iScience, Volume *23*

Supplemental Information

Tungstate-Catalyzed Biomimetic Oxidative Halogenation of (Hetero)Arene under Mild Condition

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Transparent Methods

I. General Information

Glassware and stir bars were dried in an oven at 70 °C for at least 12h and then cooled in a desiccator cabinet over Drierite prior to use. Optimization and substrate screen were performed in 20 mL vials. All other reactions were performed in round-bottom flasks sealed with rubber septa. Plastic syringes or pipets were used to transfer liquid reagents. Reactions were stirred magnetically using Teflon-coated, magnetic stir bars. Analytical thin-layer chromatography (TLC) was performed using glass plates pre-coated with 0.25 mm of 230–400 mesh silica gel impregnated with a fluorescent indicator (254 nm and 320 nm). TLC plates were visualized by exposure to ultraviolet light and/or exposure to $KMnO_4$ stain as well as phosphomolybdic acid (PMA) and cerium molybdate stain. Organic solutions were concentrated under reduced pressure using a rotary evaporator. Flash-column chromatography was performed on silica gel (60 Å, standard grade).

Materials and Instrumentation. Nuclear magnetic resonance spectra were recorded at ambient temperature (unless otherwise stated) on Bruke 400 MHz spectrometers. All values for proton chemical shifts are reported in parts per million (δ) and are referenced to the residual protium in $CDCl_3$ (δ 7.26), CD_3OD (δ 3.31) and DMSO-D_6 (δ 2.50). All values for carbon chemical shifts are reported in parts per million (δ) and are referenced to the carbon resonances in $CDCl_3$ (δ 77.0), CD_3OD (49.00) and DMSO-D_6 (39.52). NMR data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, m = multiple, br = broad), coupling constant (Hz), and integration. Infrared spectroscopic data is reported in wavenumbers (cm^{-1}). High-resolution mass spectra were obtained using a liquid chromatography-electrospray ionization and Time-of-flight mass spectrometer.

All the starting materials, including (hetero)arenes, carbonyl compounds, catalysts, oxidants, metal halide and solvents were commercially available. All the reaction solvents were not anhydrous.

II. General procedure for oxidative halogenation

General procedure A for oxidative bromination of (hetero)arene or activated carbonyl compounds. To the mixture of (hetero)arene or carbonyl compounds (**1**, 1.0 mmol, 1.0 equivalent), Na_2WO_4-$2H_2O$ (16 mg, 0.05 mmol, 5 mol %) and NaBr (112 mg, 1.1 mmol, 1.1 equivalent) was added 5.0 mL EtOH. After compound **1** was dissolved in EtOH, HOAc (66 mg, 66 μL, 1.1 mmol, 1.1 equivalent) followed by adding H_2O_2 (30% aq., 0.6 mL, 6.0 mmol, 6.0 equivalent). The reaction was conducted at 30℃ until compound **1** was all consumed (for some substrates the reactions were stopped with conversion less than 100% due to low reaction rate). Next around 100 mL EtOAc was added to dilute the reaction solution. The reaction mixture was then washed by H_2O (20 mL), $NaHCO_3$ (aq., 20 mL), brine (20 mL), and dried with Na_2SO_4. The desired product **2** was isolated after filtration, concentration, and flash chromatography. The dibromination reaction was conducted with 2.2 equivalent of NaBr and HOAc (**Figure S1**).

Figure S1. Oxidative bromination of (hetero)arenes and carbonyl compounds, related to Table 2

General procedure B for oxidative bromination of (hetero)arene in water. The reactions were conducted in the similar manner as **General Procedure A**: Na_2WO_4-$2H_2O$ (2.5 mol%), NaBr (1.1 equivalent), H_2O_2 (30% aq., 1.1 equivalent) and HOAc (1.1 equivalent) in 5.0 mL H_2O (**Figure S2**).

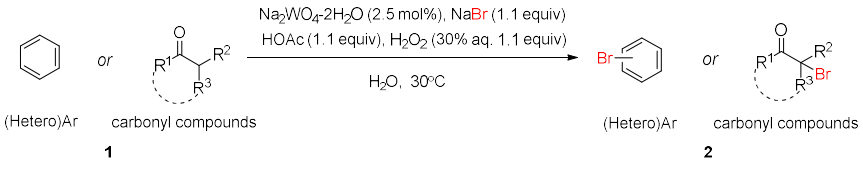


Figure S2. Oxidaive bromination of (hetero)arene in water, related to Table 2

General procedure C for oxidative chlorination of (hetero)arene and carbonyl compounds. To the mixture of (hetero)arene or carbonyl compounds (**1**, 1.0 mmol, 1.0 equivalent), K_2WO_4 (16 mg, 0.05 mmol, 5 mol %) and

$BaCl_2 \cdot 2H_2O$ (293 mg, 1.2 mmol, 1.2 equivalent) was added 5.0 mL MeCN. After compound **1** was dissolved in MeCN, HOAc (66 mg, 60 μL, 1.0 mmol, 1.0 equivalent) followed by adding H_2O_2 (30% aq., 0.4 mL, 4.0 mmol, 4.0 equivalent). The reaction was conducted at 50℃ until compound **1** was all consumed (for some substrates the reactions were stopped with conversion less than 100% due to low reaction rate). Next EtOAc (100 mL) was added to dilute the reaction solution, followed by being washed with H_2O (20 mL), $NaHCO_3$ (aq., 20 mL), brine (20 mL), and dried by Na_2SO_4. The chlorination product **2** were isolated after filtration, concentration and flash chromatography (**Figure S3**).

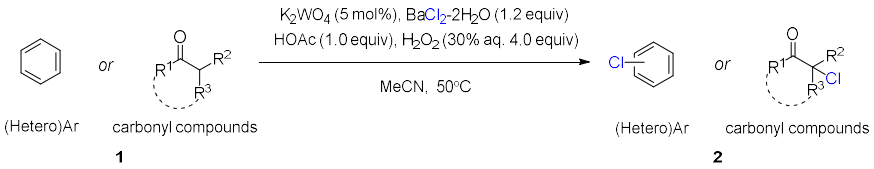


Figure S3. Oxidative chlorination of (hetero)arenes and carbonyl compounds, related Table 3

General procedure D for oxidative iodination of (hetero)arene. The reactions were conducted in the same manner as **General Procedure A** by employing KI at room temperature. The diiodination reaction was conducted with 2.2 equivalent of KI and HOAc (**Figure S4**).

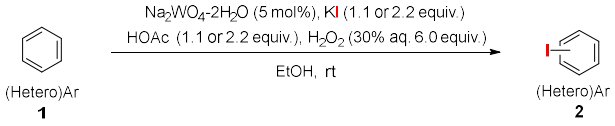


Figure S4. Oxidative iodination of (hetero)arenes, related Table 3

General procedure E 100-gram scale reaction. The reactions were conducted in the similar fashion as **General Procedure A**. The starting material (hetero)arene, $Na_2WO_4 \cdot 2H_2O$, NaBr and HOAc was dissolved in minimum amount of EtOH/H_2O, followed by adding H_2O_2 slowly at room temperature. Upon completion, the desired product **2** participated as solid due to lower solubility. Thus, the pure product was obtained simply by filtration, washed with H_2O and EtOH, and dried in *vacuum* (**Figure S5**).

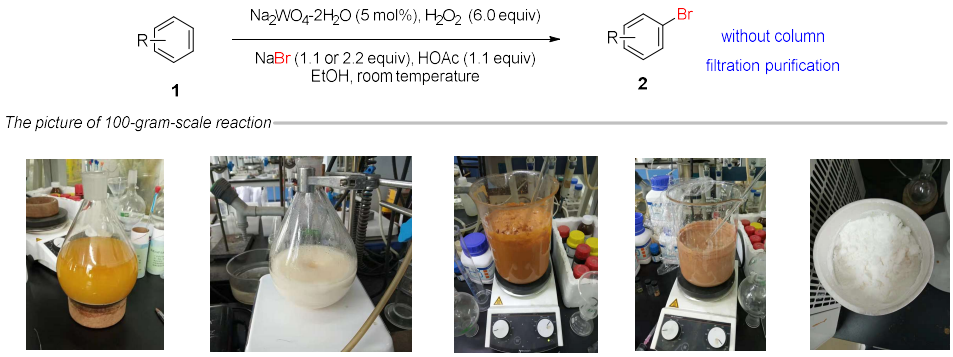
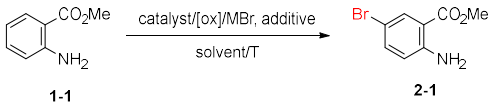


Figure S5. 100 g scale reactions, related to Table 4

III. Condition optimization

Table S1. Condition optimization for tungstate-catalyzed oxidative bromination 1, relate Table 1

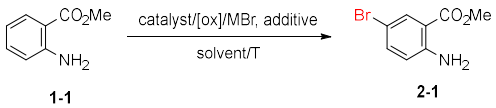


1-1 2-1

Entry	Catalyst (mol%)	[ox] (eq.)	MBr (eq.)	additive (eq.)	solvent	T/°C	yeild(%)[a]
MBr source screeing							
1	Na_2WO_4-$2H_2O$ (5)	H_2O_2 (6.0)	LiBr (1.0)	HOAc (1.0)	EtOH	50	62
2	Na_2WO_4-$2H_2O$ (5)	H_2O_2 (6.0)	LiBr (1.5)	HOAc (2.0)	EtOH	50	66
3	Na_2WO_4-$2H_2O$ (5)	H_2O_2 (6.0)	KBr (1.5)	HOAc (2.0)	EtOH	50	75
4	Na_2WO_4-$2H_2O$ (5)	H_2O_2 (6.0)	NaBr (1.5)	HOAc (2.0)	EtOH	50	84
5	Na_2WO_4-$2H_2O$ (5)	H_2O_2 (6.0)	NaBr (1.1)	HOAc (1.5)	EtOH	50	79
6	Na_2WO_4-$2H_2O$ (5)	H_2O_2 (6.0)	NaBr (1.1)	HOAc (1.5)	EtOH	30	78
7	Na_2WO_4-$2H_2O$ (5)	H_2O_2 (6.0)	NaBr (1.1)	HOAc (1.1)	EtOH	30	77-83
Catalyst screening							
8	$(NH_4)_{10}(H_2W_{12}O_{42})$-$xH_2O$ (5)	H_2O_2 (6.0)	NaBr (1.5)	HOAc (2.0)	EtOH	30	77
9	$H_3O_{40}PW_{12}$•xH_2O (5)	H_2O_2 (6.0)	NaBr (1.5)	HOAc (2.0)	EtOH	30	64
10	K_2WO_4 (5)	H_2O_2 (6.0)	NaBr (1.5)	HOAc (2.0)	EtOH	30	74
11	$CaWO_4$ (5)	H_2O_2 (6.0)	NaBr (1.5)	HOAc (2.0)	EtOH	30	71
12	Na_2WO_4-$2H_2O$ (1)	H_2O_2 (6.0)	NaBr (1.1)	HOAc (1.1)	EtOH	30	67
13	--	H_2O_2 (6.0)	NaBr (1.5)	HOAc (2.0)	EtOH	30	trace
Oxidant screening							
14	Na_2WO_4-$2H_2O$ (5)	^{t}BuOOH (6.0)	NaBr (1.5)	HOAc (2.0)	EtOH	30	N.R
15	Na_2WO_4-$2H_2O$ (5)	SPB (6.0)	NaBr (1.5)	HOAc (2.0)	EtOH	30	N.R
16	Na_2WO_4-$2H_2O$ (5)	--	NaBr (1.5)	HOAc (2.0)	EtOH	30	N.R
17	Na_2WO_4-$2H_2O$ (5)	H_2O_2 (4.0)	NaBr (1.5)	HOAc (2.0)	EtOH	30	conversion<50%
18	Na_2WO_4-$2H_2O$ (5)	H_2O_2 (2.0)	NaBr (1.1)	HOAc (1.1)	EtOH	30	57

a: all the reaction was conducted in 1.0 mmol scale (**1-1**), stirring for 12h, isolated yield

Table S2. Condition optimization for tungstate-catalyzed oxidative bromination 2, relate Table 1 and Figure 3

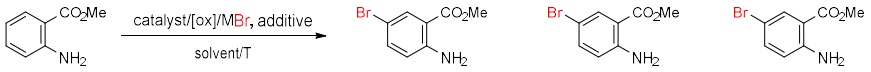


1-1 **2-1**

Entry	Catalyst (mol%)	[ox] (eq.)	MBr (eq.)	additive (eq.)	solvent	T/°C	yeild(%)[a]
Solvent screening							
1	Na_2WO_4-$2H_2O$ (5)	H_2O_2 (6.0)	*NaBr (1.1)*	HOAc (1.0)	EtOH	30	*78-83*
2	Na_2WO_4-$2H_2O$ (5)	H_2O_2 (6.0)	*NaBr (1.1)*	HOAc (2.0)	MeOH	30	67
3	Na_2WO_4-$2H_2O$ (5)	H_2O_2 (6.0)	*NaBr (1.1)*	HOAc (2.0)	iPrOH	30	85
4	Na_2WO_4-$2H_2O$ (5)	H_2O_2 (6.0)	*NaBr (1.1)*	HOAc (2.0)	THF	30	conversion<50%
5	Na_2WO_4-$2H_2O$ (5)	H_2O_2 (6.0)	NaBr (1.1)	HOAc (1.5)	MeCN	30	conversion<50%
6	*Na_2WO_4-$2H_2O$ (5)*	*H_2O_2 (6.0)*	*NaBr (1.1)*	*HOAc (1.5)*	*EtOAc*	30	conversion<50%
7	Na_2WO_4-$2H_2O$ (5)	H_2O_2 (6.0)	NaBr (1.1)	HOAc (1.1)	Toluene	30	N.R
8	Na_2WO_4-$2H_2O$ (5)	H_2O_2 (6.0)	NaBr (1.1)	HOAc (1.1)	DCM	30	N.R
9	Na_2WO_4-$2H_2O$ (5)	H_2O_2 (6.0)	NaBr (1.1)	HOAc (1.1)	DMF	30	N.R

a: all the reactions were conducted in 1.0 mmol scale (**1-1**), 12h, isolated yield; N.R = No reaction

Table S3. Condition optimization for tungstate-catalyzed oxidative bromination in water, relate Table 1 and 2



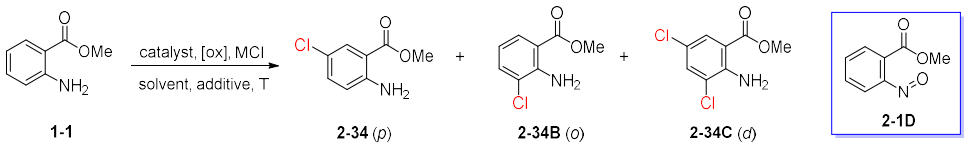
1-1 **2-1** **2-1B** **2-1C**

entry	Catalyst (mol%)	[ox] (equiv.)	MBr (equiv.)	Additive (equiv.)	solvent	T/°C	time	**2-1:2-1B:2-1C** [a]
1	$NaWO_4$-$2H_2O$ (5.0)	H_2O_2 (6)	NaBr (1.2)	HOAc (1.1)	H_2O	30	24	12:1.5:1
2	$NaWO_4$-$2H_2O$ (2.5)	H_2O_2 (6)	NaBr (1.2)	HOAc (1.1)	H_2O	30	24	>20:1:1
3	$NaWO_4$-$2H_2O$ (1.0)	H_2O_2 (6)	NaBr (1.2)	HOAc (1.1)	H_2O	30	18	10:1:0
4	$NaWO_4$-$2H_2O$ (2.5)	H_2O_2 (3)	NaBr (1.2)	HOAc (1.1)	H_2O	30	18	10:1:0
5	$NaWO_4$-$2H_2O$ (2.5)	H_2O_2 (1.5)	NaBr (1.2)	HOAc (1.1)	H_2O	30	16.5	>98:1:1
6	$NaWO_4$-$2H_2O$ (2.5)	H_2O_2 (1.1)	NaBr (1.2)	HOAc (1.1)	H_2O	30	21.5	10.0:1
Control experiment								
7	--	H_2O_2 (1.1)	NaBr (1.1)	HOAc (1.1)	H_2O	30	16	trace
8	$NaWO_4$-$2H_2O$ (5)	H_2O_2 (1.1)	NaBr (1.1)	--	H_2O	30	16	conversion<10%
9	--	H_2O_2 (1.1)	NaBr (1.1)	--	H_2O	30	16	N.R

a: all the reactions were run in 1.0 mmol scale (**1-1**), the ration between **2-1**, **2-1B** and **2-1C** was determined by H-NMR of crude products without purfication, and the conversion = 100%; N.R = No Reaction

Although this reaction work well in water, however, only limited substrates can be solved in H_2O. Therefore, currently the reaction in EtOH is still favored.

Table S4. Condition optimization for tungstate-catalyzed oxidative chlorination, related to Table 3 and Figure 3

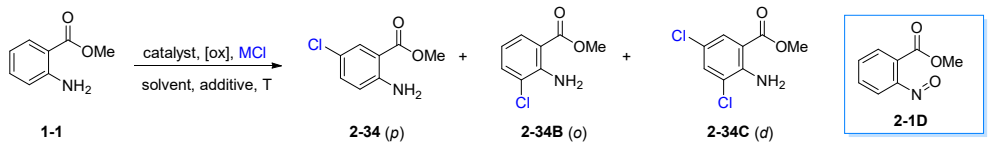


1-1 **2-34** (*p*) **2-34B** (*o*) **2-34C** (*d*) **2-1D**

entry[a]	MCl (eq.)	cat (mol%)	solvent	additive (eq.)	[ox] (eq.)	T(°C)	time (h)	yield (%*p*/*o*/*d*[b])
Chloride source screening								
1	NaCl (1.2)	Na_2WO_4 (5)	EtOH	AcOH (1.0)	H_2O_2 (6.0)	50	34	N.D[c]
2	KCl (1.2)	Na_2WO_4 (5)	EtOH	AcOH (1.0)	H_2O_2 (6.0)	50	22	N.D[c]
3	LiCl (1.2)	Na_2WO_4 (5)	EtOH	AcOH (1.0)	H_2O_2 (6.0)	50	22	N.D[c]
4	NH_4Cl(1.2)	Na_2WO_4 (5)	EtOH	AcOH(1.0)	H_2O_2 (6.0)	50	11	N.D[c]
5	$CaCl_2$(1.2)	Na_2WO_4 (5)	EtOH	AcOH (1.0)	H_2O_2 (6.0)	50	5.5	8/0/38
6	$BaCl_2$-$2H_2O$ (1.2)	Na_2WO_4 (5)	EtOH	AcOH (1.0)	H_2O_2 (6.0)	50	8.5	63(*p*+*o*)/0
7	$CdCl_2$(1.2)	Na_2WO_4 (5)	EtOH	AcOH (1.0)	H_2O_2 (6.0)	50	21.5	N.D[c]
8	$SrCl_2$(1.2)	Na_2WO_4 (5)	EtOH	AcOH (1.0)	H_2O_2 (6.0)	50	9.5	0//0/44
9	$ScCl_3$(1.2)	Na_2WO_4 (5)	EtOH	AcOH (1.0)	H_2O_2 (6.0)	50	9.5	0/0/43
10	$ZrCl_4$(1.2)	Na_2WO_4 (5)	EtOH	AcOH (1.0)	H_2O_2 (6.0)	50	8.5	0/0/17

a: all the reactions were conducted in 1.0 mmol scale (**1-1**); b: isolated yield after silica gel column; c: trace or no desired product, the nitroso byproduct **2-1D** was isolated as major product; N.D = not determined

Table S5. Condition optimization for tungstate-catalyzed oxidative chlorination 2, related to Table 3 and Figure 3



1-1 **2-34** (*p*) **2-34B** (*o*) **2-34C** (*d*)

entry[a]	MCl (eq.)	cat (mol%)	solvent	additive (eq.)	[ox] (eq.)	T(°C)	time (h)	yield (%, *p*/*o*/*d*[b])
Solvent screening								
6	$BaCl_2$-$2H_2O$ (1.2)	Na_2WO_4-$2H_2O$ (5)	EtOH	AcOH (1.0)	H_2O_2 (6.0)	50	8.5	63 (*p*+*o*)/0
11	$BaCl_2$-$2H_2O$ (1.2)	Na_2WO_4-$2H_2O$ (5)	^{i}PrOH	AcOH (1.0)	H_2O_2 (6.0)	50	85.5	N.D[c]
12	$BaCl_2$-$2H_2O$ (1.2)	Na_2WO_4-$2H_2O$ (5)	MeOH	AcOH (1.0)	H_2O_2 (6.0)	50	63	N.D[c]
13	$BaCl_2$-$2H_2O$ (1.2)	Na_2WO_4-$2H_2O$ (5)	CH_3CN	AcOH (1.0)	H_2O_2 (6.0)	50	65.5	57/22/0
14	$BaCl_2$-$2H_2O$ (1.2)	Na_2WO_4-$2H_2O$ (5)	EtOAc	AcOH (1.0)	H_2O_2 (6.0)	50	97	N.D[c]
15	$BaCl_2$-$2H_2O$ (1.2)	Na_2WO_4-$2H_2O$ (5)	THF	AcOH (1.0)	H_2O_2 (6.0)	50	97	N.D[c]
16	$BaCl_2$-$2H_2O$ (1.2)	Na_2WO_4-$2H_2O$ (5)	H_2O	AcOH (1.0)	H_2O_2 (6.0)	50	16.5	trace
17	$BaCl_2$-$2H_2O$ (1.2)	Na_2WO_4-$2H_2O$ (5)	toluene	AcOH (1.0)	H_2O_2 (6.0)	50	47	N.D[c]
18	$BaCl_2$-$2H_2O$ (1.2)	Na_2WO_4-$2H_2O$ (5)	TFE	AcOH (1.0)	H_2O_2 (6.0)	50	40	N.D[c]
19	$BaCl_2$-$2H_2O$ (1.2)	$(NH_4)_{10}[H_2W_{12}O_{42}]$ (5)	EtOH	AcOH (1.0)	H_2O_2 (6.0)	50	27	24/20/0
20	$BaCl_2$-$2H_2O$ (1.2)	$H_3O_{40}PW_{12}$ (5)	EtOH	AcOH (1.0)	H_2O_2 (6.0)	50	22.5	3/20/0
21	$BaCl_2$-$2H_2O$ (1.2)	K_2WO_4 (5)	CH_3CN	AcOH (1.0)	H_2O_2 (6.0)	50	11	57/23/0
22	$BaCl_2$-$2H_2O$ (1.2)	$CaWO_4$ (5)	CH_3CN	AcOH (1.0)	H_2O_2 (6.0)	50	57.5	N.D[c]
Additive screening								
23	$BaCl_2$-$2H_2O$ (1.2)	Na_2WO_4-$2H_2O$ (5)	EtOH	CCl_3COOH (1.0)	H_2O_2 (6.0)	50	23	N.D[c]
24	$BaCl_2$-$2H_2O$ (1.2)	Na_2WO_4-$2H_2O$ (5)	EtOH	CF_3COOH(1.0)	H_2O_2 (6.0)	50	23	0/0/12
25	$BaCl_2$-$2H_2O$ (1.2)	Na_2WO_4-$2H_2O$ (5)	EtOH	Benzoic acid (1.0)	H_2O_2 (6.0)	50	35	32/8/0
26	$BaCl_2$-$2H_2O$ (1.2)	Na_2WO_4-$2H_2O$ (5)	EtOH	Crylic acid (1.0)	H_2O_2 (6.0)	50	35	18/9/0
Oxidant screening and control experiments								
27	$BaCl_2$-$2H_2O$ (1.2)	K_2WO_4 (5)	CH_3CN	AcOH (1.0)	H_2O_2 (4.0)	50	11	56/26/0
28	$BaCl_2$-$2H_2O$ (1.2)	K_2WO_4 (5)	CH_3CN	AcOH (1.0)	H_2O_2 (3.0)	50	47	44/33/0
29	$BaCl_2$-$2H_2O$ (1.2)	Na_2WO_4 (5)	EtOH	AcOH (1.0)	SPB (3.0)	50	59	N.D[c]
30	$BaCl_2$-$2H_2O$ (1.2)	K_2WO_4(5)	CH_3CN	AcOH(1.0)	H_2O_2(2.0)	50	110.5	60/20/0
31	$BaCl_2$-$2H_2O$ (1.2)	K_2WO_4(5)	CH_3CN	AcOH (1.0)	H_2O_2 (1.0)	50	153.5	conversion low
32	$BaCl_2$-$2H_2O$ (1.2)	K_2WO_4(2.5)	CH_3CN	AcOH (1.0)	H_2O_2 (4.0)	50	142	conversion low
33	$BaCl_2$-$2H_2O$ (1.2)	K_2WO_4 (5)	CH_3CN	AcOH (1.0)	H_2O_2 (4.0)	RT	84	conversion low
34	$BaCl_2$-$2H_2O$ (1.2)	none	CH_3CN	AcOH (1.0)	H_2O_2 (4.0)	50	11.5	N.R
35	$BaCl_2$-$2H_2O$ (1.2)	K_2WO_4(5)	CH_3CN	AcOH (1.0)	none	50	11.5	N.R

a. all the reactions were conducted in 1.0 mmol scale (**1-1**); b: isolated yield; c: major product is 2-1D; N.D = not determined; N.R = No reaction; TFE = trifluroethanol; SPB = sodium perborat.

V. Byproducts detection

For some substrates, the chemo- or regioselectivivties are not good, and more than one products were isolated as shown in following. The most frequently encountered byproducts in this reaction come from dibromination. But for some free anilines, the formation of nitroso or azoxy might also be involved.

During the condition optimization, the major byproduct **2-1D** was observed during condition optimization along with the isomer of bromination product (**2-1B**, methyl 2-amino-3-bromobenzoate) and dibromination product **2-1C**. Product **2-1B** and **2-1C** were very close to each other on TLC plate and difficult for isolation (**Figure S6**).

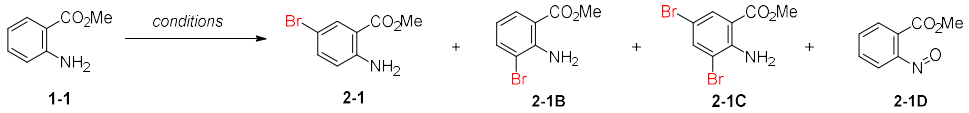


Figure S6. Byproducts formation during condition optimization, related to Table 1

The bromination of methyl 1*H*-pyrrole-2-carboxylate proceeded according to according to **General Procedure A** for 24h, affording two products (**2-20** and **2-20B**) (**Figure S7**).

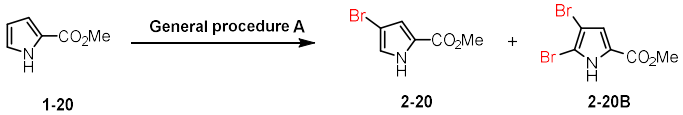


Figure S7. Bromination of 1*H*-pyrrole-2-carboxylate, related to Table 2

The bromination of isoquinolin-5-amine proceeded according to according to **General Procedure A** for 24 h, and two products (**2-24** and **2-24B**) were isolated (**Figure S8**).

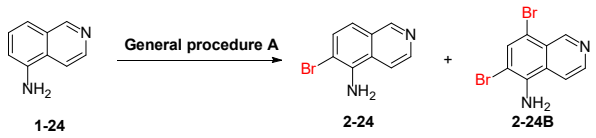


Figure S8. Bromination of isoquinolin-5-amine, related to Table 2

The bromination of estrone proceeded according to according to **General Procedure A** for 6 days, affording products **2-28** (153 mg, 44% yield) and **2-28B** (16 mg, 4% yield), and estrone was recycled 37.2 mg (14% yield) (**Figure S9**).

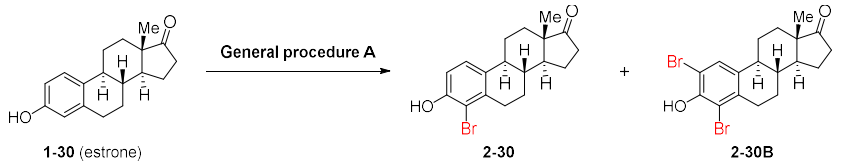


Figure S9. Bromination of estrone, related to Table 2

The bromination of cytarabine was conducted according to **General Procedure A** in water for 5.5h. Given that cytarabine and its bromination product **2-31** were well dissolved in water, the yield was determined by H-NMR of crude product after simply removing all the reaction solvent as a white liquid (396 mg) (**Figure S10**).

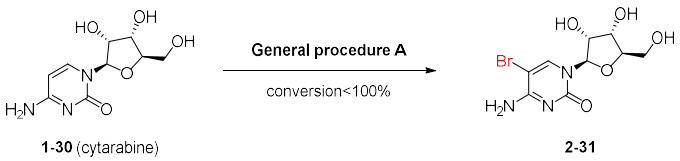


Figure S10. Bromination of cytarabine, related to Table 2

The oxidative bromination of naringin proceeded according to **General Procedure A** in 1.0 mmol scale. The crude mixture of products was obtained after the reaction went on for 35h as white solid. Both naringin and the bromination products (**2-32** and **2-32B**) were well dissolved in water due to the disaccharide chain, thus the conversion and yield was determined by H-NMR of this crude mixture (**Figure S11**).

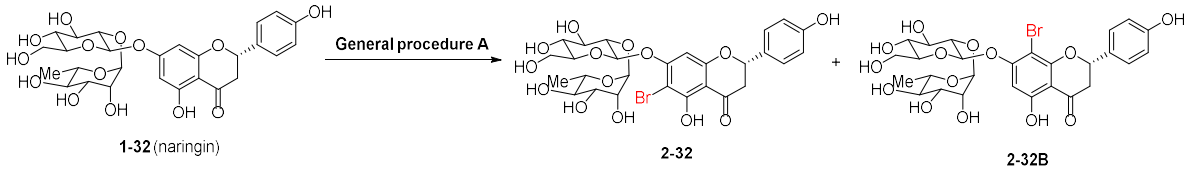


Figure S11. Bromination of cytarabine, related Table 2

The chlorination of methyl 2-aminobenzoate proceeded according to according to **General Procedure C** for 11h, affording products **2-34** and **2-34B** (**Figure S12**).

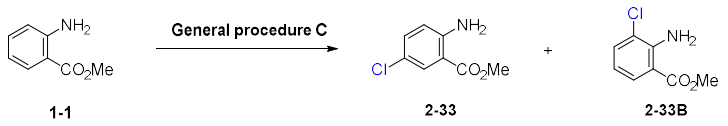


Figure S12. Chlorination of methyl 2-aminobenzoate, related to Table 3

The chlorination of methyl 4-phenylmorpholine was conducted according to **General Procedure C** for 16.5h, affording products **2-35** and **2-35B** (**Figure S13**).

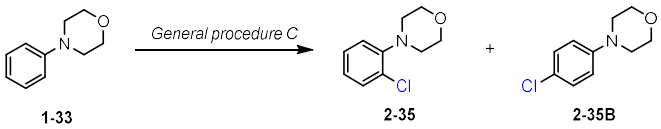


Figure S13. Chlorination of 4-phenylmorpholine, related to Table 3

VI. Mechanism study

In order to dig out more details of the reaction mechanism, compound 1, 2-dimethoxy-3-methylbenzene (**1-45**) was probed in bromiantion reactions. Product **2-61** was isolated in moderate yield, while **2-62** was not observed, thus excluding the existence of bromine radical intermediate during the reaction (**Figure S14, Figure 3a**).

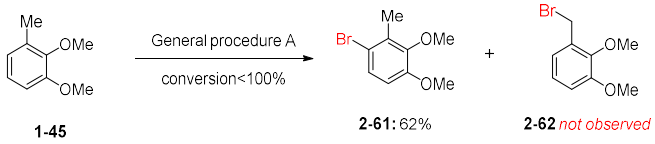


Figure S14. Primary mechanism study, related Figure 3

VII. NMR Spectrums of intermediates and products

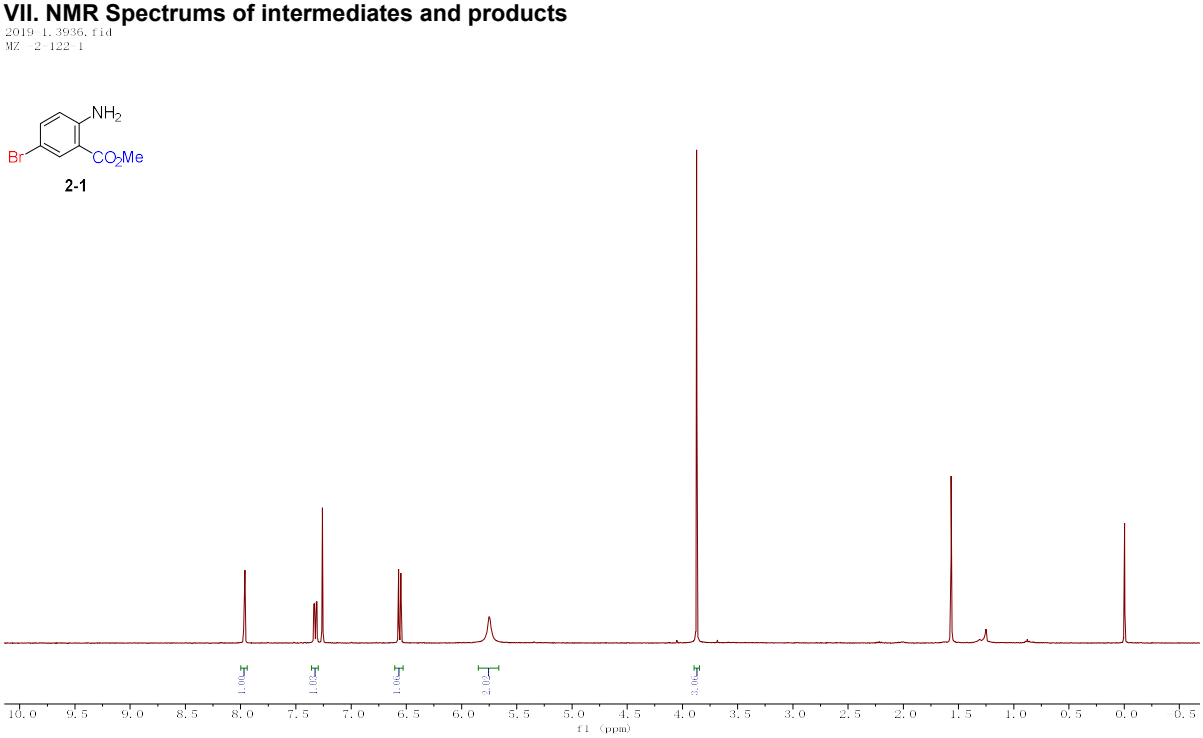


Figure S15. ^{1}H NMR of product **2-1**, related Table 2

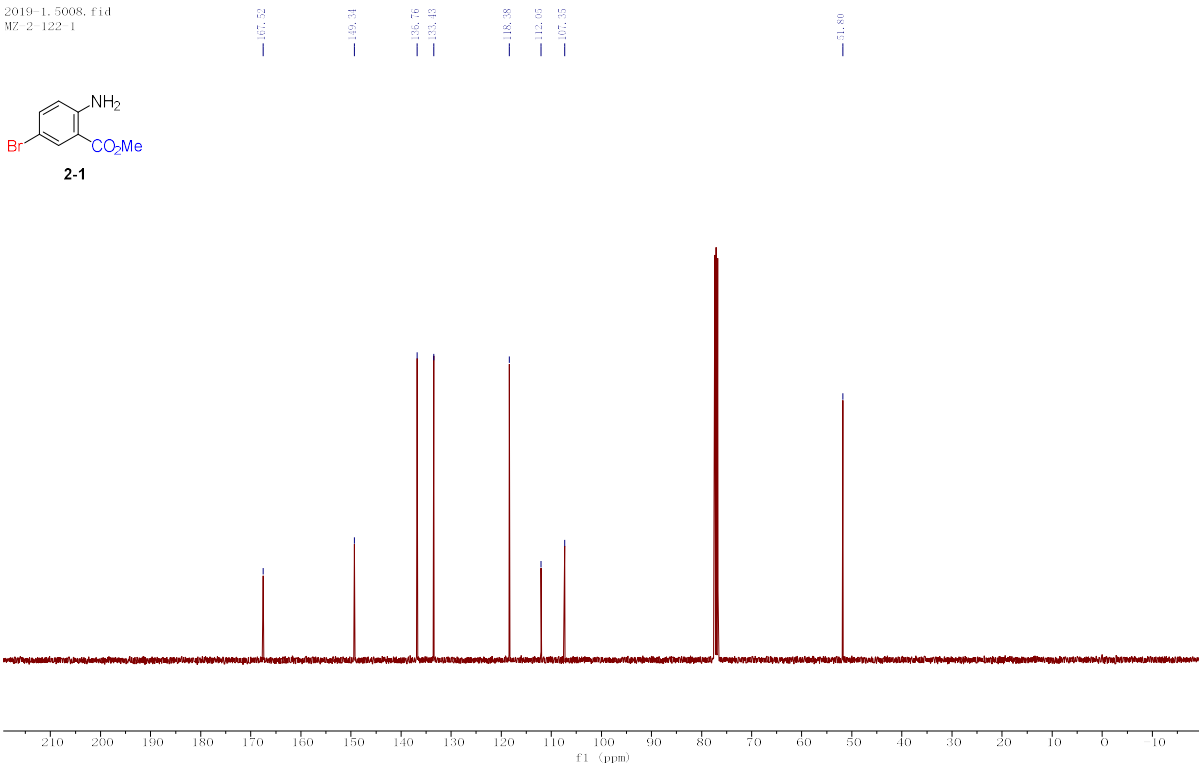


Figure S16. ^{13}C NMR of product **2-1**, related Table 2

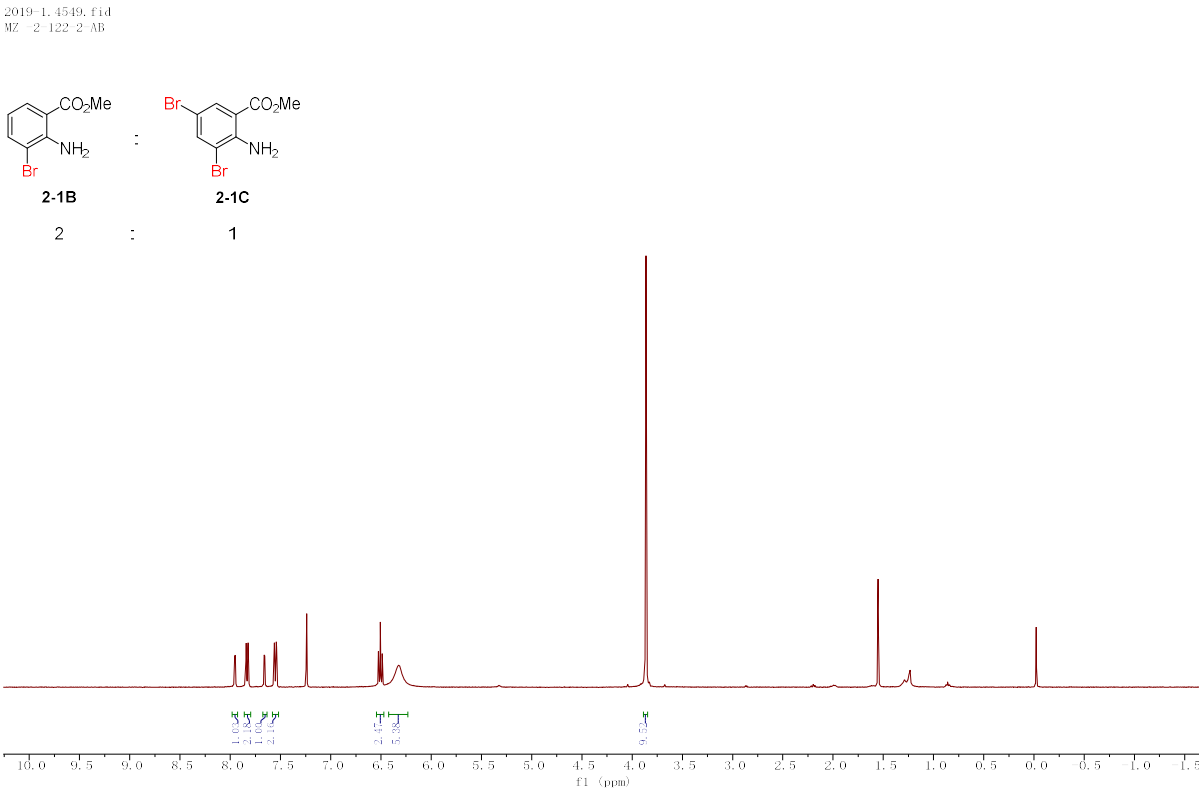


Figure S17. ^{1}H-NMR of products **2-1B** and **2-1C**, related Table 1

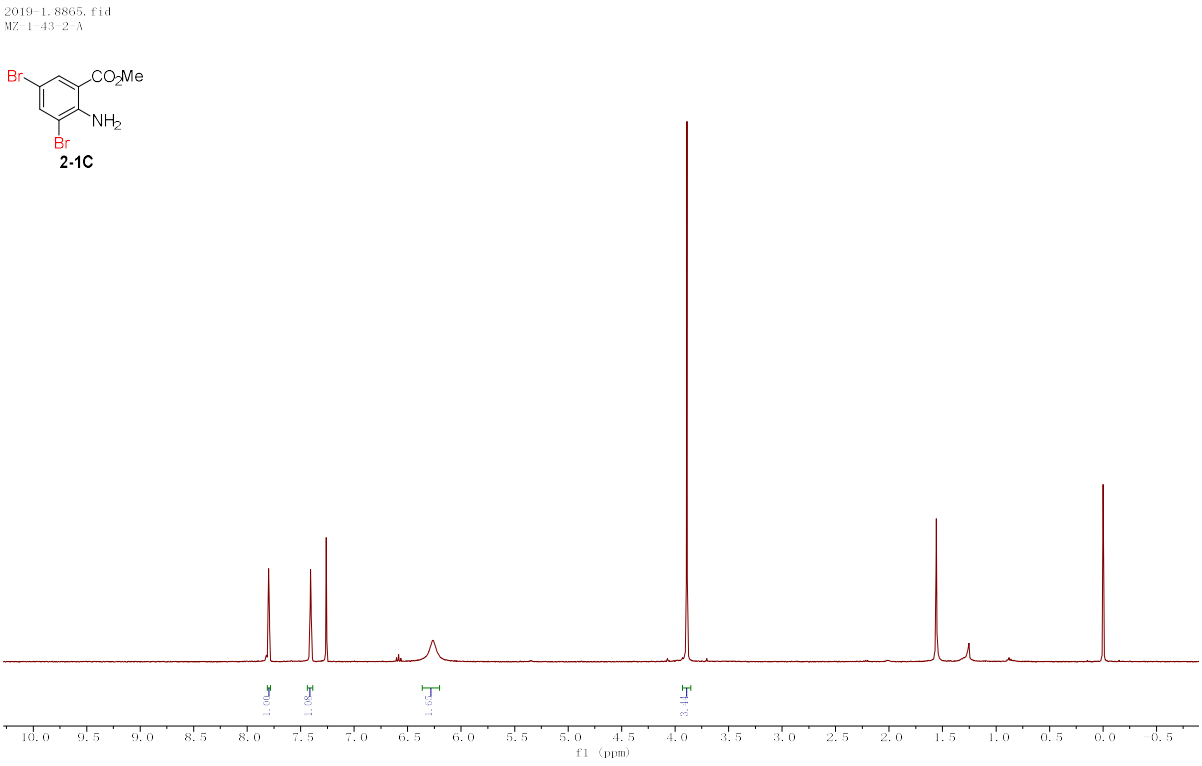


Figure S18. ^{1}H NMR of product **2-1C**, related Table 1

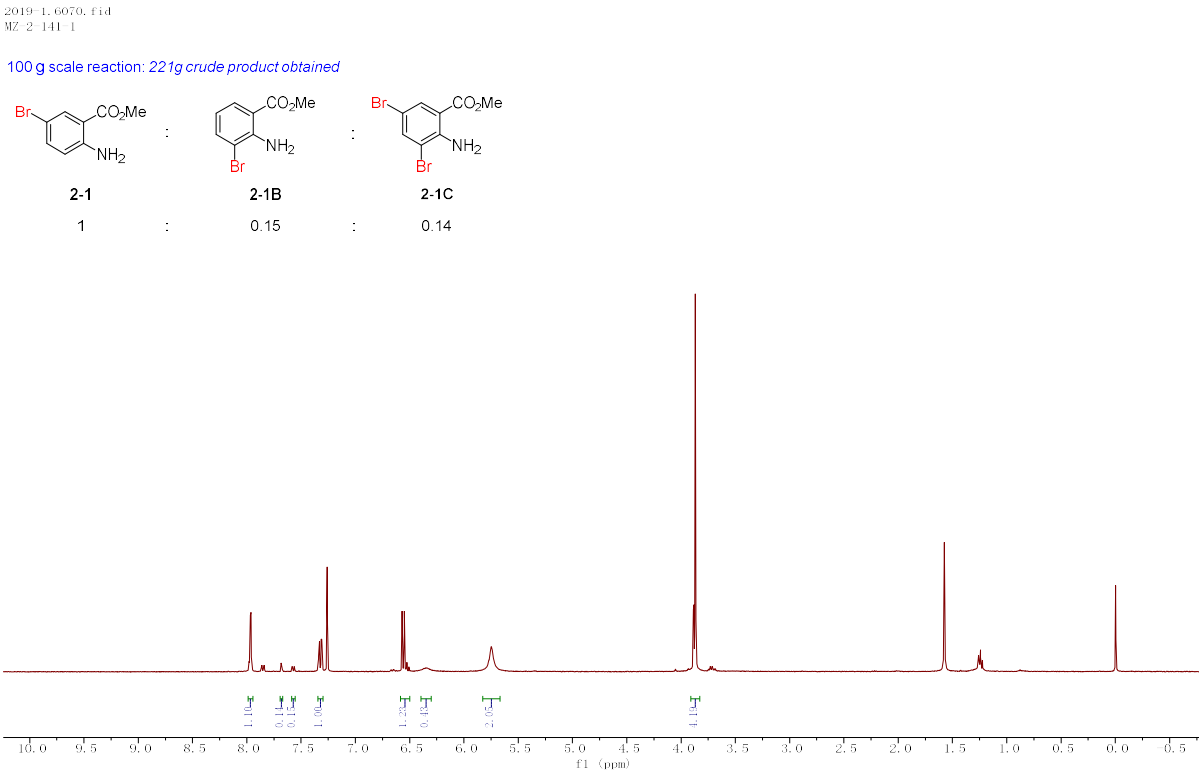


Figure S19. ^{1}H NMR of crude product **2-1** in 100 g scale, related Table 2

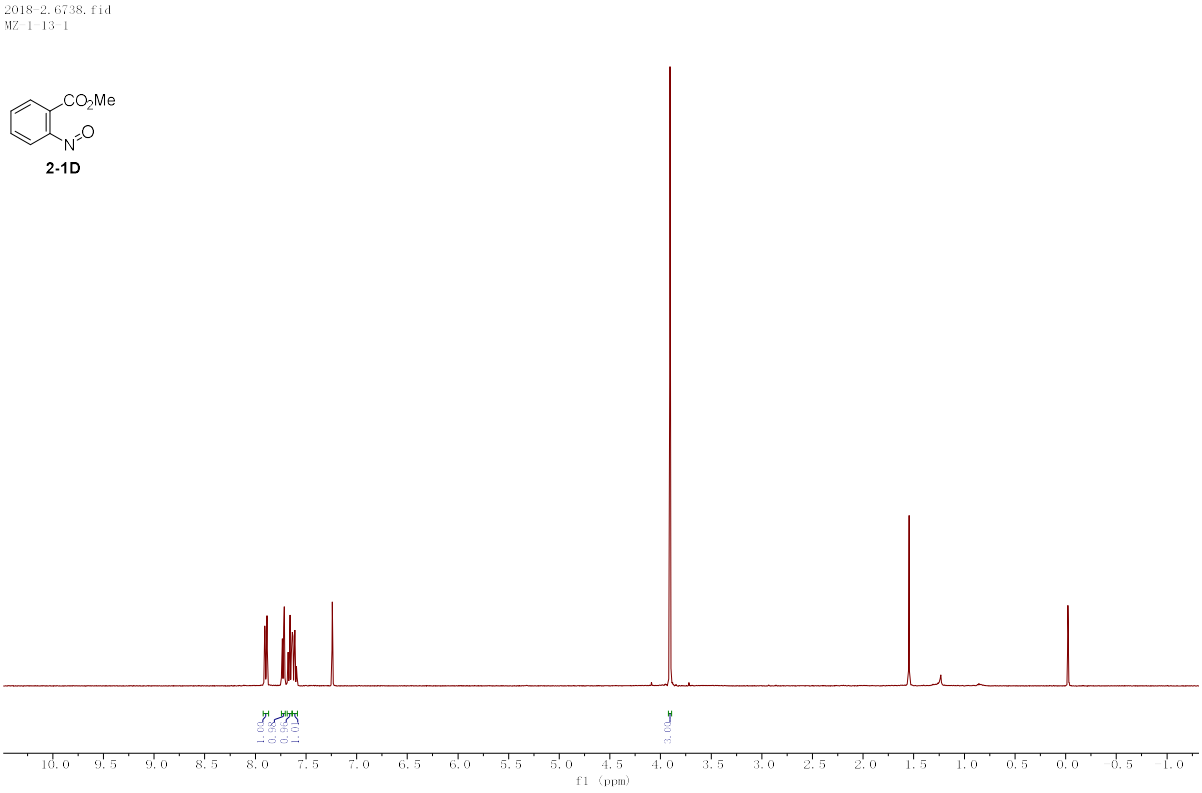


Figure S20. ^{1}H NMR of product **2-1D**, related Table 1

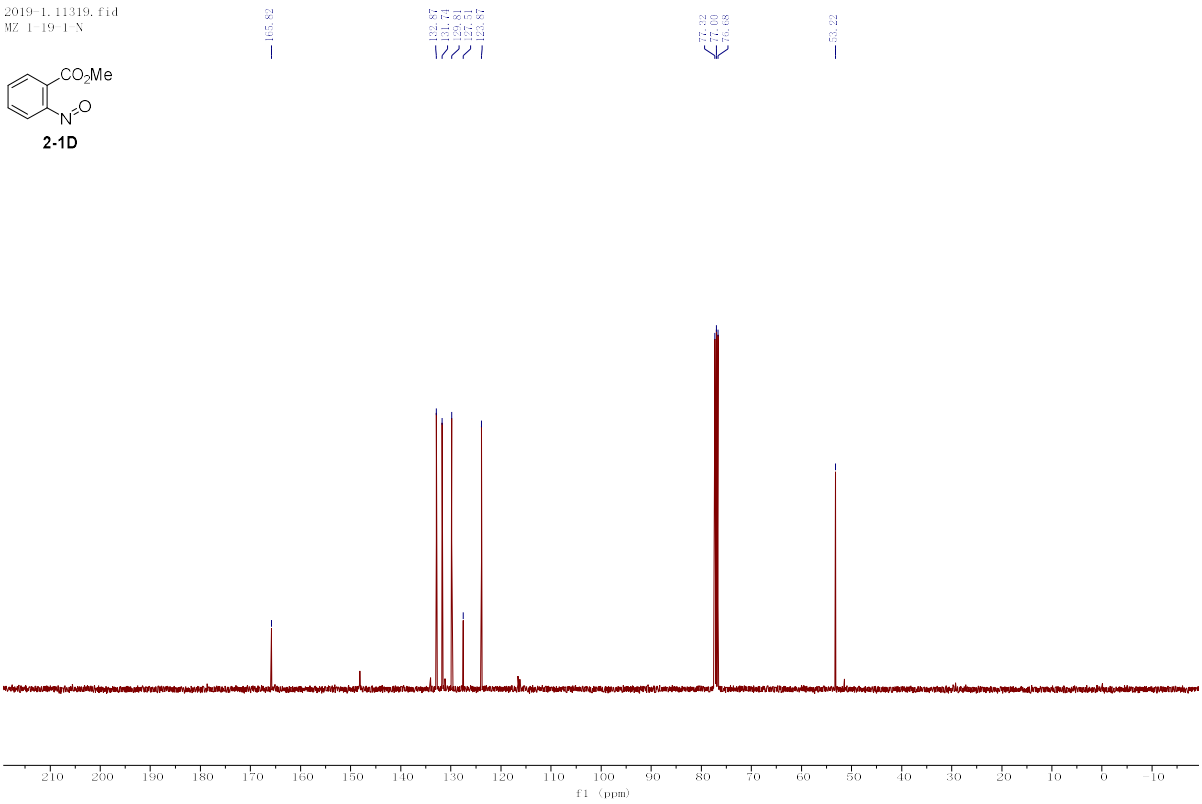


Figure S21. ^{13}C NMR of product **2-1D**, related Table 1

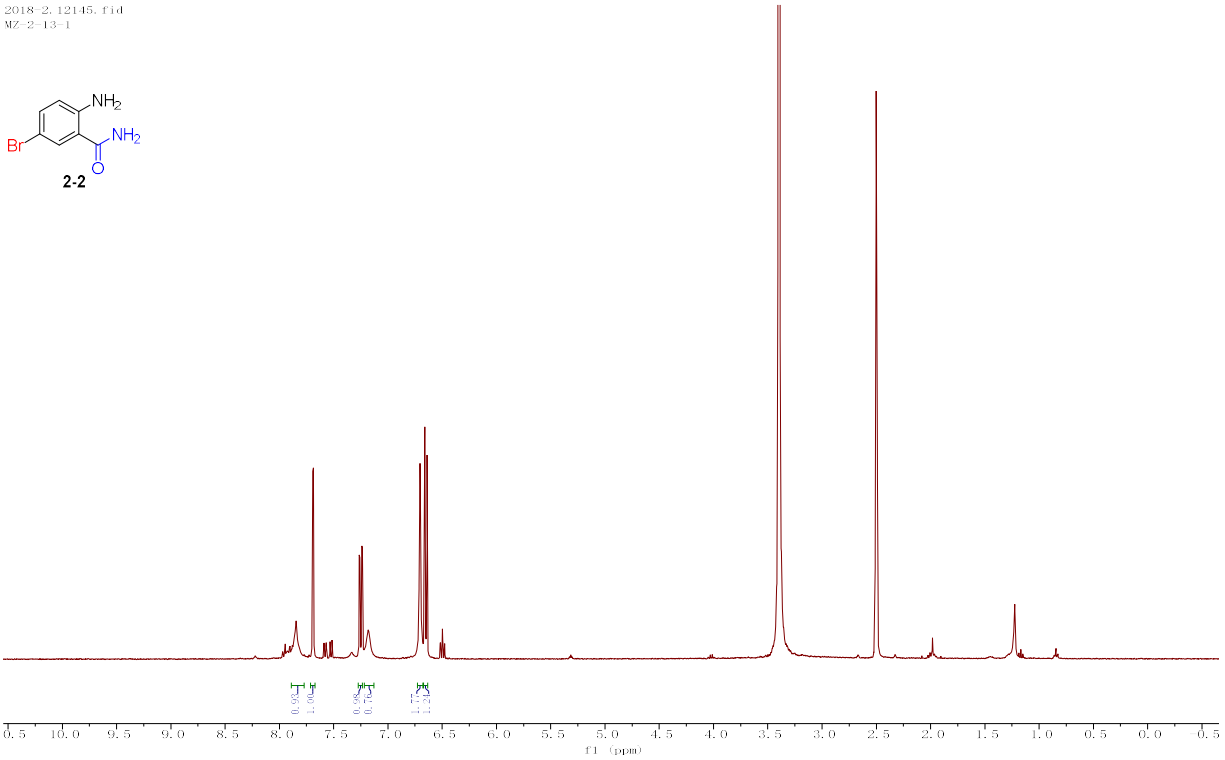


Figure S22. ^{1}H NMR of product **2-2**, related Table 2

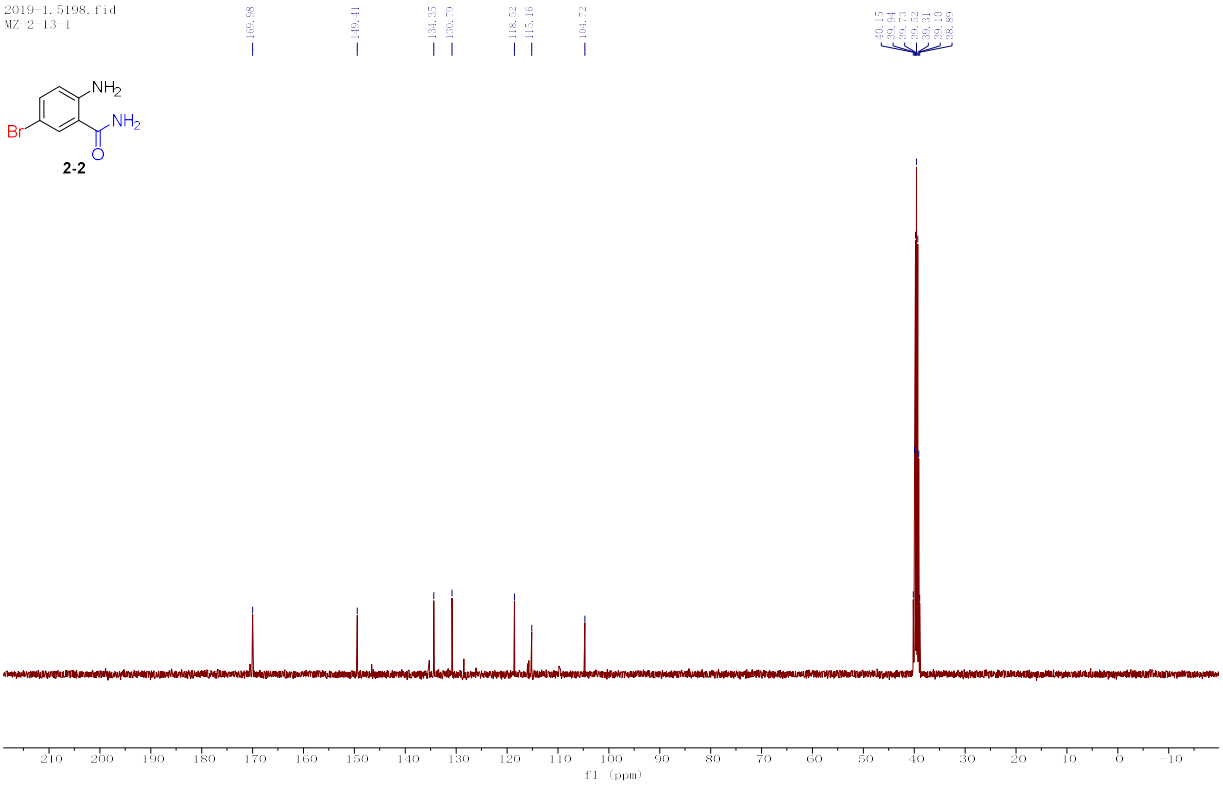


Figure S23. ^{13}C NMR of product **2-2**, related Table 2

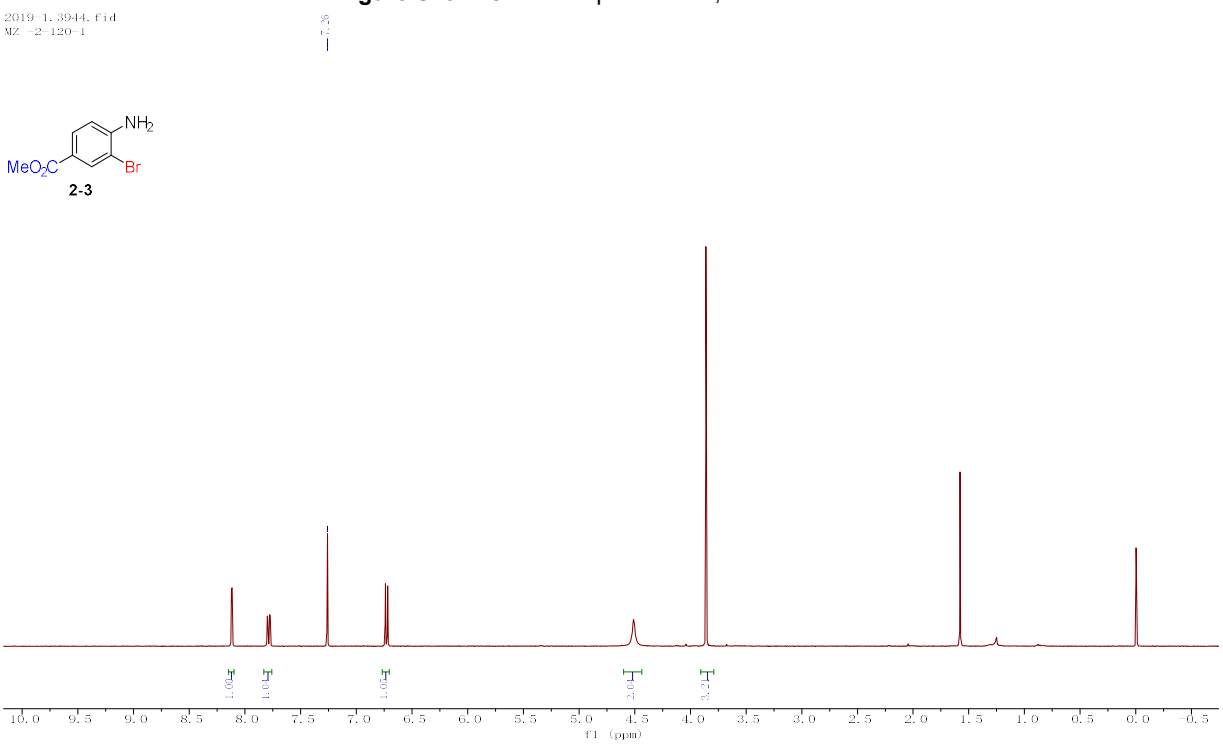


Figure S24. ^{1}H NMR of product **2-3**, related Table 2

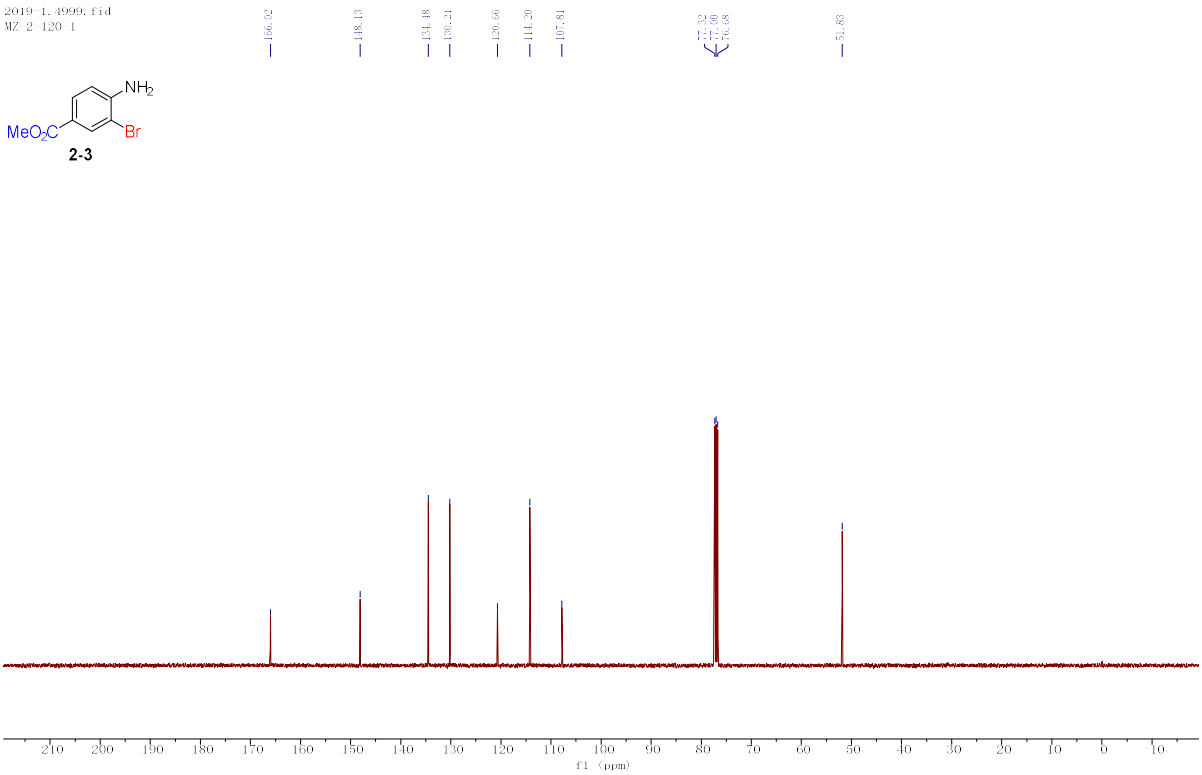


Figure S25. ^{13}C NMR of product **2-3**, related Table 2

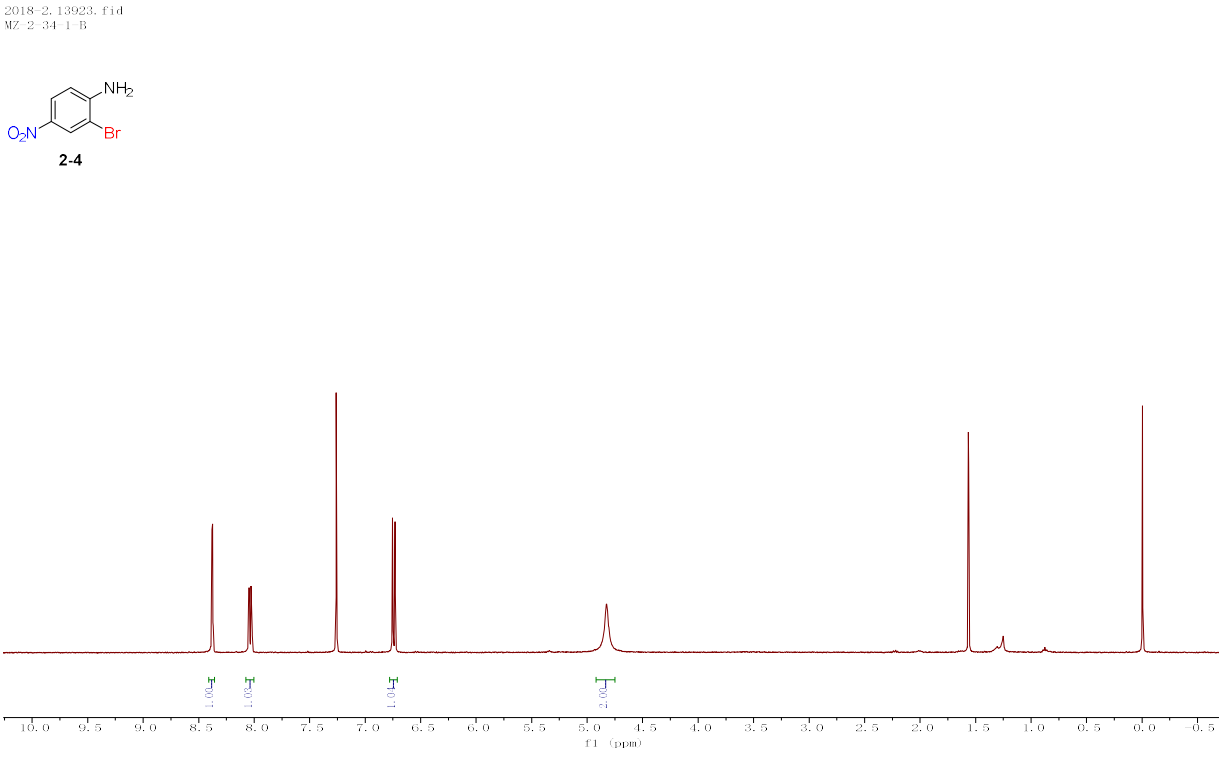


Figure S26. ^{1}H NMR of product **2-4**, related Table 2

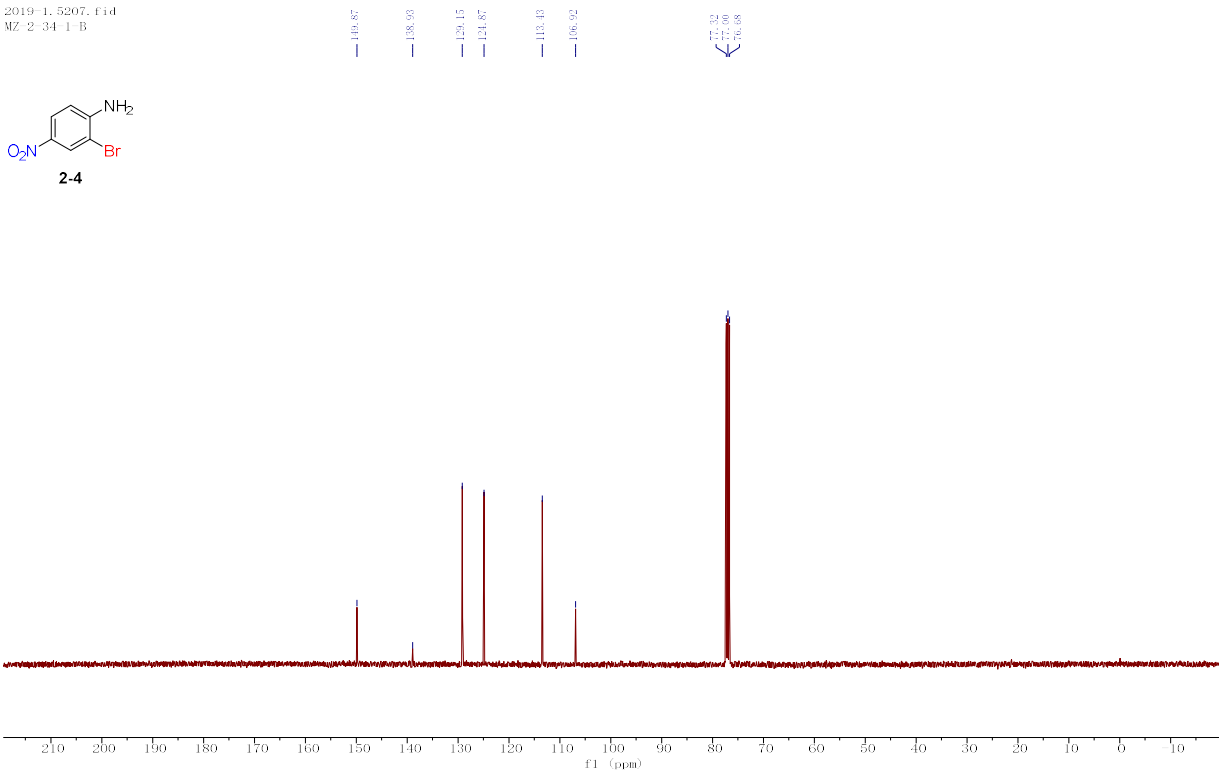


Figure S27. ^{13}C NMR of product **2-4**, related Table 2

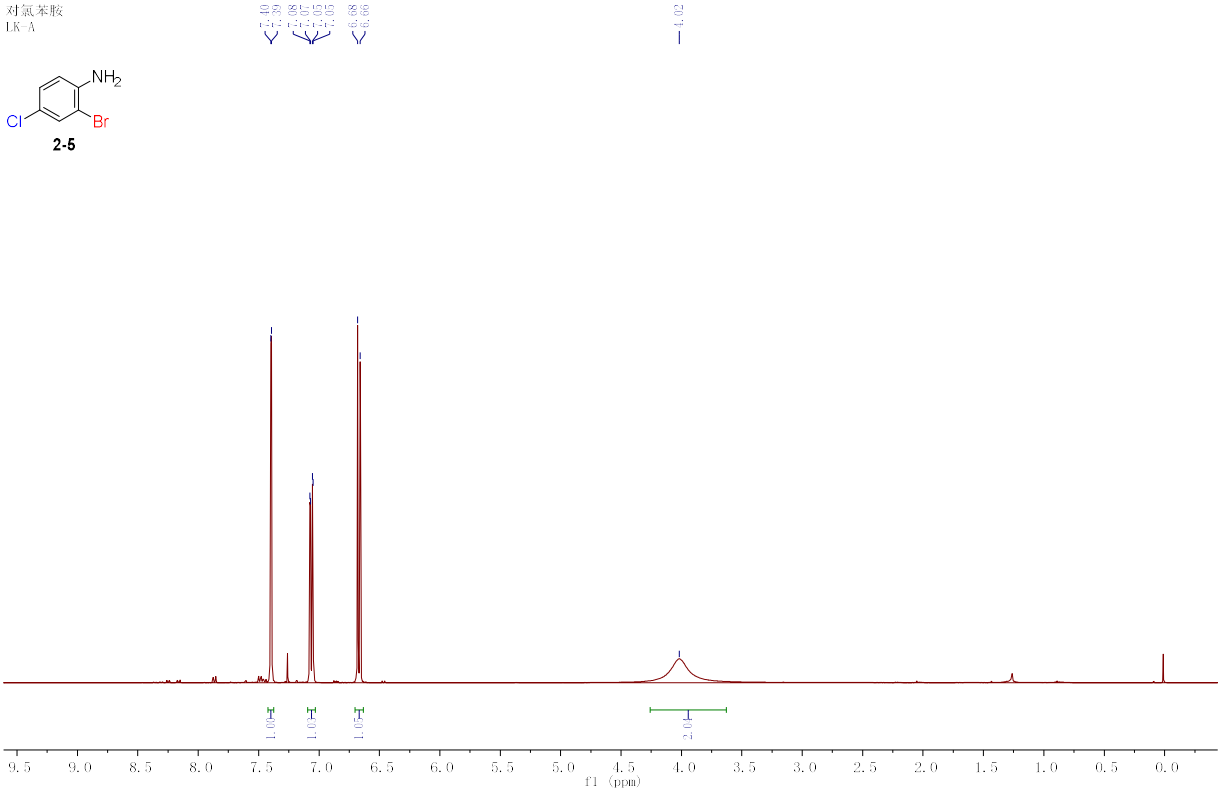


Figure S28. ^{1}H NMR of product **2-5**, related Table 2

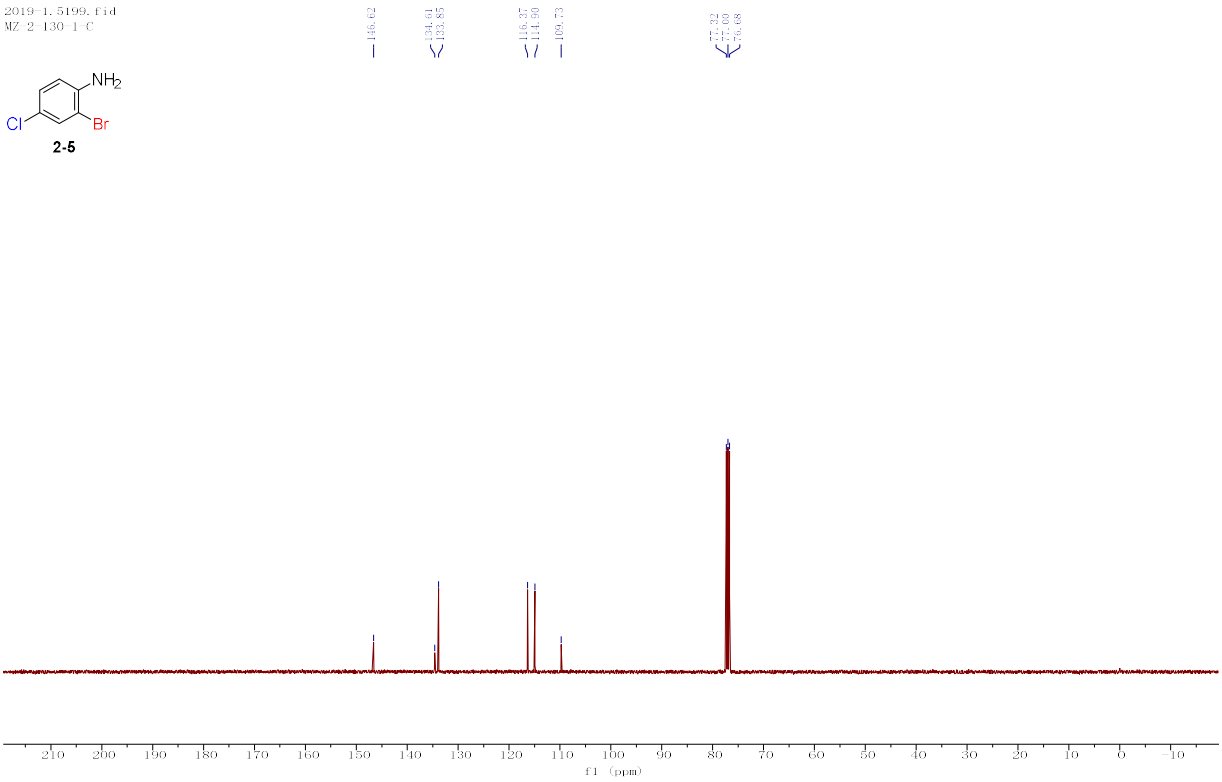


Figure S29. ^{13}C NMR of product **2-5**, related Table 2

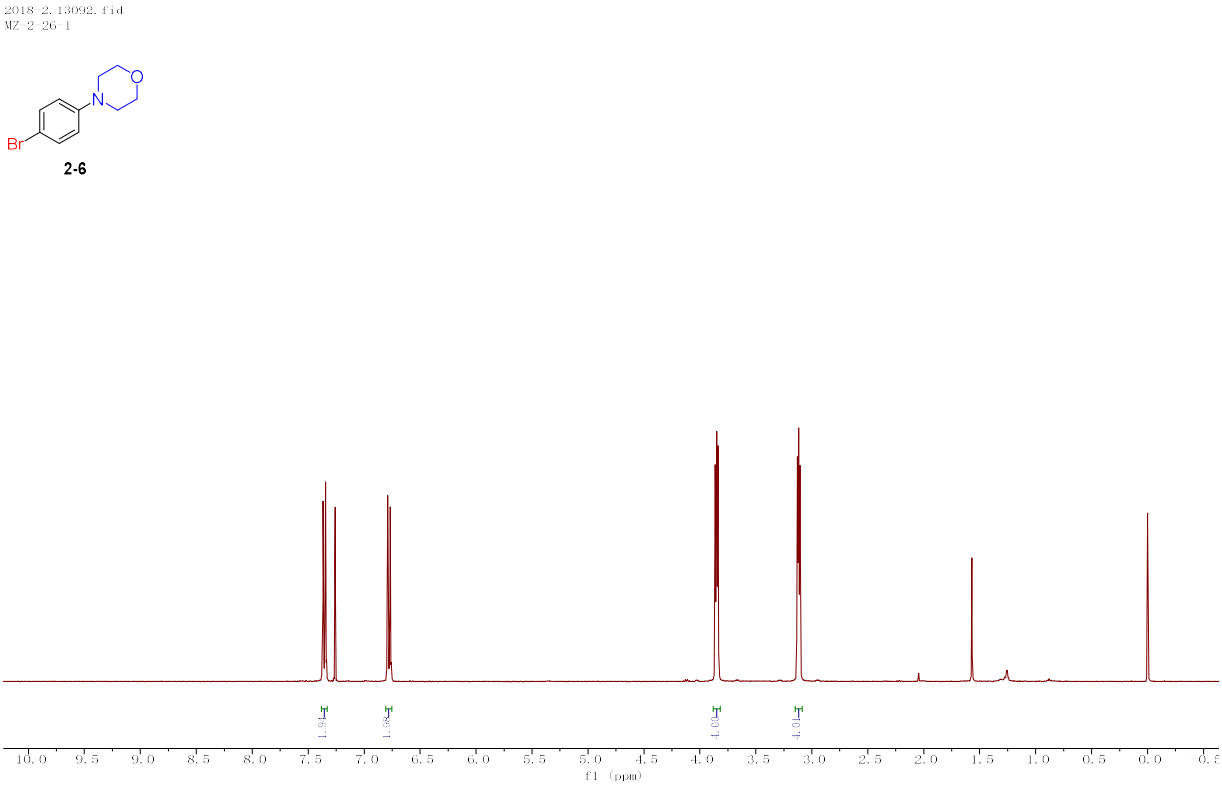


Figure S30. ^{1}H NMR of product **2-6**, related Table 2

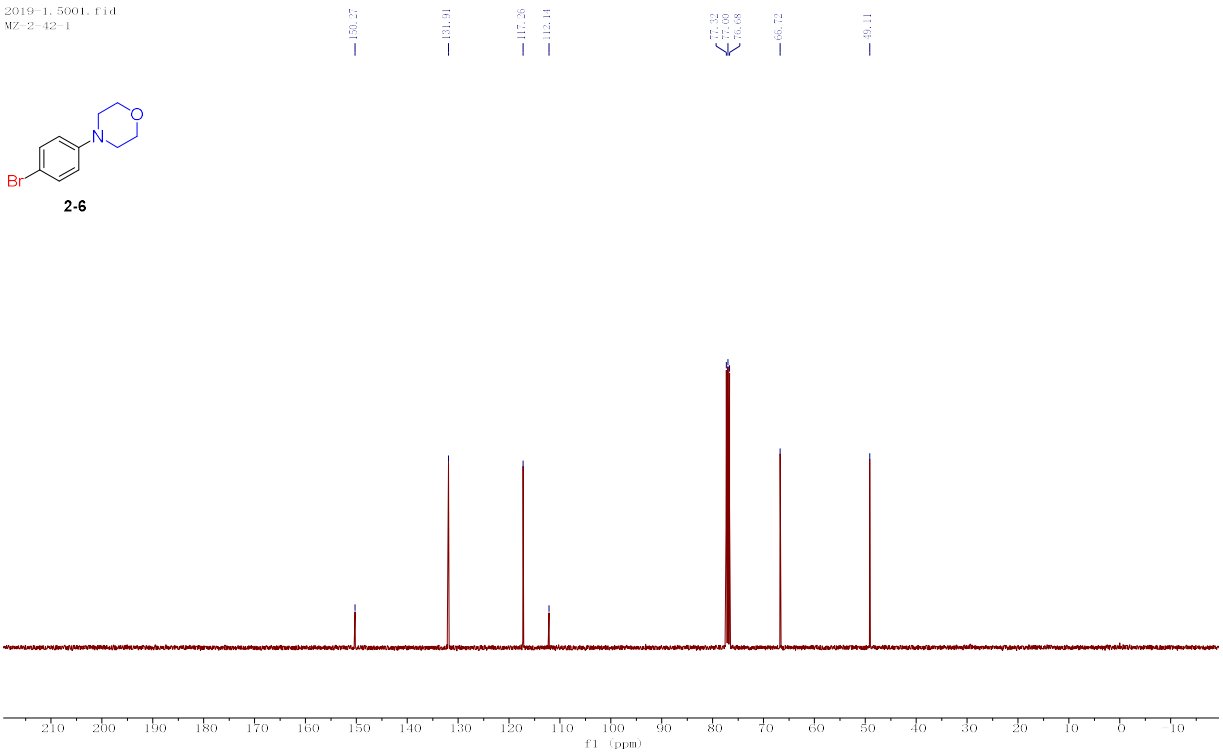


Figure S31. ^{13}C NMR of product **2-6**, related Table 2

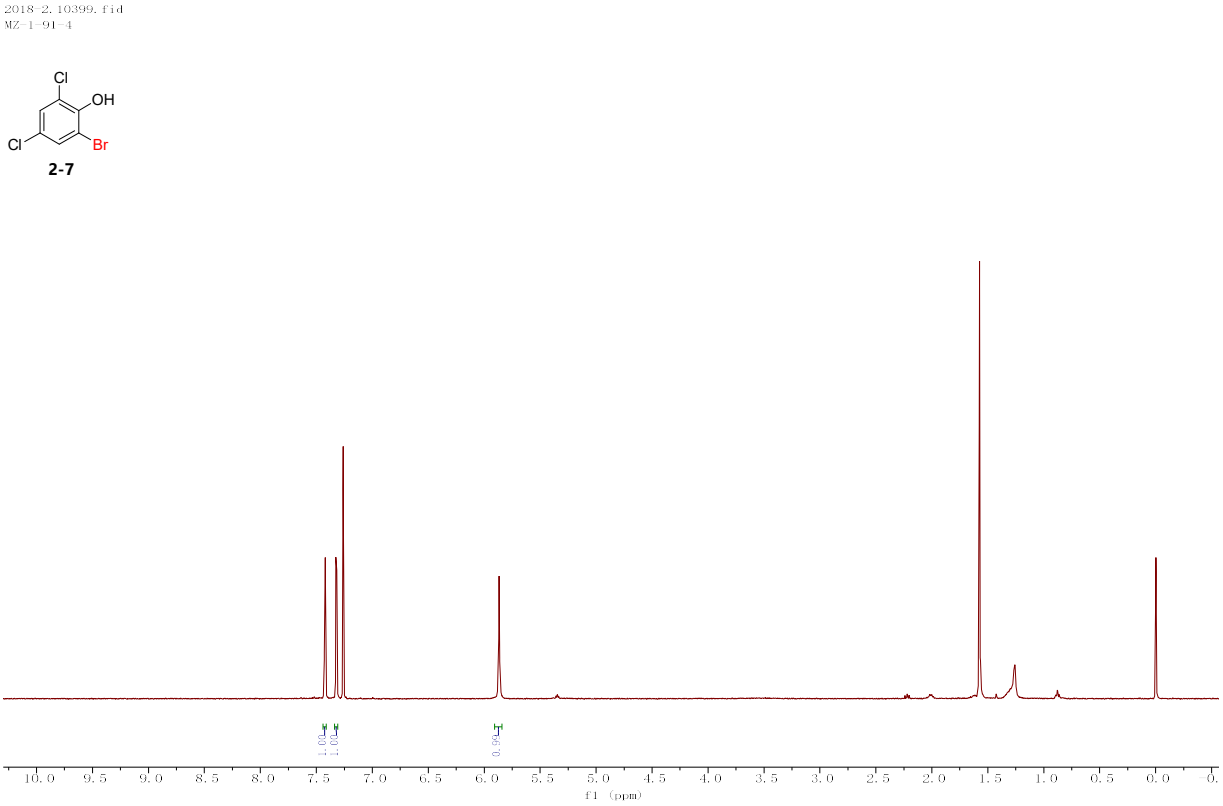


Figure S32. ^{1}H NMR of product **2-7**, related Table 2

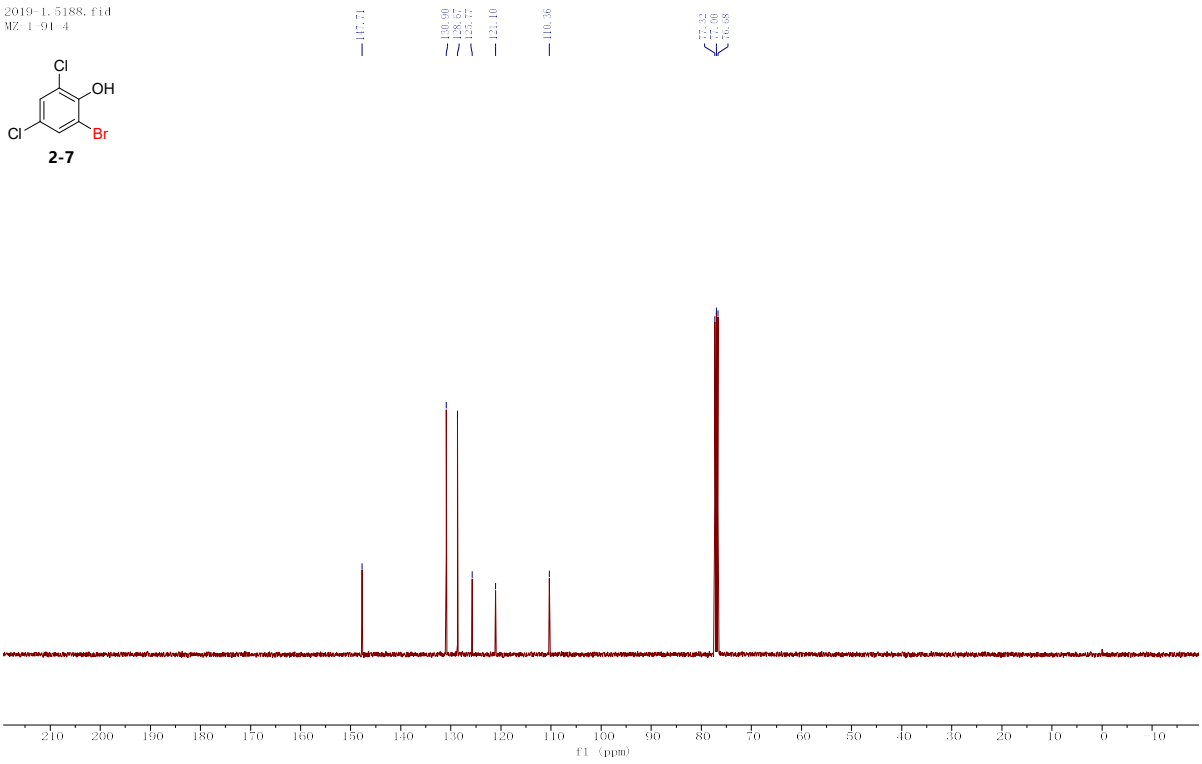


Figure S33. ^{13}C NMR of product **2-7**, related Table 2

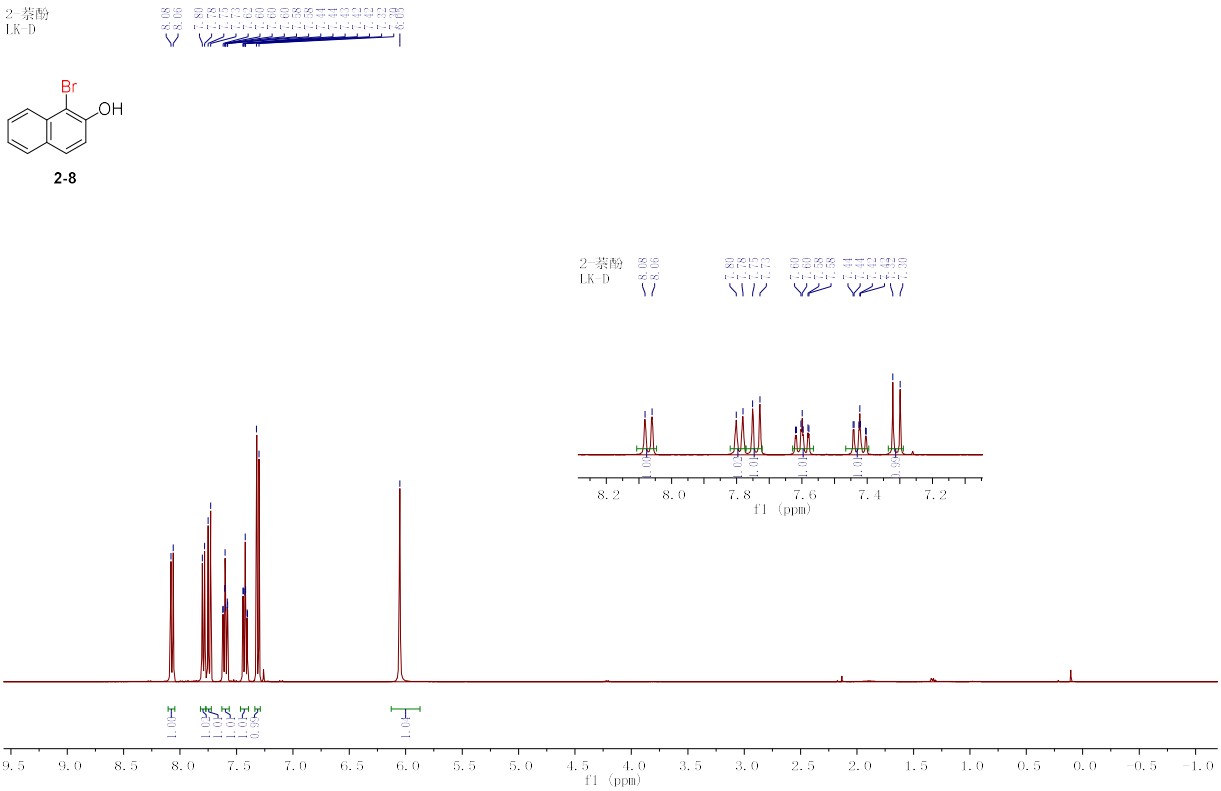


Figure S34. ^{1}H NMR of product **2-8**, related Table 2

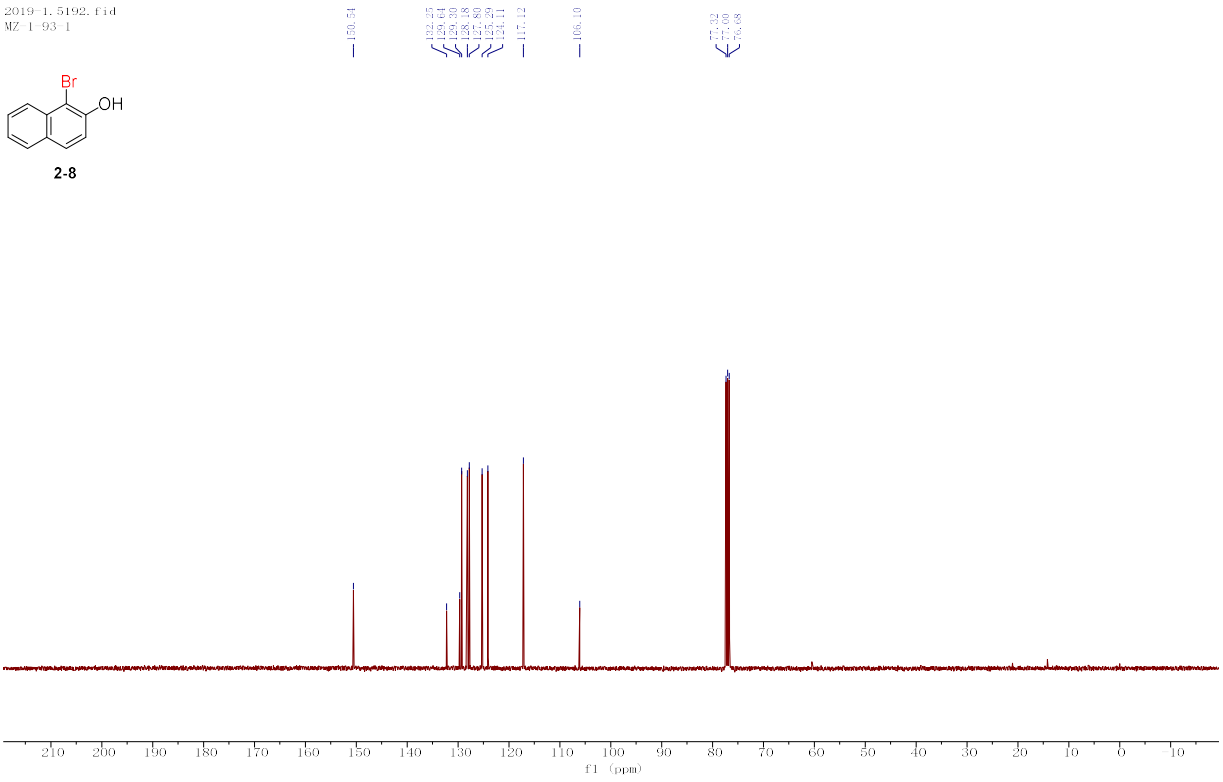


Figure S35. ^{13}C NMR of product **2-8**, related Table 2

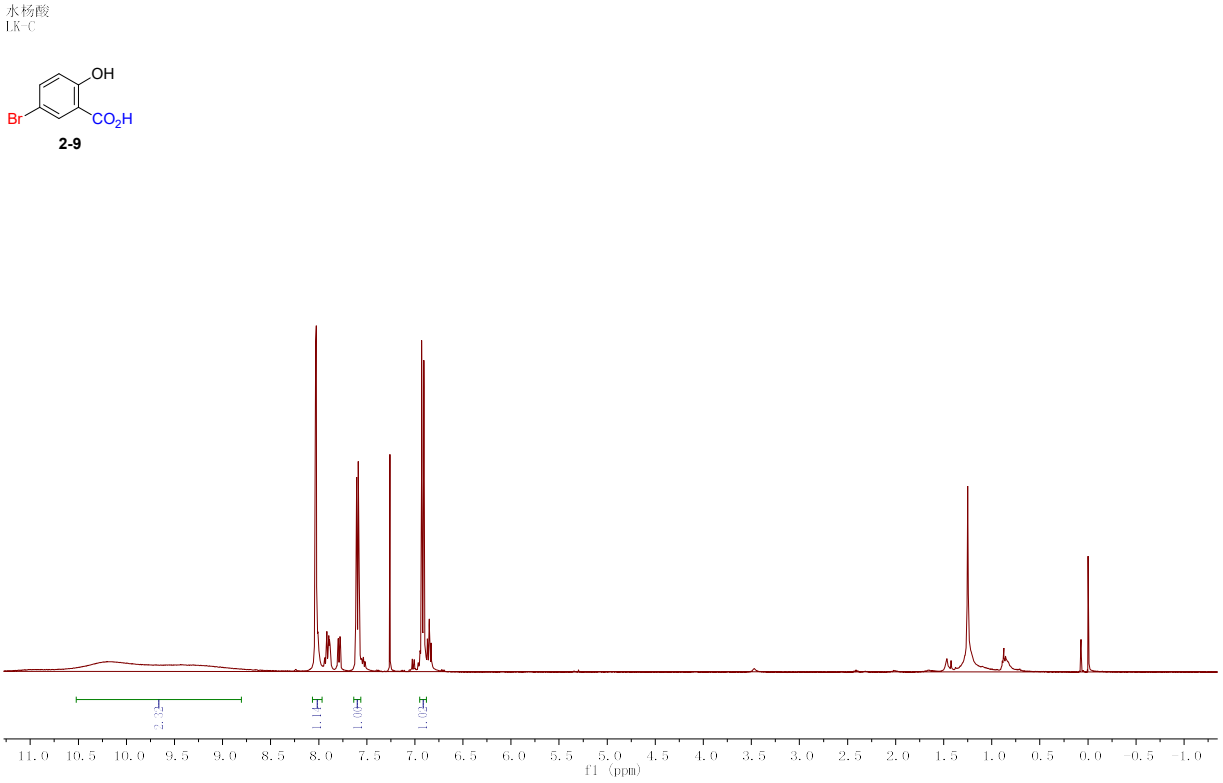


Figure S36. ^{1}H NMR of product **2-9**, related Table 2

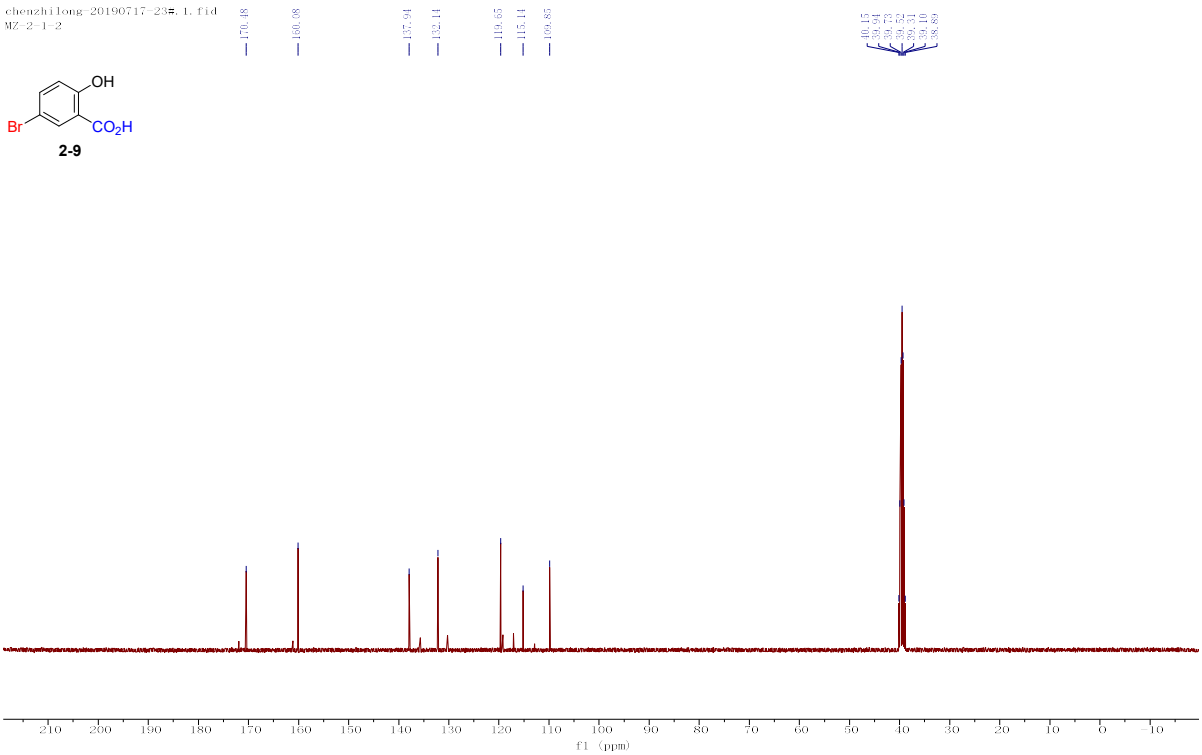


Figure S37. ^{13}C NMR of product **2-9**, related Table 2

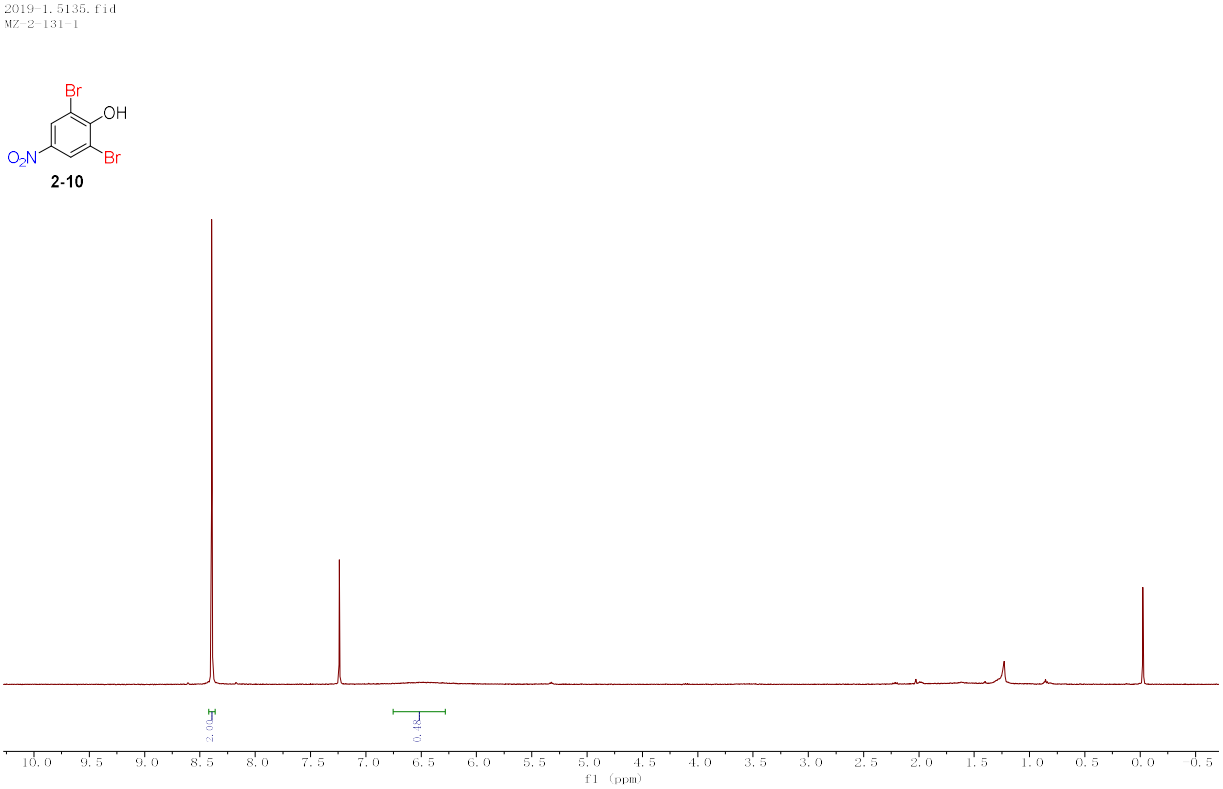


Figure S38. ^{1}H NMR of product **2-10**, related Table 2

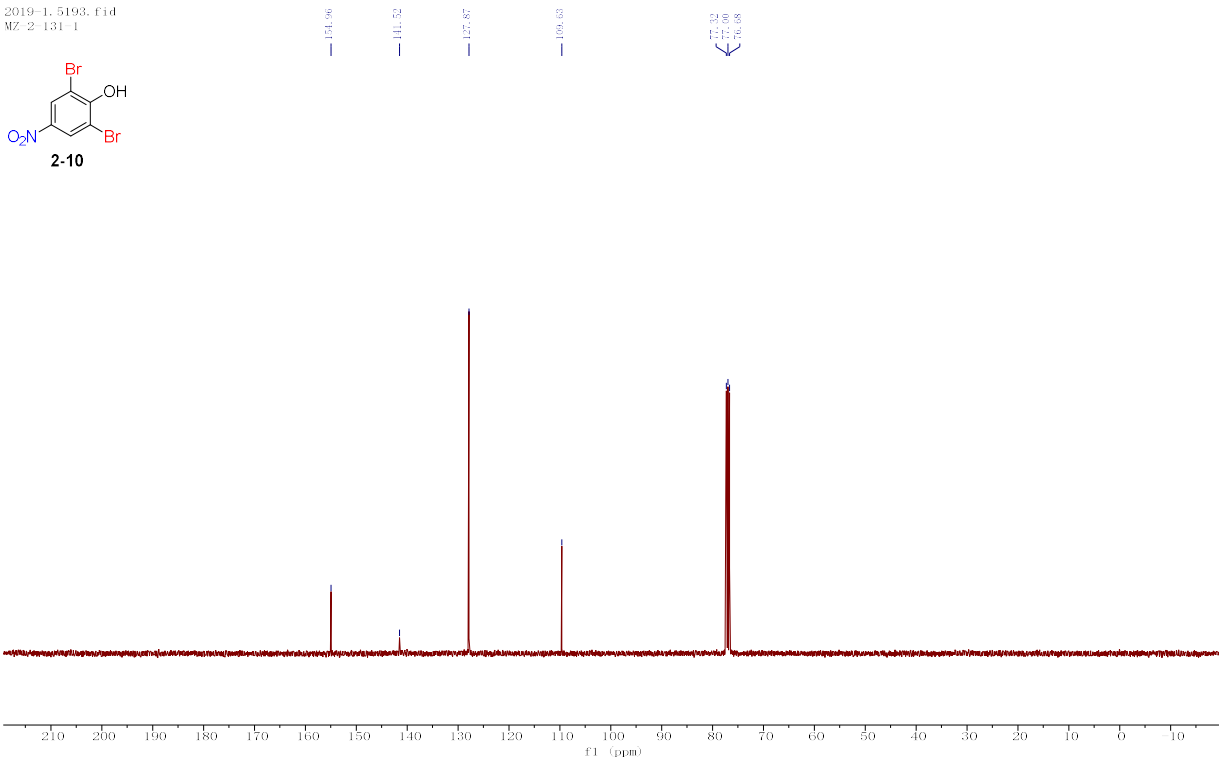


Figure S39. ^{13}C NMR of product **2-10**, related Table 2

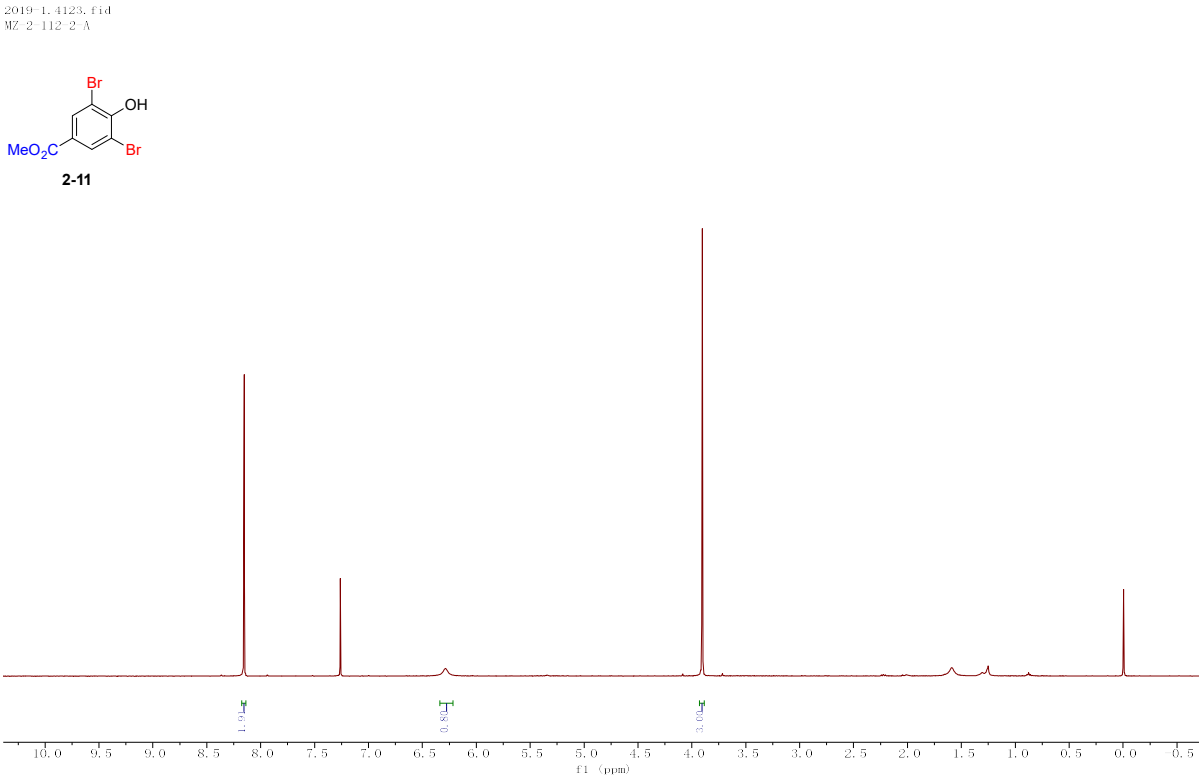


Figure S40. ^{1}H NMR of product **2-11**, related Table 2

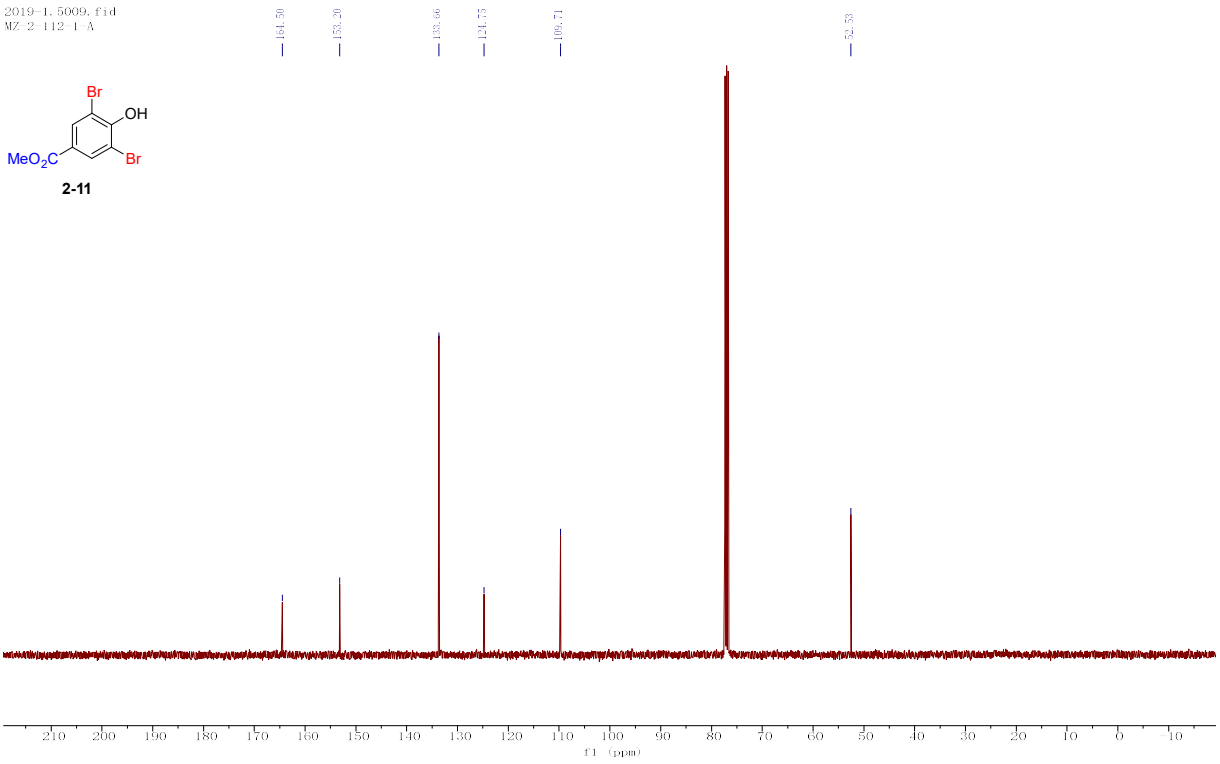


Figure S41. ^{13}C NMR of product **2-11**, related Table 2

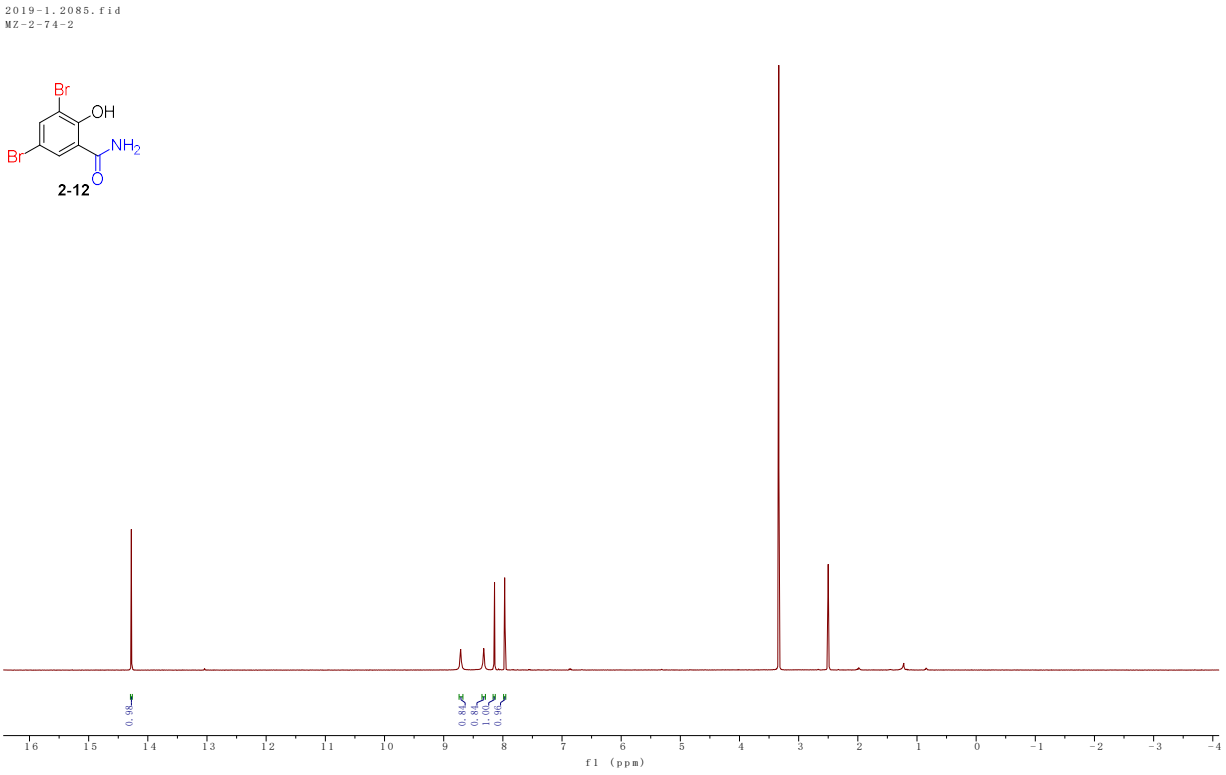


Figure S42. ^{1}H NMR of product **2-12**, related Table 2

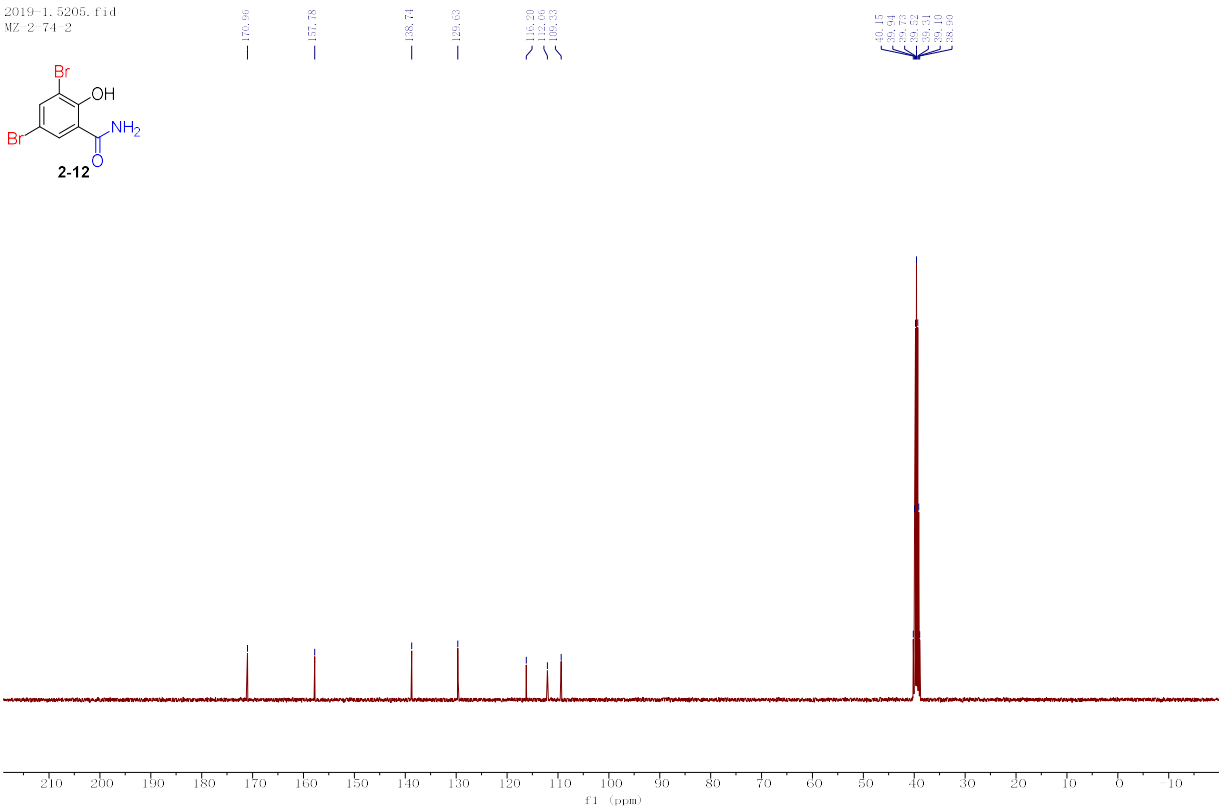


Figure S43. ^{13}C NMR of product **2-12**, related Table 2

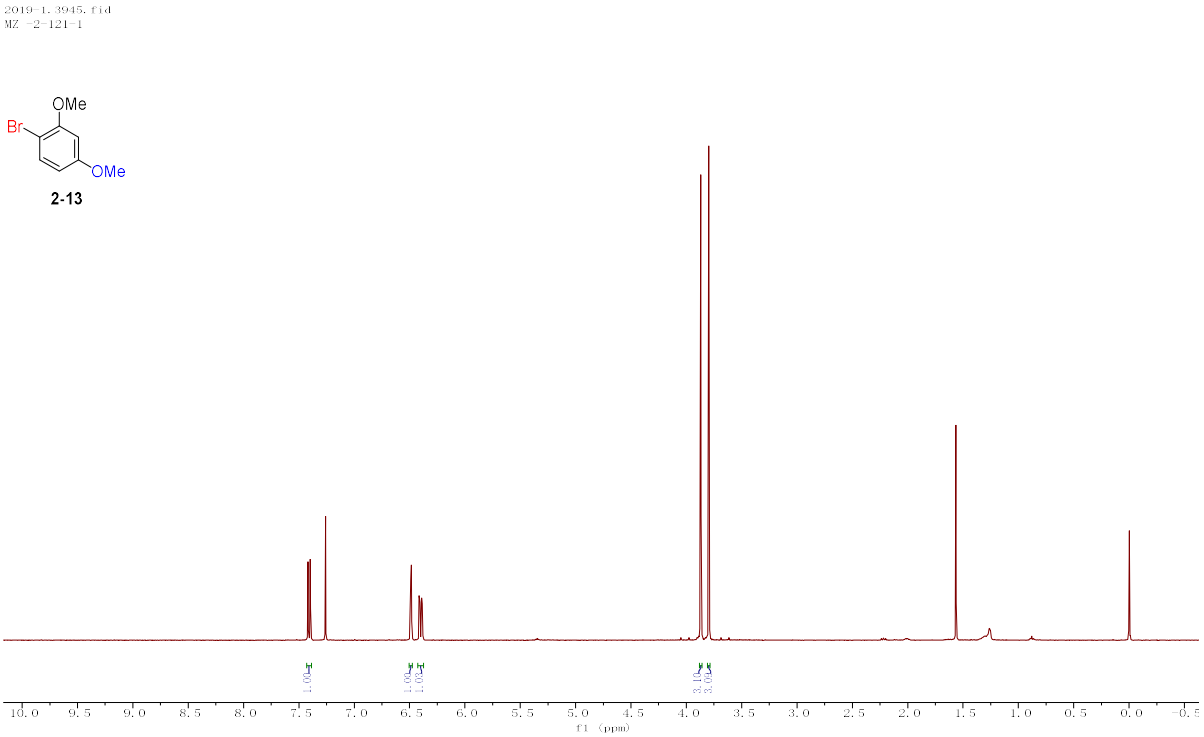


Figure S44. ^{1}H NMR of product **2-13**, related Table 2

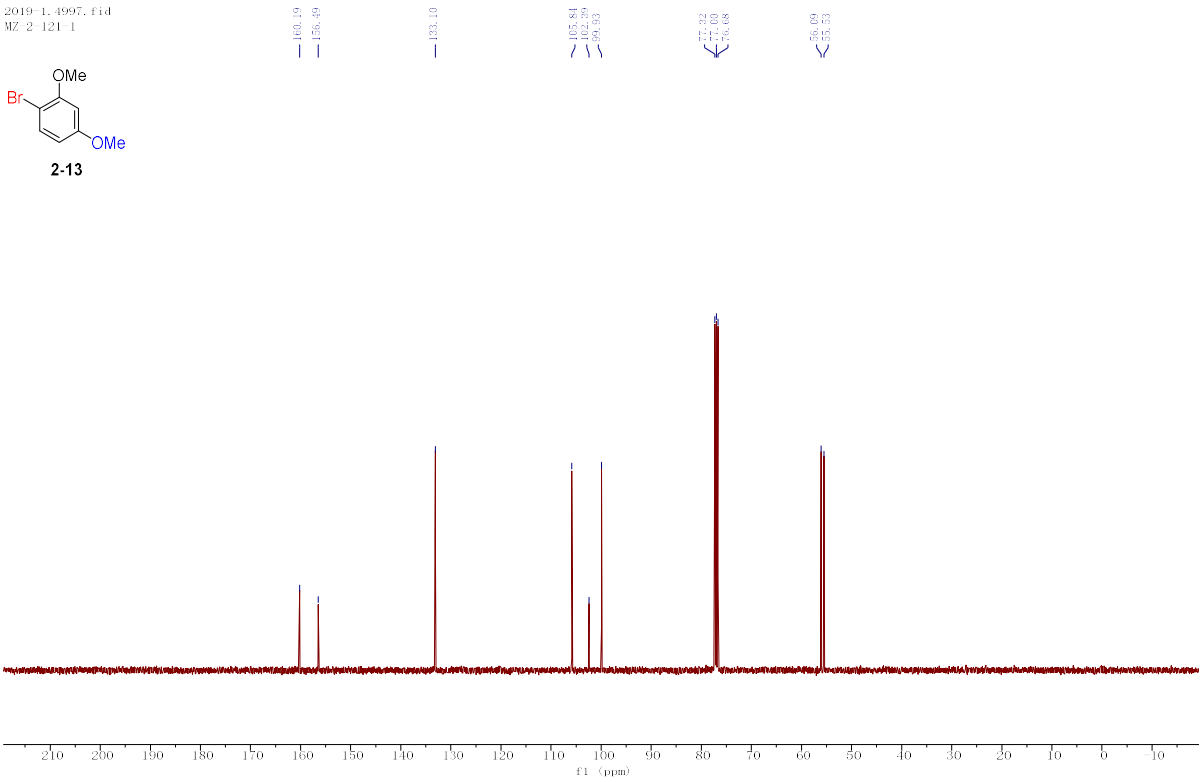


Figure S45. ^{13}C NMR of product **2-13**, related Table 2

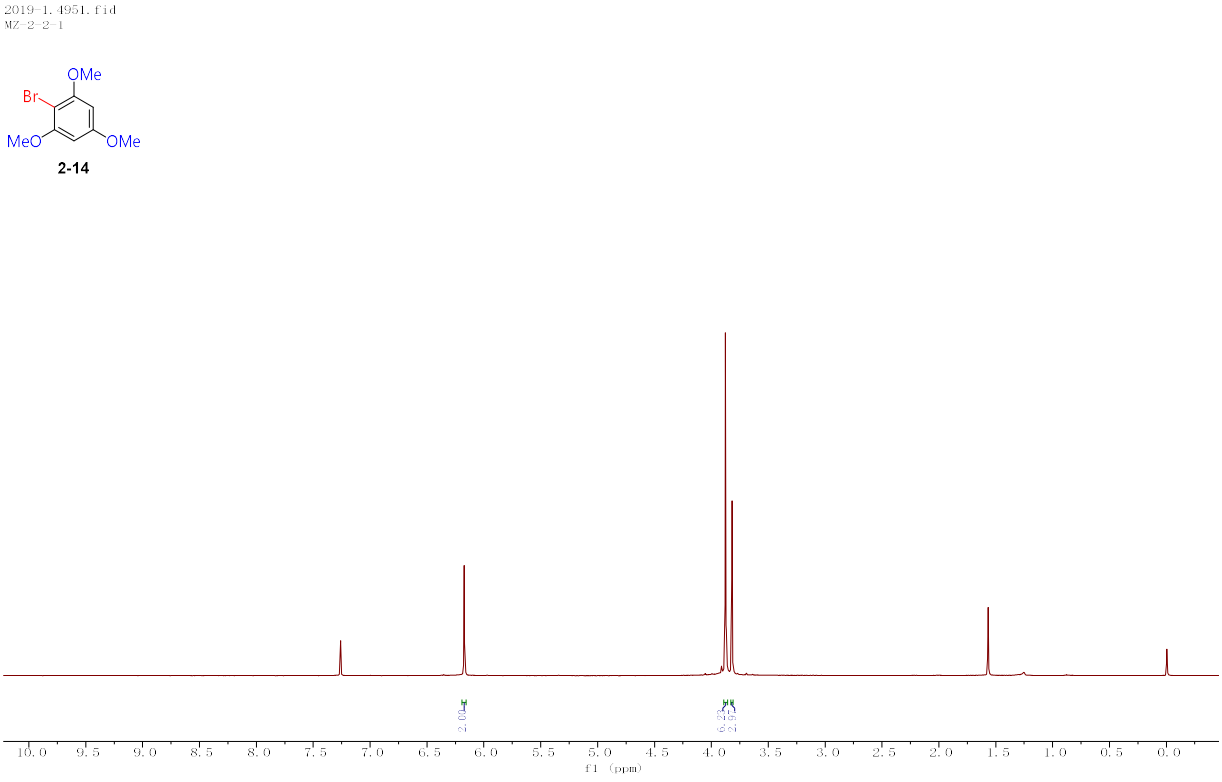


Figure S46. ^{1}H NMR of product **2-14**, related Table 2

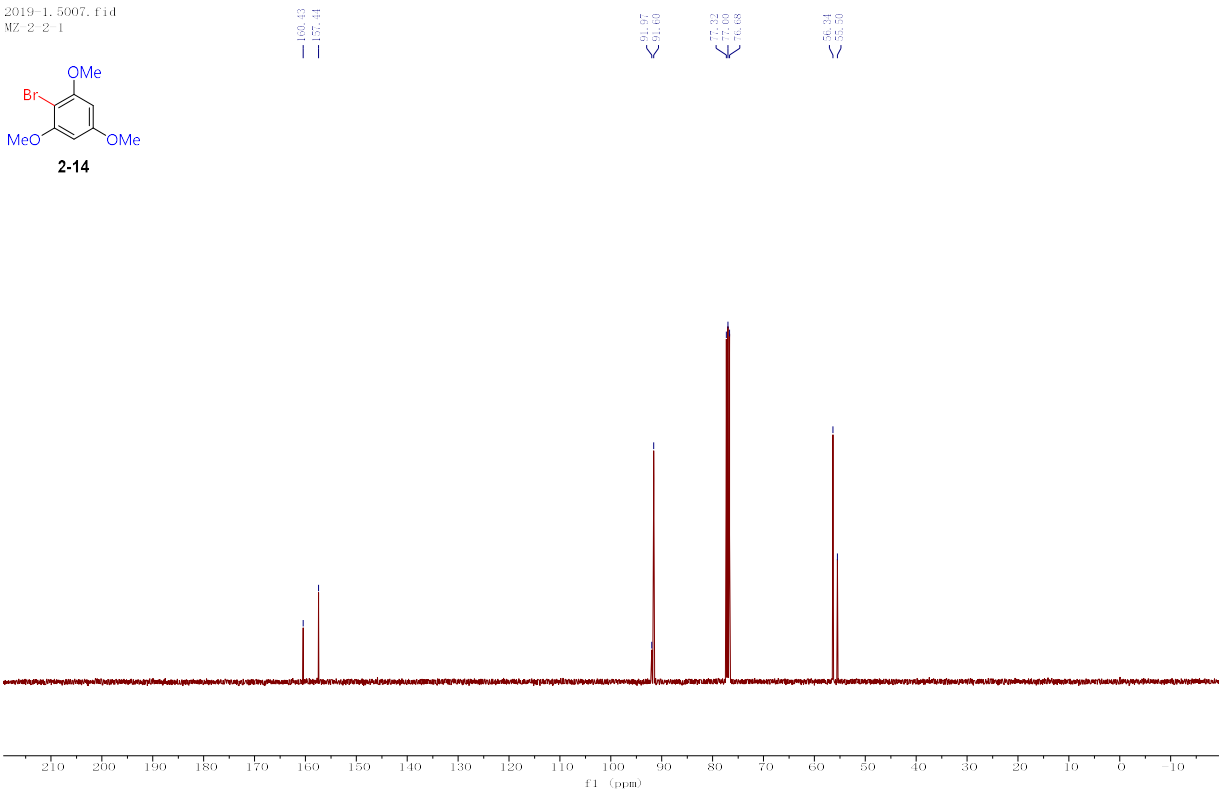


Figure S47. ^{13}C NMR of product **2-14**, related Table 2

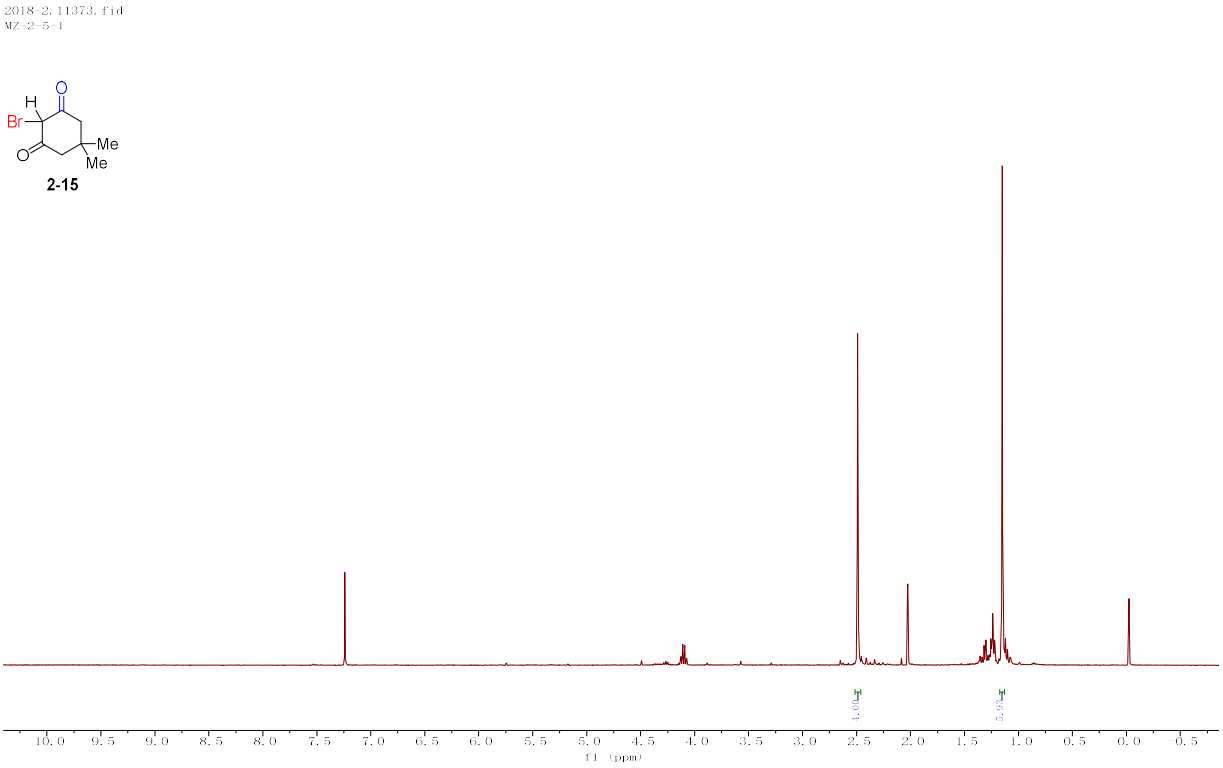


Figure S48. ^{1}H NMR of product **2-15**, related Table 2

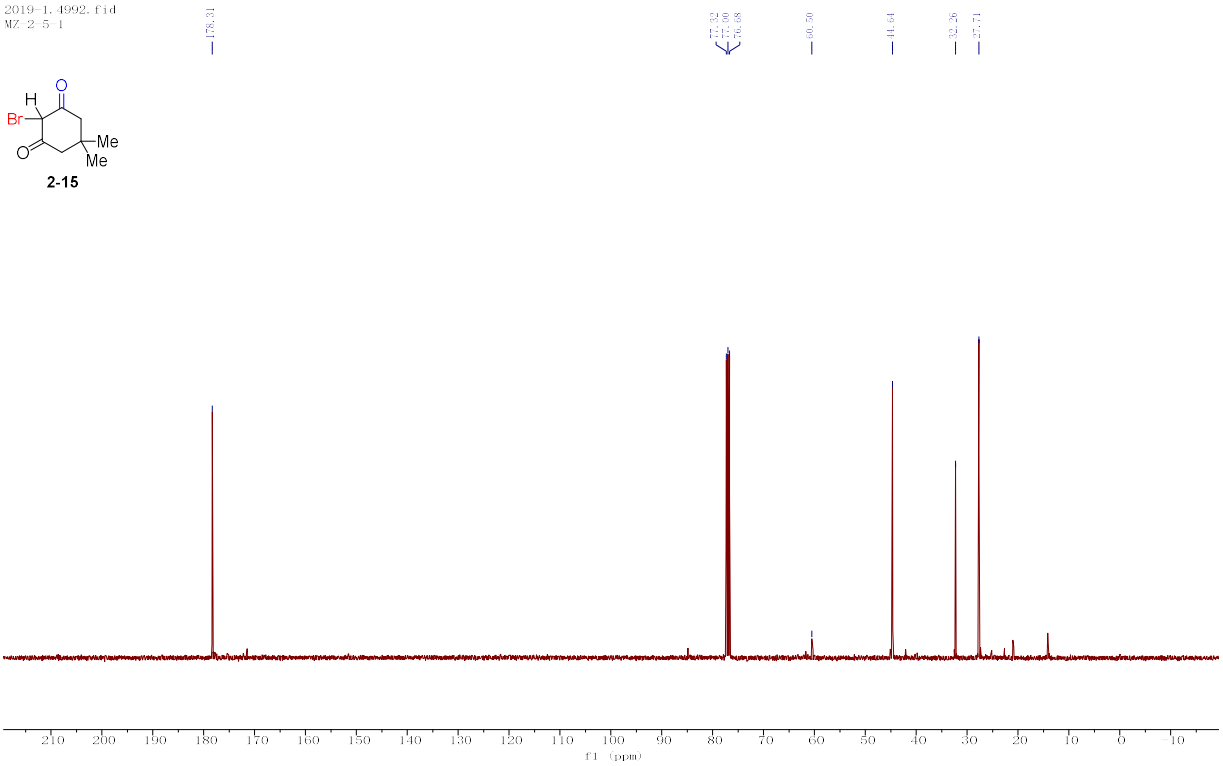


Figure S49. ^{13}C NMR of product **2-15**, related Table 2

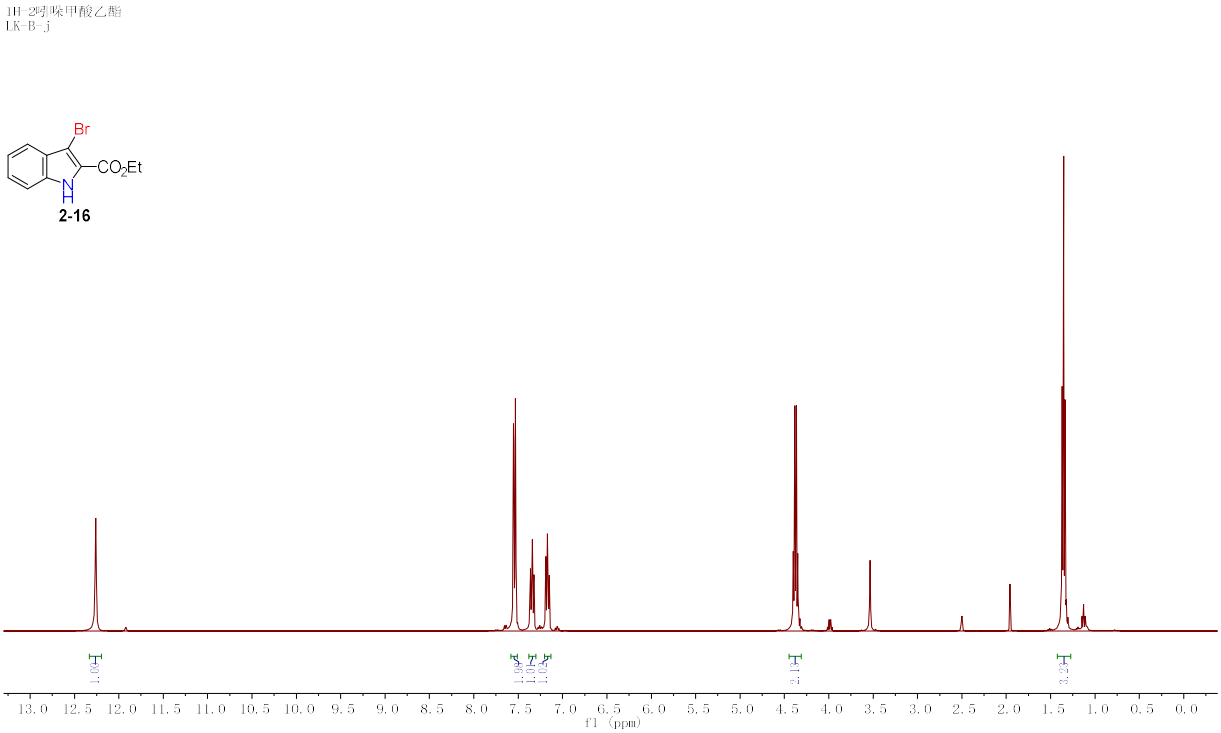


Figure S50. ^{1}H NMR of product **2-16**, related Table 2

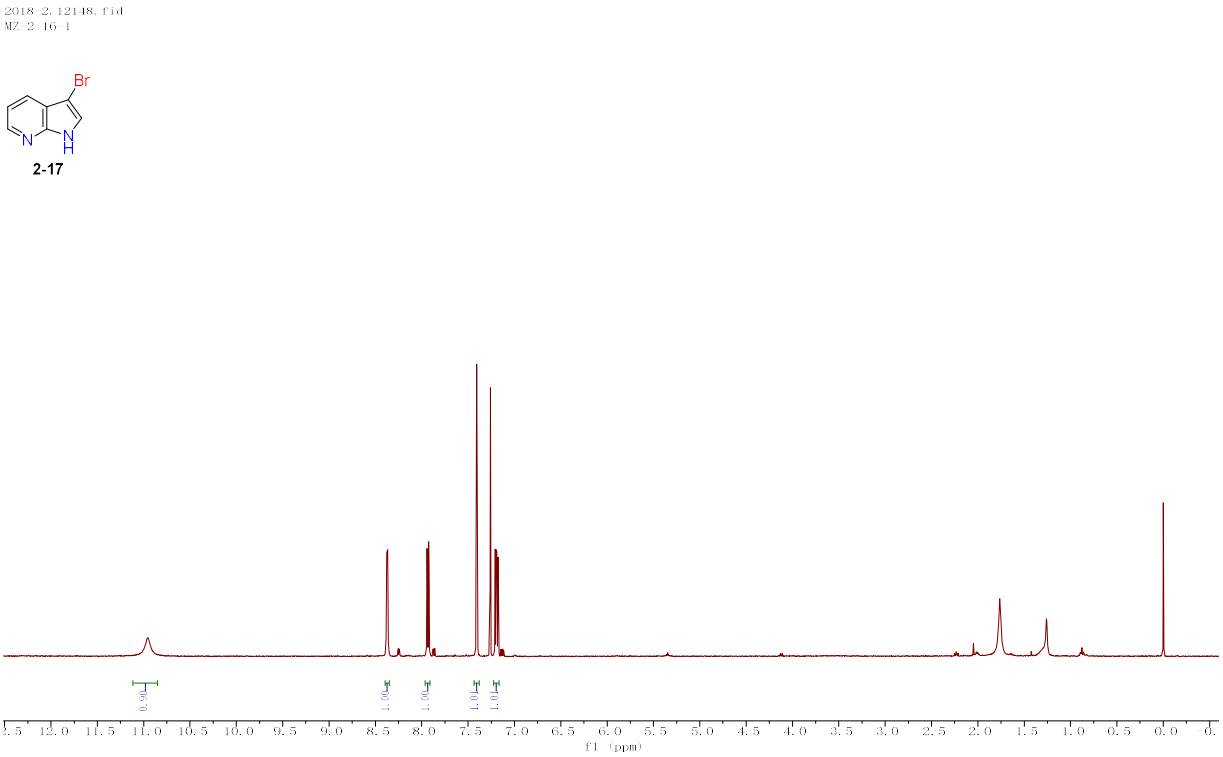


Figure S51. ^{1}H NMR of product **2-17**, related Table 2

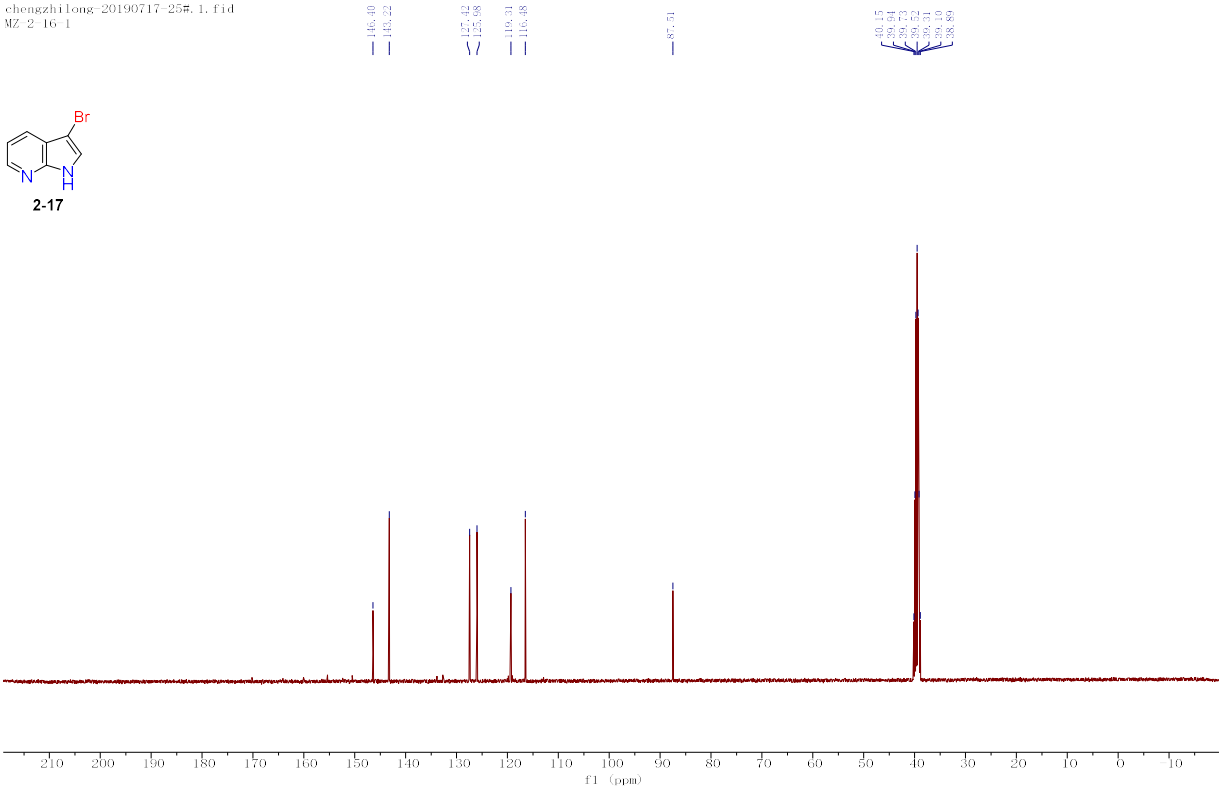


Figure S52. ^{13}C NMR of product **2-17**, related Table 2

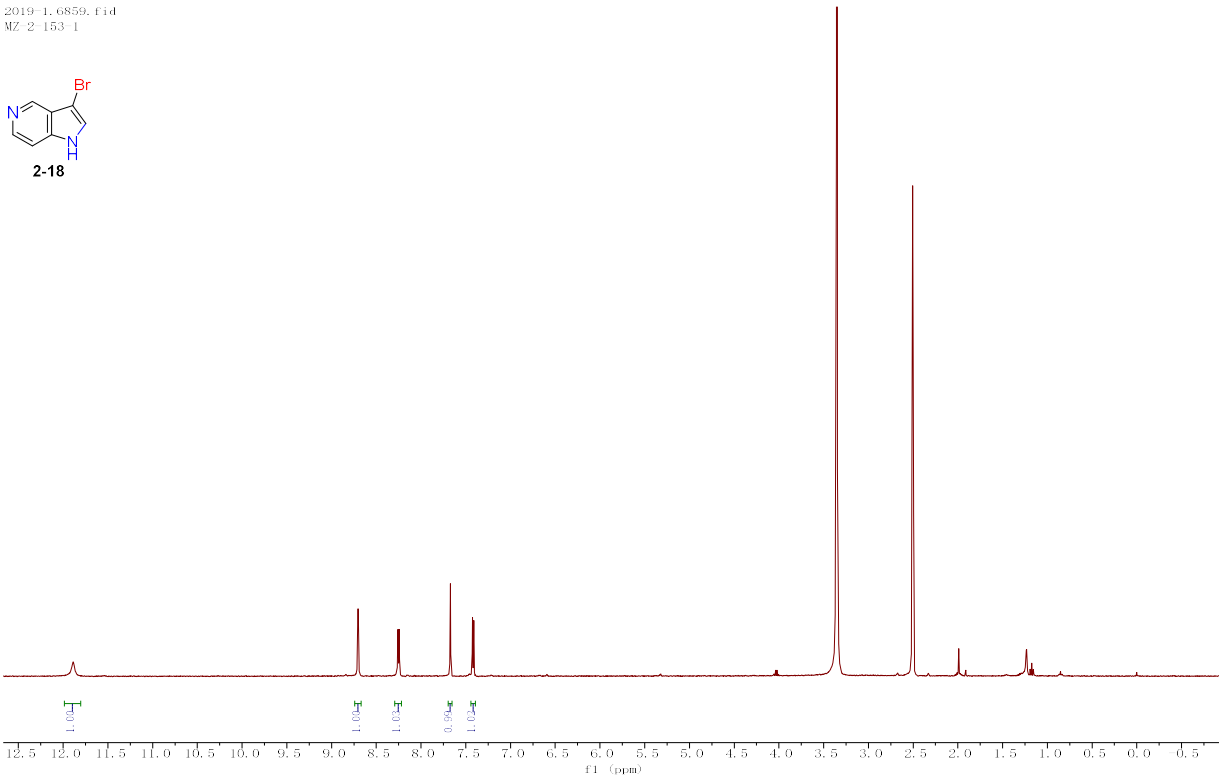


Figure S53. ^{1}H NMR of product **2-18**, related Table 2

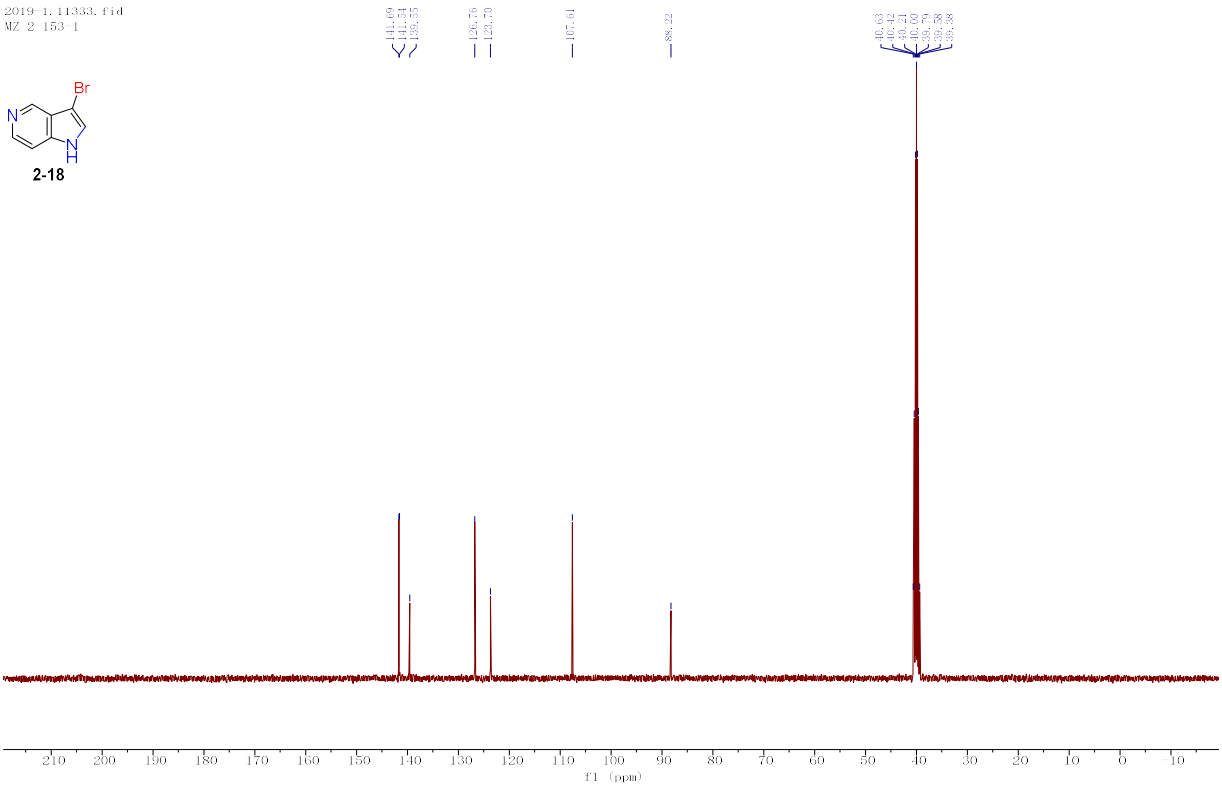


Figure S54. ^{13}C NMR of product **2-18**, related Table 2

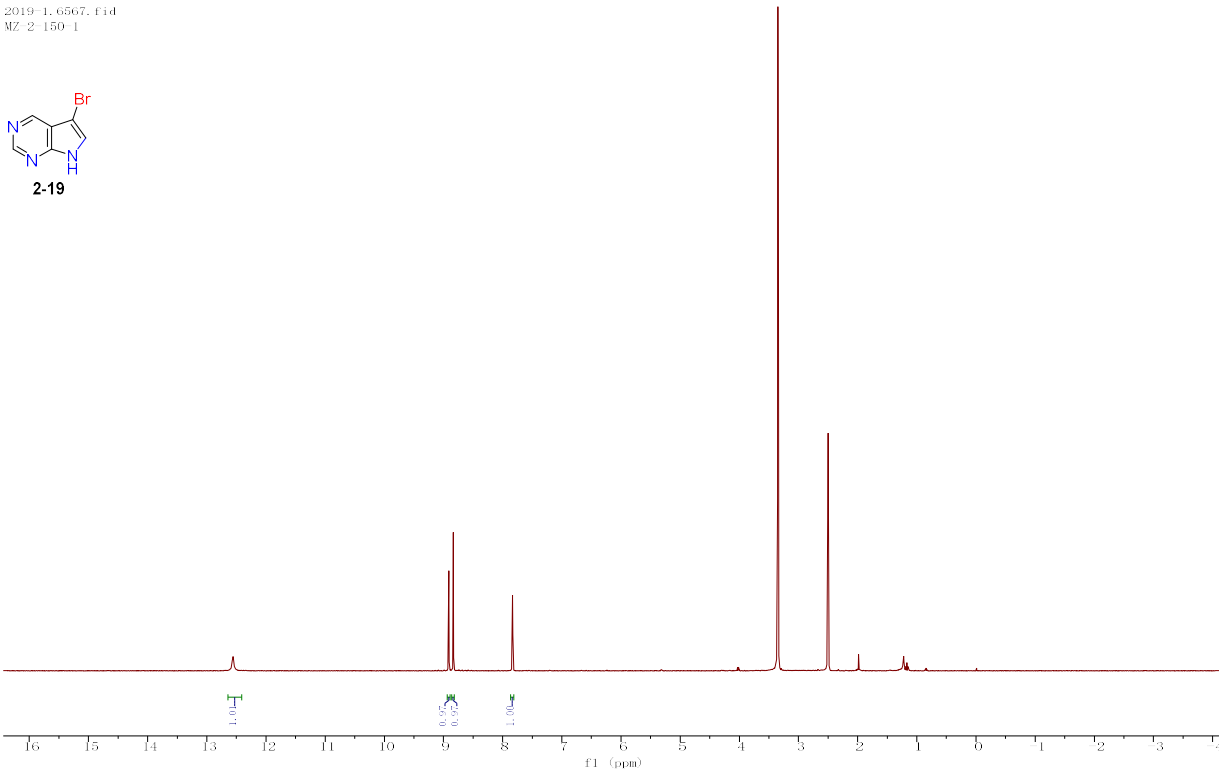


Figure S55. ^{1}H NMR of product **2-19**, related Table 2

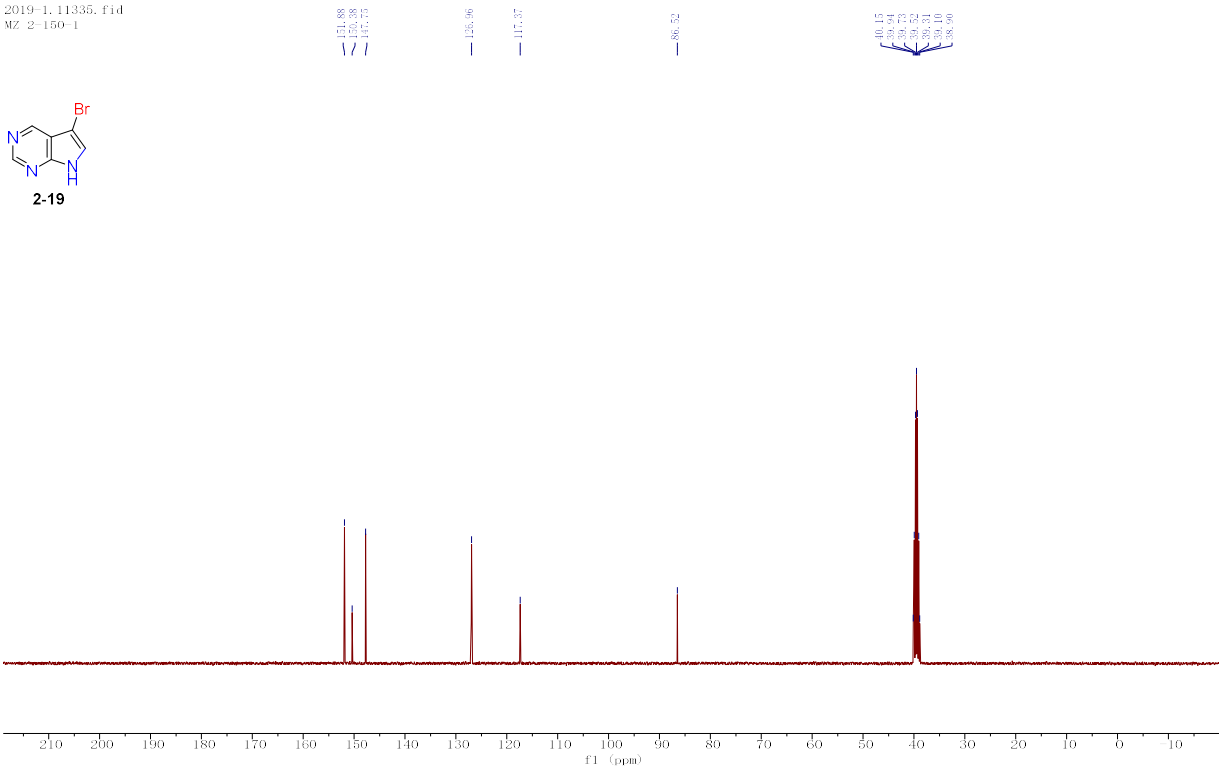


Figure S56. ^{1}H NMR of product **2-19**, related Table 2

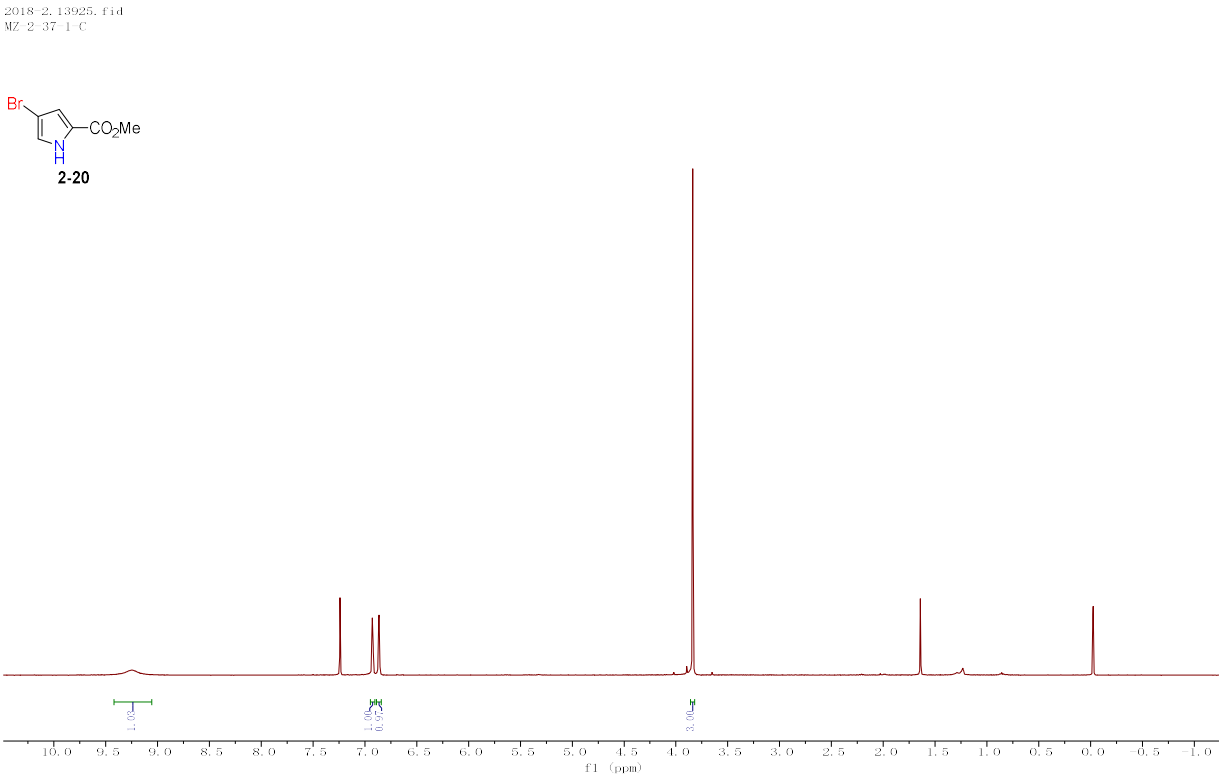


Figure S57. ^{1}H NMR of product **2-20**, related Table 2

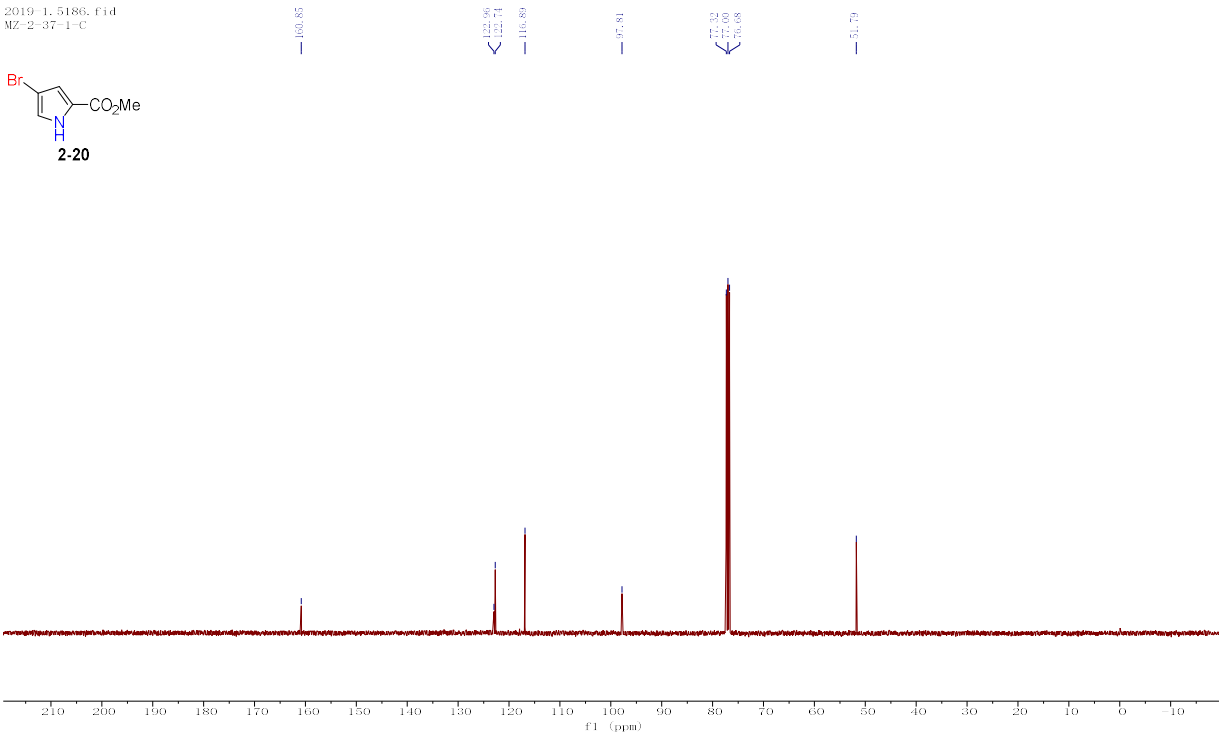


Figure S58. ^{13}C NMR of product **2-20**, related Table 2

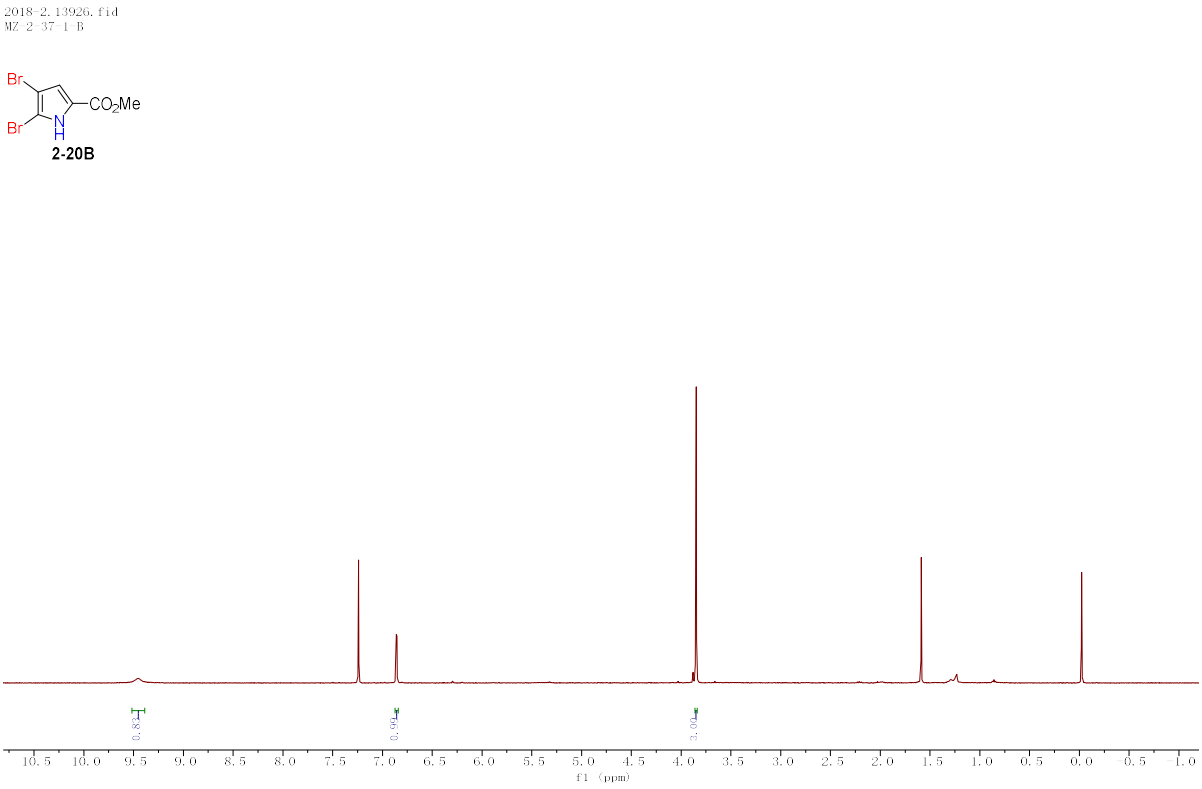


Figure S59. ^{1}H NMR of product **2-20B**, related Table 2

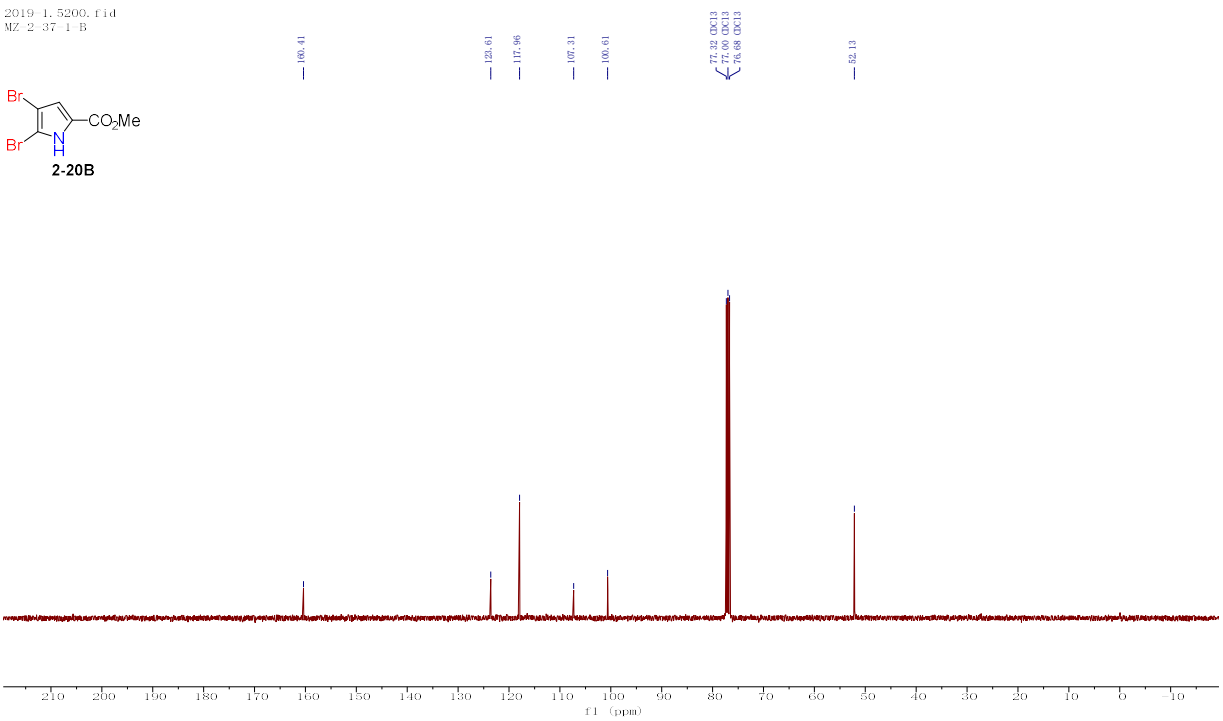


Figure S60. ^{13}C NMR of product **2-20B**, related Table 2

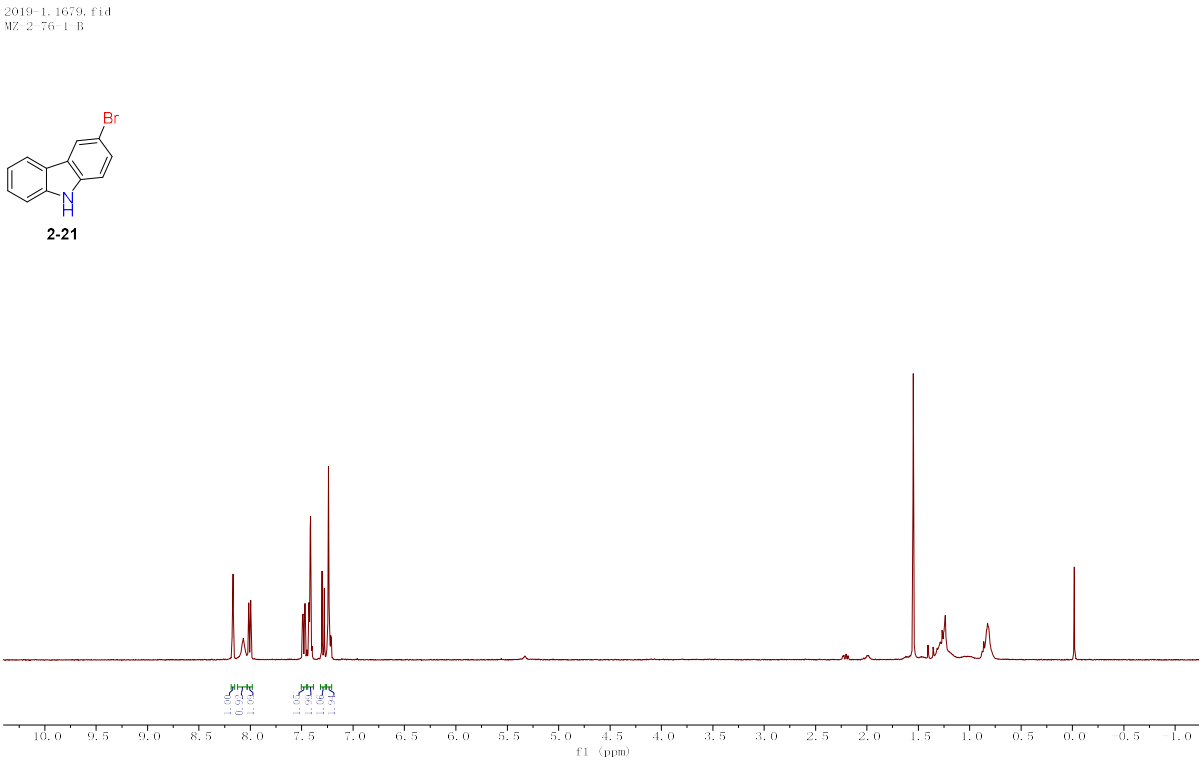


Figure S61. ^{1}H NMR of product **2-21**, related Table 2

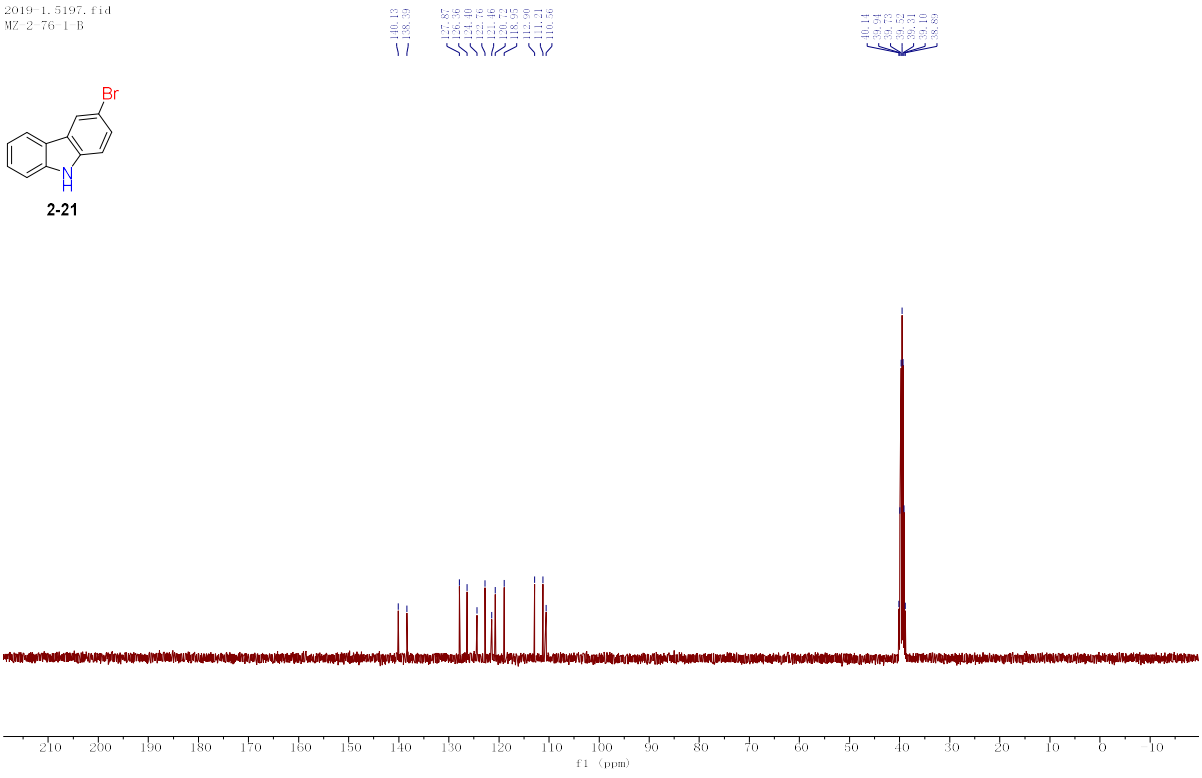


Figure S62. ^{13}C NMR of product **2-21**, related Table 2

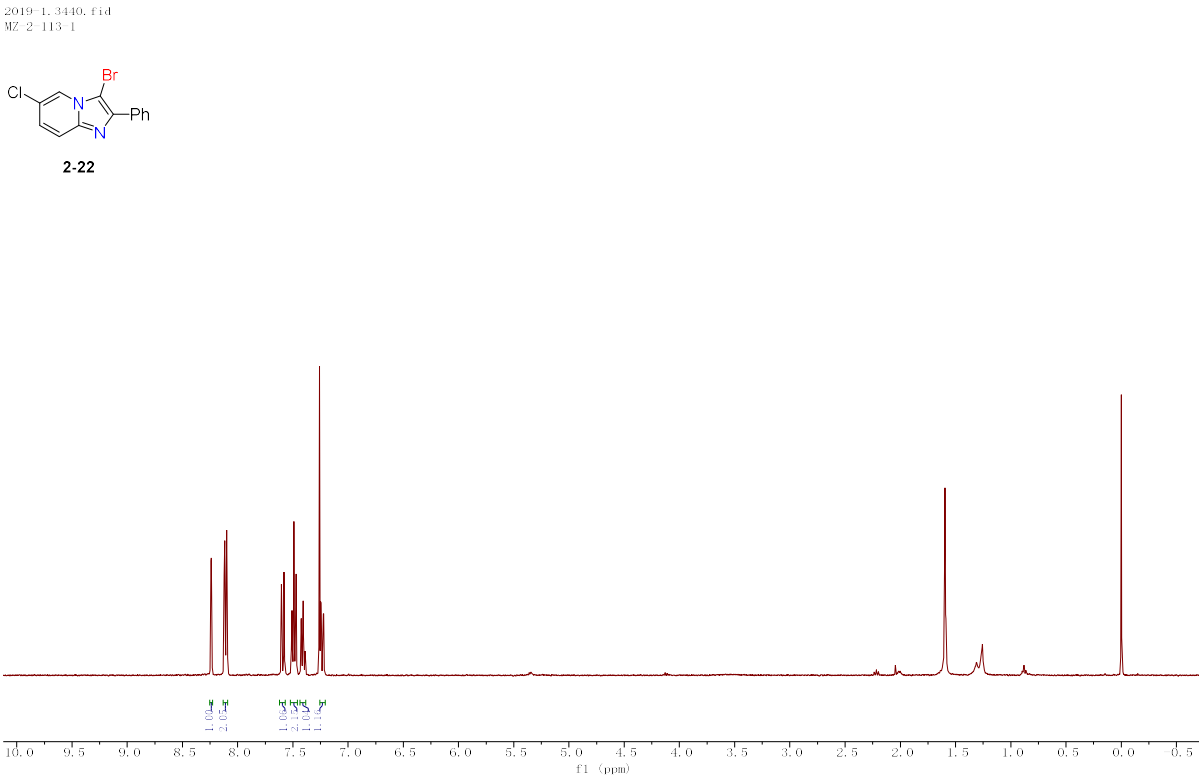


Figure S63. ^{1}H NMR of product **2-22**, related Table 2

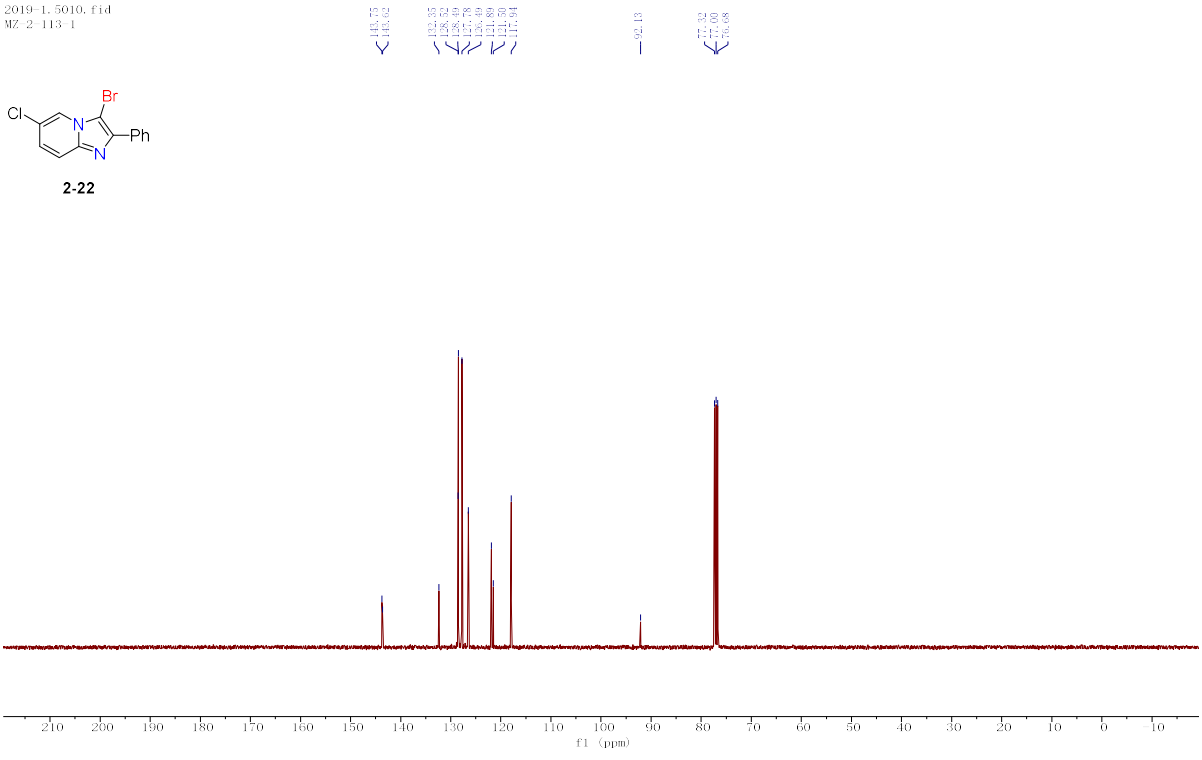


Figure S64. ^{13}C NMR of product **2-22**, related Table 2

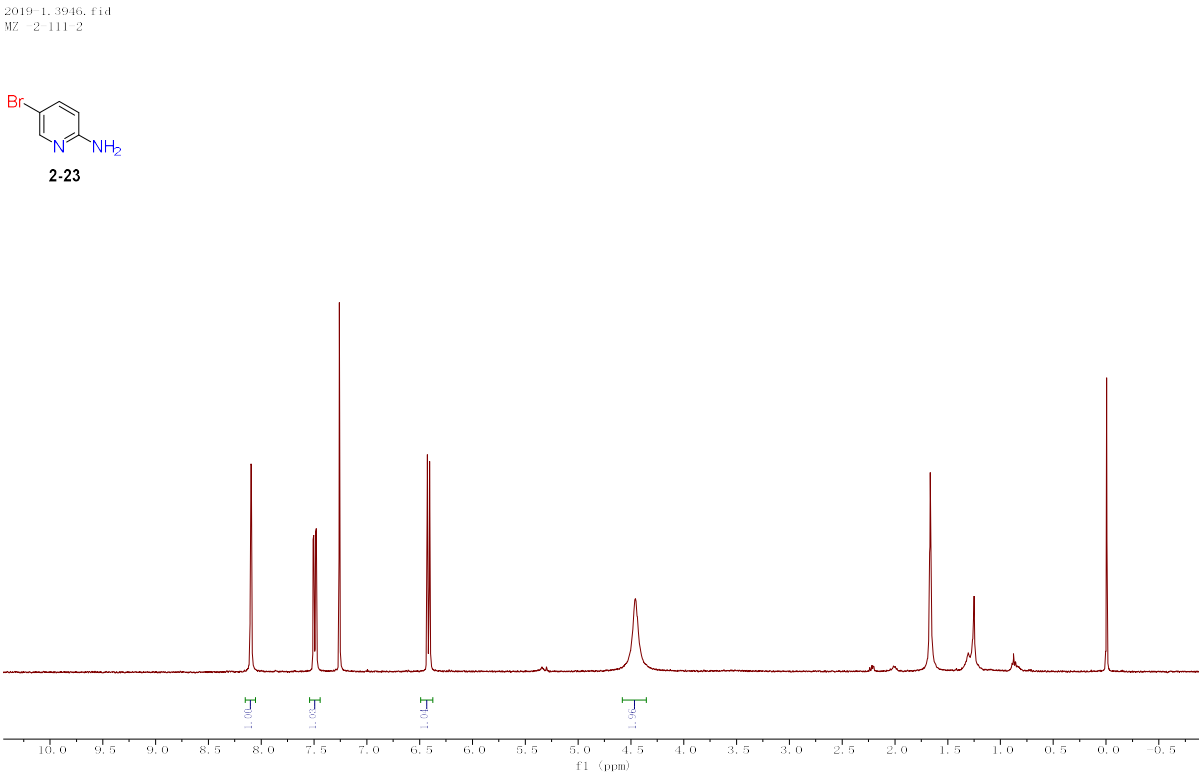


Figure S65. ^{1}H NMR of product **2-23**, related Table 2

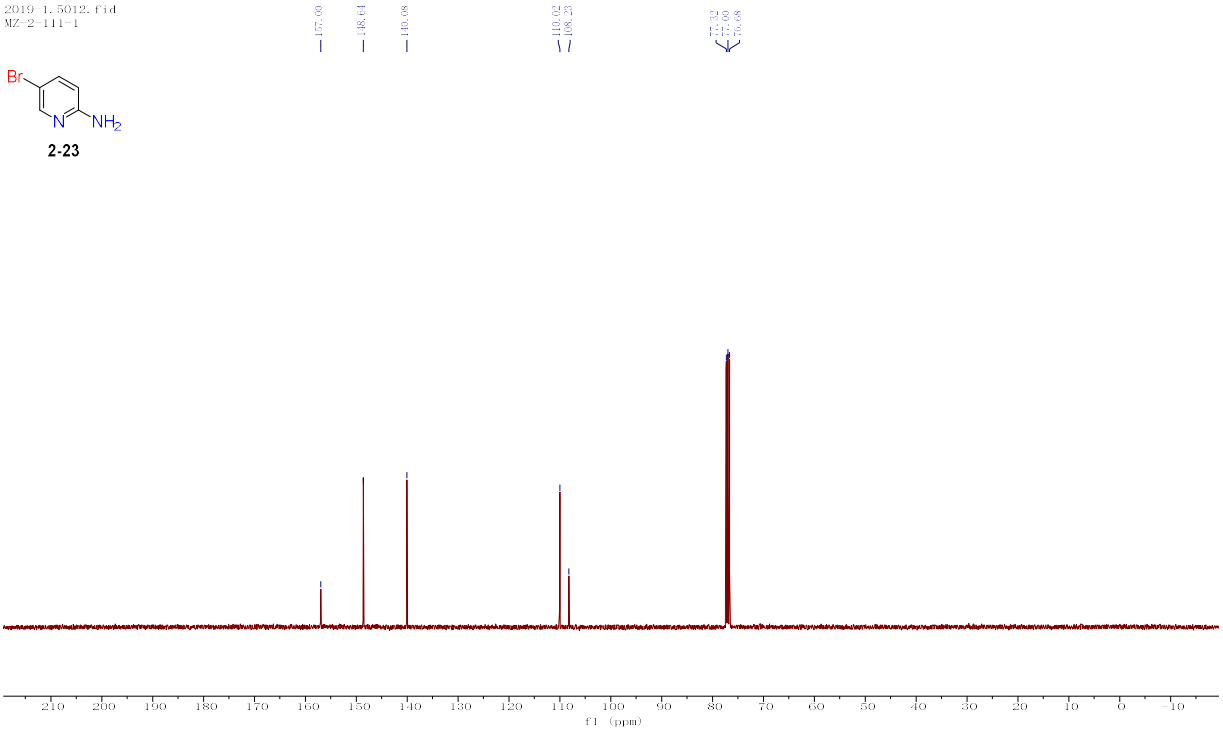


Figure S66. ^{13}C NMR of product **2-23**, related Table 2

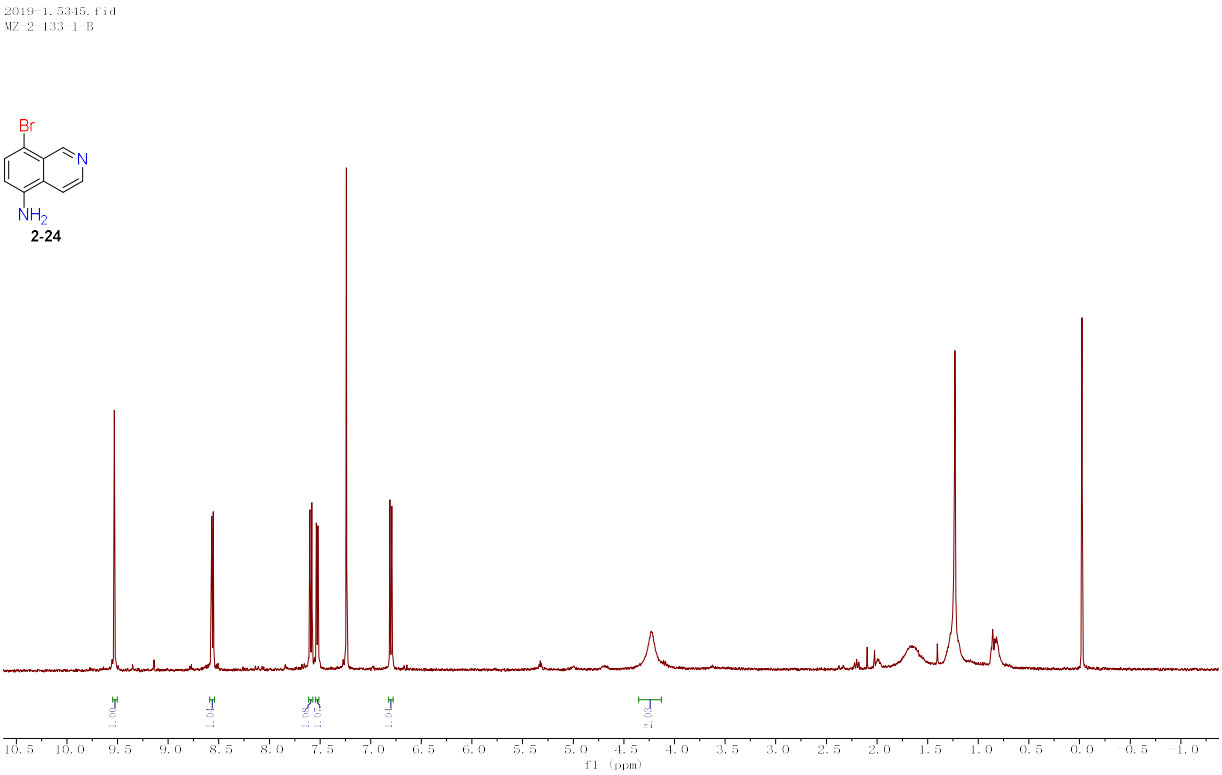


Figure S67. ^{1}H NMR of product **2-24**, related Table 2

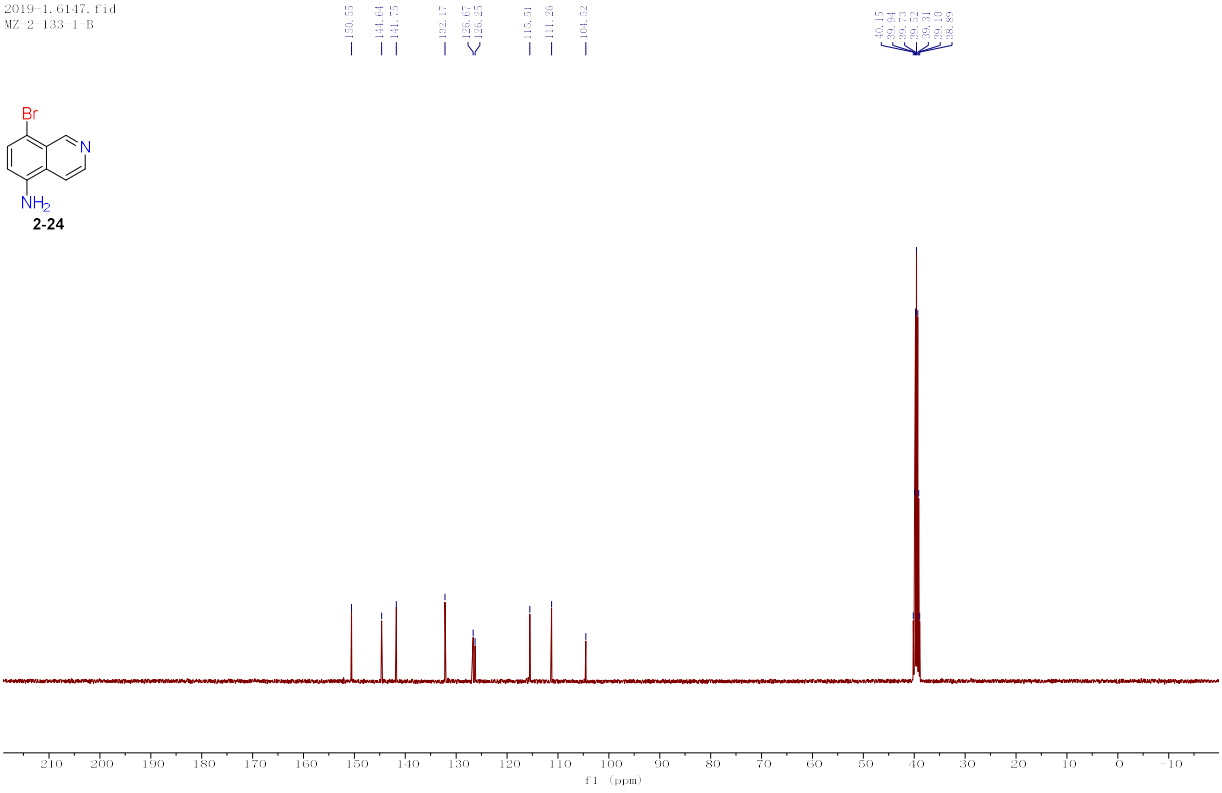


Figure S68. ^{13}C NMR of product **2-23**, related Table 2

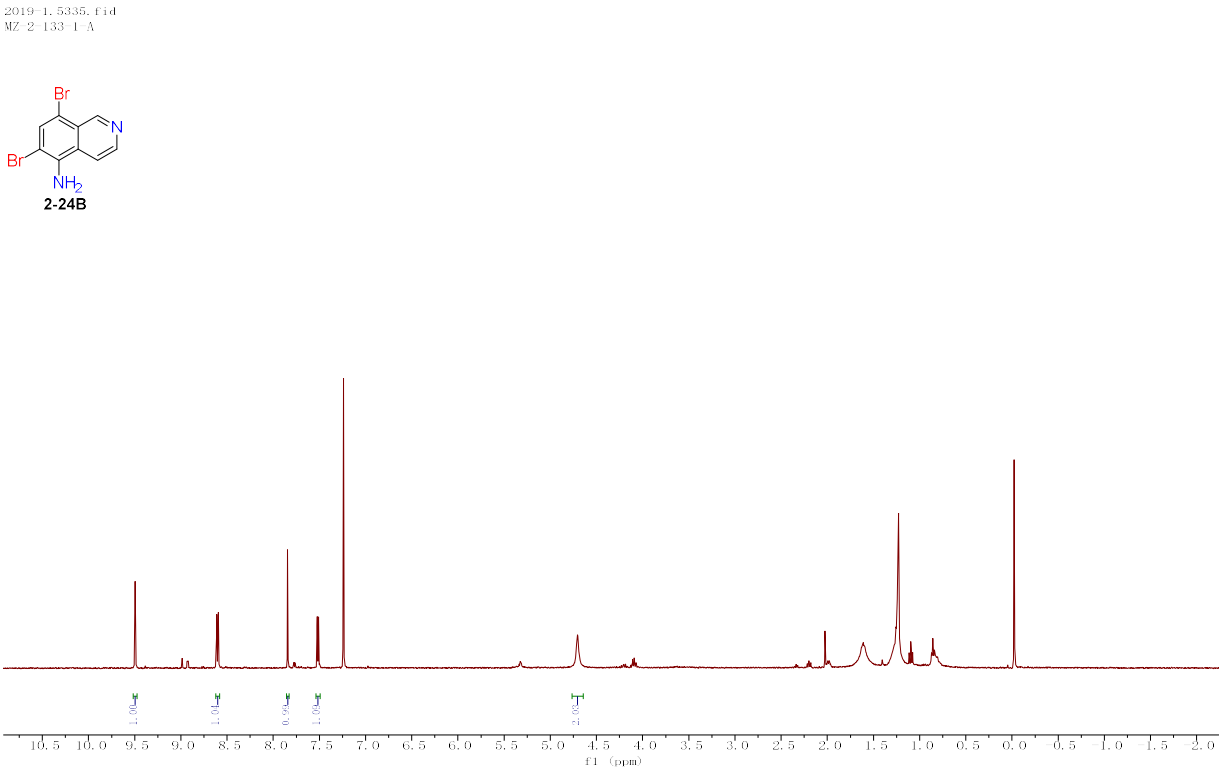


Figure S69. ^{1}H NMR of product **2-24B**, related Table 2

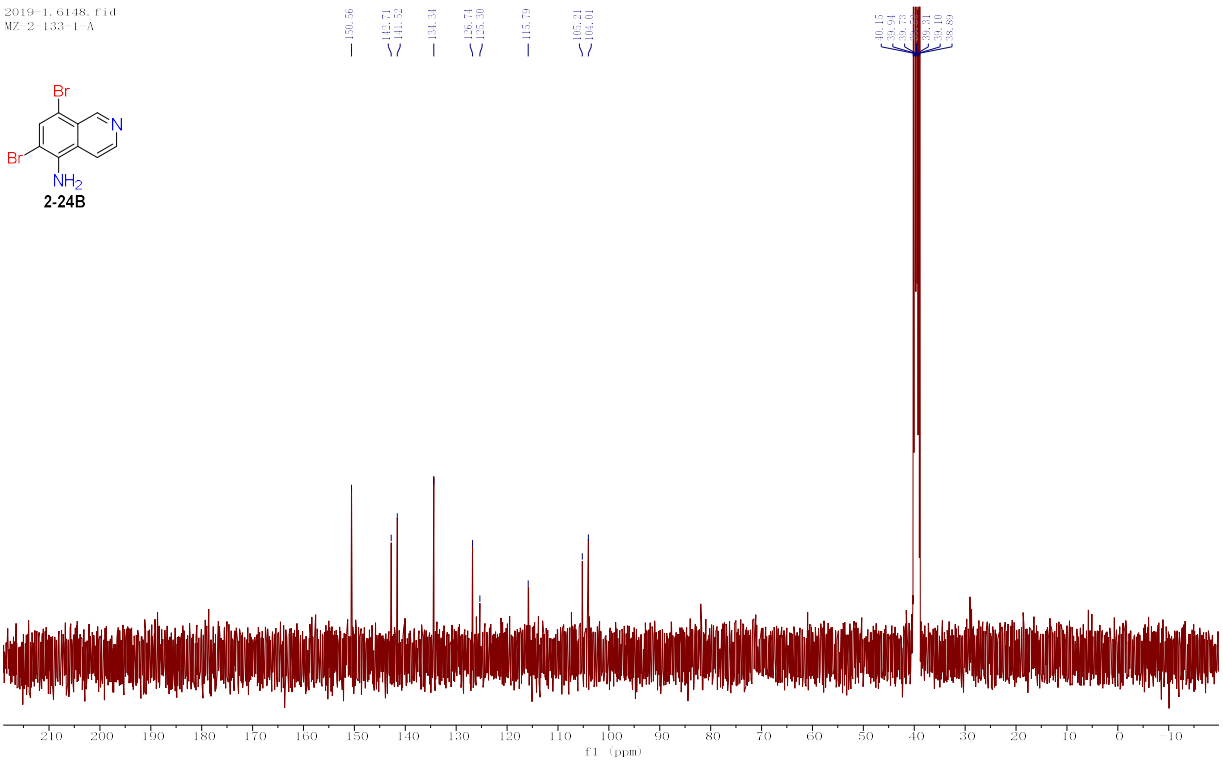


Figure S70. ^{13}C NMR of product **2-24B**, related Table 2

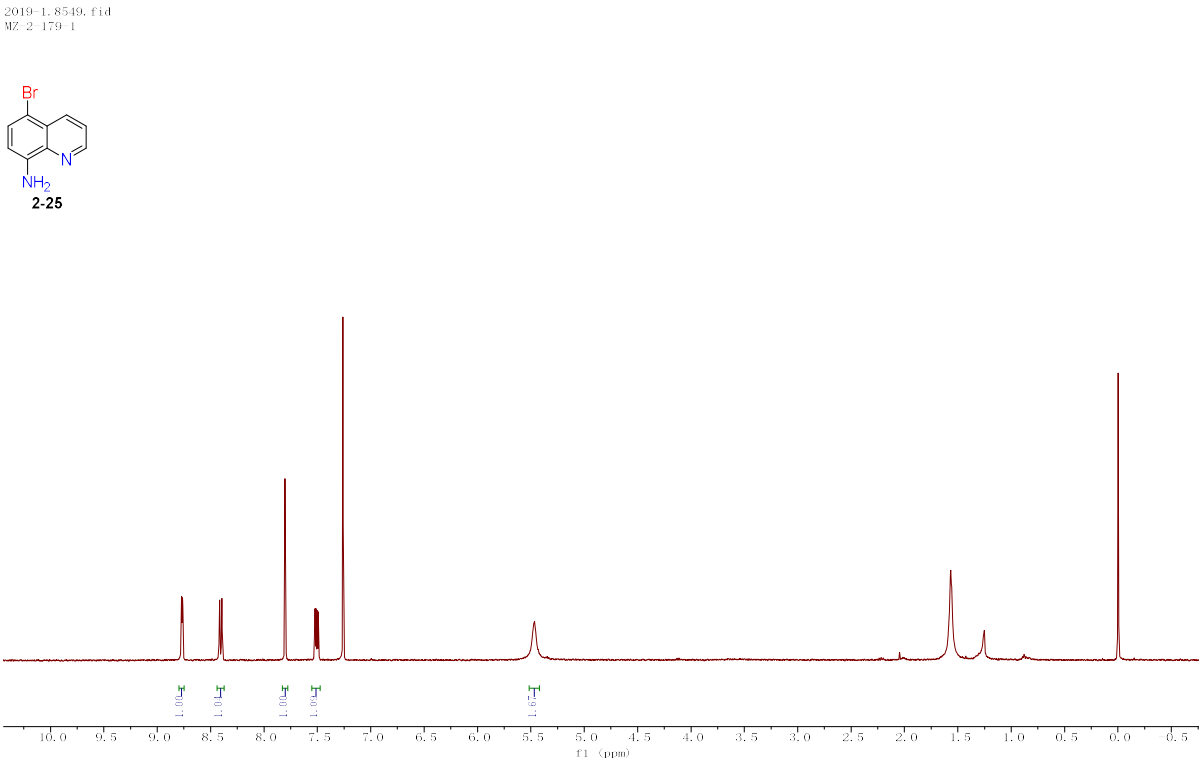


Figure S71. ^{1}H NMR of product **2-25**, related Table 2

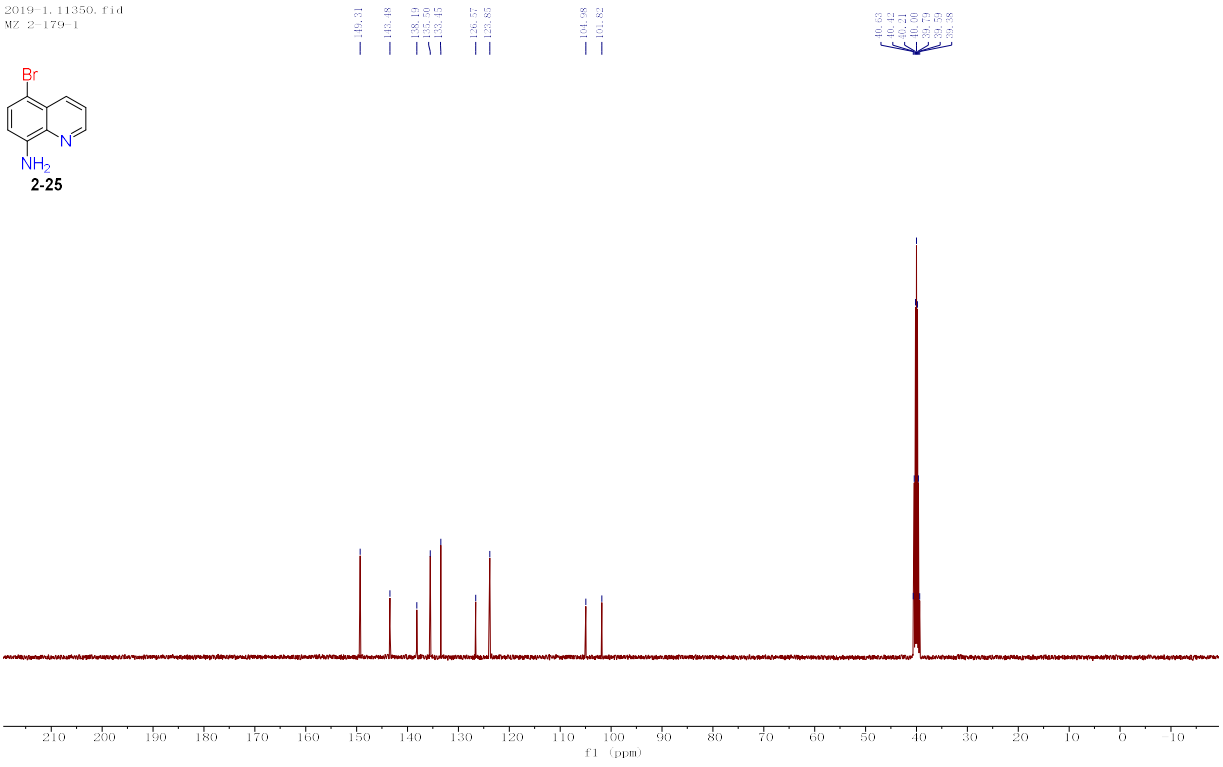


Figure S72. ^{13}C NMR of product **2-25**, related Table 2

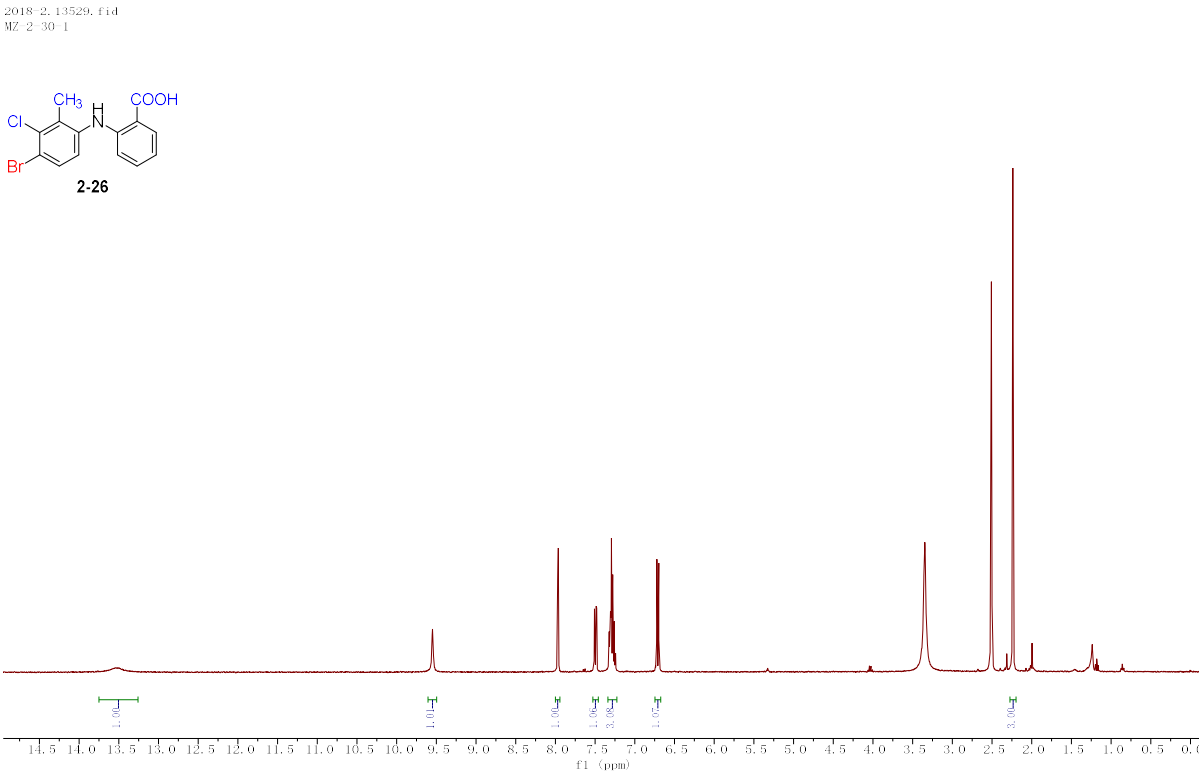


Figure S73. ^{1}H NMR of product **2-26**, related Table 2

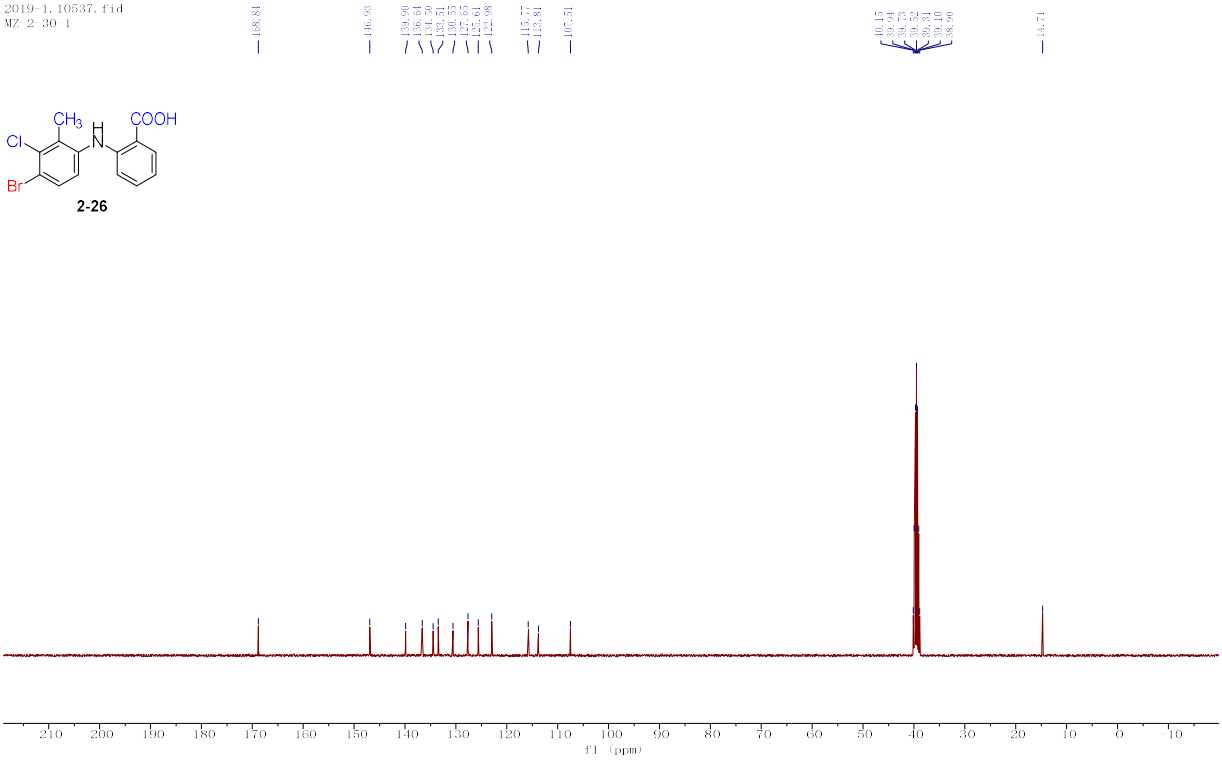


Figure S74. ^{13}C NMR of product **2-26**, related Table 2

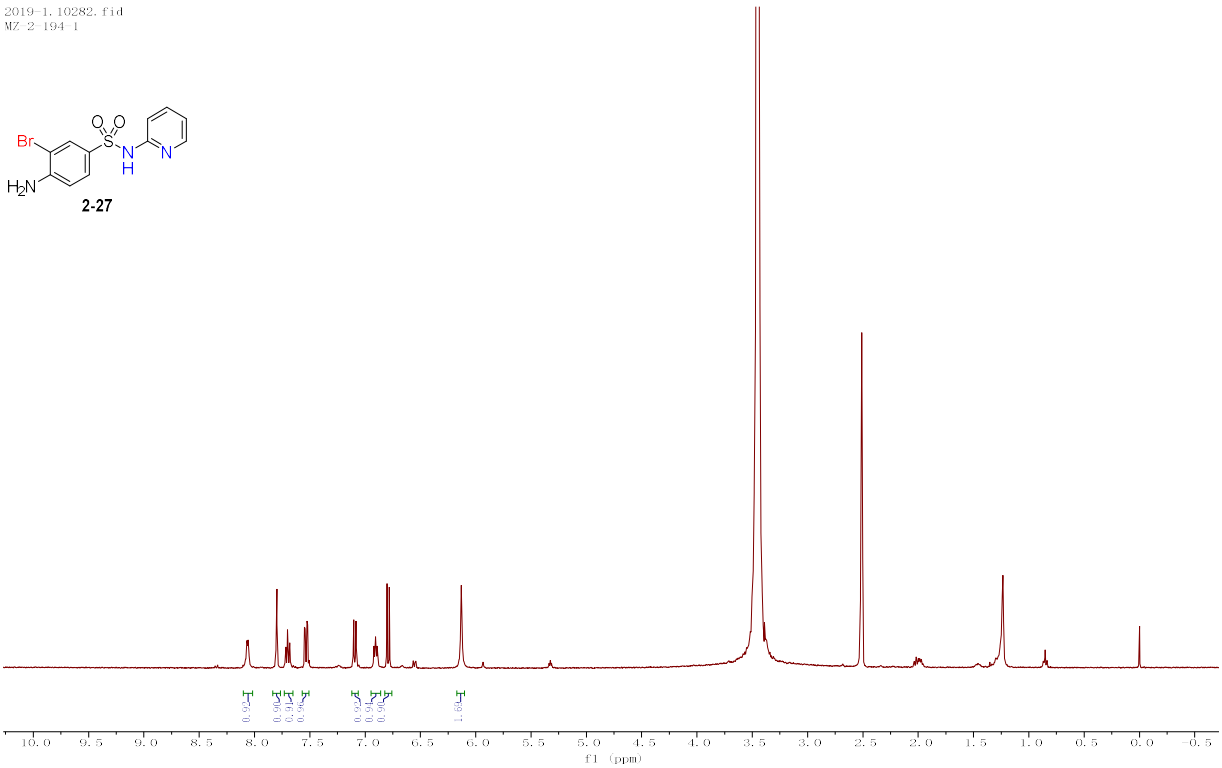


Figure S75. ^{1}H NMR of product **2-27**, related Table 2

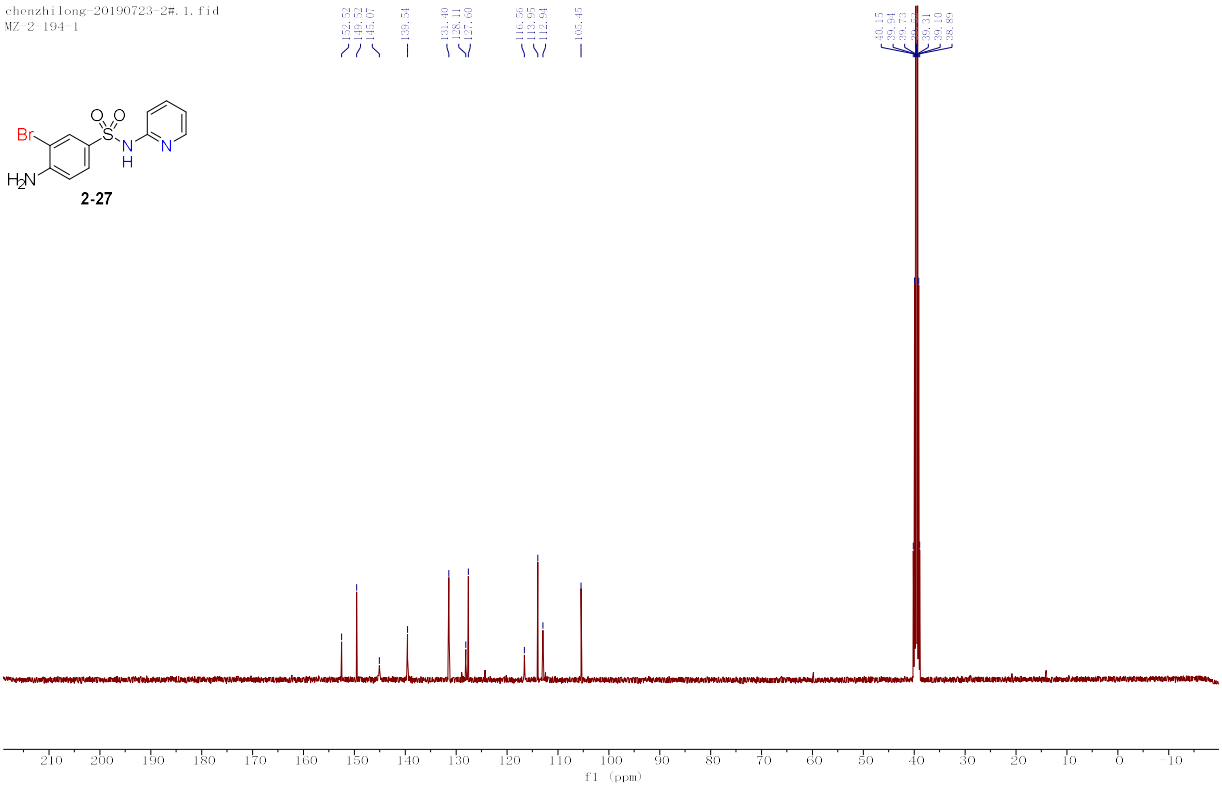


Figure S76. ^{13}C NMR of product **2-27**, related Table 2

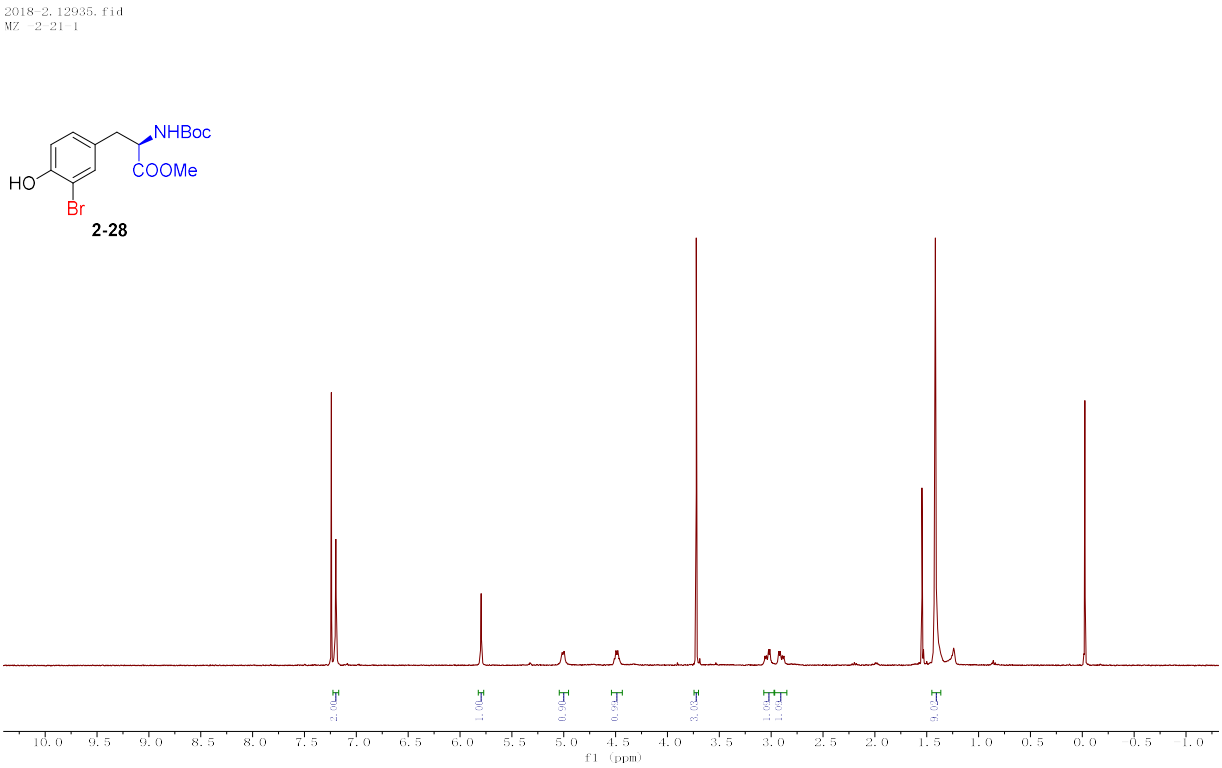


Figure S77. ^{1}H NMR of product **2-28**, related Table 2

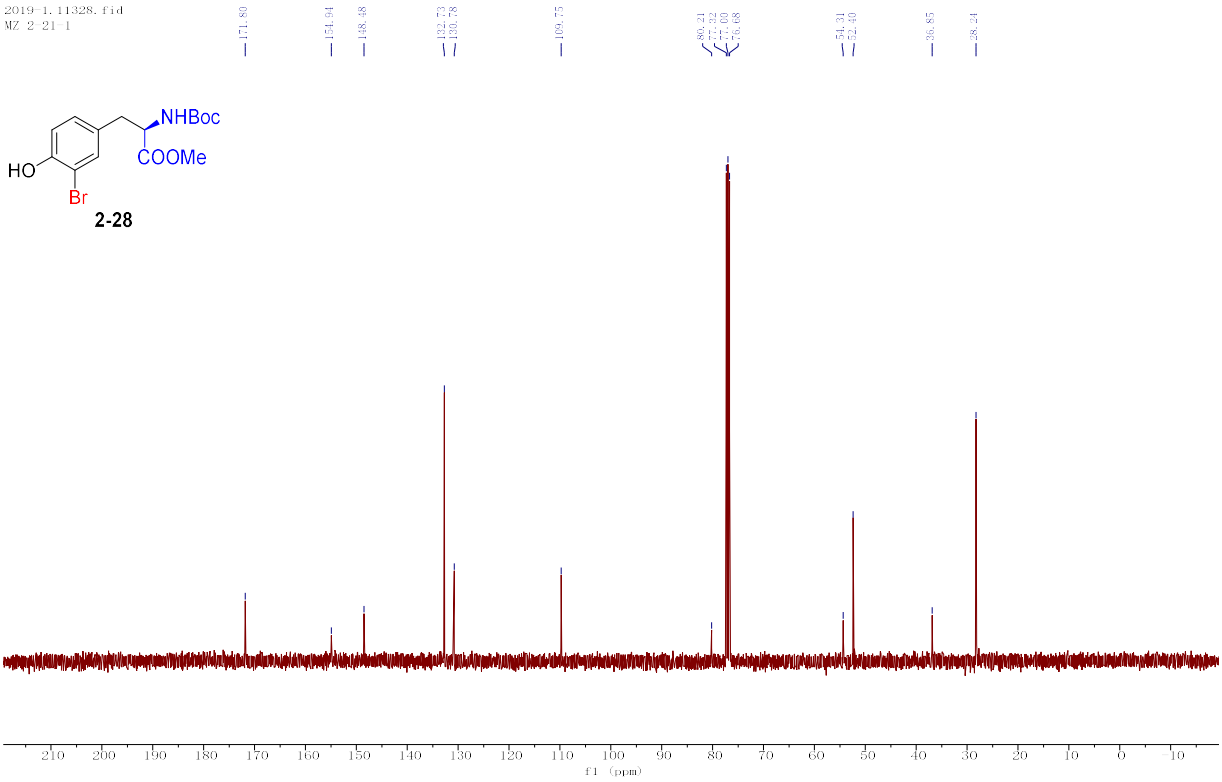


Figure S78. ^{13}C NMR of product **2-28**, related Table 2

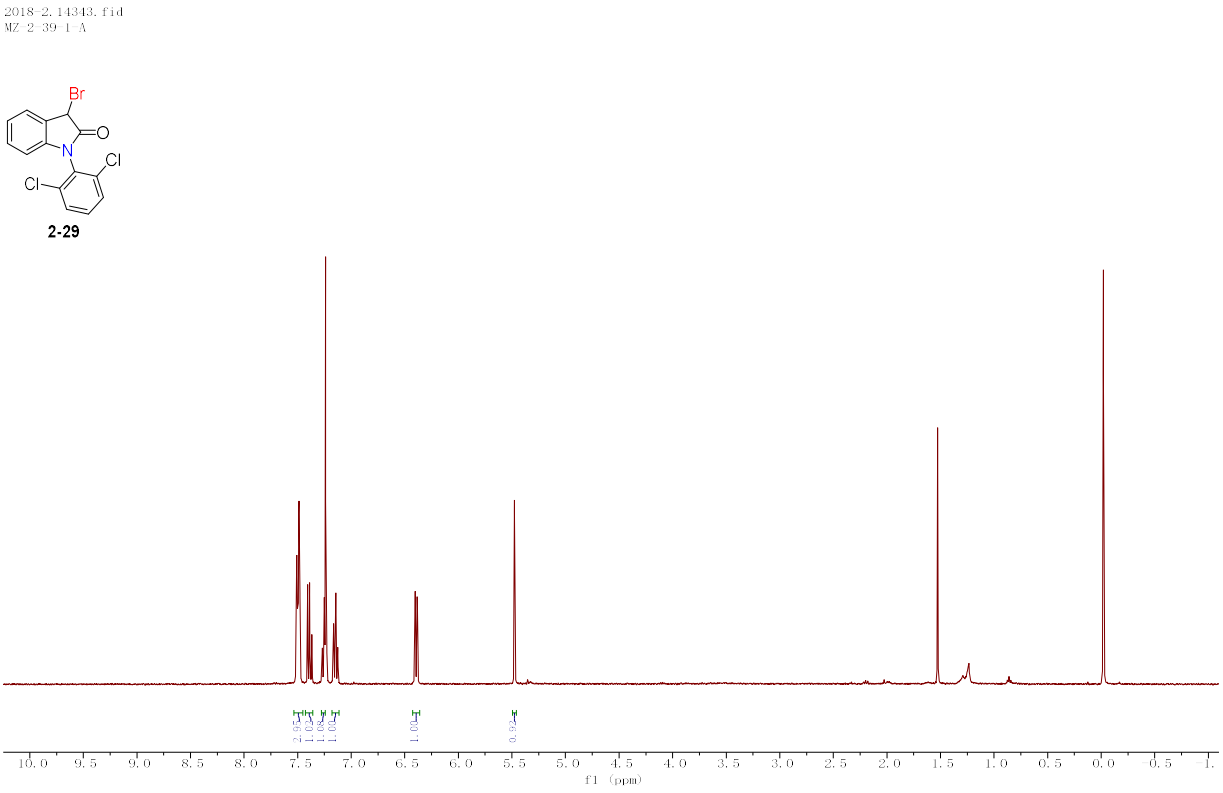


Figure S79. ^{1}H NMR of product **2-29**, related Table 2

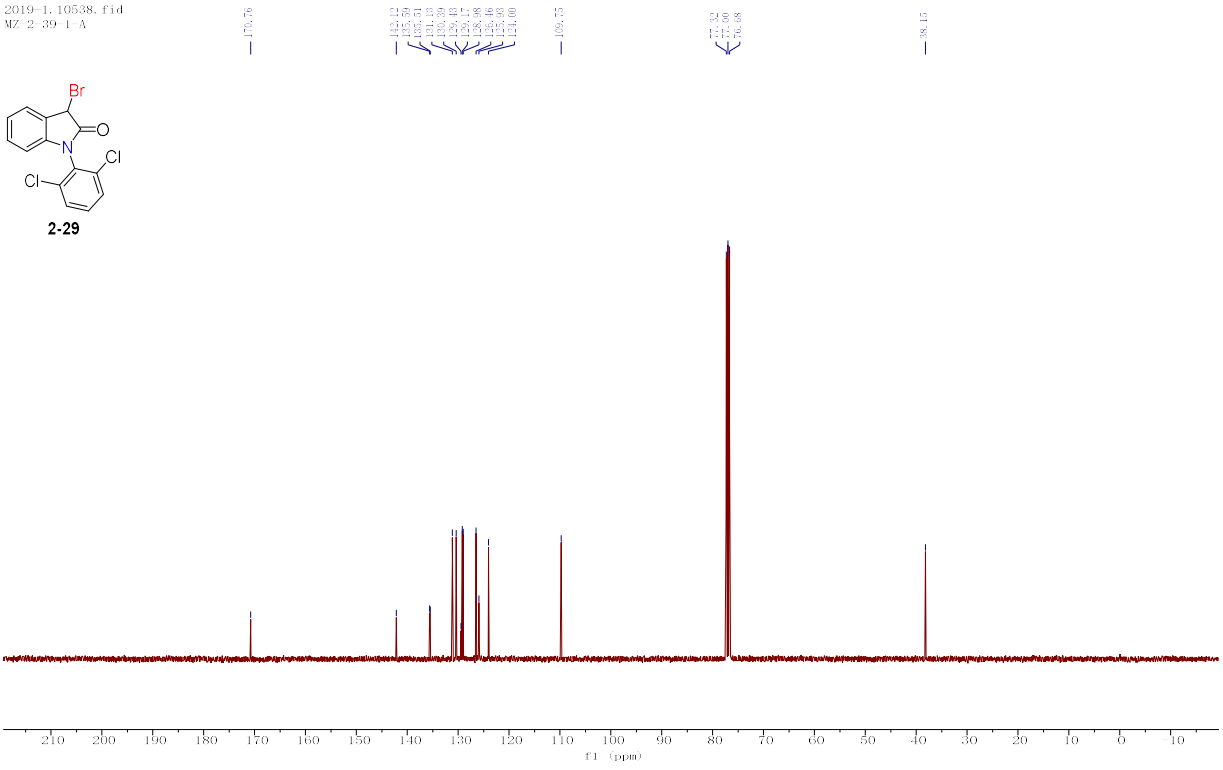


Figure S80. ^{13}C NMR of product **2-29**, related Table 2

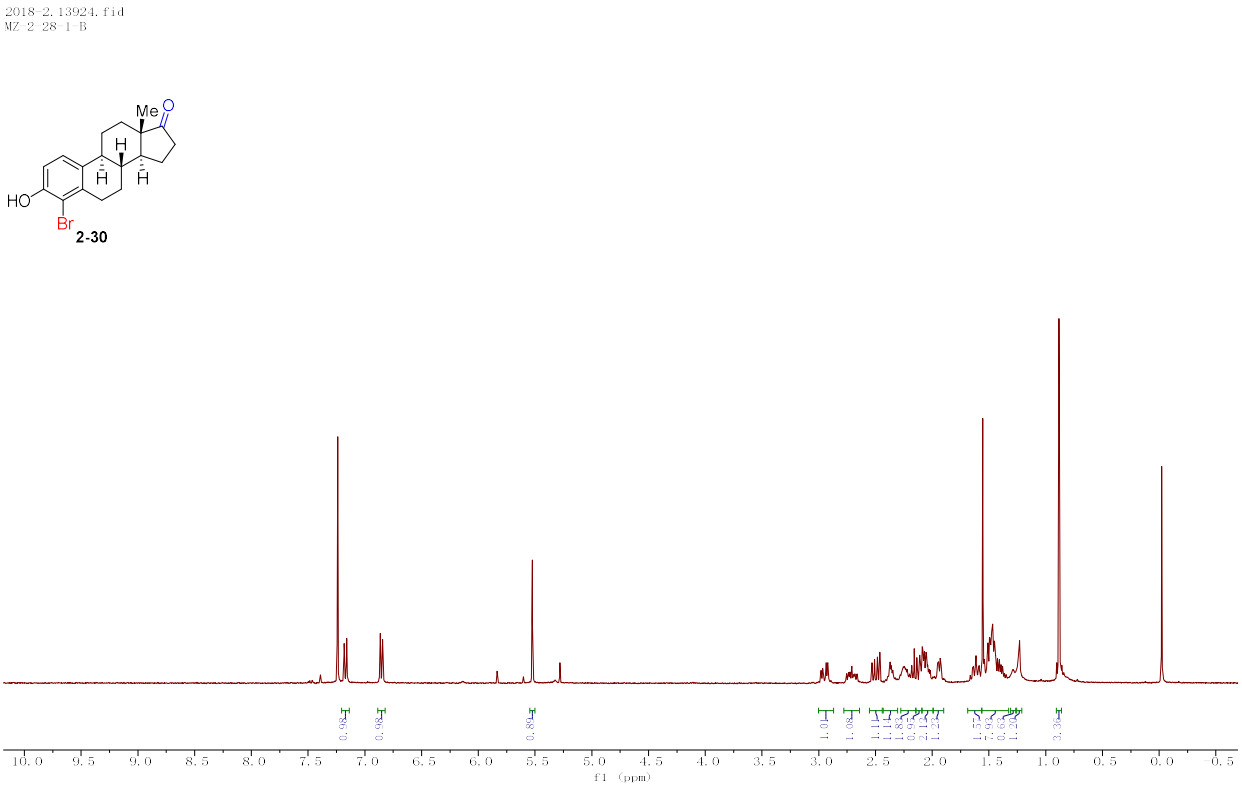


Figure S81. ^{1}H NMR of product **2-30**, related Table 2

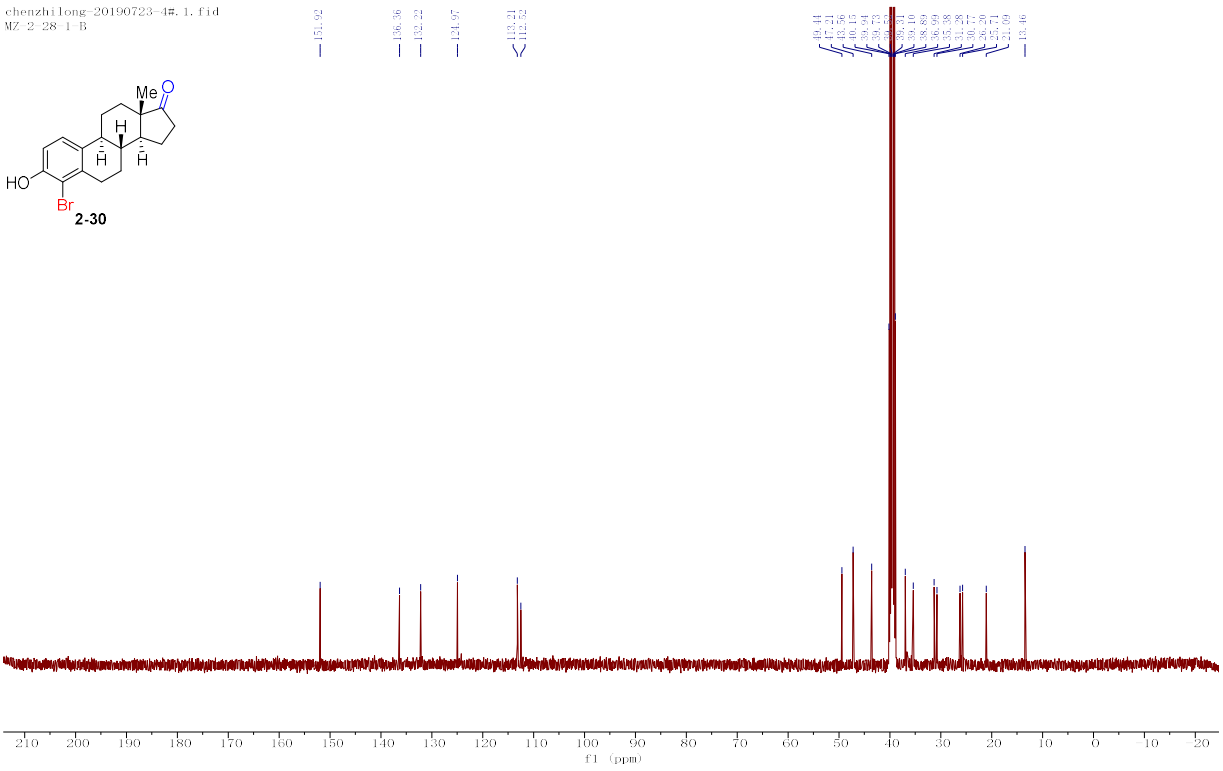


Figure S82. ^{13}C NMR of product **2-30**, related Table 2

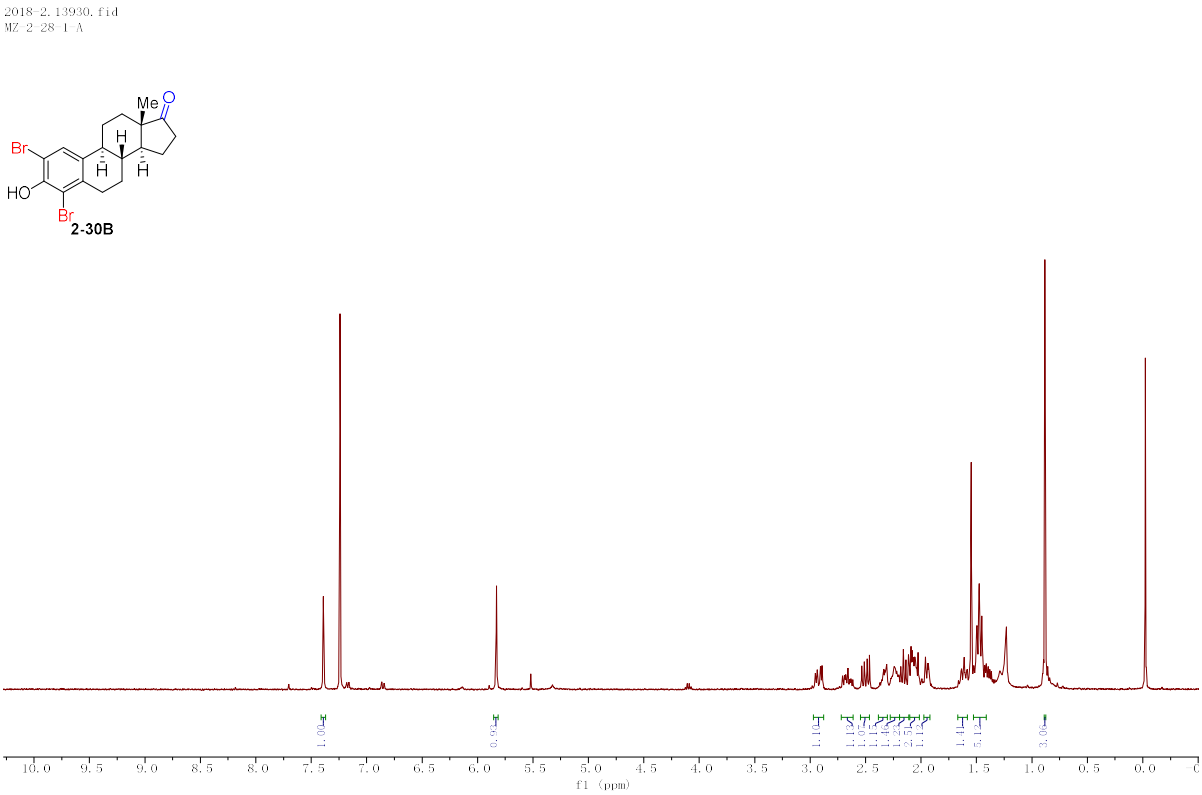


Figure S83. ^{1}H NMR of product **2-30B**, related Table 2

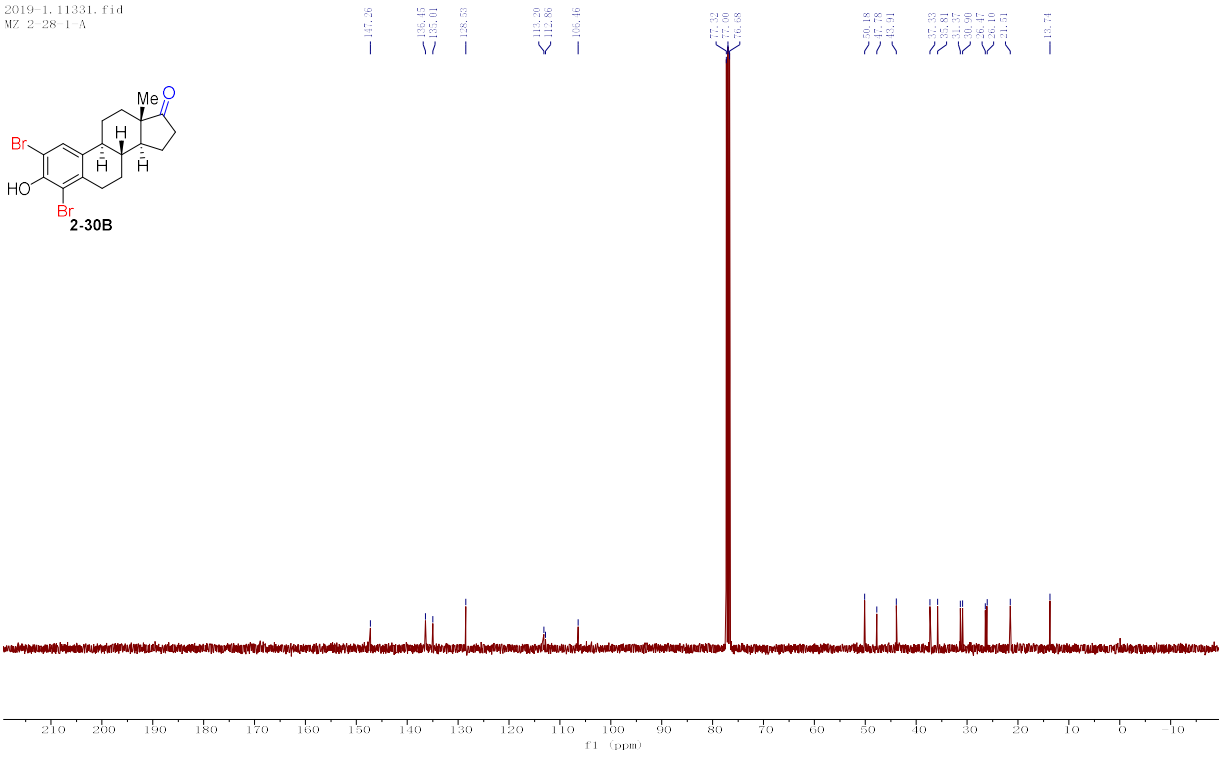


Figure S84. ^{13}C NMR of product **2-30**, related Table 2

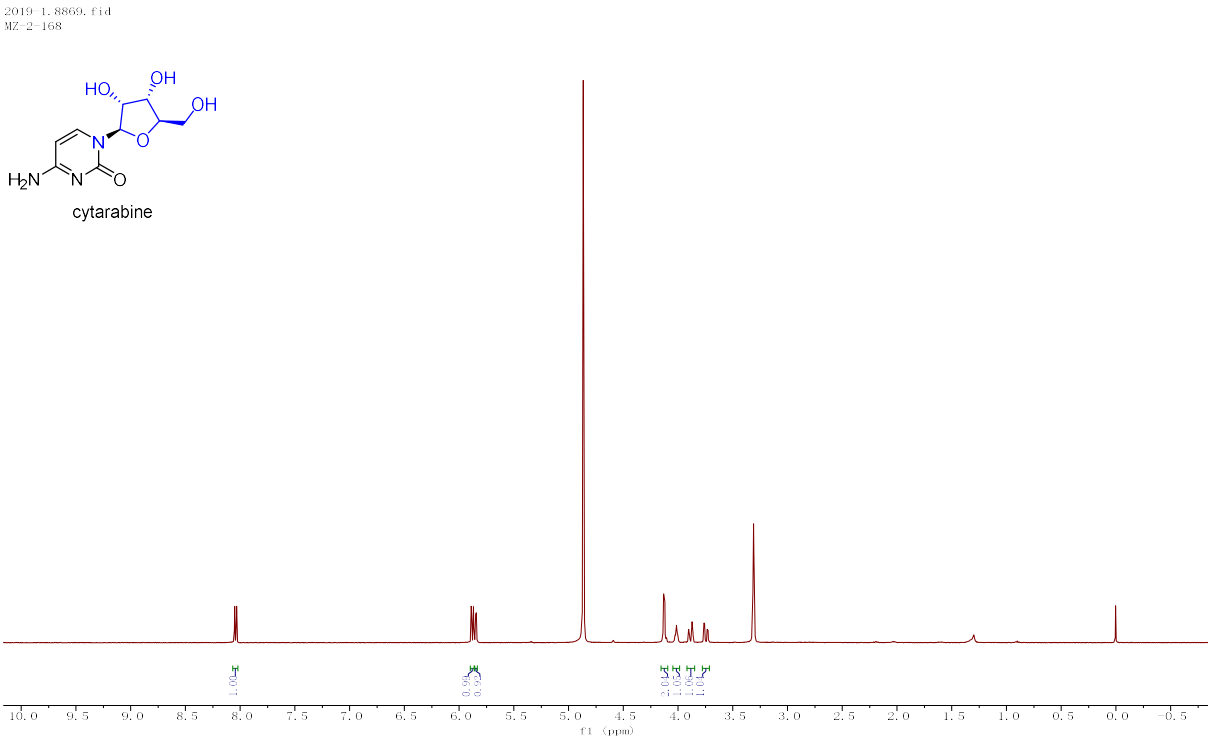


Figure S85. ^{1}H NMR of product cytarabine, related Table 2

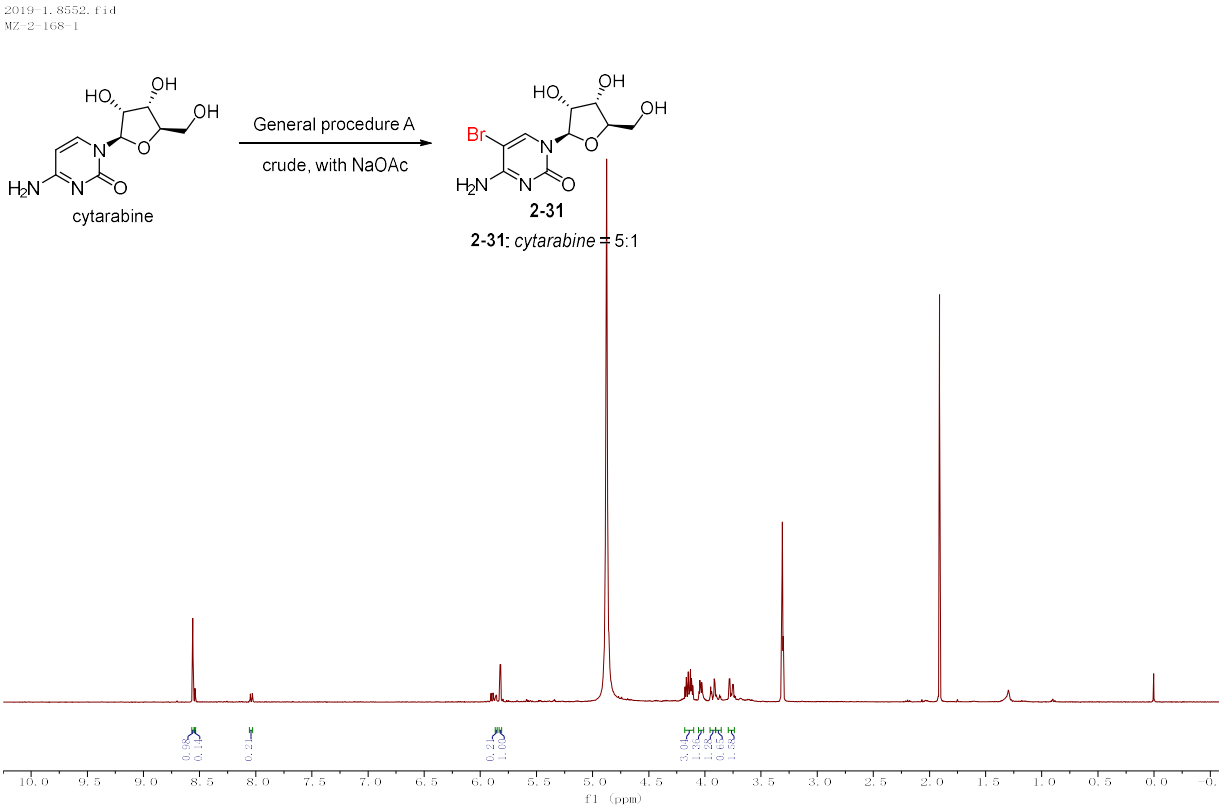


Figure S86. ^{1}H NMR of crude product from bromination of cytarabine, related Table 2

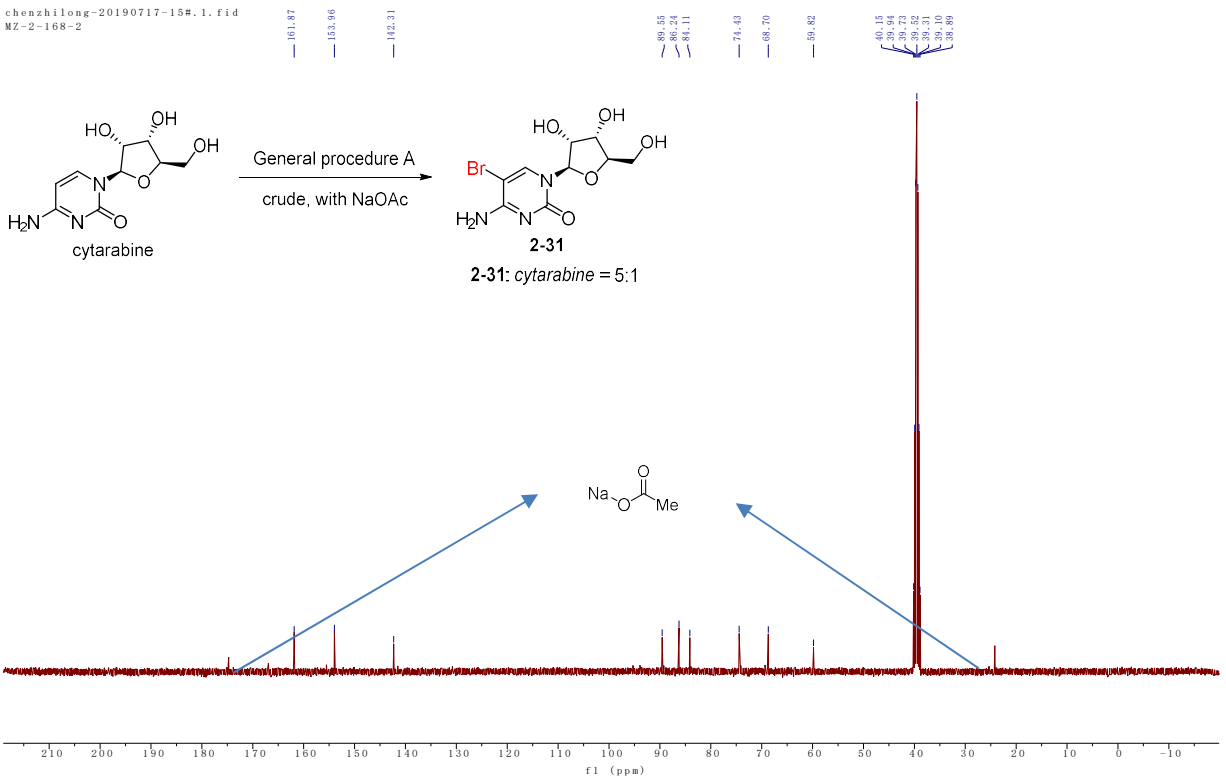


Figure S87. ^{13}C NMR of crude product from bromination of cytarabine, related Table 2

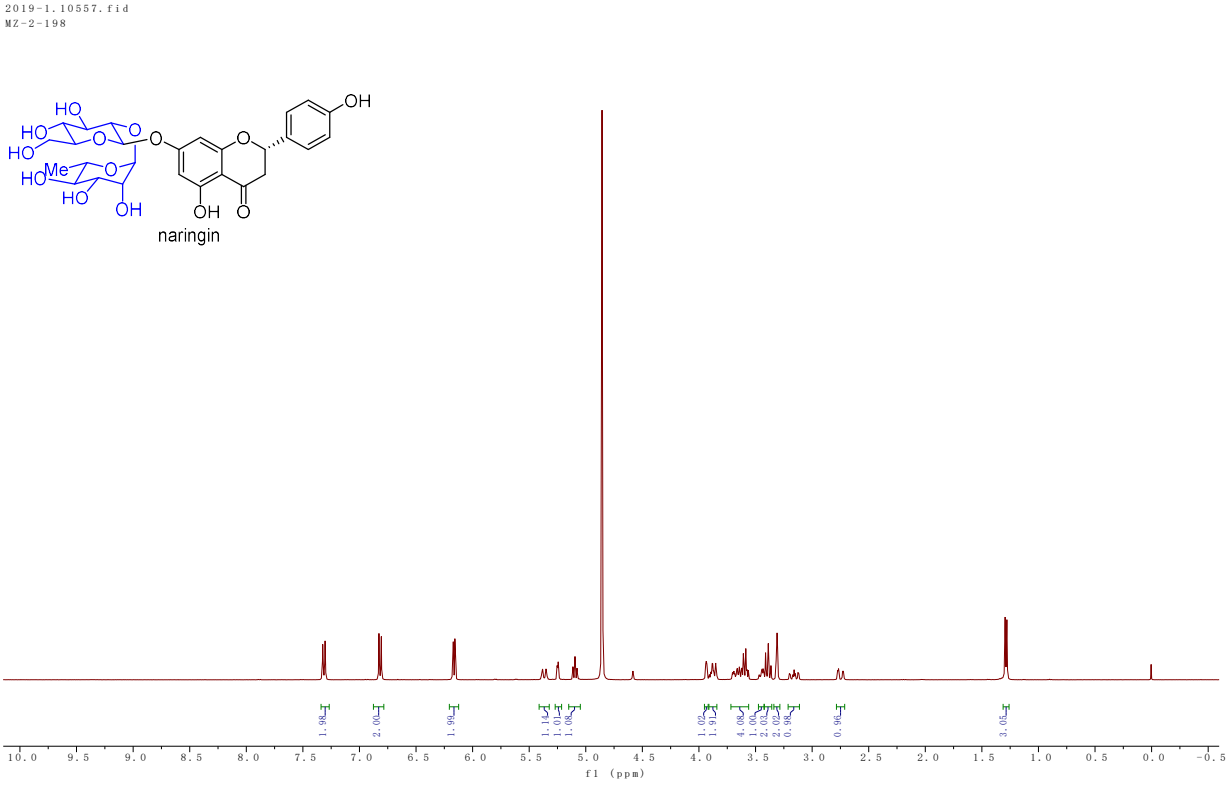


Figure S88. ^{1}H NMR of product naringin, related Table 2

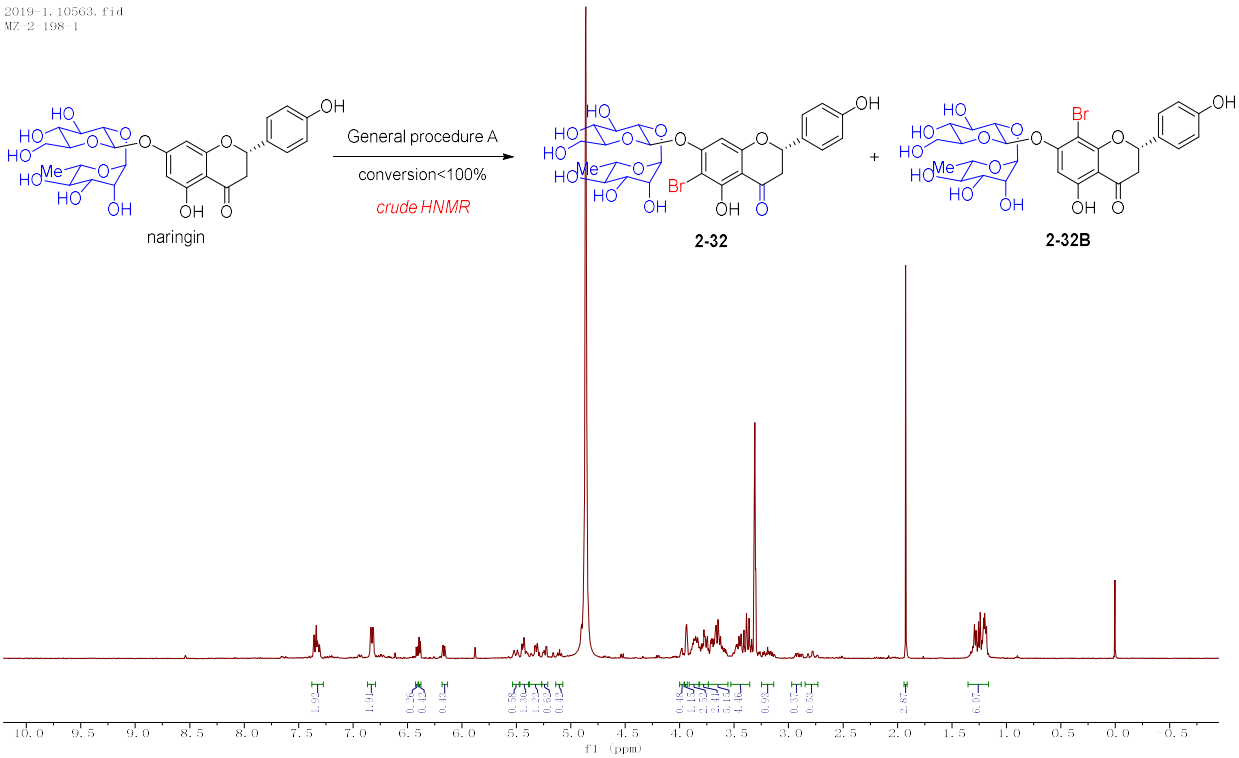


Figure S89. ^{1}H NMR of crude products from bromination of naringin, related Table 2

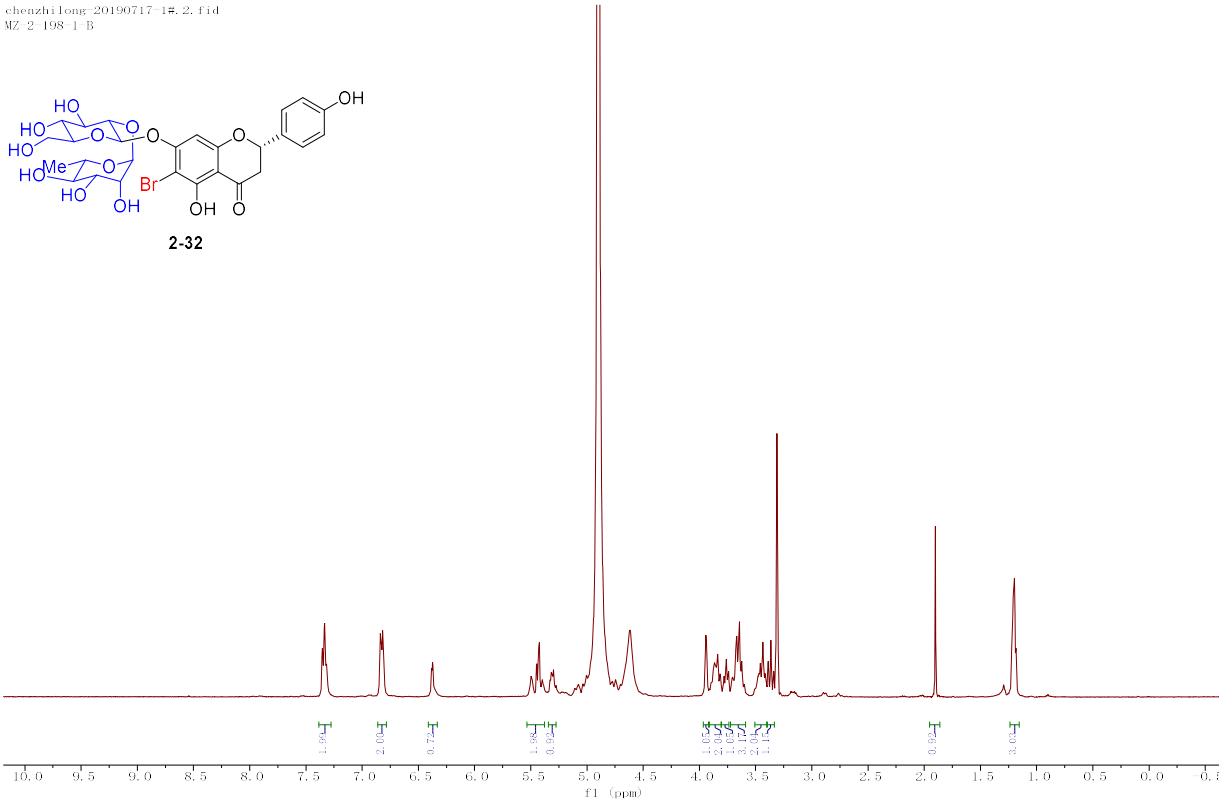


Figure S90. ^{1}H NMR of crude product **2-32**, related Table 2

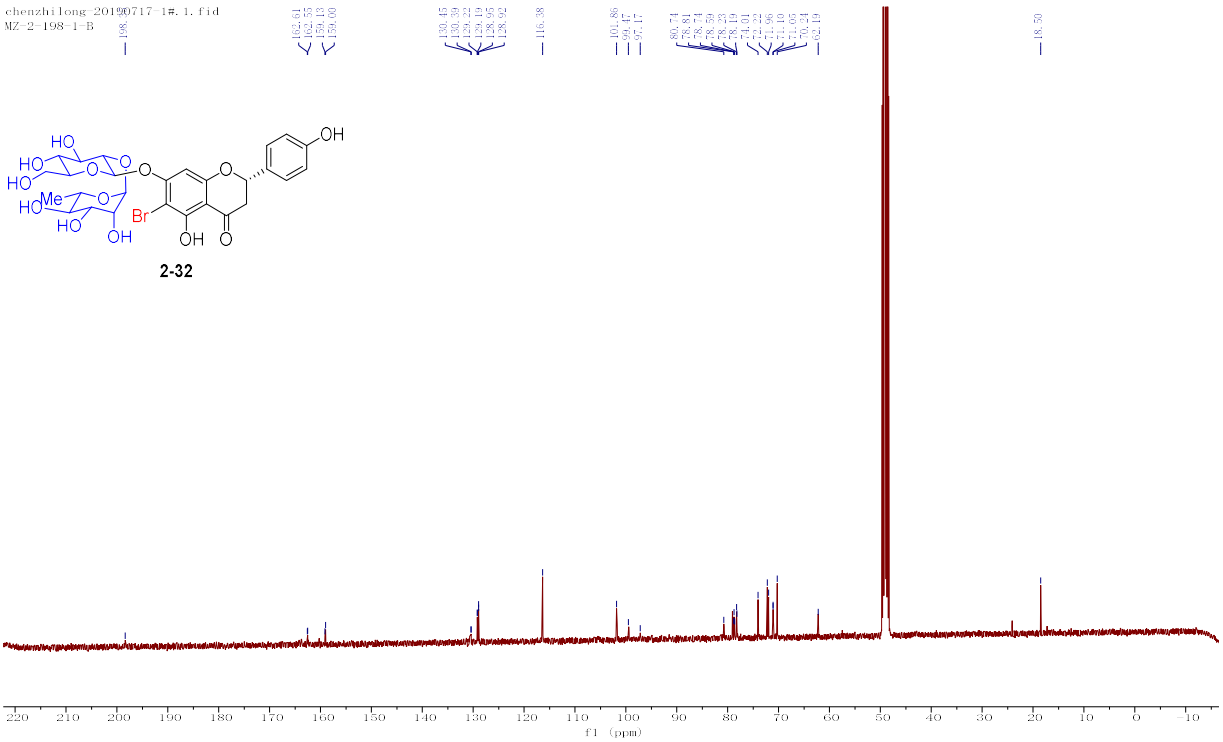


Figure S91. ^{13}C NMR of crude product **2-32**, related Table 2

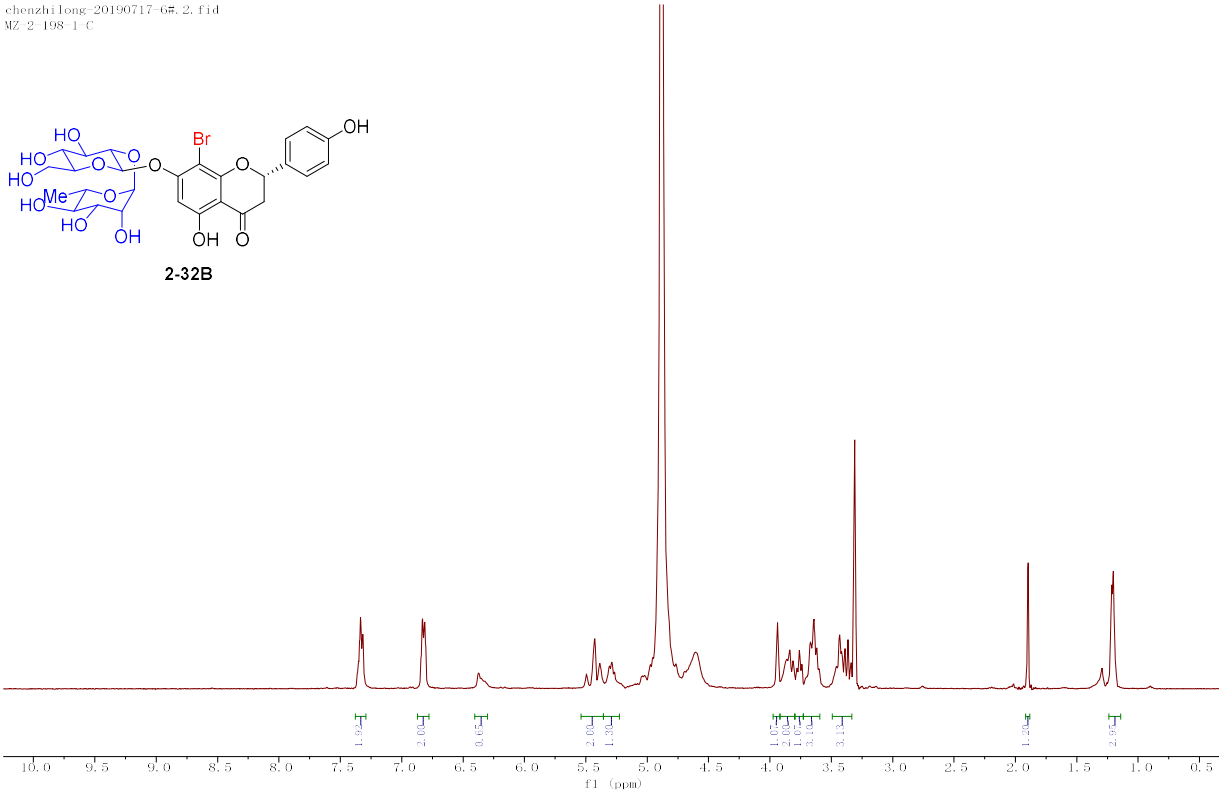


Figure S91. ^{1}H NMR of crude product **2-32B**, related Table 2

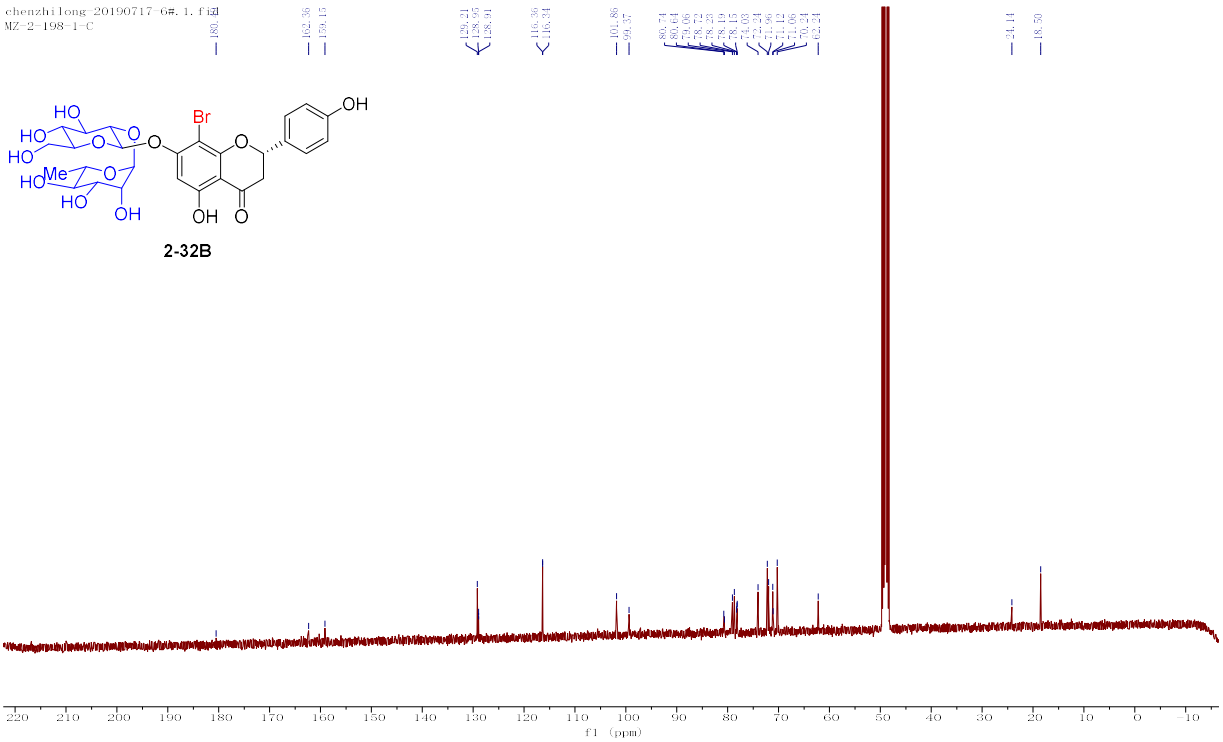


Figure S93. ^{13}C NMR of crude product **2-32B**, related Table 2

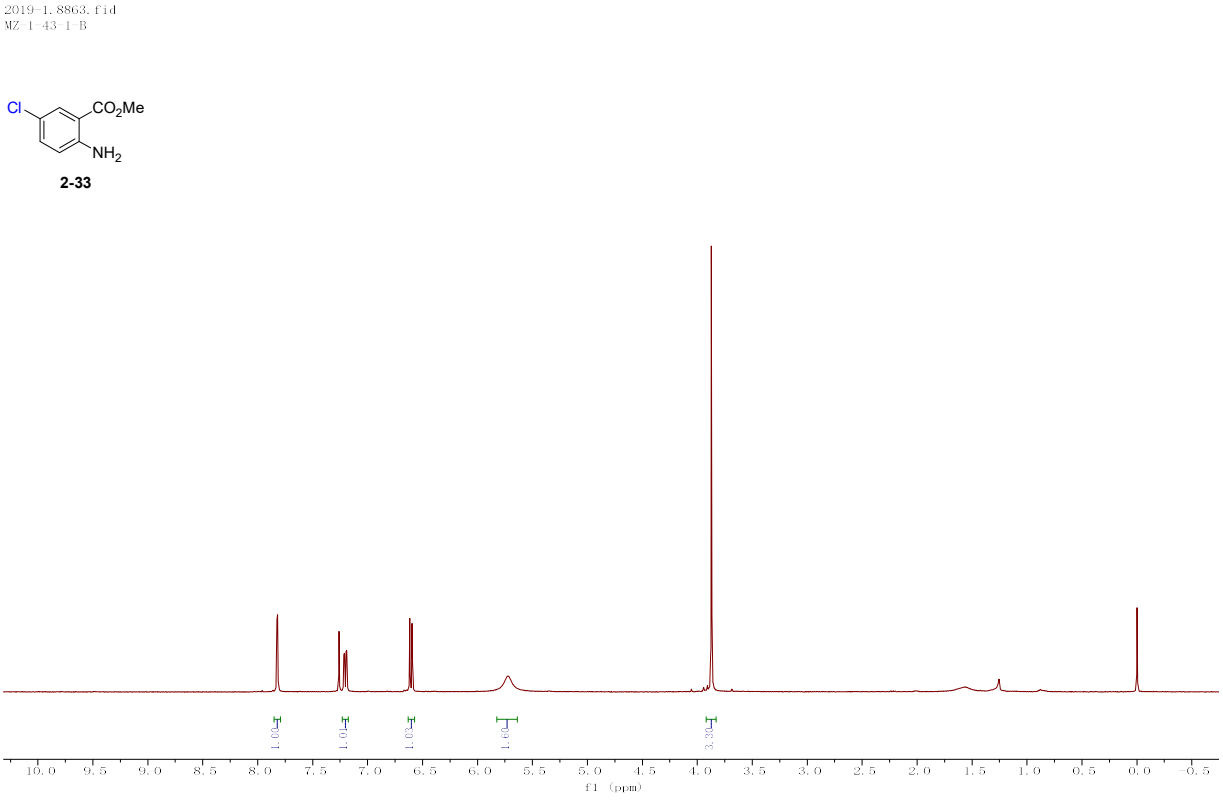


Figure S94. ^{1}H NMR of crude product **2-33**, related Table 3

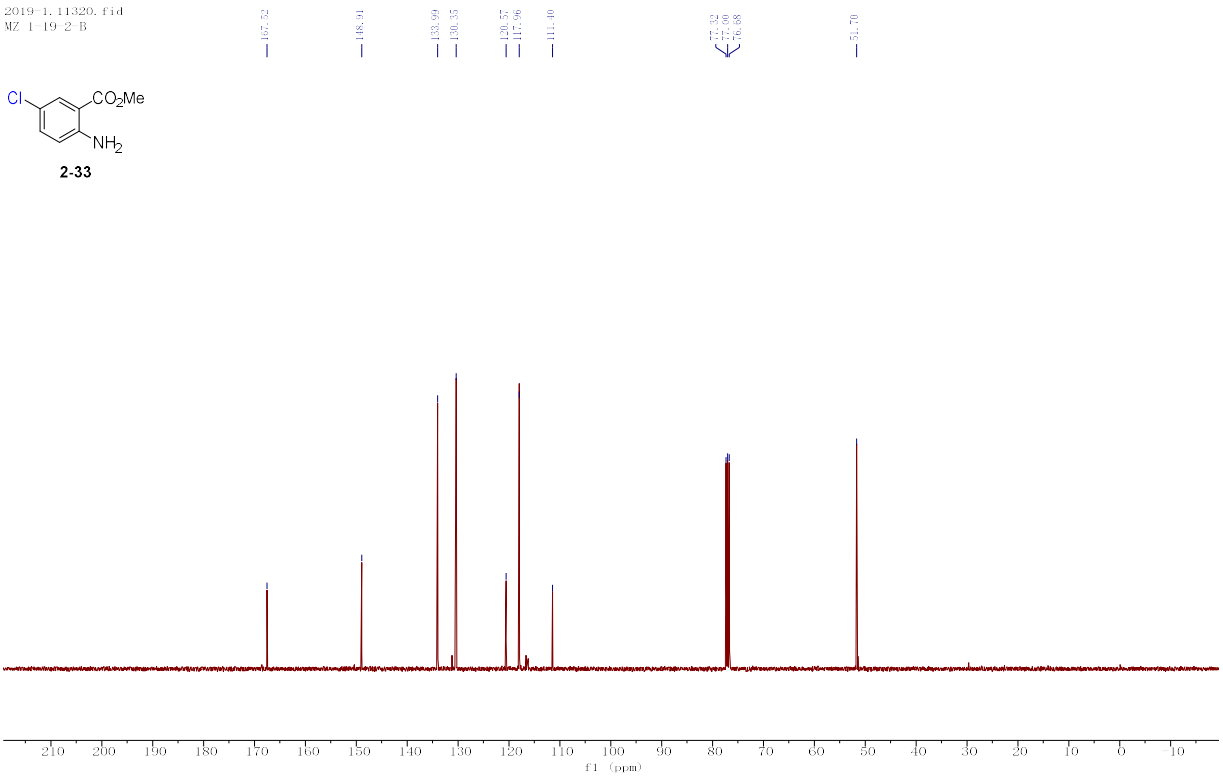


Figure S95. ^{13}C NMR of crude product **2-33**, related Table 3

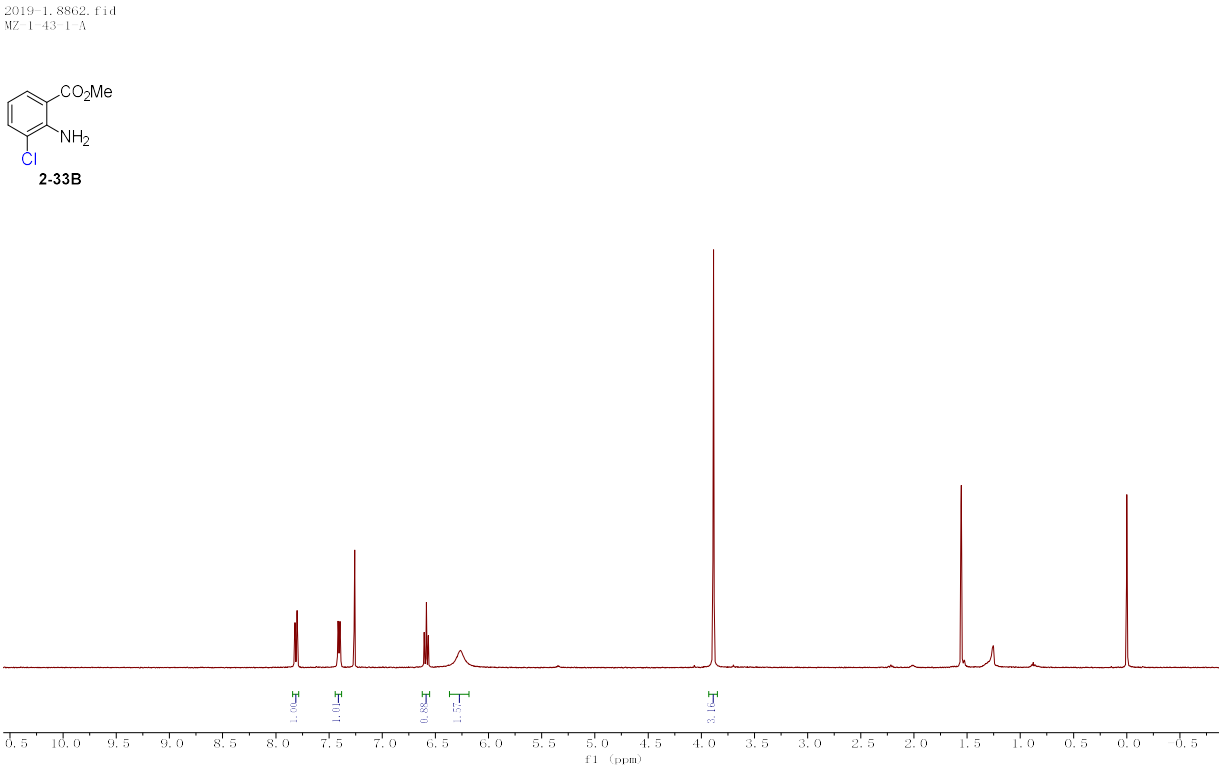


Figure S96. ^{1}H NMR of crude product **2-33B**, related Table 3

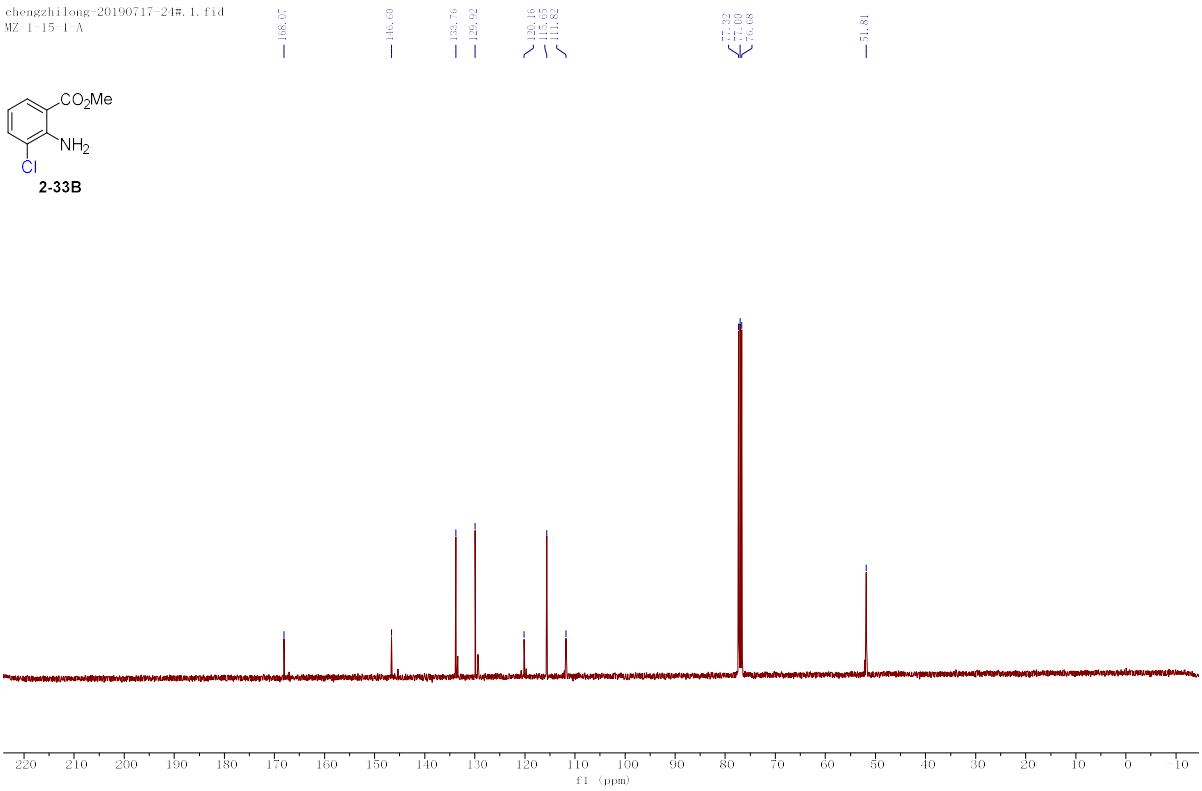


Figure S97. ^{13}C NMR of crude product **2-33B**, related Table 3

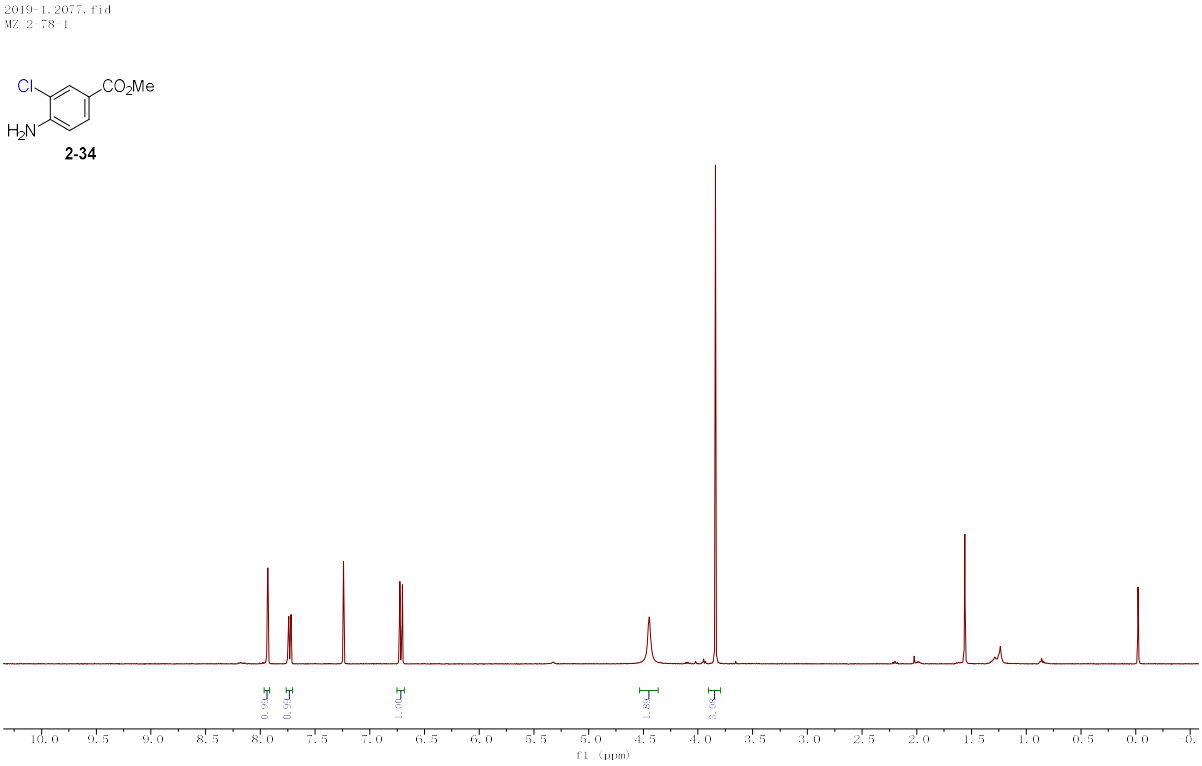


Figure S98. ^{1}H NMR of crude product **2-34**, related Table 3

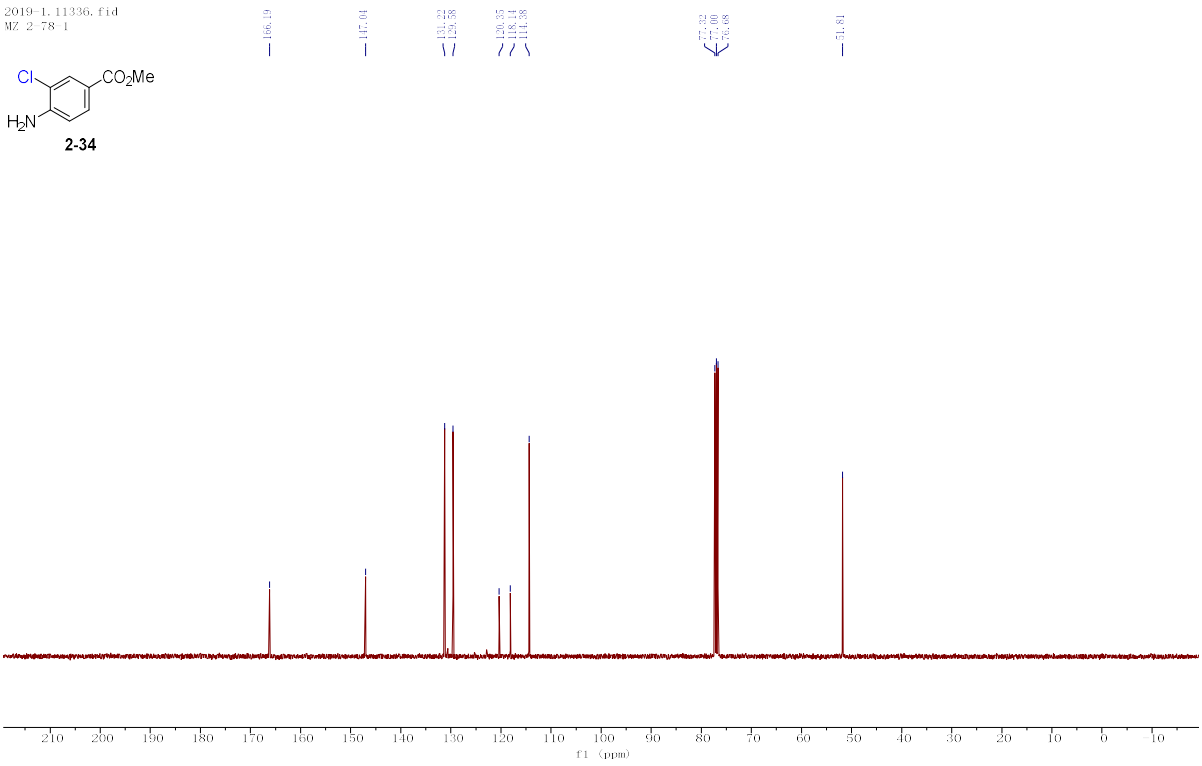


Figure S99. ^{13}C NMR of crude product **2-34**, related Table 3

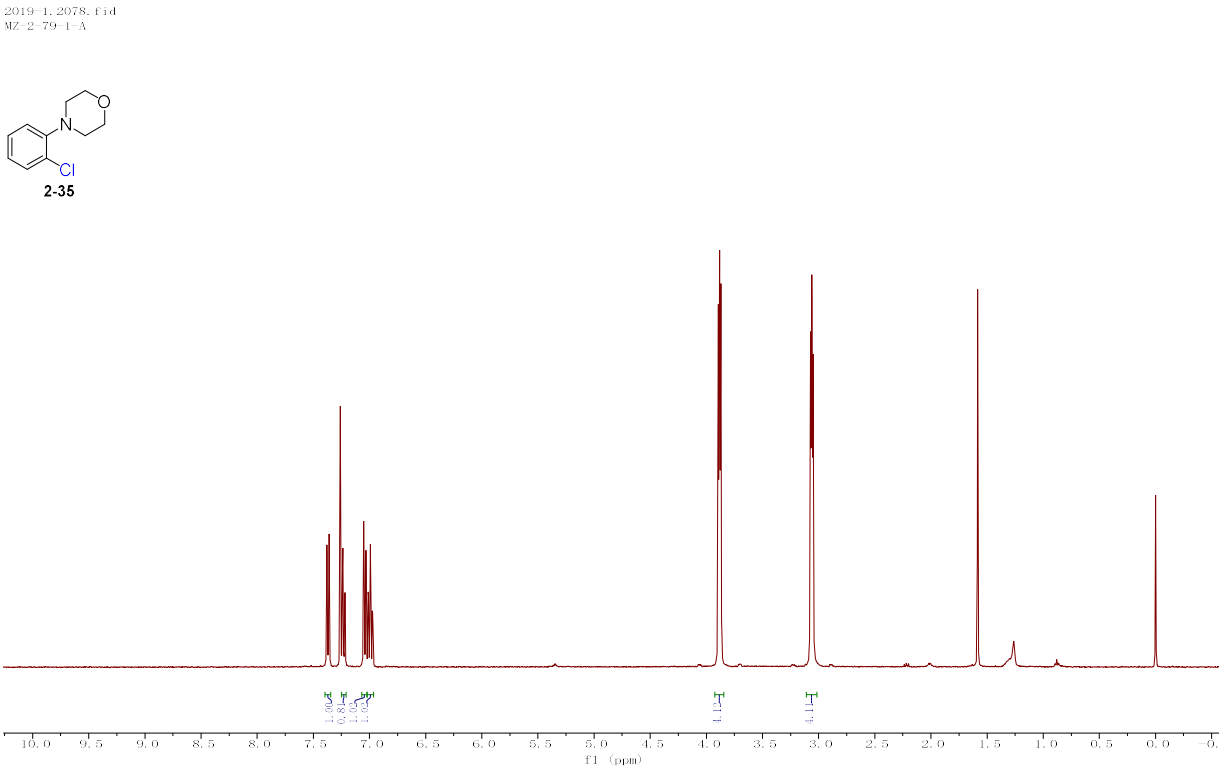


Figure S100. ^{1}H NMR of crude product **2-35**, related Table 3

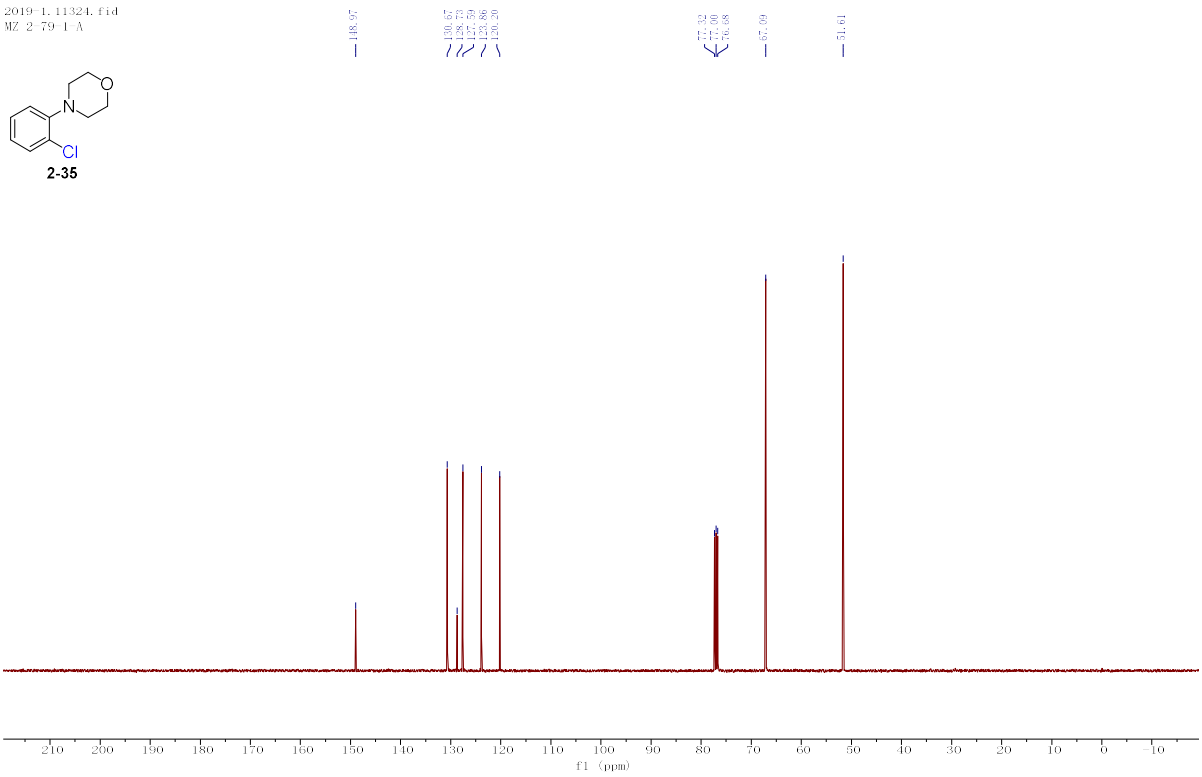


Figure S101. ^{13}C NMR of crude product **2-35**, related Table 3

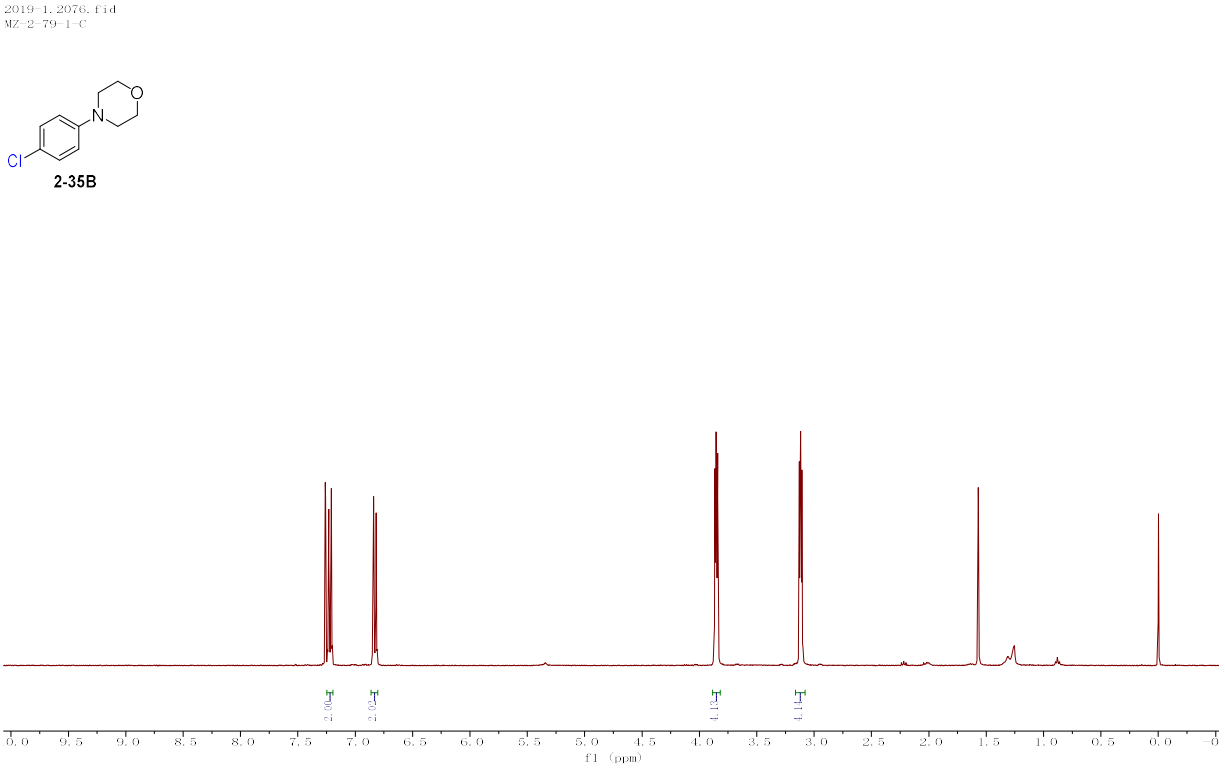


Figure S102. ^{1}H NMR of crude product **2-35B**, related Table 3

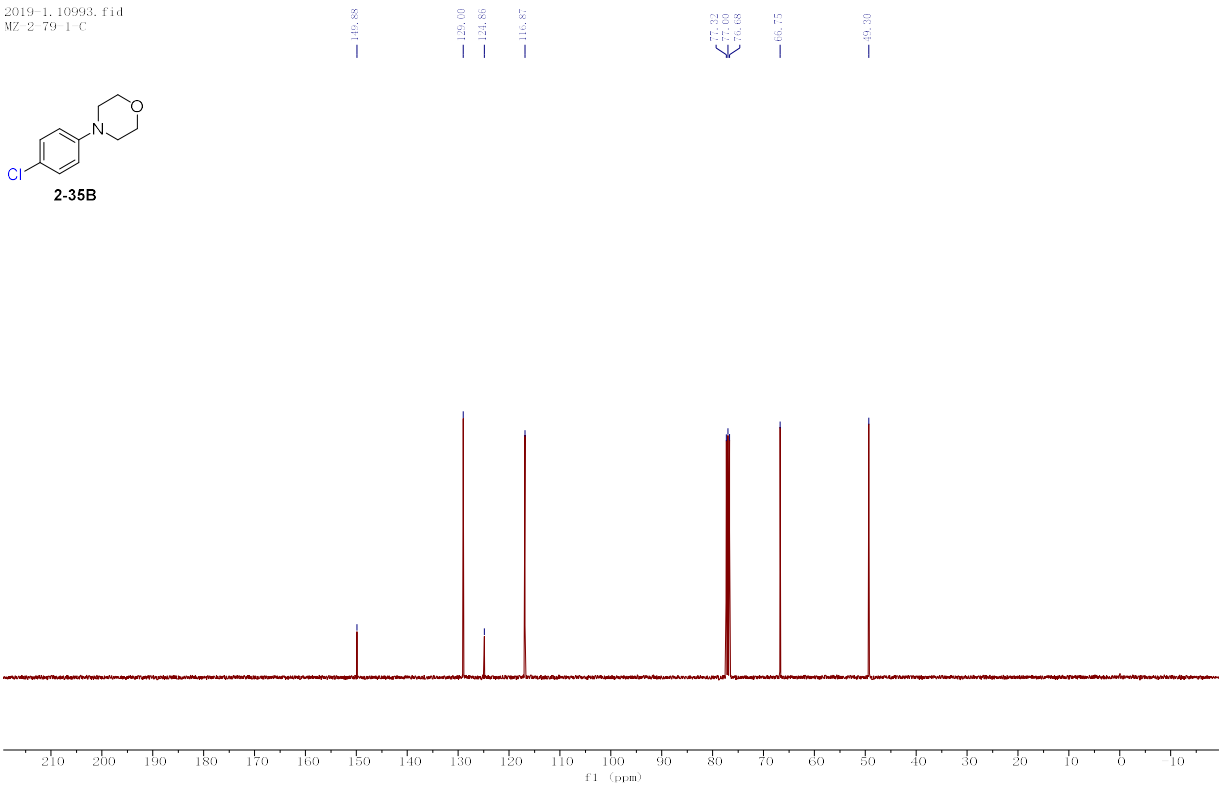


Figure S103. ^{13}C NMR of crude product **2-35B**, related Table 3

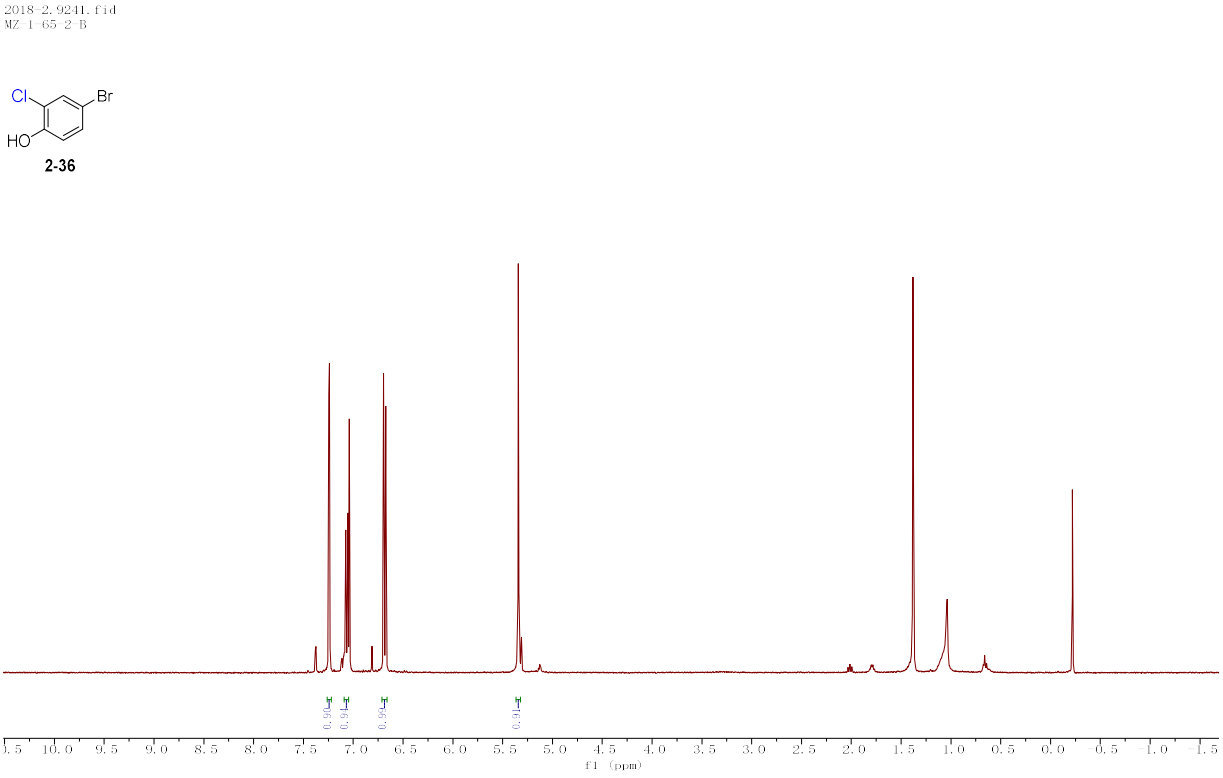


Figure S104. ^{1}H NMR of crude product **2-36**, related Table 3

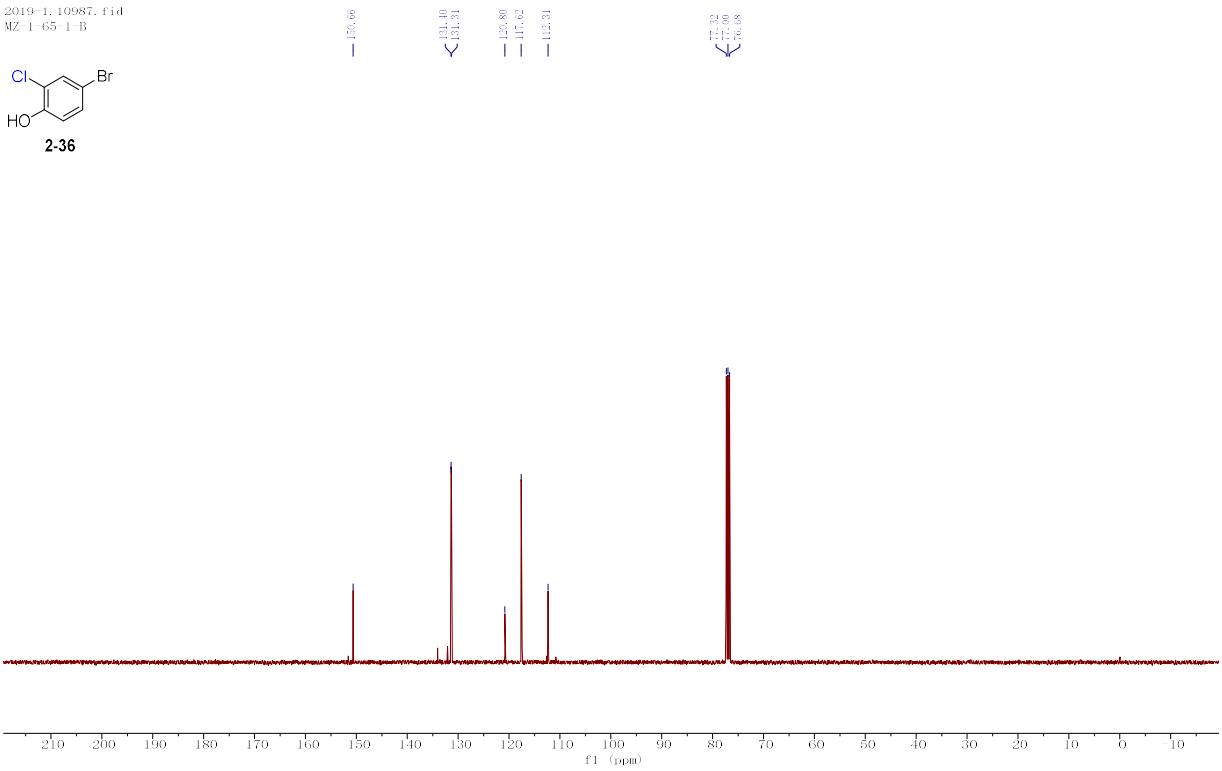


Figure S105. ^{13}C NMR of crude product **2-36**, related Table 3

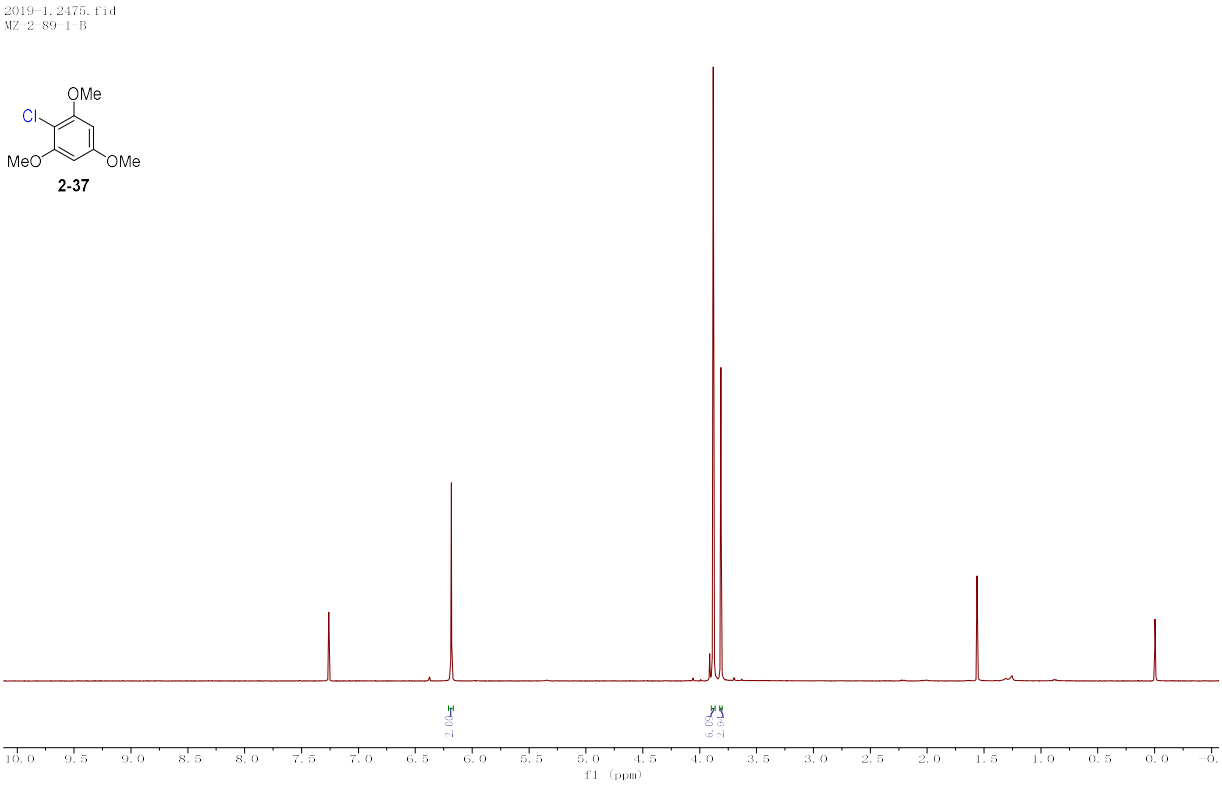


Figure S106. ^{1}H NMR of crude product **2-37**, related Table 3

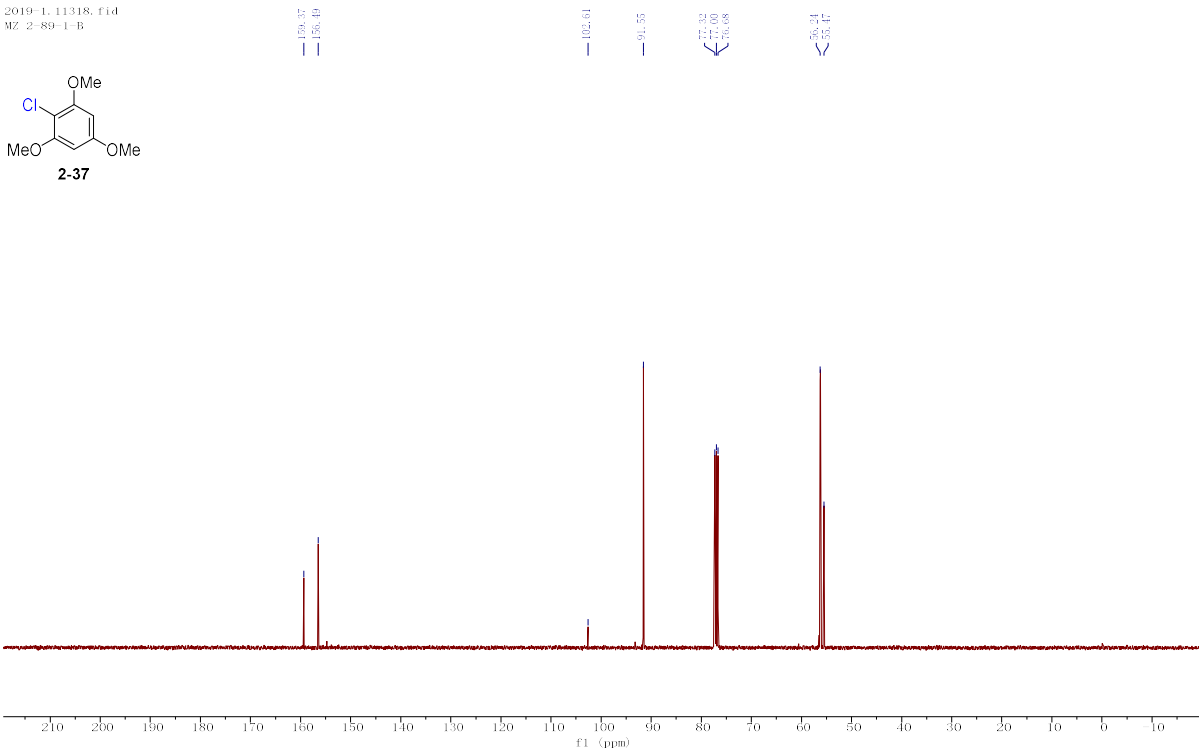


Figure S107. ^{13}C NMR of crude product **2-37**, related Table 3

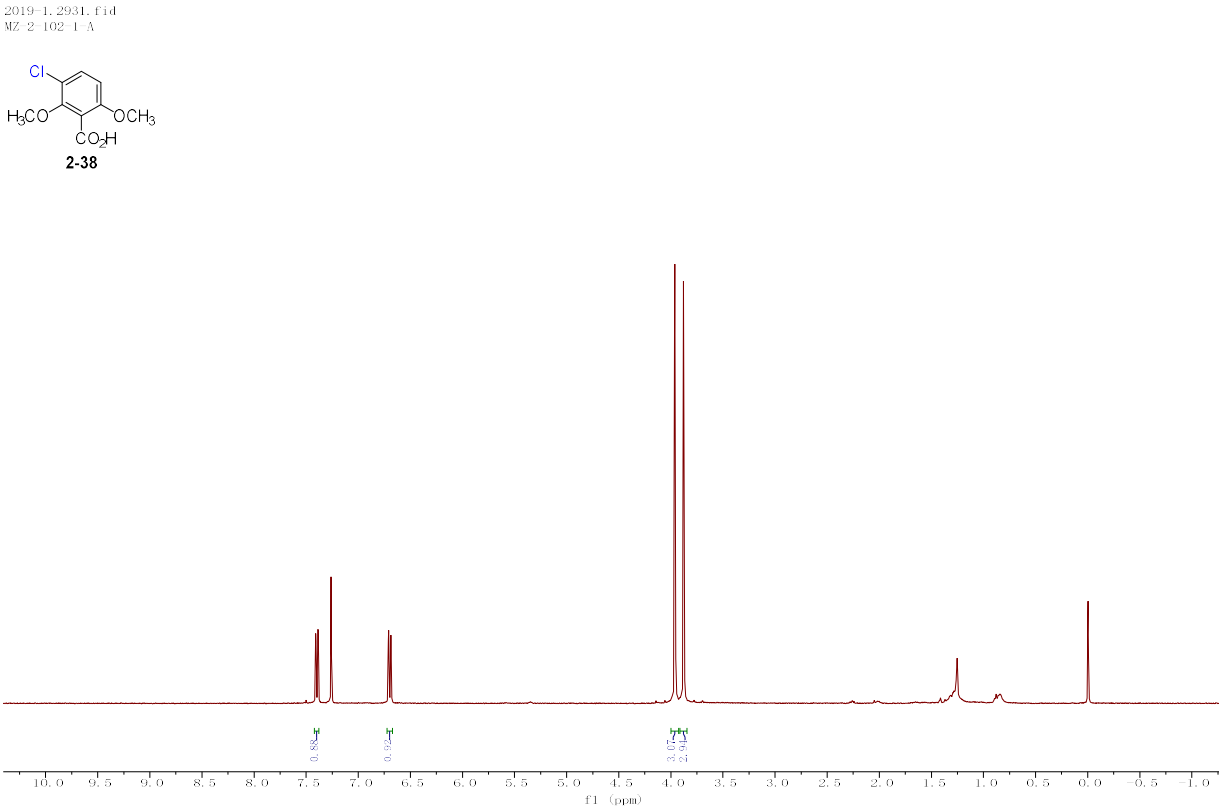


Figure S108. ^{1}H NMR of crude product **2-38**, related Table 3

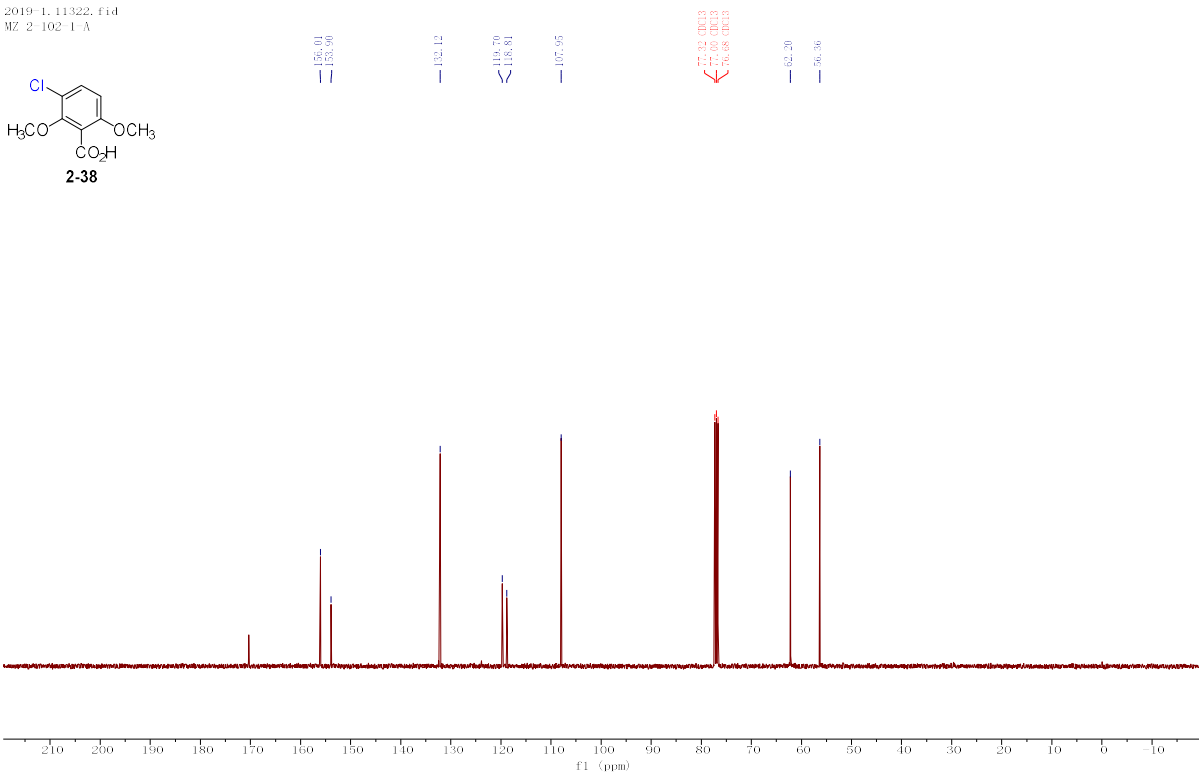


Figure S109. ^{13}C NMR of crude product **2-38**, related Table 3

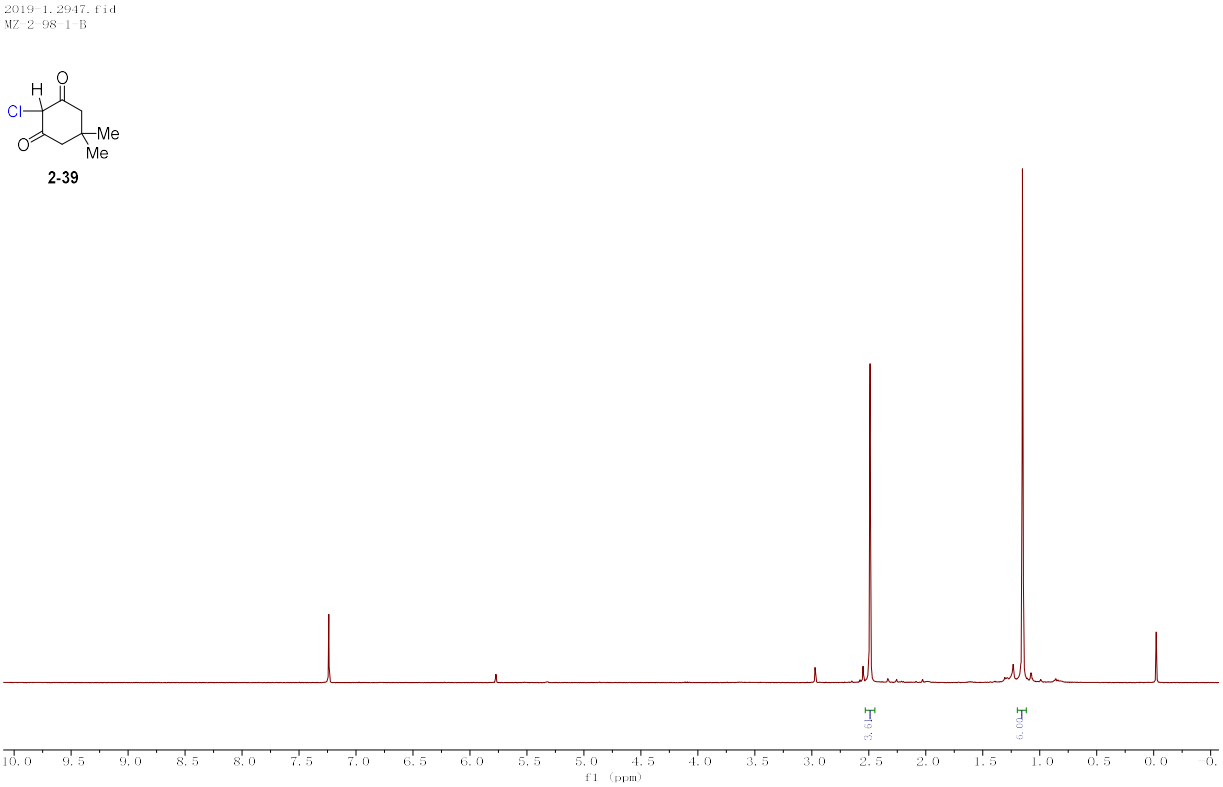


Figure S110. ^{1}H NMR of crude product **2-39**, related Table 3

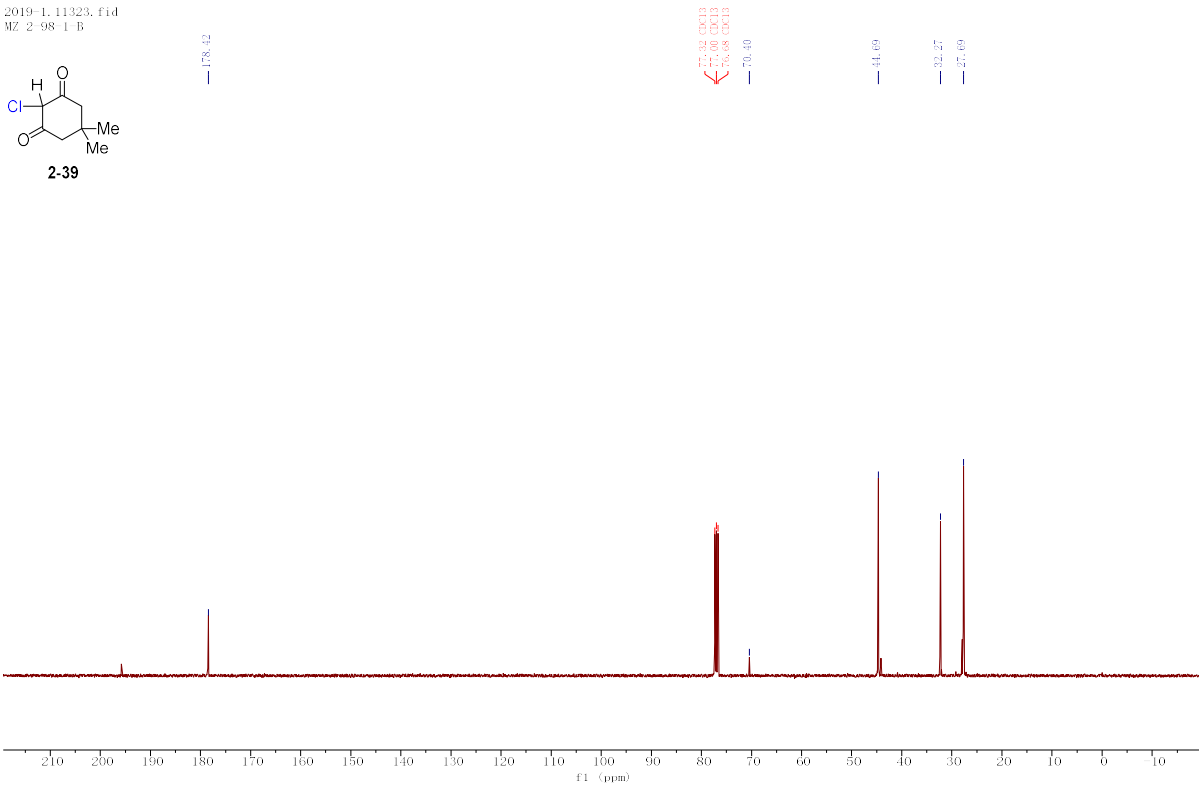


Figure S111. ^{13}C NMR of crude product **2-39**, related Table 3

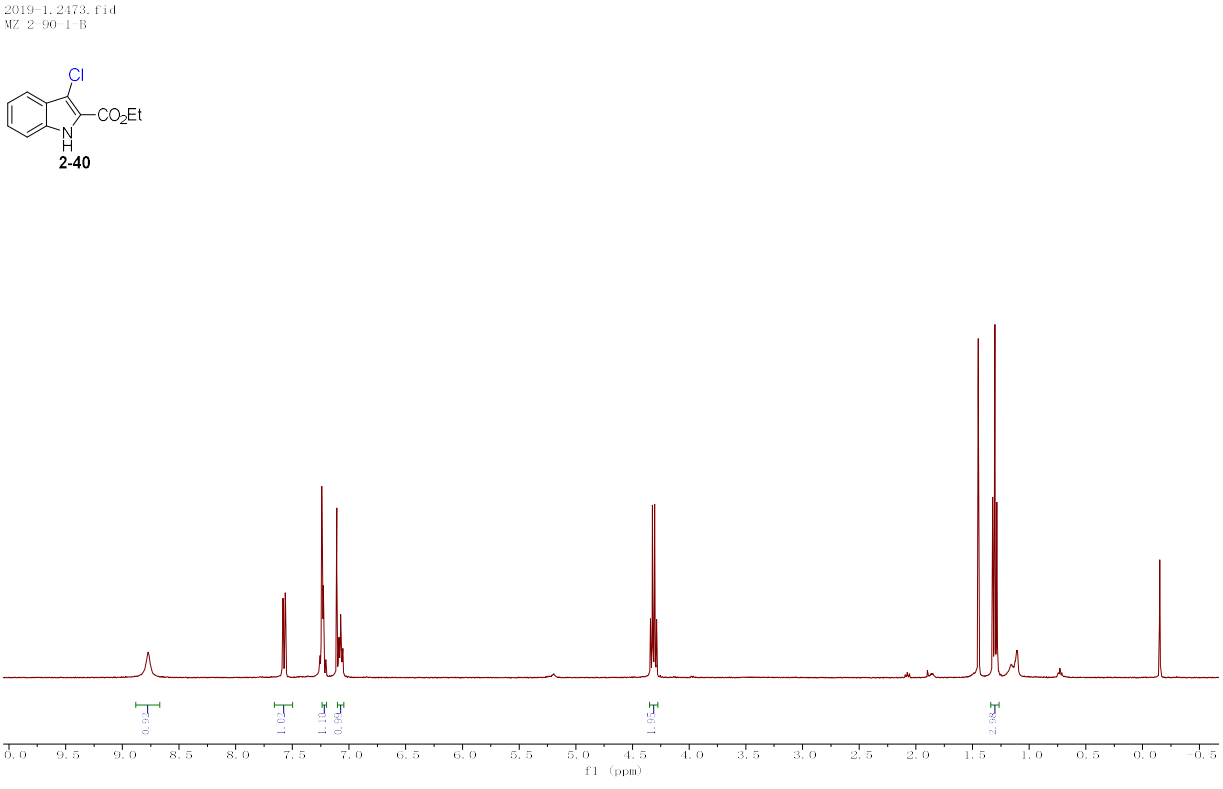


Figure S112. ^{1}H NMR of crude product **2-40**, related Table 3

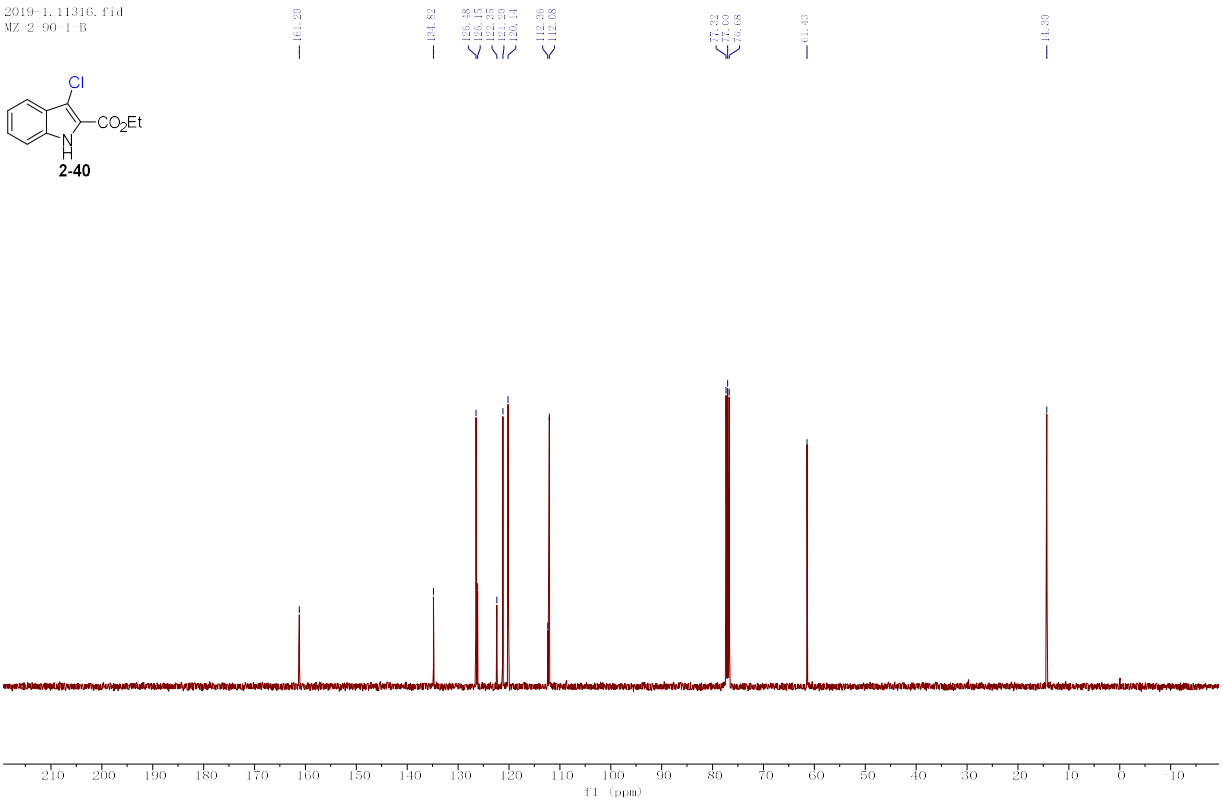


Figure S1113. ^{13}C NMR of crude product **2-40**, related Table 3

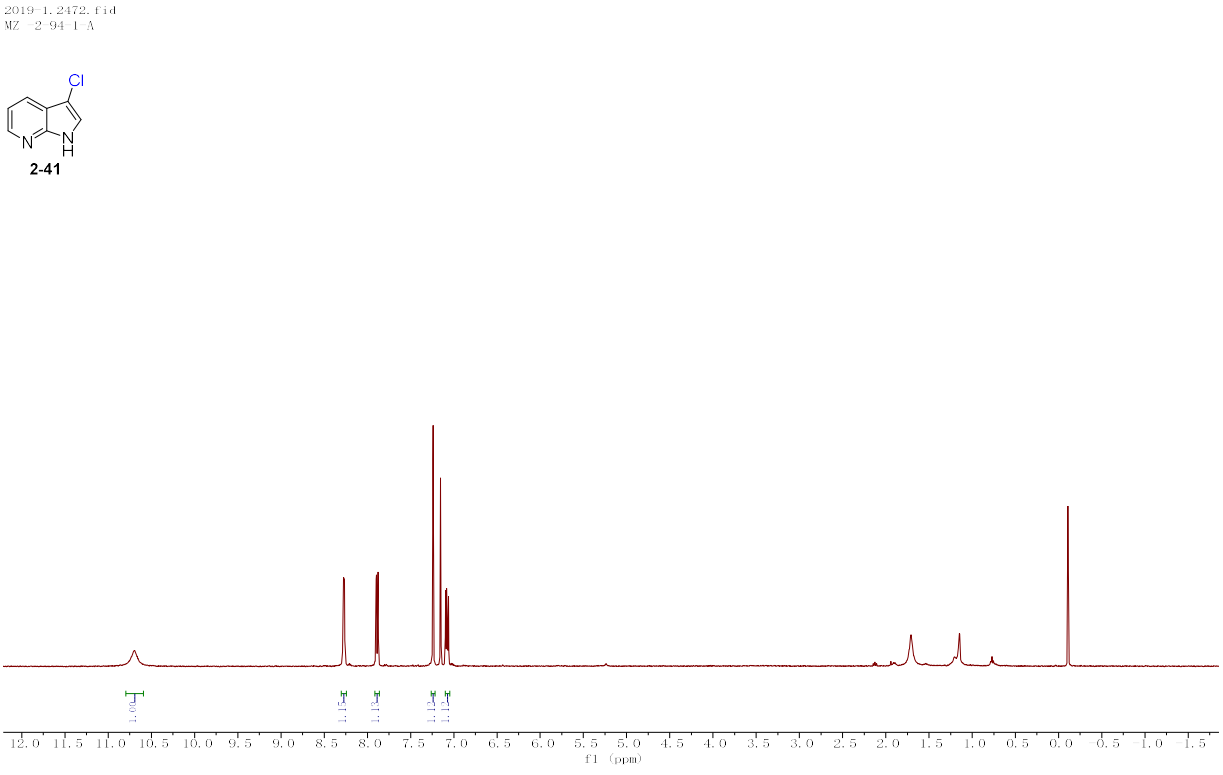


Figure S114. ^{1}H NMR of crude product **2-41**, related Table 3

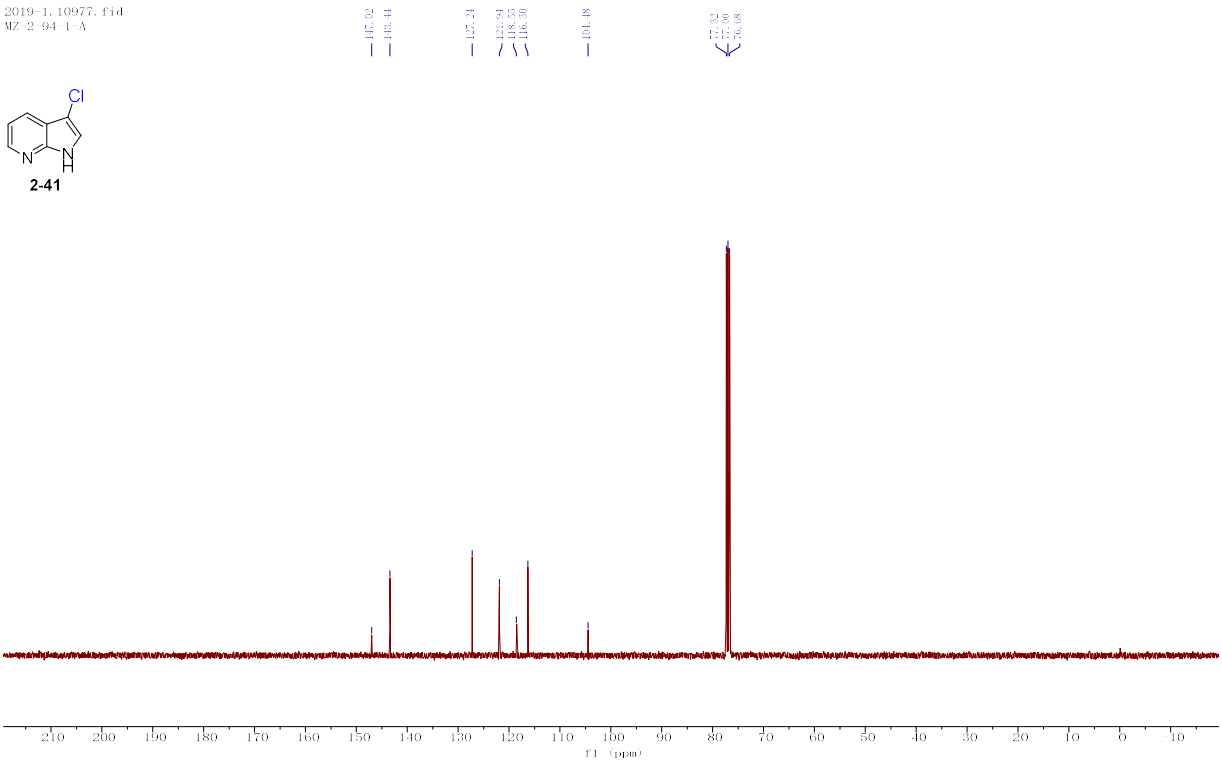


Figure S115. ^{13}C NMR of crude product **2-41**, related Table 3

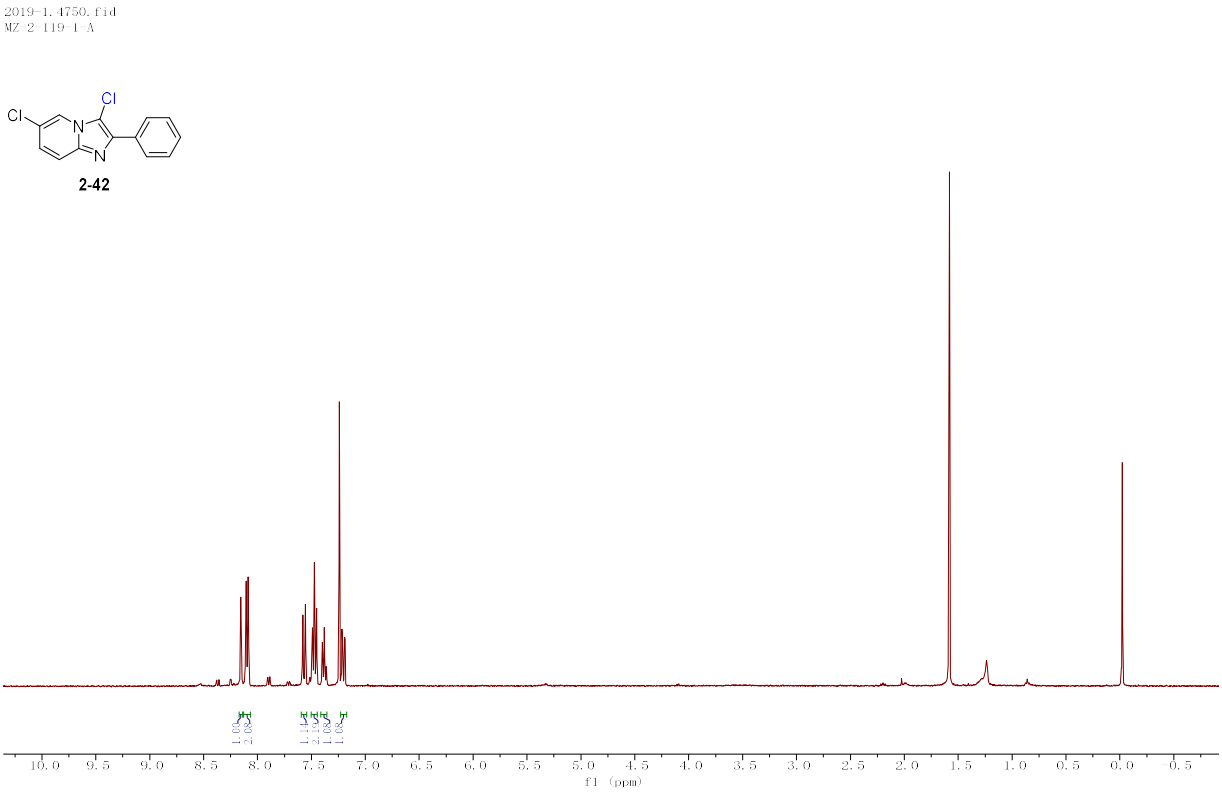


Figure S116. ^{1}H NMR of crude product **2-42**, related Table 3

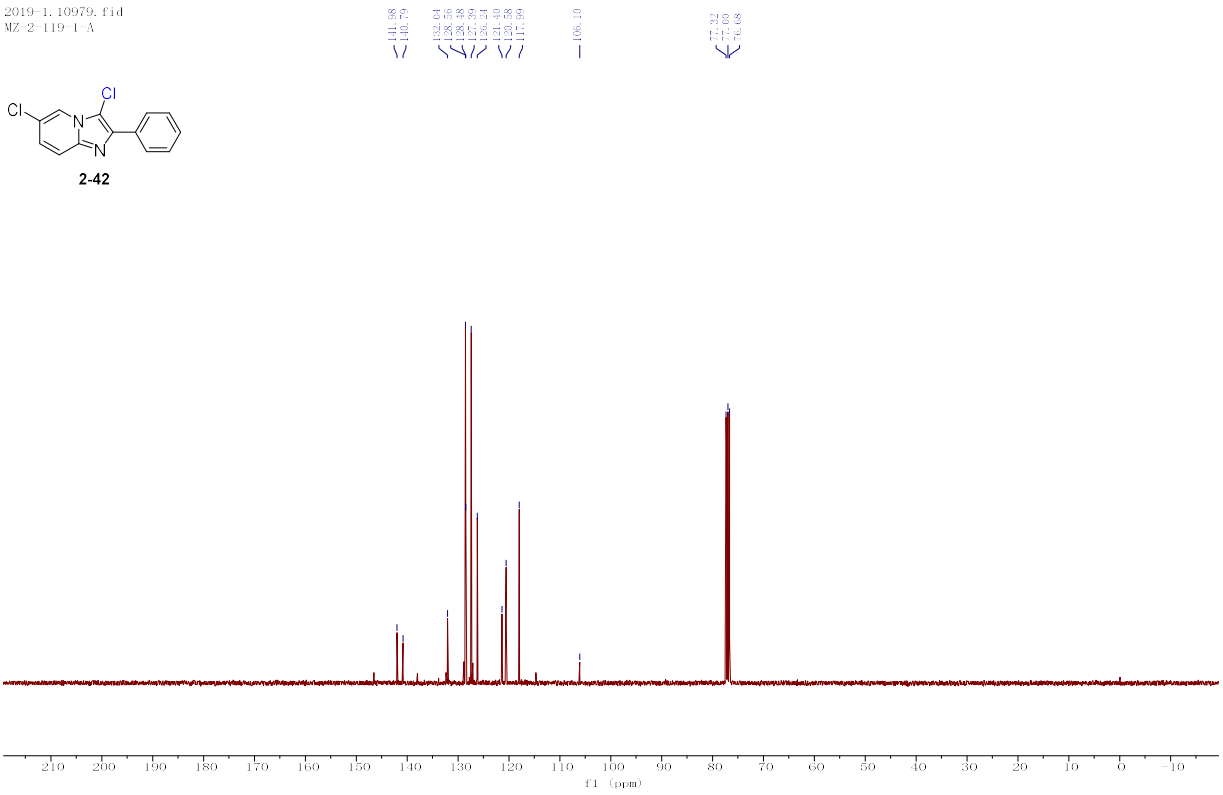


Figure S117. ^{13}C NMR of crude product **2-41**, related Table 3

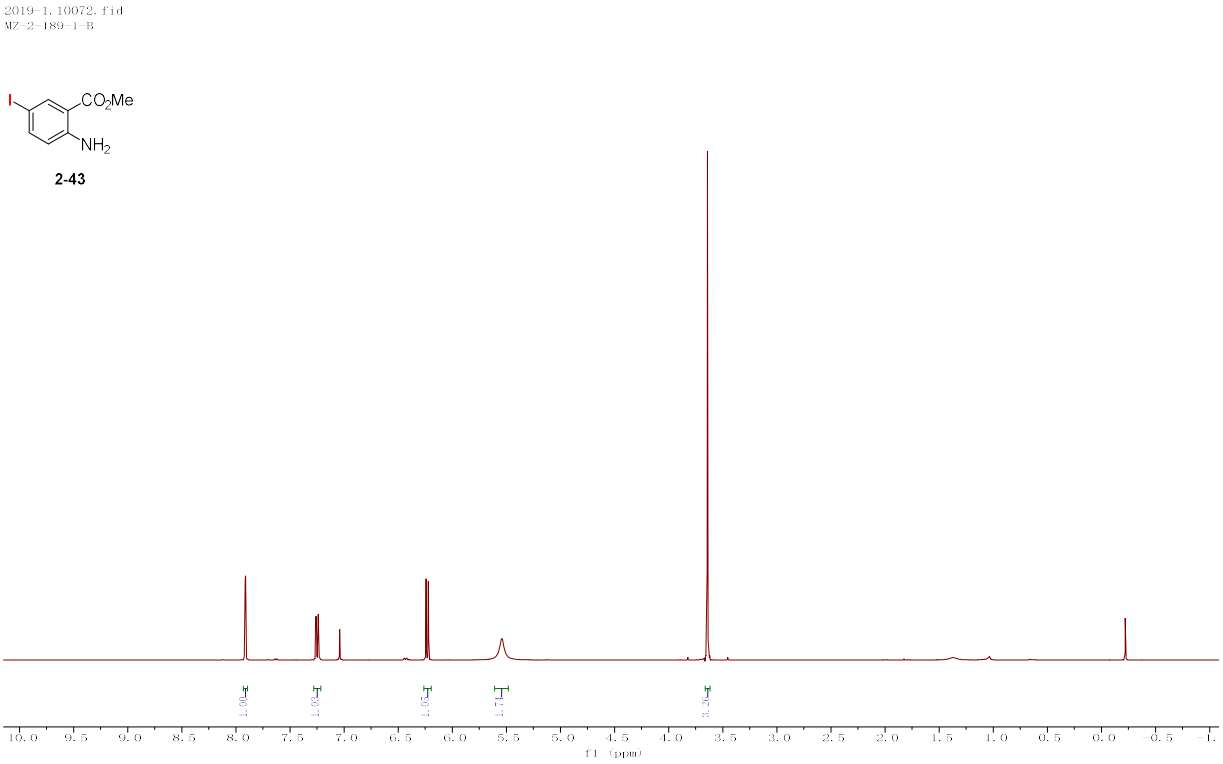


Figure S118. ^{1}H NMR of crude product **2-43**, related Table 3

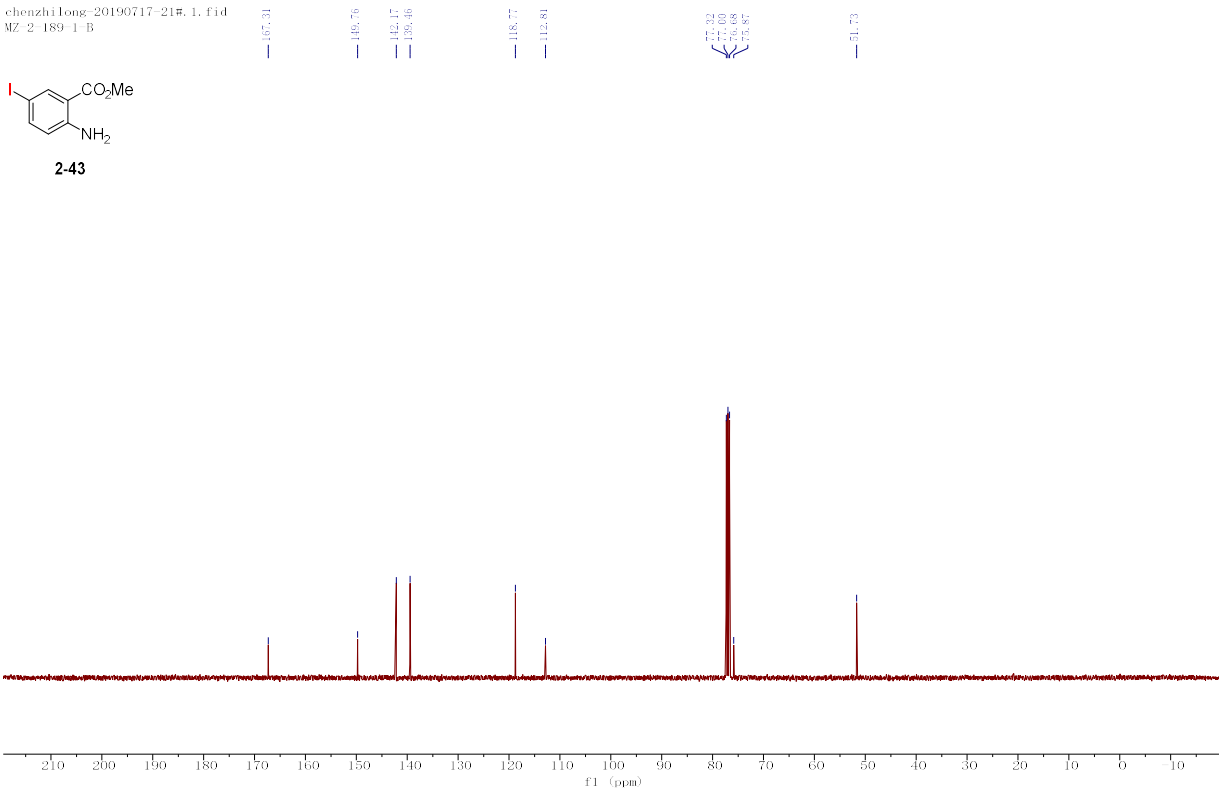


Figure S119. ^{13}C NMR of crude product **2-43**, related Table 3

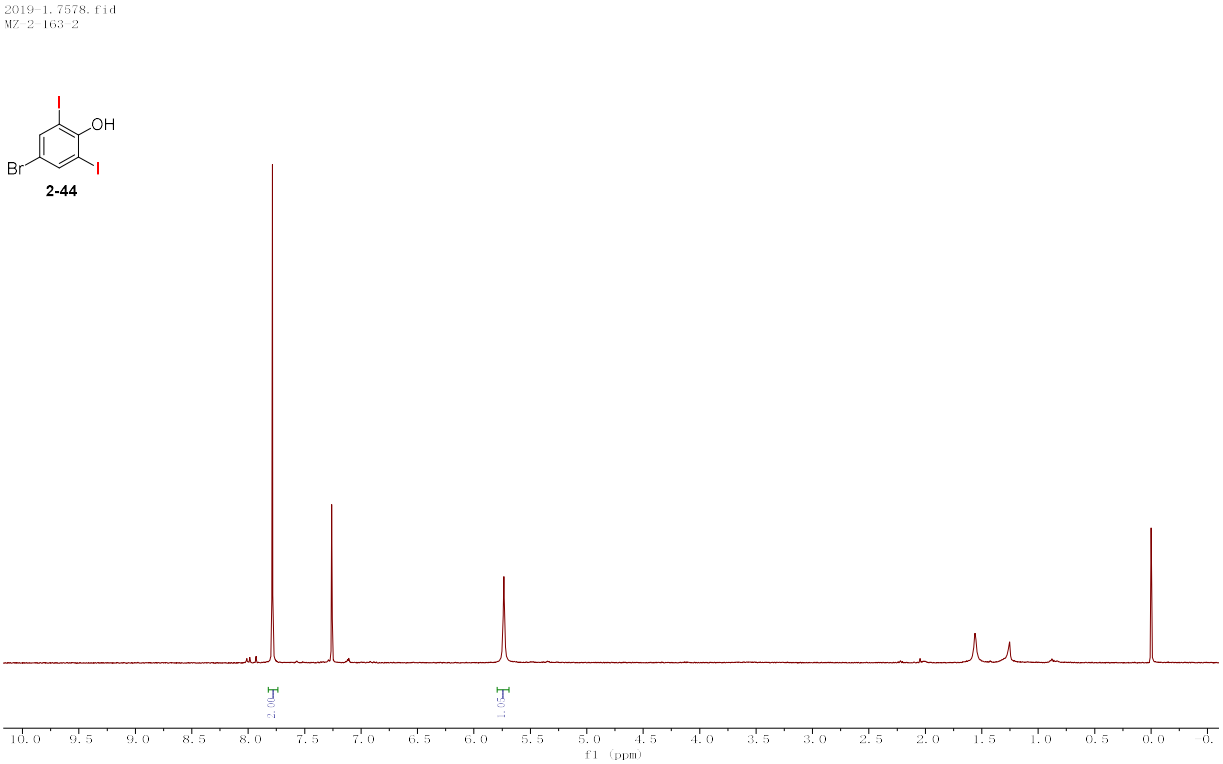


Figure S120. ^{1}H NMR of crude product **2-44**, related Table 3

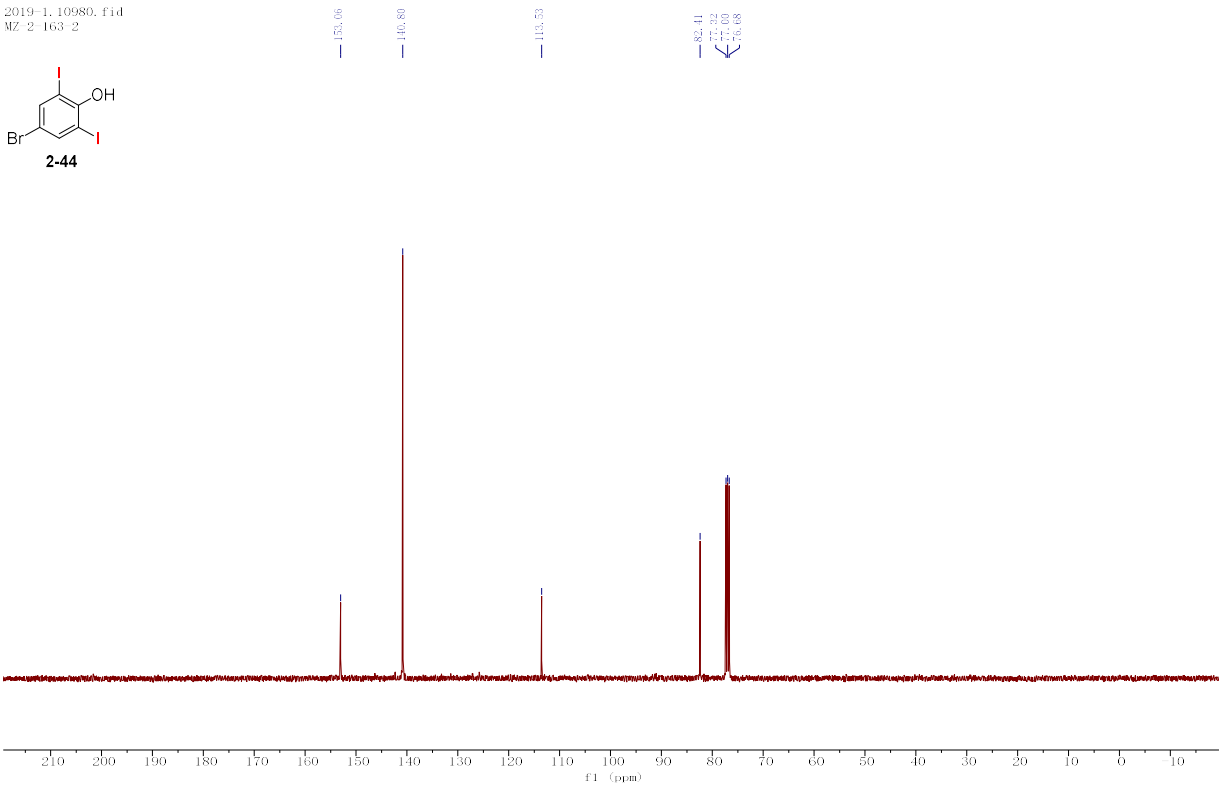


Figure S121. ^{13}C NMR of crude product **2-44**, related Table 3

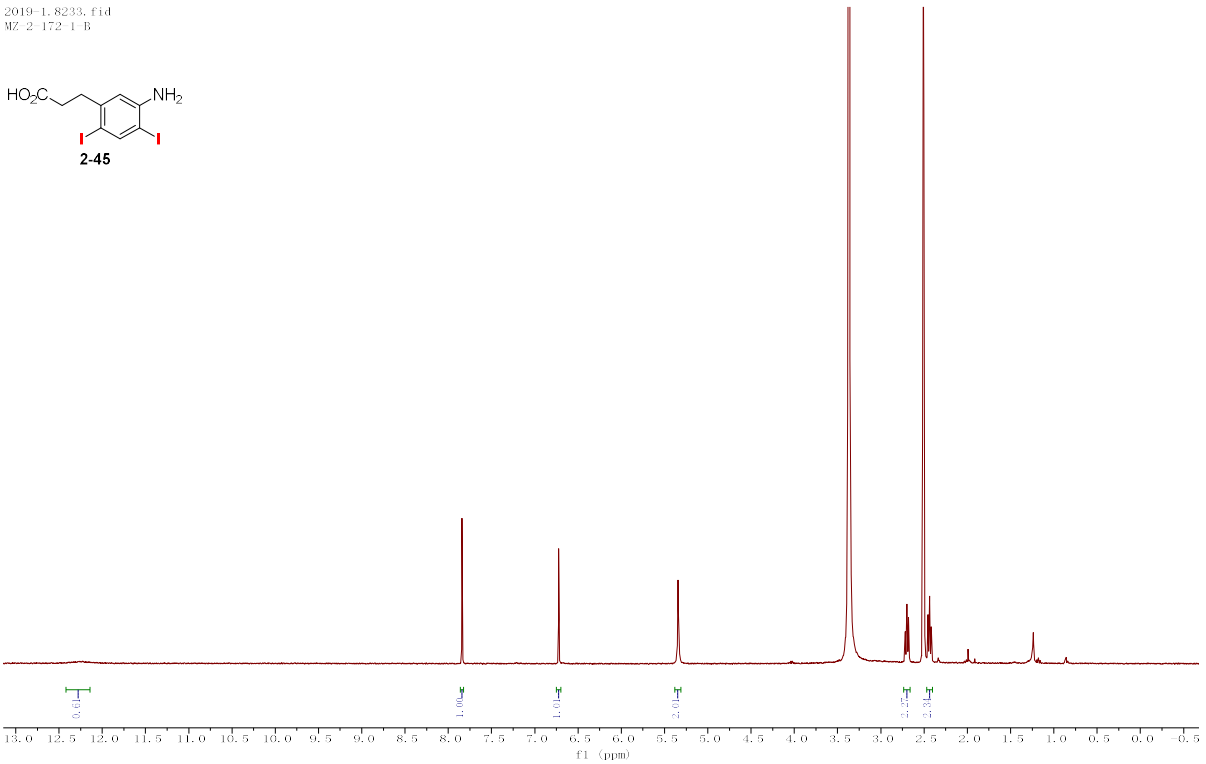


Figure S122. ^{1}H NMR of crude product **2-45**, related Table 3

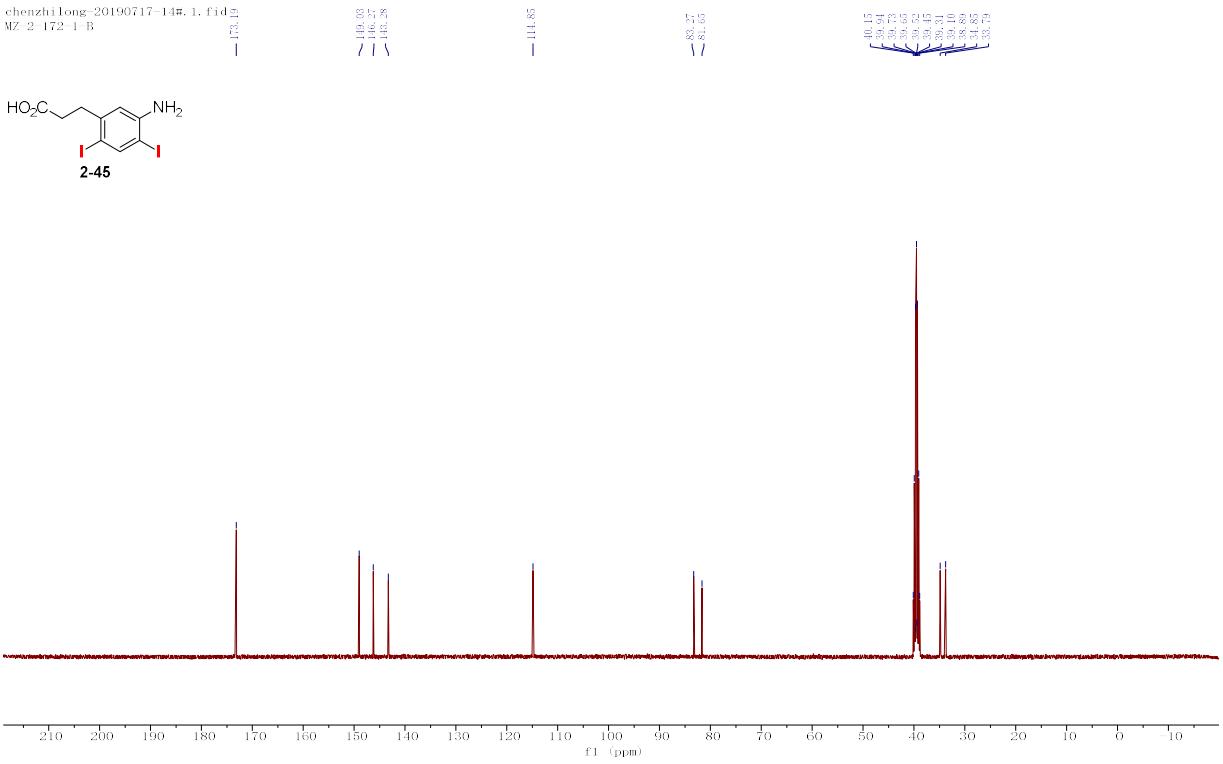


Figure S123. ^{13}C NMR of crude product **2-45**, related Table 3

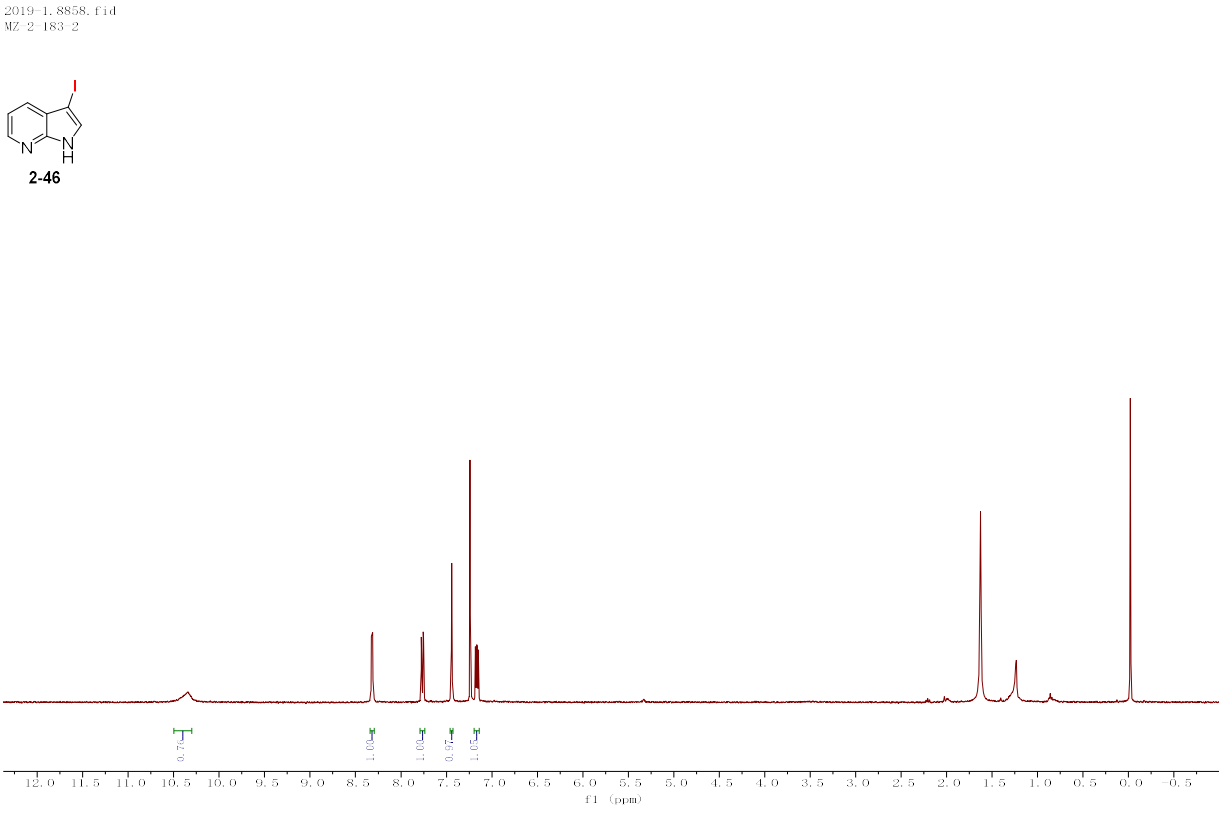


Figure S124. ^{1}H NMR of crude product **2-46**, related Table 3

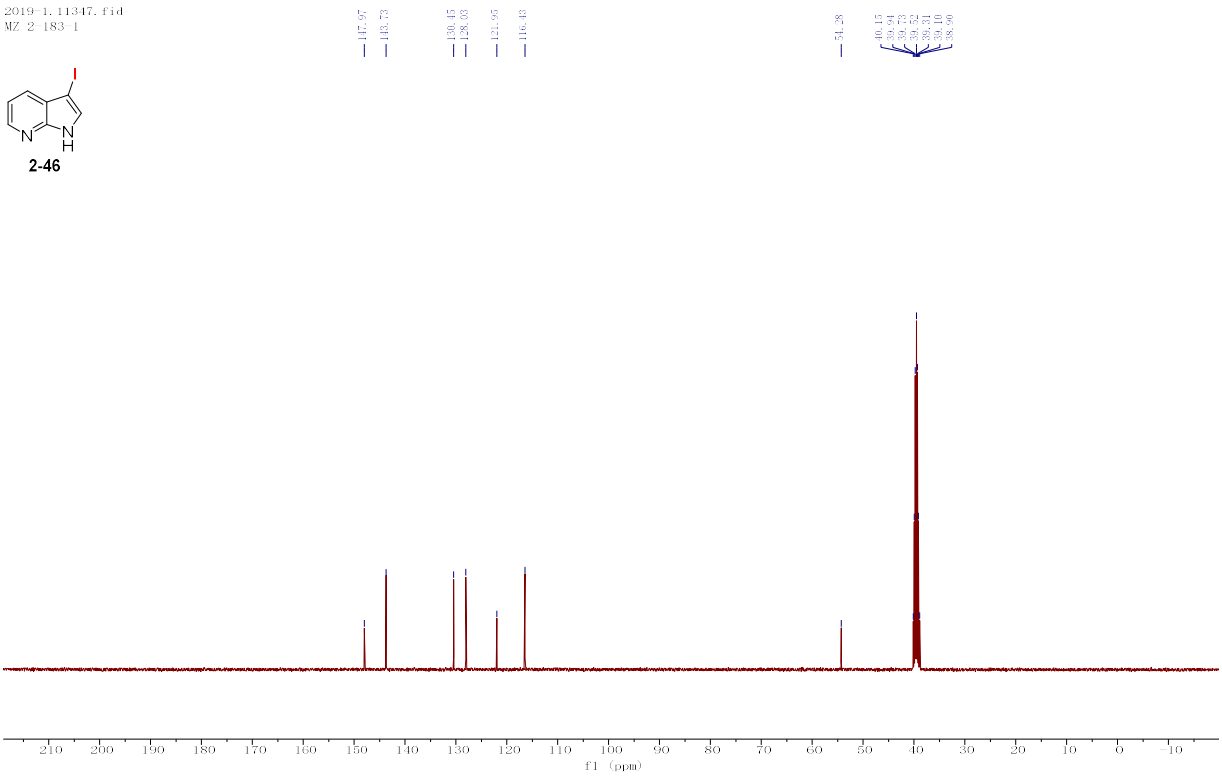


Figure S125. ^{13}C NMR of crude product **2-46**, related Table 3

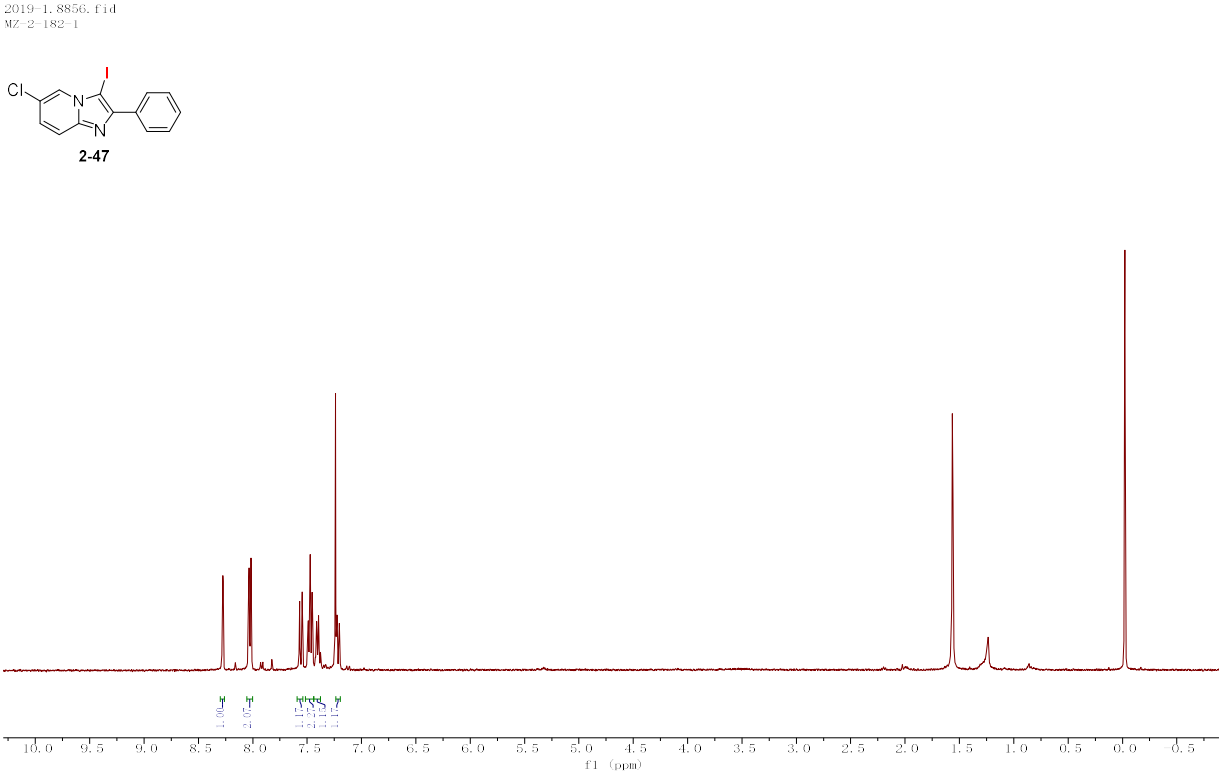


Figure S126. ^{1}H NMR of crude product **2-47**, related Table 3

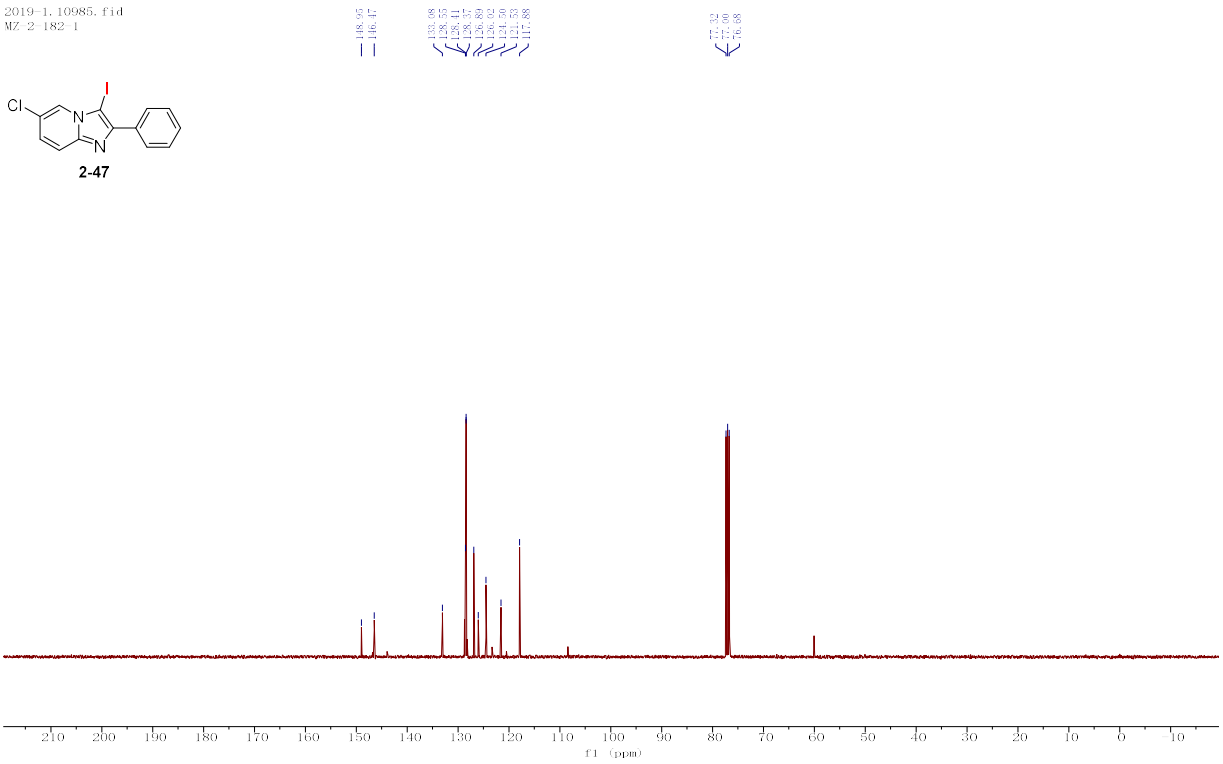


Figure S127. ^{13}C NMR of crude product **2-47**, related Table 3

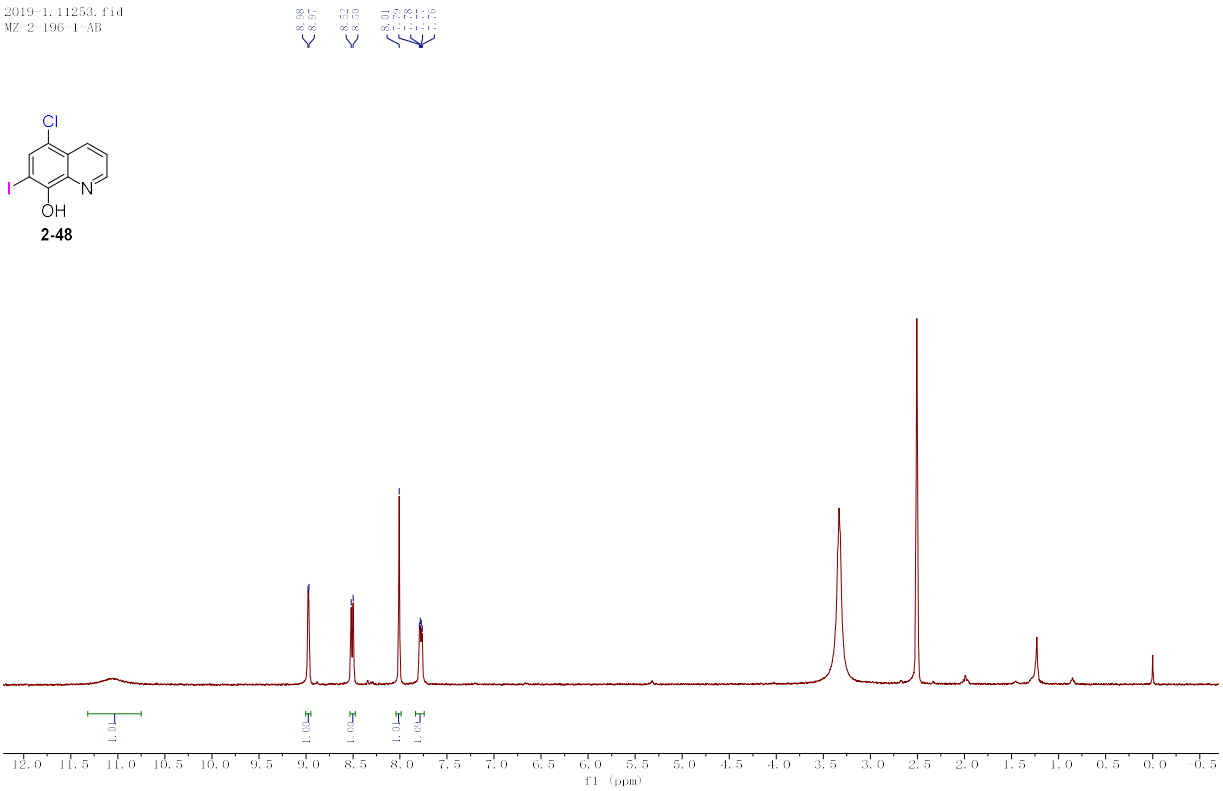


Figure S128. ^{1}H NMR of crude product **2-48**, related Figure 2

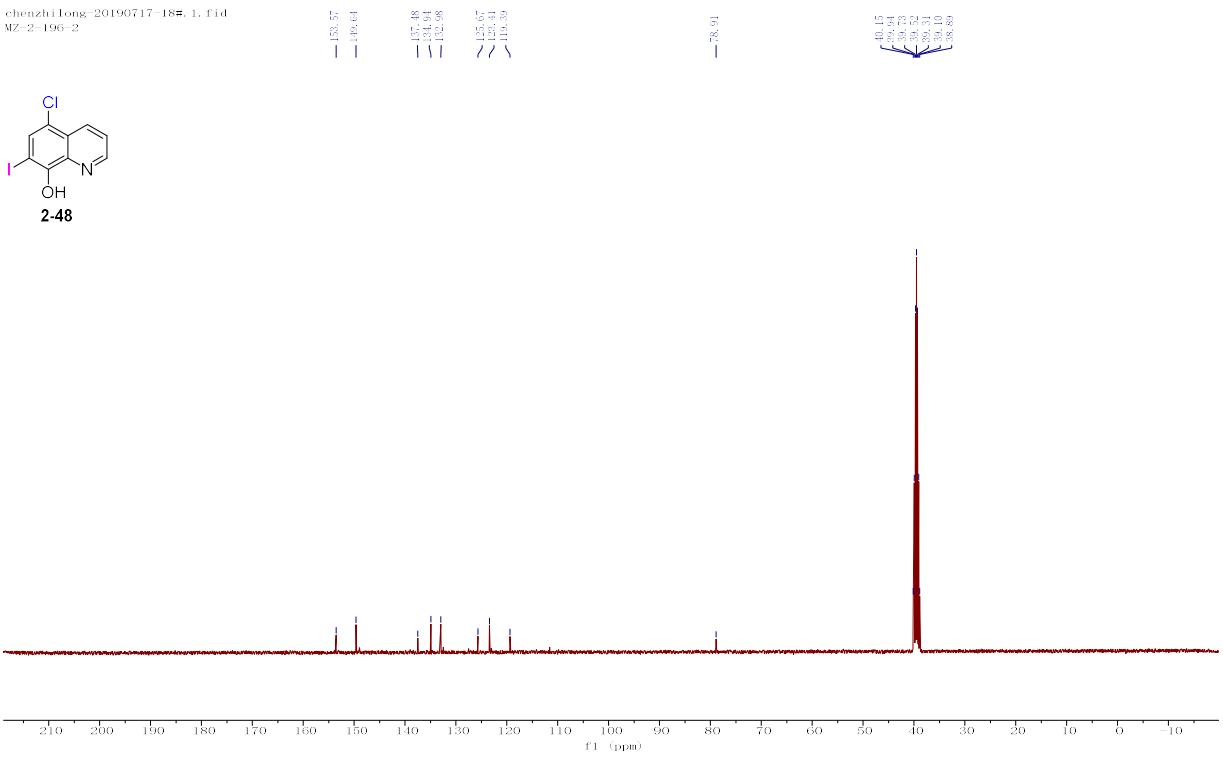


Figure S129. ^{13}C NMR of crude product **2-48**, related Figure 2

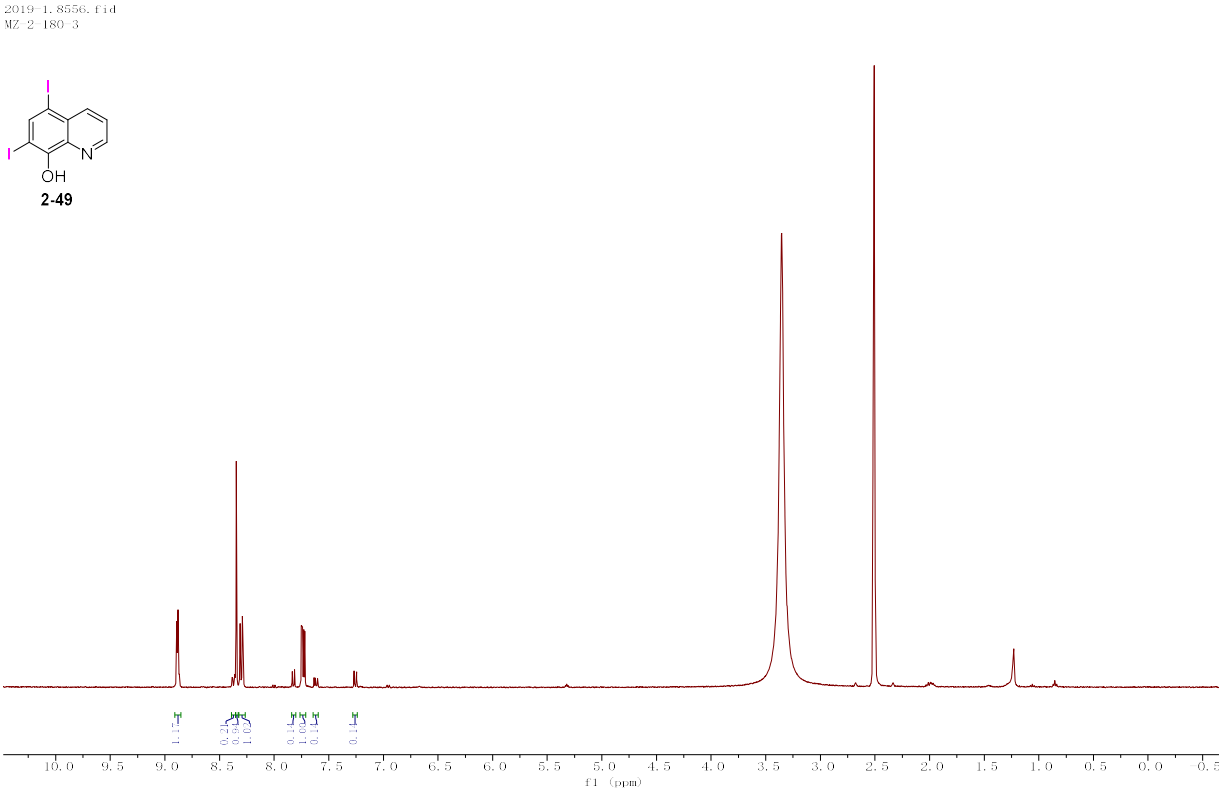


Figure S130. ^{1}H NMR of crude product **2-49**, related Figure 2

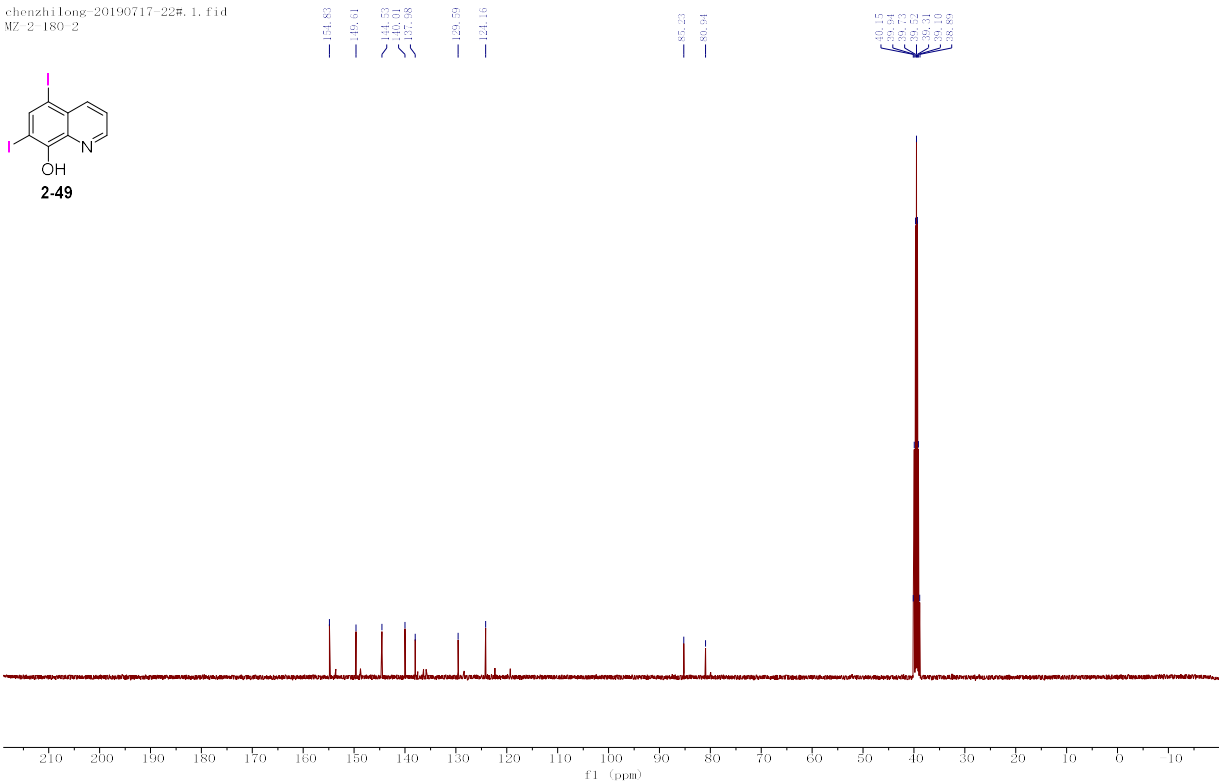


Figure S131. ^{13}C NMR of crude product **2-49**, related Figure 2

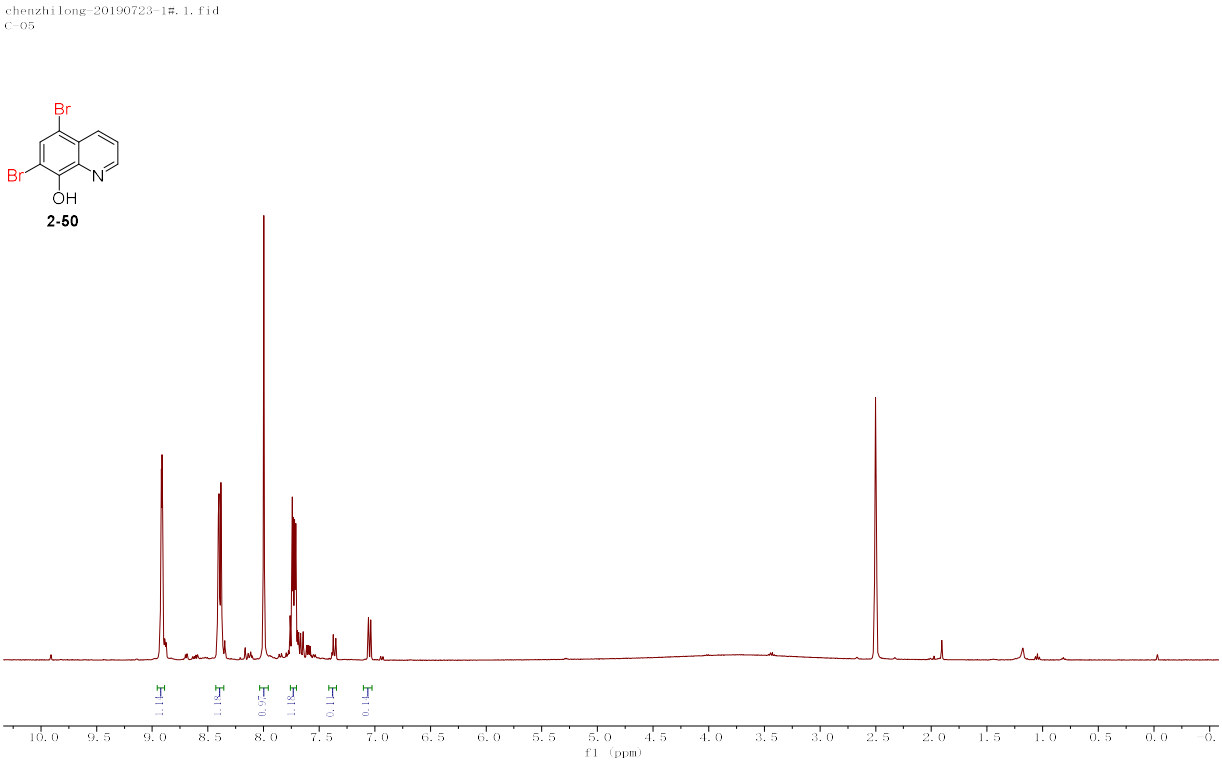


Figure S132. ^{1}H NMR of crude product **2-50**, related Figure 2

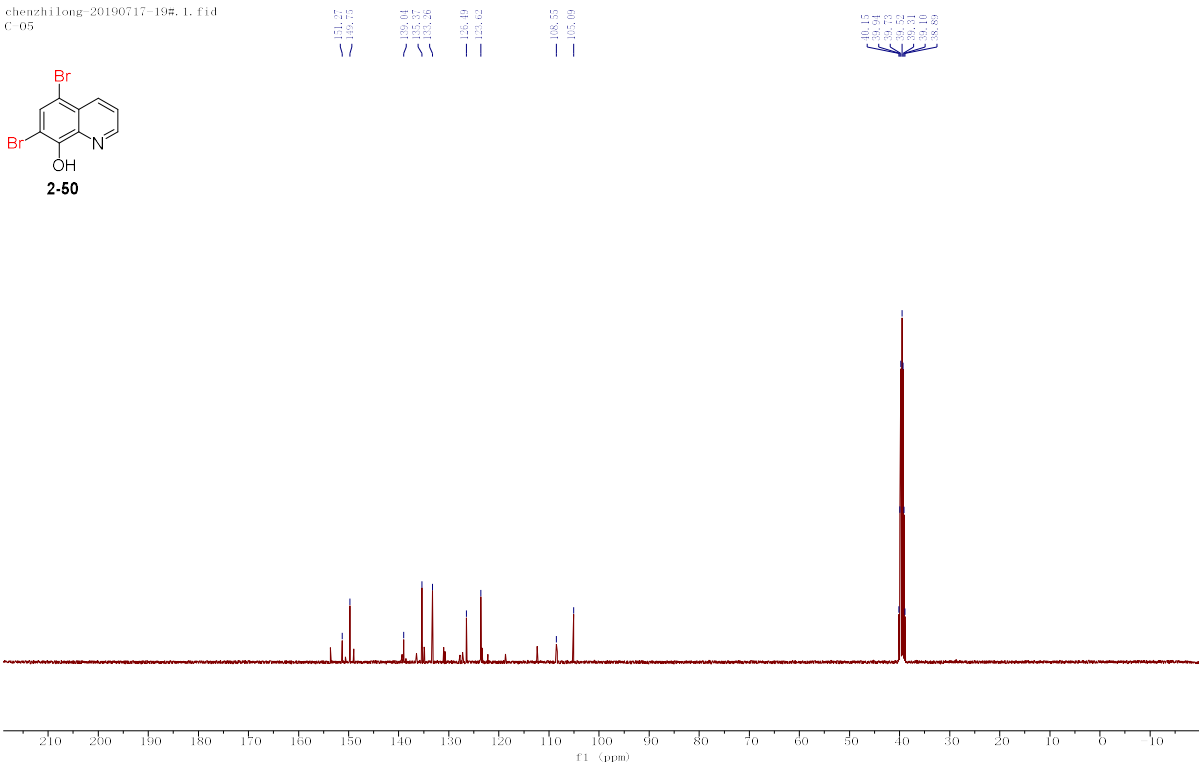


Figure S133. ^{13}C NMR of crude product **2-50**, related Figure 2

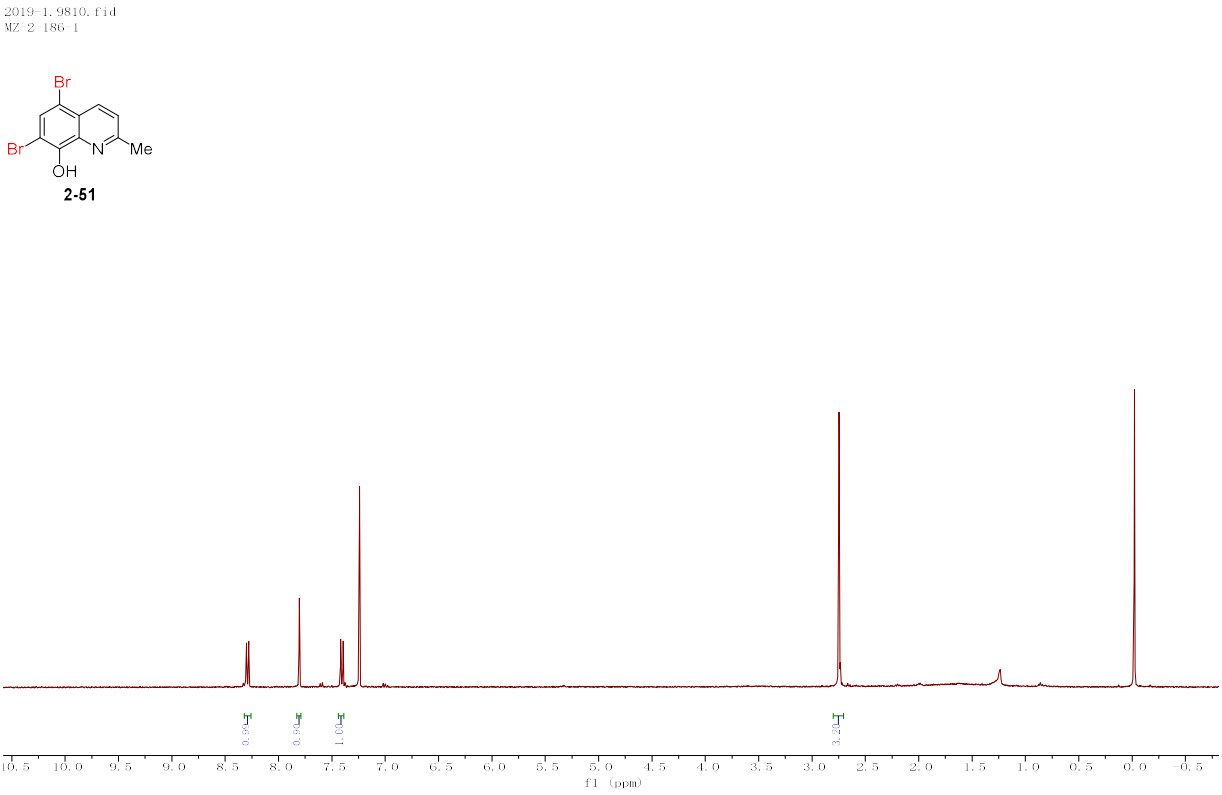


Figure S134. ^{1}H NMR of crude product **2-51**, related Figure 2

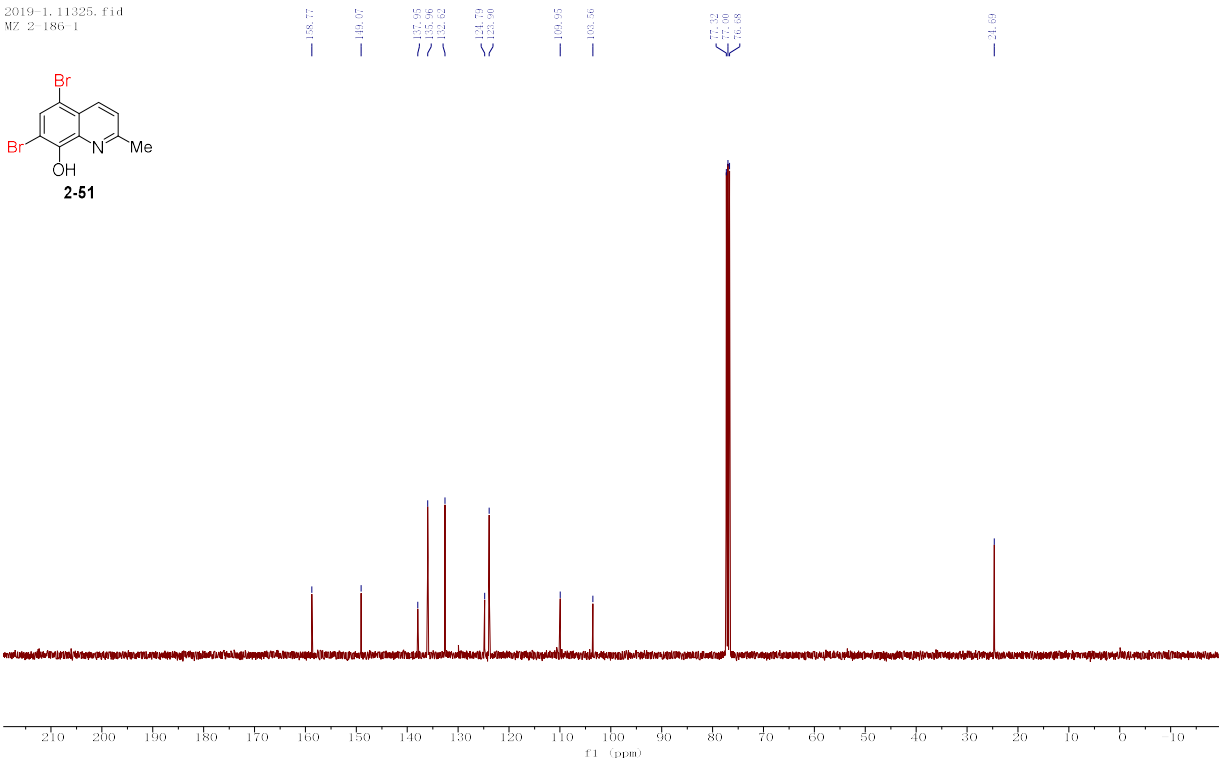


Figure S135. ^{13}C NMR of crude product **2-51**, related Figure 2

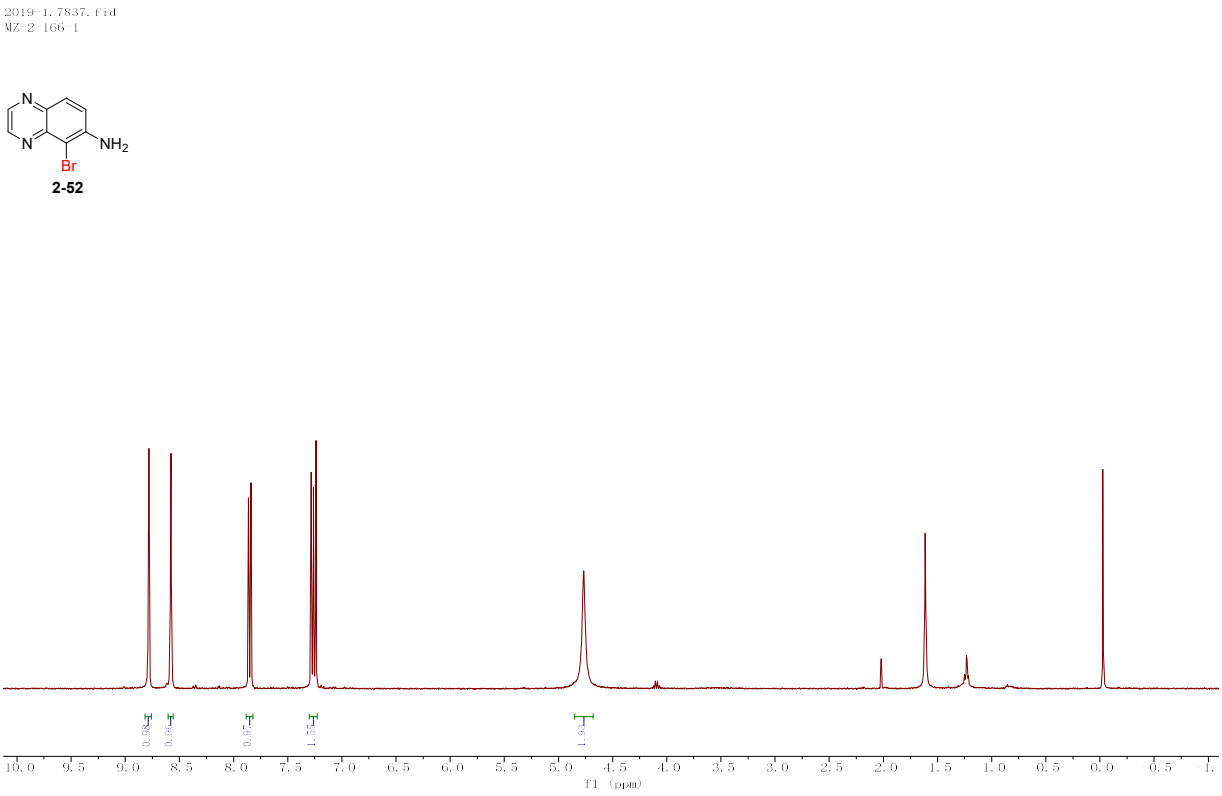


Figure S136. ^{1}H NMR of crude product **2-52**, related Figure 2

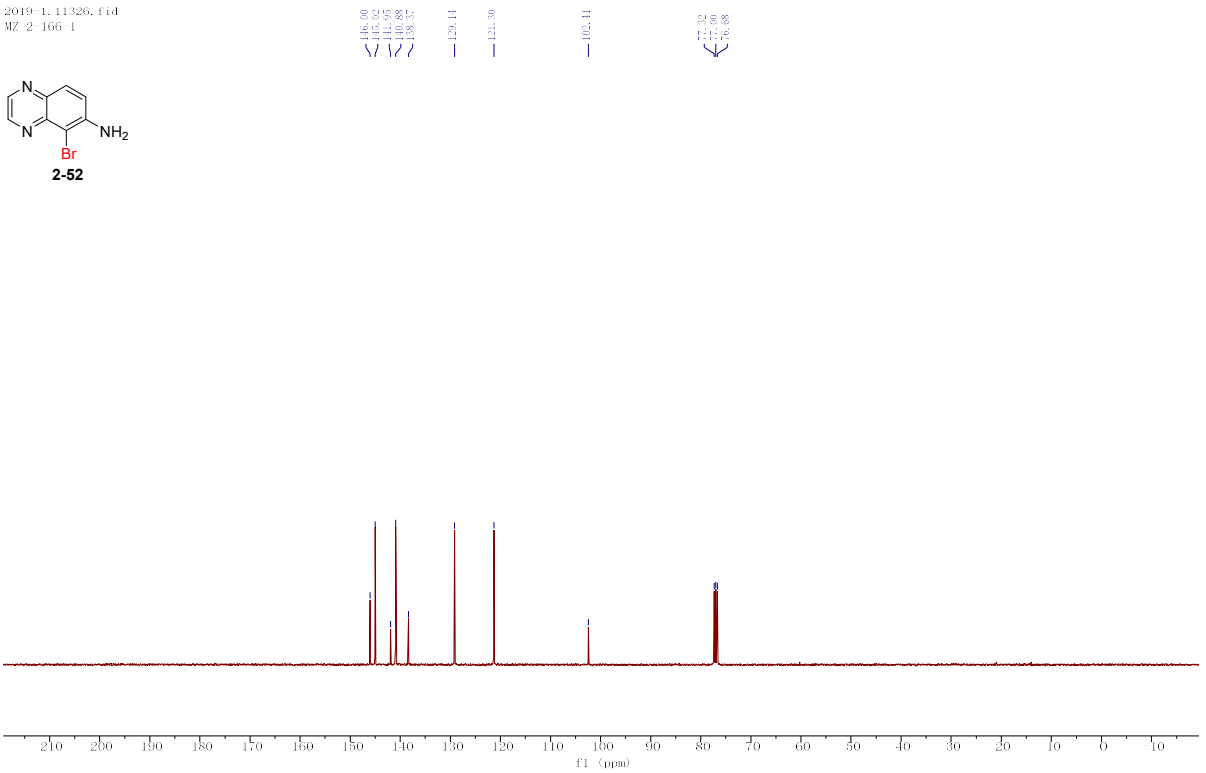


Figure S137. ^{13}C NMR of crude product **2-52**, related Figure 2

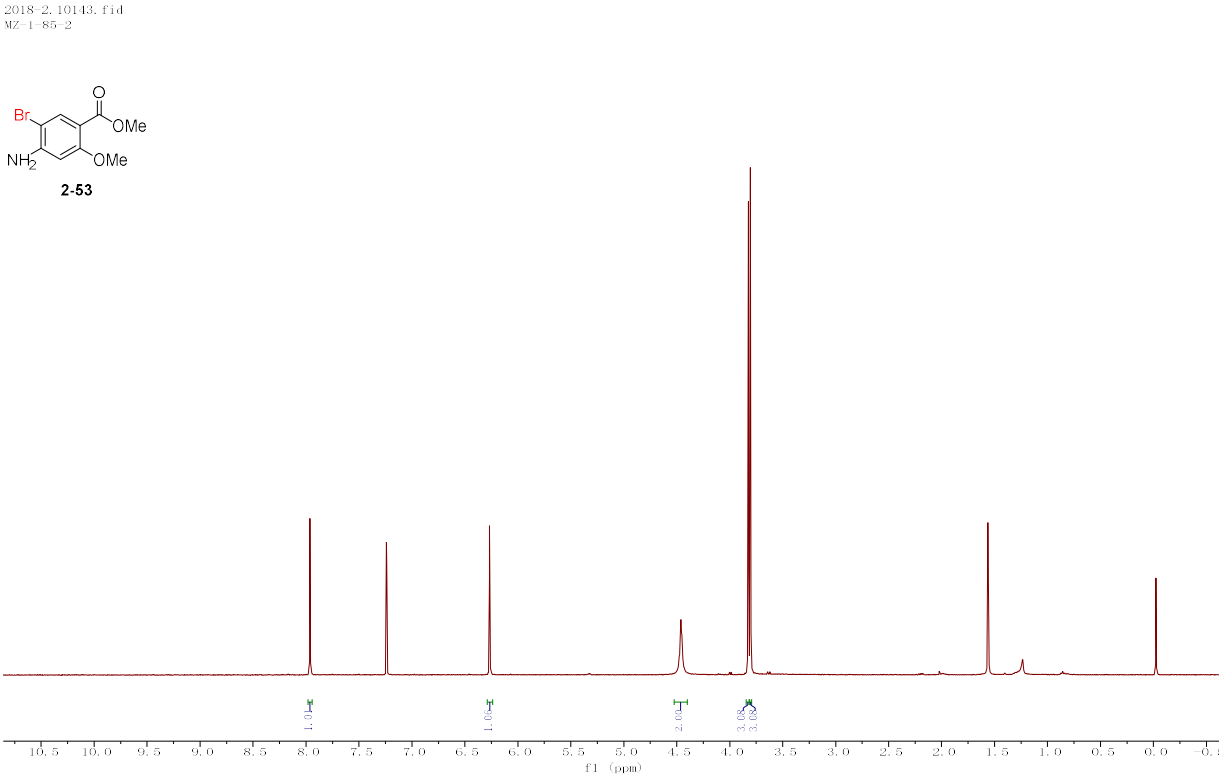


Figure S138. ^{1}H NMR of crude product **2-53**, related Figure 2

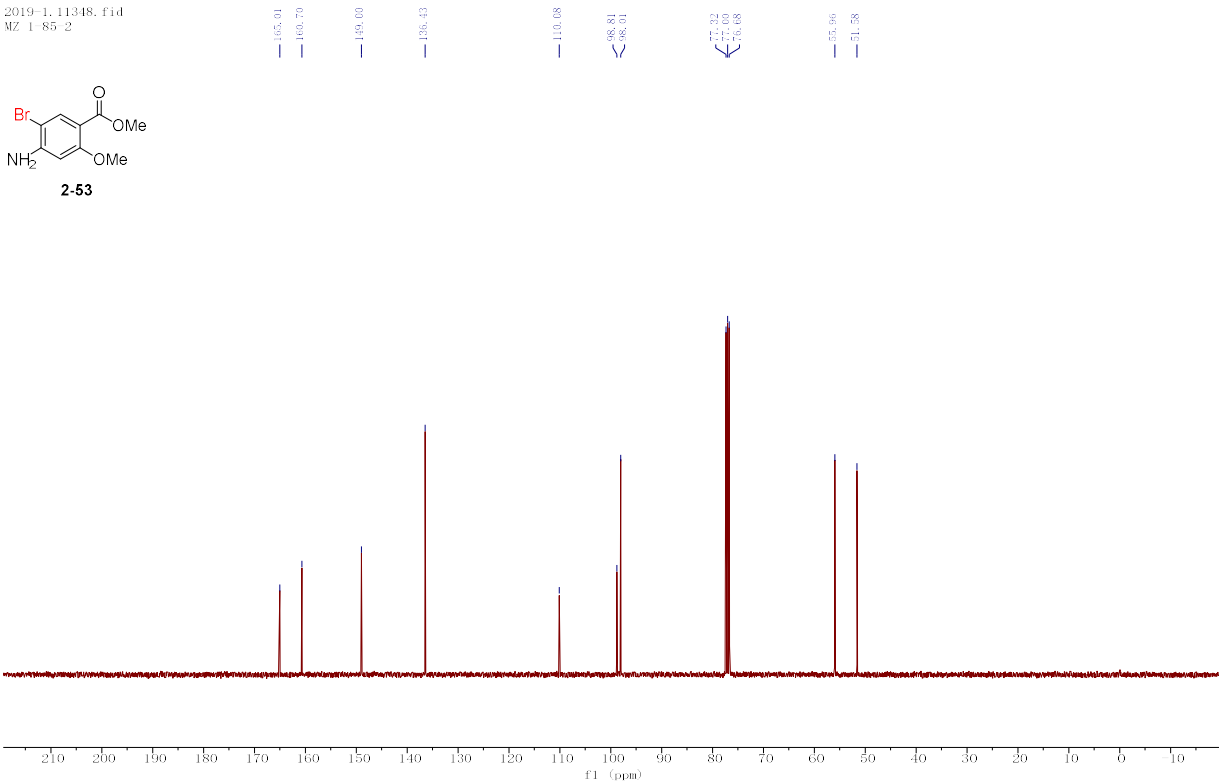


Figure S139. ^{13}C NMR of crude product **2-53**, related Figure 2

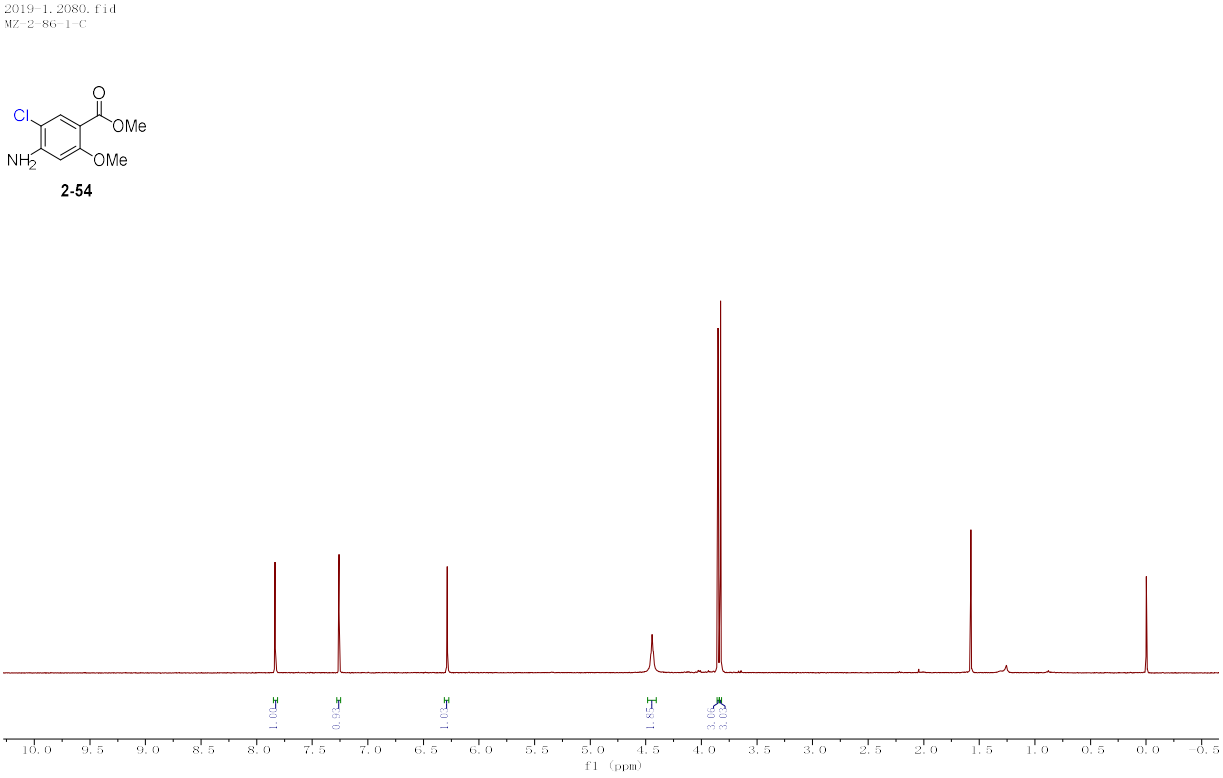


Figure S140. ^{1}H NMR of crude product **2-54**, related Figure 2

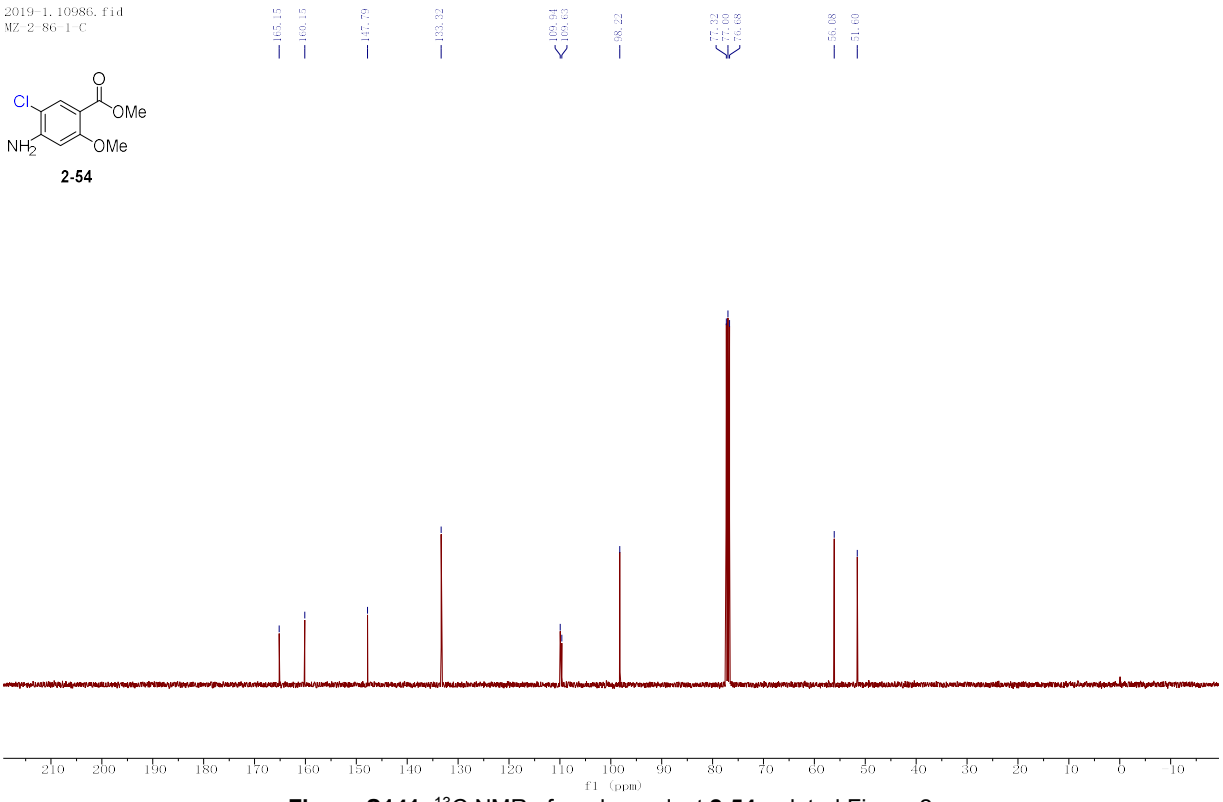


Figure S141. ^{13}C NMR of crude product **2-54**, related Figure 2

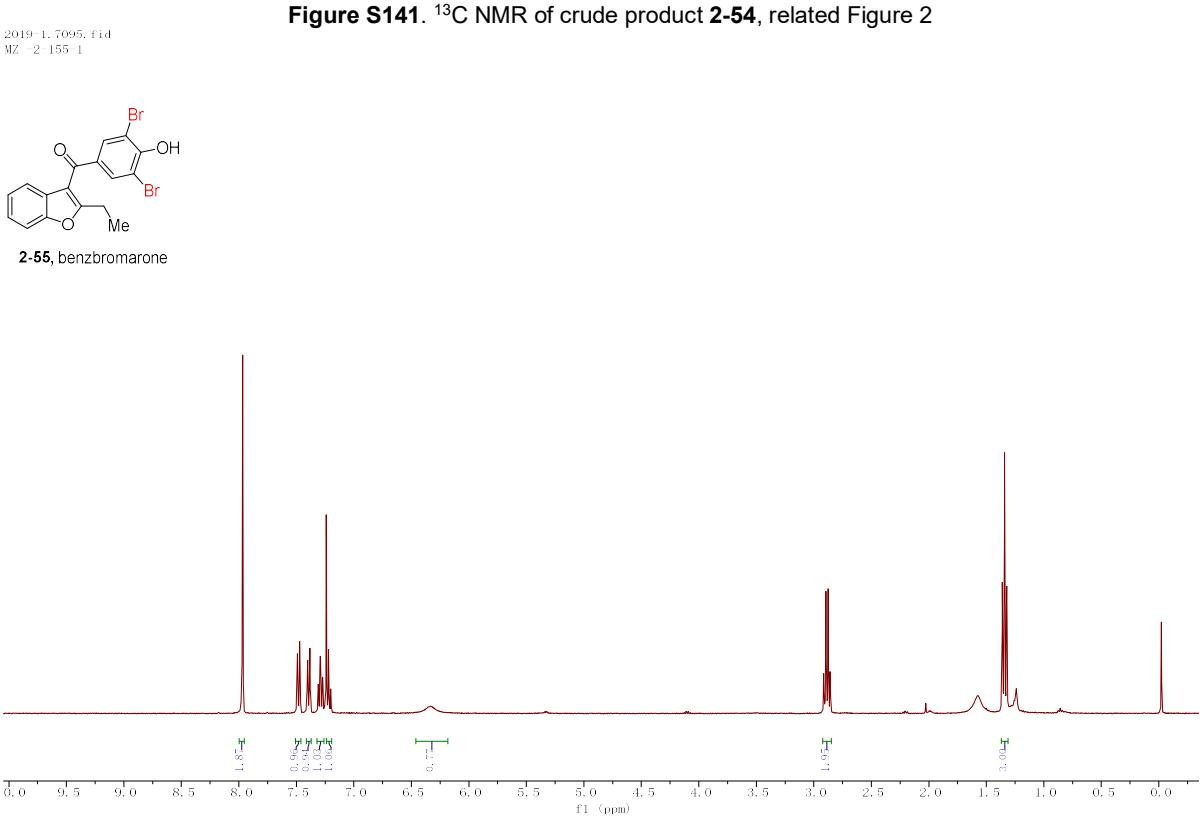
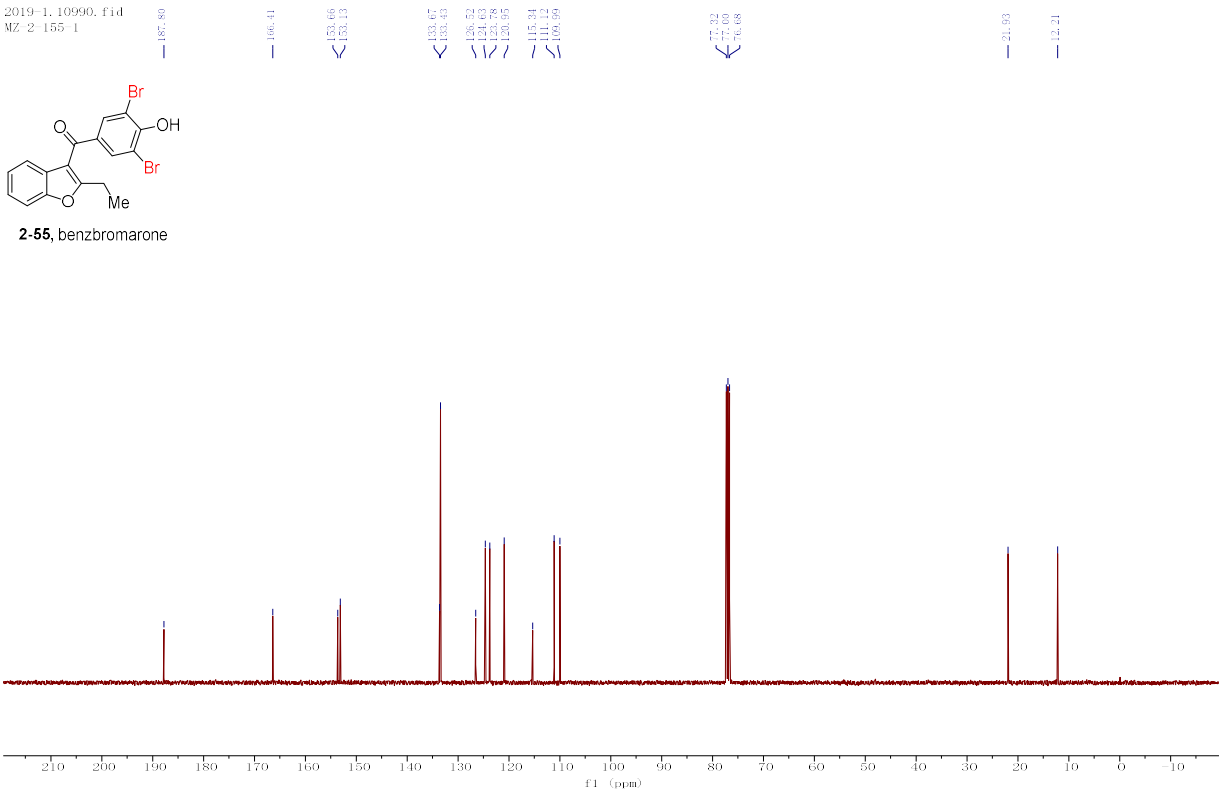
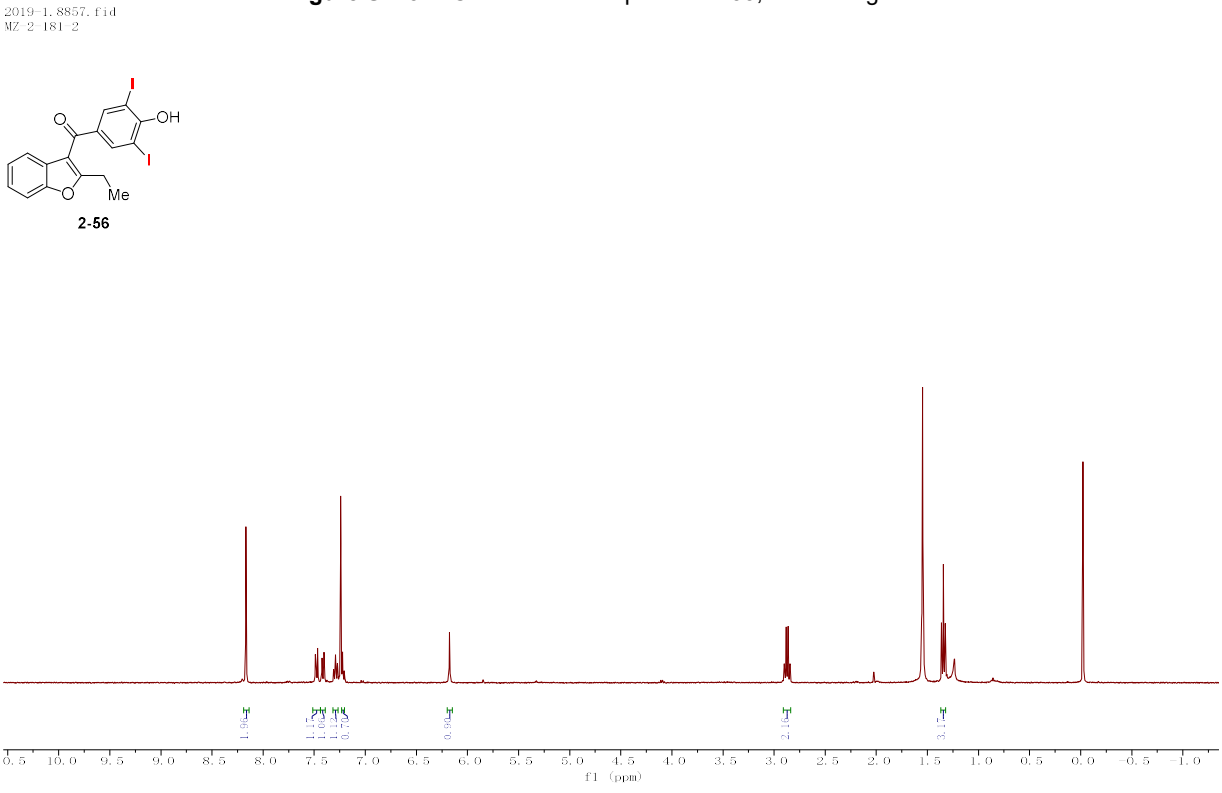


Figure S142. ^{1}H NMR of crude product **2-55**, related Figure 2



2-55, benzbromarone

Figure S143. ^{13}C NMR of crude product **2-55**, related Figure 2



2-56

Figure S144. ^{1}H NMR of crude product **2-56**, related Figure 2

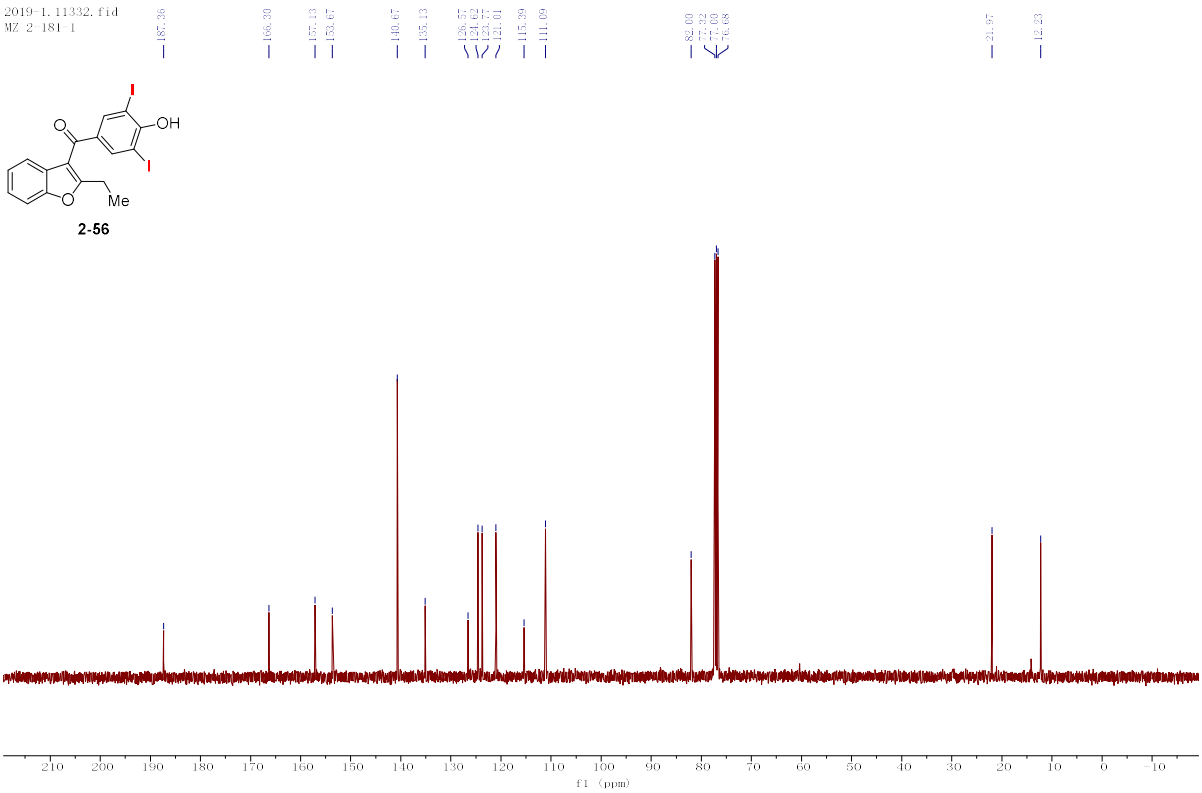


Figure S145. ^{13}C NMR of crude product **2-56**, related Figure 2

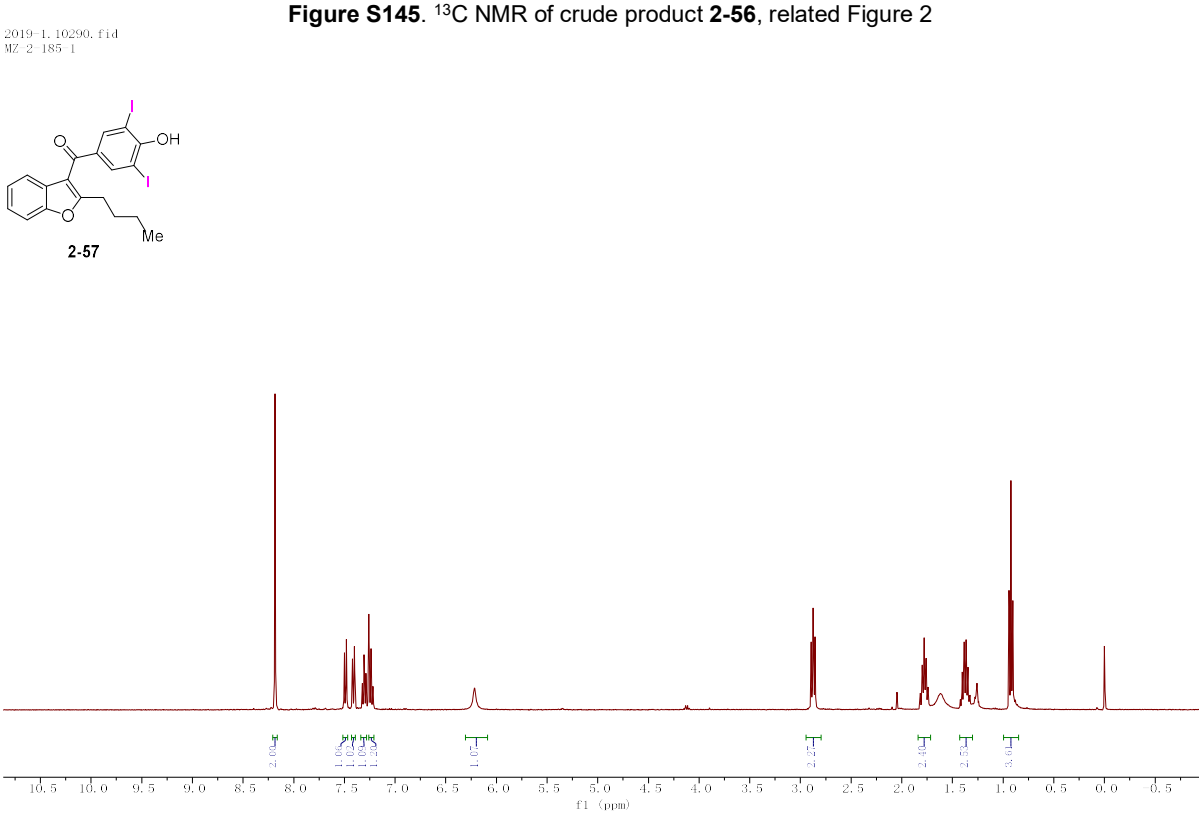


Figure S146. ^{1}H NMR of crude product **2-57**, related Figure 2

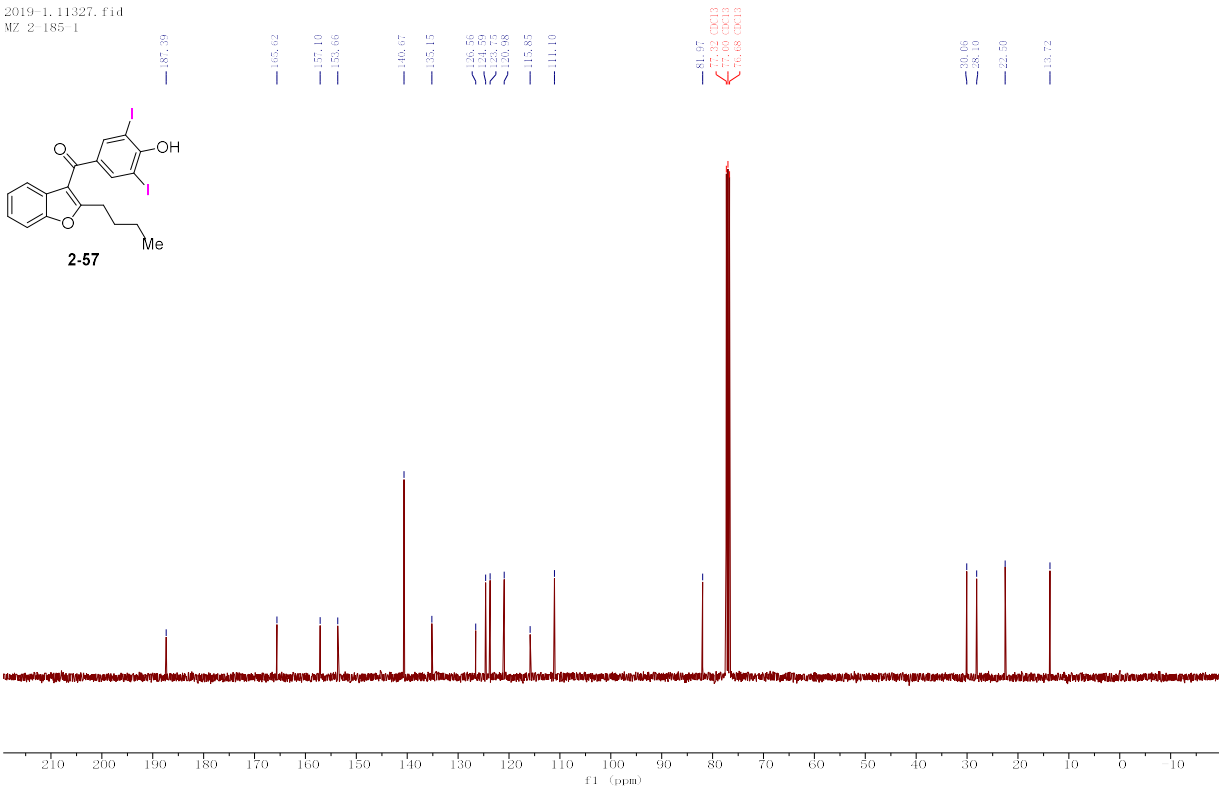


Figure S147. ^{13}C NMR of crude product **2-57**, related Figure 2

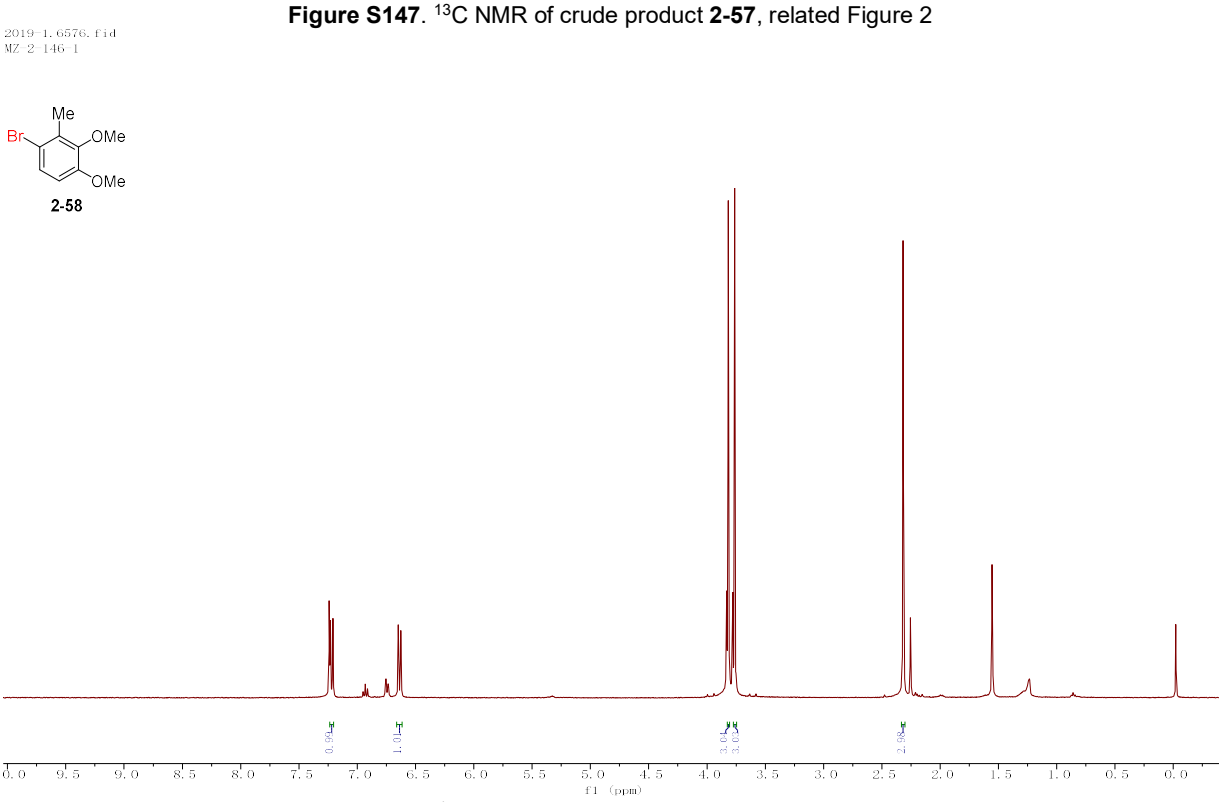


Figure S148. ^{1}H NMR of crude product **2-58**, related Figure 3

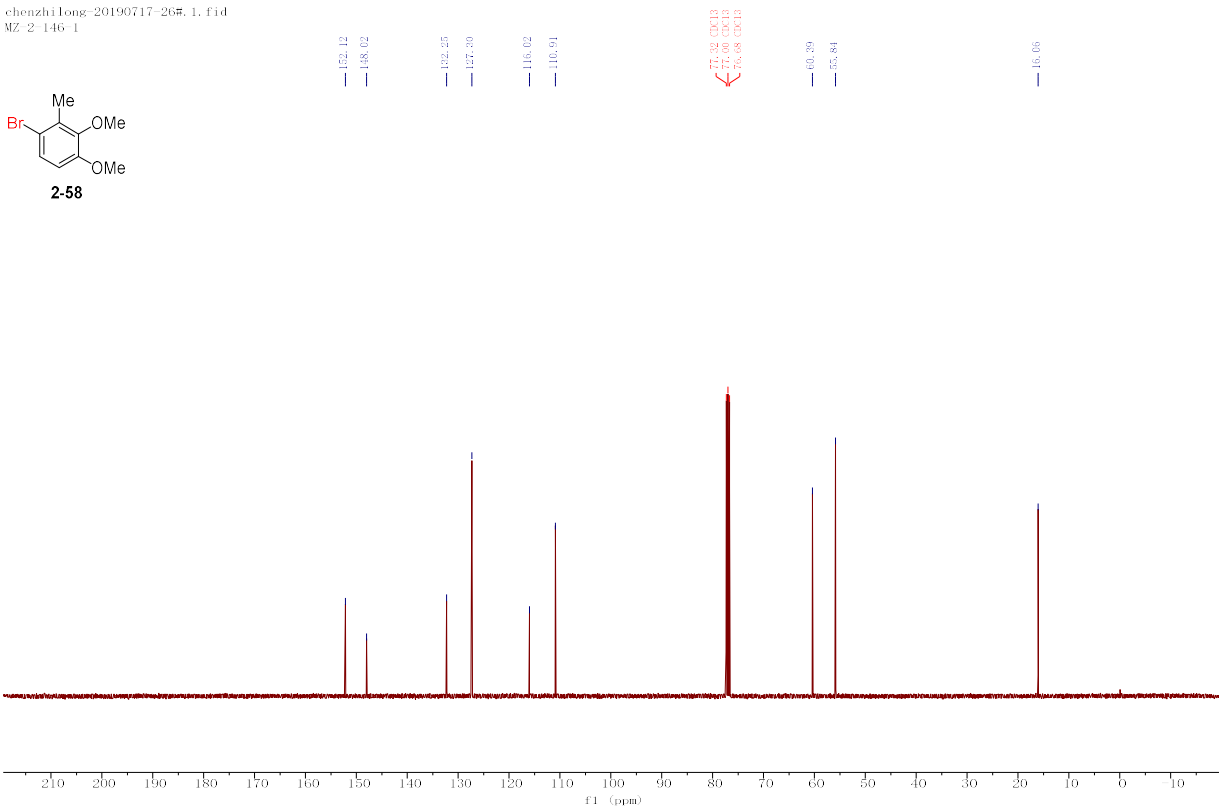
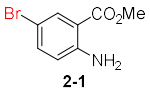


Figure S149. ^{13}C NMR of crude product **2-58**, related Figure 3

Data S1. Characterization of intermediates and products (related to Table 2, 3 and 4, Figure 2)



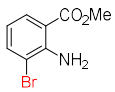
Methyl 2-amino-5-bromobenzoate (**2-1**) (Lehmann, 2007) was obtained as brown solid (192 mg, 91% yield) according to **General Procedure A** for 12h.

221g (93% yield) product **2-1** was isolated as a mixture with **2-1B** and **2-1C** when scaled up to 1.0 mol scale according to **General Procedure E**.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.95 (d, *J* = 2.5 Hz, 1H), 7.30 (dd, *J* = 8.8, 2.3 Hz, 1H), 6.54 (d, *J* = 8.8 Hz, 1H), 5.73 (brs, 2H), 3.85 (s, 3H)

^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.5, 149.3, 136.8, 133.4, 118.4, 112.1, 107.4, 51.8

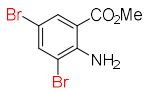
Compounds **2-1B** and **2-1C** was obtained as mixture, (22 mg, **2-1B**: **2-1C** = 5:2 by ^{1}H NMR)



2-1B

Methyl 2-amino-3-bromobenzoate (**2-1B**) (Pierre et al., 2011)

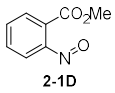
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.85 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.57 (dd, *J* = 7.8, 1.5 Hz, 1H), 6.53 (t, *J* = 8.0 Hz, 1H), 6.34 (brs, 2H), 3.88 (s, 3H)



2-1C

Methyl 2-amino-3,5-dibromobenzoate (**2-1C**) (Zhou and Song, 2018)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.97 (d, *J* = 2.3 Hz, 1H), 7.68 (d, *J* = 2.3 Hz, 1H), 6.34 (brs, 2H), 3.88 (s, 3H)

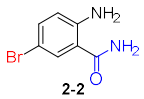


2-1D

Methyl 2-nitrosobenzoate (**2-1D**) (Leronimo et al., 2018) was obtained as a white solid as byproducts in condition screening.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.92 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.75 (dd, *J* = 7.4, 1.7 Hz, 1H), 7.68 (td, *J* = 7.4, 1.4 Hz, 1H), 7.63 (td, *J* = 7.6, 1.8 Hz, 1H), 3.93 (s, 3H)

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.8, 132.9, 131.7, 129.8, 127.5, 123.9, 53.2

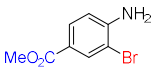


2-2

2-amino-5-bromobenzamide (**2-2**) (Latham et al., 2016) was obtained as yellow solid (112 mg, 52% yield) according to **General Procedure A** for 18.5h.

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.89-7.77 (m, 1H), 7.69 (d, *J* = 2.4 Hz, 1H), 7.25 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.18 (brs, 1H), 6.70 (brs, 2H), 6.65 (d, *J* = 8.8 Hz, 1H)

^{13}C NMR (101 MHz, DMSO-d_6) δ 170.0, 149.4, 134.4, 131.1, 118.5, 115.2, 104.7



2-3

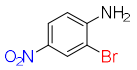
Methyl 4-amino-3-bromobenzoate (**2-3**) (Song et al., 2016) was obtained as yellow solid (194 mg, 85% yield) according to **General Procedure A** for 35h.

Product **2-3** was obtained in water (205 mg, 89% yield) according to **General Procedure B** for 24h.

100g-scale reaction afforded 107 g (94% yield, 0.5 mol scale) product **2-3** according to **General Procedure E**.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.12 (d, *J* = 1.9 Hz, 1H), 7.79 (dd, *J* = 8.4, 1.9 Hz, 1H), 6.73 (d, *J* = 8.5 Hz, 1H), 4.51 (brs, 2H), 3.86 (s, 3H)

^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.0, 148.1, 134.5, 130.2, 120.7, 114.2, 107.8, 51.8

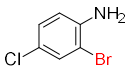


2-4

2-bromo-4-nitroaniline (**2-4**) (Kumar et al., 2011) was obtained as yellow solid (162 mg, 75% yield, 90% yield brsm; 23 mg starting material was recycled, 17% yield) according to **General Procedure A** for 24h.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.38 (d, *J* = 2.5 Hz, 1H), 8.04 (dd, *J* = 9.0, 2.5 Hz, 1H), 6.74 (d, *J* = 8.9 Hz, 1H), 4.82 (brs, 2H)

^{13}C NMR (101 MHz, Chloroform-*d*) δ 149.9, 138.9, 129.2, 124.9, 113.4, 106.9

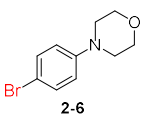


2-5

2-bromo-4-chloroaniline (**2-5**) (Gayakwad et al., 2019) was obtained as yellow solid (708 mg, 69% yield, 5.0 mmol scale) according to **General Procedure A** for 24h.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 (d, *J* = 2.3 Hz, 1H), 7.06 (dd, *J* = 8.6, 2.4 Hz, 1H), 6.67 (d, *J* = 8.6 Hz, 1H), 4.02 (s, 2H)

^{13}C NMR (101 MHz, Chloroform-*d*) δ 146.6, 134.6, 133.9, 116.4, 114.9, 109.7

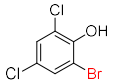


2-6

4-(4-bromophenyl) morpholine (**2-6**) (Song et al., 2015) was obtained as a white solid (139 mg, 57% yield) according to **General Procedure A** for 24h.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38-7.33 (m, 2H), 6.81-6.75 (m, 2H), 3.88-3.82 (m, 4H), 3.15-3.09 (m, 4H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 150.3, 131.9, 117.3, 112.1, 66.7, 49.1



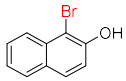
2-7

2-bromo-4,6-dichlorophenol (**2-7**) (Xiong and Yeung, 2018) was obtained as a white solid (157 mg, 65% yield) according to **General Procedure A** for 51h.

Product **2-7** was obtained in water (184 mg, 76% yield) according to **General Procedure B** for 24h.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 (d, *J* = 2.4 Hz, 1H), 7.30 (d, *J* = 2.4 Hz, 1H), 5.85 (brs, 1H)

^{13}C NMR (101 MHz, Chloroform-*d*) δ 147.7, 130.9, 128.7, 125.8, 121.2, 110.4

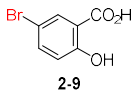


2-8

1-bromonaphthalen-2-ol (**2-8**) (Song et al., 2015) was obtained as a yellow solid (89 mg, 54% yield) according to **General Procedure A** for 15.5h.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.10 (dt, *J* = 8.5, 0.9 Hz, 1H), 7.86-7.80 (m, 1H), 7.77 (d, *J* = 8.8 Hz, 1H), 7.63 (ddd, *J* = 8.4, 6.9, 1.3 Hz, 1H), 7.45 (ddd, *J* = 8.1, 6.9, 1.2 Hz, 1H), 7.34 (d, *J* = 8.8 Hz, 1H)

^{13}C NMR (101 MHz, Chloroform-*d*) δ 150.5, 132.3, 129.6, 129.3, 128.2, 127.8, 125.3, 124.1, 117.1, 106.1

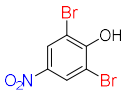


2-9

5-bromo-2-hydroxybenzoic acid (**2-9**) (Oberhauser, 1997) was obtained as white solid (193 mg, 70% yield) according to **General Procedure A** for 18h.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.19 (brs, 1H), 9.46 (brs, 1H), δ 8.06 (d, *J* = 2.5 Hz, 1H), 7.63 (dd, *J* = 8.9, 2.5 Hz, 1H), 6.95 (d, *J* = 8.9 Hz, 1H)

^{13}C NMR (101 MHz, DMSO-d_6) δ 170.5, 160.1, 137.9, 132.1, 119.7, 115.1, 109.9

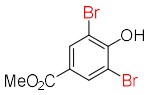


2-10

2,6-dibromo-4-nitrophenol (**2-10**) (Jiang and Yang, 2016) was obtained as a yellow solid (275 mg, 93% yield) according to **General Procedure A** with 2.2 equivalent of NaBr and HOAc for 22h.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.39 (s, 2H)

^{13}C NMR (101 MHz, Chloroform-*d*) δ 155.0, 141.5, 127.9, 109.6



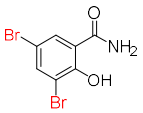
2-11

Methyl 3,5-dibromo-4-hydroxybenzoate (**2-11**) (Kansal et al., 2016) was obtained as a white solid (265 mg, 86% yield) according to **General Procedure A** with 2.2 equivalent of NaBr and HOAc for 60h.

136 g (88% yield) product **2-11** was isolated in 0.5 mol scale according to **General Procedure E**.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.13 (s, 2H), 6.27 (s, 1H), 3.88 (s, 3H)

^{13}C NMR (101 MHz, Chloroform-*d*) δ 164.5, 153.2, 133.7, 124.8, 109.7, 52.5

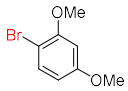


2-12

3,5-dibromo-2-hydroxybenzamide (**2-12**) (Capilato et al., 2017) was obtained as a yellow solid (243 mg, 83% yield) according to **General Procedure A** with 2.2 equivalent of NaBr and HOAc for 28h.

^{1}H NMR (400 MHz, DMSO-d_6) δ 14.29 (s, 1H), 8.72 (s, 1H), 8.33 (s, 1H), 8.15 (d, *J* = 2.3 Hz, 1H), 7.97 (d, *J* = 2.3 Hz, 1H)

^{13}C NMR (101 MHz, DMSO-d_6) δ 171.0, 157.8, 138.4, 129.6, 116.2, 112.1, 109.3

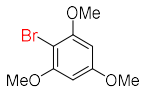


2-13

1-bromo-2,4-dimethoxybenzene (**2-13**) (Song et al., 2015) was obtained as a white solid (186 mg, 86% yield) according to **General Procedure A** for 24h.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 (d, *J* = 8.7 Hz, 1H), 6.47 (d, *J* = 2.7 Hz, 1H), 6.38 (dd, *J* = 8.7, 2.7 Hz, 1H), 3.85 (s, 3H), 3.78 (s, 3H)

^{13}C NMR (101 MHz, Chloroform-*d*) δ 160.2, 156.5, 133.1, 105.8, 102.4, 99.9, 56.1, 55.5



2-14

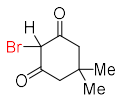
2-bromo-1,3,5-trimethoxybenzene (**2-14**) (Song et al., 2015) was obtained as a white solid (242 mg, 98% yield) according to **General Procedure A** for 24h.

Product **2-14** was also obtained in water (228 mg, 92% yield) according to **General Procedure B**.

123 g (99% yield) product **2-14** was isolated in 0.5 mol scale reaction according to **General Procedure E.**

^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.15 (s, 2H), 3.86 (s, 6H), 3.80 (s, 3H)

^{13}C NMR (101 MHz, Chloroform-*d*) δ 160.4, 157.4, 92.0, 91.6, 56.3, 55.5

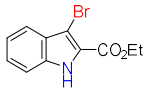


2-15

2,2-dibromo-5,5-dimethylcyclohexane-1,3-dione (**2-15**) (Podgoršek et al., 2017) was obtained as a brown solid (136 mg, 62% yield) according to **General Procedure A** for 24h.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 2.49 (s, 4H), 1.15 (s, 6H)

^{13}C NMR (101 MHz, Chloroform-*d*) δ 178.4, 60.5, 44.7, 32.3, 27.8



2-16

Ethyl 3-bromo-1*H*-indole-2-carboxylate (2-16) (Song et al., 2015) was obtained as a yellow solid (217 mg, 81% yield) according to **General Procedure A** for 16h.

^{1}H NMR (400 MHz, DMSO-d_6) δ 12.28 (brs, 1H), 7.57 (d, *J* = 1.2 Hz, 1H), 7.55 (d, *J* = 1.2 Hz, 1H), 7.36 (ddd, *J* = 8.0, 7.0, 1.2 Hz, 1H), 7.23-7.15 (ddd, *J* = 8.0, 7.0, 1.2 Hz, 1H), 4.39 (q, *J* = 7.1 Hz, 2H), 1.37 (t, *J* = 7.1 Hz, 3H).

2-17

3-bromo-1*H*-pyrrolo[2,3-b] pyridine (**2-17**) (Song et al., 2015) was obtained as a yellow solid (146 mg, 74% yield) according to **General Procedure A** for 40h.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.96 (brs, 1H), 8.37 (dd, *J* = 4.8, 1.5 Hz, 1H), 7.93 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.41 (s, 1H), 7.19 (dd, *J* = 7.9, 4.8 Hz, 1H)

^{13}C NMR (101 MHz, DMSO-d_6) δ 146.4, 143.2, 127.4, 126.0, 119.3, 116.5, 87.5

2-18

3-bromo-1*H*-pyrrolo[3,2-c] pyridine (**2-18**) (Gallou et al., 2007) was obtained as a brown solid (143 mg, 73% yield) according to **General Procedure A** for 18h.

^{1}H NMR (400 MHz, DMSO-d_6) δ 11.89 (brs, 1H), 8.70 (s, 1H), 8.25 (d, *J* = 5.8 Hz, 1H), 7.67 (s, 1H), 7.42 (dd, *J* = 5.8, 1.1Hz, 1H)

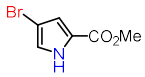
^{13}C NMR (101 MHz, DMSO-d_6) δ 141.7, 141.6, 139.5, 126.8, 123.7, 107.6, 88.2

2-19

5-bromo-7*H*-pyrrolo[2,3-d] pyrimidine (**2-19**) (Jonckers et al., 2016) was obtained as a brown solid (142 mg, 72% yield) according to **General Procedure A** for 48h.

^{1}H NMR (400 MHz, DMSO-d_6) δ 12.6 (s, 1H), 8.9 (d, *J* = 0.8 Hz, 1H), 8.8 (s, 1H), 7.8 (d, *J* = 2.5 Hz, 1H)

^{13}C NMR (101 MHz, DMSO-d_6) δ 151.9, 150.4, 147.8, 127.0, 117.4, 86.5

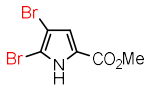


2-20

Methyl 4-bromo-1*H*-pyrrole-2-carboxylate (**2-20**) (Wischang et al., 2011) was obtained as a white solid (87 mg, 43% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.25 (brs, 1H), 6.93 (dd, *J* = 2.9, 1.6 Hz, 1H), 6.86 (dd, *J* = 2.7, 1.6 Hz, 1H), 3.84 (s, 3H)

^{13}C NMR (101 MHz, Chloroform-*d*) δ 160.9, 123.0, 122.8, 116.9, 97.8, 51.8

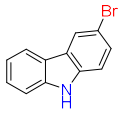


2-20B

Methyl 4,5-dibromo-1*H*-pyrrole-2-carboxylate (**2-20B**) (Wischang and Hartung, 2011) was obtained as a white solid (24 mg, 9% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.45 (s, 1H), 6.86 (d, *J* = 2.9 Hz, 1H), 3.85 (s, 3H)

^{13}C NMR (101 MHz, Chloroform-*d*) δ 160.4, 123.6, 118.0, 107.3, 100.6, 52.1

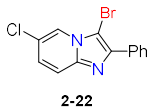


2-21

3-bromo-9*H*-carbazole (**2-21**) (Yang et al.,2018) was obtained as a white solid (90.5 mg, 38% yield; 79% yield based on starting material (brsm); starting material was recycled in 87 mg, 52% yield) according to **General Procedure A** for 22h.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.17 (d, *J* = 1.9 Hz, 1H), 8.07 (brs, 1H), 8.02-7.98 (m, 1H), 7.48 (dd, *J* = 8.6, 1.9 Hz, 1H), 7.45-7.39 (m, 2H), 7.29 (d, *J* = 8.6 Hz, 1H), 7.26-7.20 (m, 1H)

^{13}C NMR (101 MHz, DMSO-d_6) δ 140.1, 138.4, 127.9, 126.4, 124.4, 122.8, 121.5, 120.7, 119.0, 112.9, 111.2, 110.6

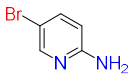


2-22

3-bromo-6-chloro-2-phenylimidazo[1,2-a] pyridine (**2-22**) (Yuan et al., 2019) was obtained as a yellow solid (283 mg, 92% yield) according to **General Procedure A** for 30h.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.22 (d, *J* = 2.0 Hz, 1H), 8.09 (dd, *J* = 7.3, 1.8 Hz, 2H), 7.57 (d, *J* = 9.5 Hz, 1H), 7.47 (dd, *J* = 8.4, 6.8 Hz, 2H), 7.39 (t, *J* = 7.4 Hz, 1H), 7.22 (dd, *J* = 9.5, 2.0 Hz, 1H)

^{13}C NMR (101 MHz, Chloroform-*d*) δ 143.8, 143.6, 132.4, 128.5, 128.5, 127.8, 126.5, 121.9, 121.5, 117.9, 92.1



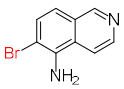
2-23

5-bromopyridin-2-amine (**2-23**) (Song et al., 2015) was obtained as a yellow solid (137 mg, 79% yield) according to **General Procedure A** for 24h.

146 g (85% yield) product **6-10** was isolated in 1.0 mol scale reaction according to **General Procedure E**.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.08 (d, *J* = 2.4 Hz, 1H), 7.47 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.42-6.37 (m, 1H), 4.44 (s, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 157.0, 148.6, 140.1, 110.0, 108.2



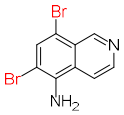
2-24

8-bromoisoquinolin-5-amine (**2-24**) (Gordon and Pearson, 1964) was obtained as a brown liquid (88 mg, 40% yield) according to **General Procedure A** for 21h.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.53 (s, 1H), 8.56 (d, *J* = 5.9 Hz, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.53 (d, *J* = 6.0 Hz, 1H), 6.80 (d, *J* = 8.1 Hz, 1H), 4.23 (brs, 2H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 150.6, 144.6, 141.8, 132.2, 126.7, 126.3, 115.5, 111.3, 104.5

HRMS (ESI): Calculated for [M+1] ($C_9H_8BrN_2^+$) 224.9845; found: 224.9845



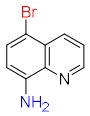
2-24B

6, 8-dibromoisoquinolin-5-amine (**2-24B**) (Gordon and Pearson, 1964) was obtained as a yellow solid (63 mg, 21% yield) according to **General Procedure A**.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.50 (s, 1H), 8.60 (d, *J* = 6.0 Hz, 1H), 7.84 (s, 1H), 7.52 (d, *J* = 6.0 Hz, 1H), 4.71 (brs, 2H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 150.6, 142.7, 141.5, 134.3, 126.7, 125.3, 115.8, 105.2, 104.1

HRMS (ESI): Calculated for [M+1] ($C_9H_7Br_2N_2^+$) 302.8950; found: 302.8949

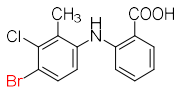


2-25

5-bromoquinolin-8-amine (**2-25**) (Chen et al., 2017) was obtained as a brown solid (74 mg, 33% yield) according to **General Procedure A** for 7h.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.77 (dd, *J* = 4.3, 1.5 Hz, 1H), 8.41 (dd, *J* = 8.5, 1.6 Hz, 1H), 7.80 (s, 1H), 7.51 (dd, *J* = 8.5, 4.2 Hz, 1H), 5.47 (s, 2H)

^{13}C NMR (101 MHz, DMSO-d_6) δ 149.3, 143.5, 138.2, 135.5, 133.5, 126.6, 123.8, 105.0, 101.8



2-26

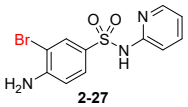
2-((4-bromo-3-chloro-2-methylphenyl) amino) benzoic acid (**2-26**) was obtained as a white solid (330 mg, 97% yield) according to **General Procedure A** for 40h.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.57 (d, *J* = 2.4 Hz, 1H), 7.26 (dd, *J* = 8.5, 2.3 Hz, 1H), 6.99 (d, *J* = 8.6 Hz, 1H), 3.38 (t, *J* = 4.8 Hz, 4H), 3.29 (t, *J* = 4.8 Hz, 4H)

^{13}C NMR (101 MHz, DMSO-d_6) δ 168.8, 146.9, 139.0, 136.4, 134.0, 133.1, 130.6, 127.7, 125.6, 123.0, 115.8, 113.8, 107.5, 14.7

HMRS (ESI): Calculated [M-H] ($C_{14}H_{10}BrClNO_2^-$) 337.9589; found 337.9591

M.p. 176.1-177.0℃



2-27

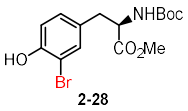
4-amino-3-bromo-N-(pyridin-2-yl) benzene sulfonamide (**2-27**) was obtained as a white solid (242 mg, 74% yield) according to **General Procedure A** for 24 h.

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.10-8.02 (m, 1H), 7.80 (d, *J* = 2.2 Hz, 1H), 7.70 (ddd, *J* = 8.9, 7.3, 1.9 Hz, 1H), 7.53 (dd, *J* = 8.6, 2.2 Hz, 1H), 7.09 (d, *J* = 8.6 Hz, 1H), 6.91 (t, *J* = 6.3 Hz, 1H), 6.79 (d, *J* = 8.6 Hz, 1H), 6.13 (brs, 2H)

^{13}C NMR (101 MHz, DMSO-d_6) δ 152.5, 149.5, 145.1, 139.5, 131.4, 128.1, 127.6, 116.6, 114.0, 112.9, 105.5

HMRS (ESI): Calculated [M+1] ($C_{11}H_{11}BrN_3O_2S^+$): 327.9750; found 327.9751

M.p. 155.9-156.8℃

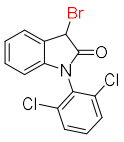


2-28

(*R*)-Methyl 3-(3-bromo-4-hydroxyphenyl)-2-((tert-butoxycarbonyl) amino) propanoate (**2-28**) (Georgiev et al., 2016) was obtained as a white solid (118 mg, 32 % yield, 98% yield brsm; starting material was recycled in 200 mg, 68 % yield) according to **General Procedure A** for 64h.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.20 (s, 2H), 5.80 (s, 1H), 5.01 (d, *J* = 7.9 Hz, 1H), 4.49 (d, *J* = 7.3 Hz, 1H), 3.72 (s, 3H), 3.04 (dd, *J* = 13.9, 5.8 Hz, 1H), 2.90 (dd, *J* = 14.0, 6.1 Hz, 1H), 1.42 (s, 9H), 1.24 (s, 1H)

^{13}C NMR (101 MHz, Chloroform-*d*)) δ 171.8, 154.9, 148.5, 132.8 (two carbons), 130.8, 109.8, 80.2, 54.4, 52.4, 36.9, 28.3



2-29

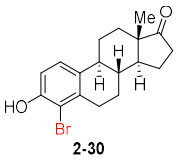
3-bromo-1-(2,6-dichlorophenyl) indolin-2-one (**2-29**) was obtained as a yellow solid (110 mg, 31% yield, 45% yield brsm; 85 mg starting material was recycled, 31% yield) according to **General Procedure A** for 64h.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.5-7.47 (m, 3H), 7.39 (dd, *J* = 8.5, 7.7 Hz, 1H), 7.26 (d, *J* = 7.9 Hz, 1H), 7.15 (td, *J* = 7.6, 1.1 Hz, 1H), 6.39 (d, *J* = 7.8 Hz, 1H), 5.48 (s, 1H)

^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.8, 142.1, 135.6, 135.5, 131.2, 130.4, 129.4, 129.2, 129.0, 126.5, 125.9, 124.0, 109.8, 38.2

HRMS (ESI): Calculated for [M+1] ($C_{14}H_9BrCl_2NO^+$) 357.9219; found 357.9222

M.p. 133.5-134.0℃

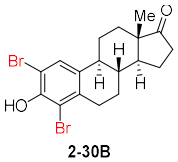


2-30

(8*R*, 9*S*, 13*S*, 14*S*)-4-bromo-3-hydroxy-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-17*H*-cyclopenta[α]phenanthren-17-one (**2-30**) (Slaunwhite and Neely, 1962) was obtained as a yellow solid (153 mg, 44% yield, 51% brsm)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.17 (d, *J* = 8.6 Hz, 1H), 6.85 (d, *J* = 8.5 Hz, 1H), 5.52 (s, 1H), 2.95 (dd, *J* = 17.8, 6.2 Hz, 1H), 2.77-2.65 (m, 1H), 2.50 (dd, *J* = 18.8, 8.7 Hz, 1H), 2.40-2.33 (m, 1H), 2.30- 2.22 (m, 1H), 2.21-2.13 (m, 1H), 2.08 (dd, *J* = 15.3, 7.3 Hz, 2H), 1.95 (s, 1H), 1.67-1.59 (m, 1H), 1.48 (dt, *J* = 9.7, 5.9 Hz, 5H), 0.88 (s, 1H)

^{13}C NMR (101 MHz, DMSO-D_6) 151.9, 136.4, 133.2, 125.0, 113.2, 112.5, 49.4, 47.2, 43.6, 37.0, 35.4, 31.3, 30.7, 26.2, 25.7, 21.7, 21.1, 13.5 (carbonyl missing)

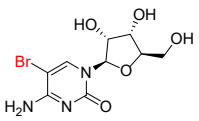


2-30B

(8*R*, 9*S*, 13*S*, 14*S*)-2,4-dibromo-3-hydroxy-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-17H-cyclopenta[a]phenanthren-17-one (**2-30B**) (Slaunwhite and Neely, 1962) was obtained as a yellow solid (16 mg, 4% yield; 5% brsm).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 (s, 1H), 5.83 (s, 1H), 2.92 (dd, *J* = 18.0, 6.2 Hz, 1H), 2.66 (ddd, *J* = 18.2, 11.9, 7.3 Hz, 1H), 2.50 (dd, *J* = 18.8, 8.8 Hz, 1H), 2.38-2.30 (m, 1H), 2.23 (d, *J* = 8.4 Hz, 1H), 2.19 – 2.11 (m, 1H), 2.10-2.02 (m, 2H), 1.97-1.92 (m, 1H), 1.67-1.58 (m, 1H), 1.46 (q, *J* = 10.6, 9.5 Hz, 5H), 0.88 (s, 3H)

^{13}C NMR (101 MHz, Chloroform-*d*) δ 147.3, 136.5, 135.0, 128.6, 113.2, 106.5, 50.2, 47.8, 43.9, 37.3, 35.8, 31.4, 30.9, 26.5, 26.1, 21.5, 13.8 (carbonyl missing)

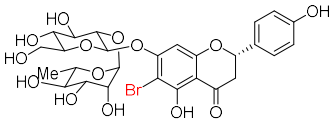


2-31 (crude)

4-amino-5-bromo-1-((2*R*,3*R*,4*R*,5*R*)-3,4-dihydroxy-5-(hydroxymethyl)-3-methyl-tetrahydrofuran-2-yl) pyrimidin-2(1*H*)-one (**2-31**) (Kumar et al., 2009)

^{1}H NMR (400 MHz, Methanol-d_4) δ 8.56 (s, 1H), 5.82 (d, *J* = 3.0 Hz, 1H), 4.17 – 4.10 (m, 2H), 4.05 – 4.01 (m, 1H), 3.93 (dd, *J* = 12.3, 2.5 Hz, 1H), 3.77 (dd, *J* = 12.3, 2.5 Hz, 1H), 1.91 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 161.9, 154.0, 142.3, 89.6, 86.2, 84.1, 74.4, 68.7, 59.8



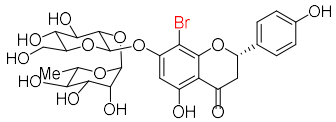
2-32

(*S*)-6-bromo-7-(((2*R*,3*S*,4*R*,5*R*,6*S*)-4,5-dihydroxy-6-(hydroxymethyl)-3-(((2*S*,3*R*,4*R*,5*R*,6*S*)-3,4,5-trihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)tetrahydro-2*H*-pyran-2-yl)oxy)-5-hydroxy-2-(4-hydroxyphenyl)chroman-4-one (**2-32**) was obtained as a white solid after HPLC purification (MeCN: H_2O = 25:75, 2 mL/min, 13.1 min) according to **General procedure A**.

^{1}H NMR (400 MHz, Methanol-d_4) δ 7.33 (t, *J* = 7.5 Hz, 2H), 6.86-6.78 (m, 2H), 6.38 (d, *J* = 3.7 Hz, 1H), 5.53-5.38 (m, 2H), 5.31 (dd, *J* = 7.7, 4.4 Hz, 1H), 3.94 (m, 1H), 3.91-3.81 (m, 2H), 3.76 (m, 1H), 3.72-3.59 (m, 3H), 3.45 (m, 2H), 3.36 (t, *J* = 9.5 Hz, 1H), 1.20 (m, 3H).

^{13}C NMR (101 MHz, Methanol-d_4) 198.3, 162.5, 159.0, 130.4, 129.2, 129.0, 116.4, 101.9, 101.7, 99.5, 97.2, 80.7, 79.1, 78.7, 78.6, 78.2, 74.1, 72.2, 72.0, 71.10, 71.05, 70.2, 62.2, 24.1, 18.5

HRMS (ESI): Calculated for [M+Na] ($C_{27}H_{31}BrNaO_{14}^{+}$) 681.0789; found 681.0783



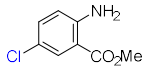
2-32B

(*S*)-8-bromo-7-(((2*R*,3*S*,4*R*,5*R*,6*S*)-4,5-dihydroxy-6-(hydroxymethyl)-3-(((2*S*,3*R*,4*R*,5*R*,6*S*)-3,4,5-trihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)tetrahydro-2*H*-pyran-2-yl)oxy)-5-hydroxy-2-(4-hydroxyphenyl)chroman-4-one (**2-32B**) was obtained as a pale-yellow solid by HPLC (MeCN:H_2O = 25:75, 2 mL/min, 16.3 min) according to **General procedure A**.

^{1}H NMR (400 MHz, Methanol-d_4) δ 7.33 (d, *J* = 7.9 Hz, 2H), 6.82 (dd, *J* = 8.6, 2.8 Hz, 2H), 6.40-6.30 (s, 1H), 5.54-5.36 (m, 2H), 5.36-5.22 (m, 1H), 3.94 (s, 1H), 3.85 (dd, *J* = 16.9, 8.5 Hz, 2H), 3.76 (t, *J* = 8.4 Hz, 1H), 3.63 (dt, *J* = 16.8, 9.0 Hz, 3H), 3.40 (dt, *J* = 29.8, 10.9 Hz, 3H), 1.90 (d, *J* = 2.4 Hz, 1H), 1.21 (d, *J* = 6.2 Hz, 3H).

^{13}C NMR (101 MHz, Methanol-d_4) 162.4, 159.2, 129.2, 129.0, 128.9, 116.4, 116.3, 101.9, 101.8, 99.4, 80.7, 79.1, 78.7, 78.19, 78.15, 74.0, 72.2, 72.0, 71.12, 71.06, 70.2, 62.2, 24.1, 18.5 (carbonyl not seen)

HRMS (ESI): Calculated for [M+Na] ($C_{27}H_{31}BrNaO_{14}^+$) 681.0789; found 681.0783

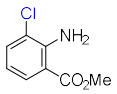


2-33

Methyl 2-amino-5-chlorobenzoate (**2-33**) (Zhou et al., 2017) was obtained as a yellow solid (104 mg, 56% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.80 (d, *J* = 2.5 Hz, 1H), 7.18 (dd, *J* = 8.8, 2.5 Hz, 1H), 6.59 (d, *J* = 8.8 Hz, 1H), 5.70 (brs, 2H), 3.85 (s, 3H)

^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.5, 148.9, 134.0, 130.4, 120.6, 118.0, 111.4, 51.7

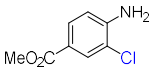


2-33B

Methyl 2-amino-3-chlorobenzoate (**2-33B**) (Cai et al., 2018) was obtained as yellowish oil (47 mg, 25% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.84-7.78 (m, 1H), 7.44-7.38 (m, 1H), 6.58 (t, *J* = 7.9 Hz, 1H), 6.27 (brs, 2H), 3.88 (d, *J* = 0.8 Hz, 3H)

^{13}C NMR (101 MHz, DMSO-d_6) δ 168.1, 146.6, 133.8, 129.9, 120.2, 115.7, 111.8, 51.8

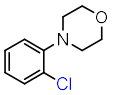


2-34

Methyl 4-amino-3-chlorobenzoate (**2-34**) (Yang et al., 2018) was obtained as a yellow solid (91 mg, 49% yield, 64 yield brsm; 35 mg starting materisl was recycled, 23% yield) according to **General Procedure C** for 27h.

^{1}H NMR (400 MHz, Methanol-d_4) δ 7.93 (d, *J* = 1.9 Hz, 1H), 7.73 (dd, *J* = 8.4, 1.9 Hz, 1H), 6.71 (d, *J* = 8.4 Hz, 1H), 4.45 (brs, 2H), 3.84 (s, 3H)

^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.2, 147.0, 131.2, 129.6, 120.4, 118.2, 114.4, 51.8

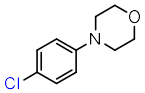


2-35

4-(2-chlorophenyl) morpholine (**2-35**) (Hendrick and Wang, 2015) was obtained as a pale-yellow liquid (89 mg, 45% yield)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.35 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.25-7.19 (m, 2H), 7.02 (dd, *J* = 8.1, 1.5 Hz, 1H), 6.97 (td, *J* = 7.7, 1.5 Hz, 1H), 3.89-3.84 (m, 4H), 3.07 – 3.02 (m, 4H)

^{13}C NMR (101 MHz, Chloroform-*d*) δ 149.0, 130.7, 128.7, 127.6, 123.9, 120.2, 67.1, 51.6

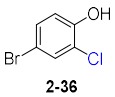


2-35B

4-(4-chlorophenyl) morpholine (**2-35B**) (Berman and Johnson, 2004) was obtained as a yellow solid (25 mg, 13% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.22 (d, *J* = 9.0 Hz, 2H), 6.83 (d, *J* = 8.9 Hz, 2H), 3.90-3.81 (m, 4H), 3.16-3.07 (m, 4H)

^{13}C NMR (101 MHz, Chloroform-*d*) δ 149.9, 129.0, 124.9, 116.9, 66.8, 49.3

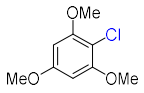


2-36

4-bromo-2-chlorophenol (**2-36**) (Oberhauser, 1997) was obtained as a yellow solid (169 mg, 82% yield) according to **General Procedure C** except using TFA instead of HOAc for 88h.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.25 (s, 1H), 7.07 (dd, *J* = 8.7, 2.3 Hz, 1H), 6.68 (d, *J* = 8.7 Hz, 1H), 5.34 (s, 1H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 150.7, 131.4, 131.3, 120.8, 117.6, 112.3

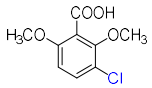


2-37

2-chloro-1,3,5-trimethoxybenzene (**2-37**) (Seel et al., 2018) was obtained as a white solid (103 mg, 51% yield, 74% yield brsm; 52 mg starting material was recycled, 31% yield) according to **General Procedure C** for 69h.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.18 (s, 2H), 3.88 (s, 6H), 3.81 (s, 3H)

^{13}C NMR (101 MHz, Chloroform-*d*) δ 159.4, 156.5, 102.6, 91.6, 56.2, 55.5

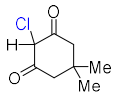


2-38

3-chloro-2,6-dimethoxybenzoic acid (**2-38**) (Florvall and Oegren, 1982) was obtained as a white solid (94 mg, 44% yield, 56% yield brsm; 38 mg starting material was recycled, 21% yield) according to **General Procedure C** for 46h.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 (d, *J* = 8.9 Hz, 1H), 6.70 (d, *J* = 8.9 Hz, 1H), 3.96 (s, 3H), 3.88 (s, 3H)

^{13}C NMR (101 MHz, Chloroform-*d*) δ 156.0, 153.9, 132.1, 119.7, 118.8, 108.0, 62.0, 56.4

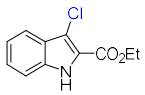


2-39

2,2-dichloro-5,5-dimethylcyclohexane-1,3-dione (2-39) (China et al., 2015) was obtained as a white solid (74 mg, 43% yield) according to **General procedure C** for 40h.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 2.49 (s, 4H), 1.15 (s, 6H)

^{13}C NMR (101 MHz, Chloroform-*d*) δ 178.5, 70.4, 44.7, 32.3, 27.7



2-40

Ethyl 3-chloro-1H-indole-2-carboxylate (**2-40**) (Wang et al., 2016) was obtained as a white solid (155.5 mg, 70% yield, 91% yield brsm; 38 mg starting material was recycled, 23% yield) according to **General Procedure C** for 70h.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.77 (brs, 1H), 7.57 (d, *J* = 8.2 Hz, 1H), 7.27-7.20 (m, 2H), 7.07 (ddd, *J* = 8.0, 5.6, 2.3 Hz, 1H), 4.31 (q, *J* = 7.1 Hz, 2H), 1.30 (t, *J* = 7.1 Hz, 3H)

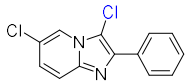
^{13}C NMR (101 MHz, Chloroform-*d*) δ 161.2, 134.8, 126.5, 126.2, 122.4, 121.2, 120.1, 112.4, 112.1, 61.4, 14.3

2-41

3-chloro-1*H*-pyrrolo[2,3-b] pyridine (**2-41**) (Wang et al., 2016) was obtained as a yellow solid (85 mg, 56% yield, 62% yield brsm; 12 mg starting material was recycled, 10% yield) for 18h.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.72 (brs, 1H), 8.29 (dd, *J* = 4.8, 1.5 Hz, 1H), 7.94-7.88 (m, 1H), 7.17 (s, 1H), 7.10 (dd, *J* = 7.9, 4.8 Hz, 1H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 147.0, 143.4, 127.2, 121.9, 118.6, 116.3, 104.4

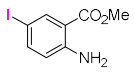


2-42

3, 6-dichloro-2-phenylimidazo[1,2-a] pyridin (**2-42**) (Xiao et al., 2015) was obtained as a white solid (92 mg, 35% yield, 78% yield brsm; 126 mg starting material was recycled, 55% yield) according to **General Procedure C** for 24h.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.17 (d, *J* = 2.0 Hz, 1H), 8.15-8.09 (m, 2H), 7.59 (d, *J* = 9.5 Hz, 1H), 7.49 (dd, *J* = 8.5, 6.9 Hz, 2H), 7.40 (t, *J* = 7.3 Hz, 1H), 7.22 (dd, *J* = 9.5, 2.0 Hz, 1H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 142.0, 140.8, 132.0, 128.6, 128.5, 127.4, 126.2, 121.4, 120.6, 118.0, 106.1

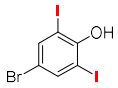


2-43

Methyl 2-amino-5-iodobenzoate (**2-43**) (Zhou and Song, 2018) was obtained as a brown solid (106 mg, 39% yield, 48% yield brsm; 28 mg starting material was recycled, 18% yield) according to **General Procedure D** for 17h.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.91 (d, *J* = 2.2 Hz, 1H), 7.25 (dd, *J* = 8.7, 2.2 Hz, 1H), 6.23 (d, *J* = 8.7 Hz, 1H), 5.54 (brs, 2H), 3.64 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.3, 149.8, 142.2, 139.5, 118.8, 112.8, 75.9, 51.8

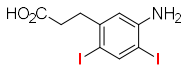


2-44

4-bromo-2,6-diiodophenol (**2-44**) (Satkar et al., 2019) was obtained as a brown solid (413 mg, 97% yield) according to **General Procedure D** for 13 h. Product **2-44** was also obtained (394 mg, 93% yield) in control experiment without catalyst for 17h.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.79 (s, 2H), 5.73 (brs, 1H)

^{13}C NMR (101 MHz, Chloroform-*d*) δ 153.1, 140.8, 113.5, 82.4



2-45

3-(5-amino-2,4-diiodophenyl) propanoic acid (**2-45**) was obtained as a brown solid (274 mg, 65% yield) according to **General Procedure D** for 40 min. Without catalyst, the reaction required 6 h to complete (279 mg, 66% yield).

^{1}H NMR (400 MHz, DMSO-d_6) δ 12.23 (brs, 1H), 7.83 (s, 1H), 6.72 (s, 1H), 5.34 (br, 2H), 2.69 (dd, *J* = 8.6, 7.0 Hz, 2H), 2.43 (dd, *J* = 8.6, 7.0 Hz, 2H)

^{13}C NMR (101 MHz, DMSO-d_6) δ 173.2, 149.0, 146.3, 143.3, 114.9, 83.3, 81.7, 34.4, 33.8

HRMS (ESI): Calculated for [M+1] ($C_9H_{10}I_2NO_2^+$): 417.8795; found 417.8797

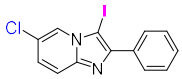
M.p. 134.9-135.6℃

2-46

3-iodo-1H-pyrrolo[2,3-*b*] pyridine (**2-46**) (Iida et al., 2019) was obtained as a brown solid (217 mg, 89% yield) according to **General Procedure D** for 15 min. Product **2-44** was obtained (233.8 mg, 96% yield) in a control experiment without catalyst in 15 min.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.35 (brs, 1H), 8.32 (dd, *J* = 4.7, 1.5 Hz, 1H), 7.76 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.44 (s, 1H), 7.16 (dd, *J* = 7.9, 4.8 Hz, 1H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 148.0, 143.7, 130.5, 128.0, 122.0, 116.4, 54.3

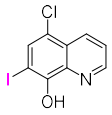


2-47

6-chloro-3-iodo-2-phenylimidazo[1,2-*a*] pyridine (**2-47**) (Zhou et al., 2019) was obtained as a yellow (172 mg, 97% yield) according to **General Procedure D** for 20 min. Product **2-47** was obtained (175 mg, 99% yield) without catalyst in a control experiment in 1h.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.28 (t, *J* = 1.2 Hz, 1H), 8.03 (d, *J* = 7.6 Hz, 2H), 7.56 (d, *J* = 9.5 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.40 (d, *J* = 7.2 Hz, 1H), 7.21 (dd, *J* = 9.5, 1.9 Hz, 1H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 149.0, 146.5, 133.1, 128.6, 128.41, 128.37, 126.9, 126.0, 124.5, 121.1, 117.9



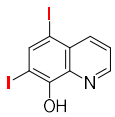
2-48

5-chloro-7-iodoquinolin-8-ol (**2-48**) (Deshmukh et al., 2015) was obtained as a brown solid (9 g, 89% yield for 50 mmol scale, isolated by filtration) according to **General Procedure E** for 1h.

^{1}H NMR (400 MHz, DMSO-d_6) δ 11.03 (s, 1H), 8.96 (d, *J* = 4.2 Hz, 1H), 8.49 (d, *J* = 8.0, 1H), 7.99 (s, 1H), 7.77 (dd, J_1 = 8.0 Hz, J_2 = 4.0 Hz, 1H)

^{13}C NMR (101 MHz, DMSO-d_6) δ 153.6, 149.6, 137.5, 134.9, 133.0, 125.7, 123.4, 119.4, 78.9

HRMS (ESI): Calculated for [M-H] ($C_9H_4ClINO^-$) 303.9032; found 303.9033

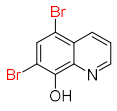


2-49

5, 7-diiodoquinolin-8-ol (**2-49**) (Swamy et al., 2016) was obtained as a brown solid (with catalyst, 3.8 g, mixture, diiodination product (di): monoiodination product (mo) = 5:1) by 1H-NMR, 83% yield) according to **General Procedure E** for 3h.

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.88 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.34 (s, 1H), 8.29 (dd, *J* = 8.5, 1.5 Hz, 1H), 7.73 (dd, *J* = 8.5, 4.2 Hz, 1H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 154.8, 149.6, 144.5, 140.0, 138.0, 129.6, 124.2, 85.2, 80.9

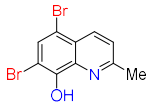


2-50

5, 7-dibromoquinolin-8-ol[xx] **(2-50)** was obtained as a yellow solid (19.3 g, 64% yield, 100 mmol scale) according to **General Procedure E** for 2h.

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.94 (dt, *J* = 3.9, 1.9 Hz, 1H), 8.44 (dd, *J* = 8.6, 1.6 Hz, 1H), 8.04 (s, 1H), 7.76 (dd, *J* = 8.7, 4.2 Hz, 1H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 151.3, 149.8, 139.0, 135.4, 133.3, 126.5, 123.6, 108.6, 105.1

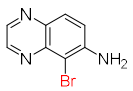


2-51

5,7-dibromo-2-methylquinolin-8-ol (**2-51**) (Bakewell et al., 2012) was obtained as a yellow solid (81.6 g, 52% yield) according to **General Procedure E** for 1.5h.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.29 (d, *J* = 8.6 Hz, 1H), 7.80 (s, 1H), 7.41 (d, *J* = 8.6 Hz, 1H), 2.75 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 158.8, 149.1, 138.0, 136.0, 132.7, 124.8, 123.9, 110.0, 103.6, 24.7

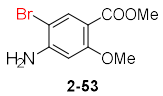


2-52

5-bromoquinoxalin-6-amine (**2-52**) (Munk et al., 1997) was obtained as a yellow solid (161 mg, 72% yield) according to **General Procedure A** for 5.5h.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.80 (s, *J* = 2.0 Hz, 1H), 8.60 (d, *J* = 2.0 Hz, 1H), 7.87 (d, *J* = 9.0 Hz, 1H), 7.29 (d, *J* = 9.0 Hz, 1H), 4.79 (brs, 2H)

^{13}C NMR (101 MHz, Chloroform-*d*) δ 146.0, 145.0, 142.0, 140.9, 138.4, 129.2, 121.3, 102.4



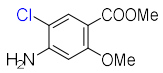
2-53

Methyl 4-amino-5-bromo-2-methoxybenzoate (**2-53**) (Lai et al., 2016) was obtained as a yellow solid (224 mg, 86% yield) according to **General Procedure A** for 5.5h.

Product **2-53** was obtained with water as solvent according to **General Procedure B** (195 mg, 75% yield; 2.5 mol% Na_2WO_4-$2H_2O$, 1.1 equivalent H_2O_2, 24h)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.98 (s, 1H), 6.29 (s, 1H), 4.48 (brs, 2H), 3.84 (s, 3H), 3.83 (s, 3H)

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.0, 160.7, 149.0, 136.4, 110.1, 98.8, 98.0, 56.0, 51.6

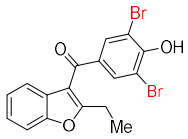


2-54

Methyl 4-amino-5-chloro-2-methoxybenzoate (**2-54**) (Selvakumar et al., 2016) was obtained as a yellow solid (91 mg, 42% yield) for 10h.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.83 (s, 1H), 6.29 (s, 1H), 4.44 (brs, 2H), 3.85 (s, 3H), 3.83 (s, 3H)

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.2, 160.2, 147.8, 133.3, 109.9, 109.6, 98.2, 56.1, 51.6

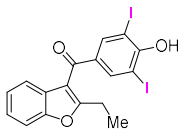


2-55

(3, 5-dibromo-4-hydroxyphenyl) (2-ethylbenzofuran-3-yl) methanone (**2-55**) (Huang et al., 2019) was obtained as a yellow solid (413 mg, 97% yield) according to **General Procedure A** by utilizing 2.2 equivalent of NaBr and HOAc for 48h.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.99 (s, 2H), 7.50 (d, *J* = 8.2 Hz, 1H), 7.41 (d, *J* = 7.7 Hz, 1H), 7.31 (td, *J* = 8.2, 7.7, 1.4 Hz, 1H), 7.23 (d, *J* = 7.5 Hz, 1H), 6.37 (brs, 1H), 2.91 (q, *J* = 7.5 Hz, 2H), 1.36 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 187.8, 166.4, 153.7, 153.1, 133.7, 133.4, 126.5, 124.6, 123.8, 121.00, 115.4, 111.1, 110.0, 21.9, 12.2

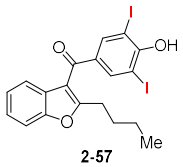


2-56

(2-ethylbenzofuran-3-yl) (4-hydroxy-3,5-diiodophenyl) methanone (**2-56**) (Huang et al., 2019) was obtained as a white solid (255 mg, 98% yield) according to **General Procedure D** for 40 min.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.17 (s, 2H), 7.48 (d, *J* = 8.2 Hz, 1H), 7.41 (d, *J* = 7.8 Hz, 1H), 7.29 (t, *J* = 7.5 Hz, 1H), 7.21 (d, *J* = 7.4 Hz, 1H), 6.18 (s, 1H), 2.87 (q, *J* = 7.5 Hz, 2H), 1.34 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 187.4, 166.3, 157.1, 153.7, 140.7, 135.1, 126.6, 124.6, 123.8, 121.0, 115.4, 111.1, 82.0, 22.0, 12.2

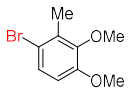


2-57

(2-butylbenzofuran-3-yl) (4-hydroxy-3,5-diiodophenyl) methanone (**2-57**) (Huang et al., 2019) was obtained as a brown solid (96 mg, 88% yield, 0.2 mmol scale) according to **General Procedure D** by utilizing 2.2 equivalent of KI and HOAc for 2h.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.18 (s, 2H), 7.49 (d, *J* = 8.2 Hz, 1H), 7.41 (d, *J* = 7.7 Hz, 1H), 7.34 – 7.28 (m, 1H), 7.24 (t, *J* = 7.4 Hz, 1H), 6.22 (brs, 1H), 2.88 (t, *J* = 7.7 Hz, 2H), 1.78 (p, *J* = 7.7 Hz, 2H), 1.38 (h, *J* = 7.4 Hz, 3H), 0.92 (t, *J* = 7.3 Hz, 4H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 187.4, 165.6, 157.1, 153.7, 140.7, 135.2, 126.6, 124.6, 123.8, 121.0, 115.9, 111.1, 82.0, 30.1, 28.1, 22.5, 13.7



2-58

1-bromo-3,4-dimethoxy-2-methylbenzene (**2-58**) (Connolly et al., 2004) was obtained as a yellow liquid (145 mg, 63% yield) according to **General procedure A** for 82h.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.24 (d, *J* = 8.8 Hz, 1H), 6.66 (d, *J* = 8.8 Hz, 1H), 3.84 (s, 3H), 3.78 (s, 3H), 2.34 (s, 3H)

^{13}C NMR (101 MHz, Chloroform-*d*) δ 152.1, 148.0, 132.3, 127.3, 116.0, 110.9, 60.4, 55.8, 16.1

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