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Highly selective synthesis of functionalized polyhydroisoquinoline derivatives via three-component domino reaction

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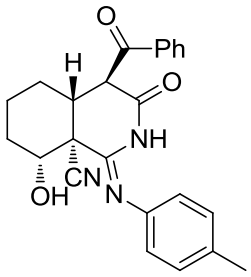
1. Experimental section

All reagents were obtained from commercial sources, and were used without further purification. Column chromatography was generally performed on silica gel (300-400 mesh) and reactions were monitored by thin-layer chromatography (TLC) using UV light to visualize the course of the reactions. IR spectra were recorded on a Varian F-1000 spectrometer in KBr with absorptions in cm^{-1}. ^{1}H NMR(400 MHz or 300 MHz) and ^{13}C NMR(100 MHz or 75 MHz) spectra were recorded on a Bruker Avance Ⅲ HD-400 MHz, Varian Inova-300 MHz and Varian Inova-400 MHz in DMSO-d_6 solution. *J* values are in Hz. Chemical shifts are expressed in ppm downfield from internal standard TMS. High-resolution mass spectra (HRMS) for all the compounds were determined on Bruker MicrOTOF-QII mass spertrometer with ESI resource. X-Ray diffraction analysis were recorded on a Rigaku Mercury CCD/AFC diffractometer.

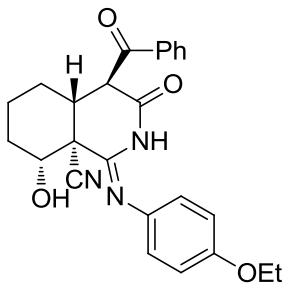
2. General procedure

A mixture of glutaraldehyde **1** (1.0 mmol), malononitrile **2** (1.0 mmol) and ß-keto amide **3** (1.0 mmol)was introduced in a 5 mL vial with EtOH (2 mL) as solution and 10 mmol% Et_3N. The reaction vial was closed and prestirred for 20 s. The mixture was irradiated at 100 ^{o}C. The reaction was monitored by TLC. After the completion, the reaction mixture was then cooled to room temperature, then filtered, the precipitate was collected and purified by recrystallization from 95% EtOH or by flash column chromatography (petroleum ether : ethyl acetate = 3:1), The analytical data for represent compounds are shown below.

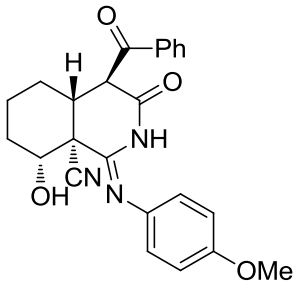
3. Characterizations for all compounds



(*Z*)-4-Benzoyl-8-hydroxy-3-oxo-1-(*p*-tolylimino)decahydroisoquinoline-8a-carbonitrile (4a) white solid (75%); m.p.: 206-208 ℃; IR (KBr, cm^{-1}) *v*: 3356, 3188, 3085, 2938, 2866, 2369, 2234, 1688, 1666, 1507, 1446, 1336, 1277, 1225, 1120, 1082, 950, 840, 820, 763, 686; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 10.56 (s, 1H, NH), 8.08 (d, *J* = 7.6 Hz, 2H, ArH), 7.72 (t, *J* = 7.2 Hz, 1H, ArH), 7.60 (t, *J* = 7.2 Hz, 2H, ArH), 7.21-6.99 (m, 4H, ArH), 5.70 (s, 1H, OH), 4.65 (d, *J* = 11.6 Hz, 1H, CH), 4.32-4.30 (m, 1H, CH), 2.91-2.86 (m, 1H, CH), 2.30 (s, 3H, CH_3), 1.98-1.96 (m, 1H, CH_2), 1.66-1.57 (m, 2H, CH_2), 1.44-1.32 (m, 3H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 196.7, 137.4, 134.6, 130.1, 129.6, 129.4, 122.0, 116.8, 71.0, 53.6, 49.4, 39.0, 31.2, 27.6, 22.0, 21.0; HRMS calcd for $C_{24}H_{22}N_3O_3$ [M-H]:$^-$ 400.1661, found: 400.1656.

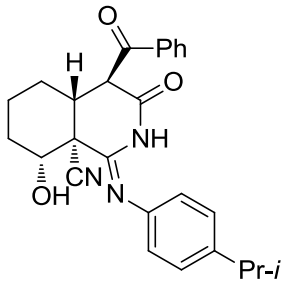


(*Z*)-4-Benzoyl-1-((4-ethoxyphenyl)imino)-8-hydroxy-3-oxo decahydroisoquinoline-8a-carbonitrile (4b) white solid (71%); m.p.: 162-163 ℃; IR (KBr, cm^{-1}) *v*:3360, 3145, 2940, 2876, 2184, 1683, 1665, 1510, 1446, 1397, 1334, 1276, 1251, 1118, 1083, 1084, 950, 840, 766; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 9.72 (s, 1H, NH), 8.09 (d, *J* = 7.2 Hz, 2H, ArH), 7.72 (t, *J* = 7.2 Hz, 1H, ArH), 7.60 (t, *J* = 7.6 Hz, 2H, ArH), 7.17-6.91 (m, 4H, ArH), 5.75 (s, 1H, OH), 4.66 (d, *J* = 11.6 Hz, 1H, CH), 4.32-4.30 (m, 1H, CH), 4.04-3.98 (m, 2H, CH_2), 2.89 (t, *J* = 10.4 Hz, 1H, CH), 2.00-1.97 (m, 1H, CH_2), 1.68-1.59 (m, 2H, CH_2), 1.44-1.31 (m, 6H, CH_2 + CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 196.8, 156.5, 137.4, 134.6, 129.6, 129.4, 123.5, 116.8, 115.3, 71.1, 63.7, 53.7, 31.3, 27.6, 22.1, 15.1; HRMS calcd for $C_{25}H_{24}N_3O_4$ [M-H]:$^-$ 430.1767, found: 430.1763.

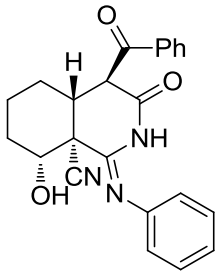


(*Z*)-4-Benzoyl-8-hydroxy-1-((4-methoxyphenyl)imino)-3-oxodecahydroisoquinoline-8a-carbonitrile (4c) white solid (75%); m.p.: 204-205 ℃; IR (KBr, cm^{-1}) *v*: 3355, 3188, 3085, 2932, 2869, 2183, 1683, 1664, 1507, 1446, 1336, 1277, 1247, 1226, 1120, 1082, 1031, 950, 839, 787, 765; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 10.42 (s, 1H, NH),

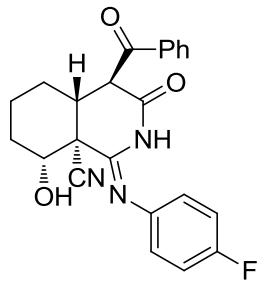
8.08 (d, *J* = 7.6 Hz, 2H, ArH), 7.72 (t, *J* = 7.2 Hz, 1H, ArH), 7.60 (t, *J* = 7.6 Hz, 2H, ArH), 7.15-6.96 (m, 4H, ArH), 5.73 (s, 1H, OH), 4.64 (d, *J* = 11.6 Hz, 1H, CH), 4.31-4.29 (m, 1H, CH), 3.36 (s, 3H, OCH_3), 2.91-2.86 (m, 1H, CH), 1.99-1.96 (m, 1H, CH_2), 1.68-1.58 (m, 2H, CH_2), 1.44-1.32 (m, 3H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 196.8, 157.2, 137.4, 134.6, 129.6, 129.4, 123.5, 116.8, 114.9, 71.0, 55.7, 53.7, 31.2, 27.6, 22.1; HRMS calcd for $C_{24}H_{22}N_3O_4$ [M-H]:$^-$ 416.1610, found :416.1605.



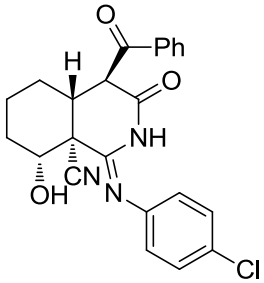
(*Z*)-4-Benzoyl-8-hydroxy-1-((4-isopropylphenyl)imino)-3-oxodecahydroisoquinoline-8a-carbonitrile (4d) white solid (78%); m.p.: 207-209 ℃; IR (KBr, cm^{-1}) *v*: 3359, 3192, 3084, 2955, 2869, 2366, 2233, 1686, 1654, 1507, 1446, 1335, 1279, 1120, 1108, 951, 841, 782, 758; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 9.92 (s, 1H, NH), 8.08 (d, *J* = 7.6 Hz, 2H, ArH), 7.72 (t, *J* = 7.2 Hz, 1H, ArH), 7.60 (t, *J* = 7.6 Hz, 2H, ArH), 7.27-7.12 (m, 4H, ArH), 5.74 (s, 1H, OH), 4.65 (d, *J* = 11.6 Hz, 1H, CH), 4.31-4.29 (m, 1H, CH), 2.90-2.85 (m, 2H, CH × 2), 1.99-1.96 (m, 1H, CH_2), 1.68-1.55 (m, 2H, CH_2), 1.44-1.32 (m, 3H, CH_2), 1.21 (s, 3H, CH_3), 1.20 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 196.7,137.4, 134.6, 129.6, 129.4, 127.4, 122.1, 116.8, 71.1, 53.7, 33.5, 31.2, 27.6, 24.4, 24.3, 22.0 ; HRMS calcd for $C_{26}H_{26}N_3O_3$ [M-H]:$^-$ 428.1974, found: 428.1953.



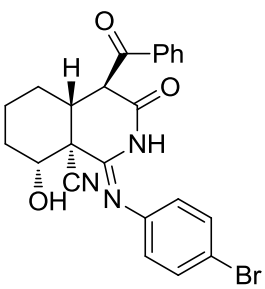
(*Z*)-4-Benzoyl-8-hydroxy-3-oxo-1-(phenylimino)decahydroisoquinoline-8a-carbonitrile (4e) white solid (70%); m.p.: 210-212 ℃; IR (KBr, cm^{-1}) *v*: 3388, 3181, 3079, 2935, 2874, 2186, 1685, 1668, 1596, 1447, 1339, 1276, 1228, 1195, 115, 1082, 952, 828, 779, 764, 689; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 10.52 (s, 1H, NH), 8.09 (d, *J* = 7.6 Hz, 2H, ArH), 7.73 (t, *J* = 7.6 Hz, 1H, ArH), 7.60 (t, *J* = 7.6 Hz, 2H, ArH), 7.39 (t, *J* = 8.0 Hz, 2H, ArH), 7.19-7.16 (m, 3H, ArH), 5.71 (s, 1H, OH), 4.67 (d, *J* = 11.2 Hz, 1H, CH), 4.32-4.30 (m, 1H, CH), 2.90 (t, *J* = 10.4 Hz, 1H, CH), 1.99-1.96 (m, 1H, CH_2), 1.69-1.63 (m, 1H, CH_2), 1.60-1.57 (m, 1H, CH_2), 1.45-1.33 (m, 3H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 196.7, 137.3, 134.7, 129.6, 129.5, 125.4, 122.0, 116.8, 71.0, 53.6, 49.6, 31.3, 27.6, 22.0; HRMS calcd for $C_{23}H_{20}N_3O_3$ [M-H]:$^-$ 386.1505, found: 386.1520.



(*Z*)-4-Benzoyl-1-((4-fluorophenyl)imino)-8-hydroxy-3-oxod ecahydroisoquinoline-8a-carbonitrile (4f) white solid (67%); m.p.: 220-222 ℃; IR (KBr, cm^{-1}) *v*: 3374, 3178, 3074, 2938, 2865, 2237, 1714, 1696, 1597, 1503, 1450, 1338, 1278, 1228, 1117, 1082, 951, 838, 789, 768; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 10.29 (s, 1H, NH), 8.10 (d, *J* = 7.6 Hz, 2H, ArH), 7.73 (t, *J* = 7.6 Hz, 1H, ArH), 7.61 (t, *J* = 7.6 Hz, 2H, ArH), 7.24-7.16 (m, 4H, ArH), 6.01 (s, 1H, OH), 4.69 (d, *J* = 11.6 Hz, 1H, CH), 4.31-4.28 (m, 1H, CH), 2.93-2.88 (m, 1H, CH), 1.99-1.95 (m, 1H, CH_2), 1.69-1.67 (m, 1H, CH_2), 1.63-1.54 (m, 1H, CH_2), 1.45-1.33 (m, 3H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 196.6, 160.0 (*J* = 230 Hz), 137.3, 134.7, 129.7, 129.5, 123.8 (*J* = 7 Hz), 116.8, 116.3 (*J* = 22 Hz), 70.9, 53.6, 50.0, 49.9, 38.8, 31.0, 27.5, 22.0; HRMS calcd for $C_{23}H_{19}FN_3O_3$ $[M-H]^{-\cdot}$ 404.1410, found: 404.1412.

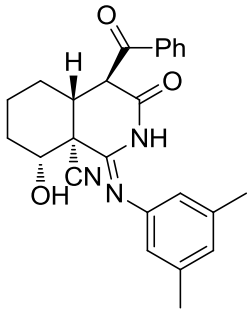


(Z)-4-Benzoyl-1-((4-chlorophenyl)imino)-8-hydroxy-3-oxod ecahydroisoquinoline-8a-carbonitrile (4g) white solid (78%); m.p.: 222-224 ℃; IR (KBr, cm^{-1}) *v*:3415, 3142, 2941, 2200, 1692, 1668, 1523, 1487, 1384, 1276, 1226, 1119, 1084, 952, 840, 779, 755; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 10.68 (s, 1H, NH), 8.09 (d, *J* = 7.6 Hz, 2H, ArH), 7.73 (t, *J* = 7.2 Hz, 1H, ArH), 7.60 (t, *J* = 7.6 Hz, 2H, ArH), 7.43 (d, *J* = 8.4 Hz, 2H, ArH), 7.09-6.89 (m, 2H, ArH), 5.68 (s, 1H, OH), 4.68 (d, *J* = 11.6 Hz, 1H, CH), 4.30-4.28 (m, 1H, CH), 2.94-2.88 (m, 1H, CH), 1.97-1.94 (m, 1H, CH_2), 1.68-1.66 (m, 1H, CH_2), 1.61-1.52 (m, 1H, CH_2), 1.44-1.32 (m, 3H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 196.5, 137.3, 134.7, 129.7, 129.6, 129.5, 129.4, 127.9, 123.7, 116.8, 70.9, 53.5, 50.0, 38.7, 30.9, 27.5, 22.0; HRMS calcd for $C_{23}H_{19}ClN_3O_3$ $[M-H]^{-}$ 420.1115, found: 420.1102

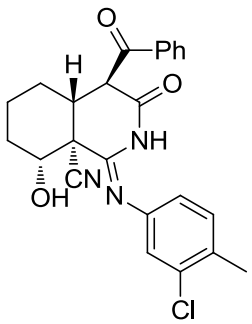


(*Z*)-4-Benzoyl-1-((4-bromophenyl)imino)-8-hydroxy-3-oxode cahydroisoquinoline-8a-carbonitrile (4h) white solid (69%); m.p.: 230-231 ℃; IR (KBr, cm^{-1}) *v*: 3312, 3190, 3085, 2941, 2867, 2370, 1686, 1665, 1484, 1446, 1335, 1277, 1227, 1120, 1082, 838, 780; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 10.46 (s, 1H, NH), 8.09 (d, *J* = 7.6 Hz, 2H, ArH), 7.73 (t, *J* = 6.8 Hz, 1H,

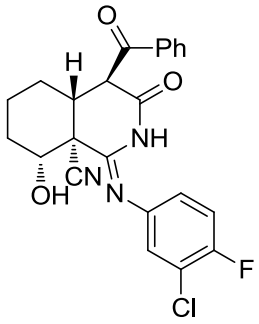
ArH), 7.62-7.50 (m, 4H, ArH), 7.05-6.83 (m, 2H, ArH), 5.77 (s, 1H, OH), 4.68 (d, *J* = 11.6 Hz, 1H, CH), 4.29-4.27 (m, 1H, CH), 2.93-2.88 (m, 1H, CH), 1.97-1.94 (m, 1H, CH_2), 1.68-1.66 (m, 1H, CH_2), 1.60-1.52 (m, 1H, CH_2), 1.40-1.32 (m, 3H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 196.5, 137.3, 134.7, 132.5, 129.7, 129.5, 129.4, 124.2, 117.5, 116.8, 70.9, 53.2, 38.7, 30.9, 27.5, 24.5, 22.0; HRMS calcd for $C_{23}H_{19}BrN_3O_3$ $[M-H]^-$ 464.0610, found: 464.0610.



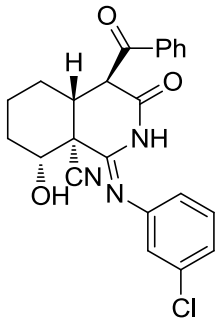
(*Z*)-4-Benzoyl-1-((3,5-dimethylphenyl)imino)-8-hydroxy-3-oxodecahydroisoquinoline-8a-carbonitrile (4i) white solid (75%); m.p.: 194-196 ℃; IR (KBr, cm^{-1}) *v*: 3341, 3092, 2938, 2203, 1713, 1666, 1597, 1447, 1357, 1279, 1221, 1121, 1083, 1043, 848, 756; ^1H NMR (400 MHz, DMSO-d_6) δ: 10.53 (s, 1H, NH), 8.09 (d, *J* = 8.0 Hz, 2H, ArH), 7.73 (t, *J* = 7.2 Hz, 1H, ArH), 7.60 (t, *J* = 7.6 Hz, 2H, ArH), 6.81-6.63 (m, 3H, ArH), 5.72 (s, 1H, OH), 4.66 (d, *J* = 11.6 Hz, 1H, CH), 4.30-4.28 (m, 1H, CH), 2.91-2.86 (m, 1H, CH), 2.27 (s, 6H, CH_3 × 2), 1.98-1.95 (m, 1H, CH_2), 1.69-1.66 (m, 1H, CH_2), 1.59-1.56 (m, 1H, CH_2), 1.44-1.32 (m, 3H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 196.6, 138.8, 137.4, 134.7, 129.6, 129.5, 126.9, 119.5, 119.4, 116.8, 71.2, 53.5, 31.0, 27.5, 22.0, 21.4; HRMS calcd for $C_{25}H_{24}N_3O_3$ $[M-H]^{-\cdot}$ 414.1818, found: 414.1813.



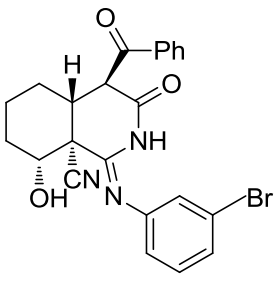
(*Z*)-4-Benzoyl-1-((3-chloro-4-methylphenyl)imino)-8-hydroxy-3-oxodecahydroisoquinoline-8a-carbonitrile (4j) white solid (66%); m.p.: 219-221 ℃; IR (KBr, cm^{-1}) *v*: 3349, 3198, 3086, 2944, 2872, 2233, 1685, 1669, 1594, 1492, 1447, 1335, 1279, 1122, 1083, 1047, 825, 789, 767; ^1H NMR (400 MHz, DMSO-d_6) δ: 10.46 (s, 1H, NH), 8.09 (d, *J* = 7.6 Hz, 2H, ArH), 7.73 (t, *J* = 7.2 Hz, 1H, ArH), 7.60 (t, *J* = 7.6 Hz, 2H, ArH), 7.34-7.21 (m, 2H, ArH), 6.94-6.92 (m, 1H, ArH), 5.74 (s, 1H, OH), 4.67 (d, *J* = 11.6 Hz, 1H, CH), 4.29-4.25 (m, 1H, CH), 2.95-2.89 (m, 1H, CH), 2.31 (s, 3H, CH_3), 1.97-1.94 (m, 1H, CH_2), 1.68-1.66 (m, 1H, CH_2), 1.60-1.52 (m, 1H, CH_2), 1.44-1.31 (m, 3H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 196.5, 137.3, 134.7, 133.9, 132.1, 131.9, 129.7, 129.5, 122.2, 120.8, 116.8, 70.9, 53.5, 50.1, 38.7, 30.9, 27.5, 22.0, 19.5; HRMS calcd for $C_{24}H_{21}ClN_3O_3$ $[M-H]^-$ 434.1271, found: 434.1271.



(*Z*)-4-Benzoyl-1-((3-chloro-4-fluorophenyl)imino)-8-hydroxy-3-oxodecahydroisoquinoline-8a-carbonitrile (4k) white solid (76%); m.p.: 217-218 ℃; IR (KBr, cm^{-1}) *v*:3368, 3204, 2946, 2873, 2203, 1667, 1496, 1337, 1279, 1259, 1121, 1083, 953, 825, 773; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 10.76 (s, 1H, NH), 8.09 (d, *J* = 7.6 Hz, 2H, ArH), 7.73 (t, *J* = 7.2 Hz, 1H, ArH), 7.62-7.59 (m, 2H, ArH), 7.40 (t, *J* = 8.8 Hz, 1H, ArH), 7.32 (s, 1H, ArH), 7.02 (s, 1H, ArH), 5.68 (s, 1H, OH), 4.69 (d, *J* = 11.6 Hz, 1H, CH), 4.28-4.24 (m, 1H, CH), 2.97-2.92 (m, 1H, CH), 1.97-1.94 (m, 1H, CH_2), 1.69-1.67 (m, 1H, CH_2), 1.59-1.51 (m, 1H, CH_2), 1.44-1.31 (m, 3H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 196.4, 155.1 (*J* = 241 Hz), 137.3, 134.8, 129.7, 129.5, 123.8, 122.4, 122.3, 120.3, 120.1, 120.0, 117.8 (*J* = 22 Hz), 116.8, 70.9, 53.4, 50.2, 38.5, 30.7, 27.4, 22.1; HRMS calcd for $C_{23}H_{18}ClFN_3O_3$ [M-H]:$^{-}$ 438.1021, found: 438.1026.

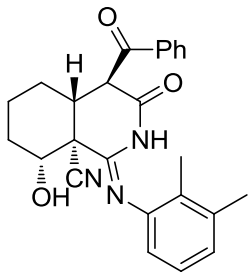


(*Z*)-4-Benzoyl-1-((3-chlorophenyl)imino)-8-hydroxy-3-oxodecahydroisoquinoline-8a-carbonitrile 4(l) white solid (75%); m.p.: 228-230 ℃; IR (KBr, cm^{-1}) *v*: 3362, 3191, 3077, 2953, 2865, 2344, 2234, 1694, 1665, 1615, 1446, 1350, 1279, 1227, 1119, 1082, 953, 881, 795, 786; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 10.79 (s, 1H, NH), 8.09 (d, *J* = 7.6 Hz, 2H, ArH), 7.73 (t, *J* = 7.6 Hz, 1H, ArH), 7.60 (t, *J* = 7.6 Hz, 2H, ArH), 7.39 (t, *J* = 8.0 Hz, 1H, ArH), 7.21-7.19 (m, 2H, ArH), 6.98 (s, 1H, ArH), 5.69 (s, 1H, OH), 4.68 (d, *J* = 11.6 Hz, 1H, CH), 4.29-4.25 (m, 1H, CH), 2.93 (t, *J* = 10.8 Hz, 1H, CH), 1.97-1.93 (m, 1H, CH_2), 1.69-1.66 (m, 1H, CH_2), 1.60-1.51 (m, 1H, CH_2), 1.45-1.31 (m, 3H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 196.5, 137.3, 134.8, 133.9, 131.3, 129.7, 129.5, 124.9, 121.8, 120.6, 116.8, 70.9, 53.5, 50.3, 38.6, 30.8, 27.5, 22.1; HRMS calcd for $C_{23}H_{19}ClN_3O_3$ [M-H]:$^{-}$ 420.1115, found: 420.1102.

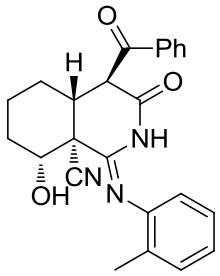


(Z)-4-Benzoyl-1-((3-bromophenyl)imino)-8-hydroxy-3-oxodecahydroisoquinoline-8a-carbonitrile (4m) white solid (70%); m.p.: 229-231 ℃; IR (KBr, cm^{-1}) *v*:3352, 3182, 3080, 2946, 2855, 2231, 1695, 1656, 1592, 1473, 1358, 1286, 1228, 1083, 952, 871; ^{1}H NMR (400 MHz, DMSO-d_6) δ:

10.76 (s, 1H, NH), 8.10 (d, *J* = 7.6 Hz, 2H, ArH), 7.73 (t, *J* = 7.2 Hz, 1H, ArH), 7.60 (t, *J* = 7.6 Hz, 2H, ArH), 7.33-7.30 (m, 3H, ArH), 7.03 (s, 1H, ArH), 5.76 (s, 1H, OH), 4.69 (d, *J* = 11.6 Hz, 1H, CH), 4.29-4.27 (m, 1H, CH), 2.97-2.92 (m, 1H, CH), 1.97-1.94 (m, 1H, CH_2), 1.69-1.52 (m, 2H, CH_2), 1.45-1.32 (m, 3H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 196.5, 137.3, 134.8, 131.5, 129.7, 129.5, 127.8, 124.6, 122.4, 121.0, 116.8, 70.9, 53.5, 38.5, 30.8, 27.5, 22.1; HRMS calcd for $C_{23}H_{20}BrN_3NaO_3$ [M+Na]:$^+$ 488.0586, found: 488.0597

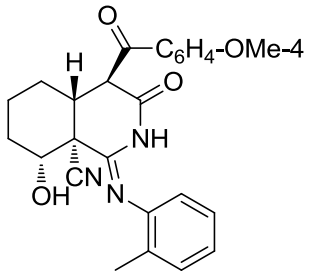


(*Z*)-4-Benzoyl-1-((2,3-dimethylphenyl)imino)-8-hydroxy-3-oxodecahydroisoquinoline-8a-carbonitrile (4n) white solid (67%); m.p.: 185-186 ℃; IR (KBr, cm^{-1}) *v*: 3449, 3196, 3070, 2940, 2858, 2368, 2236, 1696, 1664, 1593, 1580, 1446, 1334, 1273, 1258, 1229, 1194, 1080, 950, 801, 775^{1}H NMR (400 MHz, DMSO-d_6) δ: 10.36 (s, 1H, NH), 8.09 (d, *J* = 7.6 Hz, 2H, ArH), 7.75-7.71 (m, 1H, ArH), 7.62-7.58 (m, 2H, ArH), 7.10-7.07 (m, 1H, ArH), 6.98-6.96 (m, 1H, ArH), 6.73 (s, 1H, ArH), 5.83 (s, 1H, OH), 4.70 (d, *J* = 11.6 Hz, 1H, CH), 4.34-4.32 (m, 1H, CH), 2.91-2.86 (m, 1H, CH), 2.26 (s, 3H, CH_3), 2.00-1.96 (m, 4H, CH_2 + CH_3), 1.69-1.67 (m, 1H, CH_2), 1.60-1.53 (m, 1H, CH_2), 1.44-1.33 (m, 2H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 196.6, 137.4, 134.7, 131.0, 129.7, 129.5, 127.1, 125.3, 116.8, 71.3, 53.3, 49.7, 38.8, 30.8, 27.6, 22.0, 17.9; HRMS calcd for $C_{25}H_{24}N_3O_3$ [M-H]:$^-$ 414.1818, found: 414.1800.

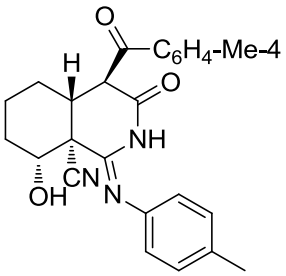


(*Z*)-4-Benzoyl-8-hydroxy-3-oxo-1-(o-tolylimino)decahydroisoquinoline-8a-carbonitrile (4o) white solid (65%); m.p.: 203-205 ℃; IR (KBr, cm^{-1}) *v*: 3434, 3182, 2938, 2874, 2187, 1681, 1596, 1446, 1337, 1274, 1255, 1229, 1192, 1113, 1083, 950, 772; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 10.55 (s, 1H, NH), 8.09 (d, *J* = 8.0 Hz, 2H, ArH), 7.73 (t, *J* = 7.2 Hz, 1H, ArH), 7.60 (t, *J* = 7.6 Hz, 2H, ArH), 7.24-7.18 (m, 2H, ArH), 7.09-7.06 (m, 1H, ArH), 6.89 (s, H, ArH), 5.79 (s, 1H, OH), 4.70 (d, *J* = 11.2 Hz, 1H, CH), 4.34-4.32 (m, 1H, CH), 2.90-2.85 (m, 1H, CH), 2.13 (s, 1H, CH_3), 1.99-1.96 (m, 1H, CH_2), 1.69-1.67 (m, 1H, CH_2), 1.61-1.55 (m, 1H, CH_2), 1.45-1.37 (m, 3H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 196.6,137.4, 134.7, 129.7, 129.5, 129.3, 127.1, 116.8, 71.4, 53.4, 38.7,

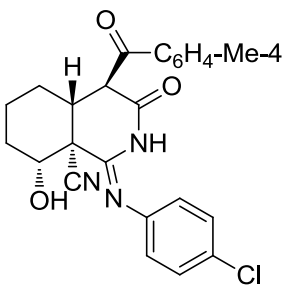
30.8, 27.5, 22.0, 17.9 ; HRMS calcd for $C_{24}H_{22}N_3O_3$ [M-H]:$^-$ 400.1661, found: 400.1659.



(*Z*)-8-Hydroxy-4-(4-methoxybenzoyl)-3-oxo-1-(*o*-tolylimino)decahydroisoquinoline-8a-carbonitrile (4p) white solid (70%); m.p.: 205-206 ℃; IR (KBr, cm^{-1}) *v*: 3448, 3223, 2932, 2861, 2248, 1703, 1654, 1596, 1330, 1272, 1233, 1168, 1115, 1077,1020, 831; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 10.38 (s, 1H, NH), 8.09 (d, *J* = 9.2 Hz, 2H, ArH), 7.24-7.18 (m, 2H, ArH), 7.12-7.05 (m, 4H, ArH), 5.86 (s, 1H, OH), 4.65 (d, *J* = 11.6 Hz, 1H, CH), 4.34-4.30 (m, 1H, CH), 3.88 (s, 3H, OCH_3), 2.88-2.82 (m, 1H, CH), 2.13 (s, 3H, CH_3), 1.99-1.96 (m, 1H, CH_2), 1.70-1.58 (m, 1H, CH_2), 1.44-1.32 (m, 3H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 194.5, 164.5, 132.2, 132.0, 131.0, 130.4, 127.1, 125.2, 116.9, 114.7, 71.3, 56.2, 53.0, 49.8, 30.9, 27.6, 22.0, 19.0, 17.9; HRMS calcd for $C_{25}H_{25}N_3NaO_4$ [M+Na]:$^+$ 454.1743, found: 454.1744

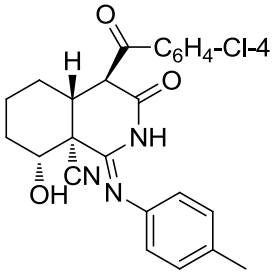


(*Z*)-8-Hydroxy-4-(4-methylbenzoyl)-3-oxo-1-(*p*-tolylimino)decahydroisoquinoline-8a-carbonitrile (4q) white solid (70%); m.p.: 210-211 ℃; IR (KBr, cm^{-1}) *v*:3358, 3176, 3082, 2932, 2867, 2184, 1681, 1606, 1508, 1449, 1337, 1279, 1258, 1227, 1121, 1085, 953, 818; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 9.76 (s, 1H, NH), 7.98 (d, *J* = 8.4 Hz, 2H, ArH), 7.40 (d, *J* = 8.4 Hz, 2H, ArH), 7.21-7.09 (m, 4H, ArH), 5.74 (s, 1H, OH), 4.60 (d, *J* = 11.2 Hz, 1H, CH), 4.31-4.27 (m, 1H, CH), 2.88-2.82 (m, 1H, CH), 2.41 (s, 3H, CH_3), 2.30 (s, 3H, CH_3), 1.98-1.94 (m, 1H, CH_2), 1.68-1.56 (m, 2H, CH_2), 1.41-1.30 (m, 3H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 196.1, 145.3, 135.0, 134.5, 130.1, 130.0, 129.8, 122.0, 116.9, 71.1, 53.5, 49.5, 39.1, 31.2, 27.6, 22.0, 21.7, 21.0; HRMS calcd for $C_{25}H_{25}N_3NaO_3$ [M+Na]:$^+$ 438.1794, found: 438.1804.

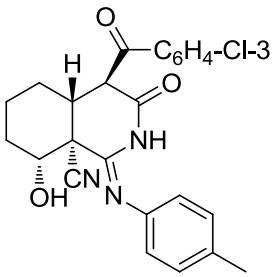


(*Z*)-1-((4-Chlorophenyl)imino)-8-hydroxy-4-(4-methylbenzoyl)-3-oxodecahydroisoquinoline-8a-carbonitrile (4r) white solid (68%); m.p.: 220-222 ℃; IR (KBr, cm^{-1}) *v*: 3366, 3165, 3077, 2926, 2870, 2236, 1652, 1598, 1481, 1444, 1331, 1274, 1220, 1121, 1084, 950, 840, 823; ^{1}H

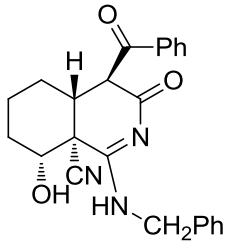
NMR (400 MHz, DMSO-d_6) δ:10.41 (s, 1H, NH), 7.99 (d, J = 8.0 Hz, 2H, ArH), 7.41 (t, J = 8.4 Hz, 4H, ArH), 7.11-6.88 (m, 2H, ArH), 6.18 (s, 1H, OH), 4.63 (d, J = 11.2 Hz, 1H, CH), 4.29-4.27 (m, 1H, CH), 2.90-2.85 (m, 1H, CH), 2.41 (s, 3H, CH_3), 1.96-1.93 (m, 1H, CH_2), 1.66-1.52 (m, 2H, CH_2), 1.42-1.31 (m, 3H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 195.9, 145.5, 134.9, 130.0, 129.8, 129.6, 129.3, 123.8, 116.8, 70.9, 53.4, 50.1, 38.8, 30.9, 27.6, 22.1, 21.7; HRMS calcd for $C_{24}H_{22}ClN_3NaO_3$ [M+Na]:$^+$ 458.1247, found: 458.1246.



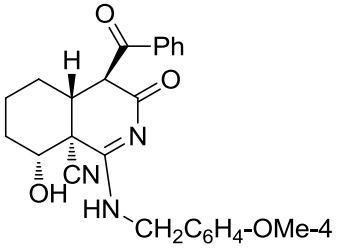
(*Z*)-4-(4-Chlorobenzoyl)-8-hydroxy-3-oxo-1-(*p*-tolylimino)decahydroisoquinoline-8a-carbonitrile (4s) white solid (65%); m.p.: 218-219 ℃; IR (KBr, cm^{-1}) v: 3176, 3082, 2938, 2864, 2273, 1686, 1661, 1588, 1507, 1400, 1336, 1278, 1256, 1085, 953, 841, 820; ^{1}H NMR (400 MHz, DMSO-d_6) δ:9.78 (s, 1H, NH), 8.12 (d, J = 8.8 Hz, 2H, ArH), 7.65 (d, J = 8.4 Hz, 2H, ArH), 7.21-7.12 (m, 4H, ArH), 5.74 (s, 1H, OH), 4.67 (d, J = 11.2 Hz, 1H, CH), 4.32-4.29 (m, 1H, CH), 2.92-2.86 (m, 1H, CH), 2.30 (s, 3H, CH_3), 1.99-1.96 (m, 1H, CH_2), 1.68-1.58 (m, 2H, CH_2), 1.44-1.32 (m, 3H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 195.7, 139.7, 136.0, 134.6, 131.6, 130.1, 129.5, 122.0, 116.7, 71.1, 53.7, 49.3, 39.0, 31.3, 27.5, 22.1, 21.0; HRMS calcd for $C_{24}H_{22}ClN_3NaO_3$ [M+Na]:$^+$ 458.1247, found: 458.1239.



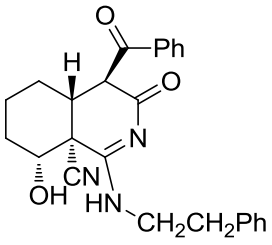
(*Z*)-4-(3-Chlorobenzoyl)-8-hydroxy-3-oxo-1-(*p*-tolylimino)decahydroisoquinoline-8a-carbonitrile (4t) white solid (74%); m.p.: 192-193 ℃; IR (KBr, cm^{-1}) v: 3365, 3183, 2945, 2867, 2344, 1685, 1668, 1569, 1508, 1339, 1280, 1257, 1199, 1118, 1083, 842; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 9.83 (s, 1H, NH), 8.14 (s, 1H, ArH), 8.06 (d, J = 7.6 Hz, 1H, ArH), 7.80-7.77 (m, 1H, ArH), 7.62 (t, J = 7.6 Hz, 1H, ArH), 7.21-7.12 (m, 4H, ArH), 5.67 (s, 1H, OH), 4.72 (d, J = 11.6 Hz, 1H, CH), 4.32-4.30 (m, 1H, CH), 2.92-2.87 (m, 1H, CH), 2.30 (s, 3H, CH_3), 1.99-1.96 (m, 1H, CH_2), 1.68-1.58 (m, 2H, CH_2), 1.45-1.35 (m, 3H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 195.8, 139.1, 134.3, 134.2, 131.3, 130.1, 129.3, 128.4, 122.0, 116.7, 71.1, 53.9, 27.4, 22.1, 21.0; HRMS calcd for $C_{24}H_{22}ClN_3NaO_3$ [M+Na]$^+$: 458.1247, found: 458.1239



4-Benzoyl-1-(benzylamino)-8-hydroxy-3-oxo-3,4,4a,5,6,7,8,8a-octahydroisoquinoline-8a-carbonitrile (5a) white solid (58%); m.p.:179-181 ℃; IR (KBr, cm^{-1}) *v*:3381, 3254, 2956, 2865, 2239, 1973, 1680, 1650, 1590, 1543, 1424, 1286, 1193, 1120, 1059, 1005, 845, 782, 757; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 9.40 (s, 1H, NH), 8.06 (d, *J* = 8.0 Hz, 2H, ArH), 7.71-7.67 (m, 1H, ArH), 7.59-7.53 (m, 2H, ArH), 7.41-7.31 (m, 5H, ArH), 6.99 (s, 1H, OH), 4.73-4.63 (m, 2H, CH_2), 4.56-4.54 (m, 1H, CH), 4.26-4.24 (m, 1H, CH), 2.83-2.78 (m, 1H, CH), 2.02-2.00 (m, 1H, CH_2), 1.64-1.62 (m, 2H, CH_2), 1.40-1.28 (m, 3H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ:197.4, 137.8, 134.2, 129.7, 129.5, 129.3, 129.1, 128.7, 127.8, 127.5, 116.6, 71.1, 54.2, 47.5, 32.5, 27.4, 22.0; HRMS calcd for $C_{24}H_{24}N_3O_3$ $[M+H]^+$: 402.1818, found: 402.1840.

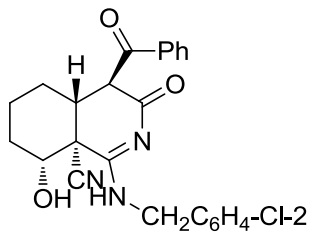


4-Benzoyl-8-hydroxy-1-((4-methoxybenzyl)amino)-3-oxo-3,4,4a,5,6,7,8,8a-octahydroisoquinoline-8a-carbonitrile (5b) white solid (61%); m.p.:168-170 ℃; IR (KBr, cm^{-1}) *v*:3433, 3242, 2942, 2856, 2203, 1685, 1640, 1560, 1541, 1458, 1274, 1250, 1200, 1178, 1060, 1035, 814, 770, 740, 704, 686; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 9.28 (s, 1H, NH), 8.03 (d, *J* = 7.6 Hz, 2H, ArH), 7.71-7.68 (m, 1H, ArH), 7.57 (t, *J* = 7.6 Hz, 2H, ArH), 7.29 (d, *J* = 8.4 Hz, 2H, ArH), 6.95-6.88 (m, 3H, ArH + OH), 4.62-4.48 (m, 3H, CH + CH_2), 4.22-4.20 (m, 1H, CH), 3.75 (s, 3H, CH_3), 2.79-2.73 (m, 1H, CH), 1.99-1.96 (m, 1H, CH_2), 1.60-1.57 (m, 2H, CH_2), 1.39-1.25 (m, 3H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ:197.5, 159.1, 137.8, 134.2, 129.7, 129.5, 129.4, 129.3, 129.0, 116.5, 114.5, 114.1, 71.0, 55.6, 54.2, 44.8, 32.5, 27.4, 22.0; HRMS calcd for $C_{25}H_{24}N_3O_3$ $[M-H]^-$: 430.1767, found: 430.1753.



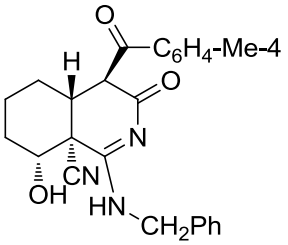
4-Benzoyl-8-hydroxy-3-oxo-1-(phenethylamino)-3,4,4a,5,6,7,8,8a-octahydroisoquinoline-8a-carbonitrile (5c) white solid (64%); m.p.: 176-178 ℃; IR (KBr, cm^{-1}) *v*:3387, 3244, 2940, 2184, 1681, 1650, 1574, 1532, 1460, 1383, 1291, 1195, 1123, 1001, 752, 698; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 9.01 (s, 1H, NH), 8.02 (d, *J* = 7.6 Hz, 2H, ArH), 7.71-7.67 (m, 1H, ArH), 7.59-7.56

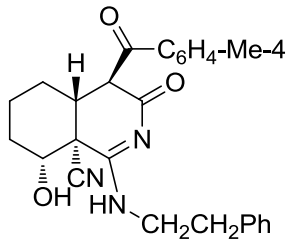
(m, 2H, ArH), 7.34-7.22 (m, 5H, ArH), 6.86 (s, 1H, OH), 4.46 (d, *J* = 9.2 Hz, 1H, CH), 4.07-4.05 (m, 1H, CH), 3.66-3.65 (m, 2H, CH_2), 2.89 (t, *J* = 6.8 Hz, 2H, CH_2), 2.67 (t, *J* = 6.8 Hz, 1H, CH), 1.98-1.96 (m, 1H, CH_2), 1.62-1.55 (m, 2H, CH_2), 1.34-1.23 (m, 3H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 175.7, 139.3, 137.8, 134.2, 129.7, 129.5, 129.3, 129.2, 128.9, 127.9, 126.8, 116.5, 71.1, 56.5, 54.1, 34.4, 27.4, 22.0; HRMS calcd for $C_{25}H_{24}N_3O_3$ [M-H]:$^-$ 414.1818, found: 414.1814.



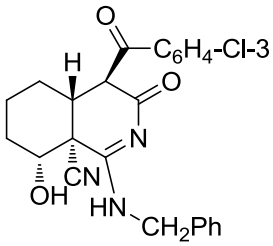
4-Benzoyl-1-((2-chlorobenzyl)amino)-8-hydroxy-3-oxo-3,4,4a,5,6,7,8,8a-octahydroisoquinoline-8a-carbonitrile (5d) white solid (77%); m.p.:192-194 ℃; IR (KBr, cm^{-1}) *v*:3228, 2917, 2893, 2180, 1684, 1642, 1557, 1536, 1362, 1270, 1249, 1194, 1125, 1060, 1002, 841, 783, 752, 685; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 9.46 (s, 1H, NH), 8.04-8.02 (m, 2H, ArH), 7.71-7.68 (m, 1H, ArH), 7.57 (t, *J* = 7.6 Hz, 2H, ArH), 7.52-7.50 (m, 1H, ArH), 7.42-7.34 (m, 3H, ArH), 7.01 (s, 1H, OH), 4.72-4.70 (m, 2H, CH_2), 4.50-4.49 (m, 1H, CH), 4.27-4.23 (m, 1H, CH), 2.81-2.76 (m, 1H, CH), 2.02-1.97 (m, 1H, CH_2), 1.64-1.62 (m, 2H, CH_2), 1.40-1.27 (m, 3H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ:197.3, 137.7, 134.3, 132.9, 129.9, 129.7, 129.5, 129.3, 127.9, 116.5, 71.1, 54.1, 47.3, 32.4, 27.4, 22.0; HRMS calcd for $C_{24}H_{23}ClN_3O_3$ [M+H]$^+$: 436.1428, found: 436.1456.

1-(Benzylamino)-8-hydroxy-4-(4-methylbenzoyl)-3-oxo-3,4,4a,5,6,7,8,8a-octahydroisoquinoline-8a-carbonitrile (5e) white solid (70%); m.p.:192-193 ℃; IR (KBr, cm^{-1}) *v*: 3206, 3090, 2933, 2866, 2235, 1698, 1680, 1606, 1446, 1357, 1292, 1180, 1124, 1087, 1002, 814, 753, 738, 666; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 9.40 (s, 1H, NH), 7.94 (d, *J* = 8.0 Hz, 2H, ArH), 7.41-7.29 (m, 7H, ArH), 6.99 (s, 1H, OH), 4.72-4.761 (m, 2H, CH_2), 4.50-4.48 (m, 1H, CH), 4.24-4.23 (m, 1H, CH), 2.80-2.74 (m, 1H, CH), 2.39 (s, 3H, CH_3), 2.01-1.99 (m, 1H, CH_2), 1.63-1.61 (m, 2H, CH_2), 1.42-1.26 (m, 3H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ:196.8, 144.9, 135.3, 129.9, 129.7, 129.1, 128.8, 127.8, 116.5, 71.0, 54.1, 27.4, 22.0, 21.7; HRMS calcd for $C_{25}H_{26}N_3O_3$ [M+H]$^+$: 416.1974, found: 416.1993.

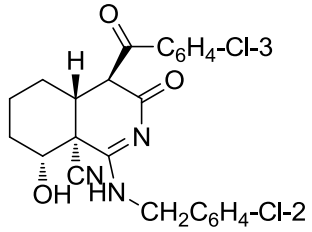




8-Hydroxy-4-(4-methylbenzoyl)-3-oxo-1-(phenethylamino)-3,4,4a,5,6,7,8,8a-octahydroisoquinoline-8a-carbonitrile (5f) white solid (66%); m.p.:178-180 ℃; IR (KBr, cm^{-1}) *v*:3188, 2941, 2854, 2233, 1681, 1657, 1581, 1530, 1459, 1353, 1274, 1203, 1184, 1078, 1024, 866, 845, 747, 716, 624; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 9.00 (s, 1H, NH), 7.94 (d, *J* = 7.6 Hz, 2H, ArH), 7.38-7.22 (m, 7H, ArH), 6.86 (s, 1H, OH), 4.47-4.44 (m, 1H, CH), 4.05-4.03 (m, 1H, CH), 3.66-3.64 (m, 2H, CH_2), 2.89 (t, *J* = 6.8 Hz, 2H, ArH), 2.69-2.63 (m, 1H, CH), 2.39 (s, 3H, CH_3), 1.98-1.95 (m, 1H, CH_2), 1.59-1.56 (m, 2H, CH_2), 1.34-1.22 (m, 3H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ:196.8, 144.8, 139.3, 135.4, 129.9, 129.7, 129.2, 128.9, 126.8, 116.5, 71.1, 56.6, 54.0, 34.5, 27.4, 22.1, 21.7; HRMS calcd for $C_{26}H_{28}N_3O_3$ $[M+H]^+$: 430.2131, found: 430.2143.



1-(Benzylamino)-4-(3-chlorobenzoyl)-8-hydroxy-3-oxo-3,4,4a,5,6,7,8,8a-octahydroisoquinoline-8a-carbonitrile (5g) white solid (73%); m.p.:202-203 ℃; IR (KBr, cm^{-1}) *v*:3347, 3236, 2946, 2863, 2236, 1683, 1647, 1575, 1529, 1448, 1359, 1280, 1186, 1123, 1056, 1026,1011, 894, 775, 754, 697; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 9.25 (s, 1H, NH), 8.08 (s, 1H, ArH), 8.02 (d, *J* = 7.6 Hz, 1H, ArH), 7.76-7.74 (m, 1H, ArH), 7.62-7.58 (m, 1H, ArH), 7.40-7.30 (m, 6H, ArH + OH), 4.72-4.57 (m, 3H, CH_2 + CH), 4.26-4.24 (m, 1H, CH), 2.82-2.77 (m, 1H, CH), 2.02-1.99 (m, 1H, CH_2), 1.64-1.62 (m, 2H, CH_2), 1.41-1.30 (m, 3H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ:196.5, 139.5, 134.2, 133.9, 131.2, 129.1, 129.0, 128.7, 128.3, 127.8, 127.5, 116.4, 71.1, 54.4, 32.6, 27.3, 22.1; HRMS calcd for $C_{24}H_{23}ClN_3O_3$ $[M+H]^+$: 436.1428, found: 436.1445.



4-(3-chlorobenzoyl)-1-((2-chlorobenzyl)amino)-8-hydroxy-3-oxo-3,4,4a,5,6,7,8,8a-octahydroisoquinoline-8a-carbonitrile (5h) white solid (52%); m.p.:210-212 ℃; IR (KBr, cm^{-1}) *v*:3369, 3239, 2943, 2865, 2237, 1683, 1646, 1576, 1536, 1442, 1381, 1358, 1280, 1187, 1121, 1060, 1023, 895, 756, 737, 694; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 9.43 (s, 1H, NH),

8.08-8.01 (m, 2H, ArH), 7.76-7.73 (m, 1H, ArH), 7.63-7.57 (m, 1H, ArH), 7.48-7.36 (m, 5H, ArH + OH), 4.72-4.761 (m, 3H, CH_2 + CH), 4.24-4.23 (m, 1H, CH), 2.80-2.74 (m, 1H, CH), 2.01-1.99 (m, 1H, CH_2), 1.65-1.60 (m, 2H, CH_2), 1.44-1.30 (m, 3H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ:196.4, 139.5, 134.3, 133.9, 132.9, 131.2, 129.9, 129.7, 129.1, 128.3, 127.9, 116.4, 71.2, 54.3, 32.5, 27.3, 22.1; HRMS calcd for $C_{24}H_{22}Cl_2N_3O_3$ $[M+H]^+$: 470.1038, found: 470.1058.

4. Crystal date of compound 4c

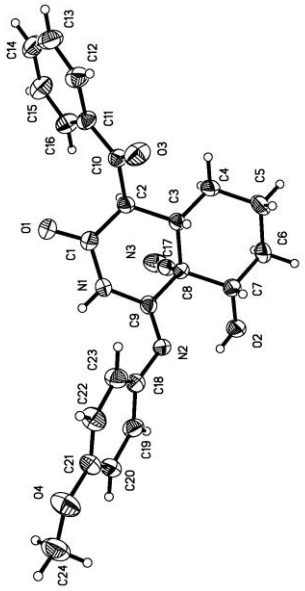


Figure 1. The Crystal Structure of **4c**

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

Empirical formula	$C_{24}H_{23}N_3O_4$
Formula weight	417.45
Temperature	298(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
space group	P2(1)
Unit cell dimensions	a = 6.8289(7) Å α = 90 °
	b = 13.5136(12) Å β = 106.143(2) °

	c = 12.1421(11) Å γ = 90 °
Volume	1076.33(18) $Å^3$
Z	2
Calculated density	1.288 Mg/m^3
Absorption coefficient	0.089 mm^{-1}
F(000)	440
Crystal size	0.27 × 0.25 ×0.12 mm
Theta range for data collection	3.01 °to 25.02 °
Limiting indices	-6≤h≤8, -14≤k≤16, -14≤l≤13
Reflections collected	5526
Independent reflections	3310 [R(int) = 0.0651]
Data / restraints / parameters	3310 / 1 / 282
Goodness-of-fit on F^2	0.908
Final R indices [I>2σ(I)]	R_1 = 0.0544, wR_2 = 0.0710
R indices (all data)	R_1 = 0.1146, wR_2 = 0.0817
Largest diff. peak and hole	0.155 and -0.140 e. $Å^{-3}$

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

Bond	Bond Lengths	Bond	Bond Lengths	Bond	Bond Lengths

N(1)-C(1)	1.372(5)	N(1)-C(9)	1.409(5)	N(2)-C(9)	1.268(5)
N(2)-C(18)	1.427(5)	N(3)-C(17)	1.141(5)	O(1)-C(1)	1.229(5)
O(2)-C(7)	1.432(5)	O(3)-C(10)	1.228(4)	O(4)-C(21)	1.368(5)
O(4)-C(24)	1.421(6)	C(1)-C(2)	1.513(6)	C(2)-C(3)	1.523(5)
C(2)-C(10)	1.544(6)	C(3)-C(4)	1.525(5)	C(3)-C(8)	1.547(5)
C(4)-C(5)	1.530(5)	C(5)-C(6)	1.522(6)	C(6)-C(7)	1.504(5)
C(7)-C(8)	1.551(6)	C(8)-C(17)	1.490(5)	C(8)-C(9)	1.516(5)
C(10)-C(11)	1.470(6)	C(11)-C(16)	1.401(5)	C(11)-C(12)	1.401(6)
C(12)-C(13)	1.389(6)	C(13)-C(14)	1.379(7)	C(14)-C(15)	1.382(7)
C(15)-C(16)	1.387(6)	C(18)-C(23)	1.387(5)	C(18)-C(19)	1.392(6)
C(19)-C(20)	1.390(6)	C(20)-C(21)	1.373(5)	C(21)-C(22)	1.377(7)
C(22)-C(23)	1.378(6)				

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

Angles	(°)	Angles	(°)
C(1)-N(1)-C(9)	126.6(4)	C(9)-N(2)-C(18)	124.1(4)
C(21)-O(4)-C(24)	118.3(4)	O(1)-C(1)-N(1)	121.1(5)
O(20)-C(1)-C(2)	121.2(4)	N(1)-C(1)-C(2)	117.7(4)
C(1)-C(2)-C(3)	114.4(3)	C(1)-C(2)-C(10)	108.0(3)
C(3)-C(2)-C(10)	111.6(4)	C(4)-C(3)-C(2)	112.1(4)
C(4)-C(3)-C(8)	111.2(3)	C(2)-C(3)-C(8)	110.3(3)
C(3)-C(4)-C(5)	110.7(4)	C(6)-C(5)-C(4)	110.0(4)

C(7)-C(6)-N(5)	112.8(4)	O(2)-C(7)-C(6)	107.5(4)
O(2)-C(7)-C(8)	111.0(4)	C(6)-C(7)-C(8)	111.2(4)
C(17)-C(8)-C(9)	107.9(4)	C(17)-C(8)-C(3)	109.2(4)
C(9)-C(8)-C(3)	109.4(3)	C(17)-C(8)-C(7)	108.4(4)
C(9)-C(8)-C(7)	111.5(4)	C(3)-C(8)-C(7)	110.3(3)
N(2)-C(9)-N(1)	124.2(4)	N(2)-C(9)-C(8)	119.5(4)
N(1)-C(9)-C(8)	116.3(4)	O(3)-C(10)-C(11)	121.8(4)
O(3)-C(10)-C(2)	116.5(4)	C(11)-C(10)-C(2)	121.6(4)
C(16)-C(11)-C(12)	117.4(4)	C(16)-C(11)-C(10)	123.9(4)
C(12)-C(11)-C(10)	118.7(4)	C(13)-C(12)-C(11)	121.5(5)
C(14)-C(13)-C(12)	119.3(5)	C(13)-C(14)-C(15)	121.0(5)
C(14)-C(15)-C(16)	119.4(5)	C(15)-C(16)-C(11)	121.4(5)
N(3)-C(17)-C(8)	176.9(5)	C(23)-C(18)-C(19)	118.2(4)
C(23)-C(18)-N(2)	124.0(5)	C(19)-C(18)-N(2)	117.3(4)
C(20)-C(19)-C(18)	120.9(5)	C(21)-C(20)-C(19)	119.8(5)
O(4)-C(21)-C(20)	124.7(5)	O(4)-C(21)-C(22)	115.6(5)
C(20)-C(21)-C(22)	119.7(5)	C(21)-C(22)-C(23)	120.8(5)
C(22)-C(23)-C(18)	120.6(5)		

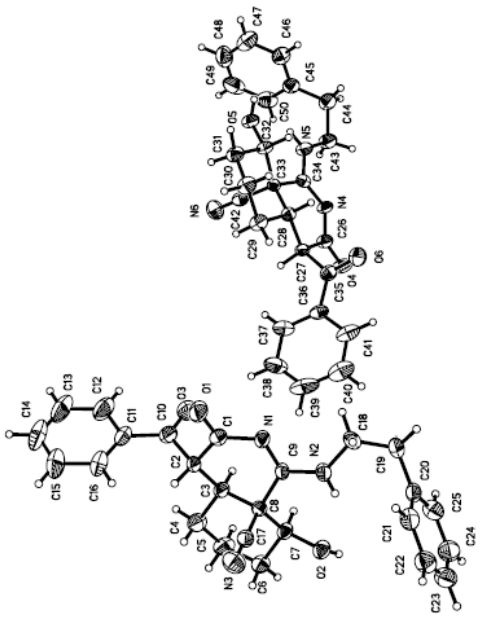


Figure 2. The Crystal Structure of **5c**

Table 4 Crystallographic Data of Compound **5c**

Empirical formula	$C_{25}H_{25}N_3O_3$
Formula weight	415.48
Temperature	298(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
space group	P2(1)/c
Unit cell dimensions	a = 18.9871(17) Å α = 90 °
	b = 18.0668(16) Å β = 94.4380(10) °
	c = 12.5460(11) Å γ = 90 °

Volume	4290.8(7) $Å^3$
Z	8
Calculated density	1.286 Mg/m^3
Absorption coefficient	0.086 mm^{-1}
F(000)	1760
Crystal size	0.32 × 0.17 ×0.14 mm
Theta range for data collection	2.19 °to 25.02 °
Limiting indices	-22≤h≤18, -21≤k≤18, -14≤l≤14
Reflections collected	21692
Independent reflections	7559 [R(int) = 0.0960]
Data / restraints / parameters	7559 / 0 / 561
Goodness-of-fit on F^2	0.884
Final R indices [I>2σ(I)]	R_1 = 0.0540, wR_2 = 0.0692
R indices (all data)	R_1 = 0.1807, wR_2 = 0.0846
Largest diff. peak and hole	0.169 and -0.211 e. $Å^{-3}$

Table 5 Selected Bond Lengths (Å) of Compound **5c**

Bond	Bond Lengths	Bond	Bond Lengths	Bond	Bond Lengths
N(1)-C(9)	1.320(3)	N(1)-C(1)	1.379(3)	N(2)-C(9)	1.305(3)

N(2)-C(18)	1.454(3)	N(3)-C(17)	1.139(4)	O(1)-C(1)	1.225(3)
O(2)-C(7)	1.444(3)	O(3)-C(10)	1.220(4)	C(1)-C(2)	1.516(4)
C(2)-C(10)	1.527(4)	C(2)-C(3)	1.528(3)	C(3)-C(4)	1.530(4)
C(3)-C(8)	1.534(4)	C(4)-C(5)	1.527(4)	C(5)-C(6)	1.507(4)
C(6)-C(7)	1.500(4)	C(7)-C(8)	1.543(3)	C(8)-C(17)	1.473(4)
C(8)-C(9)	1.538(4)	C(10)-C(11)	1.471(4)	C(11)-C(16)	1.359(4)
C(11)-C(12)	1.370(5)	C(12)-C(13)	1.383(5)	C(13)-C(14)	1.346(6)
C(14)-C(15)	1.357(6)	C(15)-C(16)	1.390(4)	C(18)-C(19)	1.514(3)
C(19)-C(20)	1.490(4)	C(20)-C(21)	1.381(4)	C(20)-C(25)	1.391(4)
C(21)-C(22)	1.375(4)	C(22)-C(23)	1.368(4)	C(23)-C(24)	1.364(5)
C(24)-C(25)	1.374(4)				

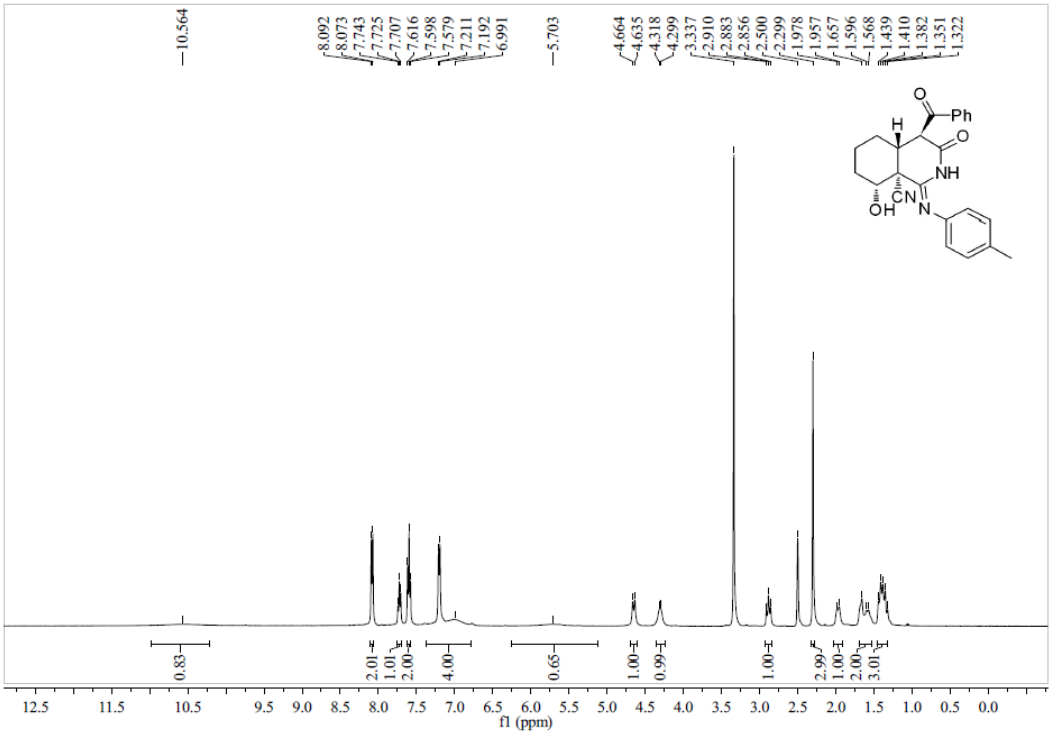
Table 6 Selected Bond Angles (°) for Compound **5c**

Angles	(°)	Angles	(°)
C(1)-N(1)-C(9)	119.6(3)	C(9)-N(2)-C(18)	125.9(3)
O(1)-C(1)-N(1)	119.5(3)	O(1)-C(1)-C(2)	118.6(3)
N(1)-C(1)-C(2)	121.8(3)	C(1)-C(2)-C(10)	107.2(3)
C(1)-C(2)-C(3)	113.5(3)	C(10)-C(2)-C(3)	109.4(3)
C(2)-C(3)-C(4)	111.5(3)	C(2)-C(3)-C(8)	111.2(3)
C(4)-C(3)-C(8)	112.4(2)	C(5)-C(4)-C(3)	111.2(3)
C(6)-C(5)-C(4)	111.4(3)	C(7)-C(6)-C(5)	111.3(3)
O(2)-C(7)-C(6)	109.6(2)	O(2)-C(7)-C(8)	108.5(3)

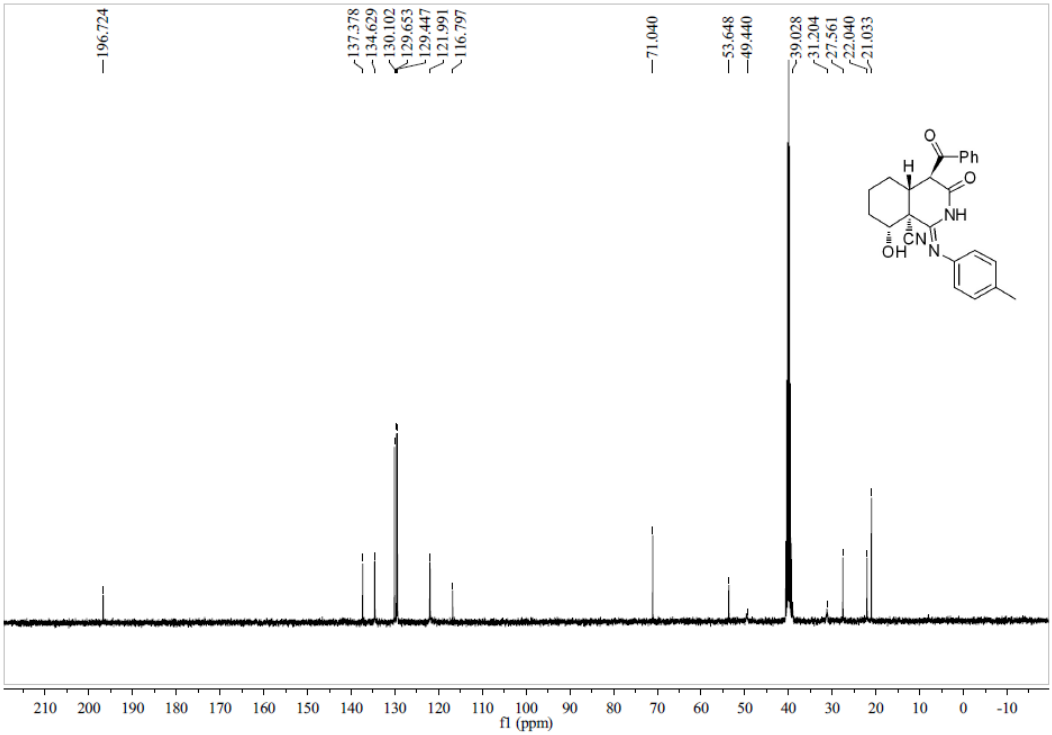
C(6)-C(7)-C(8)	111.4(3)	C(17)-C(8)-C(3)	110.2(3)
C(17)-C(8)-C(9)	106.8(3)	C(3)-C(8)-C(9)	106.6(2)
C(17)-C(8)-C(7)	111.2(3)	C(3)-C(8)-C(7)	107.3(3)
C(9)-C(8)-C(7)	114.6(3)	N(2)-C(9)-N(1)	119.7(3)
N(2)-C(9)-C(8)	116.8(3)	N(1)-C(9)-C(8)	123.5(3)
O(3)-C(10)-C(11)	120.9(4)	O(3)-C(10)-C(2)	116.8(3)
C(11)-C(10)-C(2)	122.3(4)	C(16)-C(11)-C(12)	118.0(4)
C(16)-C(11)-C(10)	123.1(4)	C(12)-C(11)-C(10)	119.0(4)
C(11)-C(12)-C(13)	121.2(5)	C(14)-C(13)-C(12)	120.2(6)
C(13)-C(14)-C(15)	119.6(6)	C(14)-C(15)-C(16)	120.2(5)
C(11)-C(16)-C(15)	120.8(4)	N(3)-C(17)-C(8)	179.0(4)
N(2)-C(18)-C(19)	109.7(3)	C(20)-C(19)-C(18)	115.9(3)
C(21)-C(20)-C(25)	117.3(4)	C(21)-C(20)-C(19)	122.7(4)
C(25)-C(20)-C(19)	120.0(4)	C(22)-C(21)-C(20)	121.6(4)
C(23)-C(22)-C(21)	120.0(4)	C(24)-C(23)-C(22)	119.5(4)
C(23)-C(24)-C(25)	120.8(4)	C(24)-C(25)-C(20)	120.7(4)

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

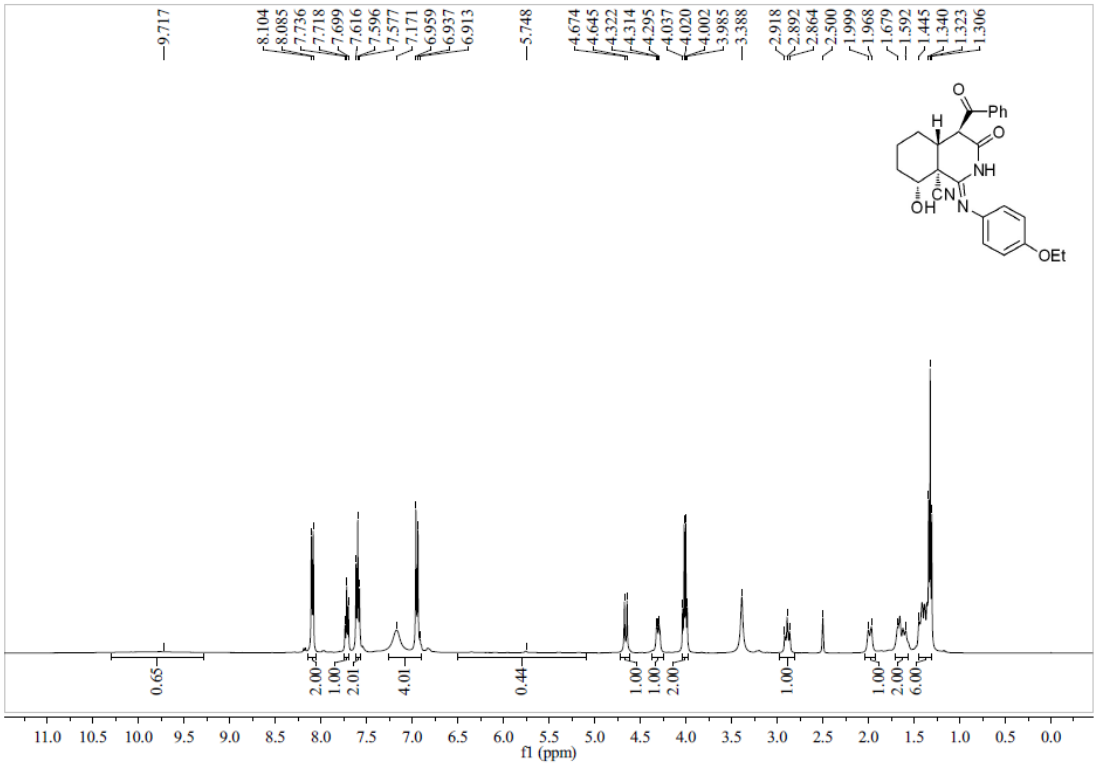
^{1}H NMR of compound **4a**



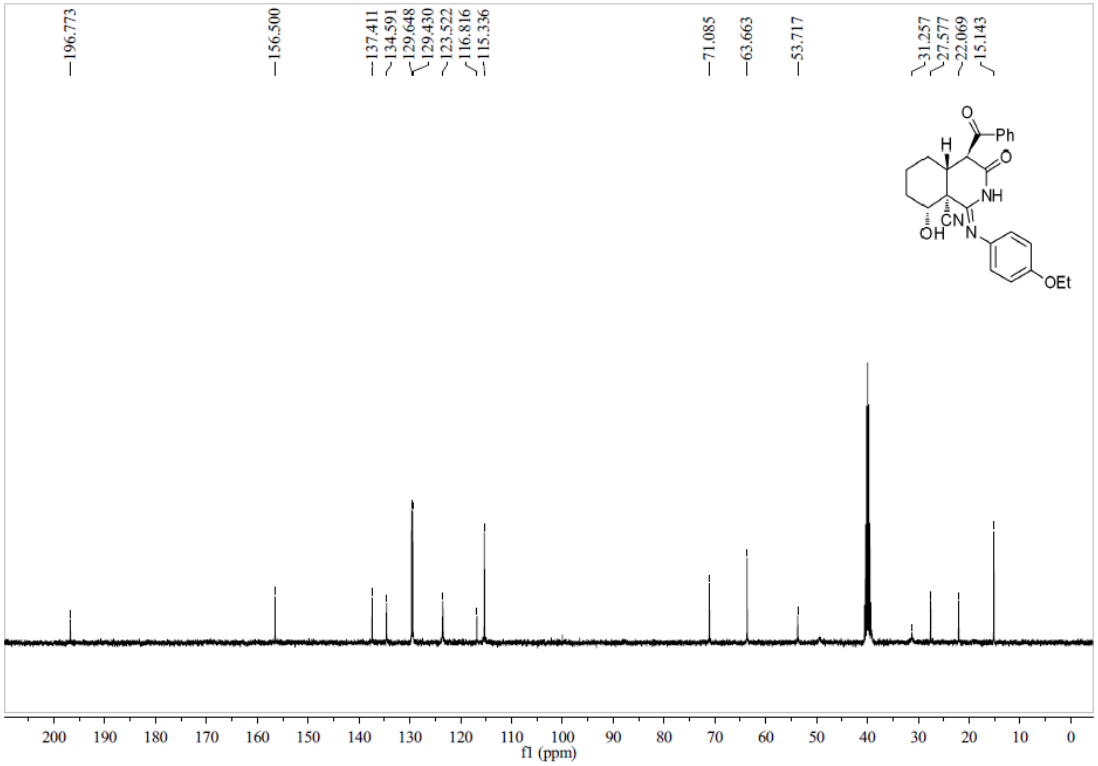
^{13}C NMR of compound **4a**



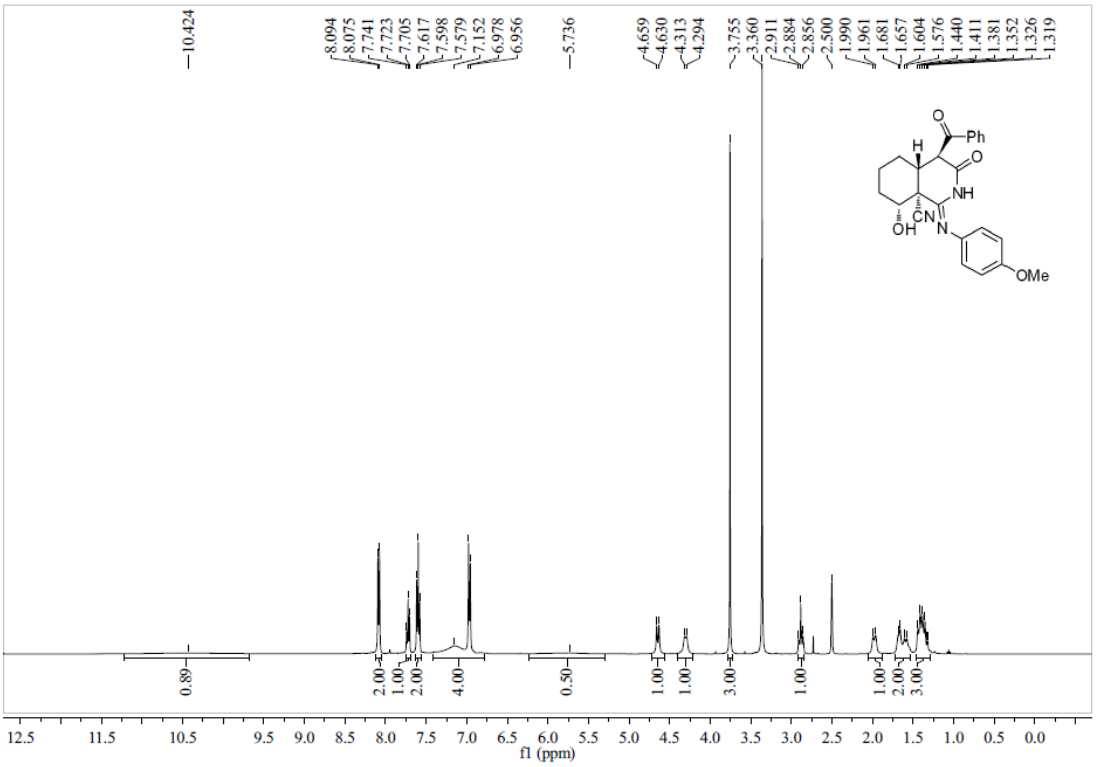
^{1}H NMR of compound **4b**



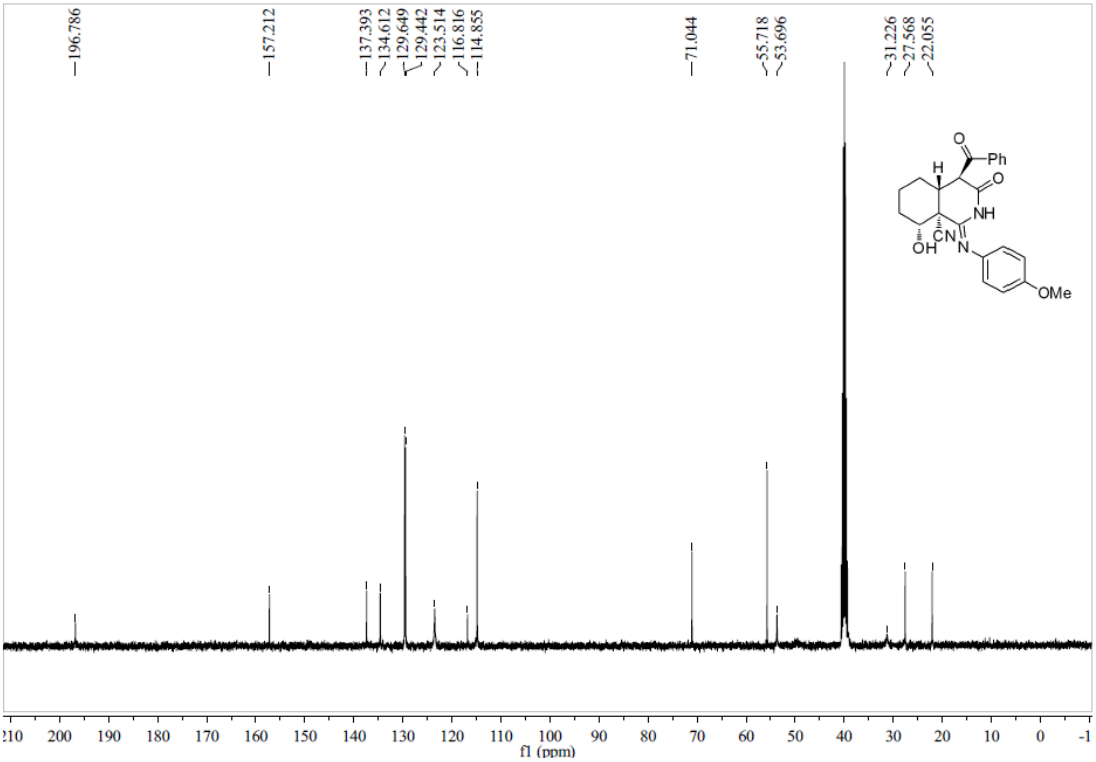
^{13}C NMR of compound **4b**



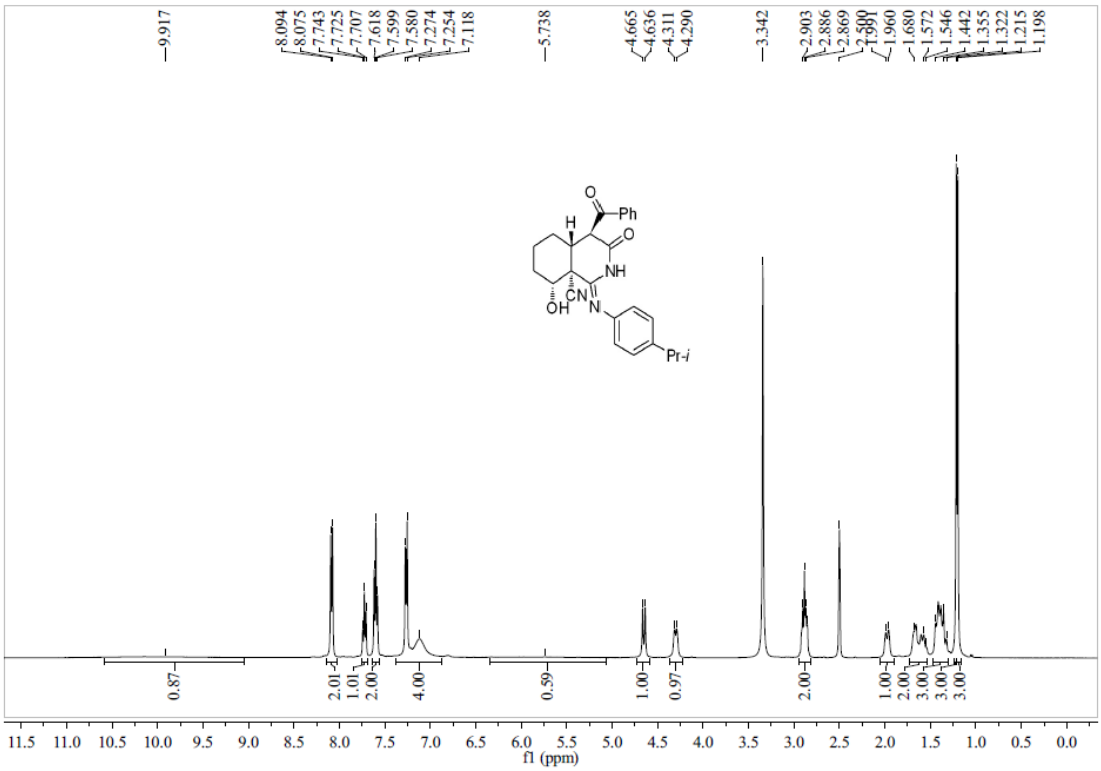
^{1}H NMR of compound **4c**



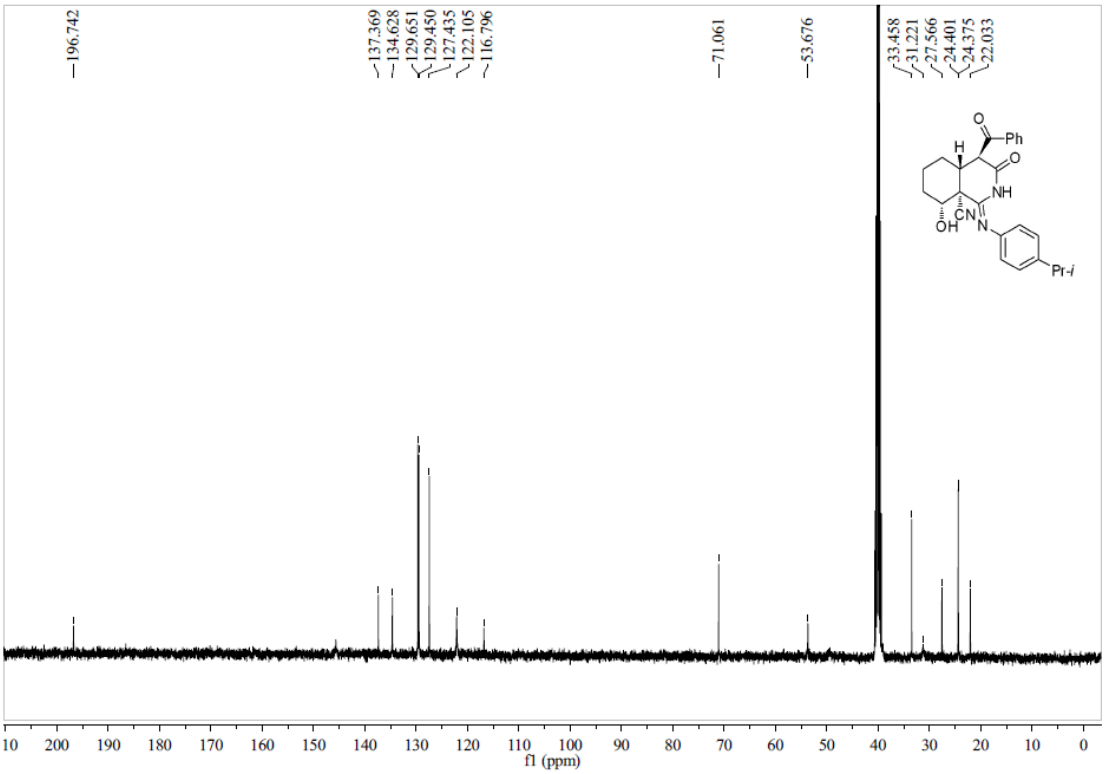
^{13}C NMR of compound **4c**



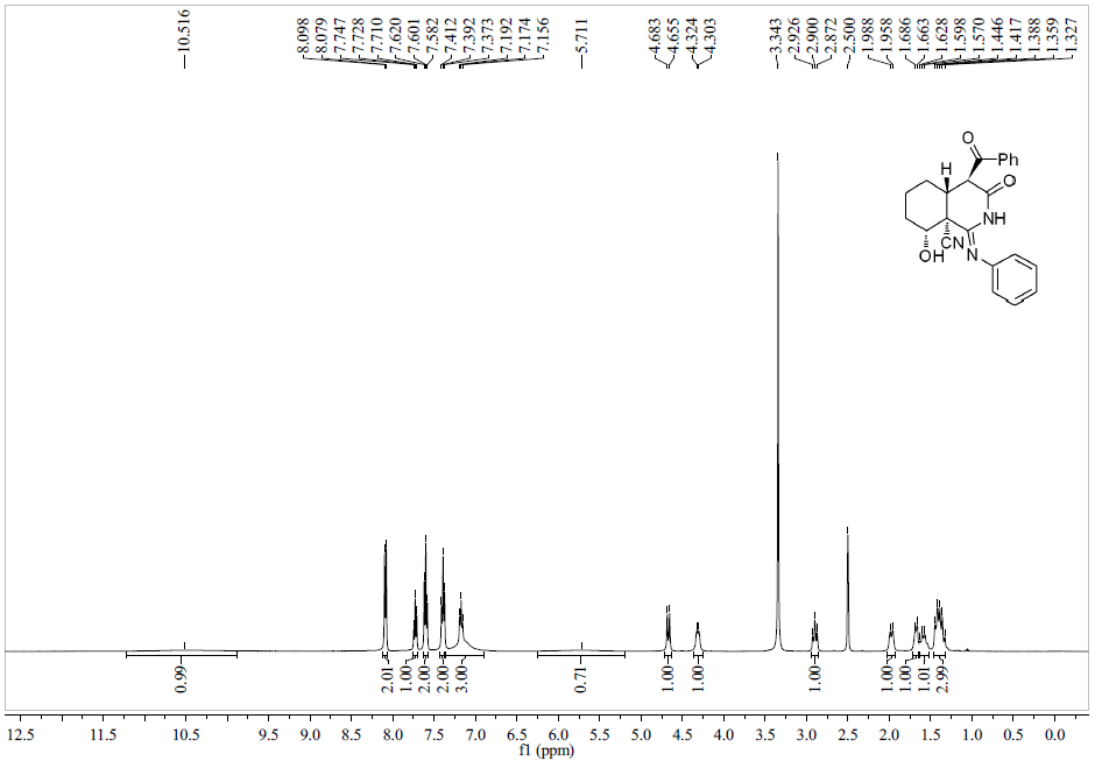
^{1}H NMR of compound **4d**



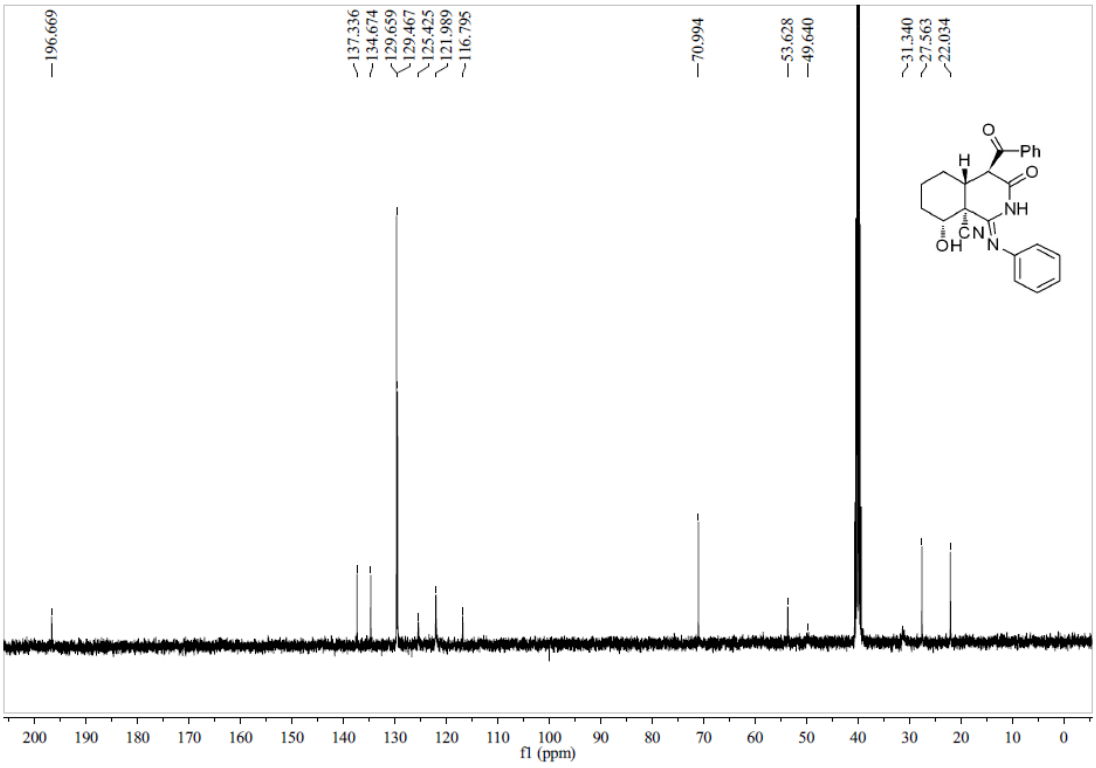
^{13}C NMR of compound **4d**



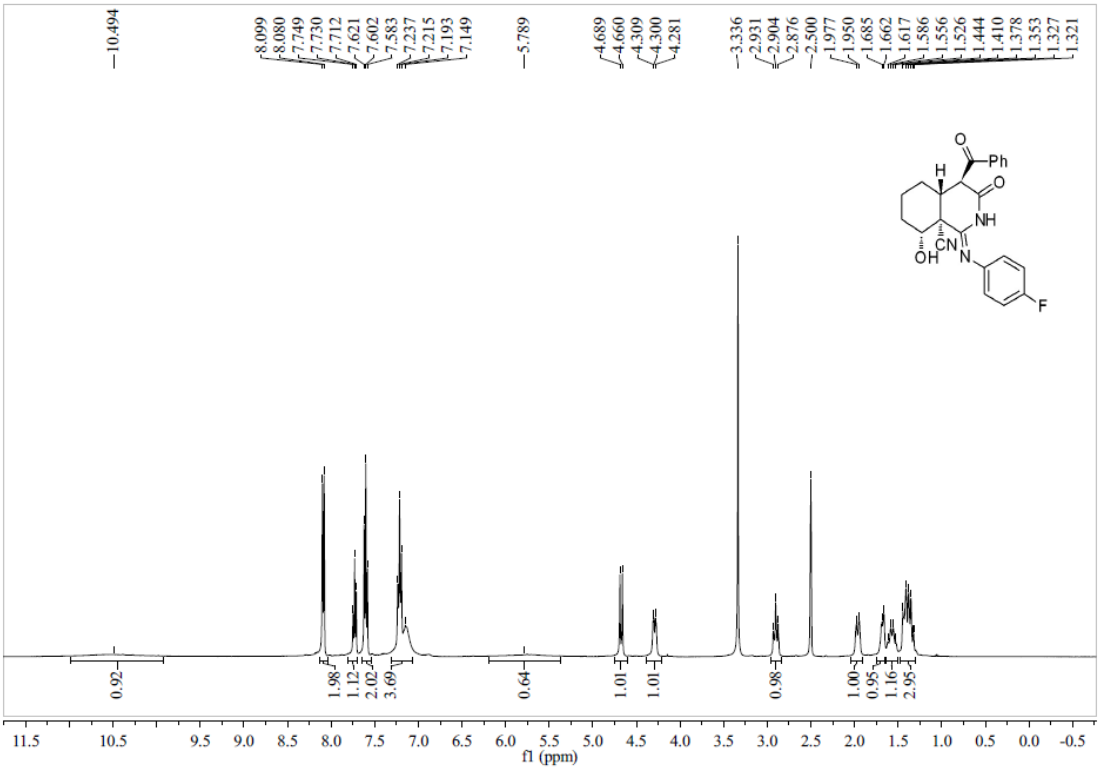
^{1}H NMR of compound **4e**



^{13}C NMR of compound **4e**



^{1}H NMR of compound **4f**



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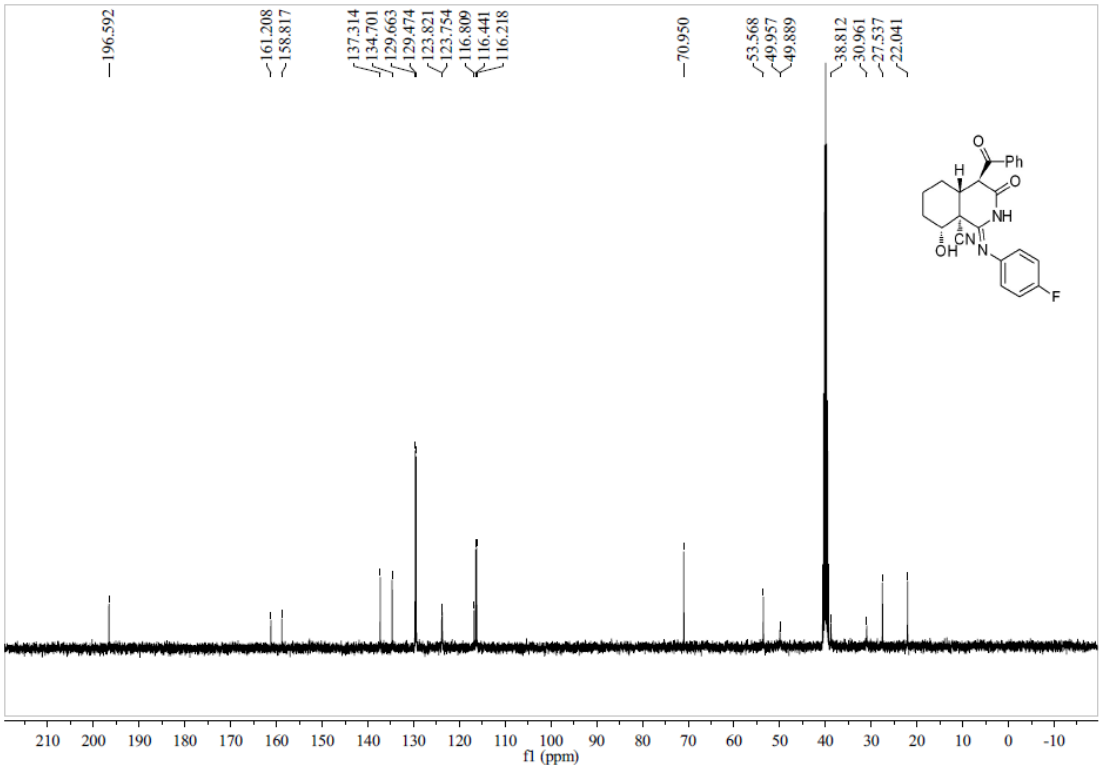
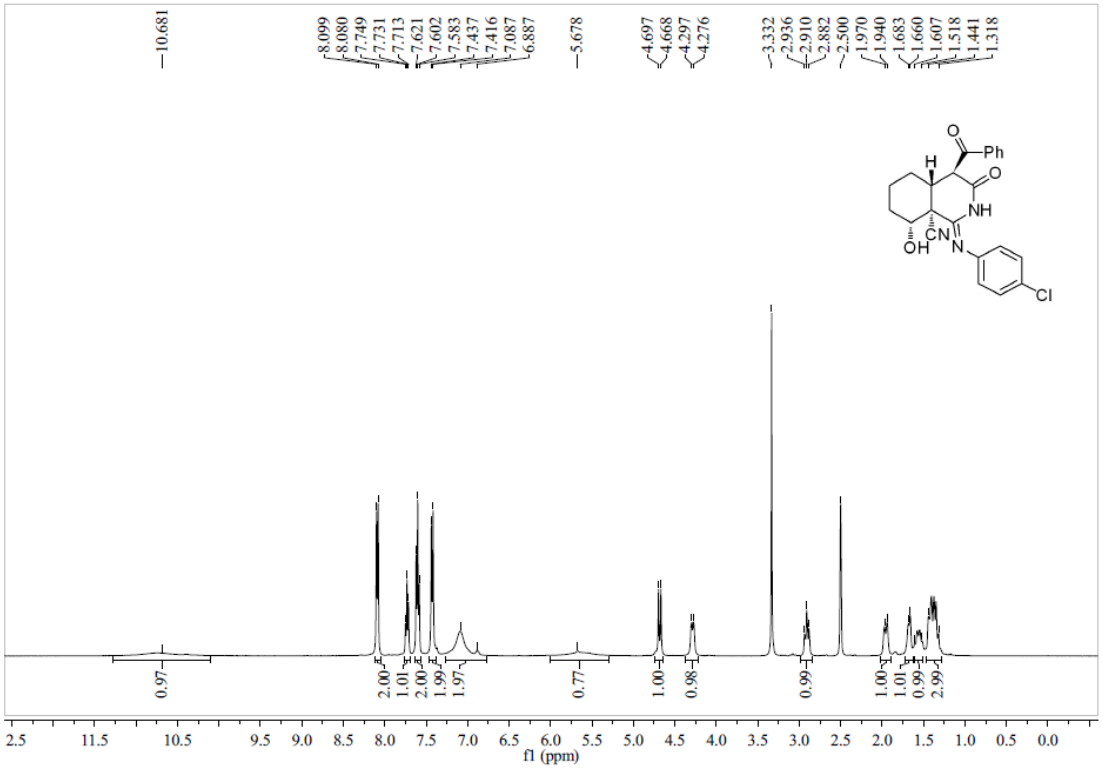
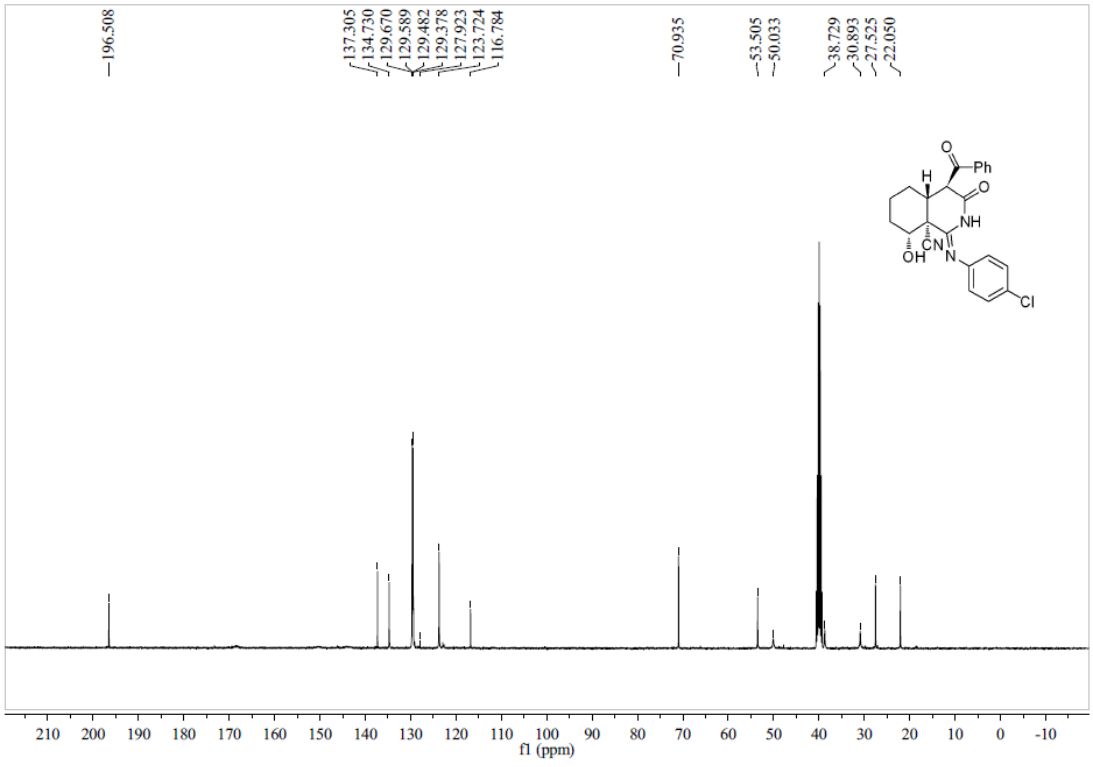


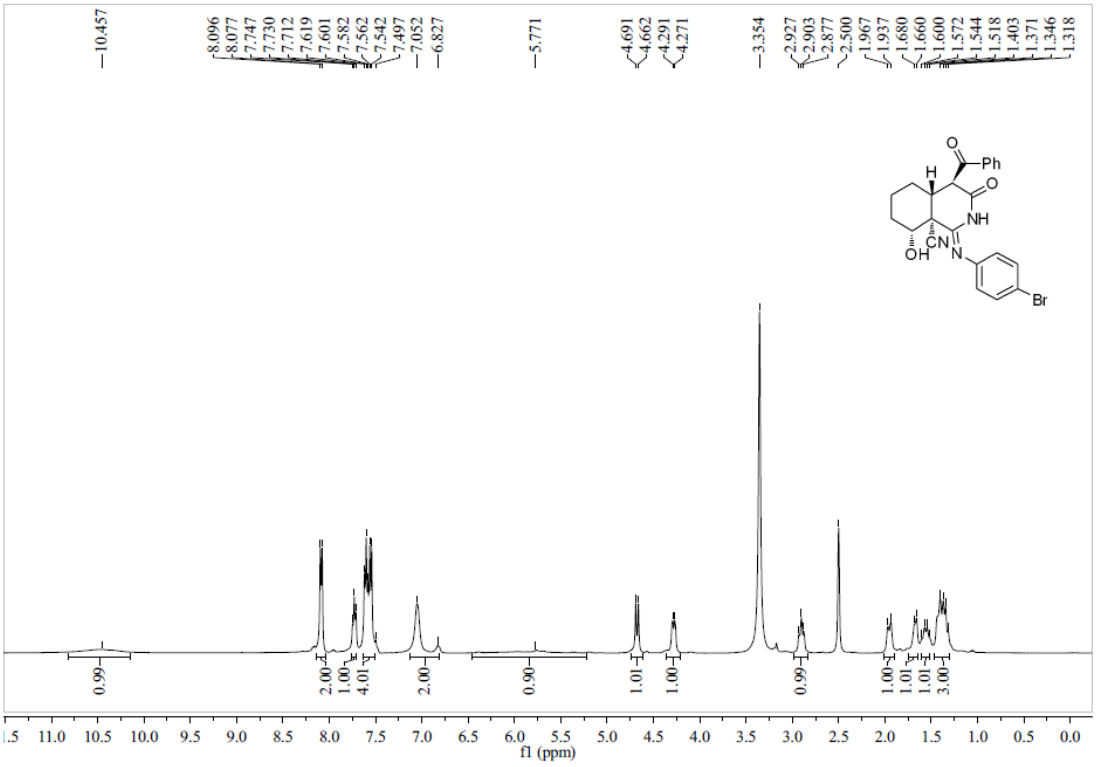
^{1}H NMR of compound **4g**



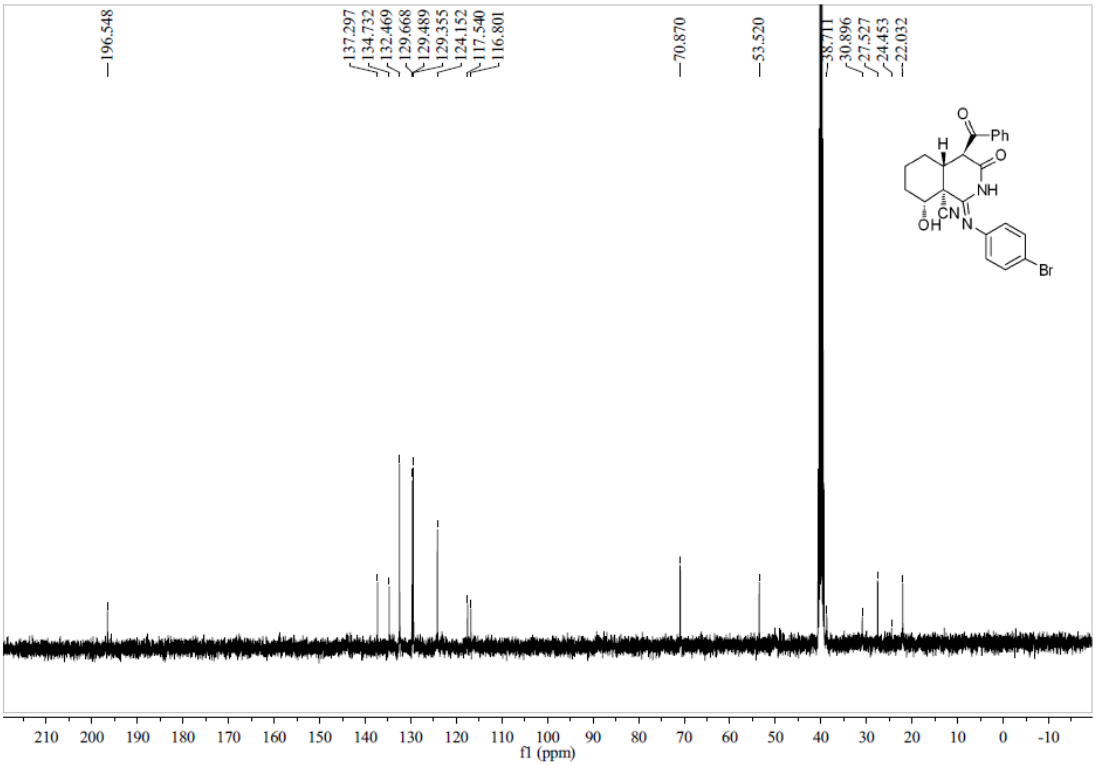
^{13}C NMR of compound **4g**



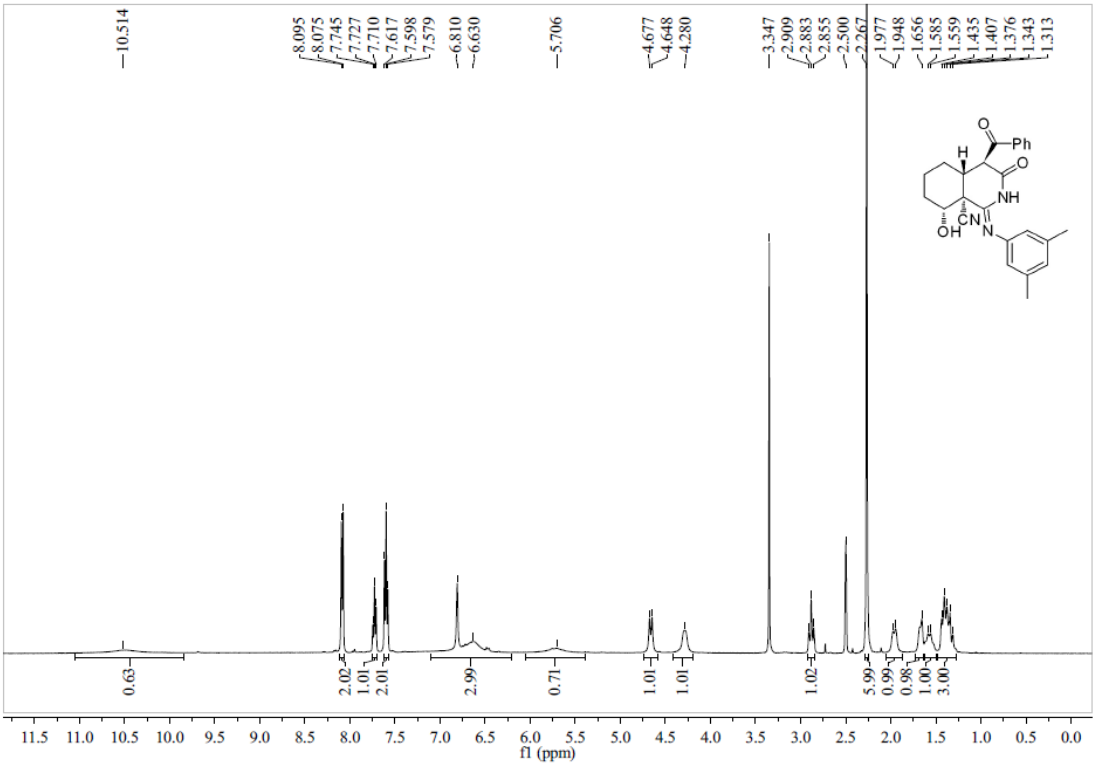
^{1}H NMR of compound **4h**



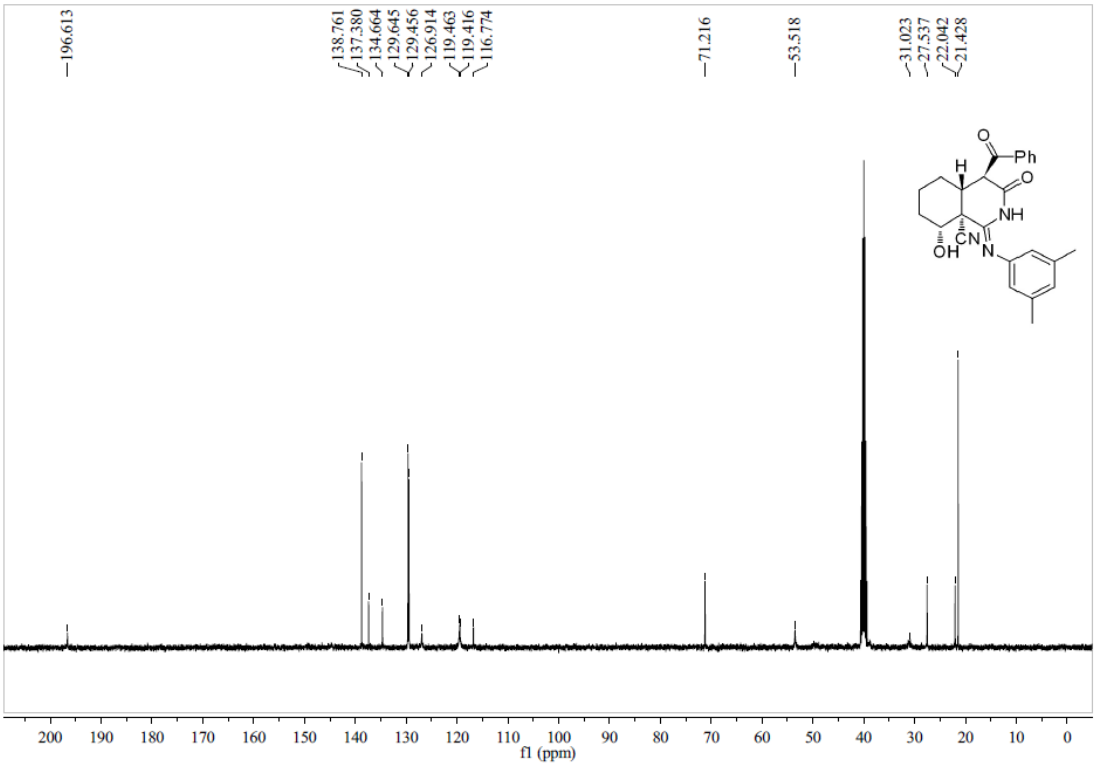
^{13}C NMR of compound **4h**



^{1}H NMR of compound **4i**



^{13}C NMR of compound **4i**



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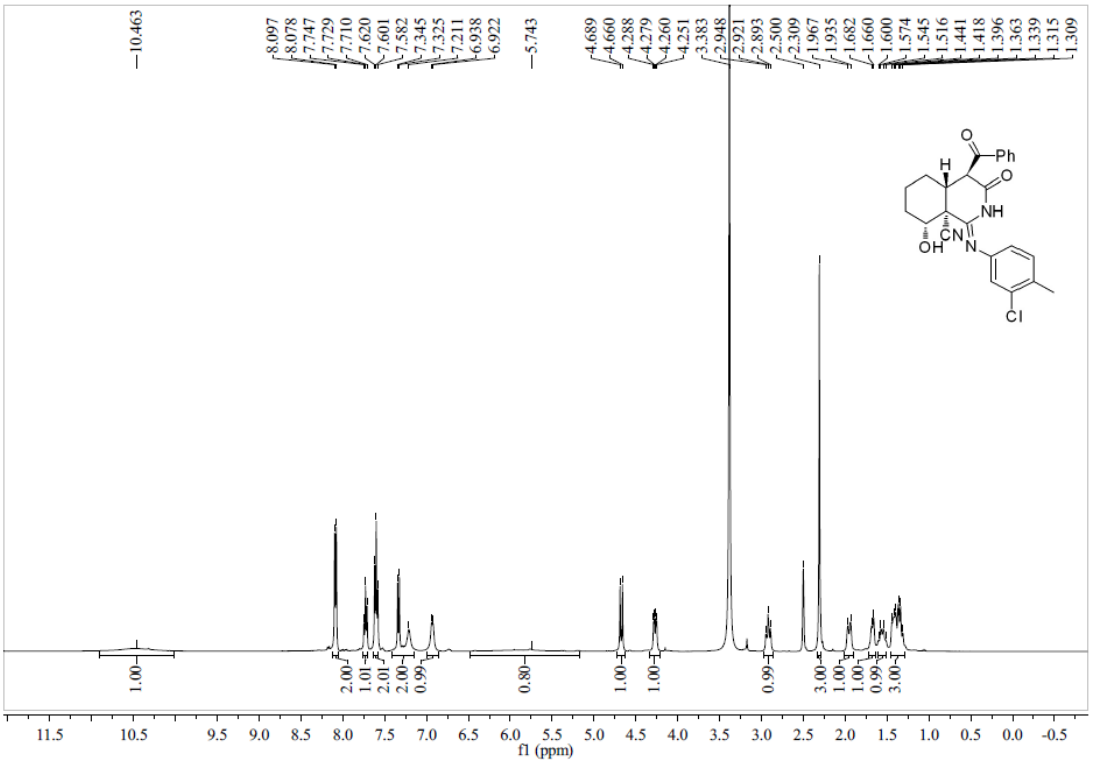

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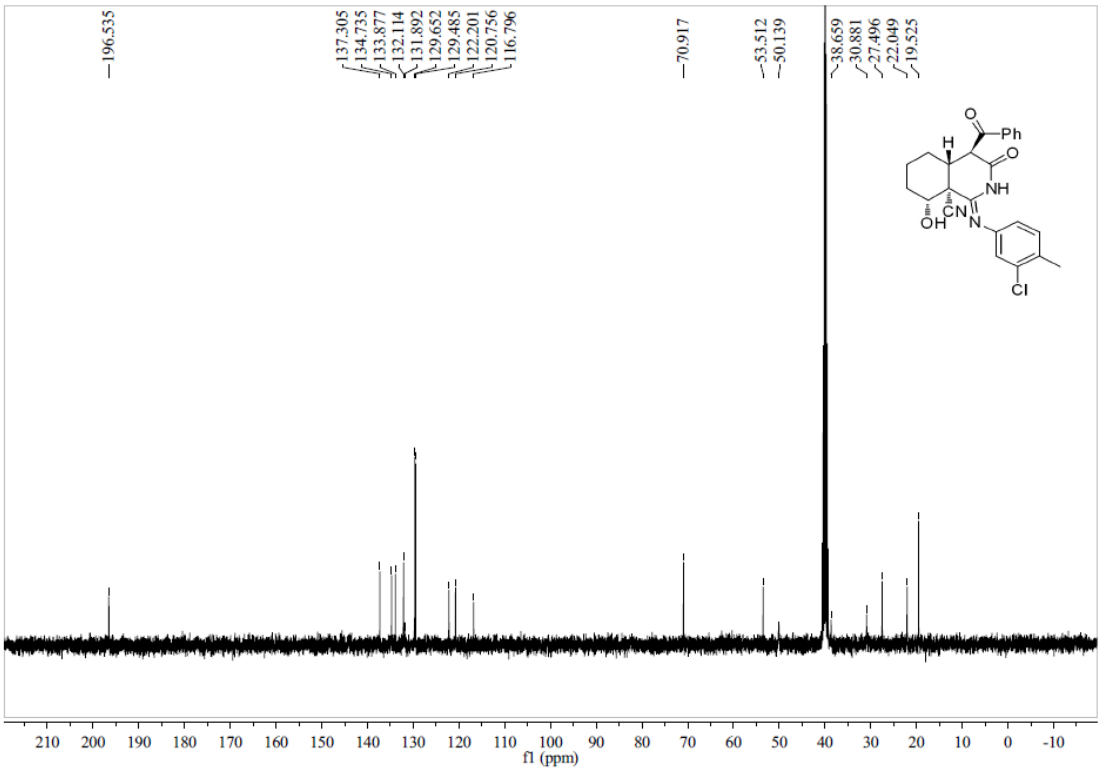

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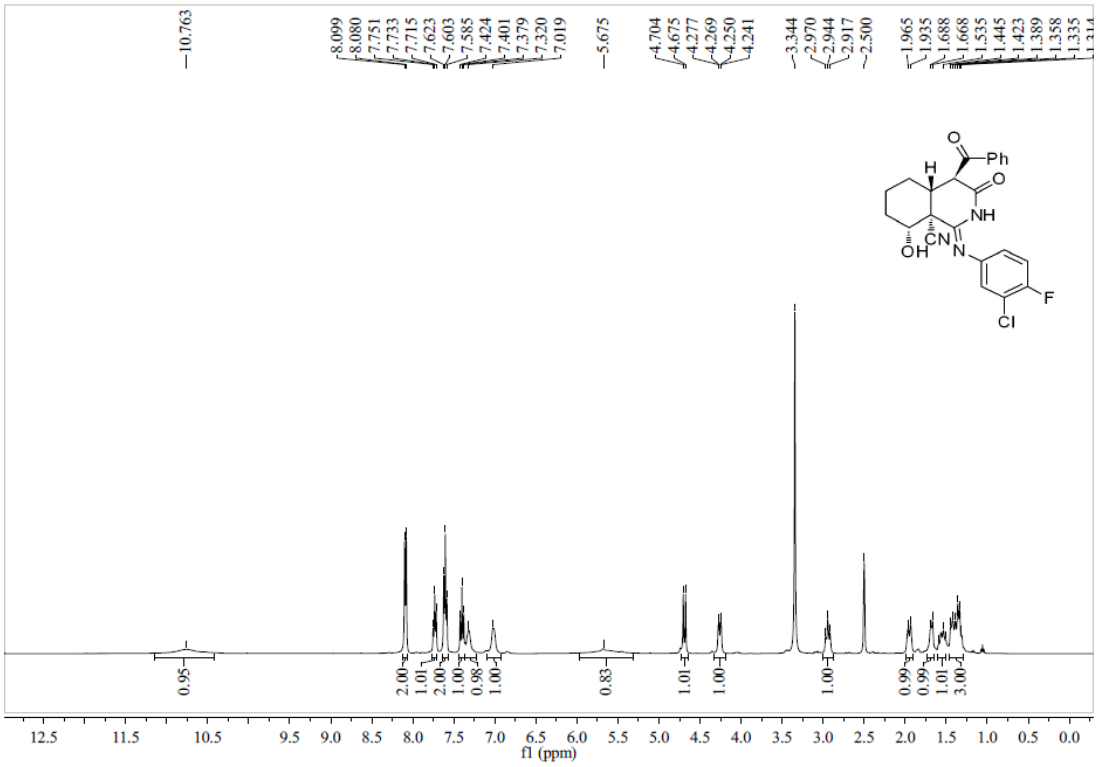

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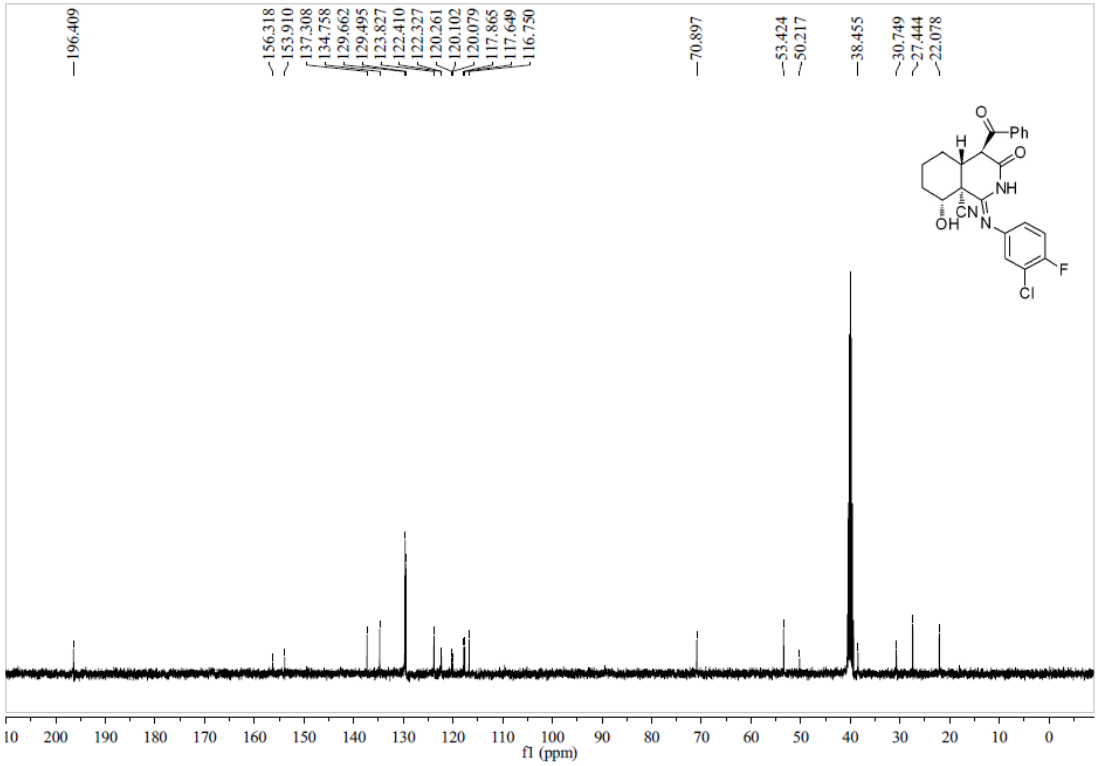
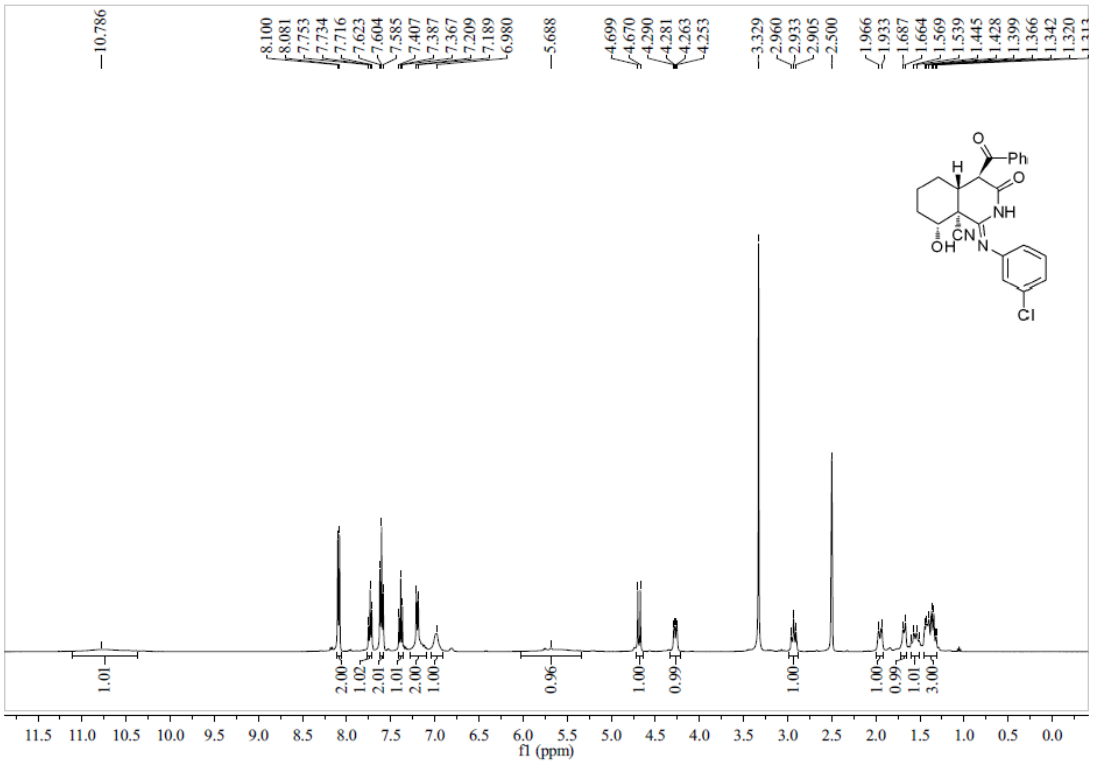
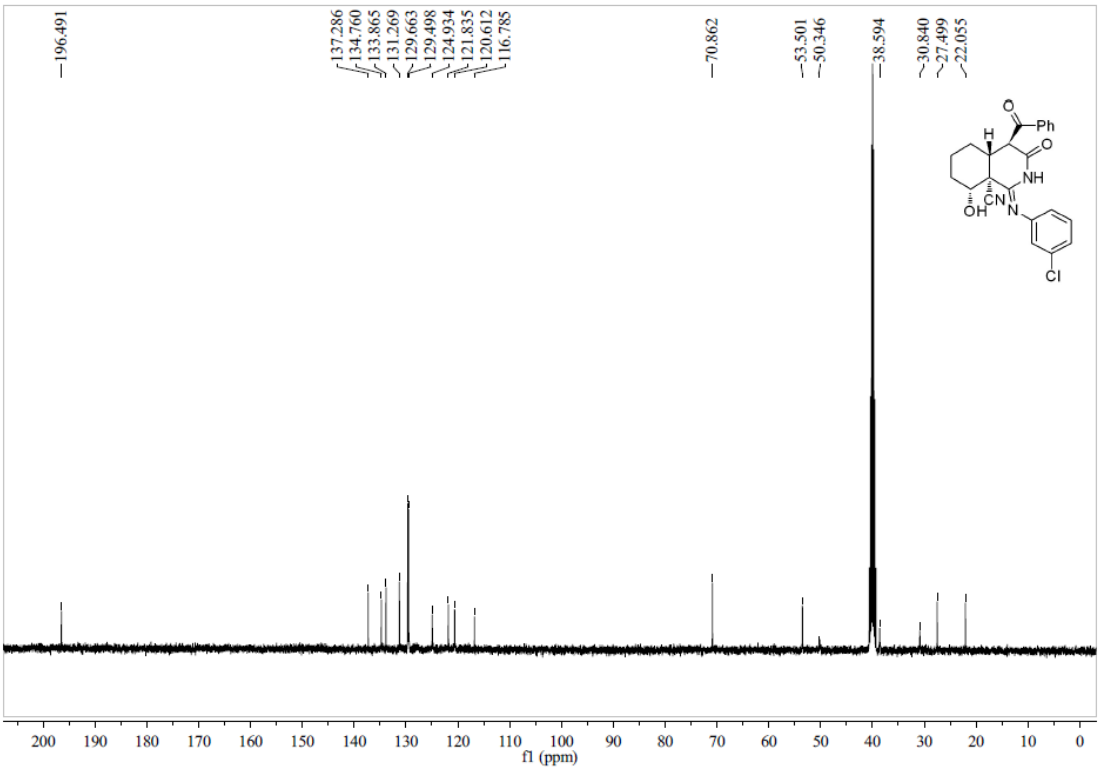


^{1}H NMR of compound **4l**



^{13}C NMR of compound **4l**



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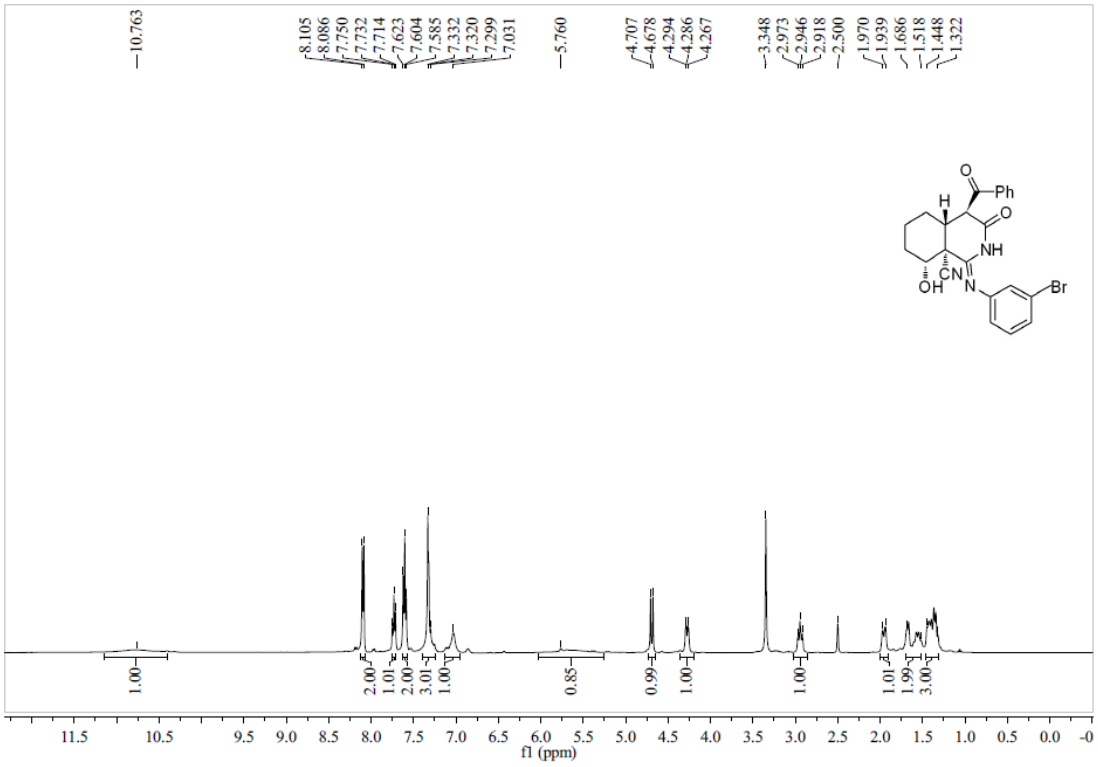
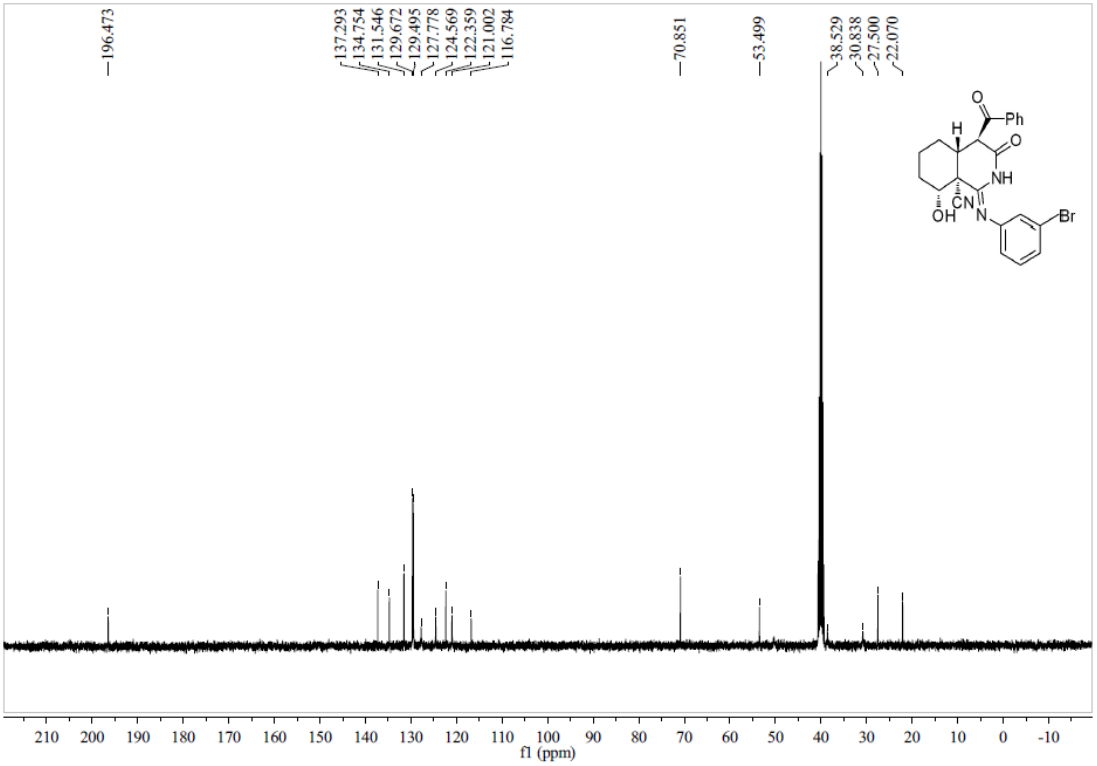
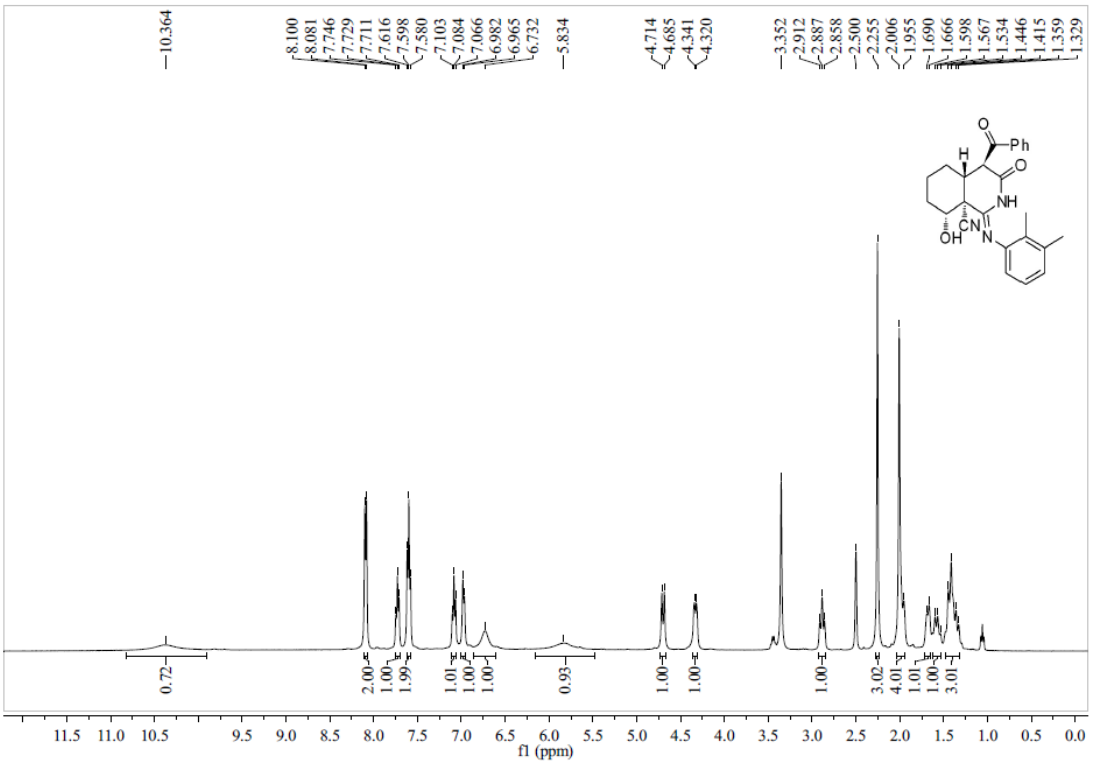


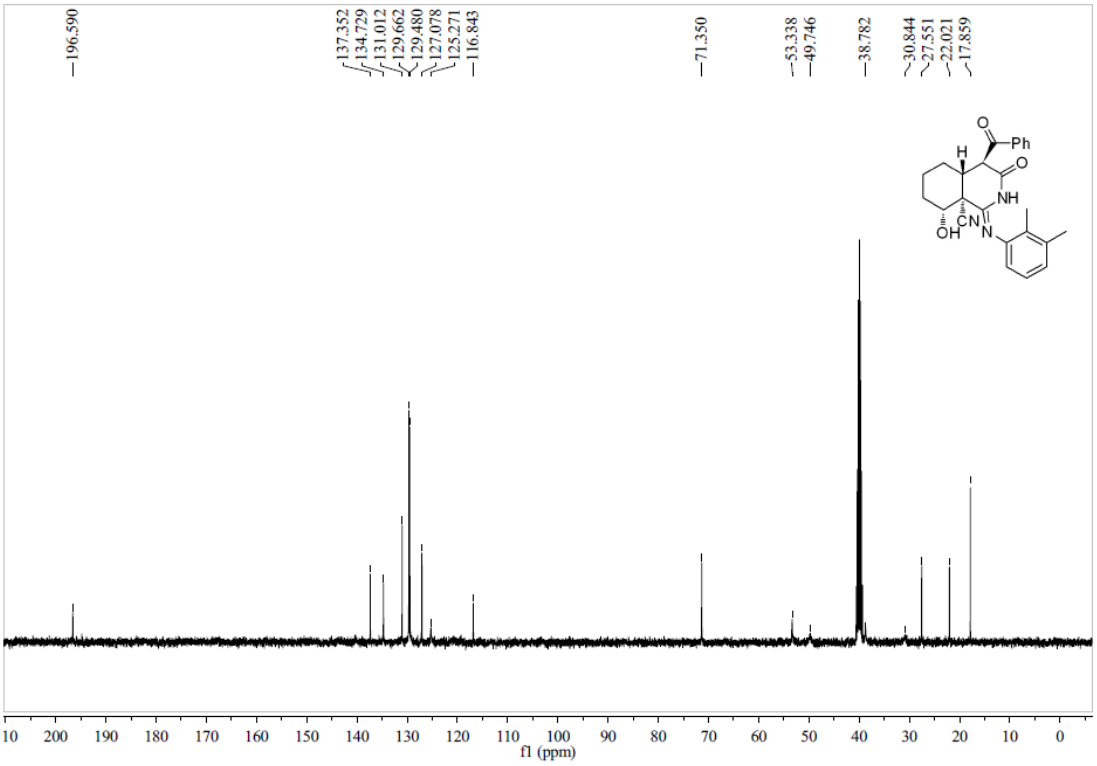
^{13}C NMR of compound **4m**



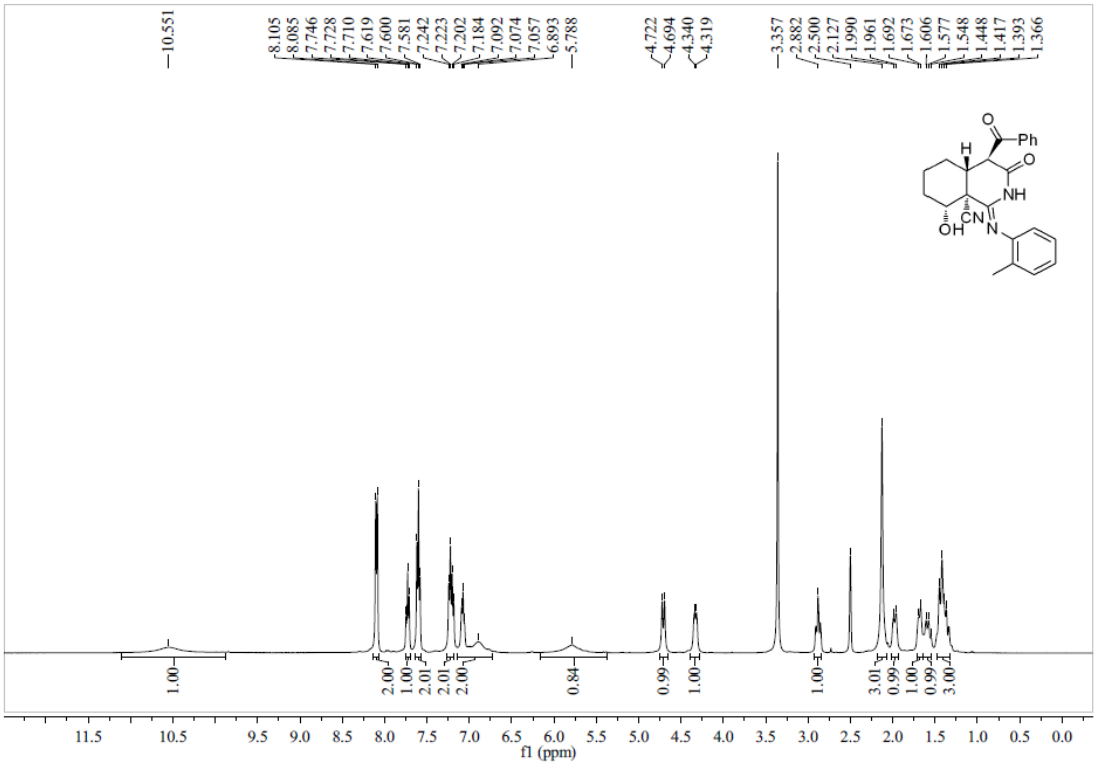
^{1}H NMR of compound **4n**



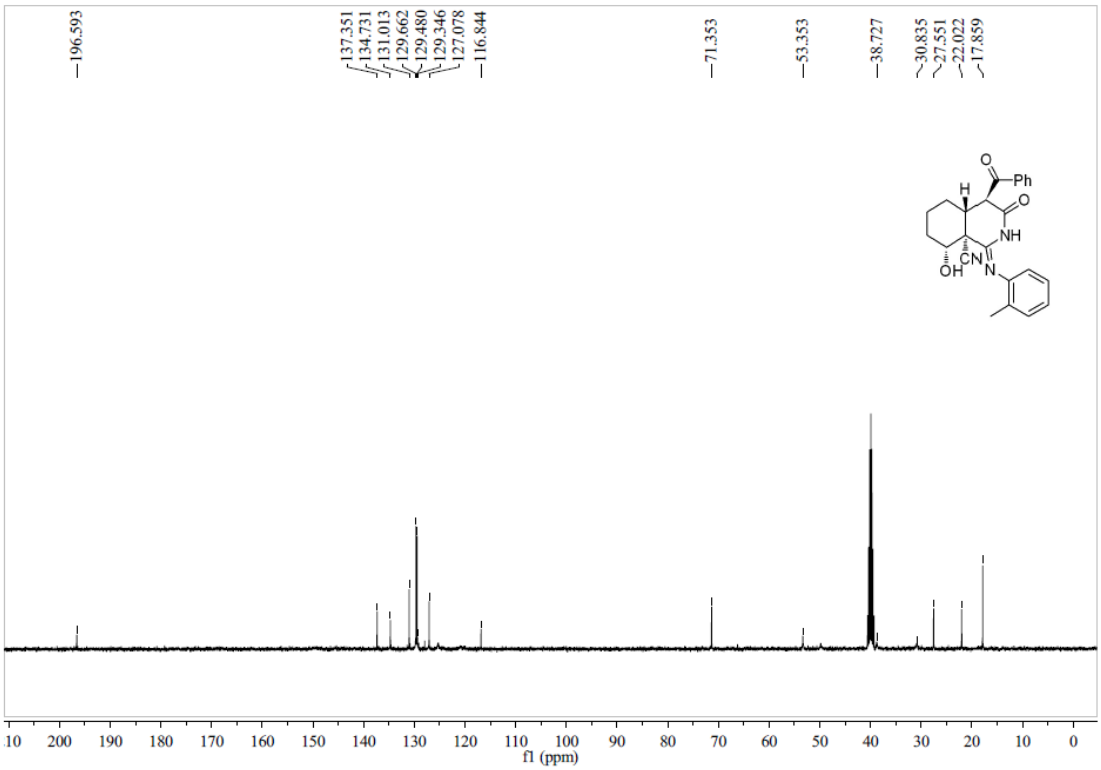
^{13}C NMR of compound **4n**



^{1}H NMR of compound **4o**



^{13}C NMR of compound **4o**



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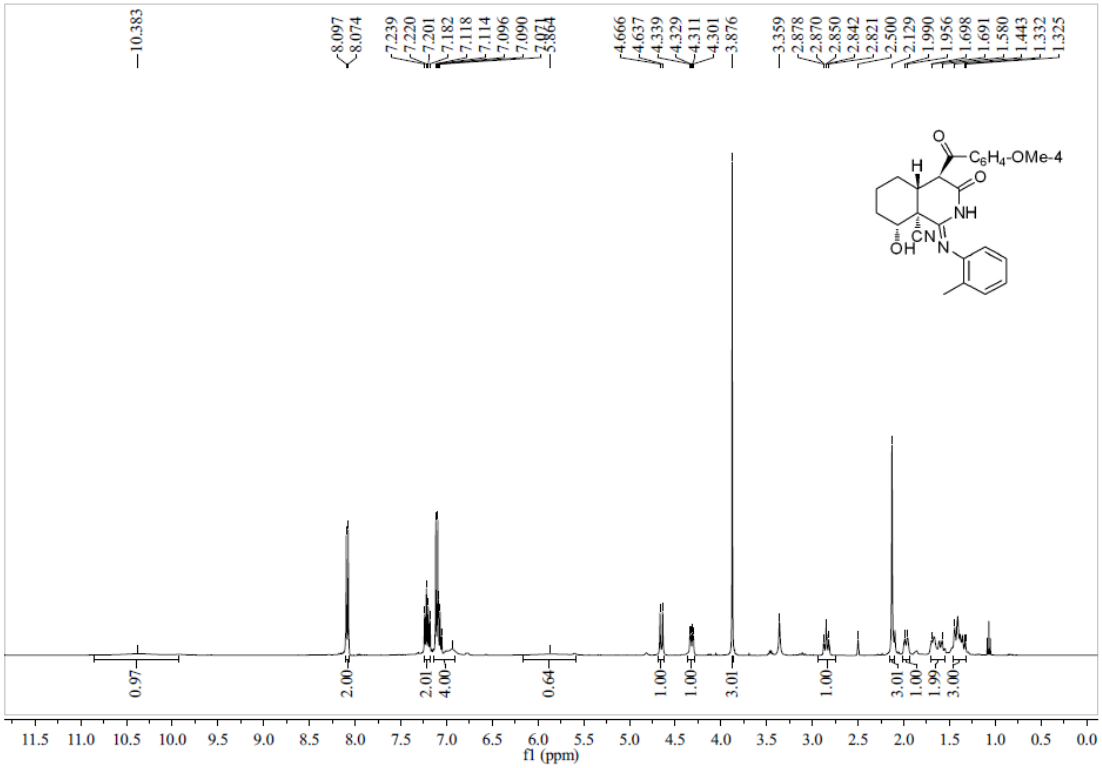
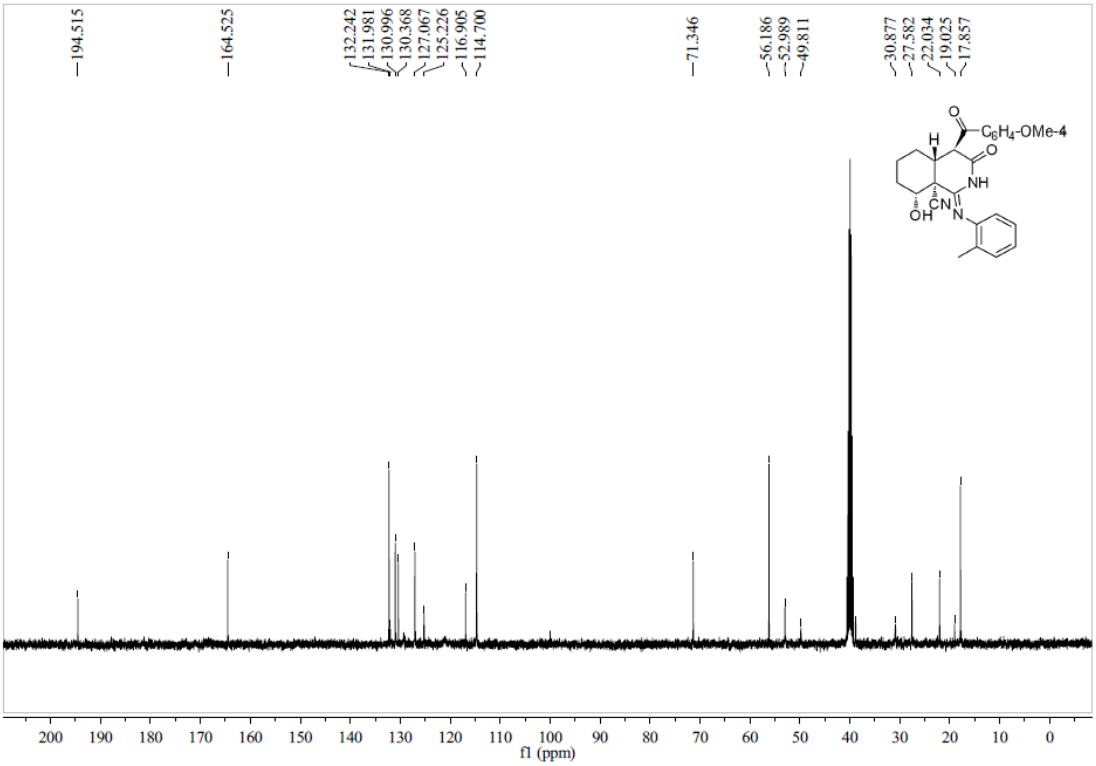
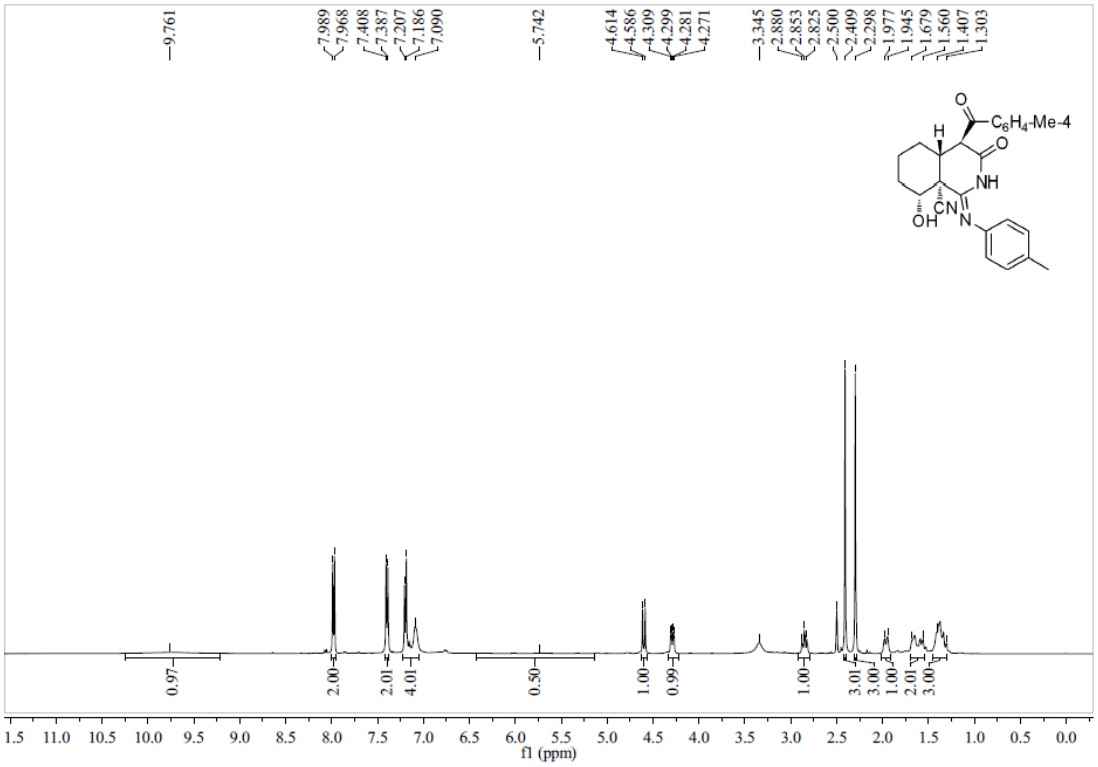


^{13}C NMR of compound **4p**



^{1}H NMR of compound **4q**



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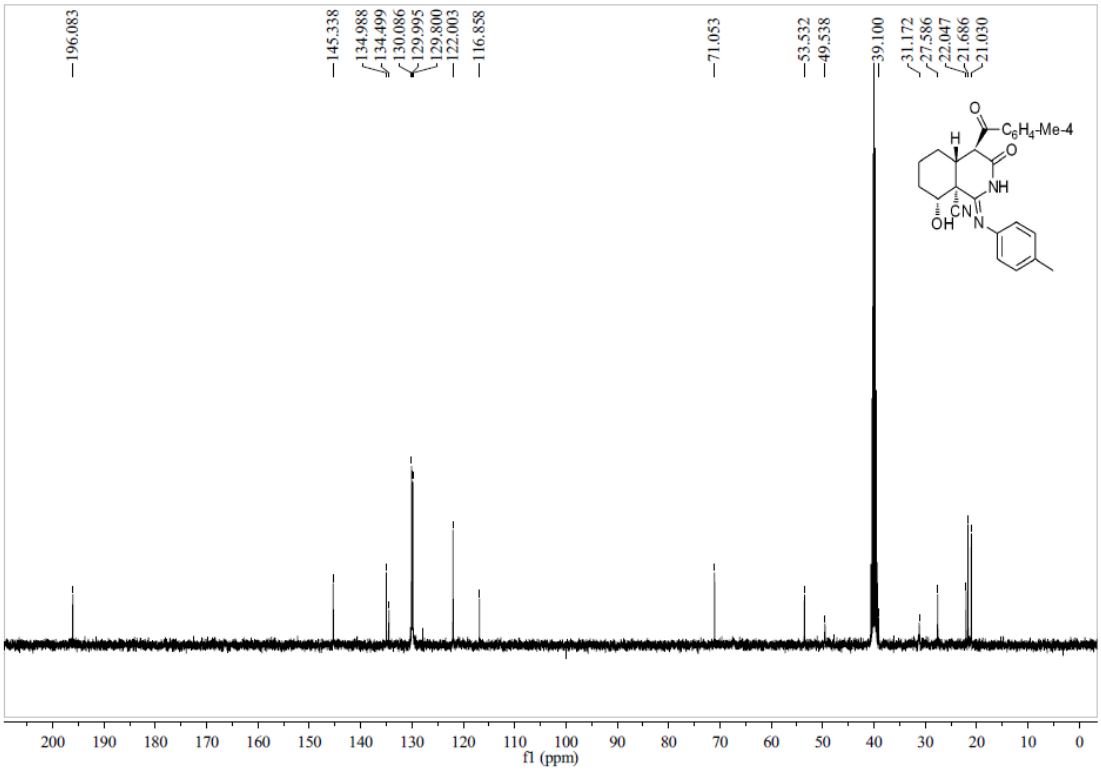

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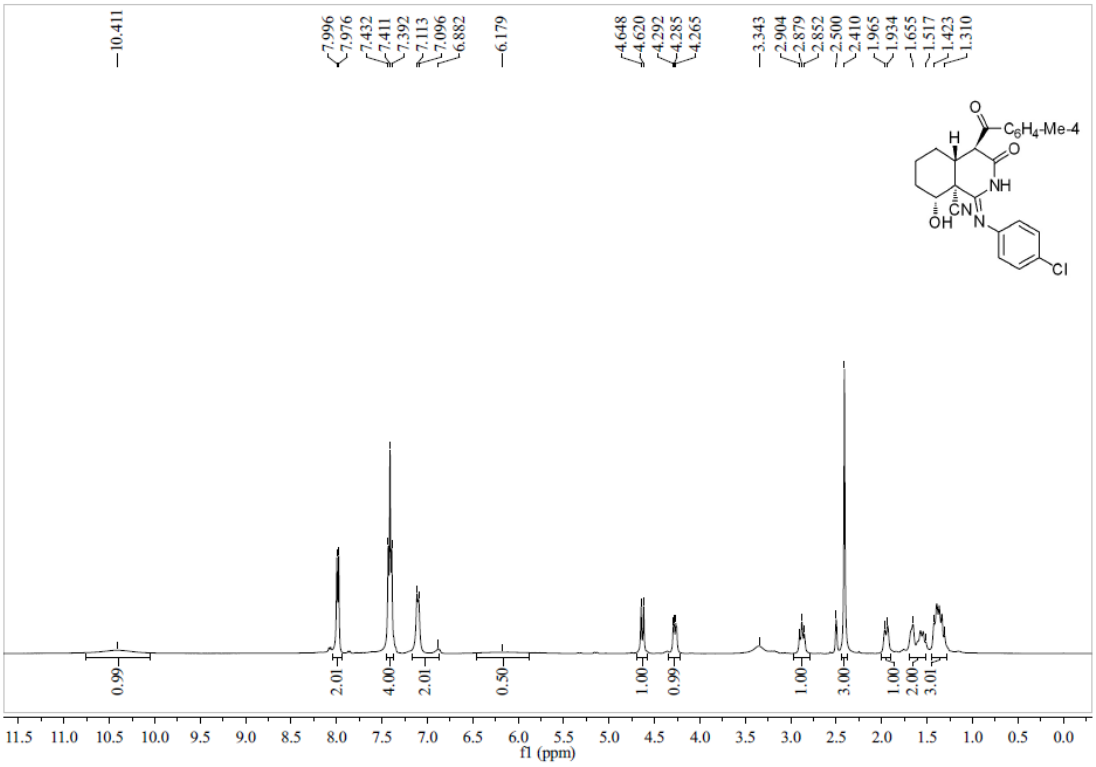

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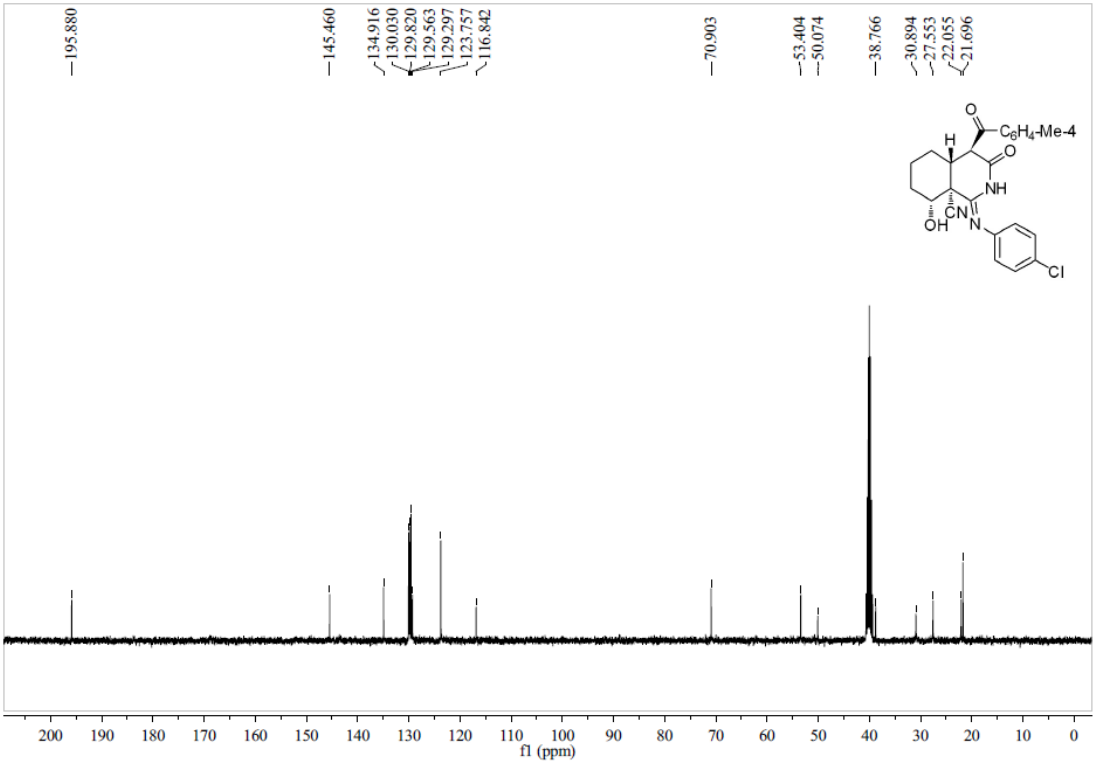

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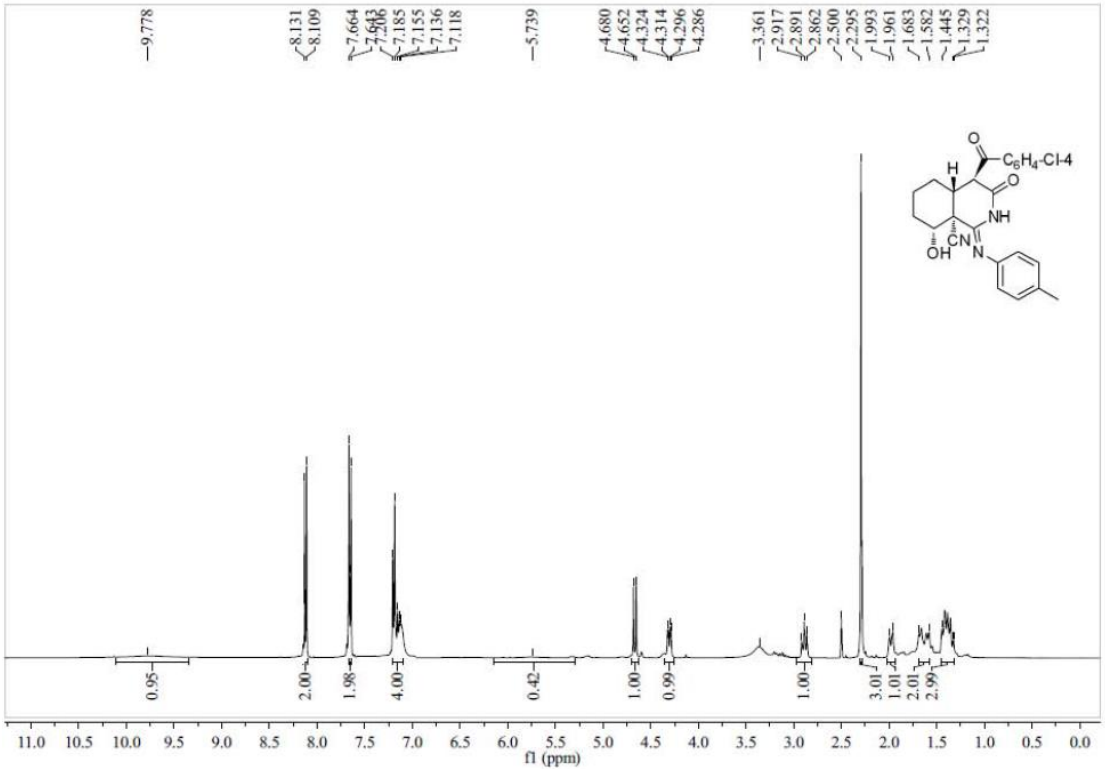

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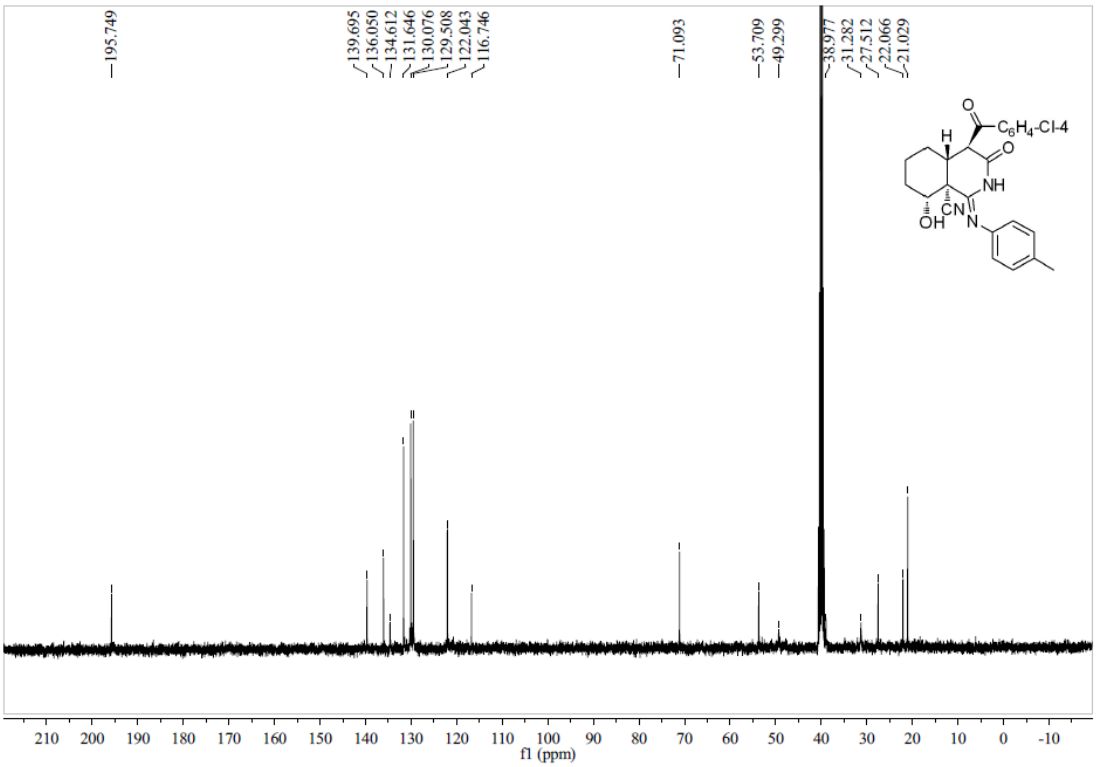
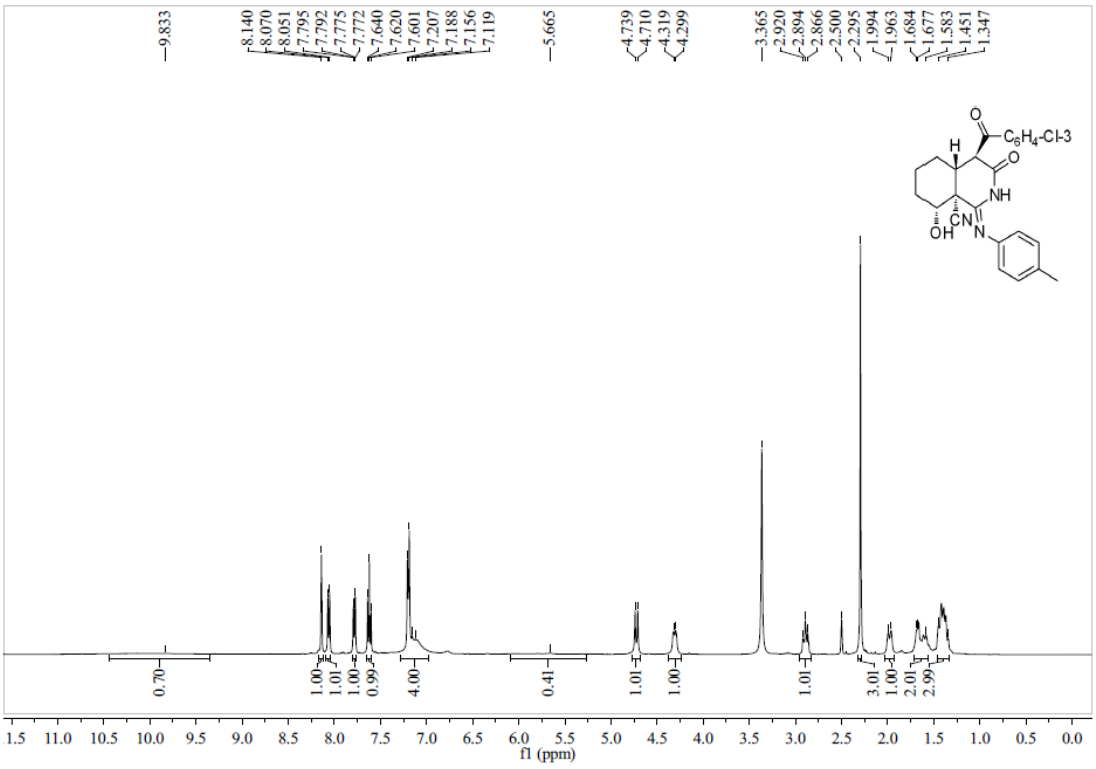


^{1}H NMR of compound **4t**



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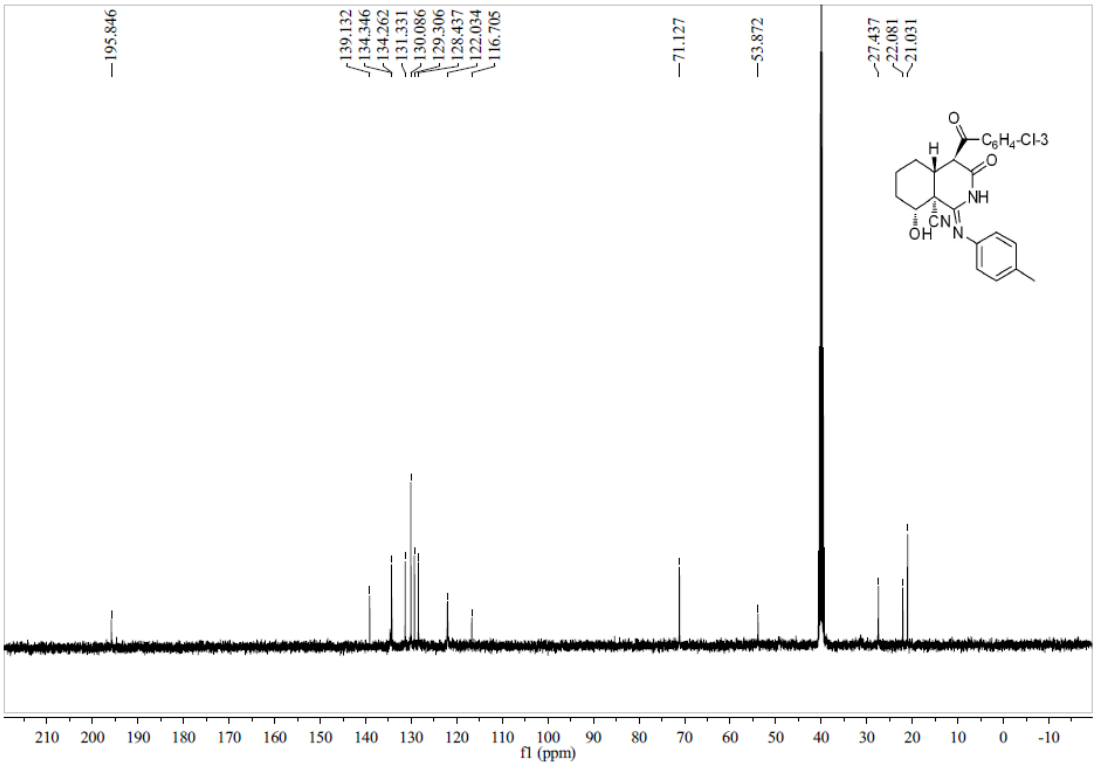
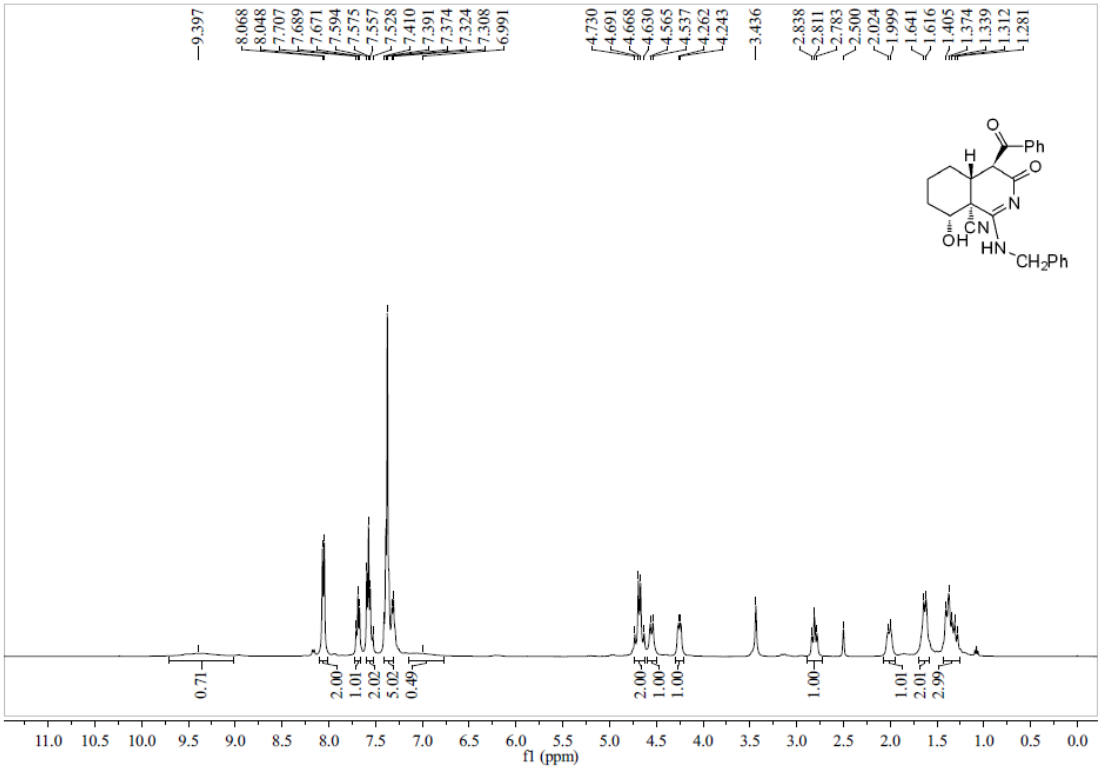
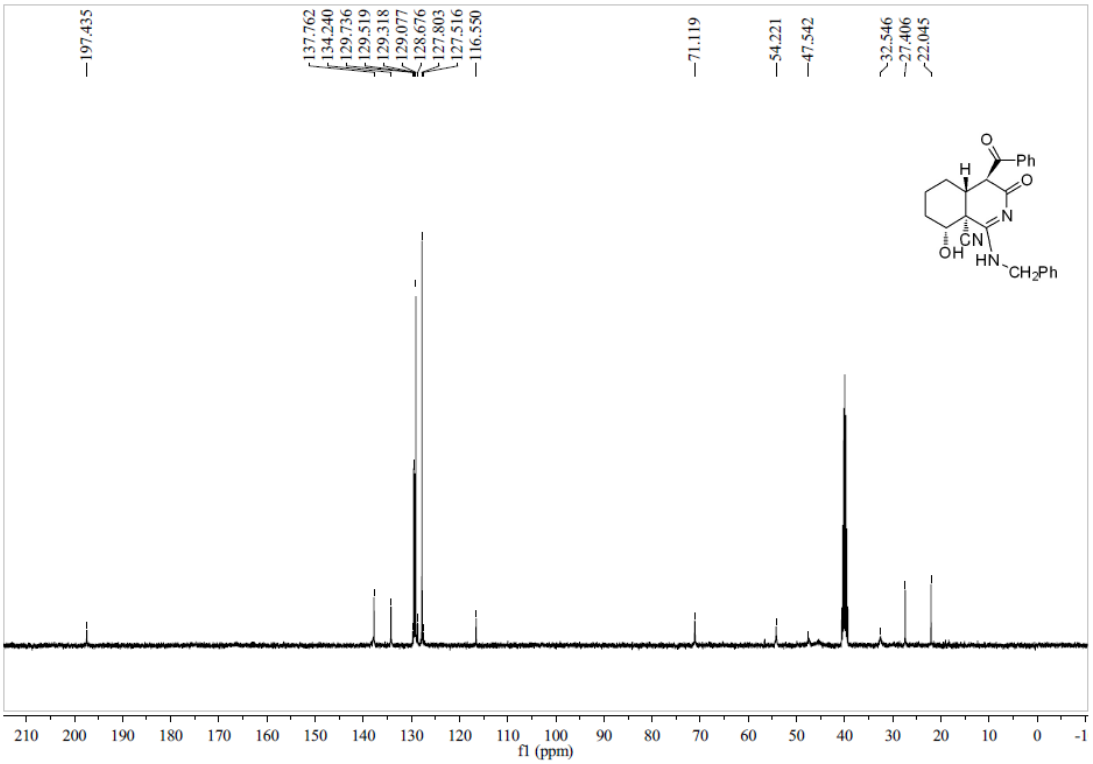


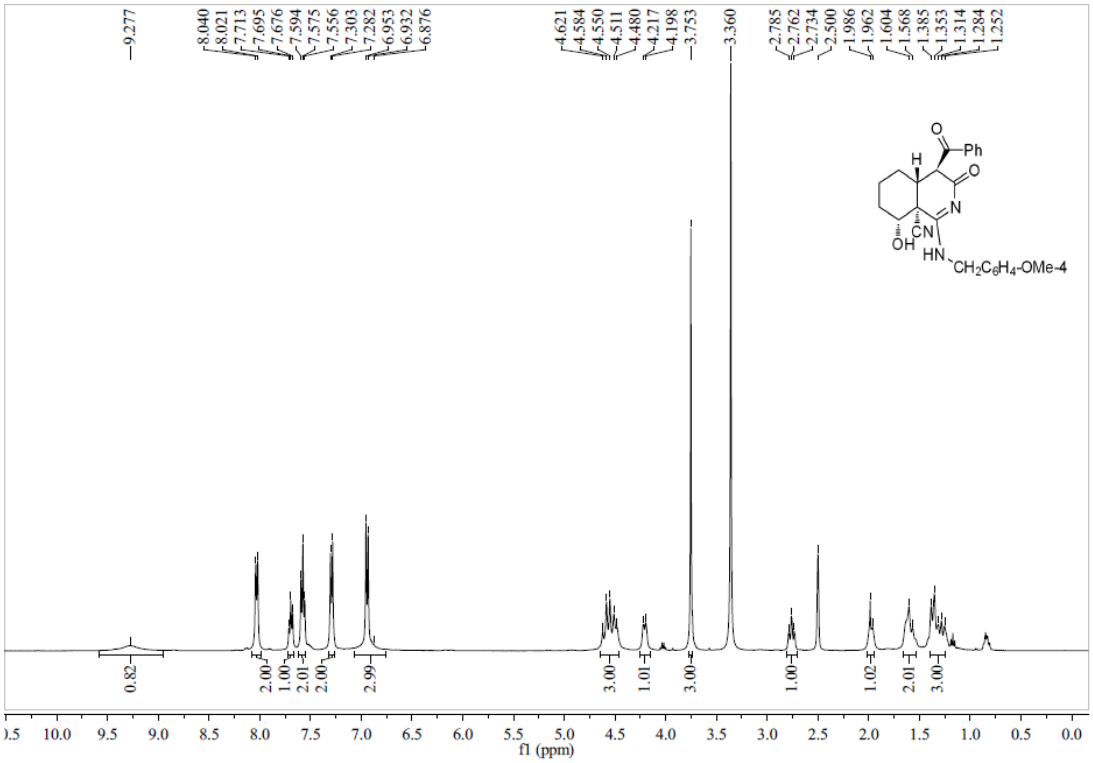
^{1}H NMR of compound **5a**



^{13}C NMR of compound **5a**



^{1}H NMR of compound **5b**



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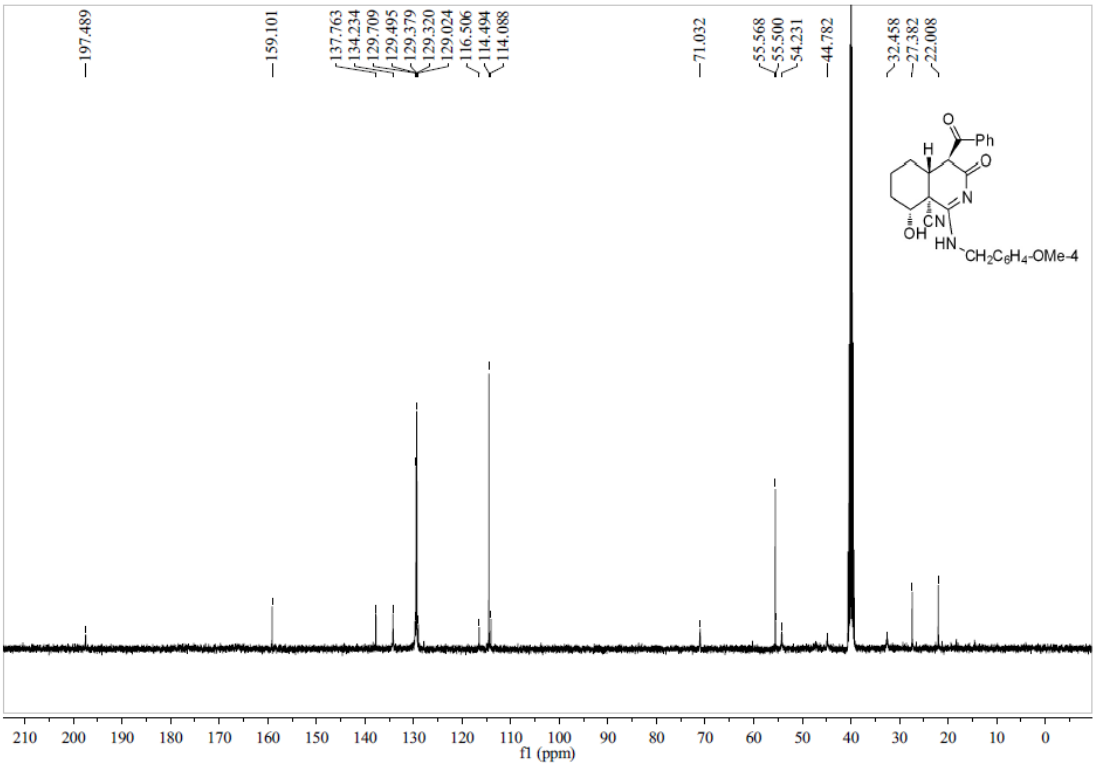

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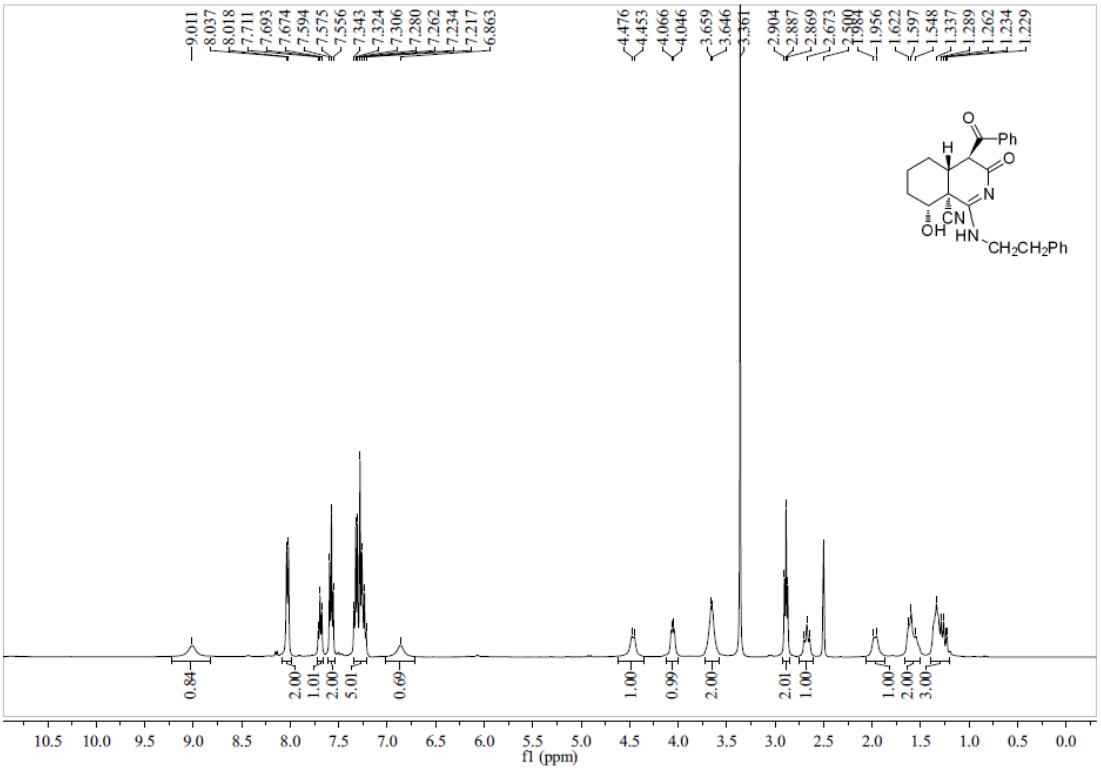

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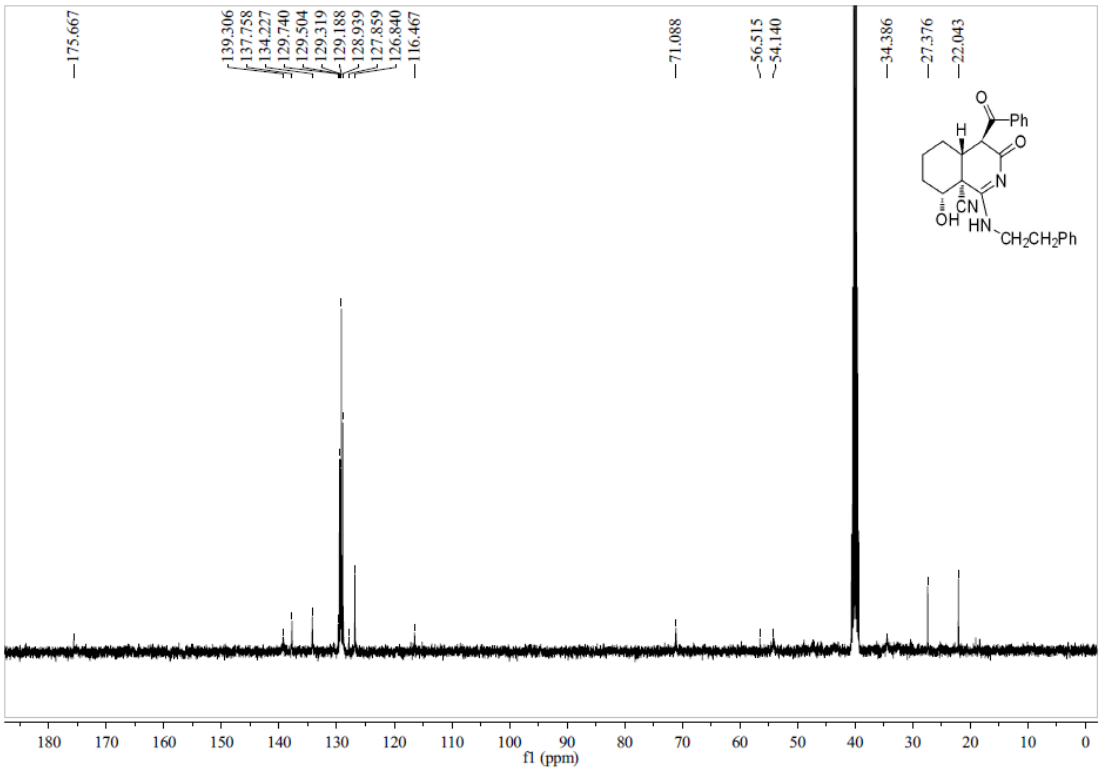
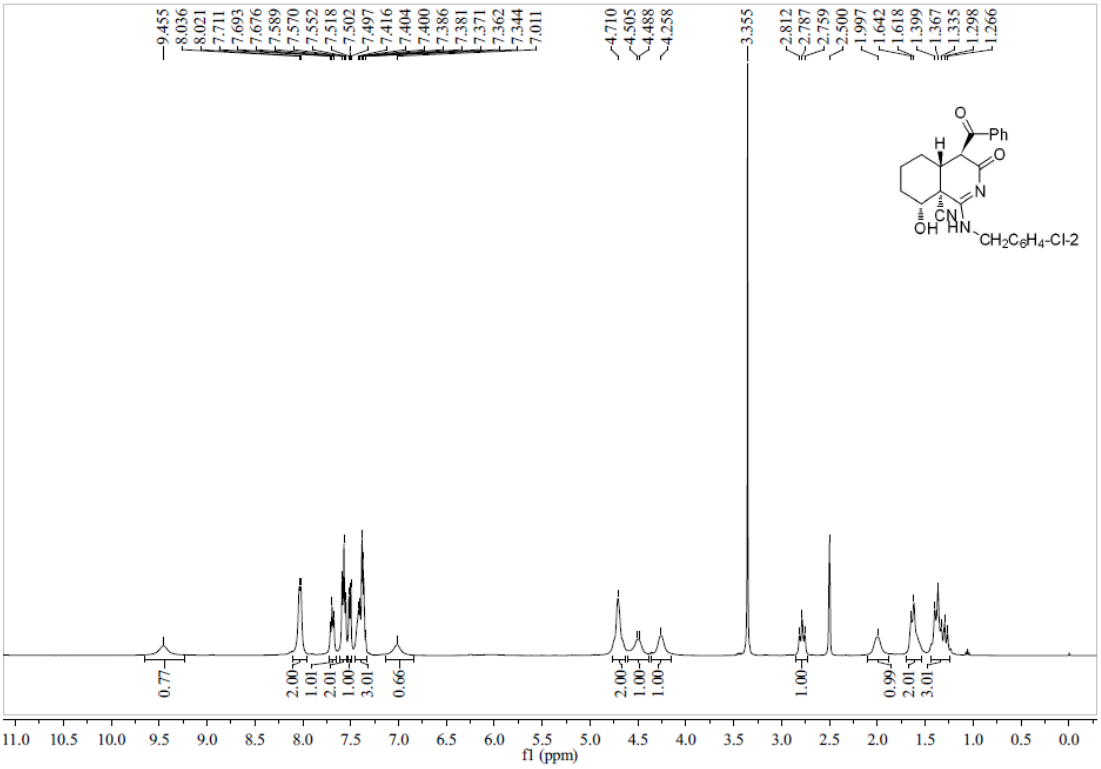
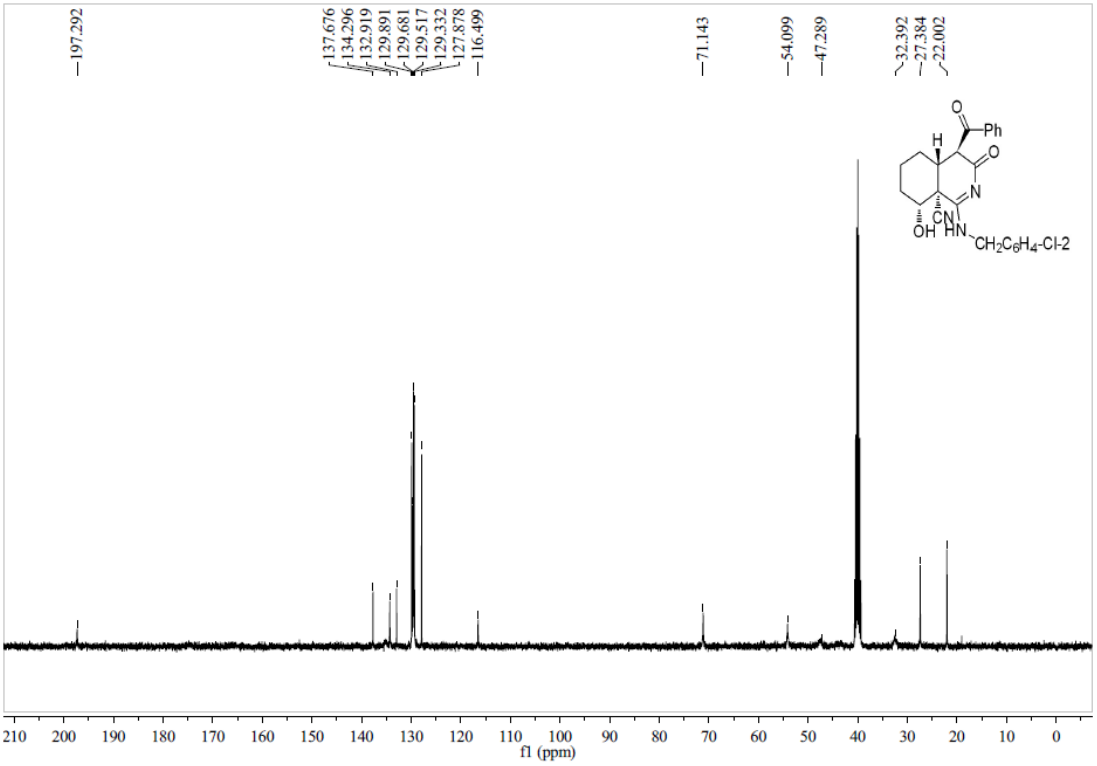


^{1}H NMR of compound **5d**



^{13}C NMR of compound **5d**



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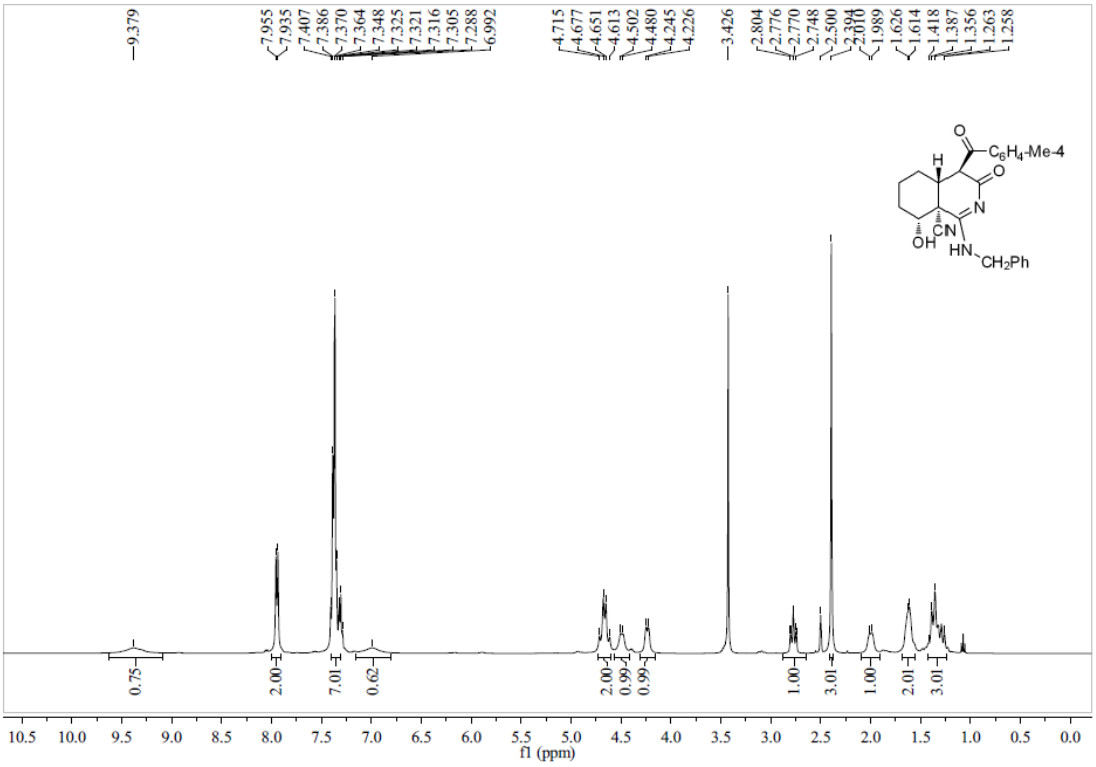

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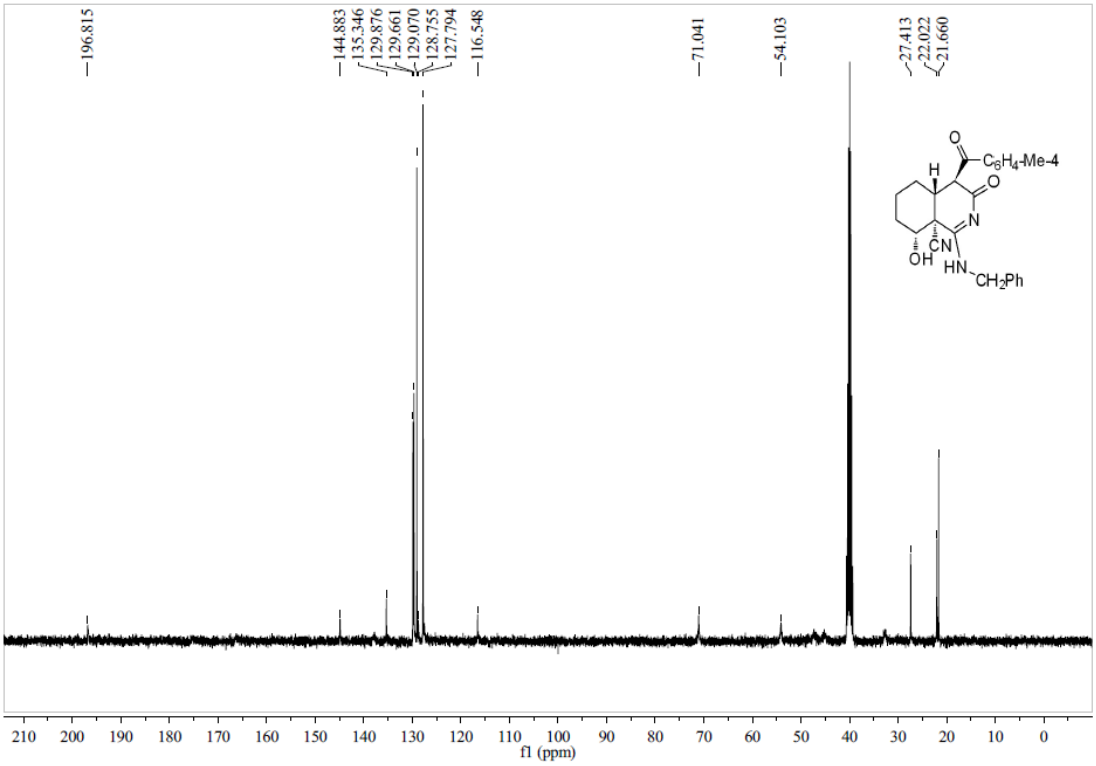

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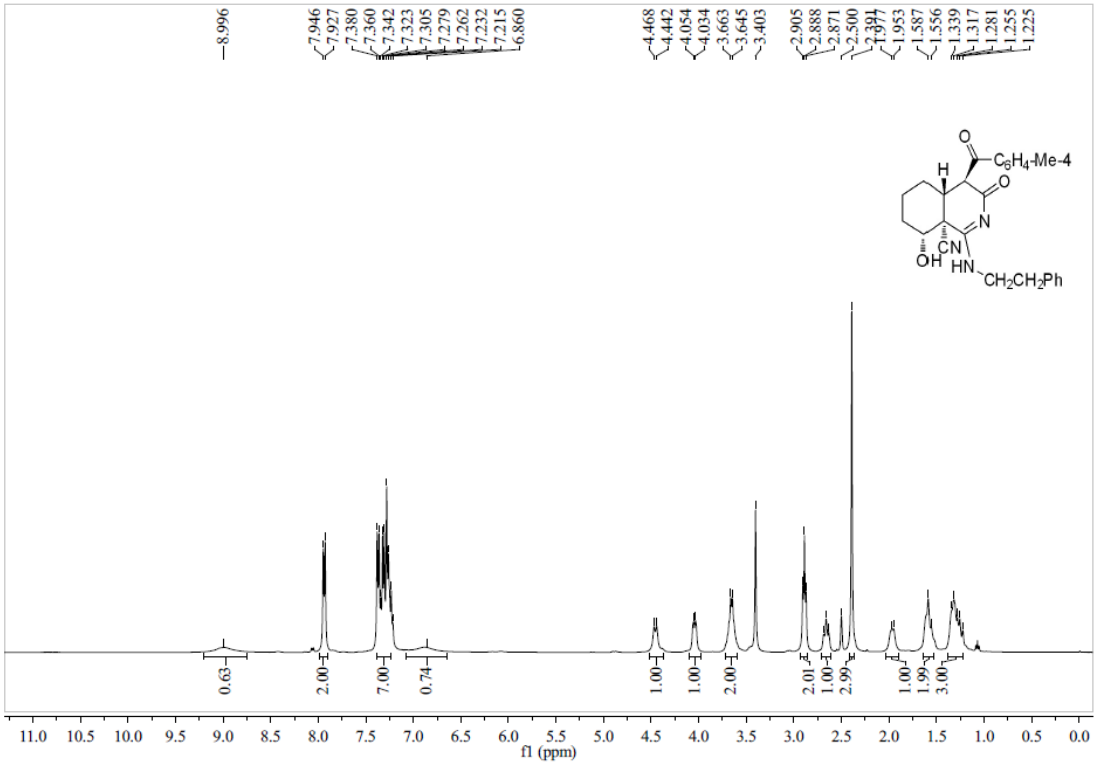
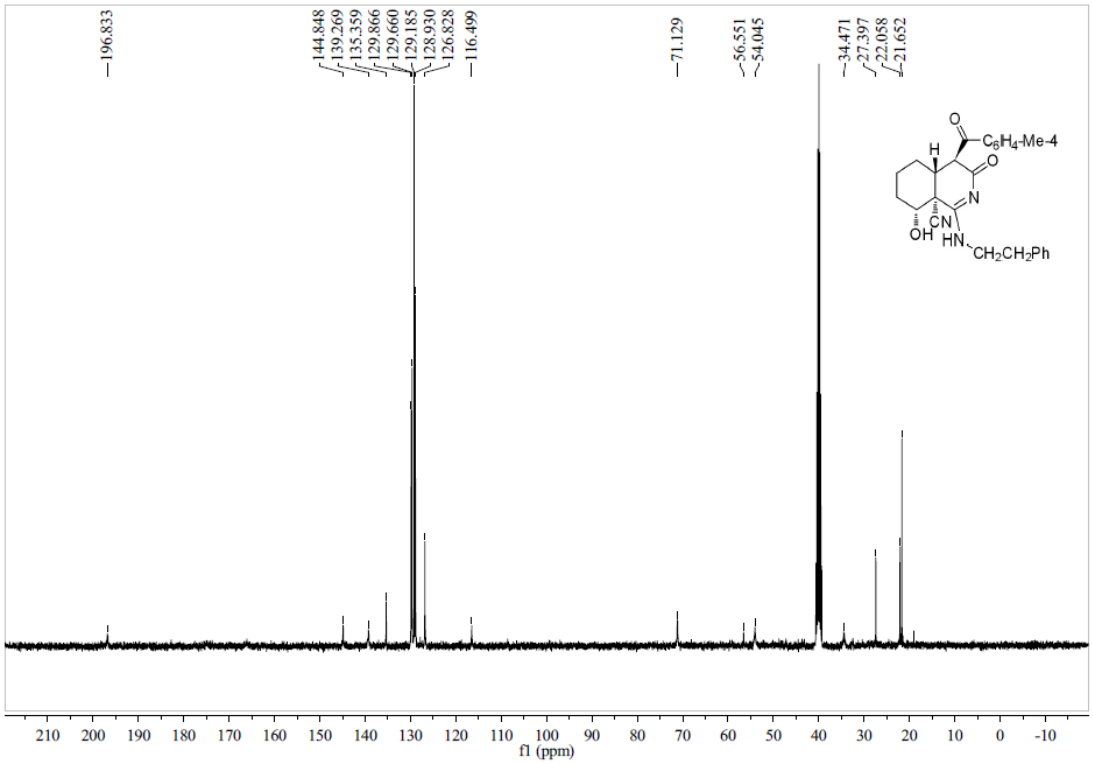
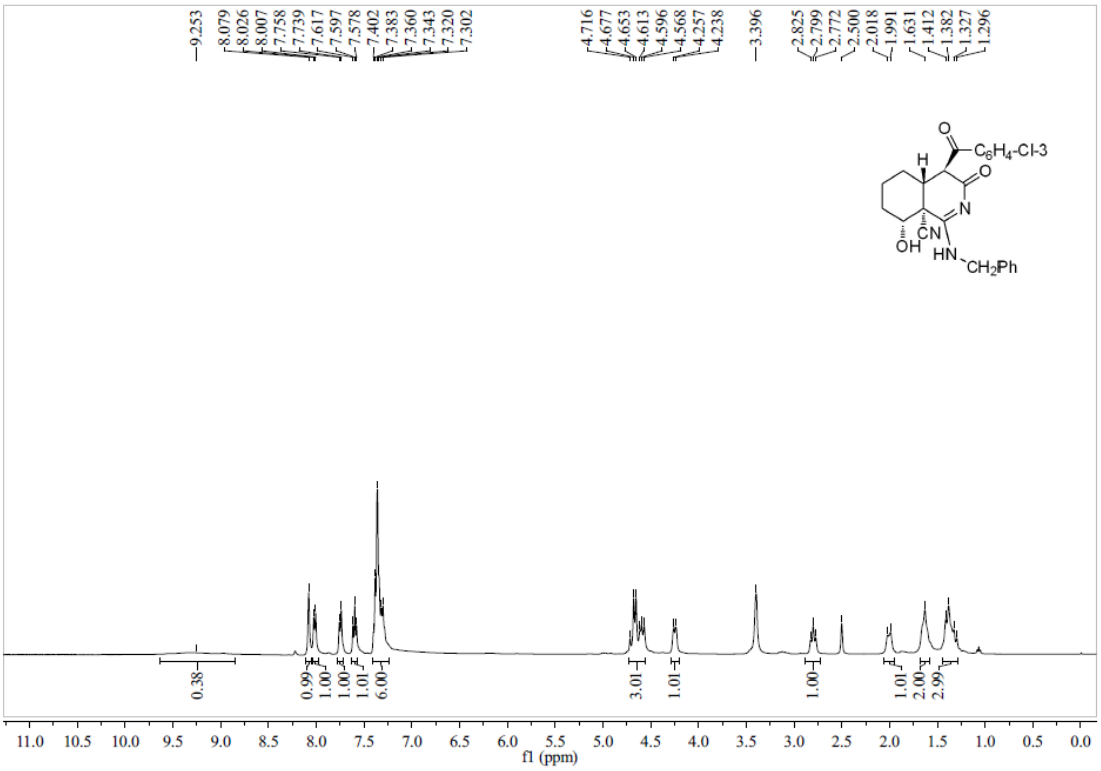


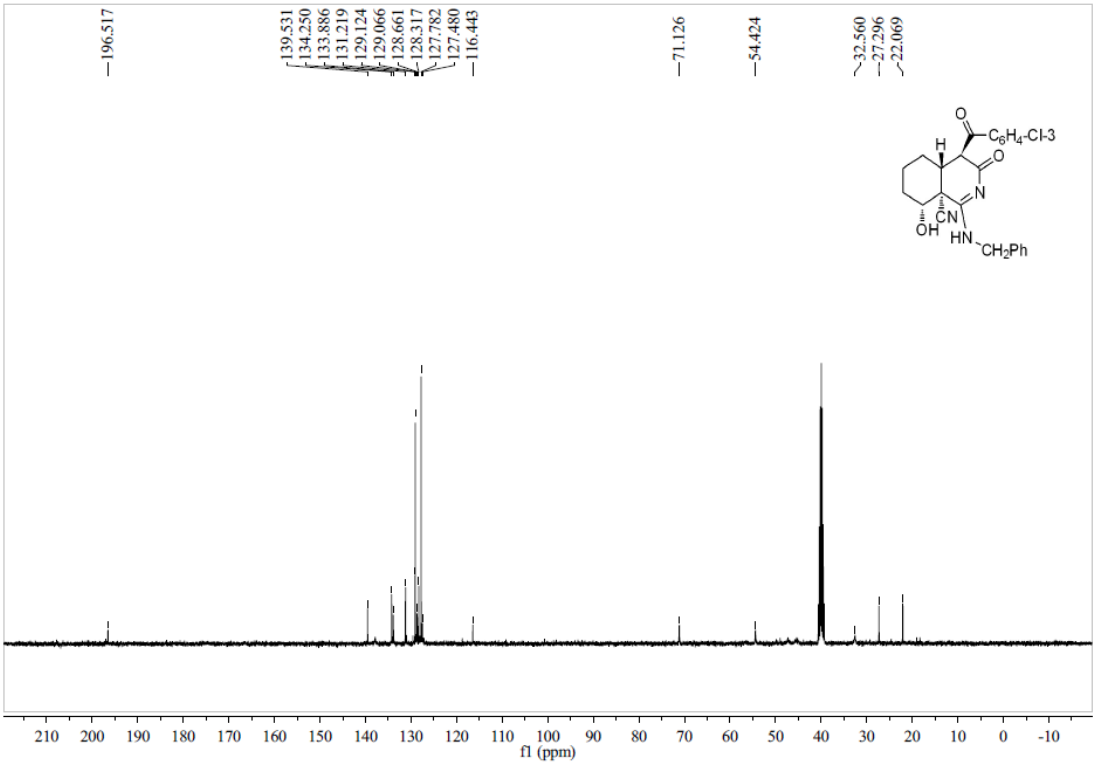
^{13}C NMR of compound **5f**



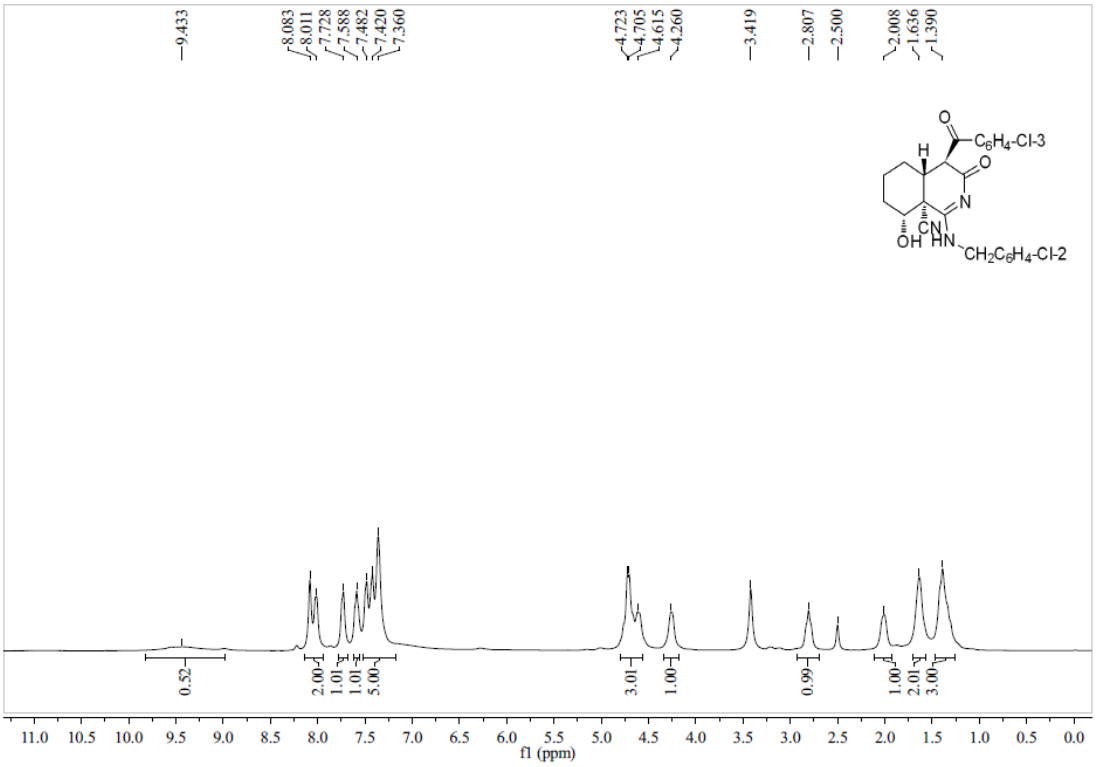
^{1}H NMR of compound **5g**



^{13}C NMR of compound **5g**



^{1}H NMR of compound **5h**



^{13}C NMR of compound **5h**