Pd-catalyzed oxidative C–H/C–H cross-coupling of pyridines with heteroarenes

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Supporting Information

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I. General Remarks

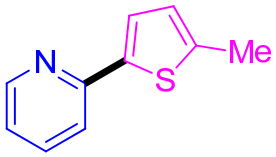
NMR spectra were obtained on a Bruker AMX-400. The ^{1}H NMR (400 MHz) chemical shifts were measured relative to $CDCl_3$ as the internal reference ($CDCl_3$: δ = 7.26 ppm). The ^{13}C NMR (100 MHz) chemical shifts were given using $CDCl_3$ as the internal standard ($CDCl_3$: δ = 77.16 ppm). Low-resolution mass spectra (MS) were obtained by a LCMS-IT-TOF. High-resolution mass spectra (HR-MS) were obtained with a Waters-Q-TOF-Premier (ESI). X-Ray single-crystal diffraction data were collected on a Bruker SMART 1000 CCD areadetector diffractometer. Melting points were determined with XRC-1 and are uncorrected.

Unless otherwise noted, all reagents were obtained from commercial suppliers and used without further purification. 3,7-Diethyl-1-methyl-xanthine[1] and 2-methyl-5-nitro-2*H*-indazole[2] were prepared according to the literature procedures. Pyridine and DMF were dried by refluxing over CaH_2 for at least 24 h, and freshly distilled prior to use. Unless otherwise indicated, all syntheses and manipulations were carried out under an N_2 atmosphere.

II. General procedure for the oxidative C–H/C–H cross-coupling of pyridines with heteroarenes

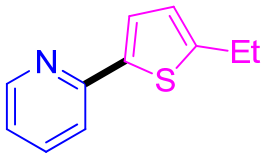
A flame-dried Schlenk test tube with a magnetic stirring bar was charged with $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), N-heteroarene (0.50 mmol), AgOAc (251 mg, 1.5 mmol), 1,10-phenanthroline monohydrate (49.5 mg, 0.25 mmol), PivOH (51 mg, 0.50 mmol), and pyridines (1.0 mL) under an N_2 atmosphere. The rubber septum was replaced with a teflon stopper, and the system was then evacuated and back filled with N_2 for twice. The reaction mixture was stirred for 5 min at room temperature, and then heated at 140 ^{o}C for 24 h. The resulting solution was cooled to ambient temperature, diluted with 20 mL of CH_2Cl_2, filtered through a celite pad, and washed with 10-20 mL of CH_2Cl_2. The combined organic extracts were concentrated and the resulting residue was purified by column chromatography on silica gel to provide the desired product.

III. Experimental data for the described substances



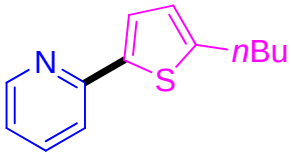
2-(5-Methylthiophen-2-yl)pyridine (3a)

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 6/1, v/v) afforded **3a** as a pale yellow solid (64 mg, 73% yield). For gram-scale, $Pd(OAc)_2$ (224 mg, 1.0 mmol), 2-methylthiophene (980 μL, 10 mmol), AgOAc (5.0 g, 30 mmol), 1,10-phenanthroline monohydrate (990 mg, 5 mmol), PivOH (1.02 g, 10 mmol), and pyridine (20 mL) at 140 °C for 24 h. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 6/1, v/v) afforded **3a** as a pale yellow solid (1.25 g, 71% yield). M.p.: 64-65 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.52 (s, 3H), 6.76 (d, J = 2.8 Hz, 1H), 7.08 (t, J = 6.4 Hz, 1H), 7.37 (d, J = 3.6 Hz, 1H), 7.57 (d, J = 8.0 Hz, 1H), 7.62 (t, J = 7.6 Hz, 1H), 8.52 (d, J = 4.4 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.7, 118.4, 121.5, 124.8, 126.5, 136.6, 142.3, 142.6, 149.5, 152.9 ppm. HRMS (ESI$^+$): calcd for $C_{10}H_9NNaS$ $[M+Na]^+$ 198.0353, found 198.0356.



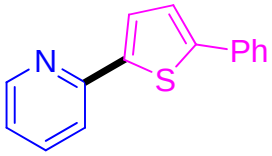
2-(5-Ethylthiophen-2-yl)pyridine (3b)

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 6/1, v/v) afforded **3b** as colorless oil (61 mg, 64% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.33 (t, J = 7.6 Hz, 3H), 2.85 (q, J = 7.6 Hz, 2H), 6.80 (d, J = 3.2 Hz, 1H), 7.09 (t, J = 6.0 Hz, 1H), 7.43 (d, J = 3.2 Hz, 1H), 7.59 (d, J = 8.0 Hz, 1H), 7.64 (t, J = 7.2 Hz, 1H), 8.53 (d, J = 4.8 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.9, 23.9, 118.5, 121.5, 124.6, 124.7, 136.7, 141.8, 149.4, 150.4, 152.9 ppm. HRMS (ESI$^+$): calcd for $C_{11}H_{12}NS$ $[M+H]^+$ 190.0690, found 190.0687.



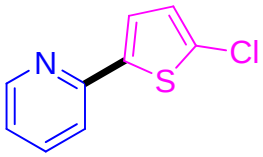
2-(5-Butylthiophen-2-yl)pyridine (3c)

Following the general procedure, the reaction mixture was stirred at 140 °C for 24 h. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 6/1, v/v) afforded **3c** as colorless oil (70 mg, 64% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.92 (t, J = 7.6 Hz, 3H), 1.37-1.46 (m, 2H), 1.66-1.74 (m, 2H), 2.82 (t, J = 7.6 Hz, 2H), 6.77 (d, J = 3.6 Hz, 1H), 7.07 (t, J = 5.6 Hz, 1H), 7.39 (d, J = 3.6 Hz, 1H), 7.58 (d, J = 8.0 Hz, 1H), 7.62 (t, J = 8.4 Hz, 1H), 8.52 (d, J = 4.8 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9, 22.2, 30.1, 33.7, 118.4, 121.4, 124.5, 125.3, 136.6, 142.1, 148.7, 149.5, 153.0 ppm. HRMS (ESI$^+$): calcd for $C_{13}H_{16}NS$ $[M+H]^+$ 218.1003, found 218.1003.



2-(5-Phenylthiophen-2-yl)pyridine (3d)

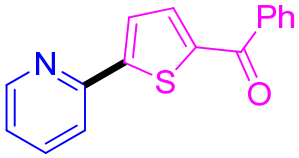
Following the general procedure, the reaction mixture was stirred at 140 °C for 24 h. Purification by column chromatography on silica gel (petroleum ether/CH_2Cl_2 = 1/1, v/v) afforded **3d** as a white solid (74 mg, 62% yield). M.p.: 101-103 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.19 (t, J = 5.6 Hz, 1H), 7.30 (t, J = 7.2 Hz, 1H), 7.35 (d, J = 4.0 Hz, 1H), 7.39 (t, J = 8.0 Hz, 2H), 7.67-7.79 (m, 5H), 8.60 (d, J = 4.8 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 118.8, 122.0, 124.2, 125.9, 128.0, 129.1, 134.3, 137.0, 146.5, 149.4 ppm. HRMS (ESI$^+$): calcd for $C_{15}H_{12}NS$ $[M+H]^+$ 238.0690, found 238.0690.



2-(5-Chlorothiophen-2-yl)pyridine (3e)

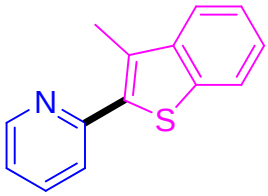
Following the general procedure, the reaction mixture was stirred at 140 °C for 24 h. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate =

6/1, v/v) afforded **3e** as a yellow solid (56 mg, 58% yield). M.p.: 63-64 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.92 (d, J = 4.0 Hz, 1H), 7.15-7.18 (m, 1H), 7.38 (d, J = 3.6 Hz, 1H), 7.57 (d, J = 8.0 Hz, 1H), 7.68 (td, J = 7.6 Hz, 1.6 Hz, 1H), 8.53 (d, J = 4.8 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 118.2, 122.3, 123.8, 127.4, 132.6, 137.0, 143.4, 149.5, 151.8 ppm. HRMS (ESI$^+$): calcd for C_9H_7ClNS $[M+H]^+$ 195.9988, found 195.9987.



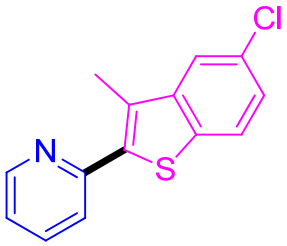
Phenyl(5-(pyridin-2-yl)thiophen-2-yl)methanone (3f)

Following the general procedure, the reaction mixture was stirred at 140 °C for 24 h. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 5/1, v/v) afforded **3f** as a yellow solid (74 mg, 56% yield). M.p.: 112-114 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.27 (d, J = 5.6 Hz, 1H), 7.49 (t, J = 7.6 Hz, 2H), 7.59 (t, J = 7.2 Hz, 1H), 7.69 (s, 2H), 7.74-7.80 (m, 2H), 7.90 (d, J = 7.6 Hz, 2H), 8.64 (d, J = 4.8 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 120.0, 123.5, 125.5, 128.6, 129.3, 132.5, 135.6, 137.5, 138.1, 144.1, 149.7, 151.3, 188.2 ppm. HRMS (ESI$^+$): calcd for $C_{16}H_{11}NNaOS$ $[M+Na]^+$ 288.0459, found 288.0460.



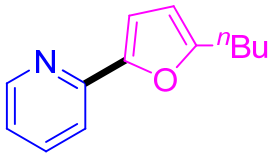
2-(3-Methylbenzo[*b*]thiophen-2-yl)pyridine (3g)

Following the general procedure, the reaction mixture was stirred at 140 °C for 24 h. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 5/1, v/v) afforded **3g** as a white solid (71 mg, 63% yield). M.p.: 52-54 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.69 (s, 3H), 7.23 (d, J = 6.8 Hz, 1H), 7.36-7.43 (m, 2H), 7.69 (d, J = 7.6 Hz, 1H), 7.77 (d, J = 7.6 Hz, 2H), 7.85 (d, J = 7.6 Hz, 1H), 8.72 (d, J = 4.4 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.5, 122.1, 122.5, 122.6, 123.3, 124.2, 125.2, 129.9, 136.6, 138.1, 139.6, 141.7, 149.8, 153.6 ppm. HRMS (ESI$^+$): calcd for $C_{14}H_{12}NS$ $[M+H]^+$ 226.0690, found 226.0687.



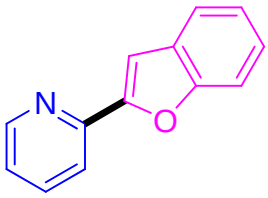
2-(5-Chloro-3-methylbenzo[*b*]thiophen-2-yl)pyridine (3h)

Following the general procedure, the reaction mixture was stirred at 140 °C for 24 h. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 6/1, v/v) afforded **3h** as a white solid (71 mg, 55% yield). M.p.: 90-92 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.58 (s, 3H), 7.19 (s, 1H), 7.23-7.29 (m, 1H), 7.63-7.71 (m, 3H), 7.76 (t, J = 7.6 Hz, 1H), 8.67 (d, J = 4.8 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.5, 122.3, 122.5, 123.3, 123.5, 125.6, 129.2, 130.6, 136.8, 137.7, 140.1, 142.9, 149.8, 153.1 ppm. HRMS (ESI$^+$): calcd for $C_{14}H_{11}ClNS$ $[M+H]^+$ 260.0301, found 260.0296.



2-(5-Butylfuran-2-yl)pyridine (3i)

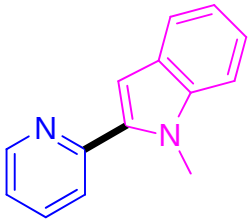
Following the general procedure, the reaction mixture was stirred at 140 °C for 24 h. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 6/1, v/v) afforded **3i** as colorless oil (58 mg, 57% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.92 (t, J = 7.2 Hz, 3H), 1.36-1.46 (m, 2H), 1.65-1.72 (m, 2H), 2.69 (t, J = 7.6 Hz, 2H), 6.11 (d, J = 3.2 Hz, 1H), 6.94 (d, J = 3.2 Hz, 1H), 7.06-7.09 (m, 1H), 7.60-7.68 (m, 2H), 8.55 (d, J = 4.4 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9, 22.4, 28.1, 30.3, 107.6, 109.6, 118.3, 121.4, 136.6, 149.6, 149.8, 151.9, 158.2 ppm. HRMS (ESI$^+$): calcd for $C_{13}H_{16}NO$ $[M+H]^+$ 202.1232, found 202.1231.



2-(Benzofuran-2-yl)pyridine (3j)

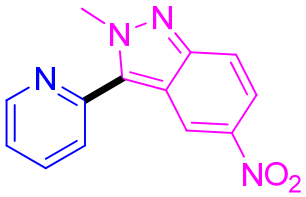
Following the general procedure, the reaction mixture was stirred at 140 °C for 24 h.

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 6/1, v/v) afforded **3j** as a white solid (54 mg, 55% yield). M.p.: 79-81 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.16-7.20 (m, 2H), 7.24-7.28 (td, J = 8.4 Hz, 1.6 Hz, 1H), 7.41 (s, 1H), 7.48 (dd, J = 8.4 Hz, 0.8 Hz, 1H), 7.56 (d, J = 8.4 Hz, 1H), 7.70 (td, J = 7.6 Hz, 1.6 Hz, 1H), 7.82 (d, J = 8.0 Hz, 1H), 8.60 (d, J = 6.4 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 105.3, 111.7, 120.0, 121.9, 123.1, 123.4, 125.4, 128.9, 137.1, 149.2, 149.8, 154.9, 155.5 ppm. HRMS (ESI$^+$): calcd for $C_{13}H_9NNaO$ $[M+Na]^+$ 218.0582, found 218.0584.



1-Methyl-2-(pyridin-2-yl)-1*H*-indole (3k)

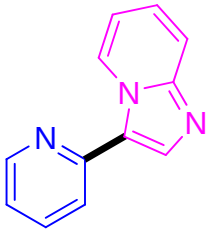
Following the general procedure, the reaction mixture was stirred at 140 °C for 24 h. Purification by column chromatography on silica gel (petroleum ether/CH_2Cl_2 = 1/1, v/v) afforded **3k** as a pale yellow solid (42 mg, 40% yield). M.p.: 86-87 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.08 (s, 3H), 6.87 (s, 1H), 7.13 (t, J = 7.6 Hz, 1H), 7.22-7.30 (m, 2H), 7.40 (d, J = 8.0 Hz, 1H), 7.65 (d, J = 8.0 Hz, 1H), 7.71-7.78 (m, 2H), 8.70 (d, J = 4.4 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 32.1, 104.2, 110.0, 120.1, 121.2, 122.0, 122.9, 123.9, 127.6, 137.2, 138.5, 139.6, 148.7, 152.1 ppm. HRMS (ESI$^+$): calcd for $C_{14}H_{13}N_2$ $[M+H]^+$ 209.1079, found 209.1076.



2-Methyl-5-nitro-3-(pyridin-2-yl)-2*H*-indazole (3l)

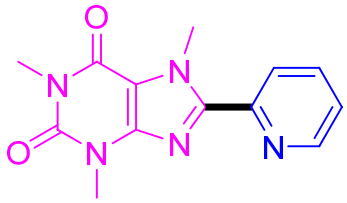
Following the general procedure, the reaction mixture was stirred at 140 °C for 24 h. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate/CH_2Cl_2 = 3/1/1, v/v/v) afforded **3l** as a yellow solid (79 mg, 62% yield). M.p.: 213-215 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.50 (s, 3H), 7.49-7.53 (m, 1H),

7.80-7.84 (m, 2H), 8.03 (t, J = 8.0 Hz, 1H), 8.15 (dd, J = 9.2 Hz, 2.0 Hz, 1H), 8.81 (d, J = 2.0 Hz, 1H), 8.88 (d, J = 4.4 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 40.7, 118.6, 119.4, 119.8, 120.6, 123.8, 124.7, 137.6, 138.0, 143.9, 147.9, 149.0, 150.5 ppm. HRMS (ESI$^+$): calcd for $C_{13}H_{11}N_4O_2$ $[M+H]^+$ 255.0882, found 255.0879.



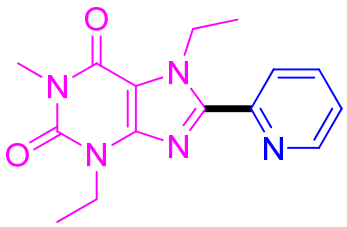
3-(Pyridin-2-yl)imidazo[1,2-*a*]pyridine (3m)

Following the general procedure, the reaction mixture was stirred at 140 °C for 24 h. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1, v/v) afforded **3m** as a white solid (49 mg, 50% yield). M.p.: 77-78 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.97 (td, J = 6.8 Hz, 1.2 Hz, 1H), 7.17-7.20 (m, 1H), 7.33-7.37 (m, 1H), 7.73-7.78 (m, 3H), 8.16 (s, 1H), 8.66 (dt, J = 4.8 Hz, 1.2 Hz, 1H), 9.96 (d, J = 7.2 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 113.1, 117.6, 120.6, 121.1, 123.8, 125.8, 128.2, 134.4, 136.7, 147.4, 148.8, 150.6 ppm. HRMS (ESI$^+$): calcd for $C_{12}H_9N_3Na$ $[M+Na]^+$ 218.0694, found 218.0698.



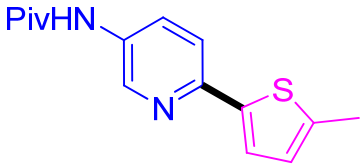
1,3,7-Trimethyl-8-(pyridin-2-yl)-xanthine (3n)

Following the general procedure, the reaction mixture was stirred at 140 °C for 24 h. Purification by column chromatography on silica gel (petroleum ether/acetone/CH_2Cl_2 = 3/1/1, v/v/v) afforded **3n** as a white solid (69 mg, 51% yield). M.p.: 275-276 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.44 (s, 3H), 3.64 (s, 3H), 4.47 (s, 3H), 7.34-7.37 (m, 1H), 7.82 (t, J = 7.6 Hz, 1H), 8.20 (d, J = 8.0 Hz, 1H), 8.68 (d, J = 4.4 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.2, 29.9, 35.3, 109.6, 124.2, 124.8, 137.0, 147.9, 148.4, 149.0, 149.4, 151.9, 155.8 ppm. HRMS (ESI$^+$): calcd for $C_{13}H_{14}N_5O_2$ $[M+H]^+$ 272.1147, found 272.1147.



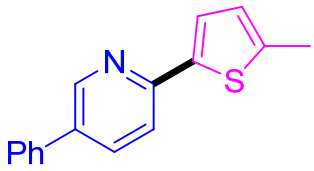
3,7-Diethyl-1-methyl-8-(pyridin-2-yl)-xanthine (3o)

Following the general procedure, the reaction mixture was stirred at 140 °C for 24 h. Purification by column chromatography on silica gel (petroleum ether/acetone/CH_2Cl_2 = 6/1/1, v/v/v) afforded **3o** as a white solid (73 mg, 49% yield). M.p.: 222-223 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.37 (t, J = 6.8 Hz, 3H), 1.48 (t, J = 7.2 Hz, 3H), 3.44 (s, 3H), 4.21 (q, J = 7.2 Hz, 2H), 5.03 (q, J = 6.8 Hz, 2H), 7.33 (t, J = 6.4 Hz, 1H), 7.81 (t, J = 7.6 Hz, 1H), 8.22 (d, J = 8.0 Hz, 1H), 8.67 (d, J = 4.4 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.5, 16.6, 28.1, 38.6, 42.8, 108.9, 124.1, 124.8, 136.9, 147.6, 147.8, 149.1, 149.4, 151.3, 155.5 ppm. HRMS (ESI$^+$): calcd for $C_{15}H_{18}N_5O_2$ $[M+H]^+$ 300.1460, found 300.1463.



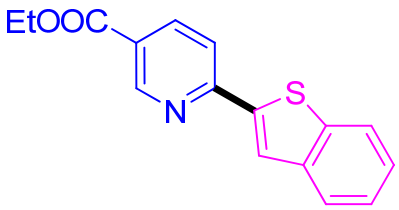
***N*-(6-(5-Methylthiophen-2-yl)pyridin-3-yl)pivalamide (4a)**

N-(Pyridin-3-yl)pivalamide (890 mg, 5.0 mmol), 2-methylthiophene (49 μL, 0.50 mmol), $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), AgOAc (251 mg, 1.5 mmol), 1,10-phenanthroline monohydrate (49.5 mg, 0.25 mmol), PivOH (51 mg, 0.50 mmol), and DMF (0.5 mL) at 140 °C for 24 h. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1, v/v) afforded **4a** as a white solid (87 mg, 63% yield). M.p.: 102-104 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.30 (s, 9H), 2.56 (s, 3H), 6.84 (d, J = 2.4 Hz, 1H), 7.23-7.25 (m, 1H), 7.29 (s, 1H), 7.99 (s, 1H), 8.36 (d, J = 4.4 Hz, 1H), 8.65 (d, J = 8.4 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.5, 27.6, 40.1, 122.6, 126.0, 126.8, 129.8, 131.7, 138.3, 143.2, 143.4, 144.8, 177.1 ppm. HRMS (ESI$^+$): calcd for $C_{15}H_{19}N_2OS$ $[M+H]^+$ 275.1218, found 275.1213.



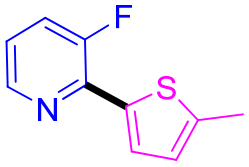
2-(5-Methylthiophen-2-yl)-5-phenylpyridine (4b)

Following the general procedure, the reaction mixture was stirred at 140 °C for 24 h. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 6/1, v/v) afforded **4b** as a white solid (52 mg, 41% yield). M.p.: 126-127 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.55 (s, 3H), 6.80 (d, J = 2.8 Hz, 1H), 7.39 (t, J = 7.6 Hz, 1H), 7.47 (t, J = 8.0 Hz, 2H), 7.54 (bs, 1H), 7.59-7.61 (m, 2H), 7.66 (d, J = 8.4 Hz, 1H), 7.89 (dd, J = 8.0 Hz, 2.0 Hz, 1H), 8.79 (d, J = 2.4 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.8, 118.4, 125.0, 126.6, 126.9, 128.1, 129.2, 134.3, 135.1, 137.7, 141.9, 142.8, 147.8, 151.6 ppm. HRMS (ESI$^+$): calcd for $C_{16}H_{14}NS$ $[M+H]^+$ 252.0847, found 252.0847.



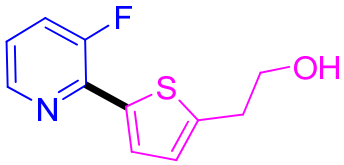
Ethyl 6-(benzo[*b*]thiophen-2-yl)nicotinate (4c)

Following the general procedure, the reaction mixture was stirred at 140 °C for 24 h. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 6/1, v/v) afforded **4c** as a pale yellow solid (57 mg, 40% yield). M.p.: 168-169 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.41 (t, J = 7.2 Hz, 3H), 4.40 (q, J = 7.2 Hz, 2H), 7.36-7.40 (m, 2H), 7.83-7.89 (m, 3H), 8.00 (s, 1H), 8.32-8.35 (m, 1H), 9.22 (d, J = 1.2 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.4, 61.6, 119.1, 122.8, 123.5, 124.7, 124.89, 124.92, 125.9, 138.0, 140.4, 141.4, 143.4, 150.9, 155.7, 165.1 ppm. HRMS (ESI$^+$): calcd for $C_{16}H_{14}NO_2S$ $[M+H]^+$ 284.0745, found 284.0746.



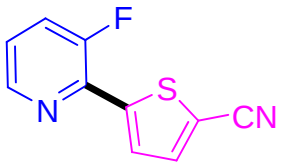
3-Fluoro-2-(5-methylthiophen-2-yl)pyridine (4d)

Following the general procedure, the reaction mixture was stirred at 140 °C for 24 h. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 6/1, v/v) afforded **4d** as colorless oil (69 mg, 71% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.54 (s, 3H), 6.81 (d, J = 3.2 Hz, 1H), 7.10-7.15 (m, 1H), 7.40-7.44 (m, 1H), 7.62 (t, J = 2.8 Hz, 1H), 8.36 (dd, J = 3.2 Hz, 1.6 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.6, 122.1, 122.2, 123.6, 123.8, 126.8, 126.9, 128.7, 137.3, 141.6, 141.7, 143.3, 145.0, 154.5, 157.1 ppm. HRMS (ESI^+): calcd for $C_{10}H_9FNS$ $[M+H]^+$ 194.0440, found 194.0437.



2-(5-(3-Fluoropyridin-2-yl)thiophen-2-yl)ethanol (4e)

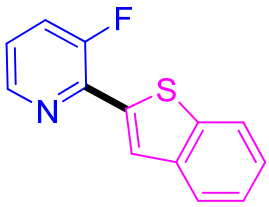
Following the general procedure, the reaction mixture was stirred at 140 °C for 24 h. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 6/1, v/v) afforded **4e** as colorless oil (85 mg, 76% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.08 (s, 1H), 3.17 (t, J = 6.4 Hz, 2H), 4.32 (t, J = 6.4 Hz, 2H), 6.92 (d, J = 3.6 Hz, 1H), 7.15-7.19 (m, 1H), 7.44-7.49 (m, 1H), 7.72 (s, 1H), 8.38 (d, J = 4.0 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.1, 64.5, 122.49, 122.53, 123.9, 124.1, 127.16, 127.18, 128.5, 128.7, 138.1, 141.3, 143.6, 144.9, 154.6, 157.2, 171.0 ppm. HRMS (ESI^+): calcd for $C_{11}H_9FNS$ $[M-H_2O+H]^+$ 206.0440, found 206.0443.



5-(3-Fluoropyridin-2-yl)thiophene-2-carbonitrile (4f)

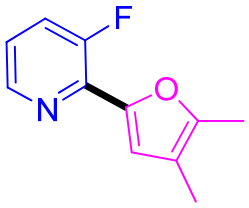
Following the general procedure, the reaction mixture was stirred at 140 °C for 24 h. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 6/1, v/v) afforded **4f** as a greenish yellow solid (44 mg, 43% yield). M.p.: 113-114 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.29-7.33 (m, 1H), 7.50-7.55 (m, 1H), 7.64 (d, J = 4.0 Hz, 1H), 7.75 (dd, J = 4.0 Hz, 1.6 Hz, 1H), 8.42-8.44 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 111.3, 111.4, 114.4, 124.4, 124.6, 124.9, 125.0, 127.4, 127.5,

138.49, 138.51, 139.3, 139.4, 145.66, 145.70, 147.1, 147.2, 155.1, 157.8 ppm. HRMS (ESI^+): calcd for $C_{10}H_6FN_2S$ $[M+H]^+$ 205.0236, found 205.0233.



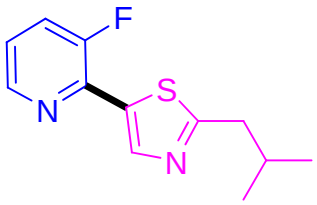
2-(Benzo[*b*]thiophen-2-yl)-3-fluoropyridine (4g)

Following the general procedure, the reaction mixture was stirred at 140 °C for 24 h. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 6/1, v/v) afforded **4g** as a white solid (70 mg, 61% yield). M.p.: 123-125 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.22-7.25 (m, 1H), 7.35-7.39 (m, 2H), 7.48-7.53 (m, 1H), 7.83-7.90 (m, 2H), 8.06 (d, J = 1.6 Hz, 1H), 8.46-8.48 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 122.4, 123.54, 123.58, 123.8, 124.0, 124.6, 124.7, 125.1, 125.3, 125.5, 140.1, 140.2, 140.41, 140.43, 140.91, 140.93, 141.3, 141.5, 145.38, 145.43, 155.5, 158.2 ppm. HRMS (ESI^+): calcd for $C_{13}H_9FNS$ $[M+H]^+$ 230.0440, found 230.0440.



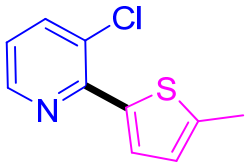
2-(4,5-Dimethylfuran-2-yl)-3-fluoropyridine (4h)

Following the general procedure, the reaction mixture was stirred at 140 °C for 24 h. Purification by column chromatography on silica gel (petroleum ether/CH_2Cl_2 = 1/1, v/v) afforded **4h** as colorless oil (65 mg, 68% yield). ^1H NMR (400 MHz, $CDCl_3$): δ = 2.02 (s, 3H), 2.35 (s, 3H), 6.90 (d, J = 4.0 Hz, 1H), 7.10-7.13 (m, 1H), 7.38-7.44 (m, 1H), 8.44-8.46 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 10.0, 11.8, 116.97, 116.99, 117.2, 117.3, 121.71, 121.74, 123.25, 123.4, 138.1, 138.2, 145.1, 145.19, 145.24, 150.2, 154.1, 156.7 ppm. HRMS (ESI^+): calcd for $C_{11}H_{11}FNO$ $[M+H]^+$ 192.0825, found 192.0822.



5-(3-Fluoropyridin-2-yl)-2-isobutylthiazole (4i)

Following the general procedure, the reaction mixture was stirred at 140 °C for 24 h. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 6/1, v/v) afforded **4i** as colorless oil (98 mg, 83% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.99 (d, J = 6.8 Hz, 6H), 2.11-2.18 (m, 1H), 2.89 (d, J = 6.8 Hz, 2H), 7.16-7.19 (m, 1H), 7.42-7.47 (m, 1H), 8.27 (d, J = 1.6 Hz, 1H), 8.36 (d, J = 4.4 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.4, 29.9, 42.5, 123.08, 123.12, 123.6, 123.8, 134.67, 134.75, 139.8, 139.9, 142.2, 142.3, 145.4, 145.5, 154.7, 157.3, 172.65, 172.68 ppm. HRMS (ESI$^+$): calcd for $C_{12}H_{14}FN_2S$ $[M+H]^+$ 237.0862, found 237.0860.



3-Chloro-2-(5-methylthiophen-2-yl)pyridine (4j)

Following the general procedure, the reaction mixture was stirred at 140 °C for 24 h. Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 6/1, v/v) afforded **4j** as colorless oil (47 mg, 45% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.53 (s, 3H), 6.81 (d, J = 1.6 Hz, 1H), 7.06-7.09 (m, 1H), 7.72 (d, J = 8.0 Hz, 1H), 7.93 (d, J = 3.6 Hz, 1H), 8.47 (d, J = 4.8 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.4, 121.7, 126.4, 127.5, 129.5, 138.7, 139.8, 143.8, 147.2, 149.5 ppm. HRMS (ESI$^+$): calcd for $C_{10}H_9ClNS$ $[M+H]^+$ 210.0144, found 210.0143.

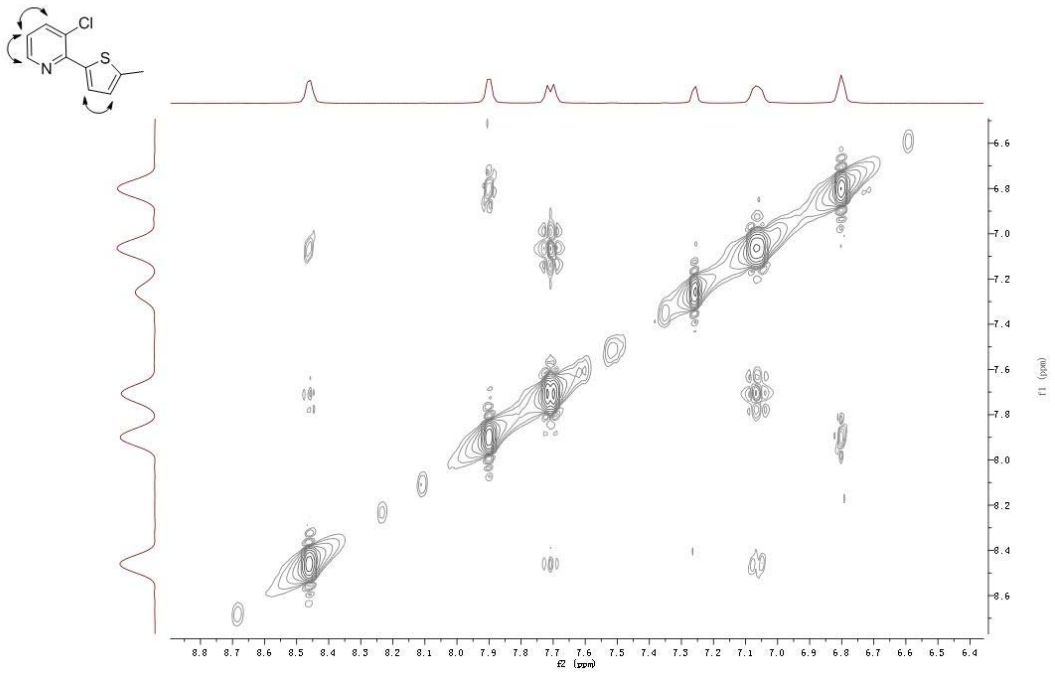
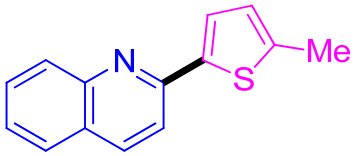
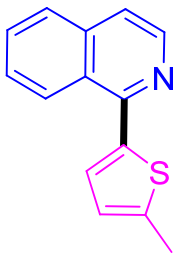


Fig. S1 ^{1}H-^{1}H NOESY spectrum of compound **4j.**



2-(5-Methylthiophen-2-yl)quinoline (4k)

Following the general procedure, the reaction mixture was stirred at 140 °C for 24 h. Purification by column chromatography on silica gel (petroleum ether/CH_2Cl_2 = 1/1, v/v) afforded **4k** as a pale yellow solid (65 mg, 58% yield). M.p.: 122-124 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.56 (s, 3H), 6.83 (d, J = 2.8 Hz, 1H), 7.46 (t, J = 7.6 Hz, 1H), 7.60 (bs, 1H), 7.67 (t, J = 7.6 Hz, 1H), 7.73 (t, J = 8.4 Hz, 2H), 8.11 (d, J = 8.8 Hz, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.8, 117.4, 125.9, 126.1, 126.5, 127.1, 127.6, 129.3, 129.8, 136.5, 143.0, 143.7, 148.3, 152.6 ppm. HRMS (ESI^{+}): calcd for $C_{14}H_{12}NS$ $[M+H]^{+}$ 226.0690, found 226.0686.



1-(5-Methylthiophen-2-yl)isoquinoline (4l)

Following the general procedure, the reaction mixture was stirred at 140 °C for 24 h. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 6/1, v/v) afforded **4l** as pale green oil (64 mg, 57% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.59 (s, 3H), 6.88 (d, J = 2.8 Hz, 1H), 7.46 (d, J = 3.2 Hz, 1H), 7.56 (d, J = 5.6 Hz, 1H), 7.60 (t, J = 7.2 Hz, 1H), 7.69 (t, J = 7.2 Hz, 1H), 7.85 (d, J = 8.0 Hz, 1H), 8.52 (d, J = 5.6 Hz, 1H), 8.55 (d, J = 8.4 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.6, 119.6, 126.0, 126.1, 127.0, 127.3, 127.6, 129.2, 130.2, 137.3, 140.3, 142.0, 143.1, 153.7 ppm. HRMS (ESI$^+$): calcd for $C_{14}H_{12}NS$ $[M+H]^+$ 226.0690, found 226.0694.

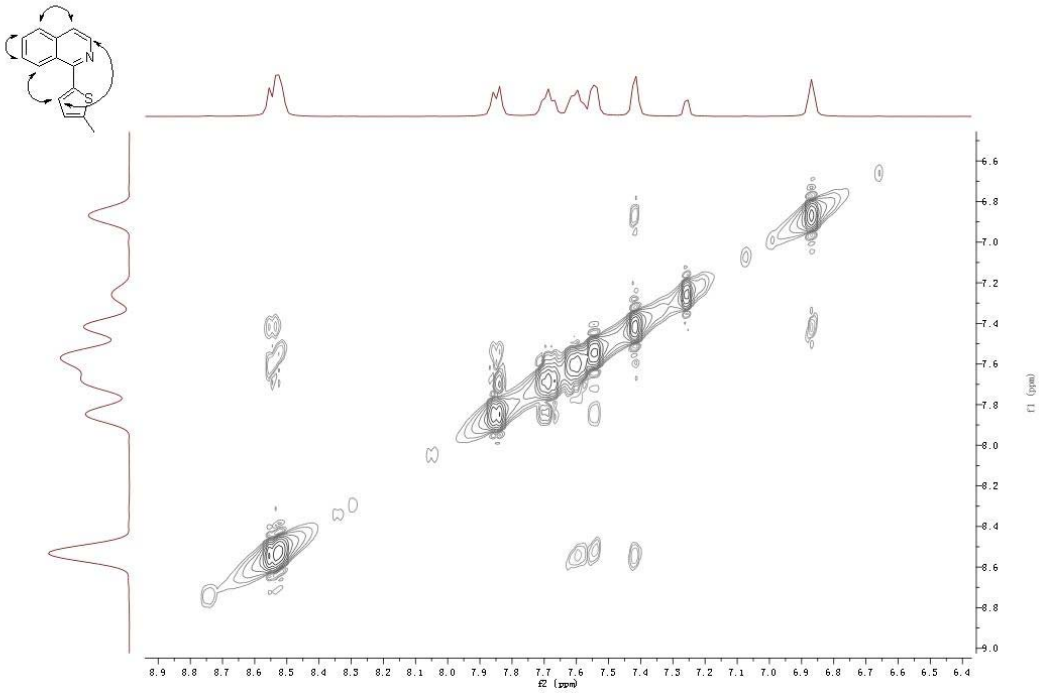
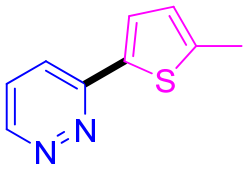
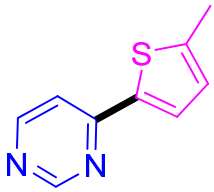


Fig. S2 ^{1}H-^{1}H NOESY spectrum of compound **4l.**



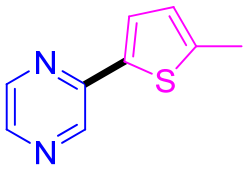
3-(5-Methylthiophen-2-yl)pyridazine (4m)

Following the general procedure, the reaction mixture was stirred at 140 °C for 24 h. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1, v/v) afforded **4m** as a white solid (36 mg, 41% yield). M.p.: 91-93 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.57 (s, 3H), 6.83-6.84 (m, 1H), 7.54-7.57 (m, 2H), 7.80 (d, J = 8.4 Hz, 1H), 9.04 (d, J = 4.8 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.8, 122.3, 126.7, 126.9, 127.0, 137.9, 145.0, 149.2, 155.5 ppm. HRMS (ESI^+): calcd for $C_9H_8N_2NaS$ $[M+Na]^+$ 199.0306, found 199.0305.



4-(5-Methylthiophen-2-yl)pyrimidine (4n)

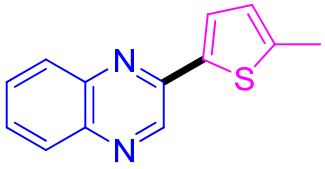
Following the general procedure, the reaction mixture was stirred at 140 °C for 24 h. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 4/1, v/v) afforded **4n** as a pale yellow solid (39 mg, 44% yield). M.p.: 83-85 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.56 (s, 3H), 6.84 (dd, J = 3.6 Hz, 1.2 Hz, 1H), 7.51 (dd, J = 5.2 Hz, 1.2 Hz, 1H), 7.62 (d, J = 4.0 Hz, 1H), 8.62 (d, J = 5.2 Hz, 1H), 9.08 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.9, 114.8, 127.1, 128.2, 139.3, 146.1, 156.8, 158.97, 159.04 ppm. HRMS (ESI^+): calcd for $C_9H_9N_2S$ $[M+H]^+$ 177.0486, found 177.0482.



2-(5-Methylthiophen-2-yl)pyrazine (4o)

Following the general procedure, the reaction mixture was stirred at 140 °C for 24 h. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate =

6/1, v/v) afforded **4o** as a pale greenish yellow solid (72 mg, 82% yield). M.p.: 85-87 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.55 (s, 3H), 6.81 (d, J = 3.6 Hz, 1H), 7.49 (d, J = 3.6 Hz, 1H), 8.34 (d, J = 2.4 Hz, 1H), 8.46 (s, 1H), 8.88 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.8, 126.2, 126.9, 138.9, 140.4, 141.8, 144.0, 144.3, 148.9 ppm. HRMS (ESI^+): calcd for $C_9H_9N_2S$ $[M+H]^+$ 177.0486, found 177.0480.



2-(5-Methylthiophen-2-yl)quinoxaline (4p)

Following the general procedure, the reaction mixture was stirred at 140 °C for 24 h. Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 6/1, v/v) afforded **4p** as a pale greenish yellow solid (51 mg, 45% yield). M.p.: 113-115 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.58 (s, 3H), 6.86 (s, 1H), 7.64-7.68 (m, 2H), 7.71 (t, J = 8.0 Hz, 1H), 8.03 (d, J = 8.4 Hz, 2H), 9.17 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.9, 127.0, 127.4, 128.9, 129.1, 129.2, 130.4, 139.9, 141.2, 142.0, 142.3, 145.3, 147.7 ppm. HRMS (ESI^+): calcd for $C_{13}H_{11}N_2S$ $[M+H]^+$ 227.0643, found 227.0639.

IV. ORTEP diagrams of compounds 3f, 3k, 3o, 4c and 4f.

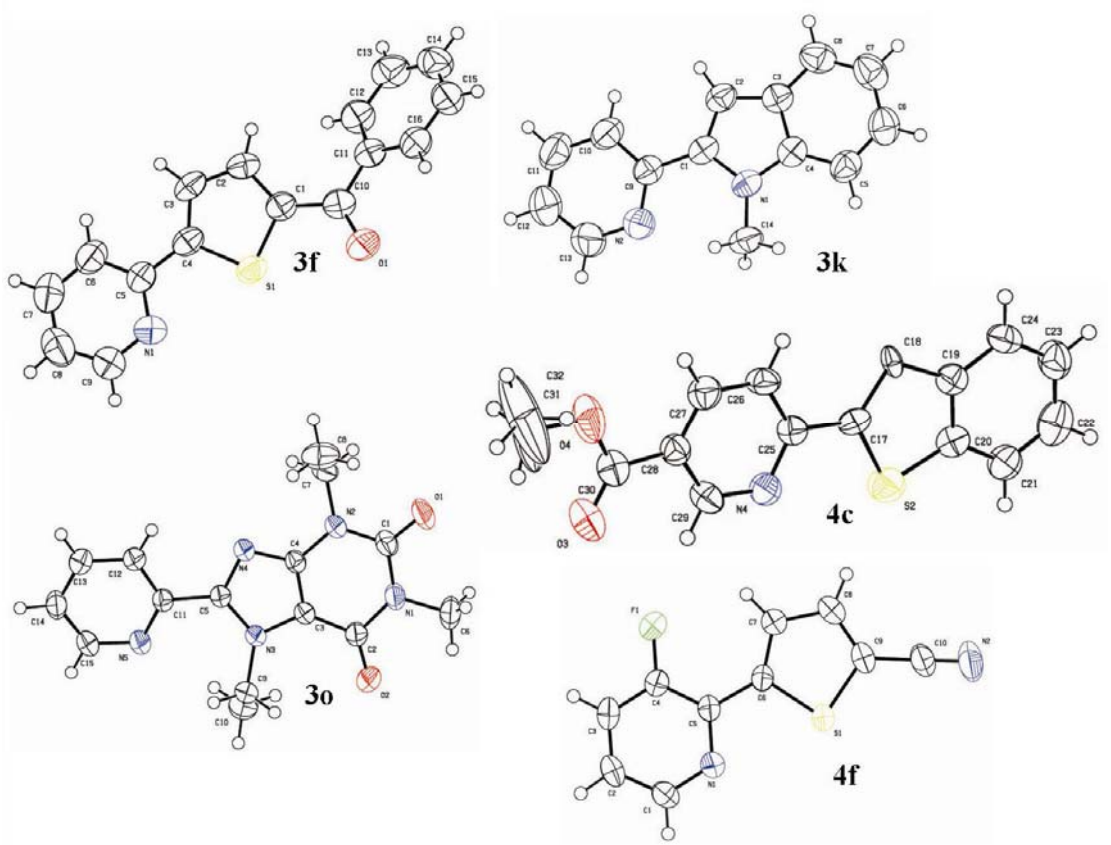
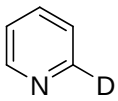


Fig. S3 ORTEP diagrams of **3f**, **3k**, **3o**, **4c** and **4f**. Thermal ellipsoids are shown at the 50% probability level.

V. Mechanistic Experiments

(1) Synthesis of pyridine-d_1 and benzofuran-d_1



Pyridine-d_1 was prepared by following a modified procedure from Brandsma *et al*.[3]

n-Butyllithium (2.5 M solution in hexane, 14.4 mL, 36 mmol, 1.2 equiv) was added dropwise to a solution of 2-bromopyridine (4.74 g, 30 mmol, 1.0 equiv) in dry Et_2O (80 mL) at -78 °C. The resulting mixture was stirred for 2 h at -78 °C and D_2O (3.0 mL) was added. The brown suspension was warmed to room temperature and stirred for an additional hour. A mixture of 10 mL of 36% hydrochloric acid and 10 mL of

water was added after this quenching procedure. The aqueous layer was separated and the organic layer was washed with 10 mL of water. The combined aqueous layers were freed from organic solvents by heating them in vacuo (rotary evaporator). Subsequently potassium hydroxide pellets (10 g) were added with shaking and cooling in ice-water. The deuterated pyridine liberated was isolated by extraction (5 times) with diethyl ether, drying the extracts over powder KOH, and subsequently distilling at normal pressure to afford pyridine-d_1 as colorless oil (2.1 g, 88% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.26-7.29 (m, 2H), 7.66 (td, J = 7.6 Hz, J = 1.2 Hz 1H), 8.60 (d, J = 4.0 Hz, 1H) ppm.

The deuterium incorporation amounts up to >99% determined by ^{1}H NMR.

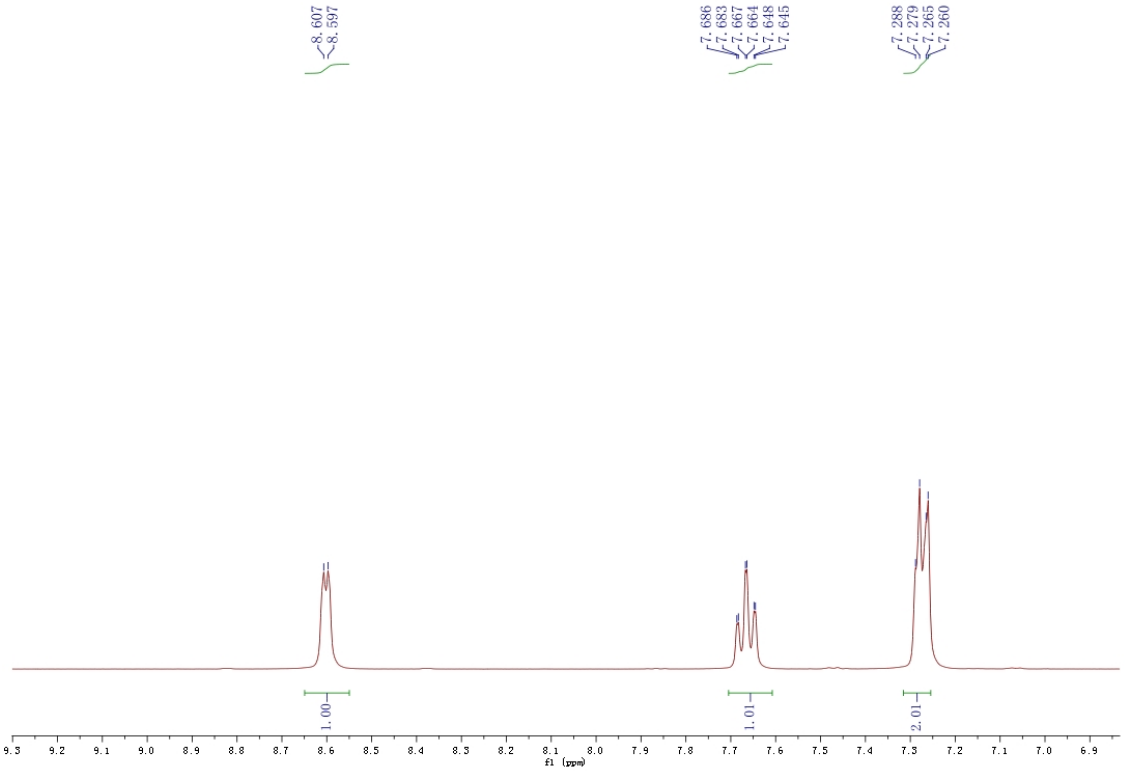
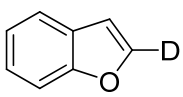


Fig. S4 ^{1}H NMR of **pyridine-d_1** measured in $CDCl_3$.

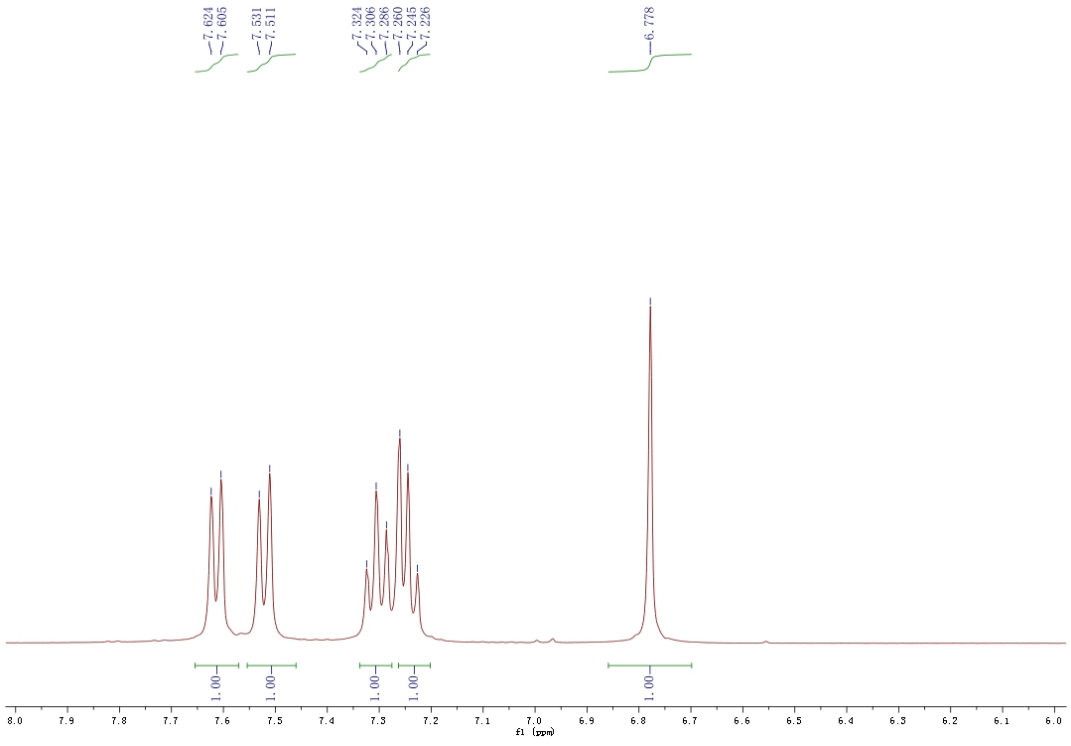


Benzofuran-d_1 was prepared by following a modified procedure from Fagnou *et al.*[4]

n-Butyllithium (2.5 M solution in hexane, 6.0 mL, 15 mmol, 1.5 equiv) was added

dropwise to a solution of benzofuran (1.18 g, 10 mmol, 1.0 equiv) in dry THF (20 mL) at -40 °C. The resulting mixture was stirred for 4 h at -40 °C and D_2O (2.0 mL) was added. The resulting mixture was stirred for an additional 2 h at room temperature before H_2O was added (5 mL). The two phases were separated and the aqueous phase was extracted with Et_2O (3×5 mL). The organic phases were combined, washed with brine and dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by short column chromatography on silica gel (eluent: pentane) to afford benzofuran-d_1 as colorless oil (1.1 g, 93%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.78 (s, 1H), 7.23-7.26 (m, 1H), 7.29-7.32 (m, 1H), 7.52 (d, J = 8.0 Hz, 1H), 7.61 (d, J = 7.6 Hz, 1H) ppm.

The deuterium incorporation amounts up to >99% determined by ^{1}H NMR.



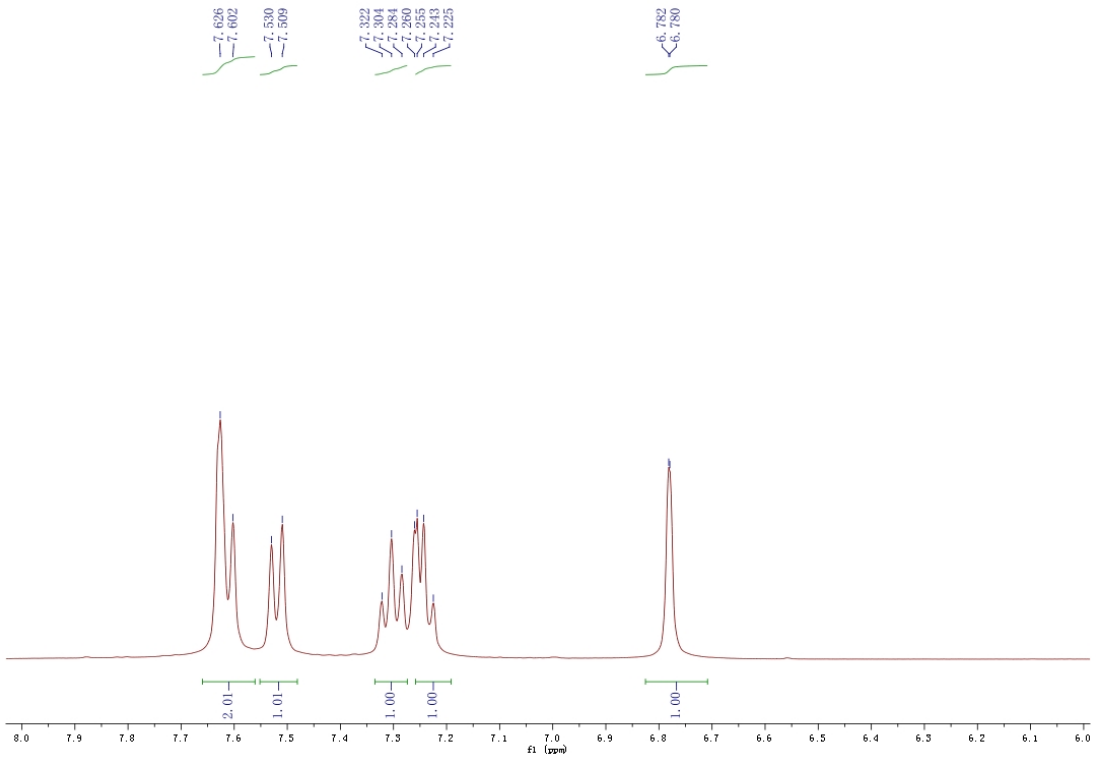
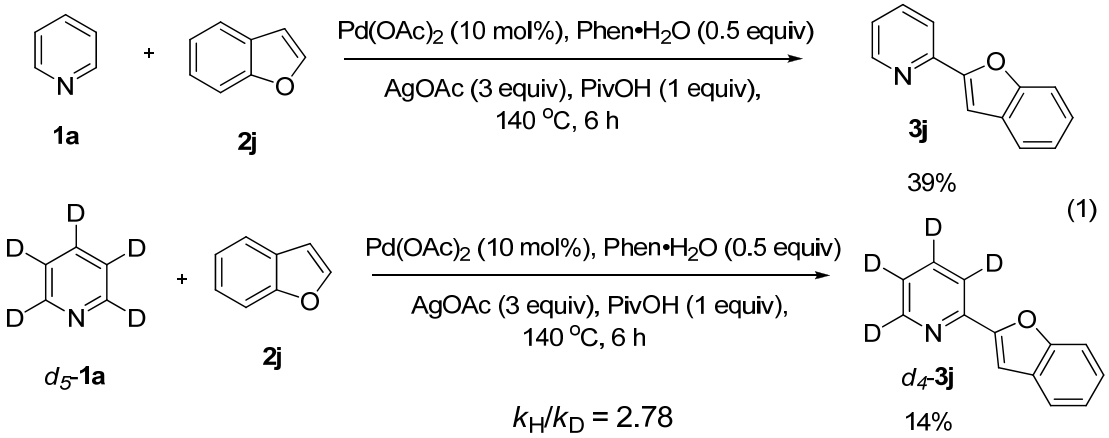


Fig. S5 ^{1}H NMR of benzofuran-d_1 (top) and benzofuran (bottom) measured in $CDCl_3$.

(2) Kinetic isotope effect experiments



Two sets of reactions were carried out in a parallel manner. In each case benzofuran was allowed to react with pyridine and pyridine-d_5, respectively. The sealed tube was screw capped and heated to 140 °C (oil bath). After being stirred for 6 h, the reaction mixture was cooled to room temperature, and diluted with 20 mL of CH_2Cl_2. The reaction mixture was filtered through a celite pad, and washed with CH_2Cl_2. The filtrate was concentrated in *vacuo*. Purification by column

chromatography on silica gel (petroleum ether/ethyl acetate = 6/1, v/v) afforded **3j** and d_4-**3j** in the yields of 39% and 14%, respectively.

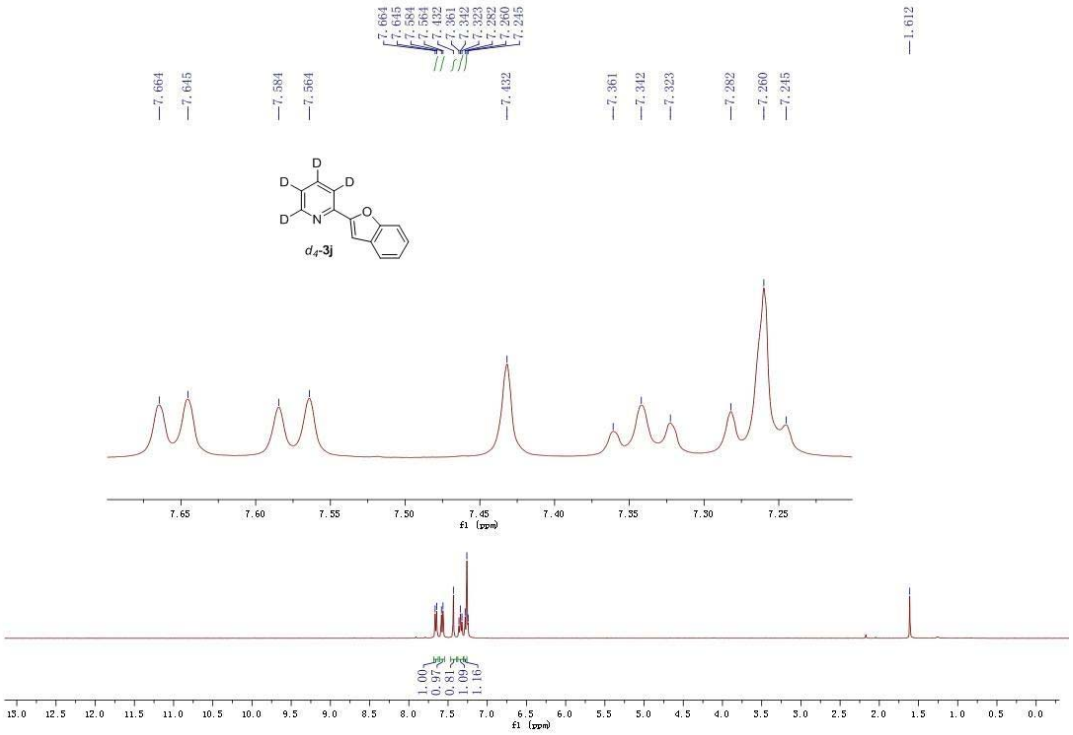
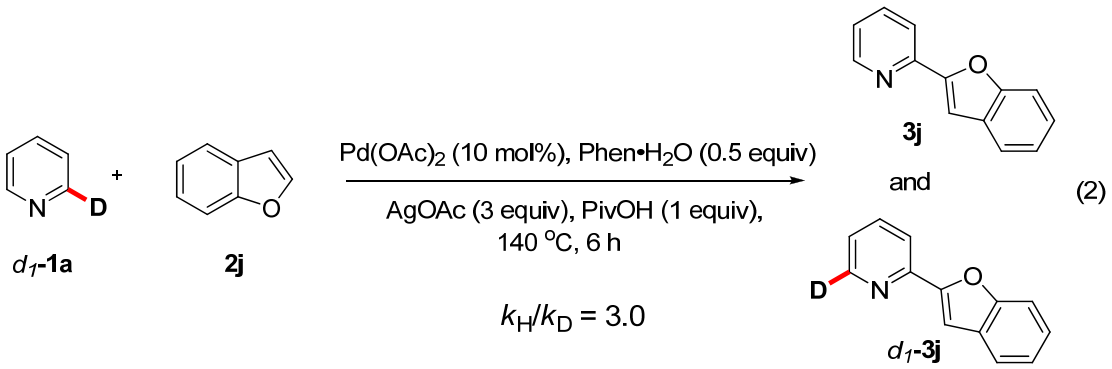


Fig. S6 ^{1}H NMR of d_4-**3j** measured in $CDCl_3$.



To a 25 mL sealed tube were added $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), AgOAc (251 mg, 1. 5 mmol), 1,10-phenanthroline monohydrate (49.5 mg, 0.25 mmol), PivOH (51 mg, 0.50 mmol), benzofuran (49 μL, 0.50 mmol) and pyridine-d_1 (1.0 mL, 12.5 mmol). The reaction mixture was stirred at 140 °C under an N_2 atmosphere for 6 h. The reaction vessel was cooled to room temperature and diluted with CH_2Cl_2. The reaction mixture was filtered through a celite pad, and washed with CH_2Cl_2. The filtrate was concentrated in *vacuo*. The resulting residue was analyzed by ^{1}H NMR.

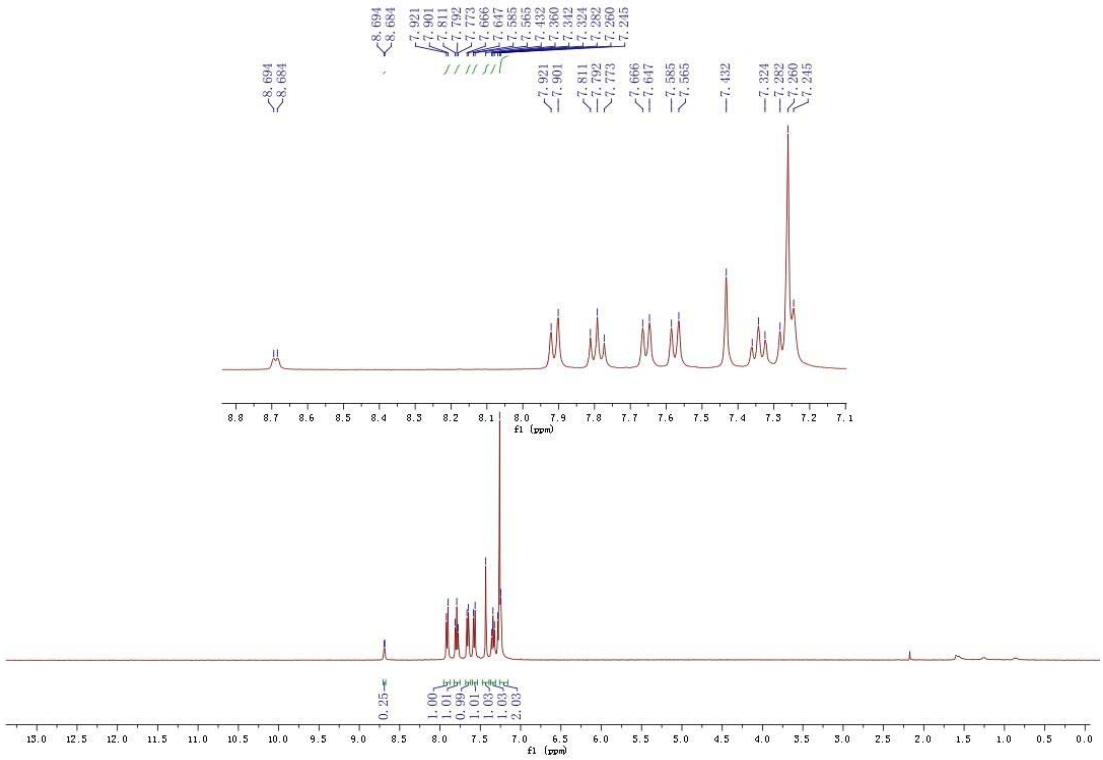
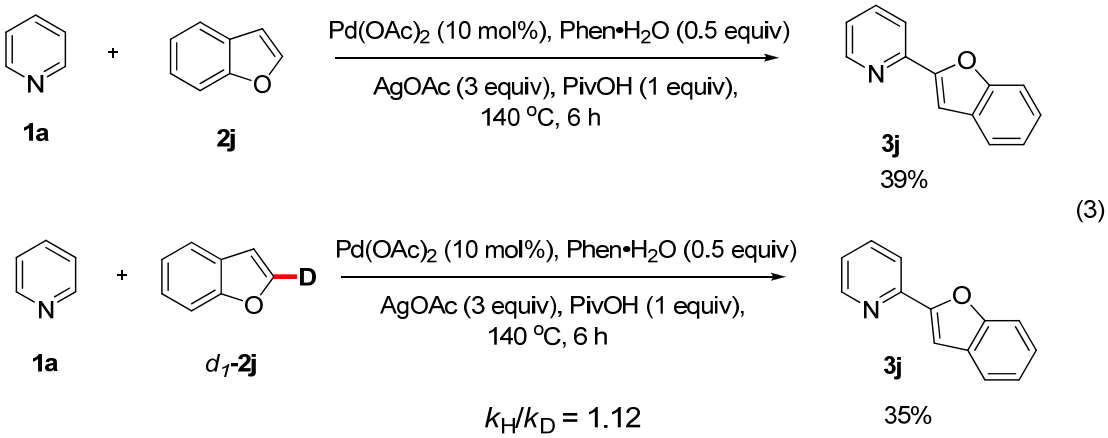


Fig. S7 ^{1}H NMR spectrum of the mixture of d_1-**3j** and **3j** measured in $CDCl_3$



Two sets of reactions were carried out in a parallel manner. In each case pyridine was allowed to react with benzofuran and benzofuran-d_1, respectively. The sealed tube was screw capped and heated to 140 °C (oil bath). After being stirred for 6 h, the reaction mixture was cooled to room temperature, and diluted with 20 mL of CH_2Cl_2. The reaction mixture was filtered through a celite pad, and washed with CH_2Cl_2. The filtrate was concentrated in *vacuo*. The yield of **3j** was determined by column chromatography on silica gel (petroleum ether/ethyl acetate = 6/1, v/v).

VI. The effect of radical scavenger TEMPO on the coupling reaction

A flame-dried Schlenk test tube with a magnetic stirring bar was charged with TEMPO (15.6 mg, 0.1 mmol), $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), 2-methylthiophene **2a** (49 μL, 0.50 mmol), AgOAc (251 mg, 1.5 mmol), 1,10-phenanthroline monohydrate (49.5 mg, 0.25 mmol), PivOH (51 mg, 0.50 mmol), and pyridine (1.0 mL) under an N_2 atmosphere. The rubber septum was replaced with a teflon stopper, and the system was then evacuated and back filled with N_2 for twice. The reaction mixture was stirred for 5 min at room temperature, and then heated at 140 ^oC for 24 h. The resulting solution was cooled to ambient temperature, diluted with 20 mL of CH_2Cl_2, filtered through a celite pad, and washed with 10-20 mL of CH_2Cl_2. The combined organic extracts were concentrated and the resulting residue was purified by column chromatography on silica gel to provide the desired product **3a**.

VII. References

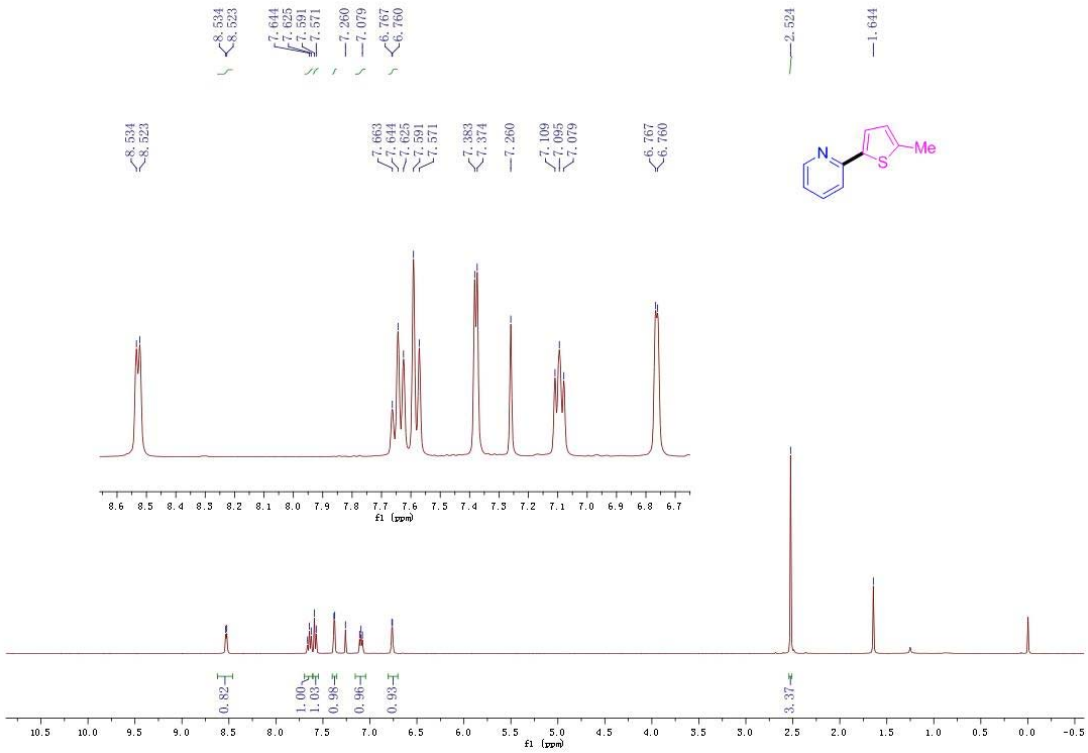
1. (a) P. Xi, F. Yang, S. Qin, D. Zhao, J. Lan, G. Gao, C. Hu and J. You, *J. Am. Chem. Soc.* 2010, **132**, 1822; (b) D. van den Berg, K. R. Zoellner, M. O. Ogunrombi, S. F. Malan, G. Terre'Blanche, N. Castagnoli, Jr., J. J. Bergh and J. P. Petzer, *Bioorg. Med. Chem.* 2007, **15**, 3692.

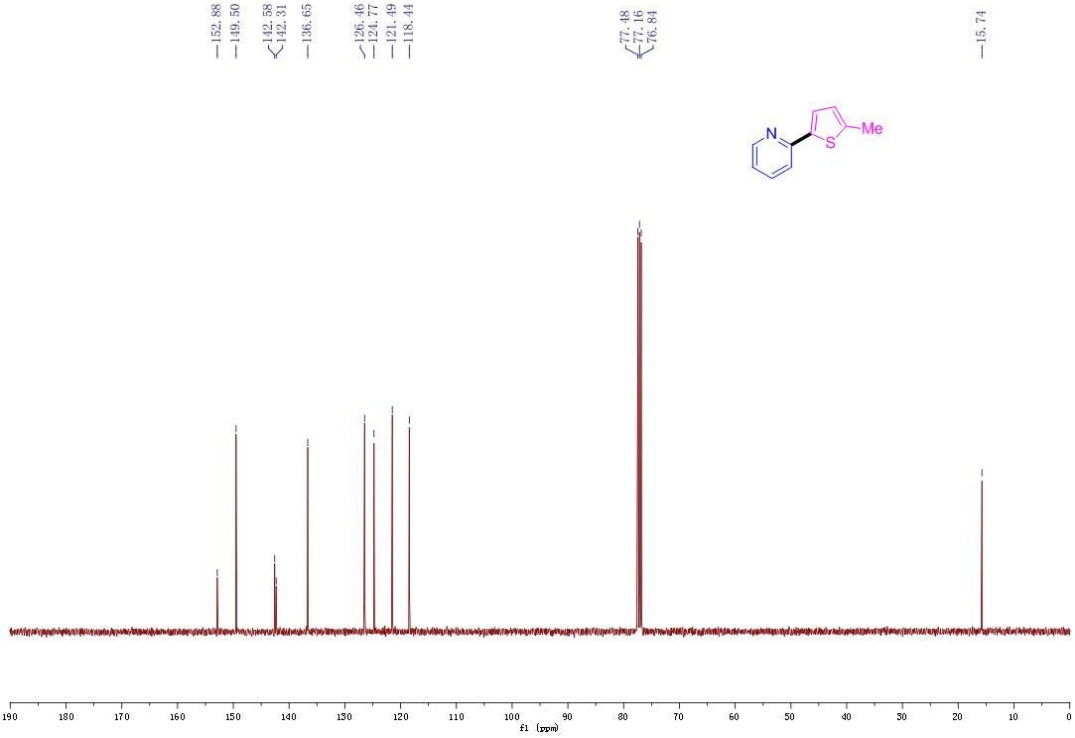
2. M. Chakrabarty, T. Kundu, S. Arima and Y. Harigaya, *Tetrahedron,* 2008, **64**, 6711.

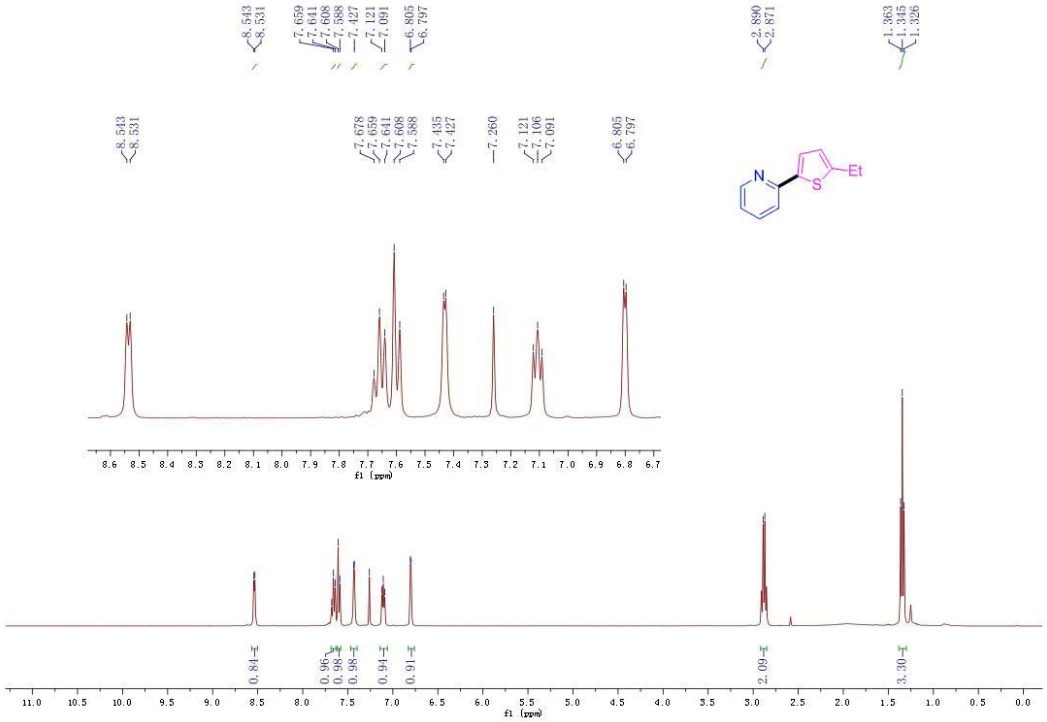
3. J. Verbeek and L. Brandsma, *J. Org. Chem.* 1984, **49**, 3857.

4. O. René and K. Fagnou, *Adv. Synth. Catal.* 2010, **352**, 2116.

VIII. Copies of ^{1}H and ^{13}C NMR spectra



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7.641
7.608
7.588
7.427
7.121
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6.805
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2.871
1.363
1.345
1.326
7.678
7.659
7.641
7.608
7.588
7.435
7.427
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7.121
7.106
7.091
6.805
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Et
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0.98
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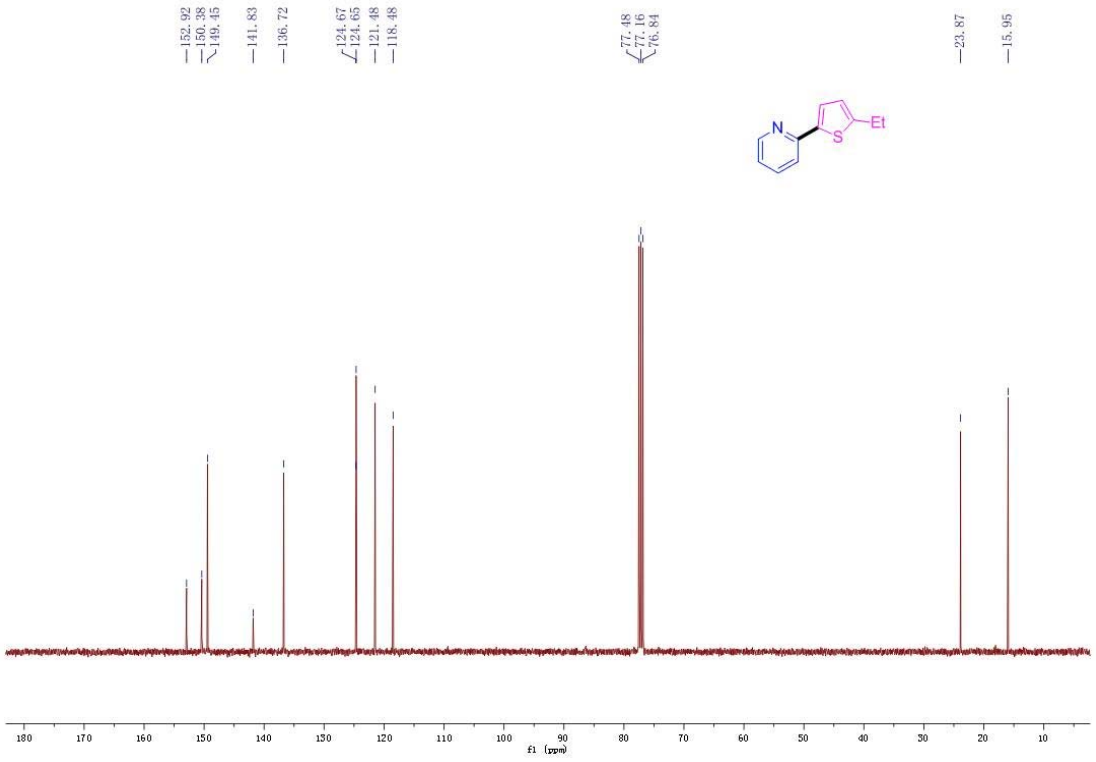
3.30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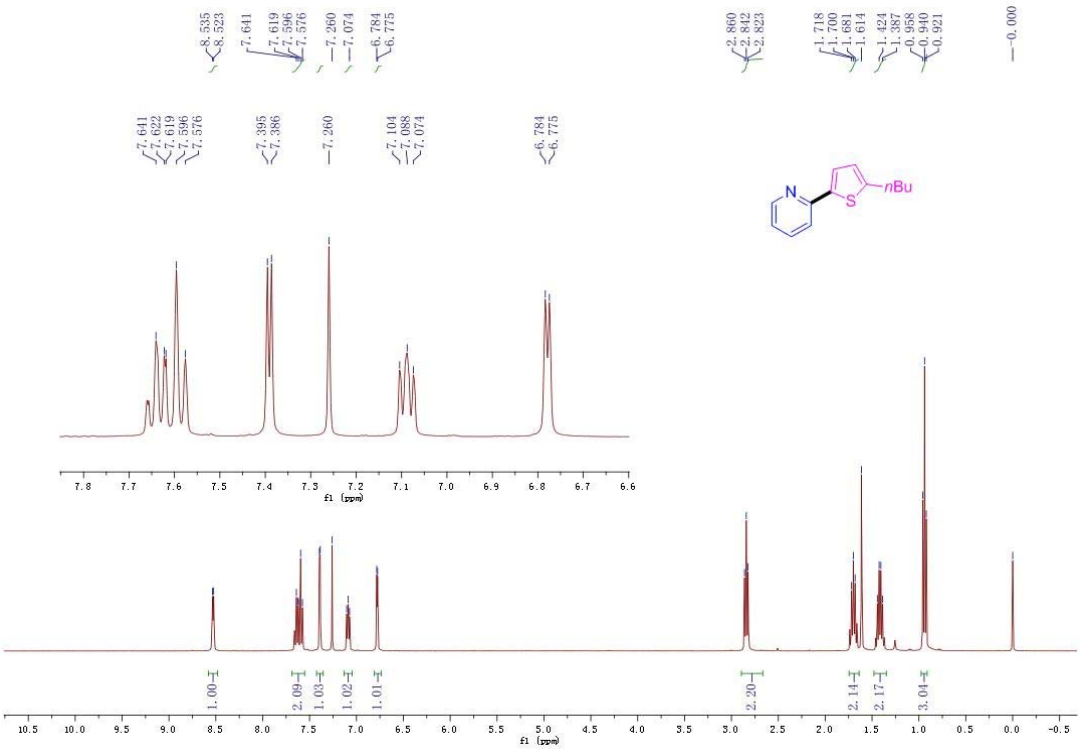
23.87
15.95
N
S
Et
f1 (ppm)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2.823
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1.700
1.681
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0.940
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nBu
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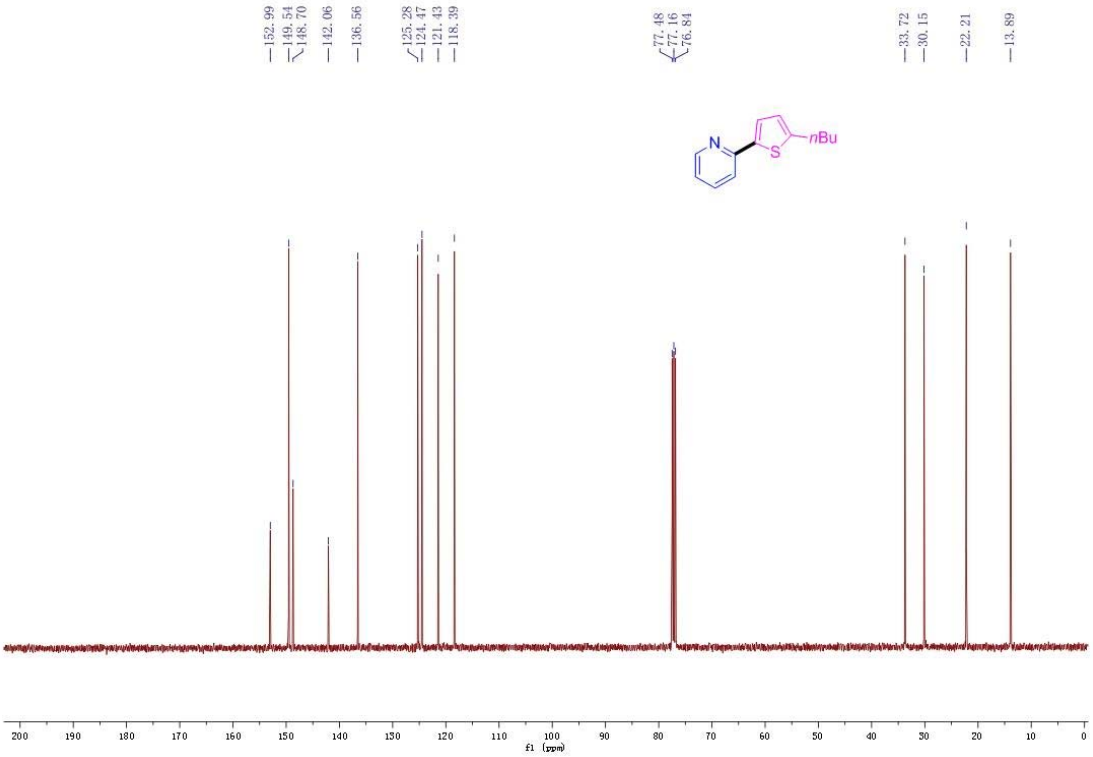
2.17
3.04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30.15
22.21
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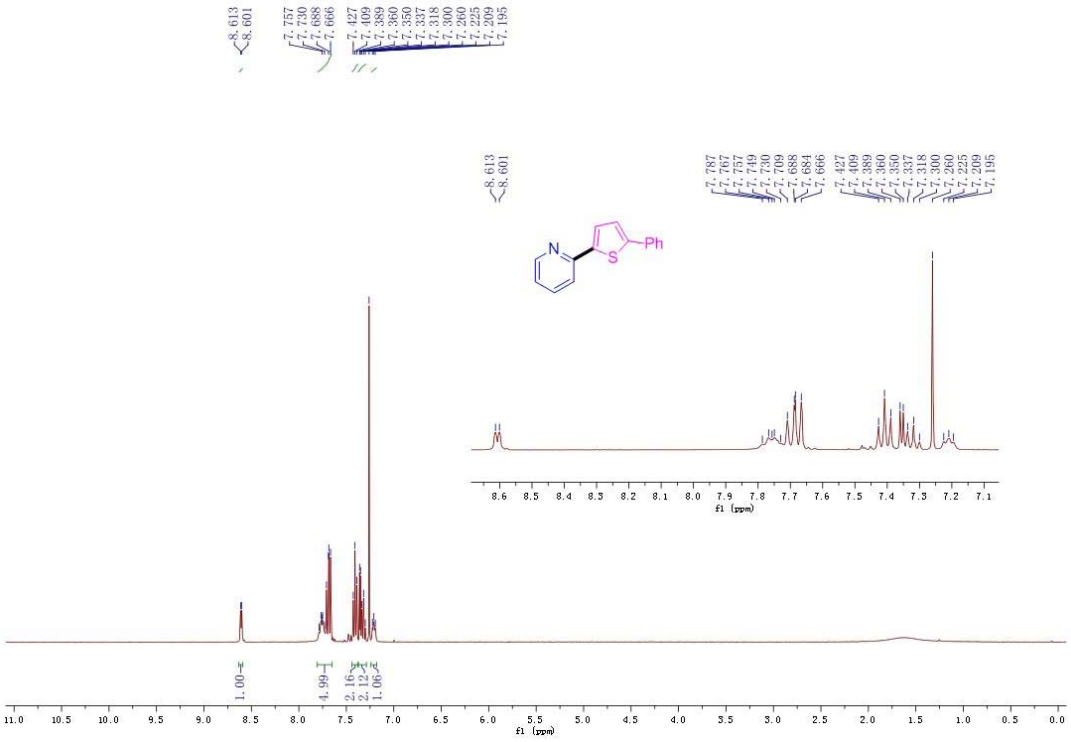
nBu
f1 (ppm)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7.300
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S
Ph
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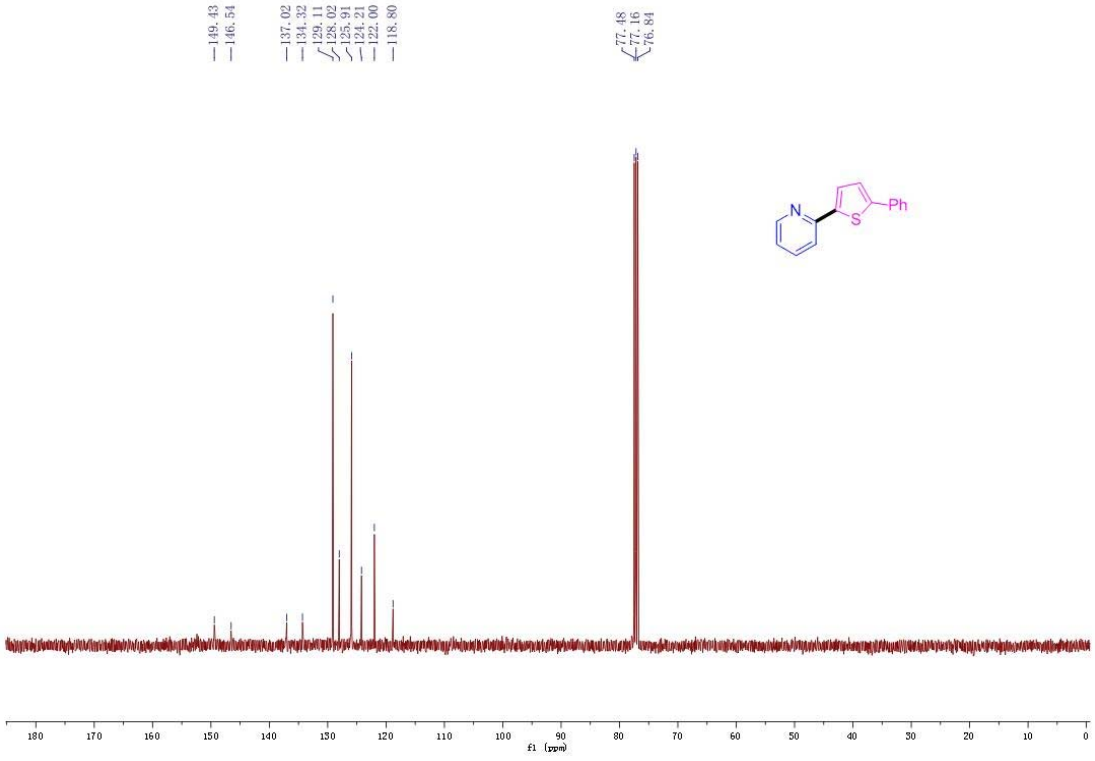
1.06
f1 (ppm)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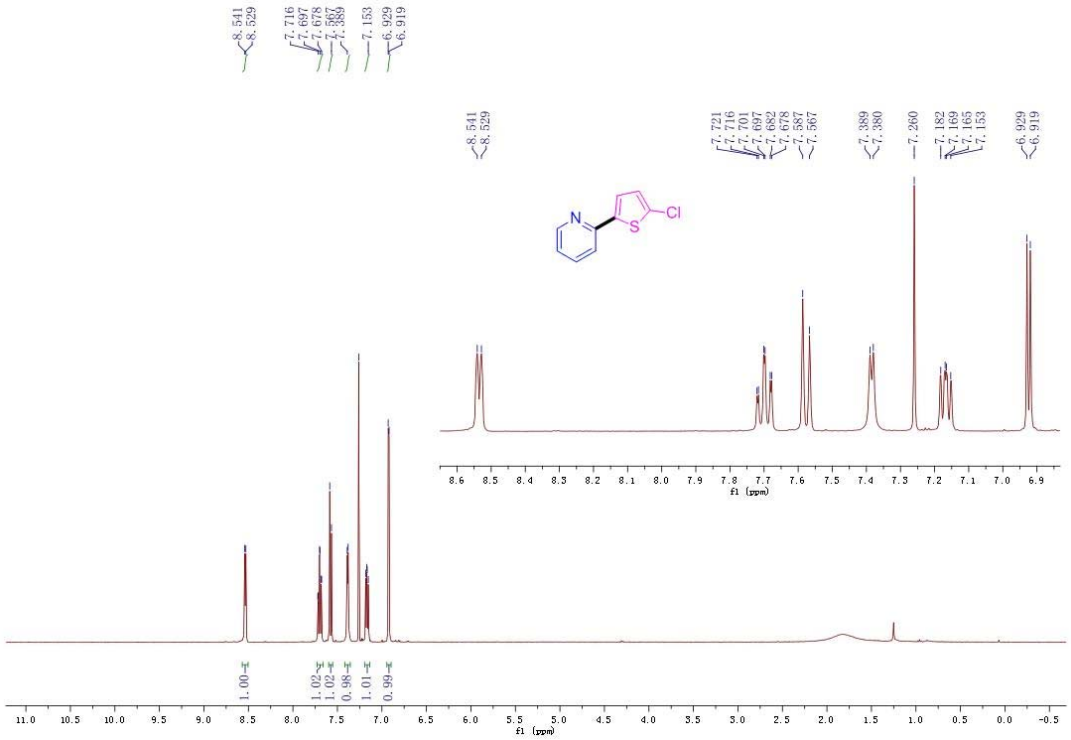
N
S
Ph
f1 (ppm)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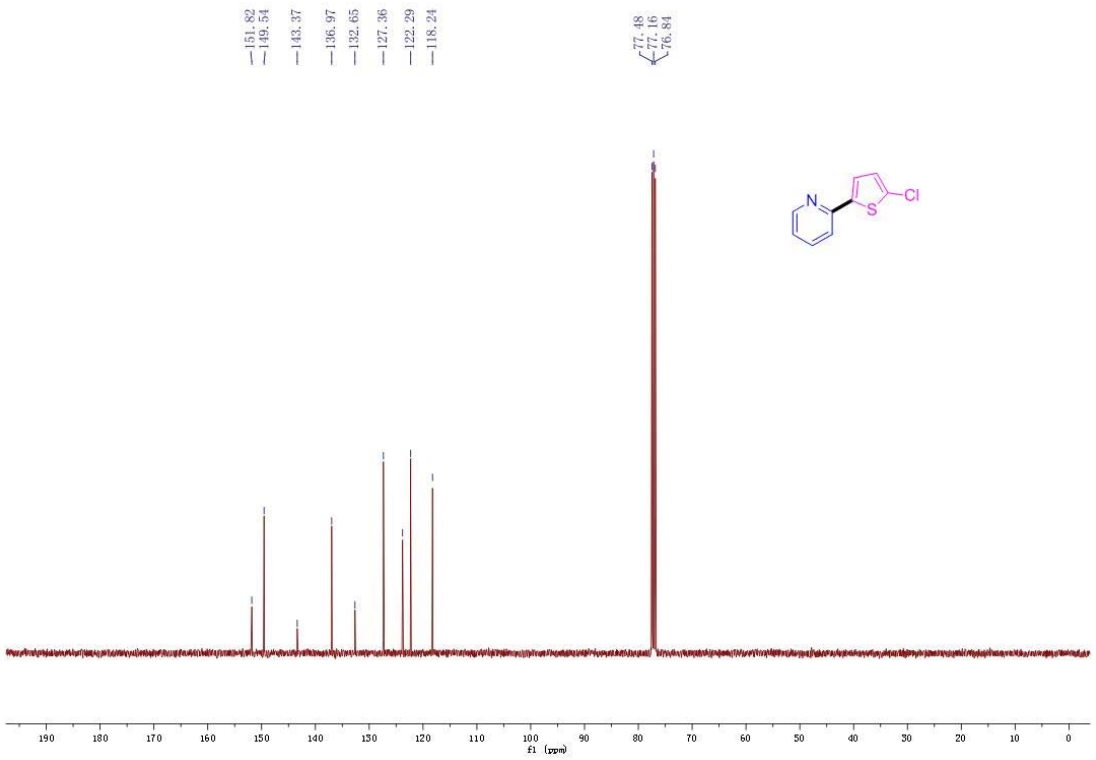
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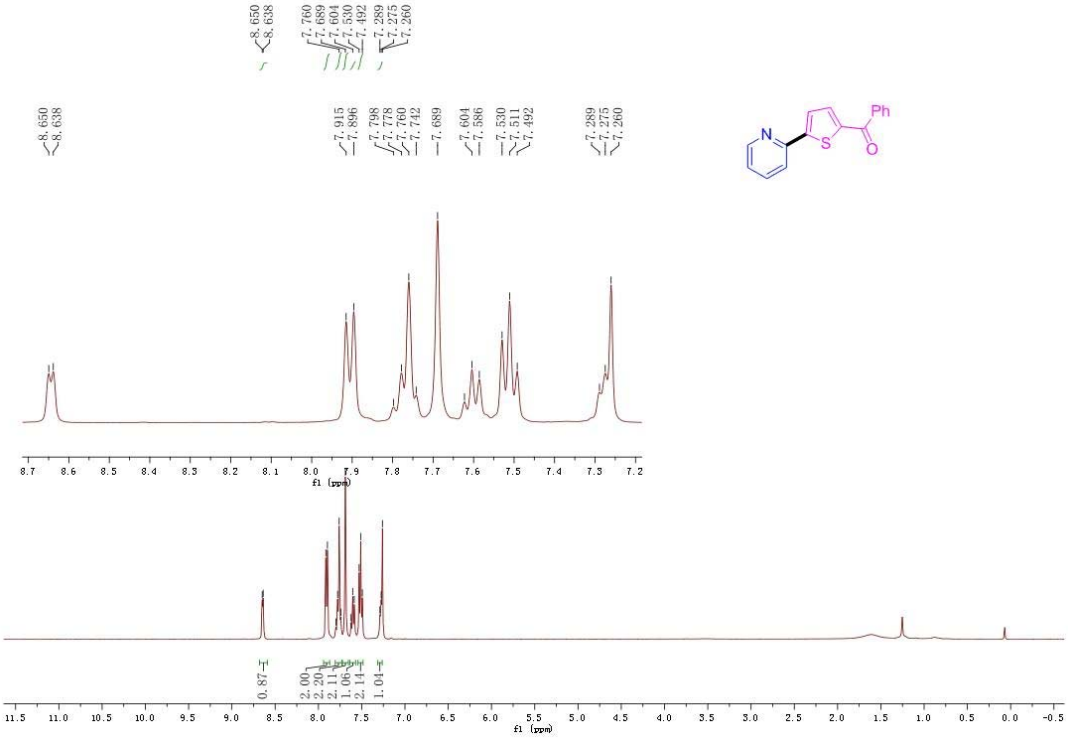
f1 (ppm)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7.289
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S
O
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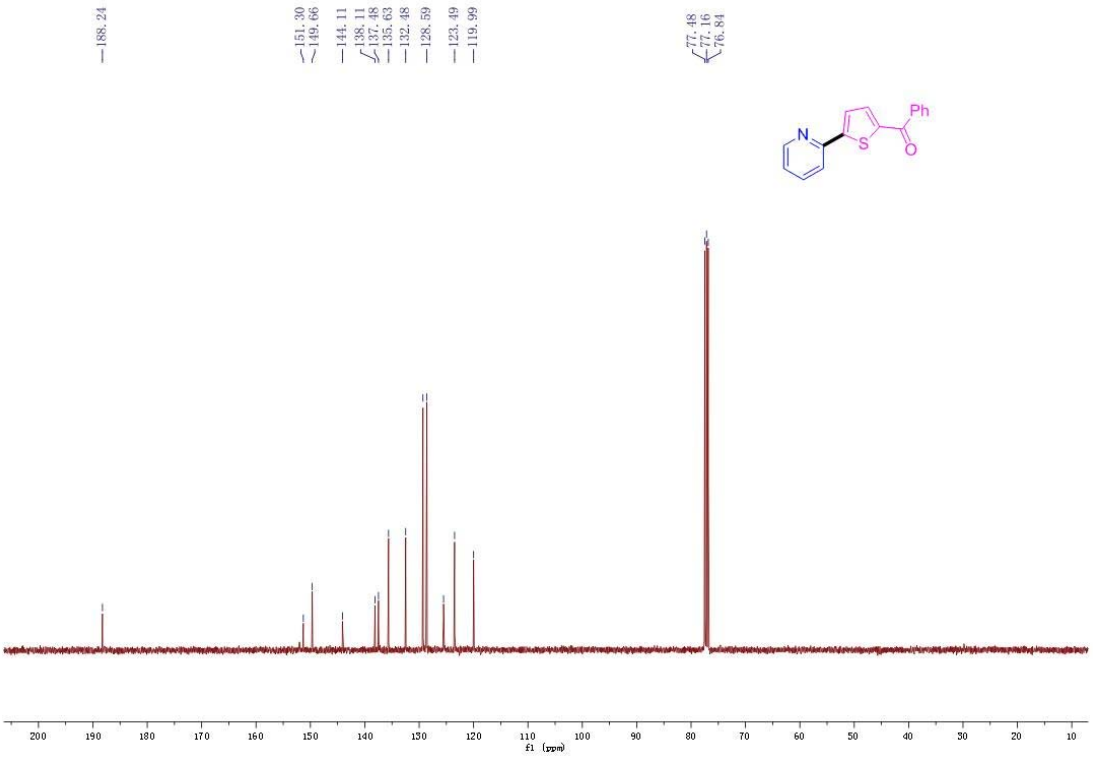
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Ph
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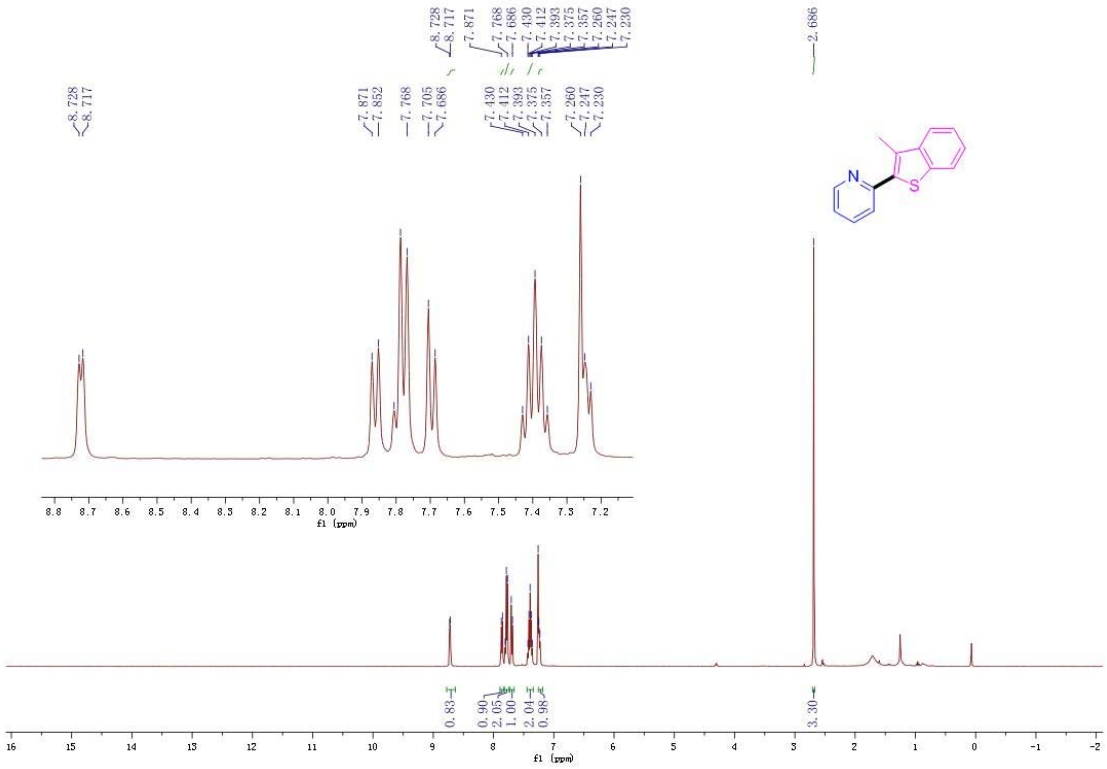
S
O
f1 (ppm)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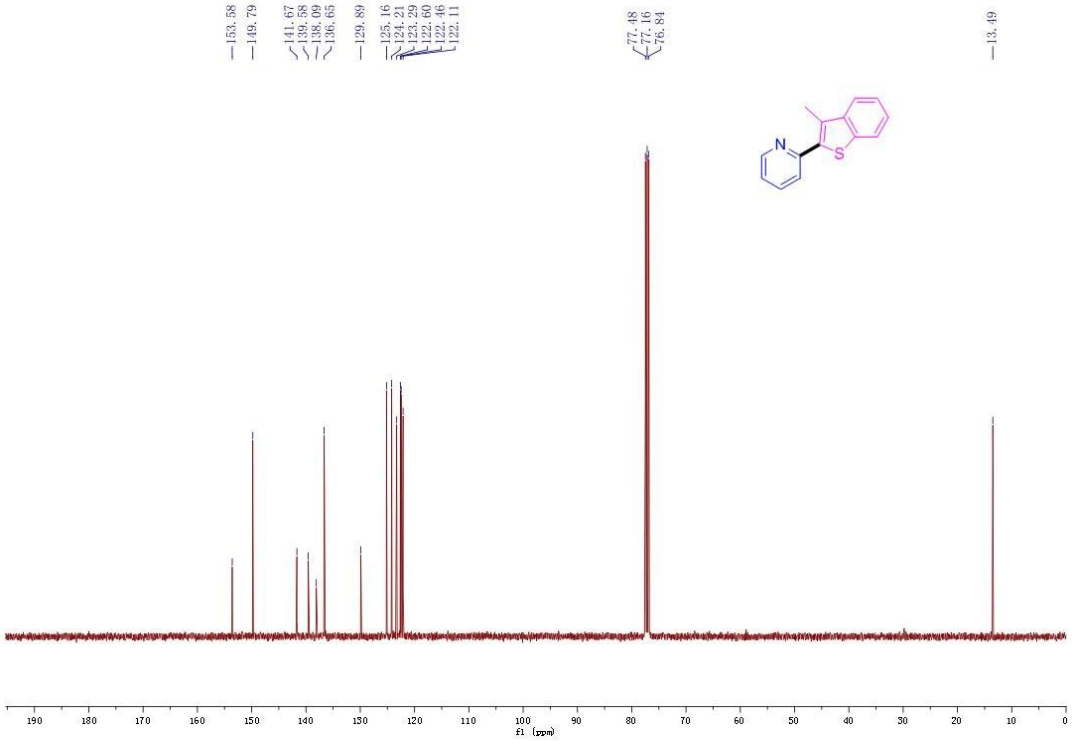
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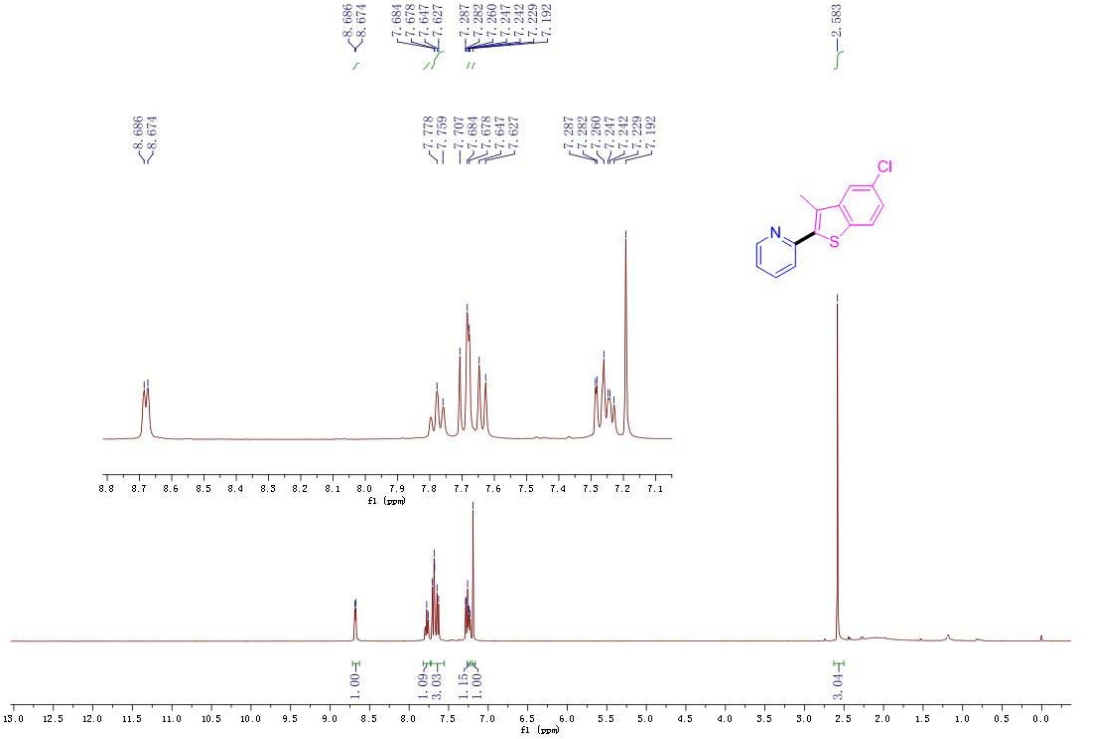
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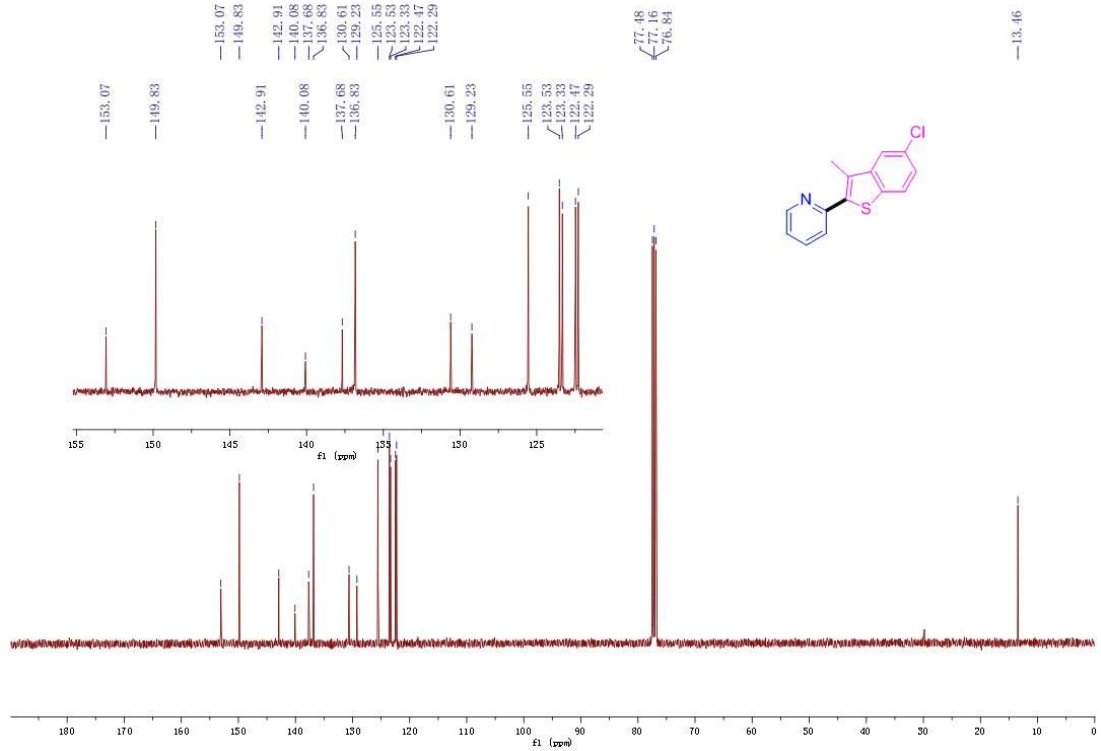
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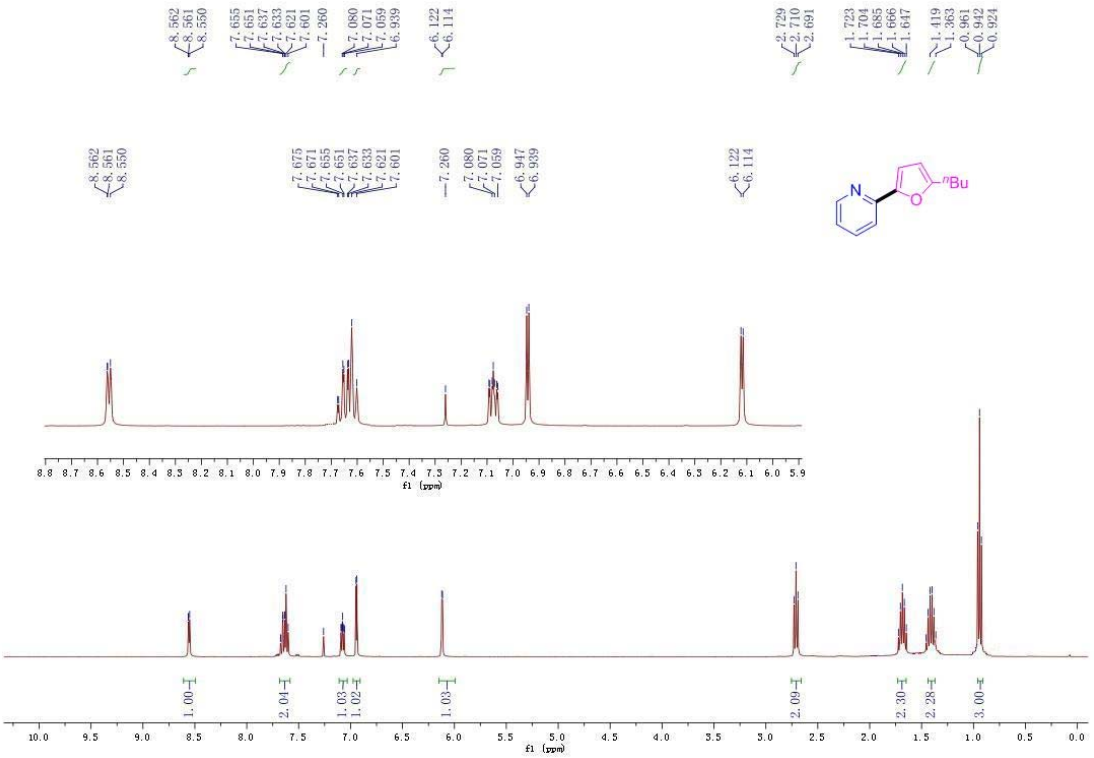
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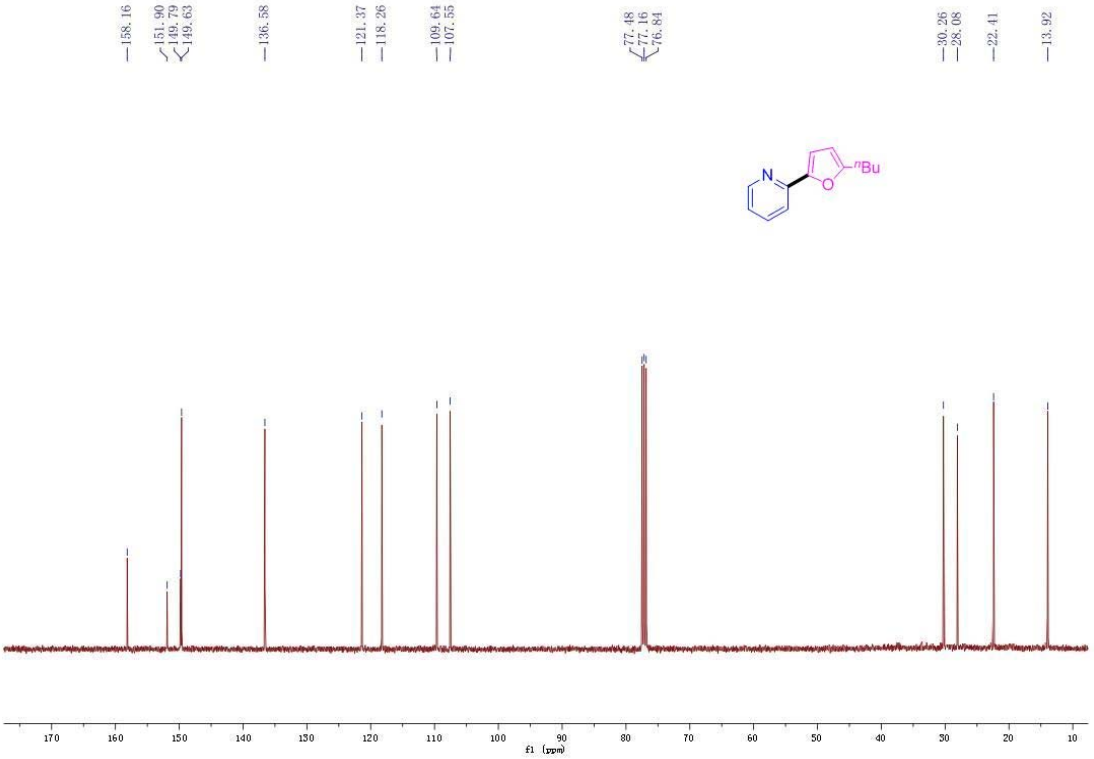
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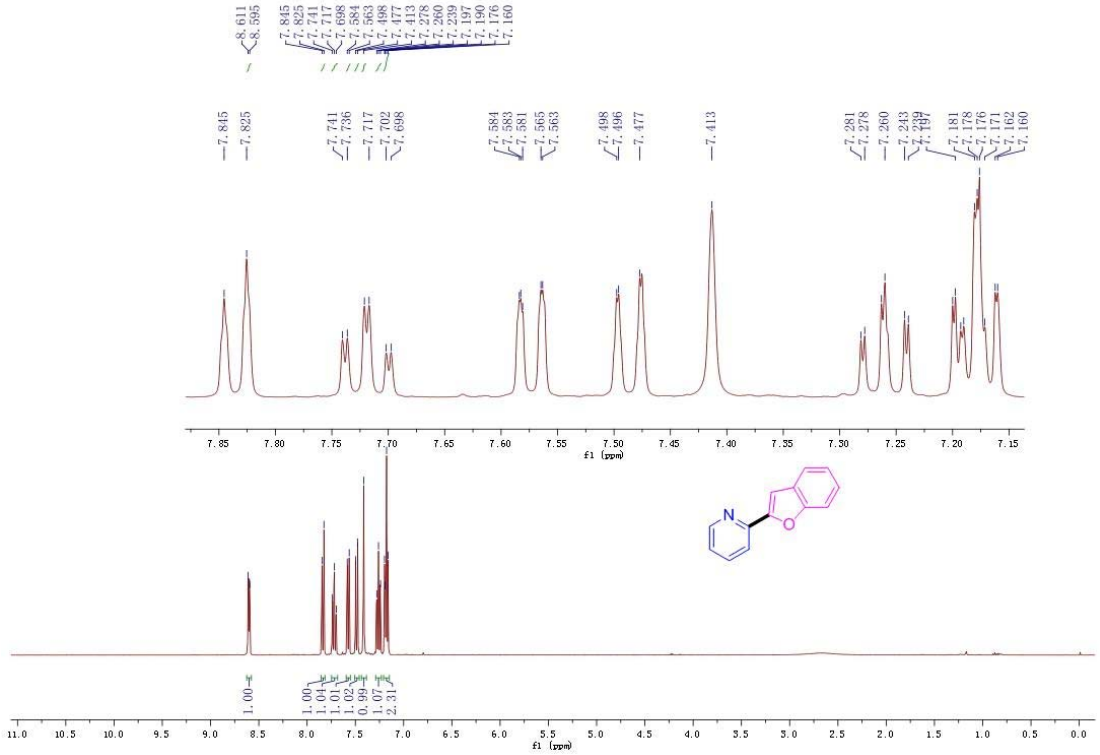
f1 (ppm)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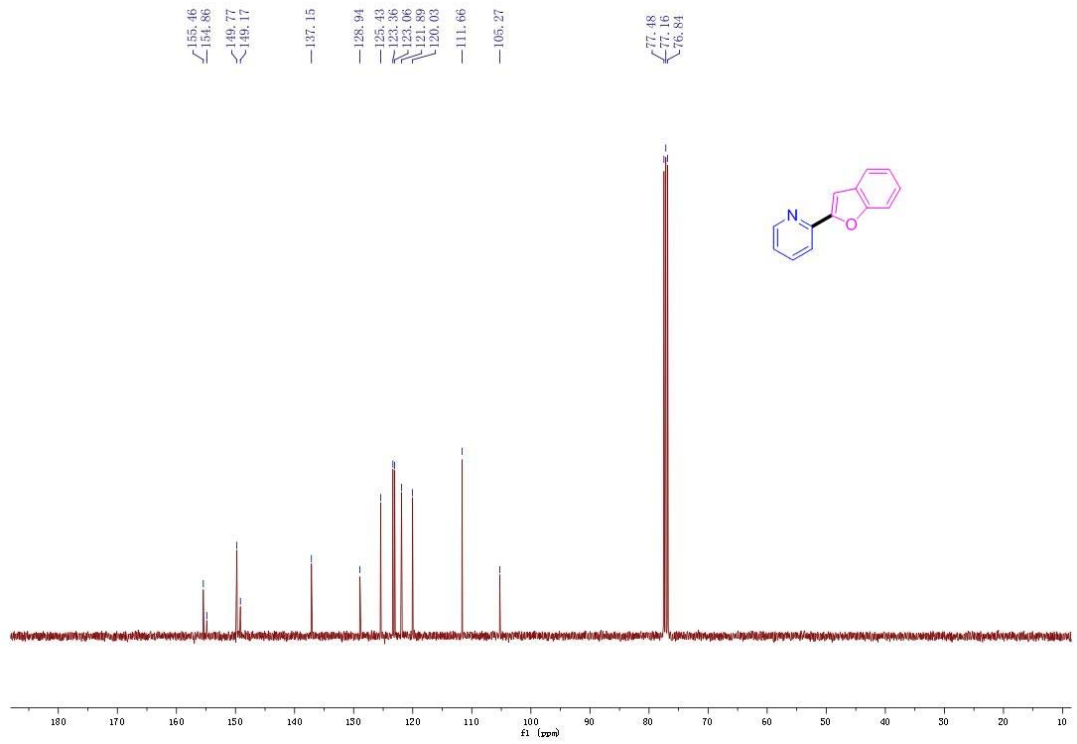
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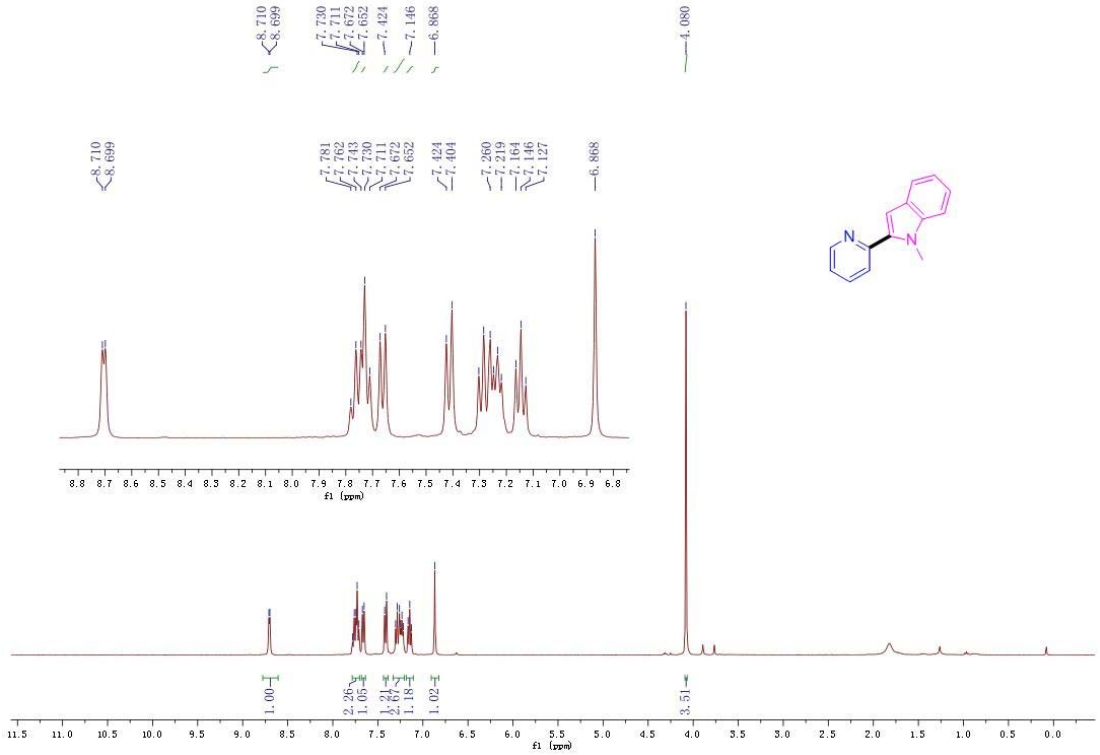
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7.730
7.711
7.672
7.652
7.424
7.146
6.868
4.080
7.781
7.762
7.743
7.730
7.711
7.672
7.652
7.424
7.404
7.260
7.219
7.164
7.146
7.127
f1 (ppm)
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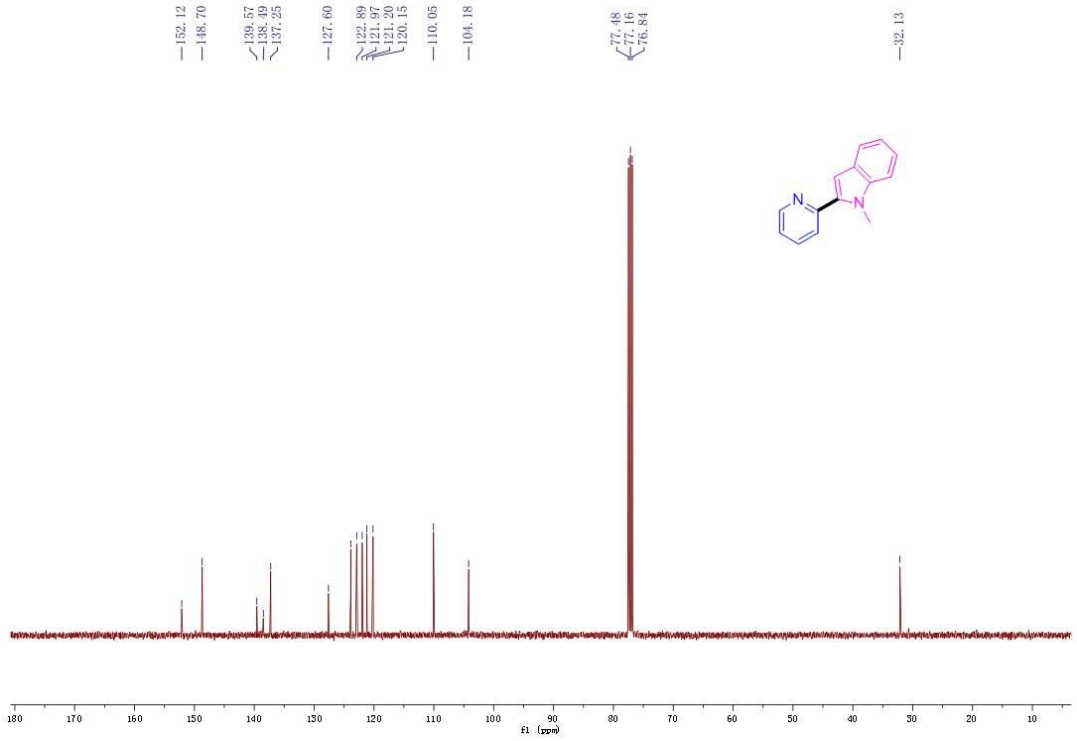
2.26
1.05
1.21
2.67
1.18
1.02
3.51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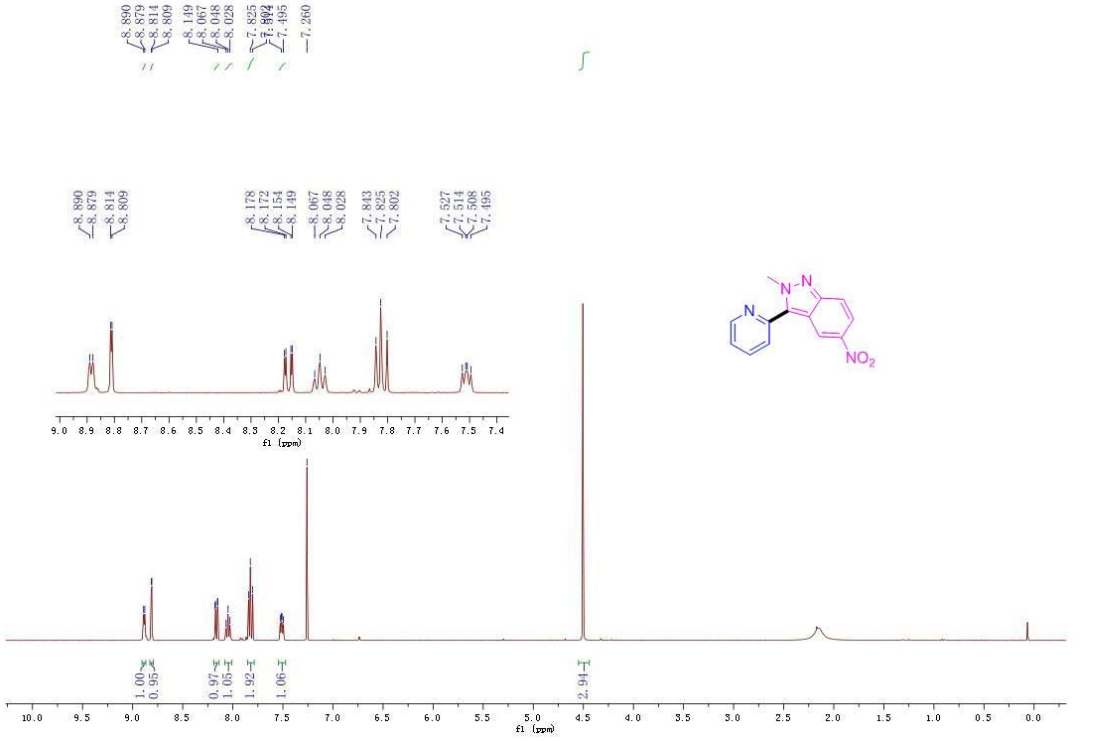
148.70
139.57
138.49
137.25
127.60
122.89
121.97
121.20
120.15
110.05
104.18
77.48
77.16
76.84
32.13
f1 (ppm)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8.814
8.809
8.178
8.172
8.154
8.149
8.067
8.048
8.028
7.843
7.825
7.802
7.527
7.514
7.508
7.495
7.260
NO2
f1 (ppm)
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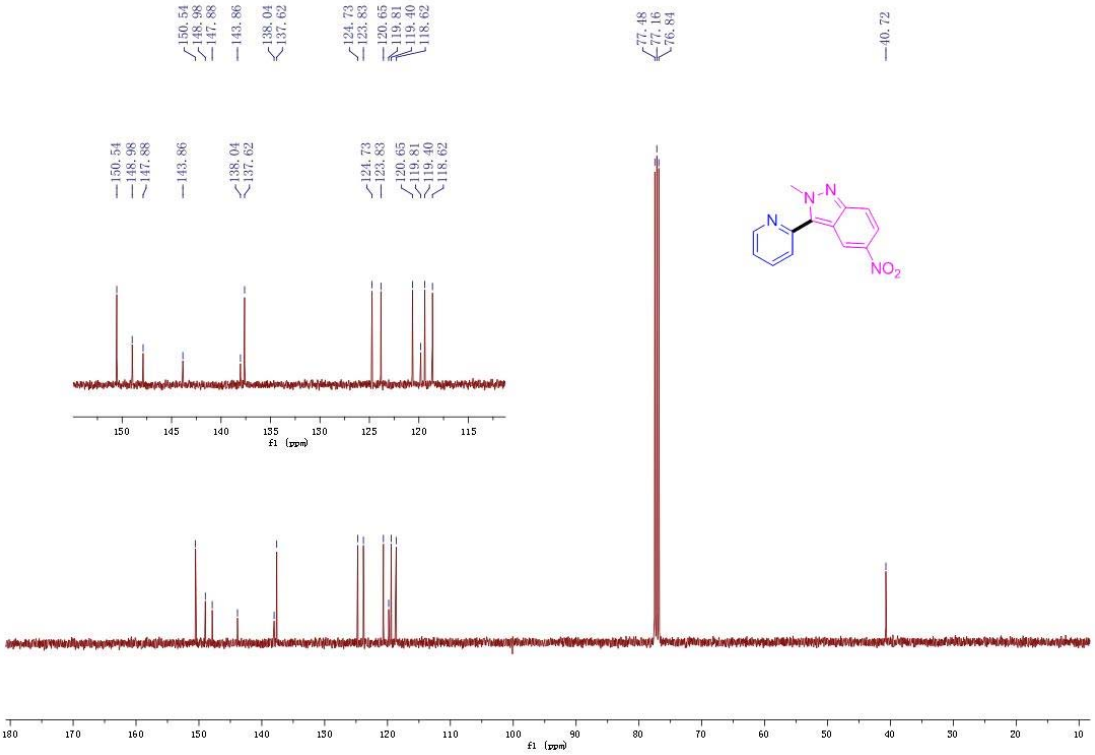
0.95
0.97
1.05
1.92
1.06
2.94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138.04
137.62
124.73
123.83
120.65
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119.40
118.62
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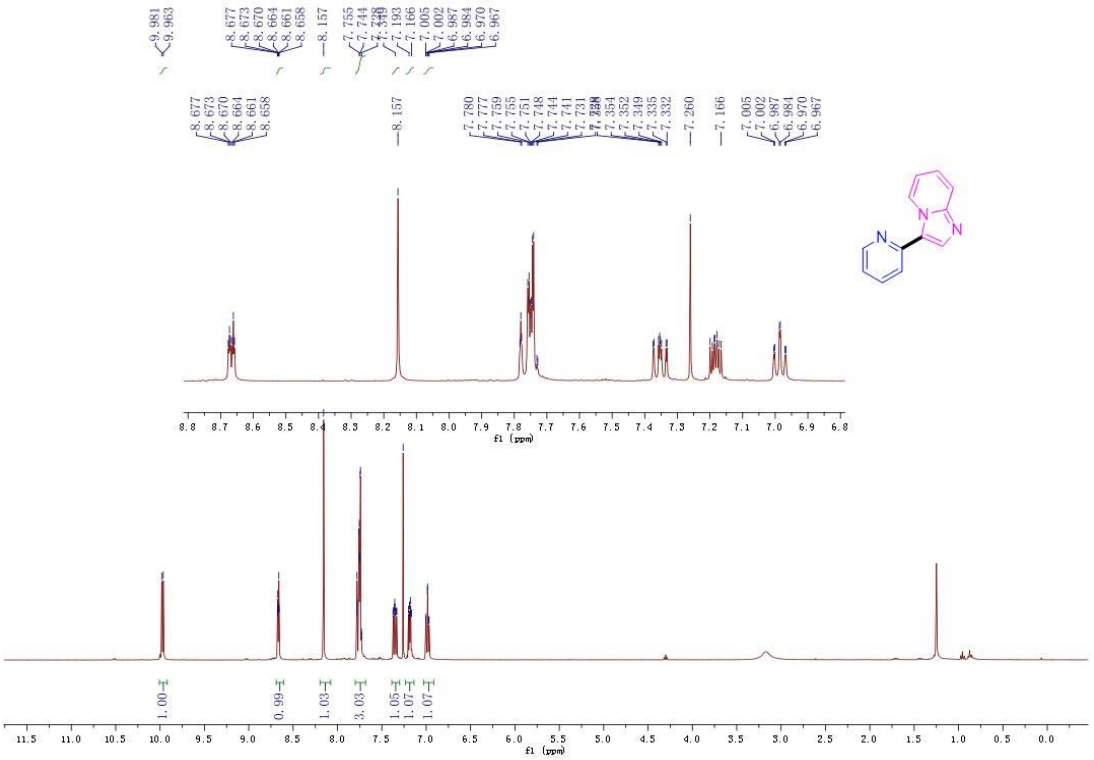
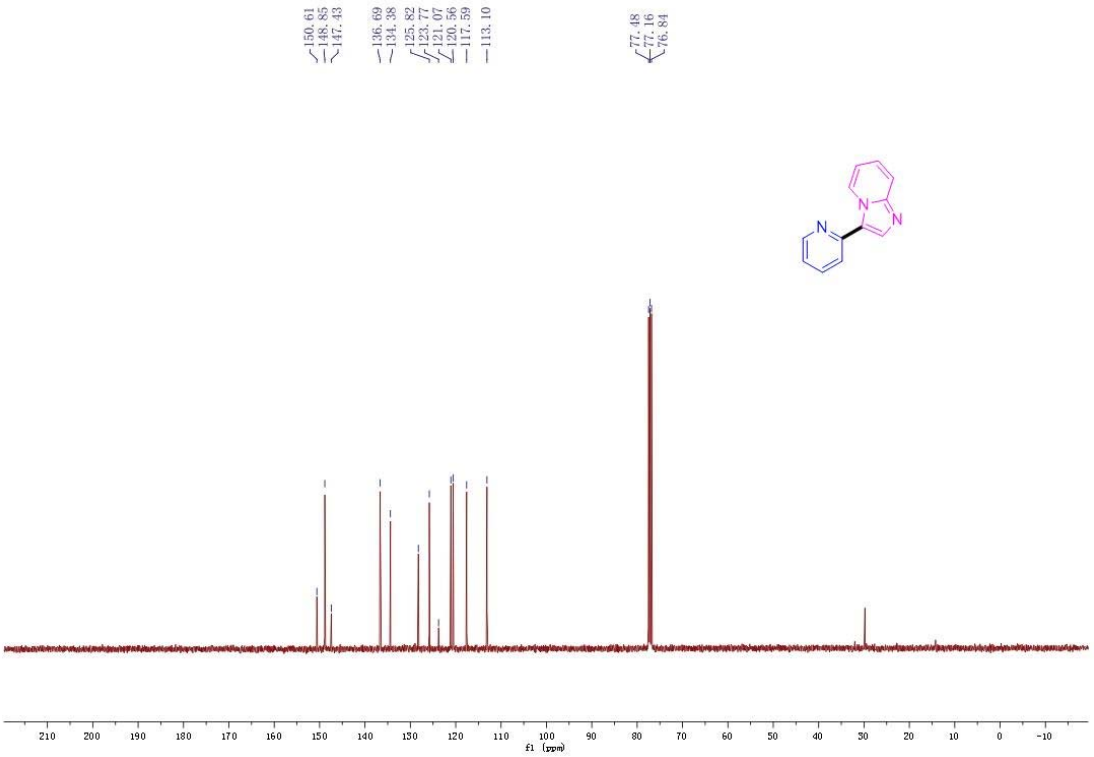
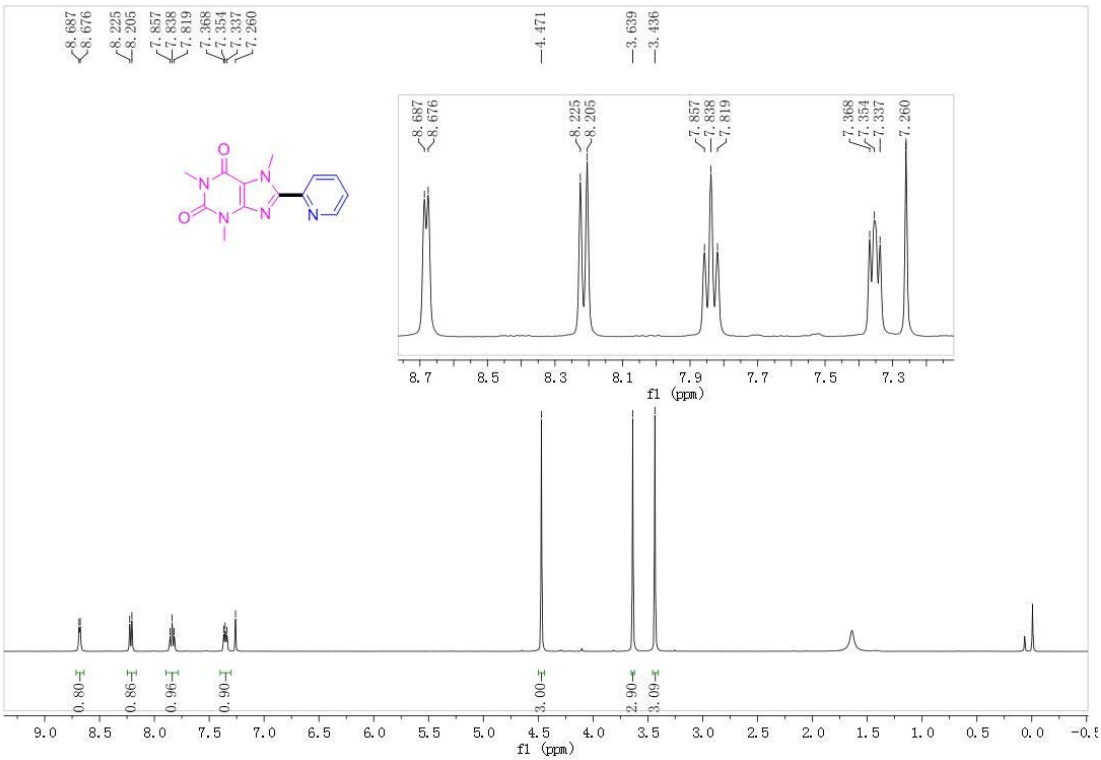
77.16
76.84
40.72
NO2
f1 (ppm)



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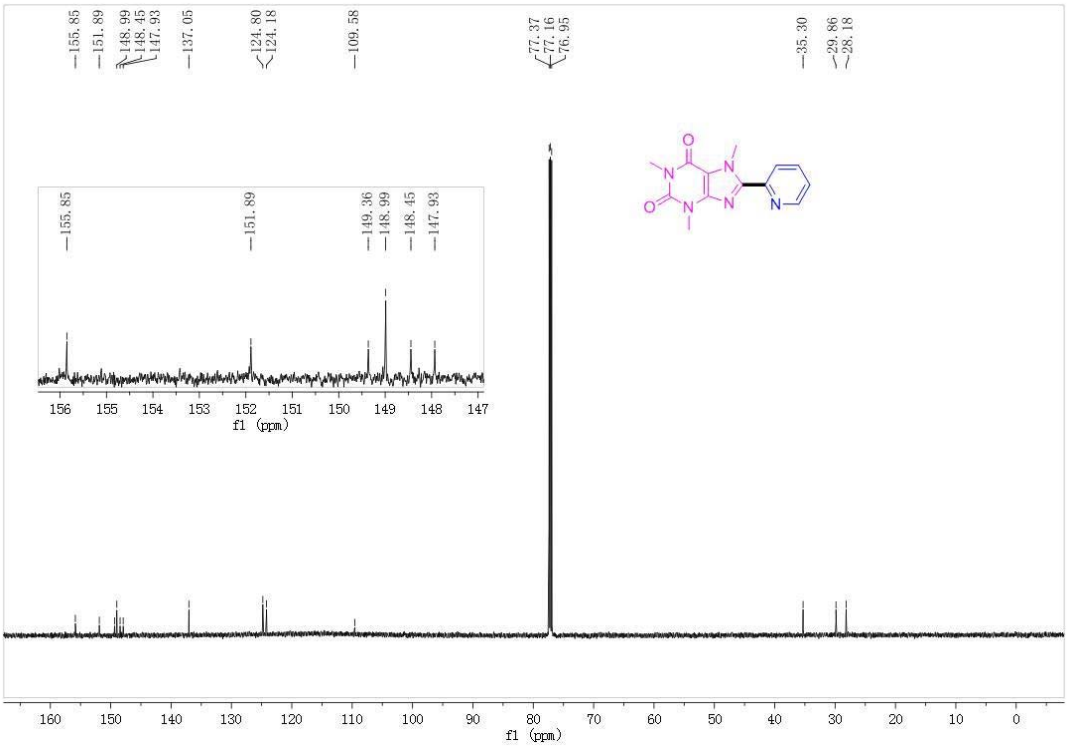
8.676
8.225
8.205
7.857
7.838
7.819
7.368
7.354
7.337
7.260
4.471
3.639
3.436
0.80
0.86
0.96
0.90
3.00
2.90
3.09
f1 (ppm)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147.93
137.05
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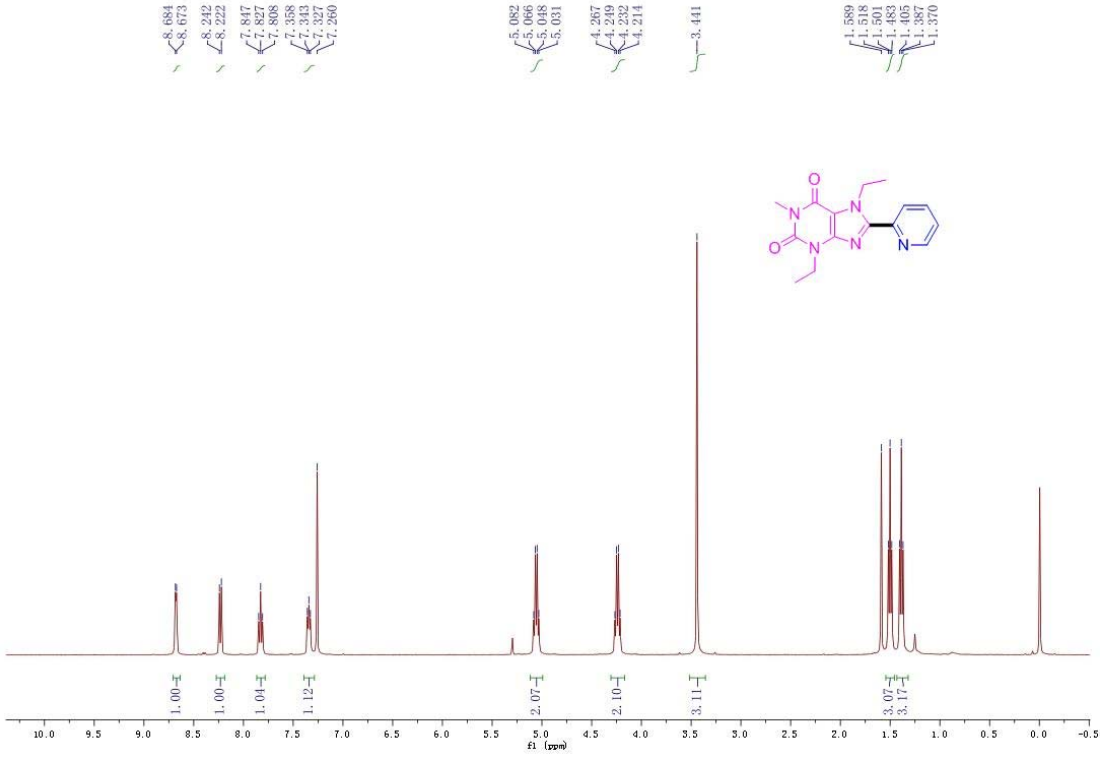
124.18
109.58
77.37
77.16
76.95
35.30
29.86
28.18
f1 (ppm)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8.673
8.242
8.222
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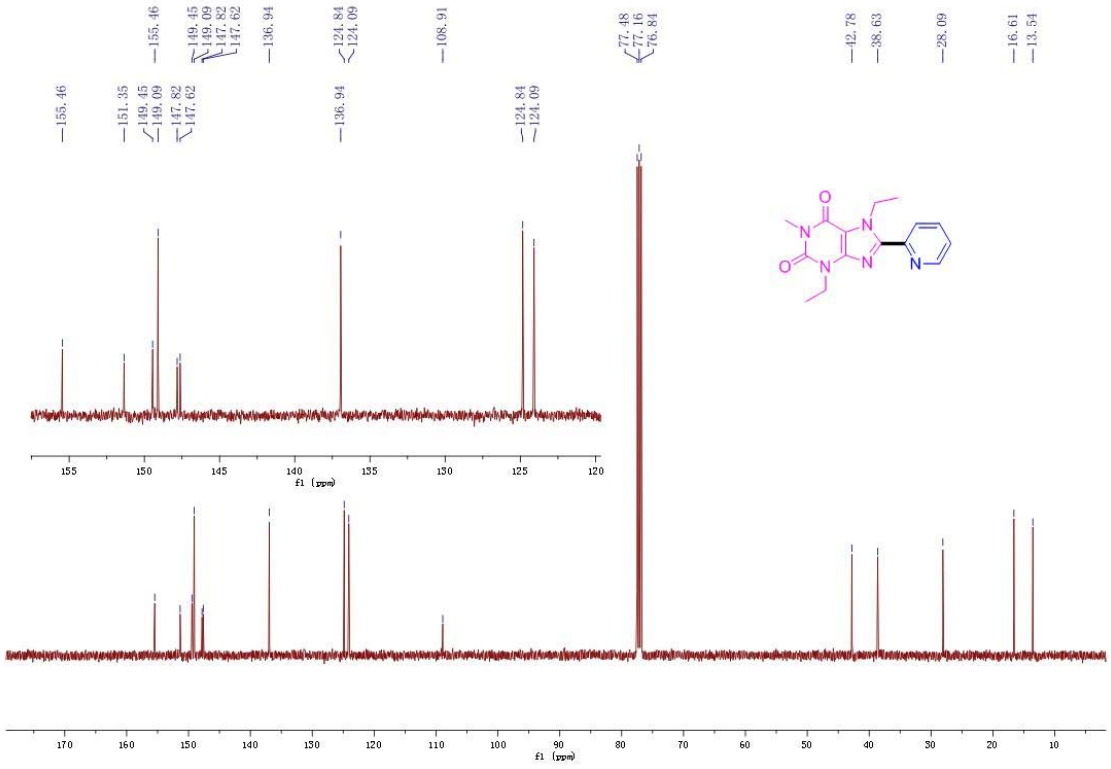
7.827
7.808
7.358
7.343
7.327
7.260
5.082
5.066
5.048
5.031
4.267
4.249
4.232
4.214
3.441
1.589
1.518
1.501
1.483
1.465
1.387
1.370
1.00
1.00
1.04
1.12
2.07
2.10
3.11
3.07
3.17
f1 (ppm)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151.35
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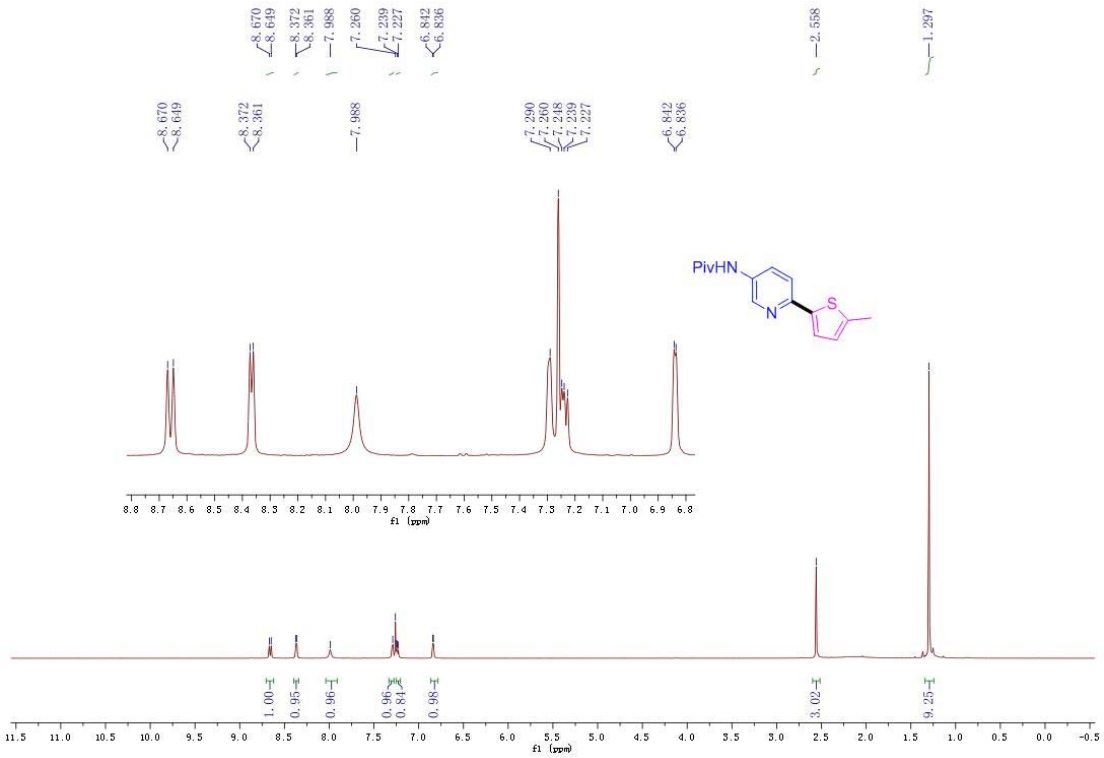
147.82
147.62
136.94
124.84
124.09
108.91
77.48
77.16
76.84
42.78
38.63
28.09
16.61
13.54
f1 (ppm)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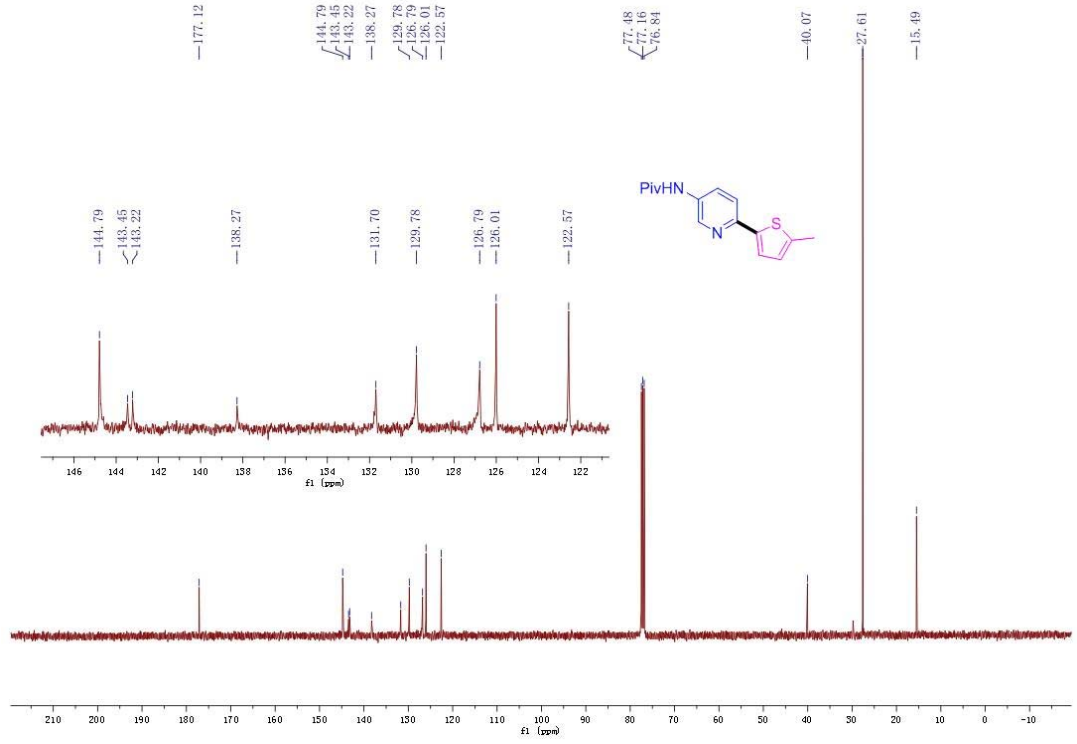
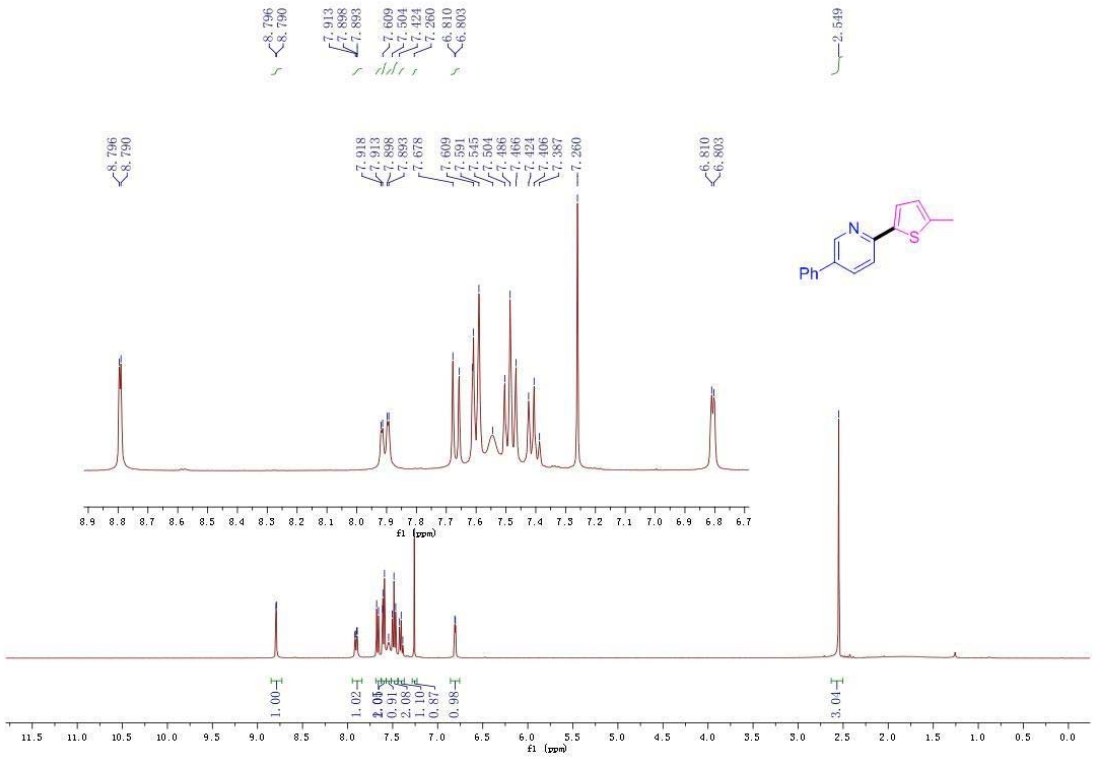
8.649
8.372
8.361
7.988
7.260
7.239
7.227
6.842
6.836
2.558
1.297
PivHN
N
S
f1 (ppm)
1.00
0.95
0.96
0.96
0.84
0.98
3.02
9.25


177.12
144.79
143.45
143.22
138.27
129.78
126.79
126.01
122.57
77.48
77.16
76.84
40.07
27.61
15.49
PivHN
N
S
131.70
f1 (ppm)


8.796
8.790
7.913
7.898
7.893
7.609
7.504
7.424
7.260
6.810
6.803
2.549
7.918
7.591
7.545
7.486
7.466
7.406
7.387
7.678
7.260
N
S
Ph
f1 (ppm)
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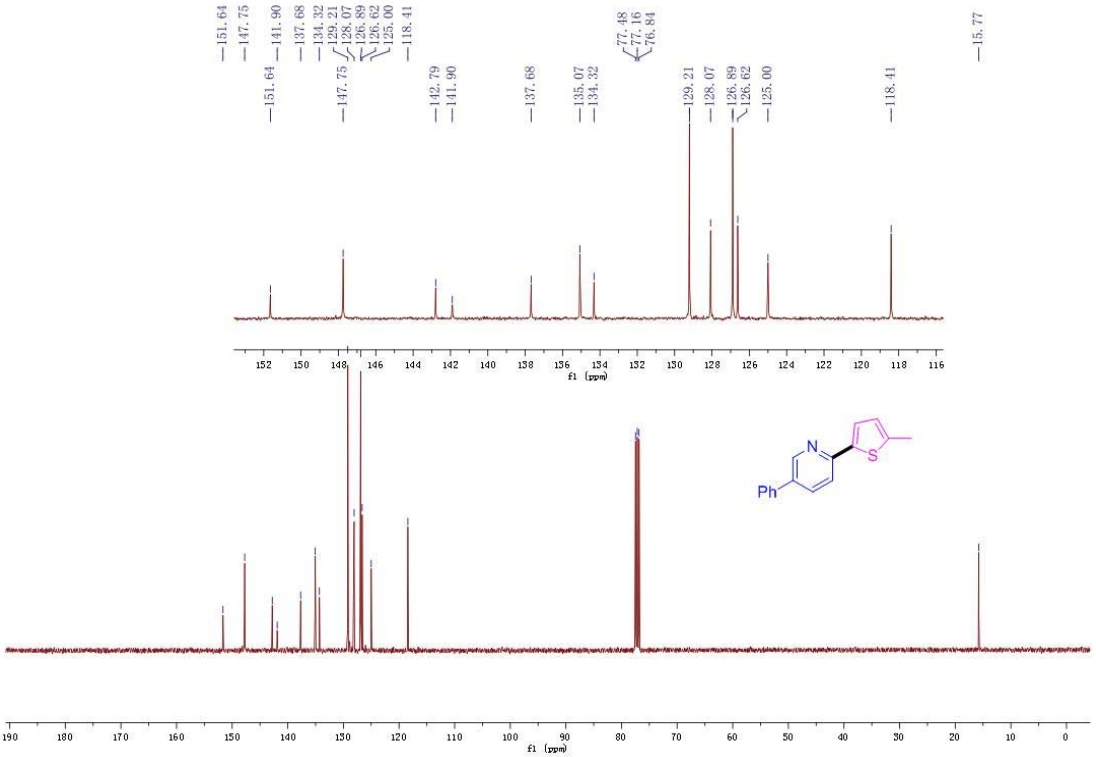
1.02
0.91
2.08
1.10
0.87
0.98
3.04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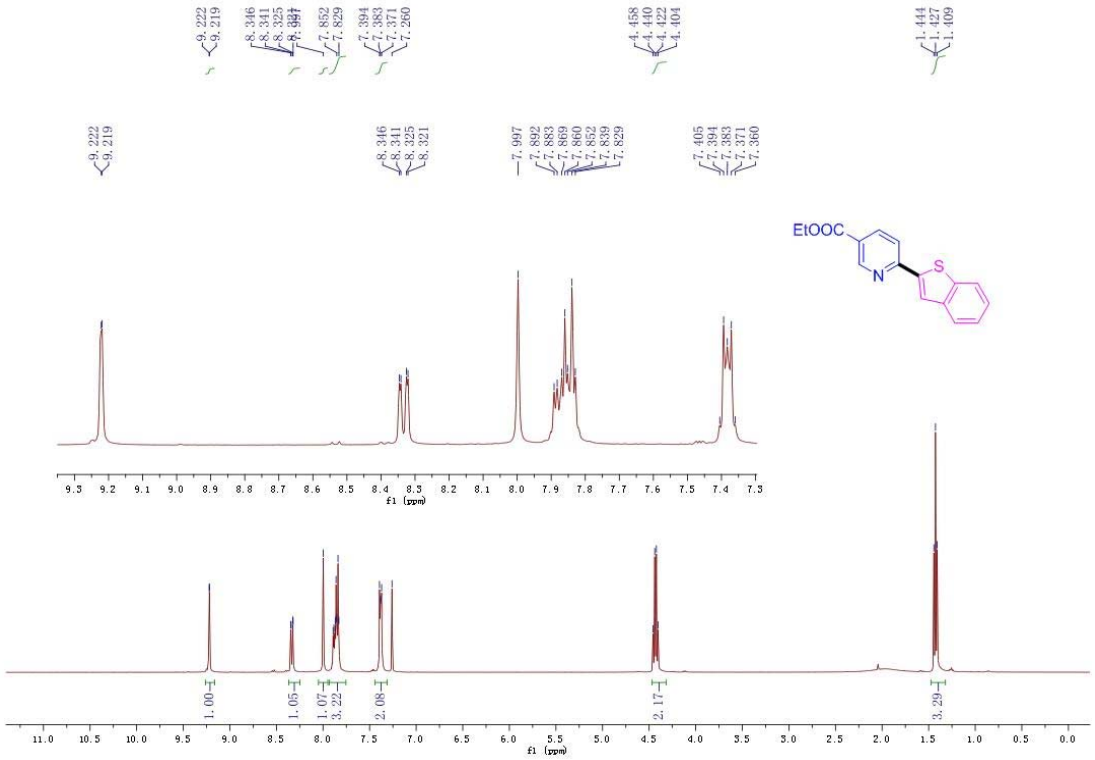
147.75
141.90
137.68
134.32
129.21
128.07
126.89
126.62
125.00
118.41
77.48
77.16
76.84
15.77
142.79
135.07
N
S
Ph
f1 (ppm)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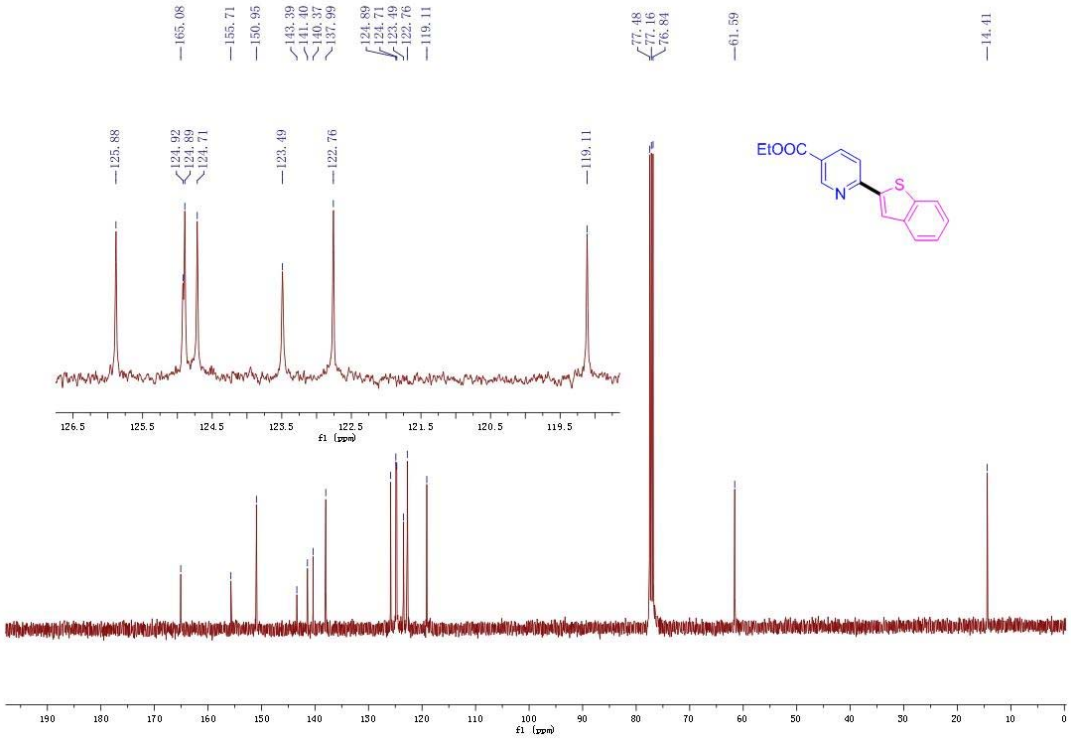
9.219
8.346
8.341
8.325
8.321
7.997
7.892
7.883
7.869
7.860
7.852
7.839
7.829
7.405
7.394
7.383
7.371
7.360
4.458
4.440
4.422
4.404
1.444
1.427
1.409
EtOOC
N
S
1.00
1.05
1.07
3.22
2.08
2.17
3.29
f1 (ppm)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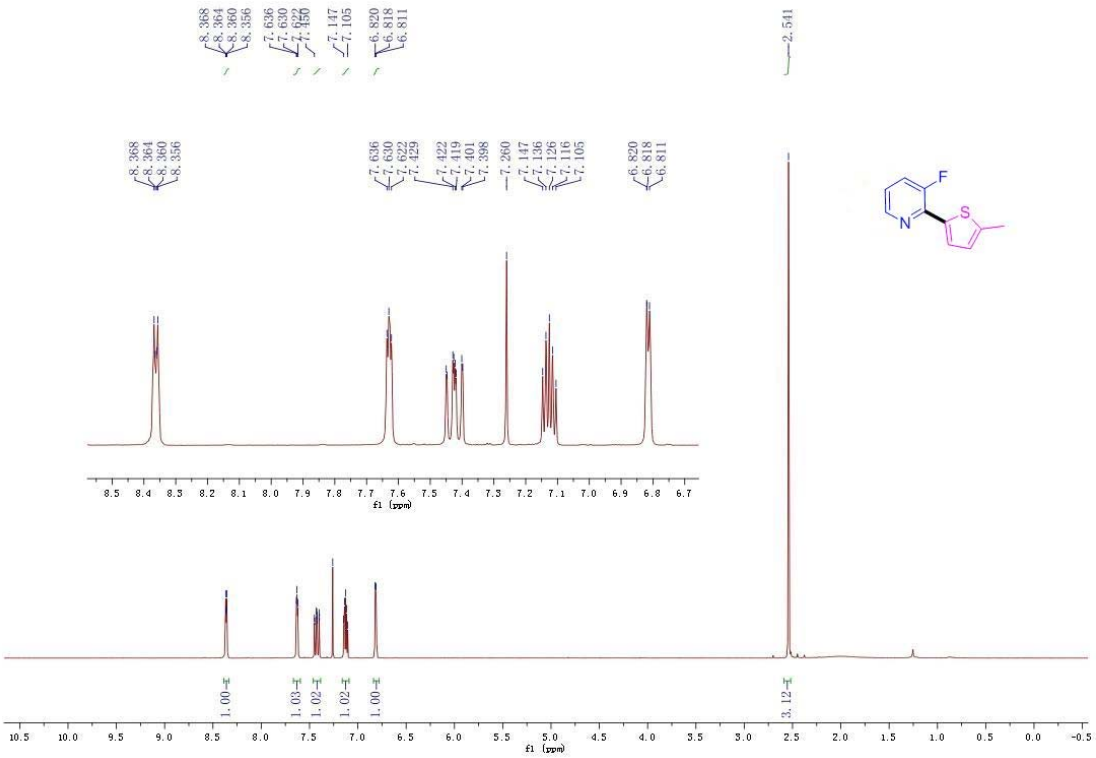
155.71
150.95
143.39
141.40
140.37
137.99
124.89
124.71
123.49
122.76
119.11
77.48
77.16
76.84
61.59
14.41
125.88
124.92
124.89
124.71
123.49
122.76
119.11
EtOOC
N
S
f1 (ppm)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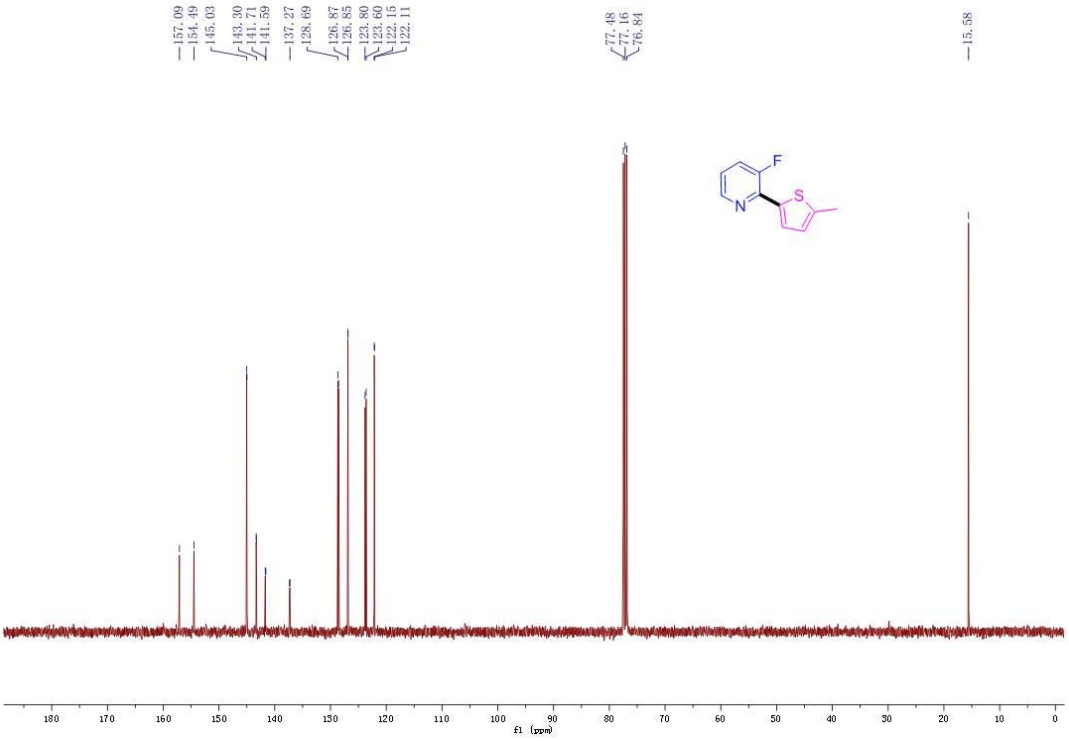
8.360
8.356
7.636
7.630
7.622
7.450
7.429
7.422
7.419
7.401
7.398
7.260
7.147
7.136
7.126
7.116
7.105
6.820
6.818
6.811
2.541
1.00
1.03
1.02
1.02
1.00
3.12
f1 (ppm)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154.49
145.03
143.30
141.71
141.59
137.27
128.69
126.87
126.85
123.80
123.60
122.15
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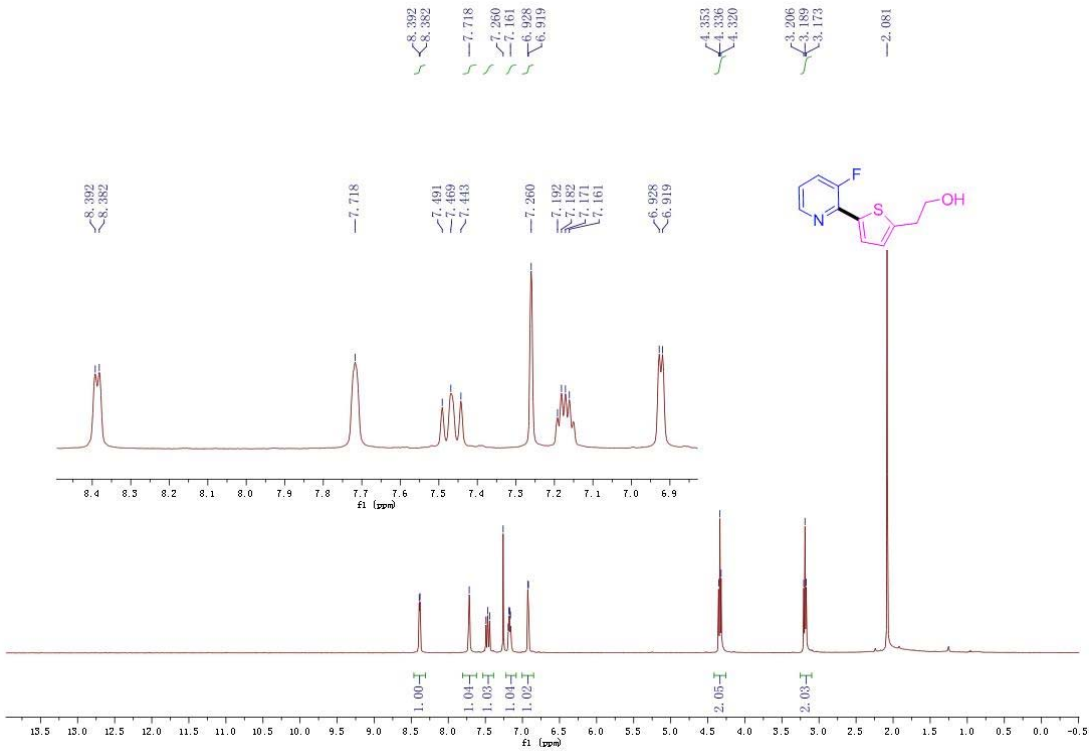
77.48
77.16
76.84
15.58
f1 (ppm)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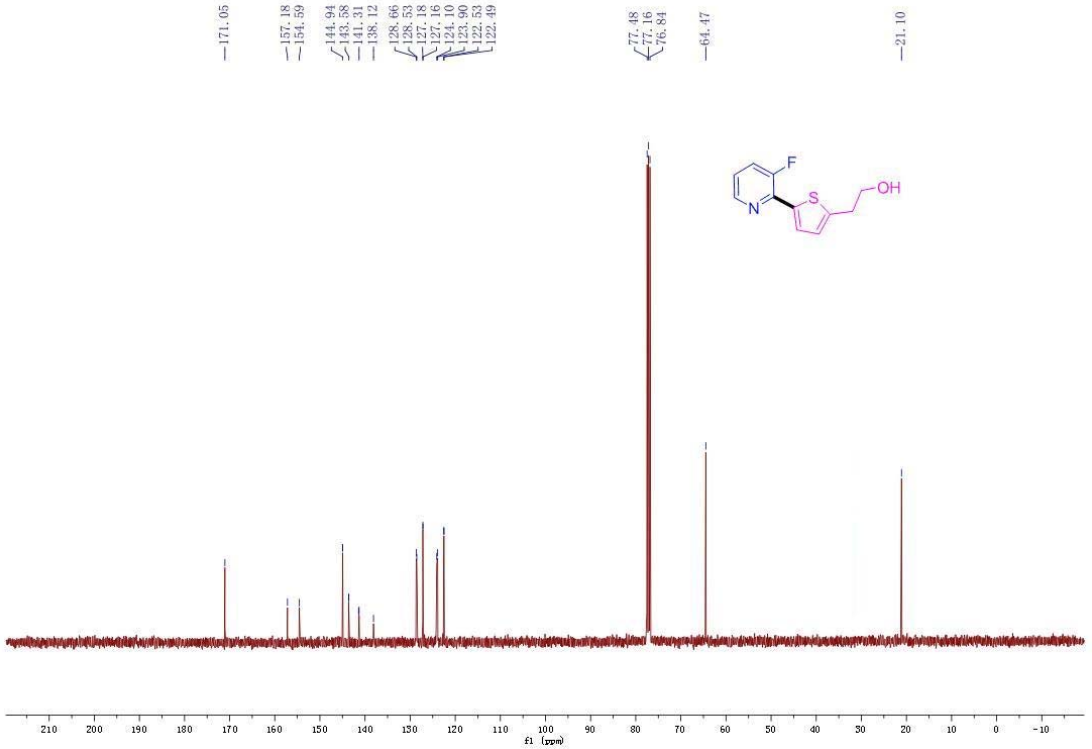
8.382
7.718
7.491
7.469
7.443
7.260
7.192
7.182
7.171
7.161
6.928
6.919
4.353
4.336
4.320
3.206
3.189
3.173
2.081
F
N
S
OH
1.00
1.04
1.03
1.04
1.02
2.05
2.03
f1 (ppm)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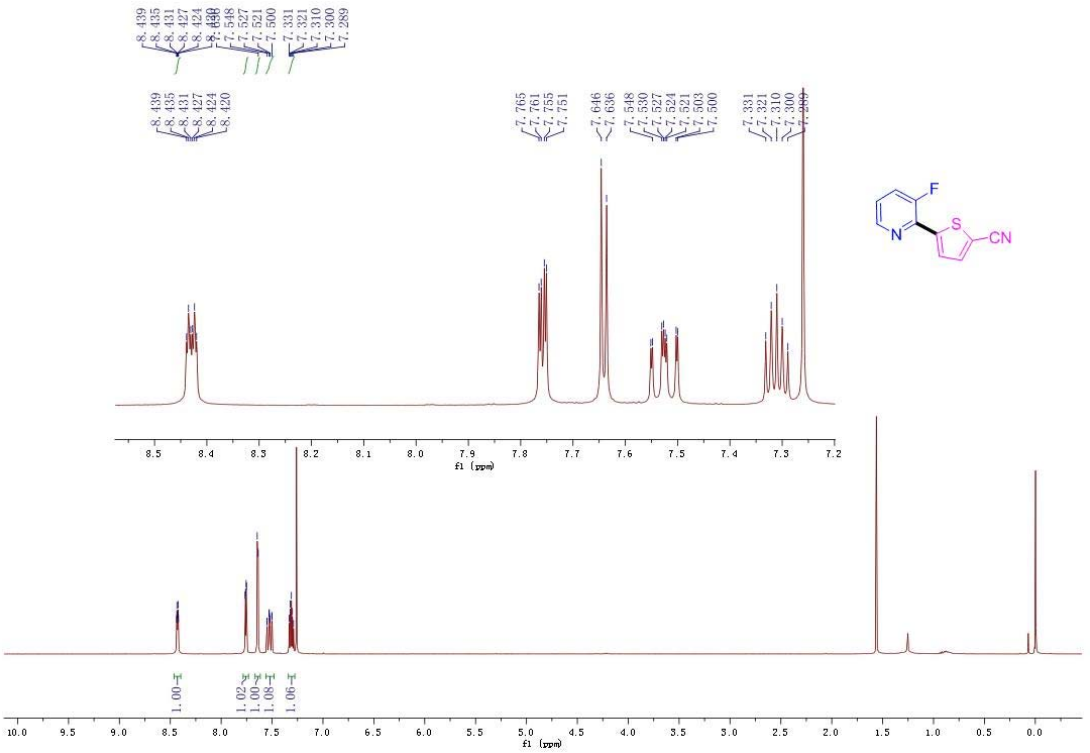
154.59
144.94
143.88
141.31
138.12
128.66
128.53
127.18
127.16
124.10
123.90
122.53
122.49
77.48
77.16
76.84
64.47
21.10
F
N
S
OH
f1 (ppm)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8.431
8.427
8.424
8.420
7.765
7.761
7.755
7.751
7.646
7.636
7.548
7.530
7.527
7.524
7.521
7.503
7.500
7.331
7.321
7.310
7.300
7.289
F
N
S
CN
f1 (ppm)
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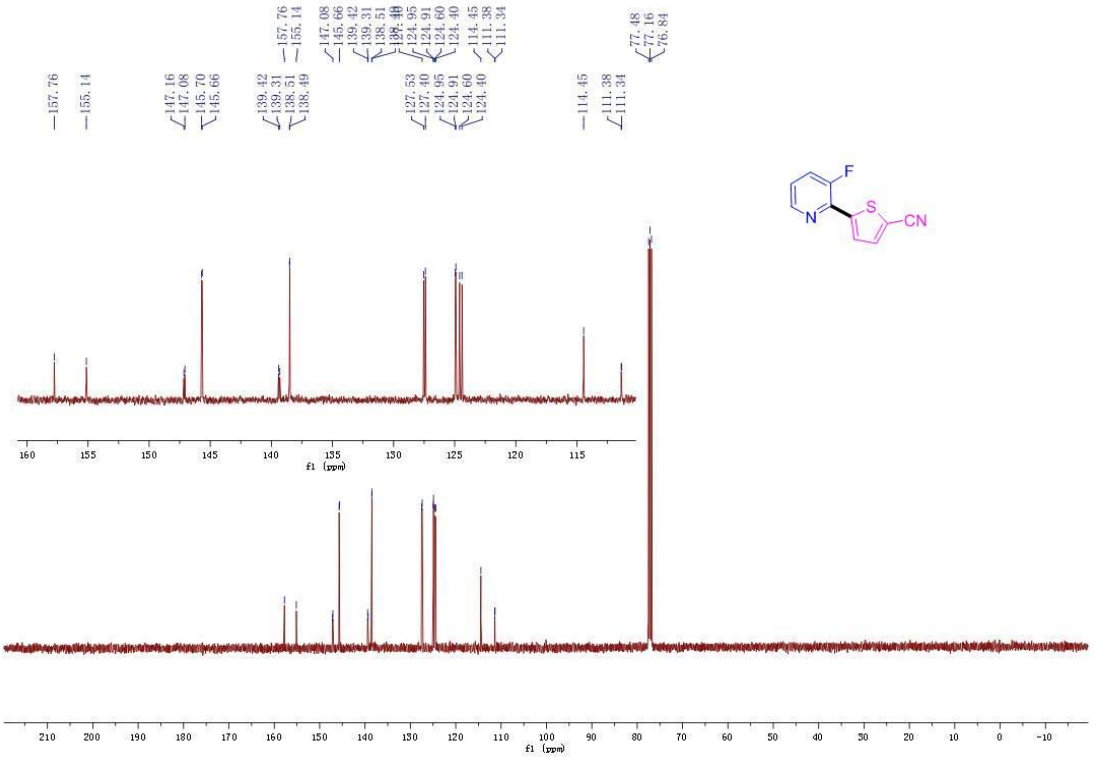
1.02
1.00
1.08
1.06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147.08
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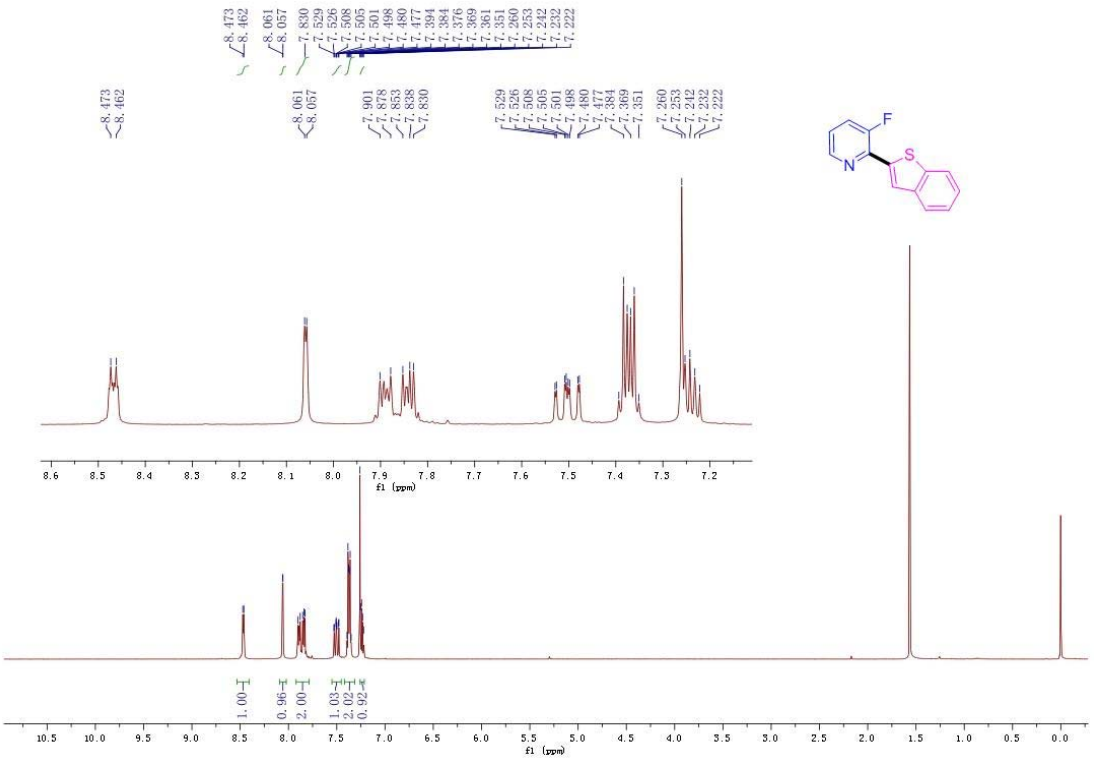
145.66
139.42
139.31
138.51
138.49
127.53
127.40
124.95
124.91
124.60
124.40
114.45
111.38
111.34
77.48
77.16
76.84
F
N
S
CN
f1 (ppm)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7.529
7.526
7.508
7.505
7.501
7.498
7.480
7.477
7.394
7.384
7.376
7.369
7.361
7.351
7.260
7.253
7.242
7.232
7.222
7.901
7.878
7.853
7.838
7.830
F
N
S
f1 (ppm)
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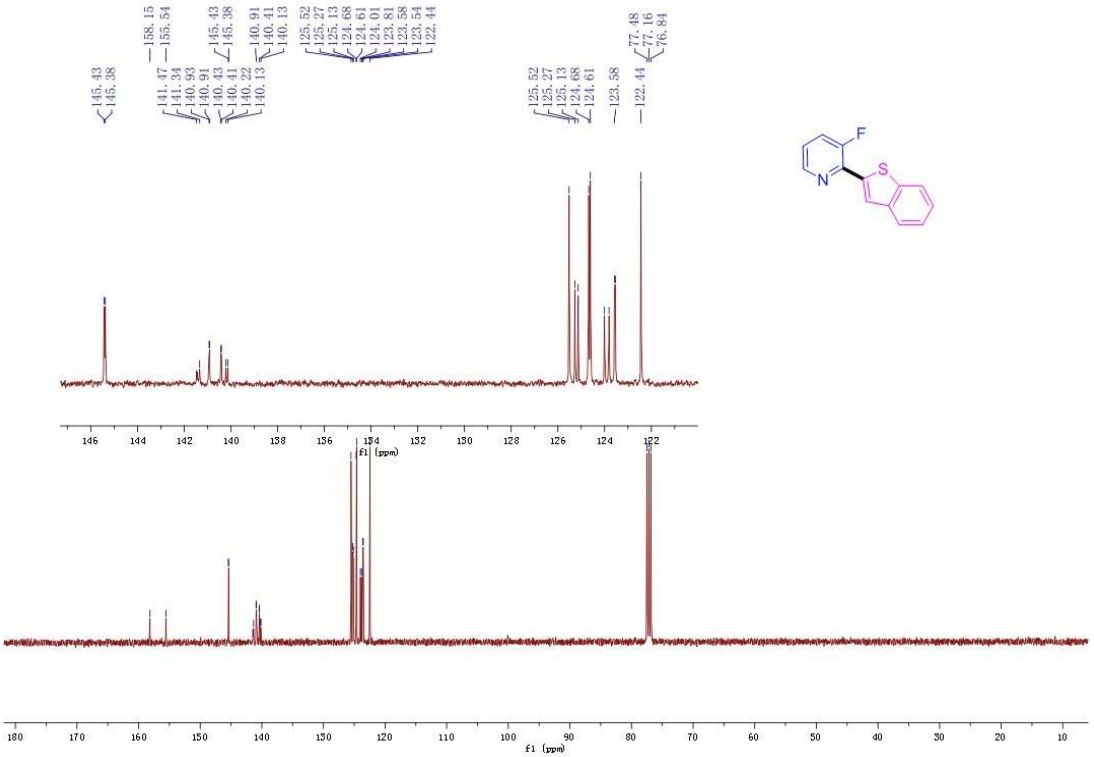
0.96
2.00
1.03
2.02
0.92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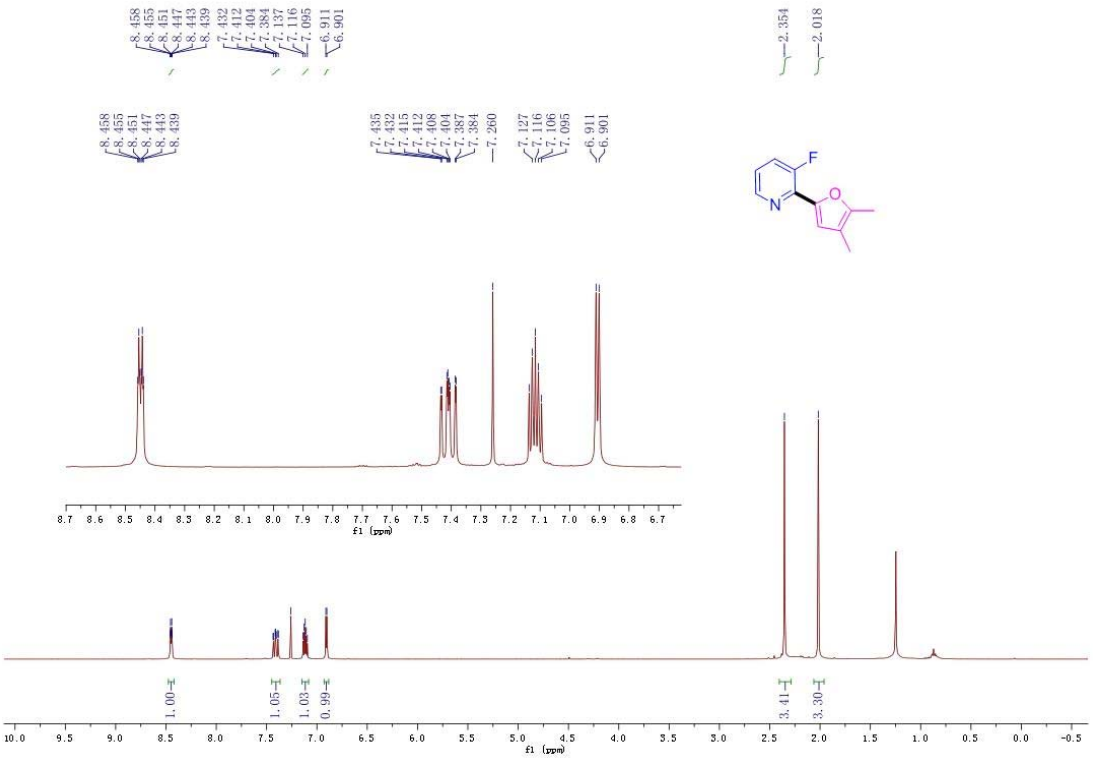
141.47
141.34
140.93
140.91
140.43
140.41
140.22
140.13
125.52
125.27
125.13
124.68
124.61
124.01
123.81
123.58
123.54
122.44
77.48
77.16
76.84
F
N
S
f1 (ppm)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8.447
8.443
8.439
7.432
7.412
7.404
7.384
7.137
7.116
7.095
6.911
6.901
2.354
2.018
7.435
7.432
7.415
7.412
7.408
7.404
7.387
7.384
7.260
7.127
7.116
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7.095
F
N
O
f1 (ppm)
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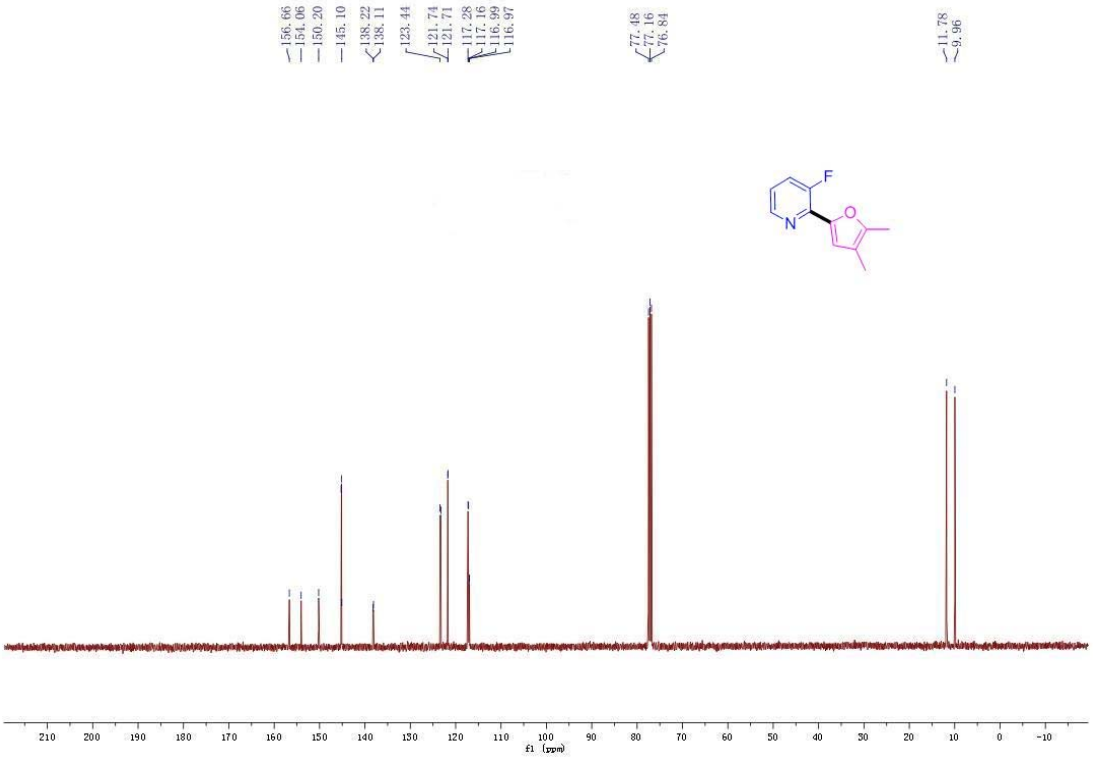
1.05
1.03
0.99
3.41
3.30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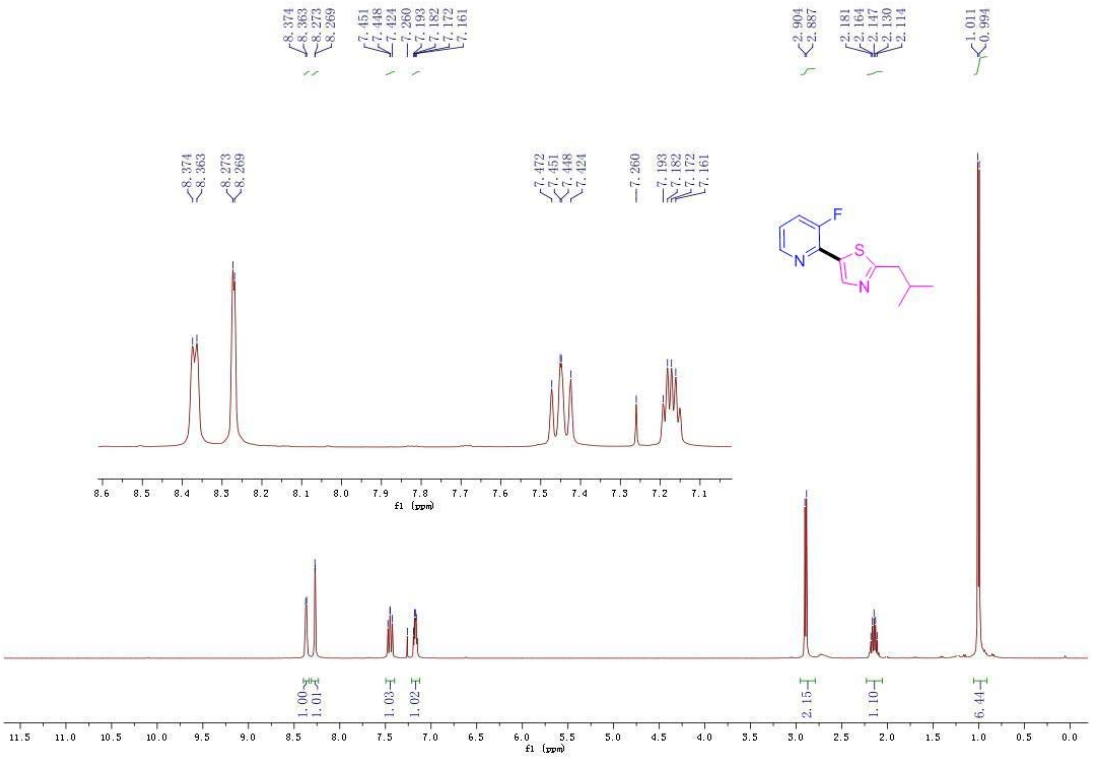
138.22
138.11
123.44
121.74
121.71
117.28
117.16
116.99
116.97
77.48
77.16
76.84
11.78
9.96
F
N
O
f1 (ppm)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8.269
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7.448
7.424
7.260
7.193
7.182
7.172
7.161
2.904
2.887
2.181
2.164
2.147
2.130
2.114
1.011
0.994
F
N
S
N
f1 (ppm)
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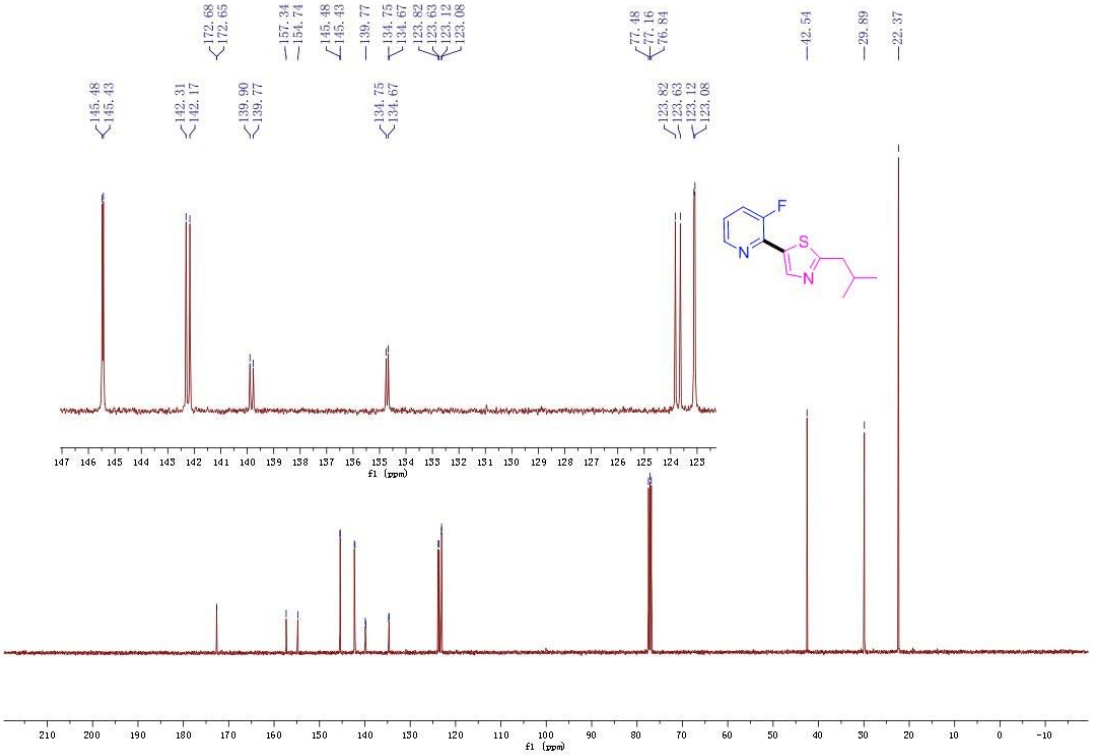
1.01
1.03
1.02
2.15
1.10
6.44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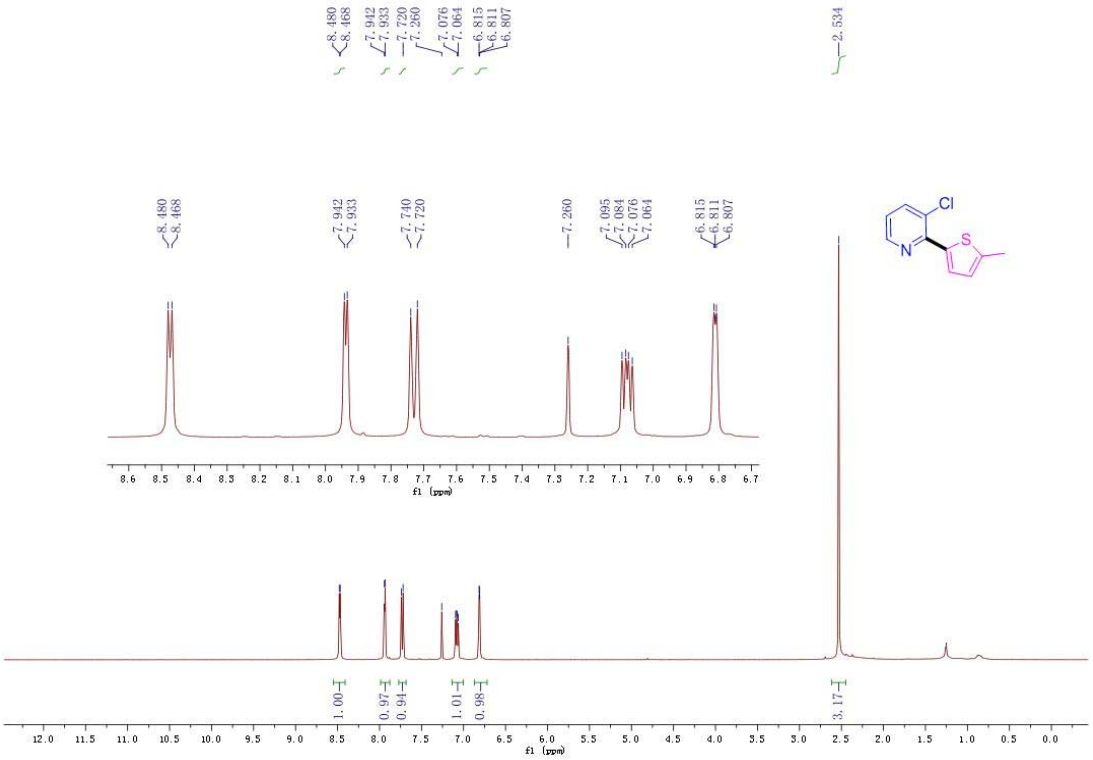
172.65
157.34
154.74
145.48
145.43
139.77
134.75
134.67
123.82
123.63
123.12
123.08
77.48
77.16
76.84
42.54
29.89
22.37
F
N
S
N
f1 (ppm)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8.468
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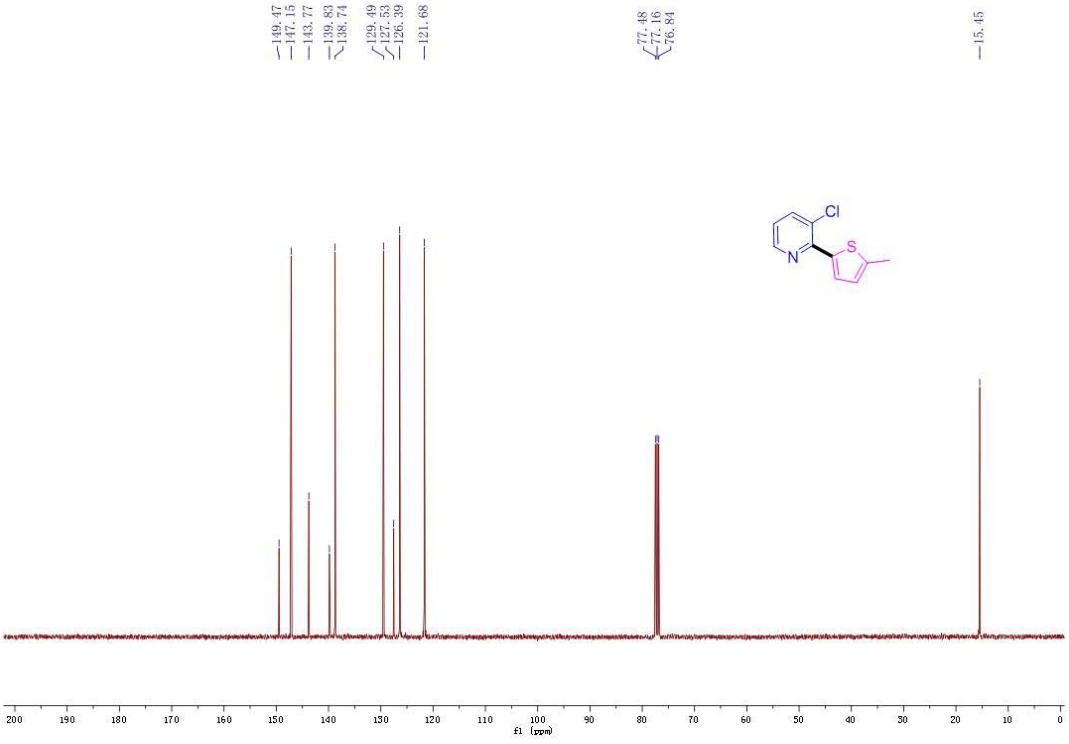
7.933
7.740
7.720
7.260
7.095
7.084
7.076
7.064
6.815
6.811
6.807
2.534
Cl
N
S
1.00
0.97
0.94
1.01
0.98
3.17
f1 (ppm)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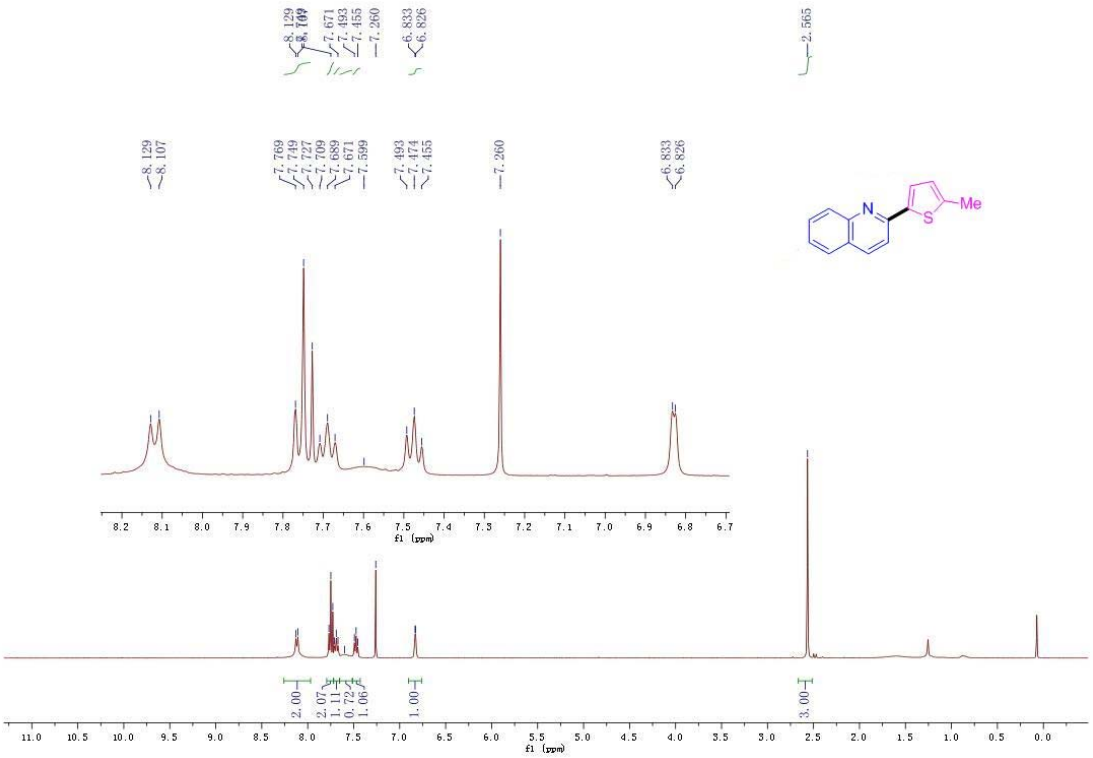
143.77
139.83
138.74
129.49
127.53
126.39
121.68
77.48
77.16
76.84
15.45
Cl
N
S
f1 (ppm)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8.107
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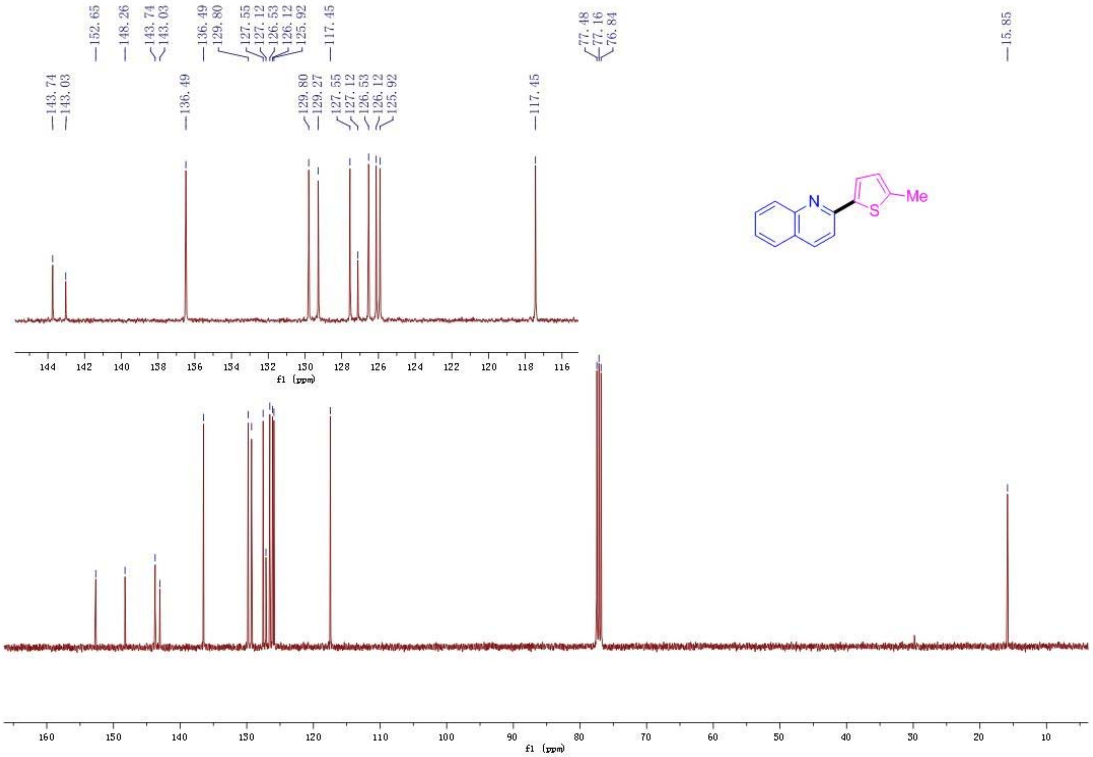
7.749
7.727
7.709
7.689
7.671
7.599
7.493
7.474
7.455
7.260
6.833
6.826
2.565
N
S
Me
f1 (ppm)


152.65
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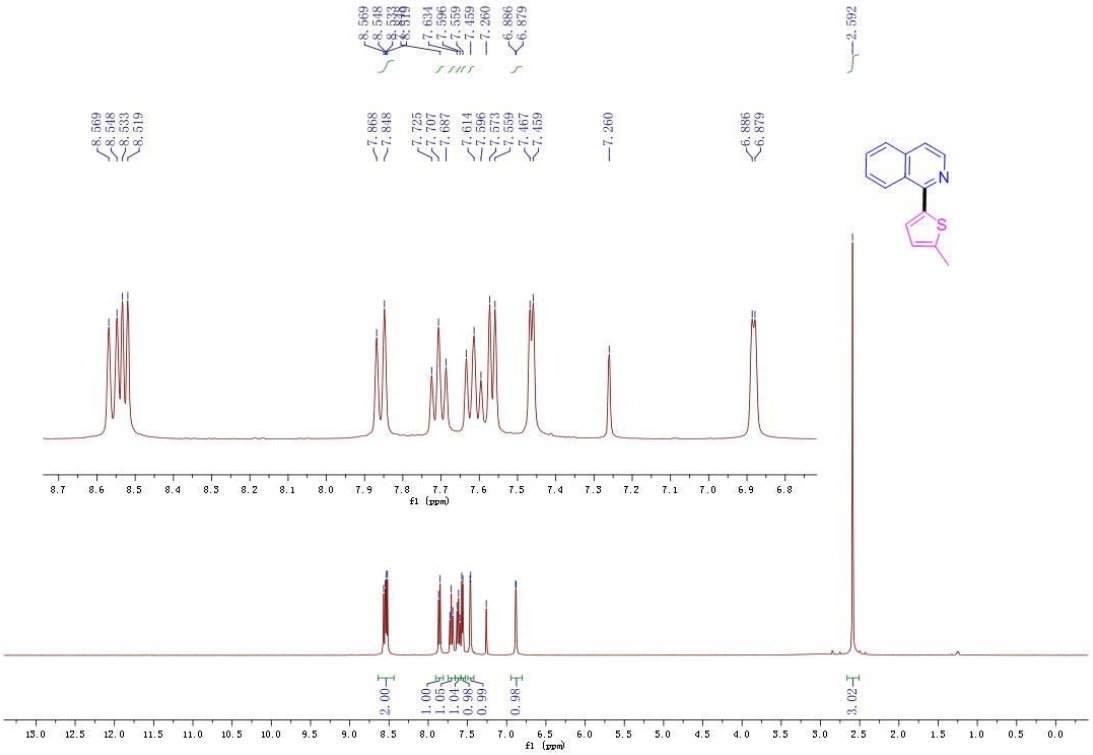
143.03
136.49
129.80
127.55
127.12
126.53
126.12
125.92
117.45
77.48
77.16
76.84
15.85
N
S
Me
f1 (ppm)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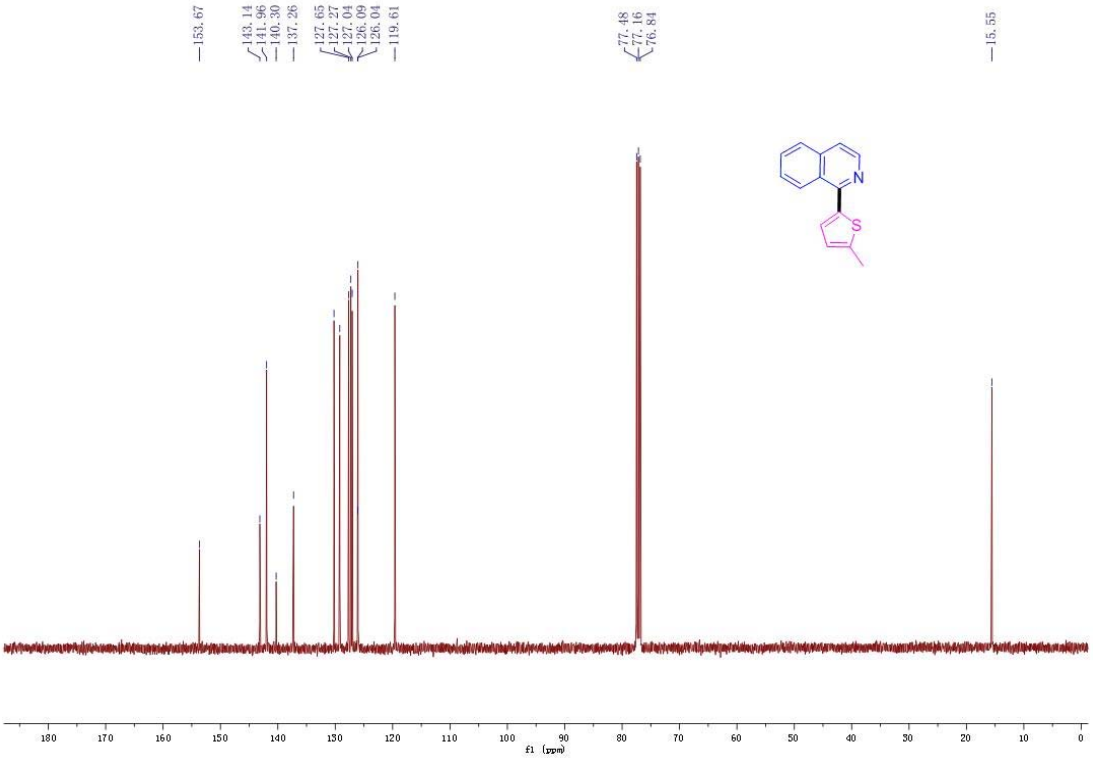
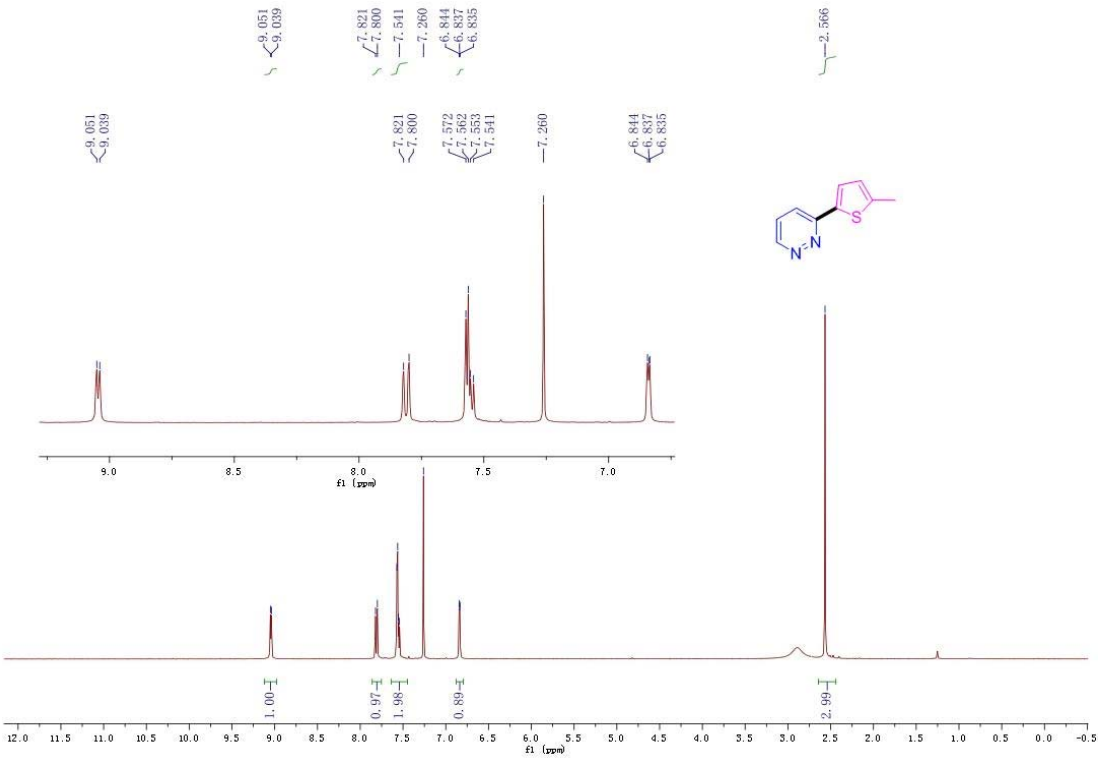
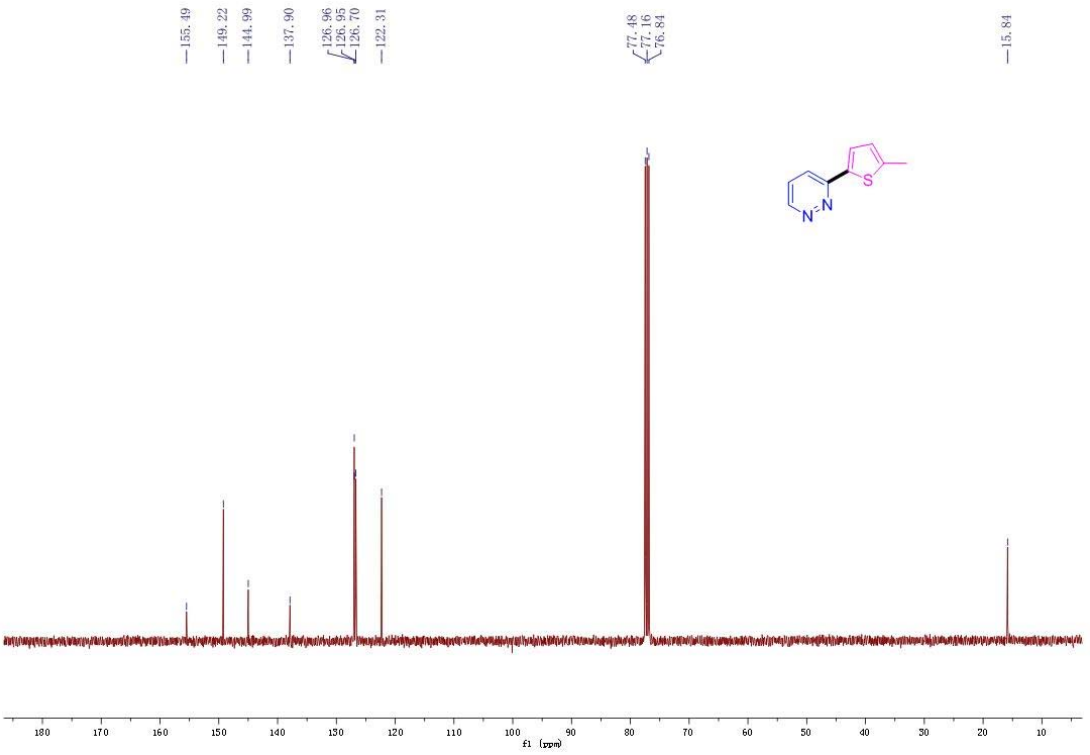
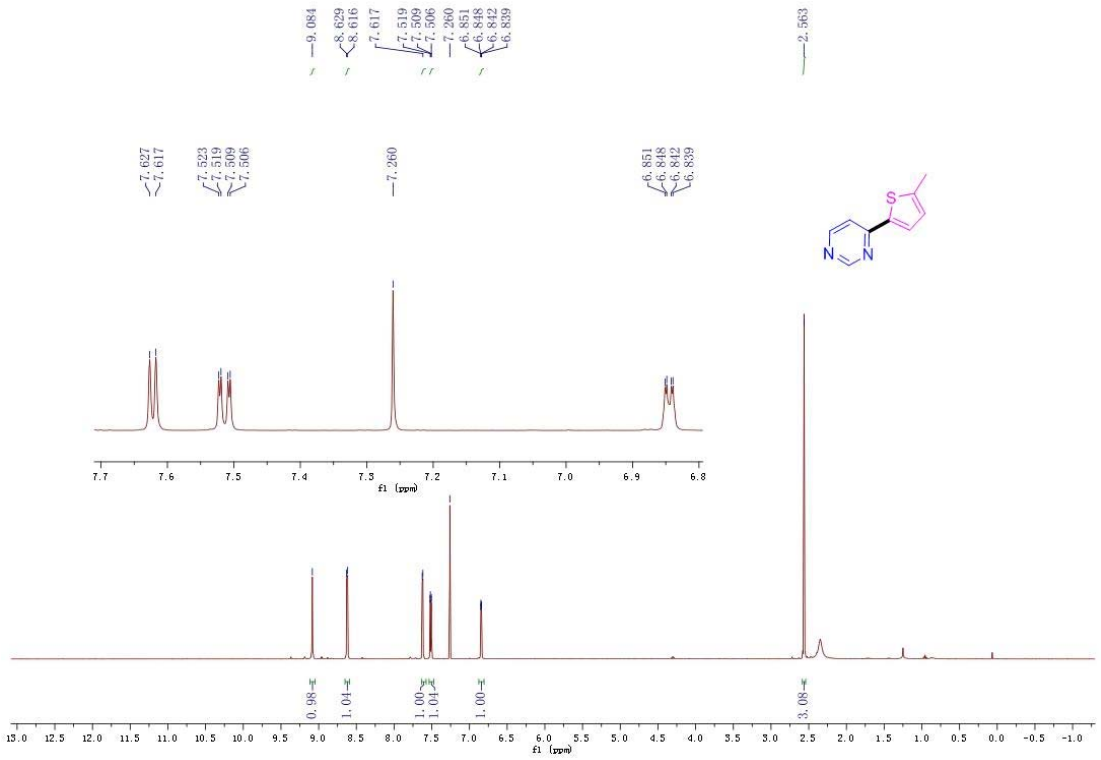
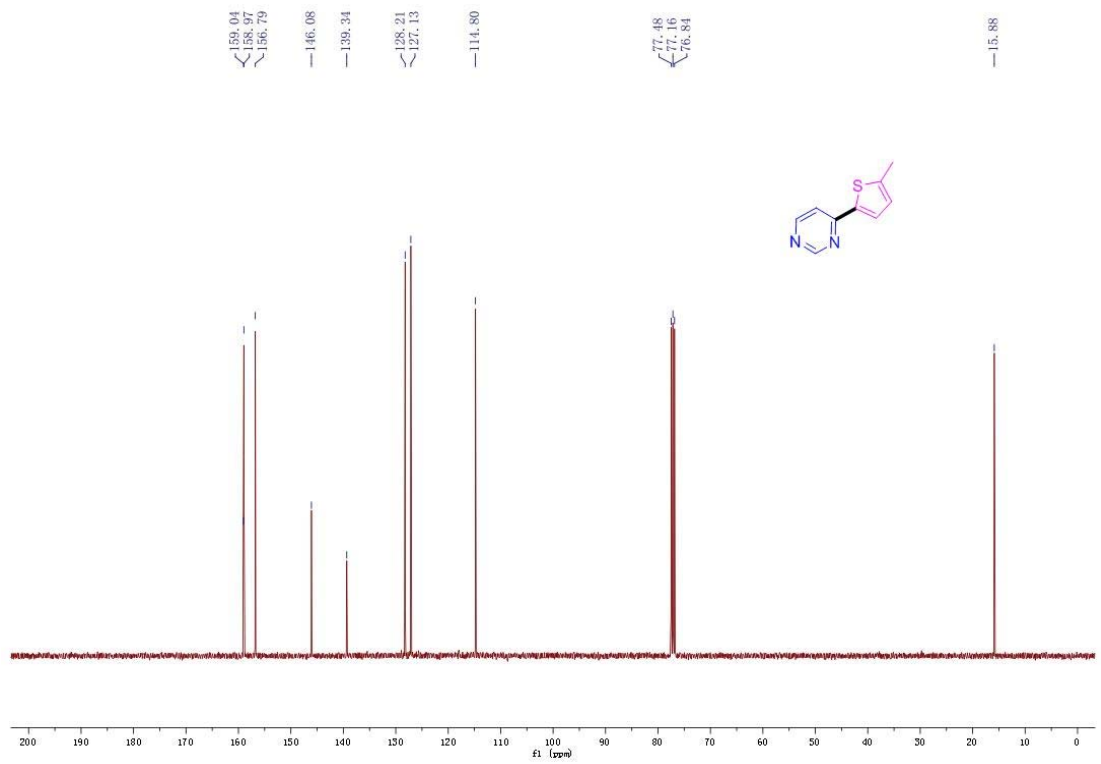
7.634
7.614
7.596
7.573
7.559
7.467
7.459
7.260
6.886
6.879
2.592
2.00
1.00
1.05
1.04
0.98
0.99
0.98
3.02
f1 (ppm)

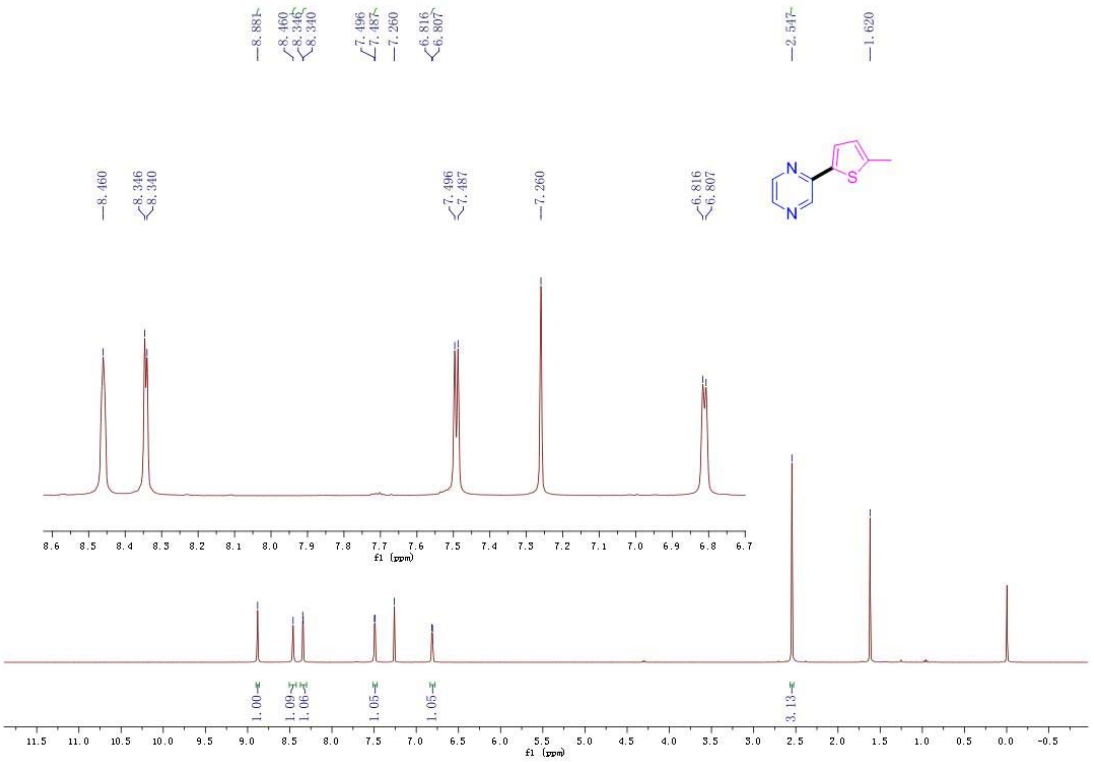

153.67
143.14
141.96
140.30
137.26
127.65
127.27
127.04
126.09
126.04
119.61
77.48
77.16
76.84
15.55
f1 (ppm)

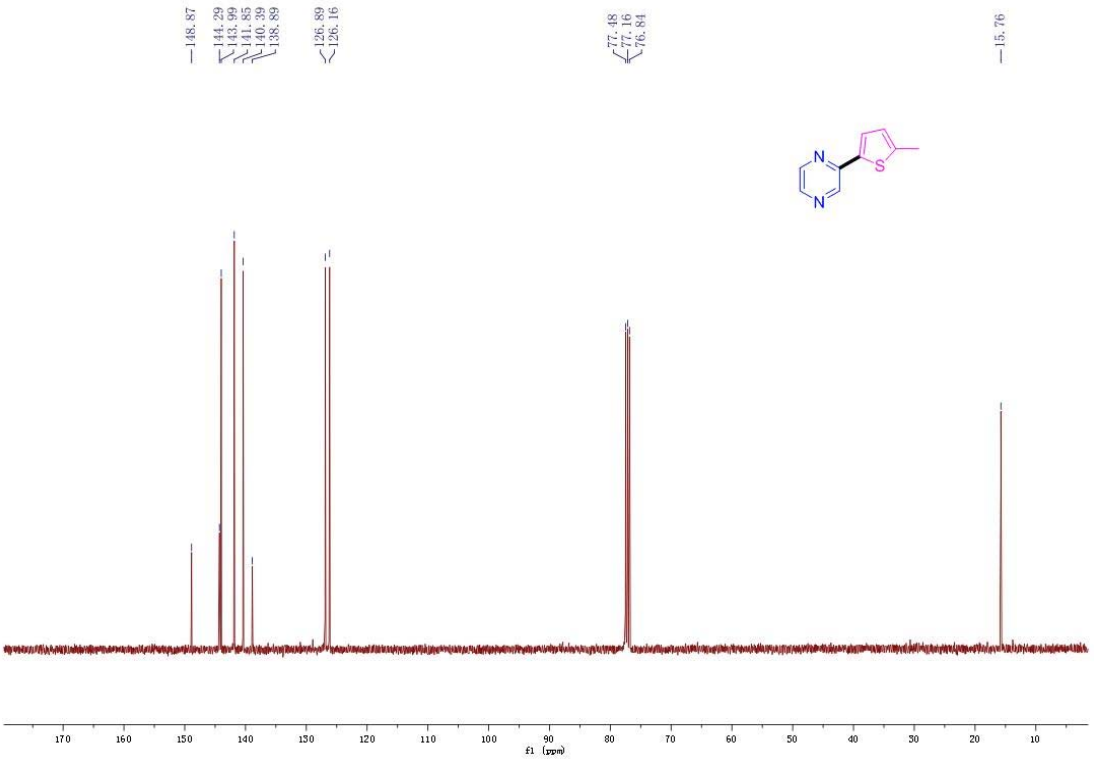

9.051
9.039
7.821
7.800
7.572
7.562
7.553
7.541
7.260
6.844
6.837
6.835
2.566
1.00
0.97
1.98
0.89
2.99
f1 (ppm)

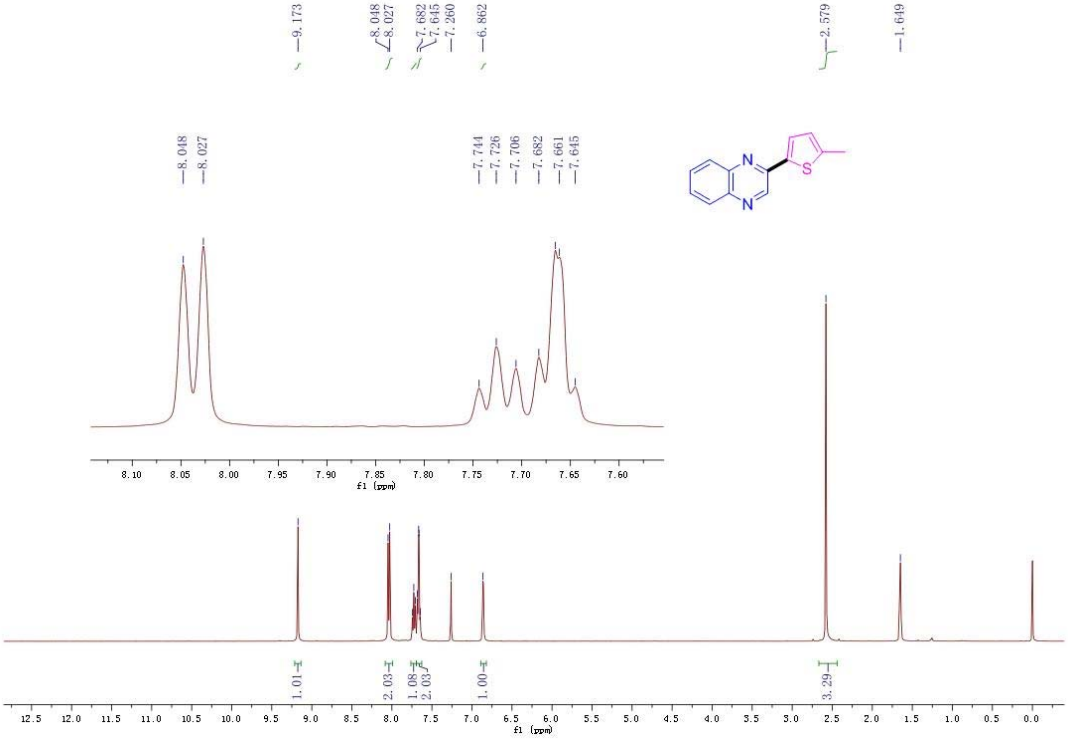

155.49
149.22
144.99
137.90
126.96
126.95
126.70
122.31
77.48
77.16
76.84
15.84
f1 (ppm)

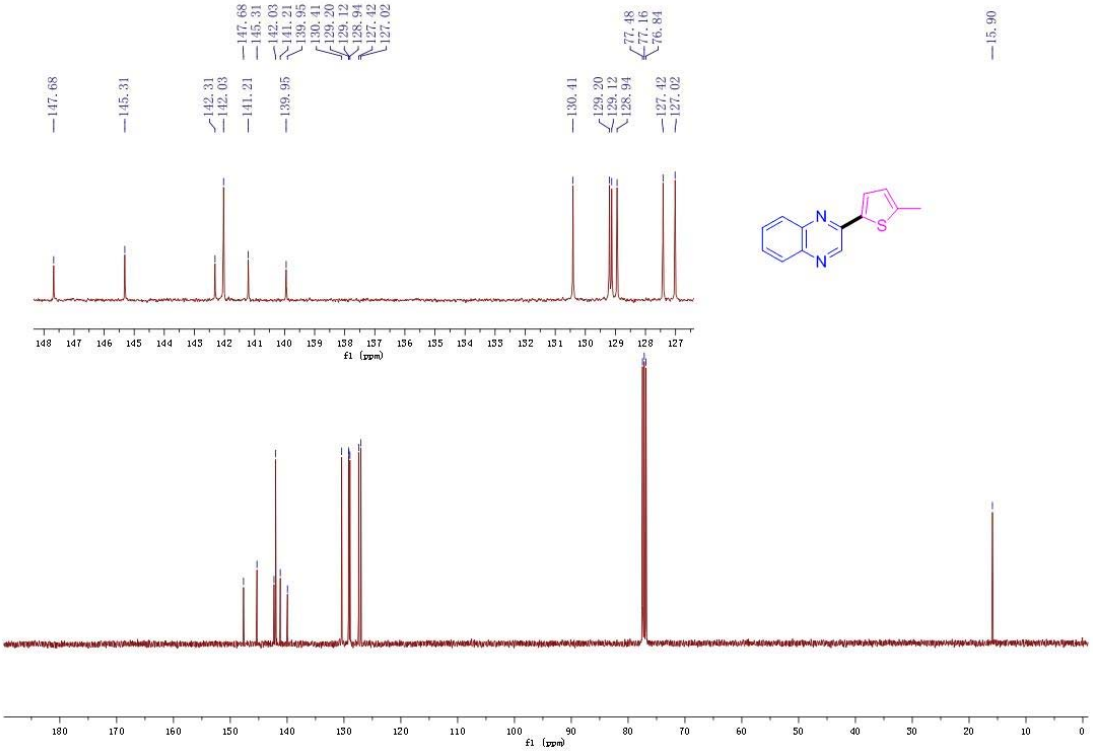

9.084
8.629
8.616
7.617
7.627
7.617
7.523
7.519
7.509
7.506
7.260
6.851
6.848
6.842
6.839
2.563
0.98
1.04
1.00
1.04
1.00
3.08
f1 (ppm)


159.04
158.97
156.79
146.08
139.34
128.21
127.13
114.80
77.48
77.16
76.84
15.88
f1 (ppm)


8.881
8.460
8.346
8.340
7.496
7.487
7.260
6.816
6.807
2.547
1.620
f1 (ppm)
1.00
1.09
1.06
1.05
1.05
3.13


148.87
144.29
143.99
141.85
140.39
138.89
126.89
126.16
77.48
77.16
76.84
15.76
f1 (ppm)


9.173
8.048
8.027
7.682
7.645
7.260
6.862
2.579
1.649
7.744
7.726
7.706
7.682
7.661
7.645
1.01
2.03
1.08
2.03
1.00
3.29
f1 (ppm)


147.68
145.31
142.31
142.03
141.21
139.95
130.41
129.20
129.12
128.94
127.42
127.02
77.48
77.16
76.84
15.90
f1 (ppm)