Copper(II)-Catalyzed Methoxylation of Unactivated (Hetero)aryl C-H Bonds Using a Removable Bidentate Auxiliary

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Table of Contents:

1. General information S2

2. Experimental Section S2

2.1 Preparation of 2-(Pyridin-2-yl)isopropyl (PIP) Amine S2

2.2 General Procedure for the Preparation of Starting Materials S3

2.3 Optimization of Reaction Conditions S16

2.4 Effect of the Directing Groups S16

2.5 General Procedure for the Methoxylation S17

2.6 Mechanistic Investigation S32

2.7 Removal of Directing Group S34

3. References S36

4. Spectra S37

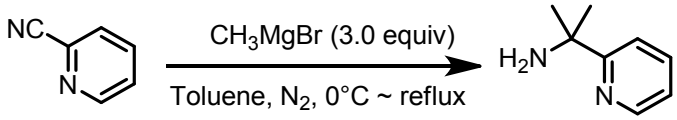
5. X-Ray Data of **2p**, **2s** and **5d** S105

1. General Information:

Methanol was dried by Sodium, distilled under reduced pressure and stored under nitrogen. KOCN and $Cu_2(OH)_2CO_3$ was obtained from Aladdin® and $Cu(OAc)_2$ from Energy®. The other materials and solvents were purchased from Adamas® and other commercial suppliers and used without additional purification. NMR spectra were recorded on a Bruke Avance operating for ^1H NMR at 400 MHz, ^{13}C NMR at 100 MHz, and ^{19}F NMR at 376 MHz, using TMS as internal standard. The peaks were internally referenced to TMS (0.00 ppm) or residual undeuterated solvent signal (77.16 ppm for ^{13}C NMR). The following abbreviations (or combinations thereof) were used to explain multiplicities: s = singlet, d = doublet, t = triplet, m = multiplet, brs = broad singlet. Mass spectroscopy data of the products were collected on an HRMS-TOF instrumentor a low-resolution MS instrument using EI ionization.

2. Experimental Section

2.1 Preparation of 2-(Pyridin-2-yl)isopropyl (PIP) Amine

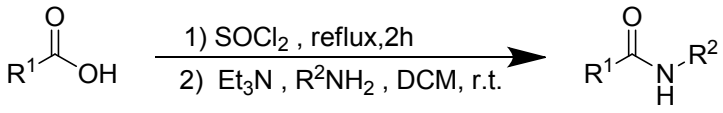


An improvement of the work-up procedure to the literature[1] was used: To a solution of 2-cyanopyridine (33.0 g, 0.32 mol) in 500 ml of toluene was added CH_3MgBr (3.2 M in 2-methyl tetrahydrofuran, 300 ml, 0.96 mol) dropwise at 0 °C in a nitrogen atmosphere by vigorous magnetometric stirring. Upon completion of addition, the mixture was refluxed overnight. The reaction was quenched by adding saturated aqueous NH_4Cl dropwise at 0 °C until the dark mixture changed to yellow. The suspension was filtrated through a pad of celite® and the filtration was acidified by aqueous HCl (6 M, 10 ml). The resulting water phase combined with the filter residue was basified by saturated aqueous NaOH until the yellow colored mixture turned dark brown with slurry sticky to the bottom. The mixture was washed with dichloromethane (500 ml×4) carefully and the supernatant was combined and

concentrated using a rotary evaporator. The crude product was further purified by distillation under reduced pressure. The target product was obtained as a light yellow liquid (>98% purity. 24 g, 55%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (d, J = 4.2 Hz, 1 H), 7.63 (td, J = 7.8, 1.8 Hz, 1 H), 7.45 (d, J = 8.0 Hz, 1 H), 7.12 (ddd, J = 7.4, 4.8, 0.8 Hz, 1 H), 1.87 (s, 2 H), 1.50 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.32, 148.78, 136.55, 121.41, 118.53, 54.14, 31.35.

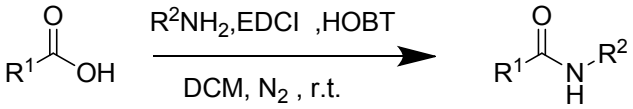
2.2 General Procedure for the Preparation of Starting Materials

General Procedure for the Preparation of Starting Materials (Method A):



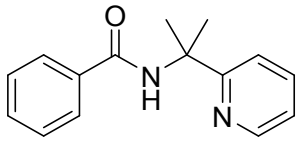
A solution of an acid (5 mmol) was refluxed in 5 mL $SOCl_2$ for 2 h and cooled to RT. The excess of $SOCl_2$ was removed under vacuum to give corresponding acid choloride. The acid choloride was then re-dissolved in 5 mL dry CH_2Cl_2 and added dropwiseto a 20 mL dry CH_2Cl_2 solution containing amine (5 mmol) and Et_3N (10 mmol) at 0 ^{o}C. After stirring for 6h at ambient temperature, the resulting mixture was washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography to give the desired product.

General Procedure for the Preparation of Starting Materials (Method B):



A mixture of amine (5 mmol), 6-bromohexanoic acid (5 mmol), EDCI (5.5 mmol) and HOBT (5.5 mmol) in anhydrous DCM (20 mL) was stirred at room temperature overnight. Water was added and the mixture was extracted with diethyl ether. The combined organic layer was washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography to give the desired product.

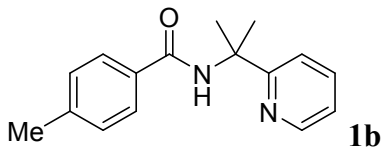
***N*-(2-(pyridin-2-yl)propan-2-yl)benzamide**



1a

The title compound **1a** was prepared according to the **General Procedure (Method A)**. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.86 (s, 1H), 8.56 (ddd, *J* = 4.8, 1.6, 0.8 Hz, 1H), 7.92-7.90 (m, 2H), 7.75 (td, *J* = 8.0, 2.0 Hz, 1H), 7.50-7.43 (m, 4H), 7.23 (ddd, *J* = 7.6, 4.8, 0.8 Hz, 1H), 1.88 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.4, 164.8, 147.7, 137.4, 136.2, 128.6, 127.1, 122.1, 119.7, 56.8, 27.6; HRMS (EI-TOF) calcd for $C_{15}H_{16}N_2O$ (M^+): 240.1263, found: 240.1259.

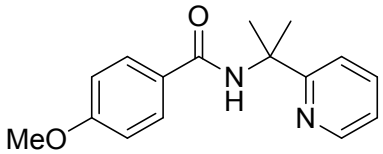
4-Methyl-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide



1b

The title compound **1b** was prepared according to the **General Procedure (Method A)**. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.77 (s, 1H), 8.56 (d, *J* = 4.4 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 2H), 7.75 (td, *J* = 8.0, 1.6 Hz, 1H), 7.46 (d, *J* = 8.0 Hz, 1H), 7.26-7.22 (m, 3H), 2.40 (s, 3H), 1.88 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.4, 165.0, 147.7, 141.4, 137.3, 133.4, 129.2, 127.1, 122.0, 119.7, 56.7, 27.7, 21.6; HRMS (EI-TOF) calcd for $C_{16}H_{18}N_2O$ (M^+): 254.1419, found: 254.1421.

4-Methoxy-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide

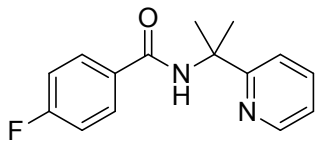


1c

The title compound **1c** was prepared according to the **General Procedure (Method A)**.^{1}H NMR (400 MHz, $CDCl_3$): δ 8.72 (s, 1H), 8.56 (d, *J* = 4.4 Hz, 1H), 7.87 (d, *J* = 8.8 Hz, 2H), 7.75 (td, *J* = 8.0, 1.6 Hz, 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.22 (dd, *J* = 6.8, 5.2 Hz, 1H), 6.95 (d, *J* = 8.8 Hz, 2H), 3.86 (s, 3H), 1.87 (s, 6H); ^{13}C NMR (100 MHz,

$CDCl_3$): δ 166.4, 165.0, 147.7, 141.4, 137.3, 133.4, 127.1, 122.0, 119.7, 56.7, 27.7, 21.6; HRMS (EI-TOF) calcd for $C_{16}H_{18}N_2O_2$ (M^+): 270.1368, found: 270.1367.

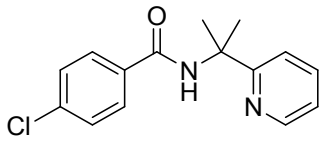
4-Fluoro-N-(2-(pyridin-2-yl)propan-2-yl)benzamide



1d

The title compound **1d** was prepared according to the **General Procedure (Method A)**. ^{1}H NMR (400 MHz, CDCl3) δ 8.88 (br, 1H), 8.56 (d, *J* = 4.8 Hz, 1H), 7.92-7.89 (m, 2H), 7.76 (td, *J* = 8.0, 1.6 Hz, 1H), 7.47 (d, *J* = 8.4 Hz, 1H), 7.24 (dd, *J* = 7.2, 4.8 Hz, 1H), 7.12 (t, *J* = 8.4 Hz, 2H), 1.87 (s, 6H).; 13C NMR (100 MHz, CDCl3) δ 166.0, 165.1(d, *J* = 54.6 Hz) , 163.5, 147.7, 137.5, 132.4 (d, *J* = 3.0 Hz), 129.4 (d, *J* = 8.7 Hz), 122.2, 119.7, 115.5 (d, *J* = 21.6 Hz), 115.4, 56.8, 27.6; HRMS (EI-TOF) calcd for $C_{15}H_{15}FN_2O$ (M+): 258.1168, found: 258.1172.

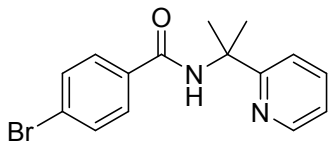
4-Chloro-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide 1e



1e

The title compound **1e** was prepared according to the **General Procedure (Method A)**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.92 (s, 1H), 8.53 (d, *J* = 4.4 Hz, 1H), 7.82 (d, *J* = 8.4 Hz, 2H), 7.73 (m , 1H), 7.43 (d, *J* = 8.4 Hz, 1H), 7.41-7.36 (m, 2H), 7.20 (m, 1H), 1.85 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.1, 164.5, 147.5, 137.3, 137.2, 134.5, 128.6, 128.5, 122.0, 119.5, 56.7, 27.4; HRMS (EI-TOF) calcd for $C_{15}H_{15}ClN_2O$ (M^+): 274.0873, found: 274.0875.

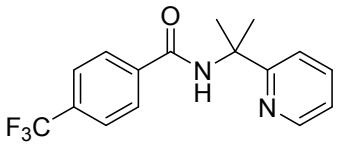
4-Bromo-N-(2-(pyridin-2-yl)propan-2-yl)benzamide



1f

The title compound **1f** was prepared according to the **General Procedure (Method A)**. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.94 (s, 1H), 8.56-8.55 (m, 1H), 7.78-7.74 (m, 3H), 7.60-7.57 (m, 2H), 7.46 (d, *J* = 8.0 Hz, 1H), 7.25-7.22 (m, 1H), 1.87 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.4, 164.7, 147.7, 137.5, 135.1, 131.8, 128.8, 125.8, 122.2, 119.7, 56.8, 27.6; HRMS (EI-TOF) calcd for $C_{15}H_{15}BrN_2O$ (M^+): 318.0368, found: 318.0369.

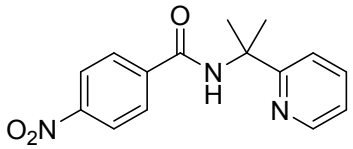
***N*-(2-(pyridin-2-yl)propan-2-yl)-4-(trifluoromethyl)benzamide**



1g

The title compound **1g** was prepared according to the **General Procedure (Method B)**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.09 (s, 1H), 8.56 (ddd, *J* = 4.4, 2.0, 0.8 Hz, 1H), 8.01 (d, *J* = 8.0 Hz, 2H), 7.78 (td, *J* = 8.0, 1.6 Hz, 1H), 7.72 (d, *J* = 8.0 Hz, 2H), 7.47 (d, *J* = 8.4 Hz, 1H), 7.27-7.23 (m, 1H), 1.89 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.0, 164.5, 147.6, 139.5, 137.5, 132.9 (q, $J_{C\text{-}F}$ = 32.4 Hz), 127.6, 125.6 (q, $J_{C\text{-}F}$ = 3.7 Hz) , 124.0 (q, $J_{C\text{-}F}$ = 270.8 Hz), 122.2, 119.7, 56.9, 27.5; HRMS (EI-TOF) calcd for $C_{16}H_{15}F_3N_2O$ (M^+): 308.1136, found: 308.1134.

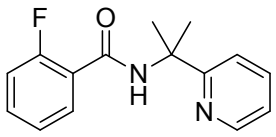
4-Nitro-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide



1h

The title compound **1h** was prepared according to the **General Procedure (Method B)**. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.23 (s, 1H), 8.57 (ddd, *J* = 4.8, 1.2, 0.8 Hz, 1H), 8.32 (d, *J* = 8.8 Hz, 2H), 8.07 (d, *J* = 8.8 Hz, 2H), 7.80 (td, *J* = 8.0, 2.0 Hz, 1H), 7.48 (d, *J* = 8.0 Hz, 1H), 7.29-7.25 (m, 2H), 1.89 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.3, 164.2, 149.6, 147.6, 141.9, 137.7, 128.3, 123.9, 122.4, 119.7, 57.0, 27.5 ; HRMS (EI-TOF) calcd for $C_{15}H_{15}N_3O_3$ (M^+): 285.1113, found: 285.1115.

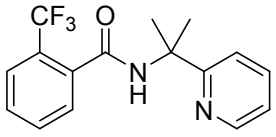
2-Fluoro-N-(2-(pyridin-2-yl)propan-2-yl)benzamide



1i

The title compound **1i** was prepared according to the **General Procedure (Method A)**. ^{1}H NMR (400 MHz, CDCl3) δ 8.85 (d, *J* = 11.0 Hz, 1H), 8.56 (d, *J* = 4.2 Hz, 1H), 8.06 (td, *J* = 7.9, 1.8 Hz, 1H), 7.73 (td, *J* = 7.8, 1.7 Hz, 1H), 7.49 – 7.40 (m, 2H), 7.25 – 7.17 (m, 2H), 7.14 (dd, *J* = 11.8, 8.3 Hz, 1H), 1.88 (s, 6H); 13C NMR (100 MHz, CDCl3) δ 164.6 , 162.4, 160.8 (d, $J_{C\text{-}F}$ = 246.5 Hz), 148.0, 137.1,132.9 (d, $J_{C\text{-}F}$ = 3.0 Hz), 131.9, 124.7 (d, $J_{C\text{-}F}$ = 3.3 Hz), 122.9, 122.0 , 119.6, 116.1 (d, $J_{C\text{-}F}$ = 24.6 Hz), 57.66, 27.80; HRMS (EI-TOF) calcd for $C_{15}H_{15}FN_2O$ (M^+): 258.1168, found: 258.1172.

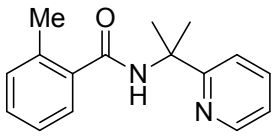
***N*-(2-(pyridin-2-yl)propan-2-yl)-2-(trifluoromethyl)benzamide**



1j

The title compound **1j** was prepared according to the **General Procedure (Method B)**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44-8.42 (m, 1H), 8.30 (s, 1H), 7.75-7.68 (m, 2H), 7.60-7.58 (m, 2H), 7.51 (t, *J* = 6.8 Hz, 1H), 7.45 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.20-7.16(m, 1H), 1.88 (d, *J* = 2.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 164.2, 147.6, 137.5 (q, $J_{C\text{-}F}$ = 2.0 Hz), 137.3, 132.0, 129.4, 128.7, 127.7 (q, $J_{C\text{-}F}$ = 31.7 Hz), 126.4 (q, $J_{C\text{-}F}$ = 5.0 Hz), 123.9 (q, $J_{C\text{-}F}$ = 272.1 Hz), 122.1, 119.6, 57.4, 27.2; HRMS (EI-TOF) calcd for $C_{16}H_{15}F_3N_2O$ (M^+): 308.1136, found: 308.1133.

2-Methyl-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide

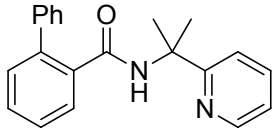


1k

The title compound **1k** was prepared according to the **General Procedure (Method A)**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48-8.47 (m, 1H), 8.11 (s, 1H), 7.73 (td, *J* = 8.0,

1.6 Hz, 1H), 7.49-7.45 (m, 2H), 7.31-7.27 (m, 1H), 7.23-7.17 (m, 3H), 2.48 (s, 3H), 1.89 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 164.6, 147.7, 138.0, 137.2, 135.8, 131.0, 129.5, 127.0, 125.8, 122.0, 119.6, 57.1, 27.7, 20.0; HRMS (EI-TOF) calcd for $C_{16}H_{18}N_2O$ (M^+): 254.1419, found: 254.1415.

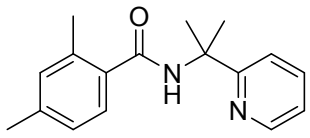
N-(2-(pyridin-2-yl)propan-2-yl)-[1,1'-biphenyl]-2-carboxamide



1l

The title compound **1l** was prepared according to the **General Procedure (Method A)**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, *J* = 4.8 Hz, 1H), 7.73 (d, *J* = 7.2 Hz, 1H), 7.61 (td, *J* = 7.6, 1.7 Hz, 1H), 7.49 – 7.32 (m, 8H), 7.25 (dd, *J* = 12.4, 7.7 Hz, 2H), 7.09 (dd, *J* = 7.4, 4.9 Hz, 1H), 1.60 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.5, 164.3, 147.6, 140.7, 139.9, 137.3, 136.9, 130.3, 129.8, 129.3, 128.9, 128.4, 127.6, 121.7, 119.3, 57.1, 27.1; HRMS (EI-TOF) calcd for $C_{21}H_{20}N_2O$ (M^+): 316.1576, found: 316.1581.

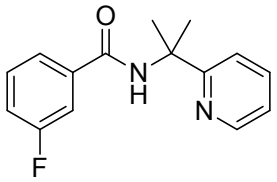
2,4-Dimethyl-N-(2-(pyridin-2-yl)propan-2-yl)benzamide



1m

The title compound **1m** was prepared according to the **General Procedure (Method A)**. 1H NMR (400 MHz, CDCl3) δ 8.47 (dd, J = 4.8, 0.7 Hz, 1H), 8.06 (brs, 1H), 7.72 (td, J = 7.8, 1.8 Hz, 1H), 7.46 (d, J = 8.1 Hz, 1H), 7.39 (d, J = 8.3 Hz, 1H), 7.18 (ddd, J = 7.4, 4.9, 0.8 Hz, 1H), 7.05-6.99 (m, 2H), 2.45 (s, 3H), 2.33 (s, 3H), 1.88 (s, 6H). 13C NMR (101 MHz, CDCl3) δ 169.4, 164.6, 147.6, 139.3, 137.1, 135.9, 135.1, 131.7, 127.1, 126.3, 121.8, 119.5, 57.0, 27.6, 21.2, 19.9; HRMS (EI-TOF) calcd for $C_{17}H_{20}N_2O$ (M+): 268.1576, found: 268.1577.

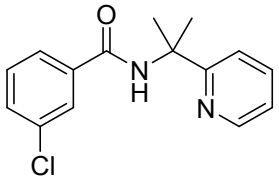
3-Fluoro-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide



1n

The title compound **1n** was prepared according to the **General Procedure (Method A)**. ^{1}H NMR (400 MHz, CDCl3) δ 8.96 (s, 1H), 8.57-8.55(m, 1H), 7.76 (td, *J* = 7.8, 1.8 Hz, 1H), 7.67 (d, *J* = 8.0Hz, 1H), 7.63-7.60(m, 1H), 7.46 (d, *J* = 8.4, 1H), 7.44-7.39 (m, 1H), 7.23 (ddd, *J* = 7.2, 5.6, 0.8 Hz, 1H), 7.20-7.16 (m, 1H), 1.87 (s, 6H); 13C NMR (100 MHz, CDCl3) δ 165.0 (d, J_{C-F} = 2.3 Hz)，164.9 (d, J_{C-F} = 245.4 Hz), 164.6, 147.7, 138.6 (d, J_{C-F} = 6.5 Hz), 137.5, 130.2 (d, J_{C-F} = 7.8 Hz), 122.6 (d, J_{C-F} = 2.9 Hz), 119.7, 118.1 (d, J_{C-F} = 21.3 Hz), 114.5 (d, J_{C-F} = 22.6 Hz), 56.8, 27.5; HRMS (EI-TOF) calcd for $C_{15}H_{15}FN_2O$ (M+): 258.1168, found: 258.1165.

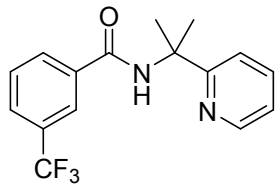
3-Chloro-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide



1o

The title compound **1o** was prepared according to the **General Procedure (Method A)**. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.92 (s, 1H), 8.57 (d, *J* = 4.0 Hz, 1H), 7.89 (br, 1H), 7.76 (t, *J* = 7.2 Hz, 2H), 7.46 (d, *J* = 7.6 Hz, 2H), 7.39 (t, *J* = 8.0 Hz, 1H), 7.26-7.23 (m, 1H) , 1.87 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.0, 164.6, 147.7, 138.0, 137.5, 134.8, 131.2, 129.9, 127.6, 125.2, 122.2, 119.7, 56.9, 27.5; HRMS (EI-TOF) calcd for $C_{15}H_{15}ClN_2O$ (M^+): 274.0873, found: 274.0877.

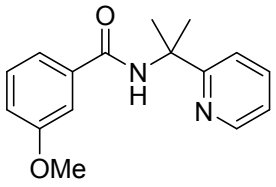
***N*-(2-(pyridin-2-yl)propan-2-yl)-3-(trifluoromethyl)benzamide**



1p

The title compound **1p** was prepared according to the **General Procedure (Method B).** ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.06 (s, 1H), 8.57 (ddd, J = 4.4, 2.0, 0.8 Hz, 1H), 8.19 (s, 1H), 8.07 (d, J = 8.0 Hz, 1H), 7.80-7.74 (m, 2H), 7.59 (t, J = 7.8 Hz, 1H), 7.47 (d, J = 8.0 Hz, 1H), 7.26-7.23 (m, 1H), 1.89 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 164.5, 147.7, 137.5, 137.0, 131.2 (q, J_{C-F} = 32.5 Hz), 130.2, 129.1, 127.8 (q, J_{C-F} = 3.6 Hz), 124.4 (q, J_{C-F} = 3.9 Hz), 124.0 (q, J_{C-F} = 270.9 Hz), 122.2, 119.7, 56.9, 27.5; HRMS (EI-TOF) calcd for $C_{16}H_{15}F_3N_2O$ (M^+): 308.1136, found: 308.1136.

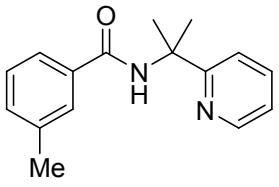
3-Methoxy-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide



1q

The title compound **1q** was prepared according to the **General Procedure (Method B)**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 (s, 1H), 8.56 (dd, J = 4.8, 0.4Hz, 1H), 7.75 (td, J = 7.6, 1.6Hz, 1H), 7.50-7.42 (m, 3H), 7.35 (t, J = 8.0 Hz, 1H), 7.23 (ddd, J = 7.6, 4.8, 0.8 Hz, 1H), 7.04-7.02 (m, 1H), 3.86 (s, 3H), 1.88 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 164.6, 159.8, 147.6, 137.4, 137.4, 129.4, 122.0, 119.6, 118.9, 117.47, 112.3, 56.7, 55.4, 27.6; HRMS (EI-TOF) calcd for $C_{16}H_{18}N_2O_2$(M^+): 270.1368, found: 270.1371.

3-Methyl-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide

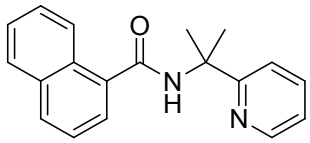


1r

The title compound **1r** was prepared according to the **General Procedure (Method A)**. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.73 (s, 1H), 8.57 (d, J = 4.8 Hz, 1H), 7.77-7.72 (m, 2H), 7.68 (d, J = 7.2 Hz, 1H), 7.47 (d, J = 8.0 Hz, 1H), 7.35-7.29 (m, 2H), 7.22 (dd, J = 7.2, 4.8 Hz, 1H) 2.42 (s, 3H), 1.88 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ

166.6, 164.9,147.3, 138.3, 137.3, 136.1, 131.9, 128.4, 127.9, 124.0, 122.0, 119.7, 56.8, 27.6, 21.5; HRMS (EI-TOF) calcd for $C_{16}H_{18}N_2O$ (M^+): 254.1419, found: 254.1418.

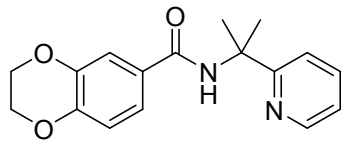
N-(2-(pyridin-2-yl)propan-2-yl)-1-naphthamide



1s

The title compound **1s** was prepared according to the **General Procedure (Method A)**. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.47 (ddd, *J* = 4.4, 2.0, 0.8 Hz, 1H), 8.39 (m, 1H), 8.34 (s, 1H), 7.91 (d, *J* = 8.0 Hz, 1H), 7.88 (m, 1H), 7.78-7.69 (m, 2H), 7.57-7.45 (m, 4H), 7.20 (ddd, *J* = 7.0, 5.4, 1.0 Hz, 1H), 1.98 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.9, 164.4, 147.7, 137.2, 135.9, 133.8, 130.4, 130.1, 128.2, 126.9, 126.2, 125.7, 124.9, 121.9, 119.5, 57.3, 27.7; HRMS (EI-TOF) calcd for $C_{19}H_{18}N_2O$ (M+): 290.1419, found: 290.1425.

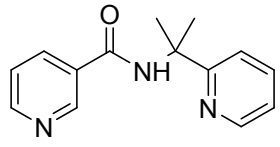
N-(2-(pyridin-2-yl)propan-2-yl)-2,3-dihydrobenzo[b][1,4]dioxine-6-carboxamide



1t

The title compound **1t** was prepared according to the **General Procedure (Method A)**. 1H NMR (400 MHz, CDCl3) δ 8.69 (s, 1H), 8.56 (d, J = 4.8 Hz, 1H), 7.74 (td, J = 7.6, 1.2 Hz, 1H), 7.46-7.44 (m, 2H), 7.41 (dd, J = 8.4, 2.0 Hz, 1H), 7.22 (dd, J = 7.2, 4.8 Hz, 1H), 6.91 (d, J = 8.4 Hz, 1H), 4.30 (s, 4H), 1.85 (s, 6H); 13C NMR (100 MHz, CDCl3) δ 165.6, 164.9, 147.7, 146.2, 143.4, 137.3, 129.6, 122.0, 120.6, 119.6, 117.2, 116.6, 64.7, 64.4, 56.7, 27.7; HRMS (EI-TOF) calcd for $C_{17}H_{18}N_2O_3$ (M+): 298.1317, found: 298.1315.

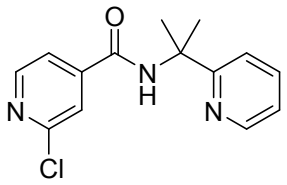
N-(2-(pyridin-2-yl)propan-2-yl)nicotinamide



4a

The title compound **4a** was prepared according to the **General Procedure (Method B)**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.09 (d, *J* = 1.6 Hz, 2H), 8.65 (dd, *J* = 4.8, 1.6 Hz, 1H), 8.48 (ddd, *J* = 4.8, 1.2, 0.8 Hz, 1H), 8.15 (dt, *J* = 8.0, 2.0 Hz ,1H), 7.71 (td, *J* = 8.0, 2.0 Hz, 1H), 7.41 (d, *J* = 8.0 Hz, 1H), 7.33 (ddd, *J* = 8.0, 4.8, 0.4Hz, 1H), 7.18 (ddd, *J* = 7.2, 4.8, 0.8 Hz, 1H), 1.82 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 164.2, 151.8, 148.3, 147.5, 137.4, 134.9, 131.5, 123.4, 122.1, 119.5, 56.8, 27.4; HRMS (EI-TOF) calcd for $C_{14}H_{15}N_3O$ (M^+): 241.1215, found: 241.1217.

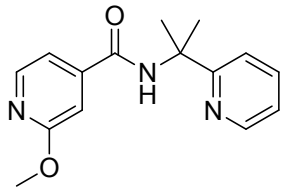
2-Chloro-*N*-(2-(pyridin-2-yl)propan-2-yl)isonicotinamide



4b

The title compound **4b** was prepared according to the **General Procedure (Method B)**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.25 (br, 1H), 8.57 (ddd, *J* = 4.8, 1.6, 0.8 Hz, 1H), 8.53 (dd, *J* = 4.8, 0.4 Hz, 1H), 7.82-7.77 (m, 2H), 7.67 (dd, *J* = 4.8, 1.6 Hz, 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.29-7.26 (m, 1H), 1.86 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.8, 162.8, 152.5, 150.4, 147.6, 146.3, 137.7, 122.3, 119.9, 119.6, 57.0, 27.3; HRMS (EI-TOF) calcd for $C_{14}H_{14}ClN_3O$ (M^+): 275.0825, found: 275.0823.

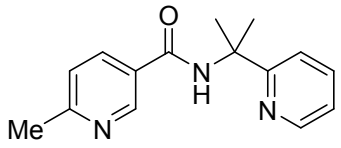
2-Methoxy-N-(2-(pyridin-2-yl)propan-2-yl)isonicotinamide



4c

The title compound 4c was prepared according to the General Procedure (Method B). 1H NMR (400 MHz, CDCl3) δ 9.10 (s, 1H), 8.55 (dd, J = 4.9, 0.9 Hz, 1H), 8.28 (d, J = 5.3 Hz, 1H), 7.77 (td, J = 7.8, 1.7 Hz, 1H), 7.46 (d, J = 8.1 Hz, 1H), 7.32 (dd, J = 5.3, 1.4 Hz, 1H), 7.26 – 7.23 (m, 1H), 7.20 (s, 1H), 3.99 (s, 3H), 1.86 (s, 6H). 13C NMR (101 MHz, CDCl3) δ 164.85, 164.10, 149.13, 147.61,147.48, 146.15 , 137.44, 122.14 , 119.51, 114.26, 108.77, 56.71, 53.78, 27.27 .

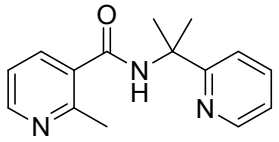
6-Methyl-N-(2-(pyridin-2-yl)propan-2-yl)nicotinamide



4d

The title compound **4d** was prepared according to the **General Procedure (Method B)**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.05 (s, 1H), 9.02 (d, *J* = 2.0 Hz, 1H), 8.54 (ddd, *J* = 5.2, 1.6, 1.2 Hz, 1H), 8.10 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.77 (td, *J* = 7.6, 2.0 Hz, 1H), 7.46 (d, *J* = 8.0 Hz, 1H), 7.26-7.23 (m, 2H), 2.62 (s, 3H), 1.88 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.5, 164.7, 161.2, 147.8, 147.5, 137.5, 135.3, 128.9, 123.0, 122.2, 119.6, 56.7, 27.5, 24.6; HRMS (EI-TOF) calcd for $C_{15}H_{17}N_3O$ (M^+): 255.1372, found: 255.1370.

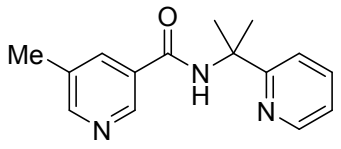
2-Methyl-N-(2-(pyridin-2-yl)propan-2-yl)nicotinamide



4e

The title compound **4e** was prepared according to the **General Procedure (Method A)**.1H NMR (400 MHz, CDCl3) δ 8.55 (dd, J = 4.8, 1.4 Hz, 1H), 8.50 – 8.45 (m, 1H), 8.38 (s, 1H), 7.81 – 7.73 (m, 2H), 7.47 (d, J = 8.1 Hz, 1H), 7.21 (ddd, J = 13.5, 6.7, 4.9 Hz, 2H), 2.72 (s, 3H), 1.90 (s, 6H). 13C NMR (101 MHz, CDCl3) δ 167.80, 164.11 , 156.03, 149.82, 147.61, 137.42, 134.95 , 133.25, 122.17 , 120.90 , 119.56, 57.20 , 27.51, 23.18 .

5-Methyl-*N*-(2-(pyridin-2-yl)propan-2-yl)nicotinamide

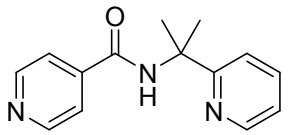


4f

The title compound **4f** was prepared according to the **General Procedure (Method A)**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.05 (s, 1H), 8.93 (d, *J* = 2.0 Hz, 1H), 8.57 – 8.55 (m, 2H), 8.02 (br, 1H), 7.77 (td, *J* = 8.0, 1.6 Hz 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.26 –

7.23 (m, 1H), 2.41 (s, 3H), 1.88 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6, 164.4, 152.4, 147.6, 145.4, 137.5, 135.6, 133.2, 131.3, 122.2, 119.6, 56.9, 27.5, 18.5; HRMS (EI-TOF) calcd for $C_{15}H_{17}N_3O$ (M^+): 255.1372, found: 255.1373.

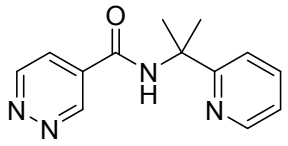
***N*-(2-(pyridin-2-yl)propan-2-yl)isonicotinamide**



4g

The title compound **4g** prepared according to the **General Procedure (Method B)**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.17 (s, 1H), 8.72-8.70 (m, 2H), 8.52 (s, 1H), 7.74-7.70 (m, 3H), 7.46-7.41 (m, 1H), 7.22-7.21 (m, 1H), 1.87-1.79 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2, 164.1，150.5, 147.5, 143.1, 137.5, 122.2, 121.0, 119.6, 56.8, 27.3; HRMS (EI-TOF) calcd for $C_{14}H_{15}N_3O$ (M^+): 241.1215, found: 241.1213.

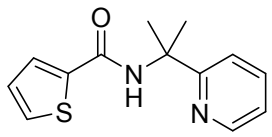
N-(2-(pyridin-2-yl)propan-2-yl)pyridazine-4-carboxamide



4h

The title compound **4h** was prepared according to the **General Procedure (Method B)**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.60 (dd, *J* = 2.0, 1.2 Hz, 1H), 9.46 (s, 1H), 9.33 (dd, *J* = 5.2, 1.2 Hz, 1H), 8.50 (ddd, *J* = 4.8, 1.6, 0.8 Hz, 1H), 7.88 (dd, *J* = 5.2, 2.4 Hz, 1H), 7.78-7.72 (m, 1H), 7.43 (d, *J* = 8.0 Hz, 1H), 7.23 (ddd, *J* = 7.2, 5.6, 0.8 Hz, 1H), 1.82 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5, 161.9, 151.9, 148.7, 147.4, 137.7, 133.0, 123.8, 122.4, 119.6, 57.0, 27.2; HRMS (EI-TOF) calcd for $C_{13}H_{14}N_4O$ (M^+): 242.1168, found: 242.1164.

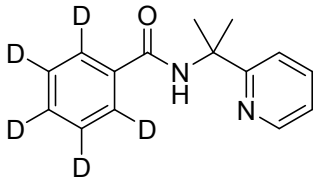
N-(2-(pyridin-2-yl)propan-2-yl)thiophene-2-carboxamide



4i

The title compound **4i** was prepared according to the **General Procedure (Method B)**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (s, 1H), 8.56 (dd, *J* = 4.8, 0.8 Hz, 1H), 7.76 (td, *J* = 8.0, 2.0 Hz, 1H), 7.60 (dd, *J* = 4,.0 1.2 Hz, 1H), 7.47-7.45 (m, 2H), 7.23 (ddd, *J* = 7.6, 4.8, 0.8 Hz, 1H), 7.09 (dd, *J* = 5.2, 4.0 Hz, 1H), 1.87 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4, 161.1, 147.6, 141.2, 137.4, 129.5, 127.6, 127.5, 122.1, 119.6, 56.9, 27.7; HRMS (EI-TOF) calcd for $C_{13}H_{14}N_2OS$ (M^+): 246.0827, found: 246.0825.

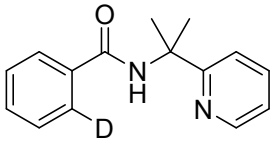
***N*-(2-(pyridin-2-yl)propan-2-yl)benzamide-2,3,4,5,6-d_5**



d_5-**1a**

The title compound *d_5*-**1a** was prepared according to the **General Procedure (Method A)**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (s, 1H), 8.56 (d, *J* = 4.4 Hz, 1H), 7.76 (td, *J* = 8.4, 2.0 Hz,1H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.26-7.23 (m, 1H), 1.88 (s, 6H); 13C NMR (101 MHz, CDCl3) δ 166.4, 164.8, 147.7, 137.4, 136.0, 130.7 (t, J_{C-F} =24.5 Hz, 1C), 128.1 (t, J_{C-F} =24.7 Hz, 2C), 126.7 (t, J_{C-F} =24.4 Hz, 2C), 122.1, 119.7, 56.8, 27.6; HRMS (EI-TOF) calcd for $C_{15}H_{11}D_5N_2O$ (M^+): 245.1576, found: 245.1579.

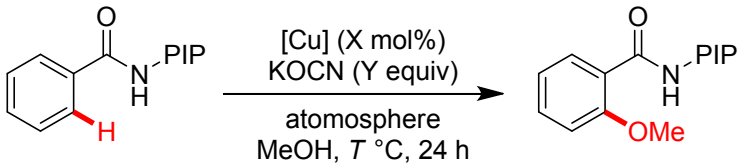
***N*-(2-(pyridin-2-yl)propan-2-yl)benzamide-2-d_1**



d_1-**1a**

The title compound *d_1*-**1a** was prepared according to the general **General Procedure (Method A)**. 1H NMR (400 MHz, CDCl3) δ 8.85 (brs, 1H), 8.56 (dd, J = 4.8, 0.7 Hz, 1H), 7.95 – 7.85 (m, 1H), 7.74 (td, J = 8.0, 1.8 Hz, 1H), 7.50 – 7.39 (m, 4H), 7.22 (ddd, J = 7.4, 4.9, 0.9 Hz, 1H), 1.88 (s, 6H)； 13C NMR (101 MHz, CDCl3) δ 166.4, 164.8, 147.7, 137.4, 136.0, 131.2, 128.5, 128.4, 127.1, 126.8 (t, J_{C-D} =24.4 Hz), 122.1, 119.7, 56.7; HRMS (EI-TOF) calcd for $C_{15}H_{15}DN_2O$ (M^+): 241.1325, found: 241.1329.

2.3 Optimization of Reaction Conditions

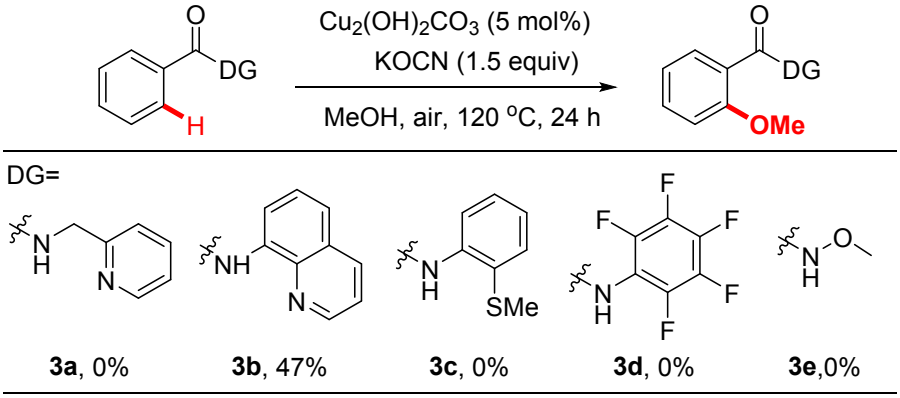


1a **2a**

Entry	[Cu] (X mol%)	KOCN (Y equiv)	*T* (ºC)/ Atmosphere	Yield (%)[b]
1	$Cu(OAc)_2$ (10)	1.5	100 ºC/O_2	75
2	$CuBr_2$ (10)	1.5	100 ºC/O_2	69
3	$Cu(OTf)_2$ (10)	1.5	100 ºC/O_2	70
4	$(CuOH)_2CO_3$ (10)	1.5	100 ºC/O_2	78
5	$(CuOH)_2CO_3$ (10)	1.5	120 ºC/O_2	86
6	$(CuOH)_2CO_3$ (10)	3.0	140 ºC/O_2	72
7	$(CuOH)_2CO_3$ (10)	3.0	120 ºC/Air	84
8	**$(CuOH)_2CO_3$ (5)**	**1.5**	**120 ºC/Air**	**88 (86)[c]**

[a]Reaction Conditions: **1a** (0.15 mmol), [Cu] (X mol%), KOCN (Y equiv), in MeOH (2 mL). [b]^{1}H NMR yield using CH_2Br_2 as the internal standard. [c]Isolated yields.

2.4 Effect of the Directing Groups:

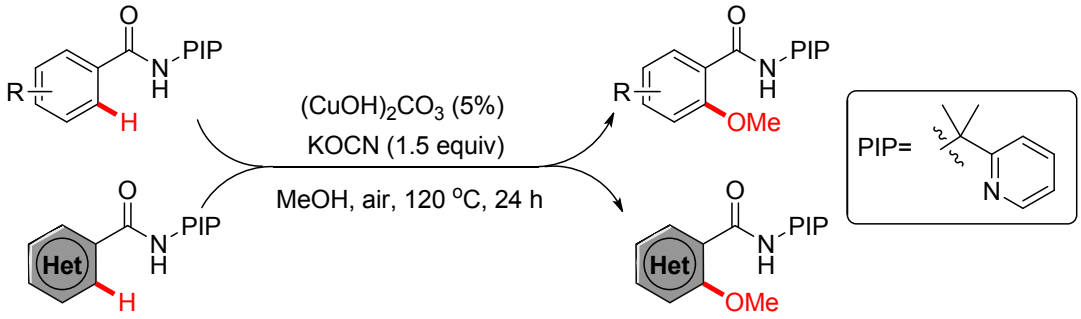


3a, 0% **3b**, 47% **3c**, 0% **3d**, 0% **3e**,0%

To a 50 mL sealed tube was added substrate (0.15 mmol), $(CuOH)_2CO_3$ (1.6 mg, 0.0075 mmol), KOCN (18.2 mg, 0.225 mmol) and Methanol (2 mL). The mixture was stirred at 120 °C oil bath for 24 hours. Then the reaction mixture was cooled to room temperature, diluted with dichloromethane and quenched with saturated sodium sulfide solution. The aqueous phase was extracted with dichloromethane (3×10 mL). The combined organic phase was dried with

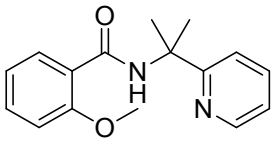
anhydrous magnesium sulfate. After concentration, the resulting residue was purified by preparative TLC to afford the product.

2.5 General Procedure for the Alkoxylation



To a 50 mL sealed tube was added substrate (0.15 mmol), $(CuOH)_2CO_3$ (1.6 mg, 0.0075 mmol), KOCN (18.2 mg, 0.225 mmol) and Methanol (2 mL). The mixture was stirred at 120 °C oil bath for 24 hours.Then the reaction mixture was cooled to room temperature, diluted with dichloromethane and quenched with saturated sodium sulfide solution. The aqueous phase was extracted with dichloromethane (3×10 mL). The combined organic phase was dried with anhydrous magnesium sulfate. After concentration, the resulting residue was purified by preparative TLC to afford the product.

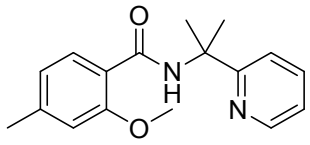
2-Methoxy-N-(2-(pyridin-2-yl) propan-2-yl)benzamide



2a

The title compound **2a** was prepared according to **General Procedure.** A purification by flash chromatography in petroleum ether : tetrahydrofuran = 3 : 1 gave **2a** as a white solid (34.9 mg, 86%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.64 (brs, 1H), 8.58 (d, J = 4.4, 1H), 8.19 (dd, J = 7.8, 1.6 Hz, 1H), 7.70 (td, J = 7.5, 1.1 Hz, 1H), 7.50-7.41 (m, 2H), 7.21-7.13 (dd, J = 7.4, 4.9 Hz, 1H), 7.06 (t, J = 7.4 Hz, 1H), 6.99 (d, J = 8.3 Hz, 1H), 4.04 (s, 3H), 1.87 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.4, 164.2, 157.8, 148.1, 136.9, 132.5, 132.2, 121.8, 121.3, 119.7, 111.5, 57.5, 56.1, 28.0; HRMS (EI-TOF) calcd for $C_{16}H_{18}N_2O_2$ (M+): 270.1368, found: 270.1367.

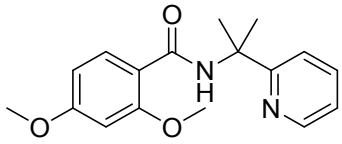
2-Methoxy-4-methyl-N-(2-(pyridin-2-yl)propan-2-yl)benzamide



2b

The title compound **2b** was prepared according to **General Procedure.** A purification by flash chromatography in petroleum ether : tetrahydrofuran = 3 : 1 gave **2b** as a colorless oil (35.9 mg, 84%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.56 (brs, 1H), 8.57 (d, *J* = 4.8 Hz, 1H), 8.07 (d, *J* = 8.0 Hz, 1H), 7.68 (td, *J* = 7.7, 1.7 Hz, 1H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.22 – 7.11 (m, 1H), 6.86 (d, *J* = 8.0 Hz, 1H), 6.78 (s, 1H), 4.02 (s, 3H), 2.38 (s, 3H), 1.85 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.5, 164.3, 157.7, 148.1, 143.2, 136.9, 132.1, 122.1, 121.7, 120.2, 119.7, 112.2, 57.5, 56.0, 28.0, 21.8; HRMS (EI-TOF) calcd for $C_{17}H_{20}N_2O_2$ (M^+): 284.1525, found: 284.1526.

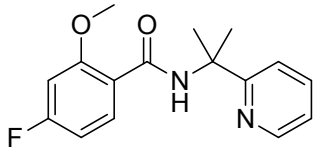
2,4-Dimethoxy-N-(2-(pyridin-2-yl)propan-2-yl)benzamide



2c

The title compound **2c** was prepared according to **General Procedure.** A purification by flash chromatography in petroleum ether : ethyl acetate = 3 : 1 gave **2c** as a colorless oil (36.3 mg, 81%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.47 (brs, 1H), 8.56 (dd, *J* = 4.8, 0.8 Hz, 1H), 8.15 (d, *J* = 8.8 Hz, 1H), 7.68 (td, *J* = 7.6, 1.8 Hz, 1H), 7.45 (d, *J* = 8.1 Hz, 1H), 7.21 – 7.09 (m, 1H), 6.57 (dd, *J* = 8.8, 2.3 Hz, 1H), 6.49 (d, *J* = 2.2 Hz, 1H), 4.00 (s, 3H), 3.83 (s, 3H), 1.84 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.6, 164.1, 163.3, 159.0, 148.1, 136.9, 133.7, 121.7, 119.7, 115.9, 105.2, 98.7, 57.4, 56.0, 55.6, 28.1; HRMS (EI-TOF) calcd for $C_{17}H_{20}N_2O_3$ (M^+): 300.1474, found: 300.1479.

4-Fluoro-2-methoxy-N-(2-(pyridin-2-yl)propan-2-yl)benzamide

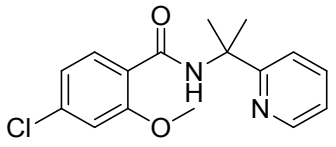


2d

The title compound **2d** was prepared according to **General Procedure.** A purification by flash chromatography in petroleum ether : tetrahydrofuran = 3 : 1 gave **2d** as a

yellow solid (31.9 mg, 74%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.61 (brs, 1H), 8.56 (dd, *J* = 4.0, 0.8 Hz, 1H), 8.19 (dd, *J* = 8.7, 7.2 Hz, 1H), 7.70 (td, *J* = 7.8, 1.7 Hz, 1H), 7.45 (d, *J* = 8.1 Hz, 1H), 7.18 (dd, *J* = 7.4, 4.9 Hz,, 1H), 6.78-6.71 (m, 1H), 6.69 (dd, *J* = 10.6, 2.3 Hz, 1H), 4.02 (s, 3H), 1.85 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.3 (d, $J_{C\text{-}F}$ =249.9 Hz), 165.30, 163.28, 159.1 (d, $J_{C\text{-}F}$ = 10.2 Hz), 148.0, 137.0, 134.0 (d, $J_{C\text{-}F}$ =10.5 Hz), 121.8, 119.7, 119.3, 108.0 (d, $J_{C\text{-}F}$ = 21.0 Hz), 99.5 (d, $J_{C\text{-}F}$ = 26.0 Hz), 57.5, 56.3, 27.9; HRMS (EI-TOF) calcd for $C_{16}H_{17}FN_2O_2$ (M^+): 288.1274, found: 288.1268.

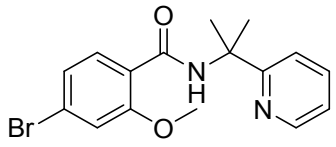
4-Chloro-2-methoxy-N-(2-(pyridin-2-yl)propan-2-yl)benzamide



2e

The title compound **2e** was prepared according to **General Procedure.** A purification by flash chromatography in petroleum ether : diethyl ether = 3 : 1 gave **2e** as a colorless oil (40.7 mg, 89%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.67 (brs, 1H), 8.55 (d, *J* = 4.7 Hz, 1H), 8.12 (d, *J* = 8.4 Hz, 1H), 7.76 – 7.64 (m, 1H), 7.44 (d, *J* = 8.0 Hz, 1H), 7.21-7.14 (m, 1H), 7.03 (d, *J* = 8.4 Hz, 1H), 6.96 (s, 1H), 4.02 (s, 3H), 1.85 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.2, 163.2, 158.1, 147.9, 138.0, 137.0, 133.2, 121.8, 121.6, 121.4, 119.7, 112.1, 57.6, 56.3, 27.8; HRMS (EI-TOF) calcd for $C_{16}H_{17}ClN_2O_2$ (M+): 304.0979, found: 304.0980.

4-Bromo-2-methoxy-N-(2-(pyridin-2-yl)propan-2-yl)benzamide

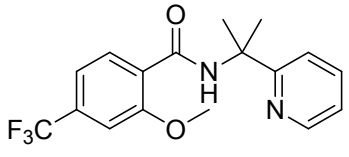


2f

The title compound **2f** was prepared according to **General Procedure.** A purification by flash chromatography in petroleum ether : ethyl acetate = 2 : 1 gave **2f** as a colorless oil (45.9 mg, 88%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.67 (brs, 1H), 8.56 (d, *J* = 4.8 Hz, 1H), 8.05 (d, *J* = 8.4 Hz, 1H), 7.70 (td, *J* = 7.7, 1.7 Hz, 1H), 7.44 (d, *J* = 8.1 Hz, 1H), 7.19 (m, 2H), 7.12 (d, *J* = 1.6 Hz, 1H), 4.03 (s, 3H), 1.85 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.2, 163.3, 158.1, 148.0, 137.1, 133.4, 126.3, 124.5,

122.2, 121.9, 119.7, 115.0, 57.6, 56.4, 27.8; HRMS (EI-TOF) calcd for $C_{16}H_{17}BrN_2O_2$ (M^+): 348.0473, found: 348.0473.

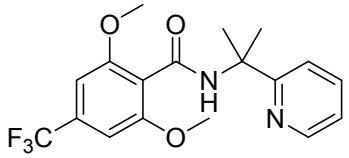
2-Methoxy-N-(2-(pyridin-2-yl)propan-2-yl)-4-(trifluoromethyl)benzamide



2ga

The title compound **2ga** was prepared according to **General Procedure.** A purification by flash chromatography in petroleum ether : diethyl ether = 3 : 4 gave **2ga** as a colorless solid (31.2 mg, 61%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.82 (brs, 1H), 8.57 (d, *J* = 4.2 Hz, 1H), 8.29 (d, *J* = 8.1 Hz, 1H), 7.72 (td, *J* = 7.7, 1.7 Hz, 1H), 7.46 (d, *J* = 8.1 Hz, 1H), 7.32 (d, *J* = 8.1 Hz, 1H), 7.23-7.17 (m, 2H), 4.09 (s, 3H), 1.87 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.1, 162.9, 157.7, 148.0, 137.1, 134.0((q, $J_{C\text{-}F}$ =32.4 Hz), 132.8, 126.4, 123.8 (q, $J_{C\text{-}F}$ =271.0 Hz), 122.0, 119.7, 117.9 (q, $J_{C\text{-}F}$ =3.8 Hz), 108.5(q, $J_{C\text{-}F}$ =3.7 Hz), 57.70, 56.38, 27.75; HRMS (EI-TOF) calcd for $C_{17}H_{17}F_3N_2O_2$ (M^+): 338.1242, found: 338.1241.

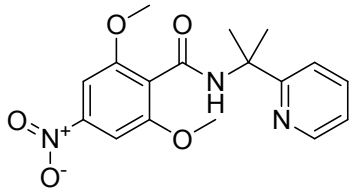
2,6-Dimethoxy-N-(2-(pyridin-2-yl)propan-2-yl)-4-(trifluoromethyl)benzamide



2gb

The title compound **2gb** was prepared according to **General Procedure.** A purification by flash chromatography in petroleum ether : diethyl ether = 3 : 4 gave **2gb** as a colorless solid (19.3 mg, 35%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (d, *J* = 4.6 Hz, 1H), 7.77 (brs, 1H), 7.71 (td, *J* = 7.7, 1.5 Hz, 1H), 7.52 (d, *J* = 8.0 Hz, 1H), 7.17 (dd, *J* = 7.0, 5.1 Hz, 1H), 6.80 (s, 2H), 3.86 (s, 6H), 1.88 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.6, 163.8, 157.7, 147.7, 137.1, 132.4 (q, $J_{C\text{-}F}$ =32.5 Hz), 121.9, 119.7, 101.5 (q, $J_{C\text{-}F}$ =3.7 Hz), 57.7, 56.5, 27.9; HRMS (EI-TOF) calcd for $C_{18}H_{19}F_3N_2O_3$ (M^+): 368.1348, found: 368.1346.

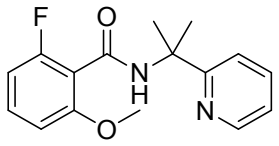
2,6-Dimethoxy-4-nitro-N-(2-(pyridin-2-yl)propan-2-yl)benzamide



2h

The title compound **2h** was prepared according to **General Procedure.** A purification by flash chromatography in petroleum ether : ethyl acetate = 3 : 1 gave **2h** as a yellow oil (18.3 mg, 35%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (d, J = 4.8 Hz, 1H), 7.94 (brs, 1H), 7.73 (td, J = 7.9, 1.6 Hz, 1H), 7.50 (d, J = 8.1 Hz, 1H), 7.46 (s, 2H), 7.18 (dd, J = 7.2, 5.0 Hz, 1H), 3.90 (s, 6H), 1.89 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.3, 163.0, 157.7, 149.5, 147.7, 137.3, 122.9, 122.0, 119.6, 100.1, 57.7, 56.7, 27.8; HRMS (EI-TOF) calcd for $C_{17}H_{19}N_3O_5$ (M^+): 345.1325, found: 345.1319.

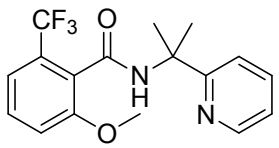
2-Fluoro-6-methoxy-N-(2-(pyridin-2-yl)propan-2-yl)benzamide



2i

The title compound **2i** was prepared according to **General Procedure.** A purification by flash chromatography in petroleum ether : tetrahydrofuran = 3 : 1 gave **2i** as a yellow solid (18.3 mg, 42%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (ddd, J = 4.8, 1.6, 0.9 Hz, 1H), 8.00 (s, 1H), 7.75 – 7.66 (m, 1H), 7.49 (d, J = 8.1 Hz, 1H), 7.33 – 7.23 (m, 1H), 7.17 (ddd, J = 7.4, 4.9, 1.0 Hz, 1H), 6.77-6.68 (m, 2H), 3.86 (s, 3H), 1.88 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.3 (d, $J_{C\text{-}F}$ = 226.1 Hz), 157.9, 147.7, 137.2, 130.7, 130.6, 121.9 (d, $J_{C\text{-}F}$ = 6.7 Hz), 119.6 (d, $J_{C\text{-}F}$ = 7.2 Hz), 108.62, 108.5 (d, $J_{C\text{-}F}$ = 22.1 Hz), 108.4 (d, $J_{C\text{-}F}$ = 22.1 Hz), 107.0, 57.70, 56.45, 27.81; HRMS (EI-TOF) calcd for $C_{16}H_{17}FN_2O_2$ (M^+): 288.1274, found: 288.1277.

2-Methoxy-N-(2-(pyridin-2-yl)propan-2-yl)-6-(trifluoromethyl)benzamide

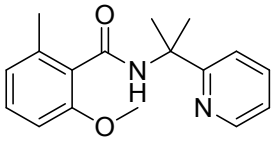


2j

The title compound **2j** was prepared according to **General Procedure.** A purification by flash chromatography in petroleum ether : tetrahydrofuran = 3 : 1 gave **2j** as a

white solid (27.3 mg, 54%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (d, J = 4.8, 1H), 8.02 (brs, 1H), 7.73 (td, J = 7.8, 1.6 Hz, 1H), 7.51 (d, J = 8.1 Hz, 1H), 7.44 (t, J = 8.0 Hz, 1H), 7.27 (d, J = 7.8, 1H), 7.18 (dd, J = 7.2, 5.0 Hz, 1H), 7.13 (d, J = 8.4 Hz, 1H), 3.87 (s, 3H), 1.89 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.4, 164.0, 157.2, 147.6, 137.2, 130.1, 128.6 (q, $J_{C\text{-}F}$ =31.5 Hz), 126.8 (d, $J_{C\text{-}F}$ =2.0 Hz), 123.8 (d, $J_{C\text{-}F}$ =272.5 Hz), 118.1(q, $J_{C\text{-}F}$ =4.9 Hz), 121.9, 119.7, 115.0, 57.6, 56.5, 27.4; HRMS (EI-TOF) calcd for $C_{17}H_{17}F_3N_2O_2$ (M^+): 338.1242, found: 338.1248.

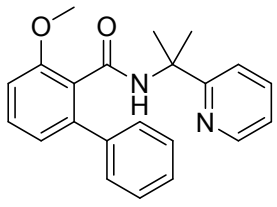
2-Methoxy-6-methyl-N-(2-(pyridin-2-yl)propan-2-yl)benzamide



2k

The title compound **2k** was prepared according to **General Procedure.** A purification by flash chromatography in petroleum ether : ethyl acetate = 3 : 1 gave **2k** as a yellow oil (18.7 mg, 44%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (dd, J = 4.8, 0.7 Hz, 1H), 7.75-7.65 (m, 2 H), 7.52 (d, J = 8.1 Hz, 1H), 7.20 (t, J = 8.0 Hz, 1H), 7.16 (ddd, J = 7.4, 4.9, 0.9 Hz, 1H), 6.81 (d, J = 7.6 Hz, 1H), 6.76 (d, J = 8.3 Hz, 1H), 3.82 (s, 3H), 2.36 (s, 3H), 1.89 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.3, 164.7, 156.4, 147.8, 137.0, 136.9, 129.4, 128.2, 122.8, 121.8, 119.6, 108.7, 57.5, 56.0, 27.9, 19.2; HRMS (EI-TOF) calcd for $C_{17}H_{20}N_2O_2$ (M^+): 284.1525, found: 284.1530.

3-Methoxy-N-(2-(pyridin-2-yl)propan-2-yl)-[1,1'-biphenyl]-2-carboxamide

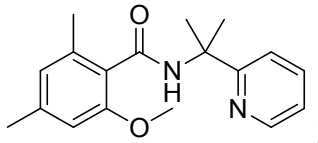


2l

The title compound **2l** was prepared according to **General Procedure.** A purification by flash chromatography in petroleum ether : tetrahydrofuran = 3 : 1 gave **2l** as a yellow solid (13.2 mg, 25%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (dd, J = 4.8, 0.8 Hz, 1H), 7.60 (td, J = 7.8, 1.6 Hz, 1H), 7.54 – 7.46 (m, 2H), 7.43 – 7.21 (m, 6H), 7.10 (ddd, J = 7.4, 4.9, 0.9 Hz, 1H), 7.03 – 6.91 (m, 2H), 3.89 (s, 3H), 1.57 (s, 6H). ^{13}C

NMR (101 MHz, $CDCl_3$) δ 166.5, 164.6, 156.7, 147.6, 141.3, 140.3, 136.9, 129.6, 129.1, 128.1, 127.8, 127.4, 122.3, 121.6, 119.5, 110.2, 57.4, 56.3, 27.4; HRMS (EI-TOF) calcd for $C_{22}H_{22}N_2O_2$ (M+): 346.1681, found: 346.1677.

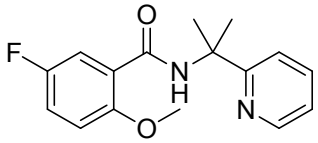
2-Methoxy-4,6-dimethyl-N-(2-(pyridin-2-yl)propan-2-yl)benzamide



2m

The title compound **2m** was prepared according to **General Procedure.** A purification by flash chromatography in petroleum ether : diethyl ether = 3 : 5 gave **2m** as a light yellow oil (13.8 mg, 31%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (dd, *J* = 4.8, 0.8 Hz, 1H), 7.70 (td, *J* = 7.7, 1.6 Hz, 1H), 7.66 (brs, 1H), 7.52 (d, *J* = 8.1 Hz, 1H), 7.16 (dd, *J* = 7.4, 4.9 Hz, 1H), 6.63 (s, 1H), 6.57 (s, 1H), 3.81 (s, 3H), 2.32 (s, 6H) , 1.87 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.5, 164.8, 156.5, 147.8, 139.6, 137.0, 136.8, 125.5, 123.5, 121.8, 119.7, 109.5, 57.5, 56.0, 27.9, 21.7, 19.2; HRMS (EI-TOF) calcd for $C_{18}H_{22}N_2O_2$ (M^+): 298.1681, found: 298.1685.

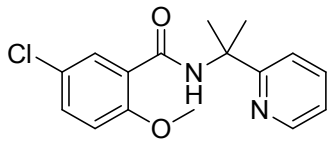
3-fluoro-2-methoxy-N-(2-(pyridin-2-yl)propan-2-yl)benzamide



2n

The title compound **2n** was prepared according to **General Procedure.** A purification by flash chromatography in petroleum ether : diethyl ether = 3 : 5 gave **2n** as a colorless oil (21.3 mg, 49%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (brs, 1H), 8.57 (d, *J* = 4.2 Hz, 1H), 7.90 (dd, *J* = 9.7, 3.3 Hz, 1H), 7.71 (td, *J* = 7.8, 1.8 Hz, 1H), 7.45 (d, *J* = 8.1 Hz, 1H), 7.19 (ddd, *J* = 7.3, 4.8, 0.8 Hz, 1H), 7.11 (ddd, *J* = 9.0, 7.2, 3.3 Hz, 1H), 6.93 (dd, *J* = 9.0, 4.1 Hz, 1H), 4.03 (s, 3H), 1.86 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.1 (d, $J_{C\text{-}F}$ =230.2 Hz), 158.5, 156.2, 153.9, 148.1, 137.1, 124.6 (d, $J_{C\text{-}F}$ =3.1 Hz), 121.9, 119.7, 118.7(d, $J_{C\text{-}F}$ =25.4 Hz), 118.5 (d, $J_{C\text{-}F}$ =25.2 Hz), 112.9 (d, $J_{C\text{-}F}$ =7.3 Hz), 57.65, 56.74, 27.85; HRMS (EI-TOF) calcd for $C_{16}H_{17}FN_2O_2$ (M+): 288.1274, found: 288.1266.

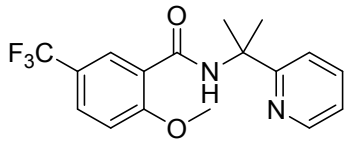
5-Chloro-2-methoxy-N-(2-(pyridin-2-yl)propan-2-yl)benzamide



2o

The title compound **2o** was prepared according to **General Procedure.** A purification by flash chromatography in petroleum ether : tetrahydrofuran = 3 : 1 gave **2o** as a white solid (37.7 mg, 82%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.73 (brs, 1H), 8.56 (dd, *J* = 4.1, 0.8 Hz, 1H), 8.16 (d, *J* = 2.8 Hz, 1H), 7.78 – 7.65 (m, 1H), 7.45 (d, *J* = 8.1 Hz, 1H), 7.35 (dd, *J* = 8.8, 2.8 Hz, 1H), 7.18 (dd, *J* = 7.4, 4.9 Hz, 1H), 6.91 (d, *J* = 8.8 Hz, 1H), 4.02 (s, 3H), 1.85 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.1, 162.8, 156.3, 148.0, 137.0, 132.0, 131.9, 126.6, 124.5, 121.9, 119.7, 113.0, 57.6, 56.4, 27.8; HRMS (EI-TOF) calcd for $C_{16}H_{17}ClN_2O_2$ (M+): 304.0979, found: 304.0982.

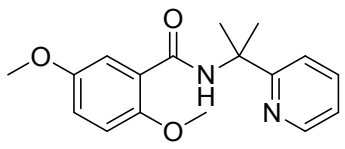
2-Methoxy-N-(2-(pyridin-2-yl)propan-2-yl)-5-(trifluoromethyl)benzamide



2p

The title compound **2p** was prepared according to **General Procedure.** A purification by flash chromatography in petroleum ether : diethyl ether = 3 : 4 gave **2p** as a colorless solid (37.3 mg, 74%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.82 (brs, 1H), 8.57 (d, *J* = 4.8 Hz, 1H), 8.51 (d, *J* = 1.9 Hz, 1H), 7.72 (td, *J* = 7.8, 1.6 Hz, 1H), 7.67 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.46 (d, *J* = 8.1 Hz, 1H), 7.24 – 7.16 (m, 1H), 7.06 (d, *J* = 8.7 Hz, 1H), 4.10 (s, 3H), 1.87 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.1, 162.7, 159.9, 147.9, 137.1, 129.8 (q, $J_{C\text{-}F}$ = 3.7 Hz), 129.5 (q, $J_{C\text{-}F}$ = 3.6 Hz), 123.6 (q, $J_{C\text{-}F}$ = 33.1 Hz), 124.2(q, $J_{C\text{-}F}$ = 269.8 Hz), 123.5,122.0, 119.7, 111.7, 57.7, 56.4, 27.7; HRMS (EI-TOF) calcd for $C_{17}H_{17}F_3N_2O_2$ (M^+): 338.1242, found: 338.1248.

2,5-Dimethoxy-N-(2-(pyridin-2-yl)propan-2-yl)benzamide

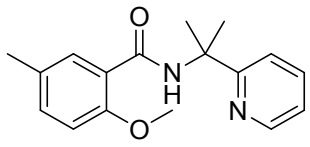


2q

The title compound **2q** was prepared according to **General Procedure.** A purification by flash chromatography in petroleum ether : diethyl ether = 3 : 5 gave **2q** as a colorless oil (28.7 mg, 64%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.72 (brs, 1H), 8.57 (d, *J*

= 4.8 Hz, 1H), 7.76 (d, *J* = 3.2 Hz, 1H), 7.69 (td, *J* = 7.8, 1.7 Hz, 1H), 7.46 (d, *J* = 8.1 Hz, 1H), 7.17 (dd, *J* = 7.2, 4.9 Hz, 1H), 7.03-6.88 (m, 2H), 3.99 (s, 3H), 3.80 (s, 3H), 1.86 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.4, 163.9, 154.0, 152.1, 148.1, 136.9, 123.4, 121.7, 119.6, 119.5, 115.2, 113.3, 57.6, 56.8, 55.9, 28.0; HRMS (EI-TOF) calcd for $C_{17}H_{20}N_2O_3$ (M+): 300.1474, found: 300.1479.

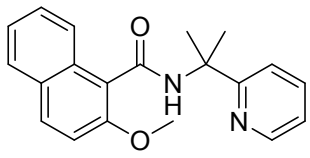
2-methoxy-5-methyl-N-(2-(pyridin-2-yl)propan-2-yl)benzamide



2r

The title compound **2r** was prepared according to **General Procedure.** A purification by flash chromatography in petroleum ether : diethyl ether = 3 : 5 gave **2r** as a colorless solid (29.9 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.59 (brs, 1H), 8.57 (dd, *J* = 4.8, 0.8 Hz, 1H), 8.00 (d, *J* = 2.0 Hz, 1H), 7.69 (td, *J* = 7.8, 1.8 Hz, 1H), 7.46 (d, *J* = 8.1 Hz, 1H), 7.21 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.17 (ddd, *J* = 7.4, 4.9, 0.9 Hz, 1H), 6.88 (d, *J* = 8.3 Hz, 1H), 4.00 (s, 3H), 2.30 (s, 3H), 1.86 (s,6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.5, 164.4, 155.8, 148.1, 136.9, 132.9, 132.5, 130.6, 122.4, 121.7, 119.7, 111.5, 57.5, 56.2, 28.0, 20.5; HRMS (EI-TOF) calcd for $C_{17}H_{20}N_2O_2$ (M^+): 284.1525, found: 284.1526.

2-Methoxy-N-(2-(pyridin-2-yl)propan-2-yl)-1-naphthamide

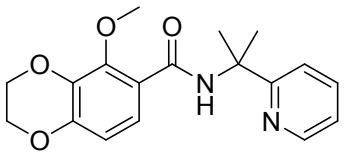


2s

The title compound **2s** was prepared according to **General Procedure.** A purification by flash chromatography in petroleum ether : tetrahydrofuran = 3 : 1 gave **2s** as a light yellow solid (23.3 mg, 48%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (d, *J* = 4.4 Hz, 1H), 7.98 (d, *J* = 8.5 Hz, 1H), 7.93 (brs, 1H), 7.86 (d, *J* = 9.0 Hz, 1H), 7.79 (d, *J* = 8.2 Hz, 1H), 7.73 (td, *J* = 7.9, 1.7 Hz, 1H), 7.57 (d, *J* = 8.1 Hz, 1H), 7.51-7.42 (m, 1H), 7.369-7.33 (m, 1H), 7.29 (d, *J* = 9.1 Hz, 1H), 7.16 (dd, *J* = 7.2, 5.0 Hz, 1H), 3.97 (s, 3H), 1.99 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.8, 164.7, 153.6, 147.8, 137.1, 131.8,

130.7, 129.0, 128.0, 127.4, 124.6, 124.1, 122.5, 121.9, 119.7, 113.7, 57.7, 57.1, 28.0; HRMS (EI-TOF) calcd for $C_{20}H_{20}N_2O_2$ (M^+): 320.1525, found: 320.1520.

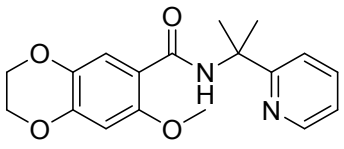
5-Methoxy-N-(2-(pyridin-2-yl)propan-2-yl)-2,3-dihydrobenzo[b][1,4]dioxine-6-carboxamide



2ta

The title compound **2ta** was prepared according to **General Procedure.** A purification by flash chromatography in petroleum ether : tetrahydrofuran = 3 : 1 gave **2ta** as a colorless oil (19.6 mg, 40%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.58 (brs, 1H), 8.55 (dd, *J* = 4.8, 0.8 Hz, 1H), 7.68 (td, *J* = 7.9, 1.8 Hz, 1H), 7.62 (d, *J* = 8.9 Hz, 1H), 7.44 (d, *J* = 8.1 Hz, 1H), 7.16 (ddd, *J* = 7.4, 4.8, 0.8 Hz, 1H), 6.71 (d, *J* = 8.9 Hz, 1H), 4.35-4.26 (m, 4H), 4.00 (s, 3H), 1.85 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.3, 163.9, 148.1, 147.9, 147.1, 136.8, 136.8, 122.9, 121.7, 120.5, 119.5, 113.0, 64.4, 64.4, 61.6, 57.4, 28.0; HRMS (EI-TOF) calcd for $C_{18}H_{20}N_2O_4$ (M^+): 328.1423, found: 328.1425.

7-Methoxy-N-(2-(pyridin-2-yl)propan-2-yl)-2,3-dihydrobenzo[b][1,4]dioxine-6-carboxamide

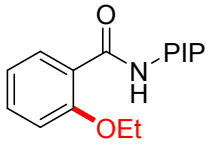


2tb

The title compound **2tb** was prepared according to **General Procedure.** A purification by flash chromatography in petroleum ether : tetrahydrofuran = 3 : 1 gave **2tb** as a colorless oil (17.5 mg, 36%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.49 (brs, 1H), 8.56 (dd, *J* = 4.8, 0.8 Hz, 1H), 7.72 (s, 1H), 7.68 (td, *J* = 8.0, 1.8 Hz, 1H), 7.44 (d, *J* = 8.1 Hz, 1H), 7.16 (ddd, *J* = 7.4, 4.9, 0.9 Hz, 1H), 6.49 (s, 1H), 4.31 – 4.24 (m, 2H), 4.23-4.18 (m,, 2H), 3.95 (s, 3H), 1.84 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.5, 163.7, 152.7, 148.1, 146.6, 137.8, 136.9, 121.7, 120.6, 119.7, 116.4, 101.0, 65.1, 64.1,

57.5, 56.6, 28.1; HRMS (EI-TOF) calcd for $C_{18}H_{20}N_2O_4$ (M^+): 328.1423, found: 328.1426.

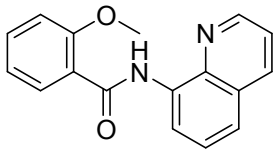
2-Ethoxy-N-(2-(pyridin-2-yl)propan-2-yl)benzamide 2u



2u

The title compound **2u** was prepared according to **General Procedure** using $Cu(OAc)_2$ (5 mol%) as catalyst**.** A purification by flash chromatography in petroleum ether : tetrahydrofuran = 3 : 1 gave **2u** as a white solid (34.9 mg, 86%). ^{1}H NMR (400 MHz, $CDCl_3$) δ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.26 (brs, 1H), 8.56 (dd, *J* = 4.8, 0.8 Hz, 1H), 8.16 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.67 (td, *J* = 7.9, 1.8 Hz, 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.40 (ddd, *J* = 8.4, 7.4, 1.8 Hz, 1H), 7.16 (ddd, *J* = 7.4, 4.8, 1.0 Hz, 1H), 7.08 – 7.00 (m, 1H), 6.96 (d, *J* = 8.3 Hz, 1H), 4.24 (q, *J* = 7.0 Hz, 2H), 1.86 (s, 6H), 1.55 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ165.4, 164.4, 157.2, 148.3, 136.8, 132.5, 132.3, 123.0, 121.7, 121.2, 119.7, 112.4, 64.9, 57.7, 28.2, 15.1.; HRMS (EI-TOF) calcd for $C_{17}H_{20}N_2O_2$ (M+): 284.1525, found: 284.1532.

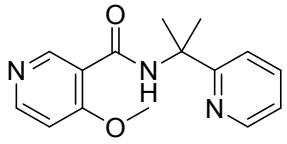
2-Methoxy-N-(quinolin-8-yl)benzamide



3b

The title compound **3b** was prepared according to **General Procedure.** A purification by flash chromatography in petroleum ether : tetrahydrofuran = 3 : 1 gave **3b** as a brown solid (19.5 mg, 47%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.34 (brs, 1H), 9.04 (dd, *J* = 7.6, 1.2 Hz, 1H), 8.88 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.36 (dd, *J* = 7.8, 1.8 Hz, 1H), 8.17 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.59 (t, *J* = 7.9 Hz, 1H), 7.55-7.48 (m, 2H), 7.46 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.18 – 7.11 (m, 1H), 7.08 (d, *J* = 8.3 Hz, 1H), 4.21 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.8, 157.9, 148.4, 139.5, 136.4, 135.9, 133.3, 132.5, 128.3, 127.7, 122.6, 121.6, 121.6, 121.5, 117.5, 111.8, 56.3; HRMS (EI-TOF) calcd for $C_{17}H_{14}N_2O_2$ (M^+): 278.1055, found: 278.1057.

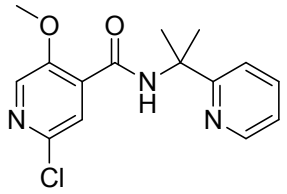
4-Methoxy-N-(2-(pyridin-2-yl)propan-2-yl)nicotinamide



5a

The title compound **5a** was prepared according to **General Procedure.** A purification by flash chromatography in ethyl acetate gave **5a** as a white solid (37.3 mg, 92%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.61 (brs, 1H), 9.20 (s, 1H), 8.53 (d, *J* = 5.7 Hz, 2H), 7.71 (td, *J* = 7.9, 1.7 Hz, 1H), 7.44 (d, *J* = 8.1 Hz, 1H), 7.18 (dd, *J* = 6.7, 4.9 Hz, 1H), 6.88 (d, *J* = 5.8 Hz, 1H), 4.07 (s, 3H), 1.85 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.9, 163.5, 162.7, 153.6, 153.5, 147.8, 137.2, 121.9, 119.7, 118.5, 106.5, 57.6, 56.0, 27.7; HRMS (EI-TOF) calcd for $C_{15}H_{17}N_3O_2$ (M^+): 271.1321, found: 271.1317.

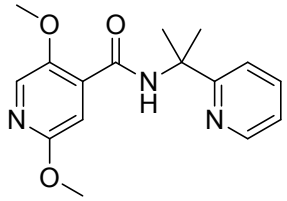
2-chloro-5-methoxy-N-(2-(pyridin-2-yl)propan-2-yl)isonicotinamide



5b

The title compound **5b** was prepared according to **General Procedure.** A purification by flash chromatography in petroleum ether : diethyl ether = 3 : 5 gave **5b** as a yellow solid (27.3 mg, 60%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.92 (brs, 1H), 8.61 – 8.52 (m, 1H), 8.18 (s, 1H), 8.02 (s, 1H), 7.75 (td, *J* = 7.8, 1.8 Hz, 1H), 7.45 (d, *J* = 8.1 Hz, 1H), 7.23 (ddd, *J* = 7.4, 4.9, 0.9 Hz, 1H), 4.15 (s, 3H), 1.85 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.5, 160.8, 152.1, 147.9, 144.4, 137.3, 134.4, 133.0, 125.5, 122.2, 119.7, 57.9, 57.2, 27.5; HRMS (EI-TOF) calcd for $C_{15}H_{16}ClN_3O_2$ (M+): 305.0931, found: 305.0929.

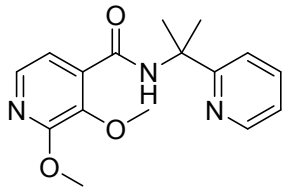
2,5-Dimethoxy-N-(2-(pyridin-2-yl)propan-2-yl)isonicotinamide



5ca

The title compound **5ca** was prepared according to **General Procedure.** A purification by flash chromatography in petroleum ether : ethyl acetate = 1 : 1 gave **5ca** as a white solid (19.3 mg, 43%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (brs, 1H), 8.57 (d, *J* = 4.7 Hz, 1H), 7.93 (s, 1H), 7.78 – 7.66 (m, 1H), 7.47 (s, 1H), 7.44 (d, *J* = 8.1 Hz, 1H), 7.20 (dd, *J* = 7.2, 5.0 Hz, 1H), 4.06 (s, 3H), 3.90 (s, 3H), 1.85 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.8, 162.0, 159.9, 148.4, 148.0, 137.2, 134.0, 131.1, 122.0, 119.7, 111.9, 57.8, 57.4, 53.9, 27.6; HRMS (EI-TOF) calcd for $C_{16}H_{19}N_3O_3$ (M^+): 301.1426, found: 301.1437.

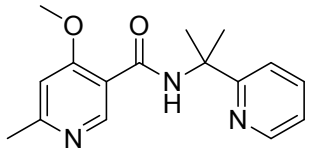
2,3-Dimethoxy-N-(2-(pyridin-2-yl)propan-2-yl)isonicotinamide



5cb

The title compound **5cb** was prepared according to **General Procedure.** A purification by flash chromatography in petroleum ether : ethyl acetate = 1 : 1 gave **5cb** as a colorless oil (18.9 mg, 42%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.87 (brs, 1H), 8.56 (d, *J* = 4.8 Hz, 1H), 7.95 (d, *J* = 5.2 Hz, 1H), 7.78-7.69 (m, 1H), 7.49 (d, *J* = 5.2 Hz, 1H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.21 (dd, *J* = 7.2, 5.0 Hz, 1H), 4.04 (s, 3H), 4.02 (s, 3H), 1.87 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.6, 162.4, 158.3, 147.9, 141.8, 141.2, 137.3, 134.8, 122.1, 119.6, 117.30, 61.3, 57.6, 54.1, 27.7; HRMS (EI-TOF) calcd for $C_{16}H_{19}N_3O_3$ (M^+): 301.1426, found: 301.1418.

4-Methoxy-6-methyl-N-(2-(pyridin-2-yl)propan-2-yl)nicotinamide

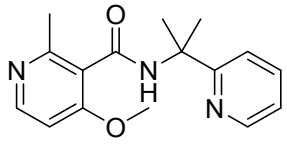


5d

The title compound **5d** was prepared according to **General Procedure.** A purification by flash chromatography in petroleum ether : tetrahydrofuran = 3 : 1 gave **5d** as a white solid (31.8 mg, 74%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.52 (brs, 1H), 9.08 (s, 1H), 8.53 (d, *J* = 4.7 Hz, 1H), 7.74-7.65 (m, 1H), 7.43 (d, *J* = 8.0 Hz, 1H), 7.22 – 7.11 (m, 1H), 6.72 (s, 1H), 4.05 (s, 3H), 2.55 (s, 3H), 1.84 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.0, 163.7, 163.1, 162.9, 153.1, 147.9, 137.1, 121.9, 119.7, 116.3, 105.7,

57.6, 55.9, 27.8, 24.8; HRMS (EI-TOF) calcd for $C_{16}H_{19}N_3O_2$ (M^+): 285.1477, found: 285.1484.

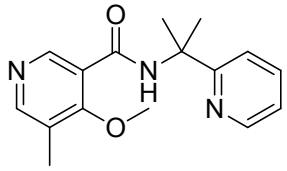
4-Methoxy-2-methyl-N-(2-(pyridin-2-yl)propan-2-yl)nicotinamide



5e

The title compound **5e** was prepared according to **General Procedure.** A purification by flash chromatography in dichloromethane : diethyl ether = 1 : 1 gave **5e** as a colorless oil (26.1 mg, 61%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 – 8.41 (m, 1H), 8.37 (d, *J* = 5.9 Hz, 1H), 8.03 (brs, 1H), 7.72 (td, *J* = 8.0, 1.8 Hz, 1H), 7.47 (d, *J* = 8.1 Hz, 1H), 7.18 (ddd, *J* = 7.4, 4.9, 0.9 Hz, 1H), 6.71 (d, *J* = 5.95Hz, 1H), 3.85 (s, 3H), 2.55 (s, 3H), 1.88 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.5, 164.3, 162.8, 156.6, 150.6, 147.7, 137.3, 123.3, 122.0, 119.6, 104.5, 57.4, 55.8, 27.6, 22.1; HRMS (EI-TOF) calcd for $C_{16}H_{19}N_3O_2$ (M^+): 285.1477, found: 285.1475.

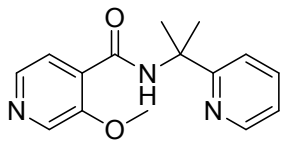
4-Methoxy-5-methyl-N-(2-(pyridin-2-yl)propan-2-yl)nicotinamide



5f

The title compound **5f** was prepared according to **General Procedure.** A purification by flash chromatography in petroleum ether : tetrahydrofuran = 2 : 1 gave **5f** as a colorless oil (20.4 mg, 48%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.36 (brs, 1H), 8.94 (s, 1H), 8.59 – 8.50 (m, 1H), 8.45 (s, 1H), 7.78-7.68 (m, 1H), 7.46 (d, *J* = 8.1 Hz, 1H), 7.25 – 7.16 (m, 1H), 3.95 (s, 3H), 2.32 (s, 3H), 1.88 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.6, 163.6, 163.2, 154.4, 151.2, 147.9, 137.2, 126.4, 123.3, 122.1, 119.6, 61.2, 57.5, 27.6, 13.4; HRMS (EI-TOF) calcd for $C_{16}H_{19}N_3O_2$ (M^+): 285.1477, found: 285.1487.

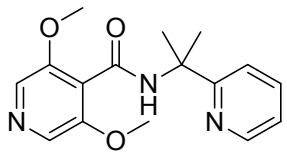
3-Methoxy-N-(2-(pyridin-2-yl)propan-2-yl)isonicotinamide



5ga

The title compound **5ga** was prepared according to **General Procedure.** A purification by flash chromatography in ethyl acetate gave **5ga** as a colorless oil (30.8 mg, 76%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.85 (brs, 1H), 8.54 (dd, *J* = 4.8, 0.7 Hz, 1H), 8.44 (s, 1H), 8.35 (d, *J* = 4.9 Hz, 1H), 7.97 (d, *J* = 4.9 Hz, 1H), 7.70 (td, *J* = 7.9, 1.8 Hz, 1H), 7.43 (d, *J* = 8.1 Hz, 1H), 7.18 (ddd, *J* = 7.4, 4.9, 0.8 Hz, 1H), 4.13 (s, 3H), 1.84 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.7, 162.0, 152.7, 147.9, 143.4, 137.2, 135.0, 129.6, 124.5, 122.0, 119.6, 57.7, 56.8, 27.6; HRMS (EI-TOF) calcd for $C_{15}H_{17}N_3O_2$ (M^+): 271.1321, found: 271.1318.

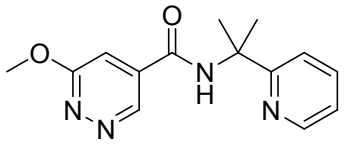
3,5-Dimethoxy-N-(2-(pyridin-2-yl)propan-2-yl)isonicotinamide



5gb

The title compound **5gb** was prepared according to **General Procedure.** A purification by flash chromatography in ethyl acetate gave **5gb** as a colorless oil (8.8 mg, 19%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (dd, *J* = 4.1, 0.9 Hz, 1H), 8.07 (s, 2H), 7.93 (brs, 1H), 7.72 (td, *J* = 8.0, 1.8 Hz, 1H), 7.50 (d, *J* = 8.1 Hz, 1H), 7.18 (ddd, *J* = 7.4, 4.9, 0.9 Hz, 1H), 3.92 (s, 6H), 1.88 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.3, 162.6, 152.7, 147.7, 137.2, 128.0, 122.0, 119.6, 100.1, 57.7, 57.1, 27.8; HRMS (EI-TOF) calcd for $C_{16}H_{19}N_3O_3$ (M^+): 301.1426, found: 301.1430.

6-Methoxy-N-(2-(pyridin-2-yl)propan-2-yl)pyridazine-4-carboxamide

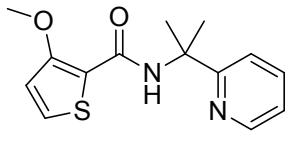


5h

The title compound **5h** was prepared according to **General Procedure.** A purification by flash chromatography in ethyl acetate : tetrahydrofuran = 3 : 2 gave **5h** as a white solid (11.2 mg, 27%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.48 (brs, 1H), 8.67 (s, 1H),

8.60 (d, J = 4.0 Hz, 1H), 8.07 (s, 1H), 7.64 (td, J = 7.9, 1.8 Hz, 1H), 7.41 (d, J = 8.0 Hz, 1H), 7.14 (ddd, J = 7.4, 4.8, 0.9 Hz, 1H), 3.95 (s, 3H), 1.82 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.5, 164.8, 161.9, 152.3, 148.7, 144.2, 141.8, 136.8, 121.8, 119.4, 57.8, 47.4, 28.1; HRMS (EI-TOF) calcd for $C_{14}H_{16}N_4O_2$ (M^+): 272.1273, found: 272.1280.

3-Methoxy-N-(2-(pyridin-2-yl)propan-2-yl)thiophene-2-carboxamide

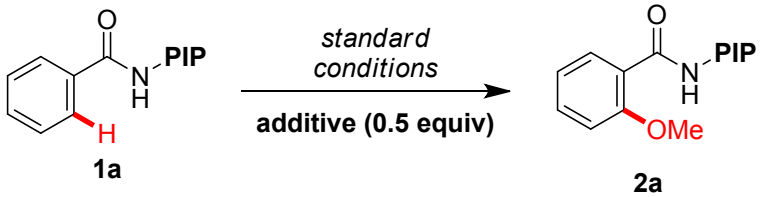


5i

The title compound **5i** was prepared according to **General Procedure.** A purification by flash chromatography in petroleum ether : tetrahydrofuran = 3 : 1 gave **5i** as a white solid (27.7 mg, 67%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (brs, 1H), 8.56 (d, J = 4.8 Hz, 1H), 7.69 (td, J = 7.6, 1.3 Hz, 1H), 7.45 (d, J = 8.1 Hz, 1H), 7.33 (d, J = 5.5 Hz, 1H), 7.17 (dd, J = 7.4, 4.9 Hz, 1H), 6.86 (d, J = 5.5 Hz, 1H), 4.05 (s, 3H), 1.84 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.1, 161.2, 156.1, 148.1, 137.0, 128.3, 121.8, 119.6, 118.8, 115.6, 59.1, 57.4, 28.1; HRMS (EI-TOF) calcd for $C_{14}H_{16}N_2O_2S$ (M^+): 276.0932, found: 276.0936.

2.6 Mechanistic Investigation

Radical Scavenger Reactions

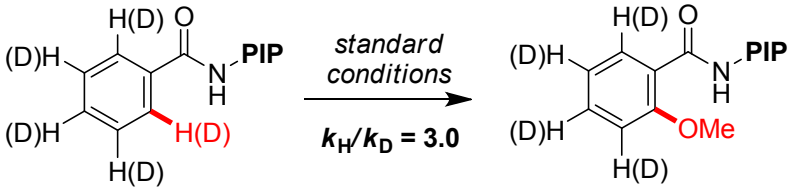


1a **2a**

Additive	Yield
no additive	88%
1,4-dinitrobenzene	32%
1,1-diphenylethylene	50%
2,6-Di-tert-butyl-4-methylphenol	35%

To a 50 mL sealed tube was added substrate (0.15 mmol), $(CuOH)_2CO_3$ (1.6 mg, 0.0075 mmol), KOCN (18.2 mg, 0.225 mmol) and additives (0.5 equiv), Methanol (2 mL). The mixture was stirred at 120 °C oil bath for 24 hours. Then the reaction mixture was cooled to room temperature, diluted with dichloromethane and quenched with saturated sodium sulfide solution. The aqueous phase was extracted with dichloromethane (3×10 mL). The combined organic phase was dried with anhydrous magnesium sulfate. After concentration, the yields were determined by 1H NMR spectroscopy

Intermolecular Competition KIE

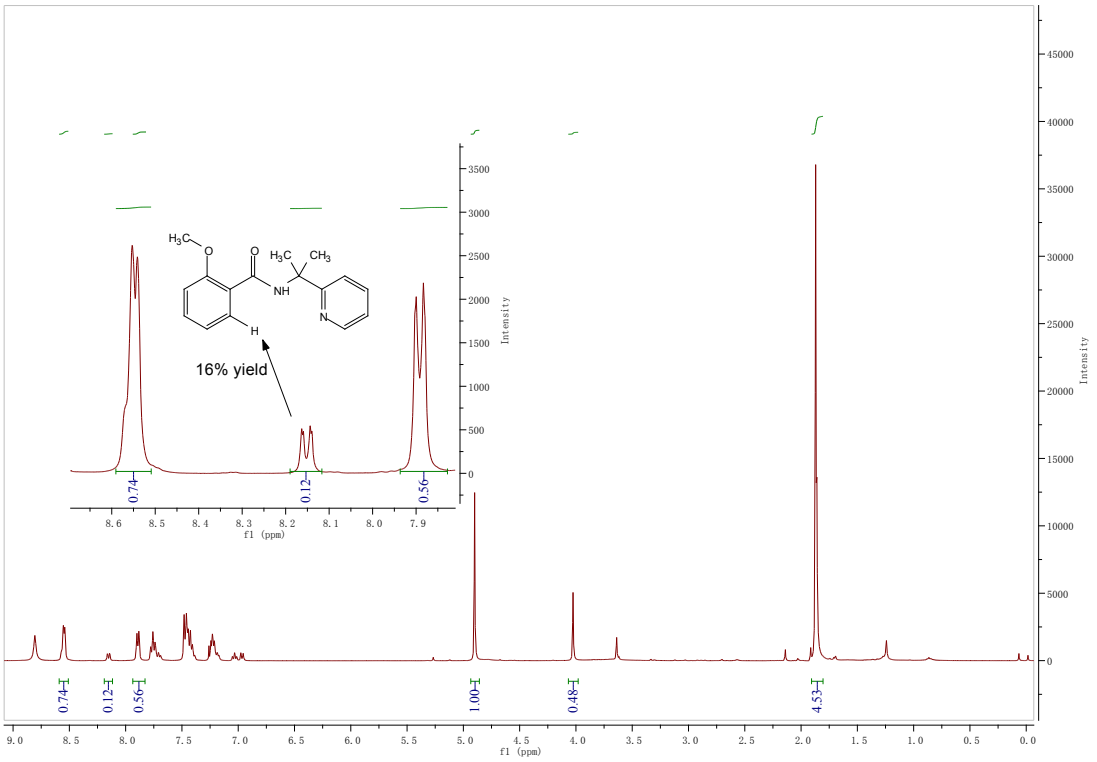


1a*/*d*$_5$-*1a

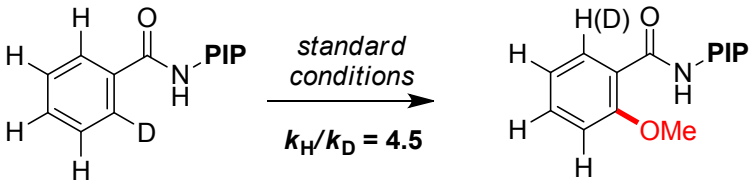
2a/*d*$_4$-**2a**, 21% yield

To a 50 mL sealed tube was added substrate **1a** (0.075 mmol) and *d*$_5$-**1a** (0.075 mmol), $(CuOH)_2CO_3$ (1.6 mg, 0.0075 mmol), KOCN (18.2 mg, 0.225 mmol) and Methanol (2 mL). The mixture was stirred at 120 °C oil bath for 6 hours.Then the reaction mixture was cooled to room temperature, diluted with dichloromethane and quenched with saturated sodium sulfide solution. The aqueous phase was extracted with dichloromethane (3×10 mL). The combined organic phase was dried with anhydrous magnesium sulfate. After concentration, The ratio of product **2a**/*d*$_4$-**2a** was analyzed by ^{1}H NMR using CH_2Br_2 as an internal standard.

^{1}H NMR spectrum of product from the intermolecular KIE experiment



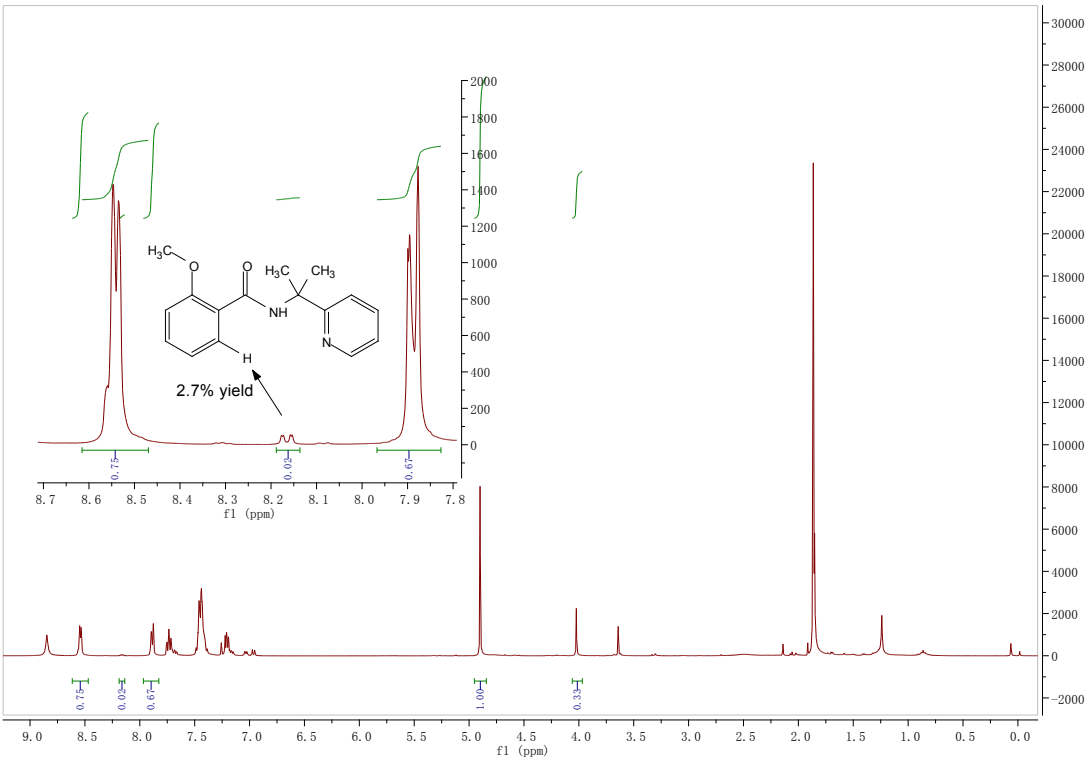
Intramolecular Competition KIE



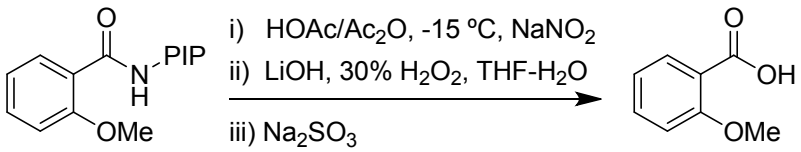
d$_1$-**1a** **2a**/*d*$_1$-**2a**,15% yield

To a 50 mL sealed tube was added substrate *d*$_1$-**1a** (0.15 mmol), $(CuOH)_2CO_3$ (1.6 mg, 0.0075 mmol), KOCN (18.2 mg, 0.225 mmol) and Methanol (2 mL). The mixture was stirred at 120 ^oC oil bath for 13 hours.Then the reaction mixture was cooled to room temperature, diluted with dichloromethane and quenched with saturated sodium sulfide solution. The aqueous phase was extracted with dichloromethane (3×10 mL). The combined organic phase was dried with anhydrous magnesium sulfate. After concentration, The ratio of product **2a**/*d*$_1$-**2a** was analyzed by 1H NMR using CH_2Br_2 as an internal standard.

^{1}H NMR spectrum of product from the intramolecular KIE experiment



2.7 Removal of Directing Group[2]



2a **6a**, 77%

A solution of substrate **2a** (67.5 mg, 0.25 mmol) in a mixture of acetic acid (0.7 mL) and acetic anhydride (3.5 mL) was cooled to -15 °C and 380 mg of granular sodium nitrite (22 equiv) was added slowly in portions. After being stirred for 48 hours at -15 °C and the mixture poured into a mixture of ice and water. (Caution! The nitrosoamide is unstable and the subsequent work-up should be carried out at 0 °C) The nitrosoamide was extracted with cold ether, and the organic phase was washed with ice water, with an aqueous solution of sodium carbonate (5%), with ice water, and then dried with anhydrous sodium sulfate under ice bath. The solvent was removed under reduce pressure under ice bath. The residue was dissolved in THF (10 mL)/ H_2O (3 mL) and cooled to -15 °C. Then 30% H_2O_2 (1.2 mL) was added followed by lithium hydroxide monohydrate (209.8 mg, 5.0 mmol). The mixture was

stirred at -15 °C for 2 hours and at 0 °C overnight, and then quenched with an aqueous solution of Na_2SO_3. The mixture was basified with 1N NaOH and washed with ethyl acetate. The aqueous phase was acidied with 1M HCl and extracted with ethyl acetate. The organic layer was washed with brine, dried over anhydrous sodium sulfate and concentrated in vacuo. The resulting residue was purified by flash chromatography (petroleum ether : ethyl acetate : acetic acid = 2 : 1 : 0.05). **6a** was obtained as a light yellow solid (29.2 mg, 77%). 1H NMR (400 MHz, CDCl3) δ 10.83（brs, 1H）,8.16 (dd, J = 7.8, 1.8 Hz, 1H), 7.57 (ddd, J = 8.4, 7.5, 1.8 Hz, 1H), 7.17 – 7.10 (m, 1H), 7.06 (d, J = 8.4 Hz, 1H), 4.07 (s, 3H). 13C NMR (101 MHz, CDCl3) δ 165.7, 158.2, 135.2, 133.9, 122.3, 117.7, 111.8, 56.8. HRMS (EI-TOF) calc. for $C_8H_8O_3$ (M+): 152.0473, found: 152.0475.

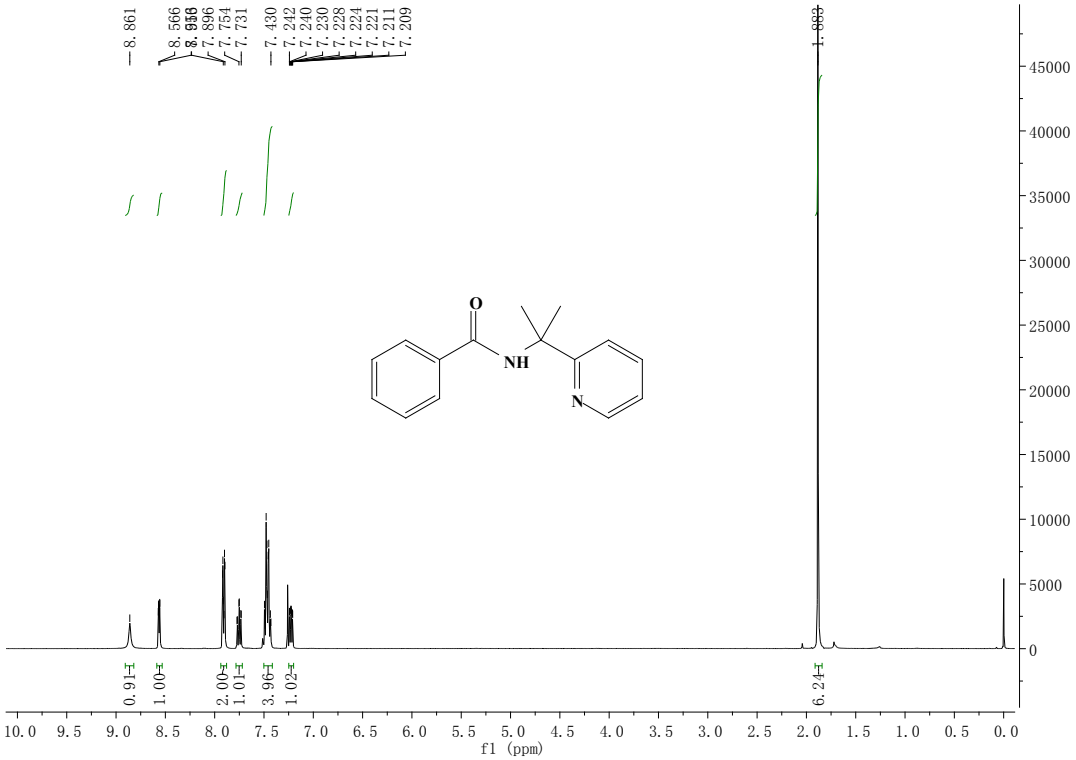
3. References:

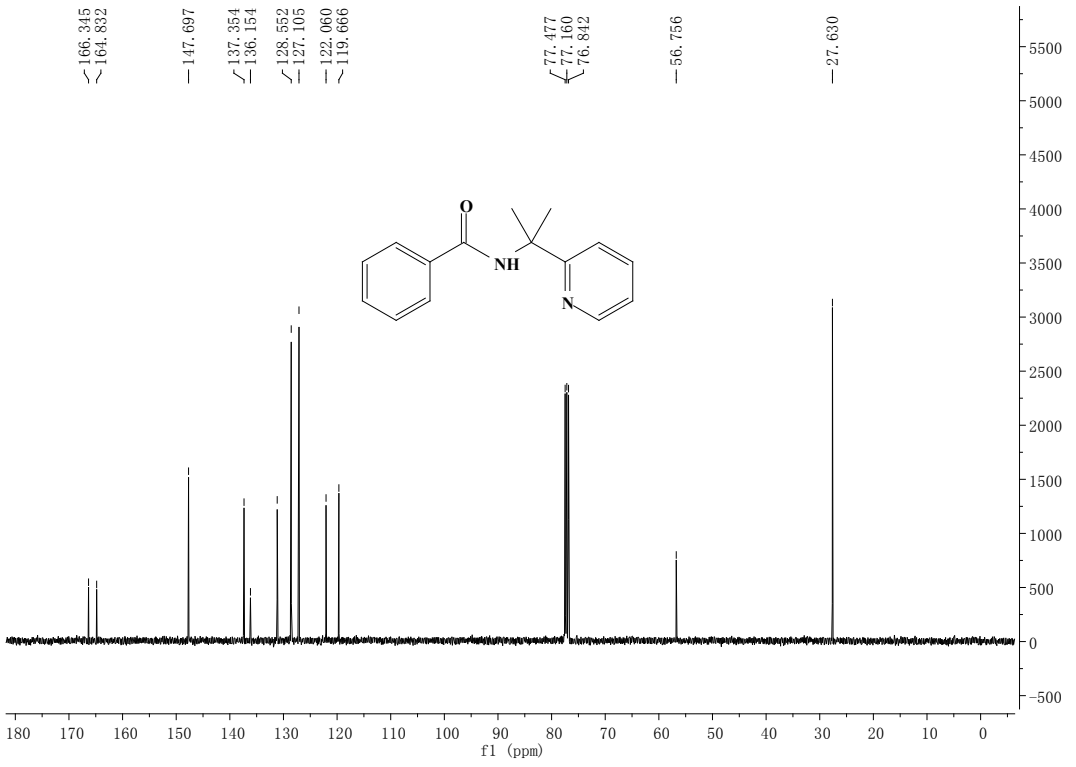
[1] Q. Zhang, X-S. Yin, S. Zhao, S-L. Fang and B-F. Shi, Chem. Commun, 2014, **50**, 8353

[2] F-J. Chen, S. Zhao, F. Hu, K. Chen, Q. Zhang, S-Q. Zhang and B-F. Shi, Chem. Sci., 2013, **4**, 4187

4. NMR Spectra

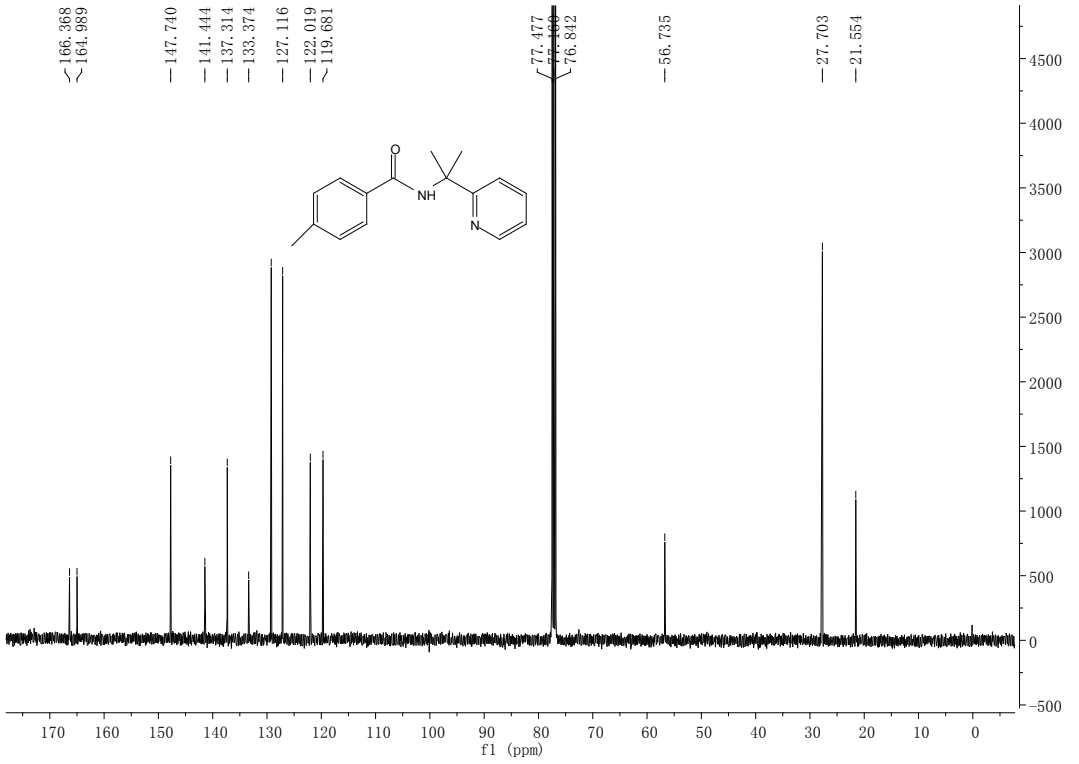
1a



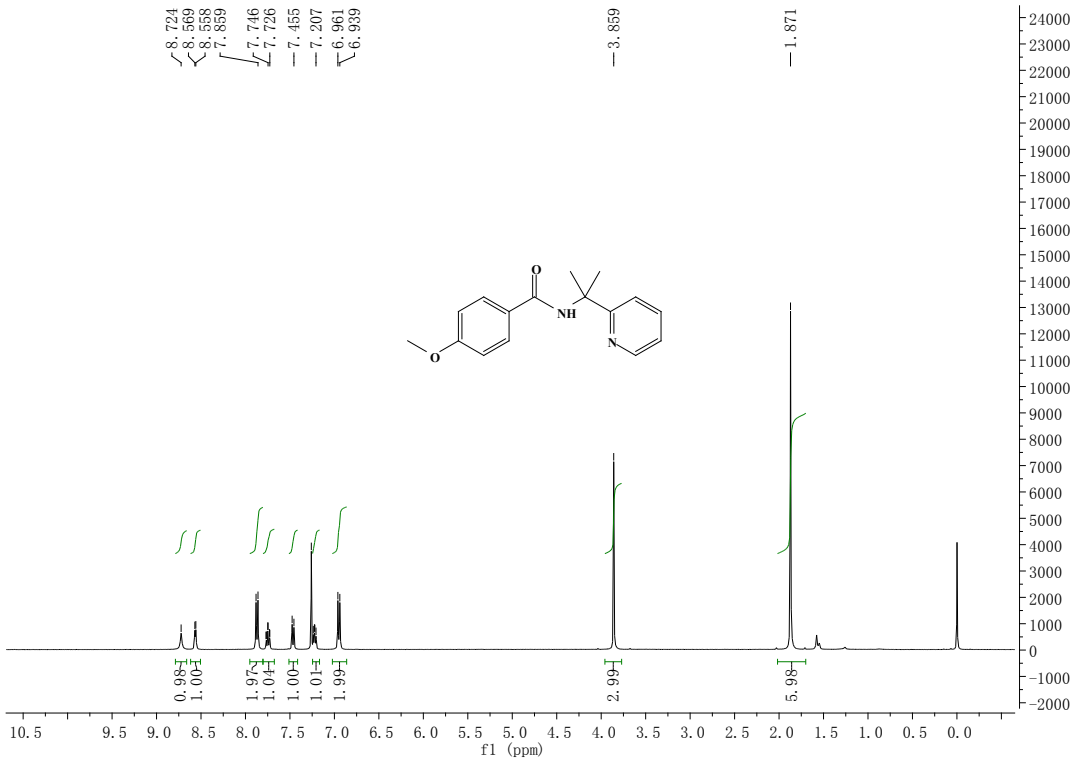


1b


8.765
8.567
8.556
7.789
7.744
7.724
7.454
7.260
7.239
7.222
7.218
7.204
2.403
1.875
O
NH
N
0.97
1.00
1.98
1.08
1.04
3.48
3.14
6.23
f1 (ppm)


166.368
164.989
147.740
141.444
137.314
133.374
127.116
122.019
119.681
77.477
77.160
76.842
56.735
27.703
21.554
O
NH
N
f1 (ppm)

1c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8.569
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7.726
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7.207
6.961
6.939
3.859
1.871
O
NH
N
O
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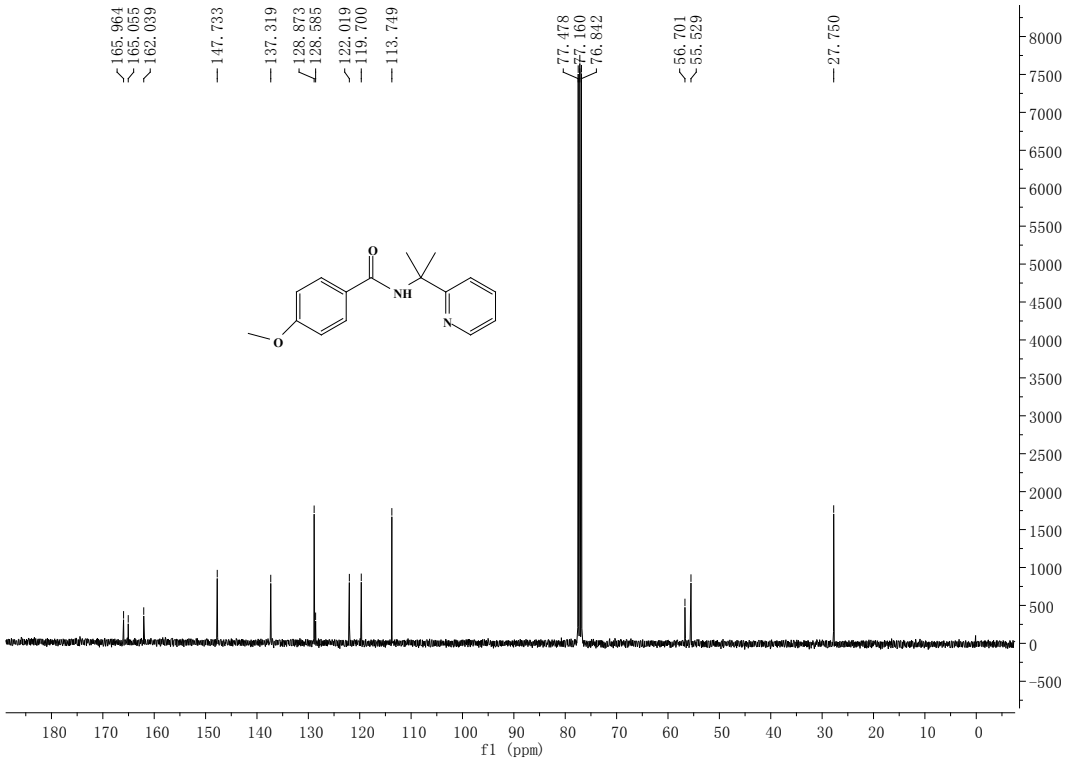
1.00
1.97
1.04
1.00
1.01
1.99
2.99
5.98
f1 (ppm)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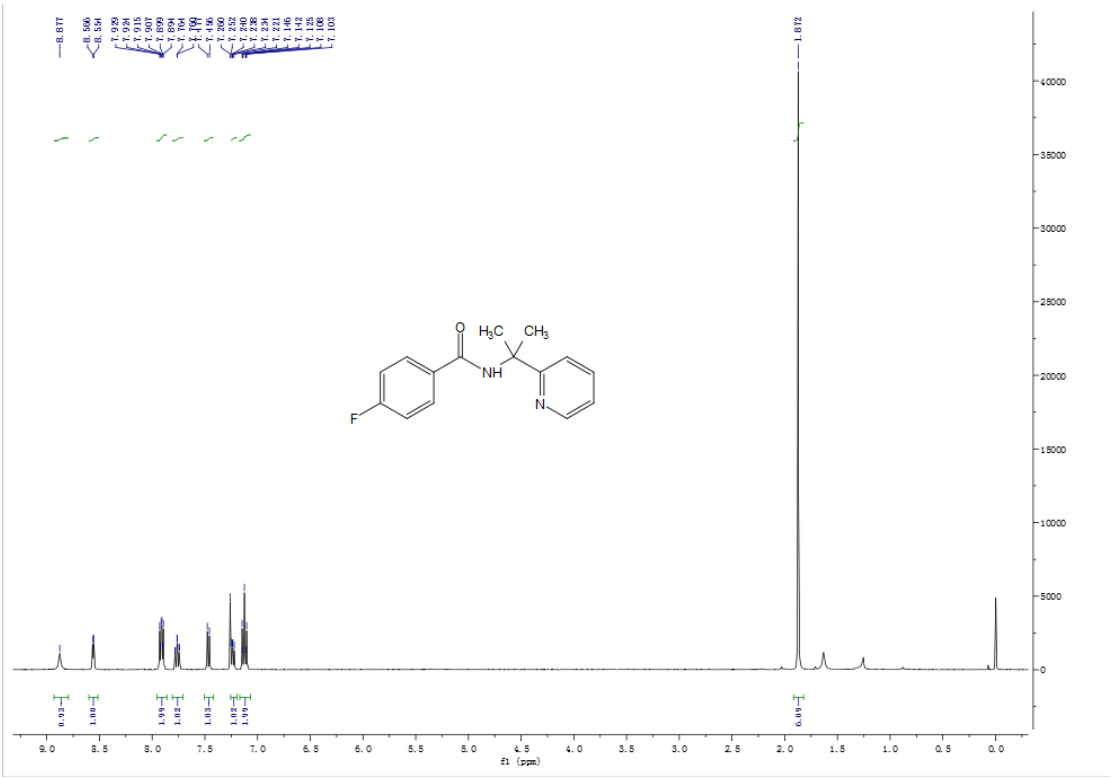
165.055
162.039
147.733
137.319
128.873
128.585
122.019
119.700
113.749
77.478
77.160
76.842
56.701
55.529
27.750
O
NH
N
O
f1 (ppm)

1d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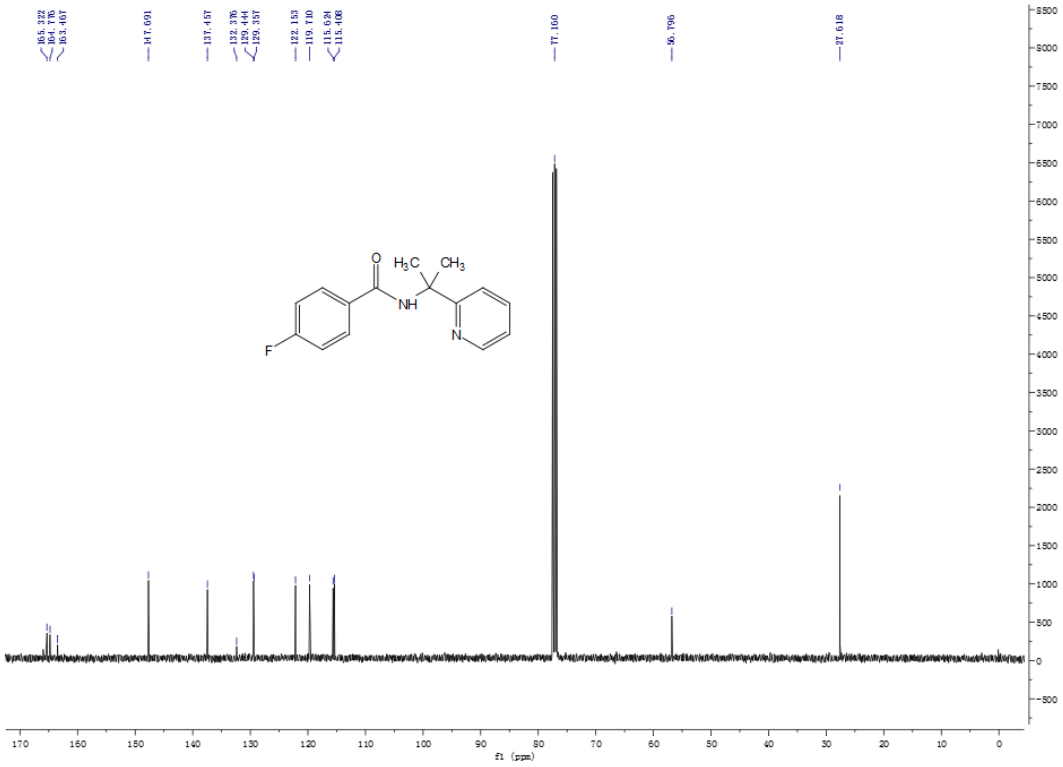
8.566
8.554
7.929
7.924
7.915
7.910
7.899
7.894
7.764
7.496
7.255
7.240
7.238
7.234
7.231
7.146
7.125
7.108
7.103
1.872
O
H3C
CH3
NH
N
F
f1 (ppm)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164.776
163.467
147.691
137.457
132.376
129.444
129.357
122.153
119.710
115.634
115.408
77.160
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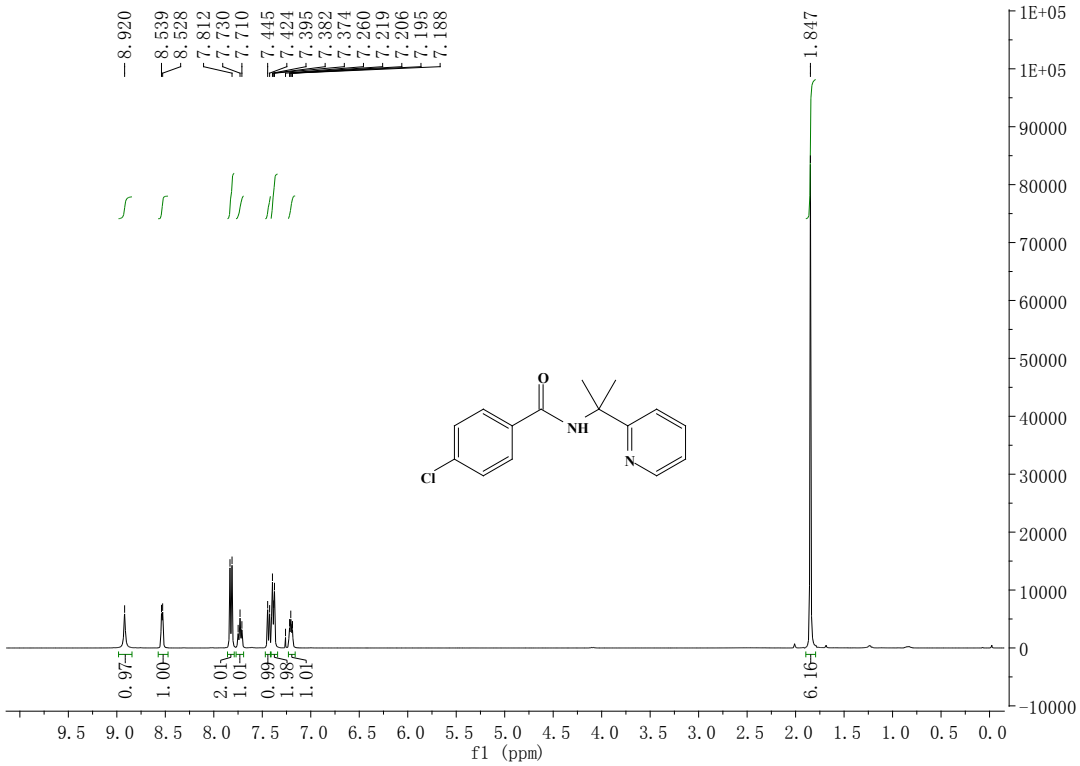
H3C
CH3
NH
N
F
f1 (ppm)

1e


8.920
8.539
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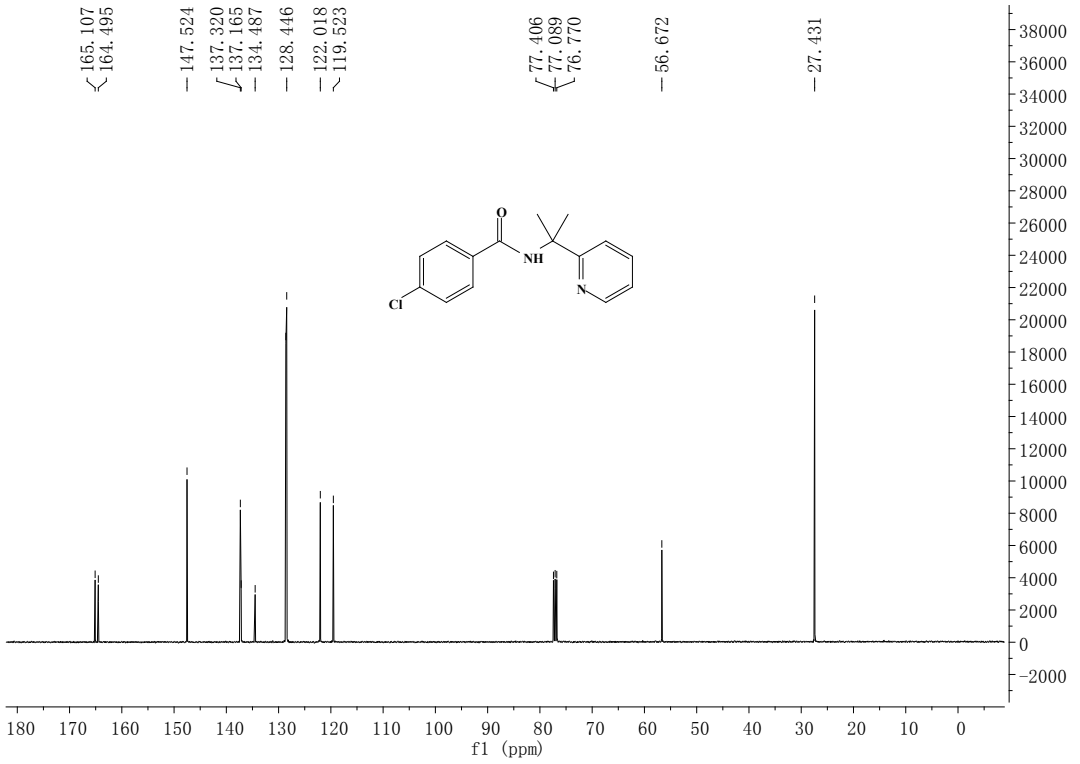
7.730
7.710
7.445
7.424
7.395
7.382
7.374
7.260
7.219
7.206
7.195
7.188
1.847
0.97
1.00
2.01
1.01
0.99
1.99
1.01
6.16
O
NH
N
Cl
f1 (ppm)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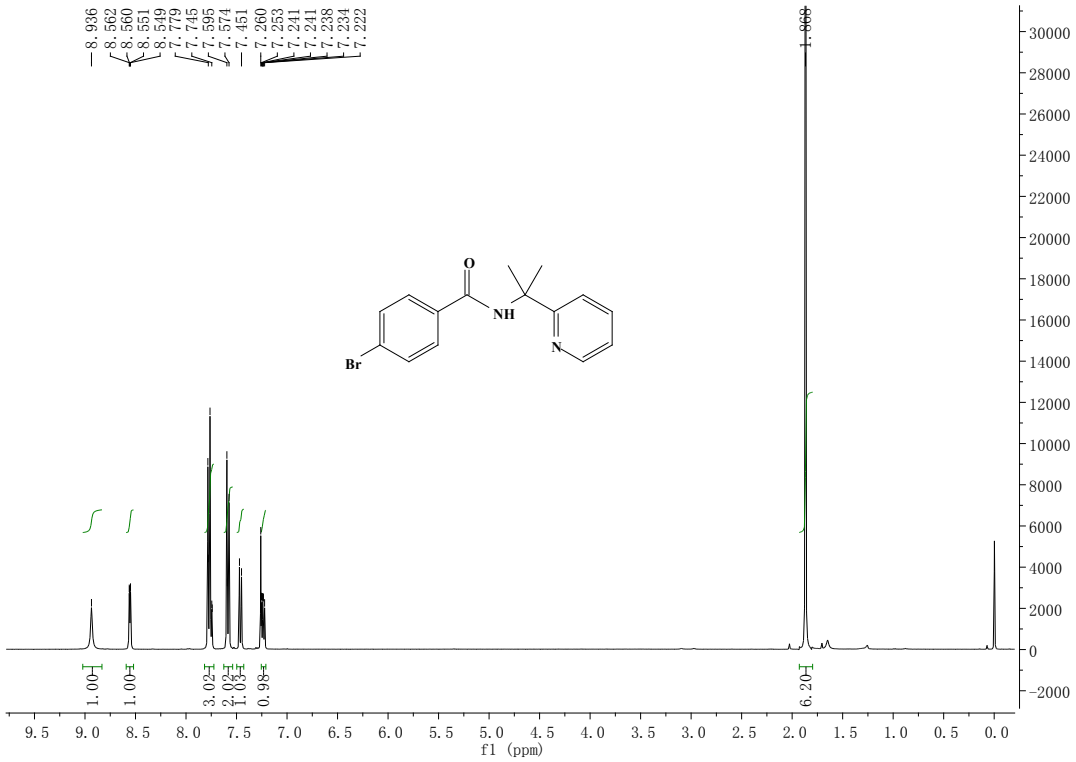
56.672
27.431
O
NH
N
Cl
f1 (ppm)

1f


8.936
8.562
8.560
8.551
8.549
7.779
7.745
7.595
7.574
7.451
7.260
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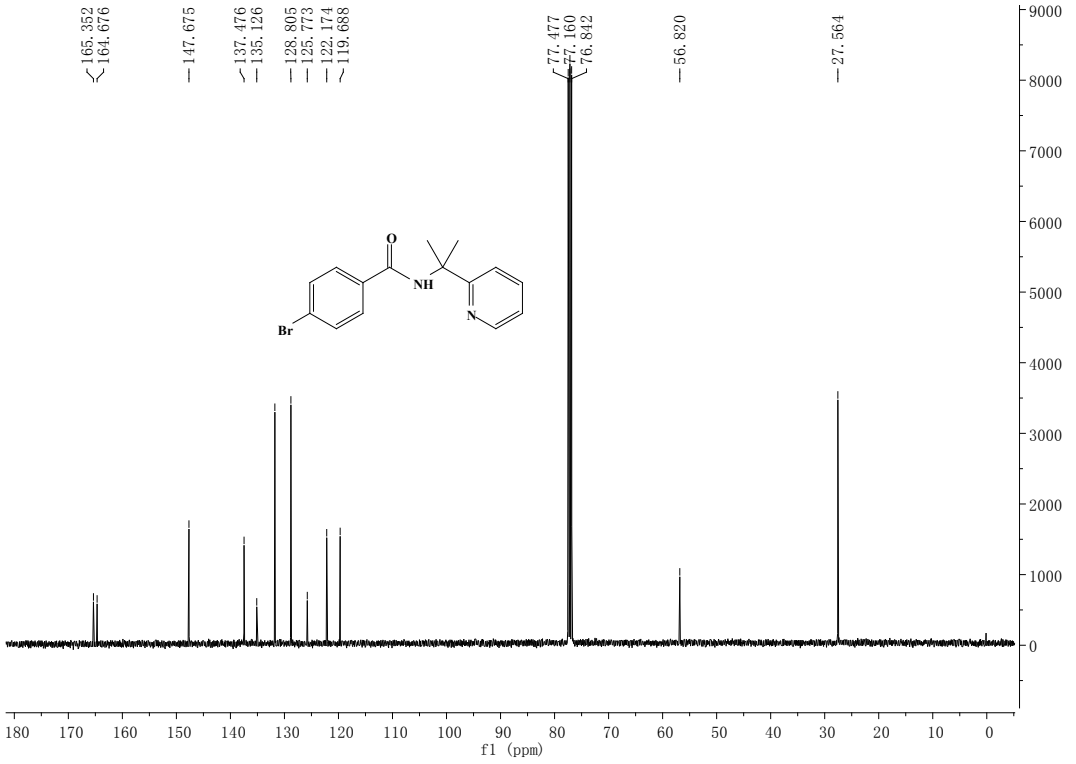
7.241
7.241
7.238
7.234
7.222
1.868
O
NH
N
Br
1.00
1.00
3.02
2.02
1.03
0.98
6.20
f1 (ppm)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137.476
135.126
128.805
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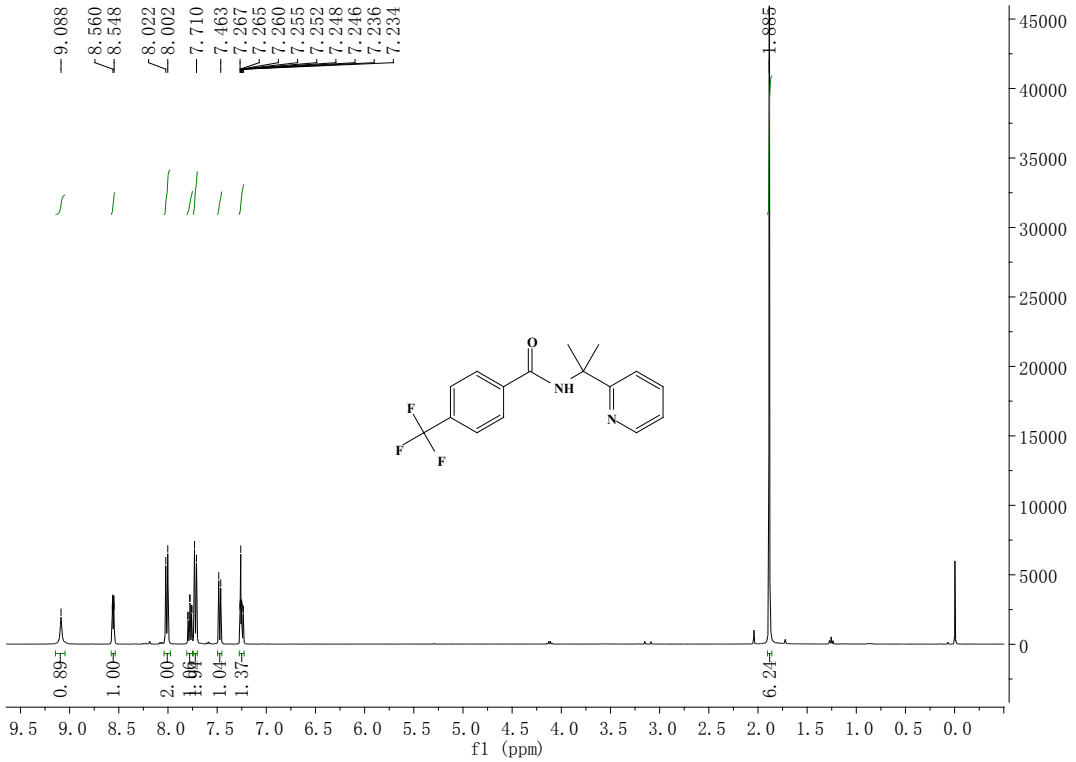
122.174
119.688
77.477
77.160
76.842
56.820
27.564
O
NH
N
Br
f1 (ppm)

1g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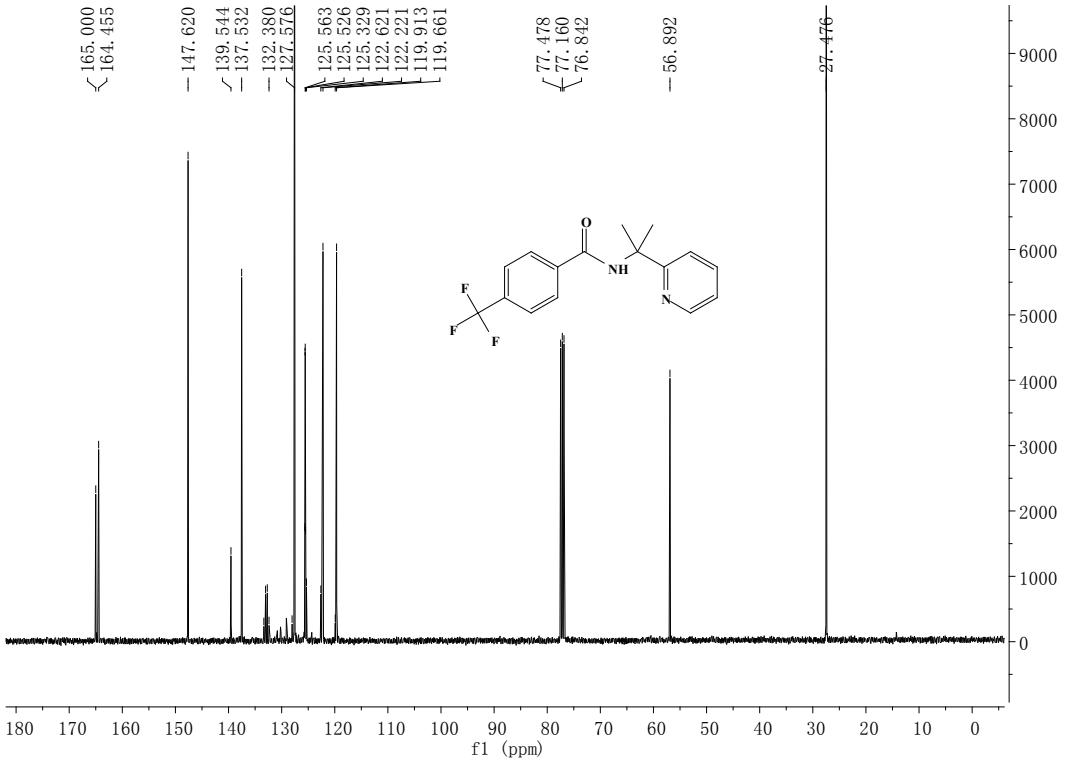
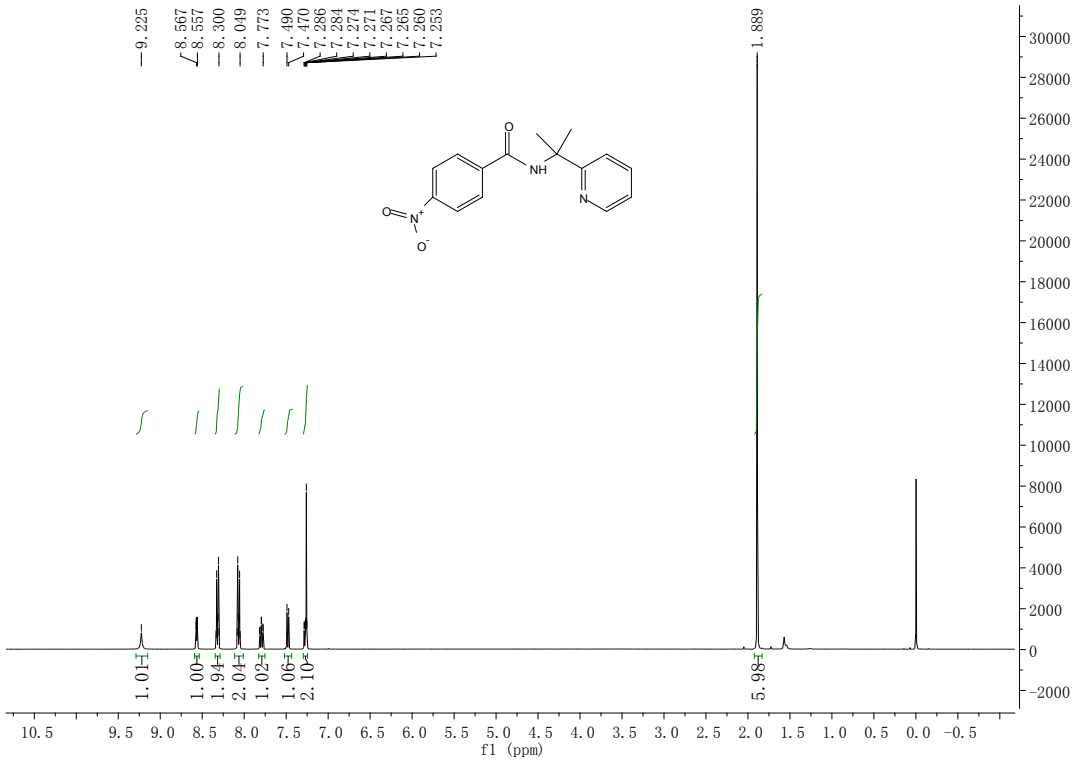
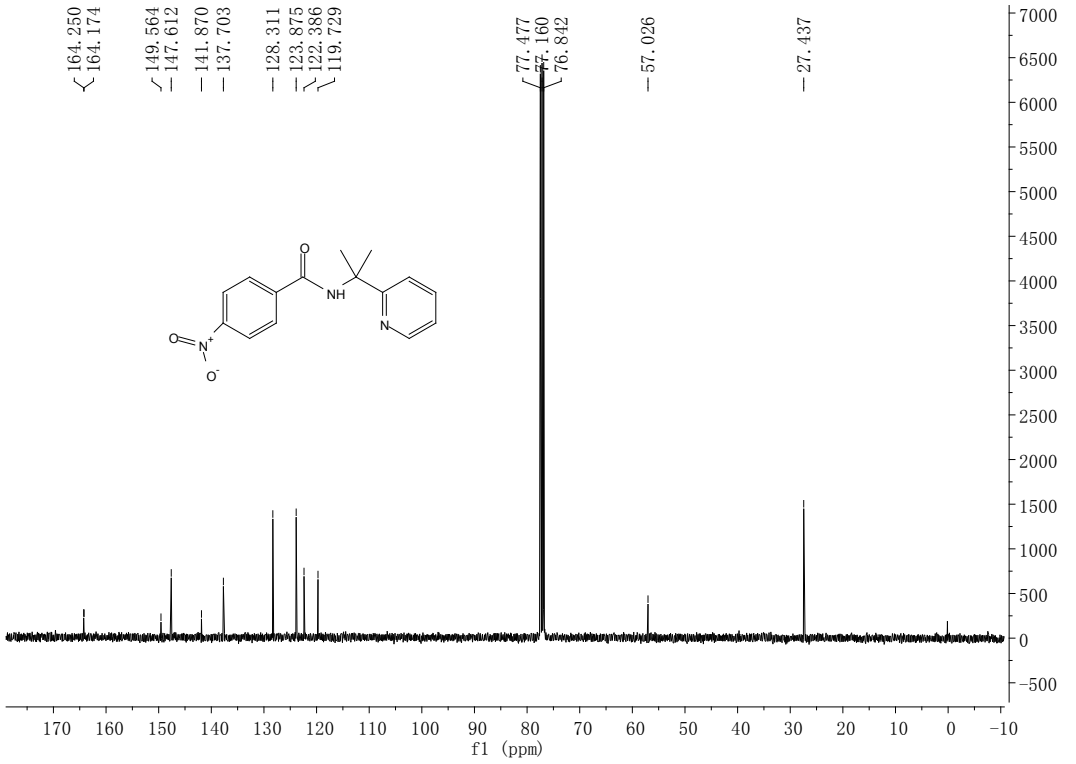
8.560
8.548
8.022
8.002
7.710
7.463
7.267
7.265
7.260
7.255
7.252
7.248
7.246
7.236
7.234
1.885
0.89
1.00
2.00
1.06
1.04
1.37
6.24
O
NH
N
F
F
F
f1 (ppm)

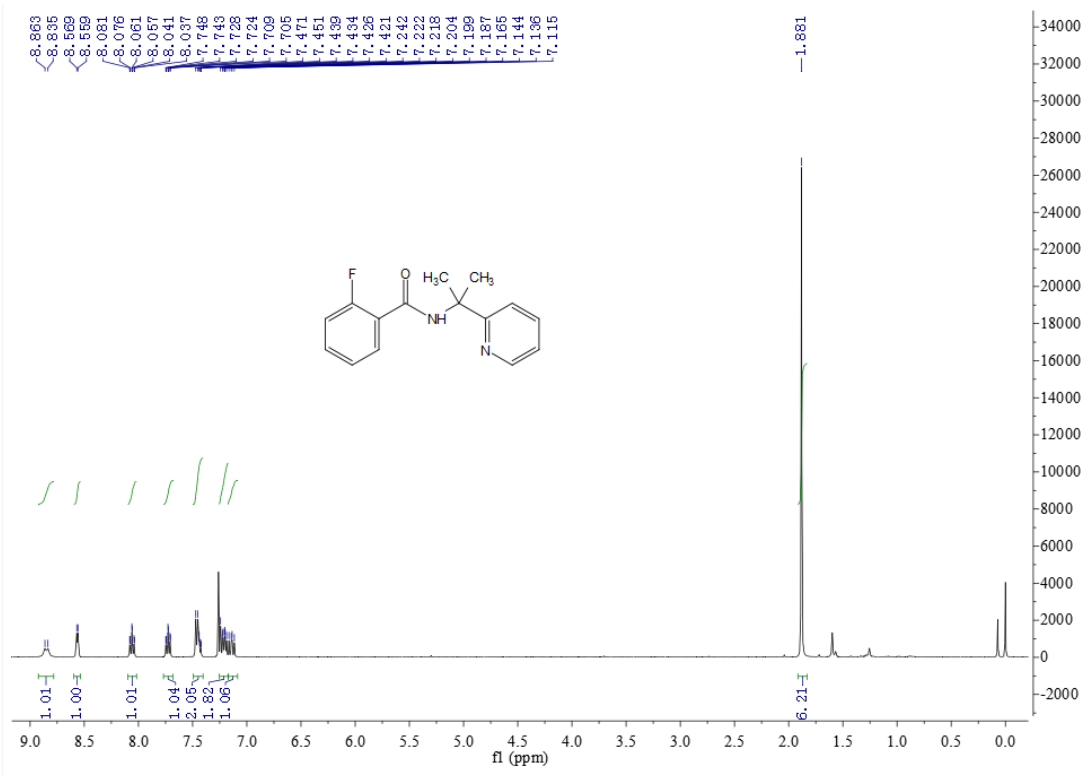

165.000
164.455
147.620
139.544
137.532
132.380
127.576
125.563
125.526
125.329
122.621
122.221
119.913
119.661
77.478
77.160
76.842
56.892
27.476
O
NH
N
F
F
F
f1 (ppm)

1h


9.225
8.567
8.557
8.300
8.049
7.773
7.490
7.470
7.286
7.284
7.274
7.271
7.267
7.265
7.260
7.253
1.889
1.01
1.00
1.94
2.04
1.02
1.06
2.10
5.98
f1 (ppm)


164.250
164.174
149.564
147.612
141.870
137.703
128.311
123.875
122.386
119.729
77.477
77.160
76.842
57.026
27.437
f1 (ppm)

1i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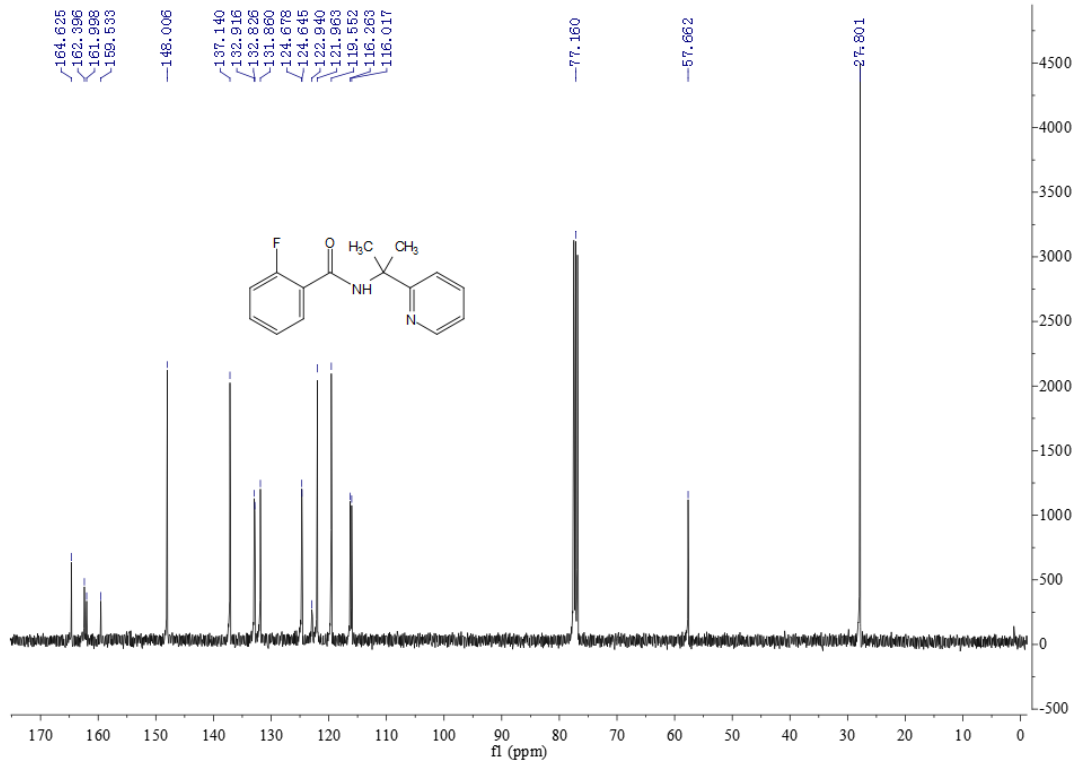
8.835
8.569
8.559
8.081
8.076
8.061
8.057
8.041
8.037
7.748
7.743
7.728
7.724
7.709
7.705
7.471
7.451
7.439
7.434
7.426
7.421
7.242
7.222
7.218
7.204
7.199
7.187
7.165
7.144
7.136
7.115
1.881
1.01
1.00
1.01
1.04
2.05
1.82
1.06
6.21
F
O
H3C
CH3
NH
N
fl (ppm)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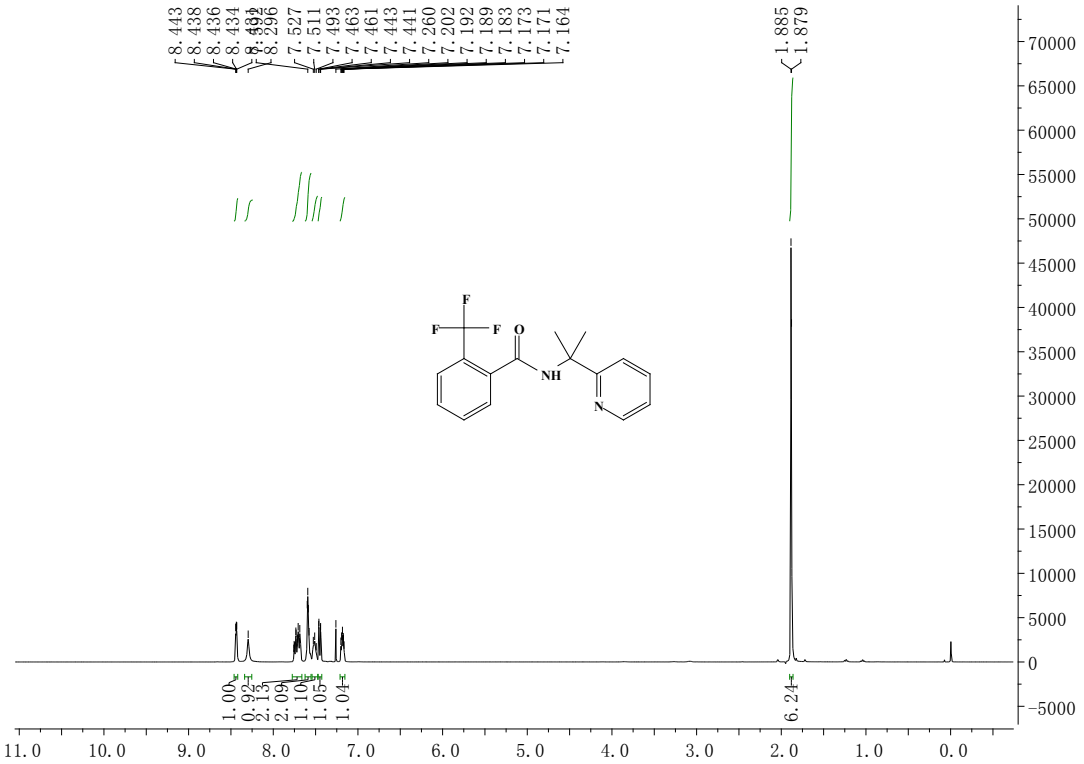
162.396
161.998
158.533
148.006
137.140
132.916
132.826
131.860
124.678
124.645
122.940
121.963
119.552
116.263
116.017
77.160
57.862
27.801
F
O
H3C
CH3
NH
N
fl (ppm)

1j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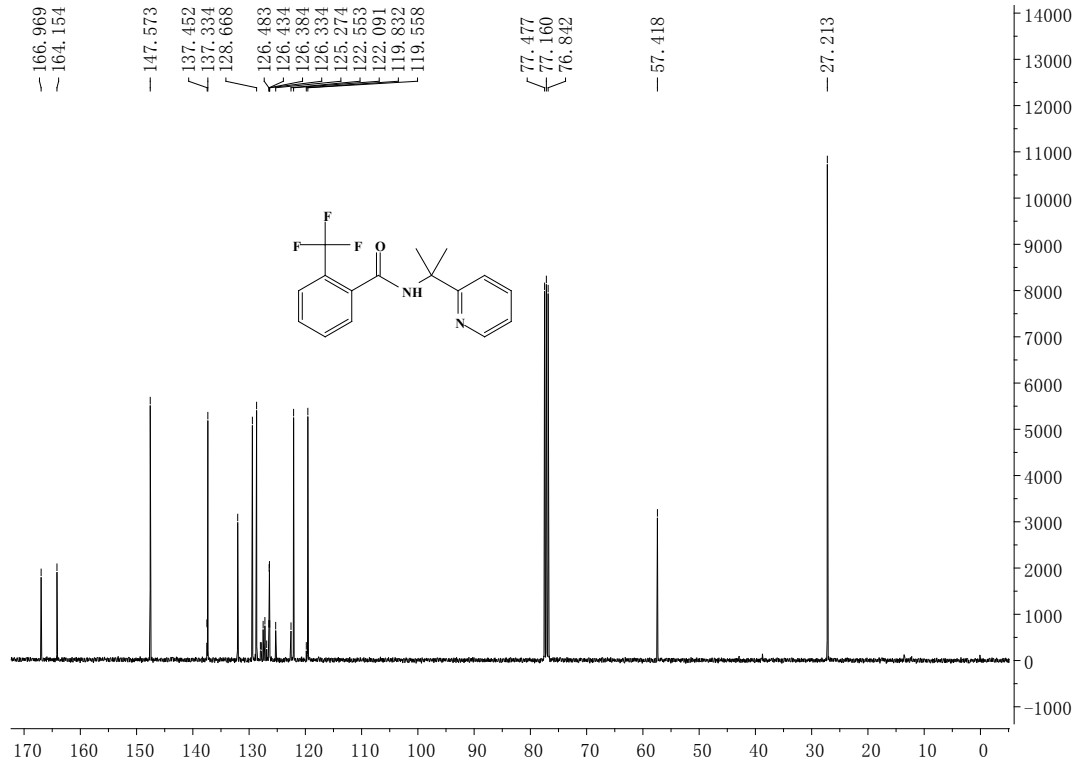
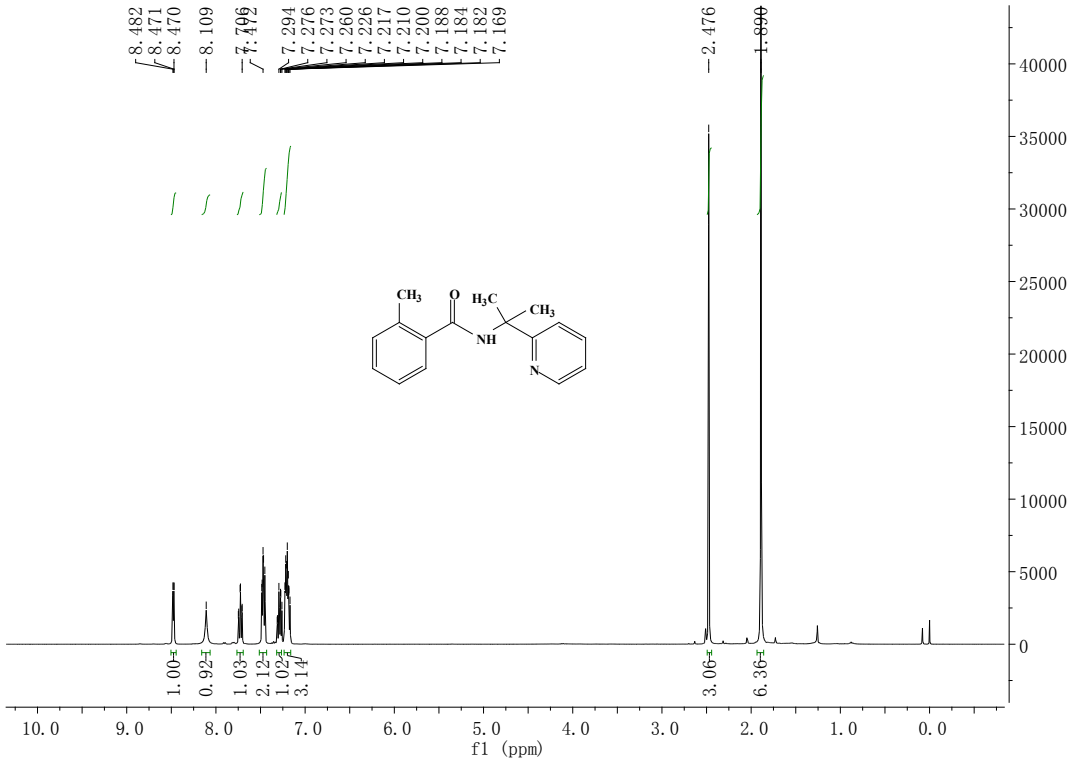
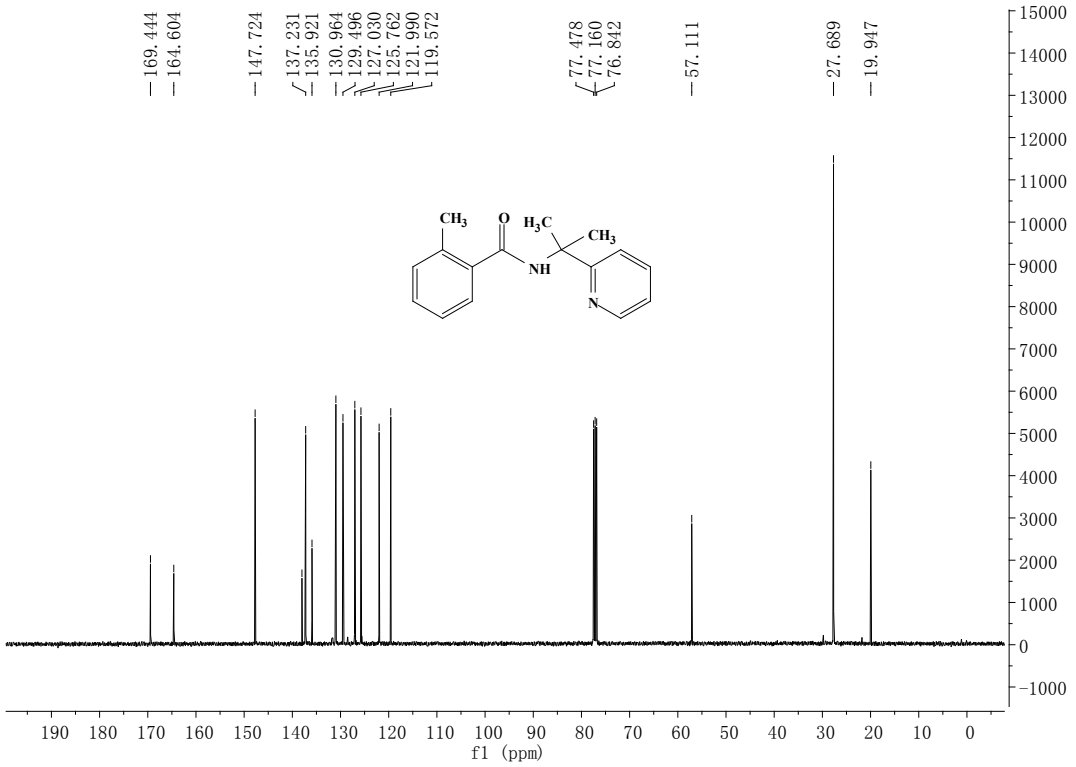
8.438
8.436
8.434
8.296
7.527
7.511
7.493
7.463
7.461
7.443
7.441
7.260
7.202
7.192
7.189
7.183
7.173
7.171
7.164
1.885
1.879
F
F
F
O
NH
N
1.00
0.92
2.15
2.09
1.10
1.05
1.04
6.24

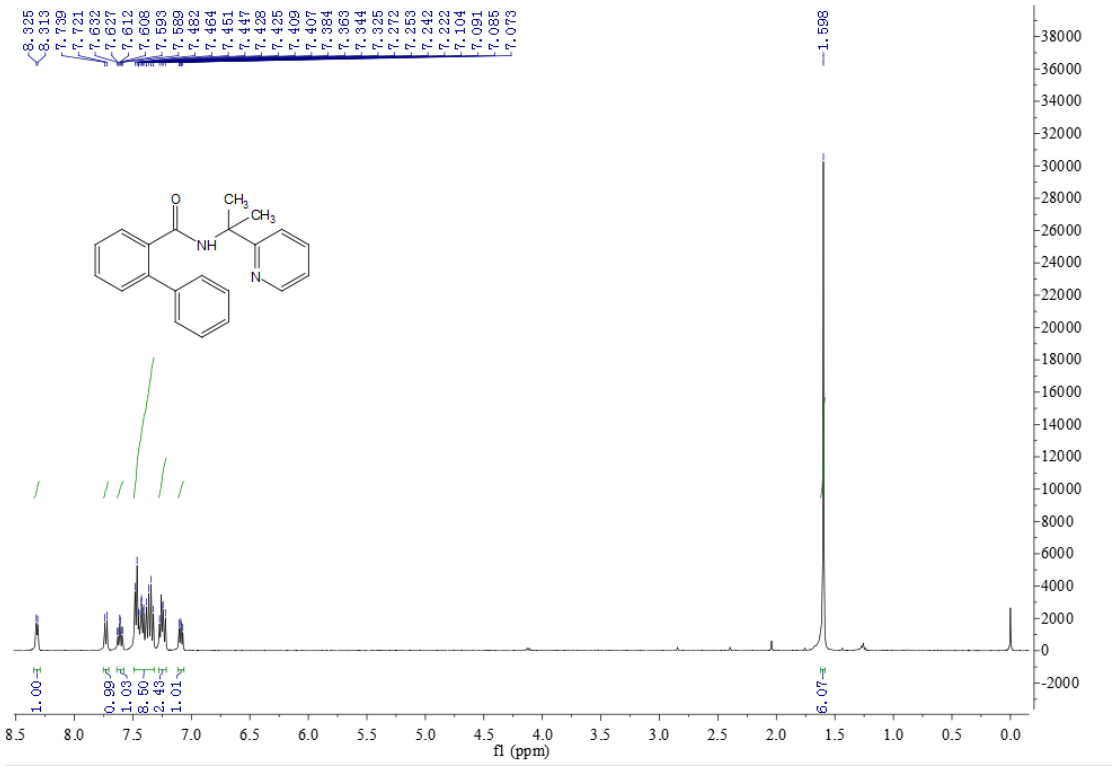

166.969
164.154
147.573
137.452
137.334
128.668
126.483
126.434
126.384
126.334
125.274
122.553
122.091
119.832
119.558
77.477
77.160
76.842
57.418
27.213
F
F
F
O
NH
N

1k


8.482
8.471
8.470
8.109
7.706
7.472
7.294
7.276
7.273
7.260
7.226
7.217
7.210
7.200
7.188
7.184
7.182
7.169
2.476
1.890
1.00
0.92
1.03
2.12
1.02
3.14
3.06
6.36
f1 (ppm)


169.444
164.604
147.724
137.231
135.921
130.964
129.496
127.030
125.762
121.990
119.572
77.478
77.160
76.842
57.111
27.689
19.947
f1 (ppm)

1l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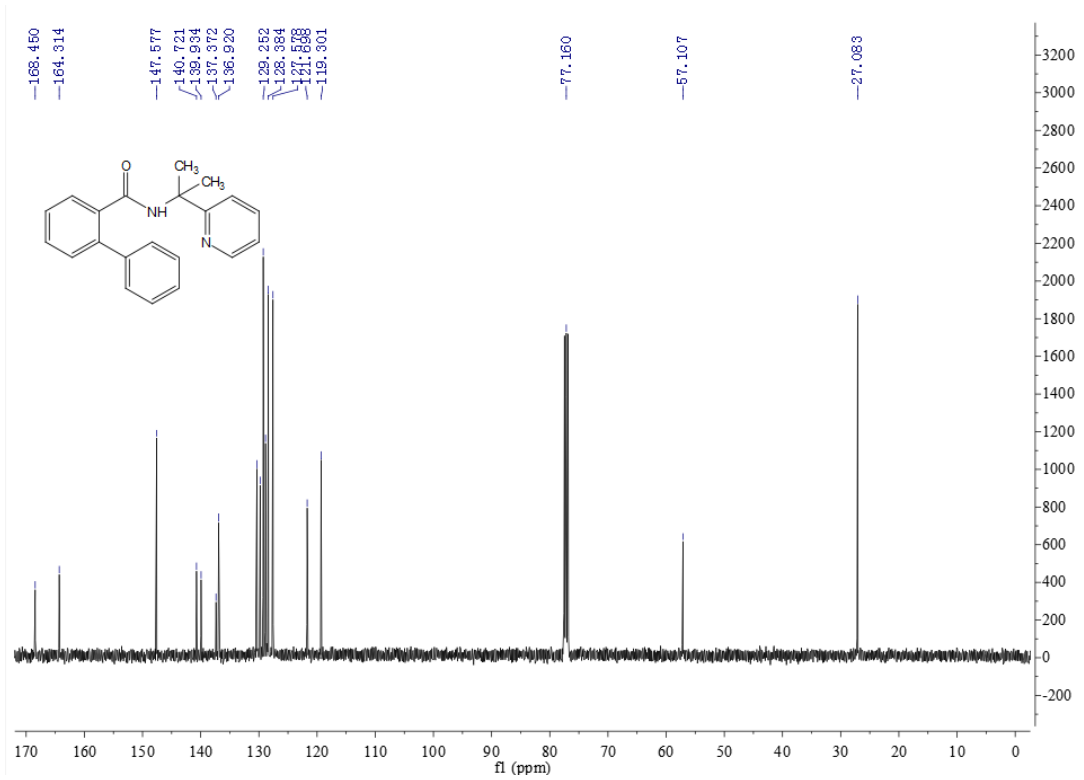
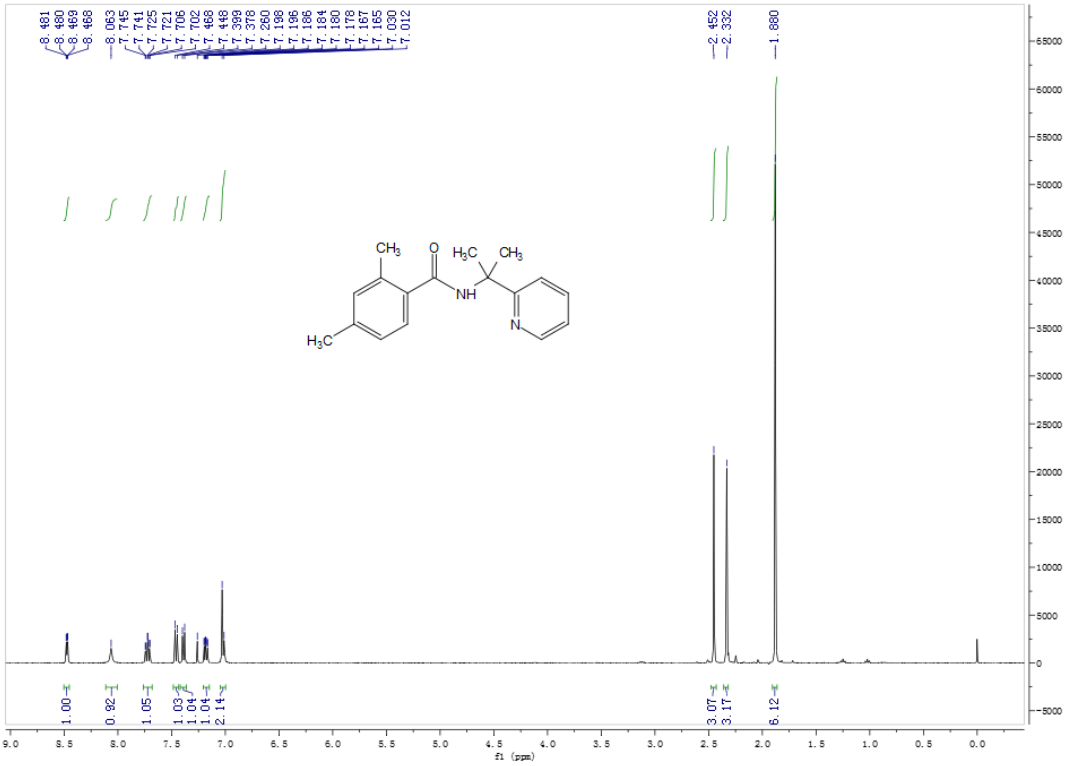
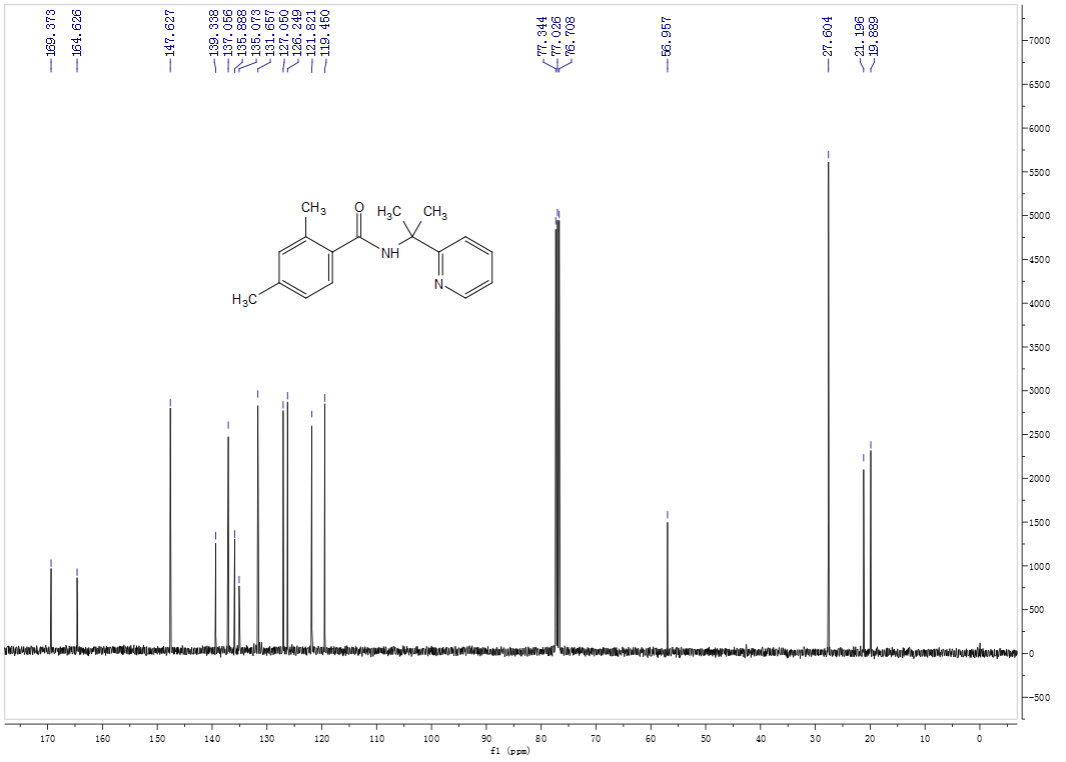
8.313
7.739
7.721
7.632
7.627
7.612
7.608
7.593
7.589
7.482
7.464
7.451
7.447
7.428
7.425
7.409
7.407
7.384
7.363
7.344
7.325
7.272
7.253
7.242
7.222
7.104
7.091
7.085
7.073
1.598
O
CH3
CH3
NH
N
1.00
0.99
1.03
8.50
2.43
1.01
6.07
f1 (ppm)

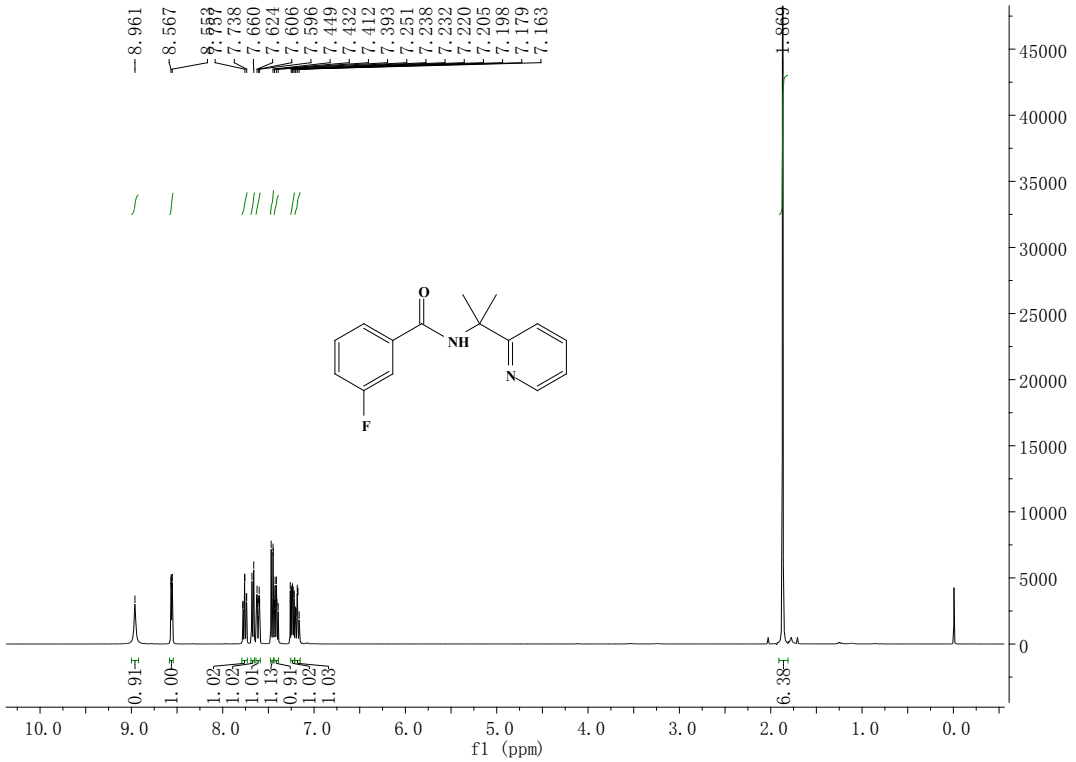

168.450
164.314
147.577
140.721
139.934
137.372
136.920
129.252
128.384
121.508
121.088
119.301
77.160
57.107
27.083
O
CH3
CH3
NH
N
f1 (ppm)

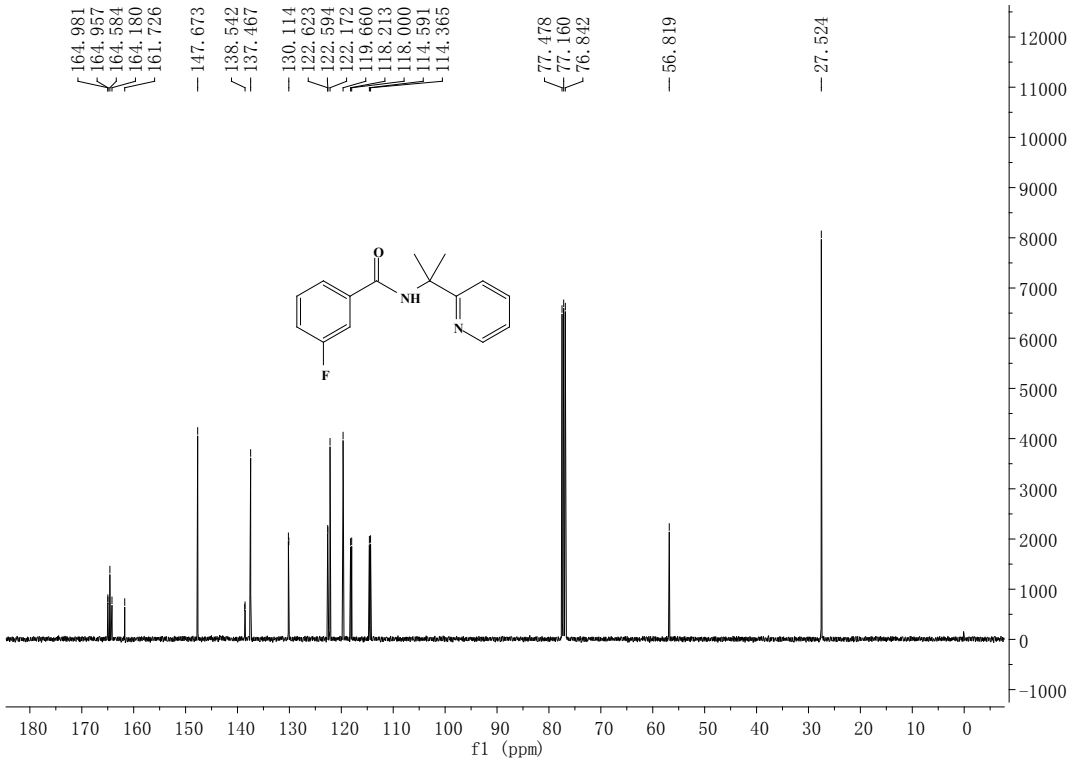
1m


8.481
8.480
8.469
8.468
8.063
7.745
7.741
7.725
7.721
7.706
7.702
7.468
7.448
7.399
7.378
7.260
7.198
7.196
7.186
7.184
7.180
7.178
7.167
7.165
7.030
7.012
2.452
2.332
1.880
CH3
O
H3C
CH3
NH
N
H3C
1.00
0.92
1.05
1.03
1.04
1.04
2.14
3.07
3.17
6.12
f1 (ppm)

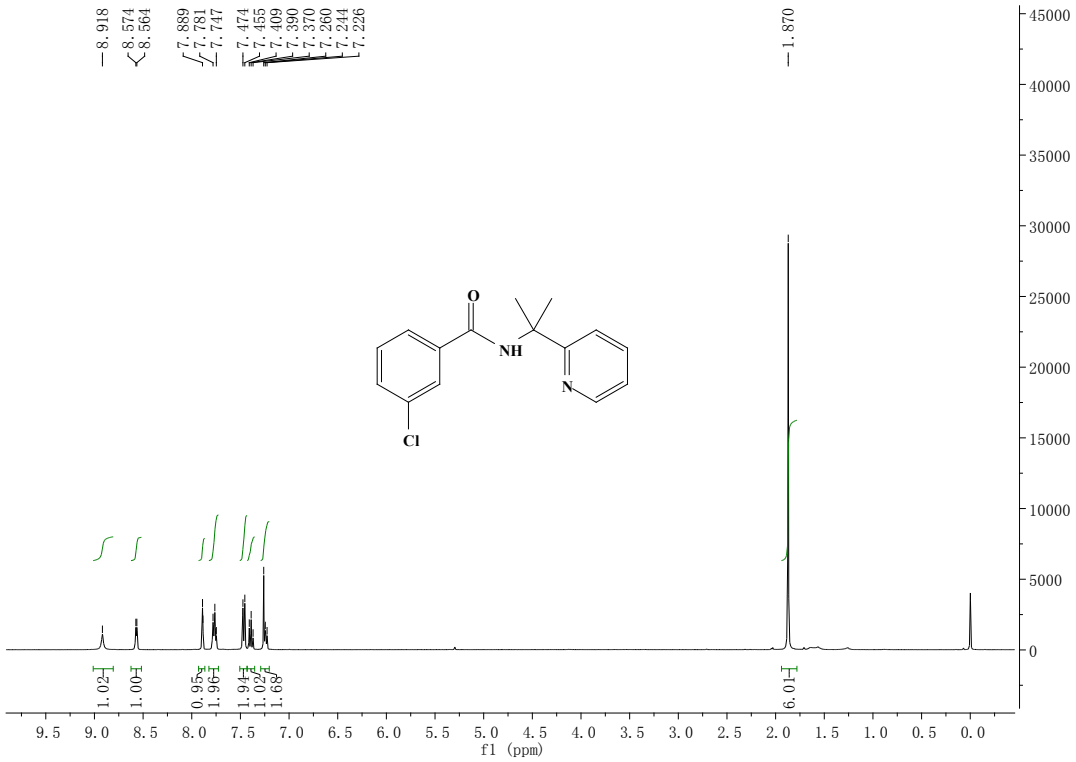

169.373
164.626
147.627
139.338
137.056
135.888
135.073
131.657
127.050
126.249
121.821
119.450
77.344
77.026
76.708
56.957
27.604
21.196
19.889
CH3
O
H3C
CH3
NH
N
H3C
f1 (ppm)

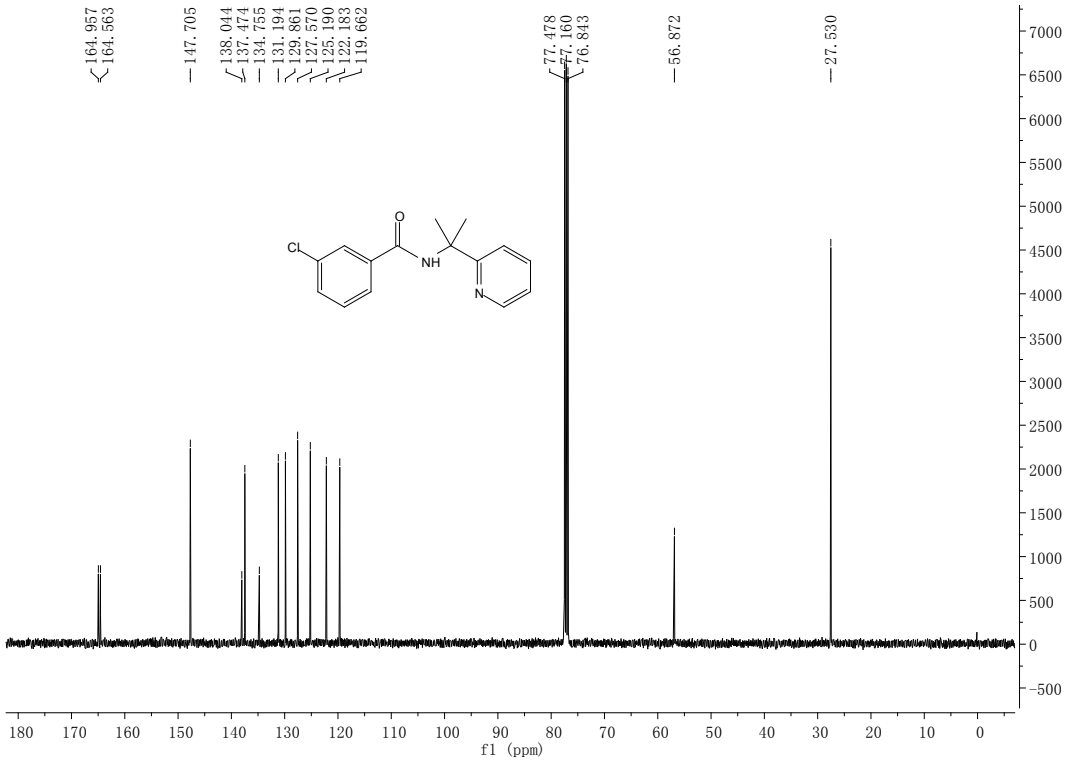
1n


8.961
8.567
8.553
8.537
7.738
7.660
7.624
7.606
7.596
7.449
7.432
7.412
7.393
7.251
7.238
7.232
7.220
7.205
7.198
7.179
7.163
1.869
O
NH
N
F
0.91
1.00
1.02
1.02
1.01
1.13
0.91
1.02
1.03
6.38
f1 (ppm)

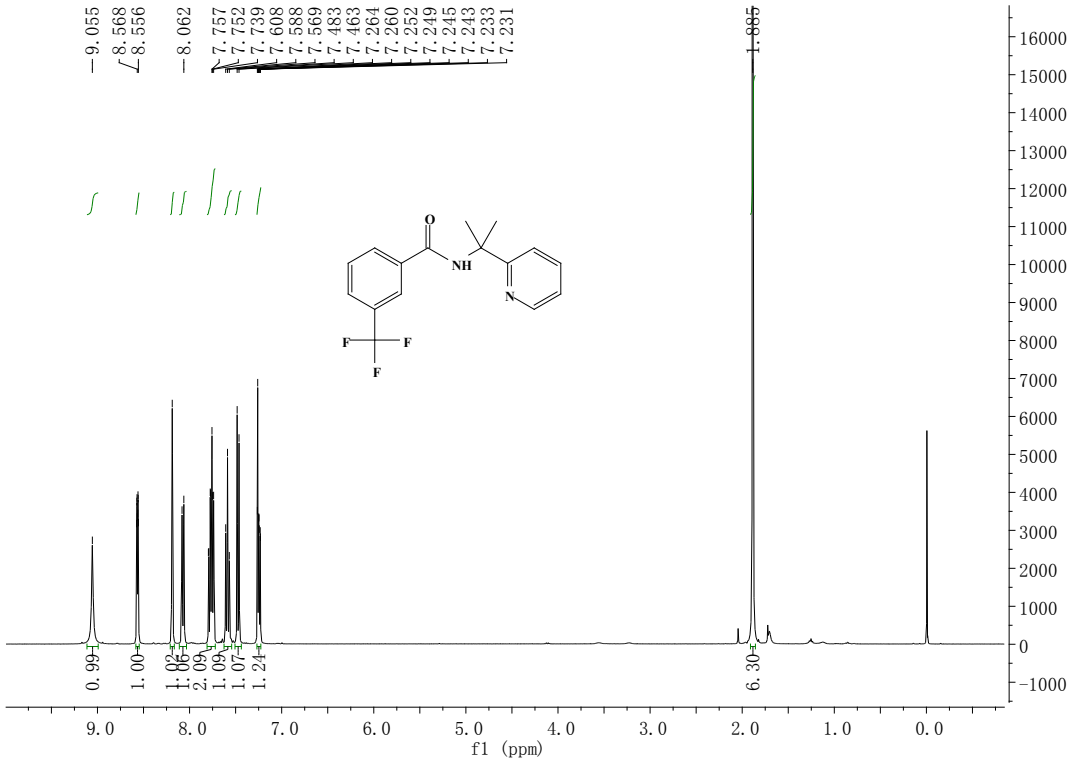

164.981
164.957
164.584
164.180
161.726
147.673
138.542
137.467
130.114
122.623
122.594
122.172
119.660
118.213
118.000
114.591
114.365
77.478
77.160
76.842
56.819
27.524
O
NH
N
F
f1 (ppm)

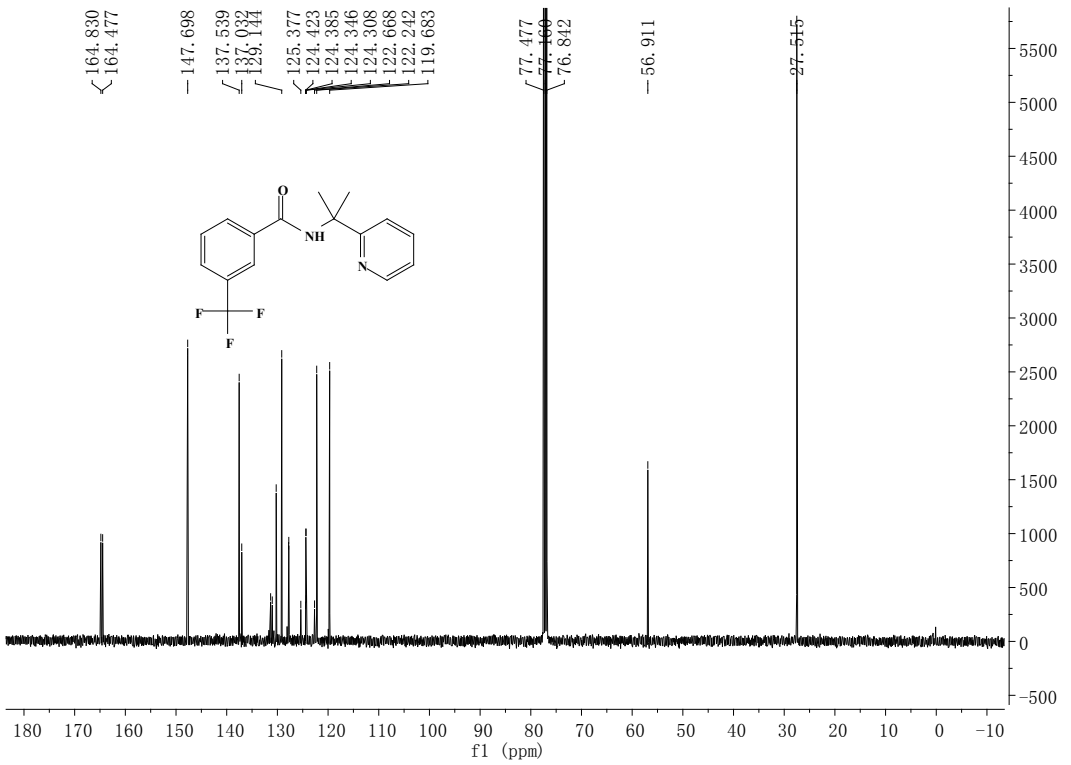
1o


8.918
8.574
8.564
7.889
7.781
7.747
7.474
7.455
7.409
7.390
7.370
7.260
7.244
7.226
1.870
O
NH
N
Cl
1.02
1.00
0.95
1.96
1.94
1.02
1.68
6.01
f1 (ppm)

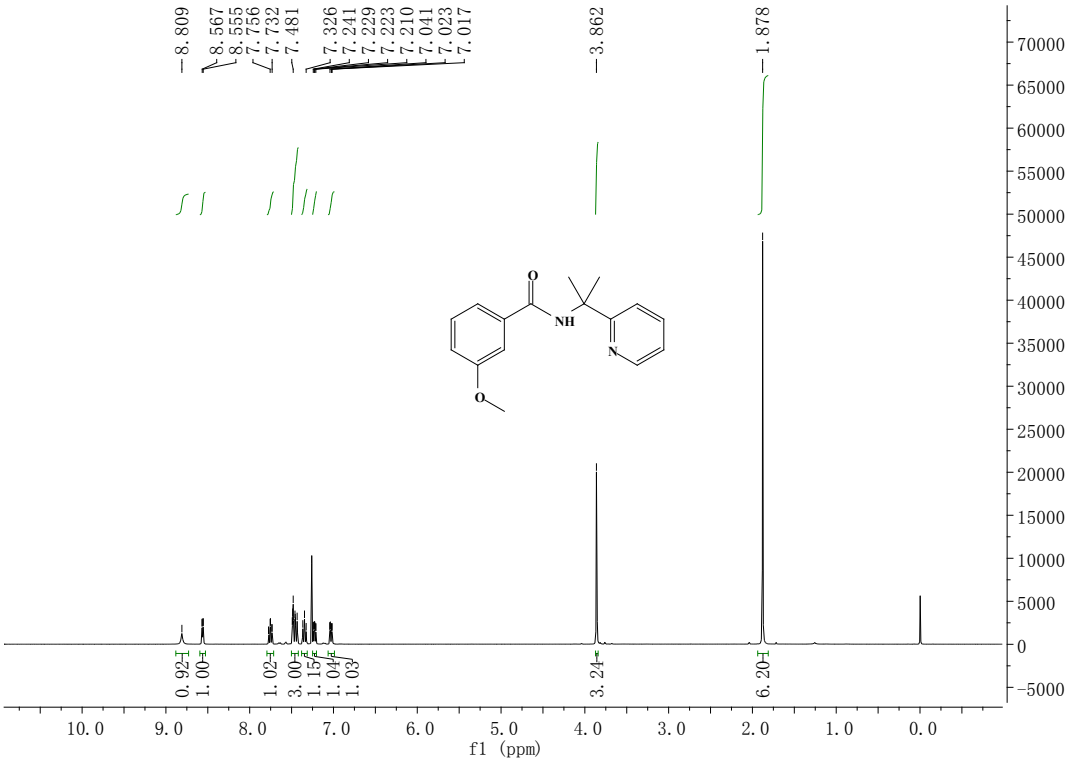

164.957
164.563
147.705
138.044
137.474
134.755
131.194
129.861
127.570
125.190
122.183
119.662
77.478
77.160
76.843
56.872
27.530
O
NH
N
Cl
f1 (ppm)

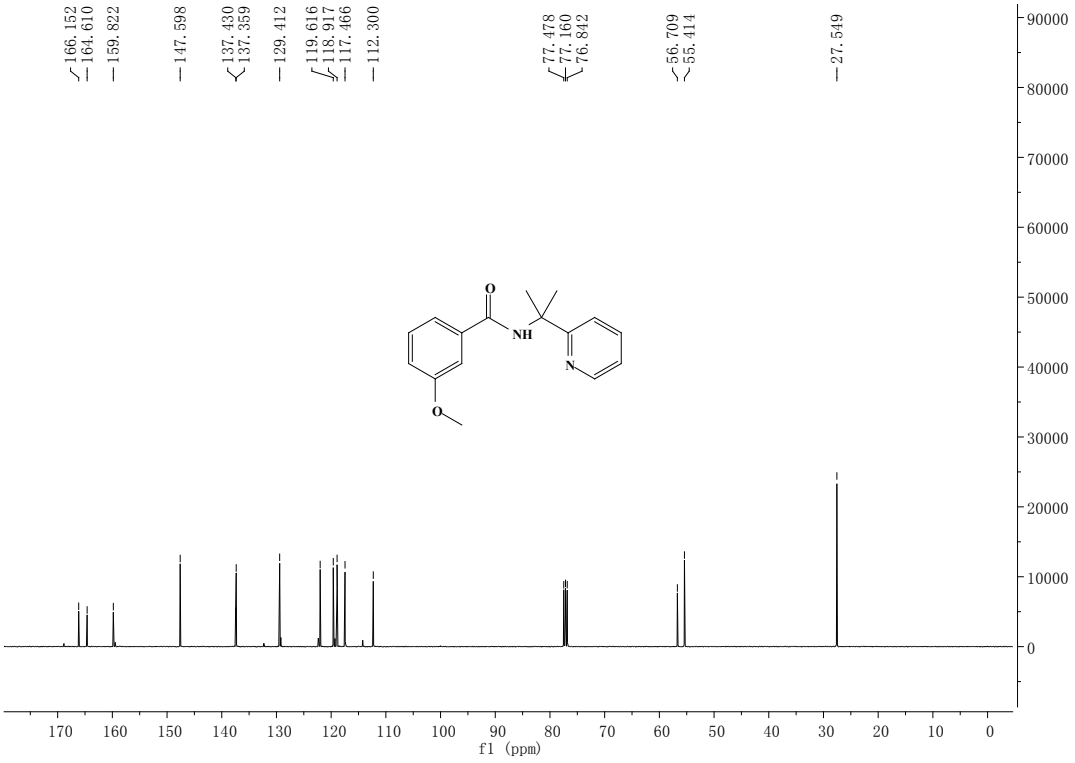
1p


9.055
8.568
8.556
8.062
7.757
7.752
7.739
7.608
7.588
7.569
7.483
7.463
7.264
7.260
7.252
7.249
7.245
7.243
7.233
7.231
1.885
O
NH
N
F
F
F
0.99
1.00
1.02
1.06
2.09
1.09
1.07
1.24
6.30
f1 (ppm)

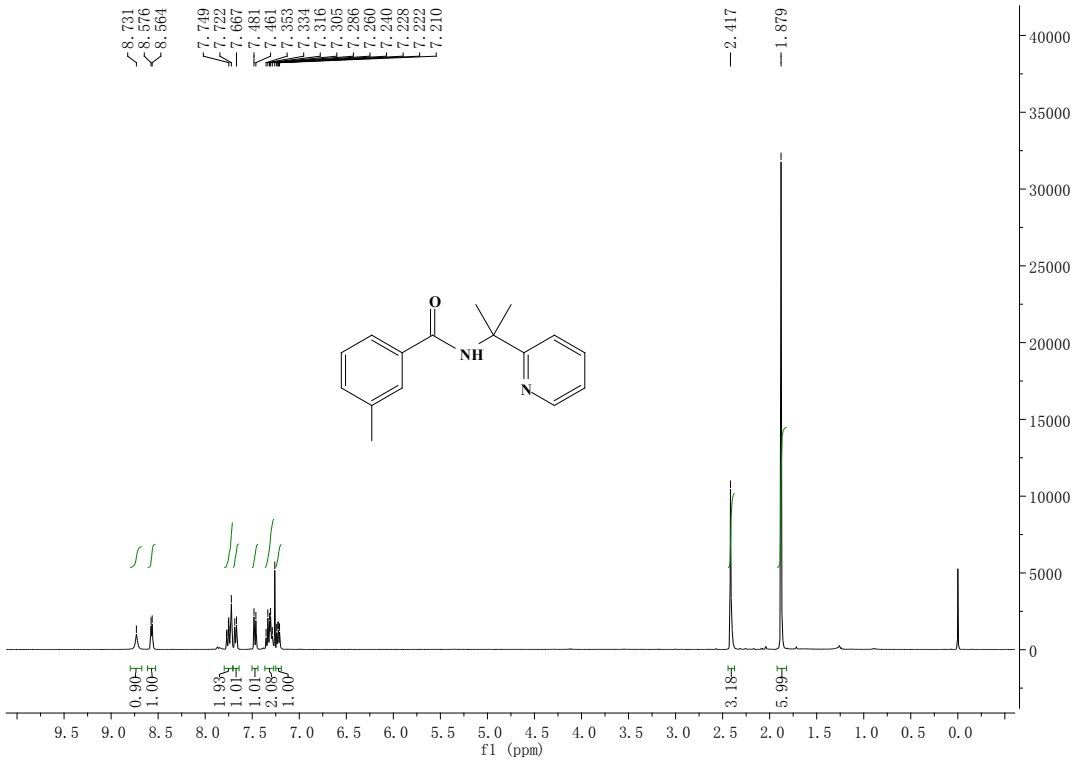

164.830
164.477
147.698
137.539
137.032
125.144
125.377
124.423
124.385
124.346
124.308
122.668
122.242
119.683
77.477
77.160
76.842
56.911
27.515
O
NH
N
F
F
F
f1 (ppm)

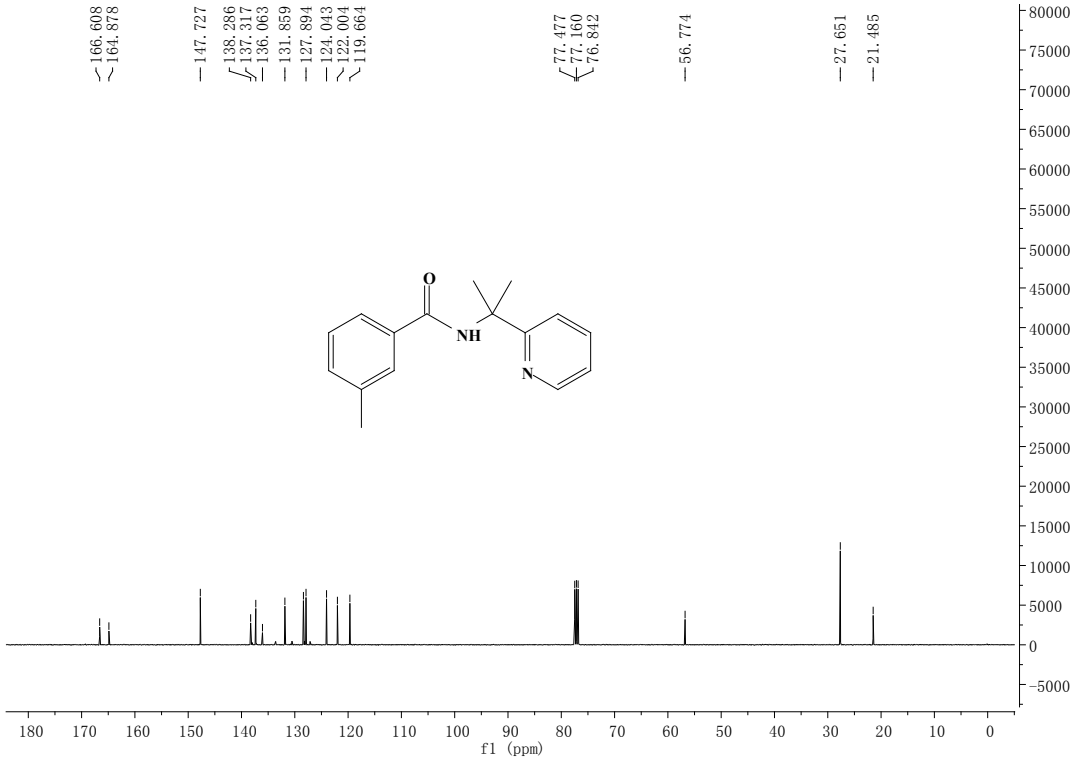
1q


8.809
8.567
8.555
7.756
7.732
7.481
7.326
7.241
7.229
7.223
7.210
7.041
7.023
7.017
3.862
1.878
O
NH
N
O
0.92
1.00
1.02
3.00
1.15
1.04
1.03
3.24
6.20
f1 (ppm)


166.152
164.610
159.822
147.598
137.430
137.359
129.412
119.616
118.917
117.466
112.300
77.478
77.160
76.842
56.709
55.414
27.549
O
NH
N
O
f1 (ppm)

1r


8.731
8.576
8.564
7.749
7.722
7.667
7.481
7.461
7.353
7.334
7.316
7.305
7.286
7.260
7.240
7.228
7.222
7.210
2.417
1.879
O
NH
N
0.90
1.00
1.93
1.01
1.01
2.08
1.00
3.18
5.99
f1 (ppm)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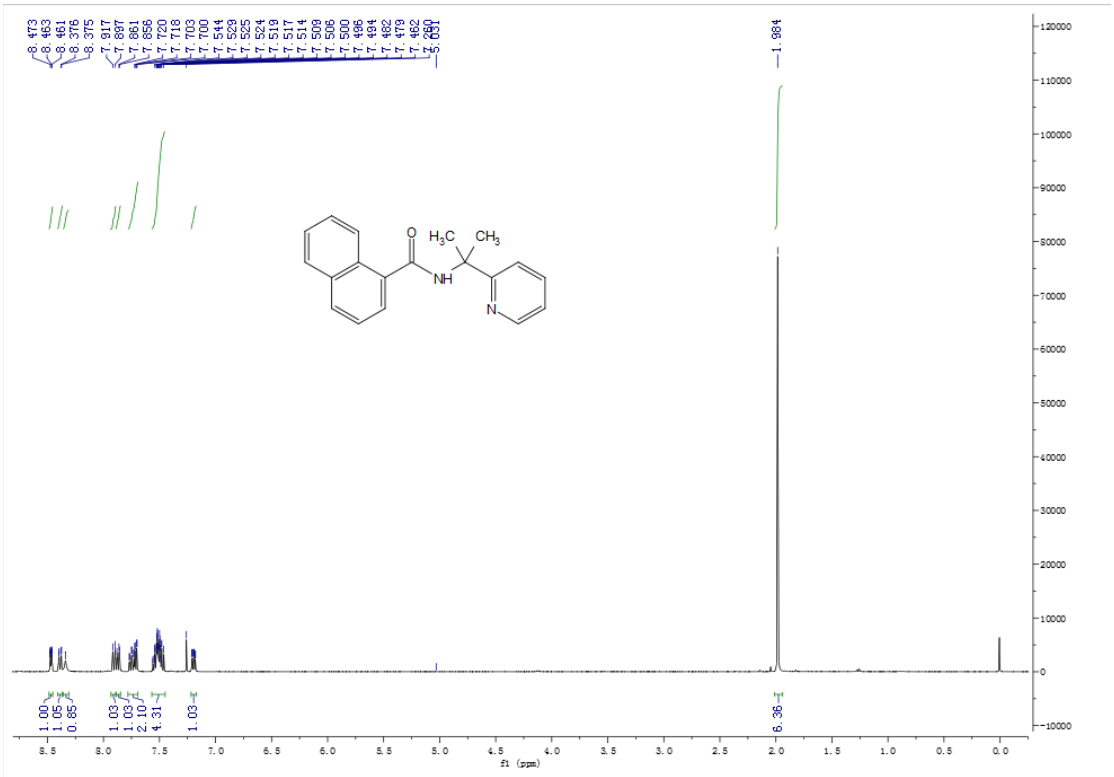
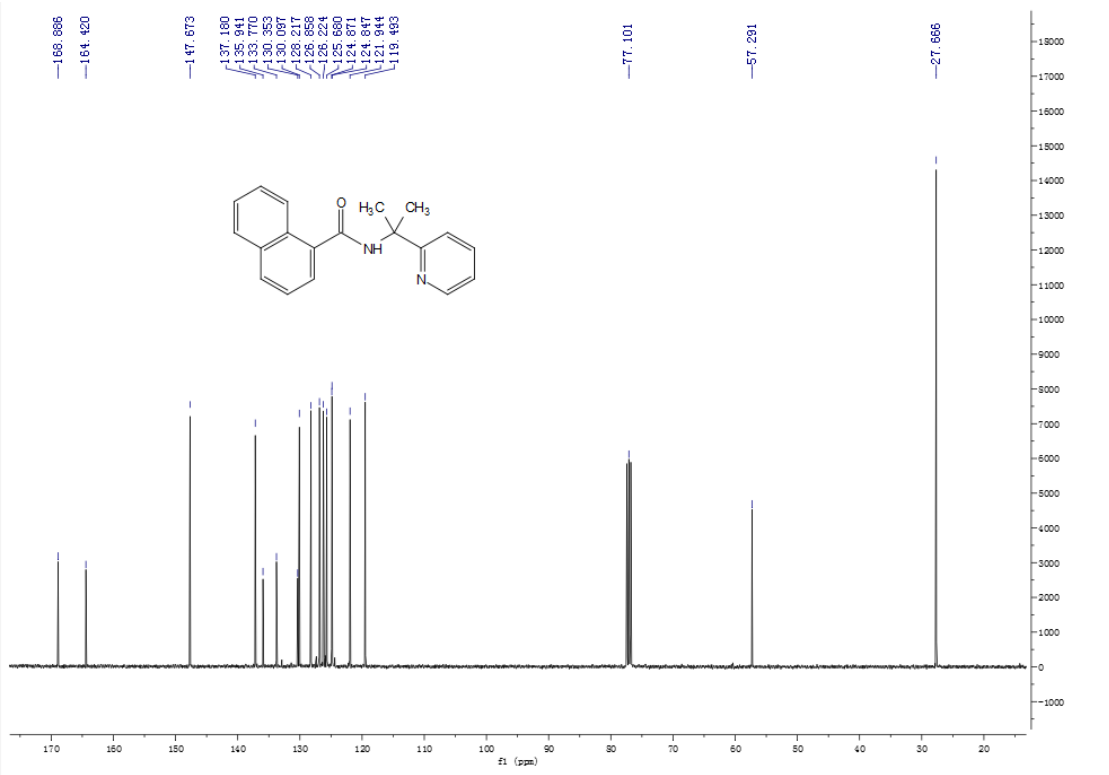
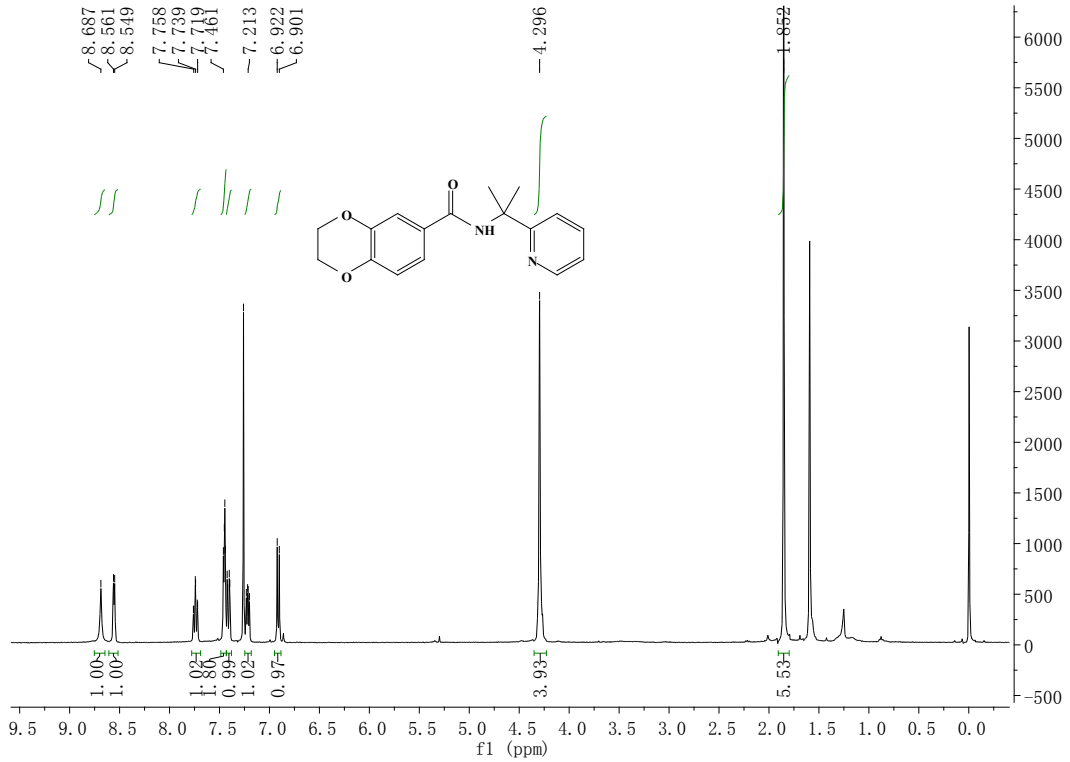
138.286
137.317
136.063
131.859
127.894
124.043
122.004
119.664
77.477
77.160
76.842
56.774
27.651
21.485
O
NH
N
f1 (ppm)

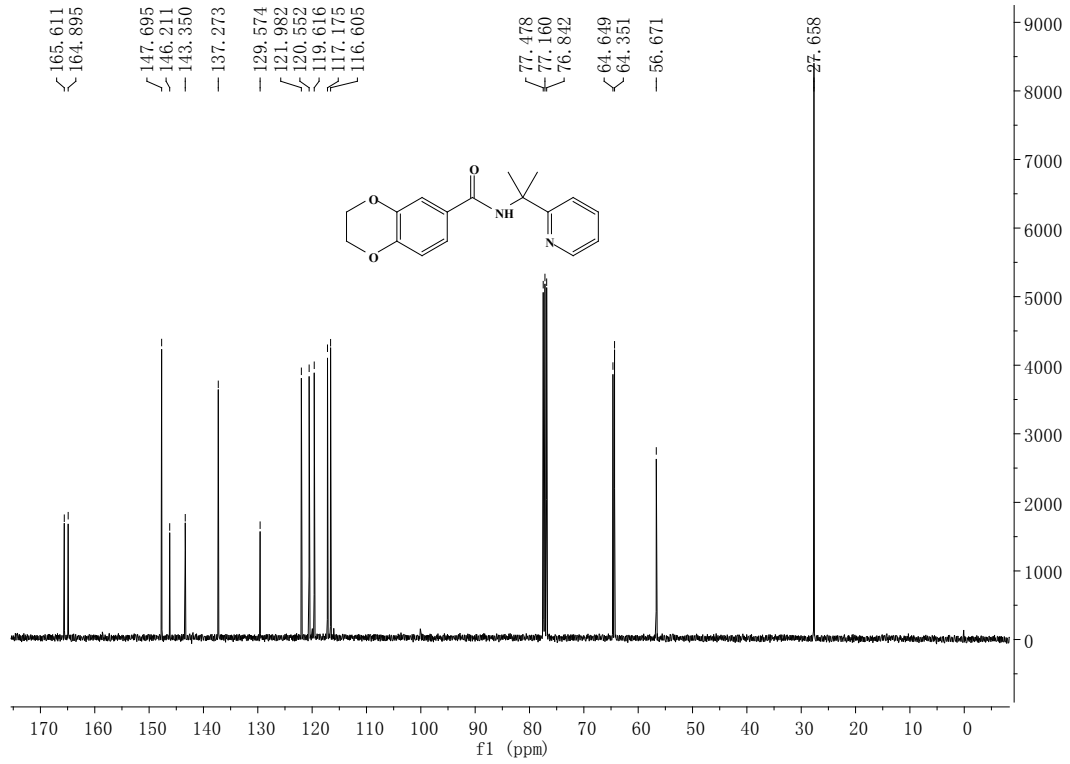
1s


8.473
8.463
8.461
8.376
8.375
7.917
7.897
7.861
7.856
7.720
7.718
7.703
7.700
7.544
7.529
7.525
7.524
7.519
7.517
7.514
7.509
7.506
7.500
7.496
7.494
7.482
7.479
7.462
7.280
5.031
1.984
O
H3C
CH3
NH
N
1.00
1.05
0.85
1.03
1.03
2.10
4.31
1.03
6.36
f1 (ppm)

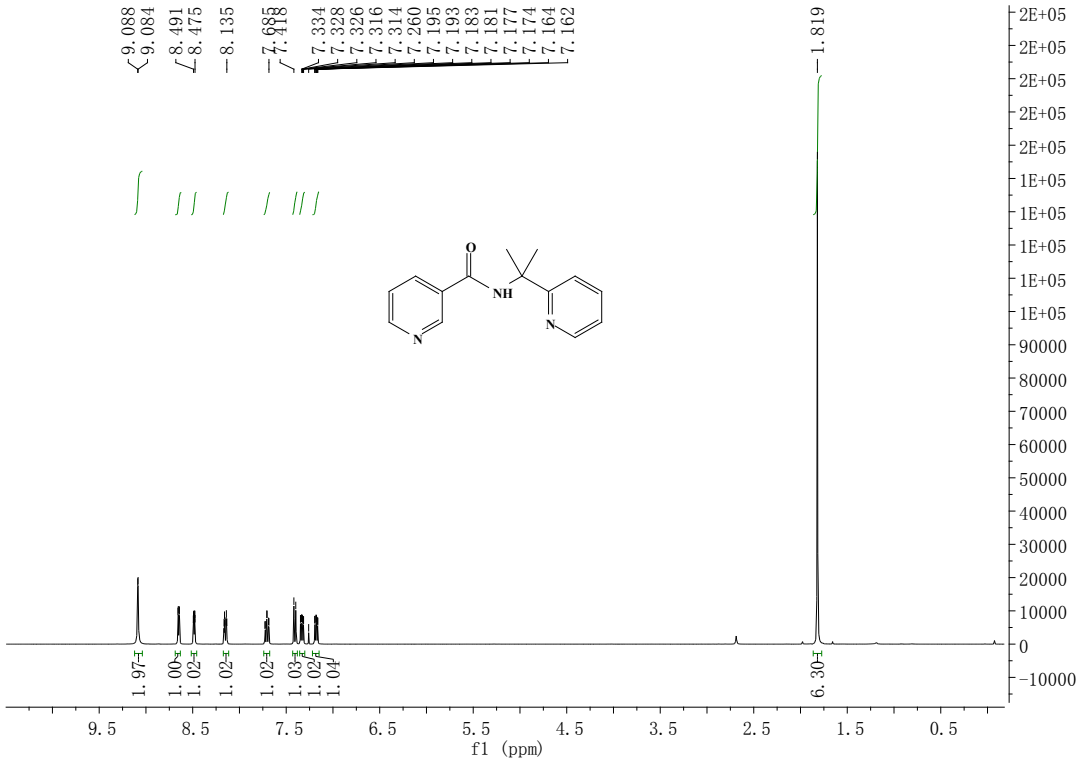

168.886
164.420
147.673
137.180
135.941
133.770
130.353
130.097
128.217
126.858
126.224
125.680
124.871
124.847
121.944
119.493
77.101
57.291
27.666
O
H3C
CH3
NH
N
f1 (ppm)

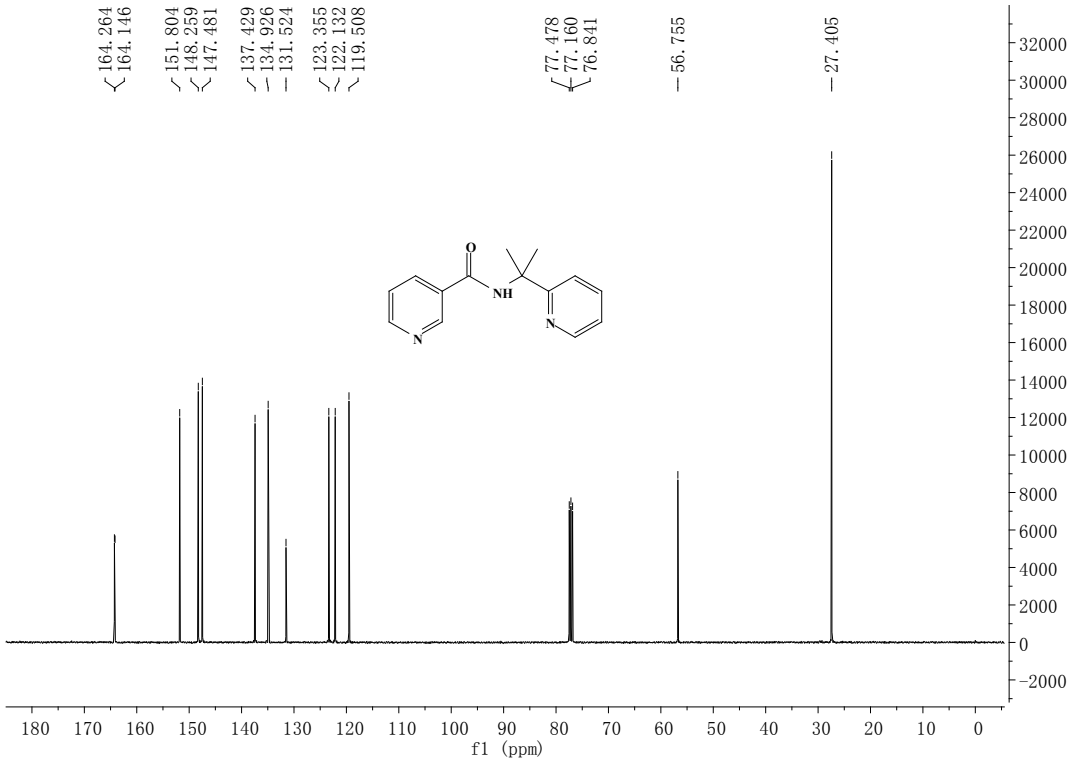
1t


8.687
8.561
8.549
7.758
7.739
7.719
7.461
7.213
6.922
6.901
4.296
1.852
1.00
1.00
1.02
1.80
0.99
1.02
0.97
3.93
5.53
f1 (ppm)

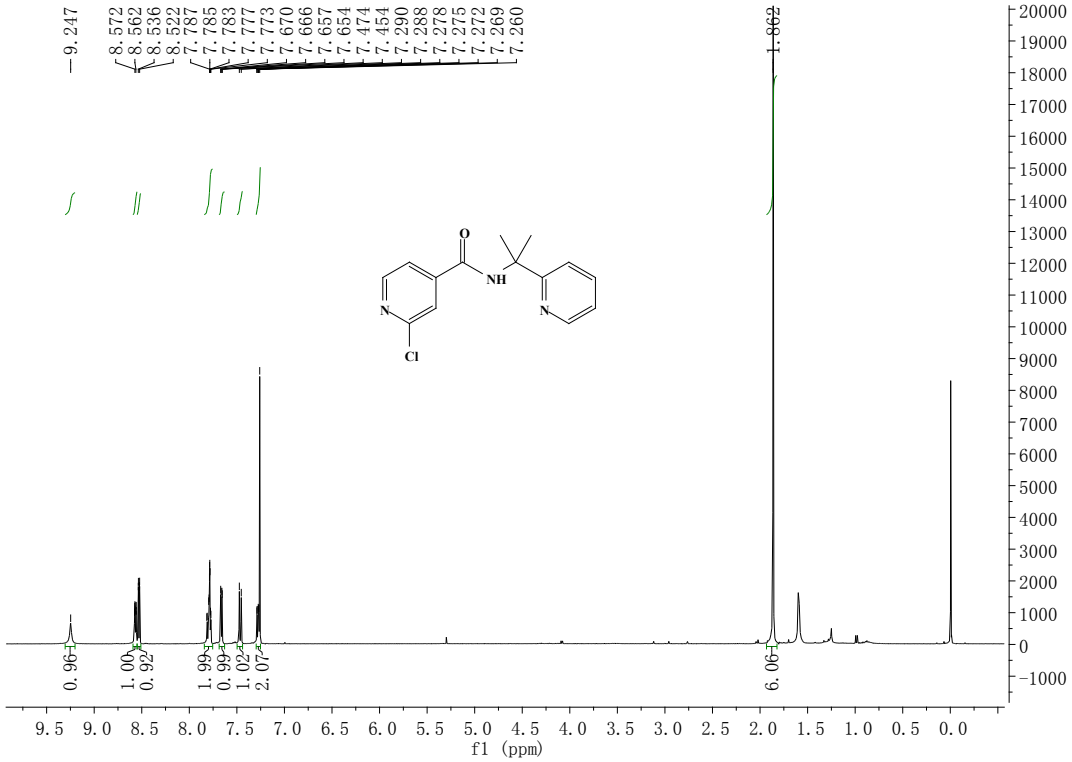

165.611
164.895
147.695
146.211
143.350
137.273
129.574
121.982
120.552
119.616
117.175
116.605
77.478
77.160
76.842
64.649
64.351
56.671
27.658
f1 (ppm)

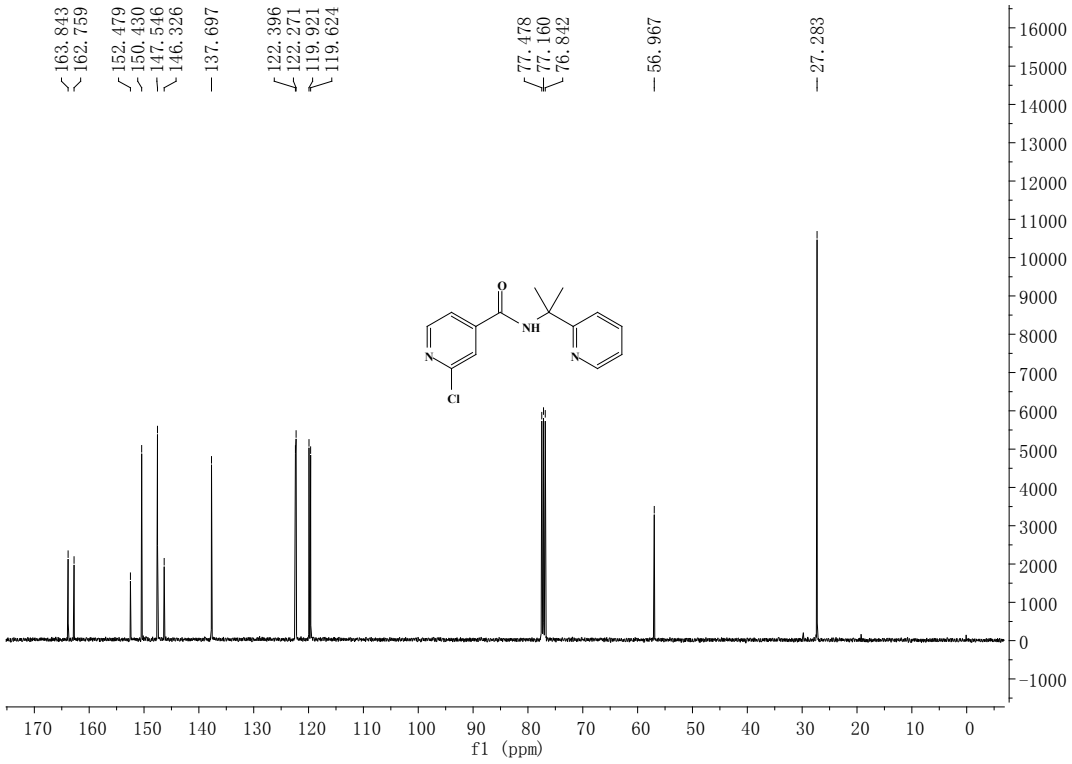
4a


9.088
9.084
8.491
8.475
8.135
7.685
7.418
7.334
7.328
7.326
7.316
7.314
7.260
7.195
7.193
7.183
7.181
7.177
7.174
7.164
7.162
1.819
1.97
1.00
1.02
1.02
1.02
1.03
1.02
1.04
6.30
f1 (ppm)

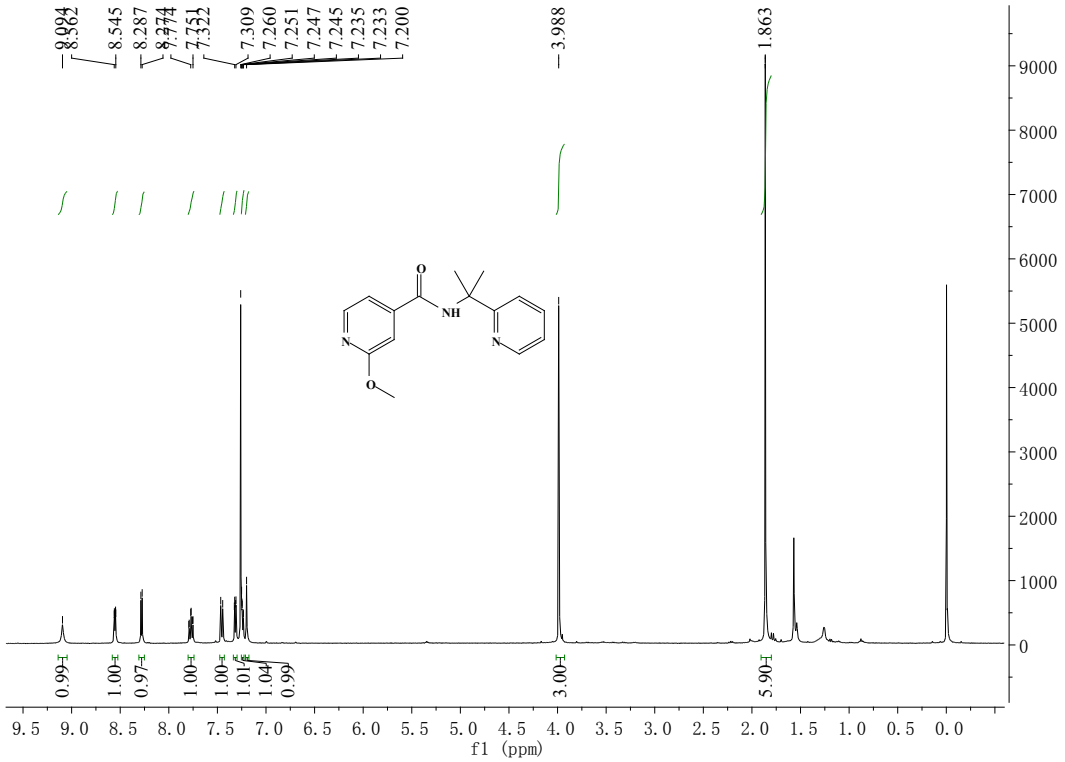

164.264
164.146
151.804
148.259
147.481
137.429
134.926
131.524
123.355
122.132
119.508
77.478
77.160
76.841
56.755
27.405
f1 (ppm)

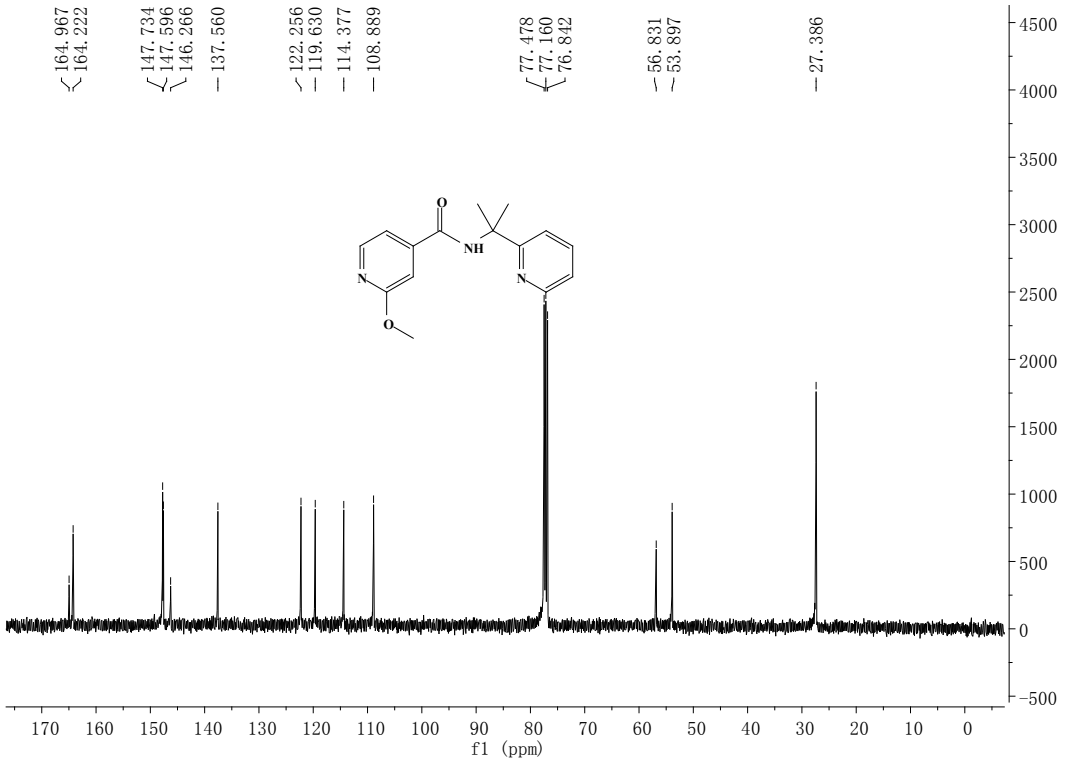
4b


9.247
8.572
8.562
8.536
8.522
7.787
7.785
7.783
7.777
7.773
7.670
7.666
7.657
7.654
7.474
7.454
7.290
7.288
7.278
7.275
7.272
7.269
7.260
1.862
0.96
1.00
0.92
1.99
0.99
1.02
2.07
6.06
f1 (ppm)

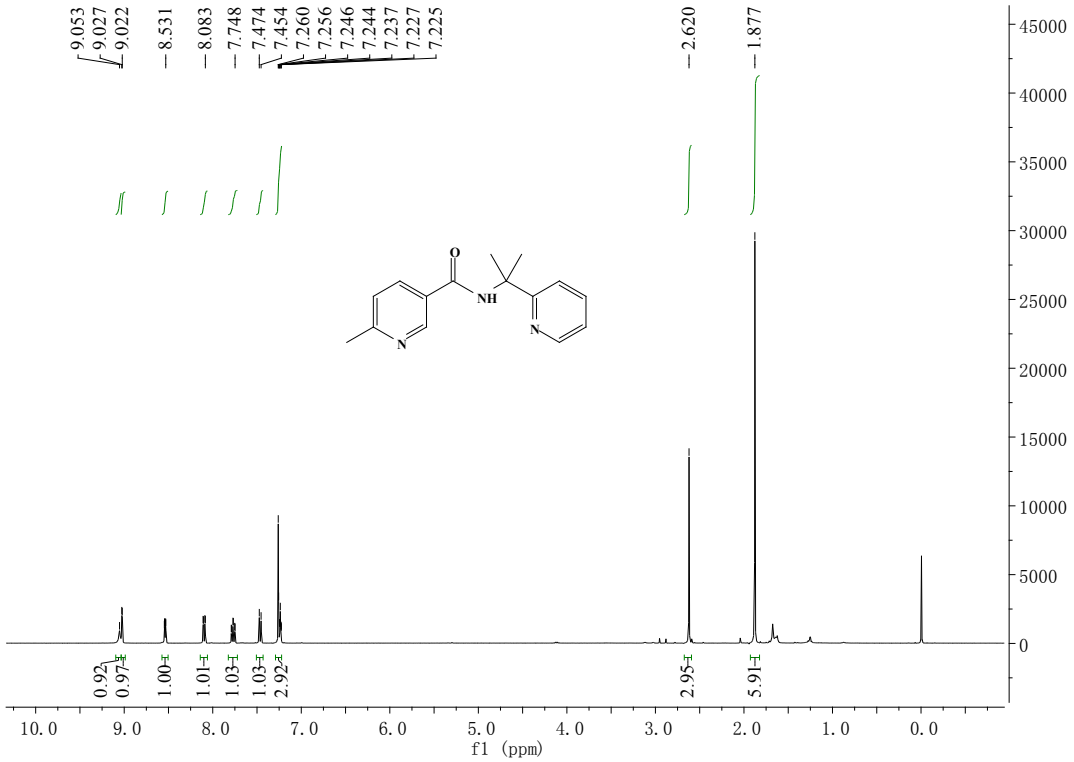

163.843
162.759
152.479
150.430
147.546
146.326
137.697
122.396
122.271
119.921
119.624
77.478
77.160
76.842
56.967
27.283
f1 (ppm)

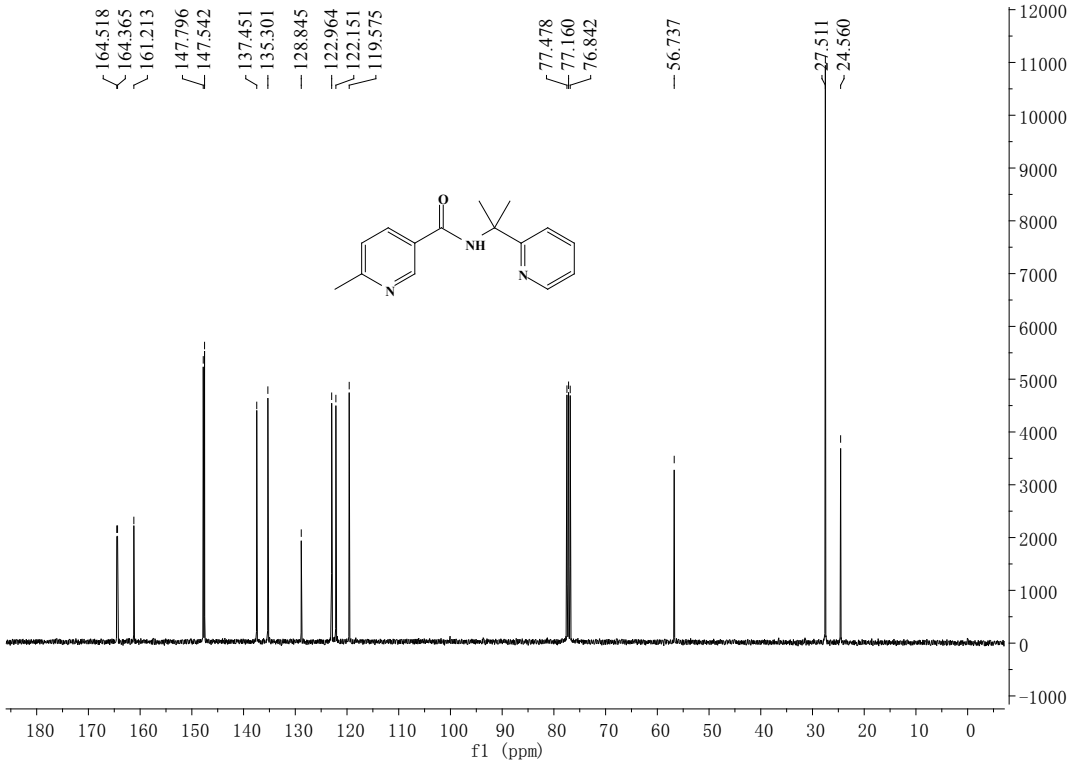
4c


9.094
8.562
8.545
8.287
8.274
7.751
7.322
7.309
7.260
7.251
7.247
7.245
7.235
7.233
7.200
3.988
1.863
0.99
1.00
0.97
1.00
1.00
1.01
1.04
0.99
3.00
5.90
f1 (ppm)

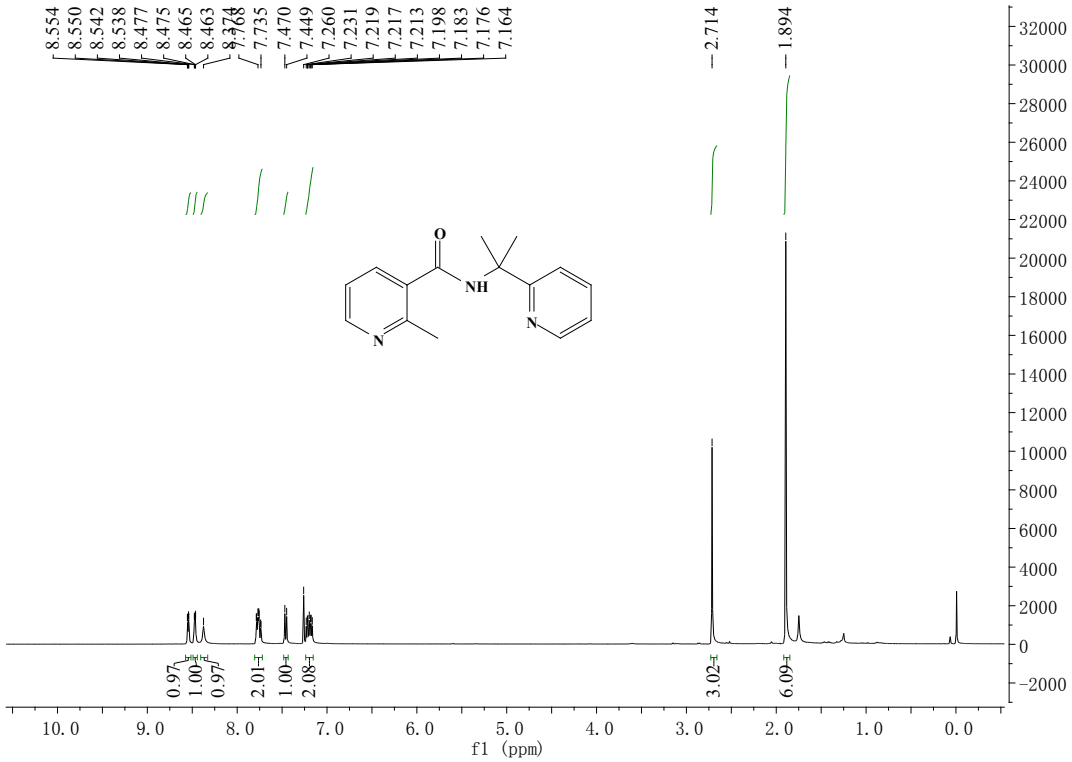

164.967
164.222
147.734
147.596
146.266
137.560
122.256
119.630
114.377
108.889
77.478
77.160
76.842
56.831
53.897
27.386
f1 (ppm)

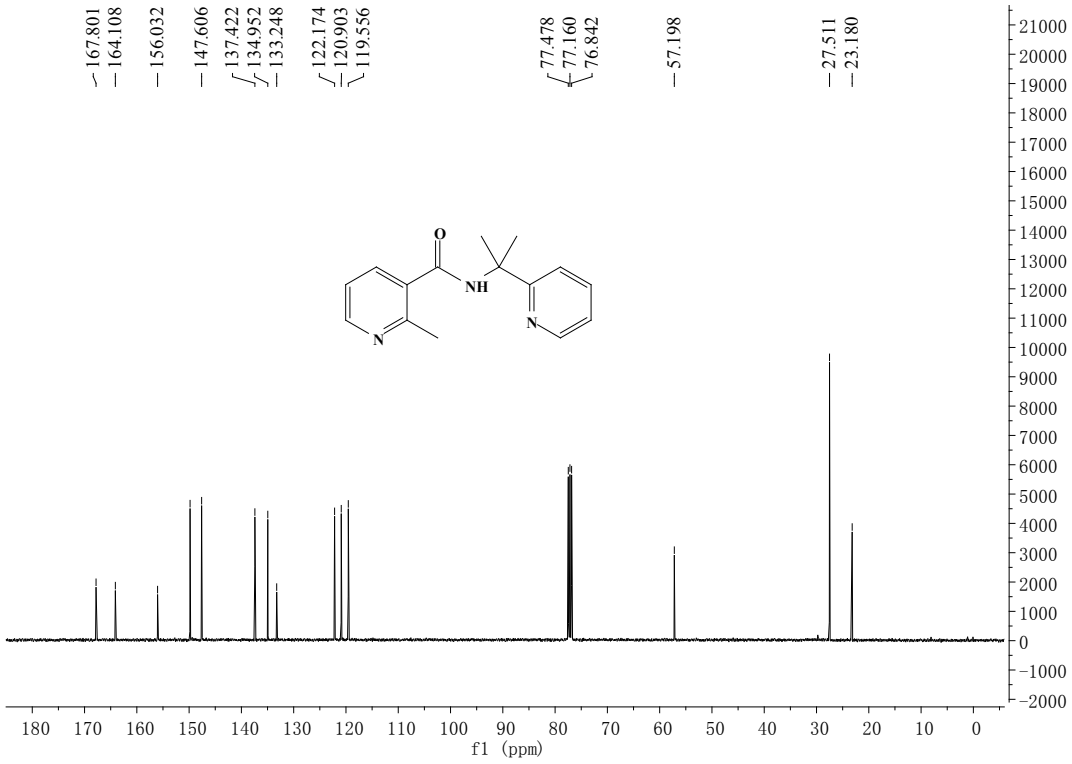
4d


9.053
9.027
9.022
8.531
8.083
7.748
7.474
7.454
7.260
7.256
7.246
7.244
7.237
7.227
7.225
2.620
1.877
0.92
0.97
1.00
1.01
1.03
1.03
2.92
2.95
5.91
f1 (ppm)

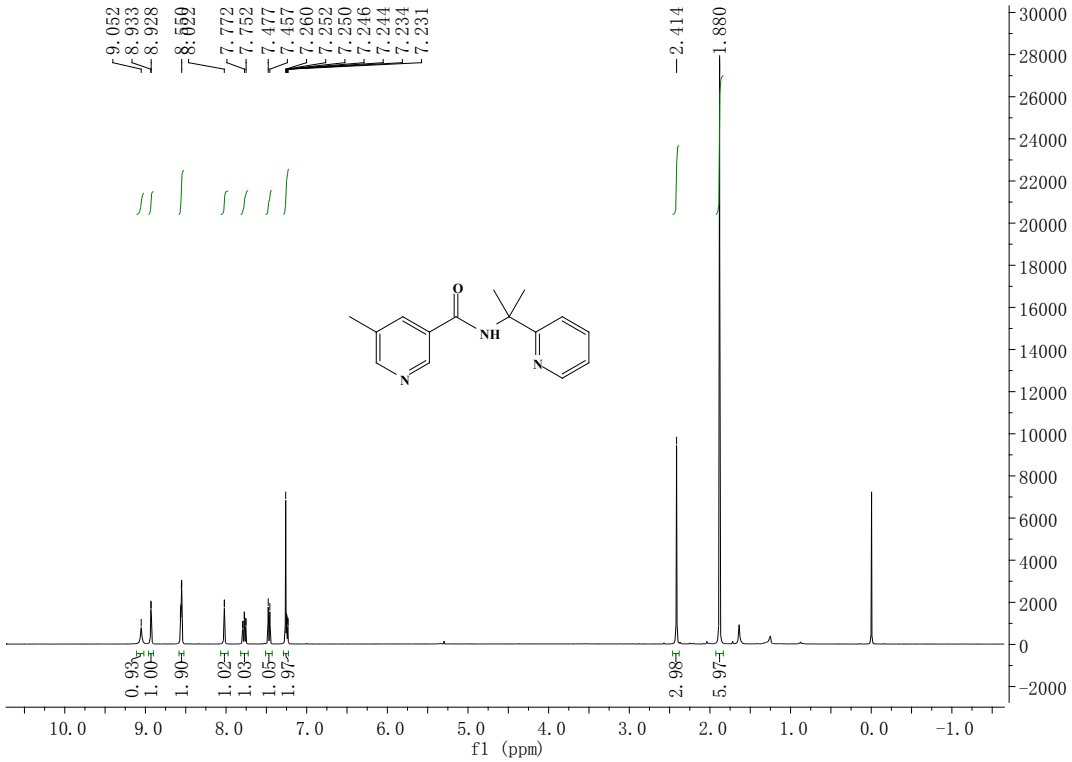

164.518
164.365
161.213
147.796
147.542
137.451
135.301
128.845
122.964
122.151
119.575
77.478
77.160
76.842
56.737
27.511
24.560
f1 (ppm)

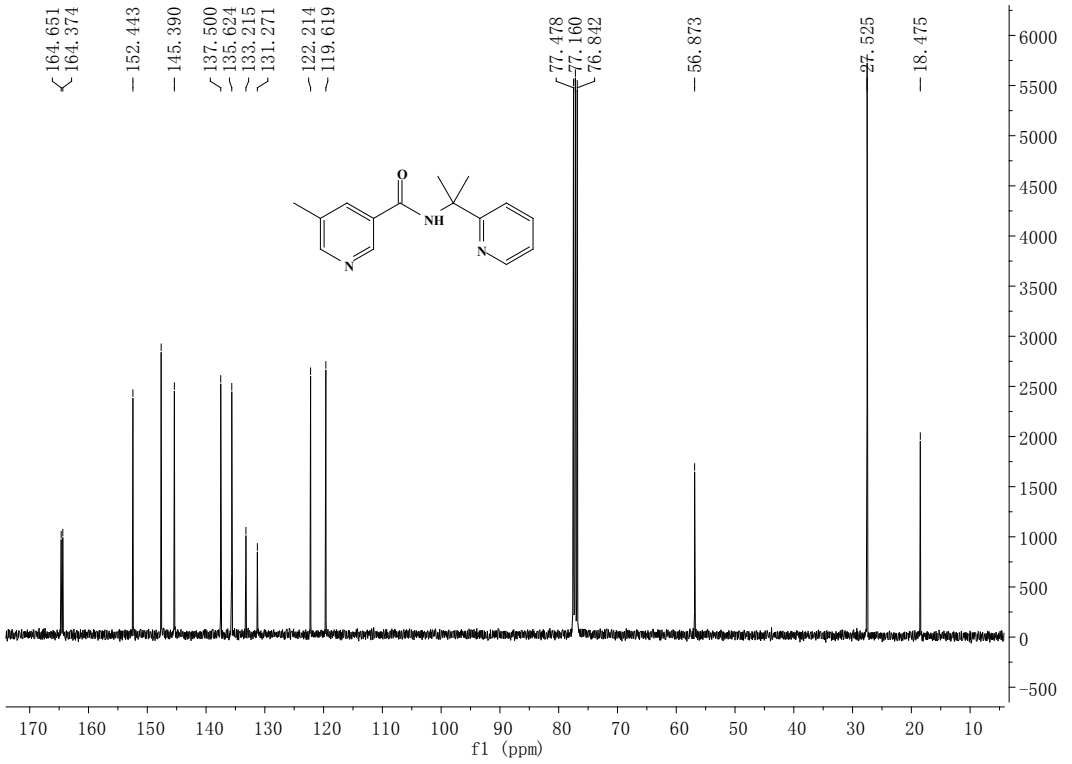
4e


8.554
8.550
8.542
8.538
8.477
8.475
8.465
8.463
7.735
7.470
7.449
7.260
7.231
7.219
7.217
7.213
7.198
7.183
7.176
7.164
2.714
1.894
O
NH
N
N
0.97
1.00
0.97
2.01
1.00
2.08
3.02
6.09
f1 (ppm)

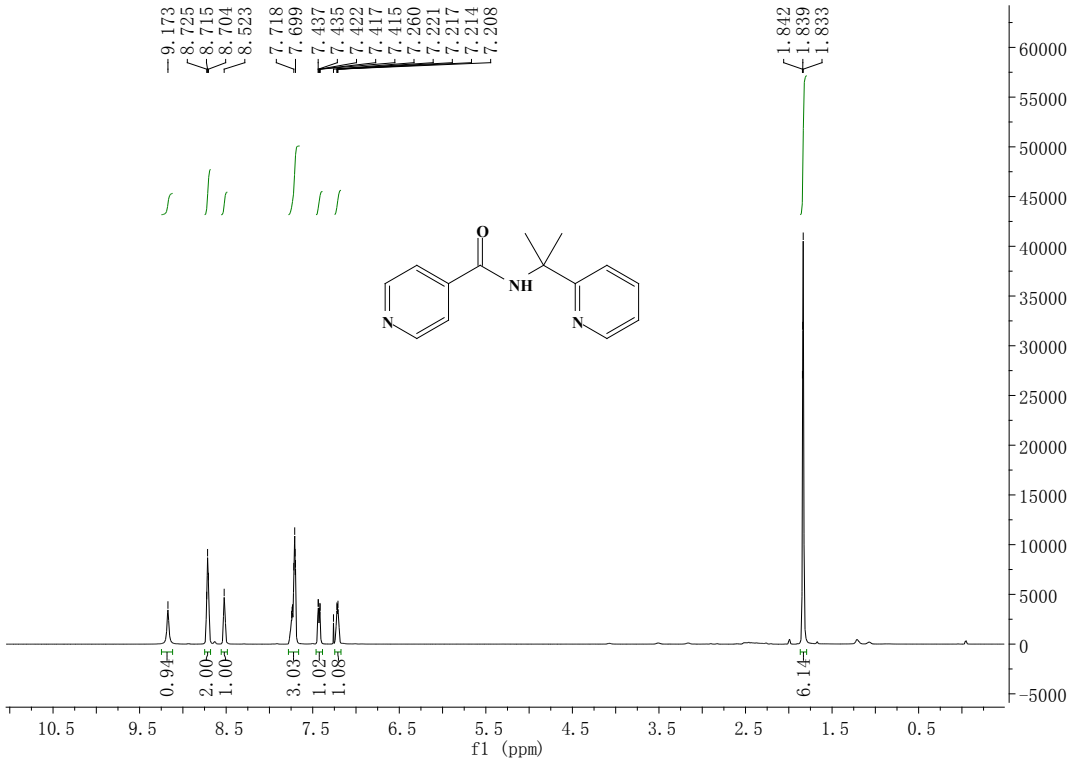

167.801
164.108
156.032
147.606
137.422
134.952
133.248
122.174
120.903
119.556
77.478
77.160
76.842
57.198
27.511
23.180
O
NH
N
N
f1 (ppm)

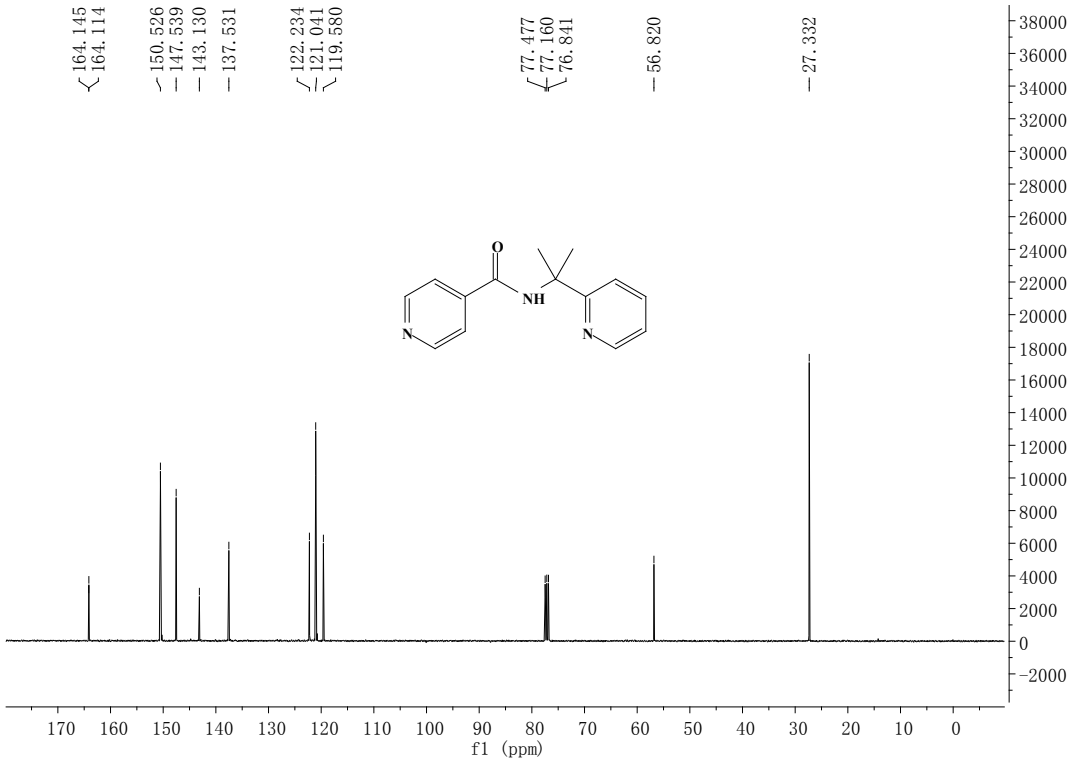
4f


9.052
8.933
8.928
8.559
8.522
7.772
7.752
7.477
7.457
7.260
7.252
7.250
7.246
7.244
7.234
7.231
2.414
1.880
0.93
1.00
1.90
1.02
1.03
1.05
1.97
2.98
5.97
O
NH
N
f1 (ppm)

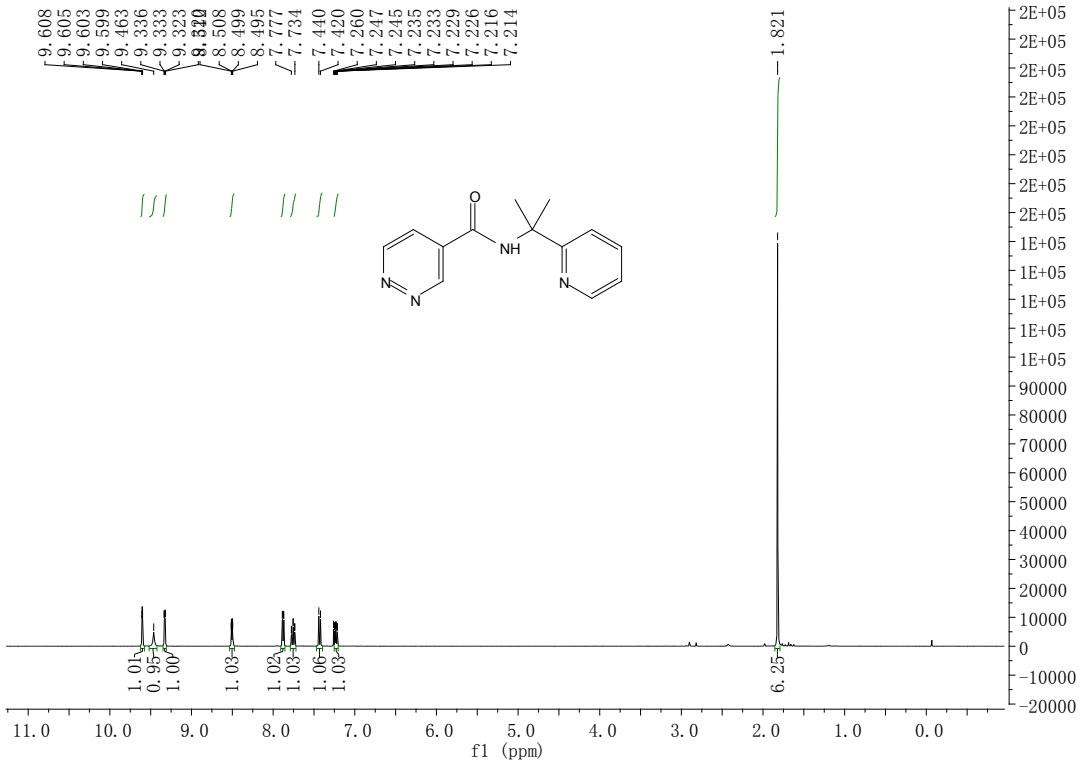

164.651
164.374
152.443
145.390
137.500
135.624
133.215
131.271
122.214
119.619
77.478
77.160
76.842
56.873
27.525
18.475
O
NH
N
f1 (ppm)

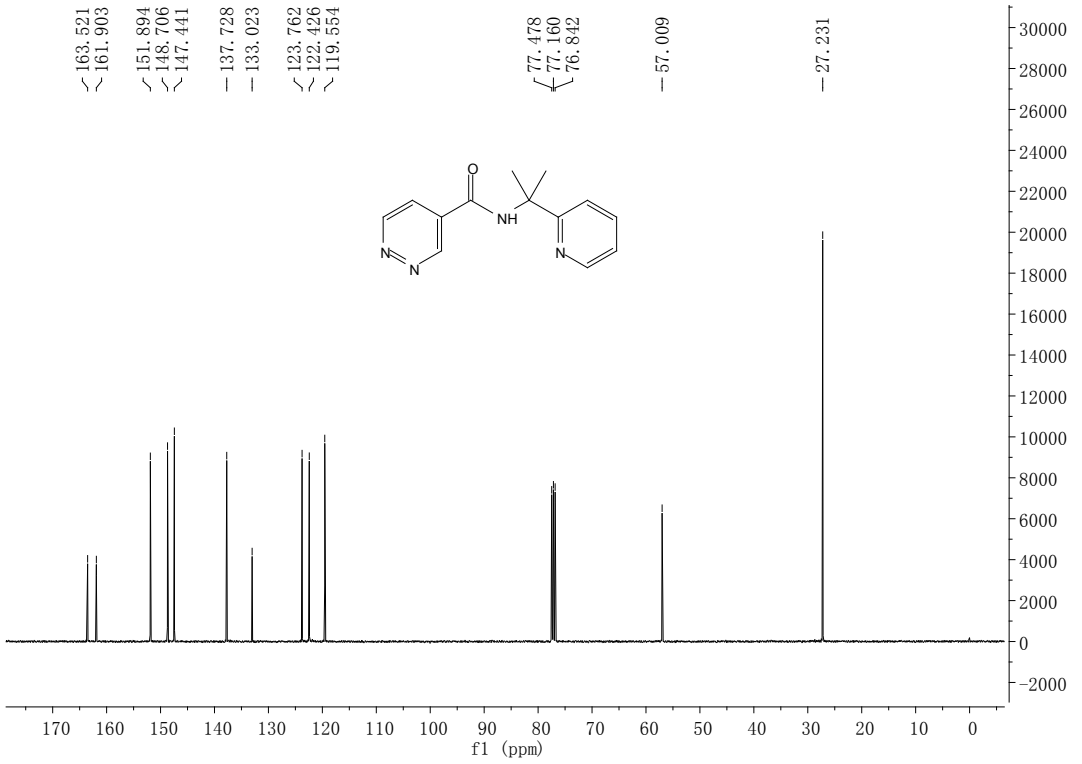
4g


9.173
8.725
8.715
8.704
8.523
7.718
7.699
7.437
7.435
7.422
7.417
7.415
7.260
7.221
7.217
7.214
7.208
1.842
1.839
1.833
O
NH
N
N
0.94
2.00
1.00
3.03
1.02
1.08
6.14
f1 (ppm)

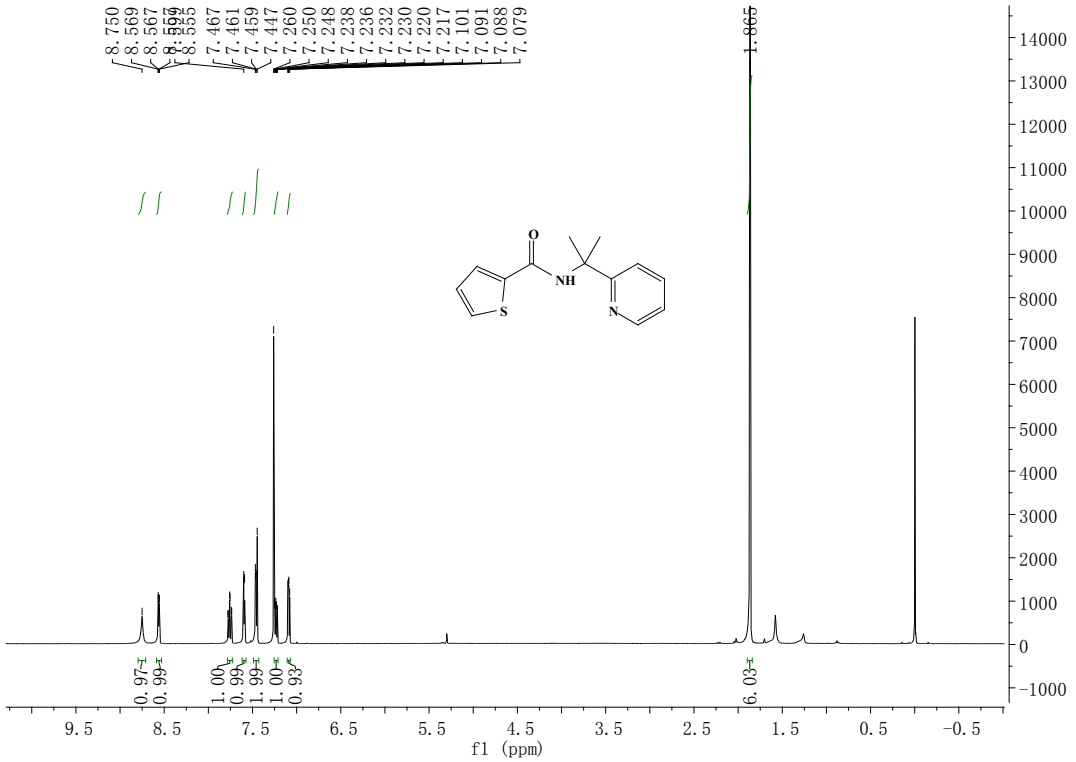

164.145
164.114
150.526
147.539
143.130
137.531
122.234
121.041
119.580
77.477
77.160
76.841
56.820
27.332
O
NH
N
N
f1 (ppm)

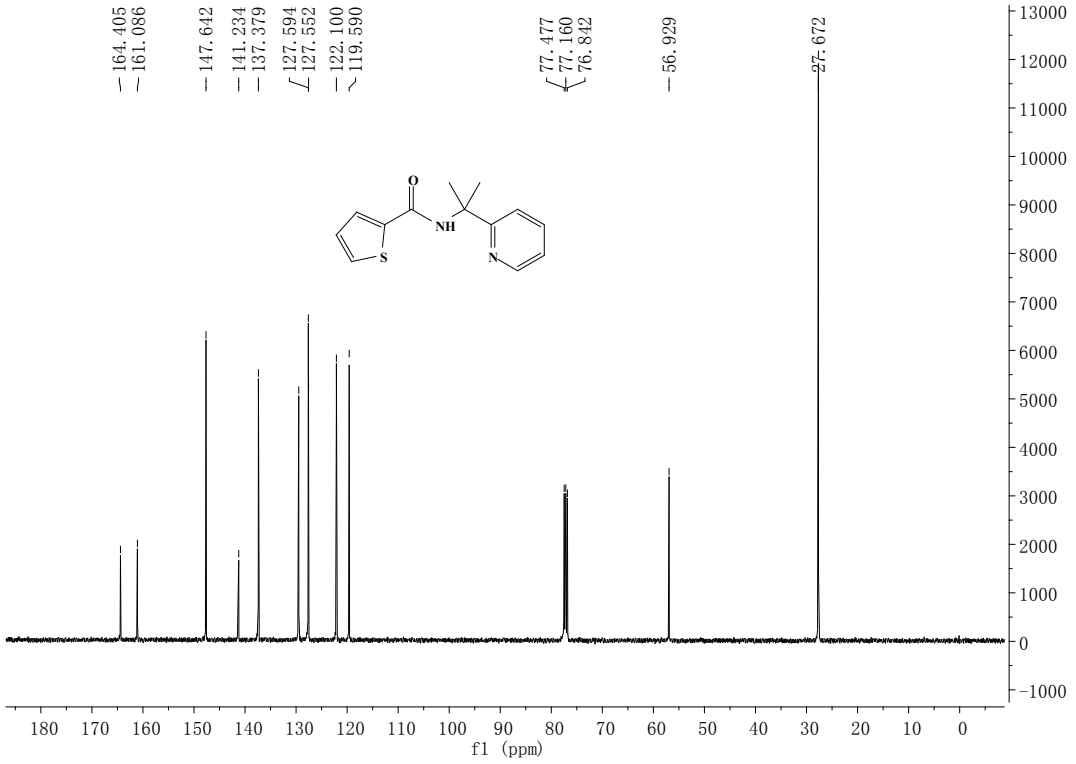
4h


9.608
9.605
9.603
9.599
9.463
9.336
9.333
9.323
8.508
8.499
8.495
7.777
7.734
7.440
7.420
7.260
7.247
7.245
7.235
7.233
7.229
7.226
7.216
7.214
1.821
O
NH
N
N
1.01
0.95
1.00
1.03
1.02
1.03
1.06
1.03
6.25
f1 (ppm)

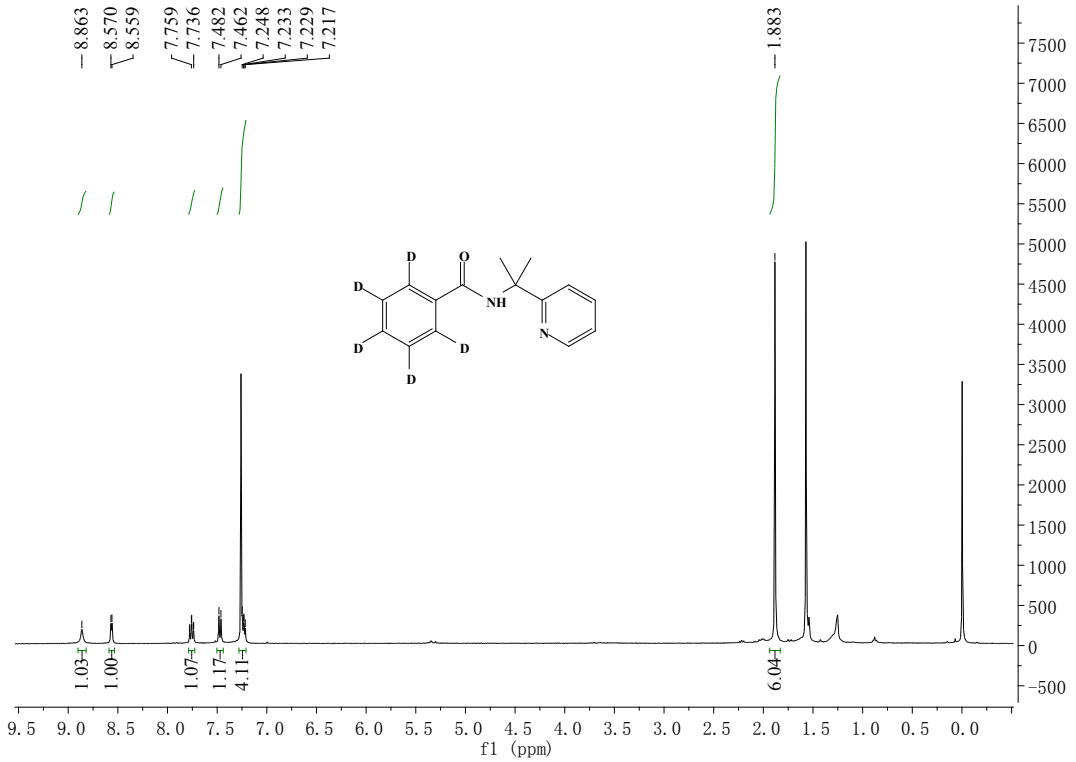

163.521
161.903
151.894
148.706
147.441
137.728
133.023
123.762
122.426
119.554
77.478
77.160
76.842
57.009
27.231
O
NH
N
N
f1 (ppm)

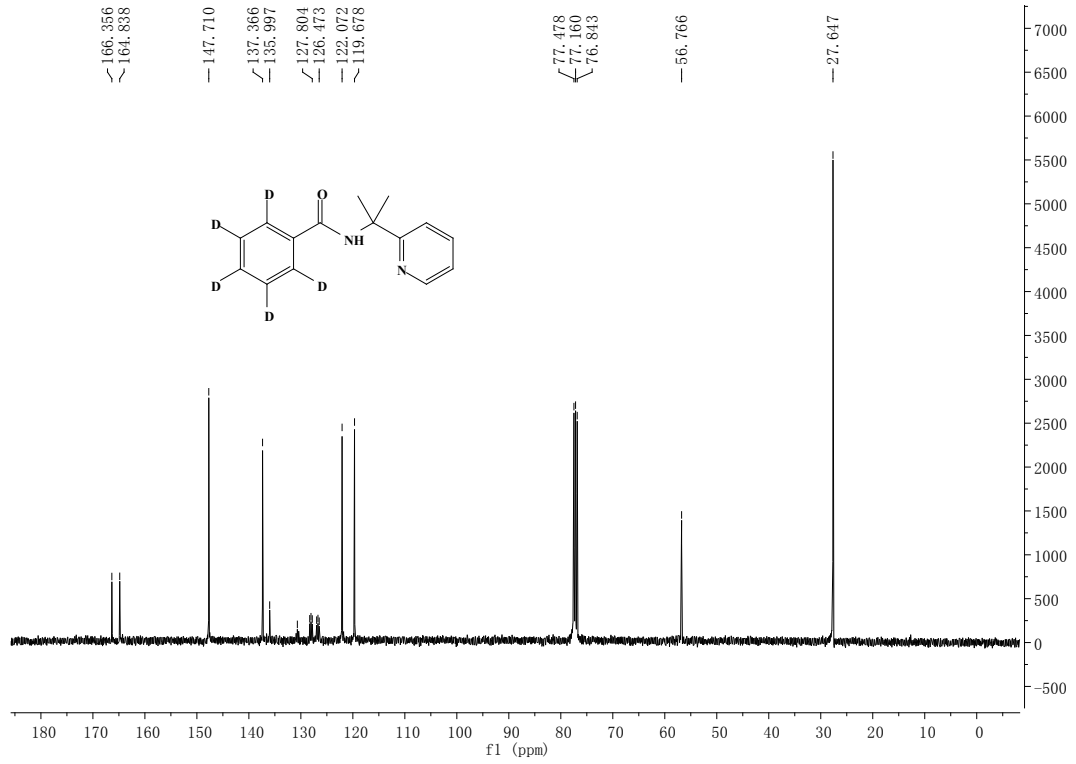
4i


8.750
8.569
8.567
8.535
7.467
7.461
7.459
7.447
7.260
7.250
7.248
7.238
7.236
7.232
7.230
7.220
7.217
7.101
7.091
7.088
7.079
1.865
O
NH
S
N
0.97
0.99
1.00
0.99
1.99
1.00
0.93
6.03
f1 (ppm)

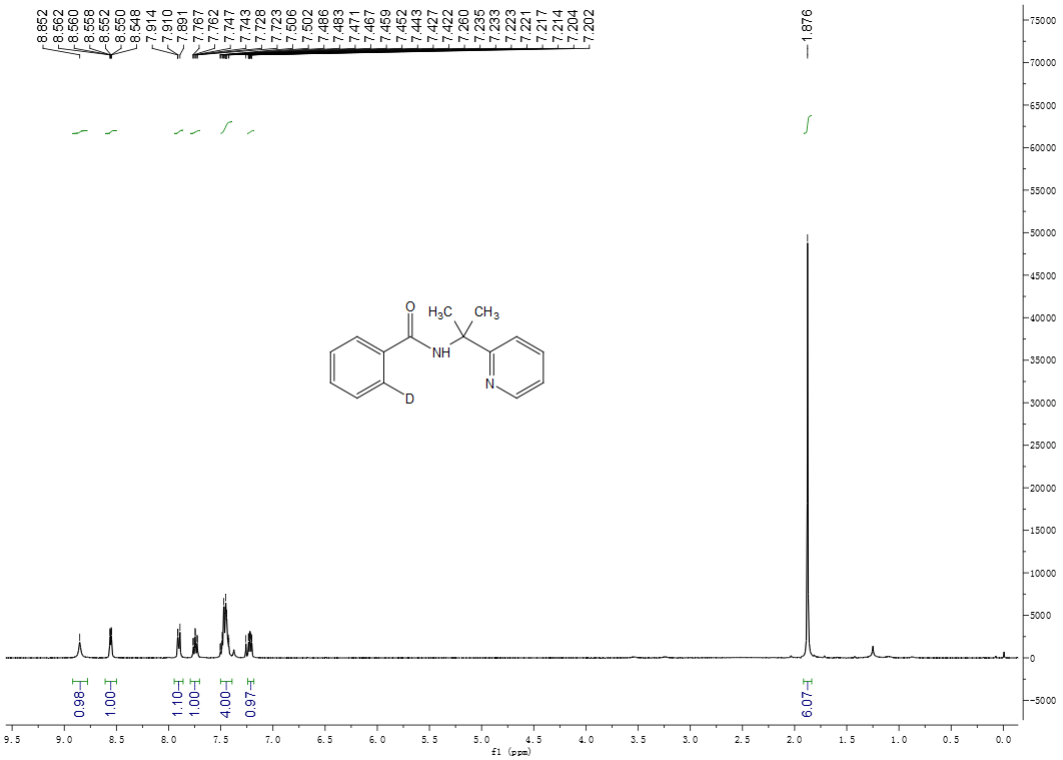

164.405
161.086
147.642
141.234
137.379
127.594
127.552
122.100
119.590
77.477
77.160
76.842
56.929
27.672
O
NH
S
N
f1 (ppm)

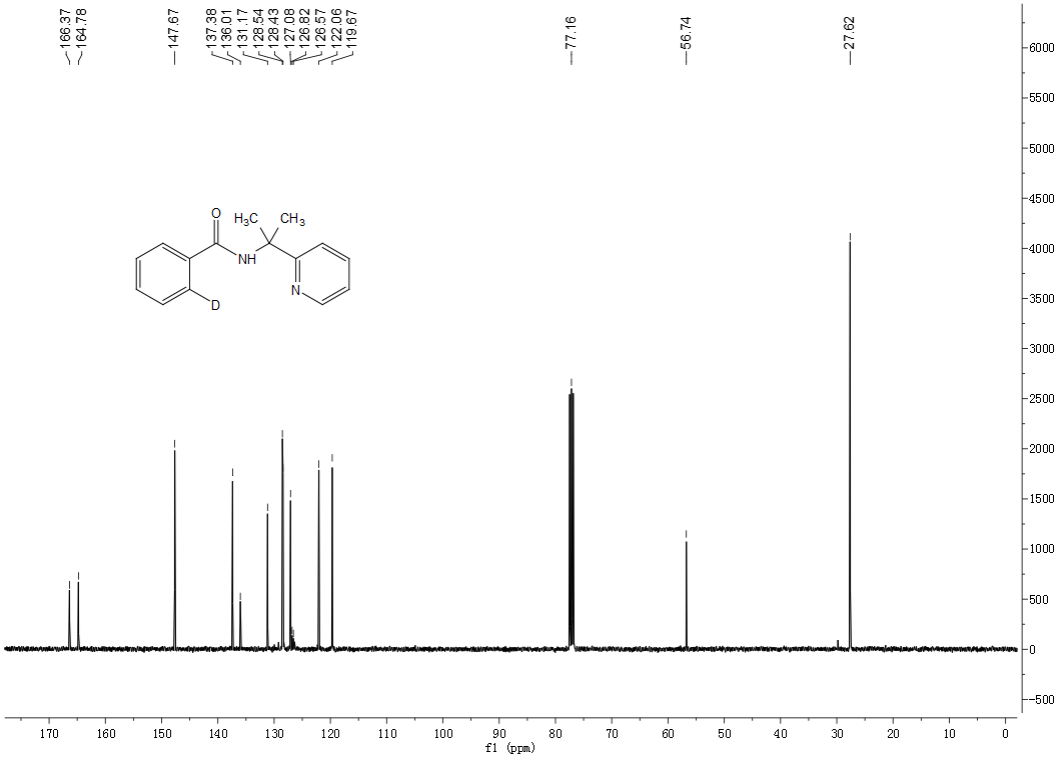
d_5-**1a**


8.863
8.570
8.559
7.759
7.736
7.482
7.462
7.248
7.233
7.229
7.217
1.883
1.03
1.00
1.07
1.17
4.11
6.04
f1 (ppm)

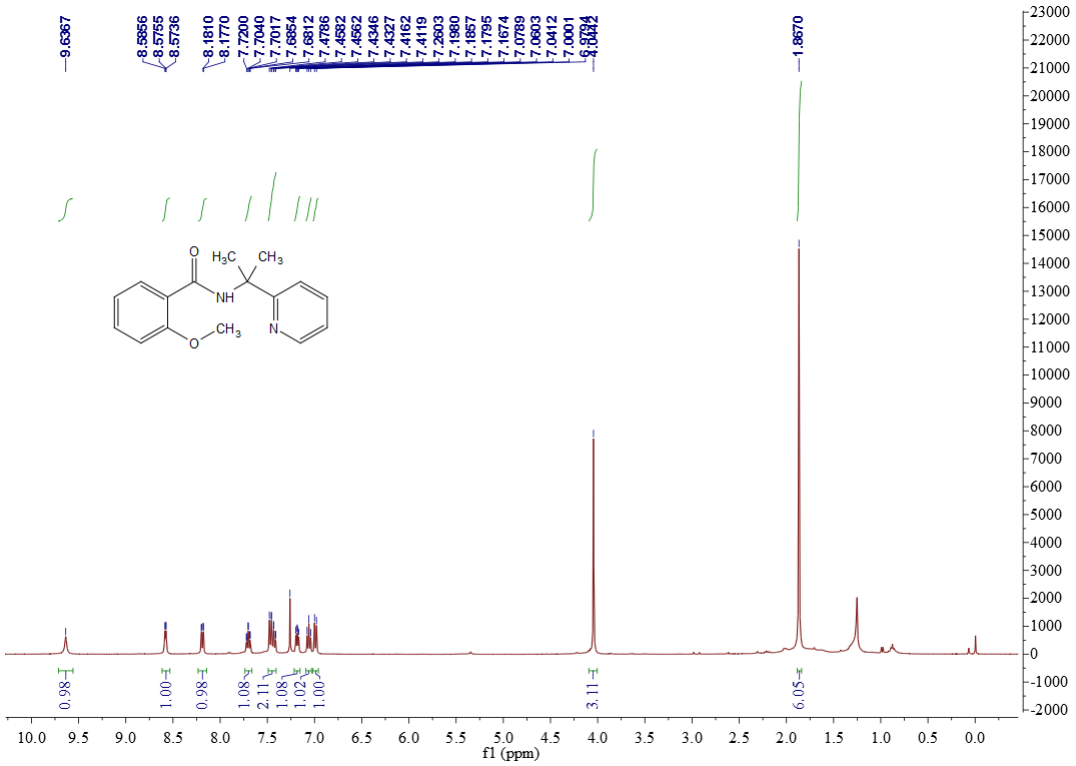

166.356
164.838
147.710
137.366
135.997
127.804
126.473
122.072
119.678
77.478
77.160
76.843
56.766
27.647
f1 (ppm)

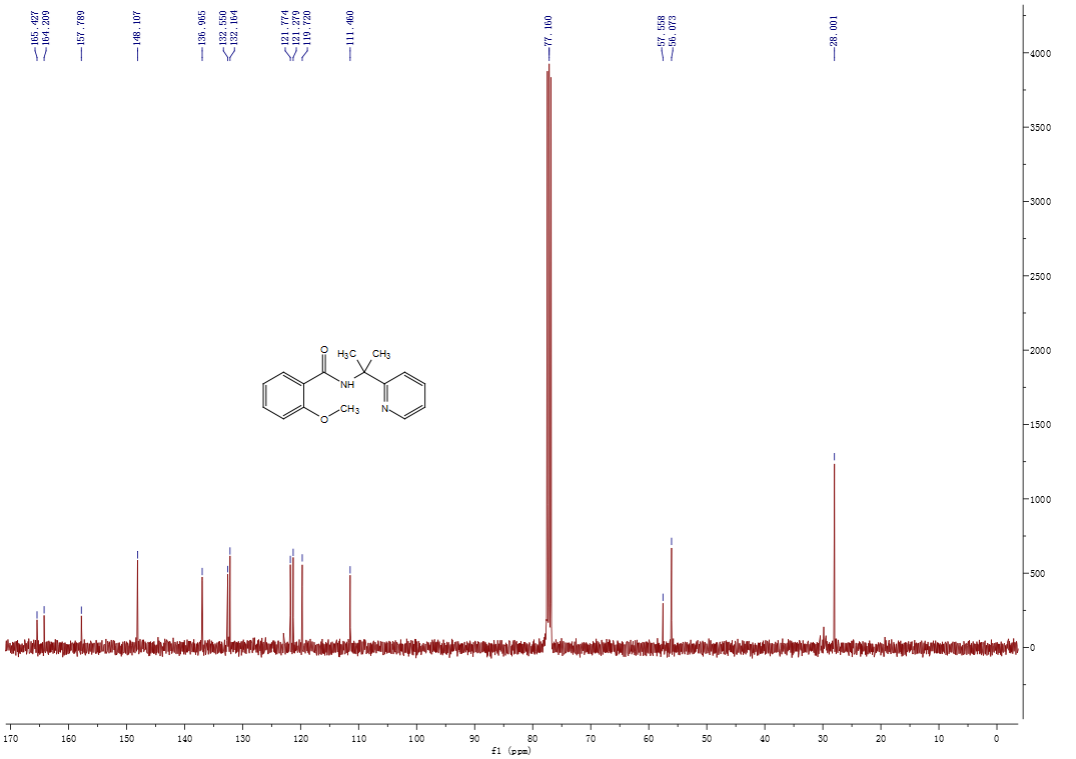
d_1-**1a**


8.852
8.562
8.560
8.558
8.552
8.550
8.548
7.914
7.910
7.891
7.767
7.762
7.747
7.743
7.728
7.723
7.506
7.502
7.486
7.483
7.471
7.467
7.459
7.452
7.443
7.427
7.422
7.260
7.235
7.233
7.223
7.221
7.217
7.214
7.204
7.202
1.876
O
H3C
CH3
NH
N
D
0.98
1.00
1.10
1.00
4.00
0.97
6.07
f1 (ppm)

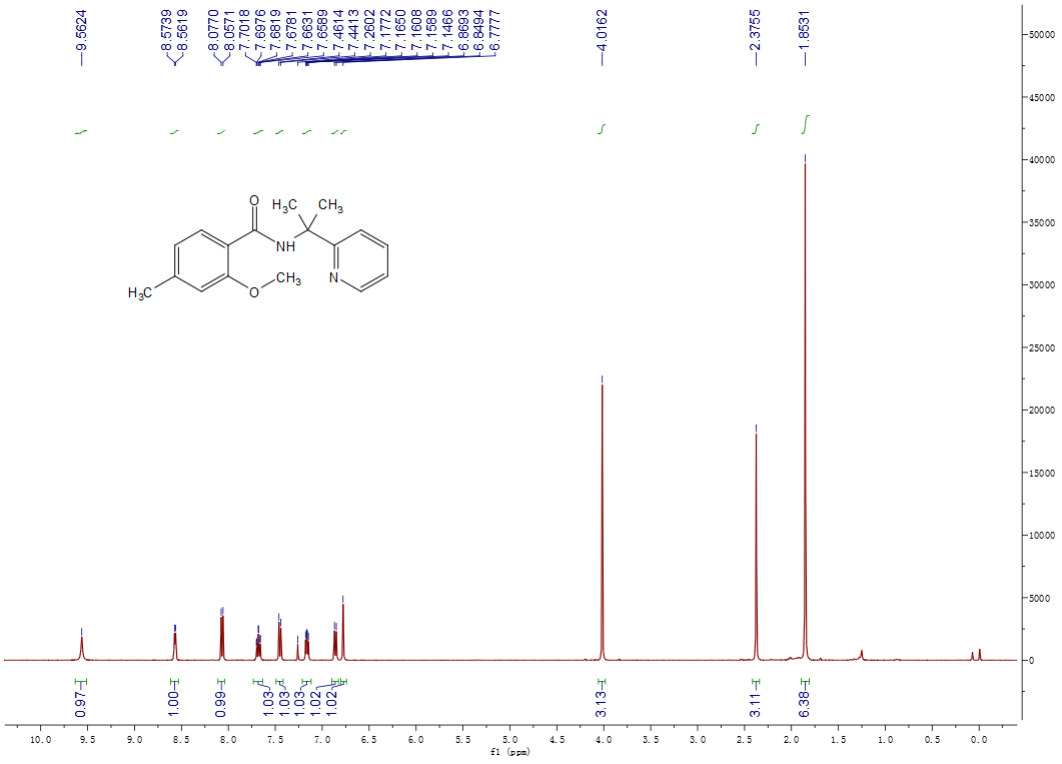

166.37
164.78
147.67
137.38
136.01
131.17
128.54
128.43
127.08
126.82
126.57
122.06
119.67
77.16
56.74
27.62
O
H3C
CH3
NH
N
D
f1 (ppm)

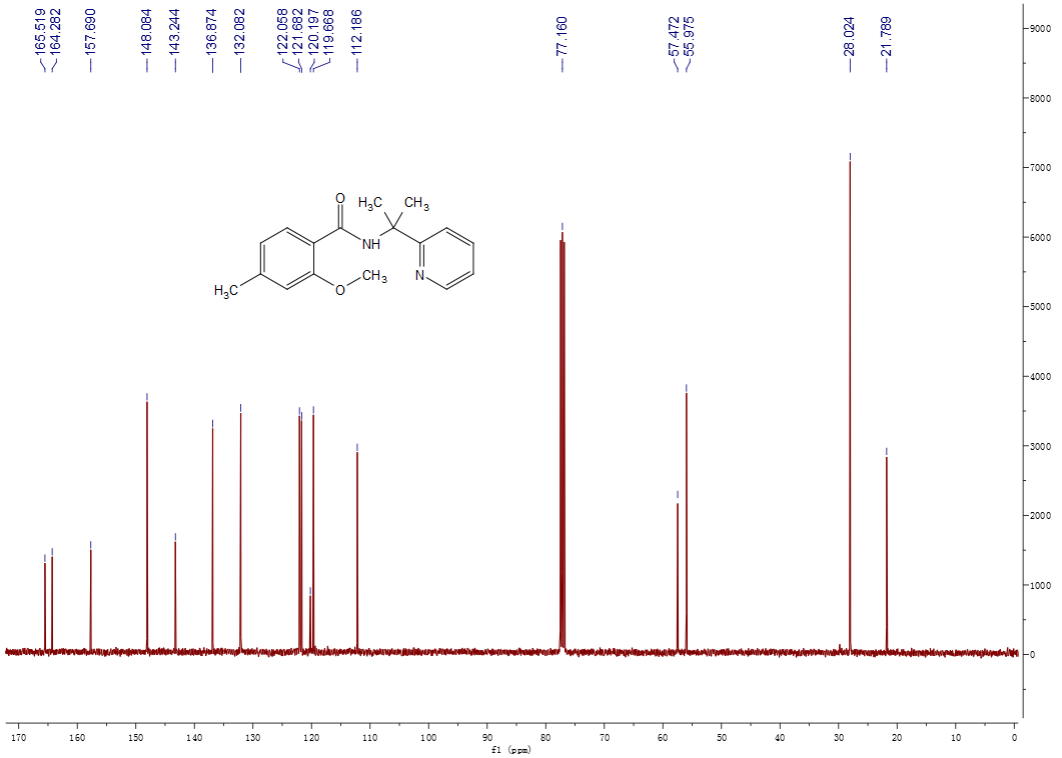
2a


9.6367
8.5856
8.5755
8.5736
8.1810
8.1770
7.7200
7.7040
7.7017
7.6854
7.6812
7.4786
7.4582
7.4562
7.4346
7.4327
7.4162
7.4119
7.2603
7.1980
7.1857
7.1795
7.1674
7.0789
7.0603
7.0412
7.0001
1.8670
0.98
1.00
0.98
1.08
2.11
1.08
1.02
1.00
3.11
6.05
f1 (ppm)

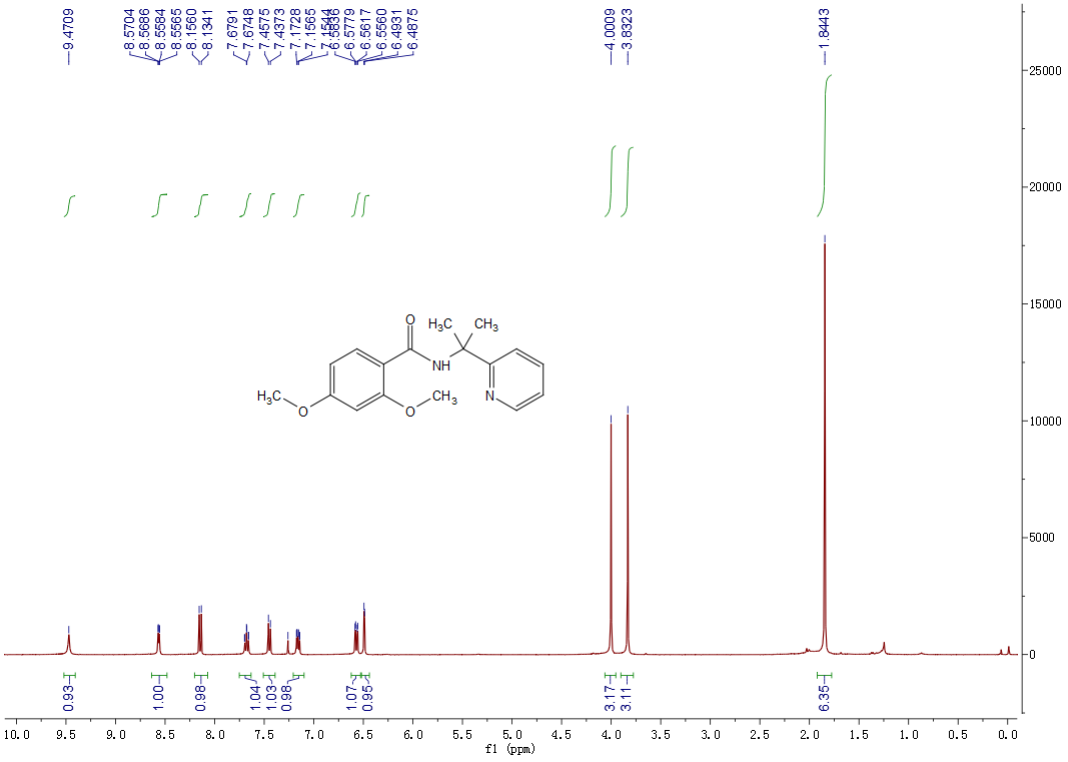

165.427
164.209
157.789
148.107
136.905
132.550
132.164
121.774
121.279
119.720
111.460
77.160
57.558
56.073
28.001
f1 (ppm)

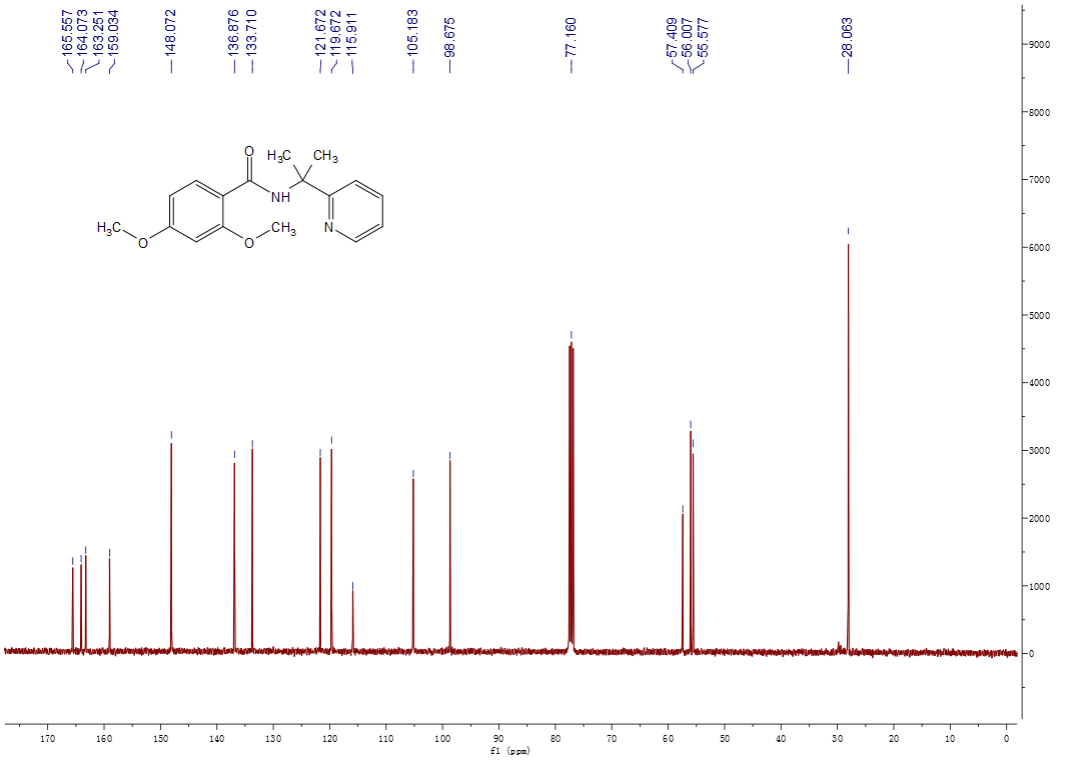
2b


9.5624
8.5739
8.5619
8.0770
8.0571
7.7018
7.6976
7.6819
7.6781
7.6631
7.6589
7.4614
7.4413
7.2602
7.1772
7.1650
7.1608
7.1589
7.1466
6.8693
6.8494
6.7777
4.0162
2.3755
1.8531
0.97
1.00
0.99
1.03
1.03
1.03
1.02
1.02
3.13
3.11
6.38
f1 (ppm)

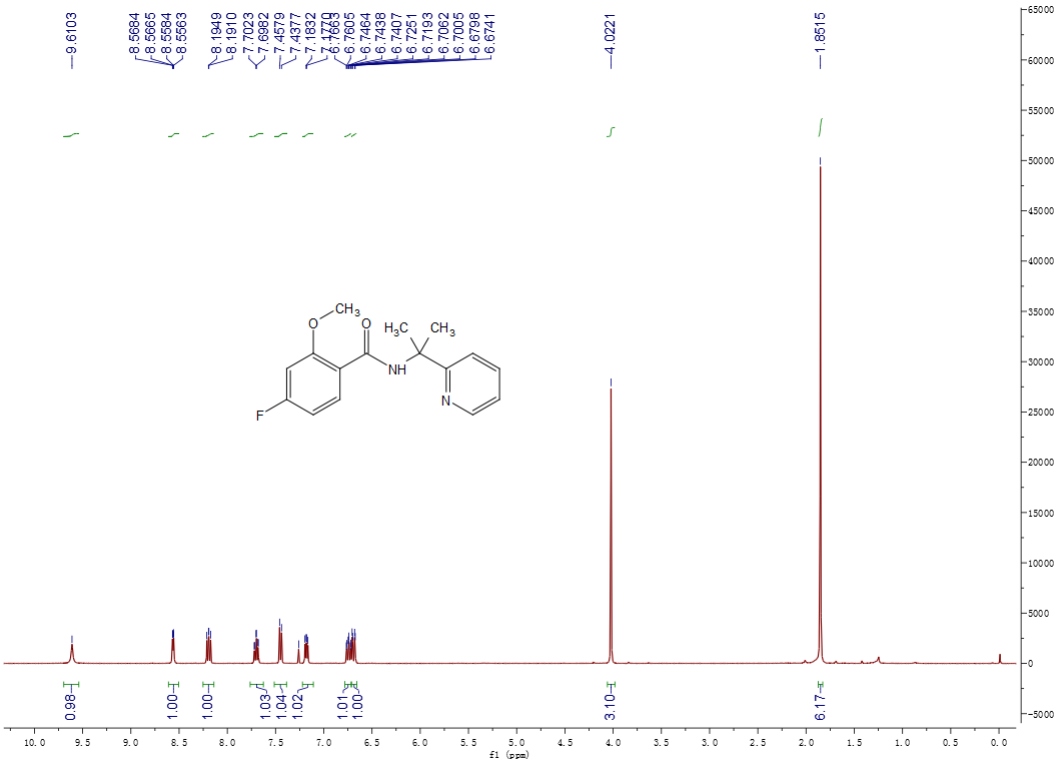

165.519
164.282
157.690
148.084
143.244
136.874
132.082
122.056
121.682
120.197
119.688
112.186
77.160
57.472
55.975
28.024
21.789
f1 (ppm)

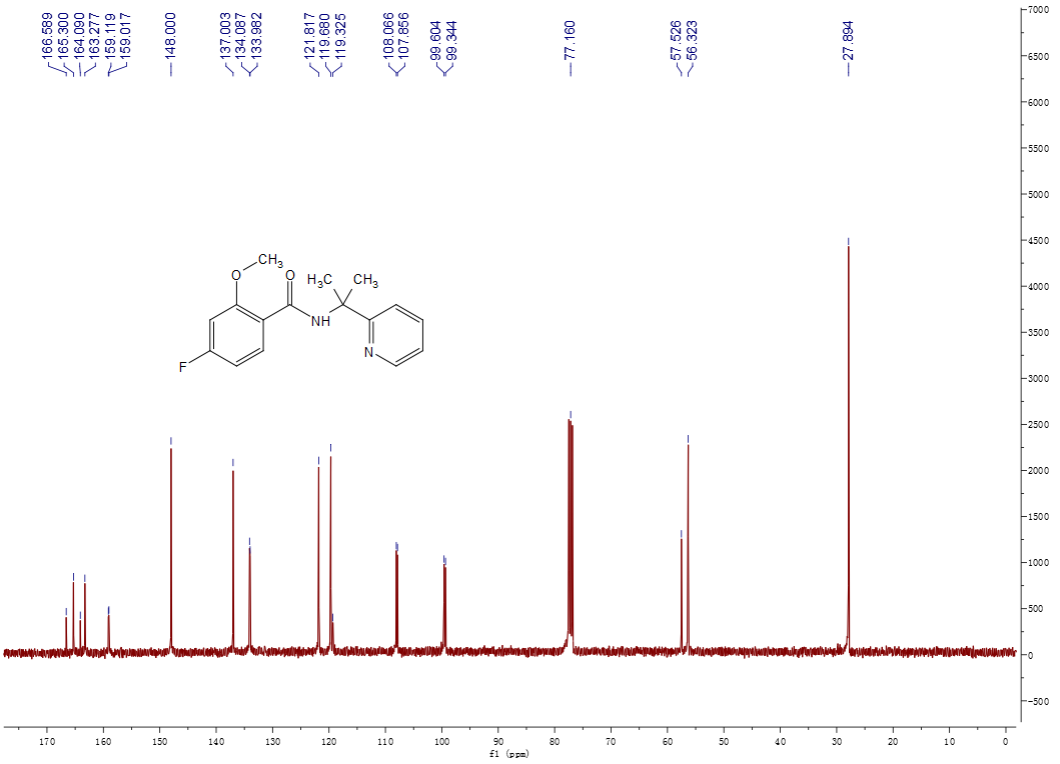
2c


9.4709
8.5704
8.5686
8.5584
8.5565
8.1560
8.1341
7.6791
7.6748
7.4575
7.4373
7.1728
7.1565
6.5779
6.5617
6.5560
6.4931
6.4875
4.0009
3.8323
1.8443
0.93
1.00
0.98
1.04
1.03
0.98
1.07
0.95
3.17
3.11
6.35
f1 (ppm)

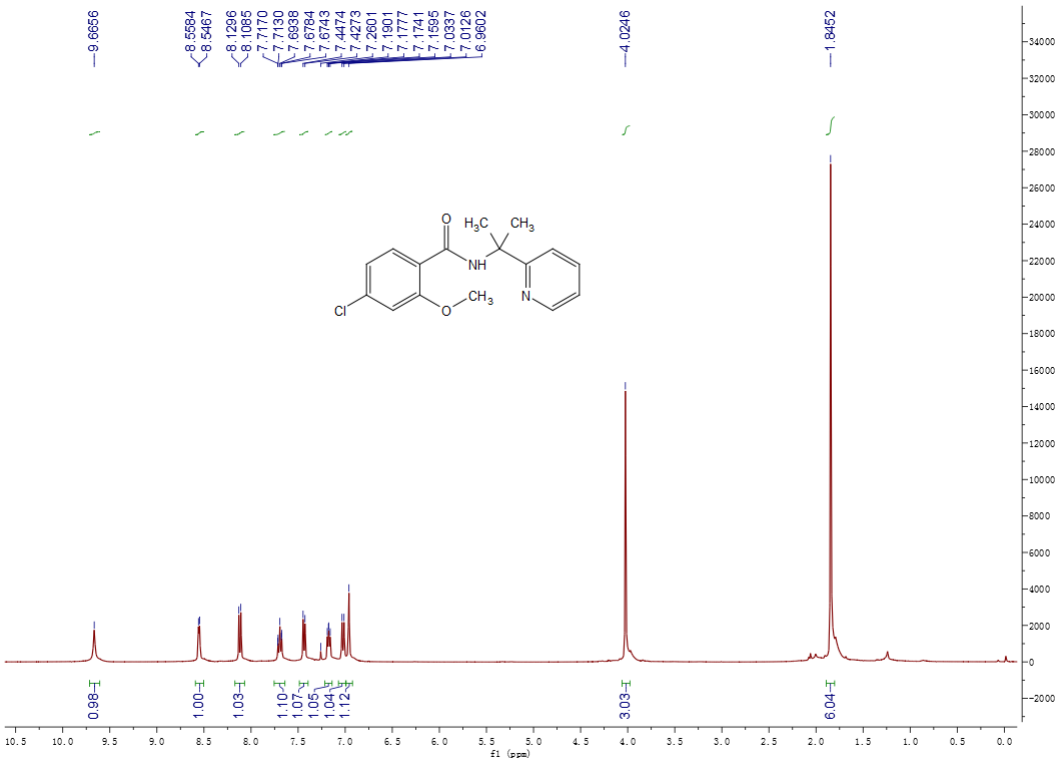

165.557
164.073
163.251
159.034
148.072
136.876
133.710
121.672
119.672
115.911
105.183
98.675
77.160
57.409
56.007
55.577
28.063
f1 (ppm)

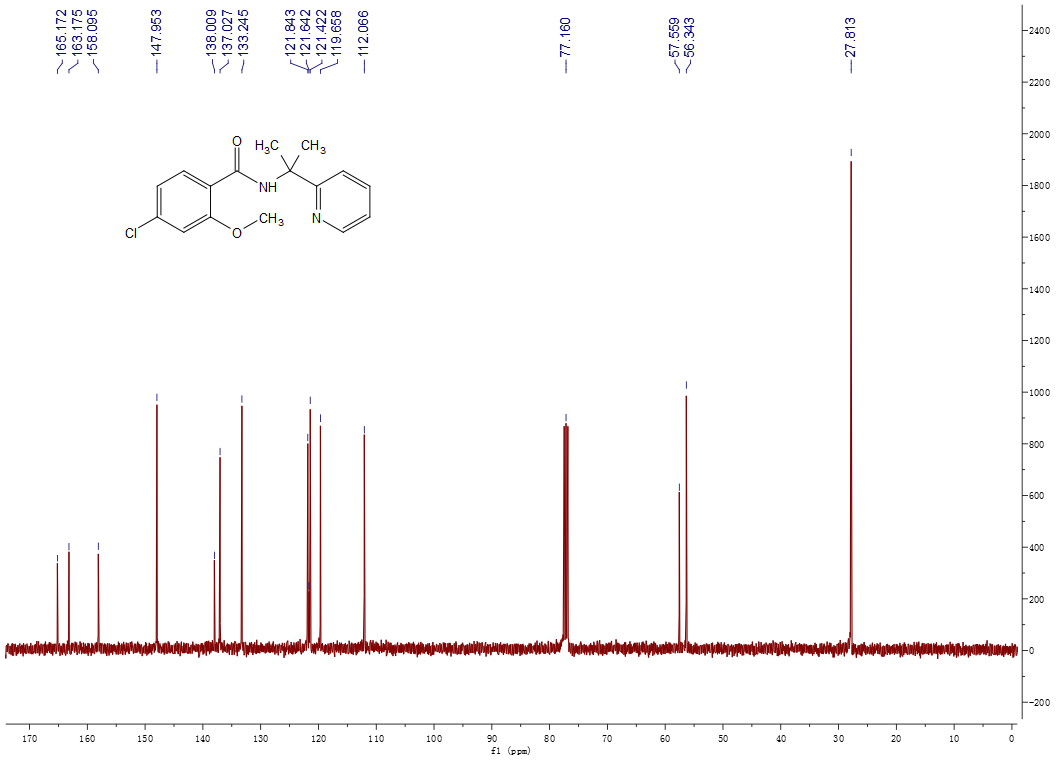
2d


9.6103
8.5684
8.5665
8.5584
8.5563
8.1949
8.1910
7.7023
7.6982
7.4579
7.4377
7.1832
7.1669
6.7605
6.7464
6.7438
6.7407
6.7251
6.7193
6.7062
6.7005
6.6798
6.6741
4.0221
1.8515
0.98
1.00
1.00
1.03
1.04
1.02
1.01
1.00
3.10
6.17
f1 (ppm)

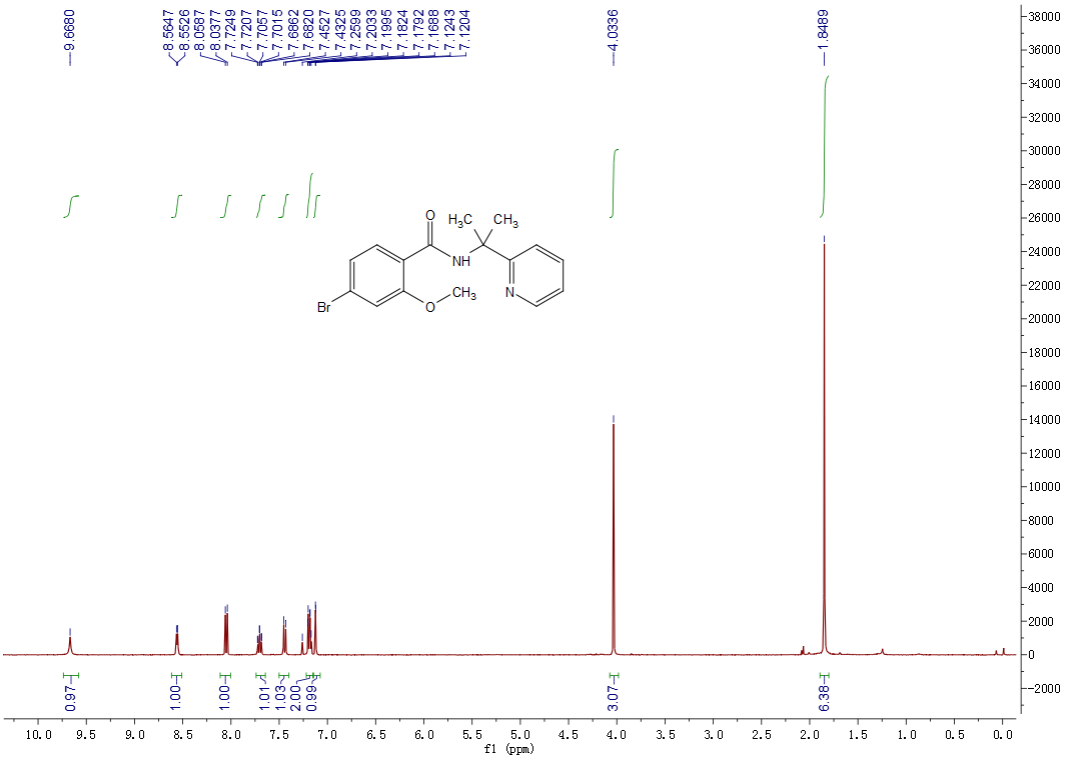

166.589
165.300
164.090
163.277
159.119
159.017
148.000
137.003
134.087
133.982
121.817
119.680
119.325
108.066
107.856
99.604
99.344
77.160
57.526
56.323
27.894
f1 (ppm)

2e


9.6656
8.5584
8.5467
8.1296
8.1085
7.7170
7.7130
7.6938
7.6784
7.6743
7.4474
7.4273
7.2601
7.1901
7.1777
7.1741
7.1595
7.0337
7.0126
6.9602
4.0246
1.8452
0.98
1.00
1.03
1.10
1.07
1.05
1.04
1.12
3.03
6.04
f1 (ppm)


165.172
163.175
158.095
147.953
138.009
137.027
133.245
121.843
121.642
121.422
119.658
112.066
77.160
57.559
56.343
27.813
f1 (ppm)

2f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8.0377
7.7249
7.7207
7.7057
7.7015
7.6862
7.6820
7.4527
7.4325
7.2599
7.2033
7.1995
7.1824
7.1792
7.1688
7.1243
7.1204
4.0336
1.8489
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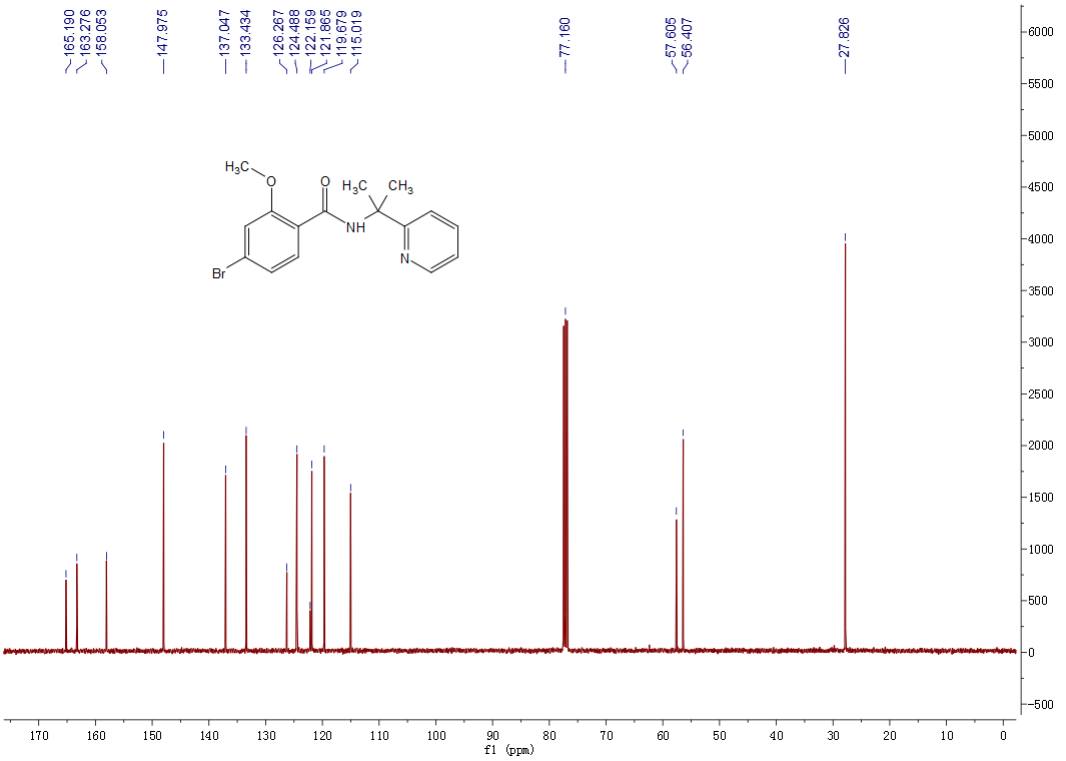
1.00
1.00
1.01
1.03
2.00
0.99
3.07
6.38
f1 (ppm)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163.276
158.053
147.975
137.047
133.434
126.267
124.488
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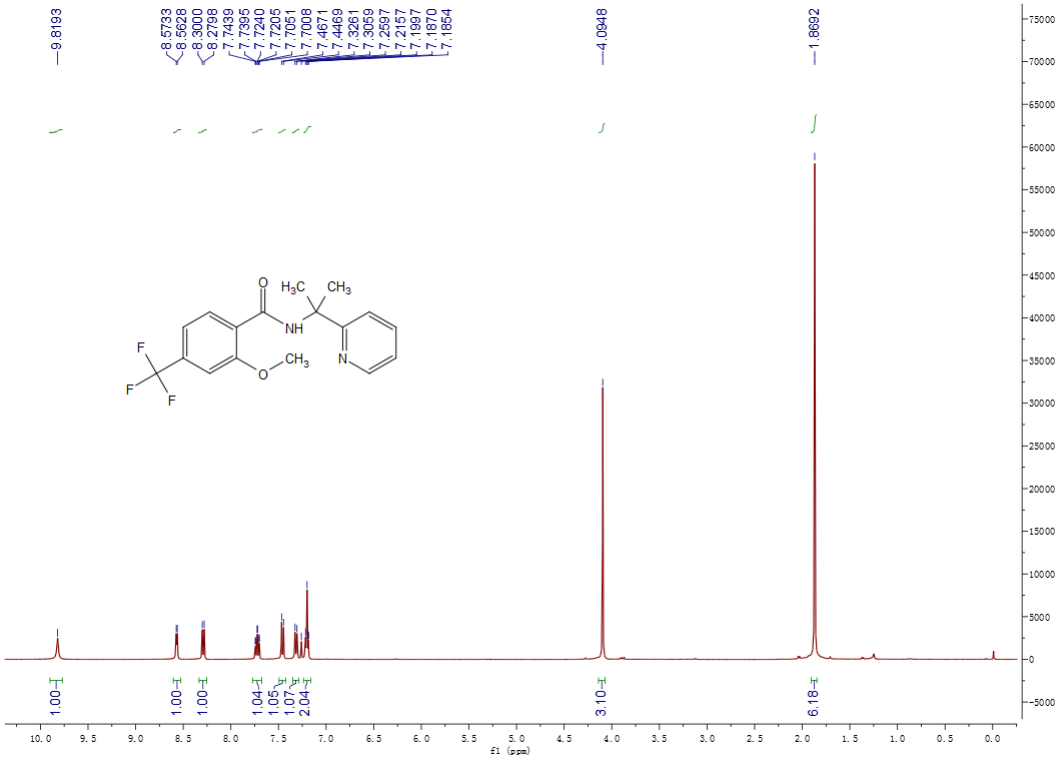
121.865
119.679
115.019
77.160
57.605
56.407
27.826
f1 (ppm)

2ga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8.5628
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8.2798
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7.7395
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7.7205
7.7051
7.7008
7.4671
7.4469
7.3261
7.3059
7.2597
7.2157
7.1997
7.1870
7.1854
4.0948
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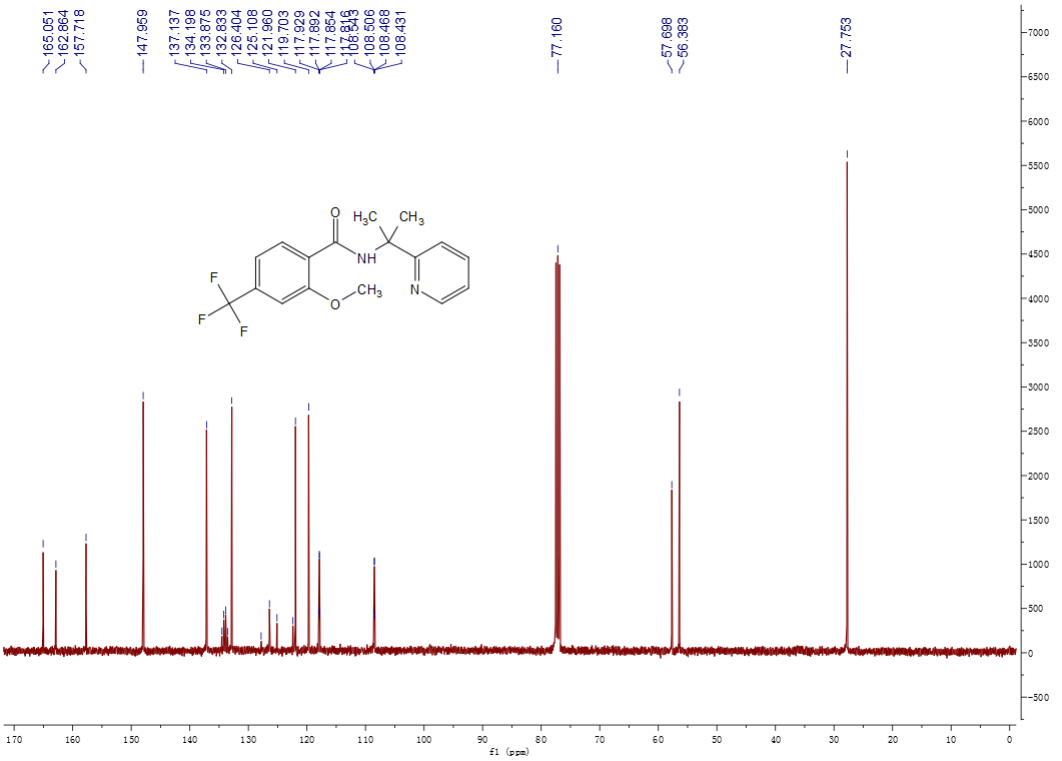
1.00
1.00
1.04
1.05
1.07
2.04
3.10
6.18
f1 (ppm)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162.864
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137.137
134.198
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132.833
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125.108
121.960
119.703
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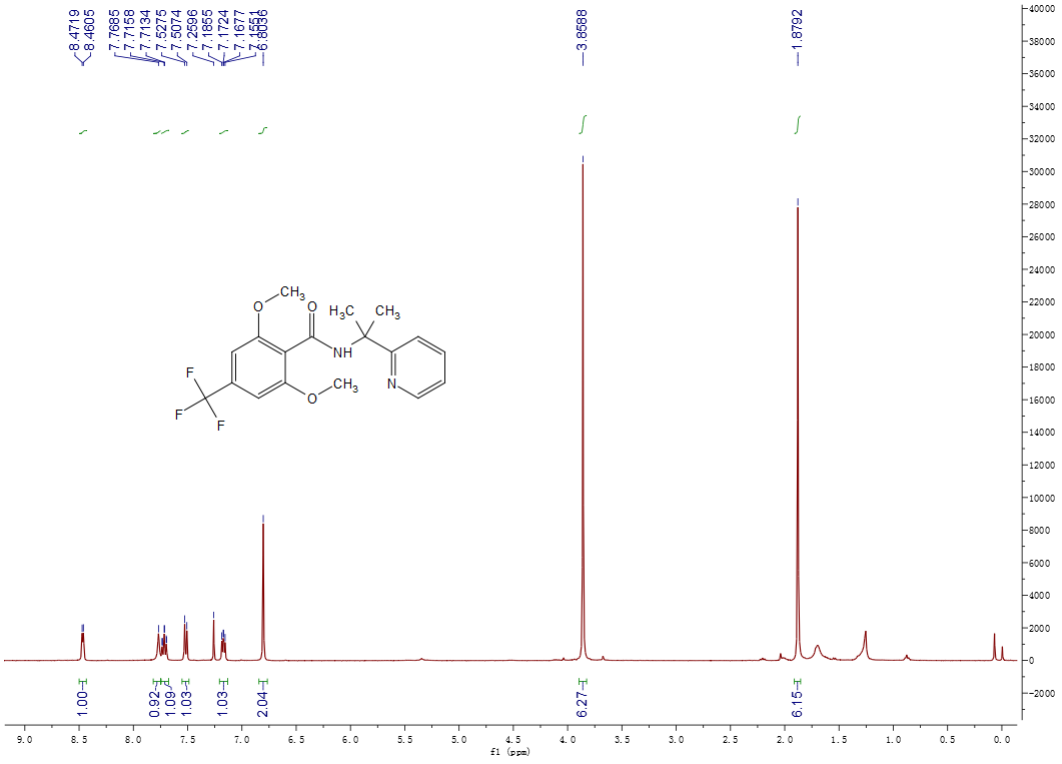
117.892
117.854
108.506
108.468
108.431
77.160
57.698
56.383
27.753
f1 (ppm)

2gb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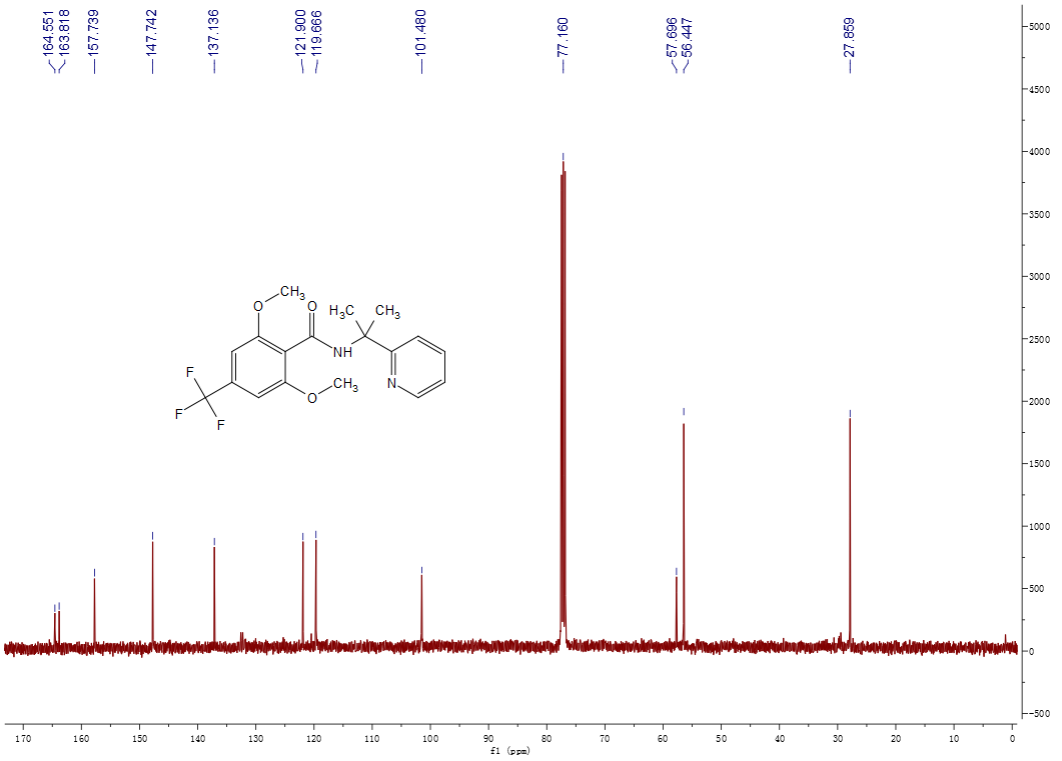
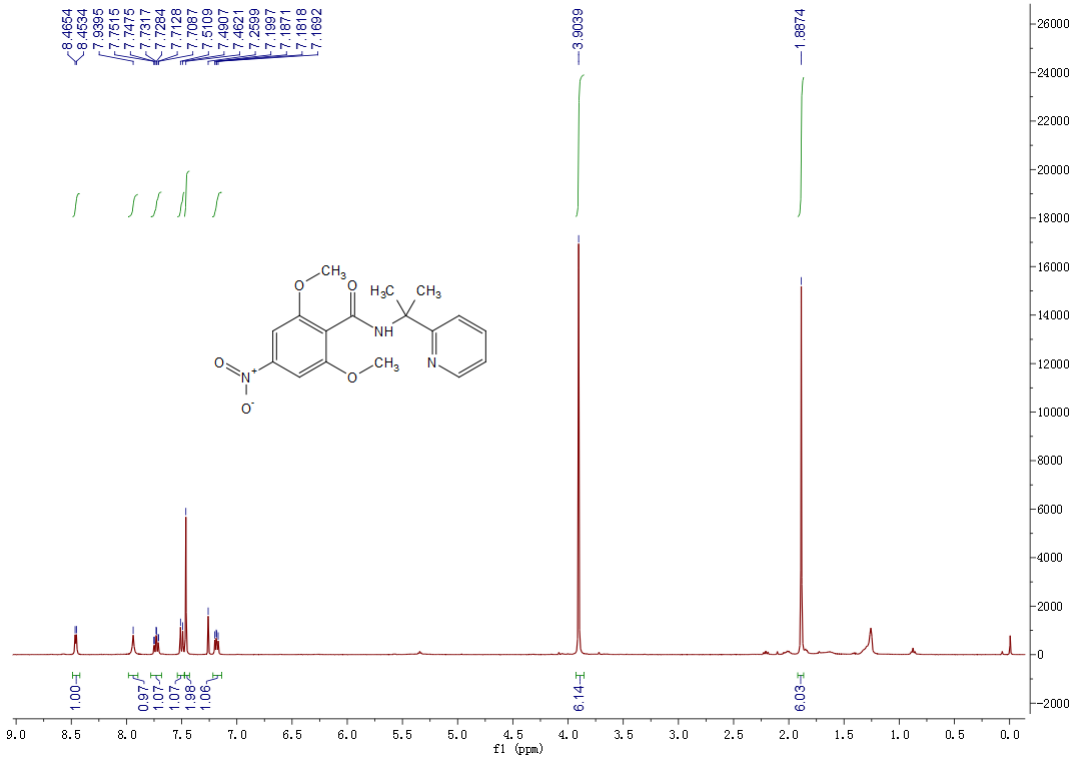
7.7685
7.7158
7.7134
7.5275
7.5074
7.2596
7.1855
7.1724
7.1677
7.1551
6.8036
3.8588
1.8792
1.00
0.92
1.09
1.03
1.03
2.04
6.27
6.15
f1 (ppm)


164.551
163.818
157.739
147.742
137.136
121.900
119.666
101.480
77.160
57.696
56.447
27.869
f1 (ppm)

2h


8.4654
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7.9396
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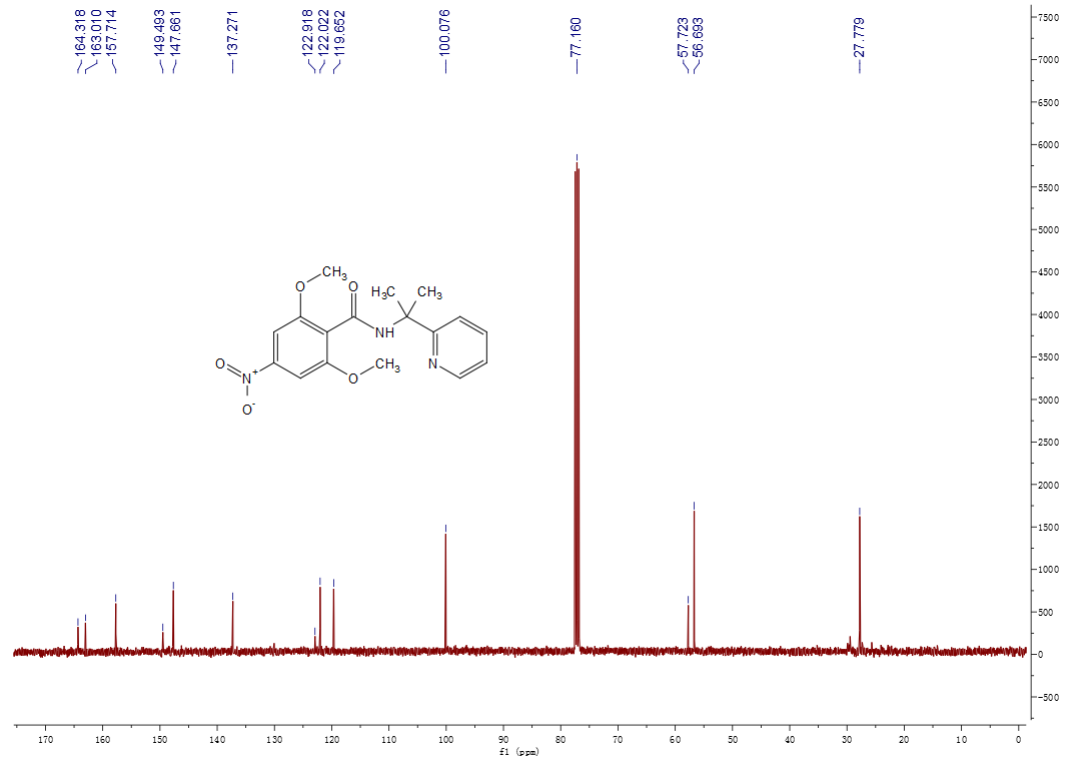
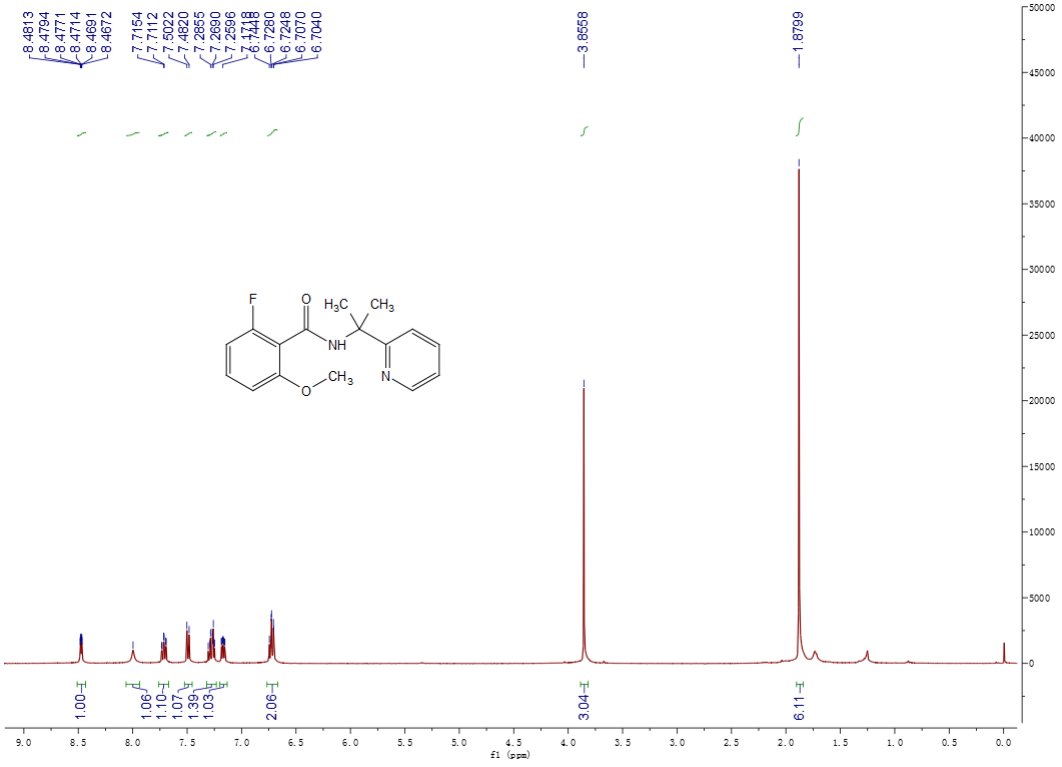
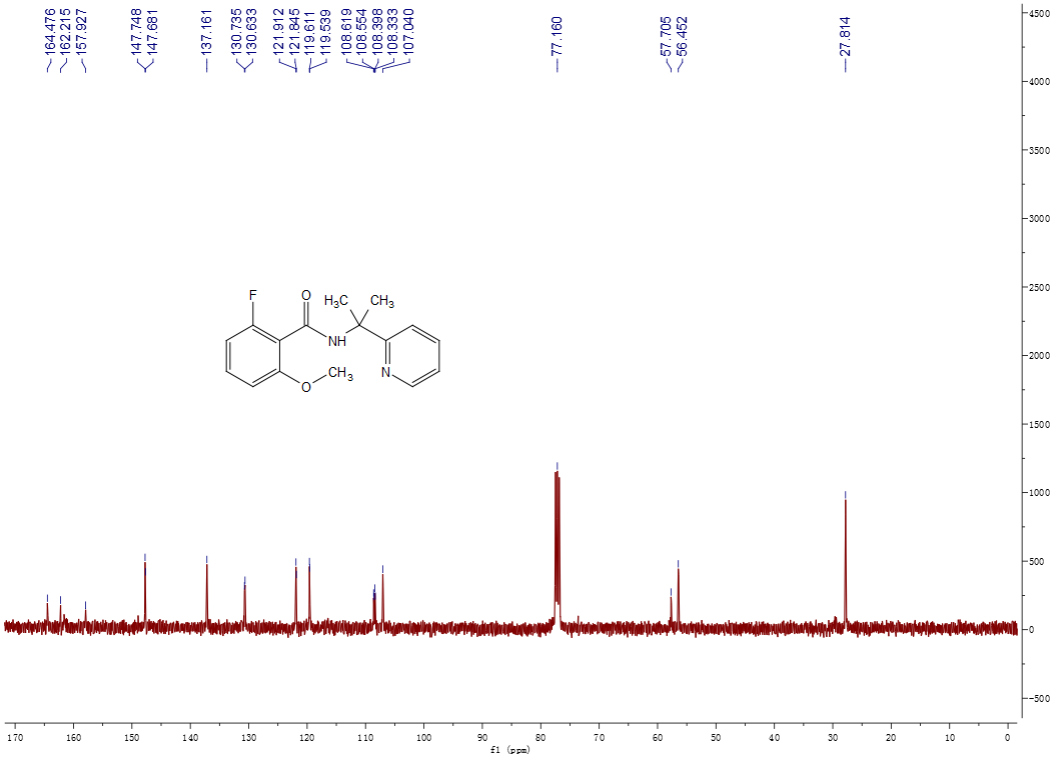
7.7475
7.7317
7.7284
7.7128
7.7087
7.5109
7.4907
7.4621
7.2599
7.1997
7.1871
7.1818
7.1692
3.9039
1.8874
1.00
0.97
1.07
1.07
1.98
1.06
6.14
6.03
f1 (ppm)

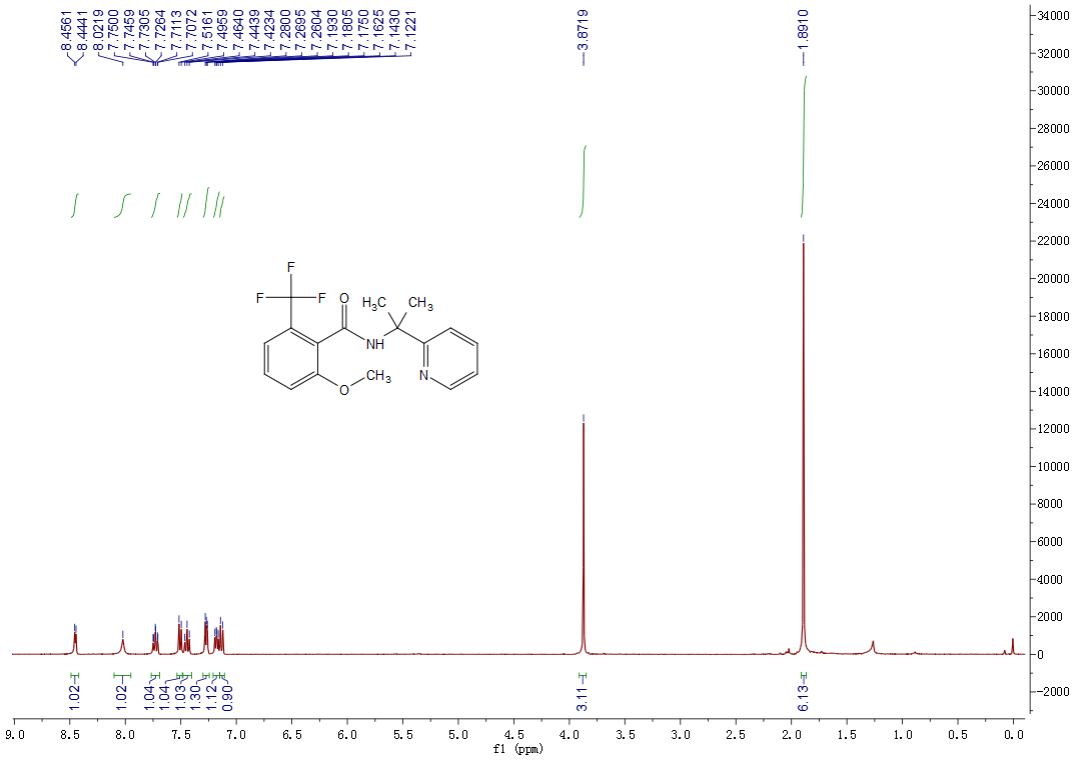

164.318
163.010
157.714
149.493
147.661
137.271
122.918
122.022
119.652
100.076
77.160
57.723
56.693
27.779
f1 (ppm)

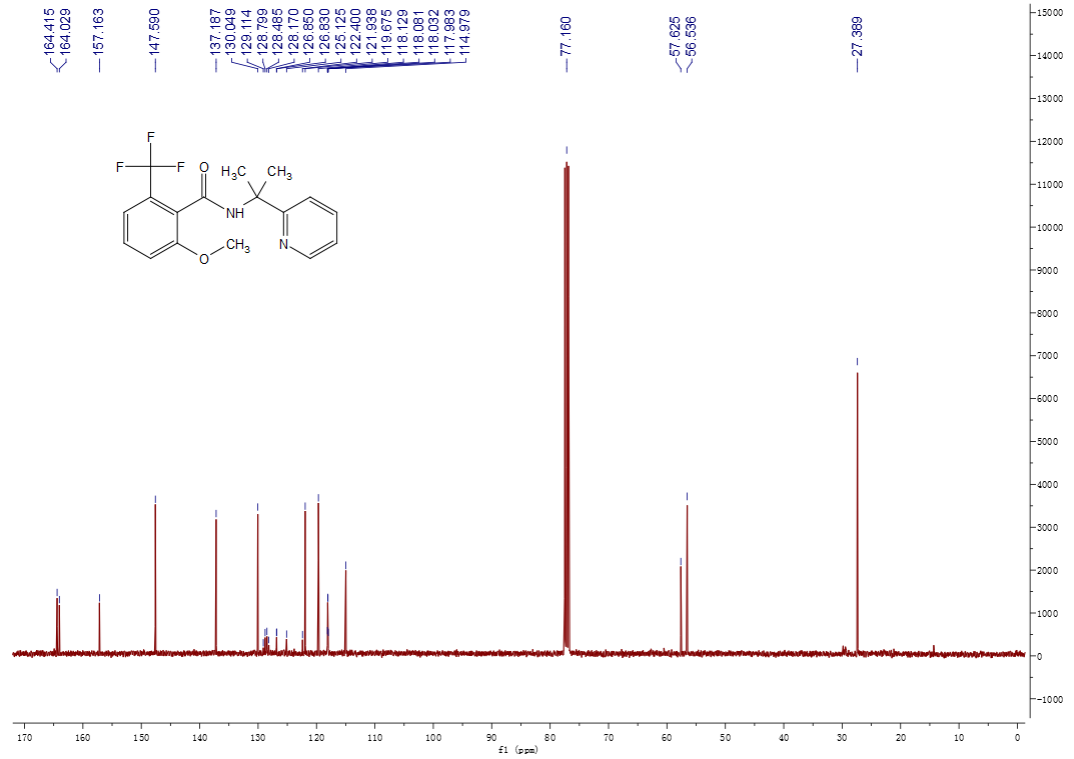
2i


8.4813
8.4794
8.4771
8.4714
8.4691
8.4672
7.7154
7.7112
7.5022
7.4820
7.2855
7.2690
7.2596
7.1418
6.7280
6.7248
6.7070
6.7040
3.8658
1.8799
F
O
H3C
CH3
NH
CH3
O
N
1.00
1.06
1.10
1.07
1.39
1.03
2.06
3.04
6.11
f1 (ppm)

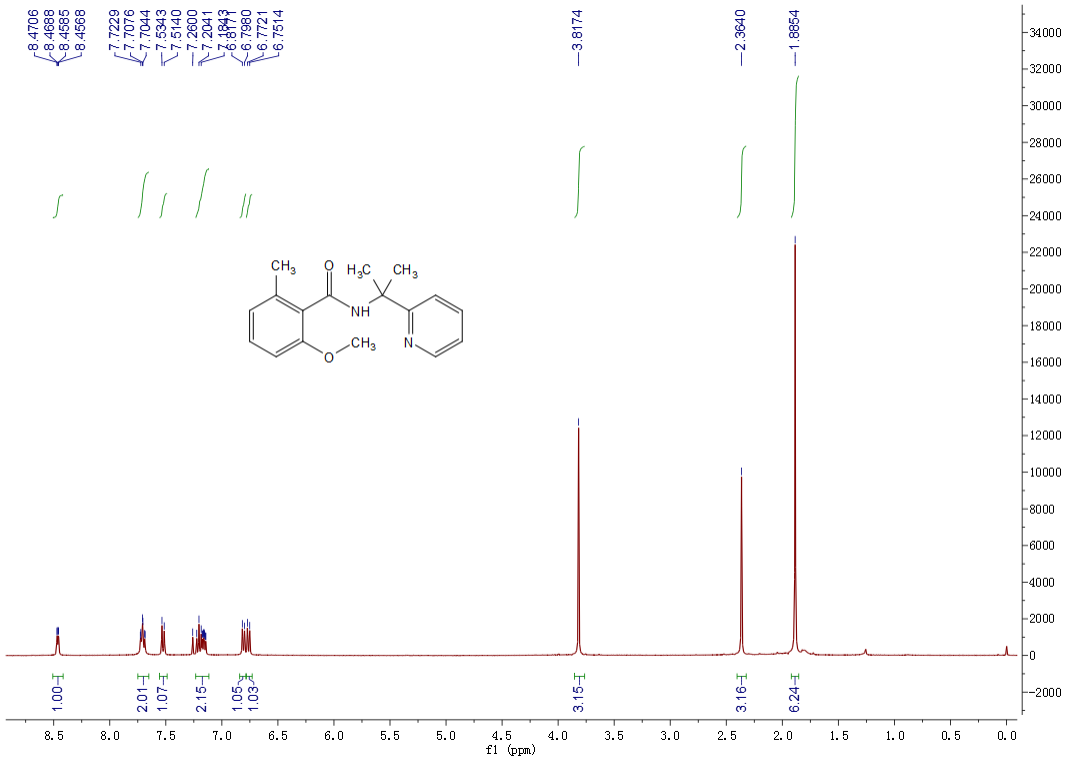

164.476
162.215
157.927
147.748
147.681
137.161
130.735
130.633
121.912
121.845
119.611
119.539
108.619
108.554
108.398
108.333
107.040
77.160
57.705
56.452
27.814
F
O
H3C
CH3
NH
CH3
O
N
f1 (ppm)

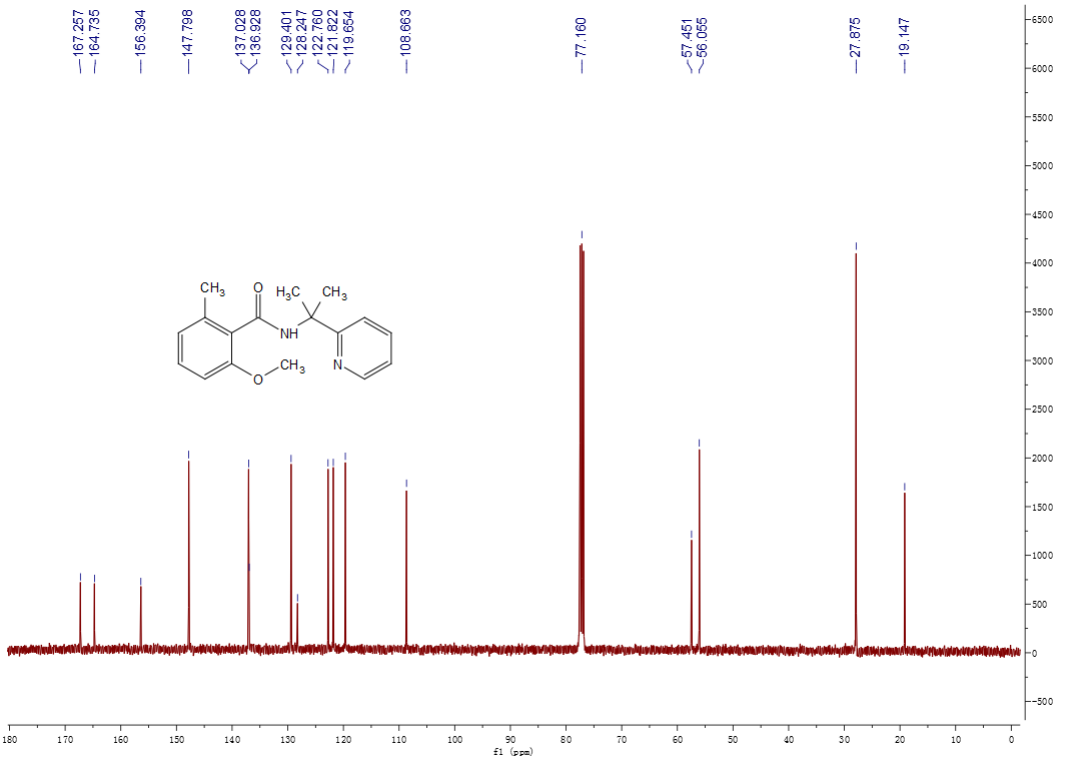
2j


8.4561
8.4441
8.0219
7.7500
7.7459
7.7305
7.7264
7.7113
7.7072
7.5161
7.4959
7.4640
7.4439
7.4234
7.2800
7.2695
7.2604
7.1930
7.1805
7.1750
7.1625
7.1430
7.1221
3.8719
1.8910
1.02
1.02
1.04
1.04
1.03
1.30
1.12
0.90
3.11
6.13
f1 (ppm)

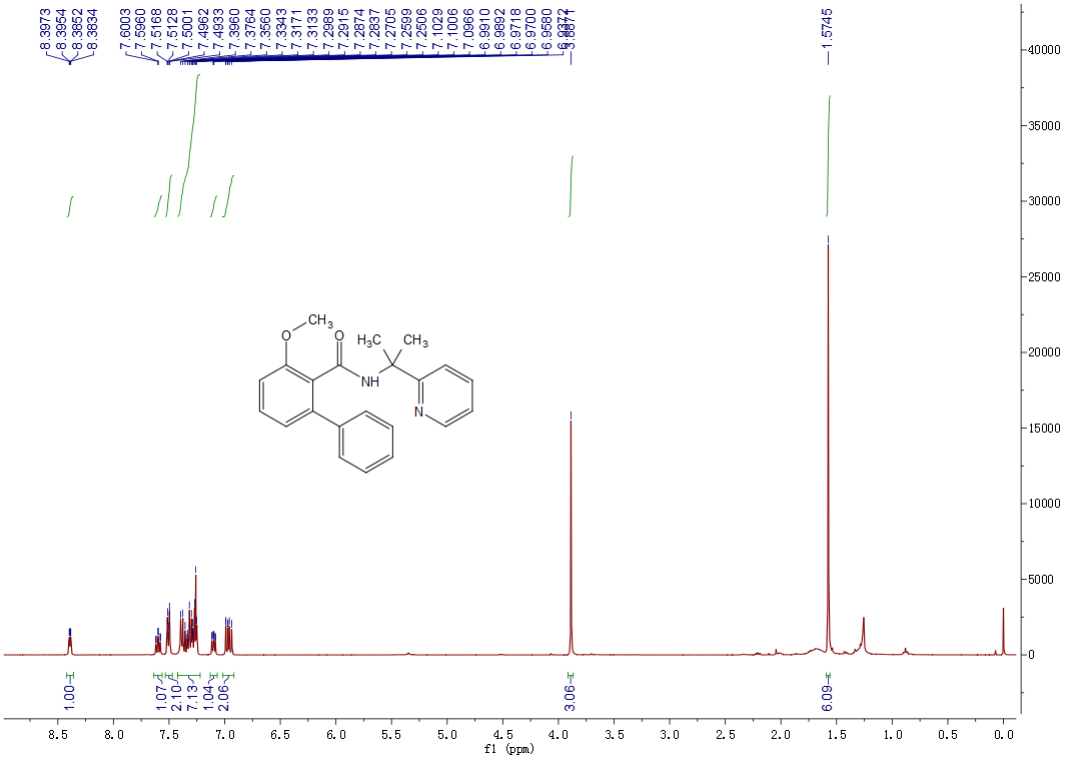

164.415
164.029
157.163
147.590
137.187
130.049
129.114
128.799
128.485
128.170
126.850
126.830
125.125
122.400
121.938
119.675
118.129
118.081
118.032
117.983
114.979
77.160
57.625
56.536
27.389
f1 (ppm)

2k


8.4706
8.4688
8.4585
8.4568
7.7229
7.7076
7.7044
7.5343
7.5140
7.2600
7.2041
7.1843
6.8177
6.7980
6.7721
6.7514
3.8174
2.3640
1.8854
1.00
2.01
1.07
2.15
1.05
1.03
3.15
3.16
6.24
f1 (ppm)


167.257
164.735
156.394
147.798
137.028
136.928
129.401
128.247
122.760
121.822
119.654
108.663
77.160
57.451
56.055
27.875
19.147
f1 (ppm)

2l


8.3873
8.3954
8.3852
8.3834
7.6003
7.5960
7.5168
7.5128
7.5001
7.4962
7.4933
7.3960
7.3764
7.3560
7.3343
7.3171
7.3133
7.2989
7.2915
7.2874
7.2837
7.2705
7.2599
7.2506
7.1029
7.1006
7.0966
6.9910
6.9892
6.9718
6.9700
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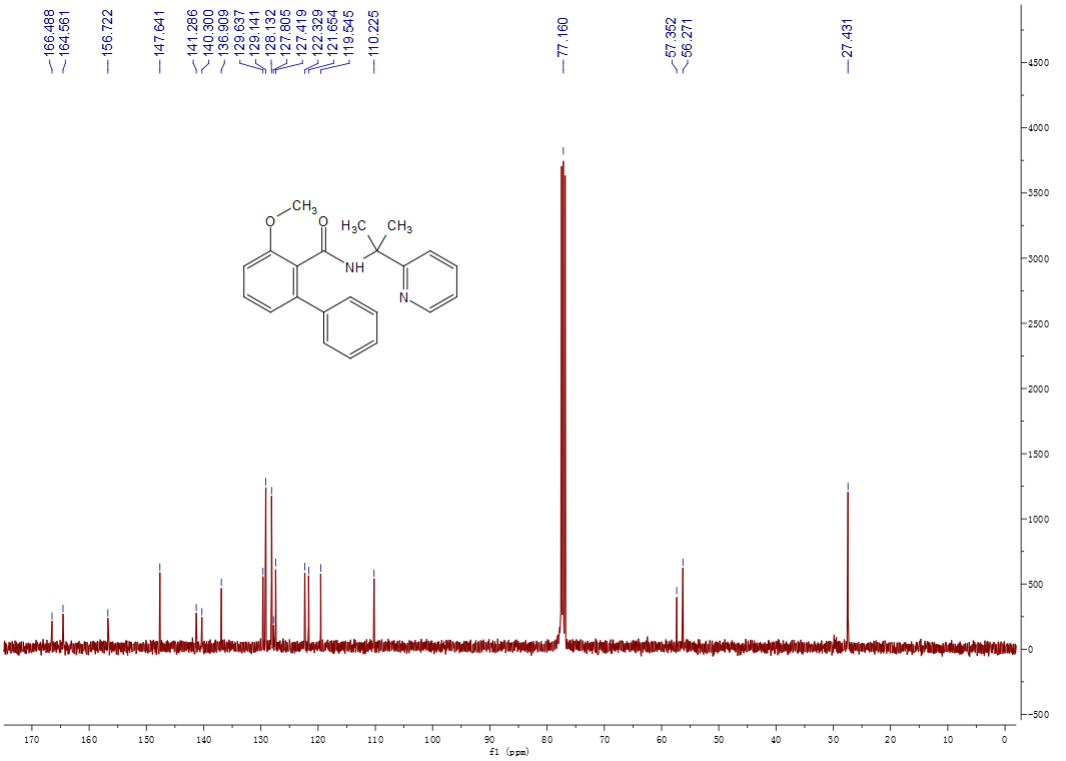
1.04
2.06
3.06
6.09
f1 (ppm)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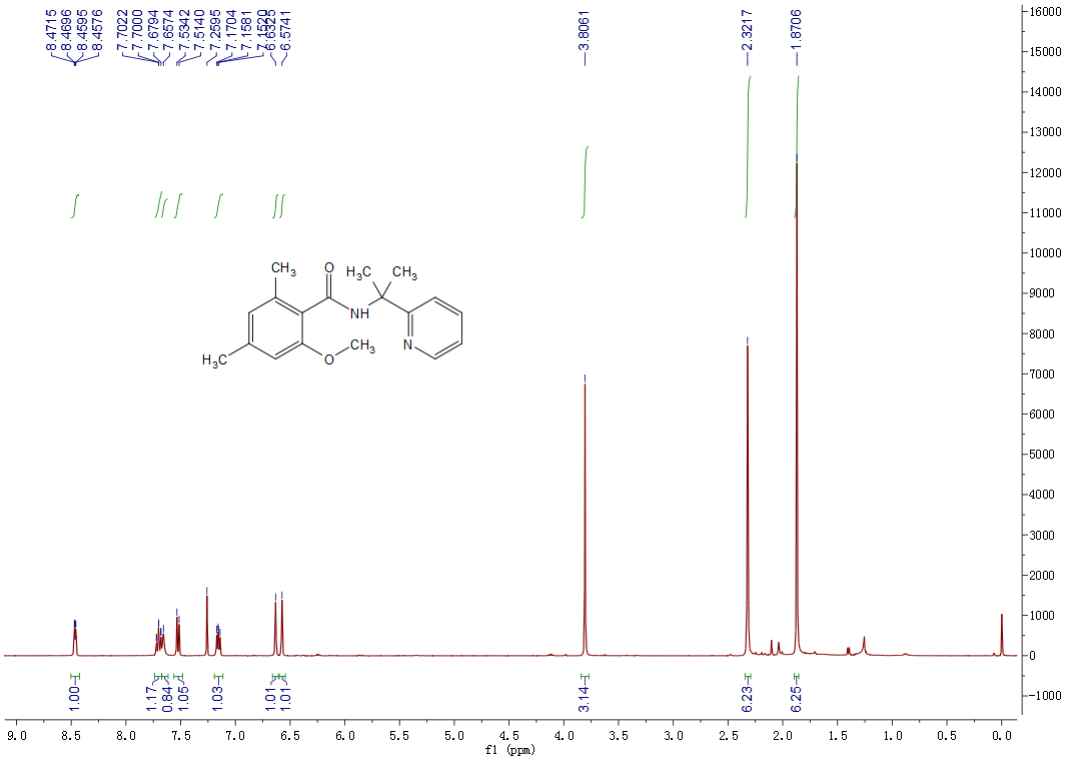
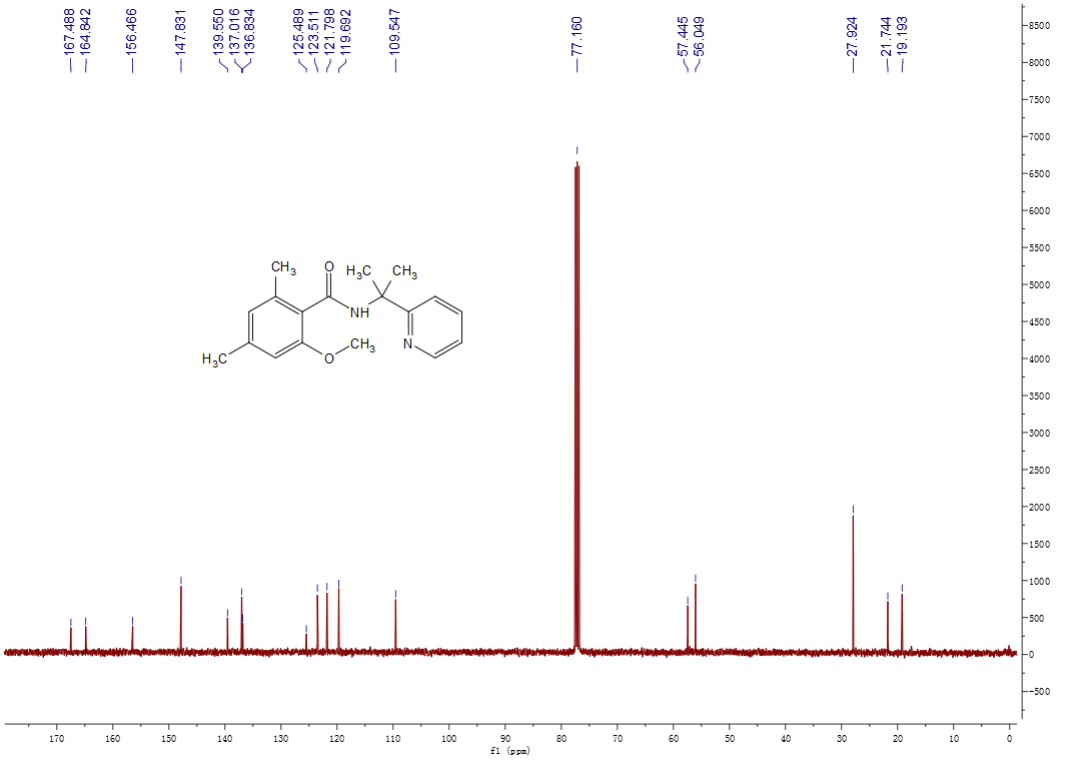
164.561
156.722
147.641
141.286
140.300
136.909
129.637
129.141
128.132
127.805
127.419
122.329
121.654
119.545
110.225
77.160
57.352
56.271
27.431
f1 (ppm)

2m


8.4715
8.4696
8.4595
8.4576
7.7022
7.7000
7.6794
7.6574
7.5342
7.5140
7.2595
7.1704
7.1581
7.1529
6.6523
6.5741
3.8061
2.3217
1.8706
1.00
1.17
0.84
1.05
1.03
1.01
1.01
3.14
6.23
6.25
f1 (ppm)


167.488
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137.016
136.834
125.489
123.511
121.798
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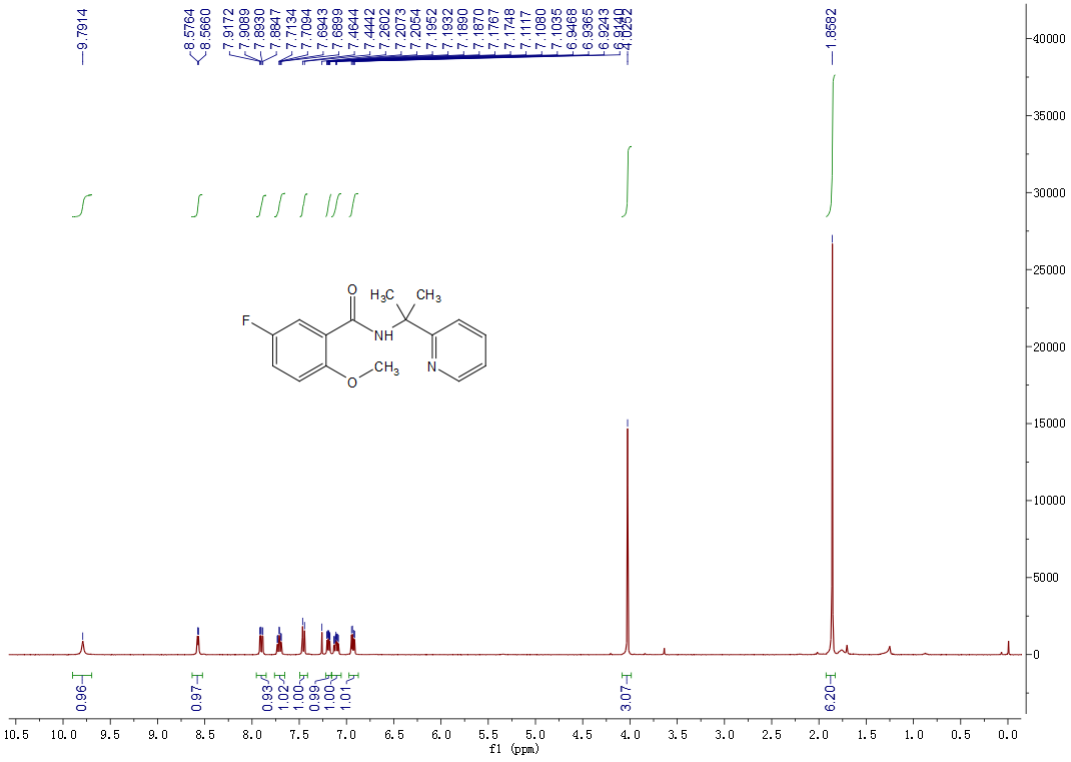
109.547
77.160
57.445
56.049
27.924
21.744
19.193
f1 (ppm)

2n


9.7914
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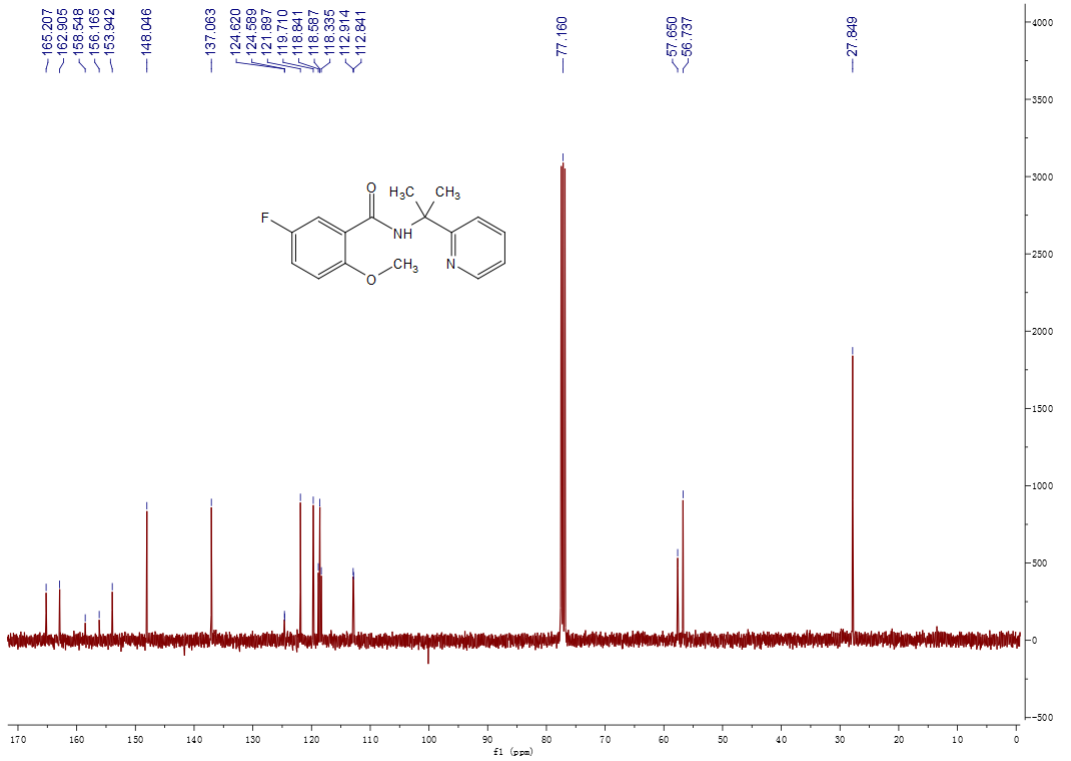
8.5660
7.9172
7.9089
7.8930
7.8847
7.7134
7.7094
7.6943
7.6899
7.4644
7.4442
7.2602
7.2073
7.2054
7.1952
7.1932
7.1890
7.1870
7.1767
7.1748
7.1117
7.1080
7.1035
6.9468
6.9365
6.9243
4.0252
1.8582
0.96
0.97
0.93
1.02
1.00
0.99
1.00
1.01
3.07
6.20
f1 (ppm)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124.620
124.589
121.897
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118.335
112.914
112.841
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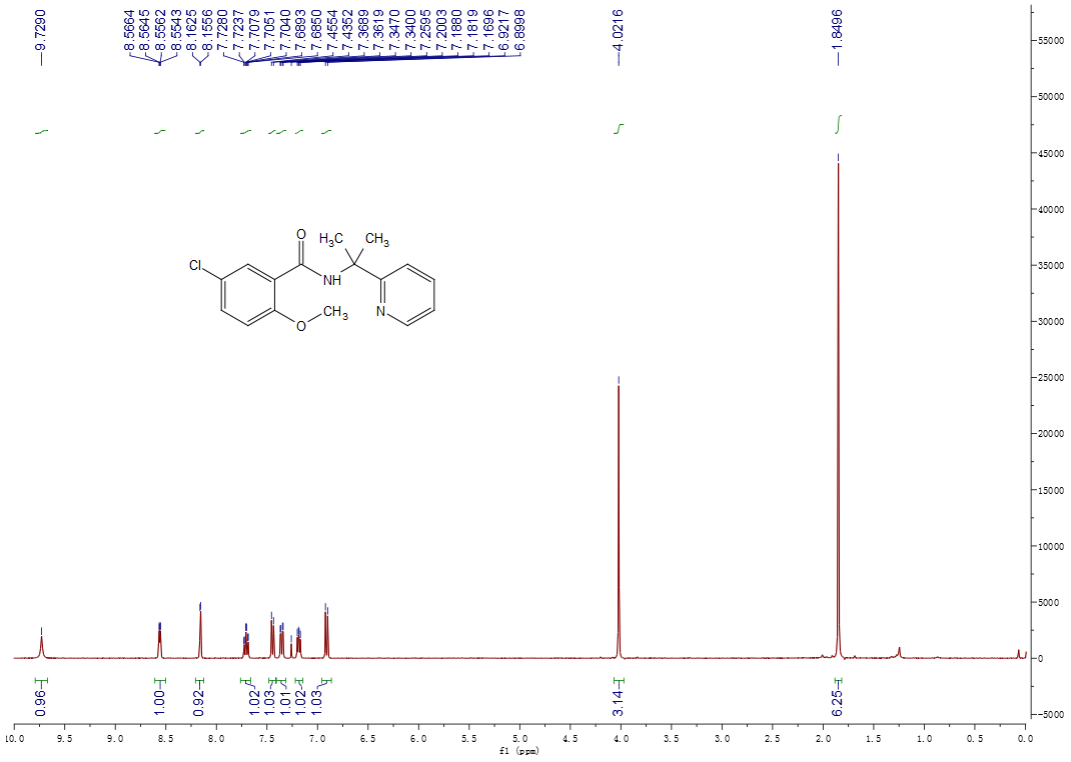
57.650
56.737
27.849
f1 (ppm)

2o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8.1556
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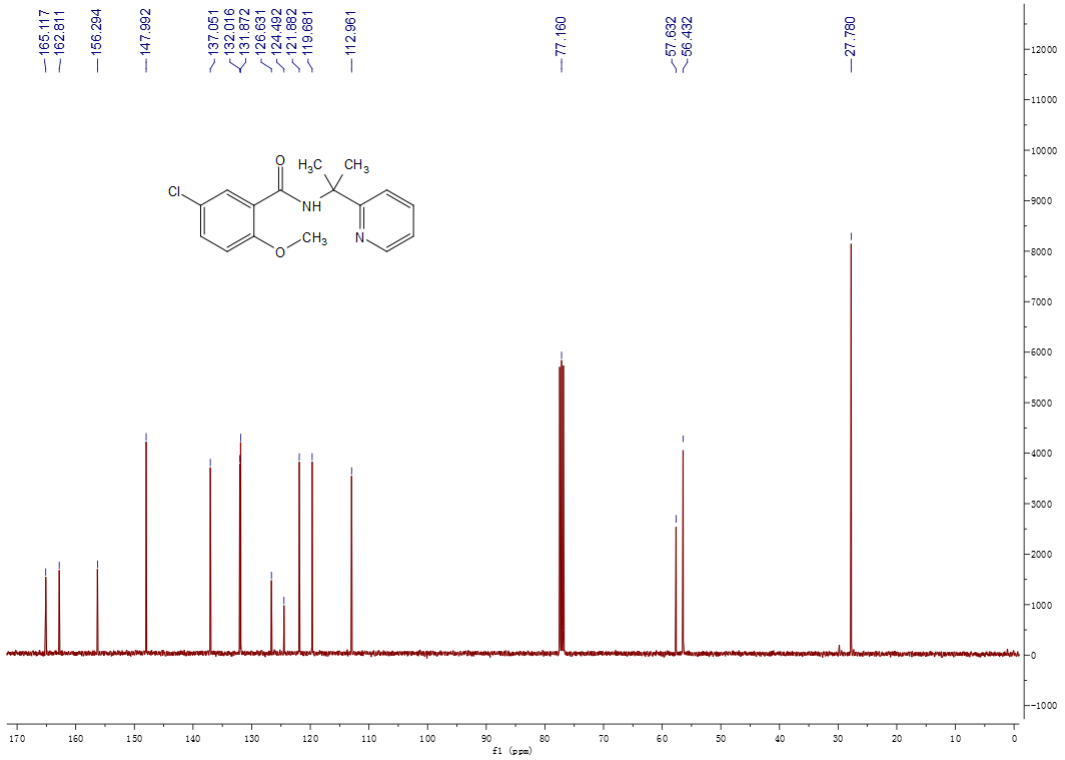
7.7237
7.7079
7.7051
7.7040
7.6893
7.6850
7.4554
7.4352
7.3689
7.3619
7.3470
7.3400
7.2595
7.2003
7.1880
7.1819
7.1696
6.9217
6.8998
4.0216
1.8496
0.96
1.00
0.92
1.02
1.03
1.01
1.02
1.03
3.14
6.25
f1 (ppm)


165.117
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156.294
147.992
137.051
132.016
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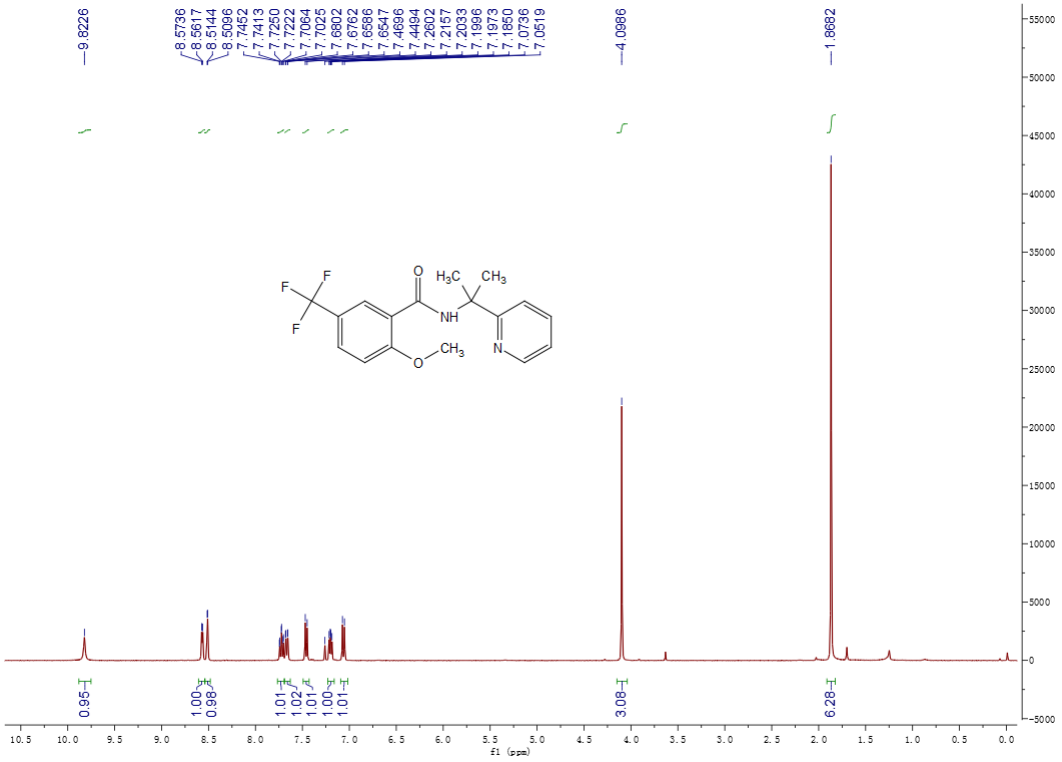
121.882
119.681
112.961
77.160
57.632
56.432
27.780
f1 (ppm)

2p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7.7413
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7.7222
7.7064
7.7025
7.6802
7.6762
7.6586
7.6547
7.4696
7.4494
7.2602
7.2157
7.2033
7.1996
7.1973
7.1850
7.0736
7.0519
4.0986
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0.95
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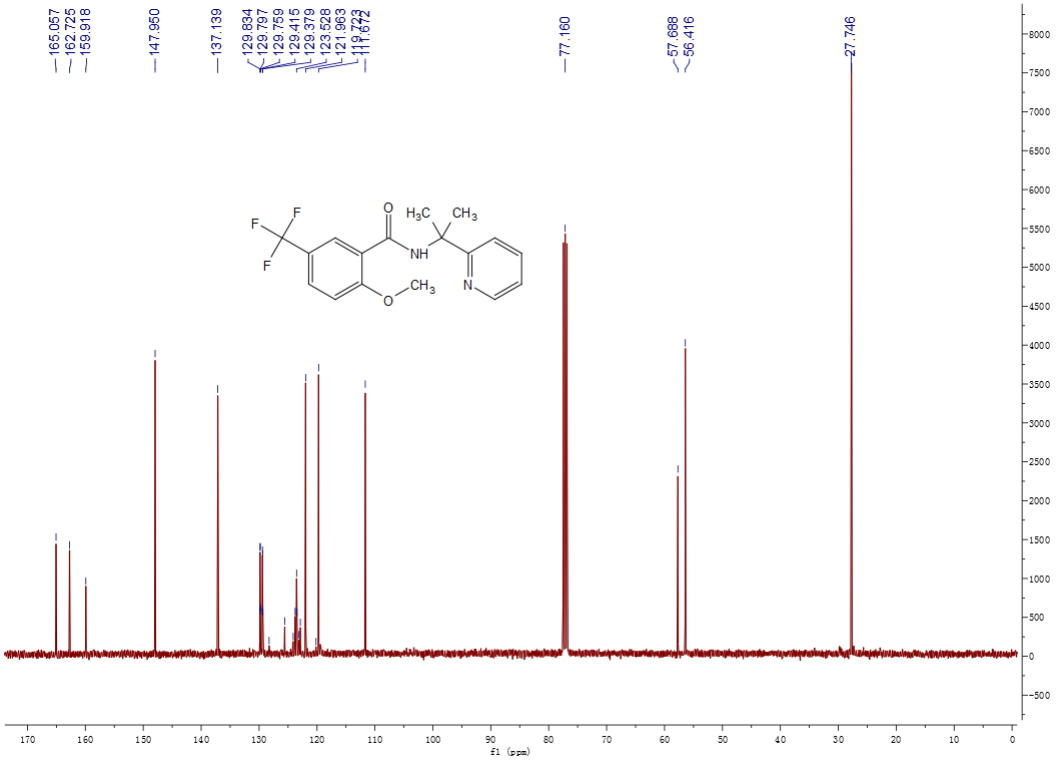
0.98
1.01
1.02
1.01
1.00
1.01
3.08
6.28
f1 (ppm)


165.057
162.725
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137.139
129.834
129.797
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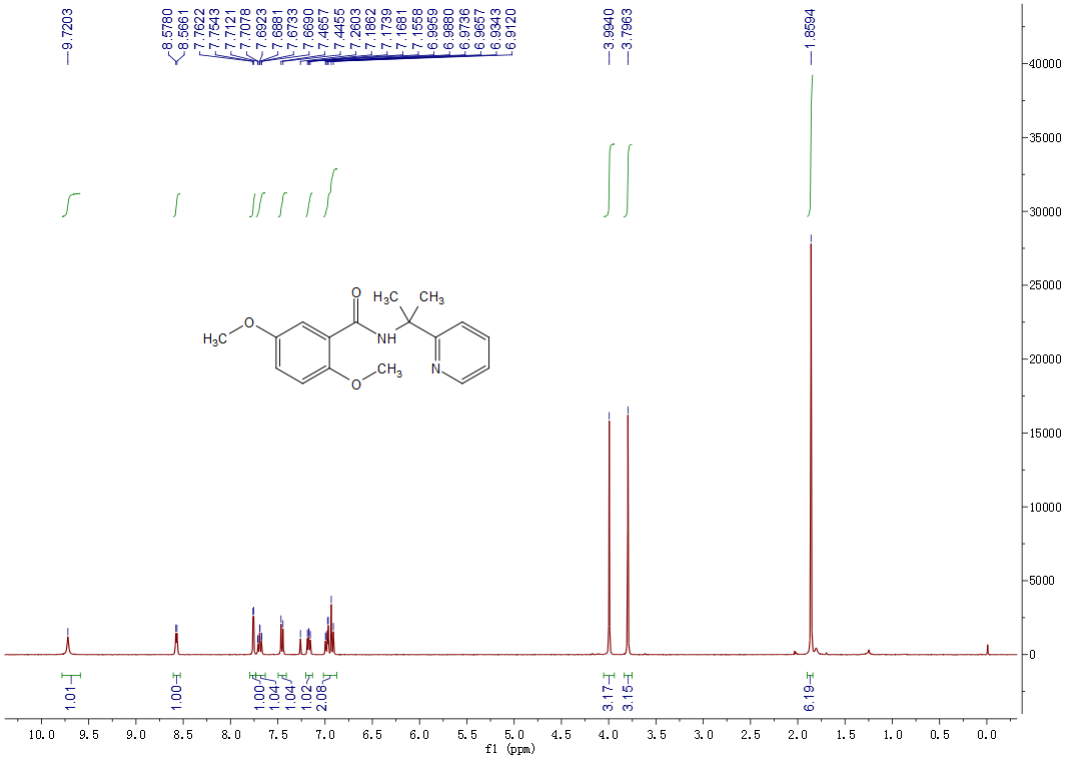
128.379
123.528
121.963
77.160
57.688
56.416
27.746
f1 (ppm)

2q


9.7203
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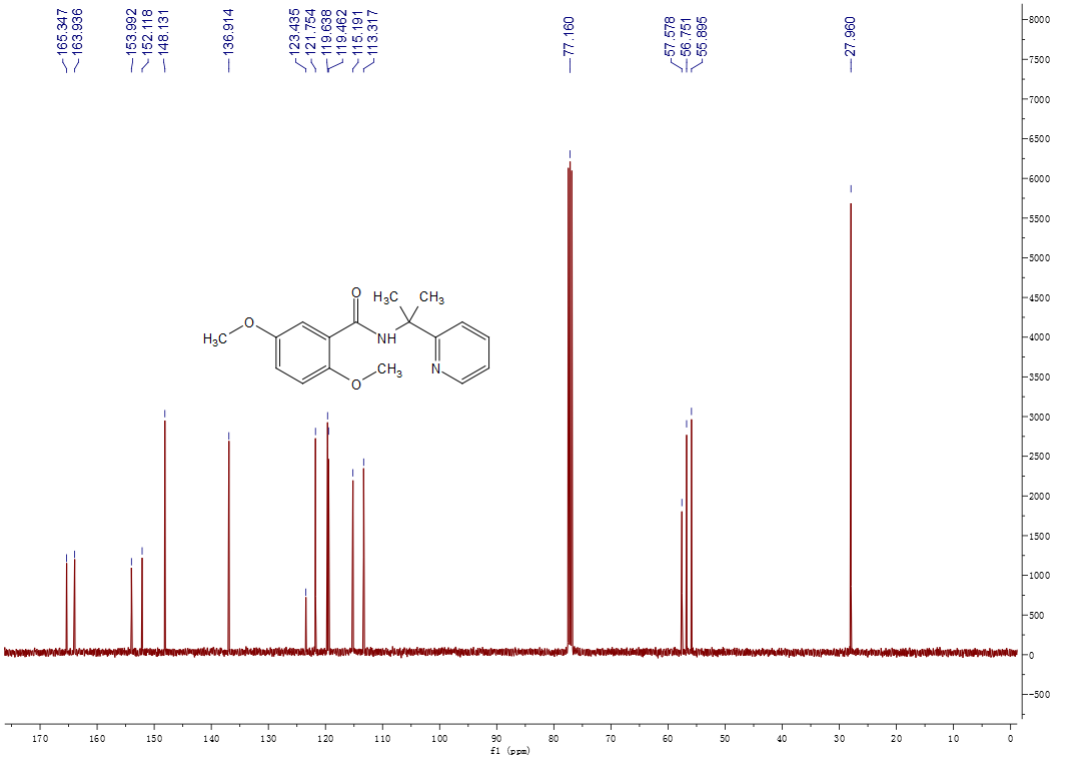
7.7121
7.7078
7.6923
7.6881
7.6733
7.6690
7.4657
7.4455
7.2603
7.1862
7.1739
7.1681
7.1558
6.9959
6.9880
6.9736
6.9657
6.9343
6.9120
3.9940
3.7963
1.8594
1.01
1.00
1.00
1.04
1.04
1.02
2.08
3.17
3.15
6.19
f1 (ppm)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163.936
153.992
152.118
148.131
136.914
123.435
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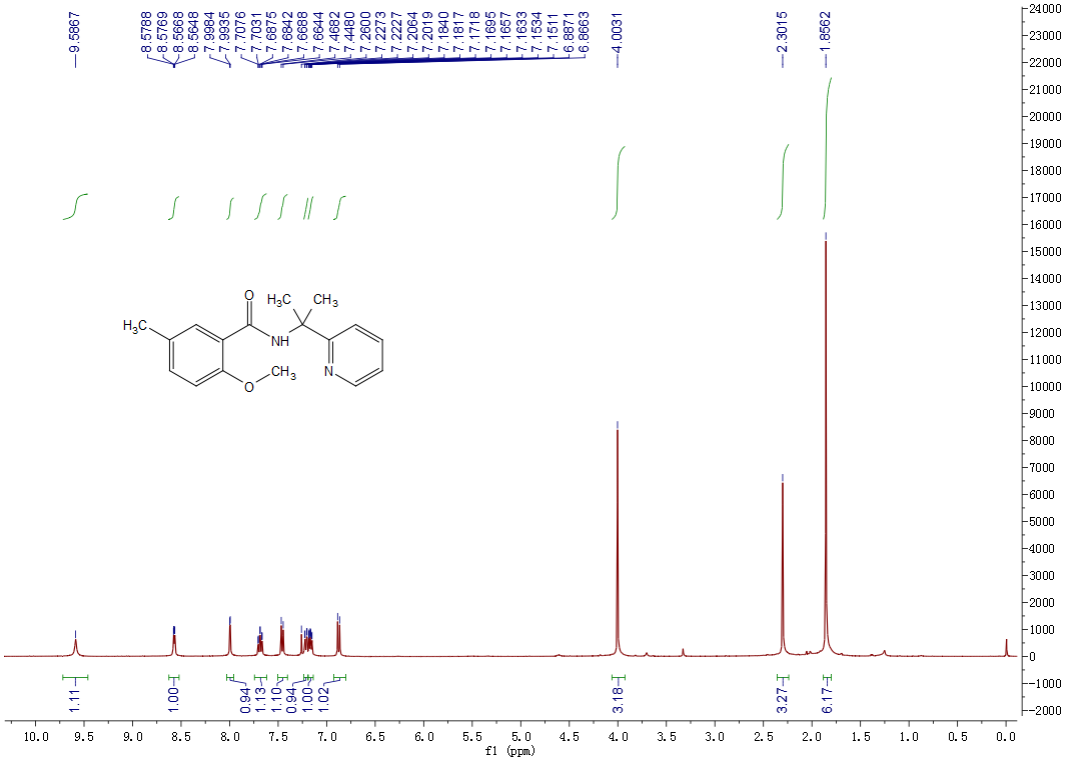
56.751
55.895
27.960
f1 (ppm)

2r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7.9935
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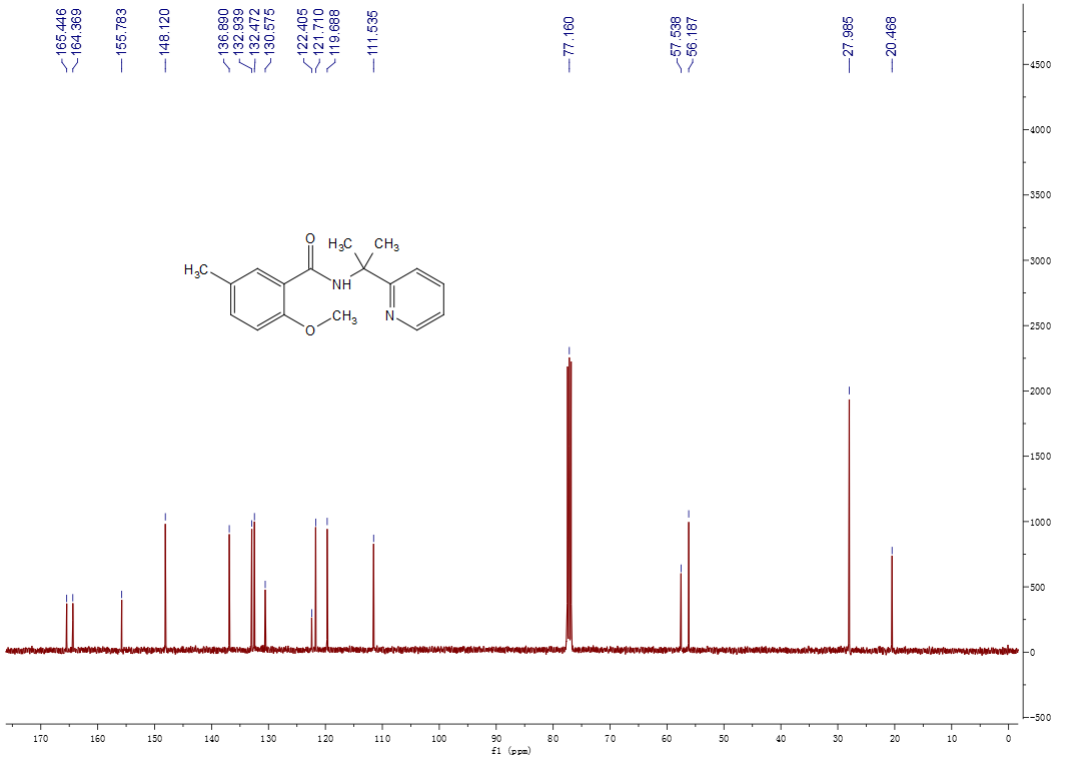
7.7031
7.6875
7.6842
7.6688
7.6644
7.4682
7.4480
7.2600
7.2273
7.2227
7.2064
7.2019
7.1840
7.1817
7.1718
7.1695
7.1657
7.1633
7.1534
7.1511
6.8871
6.8663
4.0031
2.3015
1.8562
1.11
1.00
0.94
1.13
1.10
0.94
1.00
1.02
3.18
3.27
6.17
f1 (ppm)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148.120
136.890
132.939
132.472
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122.405
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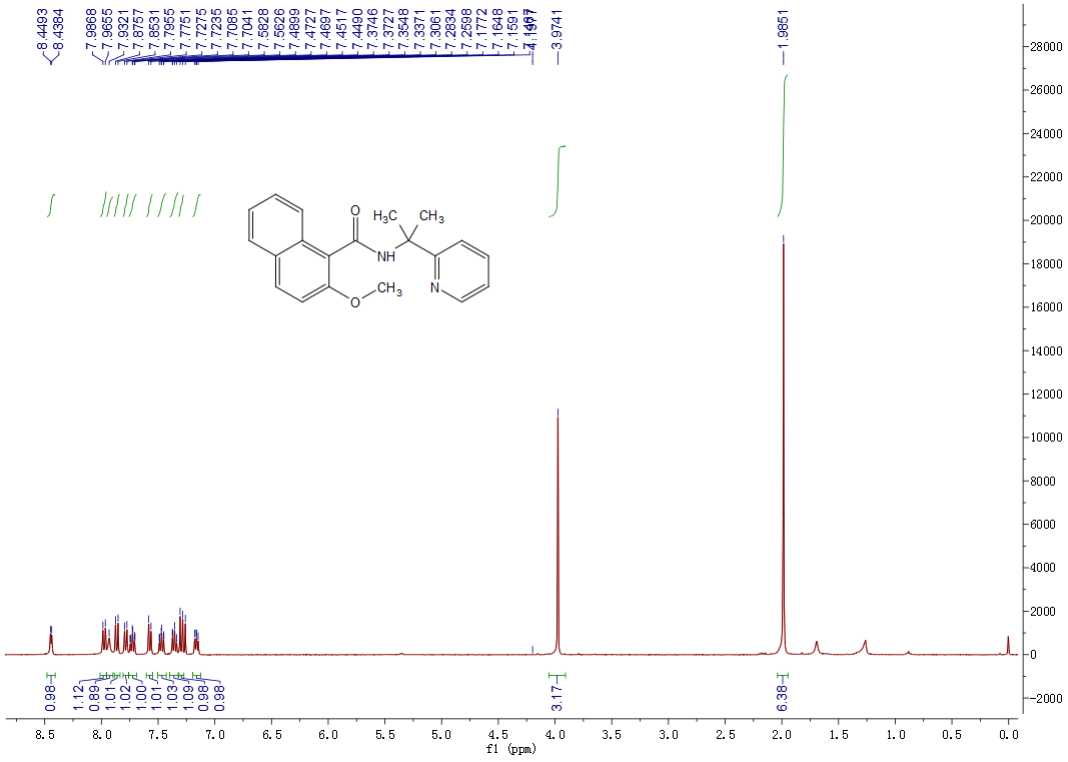
119.688
111.535
77.160
57.538
56.187
27.985
20.468
f1 (ppm)

2s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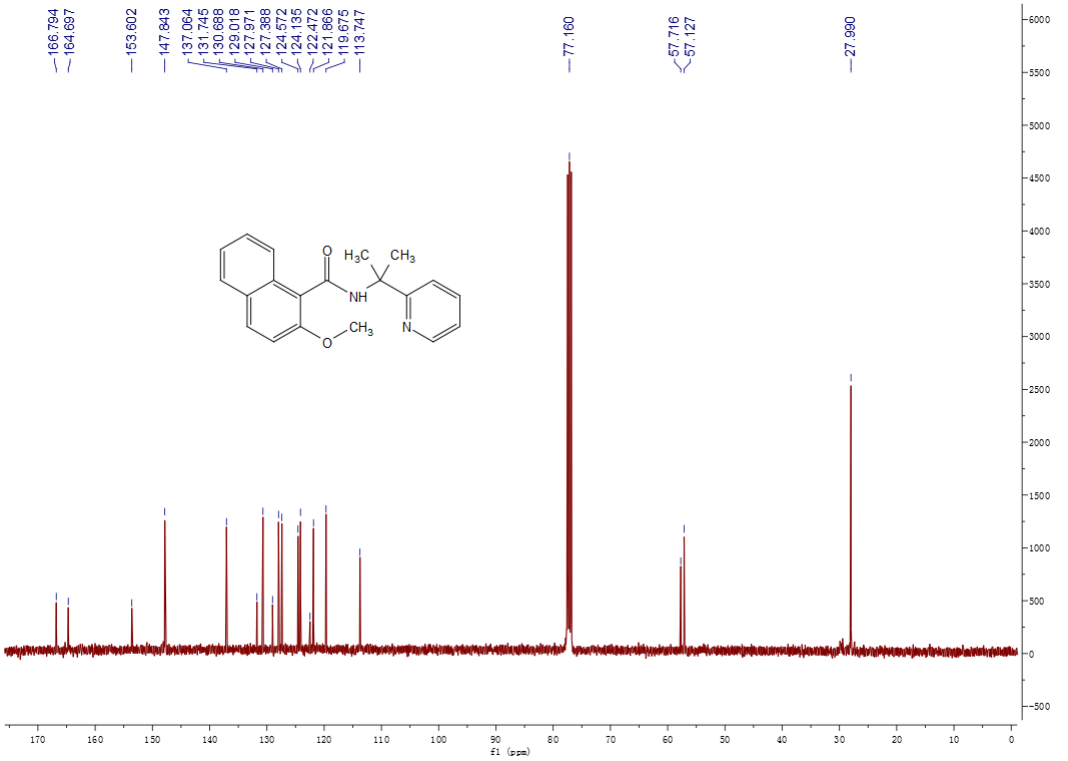
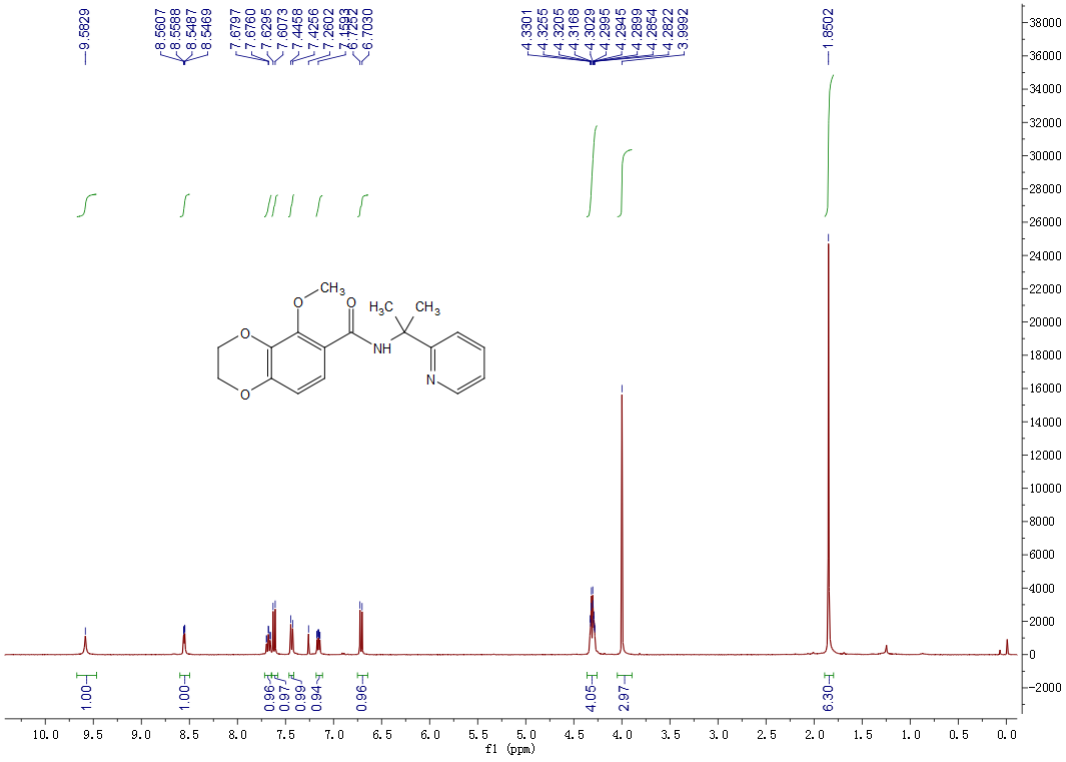
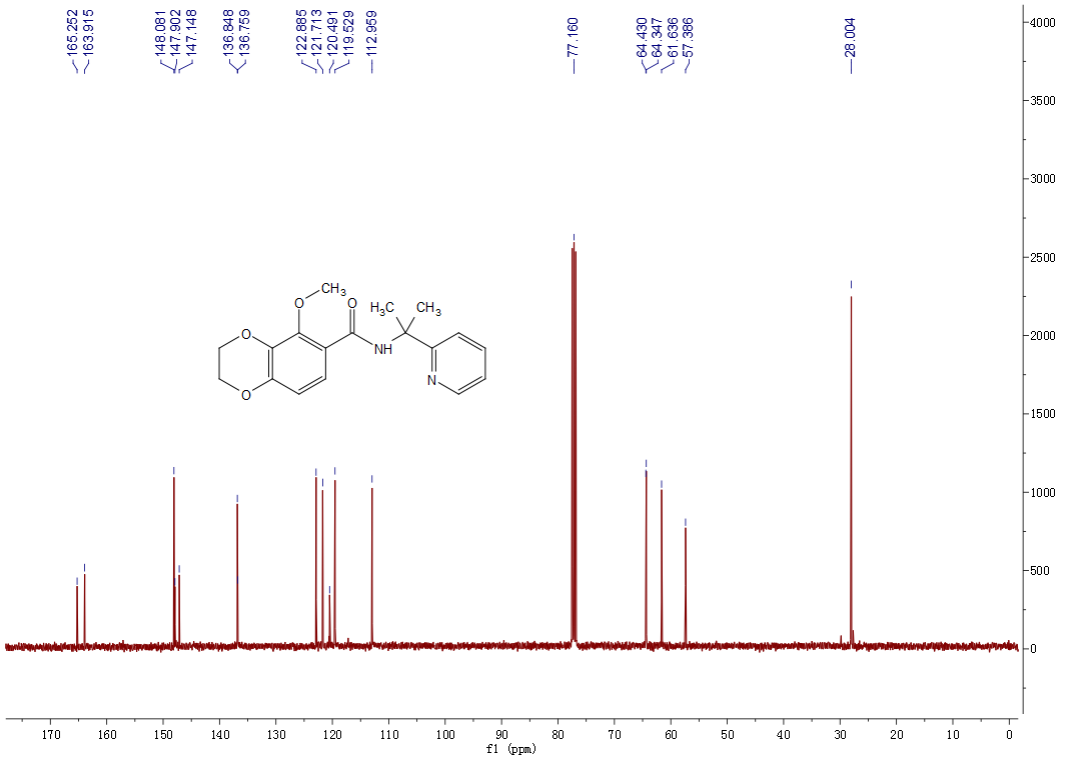
7.9321
7.8757
7.8531
7.7955
7.7751
7.7275
7.7235
7.7085
7.7041
7.5828
7.5626
7.4899
7.4727
7.4697
7.4517
7.4490
7.3746
7.3727
7.3548
7.3371
7.3061
7.2834
7.2598
7.1772
7.1648
7.1591
3.9741
1.9851
0.98
1.12
0.89
1.01
1.02
1.00
1.01
1.03
1.09
0.98
0.98
3.17
6.38
f1 (ppm)

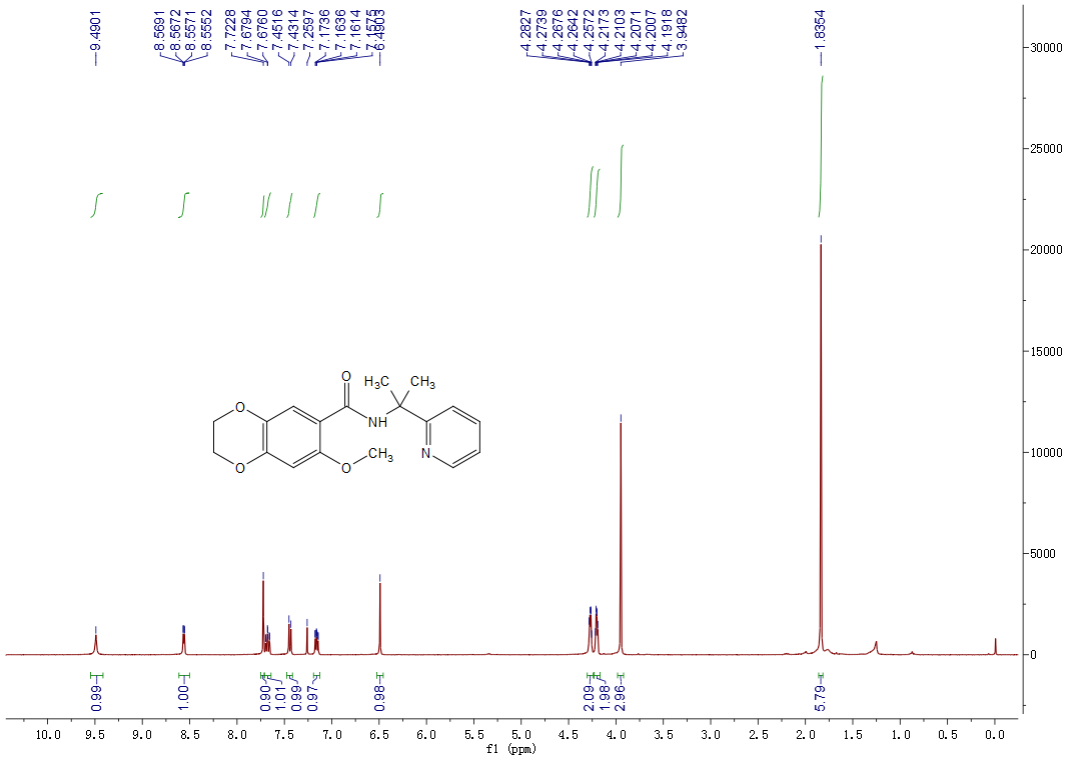

166.794
164.697
153.602
147.843
137.064
131.745
130.688
129.018
127.971
127.388
124.572
124.135
122.472
121.866
119.675
113.747
77.160
57.716
57.127
27.990
f1 (ppm)

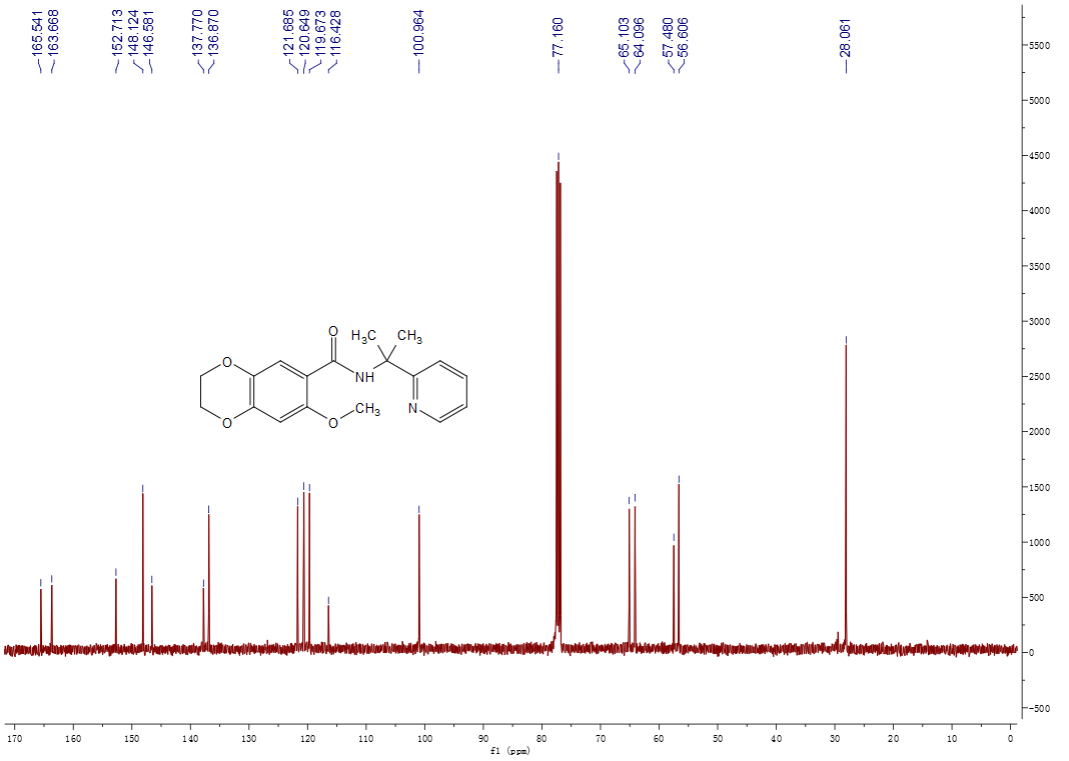
2ta


9.5829
8.5607
8.5588
8.5487
8.5469
7.6797
7.6760
7.6295
7.6073
7.4456
7.4256
7.2602
6.7030
4.3301
4.3255
4.3205
4.3168
4.3029
4.2995
4.2945
4.2899
4.2854
4.2822
3.9992
1.8502
1.00
1.00
0.96
0.97
0.99
0.94
0.96
4.05
2.97
6.30
f1 (ppm)

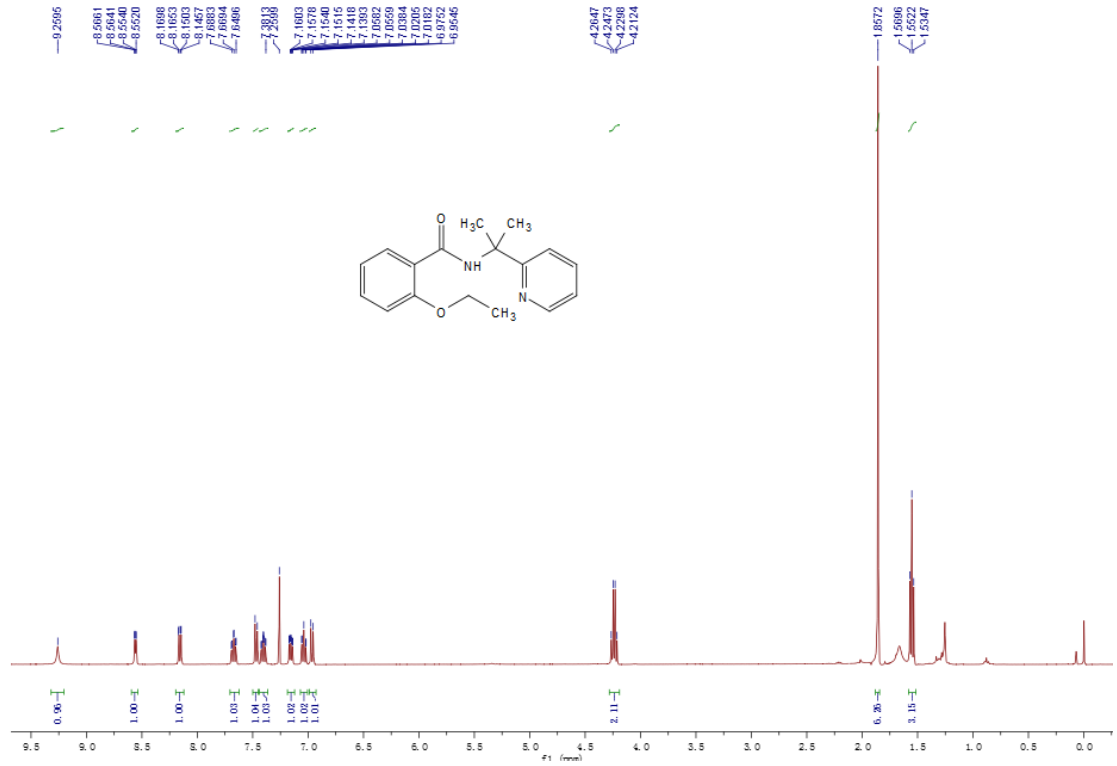

165.252
163.915
148.081
147.902
147.148
136.848
136.759
122.885
121.713
120.491
119.529
112.959
77.160
64.430
64.347
61.636
57.386
28.004
f1 (ppm)

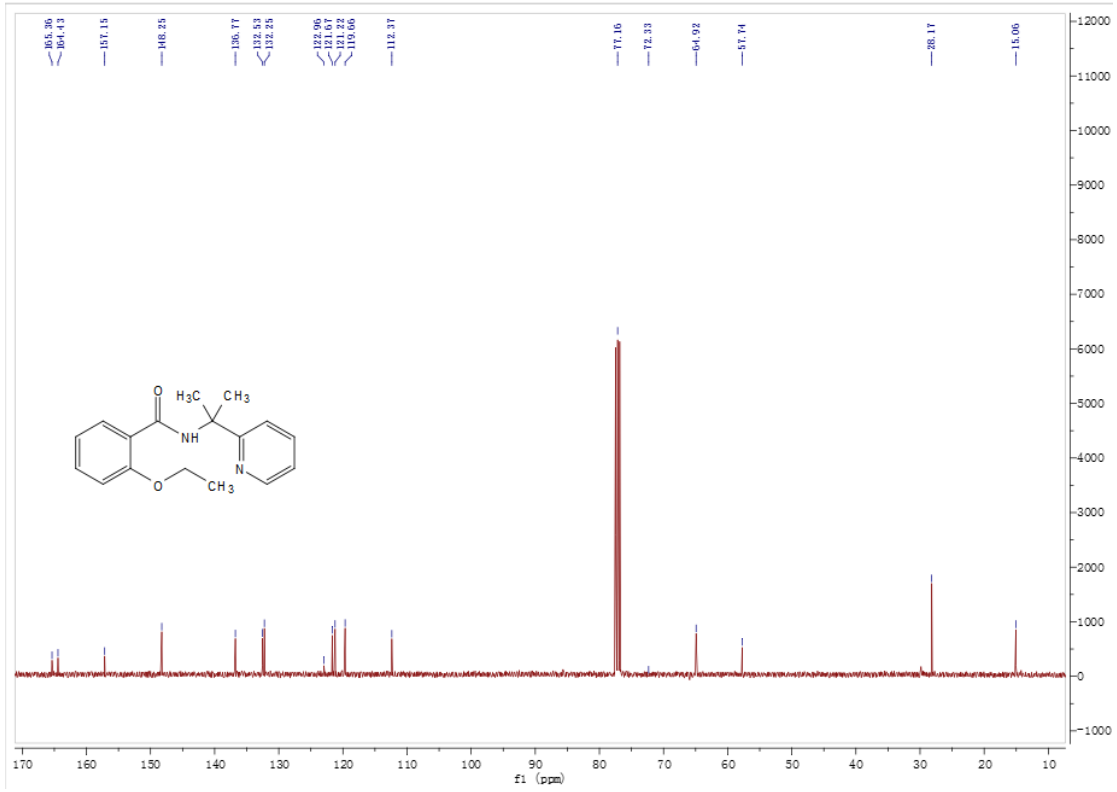
2tb


9.4801
8.5691
8.5672
8.5571
8.5552
7.7228
7.6794
7.6760
7.4516
7.4314
7.2597
7.1736
7.1636
7.1614
4.2827
4.2739
4.2676
4.2642
4.2572
4.2173
4.2103
4.2071
4.2007
4.1918
3.9482
1.8354
0.99
1.00
0.90
1.01
0.99
0.97
0.98
2.09
1.98
2.96
5.79
f1 (ppm)

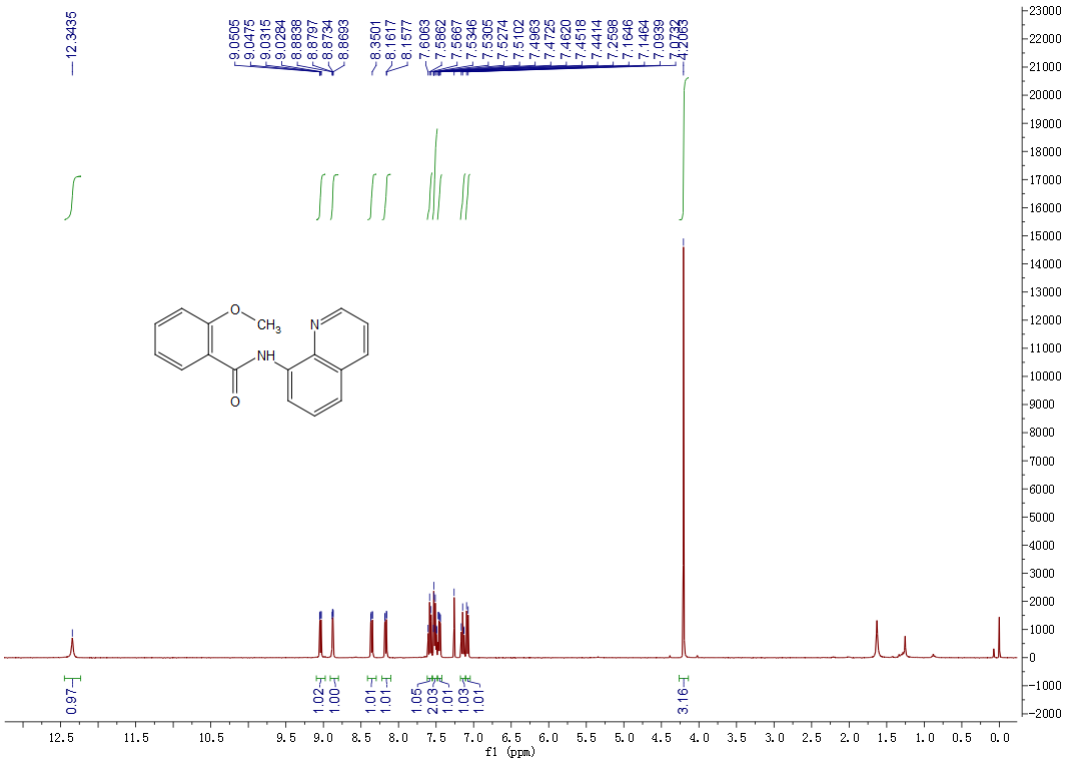

165.541
163.668
152.713
148.124
146.581
137.770
136.870
121.685
120.649
119.673
116.428
100.964
77.160
65.103
64.096
57.480
56.606
28.061
f1 (ppm)

2u





3b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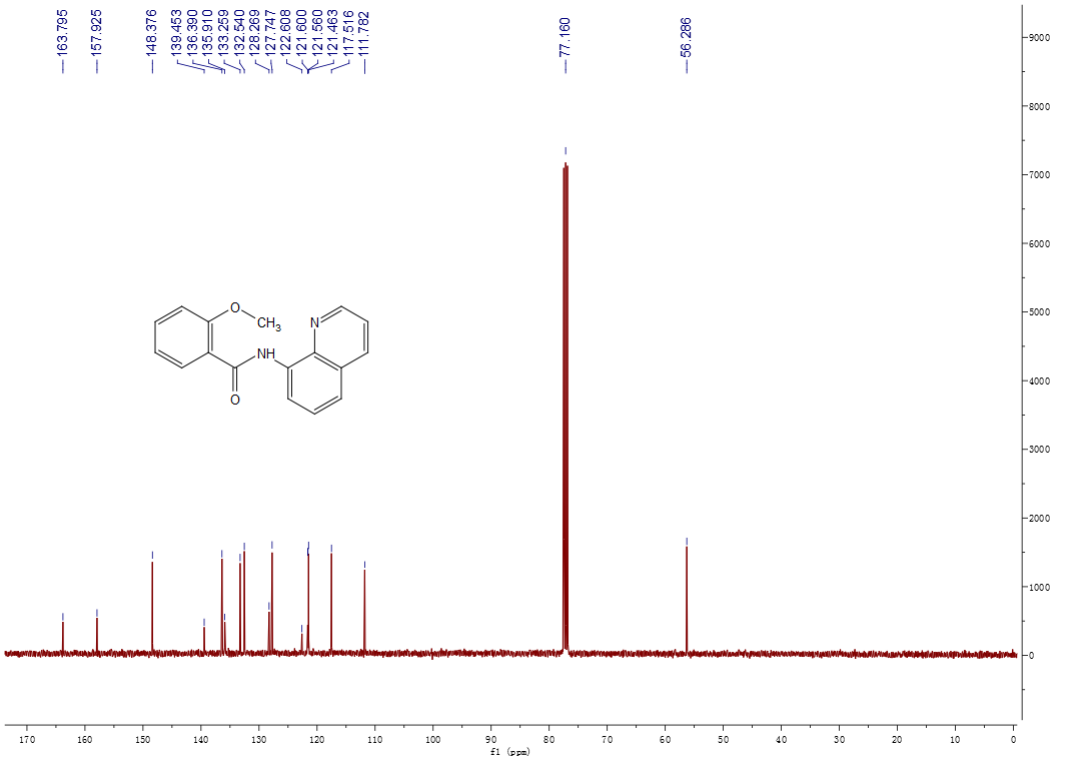
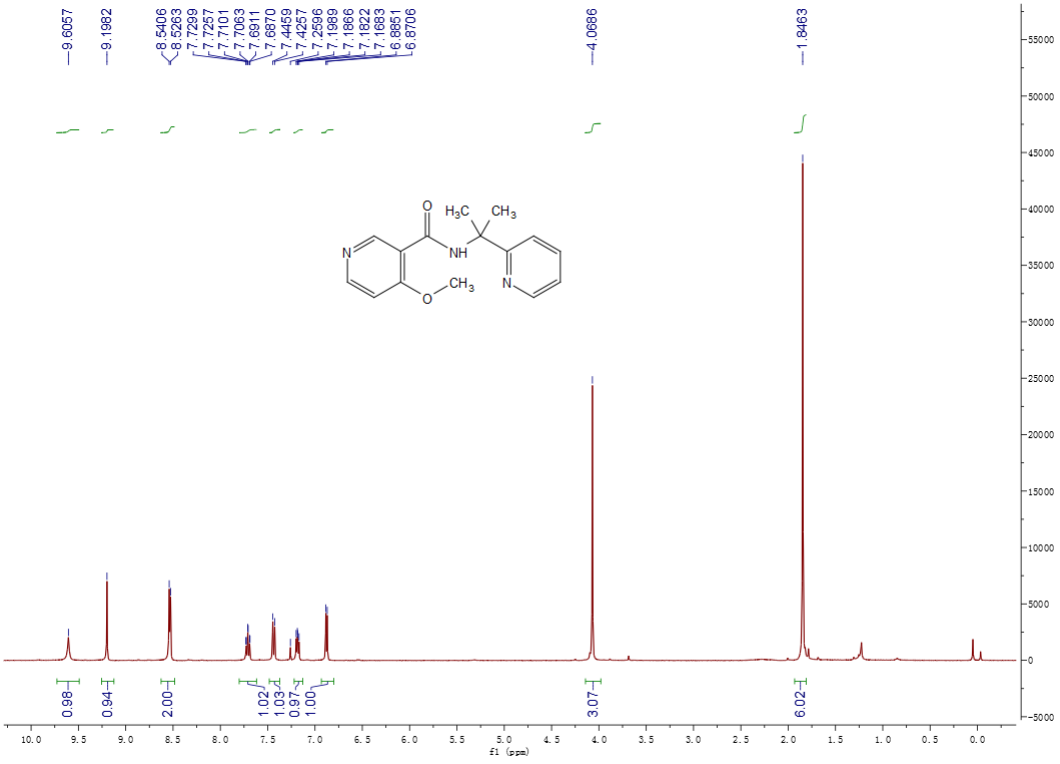
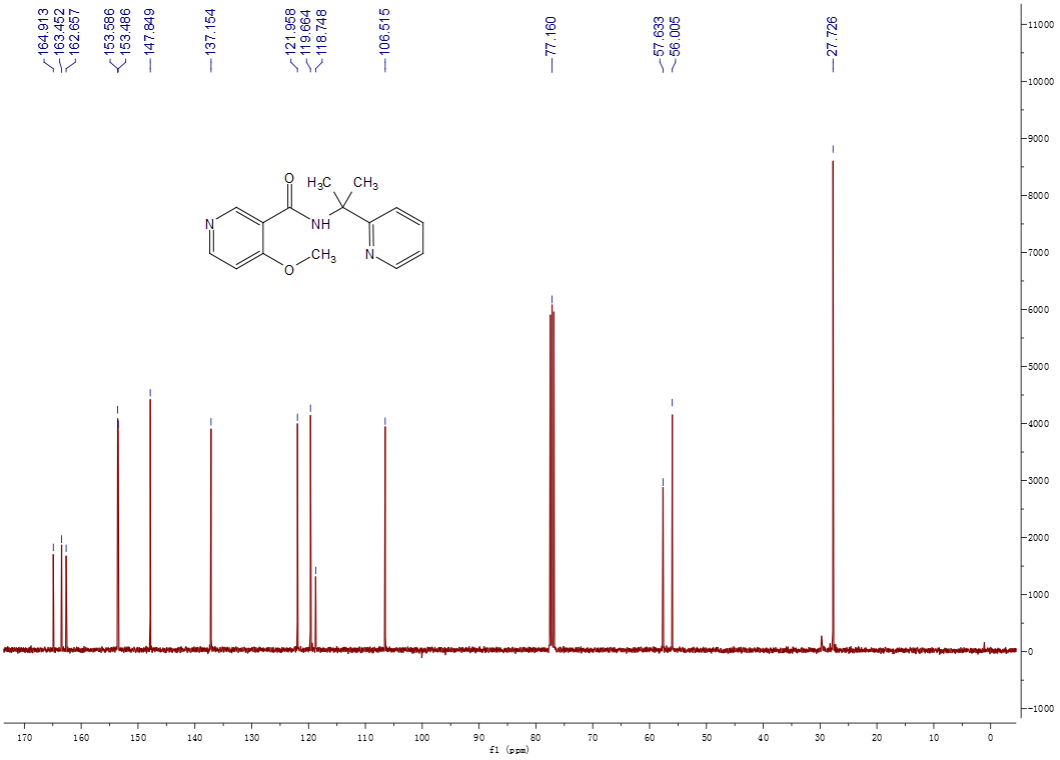
9.0505
9.0475
9.0315
9.0284
8.8838
8.8797
8.8734
8.8693
8.3501
8.1617
8.1577
7.6063
7.5862
7.5667
7.5346
7.5305
7.5274
7.5102
7.4963
7.4725
7.4620
7.4518
7.4414
7.2598
7.1646
7.1464
7.0939
7.0732
4.2063
0.97
1.02
1.00
1.01
1.01
1.05
2.03
1.01
1.03
1.01
3.16
f1 (ppm)

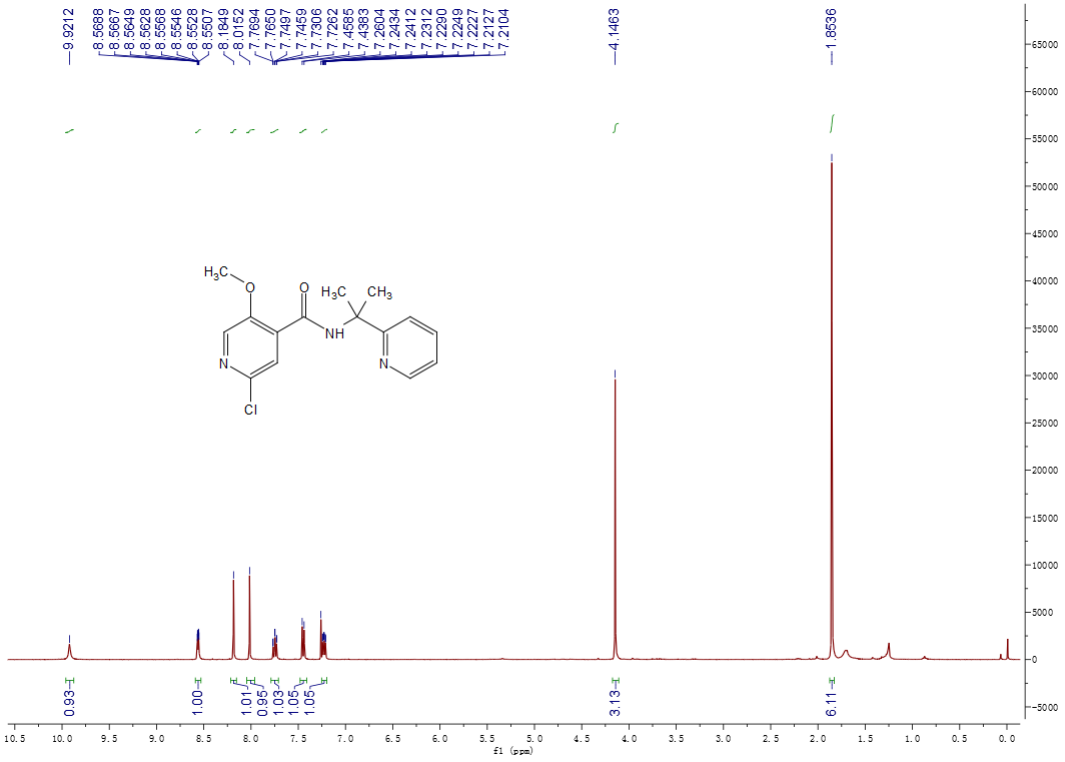

163.795
157.925
148.376
139.453
136.390
135.910
133.259
132.540
128.269
127.747
122.608
121.600
121.560
121.463
117.516
111.782
77.160
56.286
f1 (ppm)

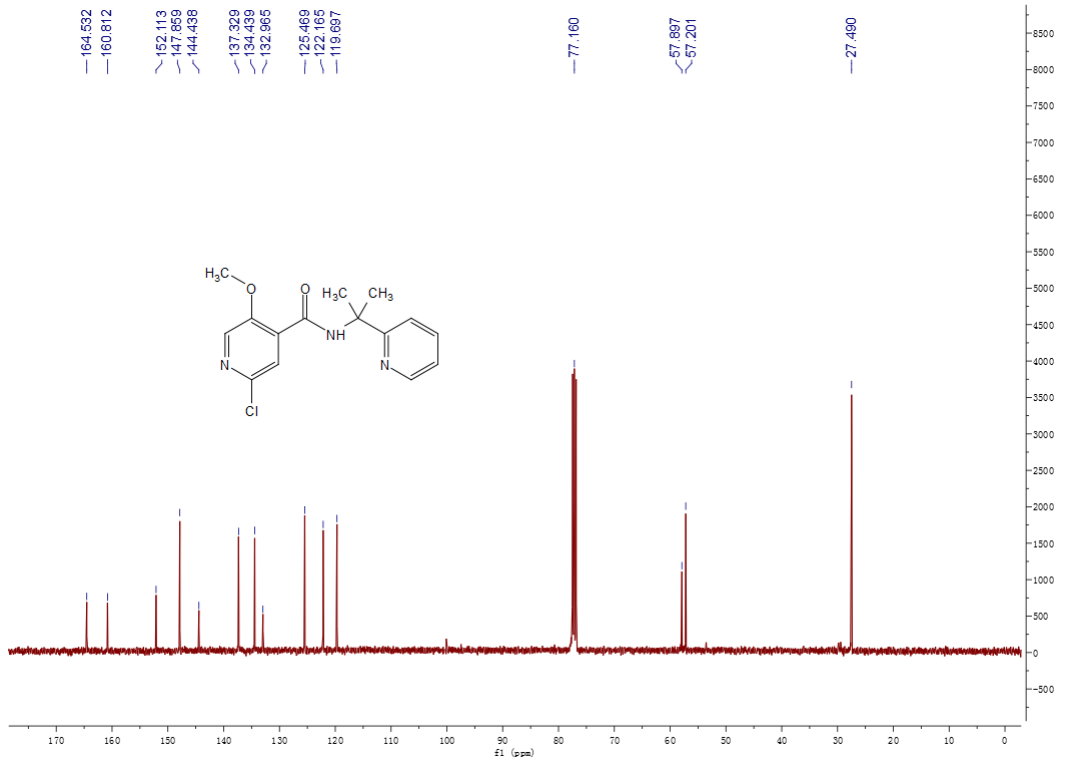
5a


9.6057
9.1982
8.5406
8.5263
7.7299
7.7257
7.7101
7.7063
7.6911
7.6870
7.4459
7.4257
7.2596
7.1989
7.1866
7.1822
7.1683
6.8851
6.8706
4.0686
1.8463
0.98
0.94
2.00
1.02
1.03
0.97
1.00
3.07
6.02
f1 (ppm)

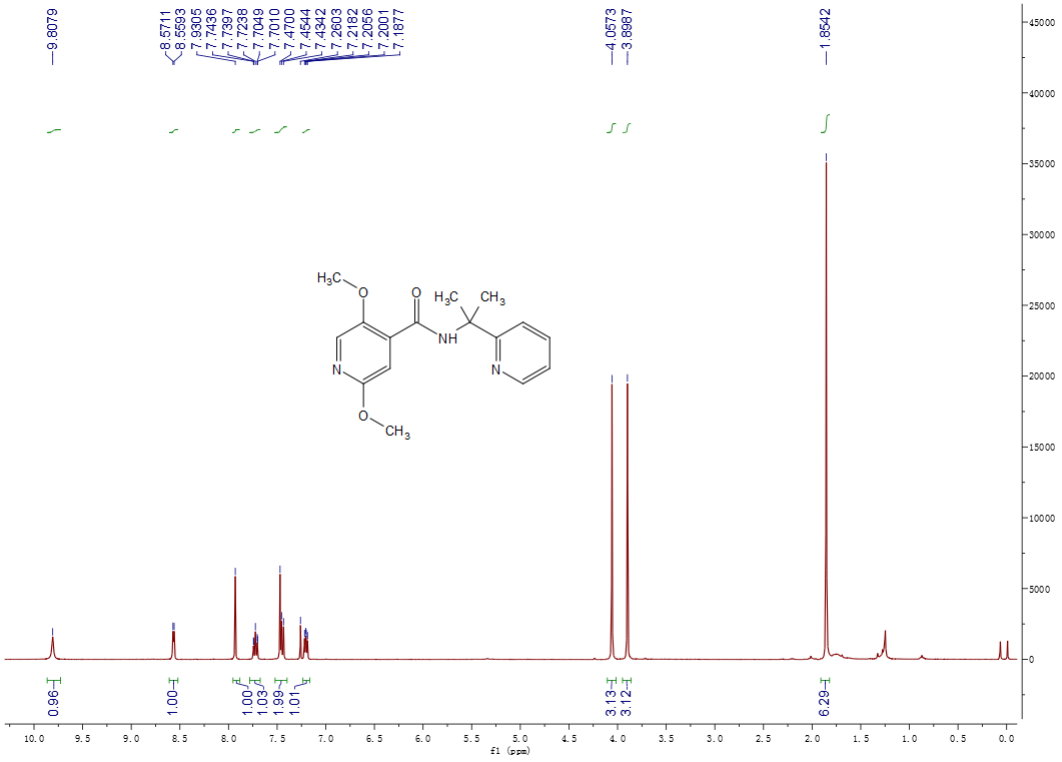

164.913
163.452
162.657
153.586
153.486
147.849
137.154
121.958
119.664
118.748
106.515
77.160
57.633
56.005
27.726
f1 (ppm)

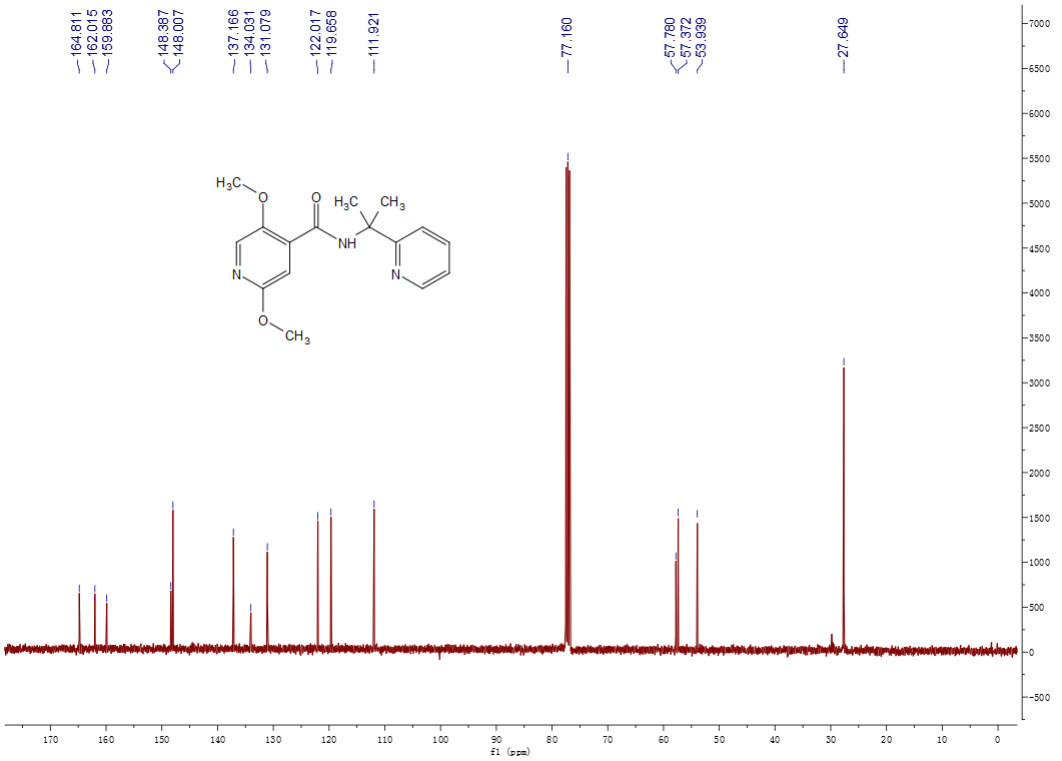
5b


9.9212
8.5688
8.5667
8.5649
8.5628
8.5568
8.5546
8.5528
8.5507
8.1849
8.0152
7.7694
7.7650
7.7497
7.7459
7.7306
7.7262
7.4585
7.4383
7.2604
7.2434
7.2412
7.2312
7.2290
7.2249
7.2227
7.2127
7.2104
4.1463
1.8536
0.93
1.00
1.01
0.95
1.03
1.05
1.05
3.13
6.11
f1 (ppm)

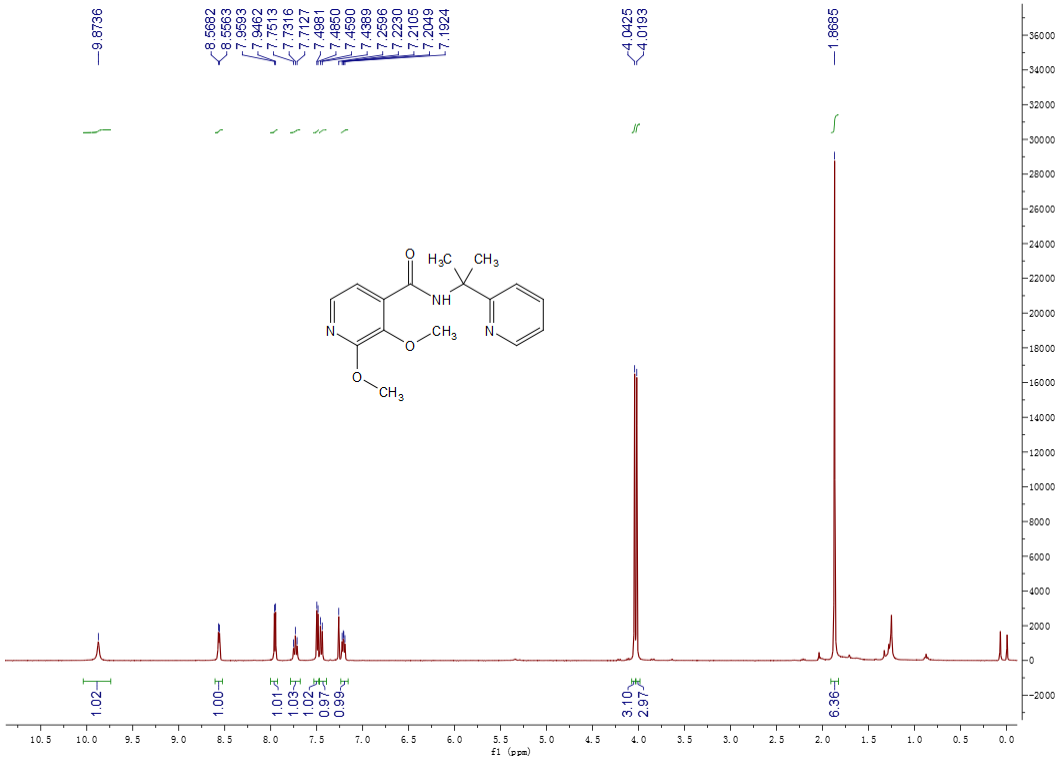

164.532
160.812
152.113
147.859
144.438
137.329
134.439
132.965
125.469
122.165
119.697
77.160
57.897
57.201
27.490
f1 (ppm)

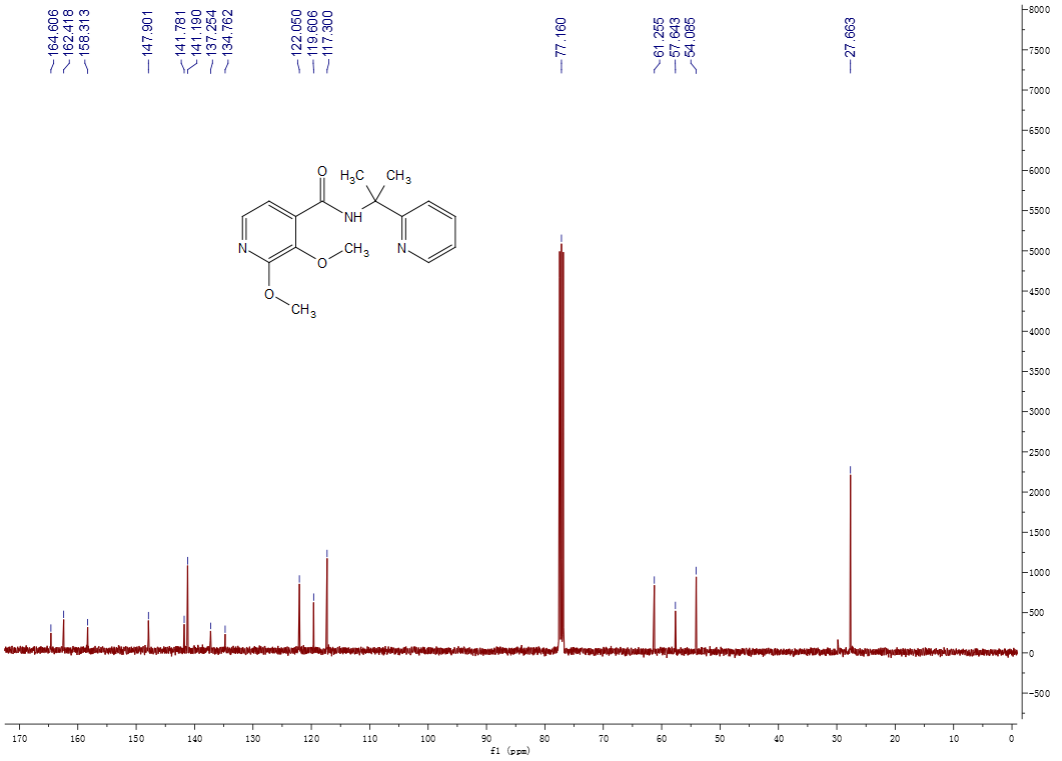
5ca


9.8079
8.5711
8.5593
7.9305
7.7436
7.7397
7.7238
7.7049
7.7010
7.4700
7.4544
7.4342
7.2603
7.2182
7.2056
7.2001
7.1877
4.0573
3.8987
1.8542
0.96
1.00
1.00
1.03
1.99
1.01
3.13
3.12
6.29
f1 (ppm)

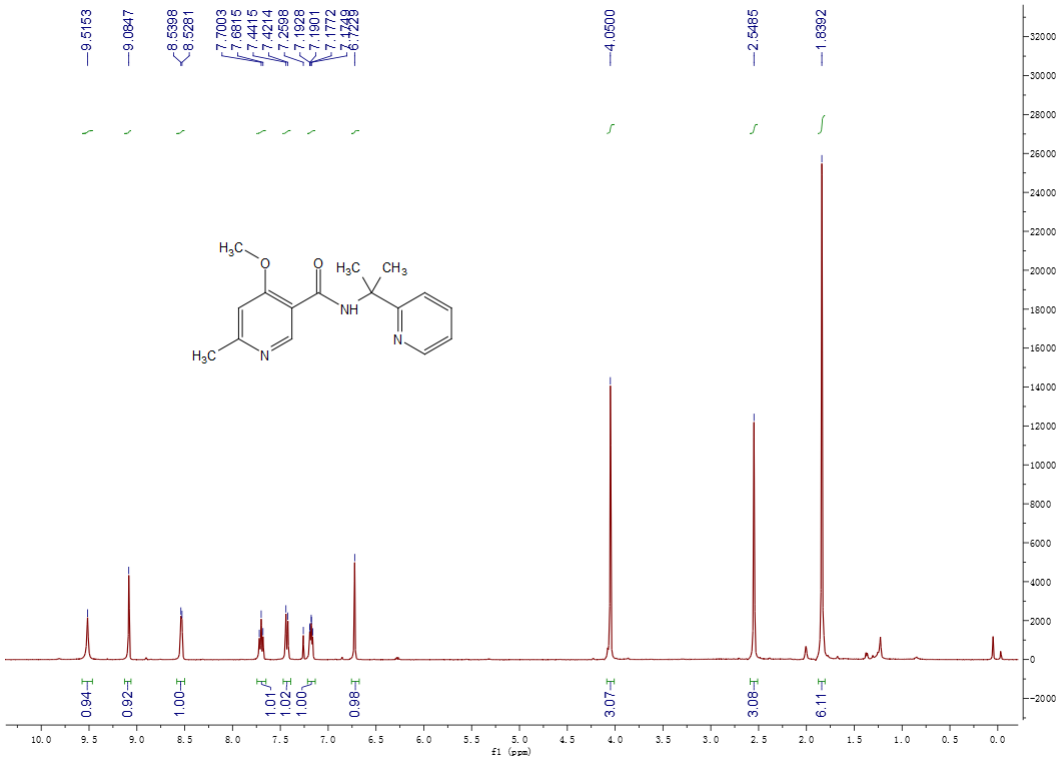

164.811
162.015
159.883
148.387
148.007
137.166
134.031
131.079
122.017
119.658
111.921
77.160
57.780
57.372
53.939
27.649
f1 (ppm)

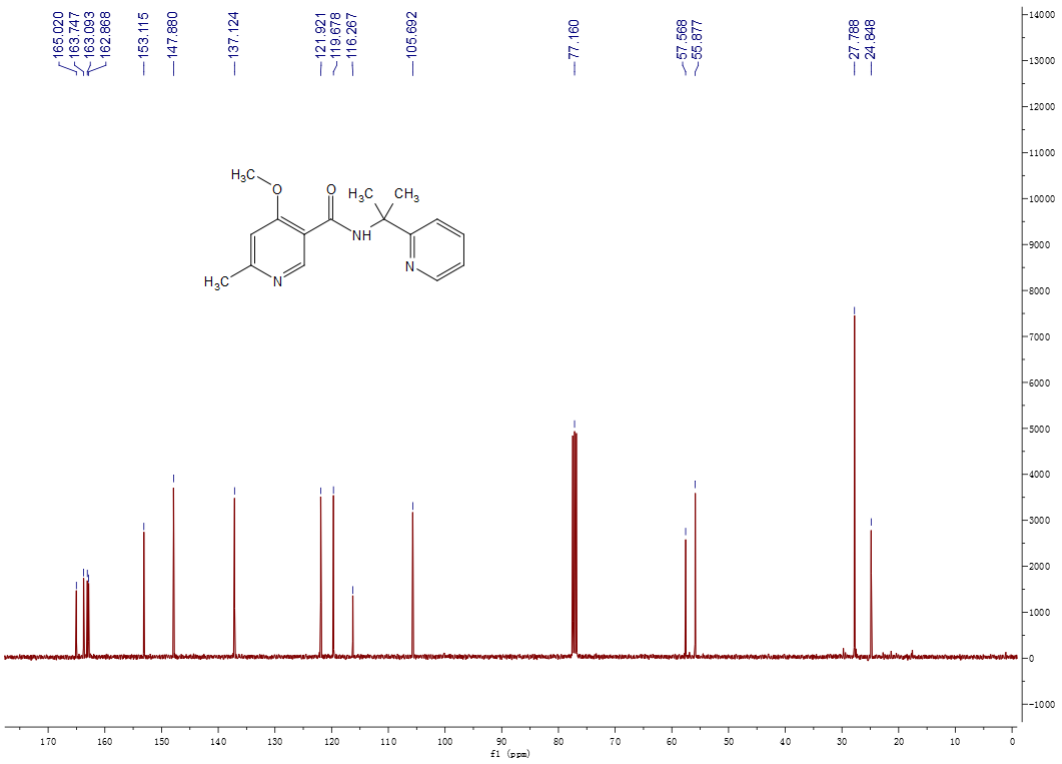
5cb


9.8736
8.5682
8.5563
7.9593
7.9462
7.7513
7.7316
7.7127
7.4981
7.4850
7.4590
7.4389
7.2596
7.2230
7.2105
7.2049
7.1924
4.0425
4.0193
1.8685
1.02
1.00
1.01
1.03
1.02
0.97
0.99
3.10
2.97
6.36
f1 (ppm)

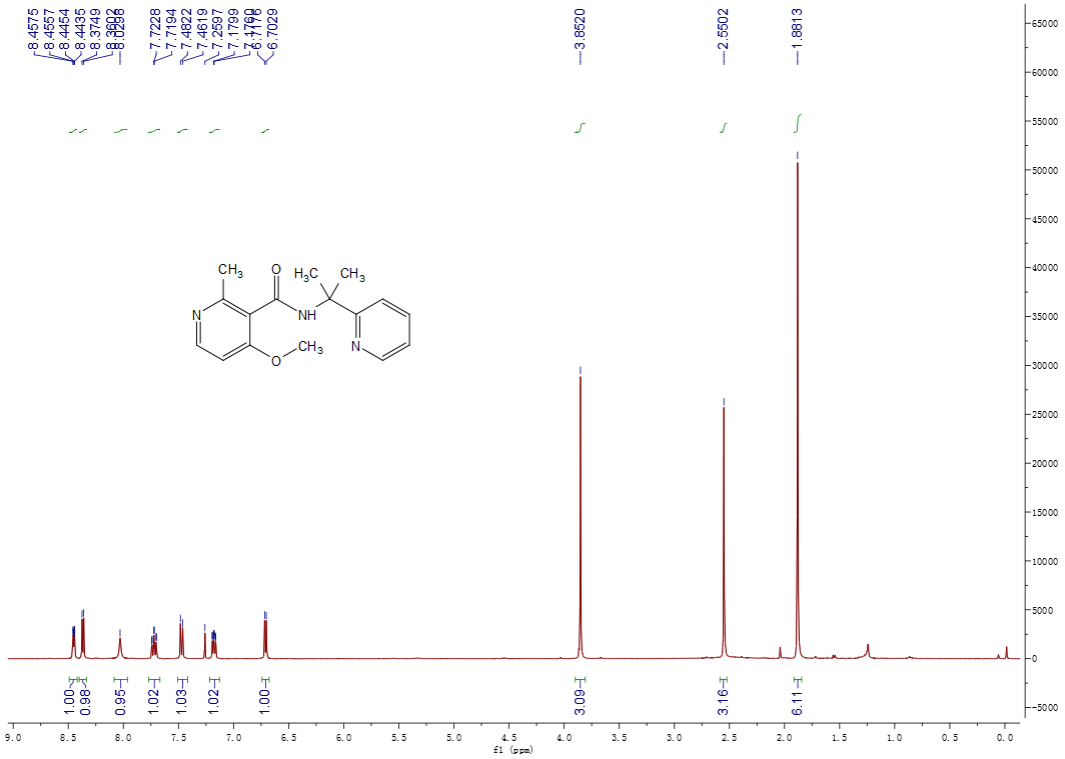

164.606
162.418
158.313
147.901
141.781
141.190
137.254
134.762
122.050
119.606
117.300
77.160
61.255
57.643
54.085
27.663
f1 (ppm)

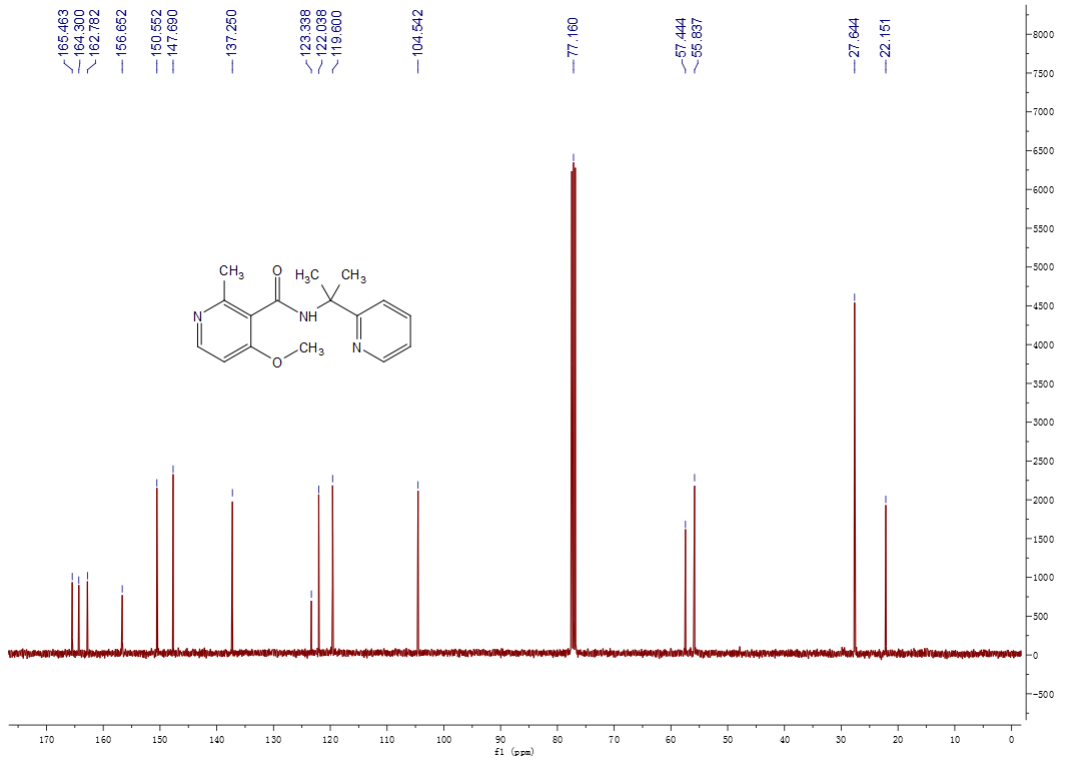
5d


9.5153
9.0847
8.5398
8.5281
7.7003
7.6815
7.4415
7.4214
7.2598
7.1928
7.1901
7.1772
4.0500
2.5485
1.8392
0.94
0.92
1.00
1.01
1.02
1.00
0.98
3.07
3.08
6.11
f1 (ppm)


165.020
163.747
163.093
162.668
153.115
147.880
137.124
121.921
119.678
116.267
105.692
77.160
57.568
55.877
27.788
24.848
f1 (ppm)

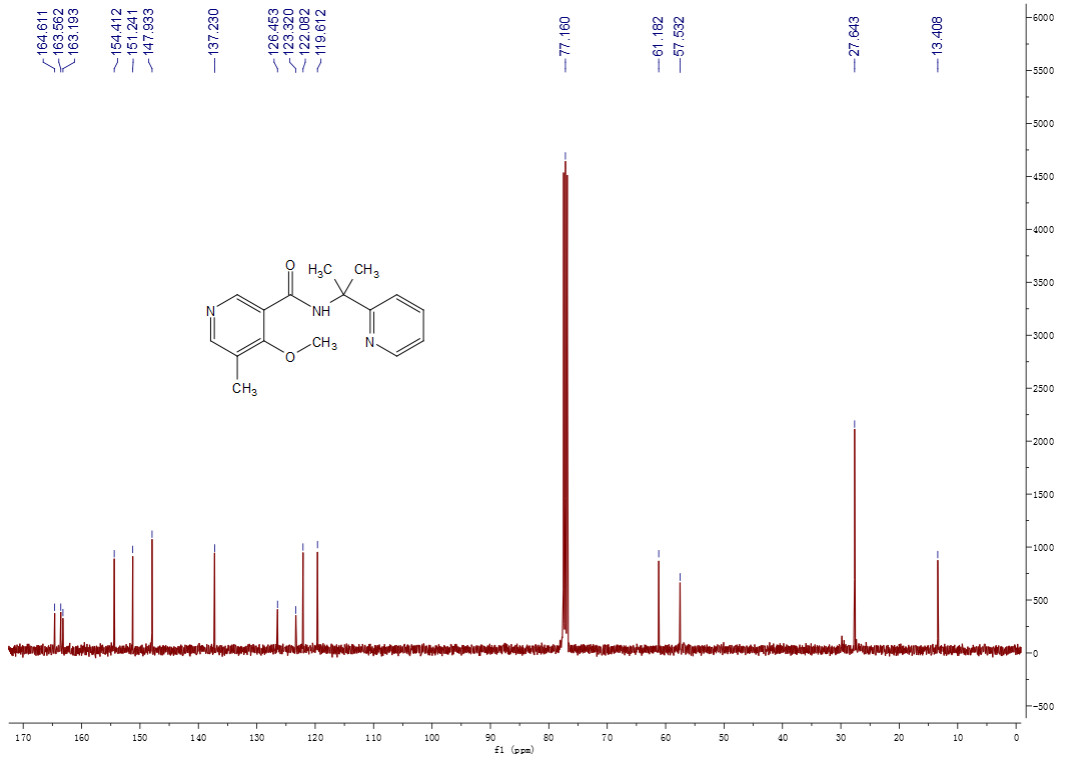
5e


8.4575
8.4557
8.4454
8.4435
8.3749
7.7228
7.7194
7.4822
7.4619
7.2597
7.1799
6.7029
3.8520
2.5502
1.8813
1.00
0.98
0.95
1.02
1.03
1.02
1.00
3.09
3.16
6.11
f1 (ppm)

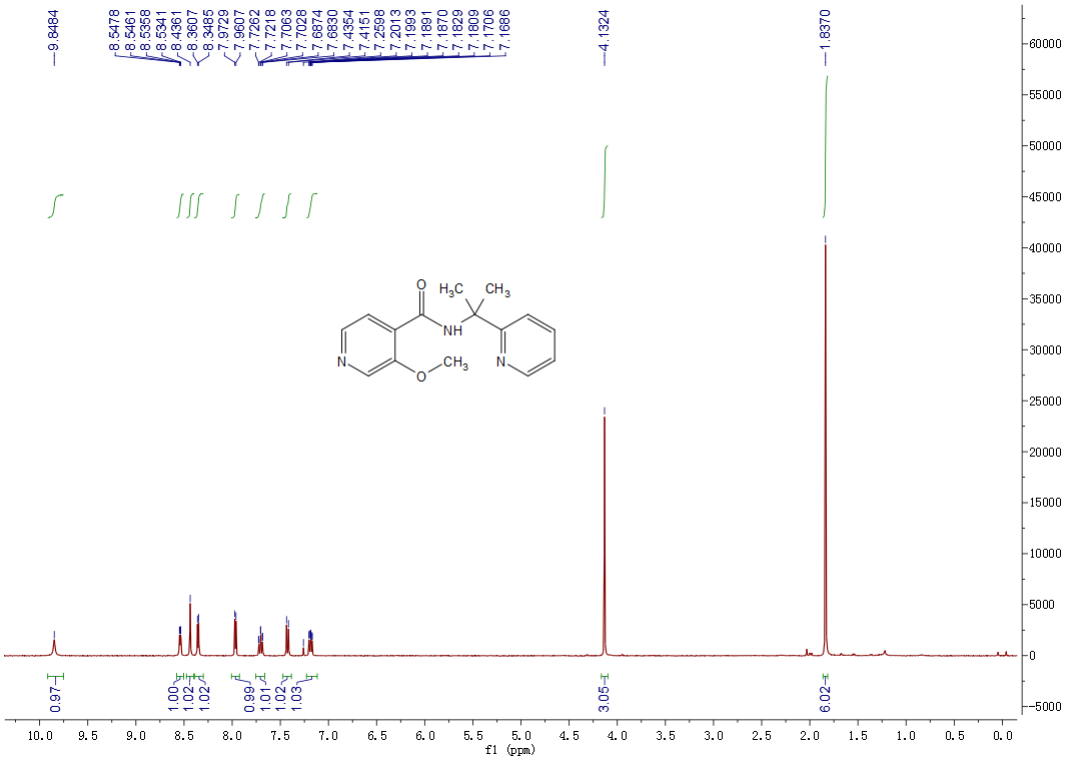

165.463
164.300
162.782
156.652
150.552
147.690
137.250
123.338
122.038
119.600
104.542
77.160
57.444
55.837
27.644
22.151
f1 (ppm)

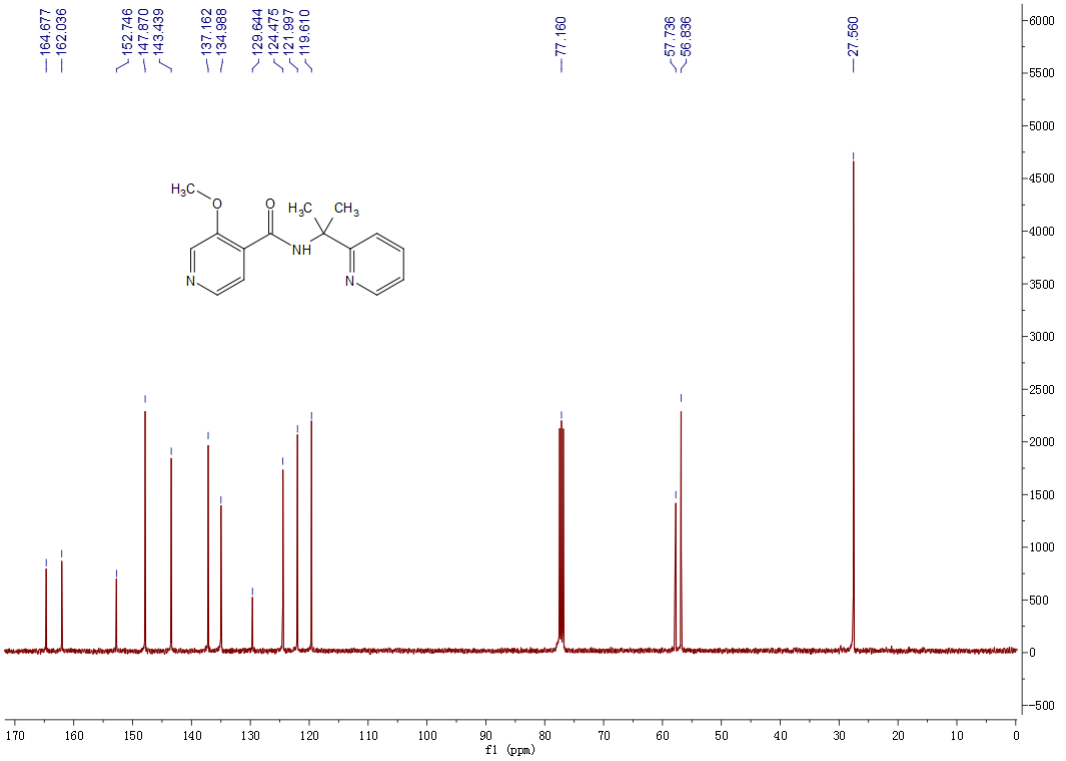
5f


9.3649
8.9373
8.5507
8.5405
8.5387
8.4451
7.7574
7.7530
7.7375
7.7332
7.7186
7.7142
7.4674
7.4472
7.2599
7.2225
7.2103
7.2062
7.2041
7.1939
7.1918
3.9548
2.3179
1.8836
0.96
0.98
1.00
0.93
1.05
1.00
0.96
3.00
3.08
6.17
f1 (ppm)

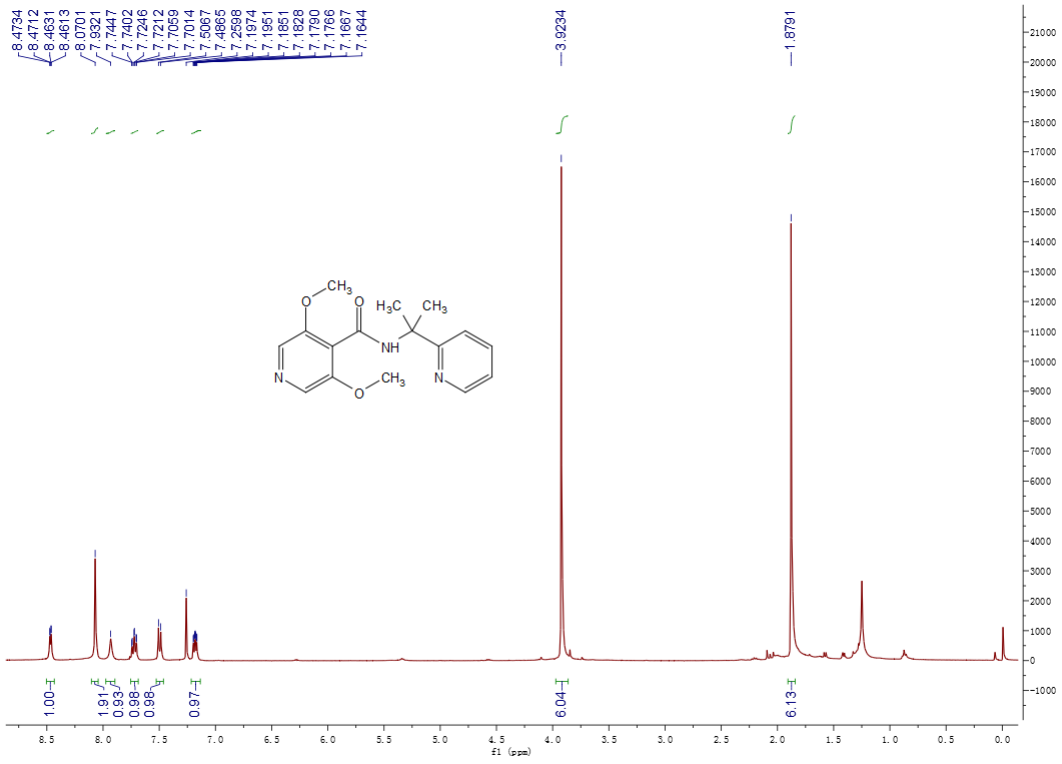

164.611
163.562
163.193
154.412
151.241
147.933
137.230
126.453
123.320
122.082
119.612
77.160
61.182
57.532
27.643
13.408
f1 (ppm)

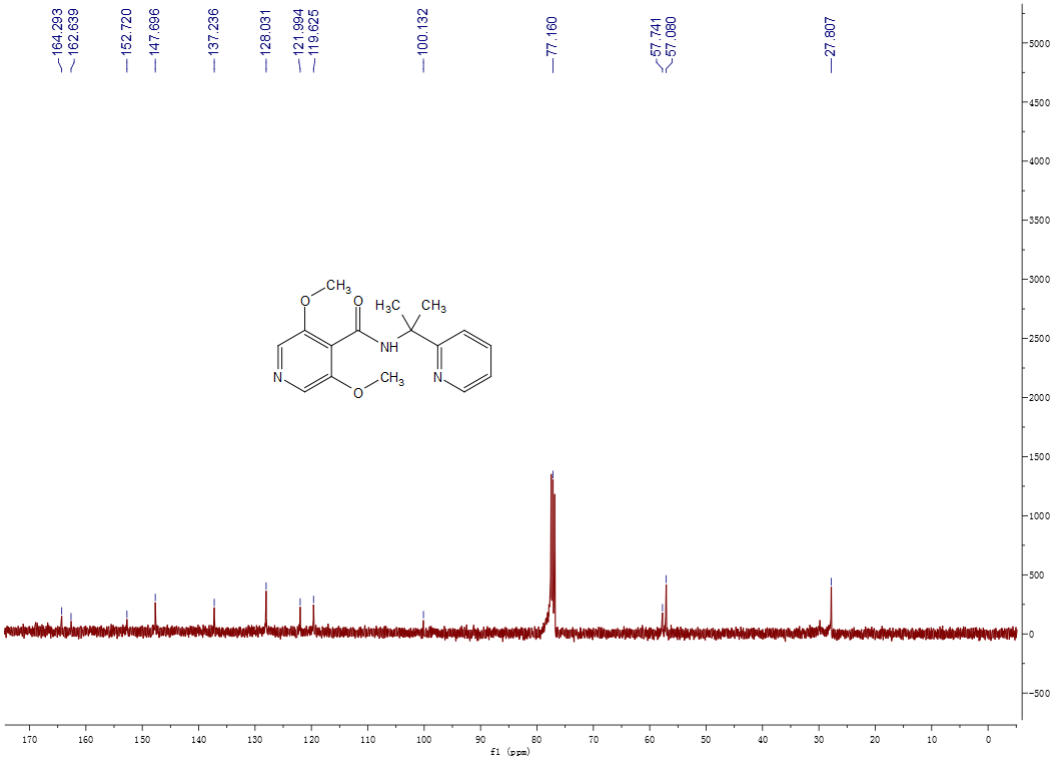
5ga


9.8484
8.5478
8.5461
8.5358
8.5341
8.4361
8.3607
8.3485
7.9729
7.9607
7.7262
7.7218
7.7083
7.7028
7.6874
7.6830
7.4354
7.4151
7.2598
7.2013
7.1993
7.1891
7.1870
7.1829
7.1809
7.1706
7.1686
4.1324
1.8370
0.97
1.00
1.02
1.02
0.99
1.01
1.02
1.03
3.05
6.02
f1 (ppm)

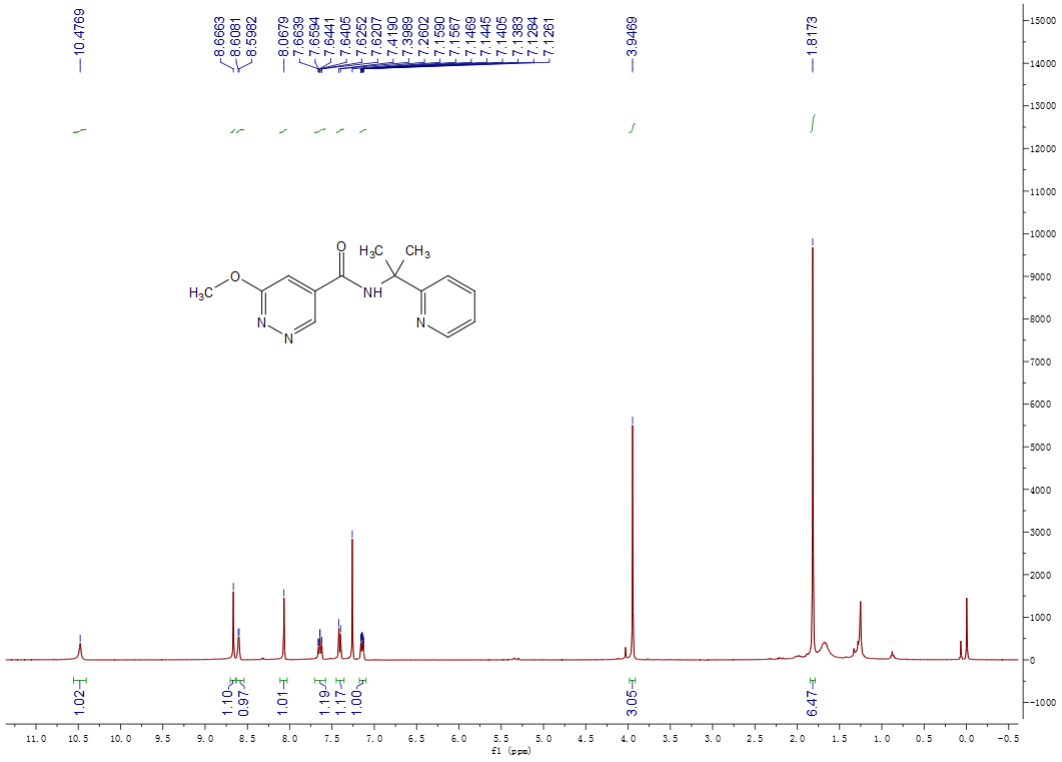

164.677
162.036
152.746
147.870
143.439
137.162
134.988
129.644
124.475
121.997
119.610
77.160
57.736
56.836
27.560
f1 (ppm)

5gb


8.4734
8.4712
8.4631
8.4613
8.0701
7.9321
7.7447
7.7402
7.7246
7.7212
7.7059
7.7014
7.5067
7.4865
7.2598
7.1974
7.1951
7.1851
7.1828
7.1790
7.1766
7.1667
7.1644
3.9234
1.8791
1.00
1.91
0.93
0.98
0.98
0.97
6.04
6.13
f1 (ppm)


164.293
162.639
152.720
147.696
137.236
128.031
121.994
119.625
100.132
77.160
57.741
57.080
27.807
f1 (ppm)

5h


10.4769
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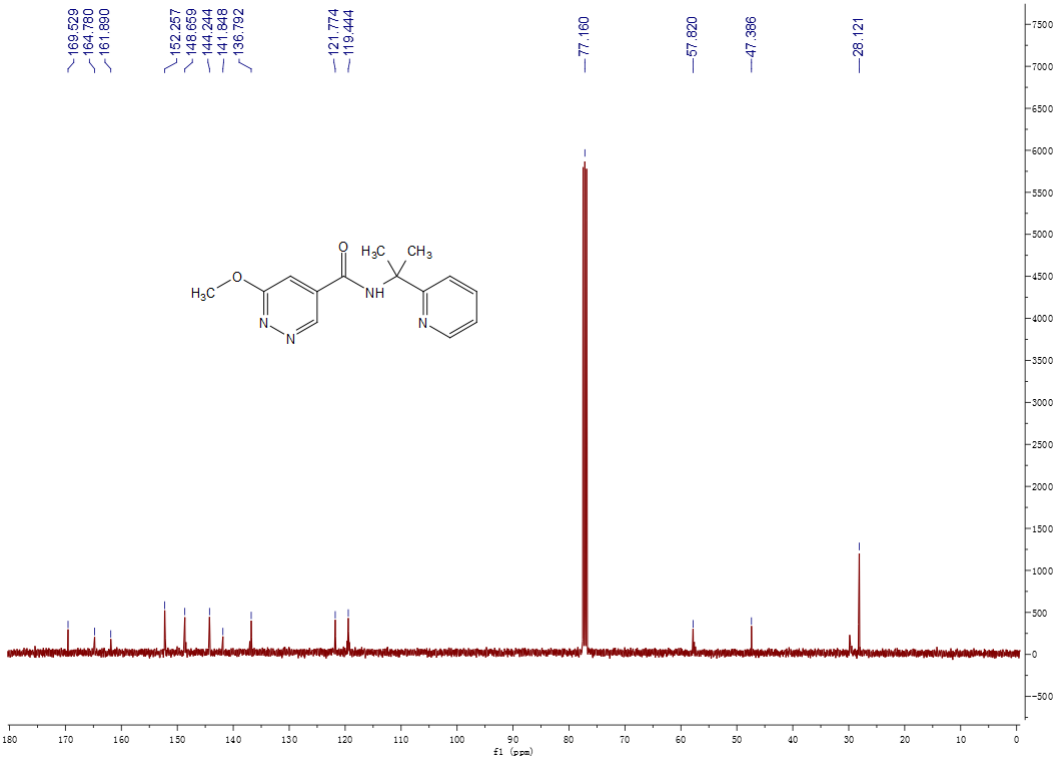
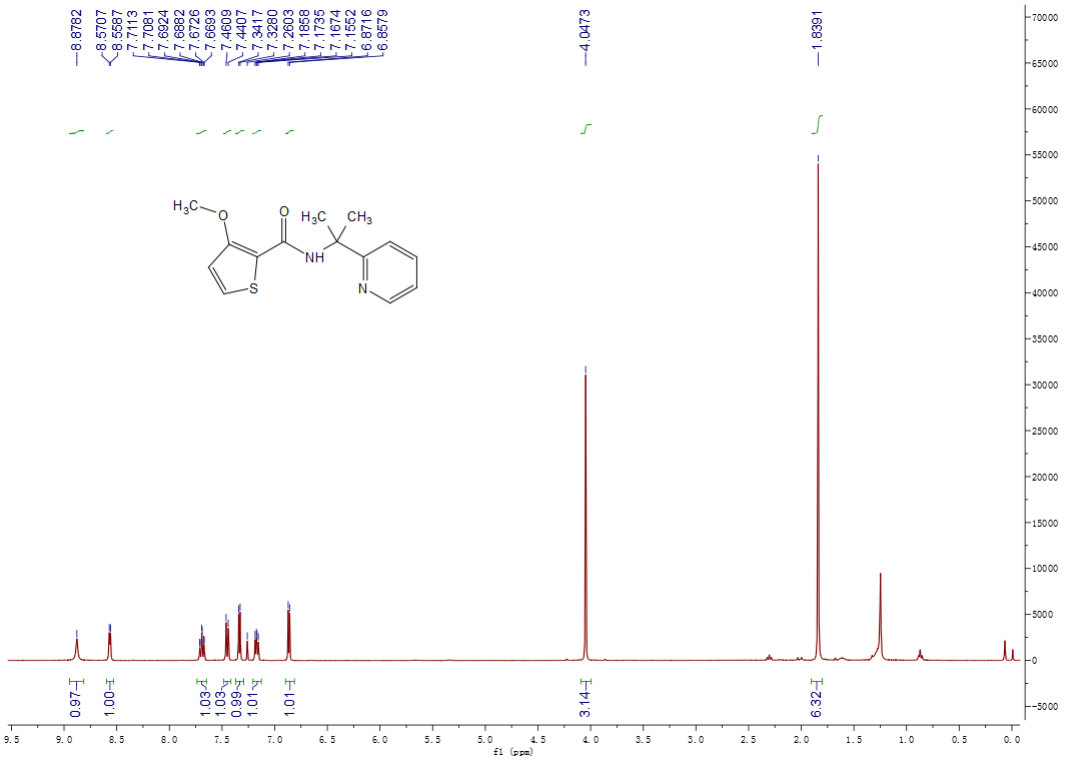
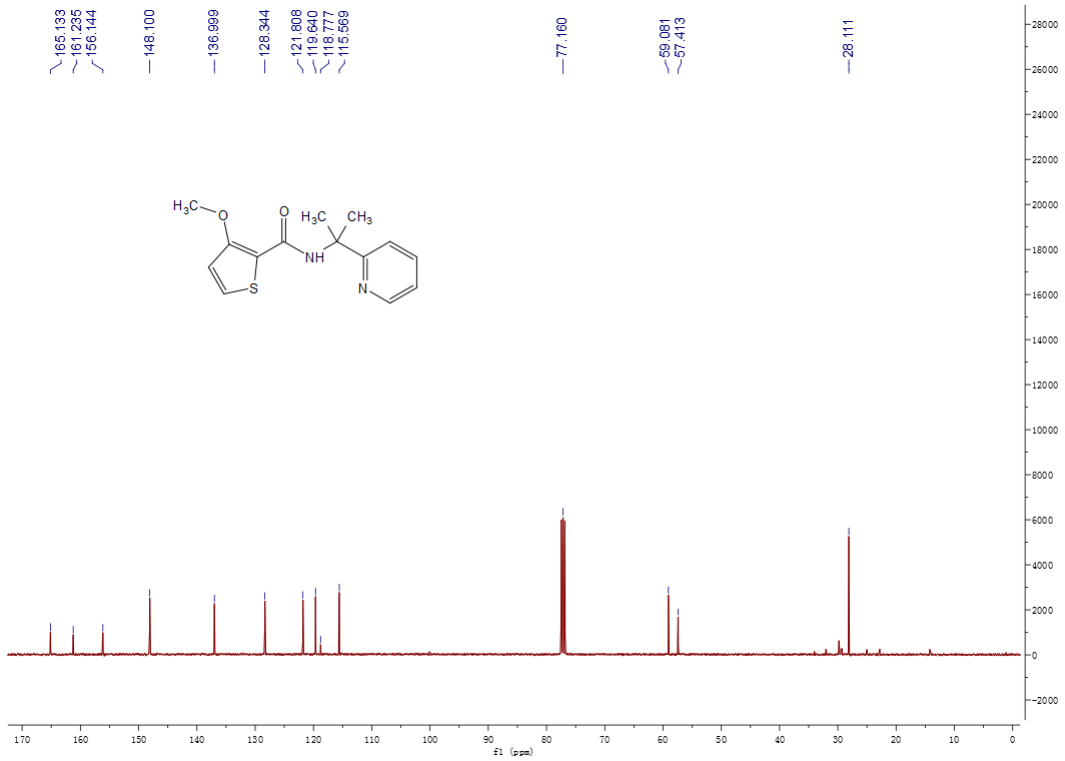
8.6081
8.5982
8.0679
7.6639
7.6594
7.6441
7.6405
7.6252
7.6207
7.4190
7.3989
7.2602
7.1590
7.1567
7.1469
7.1445
7.1405
7.1383
7.1284
7.1261
3.9469
1.8173
1.02
1.10
0.97
1.01
1.19
1.17
1.00
3.05
6.47
f1 (ppm)

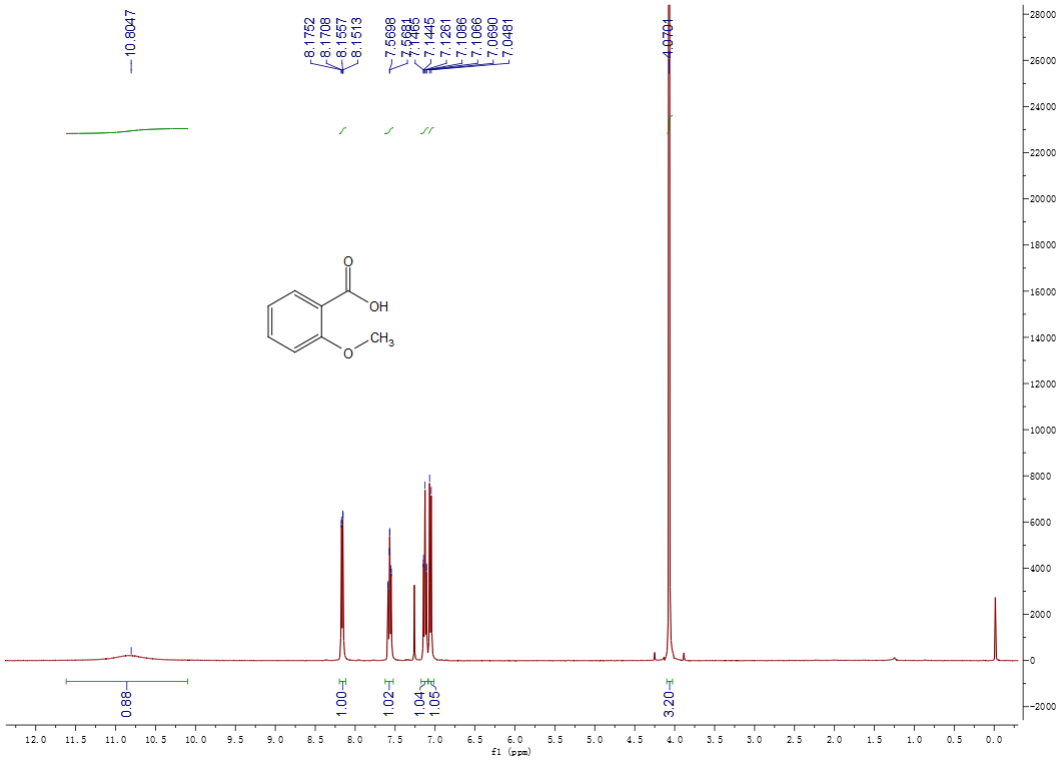

169.529
164.780
161.890
152.257
148.659
144.244
141.848
136.792
121.774
119.444
77.160
57.820
47.386
28.121
f1 (ppm)

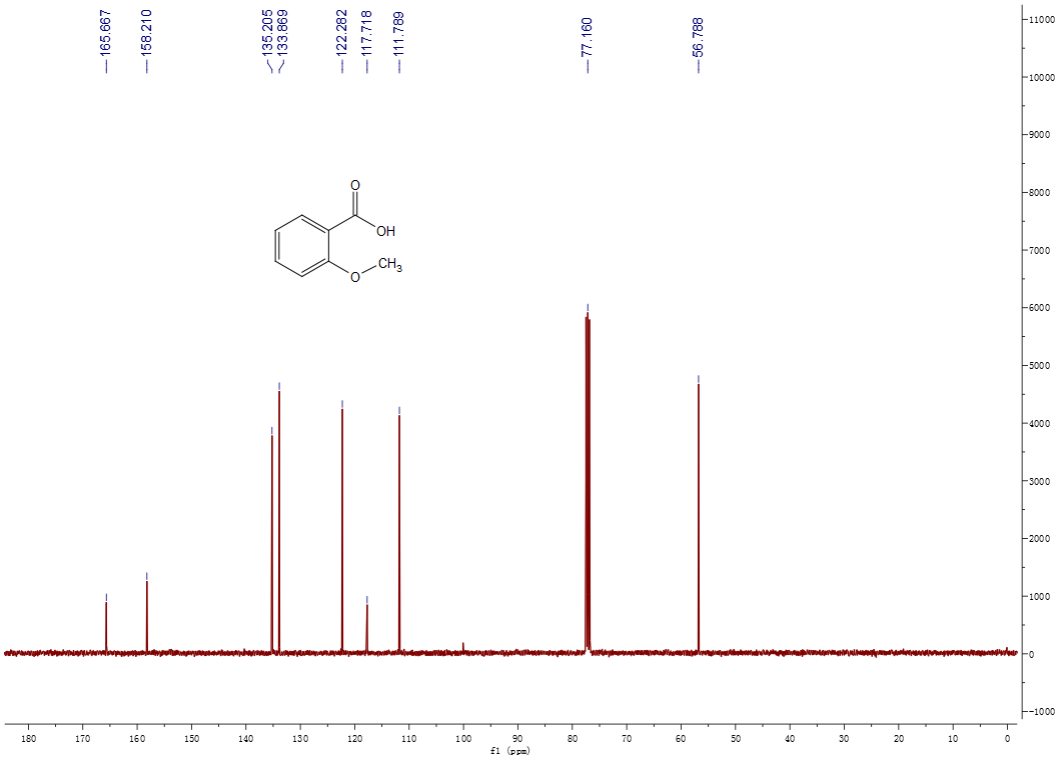
5i


8.8782
8.5707
8.5587
7.7113
7.7081
7.6924
7.6882
7.6726
7.6693
7.4609
7.4407
7.3417
7.3280
7.2603
7.1858
7.1735
7.1674
7.1552
6.8716
6.8579
4.0473
1.8391
0.97
1.00
1.03
1.03
0.99
1.01
1.01
3.14
6.32
f1 (ppm)


165.133
161.235
156.144
148.100
136.999
128.344
121.808
119.640
118.777
115.569
77.160
59.081
57.413
28.111
f1 (ppm)

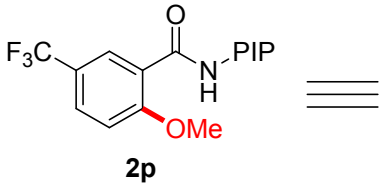
6a


10.8047
8.1752
8.1708
8.1557
8.1513
7.5698
7.5681
7.1465
7.1445
7.1261
7.1086
7.1066
7.0690
7.0481
4.0701
O
OH
CH3
O
0.88
1.00
1.02
1.04
1.05
3.20
f1 (ppm)

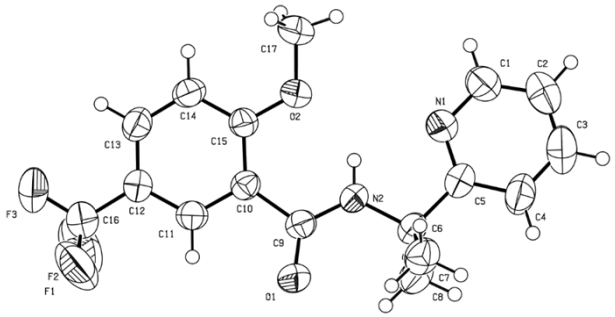

165.667
158.210
135.205
133.869
122.282
117.718
111.789
77.160
56.788
O
OH
CH3
O
f1 (ppm)

5. X-Ray Data

Crystal Data and Structure for **2p**



2p



Bond precision:	C-C = 0.0045 A		Wavelength=0.71073
Cell:	a=10.5428(12)	b=16.2625(12)	c=10.8624(15)
	alpha=90	beta=118.846(16)	gamma=90
Temperature:	293 K		
	Calculated	Reported	
Volume	1631.3(4)		1631.3(3)
Space group	P 21/c		P 1 21/c 1
Hall group	-P 2ybc		-P 2ybc
Moiety formula	C17 H17 F3 N2 O2		C17 H17 F3 N2 O2
Sum formula	C17 H17 F3 N2 O2		C17 H17 F3 N2 O2
Mr	338.33		338.33
Dx,g cm^{-3}	1.378		1.378
Z	4		4
Mu (mm-1)	0.114		0.114
F000	704.0		704.0
F000’	704.45		
h,k,lmax	12,19,13		12,19,13
Nref	2987		2981
Tmin,Tmax	0.946,0.958		0.898,1.000
Tmin’	0.946		

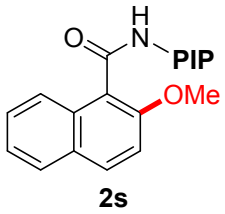
Correction method= MULTI-SCAN

Data completeness= 0.998 Theta(max)= 25.340

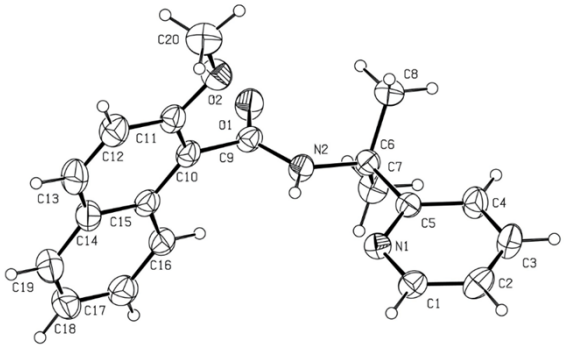
R(reflections)= 0.0549(1960) wR2(reflections)= 0.1572(2981)

S = 1.065 Npar= Npar = 221

Crystal Data and Structure for **2s**



2s



Bond precision:	C-C = 0.0060 A		Wavelength=0.71073
Cell:	a=10.255(1)	b=10.8108(12)	c=15.4763(16)
	alpha=90	beta=90	gamma=90
Temperature:	293 K		
	Calculated		Reported
Volume	1715.8(3)		1715.8(3)
Space group	P 21 21 21		P 21 21 21
Hall group	P 2ac 2ab		P 2ac 2ab
Moiety formula	C20 H20 N2 O2		C20 H20 N2 O2
Sum formula	C20 H20 N2 O2		C20 H20 N2 O2
Mr	320.38		320.38
Dx,g cm^{-3}	1.240		1.240
Z	4		4
Mu (mm-1)	0.081		0.081
F000	680.0		680.0
F000’	680.28		
h,k,lmax	12,13,18		12,13,18
Nref	3140[1807]		1803
Tmin,Tmax	0.973,0.982		0.860,1.000
Tmin’	0.972		

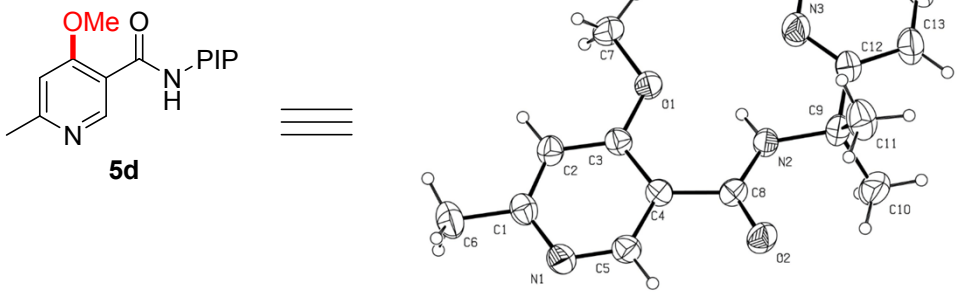
Correction method= MULTI-SCAN

Data completeness= 1.00/0.57 Theta(max)= 25.350

R(reflections)= 0.0500(1299) wR2(reflections)= 0.1290(1803)

S = 1.049 Npar= Npar = 220

Crystal Data and Structure for **5d**



Bond precision:	C-C = 0.0034 A		Wavelength=0.71073
Cell:	a=8.0742(5)	b=12.4409(10)	c=17.6473(12)
	alpha=71.940(7)	beta=79.009(6)	gamma=72.177(6)
Temperature:	293 K		
	Calculated		Reported
Volume	1595.5(2)		1595.5(2)
Space group	P -1		P -1
Hall group	-P 1		-P 1
Moiety formula	C16 H19 N3 O2		C16 H19 N3 O2
Sum formula	C16 H19 N3 O2		C16 H19 N3 O2
Mr	285.34		285.34
Dx,g cm^{-3}	1.188		1.188
Z	4		4
Mu (mm-1)	0.080		0.080
F000	608.0		608.0
F000’	608.24		
h,k,lmax	9,14,21		9,14,21
Nref	5841		5817
Tmin,Tmax	0.962,0.969		0.852,1.000
Tmin’	0.962		

Correction method= MULTI-SCAN

Data completeness= 0.996 Theta(max)= 25.350

R(reflections)= 0.0554(3700) wR2(reflections)= 0.1689(5817)

S = 1.027 Npar= Npar = 387