Supporting Information

Copper-catalysed oxidative C–H/N–H cross-coupling between formamides and amides through chelation-assisted N–H activation

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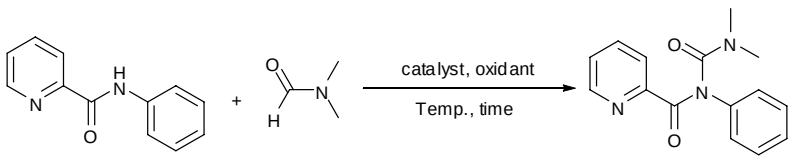
I. General remarks

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). High-resolution mass spectra (HR-MS) were obtained with a Waters-Q-TOF-Premier (ESI). 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. CuBr (99.0 %) was purchased from Shanghai Xin Bao Fine Chemical Engineering Reagent (China) CO., Ltd., TBHP (65 wt% in water) was purchased from Sinopharm Chemical Reagent (China) Co., Ltd., *N,N*-dimethylformamide was purchased from Chengdu Ke Long Chemical Engineering Reagent (China) CO., Ltd., *N,N*-diethylformamide was purchased from Chendu Best-reagent (China) CO., Ltd., and 4-formylmorpholine was purchased from Accela ChemBio (China) Co. Ltd.. *N*-Substituted-2-picolinamides[1], *N*-(pyridin-2-yl)amides[2], *N*-phenyl-3-picolinamide[1], *N*-(pyridin-3-yl)benzamide[2], 1-formylpiperidine[3], and 1-formylpyrrolidine[3] were prepared according to the literature procedures.

II. Optimization of the oxidative C–H/N–H cross-coupling of *N,N*-dimethylformamide with *N*-phenyl-2-picolinamide

***Table S1*:** Optimization of reaction conditions[a]



1a **2a** **3a**

Entry	Catalyst	Oxidant	Temp. (°C)	Time (h)	Solvent	Yield (%)[b]
1	$CuBr_2$	TBHP	80	12	none	76
2	CuBr	TBHP	80	12	none	85
3	$CuCl_2{\cdot}2H_2O$	TBHP	80	12	none	79
4	CuCl	TBHP	80	12	none	79
5	CuI	TBHP	80	12	none	46
6	$Cu(OAc)_2$	TBHP	80	12	none	72

7	$Cu(OTf)_2$	TBHP	80	12	none	79
8	$CuSO_4$	TBHP	80	12	none	54
9	$CoCl_2·6H_2O$	TBHP	80	12	none	59
10	$Pd(OAc)_2$	TBHP	80	12	none	N.D.[c]
11	$FeCl_3$	TBHP	80	12	none	N.D.
12	$NiCl_2$	TBHP	80	12	none	N.D.
13	none	TBHP	80	12	none	N.D.
14	CuBr	DTBP	80	12	none	< 5
15	CuBr	TBPB	80	12	none	< 5
16	CuBr	DDQ	80	12	none	N.D.
17	CuBr	H_2O_2	80	12	none	N.D.
18	CuBr	$K_2S_2O_8$	80	12	none	N.D.
19	CuBr	$(NH_4)_2S_2O_8$	80	12	none	N.D.
20	CuBr	TBHP	60	12	none	83
21	CuBr	TBHP	40	12	none	80
22	CuBr	TBHP	r.t.	12	none	57
23	CuBr	TBHP	120	12	none	67
24	CuBr	TBHP	80	1	none	75
25	CuBr	TBHP	80	3	none	80
26	CuBr	TBHP	80	6	none	84
27	CuBr	TBHP	80	24	none	78
28[d]	CuBr	TBHP	80	12	DMSO[e]	< 5
29[d]	CuBr	TBHP	80	12	Toluene[e]	< 5
30[d]	CuBr	TBHP	80	12	CH_3CN[e]	< 5
31[d]	CuBr	TBHP	80	12	DCE[e]	< 5
32[d]	CuBr	TBHP	80	12	none	< 5
33[f]	CuBr	TBHP	80	12	none	N.D.

[a] Reaction contidions: *N*-phenyl-2-picolinamide (**1a**, 0.5 mmol, 1.0 equiv), *N,N*-dimethylformamide (**2a**, 1 mL), catalyst (5 mol%), oxidant (1.5 equiv). [b] Isolated yield. [c] Not Detected. [d] 3.0 equiv DMF. [e] 1 mL. [f] 1.0 equiv TEMPO (2,2,6,6-tetramethylpiperidine *N*-oxide). TBHP = *tert*-butyl hydroperoxide. DTBP = di-*tert*-butyl peroxide. TBPB = *tert*-butyl perbenzoate. DDQ = 2,3-dichloro-5,6-dicyano-1,4-benzoquinone.

III. General procedure for the oxidative C–H/N–H cross-coupling of formamides with amides

TBHP (65 wt% in water, 1.5 equiv) was added to a mixture of amide (**1** or **4**, 0.5 mmol, 1.0 equiv), CuBr (5 mol%) and formamide (**2**, 1 mL) in a Schlenk tube under N_2 atmosphere. Then the reaction temperature was increased to 80 °C and the reaction mixture was stirred for 12 hours. After cooling to room temperature, the reaction mixture was extracted with ethyl acetate (20 mL), washed with water followed by

brine, and dried over anhydrous Na_2SO_4. Removal of the solvent under vacuum afforded the crude product, which was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1 ~ 1/2, v/v) to afford the required product (**3** or **5**).

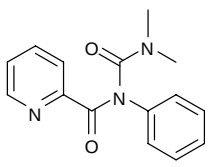
IV. Procedure for the removal of the 2-pyridoyl group

The mixture of **3a** (0.4 mmol, 1.0 equiv) and NaOH (3.0 equiv) in MeOH (2 mL) was stirred at 50 °C for 12 hours. TLC (petroleum ether/ethyl acetate/dichloromethane = 1/2/1, v/v/v) indicated that **3a** was disappeared and the product was generated. After cooling to room temperature, the reaction mixture was extracted with ethyl acetate (20 mL), washed with water followed by brine, and dried over anhydrous Na_2SO_4. Removal of the solvent under vacuum afforded the crude product, which was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1, v/v) to afford the required product **6a**.

V. Procedure for the removal of the benzoyl group

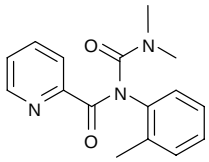
The mixture of **5a** (0.4 mmol, 1.0 equiv) and NaOH (3.0 equiv) in MeOH (2 mL) was stirred at 50 °C for 12 hours. TLC (petroleum ether/ethyl acetate/dichloromethane = 1/3/1, v/v/v) indicated that **5a** was disappeared and the product was generated. After cooling to room temperature, the reaction mixture was extracted with ethyl acetate (20 mL), washed with water followed by brine, and dried over anhydrous Na_2SO_4. Removal of the solvent under vacuum afforded the crude product, which was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/3, v/v) to afford the required product **7a**.

VI. Experimental data for the described substances



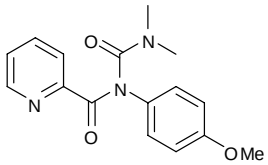
***N*-(Dimethylcarbamoyl)-*N*-phenylpicolinamide (3a)**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1, v/v) afforded **3a** as a white solid (115 mg, 85% yield). M.p.: 97-99 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.99 (s, 6H), 7.29-7.33 (m, 1H), 7.36 (d, J = 8.0 Hz, 2H), 7.40-7.46 (m, 3H), 7.84 (t, J = 7.6 Hz, 1H), 8.01 (d, J = 8.0 Hz, 1H), 8.57 (d, J = 3.2 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 37.1, 38.5, 119.8, 124.5, 125.6, 126.2, 127.0, 129.2, 129.4, 137.1, 138.5, 148.3, 152.2, 157.9, 168.3 ppm. HRMS (ESI$^+$): calcd for $C_{15}H_{15}N_3NaO_2$ $[M+Na]^+$ 292.1062, found 292.1064.



***N*-(Dimethylcarbamoyl)-*N*-(*o*-tolyl)picolinamide (3b)**

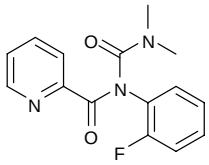
Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1, v/v) afforded **3b** as a white solid (120 mg, 85% yield). M.p.: 125-126 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.27 (s, 3H), 2.89 (s, 3H), 2.93 (s, 3H), 7.21-7.24 (m, 3H), 7.28-7.30 (m, 1H), 7.38 (t, J = 6.2 Hz, 1H), 7.81 (t, J = 7.8 Hz, 1H), 7.97 (d, J = 7.6 Hz, 1H), 8.54 (d, J = 4.4 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.4, 37.2, 37.7, 124.2, 125.7, 126.0, 126.9, 127.7, 131.3, 135.2, 136.9, 137.4, 148.3, 152.3, 158.3, 168.7 ppm. HRMS (ESI$^+$): calcd for $C_{16}H_{17}N_3NaO_2$ $[M+Na]^+$ 306.1218, found 306.1215.



***N*-(Dimethylcarbamoyl)-*N*-(4-methoxyphenyl)picolinamide (3c)**

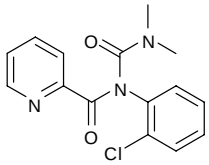
Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1, v/v) afforded **3c** as a white solid (114 mg, 76% yield). M.p.: 170-172 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.89 (s, 3H), 2.91 (s, 3H), 3.75 (s, 3H), 6.85-6.89 (m, 2H), 7.18-7.22 (m, 2H), 7.31 (dd, J = 7.6 Hz, 4.8Hz, 1H), 7.73 (td, J = 7.6 Hz, 1.6Hz, 1H), 7.90 (d, J = 7.6 Hz, 1H), 8.46 (d, J = 4.8 Hz, 1H) ppm. ^{13}C NMR (100 MHz,

$CDCl_3$): δ = 37.1, 38.5, 55.6, 114.7, 121.3, 122.4, 124.4, 126.1, 127.1, 131.2, 137.0, 148.2, 152.3, 158.0, 158.4, 168.4 ppm. HRMS (ESI^+): calcd for $C_{16}H_{17}N_3NaO_3$ $[M+Na]^+$ 322.1168, found 322.1164.



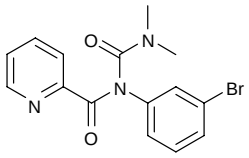
***N*-(Dimethylcarbamoyl)-*N*-(2-fluorophenyl)picolinamide (3d)**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1, v/v) afforded **3d** as a white solid (126 mg, 87% yield). M.p.: 139-141 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.97 (s, 6H), 7.16-7.21 (m, 2H), 7.30-7.36 (m, 2H), 7.39 (dd, J = 7.4 Hz, 5.0 Hz, 1H), 7.82 (t, J = 7.6 Hz, 1H), 8.02 (d, J = 7.6 Hz, 1H), 8.54 (d, J = 4.4Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 37.1, 38.1, 116.6, 116.8, 124.6, 124.9, 125.0, 126.4, 127.3, 129.2, 129.3, 137.1, 148.4, 151.3, 155.9, 157.2, 158.5, 167.4 ppm. HRMS (ESI^+): calcd for $C_{15}H_{14}FN_3NaO_2$ $[M+Na]^+$ 310.0968, found 310. 0968.



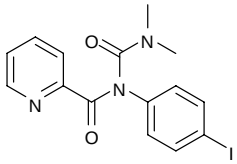
***N*-(2-Chlorophenyl)-*N*-(dimethylcarbamoyl)picolinamide (3e)**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1, v/v) afforded **3e** as a white solid (121 mg, 80% yield). M.p.: 99-100 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.97 (s, 6H), 7.27-7.40 (m, 4H), 7.49 (d, J = 7.2 Hz, 1H), 7.80 (t, J = 7.6 Hz, 1H), 8.00 (d, J = 7.6 Hz, 1H), 8.54 (d, J = 2.8 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 37.2, 38.1, 120.4, 124.6, 126.3, 128.0, 128.9, 130.7, 131.9, 136.5, 137.0, 142.1, 148.5, 151.6, 168.1 ppm. HRMS (ESI^+): calcd for $C_{15}H_{14}ClN_3NaO_2$ $[M+Na]^+$ 326.0672, found 326.0675.



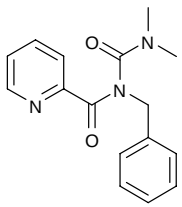
***N*-(3-Bromophenyl)-*N*-(dimethylcarbamoyl)picolinamide (3f)**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1, v/v) afforded **3f** as a white solid (133 mg, 76% yield). M.p.: 107-109 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.96 (s, 6H), 7.24-7.28 (m, 2H), 7.38-7.42 (m, 2H), 7.50 (s, 1H), 7.81 (t, J = 7.6 Hz, 1H), 7.98 (d, J = 7.6 Hz, 1H), 8.52 (d, J = 4.4 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 37.1, 38.5, 122.7, 124.2, 124.6, 126.4, 128.6, 130.1, 130.6, 137.2, 139.8, 148.3, 151.7, 157.3, 168.0 ppm. HRMS (ESI^+): calcd for $C_{15}H_{14}BrN_3NaO_2$ $[M+Na]^+$ 370.0167, found 370.0167.



***N*-(Dimethylcarbamoyl)-*N*-(4-iodophenyl)picolinamide (3g)**

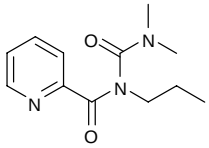
Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1, v/v) afforded **3g** as a white solid (159 mg, 80% yield). M.p.: 130-132 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.96 (s, 6H), 7.09 (d, J = 8.4 Hz, 2H), 7.40 (t, J = 6.2 Hz, 1H), 7.73 (d, J = 8.4 Hz, 2H), 7.82 (t, J = 7.6 Hz, 1H), 7.99 (d, J = 8.0 Hz, 1H), 8.53 (d, J = 4.4 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 37.1, 38.5, 121.7, 122.6, 124.6, 126.4, 127.4, 137.2, 138.1, 138.3, 138.5, 148.3, 151.8, 157.1, 168.0 ppm. HRMS (ESI^+): calcd for $C_{15}H_{14}IN_3NaO_2$ $[M+Na]^+$ 418.0028, found 418.0030.



***N*-Benzyl-*N*-(dimethylcarbamoyl)picolinamide (3h)**

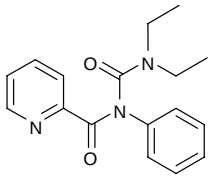
Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1, v/v) afforded **3h** as pale yellow oil (82 mg, 58% yield). Increasing the loading of

TBHP to 2.5 equiv, **3h** was afforded in 81% yield (115 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.47 (s, 3H), 2.79 (s, 3H), 4.96 (s, 2H), 7.26-7.34 (m, 3H), 7.36-7.39 (m, 1H), 7.48 (d, J = 6.8 Hz, 2H), 7.80 (td, J = 7.8 Hz, 1.2 Hz, 1H), 7.99 (d, J = 7.6 Hz, 1 H), 8.54 (d, J = 4.8 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 36.6, 37.9, 50.3, 124.3, 126.0, 127.8, 128.6, 129.1, 136.7, 137.0, 148.1, 151.7, 158.1, 166.9 ppm. HRMS (ESI$^+$): calcd for $C_{16}H_{17}N_3NaO_2$ $[M+Na]^+$ 306.1218, found 306.1220.



***N*-(Dimethylcarbamoyl)-*N*-propylpicolinamide (3i)**

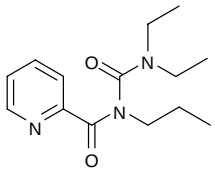
Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1, v/v) afforded **3i** as pale yellow oil (70 mg, 59% yield). Increasing the loading of TBHP to 2.5 equiv, **3i** was afforded in 78% yield (92 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.96 (t, J = 7.4 Hz, 3H), 1.70-1.79 (m, 2H), 2.85 (s, 6H), 3.65 (s, 2H), 7.33-7.37 (m, 1H), 7.78 (td, J = 7.6 Hz, 1.6Hz, 1H), 7.96 (d, J = 8.0 Hz, 1H), 8.50-8.51 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.5, 21.6, 36.6, 38.2, 48.5, 124.2, 126.7, 137.0, 148.1, 151.9, 158.6, 167.1 ppm. HRMS (ESI$^+$): calcd for $C_{12}H_{17}N_3O_2$ $[M+Na]^+$ 258.1218, found 258.1216.



***N*-(Diethylcarbamoyl)-*N*-phenylpicolinamide (3j)**

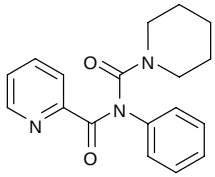
Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1, v/v) afforded **3j** as a white solid (116 mg, 78% yield), M.p.: 74-77 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.61 (t, J = 6.8 Hz, 3H), 1.09 (t, J = 6.8 Hz, 3H), 3.25 (s, 2H), 3.38 (s, 2H), 7.19-7.23 (m, 1H), 7.26-7.36 (m, 5H), 7.73 (t, J = 7.8 Hz, 1H), 7.89 (d, J = 8.0 Hz, 1H), 8.42 (d, J = 4.4 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.3, 12.1, 40.7, 42.9, 119.8, 124.4, 125.7, 126.1, 126.9, 128.8, 129.3, 137.0, 139.0, 147.8,

152.5, 156.8, 168.7 ppm. HRMS (ESI$^+$): calcd for $C_{17}H_{19}N_3NaO_2$ [M+Na]$^+$ 320.1375, found 320.1374.



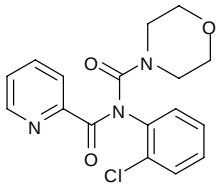
***N*-(Diethylcarbamoyl)-*N*-propylpicolinamide (3k)**

Employing the general procedure except that the loading of TBHP was 2.5 equiv, and purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1, v/v) afforded **3k** as pale yellow oil (94 mg, 71% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.96 (t, J = 7.4 Hz, 3H), 1.10 (t, J = 7.2 Hz, 6H), 1.71-1.80 (m, 2H), 3.30-3.36 (m, 6H), 7.33 (dd, J = 7.6 Hz, 4.8Hz, 1H), 7.76 (t, J = 7.8 Hz, 1H), 7.92 (d, J = 7.6 Hz, 1H), 8.46 (d, J = 4.4 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.3, 11.6, 13.2, 21.4, 40.1, 42.7, 48.8, 124.1, 125.8, 136.9, 147.7, 151.9, 157.6, 167.4 ppm. HRMS (ESI$^+$): calcd for $C_{14}H_{21}N_3NaO_2$ [M+Na]$^+$ 286.1531, found 286.1532.



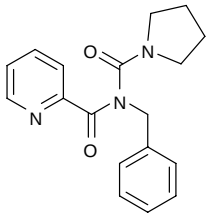
***N*-Phenyl-*N*-(piperidine-1-carbonyl)picolinamide (3l)**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1, v/v) afforded **3l** as a white solid (81 mg, 52% yield), M.p.: 96-99 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.39 (s, 2H), 1.56 (s, 4H), 3.46 (s, 4H), 7.26-7.30 (m, 1H), 7.33 (d, J = 8.0 Hz, 2H), 7.38-7.43 (m, 3H), 7.81 (t, J = 7.8 Hz, 1H), 7.97 (d, J = 7.6 Hz, 1H), 8.54 (d, J = 4.8 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.3, 25.1, 45.1, 48.0, 119.8, 124.4, 125.6, 126.2, 126.9, 128.8, 129.3, 137.0, 139.0, 148.0, 152.3, 156.3, 168.7 ppm. HRMS (ESI$^+$): calcd for $C_{18}H_{19}N_3NaO_2$ [M+Na]$^+$ 332.1375, found 332.1379.



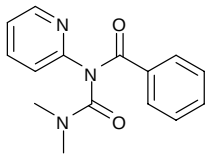
_N_-(2-Chlorophenyl)-_N_-picolinoylmorpholine-4-carboxamide (3m)

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1, v/v) afforded **3m** as a white solid (101 mg, 58 % yield), M.p.: 120-123 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.51-3.77 (m, 8H), 7.30-7.35 (m, 3H), 7.43-7.44 (m, 1H), 7.50 (d, J = 7.2 Hz, 1H), 7.84 (t, J = 7.6 Hz, 1H), 8.03 (d, J = 7.6 Hz, 1H), 8.57 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 44.4, 66.2, 121.0, 124.7, 126.6, 128.1, 129.1, 130.8, 131.5, 136.5, 137.2, 143.5, 148.1, 151.2, 168.2 ppm. HRMS (ESI^{+}): calcd for $C_{17}H_{16}ClN_3NaO_3$ $[M+Na]^{+}$ 368.0778, found 368.0775.



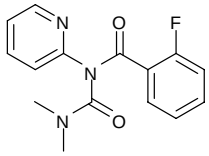
_N_-Benzyl-_N_-(pyrrolidine-1-carbonyl)picolinamide (3n)

Employing the general procedure except that the loading of TBHP was 2.5 equiv, and purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1, v/v) afforded **3n** as a white solid (99 mg, 64 % yield), M.p.: 82-83 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.48 (s, 2H), 1.63 (s, 2H), 2.80 (s, 2H), 3.33 (s, 2H), 4.98 (s, 2H), 7.26-7.33 (m, 3H), 7.38 (dd, J = 7.4 Hz, 5.0 Hz, 1H), 7.49 (d, J = 7.2Hz, 2H), 7.80 (td, J = 7.6 Hz, 1.6 Hz, 1H), 7.98 (d, J = 7.6 Hz, 1H), 8.54 (d, J = 4.8 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.4, 25.4, 46.5, 47.5, 49.8, 124.1, 125.9, 127.7, 128.5, 129.0, 136.8, 136.9, 147.9, 151.8, 155.8, 166.4 ppm. HRMS (ESI^{+}): calcd for $C_{18}H_{19}N_3NaO_2$ $[M+Na]^{+}$ 332.1375, found 332.1371.



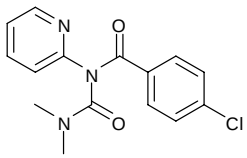
_N_-(Dimethylcarbamoyl)-_N_-(pyridin-2-yl)benzamide (5a)

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1, v/v) afforded **5a** as a white solid (108 mg, 80% yield). M.p.: 121-122 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.96 (s, 6H), 7.15 (dd, J = 7.2 Hz, 5.2Hz, 1H), 7.38 (t, J = 7.6 Hz, 3H), 7.48 (t, J = 7.0 Hz, 1H), 7.67-7.71 (m, 3H), 8.44 (d, J = 4.4 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 36.8, 37.7, 121.0, 121.7, 128.45, 128.54, 132.1, 134.9, 138.2, 148.8, 152.8, 156.3, 169.5 ppm. HRMS (ESI^+): calcd for $C_{15}H_{15}N_3NaO_2$ $[M+Na]^+$ 292.1062, found 292.1061.



_N_-(Dimethylcarbamoyl)-2-fluoro-_N_-(pyridin-2-yl)benzamide (5b)

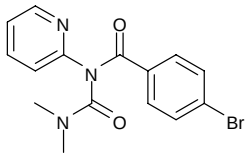
Employing the general procedure except that the reaction was carried out at room temperature, purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1, v/v) afforded **5b** as pale yellow oil (58 mg, 40% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.00 (s, 6H), 6.99 (t, J = 9.2 Hz, 1H), 7.14-7.21 (m, 2H), 7.38-7.43 (m, 2H), 7.62-7.71 (m, 2H), 8.40 (d, J = 4.4 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 36.9, 37.9, 115.7, 115.9, 119.9, 121.7, 123.7, 123.9, 124.4, 124.5, 130.31, 130.34, 132.75, 132.84, 137.9, 148.8, 152.0, 155.2, 157.7, 160.1, 165.5 ppm. HRMS (ESI^+): calcd for $C_{15}H_{14}FN_3NaO_2$ $[M+Na]^+$ 310.0968, found 310. 0969.



4-Chloro-_N_-(dimethylcarbamoyl)-_N_-(pyridin-2-yl)benzamide (5c)

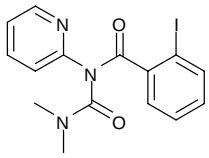
Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1, v/v) afforded **5c** as a white solid (95 mg, 63% yield). M.p.: 132-133 °C. ^{1}H NMR

(400 MHz, $CDCl_3$): δ = 2.97 (s, 6H), 7.18 (dd, J = 7.2 Hz, 5.2 Hz, 1H), 7.34-7.38 (m, 3H), 7.64 (d, J = 8.4 Hz, 2H), 7.73 (td, J = 7.8 Hz, 1.6 Hz, 1H), 8.45 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 36.3, 37.6, 120.8, 121.8, 128.8, 129.8, 133.1, 138.2, 138.5, 148.6, 152.3, 155.9, 168.4 ppm. HRMS (ESI^+): calcd for $C_{15}H_{14}ClN_3NaO_2$ $[M+Na]^+$ 326.0672, found 326.0668.



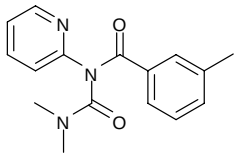
4-Bromo-*N*-(dimethylcarbamoyl)-*N*-(pyridin-2-yl)benzamide (5d)

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1, v/v) afforded **5d** as a white solid (123 mg, 71% yield). M.p.: 141-143 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.97 (s, 6H), 7.18 (t, J = 6.0 Hz, 1H), 7.36 (d, J = 8.0 Hz, 1H), 7.50-7.57 (m, 4H), 7.73 (t, J = 7.8 Hz, 1H), 8.44 (d, J = 4.8 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 36.8, 37.7, 120.9, 122.0, 126.9, 130.0, 131.9, 133.7, 138.6, 148.7, 152.4, 156.0, 168.6 ppm. HRMS (ESI^+): calcd for $C_{15}H_{14}BrN_3NaO_2$ $[M+Na]^+$ 370.0167, found 370.0169.



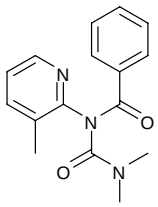
***N*-(Dimethylcarbamoyl)-2-iodo-*N*-(pyridin-2-yl)benzamide (5e)**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1, v/v) afforded **5e** as a white solid (150 mg, 76% yield). M.p.: 136-138 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.99 (s, 6H), 7.05 (t, J = 7.6 Hz, 1H), 7.14 (t, J = 5.6 Hz, 1H), 7.28 (t, J = 7.2Hz, 1H), 7.40 (d, J = 6.0 Hz, 1H), 7.58 (s, 1H), 7.70 (t, J = 7.0 Hz, 1H), 7.85 (d, J = 8.0 Hz, 1H), 8.39 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 37.0, 38.5, 93.4, 120.4, 121.9, 127.6, 128.7, 131.3, 138.4, 140.1, 148.6, 151.6, 154.7, 168.6 ppm. HRMS (ESI^+): calcd for $C_{15}H_{14}IN_3NaO_2$ $[M+Na]^+$ 418.0028, found 418.0029.



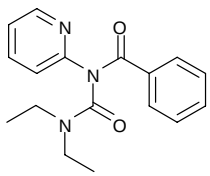
***N*-(Dimethylcarbamoyl)-3-methyl-*N*-(pyridin-2-yl)benzamide (5f)**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1, v/v) afforded **5f** as a white solid (97 mg, 69%). M.p.: 97-99°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.34 (s, 3H), 2.96 (s, 6H), 7.13 (dd, J = 7.2 Hz, 4.8 Hz, 1H), 7.21-7.28 (m, 2H), 7.33 (d, J = 8.4 Hz, 1H), 7.44 (d, J = 7.6 Hz, 1H), 7.53 (s, 1H), 7.67 (td, J = 7.8 Hz, 2.0 Hz, 1H), 8.42-8.44 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.2, 37.3, 120.8, 121.5, 125.3, 128.2, 129.0, 132.7, 134.7, 137.9, 138.3, 148.8, 152.9, 156.2, 169.6 ppm. HRMS (ESI^+): calcd for $C_{16}H_{17}N_3NaO_2$ $[M+Na]^+$ 306.1218, found 306.1222.



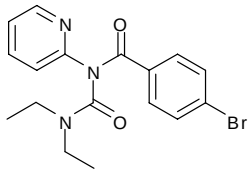
***N*-(Dimethylcarbamoyl)-*N*-(3-methylpyridin-2-yl)benzamide (5g)**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1, v/v) afforded **5g** as a white solid (89 mg, 63%). M.p.: 144-147°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.27 (s, 3H), 2.99 (s, 6H), 7.17 (dd, J = 7.4 Hz, 5.0 Hz, 1H), 7.34 (t, J = 7.2 Hz, 2H), 7.45 (t, J = 7.2 Hz, 1H), 7.57 (d, J = 6.8 Hz, 1H), 7.71 (d, J = 7.2 Hz, 2H), 8.33 (d, J = 3.6 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.6, 36.9, 38.1, 123.3, 128.4, 128.5, 132.1, 134.6, 140.7, 146.4, 151.8, 156.3, 167.3, 169.4 ppm. HRMS (ESI^+): calcd for $C_{16}H_{17}N_3NaO_2$ $[M+Na]^+$ 306.1218, found 306.1224.



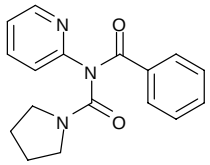
***N*-(Diethylcarbamoyl)-*N*-(pyridin-2-yl)benzamide (5i)**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1, v/v) afforded **5i** as pale yellow oil (111 mg, 75%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.97 (t, J = 7.2 Hz, 6H), 3.37 (s, 2H), 3.38 (s, 2H), 7.12 (dd, J = 7.4 Hz, 5.0 Hz, 1H), 7.36 (t, J = 7.6 Hz, 2H), 7.40-7.47 (m, 2H), 7.67 (d, J = 7.2 Hz, 3H), 8.41 (d, J = 4.4 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.4, 13.0, 40.9, 42.9, 120.3, 121.5, 128.3, 128.4, 131.7, 135.1, 138.0, 148.8, 152.9, 155.3, 170.0 ppm. HRMS (ESI$^+$): calcd for $C_{17}H_{19}N_3NaO_2$ $[M+Na]^+$ 320.1375, found 320.1373.



4-Bromo-*N*-(diethylcarbamoyl)-*N*-(pyridin-2-yl)benzamide (5j)

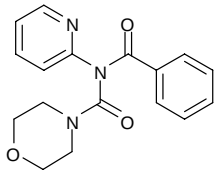
Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1, v/v) afforded **5j** as pale yellow oil (120 mg, 64 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.00 (s, 6H), 3.38 (s, 2H), 3.39 (s, 2H), 7.17 (dd, J = 7.2 Hz, 5.2 Hz, 1H), 7.40 (d, J = 8.0 Hz, 1H), 7.49-7.55 (m, 4H), 7.73 (t, J = 7.8 Hz, 1H), 8.42 (d, J = 4.8 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.5, 13.0, 40.9, 42.5, 120.3, 121.8, 126.5, 130.0, 131.7, 134.0, 138.2, 149.0, 152.7, 155.1, 169.1 ppm. HRMS (ESI$^+$): calcd for $C_{17}H_{18}BrN_3NaO_2$ $[M+Na]^+$ 398.0480, found 398.0477.



***N*-Benzoyl-*N*-(pyridin-2-yl)pyrrolidine-1-carboxamide (5k)**

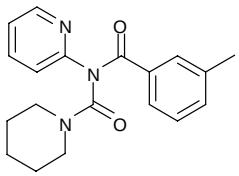
Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/2, v/v) afforded **5k** as a white solid (74 mg, 50 %). M.p.: 120-123 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.82 (s, 4H), 3.40 (s, 2H), 3.46 (s, 2H), 7.13-7.14 (m, 1H), 7.35-7.38 (m, 3H), 7.46 (t, J = 7.4 Hz, 1H), 7.68-7.72 (m, 3H), 8.43 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.6, 25.6, 47.0, 47.5, 120.8, 121.5, 128.4, 128.5, 131.9,

135.1, 138.0, 148.9, 152.8, 154.2, 169.4 ppm. HRMS (ESI^+): calcd for $C_{17}H_{17}N_3NaO_2$ $[M+Na]^+$ 318.1218, found 318.1220.



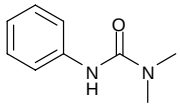
***N*-Benzoyl-*N*-(pyridin-2-yl)morpholine-4-carboxamide (5l)**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/2, v/v) afforded **5l** as a white solid (99 mg, 64 %). M.p.: 126-128 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.49 (s, 4H), 3.57-3.58 (m, 4H), 7.18 (t, J = 6.2 Hz, 1H), 7.37-7.42 (m, 3H), 7.50 (t, J = 7.4 Hz, 1H), 7.69-7.74 (m, 3H), 8.44 (d, J = 4.4 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 45.9, 66.2, 120.7, 121.8, 128.4, 128.6, 132.2, 134.7, 138.1, 149.0, 152.8, 155.2, 169.5 ppm. HRMS (ESI^+): calcd for $C_{17}H_{17}N_3NaO_3$ $[M+Na]^+$ 334.1168, found 334.1167.



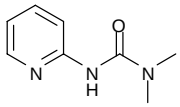
***N*-(3-Methylbenzoyl)-*N*-(pyridin-2-yl)piperidine-1-carboxamide (5m)**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1, v/v) afforded **5m** as pale yellow oil (116 mg, 72 %). ^1H NMR (400 MHz, $CDCl_3$): δ = 1.45 (s, 4H), 1.51 (s, 2H), 2.35 (s, 3H), 3.42 (s, 4H), 7.12 (t, J = 6.0 Hz, 1H), 7.22-7.29 (m, 2H), 7.41 (d, J = 8.4 Hz, 1H), 7.47 (d, J = 7.2 Hz, 1H), 7.54 (s, 1H), 7.69 (t, J = 7.8 Hz, 1H), 8.42 (d, J = 4.0 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.4, 24.1, 25.3, 46.6, 120.5, 121.5, 125.4, 128.2, 129.0, 132.7, 135.0, 138.0, 138.3, 148.9, 153.0, 155.0, 170.0 ppm. HRMS (ESI^+): calcd for $C_{19}H_{21}N_3NaO_2$ $[M+Na]^+$ 346.1531, found 346.1528.



1,1-Dimethyl-3-phenylurea (6a)[4]

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1, v/v) afforded **6a** as a white solid (63 mg, 96 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.00 (s, 6H), 6.34 (s, 1H), 7.00 (t, J = 7.2 Hz, 1H), 7.26 (t, J = 7.2 Hz, 2H), 7.36 (d, J = 8.0 Hz, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 36.5, 120.0, 123.0, 128.9, 139.3, 155.9 ppm. HRMS (ESI^+): calcd for $C_9H_{12}N_2NaO$ $[M+Na]^+$ 187.0847, found 187.0850.



1,1-Dimethyl-3-(pyridin-2-yl)urea (7a)[5]

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/3, v/v) afforded **7a** as pale yellow oil (45 mg, 68 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.03 (s, 6H), 6.91 (dd, J = 6.2 Hz, 5.8 Hz, 1H), 7.23 (s, 1H), 7.62 (t, J = 7.8 Hz, 1H), 8.04 (d, J = 8.4 Hz, 1H), 8.17 (d, J = 4.4 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 36.5, 113.2, 118.4, 138.2, 147.5, 152.9, 155.0 ppm. HRMS (ESI^+): calcd for $C_8H_{11}N_3NaO$ $[M+Na]^+$ 188.0800, found 188.0802.

VII. References

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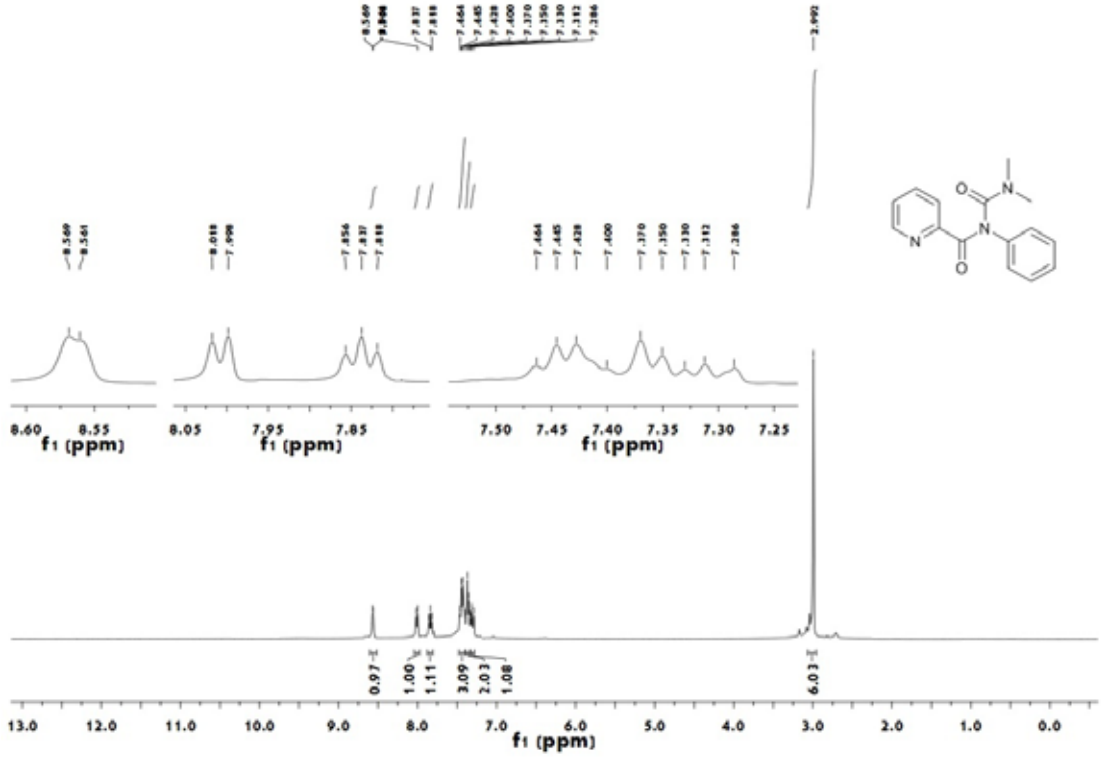
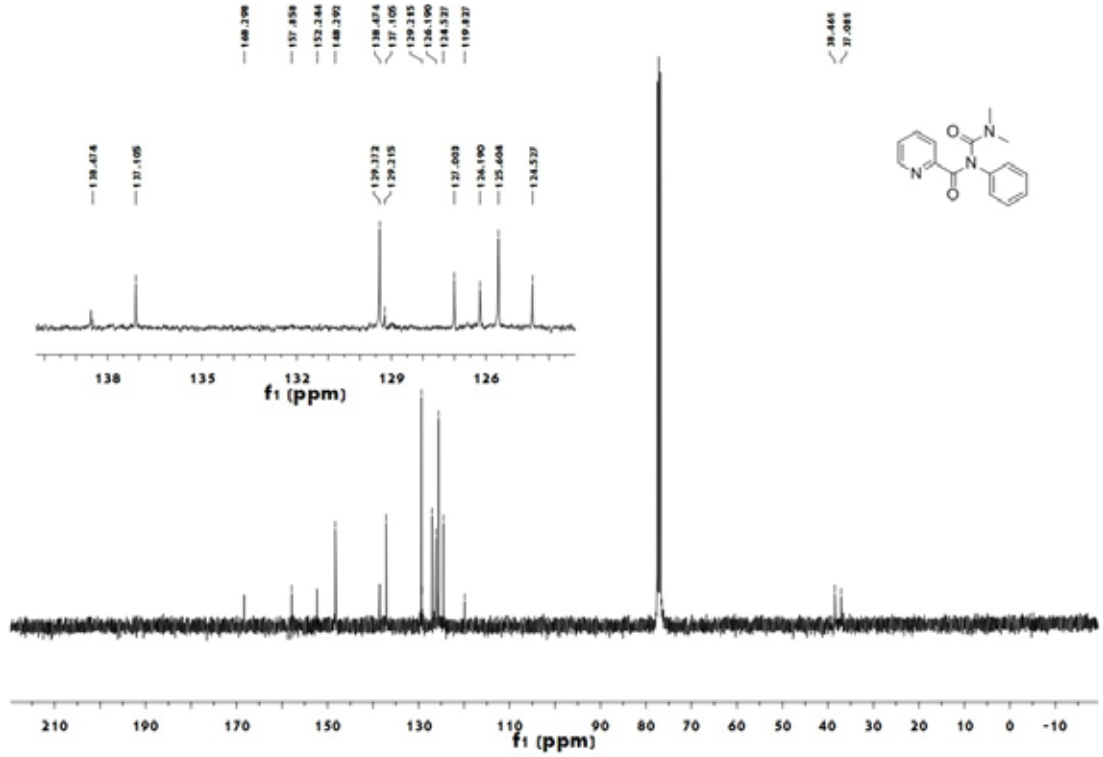
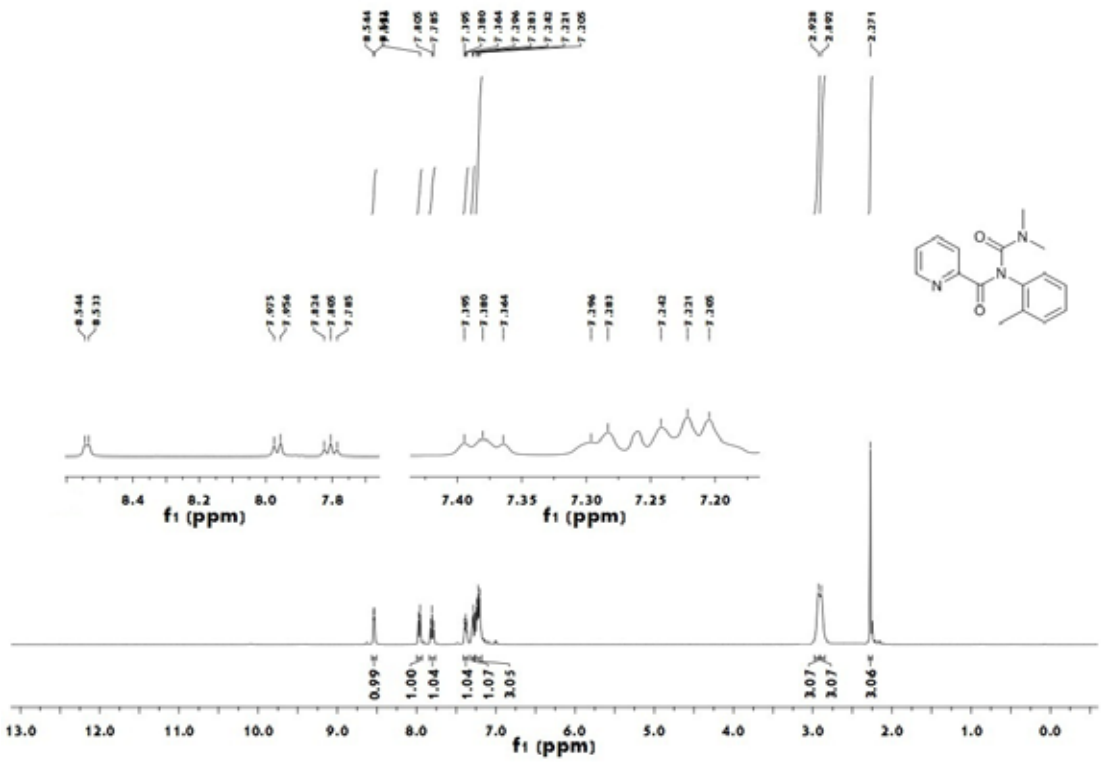
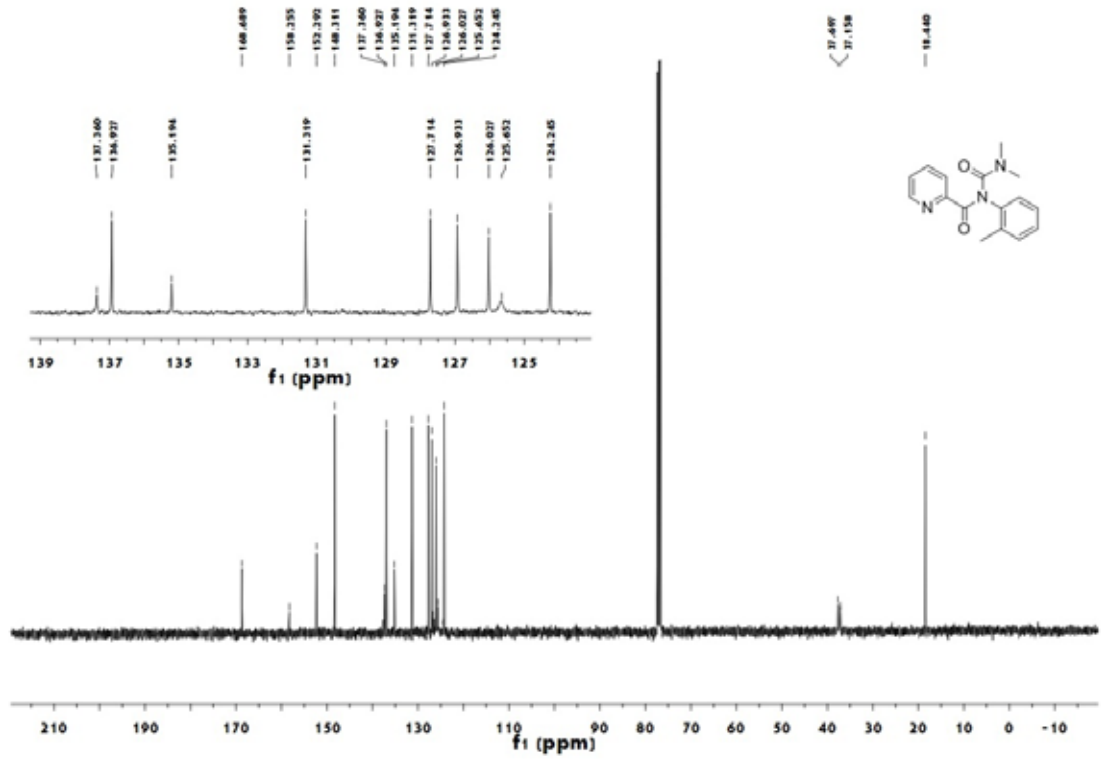
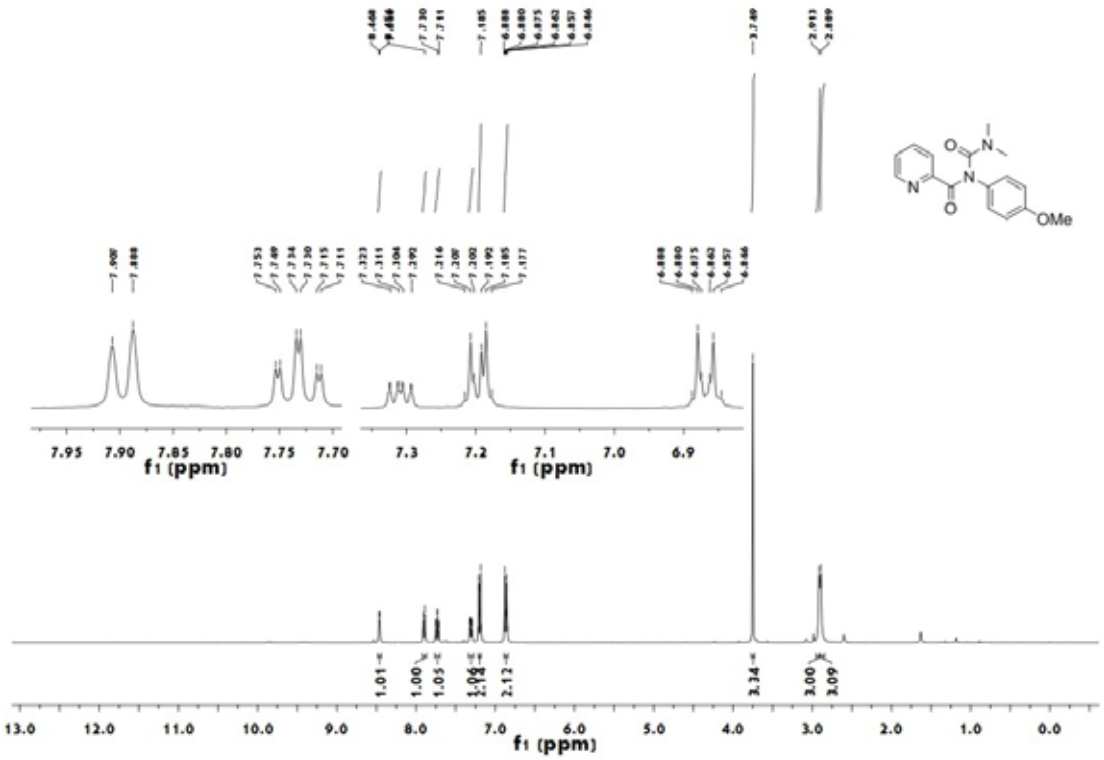
VIII. Copies of ^{1}H and ^{13}C NMR spectra

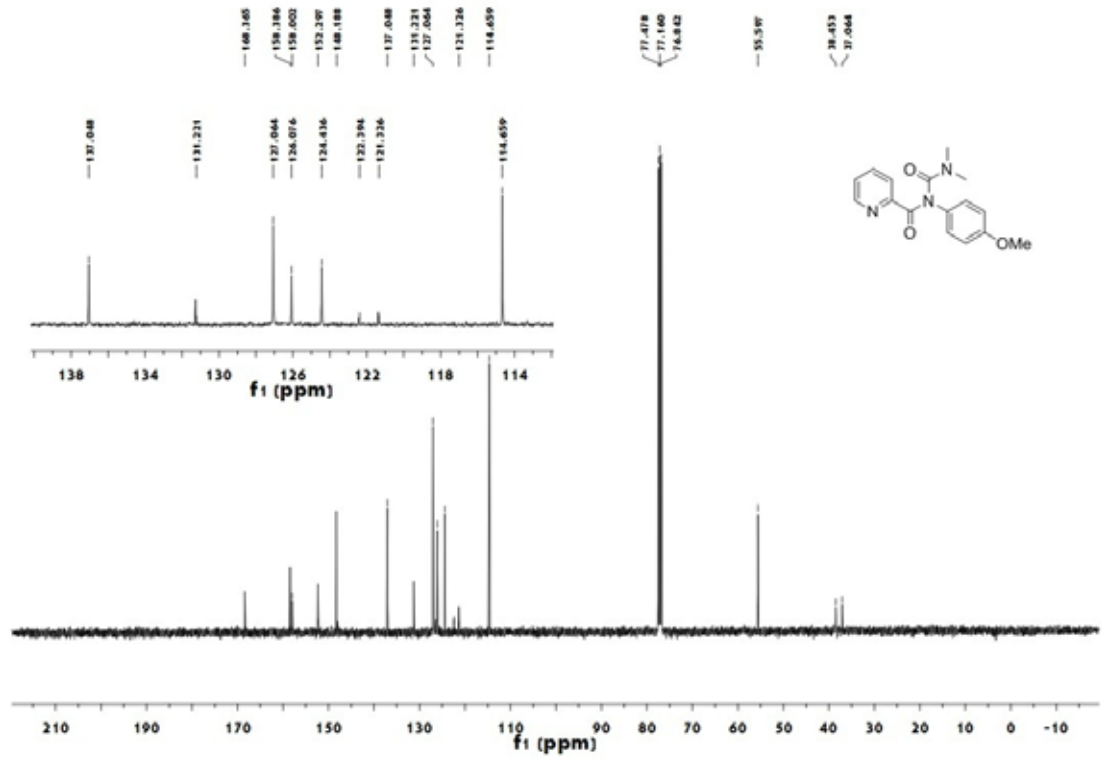


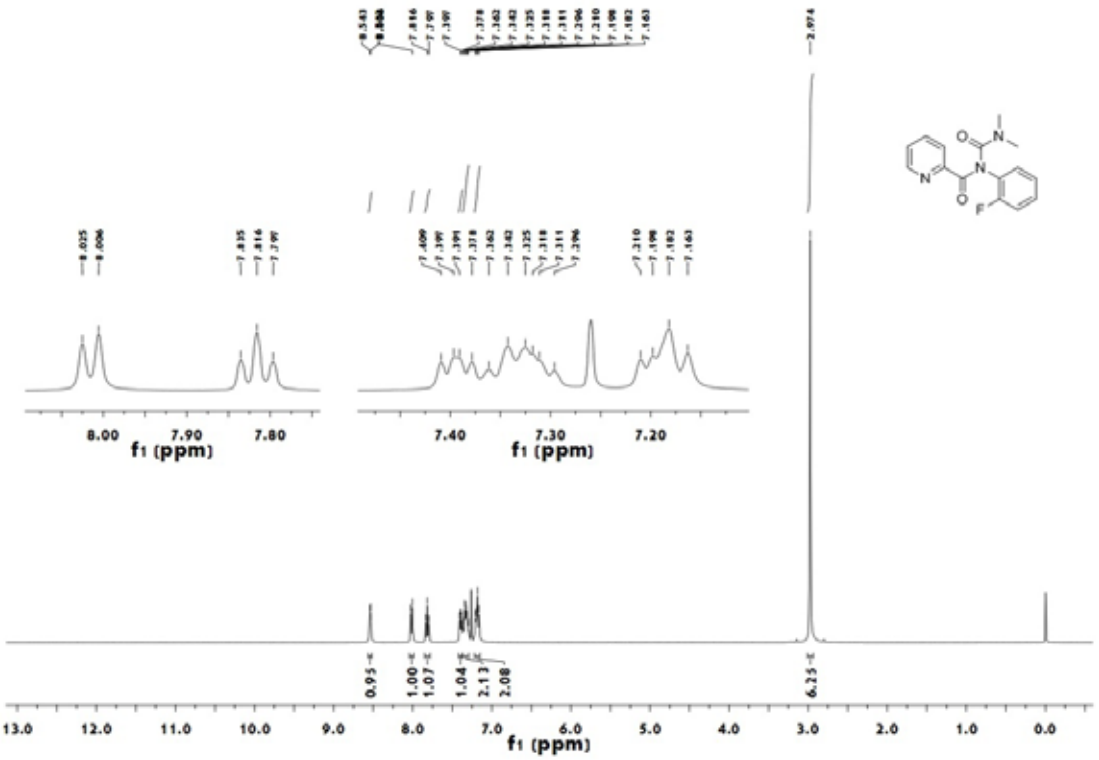


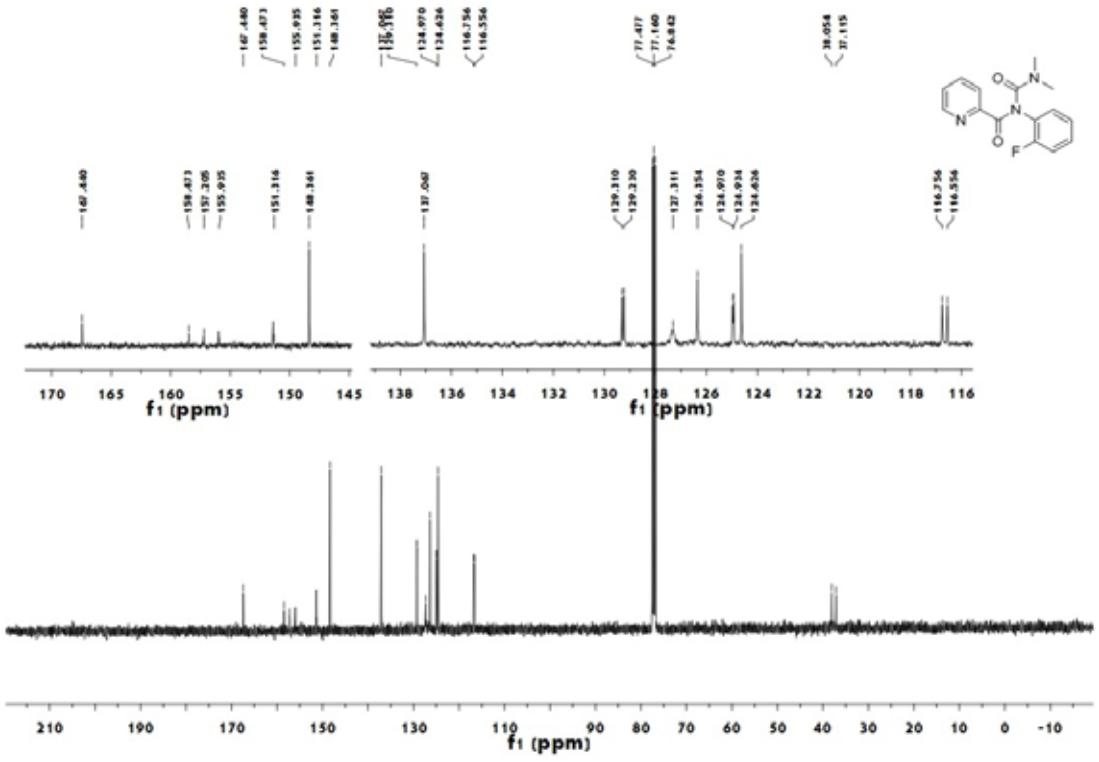


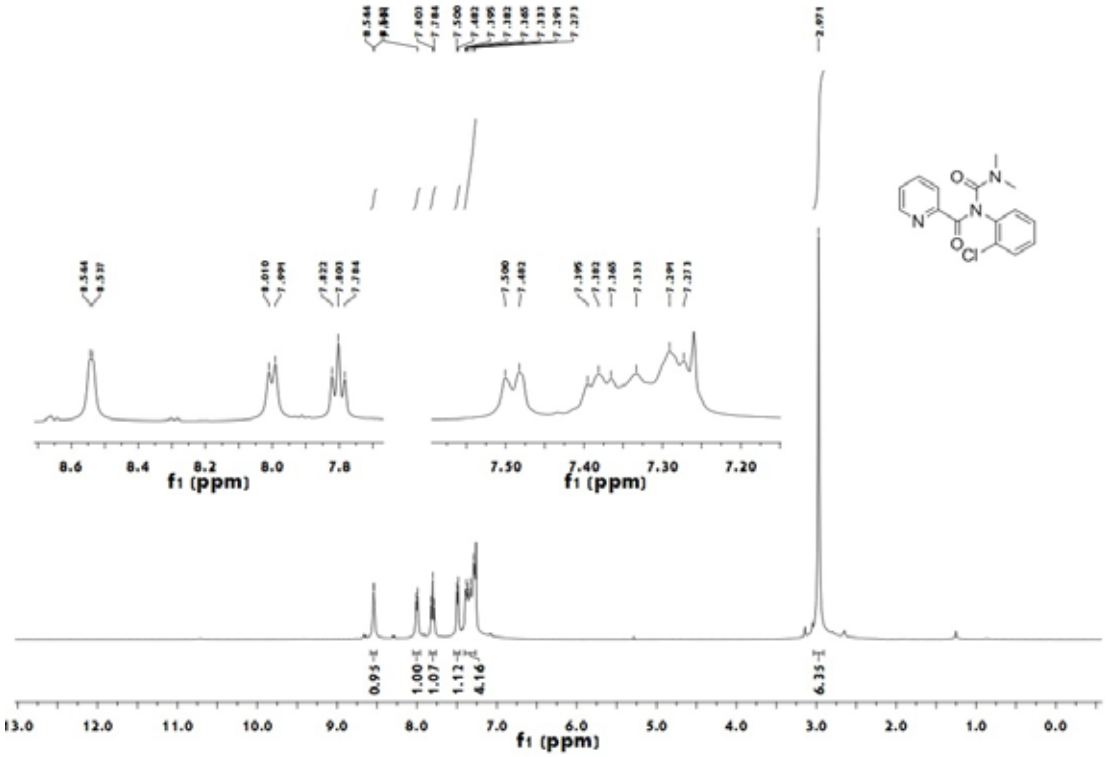


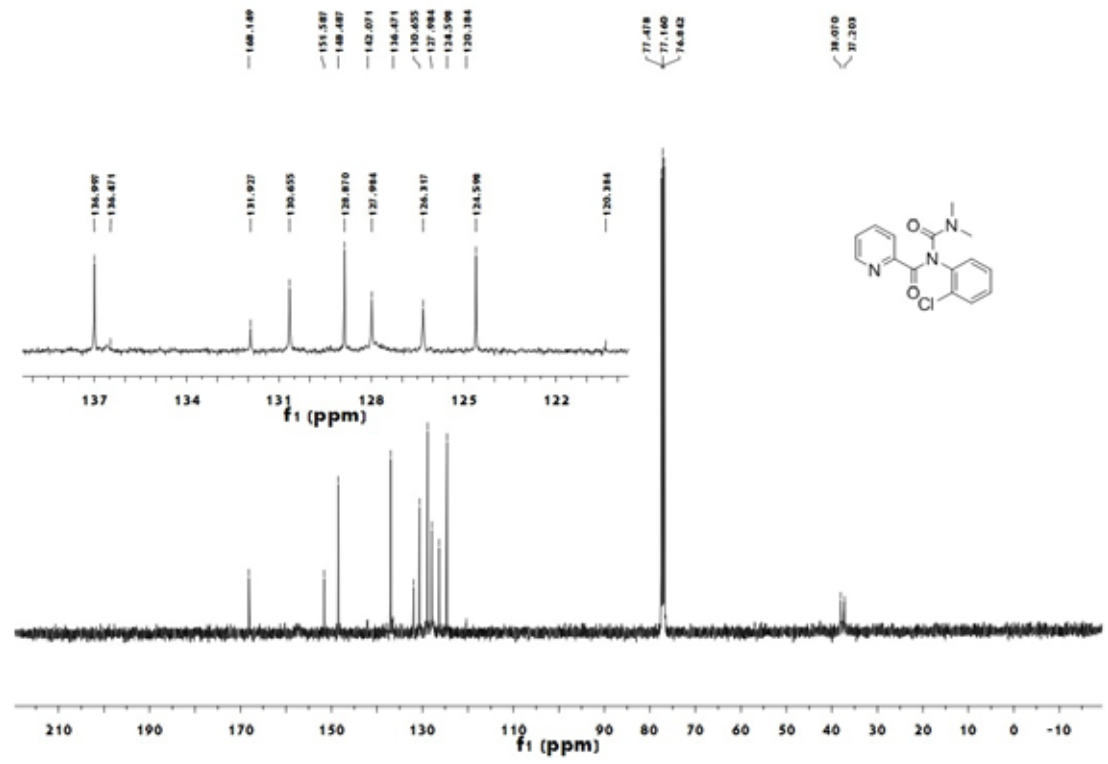


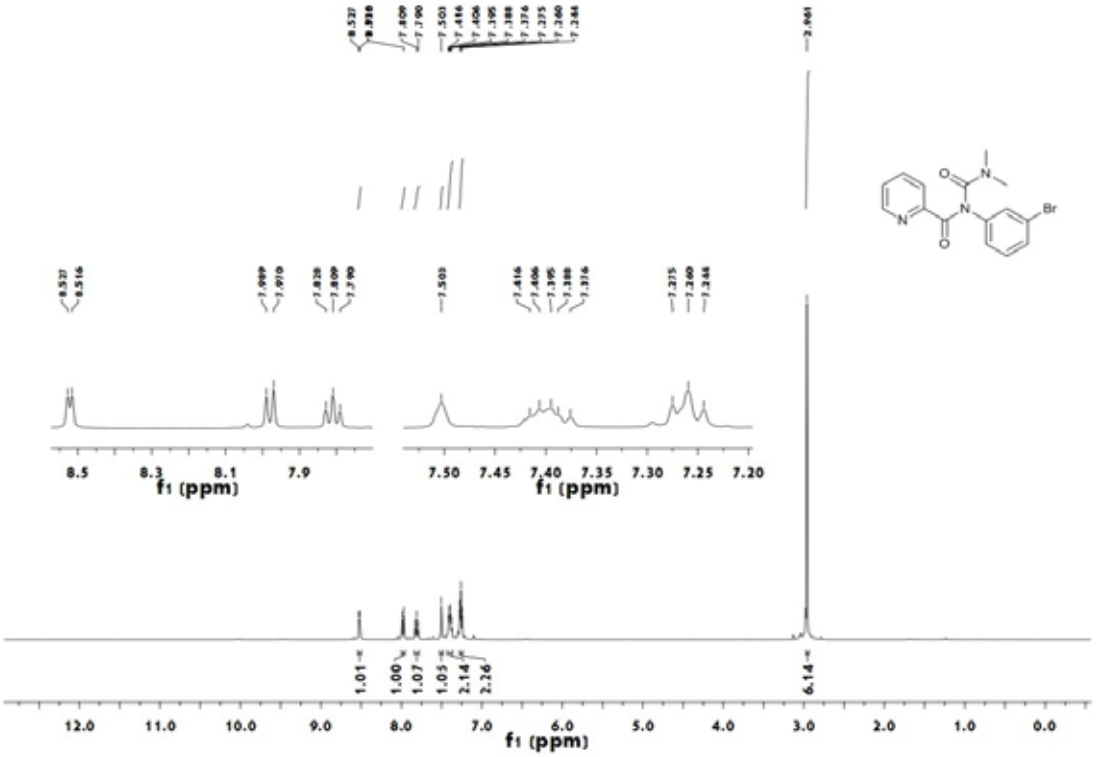


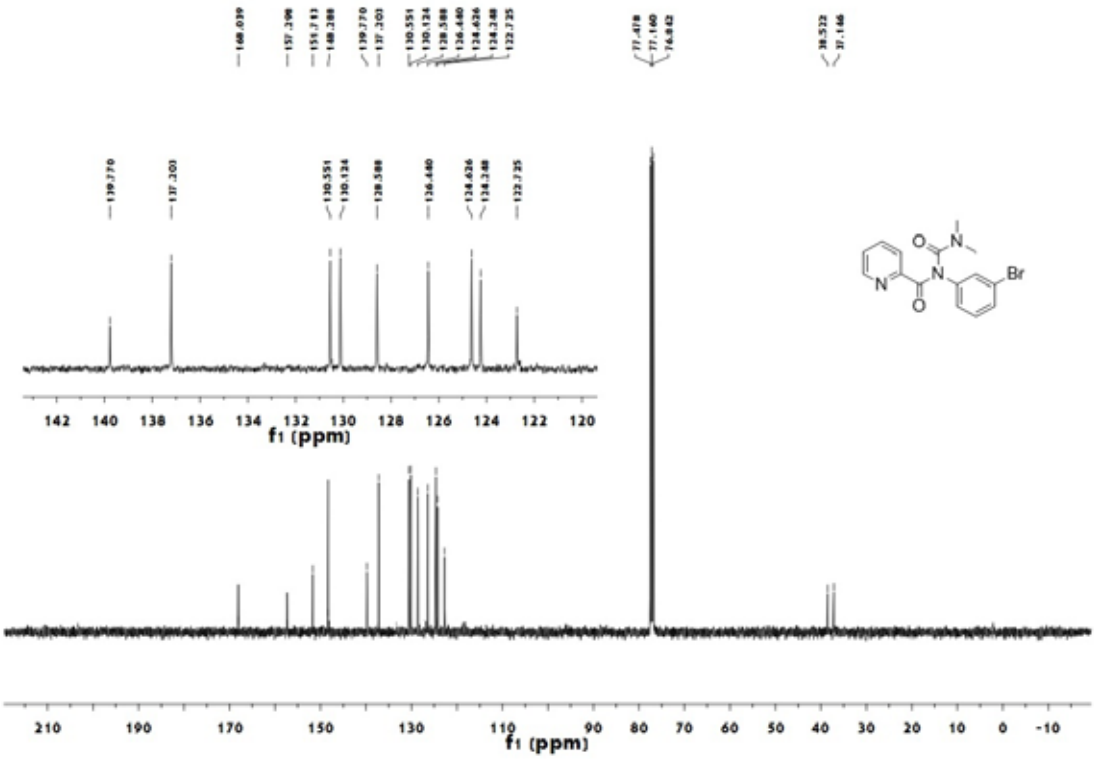


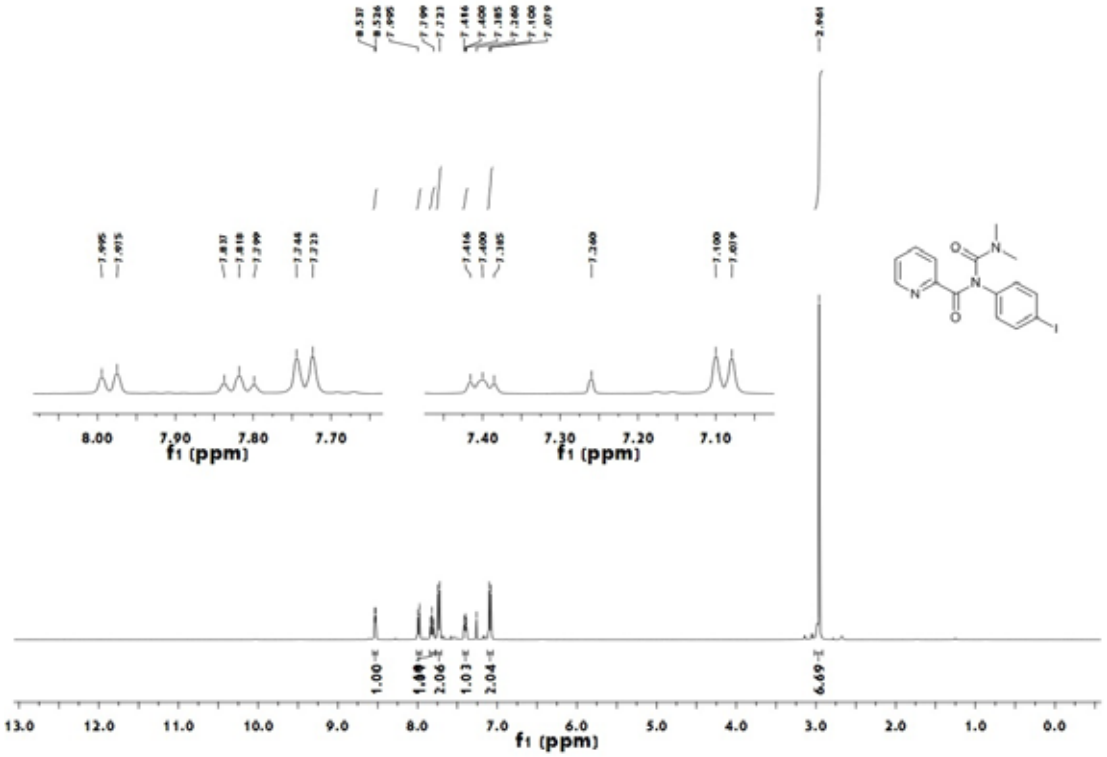


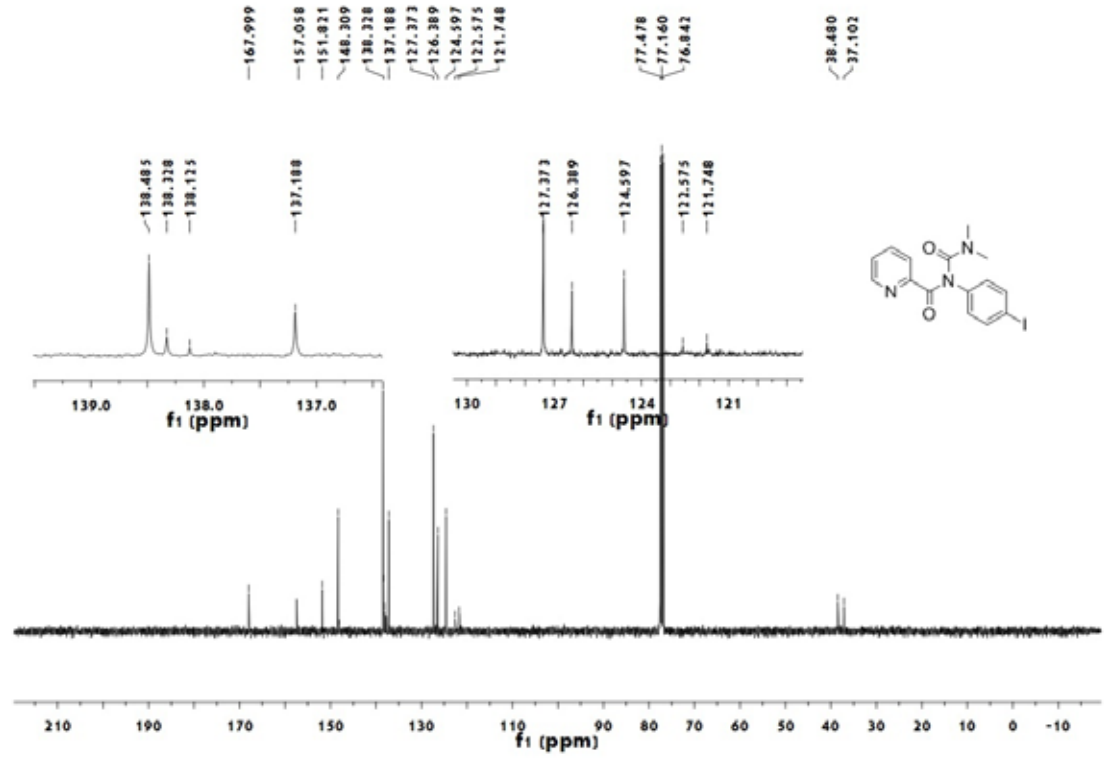


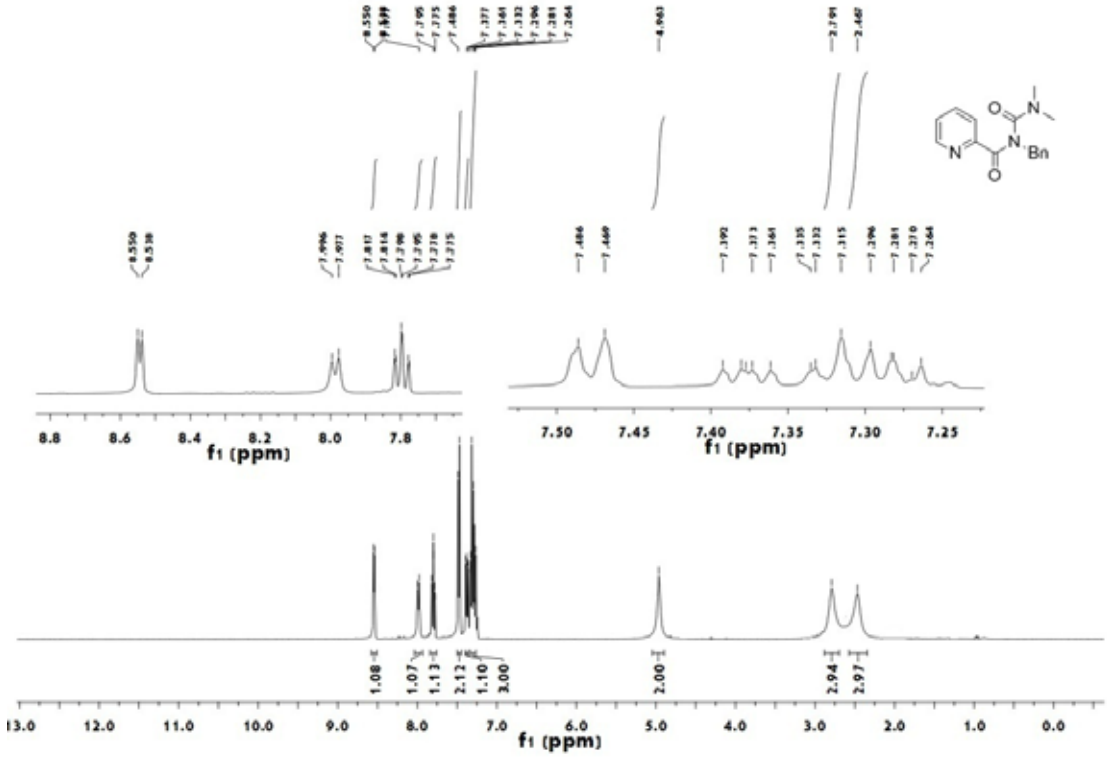


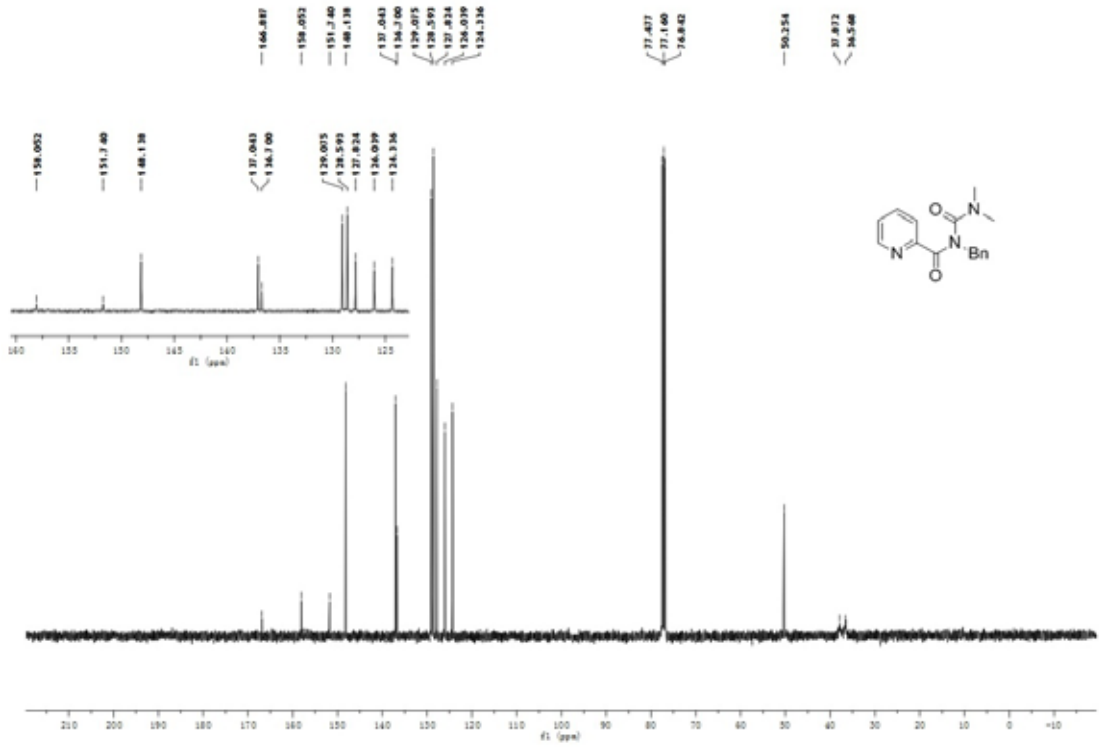


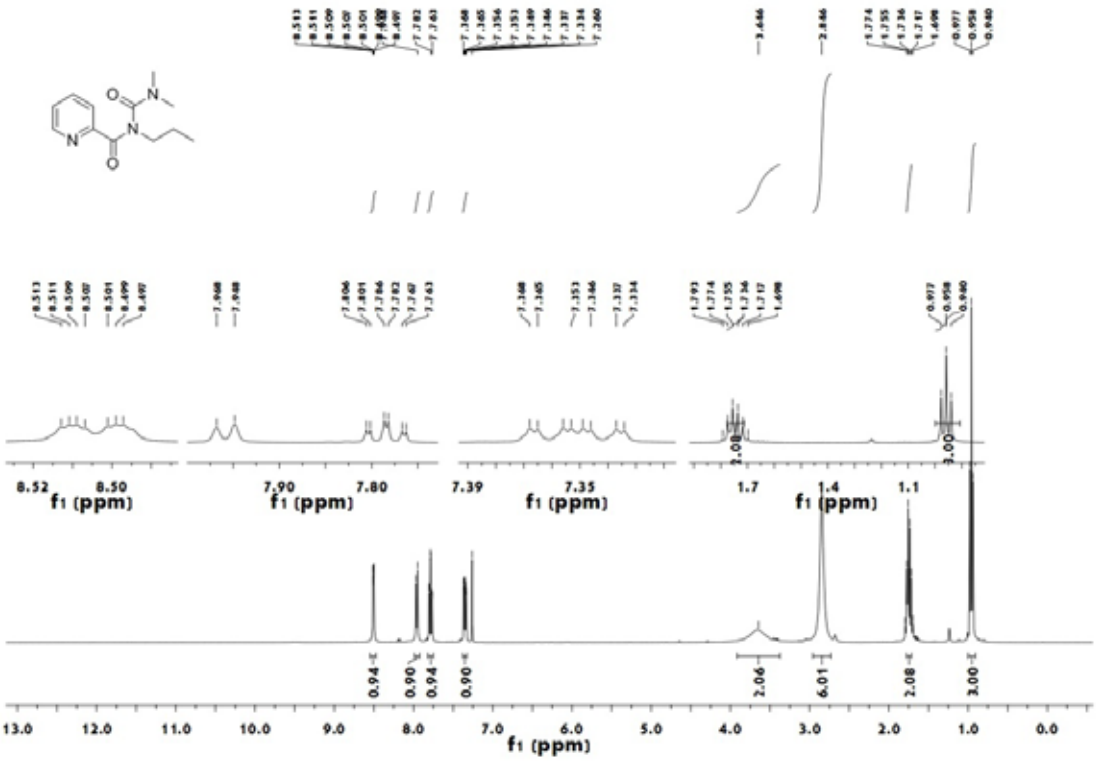


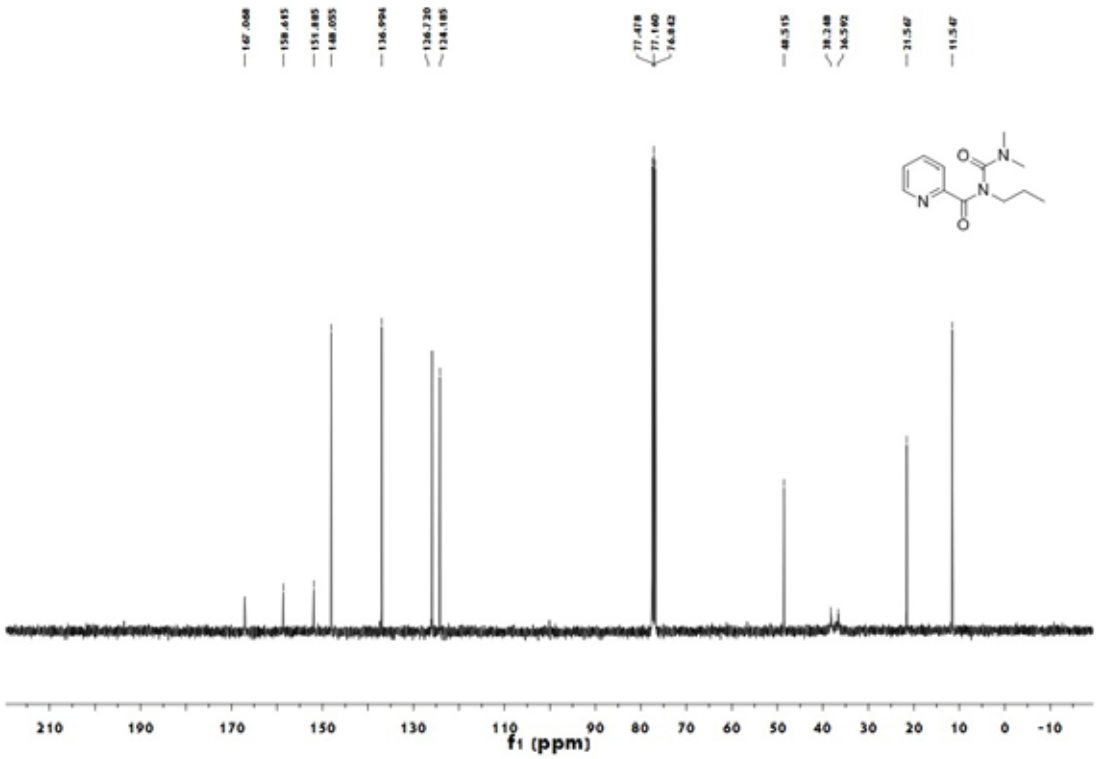


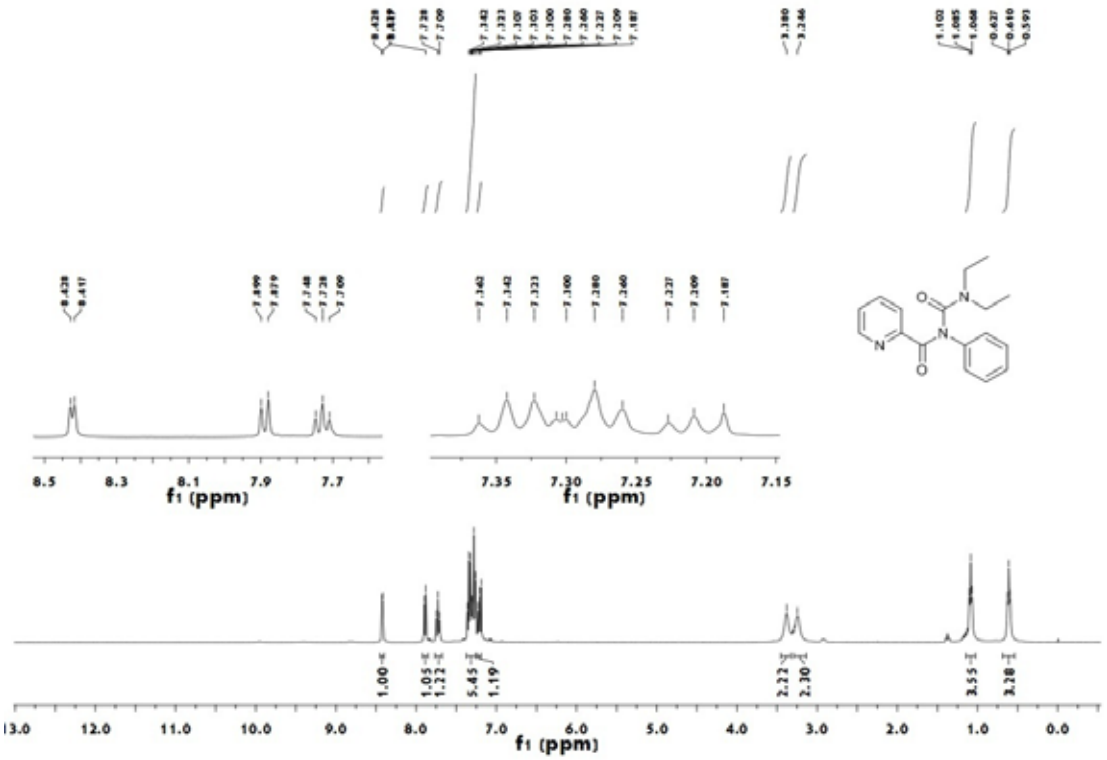


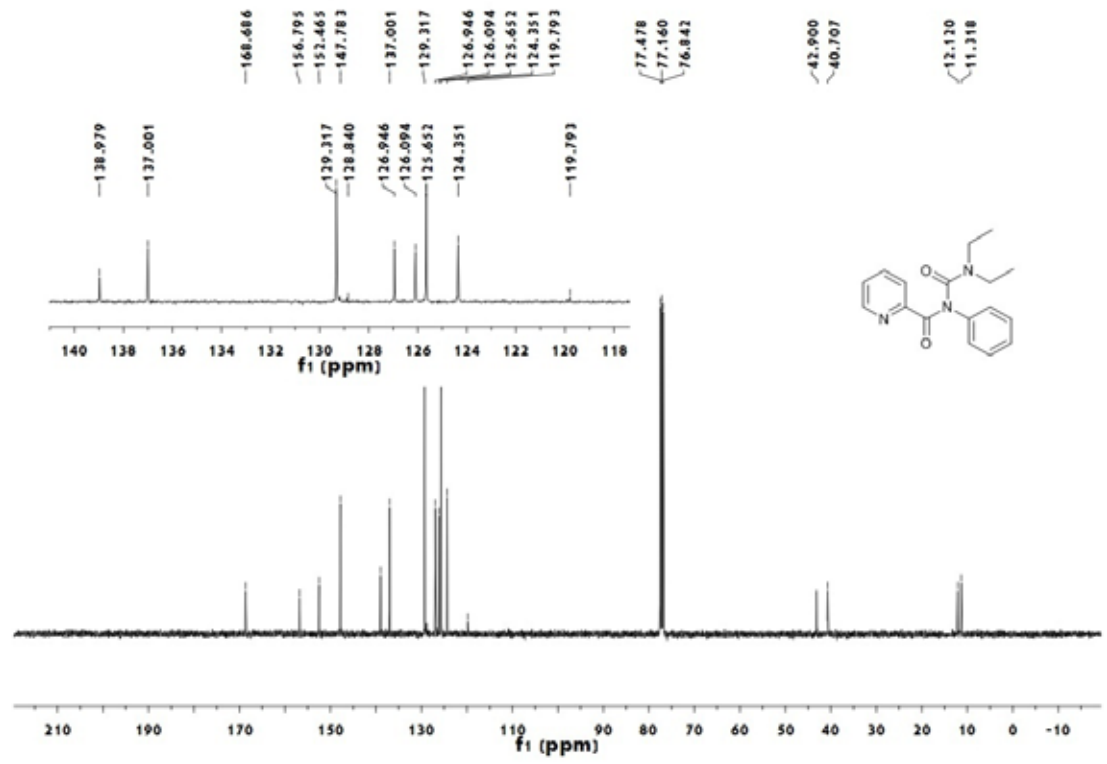









f1 (ppm)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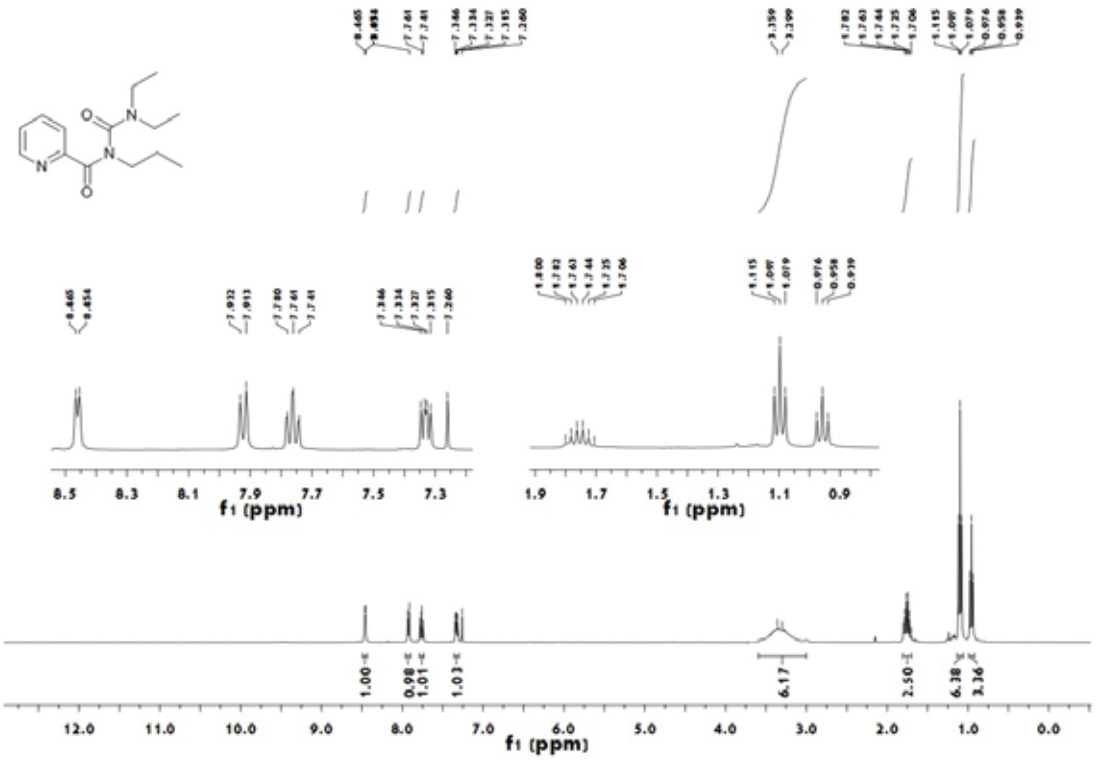
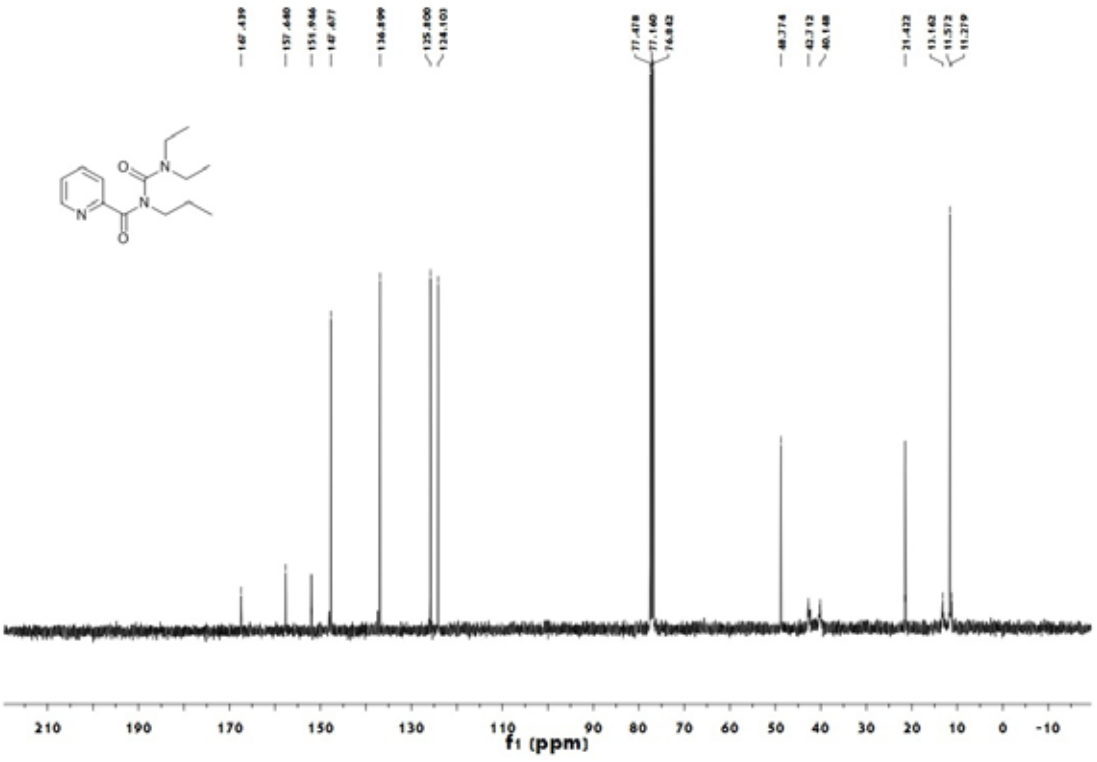
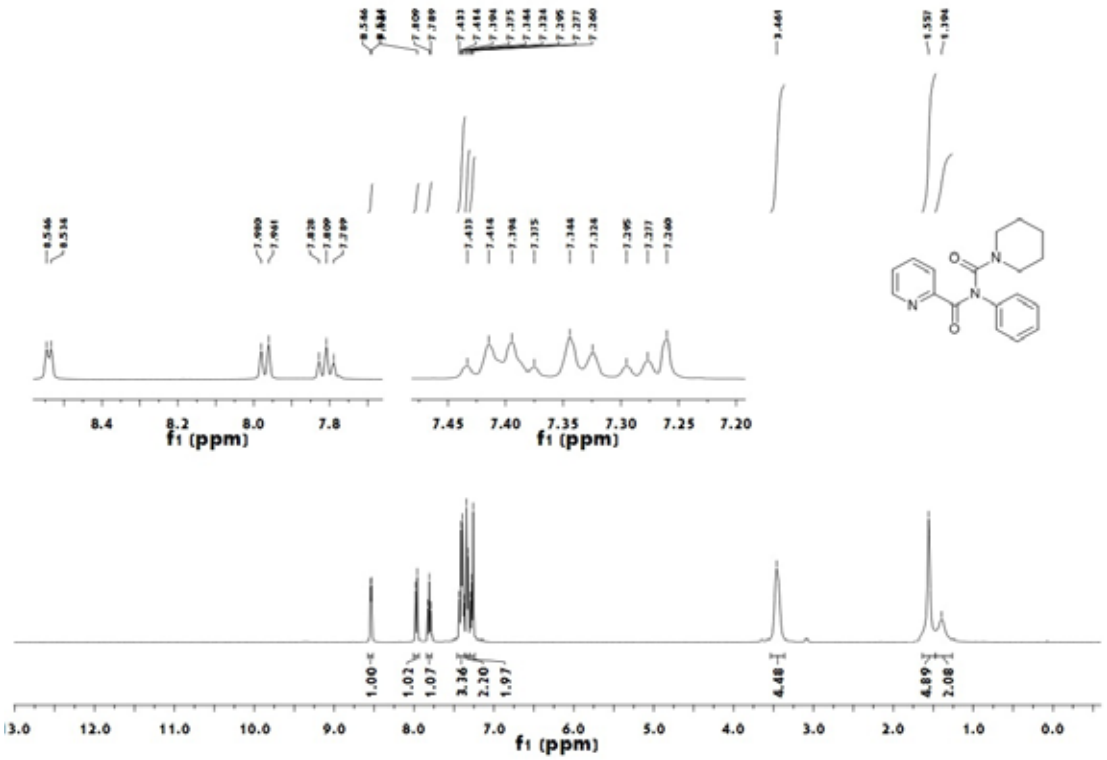

f1 (ppm)
f1 (ppm)
f1 (ppm)


f1 (ppm)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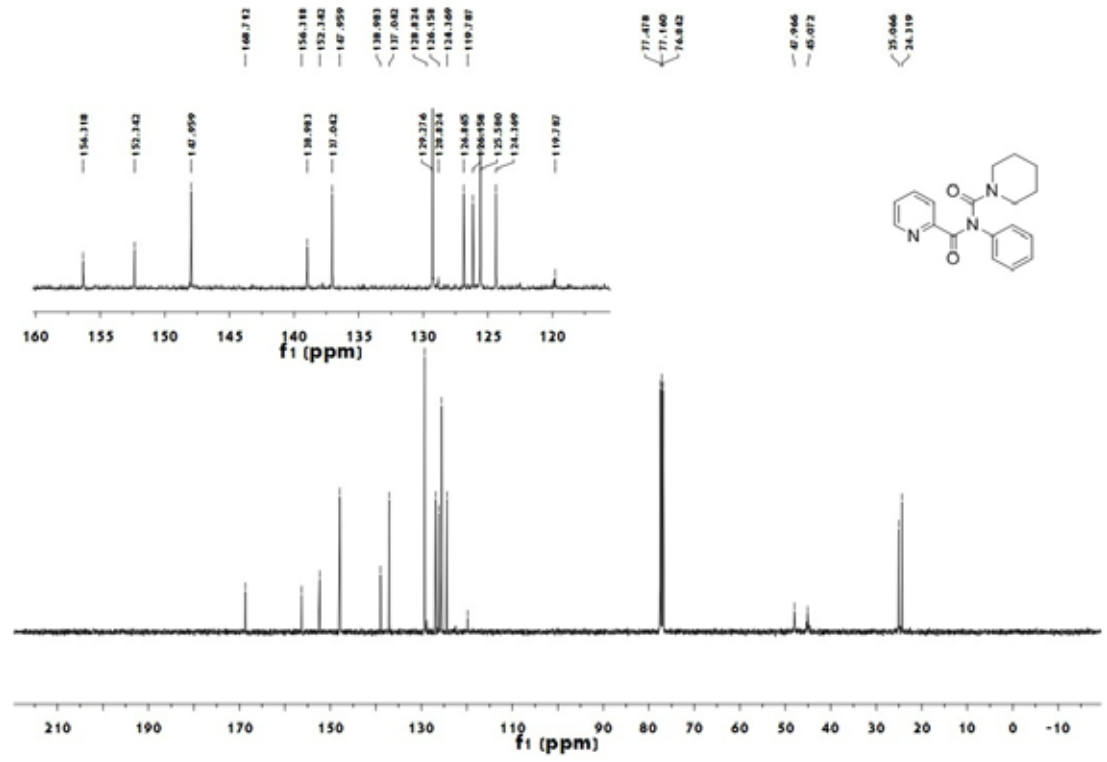
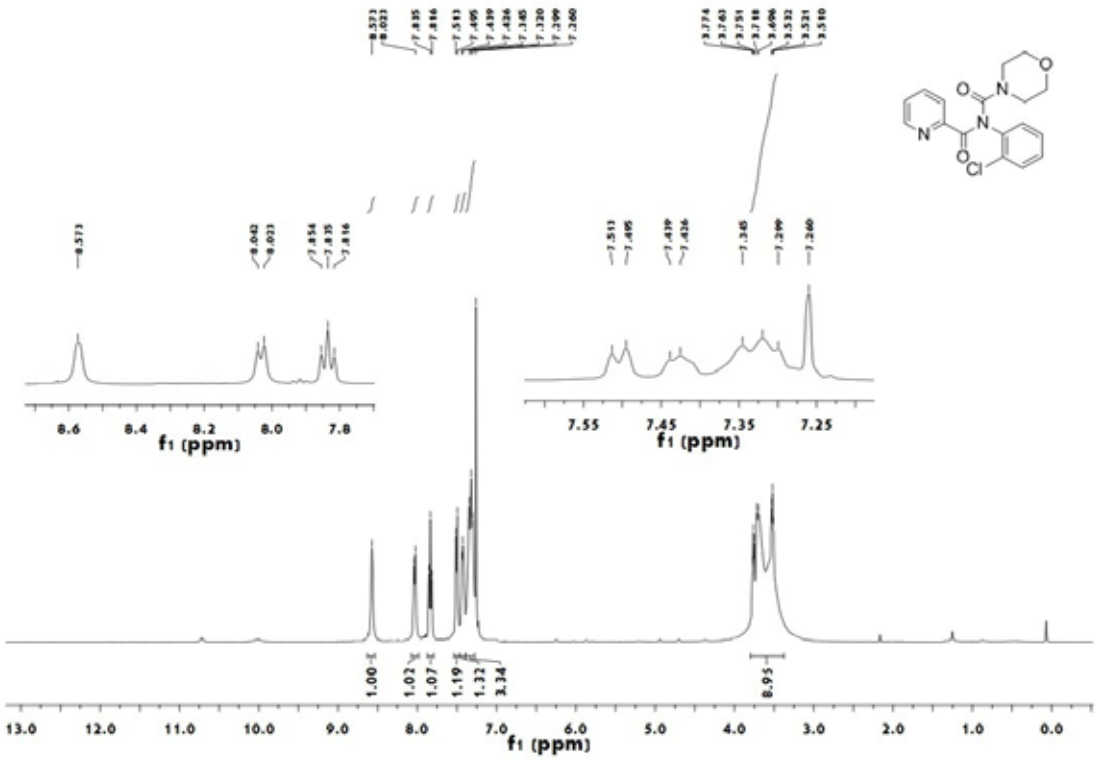
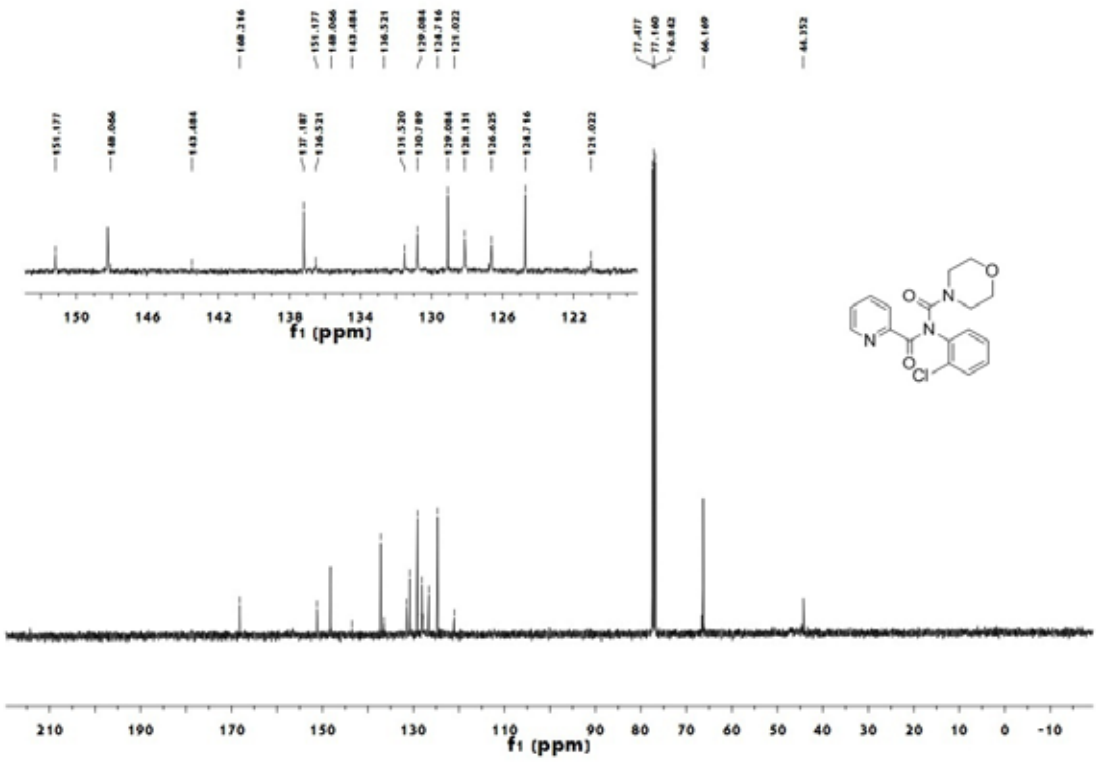
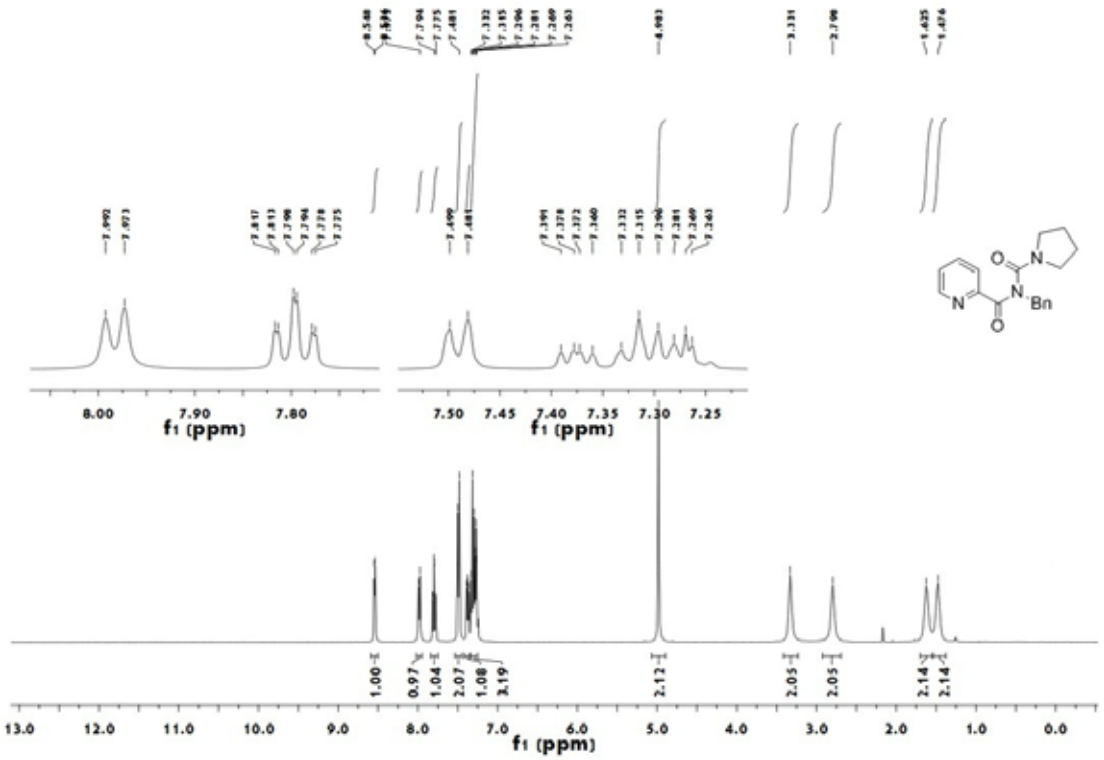
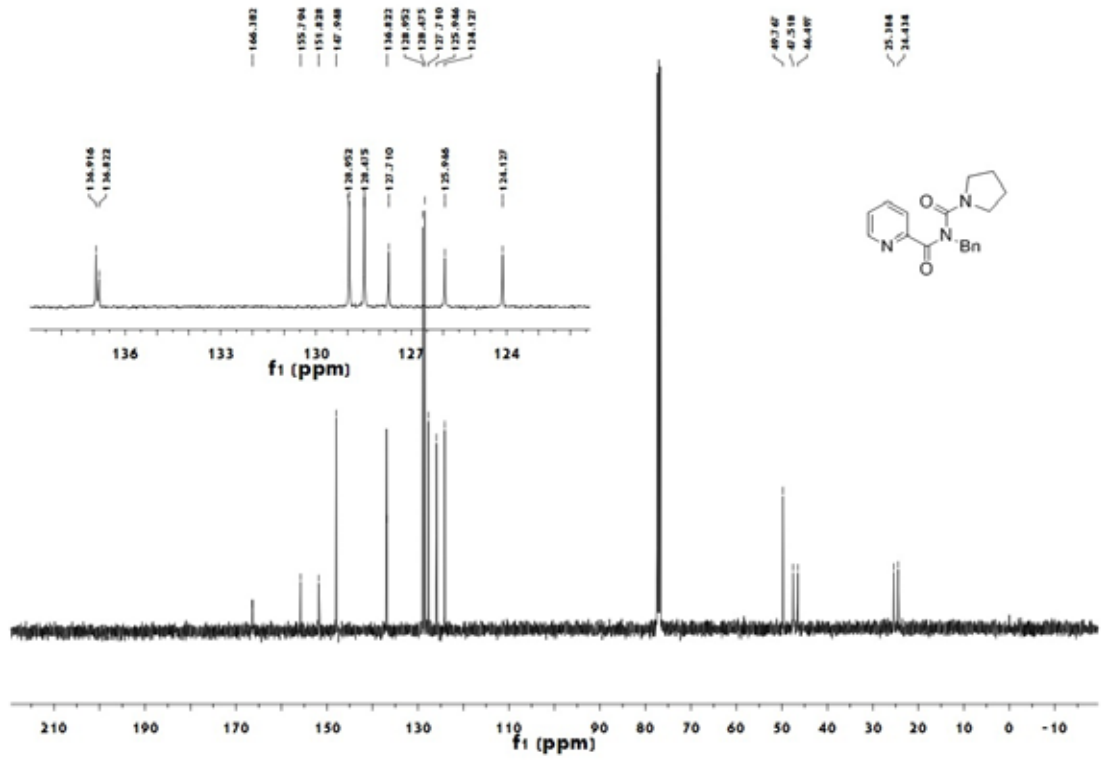
1.07
3.36
2.20
1.97
4.48
4.89
2.08

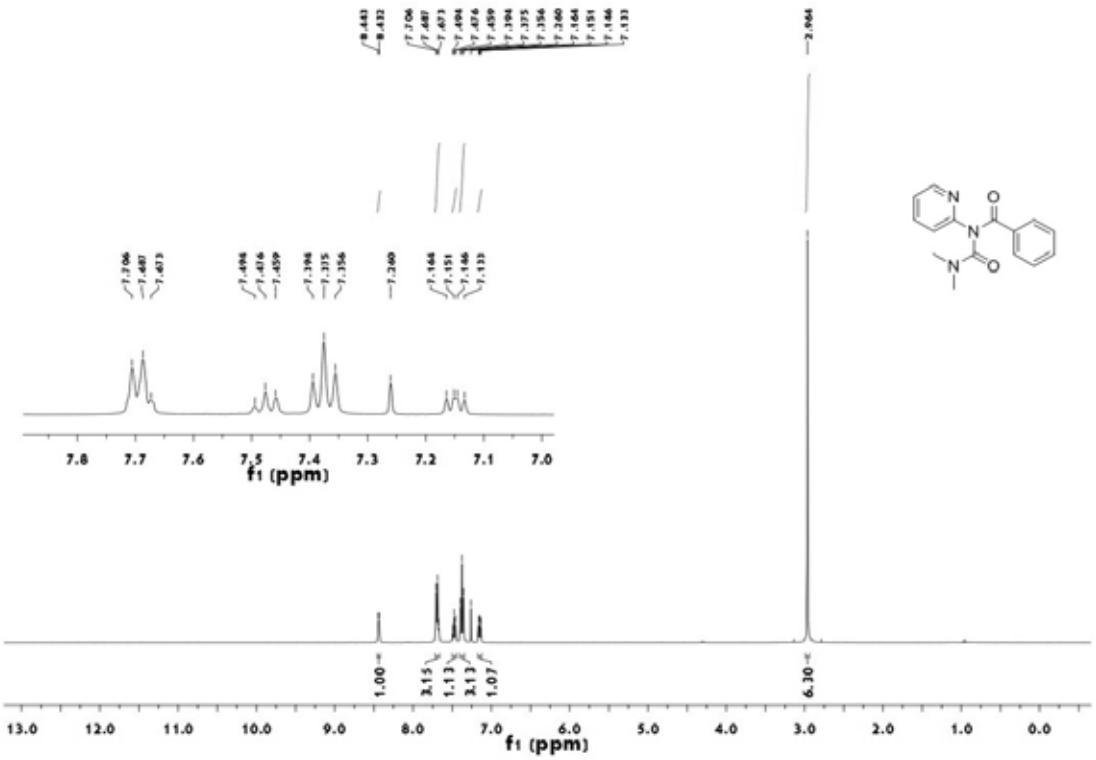

f1 (ppm)

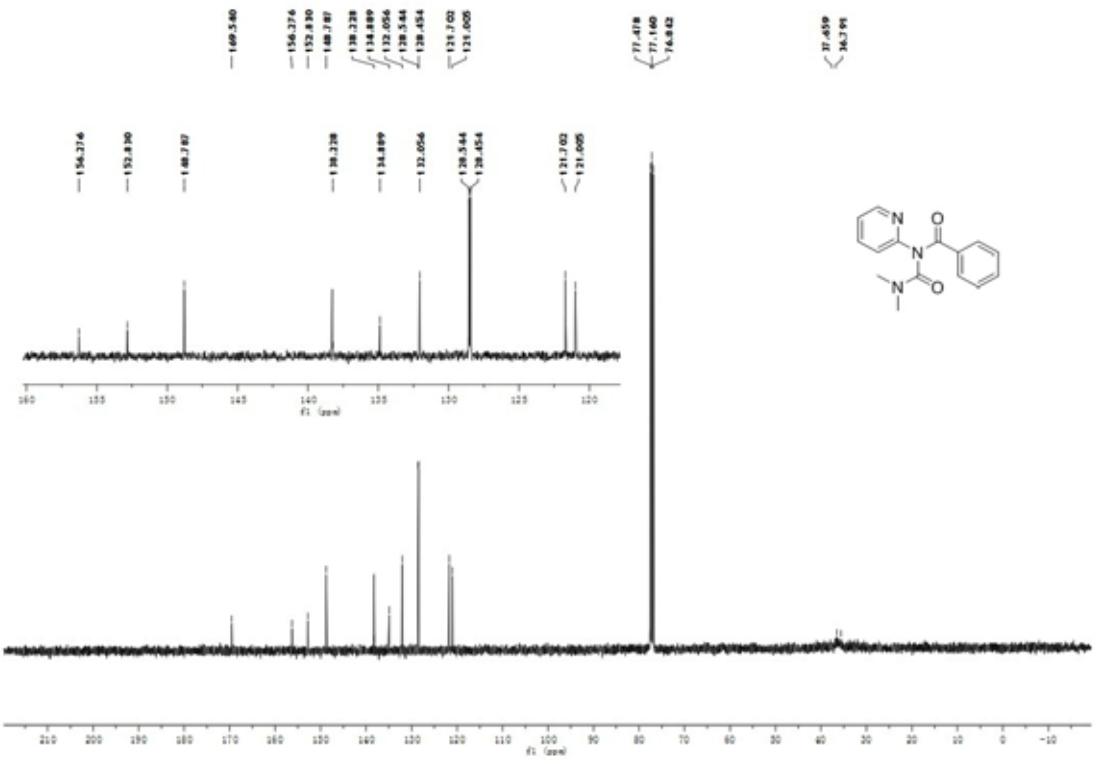


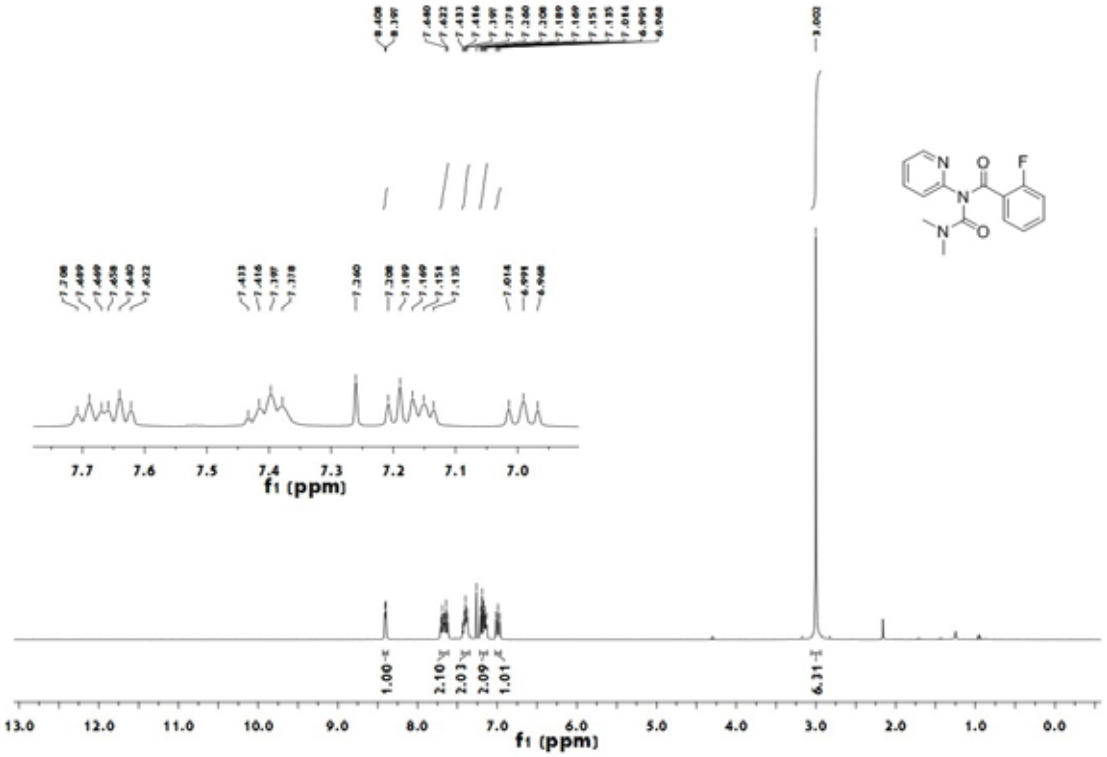


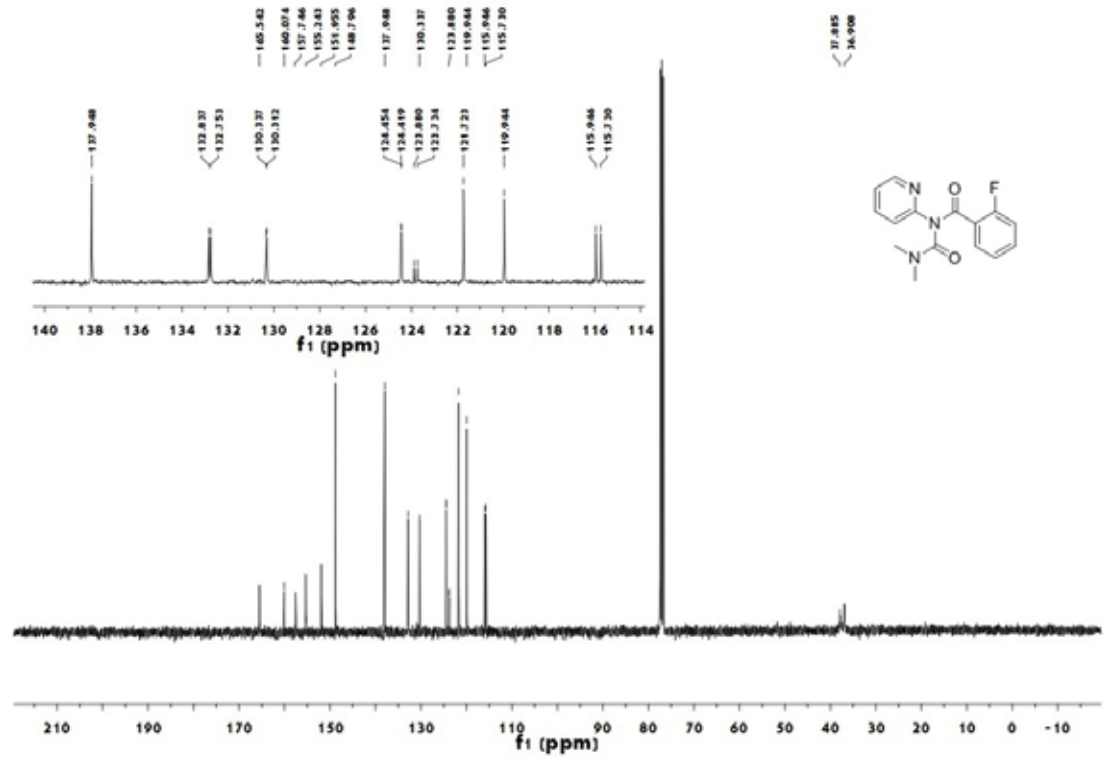


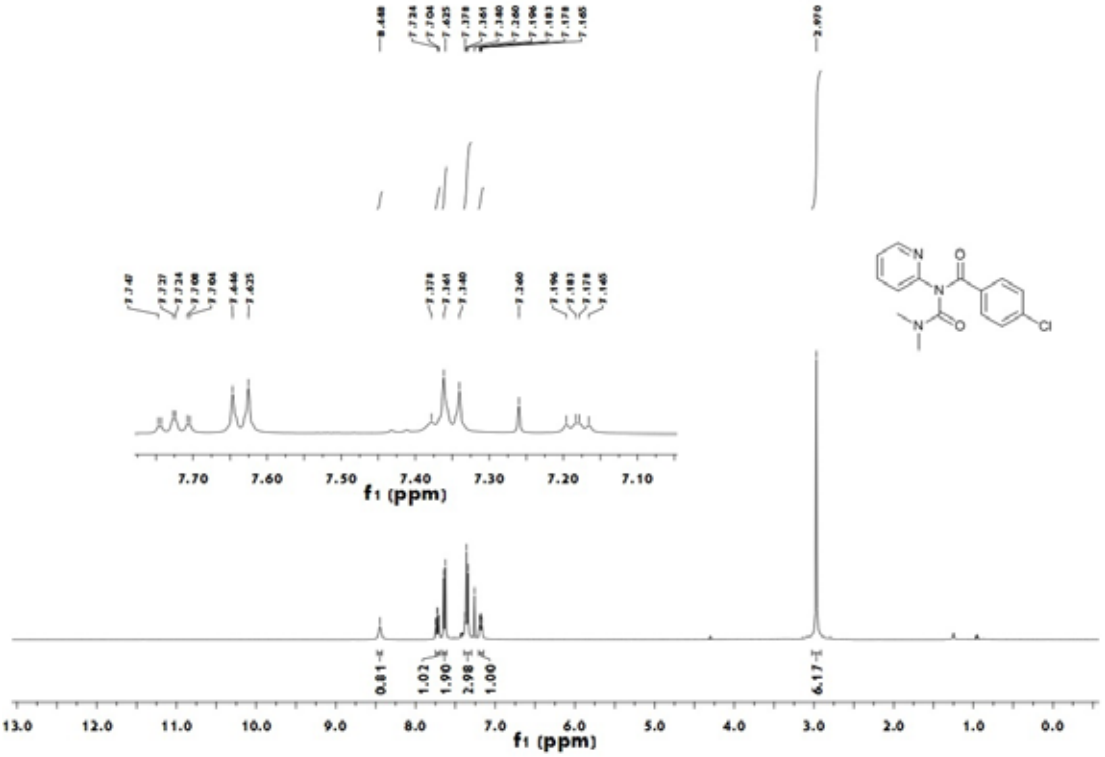


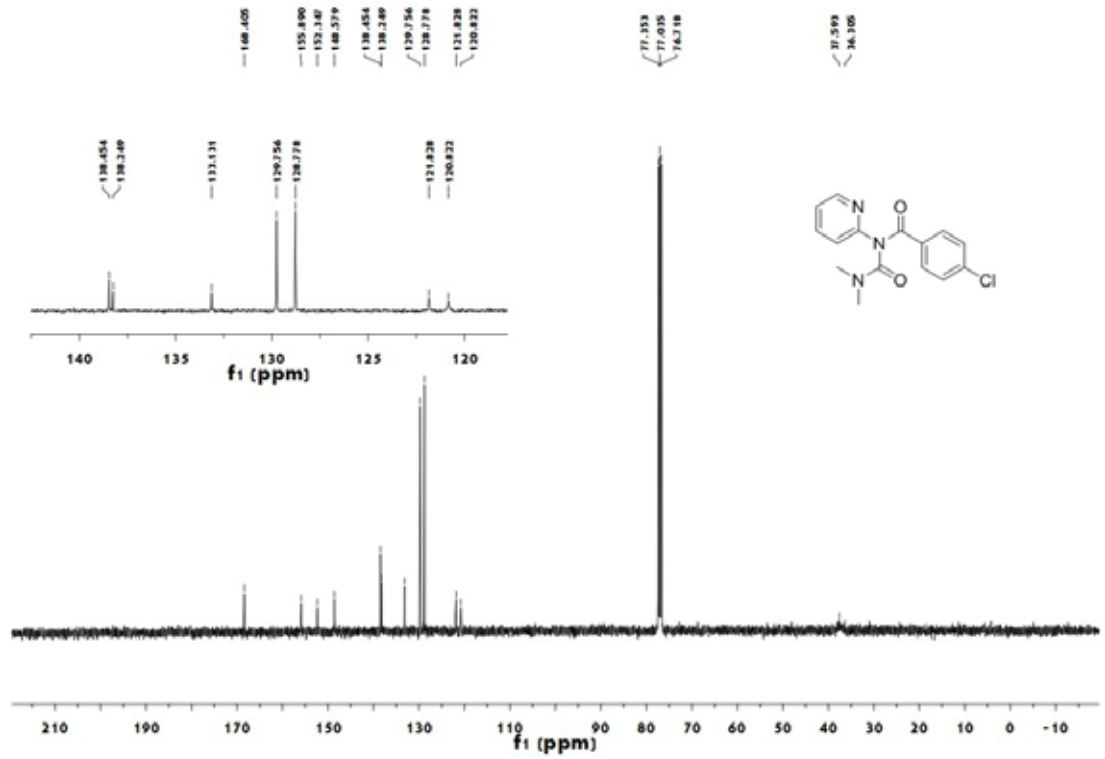

f1 (ppm)
1.00
3.15
1.13
3.13
1.07
6.30

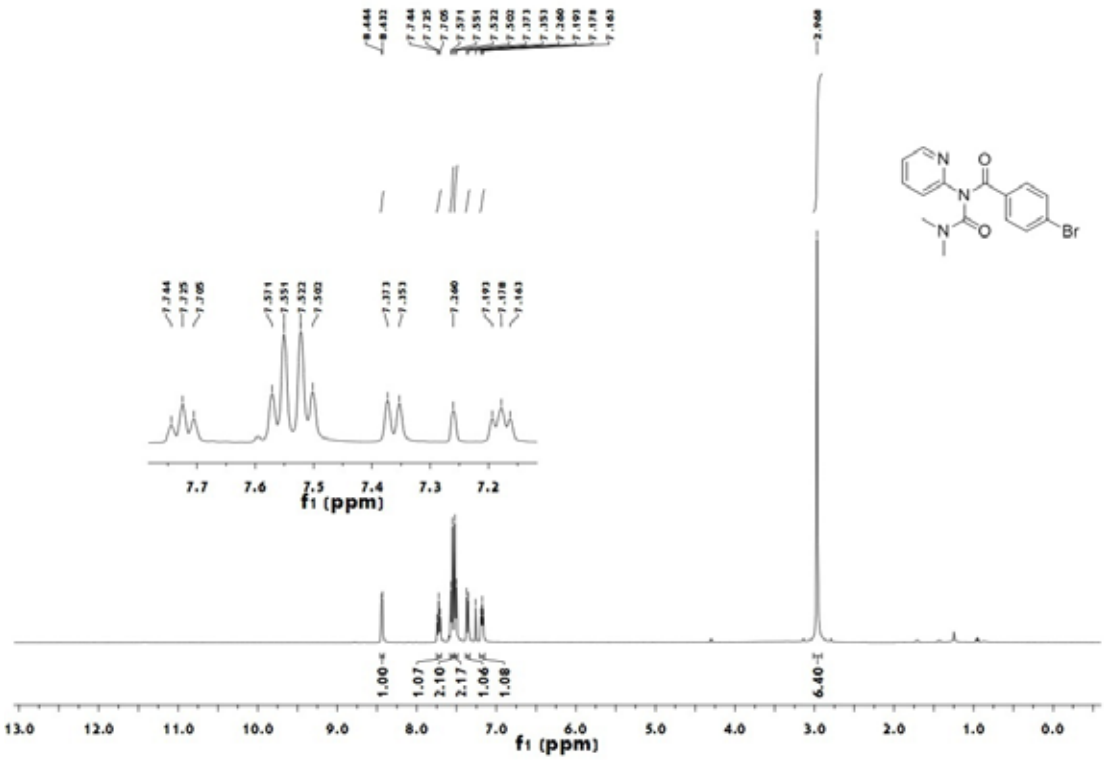

f1 (ppm)

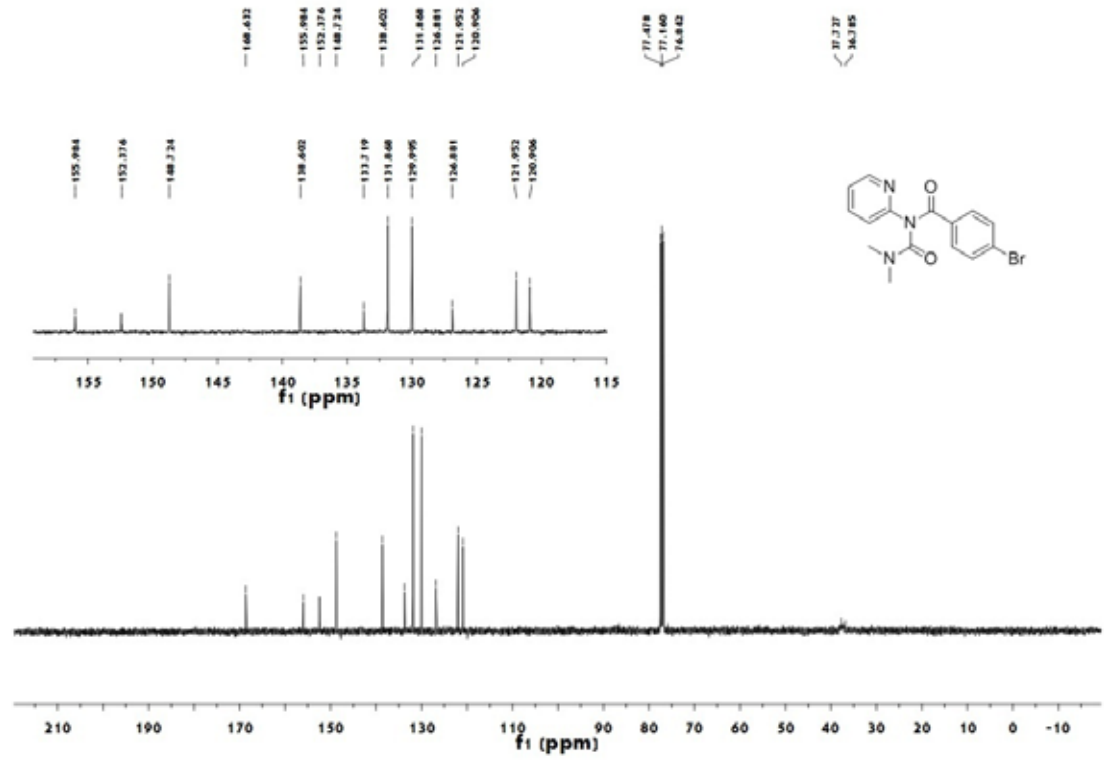

f1 (ppm)
1.00
2.10
2.03
2.09
1.01
6.31

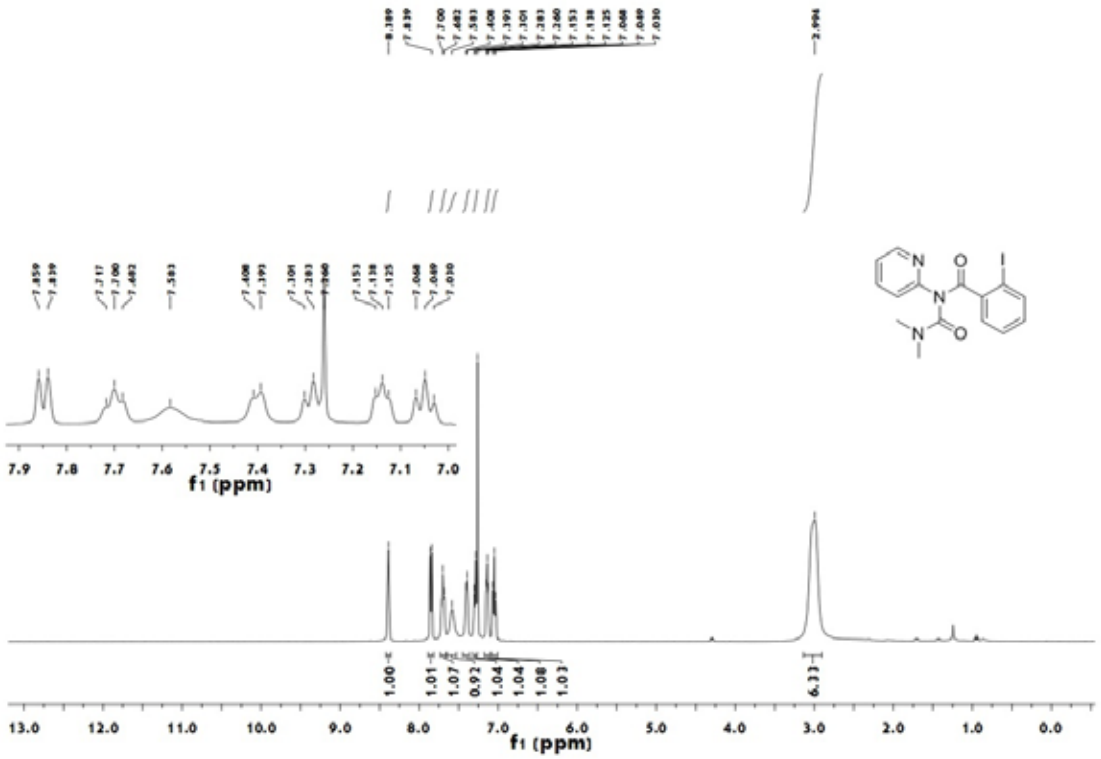

f1 (ppm)

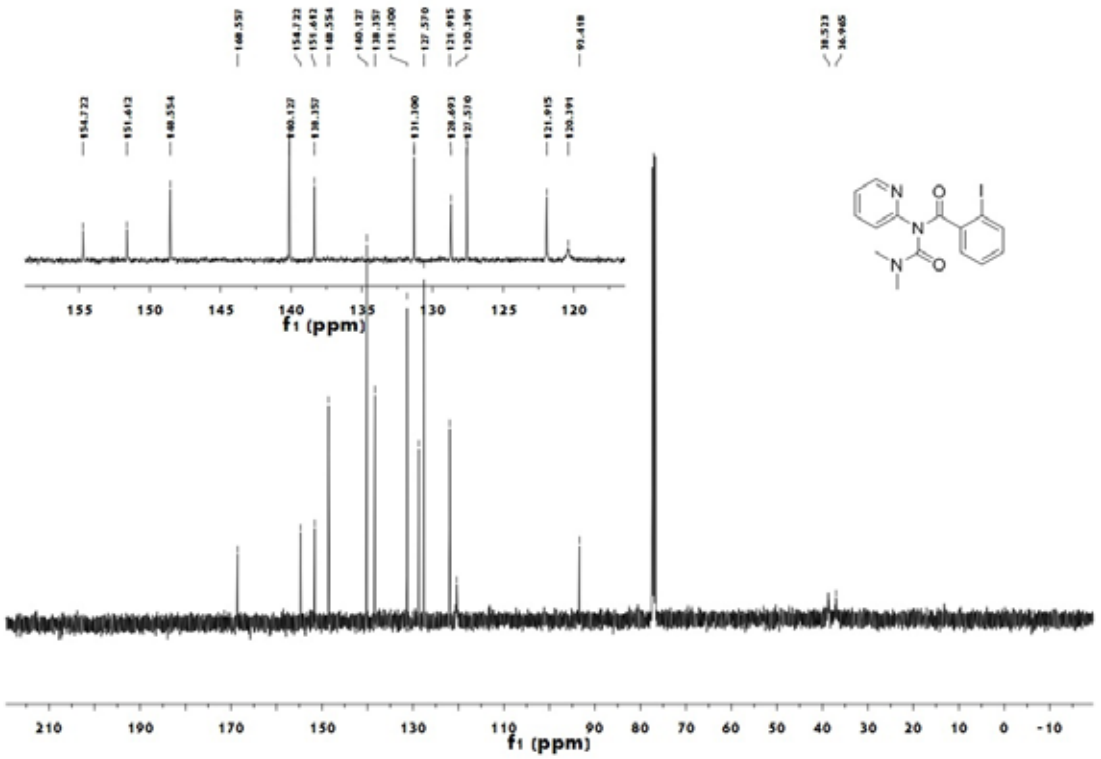


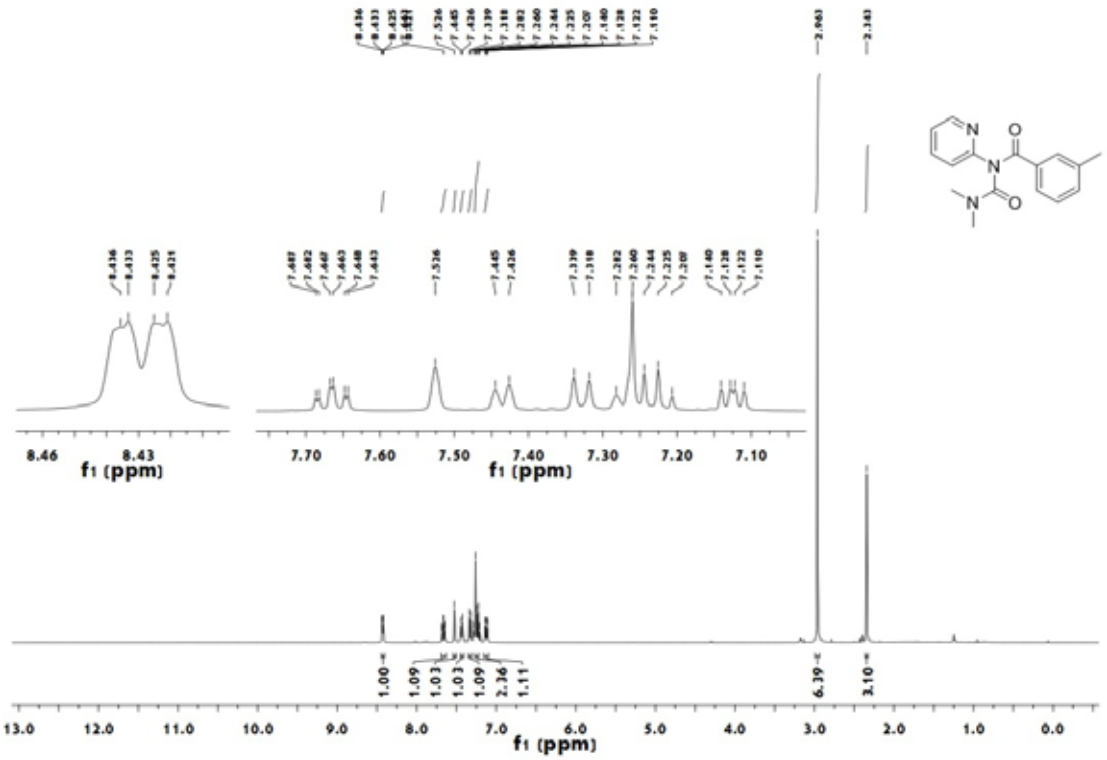







f1 (ppm)


f1 (ppm)


f1 (ppm)
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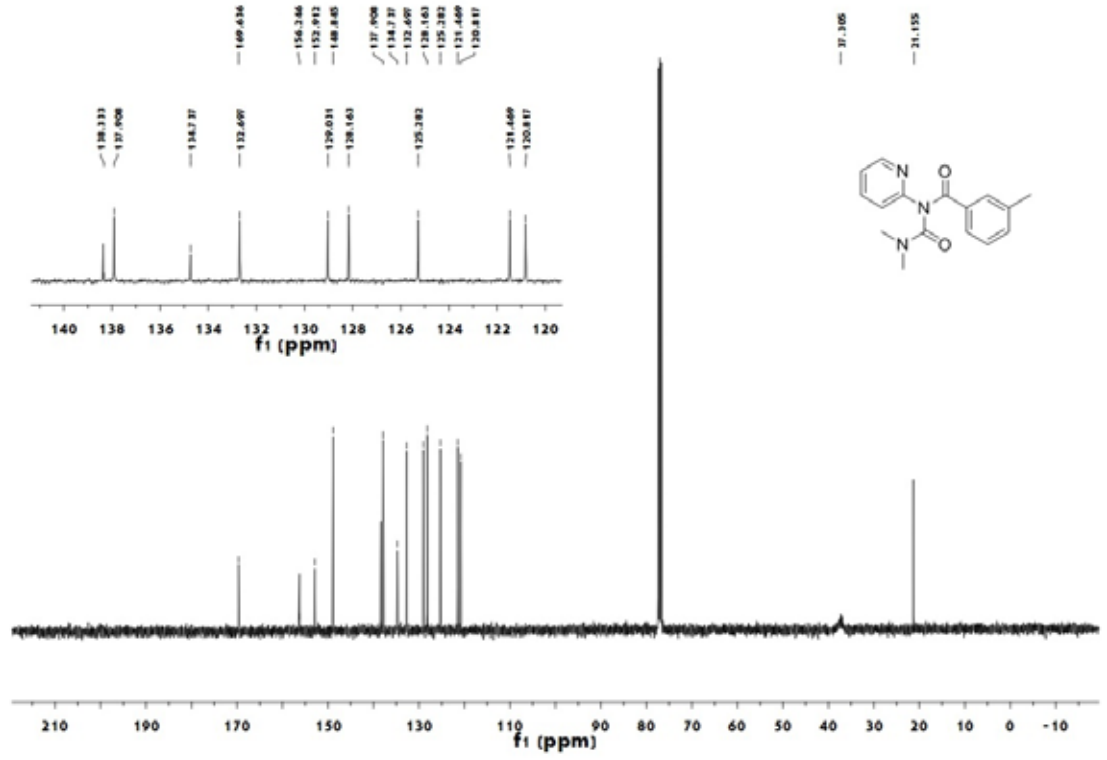
8.43
7.70
7.60
7.50
7.40
7.30
7.20
7.10
1.00
1.09
1.03
1.03
1.09
2.36
1.11
6.39
3.10
13.0
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0


f1 (ppm)
140
138
136
134
132
130
128
126
124
122
120
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
-10