Supporting information

Coordination Effect Enabled Palladium Catalyzed Regioselective *O*-Alkylation of 2-Pyridones

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1. General information

1.1 Materials

All manipulations are carried out under a nitrogen atmosphere by using standard Schlenk techniques unless otherwise stated. Solvent such as DCM/Toluene are distilled under nitrogen from sodium-benzophenone. All other starting materials are obtained commercially as analytical-grade from Innochem. Reagent Co., Ltd (BeiJing, China) and used without further purification.

Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on The German Bruker AVANCE III 400 MHz plus. spectrometer as indicated. Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on The Bruker AVANCE III 400 MHz plus (100 MHz) spectrometer as indicated. The chemical shifts of ^{1}H and ^{13}C NMR were relative to TMS. Coupling constants (*J*) are reported in Hz with the following splitting abbreviations: s = singlet, d = doublet, t = triplet, m = multiple, dd = double doublet. The melting point was determined on Shanghai INESA Physico-Optical Instrument Co., Ltd., SGWX-4 Melting-point Apparatus with Microscope. Thermo Scientific TM Q ExactiveTM (ESI mode) was employed for High resolution mass spectra determination.

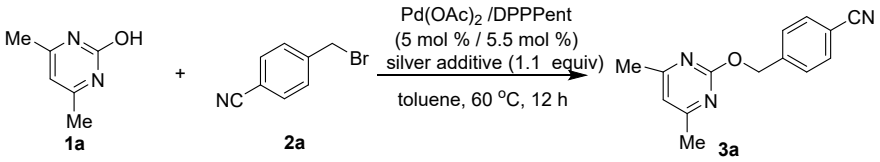
The X-ray diffraction data were collected at 290 K on an Oxford Diffraction Gemini with MoKα radiation (λ=0.71073Å). Crystalline powder of compounds (**4a, 3i-8, 3j-1**) suitable for X-ray structural analysis is obtained by slow evaporation of their ether acetate/PE mixed solutions. A crystal with approximate dimensions of 0.1 × 0.1 × 0.1 mm^3, 0.18 × 0.18 × 0.18 mm^3, 0.1 × 0.1 × 0.1 mm^3 respectively for **4a, 3i-8, 3j-1**) is mounted on a glass fiber for diffraction experiment. The Olex2 program was used as an interface, together with the SHELXT and SHELXL programs to solve the structures. All non-H atoms are refined anisotropically. Positions of hydrogen atoms were located geometrically and refined using a riding model. Crystallographic data for the structure in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplemental publication (CCDC No. is 2100786; 2100848, 2100785 respectively).

2. Experimental Section

General experimental procedure:

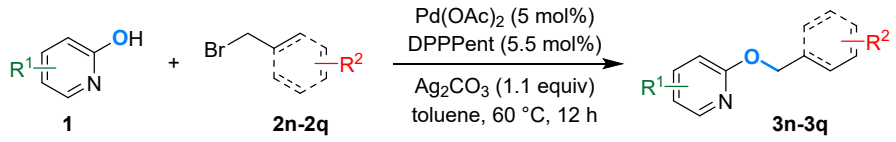
All the reaction was run following the same procedure: mixture the compound of hydroxylpyridine (0.25 mmol, 1 equiv) and the benzyl bromide (0.25 mmol, 1 equiv) in solvent of 1 mL toluene to the Schlenk tube, then add with $Pd(OAc)_2$ (5 mol%), DPPPent (5.5 mol%), silver carbonate (1.1 equiv) under N_2 atmosphere, then heating the reaction system to at 60 °C for about 12 hours. When the reaction finished, filtered and concentrated under reduced pressure. Subject the reaction mixture to the column directly, run the column by PE/EA eluent system in appropriate ratio, the ideal product will be obtained.

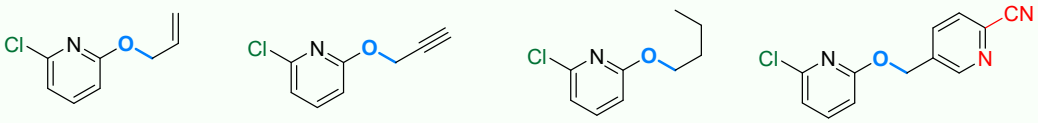
Table S1 The silver additive test in the optimization reaction condition



Entry	Silver Additive	Yield %[a]
1	AgO	45
2	$AgNO_3$	51
3	AgOAc	64
4	AgOTf	25

Reaction conditions: 1a (0.25 mmol), 2a (0.25 mmol), toluene (1 mL), $Pd(OAc)_2$ (5 mol %), DPPPent(5.5 mol %), silver (1.1 equiv), 12 h, 60 °C, under nitrogen atmosphere. [a] Isolated yields were provided.

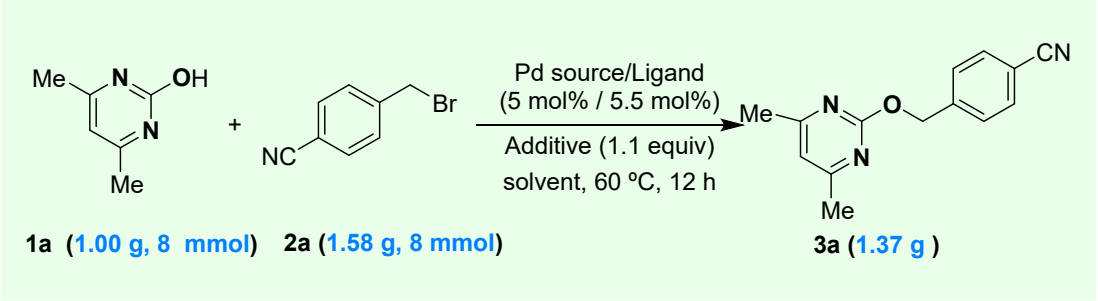




Scheme S1-1 Extensive substrate scope exploring with respect to other general halide

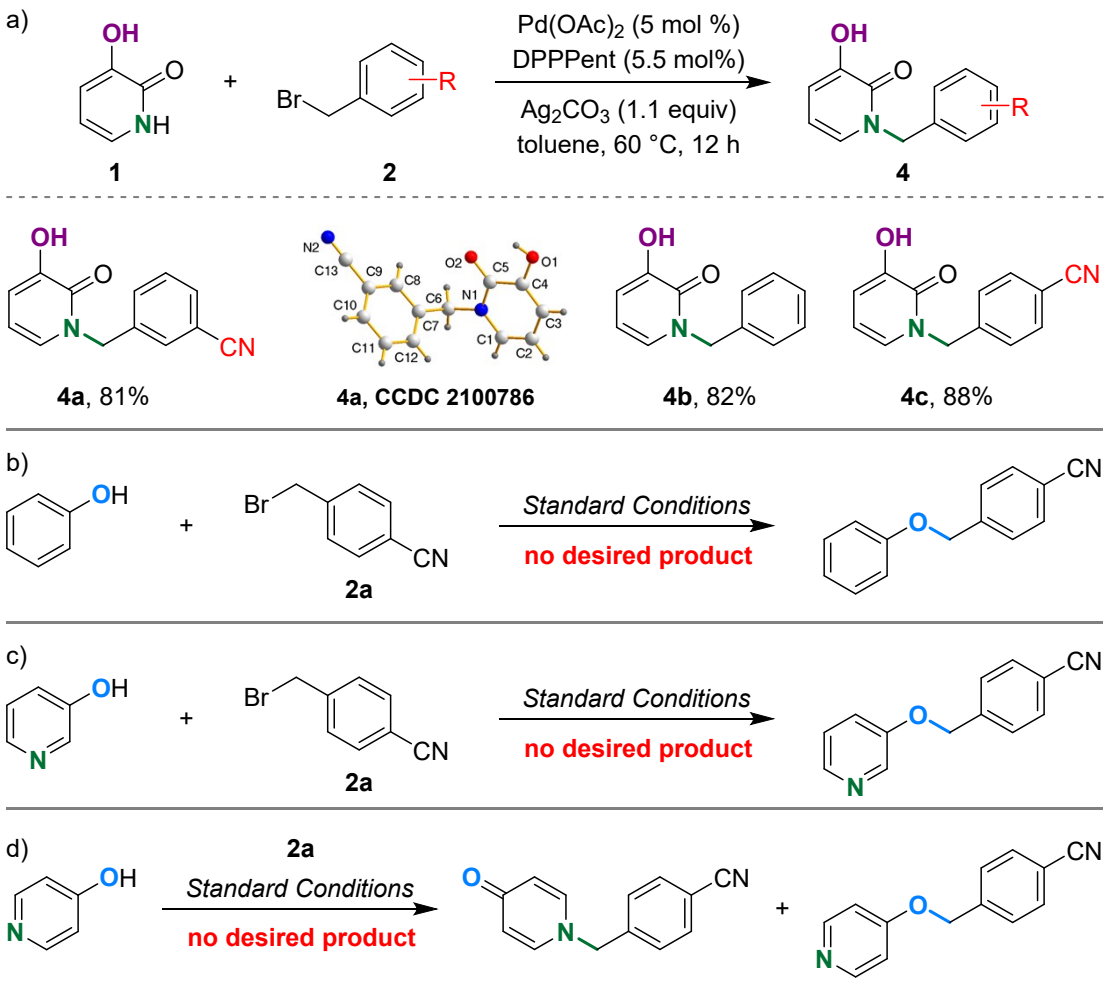
derivatives.[a]

[a]The reaction were performed with **1** (0.25 mmol), **2n-2q** (0.25 mmol), $Pd(OAc)_2$ (5 mol %), DPPPent (5.5 mol %) and Ag_2CO_3 (1.1 equiv) in toluene (1 mL) at 60 °C for 12 h under N_2 atmosphere. Isolated yields were provided.



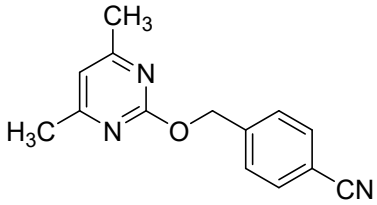
Scheme S1-2 Scale-up experiment.[a]

[a]The reaction were performed with **1a** (8 mmol), **2a** (8 mmol), $Pd(OAc)_2$ (5 mol %), DPPPent (5.5 mol %) and Ag_2CO_3 (1.1 equiv) in toluene (1 mL) at 60 °C for 12 h under N_2 atmosphere. Isolated yields were provided.



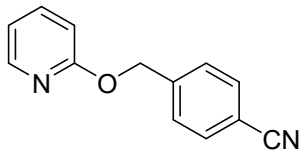
Scheme S2 Rational-Designed Substrates for *N*-Alkylation and Control Experiments.

2.1. Synthesis of 3a: *4-((4,6-dimethylpyrimidin-2-yloxy)methyl)benzonitrile*



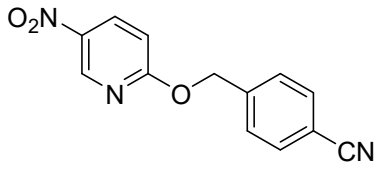
To run the reaction followed the above general procedure, and the white solid was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) 7.65 (d, J = 8.3 Hz, 2H), 7.59 (d, J = 8.1 Hz, 2H), 6.71 (s, 1H), 5.46 (s, 2H), 2.41 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.6, 164.5, 142.5, 132.3, 128.3, 119.0, 114.7, 111.6, 67.6, 24.0. IR (KBr): 2228 (s), 1602 (s), 1507 (m), 1340 (s), 1109 (s), 856 (w), 816 (s), 642 (m), 576 (m), 546 (s). m.p.: 117.0 -117.8 °C. HRMS(ESI-TOF) m/z: $[M + H]^+$: calcd. for $[C_{14}H_{13}N_3O + H]^+$ 240.1137; found 240.1139.

2.2. Synthesis of 3a-1: *4-((pyridin-2-yloxy)methyl)benzonitrile*



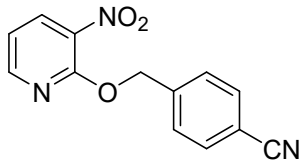
To run the reaction followed the above general procedure, and the gray solid was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, *J* = 4.8 Hz, 1H), 7.66 (d, *J* = 7.9 Hz, 2H), 7.61 (d, *J* = 7.5 Hz, 1H), 7.55 (d, *J* = 7.9 Hz, 2H), 6.98 – 6.89 (m, 1H), 6.84 (d, *J* = 8.3 Hz, 1H), 5.45 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.1, 145.0, 143.2, 139.1, 132.4, 128.0, 119.0, 117.6, 111.5, 111.4, 66.3. IR (KBr): 1560 (vs), 1541 (s), 1508 (s), 1458 (m), 1339 (m), 1140 (w). m.p.: 54.3 - 55.5 °C.

2.3. Synthesis of 3a-2: *4-((5-nitropyridin-2-yloxy)methyl)benzonitrile*



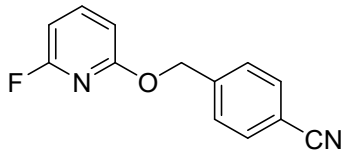
To run the reaction followed the above general procedure, and the yellow solid was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.08 (s, 1H), 8.41 (d, *J* = 8.1 Hz, 1H), 7.69 (d, *J* = 7.0 Hz, 2H), 7.57 (d, *J* = 7.3 Hz, 2H), 6.94 (d, *J* = 8.9 Hz, 1H), 5.56 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 144.8, 141.5, 140.0, 134.5, 132.5, 128.4, 118.7, 112.2, 111.6, 68.0. IR (KBr): 2230 (s), 1607 (s), 1579 (vs), 1507 (s), 1472 (s), 1458 (s), 1407 (m), 1346 (s), 1319 (m), 1115 (m), 988 (s), 895 (m), 823 (m). m.p.: 158.7 -159.7 °C. HRMS(ESI-TOF) m/z: [M + H]$^{+}$: calcd. for $[C_{13}H_9N_3O_3 + H]^{+}$ 256.0722; found 256.0716.

2.4. Synthesis of 3a-3: *4-((3-nitropyridin-2-yloxy)methyl)benzonitrile*



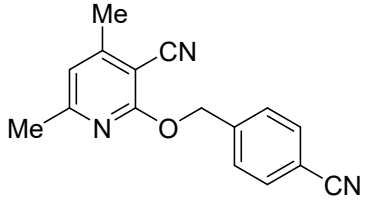
To run the reaction followed the above general procedure, and the white solid was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (dd, *J* = 4.8, 1.8 Hz, 1H), 8.34 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.69 (d, *J* = 8.3 Hz, 2H), 7.63 (d, *J* = 8.3 Hz, 2H), 7.11 (dd, *J* = 7.9, 4.8 Hz, 1H), 5.64 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.6, 151.8, 141.6, 135.5, 132.6, 127.8, 118.8, 117.5, 111.9, 94.1, 67.7. IR (KBr): 2920 (m), 1599 (s), 1572 (m), 1452 (vs), 1300 (s), 1243 (m), 1016 (m), 886 (w), 819 (w), 766 (m). m.p.: 156.1 - 157.9 °C. HRMS(ESI-TOF) m/z: $[M+H]^+$: calcd. for $[C_{13}H_9N_3O_3 + H]^+$ 256.0722; found 256.0714.

2.5. Synthesis of 3a-4: *4-((6-fluoropyridin-2-yloxy)methyl)benzonitrile*



To run the reaction followed the above general procedure, and the colorless crystal was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 – 7.68 (m, 1H), 7.66 (d, *J* = 3.8 Hz, 2H), 7.55 (d, *J* = 8.2 Hz, 2H), 6.70 (dd, *J* = 8.0, 1.1 Hz, 1H), 6.52 (dd, *J* = 7.8, 2.4 Hz, 1H), 5.40 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.4, 163.2, 143.1, 142.3, 132.4, 128.2, 118.8, 111.8, 107.5, 100.9, 67.0. IR (KBr): 2955 (w), 2944 (w), 2227 (s), 1602 (vs), 1570 (s), 1559 (s), 1508 (m), 1445 (s), 1373 (w), 1315 (s), 1228 (s), 1018 (m), 1016 (m), 795 (m), 548 (s). m.p.: 122.3 - 122.7 °C.

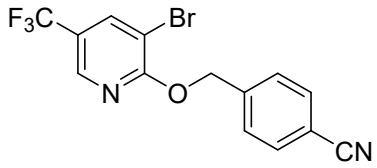
2.6. Synthesis of 3a-5: *2-((4-cyanobenzyl)oxy)-4,6-dimethylnicotinonitrile*



To run the reaction followed the above general procedure, and the white solid was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.3 Hz, 2H), 7.59 (d, *J* = 8.3 Hz, 2H), 6.74 (s, 1H), 5.53 (s, 2H), 2.47 (s, 3H), 2.44 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 162.5, 153.1, 148.3, 144.2, 141.0, 124.7, 123.7, 117.1, 109.4, 92.1, 66.7, 29.7, 27.4. IR (KBr): 2925 (m), 2223 (m), 1600 (m), 1338 (m), 1340 (m), 1156 (m), 1108 (m), 1021 (w), 862 (w), 823 (m).

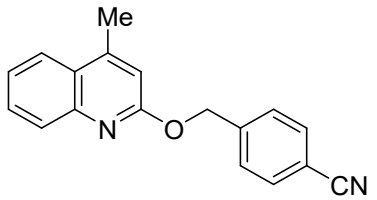
White solid , m.p.: 162.2 - 163.5 °C.

2.7. Synthesis of 3a-6: *4-((3-bromo-5-(trifluoromethyl)pyridin-2-yloxy)methyl) benzonitrile*



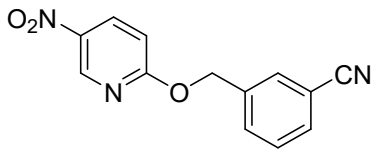
To run the reaction followed the above general procedure, and the white solid was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (s, 1H), 8.07 (d, *J* = 1.8 Hz, 1H), 7.69 (d, *J* = 8.2 Hz, 2H), 7.60 (d, *J* = 8.2 Hz, 2H), 5.56 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.2, 143.3, 141.6, 139.1, 132.5, 127.8, 124.3, 121.8, 118.7, 112.0, 107.5, 68.1. IR (KBr): 2946 (w), 2922 (w), 1606 (s), 1487 (s), 1448 (s), 1407 (s), 1317 (vs), 1156 (s), 1051 (s), 931 (m), 818 (m), 756 (m), 639 (m), 549 (s). White solid, m.p.: 126.8 - 128.4 °C. HRMS(ESI-TOF) m/z: $[M + Na]^+$: calcd. for $[C_{14}H_8N_3BrF_3N_2O + Na]^+$ 378.9670; found 378.9657.

2.8. Synthesis of 3a-7: *4-((4-methylquinolin-2-yloxy)methyl)benzonitrile*



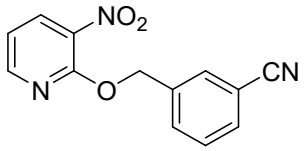
To run the reaction followed the above general procedure, and the white solid was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.86 – 7.81 (m, 2H), 7.75 (d, *J* = 8.1 Hz, 1H), 7.67 – 7.57 (m, 2H), 7.52 – 7.39 (m, 2H), 6.84 (d, *J* = 0.8 Hz, 1H), 5.57 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.2, 147.5, 144.2, 139.4, 132.4, 131.6, 131.5, 129.6, 129.3, 127.9, 125.8, 124.3, 123.9, 113.0, 66.0, 19.0. IR (KBr): 2928 (w), 2230 (m), 1655 (m), 1560 (s), 1508 (s), 1457 (s), 1395 (w), 1338 (m), 1185 (m), 1059 (m), 853 (w), 811 (w), 756 (m). White solid, m.p.: 206.1 - 208.8 °C. HRMS(ESI-TOF) m/z: $[M + H]^+$: calcd. for $[C_{18}H_{14}N_2O + H]^+$ 275.1184; found 275.1161.

2.9. Synthesis of 3b-1: *3-((5-nitropyridin-2-yloxy)methyl)benzonitrile*



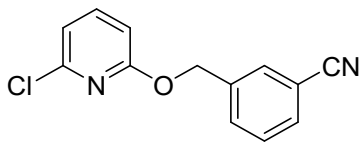
To run the reaction followed the above general procedure, and the white solid was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.08 (s, 1H), 8.41 (d, *J* = 6.7 Hz, 1H), 7.77 (s, 1H), 7.70 (d, *J* = 6.2 Hz, 1H), 7.64 (d, *J* = 6.3 Hz, 1H), 7.53 (d, *J* = 7.2 Hz, 1H), 6.94 (d, *J* = 8.8 Hz, 1H), 5.53 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 144.8, 140.0, 137.8, 134.5, 132.4, 132.0, 131.6, 129.6, 118.6, 113.0, 111.6, 67.8. IR (KBr): 2937 (m), 1654 (w), 1615 (s), 1581 (s), 1560 (m), 1490 (s), 1454 (s), 1350 (vs), 1316 (m), 1115 (w), 1033 (m), 843 (s), 792 (m). m.p.: 127.7 - 129.5 °C. HRMS(ESI-TOF) m/z: $[M + H]^+$: calcd. for $[C_{13}H_9N_3O_3 + H]^+$ 256.0722; found 256.0724.

2.10. Synthesis of 3b-2: *3-((3-nitropyridin-2-yloxy)methyl)benzonitrile*



To run the reaction followed the above general procedure, and the white solid was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (d, *J* = 2.7 Hz, 1H), 8.33 (d, *J* = 6.9 Hz, 1H), 7.78 (m, 2H), 7.62 (d, *J* = 7.0 Hz, 1H), 7.51 (t, *J* = 7.4 Hz, 1H), 7.17 – 7.05 (m, 1H), 5.61 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.6, 151.7, 137.8, 135.5, 134.2, 131.9, 131.1, 129.6, 118.8, 117.4, 112.8, 67.5. IR (KBr): 2960 (w), 2880 (w), 2360 (m), 1636 (m), 1559 (s), 1507 (m), 1458 (s), 1315 (m), 1055 (s), 972 (m), 668 (m). m.p.: 178.6 - 180.2 °C. HRMS(ESI-TOF) m/z: $[M + H]^+$: calcd. for $[C_{13}H_9N_3O + H]^+$ 256.0722; found 256.0721.

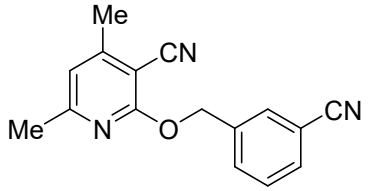
2.11. Synthesis of 3b-3: *3-((6-chloropyridin-2-yloxy)methyl)benzonitrile*



To run the reaction followed the above general procedure, and the white solid was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (s, 1H), 7.69 (d, *J* = 7.8 Hz, 1H), 7.62 (d, *J* = 7.7 Hz, 1H), 7.57 (t, *J* = 7.9 Hz,

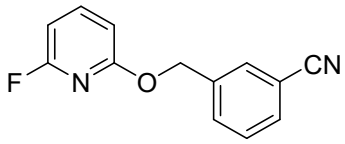
1H), 7.49 (t, *J* = 7.7 Hz, 1H), 6.95 (d, *J* = 7.5 Hz, 1H), 6.75 (d, *J* = 8.2 Hz, 1H), 5.39 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.7, 148.3, 141.1, 138.4, 132.3, 131.6, 131.4, 129.4, 118.8, 117.1, 112.7, 109.4, 66.8. IR (KBr): 2935 (w), 2835 (w), 2357 (w), 1556 (w), 1540 (w), 1506 (w), 1373 (w), 1250 (m), 1230 (m), 1125 (m), 1061 (m), 826 (w). m.p.: 187.2 - 188.4 °C. HRMS(ESI-TOF) m/z: $[M + H]^+$: calcd. for $[C_{13}H_9ClN_2O + H]^+$ 245.0482; found 245.0464.

2.12. Synthesis of 3b-4: *2-(3-cyanobenzyloxy)-4,6-dimethylnicotinonitrile*



To run the reaction followed the above general procedure, and the white solid was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, *J* = 7.2 Hz, 2H), 7.38 (t, *J* = 7.3 Hz, 2H), 7.32 (d, *J* = 7.1 Hz, 1H), 6.70 (s, 1H), 5.48 (s, 2H), 2.45 (s, 3H), 2.44 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.1, 160.7, 154.9, 138.3, 132.2, 131.7, 131.4, 129.5, 118.7, 118.3, 114.5, 112.7, 94.3, 66.9, 24.7, 24.57. IR (KBr): 2380 (w), 2310 (w), 1604 (s), 1560 (vs), 1541 (s), 1508 (vs), 1458 (s), 1419 (m), 1339 (m). m.p.: 173.2 - 175.3 °C. HRMS(ESI-TOF) m/z: $[M + H]^+$: calcd. for $[C_{16}H_{13}N_3O + H]^+$ 264.1137; found 264.1141.

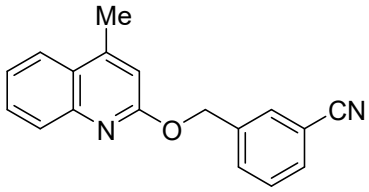
2.13. Synthesis of 3b-5: *3-((6-fluoropyridin-2-yloxy)methyl)benzonitrile*



To run the reaction followed the above general procedure, and the white solid was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (s, 1H), 7.68 (m, 2H), 7.62 (d, *J* = 6.0 Hz, 1H), 7.50 (d, *J* = 6.8 Hz, 1H), 6.71 (d, *J* = 7.0 Hz, 1H), 6.53 (d, *J* = 5.3 Hz, 1H), 5.37 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.4, 162.1, 143.1, 138.5, 132.2, 131.7, 131.5, 129.4, 118.8, 112.8, 107.5, 100.4, 66.8. IR (KBr): 1869 (m),1628 (s), 1560 (s), 1507 (s), 1470 (m), 1457 (m), 1290 (w), 1216 (m), 1069 (m), 1041 (m), 818 (w). m.p.: 189.9 - 191.6 °C. HRMS(ESI-TOF) m/z:

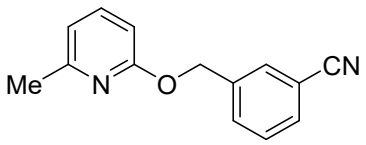
[M + H]$^+$: calcd. for [$C_{13}H_9FN_2O$ + H]$^+$ 229.0777; found 229.0782.

2.14. Synthesis of 3b-6: *3-((4-methylquinolin-2-yloxy)methyl)benzonitrile*



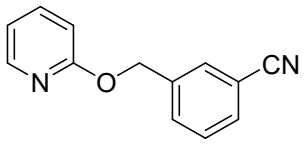
To run the reaction followed the above general procedure, and the white solid was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.1 Hz, 1H), 7.87 – 7.79 (m, 2H), 7.75 (d, *J* = 7.8 Hz, 1H), 7.69 – 7.56 (m, 2H), 7.48 (t, *J* = 7.7 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 1H), 6.84 (s, 1H), 5.57 (s, 2H), 2.65 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.2, 147.5, 146.4, 139.4, 132.4, 132.0, 131.5, 129.6, 129.3, 127.9, 125.8, 124.3, 123.9, 119.0, 112.9, 112.7, 66.0, 18.89. IR (KBr): 2229 (w), 1615 (s), 1560 (s), 1506 (s), 1456 (vs), 1340 (s), 1195 (m), 1056 (w), 753 (w). m.p.: 116.8 - 117.7 °C. HRMS(ESI-TOF) m/z: [M + H]$^+$: calcd. for [$C_{18}H_{14}N_2O$ + H]$^+$ 275.1184; found 275.1170.

2.15. Synthesis of 3b-7: *3-((6-methylpyridin-2-yloxy)methyl)benzonitrile*



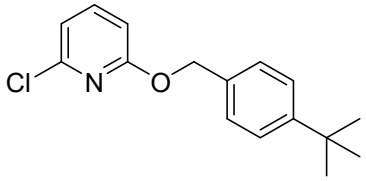
To run the reaction followed the above general procedure, and the liquid product was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 – 7.75 (m, 1H), 7.69 (d, *J* = 7.8 Hz, 1H), 7.59 (dt, *J* = 7.7, 1.5 Hz, 1H), 7.48 (q, *J* = 8.0 Hz, 2H), 6.75 (d, *J* = 7.2 Hz, 1H), 6.61 (d, *J* = 8.2 Hz, 1H), 5.40 (s, 2H), 2.44 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5, 156.3, 139.6, 139.2, 132.3, 131.5, 131.4, 129.3, 119.0, 116.6, 116.5, 107.7, 66.0, 24.3. IR (KBr): 1865 (m),1653 (m), 1648 (m), 1600 (m), 1559 (s), 1534 (vs), 1444 (m), 1312 (w), 1252 (w), 1213 (m), 1056 (s), 835 (s). HRMS(ESI-TOF) m/z: [M + Na]$^+$: calcd. for [$C_{14}H_{12}N_2O$ + Na]$^+$ 247.0847; found 247.0806.

2.16. Synthesis of 3b-8: *3-((pyridin-2-yloxy)methyl)benzonitrile*



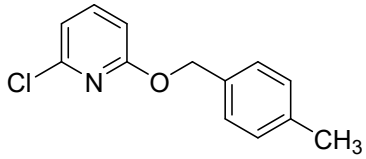
To run the reaction followed the above general procedure, and the liquid product was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, *J* = 2.2 Hz, 1H), 7.74 (s, 1H), 7.66 (d, *J* = 6.9 Hz, 1H), 7.62 – 7.51 (m, 2H), 7.45 (t, *J* = 7.4 Hz, 1H), 6.89 (d, *J* = 4.8 Hz, 1H), 6.82 (d, *J* = 8.0 Hz, 1H), 5.40 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.0, 146.9, 139.2, 139.0, 132.0, 131.3, 131.2, 129.3, 118.9, 117.4, 112.6, 111.3, 66.0. IR (KBr): 2373 (w), 2223 (w), 1611 (s), 1560 (s), 1541 (m), 1508 (s), 1472 (m), 1386 (m), 772 (w), 686 (w). HRMS(ESI-TOF) m/z: $[M + H]^+$: calcd. for $[C_{13}H_{10}N_2O + H]^+$ 211.0871; found 211.0877.

2.17. Synthesis of 3c-1: *2-(4-tert-butylbenzyloxy)-6-chloropyridine*



To run the reaction followed the above general procedure, and the white solid was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (t, *J* = 7.8 Hz, 1H), 7.47 – 7.30 (m, 4H), 6.91 (d, *J* = 7.5 Hz, 1H), 6.70 (d, *J* = 8.2 Hz, 1H), 5.32 (s, 2H), 1.33 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.4, 151.3, 148.4, 140.8, 133.7, 128.4, 125.6, 116.6, 109.6, 68.4, 34.7, 31.5. IR (KBr): 2964 (s), 1750 (m), 1682 (s), 1654 (s), 1588 (s), 1560 (vs), 1508 (s), 1438 (s), 1362 (w), 1298 (vs), 1260 (m), 1162 (s), 998 (s), 918 (m), 793 (s). m.p.: 79.6 - 81.2 °C. HRMS(ESI-TOF) m/z: $[M + H]^+$: calcd. for $[C_{16}H_{18}ClNO + H]^+$ 276.1155; found 276.1141.

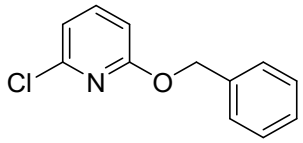
2.18. Synthesis of 3d-1: *2-chloro-6-(4-methylbenzyloxy)pyridine*



To run the reaction followed the above general procedure, and the liquid product was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, *J* = 7.2 Hz, 1H), 7.35 (d, *J* = 6.2 Hz, 2H), 7.20 (t, *J* = 11.1 Hz, 2H), 6.89 (d, *J*

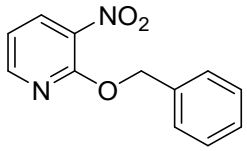
= 6.9 Hz, 1H), 6.67 (d, *J* = 7.7 Hz, 1H), 5.31 (s, 2H), 2.35 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.4, 148.4, 140.7, 138.0, 133.7, 129.3, 128.6, 116.5, 109.6, 68.4, 21.3. IR (KBr): 2967 (m), 2920 (m), 1590 (s), 1558 (s), 1440 (s), 1362 (m), 1300 (s), 1262 (w), 1159 (m), 1136 (m), 1072 (m), 919 (m), 731 (w). HRMS(ESI-TOF) m/z: $[M + H]^+$: calcd. for $[C_{13}H_{12}ClNO + H]^+$ 234.0686; found 234.0696.

2.19. Synthesis of 3e-1: *2-(benzyloxy)-6-chloropyridine*



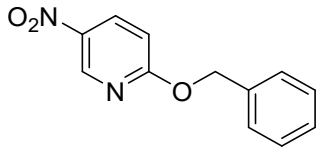
To run the reaction followed the above general procedure, and the liquid product was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 7.6 Hz, 1H), 7.49 – 7.44 (m, 2H), 7.43 – 7.30 (m, 3H), 6.91 (dd, *J* = 7.5 Hz, 0.6 Hz, 1H), 6.71 (dd, *J* = 8.2, 0.6 Hz, 1H), 5.36 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.4, 148.4, 140.8, 136.7, 128.7, 128.4, 128.2, 116.7, 109.6, 68.5. IR (KBr): 2377 (w), 2310 (w), 1588 (s), 1560 (m), 1508 (m), 1541 (m), 1458 (m), 1419 (w), 1339 (w). HRMS(ESI-TOF) m/z: $[M + Na]^+$: calcd. for $[C_{12}H_{10}ClNO + NH_4]^+$ 237.0789; found 237.0779.

2.20. Synthesis of 3e-2: *2-(benzyloxy)-3-nitropyridine*



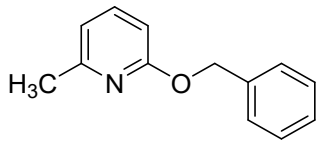
To run the reaction followed the above general procedure, and the white solid was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (d, *J* = 2.5 Hz, 1H), 8.27 (d, *J* = 6.7 Hz, 1H), 7.50 (d, *J* = 6.5 Hz, 2H), 7.37 (d, *J* = 7.0 Hz, 2H), 7.30 (t, *J* = 16.4 Hz, 1H), 7.04 (dd, *J* = 7.2, 4.6 Hz, 1H), 5.58 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.1, 151.7, 136.1, 135.2, 134.2, 128.6, 128.1, 127.7, 116.8, 68.9. IR (KBr): 1604 (vs), 1571 (s), 1518 (vs), 1435 (s), 1355 (s), 1305 (s), 1249 (m), 1152 (w), 1092 (m), 1018 (m), 886 (w), 731 (s). m.p.: 42.8 - 43.2 °C.

2.21. Synthesis of 3e-3: *2-(benzyloxy)-5-nitropyridine*



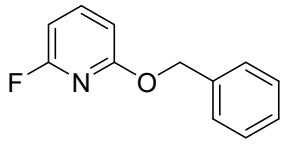
To run the reaction followed the above general procedure, and the white solid was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.09 (d, *J* = 2.6 Hz, 1H), 8.36 (dd, *J* = 9.1, 2.7 Hz, 1H), 7.46 (d, *J* = 7.1 Hz, 2H), 7.42 – 7.34 (m, 3H), 6.87 (d, *J* = 9.1 Hz, 1H), 5.49 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 144.8, 139.7, 136.0, 134.1, 128.8, 128.8, 128.3, 111.6, 69.3. IR (KBr): 1601 (s), 1578 (s), 1507 (s), 1481 (s), 1451 (s), 1400 (s), 1342 (s), 1315 (s), 1275 (s), 1113 (s), 1018 (s), 828 (m), 685 (s). m.p.: 103.5 - 104.3 °C.

2.22. Synthesis of 3e-4: *2-(benzyloxy)-6-methylpyridine*



To run the reaction followed the above general procedure, and the liquid compoundwas obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (m, 3H), 7.36 (m, 2H), 7.31 (d, *J* = 5.9 Hz, 1H), 6.71 (d, *J* = 6.2 Hz, 1H), 6.58 (d, *J* = 7.5 Hz, 1H), 5.36 (s, 2H), 2.45 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.2, 156.3, 139.0, 137.7, 128.5, 128.2, 127.8, 116.0, 107.7, 67.5, 24.3. IR (KBr): 2380 (w), 2305 (w), 1603 (m), 1560 (s), 1505 (s), 1456 (m), 1419 (m), 1339 (w), 502 (w).

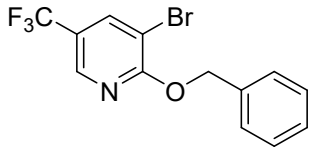
2.23. Synthesis of 3e-5: *2-(benzyloxy)-6-fluoropyridine*



To run the reaction followed the above general procedure, and the white solid compound was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 – 7.59 (m, 1H), 7.45 (s, 2H), 7.42 – 7.27 (m, 3H), 6.66 (d, *J* = 6.8 Hz, 1H), 6.48 (d, *J* = 5.1 Hz, 1H), 5.33 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5, 162.9, 142.8, 136.7, 128.7, 128.2, 107.6, 100.5, 100.1, 68.4. IR (KBr): 2925 (s), 2852 (m), 2360 (w), 1559 (s), 1458 (m), 1380 (m), 1370 (m), 1172 (m), 1122 (s),

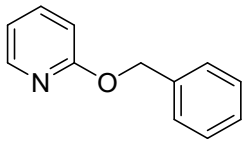
1029 (s), 832 (m), 666 (m). m.p.: 119.2 - 121.4 °C.

2.24. Synthesis of 3e-6: *2-(benzyloxy)-3-bromo-5-(trifluoromethyl)pyridine*



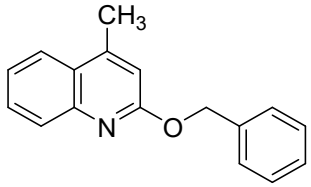
To run the reaction followed the above general procedure, and the white solid was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (m, 1H), 8.07 – 8.01 (m, 1H), 7.52 – 7.45 (m, 2H), 7.44 – 7.30 (m, 3H), 5.51 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.0, 143.4, 143.2, 138.9, 138.8, 136.2, 128.7, 128.3, 127.8, 107.6, 69.4. IR (KBr): 2946 (w), 2922 (w), 1606 (s), 1487 (s), 1448 (s), 1407 (s), 1317 (vs), 1251 (w), 1120 (m), 915 (s), 648 (m). m.p.: 49.0 - 50.9 °C.

2.25. Synthesis of 3e-7: *2-(benzyloxy)pyridine*



To run the reaction followed the above general procedure, and the white solid was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (s, 1H), 7.59 (s, 1H), 7.47 (m, 2H), 7.40 – 7.23 (m, 3H), 6.86 (d, J = 28.3 Hz 2H), 5.38 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.8, 147.0, 138.8, 137.5, 128.6, 128.1, 128.0, 117.1, 111.5, 67.7. IR (KBr): 2220 (vs), 1596 (vs), 1559 (vs), 1508 (s), 1457 (s), 1340 (vs), 1155 (m), 1092 (s), 993 (m), 848 (w), 699 (s). m.p.: 98.3 - 101.2 °C.

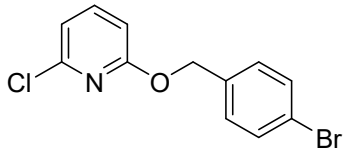
2.26. Synthesis of 3e-8: *2-(benzyloxy)-4-methylquinoline*



To run the reaction followed the above general procedure, and the white solid was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (t, J = 7.7 Hz, 2H), 7.61 (dd, J = 11.7, 4.6 Hz, 1H), 7.51 (d, J = 7.3 Hz, 2H), 7.41 – 7.34 (m, 3H), 7.31 (t, J = 7.3 Hz, 1H), 6.81 (s, 1H), 5.53 (s, 2H), 2.59 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.8, 147.0, 146.6, 137.6, 129.4, 128.9, 128.5, 128.3,

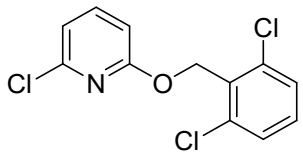
127.9, 125.6, 123.9, 123,8, 113.2, 67.5, 18.8. IR (KBr): 2935 (w), 2242 (w), 1603 (m), 1482 (m), 1451 (m), 1408 (m), 1322 (vs), 1253 (s), 1163 (m), 1128 (m), 1058 (m), 935 (w), 795 (w). HRMS(ESI-TOF) m/z: $[M + H]^+$: calcd. for $[C_{17}H_{15}NO + H]^+$ 250.1232; found 250.1243.

2.27. Synthesis of 3f-1: *2-(4-bromobenzyloxy)-6-chloropyridine*



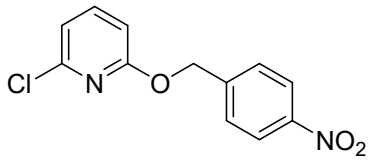
To run the reaction followed the above general procedure, and the white solid was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 – 7.47 (m, 3H), 7.38 – 7.31 (m, 2H), 6.93 (dd, *J* = 7.5, 0.7 Hz, 1H), 6.0 (dd, *J* = 8.2, 0.7 Hz, 1H), 5.31 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.1, 148.4, 140.9, 135.8, 131.8, 130.1, 122.2, 116.9, 109.5, 67.6. IR (KBr): 1606 (s), 1520 (m), 1110 (s), 1410 (w), 1407 (s), 1362 (m), 1309 (vs), 1156 (m), 1038 (w), 919 (m), 788 (m). m.p.: 182.6 - 185.3 °C.

2.28. Synthesis of 3g-1: *2-chloro-6-(2,6-dichlorobenzyloxy)pyridine*



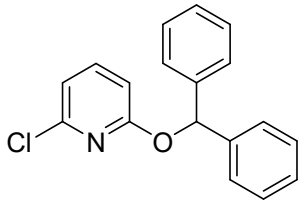
To run the reaction followed the above general procedure, and the white solid was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (t, *J* = 7.4 Hz, 1H), 7.36 (d, *J* = 7.6 Hz, 2H), 7.26 – 7.19 (m, 1H), 6.95 (d, *J* = 7.1 Hz, 1H), 6.69 (d, *J* = 7.8 Hz, 1H), 5.59 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3, 148.4, 140.8, 137.3, 132.2, 130.6, 128.6, 116.9, 109.4, 63.7. IR (KBr): 1614 (m), 1598 (s), 1569 (s), 1508 (m), 1460 (s), 1435 (s), 1361 (m), 1299 (m), 1259 (m), 1163 (w), 992 (w), 788 (m). m.p.: 111.5 - 112.3 °C. HRMS(ESI-TOF) m/z: $[M + H]^+$: calcd. for $[C_{12}H_8Cl_3NO + H]^+$ 287.9750; found 287.9738.

2.29. Synthesis of 3h-1: *2-chloro-6-(4-nitrobenzyloxy)pyridine*



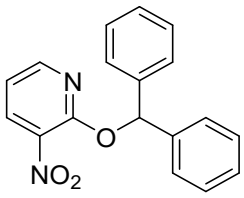
To run the reaction followed the above general procedure, and the yellow solid product was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J* = 8.2 Hz, 2H), 7.60 (dd, *J* = 21.4, 7.9 Hz, 3H), 6.96 (d, *J* = 7.3 Hz, 1H), 6.77 (d, *J* = 8.0 Hz, 1H), 5.48 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.7, 148.5, 147.7, 144.3, 141.2, 128.4, 123.9, 117.3, 109.5, 66.9. IR (KBr): 2925 (s), 1600 (m), 1559 (m), 1500 (m), 1342 (s), 1300 (m), 1260 (w), 1163 (s), 1108 (w), 1078 (m), 1029 (s), 845 (m). m.p.: 97.5 - 98.0 °C. HRMS(ESI-TOF) m/z: $[M + H]^+$: calcd. for $[C_{12}H_9ClN_2O_3 + H]^+$ 265.0380; found 265.0365.

2.30. Synthesis of 3i-1: *2-(benzhydryloxy)-6-chloropyridine*



To run the reaction followed the above general procedure, and the white solid was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (dd, *J* = 13.6, 7.6 Hz, 5H), 7.38 – 7.29 (m, 5H), 7.25 (s, 1H), 7.23 – 7.21 (m, 1H), 6.83 (d, *J* = 7.5 Hz, 1H), 6.75 (d, *J* = 8.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.1, 140.9, 140.8, 138.4, 132.2, 127.7, 127.3, 116.7, 109.7, 78.3. IR (KBr): 2346 (w), 1615 (m), 1487 (s), 1562 (s), 1508 (s), 1458 (m), 1386 (w), 1229 (s), 743 (w), 698 (m). m.p.: 122.8 - 123.4 °C.

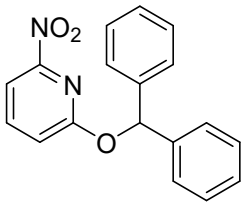
2.31. Synthesis of 3i-2: *2-(benzhydryloxy)-3-nitropyridine*



To run the reaction followed the above general procedure, and the white solid was obtained, the data of the final compound as follows: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (dd, *J* = 4.8, 1.6 Hz, 1H), 8.26 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.55 (d, *J* = 7.5 Hz, 4H),

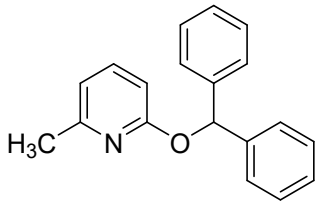
7.42 (s, 1H), 7.34 (t, *J* = 7.5 Hz, 4H), 7.25 (t, *J* = 7.3 Hz, 2H), 6.98 (dd, *J* = 7.9, 4.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.4, 151.7, 140.7, 135.3, 134.3, 128.7, 127.9, 127.1, 116.9, 79.5. IR (KBr): 2926 (w), 2855 (m), 2358 (w), 1605 (m), 1541 (s), 1520 (m), 1446 (w), 818 (m). HRMS(ESI-TOF) m/z: $[M + Na]^+$: calcd. for $[C_{18}H_{14}N_2O_3 + Na]^+$ 329.0902; found 329.0907.

2.32. Synthesis of 3i-3: *2-(benzhydryloxy)-6-nitropyridine*



To run the reaction followed the above general procedure, and the white solid was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (dt, *J* = 6.4, 3.2 Hz, 1H), 8.31 – 8.26 (m, 1H), 7.55 (ddd, *J* = 7.3, 5.1, 2.8 Hz, 4H), 7.43 (s, 1H), 7.35 (ddd, *J* = 7.8, 4.6, 1.4 Hz, 4H), 7.26 – 7.23 (m, 2H), 7.00 (dd, *J* = 7.9, 4.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.4, 151.7, 140.7, 135.4, 128.7, 128.0, 127.1, 116.9, 79.5, 77.4. IR (KBr): 2926 (w), 2855 (m), 2358 (w), 1617 (m), 1541 (s), 1520 (m), 1456 (m), 1252 (w), 1035 (w), 818 (m). m.p.: 190.5 - 193.8 °C. HRMS(ESI-TOF) m/z: $[M + Na]^+$: calcd. for $[C_{18}H_{14}N_2O_3 + Na]^+$ 329.0902; found 329.0907.

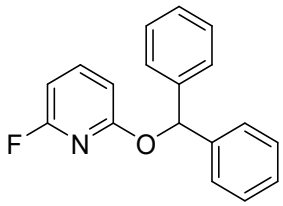
2.33. Synthesis of 3i-4: *2-(benzhydryloxy)-6-methylpyridine*



To run the reaction followed the above general procedure, and the white solid was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 – 7.40 (m, 5H), 7.35 – 7.29 (m, 4H), 7.27 (s, 1H), 7.25 – 7.21 (m, 1H), 7.20 – 7.08 (m, 1H), 6.65 (dd, *J* = 10.9, 7.7 Hz, 2H), 2.38 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4, 156.3, 142.0, 139.0, 128.4, 128.3, 127.5, 116.1, 108.0, 77.3, 24.4. IR (KBr): 2920 (m), 1599 (s), 1572 (m), 1452 (vs), 1290 (m), 1232 (m), 1150 (w), 1035 (m), 793 (s), 704 (s). m.p.: 54.0 - 55.6 °C. HRMS(ESI-TOF) m/z: $[M + H]^+$: calcd. for

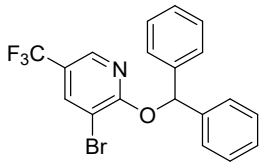
$[C_{19}H_{17}NO + H]^+$ 276.1388; found 276.1374.

2.34. Synthesis of 3i-5: *2-(benzhydryloxy)-6-fluoropyridine*



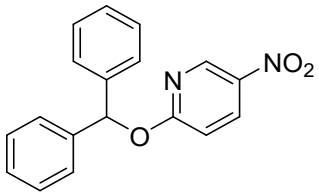
To run the reaction followed the above general procedure, and the white solid was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (q, *J* = 8.1 Hz, 1H), 7.47 – 7.42 (m, 4H), 7.36 – 7.31 (m, 4H), 7.31 – 7.26 (m, 2H), 7.15 (s, 1H), 6.73 (dd, *J* = 7.9, 1.6 Hz, 1H), 6.43 (dd, *J* = 7.8, 2.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3, 142.9, 142.8, 141.0, 128.6, 127.8, 127.4, 107.9, 100.9, 100.5, 78.5. IR (KBr): 2925 (w), 2855 (w), 2360 (w), 1616 (m), 1559 (s), 1508 (w), 1458 (w), 1507 (m), 1456 (w), 1228 (m), 1019 (w). m.p.: 86.7 - 88.3 ^{o}C. HRMS(ESI-TOF) m/z: $[M + Na]^+$: calcd. for $[C_{18}H_{14}FNO + Na]^+$ 302.0957; found 302.0937.

2.35. Synthesis of 3i-6: *2-(benzhydryloxy)-3-bromo-5-(trifluoromethyl)pyridine*



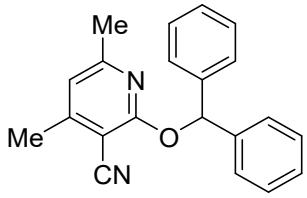
To run the reaction followed the above general procedure, and the white solid was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (s, 1H), 8.01 (s, 1H), 7.50 (d, *J* = 6.5 Hz, 4H), 7.33 (d, *J* = 7.0 Hz, 4H), 7.30 – 7.22 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1, 143.3, 140.7, 138.9, 128.7, 128.0, 127.1, 121.7, 121.3, 107.9, 79.9. IR (KBr): 2925 (w), 2855 (w), 2360 (w), 1616 (m), 1559 (s), 1508 (w), 1458 (w), 1400 (s), 1350 (m), 1200 (w), 1140 (w), 1090 (m). HRMS(ESI-TOF) m/z: $[M + NH_4]^+$: calcd. for $[C_{19}H_{13}BrF_3NO + NH_4]^+$ 425.0471; found 425.0458.

2.36. Synthesis of 3i-7: *2-(benzhydryloxy)-5-nitropyridine*



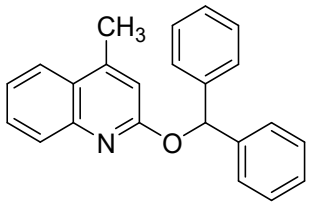
To run the reaction followed the above general procedure, and the white solid was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.02 (d, *J* = 2.8 Hz, 1H), 8.36 (dd, *J* = 9.2, 2.8 Hz, 1H), 7.46 – 7.41 (m, 4H), 7.37 – 7.33 (m, 5H), 7.32 – 7.28 (m, 2H), 6.97 (d, *J* = 9.1 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 144.9, 140.3, 139.7, 134.3, 128.7, 128.2, 127.3, 111.9, 79.8. IR (KBr): 2923 (w), 2960 (m), 2850 (m), 1460 (m), 1456 (m), 1345 (w), 1312 (w), 1112 (w), 836 (w), 699 (w). m.p.: 88.2 - 89.8 °C.

2.37. Synthesis of 3i-8: *2-(benzhydryloxy)-4,6-dimethylnicotinonitrile*



To run the reaction followed the above general procedure, and the white solid was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 6.7 Hz, 4H), 7.38 – 7.28 (m, 5H), 7.25 (d, *J* = 5.3 Hz, 2H), 6.63 (s, 1H), 2.42 (s, 3H), 2.39 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.1, 160.6, 154.6, 141.0, 128.6, 127.8, 127.2, 117.9, 115.1, 94.6, 78.5, 24.6, 20.2. IR (KBr): 2365 (s), 2325 (s), 2225 (m), 1600 (s), 1559 (s), 1458 (m), 1438 (m), 1386 (s), 1348 (m), 1155 (m), 1093 (s), 1005 (m), 862 (w), 753 (w). m.p.: 100.1 - 101.8 °C. HRMS(ESI-TOF) m/z: [M + Na]$^{+}$: calcd. for $[C_{21}H_{18}N_2O + Na]^{+}$ 337.1317; found337.1359.

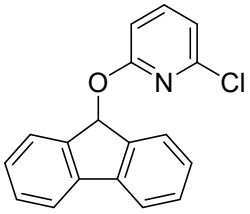
2.38. Synthesis of 3i-9: *2-(benzhydryloxy)-4-methylquinoline*



To run the reaction followed the above general procedure, and the white solid was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 – 7.79 (m, 2H), 7.63 – 7.57 (m, 1H), 7.51 – 7.46 (m, 2H), 7.34 (d, *J* = 4.4 Hz,

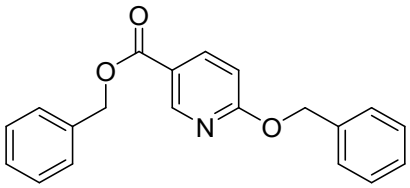
8H), 7.32 – 7.27 (m, 2H), 6.88 (s, 1H), 2.16 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.9, 151.5, 150.4, 140.3, 136.0, 132.6, 130.2, 128.6, 128.4, 128.1, 127.2, 123.2, 93.8, 77.4, 24.1. m.p.: 60.8 - 61.3 °C. IR (KBr): 2942 (w), 1494 (m), 1455 (m), 1372 (m), 1237 (vs), 1119 (w), 1025 (w), 742 (w), 701 (s), 546 (m). HRMS(ESI-TOF) m/z: $[M + H]^+$: calcd. for $[C_{23}H_{19}NO + H]^+$ 326.1545; found 326.1594.

2.39. Synthesis of 3j-1: *2-(9H-fluoren-9-yloxy)-6-chloropyridine*



To run the reaction followed the above general procedure, and the white solid was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 – 7.50 (m, 6H), 7.40 (t, *J* = 6.9 Hz, 2H), 7.26 (d, *J* = 7.2 Hz, 2H), 7.01 (d, *J* = 7.2 Hz, 1H), 6.71 (d, *J* = 7.9 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.6, 148.4, 142.9, 141.2, 129.5, 127.9, 126.2, 120.1, 117.0, 110.1, 77.5, 77.0. IR (KBr): 1624 (s), 1560 (vs), 1541 (s), 1508 (vs), 1457 (s), 1339 (m), 1162 (m), 1011 (m), 921 (w), 742 (m). m.p.: 101.2 - 101.9 °C. HRMS(ESI-TOF) m/z: $[M + Na]^+$: calcd. for $[C_{18}H_{12}ClNO + Na]^+$ 316.0505; found 316.0540.

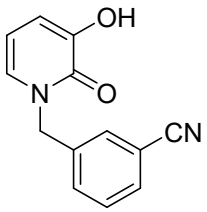
2.40. Synthesis of 3e-9: *4-(((6-fluoropyridin-2-yl)oxy)methyl)benzonitrile*



To run the reaction followed the above general procedure, and the white solid was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (d, *J* = 2.3 Hz, 1H), 8.20 (dd, *J* = 8.7, 2.4 Hz, 1H), 7.45 (ddd, *J* = 7.6, 5.8, 1.6 Hz, 4H), 7.42 – 7.31 (m, 6H), 6.82 (d, *J* = 8.7 Hz, 1H), 5.45 (s, 2H), 5.36 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.5, 165.4, 150.3, 139.9, 136.8, 136.0, 128.8, 128.7, 128.5, 128.3, 128.2, 127.2, 119.9, 111.1, 68.4, 66.8. m.p.: 122.2 - 124.4 °C. IR (KBr): 2382 (w), 2343 (w), 1692 (vs), 1607 (s), 1587 (s), 1558 (s), 1506 (s), 1456 (m), 1285

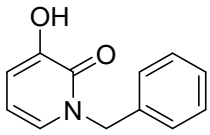
(w), 1252 (w), 1079 (m), 871 (w), 753 (m), 525 (w).

2.41. Synthesis of 4a: *3-((3-hydroxy-2-oxopyridin-1(2H)-yl)methyl)benzonitrile*



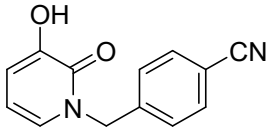
To run the reaction followed the above general procedure, and the white solid was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 7.6 Hz, 1H), 7.55 (d, *J* = 9.4 Hz, 2H), 7.47 (t, *J* = 7.7 Hz, 1H), 6.93 (s, 1H), 6.84 (d, *J* = 7.1 Hz, 2H), 6.21 (t, *J* = 7.1 Hz, 1H), 5.20 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.8, 147.0, 137.6, 132.4, 132.0, 131.4, 129.9, 126.6, 118.5, 114.1, 113.2, 107.7, 52.1. IR (KBr): 1683 (s), 1570 (s), 1524 (vs), 1437 (s), 1348 (s), 1303 (s), 1189 (m), 1083 (m), 982 (s), 758 (s), 696 (s). m.p.: 184.3 - 186.7 °C. HRMS(ESI-TOF) m/z: $[M + Na]^+$: calcd. for $[C_{13}H_{10}N_2O_2 + Na]^+$ 249.0640; found 249.0678.

2.42. Synthesis of 4b: *1-benzyl-3-hydroxypyridin-2(1H)-one*



To run the reaction followed the above general procedure, and the black solid was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33-7.30 (m, *J* = 13.2 Hz, 5H), 7.18 (br, 1H), 6.81 (dd, *J* = 12.2, 6.8 Hz, 2H), 6.13 (d, *J* = 6.2 Hz, 1H), 5.19 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.9, 146.9, 136.0, 129.0, 128.3, 128.2, 126.8, 113.8, 107.1, 52.5. m.p.: 136.9-138.3 °C. IR (KBr): 2382 (w), 2310 (w), 1680 (vs), 1490 (vs), 872 (m), 853 (s), 714 (m).

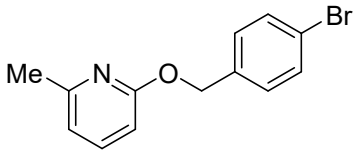
2.43. Synthesis of 4c: *4-((3-hydroxy-2-oxopyridin-1(2H)-yl)methyl)benzonitrile*



To run the reaction followed the above general procedure, and the white solid was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ

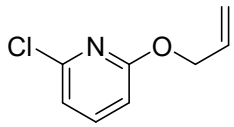
7.65 (d, *J* = 8.0 Hz, 2H), 7.38 (d, *J* = 8.0 Hz, 2H), 6.86 (s, 1H), 6.84 (s, 1H), 6.22 (t, *J* = 7.1 Hz, 1H), 5.23 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6, 158.9, 147.0, 141.2, 132.9, 128.5, 126.7, 114.0, 112.3, 107.6, 52.3. IR (KBr): 1660 (vs), 1570 (s), 1524 (vs), 1437 (s). m.p.: 137.8 - 139.4 °C. HRMS(ESI-TOF) m/z: $[M + H]^+$: calcd. for $[C_{13}H_{10}N_2O_2 + H]^+$ 227.0821; found 227.0869.

2.44. Synthesis of 3m: *2-((4-bromobenzyl)oxy)-6-methylpyridine*



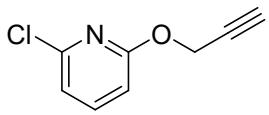
To run the reaction followed the above general procedure, and the white solid was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 – 7.43 (m, 3H), 7.34 (d, *J* = 8.3 Hz, 2H), 6.73 (d, *J* = 7.2 Hz, 1H), 6.58 (d, *J* = 8.2 Hz, 1H), 5.31 (s, 2H), 2.45 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.8, 156.2, 138.9, 136.7, 131.5, 129.8, 121.6, 116.1, 107.6, 77.3, 77.0, 76.7, 66.5, 24.1. IR (KBr): 1955 (m), 1612 (m), 1551 (s), 1410 (m), 1213 (m), 1016 (m). m.p.: 28.9-30.1 °C. HRMS(ESI-TOF) m/z: $[M + H]^+$: calcd. for $[C_{13}H_{12}BrNO + H]^+$ 278.0181; found 278.0144.

2.45. Synthesis of 3n: *2-(allyloxy)-6-chloropyridine*



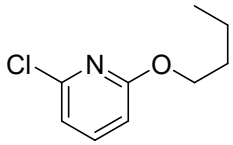
To run the reaction followed the above general procedure, and the white solid was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (t, *J* = 7.8 Hz, 1H), 6.90 (d, *J* = 7.5 Hz, 1H), 6.68 (d, *J* = 8.2 Hz, 1H), 6.16 – 5.99 (m, 1H), 5.41 (dd, *J* = 17.2, 1.5 Hz, 1H), 5.27 (dd, *J* = 10.4, 1.3 Hz, 1H), 4.88 – 4.78 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.2, 148.4, 140.8, 133.0, 118.2, 116.5, 109.4, 67.4. IR (KBr): 2913 (w), 2357 (m), 2314 (m), 1683 (s), 1559 (s), 1506 (s), 1456 (s), 1260 (m). HRMS(ESI-TOF) m/z: $[M + H]^+$: calcd. for $[C_8H_8ClNO + H]^+$ 170.0367; found 170.0349.

2.46. Synthesis of 3o: *2-chloro-6-(prop-2-yn-1-yloxy)pyridine*



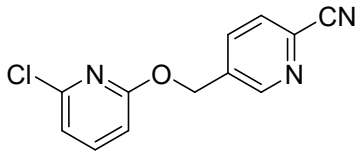
To run the reaction followed the above general procedure, and the white solid was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (s, 1H), 6.95 (d, *J* = 7.5 Hz, 1H), 6.73 (d, *J* = 8.2 Hz, 1H), 4.97 (d, *J* = 2.4 Hz, 2H), 2.50 (t, *J* = 2.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.1, 148.3, 141.0, 117.3, 109.5, 78.6, 74.9, 54.3. IR (KBr): 2918 (w), 1589 (s), 1438 (vs), 1360 (m), 1293 (s), 1163 (s). HRMS(ESI-TOF) m/z: $[M + H]^+$: calcd. for $[C_8H_6ClNO + H]^+$ 168.0211; found 168.0051.

2.47. Synthesis of 3p: *2-butoxy-6-methylpyridine*



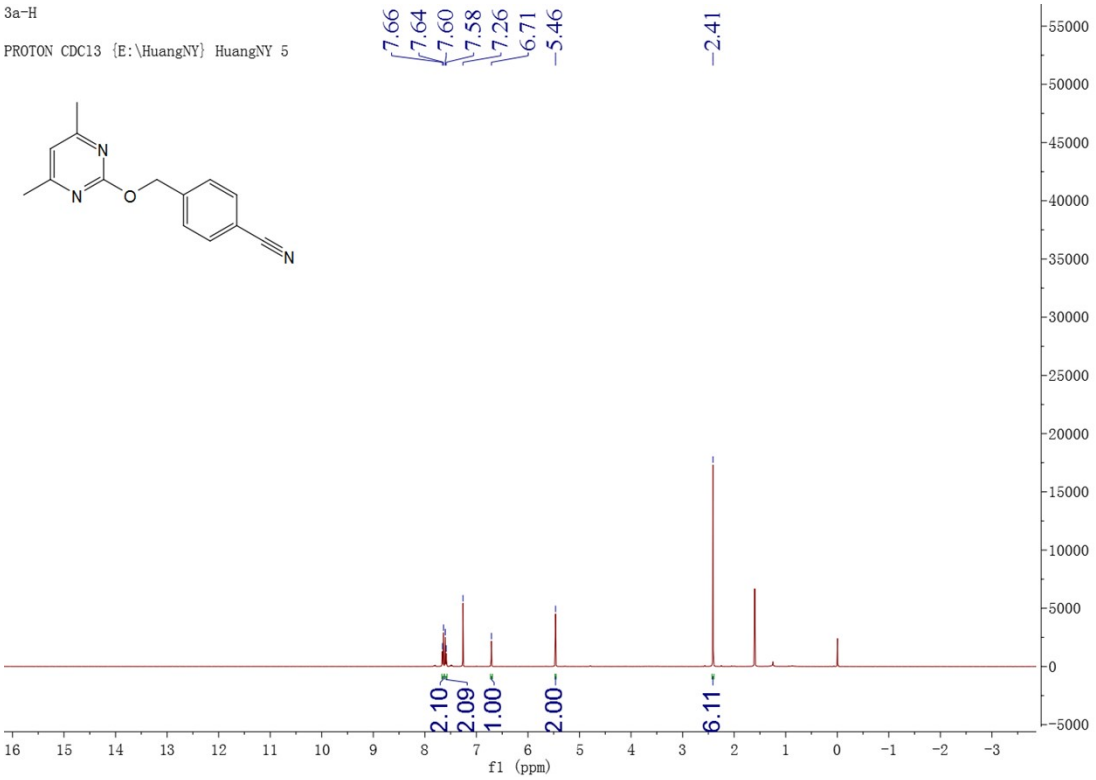
To run the reaction followed the above general procedure, and the white solid was obtained, the data of the final compound as follow: 1H NMR (400 MHz, $CDCl_3$) δ 7.50 (dd, *J* = 8.2, 7.5 Hz, 1H), 6.87 (dd, *J* = 7.5, 0.7 Hz, 1H), 6.63 (dd, *J* = 8.2, 0.7 Hz, 1H), 4.28 (t, *J* = 6.6 Hz, 2H), 1.74 (ddt, *J* = 8.9, 7.7, 6.5 Hz, 2H), 1.51 – 1.40 (m, 2H), 0.97 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) 163.8, 148.5, 140.5, 116.0, 109.1, 66.4, 31.0, 19.4, 13.9. IR (KBr): 2968 (s), 1592 (s), 1442 (vs), 1299 (s), 1162 (s). HRMS(ESI-TOF) m/z: $[M + H]^+$: calcd. for $[C_9H_{12}ClNO + H]^+$ 186.0680; found 186.0509.

2.48. Synthesis of 3q:*5-(((6-chloropyridin-2-yl)oxy)methyl)picolinonitrile*

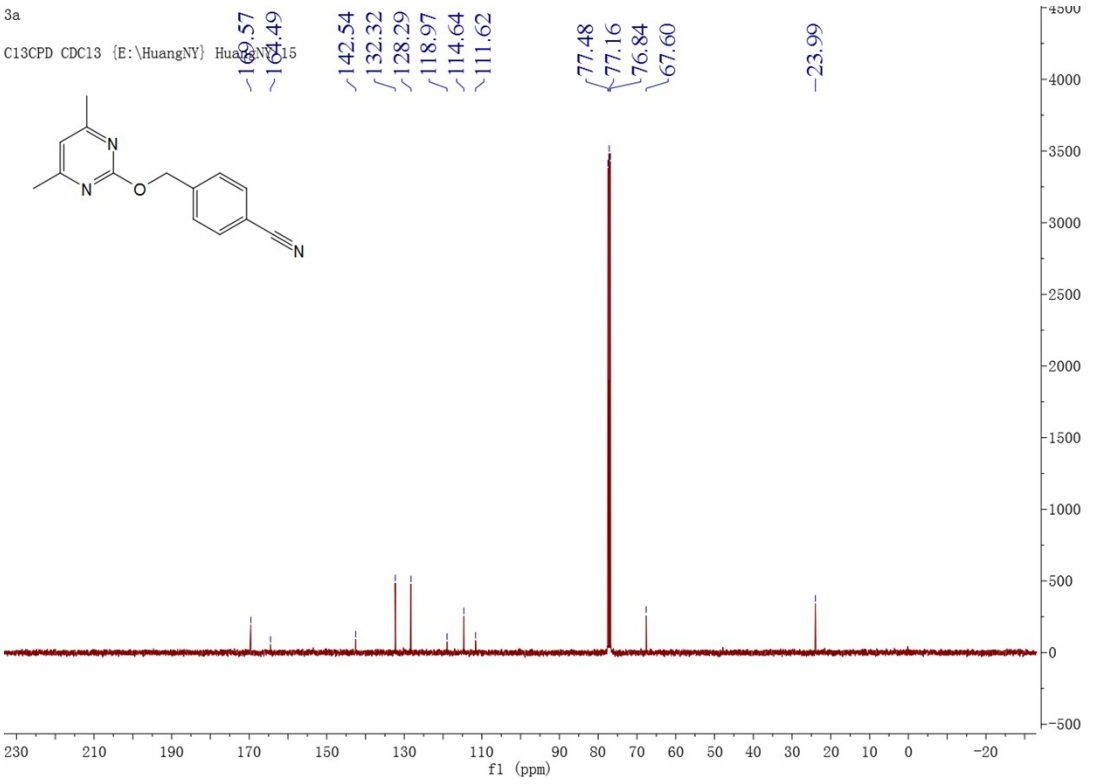


To run the reaction followed the above general procedure, and the white solid was obtained, the data of the final compound as follow: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 (s, 1H), 7.94 (d, *J* = 10.0 Hz, 1H), 7.72 (d, *J* = 8.0 Hz, 1H), 7.61 – 7.52 (m, 1H), 6.97 (d, *J* = 7.5 Hz, 1H), 6.75 (d, *J* = 8.2 Hz, 1H), 5.47 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.3, 150.8, 148.4, 141.3, 136.6, 136.5, 133.3, 128.3, 117.5, 117.3, 109.5,

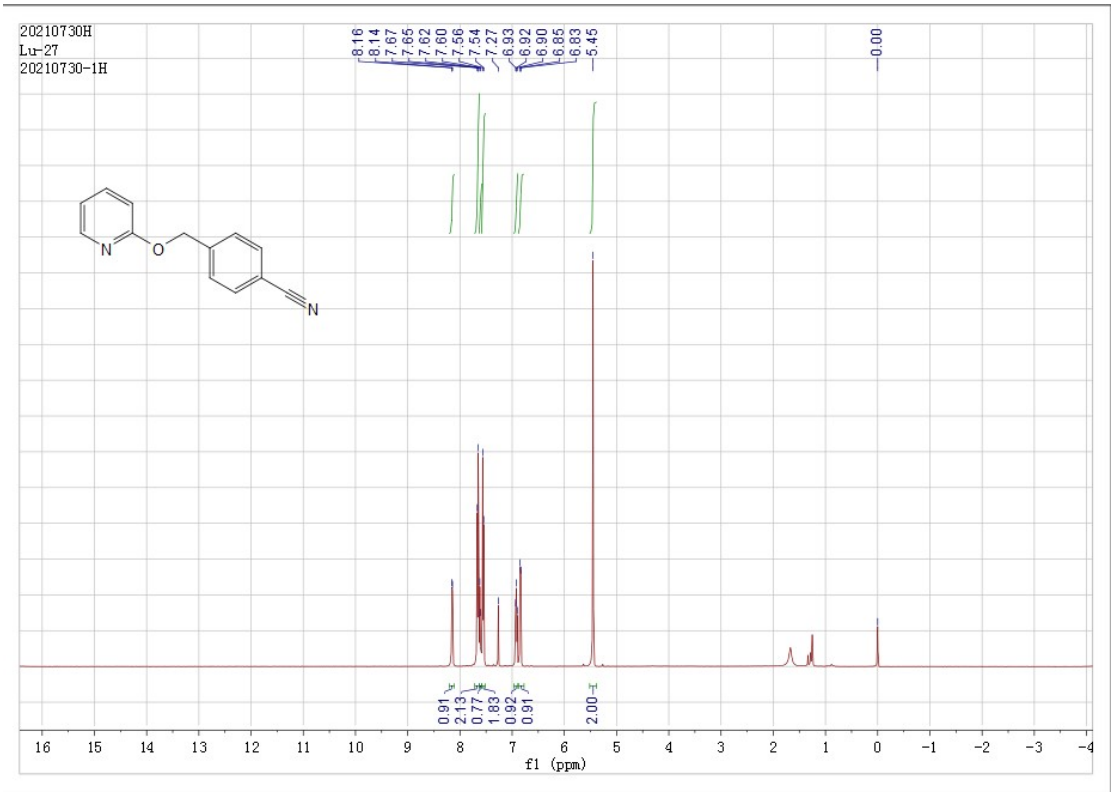
64.8. m.p.: 111.6-112.0 °C. IR (KBr): 2922 (w), 2236 (m), 1607 (s), 1591 (s), 1567 (s), 1435 (vs), 1389 (s), 1328 (m), 1308 (s). HRMS(ESI-TOF) m/z: $[M + H]^+$: calcd. for $[C_{12}H_8ClN_3O + H]^+$ 246.0429; found 246.0235.



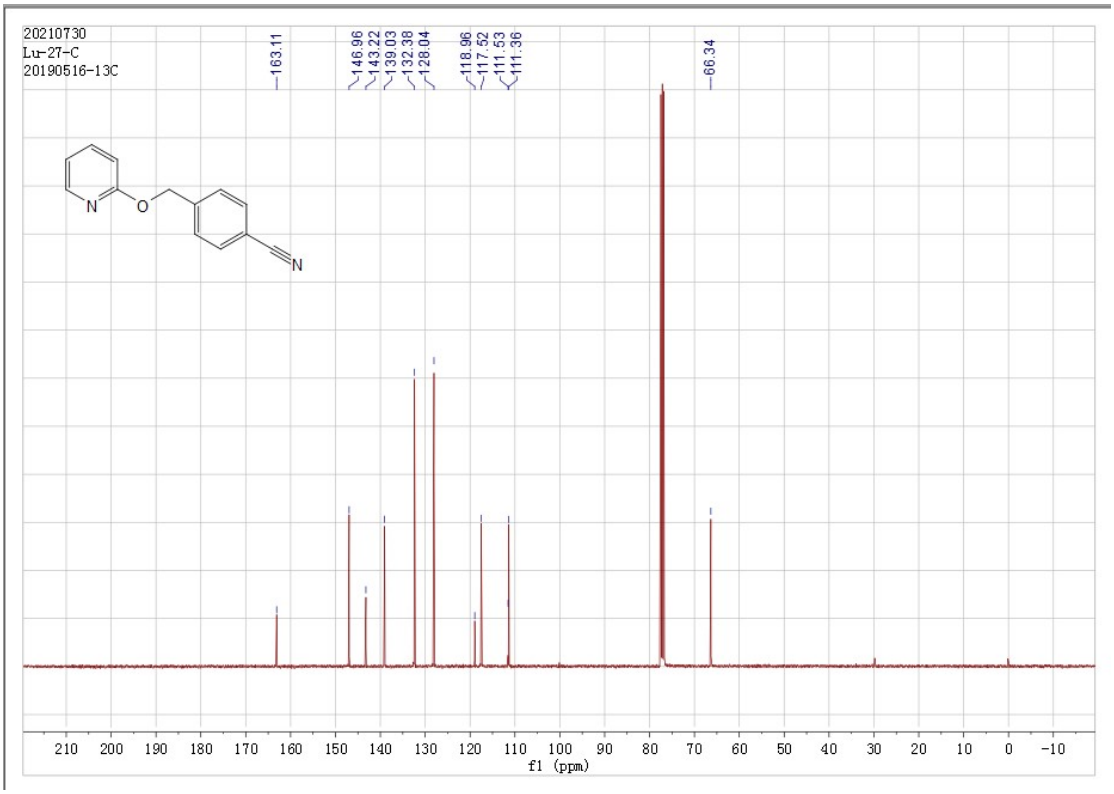
3a ^{1}H NMR



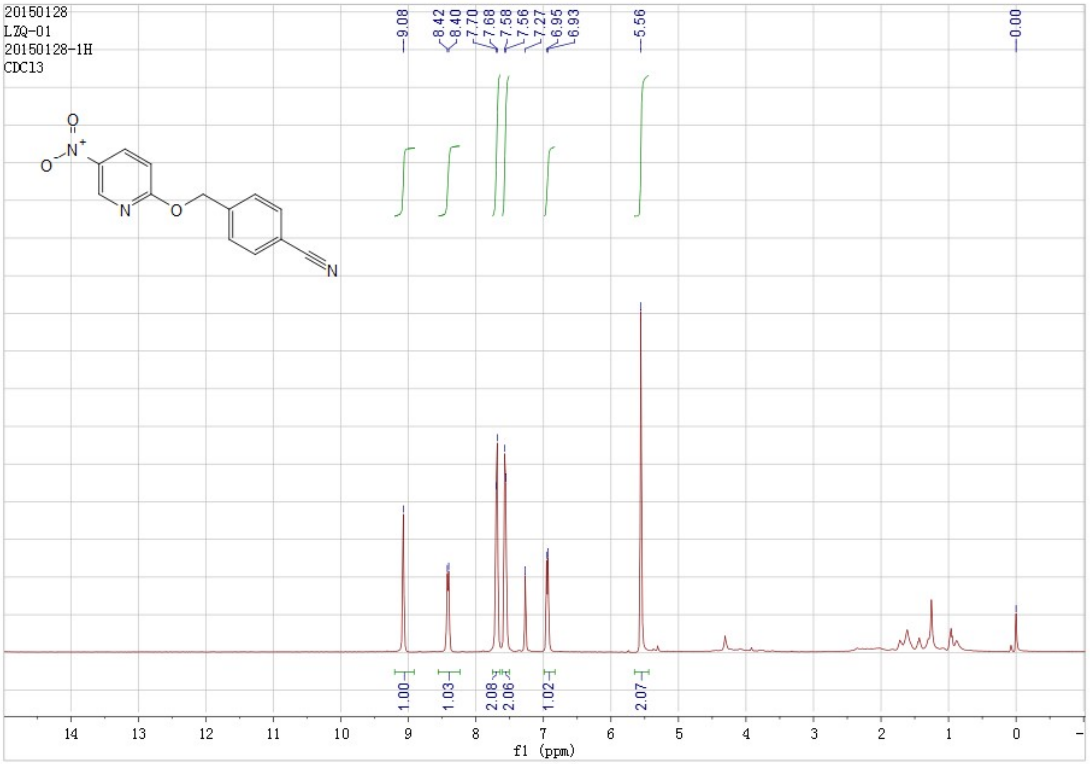
3a ^{13}C NMR



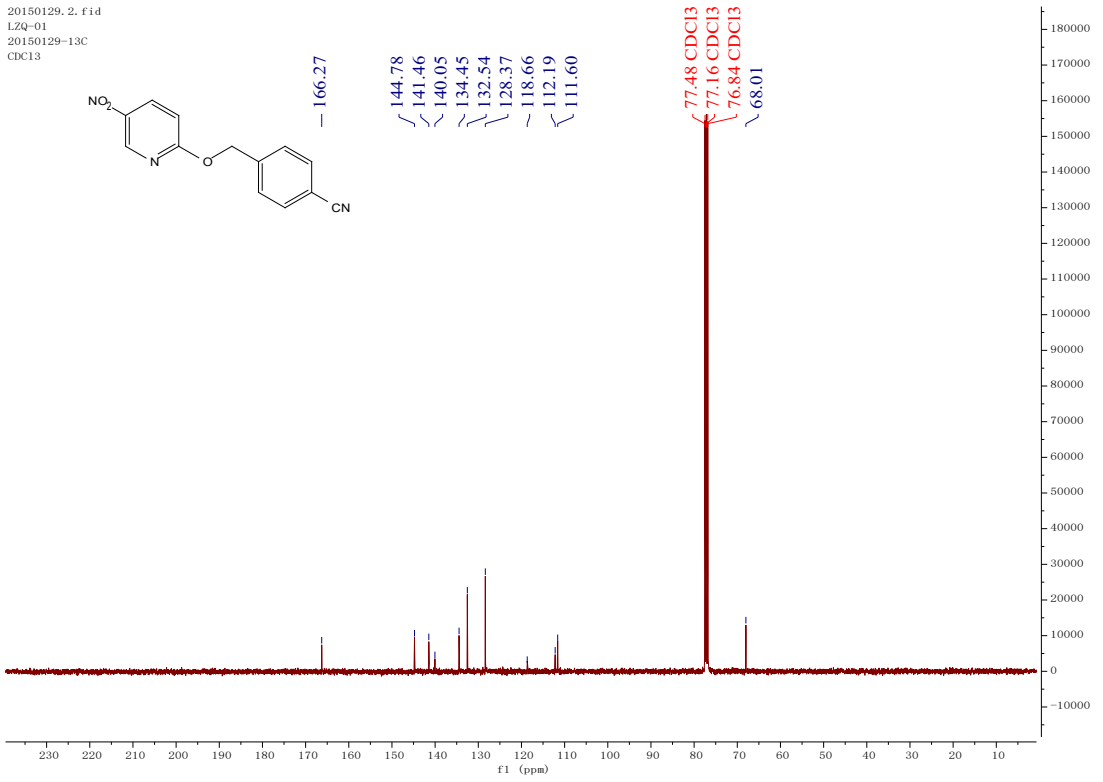
3a-1 ^{1}H NMR



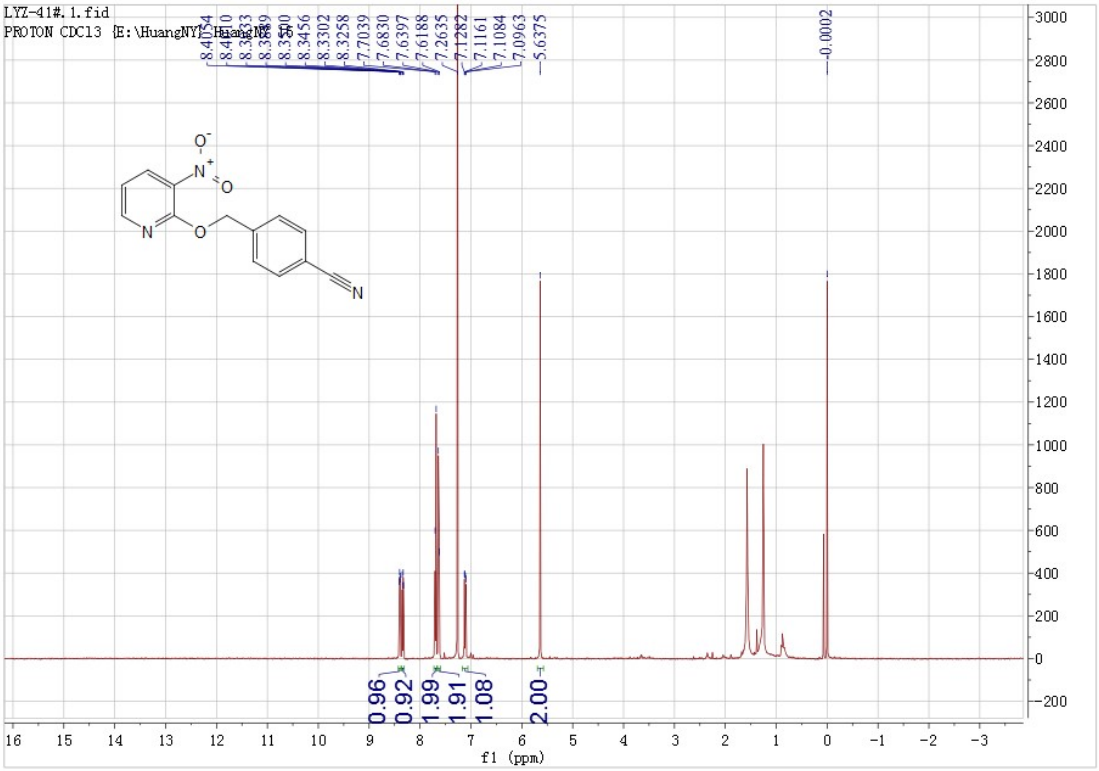
3a-1 ^{13}C NMR



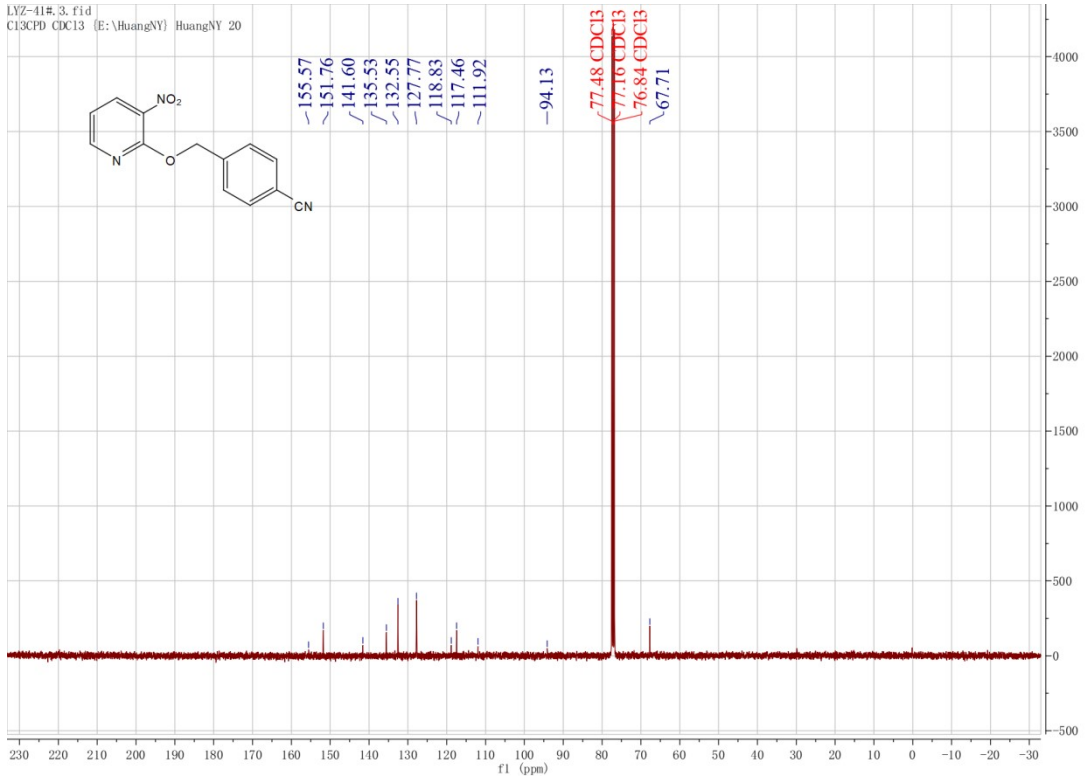
3a-2 ^{1}H NMR



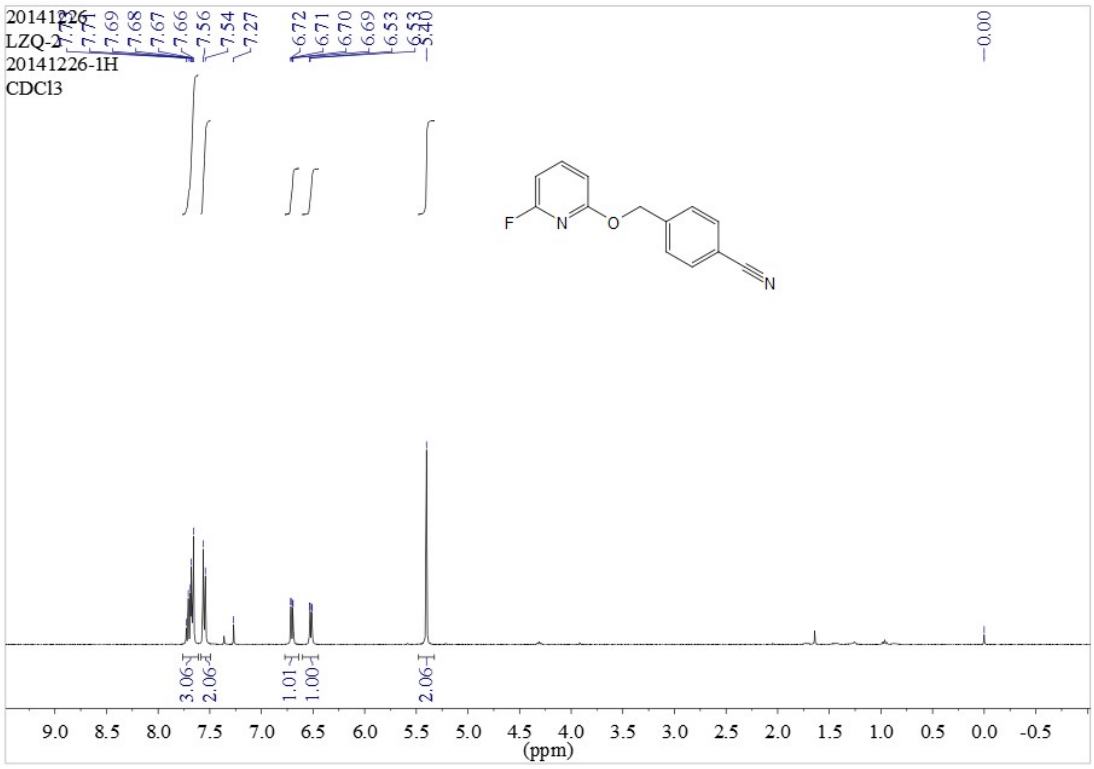
3a-2 ^{13}C NMR



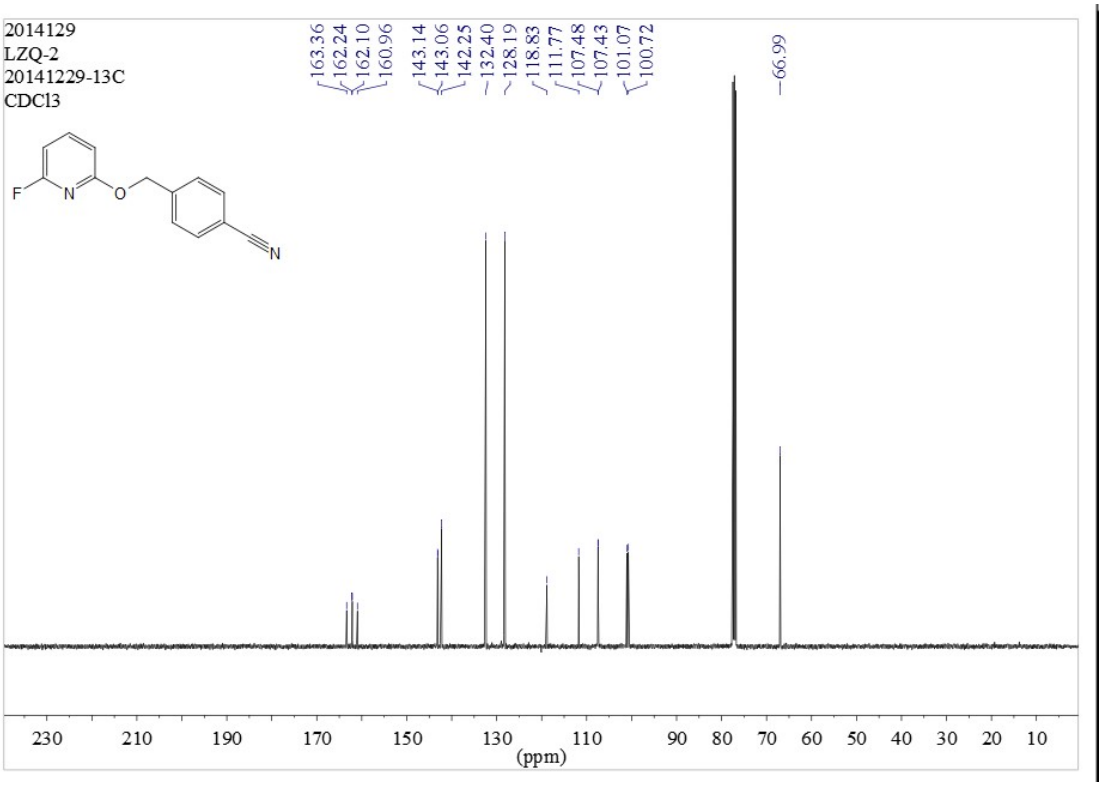
3a-3 ^{1}H NMR



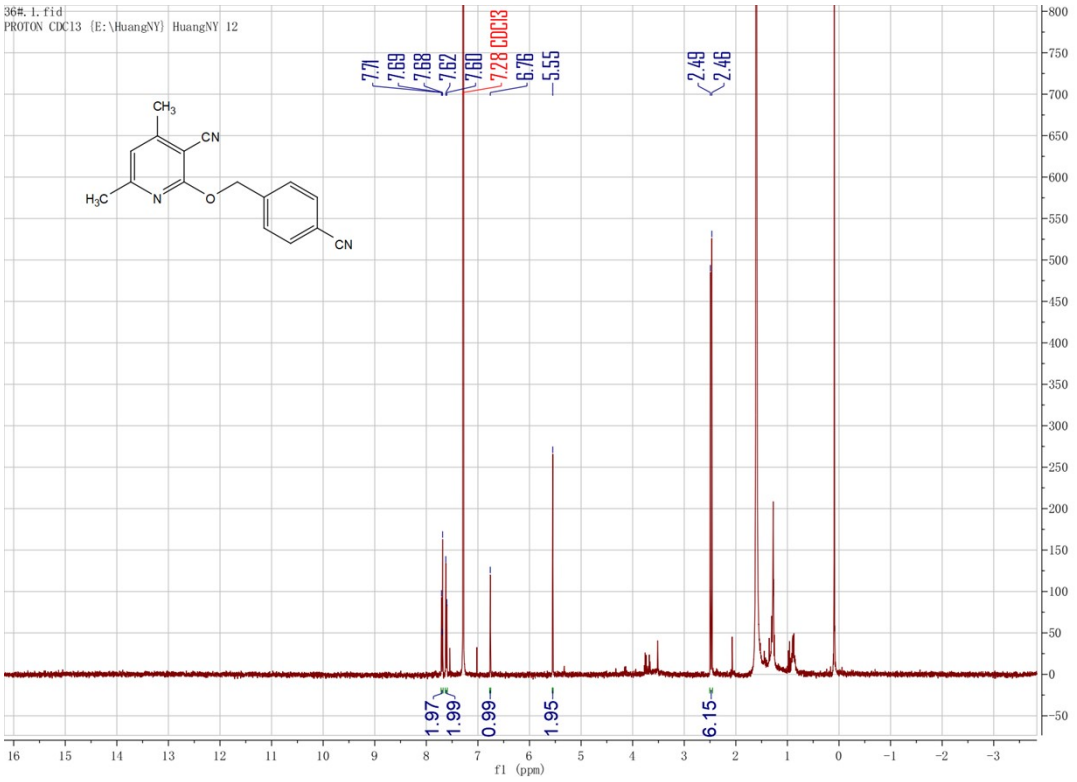
3a-3 ^{13}C NMR



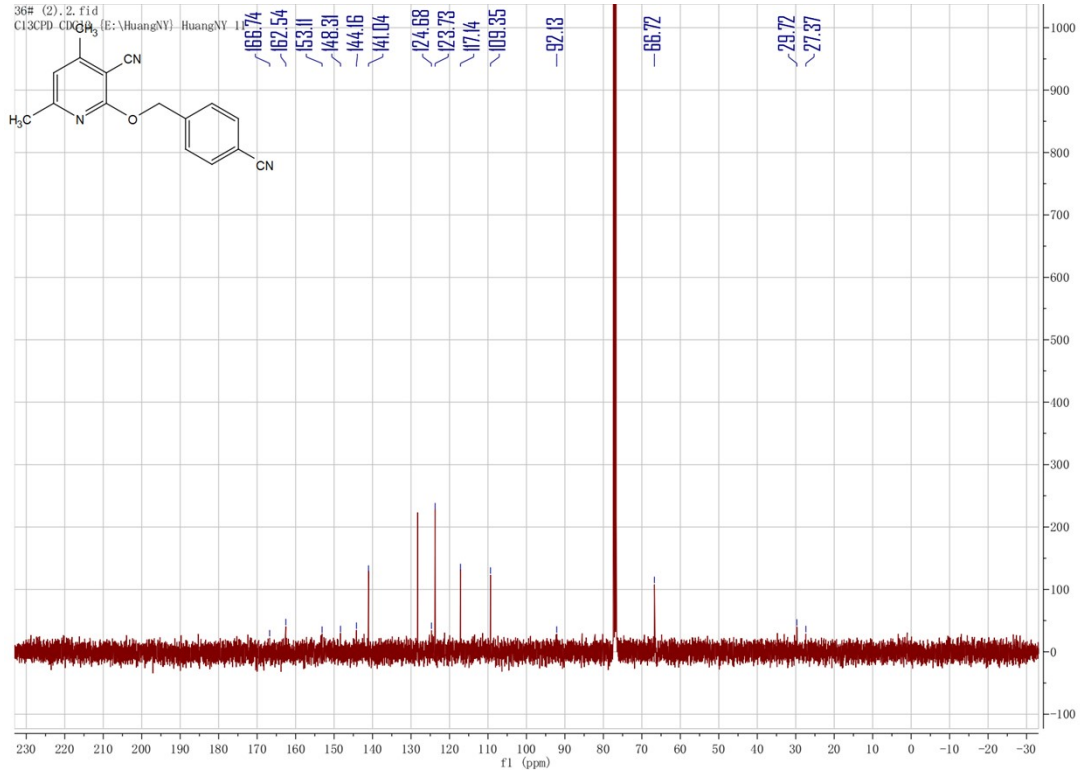
3a-4 ^{1}H NMR



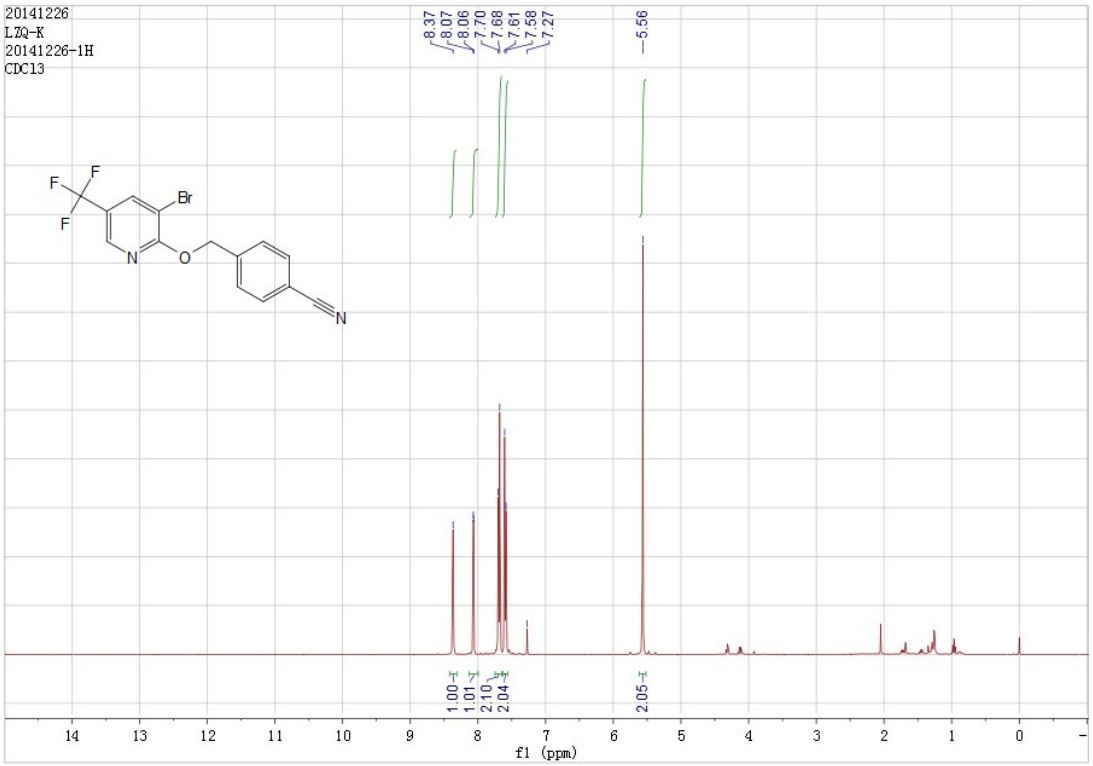
3a-4 ^{13}C NMR



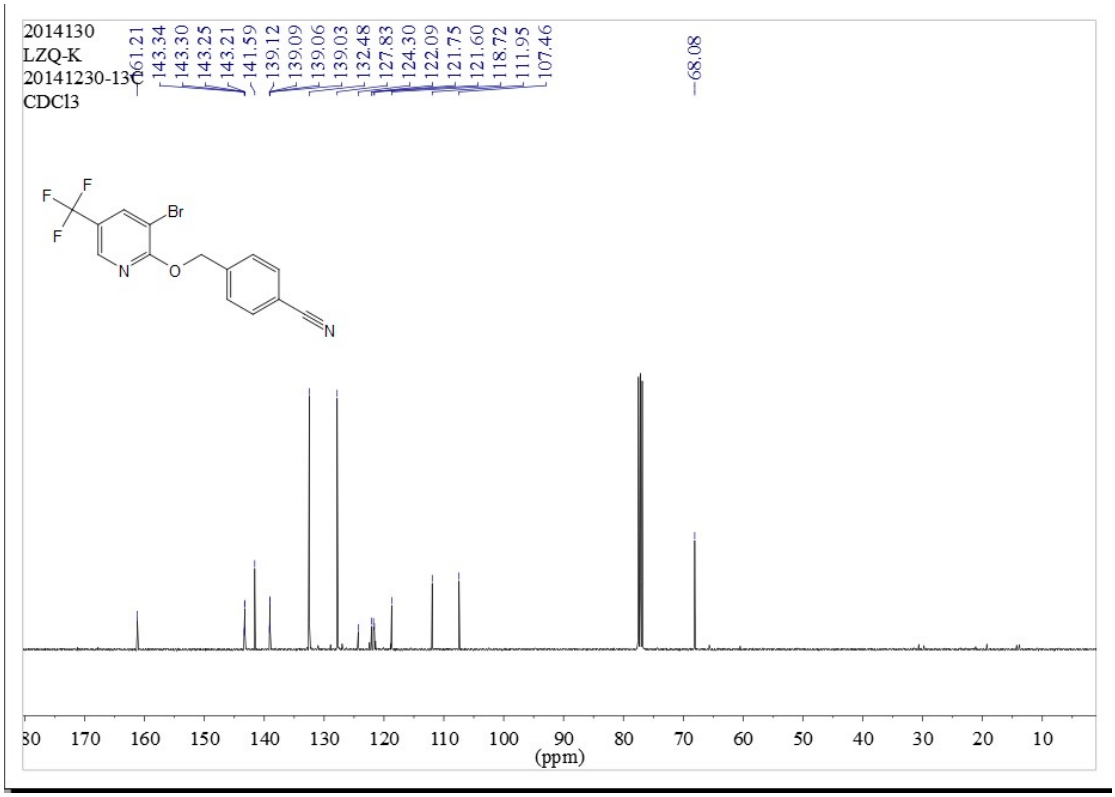
3a-5 ^{1}H NMR



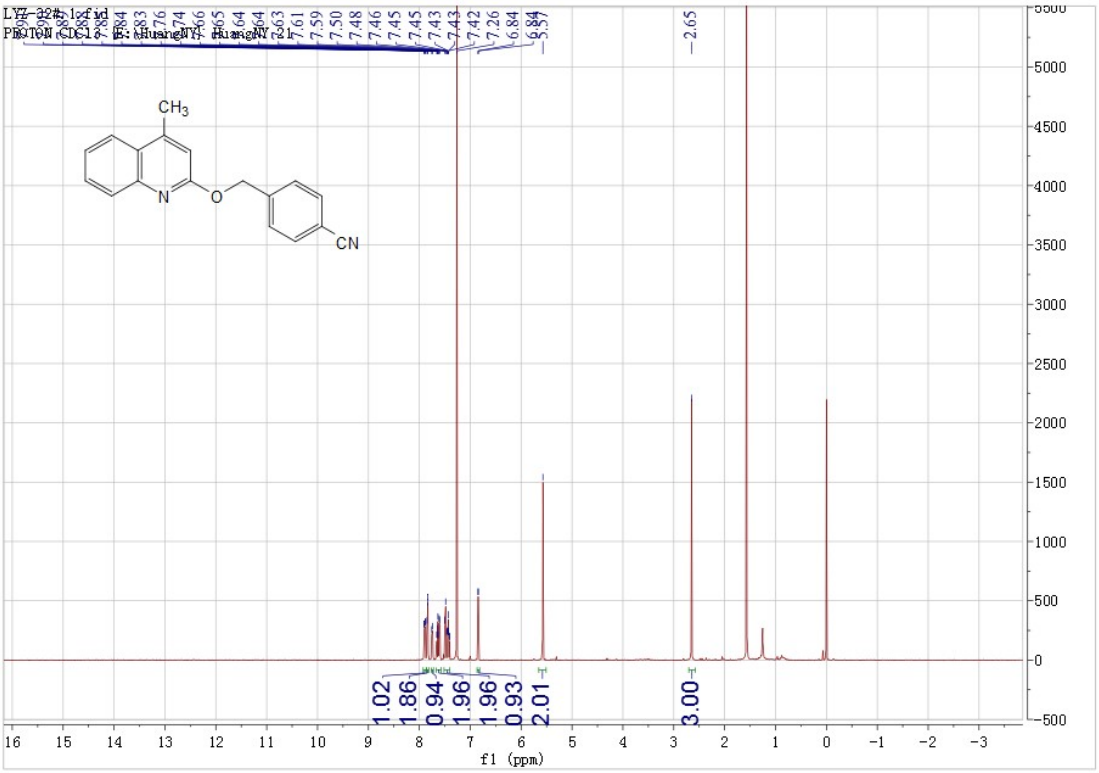
3a-5 ^{13}C NMR



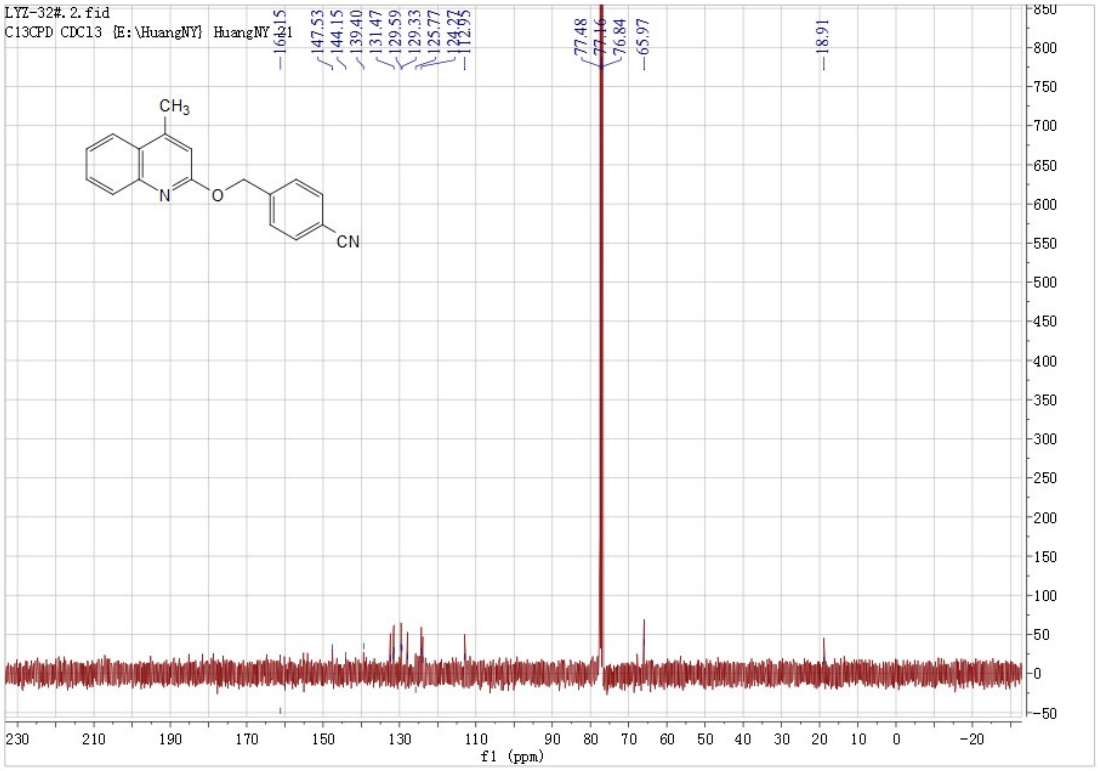
3a-6 ^{1}H NMR



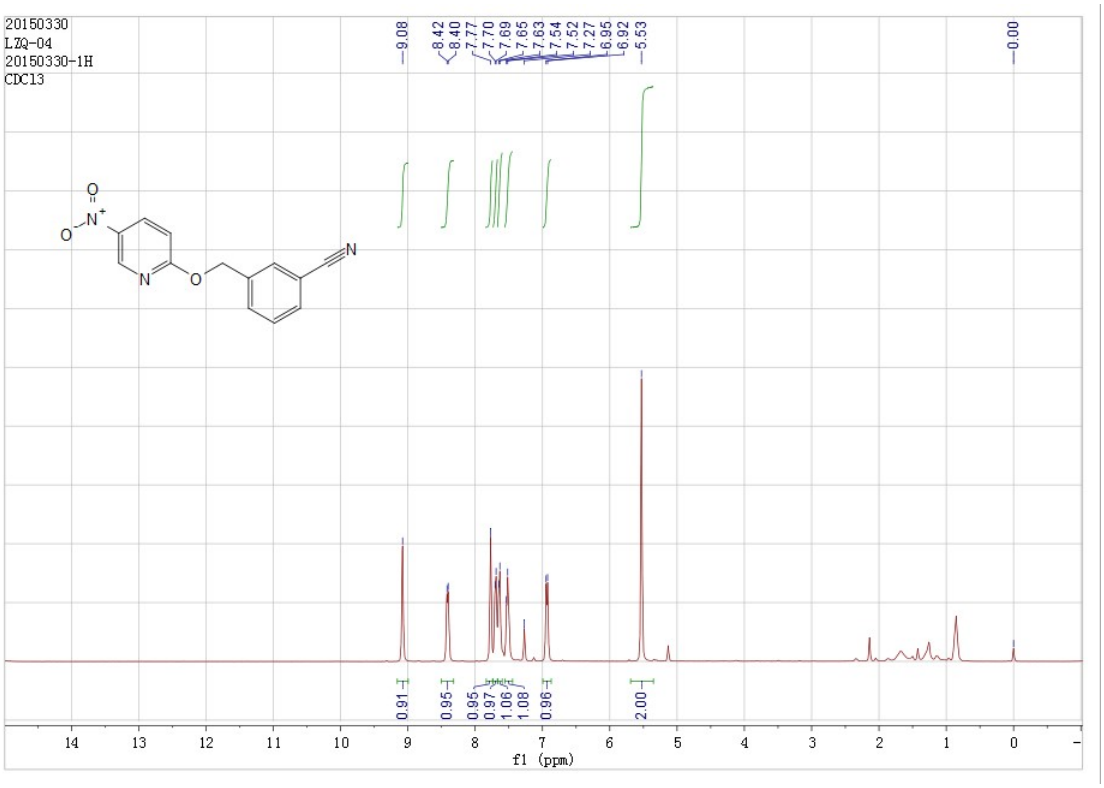
3a-6 ^{13}C NMR



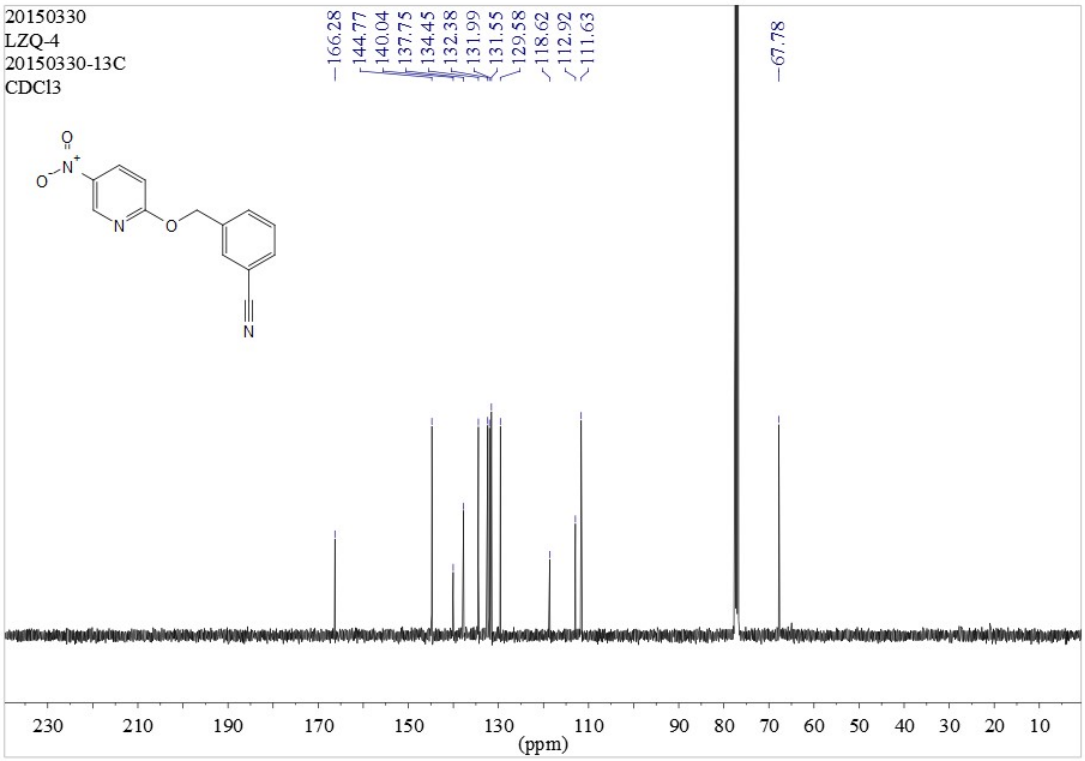
3a-7 ^{1}H NMR



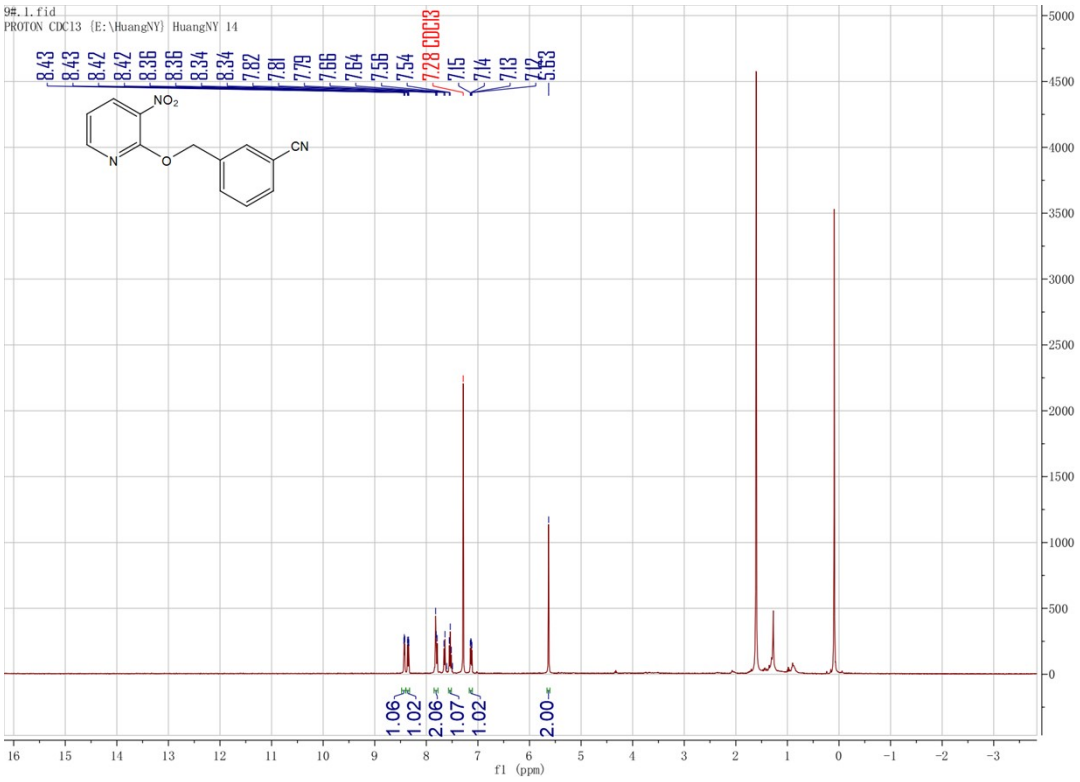
3a-7 ^{13}C NMR



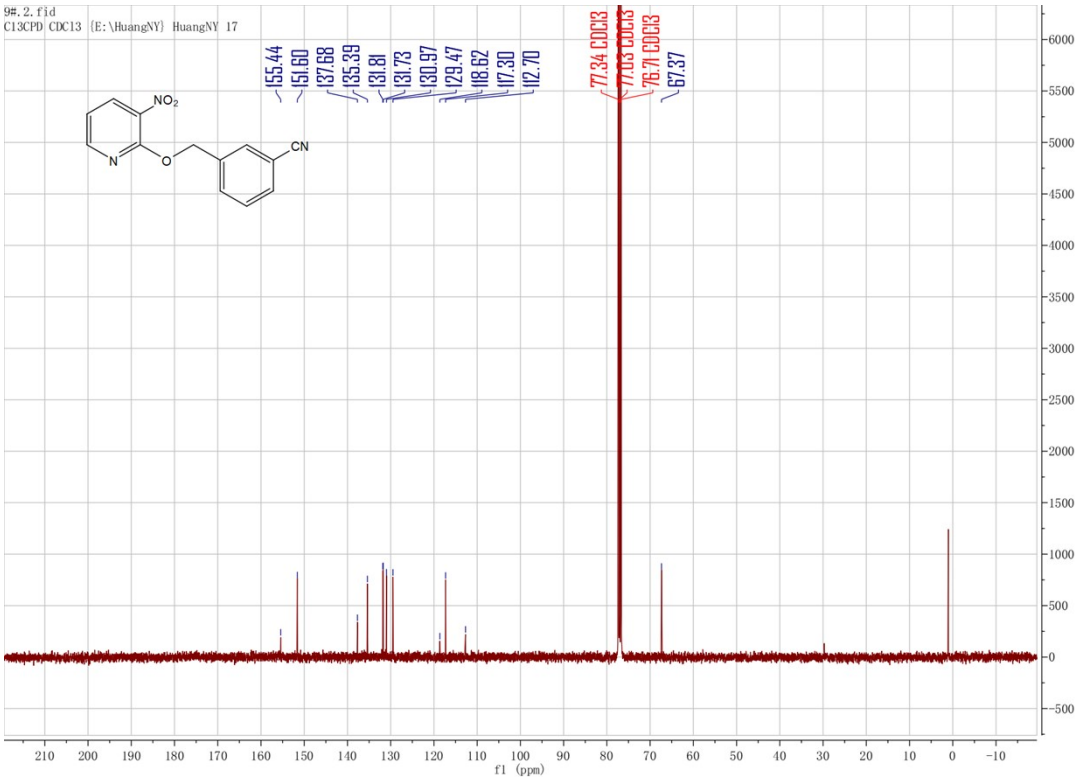
3b-1 ^{1}H NMR



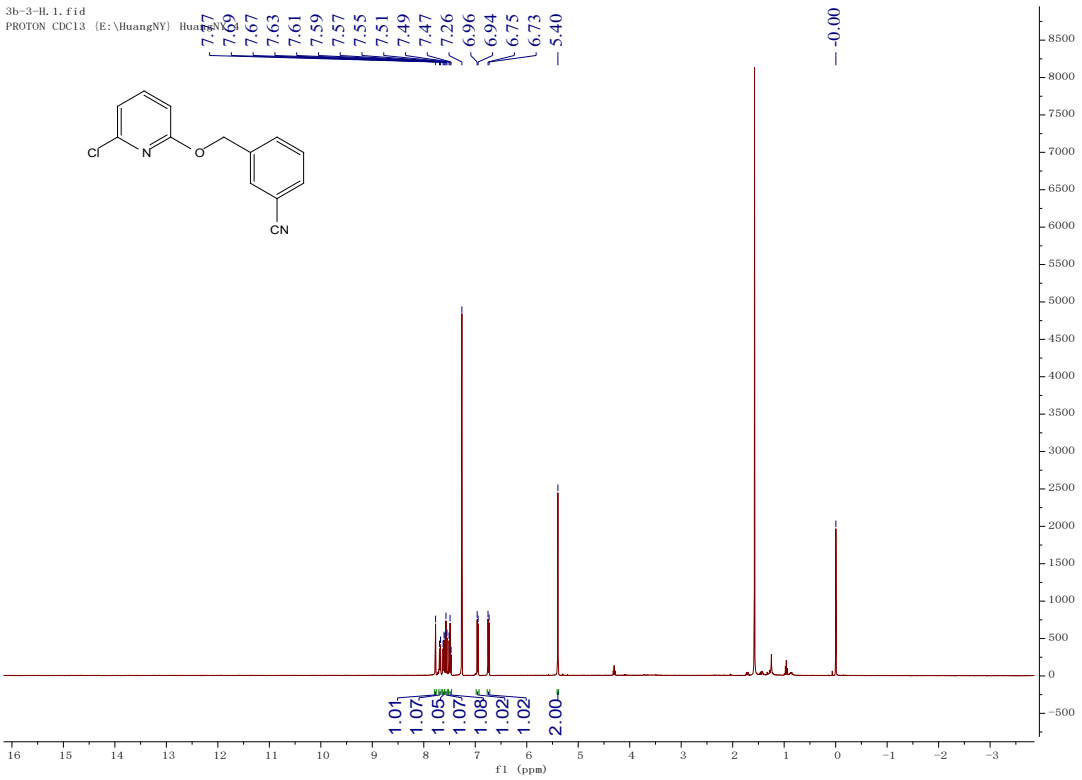
3b-1 ^{13}C NMR



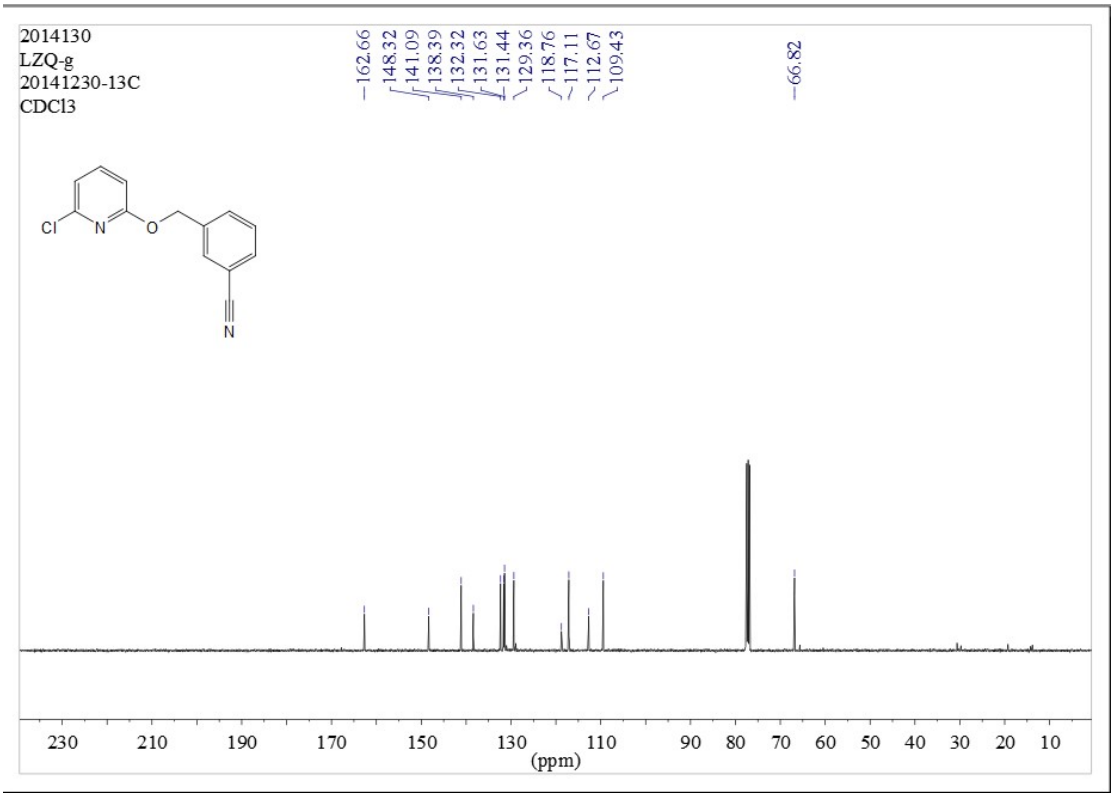
3b-2 ^{1}H NMR



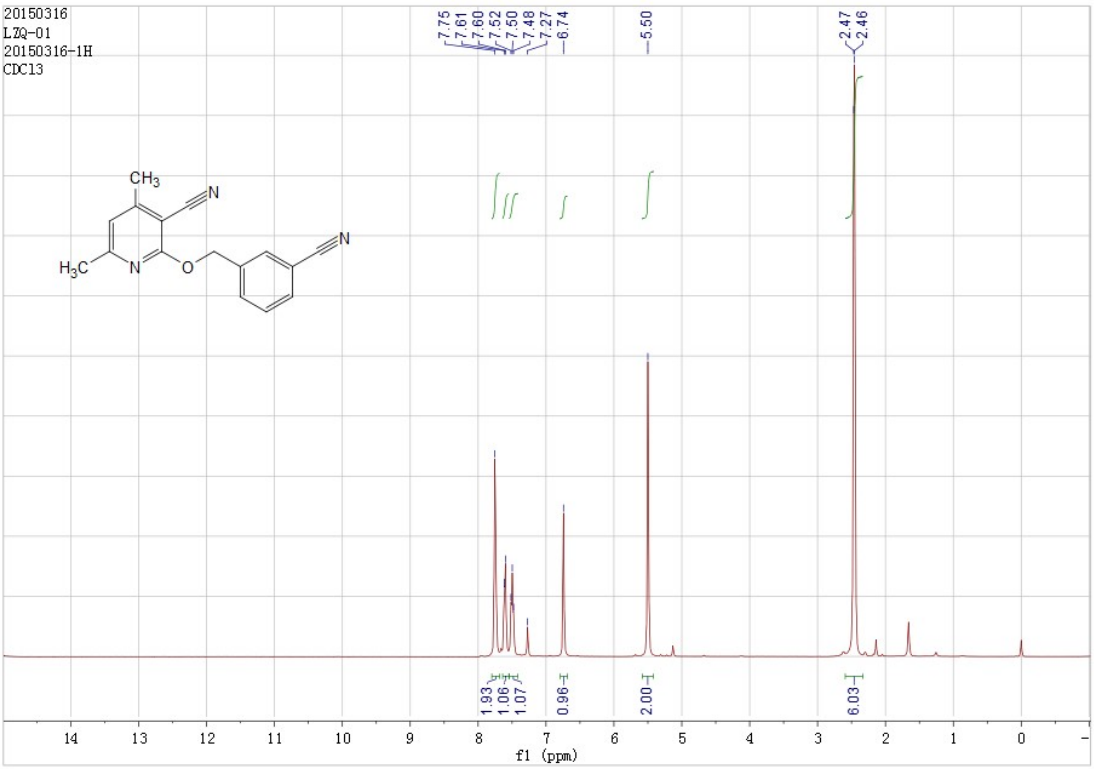
3b-2 ^{13}C NMR



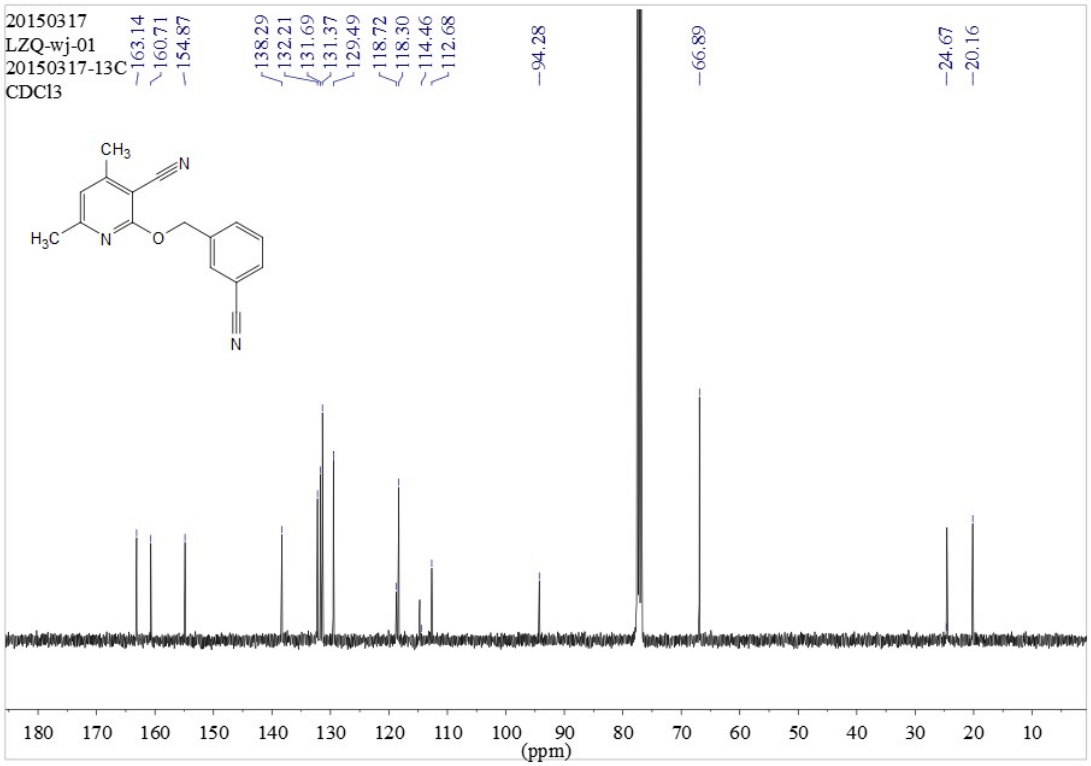
3b-3 ^{1}H NMR



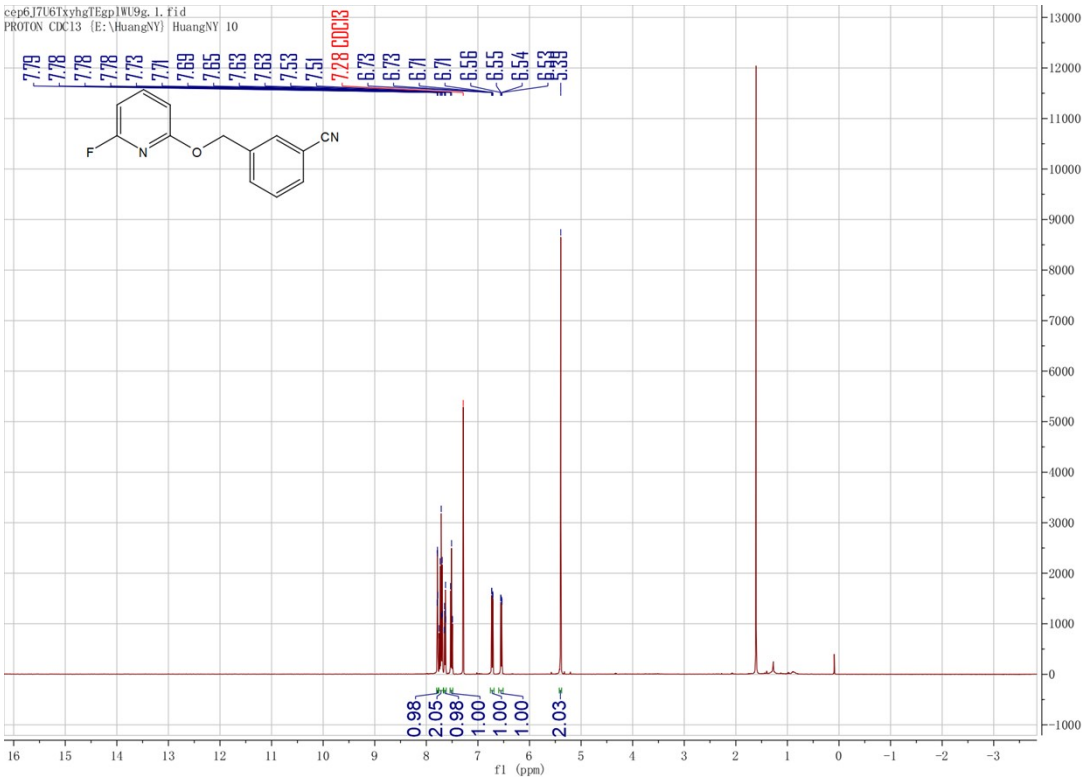
3b-3 ^{13}C NMR



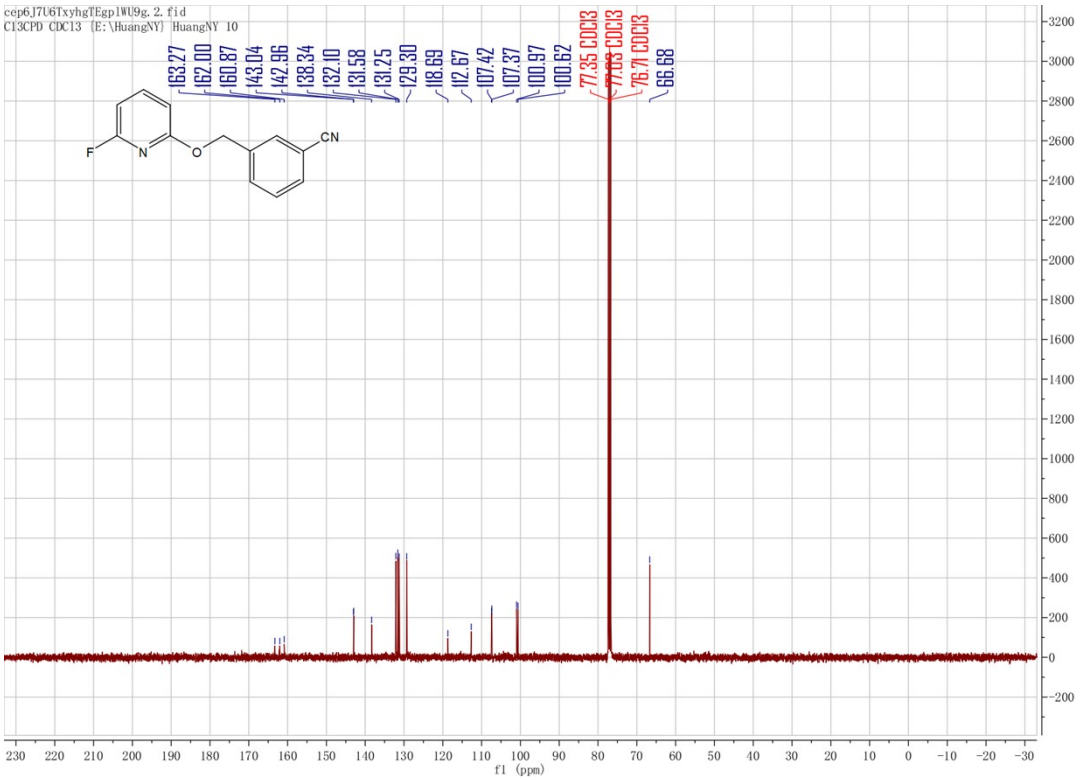
3b-4 ^{1}H NMR



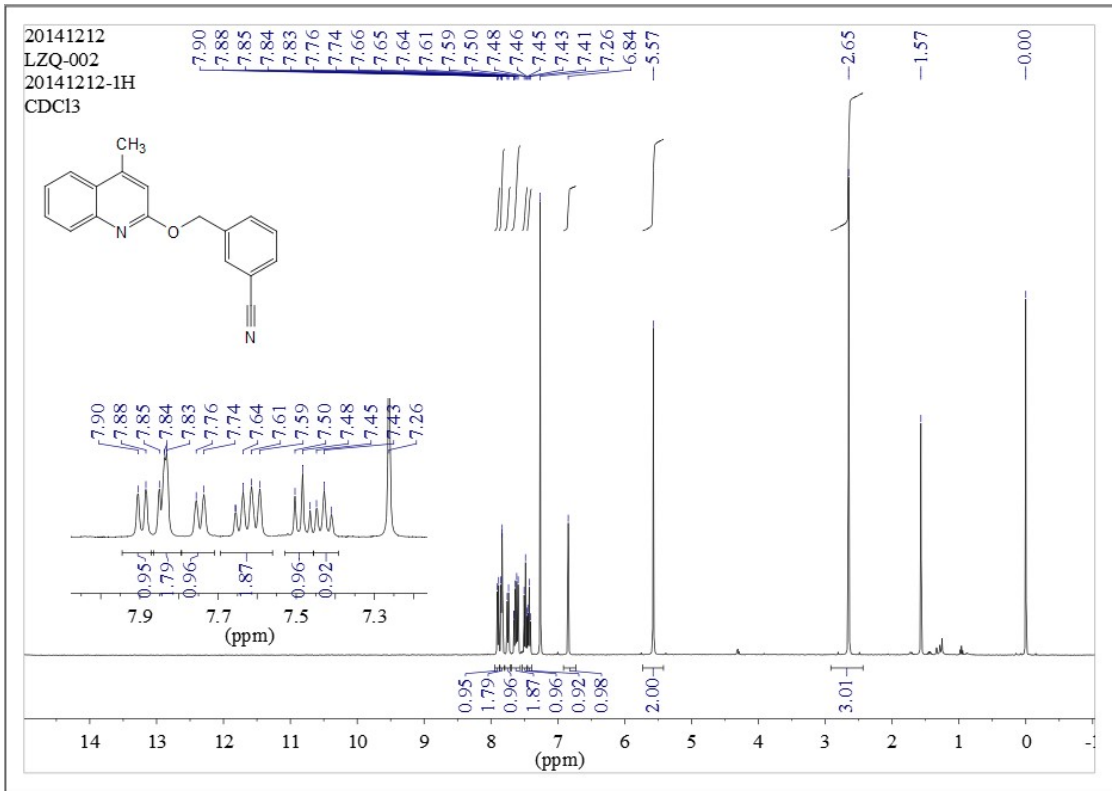
3b-4 ^{13}C NMR



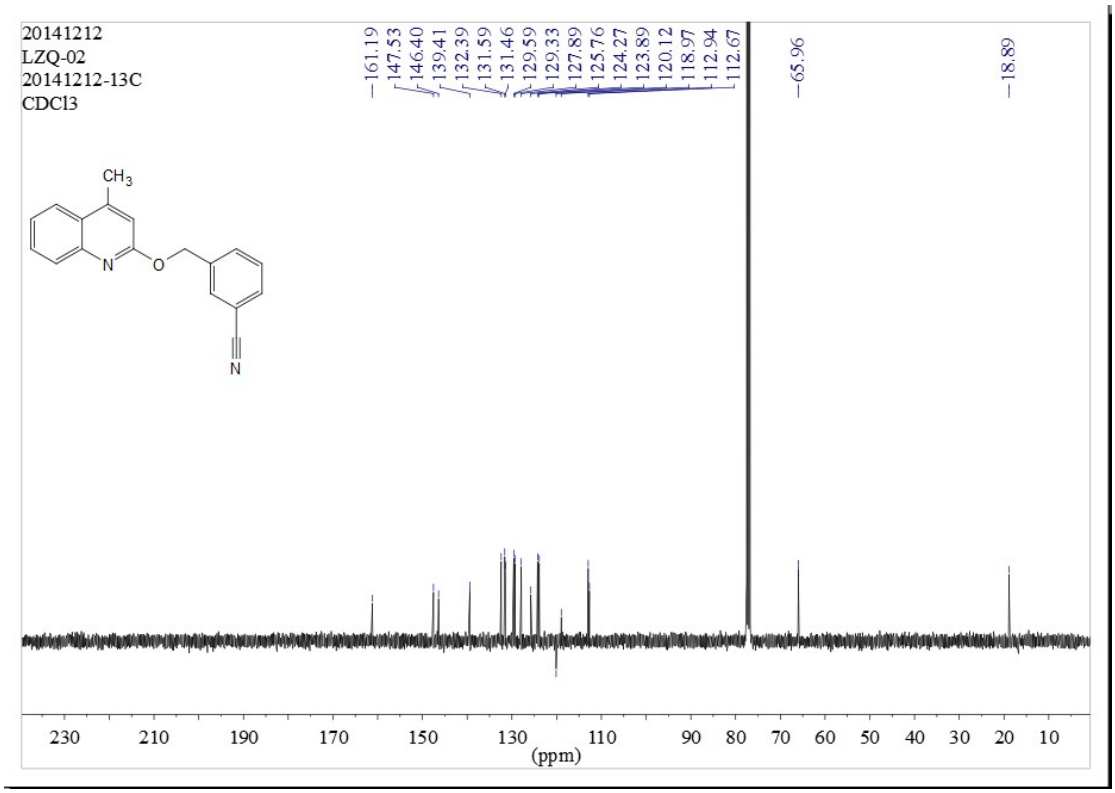
3b-5 ^{1}H NMR



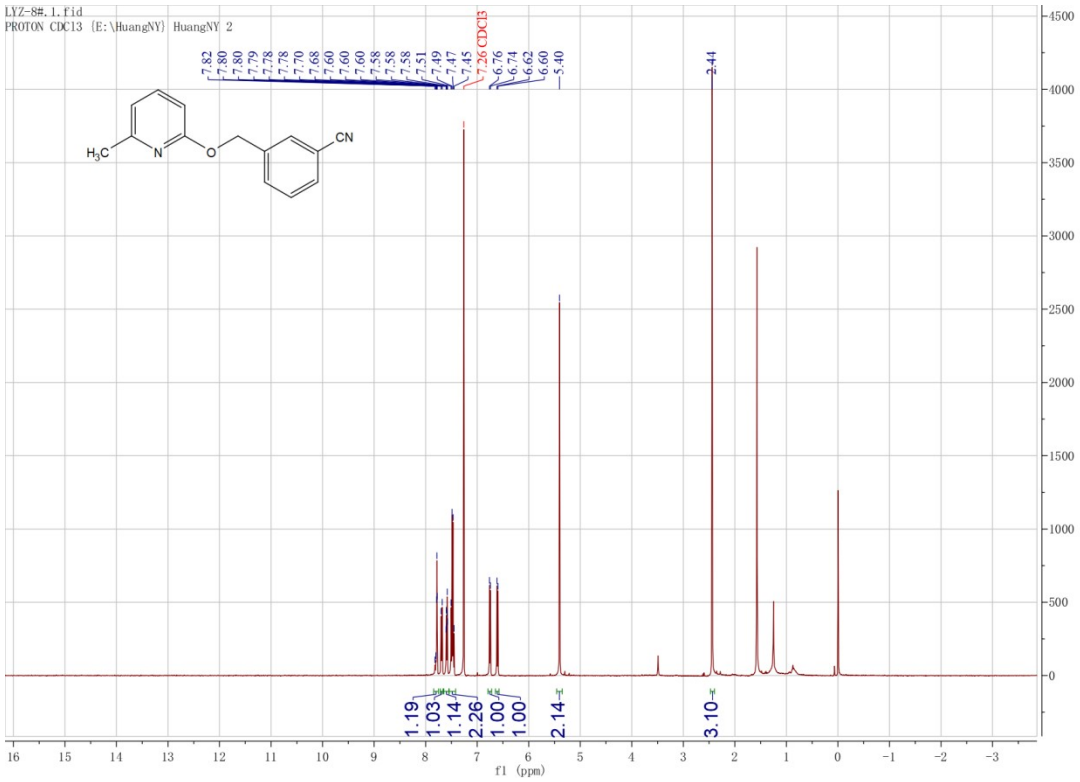
3b-5 ^{13}C NMR



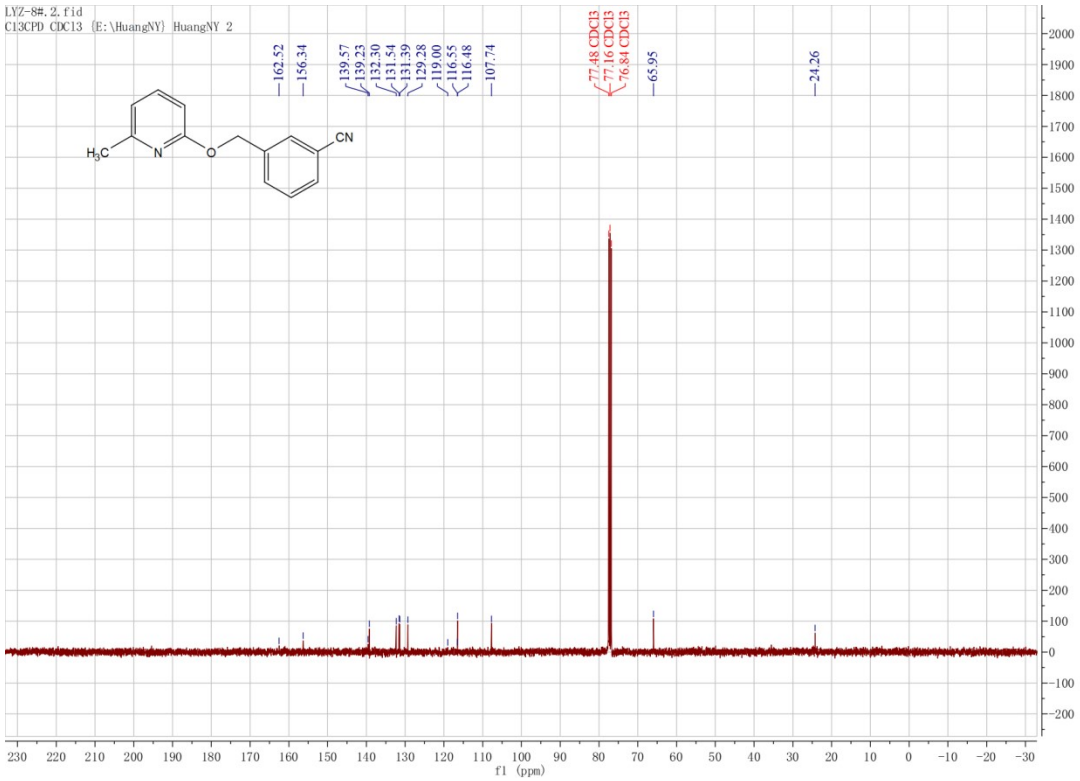
3b-6 ^{1}H NMR



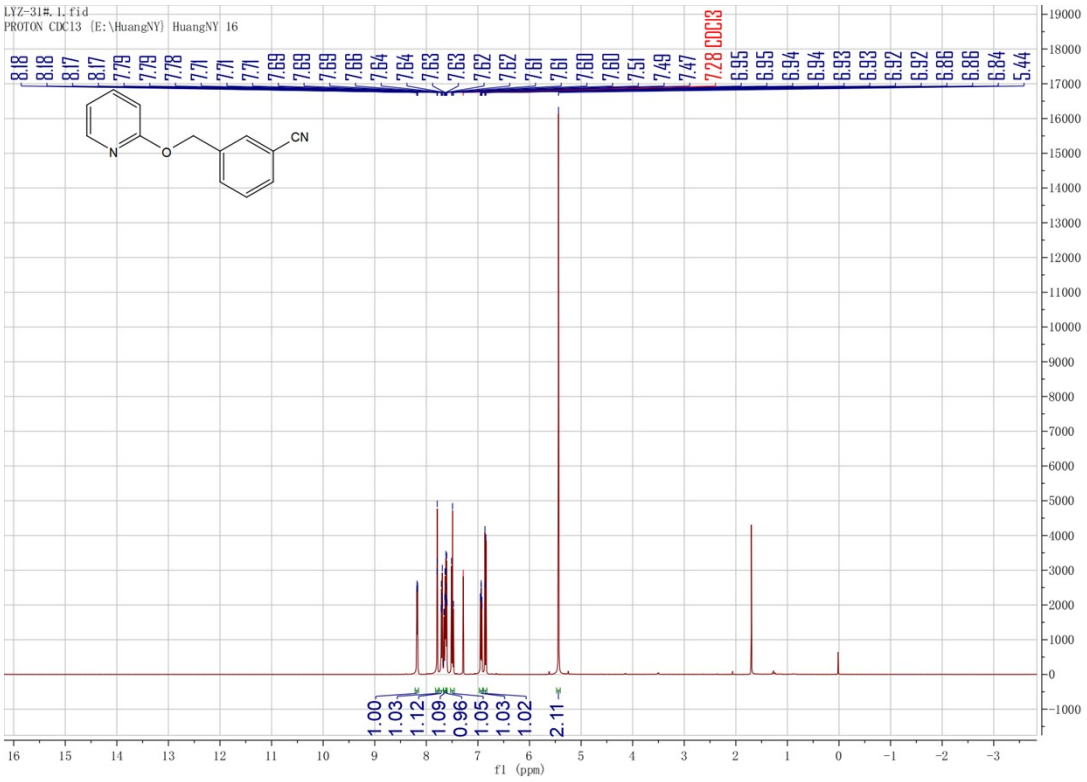
3b-6 ^{13}C NMR



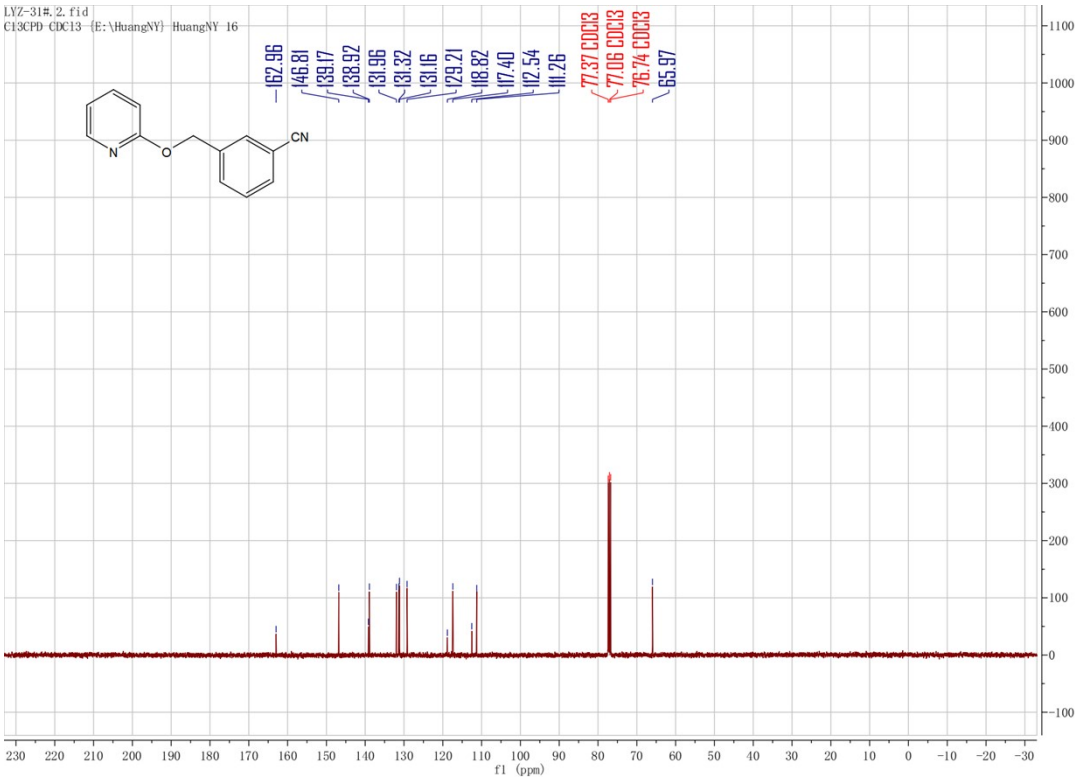
3b-7 ^{1}H NMR



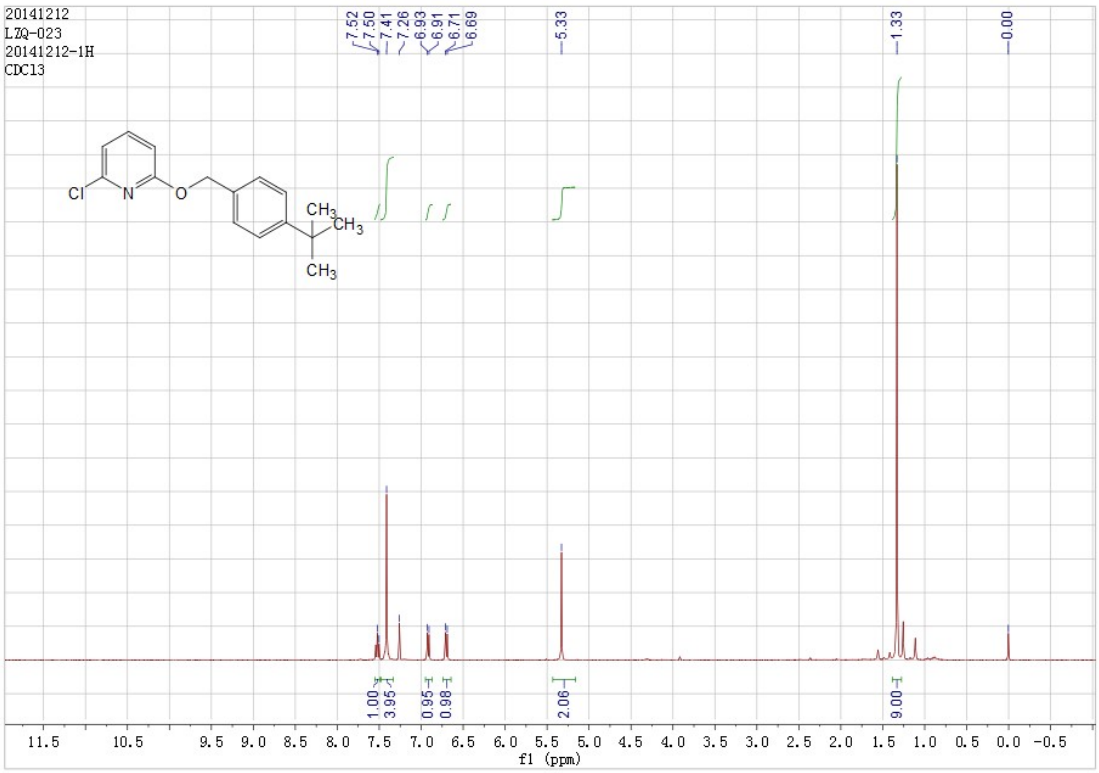
3b-7 ^{13}C NMR



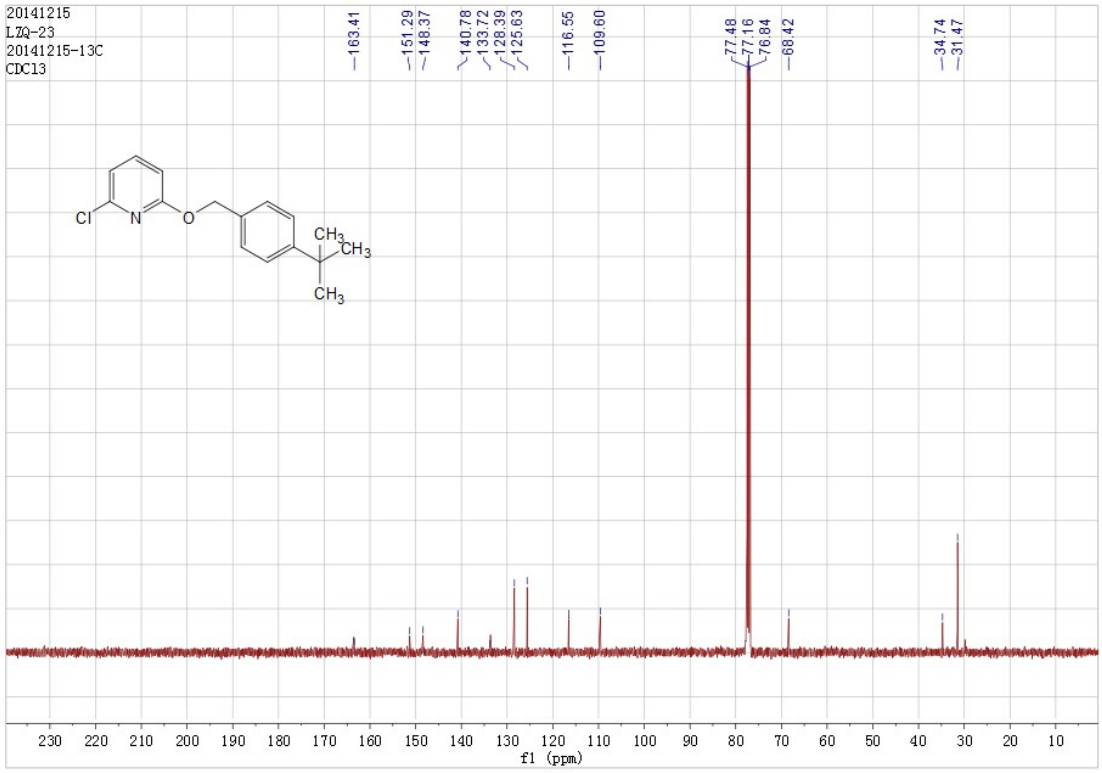
3b-8 ^{1}H NMR



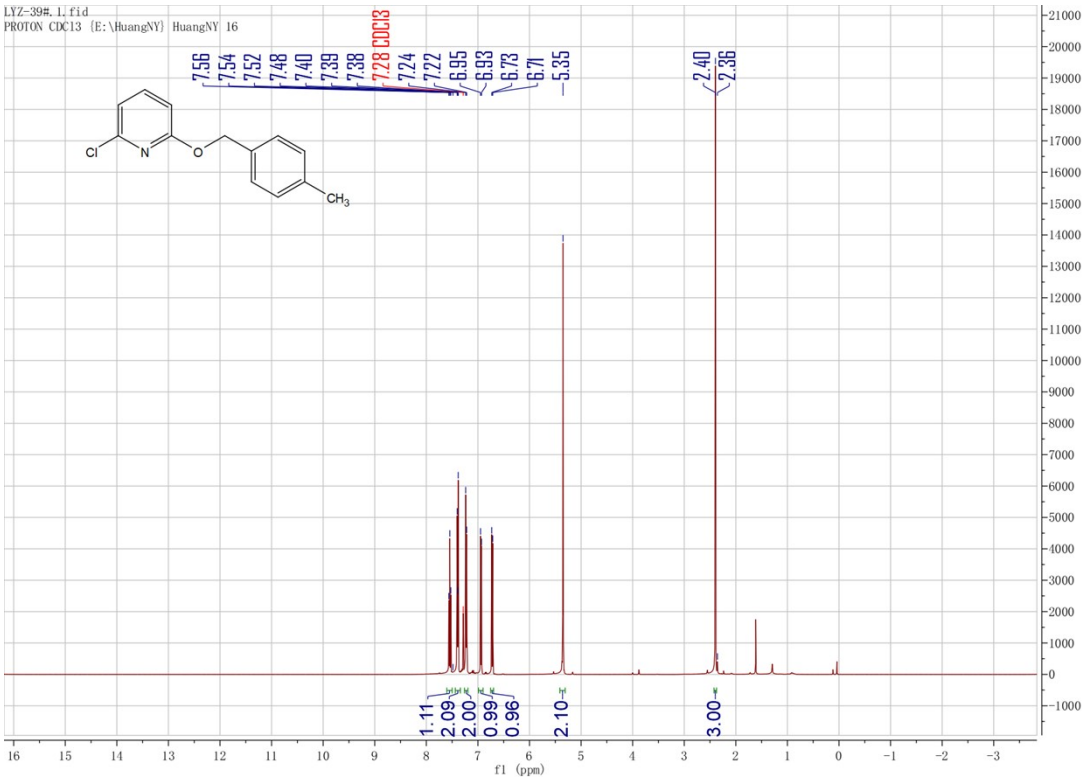
3b-8 ^{13}C NMR



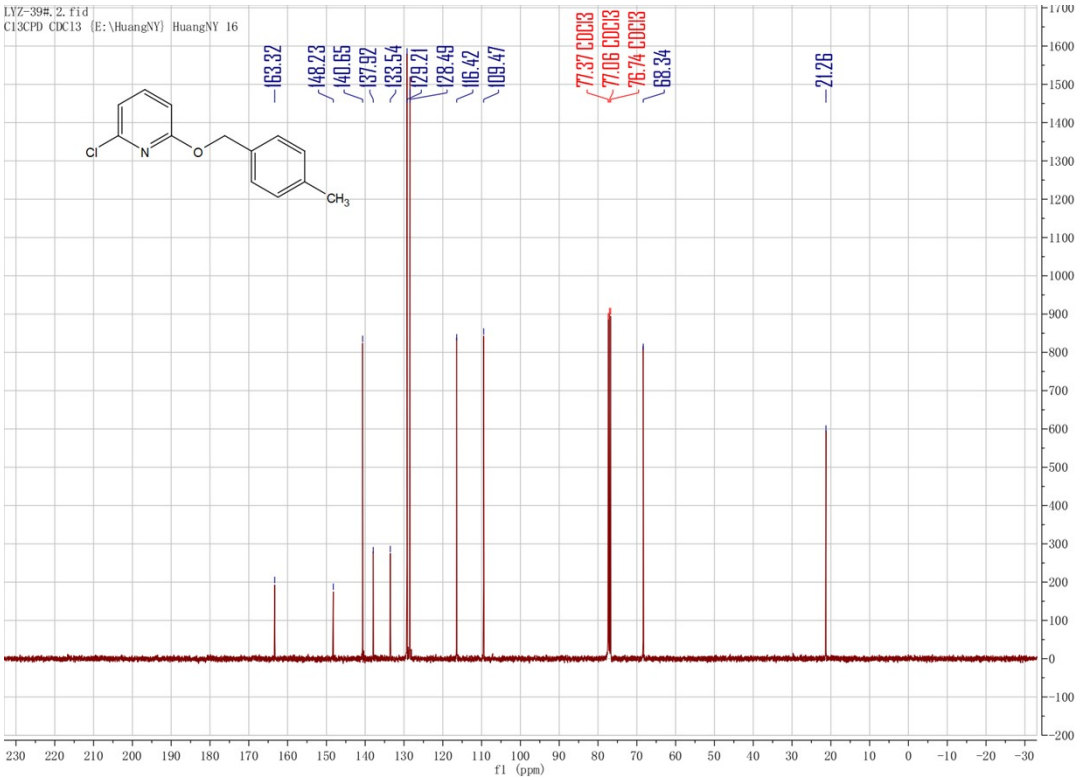
3c-1 ^{1}H NMR



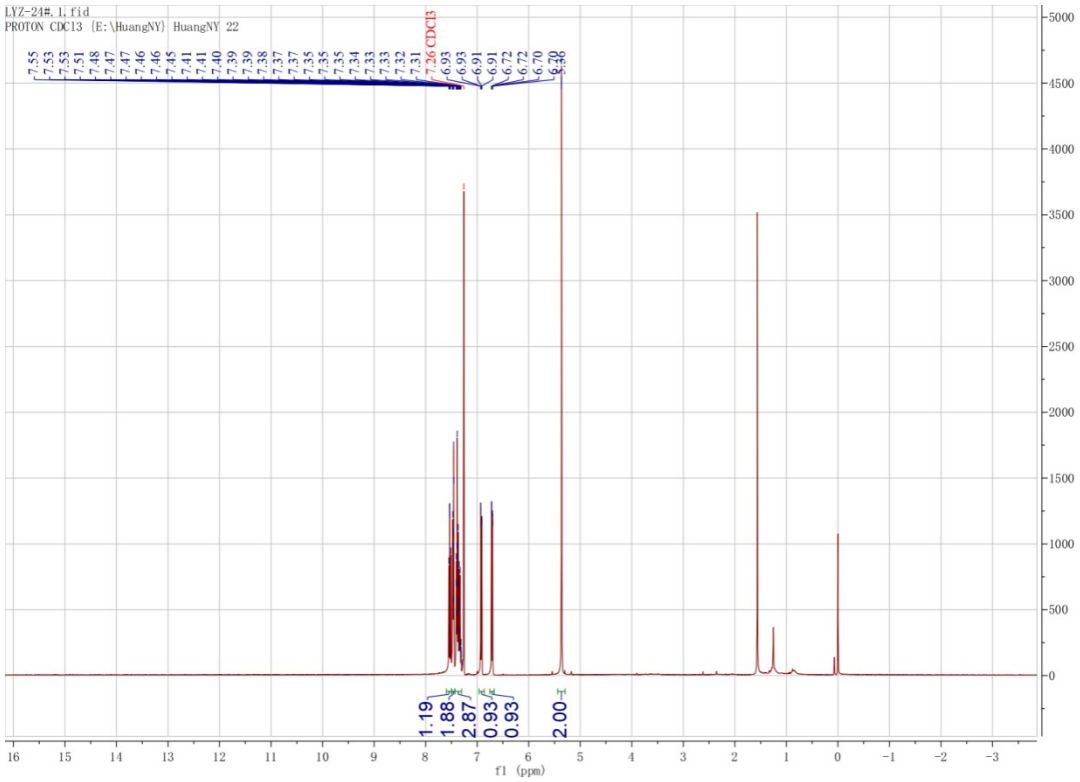
3c-1 ^{13}C NMR



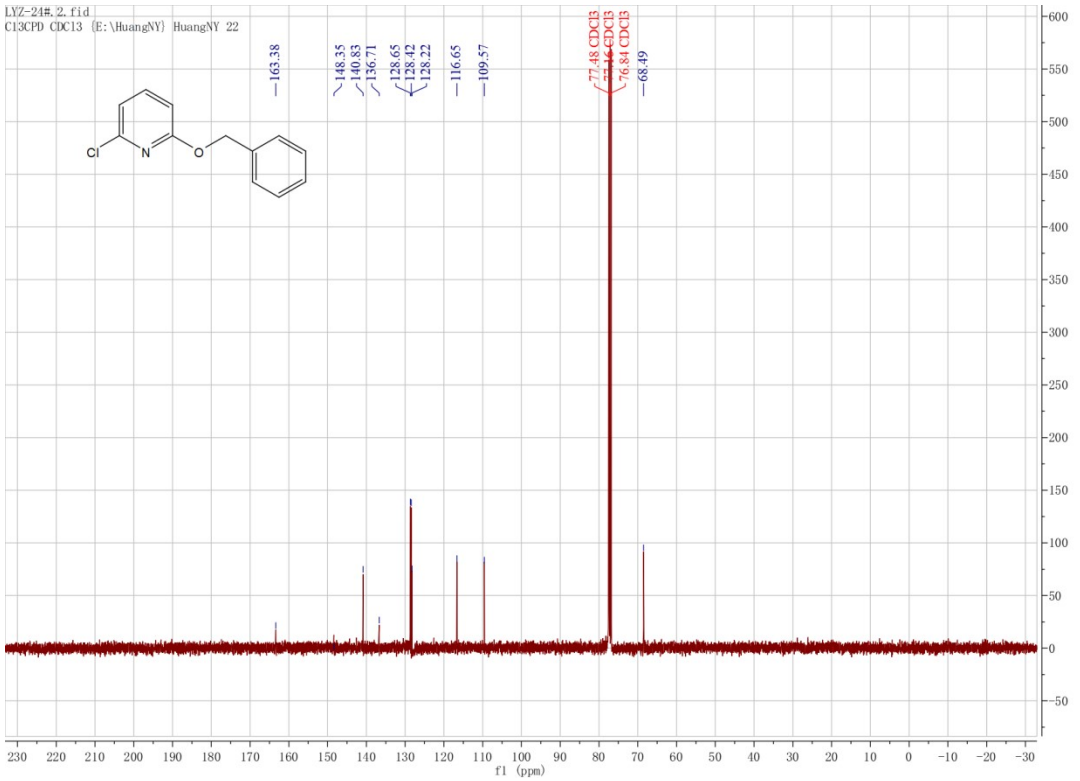
3d-1 ^{1}H NMR



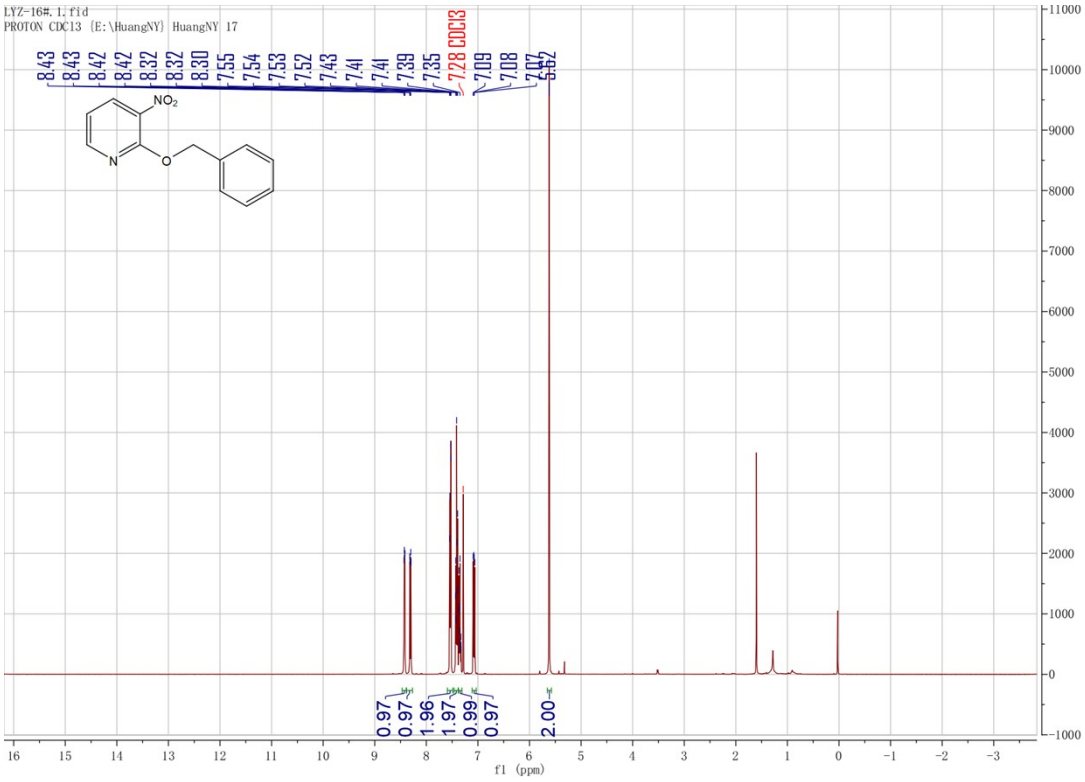
3d-1 ^{13}C NMR



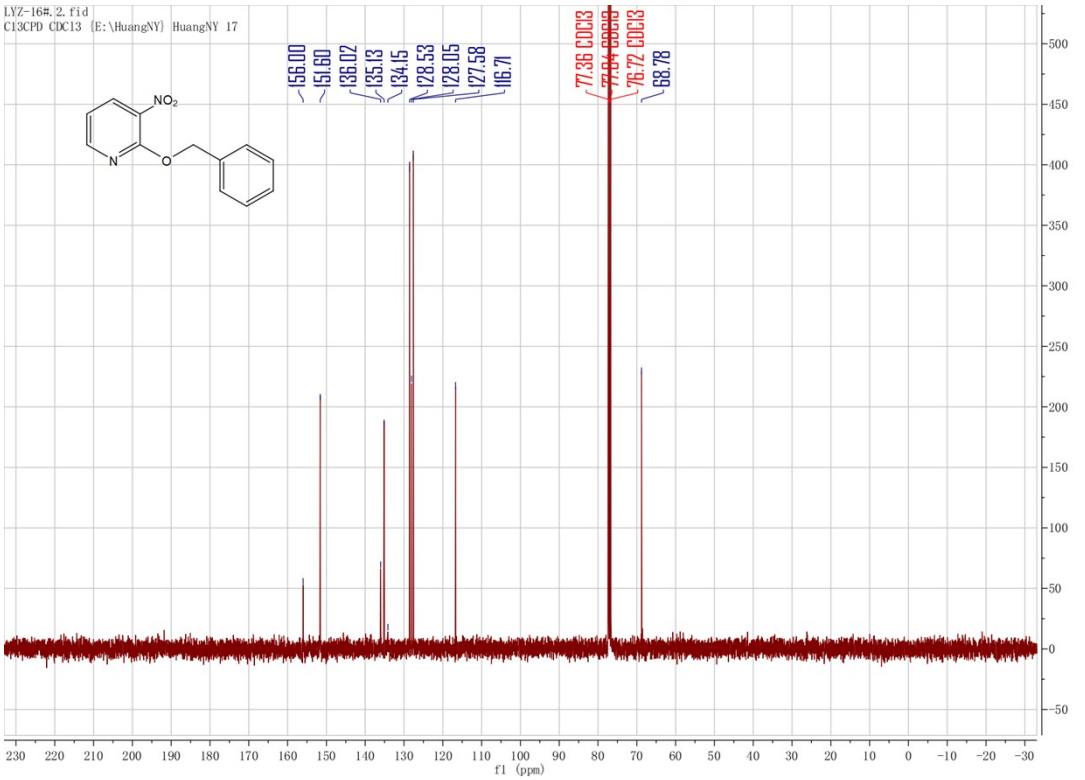
3e-1 ^{1}H NMR



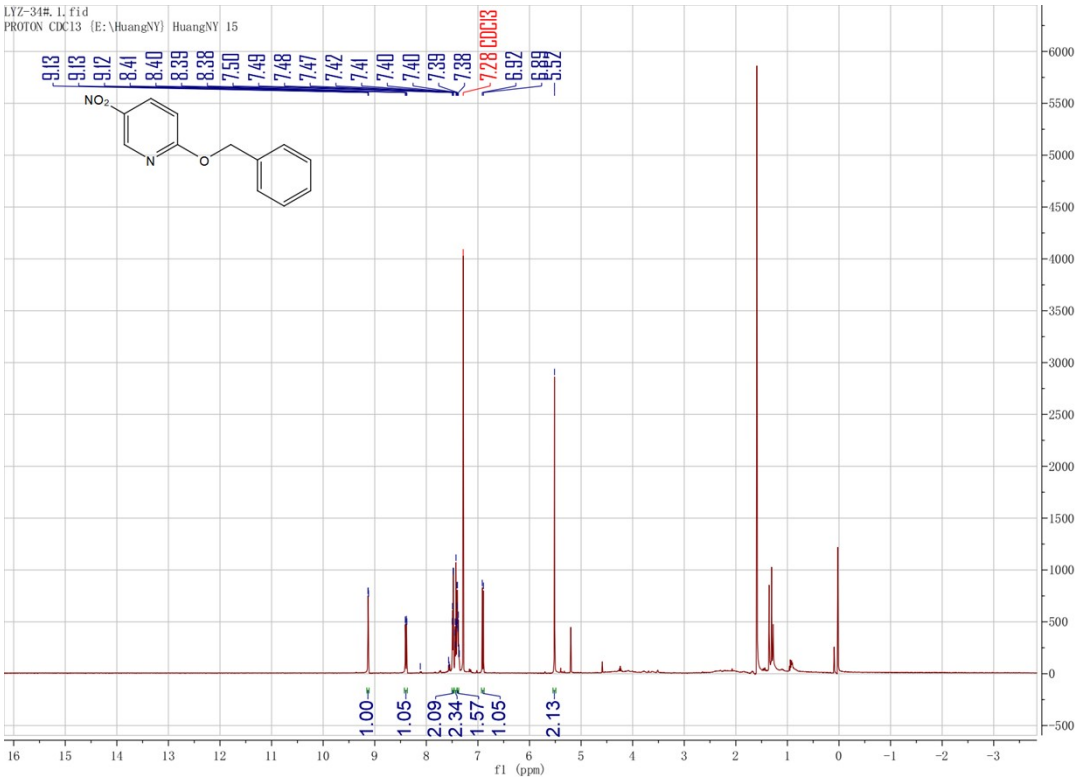
3e-1 ^{13}C NMR



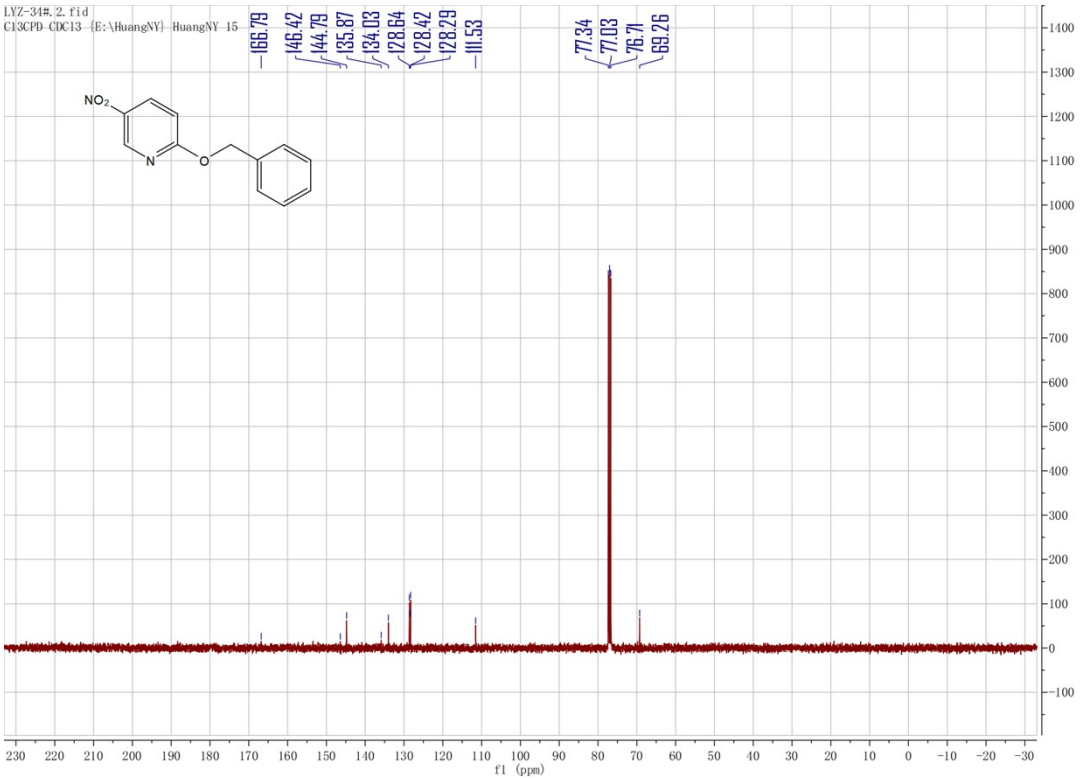
3e-2 ^{1}H NMR



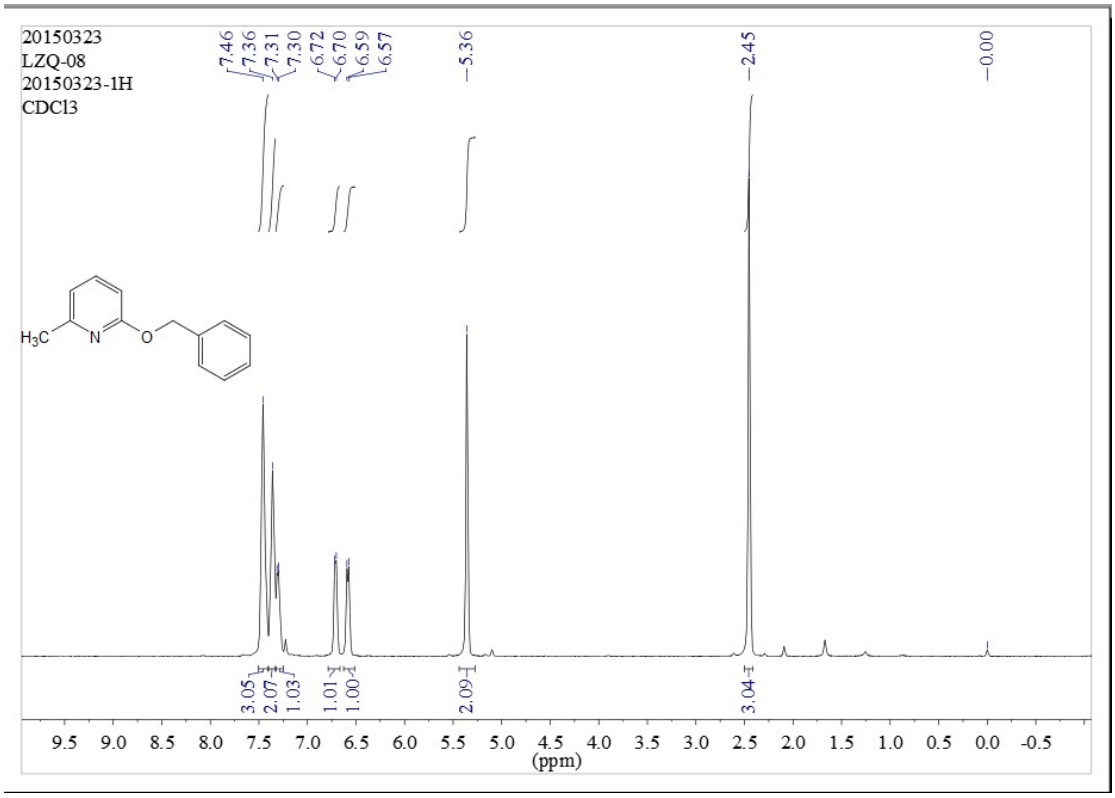
3e-2 ^{13}C NMR



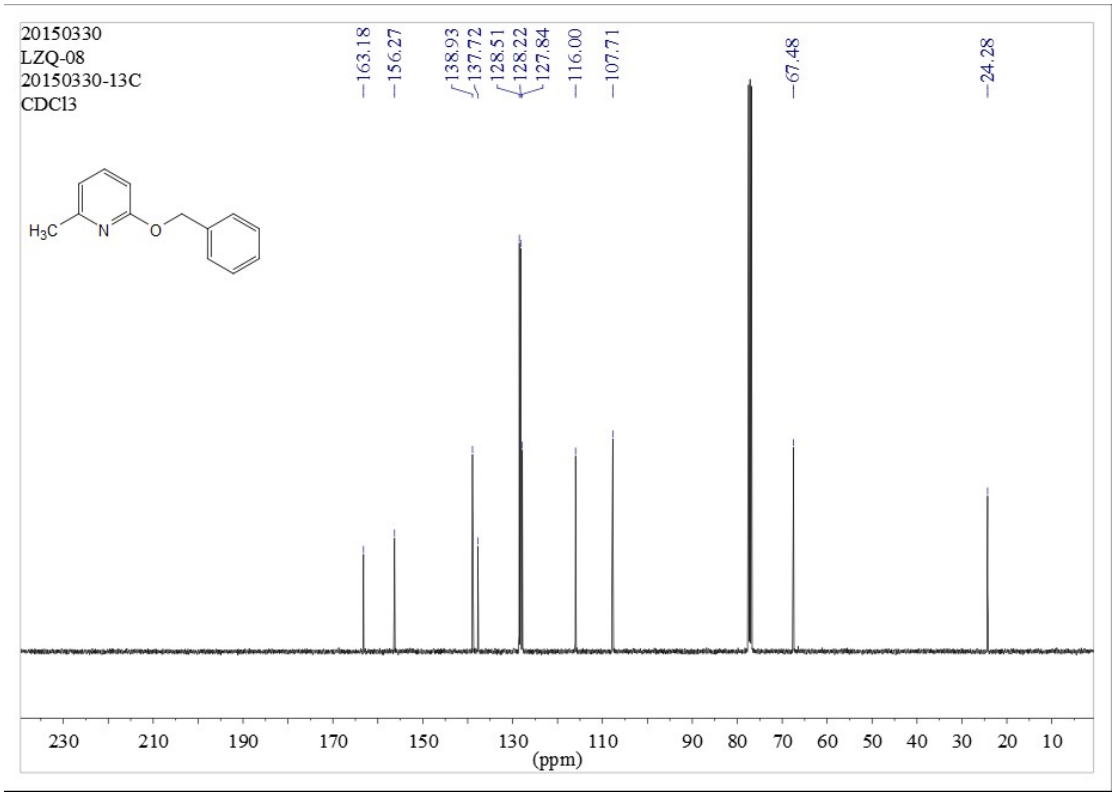
3e-3 ^{1}H NMR



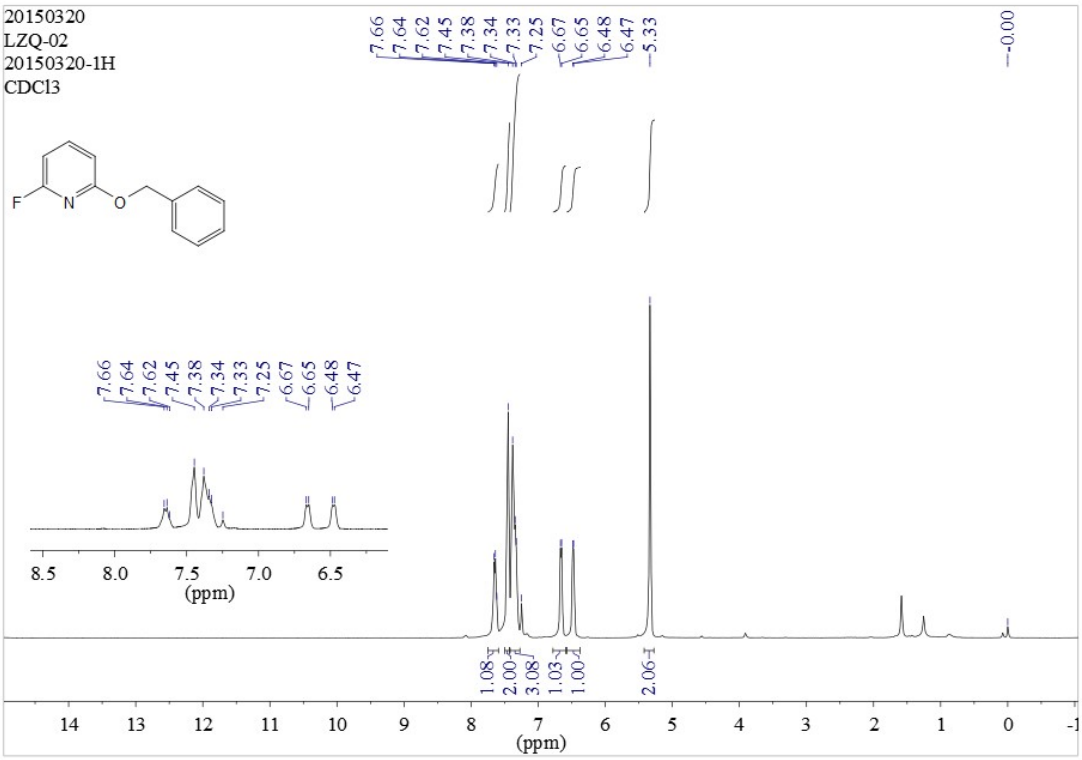
3e-3 ^{13}C NMR



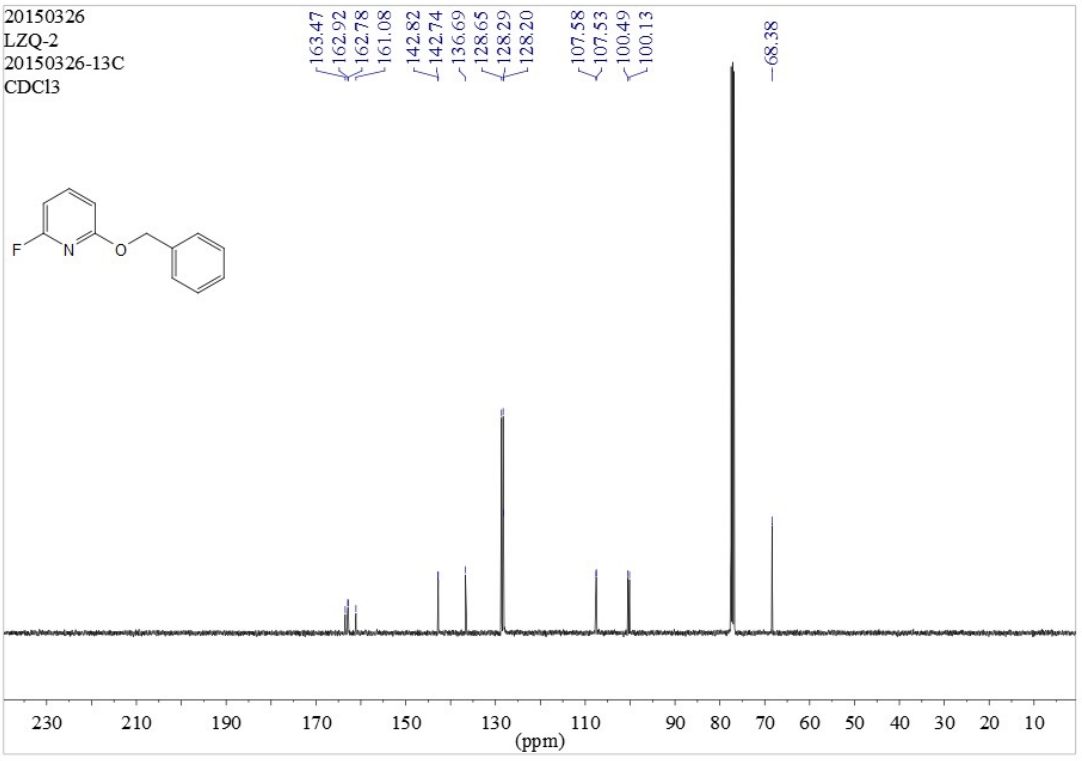
3e-4 ^{1}H NMR



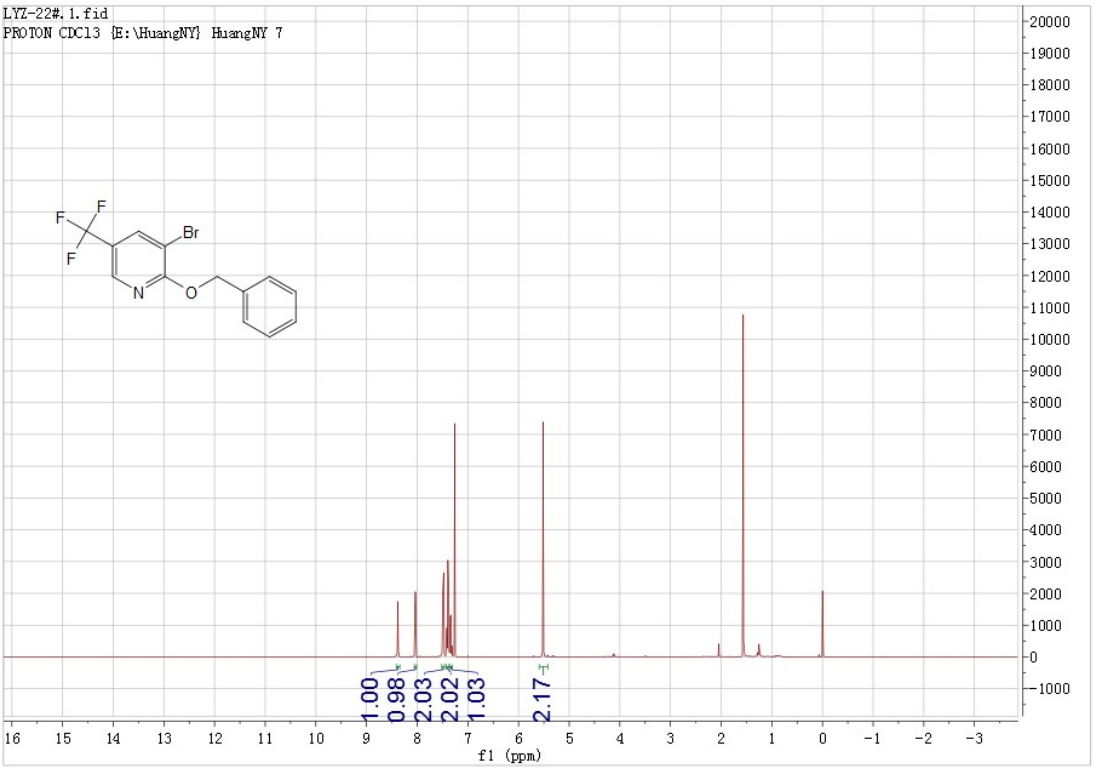
3e-4 ^{13}C NMR



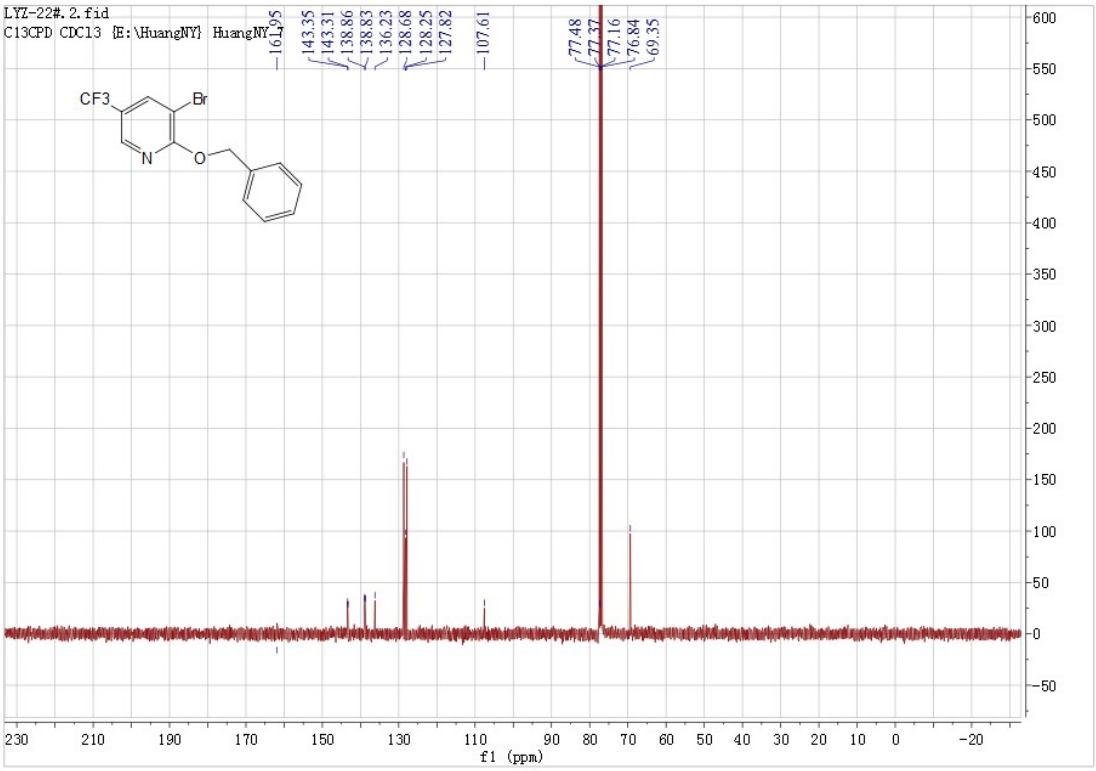
3e-5 ^{1}H NMR



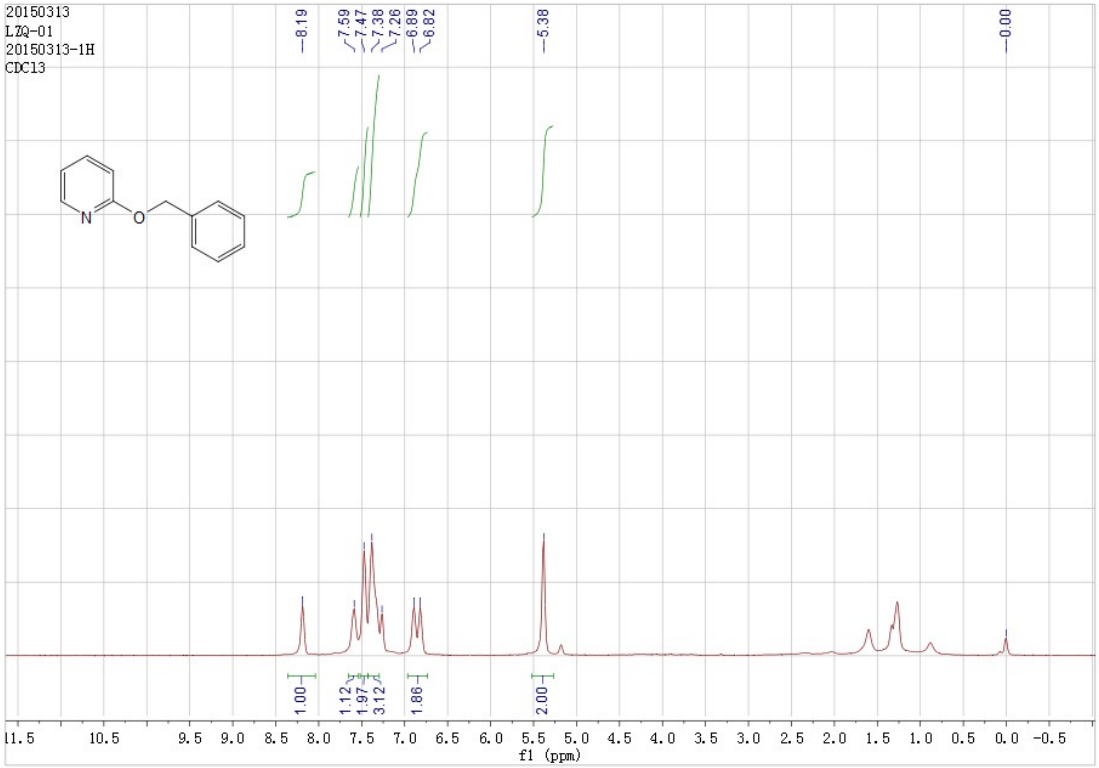
3e-5 ^{13}C NMR



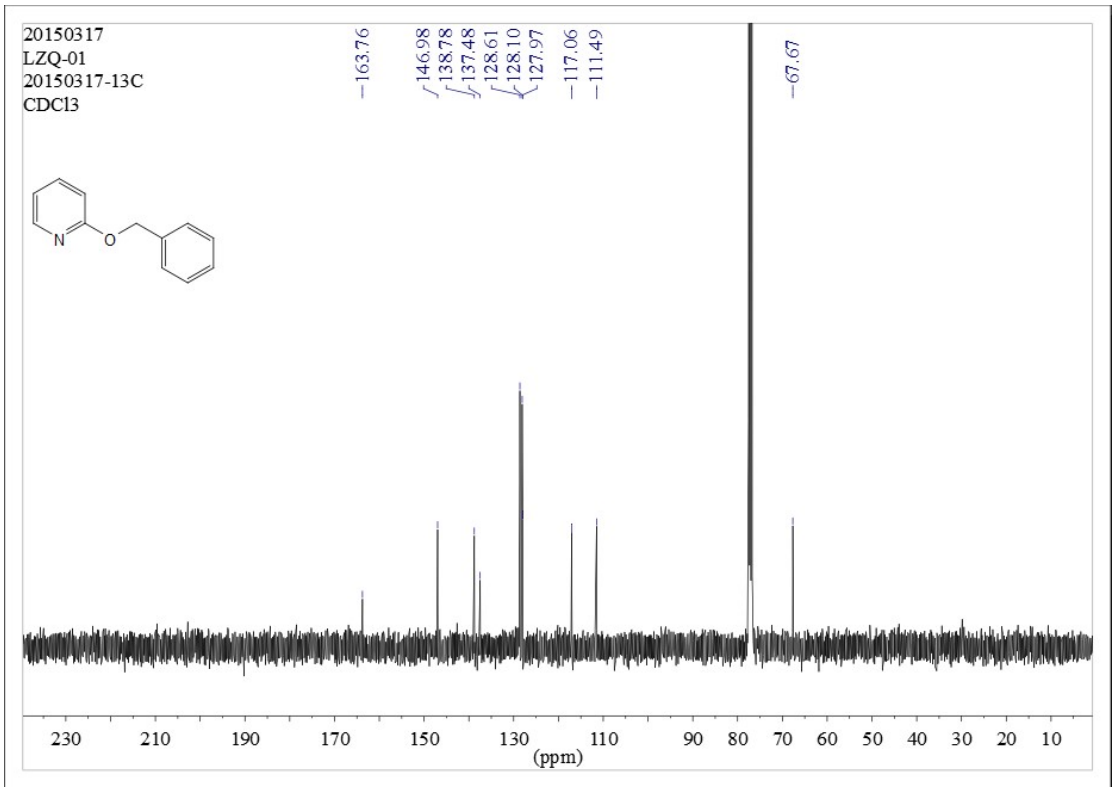
3e-6 ^{1}H NMR



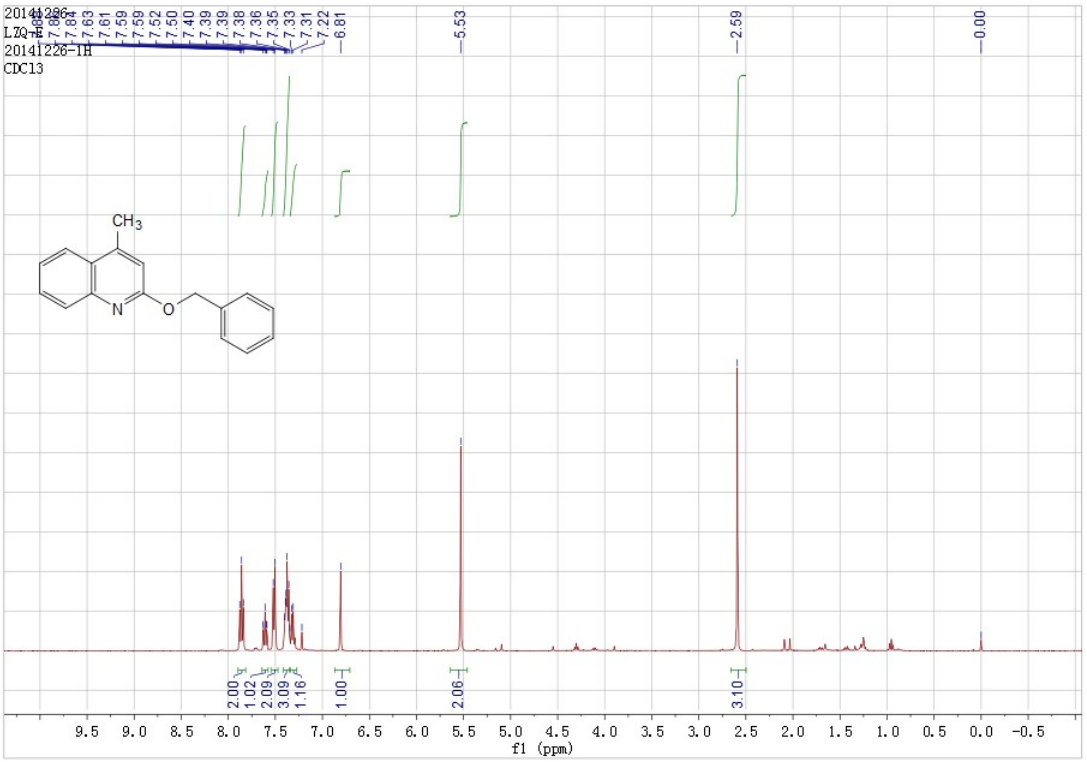
3e-6 ^{13}C NMR



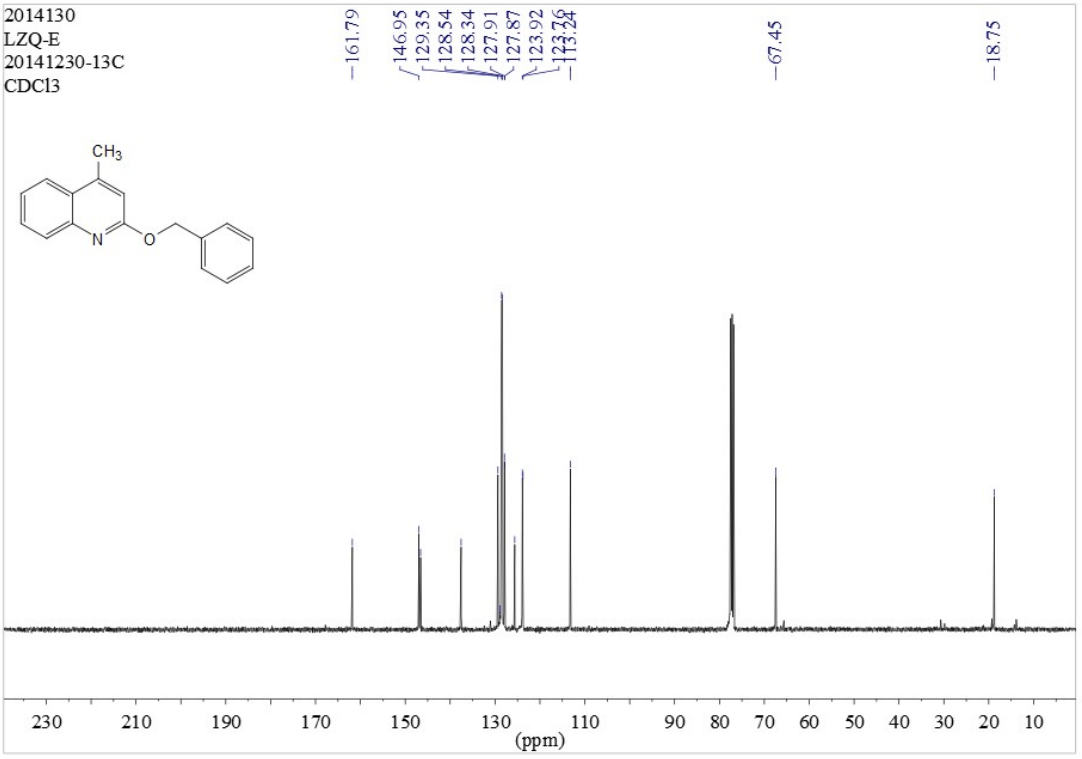
3e-7 ^{1}H NMR



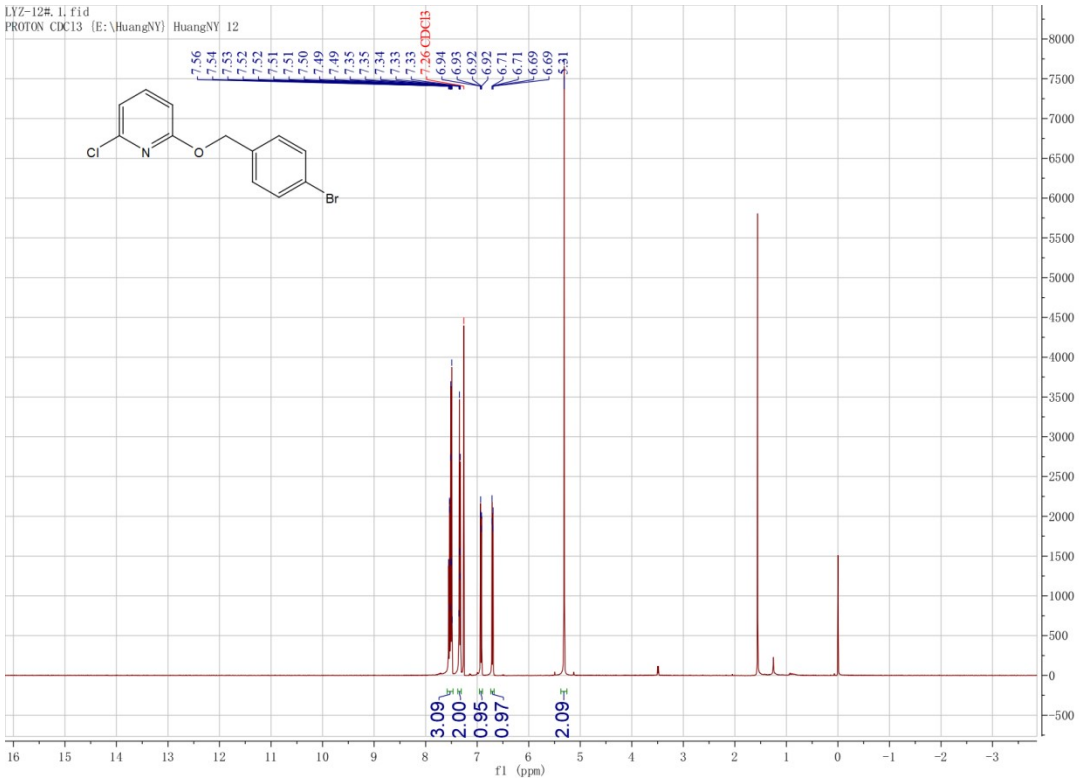
3e-7 ^{13}C NMR



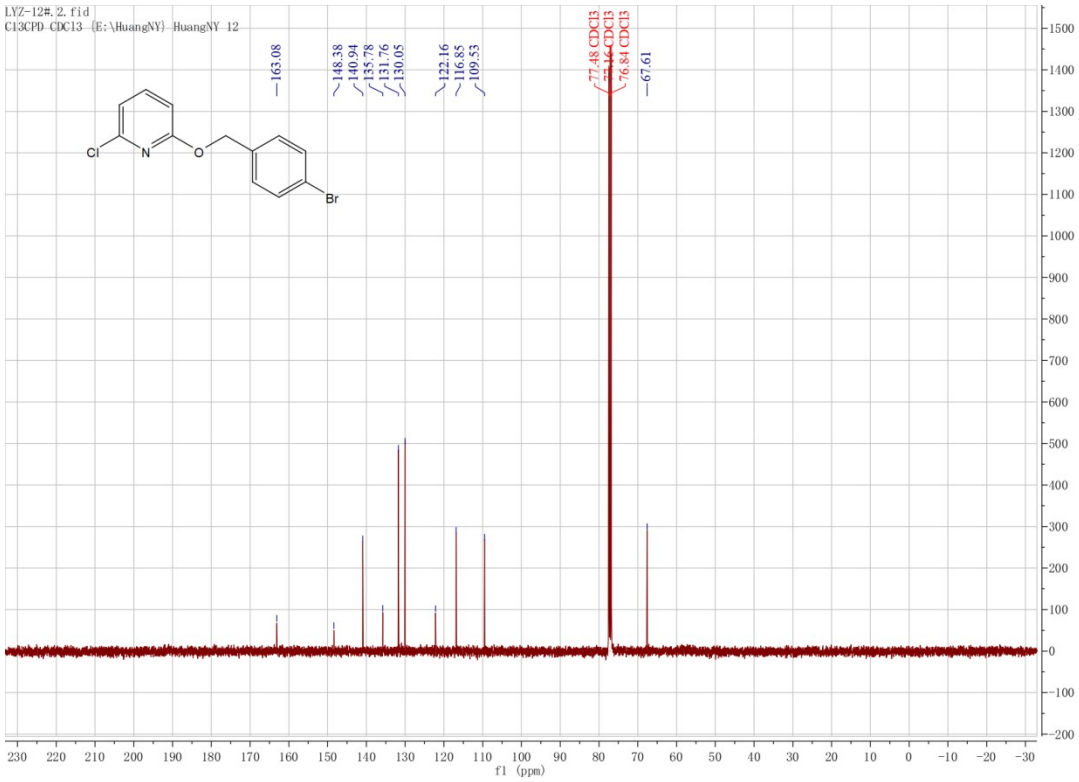
3e-8 ^{1}H NMR



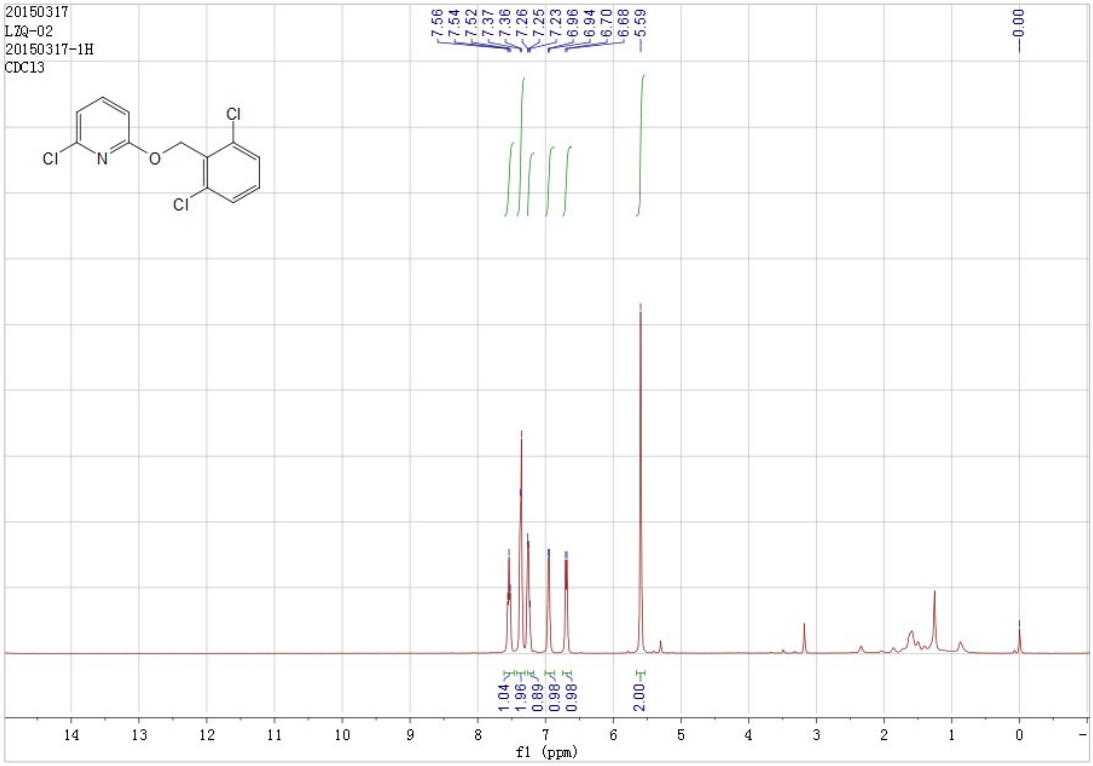
3e-8 ^{13}C NMR



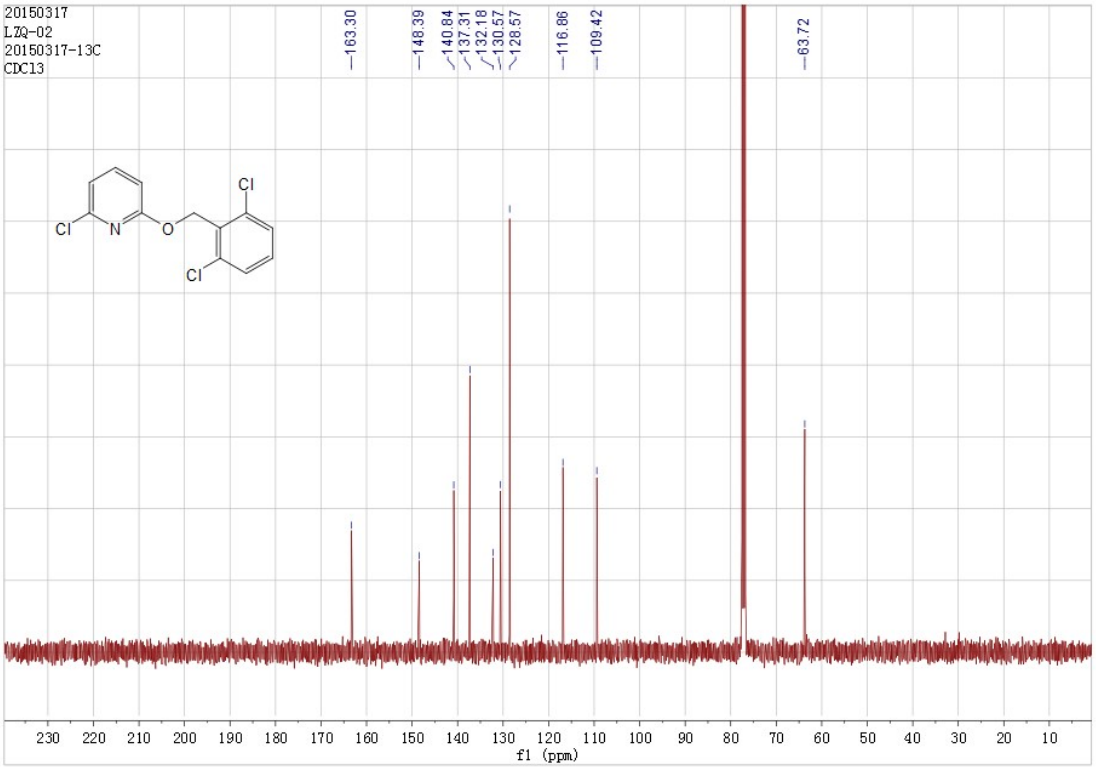
3f-1 ^{1}H NMR



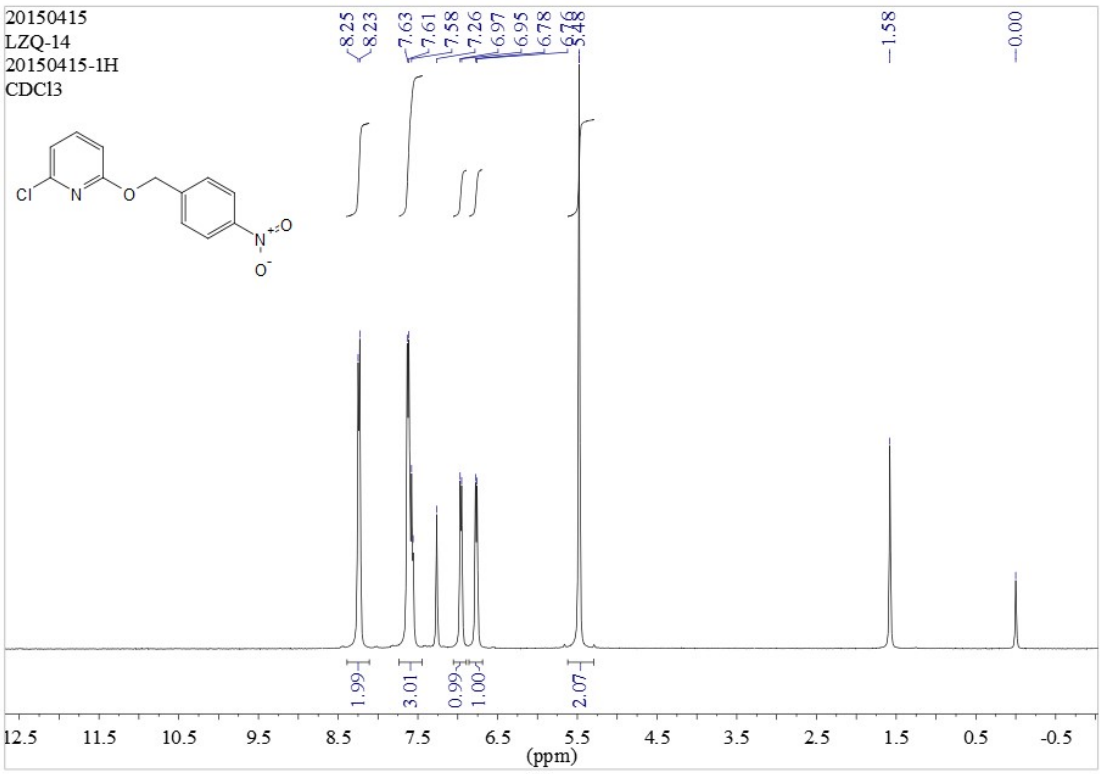
3f-1 ^{13}C NMR



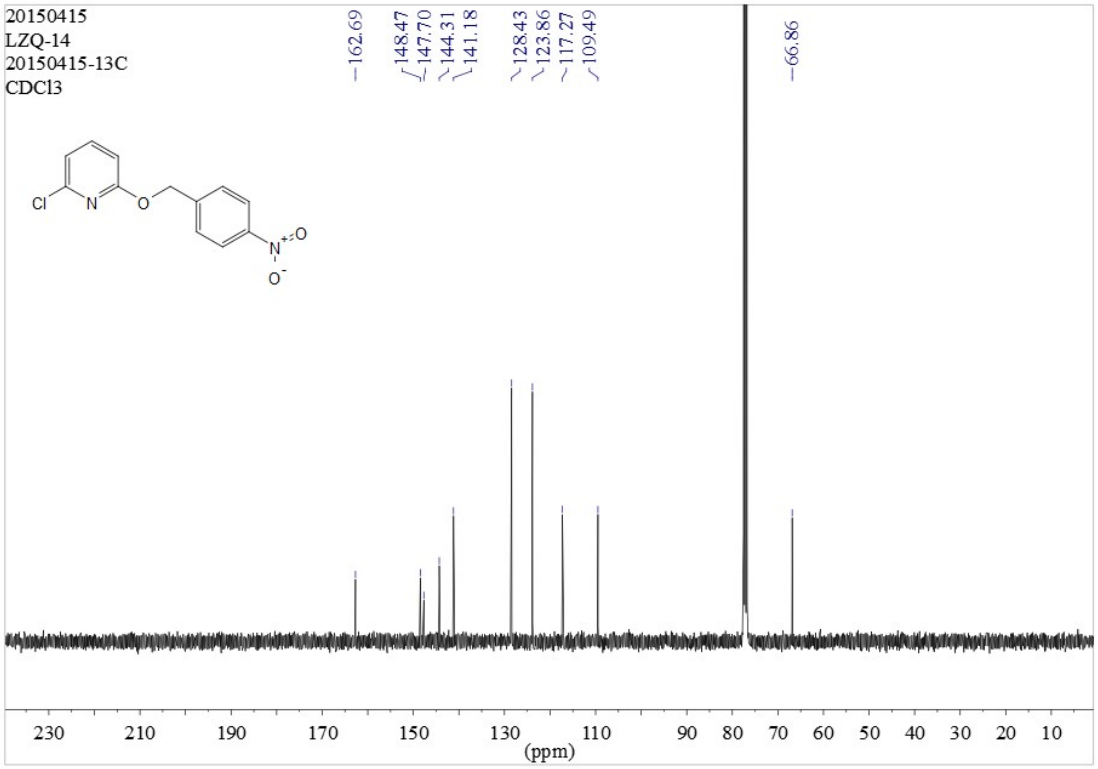
3g-1 ^{1}H NMR



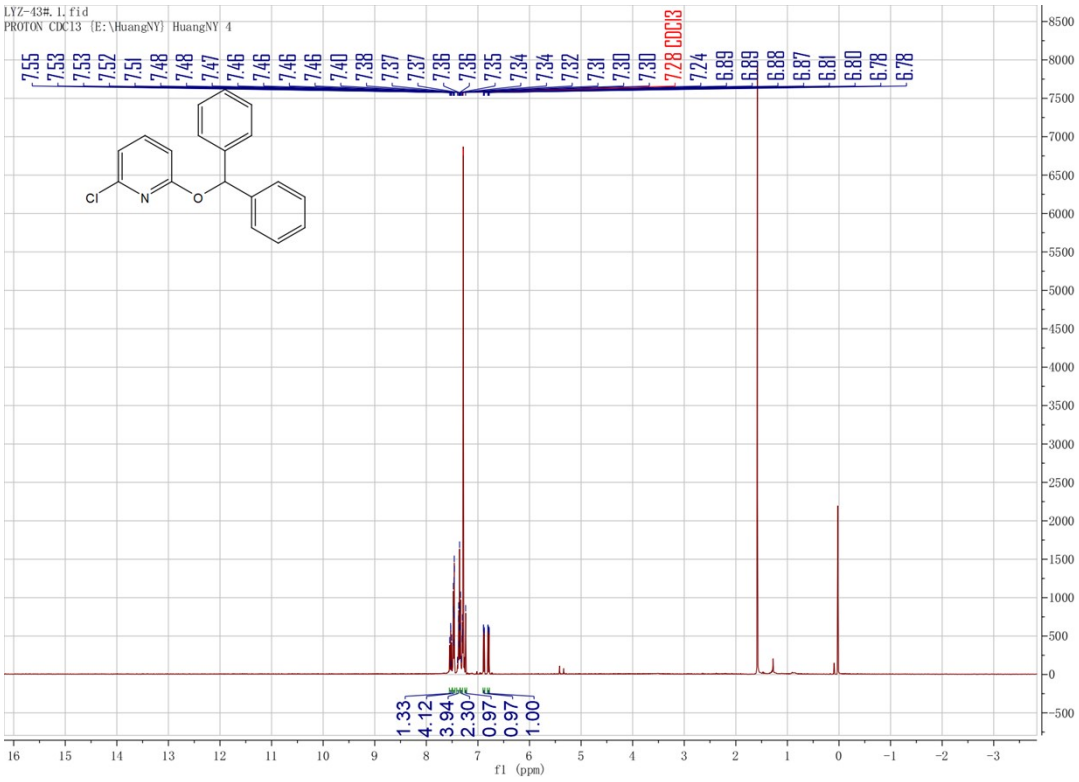
3g-1 ^{13}C NMR



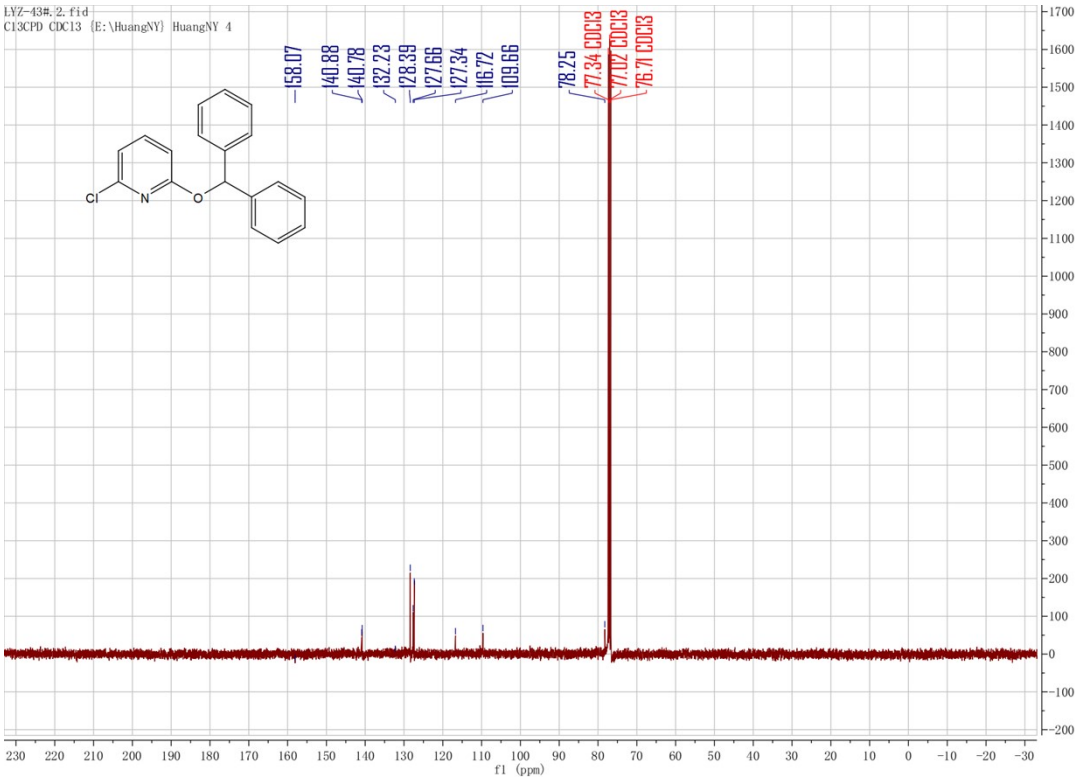
3h-1 ^{1}H NMR



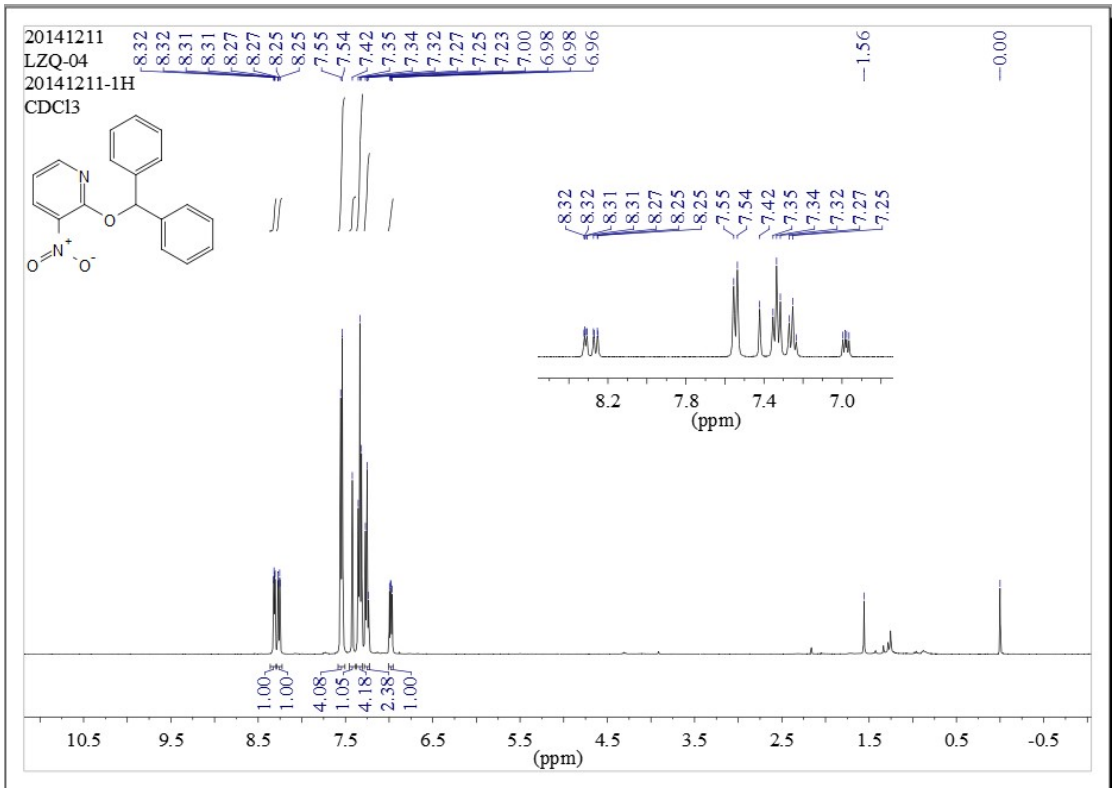
3h-1 ^{13}C NMR



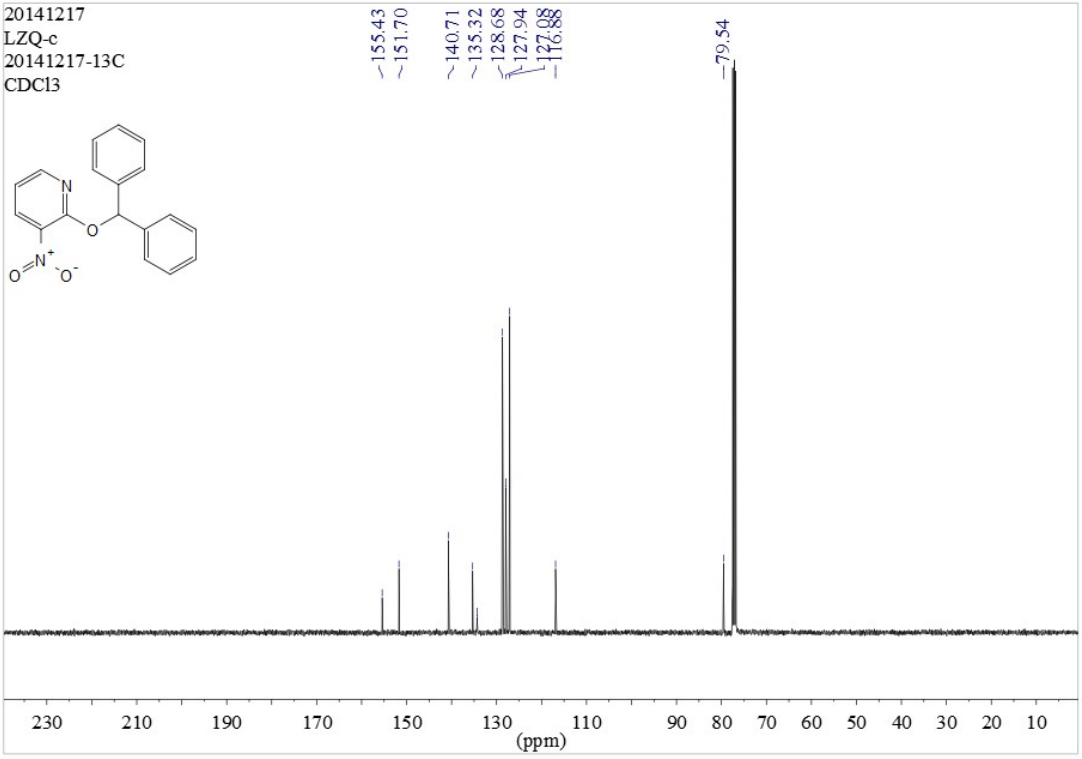
3i-1 ^{1}H NMR



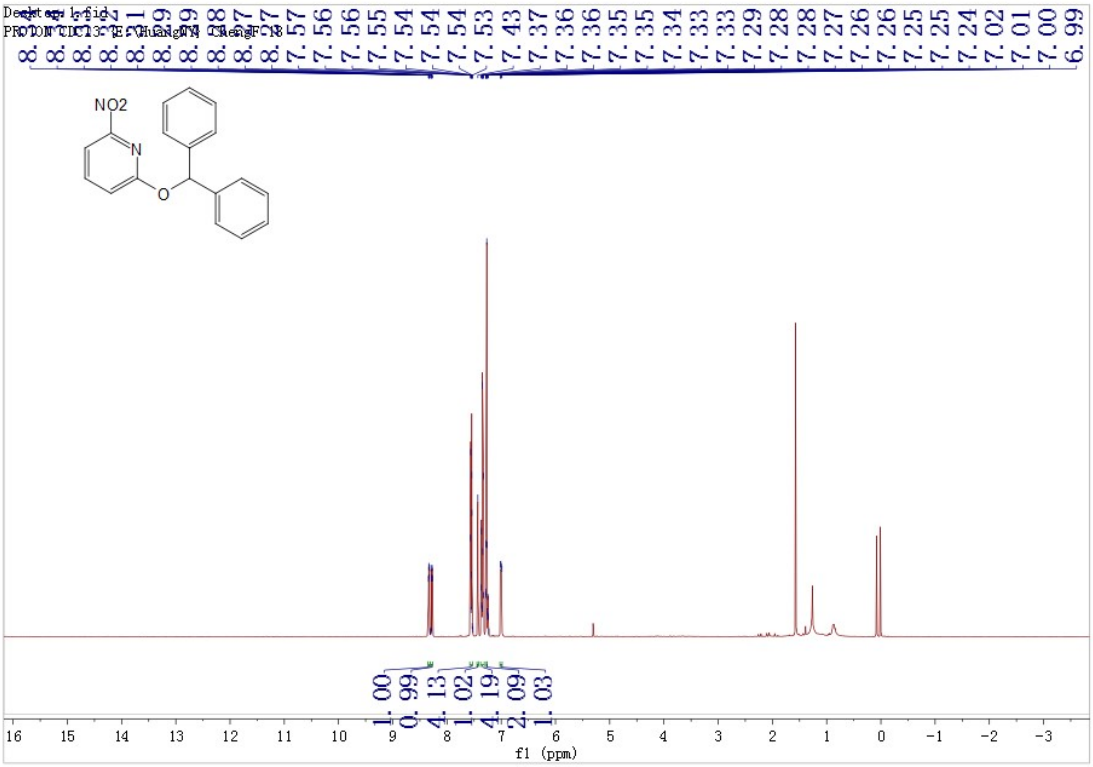
3i-1 ^{13}C NMR



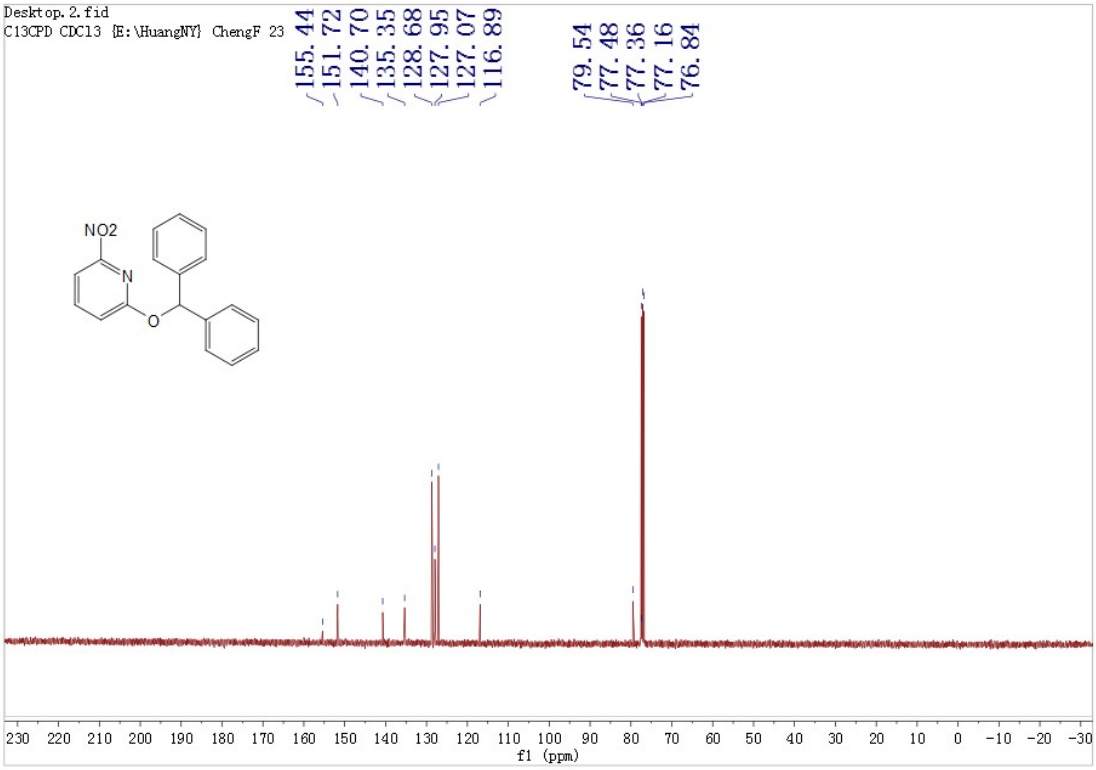
3i-2 ^{1}H NMR



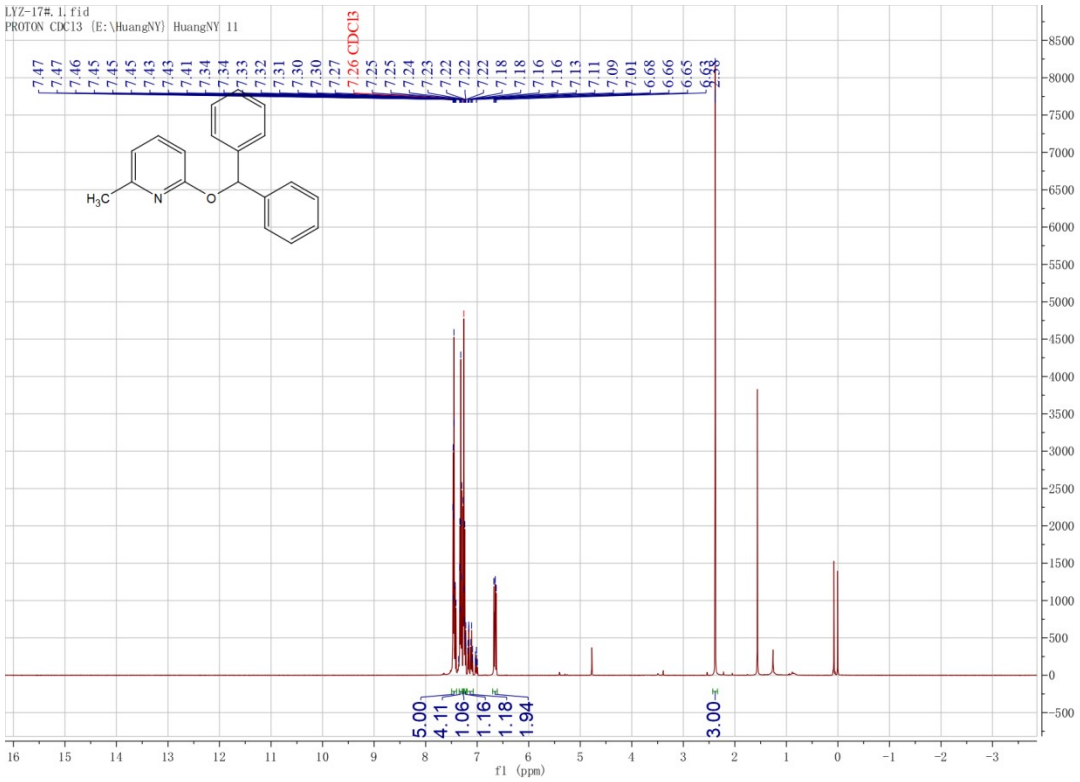
3i-2 ^{13}C NMR



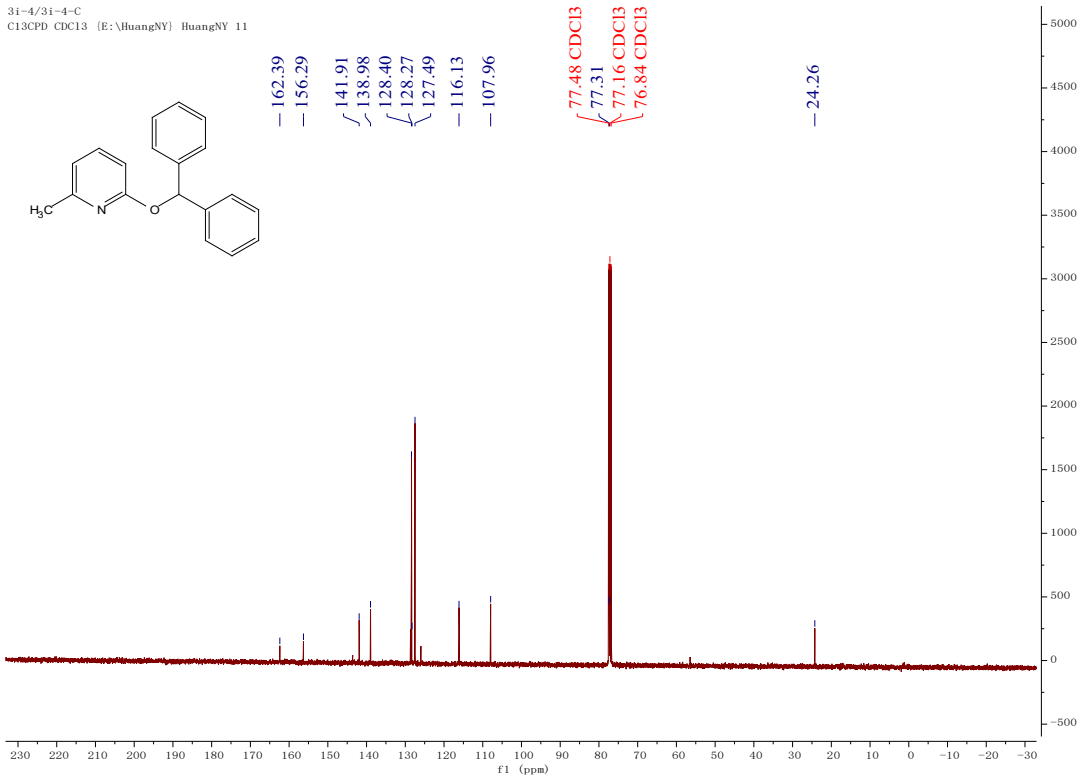
3i-3 ^{1}H NMR



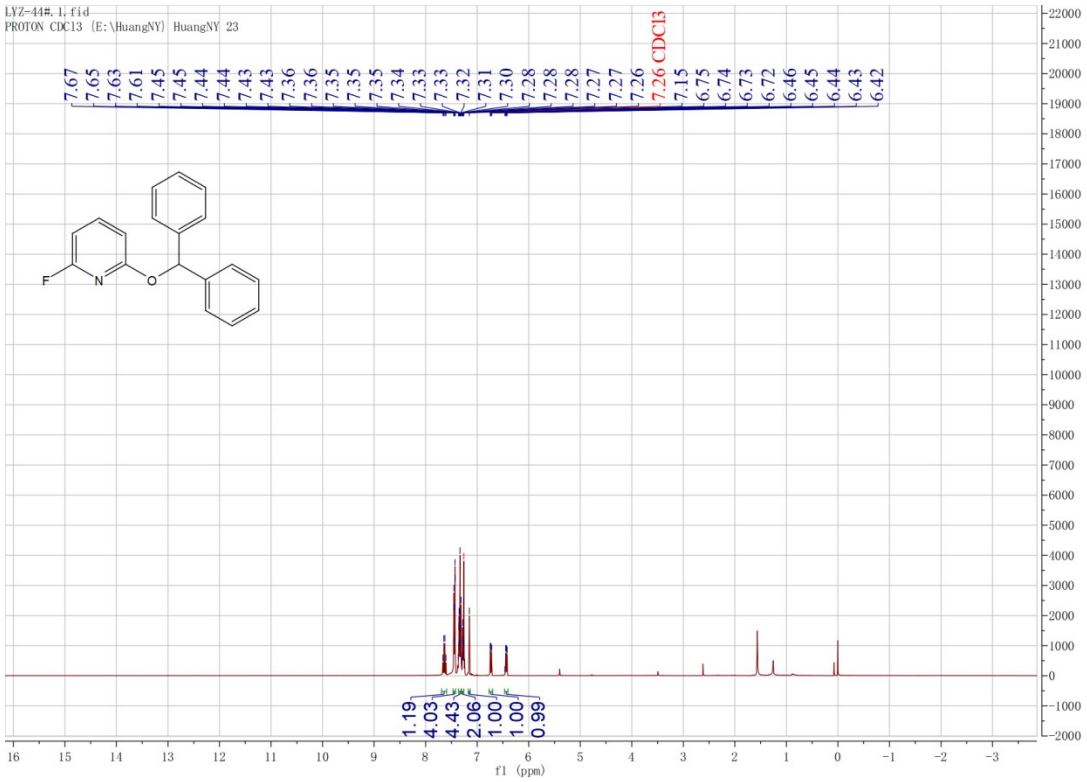
3i-3 ^{13}C NMR



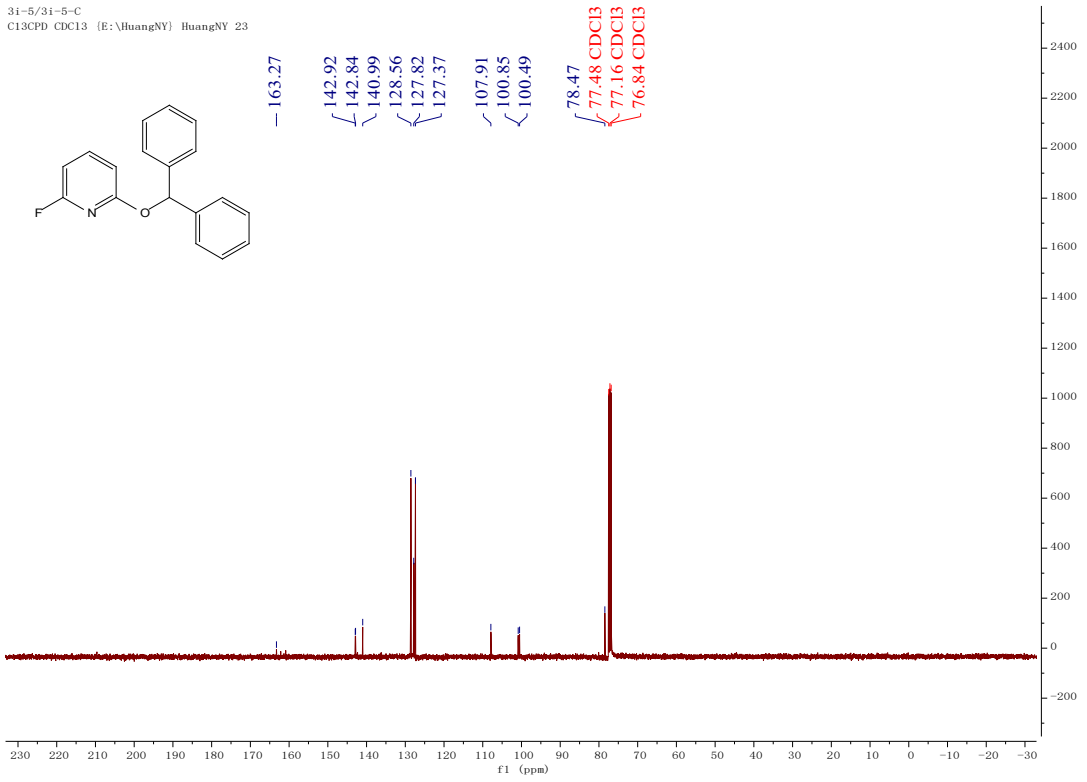
3i-4 ^{1}H NMR



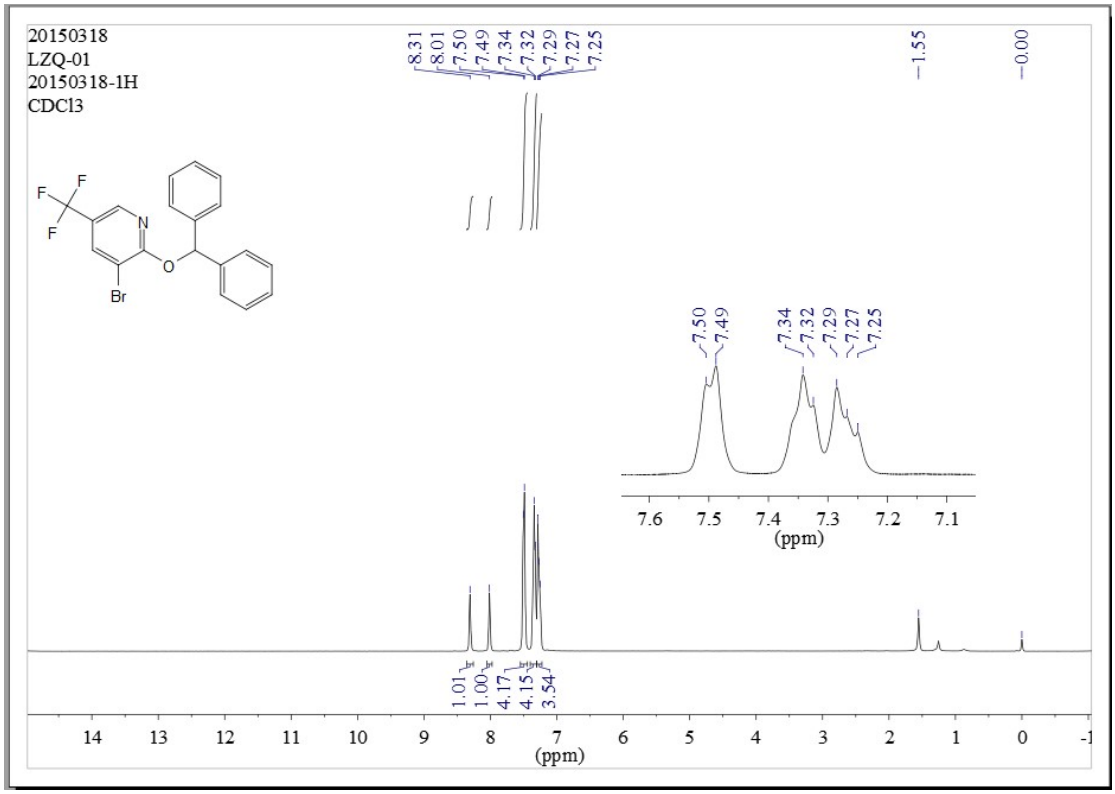
3i-4 ^{13}C NMR



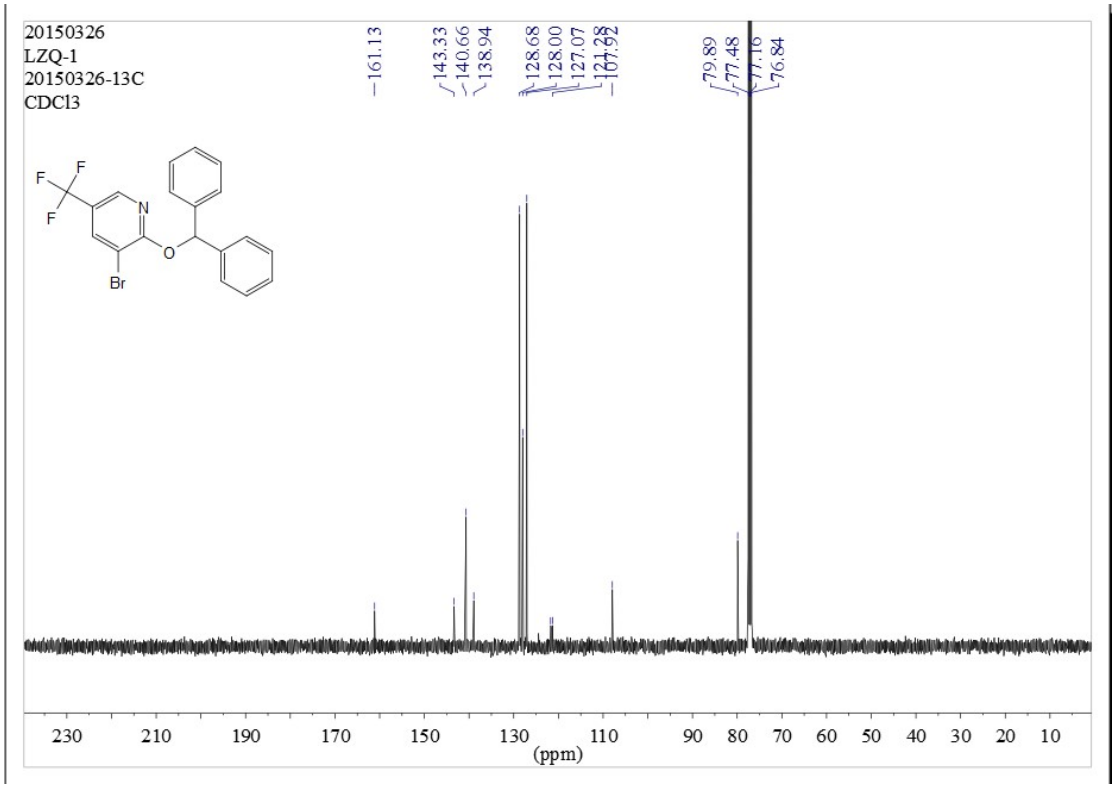
3i-5 ^{1}H NMR



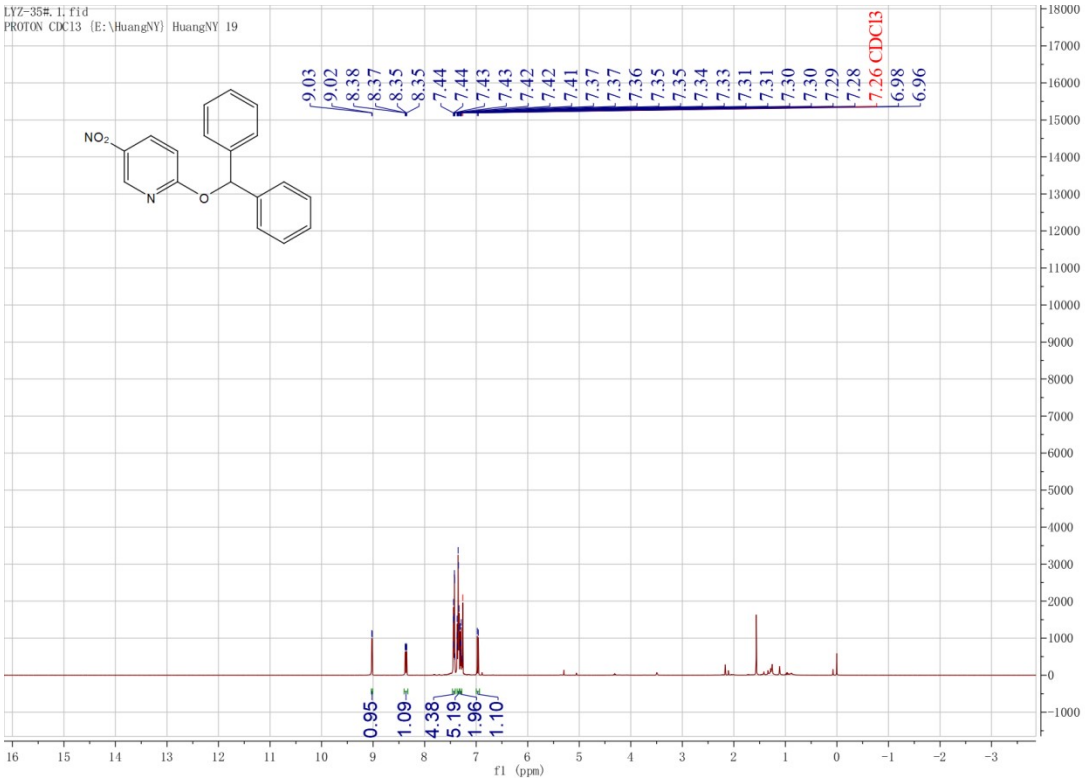
3i-5 ^{13}C NMR



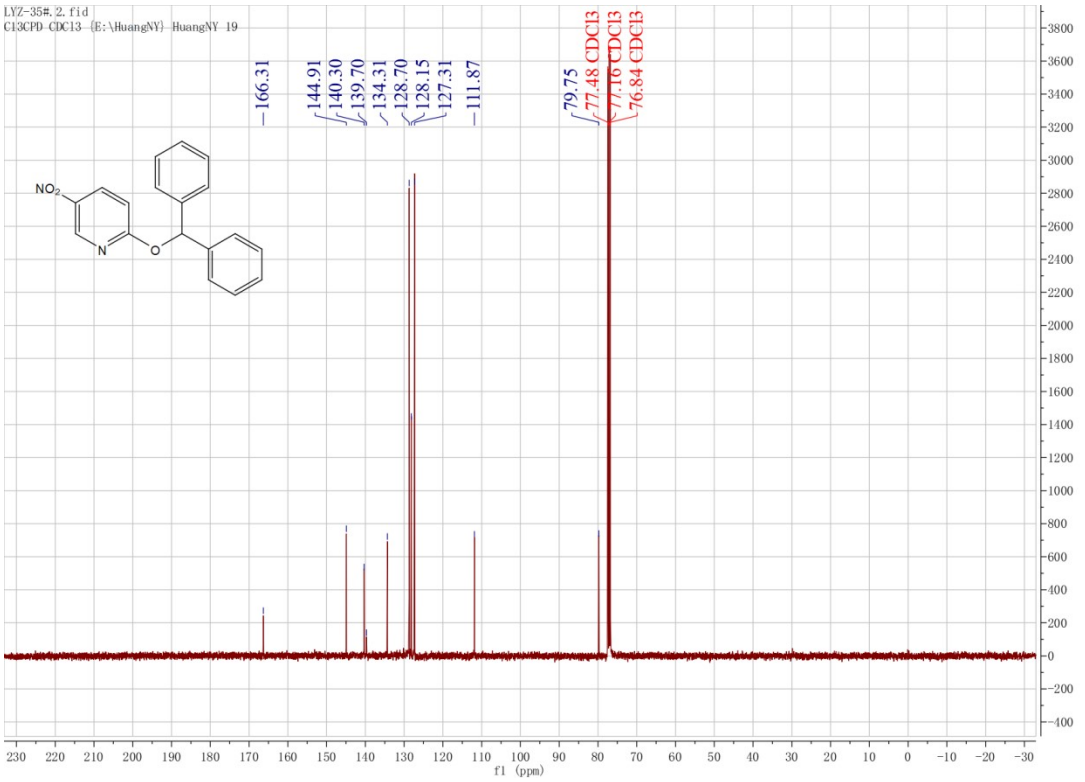
3i-6 ^{1}H NMR



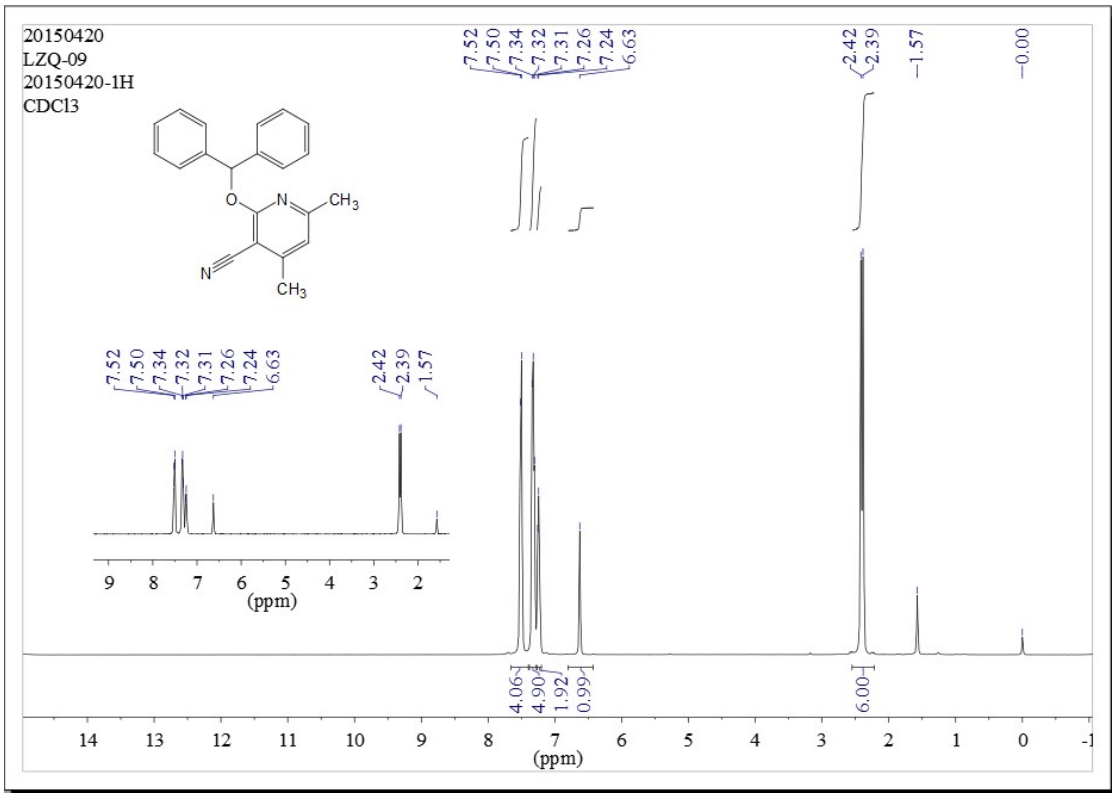
3i-6 ^{13}C NMR



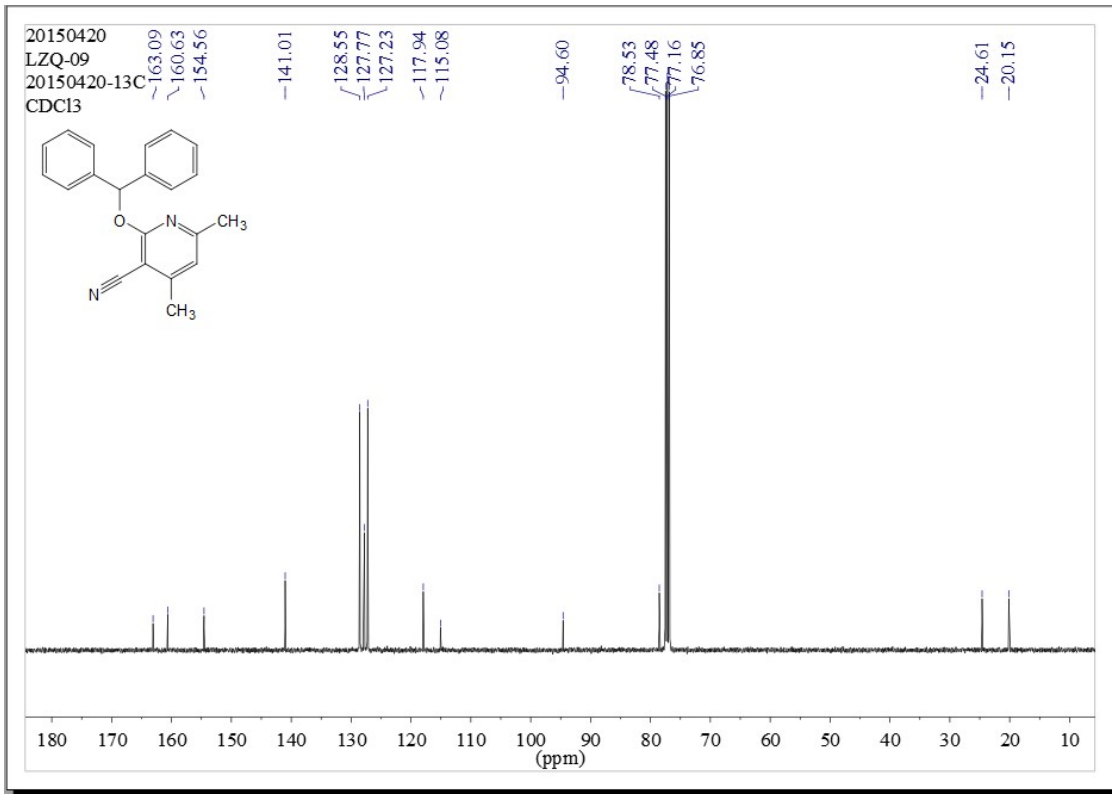
3i-7 ^{1}H NMR



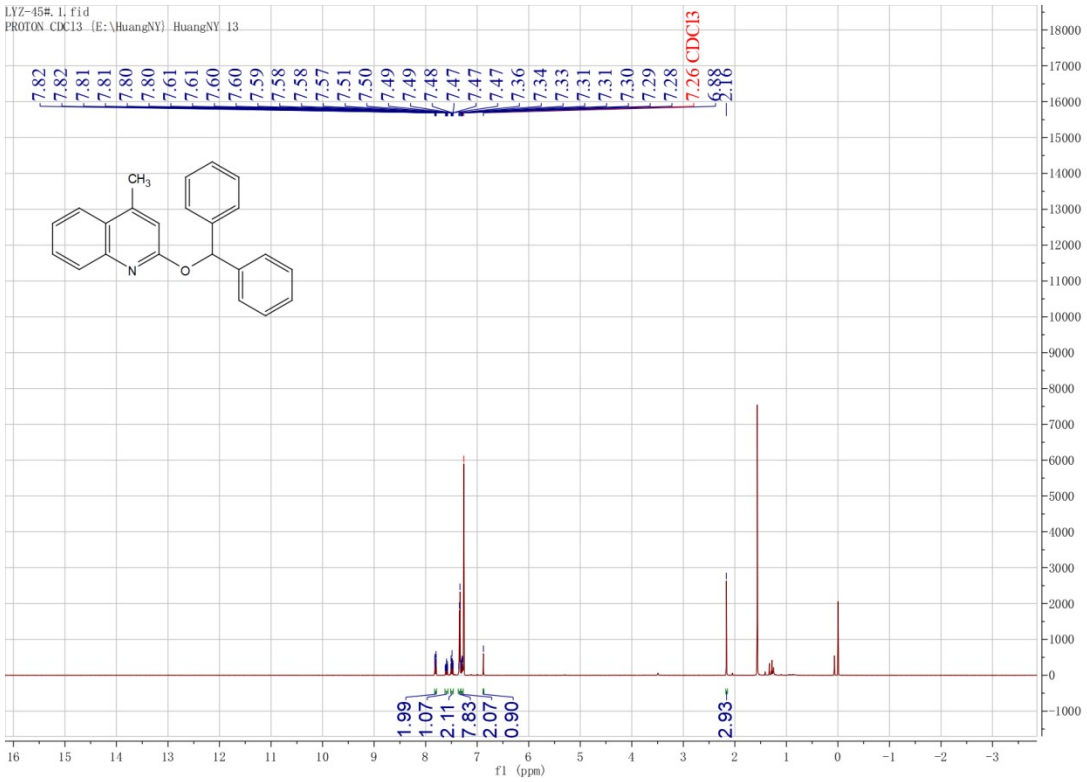
3i-7 ^{13}C NMR



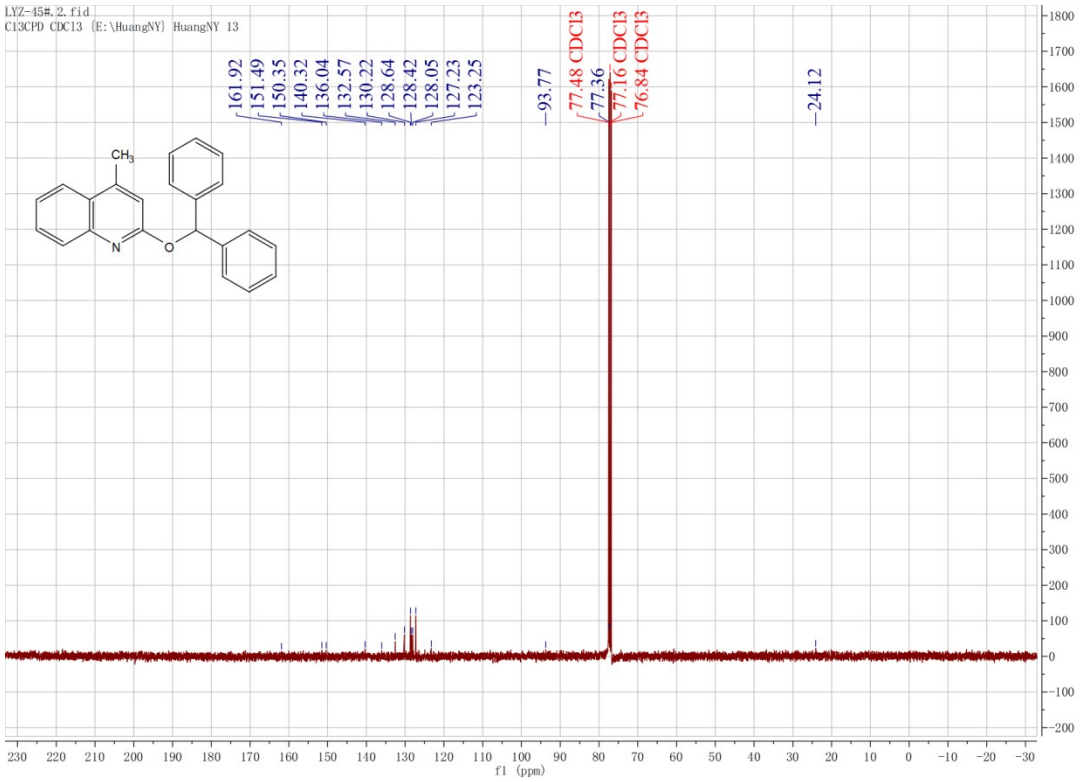
3i-8 ^{1}H NMR



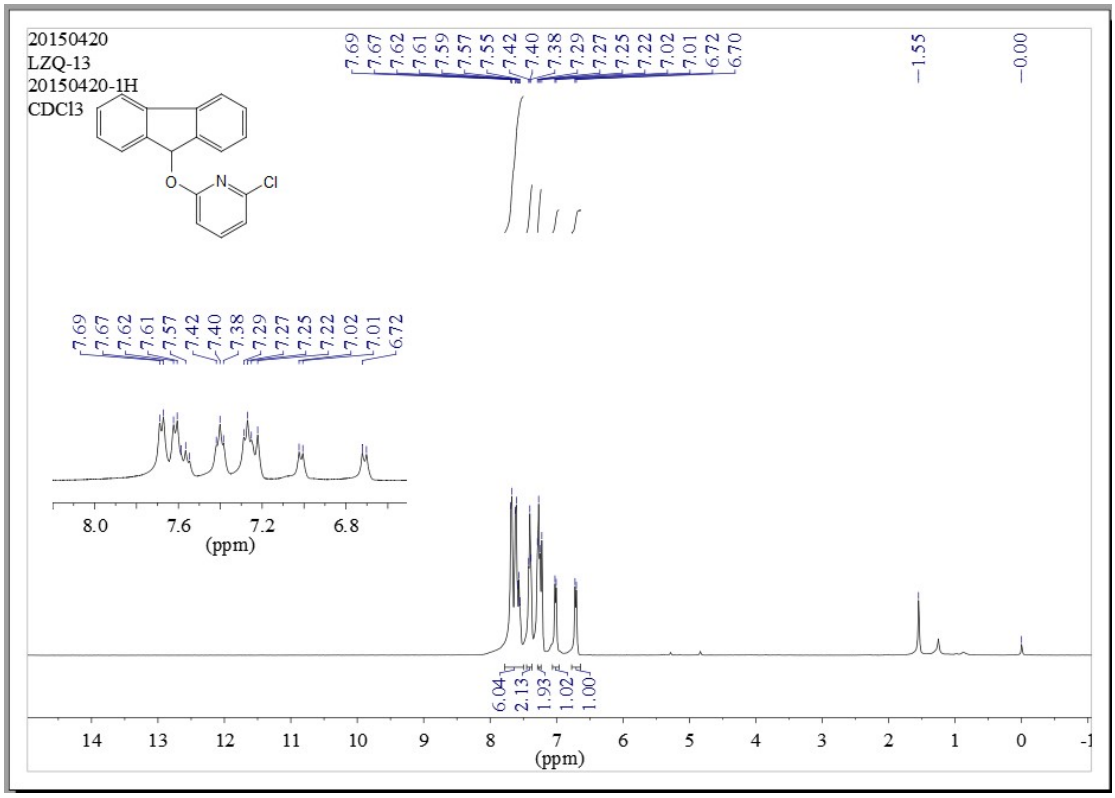
3i-8 ^{13}C NMR



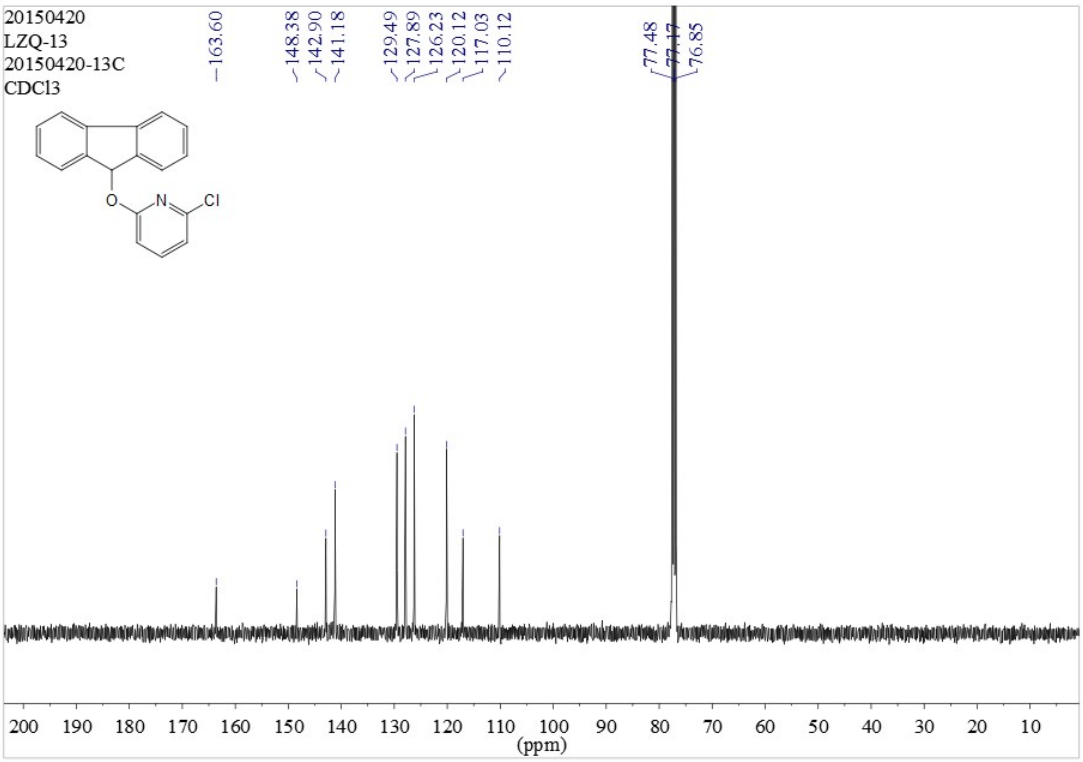
3i-9 ^{1}H NMR



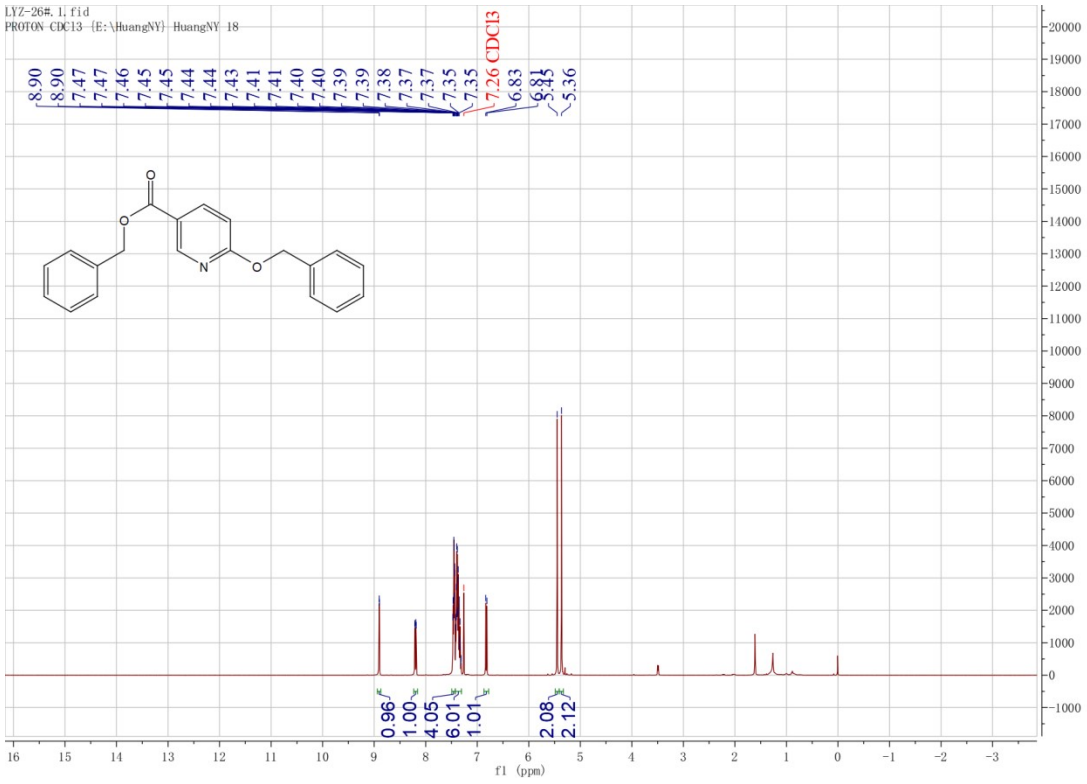
3i-9 ^{13}C NMR



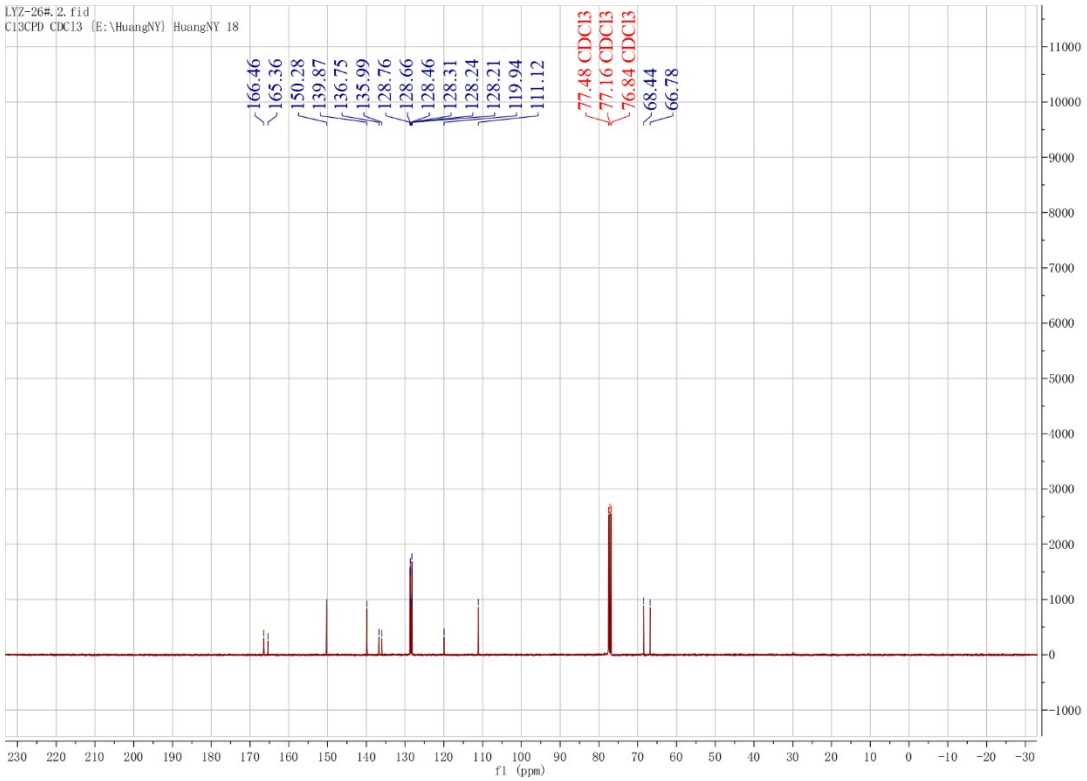
3j-1 ^{1}H NMR



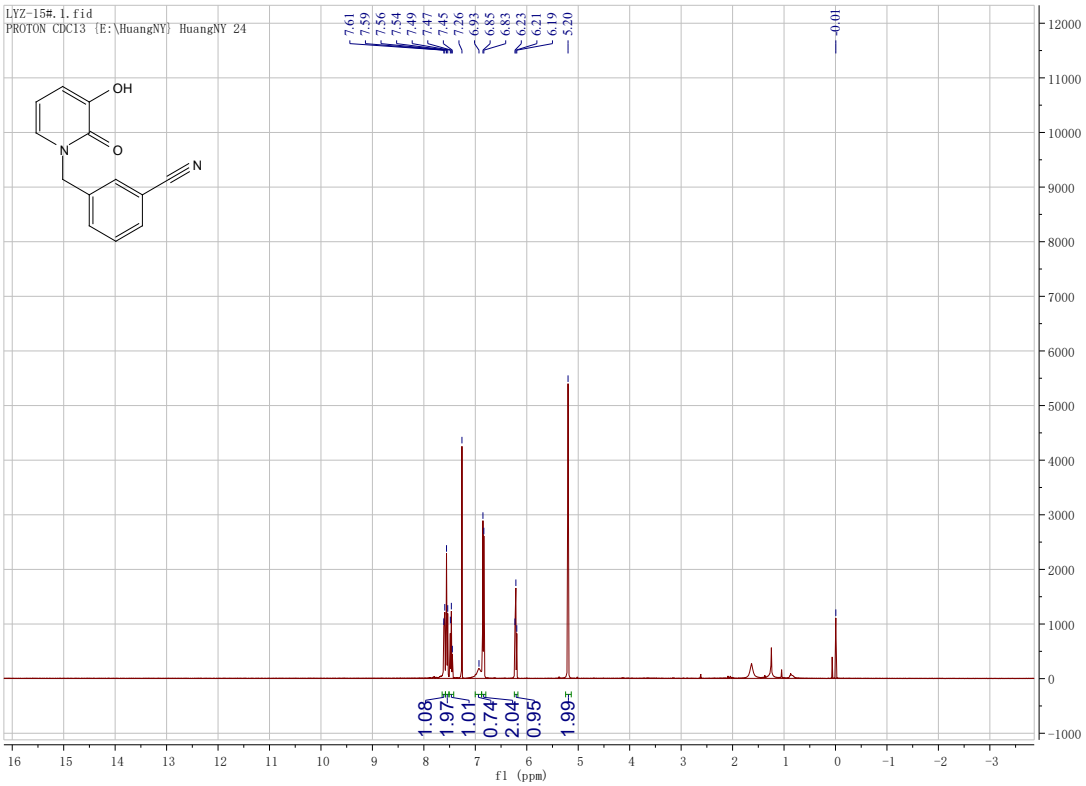
3j-1 ^{13}C NMR



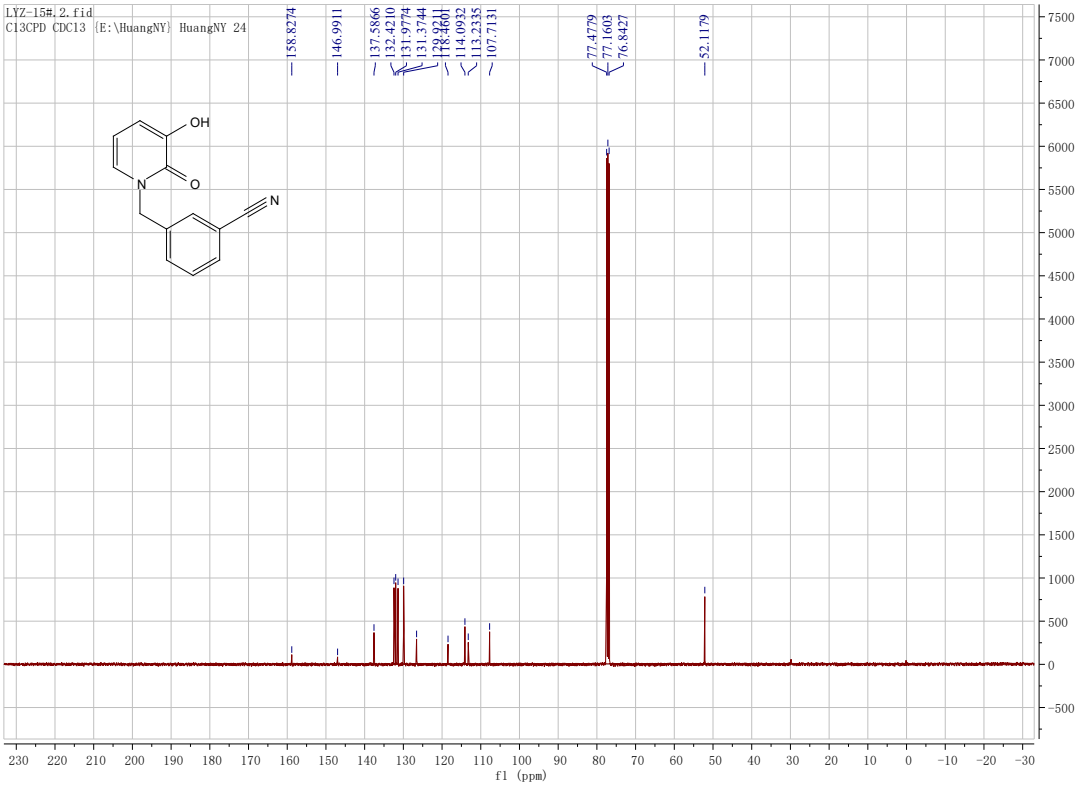
3e-9 ^{1}H NMR



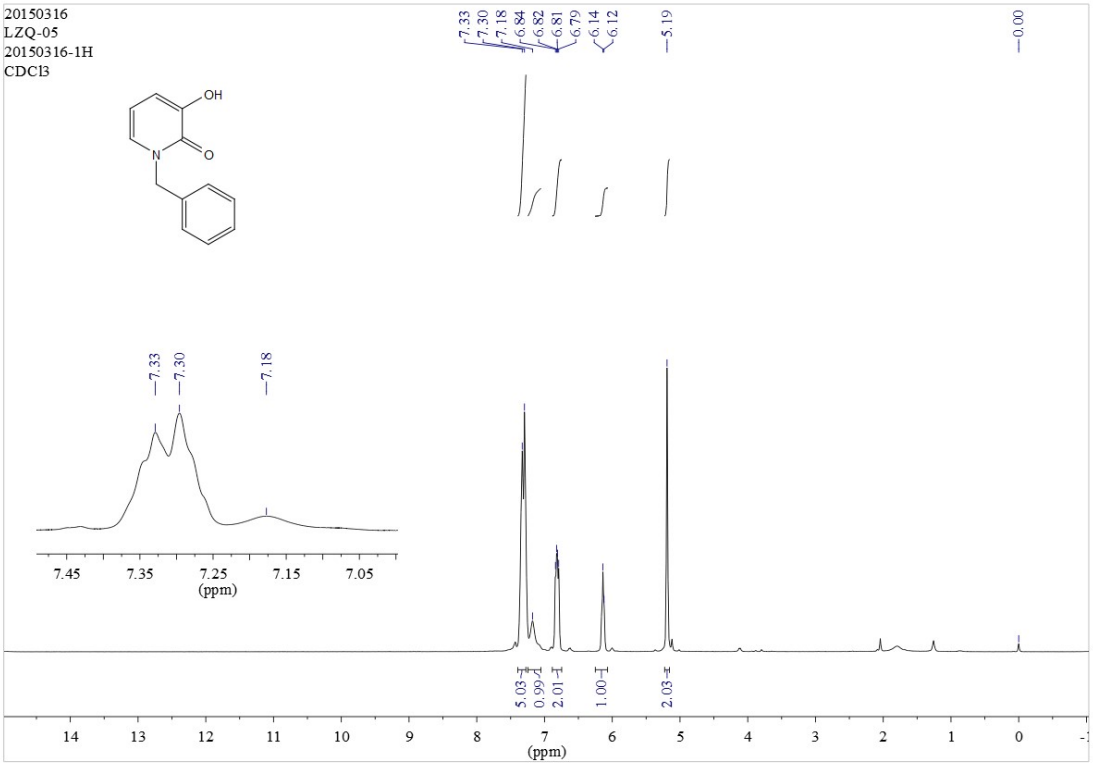
3e-9 ^{13}C NMR



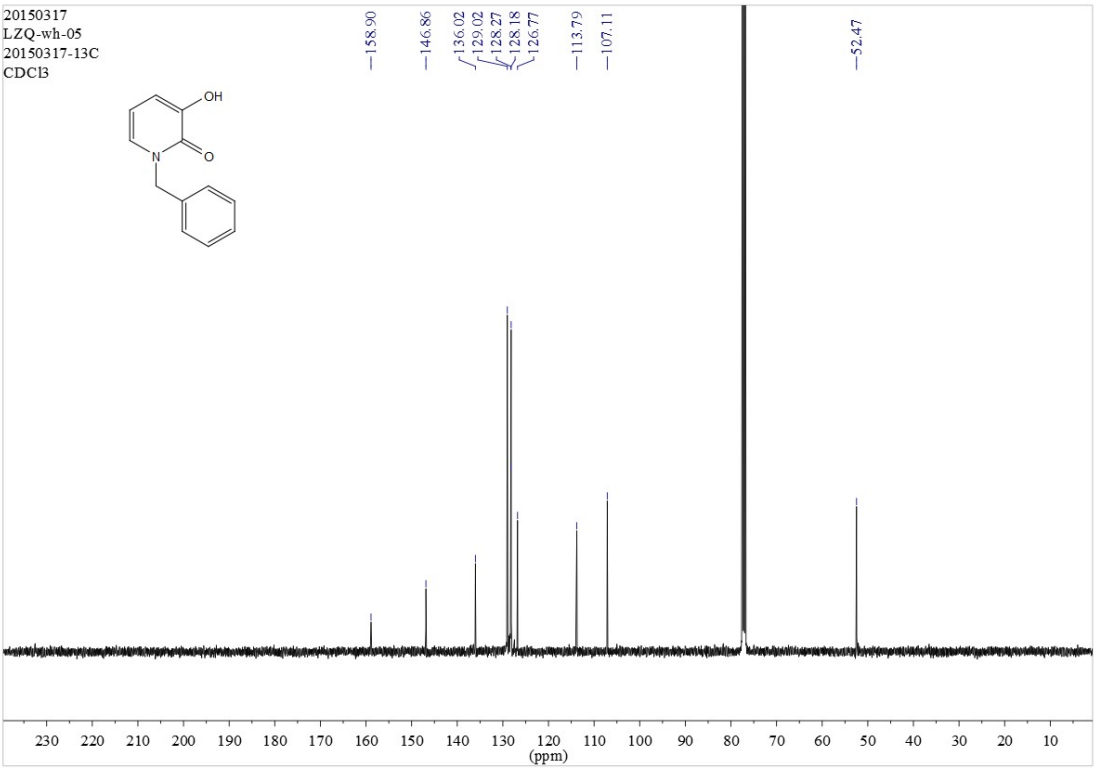
4a ^{1}H NMR



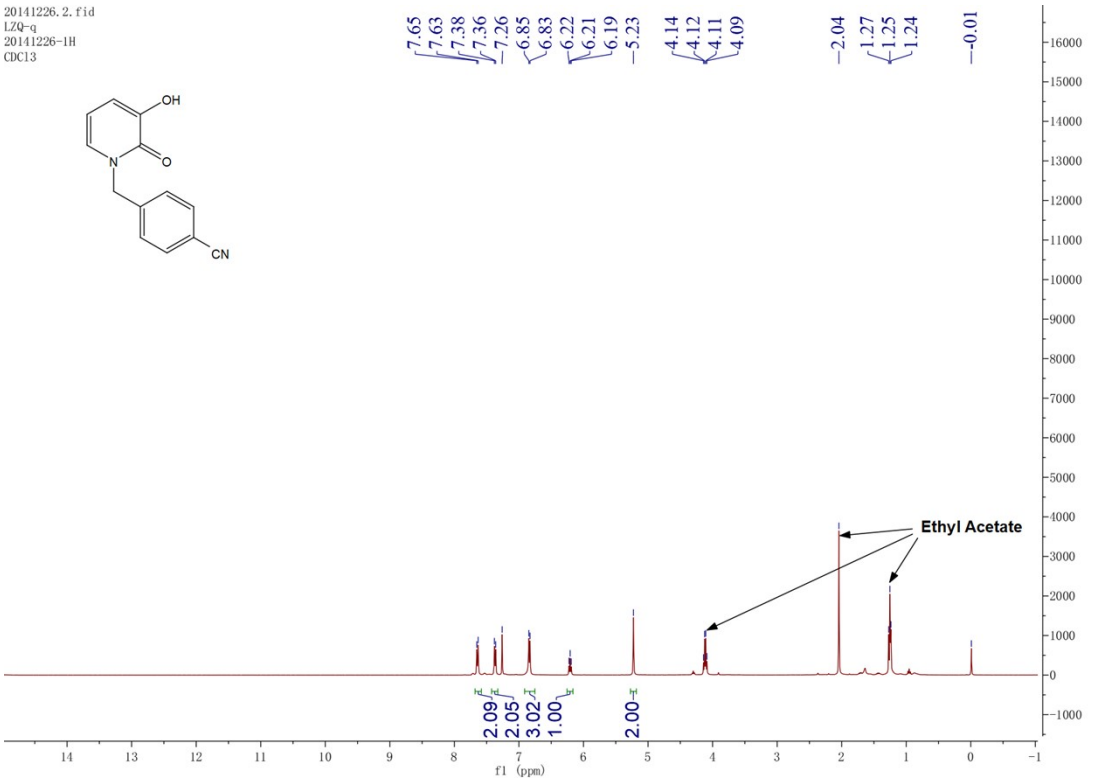
4a^{13}C NMR



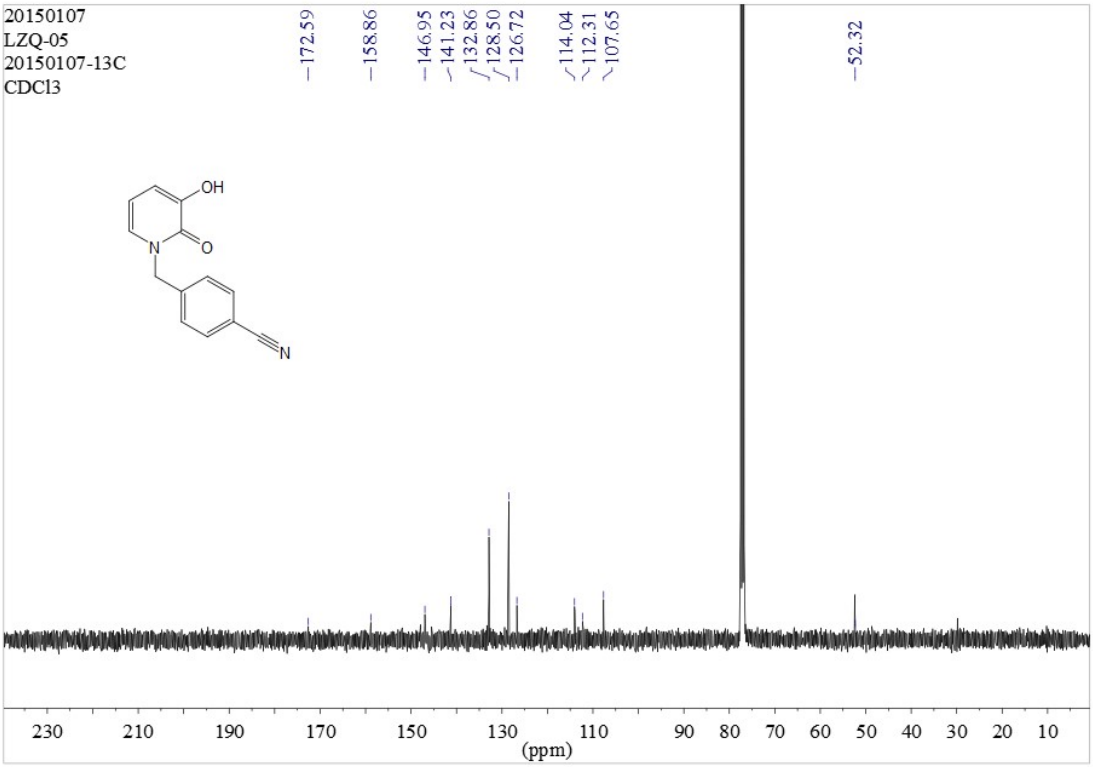
4b ^{1}H NMR



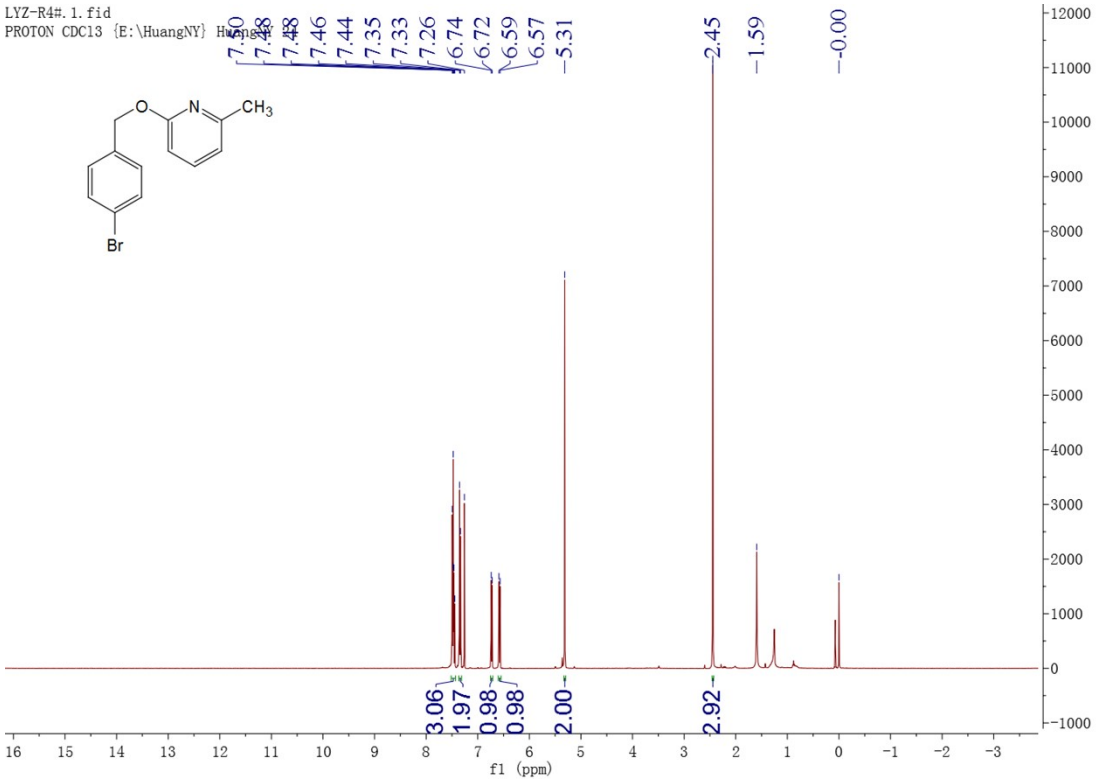
4b ^{13}C NMR



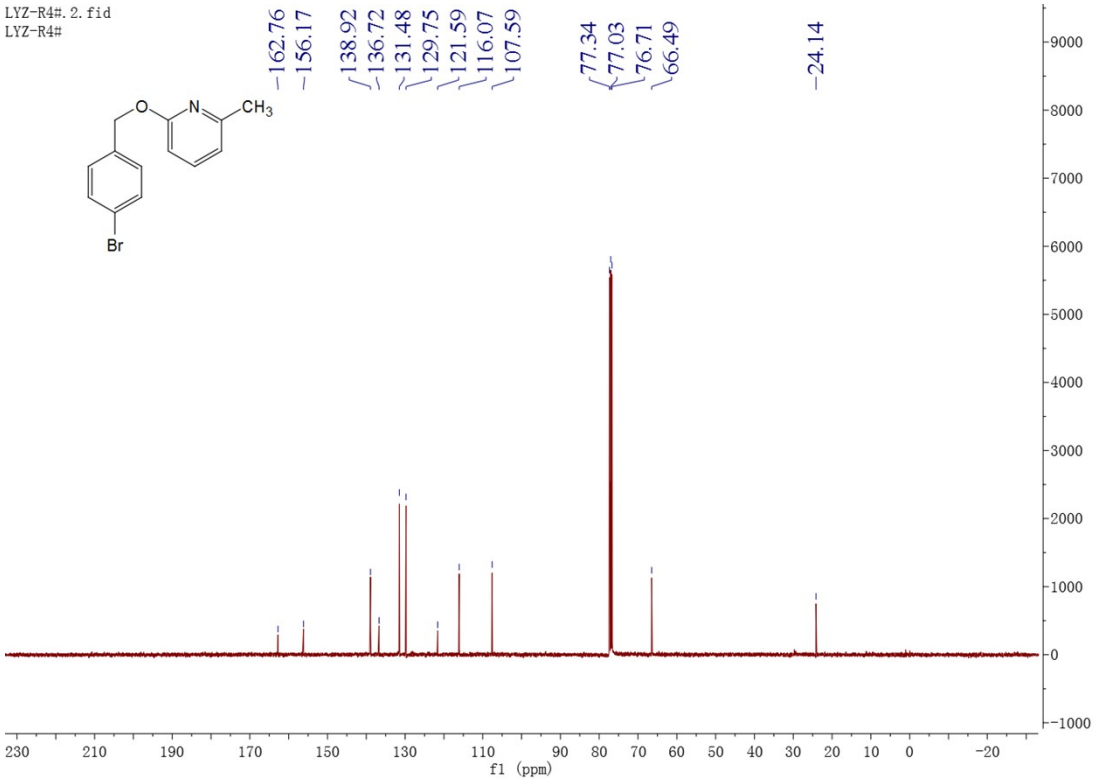
4c ^{1}H NMR



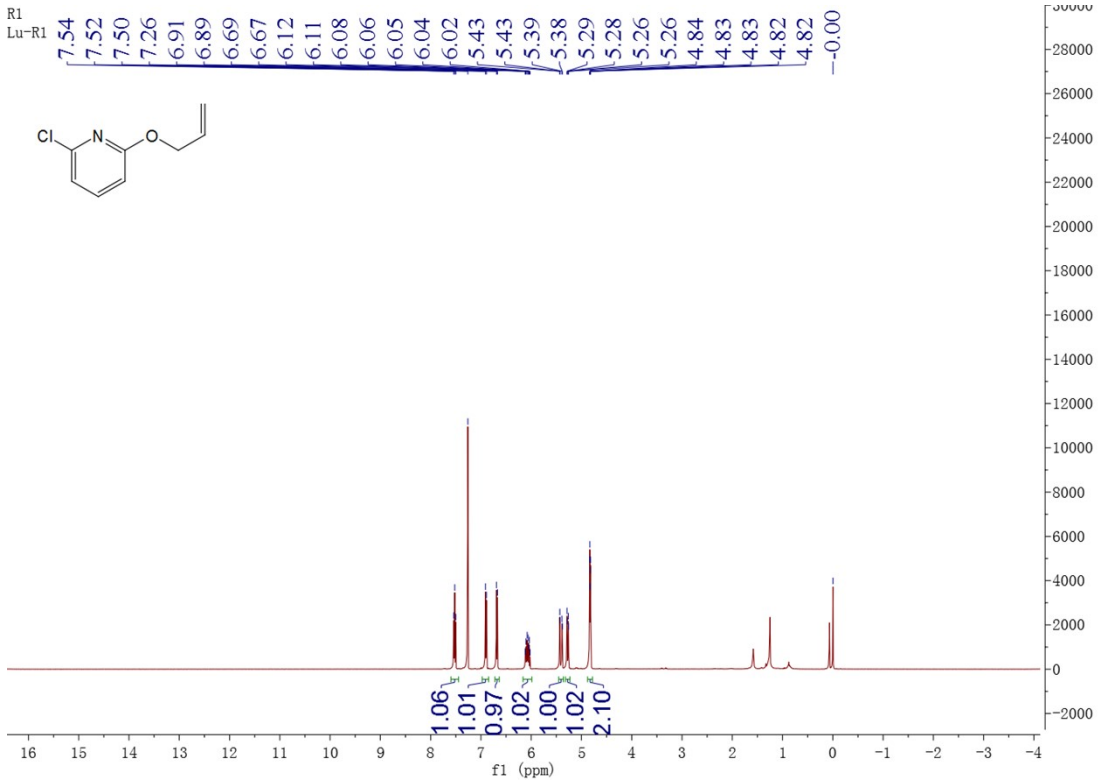
4c ^{13}C NMR



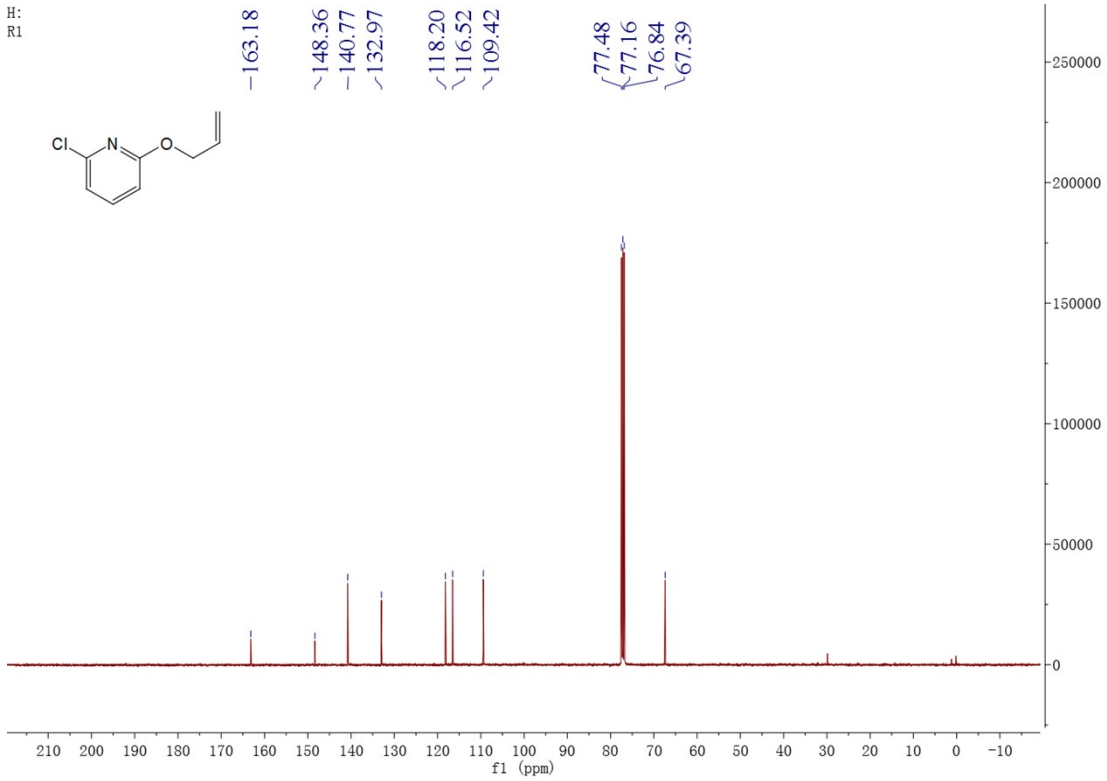
3m ^{1}H NMR



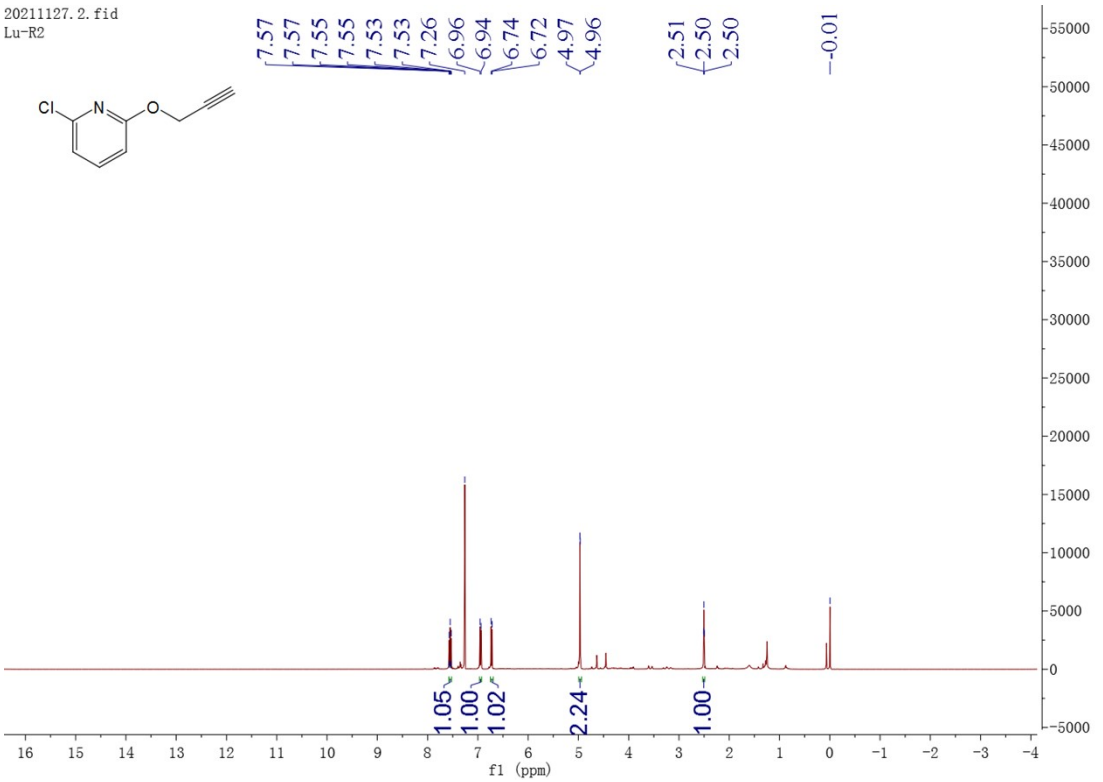
3m ^{13}C NMR



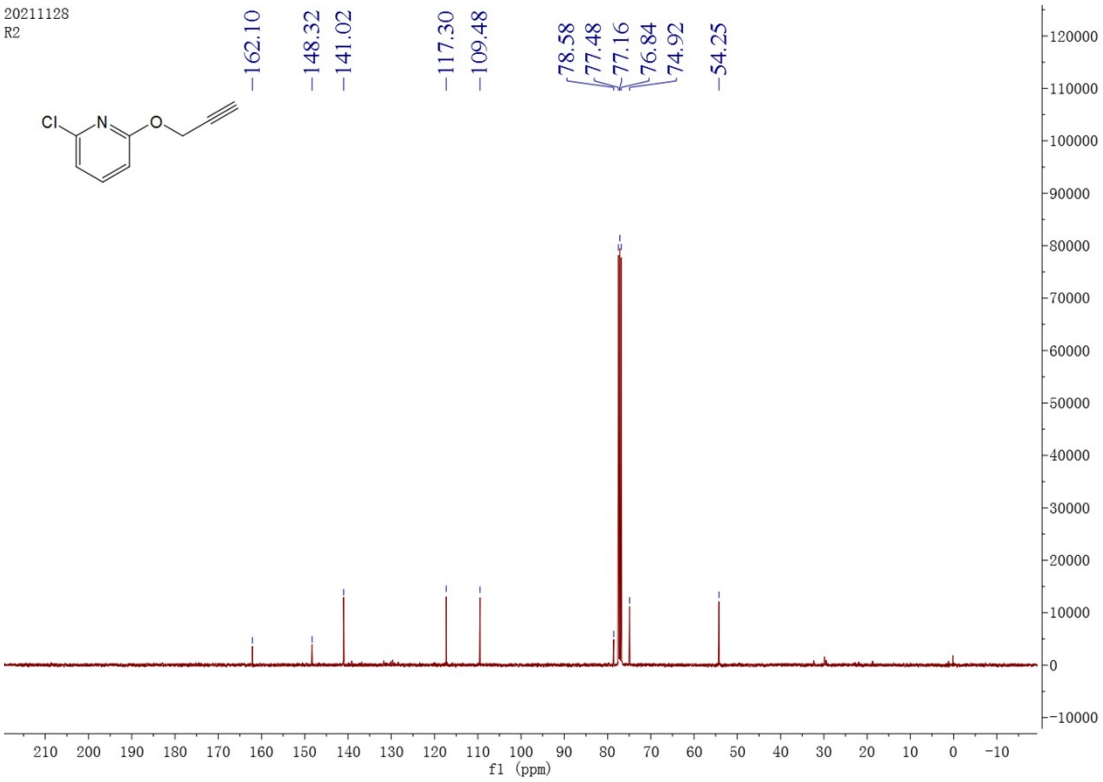
3n ^{1}H NMR



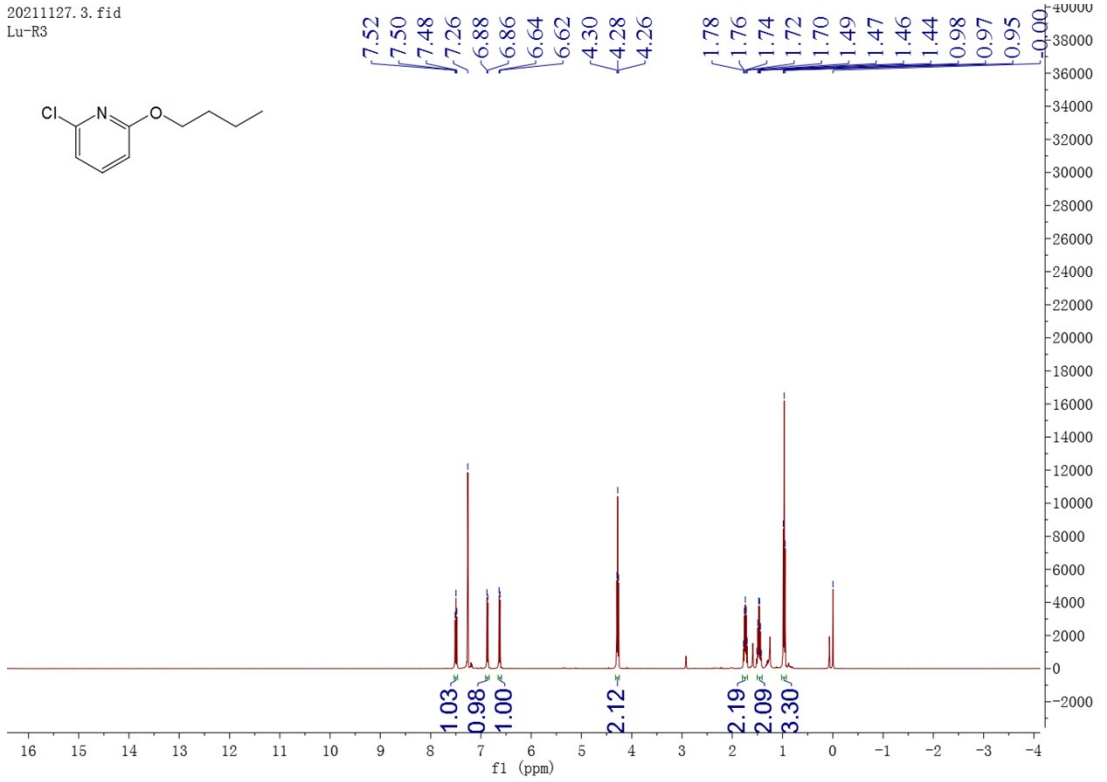
3n ^{13}C NMR



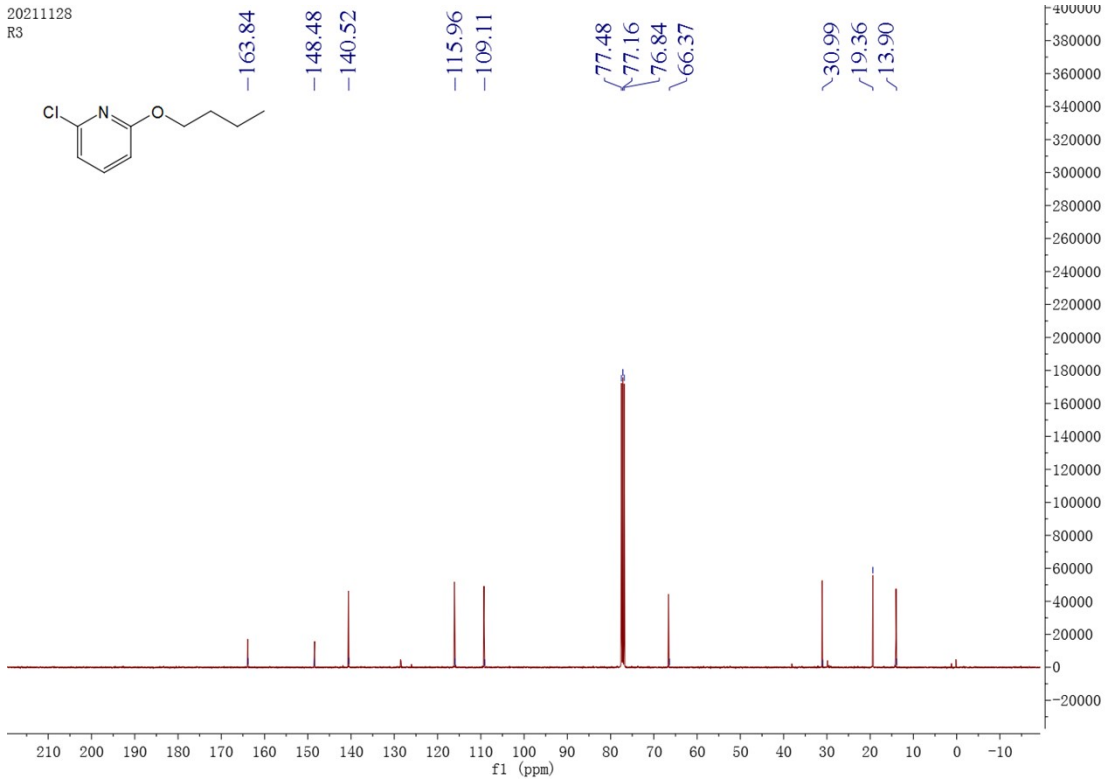
3o ^{1}H NMR



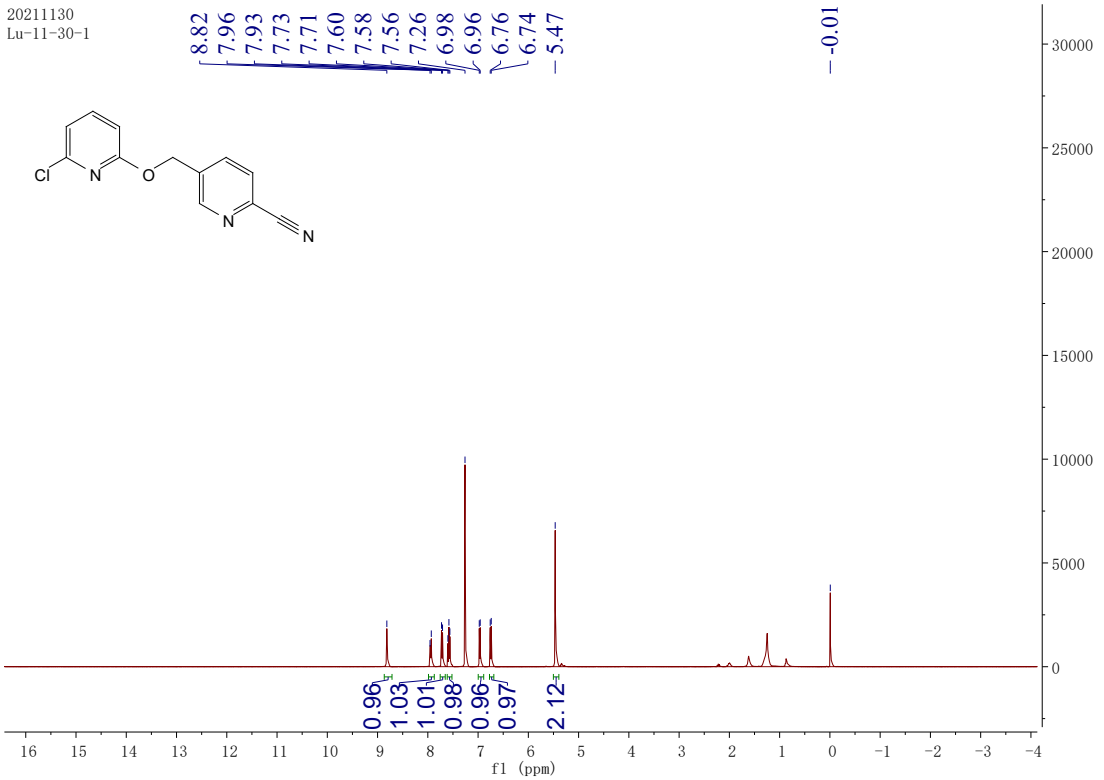
3o ^{13}C NMR



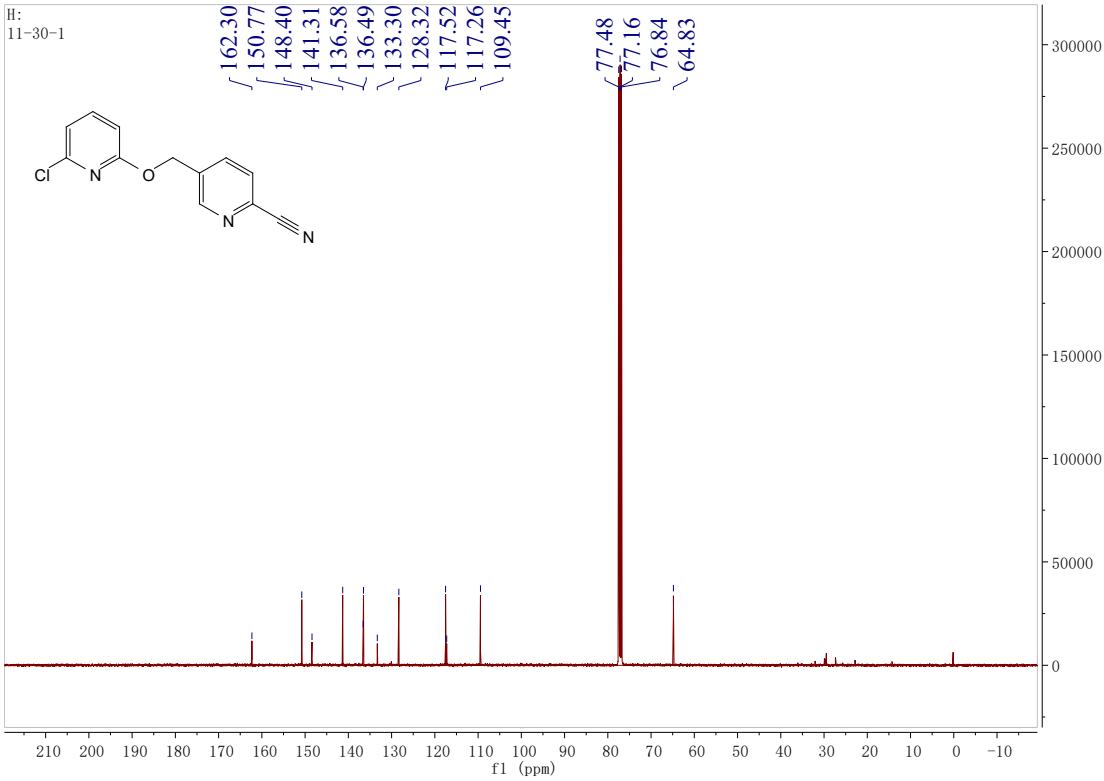
3p ^{1}H NMR



3p ^{13}C NMR



3q ^{1}H NMR



3q ^{13}C NMR

4. X-ray data determation

4.1 X-ray data of compound **4a**

Table 1 Crystal data and structure refinement for 4a.

Identification code	LZQ20210731-1
Empirical formula	$C_{11}H_{10}NO$
Formula weight	172.20
Temperature/K	293(2)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	7.4761(3)
b/Å	18.2940(7)
c/Å	8.6517(4)
α/°	90
β/°	109.547(5)
γ/°	90
Volume/Å^3	1115.08(9)
Z	5
ρ_{calc}g/cm^3	1.282
μ/mm^{-1}	0.083
F(000)	455.0
Crystal size/mm^3	0.1 × 0.1 × 0.1
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	6.636 to 56.714
Index ranges	-9 ≤ h ≤ 9, -22 ≤ k ≤ 24, -11 ≤ l ≤ 11
Reflections collected	25758
Independent reflections	2621 [R_{int} = 0.0343, R_{sigma} = 0.0235]
Data/restraints/parameters	2621/0/155
Goodness-of-fit on F^2	1.156
Final R indexes [I>=2σ (I)]	R_1 = 0.0552, wR_2 = 0.1175
Final R indexes [all data]	R_1 = 0.0705, wR_2 = 0.1228
Largest diff. peak/hole / e Å^{-3}	0.18/-0.25

4.2 X-ray data of compound **3i-8**

Table 1 Crystal data and structure refinement for 3i-8.

Identification code	LZQ20210801-1
Empirical formula	$C_{11}H_{10}NO$
Formula weight	172.20
Temperature/K	293(2)
Crystal system	triclinic
Space group	P-1
a/Å	8.2919(3)
b/Å	8.7725(4)
c/Å	13.1099(5)
α/°	101.494(3)
β/°	94.001(3)
γ/°	110.869(4)
Volume/Å^3	862.81(6)
Z	4
ρ_{calc}g/cm^3	1.326
μ/mm^{-1}	0.086
F(000)	364.0
Crystal size/mm^3	0.18 × 0.18 × 0.18
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	6.624 to 56.932
Index ranges	-11 ≤ h ≤ 11, -11 ≤ k ≤ 11, -17 ≤ l ≤ 17
Reflections collected	20397
Independent reflections	3916 [R_{int} = 0.0380, R_{sigma} = 0.0269]
Data/restraints/parameters	3916/0/219
Goodness-of-fit on F^2	1.113
Final R indexes [I>=2σ (I)]	R_1 = 0.0608, wR_2 = 0.1432
Final R indexes [all data]	R_1 = 0.0763, wR_2 = 0.1527
Largest diff. peak/hole / e Å^{-3}	0.17/-0.30

4.3 X-ray data of compound **3j-1**

Table 1 Crystal data and structure refinement for 3j-1.

Identification code	LZQ20210731-2
Empirical formula	$C_{11}H_{10}NOCl_{0.08}$
Formula weight	174.93
Temperature/K	293(2)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	10.7326(5)
b/Å	16.1644(7)
c/Å	9.2583(5)
α/°	90
β/°	115.115(7)
γ/°	90
Volume/Å^3	1454.33(15)
Z	13
ρ_{calc}g/cm^3	2.596
μ/mm^{-1}	0.212
F(000)	1200.0
Crystal size/mm^3	0.1 × 0.1 × 0.1
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	6.556 to 56.826
Index ranges	-13 ≤ h ≤ 13, -19 ≤ k ≤ 20, -11 ≤ l ≤ 12
Reflections collected	16965
Independent reflections	3254 [R_{int} = 0.0302, R_{sigma} = 0.0261]
Data/restraints/parameters	3254/0/190
Goodness-of-fit on F^2	1.056
Final R indexes [I>=2σ (I)]	R_1 = 0.0498, wR_2 = 0.1093
Final R indexes [all data]	R_1 = 0.0727, wR_2 = 0.1215
Largest diff. peak/hole / e Å^{-3}	0.16/-0.36