Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Ru(II)-Catalyzed C6-Selective C–H Amidation of 2-Pyridones

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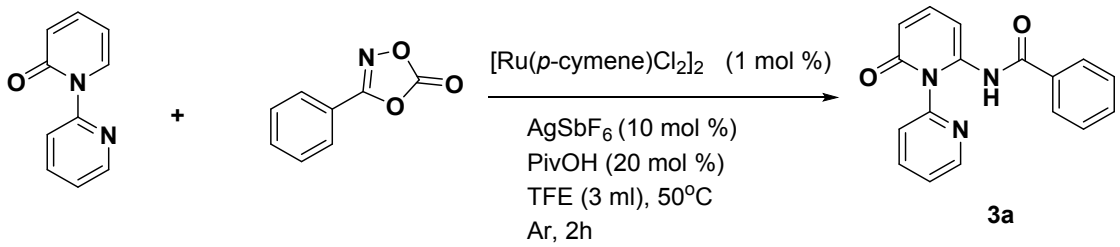
Contents

1. General information

All commercials obtained from commercial sources were used as received unless otherwise noted. Substrate **1**[1] and **2**[2] were prepared by literature reports. The progress of the reactions was monitored by TLC with silica gel plates, and the visualization was carried out under UV light (254nm). Melting points were determined using a Büchi B-540 capillary melting point apparatus. NMR spectra were recorded on 400 MHz and 600 MHz spectrometers in the solvent indicated. Chemical shifts are reported downfield from TMS (=0) for ^{1}H NMR. For ^{13}C NMR, chemical shifts are reported in the scale relative to $CDCl_3$ (= 77.0) and DMSO-d_6 (= 40.0). Infrared (IR) data were recorded as films on potassium bromide plates on a NICOLET iS50 FT-IR spectrometer. Mass spectra were measured with a low-resolution MS instrument using ESI ionization. HRMS spectra were recorded on an electrospray ionization quadrupole time-of-flight (ESI-Q-TOF) mass spectrometer.

2. General procedure for Ru(II)-catalyzed site-selective C–H amidation of pyridones .



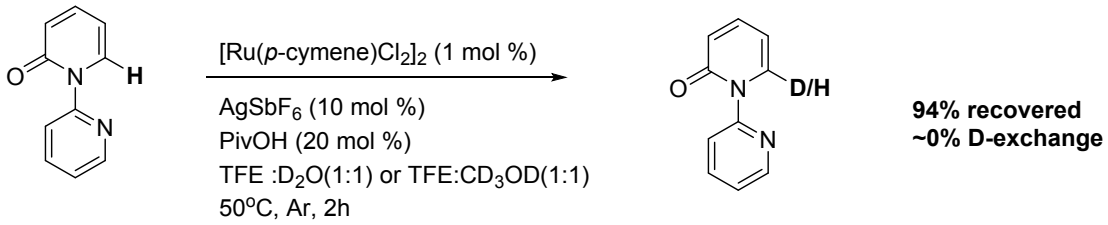
Synthesis of **3a** is representative. 2*H*-[1,2'-bipyridin]-2-one **1a** (0.4 mmol), **2a** (0.48 mmol), $[RuCl_2(p\text{-cymene})]_2$ (0.004 mmol), $AgSbF_6$ (0.04 mmol) and PivOH (0.08 mmol) were dissolved in TFE (3 mL). The mixture was stirred at 50°C under argon atmosphere for 2 hours. The resulting mixture was cooled to room temperature and then diluted with dichloromethane. The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/ethyl acetate =1/1→ethyl acetate) to give **3a** (114 mg, 98% yield) as an off-white solid.

4. Gram-scale synthesis of 3a

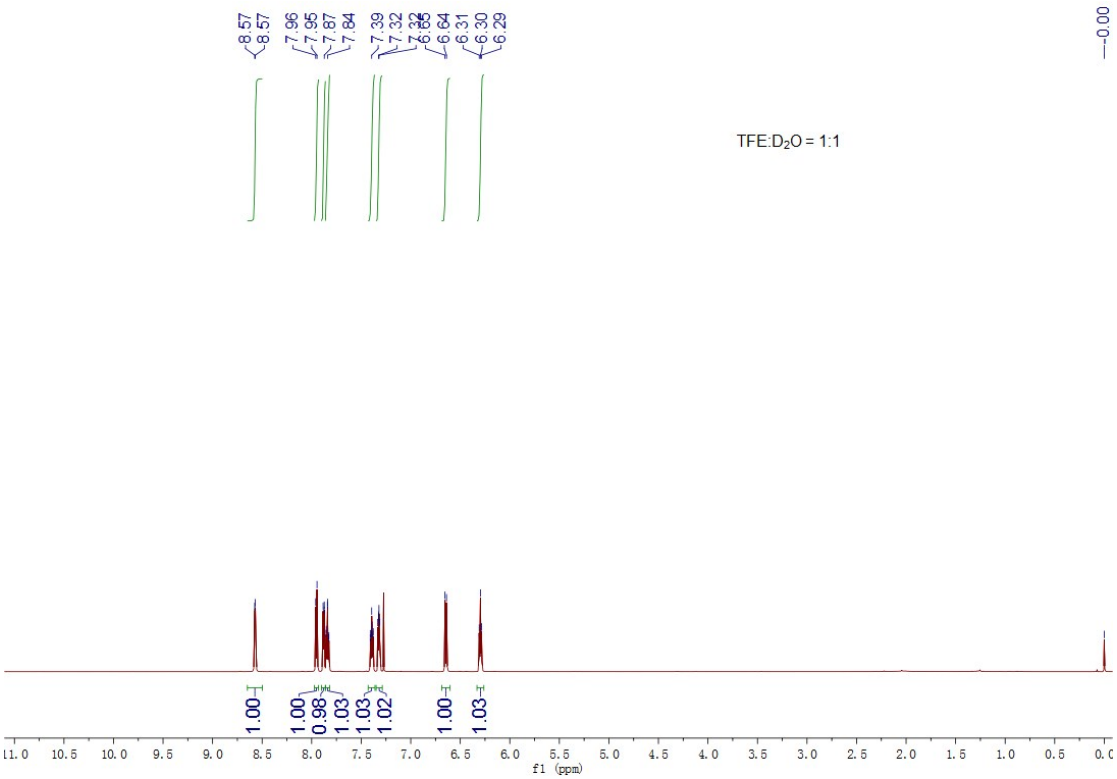
2*H*-[1,2'-bipyridin]-2-one **1a** (1.730 g，10 mmol), **2a** (1.958 g，12 mmol), $[RuCl_2(p\text{-cymene})]_2$ (32 mg，0.5 mol %), $AgSbF_6$ (351 mg，10 mol %) and PivOH (205mg，20 mol %) were dissolved in TFE (30 mL) in a three-neck flask. The mixture was stirred at 50 °C under argon atmosphere for 24 hours. The resulting mixture was cooled to room temperature and then diluted with dichloromethane. The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/ ethyl acetate =1/1→ethyl acetate) to give **3a** as an off-white solid (2.500 g，86% yield).

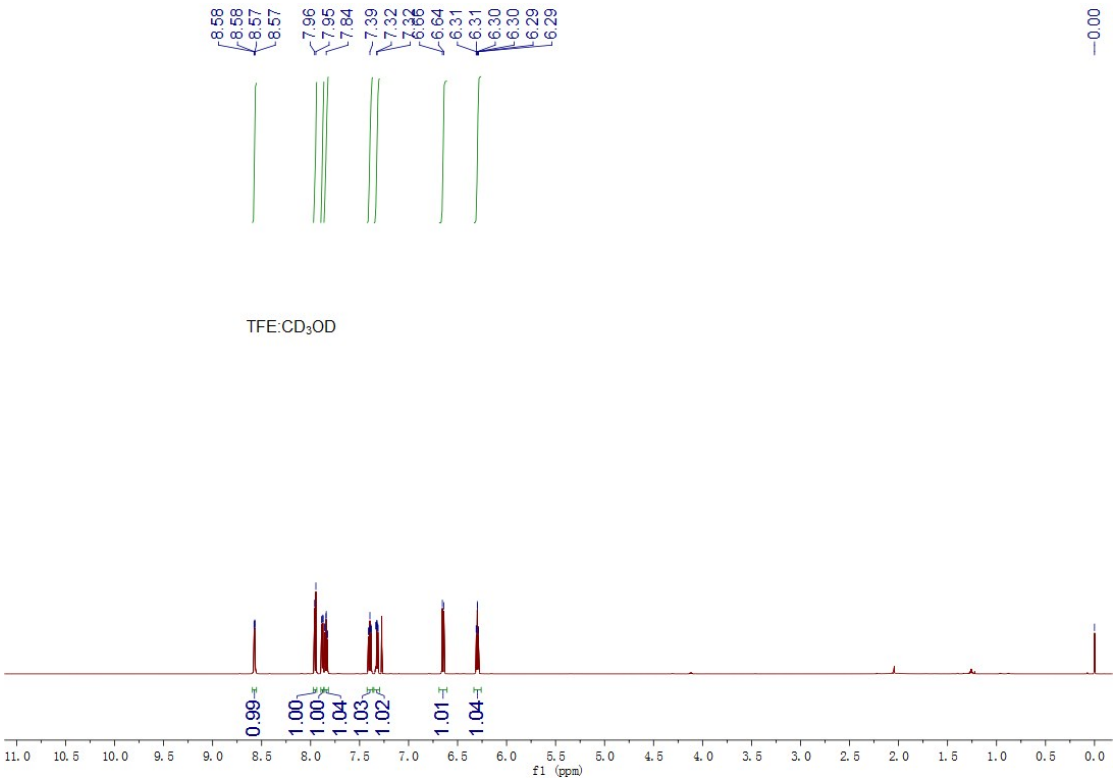
5. Mechanistic studies[3]

5.1 Deuteration experiment

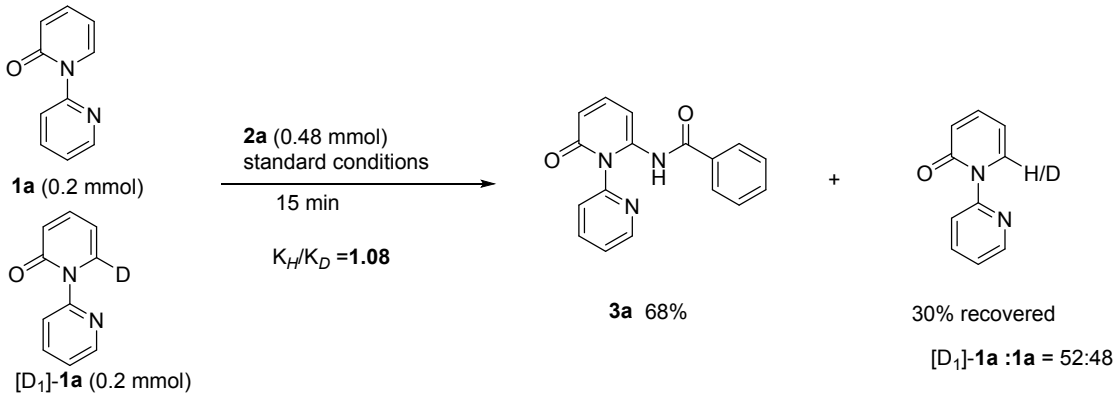


2*H*-[1,2'-bipyridin]-2-one **1a** (0.4 mmol), $[RuCl_2(p\text{-cymene})]_2$ (0.01 mmol), $AgSbF_6$ (0.04 mmol) and PivOH (0.08 mmol) were dissolved in TFE :D_2O or TFE:CD_3OD (1.5ml:1.5ml). The mixture was stirred at 50 °C under argon atmosphere for 2 hours. The resulting mixture was cooled to room temperature and then diluted with 50ml of dichloromethane, the combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (94% recovered). D-incorporation was determined by ^1H NMR (~0% D-incorporation was observed).

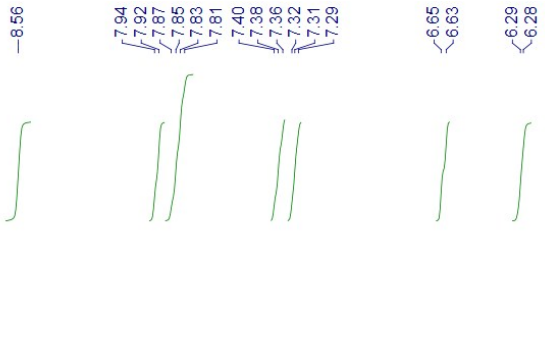

8.57
8.57
7.96
7.95
7.87
7.84
7.39
7.32
6.64
6.31
6.30
6.29
0.00
TFE:D2O = 1:1
1.00
1.00
0.98
1.03
1.03
1.02
1.00
1.03
f1 (ppm)


8.58
8.58
8.57
8.57
7.96
7.95
7.84
7.39
7.32
6.64
6.31
6.30
6.30
6.29
6.29
0.00
TFE:CD3OD
0.99
1.00
1.00
1.04
1.03
1.02
1.01
1.04
f1 (ppm)

5.2 KIE experiment



Compound **1a** (0.1 mmol) and [D_1]**-1a** (0.1 mmol), **2a** (0.48 mmol), [$RuCl_2$(*p*-cymene)]$_2$ (0.01 mmol), $AgSbF_6$ (0.04 mmol) and PivOH (0.08 mmol) were dissolved in TFE (3 mL). The mixture was stirred at 50 ^oC under argon atmosphere for 15 min. The resulting mixture was cooled to room temperature and then diluted with dichloromethane, the combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography. The remaining starting materials were recovered in 30% and analyzed by ^1H NMR to determine the ratio of **1m** and [D_1]**-1m**. ($K_{(H)}/K_{(D)}$ = (1-0.48)/0.48 = 1.08)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7.29
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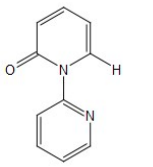
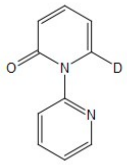
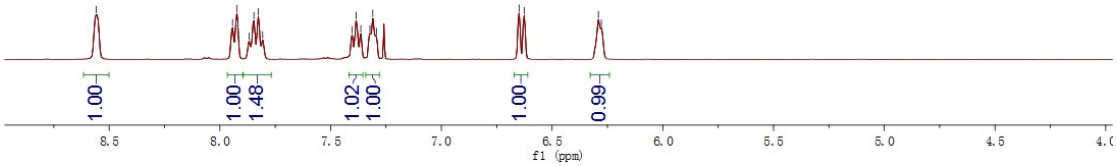
6.63
6.29
6.28


O
N
H
N

1a


O
N
D
N

[D1]-**1a**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1.00
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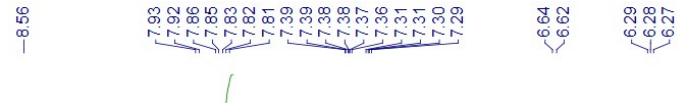
5.0
4.5
f1 (ppm)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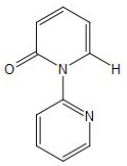
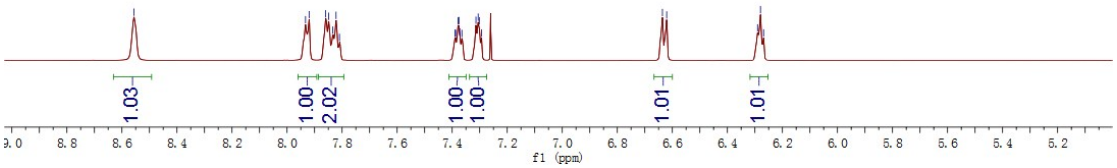
6.29
6.28
6.27


O
N
H
N

1a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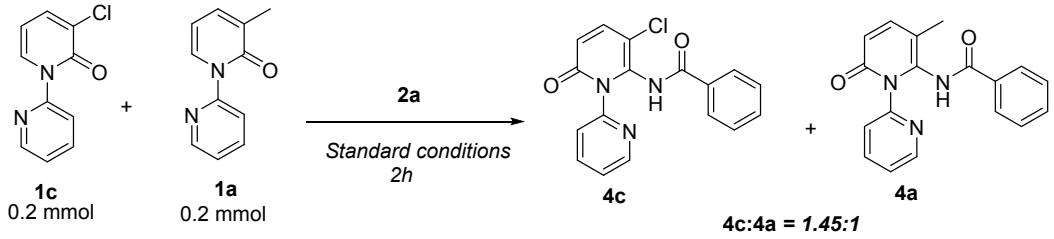
1.01
1.01
9.0
8.8
8.6
8.4
8.2
8.0
7.8
7.6
7.4
7.2
7.0
6.8
6.6
6.4
6.2
6.0
5.8
5.6
5.4
5.2
f1 (ppm)

6. Competition experiments

6.1 2-Pyridones



1c 0.2 mmol

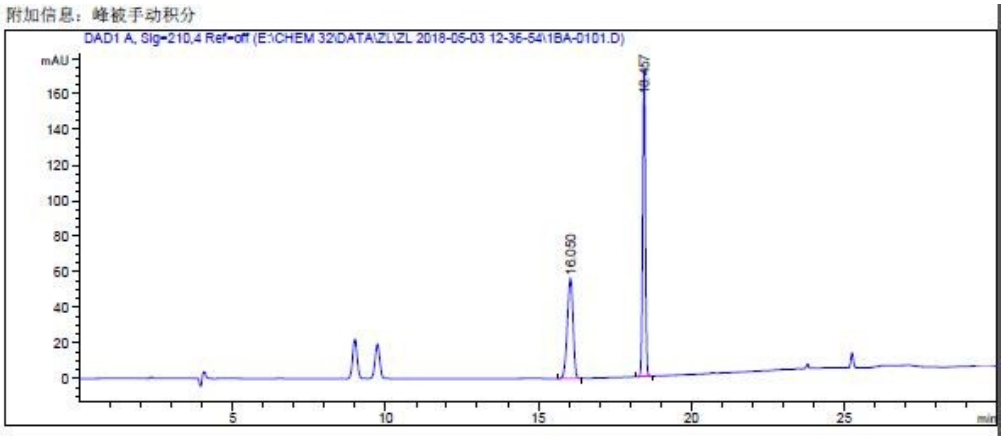
1a 0.2 mmol

4c

4a

4c:4a = *1.45:1*

To an oven-dried 10 mL pressure tube was added **1c** (42 mg, 0.20 mmol), **1a** (38 mg, 0.20 mmol), **2a** (33mg, 0.2 mmol), $[RuCl_2(p\text{-cymene})]_2$ (0.01 mmol), $AgSbF_6$ (0.04 mmol), PivOH (0.08 mmol), and TFE (3 mL) under Ar atmosphere. The mixture was stirred for 2 h at 50 °C before diluted with DCM, washed with brine, and then concentrated in vacuum. The ratio of product **4c**/**4a** was analyzed by HPLC (Welch Ultimate Plus 4.6 x 250mm, 20% ACN/H_2O, 0.8 mL/min, 210 nm. t_{4c} = 18.46 min, t_{4a}= 16.05 min).



面积百分比报告

排序 : 信号
乘积因子 : 1.0000
稀释因子 : 1.0000
内标中不使用乘积因子和稀释因子

信号 1: DAD1 A, Sig=210,4 Ref=off

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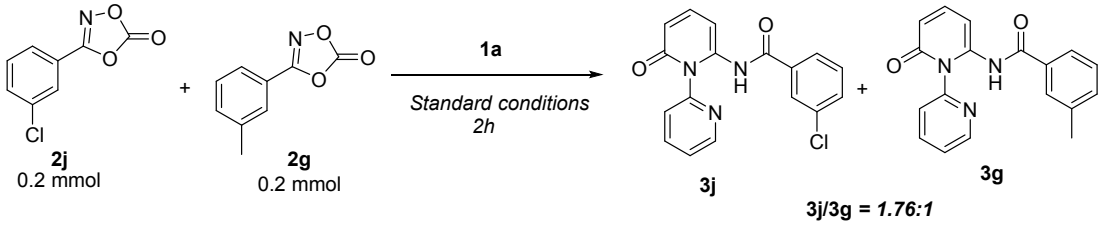
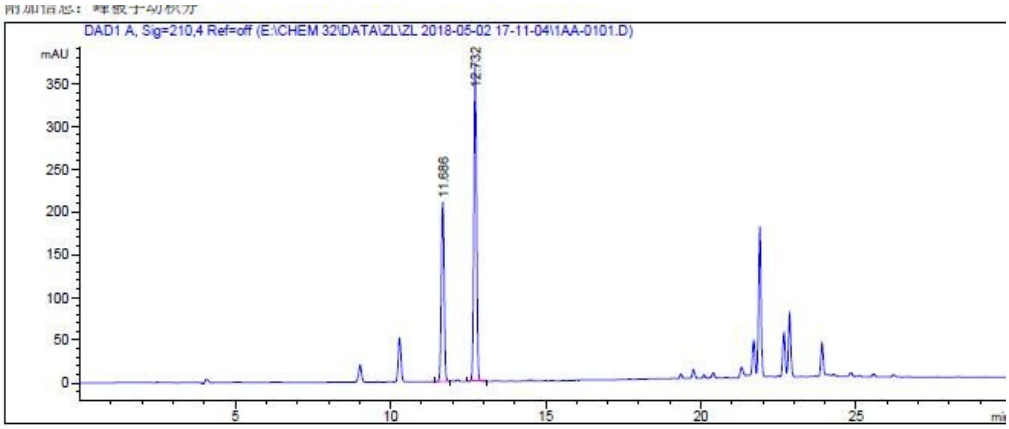
6.2 Oxazolones



To an oven-dried 10 mL pressure tube was added substrate **2j** (40 mg, 0.20 mmol), substrate **2g** (36 mg, 0.20 mmol), **1a** (35mg, 0.2 mmol), $[RuCl_2(p\text{-cymene})]_2$ (0.01 mmol), $AgSbF_6$ (0.04 mmol) and PivOH (0.08 mmol) were dissolved in TFE (3 mL) under Ar atmosphere. The mixture was stirred for 2 h at 50 °C. The mixture was then cooled to room temperature, diluted with DCM, washed with brine, concentrated in vacuum. The ratio of product **3j**/**3g** was analyzed by HPLC (Welch Ultimate Plus 4.6 x 250mm, 20% ACN/H_2O, 0.8 mL/min, 210 nm. t_{3j} = 12.73 min, t_{3g} = 11.68 min).



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面积百分比报告

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排序 : 信号
乘积因子 : 1.0000
稀释因子 : 1.0000
内标中不使用乘积因子和稀释因子

信号 1: DAD1 A, Sig=210,4 Ref=off

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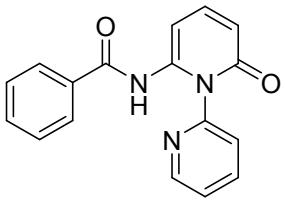
2	12.732	BB	0.0965	2320.85693	373.67096	63.7941

7. Analytical data and copies of NMR spectra

7.1 Analytical data for products.

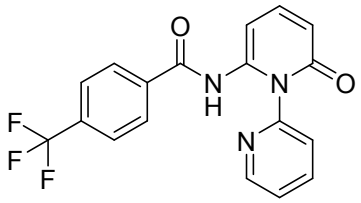
***N*-(2-oxo-2*H*-[1,2'-bipyridin]-6-yl)benzamide (3a):**



3a

Product **3a** was isolated as an off-white solid (114 mg, 98%); m.p. 151-154 °C (146-148°C)[3]**;** ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.47 (s, 1H), 8.68 (d, *J* = 3.8 Hz, 1H), 7.96 (td, *J* = 8.0, 1.6 Hz, 1H), 7.64 (d, *J* = 8.0 Hz, 1H), 7.59 – 7.55 (m, 2H), 7.54 – 7.44 (m, 3H), 7.45-7.40 (m, 2H), 7.09 (d, *J* = 7.4 Hz, 1H), 6.50 (d, *J* = 9.2 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.22, 162.52, 150.28, 148.52, 141.08, 139.48, 139.42, 133.27, 132.54, 128.85, 126.87, 125.45, 124.39, 116.74, 99.07. IR (KBr) *v* : 3442, 3137, 3061, 1676, 1600, 1529, 1367, 1275. HRMS (ESI) *m/z* calcd for $C_{17}H_{14}N_3O_2$ $[M + H]^+$ 292.1081, found 292.1085.

***N*-(2-oxo-2*H*-[1,2'-bipyridin]-6-yl)-4-(trifluoromethyl)benzamide (3b):**

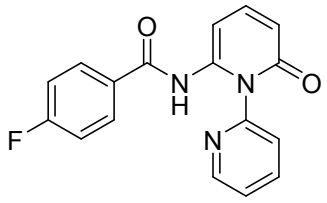


3b

Product **3b** was isolated as an off-white solid (141 mg, 98%); m.p. 179-182 °C;
^{1}H NMR (600 MHz, $CDCl_3$) δ 9.72 (s, 1H), 8.64 (d, *J* = 3.8 Hz, 1H), 7.96 (td, *J* = 8.0, 1.8 Hz, 1H), 7.72 – 7.67 (m, 4H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.52-7.42 (m, 2H), 7.06 (d, *J* = 7.2 Hz, 1H), 6.53 (d, *J* = 8.6 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.02, 162.43, 150.31, 148.39, 140.88, 139.44, 138.91, 136.57, 134.10 (d, *J* = 32.8 Hz), 127.40, 125.91 (q, *J* = 3.8 Hz), 125.43, 124.43, 123.35 (d, *J* = 272.8 Hz), 117.42,

99.39. ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.11. IR (KBr) *v* : 3439, 3059, 1678, 1601, 1532, 1330, 1268. HRMS (ESI) *m/z* calcd for $C_{18}H_{13}F_3N_3O_2$ $[M + H]^+$ 360.0954, found 360.0944.

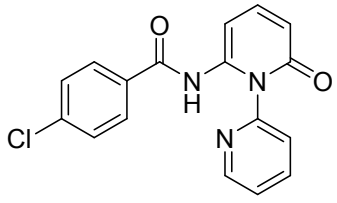
4-fluoro-*N*-(2-oxo-2*H*-[1,2'-bipyridin]-6-yl)benzamide (3c):



3c

Product **3c** was isolated as an off-white solid (120 mg, 97%); m.p. 213-215 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.51 (s, 1H), 8.64 (d, *J* = 3.6 Hz, 1H), 7.95 (t, *J* = 7.4 Hz, 1H), 7.64 (d, *J* = 8.0 Hz, 1H), 7.62-7.56 (m, 2H), 7.51 – 7.40 (m, 2H), 7.12-7.05 (m, 2H), 7.03 (d, *J* = 7.4 Hz, 1H), 6.50 (d, *J* = 9.2 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.20 (d, *J* = 254.4 Hz), 163.19, 150.35, 148.41, 140.95, 139.41, 139.27, 129.50 (d, *J* = 3.1 Hz), 129.35 (d, *J* = 9.2 Hz), 125.41, 124.36, 116.96, 116.07, 115.92, 99.18. ^{19}F NMR (376 MHz, $CDCl_3$) δ -105.78. IR (KBr) *v* : 3431, 3056, 1676, 1603, 1537, 1471, 1437, 1365, 1280. HRMS (ESI) *m/z* calcd for $C_{17}H_{13}FN_3O_2$ $[M + H]^+$ 310.0986, found 310.099.

4-chloro-*N*-(2-oxo-2*H*-[1,2'-bipyridin]-6-yl)benzamide (3d):

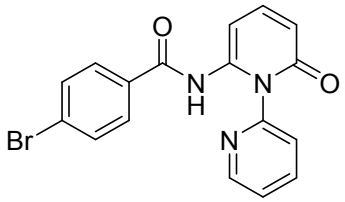


3d

Product **3d** was isolated as an off-white solid (128 mg, 98%); m.p. 202-206 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.57 (s, 1H), 8.63 (d, *J* = 4.2 Hz, 1H), 7.95 (t, *J* = 7.4 Hz, 1H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.51 (d, *J* = 8.4 Hz, 2H), 7.49 – 7.42 (m, 2H), 7.40-7.36 (m, 2H), 7.02 (d, *J* = 7.4 Hz, 1H), 6.51 (d, *J* = 9.2 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.20, 162.44, 150.36, 148.44, 140.95, 139.42, 139.13, 138.95, 131.70, 129.16, 128.27, 125.44, 124.38, 117.03, 99.05. IR (KBr) *v* : 3439, 3184, 2989, 1682,

1537, 1471, 1432, 1366, 1274. HRMS (ESI) *m/z* calcd for $C_{17}H_{13}ClN_3O_2$ $[M + H]^+$ 326.0691, found 326.0693.

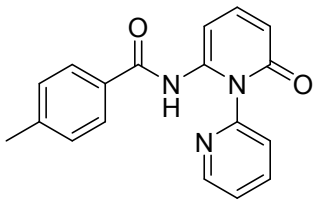
4-bromo-*N*-(2-oxo-2*H*-[1,2'-bipyridin]-6-yl)benzamide (3e):



3e

Product **3e** was isolated as an off-white solid (139 mg, 94%); m.p. 201-206 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.56 (s, 1H), 8.63 (dd, *J* = 4.8, 1.2 Hz, 1H), 7.95 (td, *J* =8.0, 1.9 Hz, 1H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.57 – 7.53 (m, 2H), 7.47 (dd, *J* = 9.2, 7.5 Hz, 1H), 7.45 – 7.42 (m, 3H), 7.03 (dd, *J* = 7.6, 0.8 Hz, 1H), 6.50 (dd, *J* = 9.2, 1.0 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.35, 162.45, 150.33, 148.41, 140.94, 139.42, 139.12, 132.15, 132.13, 128.41, 127.46, 125.42, 124.38, 117.07, 99.17. IR (KBr) *v* : 3427, 3180, 3092, 2992, 1682, 1533, 1432, 1366, 1277. HRMS (ESI) *m/z* calcd for $C_{17}H_{13}BrN_3O_2$ $[M + H]^+$ 370.0186, found 370.0175.

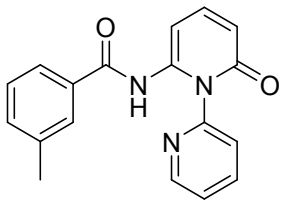
4-methyl-*N*-(2-oxo-2*H*-[1,2'-bipyridin]-6-yl)benzamide (3f):



3f

Product **3f** was isolated as an off-white solid (58 mg, 48%); m.p. 201-203 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.36 (s, 1H), 8.68 (d, *J* = 4.4 Hz, 1H), 7.94 (td, *J* = 7.8, 1.8 Hz, 1H), 7.61 (d, *J* = 8.2 Hz, 1H), 7.50 – 7.40 (m, 4H), 7.20 (d, *J* = 8.2 Hz, 2H), 7.09 (d, *J* = 7.6 Hz, 1H), 6.48 (d, *J* = 9.2 Hz, 1H), 2.37 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.14, 162.55, 150.30, 148.54, 143.29, 141.10, 139.50, 139.47, 130.40, 129.51, 126.87, 125.47, 124.38, 116.54, 98.89, 21.45. IR (KBr) *v* : 3423, 3246, 3039, 1676, 1603, 1537, 1435, 1366, 1280. HRMS (ESI) *m/z* calcd for $C_{18}H_{16}N_3O_2$ $[M + H]^+$ 306.1237, found 306.1251.

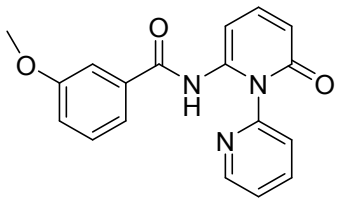
3-methyl-*N*-(2-oxo-2*H*-[1,2'-bipyridin]-6-yl)benzamide (3g):



3g

Product **3g** was isolated as an off-white solid (79 mg, 80%); m.p. 147-151 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.19 (s, 1H), 8.56 (d, J = 4.8 Hz, 1H), 7.91 (td, J = 7.8, 1.8 Hz, 1H), 7.60 (dd, J = 9.2, 7.2 Hz, 1H), 7.44 – 7.36 (m, 2H), 7.30 (d, J = 3.6 Hz, 1H), 7.28 – 7.22 (m, 3H), 6.49 (d, J = 9.2 Hz, 1H), 6.37 (d, J = 7.0 Hz, 1H), 2.27 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 166.27, 162.79, 150.75, 149.21, 141.26, 141.06, 138.51, 138.12, 133.34, 133.03, 128.67, 128.37, 125.04, 124.88, 124.46, 119.08, 104.46, 21.26. IR (KBr) v : 3169, 3058, 2987, 1671, 1586, 1518, 1468, 1377, 1280. HRMS (ESI) *m/z* calcd for $C_{18}H_{16}N_3O_2$ $[M + H]^+$ 306.1237, found 306.1243.

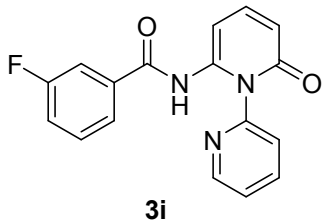
3-methoxy-*N*-(2-oxo-2*H*-[1,2'-bipyridin]-6-yl)benzamide (3h):



3h

Product **3h** was isolated as an off-white solid (123 mg, 96%); m.p. 148-151 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.43 (s, 1H), 8.68 (s, 1H), 7.96 (t, J = 7.6 Hz, 1H), 7.63 (d, J = 8.0 Hz, 1H), 7.50-7.40 (m, 2H), 7.30 (t, J = 8.4 Hz, 1H), 7.17 (s, 1H), 7.09 (d, J = 7.4 Hz, 1H), 7.07 – 6.99 (m, 2H), 6.50 (d, J = 9.2 Hz, 1H), 3.81 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.08, 162.52, 159.90, 150.29, 148.63, 141.04, 139.39, 139.33, 134.67, 129.81, 125.34, 124.35, 118.73, 118.42, 116.73, 112.25, 98.95, 55.39. IR (KBr) v : 3445, 3062, 2837, 1670, 1597, 1525, 1414, 1366, 1272. HRMS (ESI) *m/z* calcd for $C_{18}H_{15}N_3NaO_3$ $[M + Na]^+$ 344.1006, found 344.1004.

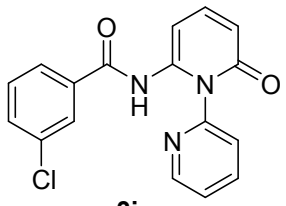
3-fluoro-*N*-(2-oxo-2*H*-[1,2'-bipyridin]-6-yl)benzamide (3i):



3i

Product **3i** was isolated as an off-white solid (117 mg, 95%); m.p. 178-182 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.12 (d, *J* = 15.6 Hz, 1H), 8.72 (dd, *J* = 5.0, 1.2 Hz, 1H), 8.06 (td, *J* = 8.0, 1.8 Hz, 1H), 7.96 (td, *J* = 7.8, 1.8 Hz, 1H), 7.55 (d, *J* = 8.0 Hz, 1H), 7.52 – 7.44 (m, 3H), 7.26 (td, 1H), 7.18 (d, *J* = 7.6 Hz, 1H), 7.02 (ddd, *J* = 12.4, 8.2, 0.8 Hz, 1H), 6.50 (dd, *J* = 9.2, 0.8 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.51, 162.94 (d, *J* = 2.5 Hz), 162.43, 161.86, 150.31, 148.46, 140.90, 139.38, 139.06, 135.52 (d, *J* = 6.9 Hz), 130.54 (d, *J* = 7.9 Hz), 124.87 (d, *J* = 150.7 Hz), 122.23 (d, *J* = 3.0 Hz), 119.56 (d, *J* = 21.3 Hz), 117.14, 114.39 (d, *J* = 23.3 Hz), 99.18. ^{19}F NMR (376 MHz, $CDCl_3$) δ -113.96. IR (KBr) *v* : 3415, 3054, 1682, 1529, 1473, 1380, 1296, 1271. HRMS (ESI) *m/z* calcd for $C_{17}H_{13}FN_3O_2$ $[M + H]^+$ 310.0986, found 310.0982.

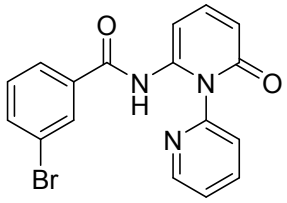
3-chloro-*N*-(2-oxo-2*H*-[1,2'-bipyridin]-6-yl)benzamide (3j):



3j

Product **3j** was isolated as an off-white solid (91 mg, 70%); m.p.188-191 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.66 (s, 1H), 8.66 (d, *J* = 3.8 Hz, 1H), 7.96 (td, *J* = 8.0, 1.4 Hz, 1H), 7.64 (d, *J* = 8.0 Hz, 1H), 7.53 (d, *J* = 1.6 Hz, 1H), 7.51 – 7.42 (m, 4H), 7.35 (t, *J* = 8.0 Hz, 1H), 7.04 (d, *J* = 7.4 Hz, 1H), 6.51 (d, *J* = 9.2 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.85, 162.41, 150.31, 148.38, 140.92, 139.49, 139.04, 135.06, 135.05, 132.49, 130.16, 127.31, 125.45, 124.94, 124.41, 117.18, 99.12. IR (KBr) *v* : 3451, 2965, 1680, 1605, 1537, 1441, 1373, 1252. HRMS (ESI) *m/z* calcd for $C_{17}H_{13}ClN_3O_2$ $[M + H]^+$ 326.0691, found 326.0684.

3-bromo-*N*-(2-oxo-2*H*-[1,2'-bipyridin]-6-yl)benzamide (3k):

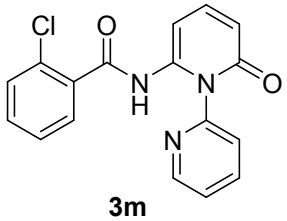


3k

Product **3k** was isolated as an off-white solid (145 mg, 98%); m.p.198 -199 °C;

^{1}H NMR (600 MHz, $CDCl_3$) δ 9.67 (s, 1H), 8.69 (d, *J* = 3.4 Hz, 1H), 7.97 (t, *J* = 7.6 Hz, 1H), 7.70-7.62 (m, 3H), 7.52 (d, *J* = 7.8 Hz, 1H), 7.51-7.44 (m, 2H), 7.30 (t, *J* = 8.0 Hz, 1H), 7.05 (d, *J* = 7.4 Hz, 1H), 6.51 (d, *J* = 9.2 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.71, 162.41, 150.34, 148.45, 140.92, 139.45, 139.02, 135.39, 135.23, 130.41, 130.15, 125.48, 125.40, 124.41, 122.97, 117.15, 99.04. IR (KBr) *v* : 3428, 3100, 2946, 1678, 1603, 1533, 1470, 1373, 1251. HRMS (ESI) *m/z* calcd for $C_{17}H_{13}BrN_3O_2$ $[M + H]^+$ 370.0186, found 370.0195.

2-chloro-*N*-(2-oxo-2*H*-[1,2'-bipyridin]-6-yl)benzamide (3m)

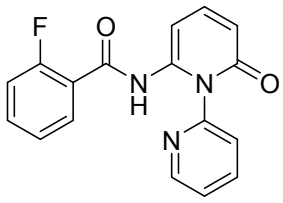


3m

Product **3m** was isolated as an off-white solid (65 mg, 50%); m.p. 170-175 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.97 (s, 1H), 8.53 (dd, *J* = 4.8, 1.2 Hz, 1H), 7.95 (td, *J* = 7.8, 1.8 Hz, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.57 – 7.52 (m, 1H), 7.48 (dd, *J* = 8.8, 7.8 Hz, 1H), 7.45 – 7.34 (m, 2H), 7.32-7.26 (m, 2H), 7.12-7.05 (m, 1H), 6.51 (d, *J* = 9.2 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.58, 162.48, 149.95, 149.32, 140.89, 139.30, 138.72, 133.51, 132.31, 130.71, 130.39, 130.18, 127.30, 125.22, 124.43, 117.30, 99.56. IR (KBr) *v* : 3443, 2965, 1677, 1604, 1519, 1429, 1370, 1252. HRMS (ESI) *m/z* calcd for $C_{17}H_{13}ClN_3O_2$ $[M + H]^+$ 326.0691, found 326.0685.

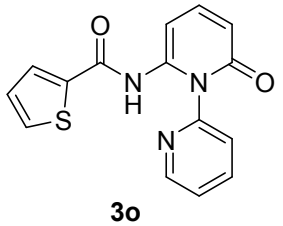
2-fluoro-*N*-(2-oxo-2*H*-[1,2'-bipyridin]-6-yl)benzamide (3n):



3n

Product **3n** was isolated as an off-white solid (108 mg, 87%); m.p. 183 -186 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.61 (s, 1H), 8.66 (dd, *J* = 4.8, 1.2 Hz, 1H), 7.95 (td, *J* = 8.0, 1.8 Hz, 1H), 7.64 (d, *J* = 8.2 Hz, 1H), 7.50 – 7.43 (m, 2H), 7.42 – 7.36 (m, 1H), 7.33 – 7.28 (m, 2H), 7.25 – 7.19 (m, 1H), 7.05 (dd, *J* = 7.4, 0.8 Hz, 1H), 6.51 (dd, *J* = 9.2, 1.0 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.46, 160.89, 160.25 (d, *J* = 3.2 Hz), 159.24, 149.72 (d, *J* = 8.4 Hz), 140.92, 139.21 (d, *J* = 3.0 Hz), 134.50 (d, *J* = 9.6 Hz), 132.34 (d, *J* = 0.8 Hz), 125.08 (d, *J* = 3.2 Hz), 124.84, 124.39, 119.80 (d, *J* = 10.6 Hz), 116.71, 116.13, 115.97, 99.09. ^{19}F NMR (376 MHz, $CDCl_3$) δ -110.79. IR (KBr) *v* : 3424, 3181, 3062, 2995, 1678, 1603, 1529, 1417, 1370, 1277. HRMS (ESI) *m/z* calcd for $C_{17}H_{13}FN_3O_2$ $[M + H]^+$ 310.0986, found 310.0981.

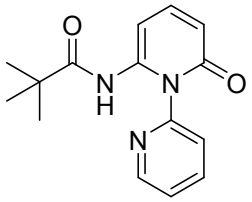
***N*-(2-oxo-2*H*-[1,2'-bipyridin]-6-yl)thiophene-2-carboxamide (3o):**



3o

Product **3o** was isolated as an off-white solid (59 mg, 50%); m.p. 166 -170 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.46 (s, 1H), 8.72 (d, *J* = 3.2 Hz, 1H), 7.97 (t, *J* = 7.4 Hz, 1H), 7.64 (d, *J* = 7.8 Hz, 1H), 7.52 (d, *J* = 4.8 Hz, 1H), 7.46 (t, *J* = 8.2 Hz, 2H), 7.30 (d, *J* = 3.4 Hz, 1H), 7.08-7.00 (m, 2H), 6.49 (d, *J* = 9.2 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.40, 158.50, 150.32, 148.55, 141.00, 139.40, 139.00, 137.89, 131.82, 129.01, 127.99, 125.37, 124.35, 116.64, 98.73. IR (KBr) *v* : 3440, 3092, 2971, 1651, 1526, 1288 HRMS (ESI) *m/z* calcd for $C_{15}H_{12}N_3O_2S$ $[M + H]^+$ 298.0645, found 298.0656.

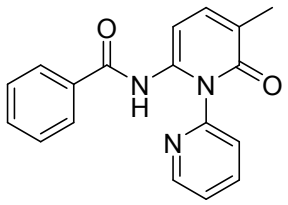
***N*-(2-oxo-2*H*-[1,2'-bipyridin]-6-yl)pivalamide (3p):**



3p

Product **3p** was isolated as an off-white solid (57 mg, 53%); m.p. 176-180 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.67 (s, 1H), 8.48 (s, 1H), 7.96 (t, *J* = 7.6 Hz, 1H), 7.56 (d, *J* = 7.8 Hz, 1H), 7.48-7.40 (m, 2H), 6.88 (d, *J* = 6.2 Hz, 1H), 6.45 (d, *J* = 9.2 Hz, 1H), 1.00 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 175.77, 162.49, 150.26, 148.85, 140.93, 139.30, 139.27, 125.13, 124.24, 116.42, 98.98, 39.74, 26.88. IR (KBr) *v* : 3161, 3083, 2964, 2870, 1683, 1605, 1540, 1385, 1270. HRMS (ESI) *m/z* calcd for $C_{15}H_{17}N_3NaO_2$ $[M + Na]^+$ 294.1213, found 294.1218.

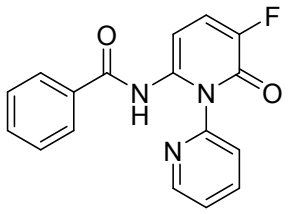
***N*-(3-methyl-2-oxo-2*H*-[1,2'-bipyridin]-6-yl)benzamide (4a):**



4a

Product **4a** was isolated as an off-white solid (100 mg, 82%); m.p. 202 -204 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.22 (s, 1H), 8.63 (d, *J* = 3.8 Hz, 1H), 7.91 (td, *J* = 8.0, 1.8 Hz, 1H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.53 (d, *J* = 7.4 Hz, 2H), 7.50 (t, *J* = 7.4 Hz, 1H), 7.44-7.36 (m, 3H), 7.34 (d, *J* = 7.6 Hz, 1H), 6.91 (d, *J* = 7.6 Hz, 1H), 2.17 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.34, 162.74, 150.70, 148.53, 139.11, 137.89, 136.63, 133.35, 132.35, 128.76, 126.81, 126.24, 125.35, 124.14, 99.59, 16.82. IR (KBr) *v* : 3451, 2923, 2778, 1667, 1615, 1559, 1434, 1280. HRMS (ESI) *m/z* calcd for $C_{18}H_{16}N_3O_2$ $[M + H]^+$ 306.1237, found 306.1247.

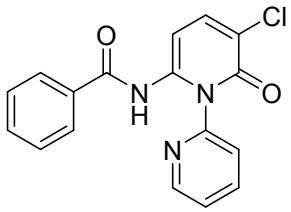
***N*-(3-fluoro-2-oxo-2*H*-[1,2'-bipyridin]-6-yl)benzamide (4b):**



4b

Product **4b** was isolated as an off-white solid (115 mg, 93%); m.p. 242-245 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.34 (s, 1H), 8.57 (d, *J* = 3.8 Hz, 1H), 7.94 (td, *J* = 7.8, 1.8 Hz, 1H), 7.62 (dd, *J* = 10.2, 8.0 Hz, 1H), 7.53 – 7.40 (m, 5H), 7.39-7.34 (m, 2H), 6.36 (dd, *J* =8.0, 4.2 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 166.55, 156.21 (d, *J* = 28.0 Hz), 152.34, 149.97, 149.90, 149.48, 138.89, 136.60 (d, *J* = 4.8 Hz), 133.16, 132.58, 128.85, 127.84, 124.88 (d, *J* = 25.4 Hz), 121.89 (d, *J* = 17.4 Hz), 103.37 (d, *J* = 5.8 Hz). ^{19}F NMR (376 MHz, DMSO-d_6) δ -133.83. IR (KBr) *v* : 3439, 3211, 2947, 1666, 1618, 1560, 1515, 1473, 1434, 1379, 1277. HRMS (ESI) *m/z* calcd for C_{17} H_{13} F N_3 O_2 $[M + H]^+$ 310.0986, found 310.0988.

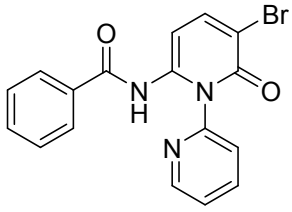
***N*-(3-chloro-2-oxo-2*H*-[1,2'-bipyridin]-6-yl)benzamide (4c):**



4c

Product **4c** was isolated as an off-white solid (106 mg, 82%); m.p. 228-233 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.39 (s, 1H), 8.57 (dd, J = 5.6, 1.8 Hz, 1H), 8.02 – 7.88 (m, 2H), 7.53 – 7.48 (m, 1H), 7.48 – 7.42 (m, 4H), 7.40-7.35 (m, 2H), 6.46 (d, J = 7.8 Hz, 1H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 166.33, 158.83, 150.40, 149.39, 140.26, 139.42, 138.84, 133.14, 132.61, 128.83, 127.85, 124.94, 124.79, 123.42, 104.60. IR (KBr) v : 3213, 3106, 2968, 1670, 1591, 1522, 1357, 1270. HRMS (ESI) m/z calcd for $C_{17}H_{13}ClN_3O_2$ $[M + H]^+$ 326.0691, found 326.0690.

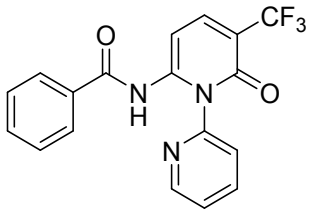
***N*-(3-bromo-2-oxo-2*H*-[1,2'-bipyridin]-6-yl)benzamide (4d):**



4d

Product **4d** was isolated as an off-white solid (136 mg, 92%); m.p. 210 -212 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.35 (s, 1H), 8.62 – 8.52 (m, 1H), 8.13 (d, J = 7.8 Hz, 1H), 7.94 (td, J = 7.8, 1.8 Hz, 1H), 7.52 – 7.48 (m, 1H), 7.48 – 7.42 (m, 4H), 7.40-7.35 (m, 2H), 6.40 (d, J = 7.8 Hz, 1H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 166.25, 158.94, 150.52, 149.37, 143.17, 141.03, 138.83, 133.12, 132.63, 128.85, 127.85, 124.93, 124.79, 113.77, 105.22. IR (KBr) v : 3443, 3057, 1670, 1628, 1592, 1529, 1472, 1434, 1358, 1262. HRMS (ESI) m/z calcd for $C_{17}H_{13}BrN_3O_2$ $[M + H]^+$ 370.0186, found 370.0174.

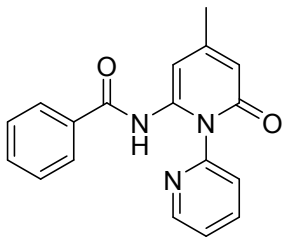
***N*-(2-oxo-3-(trifluoromethyl)-2*H*-[1,2'-bipyridin]-6-yl)benzamide (4e):**



4e

Product **4e** was isolated as an off-white solid (40 mg, 28%); m.p. 211-219 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.75 (s, 1H), 8.72 (d, *J* = 3.6 Hz, 1H), 8.00 (t, *J* = 7.8 Hz, 1H), 7.88 (d, *J* = 8.2 Hz, 1H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.62 – 7.48 (m, 4H), 7.46-7.40 (m, 2H), 7.33 (d, *J* = 8.2 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.09, 158.32, 149.27, 148.79, 143.54, 140.69 (q, *J* = 4.8 Hz), 139.64, 133.04, 132.86, 129.04, 126.93, 125.55, 124.96, 122.76 (d, *J* = 271.0 Hz), 115.50 (q, *J* = 31.6 Hz), 95.79. ^{19}F NMR (376 MHz, $CDCl_3$) δ -65.03. IR (KBr) *v* : 3408, 3152, 3058, 1682, 1560, 1525, 1375, 1252. HRMS (ESI) *m/z* calcd for $C_{18}H_{12}F_3N_3NaO_2$ $[M + Na]^+$ 382.0774, found 382.0772.

***N*-(4-methyl-2-oxo-2*H*-[1,2'-bipyridin]-6-yl)benzamide (4f):**

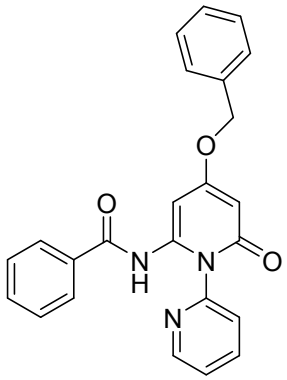


4f

Product **4f** was isolated as an off-white solid (114 mg, 93%); m.p. 197-200 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.56 (s, 1H), 8.65 (d, *J* = 4.0 Hz, 1H), 7.96– 7.88 (m, 1H), 7.62 (d, *J* = 8.0 Hz, 1H), 7.60 – 7.55 (m, 2H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.41 (t, *J* = 7.8 Hz, 3H), 6.98 (d, *J* = 1.0 Hz, 1H), 6.31 (s, 1H), 2.27 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.24, 162.34, 152.93, 150.42, 148.38, 139.21, 138.21, 133.35, 132.46, 128.81, 126.83, 125.48, 124.13, 115.33, 101.45, 21.97. IR (KBr) *v* : 3247, 3057, 2916, 1685, 1525, 1435, 1351, 1273. HRMS (ESI) *m/z* calcd for $C_{18}H_{16}N_3O_2$

$[M + H]^+$ 306.1237, found 306.1245.

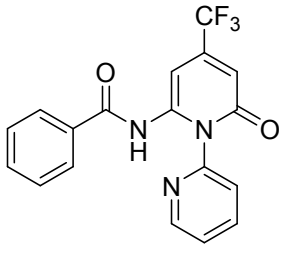
***N*-(4-(benzyloxy)-2-oxo-2*H*-[1,2'-bipyridin]-6-yl)benzamide (4g):**



4g

Product **4g** was isolated as an off-white solid (122 mg, 77%); m.p. 172-175 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.66 (s, 1H), 8.66 (s, 1H), 7.93 (t, *J* = 7.8 Hz, 1H), 7.65-7.54 (m, 3H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.46 – 7.38 (m, 7H), 7.38 – 7.34 (m, 1H), 7.03 (d, *J* = 2.0 Hz, 1H), 5.93 (s, 1H), 5.09 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.22, 164.18, 163.61, 150.35, 148.30, 139.50, 139.21, 135.21, 133.34, 132.52, 128.84, 128.66, 128.37, 127.55, 126.87, 125.66, 124.08, 94.66, 93.67, 70.32. IR (KBr) *v* : 3442, 3061, 1666, 1556, 1532, 1436, 1352, 1263. HRMS (ESI) *m/z* calcd for $C_{24}H_{20}N_3O_3$ $[M + H]^+$ 398.1499, found 398.1492.

***N*-(2-oxo-4-(trifluoromethyl)-2*H*-[1,2'-bipyridin]-6-yl)benzamide (4h):**

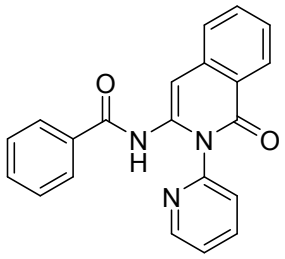


4h

Product **4h** was isolated as an off-white solid (82 mg, 57%); m.p. 173-179 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.69 (s, 1H), 8.78 – 8.65 (m, 1H), 8.01 (td, *J* =8.0, 1.8 Hz, 1H), 7.64 (d, *J* = 8.2 Hz, 1H), 7.60 – 7.53 (m, 3H), 7.51 (dd, *J* = 7.0, 5.4 Hz, 1H), 7.44 (t, *J* = 7.8 Hz, 2H), 7.40 (d, *J* = 1.6 Hz, 1H), 6.75 (s, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.08, 161.49, 149.65, 148.84, 142.63 (d, *J* = 33.8 Hz), 141.31, 139.75,

132.92, 132.90, 129.01, 126.88, 125.21, 124.87, 122.12 (d, J = 274.2 Hz), 113.56 (q, J = 4.2 Hz), 93.34 (d, J = 2.8 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -67.01. IR (KBr) v : 3146, 3078, 2927, 1702, 1614, 1525, 1438, 1358, 1284. HRMS (ESI) *m/z* calcd for $C_{18}H_{13}F_3N_3O_2$ $[M + H]^+$ 360.0954, found 360.0951.

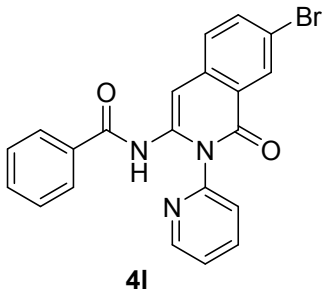
***N*-(1-oxo-2-(pyridin-2-yl)-1,2-dihydroisoquinolin-3-yl)benzamide (4k):**



4k

Product **4k** was isolated as an off-white solid (134 mg, 98%); m.p. 199-202 °C (m.p. 96-98 °C)[3]; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.36 (s, 1H), 8.55 (d, J = 4.2 Hz, 1H), 8.37 (d, J = 8.0 Hz, 1H), 7.91 (td, J = 7.8, 1.8 Hz, 1H), 7.67 – 7.61 (m, 2H), 7.59 – 7.55 (m, 2H), 7.52 – 7.47 (m, 2H), 7.46 – 7.42 (m, 1H), 7.40-7.34 (m, 3H), 7.19 (s, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.04, 162.74, 150.80, 148.41, 139.09, 136.89, 133.56, 133.21, 133.07, 132.21, 128.69, 128.04, 126.92, 126.42, 126.37, 125.49, 124.26, 123.92, 100.79. IR (KBr) v : 3165, 3059, 2965, 1666, 1517, 1372, 1269. HRMS (ESI) *m/z* calcd for $C_{21}H_{16}N_3O_2$ $[M + H]^+$ 342.1237, found 342.1238.

***N*-(7-bromo-1-oxo-2-(pyridin-2-yl)-1,2-dihydroisoquinolin-3-yl)benzamide (4l):**

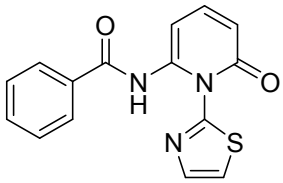


4l

Product **4l** was isolated as an off-white solid (168 mg, 98%); m.p.200 -205 °C;
^{1}H NMR (600 MHz, $CDCl_3$) δ 9.47 (s, 1H), 8.54 (d, J = 3.9 Hz, 1H), 8.19 (d, J = 8.6 Hz, 1H), 7.92 (td, J = 7.8, 1.8 Hz, 1H), 7.62 (t, J = 5.2 Hz, 2H), 7.59 – 7.54 (m, 2H), 7.54 – 7.49 (m, 2H), 7.43 – 7.37 (m, 3H), 7.12 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ

164.89, 162.25, 150.48, 148.51, 139.28, 138.41, 134.47, 133.41, 132.40, 129.80, 129.62, 128.78, 128.64, 128.53, 126.92, 125.52, 124.16, 122.75, 98.99. IR (KBr) *v* : 3443, 3057, 1670, 1628, 1592, 1529, 1472, 1434, 1358, 1262. HRMS (ESI) *m/z* calcd for $C_{21}H_{14}BrN_3NaO_2$ $[M + Na]^+$ 442.0162, found 442.0167.

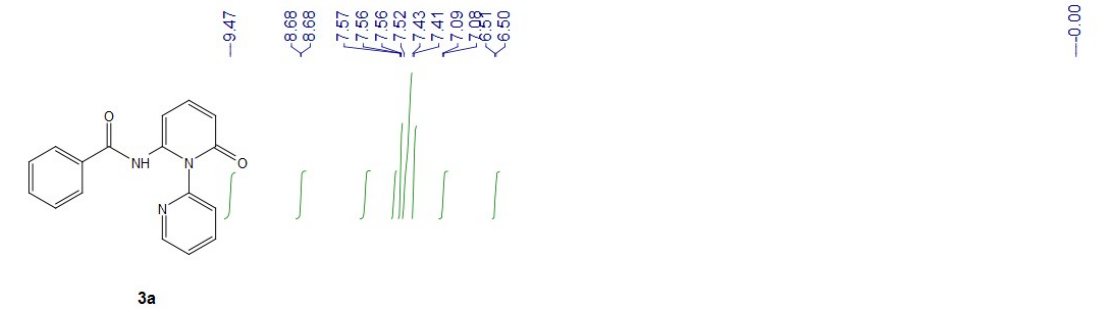
***N*-(6-oxo-1-(thiazol-2-yl)-1,6-dihydropyridin-2-yl)benzamide (4m):**



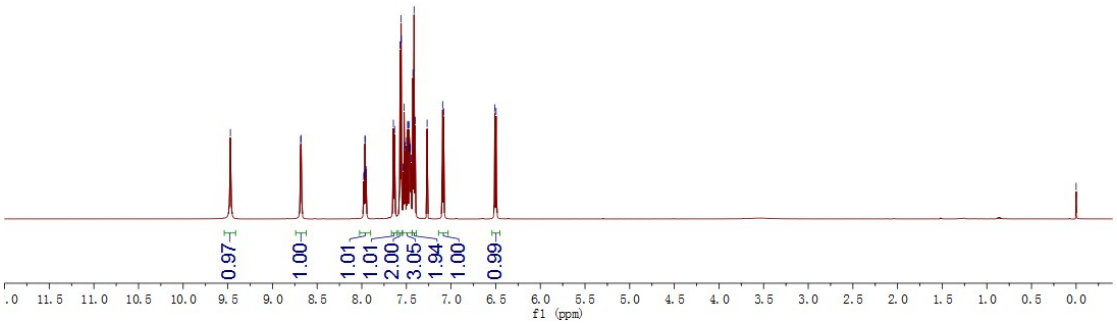
4m

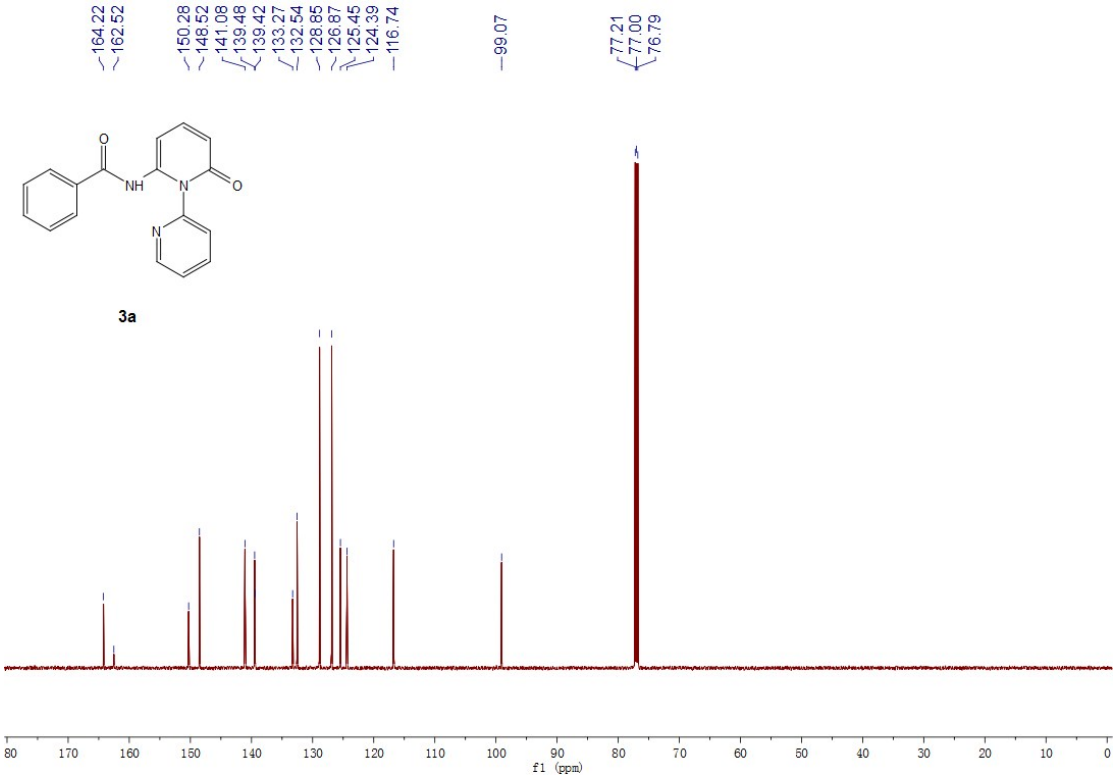
Product **4m** was isolated as an yellow solid (58 mg, 49%); m.p. 136-139 °C;
^{1}H NMR (400 MHz, DMSO) δ 11.84 (s, 1H), 7.84 (dd, *J* = 10.8, 3.6 Hz, 2H), 7.73 (d, *J* = 7.6 Hz, 2H), 7.69 – 7.56 (m, 2H), 7.50 (t, *J* = 7.6 Hz, 2H), 6.87 (d, *J* = 7.2 Hz, 1H), 6.52 (d, *J* = 9.2 Hz, 1H). ^{13}C NMR (101 MHz, DMSO) δ 166.06, 162.16, 157.01, 141.84, 141.38, 138.96, 133.66, 132.80, 129.16, 127.90, 122.81, 117.11, 103.05. IR (KBr) *v* : 3449, 2992, 1674, 1541, 1432, 1409, 1338, 1263. HRMS (ESI) *m/z* calcd for $C_{15}H_{12}N_3O_2S$ $[M + H]^+$ 298.0645, found 298.0647.

7.2 Copies of NMR spectra



3a





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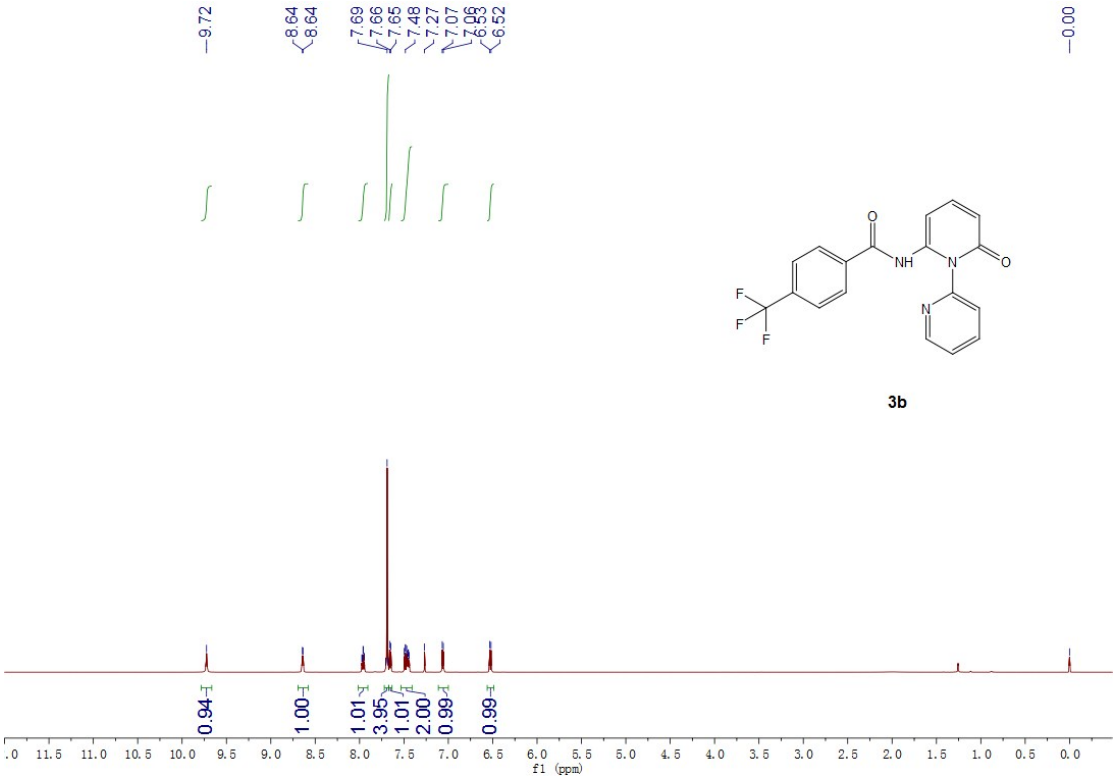
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6.52
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O
F
F
F
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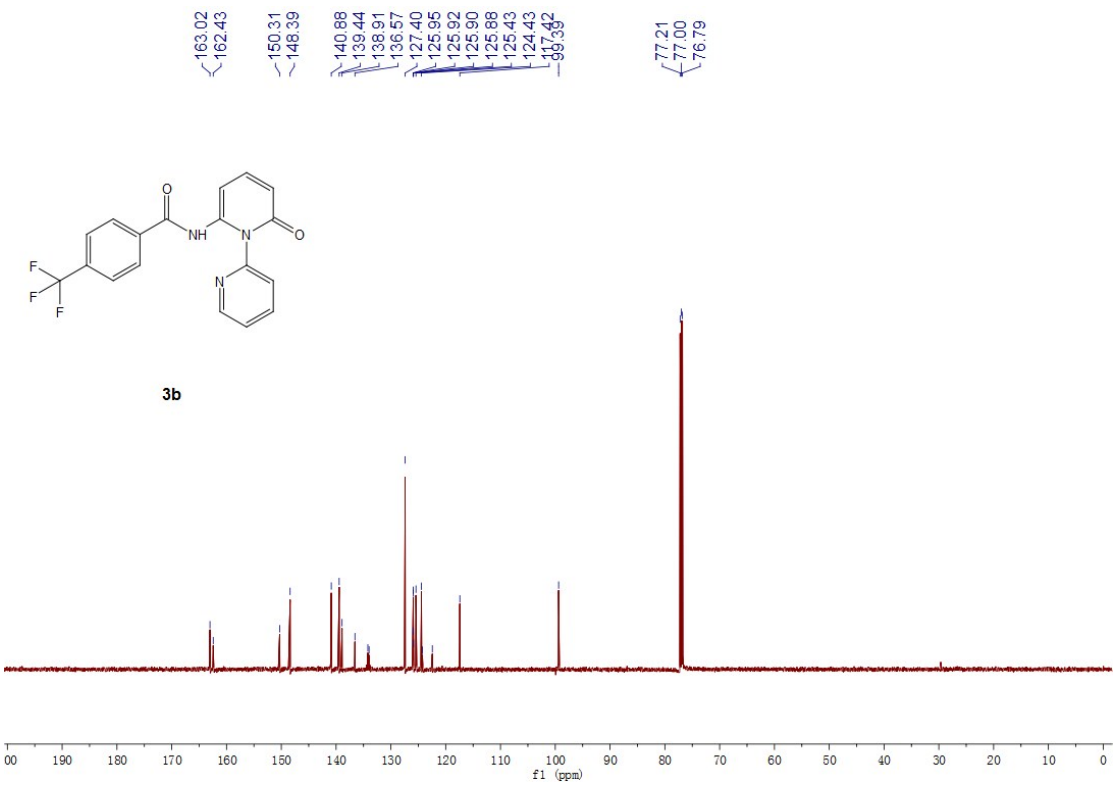
0.99
f1 (ppm)

3b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125.88
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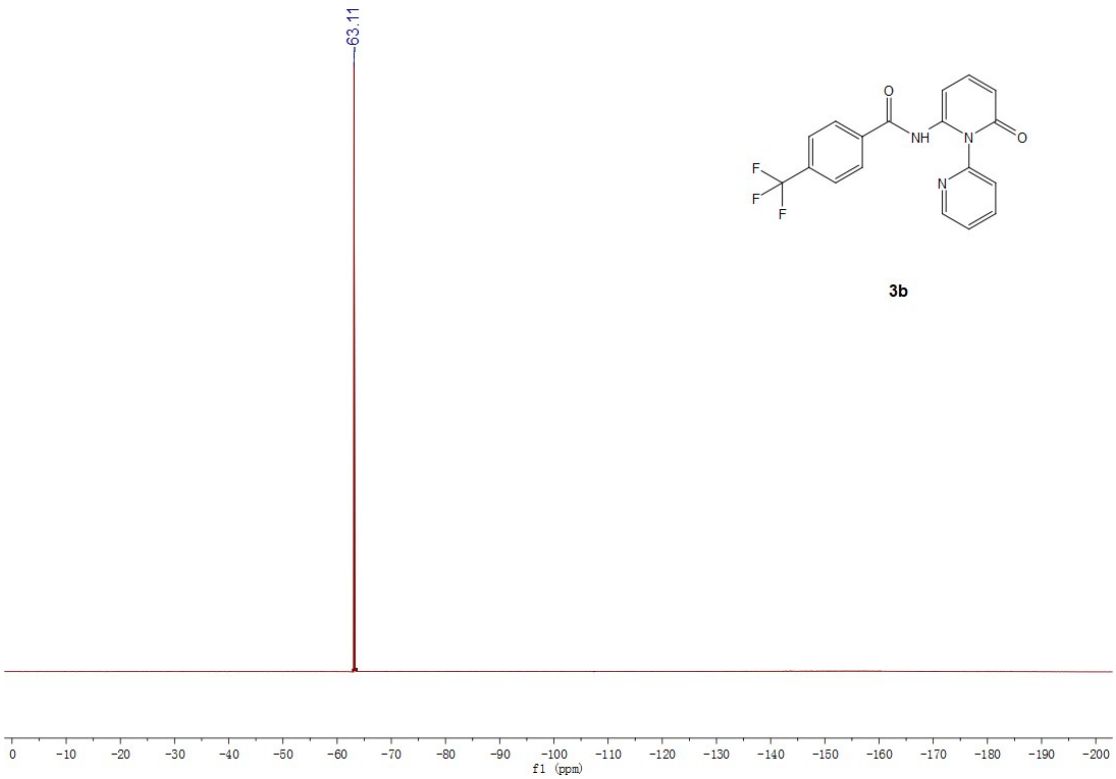
F
F
F
N
f1 (ppm)

3b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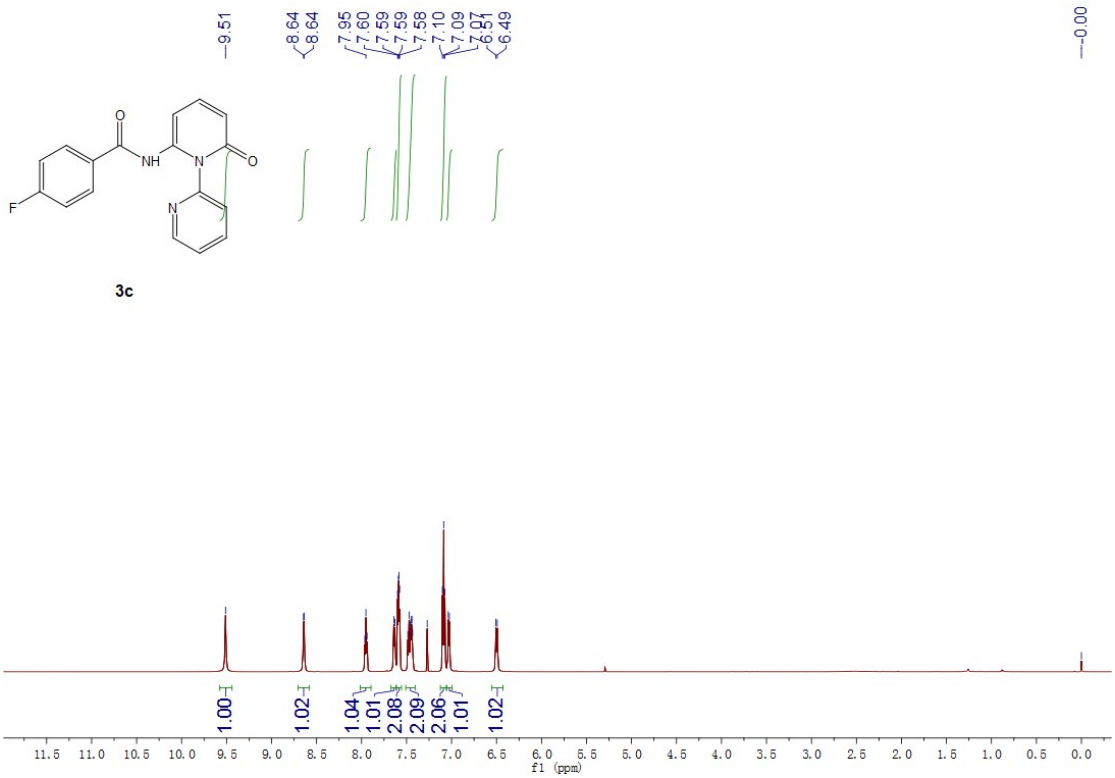
f1 (ppm)

3b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1.01
2.08
2.09
2.06
1.01
1.02
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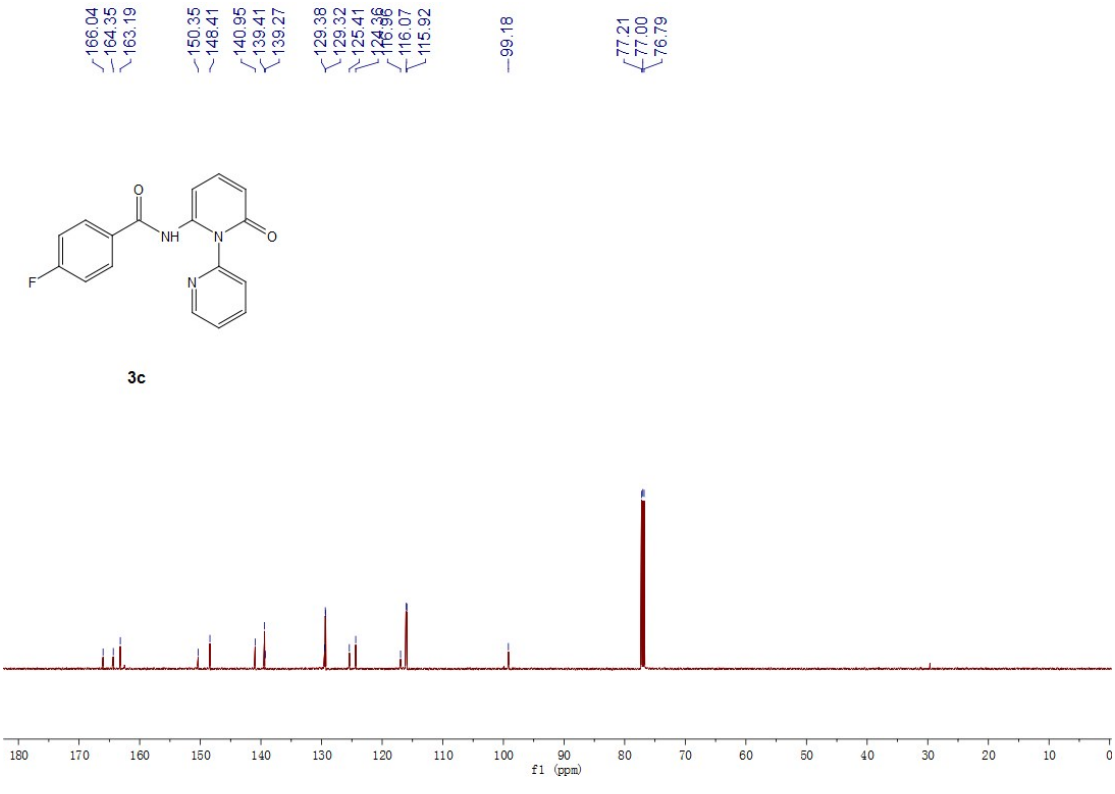
f1 (ppm)

3c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115.92
99.18
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N
O
F
N
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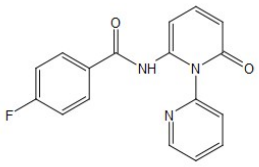
f1 (ppm)

3c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3c

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-180
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-20
f1 (ppm)


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8.62
7.64
7.52
7.51
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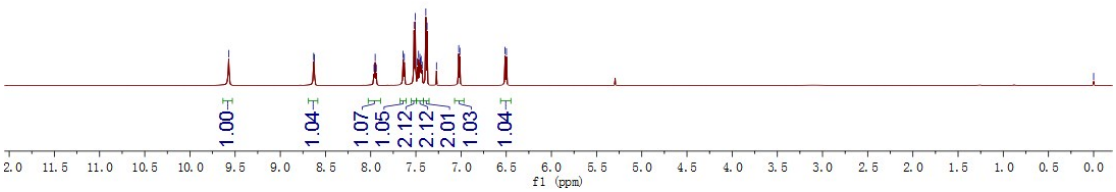
O
Cl
N

3d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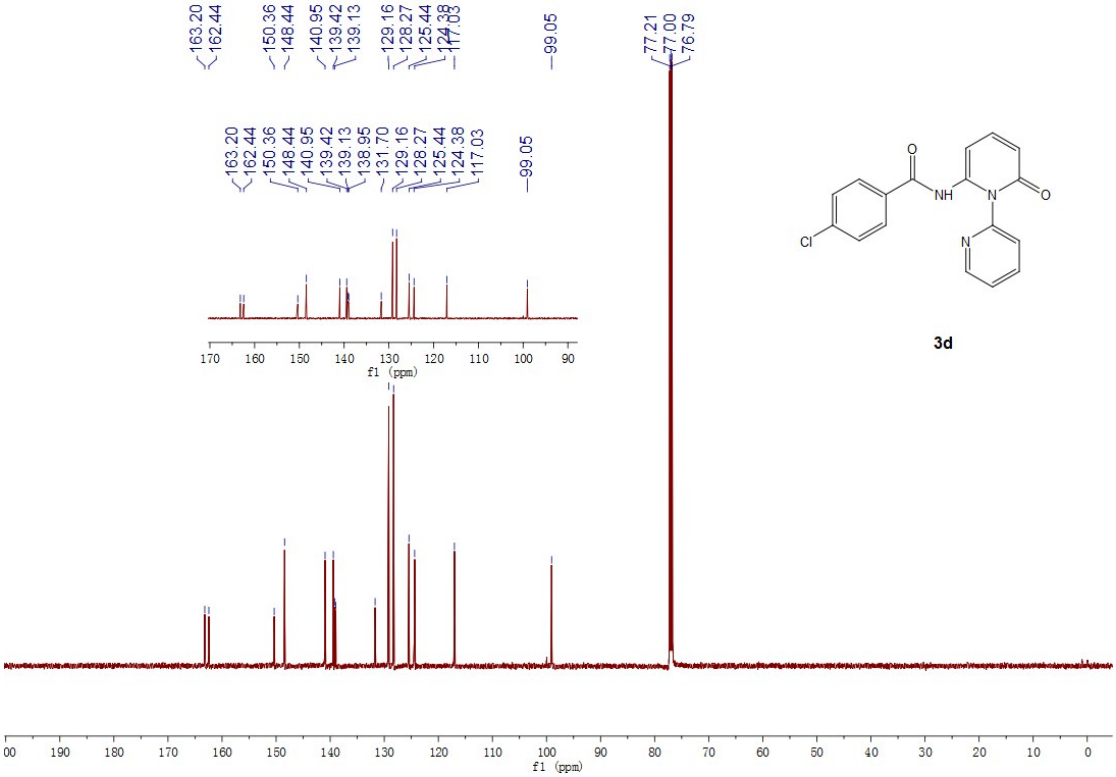
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131.70
f1 (ppm)

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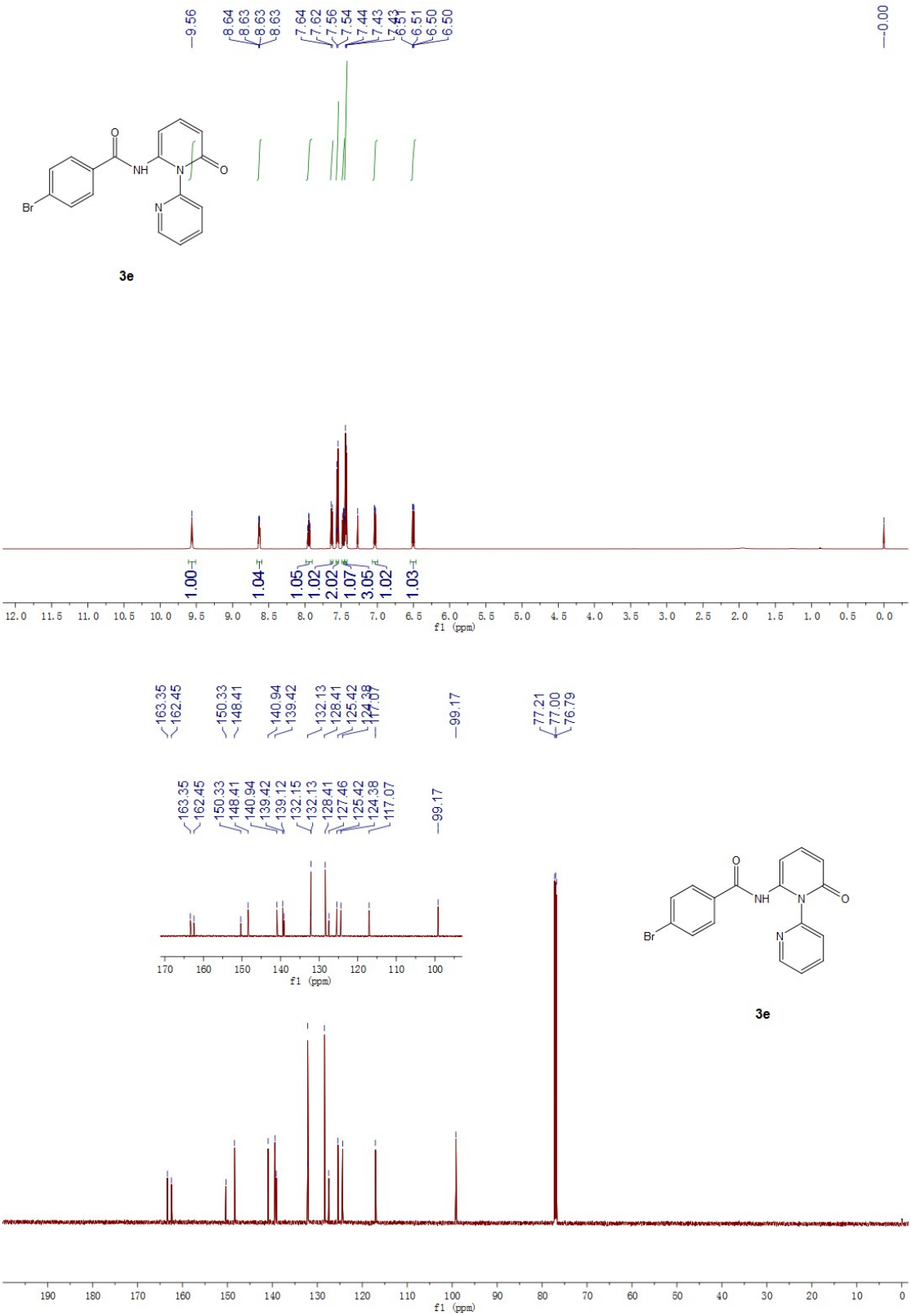
Cl
N

3d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N
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Br
N
3e
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1.04
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1.02
2.02
1.07
3.05
1.02
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124.38
117.07
99.17
170 160 150 140 130 120 110 100
f1 (ppm)
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NH
N
O
Br
N
3e
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


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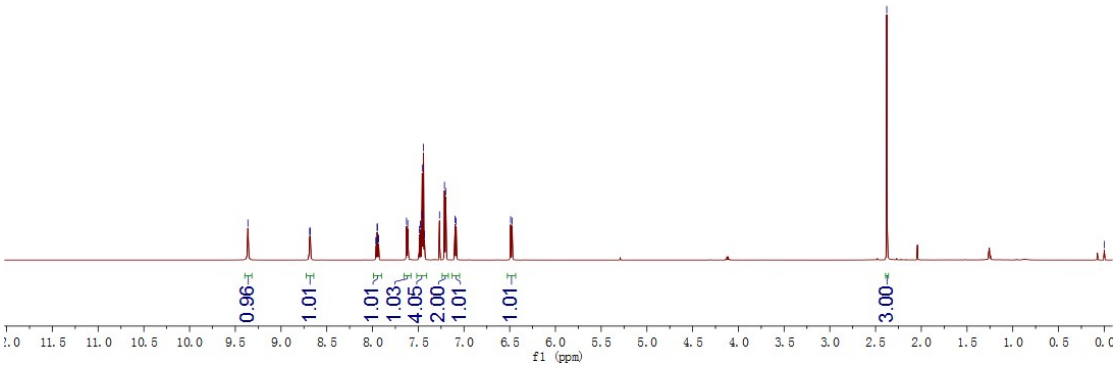
N

3f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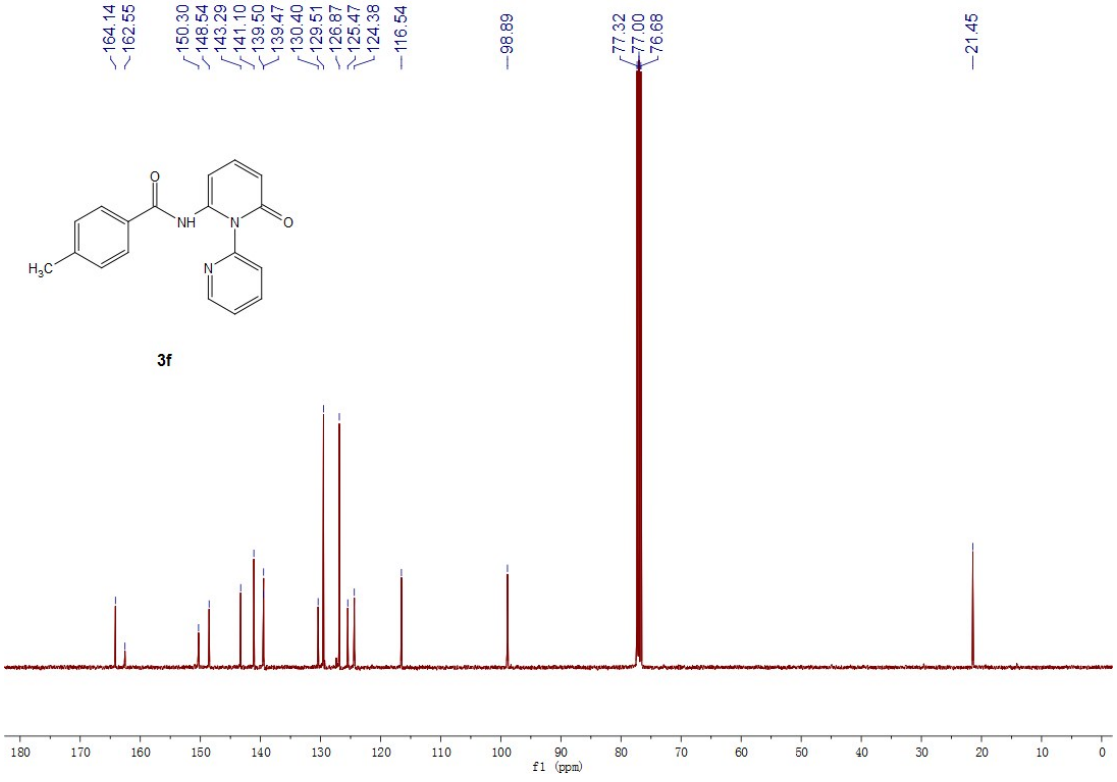
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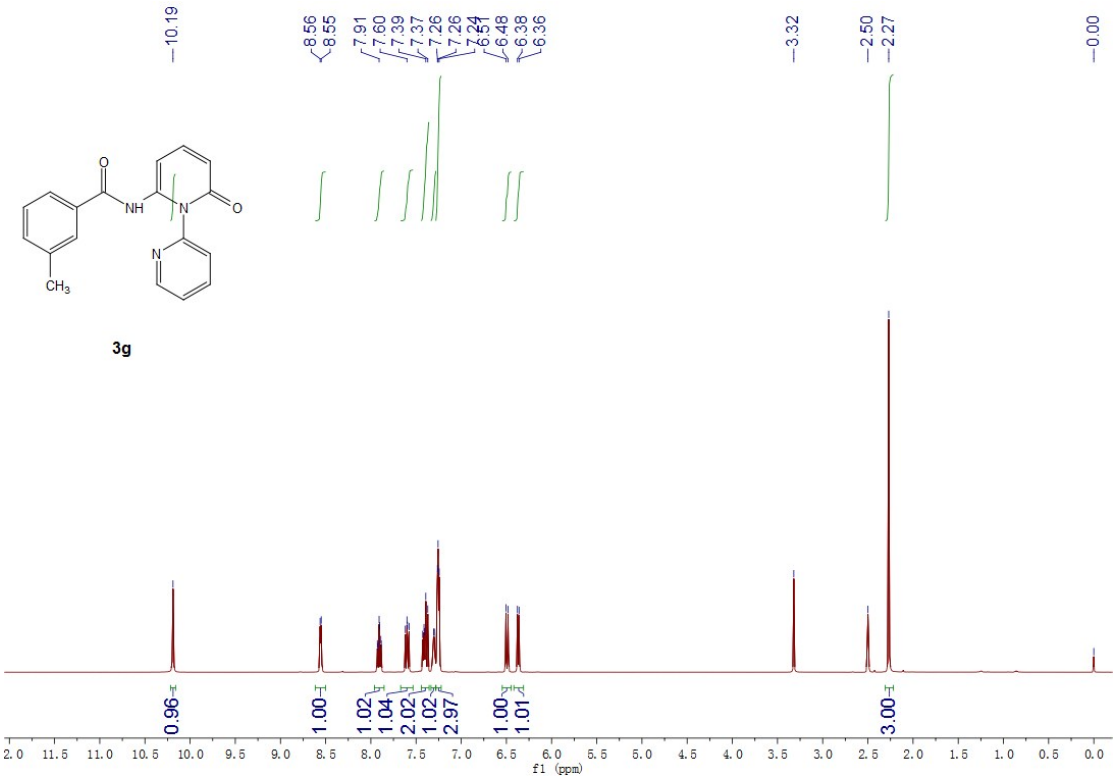
3f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CH3
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1.02
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1.00
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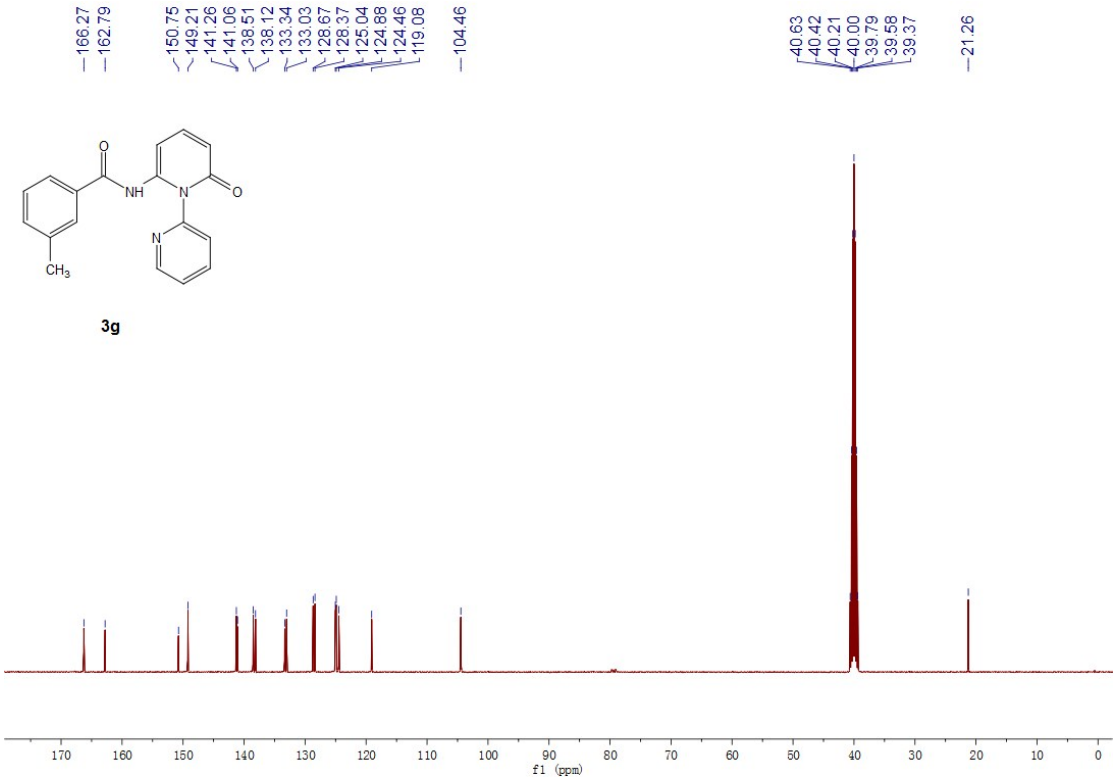
f1 (ppm)

3g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NH
N
O
N
CH3
f1 (ppm)

3g


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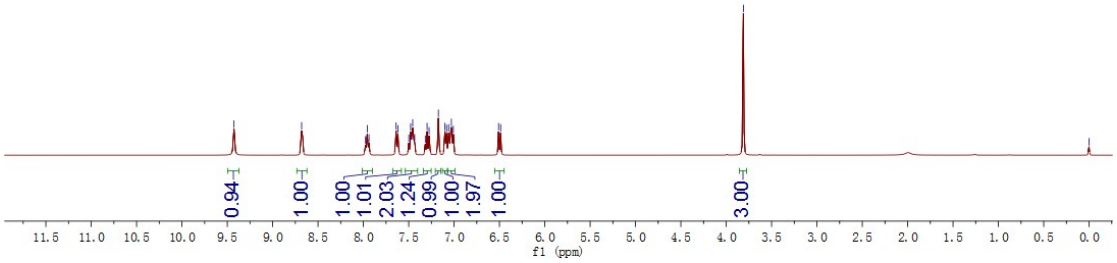
N

3h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1.00
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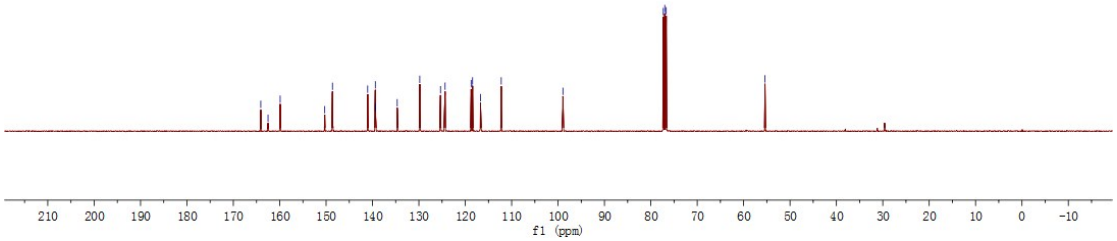
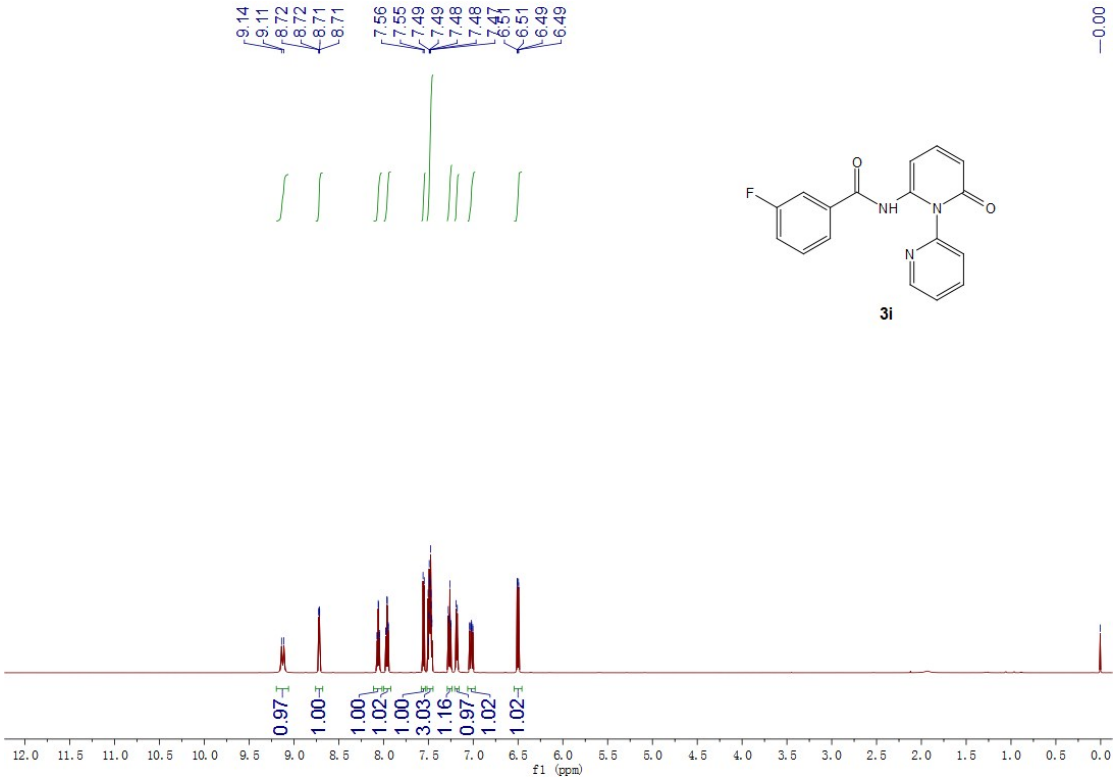
3.00
f1 (ppm)

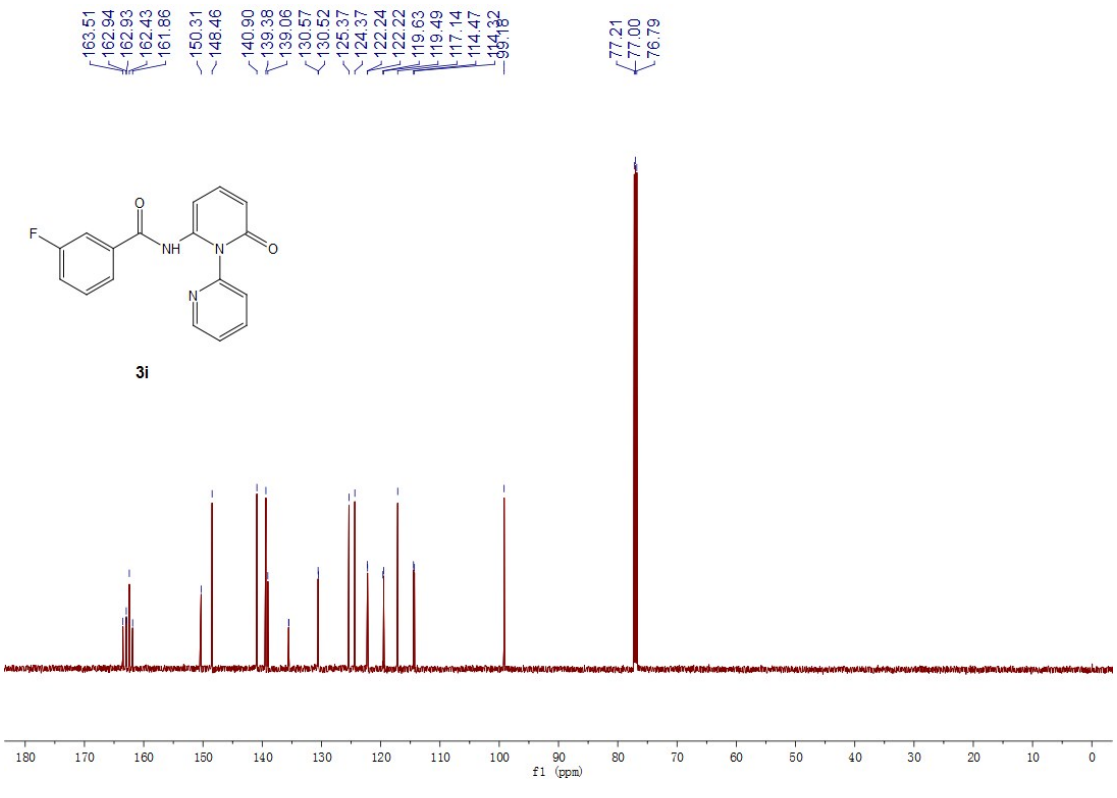

164.08
162.52
159.90
150.29
148.63
141.04
139.39
139.33
134.67
129.81
125.34
124.35
118.73
118.42
116.73
112.25
98.95
77.32
77.00
76.68
55.39

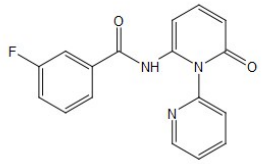

H3C
O
O
NH
N
O
N

3h


f1 (ppm)

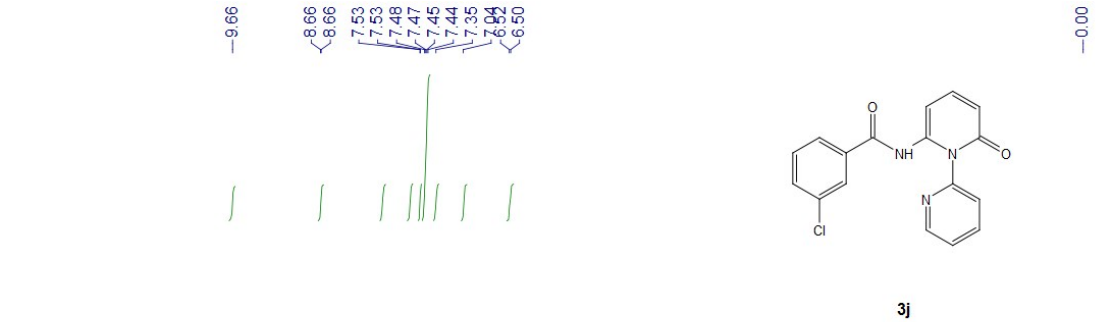

9.14
9.11
8.72
8.72
8.71
8.71
7.56
7.55
7.49
7.49
7.48
7.48
6.51
6.49
6.49
0.00
F
O
NH
N
O
N
3i
0.97
1.00
1.00
1.02
1.00
3.03
1.16
0.97
1.02
1.02
f1 (ppm)


163.51
162.94
162.93
162.43
161.86
150.31
148.46
140.90
139.38
139.06
130.57
130.52
125.37
124.37
122.24
122.22
119.63
119.49
117.14
114.47
77.21
77.00
76.79
F
O
NH
N
O
N
3i
f1 (ppm)

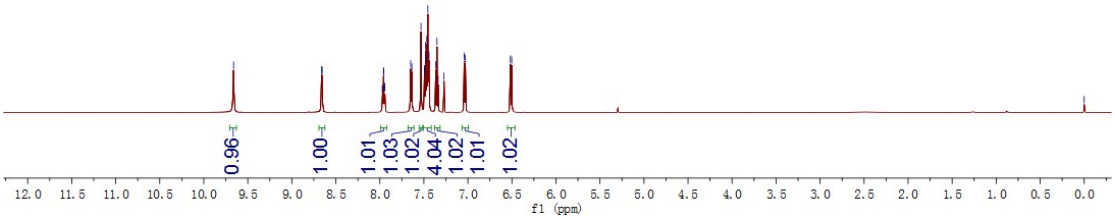

O
F
NH
N
O
N

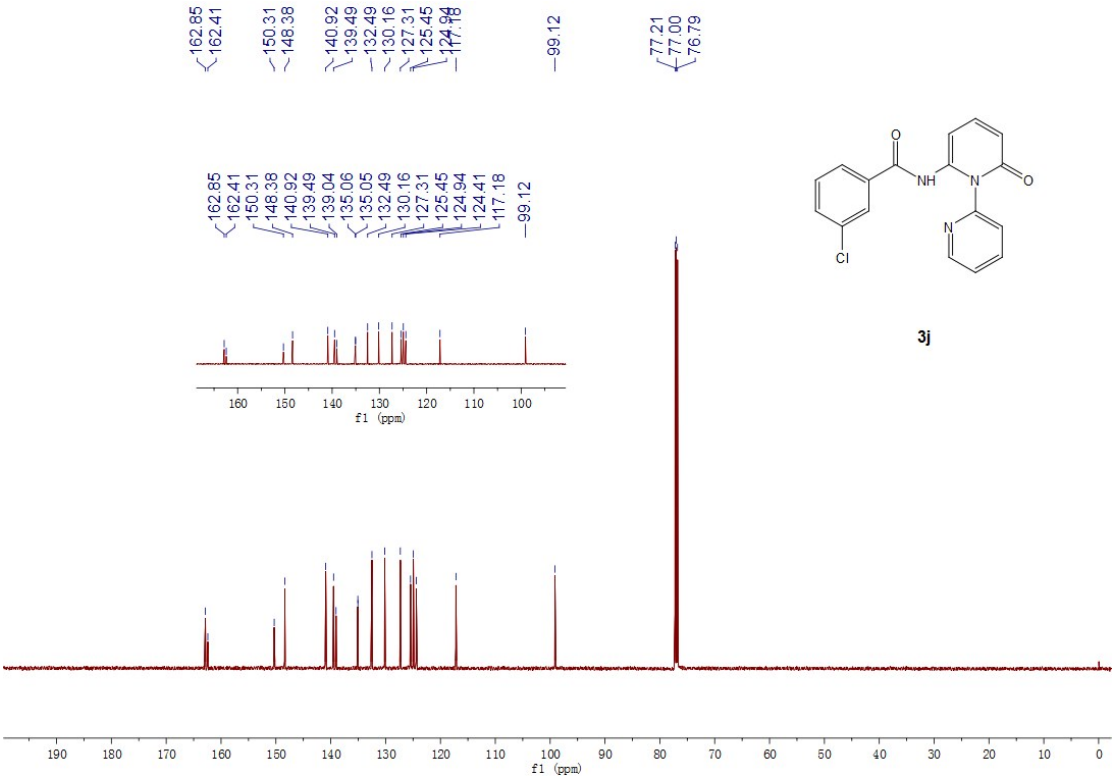
3i

-113.96
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

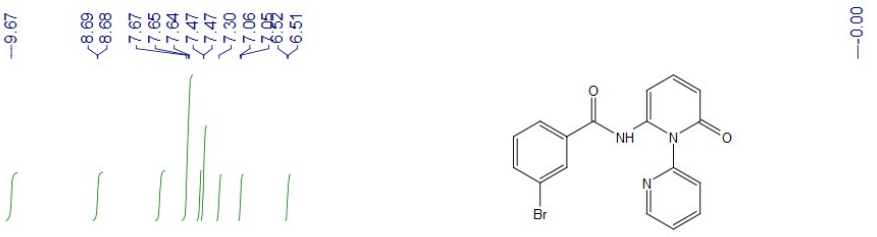

9.66
8.66
8.66
7.53
7.53
7.48
7.47
7.45
7.44
7.35
6.52
6.50
0.00
O
NH
N
O
N
Cl

3j

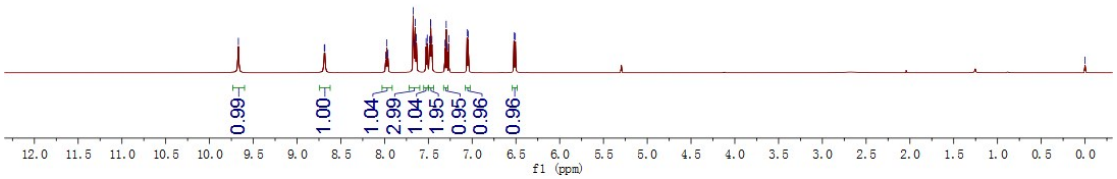

0.96
1.00
1.01
1.03
1.02
4.04
1.02
1.01
1.02
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

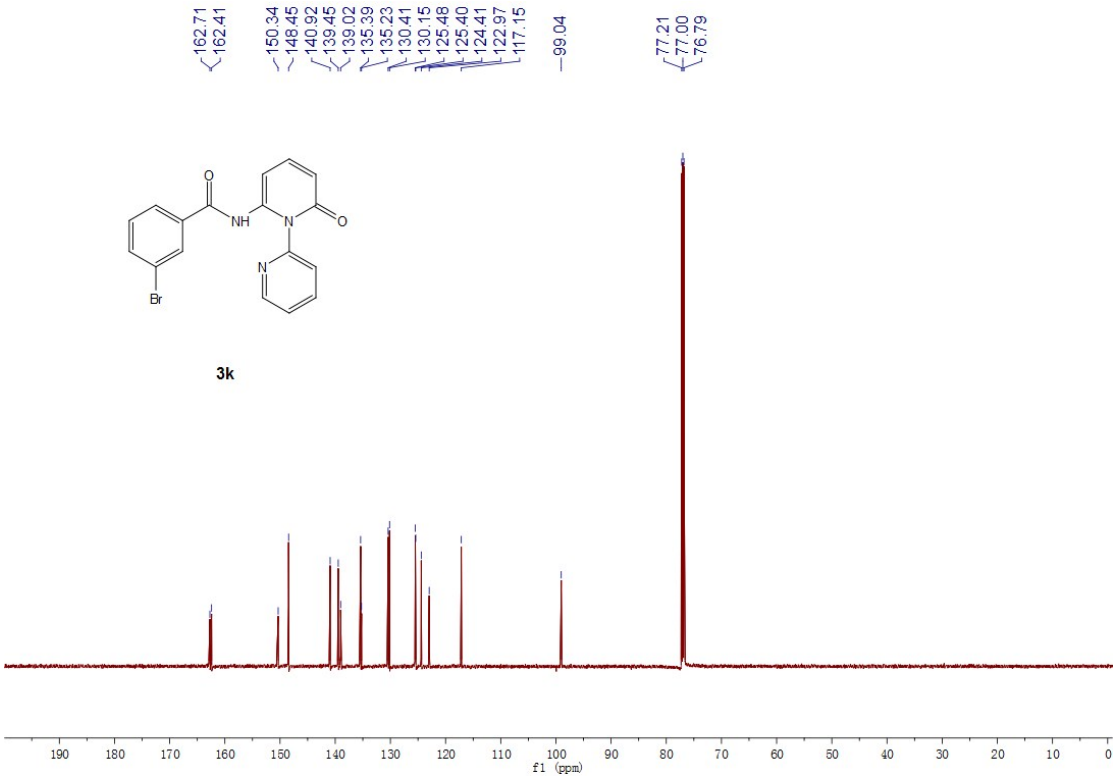

162.85
162.41
150.31
148.38
140.92
139.49
132.49
130.16
127.31
125.45
124.94
117.18
99.12
77.21
77.00
76.79
O
NH
N
O
N
Cl
160 150 140 130 120 110 100
f1 (ppm)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

3j

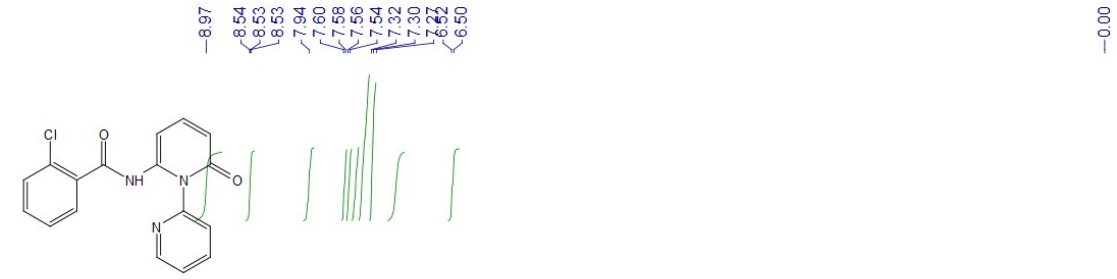

9.67
8.69
8.68
7.67
7.65
7.64
7.47
7.47
7.30
7.06
6.52
6.51
0.00
O
NH
N
O
N
Br

3k

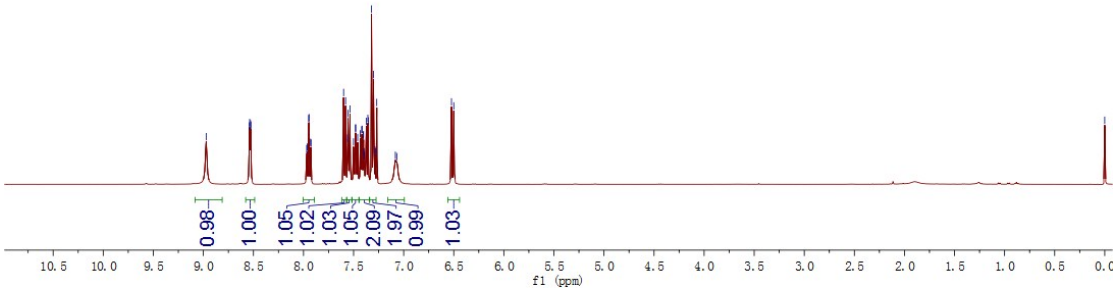

0.99
1.00
1.04
2.99
1.04
1.95
0.95
0.96
0.96
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

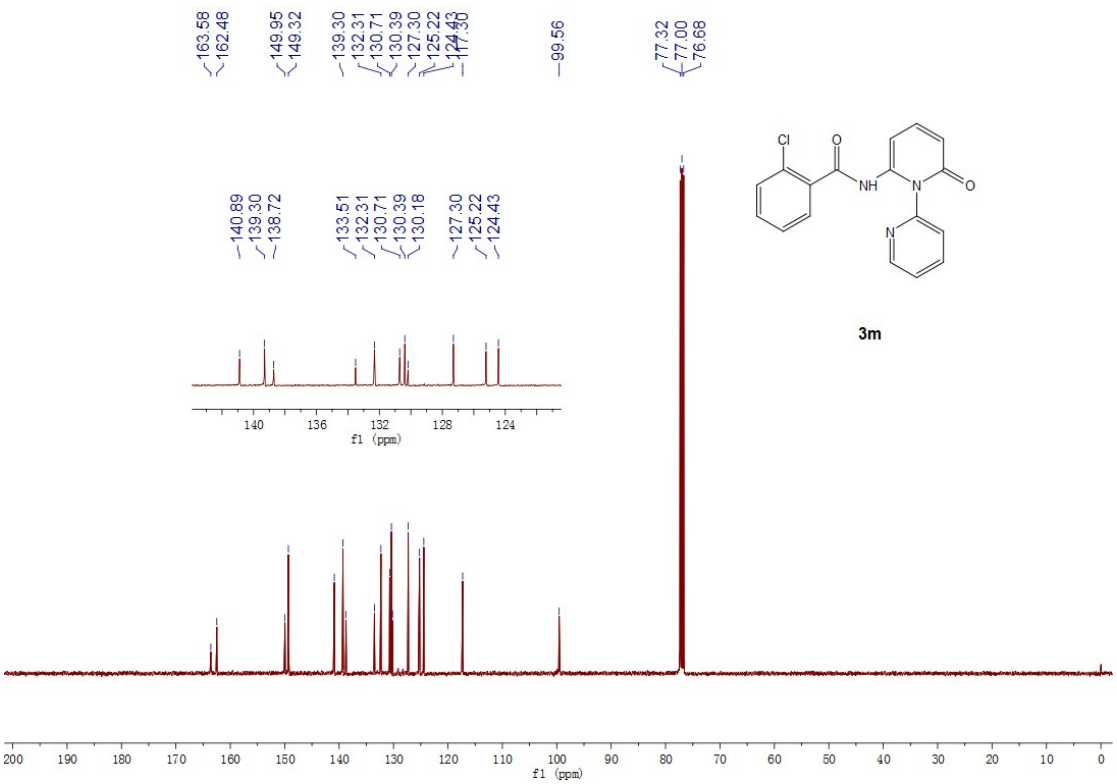

162.71
162.41
150.34
148.45
140.92
139.45
139.02
135.39
135.23
130.41
130.15
125.48
125.40
124.41
122.97
117.15
99.04
77.21
77.00
76.79
O
NH
N
O
N
Br
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

3k

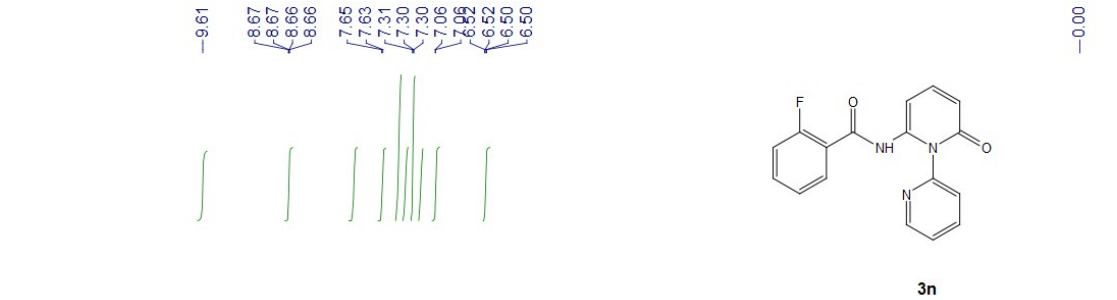

8.97
8.54
8.53
8.53
7.94
7.60
7.58
7.56
7.54
7.32
7.30
7.27
6.52
6.50
0.00
Cl
O
NH
N
O
N

3m

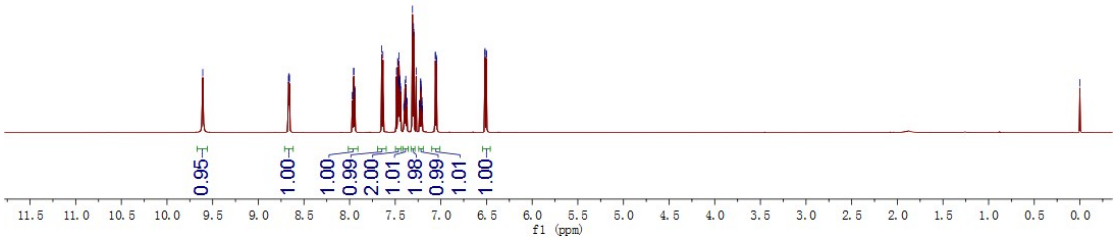

0.98
1.00
1.05
1.02
1.03
1.05
2.09
1.97
0.99
1.03
f1 (ppm)


163.58
162.48
149.95
149.32
139.30
132.31
130.71
130.39
127.30
125.22
124.43
99.56
77.32
77.00
76.68
140.89
139.30
138.72
133.51
132.31
130.71
130.39
130.18
127.30
125.22
124.43
140
136
132
128
124
f1 (ppm)
Cl
O
NH
N
O
N
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

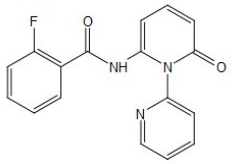
3m


9.61
8.67
8.67
8.66
8.66
7.65
7.63
7.31
7.30
7.30
7.06
6.52
6.50
6.50
0.00
F
O
NH
N
O
N

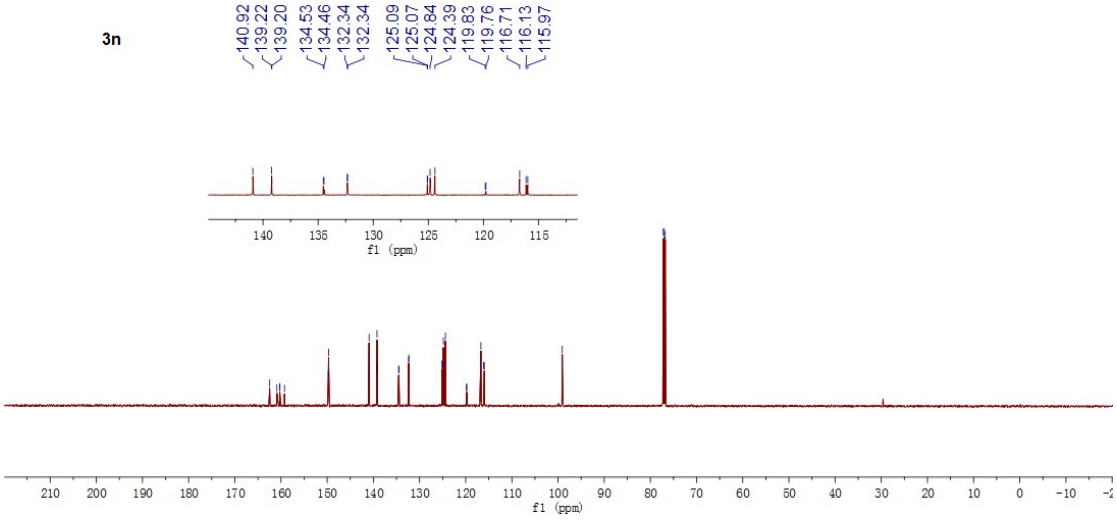
3n

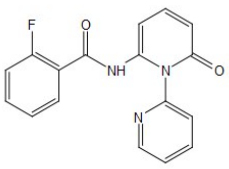

0.95
1.00
1.00
0.99
2.00
1.01
1.98
0.99
1.01
1.00
f1 (ppm)


162.46
160.89
160.26
160.24
159.24
149.75
149.70
140.92
139.22
132.34
132.34
125.09
125.07
124.84
124.39
116.71
116.13
99.09
77.21
77.00
76.79


F
O
NH
N
O
N

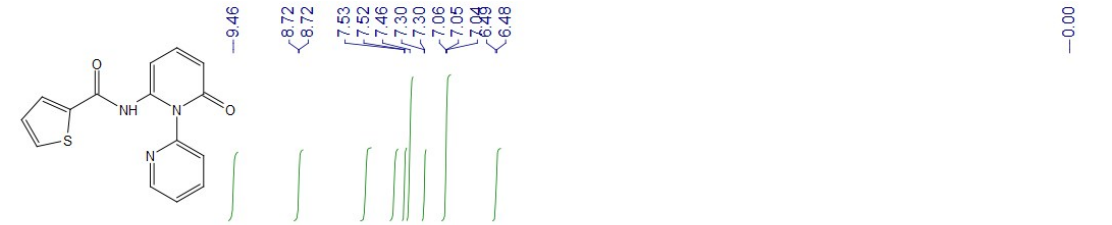
3n


140.92
139.22
139.20
134.53
134.46
132.34
132.34
125.09
125.07
124.84
124.39
119.83
119.76
116.71
116.13
115.97
140
135
130
125
120
115
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

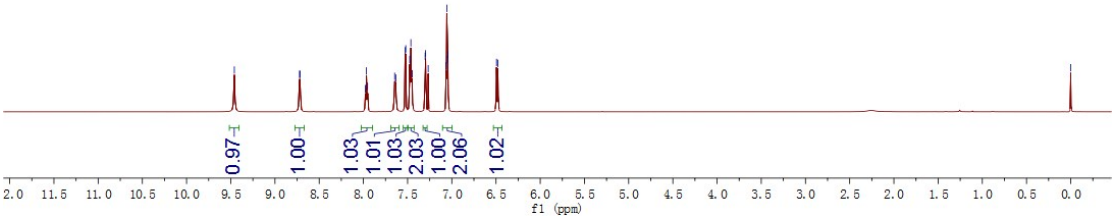

F
O
NH
N
O
N

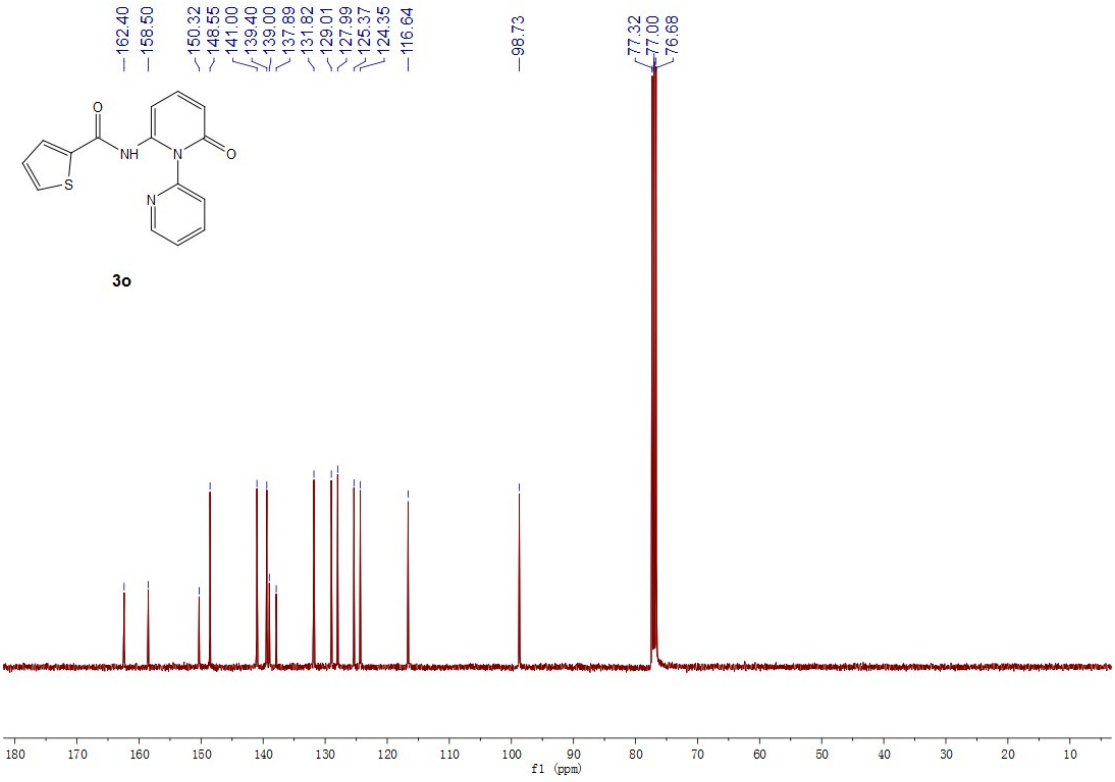
3n

-110.79
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

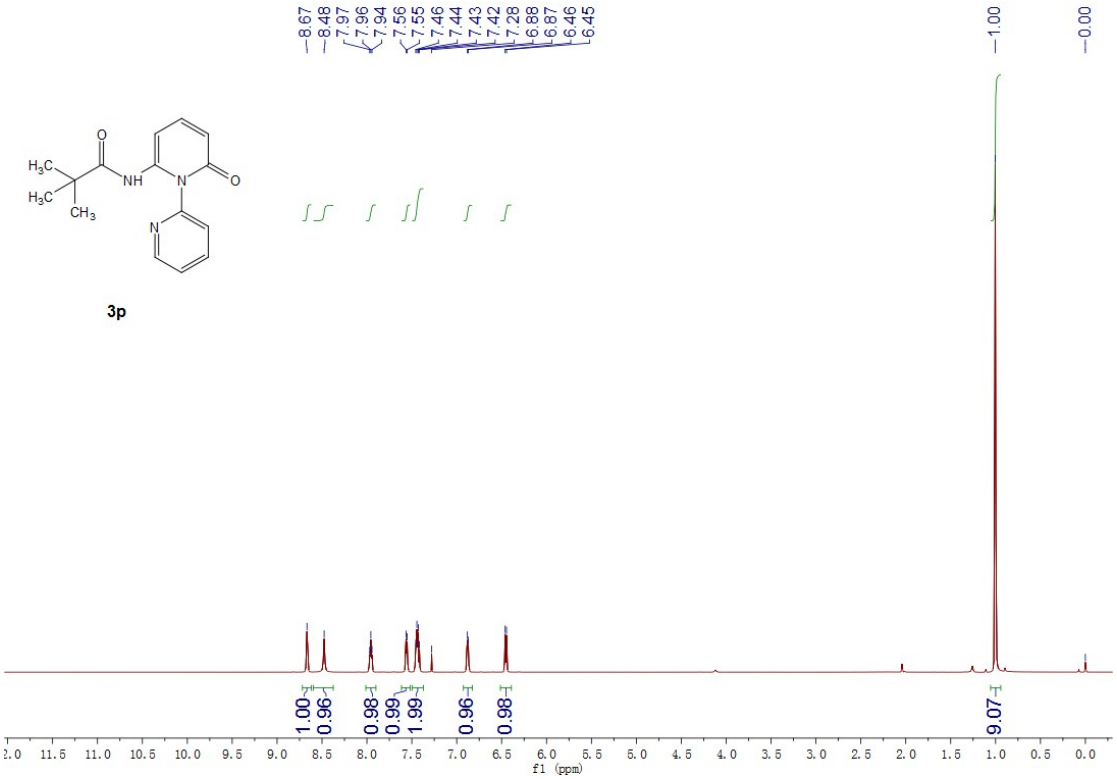

9.46
8.72
8.72
7.53
7.52
7.46
7.30
7.30
7.06
7.05
7.04
6.49
6.48
0.00
O
NH
N
O
S
N

3o

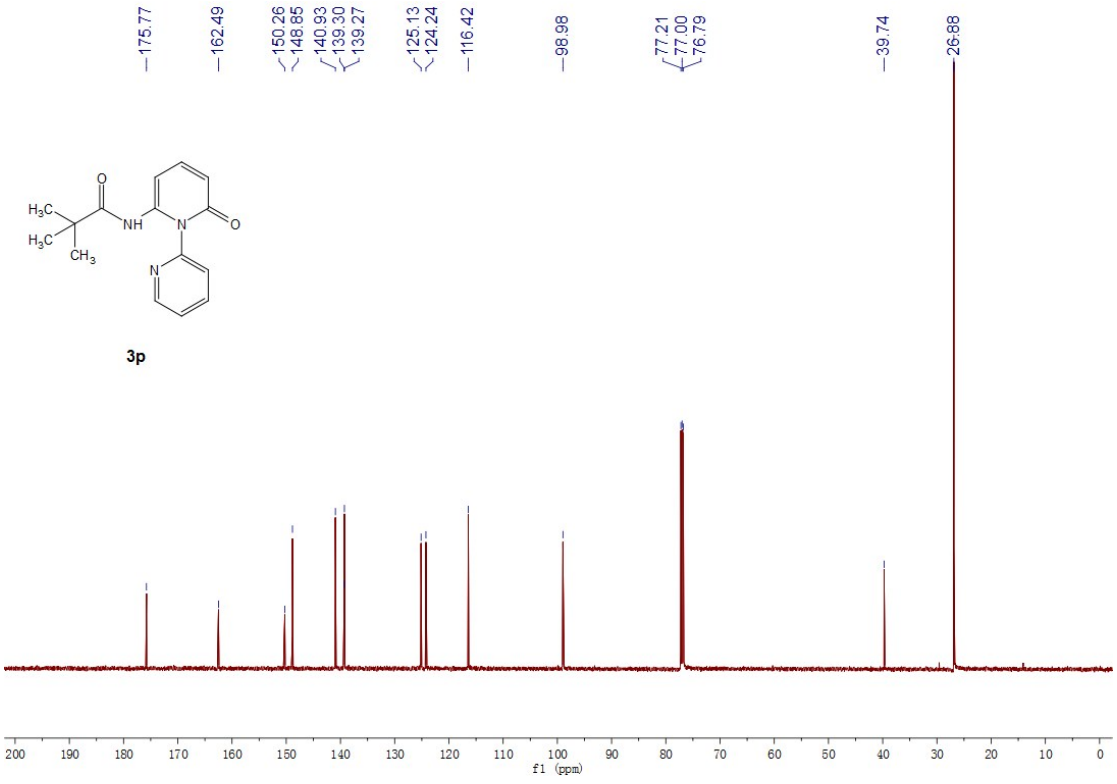

0.97
1.00
1.03
1.01
1.03
2.03
1.00
2.06
1.02
2.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


162.40
158.50
150.32
148.55
141.00
139.40
139.00
137.89
131.82
129.01
127.99
125.37
124.35
116.64
98.73
77.32
77.00
76.68
O
NH
N
O
S
N
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

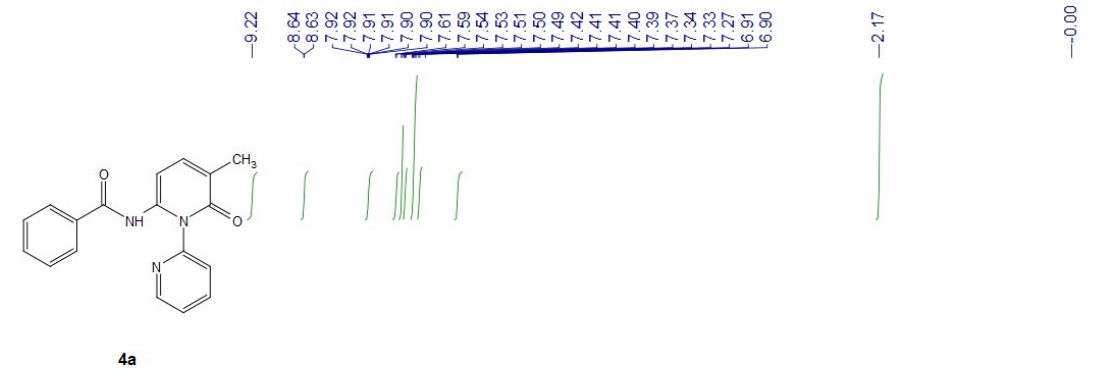
3o


8.67
8.48
7.97
7.96
7.94
7.56
7.55
7.46
7.44
7.43
7.42
7.28
6.88
6.87
6.46
6.45
1.00
0.00
1.00
0.96
0.98
0.99
1.99
0.96
0.98
9.07
f1 (ppm)

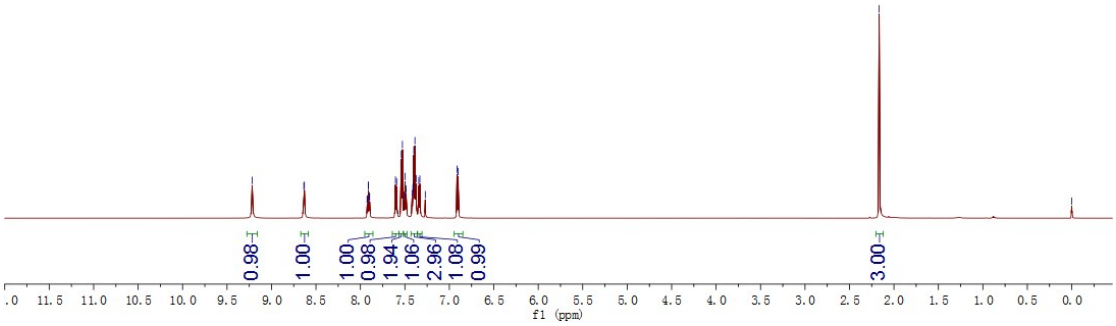
3p


175.77
162.49
150.26
148.85
140.93
139.30
139.27
125.13
124.24
116.42
98.98
77.21
77.00
76.79
39.74
26.88
f1 (ppm)

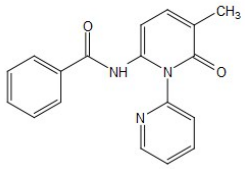
3p


9.22
8.64
8.63
7.92
7.92
7.91
7.91
7.90
7.90
7.61
7.59
7.54
7.53
7.51
7.50
7.49
7.42
7.41
7.41
7.40
7.39
7.37
7.34
7.33
7.27
6.91
6.90
2.17
0.00
O
NH
N
O
CH3
N

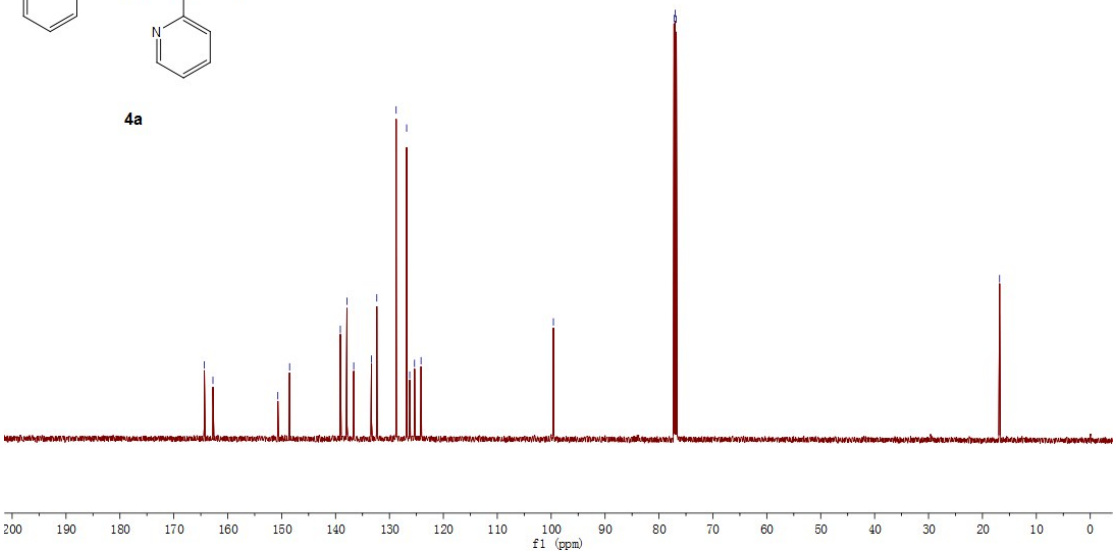
4a

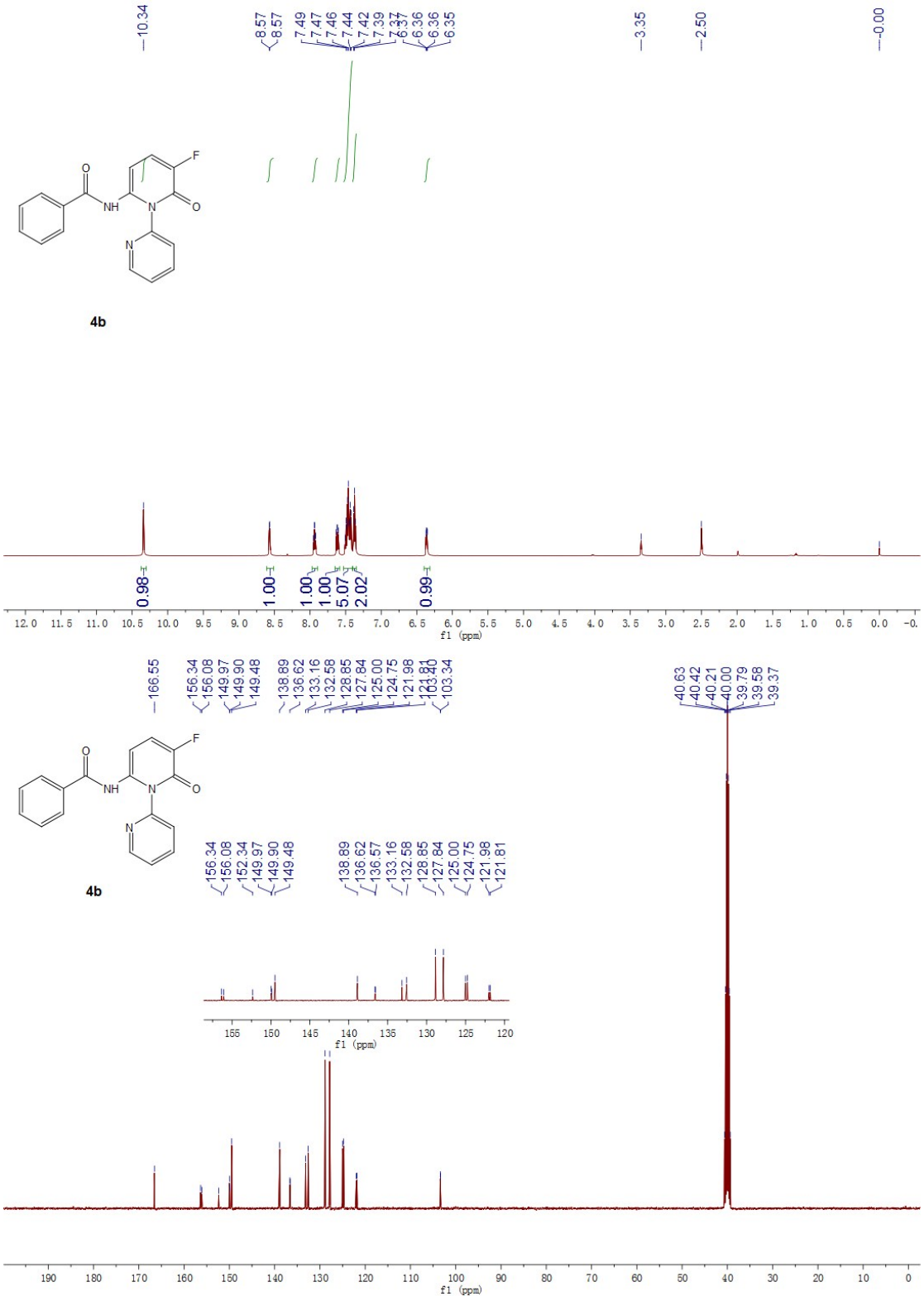

0.98
1.00
1.00
0.98
1.94
1.06
2.96
1.08
0.99
3.00
f1 (ppm)

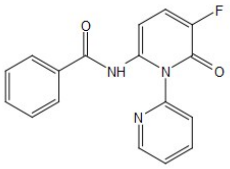

164.34
162.74
150.70
148.53
139.11
137.89
136.63
133.35
132.35
128.76
126.81
126.24
125.35
124.14
99.59
77.21
77.00
76.79
16.82


O
NH
N
O
CH3
N

4a

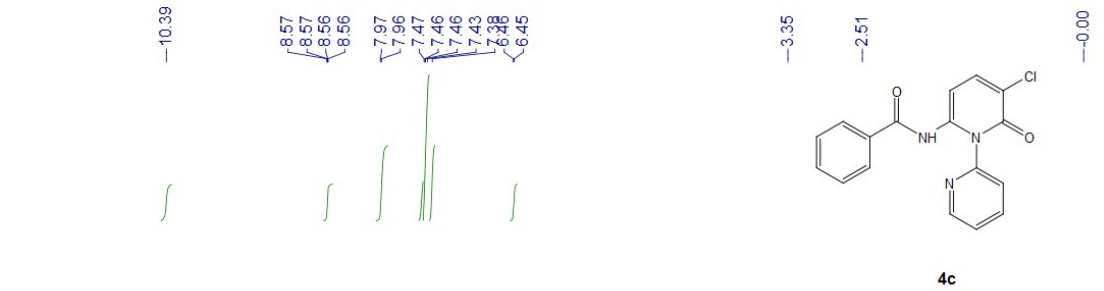

f1 (ppm)


10.34
8.57
8.57
7.49
7.47
7.46
7.44
7.42
7.39
7.37
6.37
6.36
6.35
3.35
2.50
0.00
F
O
NH
N
O
N
4b
0.98
1.00
1.00
1.00
5.07
2.02
0.99
f1 (ppm)
166.55
156.34
156.08
149.97
149.90
149.48
138.89
136.62
133.16
132.58
128.85
127.84
125.00
124.75
121.98
121.81
103.40
103.34
40.63
40.42
40.21
40.00
39.79
39.58
39.37
4b
156.34
156.08
152.34
149.97
149.90
149.48
138.89
136.62
136.57
133.16
132.58
128.85
127.84
125.00
124.75
121.98
121.81
f1 (ppm)
f1 (ppm)

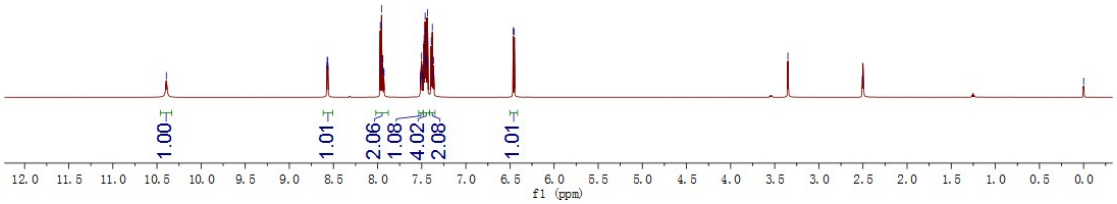

O
NH
N
O
F
N

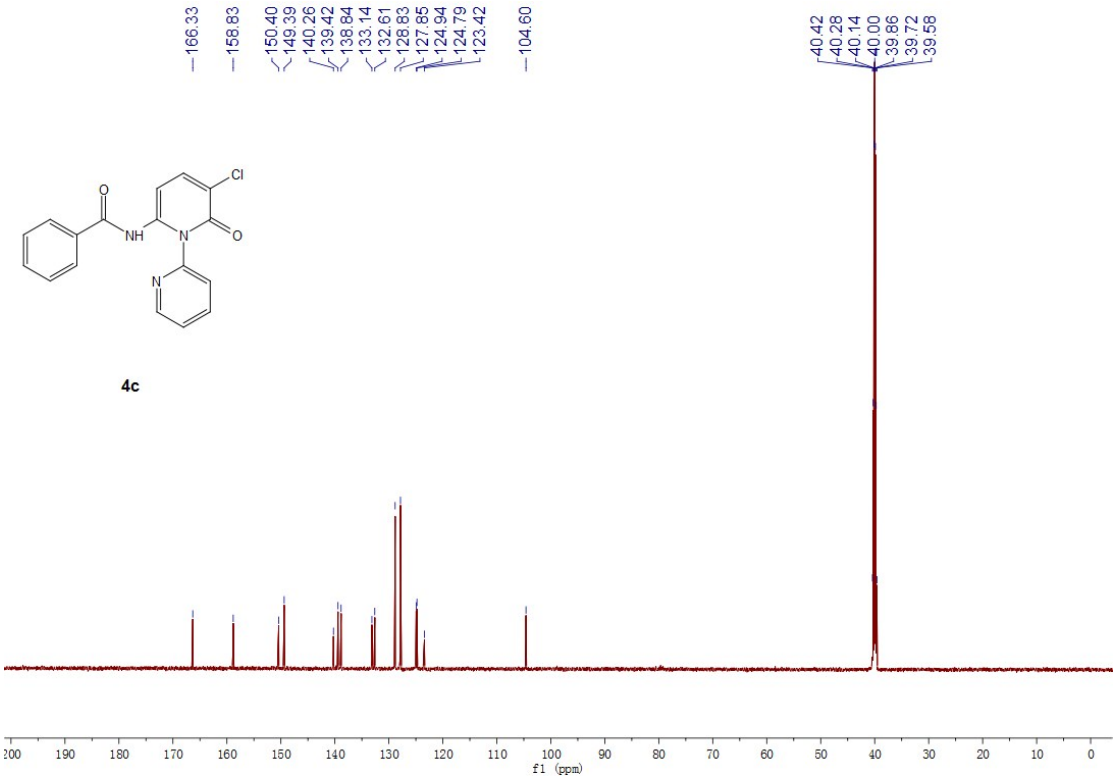
4b

-133.83
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

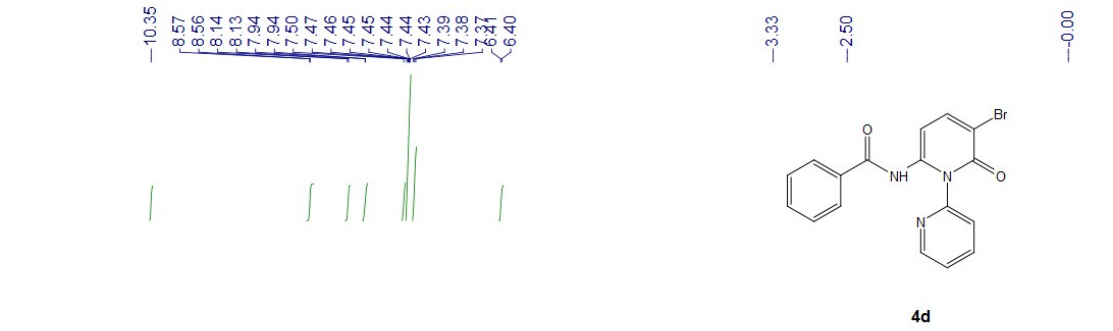

10.39
8.57
8.57
8.56
8.56
7.97
7.96
7.47
7.46
7.46
7.43
6.45
3.35
2.51
0.00
Cl
O
NH
N
O
N

4c


1.00
1.01
2.06
1.08
4.02
2.08
1.01
f1 (ppm)


166.33
158.83
150.40
149.39
140.26
139.42
138.84
133.14
132.61
128.83
127.85
124.94
124.79
123.42
104.60
40.42
40.28
40.14
40.00
39.86
39.72
39.58
Cl
O
NH
N
O
N
f1 (ppm)

4c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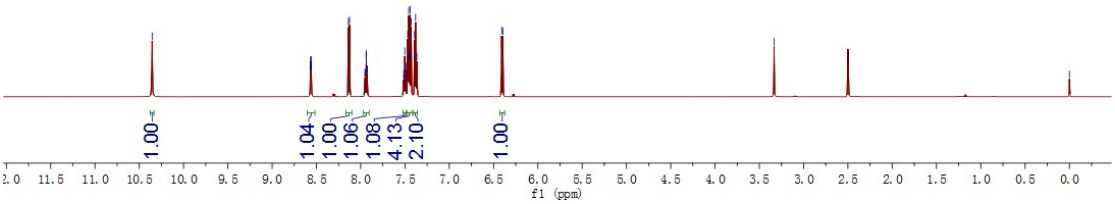
8.57
8.56
8.14
8.13
7.94
7.94
7.50
7.47
7.46
7.45
7.45
7.44
7.44
7.43
7.39
7.38
6.41
6.40
3.33
2.50
0.00
Br
O
NH
N
O
N

4d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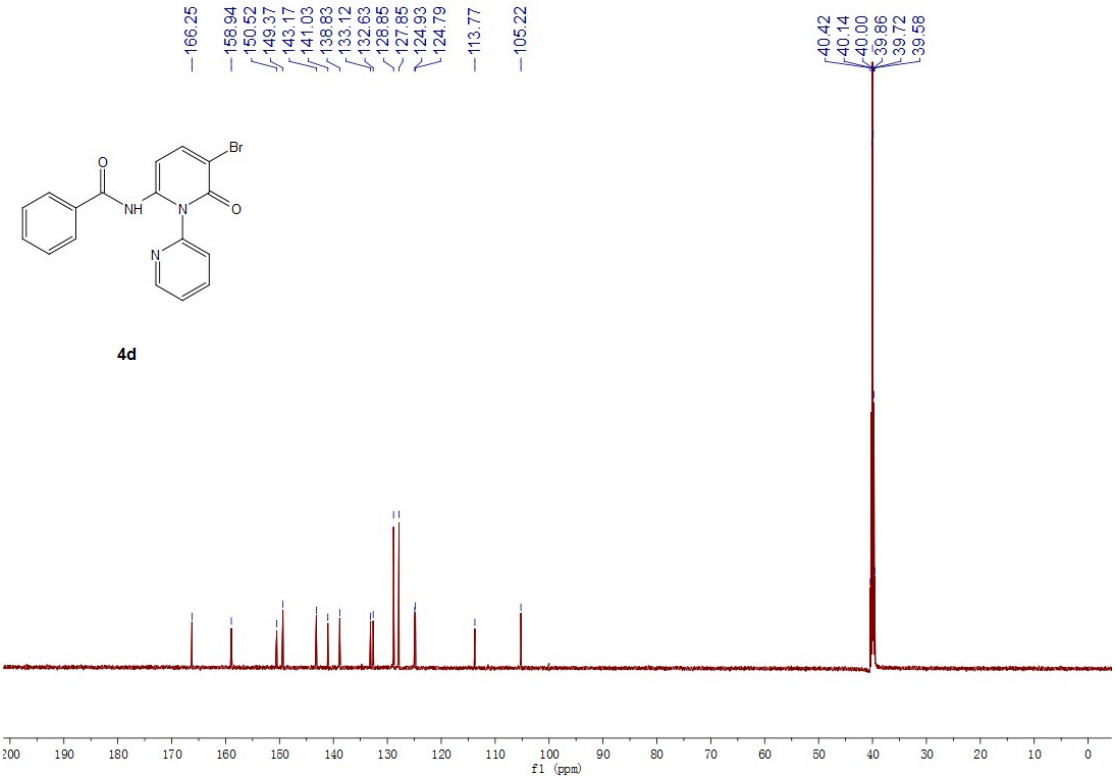
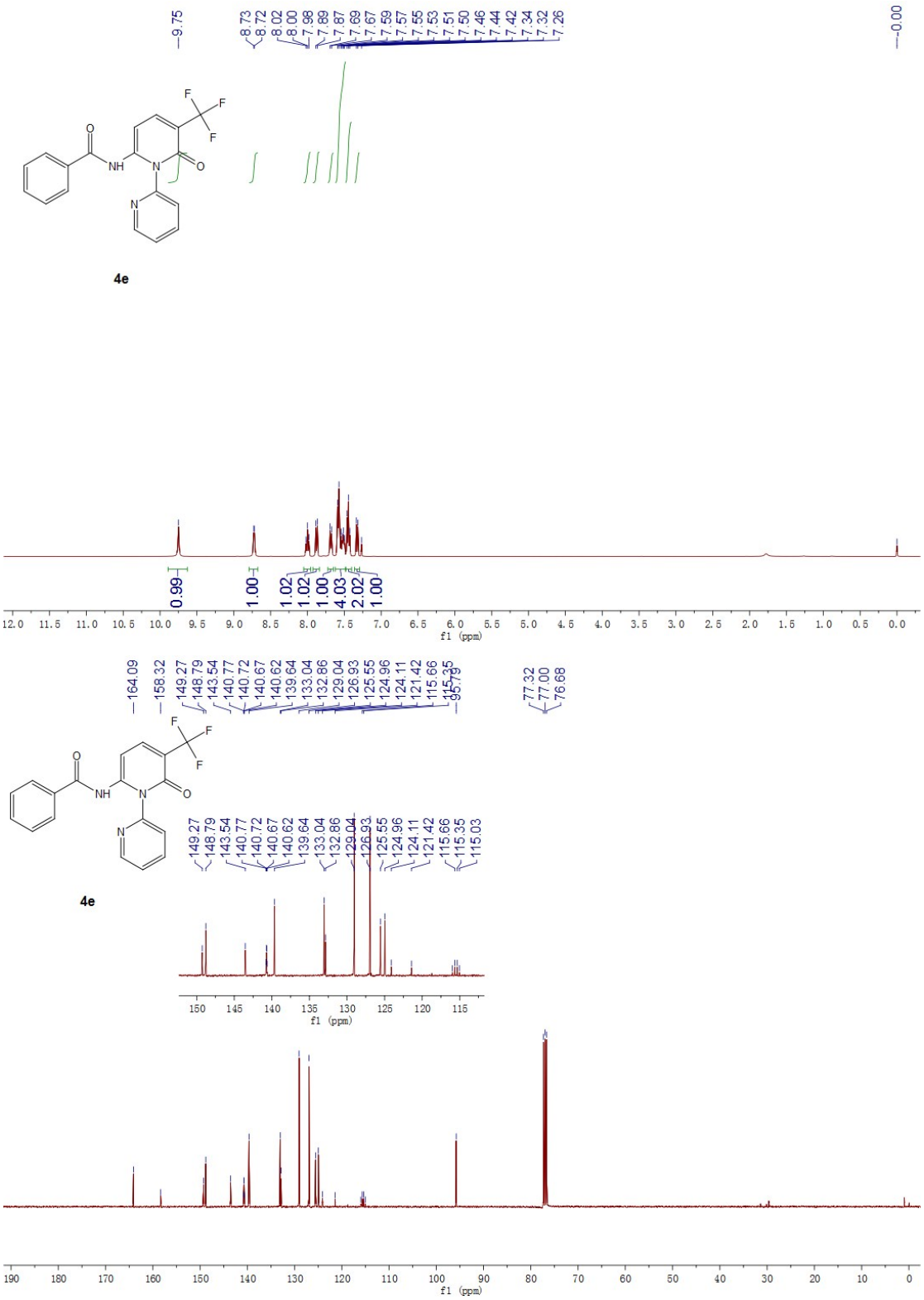
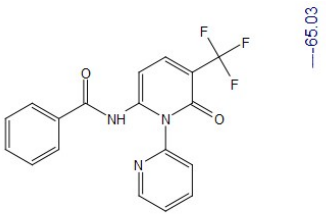
1.04
1.00
1.06
1.08
4.13
2.10
1.00
f1 (ppm)

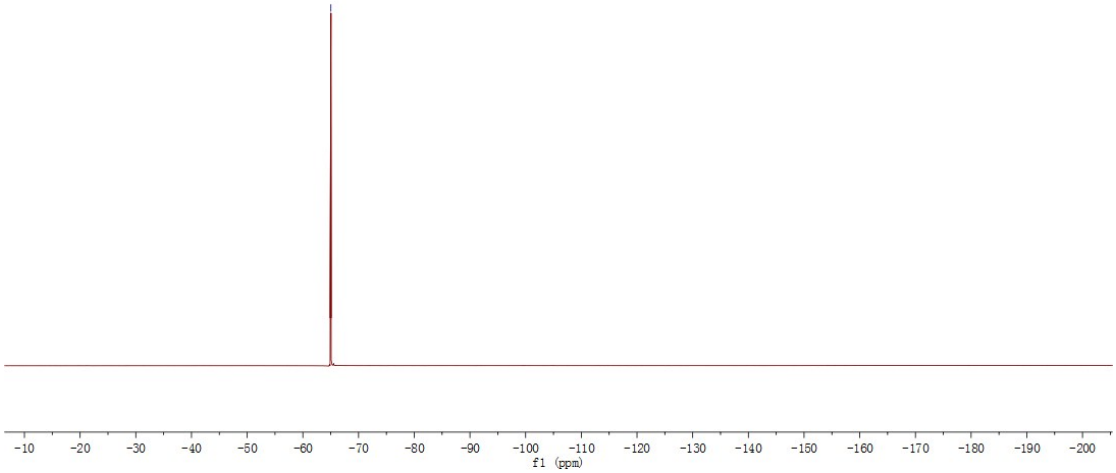

166.25
158.94
150.52
149.37
143.17
141.03
138.83
133.12
132.63
128.85
127.85
124.93
124.79
113.77
105.22
40.42
40.14
40.00
39.86
39.72
39.58
Br
O
NH
N
O
N
f1 (ppm)

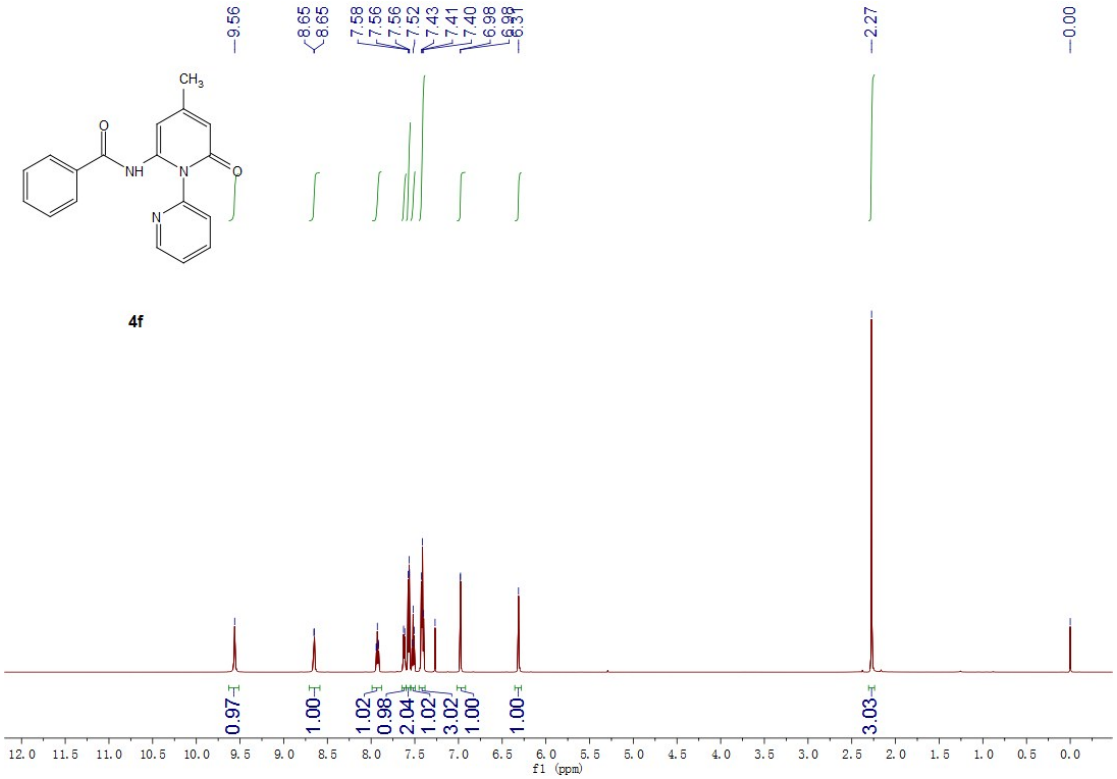
4d

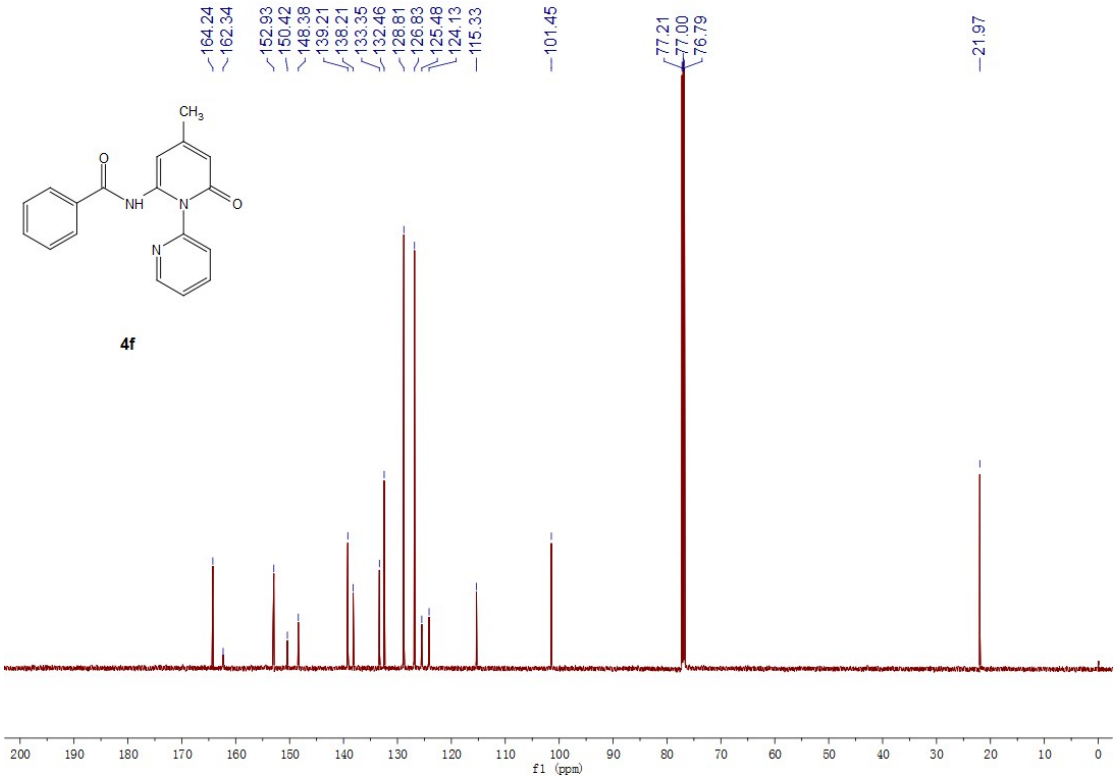

9.75
8.73
8.72
8.02
8.00
7.98
7.89
7.87
7.69
7.67
7.59
7.57
7.55
7.53
7.51
7.50
7.46
7.44
7.42
7.34
7.32
7.26
0.00
F
F
F
O
NH
N
O
N
0.99
1.00
1.02
1.02
1.00
4.03
2.02
1.00
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
164.09
158.32
149.27
148.79
143.54
140.77
140.72
140.67
140.62
139.64
133.04
132.86
129.04
126.93
125.55
124.96
124.11
121.42
115.66
115.35
115.03
77.32
77.00
76.68
4e
150 145 140 135 130 125 120 115
f1 (ppm)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

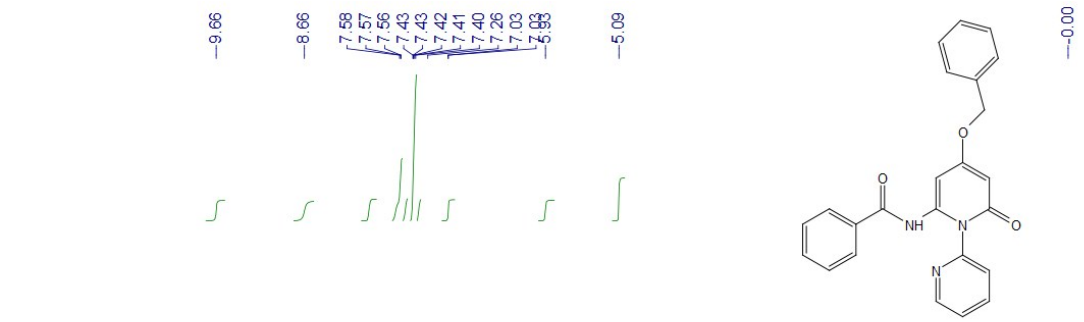

F
F
F
O
NH
N
O
N

4e

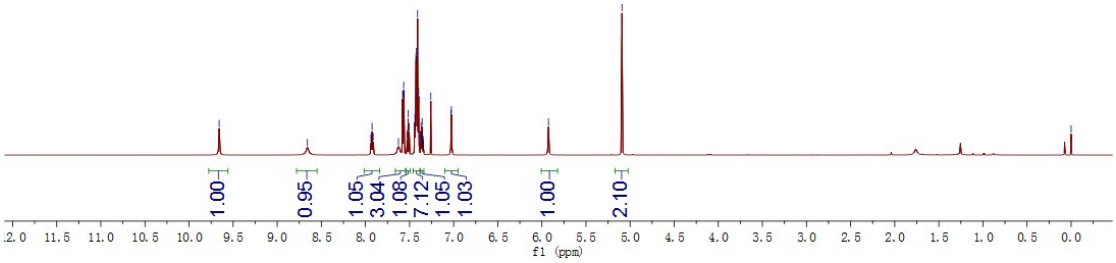

-65.03
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

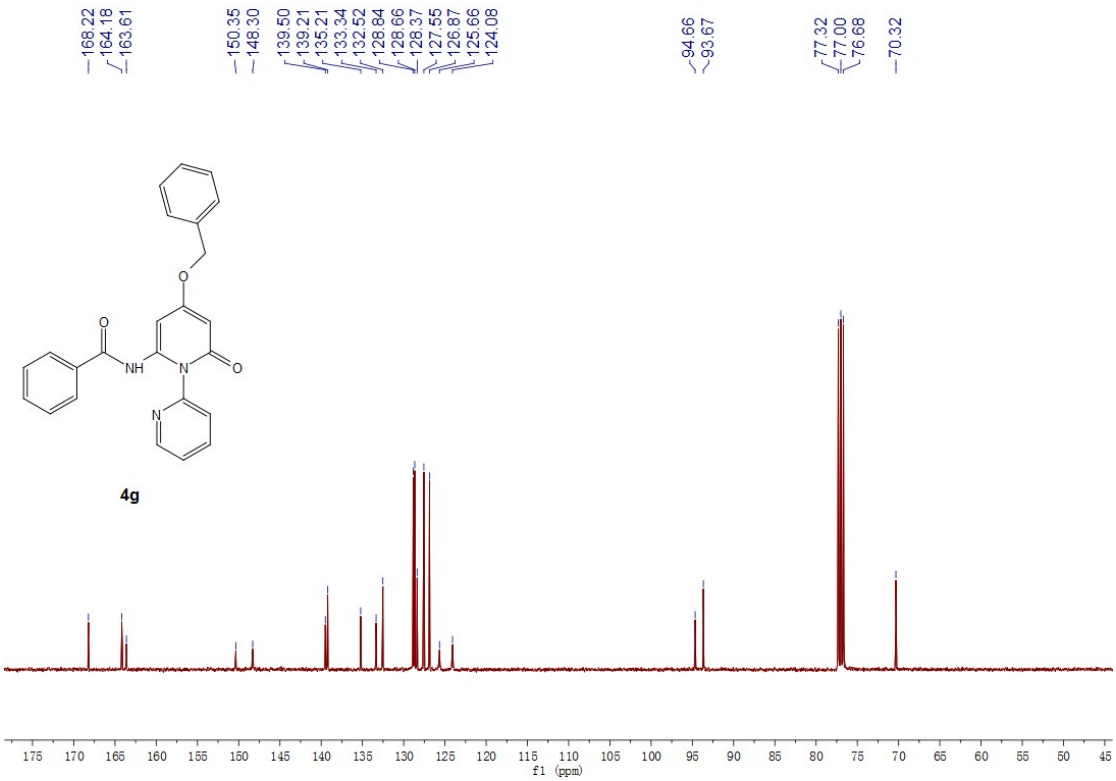

9.56
8.65
8.65
7.58
7.56
7.56
7.52
7.43
7.41
7.40
6.98
6.98
6.91
2.27
0.00
CH3
O
NH
N
O
N
4f
0.97
1.00
1.02
0.98
2.04
1.02
3.02
1.00
1.00
3.03
f1 (ppm)


164.24
162.34
152.93
150.42
148.38
139.21
138.21
133.35
132.46
128.81
126.83
125.48
124.13
115.33
101.45
77.21
77.00
76.79
21.97
CH3
O
NH
N
O
N
4f
f1 (ppm)

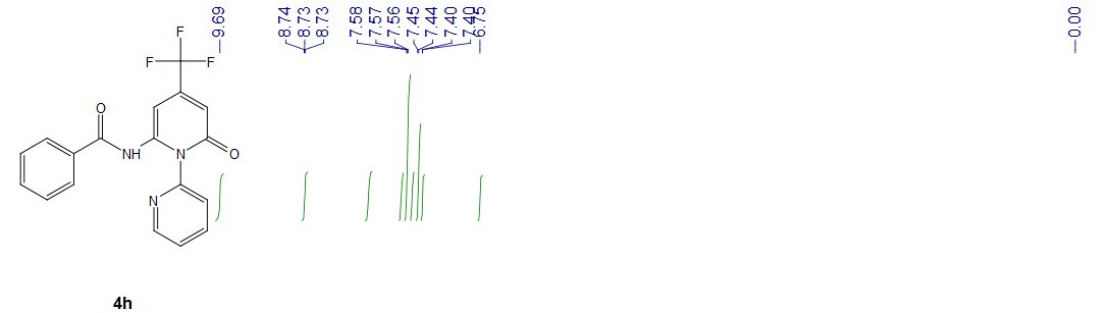

9.66
8.66
7.58
7.57
7.56
7.43
7.43
7.42
7.41
7.40
7.26
7.03
5.09
0.00

4g

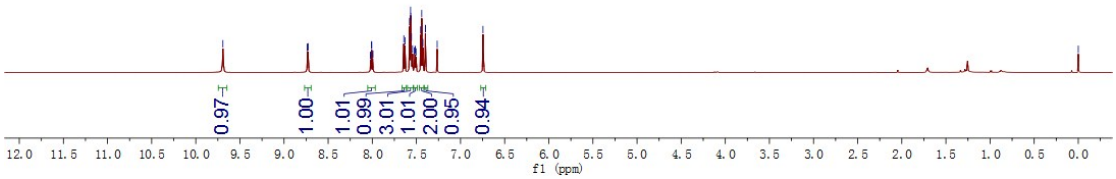

1.00
0.95
1.05
3.04
1.08
7.12
1.05
1.03
1.00
2.10
f1 (ppm)

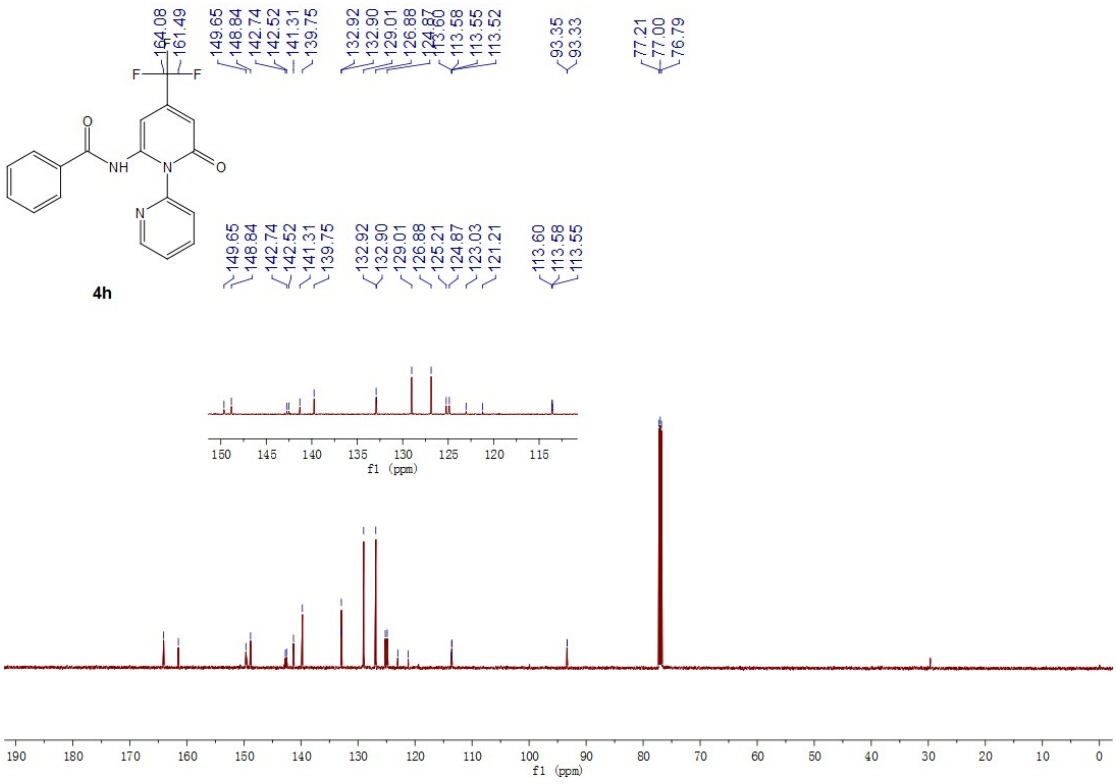

168.22
164.18
163.61
150.35
148.30
139.50
139.21
135.21
133.34
132.52
128.84
128.66
128.37
127.55
126.87
125.66
124.08
94.66
93.67
77.32
77.00
76.68
70.32
f1 (ppm)

4g

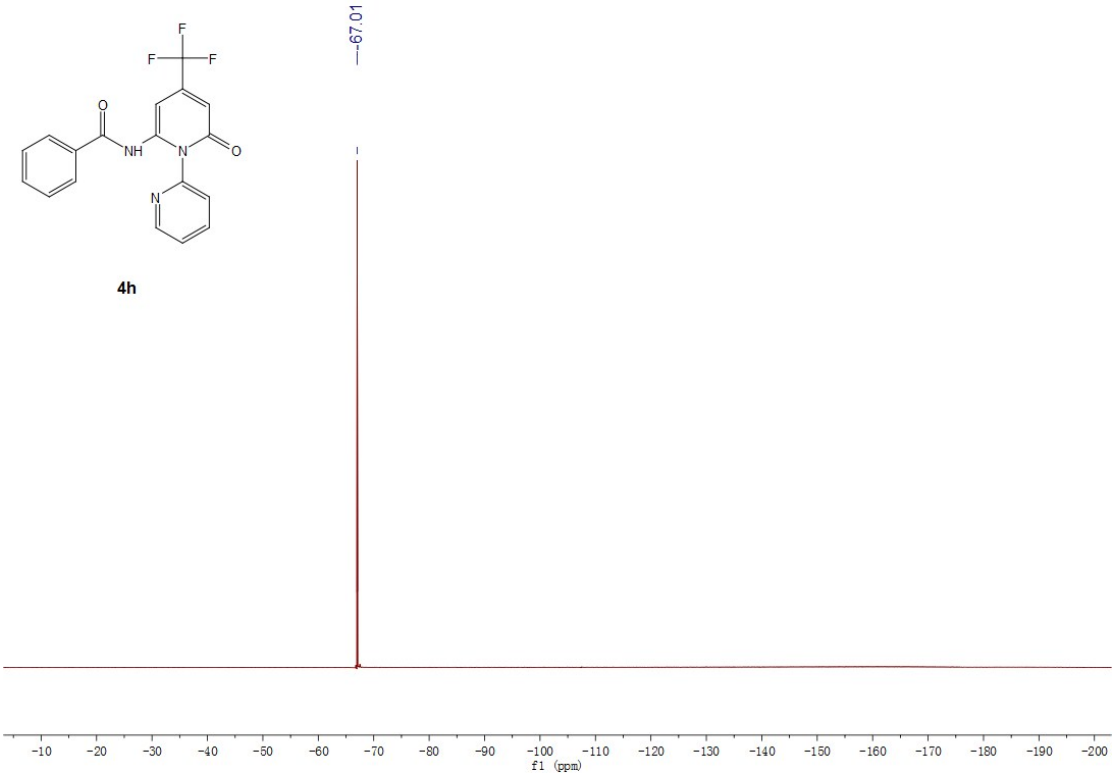

9.69
8.74
8.73
8.73
7.58
7.57
7.56
7.45
7.44
7.40
7.40
6.75
0.00
F
F
F
O
NH
N
O
N

4h

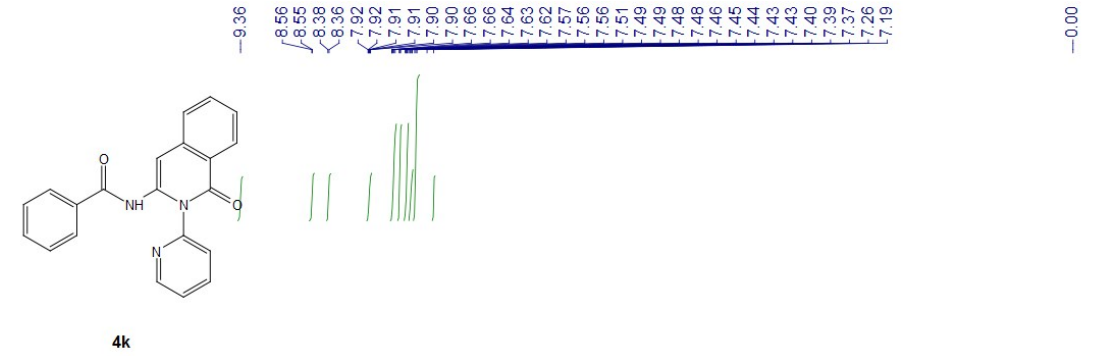

0.97
1.00
1.01
0.99
3.01
1.01
2.00
0.95
0.94
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


164.08
161.49
149.65
148.84
142.74
142.52
141.31
139.75
132.92
132.90
129.01
126.88
124.87
113.60
113.58
113.55
113.52
93.35
93.33
77.21
77.00
76.79
F
F
F
O
NH
N
O
N
149.65
148.84
142.74
142.52
141.31
139.75
132.92
132.90
129.01
126.88
125.21
124.87
123.03
121.21
113.60
113.58
113.55
150 145 140 135 130 125 120 115
f1 (ppm)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

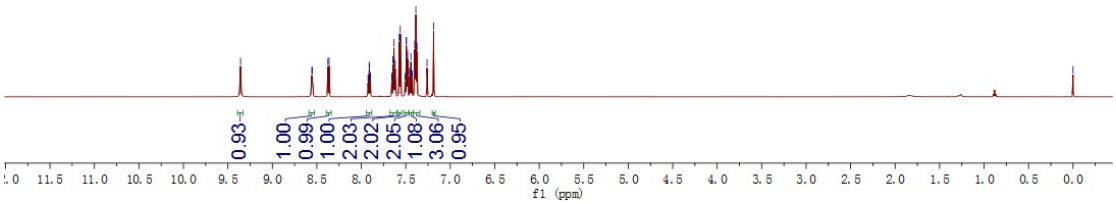
4h

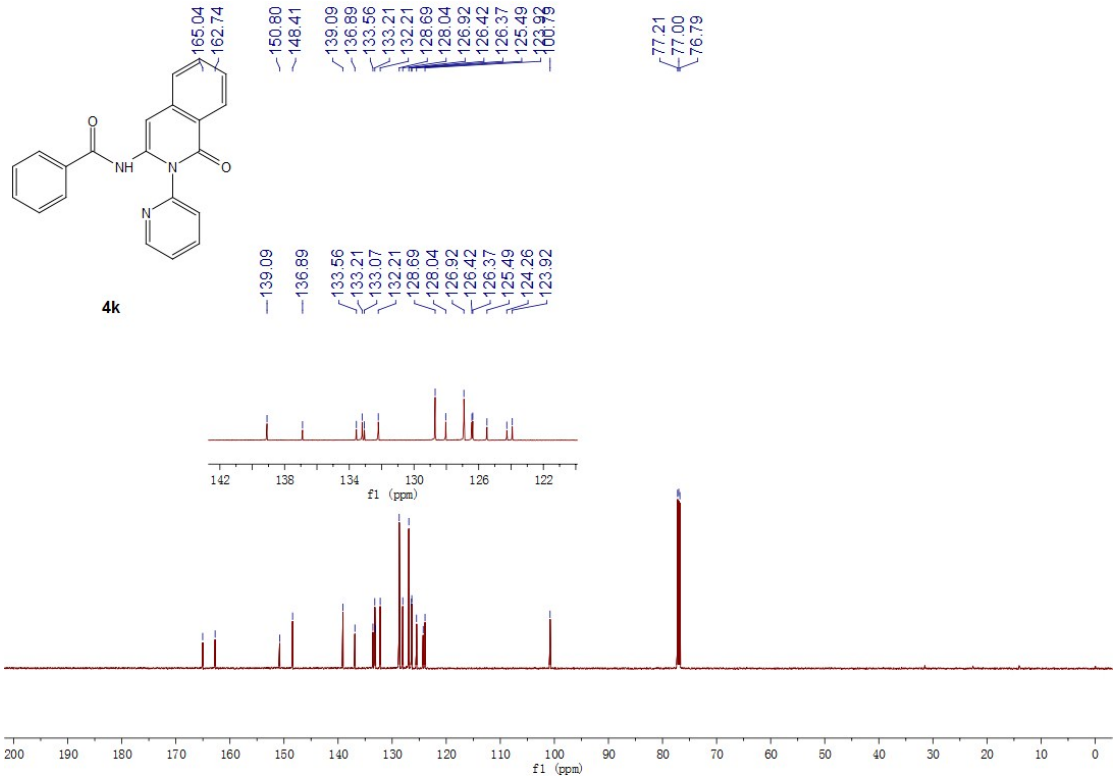

F
F
F
O
NH
N
O
N
-67.01
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

4h

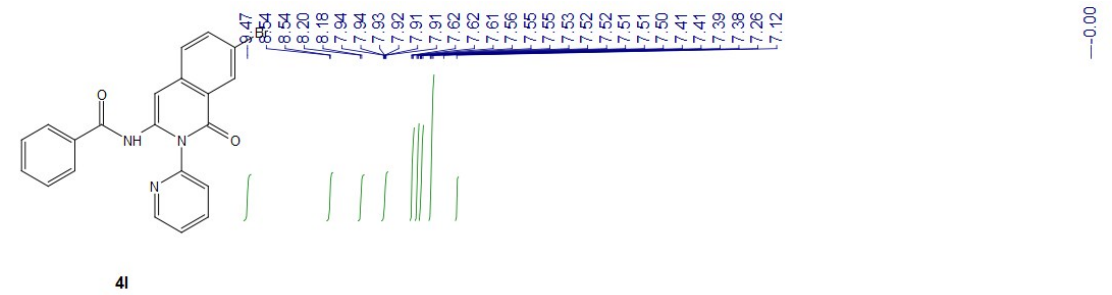

9.36
8.56
8.55
8.38
8.36
7.92
7.92
7.91
7.91
7.90
7.90
7.66
7.66
7.64
7.63
7.62
7.57
7.56
7.56
7.51
7.49
7.49
7.48
7.48
7.46
7.45
7.44
7.43
7.43
7.40
7.39
7.37
7.26
7.19
0.00
O
NH
N
O
N

4k


0.93
1.00
0.99
1.00
2.03
2.02
2.05
1.08
3.06
0.95
f1 (ppm)


165.04
162.74
150.80
148.41
139.09
136.89
133.56
133.21
132.21
128.69
128.04
126.92
126.42
126.37
125.49
77.21
77.00
76.79
O
NH
N
O
N
139.09
136.89
133.56
133.21
133.07
132.21
128.69
128.04
126.92
126.42
126.37
125.49
124.26
123.92
142
138
134
130
126
122
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

4k


9.47
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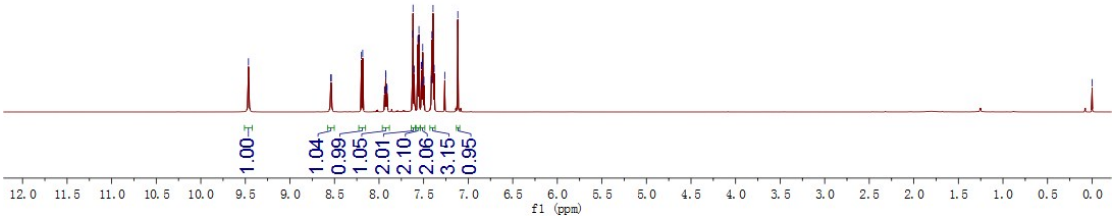
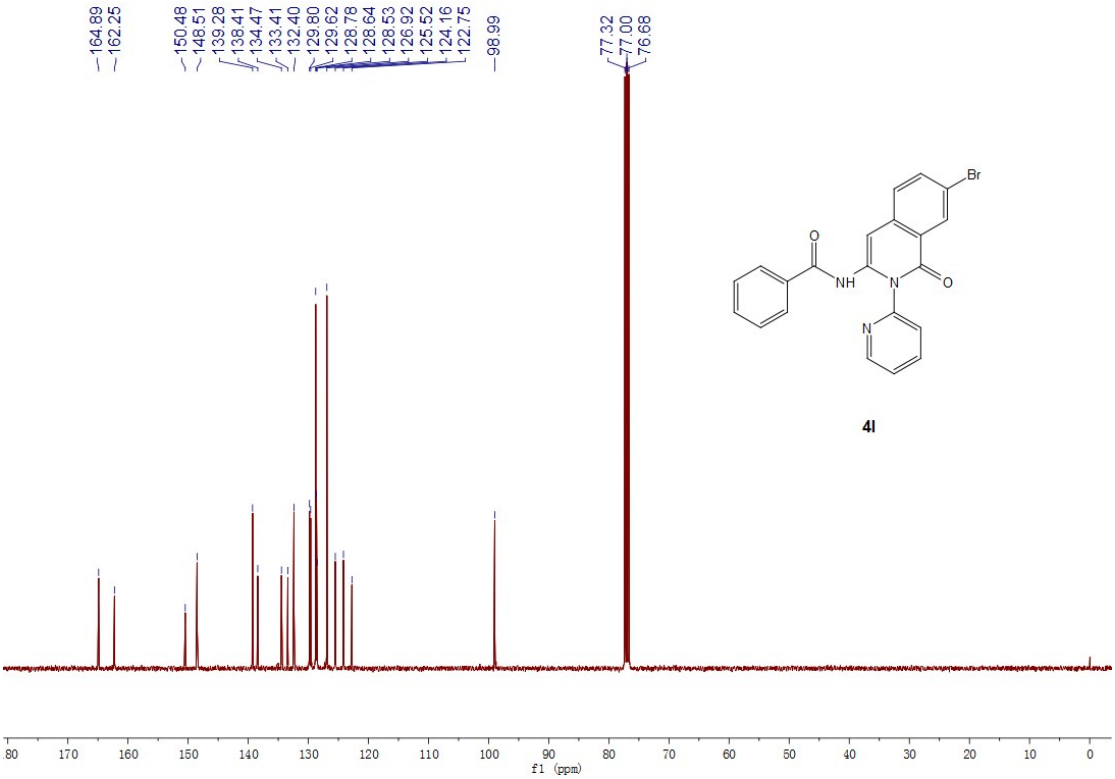
8.54
8.20
8.18
7.94
7.94
7.93
7.92
7.91
7.91
7.62
7.62
7.61
7.56
7.55
7.55
7.53
7.52
7.52
7.51
7.51
7.50
7.41
7.41
7.39
7.38
7.26
7.12
-0.00
Br
O
NH
N
O
N

4l

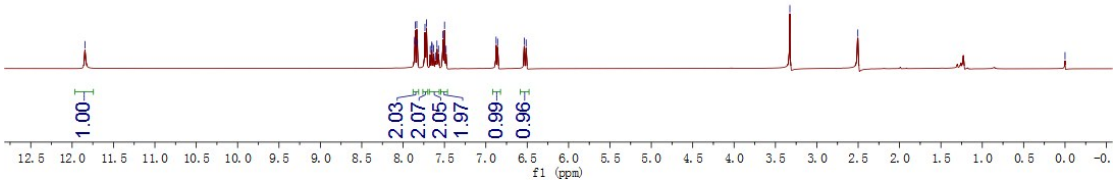

1.00
1.04
0.99
1.05
2.01
2.10
2.06
3.15
0.95
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

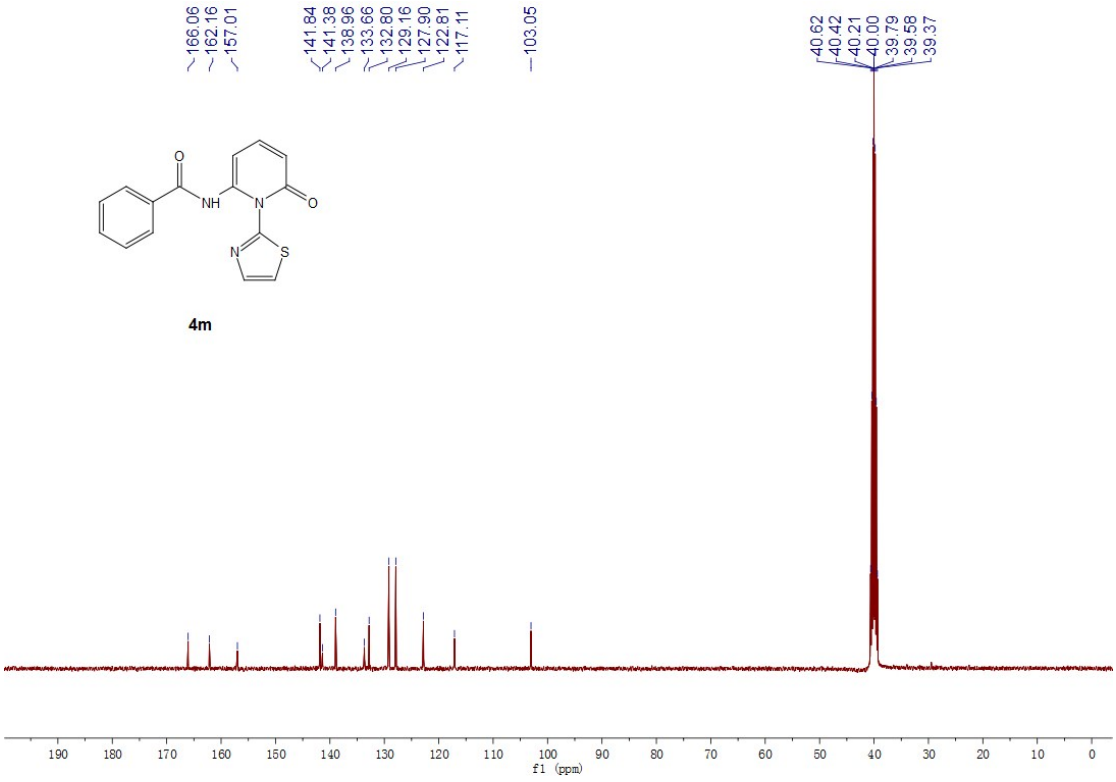

164.89
162.25
150.48
148.51
139.28
138.41
134.47
133.41
132.40
129.80
129.62
128.78
128.64
128.53
126.92
125.52
124.16
122.75
98.99
77.32
77.00
76.68
Br
O
NH
N
O
N
80 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

4l


11.84
7.86
7.85
7.83
7.83
7.74
7.72
7.67
7.65
7.65
7.63
7.61
7.59
7.57
7.52
7.50
7.48
6.88
6.86
6.54
6.51
3.33
2.50
0.00
O
NH
N
O
N
S

4m


1.00
2.03
2.07
2.05
1.97
0.99
0.96
f1 (ppm)


166.06
162.16
157.01
141.84
141.38
138.96
133.66
132.80
129.16
127.90
122.81
117.11
103.05
40.62
40.42
40.21
40.00
39.79
39.58
39.37
O
NH
N
O
N
S
f1 (ppm)

4m

8. References

[1] P. Peng, J. Wang, H. Jiang, H. Liu, *Org. Lett.* **2016**, *18*, 5376-5379.

[2] B. Jeon, U. Yeon, J.-Y. Son, P. H. Lee, *Org. Lett.* **2016**, *18*, 4610-4613.

[3] D. Das, R. Samanta, *Adv. Synth. Catal.* **2018**, *360*, 379-384.