Formal [3 +2] Cycloaddition of 1-Cyanocyclopropane 1-Ester with Pyridine, Quinoline or Isoquinoline: General and Efficient Strategy for Construction of Cyanoindolizine Skeletons

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CONTENTS

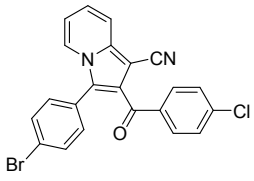
Experimental Section

General: All melting points were determined in a Yanaco melting point apparatus and are uncorrected. The ^{1}H NMR (600 MHz) and ^{13}C NMR (150 MHz) spectra were recorded in a Bruker AV-600 spectrometer with TMS as internal reference in $CDCl_3$ solutions. The *J* values are given in hertz. Only discrete or characteristic signals for the ^{1}H NMR are reported. The MS spectra were obtained on a ZAB-HS mass spectrometer with 70 eV. X-ray crystallographic analysis was performed with a Smart-1000 CCD diffractometer. Flash chromatography was performed on silica gel (230-400 mesh) eluting with ethyl acetate-hexanes mixture. All reactions were monitored by thin layer chromatography (TLC). All reagents and solvents were purchased from commercial sources and purified commonly before used.

General procedure for preparation of 1-cyanoindolizine derivatives (**2a-n**, **3a-d**, and **4a-c**).

The appropriate substituted 1-cyanocyclopropane 1-ester (6.0 mmol), pyridine (or quinoline and isoquinoline, 6.0 mmol), and molecular iodine (1.2 mmol, 0.32 g) were dissolved in 15 mL of toluene at room temperature, and the resultant mixture was stirred at 120 ^{o}C for 20 h, and the completion of reaction was confirmed by TLC (EtOAc/hexanes 1:10). After the mixture was cooled to room temperature, the solvent was removed under reduced pressure. Subsequently, the residues were added with dichloromethane (15 mL), the mixture was washed with saturated sodium thiosulfate, water and brine, dried over anhydrous sodium sulfate. The filtrate was purified by flash chromatography (silica gel, EtOAc/hexanes, 1/20) to give products.

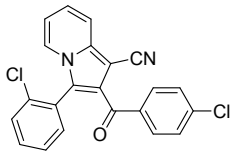
*1-Cyano-3-(4-bromophenyl)-2-(4-chlorobenzoyl)indolizine (**2a**):*



2a

Yellow solid; m.p. 209.1-209.9 ^{o}C (PE/EA); ^{1}H-NMR (DMSO-d_6, 600 MHz) δ (*ppm*): 8.26 (d, *J* = 7.2 Hz, 1H), 7.81 (d, *J* = 9.0 Hz, 1H), 7.67 (d, *J* = 7.8 Hz, 2H), 7.58 (d, *J* = 7.8 Hz, 2H), 7.41-7.38 (m, 3H), 7.36 (d, *J* = 7.2 Hz, 2H), 7.03 (t, *J* = 6.6 Hz, 1H); ^{13}C-NMR (DMSO-d_6, 150 MHz) δ (*ppm*): 189.6, 138.1, 137.7, 135.7, 132.8, 131.8, 131.3, 128.4, 127.0, 126.9, 126.0, 125.6, 125.0, 122.8, 117.7, 115.2, 115.0, 81.9; IR (KBr, cm^{-1}) ν: 2216, 1650, 1560, 1410, 1202, 1071, 1010, 986, 958, 758; MS(EI) (m/z): 434.77 [$(M+1)^{+}$] (46%); HRESIMS calcd for $C_{22}H_{12}BrClN_2O$ $(M+H)^{+}$ 434.9900; found 434.9907.

*1-Cyano-3-(2-chlorophenyl)-2-(4-chlorobenzoyl)indolizine (**2b**):*

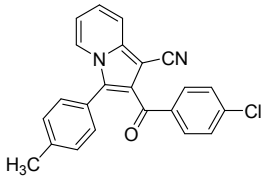


2b

Yellow solid; m.p. 212.5-213.3 ^{o}C (PE/EA); ^{1}H-NMR (DMSO-d_6, 600 MHz) δ (*ppm*): 7.90 (d, *J* = 6.6 Hz, 1H), 7.85 (d, *J* = 9.6 Hz, 1H), 7.63 (d, *J* = 8.4 Hz, 2H), 7.54 (d, *J* = 8.4 Hz, 1H), 7.47-7.41 (m, 3H), 7.39 (d, *J* = 8.4 Hz, 2H), 7.35 (t, *J* = 7.2 Hz, 1H), 7.06 (t, *J* = 6.6 Hz, 1H); ^{13}C-

NMR (DMSO-d_6, 150 MHz) δ (*ppm*): 189.2, 137.8, 137.7, 135.9, 134.2, 134.0, 131.7, 130.9, 129.8, 128.2, 127.7, 126.8, 126.7, 125.7, 125.4, 125.1, 117.7, 115.3, 114.9, 81.8; IR (KBr, cm^{-1}) ν: 2220, 1659, 1552, 1413, 1211, 1072, 1016, 990, 820, 749; MS(EI) (m/z): 391.49 [$(M+1)^+$] (100%); HRESIMS calcd for $C_{22}H_{12}Cl_2N_2O$ $(M+H)^+$ 391.0405; found 391.0411.

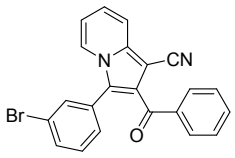
*1-Cyano-3-p-tolyl-2-(4-chlorobenzoyl)indolizine (**2c**):*



2c

Yellow solid; m.p. 178.5-179.1 °C (PE/EA); ^{1}H-NMR (DMSO-d_6, 600 MHz) δ (*ppm*): 8.24 (d, *J* = 7.2 Hz, 1H), 7.80 (d, *J* = 9.0 Hz, 1H), 7.66 (d, *J* = 8.4 Hz, 2H), 7.38-7.36 (m, 3H), 7.28 (d, *J* = 7.8 Hz, 2H), 7.20 (d, *J* = 7.8 Hz, 2H), 7.02 (t, *J* = 6.6 Hz, 1H), 2.29 (s, 3H); ^{13}C-NMR (DMSO-d_6, 150 MHz) δ (*ppm*): 189.7, 138.9, 137.9, 137.5, 136.1, 135.7, 131.3, 130.6, 129.4, 128.3, 125.7, 125.4, 124.9, 124.8, 117.7, 115.0, 81.6, 20.8; IR (KBr, cm^{-1}) ν: 2220, 1666, 1558, 1430, 1208, 1130, 982, 768; MS(EI) (m/z): 369.19 [$(M-1)^+$] (100%), 371.23 [$(M+1)^+$] (26%); HRESIMS calcd for $C_{23}H_{15}ClN_2O$ $(M+H)^+$ 371.0951; found 371.0955.

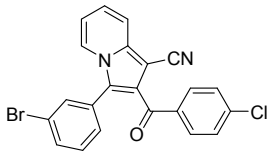
*1-Cyano-2-benzoyl-3-(3-bromophenyl)indolizine (**2d**):*



2d

Yellow solid; m.p. 192.4-193.0 °C (PE/EA); ^{1}H-NMR ($CDCl_3$, 600 MHz) δ (*ppm*): 8.01 (d, *J* = 7.2 Hz, 1H), 7.71-7.67 (m, 3H), 7.43 (t, *J* = 7.2 Hz, 1H), 7.32 (s, 1H), 7.30-7.26 (m, 3H), 7.24 (t, *J* = 7.8 Hz, 1H), 7.21-7.20 (m, 1H), 7.16-7.14 (m, 1H), 6.79 (t, *J* = 6.6 Hz, 1H); ^{13}C-NMR ($CDCl_3$, 150 MHz) δ (*ppm*): 189.7, 137.0, 136.3, 134.0, 132.3, 129.5, 129.3, 129.0, 128.9, 128.6, 127.9, 127.3, 126.7, 125.2, 123.2, 122.9, 117.7, 113.8, 113.7, 82.9; IR (KBr, cm^{-1}) ν: 2202, 1653, 1562, 1436, 1212, 1085, 985, 882, 690; MS(EI) (m/z): 399.03 [$(M-1)^+$] (42%), 401.26 [$(M+1)^+$] (29%); HRESIMS calcd for $C_{22}H_{13}BrN_2O$ $(M+H)^+$ 401.0290; found 401.0296.

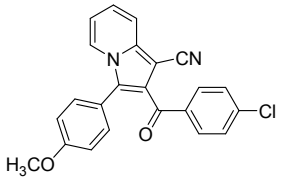
*1-Cyano-3-(3-bromophenyl)-2-(4-chlorobenzoyl)indolizine (**2e**):*



2e

Yellow solid; m.p. 171.5-172.0 °C (PE/EA); ^{1}H-NMR (DMSO-d_6, 600 MHz) δ (*ppm*): 8.27 (d, *J* = 6.6 Hz, 1H), 7.83 (d, *J* = 9.0 Hz, 1H), 7.67 (d, *J* = 8.4 Hz, 2H), 7.50 (s, 1H), 7.45-7.44 (m, 1H), 7.42-7.38 (m, 5H), 7.05 (t, *J* = 6.6 Hz, 1H); ^{13}C-NMR (DMSO-d_6, 150 MHz) δ (*ppm*): 189.5, 137.9, 137.7, 135.8, 133.4, 131.2, 130.6, 129.8, 129.5, 129.1, 128.3, 127.8, 126.6, 126.2, 125.7, 125.1, 117.7, 115.3, 115.0, 81.9; IR (KBr, cm^{-1}) ν: 2198, 1655, 1560, 1438, 1310, 1210, 1090, 982, 884, 788; MS(EI) (m/z): 432.69 (95%), 434.53 [$(M+1)^+$] (47%); HRESIMS calcd for $C_{22}H_{12}BrClN_2O$ $(M+H)^+$ 434.9900; found 434.9909.

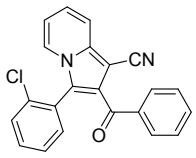
*1-Cyano-2-(4-chlorobenzoyl)-3-(4-methoxyphenyl)indolizine (**2f**):*



2f

Yellow solid; m.p.: 178.5-179.1 °C (PE/EA); ^{1}H-NMR (DMSO-d_6, 600 MHz) δ (*ppm*): 8.24 (d, *J* = 7.2 Hz, 1H), 7.80 (d, *J* = 9.0 Hz, 1H), 7.66 (d, *J* = 8.4 Hz, 2H), 7.38-7.36 (m, 3H), 7.28 (d, *J* = 7.8 Hz, 2H), 7.20 (d, *J* = 7.8 Hz, 2H), 7.02 (t, *J* = 6.6 Hz, 1H), 2.29 (s, 3H); ^{13}C-NMR (DMSO-d_6, 150 MHz) δ (*ppm*): 189.7, 138.9, 137.9, 137.5, 136.1, 135.7, 131.3, 130.6, 129.4, 128.80, 128.3, 125.7, 125.4, 124.9, 124.8, 117.7, 115.0, 81.6, 20.8; IR (KBr, cm^{-1}) ν: 2220, 1651, 1557, 1420, 1310, 1202, 1019, 999, 878, 782; MS(EI) (m/z): 385.09 (59%), 387.39 [(M+1)$^{+}$] (37%); HRESIMS calcd for $C_{23}H_{15}ClN_2O_2$ (M+H)$^{+}$ 387.0900; found 387.0893.

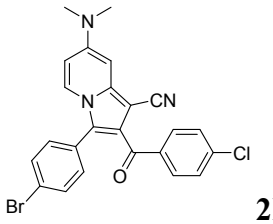
*1-Cyano-2-benzoyl-3-(2-chlorophenyl)indolizine (**2g**):*



2g

Yellow solid; m.p.: 194.2-194.7 °C (PE/EA); ^{1}H-NMR (DMSO-d_6, 600 MHz) δ (*ppm*): 7.91 (d, *J* = 7.2 Hz, 1H), 7.86 (d, *J* = 9.0 Hz, 1H), 7.63 (d, *J* = 8.4 Hz, 2H), 7.54 (d, *J* = 7.8 Hz, 1H), 7.47-7.43 (m, 3H), 7.39 (d, *J* = 8.4 Hz, 2H), 7.36-7.31 (m, 2H), 7.07 (t, *J* = 6.6 Hz, 1H); ^{13}C-NMR (DMSO-d_6, 150 MHz) δ (*ppm*): 189.2, 137.8, 137.7, 135.9, 134.2, 134.1, 131.7, 130.9, 129.8, 129.1, 128.2, 128.1, 127.6, 126.7, 125.7, 125.4, 117.7, 115.3, 114.9, 81.8; IR (KBr, cm^{-1}) ν: 2213, 1658, 1550, 1426, 1312, 1211, 1010, 989, 874, 783; MS(EI) (m/z): 357.02 [(M+1)$^{+}$] (100%); HRESIMS calcd for $C_{22}H_{13}ClN_2O$ (M+H)$^{+}$ 357.0795; found 357.0797.

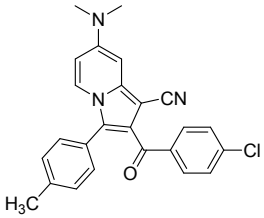
*1-Cyano-3-(4-bromophenyl)-2-(4-chlorobenzoyl)-7-(dimethylamino)indolizine (**2h**):*



2h

Yellow solid; m.p.: 256.1-256.8 °C (PE/EA); ^{1}H-NMR (DMSO-d_6, 600 MHz) δ (*ppm*): 8.03 (d, *J* = 7.8 Hz, 1H), 7.61 (d, *J* = 8.4 Hz, 2H), 7.53 (d, *J* = 7.8 Hz, 2H), 7.36 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 7.8 Hz, 2H), 6.83 (dd, *J* = 7.8, 2.4 Hz, 1H), 6.41 (d, *J* = 3.0 Hz, 1H), 3.07 (s, 6H); ^{13}C-NMR (DMSO-d_6, 150 MHz) δ (*ppm*): 189.7, 147.3, 141.4, 137.6, 136.0, 132.7, 131.6, 131.2, 128.2, 127.5, 125.5, 125.1, 124.7, 122.2, 116.7, 106.7, 90.6, 75.9; IR (KBr, cm^{-1}) ν: 2210, 1652, 1557, 1413, 1308, 1268, 1010, 972, 876, 780; MS(EI) (m/z): 478.35 [(M+1)$^{+}$] (100%); HRESIMS calcd for $C_{24}H_{17}BrClN_3O$ (M+H)$^{+}$ 478.0322; found 478.0323.

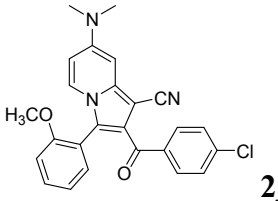
*1-Cyano-2-(4-chlorobenzoyl)-7-(dimethylamino)-3-(4-methylphenyl)indolizine (**2i**):*



2i

Yellow solid; m.p. 247.3-248.0 °C (PE/EA); ^{1}H-NMR (DMSO-d_6, 600 MHz) δ (*ppm*): 7.99 (d, *J* = 7.8 Hz, 1H), 7.60 (d, *J* = 9.0 Hz, 2H), 7.33 (d, *J* = 8.4 Hz, 2H), 7.20 (d, *J* = 7.8 Hz, 2H), 7.15 (d, *J* = 8.4 Hz, 2H), 6.82 (dd, *J* = 7.8, 2.4 Hz, 1H), 6.39 (d, *J* = 2.4 Hz, 1H), 3.06 (s, 6H), 2.27 (s, 3H); ^{13}C-NMR (DMSO-d_6, 150 MHz) δ (*ppm*): 189.8, 147.2, 141.2, 138.4, 137.4, 136.1, 131.1, 130.5, 129.3, 128.1, 126.0, 125.3, 125.2, 124.6, 116.8, 106.6, 90.6, 75.6, 20.8; IR (KBr, cm^{-1}) ν: 2214, 1650, 1551, 1410, 1302, 1278, 1010, 963, 858, 690; MS(EI) (m/z): 414.65 [(M+1)$^+$] (100%); HRESIMS calcd for $C_{25}H_{20}ClN_3O$ (M+H)$^+$ 414.1373; found 414.1376.

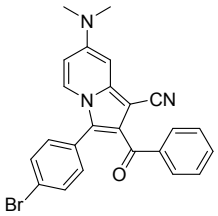
*1-Cyano-2-(4-chlorobenzoyl)-3-(2-methoxyphenyl)-7-(dimethylamino)indolizine (**2j**):*



2j

Yellow solid; m.p. 194.0-194.7 °C (PE/EA); ^{1}H-NMR (DMSO-d_6, 600 MHz) δ (*ppm*): 7.65 (d, *J* = 7.8 Hz, 1H), 7.51 (d, *J* = 8.4 Hz, 2H), 7.32 (t, *J* = 7.8 Hz, 1H), 7.28 (d, *J* = 8.4 Hz, 2H), 7.05 (d, *J* = 7.2 Hz, 1H), 7.01 (d, *J* = 7.8 Hz, 1H), 6.81 (t, *J* = 7.2 Hz, 2H), 6.40 (d, *J* = 3.0 Hz, 1H), 3.72 (s, 3H), 3.06 (s, 6H); ^{13}C-NMR (DMSO-d_6, 150 MHz) δ (*ppm*): 189.9, 157.6, 147.7, 141.7, 137.6, 136.2, 131.6, 131.1, 129.2, 128.4, 126.8, 126.8, 125.4, 123.9, 120.9, 117.4, 117.2, 111.9, 106.7, 91.0, 75.9, 55.9; IR (KBr, cm^{-1}) ν: 2220, 1645, 1530, 1400, 1302, 1270, 1012, 952, 878, 782; MS(EI) (m/z): 430.66 [(M+1)$^+$] (100%); HRESIMS calcd for $C_{25}H_{20}ClN_3O_2$ (M+H)$^+$ 430.1322; found 430.1323.

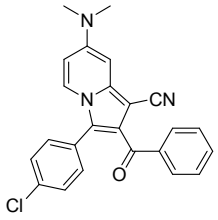
*1-Cyano-2-benzoyl-3-(4-bromophenyl)-7-(dimethylamino)indolizine (**2k**):*



2k

Yellow solid; m.p. 180.5-190.2 °C (PE/EA); ^{1}H-NMR (DMSO-d_6, 600 MHz) δ (*ppm*): 8.03 (d, *J* = 7.8 Hz, 1H), 7.62 (d, *J* = 7.2 Hz, 2H), 7.51 (d, *J* = 8.4 Hz, 2H), 7.48 (d, *J* = 7.2 Hz, 1H), 7.31 (t, *J* = 7.8 Hz, 2H), 7.29 (d, *J* = 8.4 Hz, 2H), 6.82 (dd, *J* = 7.8, 2.4 Hz, 1H), 6.41 (d, *J* = 2.4 Hz, 1H), 3.07 (s, 6H); ^{13}C-NMR (DMSO-d_6, 150 MHz) δ (*ppm*): 190.9, 147.3, 141.3, 137.2, 133.90, 132.8, 132.5, 131.6, 129.4, 128.1, 127.6, 125.6, 125.4, 124.2, 122.0, 116.7, 106.6, 90.7, 76.0; IR (KBr, cm^{-1}) ν: 2218, 1646, 1530, 1422, 1301, 1276, 1014, 988, 902, 862; MS(EI) (m/z): 442.55 (100%), 444.24 [(M+1)$^+$] (39%); HRESIMS calcd for $C_{24}H_{18}BrN_3O$ (M+H)$^+$ 444.0711; found 444.0712.

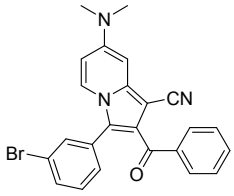
*1-Cyano-2-benzoyl-3-(4-chlorophenyl)-7-(dimethylamino)indolizine (**2l**):*



2l

Yellow solid; m.p. 193.5-194.2 °C (PE/EA); ^{1}H-NMR (DMSO-d_6, 600 MHz) δ (*ppm*): 8.02 (d, *J* = 7.8 Hz, 1H), 7.62 (d, *J* = 7.2 Hz, 2H), 7.48 (t, *J* = 7.2 Hz, 1H), 7.37-7.34 (m, 4H), 7.31 (t, *J* = 7.8 Hz, 2H), 6.82 (dd, *J* = 7.8, 3.0 Hz, 1H), 6.41 (d, *J* = 1.8 Hz, 1H), 3.07 (s, 6H); ^{13}C-NMR (DMSO-d_6, 150 MHz) δ (*ppm*): 190.9, 147.3, 141.3, 137.2, 133.3, 132.7, 132.4, 132.3, 129.4, 128.7, 128.6, 128.1, 127.2, 125.6, 125.3, 124.2, 116.7, 106.6, 90.6, 76.0; IR (KBr, cm^{-1}) ν: 2203, 1646, 1532, 1436, 1312, 1280, 1012, 990, 902, 862; MS(EI) (m/z): 400.97 [(M+1)$^+$] (78%); HRESIMS calcd for $C_{24}H_{18}ClN_3O$ (M+H)$^+$ 400.1217; found 400.1219.

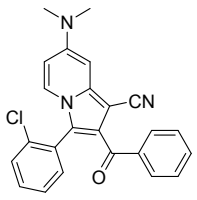
*1-Cyano-2-benzoyl-3-(3-bromophenyl)-7-(dimethylamino)indolizine (**2m**):*



2m

Yellow solid; m.p.: 199.1-199.8 °C (PE/EA); ^{1}H-NMR (DMSO-d_6, 600 MHz) δ (*ppm*): 8.04 (d, *J* = 7.8 Hz, 1H), 7.61 (d, *J* = 7.2 Hz, 2H), 7.47 (t, *J* = 7.2 Hz, 1H), 7.40 (s, 1H), 7.34-7.33 (m, 2H), 7.31-7.28 (m, 3H), 6.84 (dd, *J* = 7.8, 2.4 Hz, 1H), 6.41 (d, *J* = 1.8 Hz, 1H), 3.07 (s, 6H); ^{13}C-NMR (DMSO-d_6, 100 MHz) δ (*ppm*): 191.3, 147.8, 141.7, 137.7, 133.7, 133.2, 130.9, 130.8, 130.7, 129.7, 129.6, 129.3, 128.9, 128.5, 126.2, 125.9, 124.4, 117.1, 107.1, 91.1, 76.5; IR (KBr, cm^{-1}) ν: 2216, 1650, 1528, 1424, 1310, 1278, 1009, 972, 916, 793; MS(EI) (m/z): 444.54 [(M+1)$^+$] (68%); HRESIMS calcd for $C_{24}H_{18}BrN_3O$ (M+H)$^+$ 444.0711; found 444.0719.

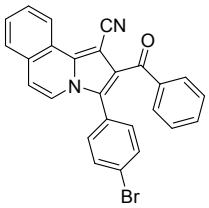
*1-Cyano-2-benzoyl-3-(2-chlorophenyl)-7-(dimethylamino)indolizine (**2n**):*



2n

Yellow solid; m.p. 169.7-170.5 °C (PE/EA); ^{1}H-NMR (DMSO-d_6, 600 MHz) δ (*ppm*): 7.62 (d, *J* = 7.8 Hz, 1H), 7.58 (d, *J* = 7.2 Hz, 2H), 7.48 (d, *J* = 7.8 Hz, 1H), 7.43 (t, *J* = 7.2 Hz, 1H), 7.36 (td, *J* = 8.4, 1.8 Hz, 1H), 7.33 (dd, *J* = 6.0, 1.8 Hz, 1H), 7.28 (t, *J* = 7.8 Hz, 2H), 7.25 (t, *J* = 7.2 Hz, 1H), 6.84 (dd, *J* = 7.8, 2.4 Hz, 1H), 6.43 (d, *J* = 2.4 Hz, 1H), 3.07 (s, 6H); ^{13}C-NMR (DMSO-d_6, 150 MHz) δ (*ppm*): 190.5, 147.3, 141.2, 137.6, 134.2, 132.5, 131.2, 129.6, 128.8, 127.9, 127.4, 126.2, 125.9, 122.7, 116.7, 106.6, 90.7, 75.7; IR (KBr, cm^{-1}) ν: 2210, 1650, 1530, 1438, 1308, 1282, 1010, 982, 913, 867; MS(EI) (m/z): 398.39 (53%), 400.21 [(M+1)$^+$] (42%); HRESIMS calcd for $C_{24}H_{18}ClN_3O$ (M+H)$^+$ 400.1217; found 400.1222.

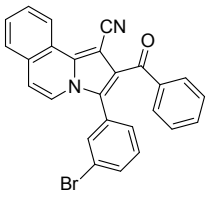
*2-benzoyl-3-(4-bromophenyl)pyrrolo[2,1-a]isoquinoline-1-carbonitrile (**3a**)*



3a

Yellow solid; m.p. 245.4-246.3 °C (PE/EA); ^{1}H-NMR (DMSO-d_6, 600 MHz) δ (*ppm*): 8.82 (d, *J* = 8.4 Hz, 1H), 8.00 (d, *J* = 7.2 Hz, 1H), 7.98 (d, *J* = 7.8 Hz, 1H), 7.81 (t, *J* = 7.2 Hz, 1H), 7.74 (t, *J* = 7.2 Hz, 1H), 7.68 (d, *J* = 8.4 Hz, 2H), 7.58 (d, *J* = 8.4 Hz, 2H), 7.52 (t, *J* = 7.2 Hz, 1H), 7.39 (d, *J* = 8.4 Hz, 2H), 7.36-7.32 (m, 3H); ^{13}C-NMR (DMSO-d_6, 150 MHz) δ (*ppm*):190.4, 137.0, 133.7, 133.1, 133.0, 131.7, 129.5, 129.4, 129.4, 129.0, 128.6, 128.3, 128.0, 127.1, 125.8, 123.7, 123.0, 122.4, 122.1, 116.7, 115.3, 84.1; IR (KBr, cm^{-1}) ν: 3064, 2206, 1637, 1592, 1524, 1454, 1400, 1260, 1207, 1073, 1010, 951, 906, 854, 779; IR (KBr, cm^{-1}) ν: 2198, 1652, 1509, 1420, 1410, 1308, 1280, 1010, 980, 915, 788; MS(EI) (m/z): 451.73 [(M+1)$^+$] (63%), 452.96 [(M+2)$^+$] (100%); HRESIMS calcd for $C_{26}H_{15}BrN_2O$ (M+H)$^+$ 451.0446; found 451.0447.

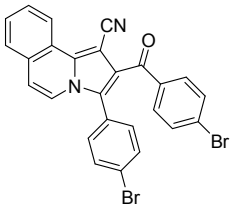
*2-benzoyl-3-(3-bromophenyl)pyrrolo[2,1-a]isoquinoline-1-carbonitrile (**3b**)*



3b

Yellow solid; m.p.: 225.6-223.0 °C (PE/EA); ^{1}H-NMR (DMSO-d_6, 600 MHz) δ (ppm): 8.83 (d, *J* = 7.8 Hz, 1H), 8.00 (d, *J* = 7.2 Hz, 1H), 7.98 (d, *J* = 7.8 Hz, 1H), 7.82 (t, *J* = 8.4 Hz, 1H), 7.74 (t, *J* = 7.2 Hz, 1H), 7.67 (d, *J* = 7.8 Hz, 2H), 7.53 (s, 1H), 7.49 (t, *J* = 7.8 Hz, 1H), 7.43-7.38 (m, 3H), 7.37 (d, *J* = 7.8 Hz, 1H), 7.32 (t, *J* = 7.8 Hz, 2H); ^{13}C-NMR (DMSO-d_6, 150 MHz) δ (ppm):190.4, 137.1, 133.7, 133.3, 133.0, 130.8, 130.5, 129.8, 129.7, 129.4, 129.3, 129.1, 129.0, 128.6, 128.1, 128.0, 125.9, 123.6, 122.4, 122.1, 116.7, 115.4, 84.1; IR (KBr, cm^{-1}) ν: 2196, 1648, 1507, 1422, 1411, 1310, 1280, 1016, 980, 869, 780; MS(EI) (m/z): 451.68 [(M+1)$^+$] (72%), 452.90 [(M+2)$^+$] (100%); HRESIMS calcd for $C_{26}H_{15}BrN_2O$ (M+H)$^+$ 451.0446; found 451.0453.

*2-(4-bromobenzoyl)-3-(4-bromophenyl)pyrrolo[2,1-a]isoquinoline-1-carbonitrile (**3b**)*

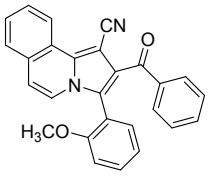


3c

Yellow solid; m.p. 293.1-293.9 °C (PE/EA); ^{1}H-NMR (DMSO-d_6, 600 MHz) δ (*ppm*): 8.81 (d, *J* = 8.4 Hz, 1H), 8.00 (d, *J* = 7.8 Hz, 1H), 7.97 (d, *J* = 7.8 Hz, 1H), 7.81 (t, *J* = 7.2 Hz, 1H), 7.74 (t, *J* = 7.2 Hz, 1H), 7.59 (t, *J* = 7.2 Hz, 4H), 7.53 (d, *J* = 8.4 Hz, 2H), 7.38 (d, *J* = 7.8 Hz, 2H), 7.35 (d, *J* = 7.8 Hz, 1H); ^{13}C-NMR (DMSO-d_6, 150 MHz) δ (*ppm*):189.4, 136.2, 133.8, 133.1, 131.8, 131.4, 131.3, 129.8, 129.4, 129.1, 128.6, 128.0, 127.0, 126.9, 125.3, 123.6, 123.1, 122.4, 122.1, 116.7, 115.4, 84.1; IR (KBr, cm^{-1}) ν:3068, 2210, 1747, 1642, 1580, 1527, 1471, 1416, 1361, 1260, 1073, 1010, 954, 904, 836, 781; IR (KBr, cm^{-1}) ν: 2199, 1647, 1515, 1420, 1410, 1310, 1282,

1012, 973, 869, 786; MS(EI) (m/z): 529.09 [(M+1)$^+$] (100%); HRESIMS calcd for $C_{26}H_{14}Br_2N_2O$ (M+H)$^+$ 530.9531; found 530.9538.

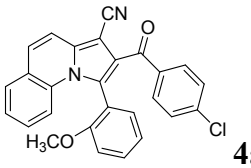
*2-benzoyl-3-(2-methoxyphenyl)pyrrolo[2,1-a]isoquinoline-1-carbonitrile (**3d**)*



3d

Yellow solid; m.p. 256.2-256.8 °C (PE/EA); ^{1}H-NMR (DMSO-d_6, 600 MHz) δ (*ppm*): 8.81 (d, *J* = 8.4 Hz, 1H), 7.96 (d, *J* = 7.2 Hz, 2H), 7.80 (t, *J* = 7.8 Hz, 1H), 7.72 (t, *J* = 7.2 Hz, 1H), 7.67 (d, *J* = 7.8 Hz, 2H), 7.49 (t, *J* = 7.2 Hz, 1H), 7.34 (t, *J* = 7.8 Hz, 3H), 7.32 (t, *J* = 7.8 Hz, 2H), 6.92 (d, *J* = 8.4 Hz, 2H), 3.73 (s, 3H); ^{13}C-NMR (DMSO-d_6, 150 MHz) δ (*ppm*): 191.1, 160.3, 137.5, 133.9, 133.4, 132.9(2C), 131.0, 129.9(2C), 129.6, 129.4, , 129.0, 128.6(2C), 128.4, 125.8, 124.2, 122.8, 122.5, 120.2, 117.4, 115.5, 114.7(2C), 84.2, 55.7; IR (KBr, cm^{-1}) ν: 2208, 1650, 1530, 1422, 1414, 1312, 1276, 1010, 975, 920, 780; MS(EI) (m/z): 403.53 [(M+1)$^+$] (100%); HRESIMS calcd for $C_{27}H_{18}N_2O_2$ (M+H)$^+$ 403.1447; found 403.1448.

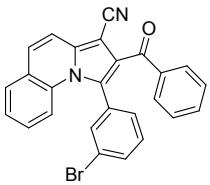
*2-(4-chlorobenzoyl)-1-(2-methoxyphenyl)pyrrolo[1,2-a]quinoline-3-carbonitrile (**4a**)*



4a

Yellow solid; m.p.: 261.1-262.0 °C (PE/EA); ^{1}H-NMR (DMSO-d_6, 600 MHz) δ (*ppm*): 7.99 (d, *J* = 7.8 Hz, 1H), 7.77 (d, *J* = 9.0 Hz, 1H), 7.71 (d, *J* = 7.2 Hz, 1H), 7.56 (d, *J* = 8.4 Hz, 2H), 7.50 (t, *J* = 7.2 Hz, 1H), 7.44 (t, *J* = 7.2 Hz, 1H), 7.39 (d, *J* = 7.8 Hz, 2H),7.36-7.32 (m, 2H), 7.24 (d, *J* = 7.8 Hz, 1H), 7.03 (d, *J* = 8.4 Hz, 1H), 6.91 (t, *J* = 7.2 Hz, 1H), 3.57 (s, 3H); ^{13}C-NMR (DMSO-d_6, 150 MHz) δ (*ppm*): 190.2, 158.1, 138.2, 137.8, 136.4, 134.3, 132.8, 132.5, 131.1, 130.1, 129.6, 129.3, 128.7, 127.2, 127.1, 126.4, 125.5, 121.2, 120.3, 116.5, 116.3, 115.1, 111.9, 85.9, 55.9; IR (KBr, cm^{-1}) ν: 2202, 1648, 1527, 1425, 1412, 1315, 1265, 1026, 988, 922, 785; MS(EI) (m/z): 437.75 [(M+1)$^+$] (100%); HRESIMS calcd for $C_{27}H_{17}ClN_2O_2$ (M+H)$^+$ 437.1057; found 437.1055.

*2-benzoyl-1-(3-bromophenyl)pyrrolo[1,2-a]quinoline-3-carbonitrile (**4b**)*

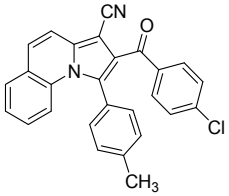


4b

Yellow solid; m.p. 200.1-200.8 °C (PE/EA); ^{1}H-NMR (DMSO-d_6, 600 MHz) δ (*ppm*): 8.02 (d, *J* = 7.8 Hz, 1H), 7.80 (d, *J* = 9.6 Hz, 1H), 7.73 (d, *J* = 9.6 Hz, 1H), 7.67 (d, *J* = 7.8 Hz, 2H), 7.61 (s, 1H), 7.56 (t, *J* = 7.2 Hz, 1H), 7.52-7.49 (m, 2H), 7.46 (d, *J* = 7.8 Hz, 1H), 7.42 (d, *J* = 7.8 Hz, 1H), 7.40 (d, *J* = 7.2 Hz, 2H), 7.38 (d, *J* = 3.6 Hz, 1H), 7.18 (d, *J* = 9.0 Hz, 1H); ^{13}C-NMR (DMSO-d_6, 150 MHz) δ (*ppm*): 190.7, 137.2, 133.3, 133.2, 130.8, 130.5, 130.0, 129.9, 129.7, 129.6, 129.4, 128.7, 128.3, 127.4, 126.8, 125.9, 125.4, 117.1, 115.8, 114.6, 85.5; IR (KBr, cm^{-1}) ν: 2189, 1642, 1520, 1426, 1410, 1310, 1260, 972, 925, 789; MS(EI) (m/z): 451.69 [(M+1)$^+$] (72%),

452.84 [(M+2)$^+$] (100%); HRESIMS calcd for $C_{26}H_{15}BrN_2O$ (M+Na)$^+$ 473.0265; found 473.0268.

*2-(4-chlorobenzoyl)-1-(4-methylphenyl)pyrrolo[1,2-a]quinoline-3-carbonitrile (**4c**)*



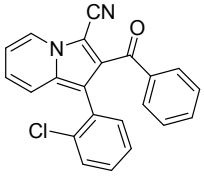
4c

Yellow solid; m.p. 258.4-259.1 ^{o}C (PE/EA); ^{1}H-NMR (DMSO-d_6, 600 MHz) δ (*ppm*): 8.00 (d, *J* = 7.8 Hz, 1H), 7.77 (d, *J* = 9.0 Hz, 1H), 7.71 (d, *J* = 9.0 Hz, 1H), 7.66 (d, *J* = 8.4 Hz, 2H), 7.49 (t, *J* = 7.2 Hz, 1H), 7.44 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 7.8 Hz, 2H), 7.31 (d, *J* = 7.8 Hz, 1H), 7.26 (d, *J* = 8.4 Hz, 1H), 7.22 (d, *J* = 7.8 Hz, 2H), 2.34 (s, 3H); ^{13}C-NMR (DMSO-d_6, 150 MHz) δ (*ppm*): 189.8, 139.3, 138.0, 137.1, 136.0, 133.5, 132.1, 131.2, 130.8, 129.8, 129.3, 128.6, 128.5, 128.1, 126.7, 125.8, 125.3, 117.0, 115.9, 114.7, 85.2, 20.9; IR (KBr, cm^{-1}) ν: 2192, 1667, 1525, 1420, 1410, 1312, 1260, 1202, 975, 922, 782; MS(EI) (m/z): 421.74 [(M+1)$^+$] (100%); HRESIMS calcd for $C_{27}H_{17}ClN_2O$ (M+Na)$^+$ 443.0927; found 443.0928.

General procedure for preparation of 3-cyanoindolizine derivatives (5a-n).

The appropriate substituted 1-cyanocyclopropane 1-ester (3.0 mmol), and molecular iodine (1.2 mmol, 0.32 g) were dissolved in 15 mL of pyridine at room temperature, and the resultant mixture was stirred at 120 ^{o}C for 15 h, and the completion of reaction was confirmed by TLC (EtOAc/hexanes 1:10). After the mixture was cooled to room temperature, the excessive pyridine was removed under reduced pressure. Subsequently, the residues were added with dichloromethane (15 mL), the mixture was washed with saturated sodium thiosulfate, water and brine, dried over anhydrous sodium sulfate. The filtrate was purified by flash chromatography (silica gel, EtOAc/hexanes, 1/20) to give product **5a**-**n**.

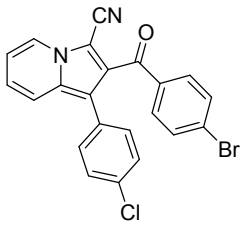
*3-Cyano-1-(2-chlorophenyl)-2-benzoylindolizine (**5a**):*



5a

Yellow solid; mp 179.0-180.0 ^{o}C (PE/EA); ^{1}H NMR (600 MHz, $CDCl_3$) δ (*ppm*): 7.70 (d, *J* = 9.0 Hz, 1H), 7.65 (d, *J* = 7.2 Hz, 2H), 7.57 (d, *J* = 7.2 Hz, 1H), 7.36 – 7.33 (m, 2H), 7.23 – 7.20 (m, 4H), 7.14 (t, *J* = 7.2 Hz, 2H), 6.77 (t, *J* = 6.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ (*ppm*): 189.6, 137.0, 136.5, 134.2, 133.1, 132.0, 130.2, 128.9, 128.6, 127.1, 126.5, 126.2, 124.2, 123.8, 123.1, 117.5, 114.0, 113.4, 82.5; IR (KBr, cm^{-1}) ν: 2209, 1648, 1597, 1540, 1504, 1417, 1173, 978, 758, 728, 690; MS(EI) (m/z): 357.4 [(M+1)$^+$] (98%); HRESIMS calcd for $C_{22}H_{13}ClN_2O$ (M + H)$^+$ 357.0795; found 357.0736.

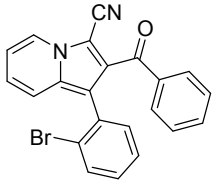
*3-Cyano-1-(4-chlorophenyl)-2-(4-bromobenzoyl)indolizine (**5b**):*



5b

Yellow solid; mp 178.5-180.5 °C (PE/EA); ^{1}H NMR (600 MHz, $CDCl_3$) δ (*ppm*) 7.98 (d, *J* = 7.2 Hz, 1H), 7.68 (d, *J* = 9.0 Hz, 1H), 7.55 (d, *J* = 8.4 Hz, 2H), 7.43 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 8.4 Hz, 2H), 7.26 (d, *J* = 8.4 Hz, 2H), 7.16 – 7.14 (m, 1H), 6.78 (t, *J* = 6.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ (*ppm*) 188.7, 137.0, 134.9, 134.8, 130.8, 130.7, 130.3, 128.5, 127.8, 125.9, 125.7, 125.4, 123.4, 122.9, 117.7, 113.9, 113.8, 82.5; IR (KBr,cm^{-1}) ν: 2213, 1651, 1584, 1539, 1478, 1422, 1259, 1012, 799, 746; MS(EI) (m/z): 435.3 [(M+1)$^+$] (100%); HRESIMS calcd for $C_{22}H_{12}BrClN_2O$ (M + H)$^+$ 434.9900; found 434.9908.

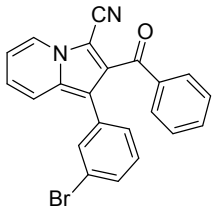
*3-Cyano-1-(2-bromophenyl)-2-benzoylindolizine (**5c**):*



5c

Yellow solid; mp 162.5-163.5 °C (PE/EA); ^{1}H NMR (600 MHz, $CDCl_3$) δ (*ppm*): 7.70 (d, *J* = 9.0 Hz, 1H), 7.68 (d, *J* = 8.4 Hz, 2H), 7.55 (d, *J* = 4.2 Hz, 1H), 7.54 (d, *J* = 4.8 Hz, 1H), 7.36 (t, *J* = 7.2 Hz, 1H), 7.24 – 7.17 (m, 4H), 7.16 – 7.13 (m, 2H), 6.77 (t, *J* = 7.2 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ (*ppm*): 189.6, 136.8, 136.6, 133.4, 132.1, 132.0, 130.3, 128.7, 128.5, 127.1, 127.0, 126.8, 125.7, 124.5, 123.8, 123.1, 117.5, 114.0, 113.3, 82.4; IR (KBr, cm^{-1}) ν: 3151, 3093, 2214, 1644, 1515, 1444, 1198, 737, 697; MS(EI) (m/z) 401.1 [(M+1)$^+$] (80%); HRESIMS calcd for $C_{22}H_{13}BrN_2O$ (M + H)$^+$ 401.0290; found 401.0278.

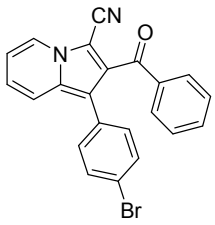
*3-Cyano-1-(3-bromophenyl)-2-benzoylindolizine (**5d**):*



5d

Yellow solid; mp 209.0-210.0 °C (PE/EA); ^{1}H NMR (600 MHz, $CDCl_3$) δ (*ppm*):7.99 (d, *J* = 6.6 Hz, 1H), 7.68 – 7.65 (m, 3H), 7.45 (s, 1H), 7.40-7.30 (m, 2H), 7.27 – 7.25 (m, 3H), 7.18 – 7.11 (m, 2H), 6.77 (t, *J* = 7.2 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ (*ppm*): 189.7, 137.0, 136.3 , 132.3, 131.4, 129.5, 129.2, 128.8, 128.3, 127.3, 126.7, 125.1, 123.2, 122.9, 121.9, 117.7, 113.8, 113.7, 82.9; IR (KBr, cm^{-1}) ν: 2924, 2212, 1658, 1593, 1509, 1468, 1448, 1304,1195.978, 712, 691; MS(EI) (m/z): 401.2 [(M+1)$^+$] (94%); HRESIMS calcd for $C_{22}H_{13}BrN_2O$ (M + H)$^+$ 401.0290; found 401.0234.

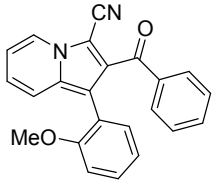
*3-Cyano-1-(4-bromophenyl)-2-benzoylindolizine (**5e**):*



5e

Yellow solid; mp 149.0-150.0 °C (PE/EA); ^{1}H NMR (600 MHz, $CDCl_3$) δ (*ppm*): 7.99 (d, *J* = 7.2 Hz, 1H), 7.68 (d, *J* = 7.2 Hz, 3H), 7.45 (d, *J* = 8.4 Hz, 2H), 7.43 (d, *J* = 7.2 Hz, 1H), 7.29 (t, *J* = 7.2 Hz, 2H), 7.20 (d, *J* = 8.4 Hz, 2H), 7.14 – 7.12 (m, 1H), 6.77 (t, *J* = 6.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ (*ppm*): 189.8, 136.9, 136.2, 132.4, 131.3, 131.1, 128.9, 127.3, 126.4, 126.1, 125.6, 123.2, 122.8, 117.7, 113.9, 113.6, 82.7; IR (KBr, cm^{-1}) ν: 2209, 1642, 1596, 1514, 1449, 1424, 1264, 1070, 1011, 979, 938, 734, 695; MS(EI) (m/z): 401.4 [(M+1)$^+$] (98%); HRESIMS calcd for $C_{22}H_{13}BrN_2O$ (M + H)$^+$ 401.0290; found 401.0305.

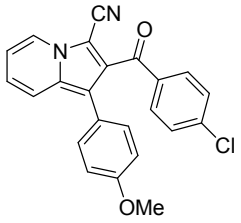
*3-Cyano-1-(2-methoxyphenyl)-2-benzoylindolizine (**5f**):*



5f

Yellow solid, mp 156.0-156.8 °C (PE/EA); ^{1}H-NMR ($CDCl_3$, 600 MHz) δ (*ppm*): 7.70-7.69 (m, 2H), 7.64 (d, *J* = 7.2 Hz, 2H), 7.32 (t, *J* = 7.2 Hz, 1H), 7.24 (dt, *J* = 7.2, 1.8 Hz, 1H), 7.13-7.09 (m, 2H), 6.81 (t, *J* = 7.8 Hz, 1H), 6.79 (d, *J* = 8.4 Hz, 1H), 6.71 (t, *J* = 6.0 Hz, 1H), 3.63 (s, 3H); ^{13}C-NMR ($CDCl_3$, 150 MHz) δ (*ppm*): 190.0, 156.3, 137.1, 136.5, 131.7, 130.3, 128.6, 126.8, 124.1, 122.7, 119.9, 117.3, 116.1, 114.5, 112.7, 109.9, 82.3, 54.3, 28.7; IR (KBr, cm^{-1}) ν: 2210, 1647, 1560, 1420, 1265, 1016, 988, 957, 780; MS(EI) (m/z): 353.3 [(M+1)$^+$] (100%); HRESIMS calcd for $C_{23}H_{16}N_2O_2$ (M+H)$^+$ 353.1290; found 353.1296.

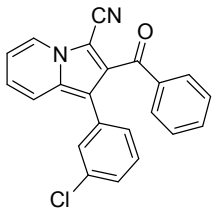
*3-Cyano-1-(4-methoxyphenyl)-2-(4-chlorobenzoyl)indolizine (**5g**):*



5g

Yellow solid, mp 173.3-173.9 °C (PE/EA); ^{1}H-NMR (DMSO-d_6, 600 MHz) δ (*ppm*): 8.22 (d, *J* = 7.2 Hz, 1H), 7.80 (d, *J* = 9.0 Hz, 1H), 7.65 (d, *J* = 8.4 Hz, 2H), 7.38-7.36 (m, 3H), 7.32 (d, *J* = 9.0 Hz, 2H), 7.02 (t, *J* = 6.6 Hz, 1H), 6.93 (d, *J* = 8.4 Hz, 2H), 3.74 (s, 3H); ^{13}C-NMR (DMSO-d_6, 150 MHz) δ (*ppm*): 189.8, 159.8, 137.8, 137.5, 132.2, 131.3, 128.3, 125.5, 125.3, 124.9, 119.7, 117.6, 115.2, 114.9, 114.3, 81.5, 55.3; IR (KBr, cm^{-1}) ν: 2208, 1642, 1550, 1420, 1255, 1106, 988, 950, 880; MS(EI) (m/z): 371.3 [(M+1)$^+$] (100%); HRESIMS calcd for $C_{23}H_{15}ClN_2O$ (M+H)$^+$ 371.0951; found 371.0926.

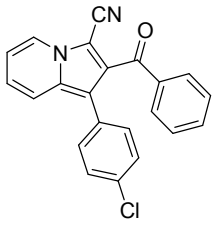
*3-Cyano-1-(3-chlorophenyl)-2-benzoylindolizine (**5h**):*



5h

Yellow solid, mp 192.5-194.0 °C (PE/EA); ^{1}H NMR (600 MHz, $CDCl_3$) δ (*ppm*): 7.99 (d, *J* = 7.2 Hz, 1H), 7.69 – 7.66 (m, 3H), 7.41 (t, *J* = 7.2 Hz, 1H), 7.31 (s, 1H), 7.28 – 7.23 (m, 4H), 7.19 (d, *J* = 8.4 Hz, 1H), 7.14 – 7.12 (m, 1H), 6.77 (t, *J* = 7.2. Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ (*ppm*): 189.7, 137.0, 136.3, 134.0, 132.3, 129.5, 129.3, 129.0, 128.8, 128.5, 127.9, 127.3, 126.7, 125.2, 123.2, 122.9, 117.7, 113.8, 113.7, 82.9; IR (KBr, cm^{-1}) ν: 2207,1641, 1595, 1511, 1425, 1262, 1087, 1013, 977, 809, 731, 691; MS(EI) (m/z): 357.5 [$(M+1)^+$] (100%); HRESIMS calcd for $C_{22}H_{13}ClN_2O$ $(M + H)^+$ 357.0795; found 357.0788.

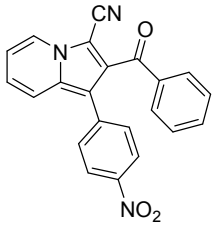
*3-Cyano-1-(4-chlorophenyl)-2-benzoylindolizine (**5i**):*



5i

Yellow solid, mp 175.0-176.0 °C (PE/EA); ^{1}H NMR (600 MHz, $CDCl_3$) δ (*ppm*): 7.97 (d, *J* = 7.2 Hz, 1H), 7.7 (d, *J* = 7.8 Hz, 3H), 7.42 (t, *J* = 7.8 Hz, 1H), 7.29 – 7.25 (m, 6H), 7.13 – 7.11 (m, 1H), 6.76 (t, *J* = 6.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ (*ppm*): 189.8, 136.9, 136.3, 134.6, 132.3, 130.9, 128.9, 128.4, 127.3, 126.6, 125.8,125.5, 123.1, 122.9, 117.7, 113.9, 113.6, 82.8; IR (KBr, cm^{-1}) ν: 2208, 1641, 1595, 1490, 1264, 1089, 1012, 977, 749, 692; MS(EI) (m/z): 357.4 [$(M+1)^+$] (100%); HRESIMS calcd for $C_{22}H_{13}ClN_2O$ $(M + H)^+$ 357.0795; found 357.0792.

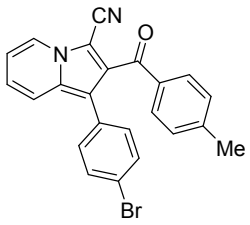
*3-Cyano-1-(4-nitrophenyl)-2-benzoylindolizine (**5j**):*



5j

Yellow solid, mp 178.5-180.5 °C (PE/EA); ^{1}H NMR (600 MHz, $CDCl_3$) δ (*ppm*) 8.18 (d, *J* = 8.4 Hz, 2H), 8.04 (d, *J* = 7.2 Hz, 1H), 7.72 (d, *J* = 9.0 Hz, 1H), 7.70 (d, *J* = 7.2 Hz, 2H), 7.55 (d, *J* = 9.0 Hz, 2H), 7.46 (t, *J* = 7.2 Hz, 1H), 7.31 (t, *J* = 7.8 Hz, 2H), 7.21 – 7.19 (m, 1H), 6.85 (t, *J* = 6.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ (*ppm*) 189.5, 146.8, 137.3, 136.0, 133.8, 132.8, 130.3, 128.9, 127.5, 124.0, 123.7, 123.3, 122.6, 117.9, 114.3, 113.5, 83.6; IR (KBr,cm^{-1}) ν: 2208, 1641, 1515, 1345, 1198, 1261, 1198, 1176, 1145, 1106, 1013, 874, 755; MS(EI) (m/z): 368.4 [$(M+1)^+$] (100%); HRESIMS calcd for $C_{22}H_{13}N_3O_3$ $(M + H)^+$ 368.1035; found 368.1052.

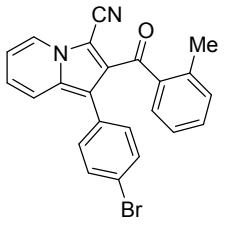
*3- Cyano-1-(4-bromophenyl)-2-(4-methylbenzoyl)indolizine (**5k**):*



5k

Yellow solid, mp 178.5-180.5 °C (PE/EA); ^{1}H NMR (600 MHz, $CDCl_3$) δ (*ppm*) 7.89 (d, *J* = 9.0 Hz, 1H), 7.61 (d, *J* = 7.8 Hz, 1H), 7.47 (d, *J* = 8.4 Hz, 1H), 7.32 (d, *J* = 7.8 Hz, 2H), 7.21 (dd, *J* = 8.4, 5.4 Hz, 2H), 7.01 (t, *J* = 6.6 Hz, 1H), 6.90 (d, *J* = 7.8 Hz, 2H), 6.87 (d, *J* = 8.4 Hz, 2H), 2.16 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ (*ppm*) 190.0, 136.8, 135.8, 135.3, 133.6, 131.4, 131.0, 129.2, 128.1, 128.0, 126.9, 126.1, 123.0, 122.8, 118.7, 117.7, 114.7, 113.5, 20.6; IR (KBr, cm^{-1}) ν: 2215, 1605, 1421, 1230, 1177, 1071, 749; MS(EI) (m/z): 415.0 [(M+1)$^+$] (90%); HRESIMS calcd for $C_{23}H_{15}BrN_2O$ (M+H)$^+$ 415.0446; found 415.0478.

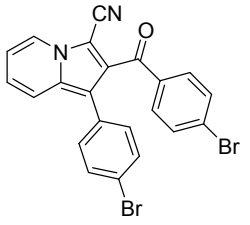
*3-Cyano-1-(4-bromophenyl)-2-(2-methylbenzoyl)indolizine (**5l**):*



5l

Yellow solid, mp 206.0-207.0 °C (PE/EA); ^{1}H NMR (600 MHz, $CDCl_3$) δ (*ppm*): 7.84 (d, *J* = 7.2 Hz, 1H), 7.66 (d, *J* = 9.0 Hz, 1H), 7.41 (d, *J* = 8.4 Hz, 2H), 7.22 – 7.19 (m, 2H), 7.11 – 7.09 (m, 3H), 7.07 (d, *J* = 7.8 Hz, 1H), 6.98 (t, *J* = 7.2 Hz, 1H), 6.73 (t, *J* = 7.2 Hz, 1H), 2.33 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ (*ppm*): 191.6, 137.1, 136.6, 131.2, 131.0, 130.3, 130.1, 128.8, 126.4, 126.1, 124.3, 123.1, 122.9, 122.8, 117.8, 113.7, 82.9, 19.2; IR (KBr, cm^{-1}) ν: 2209, 1647, 1535, 1511, 1423, 1252, 1095, 1068, 1034, 816, 748; MS(EI) (m/z): 415.5 [(M+1)$^+$] (100%); HRESIMS calcd for $C_{23}H_{15}BrN_2O$ (M+H)$^+$ 415.0446; found 415.0448.

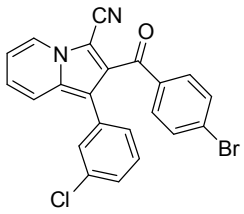
*3-Cyano-1-(4-bromophenyl)-2-(4-bromobenzoyl)indolizine (**5m**):*



5m

Yellow solid, mp 238.0-239.0 °C (PE/EA); ^{1}H NMR (600 MHz, $CDCl_3$) δ (*ppm*): 7.98 (d, *J* = 7.2 Hz, 1H), 7.69 (d, *J* = 9.0 Hz, 1H), 7.56 (d, *J* = 8.4 Hz, 2H), 7.49 (d, *J* = 8.4 Hz, 2H), 7.44 (d, *J* = 8.4 Hz, 2H), 7.20 (d, *J* = 8.4 Hz, 2H), 7.16 – 7.14 (m, 1H), 6.78 (t, *J* = 7.2 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ (*ppm*): 188.6, 137.0, 134.9, 131.5, 131.0, 130.7, 130.4, 127.8, 125.9, 125.7, 123.3, 123.1, 122.9, 117.7, 113.8, 82.6; IR (KBr, cm^{-1}) ν: 2214, 1647, 1582, 1417, 1260, 1174, 1010, 749; MS(EI) (m/z): 478.8 [(M+1)$^+$] (100%); HRESIMS calcd for $C_{22}H_{12}Br_2N_2O$ (M+H)$^+$ 478.9395; found 478.9372.

*3-Cyano-1-(3-chlorophenyl)-2-(4-bromobenzoyl)indolizine (**5n**):*



5n

Yellow solid, mp 181.0-182.0 °C (PE/EA); ^{1}H NMR (600 MHz, $CDCl_3$) δ (*ppm*): 8.00 (d, *J* = 7.2 Hz, 1H), 7.69 (d, *J* = 9.0 Hz, 1H), 7.54 (d, *J* = 8.4 Hz, 2H), 7.42 (d, *J* = 8.4 Hz, 2H), 7.31 – 7.26 (m, 3H), 7.19 (d, *J* = 6.0 Hz, 1H), 7.17 – 7.14 (m, 1H), 6.80 (t, *J* = 6.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ (*ppm*): 188.6, 137.0, 135.0, 134.1, 130.7, 130.2, 129.4, 128.8, 128.7, 127.8, 127.6, 126.1, 125.3, 123.4, 122.9, 117.7, 113.9, 113.8, 82.7; IR (KBr, cm^{-1}) ν: 2213, 1644, 1565, 1418, 1341, 1256, 1173, 1071, 1010, 980, 957, 748; MS(EI) (m/z): 435.2 [$(M+1)^+$] (90%); HRESIMS calcd for $C_{22}H_{12}BrClN_2O$ $(M+H)^+$ 434.9900; found 434.9926.

Crystal structure data

Figure 1. Molecular structure of 1-cyanoindolizine **2b**

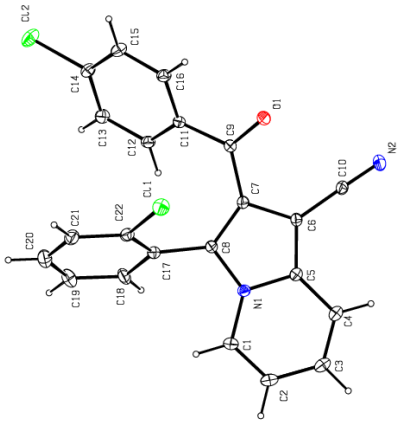


Table 1. Crystal data and structure refinement for 1-cyanoindolizine **2b**.

Identification code	1-cyanoindolizine **2b**
Empirical formula	$C_{22}H_{12}Cl_2N_2O$
Formula weight	391.24
Temperature	296(2) K
Wavelength	0.71073 A
Crystal system, space group	Triclinic, P-1

Unit cell dimensions	a = 7.7221(12) A	alpha = 80.021(2) deg.
	b = 9.0481(13) A	beta = 85.860(2) deg.
	c = 13.843(2) A	gamma = 73.874(2) deg.
Volume	914.8(2) A^3	
Z, Calculated density	2, 1.420 Mg/m^3	
Absorption coefficient	0.369 mm^-1	
F(000)	396	
Crystal size	0.35 x 0.33 x 0.30 mm	
Theta range for data collection	1.49 to 27.47 deg.	
Limiting indices	-9<=h<=9, -11<=k<=11, -17<=l<=17	
Reflections collected / unique	7959 / 4170 [R(int) = 0.0217]	
Completeness to theta = 27.47	96.1 %	
Absorption correction	None	
Refinement method	Full-matrix least-squares on F^2	
Data/restraints/parameters	4007/0/244	
Goodness-of-fit on F^2	1.041	
Final R indices [I>2sigma(I)]	R1 = 0.0761, wR2 = 0.2093	
R indices (all data)	R1 = 0.0927, wR2 = 0.2228	
Largest diff. peak and hole	1.441 and -0.496 e.A^-3	

Figure 2. Molecular structure of 1-cyanoindolizine **2h**

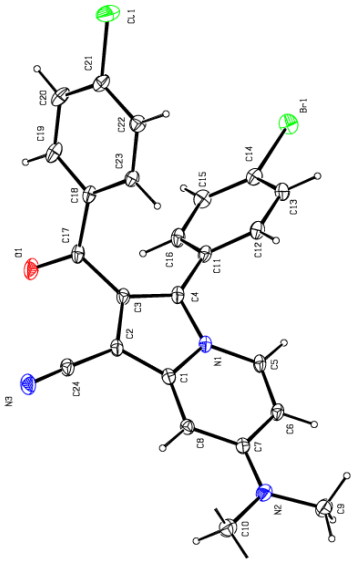


Table 2. Crystal data and structure refinement for 1-cyanoindolizine **2h**.

Identification code	1-cyanoindolizine **2h**
Empirical formula	$C_{24}H_{17}BrClN_3O$

Formula weight	478.76
Temperature	296(2) K
Wavelength	0.71073 A
Crystal system, space group	Orthorhombic, P2(1)2(1)2(1)
Unit cell dimensions	a = 10.2750(12) A alpha = 90 deg.
	b = 11.4634(14) A beta = 90 deg.
	c = 18.344(2) A gamma = 90 deg.
Volume	2160.7(5) A^3
Z, Calculated density	4, 1.472 Mg/m^3
Absorption coefficient	2.047 mm^-1
F(000)	968
Crystal size	0.35 x 0.33 x 0.31 mm
Theta range for data collection	2.09 to 24.99 deg.
Limiting indices	-11<=h<=12, -13<=k<=13, -21<=l<=19
Reflections collected / unique	18822/3799 [R(int) = 0.0443]
Completeness to theta = 24.99	100.0 %
Absorption correction	None
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3795 / 0 / 273
Goodness-of-fit on F^2	1.076
Final R indices [I>2sigma(I)]	R1 = 0.0712, wR2 = 0.1905
R indices (all data)	R1 = 0.0943, wR2 = 0.2067
Absolute structure parameter	0.99(2)
Largest diff. peak and hole	0.640 and -0.221 e.A^-3

Figure 3. Molecular structure of cyanoindolizine **4c**

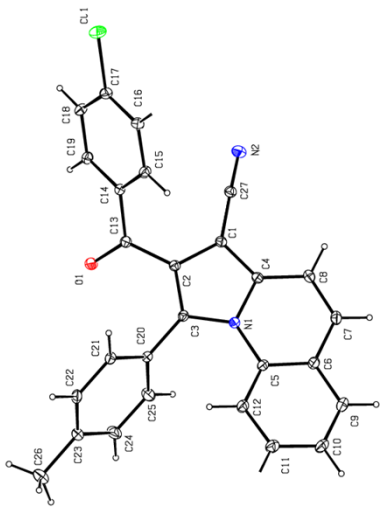


Table 3. Crystal data and structure refinement for cyanoindolizine **4c**.

Identification code	1-cyanoindolizine **4c**	
Empirical formula	$C_{27}H_{17}ClN_2O$	
Formula weight	420.88	
Temperature	296(2) K	
Wavelength	0.71073 A	
Crystal system, space group	Triclinic, P-1	
Unit cell dimensions	a = 10.4826(16) A	alpha = 71.680(5) deg.
	b = 10.6458(17) A	beta = 73.572(4) deg.
	c = 10.9600(15) A	gamma = 67.431(5) deg.
Volume	1053.7(3) A^3	
Z, Calculated density	2, 1.327 Mg/m^3	
Absorption coefficient	0.203 mm^-1	
F(000)	436	
Crystal size	0.35 x 0.33 x 0.30 mm	
Theta range for data collection	1.99 to 27.53 deg.	
Limiting indices	-13<=h<=13, -13<=k<=13, -14<=l<=14	
Reflections collected / unique	16987 / 4861 [R(int) = 0.0593]	
Completeness to theta = 27.53	99.0 %	
Absorption correction	None	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4815 / 0 / 282	
Goodness-of-fit on F^2	1.010	
Final R indices [I>2sigma(I)]	R1 = 0.0546, wR2 = 0.1073	
R indices (all data)	R1 = 0.1228, wR2 = 0.1281	
Extinction coefficient	0.0088(19)	
Largest diff. peak and hole	0.191 and -0.303 e.A^-3	

Figure 4. Molecular structure of cyanoindolizine **5a**

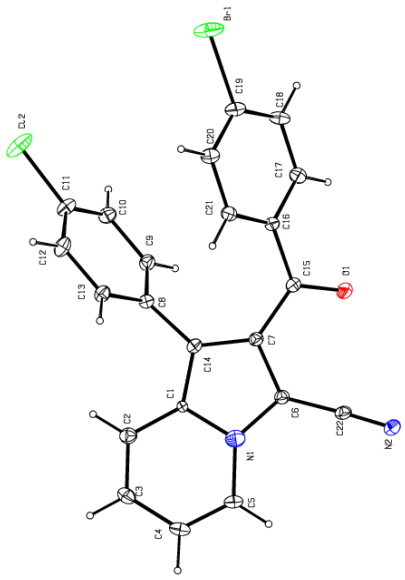


Table 4. Crystal data and structure refinement for cyanoindolizine **5a**.

Identification code	cyanoindolizine **5a**	
Empirical formula	$C_{22}H_{12}BrClN_2O$	
Formula weight	435.69	
Temperature	293(2) K	
Wavelength	0.71073 A	
Crystal system, space group	Triclinic, P-1	
Unit cell dimensions	a = 7.7273(16) A	alpha = 76.526(6) deg.
	b = 8.9408(18) A	beta = 80.859(6) deg.
	c = 14.824(3) A	gamma = 70.826(6) deg.
Volume	936.9(3) A^3	
Z, Calculated density	2, 1.544 Mg/m^3	
Absorption coefficient	2.350 mm^-1	
F(000)	484	
Crystal size	0.35 x 0.33 x 0.30 mm	
Theta range for data collection	2.46 to 25.00 deg.	
Limiting indices	-9<=h<=9, -10<=k<=10, -17<=l<=16	
Reflections collected / unique	8463 / 3220 [R(int) = 0.0370]	
Completeness to theta = 25.00	97.3 %	
Absorption correction	None	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3220 / 0 / 244	
Goodness-of-fit on F^2	1.042	
Final R indices [I>2sigma(I)]	R1 = 0.0618, wR2 = 0.1427	
R indices (all data)	R1 = 0.1006, wR2 = 0.1671	
Largest diff. peak and hole	0.564 and -0.574 e.A^-3	

Figure 5. Molecular structure of cyanoindolizine **5b**

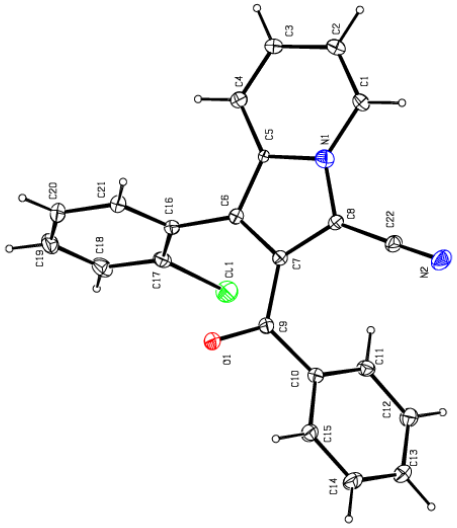


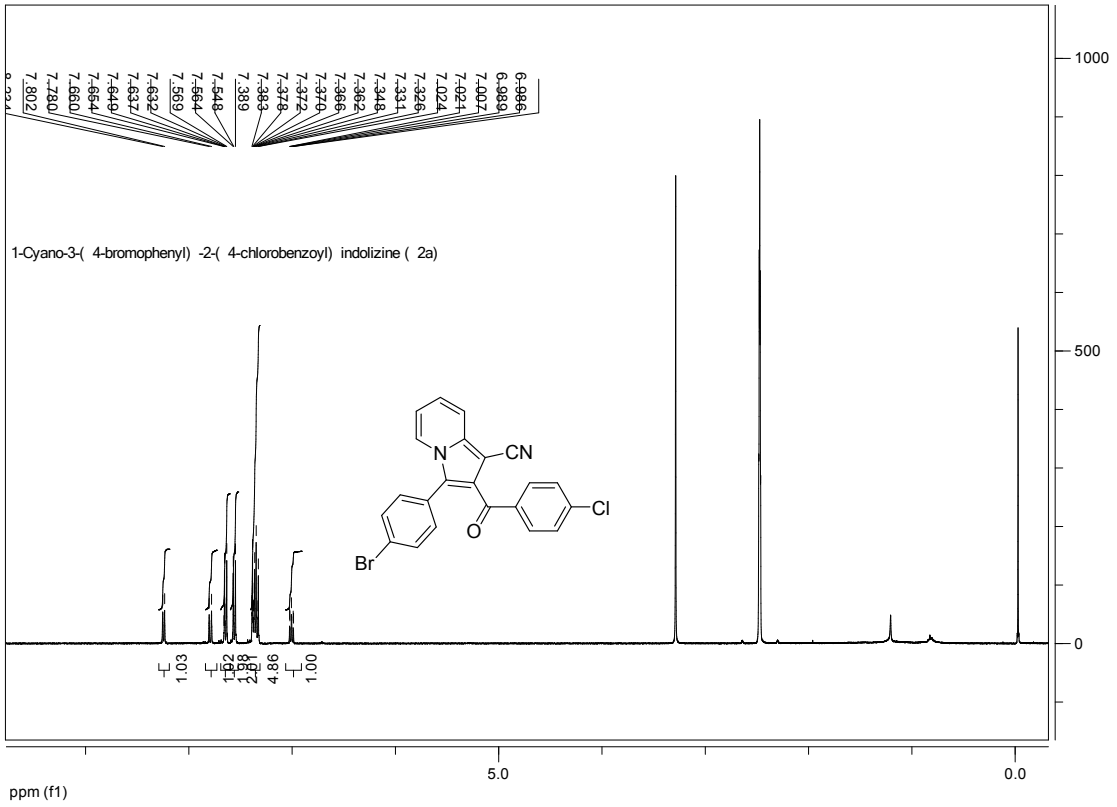
Table 5. Crystal data and structure refinement for cyanoindolizine **5b**.

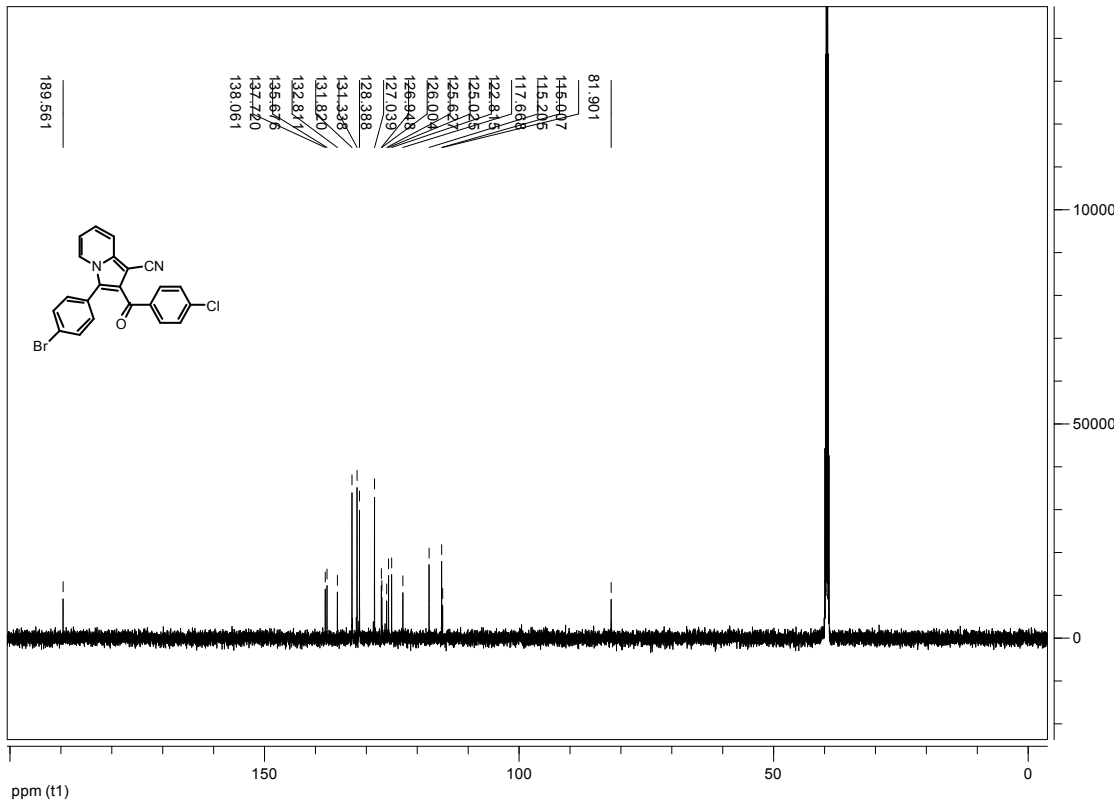
Identification code	3-cyanoindolizine **5b**	
Empirical formula	$C_{22}H_{13}ClN_2O$	
Formula weight	356.79	
Temperature	296(2) K	
Wavelength	0.71073 A	
Crystal system, space group	Monoclinic, C2/c	
Unit cell dimensions	a = 23.071(3) A	alpha = 90 deg.
	b = 10.7768(13) A	beta = 102.951(4) deg.
	c = 14.3886(19) A	gamma = 90 deg.
Volume	3486.5(7) A^3	
Z, Calculated density	8, 1.360 Mg/m^3	
Absorption coefficient	0.232 mm^-1	
F(000)	1472	
Crystal size	0.35 x 0.33 x 0.30 mm	
Theta range for data collection	2.10 to 27.54 deg.	
Limiting indices	-29<=h<=29, -14<=k<=13, -18<=l<=18	
Reflections collected / unique	23001 / 4013 [R(int) = 0.0510]	
Completeness to theta = 27.54	99.7 %	
Absorption correction	None	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4022/0/235	
Goodness-of-fit on F^2	1.033	

Final R indices [I>2sigma(I)]	R1 = 0.0698, wR2 = 0.1838
R indices (all data)	R1 = 0.1400, wR2 = 0.2268
Largest diff. peak and hole	0.553 and -0.476 e.A^-3

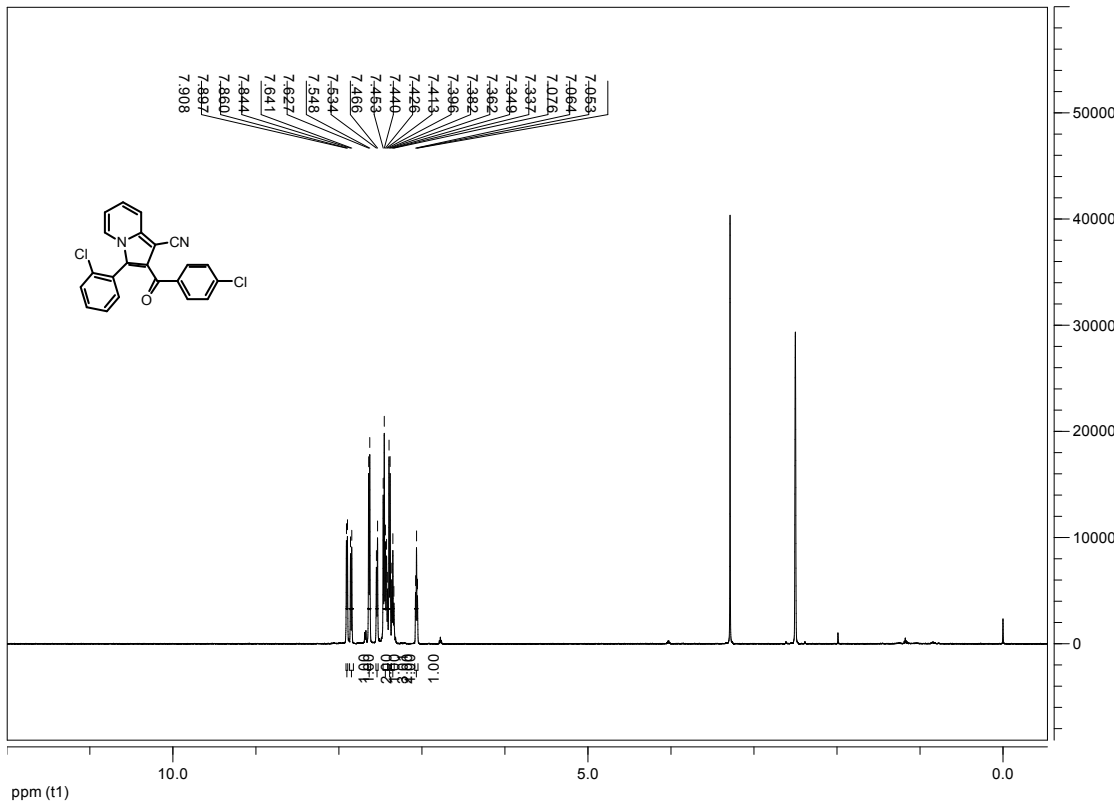
Copies of NMR Spectroscopies

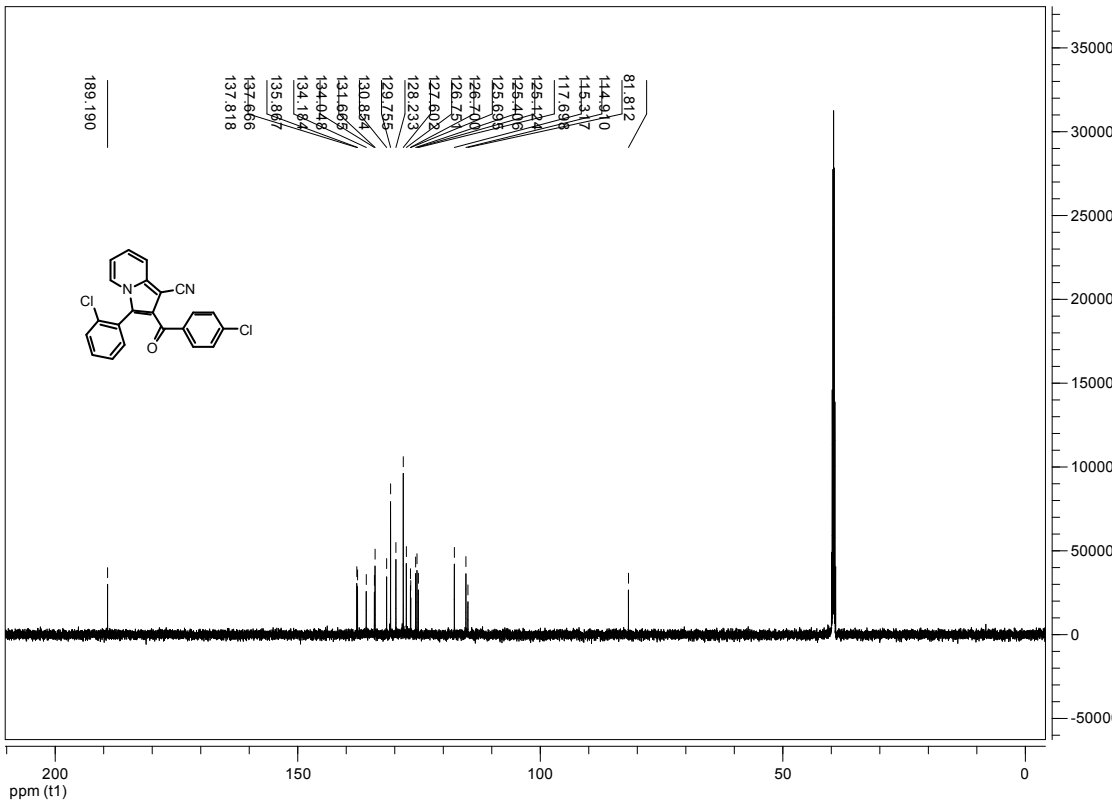
*1-Cyano-3-(4-bromophenyl)-2-(4-chlorobenzoyl)indolizine (**2a**):*



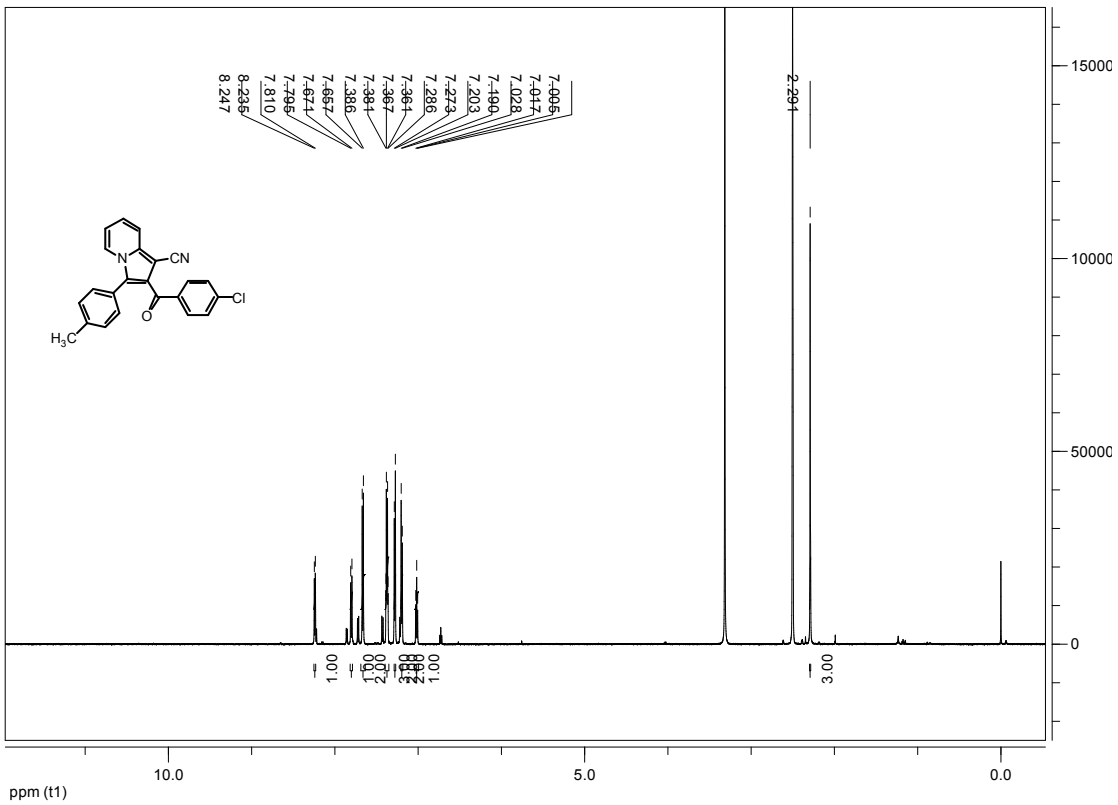


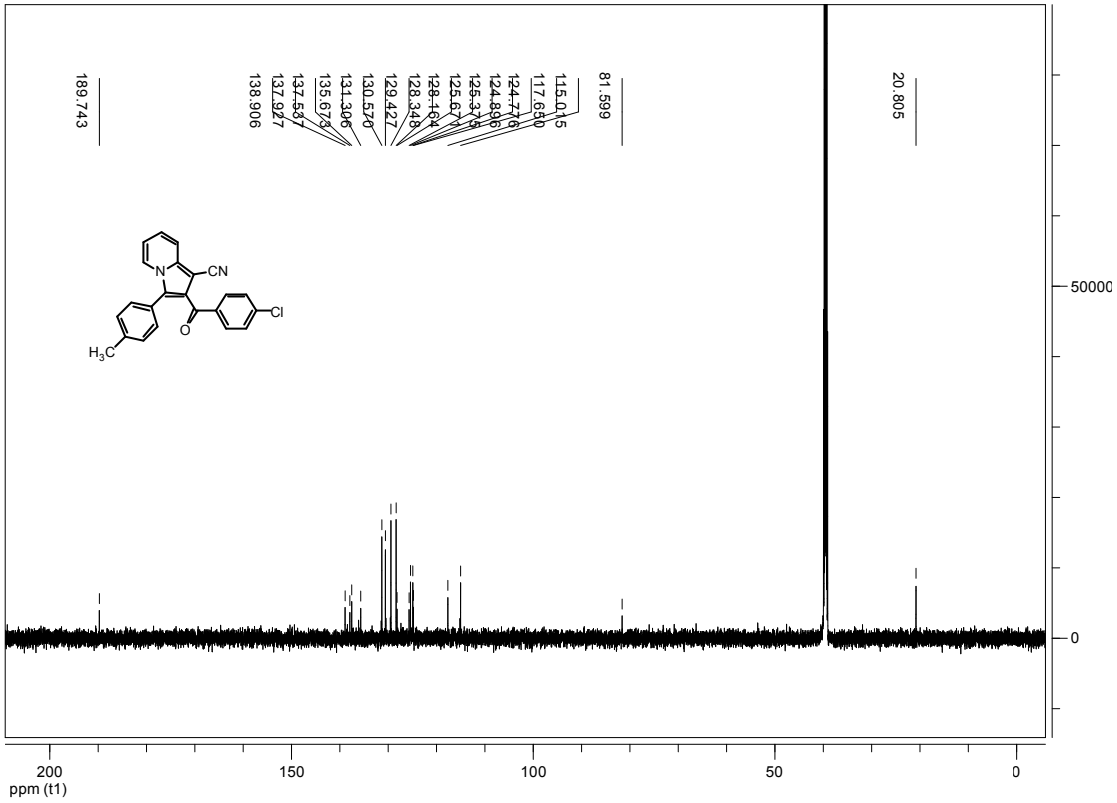
*1-Cyano-3-(2-chlorophenyl)-2-(4-chlorobenzoyl)indolizine (**2b**):*



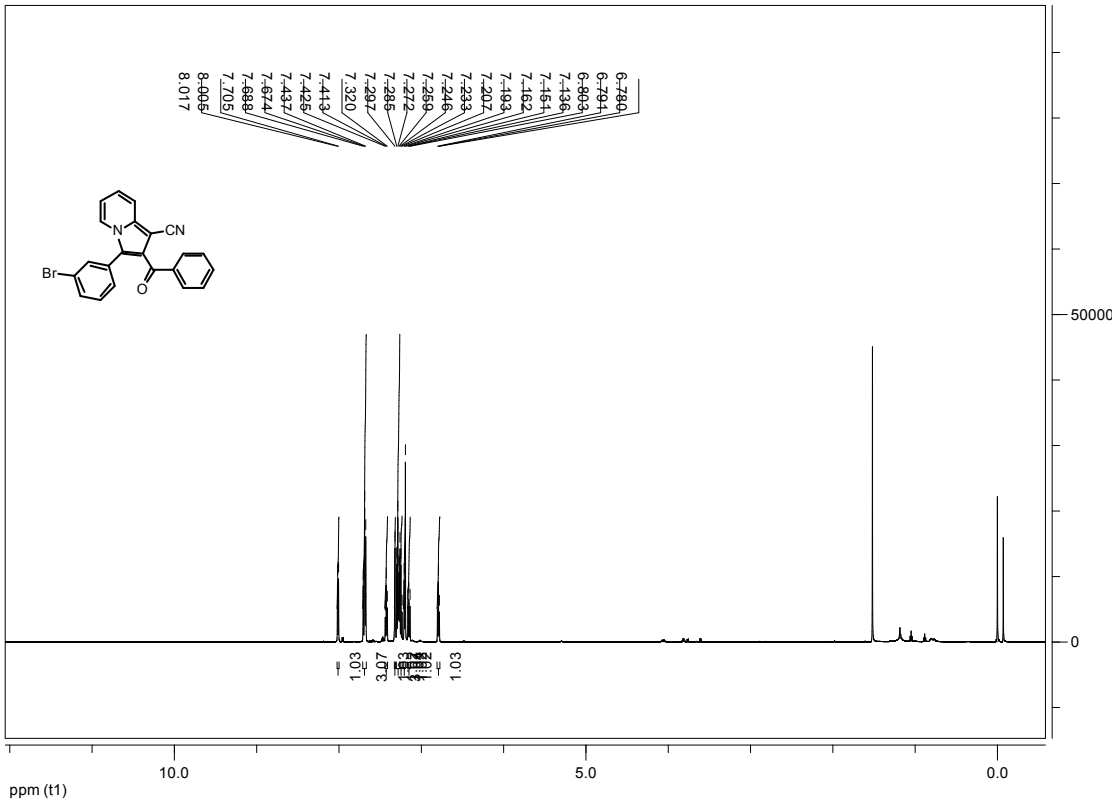


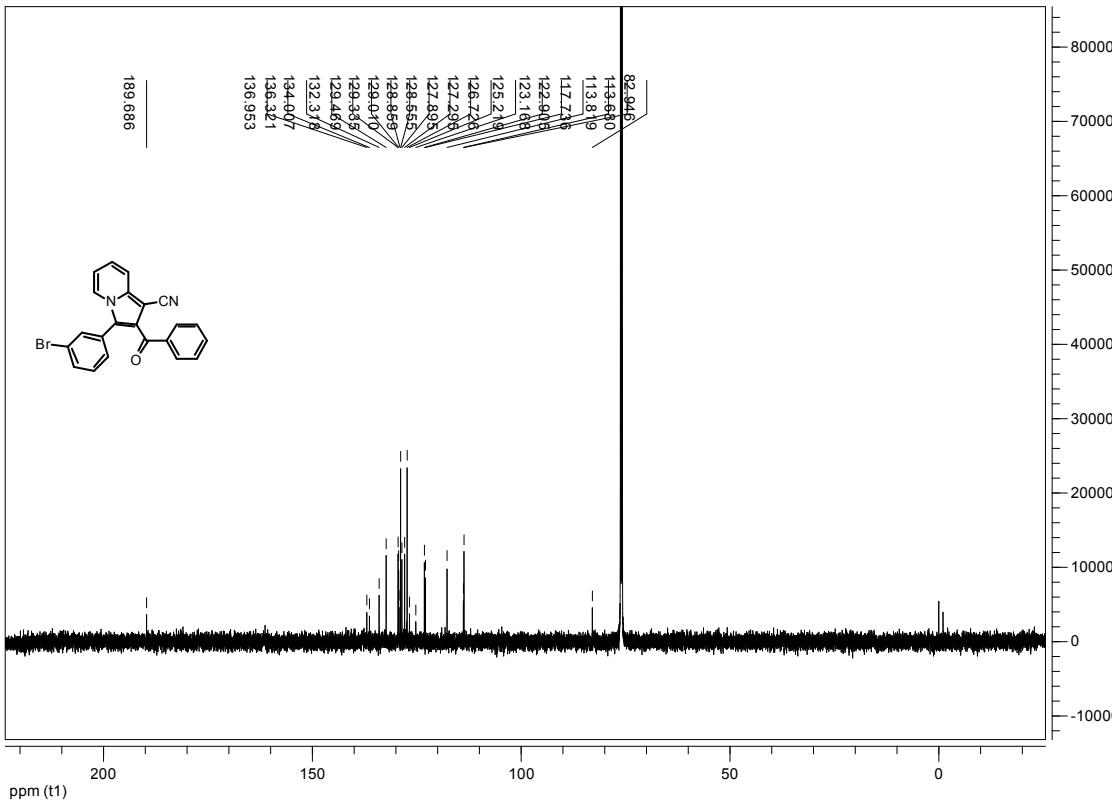
*1-Cyano-3-p-tolyl-2-(4-chlorobenzoyl)indolizine (**2c**):*



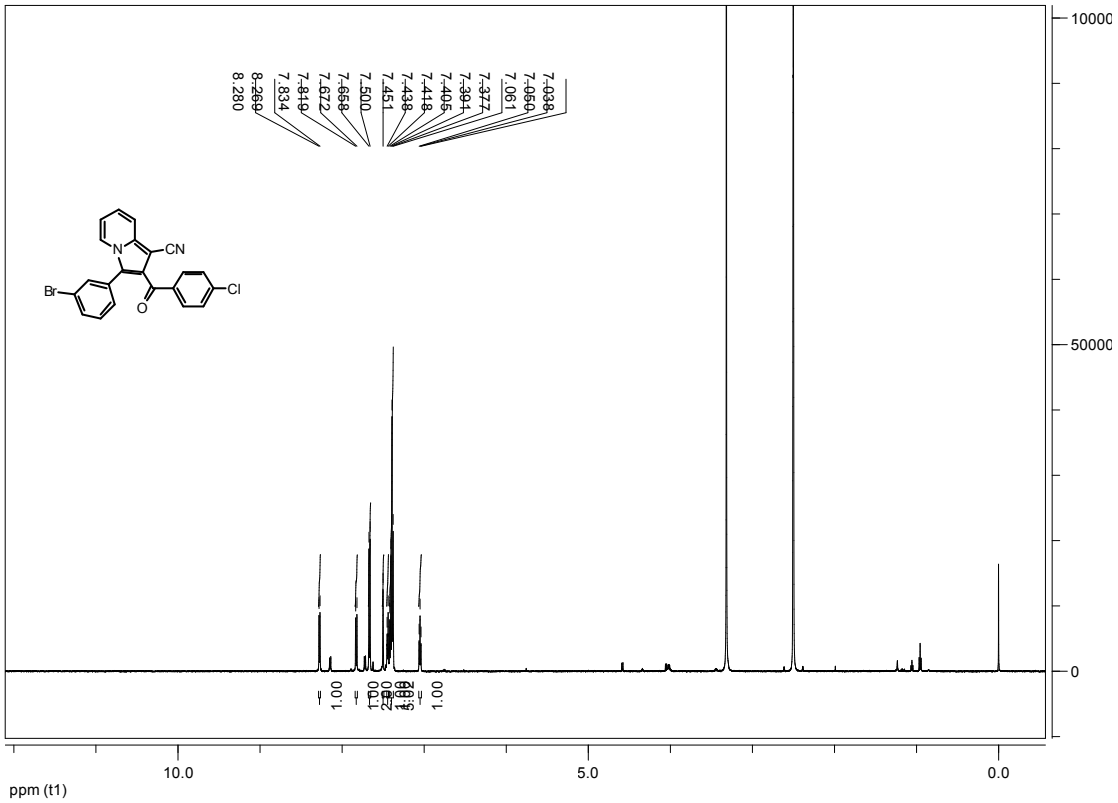


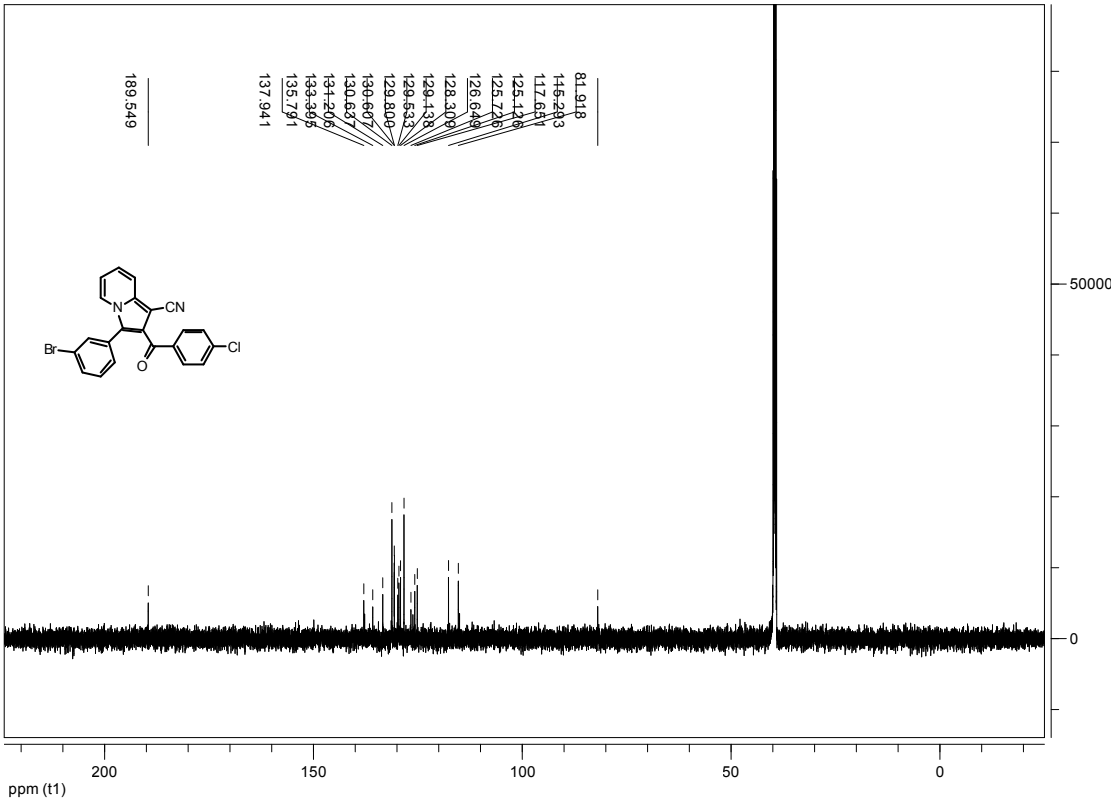
*1-Cyano-2-benzoyl-3-(3-bromophenyl)indolizine (**2d**):*



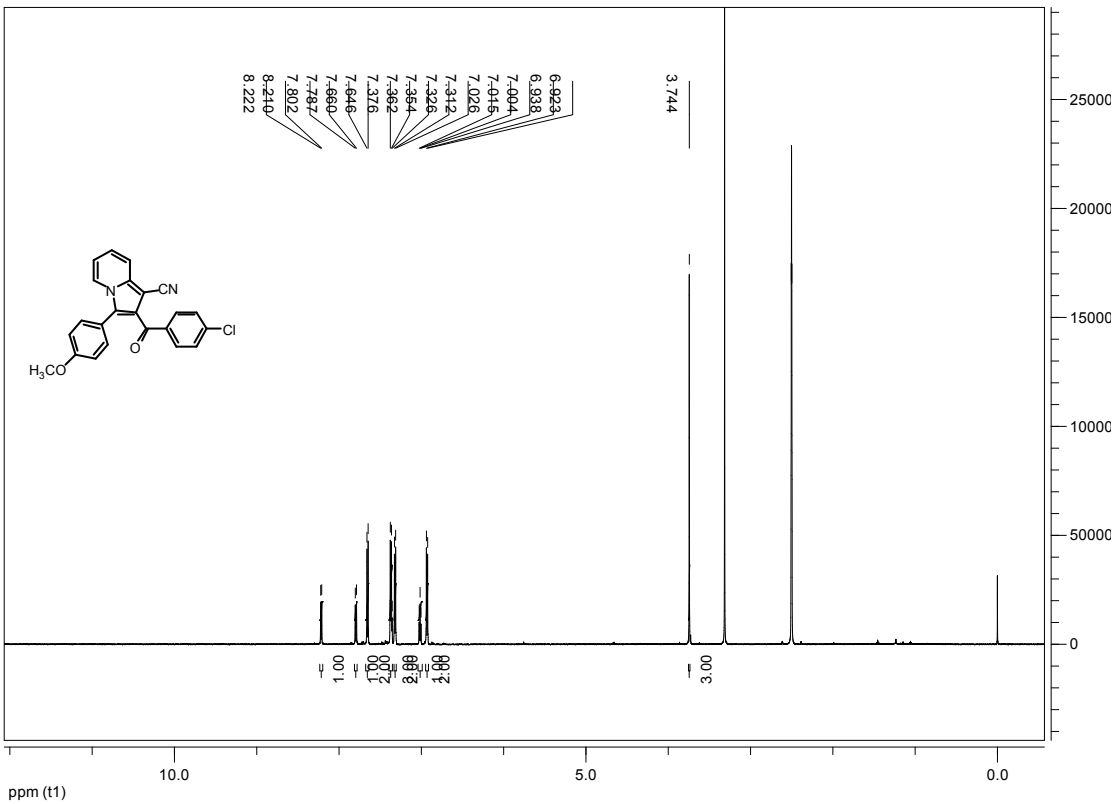


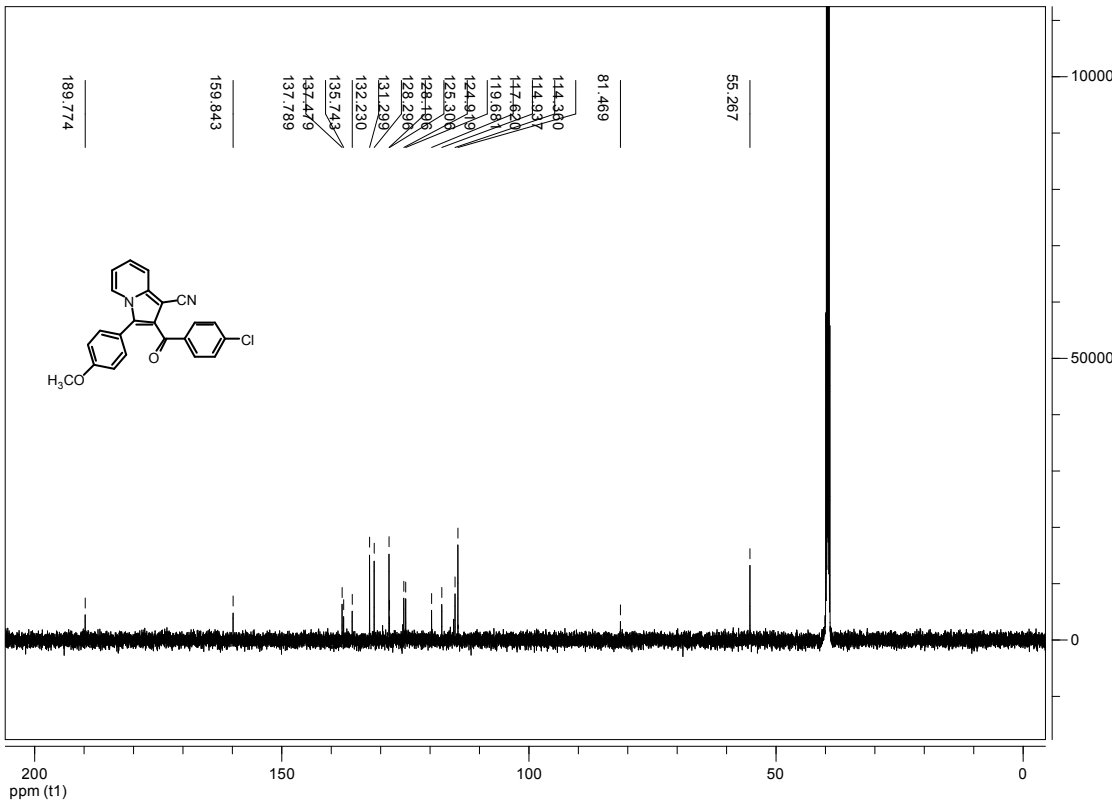
*1-Cyano-3-(3-bromophenyl)-2-(4-chlorobenzoyl)indolizine (**2e**):*



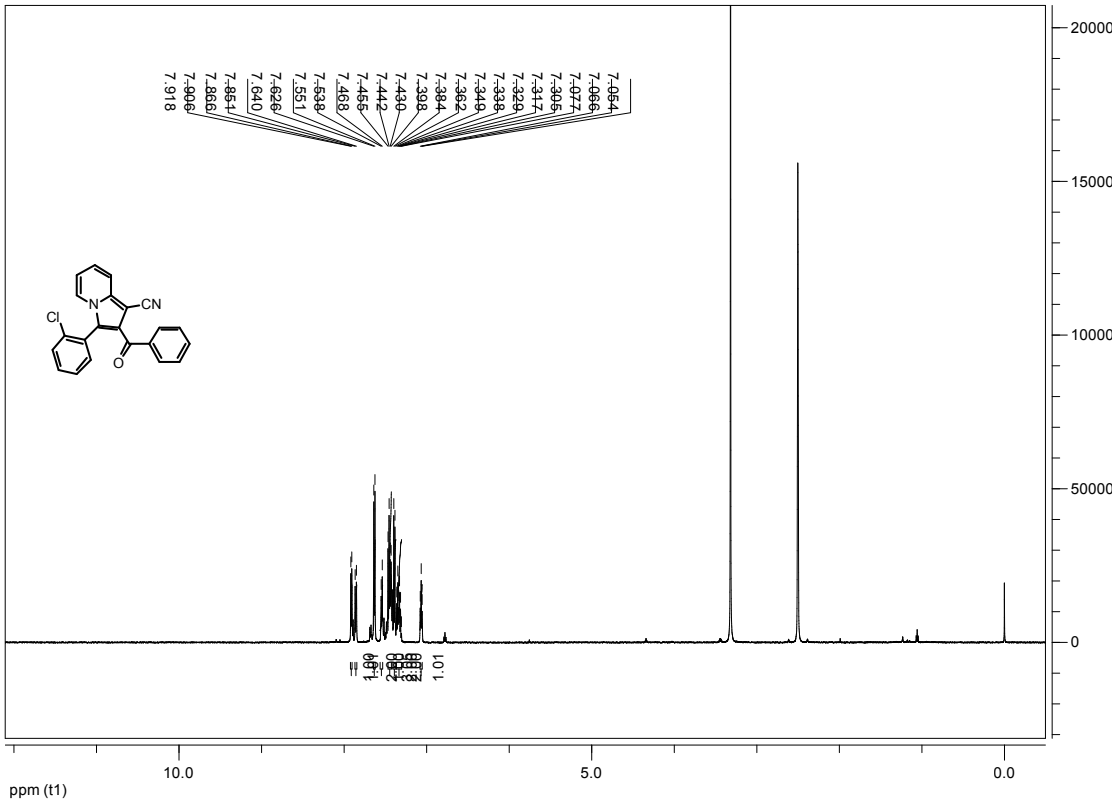


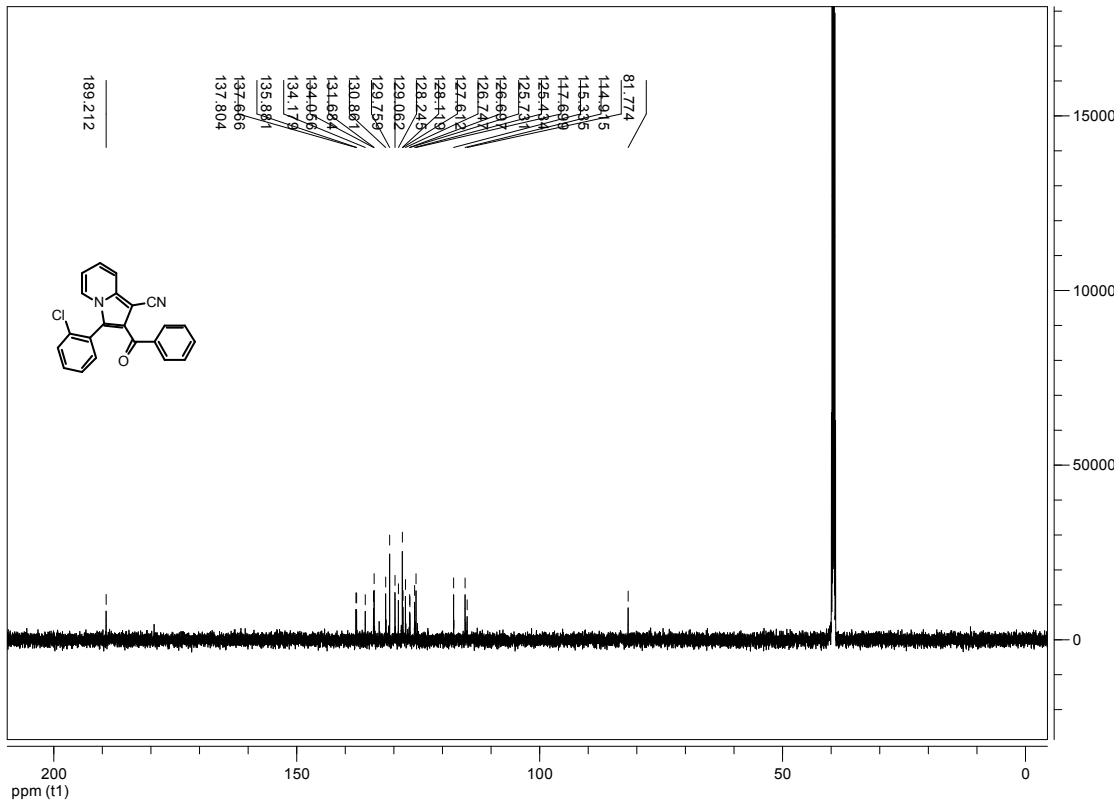
*1-Cyano-2-(4-chlorobenzoyl)-3-(4-methoxyphenyl)indolizine (**2f**):*



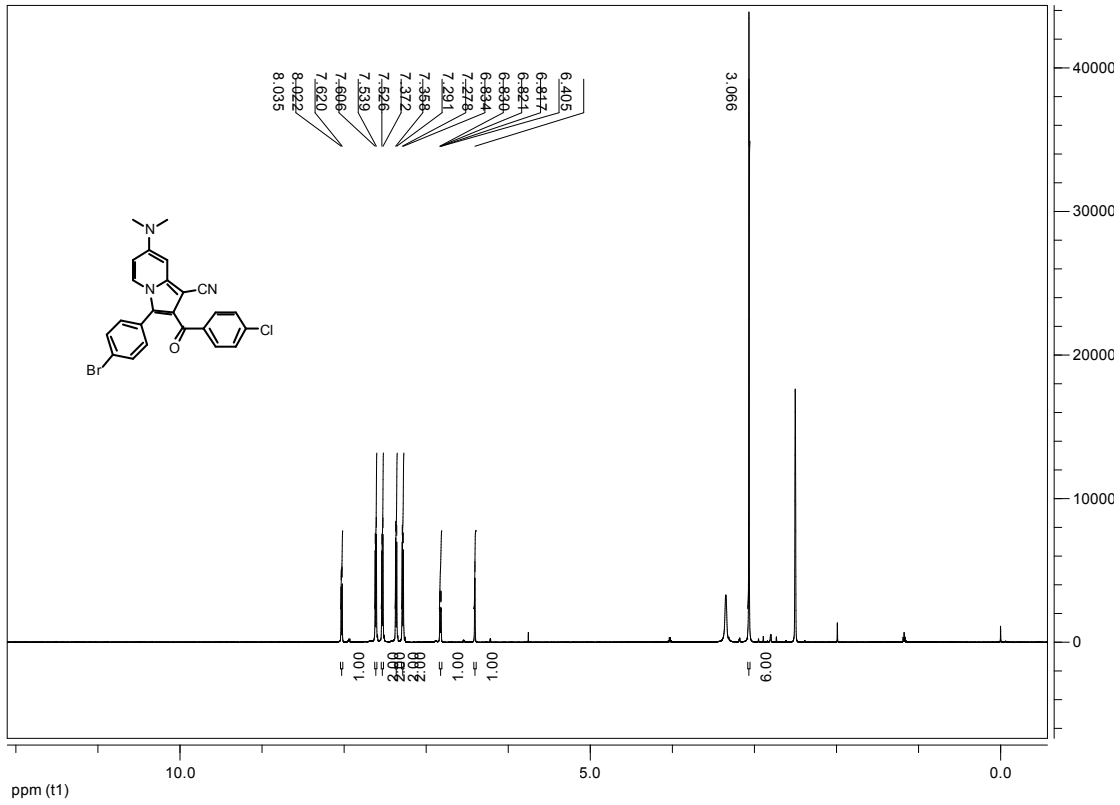


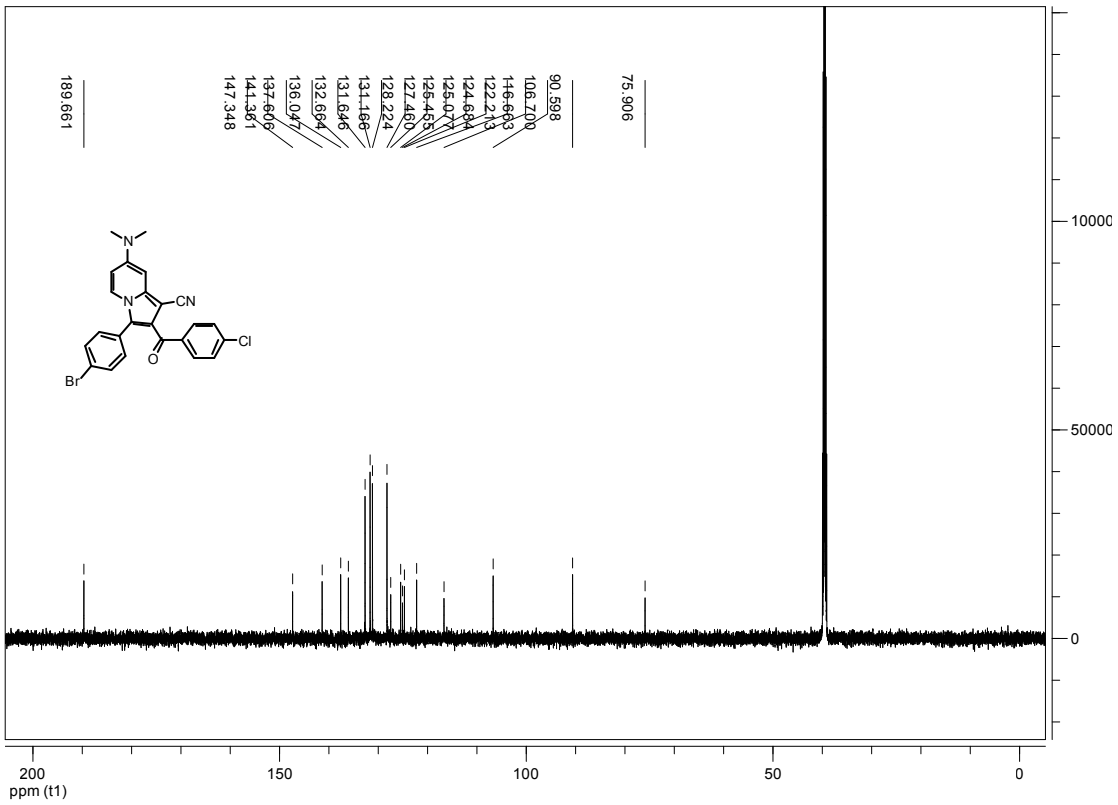
*1-Cyano-2-benzoyl-3-(2-chlorophenyl)indolizine (**2g**):*



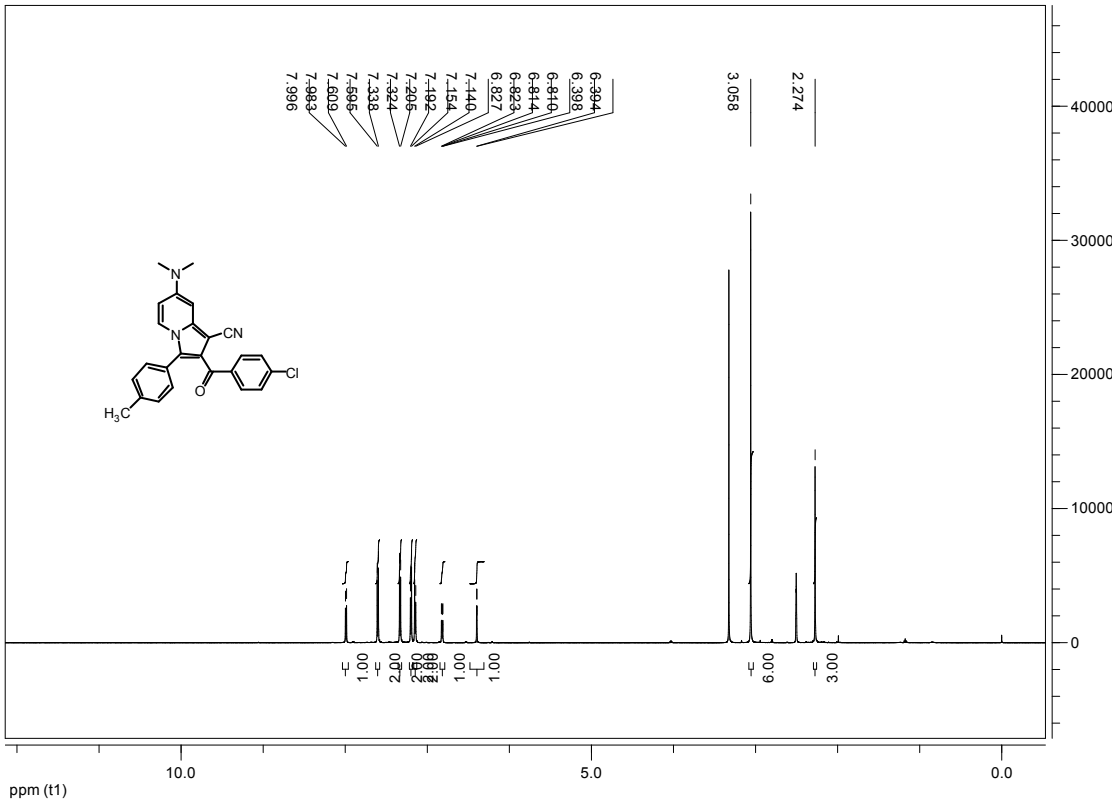


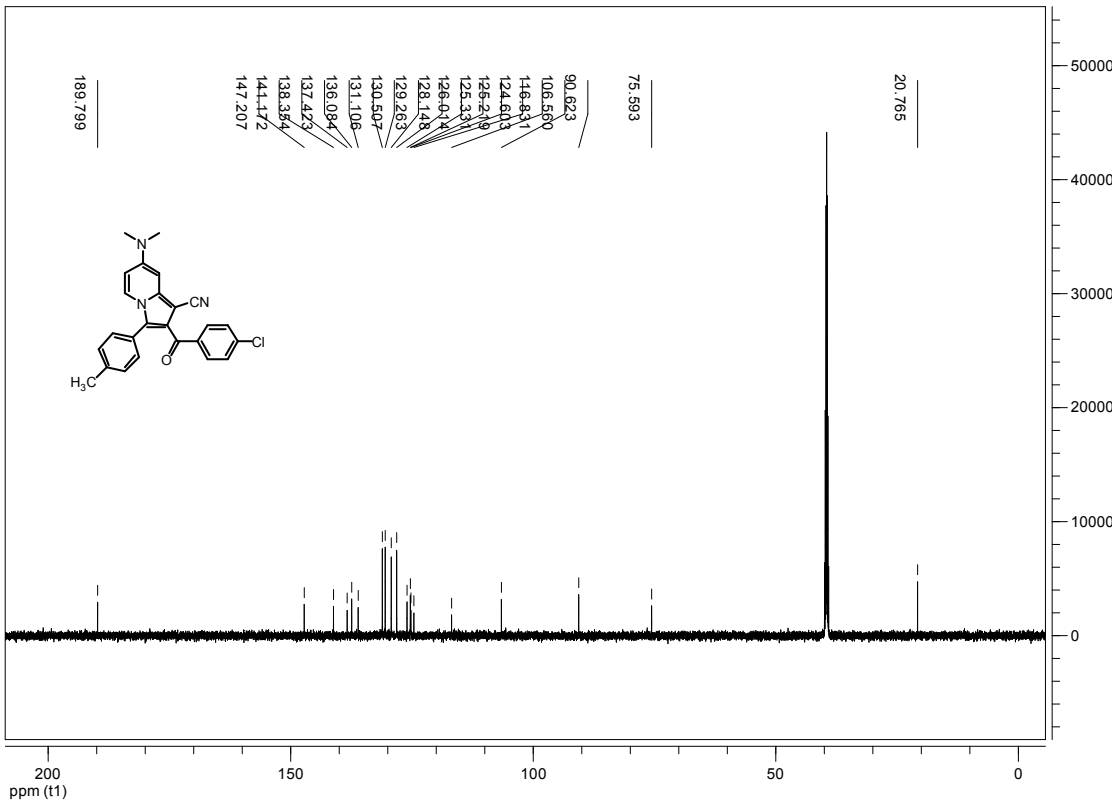
1-Cyano-3-(4-bromophenyl)-2-(4-chlorobenzoyl)-7-(dimethylamino)*indolizine (**2h**):*



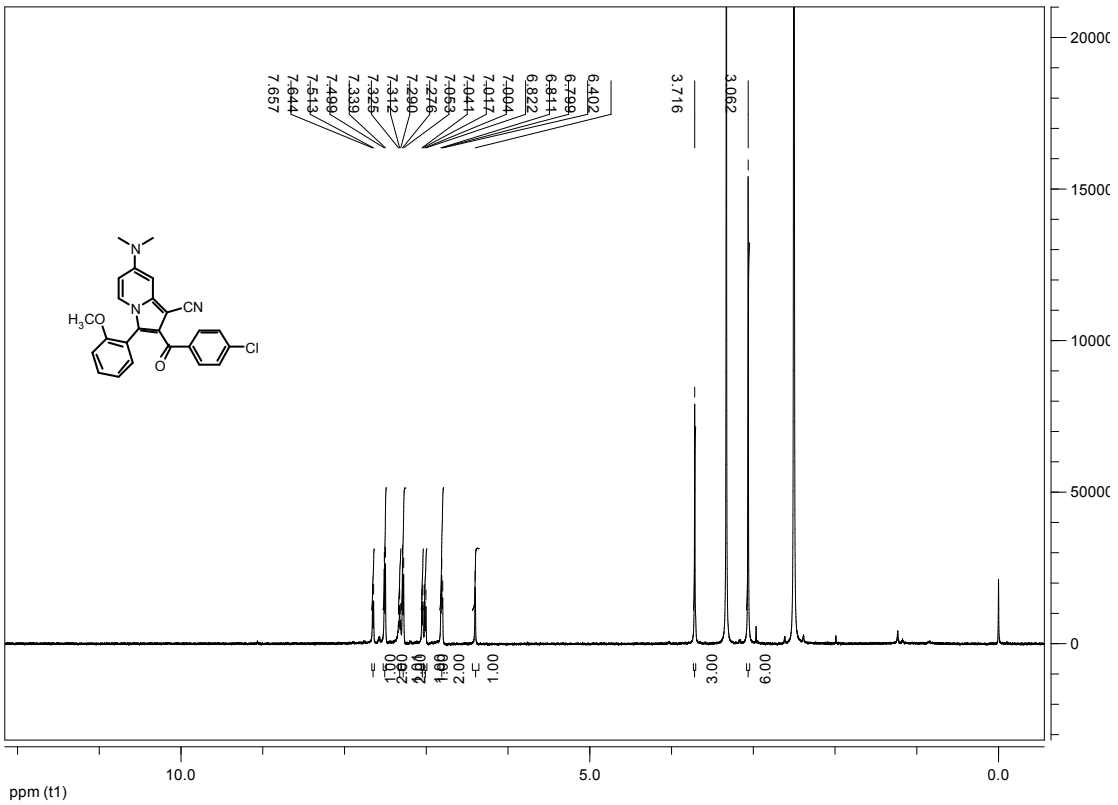


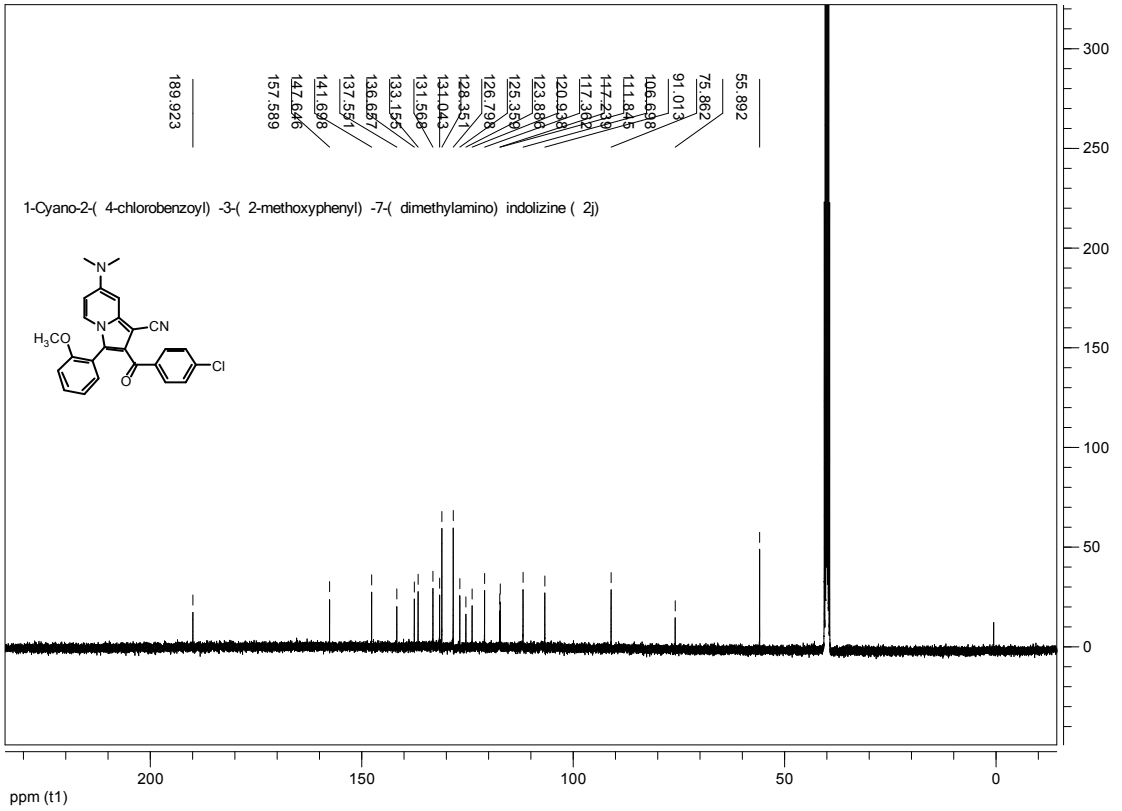
1-Cyano-2-(4-chlorobenzoyl)-7-(dimethylamino)-*3-(4-methylphenyl)indolizine (**2i**)*:



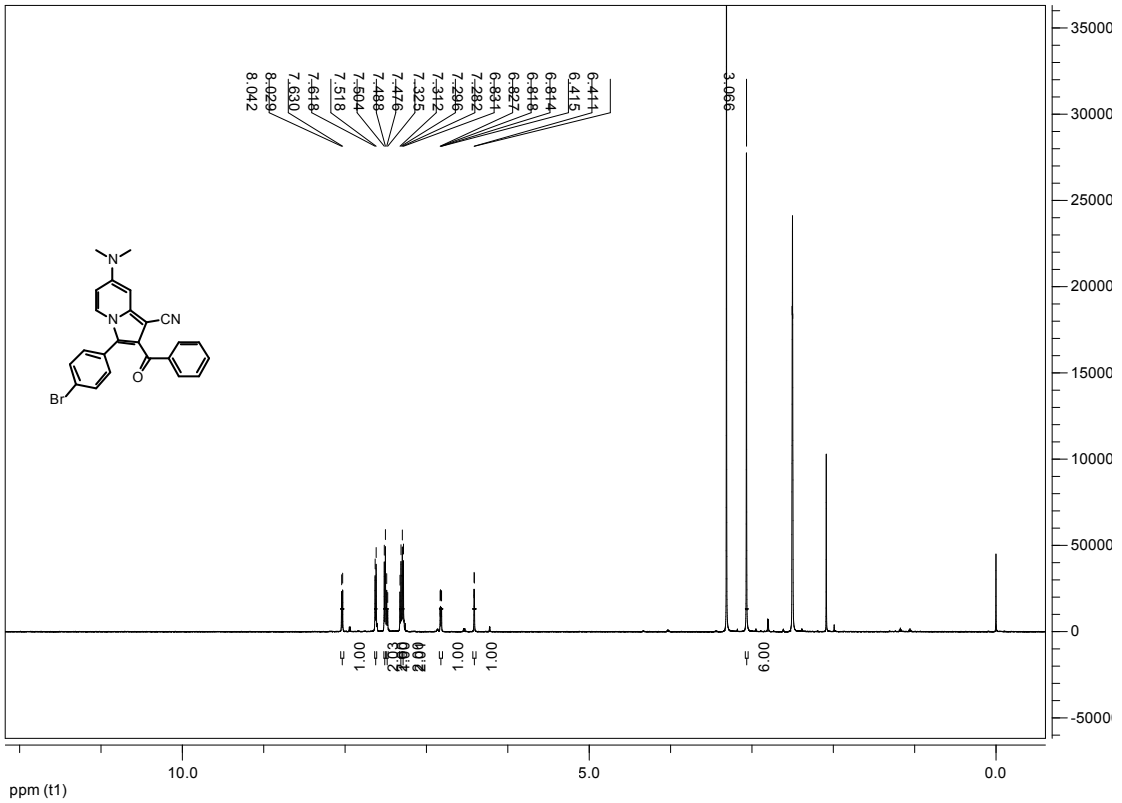


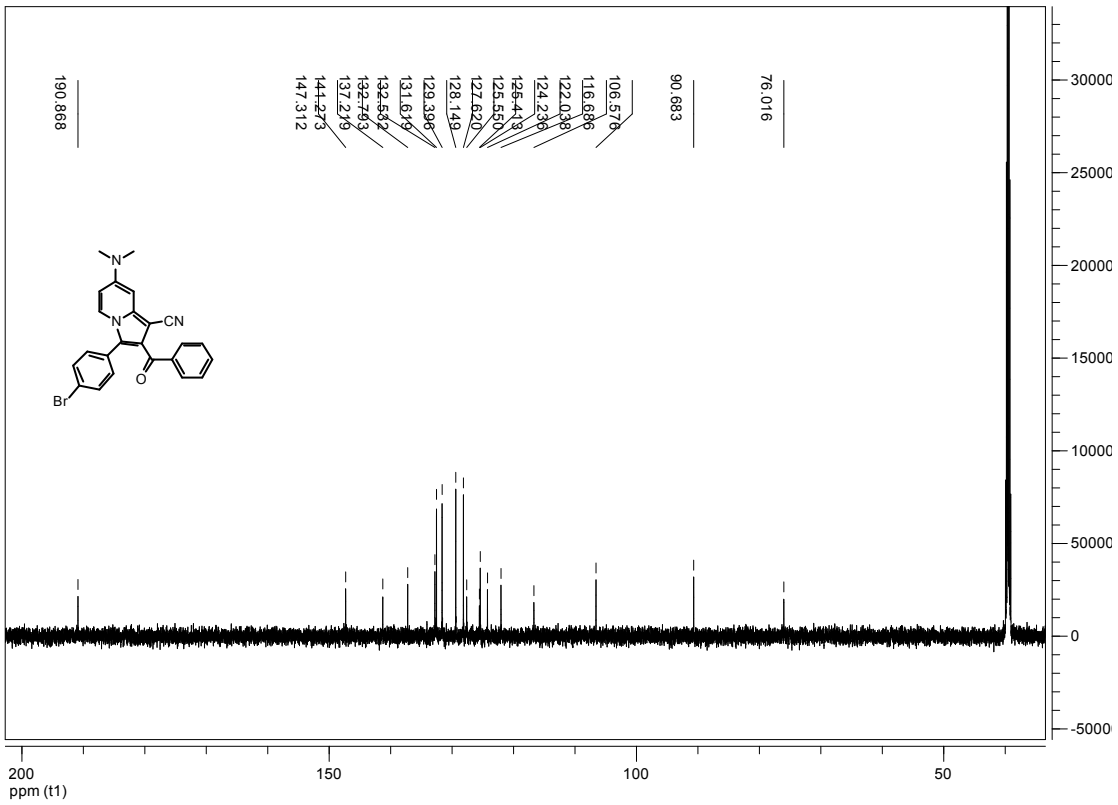
1-Cyano-2-(4-chlorobenzoyl)-3-(2-methoxyphenyl)-7-(dimethylamino)*indolizine (**2j**):*



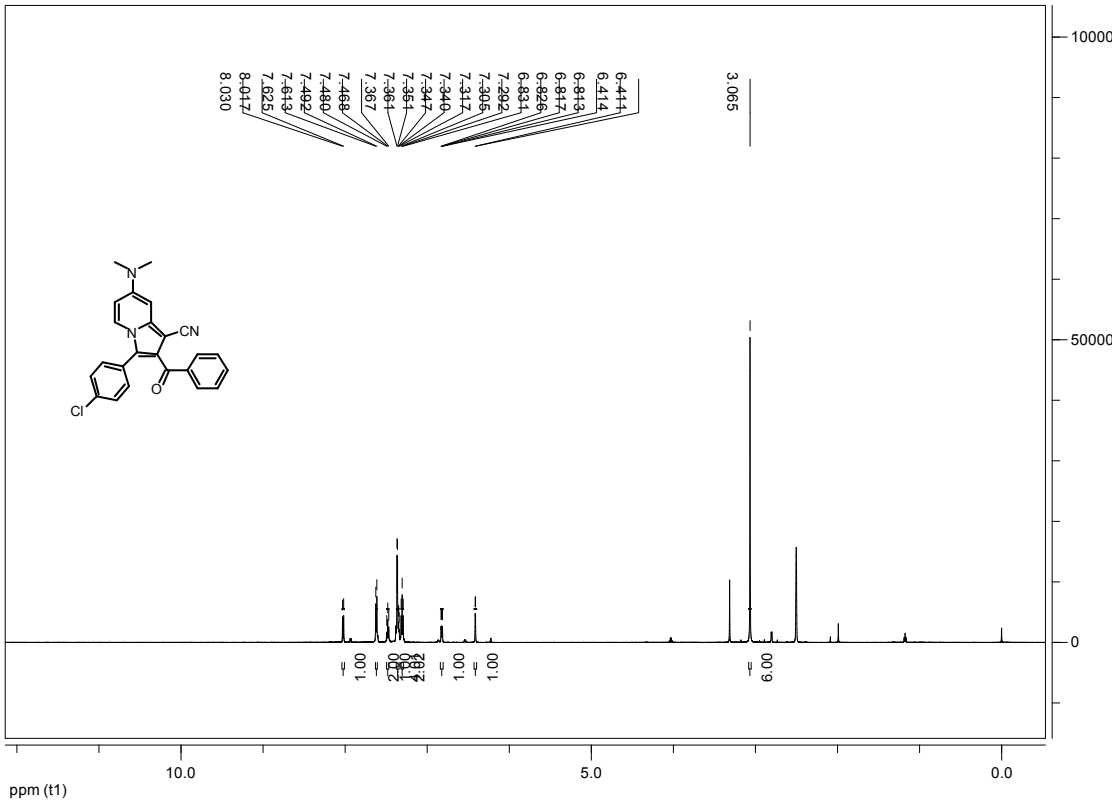


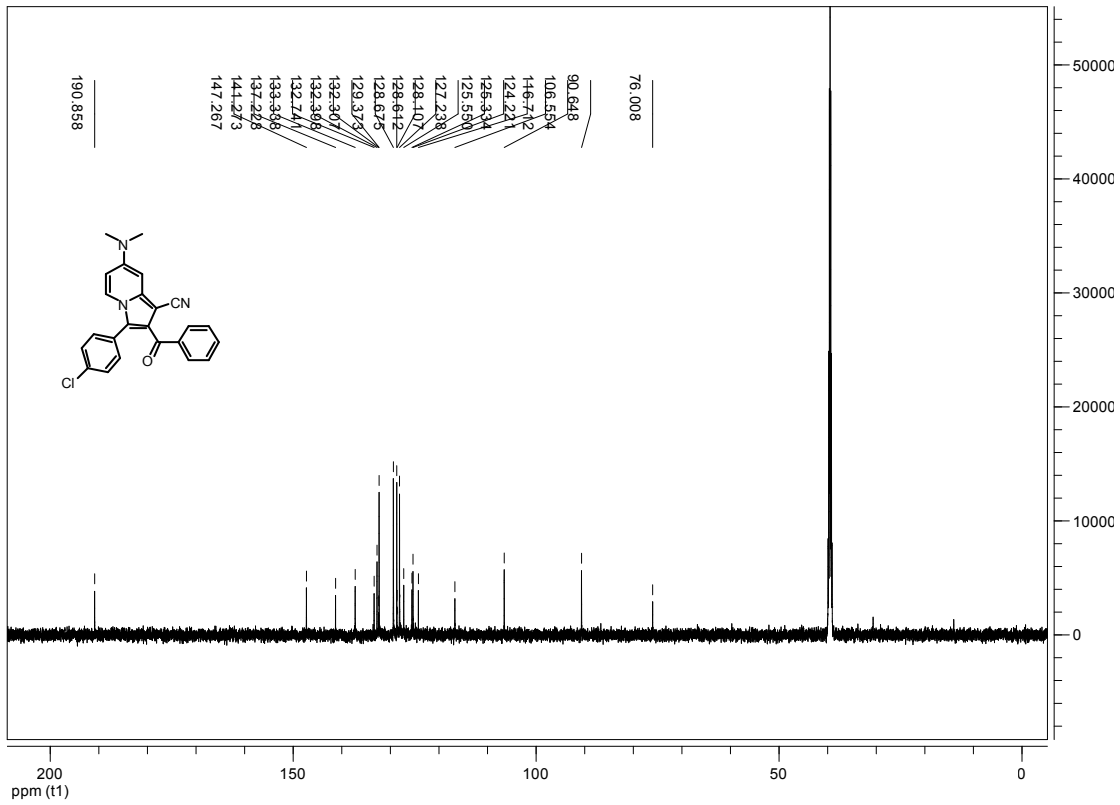
1-Cyano-2-benzoyl-3-(4-bromophenyl)-7-(dimethylamino)*indolizine (**2k**):*



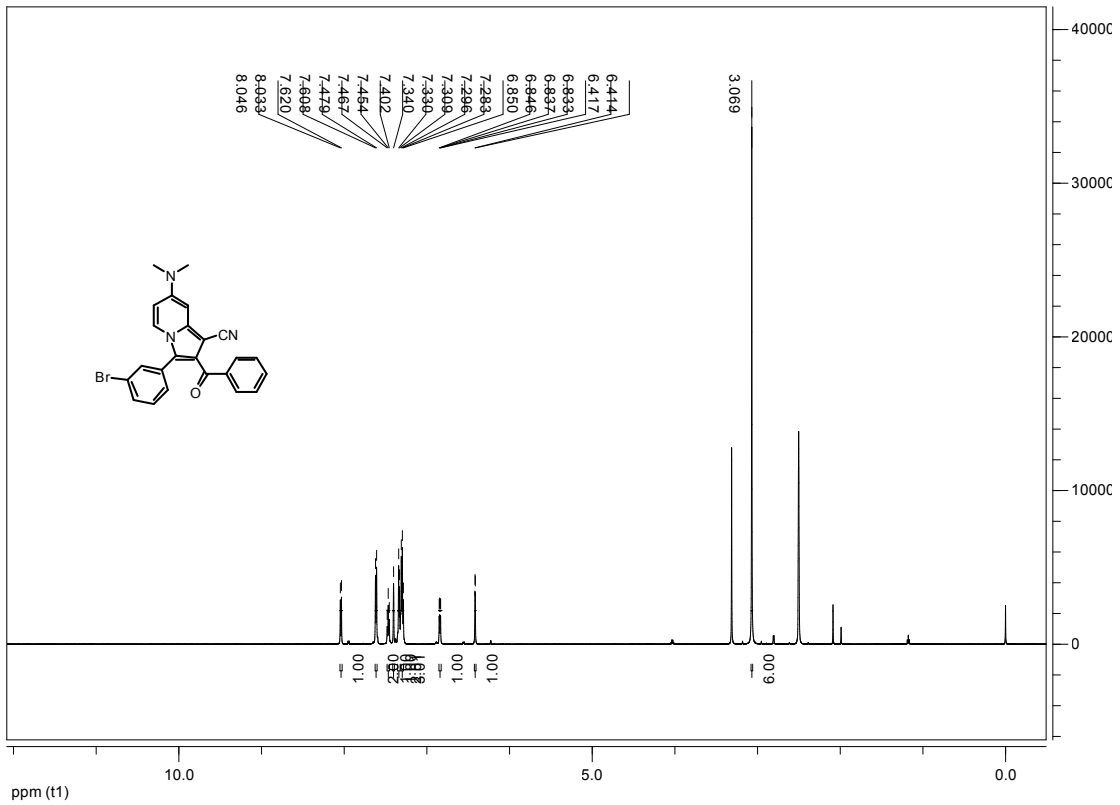


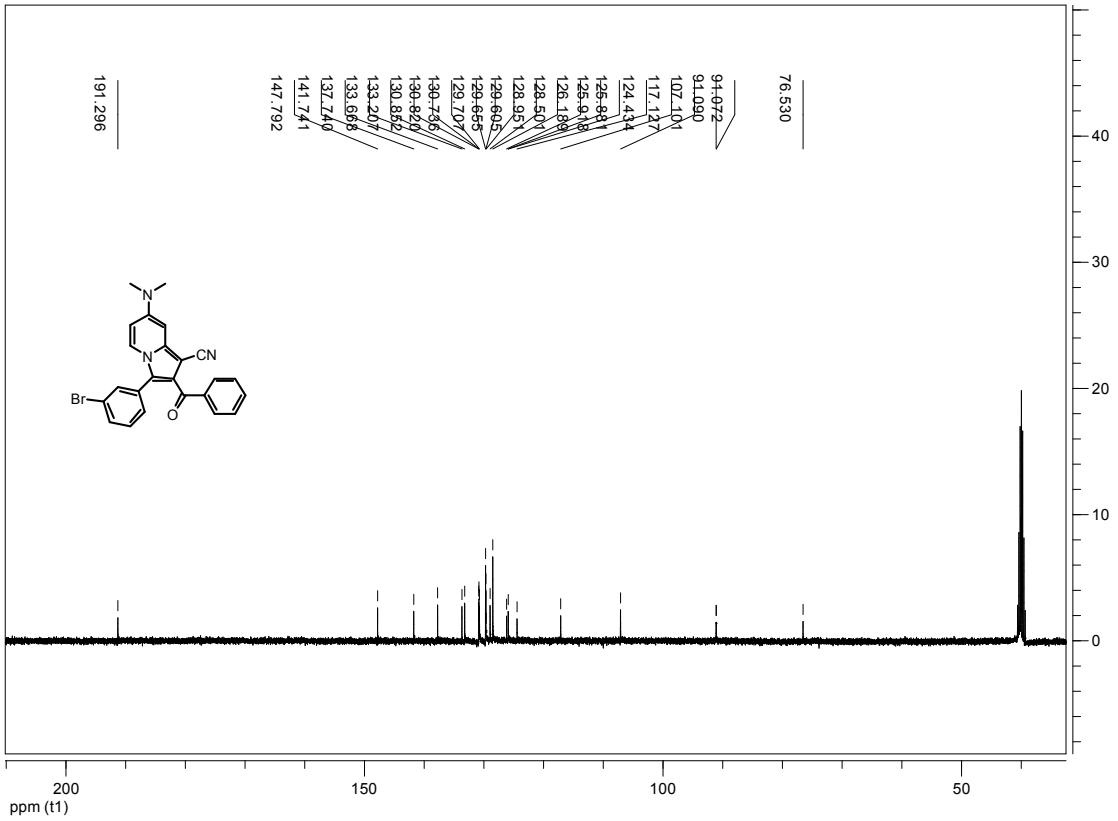
1-Cyano-2-benzoyl-3-(4-chlorophenyl)-7-(dimethylamino)*indolizine (**2l**):*



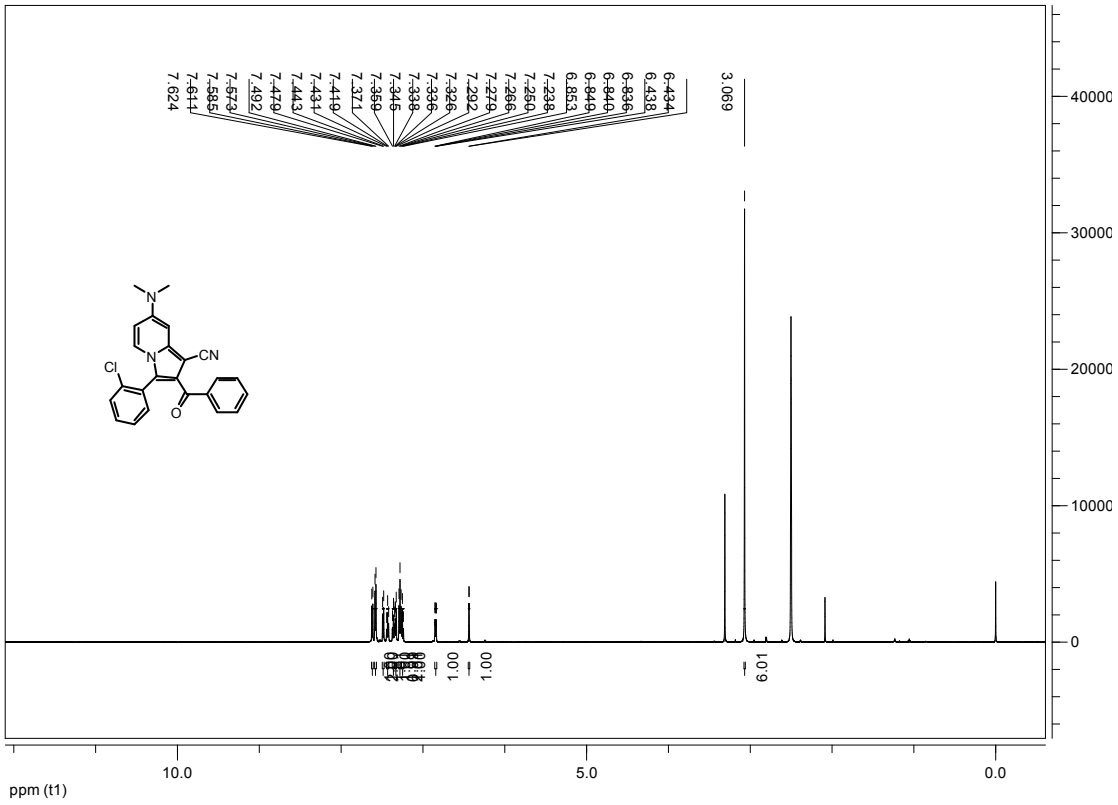


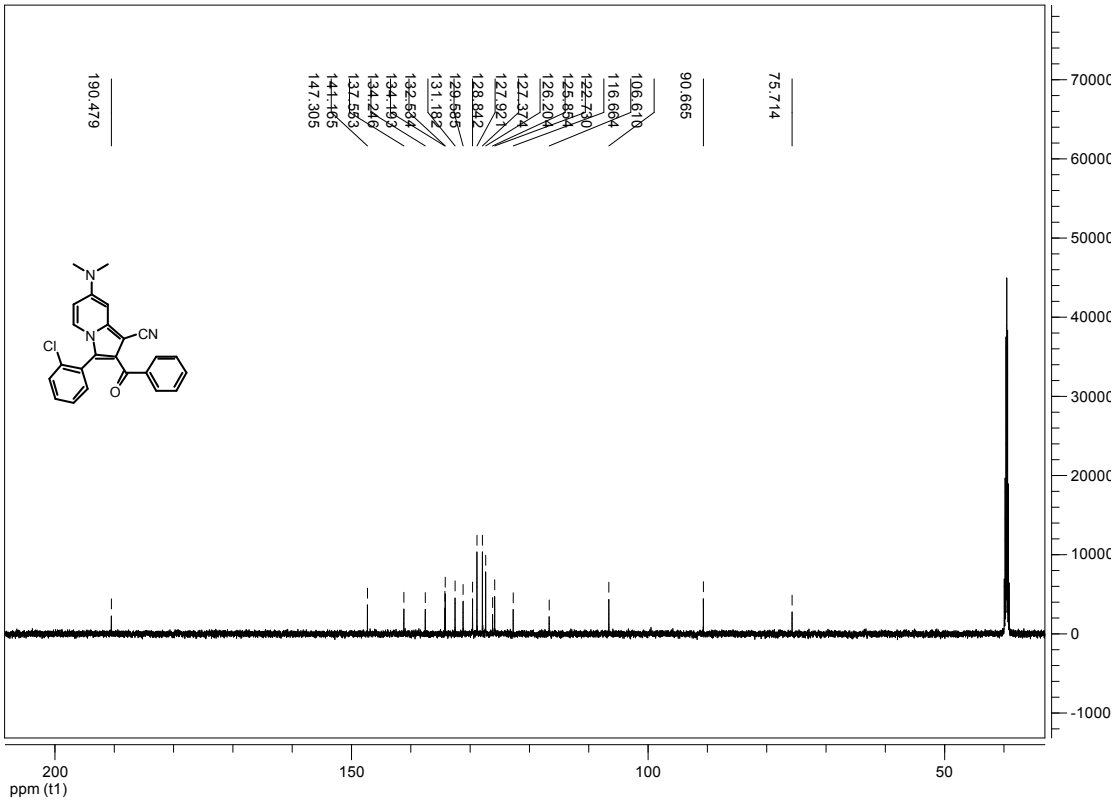
1-Cyano-2-benzoyl-3-(3-bromophenyl)-7-(dimethylamino)*indolizine (**2m**):*



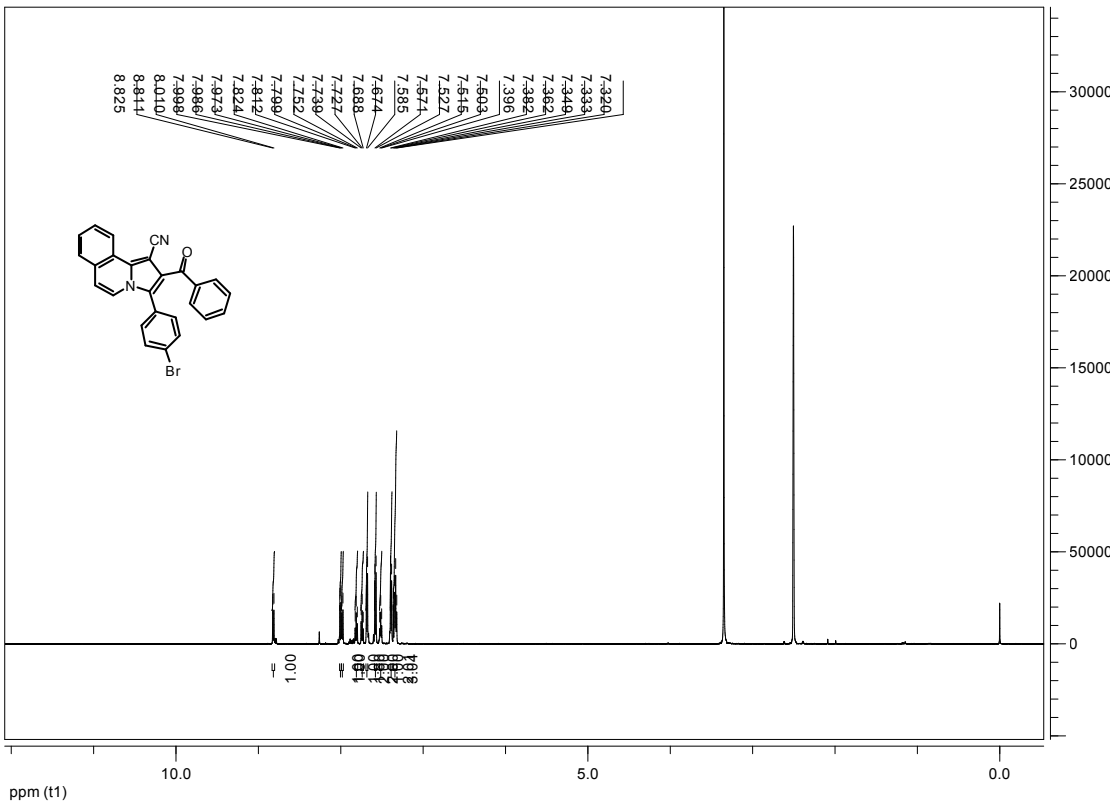


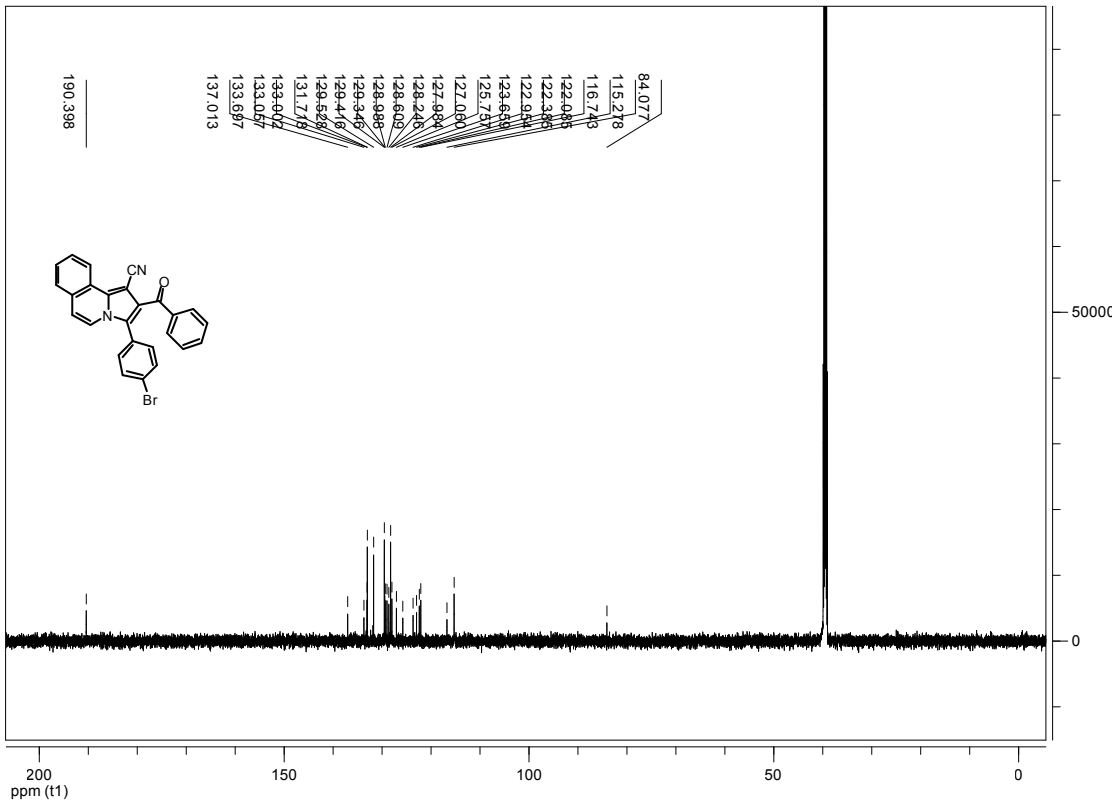
1-Cyano-2-benzoyl-3-(2-chlorophenyl)-7-(dimethylamino)*indolizine (**2n**)*:



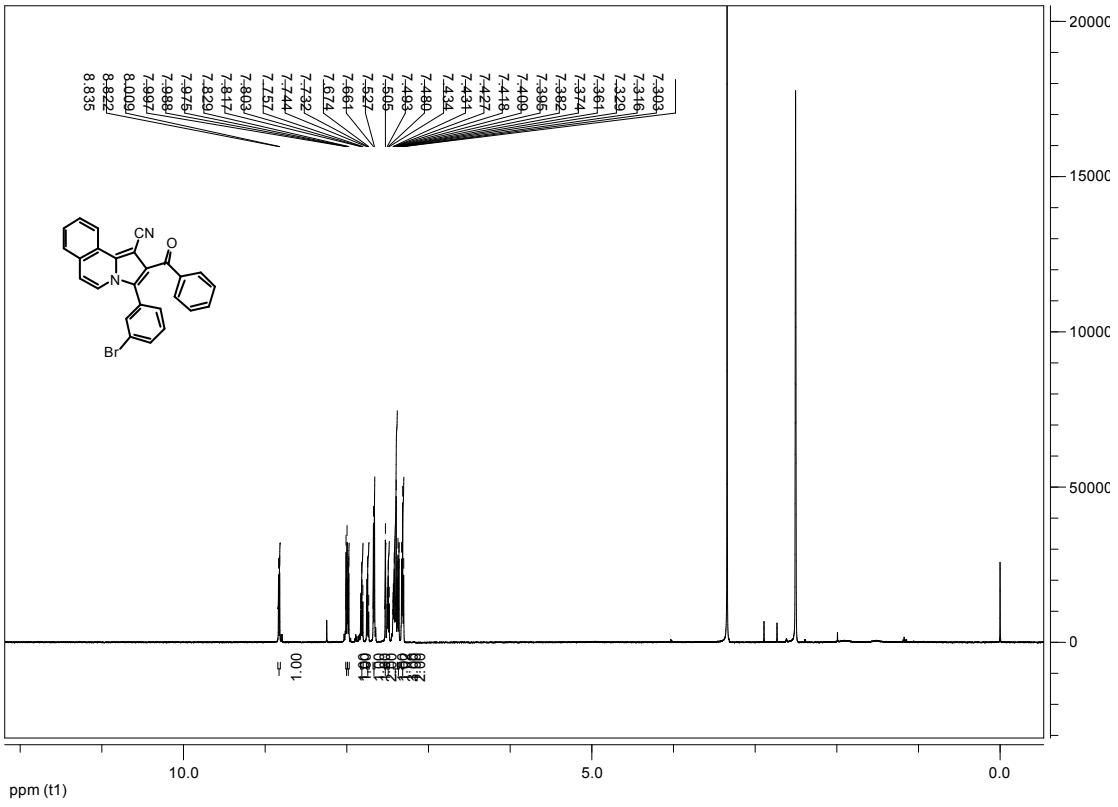


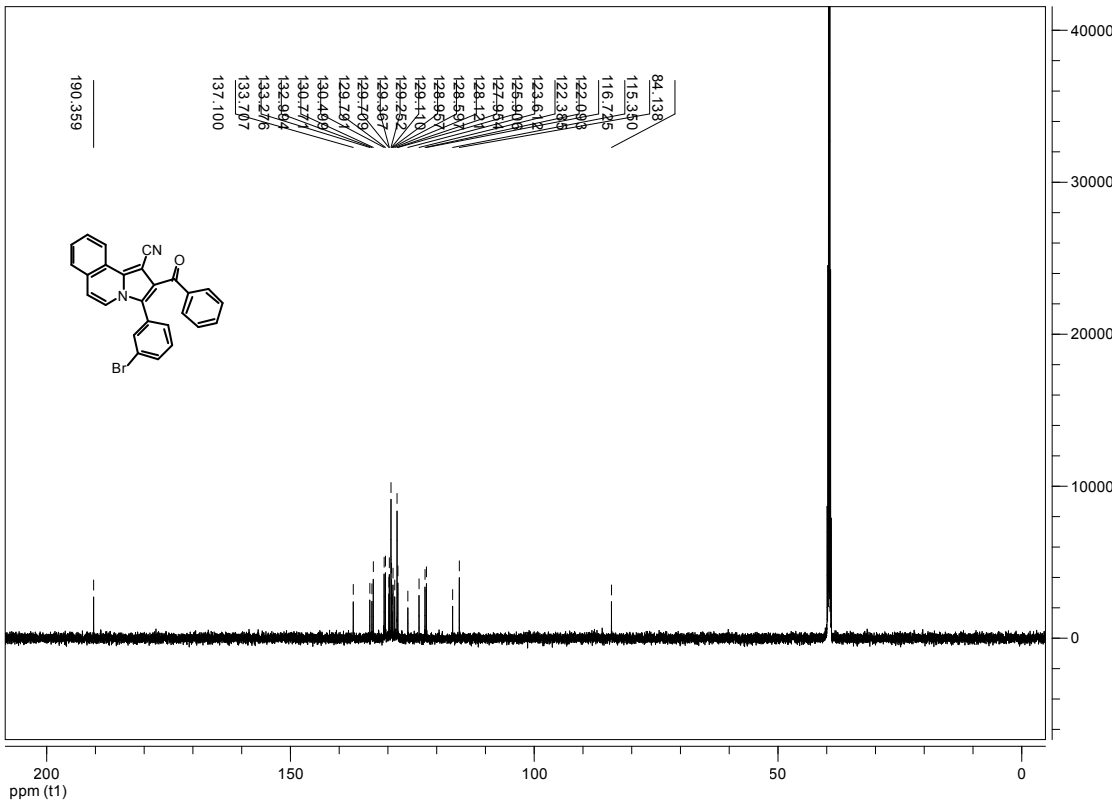
*2-benzoyl-3-(4-bromophenyl)pyrrolo[2,1-a]isoquinoline-1-carbonitrile (**3a**)*



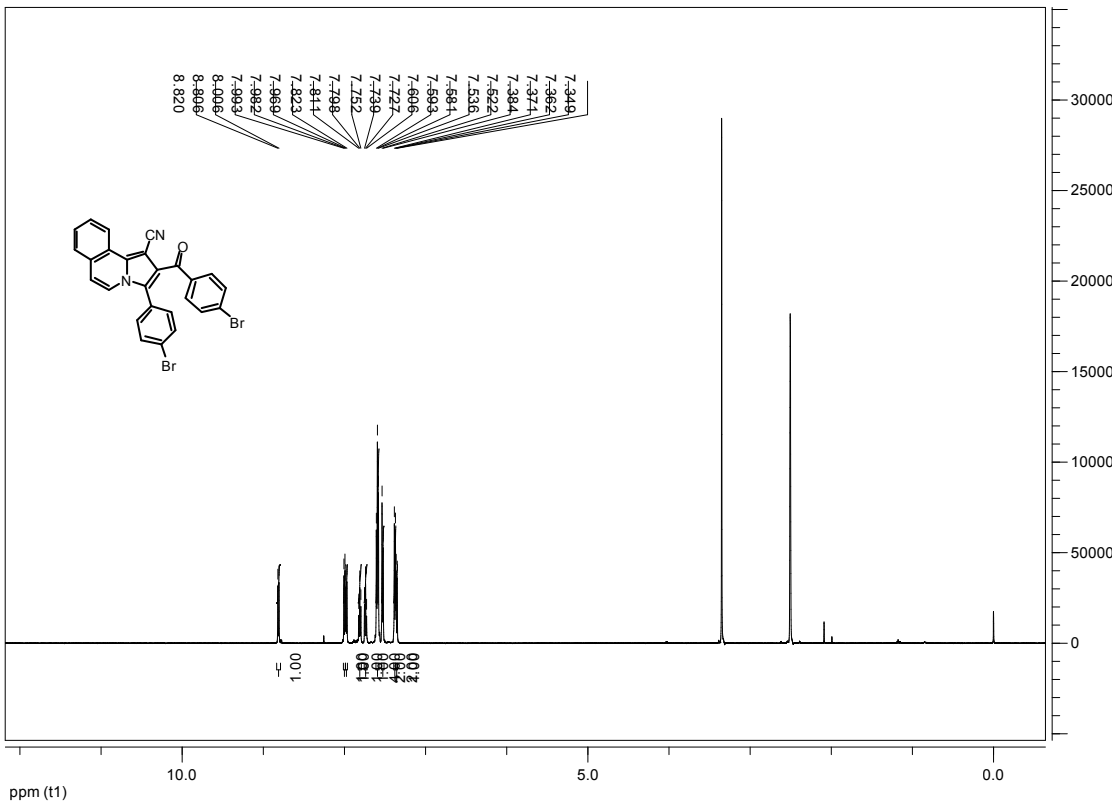


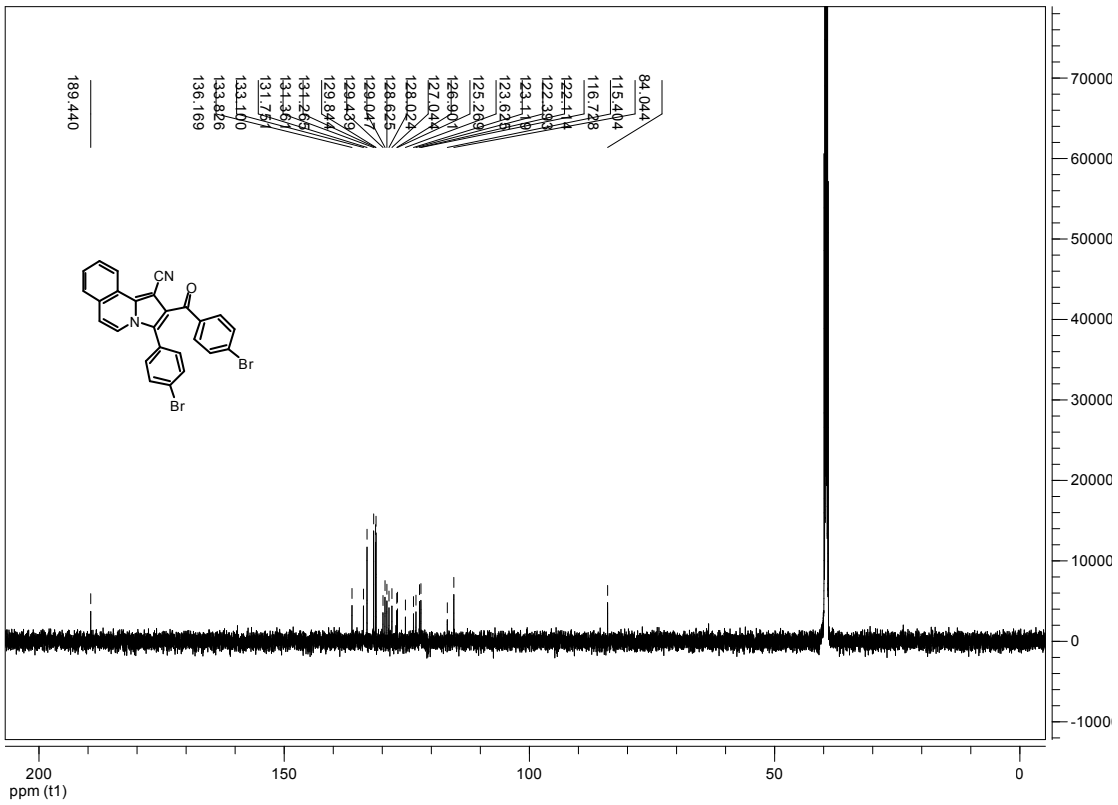
*2-benzoyl-3-(3-bromophenyl)pyrrolo[2,1-a]isoquinoline-1-carbonitrile (**3b**)*



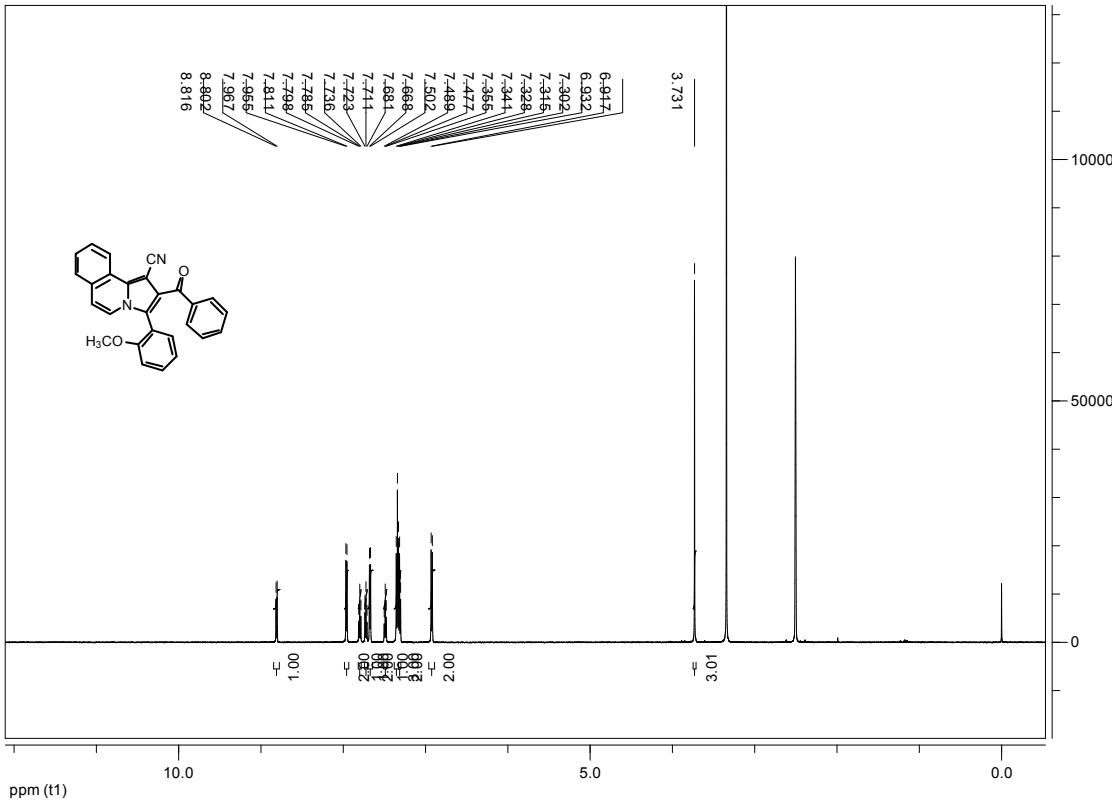


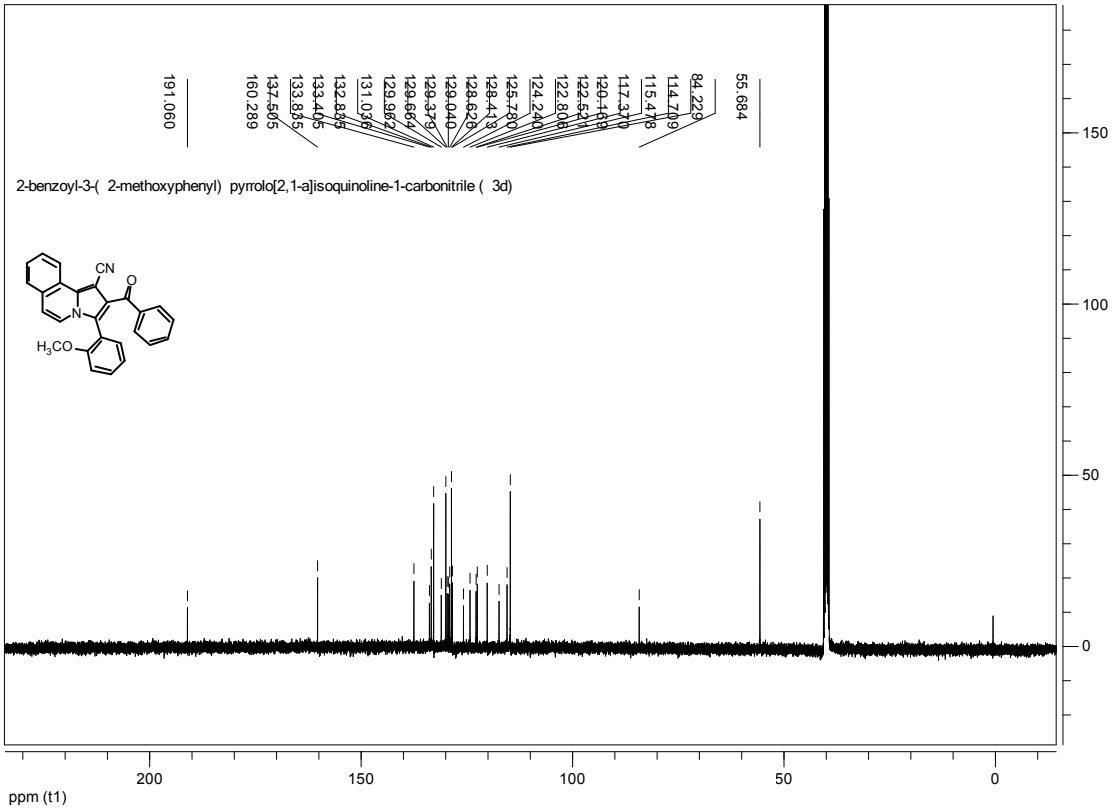
*2-(4-bromobenzoyl)-3-(4-bromophenyl)pyrrolo[2,1-a]isoquinoline-1-carbonitrile (**3b**)*



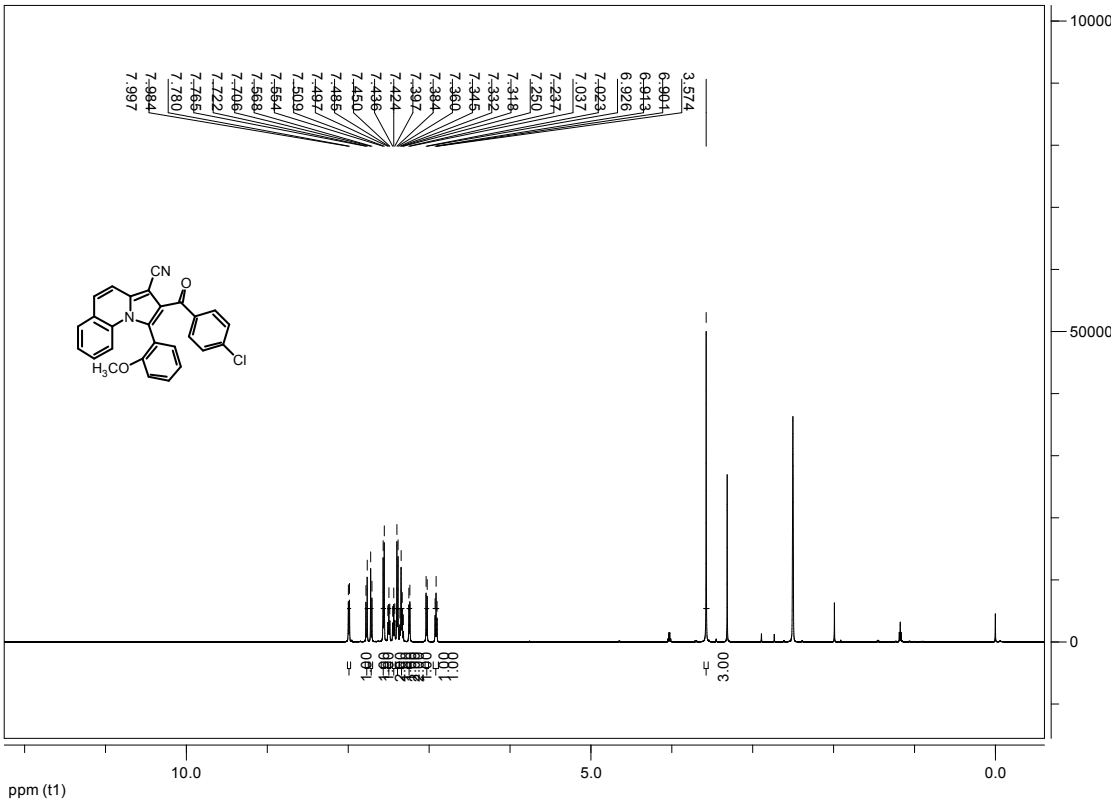


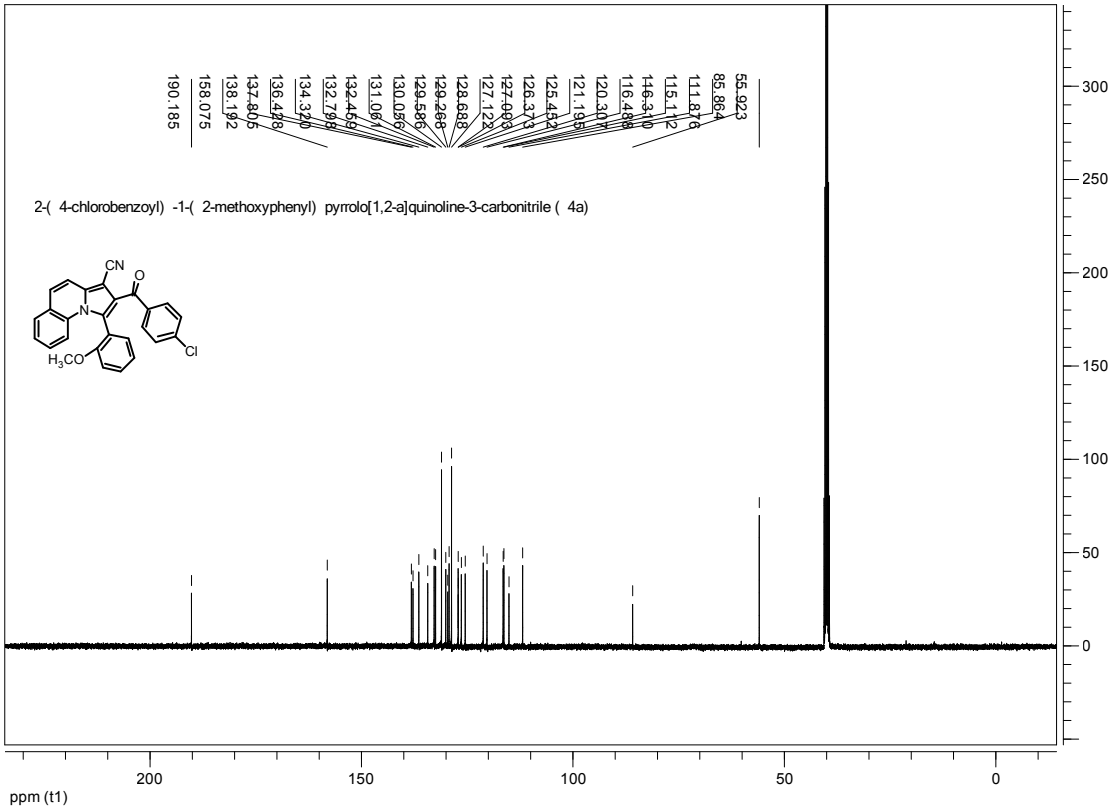
*2-benzoyl-3-(2-methoxyphenyl)pyrrolo[2,1-a]isoquinoline-1-carbonitrile (**3d**)*



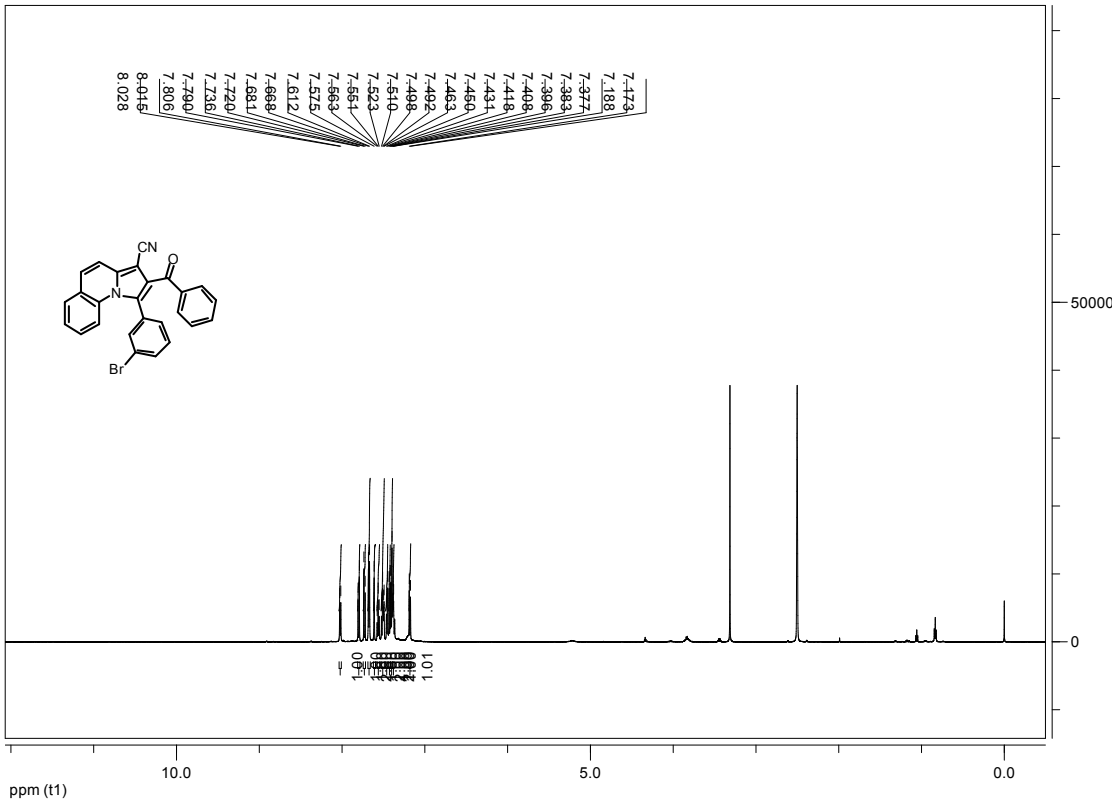


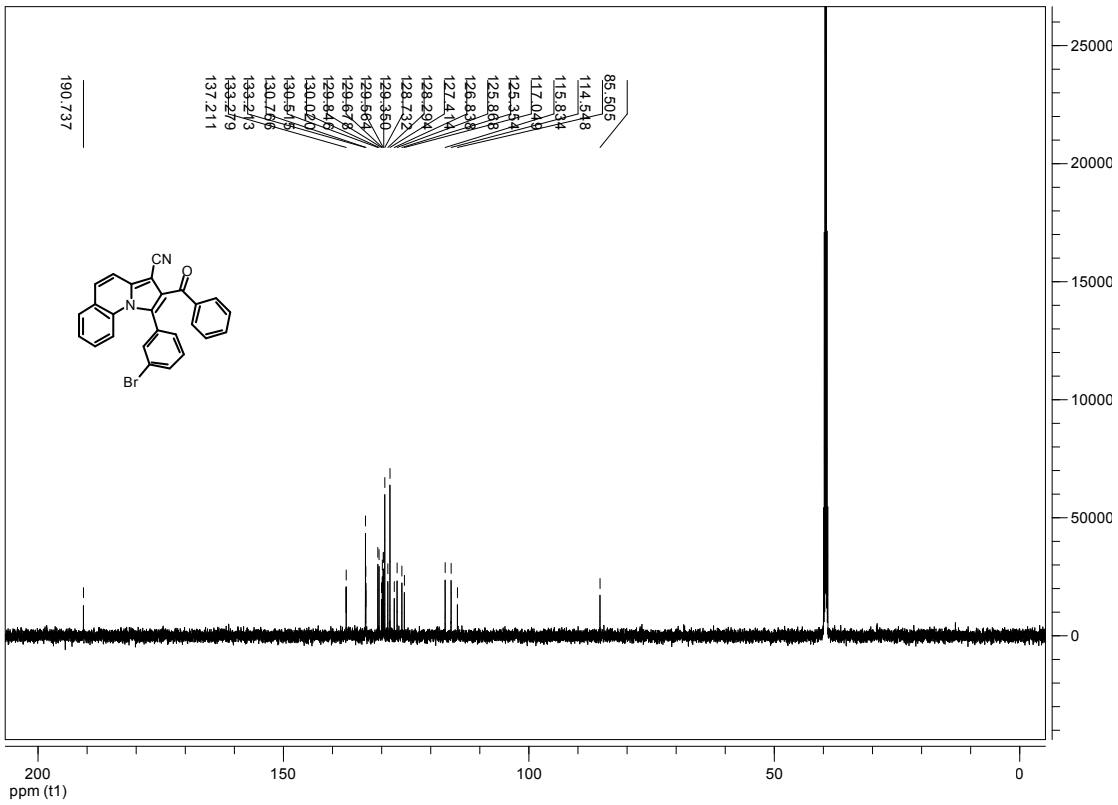
*2-(4-chlorobenzoyl)-1-(2-methoxyphenyl)pyrrolo[1,2-a]quinoline-3-carbonitrile (**4a**)*



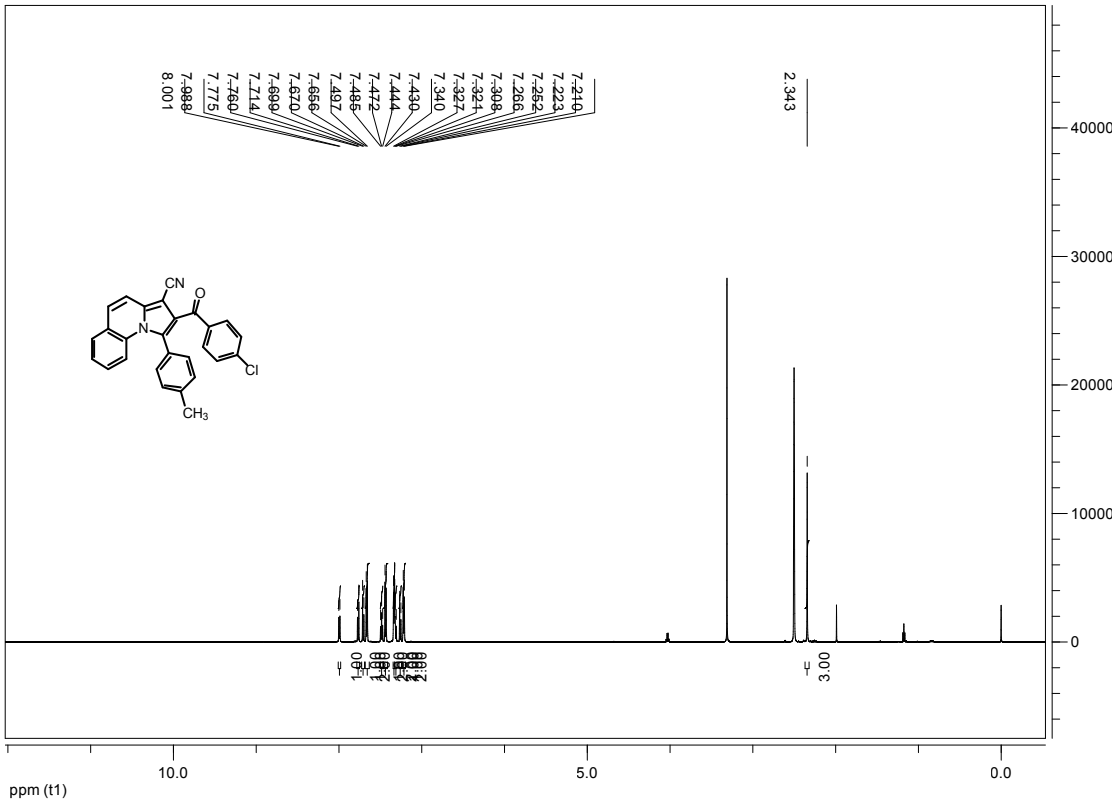


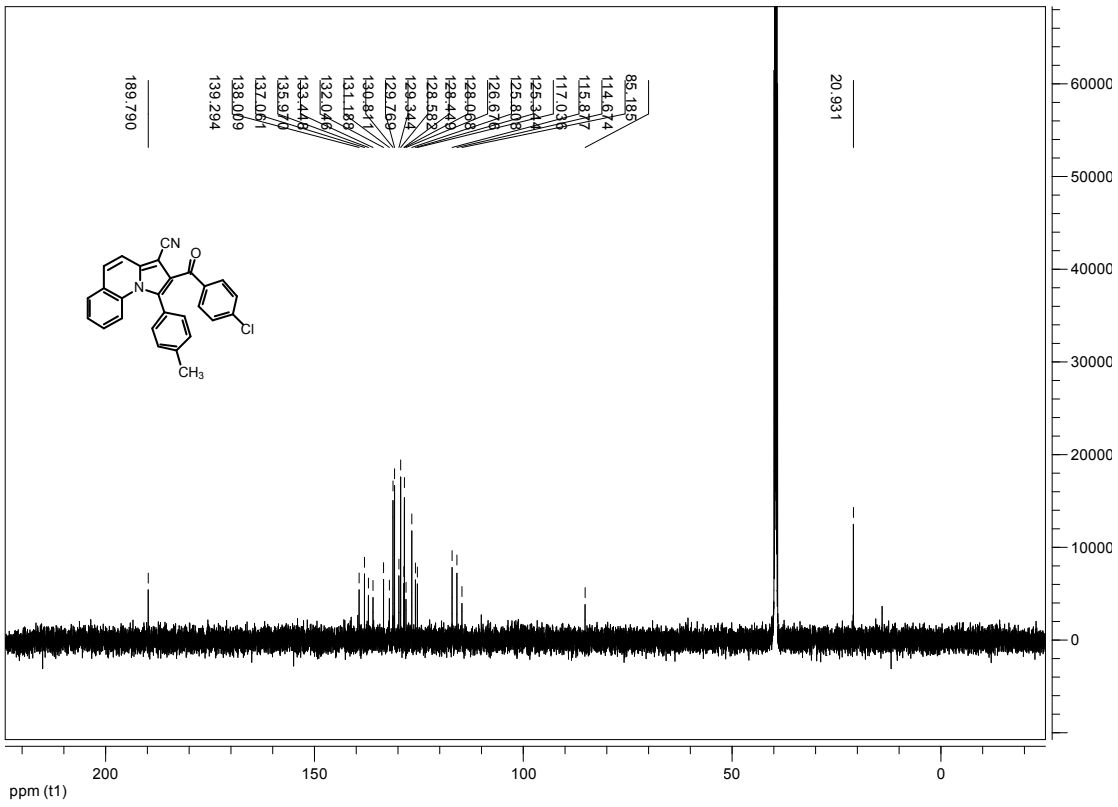
*2-benzoyl-1-(3-bromophenyl)pyrrolo[1,2-a]quinoline-3-carbonitrile (**4b**)*



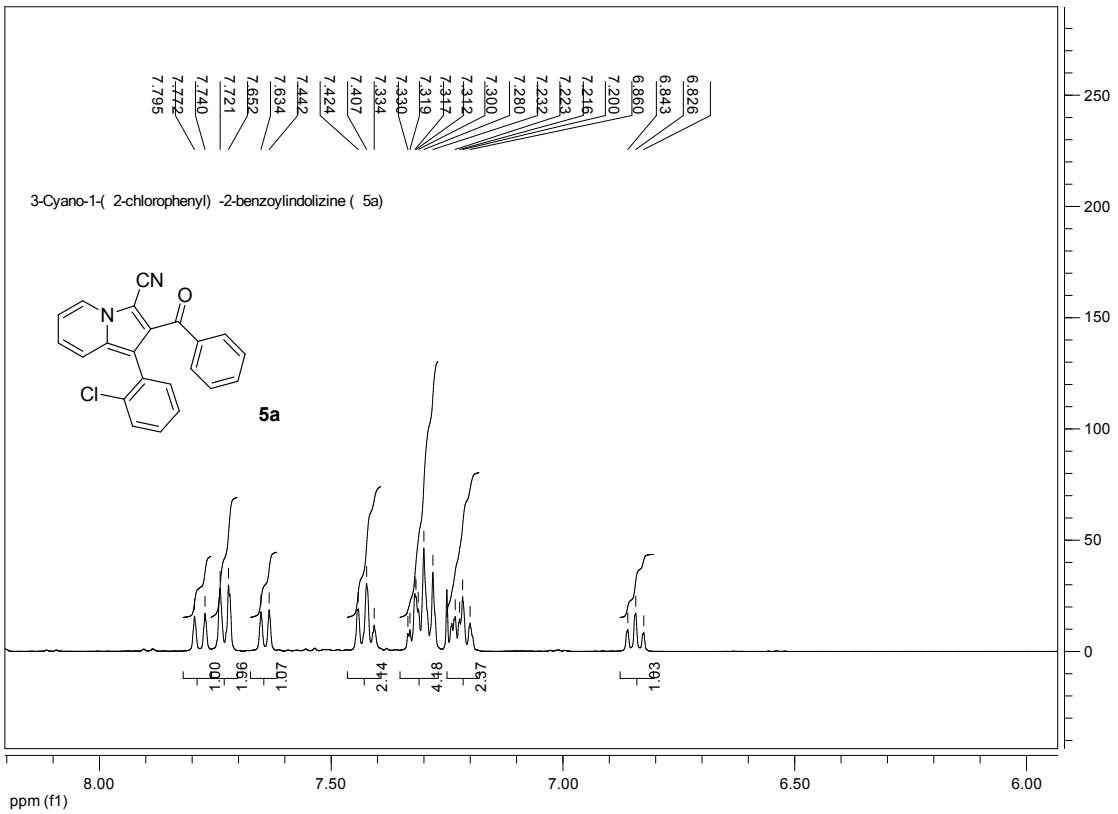


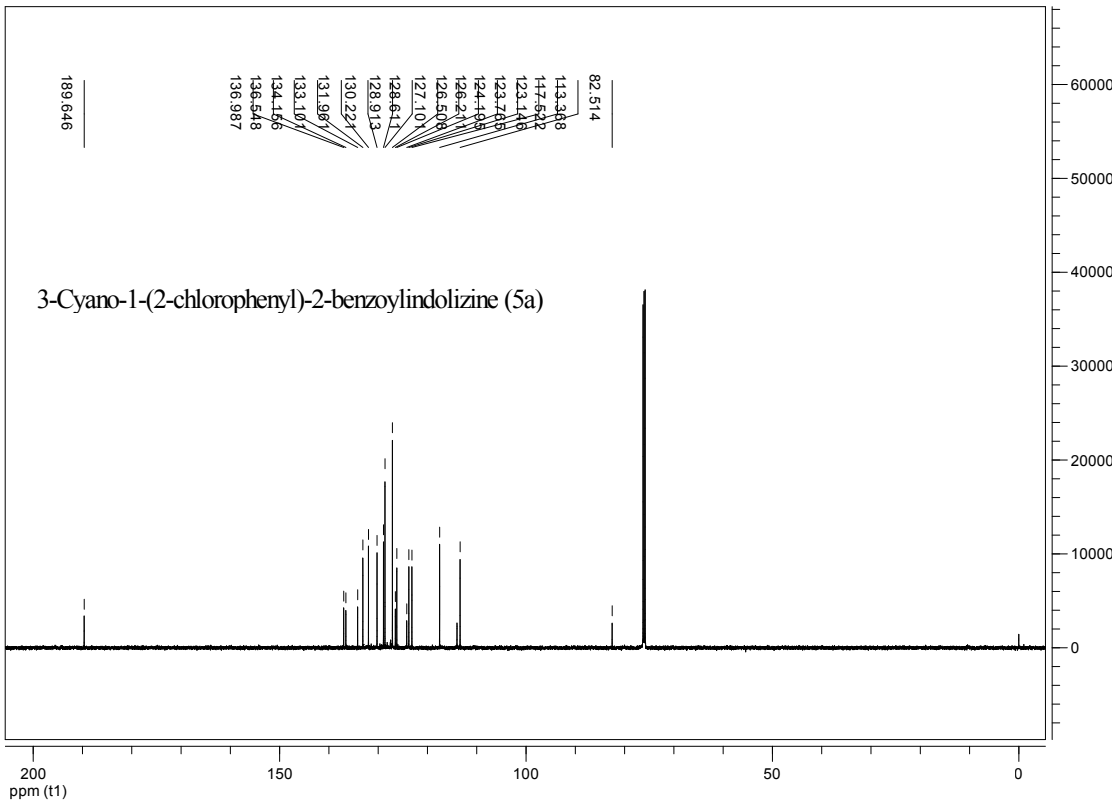
*2-(4-chlorobenzoyl)-1-(4-methylphenyl)pyrrolo[1,2-a]quinoline-3-carbonitrile (**4c**)*



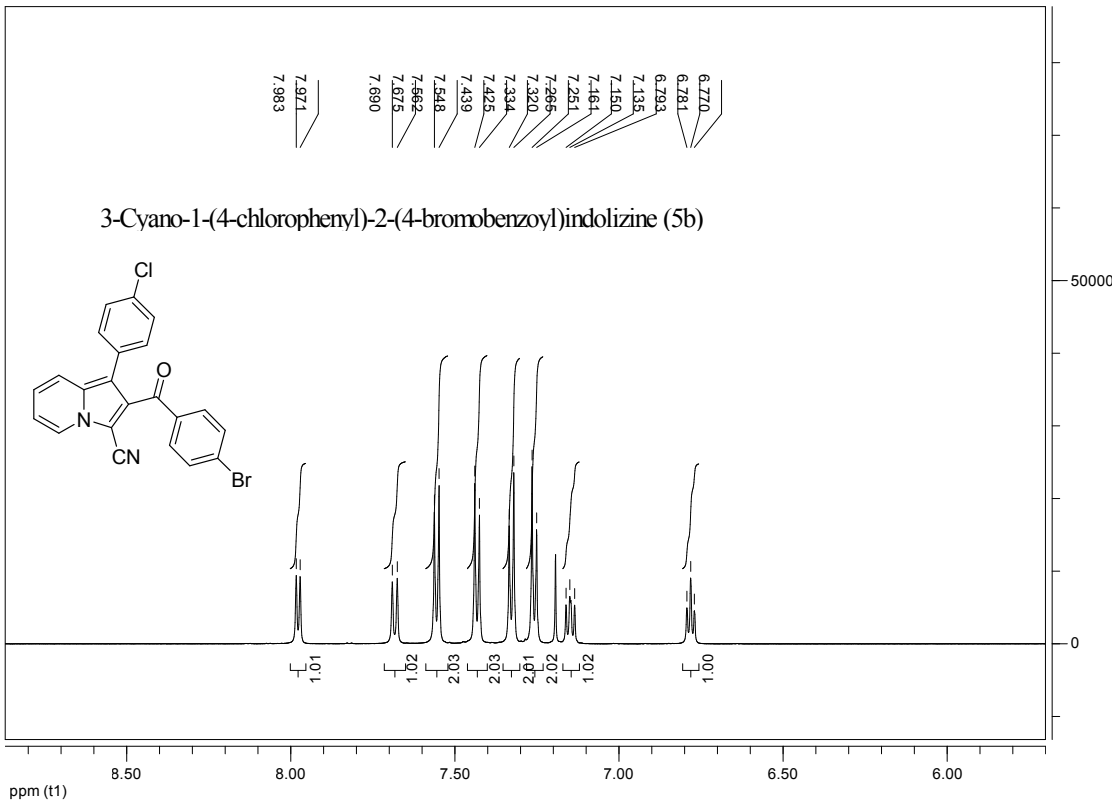


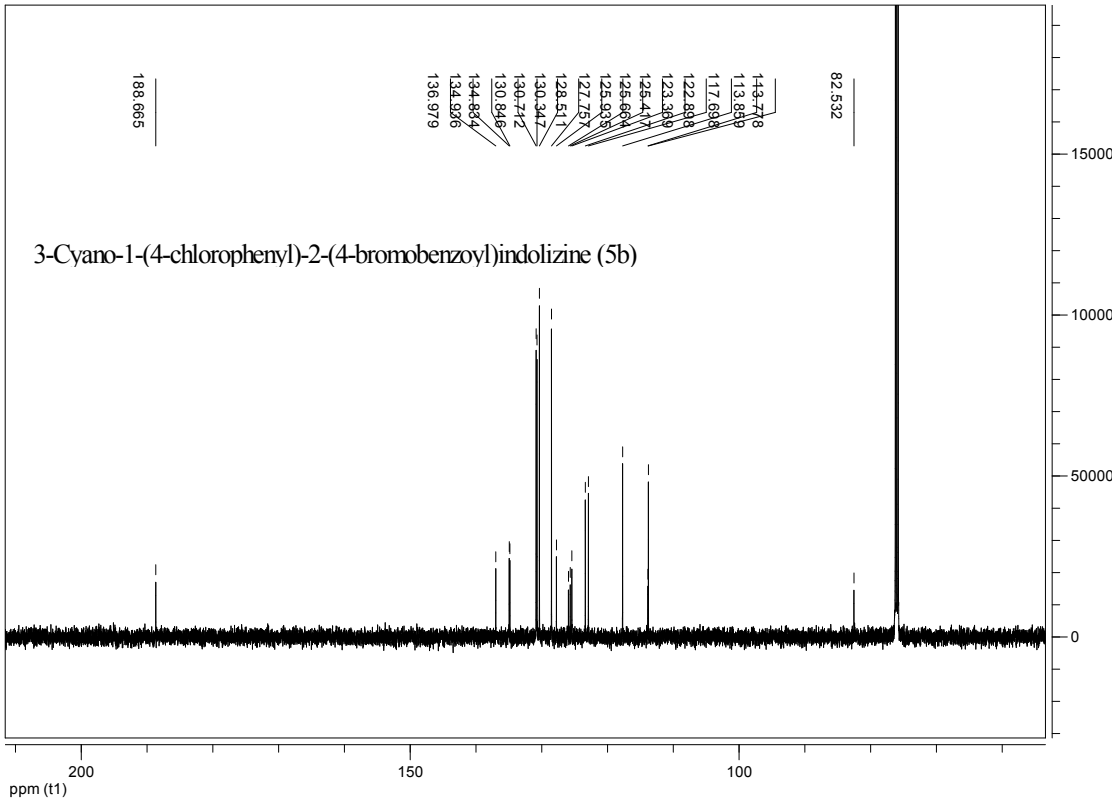
3-Cyano-1-(2-chlorophenyl)-2-benzoylindolizine (5a)



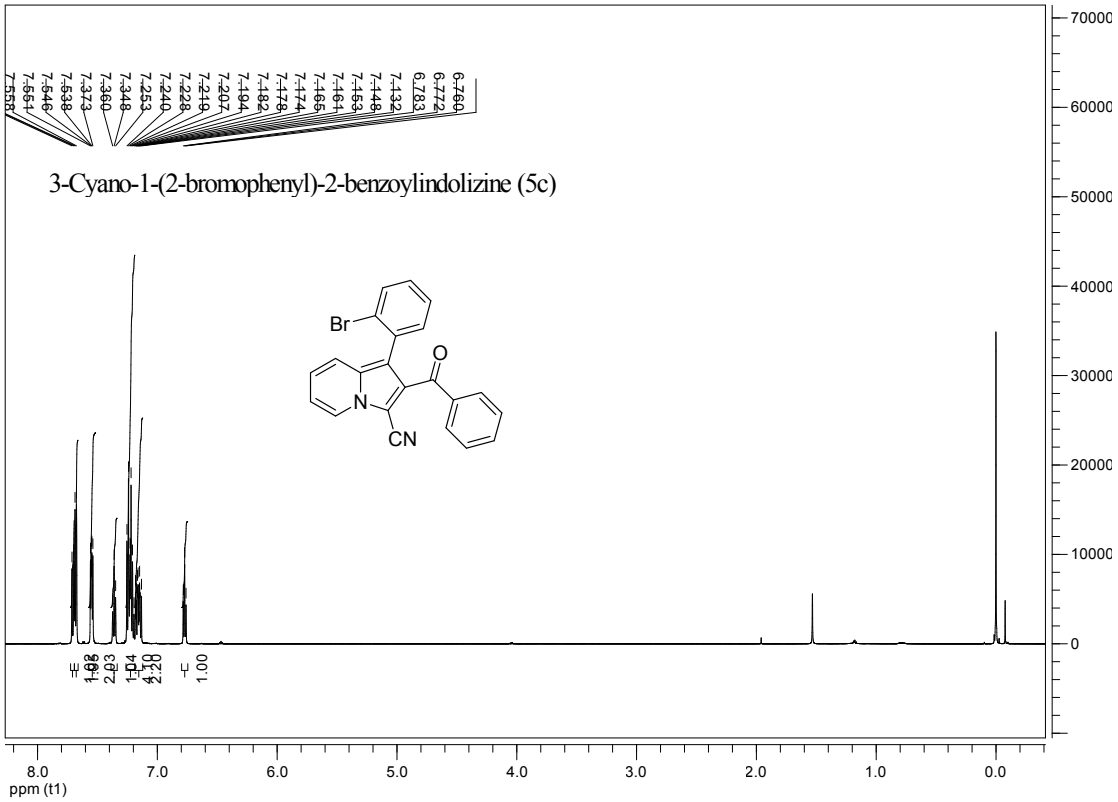


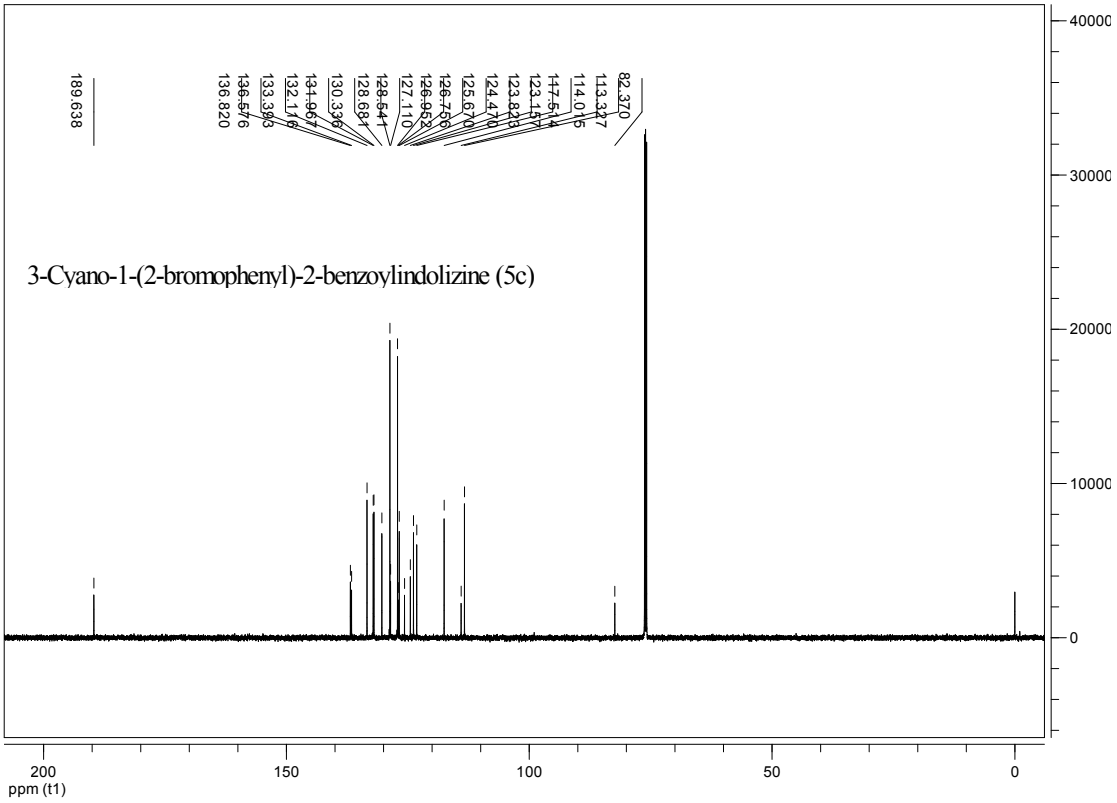
3-Cyano-1-(4-chlorophenyl)-2-(4-bromobenzoyl)indolizine (5b)



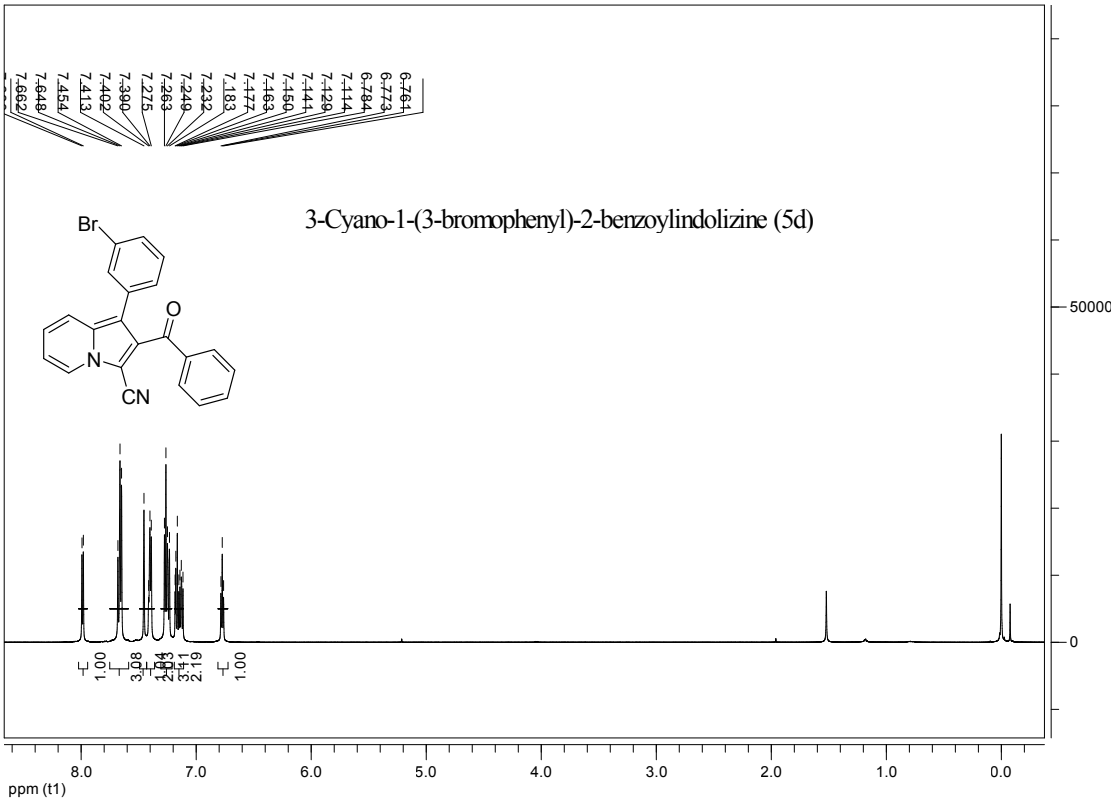


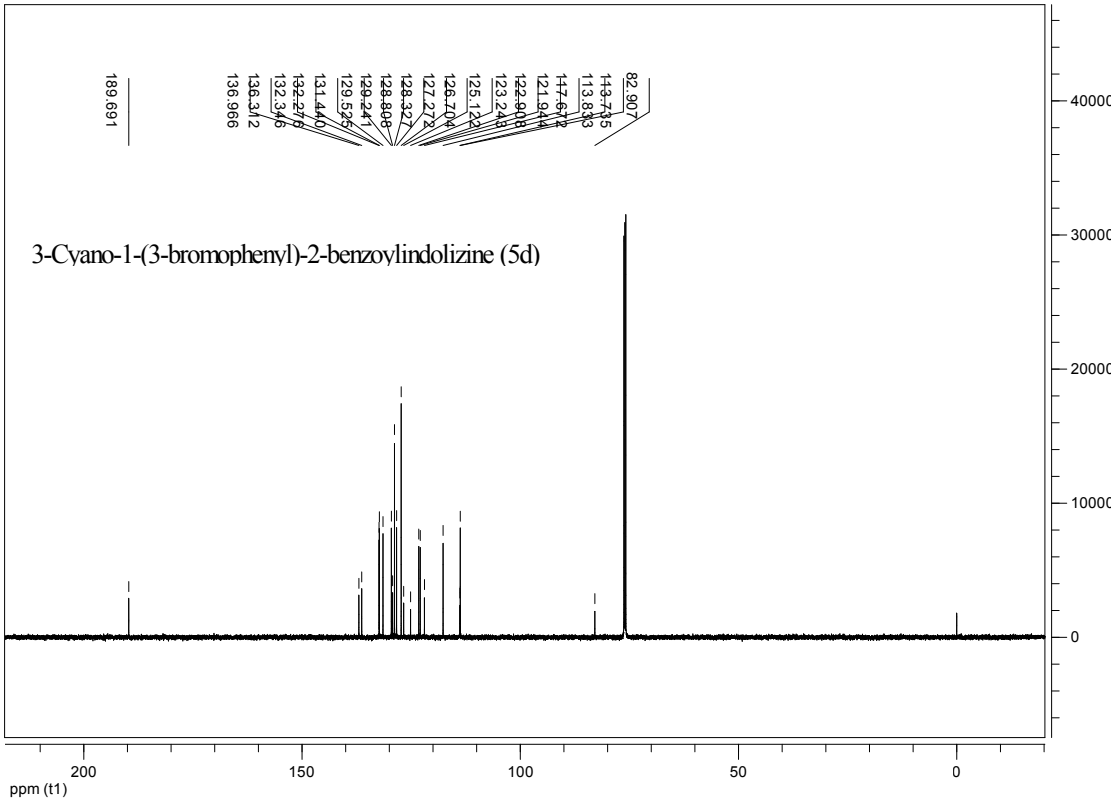
3-Cyano-1-(2-bromophenyl)-2-benzoylindolizine (5c)



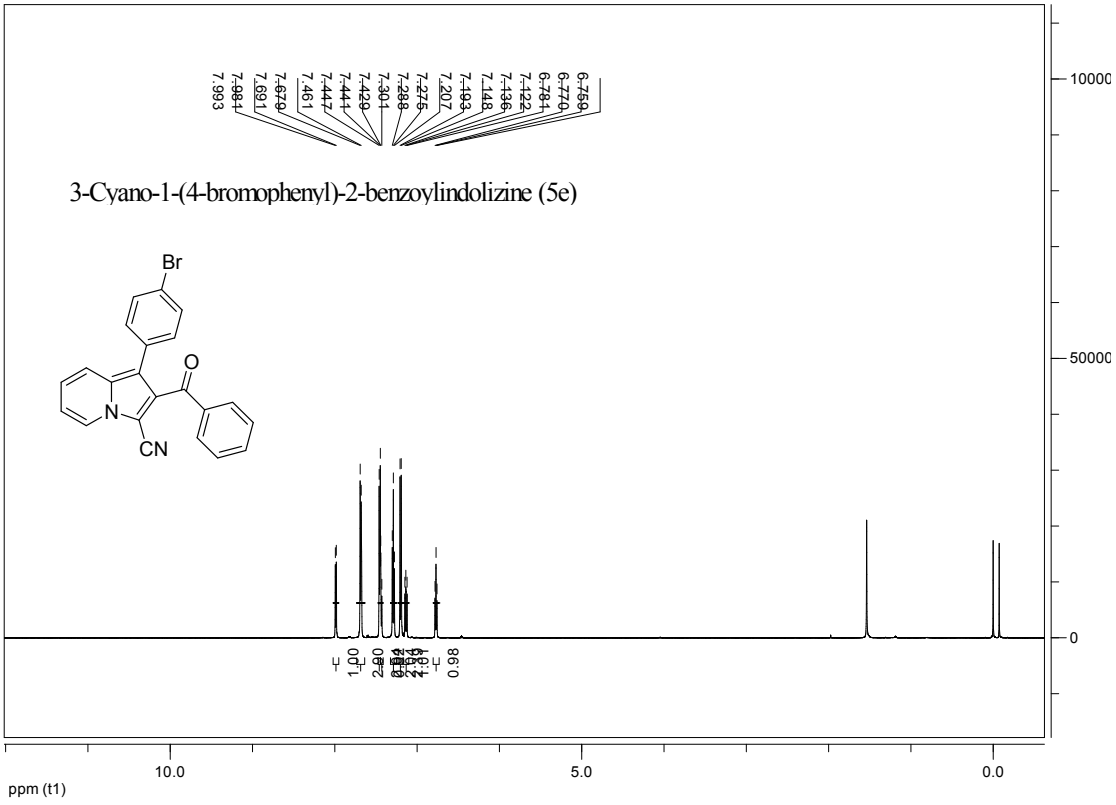


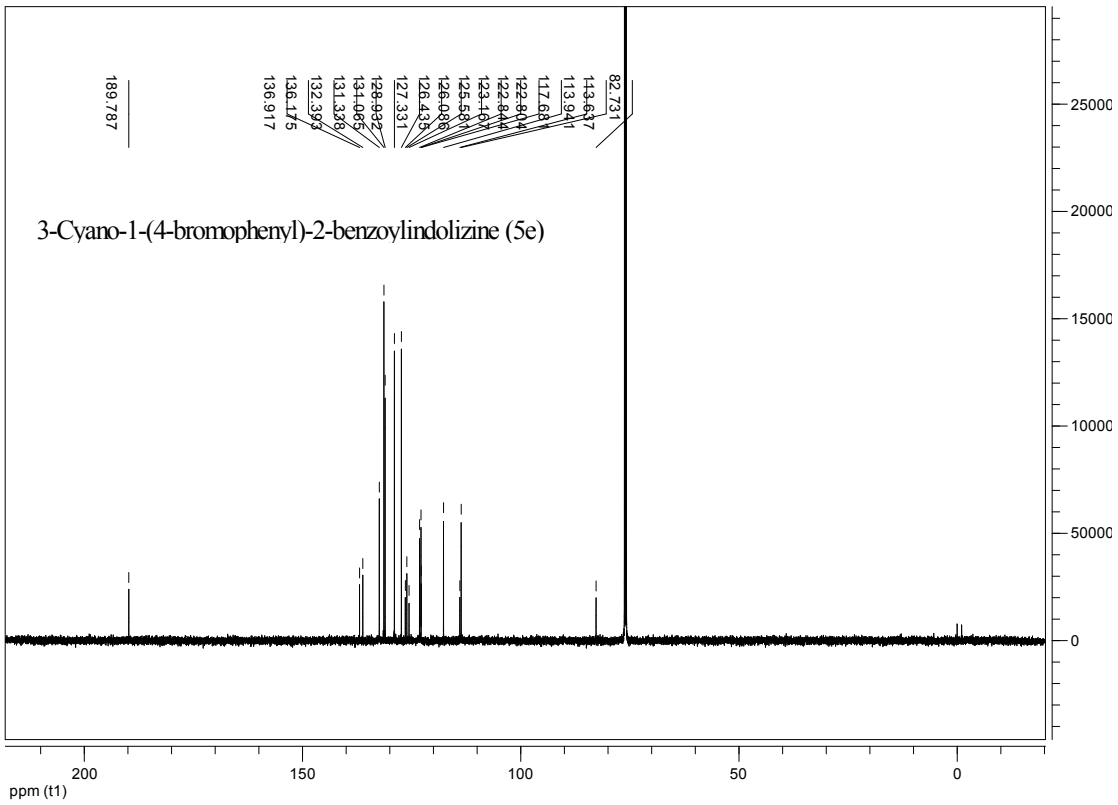
3-Cyano-1-(3-bromophenyl)-2-benzoylindolizine (5d)



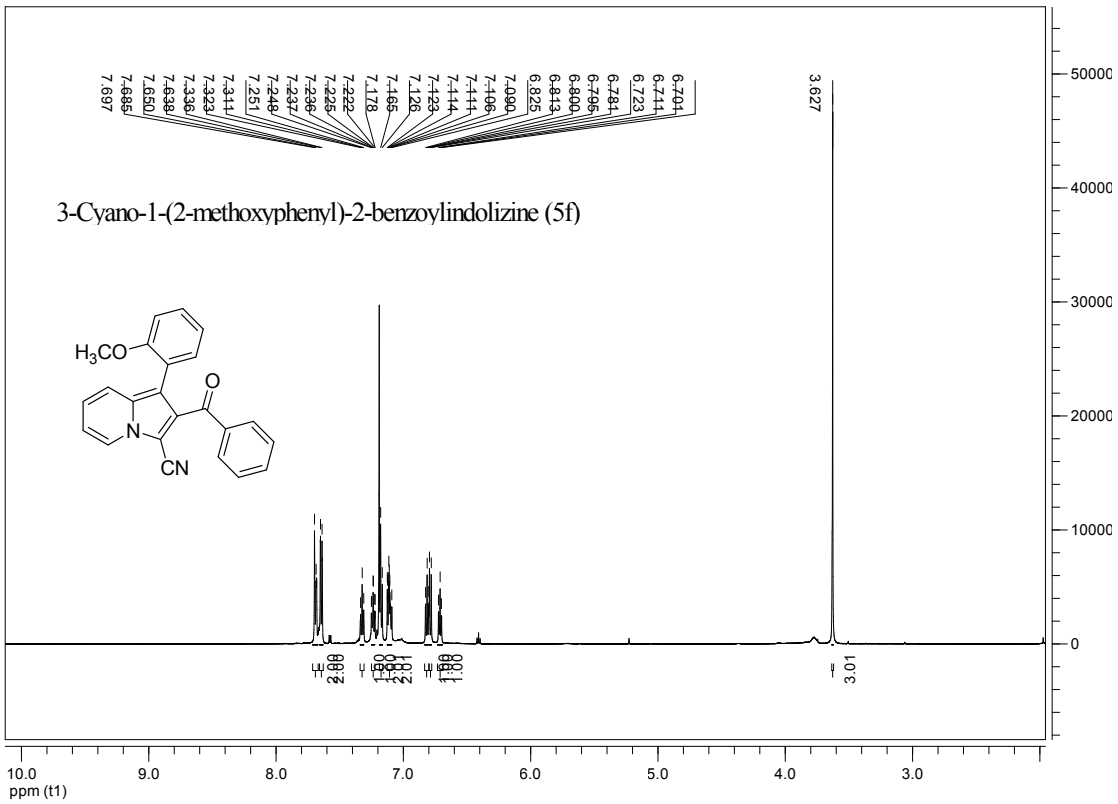


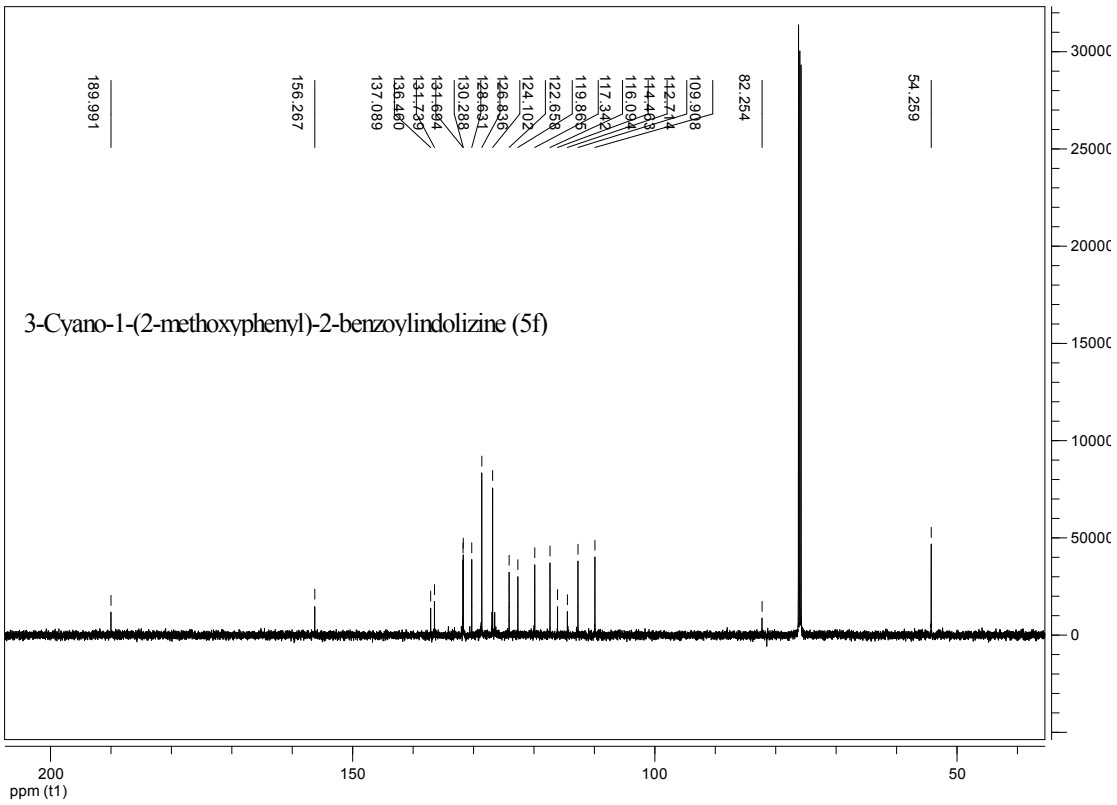
3-Cyano-1-(4-bromophenyl)-2-benzoylindolizine (5e)



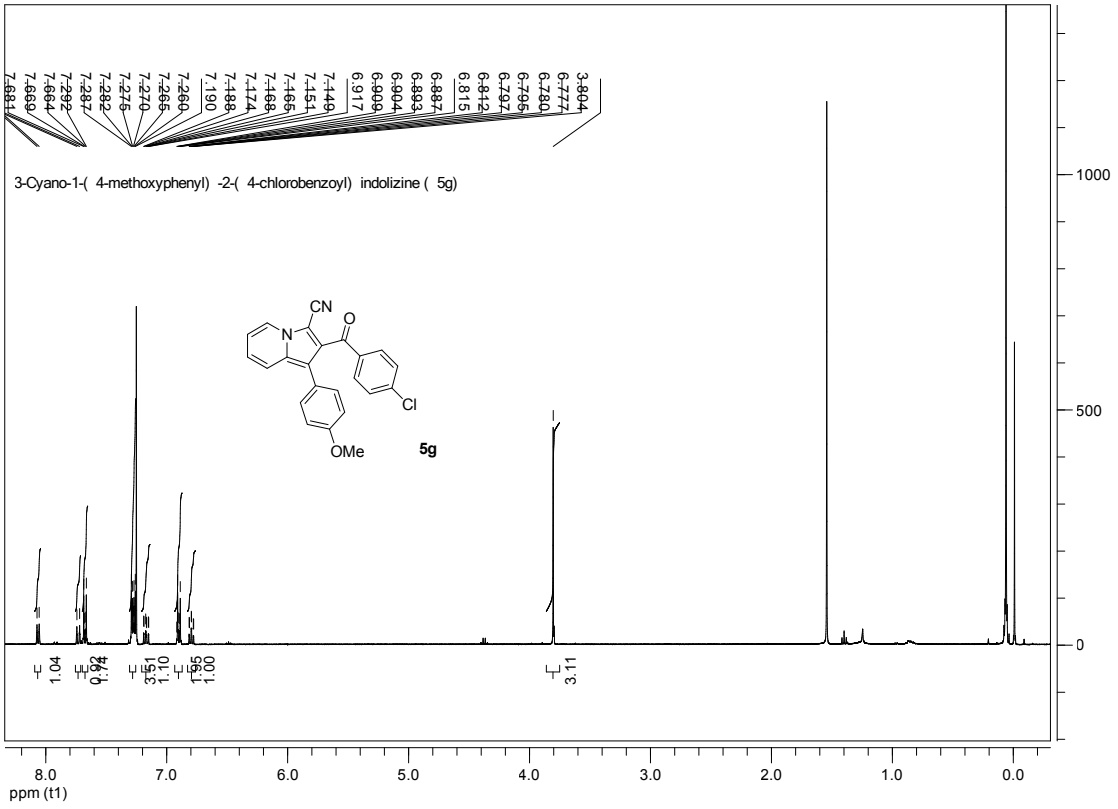


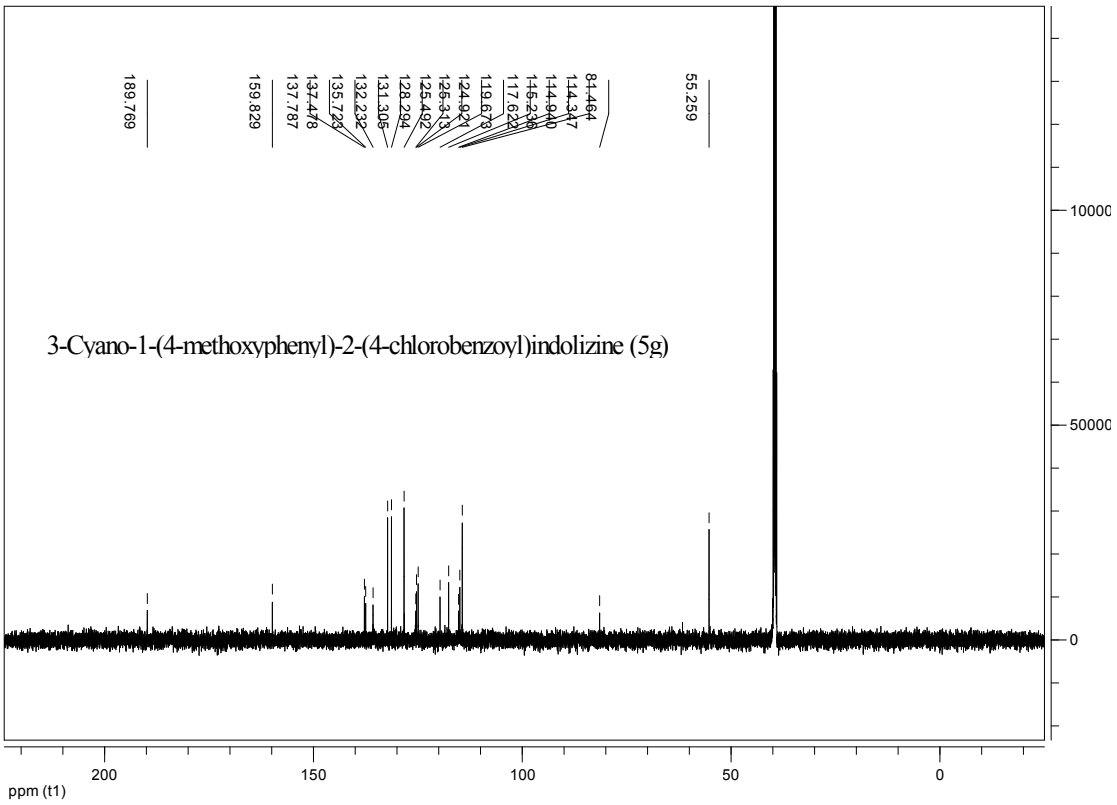
3-Cyano-1-(2-methoxyphenyl)-2-benzoylindolizine (5f)





3-Cyano-1-(4-methoxyphenyl)-2-(4-chlorobenzoyl)indolizine (5g)





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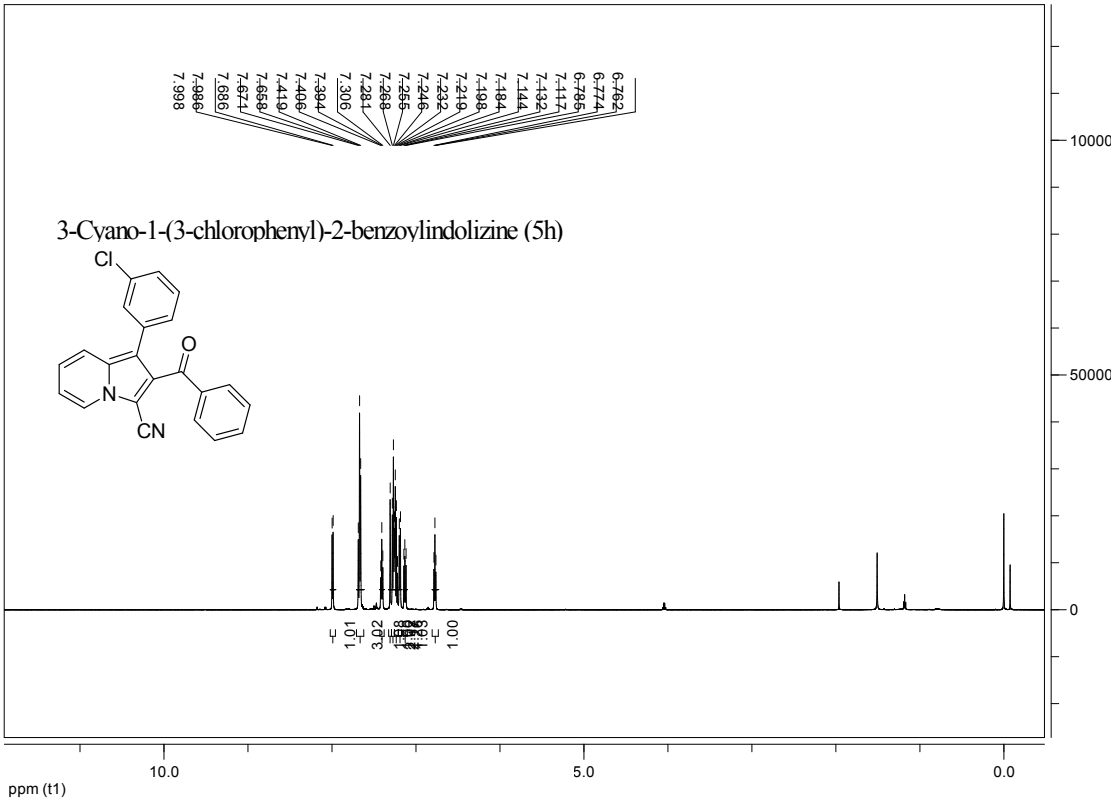

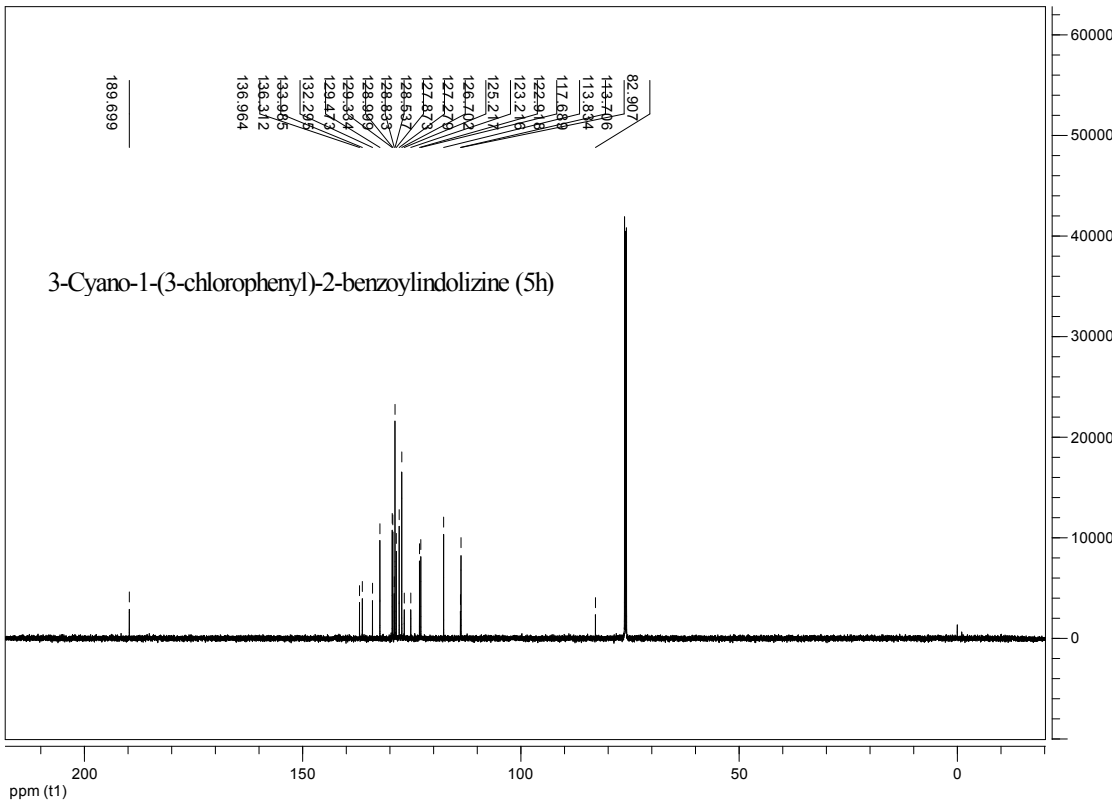

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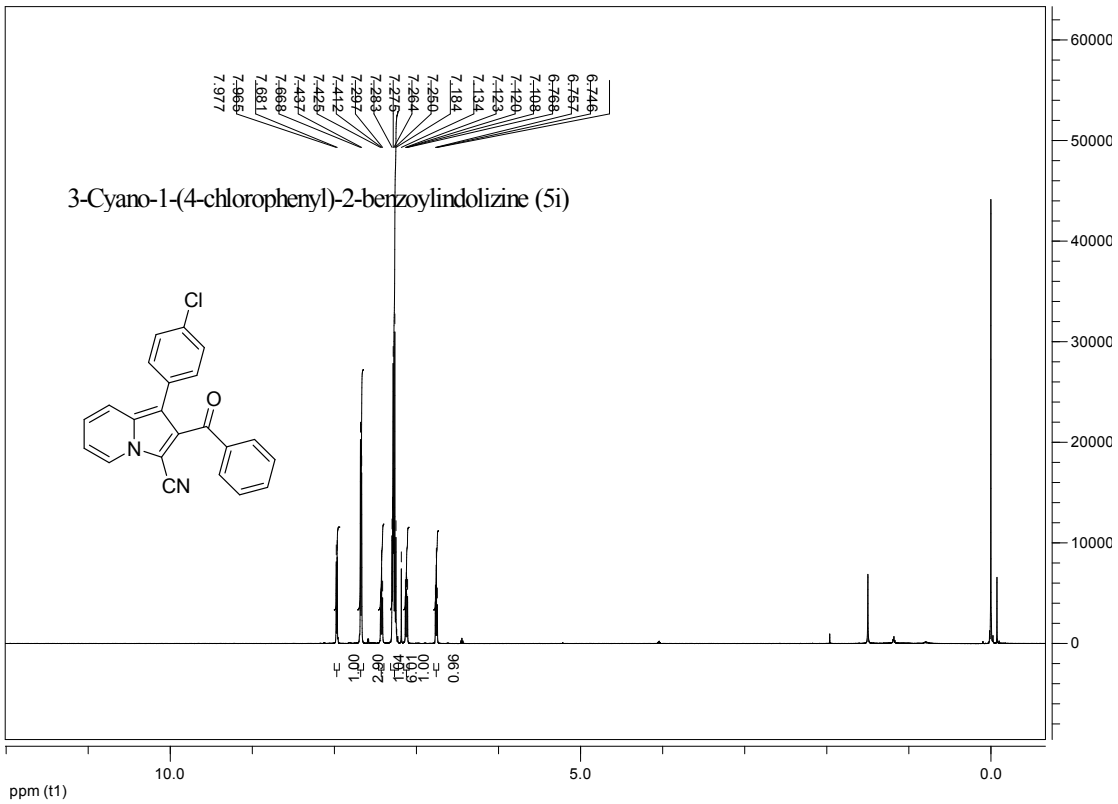

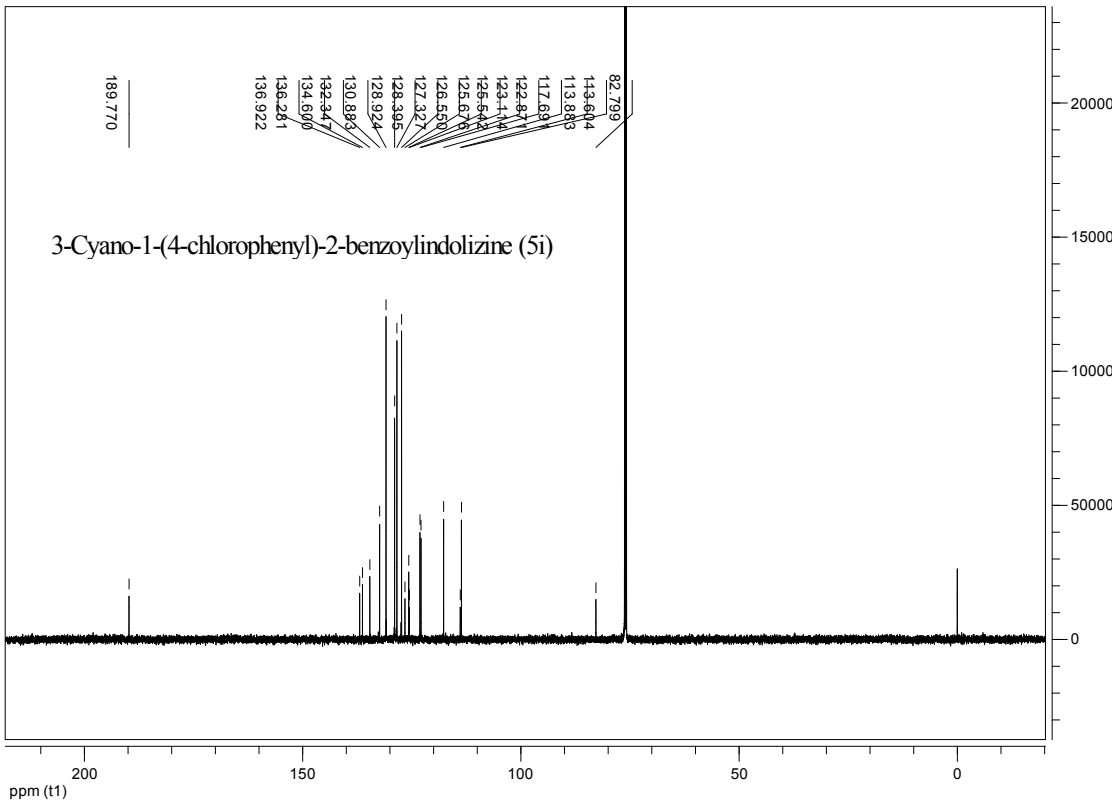

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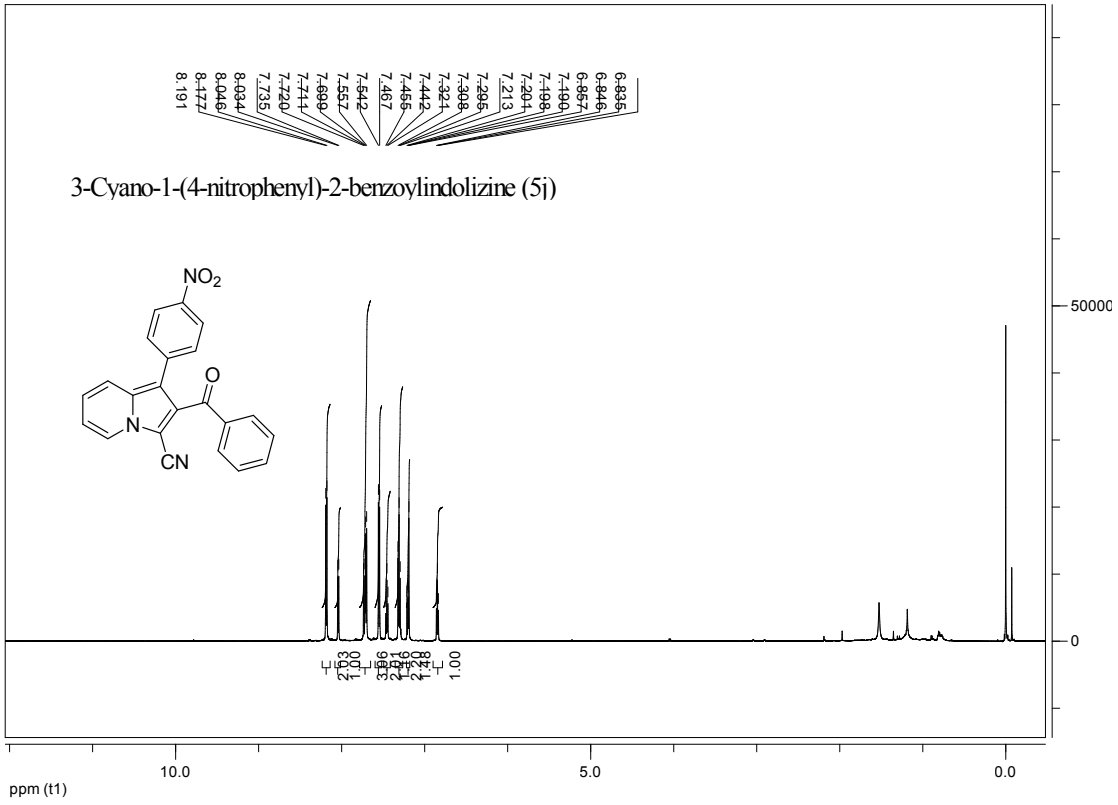
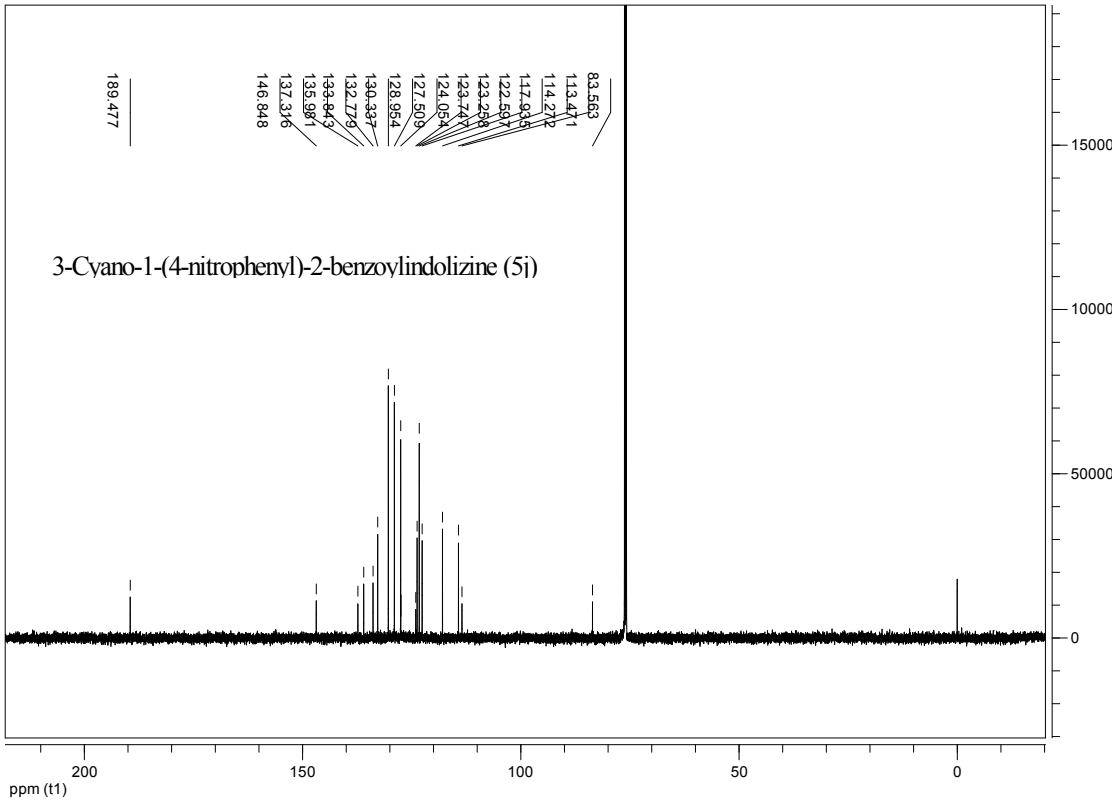
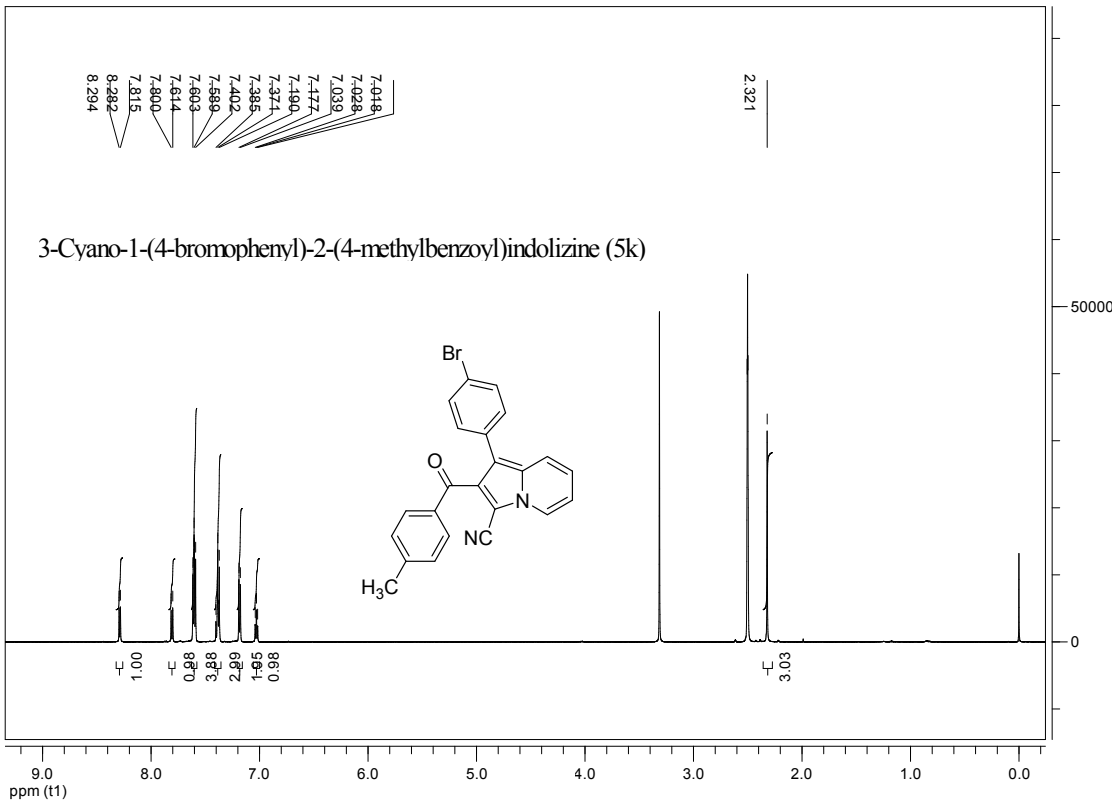
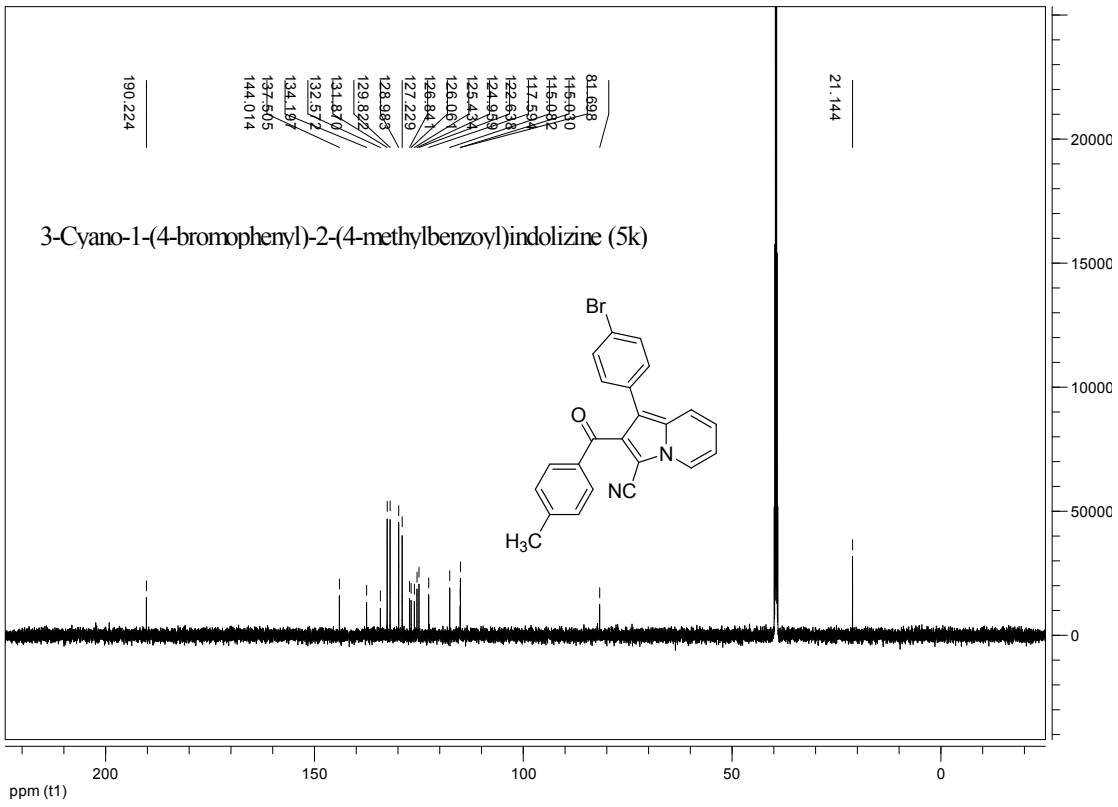


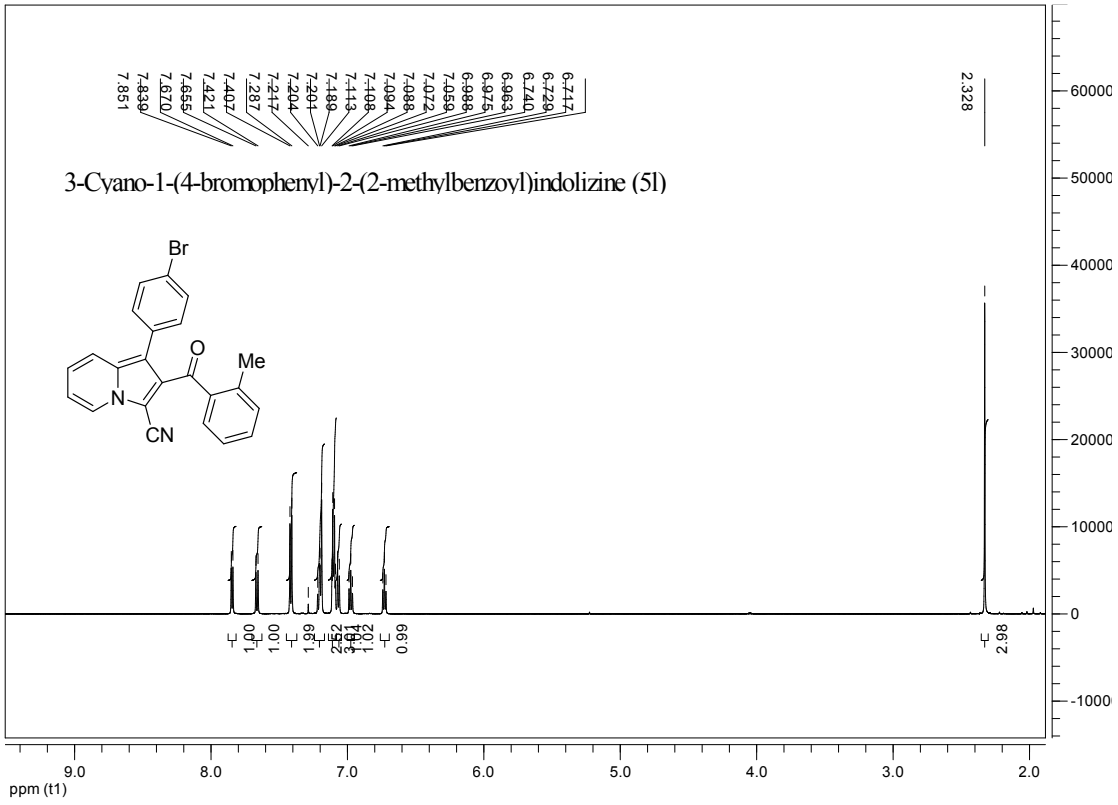


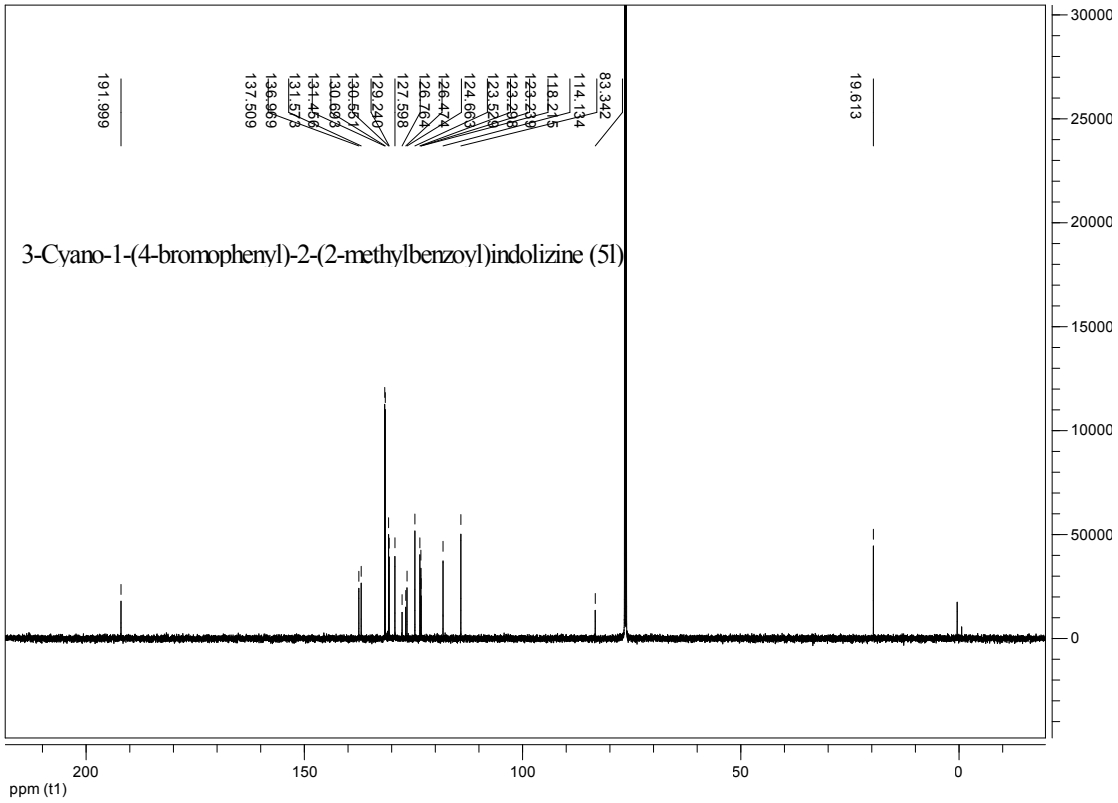
3-Cyano-1-(4-bromophenyl)-2-(4-methylbenzoyl)indolizine (5k)



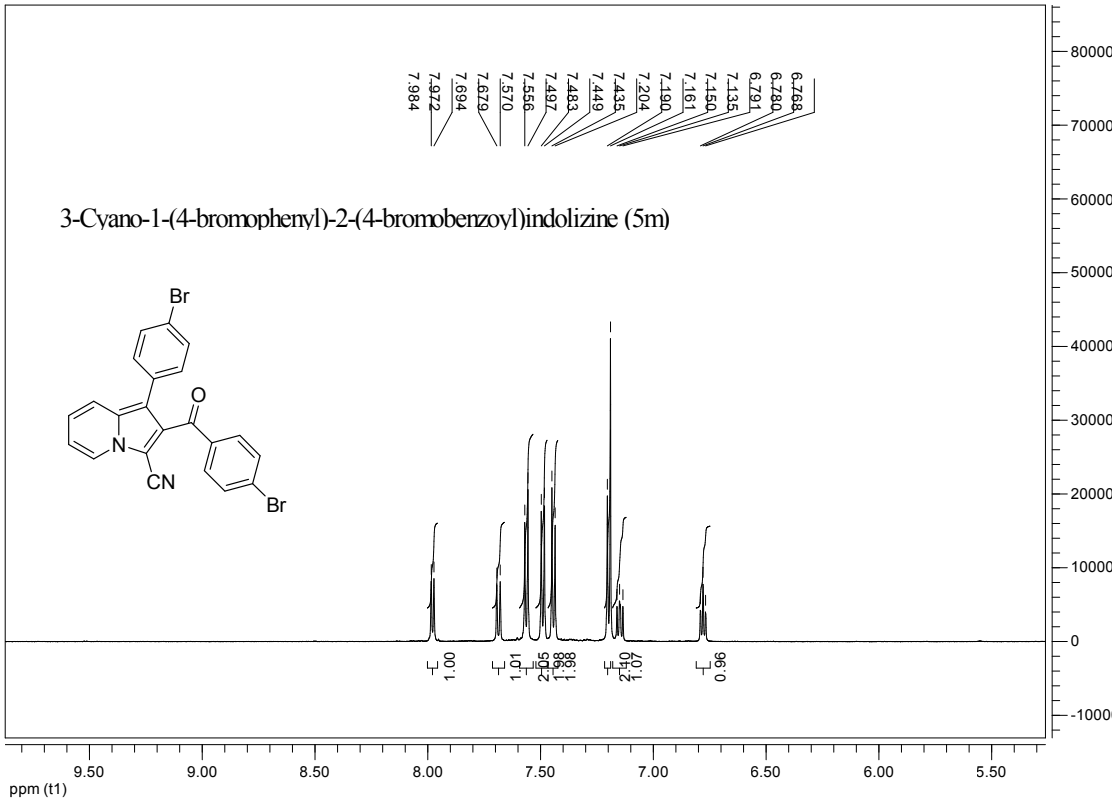


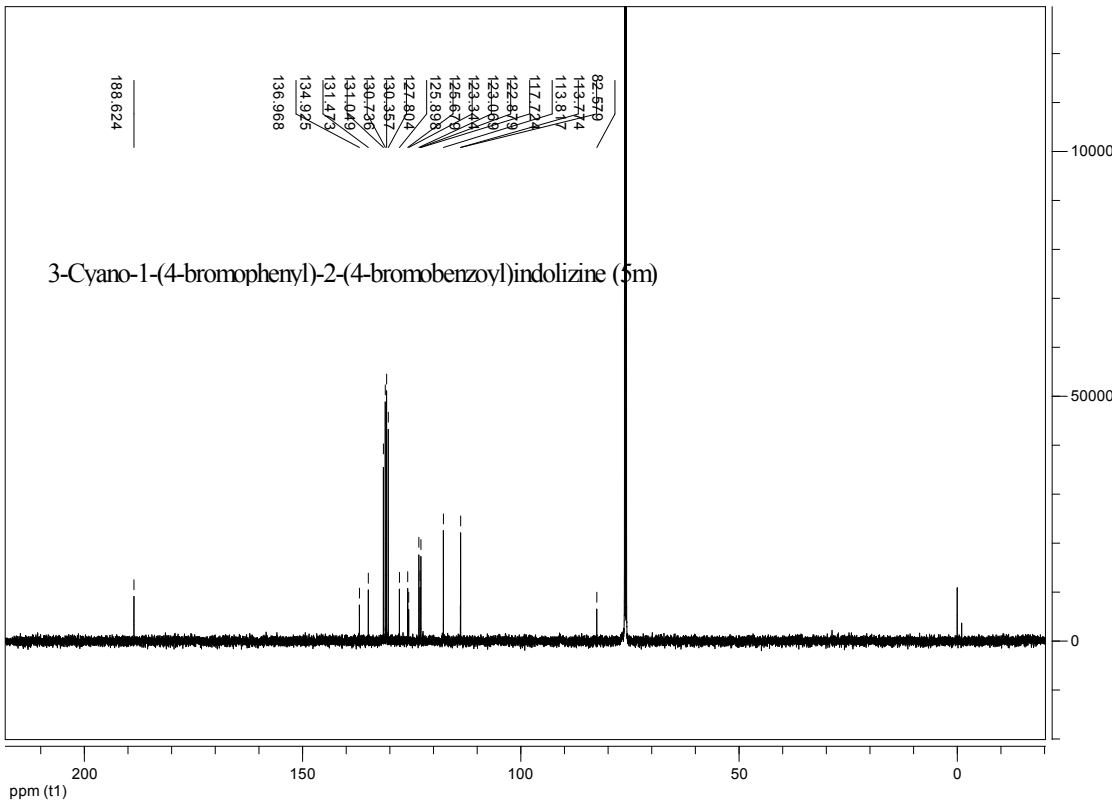
3-Cyano-1-(4-bromophenyl)-2-(2-methylbenzoyl)indolizine (5l)



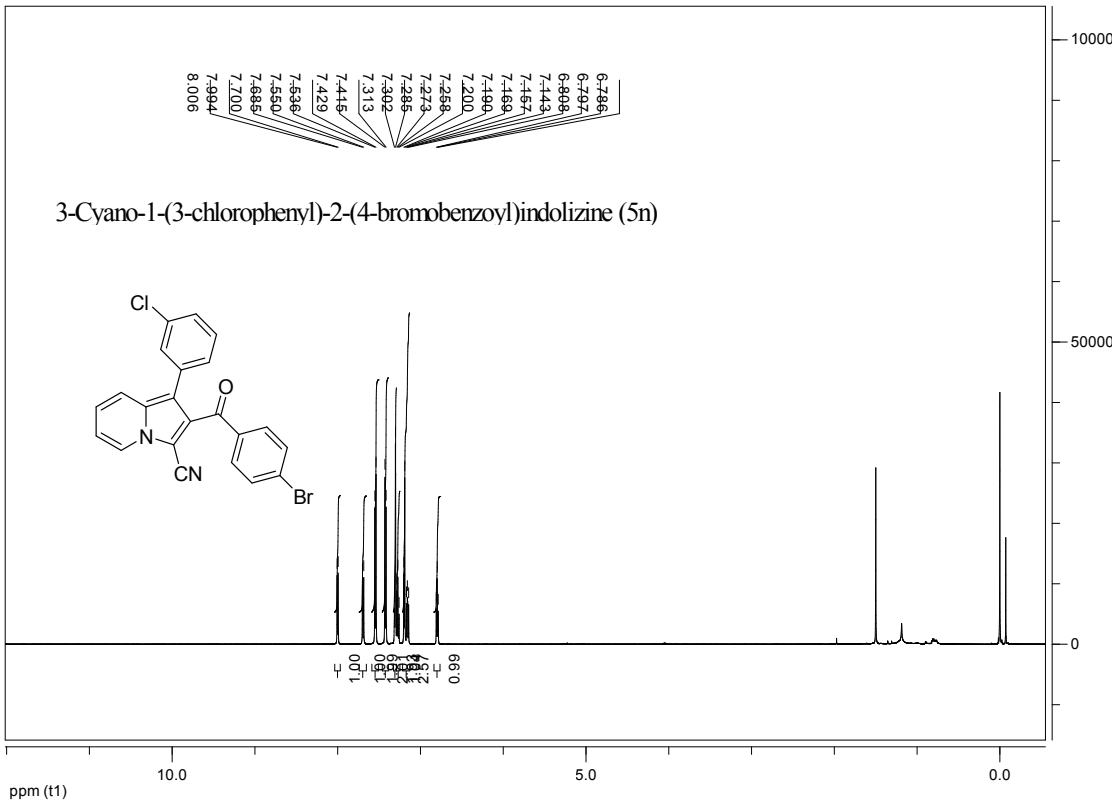


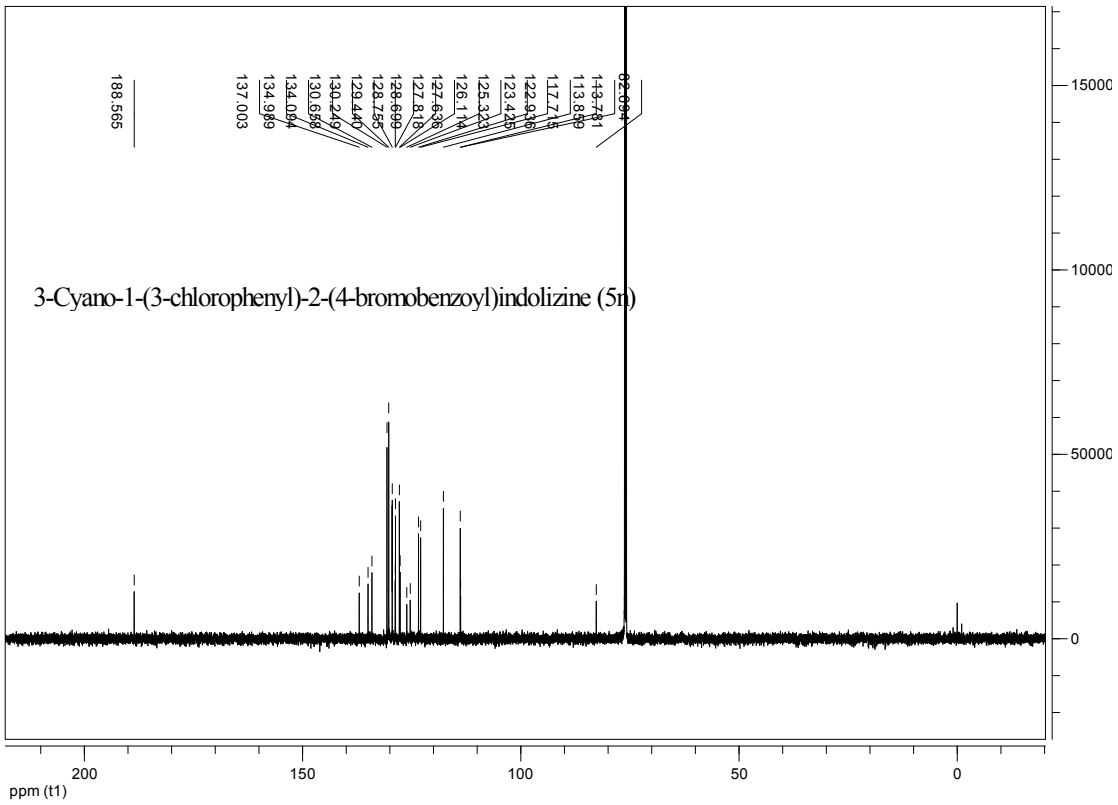
3-Cyano-1-(4-bromophenyl)-2-(4-bromobenzoyl)indolizine (5m)





3-Cyano-1-(3-chlorophenyl)-2-(4-bromobenzoyl)indolizine (5n)

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15000
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50000
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200
150
100
50
0
ppm (t1)