Electronic Supplementary Material (ESI) for RSC Advances.

A domino green method for the rapid synthesis of novel fused isoquinoline derivatives via Knoevenagel/Michael/cyclization reactions in aqueous media and their photophysical properties

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1.General Remarks

The reactions were carried out in 5 mL RB flask, fixed with reflux condenser and placed in the oilbath. Thin layer chromatography plates were visualized by the ultraviolet light and/or by exposure to iodine vapours and/or by exposure to methanolic acidic solution of *p*-anisaldehyde followed by heating (<1 min) on a hot plate (~250 °C). IR spectra were recorded on FT-IR spectrometer. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ and CF3COOH using 300, 400, 500 or 600 MHz NMR spectrometers. The chemical shifts (δ) were reported in parts per million (ppm) with respect to TMS as an internal standard. The coupling constants (*J*) are quoted in Hertz (Hz). Mass spectra were recorded on mass spectrometer by Electrospray ionization (ESI) technique.

2. General experimental procedure

A 5 ml RB flask containing 1-methyl isoquinoline (**1**) (1 mmol), malono nitrile (**2**) (1 mmol), aromatic aldehyde (**3**) (1 mmol) water (2 mL) was placed in oilbath and refluxed for the appropriate time, at 100 ^{0}C (temperature monitored by a thermometer). The progress of reaction was monitored by TLC. After completion of the reaction, the flask was removed from the oil bath and cooled to room temperature. The solid was filtered and then washed with pet-ether (2X3ml). The product were dried.

3. ICP-OES analysis report of tap water and HPLC grade water:

Validation of the water used in the reaction was analyzed by **ICP-OES** method and the analysis report is shown below.

Results:

sample	Al (mg/l)	Ca (mg/l)	Cu (mg/l)	Fe (mg/l)	K (mg/l)	Mg (mg/l)	Na (mg/l)	Ni (mg/l)	Pb (mg/l)	Zn (mg/l)
Tap water	0.01	9.95	B.D	B.D	0.53	2.19	8.87	B.D	B.D	0.21
HPLC water	B.D	0.18	B.D	B.D	B.D	0.03	0.69	B.D	B.D	B.D

B.D: Below Detection Limit

Crystal structure determination:

Figure caption: The molecular structure of 4i with the atom-numbering scheme. Displacement ellipsoids are drawn at the 20% probability level and H atoms are shown as small spheres of arbitrary radius. Only major component of the disordered trifluoromethyl fluorine atoms are shown for clarity. Dashed lines indicate N-H…O and O-H…O hydrogen bonds between the compound and solvent of crystallization.

Crystal data for 4i: The compound crystallized as a salt in the presence of strong acidic solvent trifluoroacetic acid. The asymmetric unit consists of a protonated form of compound as a cation, trifluoroacetic acetate as an anion, and a neutral trifluoroacetic acid, in 1:1:1 stoichiometric ratio with molecular formula $C_{20}H_{13}BrN_3^+.C_2F_3O_2^-.C_2F_3\ H_1O_2$. M = 602.29, orange block, 0.32 x 0.24 x 0.11 mm^3, monoclinic, space group $P2_1/n$ (No. 14), a = 11.8210(7), b = 15.0720(9), c = 14.4847(9) Å, β = 109.6100(10)°, V = 2431.0(3) Å^3, Z = 4, D_c = 1.646 g/cm^3, F_{000} = 1200, CCD area detector, MoKα radiation, λ = 0.71073 Å, T = 293(2)K, $2\theta_{max}$ = 50.0º, 23026 reflections collected, 4277 unique (R_{int} = 0.0243), Final *GooF* = 1.020, *R1* = 0.0493, *wR2* = 0.1300, *R* indices based on 3110 reflections with I >2σ(I) (refinement on F^2), 430 parameters, μ = 1.774 mm^{-1}.

CCDC 1063210 contains the supplementary crystallographic data for this paper which can be obtained free of charge at https://summary.ccdc.cam.ac.uk/structure-summary-form or from the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0) 1223 336 033; email: deposit@ccdc.cam.ac.uk.

Crystal structure determination: X-ray data for the compound were collected at room temperature using a Bruker Smart Apex CCD diffractometer with graphite monochromated Mo-Kα radiation (λ=0.71073Å) with ω-scan method.[1] Preliminary lattice parameters and orientation matrices were obtained from four sets of frames. Unit cell dimensions were determined using 6825 reflections for AW78 data. Integration and scaling of intensity data were accomplished using SAINT program.[1] The structures were solved by Direct Methods using SHELXS97[2] and refinement was carried out by full-matrix least-squares technique using SHELXL97.[2] Anisotropic displacement parameters were included for all non-hydrogen atoms. All H atoms were positioned geometrically and treated as riding on their parent C atoms, with C-H distances of 0.93--0.97 Å, and with U_{iso}(H) = 1.2U_{eq} (C) or 1.5U_{eq} for methyl atoms. H atoms bound to N

and O atoms were located in the difference Fourier map. Three fluorine atoms of trifluoromethyl groups were disordered over two sites. In the trifluoroacetate anion, two fluorine atoms have site occupancy factors (s.o.f) of 0.58 (F1/F2 atoms, major component) and 0.42 (F1D/F2D atoms, minor component) whereas the third fluorine atom has s.o.f. of 0.89 (F3, major component) and 0.11 (F3D, minor component). Similarly, in the neutral trifluoroacetic acid, two fluorine atoms have s.o.f. of 0.64 (F4/F6 atoms, major component) and 0.38 (F4D/F6D atoms, minor component) whereas the third fluorine atom has s.o.f of 0.82 (F5, major component) and 0.18 (F5D, minor component). One of oxygen atoms is disordered over two sites in trifluoroacetate anion (s.o.f of O1/O1D is 0.56/0.44) and also in trifluoroacetic acid (s.o.f of O3/O3D is 0.51/0.49). The anisotropic displacement parameters of the disordered fluorine atoms were restrained to be similar (SIMU instruction) and the direction of motion along the axis between these atoms was also restrained (DELU instruction).[3] The C-F bond distances of trifluoromethyl groups were restrained to a set target value of 1.30Å with e.s.d. of 0.005Å.

1. SMART & SAINT. Software Reference manuals. Versions 6.28a & 5.625, Bruker Analytical X-ray Systems Inc., Madison, Wisconsin, U.S.A., 2001.
2. Sheldrick, G. M. SHELXS97 and SHELXL97, Programs for crystal structure solution and refinement; University of Gottingen: Germany, 1997.
3. Muller, P, Herbst-Imer, R, Spek, A. L, Schneider, T. R, and Sawaya, M. R. Crystal Structure Refinement: A Crystallographer's Guide to SHELXL. Muller, P. Ed. 2006 Oxford University Press: Oxford, New York, pp. 57–91.

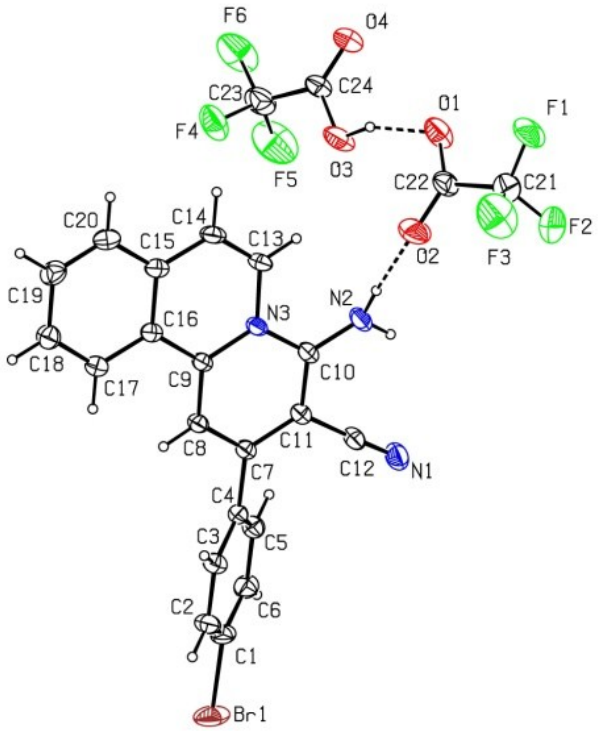


Figure S1. ORTEP diagram of compound 4i·2CF_3COOH

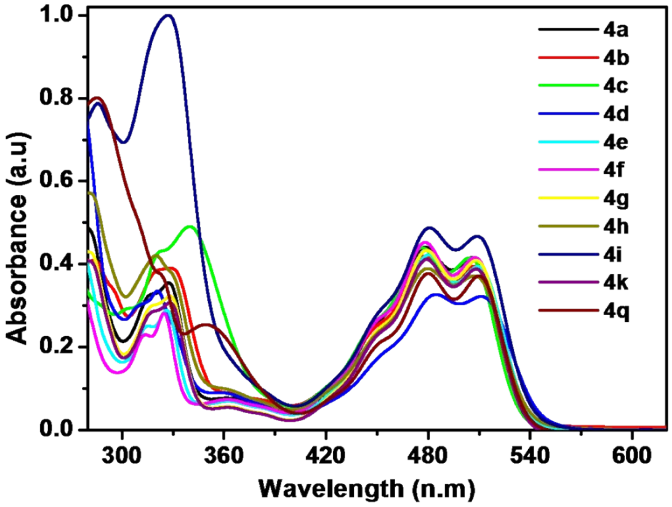


Fig. 3 UV-Vis spectra of compounds **4a-4i, 4k** and **4q** in chloroform/trifluoroacetic acid solution (1.0×10^{-5} M).

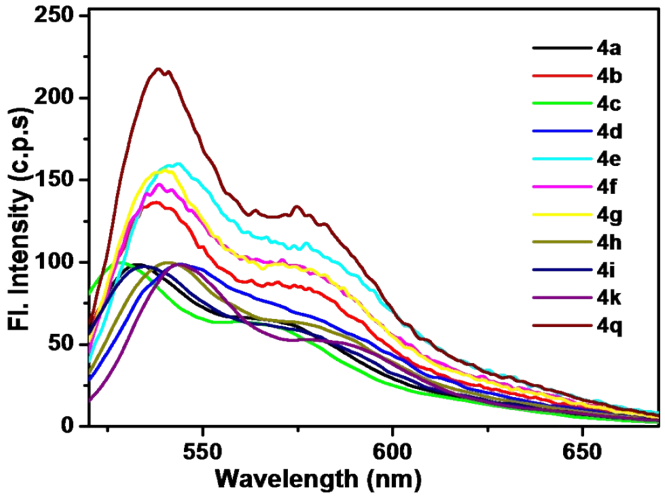


Fig. 4 Fluorescence spectra of compounds **4a-4i, 4k** and **4q** in chloroform/trifluoroacetic acid solution (1.0×10^{-5} M).

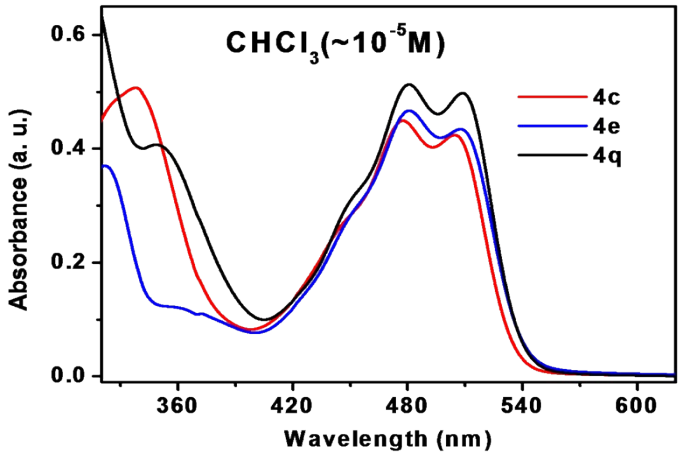


Fig. 5 UV-Vis spectra of compounds **4c, 4e, 4q** in chloroform only.

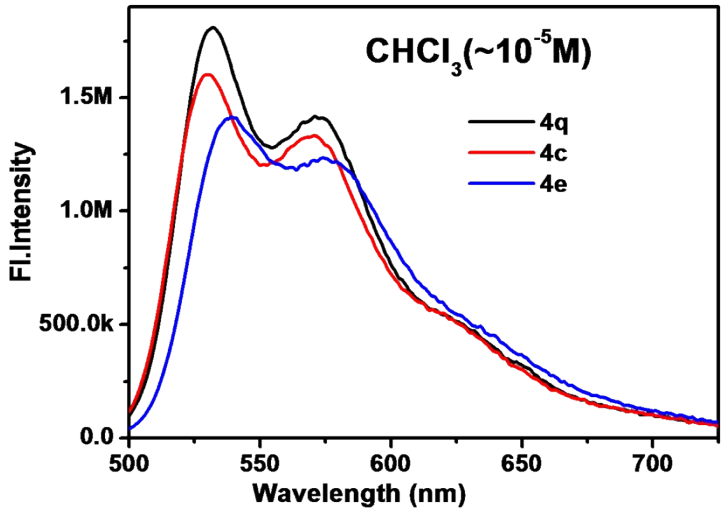
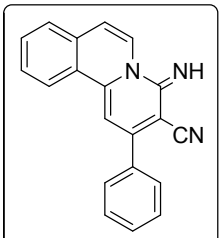


Fig. 6 Fluorescence spectra of compounds **4c, 4e,** and **4q** in chloroform.

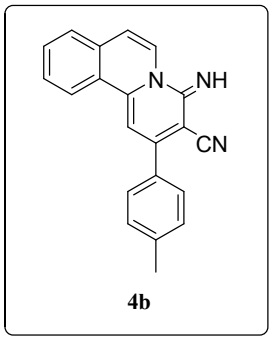
Analytical data and ^{1}H and ^{13}C NMR spectra of all compounds.

1) **4-imino-2-phenyl-4H-pyrido[2, 1-a]isoquinoline-3-carbonitrile (4a):** Pink solid. Yield 90%. Mp: 241-243 ^{o}C. IR (KBr) ν_{max} (cm^{-1}) 3315, 3054, 2201, 1641, 1609, 1534, 1503, 1392, 1275, 1130, 1080, 944, 811, 745, 693, 587; ^{1}H-NMR (500 MHz, $CDCl_3$+CF_3COOD), δ (ppm) 7.66(m, 3H), 7.77(d, *J* = 6.56 Hz, 2H), 8.00(m, 5H), 8.33(s, 1H), 8.55(br s, 1H), 8.67(d, *J* = 8.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$+CF_3COOD), δ (ppm) 155.17, 152.44, 143.79, 135.58, 133.94, 132.39, 132.08, 131.06, 129.80, 128.72, 128.48, 125.75, 124.60, 123.20, 121.29, 118.02, 115.75, 113.48, 111.22, 110.40, 91.37; ESI-MS: m/z: 296 $(M+H)^+$, HR-MS calcd for $C_{20}H_{14}N_3$: 296.1182 $[M+H]^+$, found: 296.1163.



4a

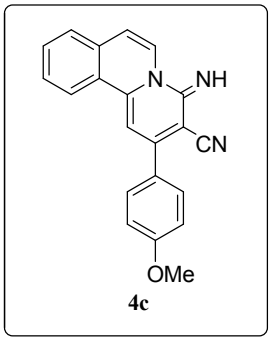
2) **4-imino-2-p-tolyl-4H-pyrido[2, 1-a]isoquinoline-3-carbonitrile (4b):** Pink solid. Yield 90%. Mp: 210-212 ^{o}C. IR (KBr) ν_{max} (cm^{-1}) 3317, 2917, 2199, 1643, 1608, 1593, 1507, 1478, 1391, 1276, 1127, 1081, 940, 806, 743; ^{1}H-NMR (500 MHz, $CDCl_3$+CF_3COOD), δ (ppm) 2.52(s, 1H), 7.47(d, *J* = 7.9 Hz, 2H), 7.69(d, *J* = 8.0 Hz, 2H), 7.93-7.99(m, 3H), 8.03-8.09(m, 2H), 8.29(s, 1H), 8.58(d, *J* = 7.6 Hz, 1H), 8.64(d, *J* = 8.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$+CF_3COOD), δ (ppm) 154.86, 152.57, 143.36, 143.24, 135.14, 131.67, 131.19, 131.05, 130.51, 128.74, 128.51, 125.49, 124.56, 122.09, 115.80, 113.52, 111.25, 109.69, 91.55, 21.54; ESI-MS: m/z: 310 $(M+H)^+$, HR-MS calcd for $C_{21}H_{16}N_3$: 310.1338 $[M+H]^+$, found: 310.1321.



4b

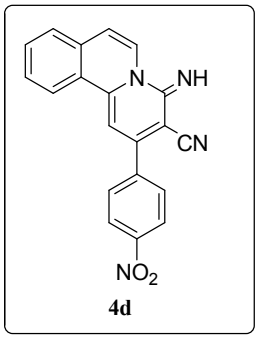
3) **4-imino-2-(4-methoxyphenyl)-4H-pyrido[2, 1-a]isoquinoline-3-carbonitrile (4c):** Pink solid. Yield 95%. Mp: 269-271 ^{o}C. IR (KBr) ν_{max} (cm^{-1}) 3326, 3114, 2198, 1644, 1609, 1543, 1514, 1410, 1349, 1274, 1147, 1078, 937, 859, 798, 609, 523; ^{1}H-NMR (300 MHz, $CDCl_3$+CF_3COOD), δ (ppm) 3.95(s, 3H), 7.16(d, *J* = 8.8 Hz, 2H), 7.79-7.90(m, 4H),

7.95-8.09(m, 3H), 8.29(s, 1H), 8.49(d, J = 7.5 Hz, 1H), 8.65(d, J = 8.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$+CF_3COOD), δ (ppm) 163.05, 154.36, 152.55, 143,34, 135.22, 131.78, 130.96, 130.54, 128.71, 126.07, 125.56, 124.56, 122.60, 121.59, 117.98, 115.71, 115.41, 113.44, 109.66, 90.84, 55.73; ESI-MS: m/z: 326 $(M+H)^+$, HR-MS calcd for $C_{21}H_{16}N_3O$: 326.1033 $[M+H]^+$, found: 326.1019.



4c

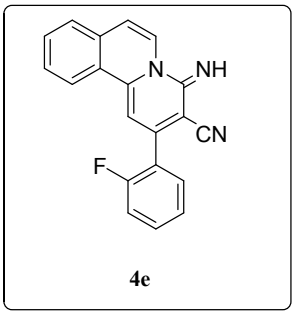
4) **4-imino-2-(4-nitrophenyl)-4H-pyrido[2, 1-a]isoquinoline-3-carbonitrile (4d):** Yield 90%. Mp: 325-327 ^{o}C. IR (KBr) ν_{max} (cm^{-1}) 3325, 3113, 2197, 1673, 1599, 1543, 1514, 1410, 1348, 1273, 1194, 1109, 1077, 1013, 935, 858, 761, 610, 525; ^{1}H-NMR (500 MHz, $CDCl_3$+CF_3COOD), δ (ppm) 6.69(d, J = 8.3 Hz, 3H), 6.78(m, 2H), 6.87(m, 2H), 7.10(d, J = 8.3 Hz, 2H), 7.34(br s, 1H), 7.44(d, J = 8.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$+CF_3COOD), δ (ppm) 152.52, 152.04, 149.61, 143.86, 140.02, 135.84, 132.15, 131.42, 129.86, 128.90, 125.71, 124.81, 124.53, 123.69, 122.18, 117.96, 115.70, 113.43, 111.16, 109.87, 91.69; ESI-MS: m/z: 341 $(M+H)^+$, HR-MS calcd for $C_{20}H_{13}N_4O_2$: 341.1033 $[M+H]^+$, found: 341.1019.



4d

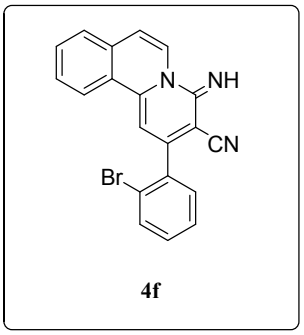
5) **2-(2-fluorophenyl)-4-imino-4H-pyrido[2, 1-a]isoquinoline-3-carbonitrile (4e):** Pink solid. Yield 85%. Mp: 274-276 ^{o}C. IR (KBr) ν_{max} (cm^{-1}) 3323, 3122, 2198, 1643, 1614, 1543, 1501, 1447, 1394, 1280, 1217, 1194, 1121, 1036, 940, 867, 808, 754, 679, 538; ^{1}H-NMR (500 MHz, $CDCl_3$+CF_3COOD), δ (ppm) 7.38(t, J = 9.0 Hz, 1H), 7.45(t, J = 7.6 Hz, 1H), 7.64-7.70(m, 2H), 7.97-8.03(m, 2H), 8.06-8.10(m, 2H), 8.34(s, 1H), 8.64(d, J = 8.3 Hz, 1H), 8.71(d, J = 6.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$+CF_3COOD), δ (ppm) 157.52, 152.30, 149.48, 143.26, 135.32, 134.18 (d, J = 8.2 Hz), 134.07, 131.80, 131.23, 130.46,

128.74, 125.64, 125.45 (d, J = 14.3 Hz), 124.56, 123.20, 122.46, 117.22, 116.94, 111.05, 93.31; ESI-MS: m/z: 314 $(M+H)^+$, HR-MS calcd for $C_{20}H_{13}FN_3$: 314.1088 $[M+H]^+$, found: 314.1088.



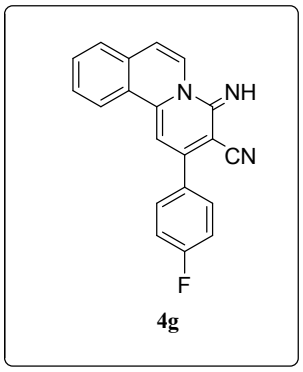
4e

6) **2-(2-bromophenyl)-4-imino-4H-pyrido[2, 1-a]isoquinoline-3-carbonitrile (4f):** Pink solid. Yield 85%. Mp: 248-250 ^oC. IR (KBr) ν_{max} (cm^{-1}) 3312, 3135, 2195, 1642, 1607, 1540, 1503, 1479, 1332, 1280, 1196, 1122, 1077, 1024, 939, 873, 795, 761, 647, 590, 531; ^{1}H-NMR (500 MHz, $CDCl_3$+CF_3COOD), δ (ppm) 7.45-7.50(m, 2H), 7.54-7.57(m, 2H), 7.79(d, J = 7.9 Hz, 1H), 7.92(s, 1H), 8.02(s, 3H), 8.59(d, J = 8.0 Hz, 1H), 9.16(s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$+CF_3COOD), δ (ppm) 154.26, 151.98, 143.37, 135.49, 133.99, 132.70, 131.98, 131.22, 130.15, 128.76, 128.43, 125.74, 124.64, 123.47, 122.17, 121.15, 115.75, 113.48, 111.58, 93.83; ESI-MS: m/z: 374 $(M+H)^+$ and $(M+3)^+$, HR-MS calcd for $C_{20}H_{13}BrN_3$: 374.0287 $[M+H]^+$, found: 374.0290.



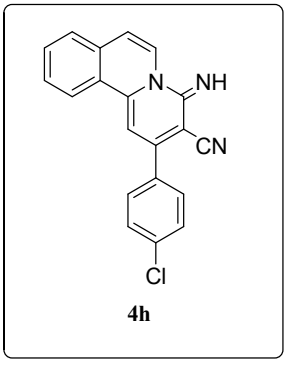
4f

7) **2-(4-fluorophenyl)-4-imino-4H-pyrido[2, 1-a]isoquinoline-3-carbonitrile (4g):** Pink solid. Yield 90%. Mp: 259-261 ^oC. IR (KBr) ν_{max} (cm^{-1}) 3317, 3124, 2202, 1607, 1533, 1502, 1477, 1454, 1412, 1377, 1336, 1279, 1217, 1063, 926, 842, 759, 690, 659, 598; ^{1}H-NMR (500 MHz, $CDCl_3$+CF_3COOD), δ (ppm) 7.37(t, J = 8.3 Hz, 2H), 7.79-7.82(m, 2H), 7.96-8.01(m, 3H), 8.05-8.11(m, 2H), 8.28(s, 1H), 8.60(d, J = 7.6 Hz, 1H), 8.66(d, J = 8.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$+CF_3COOD), δ (ppm) 153.73, 152.47, 143.59, 135.48, 131.93, 131.12, 130.94 (d, J = 8.80 Hz), 130.82, 130.10, 128.76, 125.63, 124.52, 123.06, 121.75, 117.33, 117.03 (d, J = 2.2 Hz), 116.71, 112.94, 109.94, 91.57; ESI-MS: m/z: 314 $(M+H)^+$, HR-MS calcd for $C_{20}H_{13}FN_3$: 314.1088 $[M+H]^+$, found: 314.1087.



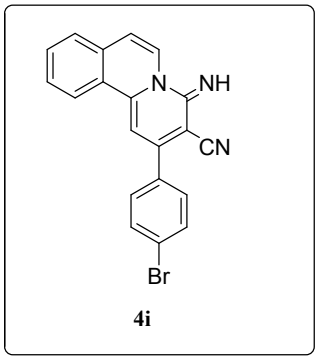
4g

8) **2-(4-chlorophenyl)-4-imino-4H-pyrido[2, 1-a]isoquinoline-3-carbonitrile (4h):** Pink solid. Yield 85%. Mp: 269-271 ^{o}C. IR (KBr) ν_{max} (cm^{-1}) 3321, 2923, 2198, 1723, 1641, 1611, 1540, 1496, 1390, 1276, 1248, 1127, 1089, 1043, 1011, 936, 874, 805, 741, 700, 646, 612, 490, 409; ^{1}H-NMR (500 MHz, $CDCl_3$+CF_3COOD), δ (ppm) 7.65(d, *J* = 8.246 Hz, 2H), 7.73(d, *J* = 8.3 Hz, 2H), 7.88(br s, 1H), 7.96(d, *J* = 7.17 Hz, 1H), 8.01(t, *J* = 7.3 Hz, 1H), 8.06(d, *J* = 7.4 Hz, 1H), 8.11(t, *J* = 7.3 Hz, 1H), 8.32(s, 1H), 8.53(d, *J* = 7.1 Hz, 1H), 8.68(d, *J* = 8.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$+CF_3COOD), δ (ppm) 153.64, 152.46, 143.78, 139.08, 135.64, 132.31, 132.09, 131.15, 130.14, 129.83, 128.76, 125.70, 124.53, 123.29, 121.54, 116.10, 113.27, 110.03, 91.29; ESI-MS: m/z: 330 $(M+H)^+$, HR-MS calcd for $C_{20}H_{13}ClN_3$: 330.1163 $[M+H]^+$, found: 330.1177.



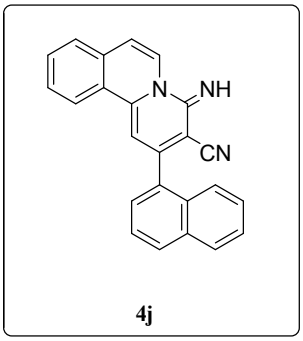
4h

9) **2-(4-bromophenyl)-4-imino-4H-pyrido[2, 1-a]isoquinoline-3-carbonitrile (4i):** Pink solid. Yidel 85%. Mp: 263-265 ^{o}C. IR (KBr) ν_{max} (cm^{-1}) 3317, 2921, 2198, 1640, 1610, 1538, 1495, 1393, 1308, 1277, 1213, 1129, 1074, 1006, 938, 875, 806, 740, 682, 611, 518, 487; ^{1}H-NMR (500 MHz, $CDCl_3$+CF_3COOD), δ (ppm) 7.64(dd, *J* = 8.08, 21.97 Hz, 2H), 7.75(dd, *J* = 8.54, 18.76 Hz, 2H), 8.01(m, 5H), 8.30(s, 1H), 8.67(d, *J* = 8.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$+CF_3COOD), δ (ppm) 153.82, 152.45, 144.01, 135.75, 133.21, 132.72, 132.19, 131.99, 131.15, 129.94, 128.78, 127.52, 125.75, 124.55, 123.42, 121.39, 115.75, 113.48, 110.09, 91.12; ESI-MS: m/z: 374 $(M+H)^+$ and 376 $(M+3)^+$, HR-MS calcd for $C_{20}H_{13}BrN_3$: 374.0287 $[M+H]^+$, found: 374.0299.



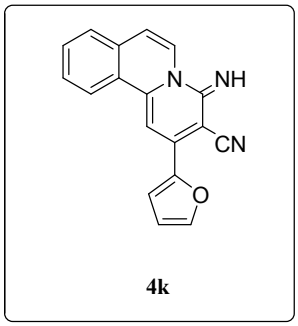
4i

10) **4-imino-2-(napthalen-1-yl)-4H-pyrido[2, 1-a]isoquinoline-3-carbonitrile (4j):** Pink solid. Yield 88%. Mp: 222-224 ^{o}C. IR (KBr) ν_{max} (cm^{-1}) 3320, 3049, 2200, 1639, 1606, 1538, 1500, 1478, 1433, 1410, 1332, 1303, 1276, 1243, 1211, 1146, 1125, 1074, 1042, 929, 869, 828, 807, 771, 744, 656, 591, 547; ^{1}H-NMR (500 MHz, $CDCl_3$+CF_3COOD), δ (ppm) 7.54-7.59(m, 2H), 7.62-7.70(m, 4H), 7.99-8.06(m, 5H), 8.12(d, *J* = 7.9 Hz, 1H), 8.40(s, 1H), 8.55(d, *J* = 8.5 Hz, 1H), 8.65(d, *J* = 7.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$+CF_3COOD), δ (ppm) 155.01, 152.29, 143.21, 135.42, 133.83, 132.08, 131.92, 131.21, 129.83, 129.26, 128.77, 128.24, 127.77, 127.29, 125.71, 125.28, 124.56, 123.25, 122.07, 117.95, 115.68, 113.40, 112.07, 94.15; ESI-MS: m/z: 346 $(M+H)^+$, HR-MS calcd for $C_{24}H_{16}N_3$: 346.13387 $[M+H]^+$, found: 346.13377.



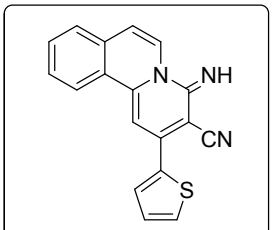
4j

11) **2-(furan-2-yl)-4-imino-4H-pyrido[2, 1-a]isoquinoline-3-carbonitrile (4k):** Pink solid. Yield 80%. Mp: 255-257 ^{o}C. IR (KBr) ν_{max} (cm^{-1}) 3320, 3093, 2198, 1641, 1611, 1581, 1544, 1509, 1482, 1414, 1382, 1307, 1271, 1217, 1130, 1151, 1084, 1037, 962, 869, 809, 747, 676, 588, 409; ^{1}H-NMR (500 MHz, $CDCl_3$+CF_3COOD), δ (ppm) 6.83-6.84(m, 1H), 7.66(br s, 1H), 7.82(d, *J* = 7.6 Hz, 1H), 7.91(s, 1H), 7.94(d, *J* = 3.6 Hz, 1H), 7.98(t, *J* = 7.9 Hz, 2H), 8.05(t, *J* = 7.6 Hz, 1H), 8.37(d, *J* = 7.7 Hz, 1H), 8.68(s, 1H), 8.71(d, *J* = 8.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$+CF_3COOD), δ (ppm) 152.64, 148.65, 146.15, 143.74, 139.85, 135.24, 131.84, 130.87, 128.62, 125.64, 124.71, 122.36, 121.47, 119.72, 116.10, 114.71, 113.26, 105.04, 85.04; ESI-MS: m/z: 286 $(M+H)^+$, HR-MS calcd for $C_{18}H_{12}N_3O$: 286.0974 $[M+H]^+$, found: 286.0963.



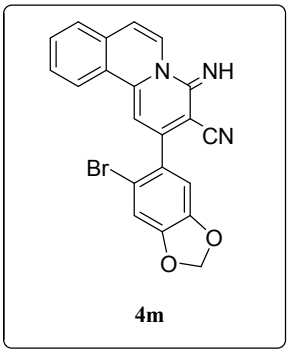
4k

12) **4-imino-2-(thiophen-2-yl)-4H-pyrido[2, 1-a]isoquinoline-3-carbonitrile (4l):** Pink solid. Yield 85%. Mp: 230-232 ^{o}C. IR (KBr) ν_{max} (cm^{-1}) 3310, 3062, 2202, 1641, 1615, 1548, 1500, 1431, 1341, 1341, 1304, 1276, 1126, 1073, 1048, 938, 857, 839, 804, 763, 745, 702, 649, 582, 524, 454; ^{1}H-NMR (300 MHz, $CDCl_3$+CF_3COOD), δ (ppm) 7.36-7.38(m, 1H), 7.85-7.88(m, 2H), 7.96-8.01(m, 2H), 8.04(t, *J* = 7.6 Hz, 1H), 8.20(d, *J* = 3.8 Hz, 1H), 8.33(s, 1H), 8.59-8.64(m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$+CF_3COOD), δ (ppm) 152.75, 145.94, 143.25, 135.33, 133.81, 132.79, 131.80, 131.00, 130.11, 128.70, 125.47, 124.41, 122.46, 121.85, 113.97, 113.59, 108.26, 88.49; ESI-MS: m/z: 302 $(M+H)^+$, HR-MS calcd for $C_{18}H_{12}N_3S$: 302.0746 $[M+H]^+$, found: 302.0746.



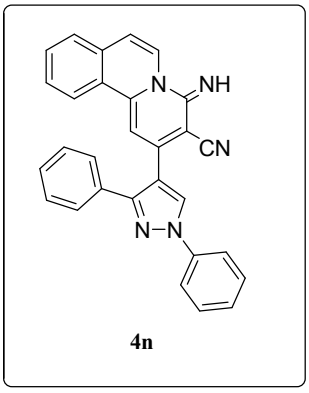
4l

13) **2-(6-bromobenzo[d][1,3]dioxol-5-yl)-4-imino-4H-pyrido[2,1-a]isoquinoline-3-carbonitrile (4m):** Pink solid. Yield 90%. Mp: 234-236 ^{o}C. IR (KBr) ν_{max} (cm^{-1}) 3309, 2913, 2207, 1608, 1545, 1500, 1479, 1407, 1278, 1234, 1120, 1075, 1032, 995, 932, 866, 803, 759, 647, 566; ^{1}H-NMR (500 MHz, $CDCl_3$+CF_3COOD), δ (ppm) 6.15(s, 2H), 6.93(s, 1H), 7.24(s, 1H), 7.96-8.10(m, 5H), 8.25(s, 1H), 8.60(d, *J* = 8.5 Hz, 1H), 8.71(d, *J* = 7.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$+CF_3COOD), δ (ppm) 154.24, 151.97, 150.93, 148.36, 143.27, 135.42, 131.96, 131.17, 128.69, 127.85, 125.76, 124.65, 123.28, 122.18, 116.86, 113.83, 112.99, 111.91, 109.64, 103.01, 94.08; ESI-MS: m/z: 418 $(M+H)^+$, HR-MS calcd for $C_{21}H_{13}BrN_3O_2$: 418.1364 $[M+H]^+$, found: 418.1352.



4m

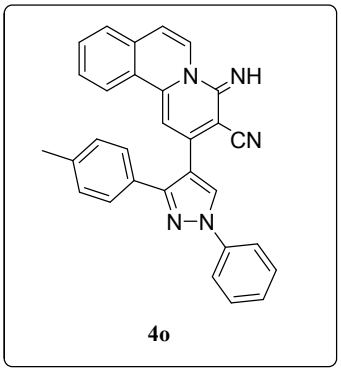
14) **2-(1,3-diphenyl-1H-pyrazol-4-yl)-4-imino-4H-pyrido[2, 1-a]isoquinoline-3-carbonitrile (4n):** Pink solid. Yield 90%. Mp: 199-201 ^{o}C. IR (KBr) $_{\nu max}$ (cm^{-1}) 3322, 3054, 2196, 1640, 1606, 1542, 1497, 1413, 1352, 1303, 1274, 1222, 1152, 1128, 1069, 957, 919, 876, 803, 753, 691, 652, 556, 506; ^{1}H-NMR (500 MHz, $CDCl_3$+CF_3COOD), δ (ppm) 6.65(s, 1H), 7.05(d, *J* = 7.7 Hz, 1H), 7.35-7.40(m, 5H), 7.47-7.52(m, 4H), 7.59-7.68(m, 4H), 7.82(d, *J* = 7.7 Hz, 2H), 8.57(s, 1H), 9.07(d, *J* = 7.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$+CF_3COOD), δ (ppm) 156.01, 152.02, 144.27, 142.73, 139.34, 132.44, 132.03, 129.54, 128.79, 128.63, 127.34, 127.15, 125.41, 124.45, 124.19, 119.58, 118.22, 117.39, 114.69, 98.84, 91.19; ESI-MS: m/z: 438 $(M+H)^+$, HR-MS calcd for $C_{29}H_{20}N_5$: 438.1713 $[M+H]^+$, found: 438.1701.



4n

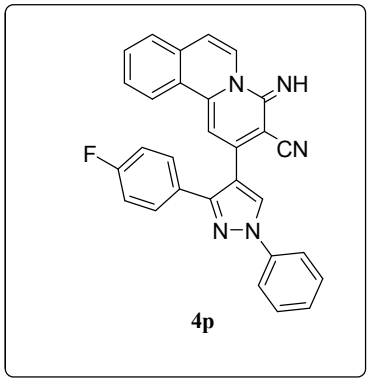
15) **4-imino-2-(1-phenyl-3-p-tolyl-1H-pyrazol-4-yl)-4H-pyrido[2, 1-a]isoquinoline-3-carbonitrile (4o):** Pink solid. Yield 90%. Mp: 212-214 ^{o}C. IR (KBr) ν_{max} (cm^{-1}) 3323, 2199, 1638, 1608, 1565, 1545, 1498, 1416, 1275, 1246, 1198, 1130, 1078, 959, 920, 876, 833, 800, 751, 688, 652, 503; ^{1}H-NMR (400 MHz, $CDCl_3$+CF_3COOD), δ (ppm) 2.36(s, 3H), 6.65(s, 1H), 7.02(d, *J* = 7.8 Hz, 1H), 7.19(d, *J* = 7.9 Hz, 2H), 7.32-7.41(m, 2H), 7.47-7.62(m, 8H), 7.80(d, *J* = 7.7 Hz, 2H), 8.54(s, 1H), 9.04(d, *J* = 7.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$+CF_3COOD), δ (ppm) 155.99, 151.98, 144.33, 142.61, 139.31, 138.42, 131.91, 129.45, 129.24, 128.58, 128.43, 127.16, 127.06, 125.39, 124.45, 124.11, 119.44, 118.26, 117.27, 114.44, 98.61,

91.17, 21.24; ESI-MS: m/z: 452 $(M+H)^+$, HR-MS calcd for $C_{30}H_{21}N_5$: 452.1869 $[M+H]^+$, found: 452.1863.



4o

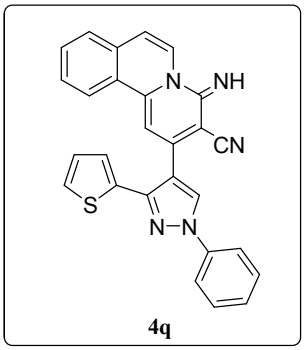
16) **2-(3-(4-fluorophenyl)-1-phenyl-1H-pyrazol-4-yl)-4-imino-4H-pyrido[2, 1-a]isoquinoline-3-carbonitrile (4p):** Pink solid. Yield 95%. Mp: 261-263 ^oC. IR (KBr) ν_{max} (cm^{-1}) 3317, 3051, 2203, 1601, 1574, 1502, 1477, 1453, 1412, 1380, 1299, 1280, 1214, 1152, 1122, 1059, 958, 877, 842, 768, 750, 688, 658, 599, 526; ^{1}H-NMR (500 MHz, $CDCl_3$+CF_3COOD), δ (ppm) 7.17-7.21(m, 2H), 7.48(t, *J* = 7.4 Hz, 1H), 7.55-7.62(m, 4H), 7.70(d, *J* = 8.3 Hz, 1H), 7.72-7.80(m, 3H), 7.84(d, *J* = 7.6 Hz, 1H), 7.91(s, 1H), 7.95-8.00(m, 3H), 8.53(d, *J* = 7.7 Hz, 1H), 8.75(s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$+CF_3COOD), δ (ppm) 152.56, 152.10, 145.33, 142.88, 138.23, 135.21, 131.78, 131.07, 130.96, 130.69, 130.01, 129.13, 128.63, 126.53, 124.76, 124.33, 122.58, 121.63, 120.71, 116.76, 116.47, 115.16, 112.83, 109.72, 90.23; ESI-MS: m/z: 456 $(M+H)^+$, HR-MS calcd for $C_{29}H_{19}FN_5$: 456.1619 $[M+H]^+$, found: 456.1609.



4p

17) **4-imino-2-(1-phenyl-3-(thiophen-2-yl)-1H-pyrazol-4-yl)-4H-pyrido[2, 1-a]isoquinoline-3-carbonitrile (4q):** Pink solid. Yield 85%. Mp: 182-184 ^oC. IR (KBr) ν_{max} (cm^{-1}) 3316, 3067, 2197, 1608, 1555, 1498, 1408, 1358, 1302, 1273, 1248, 1216, 1125, 1073, 957, 908, 850, 802, 748, 688, 653, 550; ^{1}H-NMR (300 MHz, $CDCl_3$+CF_3COOD), δ (ppm) 7.14(t, *J* = 5.0 Hz, 1H), 7.29(d, *J* = 3.5 Hz, 1H), 7.46(t, *J* = 7.0 Hz, 1H), 7.52-7.57(m, 3H), 7.79-7.82(m, 3H), 7.86(d, *J* = 7.6 Hz, 1H), 7.90(d, *J* = 8.3 Hz, 1H), 7.96-8.00(m, 2H), 8.16(s, 1H), 8.65(d, *J* = 7.7 Hz, 1H), 8.73(s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$+CF_3COOD), δ (ppm) 155.96,

145.73, 144.00, 142.93, 139.12, 133.95, 132.08, 129.51, 128.86, 128.51, 127.47, 127.34, 127.16, 126.47, 125.44, 124.62, 124.21, 119.46, 117.95, 117.39, 114.69, 98.34, 92.18; ESI-MS: m/z: 444 $(M+H)^+$, HR-MS calcd for $C_{27}H_{18}N_5S$: 444.12774 $[M+H]^+$, found: 444.12703.



4q

Figure S1: ^{1}H NMR of compound **4a**

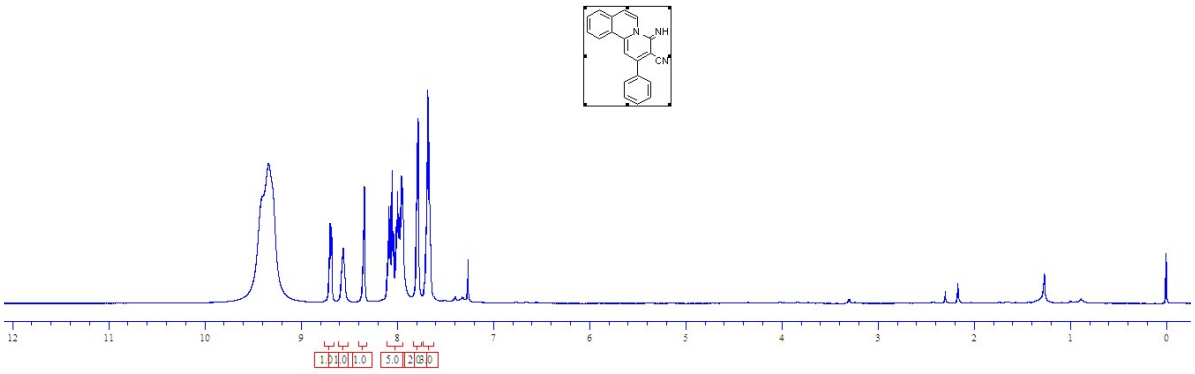


Figure S2: ^{13}C NMR of compound **4a**

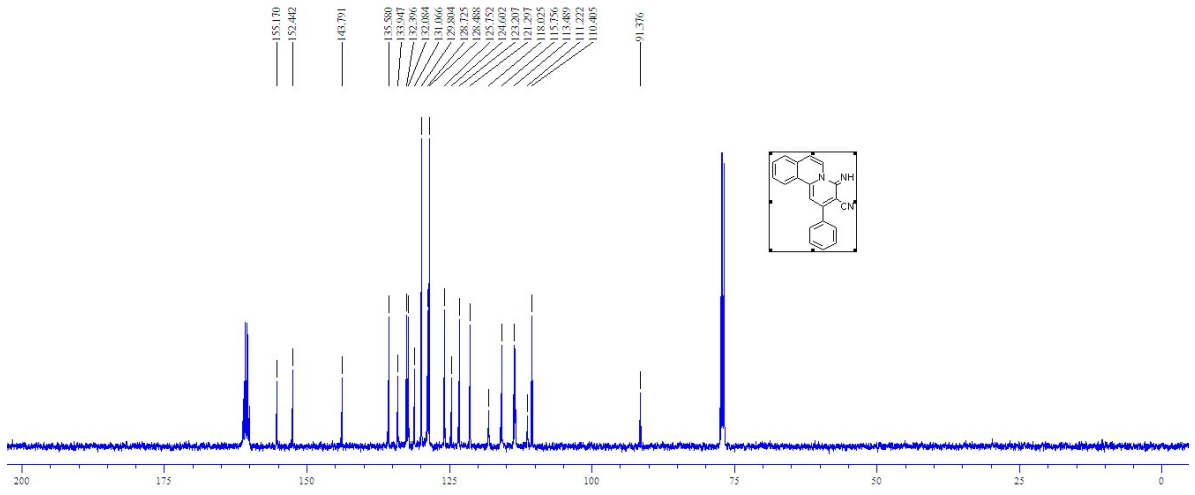


Figure S3: ^{1}H NMR of compound **4b**

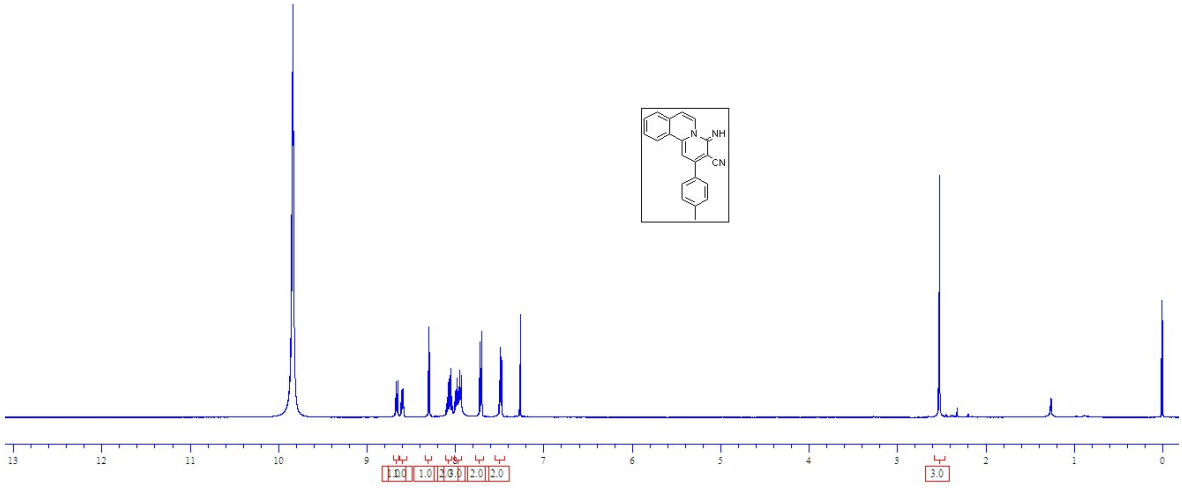


Figure S4: ^{13}C NMR of compound **4b**

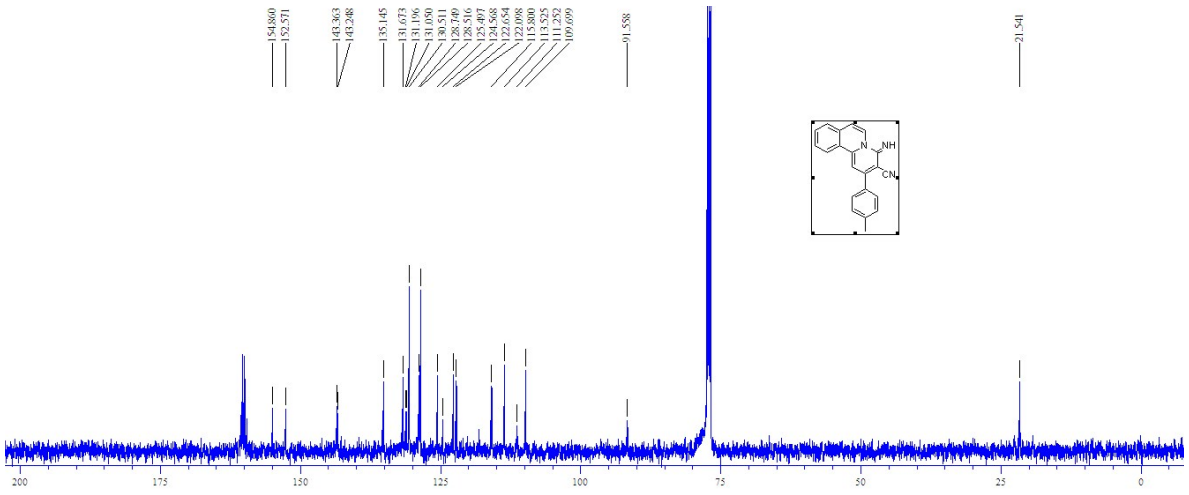


Figure S5: ^{1}H NMR of compound **4c**

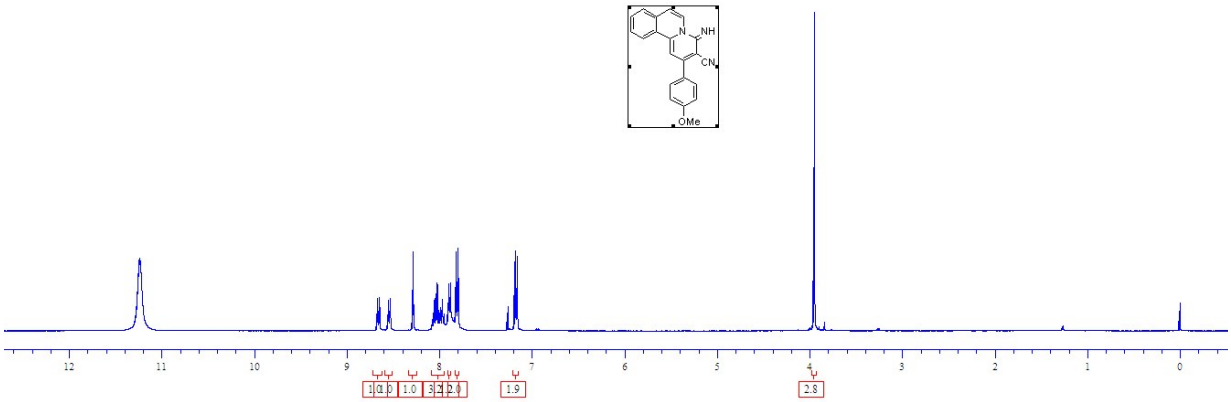


Figure S6: ^{13}C NMR of compound **4c**

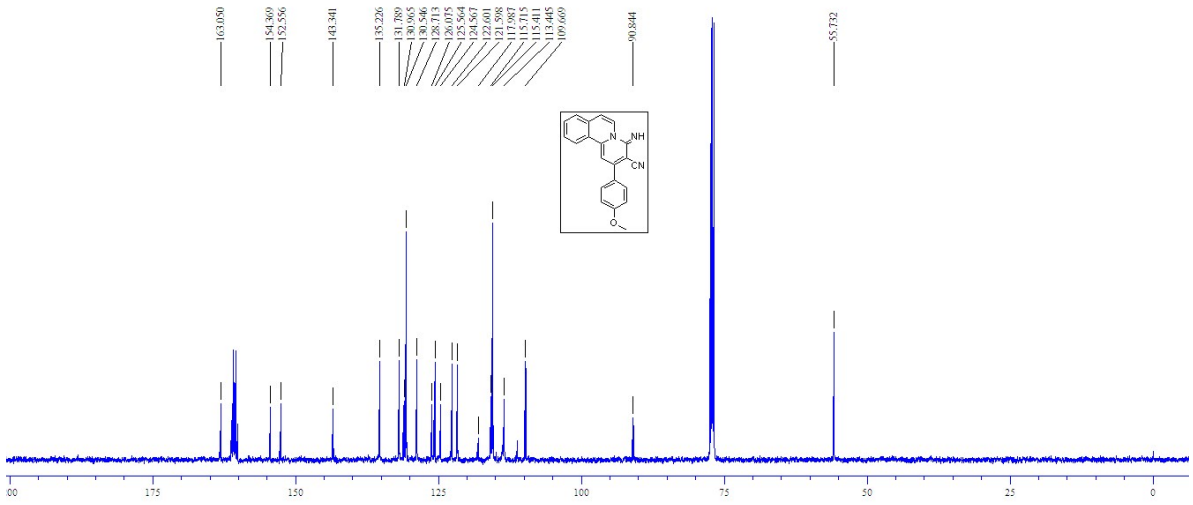


Figure S7: ^{1}H NMR of compound **4d**

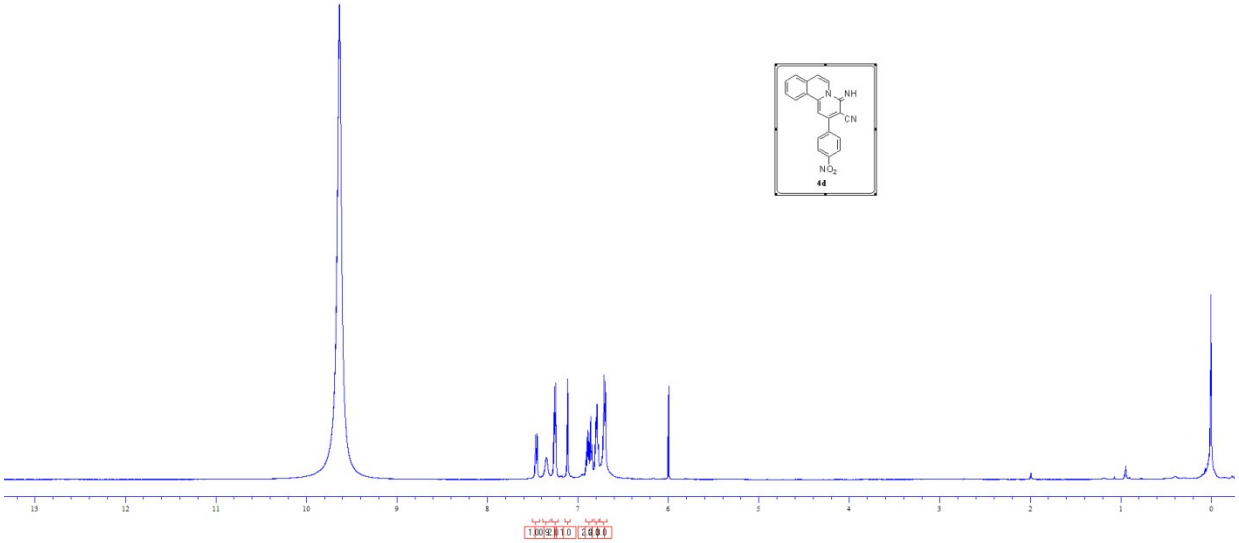


Figure S8: ^{13}C NMR of compound **4d**

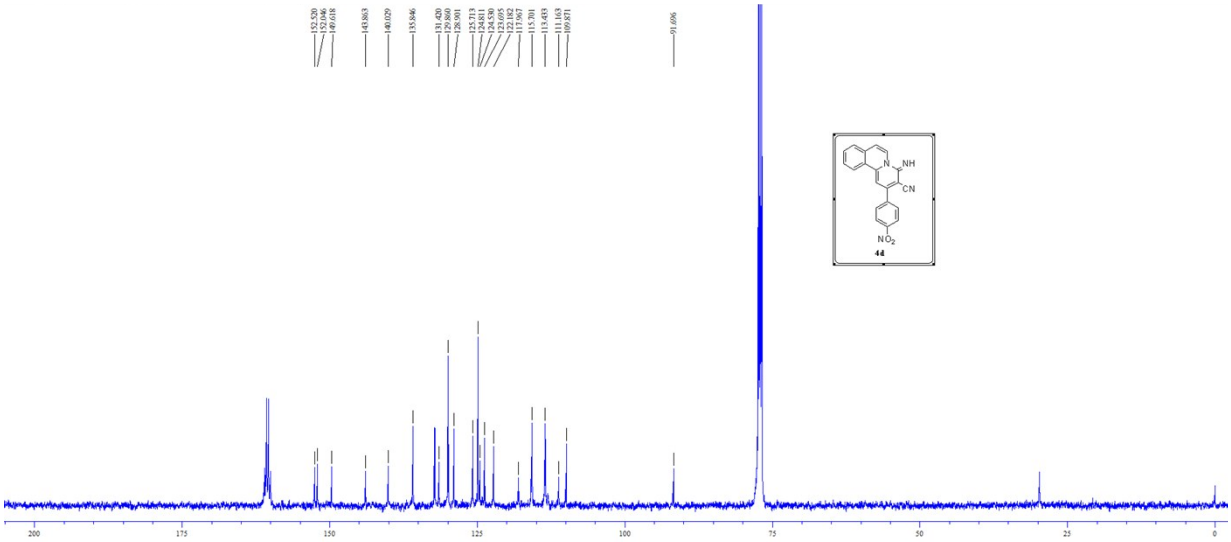


Figure S9: ^{1}H NMR of compound **4e**

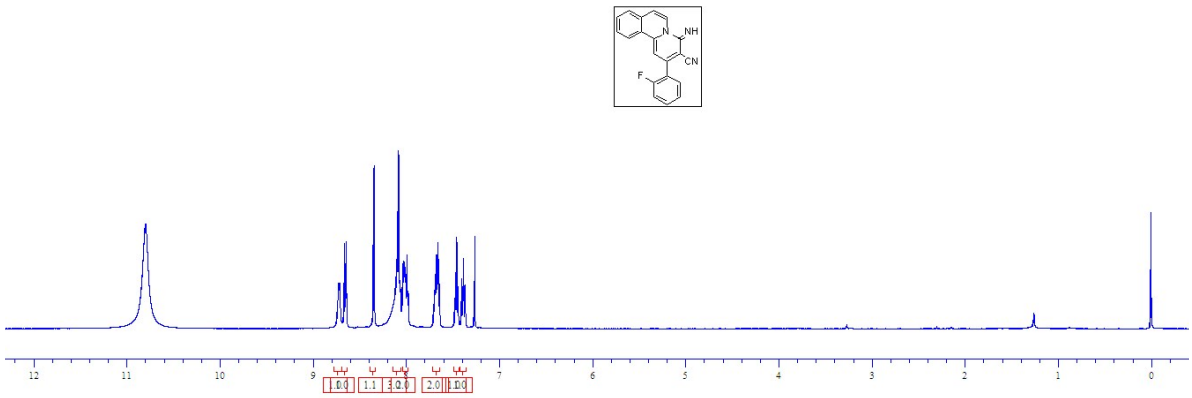


Figure S10: ^{13}C NMR of compound **4e**

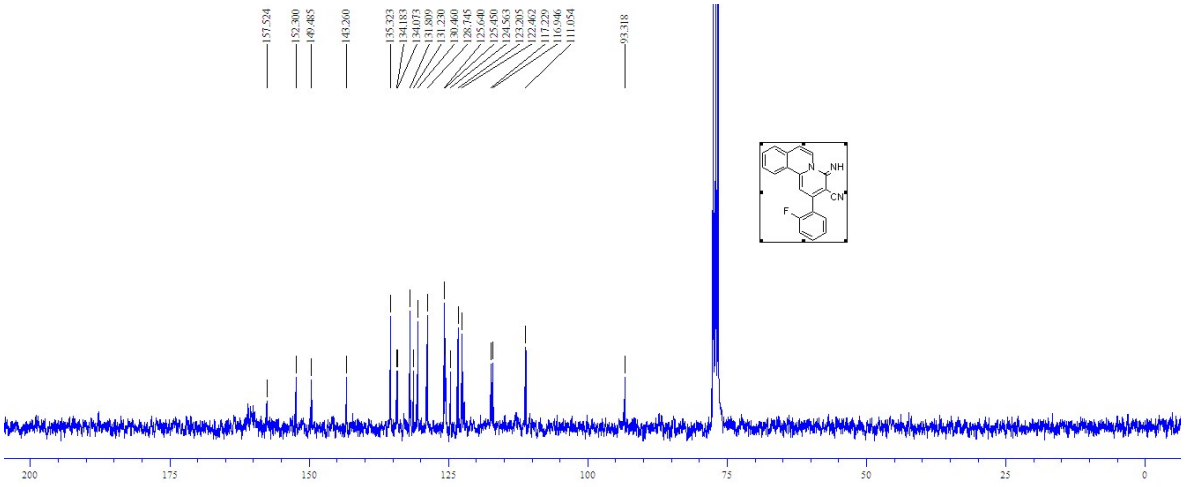


Figure S11: ^{1}H NMR of compound **4f**

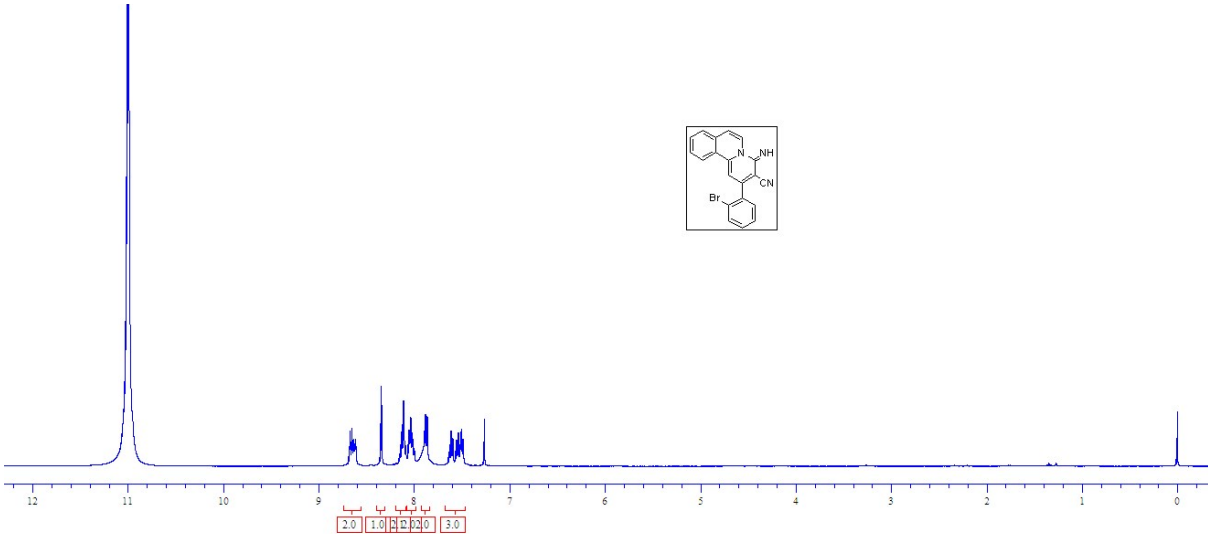


Figure S12: ^{13}C NMR of compound **4f**

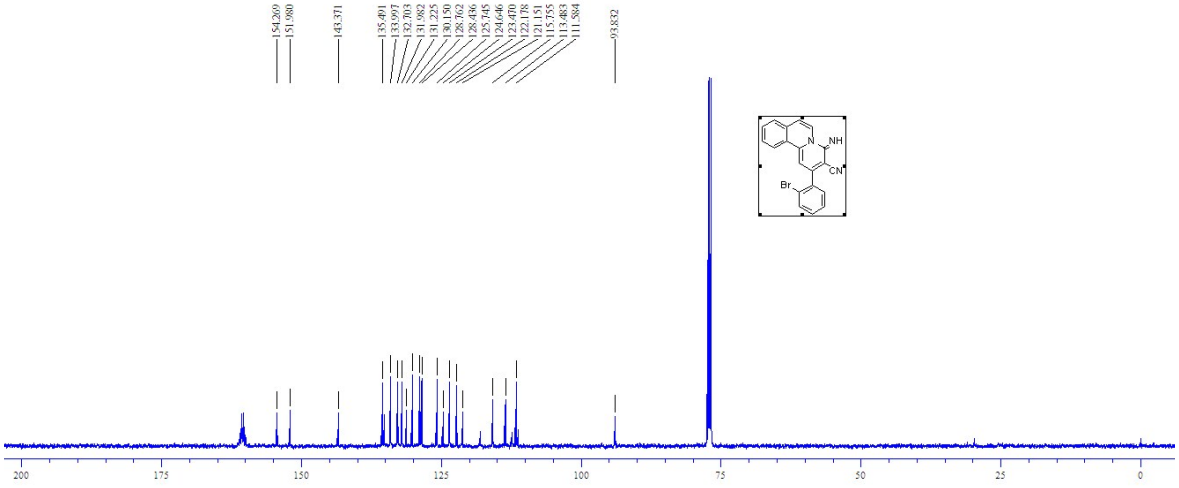


Figure S13: ^{1}H NMR of compound **4g**

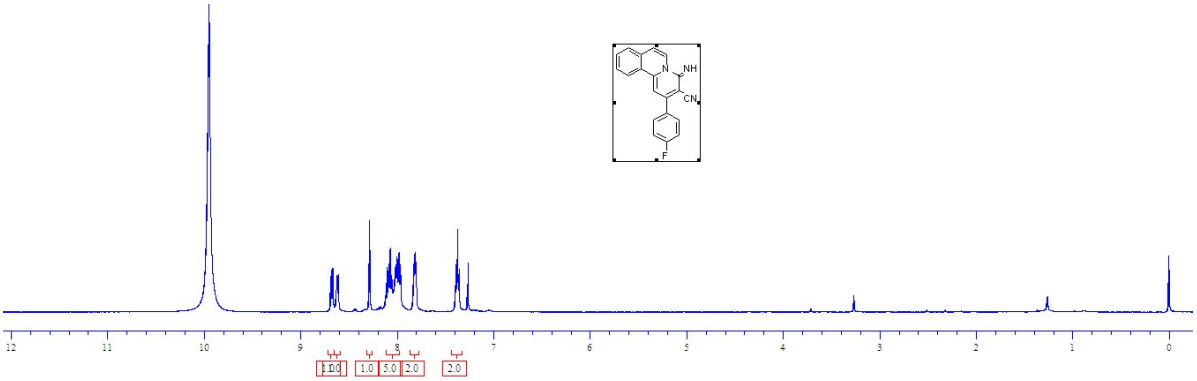


Figure S14: ^{13}C NMR of compound **4g**

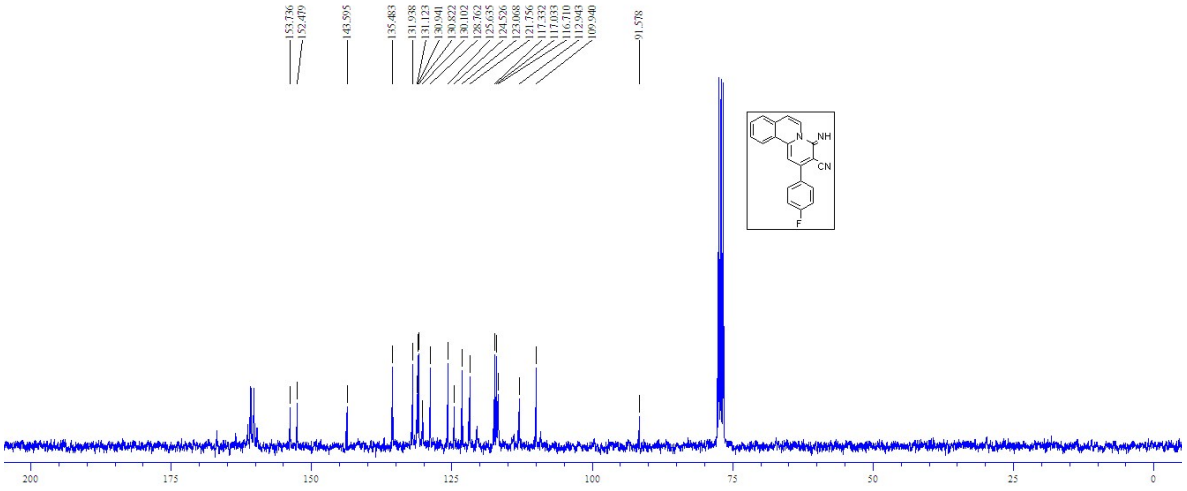


Figure S15: ^{1}H NMR of compound **4h**

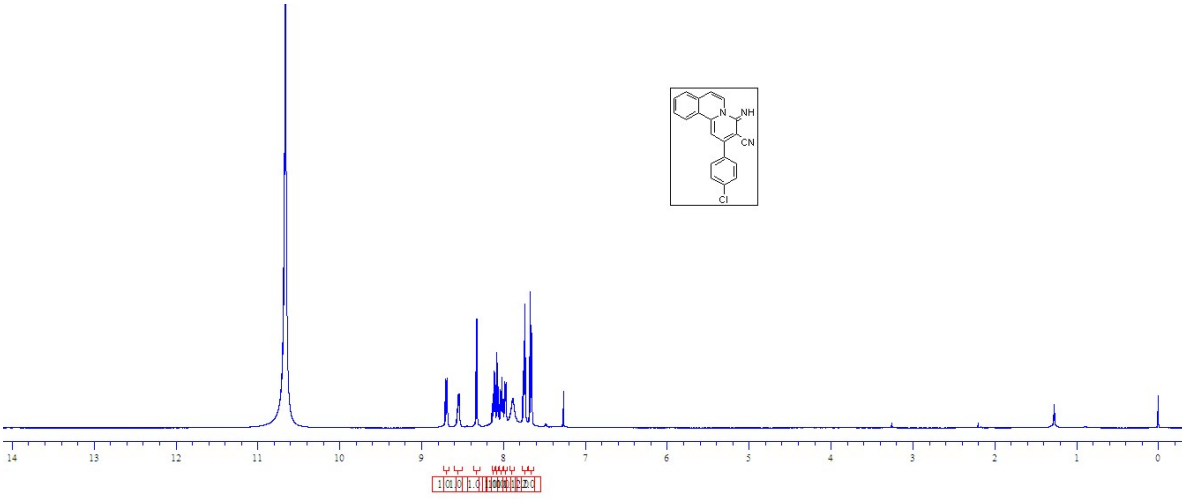


Figure S16: ^{13}C NMR of compound **4h**

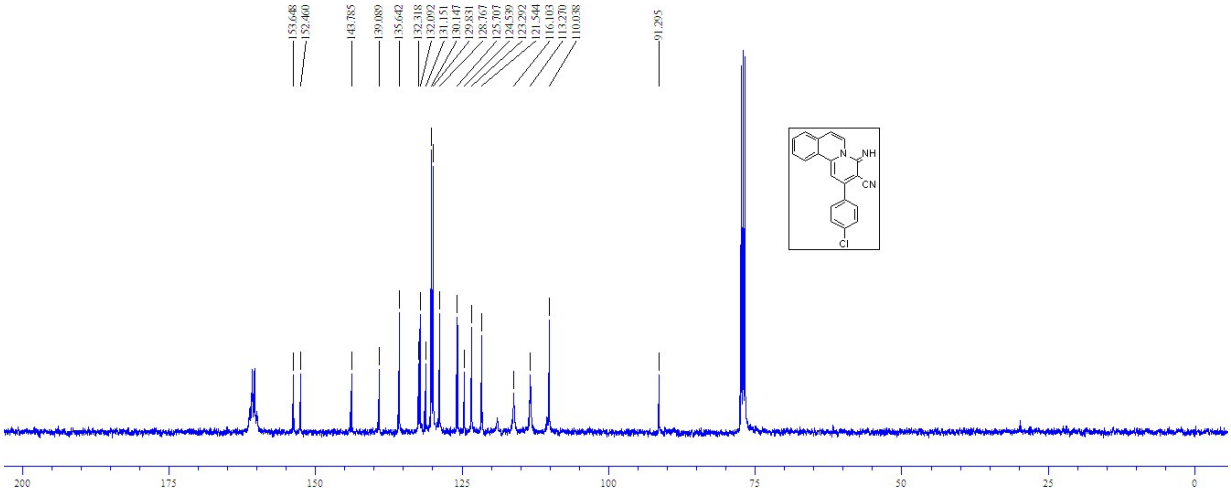


Figure S17: ^{1}H NMR of compound **4i**

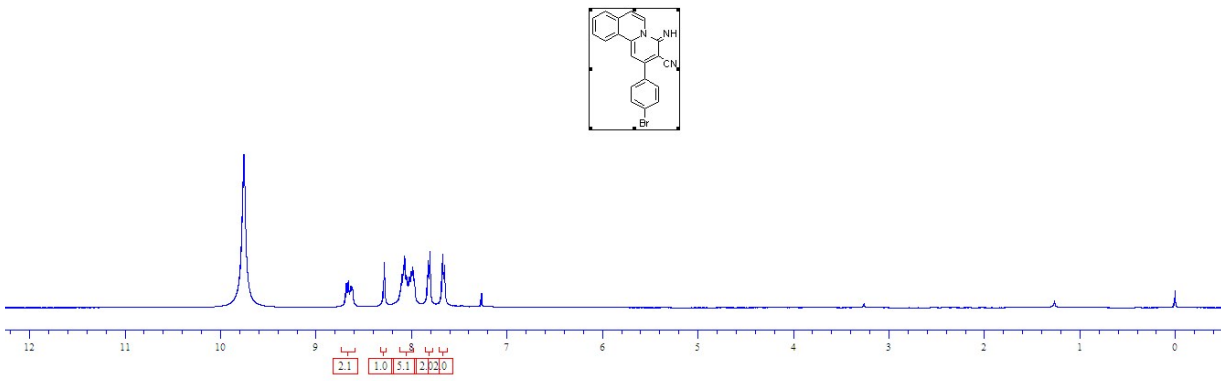


Figure S18: ^{13}C NMR of compound **4i**

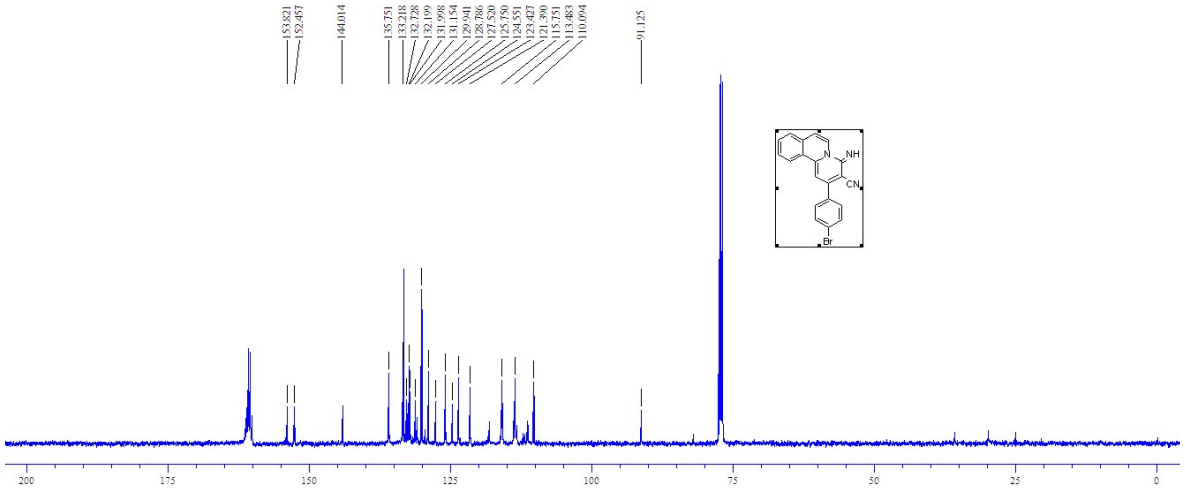


Figure S19: ^{1}H NMR of compound **4j**

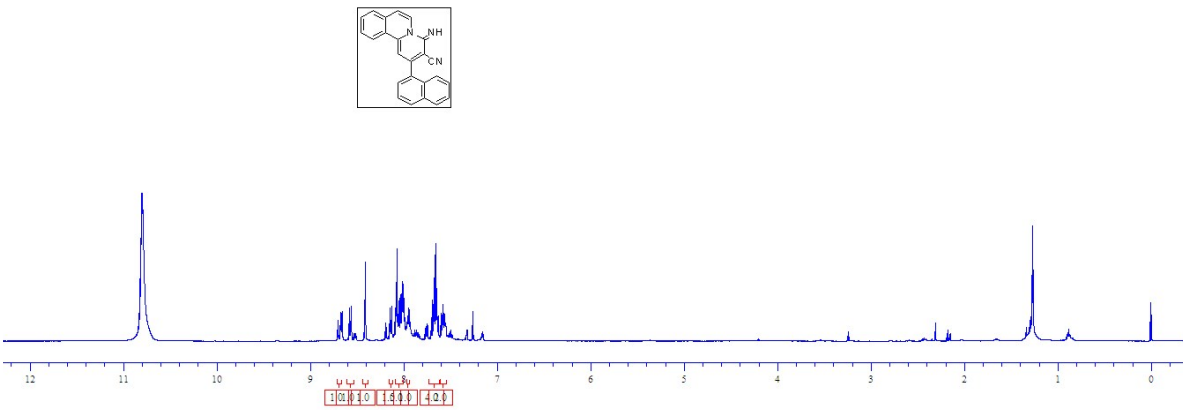


Figure S20: ^{13}C NMR of compound **4j**

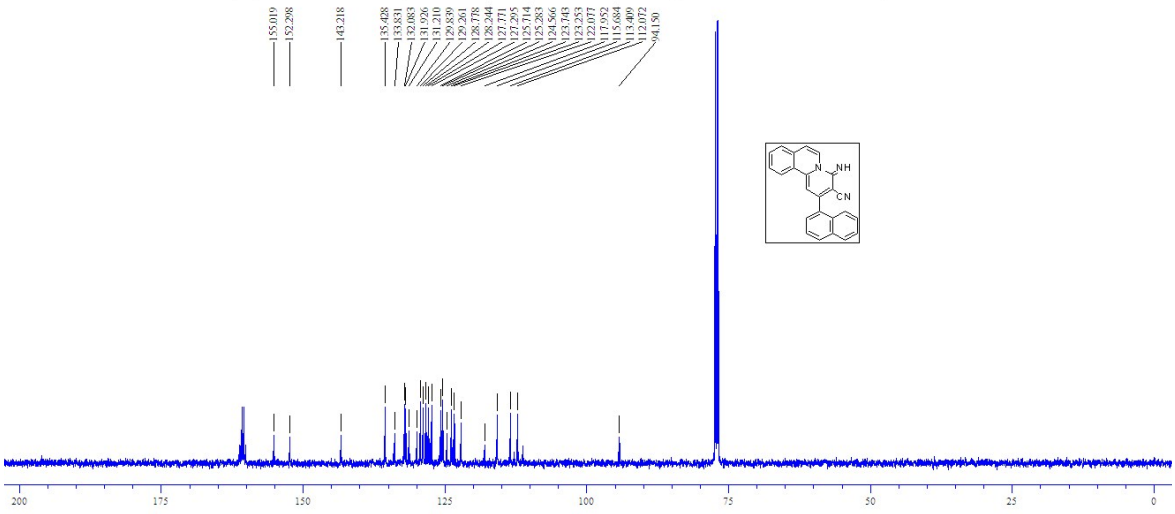


Figure S21: ^{1}H NMR of compound **4k**

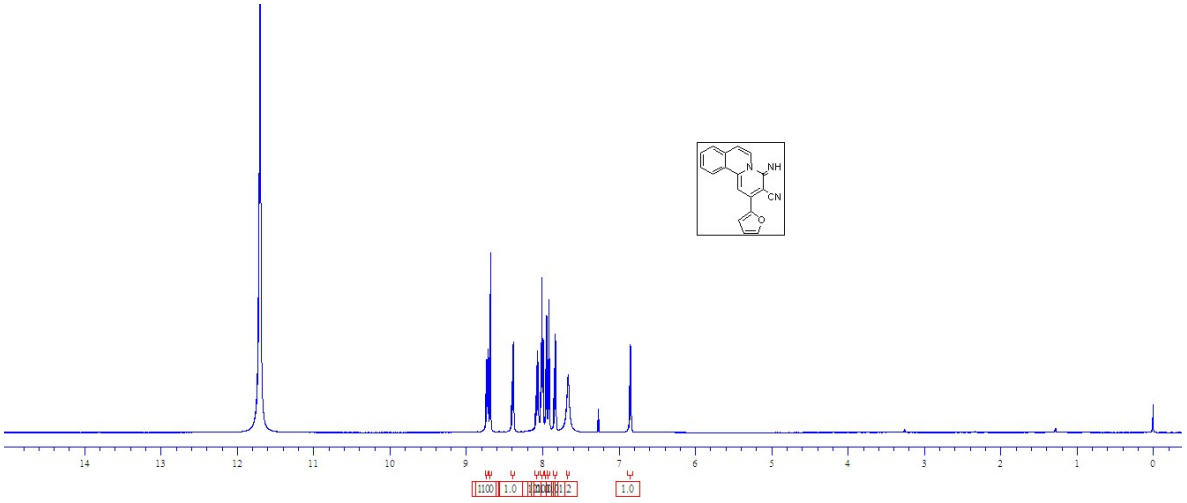


Figure S22: ^{13}C NMR of compound **4k**

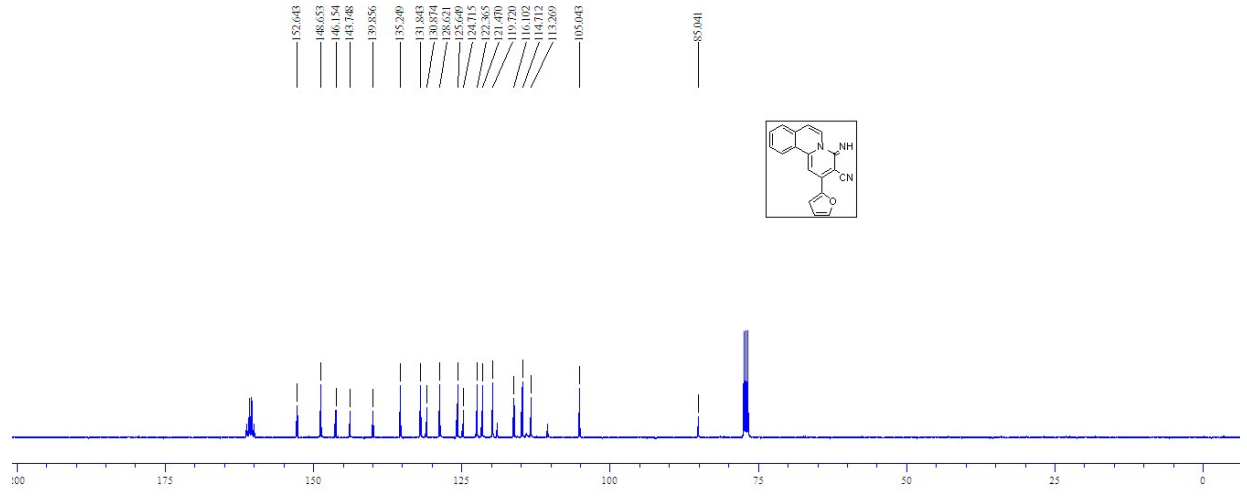


Figure S23: ^{1}H NMR of compound **4l**

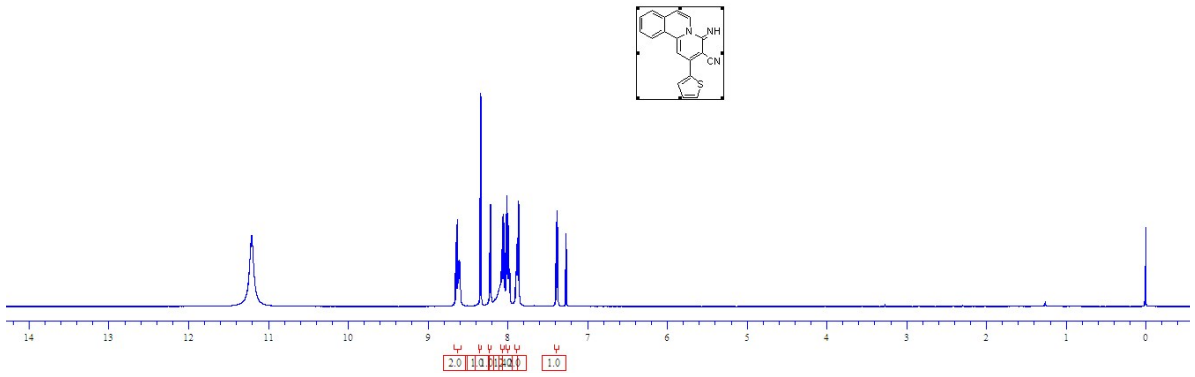


Figure S24: ^{13}C NMR of compound **4l**

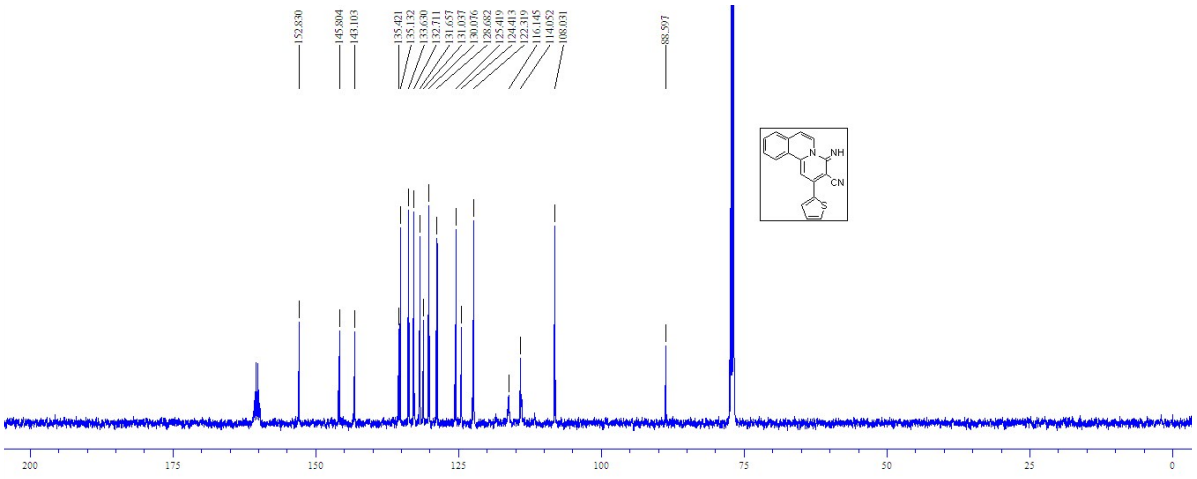


Figure S25: ^{1}H NMR of compound **4m**

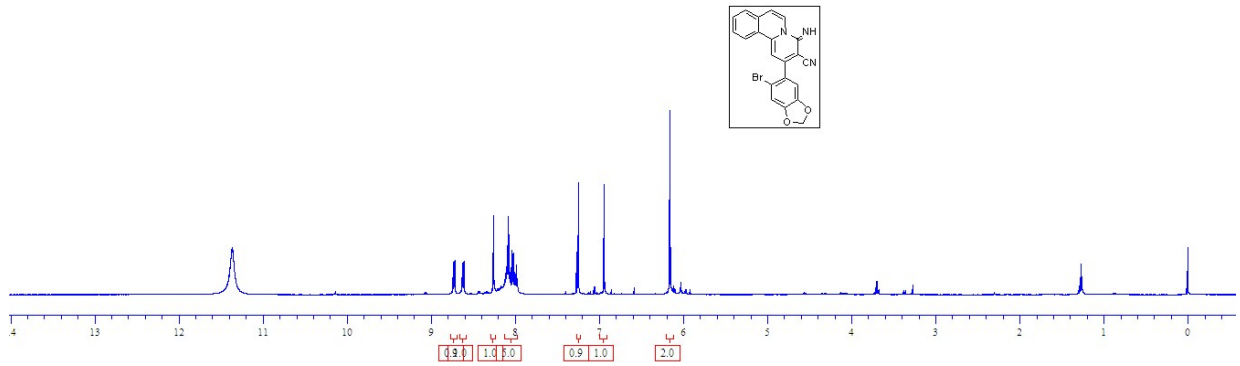


Figure S26: ^{13}C NMR of compound **4m**

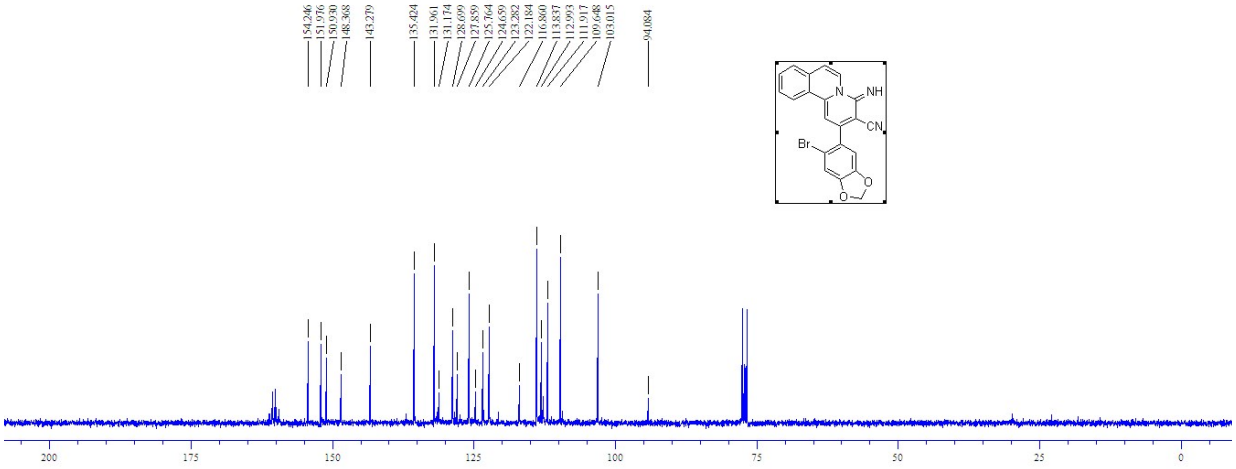


Figure S27: ^{1}H NMR of compound **4n**

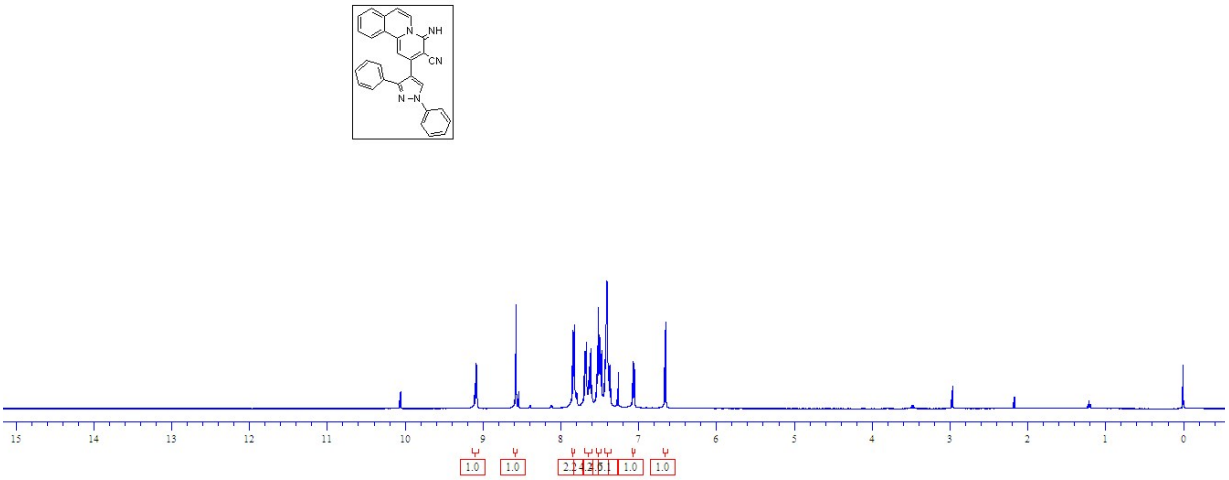


Figure S28: ^{13}C NMR of compound **4n**

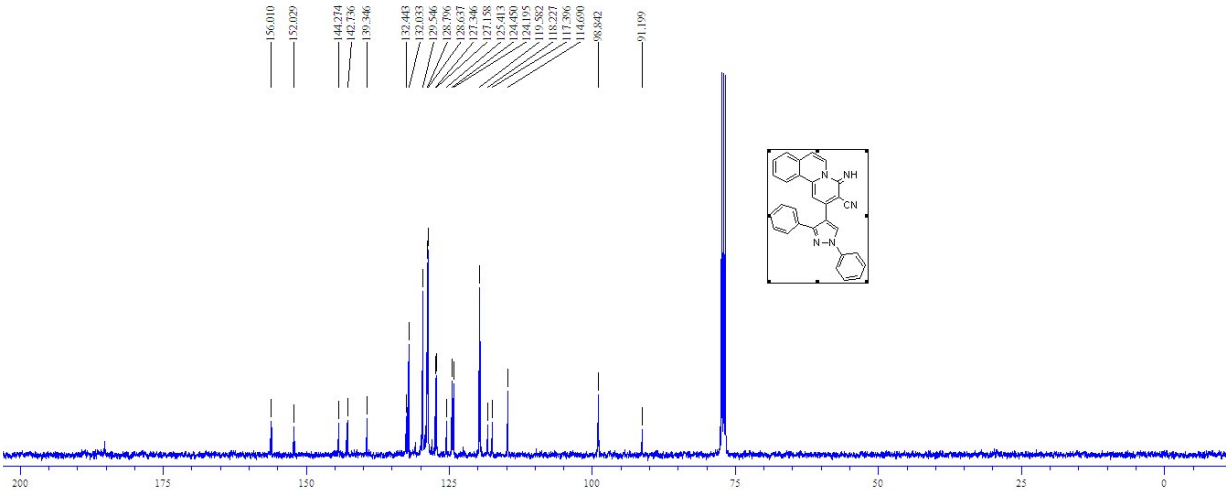


Figure S29: ^{1}H NMR of compound **4o**

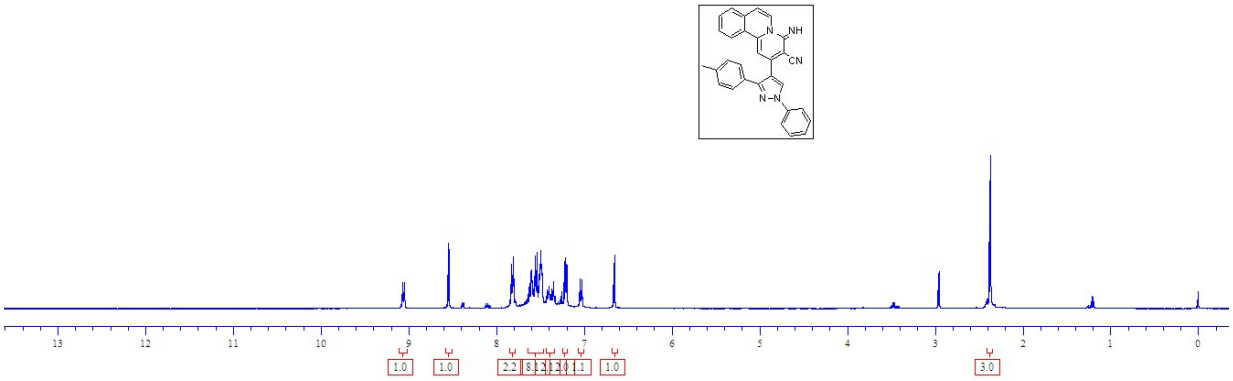


Figure S30: ^{13}C NMR of compound **4o**

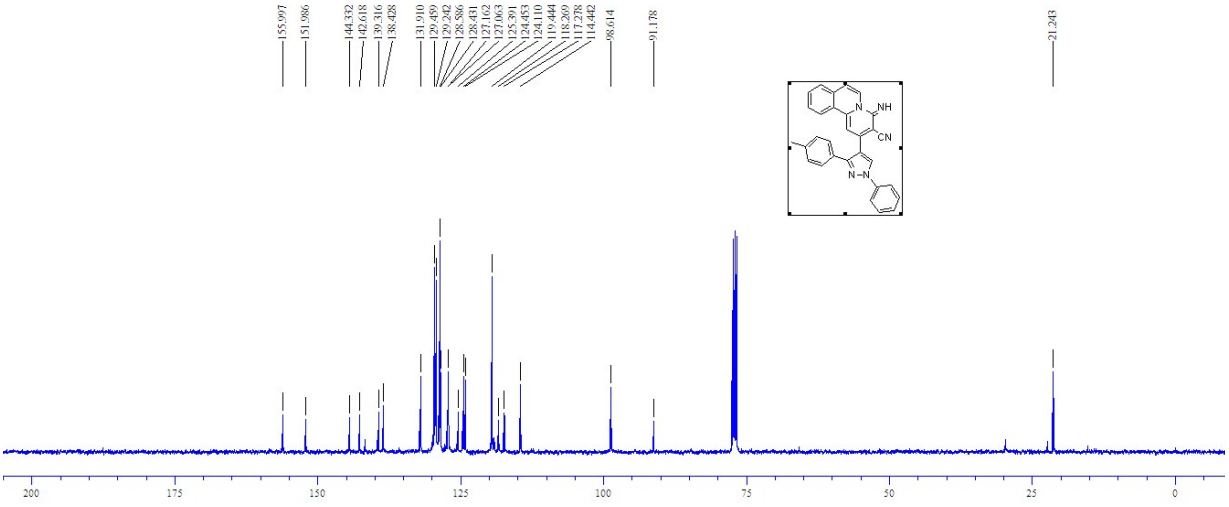


Figure S31: ^{1}H NMR of compound **4p**

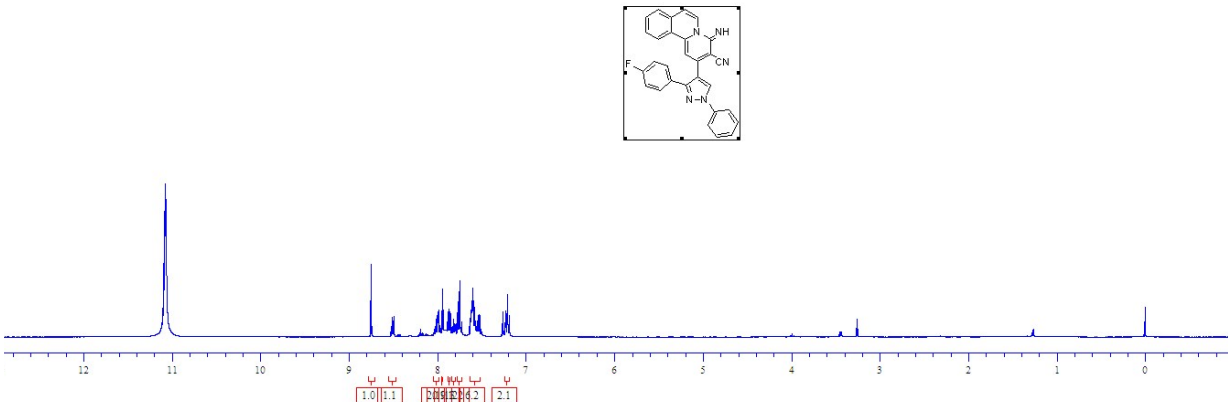


Figure S32: ^{13}C NMR of compound **4p**

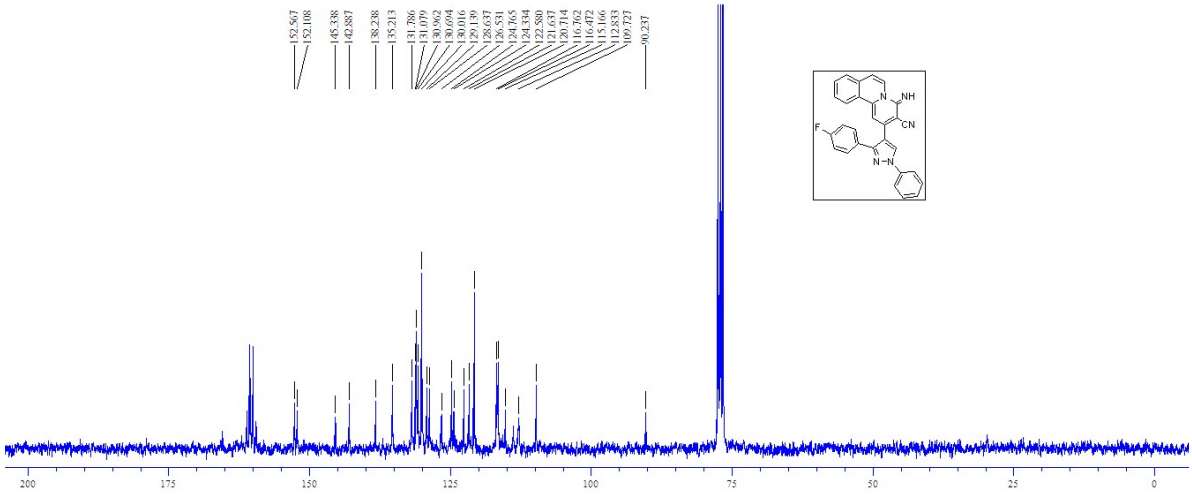


Figure S33: [1]H NMR of compound **4q**

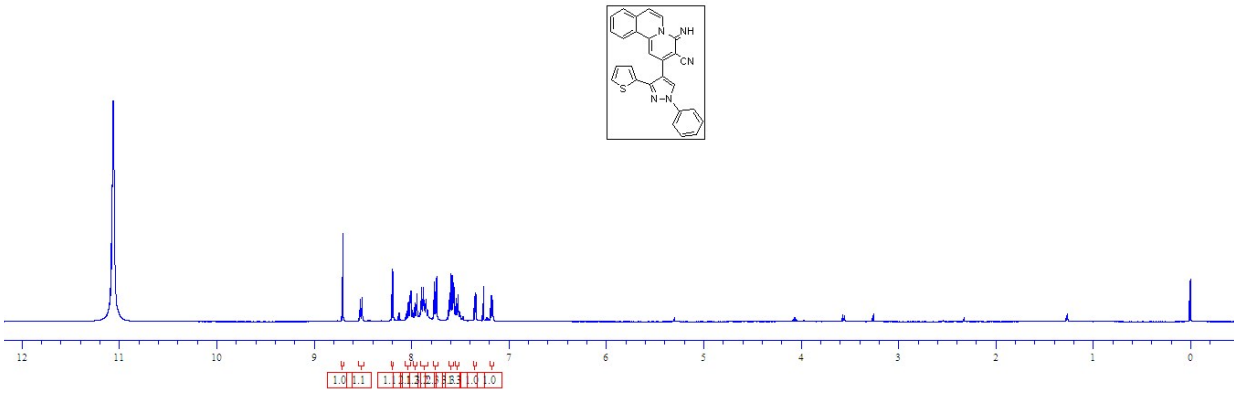


Figure S34: [13]C NMR of compound **4q**