

Supporting Information
for
Cobalt-catalyzed *peri*-selective alkoxylation of
1-naphthylamine derivatives

Jiao-Na Han, Cong Du, Xinju Zhu, Zheng-Long Wang, Yue Zhu, Zhao-Yang

Chu, Jun-Long Niu* and Mao-Ping Song*

Address: College of Chemistry and Molecular Engineering, Zhengzhou

University, Zhengzhou 450001, People's Republic of China

Email: Jun-Long Niu* - niujunlong@zzu.edu.cn; Mao-Ping Song* -

mpsong@zzu.edu.cn

*Corresponding author

Experimental details and characterization data of new
compounds, and X-ray crystal structure details for 3aa.

Table of Contents

General information	S2
Experimental section.....	S2
1. Optimization of reaction conditions.....	S2
2. General procedure for the synthesis of 3	S5
3. Control experiments and mechanistic studies	S5
4. Kinetic isotope effect measurements.....	S7
5. Removal of directing group	S7
6. X-ray crystal structure details for 3aa	S9
Reference	S10
Characterization of products	S11
NMR spectra.....	S19

General information

Unless otherwise mentioned, all materials were commercially available and used without further purification. All the procedures were completed under the ambient air. ^1H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded at 400 (or 600) MHz, 101 (or 151) MHz or 376 MHz, respectively on a Bruker DPX instrument using Me_4Si as an internal standard. Chemical shift multiplicities are represented as follows: (s = singlet, d = doublet, t = triplet, q = quadruple, p = quintuple, m = multiplet, td = tripletdoublet, dt = doublet triplet, dd = double doublet, dq = doublet quadruple). Melting points were measured on a WC-1 instrument and uncorrected. New compounds for HRMS were tested on a Waters Q-ToF Micro MS/MS System ESI spectrometer. All the naphthylamine substrates were synthesized according to literature procedures [1,2]. $[\text{D}_1]\text{-1a}$ was prepared according to the literature [3].

Experimental section

1. Optimization of reaction conditions

Table S1. Optimization of catalysts.^a

Entry	Catalyst	Yield (%)
1	$\text{Co}(\text{OAc})_2 \cdot 4\text{H}_2\text{O}$	60
2	$\text{Co}(\text{acac})_2$	34
3	$\text{Co}(\text{acac})_3$	36
4	$\text{CoCO}_3 \cdot \text{H}_2\text{O}$	n.r.
5	CoO	n.r.
6	$\text{Co}(\text{pph}_3)\text{Cl}_2$	66
7	CoF_3	60
8	$\text{CoSO}_4 \cdot \text{H}_2\text{O}$	trace
9	$\text{Co}(\text{OOC}\text{C}_6\text{H}_5)_2$	63
10	CoF_2	71
11	$\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$	57
12	$\text{CoC}_2\text{O}_4 \cdot 4\text{H}_2\text{O}$	56
13	$\text{Co}(\text{NH}_3)_6\text{Cl}_3$	53

^aReaction conditions: **1a** (0.2 mmol), **2a** (1.0 mL), Co Catalyst (20 mol %), Ag₂CO₃ (1.0 equiv), Cs₂CO₃ (1.0 equiv), 100 °C, air, 12 h. Isolated yield. HFIP = hexafluoroisopropanol. n.r. = no reaction.

Table S2. Optimization of base/acid.^a

Entry	Base	Yield(%)
1	DBU	66
2	Et ₃ N	46
3	CH ₃ ONa	72
4	^t AmONa	71
5	EtONa	70
6	^t BuONa	65
7	CsOAc	8
8	NaOAc	12
9	Li ₂ CO ₃	24
10	Na ₂ CO ₃	58
11	K ₂ CO ₃	67
12	Cs ₂ CO ₃	82

^aReaction conditions: **1a** (0.2 mmol), **2a** (1.0 mL), CoF₂ (20 mol %), Ag₂CO₃ (1.0 equiv), base (1.0 equiv), 100 °C, air, 12 h. Isolated yield.

Table S3. Optimization of oxidants.^a

Entry	Oxidant	Yield(%)
1	AgNO ₃	11
2	NaIO ₄	trace
3	Ag ₂ CO ₃	82
4	NMO	7
5	K ₂ S ₂ O ₈	n.r.
6	PhI(OAc) ₂	n.r.

7	Ag ₂ SO ₄	trace
8	Ag ₂ O	32
9	AgTFA	trace
10	AgOAc	trace
11	Mn(OAc) ₂ ·4H ₂ O	trace
12	Mn(acac) ₂	n.r.
13	Mn(acac) ₃	n,r,

^aReaction conditions: **1a** (0.2 mmol), **2a** (1.0 mL), CoF₂ (20 mol %), oxidant (2.0 equiv), Cs₂CO₃ (1.0 equiv), 100 °C, air, 12 h. Isolated yield.

Table S4. Optimization of cosolvents.^a

$\text{1a} + \text{2a} \xrightarrow[\text{cosolvent, 100 } ^\circ\text{C, air, 12 h}]{\text{CoF}_2 (20 \text{ mol}\%), \text{Cs}_2\text{CO}_3 (1.0 \text{ equiv}), \text{Ag}_2\text{CO}_3 (1.0 \text{ equiv})} \text{3aa}$

Entry	cosolvent	Yield(%)
1	DCE	84
2	PhCF ₃	80
3	dioxane	15
4	PhMe	61
5	CH ₃ CN	19
6	THF	trace
7	PhF	77
8	TCP	75
9	PhOMe	79
10	acetone	22

^aReaction conditions: **1a** (0.2 mmol), **2a** (1.0 mL), CoF₂ (20 mol %), Ag₂CO₃ (1.0 equiv), Cs₂CO₃ (1.0 equiv), cosolvent (1.0 mL), 100 °C, air, 12 h. Isolated yield. DCE = 1,2-dichloroethane. TCP = 1, 2, 3-Trichloropropane

Table S5. Optimization of temperature.^a

$\text{1a} + \text{2a} \xrightarrow[\text{DCE, T, air, 12 h}]{\text{CoF}_2 (20 \text{ mol}\%), \text{Cs}_2\text{CO}_3 (1.0 \text{ equiv}), \text{Ag}_2\text{CO}_3 (1.0 \text{ equiv})} \text{3aa}$

Entry	temperature	Yield (%)
1	60	trace

2	70	5
3	80	37
4	90	48
5	100	84
6	110	75
7	120	63

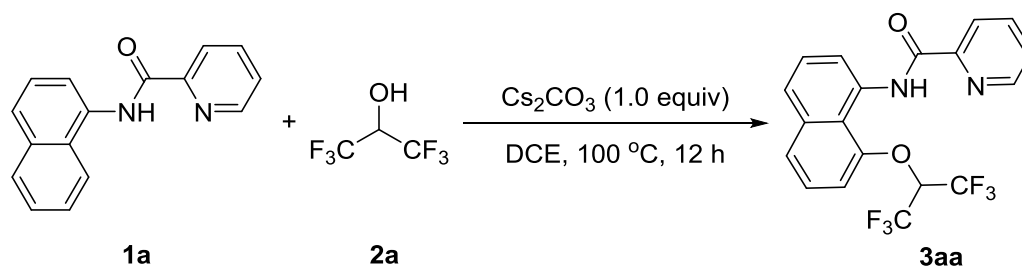
^aReaction conditions: **1a** (0.2 mmol), CoF₂ (20 mol %), Ag₂CO₃ (1.0 equiv), Cs₂CO₃ (1.0 equiv), HFIP (1.0 mL), DCE (1.0 mL), temperature, air, 12 h. Isolated yield.

2. General procedure for the synthesis of **3**

A 15 mL oven-dried screw cap tube equipped with a magnetic stir bar was filled with **1** (0.20 mmol), Ag₂CO₃ (55.2 mg, 0.20 mmol), Cs₂CO₃ (65.0 mg, 0.20 mmol), CoF₂ (3.8 mg, 20 mol %), **2** (1.0 mL) and DCE (1.0 mL). The reaction was stirred at 100 °C for 12 h and then cooled down to room temperature. The resulting mixture was diluted with 25 mL of dichloromethane, and filtered through a celite pad. The reaction solution was detected by TLC, and concentrated in vacuum. The product was purified by preparative TLC on silica gel (petroleum ether/EtOAc) to afford the target product **3**.

3. Control experiments and mechanistic studies

Control experiments

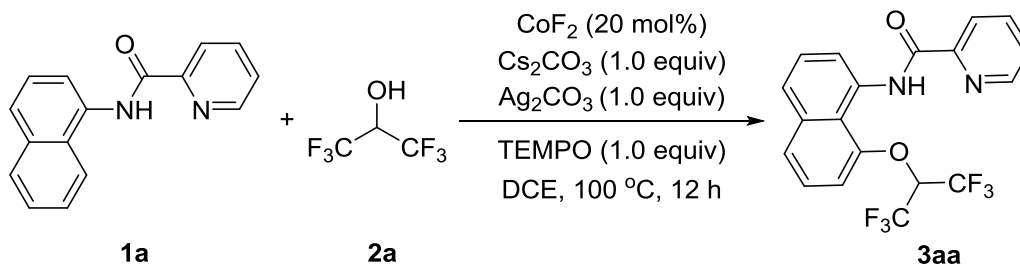


Entry	Catalyst	oxidant	atmosphere	Yield (%)
1	CoF ₂	--	Ar	n.r.
2	CoF ₂	--	air	29
3	CoF ₂	--	O ₂	51
4	--	Ag ₂ CO ₃	air	n.r.
5	CoF ₃	Ag ₂ CO ₃	Ar	67
6 ^b	CoF ₃	--	Ar	12
7 ^c	CoF ₂	Ag ₂ CO ₃	air	n.r.
8 ^d	CoF ₂	Ag ₂ CO ₃	air	39
9 ^e	CoF ₂	Ag ₂ CO ₃	air	23

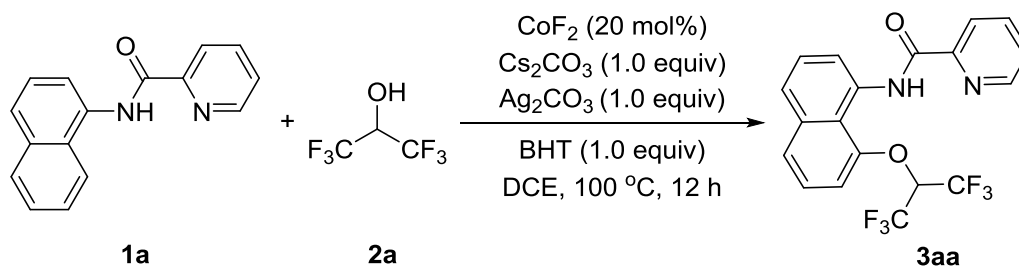
^aReaction conditions: **1a** (0.2 mmol), **2a** (1.0 mL), Co salts (20 mol %),

Ag₂CO₃(1.0 equiv), Cs₂CO₃(1.0 equiv), DCE (1.0 mL), 100 °C, air, 12 h. Isolated yield.^bCoF₃ (1.0 equiv).^cBQ (1.0 equiv) was added. ^dTEMPO (1.0 equiv) was added. ^eBHT (1.0 equiv) was added.

Reaction of radicals trapping

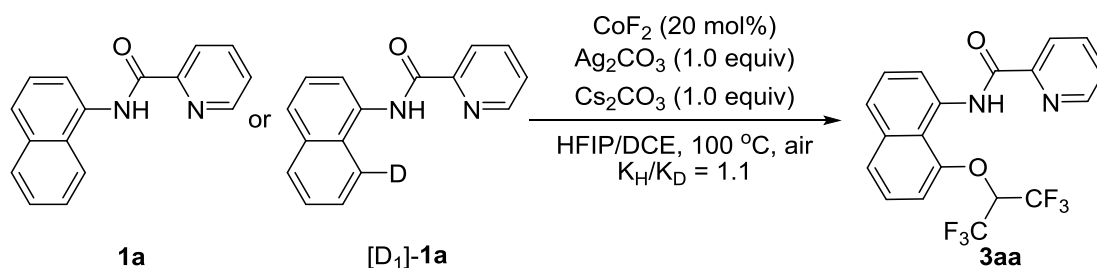


A 15 mL oven-dried screw cap tube equipped with a magnetic stir bar was filled with **1a** (49.6 mg, 0.20 mmol), Ag₂CO₃ (55.2 mg, 0.20 mmol), Cs₂CO₃ (65.0 mg, 0.20 mmol), CoF₂ (3.8 mg, 20 mol %), TEMPO (1.0 equiv), HFIP (1.0 mL) and DCE (1.0 mL). Then the reaction was stirred in an oil bath at 100 °C for 12 h and cooled down to room temperature. The resulting mixture was diluted with 25 mL of dichloromethane, and filtered through a celite pad. The reaction solution was detected by TLC, and concentrated in vacuum. The product was purified by preparative TLC on silica gel (petroleum ether/EtOAc = 5:1) to afford the target product **3aa** in 39% yield.

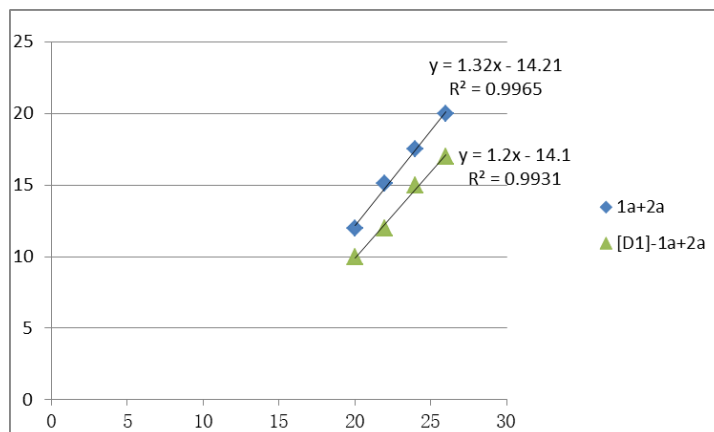


A 15 mL oven-dried screw cap tube equipped with a magnetic stir bar was filled with **1a** (49.6 mg, 0.20 mmol), Ag₂CO₃ (55.2 mg, 0.20 mmol), Cs₂CO₃ (65.0 mg, 0.20 mmol), CoF₂ (3.8 mg, 20 mol %), BHT (1.0 equiv), HFIP (1.0 mL) and DCE (1.0 mL). Then the reaction was stirred in an oil bath at 100 °C for 12 h and cooled down to room temperature. The resulting mixture was diluted with 25 mL of dichloromethane, and filtered through a celite pad. The reaction solution was detected by TLC, and concentrated in vacuum. The product was purified by preparative TLC on silica gel (petroleum ether/EtOAc = 5:1) to afford the target product **3aa** in 23% yield.

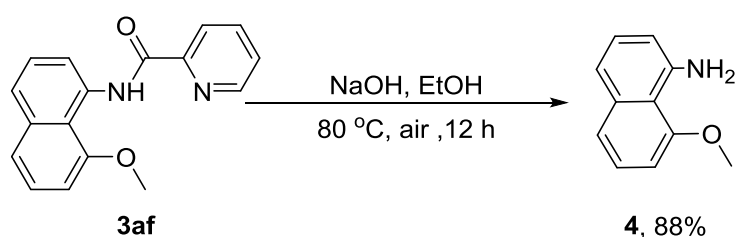
4. Kinetic isotope effect measurements



A 15 mL oven-dried screw cap tube was equipped with a magnetic stir bar and charged with **1a** (49.6 mg, 0.2 mmol) or **[D₁]-1a** (49.9 mg, 0.2 mmol), **2a** (1.0 mL), Ag_2CO_3 (55.2 mg, 0.20 mmol), Cs_2CO_3 (65.0 mg, 0.20 mmol), CoF_2 (3.8 mg, 20 mol %) and DCE (1.0 mL). Then the tubes were heated at 100 °C for 20, 22, 24, 26 minutes and quenched separately with 1 mL dichloromethane. Next, the reaction mixture was diluted with 25 mL dichloromethane and filtered through a celite pad. The solvent was removed in vacuum and ^1H NMR was taken separately using 0.1 mmol anisole (10.8 mg) as the internal standard. The KIE was determined as $k_{\text{H}}/k_{\text{D}} \approx 1.1$.

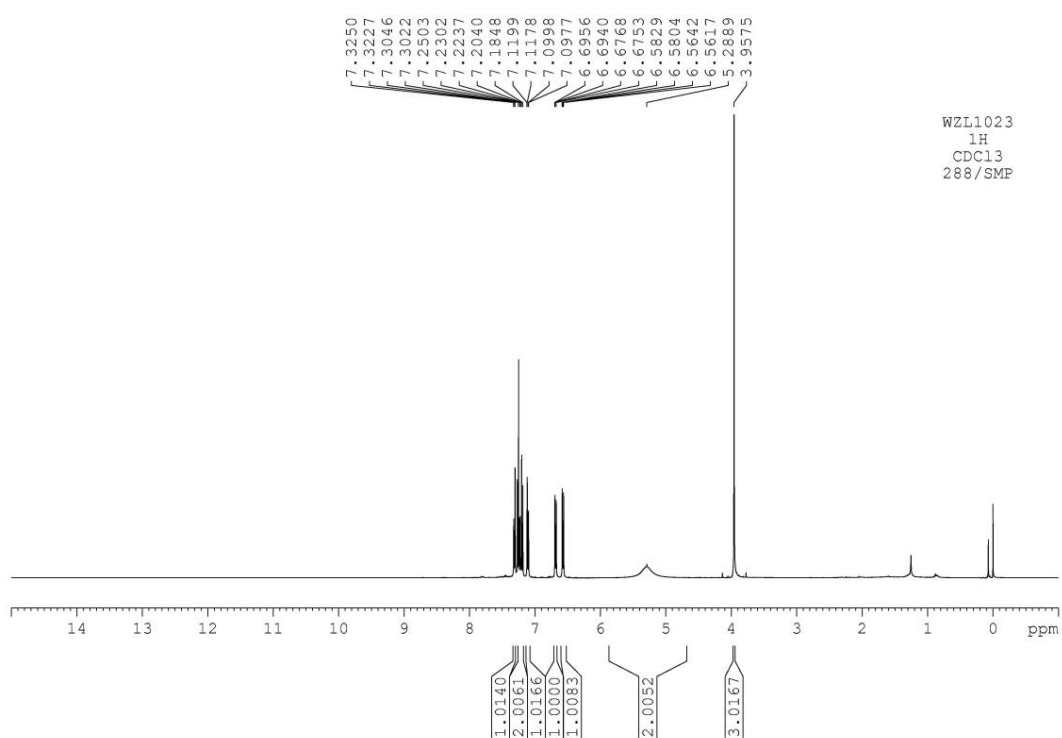


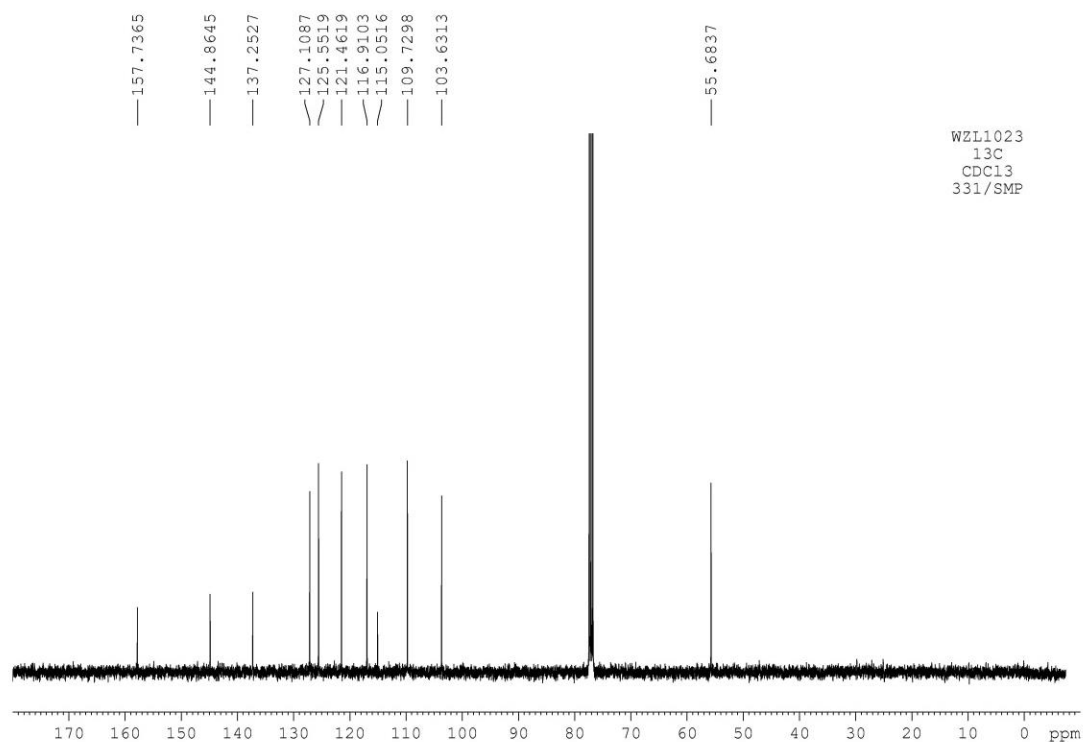
5. Removal of directing group



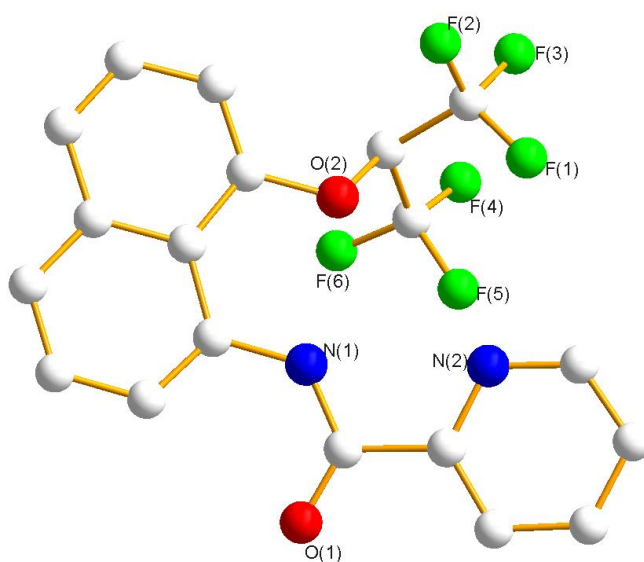
A 15 mL oven-dried screw cap tube was equipped with a magnetic stir bar and charged with **3af** (13.9 mg, 0.05 mmol), NaOH (40.0 mg, 1 mmol, 20 equiv) and MeOH (0.5 mL). Then the reaction was stirred in an oil bath at 100 °C for 12 h. After completion, the resulting mixture was cooled to room temperature, quenched with 5 mL H_2O , then treated with HCl (2.0 mol/L) until pH = 5. Next, the reaction mixture was diluted with dichloromethane

(10 ml × 2). The organic layer was collected and dried over Na₂SO₄. After concentration in vacuum, the residue was purified by preparative TLC on silica gel and the product was isolated in 88%. ¹H NMR (400 MHz, CDCl₃): δ 7.35-7.28 (m, 1H), 7.28-7.16 (m, 2H), 7.15-7.08 (m, 1H), 6.69 (dd, J = 7.5, 0.7 Hz, 1H), 6.57 (dd, J = 7.5, 1.1 Hz, 1H), 3.96 (s, 9H). ¹³C NMR (101 MHz, CDCl₃): δ 157.7, 144.9, 137.3, 127.1, 125.6, 121.5, 116.9, 115.1, 109.7, 103.6, 55.7.





6. X-ray crystal structure details for 3aa



Chemical formula	$\text{C}_{19}\text{H}_{12}\text{F}_6\text{N}_2\text{O}_2$
Formula weight	414.31 g/mol
Temperature	293(2) K

Wavelength	1.54184Å
Crystal system	orthorhombic
Space group	Pbca
Unit cell dimensions	$a = 7.3762(3)\text{\AA}$ $\alpha = 90^\circ$ $b = 17.5081(5)\text{\AA}$ $\beta = 90^\circ$ $c = 28.0730(11)\text{\AA}$ $\gamma = 90^\circ$
Volume	3625.4(2) Å ³
Z	8
Density (calculated)	1.518 g/cm ³
Absorption coefficient	1.249 mm ⁻¹
F(000)	1680.0

Data collection and structure refinement for compound 3aa.

Theta range for datacollection	10.104 to 134.16°
Index ranges	$-8 \leq h \leq 6$, $-13 \leq k \leq 20$, $-21 \leq l \leq 33$
Reflections collected	8287
Independent reflections	3240 [R(int) = 0.0291]
Absorption correction	Multi-Scan
Structure solution technique	direct methods
Structure solution program	SHELX, VERSION 2014/7

Reference:

1. Bai, P.; Sun, S.; Li, Z.; Qiao, H.; Su, X.; Yang, F.; Wu, Y. *J. Org. Chem.* **2017**, *82*, 12119-12127.
2. Li, Z.; Sun, S.; Qiao, H.; Yang, F.; Zhu, Y.; Kang, J.; Wu, Y. *J. Org. Lett.* **2016**, *18*, 4594-4597.
3. Huang, L.; Li, Q.; Wang, C.; Qi, C. *J. Org. Chem.* **2013**, *78*, 3030-3038.

Characterization of products

***N*-(8-(Hexafluoropropan-2-yl)oxy)naphthalen-1-yl)picolinamide (3aa):** purified by analytical TLC on silica gel with petroleum ether/EtOAc (5:1) as an eluent $R_f = 0.41$; light yellow solid (69.6 mg, 84%), mp 153-158°C. ^1H NMR (400 MHz, CDCl_3): δ 11.85 (s, 1H), 8.92 (dd, $J = 7.7, 1.2$ Hz, 1H), 8.65 (d, $J = 4.5$ Hz, 1H), 8.31 (d, $J = 7.8$ Hz, 1H), 7.91-7.87 (m, 1H), 7.66-7.55 (m, 3H), 7.47-7.44 (m, 1H), 7.41 (t, $J = 11.9$ Hz, 1H), 7.12 (d, $J = 11.6$ Hz, 1H), 5.24-5.15 (m, 1H). ^{13}C NMR (101 MHz, CDCl_3): δ 162.8, 154.9, 150.2, 147.9, 137.2, 136.6, 133.4, 127.4, 126.2, 125.9, 125.2, 124.3, 122.3, 120.9 (dq, $J_{\text{C-F}} = 284.7, 2.9$ Hz), 119.2, 117.8, 116.7, 78.1 (p, $J_{\text{C-F}} = 34.0$ Hz). HRMS (positive ESI) Calcd. ^{19}F NMR (376 MHz, CDCl_3): δ -72.46. For $\text{C}_{19}\text{H}_{12}\text{F}_6\text{N}_2\text{O}_2$ ($M + \text{H}$) 415.0881, Found: 415.0881.

***N*-(5-Bromo-8-(hexafluoropropan-2-yl)oxy)naphthalen-1-yl)picolinamide (3ba):** purified by analytical TLC on silica gel with petroleum ether/EtOAc (5:1) as an eluent $R_f = 0.50$; white solid (86.8 mg, 88%), mp 152-156°C. ^1H NMR (400 MHz, CDCl_3): δ 11.82 (s, 1H), 8.97 (dd, $J = 7.9, 1.0$ Hz, 1H), 8.61 (d, $J = 4.4$ Hz, 1H), 8.31 (dt, $J = 7.8, 1.0$ Hz, 1H), 8.10 (dd, $J = 8.5, 1.0$ Hz, 1H), 7.93-7.88 (m, 1H), 7.75-7.68 (m, 2H), 7.49-7.46 (m, 1H), 7.00 (d, $J = 8.4$ Hz, 1H), 5.15-5.06 (m, 1H). ^{13}C NMR (101 MHz, CDCl_3): δ 162.8, 154.7, 150.0, 147.9, 137.3, 134.2, 133.8, 129.3, 128.9, 126.4, 123.8, 122.4, 120.8 (dq, $J_{\text{C-F}} = 285.3, 3.8$ Hz), 120.3, 119.4, 119.0, 111.1, 78.5 (p, $J_{\text{C-F}} = 33.7$ Hz). ^{19}F NMR (376 MHz, CDCl_3): δ -72.42. HRMS (positive ESI) Calcd. For $\text{C}_{19}\text{H}_{11}\text{BrF}_6\text{N}_2\text{O}_2$ ($M + \text{H}$) 492.9986, Found: 492.9986.

***N*-(4-Bromo-8-(hexafluoropropan-2-yl)oxy)naphthalen-1-yl)picolinamide (3ca):** purified by analytical TLC on silica gel with petroleum ether/EtOAc (5:1) as an eluent $R_f = 0.47$; white solid (84.8 mg, 86%), mp 122-126 °C. ^1H NMR (400 MHz, CDCl_3): δ 11.88 (s, 1H), 8.82 (d, $J = 8.6$ Hz, 1H), 8.60 (d, $J = 4.4$ Hz, 1H), 8.29 (dt, $J = 7.8, 0.9$ Hz, 1H), 8.15 (dd, $J = 8.6, 0.9$ Hz, 1H), 7.91-7.86 (m, 2H), 7.57-7.42 (m, 2H), 7.22-7.21 (d, $J = 8.6$, 1H), 5.20-5.11 (m, 1H). ^{13}C NMR (101 MHz, CDCl_3): δ 162.8, 155.1, 150.0, 147.9, 137.4, 134.2, 133.5, 131.6, 126.5, 126.4, 125.3, 122.4, 120.7 (dq, $J_{\text{C-F}} = 284.8, 2.8$ Hz), 119.3, 119.2, 117.6, 112.0, 78.7 (p, $J_{\text{C-F}} = 34.6$ Hz). ^{19}F NMR (376 MHz, CDCl_3): δ -72.44. HRMS (positive ESI) Calcd. For $\text{C}_{19}\text{H}_{11}\text{BrF}_6\text{N}_2\text{O}_2$ ($M + \text{H}$) 492.9986, Found: 492.9985.

***N*-(4-Nitro-8-(hexafluoropropan-2-yl)oxy)naphthalen-1-yl)picolinamide (3da):** purified by analytical TLC on silica gel with petroleum ether/EtOAc (5:1) as an eluent $R_f = 0.40$; yellow solid (58.8 mg, 64%), mp 176-178°C. ^1H NMR (400 MHz, CDCl_3): δ 12.30 (s, 1H), 9.15 (d, $J = 8.9$ Hz, 1H), 8.62 (d, $J = 4.4$ Hz, 1H), 8.48 (dd, $J = 8.8, 0.7$ Hz, 1H), 8.33 (dd, $J = 8.3, 5.3$ Hz, 2H), 7.96-7.91 (m, 1H), 7.68 (t, $J = 8.0$, Hz 1H), 7.54-7.52 (m, 1H), 7.31 (d, $J = 7.9$ Hz, 1H), 5.21-5.07 (m, 1H). ^{13}C NMR (101 MHz, CDCl_3): δ 163.3, 155.4, 149.3, 148.1, 142.2, 139.3, 137.6, 128.7, 128.5, 126.9, 126.6, 122.7, 120.8, 120.7 (dq, $J_{\text{C-F}} = 284.5, 2.7$ Hz), 117.8, 115.9, 112.8, 79.1 (p, $J_{\text{C-F}} = 34.1$ Hz). ^{19}F NMR (376 MHz,

CDCl₃): δ -72.35. HRMS (positive ESI) Calcd. For C₁₉H₁₁F₆N₃O₂ (M + K) 498.0291, Found: 498.0287.

***N*-(4-Benzenesulfonyl-8-(hexafluoropropan-2-yl)oxy)naphthalen-1-yl)picolinamide (3ea)**: purified by analytical TLC on silica gel with petroleum ether/EtOAc (1:1) as an eluent R_f = 0.53; white solid (67.6 mg, 61%), mp 184-188°C. ¹H NMR (400 MHz, CDCl₃): δ 12.23 (s, 1H), 9.18 (d, J = 8.6 Hz, 1H), 8.64-8.52 (m, 3H), 8.30 (d, J = 7.8 Hz, 1H), 7.95-7.89 (m, 3H), 7.56-7.46 (m, 5H), 7.21 (d, J = 7.8, 1H), 5.16-5.06 (m, 1H). ¹³C NMR (101 MHz, CDCl₃): δ 163.3, 155.5, 149.4, 148.0, 141.7, 139.7, 137.5, 133.1, 132.5, 131.8, 130.3, 129.2, 127.8, 127.4, 126.8, 122.6, 121.9, 120.7 (dq, J_{C-F} = 284.5, 2.7 Hz), 118.2, 116.2, 112.3, 78.8 (p, J_{C-F} = 34.3 Hz). ¹⁹F NMR (376 MHz, CDCl₃): δ -72.35. HRMS (positive ESI) Calcd. For C₂₅H₁₆F₆N₂O₄S (M + H) 555.0813, Found: 555.0813.

***N*-(4-Benzenesulfonyl-5-bromo-8-(hexafluoropropan-2-yl)oxy)naphthalen-1-yl)picolinamide (3fa)**: purified by analytical TLC on silica gel with petroleum ether/EtOAc (3:1) as an eluent R_f = 0.29; white solid (59.5 mg, 47%), mp 232-236 °C. ¹H NMR (400 MHz, CDCl₃): δ 12.00 (s, 1H), 9.54 (d, J = 1.8 Hz, 1H), 8.77 (d, J = 1.8 Hz, 1H), 8.58 (d, J = 4.5 Hz, 1H), 8.30 (d, J = 7.8 Hz, 1H), 8.15-8.12 (m, 2H), 7.92 (td, J = 7.7, 1.7 Hz, 1H), 7.86 (d, J = 8.4 Hz, 1H), 7.63-7.53 (m, 3H), 7.51-7.48 (m, 1H), 7.15 (d, J = 8.5 Hz, 1H), 5.12-5.06 (m, 1H). ¹³C NMR (101 MHz, CDCl₃): δ 163.0, 154.5, 149.4, 148.0, 141.8, 140.8, 137.5, 136.0, 133.7, 133.6, 131.1, 129.5, 128.2, 126.7, 123.3, 122.6, 120.9 (dq, J_{C-F} = 284.7, 2.3 Hz), 120.8, 120.4, 116.0, 114.0, 78.7 (p, J_{C-F} = 34.3 Hz). ¹⁹F NMR (376 MHz, CDCl₃): δ -72.31. HRMS (positive ESI) Calcd. For C₂₅H₁₅BrF₆N₂O₄S (M + H) 632.9918, Found: 632.9913.

***N*-(5-*tert*-Butylmethylcarbamate-8-(hexafluoropropan-2-yl)oxy)naphthalen-1-yl)picolinamide (3ga)**: purified by analytical TLC on silica gel with petroleum ether/EtOAc (3:1) as an eluent R_f = 0.60; white solid (43.9 mg, 33%), mp 157-161°C. ¹H NMR (400 MHz, CDCl₃): δ 11.85 (s, 1H), 8.91 (dd, J = 7.8, 0.9 Hz, 1H), 8.62 (d, J = 4.3 Hz, 1H), 8.30 (d, J = 7.8 Hz, 1H), 7.92-7.88 (m, 1H), 7.77 (d, J = 8.0 Hz, 1H), 7.68 (d, J = 7.9 Hz, 1H), 7.58 (t, J = 8.2 Hz, 1H), 7.49-7.45 (m, 1H), 7.09 (d, J = 8.6 Hz, 1H), 6.81 (s, 1H), 5.12-5.04 (m, 1H), 1.55 (s, 9H). ¹³C NMR (101 MHz, CDCl₃): δ 162.8, 153.7, 152.0, 150.2, 148.0, 137.3, 134.0, 130.3, 127.7, 126.3, 122.4, 121.1 (dq, J_{C-F} = 286.1, 3.5 Hz), 119.4, 118.2, 116.8, 111.0, 81.0, 78.8 (p, J_{C-F} = 33.8 Hz), 28.4. ¹⁹F NMR (376 MHz, CDCl₃): δ -72.52. HRMS (positive ESI) Calcd. For C₂₄H₂₁F₆N₃O₄ (M + H) 530.1515, Found: 530.1509.

***N*-(7-Methoxy-8-(hexafluoropropan-2-yl)oxy)naphthalen-1-yl)picolinamide (3ha)**: purified by analytical TLC on silica gel with petroleum ether/EtOAc (3:1) as an eluent R_f = 0.36; light yellow solid (72.0 mg, 81%), mp 155-157°C. ¹H NMR (400 MHz, CDCl₃): δ 11.76 (s, 1H), 8.89 (dd, J = 7.8, 1.1 Hz, 1H), 8.62 (d, J = 4.3 Hz, 1H), 8.31 (dt, J = 7.8, 1.0 Hz, 1H), 7.90-7.86 (m, 1H), 7.69 (d, J = 9.1 Hz, 1H), 7.55 (dd, J = 8.1, 0.8 Hz, 1H), 7.46-7.41 (m, 2H), 7.30 (d, J = 9.0 Hz, 1H), 5.38-5.30 (m, 1H), 4.03 (s, 3H). ¹³C NMR (101 MHz, CDCl₃): δ 162.7,

150.4, 148.0, 146.8, 140.3, 137.2, 132.6, 131.0, 127.3, 126.1, 125.0, 124.2, 122.2, 121.2 (dq, $J_{C-F} = 285.2, 2.8$ Hz), 120.1, 119.5, 114.4, 76.4 (p, $J_{C-F} = 33.8$ Hz), 57.1. ^{19}F NMR (376 MHz, CDCl_3): δ -71.97. HRMS (positive ESI) Calcd. For $\text{C}_{20}\text{H}_{14}\text{F}_6\text{N}_2\text{O}_3$ ($M + H$) 445.0987, Found: 445.0982.

***N*-(8-(2,2,2-Trifluoroethoxy)naphthalen-1-yl)picolinamide (3ab)**: purified by analytical TLC on silica gel with petroleum ether/EtOAc (5:1) as an eluent $R_f = 0.31$; light yellow solid (52.6mg, 76%), mp 200-203 °C. ^1H NMR (400 MHz, CDCl_3): δ 12.50 (s, 1H), 28.94 (d, $J = 7.6$ Hz, 1H), 8.66 (d, $J = 4.6$ Hz, 1H), 8.34 (d, $J = 7.8$ Hz, 1H), 7.92 (td, $J = 7.7, 1.5$ Hz, 1H), 7.62-7.48 (m, 4H), 7.40 (t, $J = 8.0$ Hz, 1H), 7.07 (d, $J = 7.7$ Hz, 1H), 4.77 (q, $J = 8.4$ Hz, 2H). ^{13}C NMR (101 MHz, CDCl_3): δ 162.8, 154.8, 150.7, 148.1, 137.5, 136.5, 134.1, 127.1, 126.2, 125.4, 124.5, 124.2, 123.4 (q, $J_{C-F} = 285.3$ Hz) 122.1, 118.1, 117.3, 109.8, 36.2 (q, $J_{C-F} = 36.3$ Hz). ^{19}F NMR (376 MHz, CDCl_3): δ -72.83. HRMS (positive ESI) Calcd. For $\text{C}_{18}\text{H}_{13}\text{F}_3\text{N}_2\text{O}_3$ ($M + H$) 347.1007, Found: 347.1008.

***N*-(8-(3-Fluoropropoxy)naphthalen-1-yl)picolinamide (3ac)**: purified by analytical TLC on silica gel with petroleum ether/EtOAc (1:1) as an eluent $R_f = 0.65$; brown solid (50.0mg, 77%), mp 103-105 °C. ^1H NMR (400 MHz, CDCl_3): δ 12.59 (s, 1H), 8.99 (dd, $J = 7.7, 1.3$ Hz, 1H), 8.63-8.61 (m, 1H), 8.37 (dt, $J = 7.9, 1.0$ Hz, 1H), 7.91 (td, $J = 7.7, 1.7$ Hz, 1H), 7.59-7.56 (m, 1H), 7.53-7.45 (m, 3H) 7.35 (t, $J = 7.9$ Hz, 1H), 6.95 (d, $J = 7.3$ Hz, 1H), 4.71 (t, $J = 5.8$ Hz, 1H), 4.59 (t, $J = 5.8$ Hz, 1H), 4.47 (t, $J = 6.1$ Hz, 2H), 2.60-2.56 (m, 1H), 2.52-2.48 (m, 1H). ^{13}C NMR (101 MHz, CDCl_3): δ 162.6, 155.3, 151.0, 147.7, 137.6, 136.5, 134.8, 126.7, 126.2, 125.6, 124.1, 122.9, 122.3, 117.4, 117.0, 106.8, 80.9 (d, $J_{C-F} = 164.8$ Hz), 65.4 (d, $J_{C-F} = 5.4$ Hz), 29.9 (d, $J_{C-F} = 20.2$ Hz). ^{19}F NMR (376 MHz, CDCl_3): δ -72.83. HRMS (positive ESI) Calcd. For $\text{C}_{19}\text{H}_{16}\text{FN}_2\text{O}_2$ ($M + H$) 325.1352, Found: 325.1347.

***N*-(8-(2,2,3,3-Tetrafluoropropoxy)naphthalen-1-yl)picolinamide (3ad)**: purified by analytical TLC on silica gel with petroleum ether/EtOAc (3:1) as an eluent $R_f = 0.44$; light green solid (50.0mg, 66%), mp 133-136 °C. ^1H NMR (400 MHz, CDCl_3): δ 12.18 (s, 1H), 8.91 (dd, $J = 7.7, 1.2$ Hz, 1H), 8.64 (d, $J = 4.5$ Hz, 1H), 8.34 (td, $J = 7.8, 0.9$ Hz, 1H), 7.91 (td, $J = 7.7, 1.7$ Hz, 1H), 7.62-7.59 (m, 1H), 7.62-7.59 (m, 1H), 7.57-7.46 (m, 3H), 7.37 (t, $J = 8.0$ Hz, 1H), 7.05 (d, $J = 7.7$ Hz, 1H), 6.23 (tt, $J = 52.9, 4.5$ Hz, 1H), 4.76 (t, $J = 12.8$ Hz, 2H). ^{13}C NMR (101 MHz, CDCl_3): δ 162.6, 154.7, 150.5, 148.1 137.6, 136.5, 133.9, 126.9, 126.4, 125.4, 124.4, 124.2 122.7, 117.2 (tt, $J_{C-F} = 34.3, 250.3$ Hz) 118.4, 117.3, 111.7 (tt, $J_{C-F} = 34.3, 250.3$ Hz), 109.1, 67.2 (d, $J_{C-F} = 28.9$ Hz). ^{19}F NMR (376 MHz, CDCl_3): δ -123.15, -138.46. HRMS (positive ESI) Calcd. For $\text{C}_{19}\text{H}_{14}\text{F}_4\text{N}_2\text{O}_2$ ($M + H$) 379.1070, Found: 379.1064.

***N*-(8-(2,2,3,3,4,4,4-Heptafluorobutoxy)naphthalen-1-yl)picolinamide (3ae)**: purified by analytical TLC on silica gel with petroleum ether/EtOAc (5:1) as an eluent $R_f = 0.38$; white solid (65.2mg, 73%), mp 130-134 °C. ^1H NMR (400 MHz, CDCl_3): δ 12.49 (s, 1H), 8.94 (dd, $J = 7.7, 1.3$ Hz, 1H), 8.60 (d, $J = 4.3$ Hz, 1H), 8.33 (dt, $J = 7.8, 1.0$ Hz, 1H), 7.91 (td, $J = 7.7, 1.7$ Hz, 1H), 7.61-7.51 (m, 3H), 7.49-7.46 (m, 1H), 7.38 (t, $J = 8.1$ Hz, 1H), 7.07 (d, $J = 7.7$

Hz, 1H), 4.92 (t, $J = 14.7$ Hz, 2H). ^{13}C NMR (151 MHz, CDCl_3): δ 161.6, 154.0, 149.7, 146.9, 136.5, 135.5, 133.1, 126.1, 125.2, 124.4, 123.6, 123.2, 121.6, 117.5 (t, $J = 43.7$ Hz), 117.1, 115.5 (q, $J = 37.3$ Hz), 116.4, 112.8 (t, $J = 260.6$, 31.0 Hz), 109.1, 66.4 (t, $J = 23.4$ Hz). ^{19}F NMR (376 MHz, CDCl_3): δ -119.68, -119.74, -127.67. HRMS (positive ESI) Calcd. For $\text{C}_{20}\text{H}_{13}\text{F}_7\text{N}_2\text{O}_2$ ($M + H$) 447.0944, Found: 447.0938.

***N*-(8-Methoxynaphthalen-1-yl)picolinamide (3af)**: purified by analytical TLC on silica gel with petroleum ether/EtOAc (3:1) as an eluent $R_f = 0.30$; light yellow solid (30.1mg, 54%), mp 176-182°C. ^1H NMR (400 MHz, CDCl_3): δ 13.20 (s, 1H), 9.00 (dd, $J = 7.6, 1.4$ Hz, 1H), 8.71-8.69 (m, 1H), 8.35 (dt, $J = 7.9, 0.9$ Hz, 1H), 7.91 (td, $J = 7.7, 1.7$ Hz, 1H), 7.57-7.55 (m, 1H), 7.53-7.44 (m, 3H), 7.37 (t, $J = 8.0$ Hz, 1H), 6.91 (dd, $J = 7.6, 0.7$ Hz, 1H), 4.20 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3): δ 162.4, 156.3, 151.2, 148.1, 137.5, 136.4, 135.2, 126.8, 126.1, 125.6, 123.7, 122.6, 122.1, 116.6, 116.6, 105.7, 56.2. HRMS (positive ESI) Calcd. For $\text{C}_{17}\text{H}_{14}\text{N}_2\text{O}_2$ ($M + H$) 279.1134, Found: 279.1128

***N*-(8-Ethoxynaphthalen-1-yl)picolinamide (3ag)**: purified by analytical TLC on silica gel with petroleum ether/EtOAc (3:1) as an eluent $R_f = 0.39$; white solid (46.8mg, 80%), mp 105-111°C. ^1H NMR (400 MHz, CDCl_3): δ 12.75 (s, 1H), 9.01 (dd, $J = 7.7, 1.3$ Hz, 1H), 8.63-8.61 (m, 1H), 8.34 (dt, $J = 7.9, 0.9$ Hz, 1H), 7.88 (td, $J = 7.7, 1.7$ Hz, 1H), 7.57-7.55 (m, 1H), 7.52-7.40 (m, 3H), 7.33 (t, $J = 8.0$ Hz, 1H), 6.90 (d, $J = 7.4$ Hz, 1H), 4.35 (q, $J = 7.0$ Hz, 2H), 1.68 (t, $J = 7.0$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3): δ 162.8, 155.6, 151.1, 147.7, 137.4, 136.5, 135.0, 126.6, 126.1, 125.6, 124.0, 122.7, 121.9, 117.2, 117.0, 106.8, 65.4, 15.1. HRMS (positive ESI) Calcd. For $\text{C}_{18}\text{H}_{16}\text{N}_2\text{O}_2$ ($M + H$) 293.1290, Found: 293.1285.

***N*-(8-Propoxynaphthalen-1-yl)picolinamide (3ah)**: purified by analytical TLC on silica gel with petroleum ether/EtOAc (3:1) as an eluent $R_f = 0.43$; white solid (40.4mg, 66%), mp 82-84°C. ^1H NMR (400 MHz, CDCl_3): δ 12.74 (s, 1H), 8.99 (dd, $J = 7.7, 1.2$ Hz, 1H), 8.66-8.64 (m, 1H), 8.35 (d, $J = 7.8$ Hz, 1H), 7.92 (td, $J = 7.7, 1.7$ Hz, 1H), 7.58-7.56 (m, 1H), 7.52-7.46 (m, 2H), 7.45-7.43 (m, 1H), 7.35 (t, $J = 8.0$ Hz, 1H), 6.93 (d, $J = 7.8$ Hz, 1H), 4.30 (t, $J = 6.7$ Hz, 2H), 2.20-2.11 (m, 2H), 1.04 (t, $J = 7.4$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3): δ 162.8, 155.7, 151.2, 147.6, 137.4, 136.5, 135.0, 126.6, 126.1, 125.6, 124.0, 122.8, 121.8, 117.2, 117.1, 106.8, 71.5, 22.3, 10.8. HRMS (positive ESI) Calcd. For $\text{C}_{19}\text{H}_{18}\text{N}_2\text{O}_2$ ($M + H$) 307.1447, Found: 307.1441.

***N*-(8-Butoxynaphthalen-1-yl)picolinamide (3ai)**: purified by analytical TLC on silica gel with petroleum ether/EtOAc (3:1) as an eluent $R_f = 0.55$; white solid (53.8mg, 84%), mp 109-111°C. ^1H NMR (400 MHz, CDCl_3): δ 12.72 (s, 1H), 8.98 (dd, $J = 7.7, 1.2$ Hz, 1H), 8.68-8.65 (m, 1H), 8.36 (d, $J = 7.8$ Hz, 1H), 7.92 (td, $J = 7.7, 1.7$ Hz, 1H), 7.58-7.56 (m, 1H), 7.52-7.47 (m, 2H), 7.45-7.43 (m, 1H), 7.35 (t, $J = 8.0$ Hz, 1H), 6.94 (d, $J = 7.1$ Hz, 1H), 4.33 (t, $J = 6.9$ Hz, 2H), 2.14-2.07 (m, 2H), 1.53-1.43 (m, 2H), 0.92 (t, $J = 7.4$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3): δ 162.8, 155.7, 151.2, 147.7, 137.4, 136.5, 135.0, 126.6, 126.1, 125.6, 124.0, 122.8, 121.8, 117.2, 117.1, 106.8, 69.7, 31.0, 19.3,

13.9.HRMS (positive ESI) Calcd. For $C_{20}H_{20}N_2O_2$ (M + H) 321.1603, Found: 321.1598.

***N*-(8-(Pentyloxy)naphthalen-1-yl)picolinamide (3aj):** purified by analytical TLC on silica gel with petroleum ether/EtOAc (3:1) as an eluent R_f = 0.51; white solid (52.2mg, 78%), mp 106-110°C. 1H NMR (400 MHz, $CDCl_3$): δ 12.72 (s, 1H), 8.98 (dd, J = 7.8, 1.3 Hz, 1H), 8.65-8.64 (m, 1H), 8.36 (dt, J = 7.9, 0.9 Hz, 1H), 7.91 (td, J = 7.8, 1.7 Hz, 1H), 7.58-7.56 (m, 1H), 7.52-7.46 (m, 2H), 7.44-7.42 (m, 1H), 7.34 (t, J = 8.0 Hz, 1H), 6.92 (d, J = 7.1 Hz, 1H), 4.31 (t, J = 7.0 Hz, 2H), 2.15-2.08 (m, 2H), 1.45-1.27 (m, 4H), 0.85 (t, J = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 162.8, 155.7, 151.2, 147.6, 137.4, 136.5, 135.0, 126.6, 126.1, 125.6, 124.0, 122.8, 121.8, 117.2, 117.1, 106.8, 77.4, 77.1, 76.7, 70.0, 28.8, 28.3, 22.5, 14.1. HRMS (positive ESI) Calcd. For $C_{21}H_{22}N_2O_2$ (M + H) 335.1760, Found: 335.1754.

***N*-(8-(Hexyloxy)naphthalen-1-yl)picolinamide (3ak):** purified by analytical TLC on silica gel with petroleum ether/EtOAc (3:1) as an eluent R_f = 0.57; brown solid (55.8mg, 80%), mp 78-81°C. 1H NMR (400 MHz, $CDCl_3$): δ 12.72 (s, 1H), 8.98 (dd, J = 7.7, 1.2 Hz, 1H), 8.66-8.65 (m, 1H), 8.36 (d, J = 7.8 Hz, 1H), 7.91 (td, J = 7.7, 1.7 Hz, 1H), 7.58-7.56 (m, 1H), 7.52-7.46 (m, 1H), 7.44-7.42 (m, 1H), 7.37-7.33 (m, 1H), 6.92 (d, J = 7.2 Hz, 1H), 4.31 (t, J = 7.0 Hz, 2H), 2.14-2.07 (m, 2H), 1.46-1.39 (m, 2H), 1.31-1.17 (m, 4H), 0.82 (t, J = 7.2, 4.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 162.8, 155.7, 151.2, 147.7, 137.4, 136.5, 135.0, 126.6, 126.1, 125.6, 124.0, 122.8, 121.8, 117.2, 117.1, 106.8, 70.0, 31.6, 29.0, 25.8, 22.6, 14.0. HRMS (positive ESI) Calcd. For $C_{22}H_{24}N_2O_2$ (M + H) 349.1916, Found: 349.1911.

***N*-(8-Isobutoxynaphthalen-1-yl)picolinamide (3al):** purified by analytical TLC on silica gel with petroleum ether/EtOAc (5:1) as an eluent R_f = 0.55; slight yellow solid (57.0mg, 89%), mp 81-84 °C. 1H NMR (400 MHz, $CDCl_3$): δ 12.72 (s, 1H), 8.99 (dd, J = 7.7, 1.3 Hz, 1H), 8.63-8.61 (m, 1H), 8.36 (dt, J = 7.9, 1.0 Hz, 1H), 7.91 (td, J = 7.7, 1.7 Hz, 1H), 7.58-7.56 (m, 1H), 7.53-7.42 (m, 3H), 7.35 (t, J = 7.9 Hz, 1H), 6.91 (d, J = 7.6 Hz, 1H), 4.09 (d, J = 7.1 Hz, 2H), 2.69-2.56 (m, 1H), 1.03 (d, J = 6.6 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 162.8, 155.7, 151.2, 147.6, 137.4, 136.5, 135.0, 126.6, 126.1, 125.6, 124.1, 122.8, 121.8, 117.3, 117.1, 106.8, 76.4, 27.3, 19.6. HRMS (positive ESI) Calcd. For $C_{20}H_{20}N_2O_2$ (M + H) 321.1603, Found: 321.1598.

***N*-(8-(2-Methylbutoxy)naphthalen-1-yl)picolinamide (3am):** purified by analytical TLC on silica gel with petroleum ether/EtOAc (3:1) as an eluent R_f = 0.57; slight yellow oil (44.1mg, 66%). 1H NMR (400 MHz, $CDCl_3$): δ 12.71 (s, 1H), 8.98 (dd, J = 7.7, 1.3 Hz, 1H), 8.65-8.63 (m, 1H), 8.37-8.35 (m, 1H), 7.91 (td, J = 7.7, 1.7 Hz, 1H), 7.59-7.56 (m, 1H), 7.53-7.43 (m, 3H), 7.35 (t, J = 7.9 Hz, 1H), 6.92 (d, J = 7.1 Hz, 1H), 4.25-4.21 (m, 1H), 4.08-4.04 (m, 1H), 2.50-2.37 (m, 1H), 1.63-1.53 (m, 1H), 1.32-1.20 (m, 1H), 1.00 (d, J = 6.6 Hz, 3H), 0.91 (t, J = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 162.8, 155.8, 151.2, 147.7, 137.4, 136.5, 135.0, 126.6, 126.1, 125.6, 124.1, 122.8, 121.8,

117.3, 117.1, 106.8, 75.2, 33.5, 26.3, 16.6, 11.1. HRMS (positive ESI) Calcd. For $C_{17}H_{14}N_2O_2$ (M + H) 335.1760, Found: 335.1756.

N-(8-(Isopentyloxy)naphthalen-1-yl)picolinamide (3an): purified by analytical TLC on silica gel with petroleum ether/EtOAc (3:1) as an eluent R_f = 0.52; white solid (54.8mg, 82%), mp 101-104 °C. 1H NMR (400 MHz, $CDCl_3$): δ 12.69 (s, 1H), 8.98 (dd, J = 7.7, 1.2 Hz, 1H), 8.69-8.67(m, 1H), 8.36 (d, J = 7.9 Hz, 1H), 7.92 (td, J = 7.7, 1.7 Hz, 1H), 7.58-7.53(m, 1H), 7.52-7.47(m, 2H), 7.45-7.42 (m, 1H), 7.36 (t, J = 7.9 Hz, 1H), 6.94 (d, J = 7.2 Hz, 1H), 4.35 (t, J = 7.3 Hz, 2H), 2.04 (q, J = 7.3 Hz 2H), 1.79 (p, J = 6.7 Hz, 1H), 0.94 (d, J = 6.6 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 162.8, 155.7, 151.2, 147.7, 137.5, 136.5, 135.0, 126.6, 126.1, 125.6, 124.0, 122.8, 121.8, 117.2, 117.1, 106.8, 68.6, 37.6, 25.4, 22.7. HRMS (positive ESI) Calcd. For $C_{21}H_{22}N_2O_2$ (M + H) 335.1760, Found: 335.1754.

N-(8-(Cyclopropylmethoxy)naphthalen-1-yl)picolinamide (3ao): purified by analytical TLC on silica gel with petroleum ether/EtOAc (3:1) as an eluent R_f = 0.45; gray solid (28.7mg, 45%), mp 102-105 °C. 1H NMR (400 MHz, $CDCl_3$): δ 12.95 (s, 1H), 8.98 (dd, J = 7.7, 1.3 Hz, 1H), 8.56-8.54(m, 1H), 8.37-8.33 (m, 1H), 7.90 (td, J = 7.7, 1.7 Hz, 1H), 7.58-7.56(m, 1H), 7.52-7.49(m, 1H), 7.46-7.43 (m, 2H), 7.34 (dd, J = 14.1, 6.1 Hz, 1H), 6.94 (dd, J = 7.7, 0.7 Hz, 1H), 4.20 (d, J = 7.1 Hz, 2H), 1.65-1.56 (m, 1H), 0.59-0.54 (m, 2H), 0.42-0.37 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 162.7, 155.6, 151.3, 147.6, 137.4, 136.5, 135.1, 126.6, 126.1, 125.6, 124.0, 122.8, 121.9, 117.3, 117.1, 107.5, 74.8, 10.3, 3.9. HRMS (positive ESI) Calcd. For $C_{20}H_{18}N_2O_2$ (M + H) 319.1447, Found: 319.1441.

N-(8-(Cyclohexylmethoxy)naphthalen-1-yl)picolinamide (3ap): purified by analytical TLC on silica gel with petroleum ether/EtOAc (3:1) as an eluent R_f = 0.59; light yellow solid (33.2mg, 46%), mp 99-101 °C. 1H NMR (400 MHz, $CDCl_3$): δ 12.74 (s, 1H), 8.97 (dd, J = 7.7, 1.2 Hz, 1H), 8.72-8.70 (m, 1H), 8.36 (d, J = 7.8 Hz, 1H), 7.92 (td, J = 7.7, 1.7 Hz, 1H), 7.58-7.56 (m, 1H) 7.52-7.47 (m, 2H), 7.44-7.42 (m, 1H), 7.35 (t, J = 7.9 Hz, 1H), 6.91 (d, J = 7.2 Hz, 1H), 4.14 (d, J = 6.9 Hz, 2H), 2.34-2.28 (m, 1H), 1.92-1.90 (m, 2H), 1.66-1.63 (m, 3H), 1.18-0.91 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 162.7, 155.8, 151.3, 147.9, 137.5, 136.5, 135.0, 126.6, 126.0, 125.6, 124.0, 122.8, 121.7, 117.1, 106.9, 77.4, 77.1, 76.7, 75.5, 36.2, 30.0, 26.4, 25.5. HRMS (positive ESI) Calcd. For $C_{23}H_{24}N_2O_2$ (M + H) 361.1916, Found: 361.1911.

N-(8-(Adamantanylmethoxy)naphthalen-1-yl)picolinamide (3aq): purified by analytical TLC on silica gel with petroleum ether/EtOAc (3:1) as an eluent R_f = 0.57; white solid (46.2mg, 56%), mp 166-175 °C. 1H NMR (400 MHz, $CDCl_3$): δ 12.41 (s, 1H), 8.89 (dd, J = 7.7, 1.2 Hz, 1H), 8.67-8.65 (m, 1H), 8.36 (d, J = 7.8 Hz, 1H), 7.91 (td, J = 7.7, 1.7 Hz, 1H), 7.58-7.56 (m, 1H), 7.51-7.46 (m, 2H), 7.44-7.41 (m, 1H), 7.34 (t, J = 7.9 Hz, 1H), 7.04 (d, J = 7.2 Hz, 1H), 4.08 (s, 2H), 1.89 (s, 3H), 1.67-1.66 (m, 7H), 1.62 (s, 2H), 1.48 (d, J = 11.5 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 162.9, 155.1, 151.2, 147.7, 137.4, 136.7, 135.1, 126.5, 126.1, 125.7, 124.1, 122.9, 121.7, 117.8, 117.2, 108.2, 76.7,

38.3, 20.0, 19.2, 14.0. HRMS (positive ESI) Calcd. For C₂₇H₂₈N₂O₂ (M + H) 413.2229, Found: 413.2224.

***N*-(8-(3-Methoxypropoxy)naphthalen-1-yl)picolinamide (3ar):** purified by analytical TLC on silica gel with petroleum ether/EtOAc (1:1) as an eluent R_f = 0.38; white solid (45.7mg, 68%), mp 136-139 °C. ¹H NMR (400 MHz, CDCl₃): δ 12.69 (s, 1H), 8.99 (dd, *J* = 7.7, 1.2 Hz, 1H), 8.68-8.67 (m, 1H), 8.36 (d, *J* = 7.8 Hz, 1H), 7.92 (td, *J* = 7.7, 1.7 Hz, 1H), 7.58-7.56 (m, 1H), 7.53-7.46 (m, 2H), 7.45-7.42 (m, 1H) 7.36 (t, *J* = 7.9 Hz, 1H), 6.96 (d, *J* = 7.2 Hz, 1H), 4.44 (t, *J* = 6.3 Hz, 2H), 3.54 (t, *J* = 6.2 Hz, 2H), 3.23 (s, 3H), 2.42 (p, *J* = 6.2 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃): δ 162.7, 155.6, 151.1, 147.8, 137.5, 136.5, 134.9, 126.6, 126.1, 125.7, 124.1, 122.8, 122.0, 117.3, 117.0, 106.9, 69.5, 66.8, 58.7, 29.3. HRMS (positive ESI) Calcd. For C₂₀H₂₀N₂O₂ (M + H) 337.1552, Found: 337.1547.

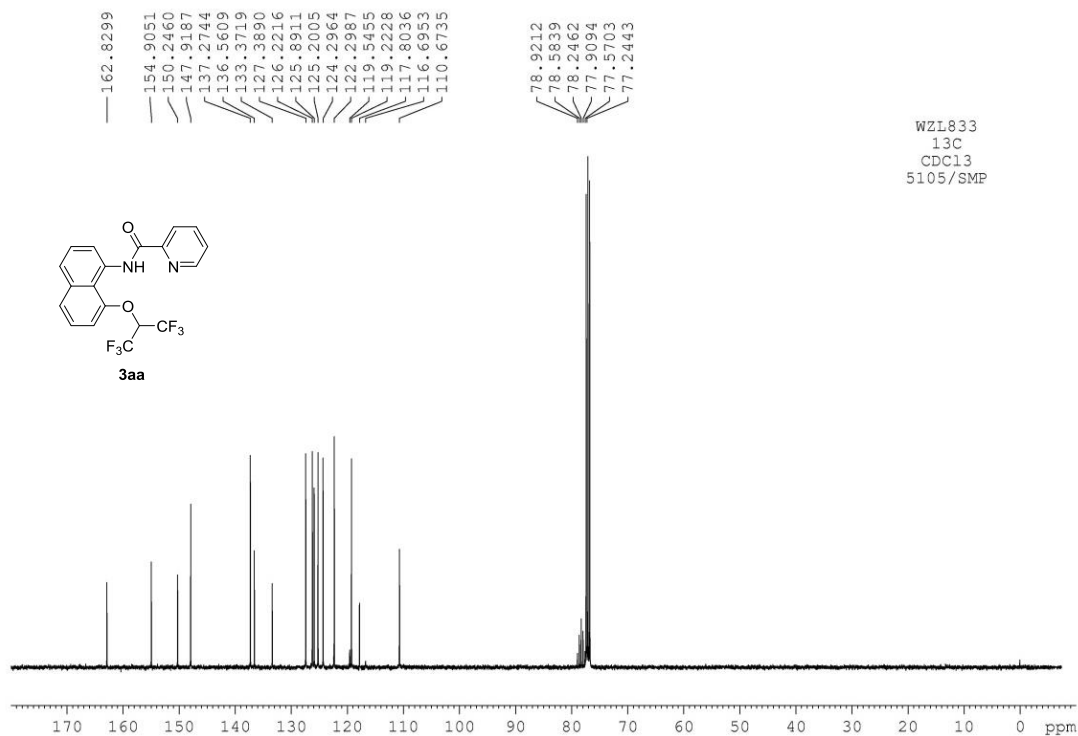
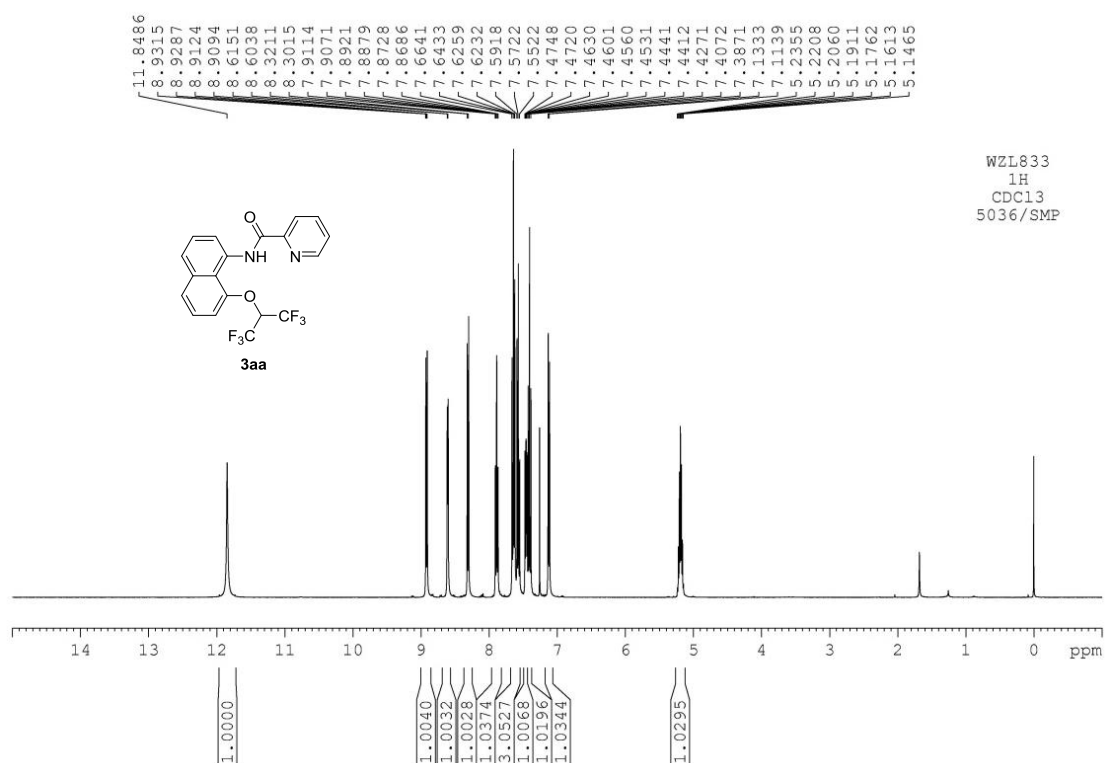
***N*-(8-((4-Bromobenzyl)oxy)naphthalen-1-yl)picolinamide (3as):** purified by analytical TLC on silica gel with petroleum ether/EtOAc (3:1) as an eluent R_f = 0.40; white solid (60.7mg, 70%), mp 127-131 °C. ¹H NMR (400 MHz, CDCl₃): δ 12.93 (s, 1H), 8.93 (dd, *J* = 7.5, 1.4 Hz, 1H), 8.27 (dd, *J* = 7.8, 0.9 Hz, 1H), 8.15-8.13 (m, 1H), 7.83 (td, *J* = 7.7, 1.7 Hz, 1H), 7.55-7.45 (m, 2H), 7.41-7.39 (m, 1H), 7.35-7.30 (m, 5H), 7.24-7.22 (m, 1H), 6.82 (d, *J* = 7.1 Hz, 1H), 5.39 (s, 2H). ¹³C NMR (101 MHz, CDCl₃): δ 162.5, 154.9, 150.7, 147.8, 137.4, 136.5, 135.7, 134.9, 131.7, 129.2, 126.8, 126.0, 125.5, 124.0, 122.5, 122.1, 117.2, 117.1, 108.0, 70.8. HRMS (positive ESI) Calcd. For C₂₃H₁₇BrN₂O₂ (M + H) 433.0552, Found: 433.0546.

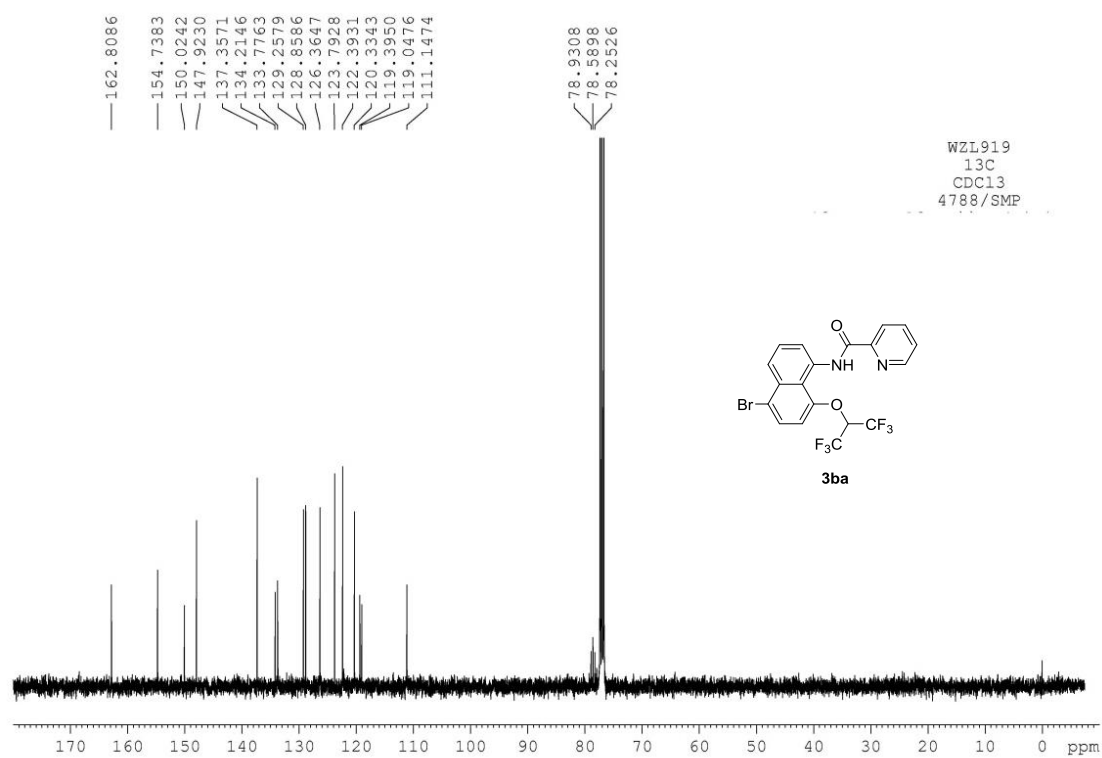
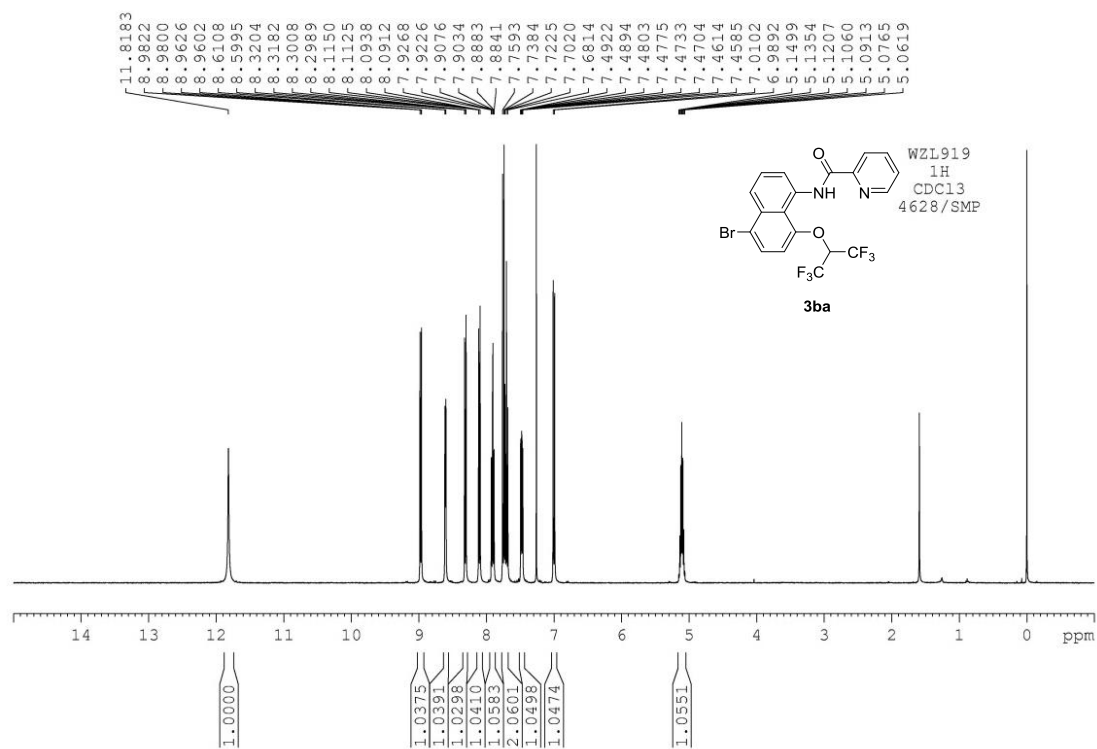
***N*-(8-Isopropoxynaphthalen-1-yl)picolinamide (3at):** purified by analytical TLC on silica gel with petroleum ether/EtOAc (3:1) as an eluent R_f = 0.48; light yellow solid (35.5mg, 58%), mp 81-83 °C. ¹H NMR (400 MHz, CDCl₃): δ 12.71 (s, 1H), 9.01 (dd, *J* = 7.7, 1.3 Hz, 1H), 8.68-8.67 (m, 1H), 8.36 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.90 (td, *J* = 7.7, 1.7 Hz, 1H), 7.58-7.56 (m, 1H), 7.52-7.46 (m, 2H), 7.43-7.42 (m, 1H) 7.35 (t, *J* = 7.9 Hz, 1H), 6.98 (d, *J* = 7.6 Hz, 1H), 4.96-4.86 (m, 1H), 1.59 (d, *J* = 6.1 Hz, 6H). ¹³C NMR (101 MHz, CDCl₃): δ 162.9, 154.7, 151.2, 147.7, 137.4, 136.6, 135.1, 126.5, 126.1, 125.7, 124.1, 122.8, 121.8, 117.8, 117.1, 108.5, 72.9, 22.0. HRMS (positive ESI) Calcd. For C₁₉H₁₈N₂O₂ (M + H) 307.1447, Found: 307.1441.

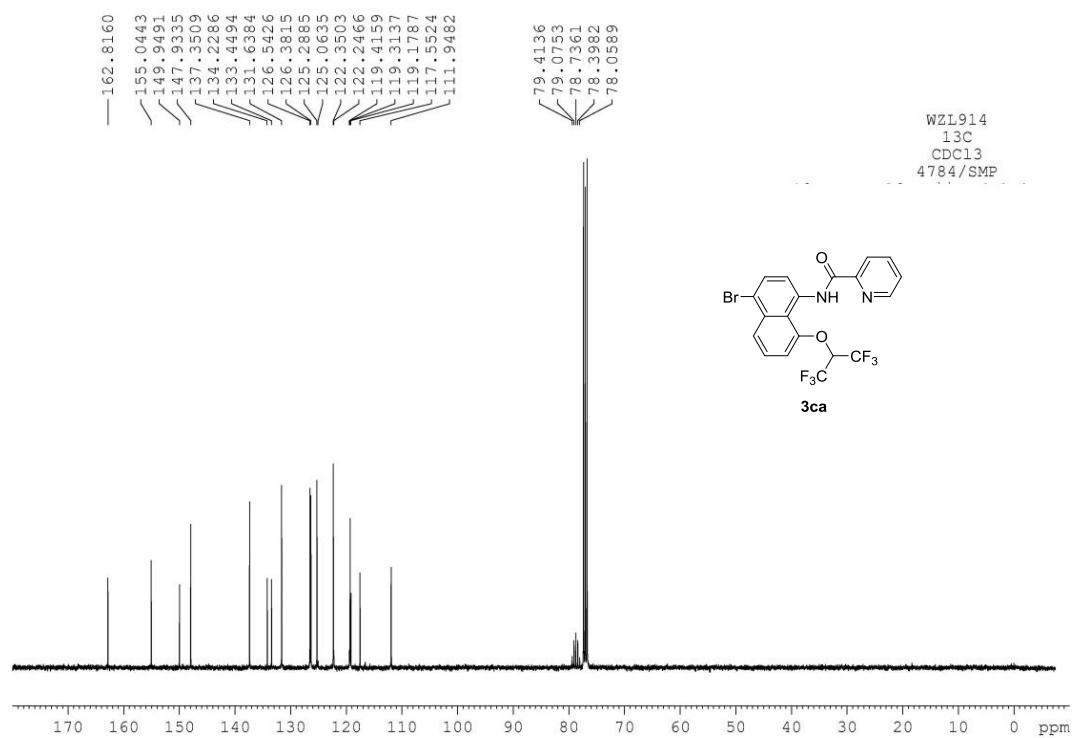
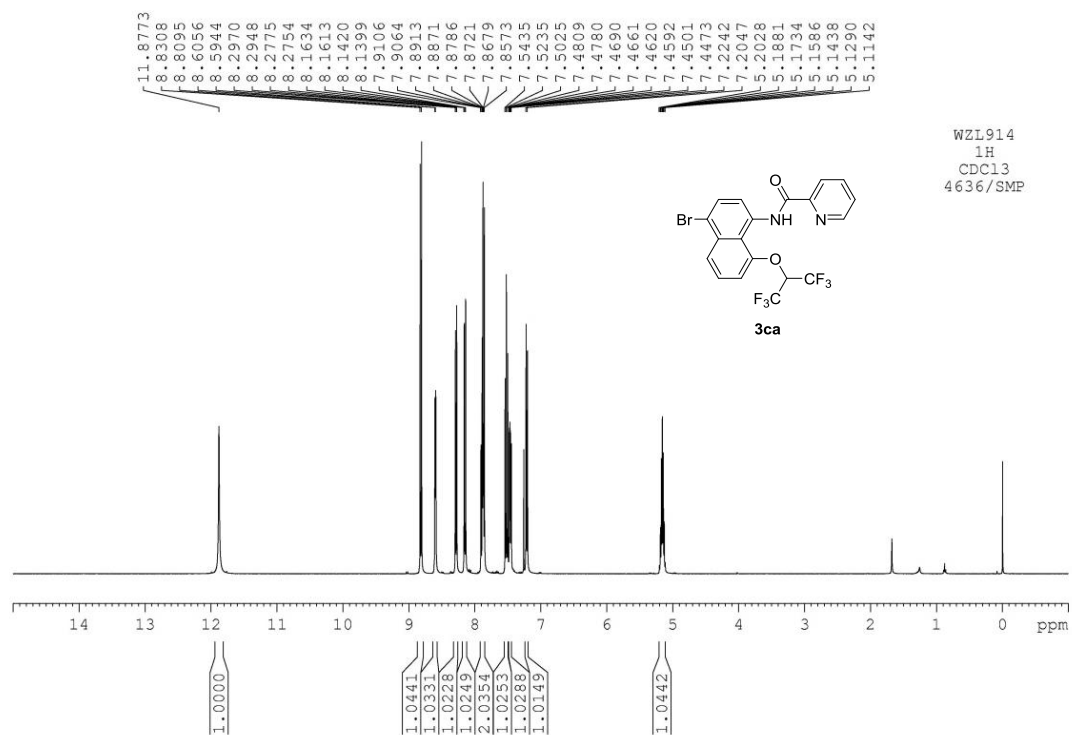
***N*-(8-(sec-Butoxy)naphthalen-1-yl)picolinimidamide(3au):** purified by analytical TLC on silica gel with petroleum ether/EtOAc (3:1) as an eluent R_f = 0.53; yellow oil (41.7mg, 65%). ¹H NMR (400 MHz, CDCl₃): δ 12.72 (s, 1H), 9.01 (dd, *J* = 7.7, 1.3 Hz, 1H), 8.67-8.65 (m, 1H), 8.36 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.91 (td, *J* = 7.7, 1.7 Hz, 1H), 7.58-7.56 (m, 1H), 7.53-7.46 (m, 2H), 7.44-7.42 (m, 1H), 7.35 (t, *J* = 7.9 Hz, 1H), 6.98 (d, *J* = 7.6 Hz, 1H), 4.710-4.62 (m, 1H), 2.25-2.13 (m, 1H), 1.90-1.79 (m, 1H), 1.54 (d, *J* = 6.1 Hz, 3H), 1.02 (t, *J* = 7.4 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃): δ 162.9, 155.1, 151.2, 147.6, 137.4, 136.7, 135.1, 126.5, 126.1, 125.7, 124.1, 122.8, 121.7, 117.8, 117.2, 108.3, 78.3, 29.0, 19.6, 10.4. HRMS (positive ESI) Calcd. For C₂₀H₂₀N₂O₂ (M + H) 321.1603, Found: 321.1598.

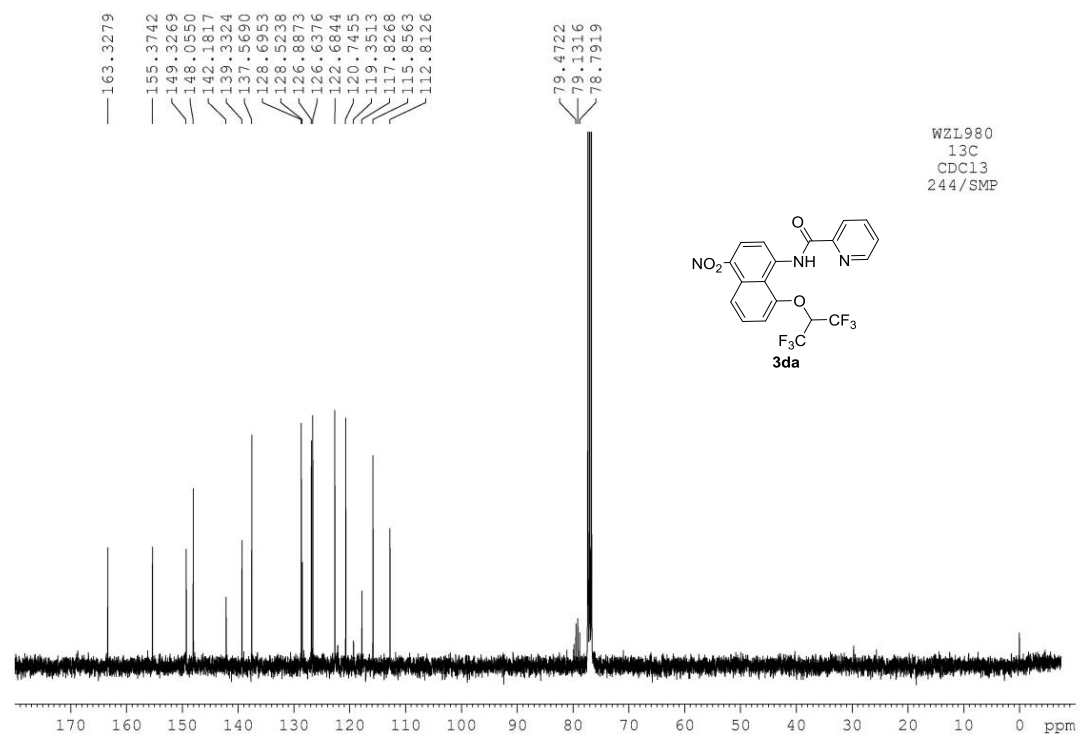
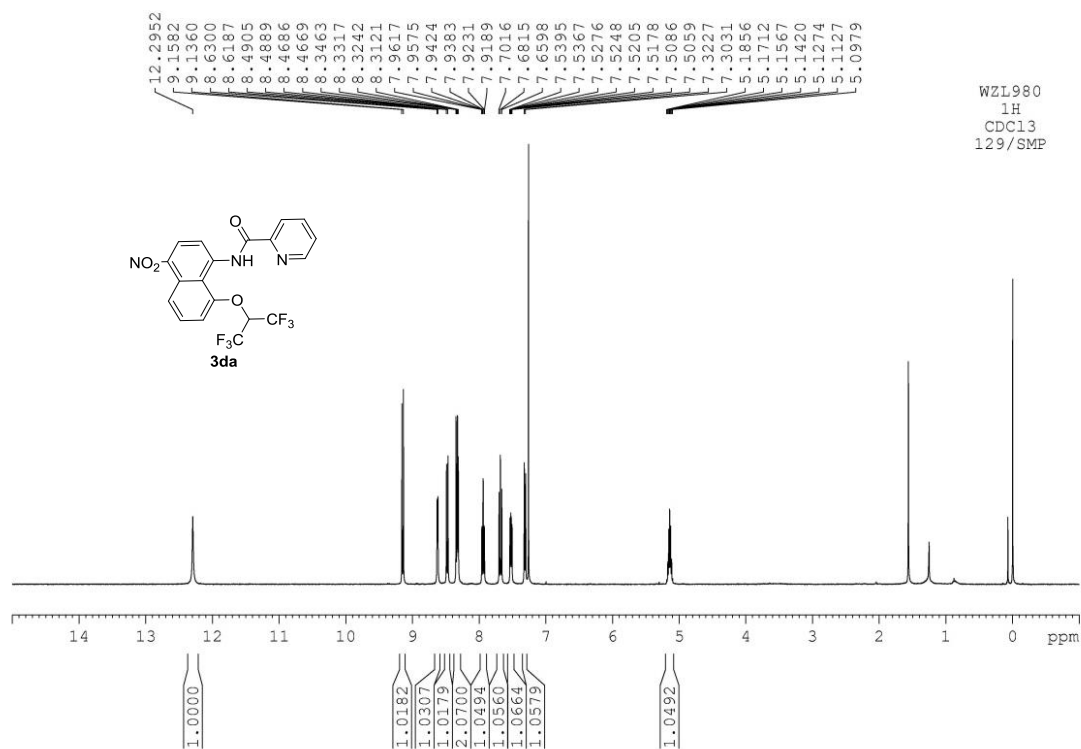
***N*-(8-(Pentan-2-yloxy)naphthalen-1-yl)picolinamide (3av):** purified by analytical TLC on silica gel with petroleum ether/EtOAc (3:1) as an eluent $R_f = 0.55$; light yellow oil (59.5mg, 89%). ^1H NMR (400 MHz, CDCl_3): δ 12.71 (s, 1H), 9.01 (dd, $J = 7.7, 1.3$ Hz, 1H), 8.69-8.67 (m, 1H), 8.36 (dt, $J = 7.9, 1.0$ Hz, 1H), 7.91 (td, $J = 7.7, 1.7$ Hz, 1H), 7.58-7.56 (dm, 1H), 7.53-7.46 (m, 2H), 7.44-7.42 (m, 1H), 7.35 (t, $J = 7.9$ Hz, 1H), 6.97 (d, $J = 7.6$ Hz, 1H), 4.77-4.70 (m, 1H), 2.27-2.16 (m, 1H), 1.80-1.70 (m, 1H), 1.53 (d, $J = 6.1$ Hz, 3H), 1.51-1.38 (m, 2H), 0.88 (t, $J = 7.4$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3): δ 162.9, 155.1, 151.2, 147.7, 137.4, 136.7, 135.1, 126.5, 126.1, 125.7, 124.1, 122.9, 121.7, 117.8, 117.2, 108.2, 76.7, 38.3, 20.0, 19.2, 14.0. HRMS (positive ESI) Calcd. For $\text{C}_{21}\text{H}_{22}\text{N}_2\text{O}_2$ ($M + H$) 335.1760, Found: 335.1754.

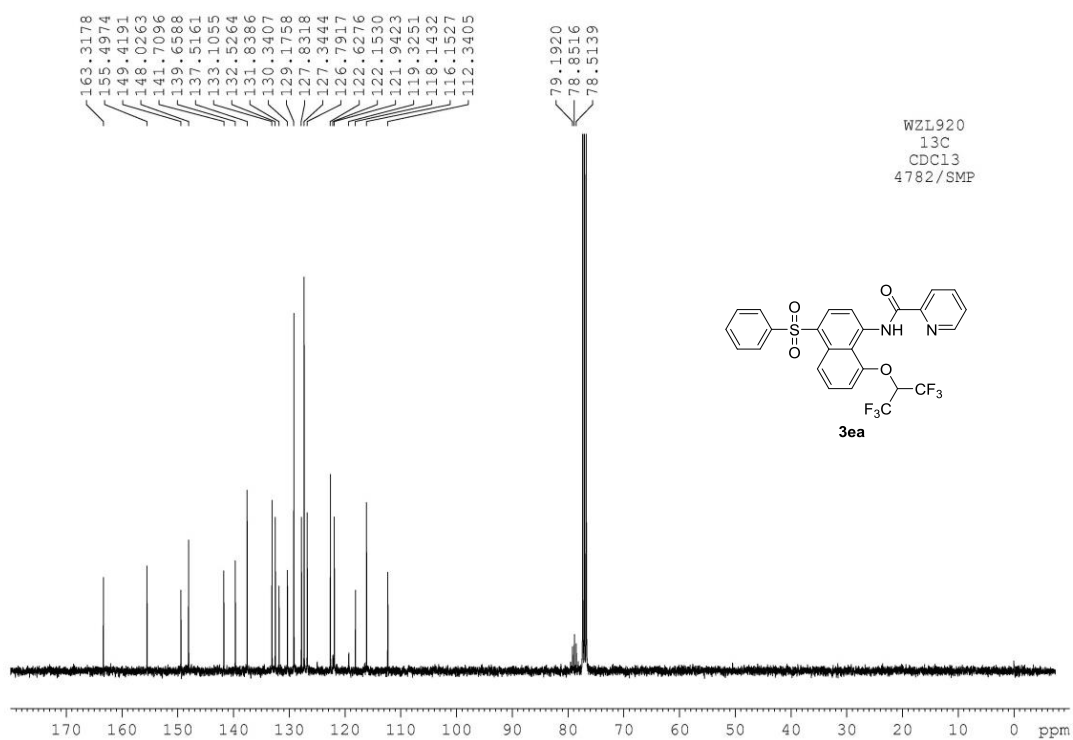
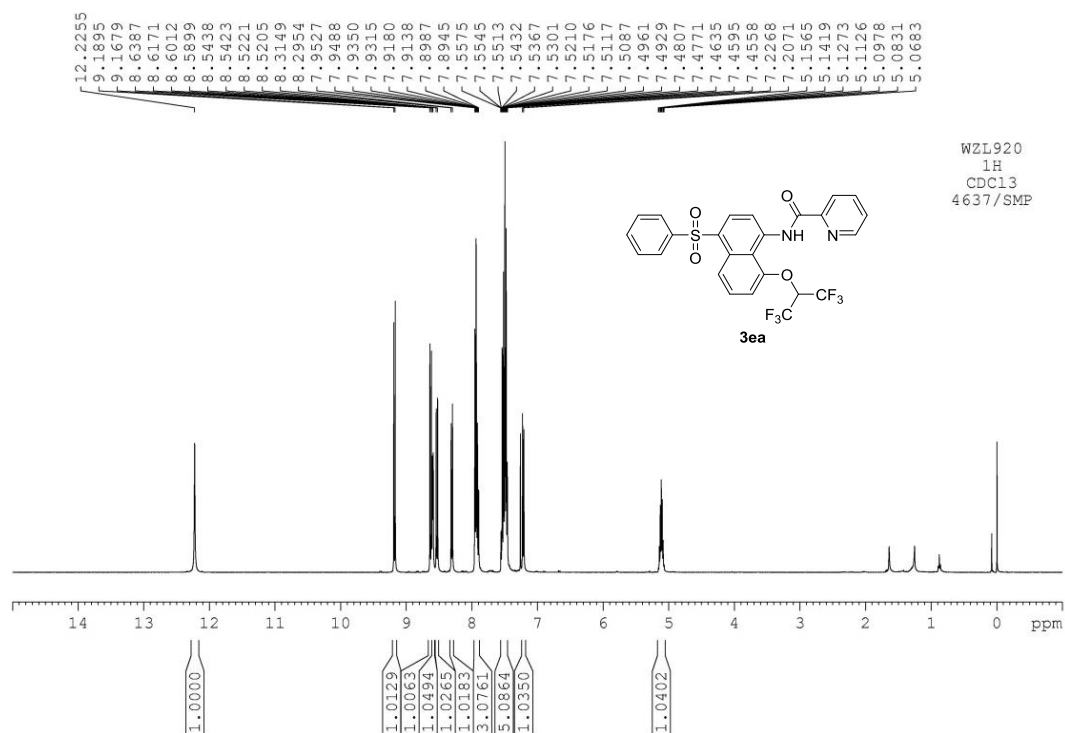
NMR spectra

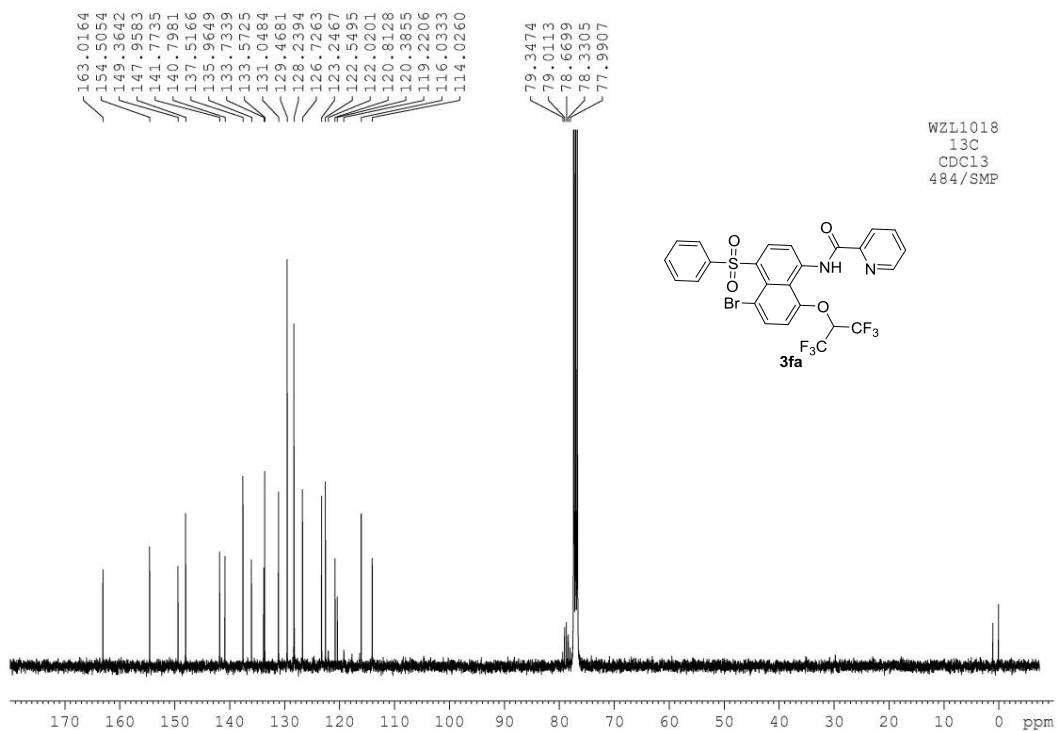
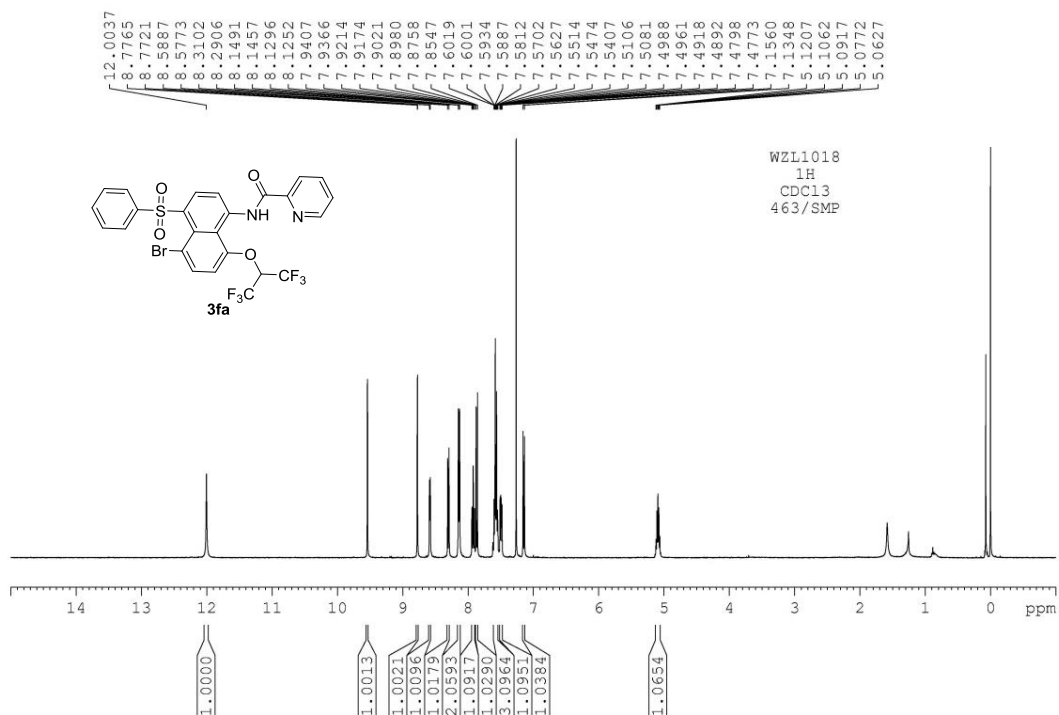


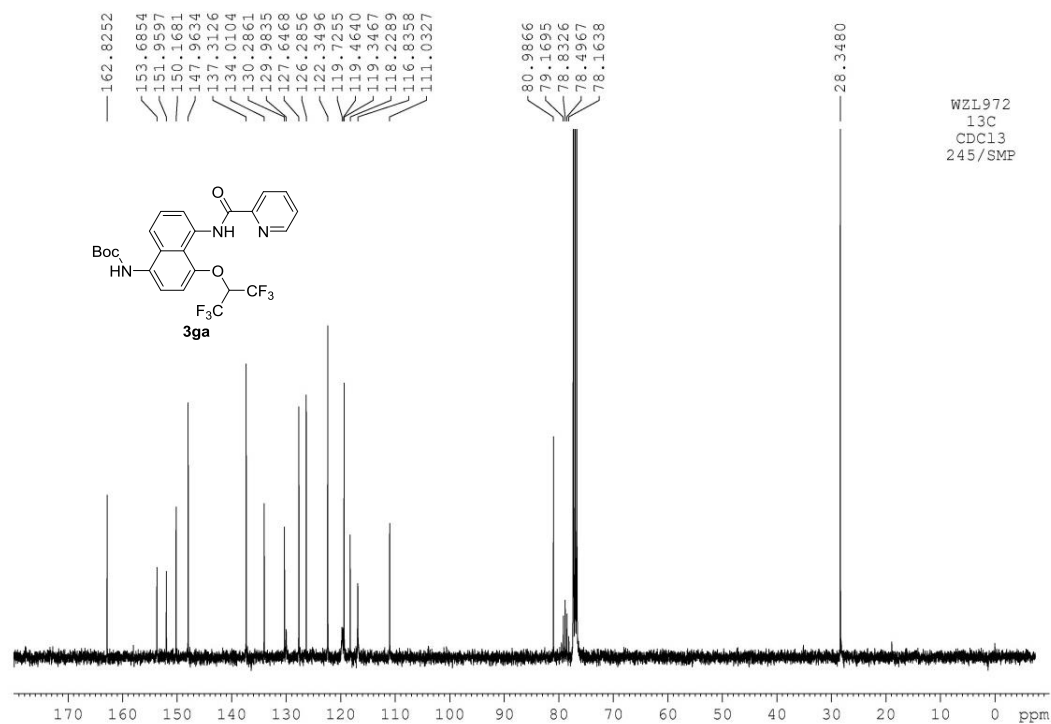
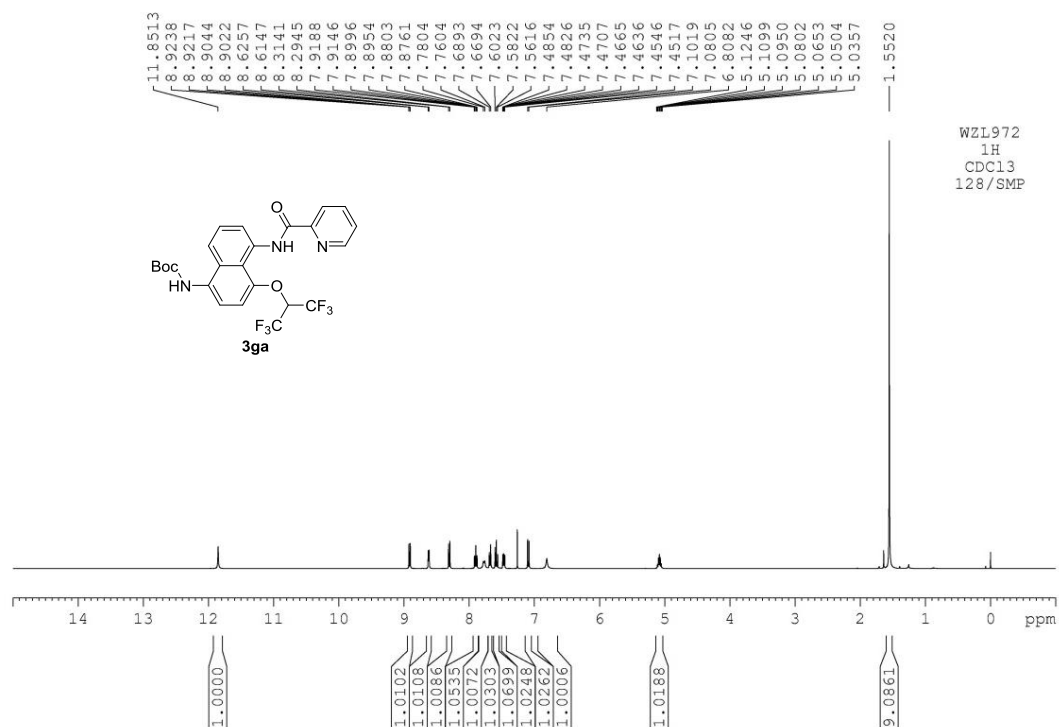


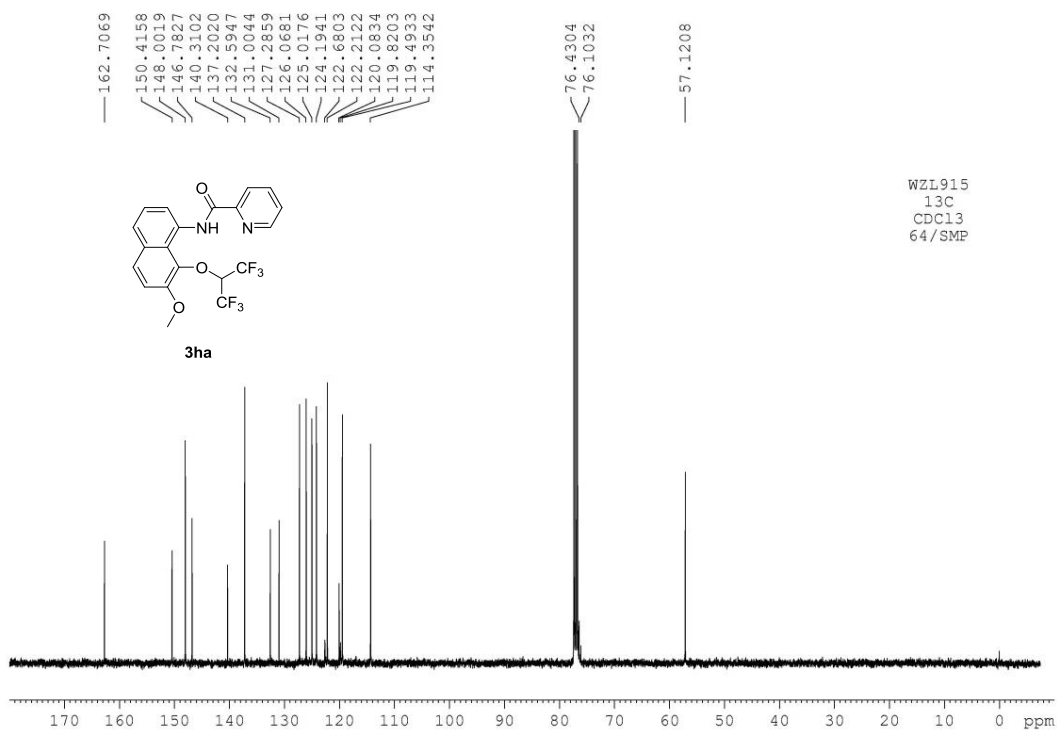
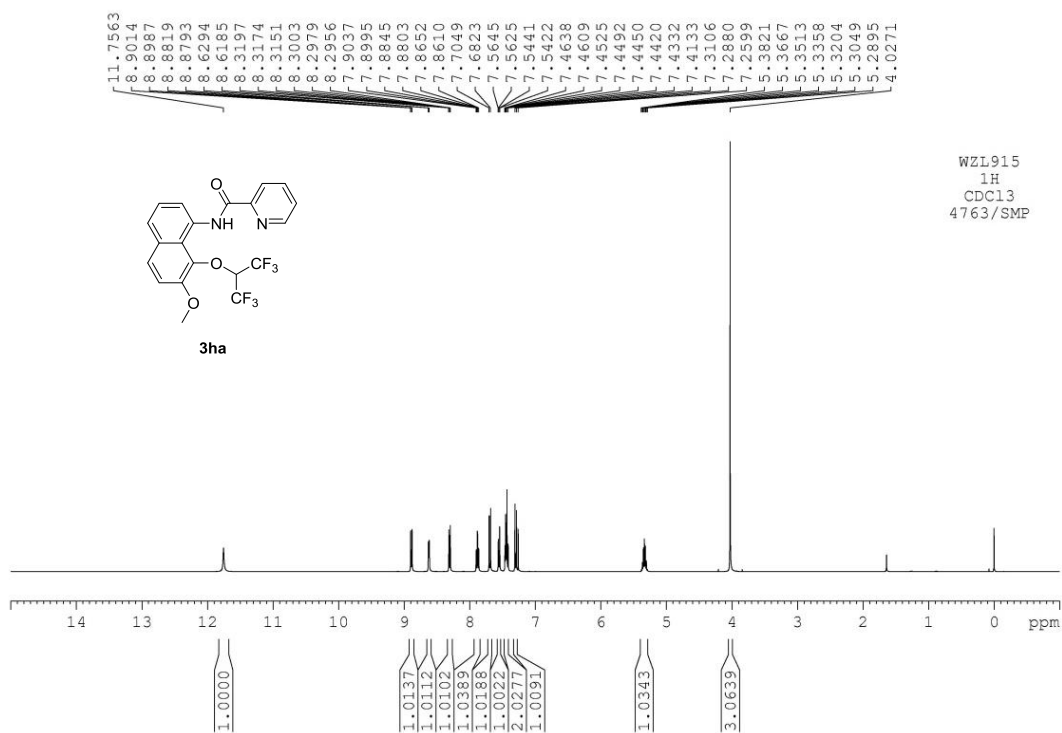


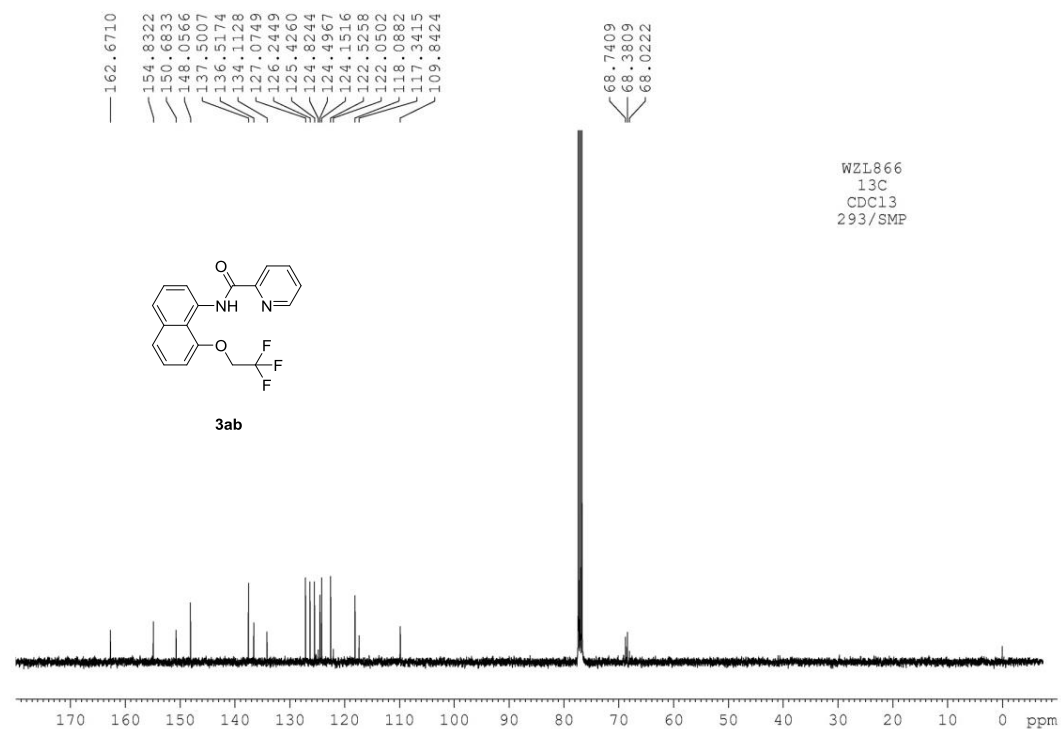
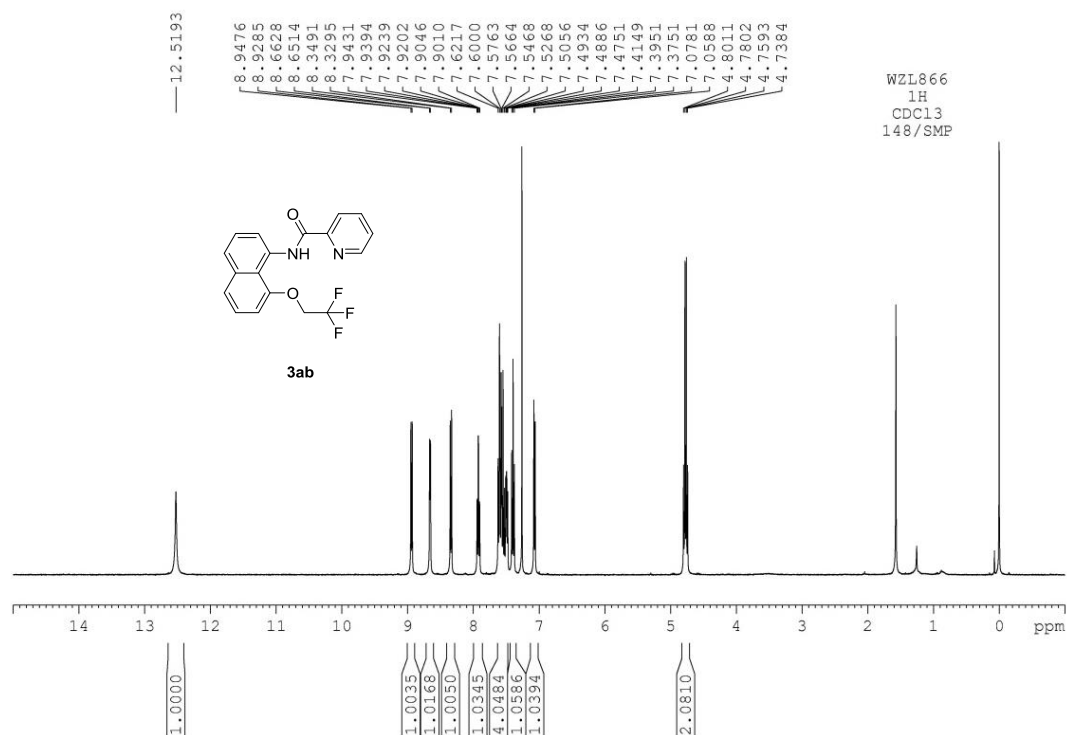


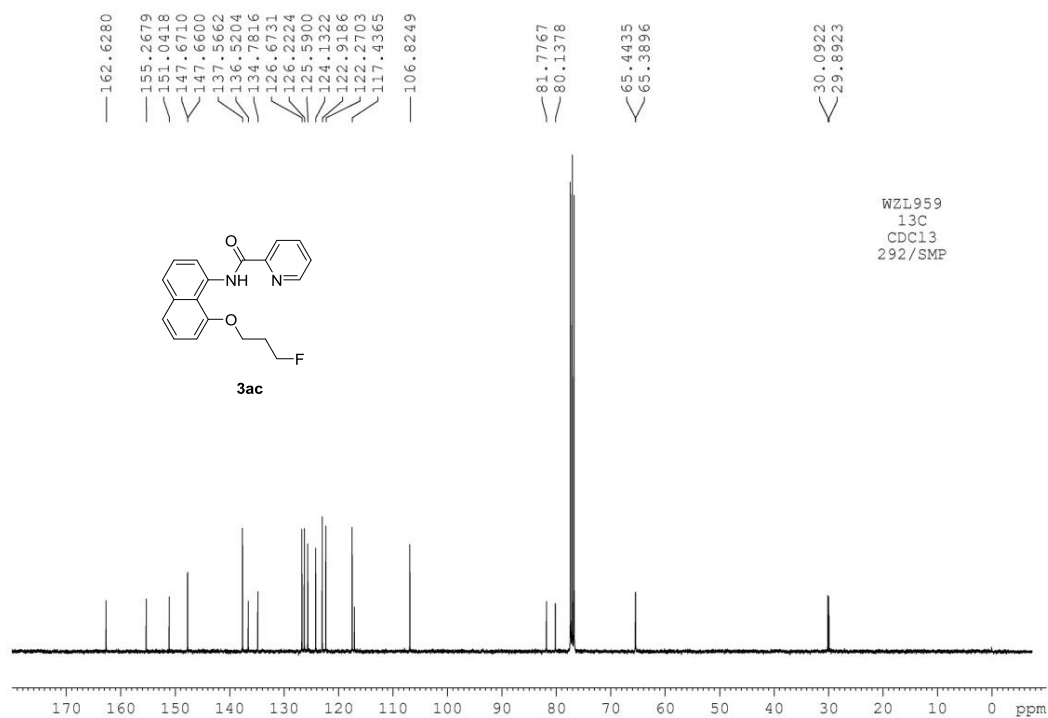
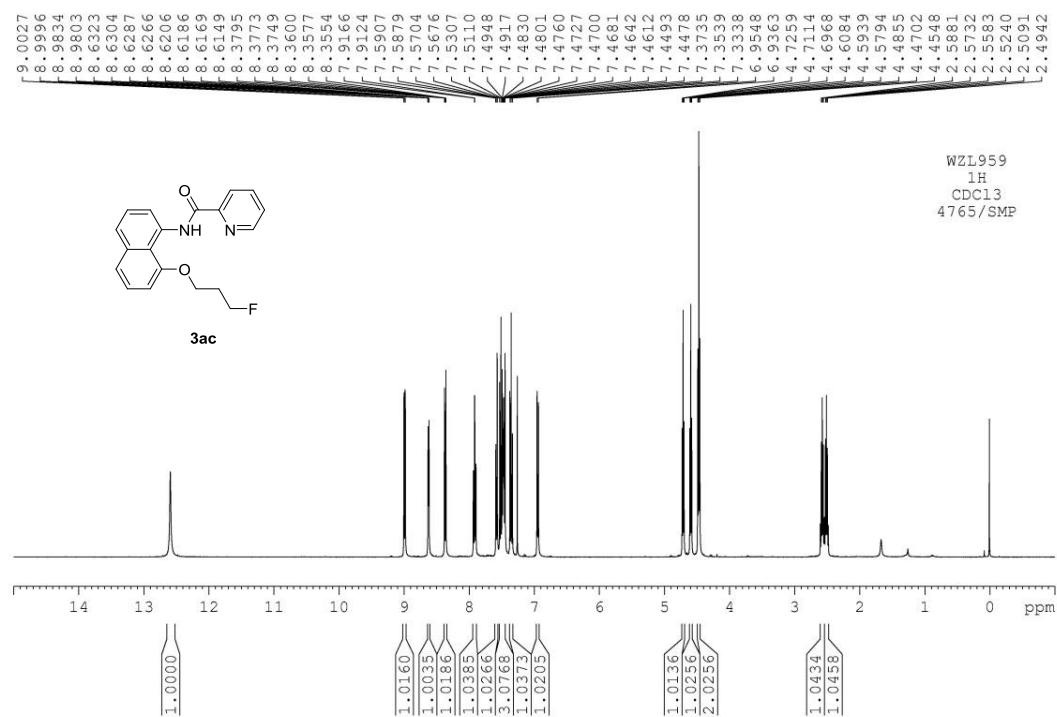


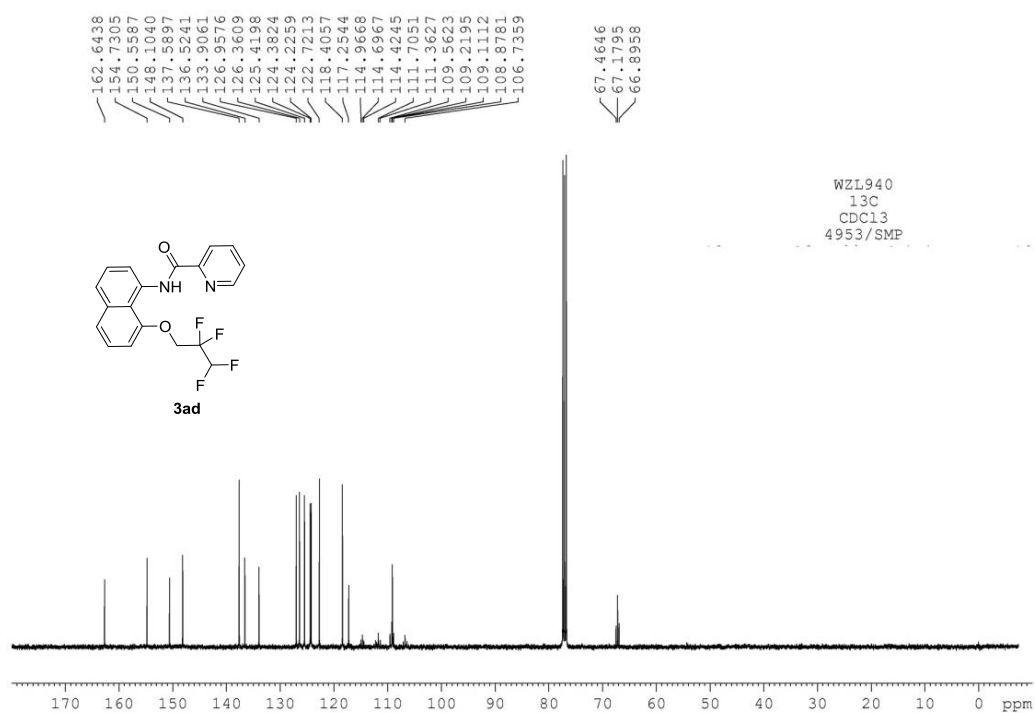
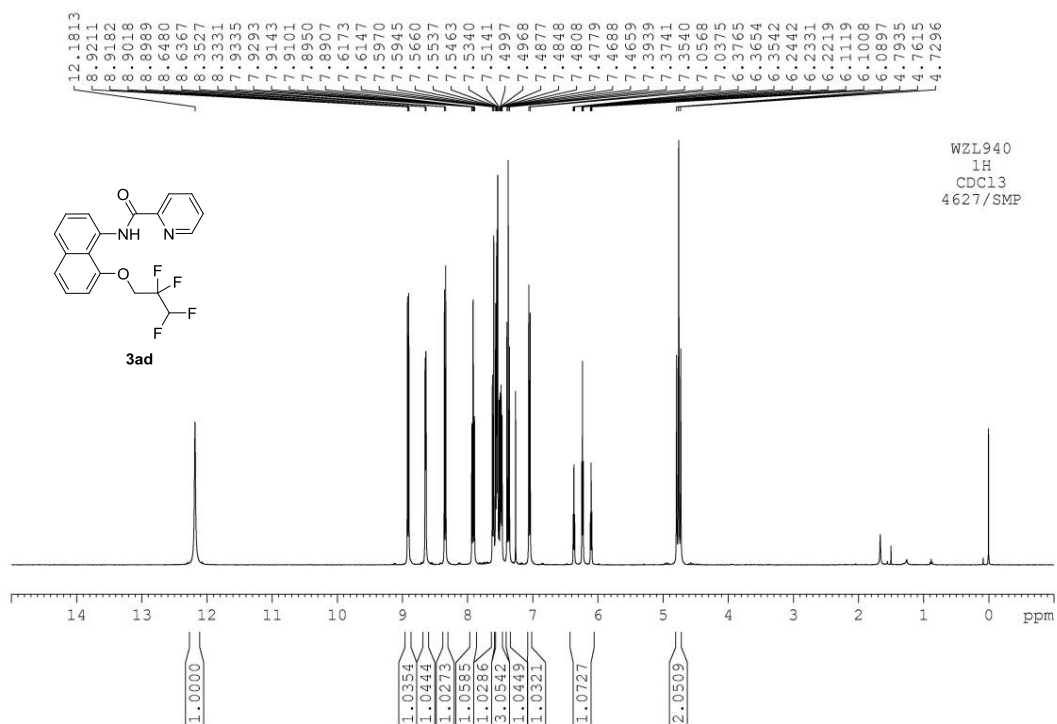


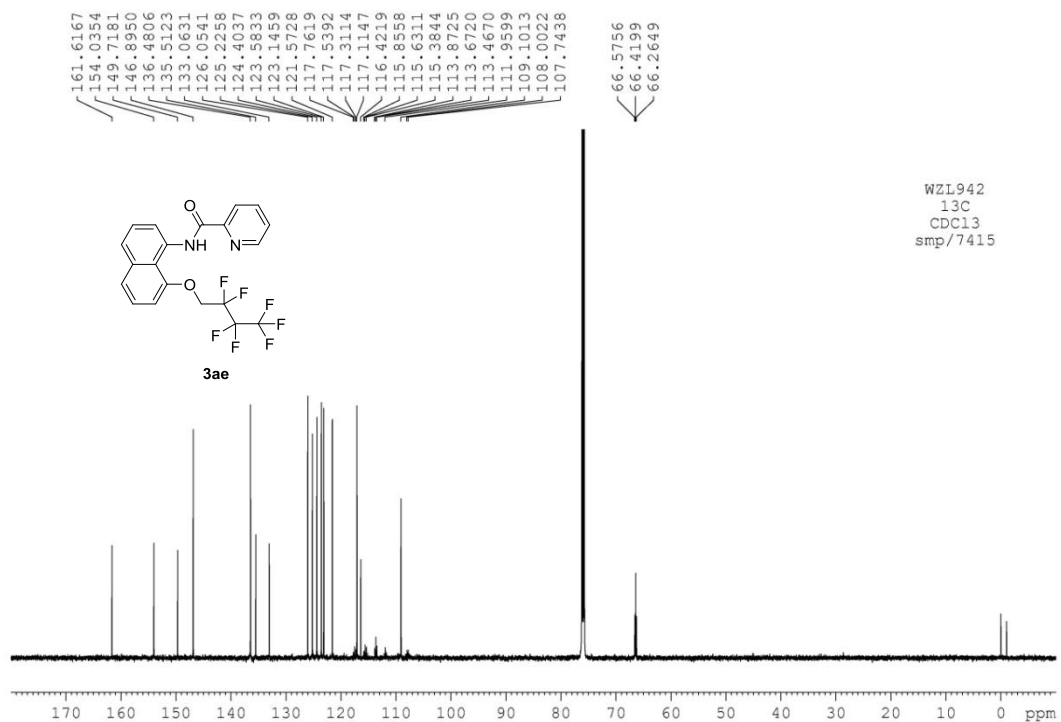
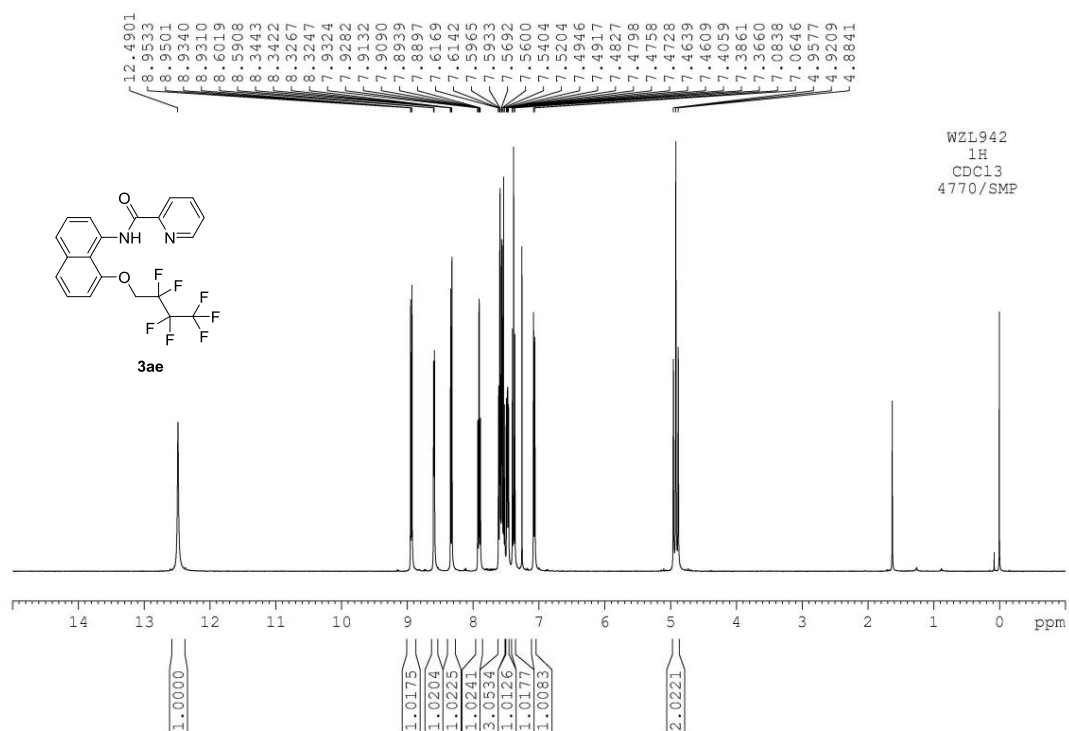


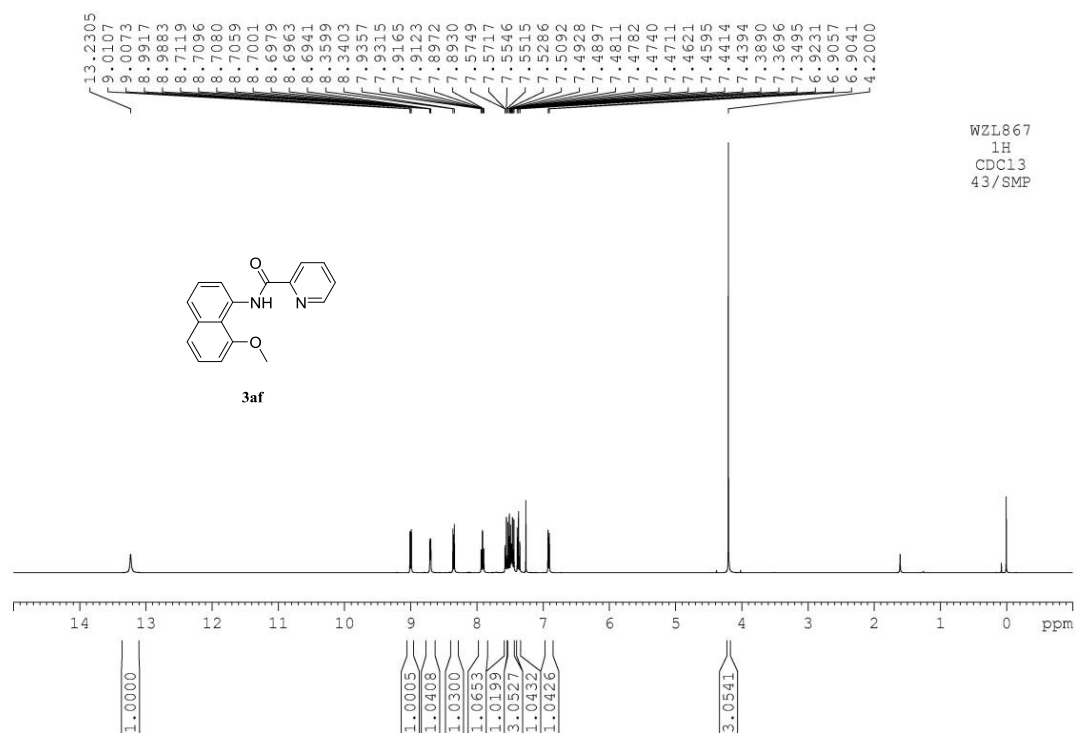




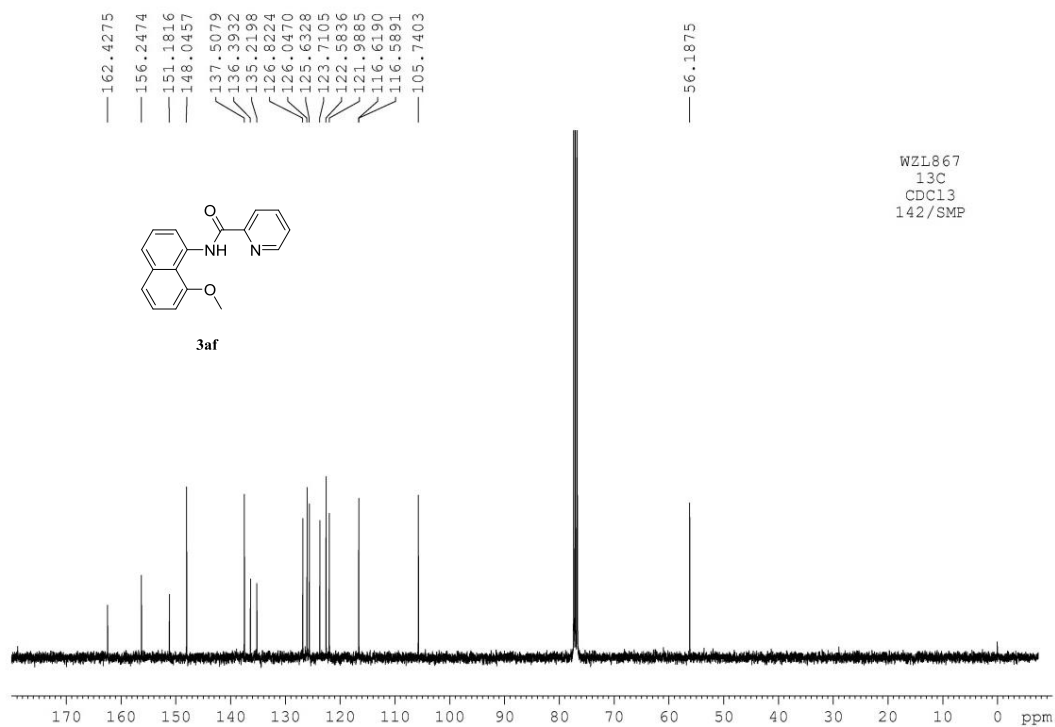




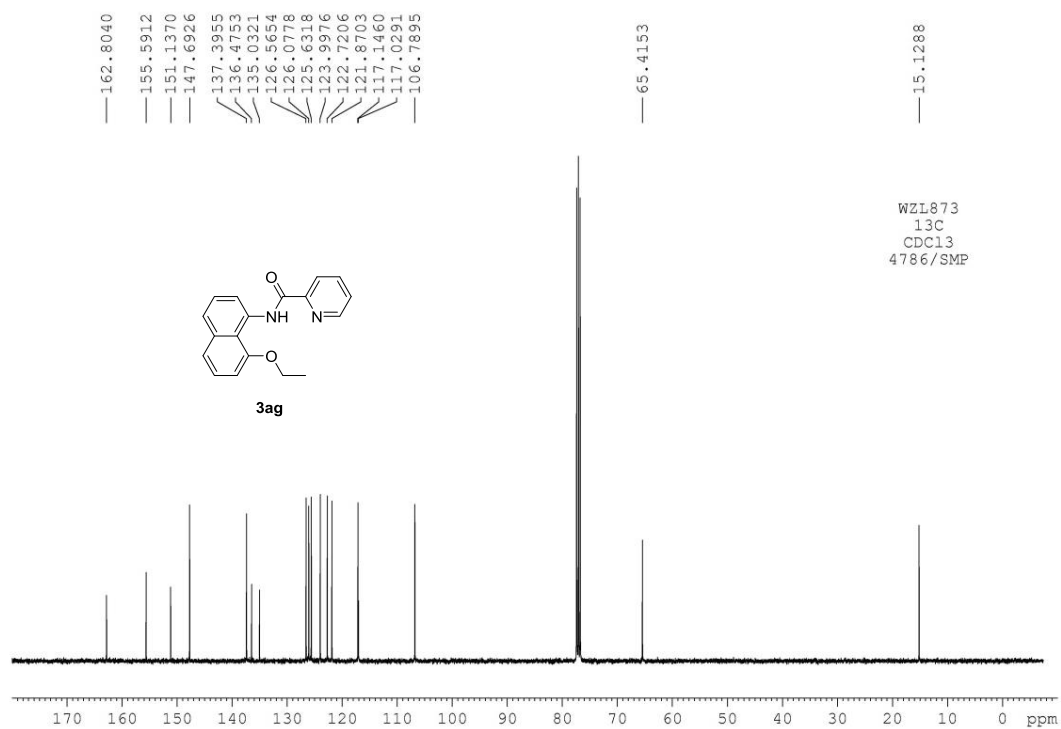
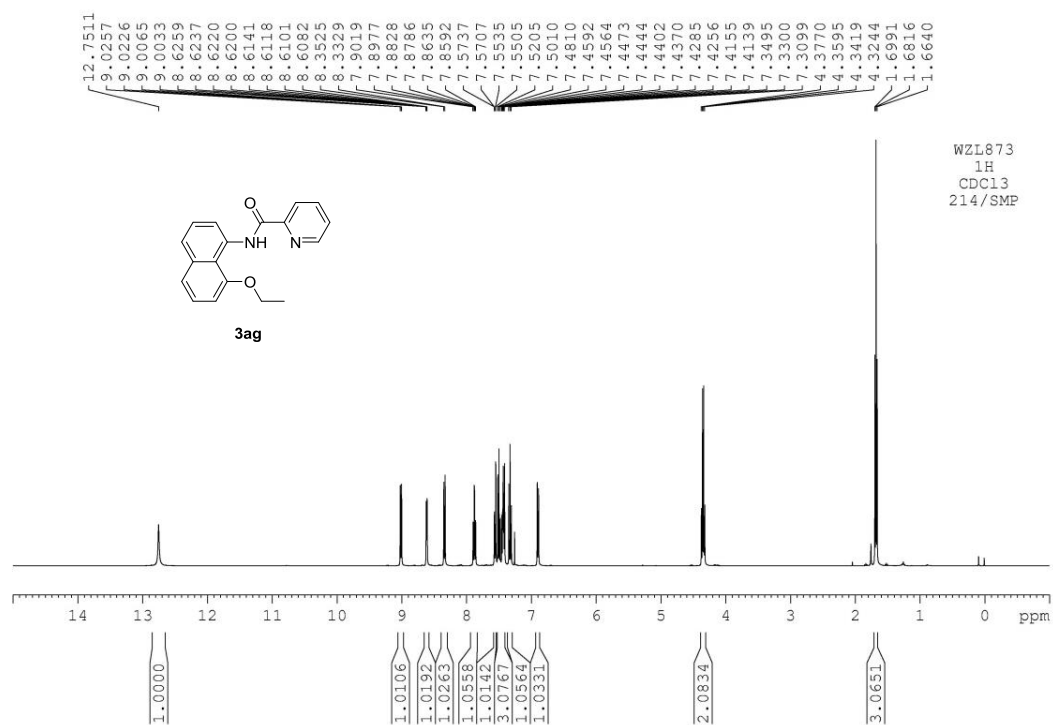


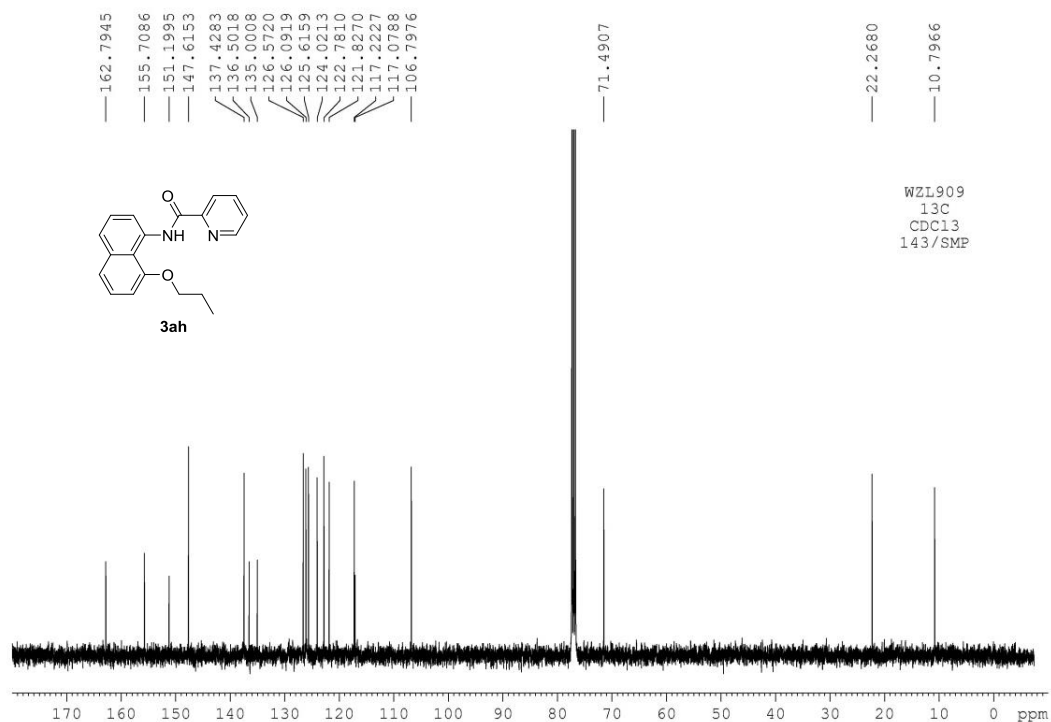
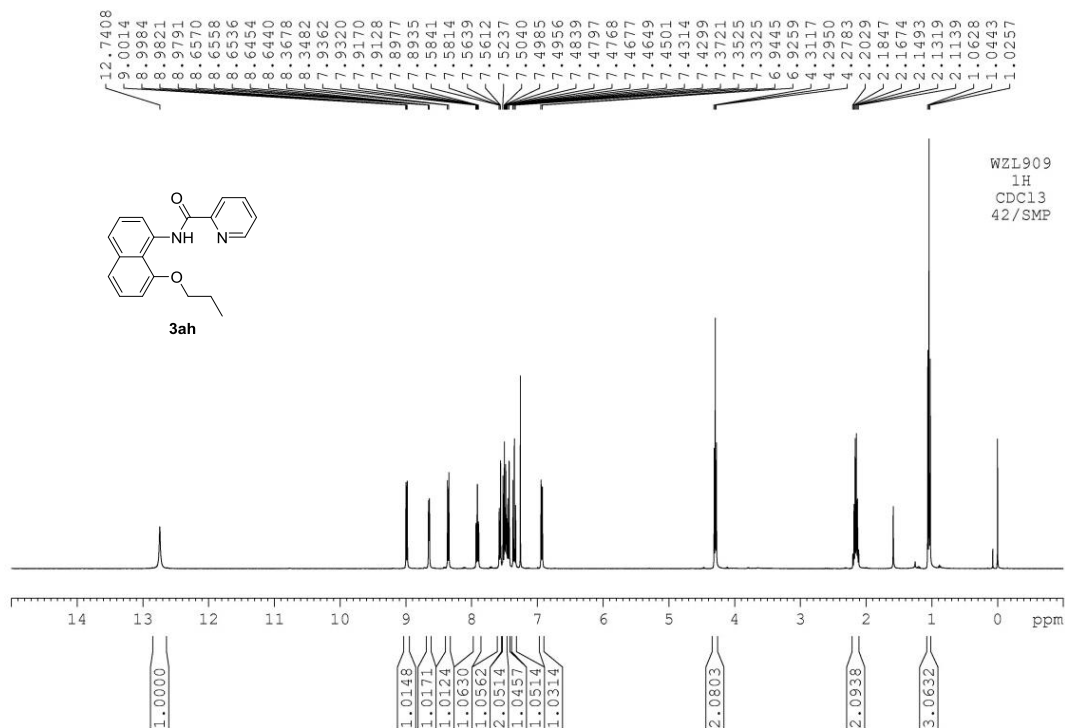


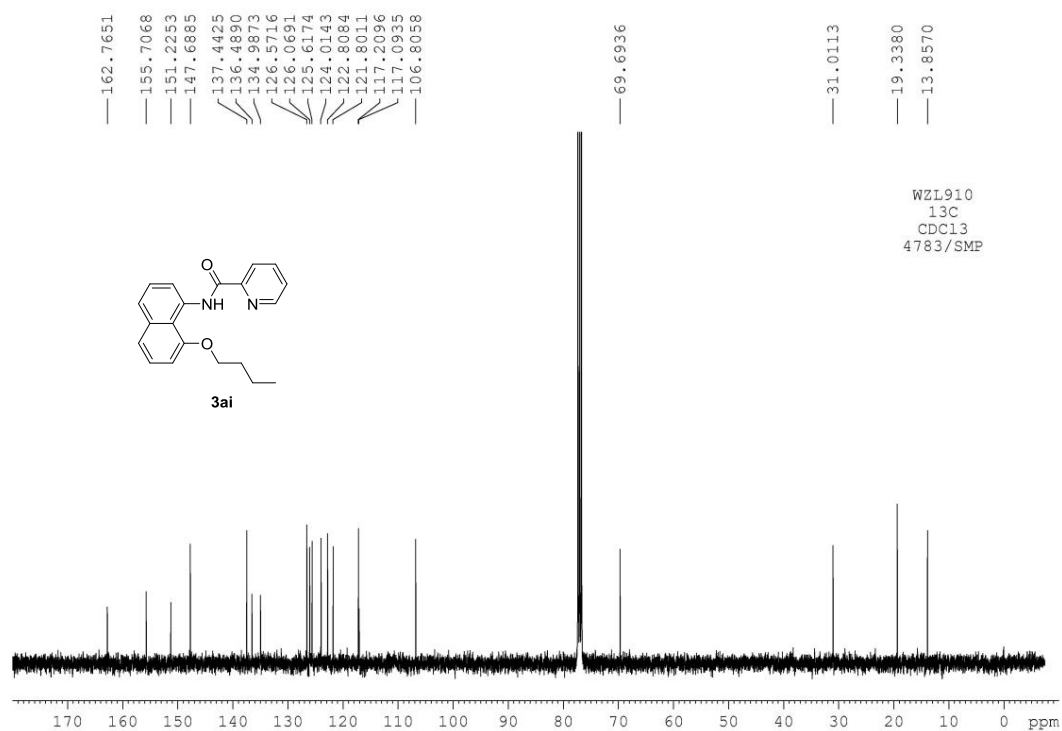
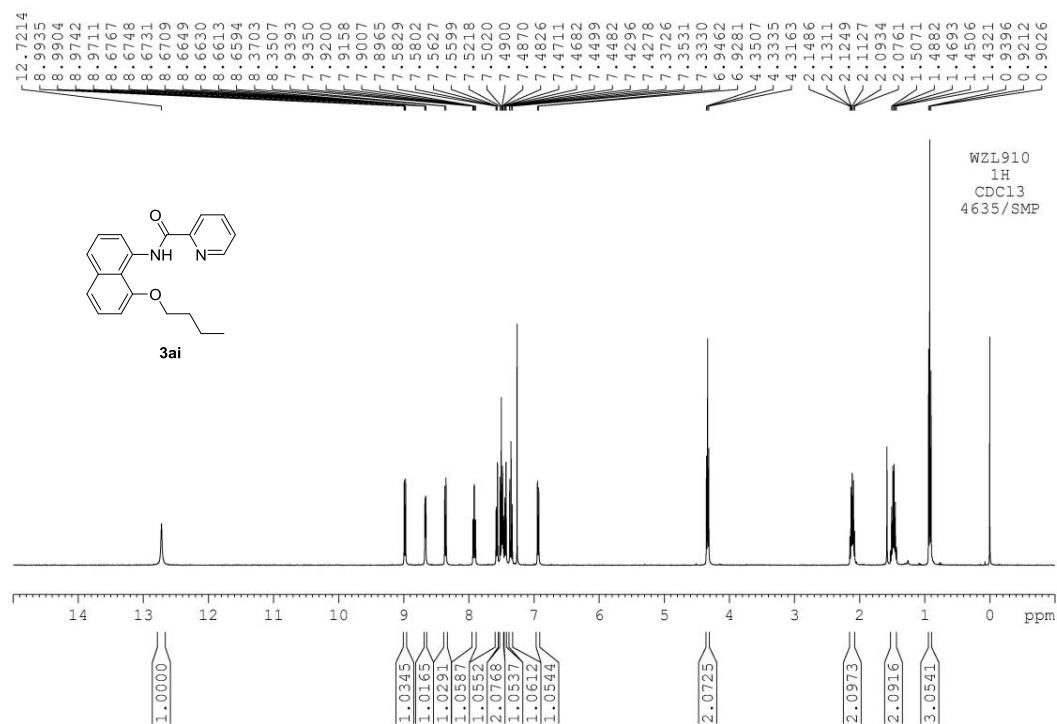
WZL867
1H
CDCl₃
43/SMP

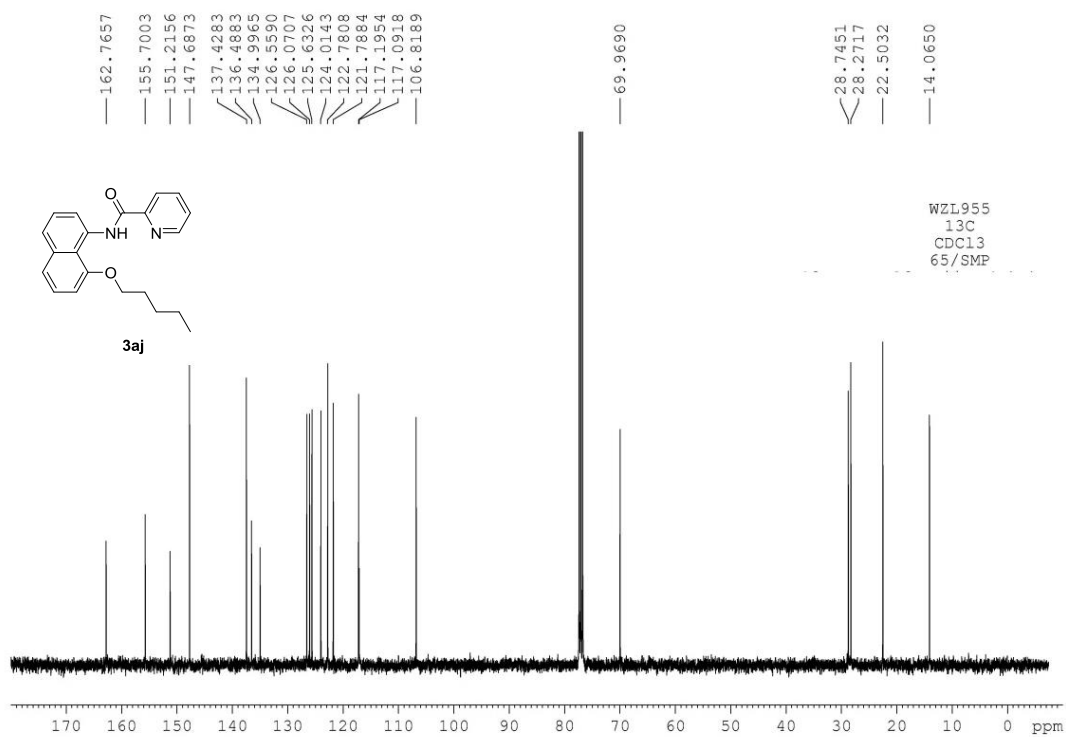
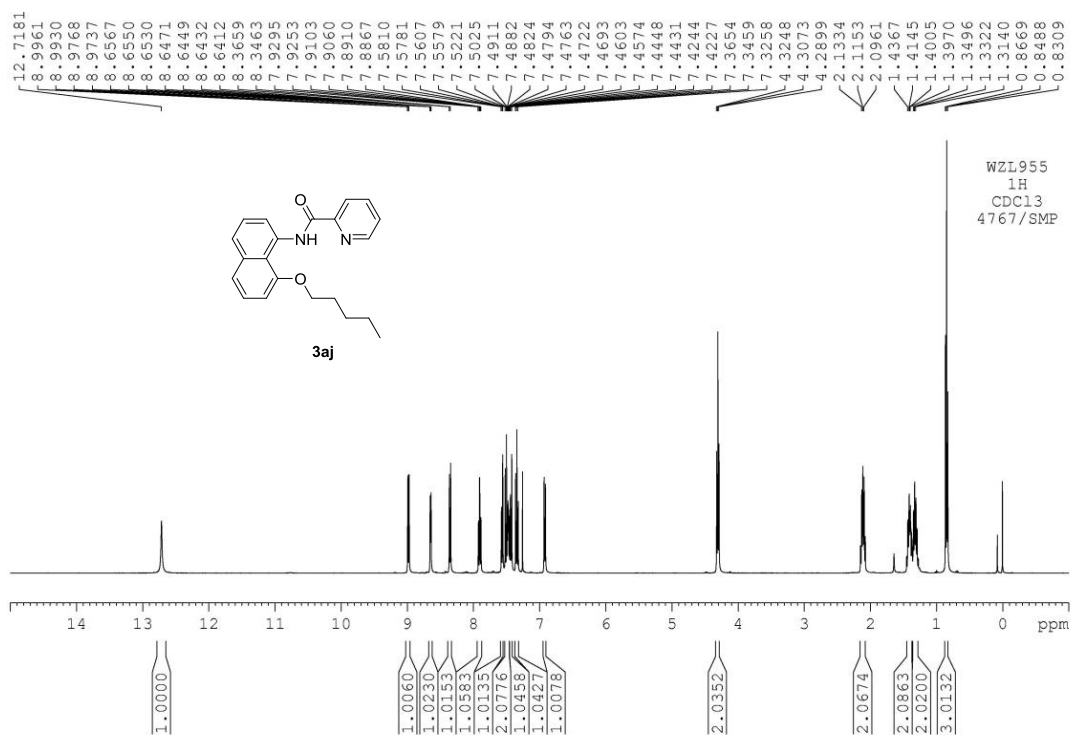


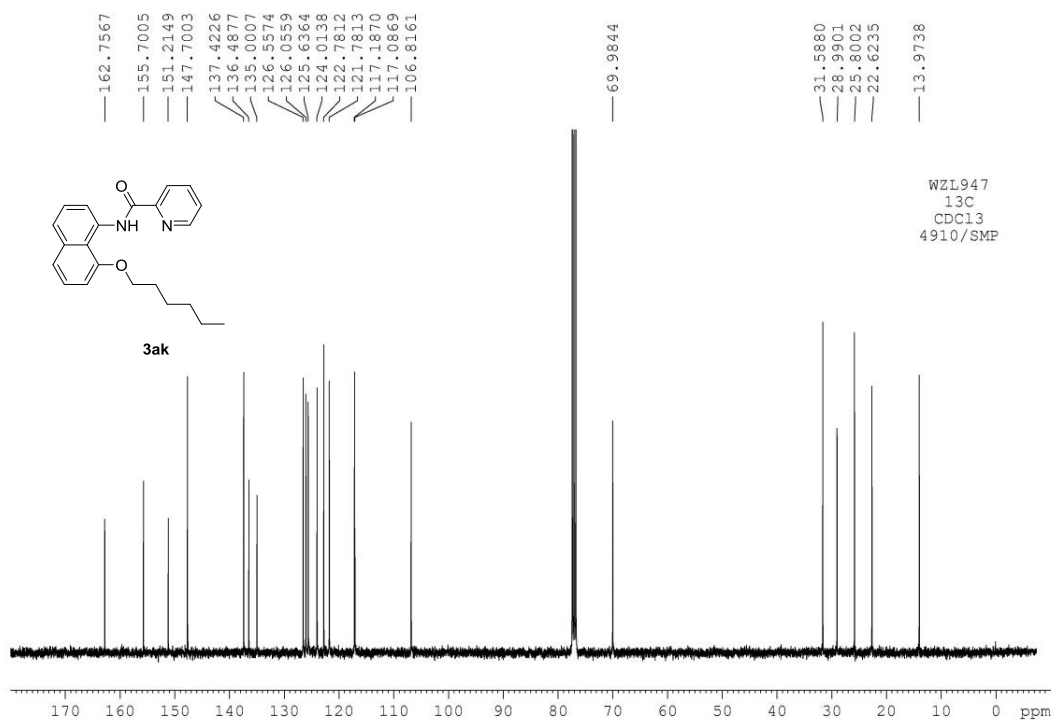
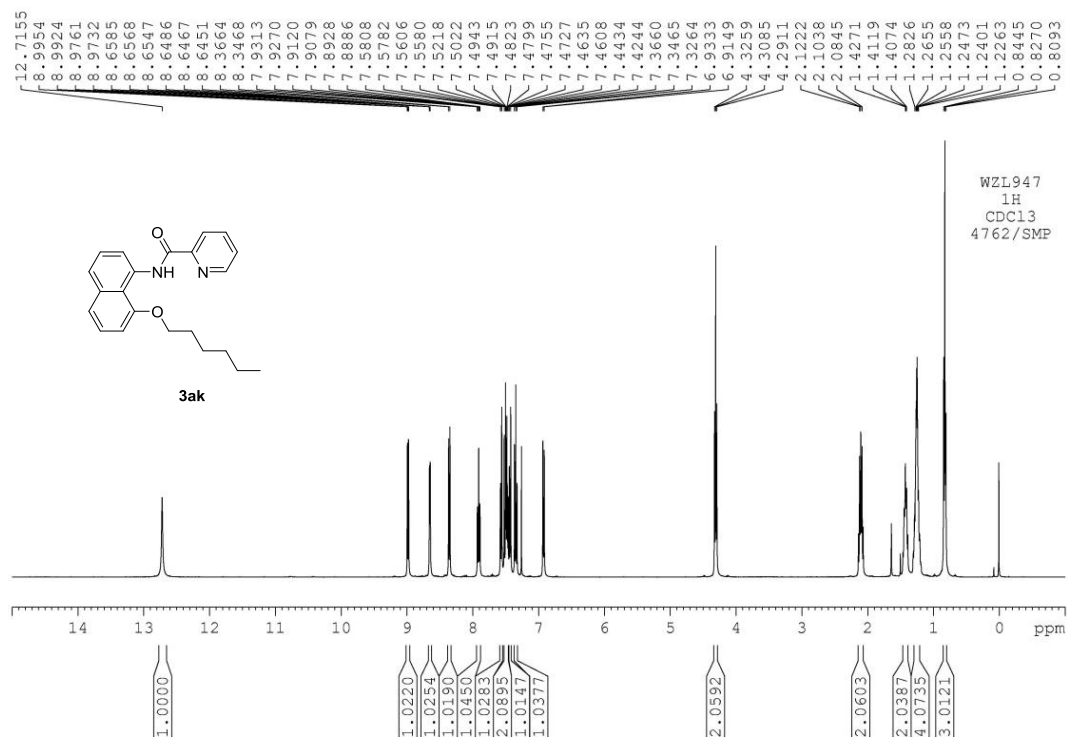
WZL867
13C
CDCl₃
142/SMP

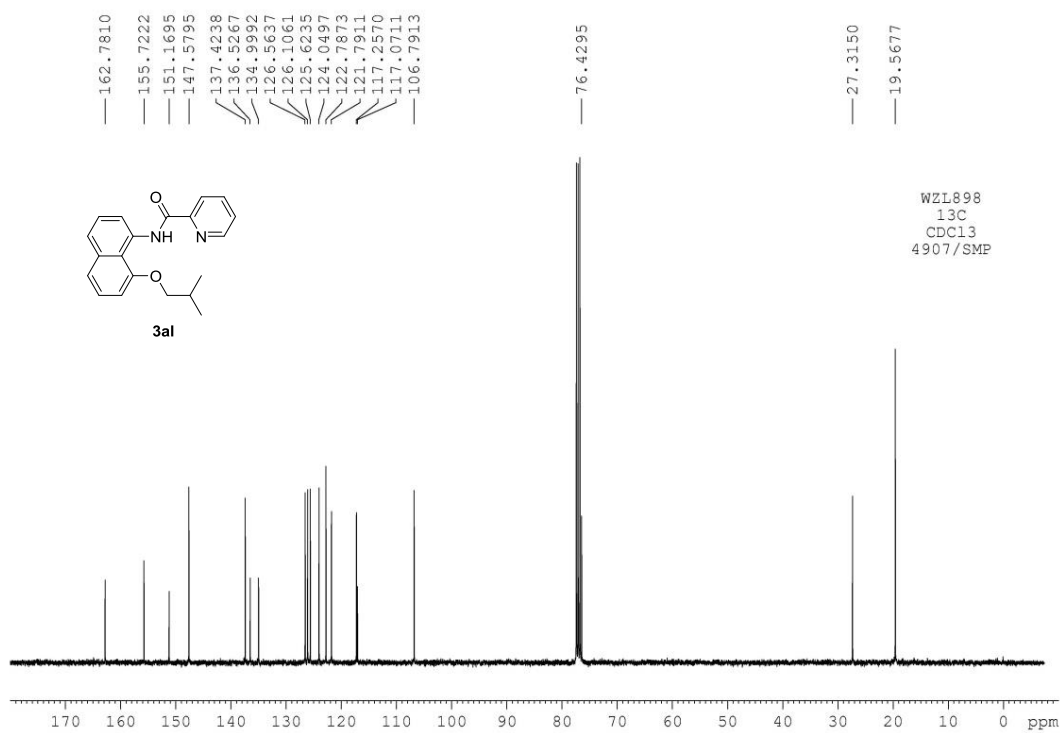
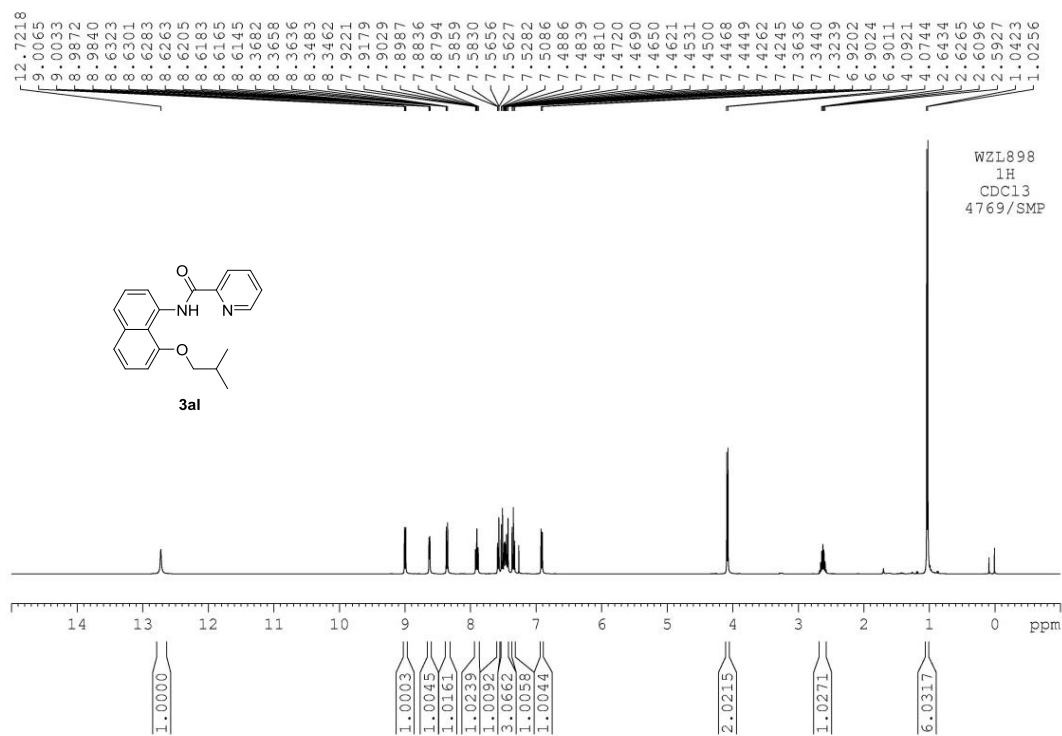


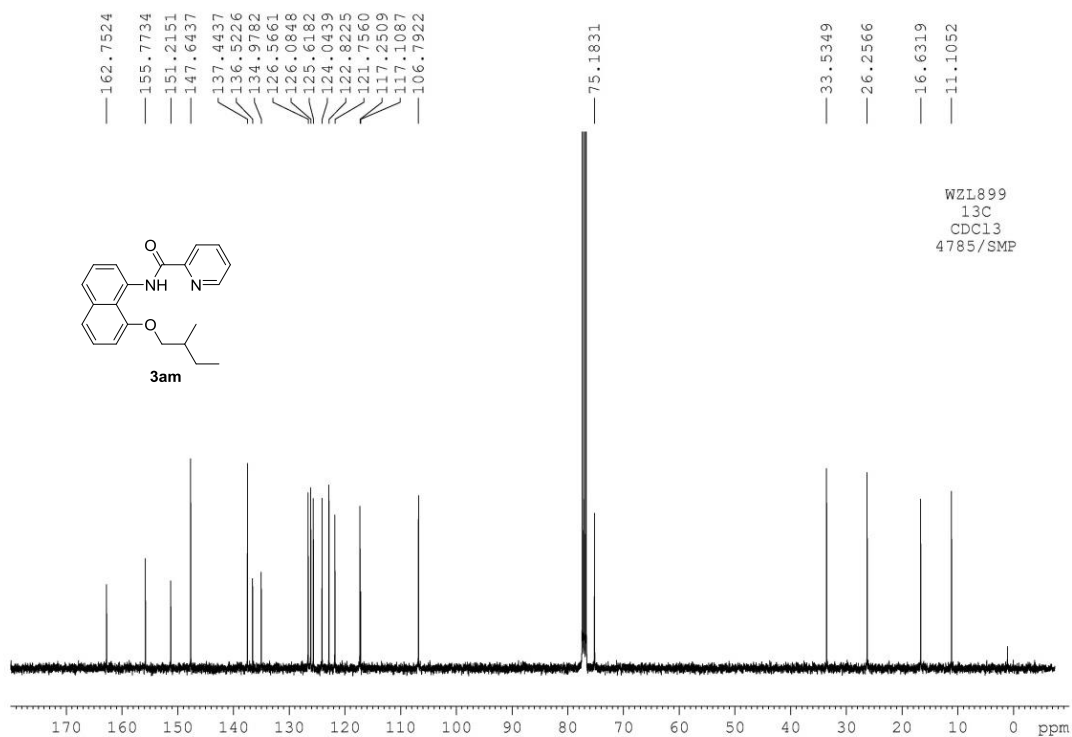
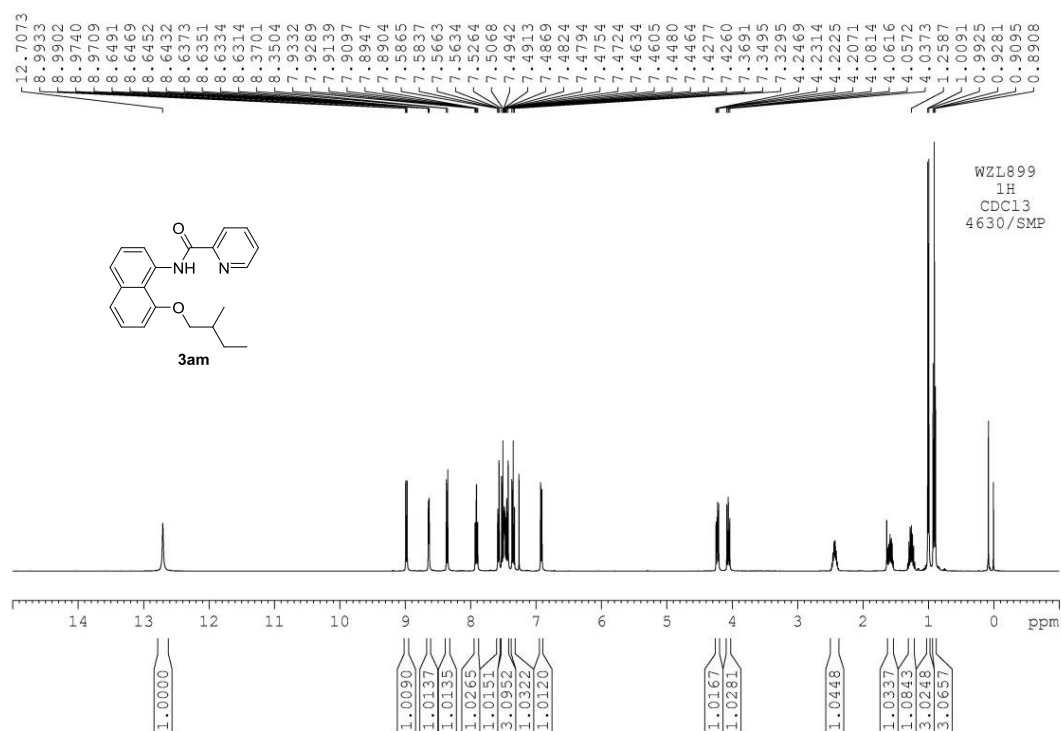


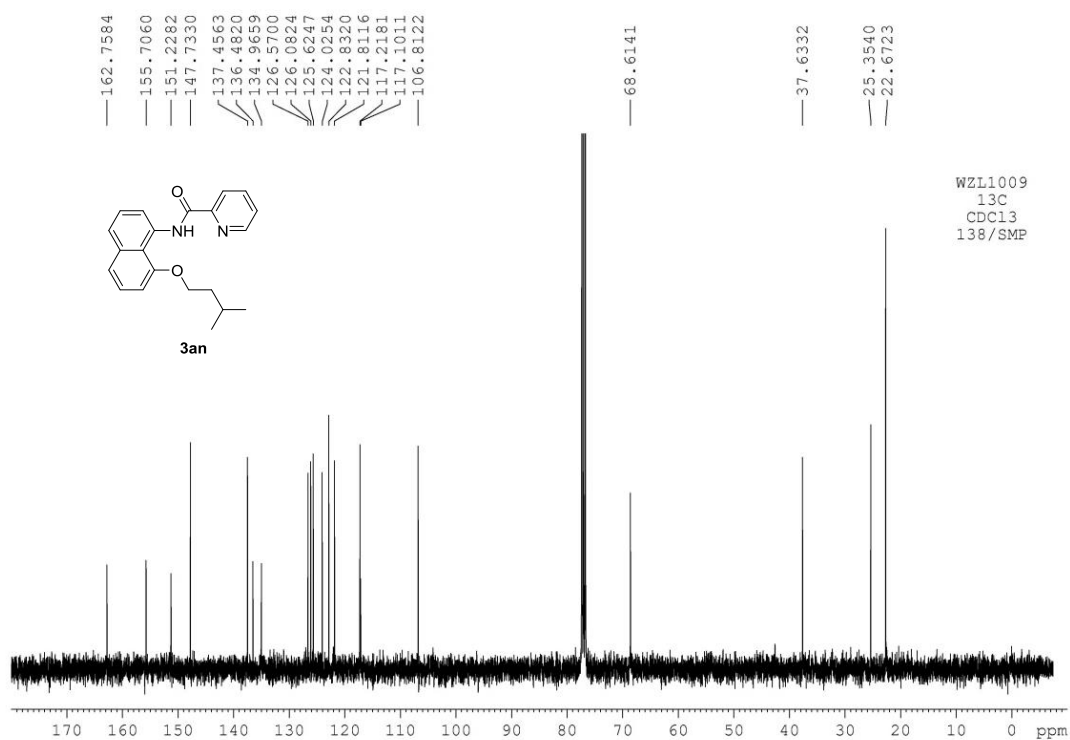
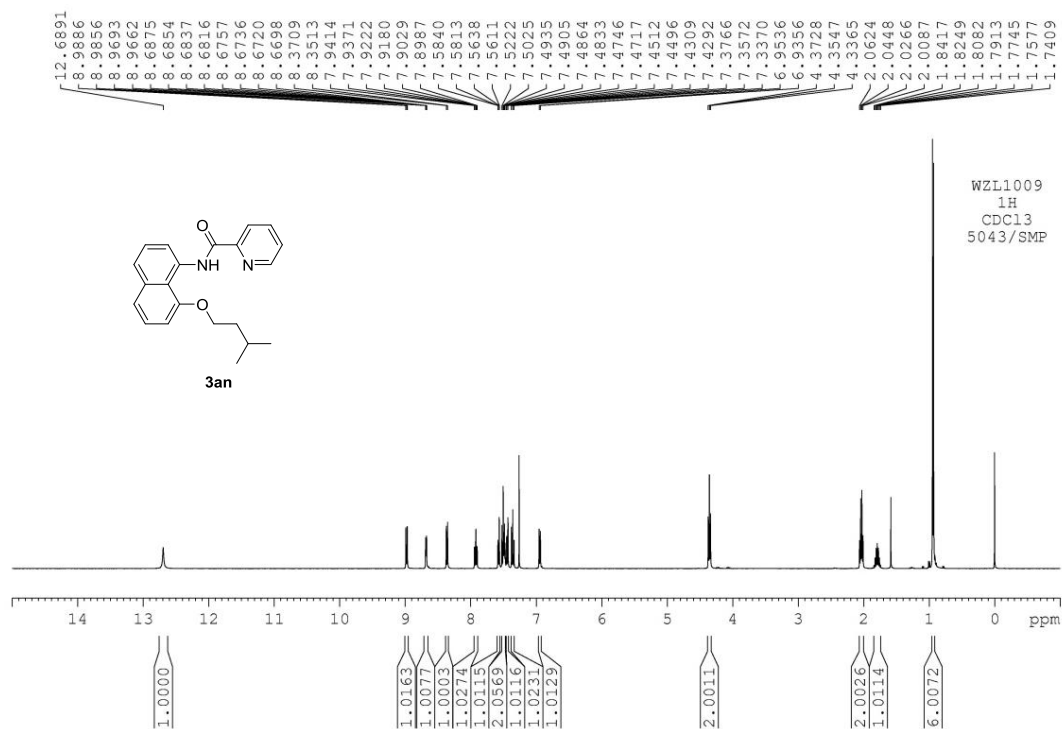


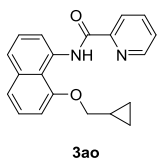
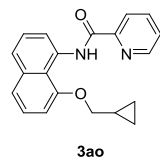


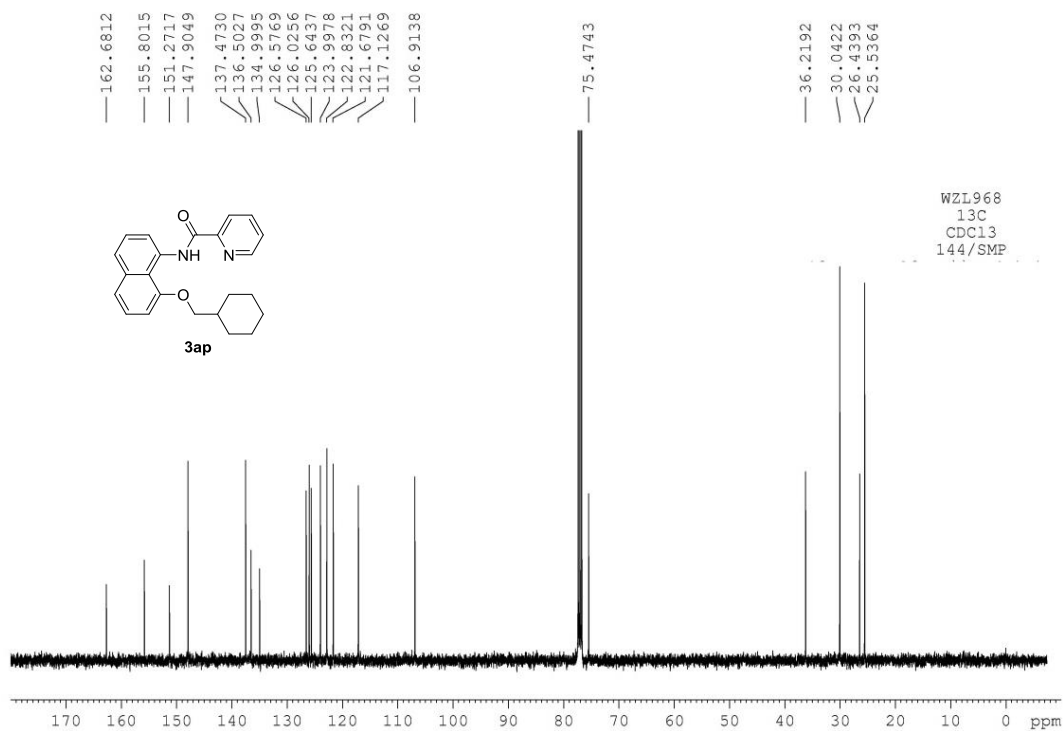
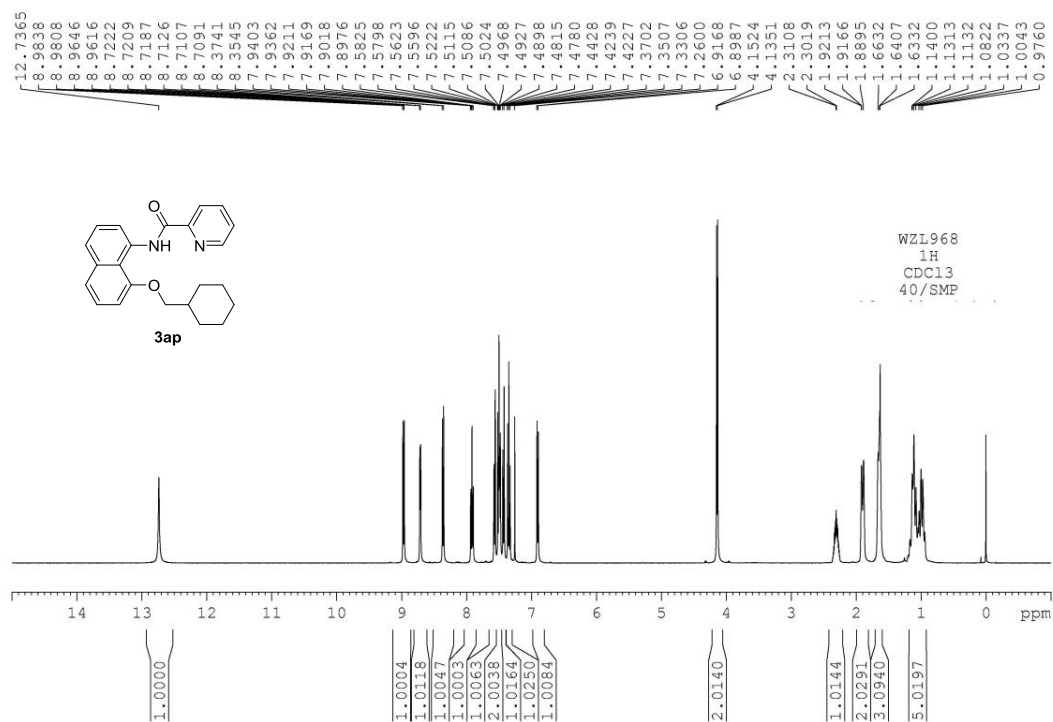


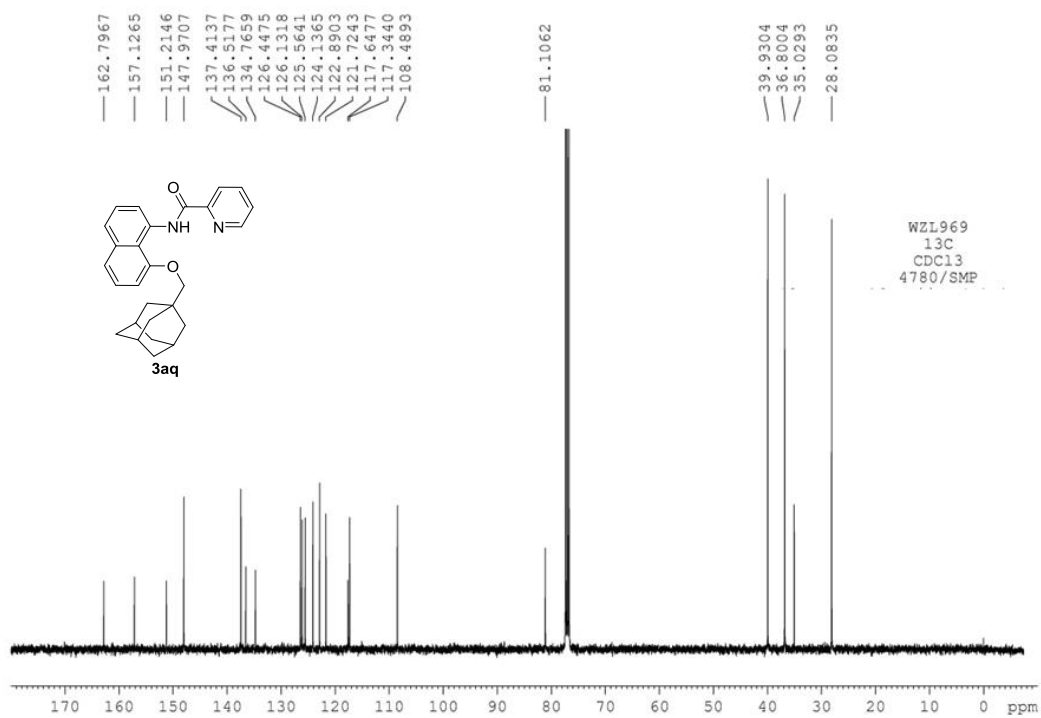
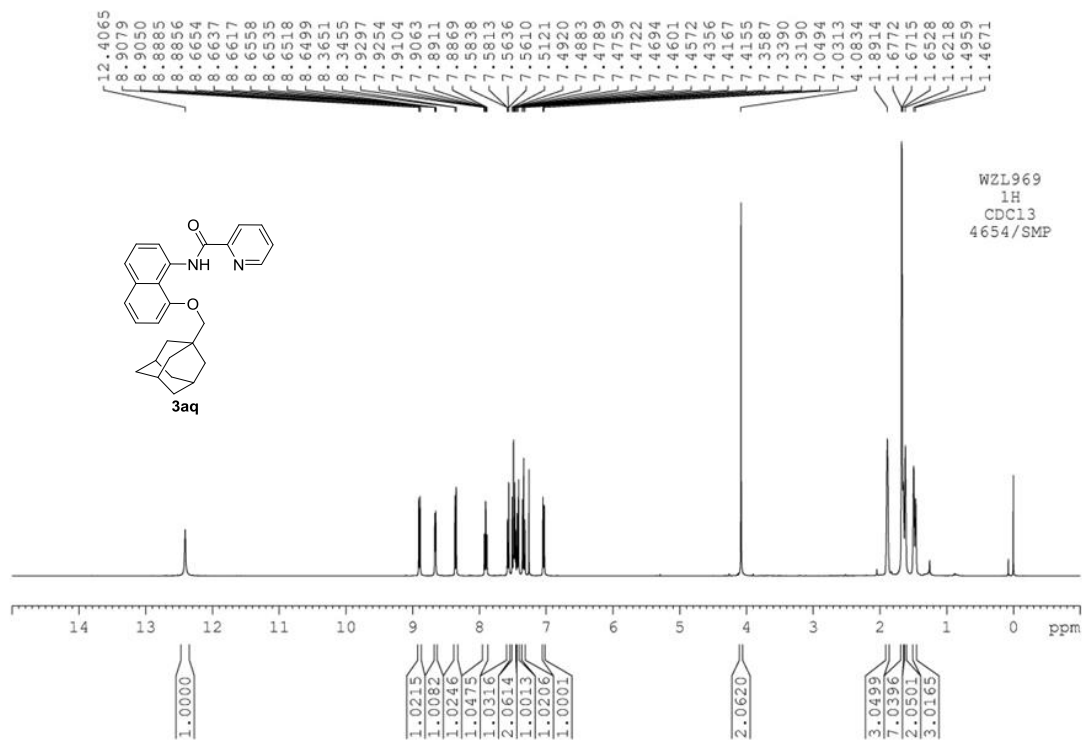


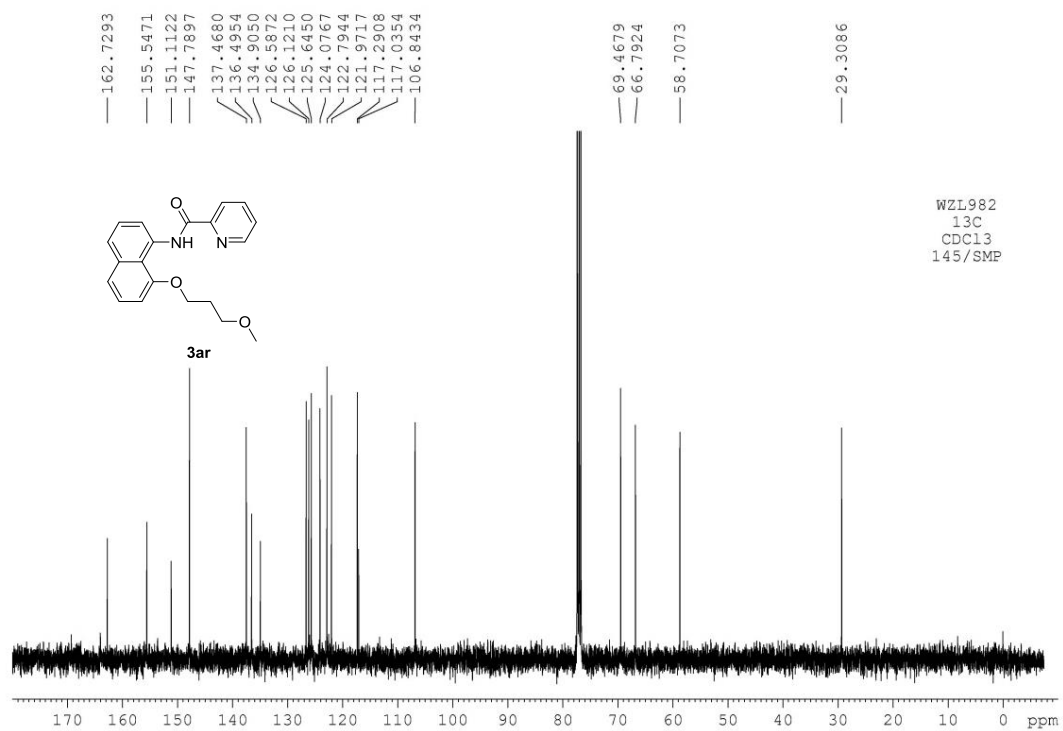
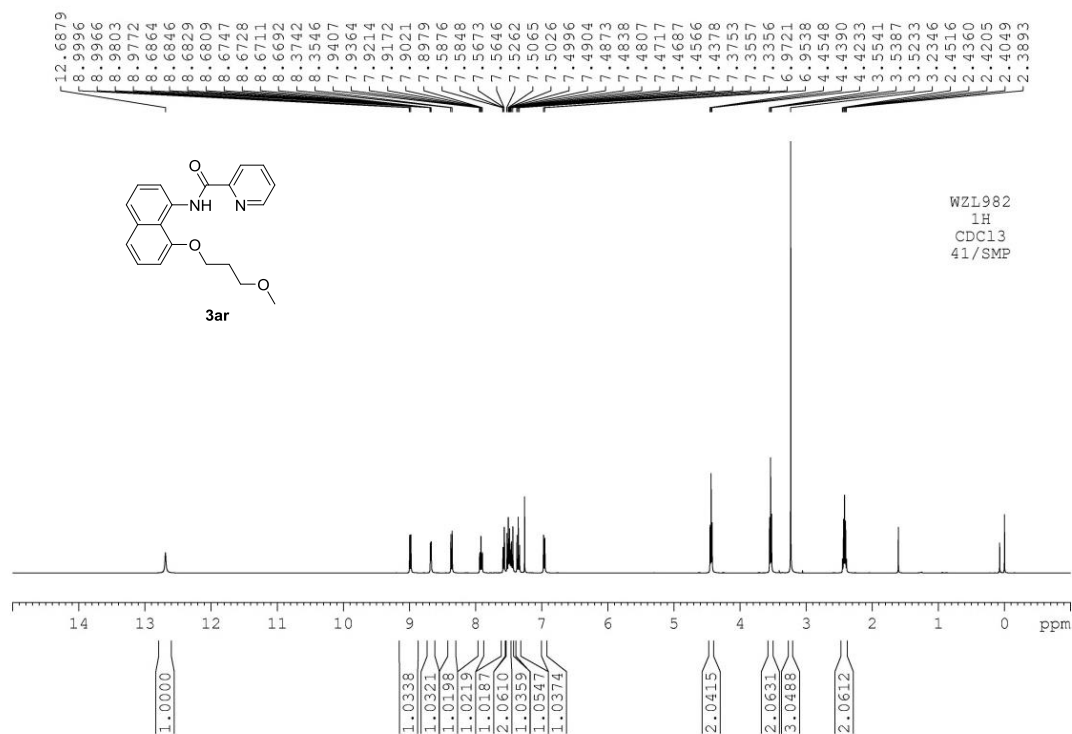


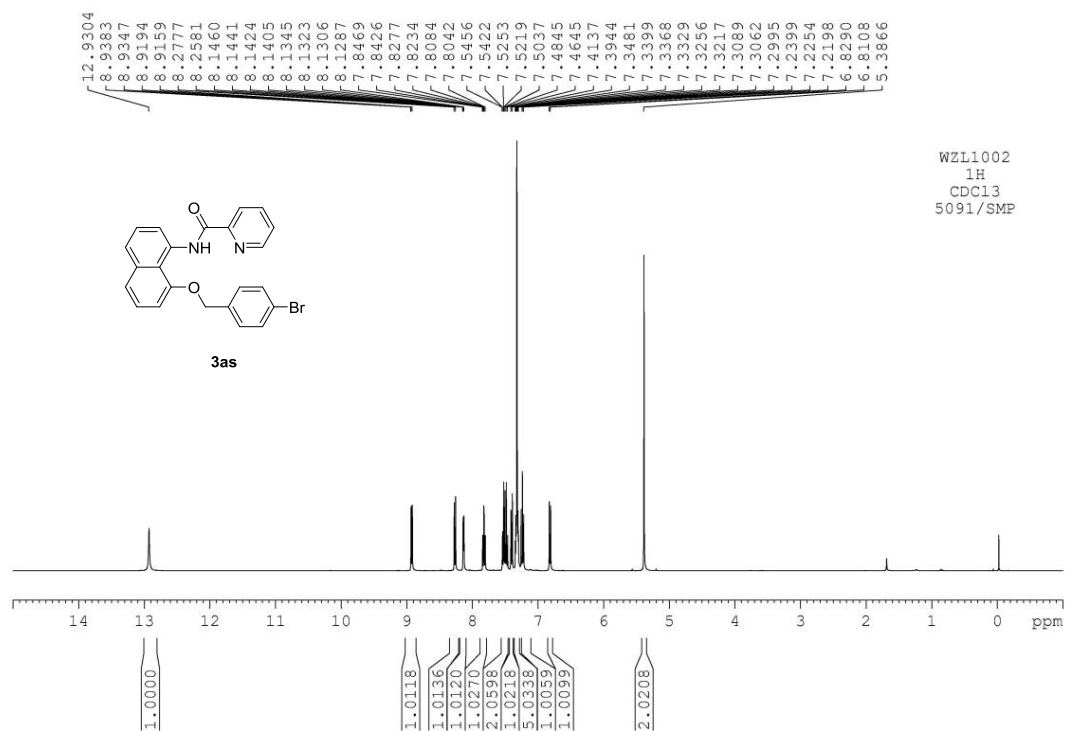




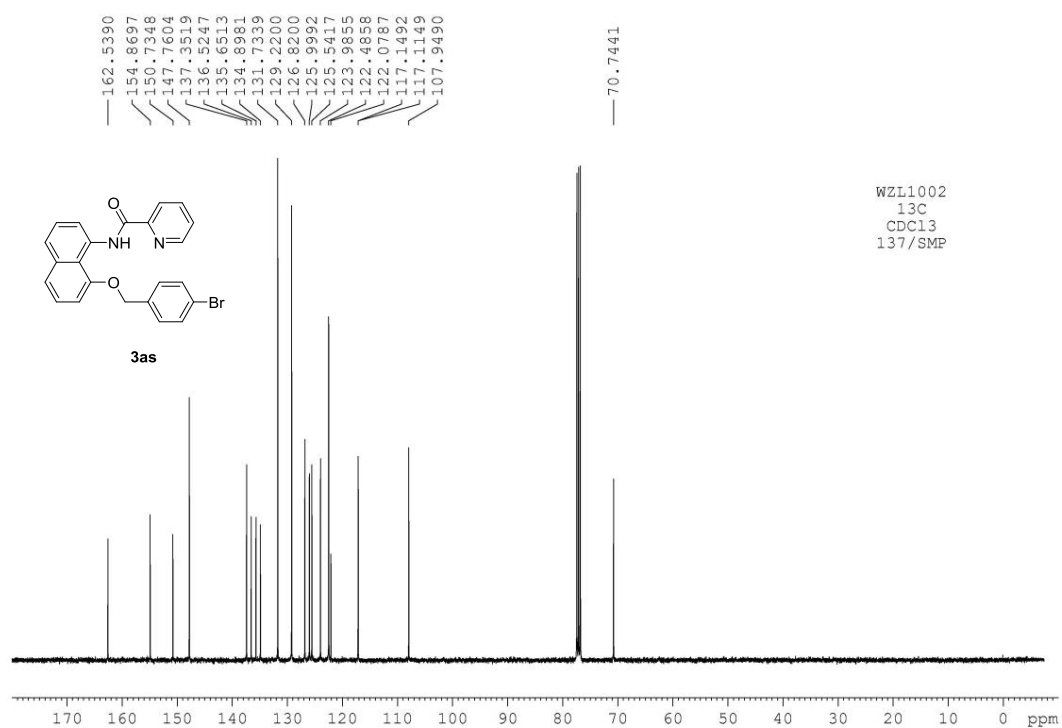








WZL1002
1H
CDCl₃
5091/SMP



WZL1002
13C
CDCl₃
137/SMP

