 2 × CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 195.8, 168.1, 158.1, 155.8, 137.3, 136.7, 134.8, 129.5, 129.4, 128.8, 128.3, 127.7, 119.7, 115.1, 58.6, 52.5, 44.9 , 43.2, 38.1, 37.4, 27.3, 26.7, 23.4; HRMS calcd for $C_{27}H_{22}N_5O_2$ [M-H]$^-$: 448.1773, found: 448.1773.



8-Amino-3-benzoyl-1-(2-chlorobenzyl)-2-oxo-2,3,3a,3a^1,4,5,6,6a-octahydro-1*H*-benzo[*de*][1,8]naphthyridine-3a^1,7-dicarbonitrile (4ax)

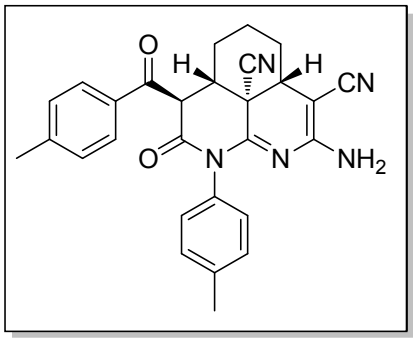
Isolated as a yellow solid; mp 258–260°C; IR (KBr, ν, cm^{-1}): 3332, 2955, 2166, 1665, 1644, 1593, 1563, 1487, 1369, 1344, 1159, 1031, 1000, 922, 736; ^1H NMR (400 MHz, DMSO-d_6) δ_H: 8.10–8.03 (m, 2H, ArH), 7.72–7.71 (m, 1H, ArH), 7.64–7.52 (m, 2H, ArH), 7.51–7.40 (m, 1H, ArH), 7.38–7.24 (m, 2H, ArH), 7.13–7.08 (m, 1H, ArH), 6.79 (s, 2H, NH_2), 5.24–5.20 (m, 2H, CH_2), 4.97 (d, J = 12.0 Hz, 1H), 3.12–3.06 (m, 2H, 2 × CH), 2.03 (s, 1H, CH_2), 1.83 (s, 1H, CH_2), 1.59–1.36 (m, 4H, 2 × CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 195.6, 168.1, 158.0, 155.9, 137.4, 134.8, 133.5, 132.0, 129.7, 129.5, 129.4, 129.1, 127.9, 127.1, 119.6,

115.1, 58.8, 52.5, 43.3, 43.1, 38.1, 37.7, 27.3, 26.6, 23.5; HRMS calcd for $C_{27}H_{21}ClN_5O$ [M-H]$^-$: 482.1384, found: 482.1384



8-Amino-3-benzoyl-1-(4-fluorobenzyl)-2-oxo-2,3,3a,3a^1,4,5,6,6a-octahydro-1*H*-benzo[*de*][1,8]naphthyridine-3a^1,7-dicarbonitrile (4ay)

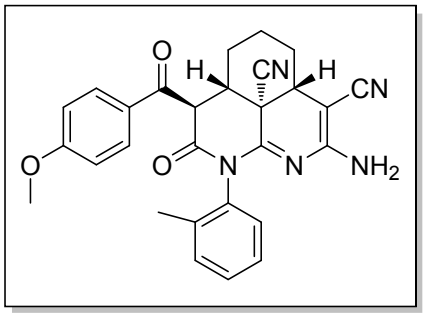
Isolated as a yellow solid; mp 268–270°C; IR (KBr, ν, cm^{-1}): 3334, 2935, 2177, 1663, 1635, 1595, 1566, 1505, 1388, 1249, 1225, 1024, 876, 745; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 8.09 (d, J = 7.6 Hz, 2H, ArH), 7.74–7.70 (m, 1H, ArH), 7.60–7.56 (m, 2H, ArH), 7.44–7.40 (m, 2H, ArH), 7.15–7.11 (m, 2H, ArH), 6.90 (s, 2H, NH_2), 5.13–5.04 (m, 2H, CH_2), 4.89 (d, J = 12.8 Hz, 1H), 2.95–2.89 (m, 2H, 2 × CH), 2.02–2.00 (m, 1H, CH_2), 1.80–1.77 (m, 1H, CH_2), 1.52–1.30 (m, 4H, 2 × CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 195.8, 168.2, 161.9 (^1J = 242 Hz), 158.1, 155.7, 137.4, 134.8, 132.9, 132.8, 131.0 (^3J = 8 Hz), 129.5, 129.4, 119.7, 115.5 (^2J = 21 Hz), 115.1, 58.6, 52.5, 44.3, 43.2, 38.1, 37.7, 27.2, 26.6, 23.4; HRMS calcd for $C_{27}H_{21}FN_5O_2$ [M-H]$^-$: 466.1679, found: 466.1680.



8-Amino-3-(4-methylbenzoyl)-2-oxo-1-(*p*-tolyl)-2,3,3a,3a^1,4,5,6,6a-octahydro-*1H*-benzo[*de*][1,8]naphthyridine-3a^1,7-dicarbonitrile (4ba)

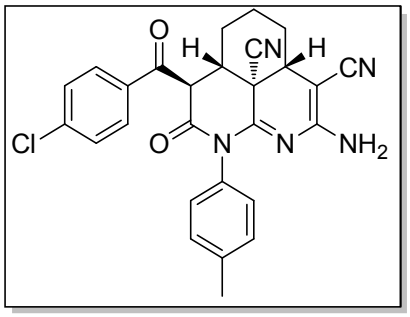
Isolated as a yellow solid; mp 236–237°C; IR (KBr, ν, cm^{-1}): 3463, 3322, 2947, 2863, 2185, 1721, 1669, 1600, 1560, 1511, 1374, 1268, 1183, 1014, 759; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 8.01 (d, J = 8.0 Hz, 2H, ArH), 7.39 (d, J = 8.0 Hz, 2H, ArH), 7.23–7.18 (m, 4H, ArH), 6.53 (s, 2H, NH_2), 4.96 (d, J = 12.8 Hz, 1H, CH), 3.17–3.10 (m, 1H, CH), 3.03–2.99 (m, 1H, CH), 2.40 (s, 3H, CH_3), 2.33 (s, 3H, CH_3), 2.05–2.02 (m, 1H, CH_2), 1.86–1.83 (m, 1H, CH_2), 1.61–1.34 (m, 4H, 2 × CH_2); ^{13}C NMR (100 MHz, DMSO-

d_6) δ_C: 195.0, 168.4, 158.5, 157.2, 145.4, 138.2, 135.2, 133.6, 130.0, 129.9, 129.6, 129.0, 119.8, 115.5, 58.7, 52.7, 43.8, 38.1, 37.6, 27.3, 26.4, 23.7, 21.7, 21.2; HRMS calcd for $C_{28}H_{24}N_5O_2$ [M-H]$^-$: 462.1930, found: 462.1911.



8-Amino-3-(4-methoxybenzoyl)-2-oxo-1-(*o*-tolyl)-2,3,3a,3a^1,4,5,6,6a-octahydro-*1H*-benzo[*de*][1,8]naphthyridine-3a^1,7-dicarbonitrile(4bb)

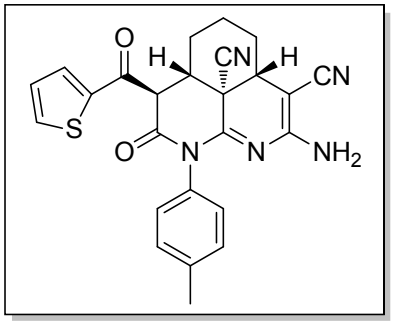
Isolated as a yellow solid; mp 250–252°C; IR (KBr, ν, cm^{-1}): 3406, 2939, 2864, 2180, 1712, 1664, 1622, 1559, 1462, 1373, 1173, 1083, 840, 754; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 8.11 (d, J = 8.8 Hz, 2H, ArH), 7.34–7.17 (m, 4H, ArH), 7.12–7.08 (m, 2H, ArH), 6.58–6.57 (m, 2H, NH_2), 5.05–4.92 (m, 1H, CH), 3.87 (s, 3H, OCH_3), 3.22–2.94 (m, 2H, 2 × CH), 2.10–2.04 (m, 4H, CH_3 + CH_2), 1.86–1.83 (m, 1H, CH_2), 1.61–1.38 (m, 4H, 2 × CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 193.7, 193.5, 168.2, 167.8, 164.6, 164.5, 158.3, 158.2, 156.4, 156.3, 136.3, 135.3, 135.1, 135.0, 132.2, 132.1, 131.1, 131.0, 130.6, 130.4, 129.4, 129.3, 128.8, 127.3, 127.1, 119.7, 115.4, 115.2, 114.7, 58.8, 58.7, 56.2, 56.1, 43.4, 43.3, 38.2, 37.6, 27.4, 23.7, 23.4, 17.4, 17.2; HRMS calcd for $C_{28}H_{24}N_5O_3$ [M-H]$^-$: 478.1879, found: 478.1852.



8-Amino-3-(4-chlorobenzoyl)-2-oxo-1-(*p*-tolyl)-2,3,3a,3a^1,4,5,6,6a-octahydro-*1H*-benzo[*de*][1,8]naphthyridine-3a^1,7-dicarbonitrile (4bc)

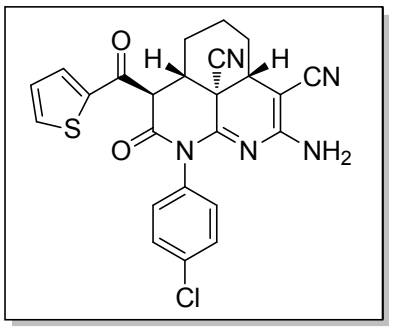
Isolated as a yellow solid; mp 213–215°C; IR (KBr, ν, cm^{-1}): 3469, 3317, 2947, 2855, 2188, 1721, 1673, 1559, 1511, 1401, 1323, 1260, 1213, 1094, 1011, 866, 795; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 8.15 (d, J = 8.8 Hz, 2H, ArH), 7.67 (d, J = 8.8 Hz, 2H, ArH), 7.27–7.19 (m, 4H, ArH), 6.54 (s, 2H, NH_2), 5.01 (d, J = 12.8 Hz, 1H, CH), 3.19–3.13 (m, 1H, CH), 3.03–3.00 (m, 1H, CH), 2.32 (s, 3H, CH_3), 2.06–2.03 (m, 1H, CH_2), 1.88–1.85 (m, 1H, CH_2), 1.66–1.36 (m, 4H, 2 × CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 194.6, 168.4, 158.4, 157.1, 139.7, 138.2, 136.2, 133.5, 131.4, 129.9, 129.5, 128.9,

119.8, 115.4, 58.7, 52.8, 43.7, 37.9, 37.6, 27.3, 26.3, 23.7, 21.2; HRMS calcd for $C_{27}H_{21}ClN_5O_2$ $[M-H]^-$: 482.1384, found: 482.1395.



8-Amino-2-oxo-3-(thiophene-2-carbonyl)-1-(*p*-tolyl)-2,3,3a,3a^1,4,5,6,6a-octahydro-*1H*-benzo[*de*][1,8]naphthyridine-3a^1,7-dicarbonitrile (4bd)

Isolated as a yellow solid; mp 288–290°C; IR (KBr, ν, cm^{-1}): 3462, 3345, 2933, 2849, 2189, 1719, 1644, 1532, 1468, 1436, 1391, 1257, 1164, 1086, 880, 772; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 8.26–8.24 (m, 1H, ArH), 8.16–8.14 (m, 1H, ArH), 7.35–8.32 (m, 1H, ArH), 7.28–7.16 (m, 4H, ArH), 6.53 (s, 2H, NH_2), 4.87 (d, J = 12.0 Hz, 1H, CH), 3.16–3.10 (m, 1H, CH), 3.03–2.99 (m, 1H, CH), 2.33 (s, 3H, CH_3), 2.05–2.03 (m, 1H, CH_2), 1.88–1.85 (m, 1H, CH_2), 1.61–1.38 (m, 4H, 2 × CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 187.7, 168.0, 158.4, 157.1, 138.2, 137.8, 136.6, 133.6, 130.0, 129.8, 128.9, 119.8, 115.4, 58.7, 43.8, 38.0, 37.6, 27.3, 26.4, 23.7, 21.2; HRMS calcd for $C_{25}H_{21}N_5NaO_2S$ $[M+Na]^+$: 478.1314, found: 478.1316.



8-Amino-1-(4-chlorophenyl)-2-oxo-3-(thiophene-2-carbonyl)-2,3,3a,3a^1,4,5,6,6a-octahydro-*1H*-benzo[*de*][1,8]naphthyridine-3a^1,7-dicarbonitrile (4be)

Isolated as a yellow solid; mp >300°C; IR (KBr, ν, cm^{-1}): 3472, 3349, 2941, 2857, 2174, 1720, 1652, 1488, 1411, 1316, 1269, 1089, 811, 770; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 8.24–8.15 (m, 2H, ArH), 7.57–7.55 (m, 2H, ArH), 7.39–7.33 (m, 3H, ArH), 6.59 (s, 2H, NH_2), 4.89 (d, J = 10.4 Hz, 1H, CH), 3.19–3.13 (m, 1H, CH), 3.02–2.99 (m, 1H, CH), 2.07–2.04 (m, 1H, CH_2), 1.89–1.87 (m, 1H, CH_2), 1.67–1.40 (m, 4H, 2 × CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 187.5, 167.9, 158.3, 156.9, 137.8, 136.5, 135.1, 133.5, 131.2, 129.8, 129.5, 119.8, 115.3, 58.7, 43.7, 37.9, 37.6, 27.3, 26.3, 23.8; HRMS calcd for $C_{24}H_{15}ClN_5O_2S$ $[M-H]^-$: 474.0791, found: 474.0764.

4. Crystal Date

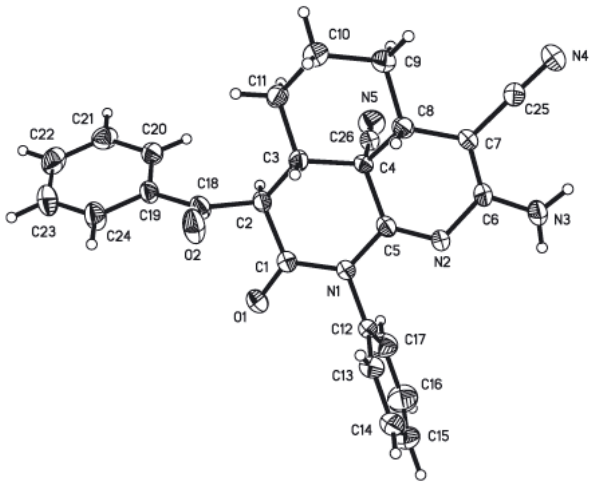


Figure 1. The Crystal Structure of **4am**

Table 1 Crystallographic Data of Compound **4am**

Empirical formula	$C_{26}H_{21}N_5O_2$
Formula weight	435.48
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
space group	P-1
Unit cell dimensions	a =9.1187(9) Å α = 66.3090(10) ° b = 10.8390(10) Å β = 88.214(2) ° c = 12.4287(11) Å γ = 81.725(2) °
Volume	112.70(18)Å^3
Z	3
Calculated density	21.3000 Mg/m^3
Absorption coefficient	0.085 mm^{-1}
F(000)	456
Crystal size	0.31 × 0.17 × 0.13 mm
Theta range for data collection	2.84 to 25.02°
Limiting indices	-10≤h≤10, -12≤k≤11, -14≤l≤14
Reflections collected	4834
Independent reflections	3921 [R(int) = 0.0382]
Data / restraints / parameters	2921 / 0 / 299
Goodness-of-fit on F^2	1.032
Final R indices [I>2σ(I)]	R_1 = 0.0595, wR_2 = 0.0957
R indices (all data)	R_1 = 0.1342, wR_2 = 0.1339
Largest diff. peak and hole	0.218 and -0.205 e. Å^{-3}

Table 2 Selected Bond Lengths (Å) of Compound **4am**

Bond	Bond Lengths	Bond	Bond Lengths
N(1)-C(5)	1.393(3)	C(3)-C(11)	1.526(4)
N(1)-C(1)	1.401(4)	C(3)-C(4)	1.530(4)
N(2)-C(12)	1.463(4)	C(4)-C(26)	1.487(4)
N(2)-C(5)	1.276(3)	C(4)-C(5)	1.520(4)
N(2)-C(6)	1.415(4)	C(4)-C(8)	1.541(4)
N(3)-C(6)	1.342(4)	C(6)-C(7)	1.360(4)
N(4)-C(25)	1.153(4)	C(7)-C(25)	1.416(4)
N(5)-C(26)	1.140(4)	C(7)-C(8)	1.500(4)
O(1)-C(1)	1.206(3)	C(8)-C(9)	1.524(4)
O(2)-C(18)	1.226(3)	C(9)-C(10)	1.526(4)
C(1)-C(2)	1.519(4)	C(10)-C(11)	1.530(4)
C(2)-C(3)	1.527(4)	C(12)-C(13)	1.362(4)
C(2)-C(18)	1.527(4)	C(12)-C(17)	1.362(4)
C(13)-C(14)	1.381(4)	C(14)-C(15)	1.363(5)
C(15)-C(16)	1.364(5)	C(16)-C(17)	1.383(5)
C(18)-C(19)	1.466(4)	C(19)-C(20)	1.384(4)
C(19)-C(24)	1.386(4)	C(20)-C(21)	1.381(4)
C(21)-C(22)	1.370(5)	C(22)-C(23)	1.371(5)
C(23)-C(24)	1.374(4)		

Table 3 Selected Bond Angles (°) for Compound **4am**

Angles	(°)	Angles	(°)
C(5)-N(1)-C(1)	125.5(3)	N(2)-C(5)-C(4)	124.0(3)
C(5)-N(1)-C(12)	117.6(3)	N(1)-C(5)-C(4)	117.6(3)
C(1)-N(1)-C(12)	116.9(2)	N(3)-C(6)-C(7)	126.7(3)
C(5)-N(2)-C(6)	118.1(3)	N(3)-C(6)-N(2)	111.4(3)
O(1)-C(1)-N(1)	120.3(3)	C(7)-C(6)-N(2)	121.9(3)
O(1)-C(1)-C(2)	121.3(3)	C(6)-C(7)-C(25)	119.3(3)
N(1)-C(1)-C(2)	118.4(3)	C(6)-C(7)-C(8)	119.2(3)
C(1)-C(2)-C(3)	112.9(3)	C(25)-C(7)-C(8)	121.3(3)
C(1)-C(2)-C(18)	106.8(3)	C(7)-C(8)-C(9)	116.2(3)
C(3)-C(2)-C(18)	109.2(2)	C(7)-C(8)-C(4)	108.8(2)
C(11)-C(3)-C(2)	113.9(3)	C(9)-C(8)-C(4)	110.0(3)
C(11)-C(3)-C(4)	110.1(2)	C(8)-C(9)-C(10)	111.0(3)
C(2)-C(3)-C(4)	111.5(2)	C(9)-C(10)-C(11)	112.9(2)
C(26)-C(4)-C(5)	106.9(2)	C(3)-C(11)-C(10)	110.6(3)
C(26)-C(4)-C(3)	109.8(3)	C(13)-C(12)-C(17)	120.9(3)
C(5)-C(4)-C(3)	112.8(2)	C(13)-C(12)-N(1)	119.5(3)
C(26)-C(4)-C(8)	109.9(2)	C(17)-C(12)-N(1)	119.6(3)

C(5)-C(4)-C(8)	108.4(2)	C(12)-C(13)-C(14)	119.8(3)
C(3)-C(4)-C(8)	109.2(2)	C(15)-C(14)-C(13)	119.7(4)
N(2)-C(5)-N(1)	118.4(3)	C(14)-C(15)-C(16)	120.1(4)
C(15)-C(16)-C(17)	120.5(4)	C(12)-C(17)-C(16)	119.0(4)
O(2)-C(18)-C(19)	119.7(3)	O(2)-C(18)-C(2)	116.9(3)
C(20)-C(19)-C(24)	118.8(3)	C(19)-C(18)-C(2)	123.4(3)
C(20)-C(19)-C(18)	122.7(3)	C(24)-C(19)-C(18)	118.3(3)
C(22)-C(21)-C(20)	120.2(4)	C(21)-C(20)-C(19)	120.0(3)
C(21)-C(22)-C(23)	120.4(4)	C(22)-C(23)-C(24)	119.7(4)
C(23)-C(24)-C(19)	120.9(4)	N(4)-C(25)-C(7)	178.0(4)
N(5)-C(26)-C(4)	177.1(4)		

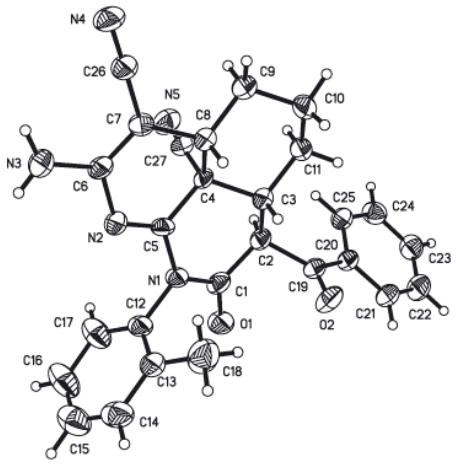


Figure 1. The Crystal Structure of **4aj**

Table 4 Crystallographic Data of Compound **4aj**

Empirical formula	$C_{267}H_{23}N_5O_2$	
Formula weight	449.50	
Temperature	293(2) K	
Wavelength	1.54178 Å	
Crystal system	Triclinic	
space group	P-1	
Unit cell dimensions	a =8.5318(10) Å	α = 74.306(14) °
	b = 10.8390(2) Å	β = 87.632(10) °
	c = 12.4287(18) Å	γ = 81.193(12) °
Volume	1140.3 (3)Å^3	
Z	3	
Calculated density	1.309 Mg/m^3	
Absorption coefficient	0.687 mm^{-1}	

F(000)	472
Crystal size	0.11 × 0.10 × 0.07 mm
Theta range for data collection	3.50 to 66.04°
Limiting indices	-10≤h≤8, -11≤k≤12, -15≤l≤15
Reflections collected	6977
Independent reflections	3859 [R(int) = 0.1181]
Data / restraints / parameters	3859 / 0 / 309
Goodness-of-fit on F^2	1.190
Final R indices [$I>2\sigma(I)$]	R_1 = 0.1399, wR_2 = 0.2392
R indices (all data)	R_1 = 0.2516, wR_2 = 0.2855
Largest diff. peak and hole	0.225 and -0.276 e. $Å^{-3}$

Table 5 Selected bond lengths (Å) of compound **4aj**

Bond	Bond Lengths	Bond	Bond Lengths
N(1)-C(5)	1.380(9)	C(7)-C(26)	1.406(12)
N(1)-C(1)	1.420(10)	C(7)-C(8)	1.526(11)
N(2)-C(12)	1.467(11)	C(8)-C(9)	1.521(11)
N(2)-C(5)	1.283(10)	C(9)-C(10)	1.522(11)
N(2)-C(6)	1.412(10)	C(10)-C(11)	1.536(12)
N(3)-C(6)	1.348(10)	C(12)-C(13)	1.368(14)
N(4)-C(26)	1.147(11)	C(12)-C(17)	1.387(14)
N(5)-C(27)	1.107(12)	C(13)-C(14)	1.398(14)
O(1)-C(1)	1.197(10)	C(13)-C(18)	1.470(14)
O(2)-C(19)	1.204(11)	C(14)-C(15)	1.348(16)
C(1)-C(2)	1.513(12)	C(15)-C(16)	1.379(17)
C(2)-C(19)	1.530(11)	C(16)-C(17)	1.385(15)
C(2)-C(3)	1.531(11)	C(19)-C(20)	1.501(12)
C(3)-C(4)	1.531(10)	C(20)-C(25)	1.389(13)
C(3)-C(11)	1.535(11)	C(20)-C(21)	1.390(11)
C(4)-C(27)	1.491(13)	C(21)-C(22)	1.391(13)
C(4)-C(5)	1.526(11)	C(22)-C(23)	1.356(14)
C(4)-C(8)	1.562(12)	C(23)-C(24)	1.381(13)
C(6)-C(7)	1.361(12)	C(24)-C(25)	1.387(12)

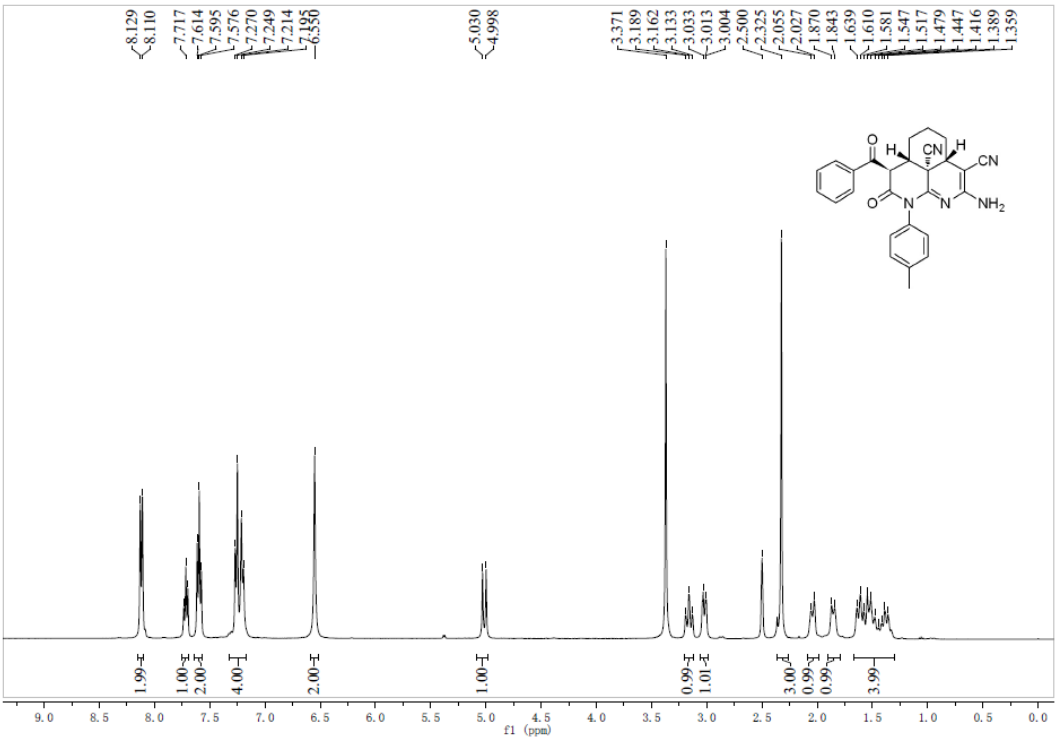
Table 6 Selected bond angles (°) of compound **4aj**

Angles	(°)	Angles	(°)
C(5)-N(1)-C(1)	124.5(7)	C(9)-C(8)-C(7)	115.5(7)
C(5)-N(1)-C(12)	118.1(7)	C(9)-C(8)-C(4)	110.2(8)
C(1)-N(1)-C(12)	116.8(7)	C(13)-C(12)-C(17)	122.5(11)
C(5)-N(2)-C(6)	117.6(8)	C(13)-C(12)-N(1)	118.1(10)
O(1)-C(1)-N(1)	120.2(9)	C(17)-C(12)-N(1)	119.4(10)

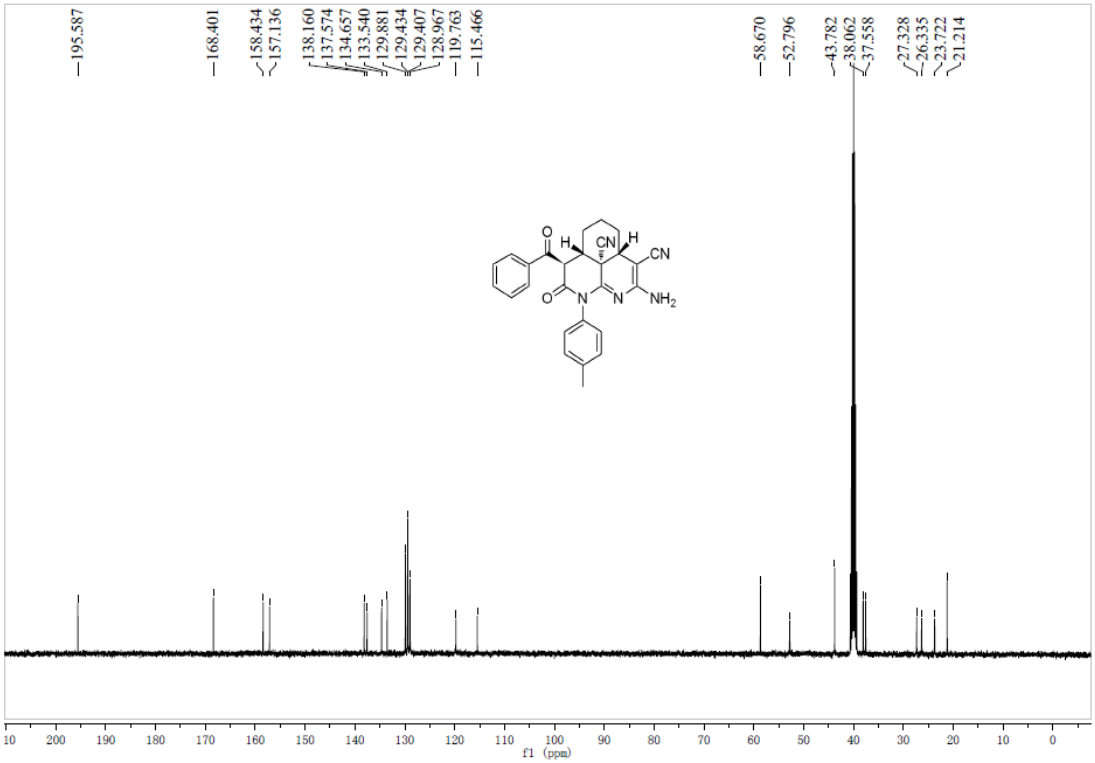
O(1)-C(1)-C(2)	121.9(8)	C(12)-C(13)-C(14)	118.6(12)
N(1)-C(1)-C(2)	117.7(8)	C(12)-C(13)-C(18)	121.5(11)
C(1)-C(2)-C(19)	105.3(7)	C(14)-C(13)-C(18)	120.0(12)
C(1)-C(2)-C(3)	113.0(7)	C(15)-C(14)-C(13)	119.1(14)
C(19)-C(2)-C(3)	108.6(7)	C(14)-C(15)-C(16)	122.6(14)
C(2)-C(3)-C(4)	109.8(7)	C(15)-C(16)-C(17)	119.3(14)
C(2)-C(3)-C(11)	113.9(7)	C(16)-C(17)-C(12)	117.9(13)
C(4)-C(3)-C(11)	110.0(7)	O(2)-C(19)-C(20)	119.8(8)
C(27)-C(4)-C(5)	108.3(7)	O(2)-C(19)-C(2)	118.9(9)
C(27)-C(4)-C(3)	111.3(8)	C(20)-C(19)-C(2)	121.2(9)
C(5)-C(4)-C(3)	112.3(7)	C(25)-C(20)-C(21)	119.0(9)
C(27)-C(4)-C(8)	109.8(7)	C(25)-C(20)-C(19)	122.9(8)
C(5)-C(4)-C(8)	107.3(7)	C(21)-C(20)-C(19)	118.0(9)
C(3)-C(4)-C(8)	107.8(7)	C(20)-C(21)-C(22)	120.3(10)
N(2)-C(5)-N(1)	119.3(8)	C(23)-C(22)-C(21)	120.1(10)
N(2)-C(5)-C(4)	123.9(7)	C(22)-C(23)-C(24)	120.6(10)
N(1)-C(5)-C(4)	116.8(7)	C(23)-C(24)-C(25)	120.0(10)
N(3)-C(6)-C(7)	125.9(8)	C(24)-C(25)-C(20)	120.0(9)
N(3)-C(6)-N(2)	111.3(8)	N(4)-C(26)-C(7)	178.1(13)
C(7)-C(6)-N(2)	122.8(8)	N(5)-C(27)-C(4)	177.7(11)
C(6)-C(7)-C(26)	120.7(9)	C(26)-C(7)-C(8)	121.5(8)
C(6)-C(7)-C(8)	117.7(8)		

5. ^{1}H NMR and ^{13}C NMR Spectra of all compounds

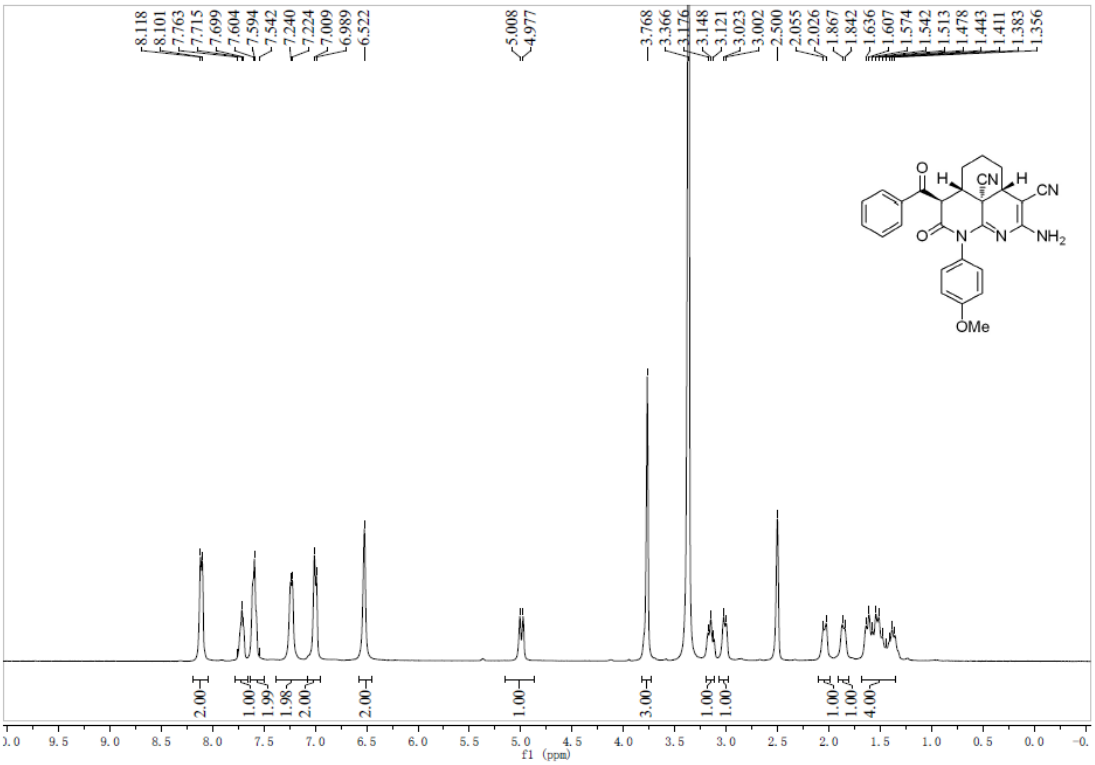
^{1}H NMR of compounds **4aa**



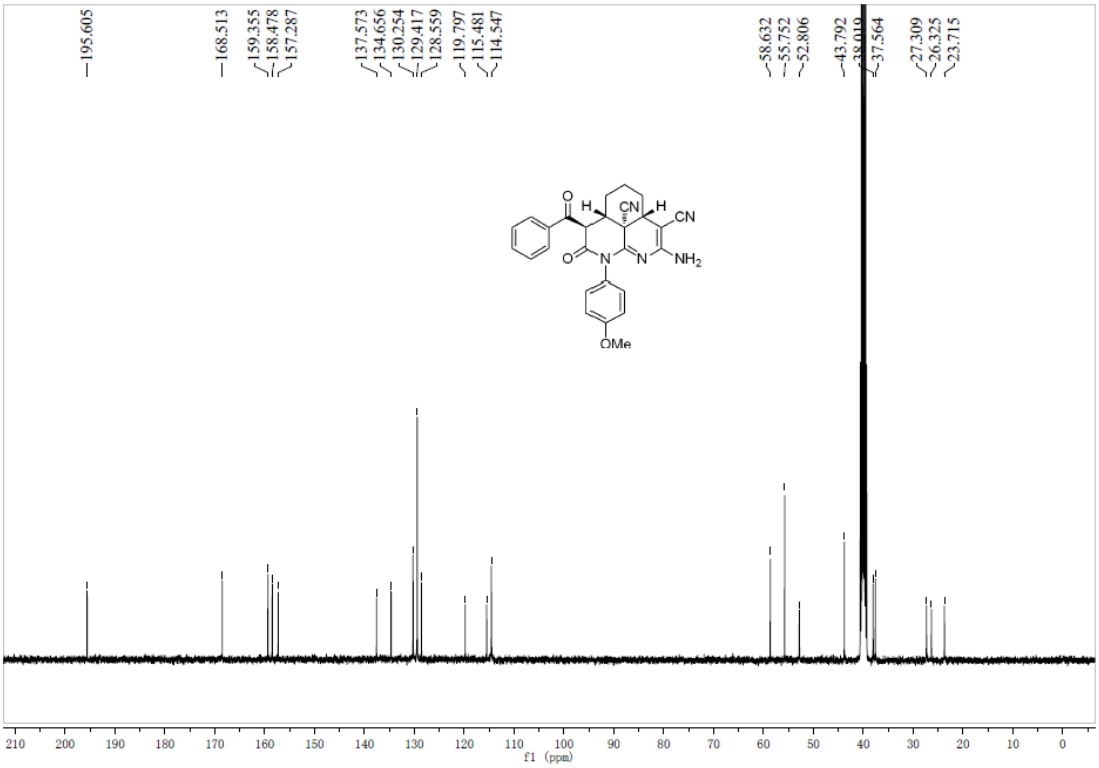
^{13}C NMR of compounds **4aa**



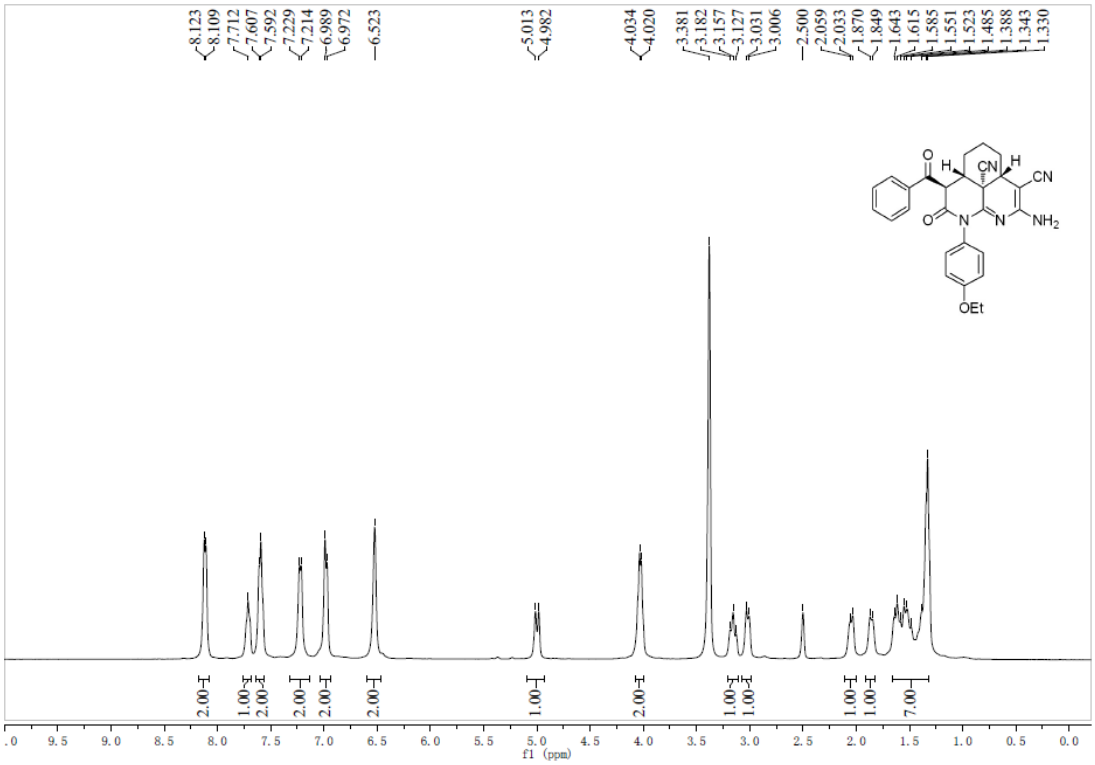
^{1}H NMR of compounds **4ab**



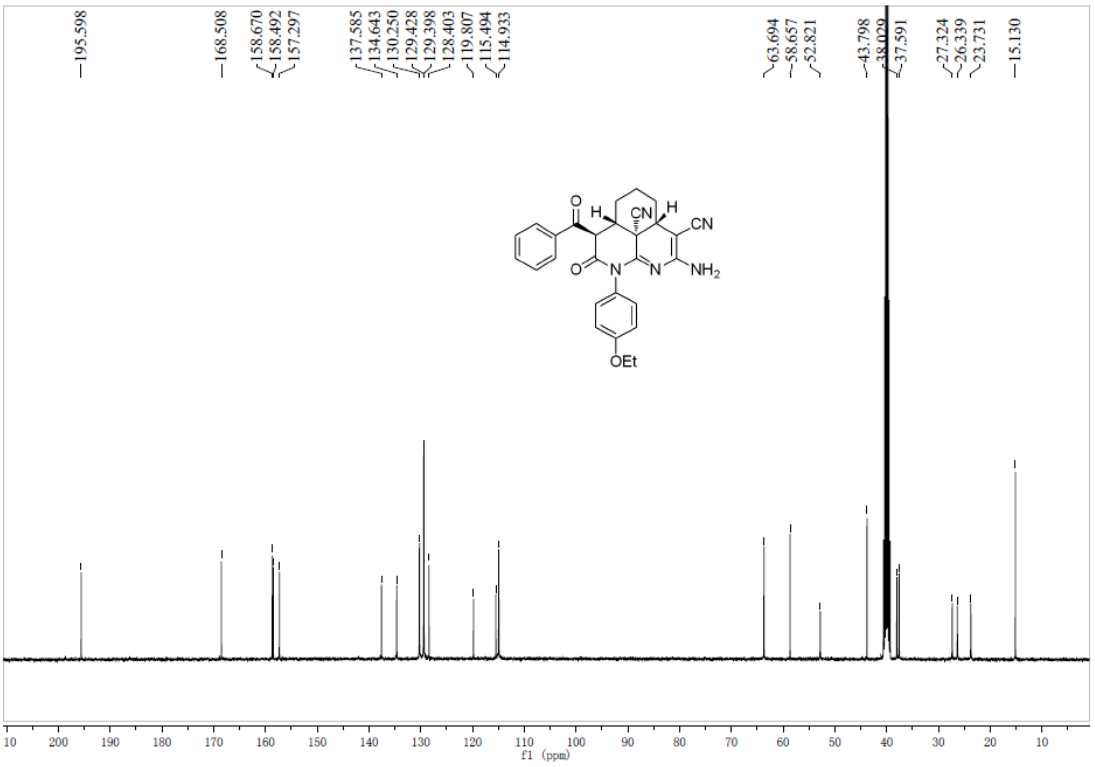
^{13}C NMR of compounds **4ab**



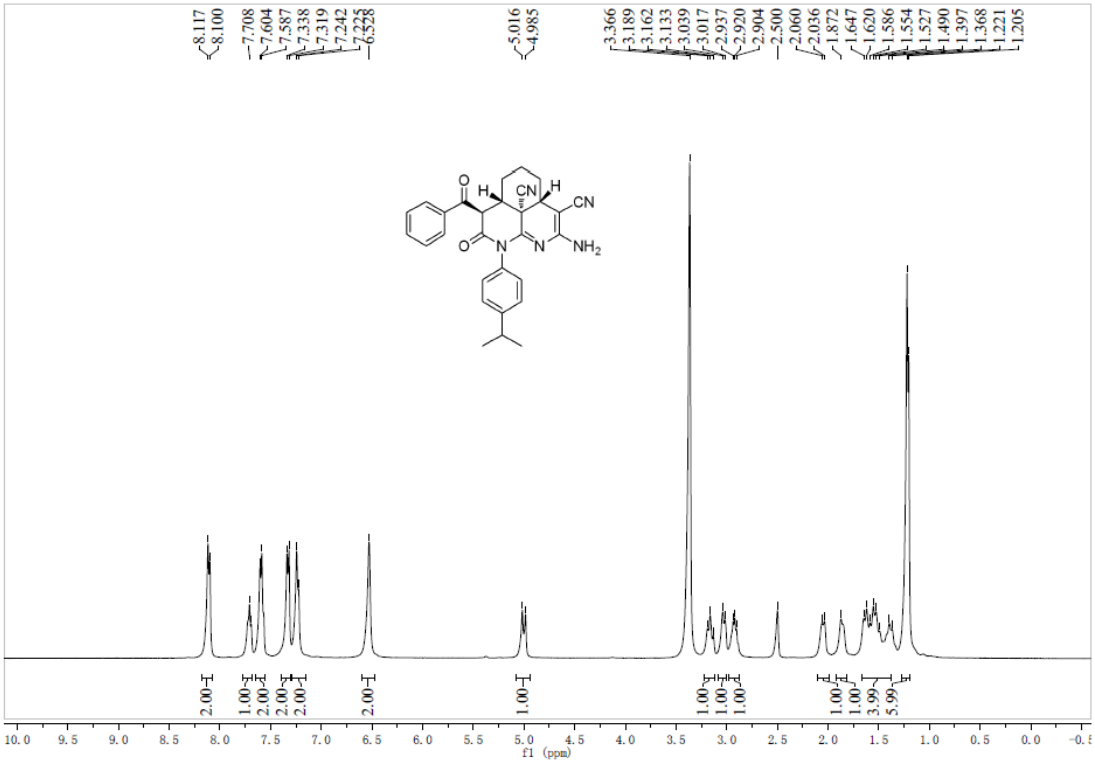
^{1}H NMR of compounds **4ac**



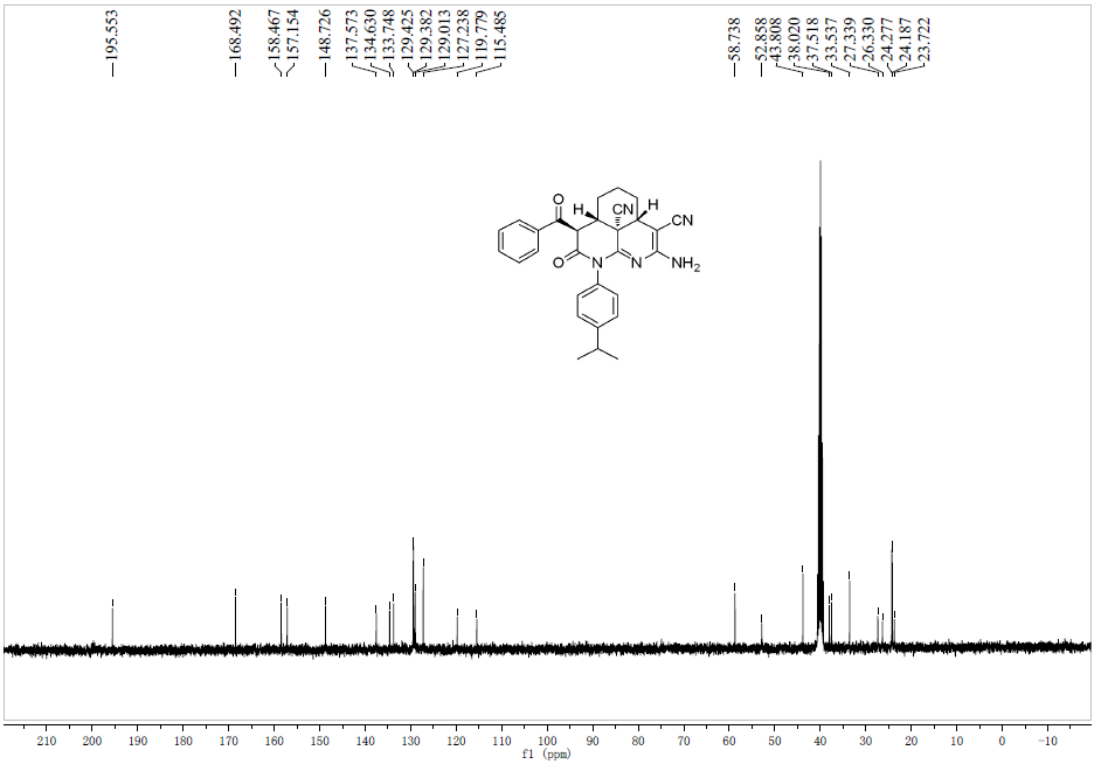
^{13}C NMR of compounds **4ac**



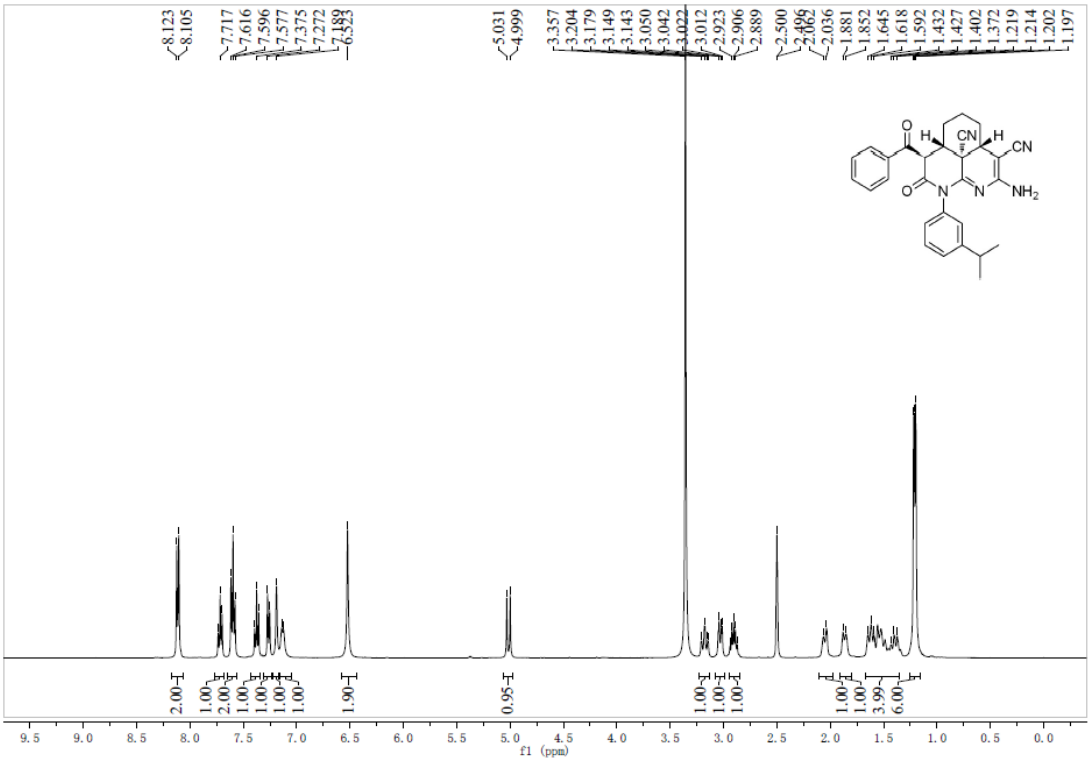
^{1}H NMR of compounds **4ad**



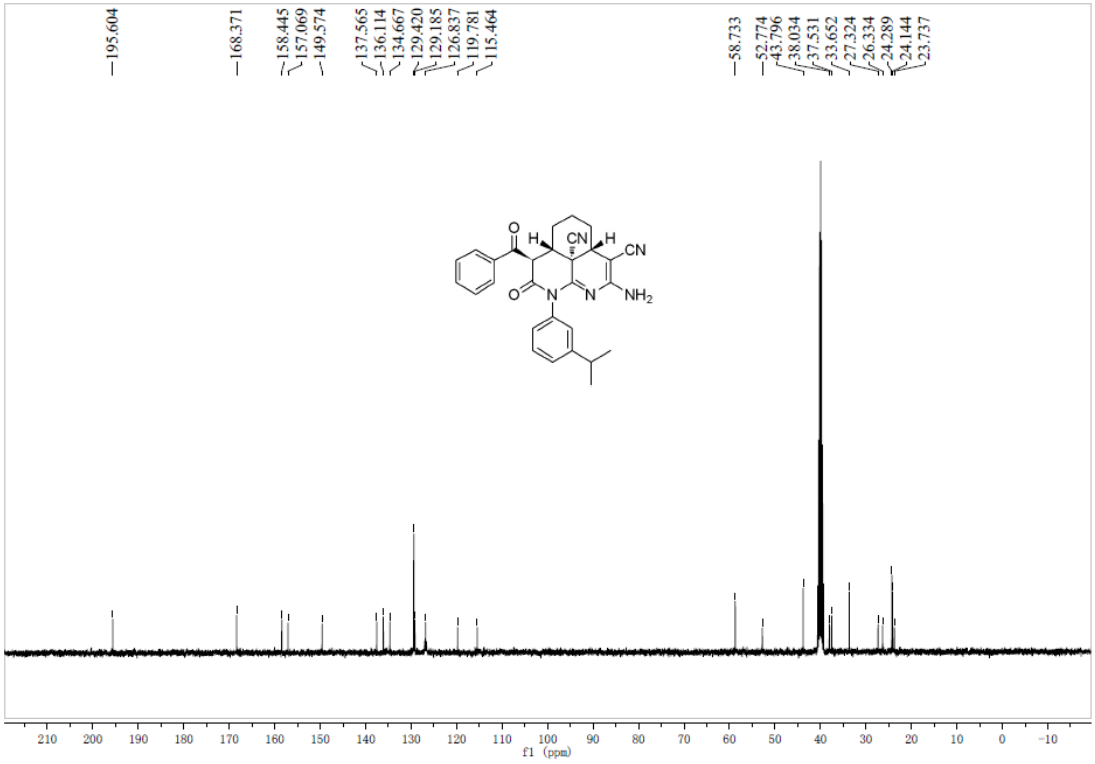
^{13}C NMR of compounds **4ad**



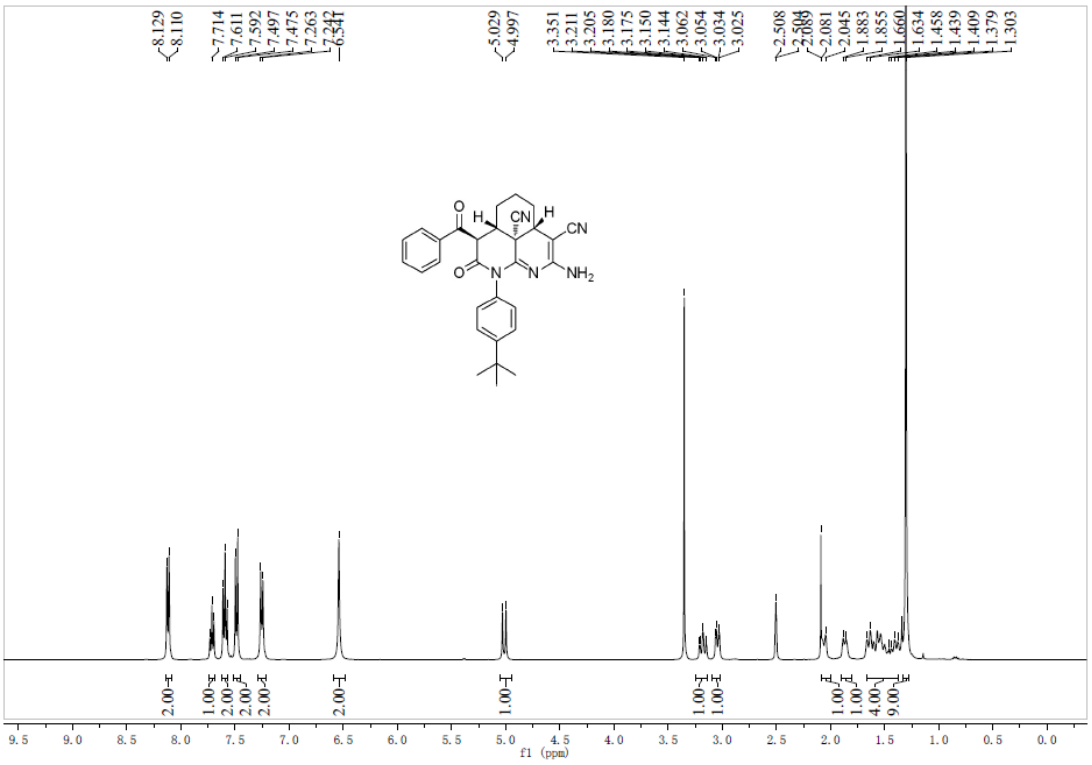
^{1}H NMR of compounds **4ae**



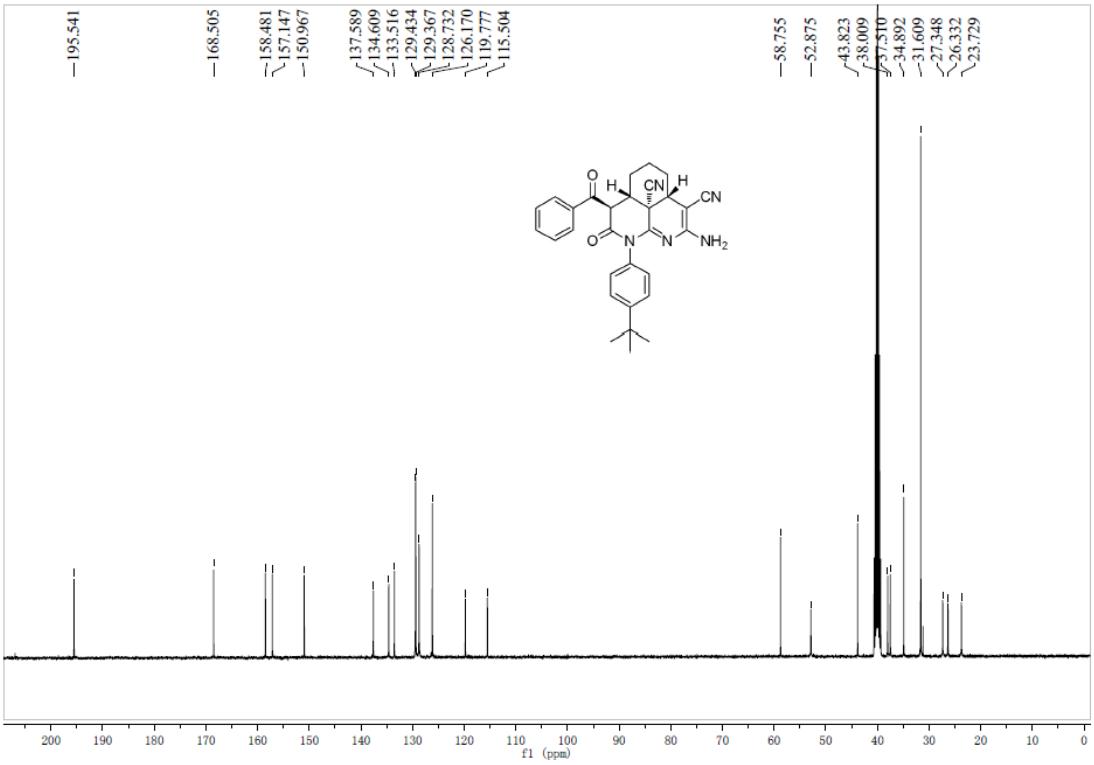
^{13}C NMR of compounds **4ae**



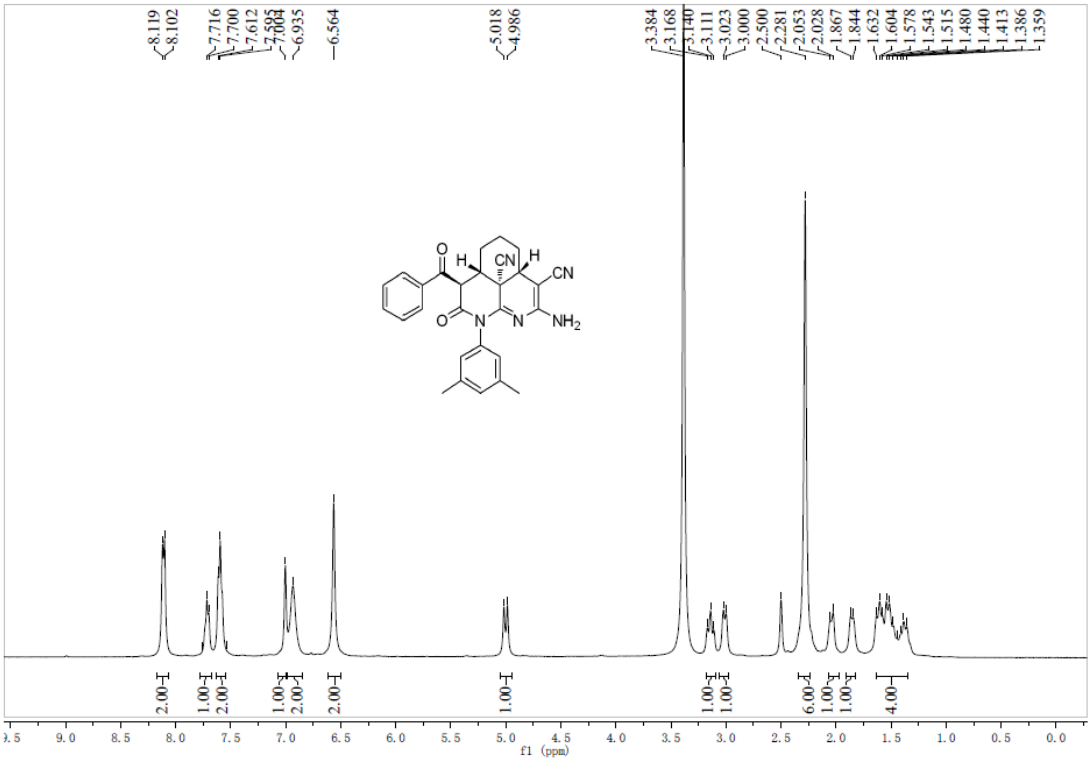
^{1}H NMR of compounds **4af**



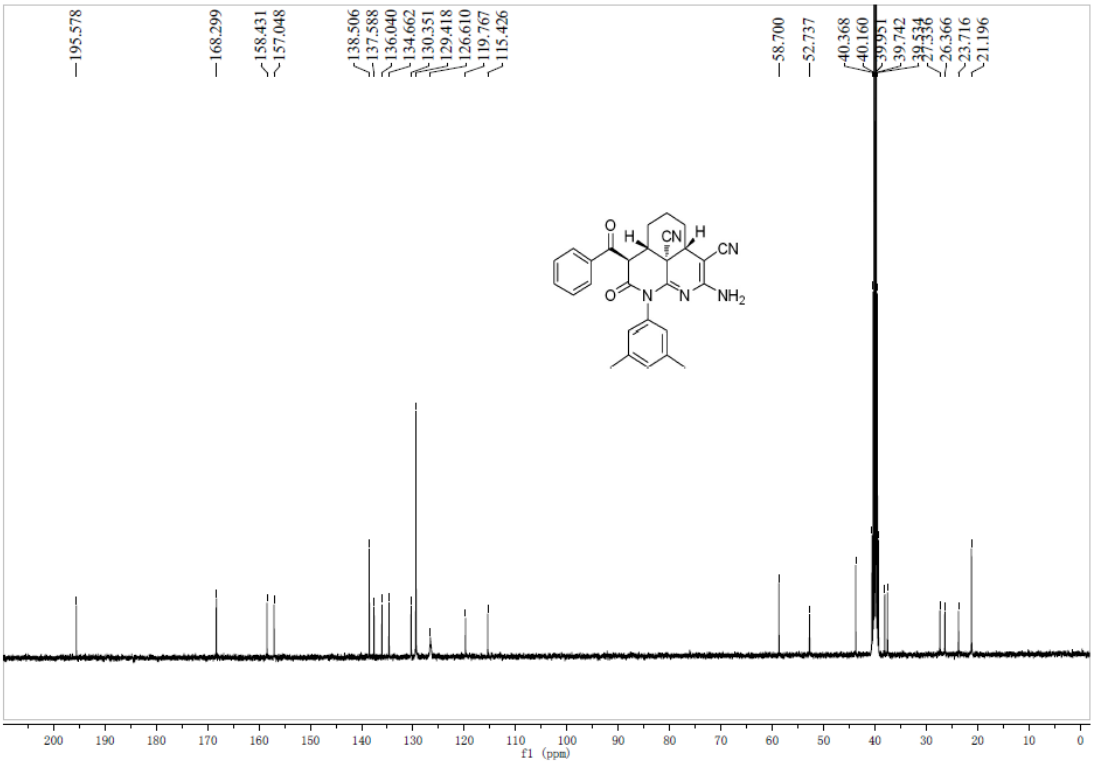
^{13}C NMR of compounds**4af**



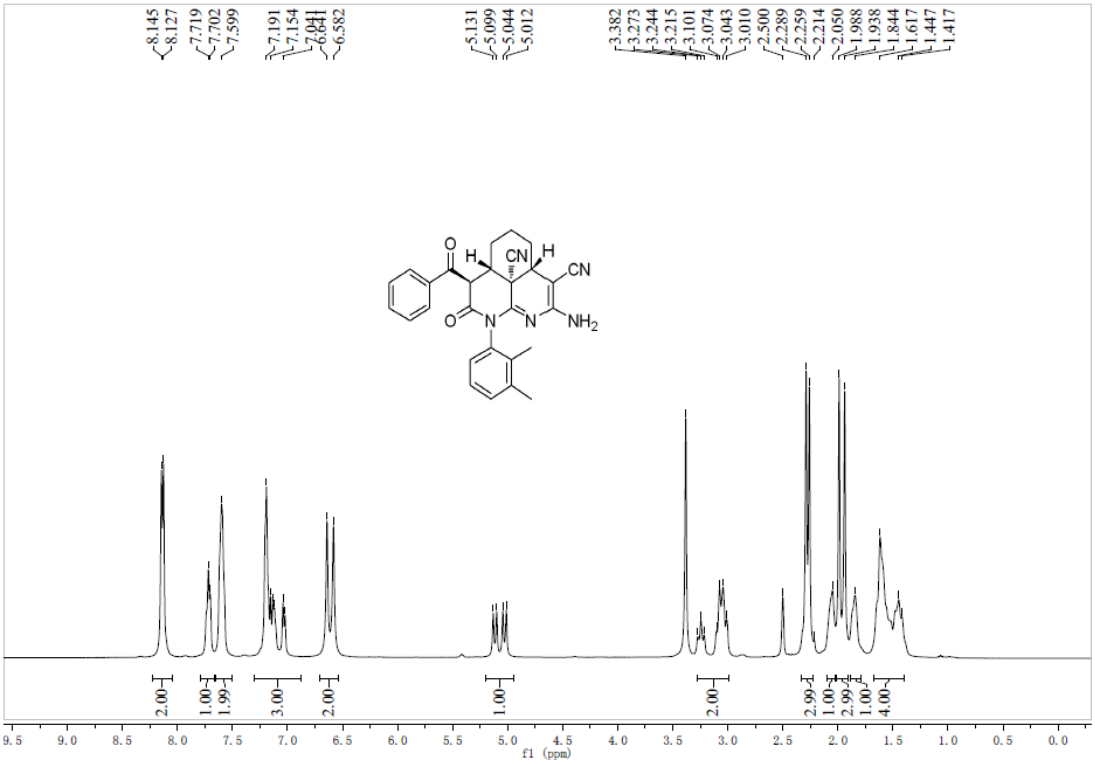
^{1}H NMR of compounds **4ag**



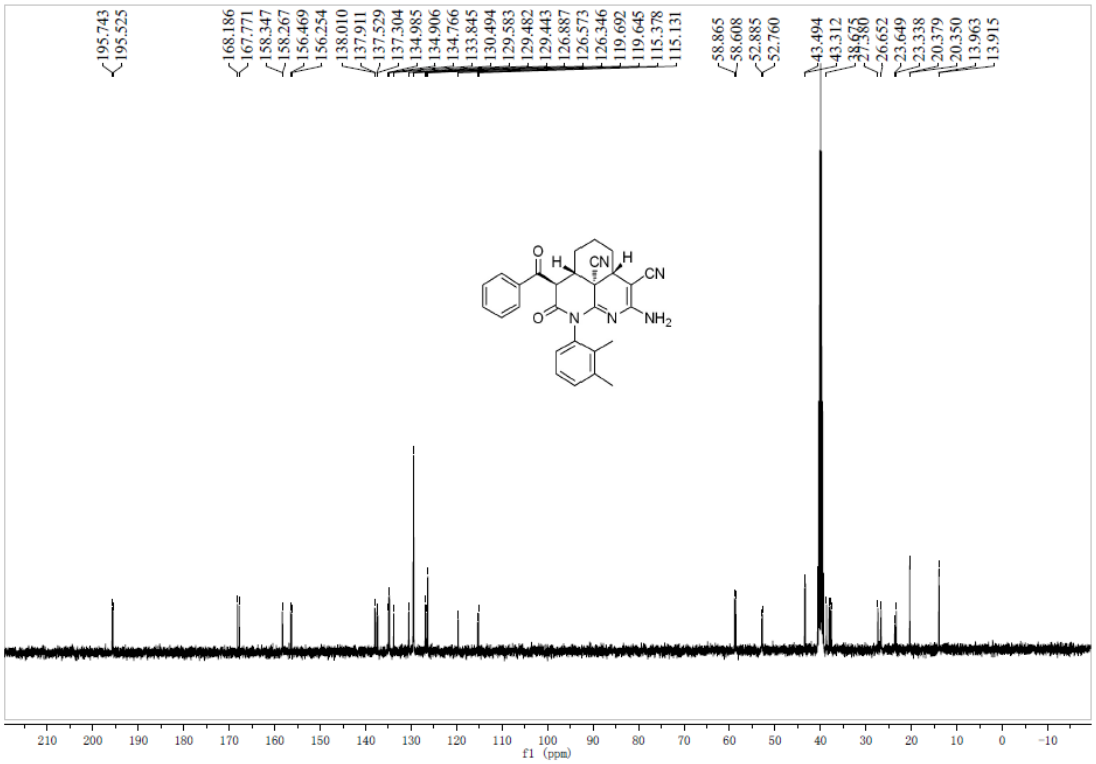
^{13}C NMR of compounds**4ag**



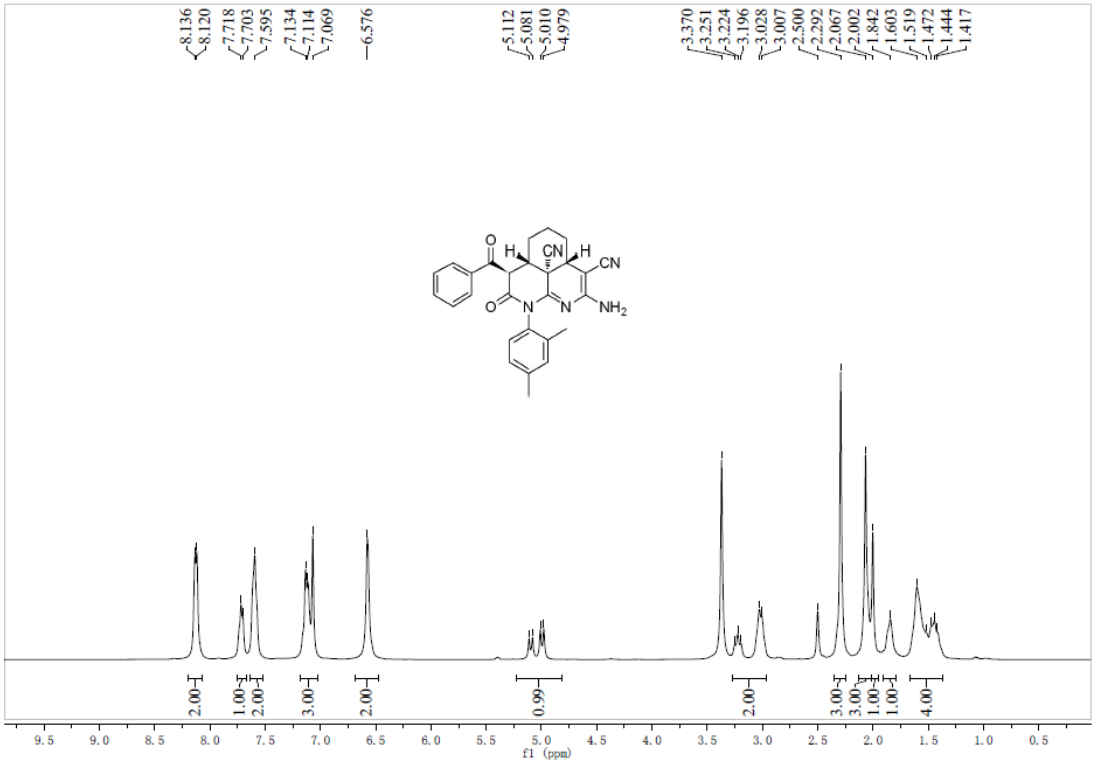
^{1}H NMR of compounds **4ah**



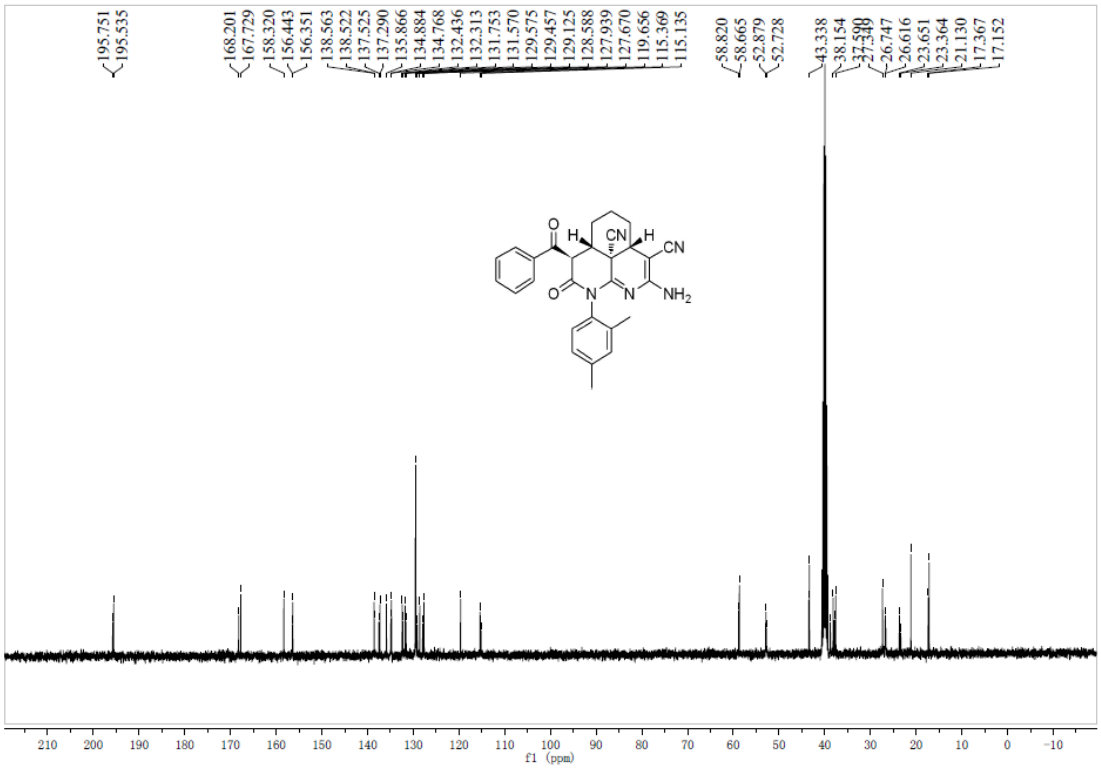
^{13}C NMR of compounds **4ah**



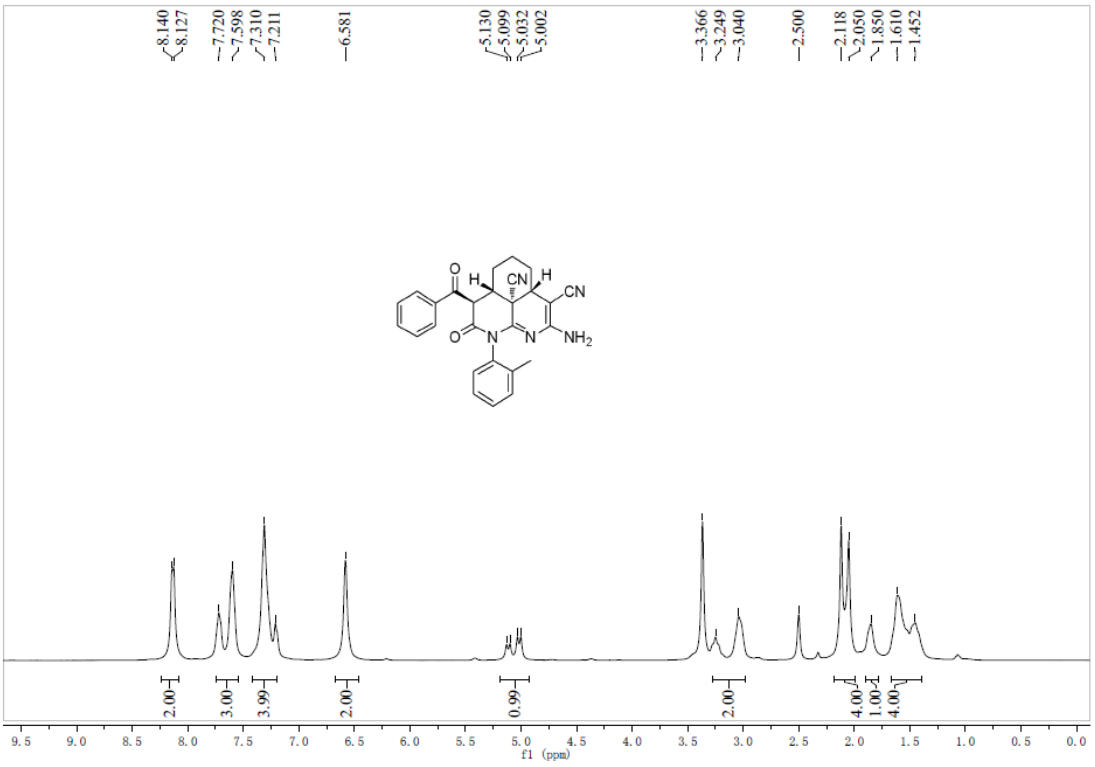
^{1}H NMR of compounds **4ai**



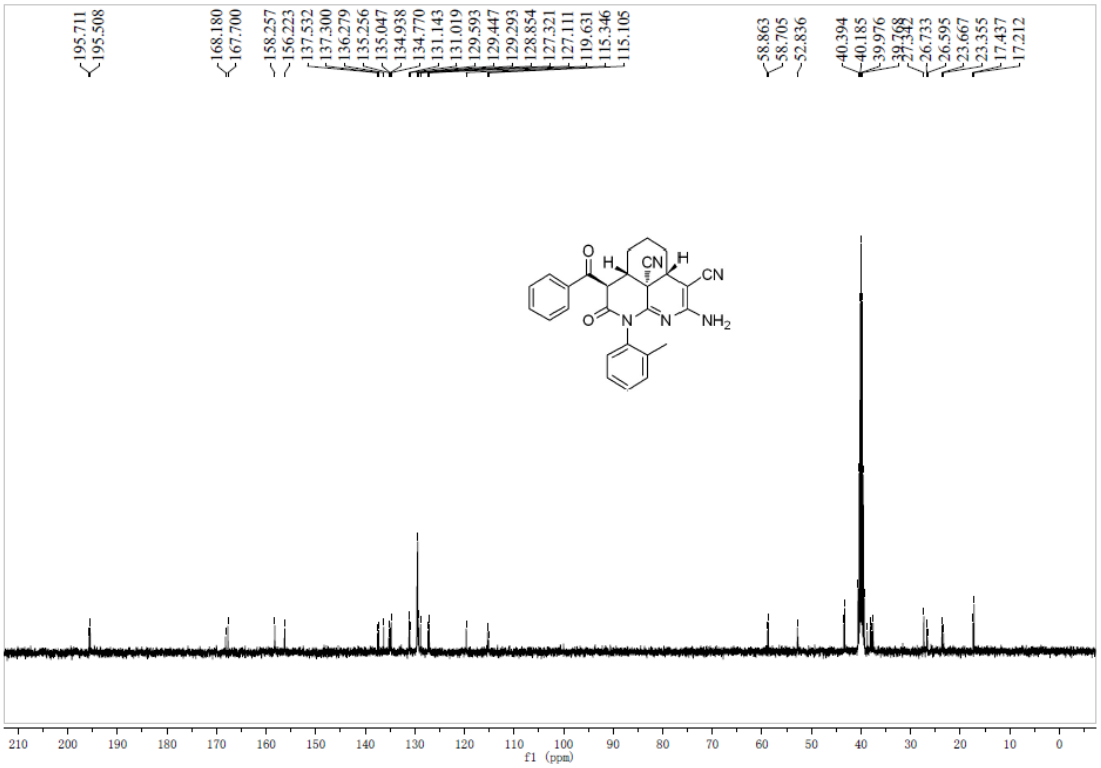
^{13}C NMR of compounds **4ai**



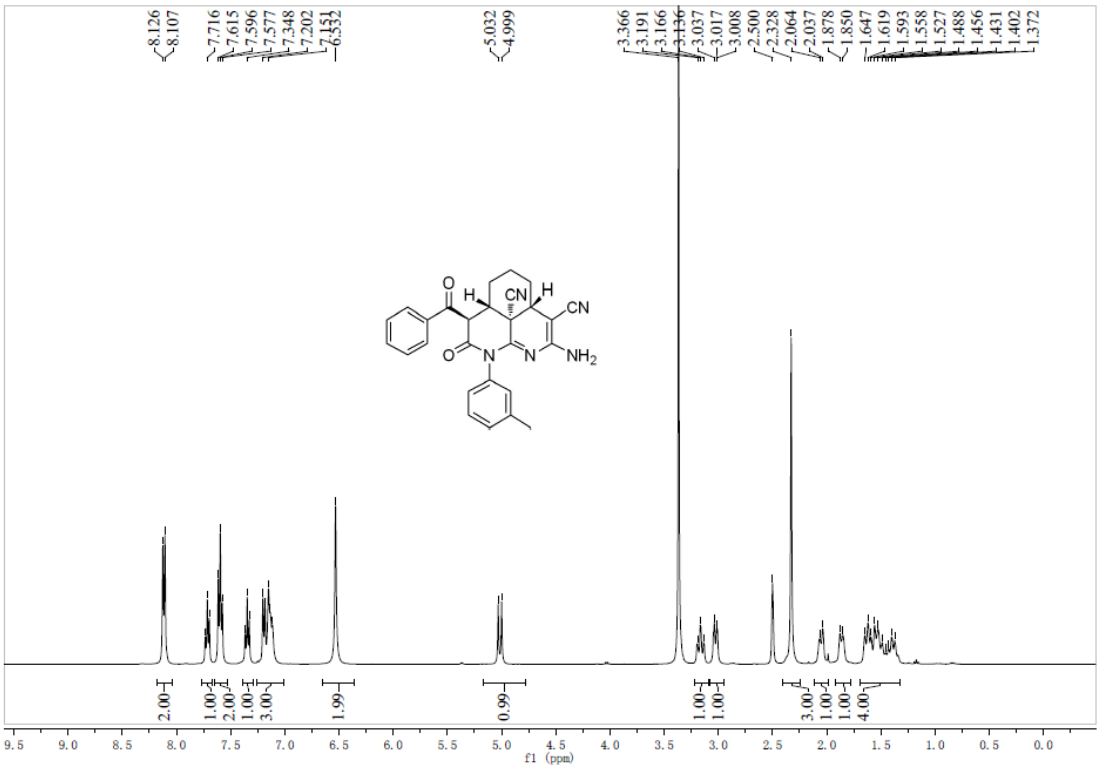
^{1}H NMR of compounds **4aj**



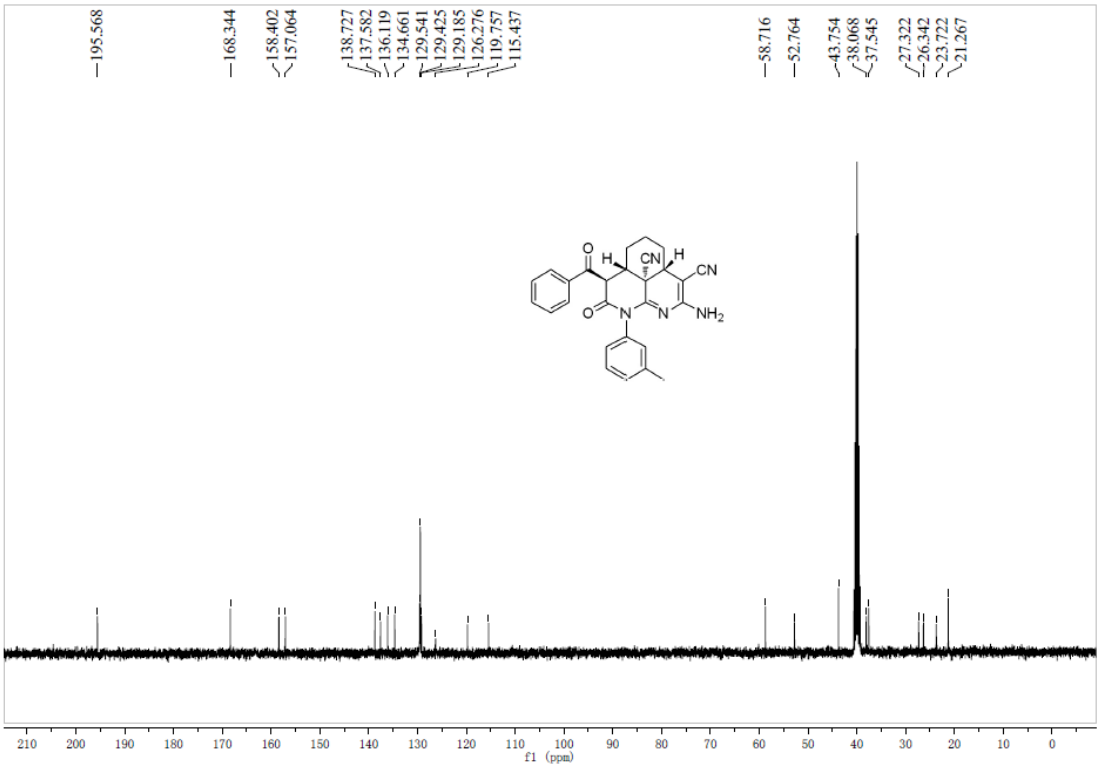
^{13}C NMR of compounds **4aj**



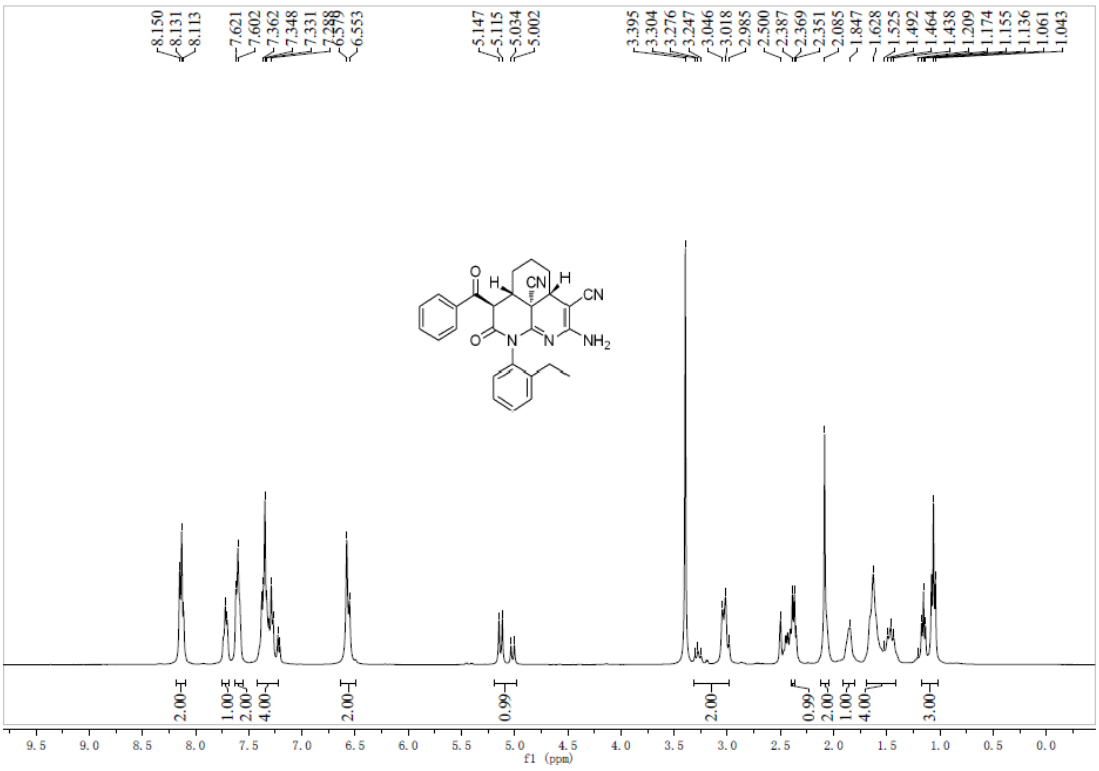
^{1}H NMR of compounds **4ak**



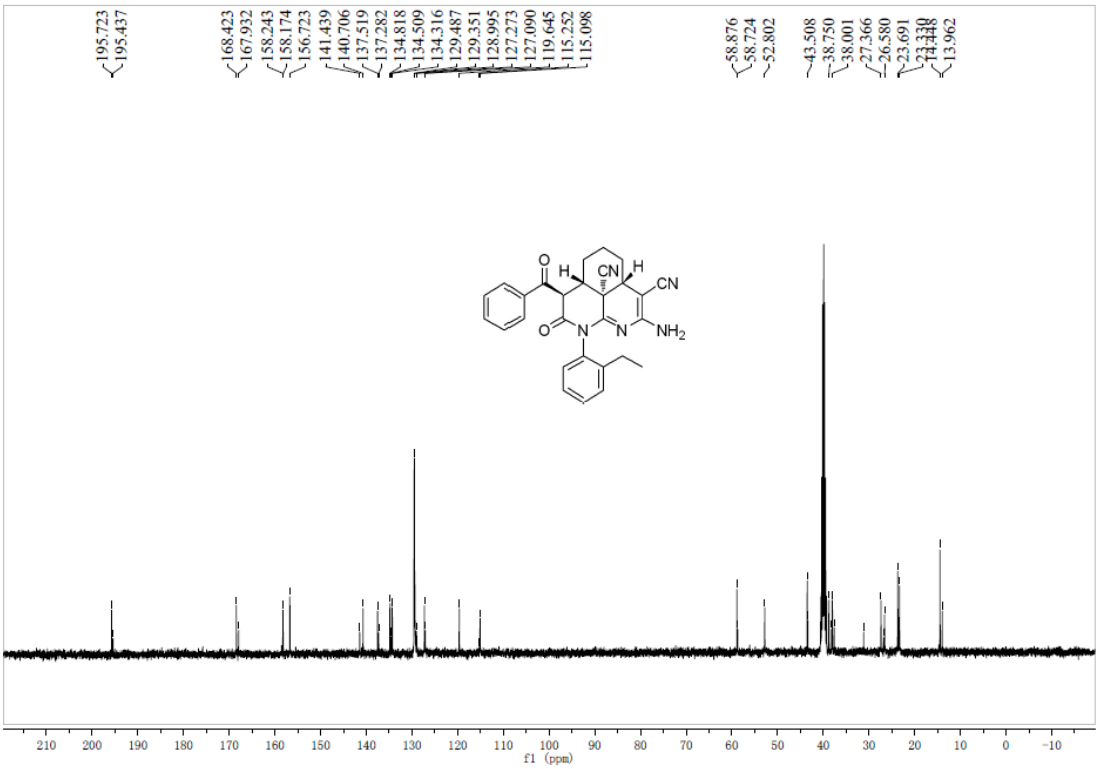
^{13}C NMR of compounds **4ak**



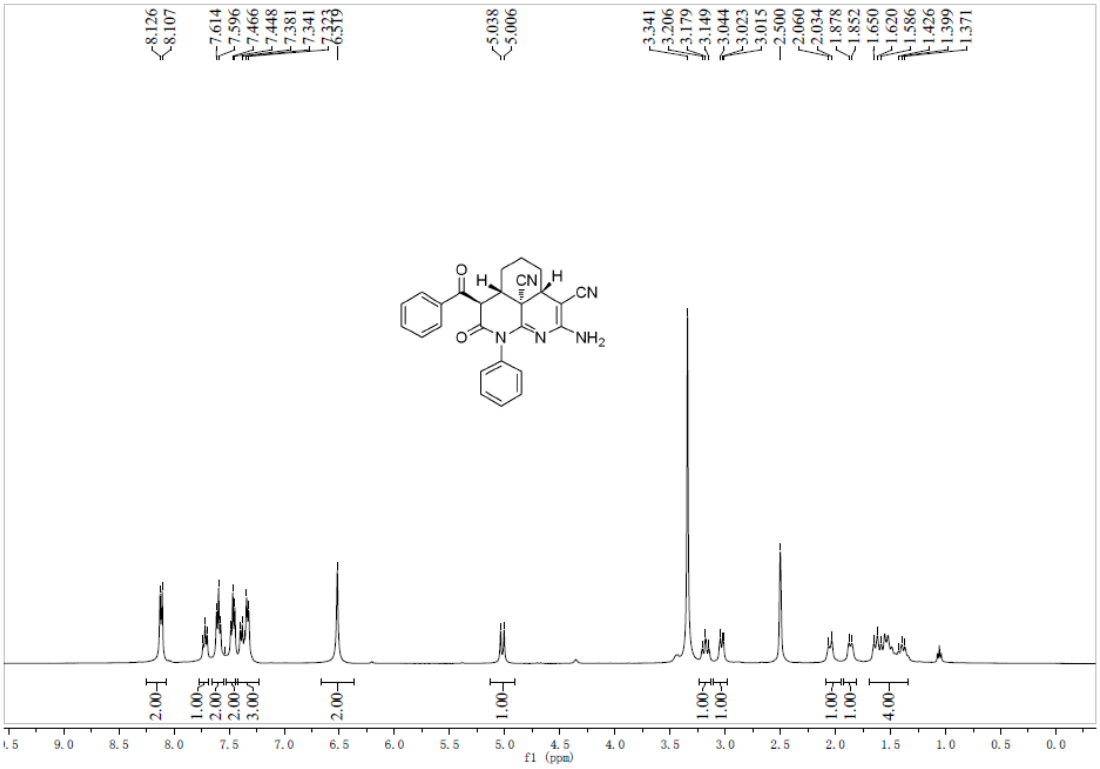
[1]H NMR of compounds **4al**



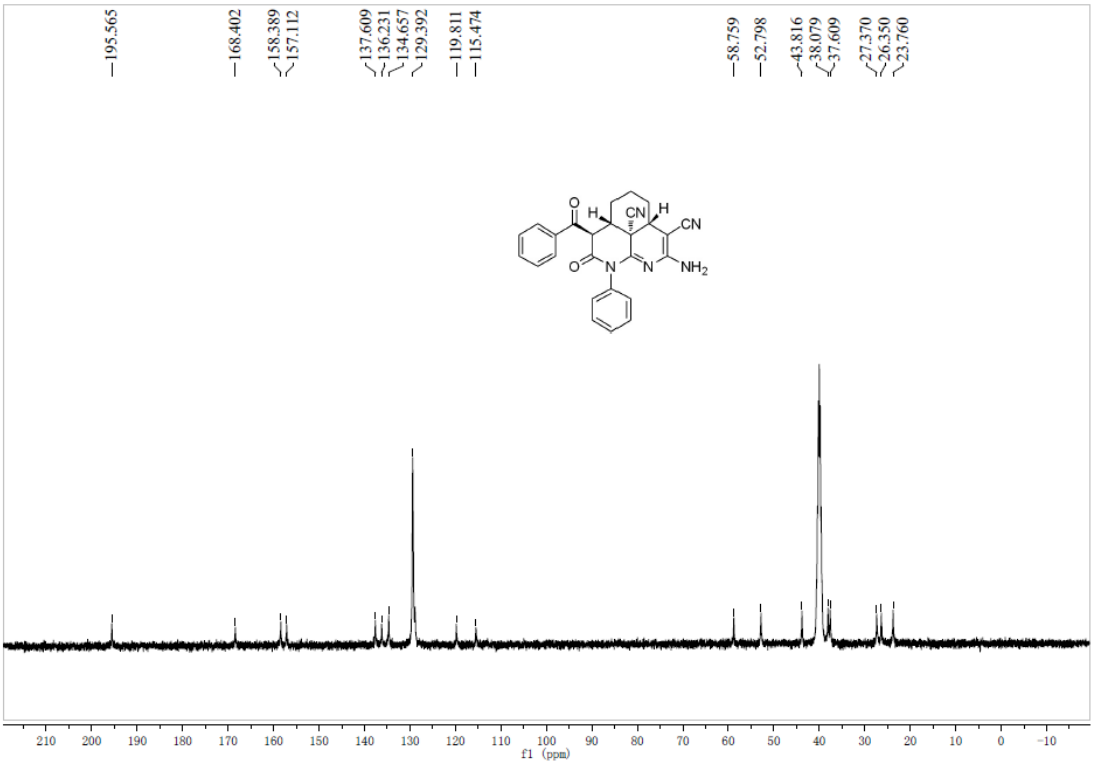
[13]C NMR of compounds**4al**



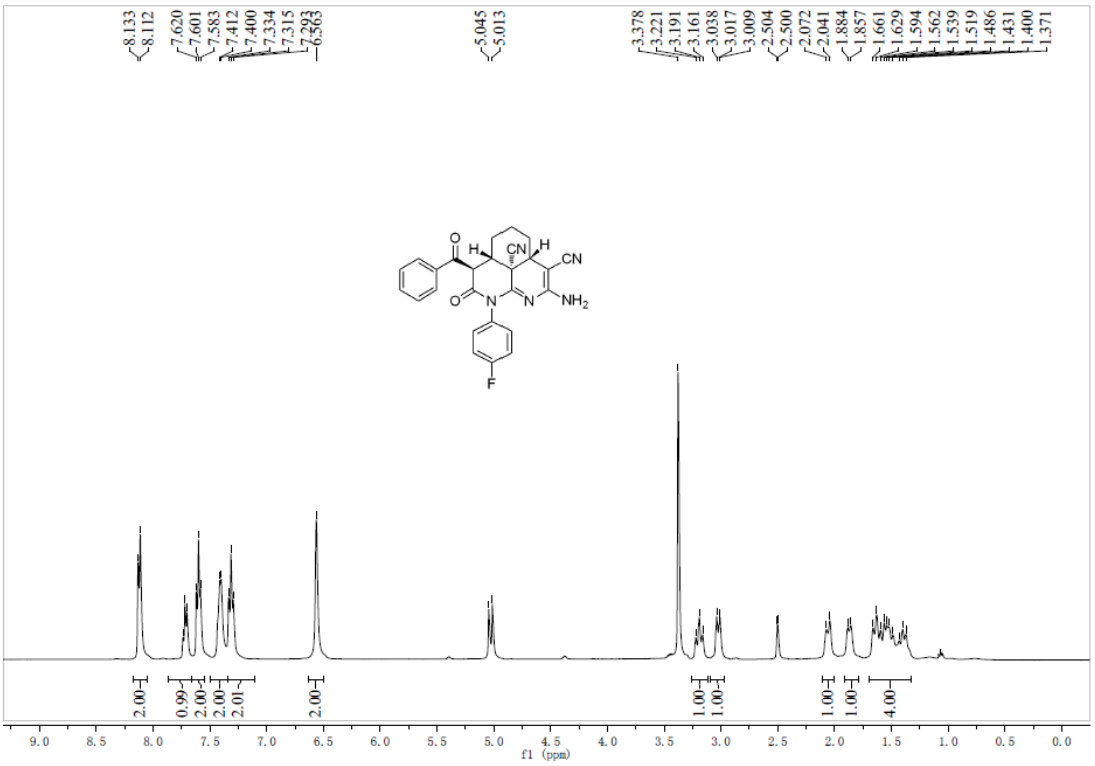
^{1}H NMR of compounds **4am**



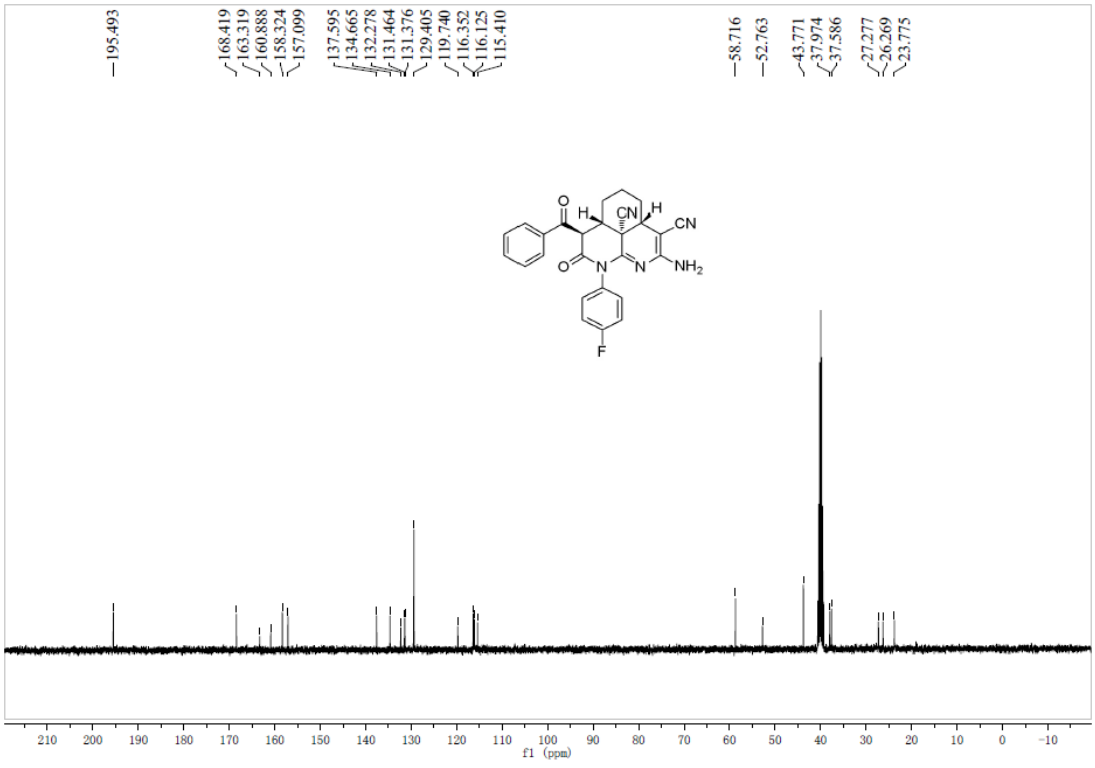
^{13}C NMR of compounds **4am**



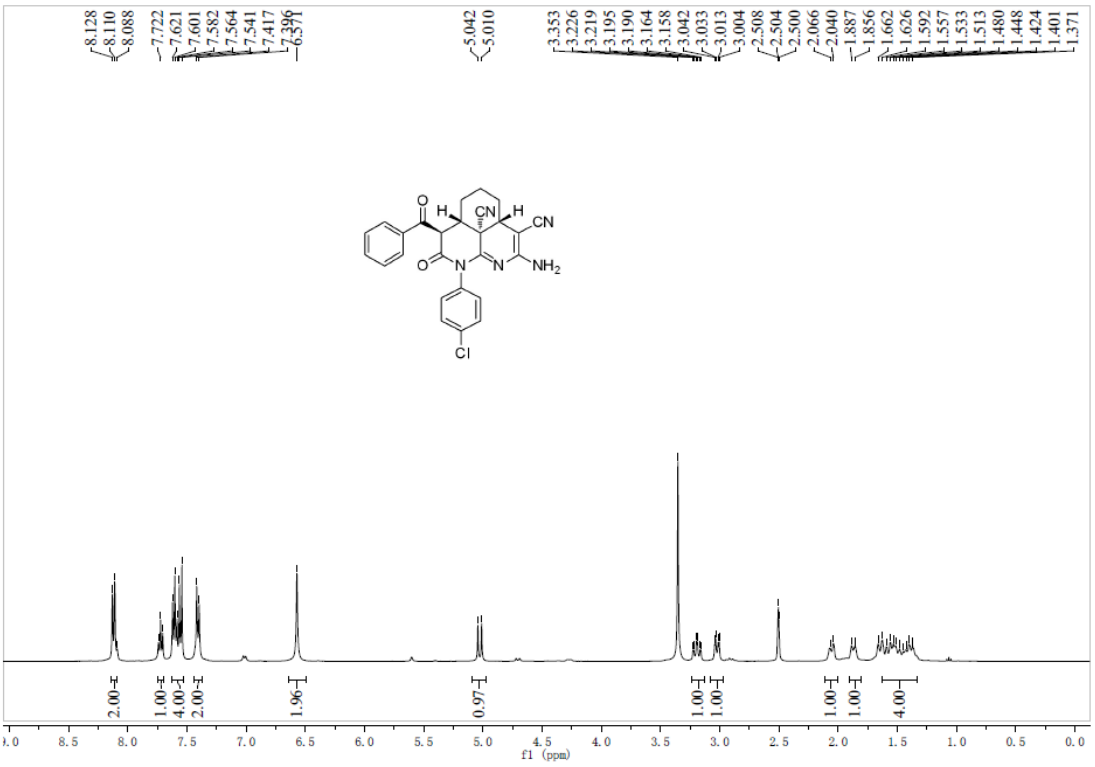
^{1}H NMR of compounds **4an**



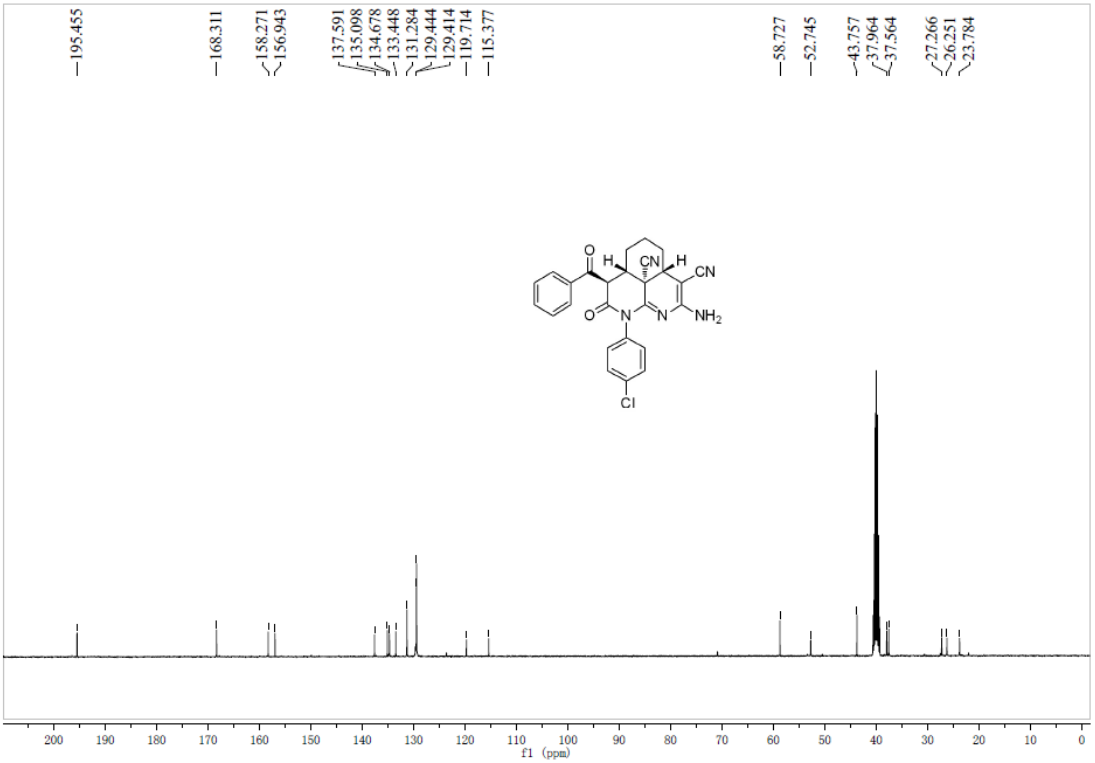
^{13}C NMR of compounds **4an**



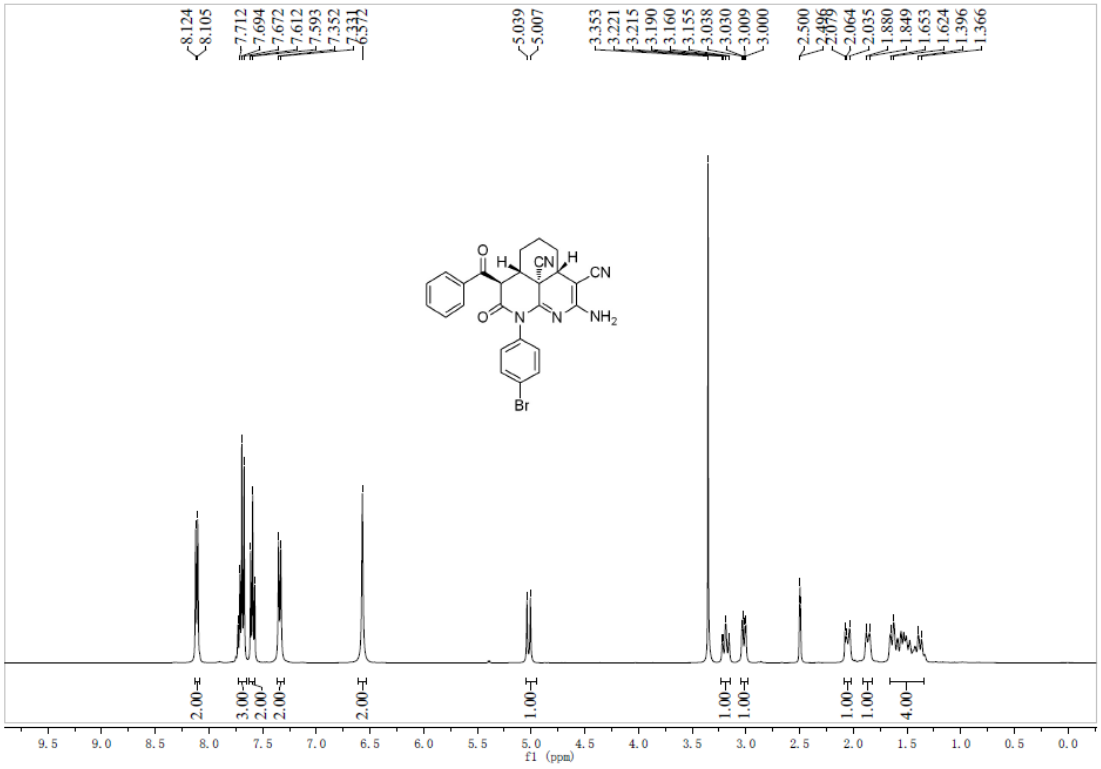
^{1}H NMR of compounds **4ao**



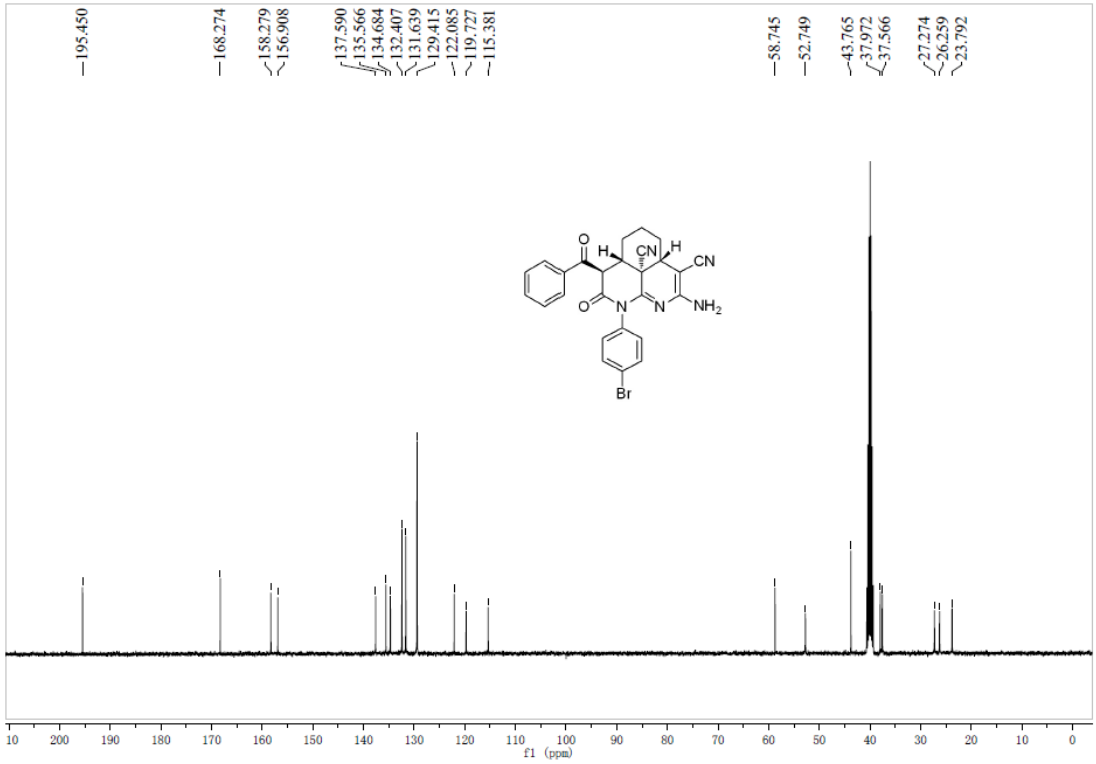
^{13}C NMR of compounds **4ao**



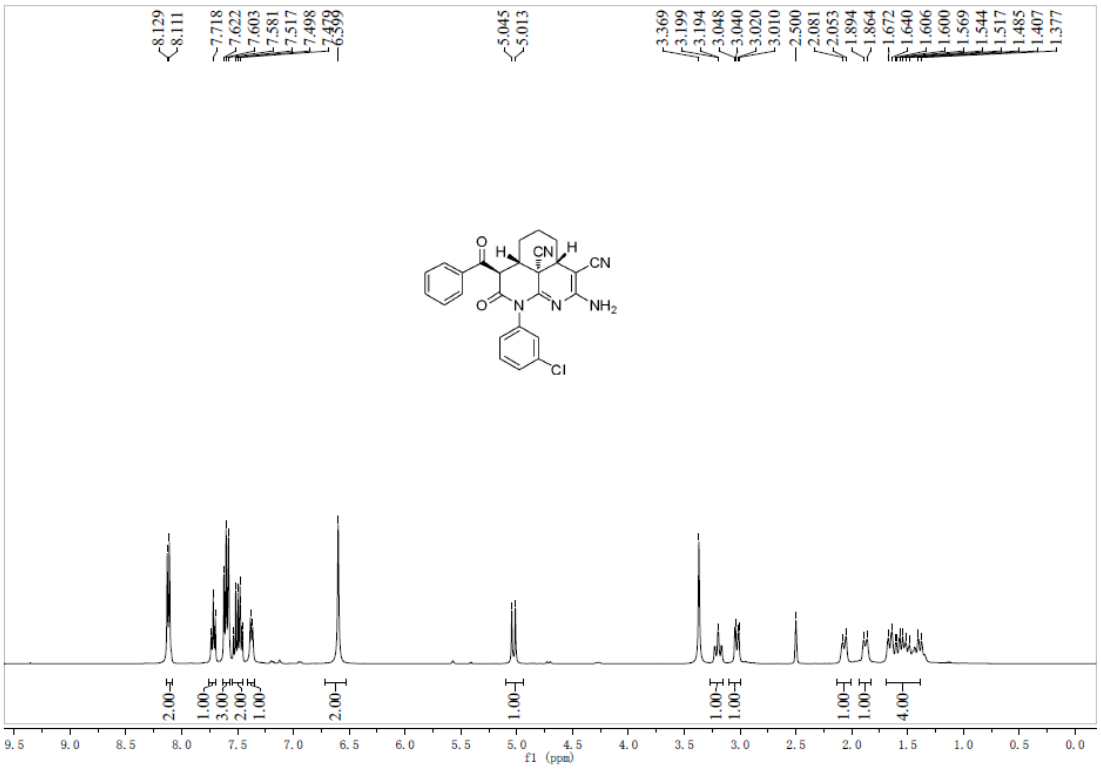
^{1}H NMR of compounds **4ap**



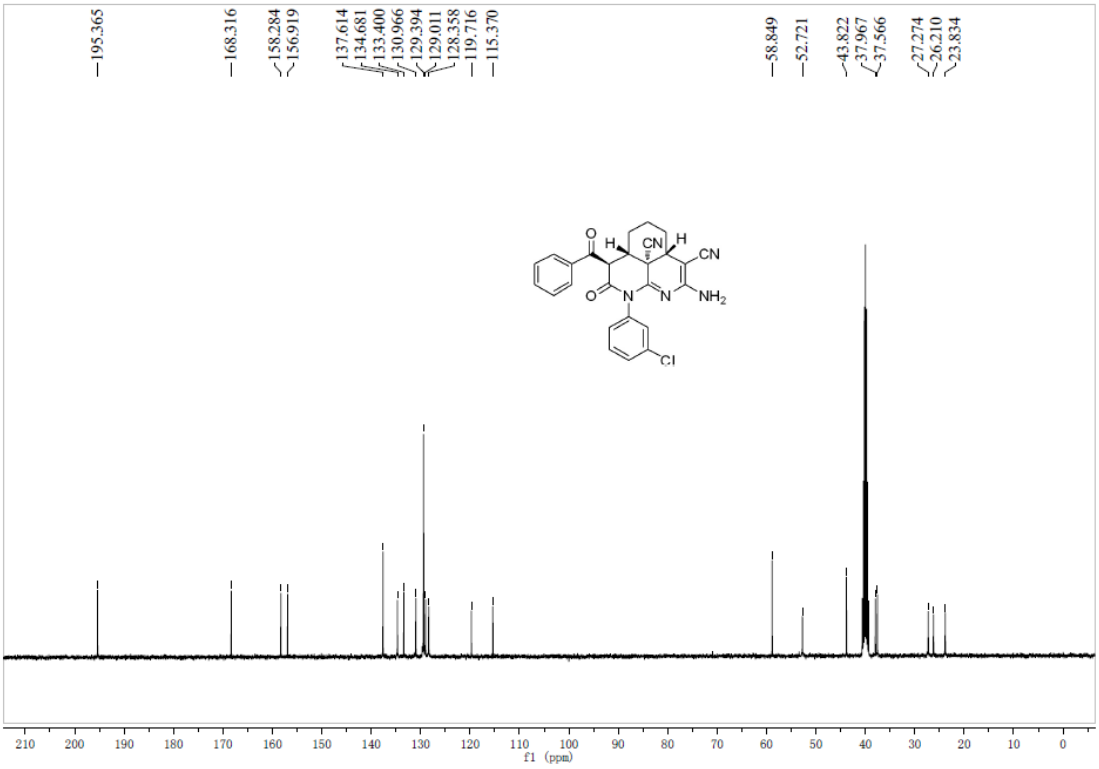
^{13}C NMR of compounds **4ap**



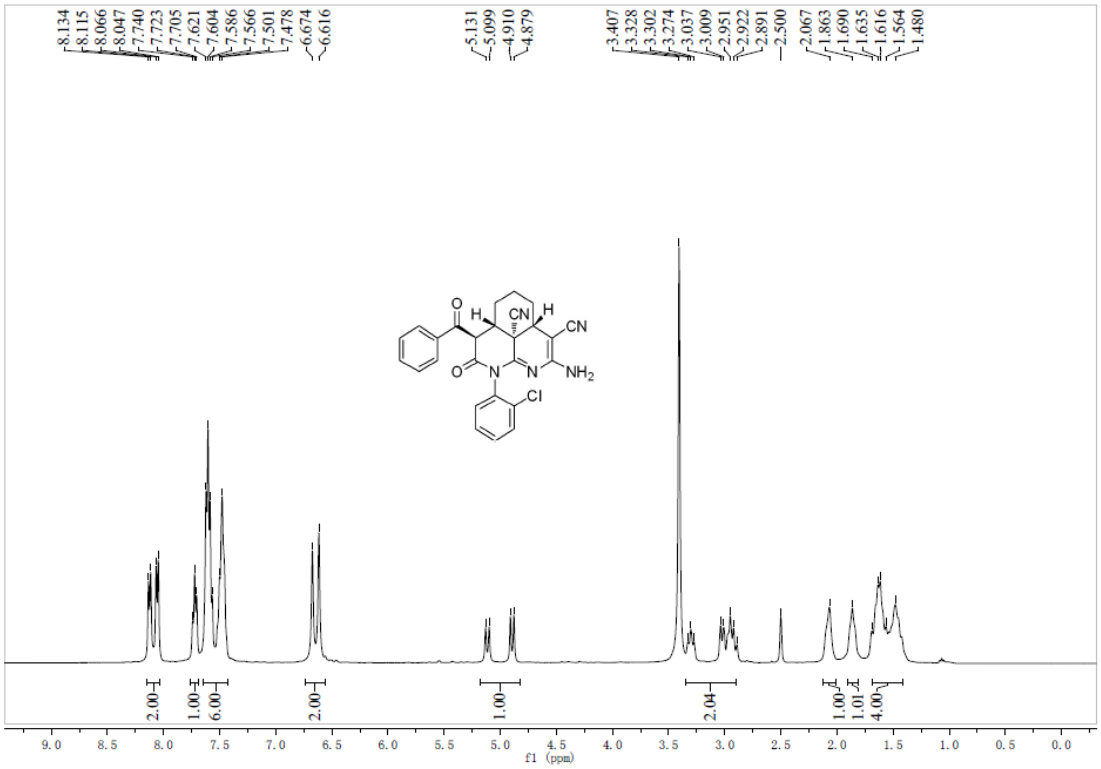
^{1}H NMR of compounds **4aq**



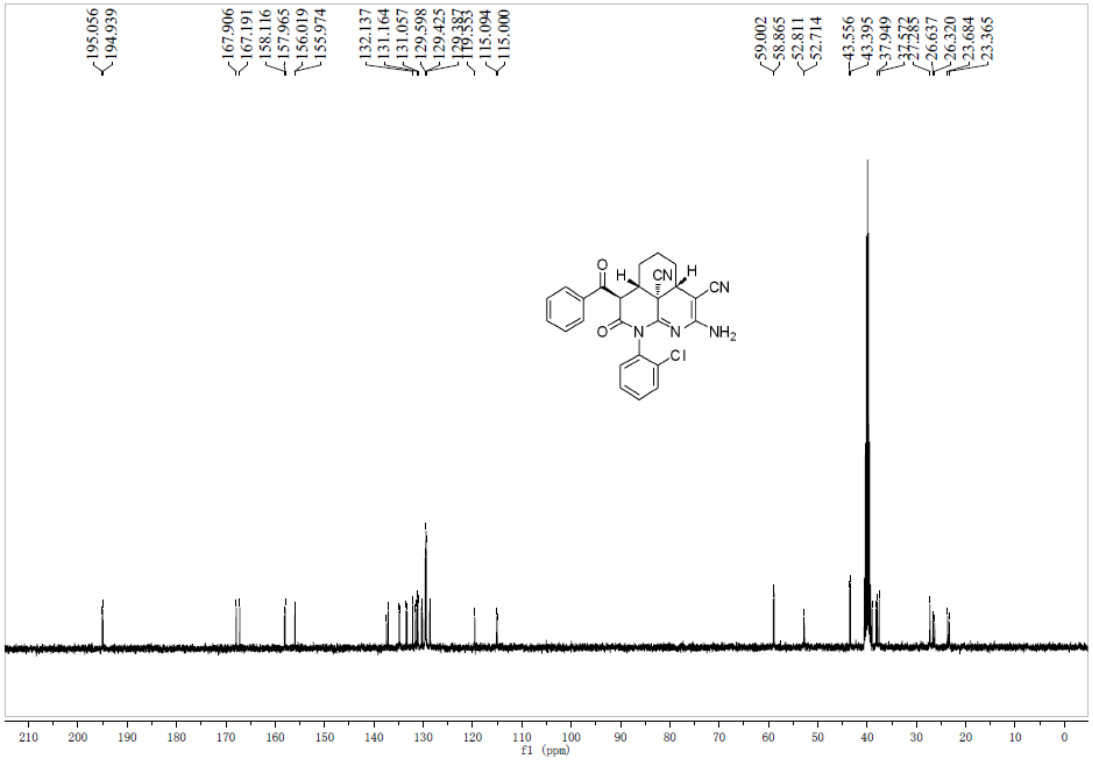
^{13}C NMR of compounds **4aq**



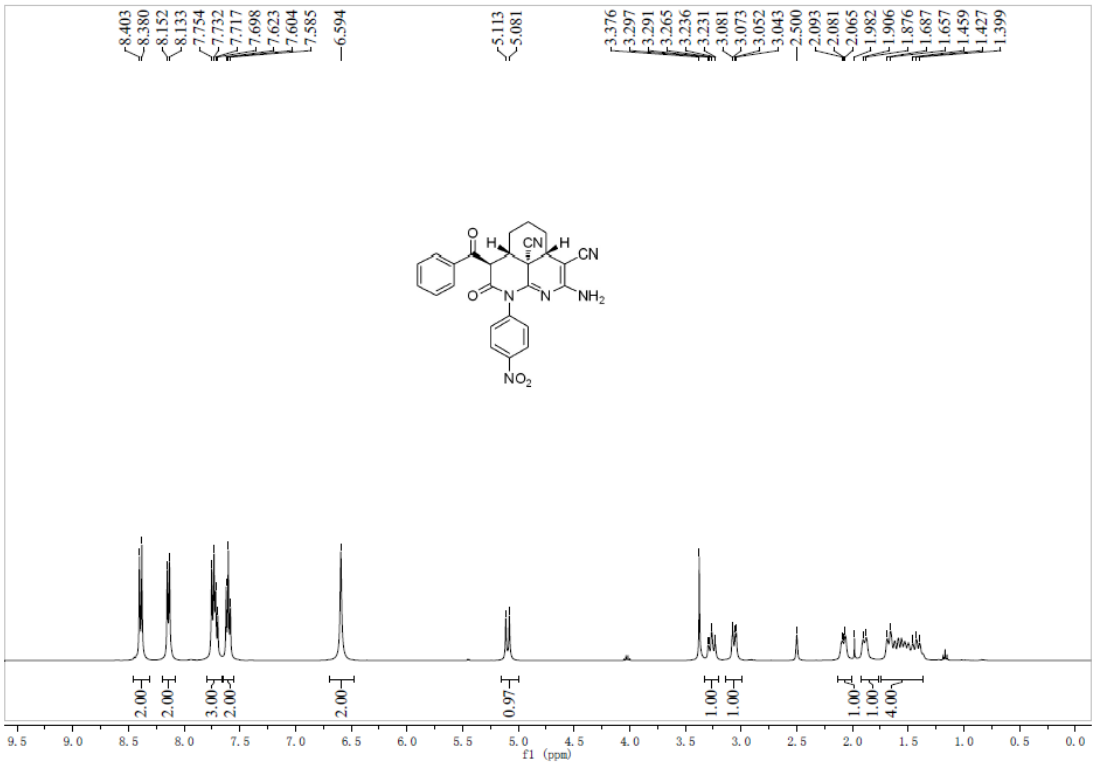
^{1}H NMR of compounds **4ar**



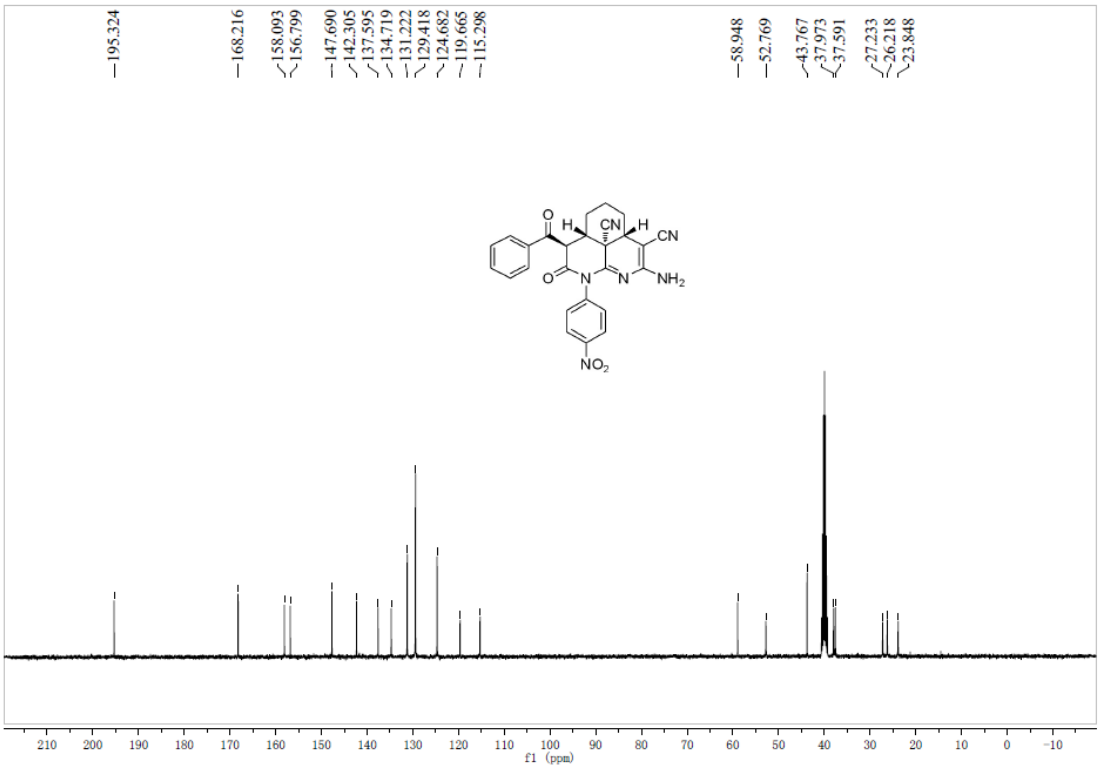
^{13}C NMR of compounds **4ar**



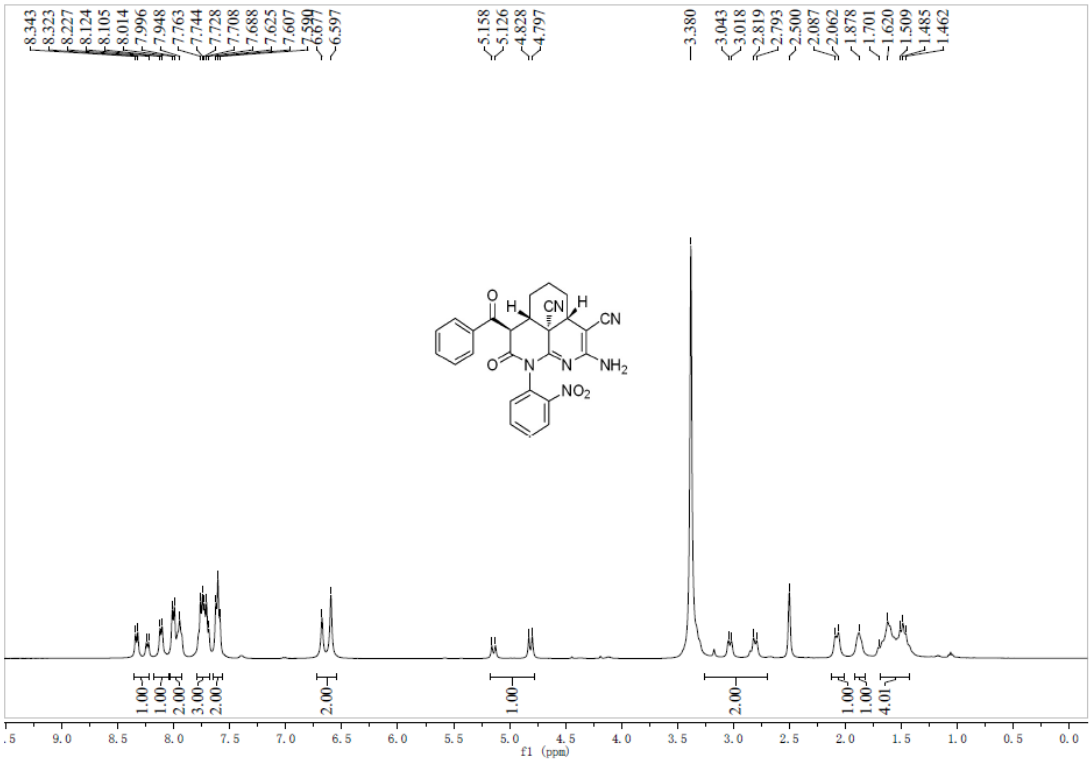
^{1}H NMR of compounds **4as**



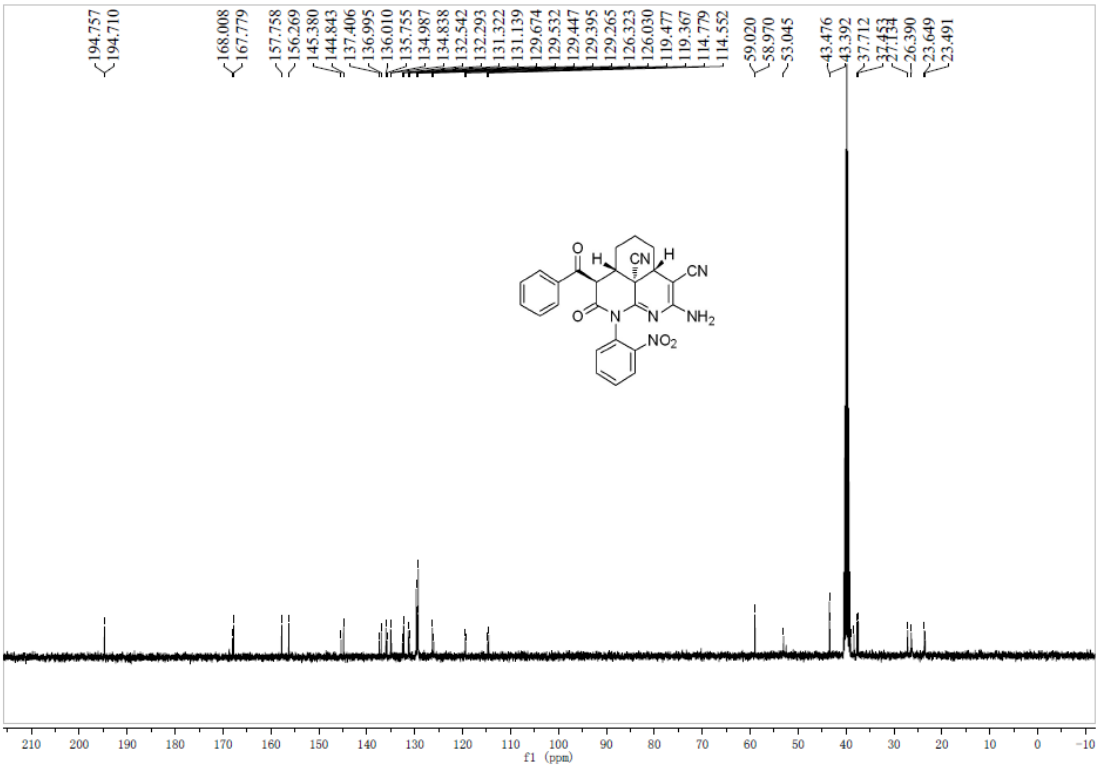
^{13}C NMR of compounds **4as**



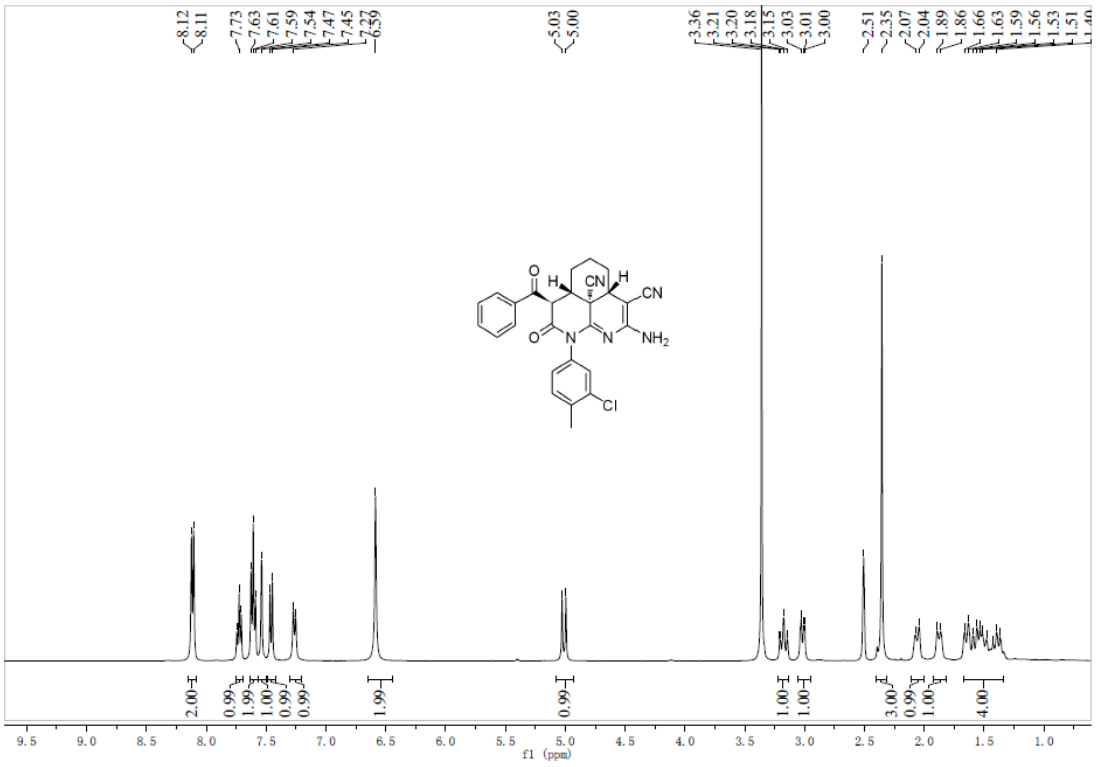
^{1}H NMR of compounds **4at**



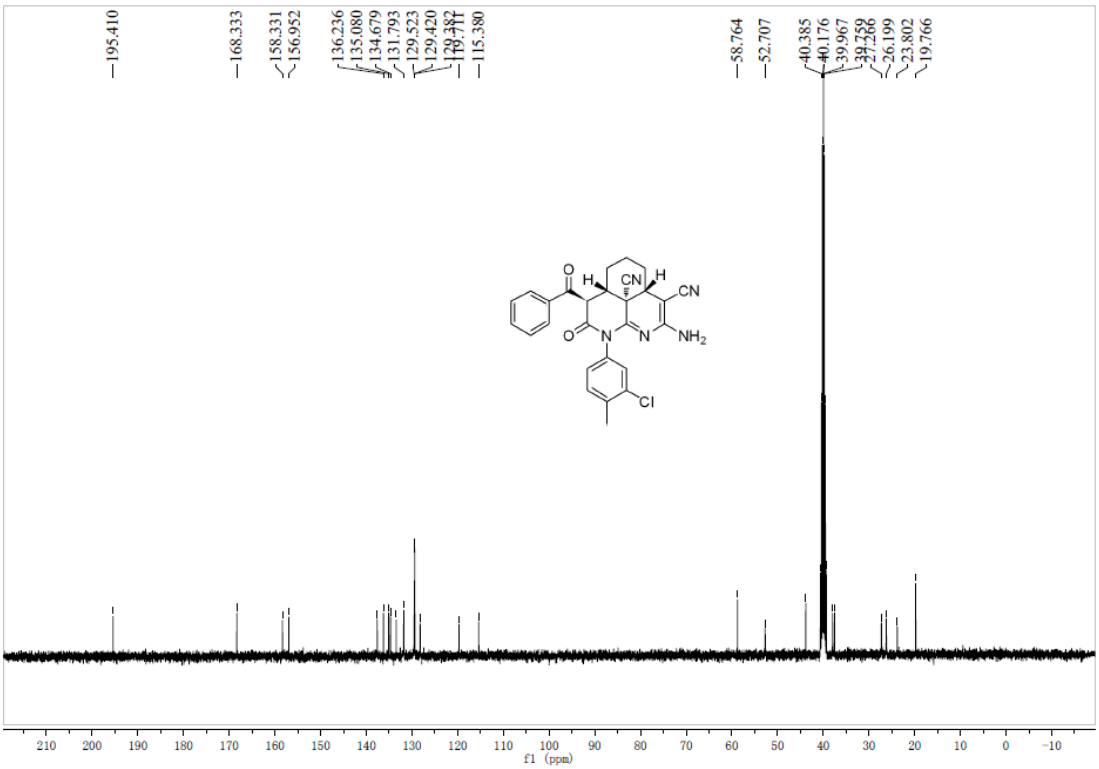
^{13}C NMR of compounds **4at**



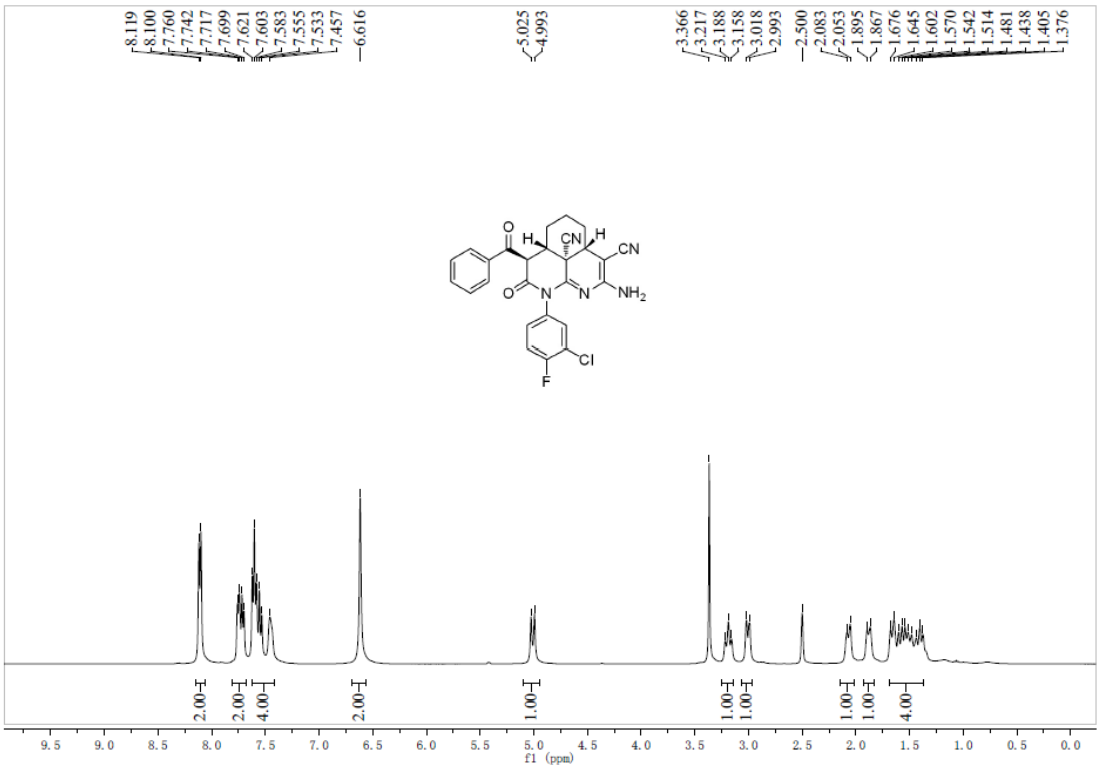
^{1}H NMR of compounds **4au**



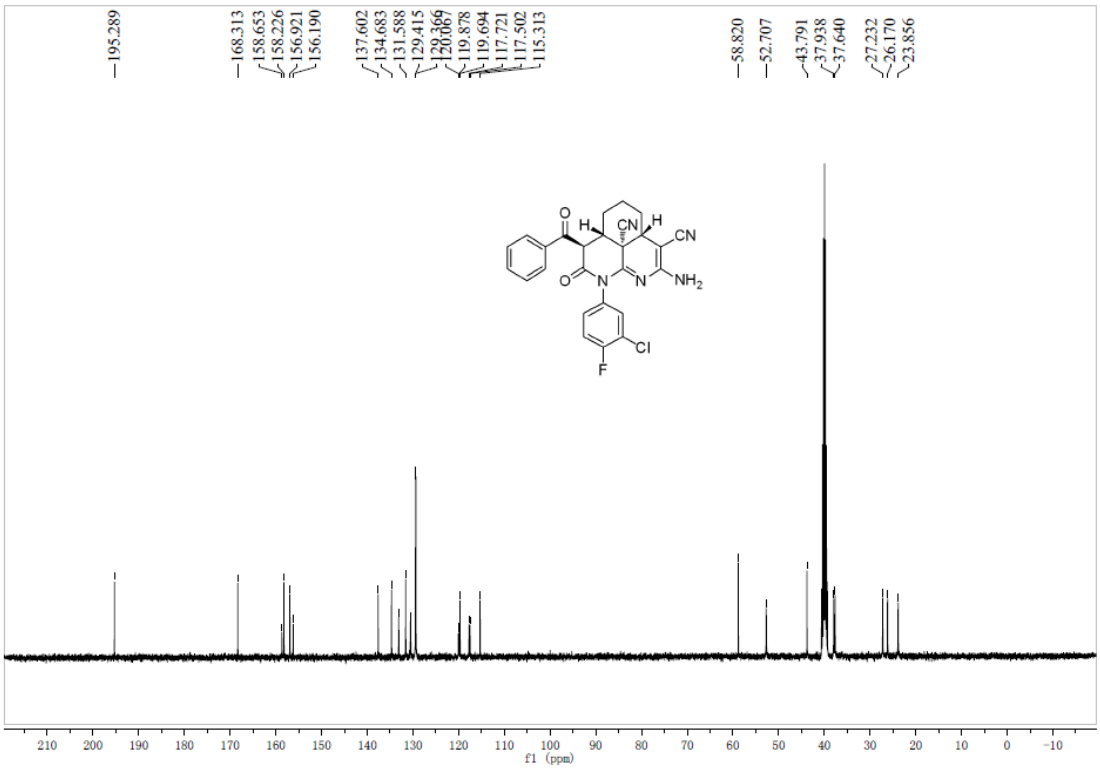
^{13}C NMR of compounds **4au**



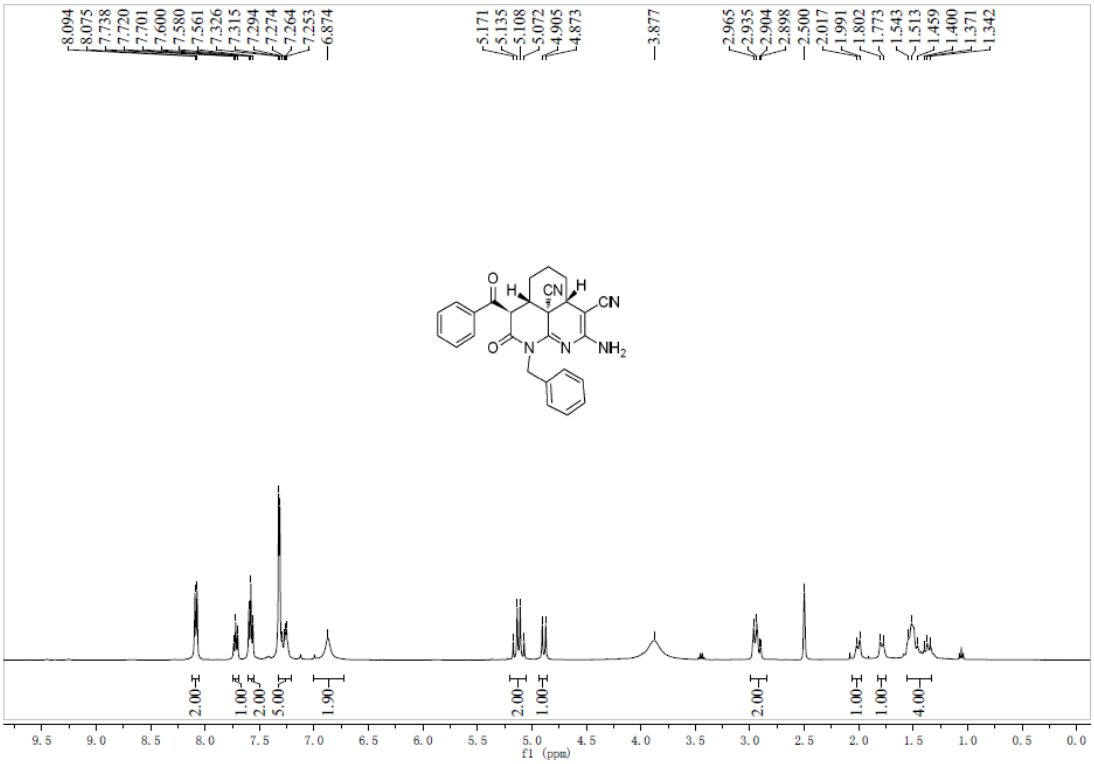
^{1}H NMR of compounds **4av**



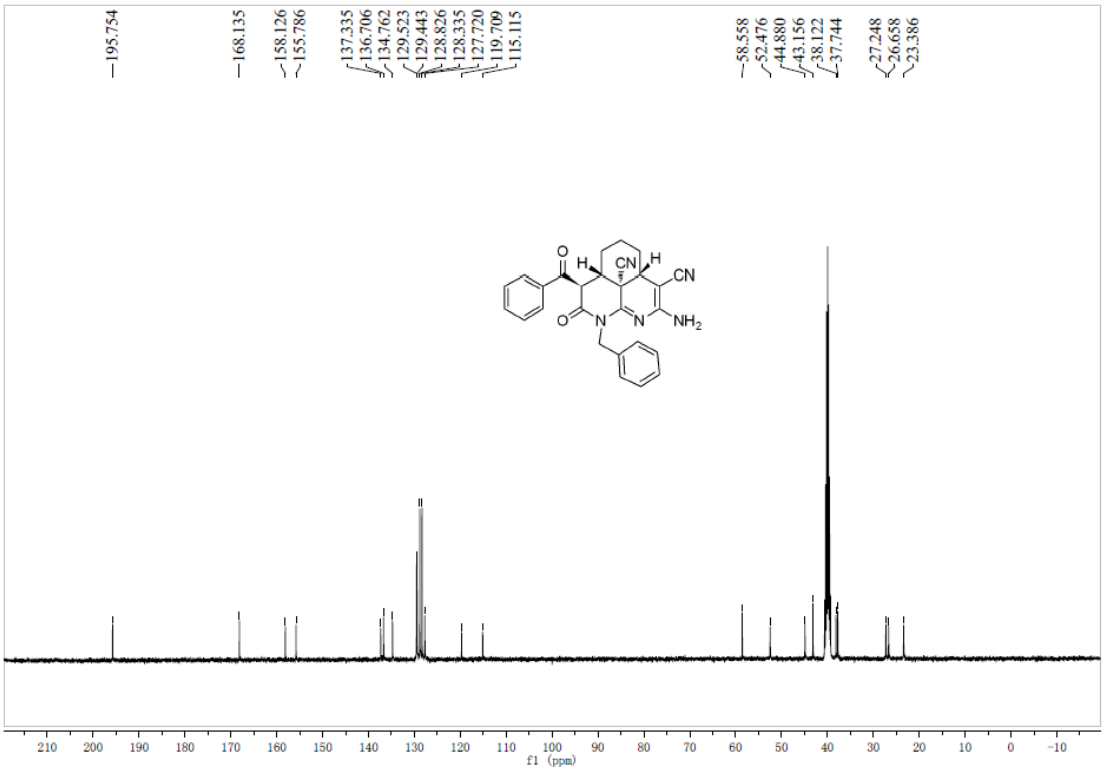
^{13}C NMR of compounds **4av**



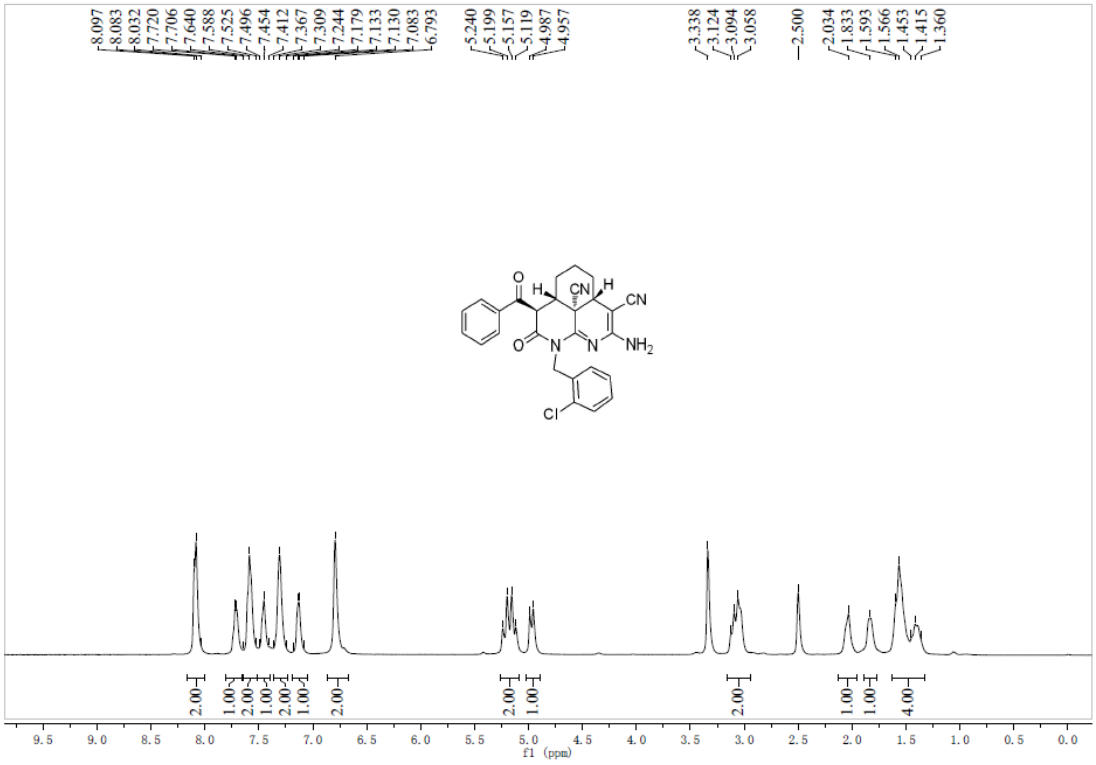
^{1}H NMR of compounds **4aw**



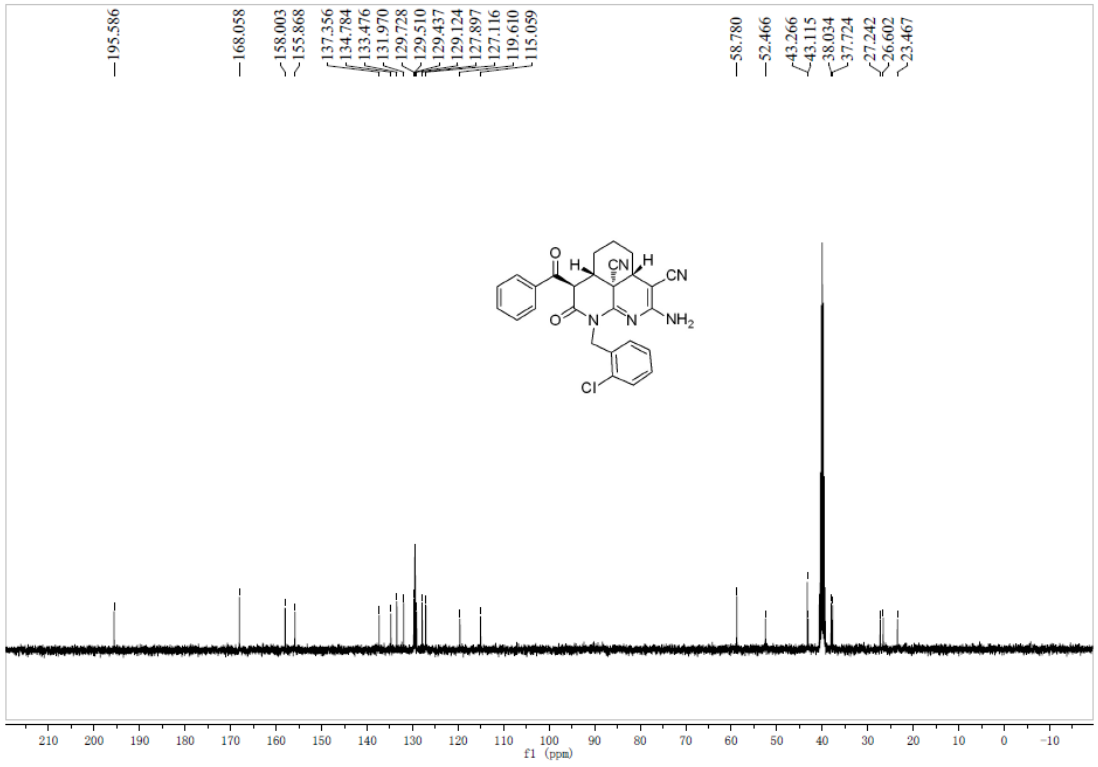
^{13}C NMR of compounds **4aw**



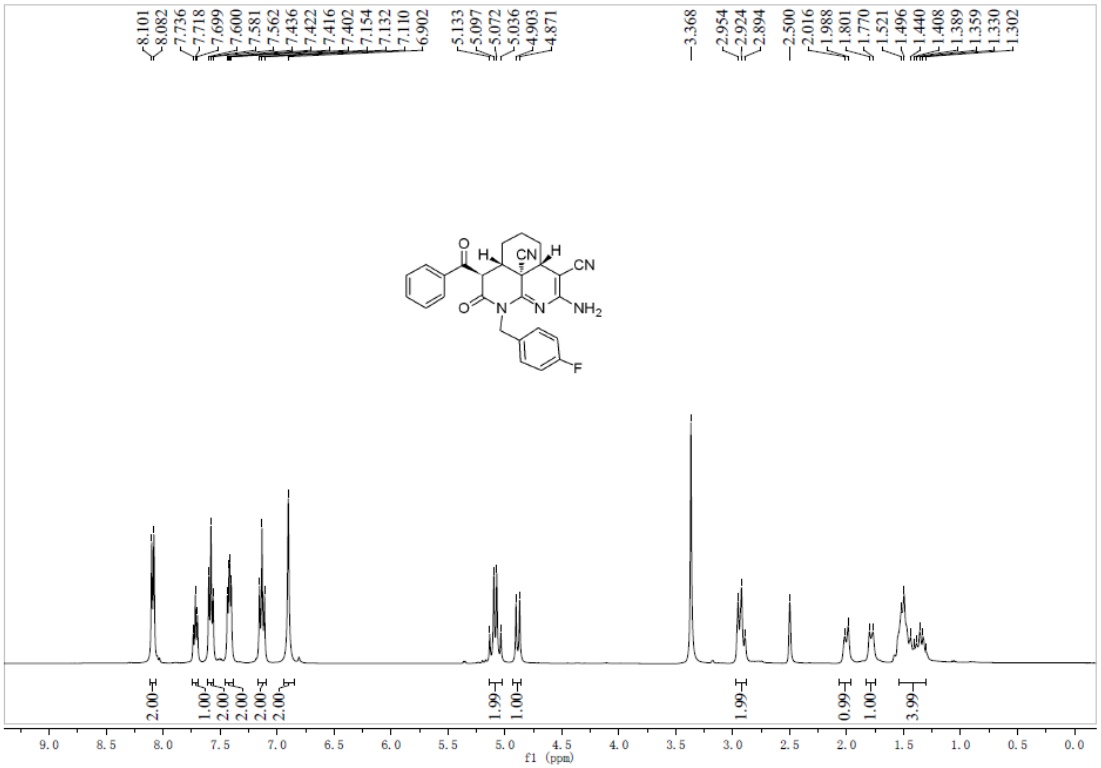
^{1}H NMR of compounds **4ax**



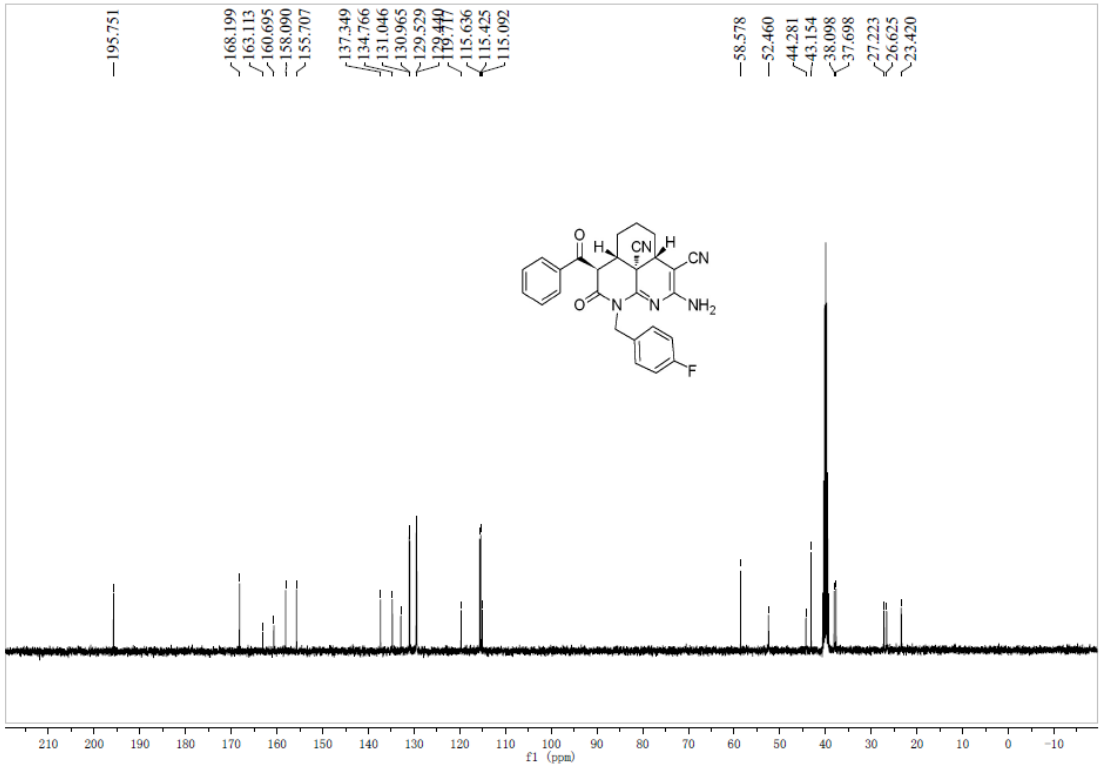
^{13}C NMR of compounds **4ax**



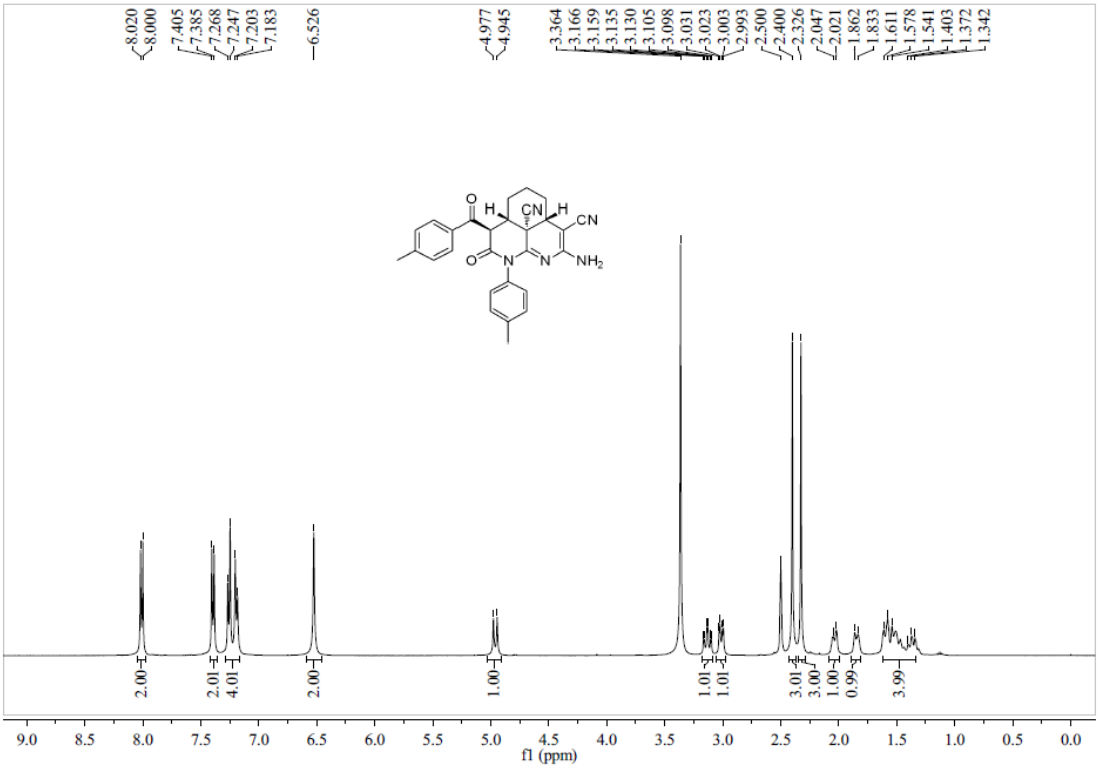
^{1}H NMR of compounds **4ay**



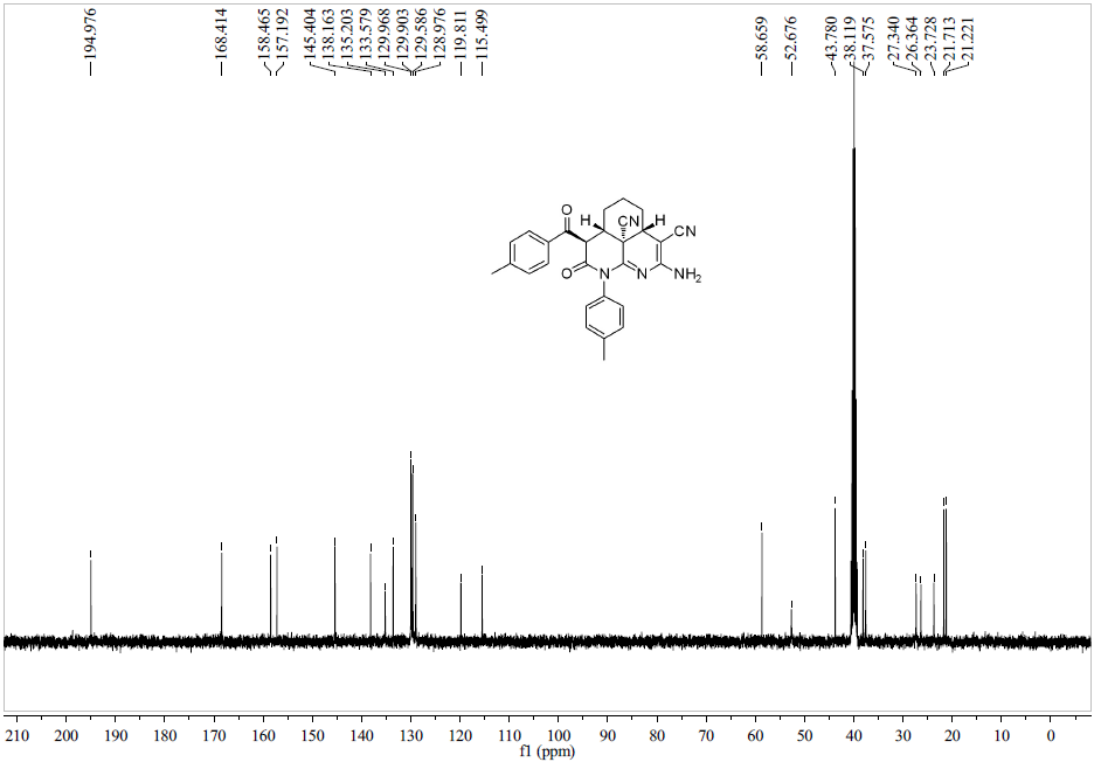
^{13}C NMR of compounds **4ay**



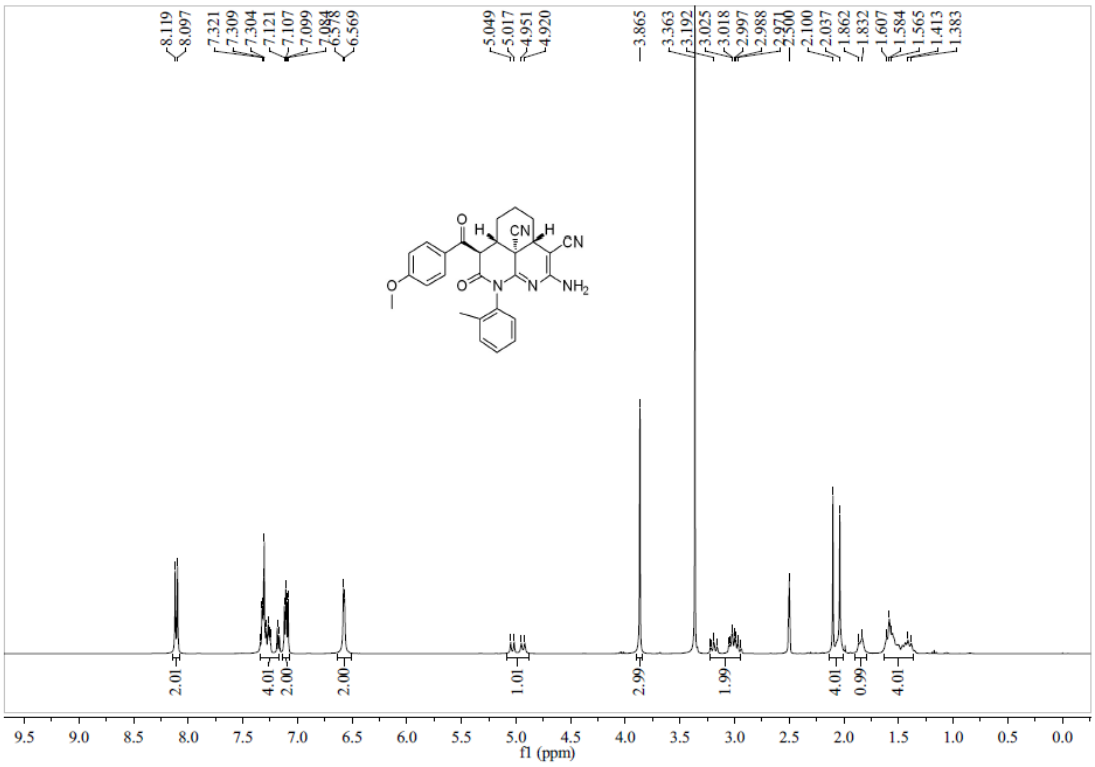
^{1}H NMR of compounds **4ba**



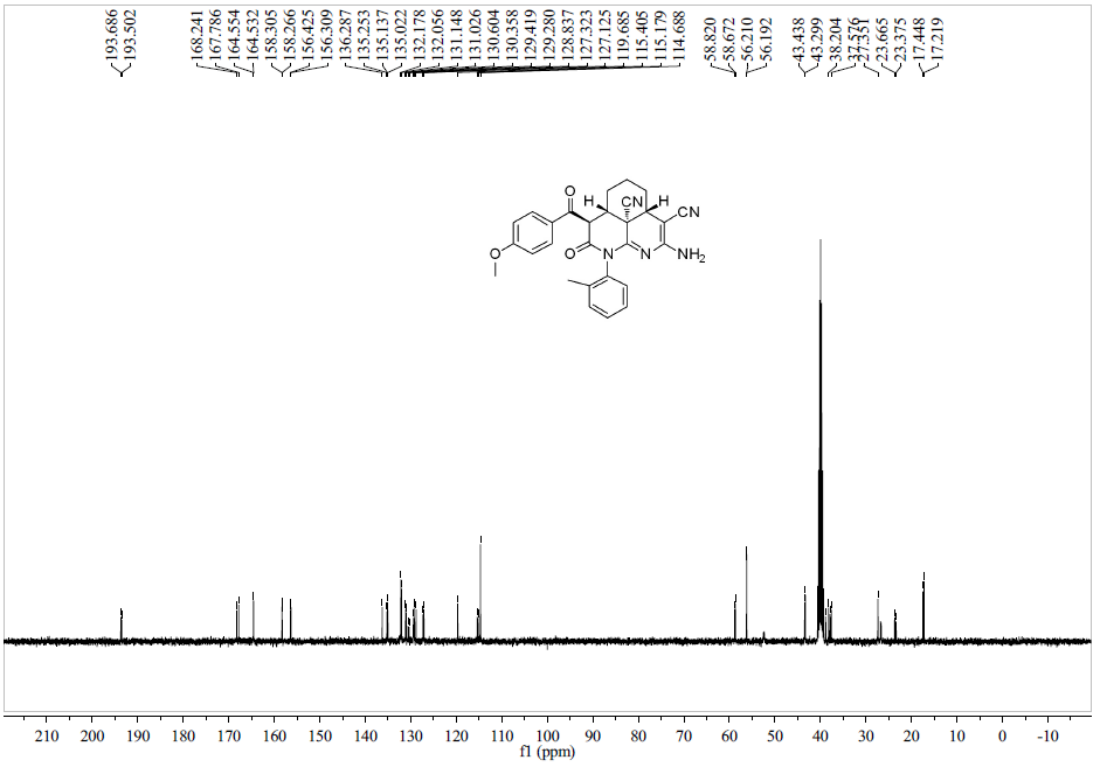
^{13}C NMR of compounds **4ba**



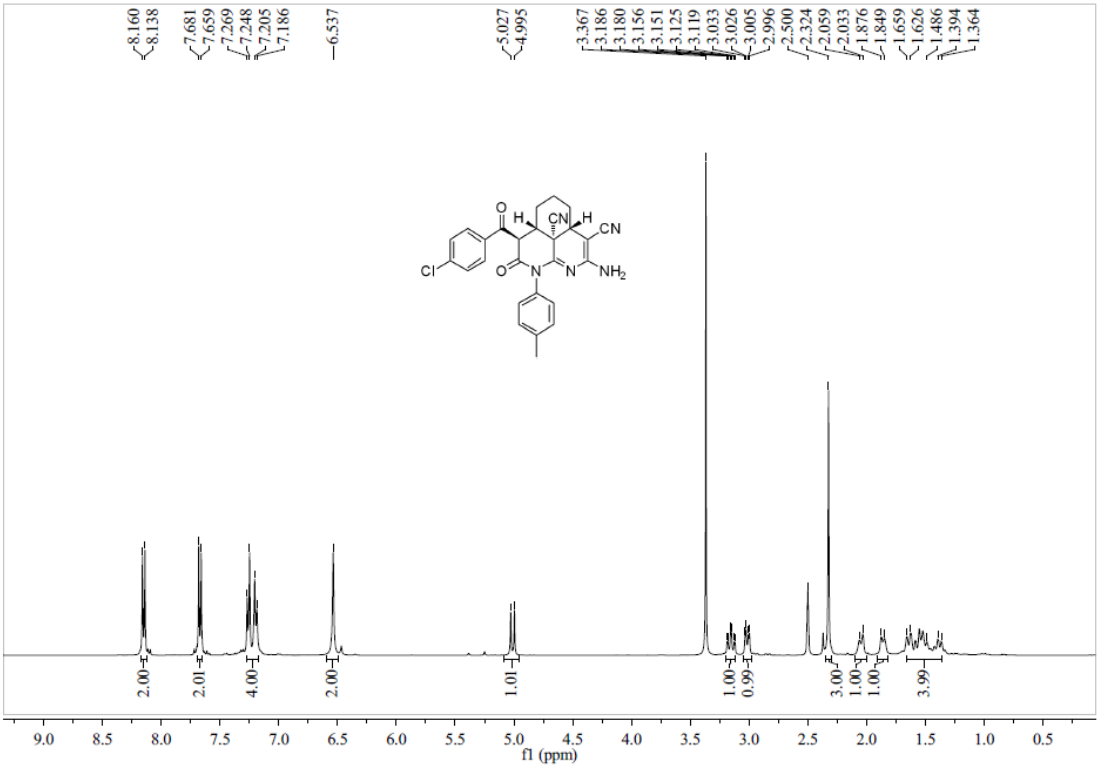
^{1}H NMR of compounds **4bb**



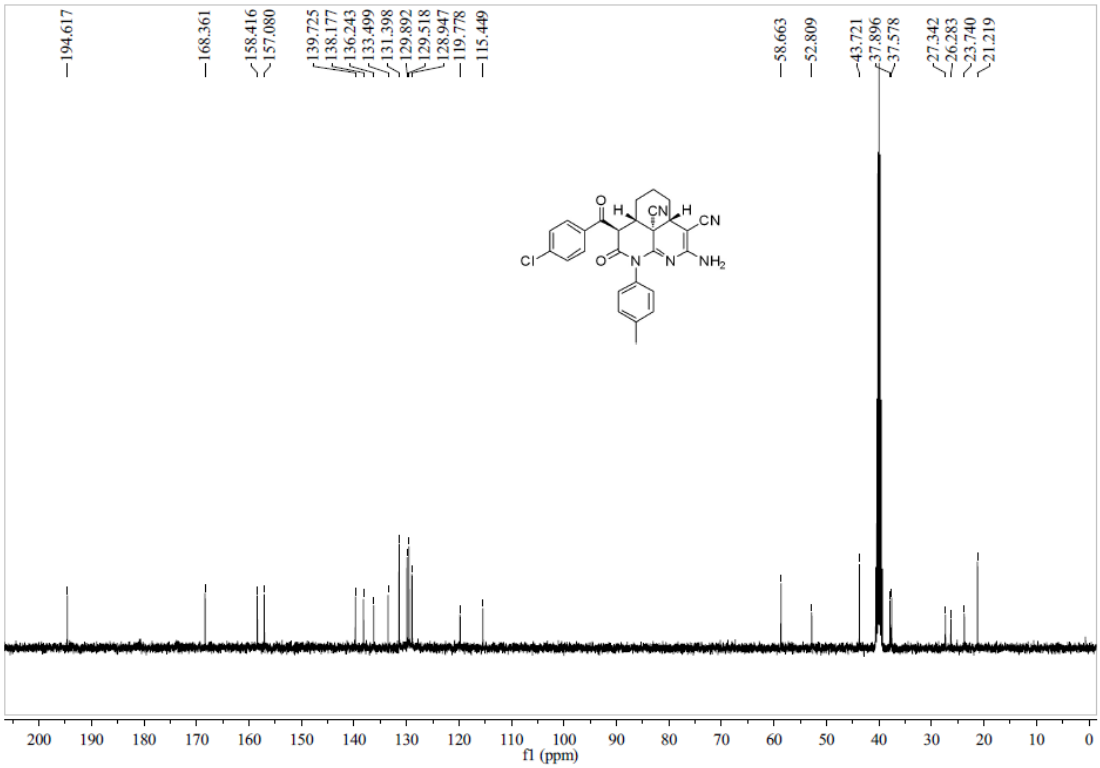
^{13}C NMR of compounds **4bb**



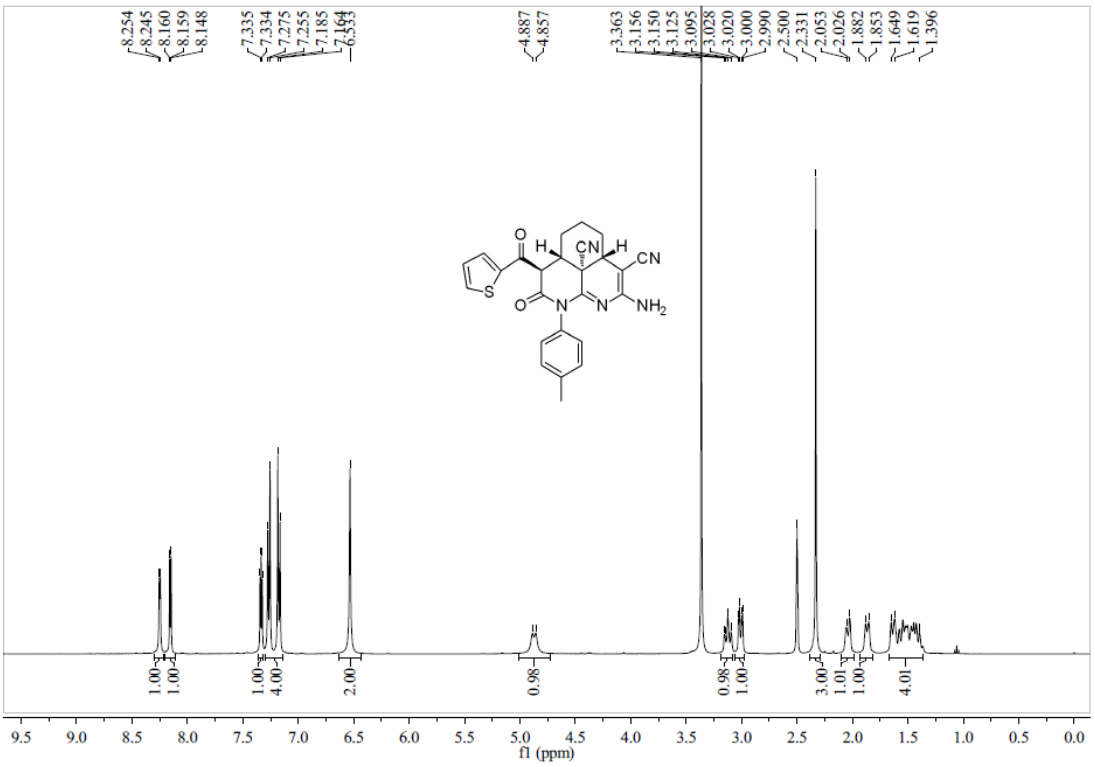
^{1}H NMR of compounds **4bc**



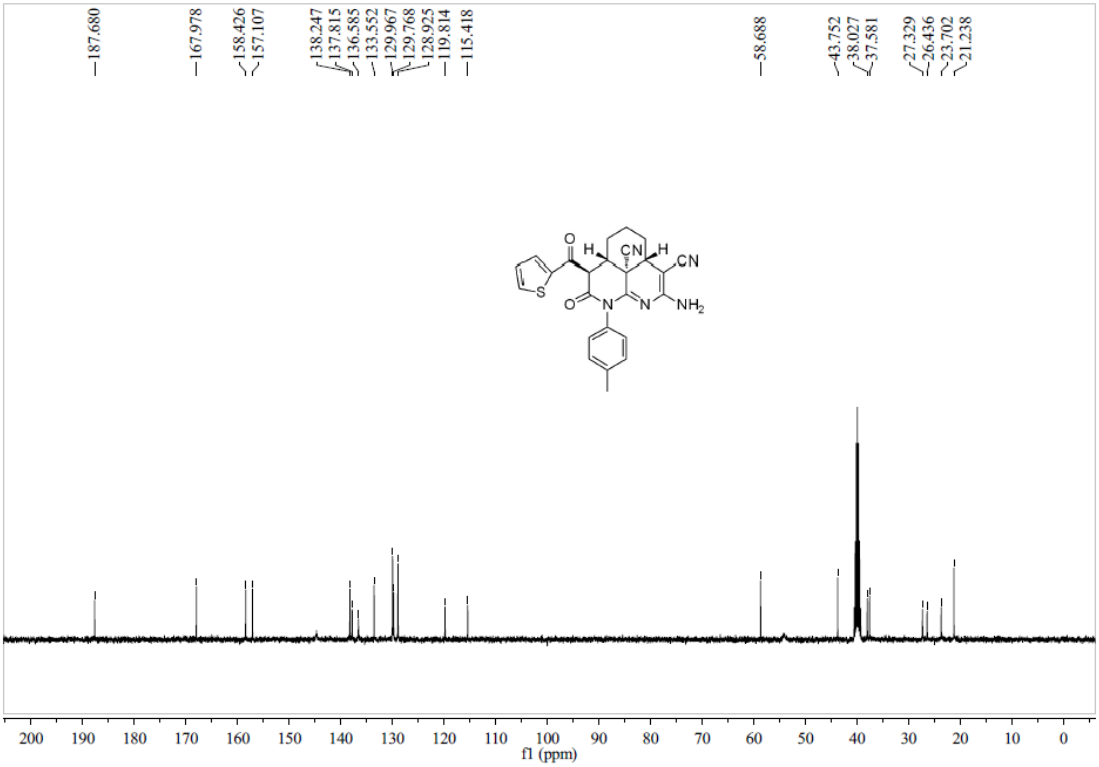
^{13}C NMR of compounds **4bc**



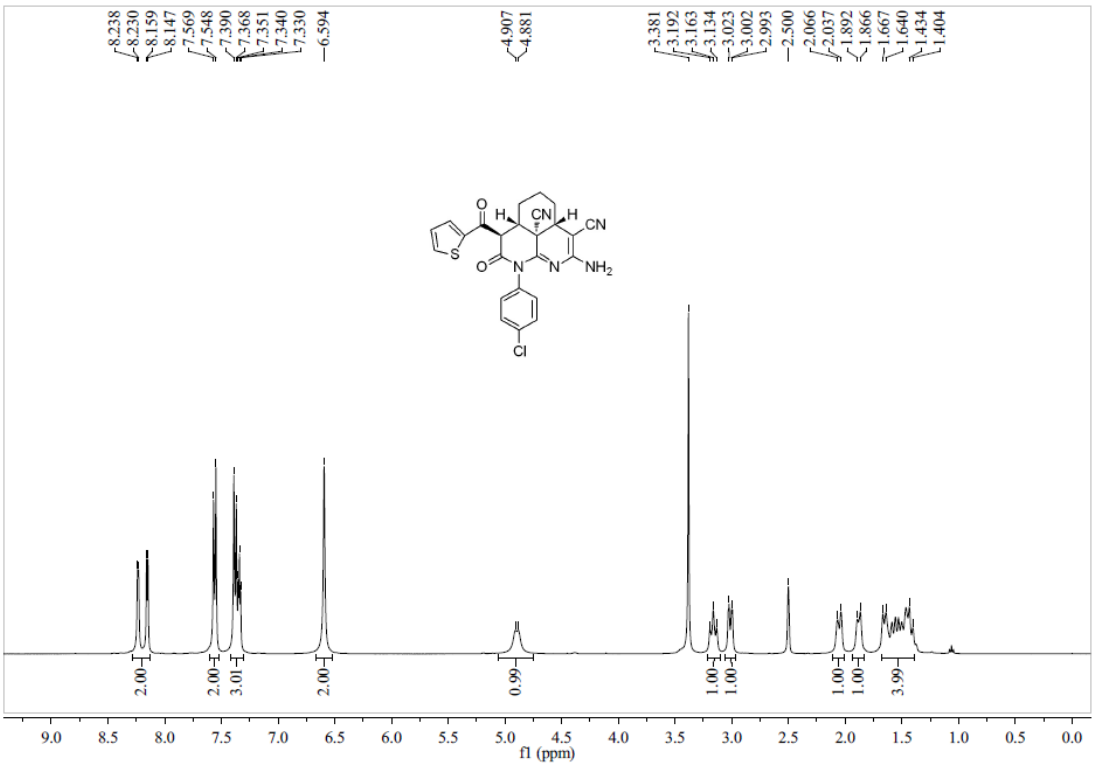
[1]H NMR of compounds **4bd**



[13]C NMR of compounds **4bd**



^{1}H NMR of compounds **4be**



^{13}C NMR of compounds **4be**