Nickel-catalyzed *ortho*-halogenation of unactivated (hetero)aryl C–H bonds with lithium halides using a removable auxiliary

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Supporting Information

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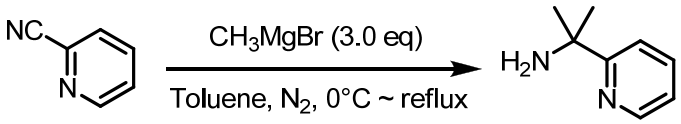
1. General Information

t-BuCNwas dried by CaH_2,distilled under reduced pressure and stored undernitrogen. $Ni(OTf)_2$and LiIwere obtained from Energy®. LiBr, LiCl and tetrahydropyranewere obtained fromaladdin.$NiCl_2(PPh_3)_2$ was obtained from SINOCOMPOUND. Dibutyl ether was obtained from Adamas.The other materials and solvents were purchased from Aladdin and other commercial suppliers and used without additional purification. NMR spectra were recorded on a BrukeAvance 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 $CDCl_3$ (7.26 ppm) or residual undeuterated solvent signal(77.20 ppm for ^{13}C NMR).The following abbreviations (or combinations thereof) were used to explain multiplicities: s = singlet, d = doublet, t = triplet, m = multiplet, b = broad. 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

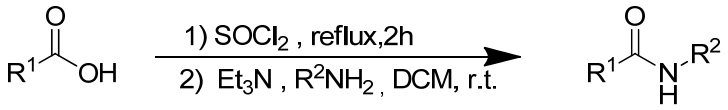


An improvement of the work-up procedure to the literature[1] was used: To a solution of 2-cyanopyridine (33.0 g, 0.32 mol) in 500 ml of toluene was added CH_3MgBr (3.2M in 2-methyl tetrahydrofuran, 300ml, 0.96mol) dropwise at 0°C in a nitrogen atmosphere by vigorous magnetometric stirring. Upon completion 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 organic phase 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. 24g, 55%).^{1}H NMR (400 MHz, $CDCl_3$) δ8.55 (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.

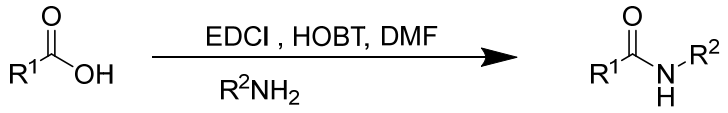
2.2 General Procedure for the Preparation of Starting Materials

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 2h 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 addeddropwiseto a 20 mL dry CH_2Cl_2 solution containing amine (5 mmol) and Et_3N (10mmol) at 0 ^{o}C. After stirring for 6h at ambient temperature, the resulting mixture waswashed with brine, dried over $MgSO_4$, filtered and concentrated under reducedpressure.The residue was purified by flash chromatography to give the desiredproduct.

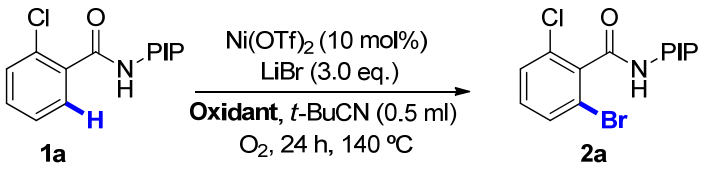
General Procedure for the Preparation of Starting Materials (Method B):



A mixture of amine (5 mmol), 6-bromohexanoic acid (5 mmol), EDCI (5.5 mmol) and HOBT (5.5 mmol) in anhydrous DMF (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.

2.3 Optimization of Reaction Conditions

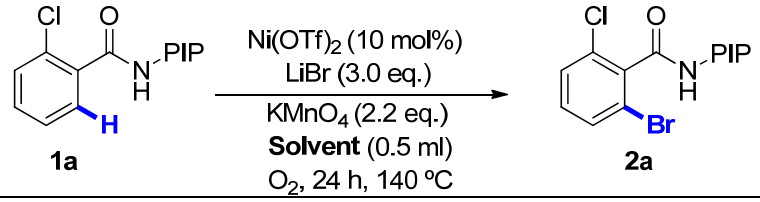
Screening of Oxidants



Entry[a]	Oxidant (2.0 eq.)	Yield[b] of 2a
1	$PhI(OAc)_2$	decomposed
2	$K_2S_2O_8$	decomposed
3	Selectfluor	decomposed
4	$KMnO_4$ (2.2 eq.)	58%
5	BQ	N.R.
6	Ag_2CO_3	trace
7	TBHP	trace

[a] The reactions were carried out **1a** (0.1 mmol), $Ni(OTf)_2$ (0.01 mmol), LiBr (0.3 mmol), oxidant (0.2 mmol), *t*-BuCN (0.5 mL), O_2, 140 °C. [b] ^1H NMR yield using CH_2Br_2 as the internal standard.

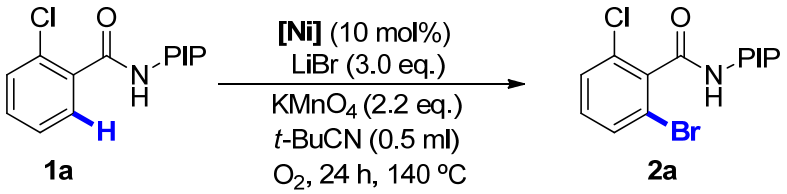
Screening of Solvents



Entry[a]	Solvent	Yield[b] of 2a
1	dioxane	trace
2	CH_3OH	N.R.
3	DCE	40%
4	*t*-BuCN	58%
5	toluene	18%

[a] The reactions were carried out **1a** (0.1 mmol), $Ni(OTf)_2$ (0.01 mmol), LiBr (0.3 mmol), $KMnO_4$ (0.22 mmol), solvent (0.5 mL), O_2, 140 °C. [b] ^1H NMR yield using CH_2Br_2 as the internal standard.

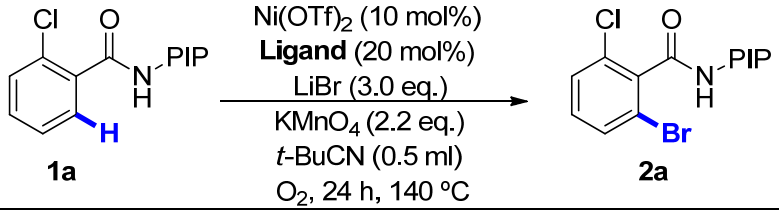
Screening of NickelCatalysts



Entry[a]	[Ni]	Yield[b] of 2a
1	/	N.R.
2	$Ni(OAc)_2$	29%
3	$Ni(OTf)_2$	60%
4	$Ni(acac)_2$	22%
5	$NiBr_2$	trace

[a] The reactions were carried out **1a** (0.1 mmol), [Ni] (0.01 mmol), LiBr (0.3 mmol), $KMnO_4$ (0.22 mmol), *t*-BuCN (0.5 mL), O_2, 140 °C. [b] ^1H NMR yield using CH_2Br_2 as the internal standard.

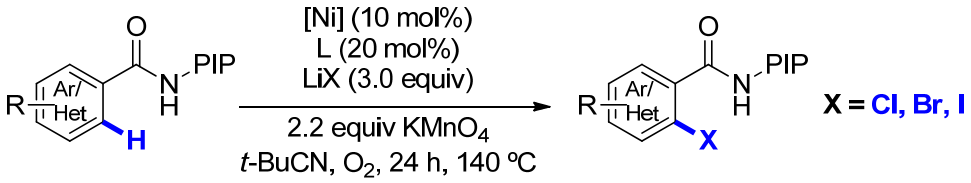
Screening of Ligands



Entry[a]	Ligand	Yield[b] of 2a
1	PPh_3	trace
2	PCy_3	60%
3	DME	20%
4	THP	92%[c]
5	DBE	47%

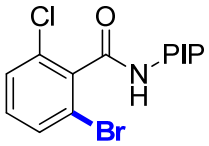
[a] The reactions were carried out **1a** (0.1 mmol), $Ni(OTf)_2$ (0.01 mmol), LiBr (0.3 mmol), $KMnO_4$ (0.22 mmol), *t*-BuCN (0.5 mL), O_2, 140 °C. [b] ^1H NMR yield using CH_2Br_2 as the internal standard. [c]Isolated yield. DME = glycol dimethyl ether, THP = tetrahydropyrane, DBE = dibutylether.

2.4 General Procedure for the Halogenations



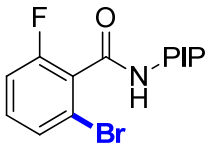
To a 50 mL sealed tube was added substrate (0.1mmol), nickel catalyst (3.7 mg, 0.01mmol), L (0.02mmol), LiX (0.3mmol), $KMnO_4$ (36mg, 0.22mmol), and *t*-BuCN (0.5 mL). The mixture was stirred at 140℃oil bathfor24 hour. The reaction mixture was cooled to room temperature, diluted with ethyl acetate and quenched with saturated ammonia solution. The aqueous phase was extracted with ethyl acetate (10 mL× 3).The combined organic phase was dried with anhydrous magnesium sulfate. After concentration, the resultin gresidue was purified by flash chromatography to afford the product.

2-Bromo-6-chloro-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide (2a)



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (d, *J* = 4.8 Hz, 1H), 8.25 (brs, 1H), 7.74 (td, *J* = 8.0, 1.6 Hz, 1H), 7.48 (d, *J* = 8.4 Hz, 2H), 7.36 (d, *J* = 8.0 Hz, 1H), 7.18 (m, 2H), 1.92 (s, 6H).^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 163.9, 147.5, 138.9, 137.4, 132.3, 131.3, 130.6, 128.7, 122.1, 120.8, 119.7, 57.7, 27.4; HRMS (EI-TOF) calcd for $C_{15}H_{14}BrClN_2O$ (M^+): 351.9978, found:351.9980.

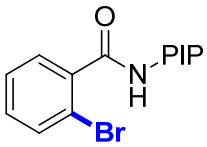
2-Bromo-6-fluoro-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide (2b)



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (dd, *J* = 4.8, 0.8 Hz, 1H), 8.26 (brs, 1H), 7.74 (td, *J* = 8.0, 1.6 Hz, 1H), 7.47 (d, *J* = 8.4 Hz, 1H), 7.38 (d, *J* = 8.4 Hz, 1H), 7.25 – 7.17 (m, 2H), 7.08 (td, *J* = 8.4, 0.8 Hz, 1H), 1.91 (s, 6H);^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0,

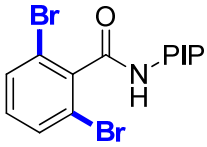
162.4, 160.8, 158.3, 147.6, 137.4, 131.0(d, J = 8.0 Hz), 128.97 – 128.46 (m), 122.2, 120.9 (d, J = 5.0 Hz), 119.6, 115.2, 115.0, 57.8, 27.5; HRMS (EI-TOF) calcd for $C_{15}H_{14}BrFN_2O$ (M^+): 336.0274, found:336.0275.

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



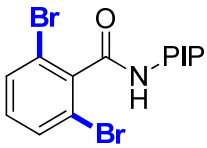
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 – 8.46 (m, 1H), 8.24 (brs, 1H), 7.75 – 7.71 (m, 1H), 7.59 (dd, J = 8.0, 0.8 Hz, 1H), 7.54 (dd, J = 7.6, 1.6 Hz, 1H), 7.47 (dt, J = 8.0, 0.8 Hz, 1H), 7.35 (td, J = 7.6, 1.2 Hz, 1H), 7.28 – 7.22 (m, 1H), 7.19 (ddd, J = 7.2, 4.8, 0.8 Hz, 1H), 1.90 (s, 6H);^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 164.3, 147.7, 139.5, 137.3, 133.4, 130.9, 129.3, 127.6, 122.1, 119.6, 57.6, 27.6; HRMS (EI-TOF) calcd for $C_{15}H_{15}BrN_2O_2$ (M^+):318.0368, found: 318.0367.

2,6-dibromo-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide (2c')



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (d, J = 4.8 Hz, 1H), 8.28 (brs, 1H), 7.74 (td, J = 8.0, 1.6 Hz, 1H), 7.53 (d, J = 8.0 Hz, 2H), 7.49 (d, J = 8.0 Hz, 1H), 7.20 (dd, J = 6.8, 4.8Hz, 1H), 7.09 (t, J = 8.0 Hz, 1H), 1.93 (s, 6H);^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 164.0, 147.6, 140.8, 137.4, 132.0, 131.0, 122.2, 120.8, 119.7, 57.7, 27.4; HRMS (EI-TOF) calcd for $C_{15}H_{14}Br_2N_2O$ (M^+): 395.9473, found:395.9479.

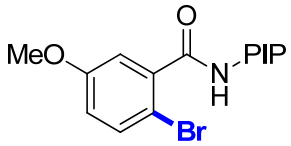
2,6-Dibromo-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide (2d)



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (d, J = 4.8 Hz, 1H), 8.28 (brs, 1H), 7.74 (td, J = 8.0, 1.6 Hz, 1H), 7.53 (d, J = 8.0 Hz, 2H), 7.49 (d, J = 8.0 Hz, 1H), 7.20 (dd, J = 6.8, 4.8Hz, 1H), 7.09 (t, J = 8.0 Hz, 1H), 1.93 (s, 6H);^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 164.0, 147.6, 140.8, 137.4, 132.0, 131.0, 122.2, 120.8, 119.7, 57.7, 27.4; HRMS (EI-TOF)

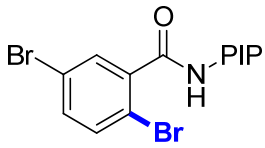
calcd for $C_{15}H_{14}Br_2N_2O$ (M^+): 395.9473, found:395.9479.

2-Bromo-5-methoxy-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide (2e)



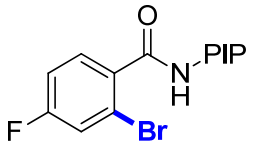
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (dd, *J* = 4.8, 0.8 Hz, 1H), 8.18 (brs, 1H), 7.78 – 7.68 (m, 2H), 7.47 (d, *J* = 8.4 Hz, 1H), 7.19 (ddd, *J* = 7.6, 4.8, 0.8 Hz, 1H), 7.02 (d, *J* = 3.2 Hz, 1H), 6.68 (dd, *J* = 8.8, 2.8 Hz, 1H), 3.80 (s, 3H), 1.91 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 164.2, 159.1, 147.8, 140.1, 137.3, 134.2, 122.1, 119.7, 117.5, 114.5, 109.8, 57.6, 55.8, 27.6; HRMS (EI-TOF) calcd for $C_{16}H_{17}BrN_2O_2$ (M^+): 348.0473, found: 348.0475.

2,5-Dibromo-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide (2f)



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 – 8.45 (m, 1H), 8.35 (brs, 1H), 7.74 (td, *J* = 8.0, 1.6 Hz, 1H), 7.65 (d, *J* = 2.4 Hz, 1H), 7.46 (d, *J* = 4.0 Hz, 1H), 7.44 (d, *J* = 4.4 Hz, 1H),7.37 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.21 (ddd, *J* = 7.2, 4.8, 0.8 Hz, 1H), 1.88 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5, 164.0, 147.7, 141.2, 137.5, 134.9, 133.8, 132.2, 122.3, 121.6, 119.7, 118.4,57.7, 27.5;HRMS (EI-TOF) calcd for $C_{15}H_{14}Br_2N_2O$ (M^+): 395.9473, found:395.9468.

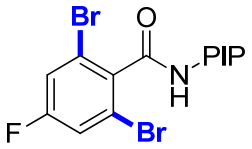
2-Bromo-4-fluoro-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide (2g)



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (dd, *J* = 4.8, 0.4 Hz, 1H), 8.33 (brs, 1H), 7.74 (td, *J* = 8.0, 2.0 Hz, 1H), 7.56 (dd, *J* = 8.8, 6.0 Hz, 1H), 7.46 (d, *J* = 8.0 Hz, 1H), 7.34 (dd, *J* = 8.4, 2.8 Hz, 1H), 7.20 (ddd, *J* = 7.2, 4.8, 0.8 Hz, 1H), 7.07 (td, *J* = 8.4, 2.4 Hz, 1H),

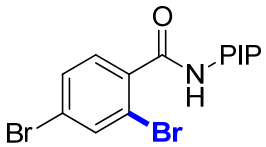
1.89 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 164.1(d, *J* = 13.0 Hz), 161.5, 147.7, 137.4, 135.8 (d, *J* = 3.6 Hz), 130.9(d, *J* = 8.8 Hz), 122.2, 120.8, 120.6, 120.3 (d, *J* = 9.6 Hz), 119.7, 115.0, 114.8, 57.6, 27.6; HRMS (EI-TOF) calcd for $C_{15}H_{14}BrFN_2O$ (M^+): 336.0274, found:336.0276.

2,6-Dibromo-4-fluoro-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide (2g')



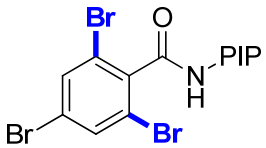
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (d, *J* = 4.8 Hz, 1H), 8.32 (brs, 1H), 7.75 (td, *J* = 7.6, 2.0 Hz, 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.23 – 7.18 (m, 1H), 1.92 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6, 163.9, 163.0, 160.5, 147.5, 137.5 (d, *J* = 5.5 Hz), 122.3, 121.1 (d, *J* = 10.2 Hz), 119.7 (d, *J* = 6.5 Hz), 119.5, 57.7, 27.3; HRMS (EI-TOF) calcd for $C_{15}H_{14}Br_2FN_2O$ (M^+): 413.9379, found:413.9375.

2,4-Dibromo-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide (2h)



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (d, *J* = 4.8 Hz, 1H), 8.35 (brs, 1H), 7.80 – 7.71 (m, 2H), 7.52 – 7.43 (m, 2H), 7.41 (d, *J* = 8.4 Hz, 1H), 7.20 (dd, *J* = 7.2, 4.8 Hz, 1H), 1.88 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 164.0, 147.7, 138.3, 137.5, 135.8, 130.8, 130.5, 123.9, 122.2, 120.4, 119.7, 57.6, 27.5; HRMS (EI-TOF) calcd for $C_{15}H_{14}Br_2N_2O$ (M^+): 395.9473, found:395.9469.

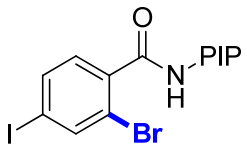
2,4,6-Tribromo-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide (2h')



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (d, *J* = 4.4 Hz, 1H), 8.36 (brs, 1H), 7.74 (t, *J* = 7.6 Hz, 1H), 7.71 (s, 2H), 7.46 (d, *J* = 8.0 Hz, 1H), 7.20 (t, *J* = 6.0 Hz, 1H), 1.91 (s, 6H);

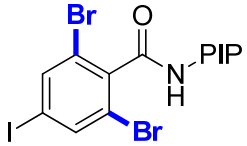
^{13}C NMR (100 MHz, $CDCl_3$) δ 164.5, 163.8, 147.5, 139.8, 137.5, 134.4, 123.2, 122.3, 121.2, 119.7, 57.7, 27.3; HRMS (EI-TOF) calcd for $C_{15}H_{13}Br_3N_2O$ (M^+): 473.8578, found:473.8573.

2-Bromo-4-iodo-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide (2i)



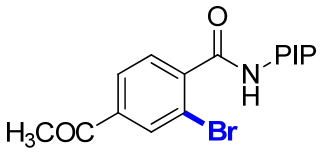
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (d, *J* = 4.4 Hz, 1H), 8.38 (brs, 1H), 7.97 (s, 1H), 7.74 (t, *J* = 8.0 Hz, 1H), 7.69 (d, *J* = 8.0 Hz, 1H), 7.46 (d, *J* = 8.0 Hz, 1H), 7.31 – 7.25 (m, 1H), 7.22 –7.16 (m, 1H), 1.89 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 164.1, 147.7, 141.4, 139.0, 137.4, 136.7, 130.5, 122.2, 120.4, 119.6, 95.6, 57.6, 27.5; HRMS (ESI-TOF) calcd for$C_{15}H_{15}BrIN_2O$ $[M+Na]^+$: 466.9226, found: 466.9222.

2,6-Dibromo-4-iodo-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide (2i')



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (d, *J* = 4.4 Hz, 1H), 8.36 (brs, 1H), 7.89 (s, 2H), 7.74 (t, *J* = 7.6 Hz, 1H), 7.46 (d, *J* = 8.0 Hz, 1H), 7.23 – 7.18 (m, 1H), 1.91 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.5, 163.9, 147.5, 140.4, 139.9, 137.5, 122.3, 121.2, 119.7, 94.4, 57.7, 27.3; HRMS (ESI-TOF)calcd for $C_{15}H_{14}Br_2IN_2O$ $[M^+H]^+$: 522.8512, found: 522.8525.

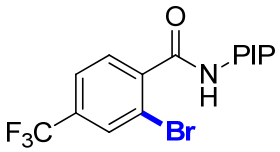
4-acetyl-2-bromo-N-(2-(pyridin-2-yl)propan-2-yl)benzamide (2j)



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, *J* = 4.4 Hz, 1H), 8.28 (brs, 1H), 8.16 (d, *J* = 1.2 Hz, 1H), 7.95 – 7.85 (m, 2H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.58 (d, *J* = 8.0 Hz, 1H), 7.34 (dd, *J* = 6.8 Hz, *J* = 5.2 Hz, 1H), 2.61 (s, 3H), 1.92 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$)

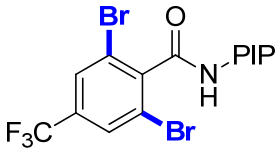
δ 196.3, 166.5, 163.4, 146.6, 142.7, 139.0, 133.3, 129.6, 127.5, 122.8, 120.3, 120.1, 57.3, 27.5, 26.9. HRMS (EI-TOF)calcd for $C_{17}H_{17}BrN_2O_2$ $[M^+H]^+$: 360.0473, found: 360.0472.

2-bromo-N-(2-(pyridin-2-yl)propan-2-yl)-4-(trifluoromethyl)benzamide (2k)



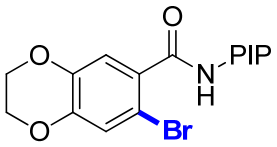
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 – 8.43 (m, 2H), 7.87 (s, 1H), 7.76 (td, *J* = 8.0, 1.6 Hz, 1H), 7.67 – 7.59 (m, 2H), 7.46 (d, *J* = 8.1 Hz, 1H), 7.22 (ddd, *J* = 7.6, 4.8, 0.8 Hz, 1H), 1.91 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 163.9, 147.6, 142.9, 137.5, 133.0, 132.7, 130.5 (d, *J* = 3.9 Hz), 129.6, 124.6 (d, *J* = 3.7 Hz), 122.3, 120.1, 119.7, 57.7, 27.5. HRMS (ESI-TOF) calcd for $C_{16}H_{14}BrF_3N_2O$ $[M+H]^+$: 387.0314, found: 387.0306.

2,6-dibromo-N-(2-(pyridin-2-yl)propan-2-yl)-4-(trifluoromethyl)benzamide (2k')



1H NMR (400 MHz, CDCl3) δ 8.48 (brs, 1H), 8.46 – 8.42 (m, 1H), 7.85 – 7.71 (m, 3H), 7.47 (d, J = 8.0 Hz, 1H), 7.24 – 7.19 (m, 1H), 1.93 (s, 6H); 13C NMR (100 MHz, CDCl3) δ 164.1, 163.6, 147.5, 143.9, 137.6, 134.1, 133.3, 132.9, 129.0 (q, J = 3.7 Hz), 123.6, 122.3, 121.2, 120.9, 119.6, 57.8, 27.3. HRMS (EI-TOF) calcd for $C_{16}H_{13}BrF_3N_2O$ (M^+): 463.9347, found: 463.9349.

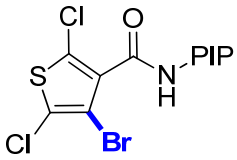
7-bromo-N-(2-(pyridin-2-yl)propan-2-yl)-2,3-dihydrobenzo[b][1,4]dioxine-6-carboxamide (2l)



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, *J* = 4.4 Hz, 1H), 8.15 (brs, 1H), 7.73 (td, *J* = 8.0,

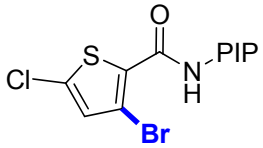
1.6 Hz, 1H), 7.46 (d, J = 8.4 Hz, 1H), 7.19 (dd, J = 7.2, 5.2 Hz, 1H), 7.13 (s, 1H), 7.08 (s, 1H), 4.25 (s, 4H), 1.86 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1, 164.1, 147.5, 145.1, 142.8, 137.2, 132.0, 121.9, 121.6, 119.6, 118.4, 110.0, 64.5, 64.2, 57.3, 27.5. HRMS (EI-TOF)calcd for $C_{17}H_{17}Br_2N_2O_3$ $[M^+H]^+$: 376.0423, found: 376.0428.

4-Bromo-2,5-dichloro-*N*-(2-(pyridin-2-yl)propan-2-yl)thiophene-3-carboxamide (2p)



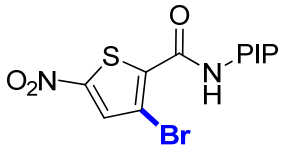
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (dd, J = 4.8, 0.8 Hz, 1H), 8.46 (brs, 1H), 7.75 (td, J = 7.6, 1.6 Hz, 1H), 7.45 (d, J = 8.0 Hz, 1H), 7.21 (ddd, J = 7.2, 4.8, 0.8 Hz, 1H), 1.88 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.8, 159.9, 147.6, 137.5, 136.3, 126.0, 124.6, 122.3, 119.6, 109.4, 57.7, 27.6; HRMS (EI-TOF) calcd for $C_{13}H_{11}BrCl_2N_2OS$ (M^+): 391.9153, found:391.9148.

3-Bromo-5-chloro-*N*-(2-(pyridin-2-yl)propan-2-yl)thiophene-2-carboxamide (2q)



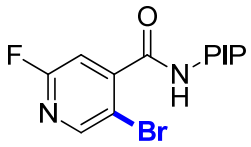
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.17 (brs, 1H), 8.54 (d, J = 4.8 Hz, 1H), 7.74 (td, J = 7.6, 1.2 Hz, 1H), 7.43 (d, J = 8.0 Hz, 1H), 7.21 (dd, J = 7.2, 5.2 Hz, 1H), 6.88 (s, 1H), 1.85 (s, 6H);^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 158.9, 147.8, 137.3, 136.1, 135.1, 131.0, 122.2, 119.5, 107.2, 58.3, 27.7; HRMS (EI-TOF) calcd for $C_{13}H_{12}BrClN_2OS$ (M^+): 357.9542, found: 357.9545.

3-Bromo-5-nitro-*N*-(2-(pyridin-2-yl)propan-2-yl)thiophene-2-carboxamide (2r)



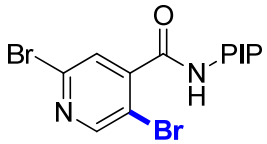
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.63 (brs, 1H), 8.54 (d, *J* = 4.4 Hz, 1H), 7.83 (s, 1H), 7.78 (td, *J* = 8.0, 1.2 Hz, 1H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.25 (m, 1H), 1.87 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.6, 157.9, 152.4, 147.7, 143.6, 137.6, 132.0, 122.5, 119.6, 107.1, 58.6, 27.5.HRMS (EI-TOF) calcd for $C_{13}H_{12}BrN_3O_3S$ (M^+): 368.9783, found:368.9785.

5-Bromo-2-fluoro-*N*-(2-(pyridin-2-yl)propan-2-yl)isonicotinamide (2s)



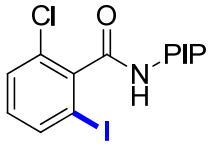
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (brs, 1H), 8.47 (m, 1H), 8.38 (s, 1H), 7.77 (td, *J* = 8.0, 1.6 Hz, 1H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.23 (ddd, *J* = 7.6, 4.8, 0.8 Hz, 1H), 7.12 (d, *J* = 3.2 Hz, 1H), 1.89 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 163.5 (d, *J* = 3.0 Hz), 161.8, 150.8 (d, *J* = 7.0 Hz), 150.6 (d, *J* = 15.0 Hz), 147.6, 137.7, 122.5, 119.6, 113.6 (d, *J* = 5.0 Hz), 110.1, 109.7, 57.8, 27.5; HRMS (EI-TOF) calcd for $C_{14}H_{13}BrFN_3O$ (M^+): 337.0226, found:337.0230.

2,5-Dibromo-N-(2-(pyridin-2-yl)propan-2-yl)isonicotinamide (2t)



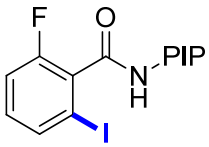
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (brs, 1H), 8.52 (s, 1H), 8.48 (d, *J* = 4.8 Hz, 1H), 7.77 (td, *J* = 8.0, 1.6 Hz, 1H), 7.60 (s, 1H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.26 – 7.21 (m, 1H), 1.87 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.4, 163.1, 152.8, 148.1, 147.5, 141.0, 137.7, 127.6, 122.4, 119.6, 116.9, 57.8, 27.4; HRMS (EI-TOF) calcd for $C_{14}H_{13}Br_2N_3O$ (M^+): 396.9425, found:396.9427.

2-Chloro-6-iodo-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide (3a)



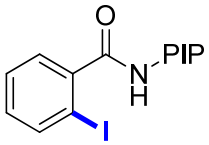
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (d, *J* = 4.8 Hz, 1H), 8.27 (brs, 1H), 7.75 (m, 2H), 7.48 (d, *J* = 8.4 Hz, 1H), 7.38 (d, *J* = 8.0 Hz, 1H), 7.19 (ddd, *J* = 7.2, 4.8, 0.8 Hz, 1H), 6.99 (t, *J* = 8.0 Hz, 1H), 1.94 (s, 6H);^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 164.0, 147.5, 142.7, 137.8, 137.4, 131.4, 130.9, 129.6, 122.2, 119.7, 93.8, 57.7, 27.4; HRMS (EI-TOF) calcd for $C_{15}H_{14}ClIN_2O$ (M^+): 399.9839, found:399.9842.

2-Fluoro-6-iodo-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide (3b)



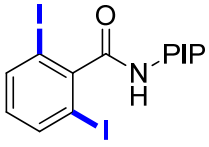
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (d, *J* = 4.8 Hz, 1H), 8.25 (brs, 1H), 7.78 – 7.70 (m, 1H), 7.63 (d, *J* = 7.6 Hz, 1H), 7.48 (d, *J* = 8.4 Hz, 1H), 7.19 (dd, *J* = 7.2, 4.8 Hz, 1H), 7.13 – 7.02 (m, 2H), 1.92 (s, 6H);^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0 (d, *J* = 6.0 Hz), 160.0, 157.5, 147.6, 137.4, 135.2 (d, *J* = 3.5 Hz), 132.5, 132.3, 131.5 (d, *J* = 8.3 Hz), 122.2, 119.7, 116.0, 115.8, 93.9 (d, *J* = 3.4 Hz), 57.8, 27.5.HRMS (EI-TOF) calcd for $C_{15}H_{14}FIN_2O$ (M^+): 384.0135, found:384.0133.

2-Iodo-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide (3c)



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (m, 1H), 8.18 (brs, 1H), 7.87 (dd, *J* =8.0, 0.8 Hz, 1H), 7.74 (td, *J* = 7.6, 1.6 Hz, 1H), 7.50 – 7.43 (m, 2H), 7.38 (td, *J* = 7.2, 1.2 Hz, 1H), 7.19 (ddd, *J* = 7.6, 4.8, 0.8 Hz, 1H), 7.08 (td, *J* = 7.6, 1.6 Hz, 1H), 1.91 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.7, 164.2, 147.7, 143.6, 139.9, 137.4, 130.8, 128.3128.2, 122.1, 119.7, 92.8, 57.5, 27.6; The analyticaldatas above were matched with literature.[2]

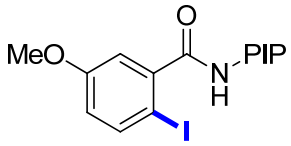
2,6-Diiodo-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide(3c')



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (d, *J* = 3.6 Hz, 1H), 8.31 (brs, 1H), 7.81 (d, *J* = 8.0

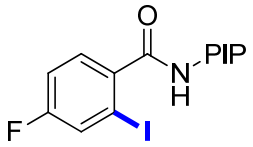
Hz, 2H), 7.75 (t, J = 7.6 Hz, 1H), 7.48 (d, J = 8.0 Hz, 1H), 7.24 – 7.15 (m, 1H), 6.72 (t, J = 8.0 Hz, 1H), 1.96 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.6, 164.1, 147.9, 147.5, 139.3, 137.4, 131.4, 122.2, 119.8, 92.6, 57.6, 27.2; HRMS (EI-TOF) calcd for $C_{15}H_{14}I_2N_2O$ (M^+): 491.9195, found:491.9199.

2-Iodo-5-methoxy-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide (3e)



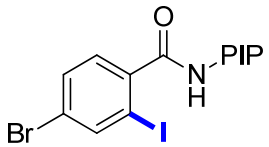
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 – 8.45 (m, 1H), 8.18 (brs, 1H), 7.77 – 7.68 (m, 2H), 7.47 (d, J = 8.4 Hz, 1H), 7.19 (ddd, J = 7.6, 4.8, 0.8 Hz, 1H), 7.02 (d, J = 3.2 Hz, 1H), 6.68 (dd, J = 8.8, 2.8 Hz, 1H), 3.80 (s, 3H), 1.91 (s, 6H);^{13}C NMR (100 MHz, $CDCl_3$) δ 168.4, 164.2, 159.9, 147.7, 144.3, 140.6, 137.4, 122.1, 119.7, 117.5, 114.1 81.0, 57.5, 55.7, 27.6; HRMS (EI-TOF) calcd for $C_{16}H_{17}IN_2O_2$(M^+): 396.0335, found:396.0338.

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



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (d, J = 4.4 Hz, 1H), 8.25 (brs, 1H), 7.74 (td, J = 7.6, 1.6 Hz, 1H), 7.59 (dd, J = 8.4, 2.4 Hz, 1H), 7.50 – 7.41 (m, 2H), 7.24 – 7.17 (m, 1H), 7.09 (td, J = 8.0, 2.4 Hz, 1H), 1.90 (s, 6H);^{13}C NMR (100 MHz, $CDCl_3$) δ 167.9, 164.13 (s), 163.6, 161.1, 147.7, 139.8 (d, J = 3.5 Hz), 137.4, 129.5 (d, J = 8.5 Hz), 127.2, 126.9, 122.2, 119.7, 115.5, 115.3, 92.6(d, J = 8.2 Hz) 57.5, 27.5; HRMS (EI-TOF) calcd for $C_{15}H_{14}FIN_2O$ (M^+): 384.0135, found:384.0137.

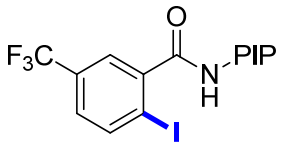
4-Bromo-2-iodo-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide (3h)



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 – 8.43 (m, 1H), 8.29 (brs, 1H), 8.02 (d, J = 1.6 Hz, 1H), 7.74 (td, J = 8.0, 2.0 Hz, 1H), 7.51 (dd, J = 8.0, 1.6 Hz, 1H), 7.45 (d, J = 8.0 Hz, 1H), 7.32 (d, J = 8.0 Hz, 1H), 7.20 (ddd, J = 7.6, 4.8, 0.8 Hz, 1H), 1.89 (s, 6H);^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 164.0, 147.6, 142.4, 141.9, 137.5, 131.4, 129.2, 123.8,

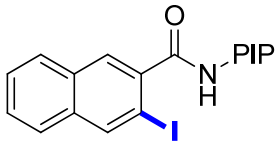
122.2, 119.7, 93.4, 57.5, 27.5; HRMS (EI-TOF) calcd for $C_{15}H_{14}BrIN_2O$ (M^+): 443.9334, found:443.9331.

2-Iodo-*N*-(2-(pyridin-2-yl)propan-2-yl)-5-(trifluoromethyl)benzamide (3m)



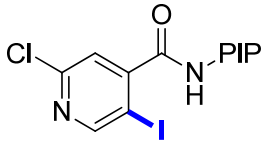
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (d, *J* = 4.4 Hz, 1H), 8.39 (brs, 1H), 8.01 (d, *J* = 8.4 Hz, 1H), 7.76 (td, *J* = 8.0, 1.6 Hz, 1H), 7.68 (d, *J* = 1.6 Hz, 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.33 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.22 (dd, *J* = 6.8, 4.8 Hz, 1H), 1.93 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 163.9, 147.6, 144.4, 140.7, 137.5, 131.1, 130.8, 127.2(d, *J* = 3.5 Hz), 124.9 (d, *J* = 3.7 Hz), 122.3, 119.7, 97.3, 57.6, 27.5;HRMS (EI-TOF) calcd for $C_{16}H_{14}F_3IN_2O$(M^+): 434.0103,found:434.0103.

3-Iodo-*N*-(2-(pyridin-2-yl)propan-2-yl)-2-naphthamide (3n)



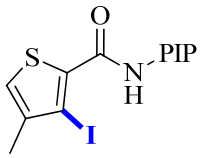
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (d, *J* = 4.0 Hz, 1H), 8.39 (s, 1H), 8.31 (brs, 1H), 7.93 (s, 1H), 7.87 – 7.79 (m, 1H), 7.76 – 7.72(m, 2H), 7.57 – 7.45 (m, 3H), 7.24 – 7.15 (m, 1H), 1.96 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.7, 164.3, 147.7, 140.0, 139.5, 137.4, 134.9, 132.2, 128.3, 127.7, 127.2, 126.8, 122.1, 119.7, 89.5, 57.5, 27.6; HRMS (EI-TOF) calcd for $C_{19}H_{17}IN_2O$(M^+): 416.0386, found: 416.0385.

2-Chloro-5-iodo-*N*-(2-(pyridin-2-yl)propan-2-yl)isonicotinamide (3u)



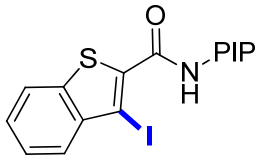
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (s, 1H), 8.58 (brs, 1H), 8.48 (d, *J* = 4.8 Hz, 1H), 7.77 (td, *J* = 8.0, 1.6 Hz, 1H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.41 (s, 1H), 7.26 – 7.21 (m, 1H), 1.90 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.0, 163.4, 158.0, 152.4, 151.9, 147.5, 137.7, 123.5, 122.5, 119.65, 89.5, 57.7, 27.4; HRMS (EI-TOF) calcd for $C_{14}H_{13}ClIN_3O$(M^+): 400.9792,found:400.9788.

4-Iodo-5-methyl-*N*-(2-(pyridin-2-yl)propan-2-yl)thiophene-3-carboxamide (3v)



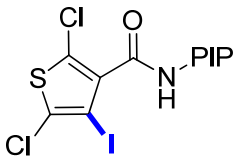
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (brs, 1H), 8.57 – 8.51 (m, 1H), 7.72 (td, *J* =8.0, 1.6 Hz, 1H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.20 (ddd, *J* = 7.2, 4.8, 0.8 Hz, 1H), 7.16 (d, *J* = 0.8 Hz, 1H), 2.29 (d, *J* = 0.4 Hz, 3H), 1.87 (s, 6H);^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4, 160.6, 147.9, 142.1, 139.6, 137.2, 123.6, 122.1, 119.6, 85.9, 58.0, 27.8, 19.8; HRMS (EI-TOF) calcd for $C_{14}H_{13}IN_2OS(M^+)$: 385.9950, found:385.9947.

3-Iodo-*N*-(2-(pyridin-2-yl)propan-2-yl)benzo[b]thiophene-2-carboxamide (3w)



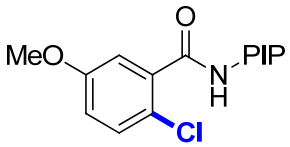
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.05 (brs, 1H), 8.56 (m, 1H), 7.89 – 7.85 (m, 1H), 7.83 – 7.78 (m, 1H), 7.75 (ddd, *J* = 8.0, 7.6, 1.8 Hz, 1H), 7.51 – 7.42 (m, 3H), 7.22 (ddd, *J* = 7.6, 4.8, 0.8 Hz, 1H), 1.92 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 160.9, 147.8, 141.9, 139.2, 138.9, 137.4, 127.4, 127.1 125.8, 122.6, 122.2, 119.6, 80.1, 58.2, 27.7; HRMS (EI-TOF) calcd for $C_{17}H_{15}IN_2OS(M^+)$: 421.9950, found:421.9948.

2,5-Dichloro-4-iodo-*N*-(2-(pyridin-2-yl)propan-2-yl)thiophene-3-carboxamide (3p)



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 – 8.47 (m, 1H), 8.43 (brs, 1H), 7.78 – 7.71 (m, 1H), 7.46 (d, *J* = 8.0 Hz, 1H), 7.24 – 7.18 (m, 1H), 1.88 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.8, 160.8, 147.6, 139.4, 137.5, 129.1, 125.9, 122.3, 119.6, 81.9, 57.6, 27.6; HRMS (EI-TOF) calcd for $C_{13}H_{11}Cl_2IN_2OS(M^+)$: 439.9014,found:439.9012.

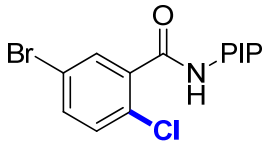
2-Chloro-5-methoxy-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide (4e)



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, *J* = 4.8 Hz, 1H), 8.39 (brs, 1H), 7.75 – 7.69 (m,

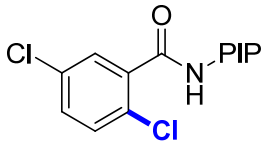
1H), 7.46 (d, *J* = 8.0 Hz, 1H), 7.28 (d, *J* = 8.8, 1H), 7.21– 7.16 (m, 2H), 6.88 (dd, *J* = 8.8, 3.2 Hz, 1H), 3.81 (s, 3H), 1.89 (s, 6H).^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7, 164.37, 158.57, 147.87, 137.5, 137.3, 131.1, 122.1, 122.1, 119.6, 117.5, 114.5, 57.7, 55.8, 27.7; HRMS (EI-TOF) calcd for $C_{16}H_{17}ClN_2O_2$ (M^+): 304.0979, found:304.0976.

5-Bromo-2-chloro-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide (4f)



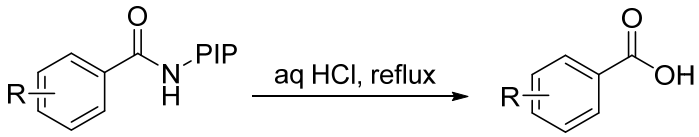
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 – 8.44 (m, 2H), 7.77 – 7.71 (m, 2H), 7.46 (m, 1H), 7.44 (d, *J* = 2.4 Hz 1H), 7.27 (d, *J* = 8.4 Hz, 1H), 7.20 (ddd, *J* = 7.2, 4.8, 0.8 Hz, 1H), 1.88 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4, 163.9, 147.7, 138.6, 137.4, 133.7 132.5, 131.7, 129.9, 122.2, 120.7, 119.6, 57.7, 27.5; HRMS (EI-TOF) calcd for $C_{15}H_{14}BrClN_2O$ (M^+): 351.9978, found: 351.9975.

2,5-Dichloro-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide (4o)



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, *J* = 4.0 Hz, 2H), 7.77 – 7.71 (m, 1H), 7.60 (d, *J* = 2.4 Hz, 1H), 7.45 (d, *J* = 8.4 Hz, 1H), 7.34 (d, *J* = 8.8 Hz, 1H), 7.32 – 7.28 (m, 1H), 7.23 – 7.17 (m, 1H), 1.88 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6, 164.06, 147.76, 138.36, 137.46, 133.16, 131.5, 130.8, 129.7, 129.3, 122.2, 119.6, 57.7, 27.6; HRMS (EI-TOF) calcd for $C_{15}H_{14}Cl_2N_2O$ (M^+): 308.0483, found:308.0486.

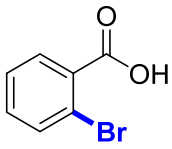
2.5 Removal of the Directing Group



5a, R = 2-Br, 89% yield
5b, R = 2-I, 82% yield

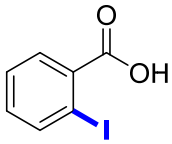
To a 50 mL Schlenk tube was added 2c (0.2 mmol) (or 3c) and conc. HCl (3 mL). The mixture was then heated at 145 °C for 48 hours. After cooling down to room temperature, aqueous NaOH (1 M) was added and the aqueous phase was extracted with DCM (10 mL x 2). Then, conc. HCl was added slowly into the aqueous phase (pH = 2) and the aqueous phase was as extracted with DCM (10 mL x 3). The combined organic phase was dried with anhydrous sodium sulfate. After concentration, the desired product **5** was obtained as a white solid.

2-Bromobenzoic acid 5a



^{1}H NMR (400 MHz, $CDCl_3$) δ 11.23 (brs, 1H), 8.05 – 7.99 (m, 1H), 7.72 (dd, *J* = 7.2, 1.6 Hz, 1H), 7.41 (m, 2H).

2-Iodobenzoic acid 5b



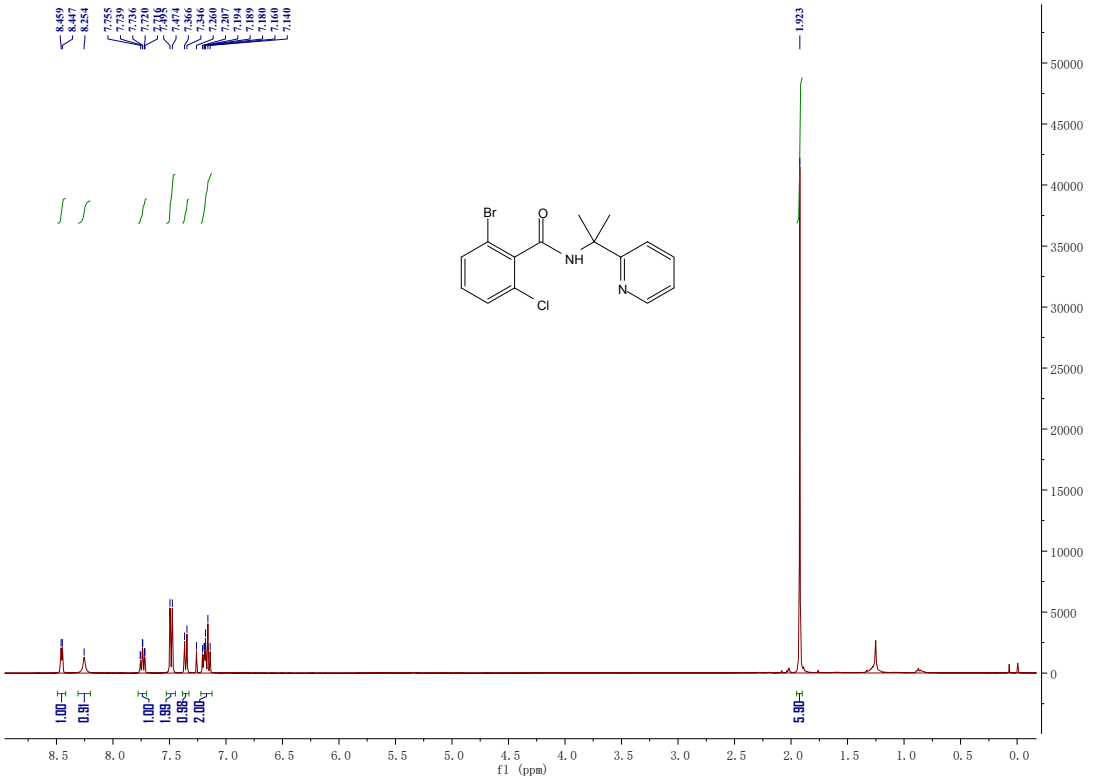
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (dd, *J* = 8.0, 1.2 Hz, 1H), 8.03 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.45 (td, *J* = 7.6, 1.2 Hz, 1H), 7.21 (td, *J* = 7.6, 1.6 Hz, 1H).

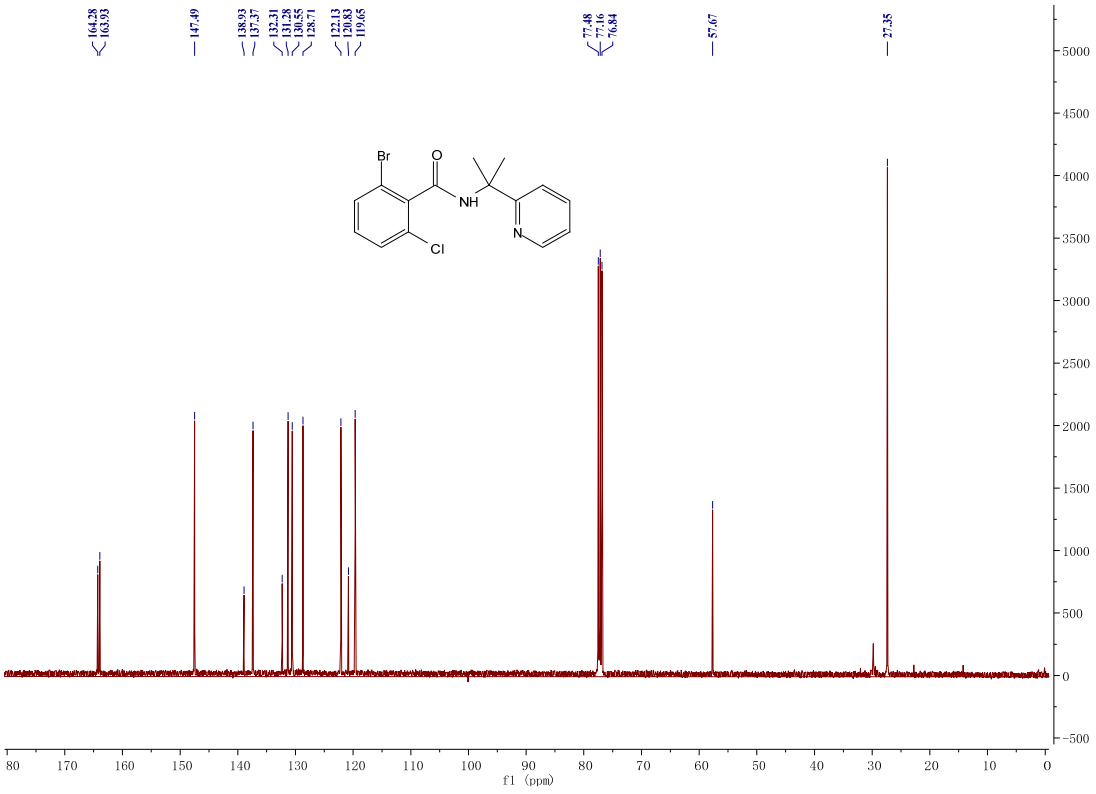
3. References:

1. K. M. Yager, E. A. Plaza, D. V. Kumar and I. C. Kim, US Pat., 20080207573 A1.
2. F-J. Chen, S. Zhao, F. Hu, K. Chen, Q. Zhang, S-Q. Zhang and B-F. Shi, Chem. Sci., 2013, **4**, 4187
3. B. Li, B. Liu and B-F.Shi, Chem. Commun., 2015, **51**, 5093.

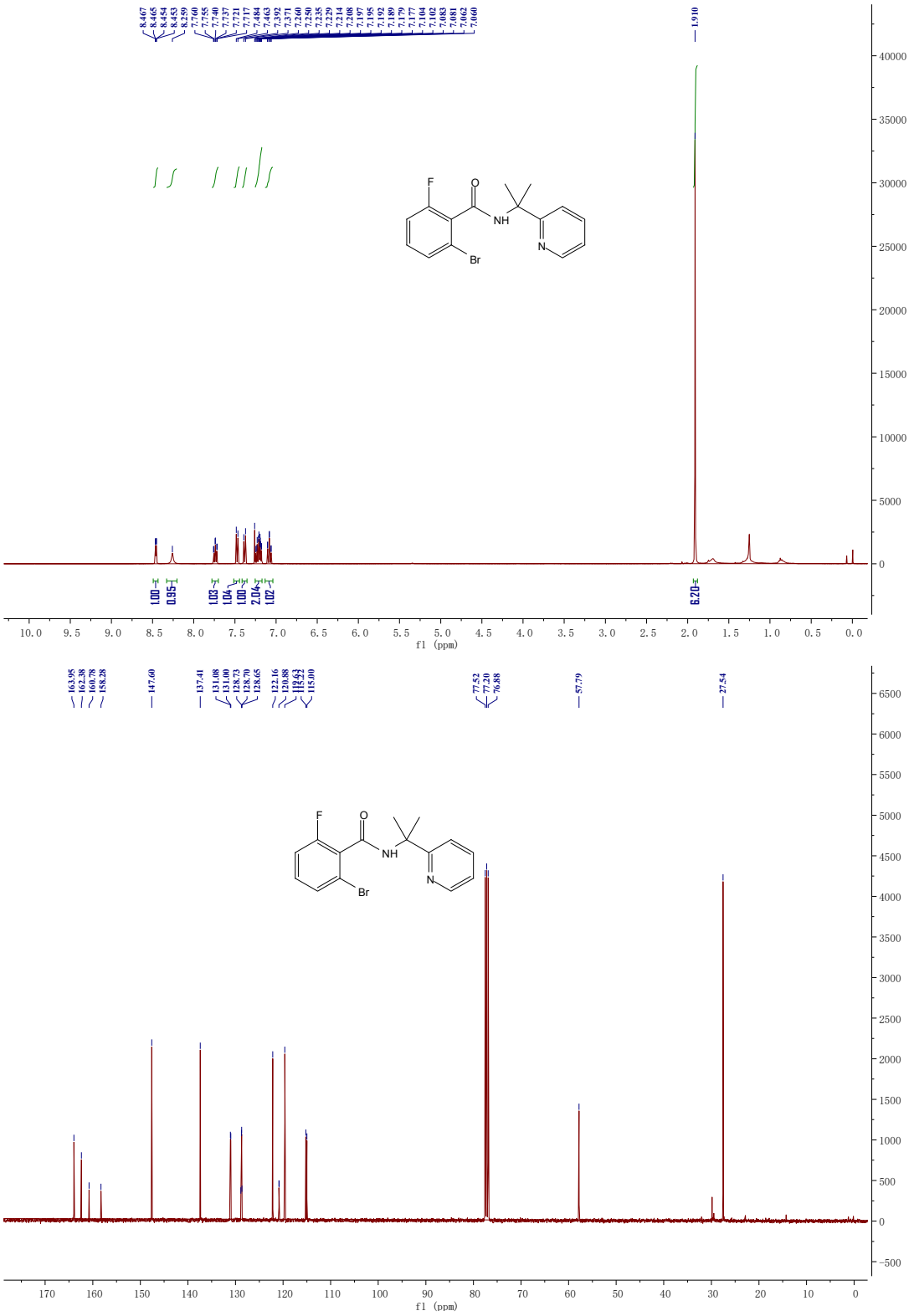
4. NMR Spectra

2a





2b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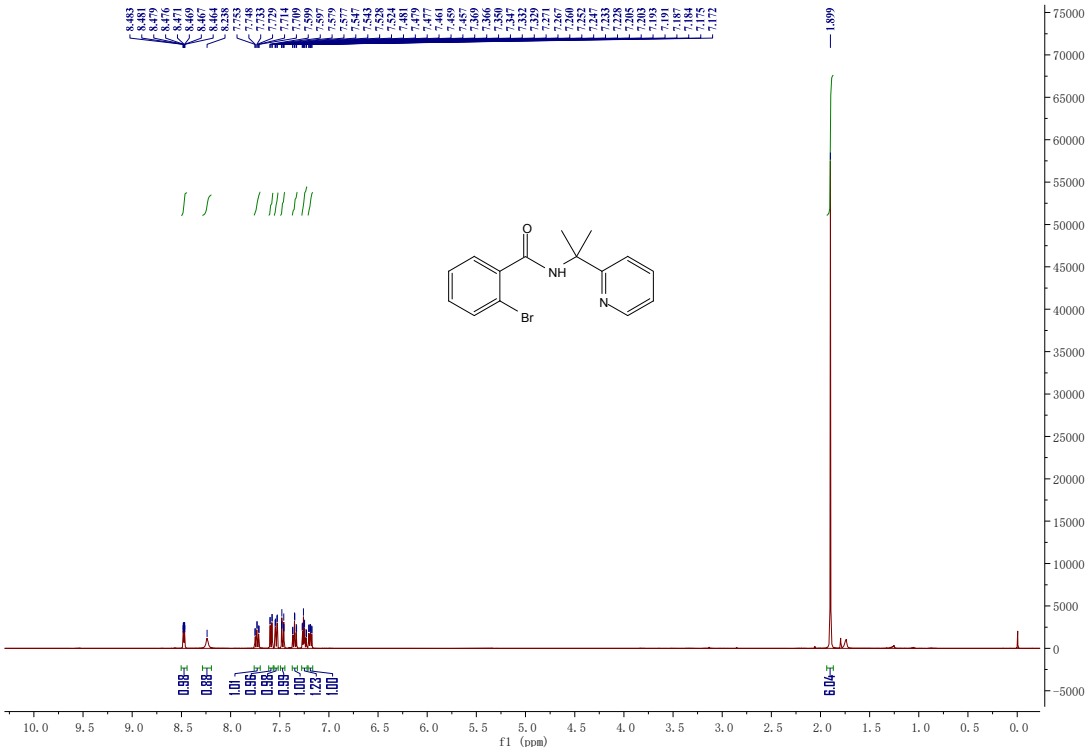
8.465
8.454
8.453
8.259
7.760
7.755
7.740
7.737
7.731
7.717
7.484
7.463
7.392
7.371
7.260
7.250
7.235
7.230
7.214
7.208
7.197
7.195
7.192
7.189
7.179
7.177
7.104
7.102
7.083
7.081
7.062
7.060
1.910
F
O
NH
N
Br
1.00
0.95
1.03
1.04
1.00
2.04
1.02
6.20
f1 (ppm)
163.95
162.38
160.78
158.28
147.60
137.41
131.08
131.00
128.73
128.70
128.65
122.16
120.88
115.43
115.00
77.52
77.20
76.88
57.79
27.54
f1 (ppm)

2c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8.481
8.479
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8.471
8.469
8.467
8.464
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7.753
7.748
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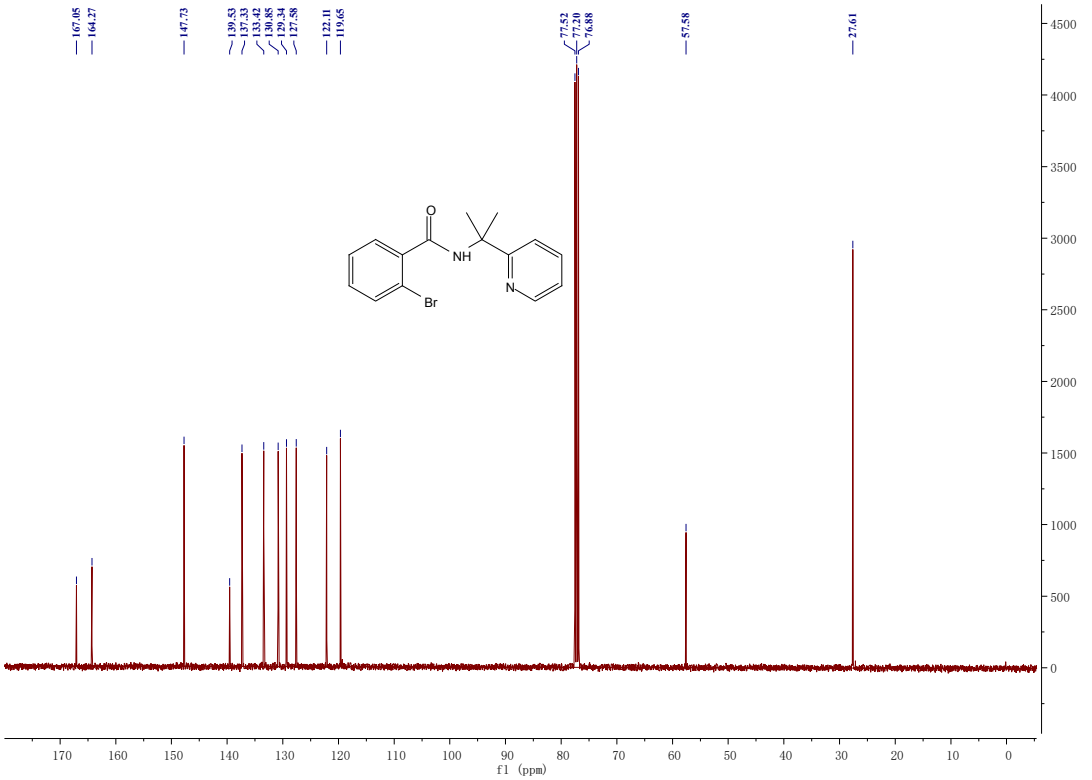
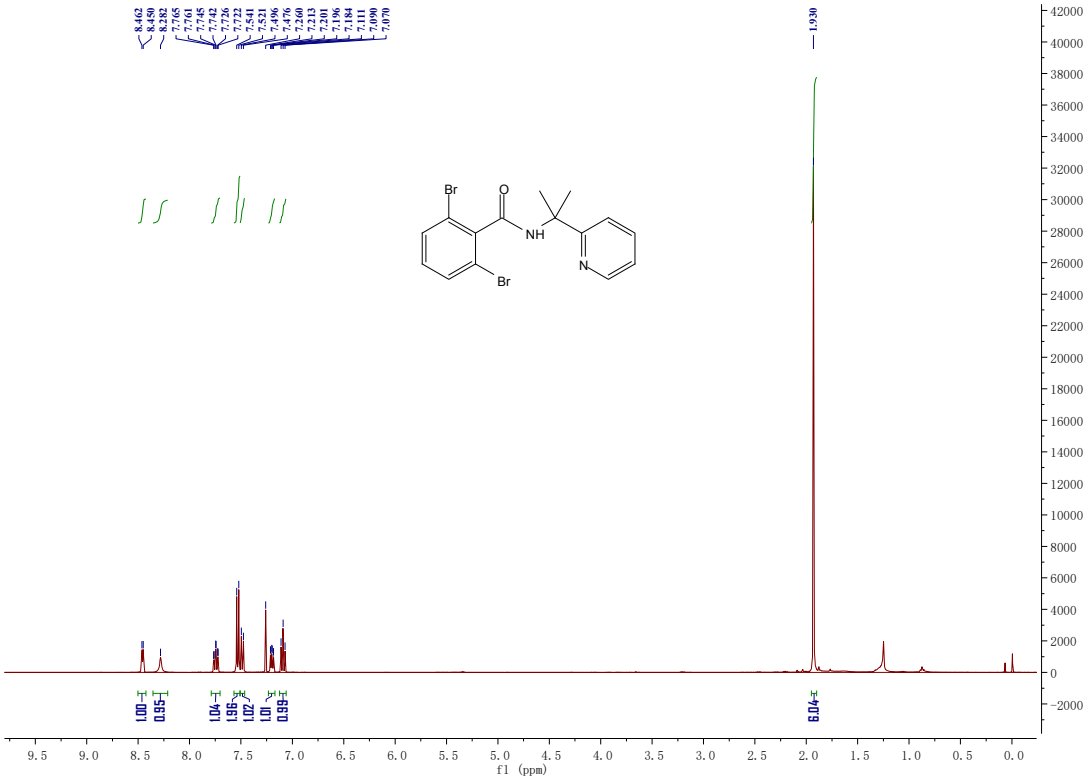
7.729
7.714
7.709
7.599
7.597
7.579
7.577
7.547
7.543
7.538
7.534
7.481
7.479
7.477
7.461
7.459
7.457
7.369
7.366
7.350
7.347
7.332
7.329
7.271
7.267
7.260
7.252
7.247
7.233
7.228
7.205
7.203
7.193
7.191
7.187
7.184
7.175
7.172
1.899
O
NH
N
Br
0.95
0.89
1.01
0.96
0.95
0.95
1.00
1.23
1.00
6.04
f1 (ppm)


167.05
164.27
147.73
139.53
137.33
133.42
130.85
130.34
127.58
122.11
119.65
77.52
77.20
76.88
57.58
27.61
O
NH
N
Br
f1 (ppm)

2c'


8.462
8.450
8.282
7.765
7.761
7.745
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7.726
7.722
7.541
7.521
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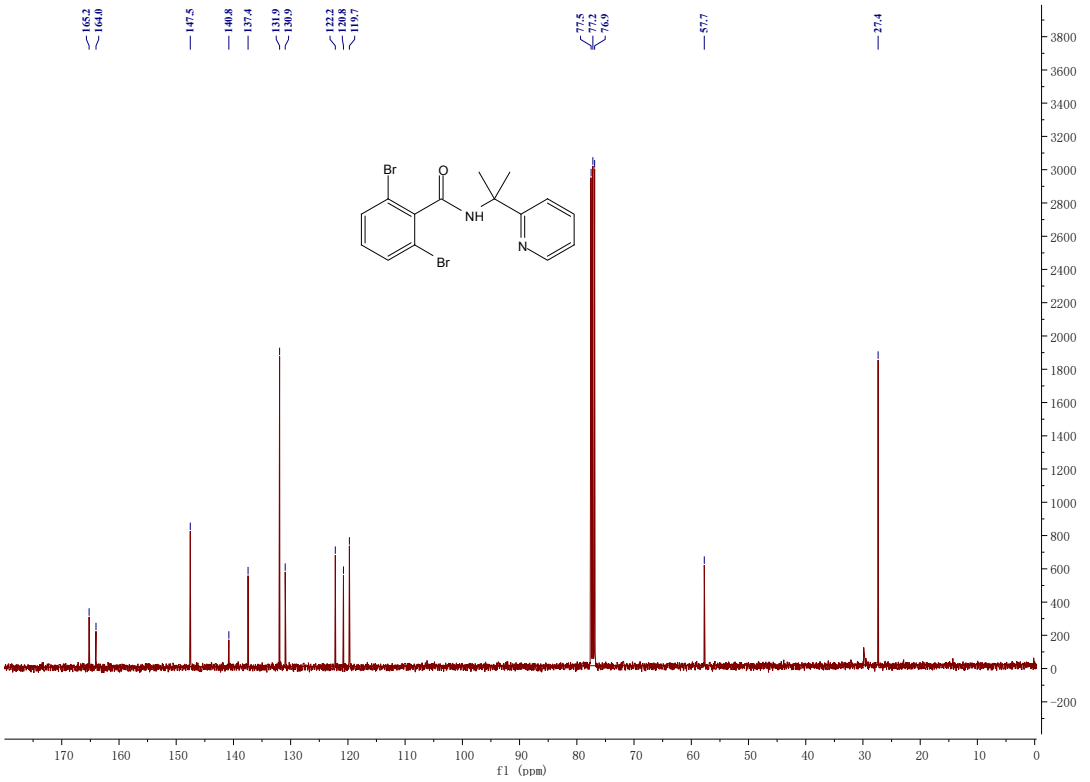
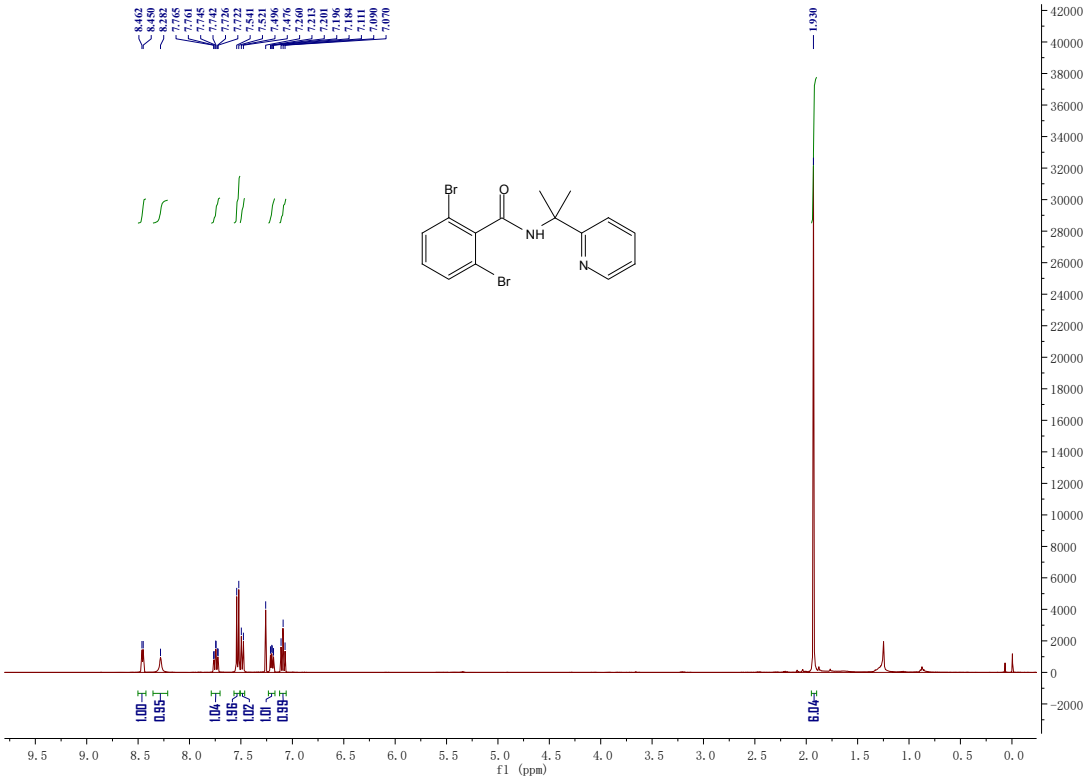
7.476
7.260
7.213
7.201
7.196
7.184
7.111
7.090
7.070
1.930
Br
O
NH
N
Br
1.00
0.95
1.04
1.36
1.02
1.01
0.99
6.04
f1 (ppm)


165.2
164.0
147.5
140.8
137.4
131.9
130.9
122.2
120.8
119.7
77.5
77.2
76.9
57.7
27.4
Br
O
NH
N
Br
f1 (ppm)

2d


8.462
8.459
8.282
7.765
7.761
7.745
7.742
7.726
7.722
7.541
7.521
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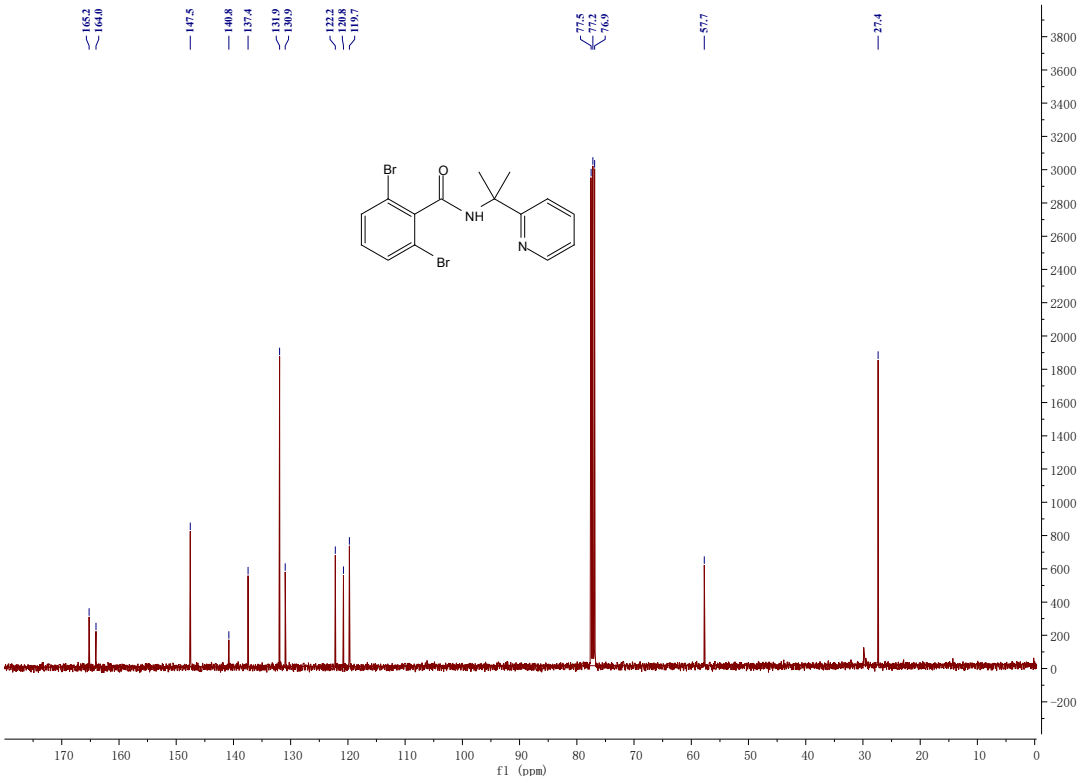
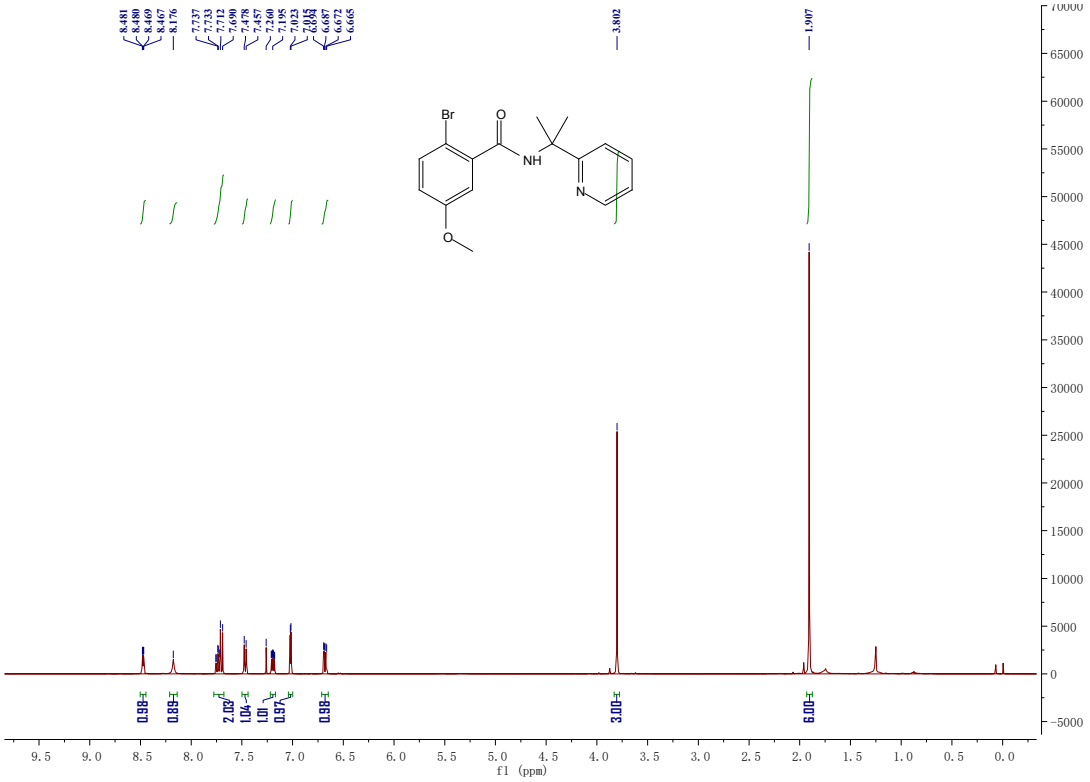
7.476
7.260
7.213
7.201
7.196
7.184
7.111
7.090
7.070
1.930
Br
O
NH
N
Br
1.00
0.95
1.04
1.36
1.02
1.01
0.99
6.04
f1 (ppm)


165.2
164.0
147.5
140.8
137.4
131.9
130.9
122.2
120.8
119.7
77.5
77.2
76.9
57.7
27.4
Br
O
NH
N
Br
f1 (ppm)

2e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7.478
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7.023
7.015
6.694
6.687
6.672
6.665
3.802
1.907
Br
O
NH
N
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0.89
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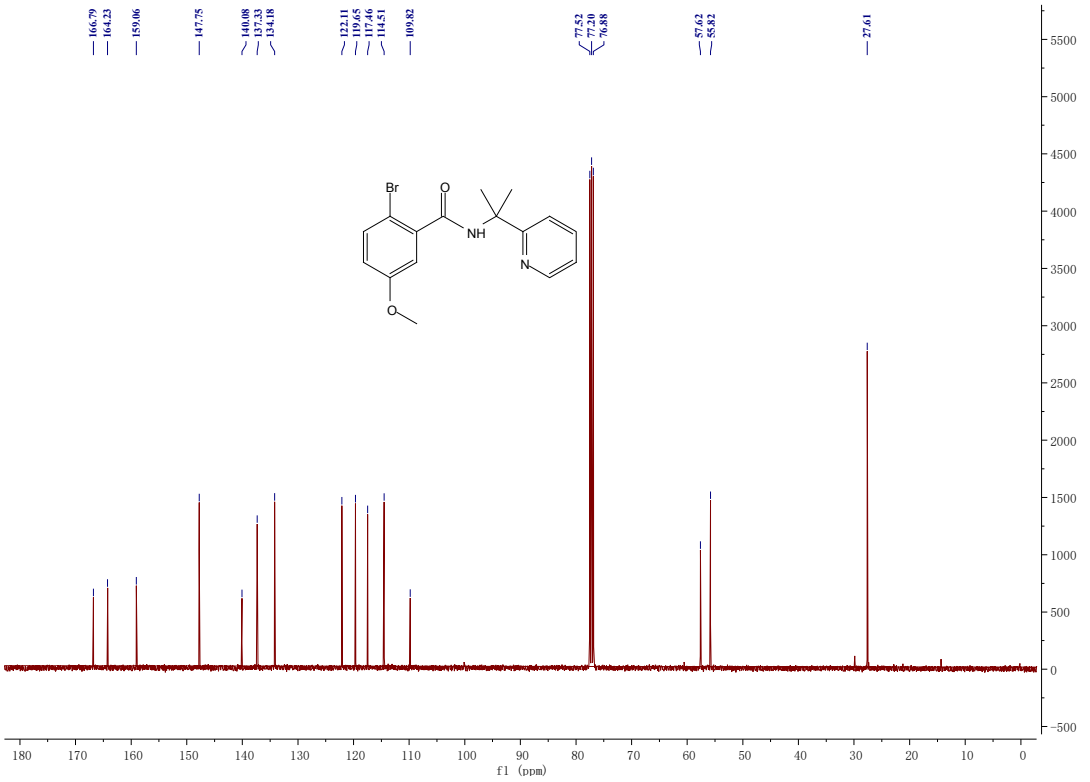
1.04
1.01
0.97
0.98
3.00
6.00
f1 (ppm)


166.79
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122.11
119.65
117.46
114.51
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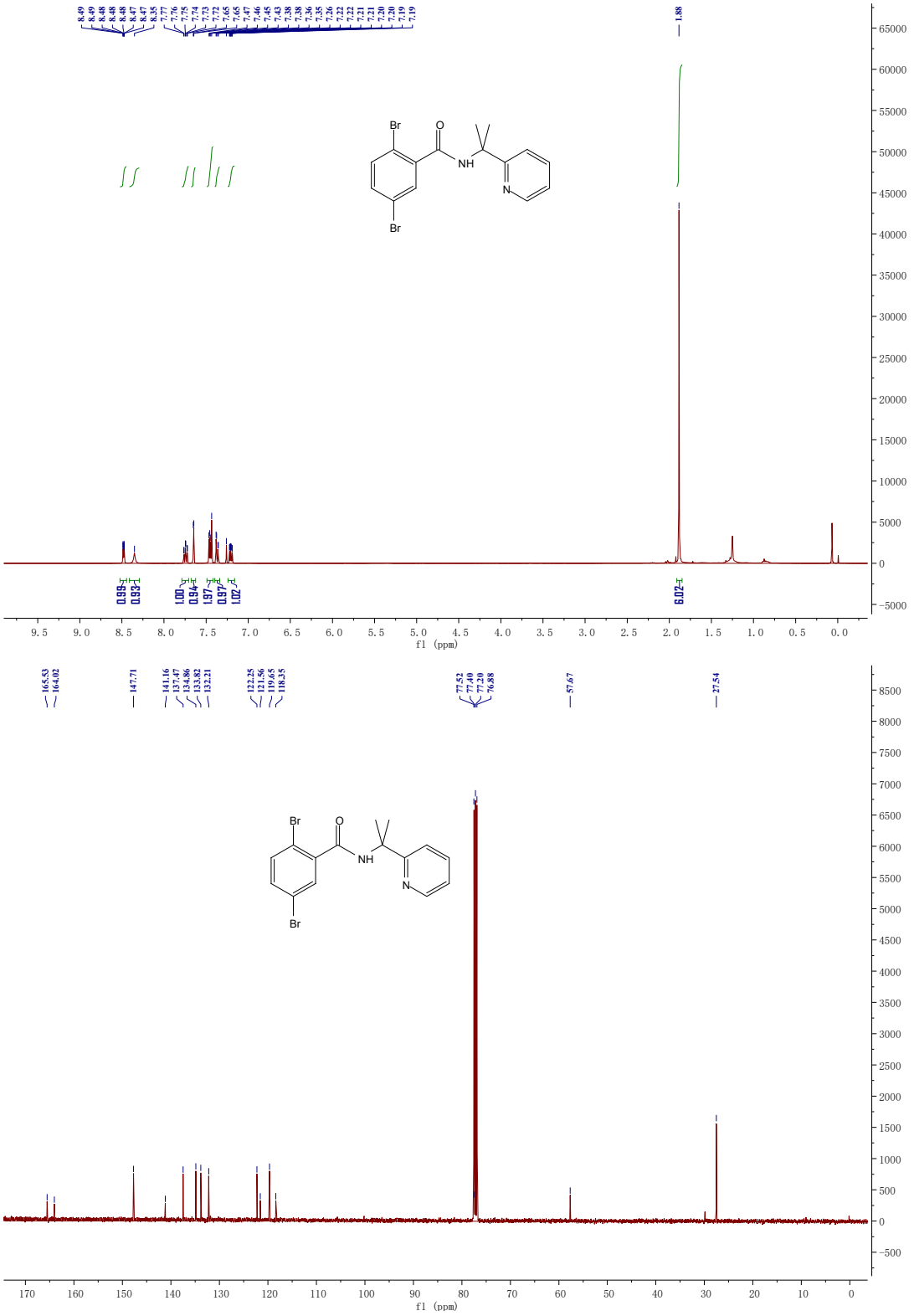
77.20
76.88
57.62
55.82
27.61
Br
O
NH
N
O
f1 (ppm)

2f


8.49
8.48
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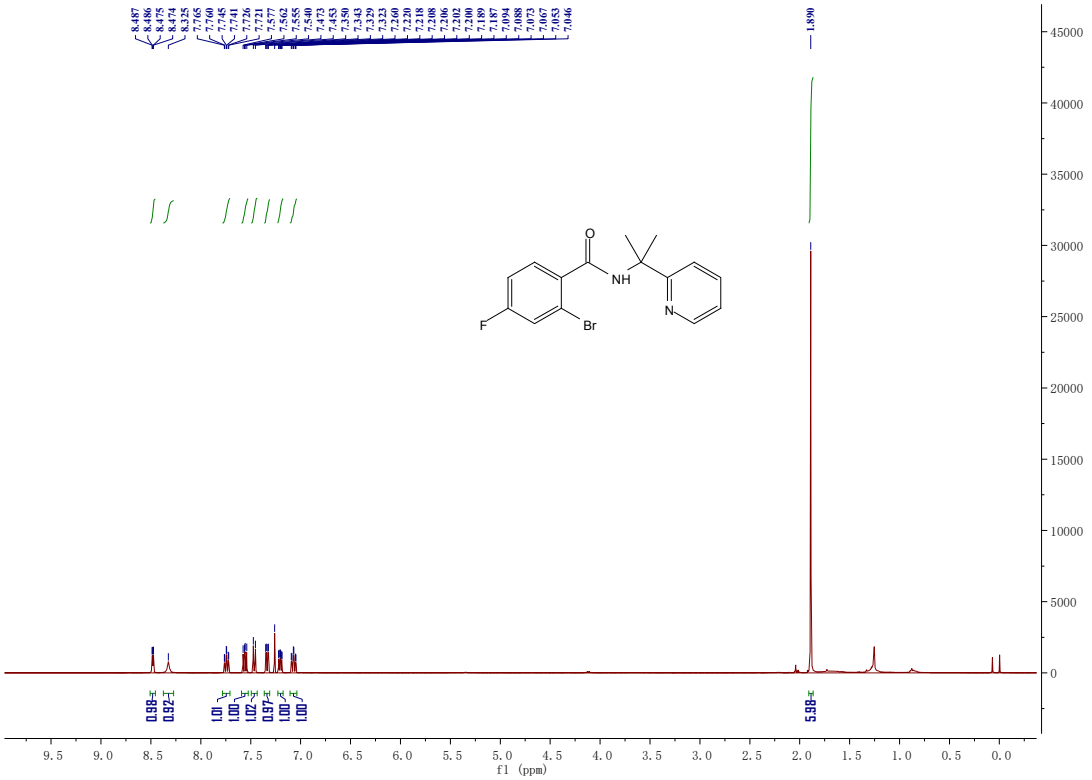
7.76
7.75
7.74
7.73
7.72
7.65
7.47
7.46
7.45
7.43
7.38
7.36
7.35
7.26
7.22
7.21
7.20
7.19
1.88
Br
O
NH
N
Br
0.99
0.93
1.00
0.94
1.97
0.97
1.02
6.02
f1 (ppm)
165.53
164.02
147.71
141.16
137.47
134.86
133.82
132.21
122.25
121.56
119.45
118.25
77.52
77.40
77.20
76.88
57.67
27.54
f1 (ppm)

2g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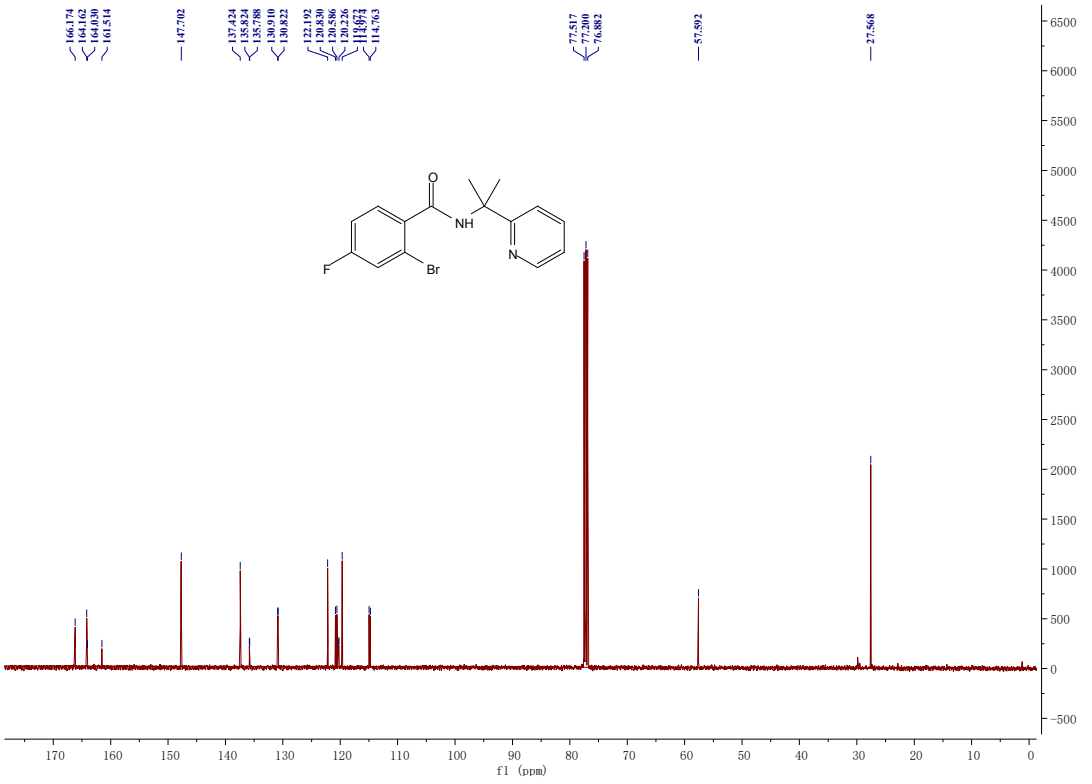
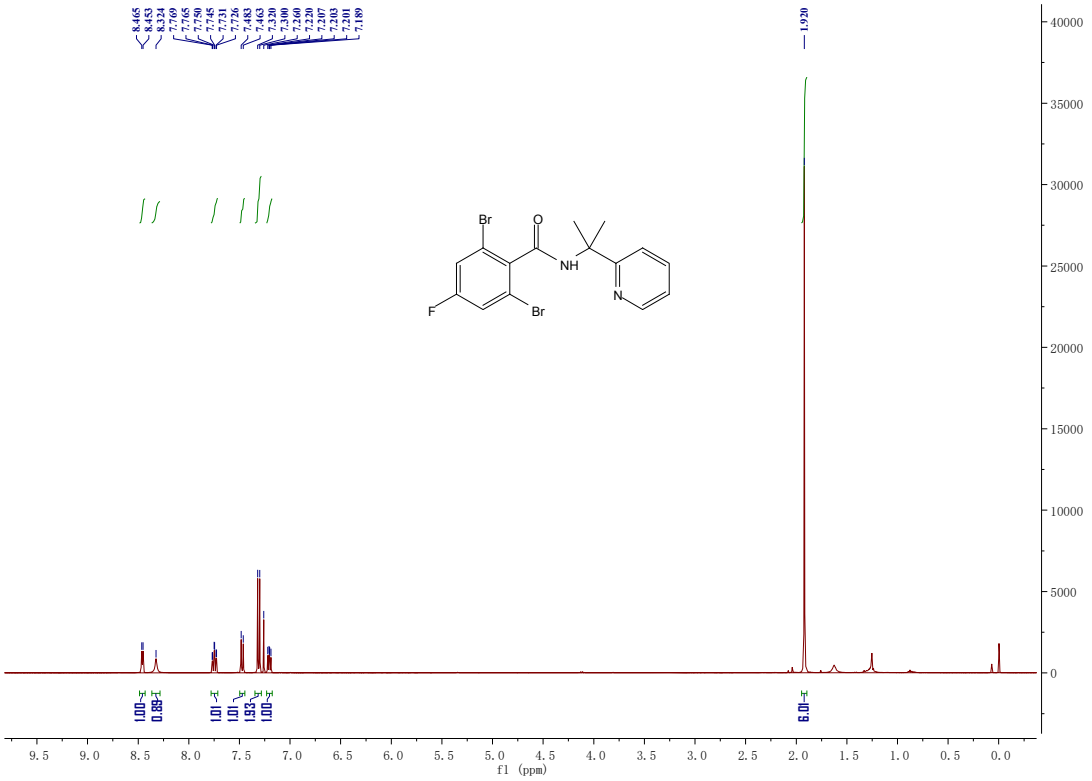
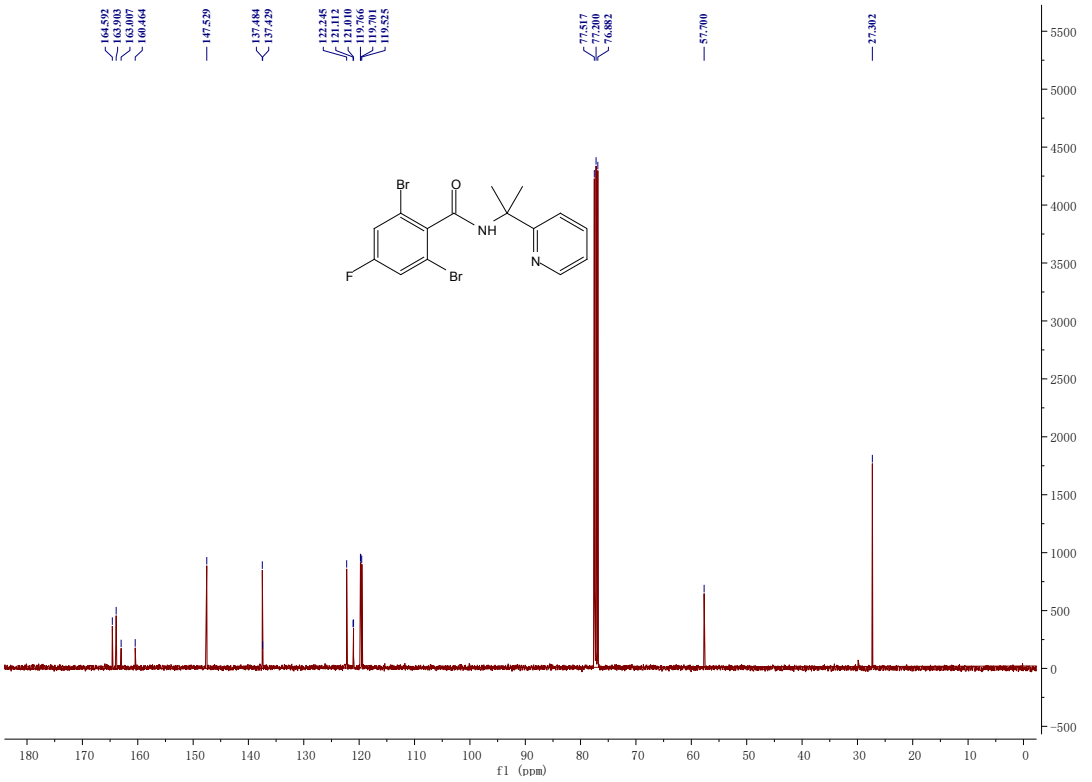
8.486
8.475
8.474
8.325
7.765
7.760
7.745
7.741
7.726
7.721
7.577
7.562
7.555
7.546
7.473
7.453
7.350
7.343
7.329
7.323
7.260
7.230
7.218
7.208
7.206
7.202
7.200
7.189
7.187
7.084
7.073
7.067
7.053
7.046
1.890
O
NH
N
F
Br
0.98
0.92
1.01
1.00
1.02
0.97
1.00
1.00
5.98
f1 (ppm)

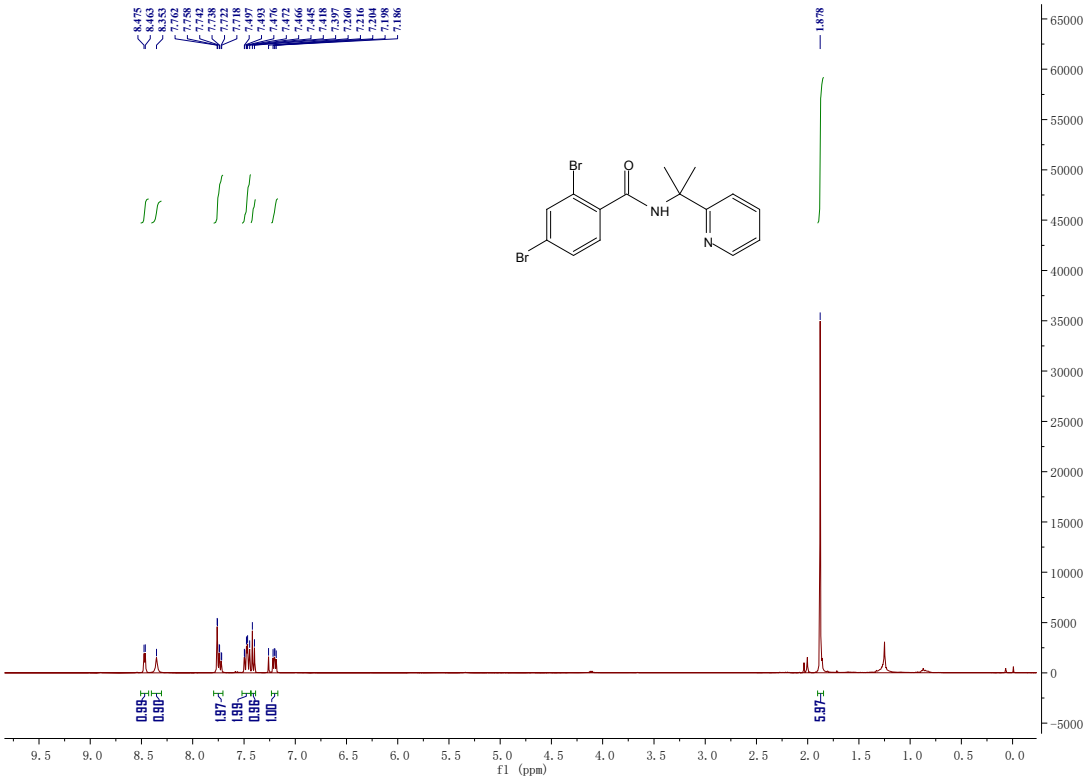

166.174
164.162
164.030
161.514
147.702
137.424
135.824
135.788
130.910
130.822
122.192
120.830
120.586
120.226
114.763
77.517
77.200
76.882
57.592
27.568
O
NH
N
F
Br
f1 (ppm)

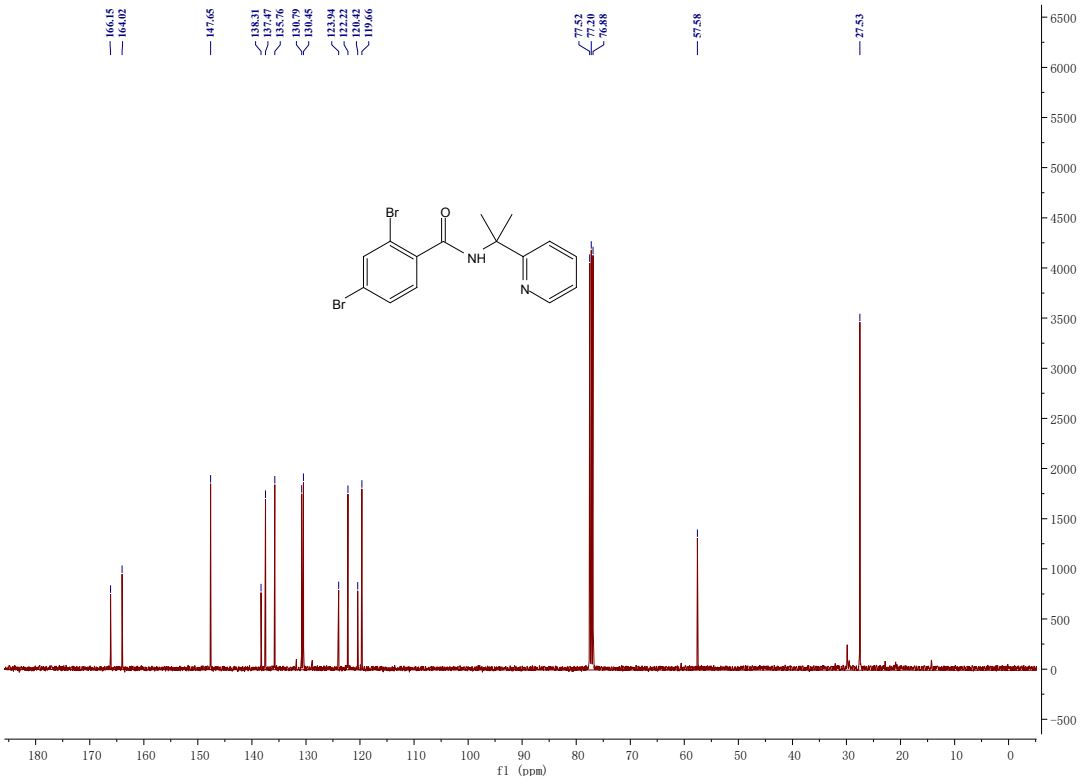
2g'


8.465
8.453
8.324
7.769
7.765
7.750
7.746
7.731
7.726
7.483
7.463
7.320
7.300
7.240
7.220
7.207
7.203
7.201
7.189
1.920
Br
O
NH
N
F
Br
1.00
0.89
1.01
1.01
1.93
1.00
6.01
f1 (ppm)

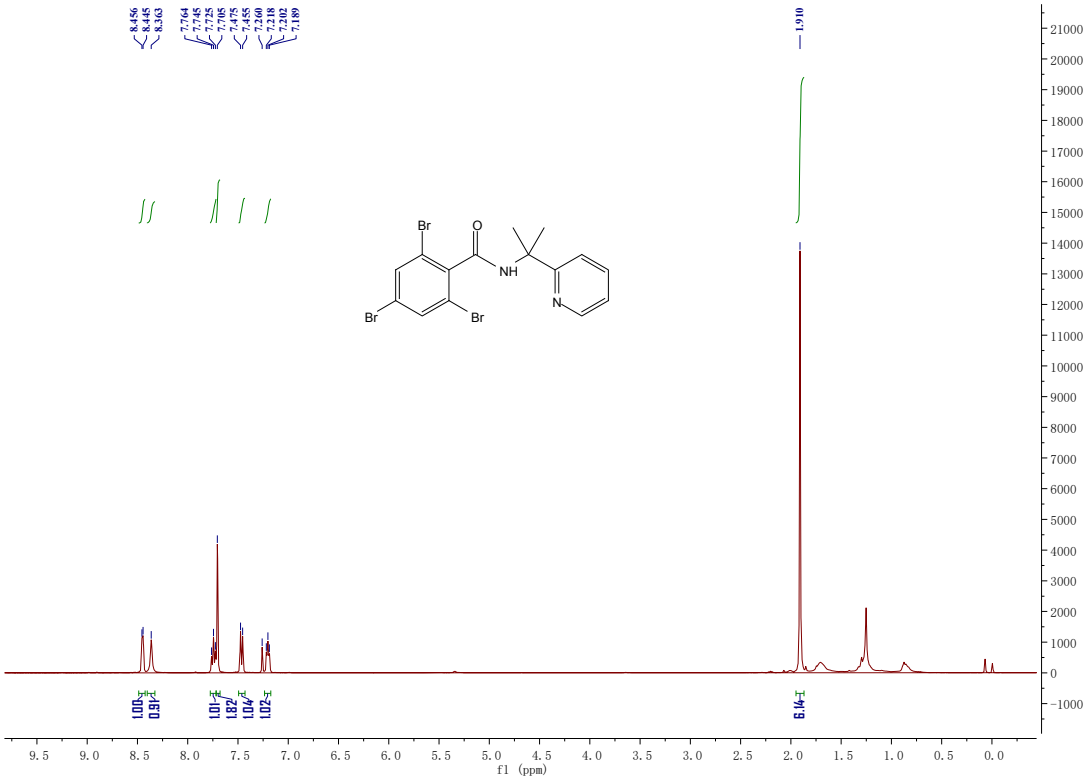

164.592
163.903
163.307
160.464
147.529
137.484
137.429
122.245
121.112
121.010
119.766
119.701
119.525
77.517
77.200
76.882
57.700
27.302
Br
O
NH
N
F
Br
f1 (ppm)

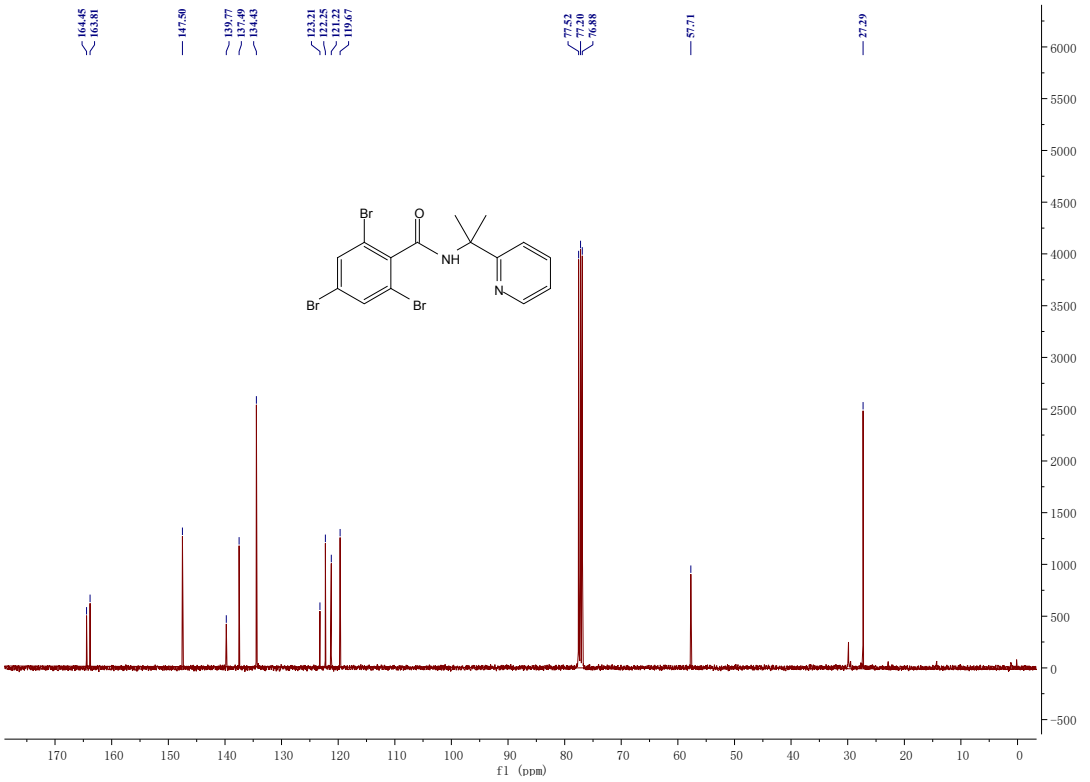
2h


8.475
8.463
8.353
7.762
7.758
7.742
7.738
7.722
7.718
7.497
7.493
7.476
7.472
7.466
7.445
7.441
7.397
7.260
7.216
7.204
7.198
7.186
1.878
Br
O
NH
N
Br
0.95
0.90
1.97
1.99
0.96
1.00
5.97
f1 (ppm)

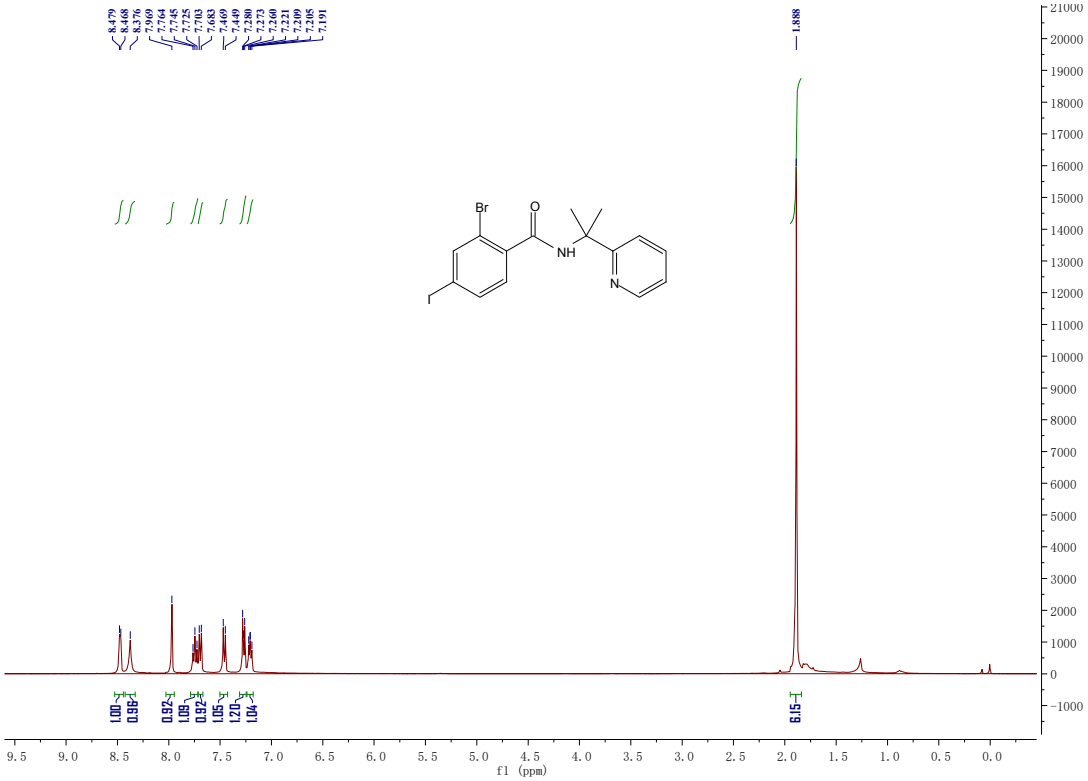

166.15
164.02
147.65
138.31
137.47
135.76
130.79
130.45
123.94
122.22
120.42
119.66
77.52
77.20
76.88
57.58
27.53
Br
O
NH
N
Br
f1 (ppm)

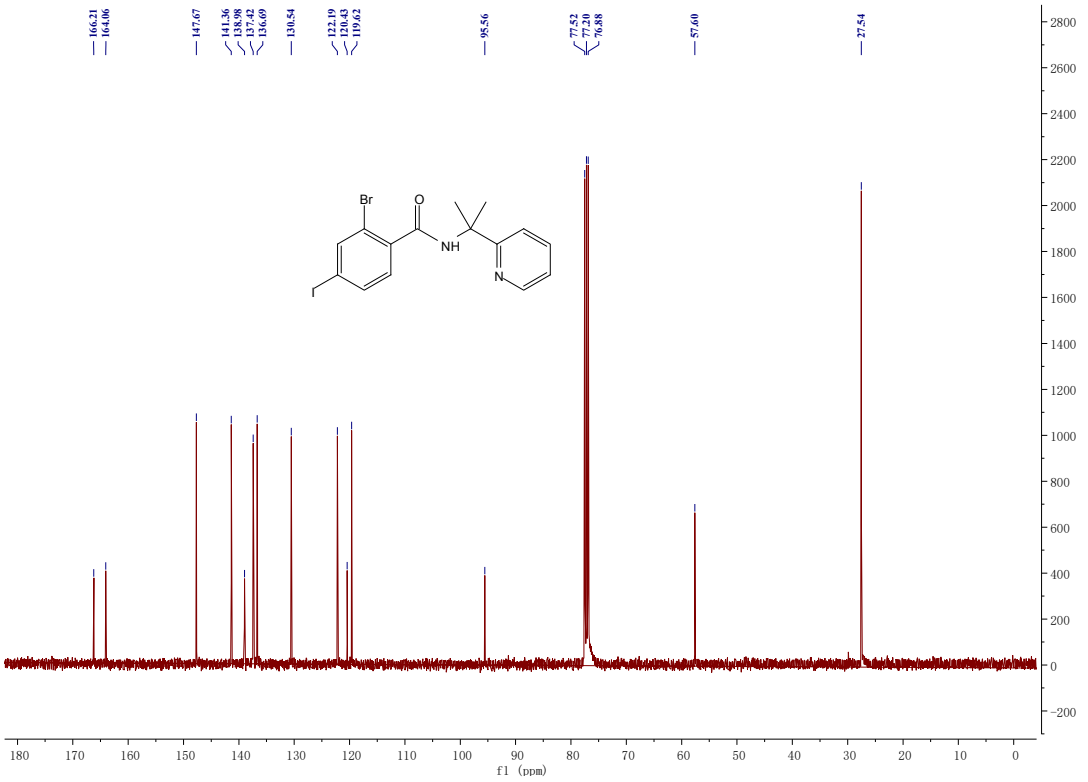
2h'


8.456
8.445
8.363
7.764
7.745
7.725
7.705
7.475
7.455
7.260
7.218
7.202
7.189
1.910
Br
O
NH
N
Br
Br
1.00
0.91
1.01
1.82
1.04
1.02
6.14
f1 (ppm)

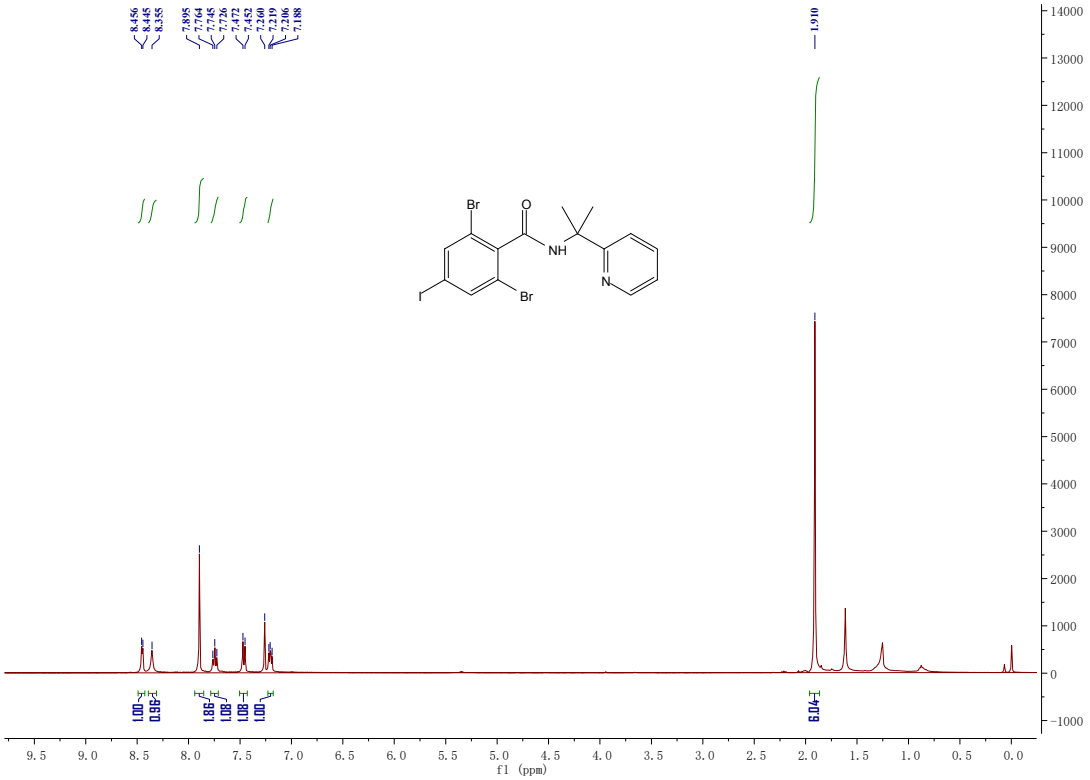

164.45
163.81
147.50
139.77
137.49
134.43
122.31
122.25
121.22
119.67
77.52
77.20
76.88
57.71
27.29
Br
O
NH
N
Br
Br
f1 (ppm)

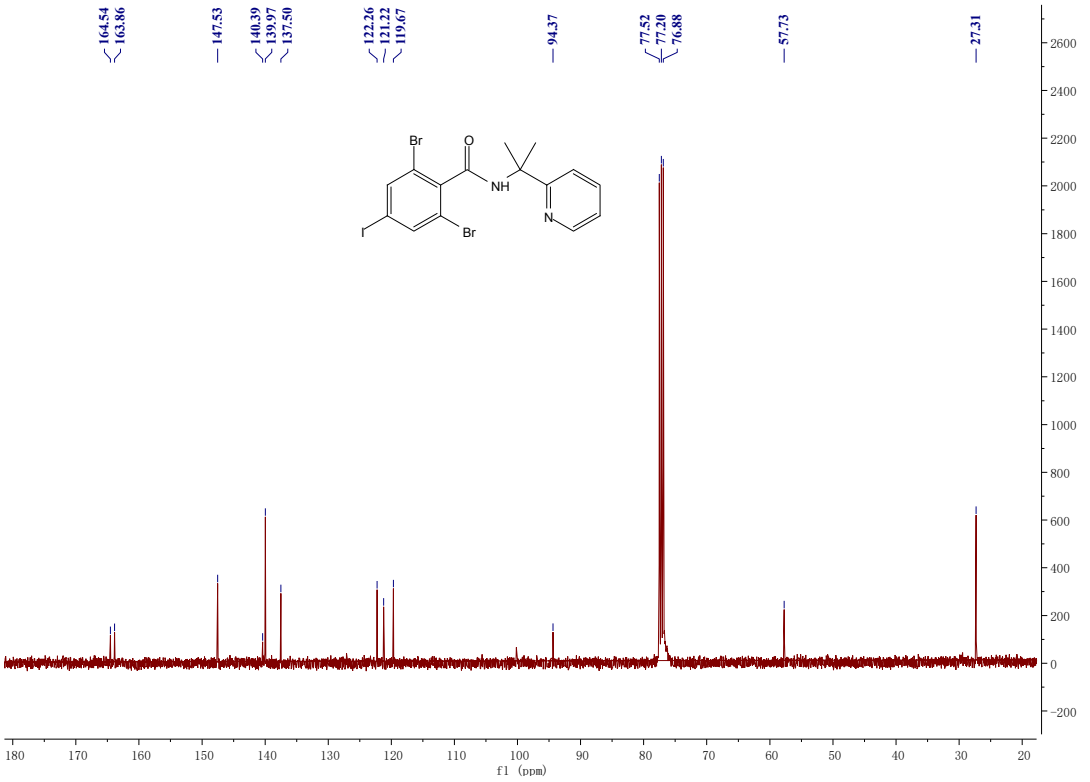
2i


8.479
8.468
8.376
7.969
7.764
7.745
7.725
7.703
7.685
7.460
7.449
7.280
7.273
7.260
7.221
7.209
7.205
7.191
1.888
Br
O
NH
N
I
1.00
0.98
0.82
1.08
0.92
1.05
1.20
1.04
6.15
f1 (ppm)

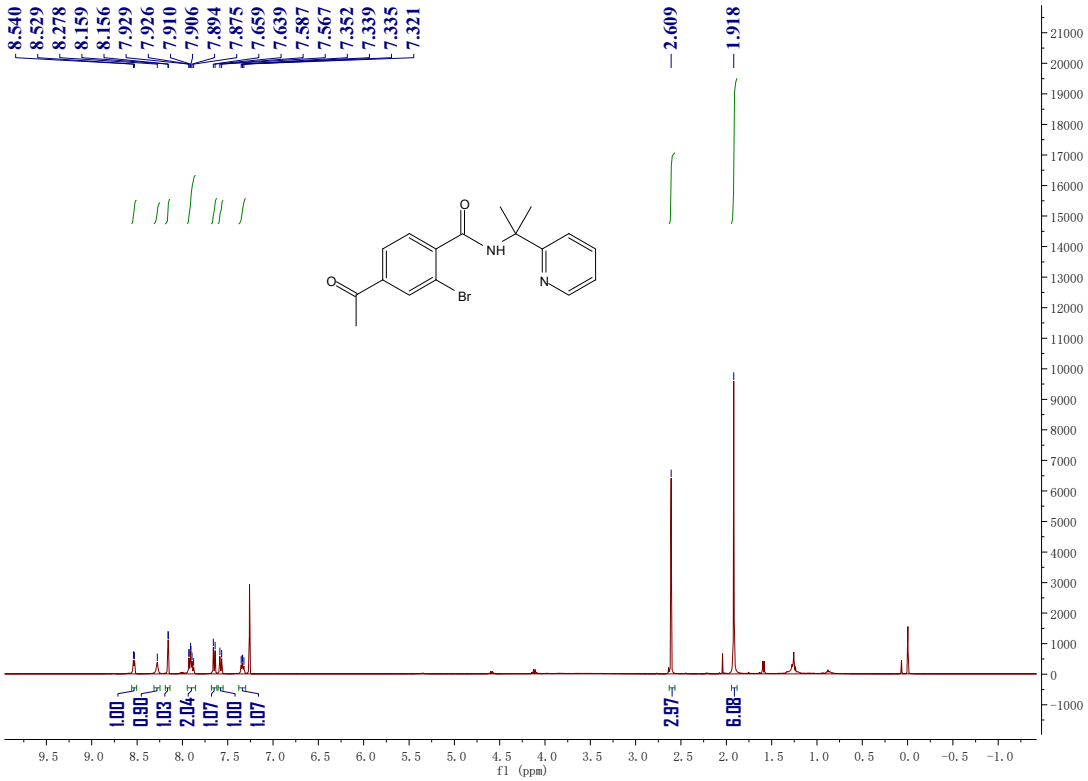

166.21
164.06
147.67
141.36
138.98
137.42
136.69
130.54
122.19
120.43
119.62
95.56
77.52
77.20
76.88
57.60
27.54
Br
O
NH
N
I
f1 (ppm)

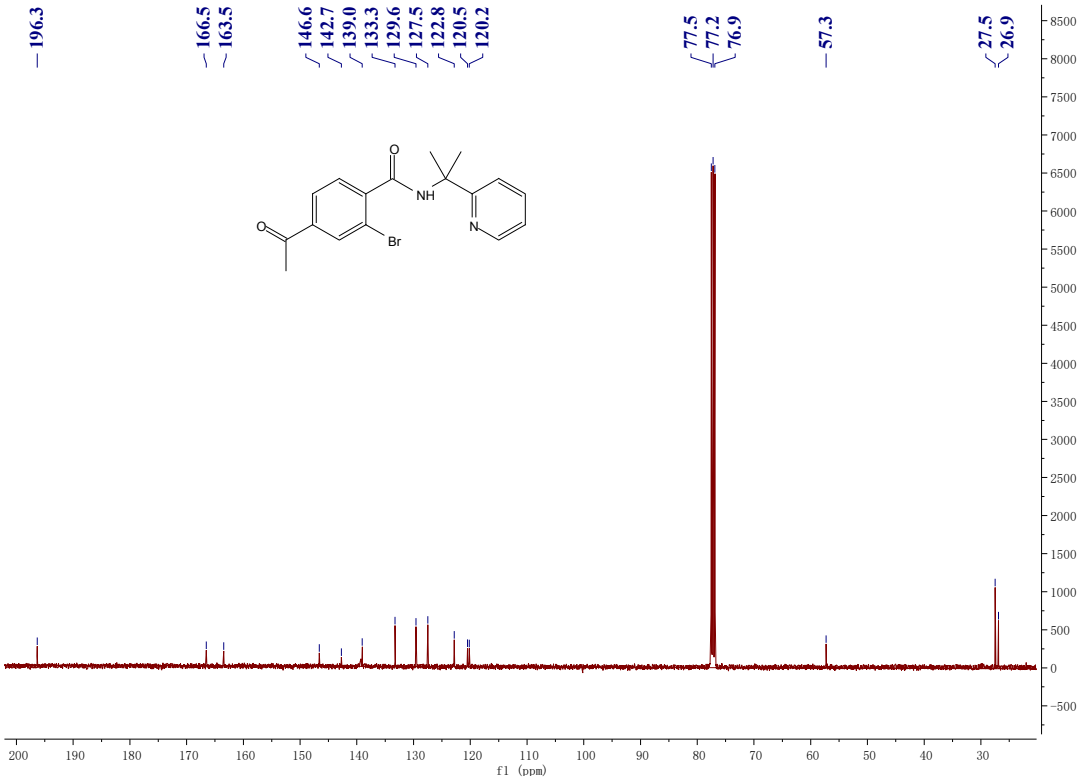
2i'


8.456
8.445
8.355
7.895
7.744
7.745
7.726
7.472
7.452
7.260
7.219
7.206
7.188
1.910
Br
O
NH
N
Br
1.00
0.98
1.86
1.08
1.08
1.00
6.04
f1 (ppm)

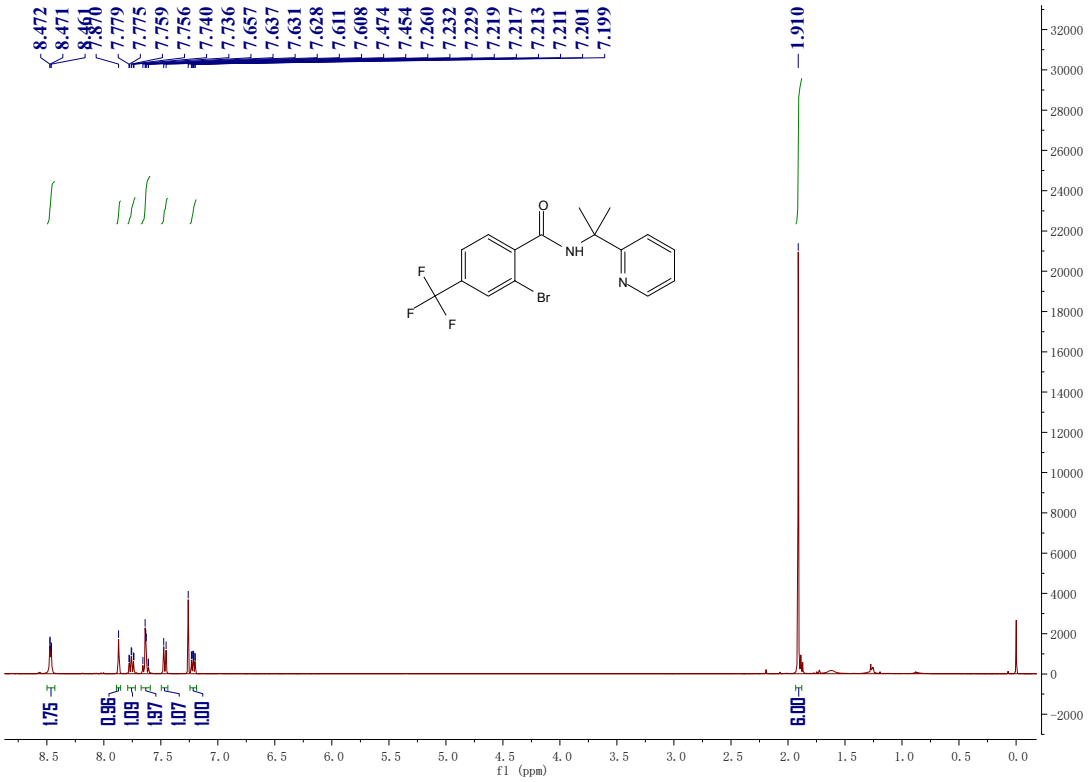

164.54
163.86
147.53
140.39
139.97
137.50
122.26
121.22
119.67
94.37
77.52
77.20
76.88
57.73
27.31
Br
O
NH
N
Br
f1 (ppm)

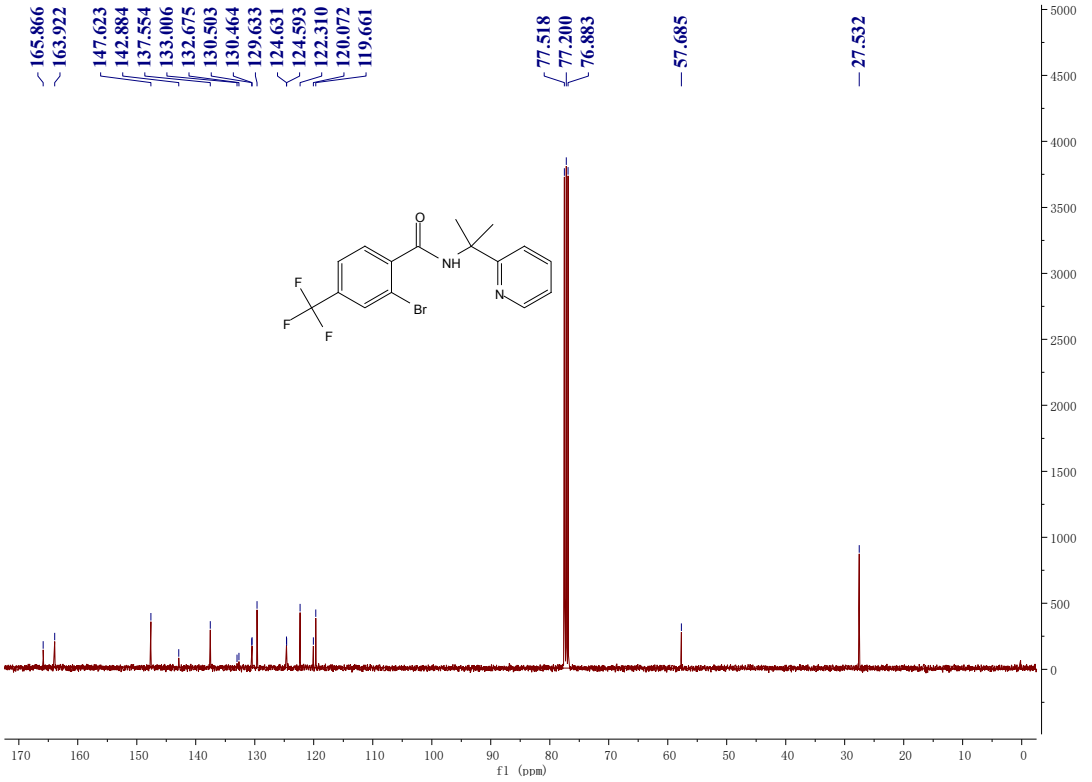
2j


8.540
8.529
8.278
8.159
8.156
7.929
7.926
7.910
7.906
7.894
7.875
7.659
7.639
7.587
7.567
7.352
7.339
7.335
7.321
2.609
1.918
1.00
0.90
1.03
2.04
1.07
1.00
1.07
2.97
6.08
f1 (ppm)

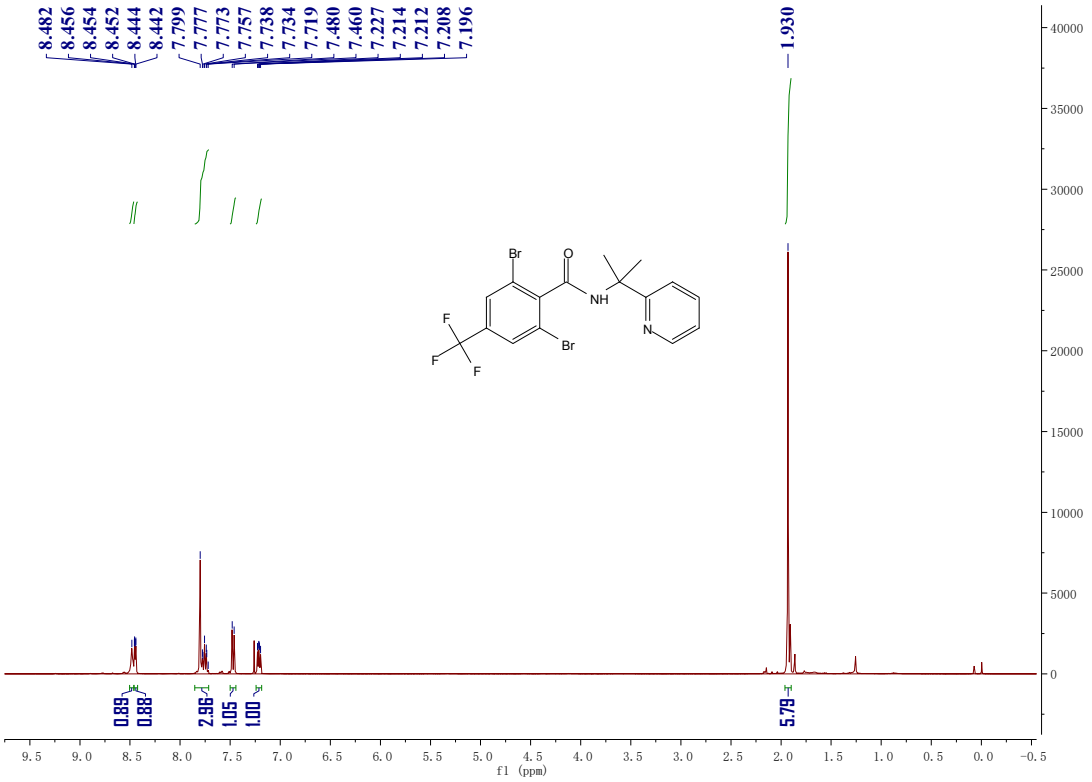

196.3
166.5
163.5
146.6
142.7
139.0
133.3
129.6
127.5
122.8
120.5
120.2
77.5
77.2
76.9
57.3
27.5
26.9
f1 (ppm)

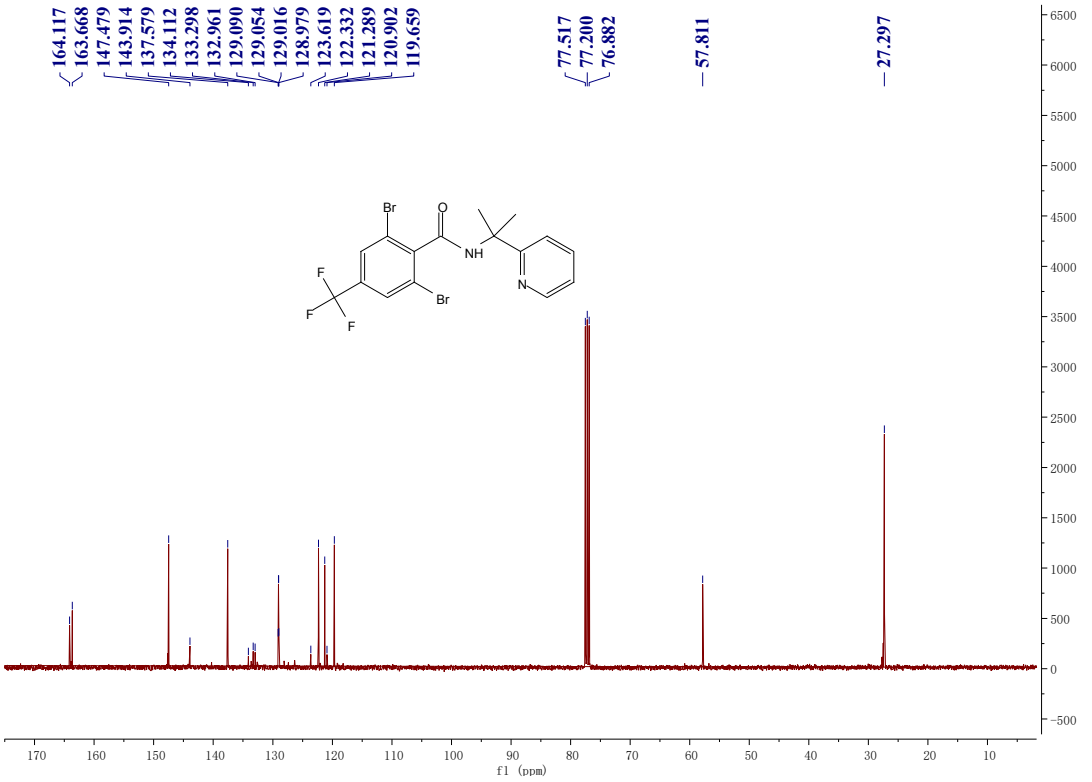
2k


8.472
8.471
8.461
7.779
7.775
7.759
7.756
7.740
7.736
7.657
7.637
7.631
7.628
7.611
7.608
7.474
7.454
7.260
7.232
7.229
7.219
7.217
7.213
7.211
7.201
7.199
1.910
1.75
0.96
1.09
1.97
1.07
1.00
6.00
O
NH
N
Br
F
F
F
f1 (ppm)

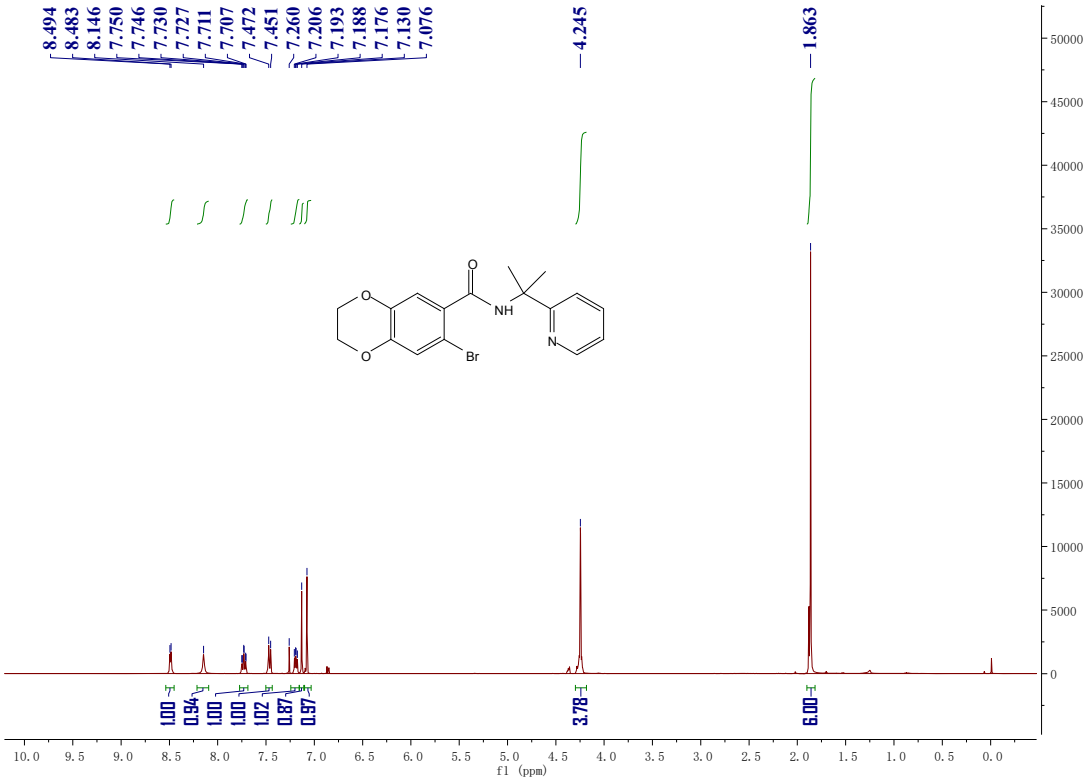

165.866
163.922
147.623
142.884
137.554
133.006
132.675
130.503
130.464
129.633
124.631
124.593
122.310
120.072
119.661
77.518
77.200
76.883
57.685
27.532
O
NH
N
Br
F
F
F
f1 (ppm)

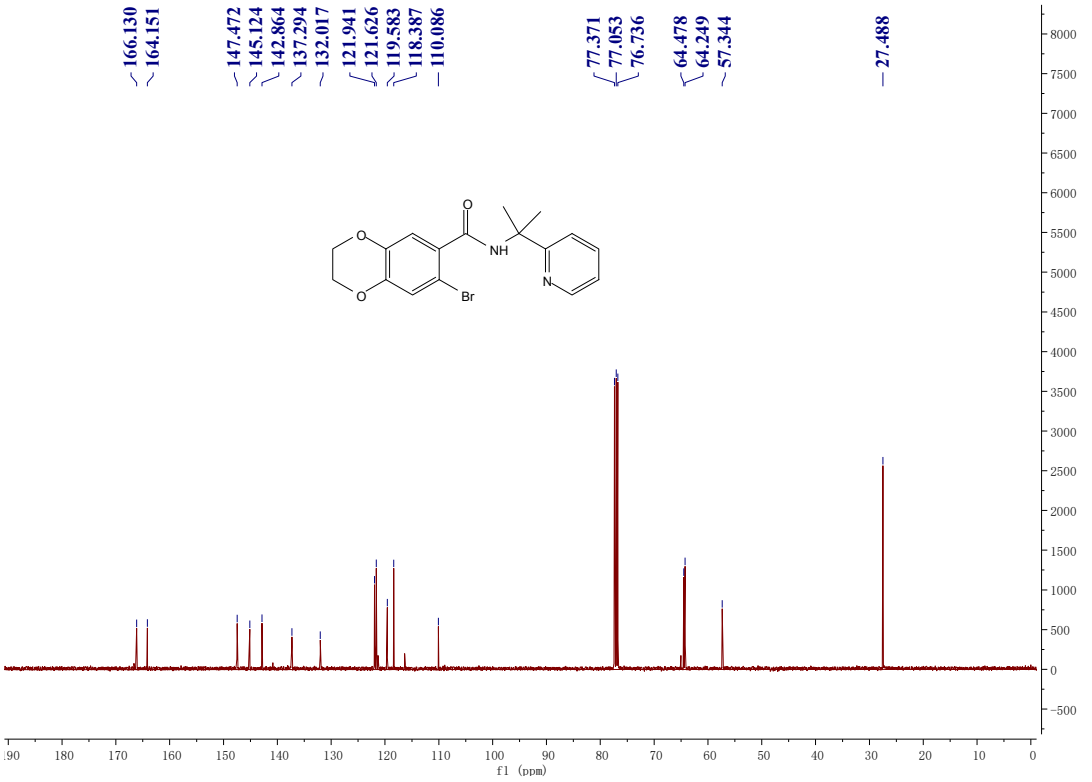
2k'


8.482
8.456
8.454
8.452
8.444
8.442
7.799
7.777
7.773
7.757
7.738
7.734
7.719
7.480
7.460
7.227
7.214
7.212
7.208
7.196
1.930
0.89
0.88
2.98
1.05
1.00
5.79
Br
O
NH
N
F
F
F
Br
f1 (ppm)

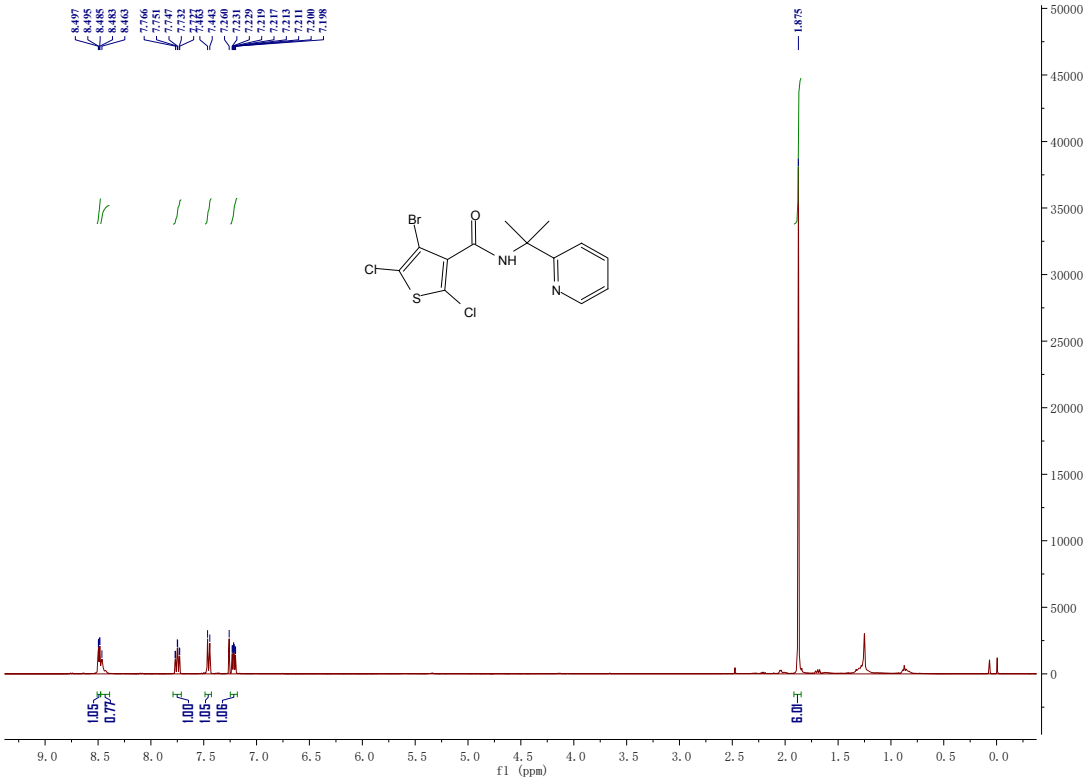

164.117
163.668
147.479
143.914
137.579
134.112
133.298
132.961
129.090
129.054
129.016
128.979
123.619
122.332
121.289
120.902
119.659
77.517
77.200
76.882
57.811
27.297
Br
O
NH
N
F
F
F
Br
f1 (ppm)

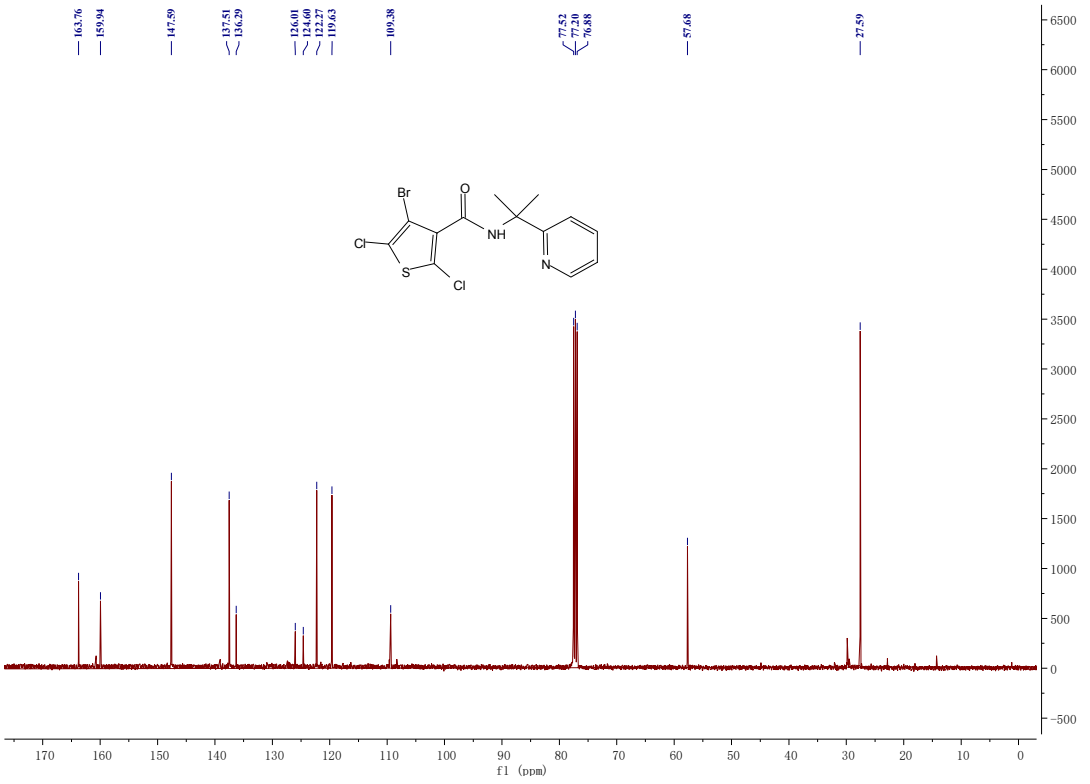
2l


8.494
8.483
8.146
7.750
7.746
7.730
7.727
7.711
7.707
7.472
7.451
7.260
7.206
7.193
7.188
7.176
7.130
7.076
4.245
1.863
1.00
0.94
1.00
1.00
1.02
0.87
0.97
3.78
6.00
O
NH
N
O
O
Br
f1 (ppm)

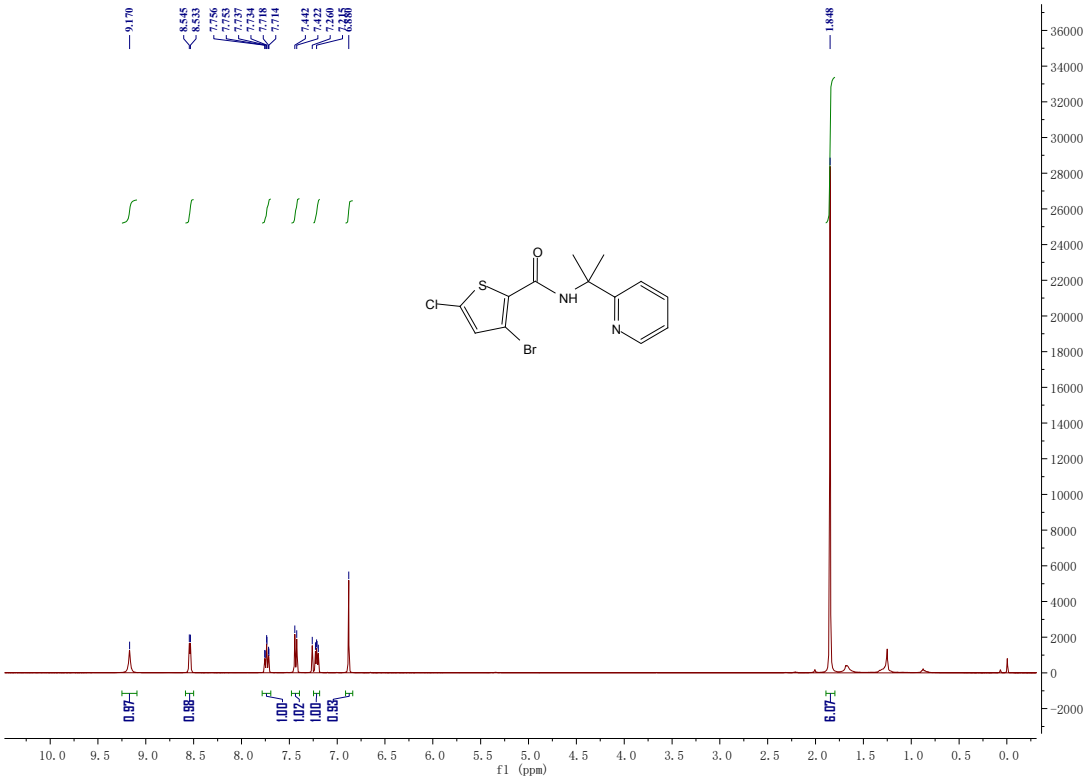

166.130
164.151
147.472
145.124
142.864
137.294
132.017
121.941
121.626
119.583
118.387
110.086
77.371
77.053
76.736
64.478
64.249
57.344
27.488
O
NH
N
O
O
Br
f1 (ppm)

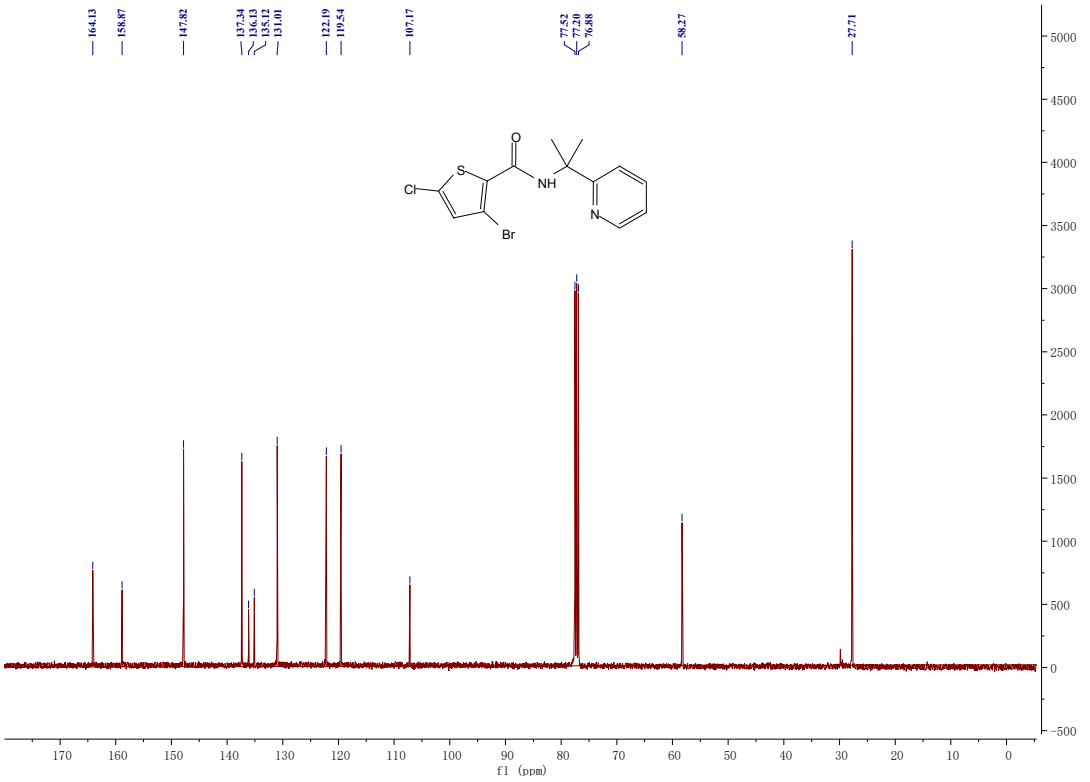
2p


8.497
8.495
8.485
8.483
8.463
7.766
7.751
7.747
7.732
7.727
7.723
7.463
7.443
7.240
7.231
7.229
7.219
7.217
7.213
7.211
7.200
7.198
1.875
Br
O
NH
Cl
S
Cl
N
1.05
0.77
1.00
1.05
1.06
6.01
f1 (ppm)

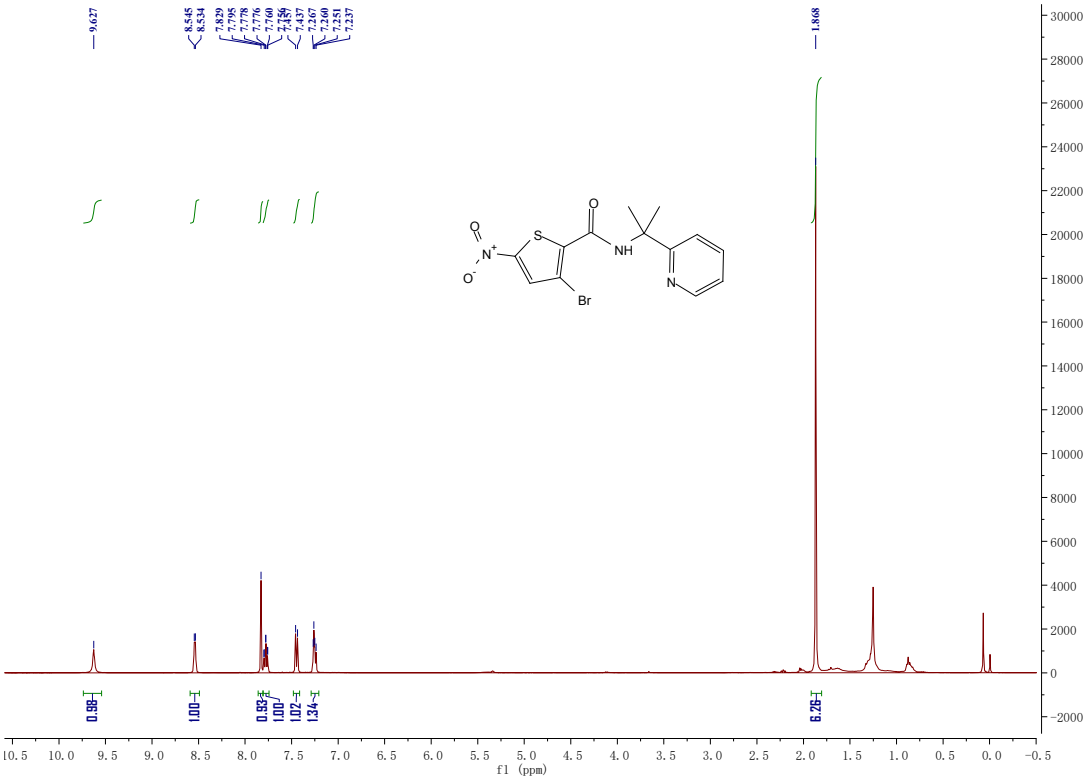

163.76
159.94
147.59
137.51
136.29
126.01
124.60
122.27
119.63
109.38
77.82
77.20
76.88
57.68
27.59
Br
O
NH
Cl
S
Cl
N
f1 (ppm)

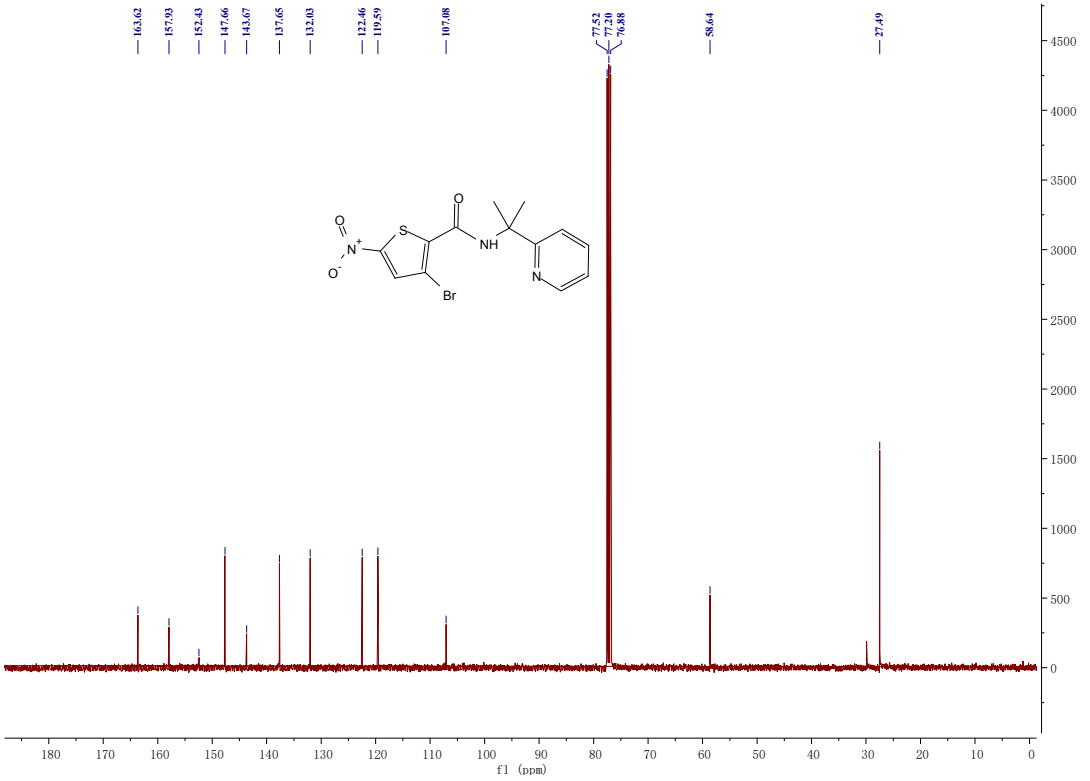
2q


9.170
8.545
8.533
7.756
7.753
7.737
7.734
7.718
7.714
7.442
7.422
7.260
7.255
7.250
1.848
0.97
0.98
1.00
1.02
1.00
0.53
6.07
f1 (ppm)

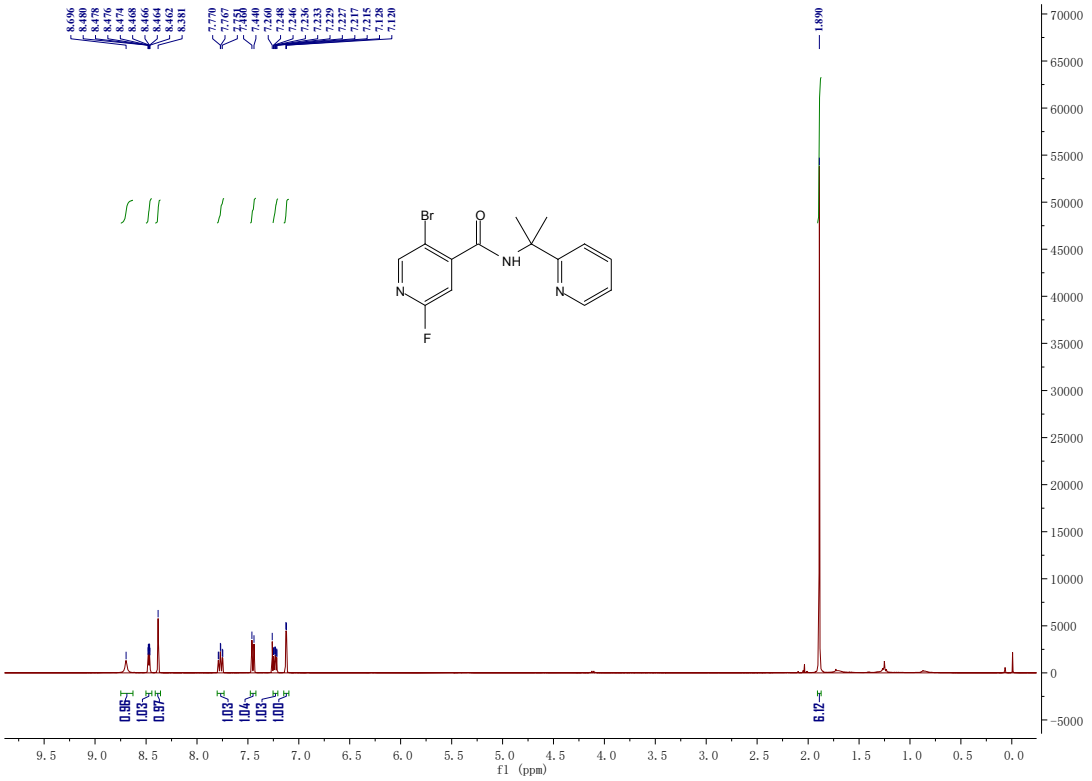

164.13
158.87
147.82
137.34
136.13
135.12
131.01
122.19
119.54
107.17
77.52
77.20
76.88
58.27
27.71
f1 (ppm)

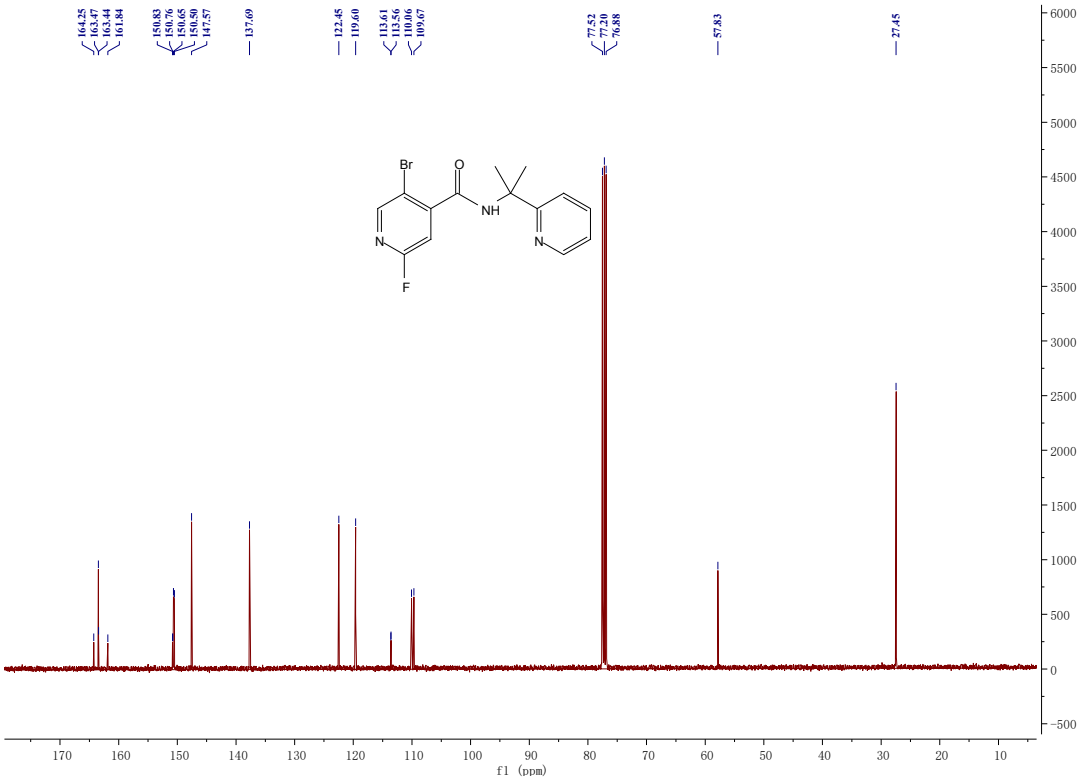
2r


9.627
8.545
8.534
7.829
7.795
7.778
7.776
7.760
7.756
7.439
7.437
7.267
7.260
7.251
7.237
1.868
0.98
1.00
0.93
1.00
1.02
1.34
6.26
f1 (ppm)

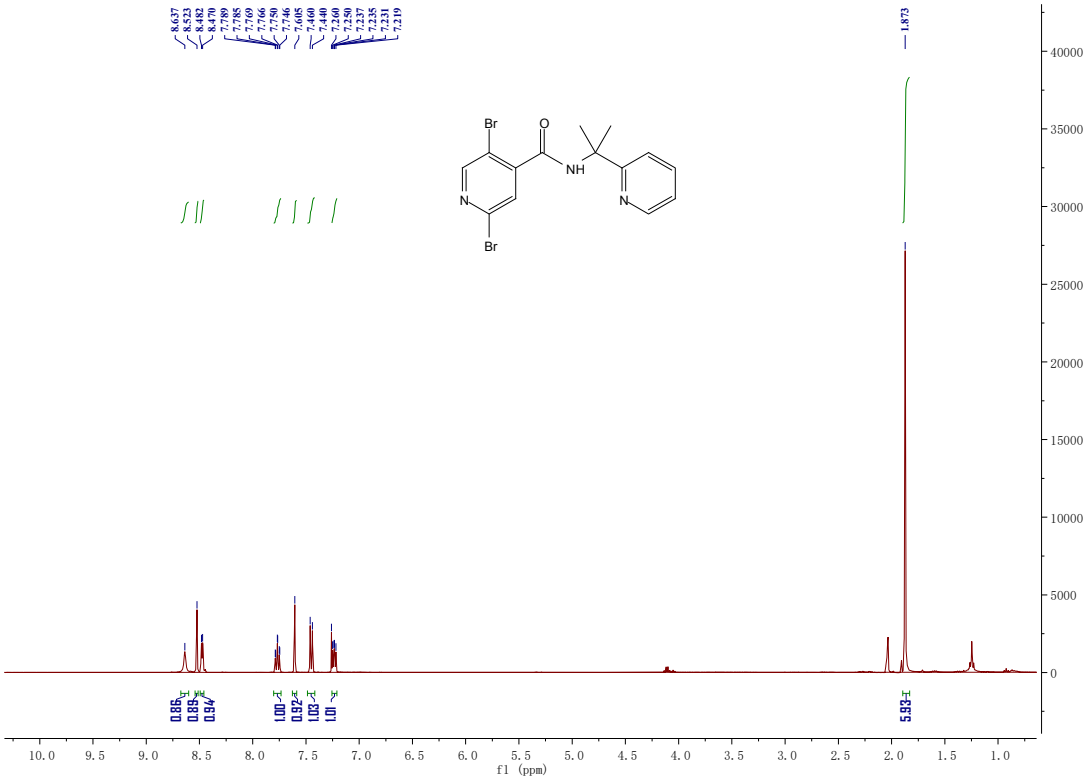

163.62
157.93
152.43
147.66
143.67
137.65
132.03
122.46
119.59
107.08
77.52
77.20
76.88
58.64
27.49
f1 (ppm)

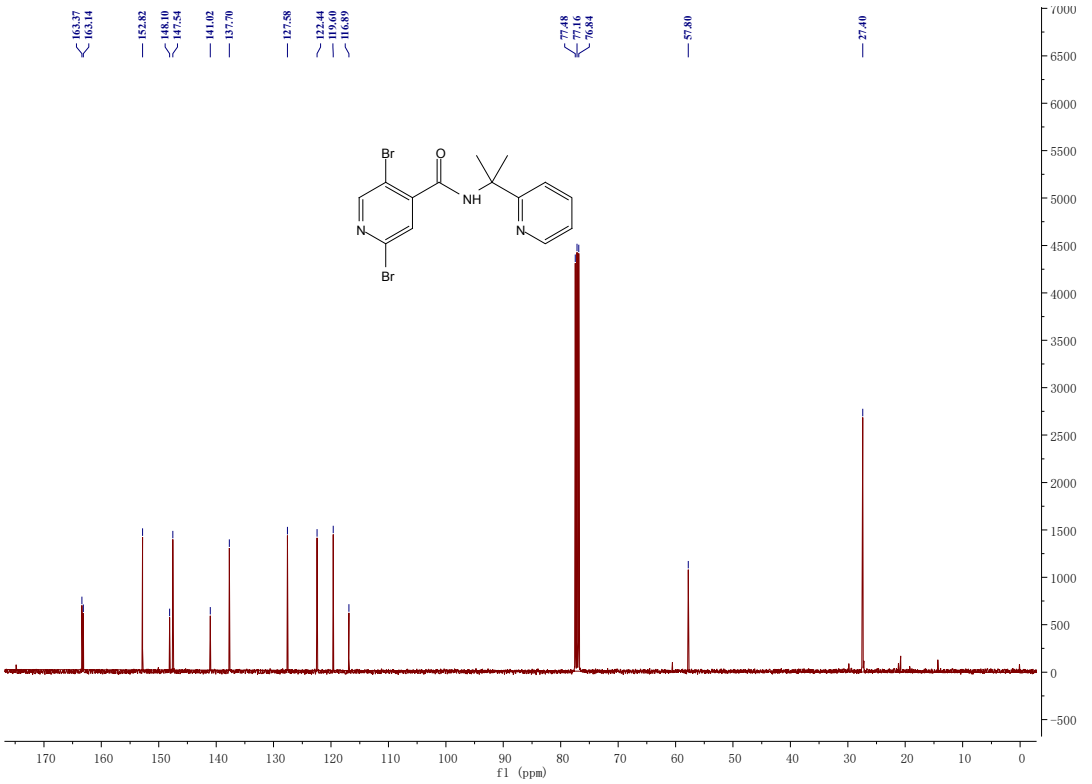
2s


8.696
8.480
8.478
8.476
8.474
8.468
8.466
8.464
8.462
8.381
7.770
7.767
7.751
7.748
7.440
7.438
7.246
7.236
7.233
7.229
7.227
7.217
7.215
7.138
7.130
1.890
Br
O
NH
N
N
F
0.95
1.03
0.97
1.03
1.04
1.03
1.00
6.12
f1 (ppm)

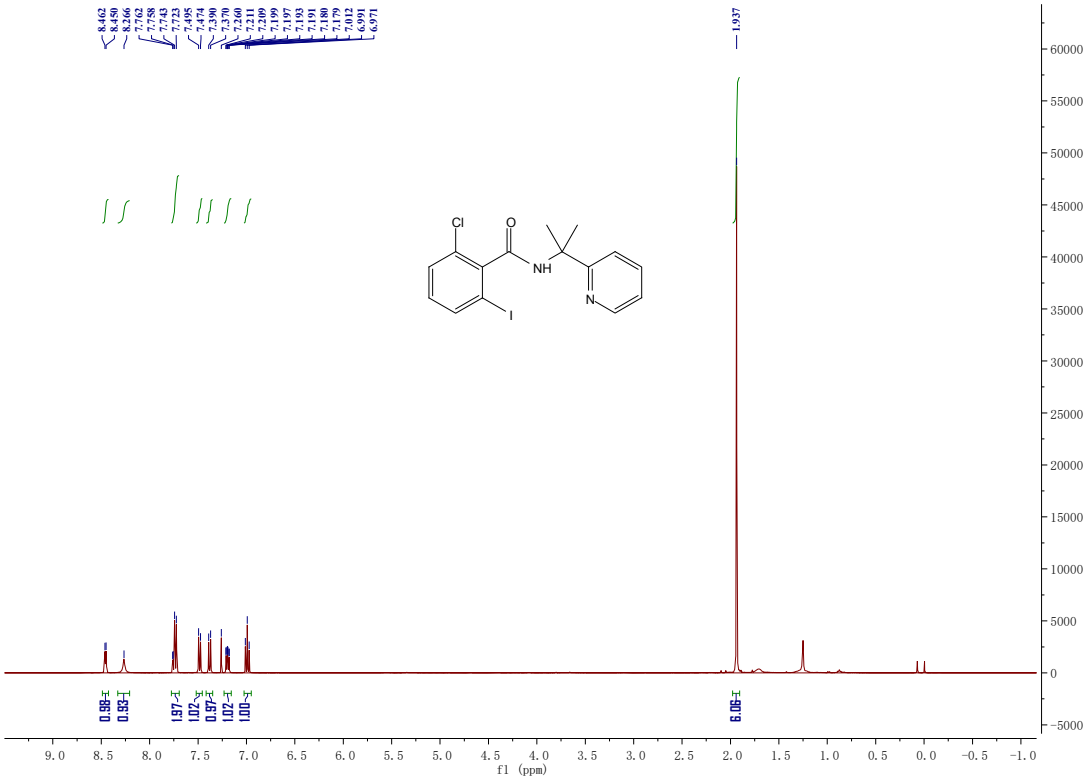

164.25
163.47
163.44
161.84
150.83
150.76
150.65
150.50
147.57
137.69
122.45
119.60
113.61
113.56
110.06
109.67
77.52
77.20
76.88
57.83
27.45
Br
O
NH
N
N
F
f1 (ppm)

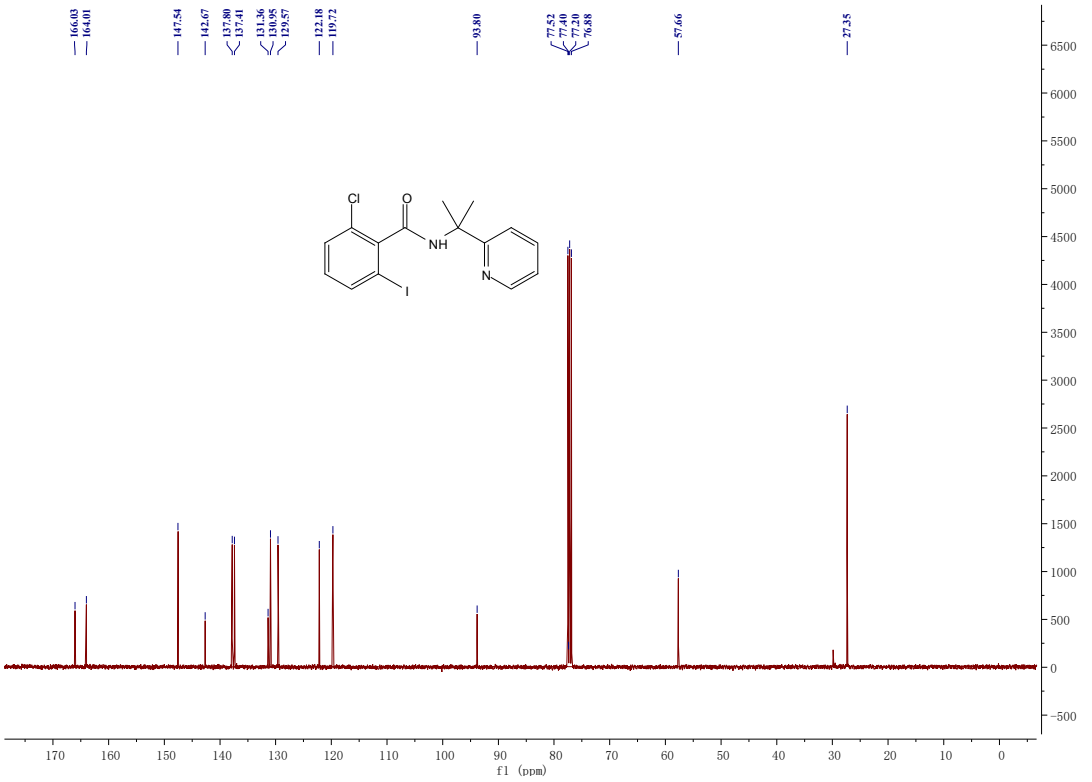
2t


8.637
8.523
8.482
8.470
7.789
7.785
7.769
7.766
7.750
7.746
7.605
7.460
7.446
7.260
7.250
7.237
7.235
7.231
7.219
1.873
Br
O
NH
N
N
Br
0.86
0.89
0.94
1.00
0.92
1.03
1.01
5.83
f1 (ppm)

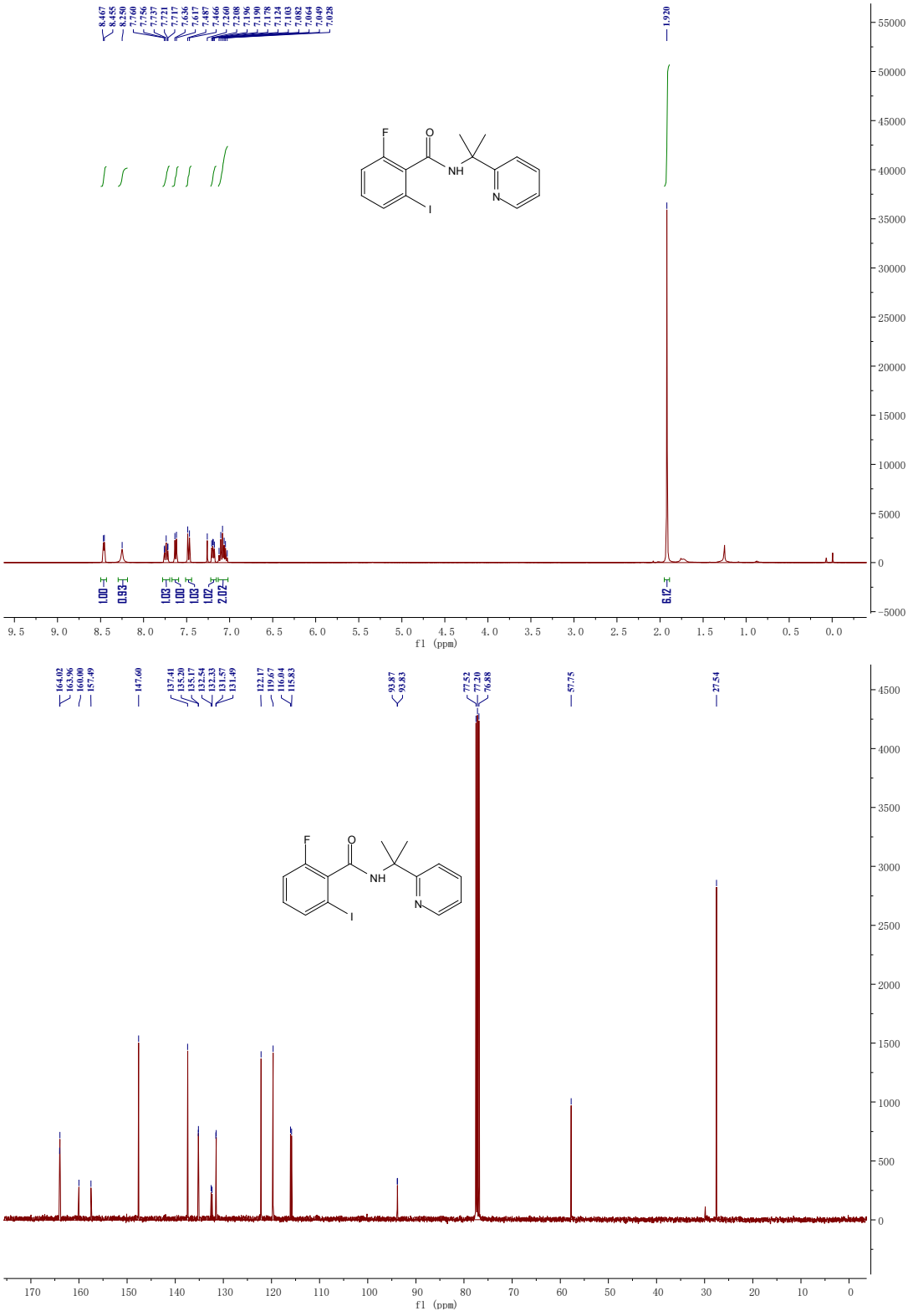

163.37
163.14
152.82
148.10
147.54
141.02
137.70
127.58
122.44
119.60
116.89
77.48
77.16
76.84
57.80
27.40
Br
O
NH
N
N
Br
f1 (ppm)

3a

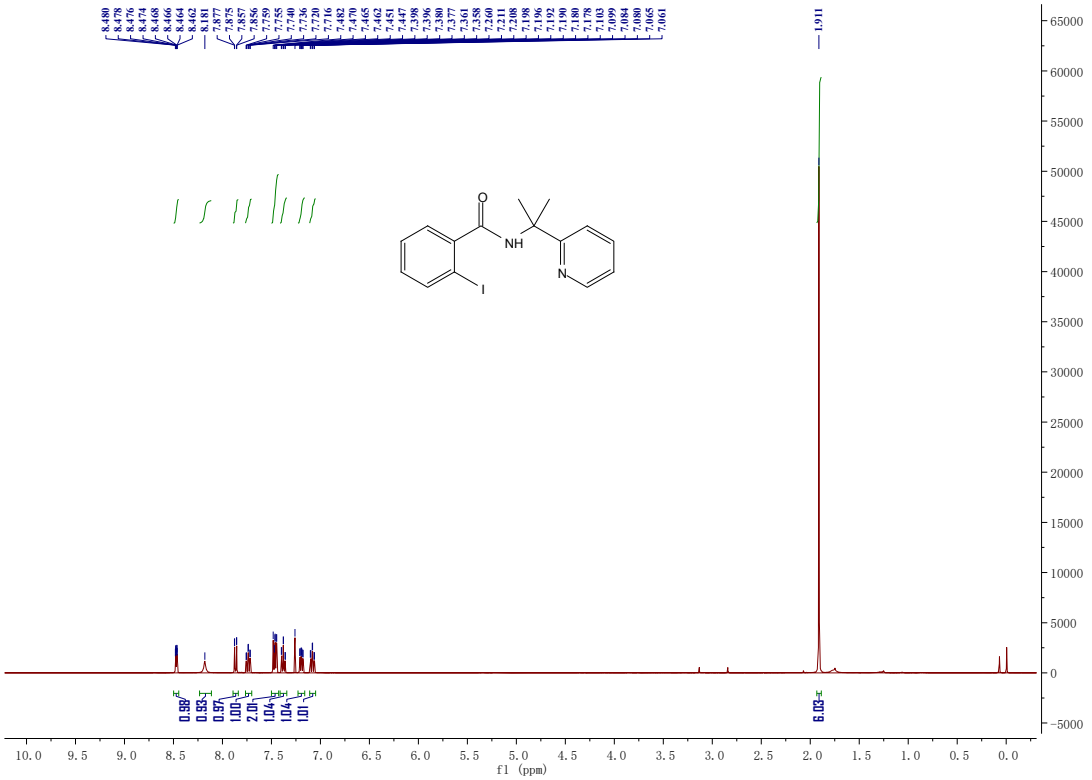

8.462
8.460
8.456
7.762
7.758
7.743
7.723
7.495
7.474
7.390
7.370
7.240
7.211
7.209
7.199
7.197
7.193
7.191
7.180
7.179
7.012
6.991
6.971
1.937
Cl
O
NH
N
I
0.58
0.53
1.37
1.02
0.97
1.02
1.00
6.06
f1 (ppm)

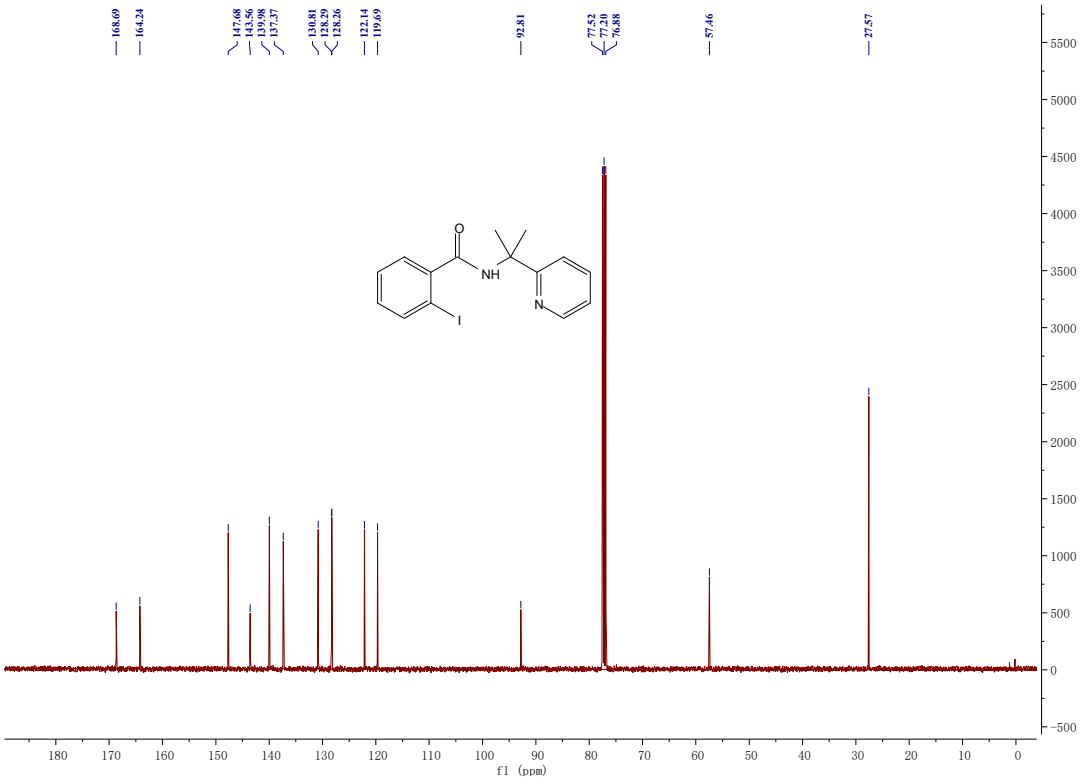

166.03
164.01
147.54
142.67
137.80
137.41
131.36
130.95
129.57
122.18
119.72
93.80
77.52
77.40
77.20
76.88
57.66
27.35
Cl
O
NH
N
I
f1 (ppm)

3b

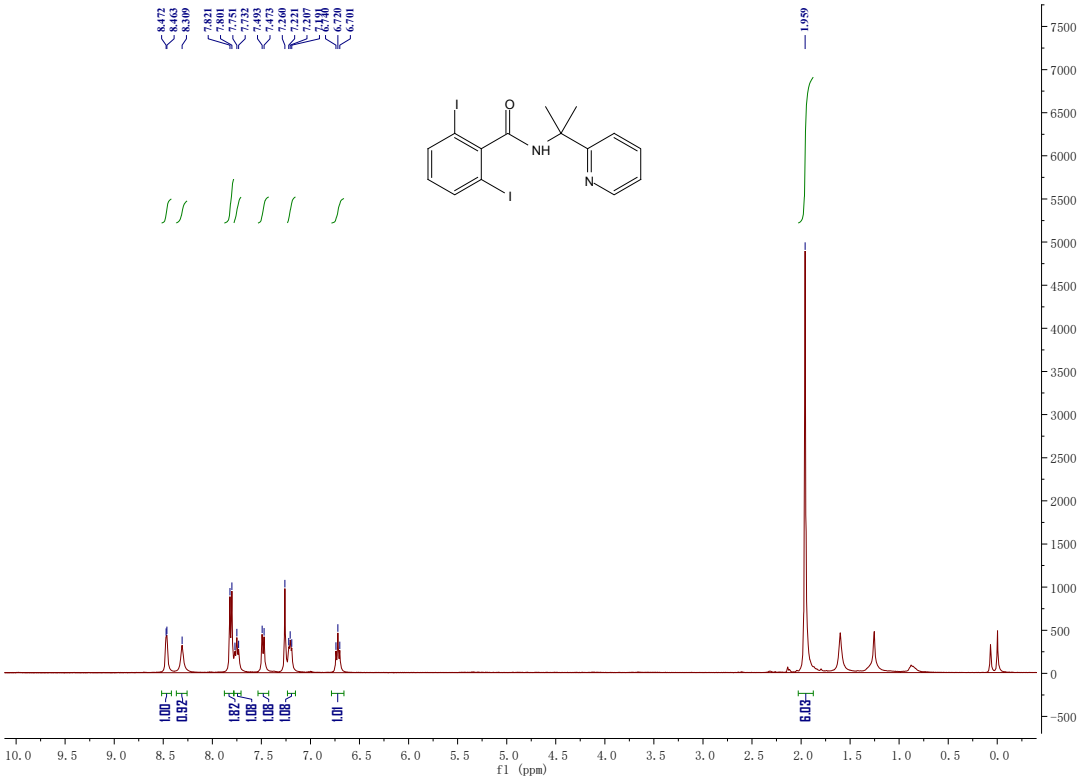

8.467
8.455
8.250
7.760
7.756
7.737
7.731
7.717
7.636
7.617
7.487
7.466
7.260
7.208
7.196
7.190
7.178
7.124
7.103
7.082
7.064
7.049
7.028
1.920
F
O
NH
N
I
1.00
0.93
1.03
1.00
1.03
1.02
2.02
6.12
f1 (ppm)
164.02
163.96
160.00
157.49
147.60
137.41
135.20
135.17
132.54
132.33
131.57
131.49
122.17
119.67
116.04
115.83
93.87
93.83
77.52
77.20
76.88
57.75
27.54
f1 (ppm)

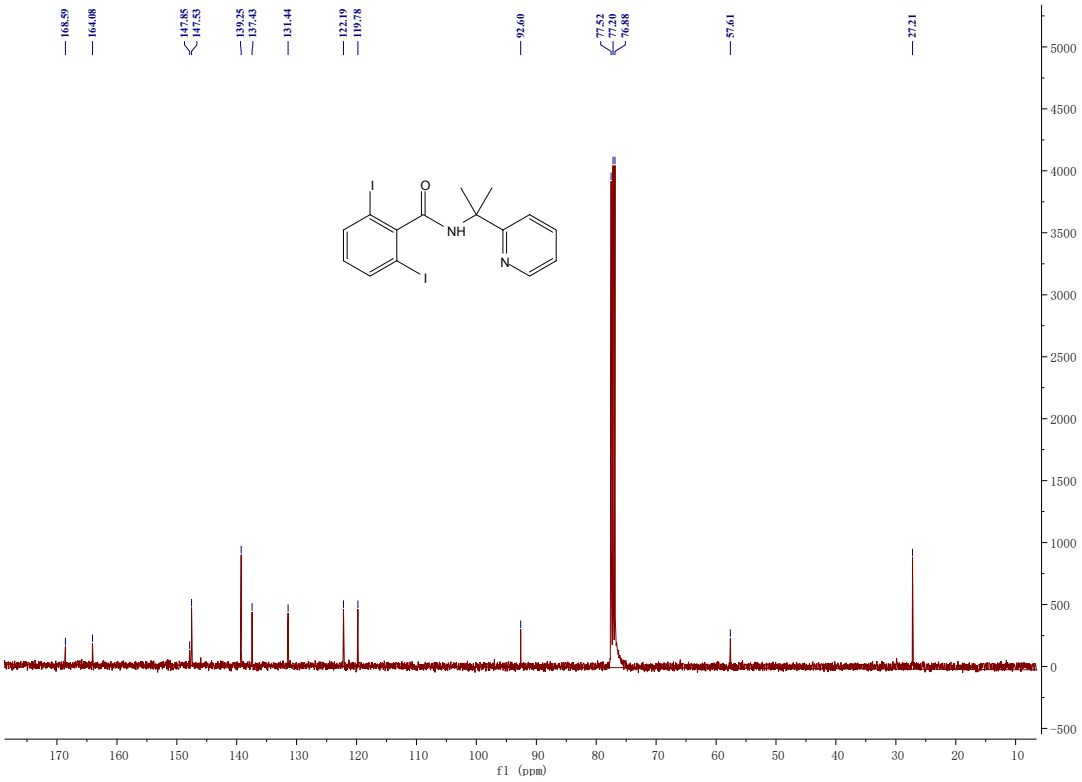
3c


8.480
8.478
8.476
8.474
8.468
8.466
8.464
8.462
8.181
7.877
7.875
7.857
7.856
7.759
7.755
7.740
7.736
7.720
7.716
7.482
7.470
7.465
7.462
7.451
7.447
7.398
7.396
7.380
7.377
7.361
7.358
7.260
7.211
7.208
7.198
7.196
7.192
7.190
7.180
7.178
7.103
7.099
7.084
7.080
7.065
7.061
1.911
O
NH
N
I
0.89
0.93
0.97
1.00
2.01
1.04
1.04
1.01
6.03
f1 (ppm)

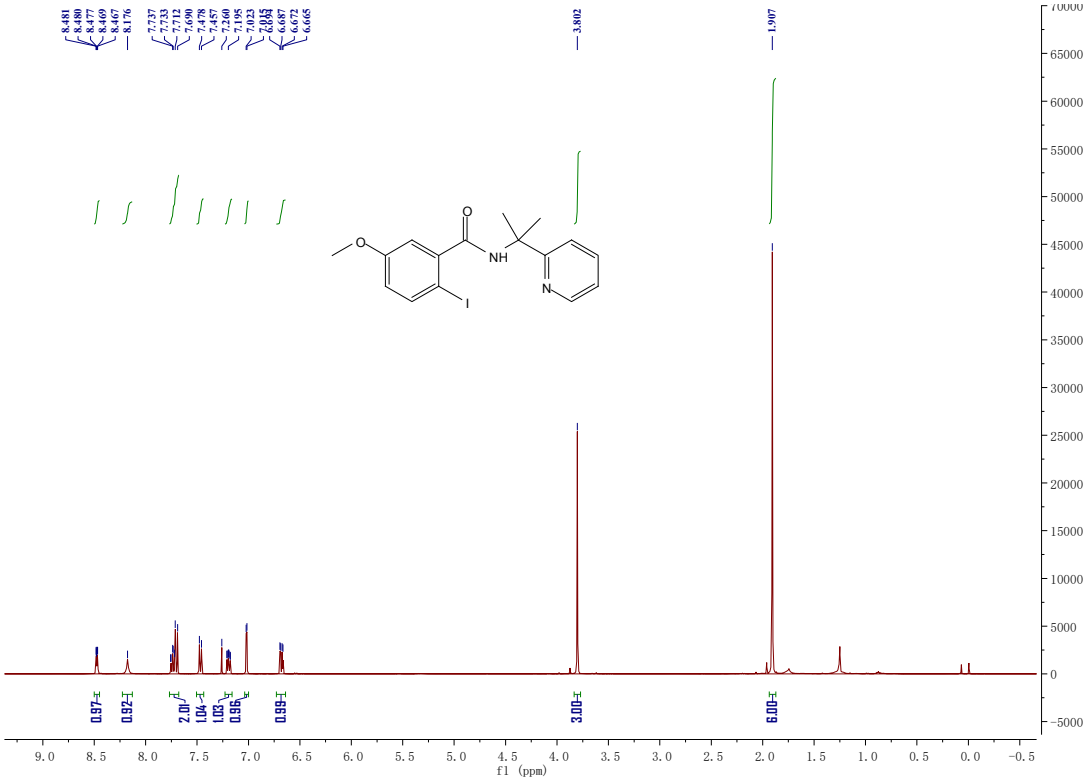

168.69
164.24
147.68
143.56
139.98
137.37
130.81
128.29
128.26
122.14
119.69
92.81
77.52
77.20
76.88
57.46
27.57
O
NH
N
I
f1 (ppm)

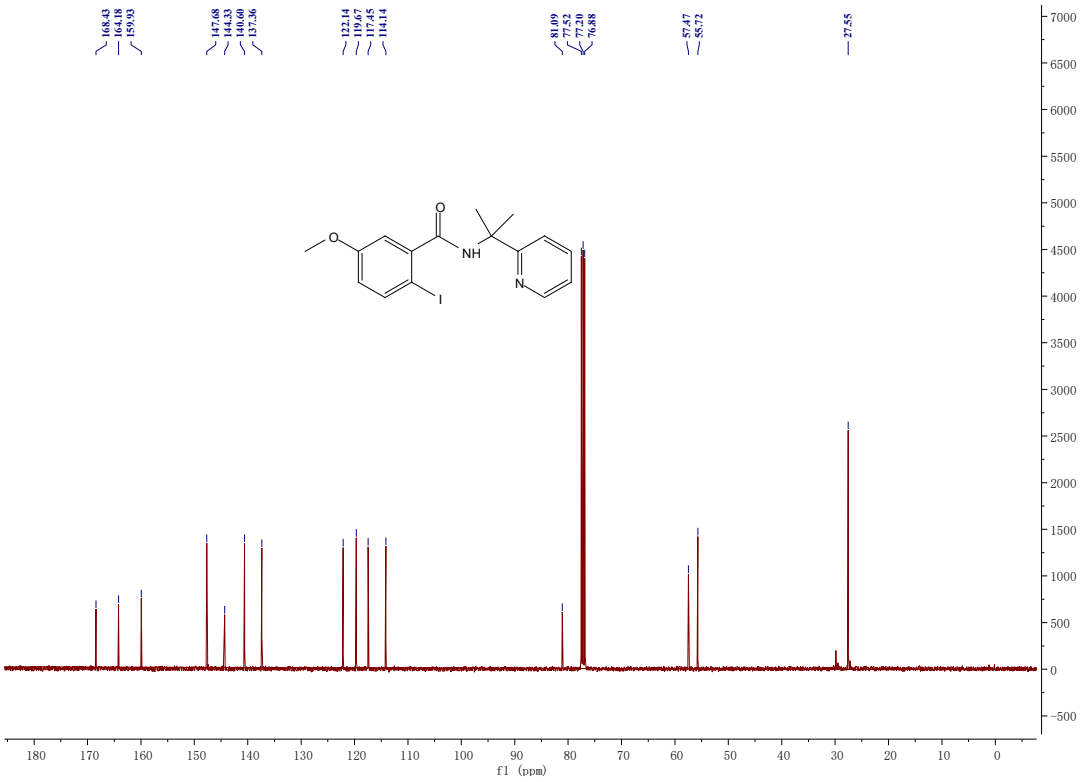
3c'


8.472
8.463
8.309
7.821
7.801
7.751
7.732
7.493
7.473
7.260
7.221
7.207
7.191
6.720
6.701
1.959
1.00
0.92
1.82
1.08
1.08
1.08
1.01
6.03
f1 (ppm)

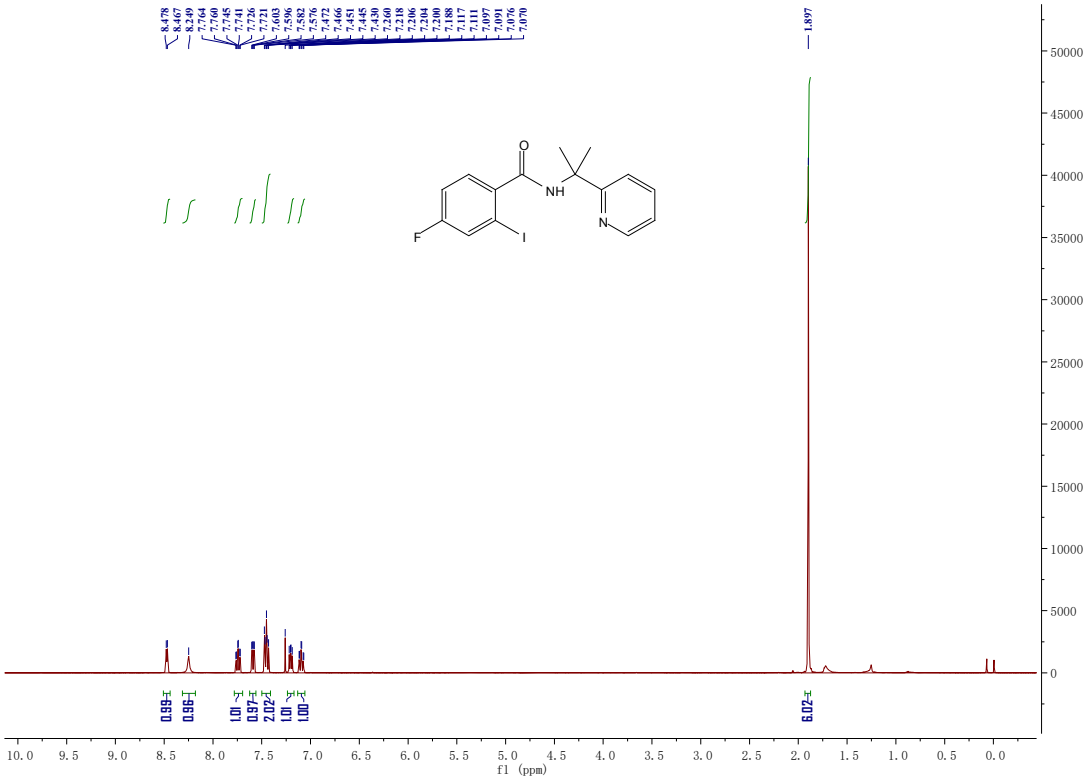

168.59
164.08
147.85
147.53
139.25
137.43
131.44
122.19
119.78
92.60
77.52
77.20
76.88
57.61
27.21
f1 (ppm)

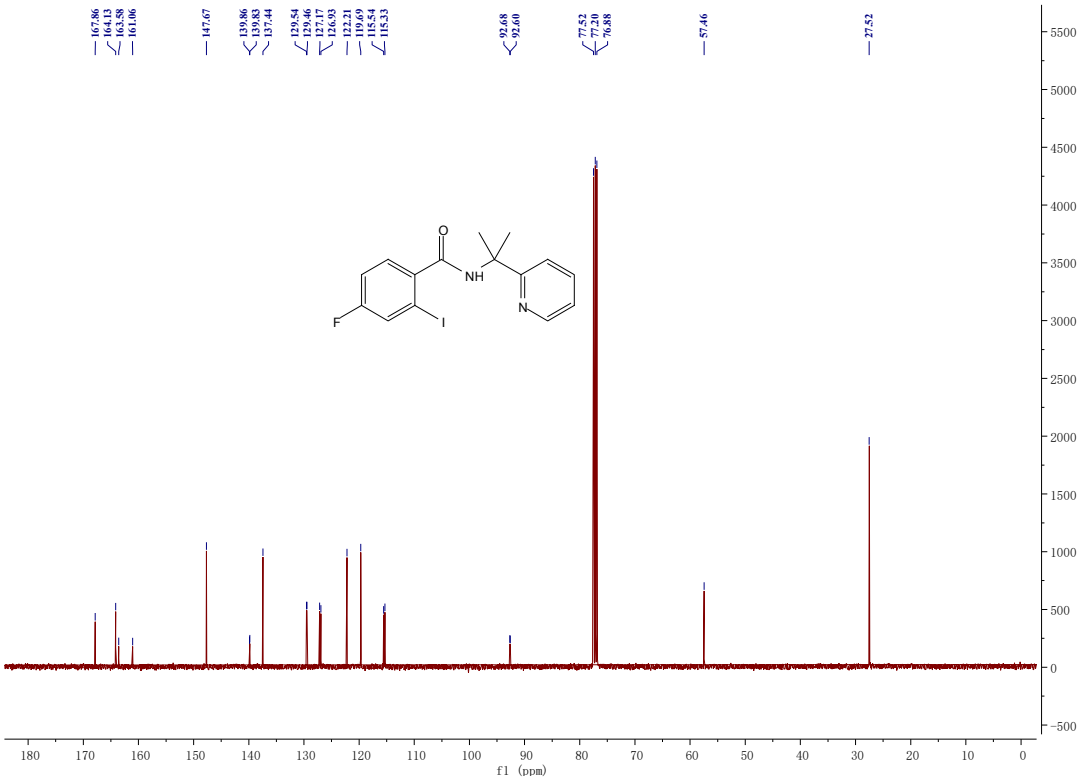
3e


8.481
8.480
8.477
8.469
8.467
8.176
7.737
7.733
7.712
7.690
7.478
7.457
7.260
7.195
7.023
6.694
6.687
6.672
6.665
3.802
1.907
0.97
0.82
2.01
1.04
1.03
0.96
0.99
3.00
6.00
f1 (ppm)

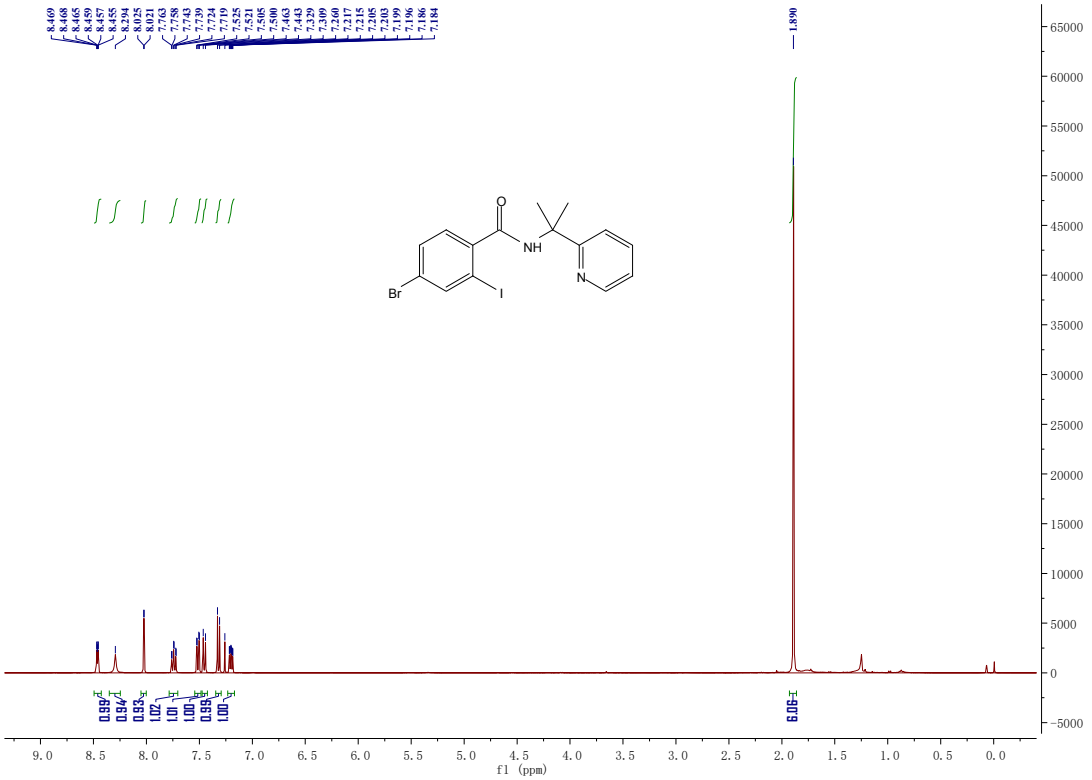

168.43
164.18
159.93
147.68
144.33
140.60
137.56
122.14
119.67
117.45
114.14
81.09
77.52
77.20
76.88
57.47
55.72
27.55
f1 (ppm)

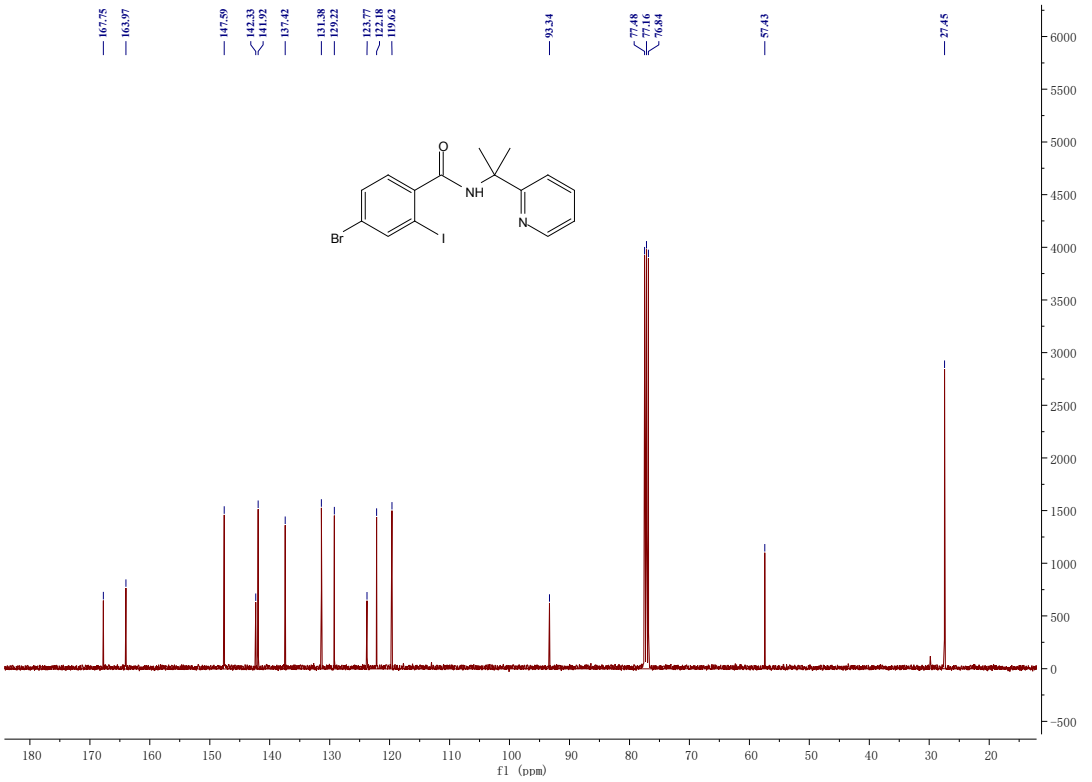
3g


8.478
8.467
8.249
7.764
7.760
7.745
7.741
7.736
7.721
7.603
7.596
7.582
7.576
7.472
7.466
7.451
7.445
7.430
7.260
7.218
7.206
7.204
7.200
7.198
7.117
7.111
7.097
7.091
7.076
7.070
1.897
O
NH
N
F
I
0.99
0.96
1.01
0.97
2.02
1.01
1.00
6.02
f1 (ppm)

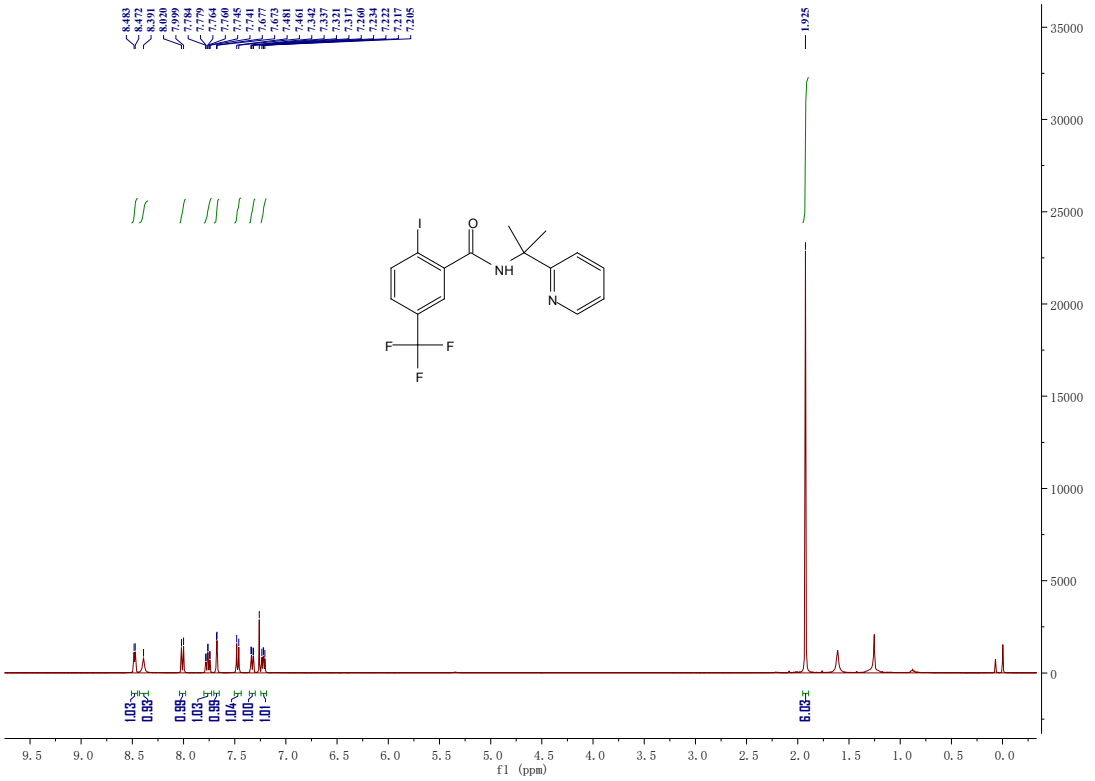

167.86
164.13
163.58
161.06
147.67
139.86
139.83
137.44
129.54
129.46
127.17
126.93
122.21
119.69
115.54
115.33
92.68
92.60
77.52
77.20
76.88
57.46
27.52
O
NH
N
F
I
f1 (ppm)

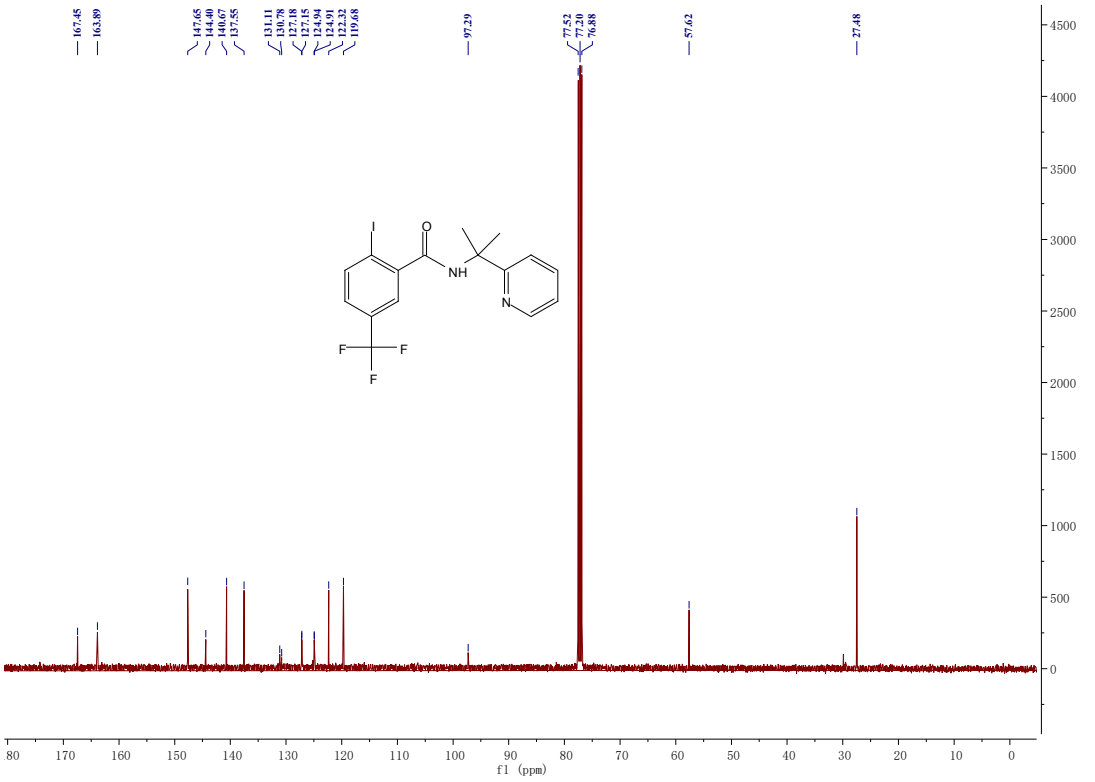
3h


8.469
8.468
8.465
8.459
8.457
8.455
8.294
8.025
8.021
7.763
7.758
7.743
7.739
7.734
7.719
7.525
7.521
7.505
7.500
7.463
7.443
7.339
7.300
7.260
7.217
7.215
7.205
7.203
7.199
7.196
7.186
7.184
1.890
0.99
0.94
0.93
1.02
1.01
1.00
0.98
1.00
6.06
O
NH
N
Br
I
f1 (ppm)

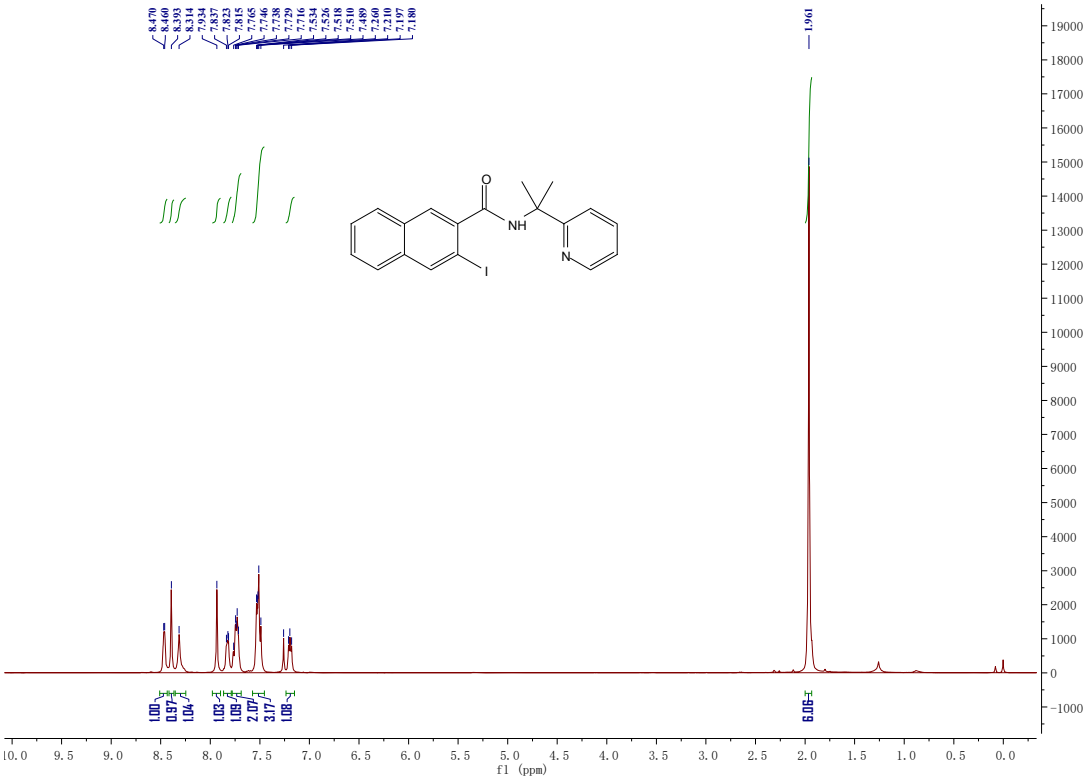

167.75
163.97
147.59
142.33
141.92
137.42
131.38
129.22
123.77
122.18
119.62
93.34
77.48
77.16
76.84
57.43
27.45
O
NH
N
Br
I
f1 (ppm)

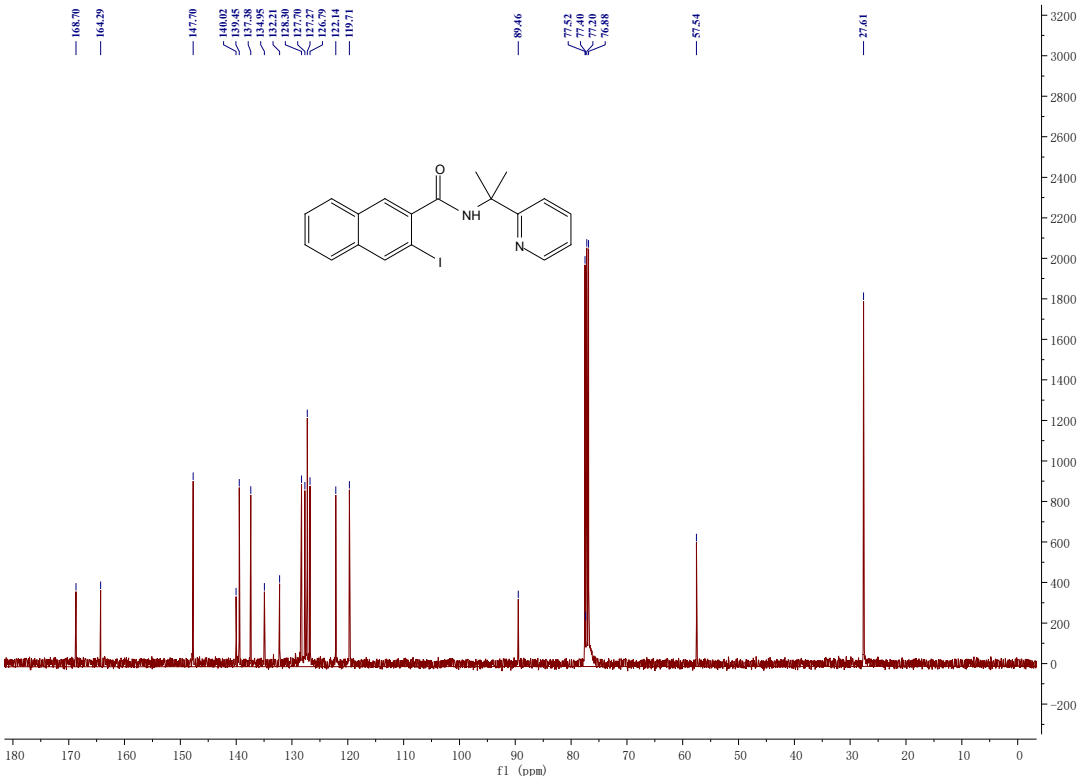
3m


8.483
8.472
8.391
8.020
7.999
7.784
7.779
7.764
7.760
7.745
7.741
7.677
7.673
7.481
7.461
7.342
7.337
7.331
7.317
7.260
7.234
7.222
7.217
7.205
1.925
I
O
NH
N
F
F
F
1.03
0.52
0.99
1.03
0.99
1.04
1.00
1.01
6.02
f1 (ppm)

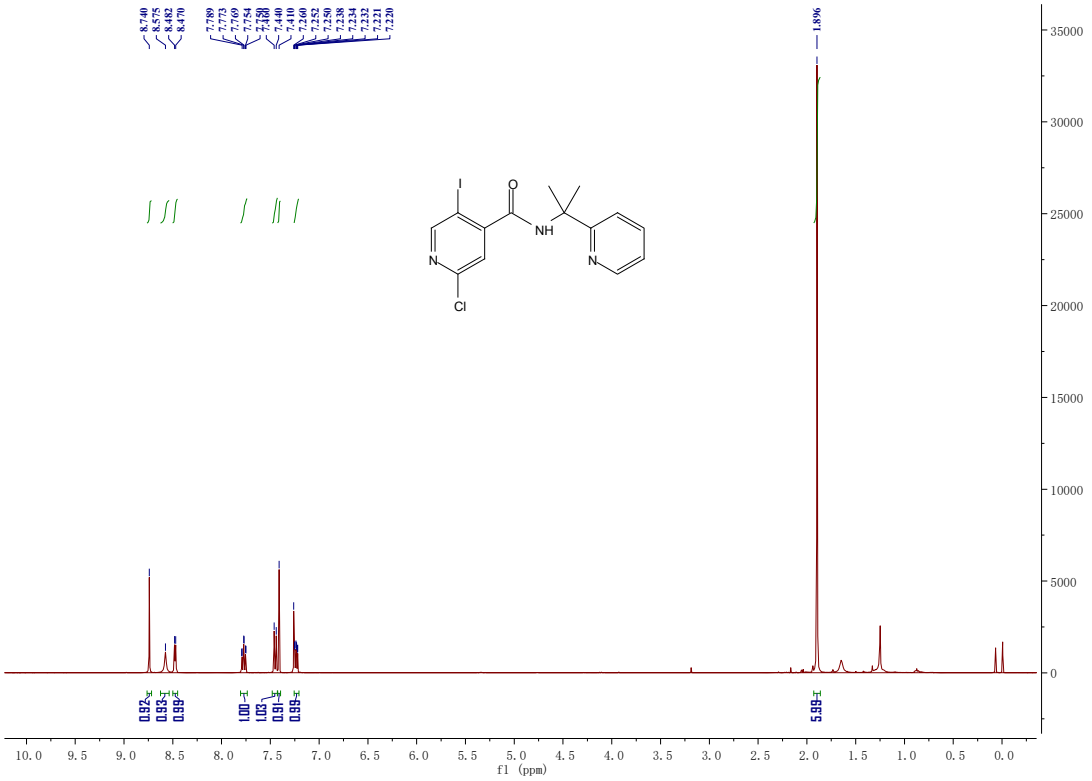

167.45
163.89
147.65
144.40
140.67
137.55
131.11
130.78
127.18
127.15
124.94
124.91
122.32
119.68
97.29
77.52
77.20
76.88
57.62
27.48
I
O
NH
N
F
F
F
f1 (ppm)

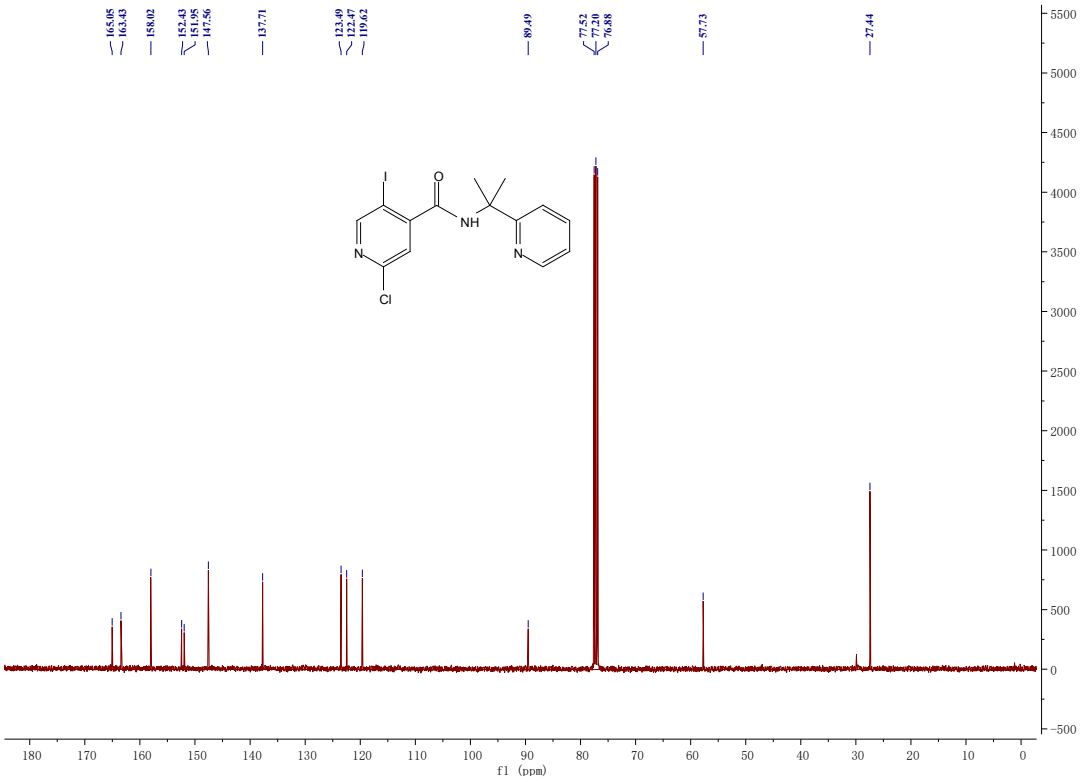
3n


8.470
8.460
8.393
8.314
7.934
7.857
7.833
7.815
7.765
7.746
7.738
7.729
7.716
7.534
7.526
7.518
7.510
7.489
7.260
7.210
7.197
7.180
1.961
O
NH
N
I
1.00
0.97
1.04
1.03
1.09
2.07
3.17
1.08
6.06
f1 (ppm)

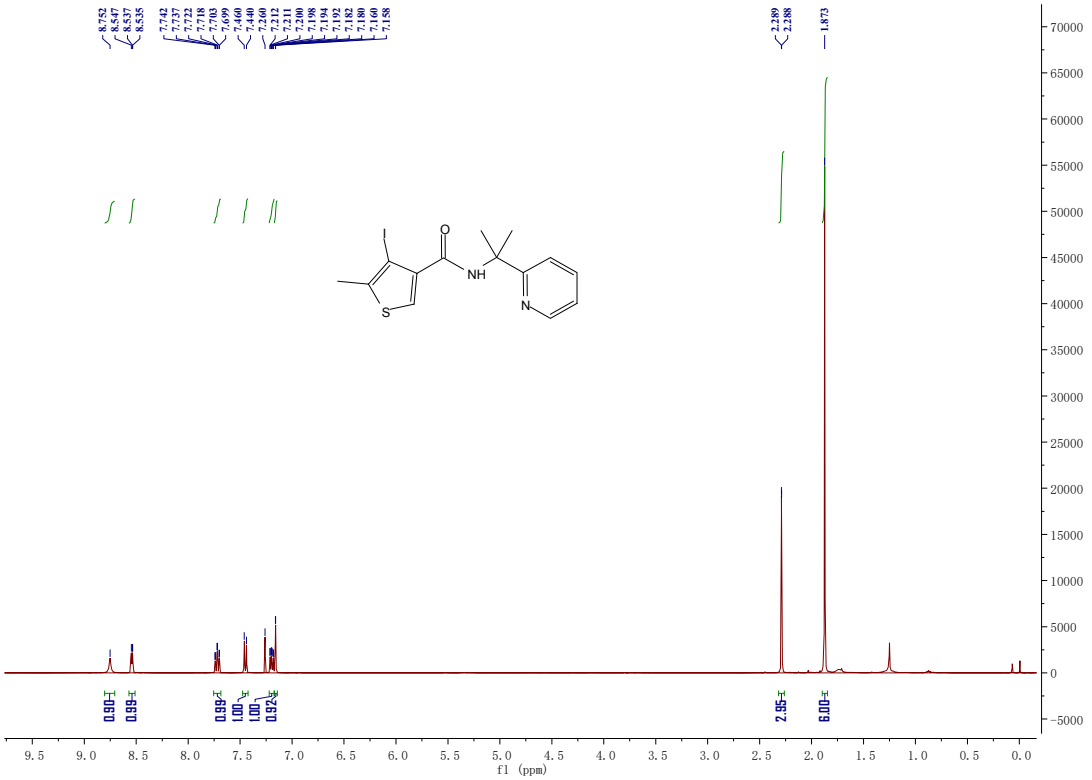

168.70
164.29
147.70
140.02
139.45
137.38
134.95
132.21
128.30
127.70
127.27
126.79
122.14
119.71
89.46
77.52
77.40
77.20
76.88
57.54
27.61
O
NH
N
I
f1 (ppm)

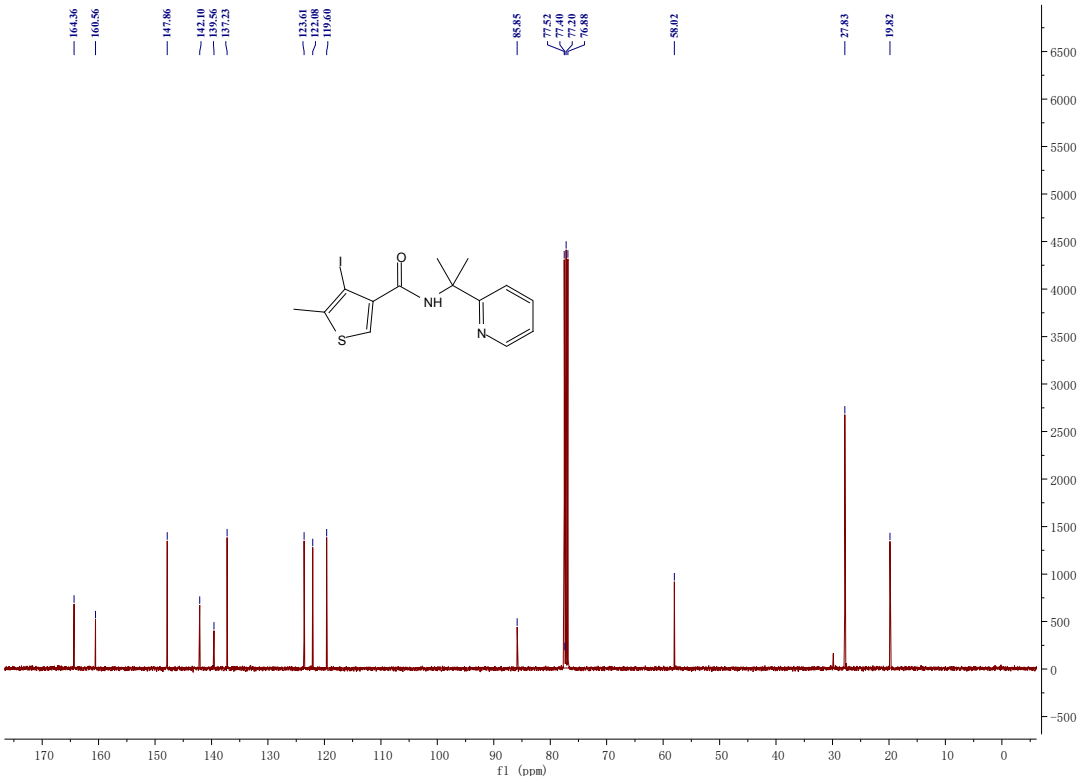
3u


8.740
8.475
8.465
8.470
7.789
7.773
7.769
7.754
7.440
7.410
7.260
7.252
7.250
7.238
7.234
7.231
7.221
7.220
1.896
I
O
NH
N
N
Cl
0.92
0.93
0.99
1.00
1.03
0.91
0.99
5.99
f1 (ppm)

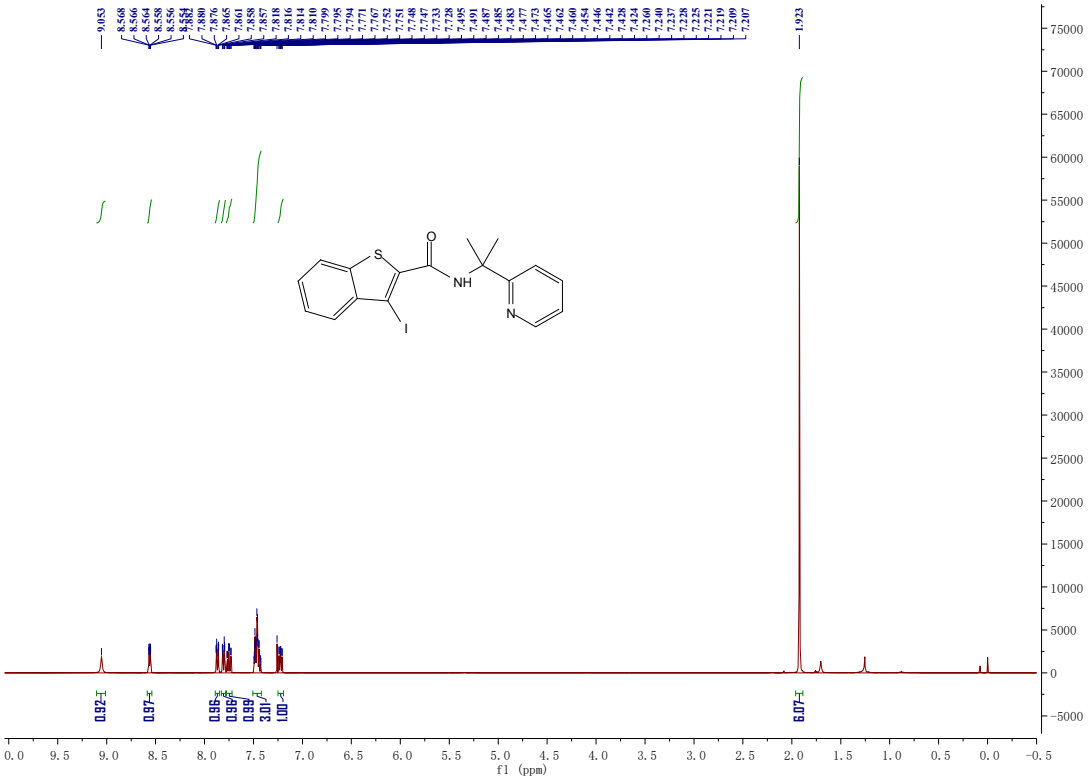

165.05
163.43
158.02
152.43
151.95
147.56
137.71
123.49
122.47
119.62
89.49
77.52
77.20
76.88
57.73
27.44
I
O
NH
N
N
Cl
f1 (ppm)

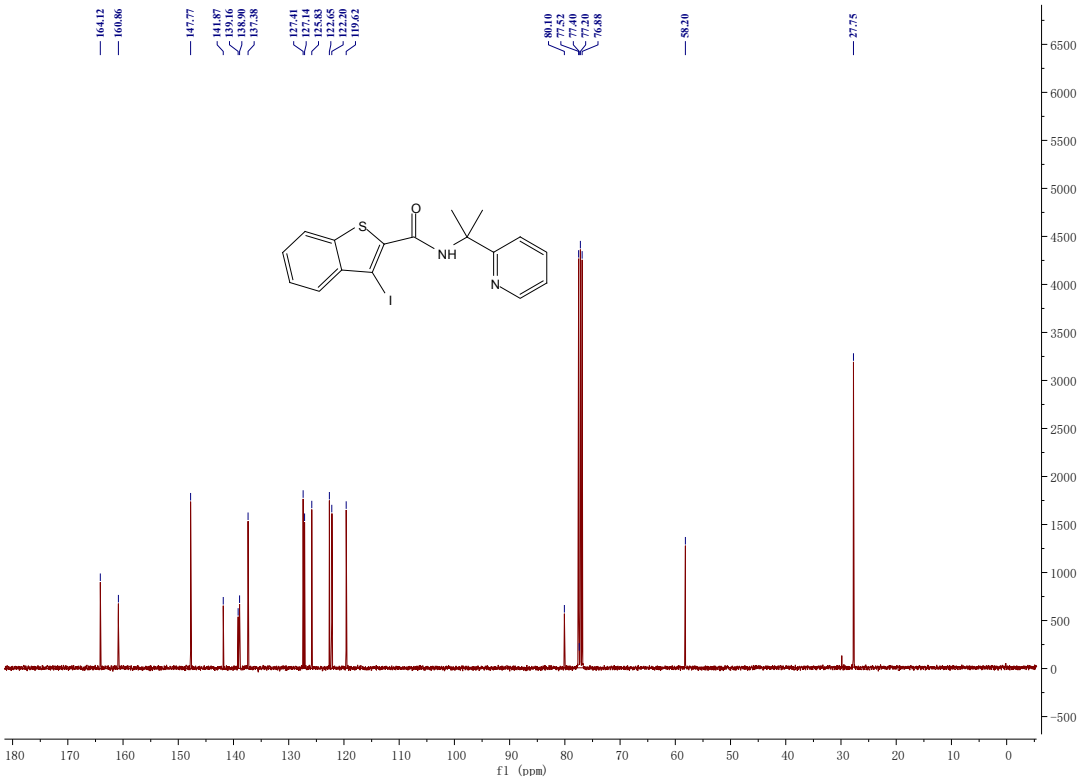
3v


8.752
8.547
8.537
8.535
7.742
7.737
7.722
7.718
7.703
7.699
7.460
7.440
7.260
7.212
7.211
7.200
7.198
7.194
7.192
7.182
7.180
7.160
7.158
2.289
2.288
1.873
I
O
NH
N
S
0.90
0.99
0.99
1.00
1.00
0.92
2.95
6.00
f1 (ppm)

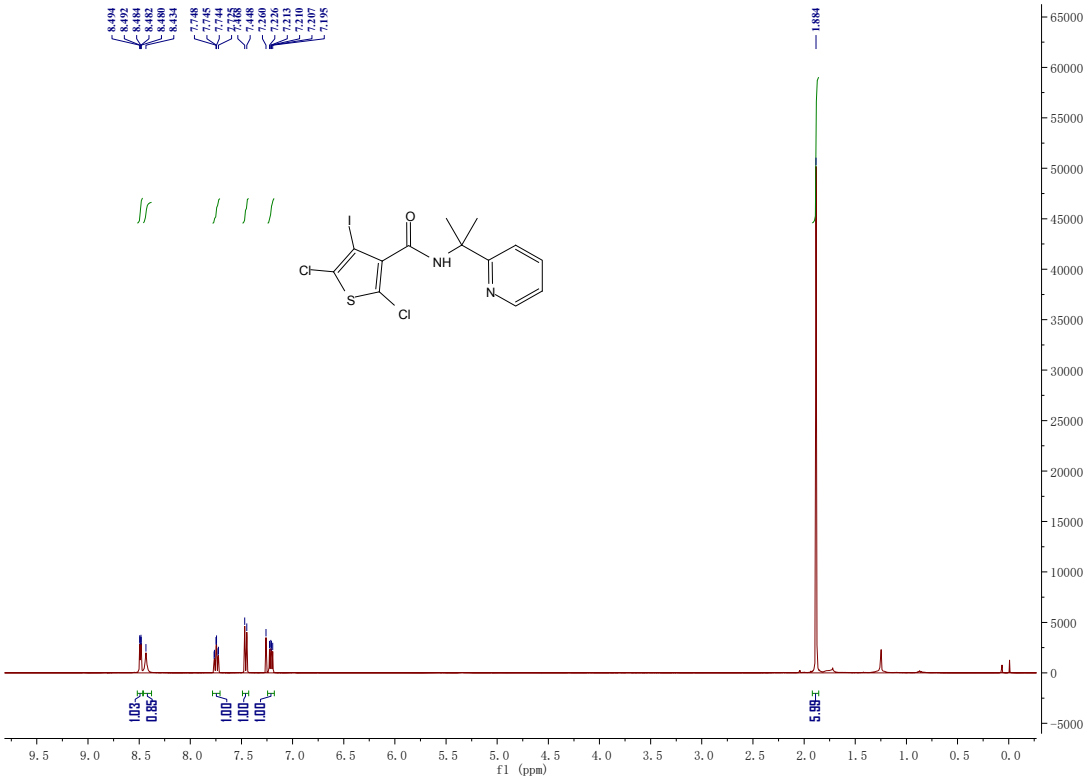

164.36
160.56
147.86
142.10
139.56
137.23
123.61
122.08
119.60
85.85
77.52
77.40
77.20
76.88
58.02
27.83
19.82
I
O
NH
N
S
f1 (ppm)

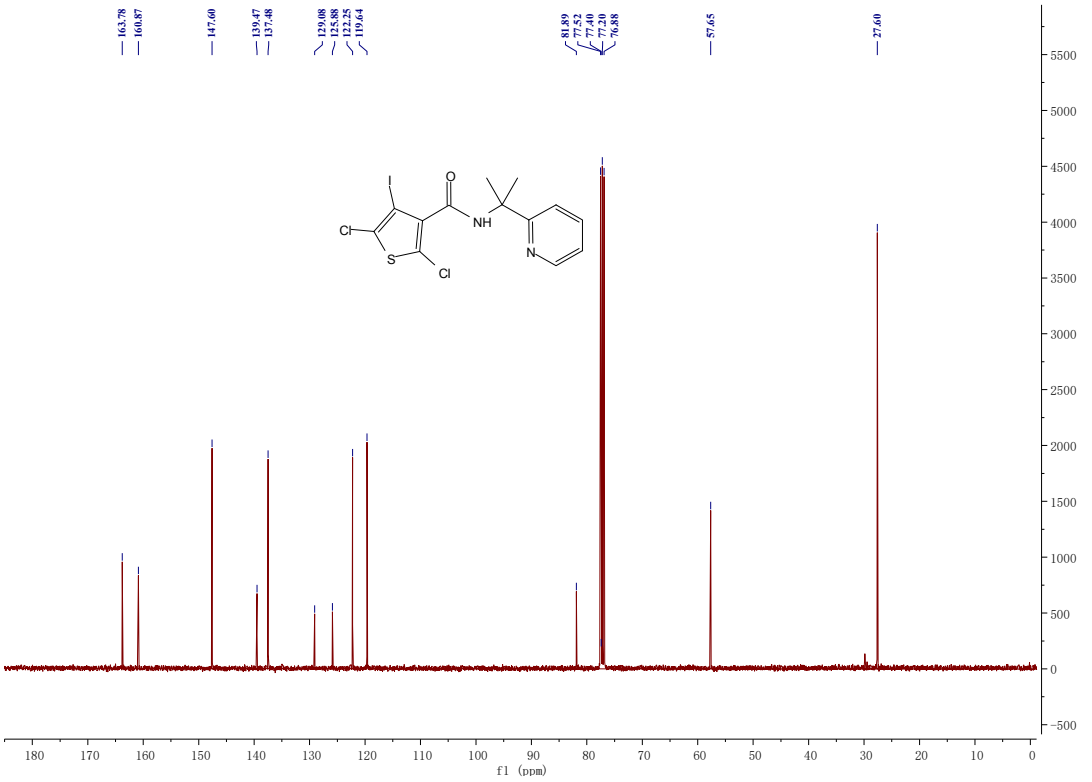
3w


9.053
8.568
8.566
8.564
8.558
8.556
7.880
7.876
7.865
7.861
7.858
7.857
7.818
7.816
7.814
7.810
7.799
7.795
7.794
7.771
7.767
7.752
7.751
7.748
7.747
7.733
7.728
7.495
7.491
7.487
7.485
7.483
7.477
7.473
7.465
7.462
7.460
7.454
7.446
7.442
7.428
7.424
7.240
7.240
7.237
7.228
7.225
7.221
7.219
7.209
7.207
1.933
0.92
0.87
0.96
0.96
0.99
3.01
1.00
6.07
O
S
NH
N
I
f1 (ppm)

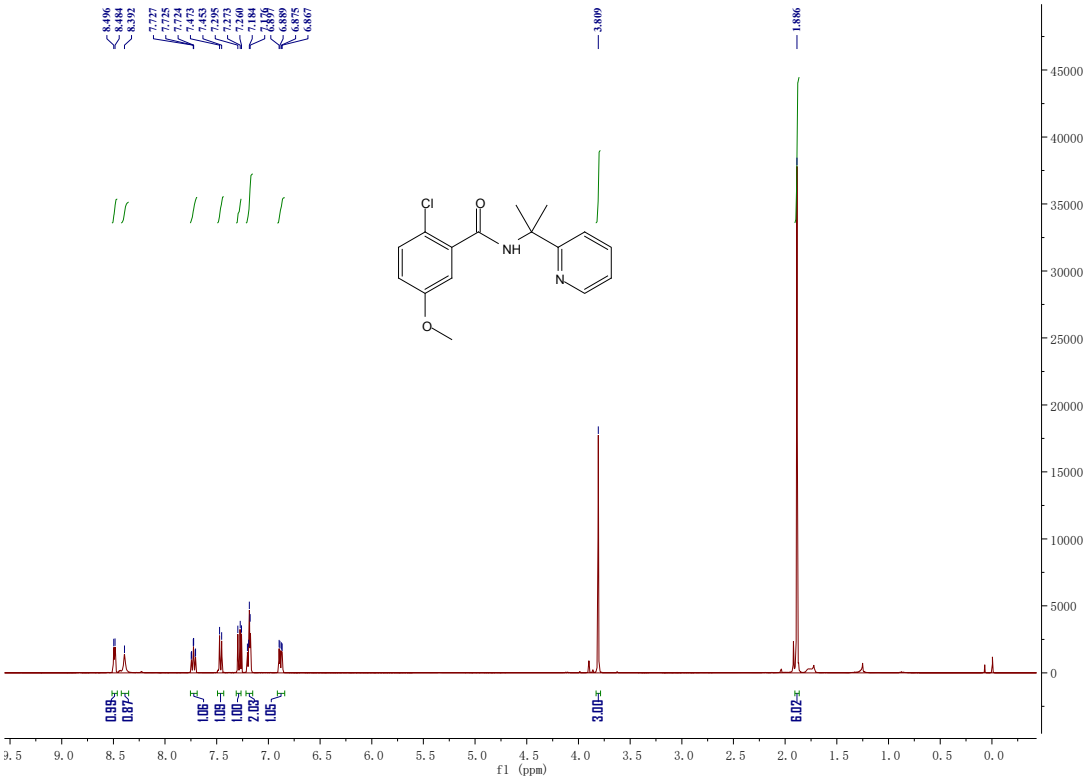

164.12
160.86
147.77
141.87
139.16
138.90
137.38
127.41
127.14
125.83
122.65
122.20
119.62
80.10
77.52
77.40
77.20
76.88
88.20
27.75
O
S
NH
N
I
f1 (ppm)

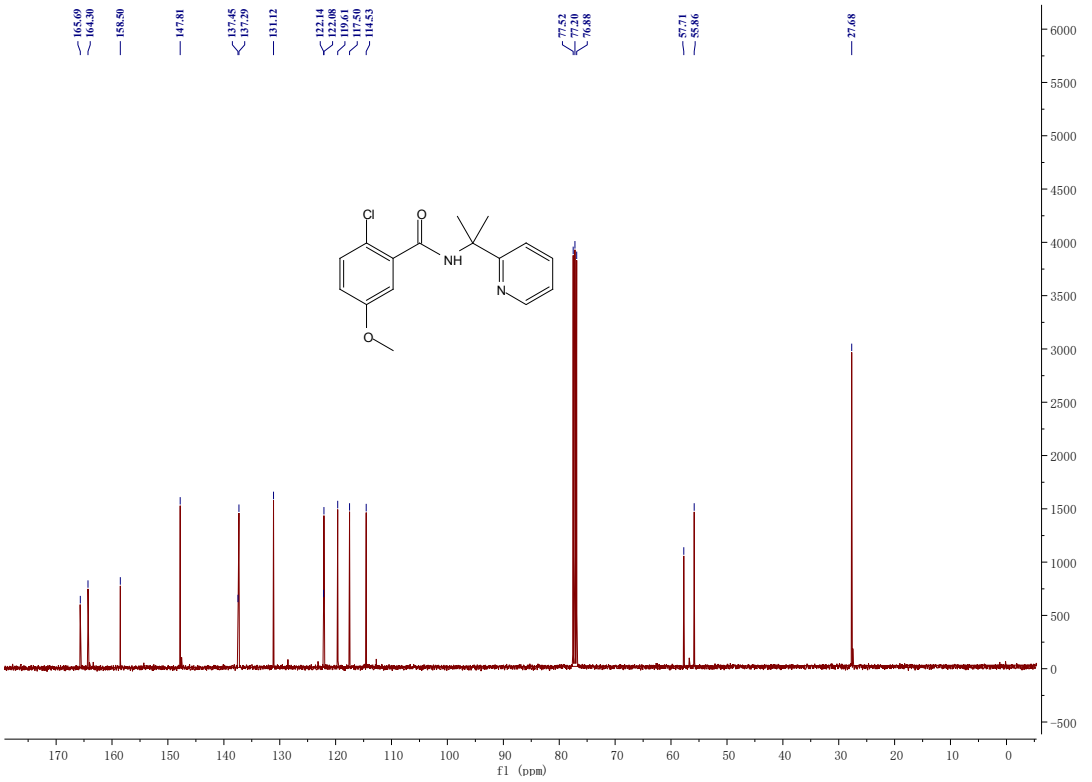
3p


8.494
8.492
8.484
8.482
8.480
8.434
7.748
7.745
7.744
7.448
7.260
7.226
7.213
7.210
7.207
7.195
1.884
1.03
0.85
1.00
1.00
1.00
5.99
I
O
NH
Cl
S
Cl
N
f1 (ppm)

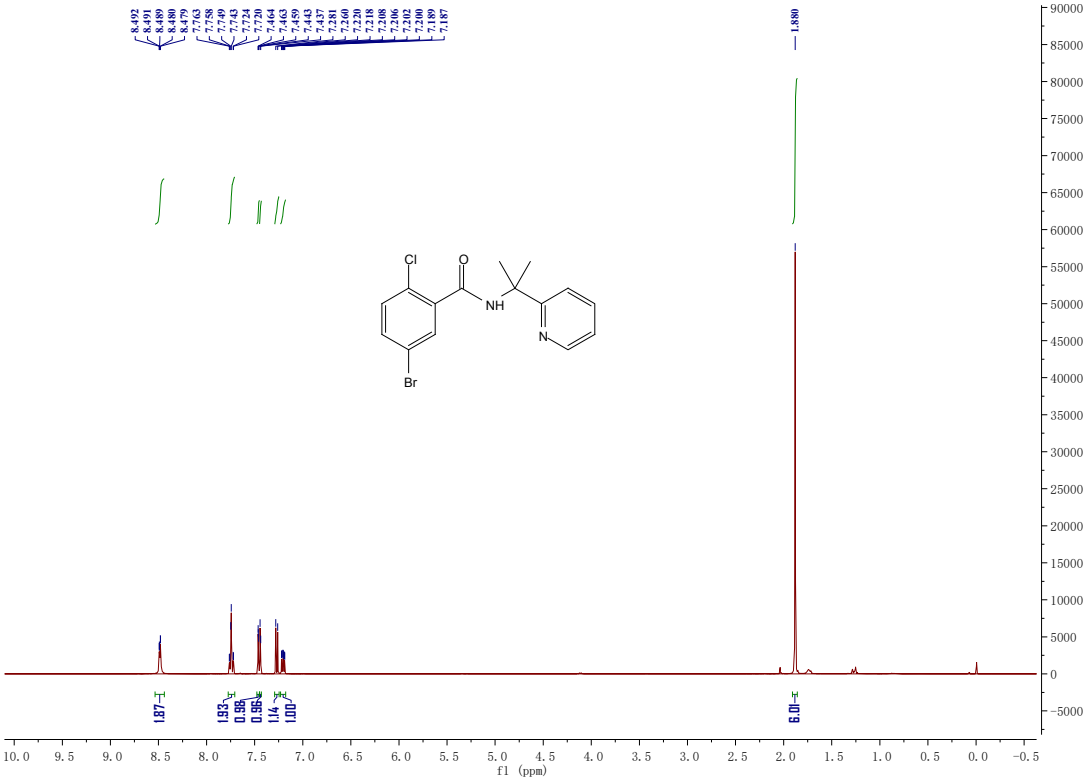

163.78
160.87
147.60
139.47
137.48
129.08
125.88
122.25
119.64
81.89
77.52
77.40
77.30
76.88
57.65
27.60
I
O
NH
Cl
S
Cl
N
f1 (ppm)

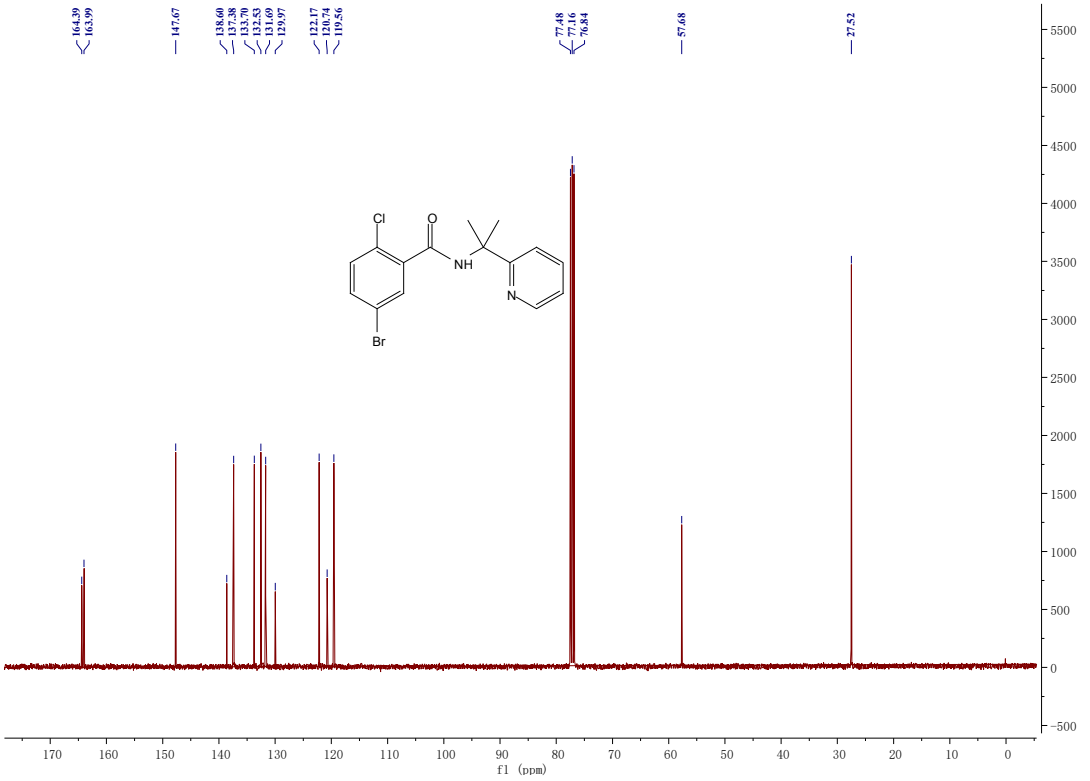
4e


8.496
8.484
8.392
7.727
7.725
7.724
7.473
7.453
7.295
7.273
7.260
7.184
6.899
6.880
6.875
6.867
3.809
1.886
Cl
O
NH
N
O
0.99
0.87
1.06
1.03
1.00
2.03
1.05
3.00
6.02
f1 (ppm)

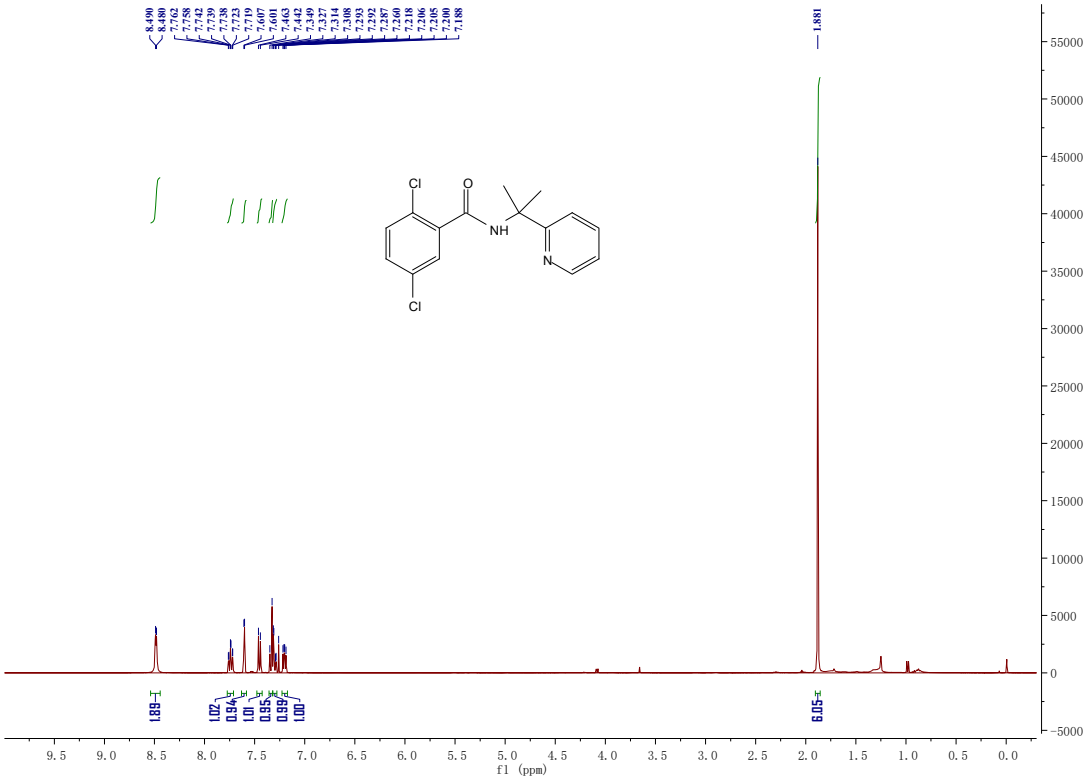

165.69
164.30
158.50
147.81
137.45
137.29
131.12
122.14
122.08
119.61
117.50
114.53
77.52
77.20
76.88
57.71
55.86
27.68
Cl
O
NH
N
O
f1 (ppm)

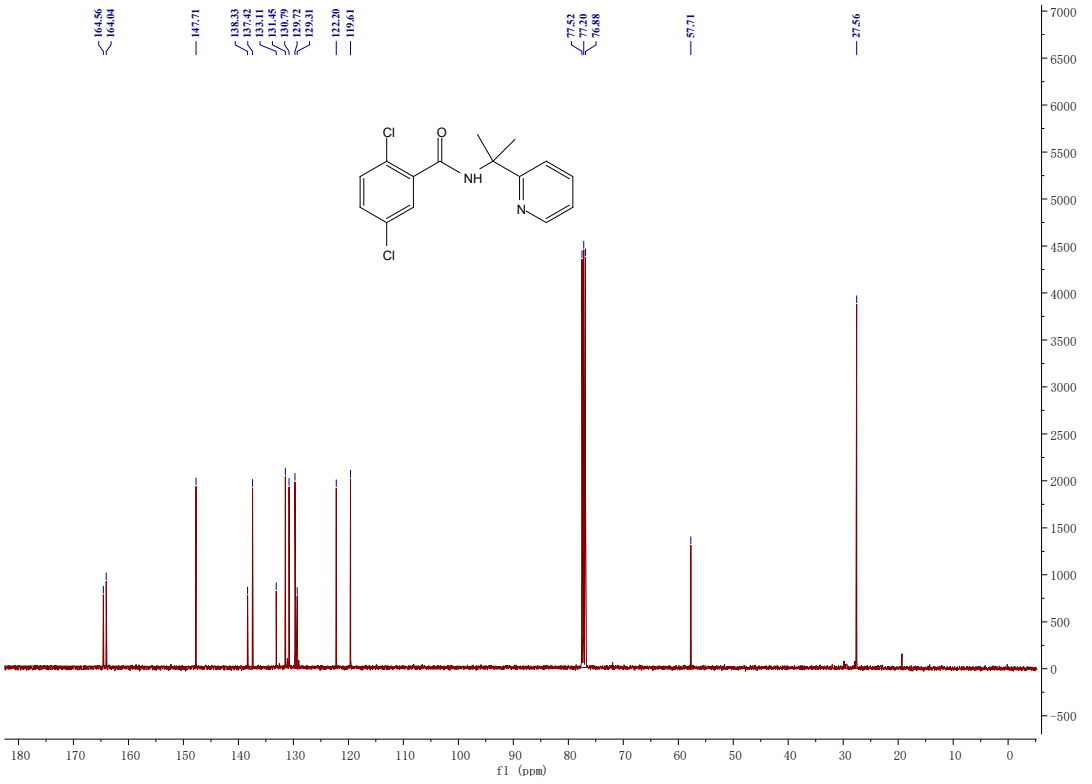
4f


8.492
8.491
8.489
8.480
8.479
7.765
7.758
7.749
7.743
7.724
7.720
7.464
7.463
7.456
7.443
7.437
7.281
7.260
7.220
7.218
7.208
7.206
7.202
7.200
7.189
7.187
1.880
Cl
O
NH
N
Br
1.87
1.93
0.98
0.96
1.14
1.00
6.01
f1 (ppm)

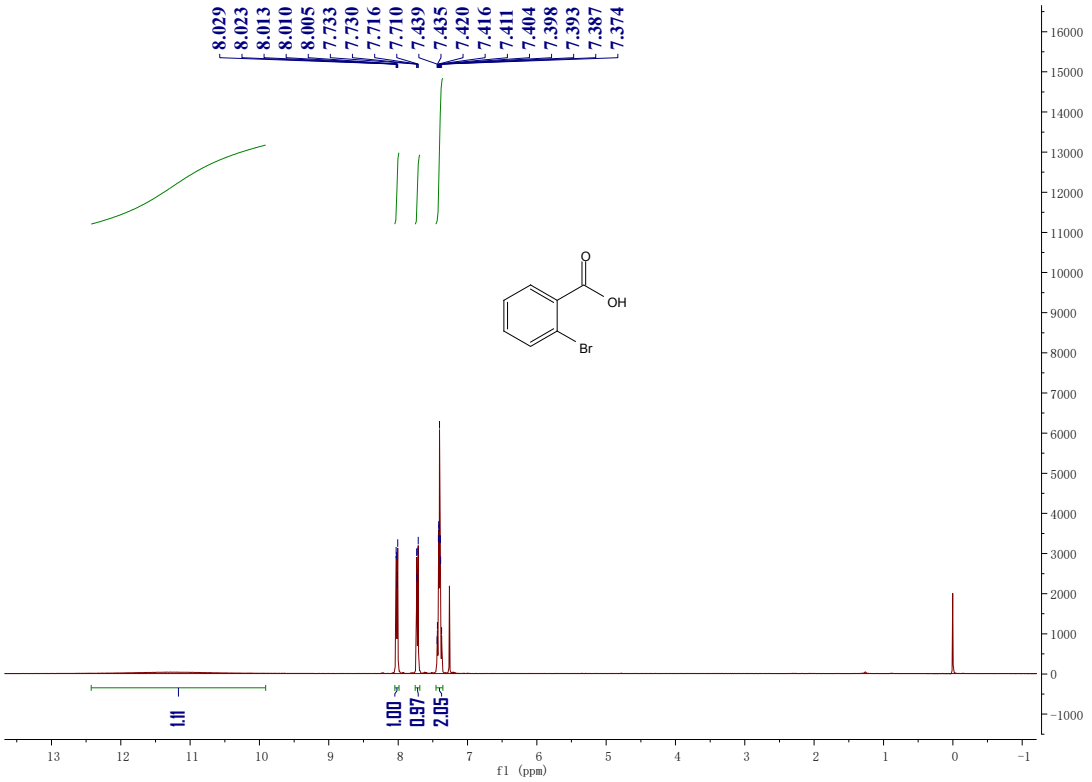

164.39
163.99
147.67
138.60
137.38
133.70
132.53
131.69
129.97
122.17
120.74
119.56
77.48
77.16
76.84
57.68
27.52
Cl
O
NH
N
Br
f1 (ppm)

4o

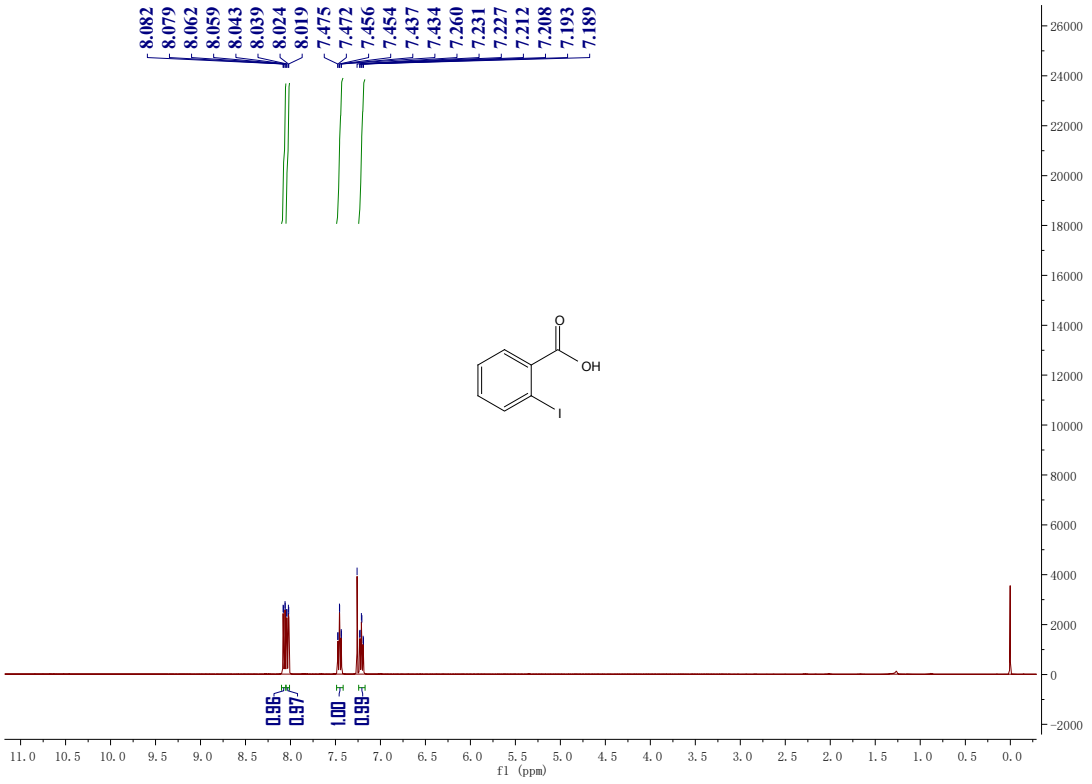

8.490
8.480
7.762
7.758
7.742
7.739
7.738
7.723
7.719
7.607
7.601
7.463
7.442
7.349
7.337
7.314
7.308
7.293
7.292
7.287
7.260
7.218
7.206
7.205
7.200
7.188
1.881
Cl
O
NH
N
Cl
1.89
1.02
0.94
1.01
0.95
0.99
1.00
6.05
f1 (ppm)


164.56
164.04
147.71
138.33
137.42
133.11
131.45
130.79
129.72
129.31
122.20
119.61
77.52
77.20
76.88
57.71
27.56
Cl
O
NH
N
Cl
f1 (ppm)

5a


8.029
8.023
8.013
8.010
8.005
7.733
7.730
7.716
7.710
7.439
7.435
7.420
7.416
7.411
7.404
7.398
7.393
7.387
7.374
O
OH
Br
1.11
1.00
0.97
2.05
f1 (ppm)

5b


8.082
8.079
8.062
8.059
8.043
8.039
8.024
8.019
7.475
7.472
7.456
7.454
7.437
7.434
7.260
7.231
7.227
7.212
7.208
7.193
7.189
O
OH
I
0.96
0.97
1.00
0.99
f1 (ppm)