Silver-Promoted Regioselective [4+2] Annulation Reaction of Indoles with Alkenes to Construct Dihydropyrimidoindolone Scaffolds

Contents

Molecular structure and crystallographic data of 3af

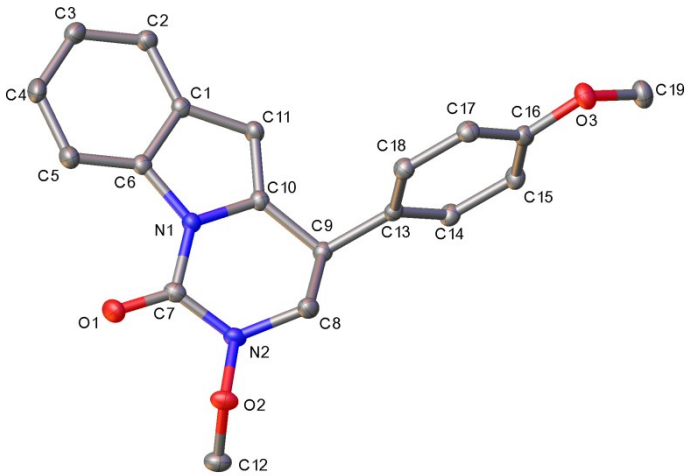


Figure S1. X-ray crystal structure of **3af**

Table S1. Crystal data and structure refinement for **3af**

Empirical formula	$C_{19}\ H_{18}\ N_2\ O_3$
CCDC number	1841255
Formula weight	322.35
Temperature	173.15 K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P 1 21/c 1
Unit cell dimensions	a = 11.350(3) Å α = 90°.
	b = 13.447(4) Å β = 108.139(4)°.
	c = 10.912(3) Å γ = 90°.
Volume	1582.6(8) $Å^3$
Z	4
Density (calculated)	1.353 Mg/m^3
Absorption coefficient	0.093 mm^{-1}
F(000)	680
Crystal size	0.455 x 0.408 x 0.264 mm^3
Theta range for data collection	1.888 to 27.468°

Index ranges	-14<=h<=13, -17<=k<=17, -13<=l<=14
Reflections collected	10516
Independent reflections	3590 [R(int) = 0.0385]
Completeness to theta = 25.242°	99.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.00000 and 0.77874
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3590 / 0 / 219
Goodness-of-fit on F^2	1.104
Final R indices [I>2sigma(I)]	R1 = 0.0474, wR2 = 0.1026
R indices (all data)	R1 = 0.0505, wR2 = 0.1050
Extinction coefficient	n/a
Largest diff. peak and hole	0.255 and -0.164 e.Å^{-3}

General methods

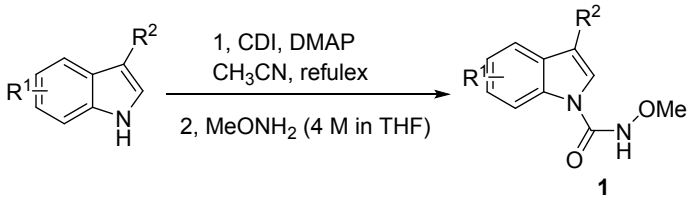
Unless noted, all commercial reagents and solvents were used without further purification. Melting points were recorded on a RY-1 microscopic melting apparatus and uncorrected. NMR spectra were recorded in $CDCl_3$ on 400 MHz or 500 MHz spectrometers. ^{1}H NMR chemical shifts (δ) are reported in parts per million relative to tetramethylsilane (0 ppm) or residual $CHCl_3$ (7.26 ppm). ^{13}C NMR chemical shifts are reported relative to the center line signal of the $CDCl_3$ triplet at 77.0 ppm. The following abbreviations are used for multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, and m = multiplet. Mass spectra were obtained on an Ultima Global spectrometer with an ESI source. The X-ray single-crystal diffraction was performed on Saturn 724+ instrument. Silica gel (200–300 mesh) for column chromatography and silica GF254 for TLC were produced by Qingdao Marine Chemical Company (China).

Preparation of the starting materials

Preparation of substrates 1

The *N*-methoxy-1*H*-indole-1-carboxamides **1** were prepared according to previously

described methods.[1]

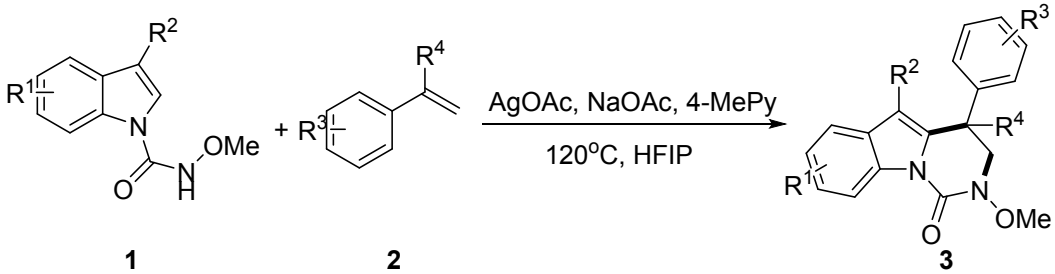


1

Preparation of $MeONH_2$ solution: To a 100 mL round bottle charged with a stirring bar was added $MeONH_2$·HCl (80.0 mmol) and 20 mL THF. To the system was then added sodium hydroxide (powder, 1.0 equiv). The system was then stirred at room temperature for about 3 h until the system became clear.

Preparation of *N*-methoxy-1*H*-indole-1-carboxamides: To a 100 mL round bottle charged with stirring bar, was added indole (5.0 mmol, 1.0 equiv), 1, 1'-carbonyldiimidazole (CDI, 7.5 mmol, 1.5 equiv) and 4-dimethylaminepyridine (DMAP, 5.0 mol%). Then 20 mL anhydrous acetonitrile was added to the bottle under the protection of nitrogen. The system was refluxed at 85 °C for 10 h. After cooled to room temperature, $MeONH_2$ solution (4 M in THF, 2 equiv) was added and then stirred at 80 °C for another 6 h (when most of indole was consumed as detected by TLC). After cooled to room temperature, the solvents were removed under reduced pressure. The residue was purified by silica chromatography to afford the corresponding *N*-methoxy-1*H*-indole-1-carboxamides **1a-1s.**

General procedure for the synthesis of compounds 3

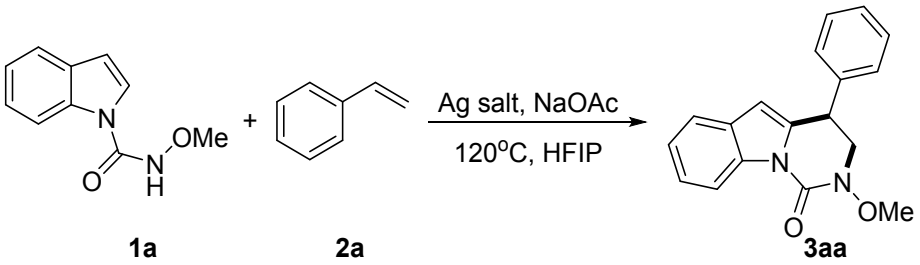


1 **2** **3**

To a solution of *N*-methoxy-1*H*-indole-1-carboxamides **1** (0.2 mmol), AgOAc (0.4 mmol, 2.0 equiv), NaOAc (0.4 mmol, 2.0 equiv), and 4-Methylpyridine (0.8 mmol, 4.0 equiv) in HFIP (2 mL) was added olefins **2** (0.4 mmol, 2.0 equiv). The reaction mixture was stirred at 120 °C for 4 h, and cooled to room temperature. The resulting mixture was diluted with 25 mL of CH_2Cl_2, and filtered through a celite pad. Evaporation of the solvent followed by purification on silica gel, provided products **3**.

Optimization of reaction conditions

Ag salt[a]

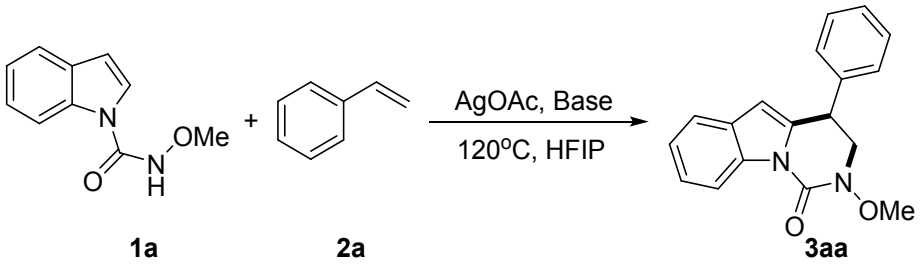


1a **2a** **3aa**

Entry	Ag salt	Yield[b]
1	**AgOAc**	**64%**
2	$AgNO_3$	60%
3	AgOPiv	59%
4	Ag_2CO_3	50%
5	Ag_2O	49%
6	AgTFA	22%
7	AgOTf	42%
8	$AgSbF_6$	38%
9	none	n.p

[a]Conditions: 0.2 mmol of **1a**, 0.4 mmol of **2a**, Ag salt (0.4 mmol, 2.0 equiv), NaOAc (0.4 mmol, 2.0 equiv), air, HFIP (2 mL), 120 °C, 4 h. [b]Isolated yields. n. p = no product.

Base[a]

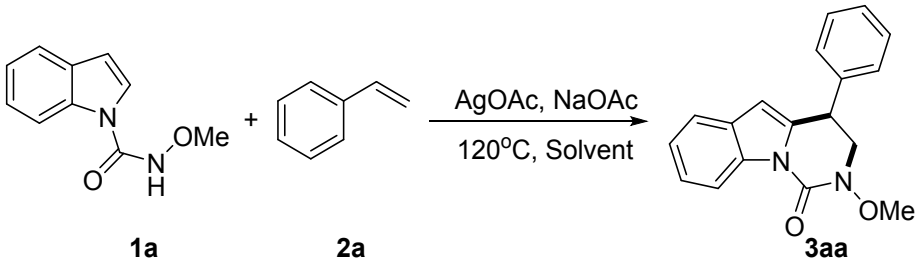


1a **2a** **3aa**

Entry	Base	Yield[b]
1	$NaOPiv{\cdot}H_2O$	35%
2	Na_2CO_3	41%
3	K_2CO_3	38%
4	Cs_2CO_3	36%
5	**NaOAc**	**64%**
6	KOAc	60%
7	CsOAc	43%
8	DIPEA	53%
9	DABCO	19%
10	TEA	25%

[a]Conditions: 0.2 mmol of **1a**, 0.4 mmol of **2a**, AgOAc (0.4 mmol, 2.0 equiv), Base (0.4 mmol, 2.0 equiv), air, HFIP (2 mL), 120 °C, 4 h. [b]Isolated yields.

Solvent[a]



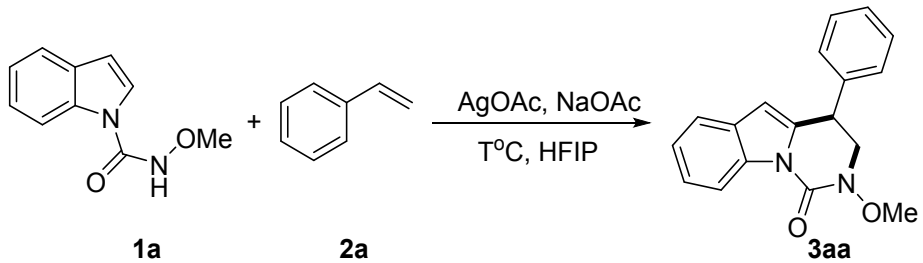
1a **2a** **3aa**

Entry	Solvent	Yield[b]
1	**HFIP**	**64%**
2	TFE	52%
3	MeOH	trace
4	DCE	trace
5	Dioxane	trace

[a]Conditions: 0.2 mmol of **1a**, 0.4 mmol of **2a**, AgOAc (0.4 mmol, 2.0 equiv), NaOAc

(0.4 mmol, 2.0 equiv), air, Solvent (2 mL), 120 °C, 4 h. [b]Isolated yields.

Temperature[a]

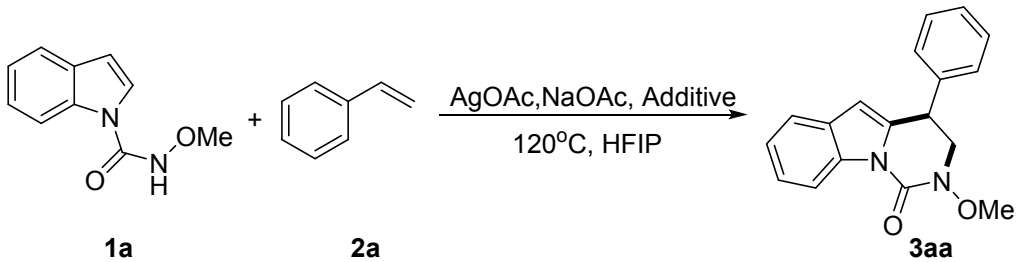


1a **2a** **3aa**

Entry	Temp/°C	Yield[b]
1	60	n.p
2	80	45%
3	100	48%
4	**120**	**64%**
5	140	32%

[a]Conditions: 0.2 mmol of **1a**, 0.4 mmol of **2a**, AgOAc (0.4 mmol, 2.0 equiv), NaOAc (0.4 mmol, 2.0 equiv), air, HFIP (2 mL), T °C, 4 h. [b]Isolated yields. n. p = no product.

Additive[a]



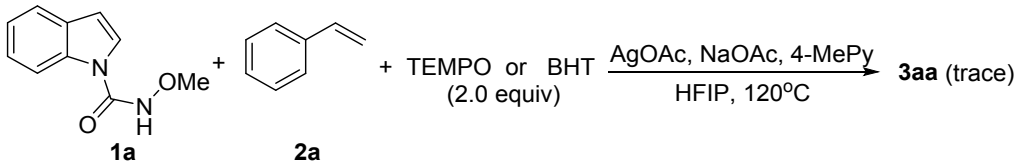
1a **2a** **3aa**

Entry	Additive	Yield[b]
1	Pyridine	78%
2	2-Chloropyridine	72%
3	**4-Methylpyridine**	**85%**
4	2,6-Dimethylpyridine	75%
5[c]	4-Methylpyridine	19%
6[d]	4-Methylpyridine	trace

[a]Conditions: 0.2 mmol of **1a**, 0.4 mmol of **2a**, AgOAc (0.4 mmol, 2.0 equiv), NaOAc (0.4 mmol, 2.0 equiv), Additive (0.8 mmol, 4.0 equiv), air, HFIP (2 mL), 120 °C, 4 h. [b]Isolated yields. [c]Condition: AgOAc (20 mol%), $K_2S_2O_8$ (2.0 equiv). [d]Condition: AgOAc (20 mol%), $PhI(OAc)_2$ (2.0 equiv).

Control experiments

TEMPO or BHT inhibiting experiment

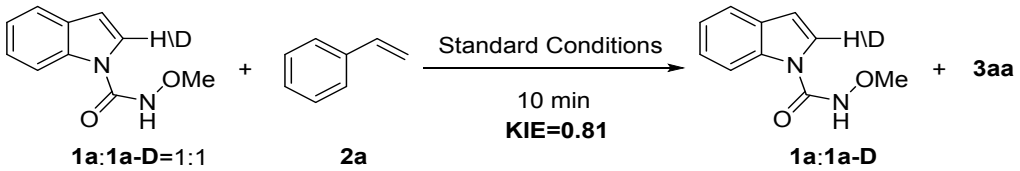


1a **2a**

The reaction was carried out according to the general procedure for the synthesis of compounds **3**, and 2 equivalent of TEMPO or BHT (0.4 mmol) was added into the reaction system. At the end of the reaction, the target product **3aa** was generated in a trace yield.

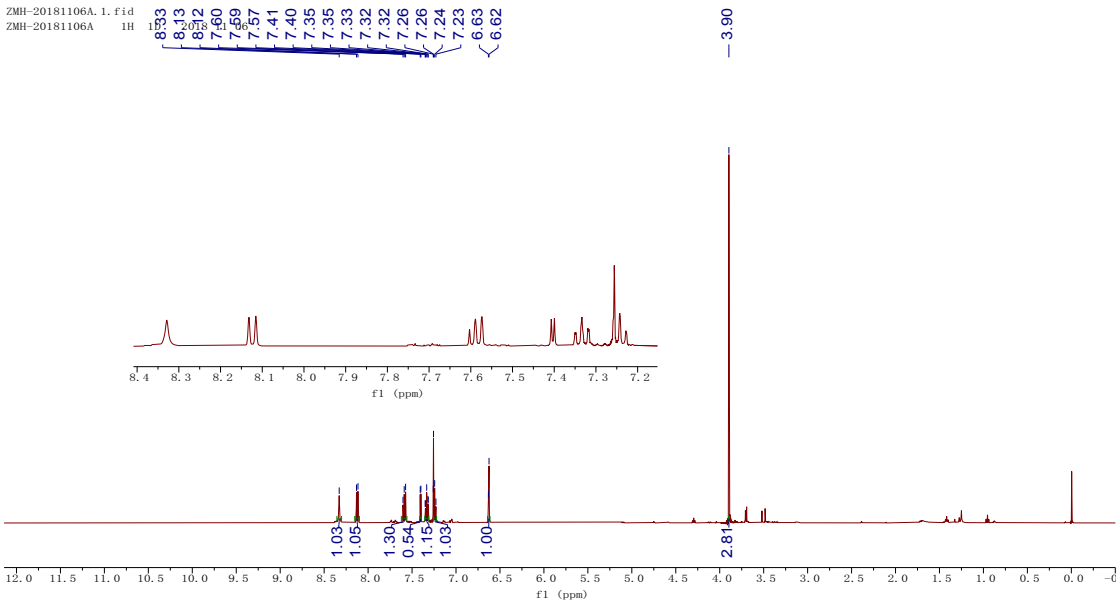
Kinetic Isotope Effect (KIE) Study

Intermolecular Kinetic Isotopic Effect

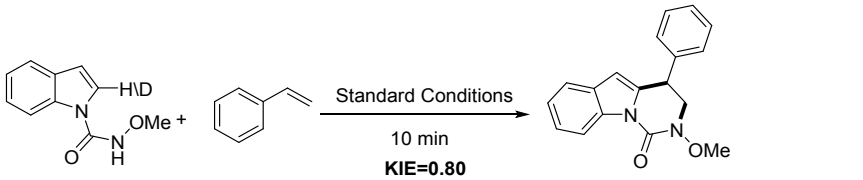


1a:**1a-D**=1:1 **2a** **1a**:**1a-D**

An equimolar mixture of **1a** (0.1 mmol) and **1a-D** (95% D, 0.1 mmol) were allowed to react with **2a** (0.1 mmol) in HFIP (2 mL) in the presence of AgOAc (0.4 mmol), NaOAc (0.4 mmol), and 4-Methylpyridine (0.8 mmol). The mixture was stirred at 120 °C. The reaction was stopped after 10 min, then the starting materials and the product were isolated by using column chromatography on silica gel. A mixture of the starting materials was analyzed by ^{1}H NMR spectroscopy. *A Kinetic isotopic effect of this reaction was determined to be* K_H/K_D *= 0.81 (0.46/0.54*0.95)*



Two parallel reactions for KIE value measurement



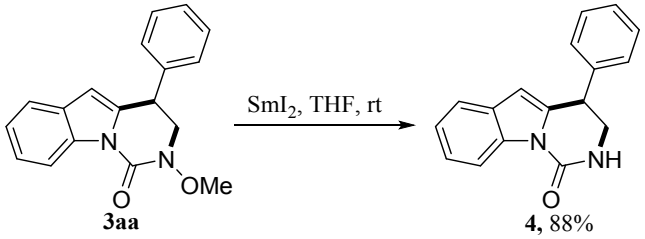
1a/1a-D **2a** **3aa, 41.4% yield starting from 1a**
3aa, 49.3% yield starting from [D]-1a

To a solution of *N*-methoxyl-1*H*-indole-1-carboxamide **1a** (0.1 mmol), AgOAc (0.2 mmol, 2.0 equiv), NaOAc (0.2 mmol, 2.0 equiv), and 4-Methylpyridine (0.4 mmol, 4.0 equiv), in HFIP (2 mL) was added styrene **2a** (0.2 mmol, 2.0 equiv). The reaction mixture was stirred at 120°C for 10 min, and cooled to room temperature. The resulting mixture was diluted with 25 mL of CH_2Cl_2, and filtered through a celite pad. Evaporation of the solvent followed by purification on silica gel, provided product **3aa** (41.4% 12.1 mg).

To a solution of *N-methoxy-1H-indole-2-d-1-carboxamide* **1a-D** (0.1 mmol), AgOAc (0.2 mmol, 2.0 equiv), NaOAc (0.2 mmol, 2.0 equiv), and 4-Methylpyridine (0.4 mmol, 4.0 equiv), in HFIP (2 mL) was added styrene **2a** (0.2 mmol, 2.0 equiv). The reaction mixture was stirred at 120 °C for 10 min, and cooled to room temperature. The resulting mixture was diluted with 25 mL of CH_2Cl_2, and filtered through a celite pad. Evaporation of the solvent followed by purification on silica gel, provided product **3aa** (49.3% 14.4 mg). *A kinetic isotopic effect of these two reactions was determined to be*

K_H/K_D = *0.80.*

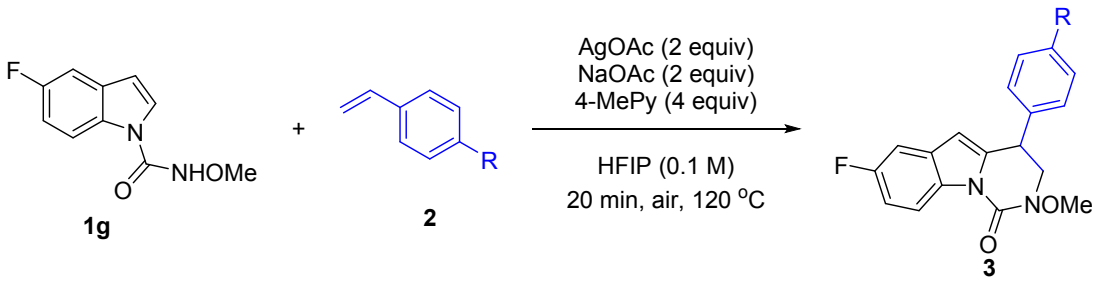
Transformation of product 3aa



In a flame-dried round-bottom flask, **3aa** (29 mg, 0.1 mmol, 1.0 equiv) was dissolved in dry THF (15 mL). SmI_2-solution (0.1 M in THF, 3 mL, 3.0 equiv) was added dropwise at room temperature. The reaction was stirred at room temperature for 3 hours under the protection of nitrogen. The solvent was removed under reduced pressure and the residue purified by flash column chromatography to afford the title compound **4** (23 mg) as a white solid in 88% yield.

Hammett-plot correlation study

To a solution of *N*-methoxy-1*H*-indole-1-carboxamides **1** (0.2 mmol), AgOAc (0.4 mmol, 2.0 equiv), NaOAc (0.4 mmol, 2.0 equiv), and 4-Methylpyridine (0.8 mmol, 4.0 equiv) in HFIP (2 mL) was added olefins **2** (0.4 mmol, 2.0 equiv). The reaction mixture was stirred at 120 °C for 20 min, and cooled to room temperature. Filtered through a celite pad, the solvents were removed under reduced pressure, then add $CDCl_3$ to the mixture to dissolve the solid. The resulting mixture was analyzed by ^{19}F NMR for determination of yield using Benzotrifluoride (0.2 mmol) as the internal standard.



R	σ	k_x/k_H	$\lg(k_x/k_H)$
***p*-OMe**	-0.268	0.31394	-0.50316
***p*-Me**	-0.170	0.51284	-0.29002

***p*-^{t}Bu**	-0.197	0.48783	-0.31173
H	0.000	1.00000	0.00000
***p*-F**	0.062	0.70957	-0.14900
***p*-Cl**	0.227	1.07411	0.03105
***p*-Br**	0.232	1.03943	0.01680

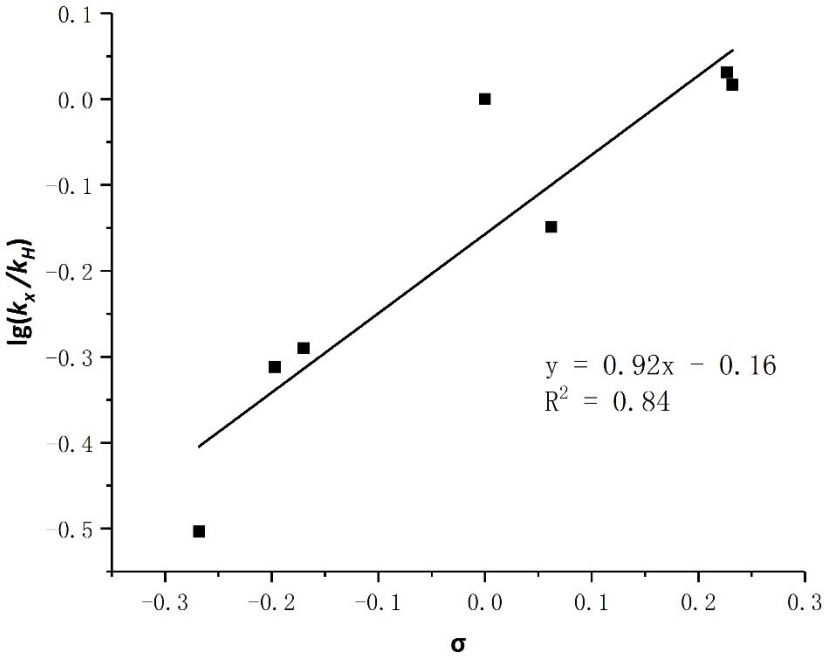


Figure S2. Hammett plot correlation of differently *para*-substituted styrene

To further explore the reaction mechanism, the reaction of different *p*-substituted styrene with substrate **1g** was studied. In the Hammett curve, lg(k_x/k_H) is linear with σ, and ρ = 0.92 indicates that the reaction is promoted by electron-withdrawing groups.[2]

DFT calculation

Computational Details

The ωB97X-D[i] functional was used for all calculations, which were carried out with the Gaussian 09 program[ii]. Two different basis sets were used. Basis set I was used for geometry optimizations and frequency calculations. The effective core potentials (ECPs) of Hay and Wadt with a double-ζ valence basis set (LANL2DZ) were employed for Ag,[iii,iv,v,vi] supplemented with polarization shells with the following exponents: Ag (f = 1.611);[vii,viii] and the all-electron 6-31G(d) basis set was used in describing all other atoms.[ix,x,xi] Geometric structures of all species in this work were optimized

as gas phase at T = 298.15 K and 1 atm pressure. The harmonic vibrational frequencies and the number of imaginary frequencies determine the nature of all intermediates (no imaginary frequency) and transition state structures (only one imaginary frequency). The latter were also confirmed to connect appropriate intermediates, reactants, or products by intrinsic reaction coordinate (IRC) calculations.[xii,xiii] The gas-phase Gibbs free energies, G, were calculated within the harmonic potential approximation at optimized structures. Based on the gas phase optimized geometries, the solvation effect of 2,2,2-trifluoroethanol was incorporated with the SMD solvent model at the level of ωB97X-D/6-311+G(d,p) theory. The solution phase Gibbs free energy is calculated by adding solvation energies on the gas phase relative Gibbs free energies. The same methodology has been widely used in many recent theoretical works.[xiv]

Calculation of Gibbs free energy of Ag(s)

The Gibbs free energy of solid Ag was calculated by taking into account available experimental data:

$Ag_{(s)} \rightarrow Ag_{(g)}$ Δ_rG = 0.08205 Eh from Ref 1[xv]

$Ag_{(g)}$ Δ_fG_g = -145.7410885 Eh from ωB97X-D

$Ag_{(s)}$ Δ_fG_s = -145.840398 Eh

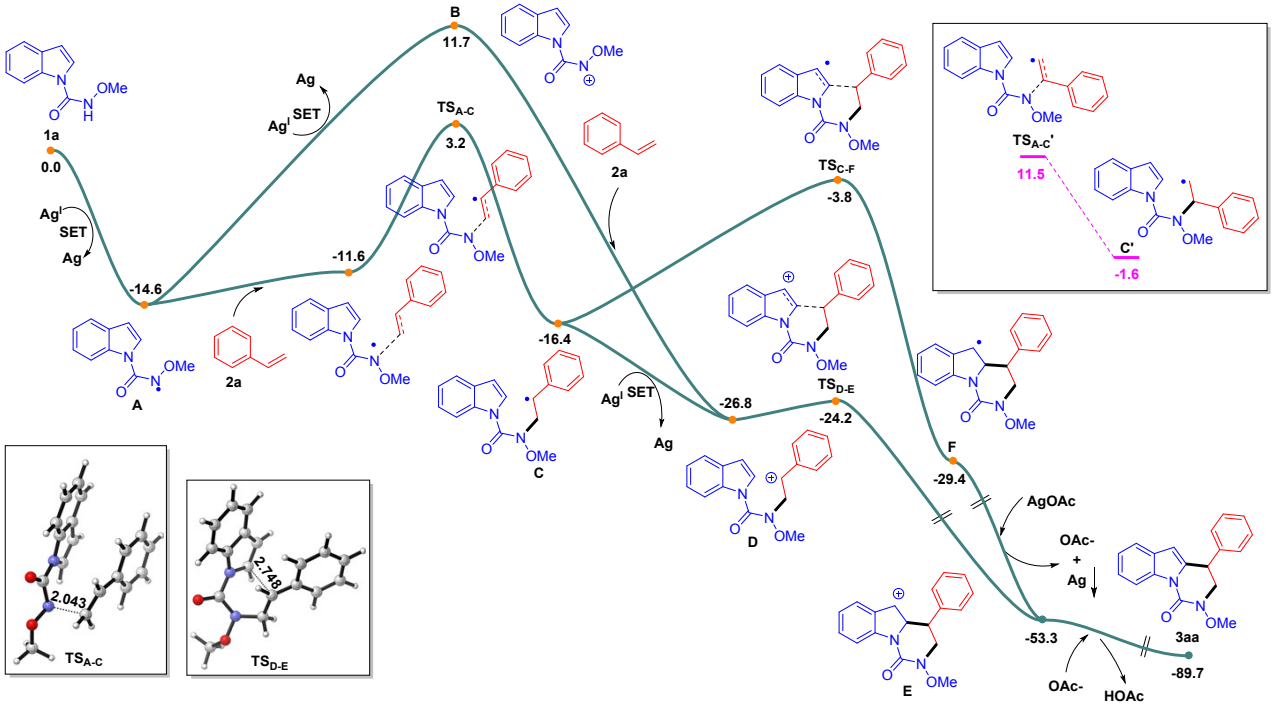


Figure S3. Computed free energy profile (in kcal mol^{-1}) of this reaction

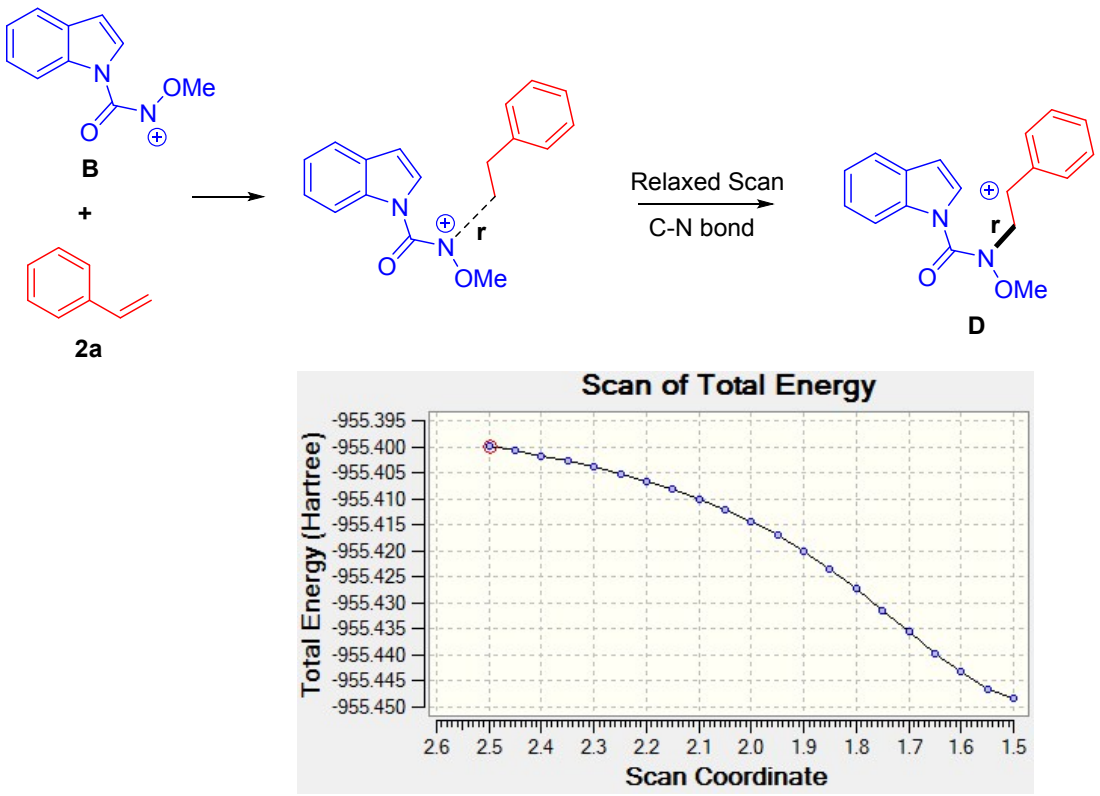


Figure S4. The relaxed scan of the cation transfer process with the formation of C-N bond.

Cartesian Coordinates of all the intermediate and transition states

1a

C	4.75000400	2.00088300	-0.12069200
C	4.91338800	0.67801300	0.32280500
C	3.87329000	-0.23871900	0.27982300
C	2.65188000	0.21114000	-0.22422500
C	2.46705500	1.53301000	-0.67602800
C	3.53422700	2.43715300	-0.62002800
N	1.43952800	-0.46534200	-0.41109200
C	0.51547100	0.43898100	-0.94857000
C	1.10039900	1.64727500	-1.12164900
C	1.22436400	-1.82066300	-0.13254800
O	1.94560400	-2.48021600	0.57665900
N	0.04337700	-2.30016600	-0.70762700
O	-0.07642700	-3.68379200	-0.65879100
C	-0.82594100	-4.06032800	0.48657600
H	5.58850700	2.68882100	-0.06869200
H	5.87580800	0.36313500	0.71480600
H	3.99190200	-1.25415300	0.63332600
H	3.40626600	3.45947700	-0.96357400

H	-0.51032700	0.14100600	-1.10600000
H	0.61633500	2.53566600	-1.50214200
H	-0.93426800	-5.14378300	0.40914800
H	-0.28672300	-3.80829500	1.40531100
H	-1.81194400	-3.58200100	0.48400100
H	-0.12204200	-2.01093100	-1.66485500

A

C	4.77142400	2.12924500	-0.31126600
C	5.06474700	0.82765200	0.12257700
C	4.08485700	-0.15348500	0.19795900
C	2.79188500	0.21093400	-0.17817700
C	2.47684500	1.51254800	-0.61676000
C	3.48235600	2.48091900	-0.68254000
N	1.60657400	-0.53681700	-0.21335400
C	0.57469300	0.29854100	-0.66974300
C	1.06437100	1.53284100	-0.92003400
C	1.49091800	-1.87567000	0.14553700
O	2.41644300	-2.55476700	0.53166300
N	0.15114900	-2.30846900	-0.00760100
O	0.10161800	-3.58583900	0.34542000
C	-1.23019800	-4.08511300	0.21813400
H	5.56487900	2.86913300	-0.35562000
H	6.08266800	0.57832200	0.40671900
H	4.30564600	-1.15803400	0.53202100
H	3.25498400	3.48840400	-1.01850000
H	-0.42279200	-0.09713200	-0.76926500
H	0.49490700	2.37697600	-1.28270000
H	-1.17639800	-5.13057800	0.52032800
H	-1.89908000	-3.52467000	0.87572000
H	-1.56072000	-3.99783800	-0.81971900

B

C	4.77637800	2.09203200	-0.31858200
C	5.04093700	0.83474500	0.21643800
C	4.04293600	-0.14037300	0.30938300
C	2.77946100	0.21749900	-0.16129900
C	2.49457900	1.48636400	-0.70443800

C	3.49516400	2.43469500	-0.78706900
N	1.59427700	-0.52673900	-0.20600000
C	0.56972200	0.28287000	-0.77507200
C	1.08634400	1.48654500	-1.07925800
C	1.51563700	-1.82356300	0.23802800
O	2.38815800	-2.49826500	0.72059400
N	0.16298800	-2.27555800	0.02272400
O	0.07108000	-3.46380800	0.39671300
C	-1.24964300	-4.07255900	0.23974300
H	5.57308500	2.82605200	-0.37534400
H	6.03870100	0.60143900	0.57095400
H	4.24201900	-1.11786500	0.72655900
H	3.30464500	3.41847700	-1.20242600
H	-0.42615300	-0.10803000	-0.89844200
H	0.54236400	2.30745000	-1.52504900
H	-1.10311700	-4.89122800	-0.46596700
H	-1.50053900	-4.45448500	1.22938600
H	-1.94724700	-3.31859400	-0.12078000

C

C	-3.28518300	-1.83101400	-0.01559300
C	-2.33644700	-2.38266800	0.85835100
C	-0.97535400	-2.16520100	0.68624500
C	-0.59183400	-1.36831100	-0.39235300
C	-1.52944500	-0.80431800	-1.27981700
C	-2.89156700	-1.04306400	-1.08655600
N	0.67794500	-0.95247200	-0.81168100
C	0.51999600	-0.13597600	-1.94222200
C	-0.79090500	-0.03301400	-2.25086700
C	1.86839600	-1.22334000	-0.14969200
O	1.95043100	-1.91761300	0.84036400
N	2.94781100	-0.57767200	-0.79940400
O	4.03953300	-0.80368200	-0.07987100
C	5.16685900	-0.16818100	-0.68162100
H	-4.34072100	-2.02409200	0.15170500
H	-2.67043000	-2.99902500	1.68783600
H	-0.23944900	-2.58964100	1.35542500
H	-3.62560200	-0.60878900	-1.75864600
H	1.38911000	0.29692200	-2.40914800
H	-1.20543000	0.53798500	-3.06930000
H	6.00993100	-0.39730100	-0.03023400

H	5.33023100	-0.57418800	-1.68294700
H	4.99877400	0.91034100	-0.73402800
C	-2.95088800	2.57173800	0.13969400
C	-2.90348200	1.61390800	1.14823600
C	-1.67743600	1.17246900	1.63098700
C	-0.47626300	1.68004600	1.12236300
C	-0.53880500	2.63666000	0.10212600
C	-1.76301100	3.08064100	-0.38177900
H	-3.90672900	2.91435700	-0.24611900
H	-3.82115700	1.19499800	1.54951700
H	-1.64650600	0.40730100	2.40148700
H	0.37841000	3.01756600	-0.33744000
H	-1.79083100	3.81989300	-1.17725300
C	0.79891700	1.16181700	1.64987700
C	2.00982000	1.70158600	1.49290300
H	0.71935900	0.23006600	2.20878800
H	2.88851800	1.21562400	1.90524800
H	2.16962200	2.63749400	0.96357400

TSC-D

C	-3.31989600	-2.26244400	0.10368600
C	-2.30448100	-2.80171300	0.91099900
C	-0.97090500	-2.46701400	0.71969700
C	-0.68283100	-1.56210200	-0.30277800
C	-1.68618400	-1.00865900	-1.12317400
C	-3.02068400	-1.37252900	-0.91568200
N	0.53104300	-0.98301800	-0.68423100
C	0.27832400	-0.08658400	-1.72721200
C	-1.04186500	-0.08603700	-2.02417400
C	1.75991300	-1.20376500	-0.05829600
O	1.98155400	-2.16258000	0.64520700
N	2.65520500	-0.14649500	-0.34734400
O	3.90505200	-0.56810900	0.01987800
C	4.86993000	0.30160600	-0.54239700
H	-4.35178900	-2.55110100	0.28089200
H	-2.56560200	-3.50398300	1.69704000
H	-0.18055200	-2.89025200	1.32598100
H	-3.80659000	-0.95130500	-1.53599300
H	1.09885300	0.46644300	-2.15474200
H	-1.51952700	0.51238700	-2.78660900
H	5.83743300	-0.14985200	-0.31770500

H	4.73098100	0.38684900	-1.62481000
H	4.81413100	1.29835300	-0.08732100
C	-2.59586100	2.92237100	-0.11228600
C	-2.72048700	1.83854000	0.75356200
C	-1.58813300	1.24852800	1.29671600
C	-0.30176800	1.72119800	0.97922200
C	-0.19539400	2.82469500	0.11031800
C	-1.32803500	3.41621400	-0.42560300
H	-3.48065100	3.38357200	-0.54087300
H	-3.70035400	1.43662500	0.99127000
H	-1.68997800	0.38250600	1.94531100
H	0.78240300	3.22075100	-0.14667700
H	-1.22686300	4.26481600	-1.09585600
C	0.84892500	1.03781700	1.53024800
C	2.16870000	1.18360400	1.12605400
H	0.63375200	0.25103700	2.25118100
H	2.94223500	0.75508200	1.75528100
H	2.46618500	2.04639700	0.53937600

D

C	1.81166100	3.37744500	1.51056000
C	2.55287900	2.56648900	0.63316300
C	2.27480200	1.21768700	0.48186800
C	1.22180300	0.70068300	1.23607200
C	0.46267800	1.49329800	2.11937700
C	0.77110900	2.85246500	2.25831100
N	0.65917600	-0.57768400	1.23794700
C	-0.41145800	-0.58507800	2.13205600
C	-0.55608100	0.64425600	2.68613900
C	1.06810900	-1.63404300	0.40755600
O	2.21625500	-1.79806400	0.07638600
N	-0.00218800	-2.48441200	0.06997100
O	0.45116700	-3.55367600	-0.71452500
C	0.79551100	-4.64408200	0.12005000
H	2.06260500	4.42989200	1.60340400
H	3.36422500	3.00571600	0.06088200
H	2.84437000	0.58638400	-0.18826900
H	0.19707500	3.48073800	2.93330100
H	-0.94521300	-1.50628600	2.31265900
H	-1.28841000	0.92072300	3.43151200
H	1.07175700	-5.44964500	-0.56308200

H	1.65331300	-4.39840100	0.75616400
H	-0.05529000	-4.95090500	0.74008100
C	-0.16104100	3.02238600	-2.37701700
C	0.20406500	2.12300400	-3.38343200
C	-0.00436000	0.76650700	-3.21588800
C	-0.58804200	0.24896000	-2.02703900
C	-0.96879300	1.18710700	-1.03052400
C	-0.74902900	2.54233600	-1.20520000
H	0.01458600	4.08601200	-2.50441900
H	0.66136000	2.48876400	-4.29820000
H	0.29497700	0.07006500	-3.99480000
H	-1.41638300	0.84775400	-0.10170000
H	-1.01928200	3.23130200	-0.41103300
C	-0.74009500	-1.15236600	-1.88827700
C	-1.15386500	-1.86755500	-0.64263500
H	-0.39744300	-1.78283800	-2.70448800
H	-1.81797600	-2.70566400	-0.86690700
H	-1.67157500	-1.21529900	0.06098500

E

C	-1.22997500	2.12923700	1.71642100
C	-0.25674800	1.85876100	0.73636300
C	0.22909900	0.57582200	0.52929600
C	-0.30767100	-0.43477200	1.32589200
C	-1.28188600	-0.18965900	2.31491800
C	-1.74018200	1.11850700	2.51553200
N	-0.09157900	-1.82086000	1.29537400
C	-0.89135300	-2.41409900	2.28177000
C	-1.61586800	-1.46021800	2.91473400
C	0.68576500	-2.46589700	0.33516900
O	1.67476400	-1.99754500	-0.16176400
N	0.16040400	-3.75195800	-0.00176800
O	0.97203600	-4.40004800	-0.93142600
C	1.91425200	-5.23838100	-0.25945900
H	-1.56619700	3.15084000	1.86286300
H	0.14667100	2.67761300	0.14875400
H	1.00339100	0.36861200	-0.19913200
H	-2.47791700	1.33353100	3.28235200
H	-0.80990300	-3.47497900	2.46959900
H	-2.28832300	-1.62552000	3.74474200
H	2.45537800	-5.74198200	-1.06076900

H	2.60920300	-4.63716200	0.33379100
H	1.39965500	-5.96918600	0.37166700
C	-2.70835800	1.09191800	-1.58148600
C	-1.88723200	0.66170900	-2.63729000
C	-1.45304400	-0.64036100	-2.66042000
C	-1.81109500	-1.54162300	-1.60155700
C	-2.65688600	-1.06905500	-0.54323300
C	-3.11353400	0.22690800	-0.55615800
H	-3.04348900	2.12465200	-1.56061200
H	-1.59913300	1.35545800	-3.41860300
H	-0.81434000	-0.99783700	-3.46265900
H	-2.92985800	-1.72624900	0.27513000
H	-3.74172700	0.59415200	0.24585800
C	-1.25961100	-2.80652000	-1.61338800
C	-1.23071800	-3.79662100	-0.49642600
H	-0.62847000	-3.07813700	-2.45940500
H	-1.40083100	-4.81250900	-0.85519600
H	-1.92292100	-3.57688600	0.31425500

TSE-F

C	0.83389800	3.01271200	0.35446700
C	1.86350800	2.18355000	-0.13338200
C	1.82545900	0.80707500	0.01854800
C	0.71464600	0.27956200	0.68190000
C	-0.33573000	1.08819900	1.17078800
C	-0.26318400	2.48092000	1.00667600
N	0.36027000	-1.04920900	0.92012200
C	-0.88673300	-1.06328800	1.56558700
C	-1.31757300	0.21210400	1.74822500
C	1.02476200	-2.15929300	0.36291400
O	2.21871000	-2.22696100	0.24266600
N	0.13455900	-3.18445600	0.00852800
O	0.76830400	-4.30164500	-0.52037900
C	1.17004600	-5.19530600	0.51936600
H	0.91426900	4.08670500	0.22263600
H	2.71737300	2.63548600	-0.62750800
H	2.62988300	0.16986000	-0.32840300
H	-1.04966900	3.12315100	1.39064200
H	-1.29318900	-1.99746800	1.92577500
H	-2.22236800	0.50375500	2.26294000
H	1.58572800	-6.05641300	-0.00415700

H	1.94174500	-4.73847800	1.14494400
H	0.30960300	-5.49802400	1.12466800
C	-4.83577600	0.59754100	-1.78167700
C	-3.59657100	1.21736500	-1.96487100
C	-2.44228100	0.49335100	-1.74601000
C	-2.51909900	-0.86885700	-1.32644700
C	-3.79705100	-1.47143900	-1.12982100
C	-4.93798500	-0.74264100	-1.36813400
H	-5.74514500	1.16385200	-1.95954700
H	-3.54465900	2.25379500	-2.27814700
H	-1.46737000	0.95493400	-1.87524400
H	-3.87268900	-2.50081100	-0.79619900
H	-5.91494800	-1.19229300	-1.23144900
C	-1.31624000	-1.52858700	-1.10909500
C	-1.09846000	-2.94476600	-0.73370800
H	-0.41873700	-0.96435700	-1.35680800
H	-0.99003400	-3.48506500	-1.69064100
H	-1.95554300	-3.38290600	-0.21444500

F

C	1.80915100	3.03241800	1.35882600
C	2.76924000	1.96444300	1.28182800
C	2.44513500	0.65898700	1.00989900
C	1.07779600	0.38624900	0.79638100
C	0.08645300	1.44917000	0.85605200
C	0.48855400	2.79526400	1.15332100
N	0.45570800	-0.77008500	0.50757600
C	-0.97689000	-0.55454800	0.36319700
C	-1.12659100	0.90323400	0.57165500
C	1.10772700	-1.99478900	0.13249200
O	2.27599900	-2.17877700	0.37486000
N	0.25507500	-2.86471500	-0.46433200
O	0.82205200	-4.02556500	-0.93330400
C	0.91519700	-5.01507000	0.09842000
H	2.16194300	4.03220300	1.58516300
H	3.81320000	2.20873400	1.45437600
H	3.18263100	-0.12991300	0.96487100
H	-0.25522700	3.58246600	1.20731700
H	-1.49949500	-1.07583000	1.18154300
H	-2.08570200	1.40550200	0.52313500
H	1.29468400	-5.90288200	-0.40709400

H	1.61978400	-4.69690400	0.87107900
H	-0.07024300	-5.22167600	0.52897600
C	-5.61856300	-0.37299200	-1.72863600
C	-4.65080100	0.09199600	-2.61421800
C	-3.30352700	-0.15838100	-2.36880900
C	-2.91252800	-0.88170300	-1.24070900
C	-3.89098300	-1.34642300	-0.35608000
C	-5.23695100	-1.09250300	-0.59854300
H	-6.66902800	-0.17879600	-1.91894700
H	-4.94255600	0.64819400	-3.49918200
H	-2.55290800	0.20410300	-3.06678000
H	-3.61480700	-1.91863500	0.52750600
H	-5.98771900	-1.45937900	0.09380500
C	-1.44309800	-1.13592200	-0.98683400
C	-1.09188100	-2.62795500	-0.97424500
H	-0.85073700	-0.64257900	-1.76625800
H	-1.12668200	-3.02994600	-1.98952100
H	-1.81168400	-3.18534000	-0.36346700

TSD-G

C	4.09787000	2.51021500	1.28387600
C	4.61771400	1.21668700	1.10708700
C	3.78853500	0.10721800	0.99589100
C	2.41586100	0.33186900	1.06518900
C	1.86786200	1.62578700	1.22953300
C	2.73163800	2.72572600	1.34682300
N	1.34859200	-0.56863600	0.97129100
C	0.14400300	0.16409500	0.99293000
C	0.44531400	1.49382900	1.23969400
C	1.45669700	-1.87510700	0.49159600
O	2.44785200	-2.55628400	0.63799500
N	0.25789900	-2.32671100	-0.06595800
O	0.33831600	-3.65953200	-0.46893500
C	0.00740300	-4.51529500	0.61177300
H	4.78077500	3.34987600	1.37182200
H	5.69347800	1.07668300	1.06232000
H	4.18109000	-0.89406000	0.87370300
H	2.32882300	3.72528200	1.48112500
H	-0.77294800	-0.35013400	1.24894600
H	-0.28301900	2.28042700	1.37586000
H	0.00269600	-5.52049400	0.18595900

H	0.76201400	-4.45700600	1.40299600
H	-0.98288100	-4.27387200	1.01565900
C	-3.29440600	2.75984400	-2.04536900
C	-1.93978900	3.08141200	-2.13590300
C	-0.97468800	2.12630700	-1.85582700
C	-1.32982400	0.81384700	-1.48003800
C	-2.70203900	0.51153400	-1.38459900
C	-3.66617000	1.47108800	-1.66705600
H	-4.05125700	3.50622600	-2.26579300
H	-1.63668500	4.08319300	-2.42659100
H	0.07919900	2.38495500	-1.92030600
H	-3.02612500	-0.47975200	-1.08218500
H	-4.71796800	1.21190400	-1.58710000
C	-0.27305800	-0.11155800	-1.12986100
C	-0.47304000	-1.59791700	-1.12399500
H	0.72952600	0.21268800	-1.40507900
H	-0.13176600	-2.01789800	-2.08072000
H	-1.52553700	-1.86746300	-1.01074500

G

C	4.24252800	2.36692900	1.80708700
C	4.66309500	1.02947000	1.78357600
C	3.79118600	-0.00898700	1.43593300
C	2.49072100	0.33212400	1.10926800
C	2.03543800	1.68527900	1.11992400
C	2.93945600	2.70708800	1.48064700
N	1.42136200	-0.48339800	0.72292300
C	0.22118900	0.31876500	0.46766900
C	0.69085700	1.71388800	0.73486900
C	1.51899200	-1.80161900	0.32163700
O	2.49126300	-2.50532700	0.51716200
N	0.32702700	-2.26937000	-0.23322600
O	0.41819400	-3.56287700	-0.73228900
C	0.12663300	-4.50311000	0.28984600
H	4.94809900	3.14359100	2.08610000
H	5.68988100	0.78896600	2.04162300
H	4.10923200	-1.04267400	1.41542500
H	2.60995400	3.74161700	1.49690600
H	-0.57851500	0.01780900	1.16510100
H	0.04939200	2.58033400	0.64780200
H	0.14270600	-5.47597300	-0.20554100

H	0.89143600	-4.47465100	1.07157500
H	-0.86439500	-4.31940600	0.72202600
C	-3.56572200	2.55796100	-2.09344600
C	-2.33879300	2.67682800	-2.73944200
C	-1.27757300	1.85022100	-2.38066000
C	-1.42504300	0.89104200	-1.37705600
C	-2.66107500	0.78399800	-0.73155600
C	-3.72336100	1.60935300	-1.08601700
H	-4.39447200	3.20164800	-2.37248800
H	-2.20522500	3.41521000	-3.52450500
H	-0.31969900	1.95191600	-2.88435100
H	-2.79999800	0.05115100	0.05984600
H	-4.67622600	1.51070300	-0.57459400
C	-0.25110800	0.02836700	-0.97248900
C	-0.55206200	-1.47180700	-1.08653800
H	0.60045600	0.26691000	-1.62054300
H	-0.42154600	-1.80375500	-2.12214700
H	-1.58732500	-1.68423900	-0.79904700

3aa

C	7.11528700	-1.07965600	-0.42072700
C	6.55413300	-2.01248900	0.46625900
C	5.23906600	-2.43788900	0.34031500
C	4.49548800	-1.89726600	-0.70905800
C	5.03900000	-0.95951000	-1.61037900
C	6.36782600	-0.54822300	-1.45906800
N	3.16471800	-2.10591500	-1.08904200
C	2.89431700	-1.31635400	-2.21667700
C	4.00401000	-0.61388300	-2.55190600
C	2.25399300	-2.95983500	-0.44808200
O	2.56557600	-3.69872000	0.46211000
N	0.98637800	-2.87086000	-0.97708200
O	0.01023100	-3.61682400	-0.35422200
C	-0.38916600	-3.04522700	0.89065400
H	8.14902200	-0.77430200	-0.28892100
H	7.16274900	-2.41527200	1.27032500
H	4.80292500	-3.16097600	1.01594000
H	6.80030800	0.17323600	-2.14620500
H	4.07959700	0.08098400	-3.37658200
H	-1.16108800	-3.71663300	1.26961300
H	0.45078600	-3.01330700	1.58949000

H	-0.81473400	-2.04375900	0.74980100
C	0.26124400	2.04633900	-5.07234700
C	0.15335100	0.77658400	-5.63094500
C	0.58544100	-0.33840000	-4.91670900
C	1.13069500	-0.19913200	-3.64038600
C	1.23471900	1.08046600	-3.08695000
C	0.80404500	2.19546400	-3.79784600
H	-0.07285300	2.91747600	-5.62786000
H	-0.26649700	0.65084300	-6.62446900
H	0.49913300	-1.32815700	-5.35864600
H	1.67356000	1.20386100	-2.10049700
H	0.89582800	3.18320500	-3.35599900
C	1.54039400	-1.42556100	-2.85151000
C	0.51759000	-1.73538700	-1.75042900
H	1.54906500	-2.29165500	-3.52757400
H	-0.44025500	-2.01993300	-2.19030000
H	0.36193700	-0.84642600	-1.12081200

TSC-D’

C	5.37682200	-0.37838400	0.82126800
C	4.76252600	0.86723200	1.03105200
C	3.48696600	1.13743000	0.55698500
C	2.83674800	0.11472900	-0.13569700
C	3.43354700	-1.14398400	-0.35504700
C	4.72358200	-1.38658500	0.13076100
N	1.55594800	0.07132200	-0.69393500
C	1.37271500	-1.18921400	-1.26939600
C	2.48170900	-1.94529800	-1.08554400
C	0.60603200	1.10107200	-0.61965000
O	0.90325200	2.25069600	-0.39682100
N	-0.69027000	0.58610400	-0.83332500
O	-1.56485200	1.63624000	-0.88347500
C	-2.53418600	1.39934200	-1.89691900
H	6.37783600	-0.54993600	1.20565000
H	5.29953000	1.64165500	1.57061300
H	3.01516100	2.10101400	0.69744000
H	5.19940800	-2.34963400	-0.02999000
H	0.44877600	-1.40230200	-1.78446800
H	2.62600600	-2.95537600	-1.44254100
H	-3.26947100	2.19784700	-1.78403100
H	-2.06689200	1.45464300	-2.88616800

H	-3.01782500	0.42751700	-1.76553000
C	-5.33825900	-0.75426900	0.41111300
C	-4.50846300	-1.79435400	-0.00146600
C	-3.13036000	-1.68278800	0.14692400
C	-2.56192500	-0.53838900	0.71459200
C	-3.40366100	0.49896400	1.12886000
C	-4.78162300	0.39086500	0.97619500
H	-6.41437000	-0.83632900	0.29162500
H	-4.93461800	-2.69077000	-0.44176700
H	-2.48231200	-2.48951400	-0.18657000
H	-2.97976400	1.40789600	1.54260700
H	-5.42372700	1.20647800	1.29519200
C	-1.08694300	-0.44037300	0.81466900
C	-0.46764900	0.25388700	1.85940000
H	-0.55845400	-1.32167000	0.45913900
H	0.59317700	0.12649600	2.04871800
H	-0.98963800	1.00881500	2.43672300

D’

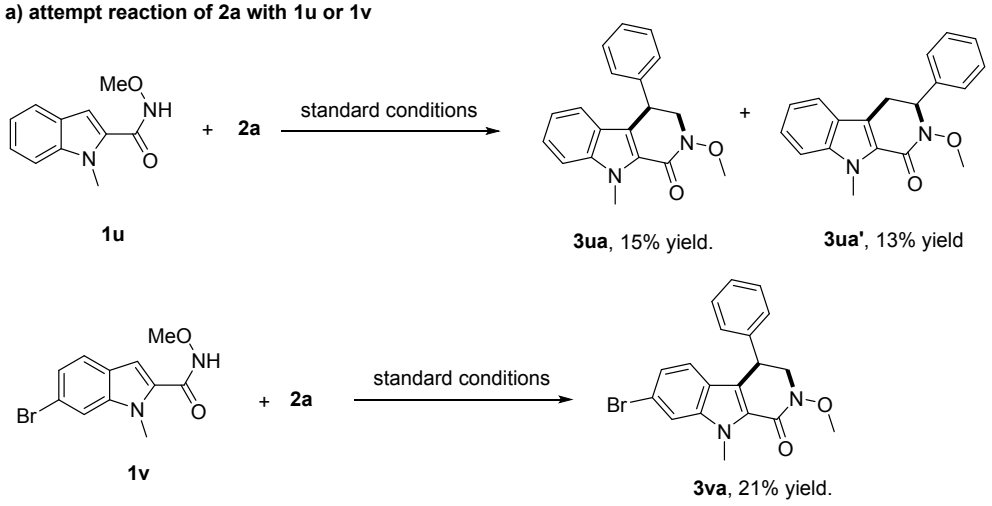
C	5.37531400	-0.20558300	0.80102800
C	4.92907700	0.70269400	-0.17393500
C	3.59753100	0.76133500	-0.55698200
C	2.71717300	-0.11992000	0.07131400
C	3.14170600	-1.03737800	1.05311900
C	4.49303900	-1.07750300	1.41732400
N	1.33530800	-0.27506700	-0.07350100
C	0.91824800	-1.30109000	0.78100600
C	1.97824500	-1.77851800	1.47607000
C	0.52852600	0.45061900	-0.96137200
O	0.94924200	0.93941100	-1.98220300
N	-0.81724000	0.46787300	-0.55363600
O	-1.62885900	1.02419800	-1.54380300
C	-2.23811200	-0.01534400	-2.29115400
H	6.42733800	-0.22438300	1.06935200
H	5.64331100	1.37147800	-0.64471500
H	3.25250100	1.44558000	-1.32153000
H	4.83873000	-1.78069800	2.16937700
H	-0.11573600	-1.61242400	0.77103400
H	1.95210300	-2.58499400	2.19530500
H	-2.88374800	0.49243300	-3.01059400
H	-1.48624000	-0.60439600	-2.82865400

H	-2.83503600	-0.66500900	-1.64164900
C	-4.90872300	-0.51333600	2.14815800
C	-3.70858900	-0.97412600	2.68153200
C	-2.50033600	-0.44528800	2.23437800
C	-2.47878300	0.54613000	1.25328900
C	-3.68736300	1.01210500	0.73041000
C	-4.89496300	0.48139200	1.17233800
H	-5.85210600	-0.92378800	2.49589400
H	-3.71142800	-1.74258700	3.44872800
H	-1.56429200	-0.80369500	2.65744700
H	-3.67104900	1.78902900	-0.02768000
H	-5.82875300	0.84924800	0.75713300
C	-1.15151100	1.09138300	0.74843700
C	-1.10399800	2.58276000	0.66687800
H	-0.37550300	0.74564700	1.44497200
H	-0.68479200	3.07702500	-0.20137300
H	-1.43508600	3.17190100	1.51461400

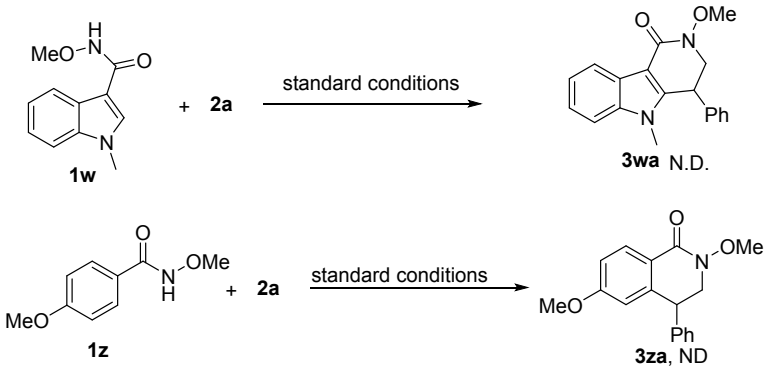
Scope for other electron-rich aromatic27

In addition to indole, we also tested some other electron rich aromatic ring substrates. At first, we tried to react **2a** with **1u**, regioisomer mixtures **3ua** and **3ua'** were obtained with the yield of 15% and 13%, respectively. Next, we tried to react **2a** with **1v**, the corresponding product **3va** was furnished with a yield of 21%. However, the directing group was installed at 3-position of indole or the arene ring (**1w** or **1z**), the reaction was totally inhibited and the corresponding product was not detected. Moreover, the substrate was decomposed during the transformation.

a) attempt reaction of 2a with 1u or 1v

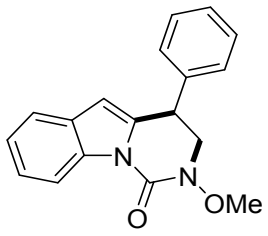


b) attempt reaction of 2a with 1w or 1z



Characterization of products

2-methoxy-4-phenyl-3, 4-dihydropyrimido[1,6-*a*]indol-1(2*H*)-one (3aa)



3aa

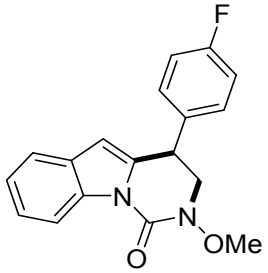
3aa was obtained in 85% (49.2 mg) as a white solid after column chromatography (eluent: petroleum ether/ethyl acetate = 8/1 v/v). Mp: 156-158 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.45 (d, J = 8.3 Hz, 1H), 7.46-7.29 (m, 7H), 7.22 (t, J = 7.5 Hz, 1H), 6.07 (s, 1H), 4.57 (dd, J = 9.8, 5.4 Hz, 1H), 3.98-3.85 (m, 2H), 3.85 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 152.5, 138.3, 137.2, 135.5, 129.5, 128.2, 128.0, 124.3, 123.1, 120.2, 115.5, 105.2, 62.7, 54.6, 40.9.

HRMS (ESI-TOF, $[M + Na]^+$): For $C_{18}H_{16}N_2NaO_2$, 315.1109, Found: 315.1113.

4-(4-fluorophenyl)-2-methoxy-3,4-dihydropyrimido[1,6-*a*]indol-1(2*H*)-one (3ab)



3ab

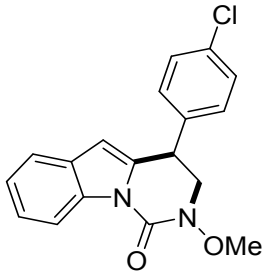
3ab was obtained in 55% yield (34.1 mg) as a white solid after column chromatography (eluent: petroleum ether/ethyl acetate = 8/1 v/v). Mp: 178-180 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.44 (d, J = 8.3 Hz, 1H), 7.44 (d, J = 7.7 Hz, 1H), 7.36-7.28 (m, 3H), 7.23 (t, J = 7.5 Hz, 1H), 7.09 (t, J = 8.6 Hz, 2H), 6.06 (s, 1H), 4.57 (dd, J = 9.4, 4.9 Hz, 1H), 3.92 (dd, J = 10.8, 5.4 Hz, 1H), 3.85 (s, 3H), 3.82 (d, J = 10.5 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 162.3 (d, J = 246.9 Hz), 152.4, 137.0, 135.5, 134.1, 129.9 (d, J = 5.0 Hz), 124.4, 123.2, 120.3, 116.0, 115.9 (d, J = 21.3 Hz), 105.2, 62.8, 54.7, 40.2.

HRMS (ESI-TOF, $[M + H]^+$): For $C_{18}H_{16}FN_2O_2$, 311.1196, Found: 311.1197.

4-(4-chlorophenyl)-2-methoxy-3,4-dihydropyrimido[1,6-*a*]indol-1(2*H*)-one (3ac)



3ac

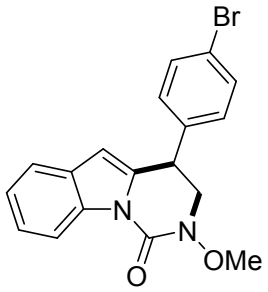
3ac was obtained in 70% (45.5 mg) as a white solid after column chromatography (eluent: petroleum ether/ethyl acetate = 8/1 v/v). Mp: 195-197 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.44 (d, J = 8.3 Hz, 1H), 7.44 (d, J = 7.7 Hz, 1H), 7.39-7.30 (m, 3H), 7.25 (m, 3H), 6.06 (s, 1H), 4.55 (dd, J = 9.5, 5.3 Hz, 1H), 3.92 (dd, J = 10.8, 5.3 Hz, 1H), 3.85 (s, 3H), 3.81 (d, J = 10.4 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 152.4, 136.9, 136.6, 135.5, 133.9, 129.6, 129.4, 129.1, 124.4, 123.3, 120.3, 115.5, 105.3, 62.8, 54.5, 40.3.

HRMS (ESI-TOF, $[M + H]^+$): For $C_{18}H_{16}ClN_2O_2$, 327.0900, Found: 327.0903.

4-(4-bromophenyl)-2-methoxy-3,4-dihydropyrimido[1,6-*a*]indol-1(2*H*)-one (3ad)



3ad

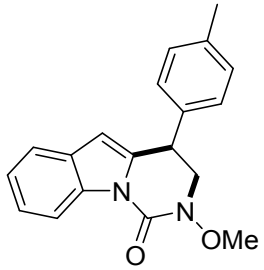
3ad was obtained in 78% (57.9 mg) as a white solid after column chromatography (eluent: petroleum ether/ethyl acetate = 8/1 v/v). Mp: 201-203 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.43 (d, J = 8.2 Hz, 1H), 7.52 (d, J = 8.2 Hz, 2H), 7.44 (d, J = 7.7 Hz, 1H), 7.33 (t, J = 7.7 Hz, 1H), 7.22 (m, 3H), 6.06 (s, 1H), 4.54 (dd, J = 9.3, 5.3 Hz, 1H), 3.92 (dd, J = 10.7, 5.3 Hz, 1H), 3.84 (s, 3H), 3.81 (d, J = 10.3 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 152.4, 137.4, 136.5, 135.5, 132.1, 129.9, 129.4, 124.4, 123.3, 122.0, 120.3, 115.5, 105.3, 62.8, 54.5, 40.3.

HRMS (ESI-TOF, [M + H]$^+$): For $C_{18}H_{16}BrN_2O_2$, 371.0395 , Found: 371.0394.

2-methoxy-4-(*p*-tolyl)-3,4-dihydropyrimido[1,6-*a*]indol-1(2*H*)-one (3ae)



3ae

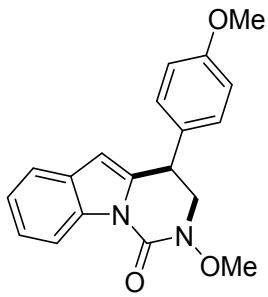
3ae was obtained in 81% (49.6 mg) as a white solid after column chromatography (eluent: petroleum ether/ethyl acetate = 8/1 v/v). Mp: 187-189 ^{o}C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.44 (d, J = 8.3 Hz, 1H), 7.42 (d, J = 7.7 Hz, 1H), 7.31 (t, J = 7.6 Hz, 1H), 7.21 (m, 5H), 6.05 (s, 1H), 4.53 (dd, J = 9.3, 5.7 Hz, 1H), 3.99-3.77 (m, 5H), 2.38 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 152.5, 137.8, 137.6, 135.5, 135.2, 129.6, 128.1, 124.2, 123.1, 120.2, 115.5, 105.1, 62.7, 54.7, 40.5, 21.1.

HRMS (ESI-TOF, [M + H]$^+$): For $C_{19}H_{19}N_2O_2$, 307.1447, Found: 307.1456.

2-methoxy-4-(4-methoxyphenyl)-3,4-dihydropyrimido[1,6-*a*]indol-1(2*H*)-one (3af)



3af

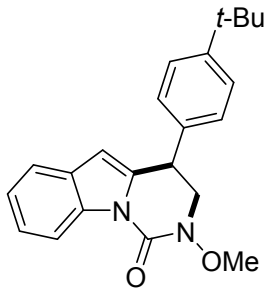
3af was obtained in 92% (59.2 mg) as a white solid after column chromatography (eluent: petroleum ether/ethyl acetate = 8/1 v/v). Mp: 198-200 ^{o}C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.44 (d, J = 8.3 Hz, 1H), 7.43 (d, J = 7.7 Hz, 1H), 7.31 (t, J = 7.8, 7.8 Hz, 1H), 7.26 – 7.18 (m, 3H), 6.92 (d, J = 8.6 Hz, 2H), 6.05 (s, 1H), 4.52 (dd, J = 5.5, 10.1 Hz, 1H), 3.89 (dd, J = 5.6, 10.7 Hz, 2H), 3.86 (s, 3H), 3.83 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): *δ* 159.3, 152.5, 137.7, 135.5, 130.2, 129.5, 124.2, 123.1, 120.2, 115.5, 114.3, 105.0, 62.7, 55.3, 54.8, 40.2.

HRMS (ESI-TOF, [M + H]$^+$): For $C_{19}H_{19}N_2O_3$, 323.1396, Found: 323.1398.

4-(4-(tert-butyl)phenyl)-2-methoxy-3,4-dihydropyrimido[1,6-*a*]indol-1(2*H*)-one (3ag)



3ag

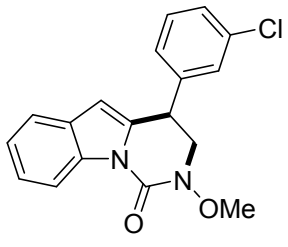
3ag was obtained in 74% (51.7 mg) as a white solid after column chromatography (eluent: petroleum ether/ethyl acetate = 8/1 v/v). Mp: 216-218 °C.

^{1}H NMR (500 MHz, $CDCl_3$): *δ* 8.45 (d, *J* = 8.3 Hz, 1H), 7.45-7.38 (m, 3H), 7.31 (t, *J* = 7.8 Hz, 1H), 7.27 (d, *J* = 8.3 Hz, 2H), 7.22 (t, *J* = 7.5 Hz, 1H), 6.08 (s, 1H), 4.54 (dd, *J* = 9.9, 5.8 Hz, 1H), 3.93-3.85 (m, 5H), 1.34 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$): *δ* 152.5, 151.0, 137.6, 135.5, 135.1, 129.6, 127.9, 125.8, 124.2, 123.1, 120.2, 115.5, 105.1, 62.7, 54.6, 40.5, 34.6, 31.3.

HRMS (ESI-TOF, [M + H]$^+$): For $C_{22}H_{25}N_2O_2$, 349.1916, Found: 349.1913.

4-(3-chlorophenyl)-2-methoxy-3,4-dihydropyrimido[1,6-*a*]indol-1(2*H*)-one (3ah)



3ah

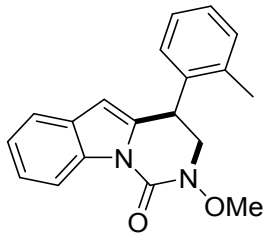
3ah was obtained in 44% (28.5 mg) as a white solid after column chromatography (eluent: petroleum ether/ethyl acetate = 8/1 v/v). Mp: 198-200 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.41 (d, J = 8.3 Hz, 1H), 7.43 (d, J = 7.8 Hz, 1H), 7.31 (m, 3H), 7.26-7.16 (m, 3H), 6.07 (s, 1H), 4.53 (dd, J = 9.4, 5.4 Hz, 1H), 4.00-3.74 (m, 5H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 152.4, 140.4, 136.2, 135.5, 134.8, 130.2, 129.4, 128.4, 128.3, 126.4, 124.5, 123.3, 120.3, 115.5, 105.4, 62.8, 54.5, 40.5.

HRMS (ESI-TOF, [M + Na]$^+$): For $C_{18}H_{15}ClN_2NaO_2$, 349.0720, Found: 349.0716.

2-methoxy-4-(*o*-tolyl)-3,4-dihydropyrimido[1,6-*a*]indol-1(2*H*)-one (3ai)



3ai

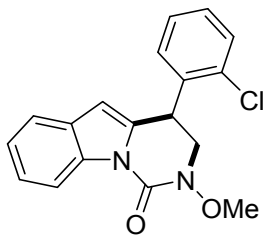
3ai was obtained in 75% (45.9 mg) as a white solid after column chromatography (eluent: petroleum ether/ethyl acetate = 8/1 v/v). Mp: 193-195 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.46 (d, J = 8.3 Hz, 1H), 7.42 (d, J = 7.7 Hz, 1H), 7.32 (t, J = 7.8 Hz, 1H), 7.30-7.16 (m, 5H), 6.00 (s, 1H), 4.82 (t, J = 7.9 Hz, 1H), 3.88 (d, J = 8.7 Hz, 2H), 3.87 (s, 3H), 2.48 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 152.5, 137.3, 136.3, 135.9, 135.5, 130.9, 129.6, 127.9, 126.6, 124.2, 123.1, 120.2, 115.5, 104.8, 62.7, 53.4, 36.9, 19.6.

HRMS (ESI-TOF, [M + Na]$^+$): For $C_{19}H_{18}N_2NaO_2$, 329.1266, Found: 329.1264.

4-(2-chlorophenyl)-2-methoxy-3,4-dihydropyrimido[1,6-*a*]indol-1(2*H*)-one (3aj)



3aj

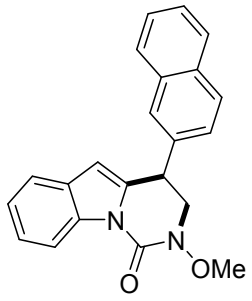
3aj was obtained in 57% (37.1 mg) as a white solid after column chromatography (eluent: petroleum ether/ethyl acetate = 8/1 v/v). Mp: 201-203 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.47 (d, J = 8.3 Hz, 1H), 7.51-7.44 (m, 2H), 7.37-7.32 (m, 1H), 7.31-7.19 (m, 3H), 7.13 (dd, J = 7.7, 1.5 Hz, 1H), 6.19 (s, 1H), 5.16-5.06 (m, 1H), 4.07-3.99 (m, 1H), 3.85 (dd, J = 11.0, 7.7 Hz, 1H), 3.77 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 152.2, 136.5, 135.5, 135.5, 133.4, 129.9, 129.5, 129.2, 127.3, 124.4, 123.2, 120.3, 115.5, 105.2, 62.6, 52.9, 37.1.

HRMS (ESI-TOF, [M + Na]$^+$): For $C_{18}H_{15}ClN_2NaO_2$, 349.0720, Found: 349.0719.

2-methoxy-4-(naphthalen-2-yl)-3,4-dihydropyrimido[1,6-*a*]indol-1(2*H*)-one (3ak)



3ak

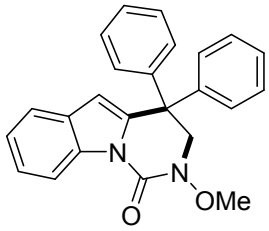
3ak was obtained in 80% (54.7 mg) as a white solid after column chromatography (eluent: petroleum ether/ethyl acetate = 8/1 v/v). Mp: 221-223 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.48 (d, J = 8.2 Hz, 1H), 7.94-7.72 (m, 4H), 7.52 (dd, J = 6.2, 3.2 Hz, 2H), 7.43 (d, J = 7.2 Hz, 2H), 7.37-7.30 (m, 1H), 7.23 (dd, J = 13.0, 5.4 Hz, 1H), 6.07 (s, 1H), 4.76-4.68 (m, 1H), 4.12-3.64 (m, 5H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 152.5, 137.2, 135.6, 135.5, 133.3, 132.9, 129.6, 128.8, 127.8, 127.7, 127.5, 126.5, 126.3, 125.7, 124.3, 123.2, 120.3, 115.5, 105.4, 62.8, 54.6, 41.1.

HRMS (ESI-TOF, [M + Na]$^+$): For $C_{22}H_{18}N_2NaO_2$, 365.1266, Found: 365.1269.

2-methoxy-4,4-diphenyl-3,4-dihydropyrimido[1,6-*a*]indol-1(2*H*)-one (3al)



3al

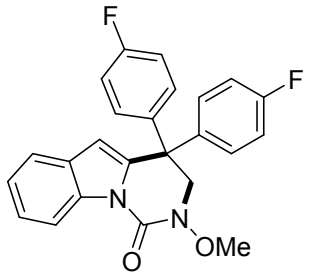
3al was obtained in 88% (65.1 mg) as a white solid after column chromatography (eluent: petroleum ether/ethyl acetate = 8/1 v/v). Mp: 234-236 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.45 (d, J = 8.3 Hz, 1H), 7.47 (d, J = 7.7 Hz, 1H), 7.33 (d, J = 7.6 Hz, 7H), 7.24 (t, J = 7.0 Hz, 1H), 7.16 (d, J = 6.4 Hz, 4H), 6.08 (s, 1H), 4.46 (s, 2H), 3.52 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 151.3, 142.0, 140.1, 135.7, 128.9, 128.5, 128.1, 127.6, 124.5, 123.1, 120.5, 115.5, 107.6, 62.3, 58.7, 50.9.

HRMS (ESI-TOF, $[M + Na]^+$): For $C_{24}H_{20}N_2NaO_2$, 391.1417, Found: 391.1420.

4,4-bis(4-fluorophenyl)-2-methoxy-3,4-dihydropyrimido[1,6-*a*]indol-1(2*H*)-one (3am)



3am

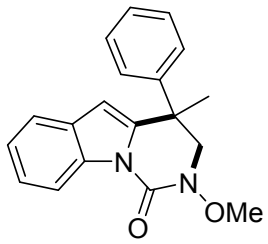
3am was obtained in 49% (39.6 mg) as a white solid after column chromatography (eluent: petroleum ether/ethyl acetate = 8/1 v/v). Mp: 219-221 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.42 (d, J = 8.3 Hz, 1H), 7.47 (d, J = 7.7 Hz, 1H), 7.35 (t, J = 7.3 Hz, 1H), 7.28-7.23 (m, 1H), 7.15-7.09 (m, 4H), 7.03 (t, J = 8.6 Hz, 4H), 6.05 (s, 1H), 4.39 (s, 2H), 3.57 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 162.1(d, J = 248.2 Hz), 151.3, 139.8, 137.5, 135.8, 129.8 (d, J = 6.6 Hz), 124.9, 123.4, 120.6, 115.5 (d, J = 20.9 Hz), 107.6, 62.5, 59.0, 50.0.

HRMS (ESI-TOF, $[M + H]^+$): For $C_{24}H_{19}F_2N_2O_2$, 405.1415, Found: 405.1413.

2-methoxy-4-methyl-4-phenyl-3,4-dihydropyrimido[1,6-*a*]indol-1(2*H*)-one (3an)



3an

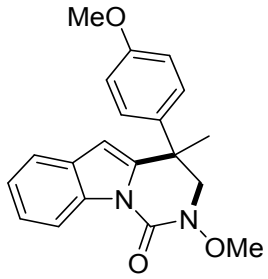
3an was obtained in 85% (52.0 mg) as a white solid after column chromatography (eluent: petroleum ether/ethyl acetate = 8/1 v/v). Mp: 225-227 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.48 (d, J = 8.2 Hz, 1H), 7.59 (d, J = 7.7 Hz, 1H), 7.43-7.27 (m, 5H), 7.21 (d, J = 7.4 Hz, 2H), 6.47 (s, 1H), 4.24-3.86 (m, 2H), 3.60 (s, 3H), 1.87 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 151.6, 143.6, 140.9, 135.5, 129.3, 128.6, 127.4, 126.1, 123.1, 120.4, 115.5, 104.4, 62.3, 60.2, 41.5, 3.

HRMS (ESI-TOF, $[M + H]^+$): For $C_{19}H_{18}N_2NaO_2$, 329.1266, Found: 329.1266.

2-methoxy-4-(4-methoxyphenyl)-4-methyl-3,4-dihydropyrimido[1,6-*a*]indol-1(2*H*)-one (3ao)



3ao

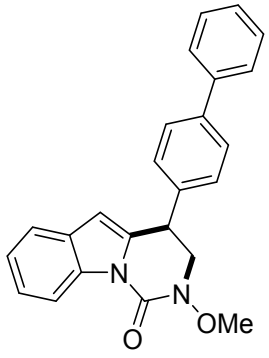
3an was obtained in 89% (59.8 mg) as a white solid after column chromatography (eluent: petroleum ether/ethyl acetate = 8/1 v/v). Mp: 239-241 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.43 (d, J = 8.3 Hz, 1H), 7.53 (d, J = 7.8 Hz, 1H), 7.33 (t, J = 7.8 Hz, 1H), 7.28-7.22 (m, 1H), 7.09 (d, J = 8.8 Hz, 2H), 6.82 (d, J = 8.8 Hz, 2H), 6.38 (s, 1H), 3.97-3.81 (m, 2H), 3.77 (s, 3H), 3.60 (s, 3H), 1.80 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 158.7, 151.5, 141.3, 135.6, 135.5, 129.3, 127.3, 124.3, 123.1, 120.4, 115.5, 113.8, 104.2, 62.3, 60.2, 55.3, 40.9, 25.7.

HRMS (ESI-TOF, [M + H]$^+$): For $C_{20}H_{21}N_2O_3$, 337.1552, Found: 337.1552.

4-([1,1'-biphenyl]-4-yl)-2-methoxy-3,4-dihydropyrimido[1,6-*a*]indol-1(2*H*)-one (3ap)



3ap

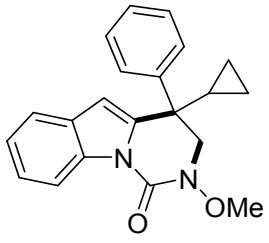
3ap was obtained in 86% (63.3 mg) as a white solid after column chromatography (eluent: petroleum ether/ethyl acetate = 8/1 v/v). Mp: 229-231 ^{o}C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.47 (d, J = 8.3 Hz, 1H), 7.62 (t, J = 7.1 Hz, 4H), 7.46 (t, J = 7.7 Hz, 3H), 7.43 – 7.31 (m, 4H), 7.28-7.20 (m, 1H), 6.13 (s, 1H), 4.62 (dd, J = 9.5, 5.5 Hz, 1H), 4.00 – 3.88 (m, 2H), 3.87 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 152.5, 141.0, 140.3, 137.3, 137.2, 135.5, 129.5, 128.8, 128.7, 127.6, 127.0, 124.3, 123.2, 120.3, 115.5, 105.3, 62.8, 54.6, 40.6.

HRMS (ESI-TOF, [M + Na]$^+$): For $C_{24}H_{20}N_2NaO_2$, 391.1422, Found: 391.1419.

(R)-4-cyclopropyl-2-methoxy-4-phenyl-3,4-dihydropyrimido[1,6-a]indol-1(2H)-one (3aq)



3aq

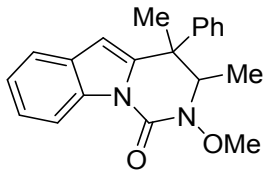
3aq was obtained in 88% (53.2 mg) as a white solid after column chromatography (eluent: petroleum ether/ethyl acetate = 8/1 v/v). Mp:112-120 ^{o}C

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.37 (d, J = 8.2 Hz, 1H), 7.48 (d, J = 7.8 Hz, 1H), 7.36 – 7.26 (m, 4H), 7.25 – 7.17 (m, 3H), 6.40 (s, 1H), 4.13 (d, J = 11.4 Hz, 1H), 3.78 (d, J = 11.4 Hz, 1H), 3.71 (s, 3H), 1.43 (tt, J = 5.5, 5.5, 8.4, 8.4 Hz, 1H), 0.70 – 0.60 (m, 1H), 0.53 (tt, J = 5.3, 5.3, 9.4, 9.4 Hz, 1H), 0.20 (dq, J = 5.5, 5.5, 5.5, 10.7 Hz, 1H), -0.01 (dq, J = 5.1, 5.3, 5.3, 10.1 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 151.62, 140.03, 139.43, 135.46, 129.15, 128.24, 127.89, 127.54, 124.36, 123.09, 120.37, 115.54, 106.11, 62.40, 58.91, 45.54, 29.70, 18.64, 2.33.

HRMS (ESI-TOF, $[M + Na]^+$): For $C_{21}H_{20}N_2NaO_2$, 355.1417, found: 355.1419

2-methoxy-3,4-dimethyl-4-phenyl-3,4-dihydropyrimido[1,6-*a*]indol-1(2*H*)-one (3as)



3as

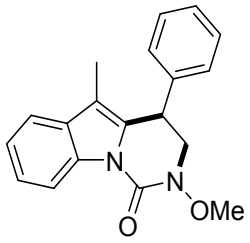
3as was obtained in 36% (23.1 mg) as a colorless oil after column chromatography (eluent: petroleum ether/ethyl acetate = 8/1 v/v).

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.44 (d, J = 8.2 Hz, 1H), 7.58 (d, J = 7.7 Hz, 1H), 7.38 – 7.32 (m, 1H), 7.31 – 7.26 (m, 2H), 7.26 – 7.20 (m, 2H), 7.04 (dd, J = 1.8, 7.2 Hz, 2H), 6.53 (s, 1H), 4.15 (q, J = 6.5, 6.5, 6.5 Hz, 1H), 3.36 (s, 3H), 1.75 (s, 3H), 1.30 (d, J = 6.5 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 150.74, 145.74, 139.23, 135.46, 129.26, 128.45, 127.11, 125.67, 124.36, 123.00, 120.31, 115.50, 105.85, 77.24, 76.98, 76.73, 65.21, 62.12, 45.45, 23.69, 13.41.

HRMS (ESI-TOF, $[M + Na]^+$): For $C_{20}H_{20}N_2NaO_2$, 343.1422, Found: 343.1424

2-methoxy-5-methyl-4-phenyl-3,4-dihydropyrimido[1,6-*a*]indol-1(2*H*)-one (3ba)



3ba

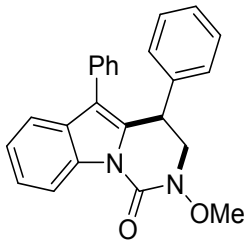
3ba was obtained in 72% (44.1 mg) as a white solid after column chromatography (eluent: petroleum ether/ethyl acetate = 8/1 v/v). Mp: 191-193 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.44 (d, J = 8.2 Hz, 1H), 7.46 (d, J = 7.7 Hz, 1H), 7.38-7.25 (m, 5H), 7.18 (d, J = 7.1 Hz, 2H), 4.58 (t, J = 4.3 Hz, 1H), 4.12 (dd, J = 10.9, 4.8 Hz, 1H), 3.80 (dd, J = 10.9, 4.4 Hz, 1H), 3.65 (s, 3H), 1.94 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 152.5, 139.8, 134.9, 130.9, 130.7, 128.8, 127.5, 124.4, 122.8, 118.3, 115.5, 112.9, 62.4, 55.0, 38.7, 8.3.

HRMS (ESI-TOF, [M + Na]$^+$): For $C_{19}H_{18}N_2NaO_2$, 329.1266, Found: 329.1267.

2-methoxy-4,5-diphenyl-3,4-dihydropyrimido[1,6-*a*]indol-1(2*H*)-one (3ca)



3ca

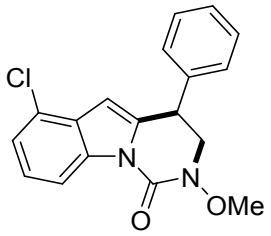
3ca was obtained in 92% (67.7 mg) as a white solid after column chromatography (eluent: petroleum ether/ethyl acetate = 8/1 v/v). Mp: 221-223 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.55 (d, J = 8.3 Hz, 1H), 7.63 (d, J = 7.9 Hz, 1H), 7.41 (ddd, J = 1.3, 7.2, 8.4 Hz, 1H), 7.30 (dtd, J = 2.6, 4.2, 4.9, 8.6 Hz, 7H), 7.25 – 7.19 (m, 2H), 7.18 – 7.09 (m, 2H), 4.63 – 4.55 (m, 1H), 4.20 (dd, J = 4.1, 11.1 Hz, 1H), 3.78 (dd, J = 2.6, 11.2 Hz, 1H), 3.54 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 151.8, 141.0, 135.3, 132.5, 130.9, 129.1, 128.8, 128.5, 127.4, 127.3, 127.2, 124.8, 123.3, 119.5, 118.7, 115.7, 62.1, 55.1, 38.3.

HRMS (ESI-TOF, [M + Na]$^+$): For $C_{24}H_{20}N_2NaO_2$, 391.1422, Found: 391.1420.

6-chloro-2-methoxy-4-phenyl-3,4-dihydropyrimido[1,6-*a*]indol-1(2*H*)-one (3da)



3da

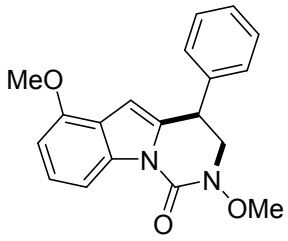
3da was obtained in 72% (46.9 mg) as a white solid after column chromatography (eluent: petroleum ether/ethyl acetate = 8/1 v/v). Mp: 195-197 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.35 (d, J = 7.1 Hz, 1H), 7.39 (m, 3H), 7.33 (d, J = 7.3 Hz, 2H), 7.23 (d, J = 7.7 Hz, 2H), 6.19 (s, 1H), 4.58 (dd, J = 9.6, 5.6 Hz, 1H), 3.99-3.87 (m, 2H), 3.85 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 152.0, 138.0, 137.8, 136.1, 129.0, 128.2, 125.4, 125.0, 122.9, 114.0, 103.3, 62.8, 54.5, 40.9.

HRMS (ESI-TOF, $[M + H]^+$): For $C_{18}H_{16}ClN_2O_2$, 327.0900, Found: 327.0904.

2,6-dimethoxy-4-phenyl-3,4-dihydropyrimido[1,6-*a*]indol-1(2*H*)-one (3ea)



3ea

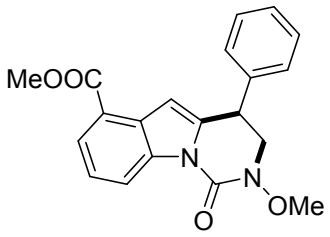
3ea was obtained in 76% (48.8 mg) as a white solid after column chromatography (eluent: petroleum ether/ethyl acetate = 8/1 v/v). Mp: 189-192 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.06 (d, J = 8.3 Hz, 1H), 7.36 (dq, J = 18.7, 6.6 Hz, 5H), 7.27-7.22 (m, 1H), 6.68 (d, J = 8.0 Hz, 1H), 6.19 (s, 1H), 4.56 (dd, J = 9.7, 5.5 Hz, 1H), 3.96 – 3.87 (m, 5H), 3.85 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 152.4, 138.3, 136.7, 135.8, 128.9, 128.3, 128.0, 125.2, 119.7, 108.6, 103.5, 102.2, 62.7, 55.3, 54.6, 40.9.

HRMS (ESI-TOF, $[M + Na]^+$): For $C_{19}H_{18}N_2NaO_3$, 345.1215, Found: 345.1216 .

Methyl2-methoxy-1-oxo-4-phenyl-1,2,3,4-tetrahydropyrimido[1,6-*a*]indole-6-carboxylate (3fa)



3fa

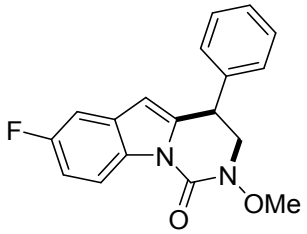
3fa was obtained in 70% (49.0 mg) as a white solid after column chromatography (eluent: petroleum ether/ethyl acetate = 8/1 v/v). Mp: 199-201 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.68 (d, J = 8.2 Hz, 1H), 7.95 (d, J = 7.5 Hz, 1H), 7.41-7.30 (m, 6H), 6.81 (s, 1H), 4.60 (dd, J = 9.0, 5.6 Hz, 1H), 3.99 – 3.89 (m, 2H), 3.88 (s, 3H), 3.84 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 167.2, 152.1, 139.2, 138.0, 136.2, 129.7, 129.0, 128.2, 128.1, 125.8, 123.6, 121.3, 120.0, 105.9, 62.7, 54.5, 51.8, 40.9.

HRMS (ESI-TOF, [M + Na]$^+$): For $C_{20}H_{18}N_2NaO_4$, 373.1164, found: 373.1165.

7-fluoro-2-methoxy-4-phenyl-3,4-dihydropyrimido[1,6-*a*]indol-1(2*H*)-one (3ga)



3ga

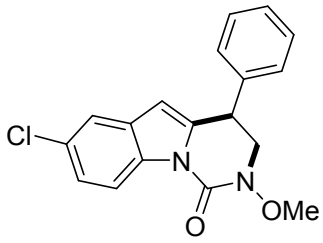
3ga was obtained in 53% (32.9 mg) as a white solid after column chromatography (eluent: petroleum ether/ethyl acetate = 8/1 v/v). Mp: 193-195 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.39 (dd, J = 9.0, 4.7 Hz, 1H), 7.40 (dt, J = 11.6, 6.7 Hz, 3H), 7.33 (d, J = 6.8 Hz, 2H), 7.08 (dd, J = 8.8, 2.3 Hz, 1H), 7.04 (td, J = 9.2, 2.4 Hz, 1H), 6.03 (s, 1H), 4.57 (dd, J = 9.6, 5.5 Hz, 1H), 3.98 – 3.87 (m, 2H), 3.85 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 159.5 (d, J = 239.2 Hz), 152.3, 138.9, 138.0, 131.8, 130.4 (d, J = 9.2 Hz), 129.0, 1228.2, 116.4 (d, J = 7.7 Hz), 112.0 (d, J = 24.8 Hz), 105.8 (d, J = 23.9 Hz), 104.9, 62.8, 54.6, 40.9.

HRMS (ESI-TOF, [M + H]$^+$): For $C_{18}H_{16}FN_2O_2$, 311.1196, found: 311.1201.

7-chloro-2-methoxy-4-phenyl-3,4-dihydropyrimido[1,6-*a*]indol-1(2*H*)-one (3ha)



3ha

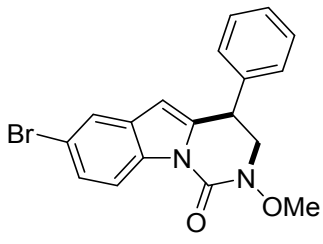
3ha was obtained in 65% (42.3 mg) as a white solid after column chromatography (eluent: petroleum ether/ethyl acetate = 8/1 v/v). Mp: 205-207 ^{o}C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.36 (d, J = 8.8 Hz, 1H), 7.46-7.33 (m, 4H), 7.34-7.30 (m, 2H), 7.29-7.23 (m, 1H), 6.00 (s, 1H), 4.56 (dd, J = 9.1, 5.6 Hz, 1H), 3.98-3.85 (m, 2H), 3.85 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 152.1, 138.7, 137.9, 133.8, 130.7, 129.0, 128.7, 128.2, 124.4, 119.8, 116.4, 104.4, 62.8, 54.5, 40.9.

HRMS (ESI-TOF, [M + H]$^+$): For $C_{18}H_{16}ClN_2O_2$, 327.0900, found: 327.0904.

7-bromo-2-methoxy-4-phenyl-3,4-dihydropyrimido[1,6-a]indol-1(2*H*)-one (3ia)



3ia

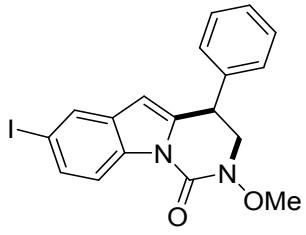
3ia was obtained in 74% (54.9 mg) as a white solid after column chromatography (eluent: petroleum ether/ethyl acetate = 8/1 v/v). Mp: 211-213 ^{o}C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.31 (d, J = 8.8 Hz, 1H), 7.55 (s, 1H), 7.43-7.35 (m, 4H), 7.31 (d, J = 6.9 Hz, 2H), 6.00 (s, 1H), 4.56 (dd, J = 9.8, 5.6 Hz, 1H), 3.97-3.86 (m, 2H), 3.84 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 156.2, 152.5, 138.4, 137.9, 130.4, 130.1, 128.9, 128.2, 128.0, 116.1 112.7, 105.0, 103.1, 62.7, 55.6, 54.8, 40.9.

HRMS (ESI-TOF, [M + Na]$^+$): For $C_{18}H_{15}BrN_2NaO_2$, 371.0395, found: 371.0397.

7-iodo-2-methoxy-4-phenyl-3,4-dihydropyrimido[1,6-*a*]indol-1(2*H*)-one (3ja)



3ja

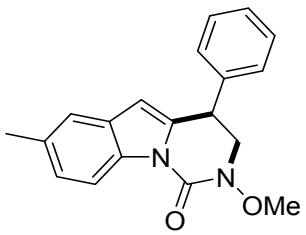
3ja was obtained in 56% (22.2 mg) as a white solid after column chromatography (eluent: petroleum ether/ethyl acetate = 8/1 v/v). Mp: 209-211 ^{o}C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.19 (d, J = 8.7 Hz, 1H), 7.75 (d, J = 1.3 Hz, 1H), 7.57 (dd, J = 8.7, 1.5 Hz, 1H), 7.44 – 7.34 (m, 3H), 7.30 (d, J = 6.5 Hz, 2H), 5.97 (s, 1H), 4.55 (dd, J = 9.1, 5.6 Hz, 1H), 3.96 – 3.84 (m, 2H), 3.84 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 152.0, 138.2, 137.9, 134.7, 132.7, 131.8, 129.0, 128.2, 117.3, 104.1, 87.2, 62.7, 54.5, 40.8.

HRMS (ESI-TOF, [M + H]$^+$): For $C_{18}H_{16}IN_2O_2$, 419.0256, found: 419.0255.

2-methoxy-7-methyl-4-phenyl-3,4-dihydropyrimido[1,6-*a*]indol-1(2*H*)-one (3ka)



3ka

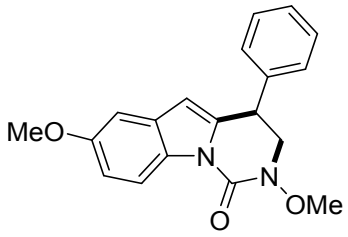
3kq was obtained in 76% (46.5 mg) as a white solid after column chromatography (eluent: petroleum ether/ethyl acetate = 8/1 v/v). Mp: 188-200 ^{o}C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.30 (d, J = 8.4 Hz, 1H), 7.38 (m, 3H), 7.34-7.30 (m, 2H), 7.22 (s, 1H), 7.14 (d, J = 8.4 Hz, 1H), 5.99 (s, 1H), 4.55 (dd, J = 9.2, 5.5 Hz, 1H), 3.96-3.84 (m, 2H), 3.84 (s, 3H), 2.42 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 152.6, 138.5, 137.2, 133.6, 132.6, 129.7, 128.9, 128.2, 128.0, 125.6, 120.2, 115.1, 104.9, 62.7, 54.7, 40.9, 21.4.

HRMS (ESI-TOF, [M + Na]$^+$): For $C_{19}H_{18}N_2NaO_2$, 329.1266, found: 329.1269.

2,7-dimethoxy-4-phenyl-3,4-dihydropyrimido[1,6-*a*]indol-1(2*H*)-one (3la)



3la

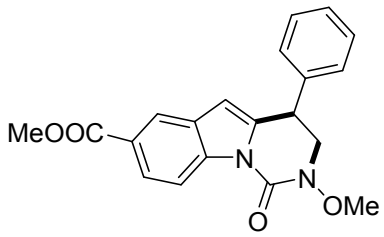
3la was obtained in 75% (48.3 mg) as a white solid after column chromatography (eluent: petroleum ether/ethyl acetate = 8/1 v/v). Mp: 191-193 ^{o}C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.32 (d, J = 9.0 Hz, 1H), 7.42-7.30 (m, 5H), 6.93 (dd, J = 9.0, 2.4 Hz, 1H), 6.90 (d, J = 2.2 Hz, 1H), 5.99 (s, 1H), 4.55 (dd, J = 9.8, 5.4 Hz, 1H), 3.95-3.85 (m, 2H), 3.84 (s, 3H), 3.82 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 156.2, 152.5, 138.4, 137.9, 130.4, 130.1, 128.9, 128.2, 128.02, 116.2, 112.7, 105.0, 103.1, 62.8, 55.6, 54.8, 40.9.

HRMS (ESI-TOF, [M + Na]$^+$): For $C_{19}H_{18}N_2NaO_3$, 345.1215, found: 345.1218.

methyl2-methoxy-1-oxo-4-phenyl-1,2,3,4-tetrahydropyrimido[1,6-*a*]indole-7-carboxylate (3ma)



3ma

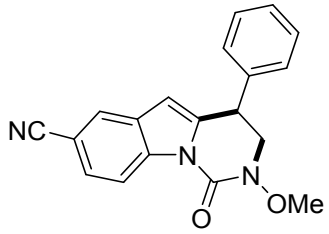
3ma was obtained in 47% (32,9 mg) as a white solid after column chromatography (eluent: petroleum ether/ethyl acetate = 8/1 v/v). Mp: 191-193 ^{o}C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.47 (d, J = 8.7 Hz, 1H), 8.16 (s, 1H), 8.01 (dd, J = 8.7, 1.4 Hz, 1H), 7.39 (m, 3H), 7.35-7.30 (m, 2H), 6.13 (s, 1H), 4.59 (dd, J = 9.2, 5.7 Hz, 1H), 3.99-3.87 (m, 5H), 3.85 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 167.4, 151.9, 138.7 138.1, 137.8, 129.3 129.0, 128.2, 125.6 125.1, 122.6, 115.1, 105.5, 62.8 54.4, 52.0, 40.9.

HRMS (ESI-TOF, [M + Na]$^+$): For $C_{20}H_{18}N_2NaO_4$, 373.1164, found: 373.1161.

2-methoxy-1-oxo-4-phenyl-1,2,3,4-tetrahydropyrimido[1,6-*a*]indole-7-carbonitrile (3na)



3na

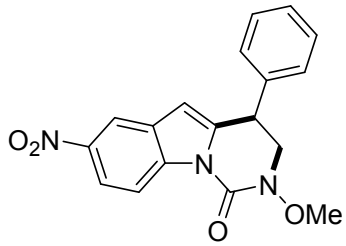
3na was obtained in 36% (22.8 mg) as a white solid after column chromatography (eluent: petroleum ether/ethyl acetate = 4/1 v/v). Mp: 209-211 ^{o}C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.54 (d, J = 8.6 Hz, 1H), 7.76 (s, 1H), 7.56 (dd, J = 8.6, 1.4 Hz, 1H), 7.45 – 7.39 (m, 3H), 7.35 – 7.32 (m, 2H), 6.13 (s, 1H), 4.61 (dd, J = 9.9, 5.8 Hz, 1H), 4.00 – 3.91 (m, 2H), 3.87 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 151.5, 139.8, 137.3, 129.5, 129.1, 128.4, 128.2, 127.4, 125.1, 119.7, 116.3, 106.4, 104.7, 62.8, 54.2, 40.8.

HRMS (ESI-TOF, [M + H]$^+$): For $C_{19}H_{16}N_3O_2$, 318.1243, found: 318.1247.

2-methoxy-7-nitro-4-phenyl-3,4-dihydropyrimido[1,6-*a*]indol-1(2*H*)-one (3oa)



3oa

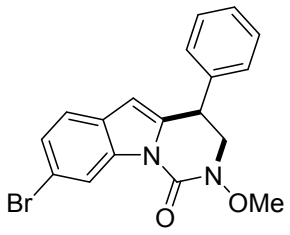
3oa was obtained in 50% (33.7 mg) as a white solid after column chromatography (eluent: petroleum ether/ethyl acetate = 4/1 v/v). Mp: 219-221 ^{o}C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.53 (d, J = 9.1 Hz, 1H), 8.33 (d, J = 1.9 Hz, 1H), 8.19 (dd, J = 9.1, 2.0 Hz, 1H), 7.42 (m, 3H), 7.34 (d, J = 6.8 Hz, 2H), 6.20 (s, 1H), 4.62 (dd, J = 9.3, 6.0 Hz, 1H), 4.03 – 3.93 (m, 2H), 3.87 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 151.3, 144.0, 140.6, 138.6, 137.2, 129.3, 129.2, 128.5, 128.2, 119.5, 116.5, 115.6, 105.6, 62.8, 54.2, 40.9.

HRMS (ESI-TOF, $[M + H]^+$): For $C_{18}H_{16}N_3O_4$, 338.1141, found: 338.1143.

8-bromo-2-methoxy-4-phenyl-3,4-dihydropyrimido[1,6-*a*]indol-1(2*H*)-one (3pa)



3pa

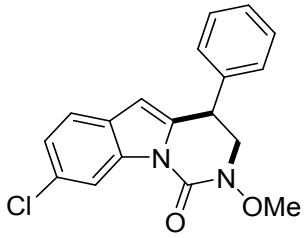
3pa was obtained in 73% (54.2 mg) as a white solid after column chromatography (eluent: petroleum ether/ethyl acetate = 8/1 v/v). Mp: 193-195 ^{o}C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.64 (s, 1H), 7.43-7.29 (m, 6H), 7.27 (d, J = 11.9 Hz, 1H), 6.02 (s, 1H), 4.54 (dd, J = 9.8, 5.6 Hz, 1H), 3.97-3.86 (m, 2H), 3.85 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 151.9, 137.9, 136.0, 129.0, 128.3, 128.2, 126.4, 121.3, 118.5, 117.8, 104.9, 62.7, 54.5, 40.9.

HRMS (ESI-TOF, $[M + H]^+$): For $C_{18}H_{16}BrN_2O_2$, 371.0395, found: 371.0397.

8-chloro-2-methoxy-4-phenyl-3,4-dihydropyrimido[1,6-*a*]indol-1(2*H*)-one (3qa)



3qa

3qa was obtained in 64% (41.9 mg) as a white solid after column chromatography (eluent: petroleum ether/ethyl acetate = 8/1 v/v). Mp: 183-185 ^{o}C.

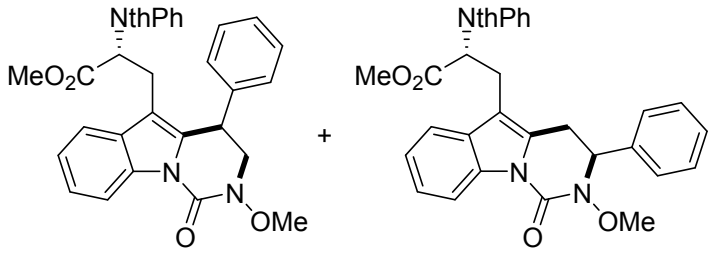
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.47 (s, 1H), 7.39 (m, 3H), 7.31 (d, J = 8.1 Hz, 3H), 7.18 (dd, J = 8.3, 1.8 Hz, 1H), 6.02 (s, 1H), 4.55 (dd, J = 9.5, 5.4 Hz, 1H), 3.98 – 3.85 (m, 2H), 3.84 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 152.0, 138.0, 135.7, 130.0, 129.0, 128.2, 128.0, 123.7, 120.9, 115.6, 104.8, 62.7, 54.5, 40.8.

HRMS (ESI-TOF, $[M + H]^+$): For $C_{18}H_{16}ClN_2O_2$, 327.0900, found: 327.0901.

methyl(2*R*)-2-(1,3-dioxoisoindolin-2-yl)-3-(2-methoxy-1-oxo-4-phenyl-1,2,3,4-tetrahydropyrimido[1,6-*a*]indol-5-yl)propanoate (3ra)

methyl(2*R*)-2-(1,3-dioxoisoindolin-2-yl)-3-(2-methoxy-1-oxo-3-phenyl-1,2,3,4-tetrahydropyrimido[1,6-*a*]indol-5-yl)propanoate (3ra')



3ra+**3ra**'
ratio 1:0.9

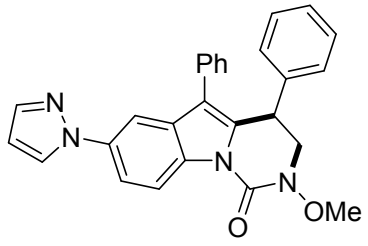
3ra and **3ra'** were obtained in 91% (95.1 mg) as white solid after column chromatography (eluent: petroleum ether/ethyl acetate = 4/1 v/v). Mp: 261-263 ^{o}C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.38 (dd, J = 13.5, 8.3 Hz, 1.91H), 7.75 (dd, J = 5.4, 3.1 Hz, 1.88H), 7.69 (dd, J = 5.4, 3.0 Hz, 1.87H), 7.61 (s, 3.98H), 7.55 (d, J = 7.7 Hz, 1.16H), 7.45 (d, J = 7.8 Hz, 1.02H), 7.27 (tq, J = 22.3, 7.2 Hz, 6.55H), 7.11 (dt, J = 34.5, 7.3 Hz, 6.81H), 7.00 (t, J = 6.5 Hz, 1.09H), 5.11 (dd, J = 9.4, 5.6 Hz, 0.99H), 5.04 (dd, J = 9.8, 6.4 Hz, 0.91H), 4.78 (t, J = 4.1 Hz, 1.01H), 4.64 – 4.57 (m, 0.90H), 4.15 (dd, J = 11.1, 4.4 Hz, 1.01H), 3.84 (dd, J = 11.0, 4.6 Hz, 1.06H), 3.71 (s, 3.09H), 3.70 (s, 3.16H), 3.54 (s, 3.00H), 3.52 (s, 3.25H), 3.49 – 3.30 (m, 4.14H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 169.1, 169.1, 167.4, 151.9, 151.9, 140.0, 139.6, 135.1, 135.0, 134.3, 133.9, 133.1, 132.8, 131.5, 131.5, 129.6, 129.3, 128.9, 128.6, 127.6, 127.5, 127.4, 127.3, 124.6, 123.5, 123.1, 123.1, 118.4, 118.3, 115.7, 115.6, 112.1, 62.2, 62.2, 55.3, 54.8, 52.9, 52.9, 51.3, 38.4, 37.9, 23.9, 23.8.

HRMS (ESI-TOF, [M + Na]$^+$): For $C_{30}H_{25}N_3NaO_6$, 546.1641, found: 546.1644.

2-methoxy-4,5-diphenyl-7-(1*H*-pyrazol-1-yl)-3,4-dihydropyrimido[1,6-*a*]indol-1(2*H*)-one (3sa)



3sa

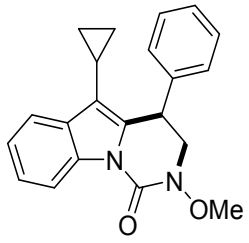
3sa was obtained in 68% (59.6 mg) as a white solid after column chromatography (eluent: petroleum ether/ethyl acetate = 4/1 v/v). Mp: 254-256 ^{o}C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.60 (d, J = 8.9 Hz, 1H), 7.92 (dd, J = 11.0, 1.8 Hz, 3H), 7.71 (d, J = 9.6 Hz, 2H), 7.36-7.27 (m, 9H), 7.22 (d, J = 7.9 Hz, 2H), 7.13 (d, J = 7.8 Hz, 2H), 6.46 (s, 1H), 4.60 (s, 1H), 4.24 (dd, J = 11.2, 4.0 Hz, 1H), 3.80 (dd, J = 11.2, 2.3 Hz, 1H), 3.56 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 151.5, 140.8, 136.6, 133.6, 132.5, 132.0, 130.0, 129.1, 128.9, 128.7, 127.5, 127.4, 127.3, 118.9, 117.0, 116.3, 110.6, 110.0, 107.3, 62.2, 55.1, 38.4.

HRMS (ESI-TOF, [M + Na]$^+$): For $C_{27}H_{22}N_4NaO_2$, 457.1640, found: 457.1638.

5-cyclopropyl-2-methoxy-4-phenyl-3,4-dihydropyrimido[1,6-*a*]indol-1(2*H*)-one (3ta)



3ta

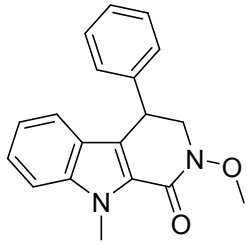
3ta was obtained in 87% (57.8 mg) as a white solid after column chromatography (eluent: petroleum ether/ethyl acetate = 8/1 v/v). Mp: 213-215^{o}C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.50 (d, J = 7.2 Hz, 1H), 7.67 (t, J = 6.4 Hz, 1H), 7.29 – 7.40 (m, 6H), 7.20 (d, J = 6.3 Hz, 2H), 4.76 (s, 1H), 4.17 -4.21 (m, 1H), 3.80-3.83 (m, 1H), 3.64 (s, 1H), 1.53 – 1.54 (m, 1H), 0.75 - 0.79 (m, 1H), 0.56 – 0.57 (m, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 152.3, 140.5, 134.9, 132.6, 130.6, 128.7, 127.5, 127.4, 124.3, 122.9, 119.2, 117.7, 115.7, 100.0, 62.3, 55.1, 38.7, 5.4, 4.9, 4.6.

HRMS (ESI-TOF, $[M + Na]^+$): For $C_{21}H_{20}N_2NaO_2$, 355.1422, found: 355.1425.

2-methoxy-9-methyl-4-phenyl-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-1-one (1ua)



3ua

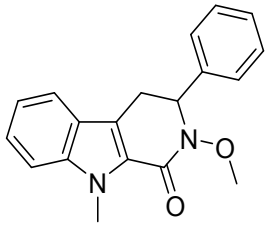
1ua was obtained in 15% (9.2 mg) as a yellow oil after column chromatography (eluent: petroleum ether/ethyl acetate = 8/1 v/v).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38 (d, J = 8.5 Hz, 1H), 7.36 – 7.27 (m, 5H), 6.99 – 6.91 (m, 2H), 4.61 (dd, J = 6.0, 8.3 Hz, 1H), 4.18 (s, 3H), 4.12 (dd, J = 6.0, 11.1 Hz, 1H), 3.86 (dd, J = 8.3, 11.1 Hz, 1H), 3.78 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 162.86, 140.47, 140.05, 128.74, 128.22, 127.52, 125.42, 125.02, 123.54, 121.25, 120.97, 120.27, 110.30, 100.00, 77.28, 77.02, 76.77, 62.42, 57.81, 39.87, 31.41.

HRMS (ESI-TOF, $[M + Na]^+$): For $C_{19}H_{18}N_2NaO_2$, 329.1266, found: 329.1269

2-methoxy-9-methyl-3-phenyl-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-1-one (3ua')



3ua'

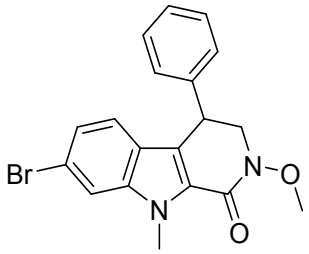
1ua' was obtained in 13% (8.0 mg) as a yellow oil after column chromatography (eluent: petroleum ether/ethyl acetate = 8/1 v/v).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.50 (d, J = 8.0 Hz, 1H), 7.39 (t, J = 8.2, 8.2 Hz, 3H), 7.36 – 7.31 (m, 2H), 7.29 (d, J = 7.2 Hz, 1H), 7.13 (ddd, J = 1.3, 6.5, 7.9 Hz, 1H), 5.16 (t, J = 6.8, 6.8 Hz, 1H), 4.16 (s, 3H), 3.77 (s, 3H), 3.56 (dd, J = 6.5, 16.2 Hz, 1H), 3.42 (dd, J = 7.1, 16.2 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 163.68, 139.94, 139.71, 128.50, 127.95, 127.09, 125.14, 123.94, 120.34, 120.25, 116.84, 110.33, 77.27, 77.02, 76.76, 65.41, 63.36, 31.36, 29.56.

HRMS (ESI-TOF, [M + Na]$^+$): For $C_{19}H_{18}N_2NaO_2$, 329.1266, found: 329.1269

7-bromo-2-methoxy-9-methyl-4-phenyl-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-1-one (3ra)



3va

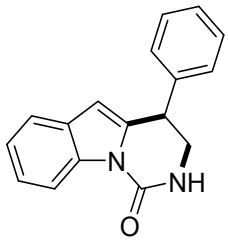
3va was obtained in 21% (16.2 mg) as a yellow solid after column chromatography (eluent: petroleum ether/ethyl acetate = 8/1 v/v). Mp: 185-187 ^{o}C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.58 (d, J = 1.7 Hz, 1H), 7.42 – 7.28 (m, 5H), 7.08 (dd, J = 1.7, 8.6 Hz, 1H), 6.79 (d, J = 8.5 Hz, 1H), 4.62 (dd, J = 6.0, 8.7 Hz, 1H), 4.18 (s, 3H), 4.13 (dd, J = 6.0, 11.1 Hz, 1H), 3.89 (dd, J = 8.8, 11.2 Hz, 1H), 3.83 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 162.44, 140.67, 140.07, 128.84, 128.19, 127.71, 125.94, 123.81, 122.47, 122.34, 121.10, 119.03, 113.38, 77.28, 77.03, 76.77, 62.46, 57.67, 39.81, 31.56.

HRMS (ESI-TOF, [M + Na]$^+$): For $C_{19}H_{17}BrN_2NaO_2$, 407.0371, found: 407.0374.

4-phenyl-3,4-dihydropyrimido[1,6-*a*]indol-1(2*H*)-one (4)



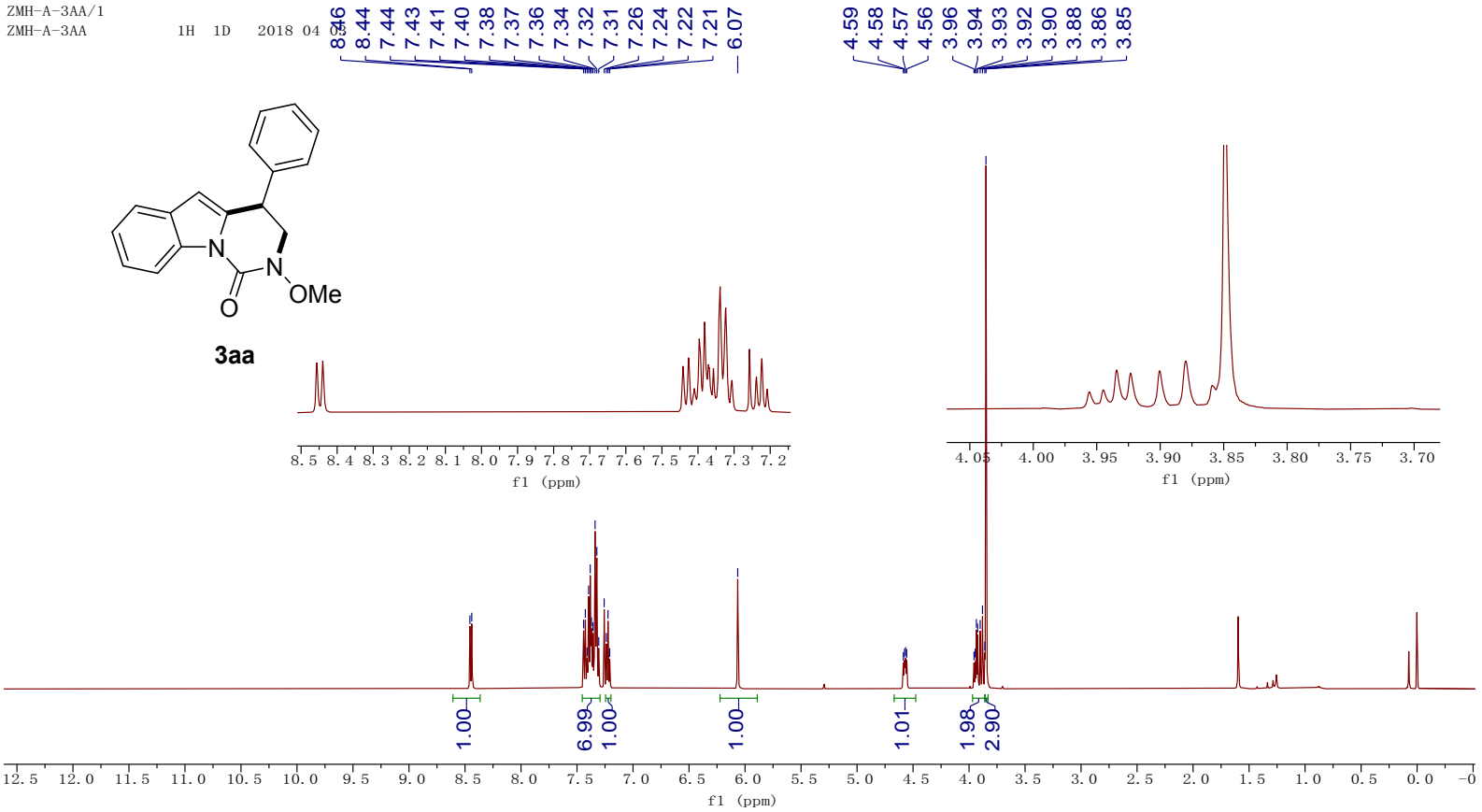
4

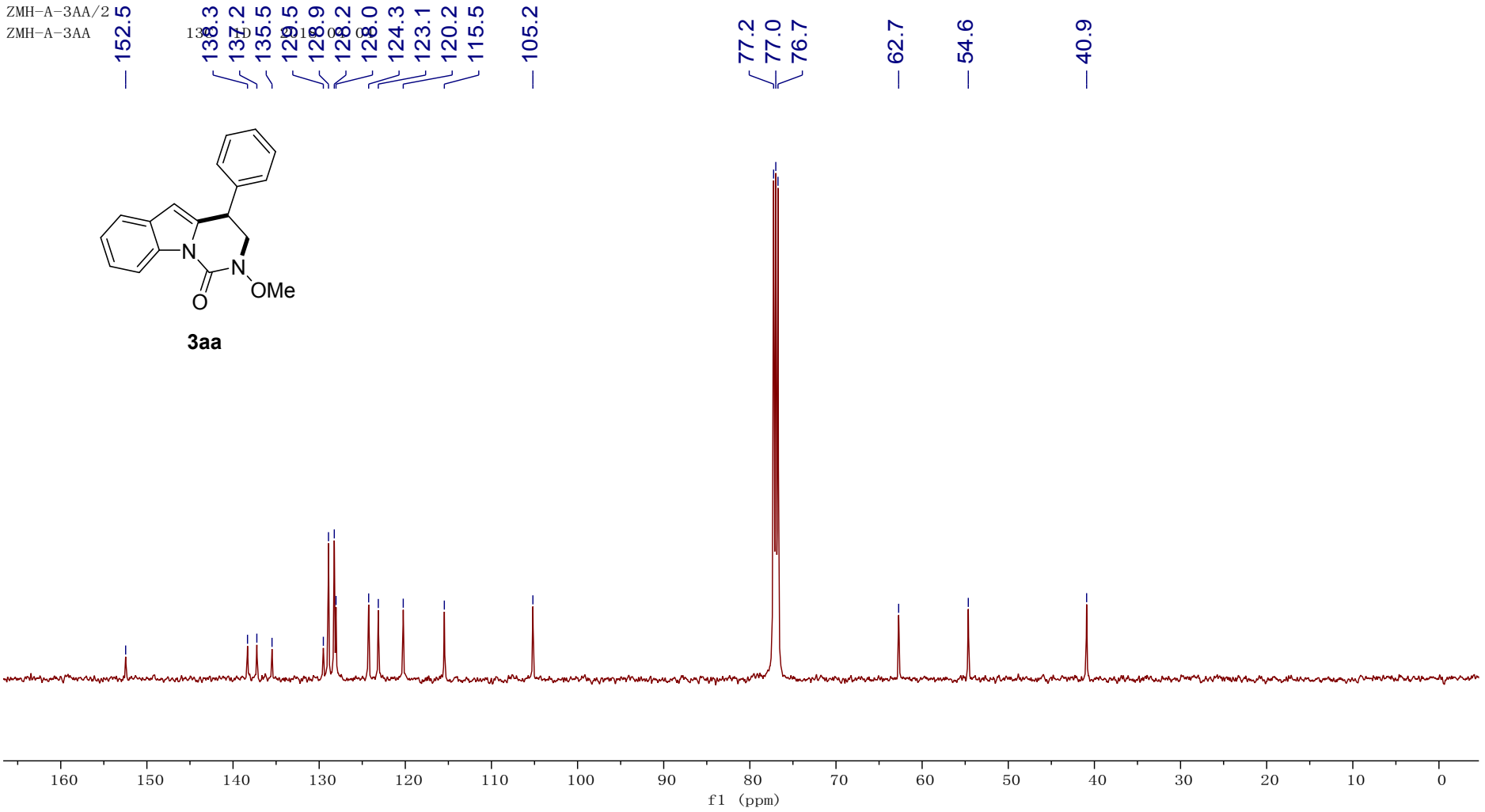
4 was obtained in 88% (23.1 mg) as a white solid after column chromatography (eluent: petroleum ether/ethyl acetate = 2/1 v/v). Mp: 175-177 ^{o}C.

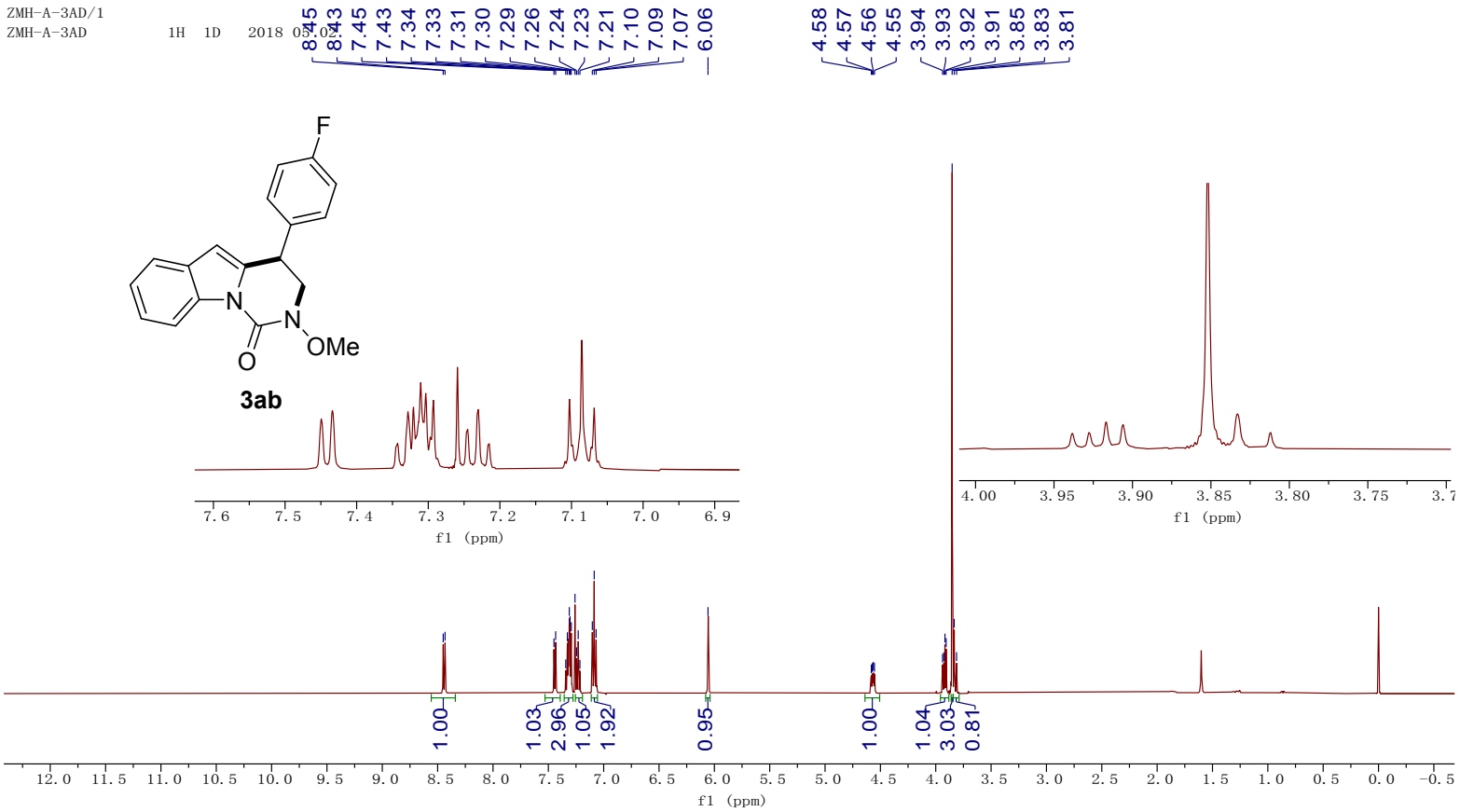
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.40 (s, 1H), 7.46 (d, J = 7.7 Hz, 1H), 7.36 (m, 7H) 7.22 (t, J = 7.4 Hz, 1H), 4.43 (s, 1H), 3.67 (s, 2H).

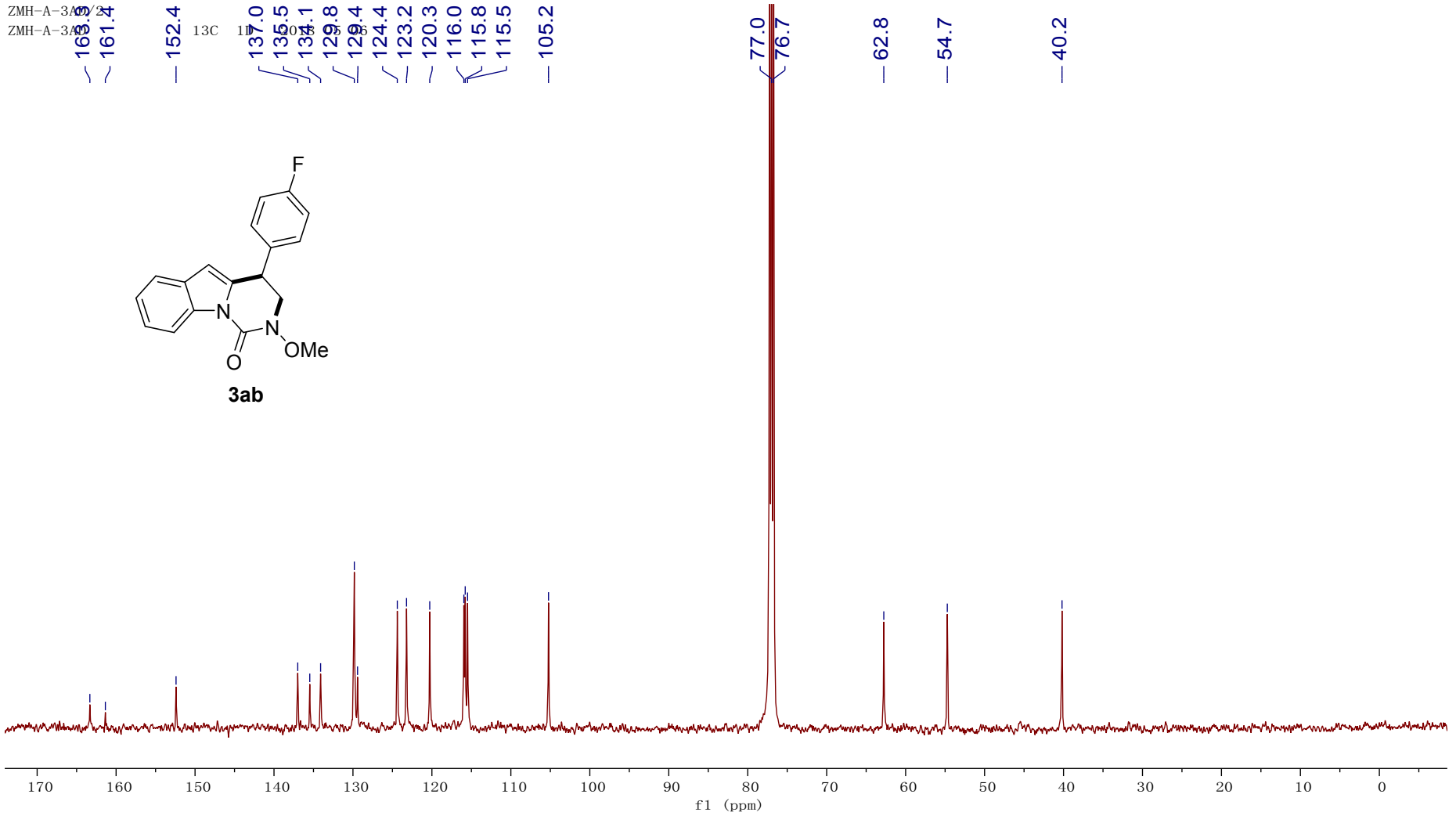
^{13}C NMR (126 MHz, $CDCl_3$): δ 138.55, 138.34, 135.43, 129.00, 128.84, 128.35, 127.84, 123.91, 122.80, 120.15, 115.23, 104.79, 77.25, 76.99, 76.74, 46.53, 40.73.

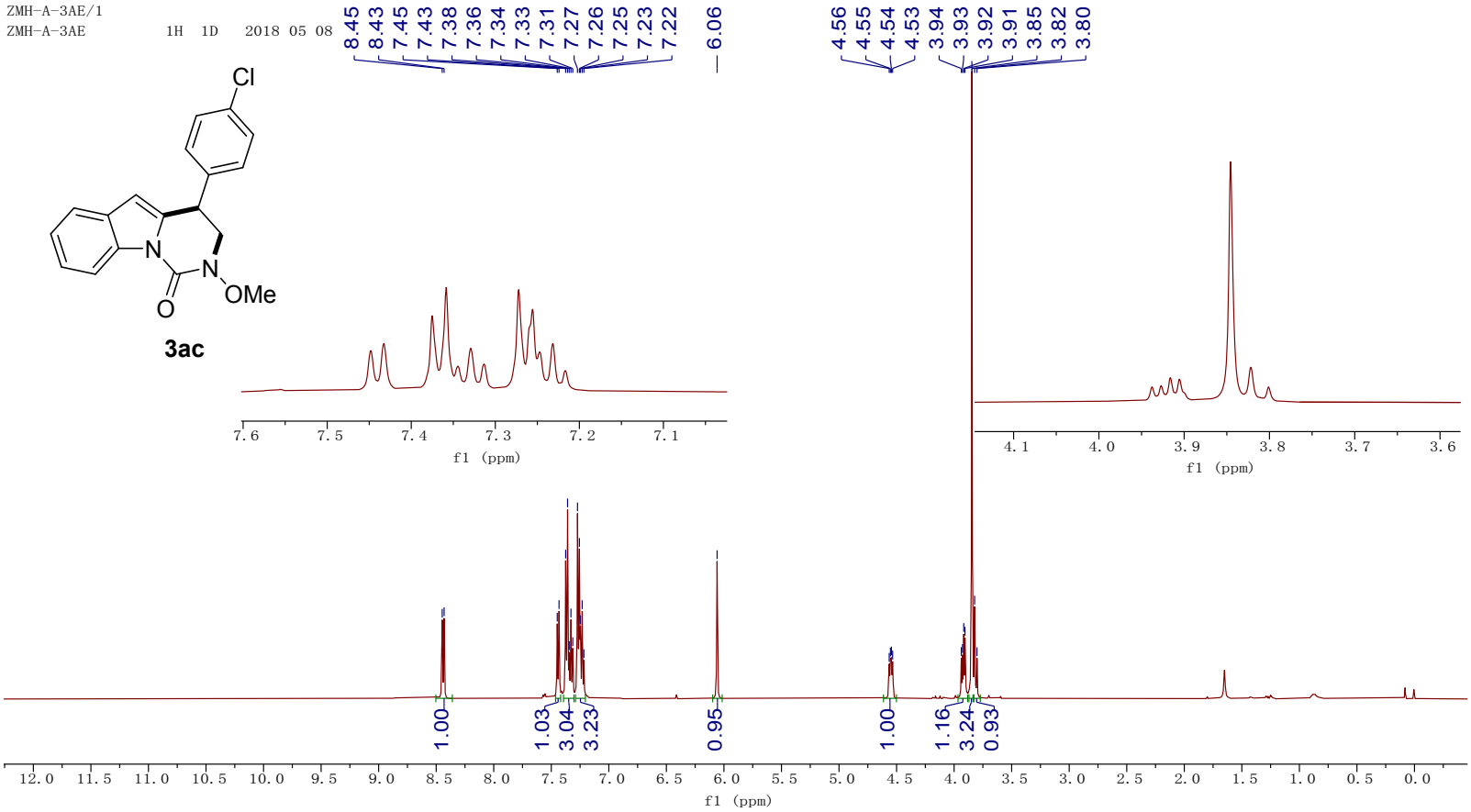
HRMS (ESI-TOF, [M + Na]$^+$): For $C_{17}H_{14}N_2NaO$, 285.1004, found: 285.1005.

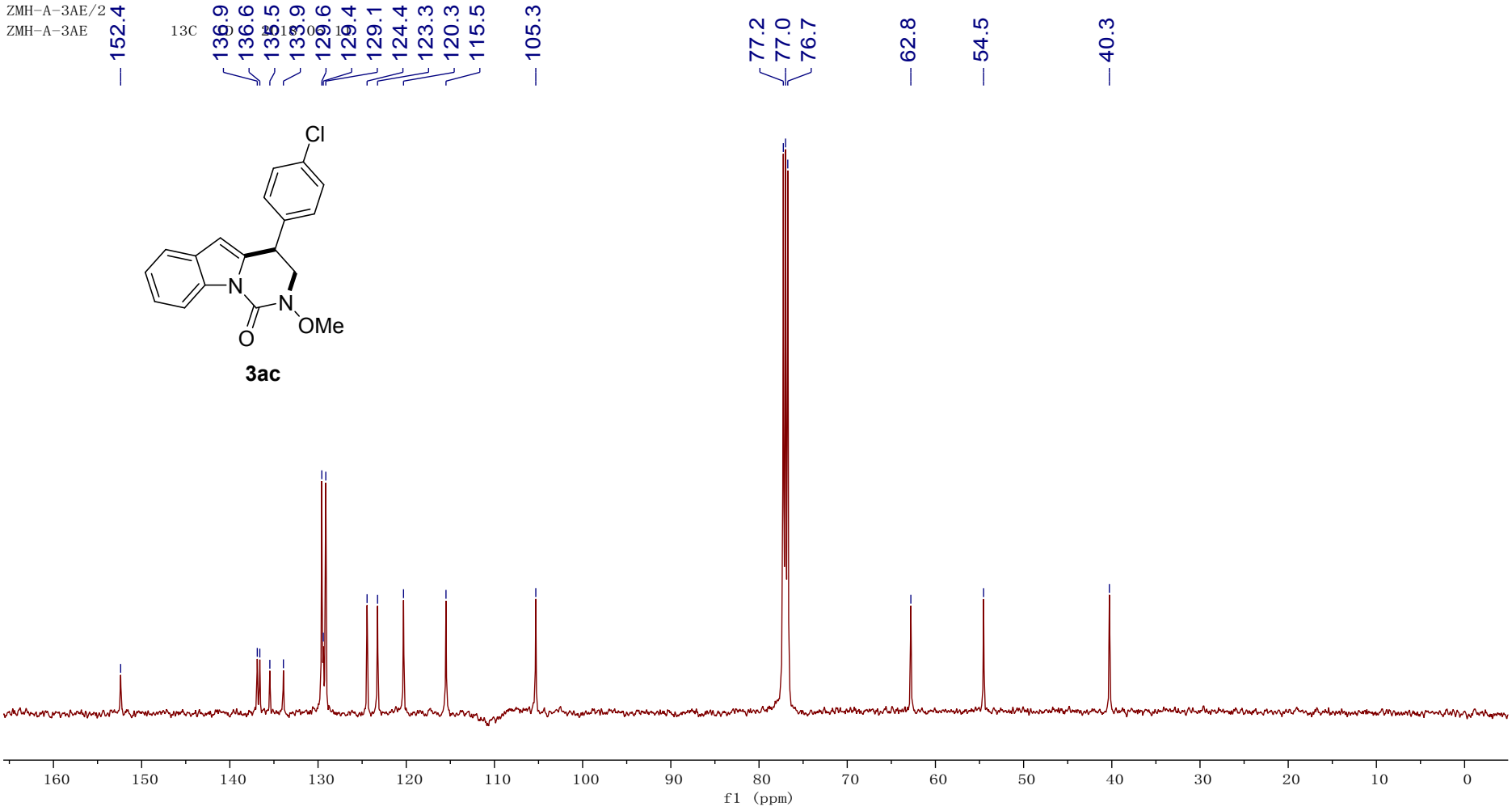

ZMH-A-3AA/1
ZMH-A-3AA 1H 1D 2018 04 05
8.46
8.44
7.44
7.43
7.41
7.40
7.38
7.37
7.36
7.34
7.32
7.31
7.26
7.24
7.22
7.21
6.07
4.59
4.58
4.57
4.56
3.96
3.94
3.93
3.92
3.90
3.88
3.86
3.85
N
N
OMe
O
3aa
f1 (ppm)
f1 (ppm)
1.00
6.99
1.00
1.00
1.01
1.98
2.90
f1 (ppm)

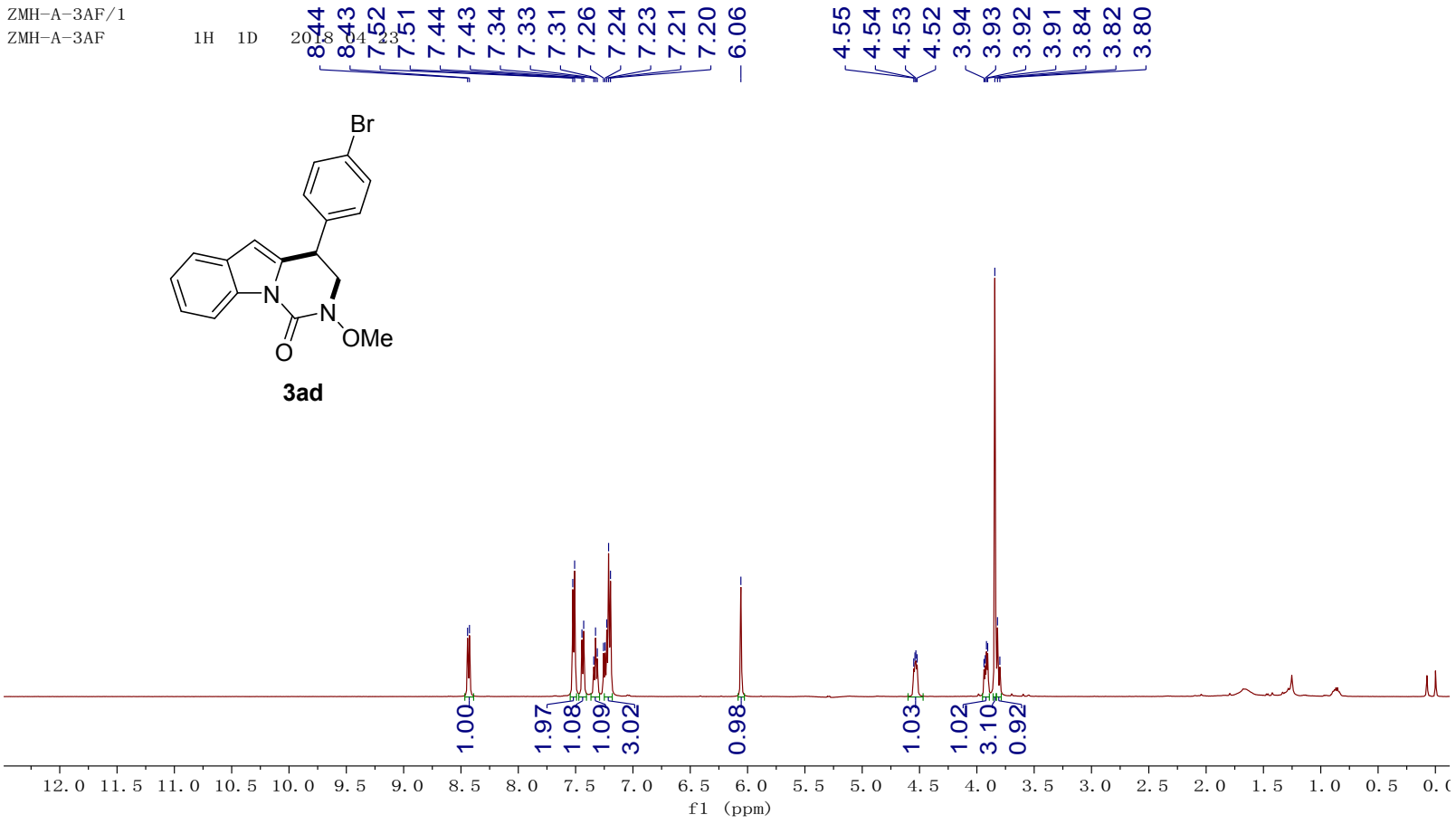

ZMH-A-3AA/2
ZMH-A-3AA
152.5
138.3
137.2
135.5
129.5
128.9
128.2
128.0
124.3
123.1
120.2
115.5
105.2
77.2
77.0
76.7
62.7
54.6
40.9
N
N
OMe
O
3aa
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

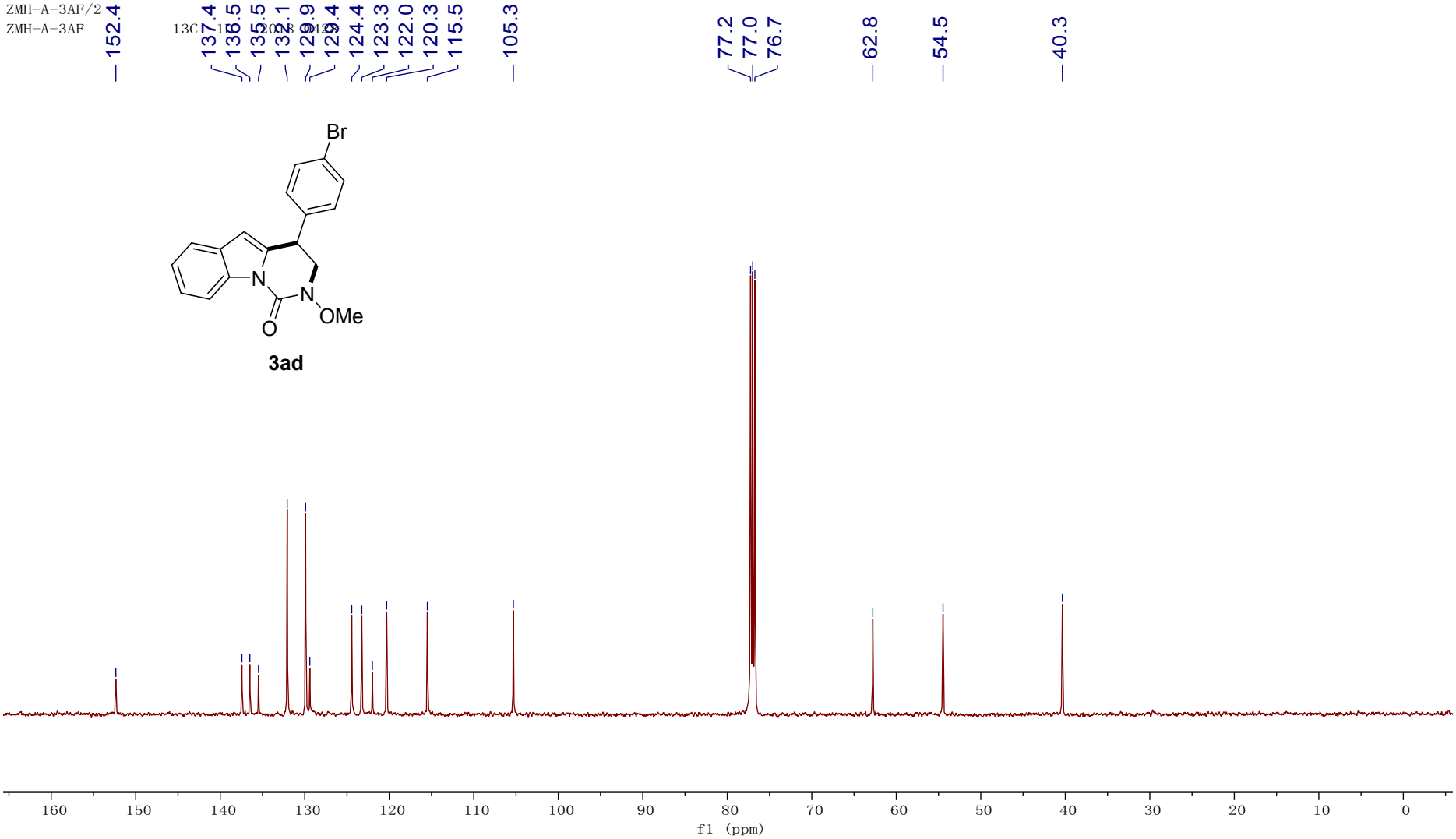

ZMH-A-3AD/1
ZMH-A-3AD 1H 1D 2018 05 02
8.45
8.43
7.45
7.43
7.34
7.33
7.31
7.30
7.29
7.26
7.24
7.23
7.21
7.10
7.09
7.07
6.06
4.58
4.57
4.56
4.55
3.94
3.93
3.92
3.91
3.85
3.83
3.81
F
N
N
OMe
O
3ab
1.00
1.03
2.96
1.05
1.92
0.95
1.00
1.04
3.03
0.81
f1 (ppm)


ZMH-A-3AB/2
ZMH-A-3AB 13C 1T 2018 5 26
163.3
161.4
152.4
137.0
135.5
134.1
129.8
129.4
124.4
123.2
120.3
116.0
115.8
115.5
105.2
77.0
76.7
62.8
54.7
40.2
F
N
N
OMe
O
3ab
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

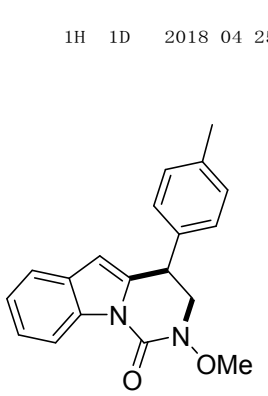

ZMH-A-3AE/1
ZMH-A-3AE 1H 1D 2018 05 08
8.45 8.43 7.45 7.43 7.38 7.36 7.34 7.33 7.31 7.27 7.26 7.25 7.23 7.22 6.06
4.56 4.55 4.54 4.53 3.94 3.93 3.92 3.91 3.85 3.82 3.80
Cl
N
N
OMe
O
3ac
7.6 7.5 7.4 7.3 7.2 7.1
f1 (ppm)
4.1 4.0 3.9 3.8 3.7 3.6
f1 (ppm)
1.00 1.03 3.04 3.23 0.95 1.00 1.16 3.24 0.93
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


ZMH-A-3AE/2
ZMH-A-3AE
152.4
136.9
136.6
135.5
133.9
129.6
129.4
129.1
124.4
123.3
120.3
115.5
105.3
77.2
77.0
76.7
62.8
54.5
40.3
Cl
N
N
OMe
O
3ac
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

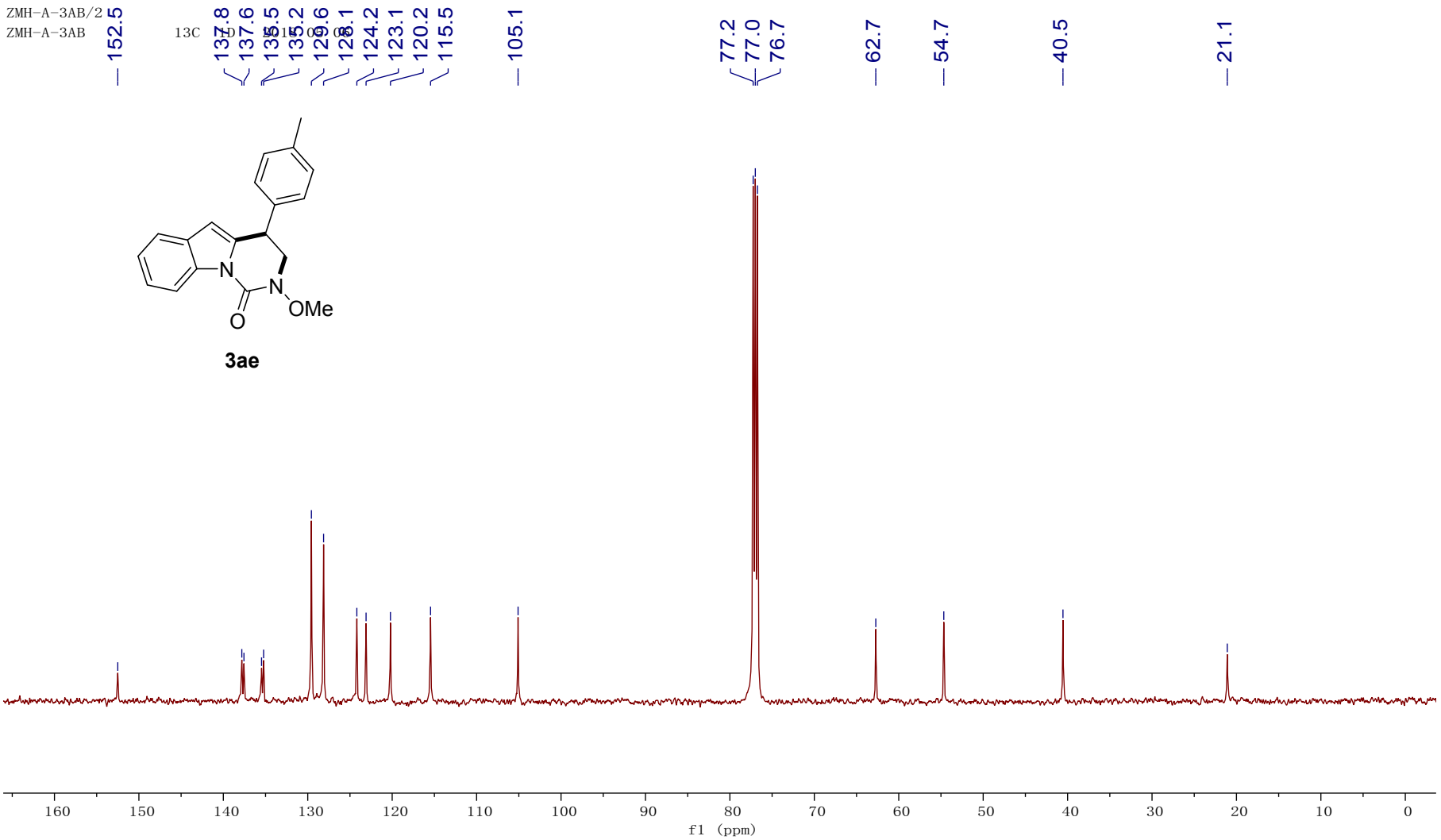

ZMH-A-3AF/1
ZMH-A-3AF 1H 1D 2018 04 23
8.44
8.43
7.52
7.51
7.44
7.43
7.34
7.33
7.31
7.26
7.24
7.23
7.21
7.20
6.06
4.55
4.54
4.53
4.52
3.94
3.93
3.92
3.91
3.84
3.82
3.80
Br
N
N
OMe
O
3ad
1.00
1.97
1.08
1.09
3.02
0.98
1.03
1.02
3.10
0.92
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

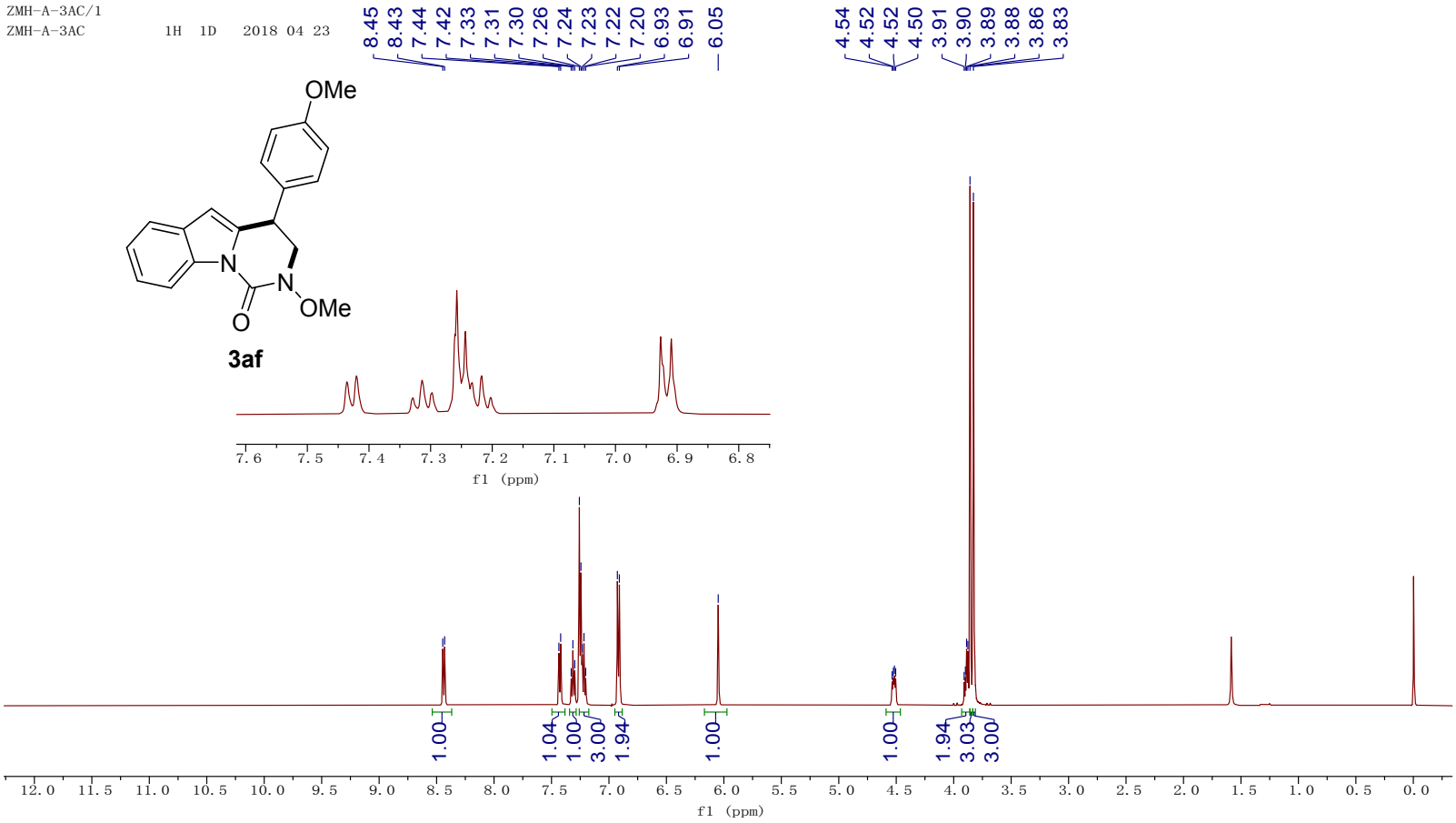

ZMH-A-3AF/2
ZMH-A-3AF
152.4
137.4
136.5
135.5
132.1
129.9
129.4
124.4
123.3
122.0
120.3
115.5
105.3
77.2
77.0
76.7
62.8
54.5
40.3
Br
N
N
OMe
O
3ad
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

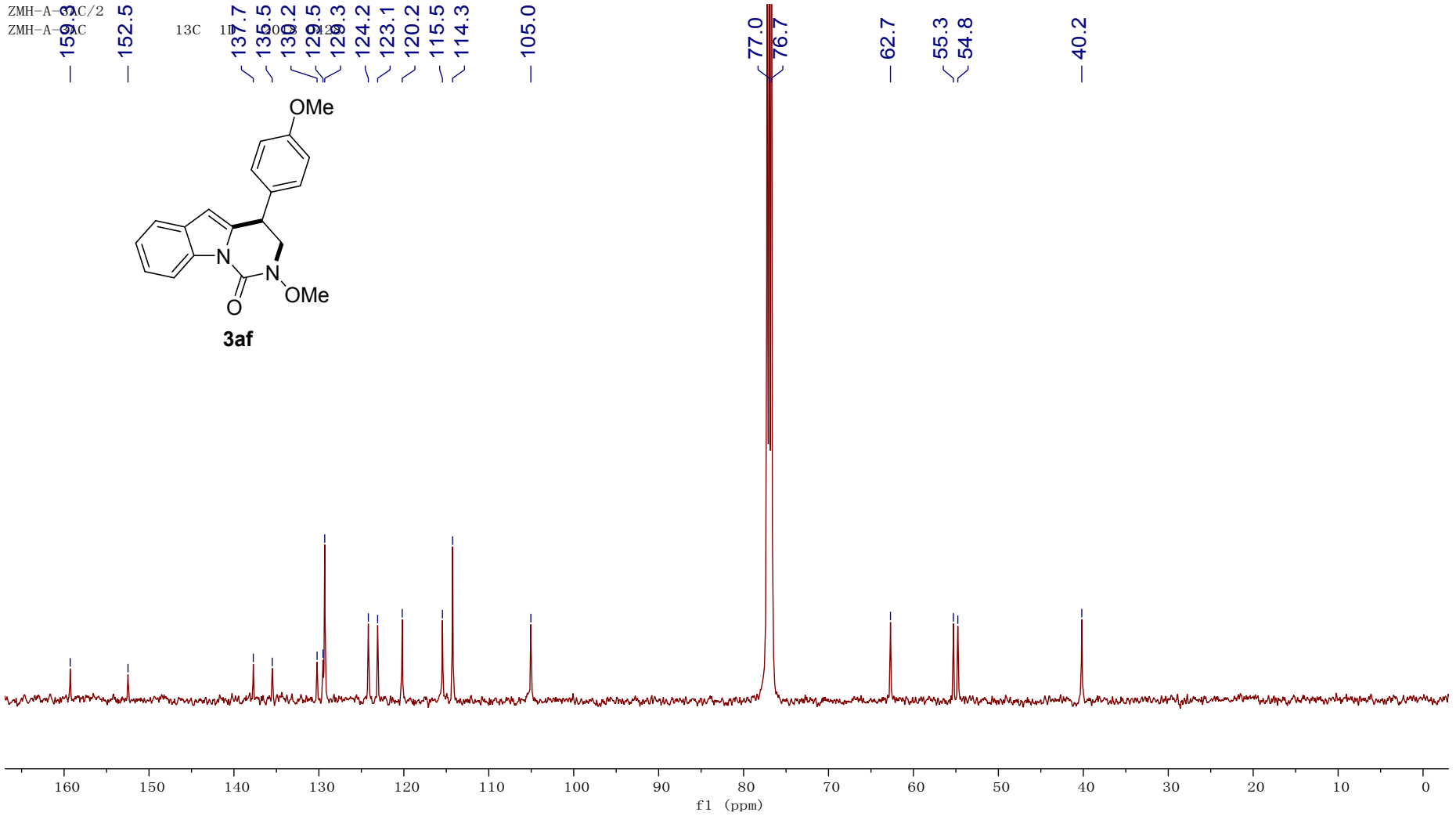
ZMH-A-3AR/1
ZMH-A-3AR 1H 1D 2018 04 25

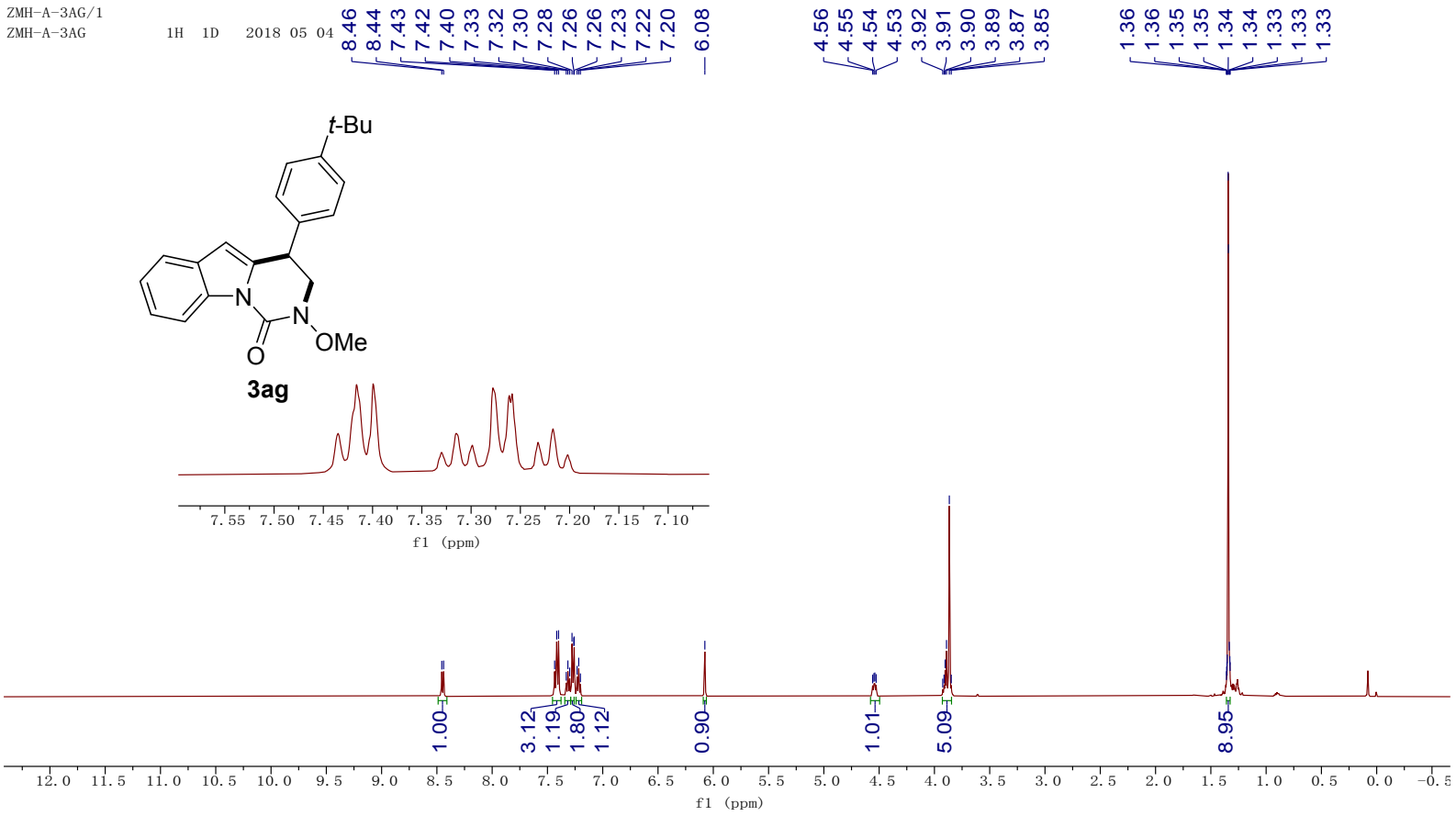


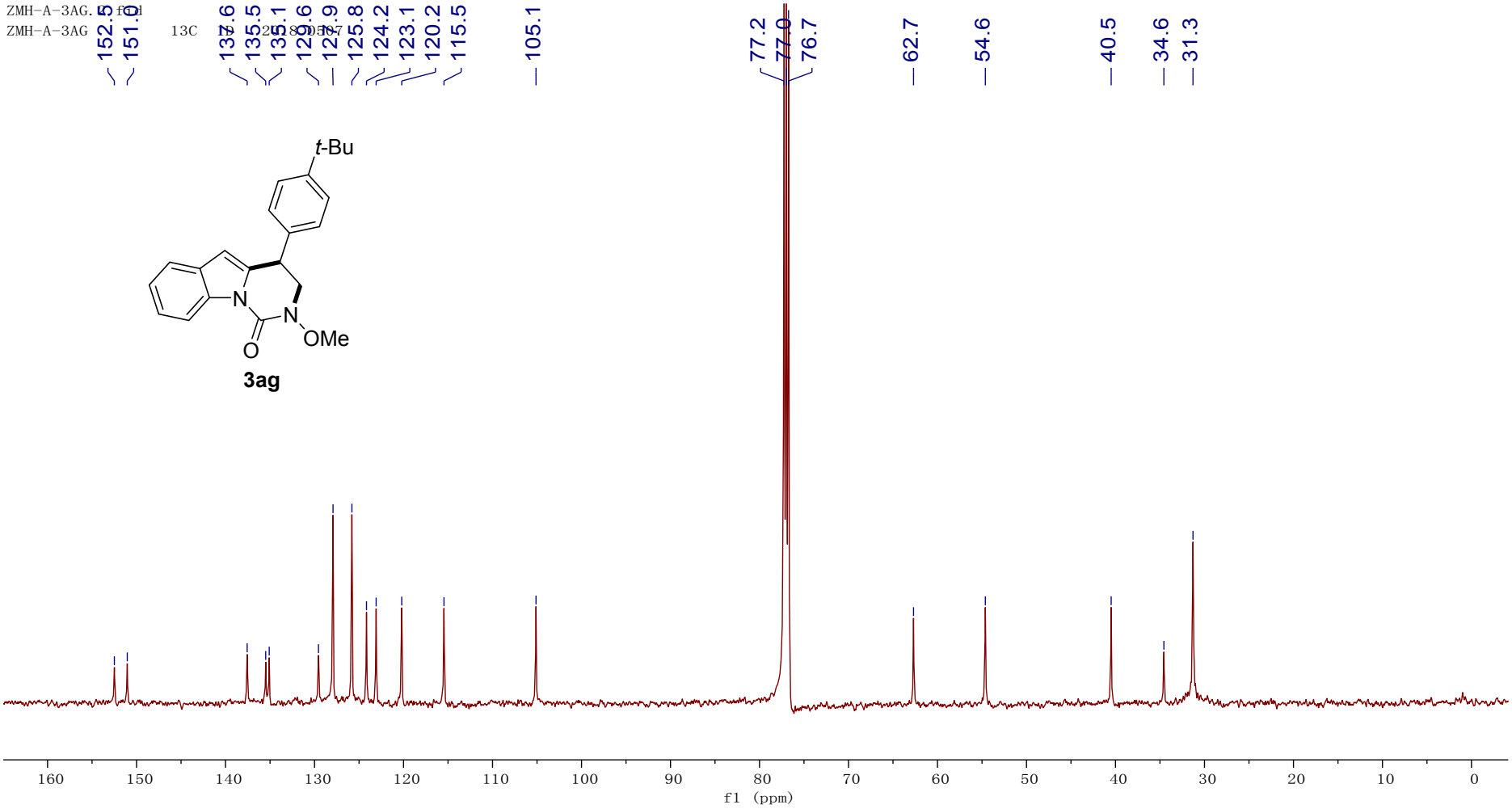
3ae

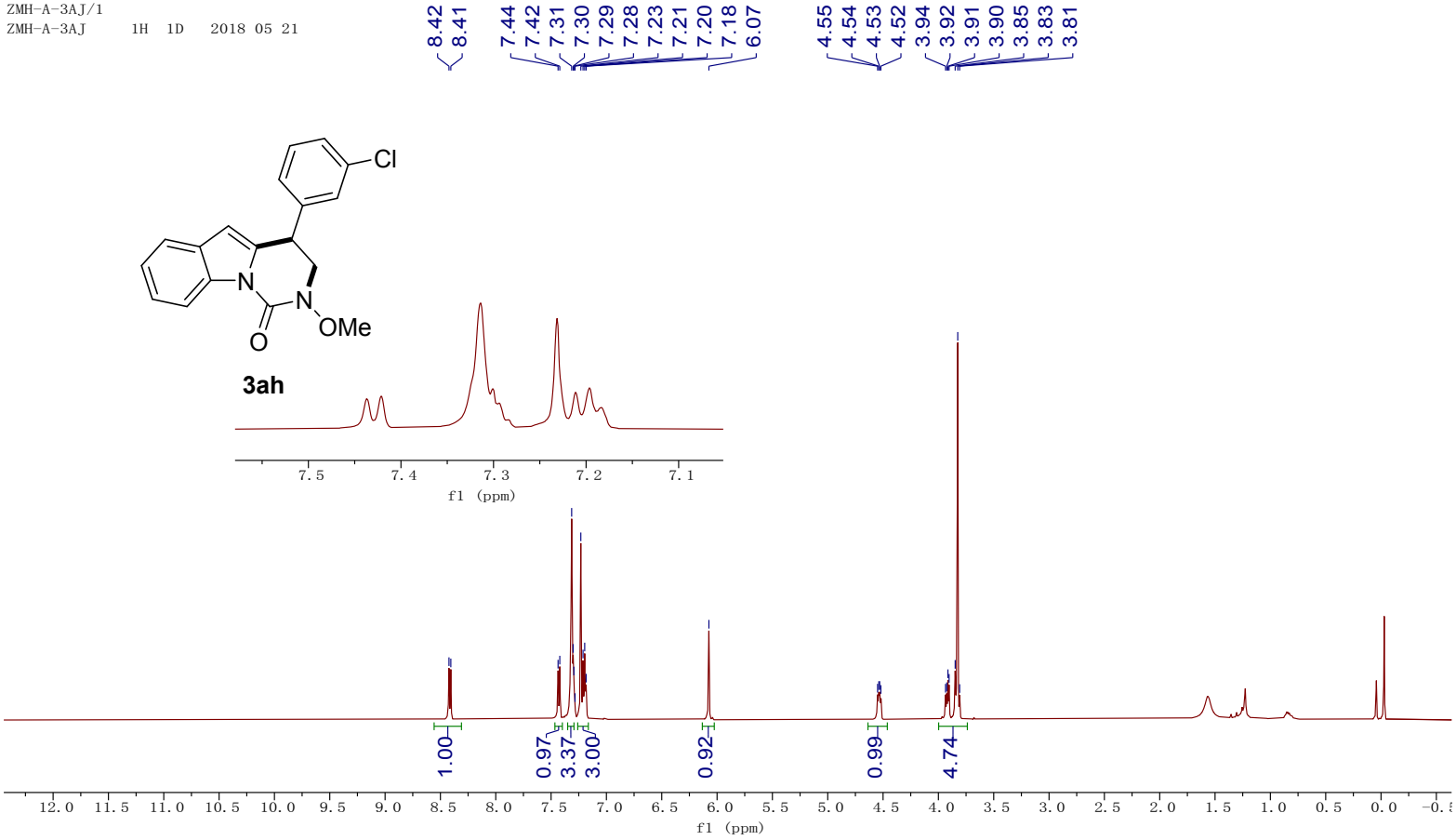

ZMH-A-3AB/2
ZMH-A-3AB
152.5
137.8
137.6
135.5
135.2
129.6
128.1
124.2
123.1
120.2
115.5
105.1
77.2
77.0
76.7
62.7
54.7
40.5
21.1
N
N
OMe
O
3ae
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

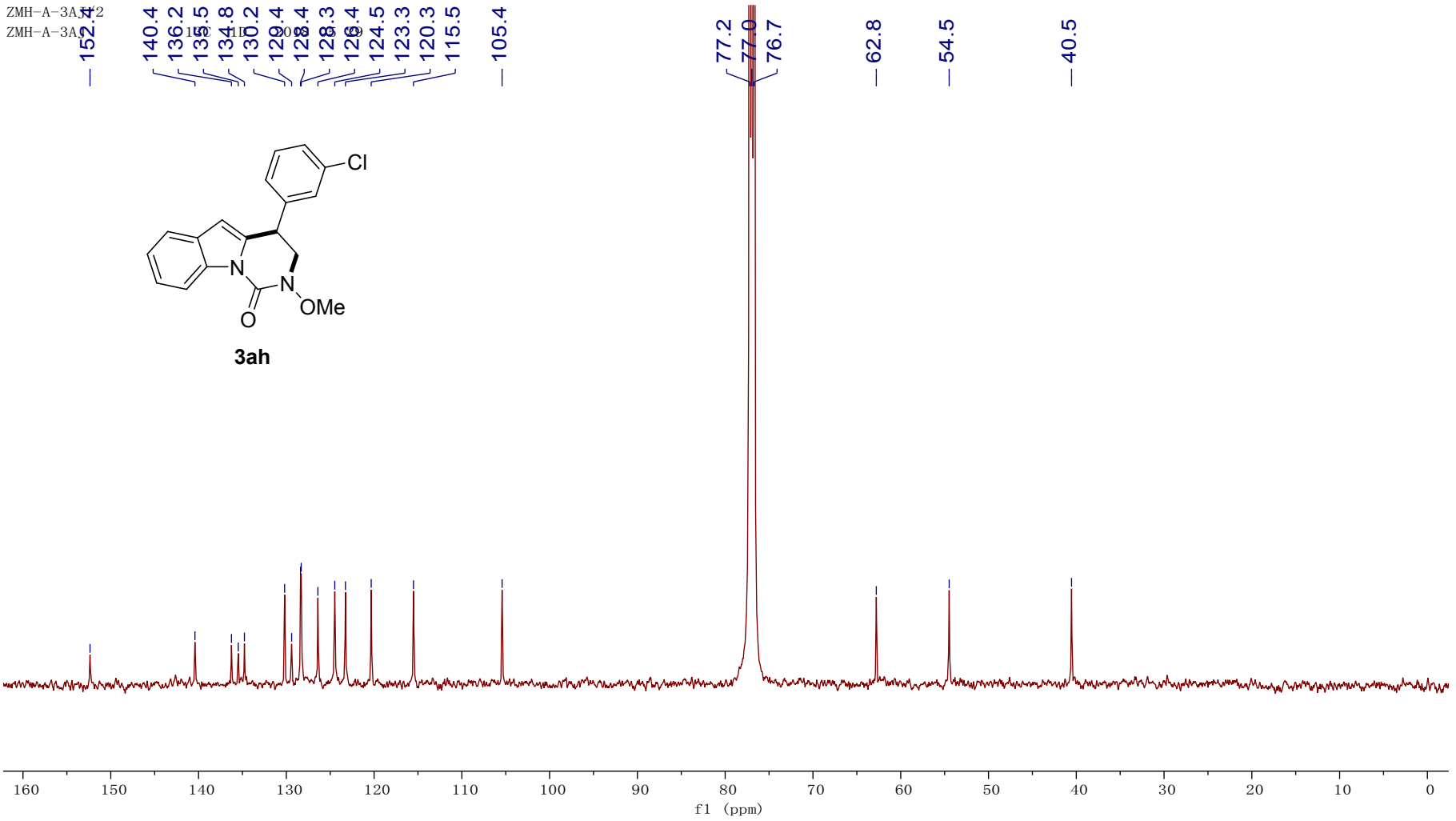

ZMH-A-3AC/1
ZMH-A-3AC 1H 1D 2018 04 23
8.45
8.43
7.44
7.42
7.33
7.31
7.30
7.26
7.24
7.23
7.22
7.20
6.93
6.91
6.05
4.54
4.52
4.52
4.50
3.91
3.90
3.89
3.88
3.86
3.83
OMe
N
N
OMe
O
3af
7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9 6.8
f1 (ppm)
1.00
1.04
1.00
3.00
1.94
1.00
1.00
1.94
3.03
3.00
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

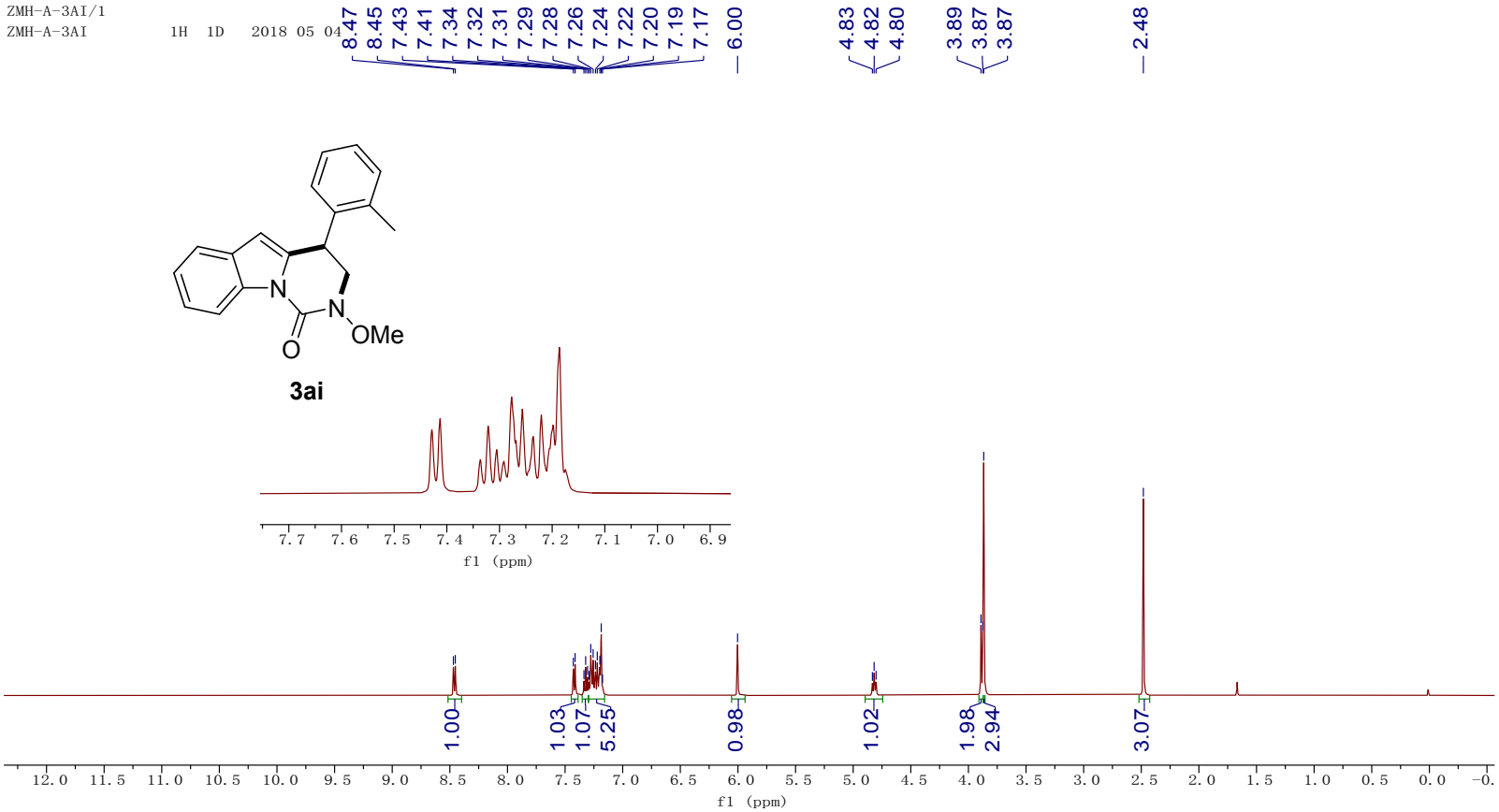

ZMH-A-3AC/2
ZMH-A-3AC
13C
159.4
152.5
137.7
135.5
130.2
129.5
129.3
124.2
123.1
120.2
115.5
114.3
105.0
77.0
76.7
62.7
55.3
54.8
40.2
OMe
N
N
OMe
O
3af
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

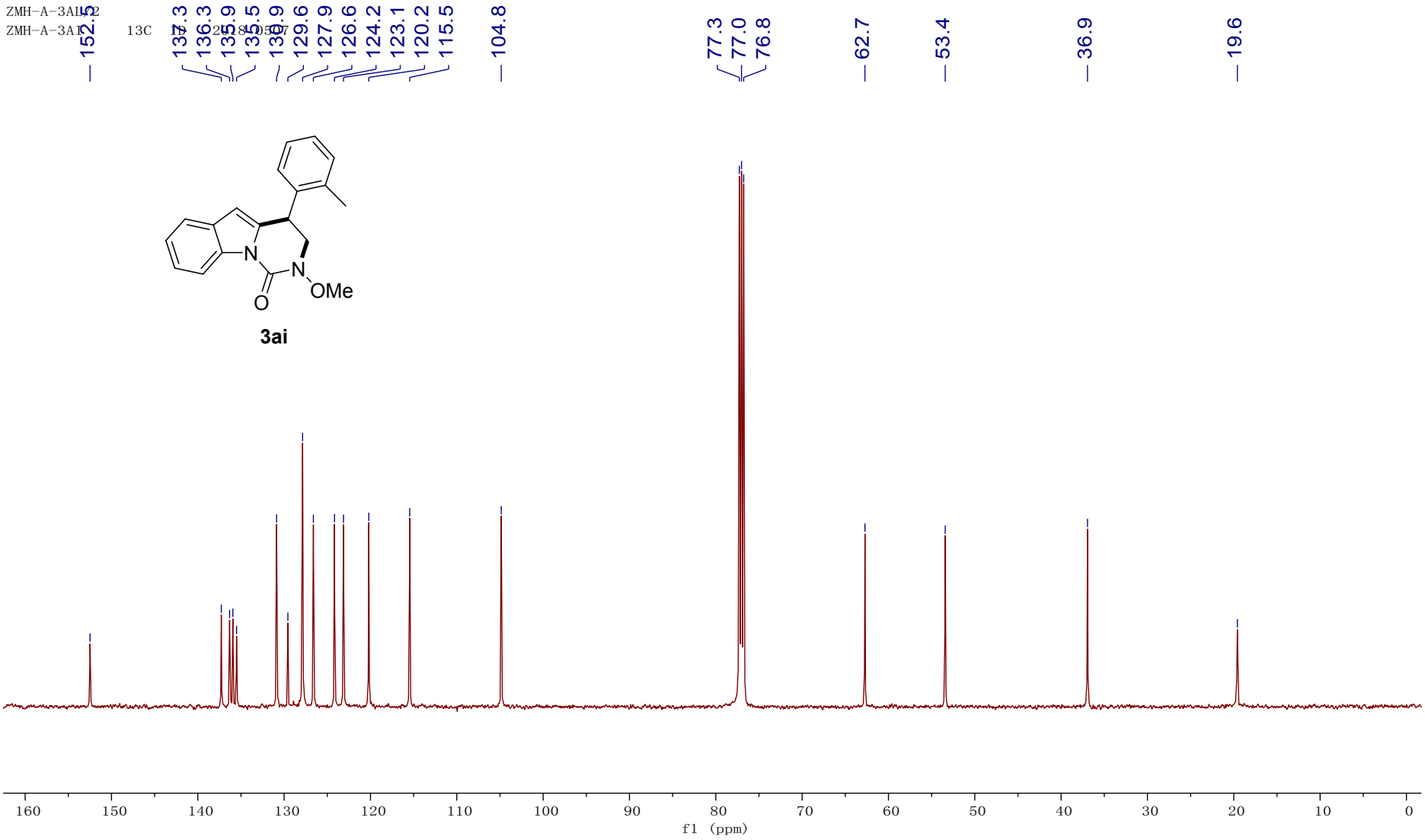

ZMH-A-3AG/1
ZMH-A-3AG 1H 1D 2018 05 04
8.46 8.44 7.43 7.42 7.40 7.33 7.32 7.30 7.28 7.26 7.26 7.23 7.22 7.20 6.08
4.56 4.55 4.54 4.53 3.92 3.91 3.90 3.89 3.87 3.85
1.36 1.36 1.35 1.35 1.34 1.34 1.33 1.33 1.33
t-Bu
N
N
OMe
O
3ag
7.55 7.50 7.45 7.40 7.35 7.30 7.25 7.20 7.15 7.10
f1 (ppm)
1.00 3.12 1.19 1.80 1.12 0.90 1.01 5.09 8.95
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5
f1 (ppm)

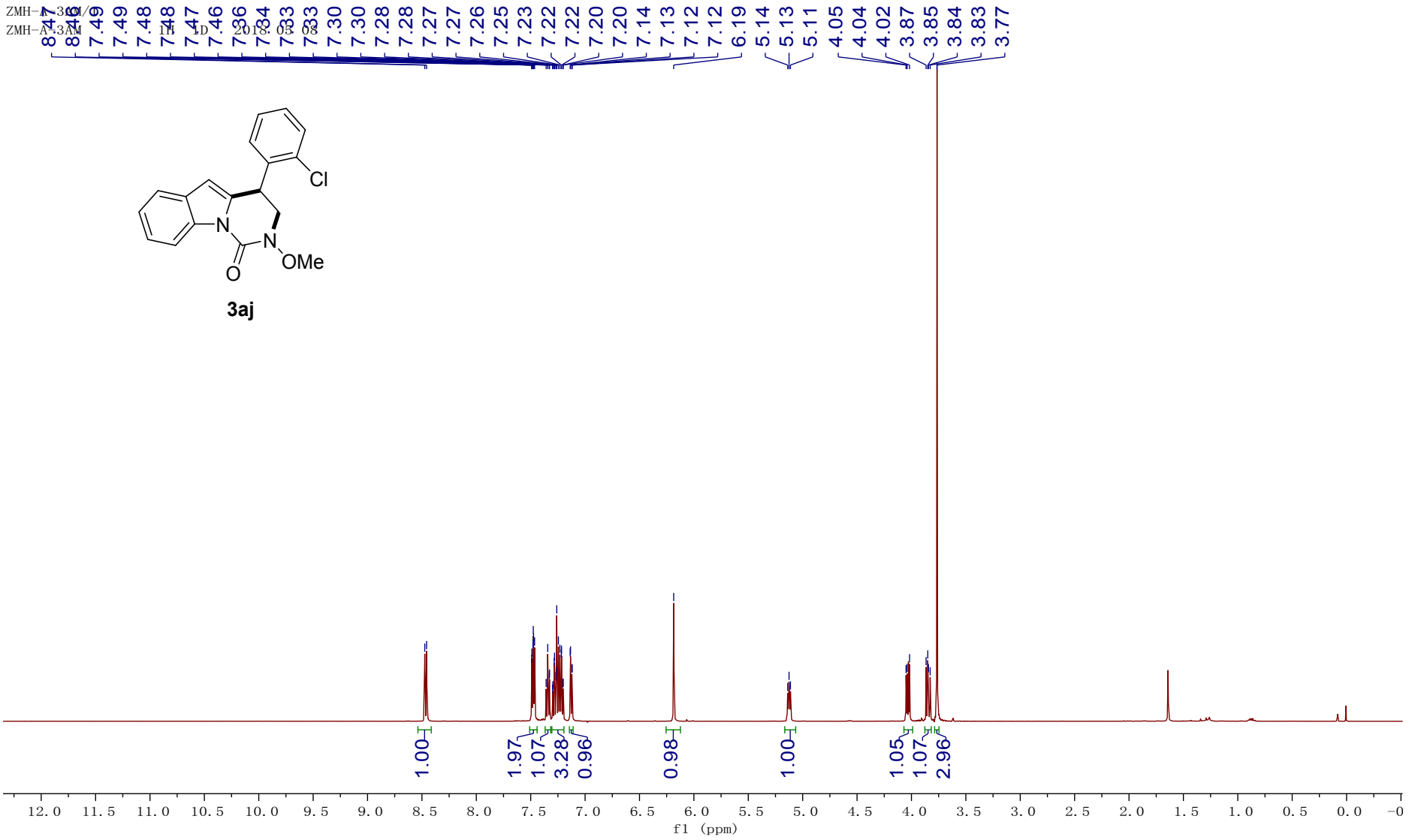

ZMH-A-3AG.fid
ZMH-A-3AG 13C
152.5
151.6
135.6
135.5
135.1
129.6
129.9
125.8
124.2
123.1
120.2
115.5
105.1
77.2
77.0
76.7
62.7
54.6
40.5
34.6
31.3
t-Bu
N
N
OMe
O
3ag
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

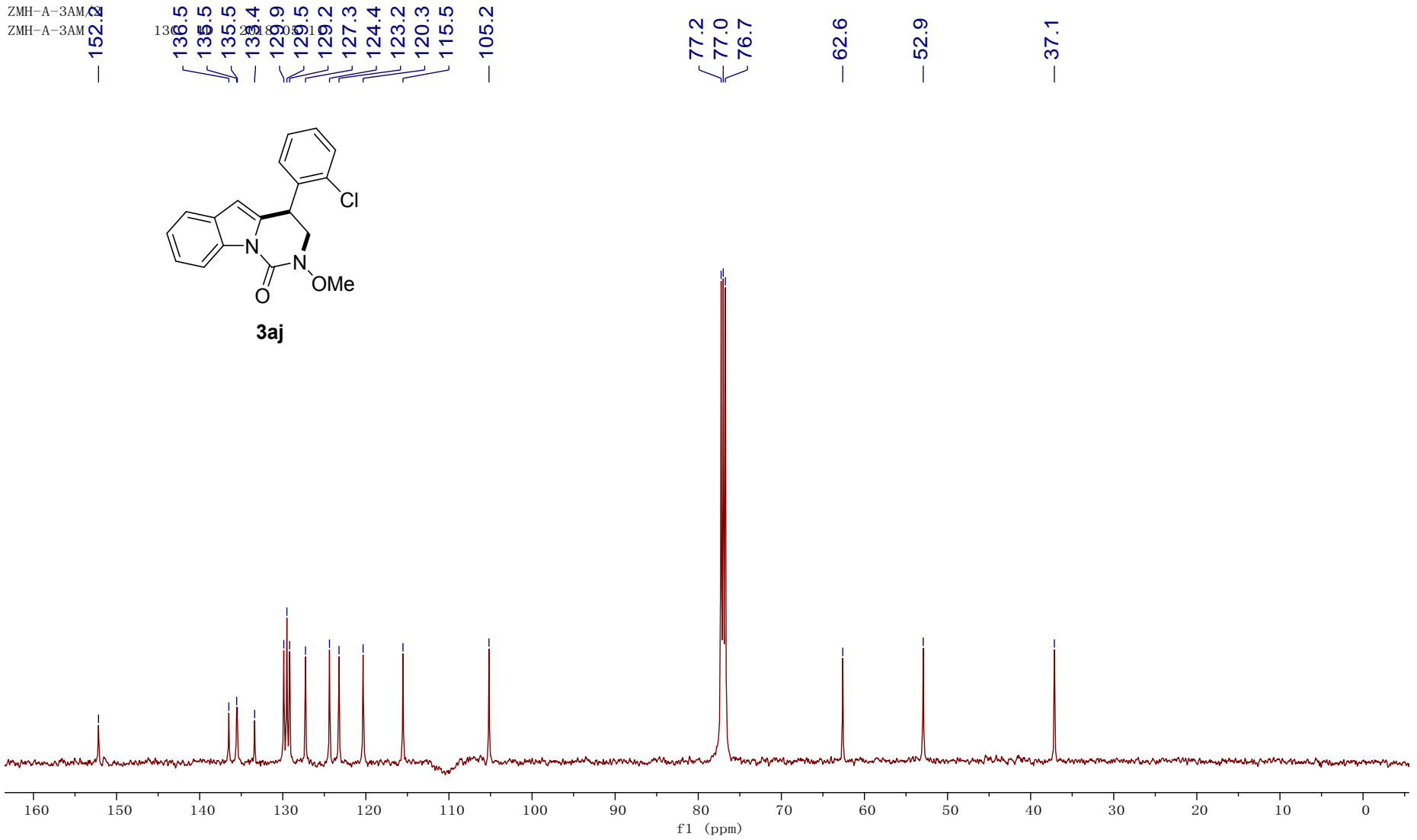

ZMH-A-3AJ/1
ZMH-A-3AJ 1H 1D 2018 05 21
8.42
8.41
7.44
7.42
7.31
7.30
7.29
7.28
7.23
7.21
7.20
7.18
6.07
4.55
4.54
4.53
4.52
3.94
3.92
3.91
3.90
3.85
3.83
3.81
Cl
N
N
OMe
O
3ah
7.5
7.4
7.3
7.2
7.1
f1 (ppm)
1.00
0.97
3.37
3.00
0.92
0.99
4.74
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

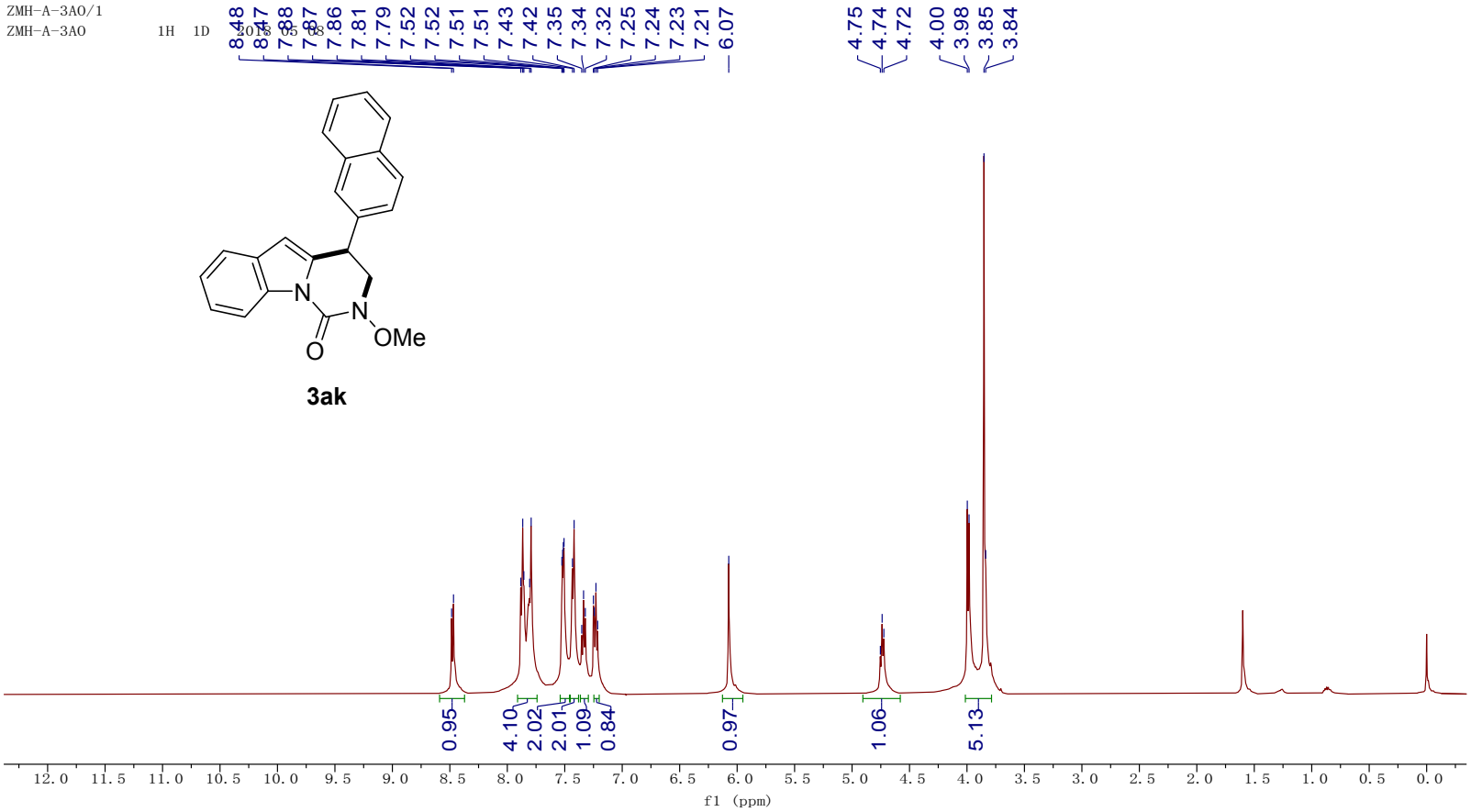

ZMH-A-3AH-2
152.4
140.4
136.2
135.5
134.8
130.2
129.4
128.4
128.3
126.4
124.5
123.3
120.3
115.5
105.4
77.2
77.0
76.7
62.8
54.5
40.5
Cl
N
N
OMe
O
3ah
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

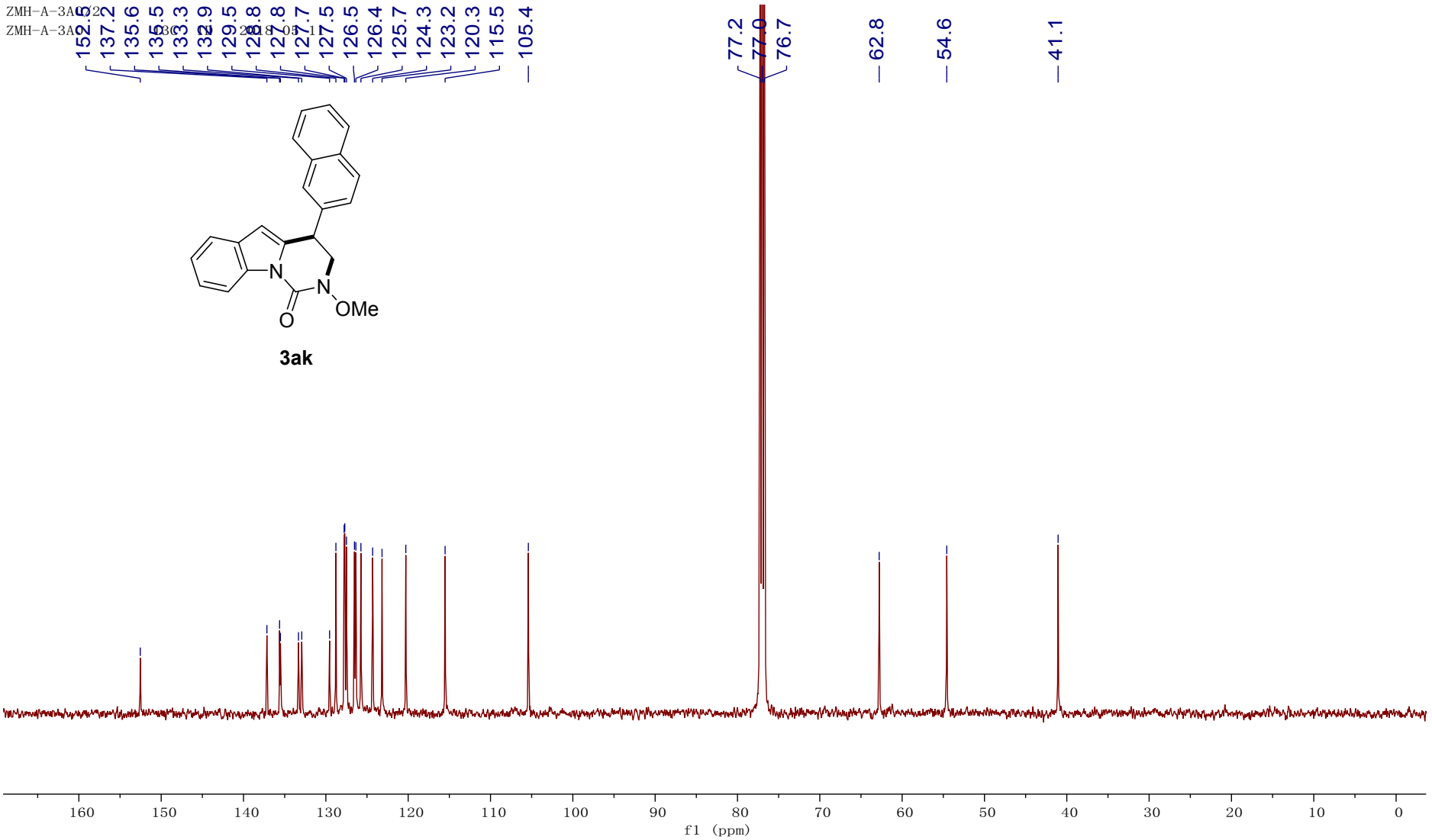

ZMH-A-3AI/1
ZMH-A-3AI 1H 1D 2018 05 04
8.47
8.45
7.43
7.41
7.34
7.32
7.31
7.29
7.28
7.26
7.24
7.22
7.20
7.19
7.17
6.00
4.83
4.82
4.80
3.89
3.87
3.87
2.48
N
N
OMe
O
3ai
7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9
f1 (ppm)
1.00
1.03
1.07
5.25
0.98
1.02
1.98
2.94
3.07
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.
f1 (ppm)


ZMH-A-3AL2
ZMH-A-3AL2 13C
152.2
137.3
136.3
135.9
135.5
130.9
129.6
127.9
126.6
124.2
123.1
120.2
115.5
104.8
77.3
77.0
76.8
62.7
53.4
36.9
19.6
N
N
OMe
O
3ai
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

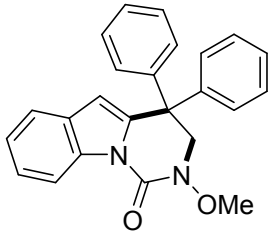

ZMH-A-3AM/9
ZMH-A-3AM 1H 1D 2018.03.08
8.47
8.46
7.49
7.49
7.48
7.48
7.47
7.46
7.36
7.34
7.33
7.33
7.30
7.30
7.28
7.28
7.27
7.27
7.26
7.25
7.23
7.22
7.22
7.20
7.20
7.14
7.13
7.12
7.12
6.19
5.14
5.13
5.11
4.05
4.04
4.02
3.87
3.85
3.84
3.83
3.77
Cl
N
N
OMe
O
3aj
1.00
1.97
1.07
3.28
0.96
0.98
1.00
1.05
1.07
2.96
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0
f1 (ppm)


ZMH-A-3AM.10.1
ZMH-A-3AM
152.2
136.5
135.5
135.5
130.4
129.9
129.5
129.2
127.3
124.4
123.2
120.3
115.5
105.2
77.2
77.0
76.7
62.6
52.9
37.1
Cl
N
N
OMe
O
3aj
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

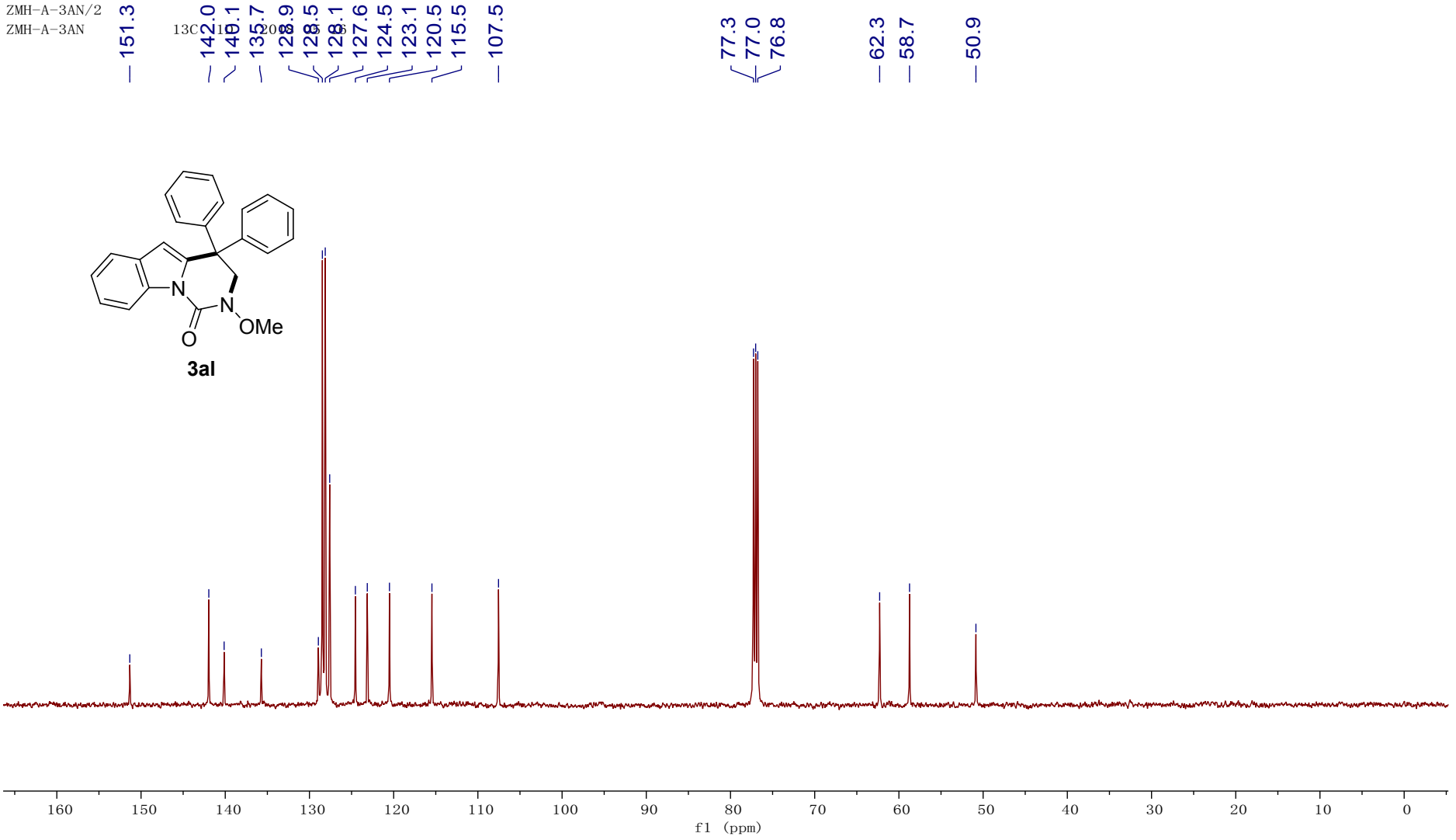

ZMH-A-3AO/1
ZMH-A-3AO 1H 1D 2018 05 08
8.48
8.47
7.88
7.87
7.86
7.81
7.79
7.52
7.52
7.51
7.51
7.43
7.42
7.35
7.34
7.32
7.25
7.24
7.23
7.21
6.07
4.75
4.74
4.72
4.00
3.98
3.85
3.84
N
N
O
OMe
3ak
0.95
4.10
2.02
2.01
1.09
0.84
0.97
1.06
5.13
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

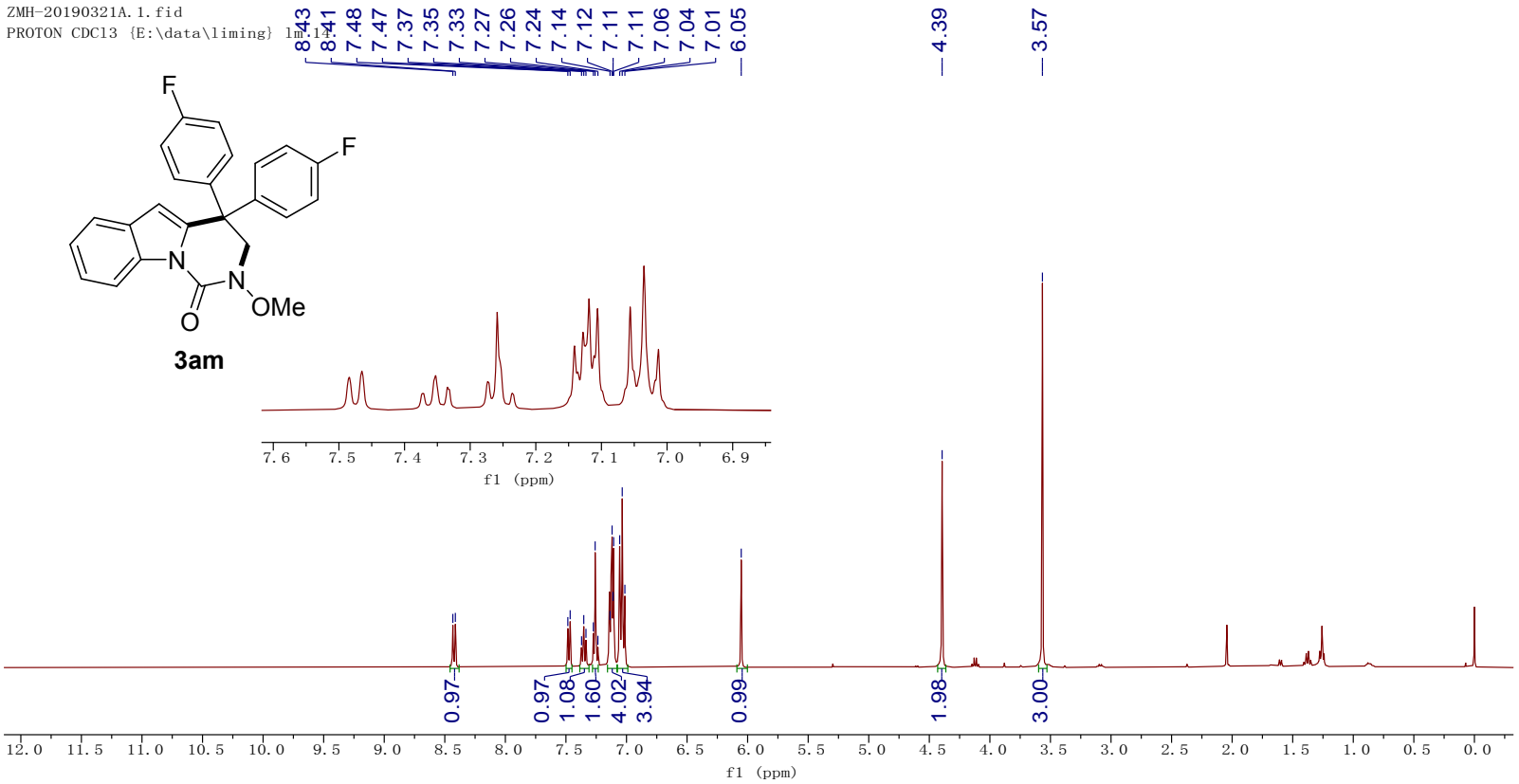

ZMH-A-3AA-2
152.5
137.2
135.6
135.5
133.3
132.9
129.5
128.8
127.8
127.7
127.5
126.5
126.4
125.7
124.3
123.2
120.3
115.5
105.4
77.2
77.0
76.7
62.8
54.6
41.1
N
N
OMe
O
3ak
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

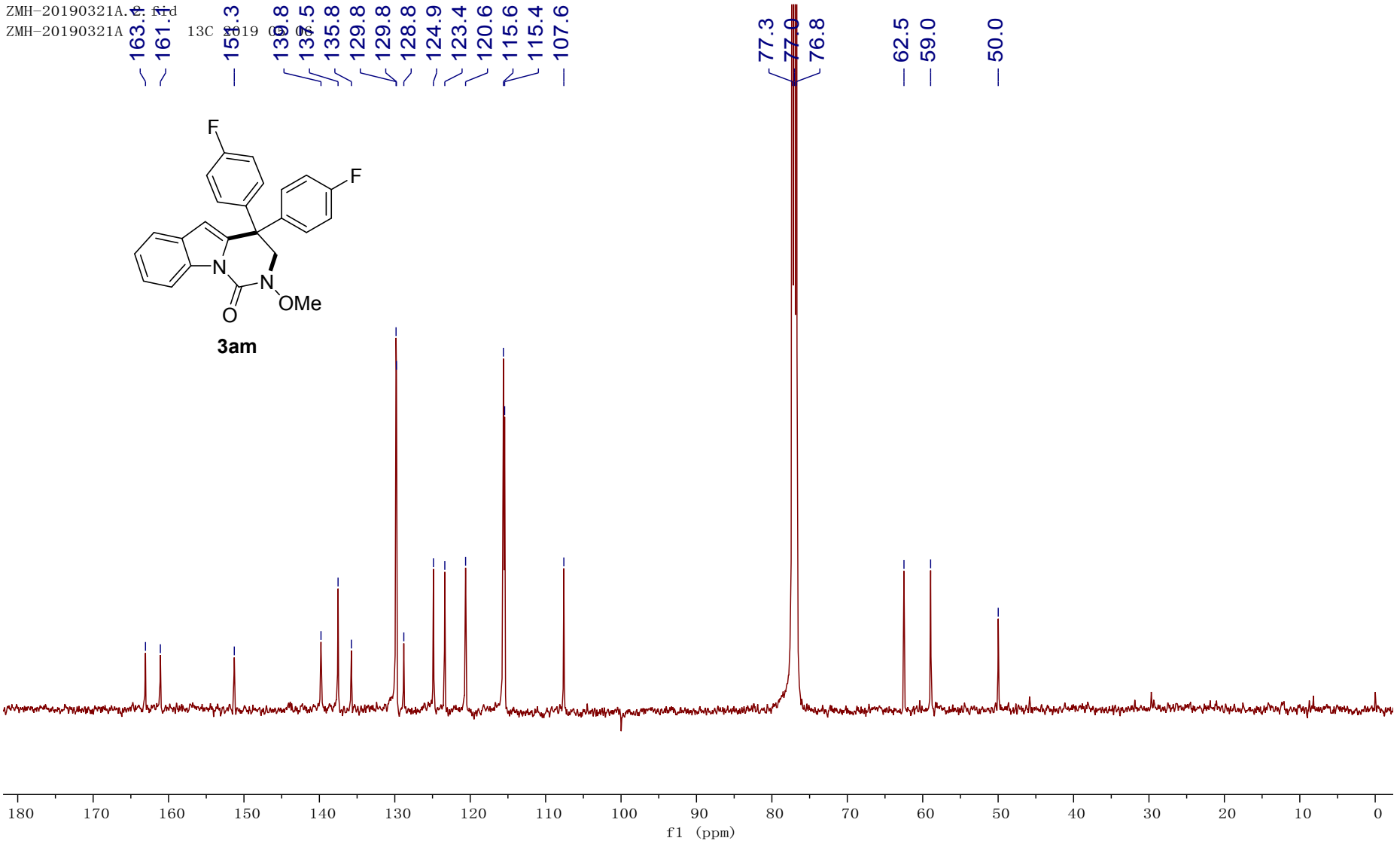
ZMH-A-3AN.1.fid
ZMH-A-3AN 1H 1D 2018 05 15

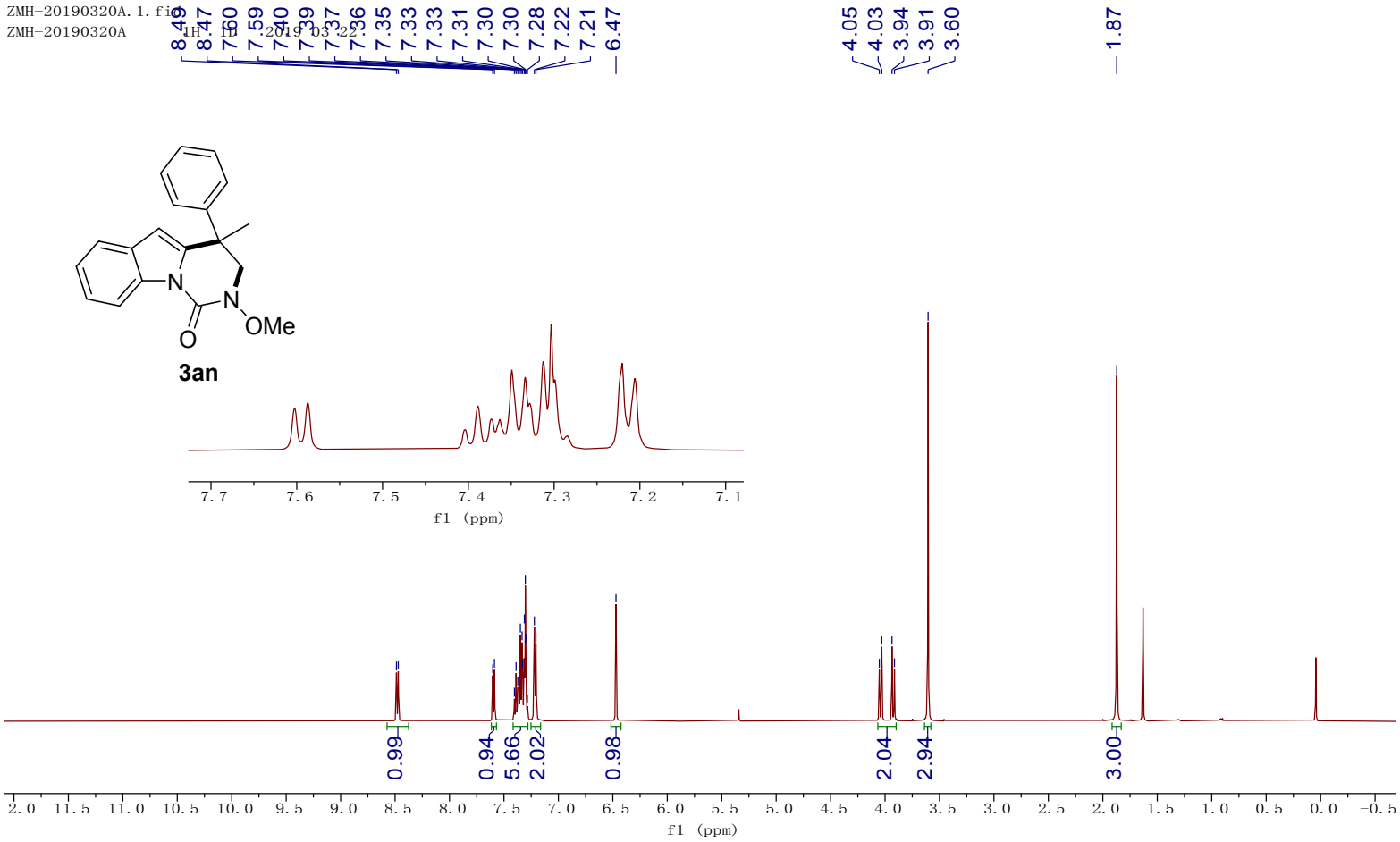


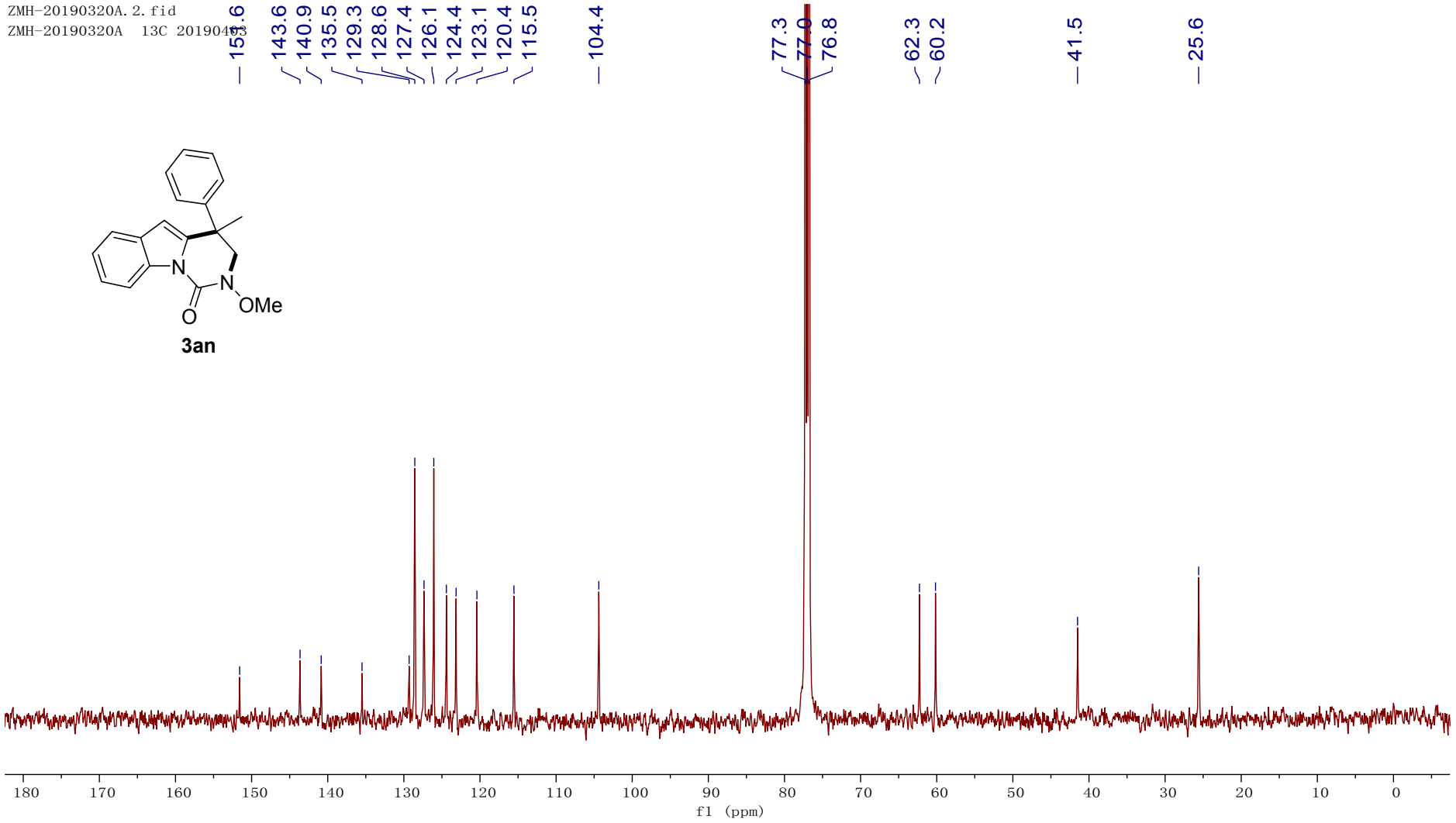
3al


ZMH-A-3AN/2
ZMH-A-3AN
151.3
142.0
140.1
135.7
128.9
128.5
128.1
127.6
124.5
123.1
120.5
115.5
107.5
77.3
77.0
76.8
62.3
58.7
50.9
N
N
OMe
O
3al
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

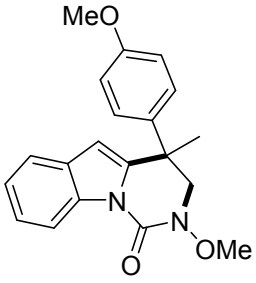

ZMH-20190321A.1.fid
PROTON CDC13 {E:\data\liming} lm-13-
8.43
8.41
7.48
7.47
7.37
7.35
7.33
7.27
7.26
7.24
7.14
7.12
7.11
7.11
7.06
7.04
7.01
6.05
4.39
3.57
F
F
N
N
OMe
O
3am
7.6
7.5
7.4
7.3
7.2
7.1
7.0
6.9
f1 (ppm)
0.97
0.97
1.08
1.60
4.02
3.94
0.99
1.98
3.00
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


ZMH-20190321A.10.fid
ZMH-20190321A 13C 2019 03 06
163.4
161.4
151.3
139.8
137.5
135.8
129.8
129.8
128.8
124.9
123.4
120.6
115.6
115.4
107.6
77.3
77.0
76.8
62.5
59.0
50.0
F
F
N
N
OMe
O
3am
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


ZMH-20190320A.1.fid
ZMH-20190320A
8.49
8.47
7.60
7.59
7.40
7.39
7.37
7.36
7.35
7.33
7.33
7.31
7.30
7.30
7.28
7.22
7.21
6.47
4.05
4.03
3.94
3.91
3.60
1.87
N
N
OMe
O
3an
7.7
7.6
7.5
7.4
7.3
7.2
7.1
f1 (ppm)
0.99
0.94
5.66
2.02
0.98
2.04
2.94
3.00
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

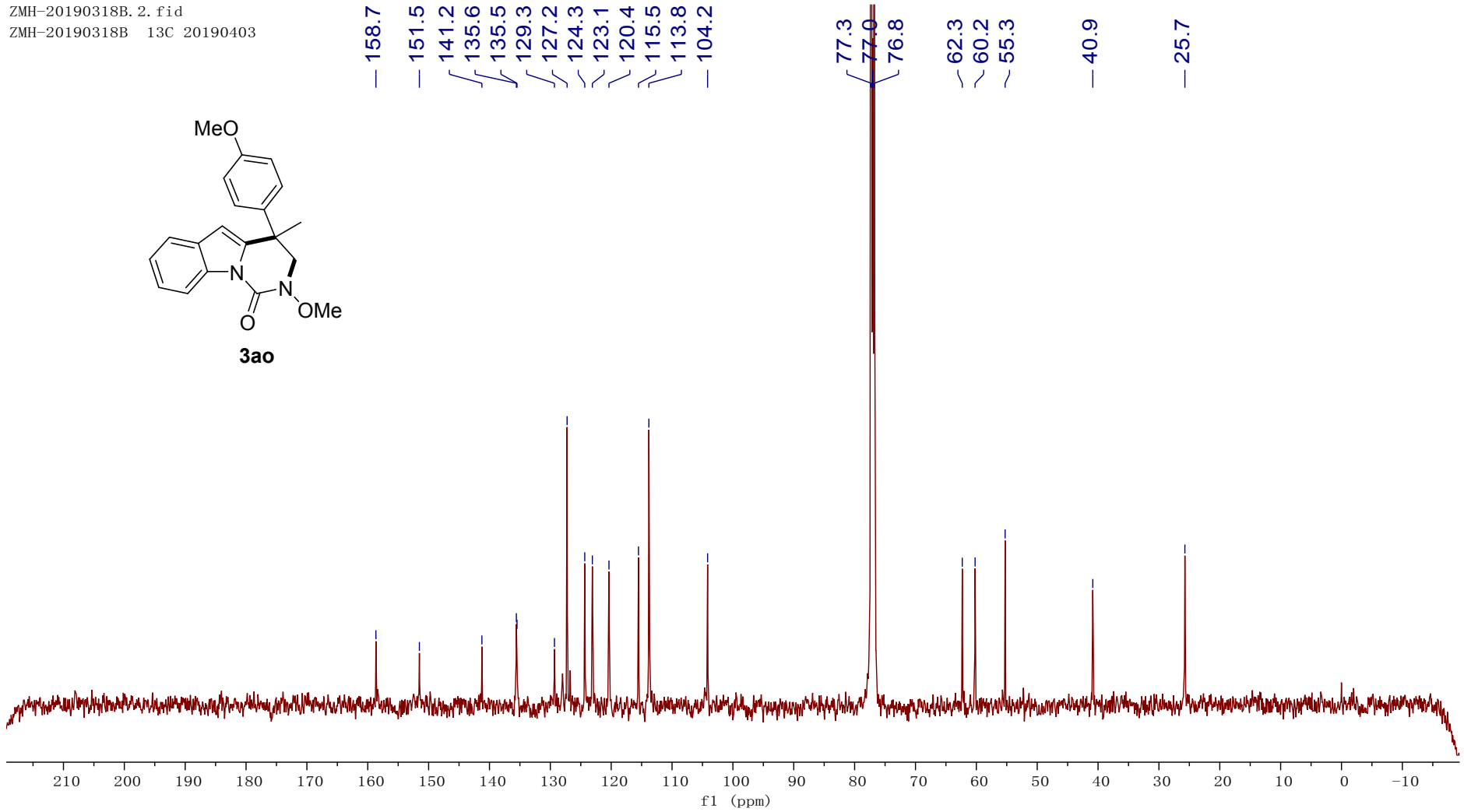

ZMH-20190320A.2.fid
ZMH-20190320A 13C 20190403
155.6
143.6
140.9
135.5
129.3
128.6
127.4
126.1
124.4
123.1
120.4
115.5
104.4
77.3
77.0
76.8
62.3
60.2
41.5
25.6
N
N
O
OMe
3an
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

ZMH-20190318B.1.fid
PROTON CDCl3 {E:\data\liming} lm 9

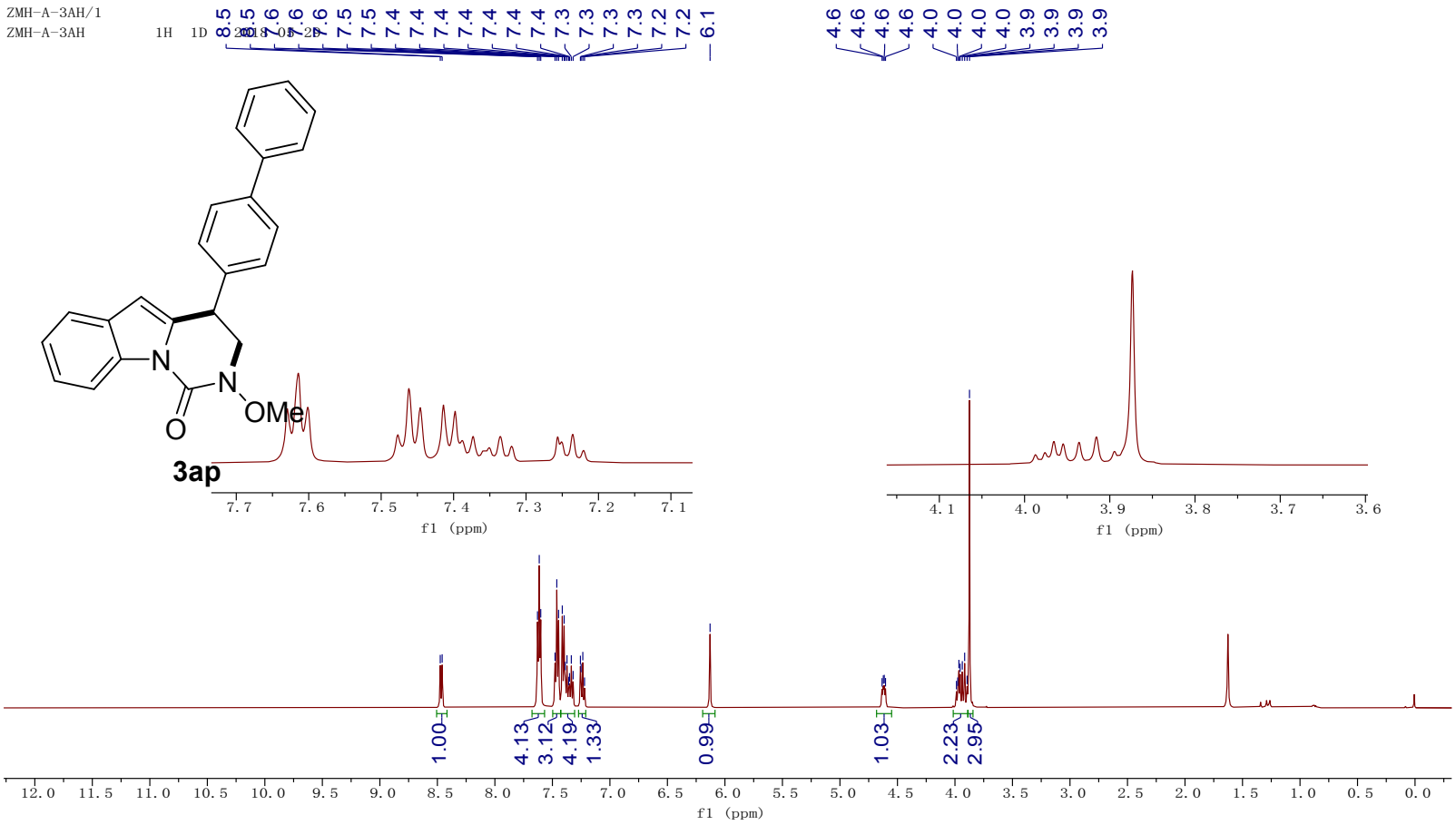


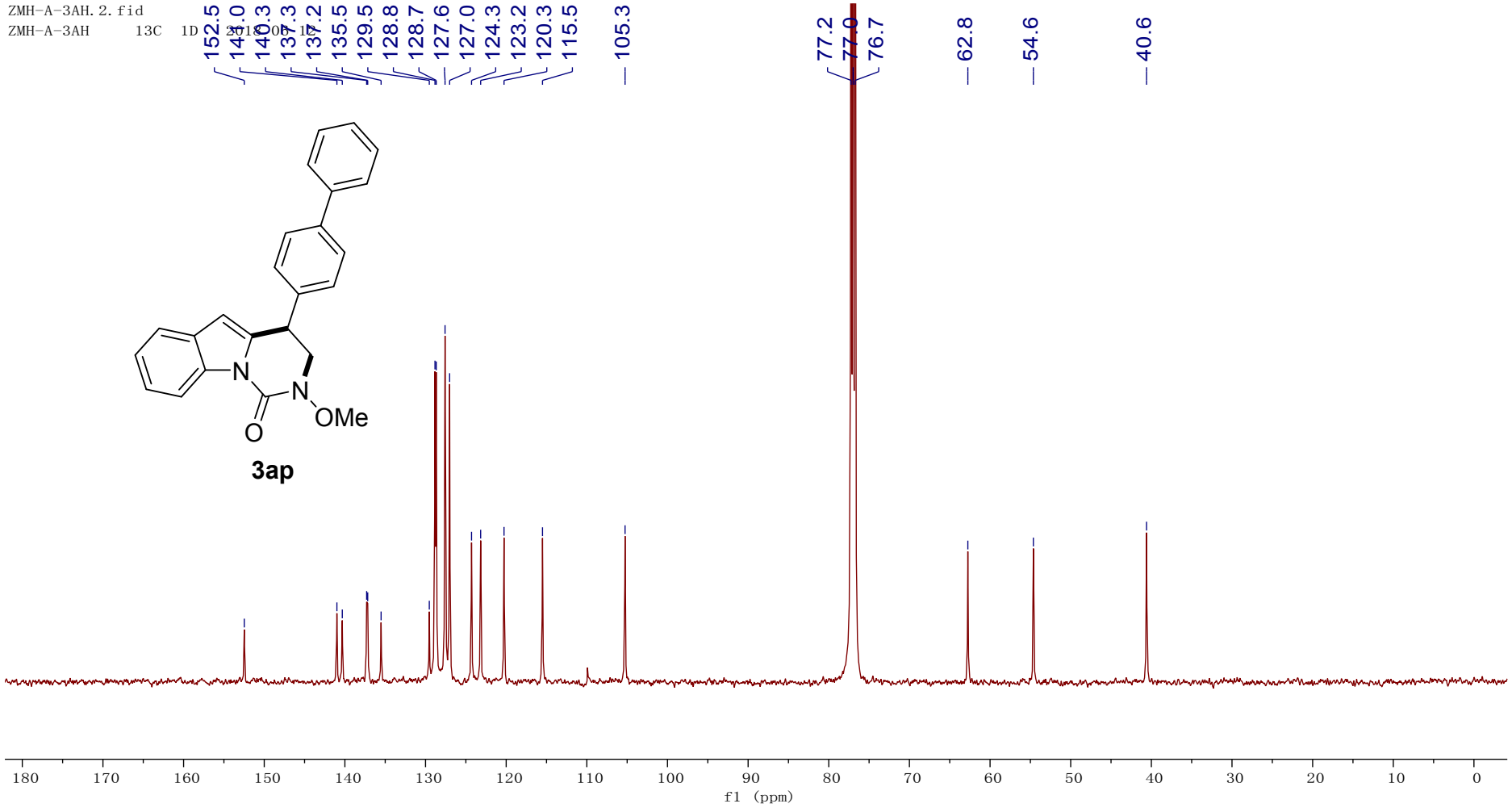
3ao

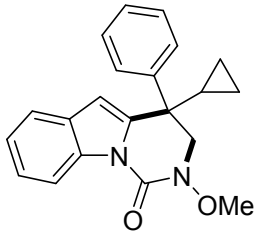
ZMH-20190318B.2.fid
ZMH-20190318B 13C 20190403



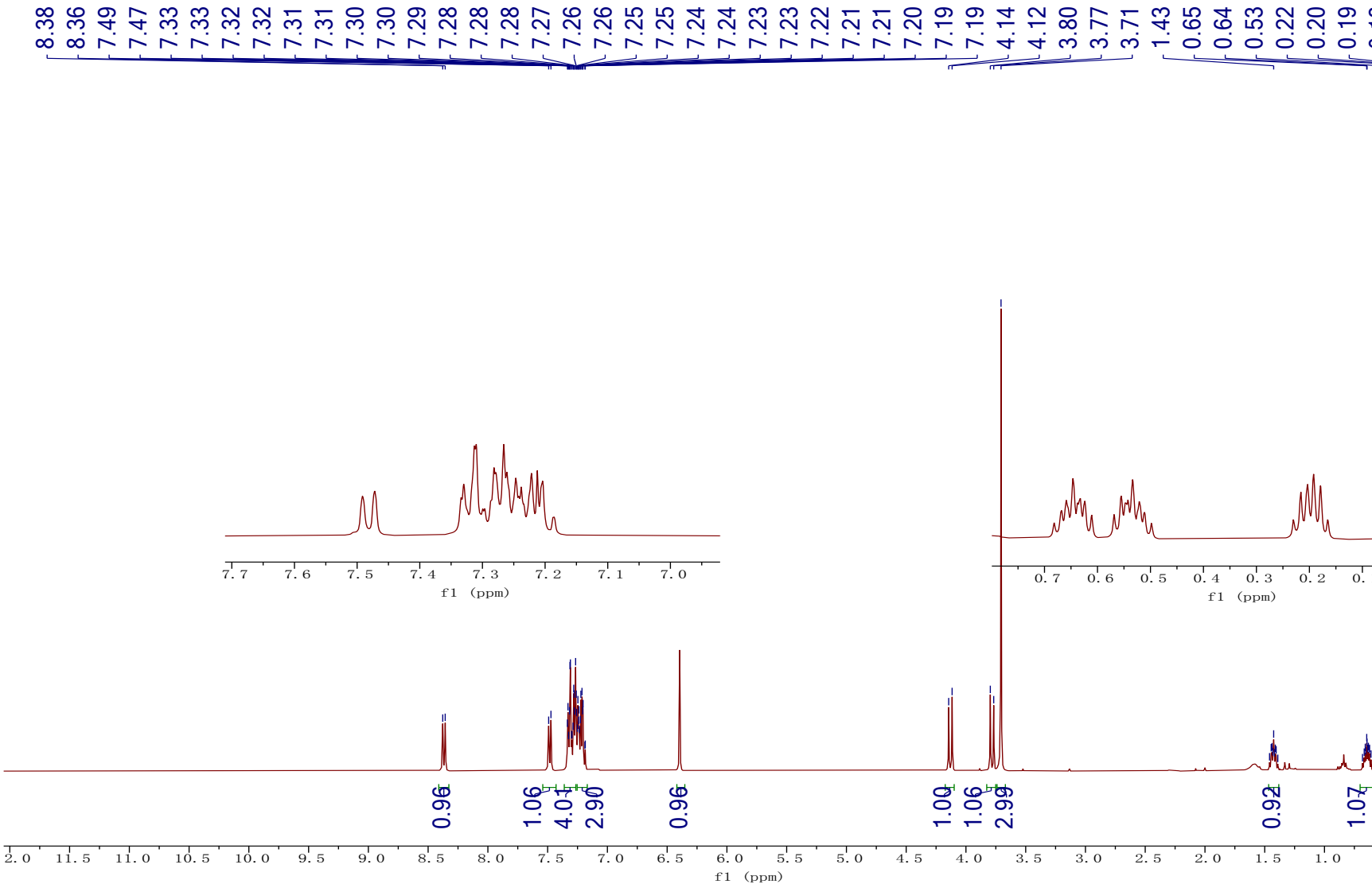
3ao

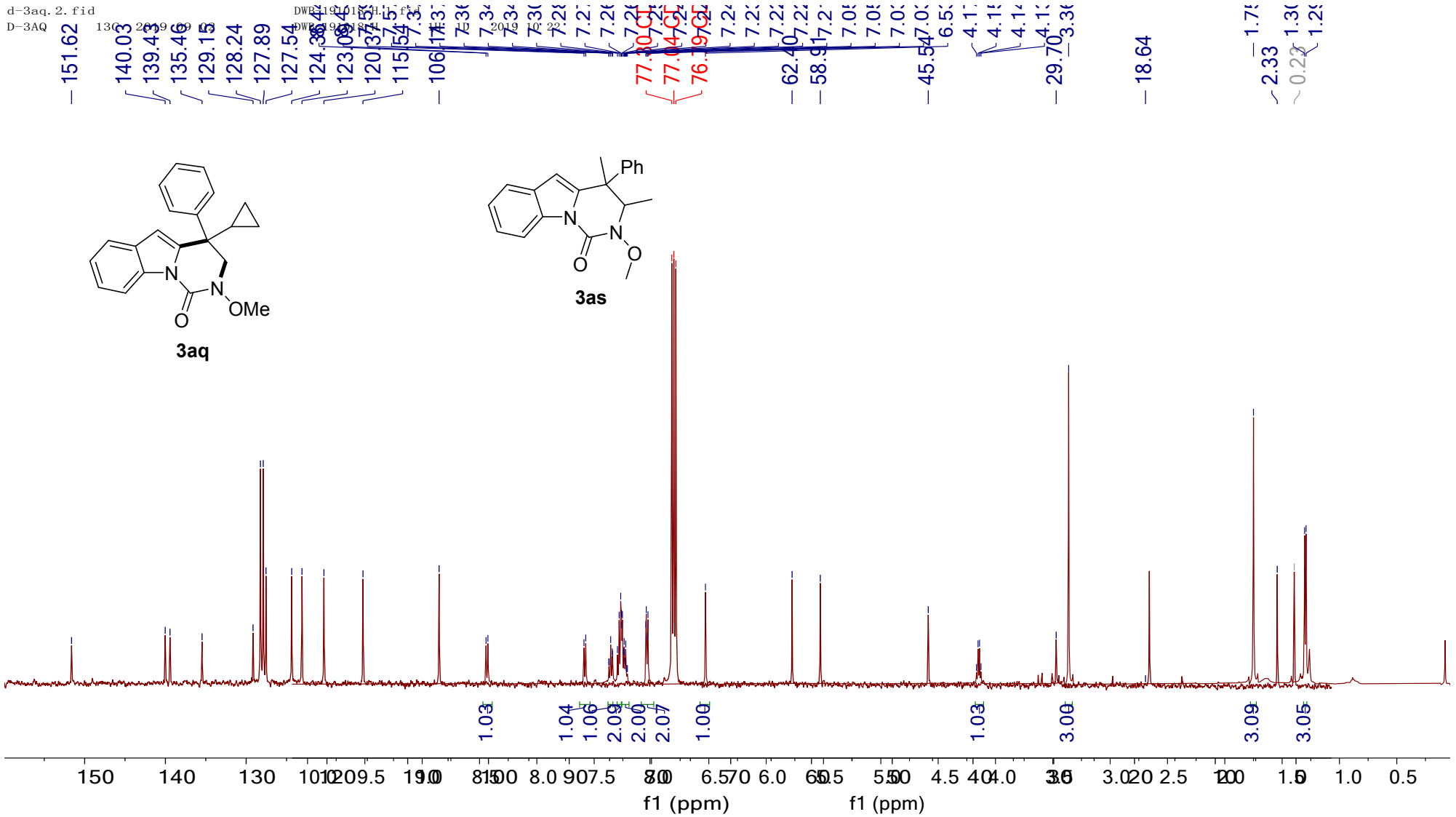

ZMH-A-3AH/1
ZMH-A-3AH 1H 1D
3ap
f1 (ppm)
1.00
4.13
3.12
4.19
1.33
0.99
1.03
2.23
2.95

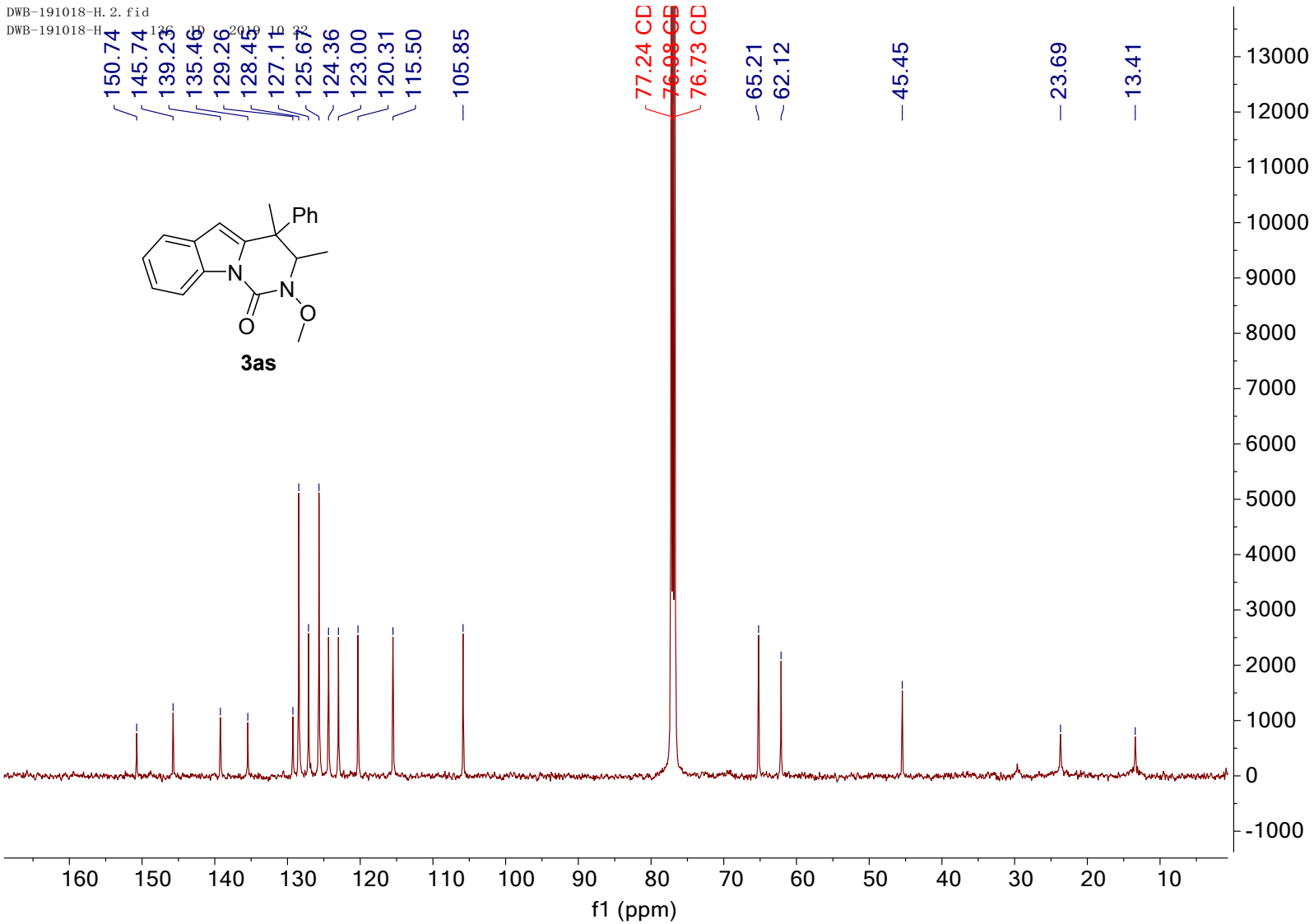

ZMH-A-3AH.2.fid
ZMH-A-3AH 13C 1D
152.5
140.0
138.3
137.3
137.2
135.5
129.5
128.8
128.7
127.6
127.0
124.3
123.2
120.3
115.5
105.3
77.2
77.0
76.7
62.8
54.6
40.6
N
N
OMe
O
3ap
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

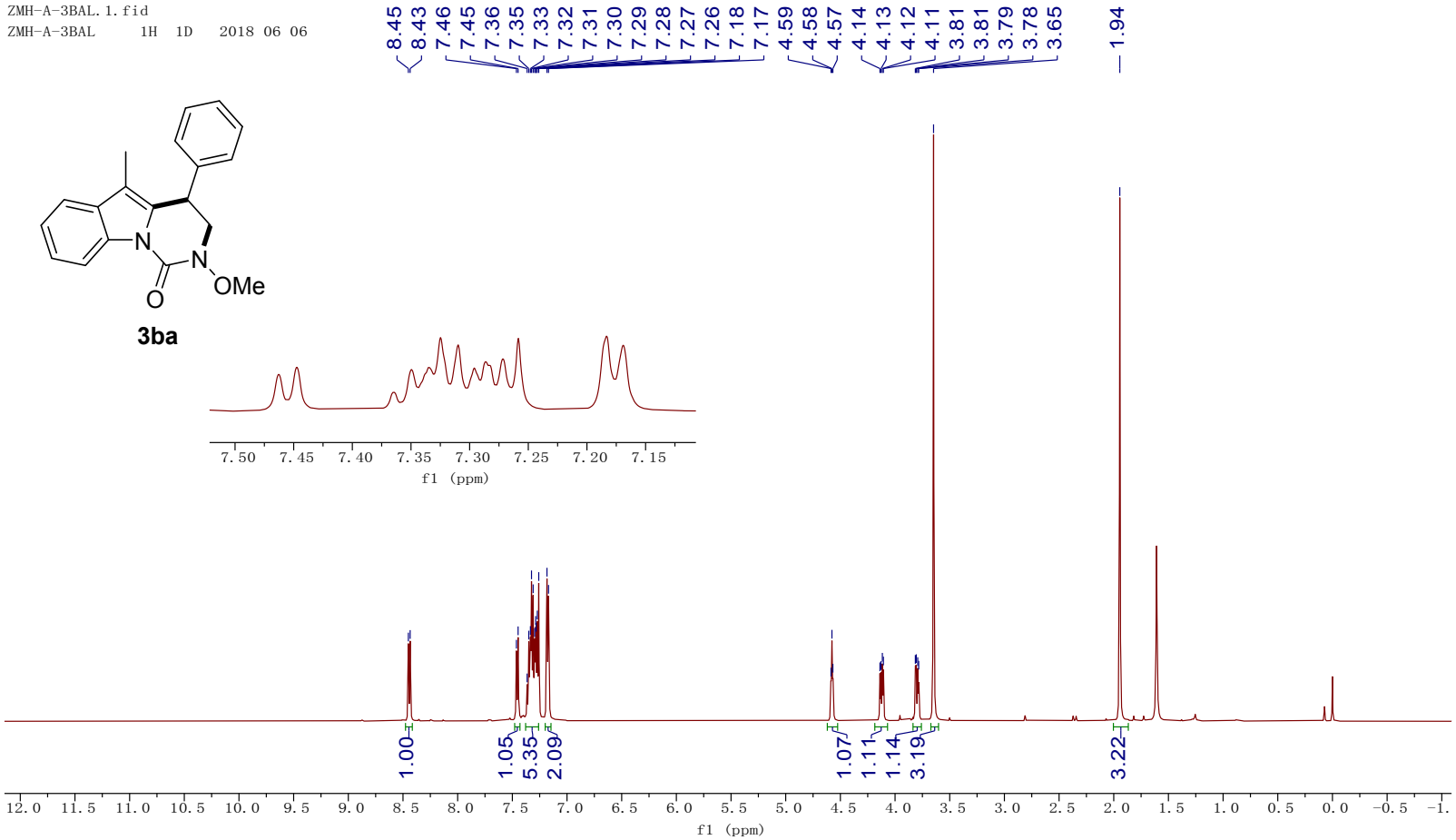

N
N
OMe
O

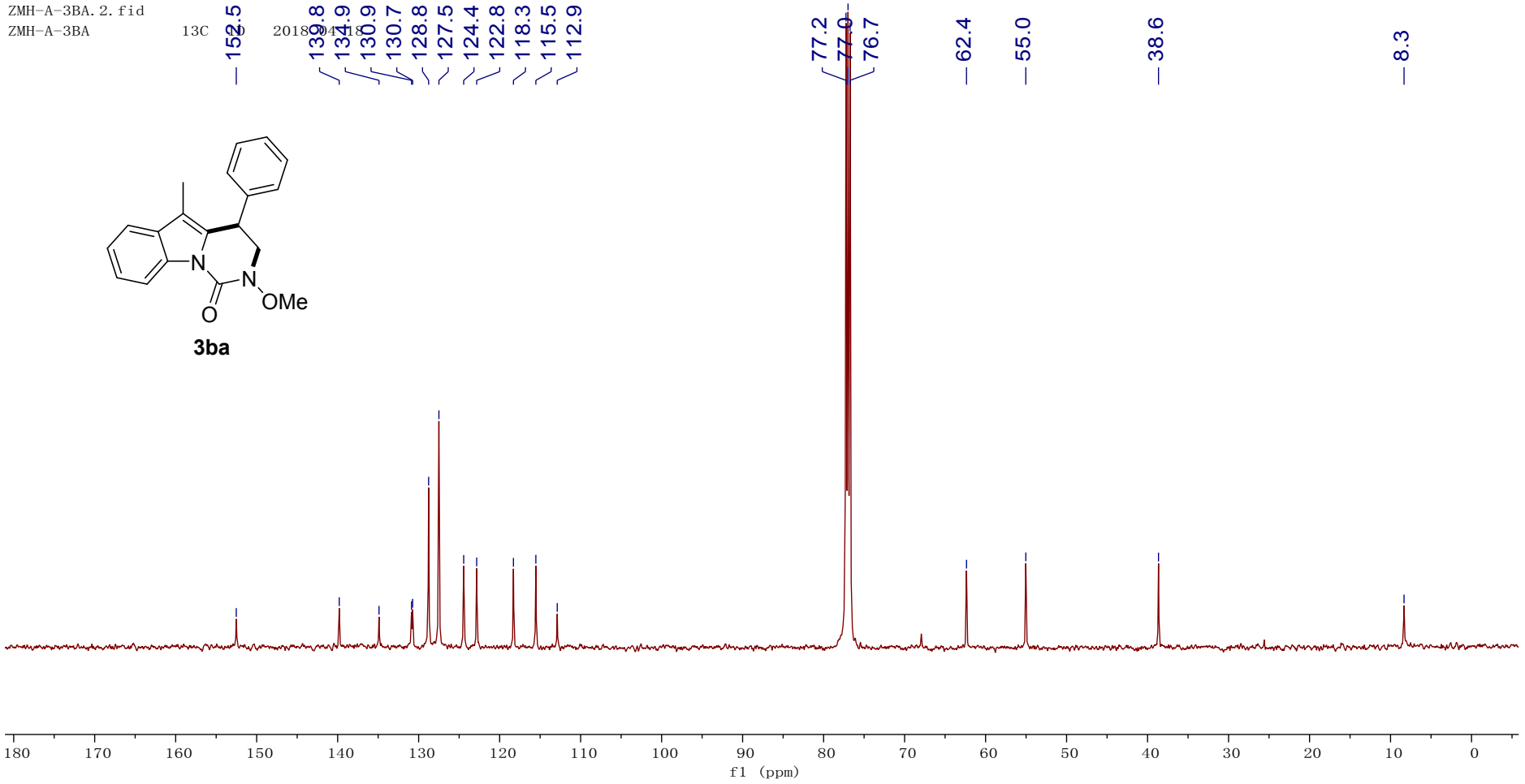
3aq


8.38
8.36
7.49
7.47
7.33
7.33
7.32
7.32
7.31
7.31
7.30
7.30
7.29
7.28
7.28
7.28
7.27
7.26
7.26
7.25
7.25
7.24
7.24
7.23
7.23
7.22
7.21
7.21
7.20
7.19
7.19
4.14
4.12
3.80
3.77
3.71
1.43
0.65
0.64
0.53
0.22
0.20
0.19
f1 (ppm)
0.96
1.06
4.01
2.90
0.96
1.00
1.06
2.99
0.92
1.07

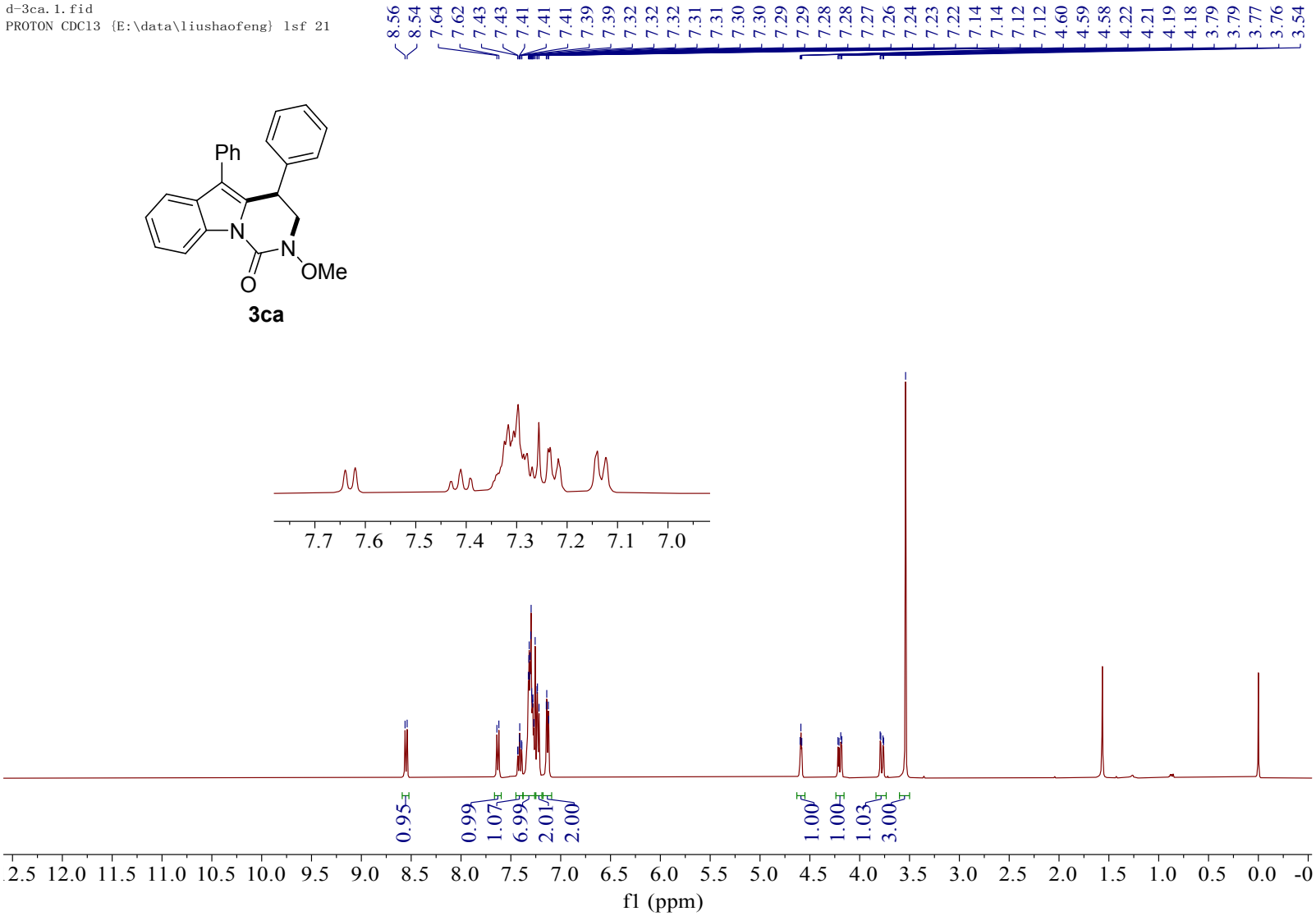

d-3aq.2.fid
D-3AQ
151.62
140.03
139.47
135.46
129.15
128.24
127.89
127.54
124.38
123.09
120.37
115.54
106.17
77.40
77.04
76.79
62.40
58.91
45.54
29.70
18.64
2.33
0.22
OMe
3aq
Ph
3as
1.03
1.04
1.06
2.09
2.00
2.07
1.00
1.03
3.00
3.09
3.05
f1 (ppm)
f1 (ppm)

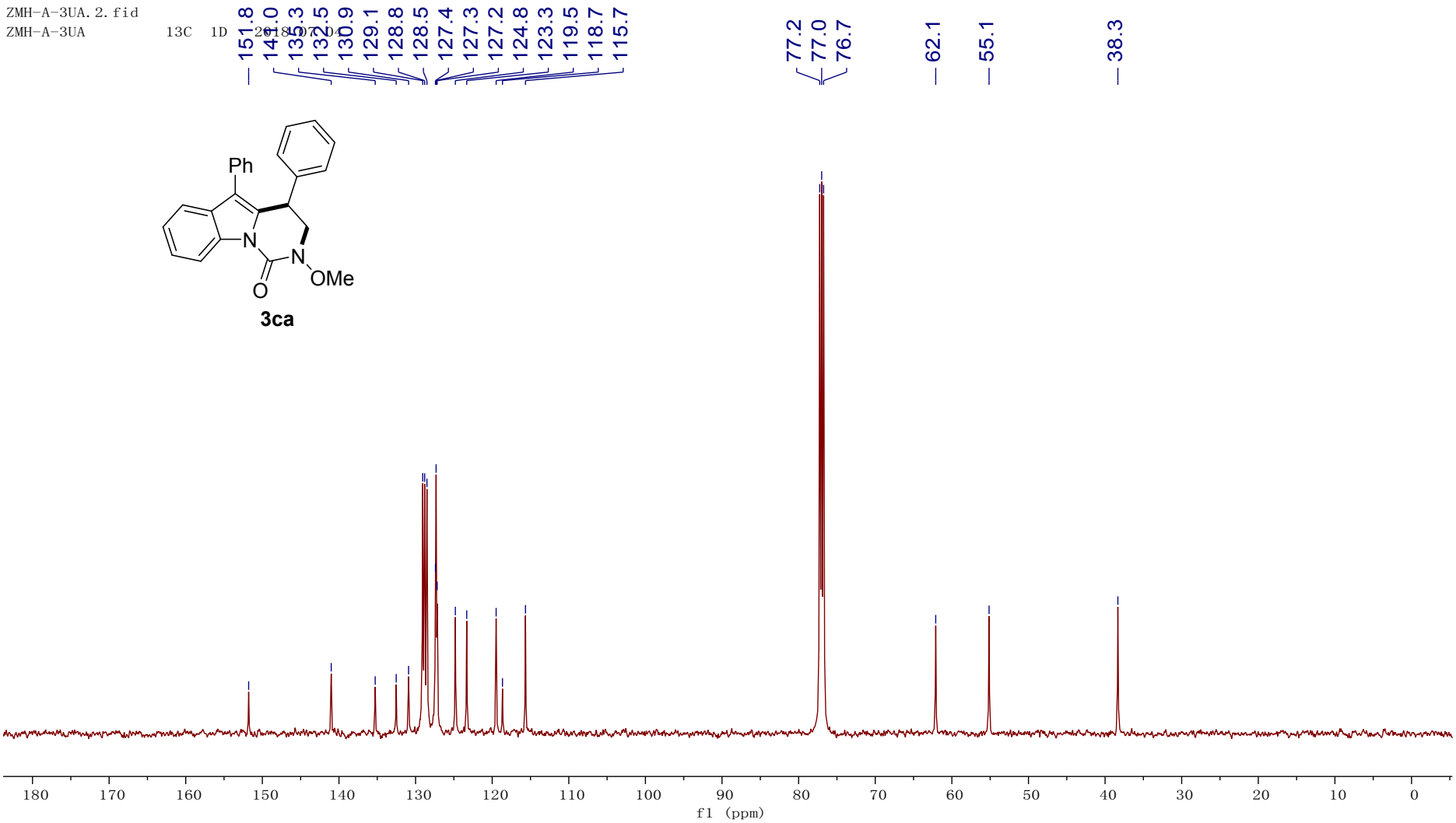

DWB-191018-H.2.fid
150.74
145.74
139.23
135.46
129.26
128.45
127.11
125.67
124.36
123.00
120.31
115.50
105.85
77.24 CD
76.73 CD
65.21
62.12
45.45
23.69
13.41
Ph
N
N
O
O
3as
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

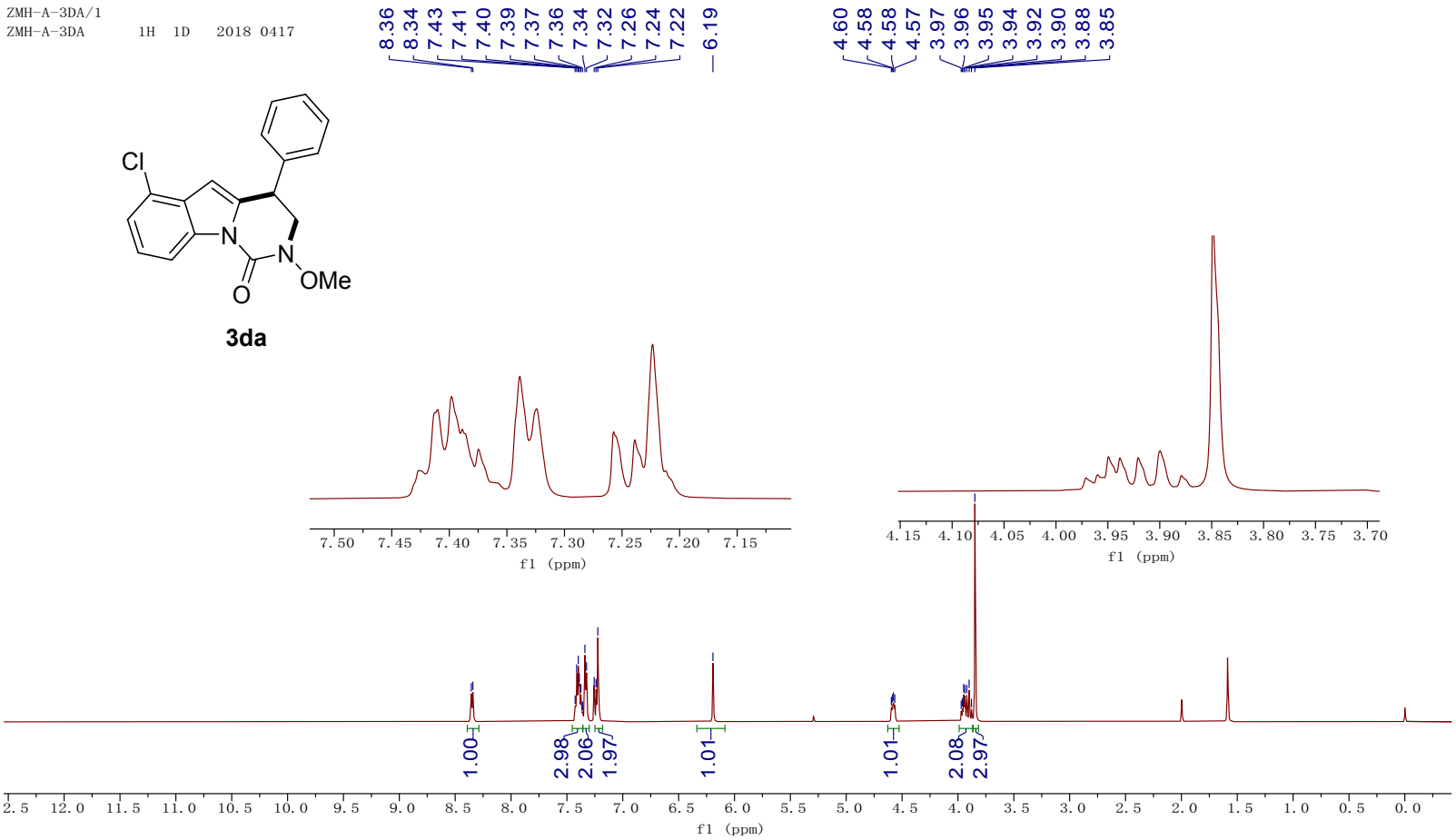

ZMH-A-3BAL.1.fid
ZMH-A-3BAL 1H 1D 2018 06 06
8.45
8.43
7.46
7.45
7.36
7.35
7.33
7.32
7.31
7.30
7.29
7.28
7.27
7.26
7.18
7.17
4.59
4.58
4.57
4.14
4.13
4.12
4.11
3.81
3.81
3.79
3.78
3.65
1.94
N
N
OMe
O
3ba
7.50 7.45 7.40 7.35 7.30 7.25 7.20 7.15
f1 (ppm)
1.00
1.05
5.35
2.09
1.07
1.11
1.14
3.19
3.22
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 −1.
f1 (ppm)

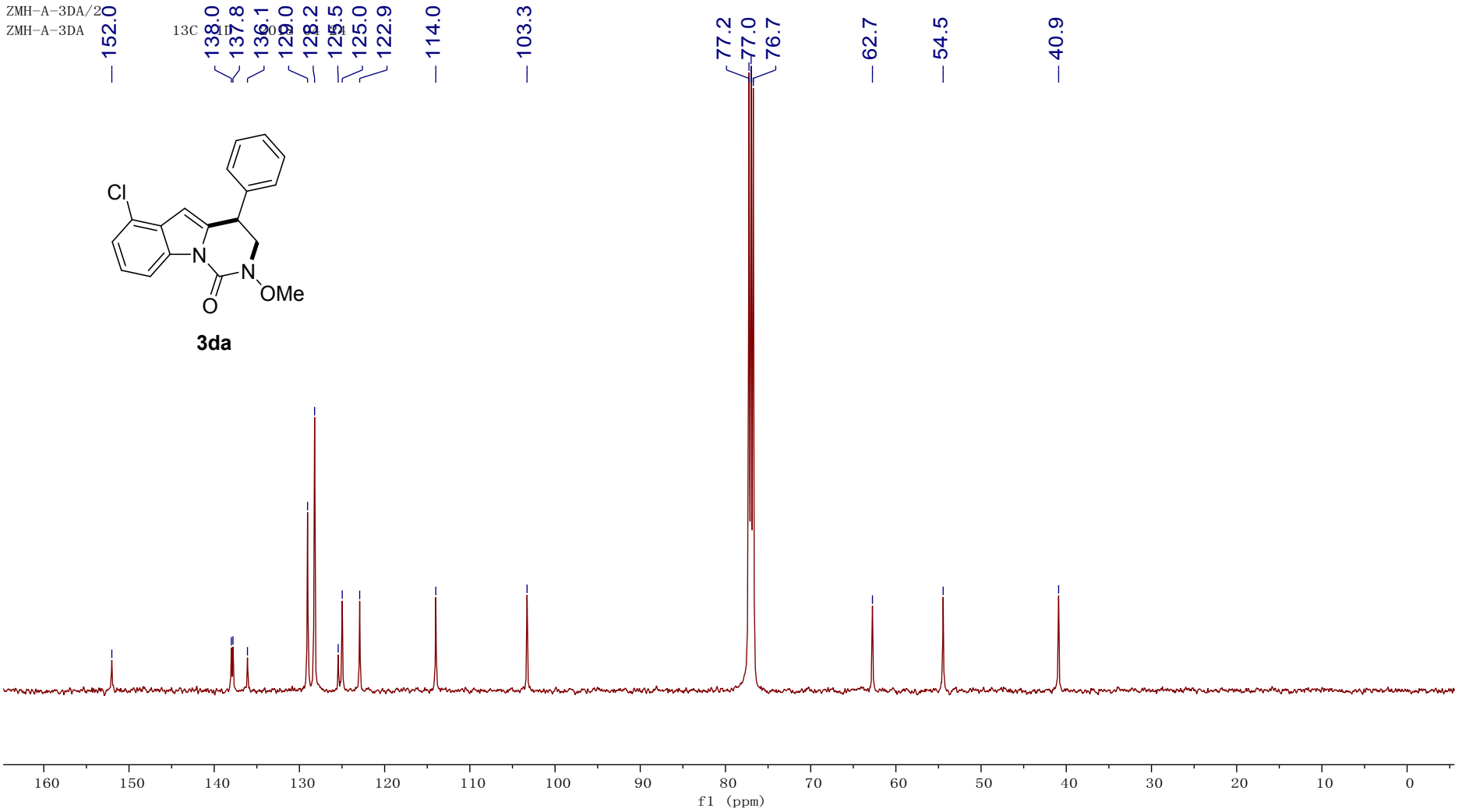

ZMH-A-3BA.2.fid
ZMH-A-3BA 13C 2D 20180404[illegible]
152.5
139.8
134.9
130.9
130.7
128.8
127.5
124.4
122.8
118.3
115.5
112.9
77.2
77.0
76.7
62.4
55.0
38.6
8.3
N
N
OMe
O
3ba
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

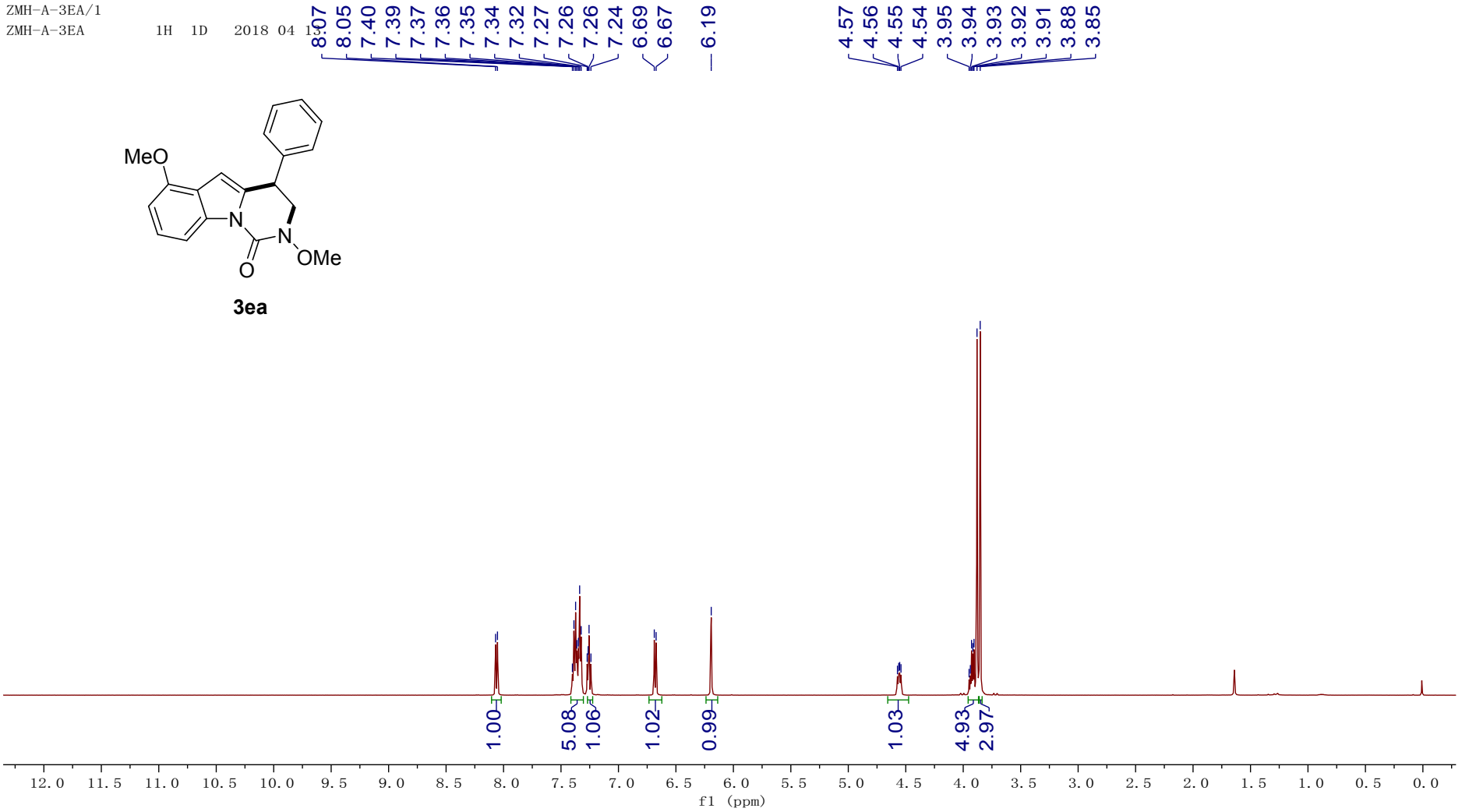
d-3ca.1.fid
PROTON CDCl3 {E:\data\liushaofeng} lsf 21

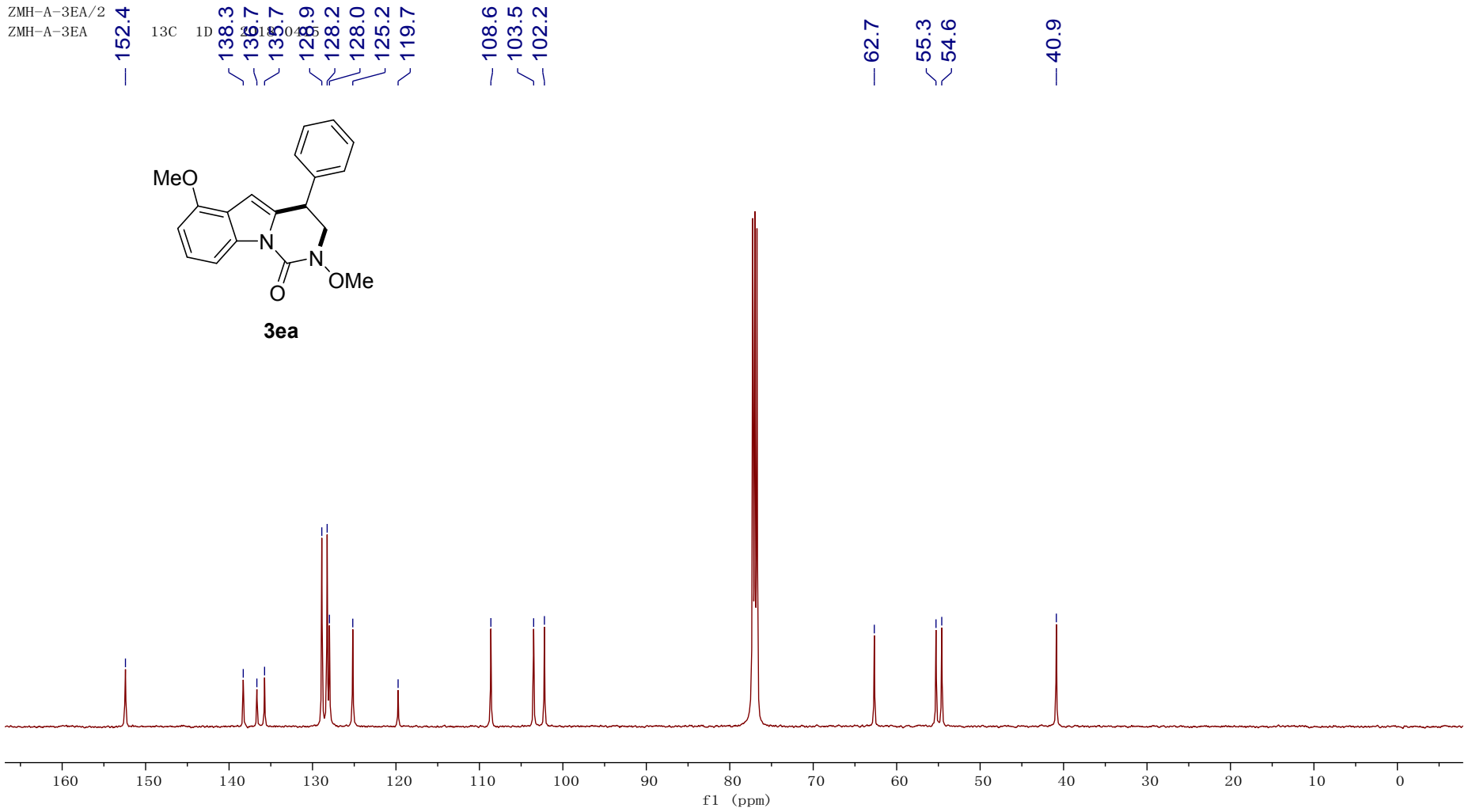


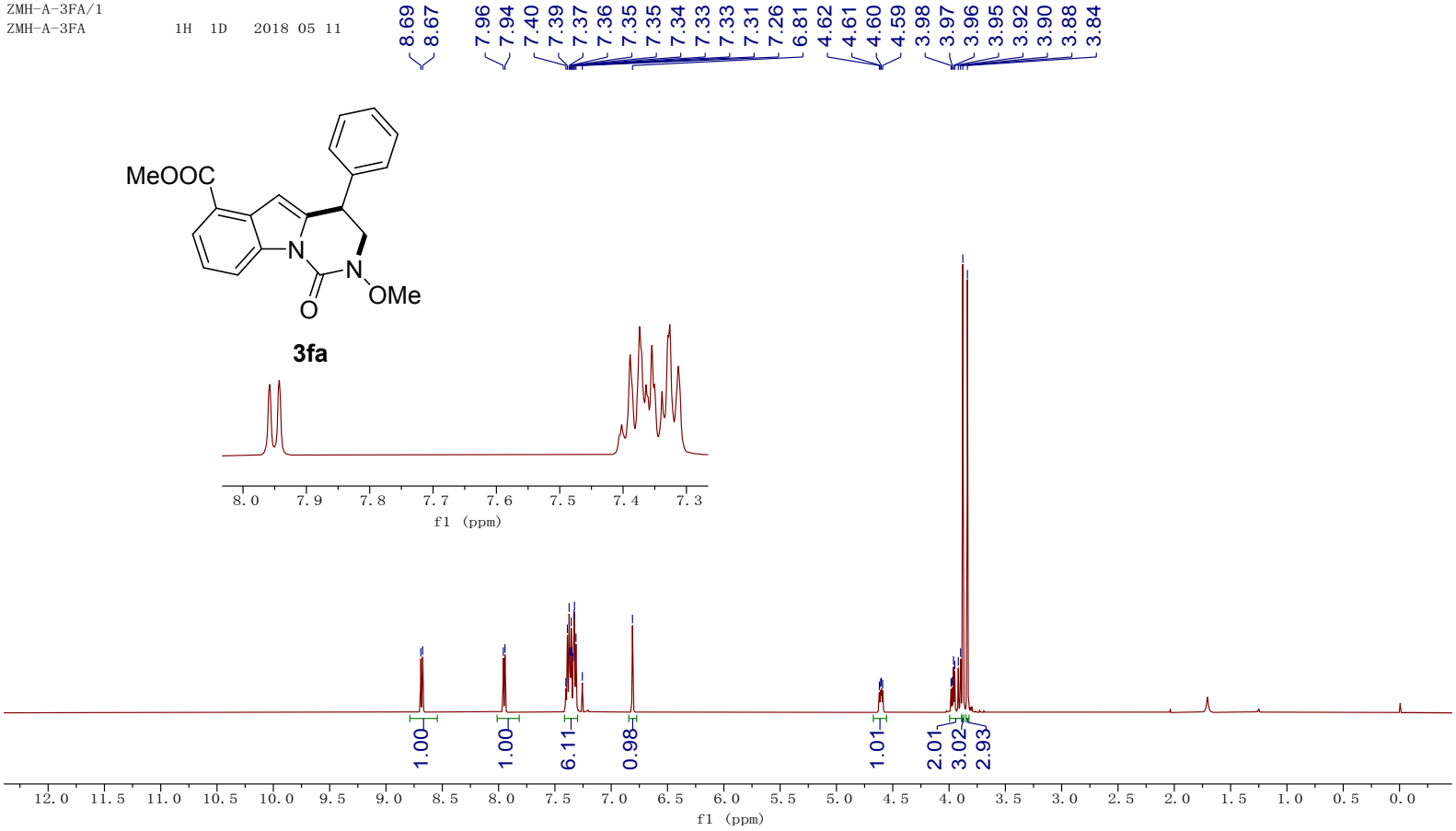

ZMH-A-3UA.2.fid
ZMH-A-3UA 13C 1D
151.8
144.0
135.3
132.5
130.9
129.1
128.8
128.5
127.4
127.3
127.2
124.8
123.3
119.5
118.7
115.7
77.2
77.0
76.7
62.1
55.1
38.3
Ph
N
N
OMe
O
3ca
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

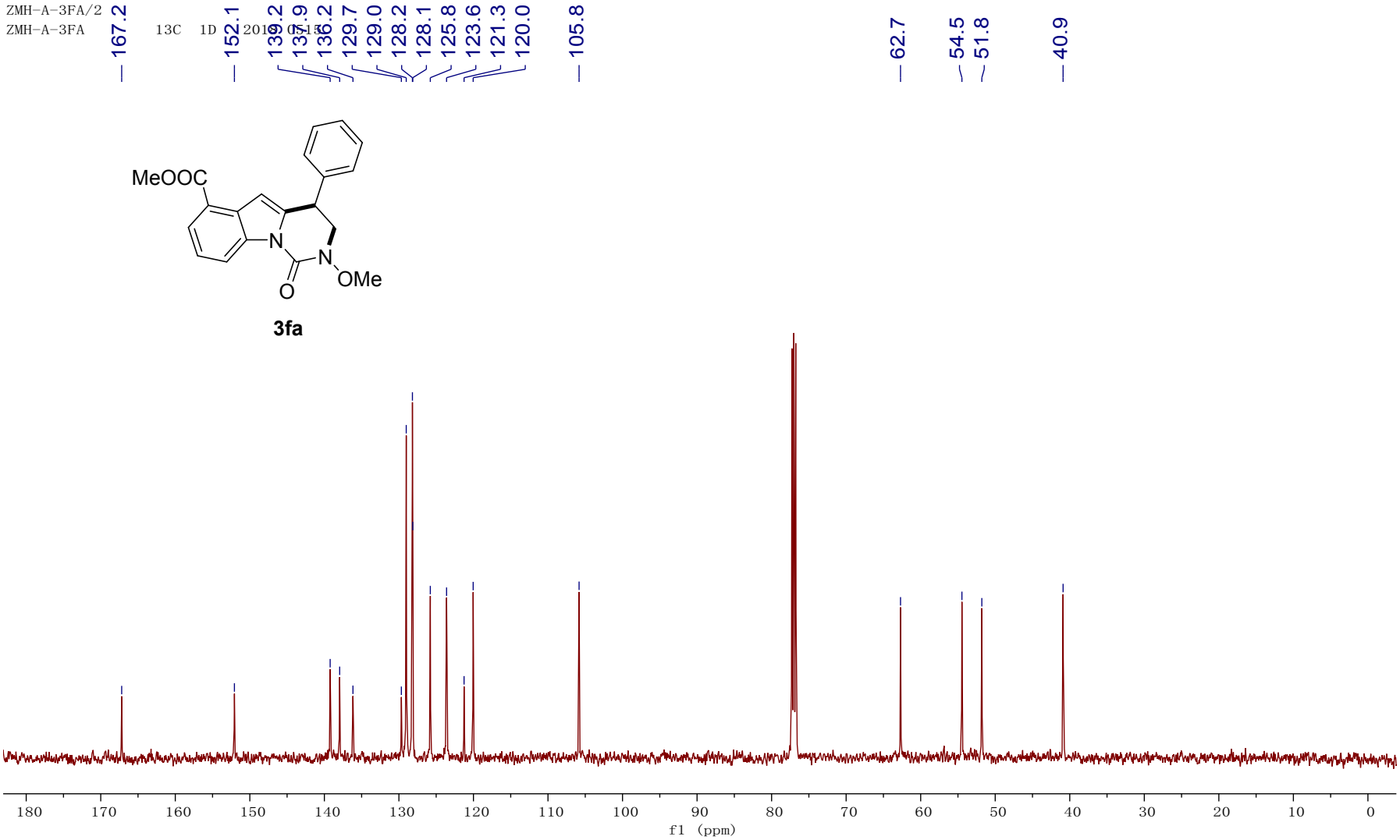

ZMH-A-3DA/1
ZMH-A-3DA 1H 1D 2018 0417
8.36
8.34
7.43
7.41
7.40
7.39
7.37
7.36
7.34
7.32
7.26
7.24
7.22
6.19
4.60
4.58
4.58
4.57
3.97
3.96
3.95
3.94
3.92
3.90
3.88
3.85
Cl
N
N
OMe
O
3da
7.50 7.45 7.40 7.35 7.30 7.25 7.20 7.15
f1 (ppm)
4.15 4.10 4.05 4.00 3.95 3.90 3.85 3.80 3.75 3.70
f1 (ppm)
1.00
2.98
2.06
1.97
1.01
1.01
2.08
2.97
2.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

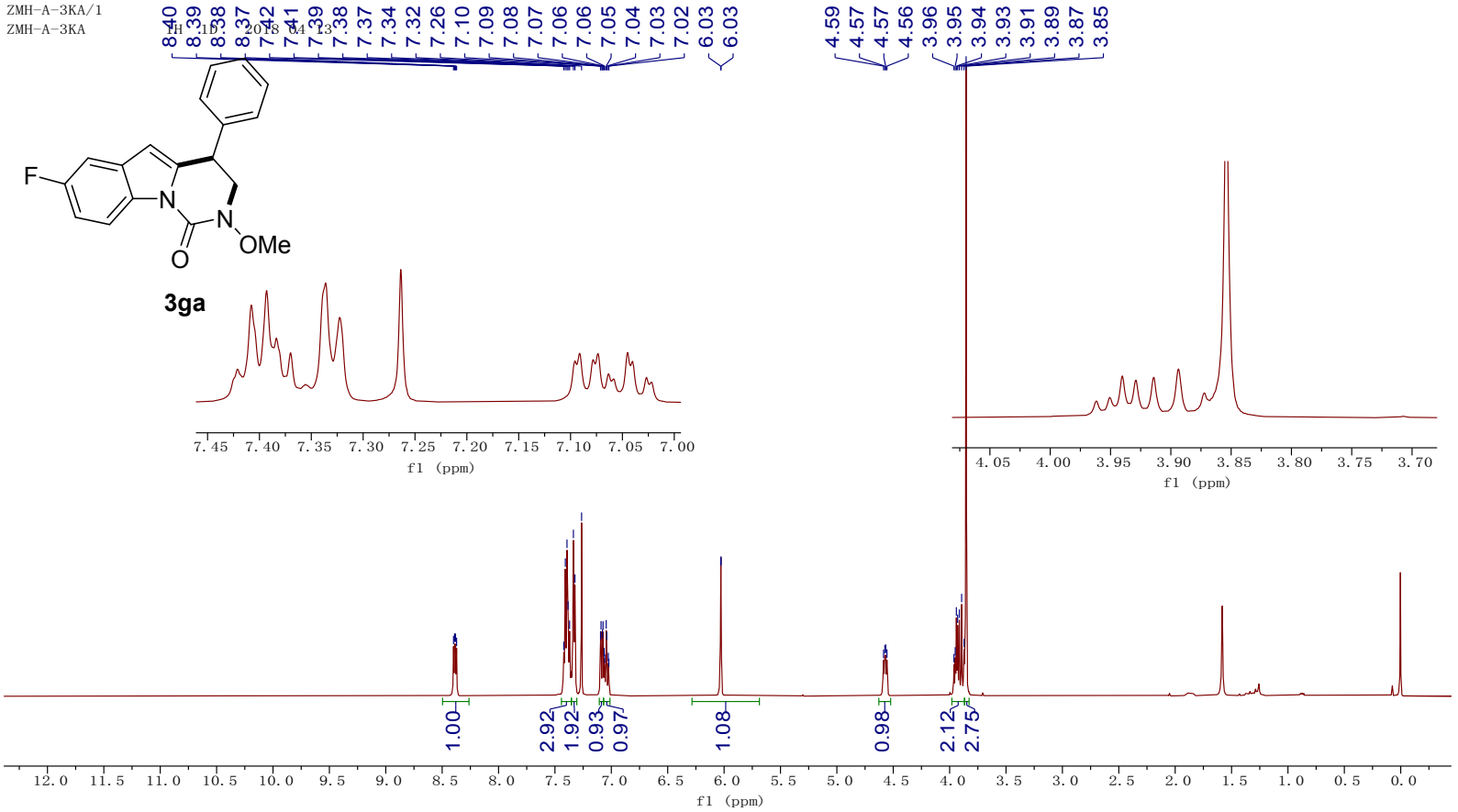

ZMH-A-3DA/2
ZMH-A-3DA
152.0
138.0
137.8
136.1
129.0
128.2
125.5
125.0
122.9
114.0
103.3
77.2
77.0
76.7
62.7
54.5
40.9
Cl
N
N
OMe
O
3da
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

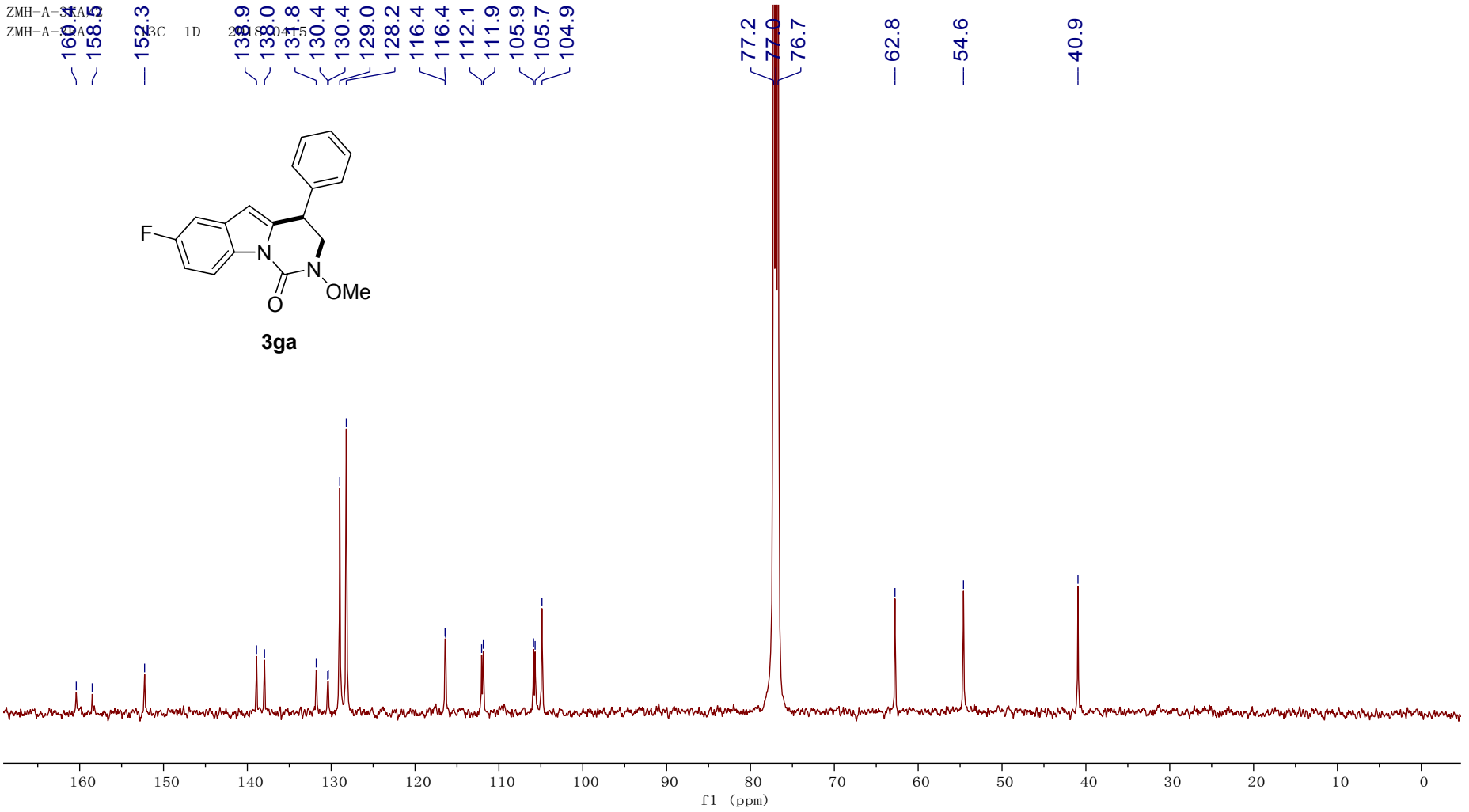

ZMH-A-3EA/1
ZMH-A-3EA 1H 1D 2018 04 13
8.07
8.05
7.40
7.39
7.37
7.36
7.35
7.34
7.32
7.27
7.26
7.26
7.24
6.69
6.67
6.19
4.57
4.56
4.55
4.54
3.95
3.94
3.93
3.92
3.91
3.88
3.85
MeO
N
N
OMe
O
3ea
1.00
5.08
1.06
1.02
0.99
1.03
4.93
2.97
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

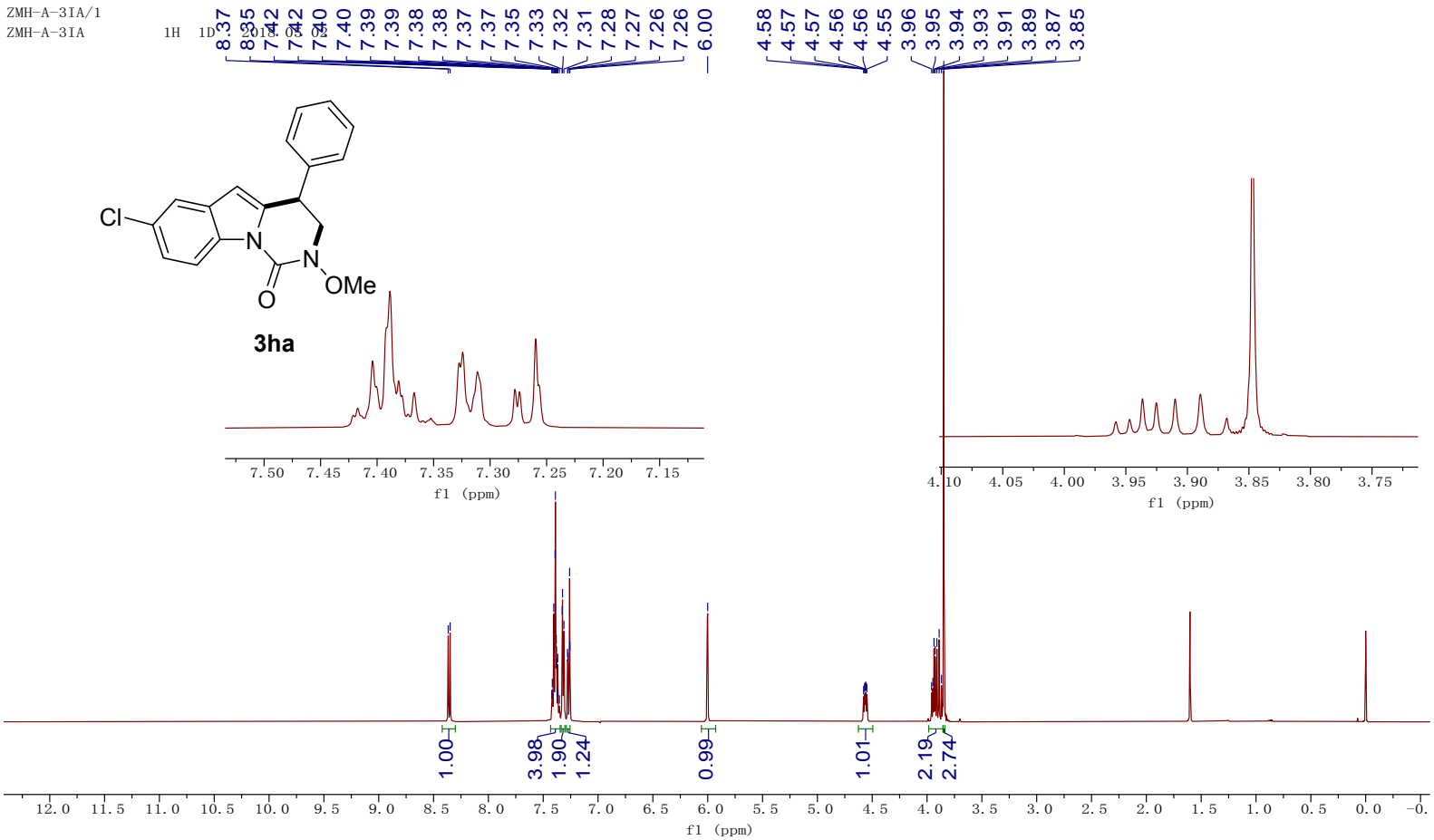

ZMH-A-3EA/2
ZMH-A-3EA 13C 1D
152.4
138.3
135.7
135.7
128.9
128.2
128.0
125.2
119.7
108.6
103.5
102.2
62.7
55.3
54.6
40.9
MeO
N
N
OMe
O
3ea
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

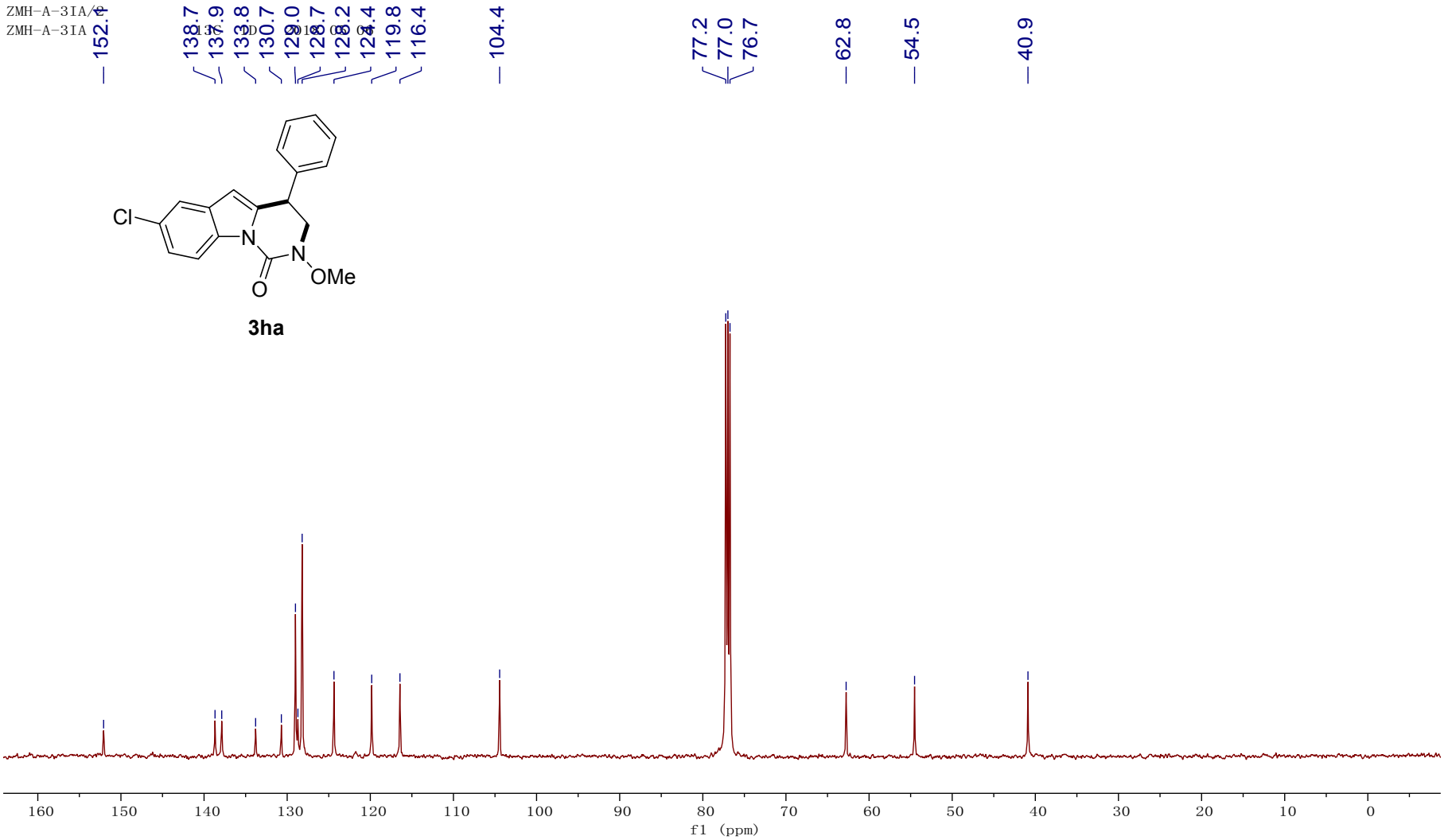

ZMH-A-3FA/1
ZMH-A-3FA 1H 1D 2018 05 11
8.69
8.67
7.96
7.94
7.40
7.39
7.37
7.36
7.35
7.35
7.34
7.33
7.33
7.31
7.26
6.81
4.62
4.61
4.60
4.59
3.98
3.97
3.96
3.95
3.92
3.90
3.88
3.84
MeOOC
N
N
OMe
O
3fa
8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3
f1 (ppm)
1.00
1.00
6.11
0.98
1.01
2.01
3.02
2.93
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

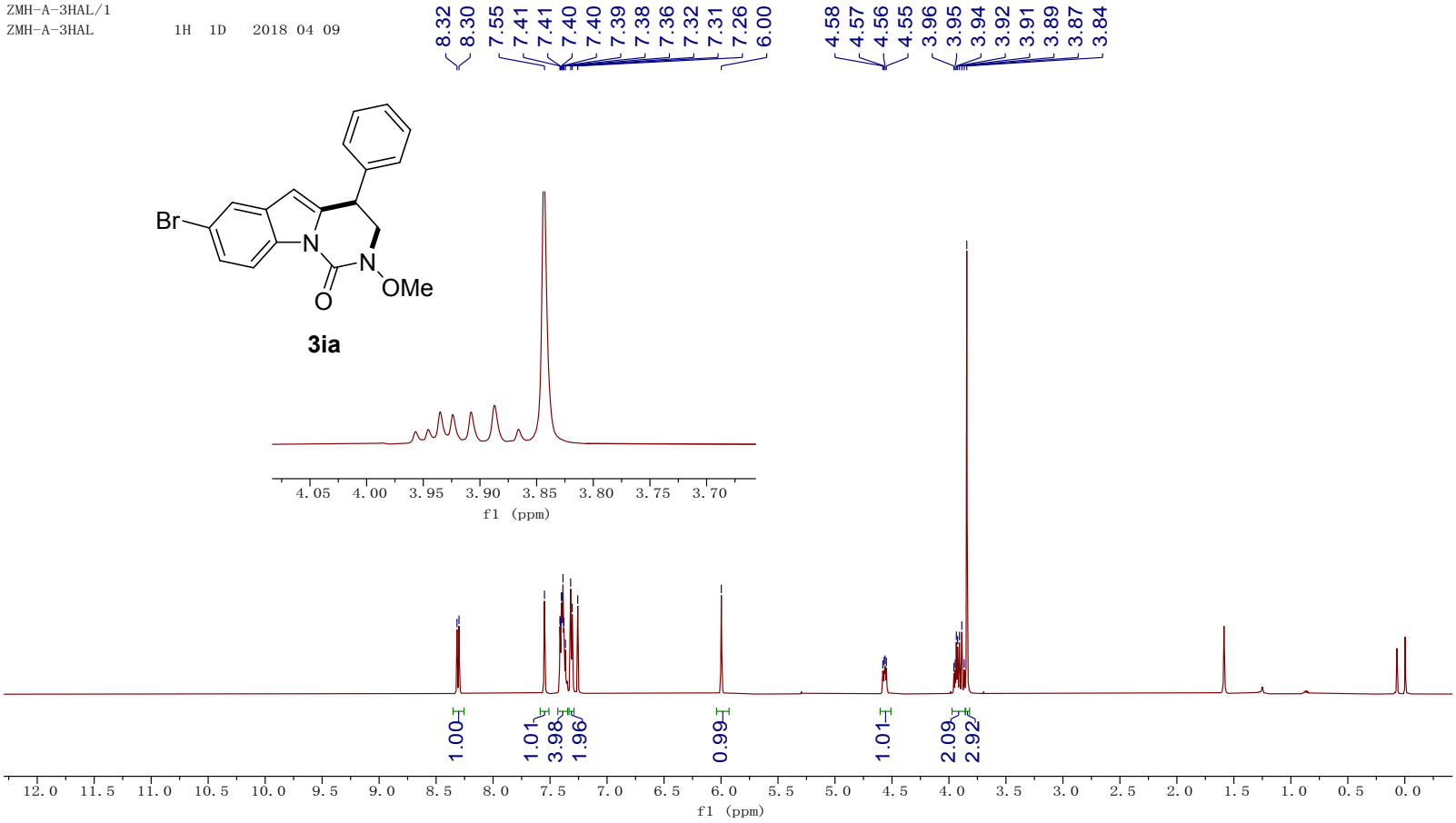

ZMH-A-3FA/2
ZMH-A-3FA 13C 1D 2019 05 15
167.2
152.1
139.2
137.9
136.2
129.7
129.0
128.2
128.1
125.8
123.6
121.3
120.0
105.8
62.7
54.5
51.8
40.9
MeOOC
N
N
OMe
O
3fa
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

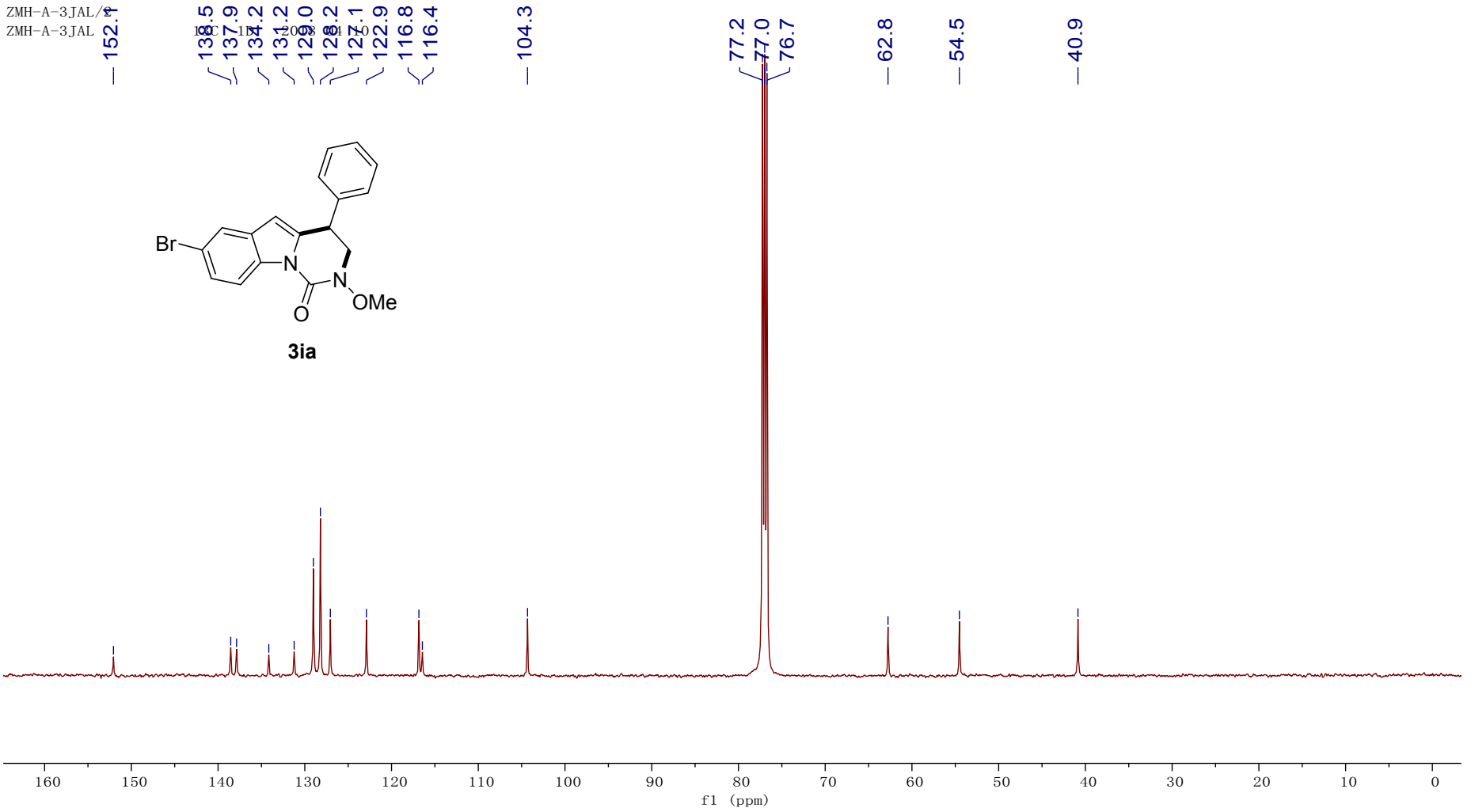

ZMH-A-3KA/1
ZMH-A-3KA
1H -1D- 2018 04 13
8.40 8.39 8.38 8.37 7.42 7.41 7.39 7.38 7.37 7.34 7.32 7.26 7.10 7.09 7.08 7.07 7.06 7.06 7.05 7.04 7.03 7.02 6.03 6.03
4.59 4.57 4.57 4.56 3.96 3.95 3.94 3.93 3.91 3.89 3.87 3.85
F
N
N
OMe
O
3ga
7.45 7.40 7.35 7.30 7.25 7.20 7.15 7.10 7.05 7.00
f1 (ppm)
4.05 4.00 3.95 3.90 3.85 3.80 3.75 3.70
f1 (ppm)
1.00 2.92 1.92 0.93 0.97 1.08 0.98 2.12 2.75
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

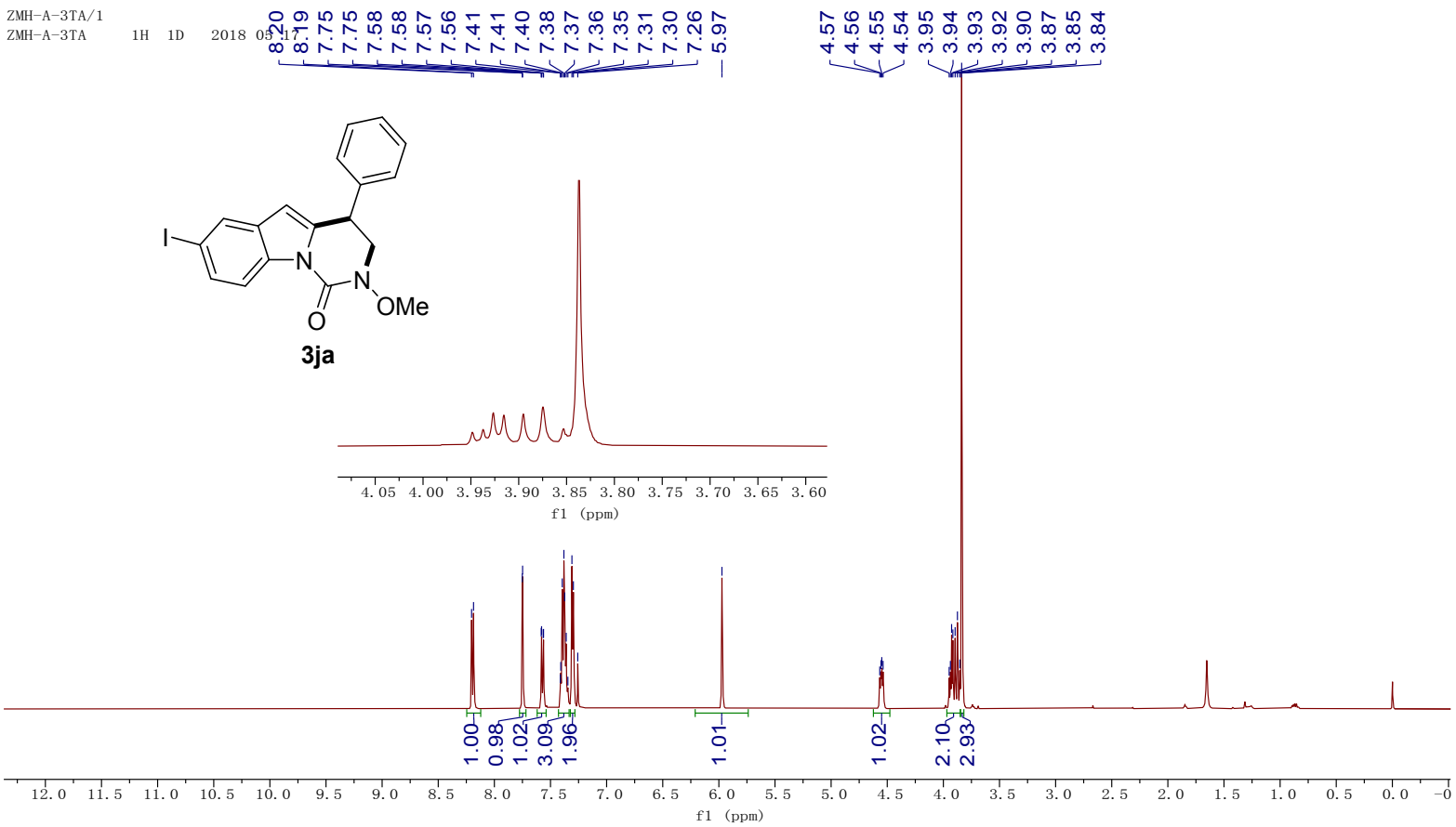

ZMH-A-3KA-2
ZMH-A-3KA 13C 1D 20180411-5
169.4
158.2
152.3
139.9
138.0
137.8
130.4
130.4
129.0
128.2
116.4
116.4
112.1
111.9
105.9
105.7
104.9
77.2
77.0
76.7
62.8
54.6
40.9
F
N
N
OMe
O
3ga
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

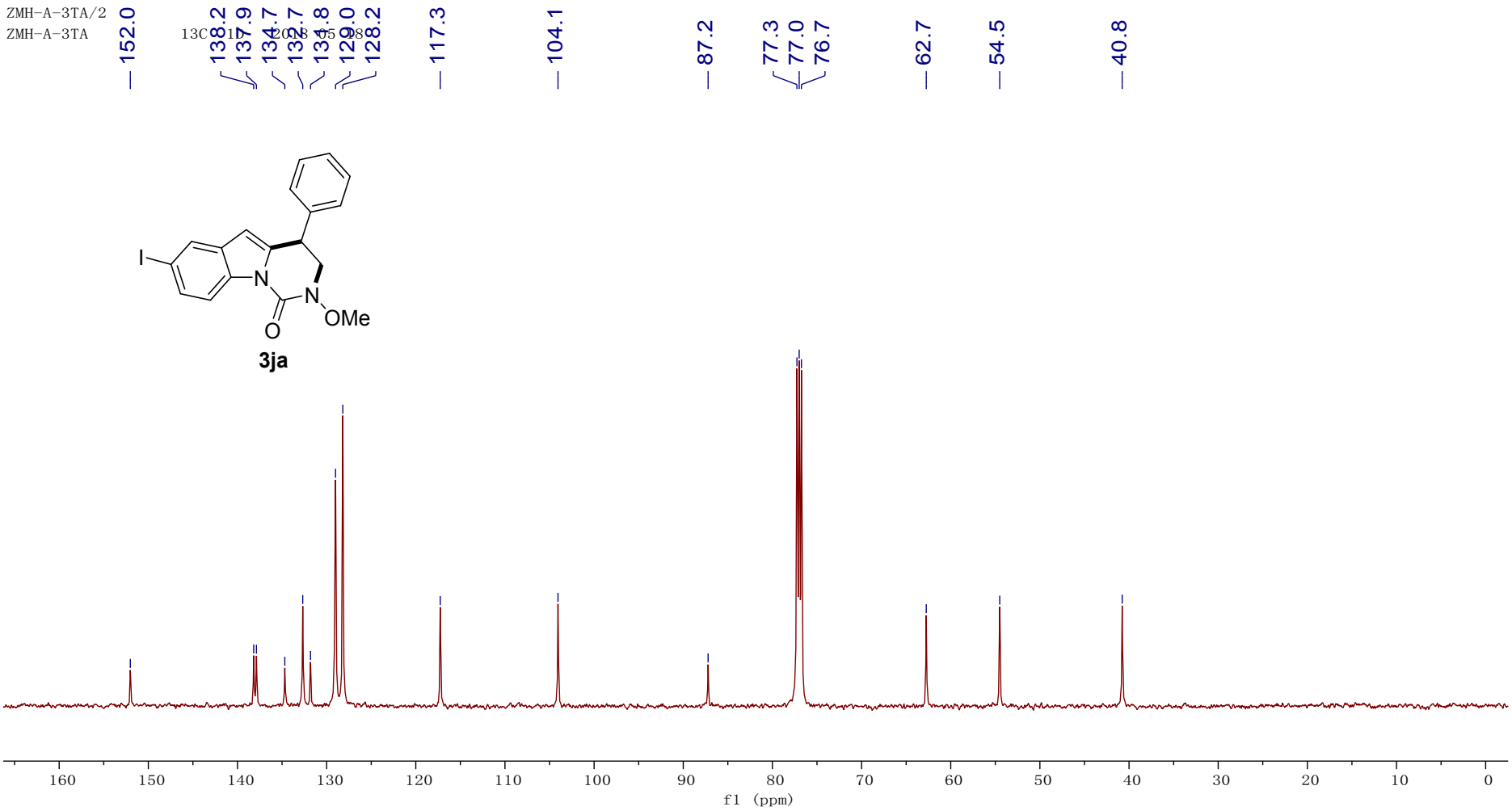

ZMH-A-3IA/1
ZMH-A-3IA 1H 1D 2018.05.02
8.37 8.35 7.42 7.42 7.40 7.40 7.39 7.39 7.38 7.38 7.37 7.37 7.35 7.33 7.32 7.31 7.28 7.27 7.26 7.26 6.00
4.58 4.57 4.57 4.56 4.56 4.55 3.96 3.95 3.94 3.93 3.91 3.89 3.87 3.85
Cl
N
N
OMe
O
3ha
7.50 7.45 7.40 7.35 7.30 7.25 7.20 7.15
f1 (ppm)
4.10 4.05 4.00 3.95 3.90 3.85 3.80 3.75
f1 (ppm)
1.00 3.98 1.90 1.24 0.99 1.01 2.19 2.74
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


ZMH-A-3IA/C
ZMH-A-3IA
152.1
138.7
137.9
133.8
130.7
129.0
128.7
128.2
124.4
119.8
116.4
104.4
77.2
77.0
76.7
62.8
54.5
40.9
Cl
N
N
OMe
O
3ha
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

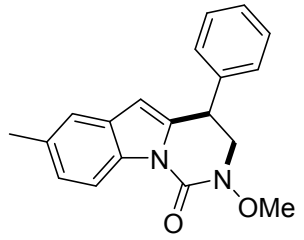

ZMH-A-3HAL/1
ZMH-A-3HAL 1H 1D 2018 04 09
8.32
8.30
7.55
7.41
7.41
7.40
7.40
7.39
7.38
7.36
7.32
7.31
7.26
6.00
4.58
4.57
4.56
4.55
3.96
3.95
3.94
3.92
3.91
3.89
3.87
3.84
Br
N
N
OMe
O
3ia
4.05 4.00 3.95 3.90 3.85 3.80 3.75 3.70
f1 (ppm)
1.00
1.01
3.98
1.96
0.99
1.01
2.09
2.92
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


ZMH-A-3JAL/1
ZMH-A-3JAL
152.1
135.5
137.9
134.2
131.2
129.0
128.2
127.1
122.9
116.8
116.4
104.3
77.2
77.0
76.7
62.8
54.5
40.9
Br
N
N
OMe
O
3ia
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

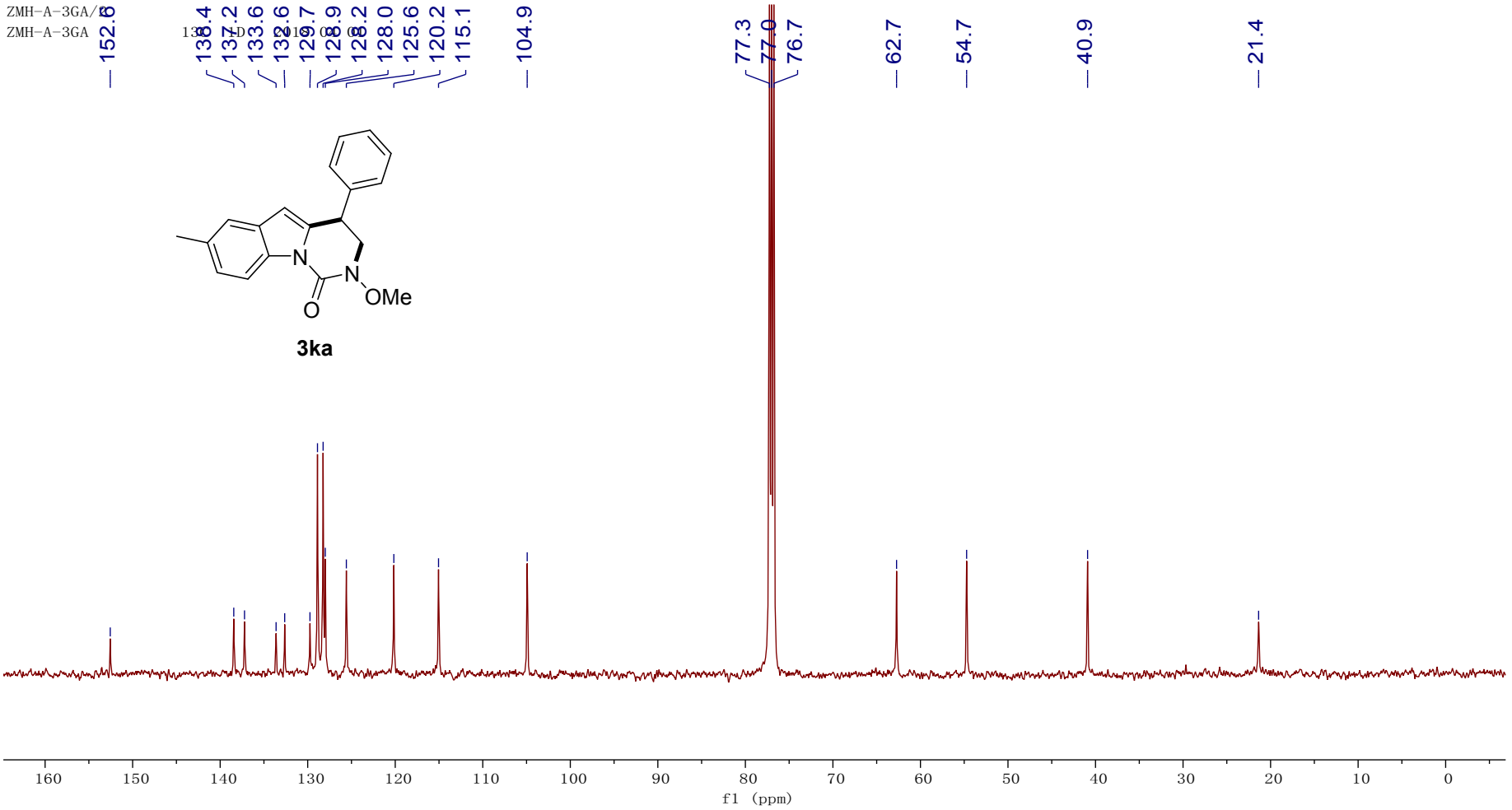

ZMH-A-3TA/1
ZMH-A-3TA 1H 1D 2018 05 17
8.20 8.19 7.75 7.75 7.58 7.58 7.57 7.56 7.41 7.41 7.40 7.38 7.37 7.36 7.35 7.31 7.30 7.26 5.97
4.57 4.56 4.55 4.54 3.95 3.94 3.93 3.92 3.90 3.87 3.85 3.84
I
N
N
OMe
O
3ja
4.05 4.00 3.95 3.90 3.85 3.80 3.75 3.70 3.65 3.60
f1 (ppm)
1.00 0.98 1.02 3.09 1.96 1.01 1.02 2.10 2.93
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

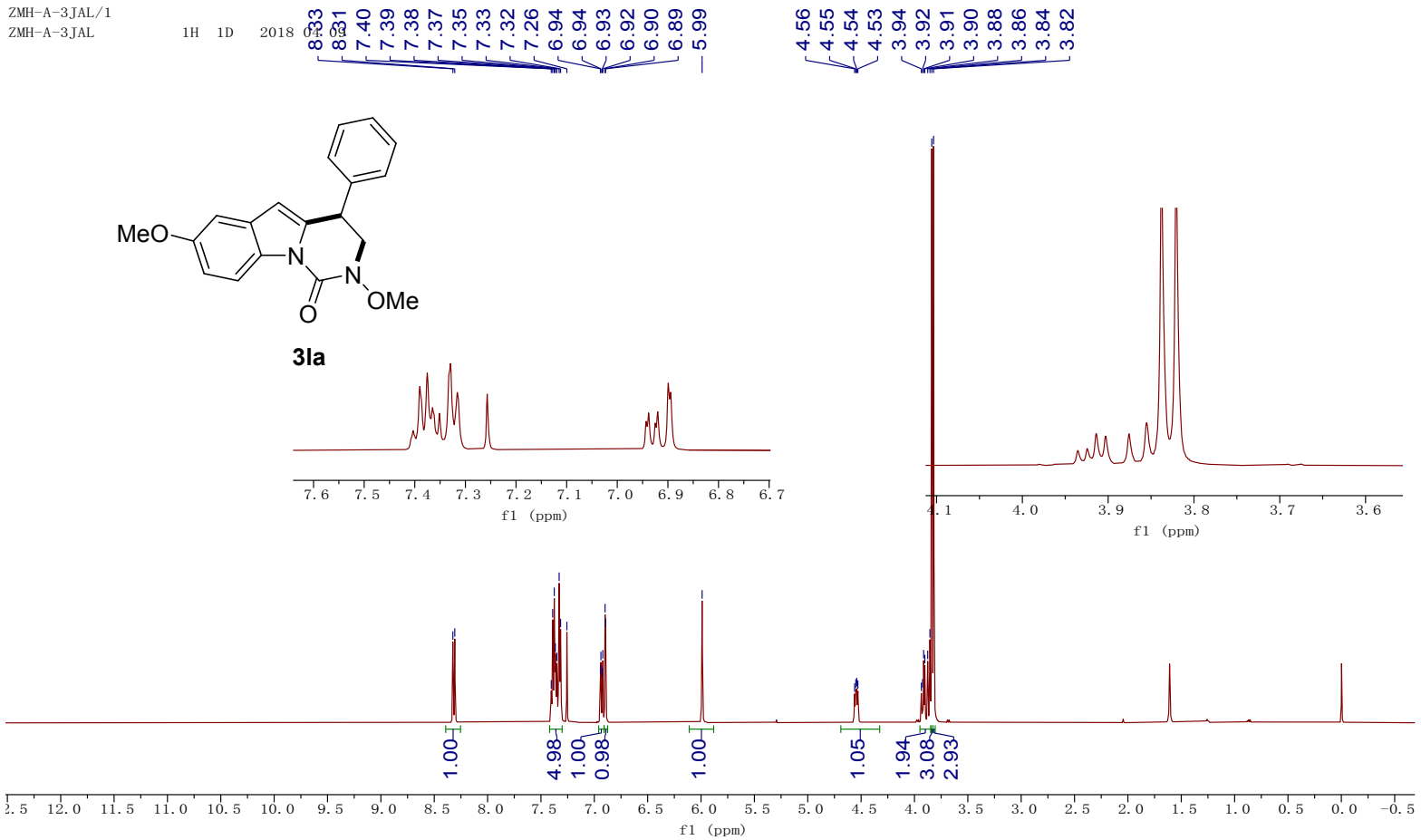

ZMH-A-3TA/2
ZMH-A-3TA
152.0
138.2
137.9
134.7
132.7
131.8
129.0
128.2
117.3
104.1
87.2
77.3
77.0
76.7
62.7
54.5
40.8
I
N
N
OMe
O
3ja
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

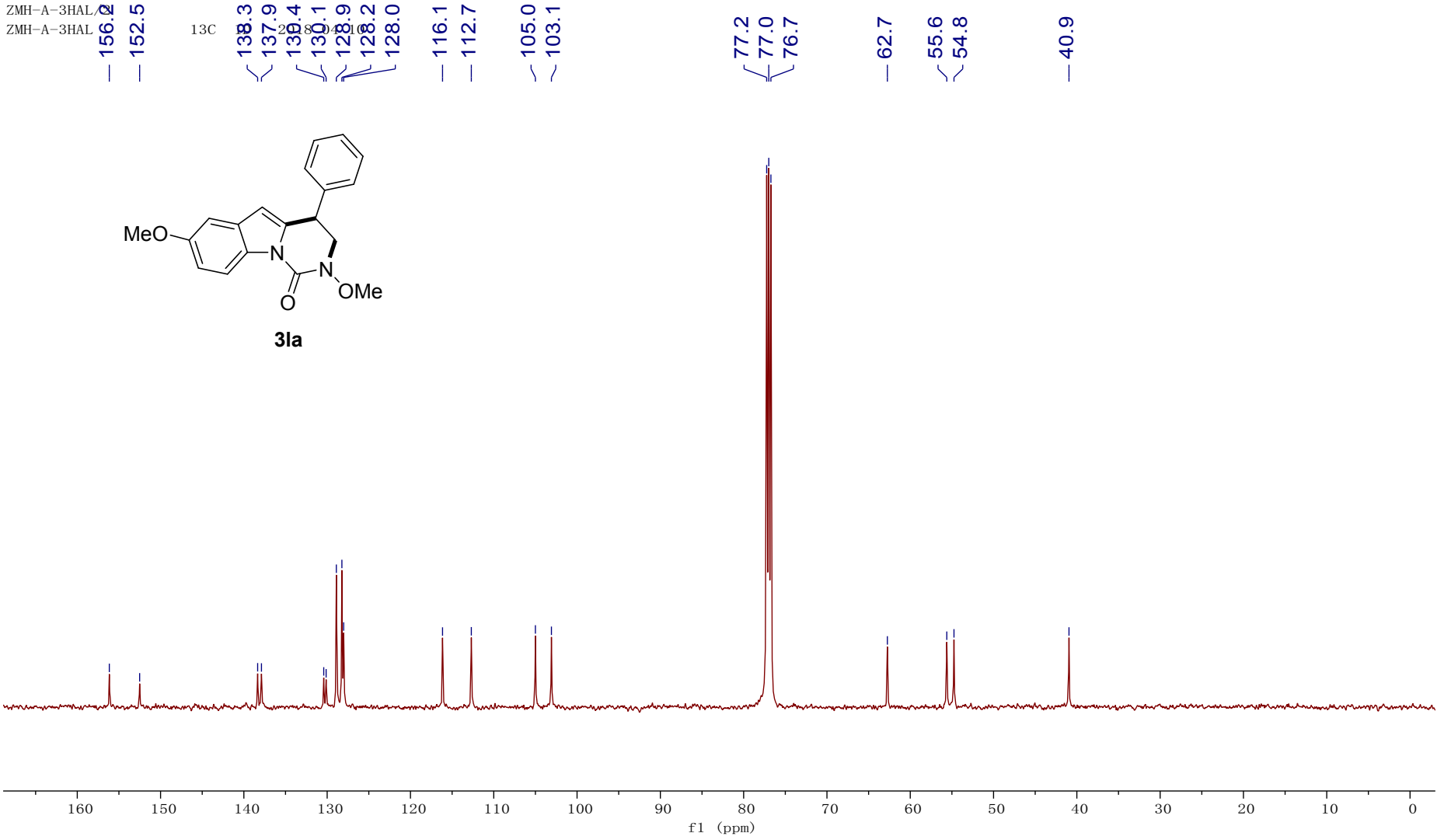
ZMH-A-3GA/1
ZMH-A-3GA 1H 1D 2018 03 30

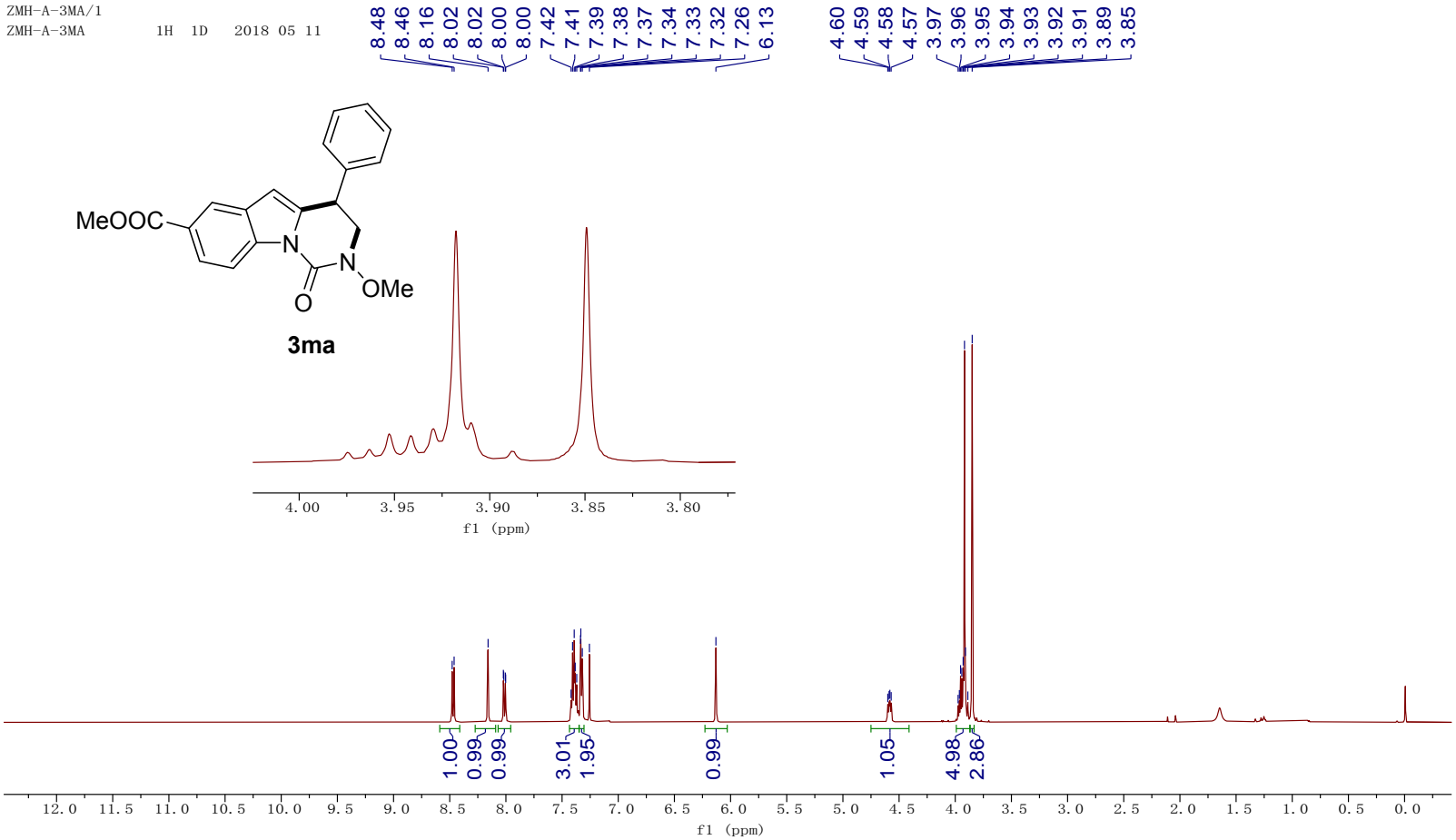


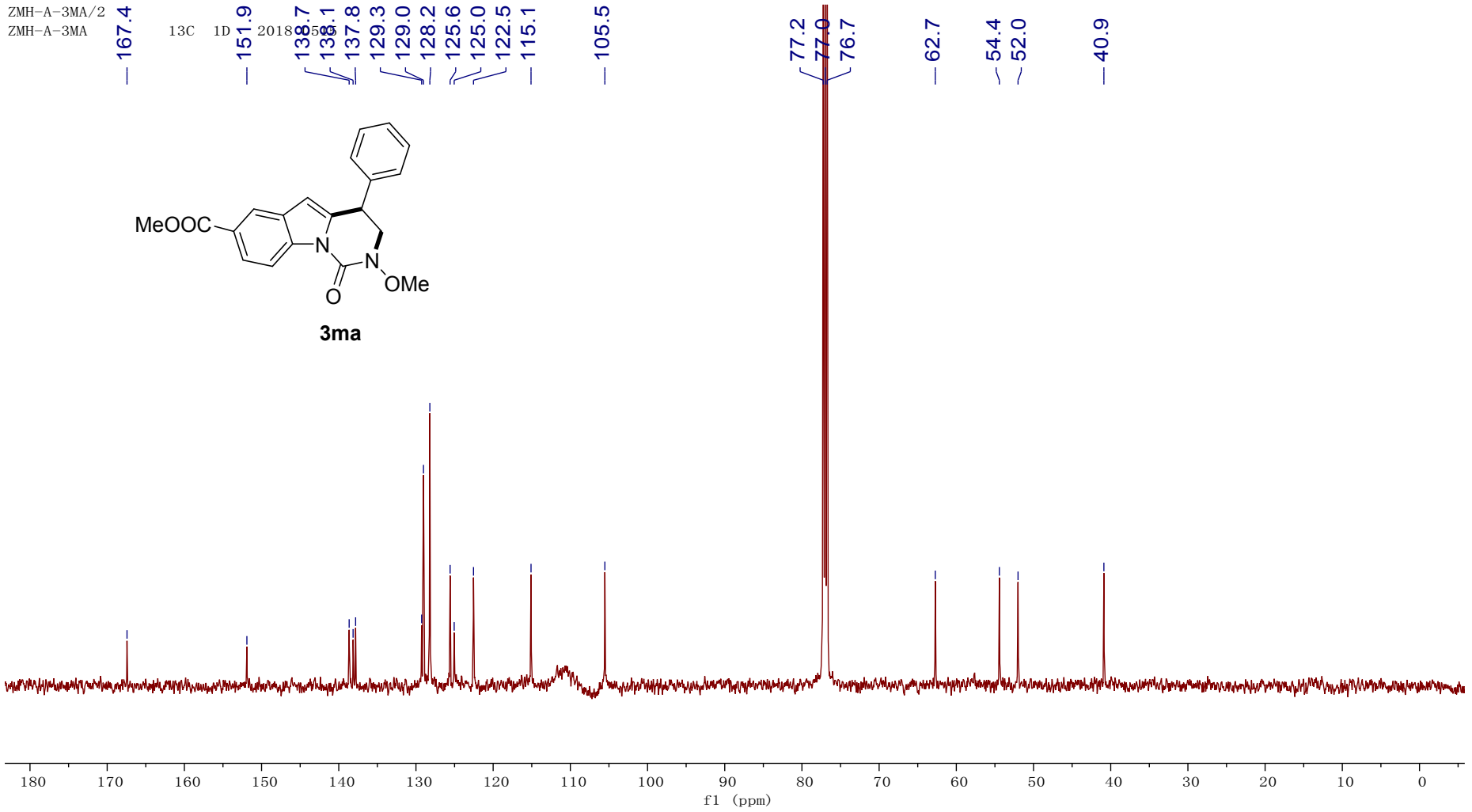
3ka

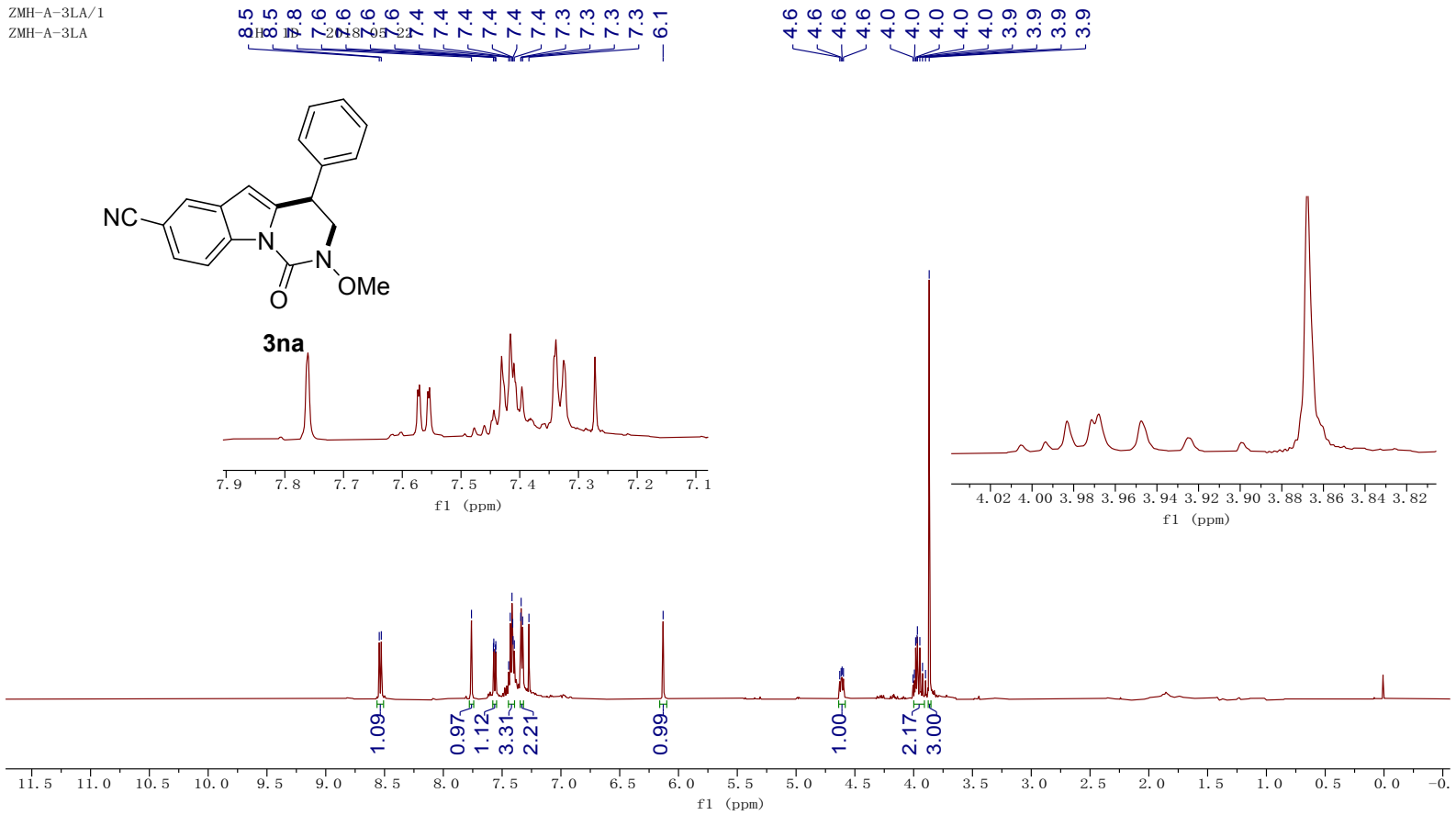

ZMH-A-3GA/C
ZMH-A-3GA
152.6
138.4
137.2
133.6
132.6
129.7
128.9
128.2
128.0
125.6
120.2
115.1
104.9
77.3
77.0
76.7
62.7
54.7
40.9
21.4
N
N
OMe
O
3ka
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

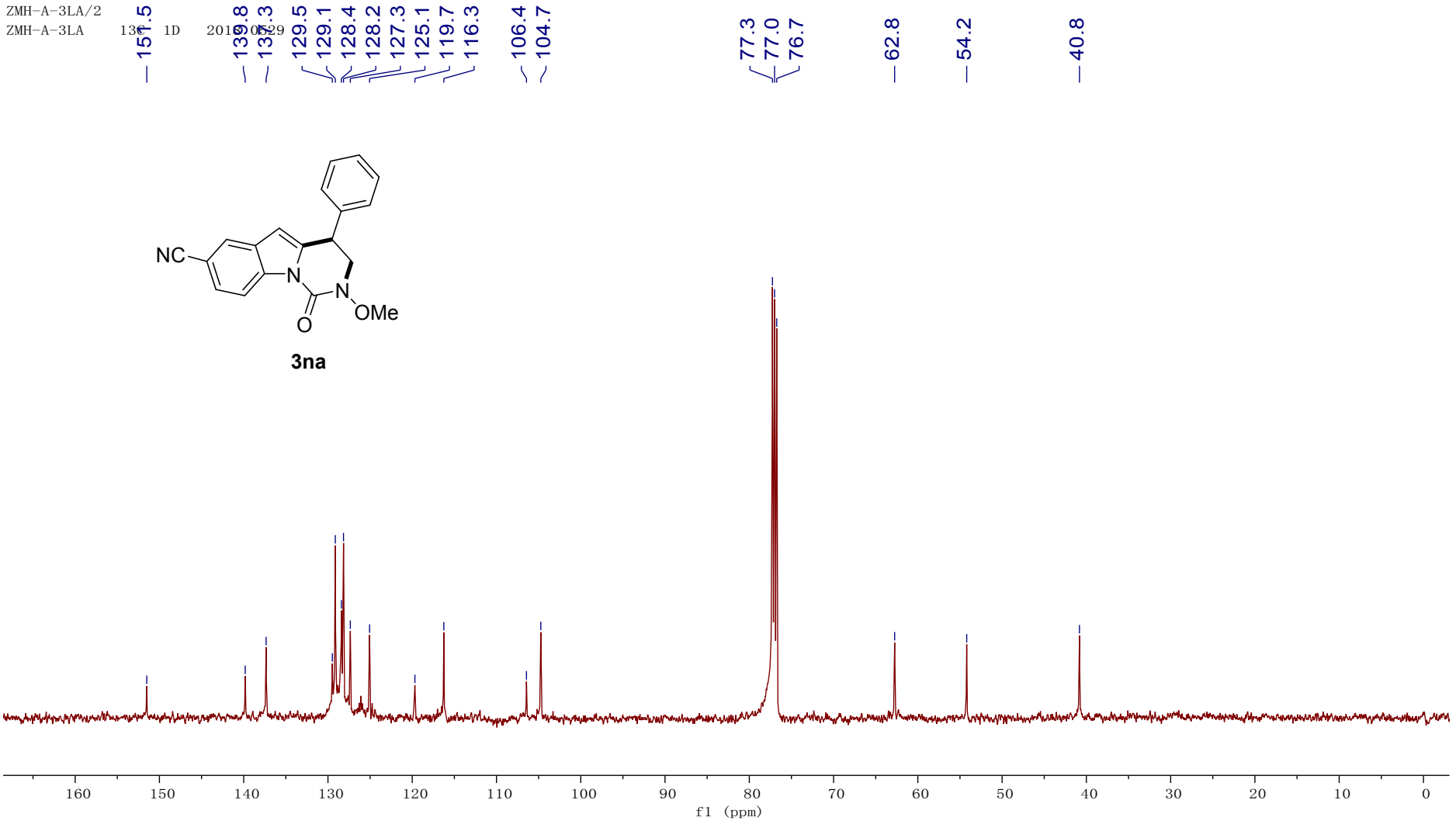

ZMH-A-3JAL/1
ZMH-A-3JAL 1H 1D 2018 04 03
8.33 8.31 7.40 7.39 7.38 7.37 7.35 7.33 7.32 7.26 6.94 6.94 6.93 6.92 6.90 6.89 5.99
4.56 4.55 4.54 4.53 3.94 3.92 3.91 3.90 3.88 3.86 3.84 3.82
MeO
N
N
OMe
O
3la
1.00 4.98 1.00 0.98 1.00 1.05 1.94 3.08 2.93
f1 (ppm)

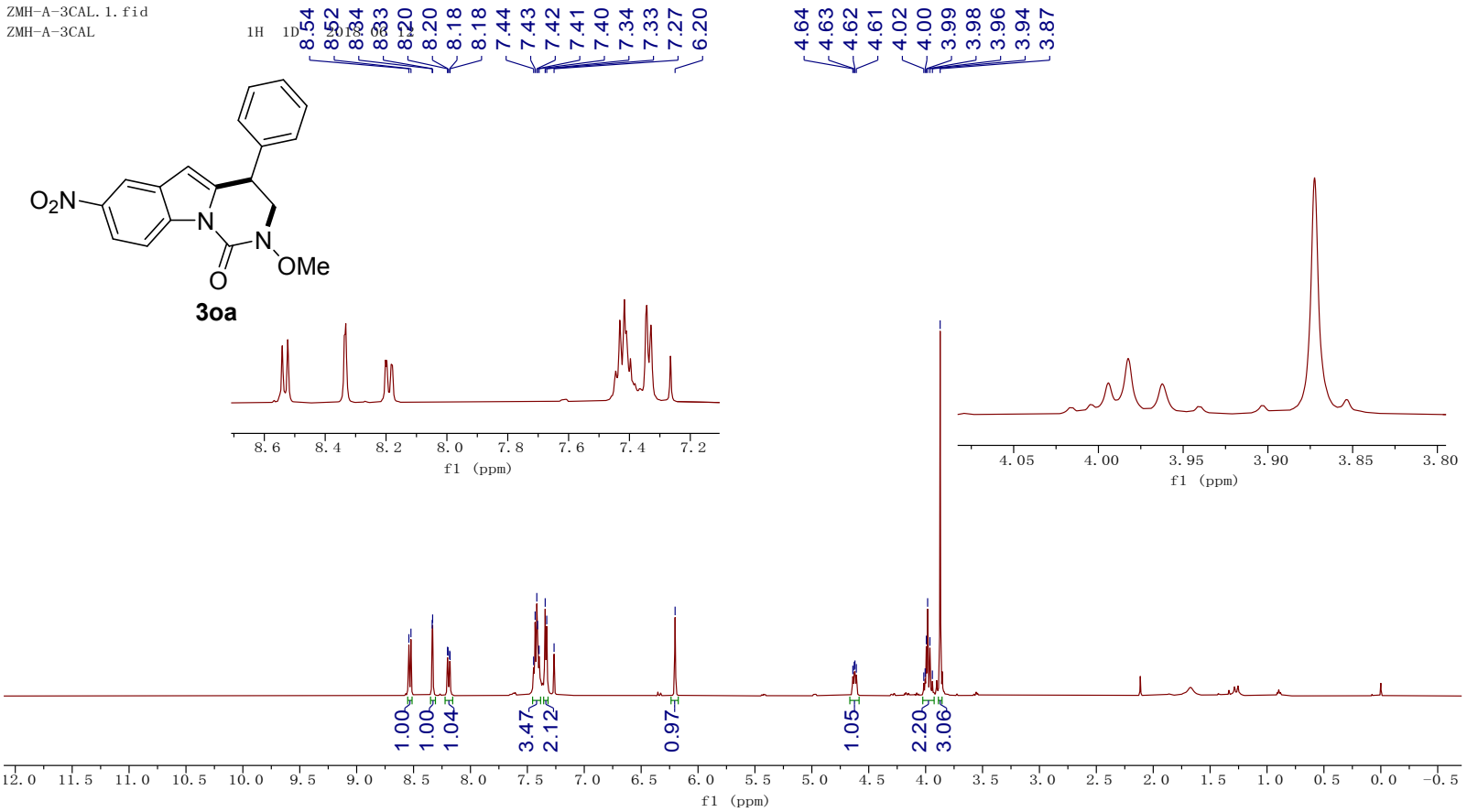

ZMH-A-3HAL/C2
ZMH-A-3HAL 13C
156.2
152.5
138.3
137.9
130.4
130.1
129.9
128.2
128.0
116.1
112.7
105.0
103.1
77.2
77.0
76.7
62.7
55.6
54.8
40.9
MeO
N
N
OMe
O
3la
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

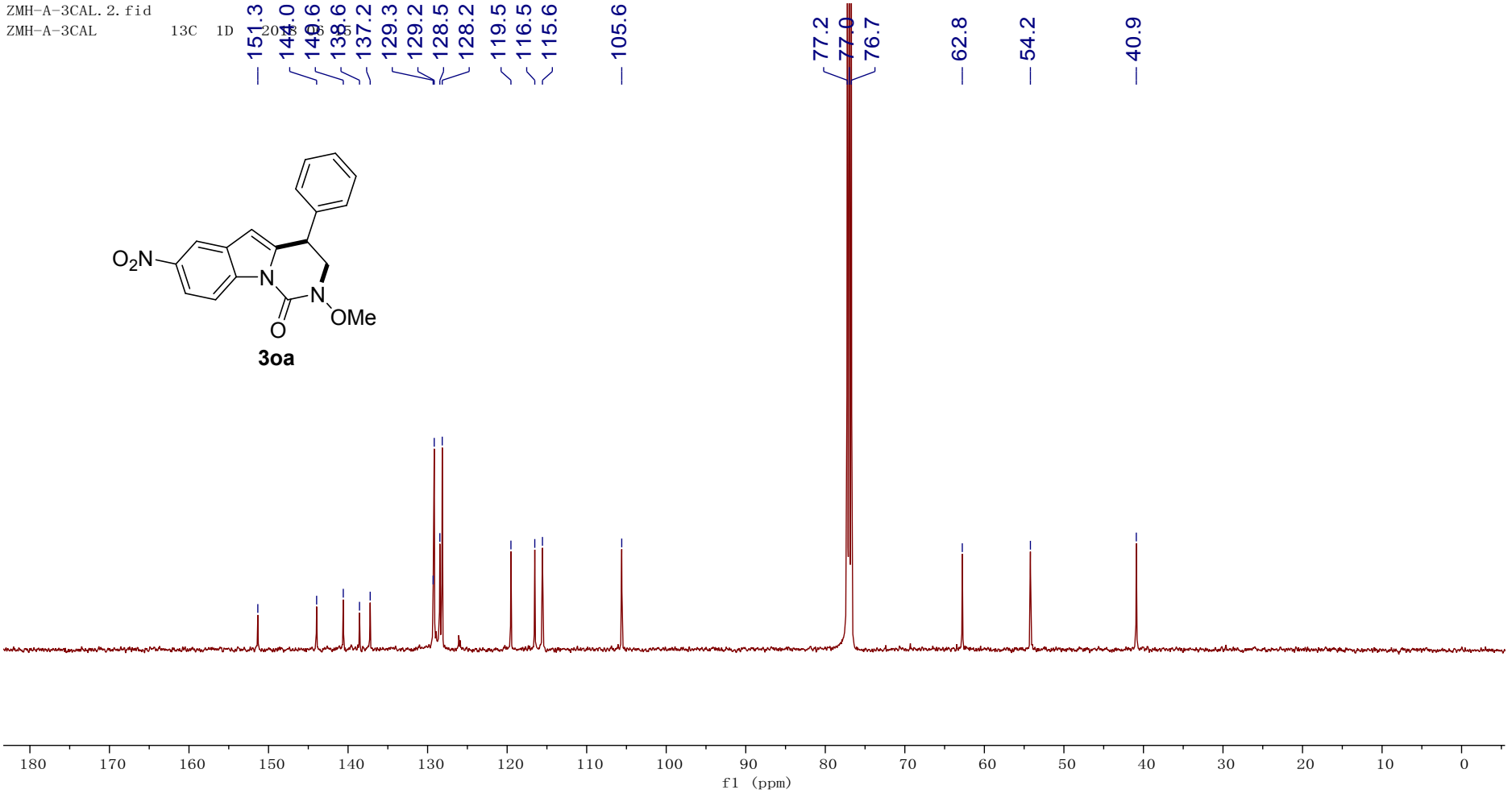

ZMH-A-3MA/1
ZMH-A-3MA 1H 1D 2018 05 11
8.48 8.46 8.16 8.02 8.02 8.00 8.00 7.42 7.41 7.39 7.38 7.37 7.34 7.33 7.32 7.26 6.13
4.60 4.59 4.58 4.57 3.97 3.96 3.95 3.94 3.93 3.92 3.91 3.89 3.85
MeOOC
N
N
OMe
O
3ma
4.00 3.95 3.90 3.85 3.80
f1 (ppm)
1.00 0.99 0.99 3.01 1.95 0.99 1.05 4.98 2.86
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

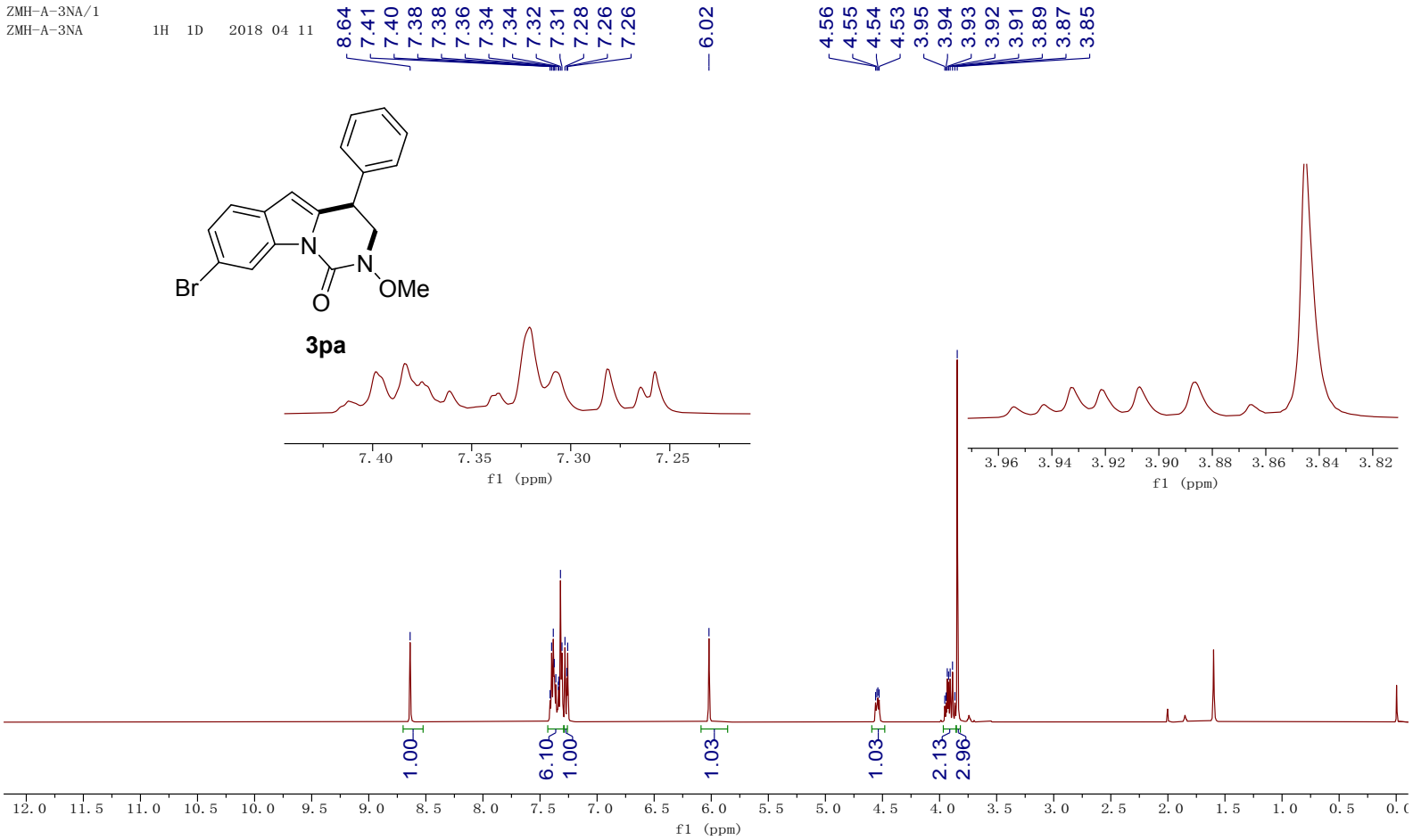

ZMH-A-3MA/2
ZMH-A-3MA 13C 1D 20180530
167.4
151.9
138.7
138.1
137.8
129.3
129.0
128.2
125.6
125.0
122.5
115.1
105.5
77.2
77.0
76.7
62.7
54.4
52.0
40.9
MeOOC
N
N
OMe
O
3ma
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

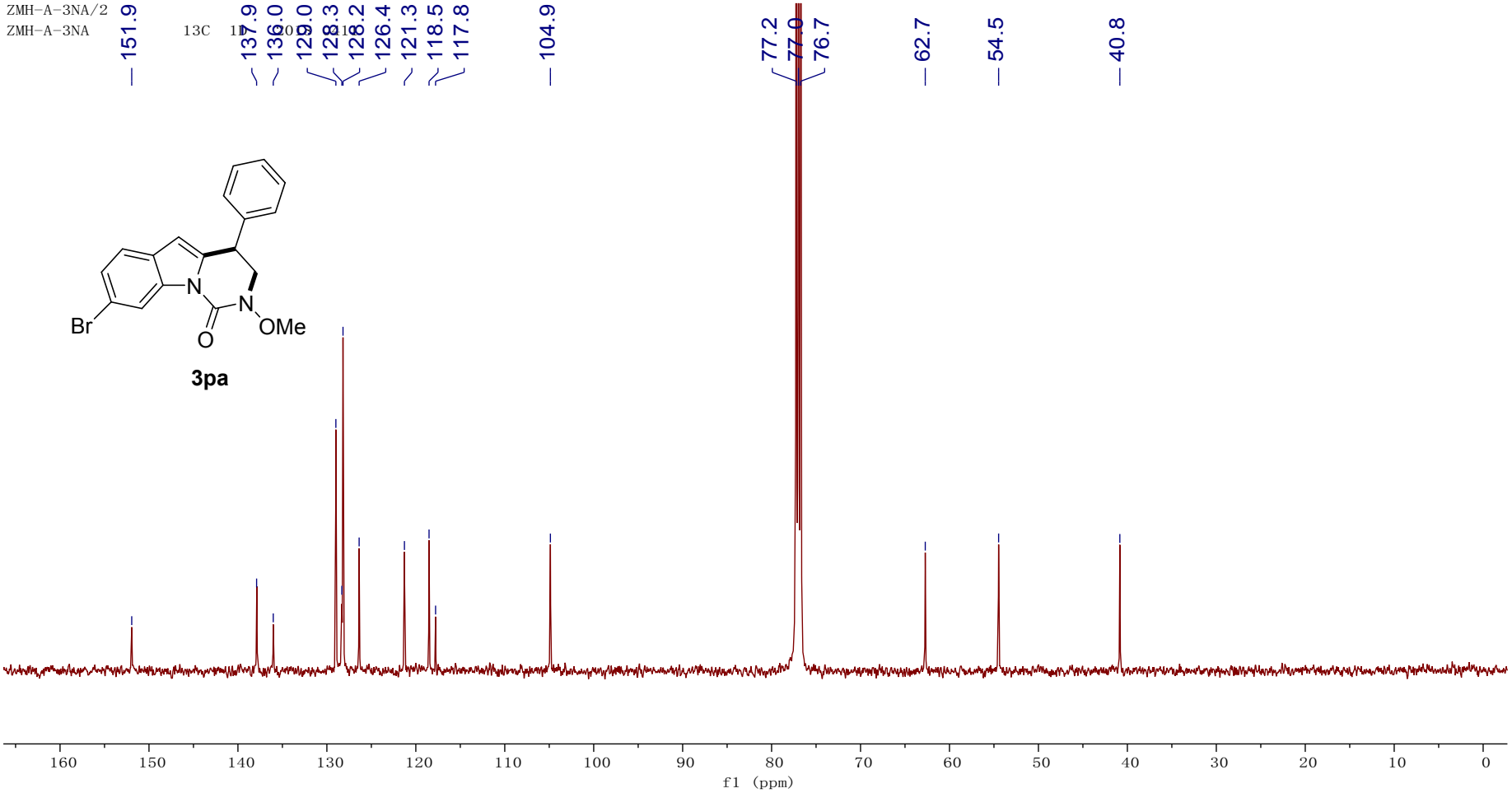

ZMH-A-3LA/1
ZMH-A-3LA
NC
N
N
O
OMe
3na
f1 (ppm)
f1 (ppm)
f1 (ppm)

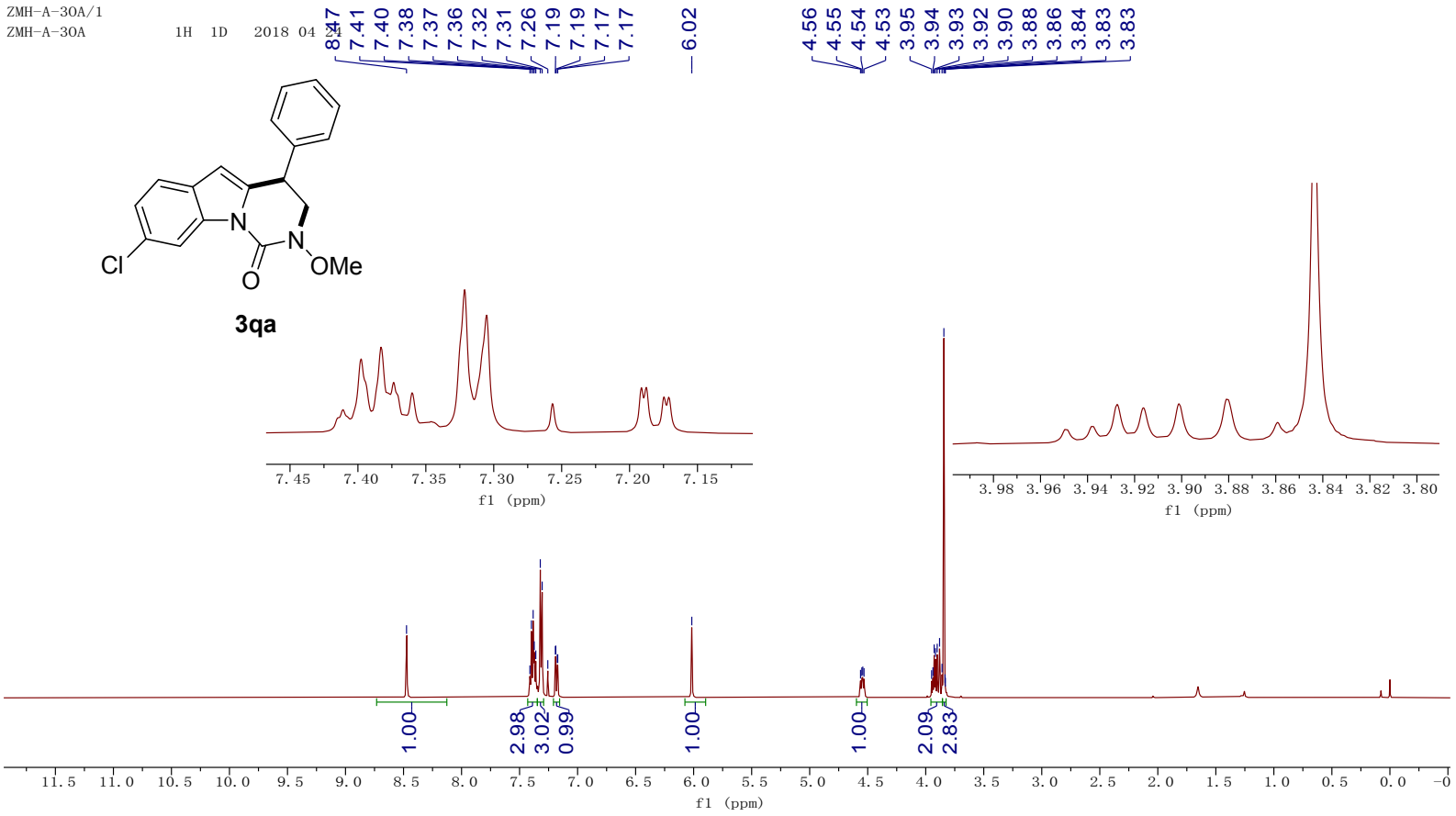

ZMH-A-3LA/2
ZMH-A-3LA 13C 1D 20190529
151.5
139.8
135.3
129.5
129.1
128.4
128.2
127.3
125.1
119.7
116.3
106.4
104.7
77.3
77.0
76.7
62.8
54.2
40.8
NC
N
N
OMe
O
3na
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

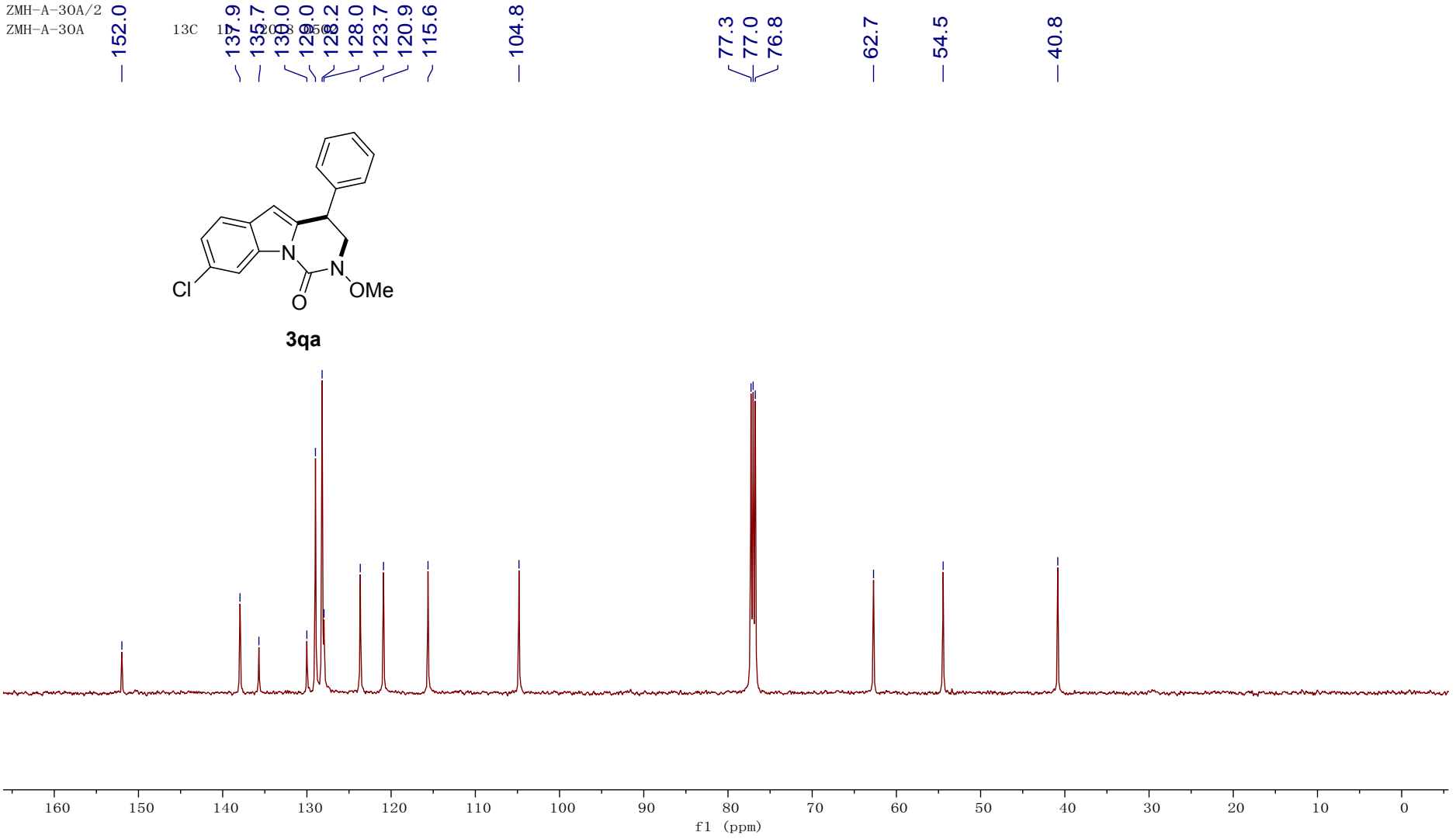

ZMH-A-3CAL.1.fid
ZMH-A-3CAL
1H 1D
8.54 8.52 8.34 8.33 8.20 8.20 8.18 8.18 7.44 7.43 7.42 7.41 7.40 7.34 7.33 7.27 6.20
4.64 4.63 4.62 4.61 4.02 4.00 3.99 3.98 3.96 3.94 3.87
O2N
N
N
OMe
O
3oa
f1 (ppm)
1.00 1.00 1.04 3.47 2.12 0.97 1.05 2.20 3.06

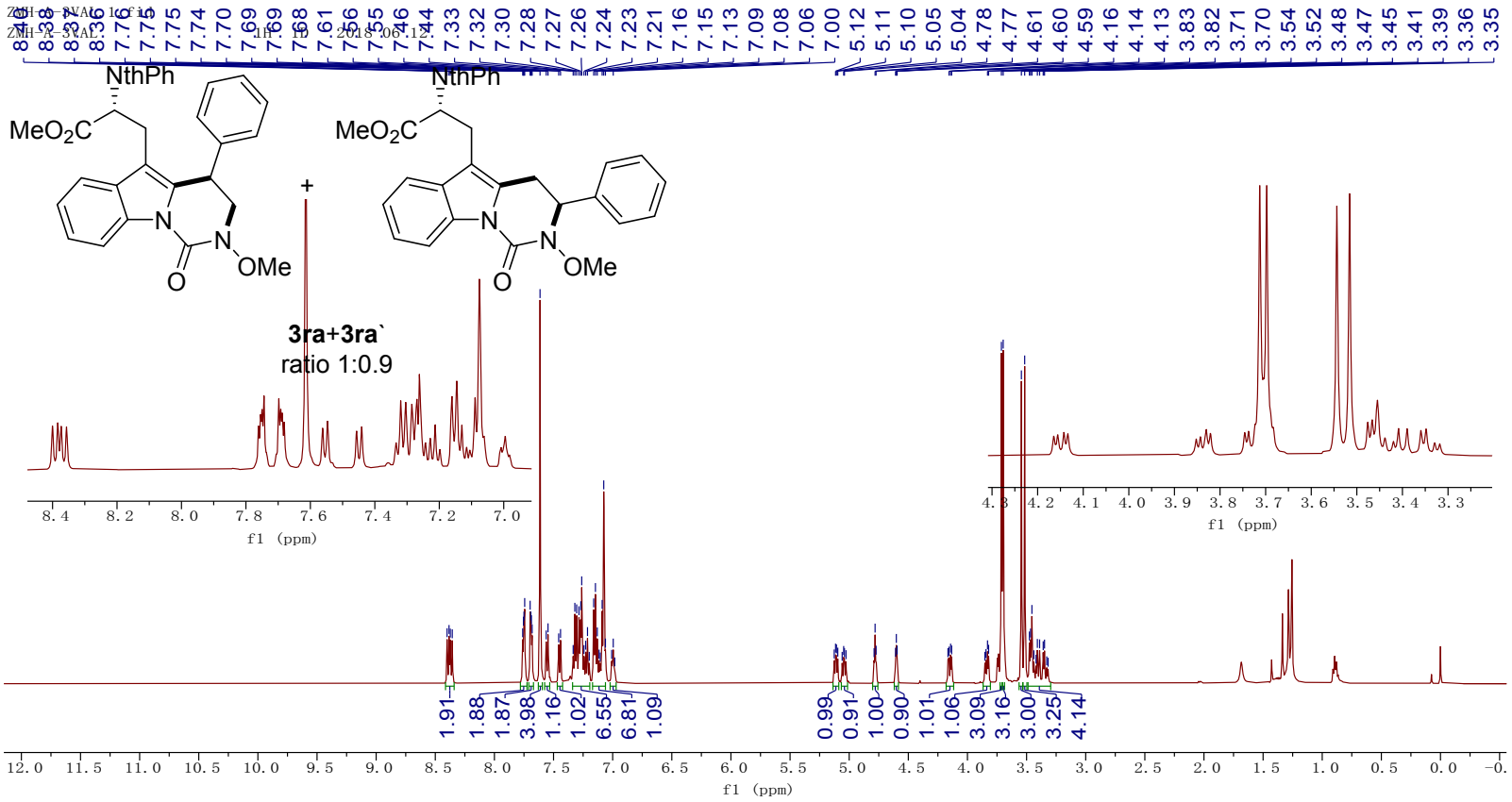

ZMH-A-3CAL.2.fid
ZMH-A-3CAL 13C 1D
151.3
144.0
140.6
138.6
137.2
129.3
129.2
128.5
128.2
119.5
116.5
115.6
105.6
77.2
77.0
76.7
62.8
54.2
40.9
O2N
N
N
OMe
O
3oa
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

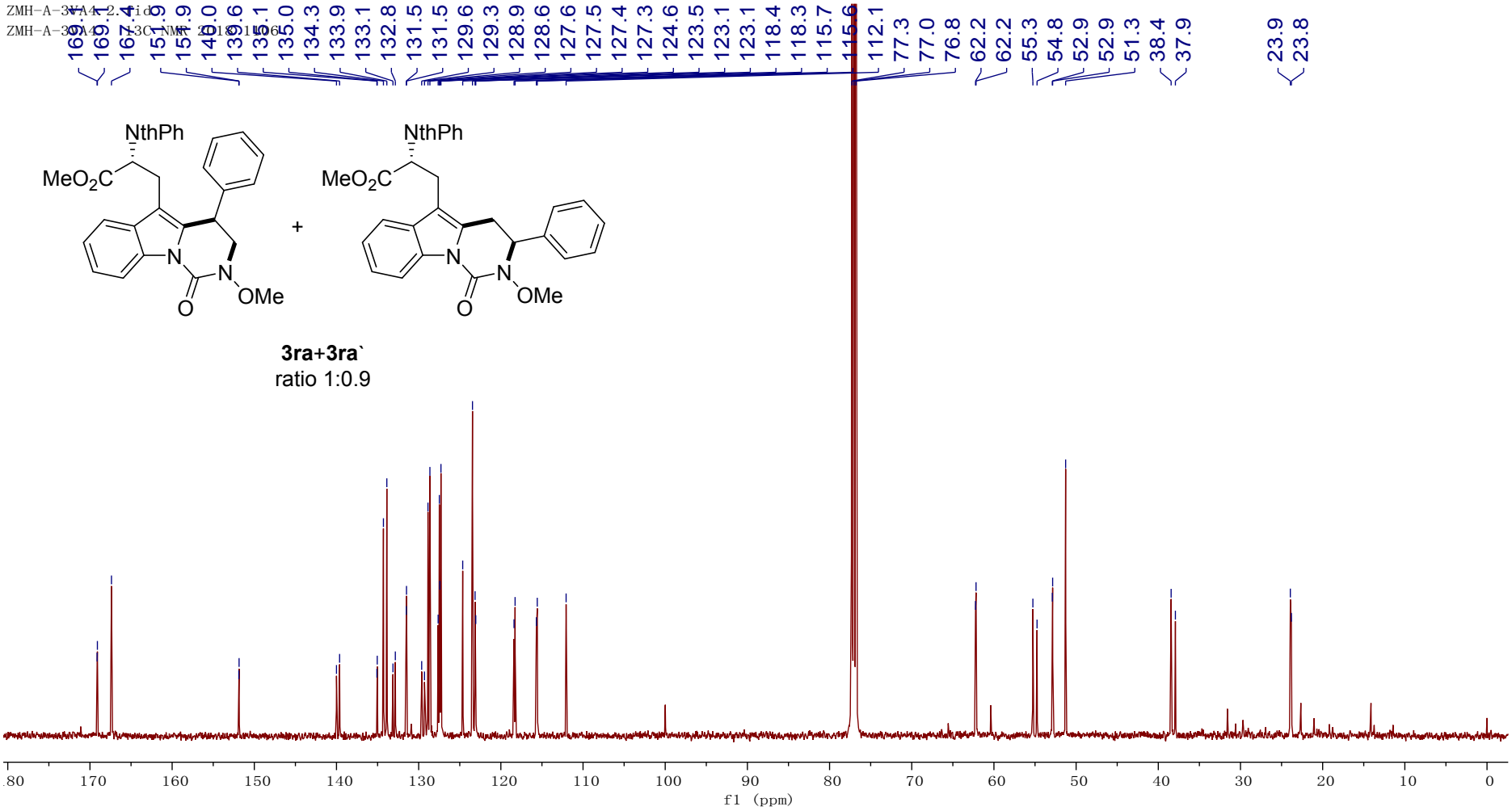

ZMH-A-3NA/1
ZMH-A-3NA 1H 1D 2018 04 11
8.64
7.41
7.40
7.38
7.38
7.36
7.34
7.34
7.32
7.31
7.28
7.26
7.26
6.02
4.56
4.55
4.54
4.53
3.95
3.94
3.93
3.92
3.91
3.89
3.87
3.85
Br
N
N
O
OMe
3pa
7.40
7.35
7.30
7.25
f1 (ppm)
3.96
3.94
3.92
3.90
3.88
3.86
3.84
3.82
f1 (ppm)
1.00
6.10
1.00
1.03
1.03
2.13
2.96
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

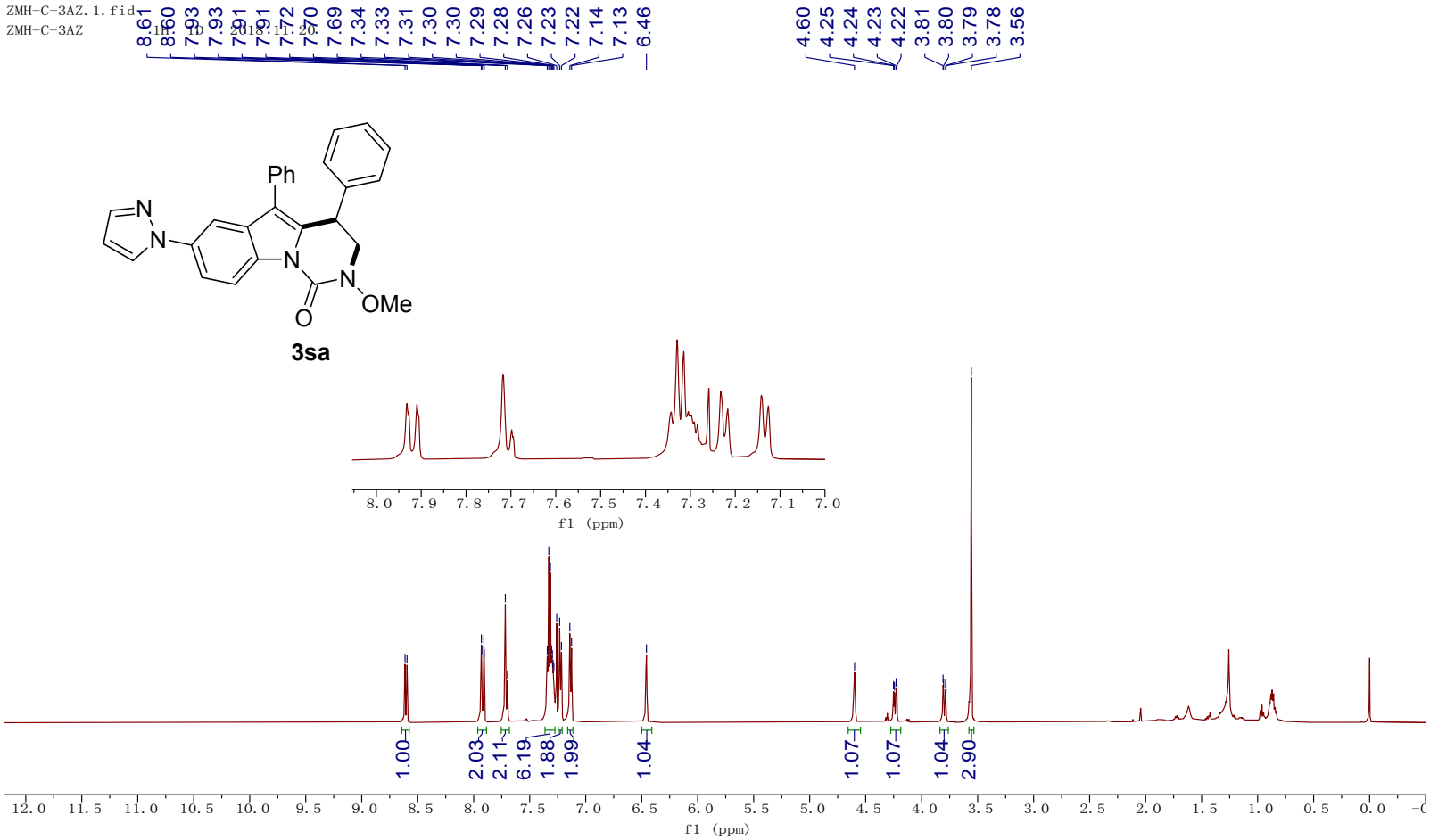

ZMH-A-3NA/2
ZMH-A-3NA
151.9
137.9
136.0
129.0
128.3
128.2
126.4
121.3
118.5
117.8
104.9
77.2
77.0
76.7
62.7
54.5
40.8
Br
N
N
OMe
O
3pa
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

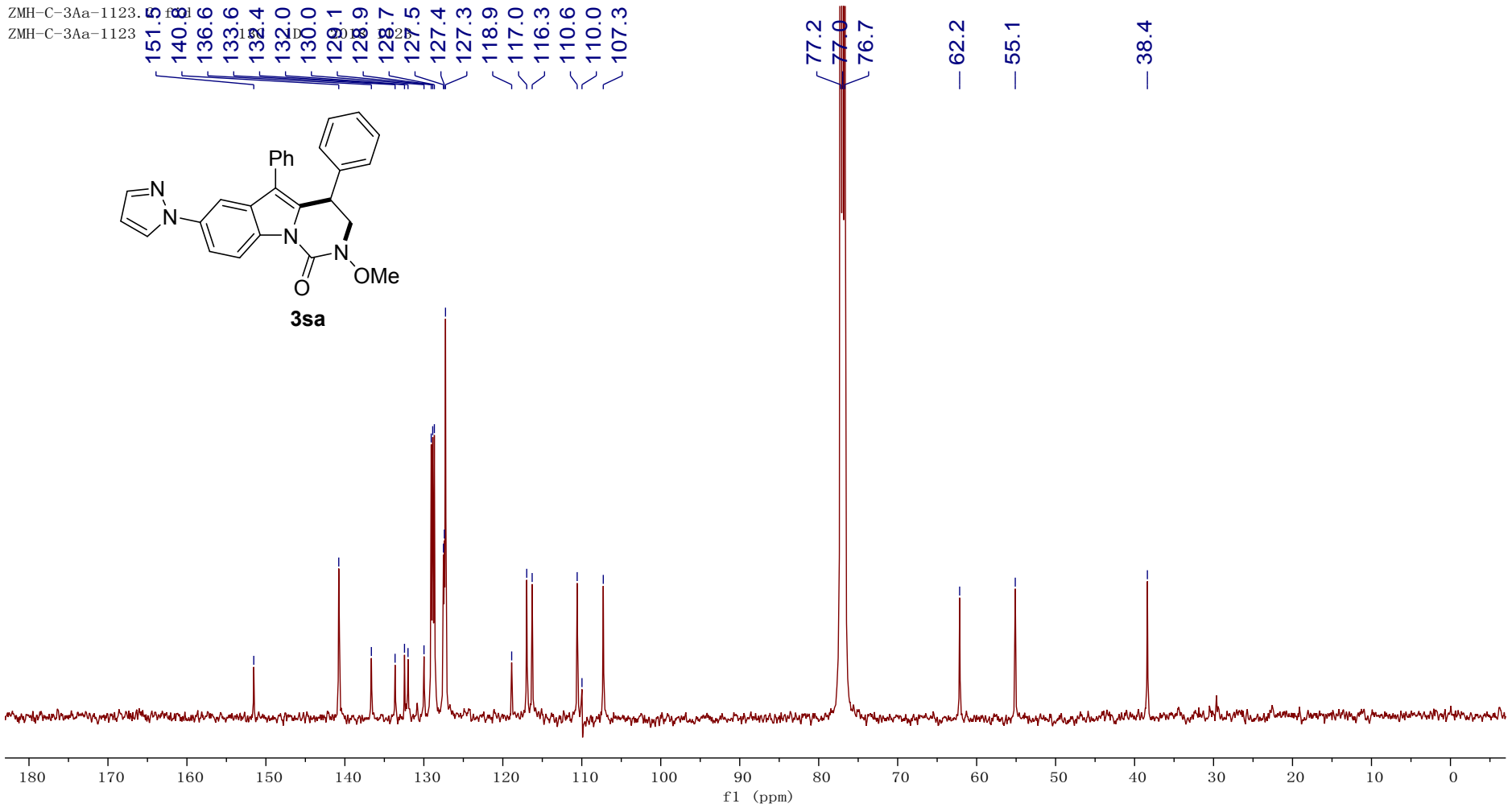

ZMH-A-30A/1
ZMH-A-30A 1H 1D 2018 04 24
8.47
7.41
7.40
7.38
7.37
7.36
7.32
7.31
7.26
7.19
7.19
7.17
7.17
6.02
4.56
4.55
4.54
4.53
3.95
3.94
3.93
3.92
3.90
3.88
3.86
3.84
3.83
3.83
Cl
N
N
OMe
O
3qa
7.45 7.40 7.35 7.30 7.25 7.20 7.15
f1 (ppm)
3.98 3.96 3.94 3.92 3.90 3.88 3.86 3.84 3.82 3.80
f1 (ppm)
1.00
2.98
3.02
0.99
1.00
1.00
2.09
2.83
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0
f1 (ppm)

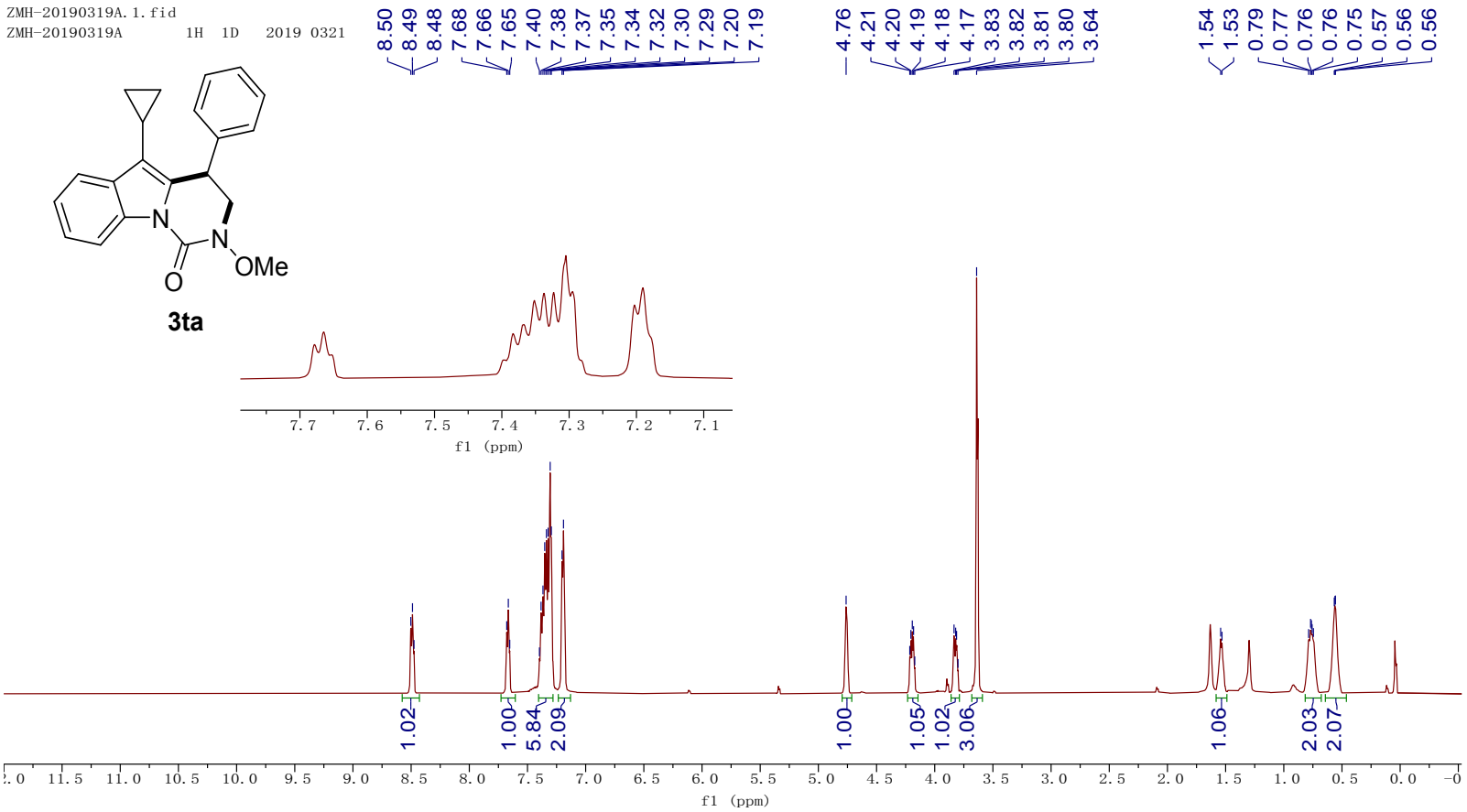

ZMH-A-30A/2
ZMH-A-30A
13C
152.0
137.9
135.7
130.0
129.0
128.2
128.0
123.7
120.9
115.6
104.8
77.3
77.0
76.8
62.7
54.5
40.8
Cl
N
N
OMe
O
3qa
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

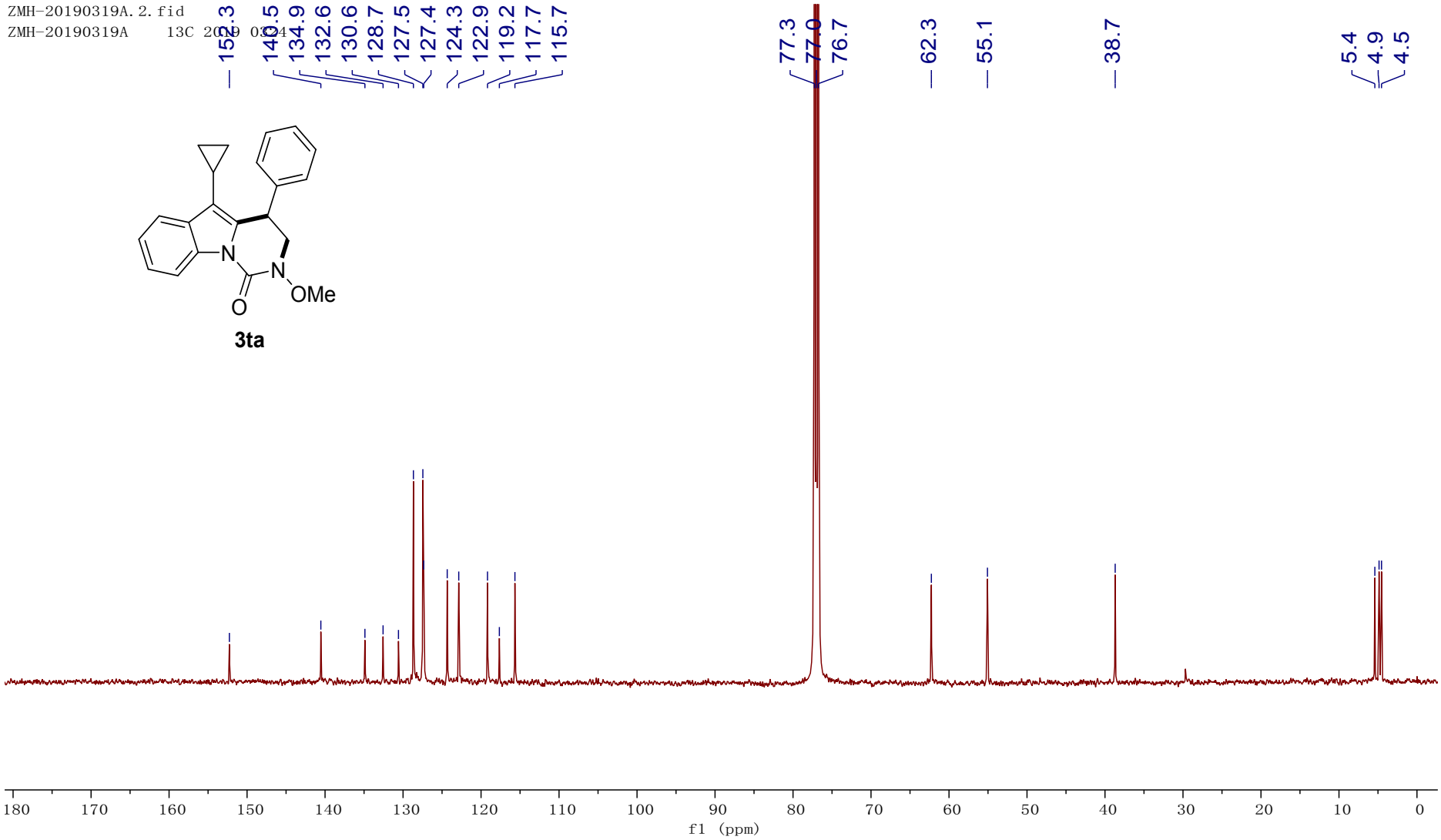

NthPh
MeO2C
N
N
OMe
O
+
3ra+3ra`
ratio 1:0.9
f1 (ppm)

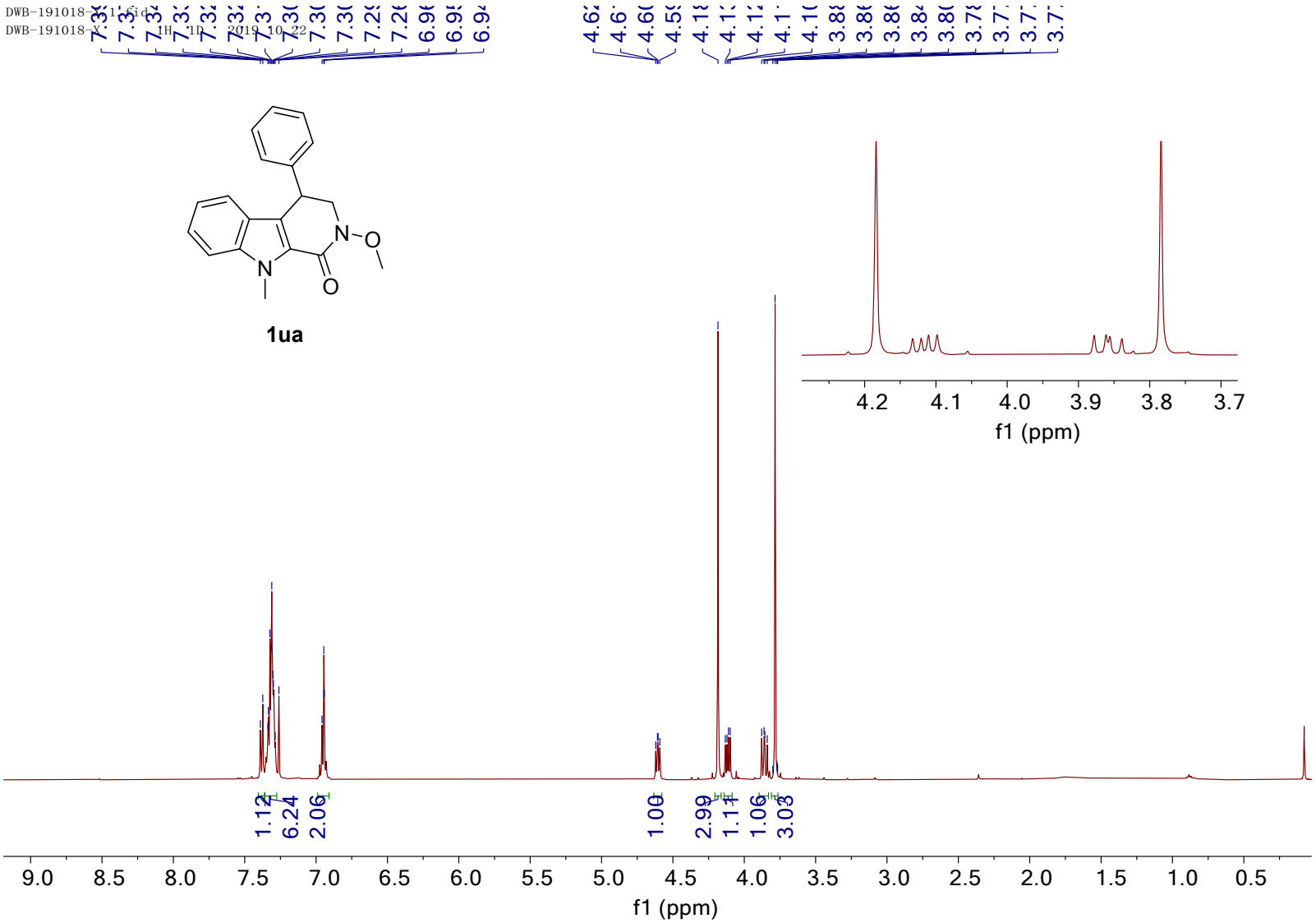

ZMH-A-3YA4-2.4.fid
ZMH-A-3YA4-13C-NMR-2018-11-06
169.4
169.2
167.4
151.9
151.9
140.0
139.6
135.1
135.0
134.3
133.9
133.1
132.8
131.5
131.5
129.6
129.3
128.9
128.6
127.6
127.5
127.4
127.3
124.6
123.5
123.1
123.1
118.4
118.3
115.7
115.6
112.1
77.3
77.0
76.8
62.2
62.2
55.3
54.8
52.9
52.9
51.3
38.4
37.9
23.9
23.8
NthPh
MeO2C
N
N
OMe
O
+
NthPh
MeO2C
N
N
OMe
O
3ra+3ra`
ratio 1:0.9
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

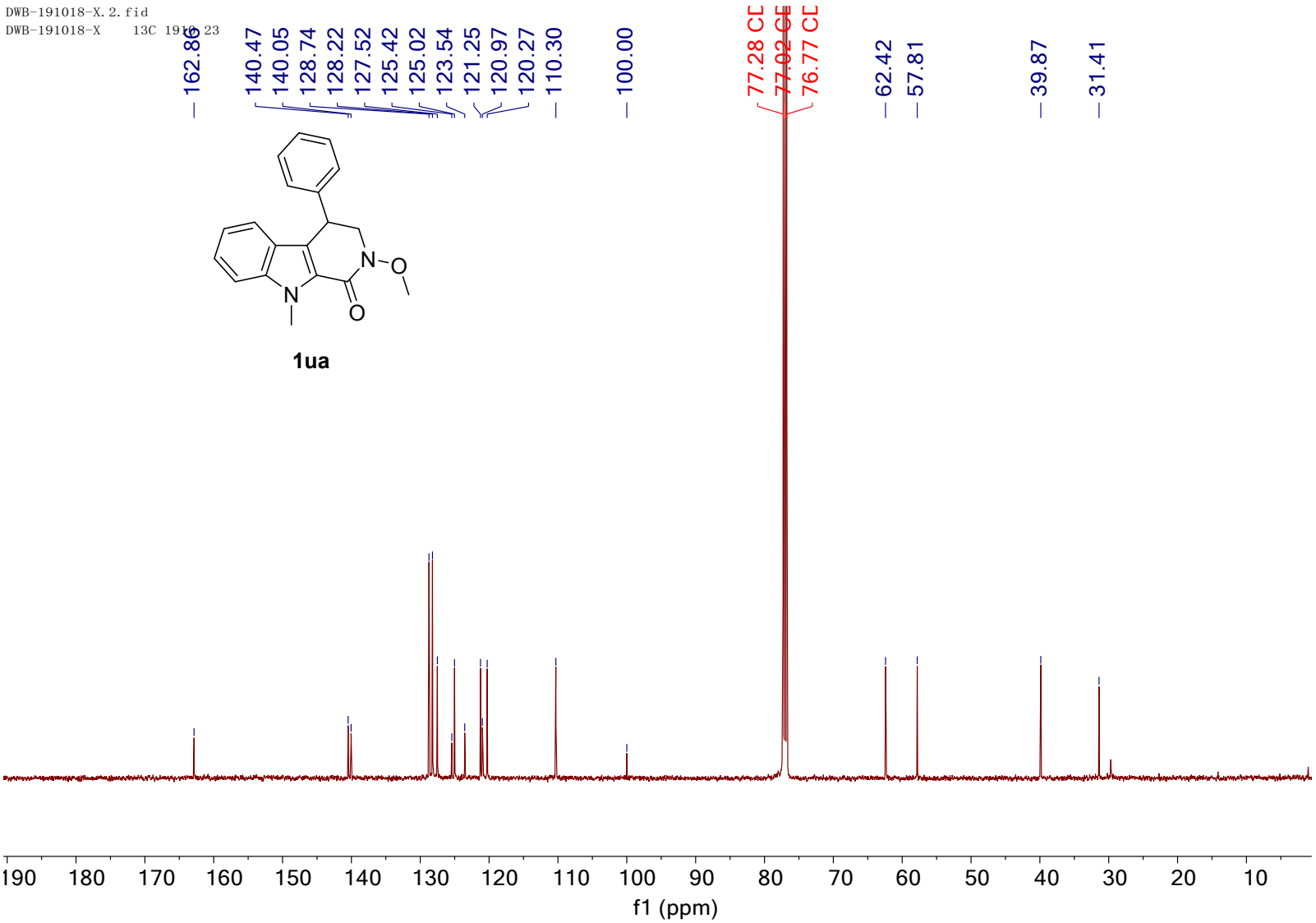

ZMH-C-3AZ.1.fid
ZMH-C-3AZ
8.61
8.60
7.93
7.93
7.91
7.91
7.72
7.70
7.69
7.34
7.33
7.31
7.30
7.30
7.29
7.28
7.26
7.23
7.22
7.14
7.13
6.46
4.60
4.25
4.24
4.23
4.22
3.81
3.80
3.79
3.78
3.56
Ph
N
N
N
N
OMe
O
3sa
f1 (ppm)
1.00
2.03
2.11
6.19
1.88
1.99
1.04
1.07
1.07
1.04
2.90
f1 (ppm)

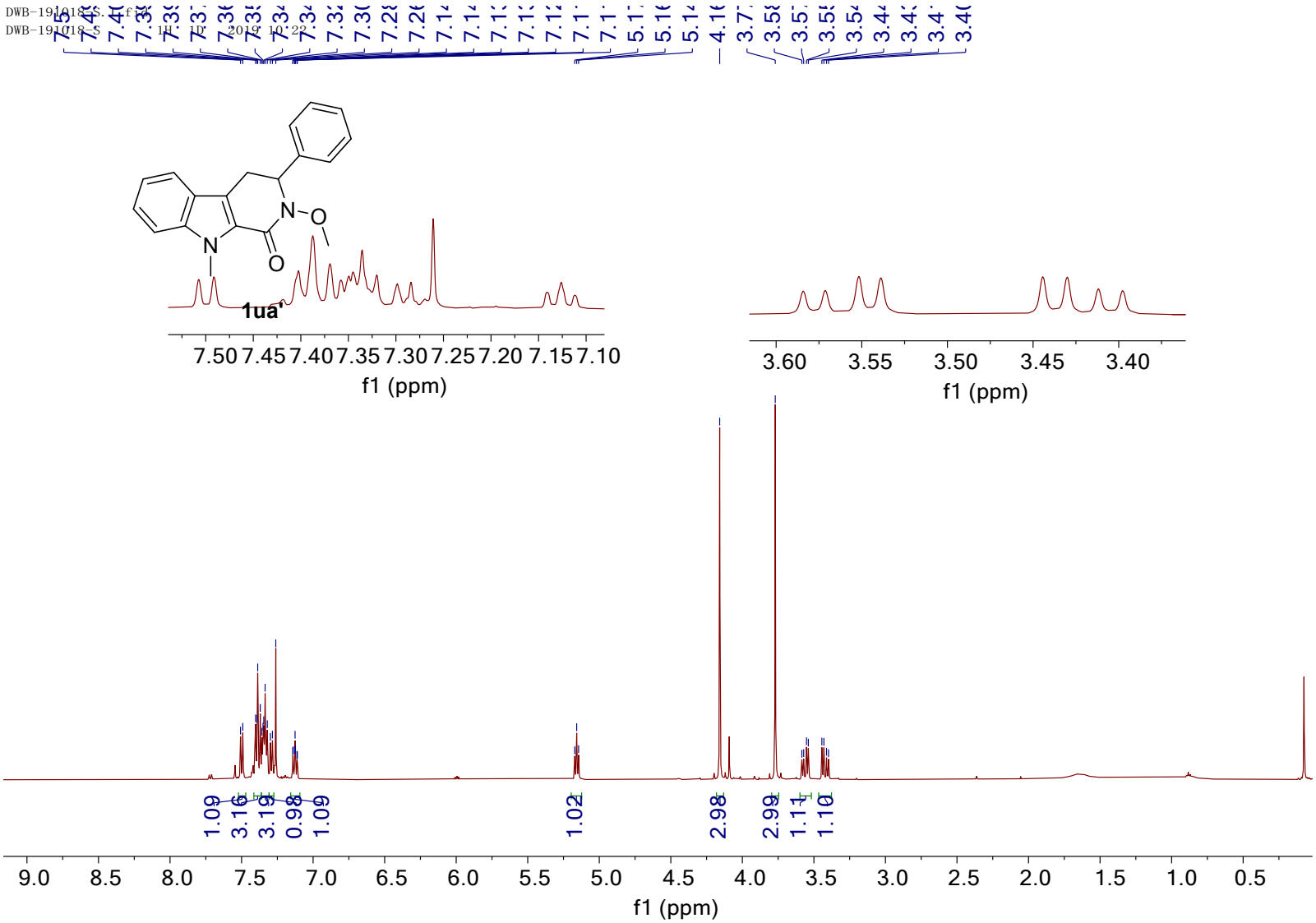

ZMH-C-3Aa-1123.
ZMH-C-3Aa-1123
151.5
140.8
136.6
133.6
132.4
132.0
130.0
129.1
128.9
128.7
127.5
127.4
127.3
118.9
117.0
116.3
110.6
110.0
107.3
77.2
77.0
76.7
62.2
55.1
38.4
Ph
N
N
N
N
OMe
O
3sa
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

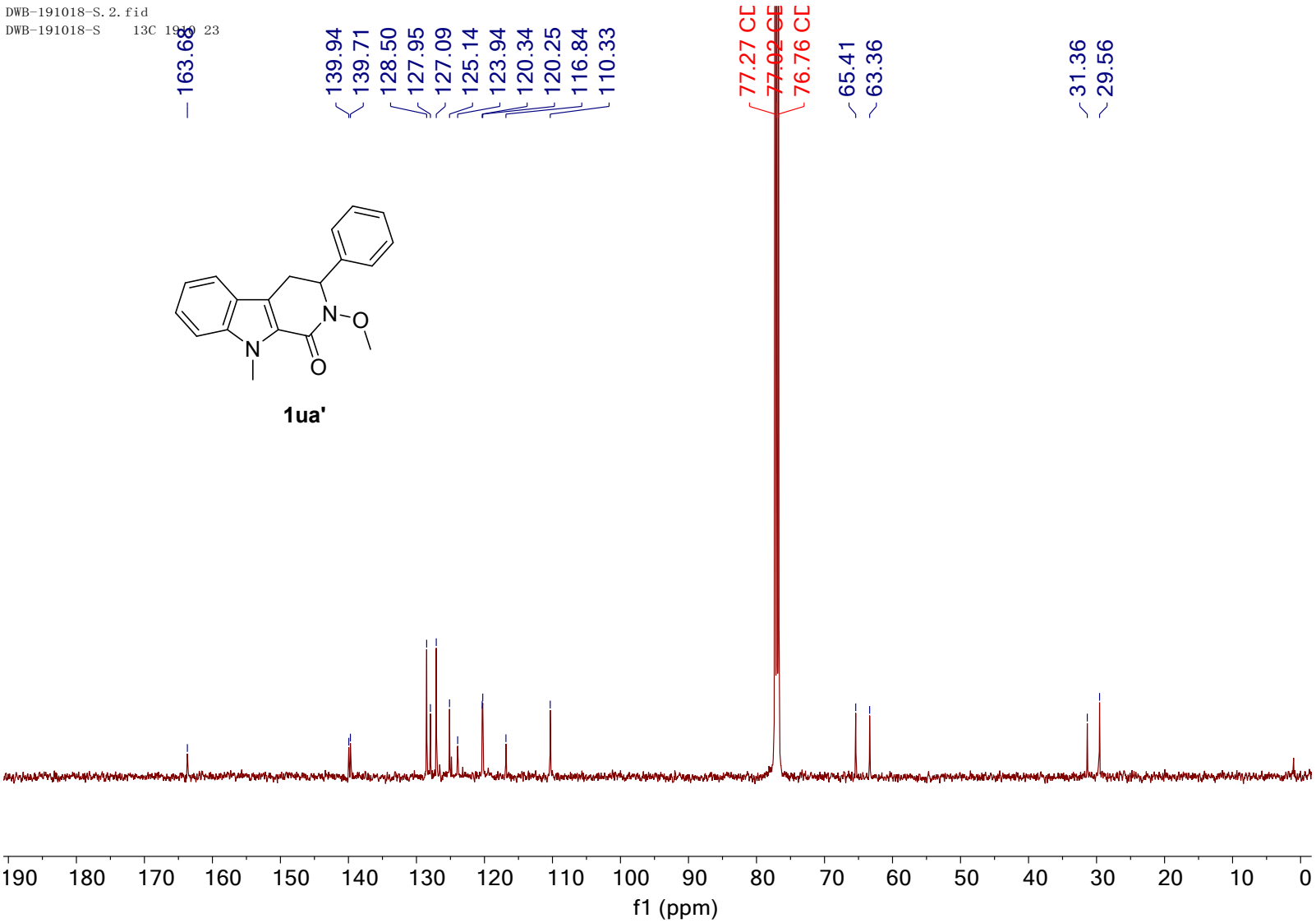

ZMH-20190319A.1.fid
ZMH-20190319A 1H 1D 2019 0321
8.50 8.49 8.48 7.68 7.66 7.65 7.40 7.38 7.37 7.35 7.34 7.32 7.30 7.29 7.20 7.19
4.76 4.21 4.20 4.19 4.18 4.17 3.83 3.82 3.81 3.80 3.64
1.54 1.53 0.79 0.77 0.76 0.76 0.75 0.57 0.56 0.56
N
N
OMe
O
3ta
7.7 7.6 7.5 7.4 7.3 7.2 7.1
f1 (ppm)
1.02 1.00 5.84 2.09 1.00 1.05 1.02 3.06 1.06 2.03 2.07
f1 (ppm)

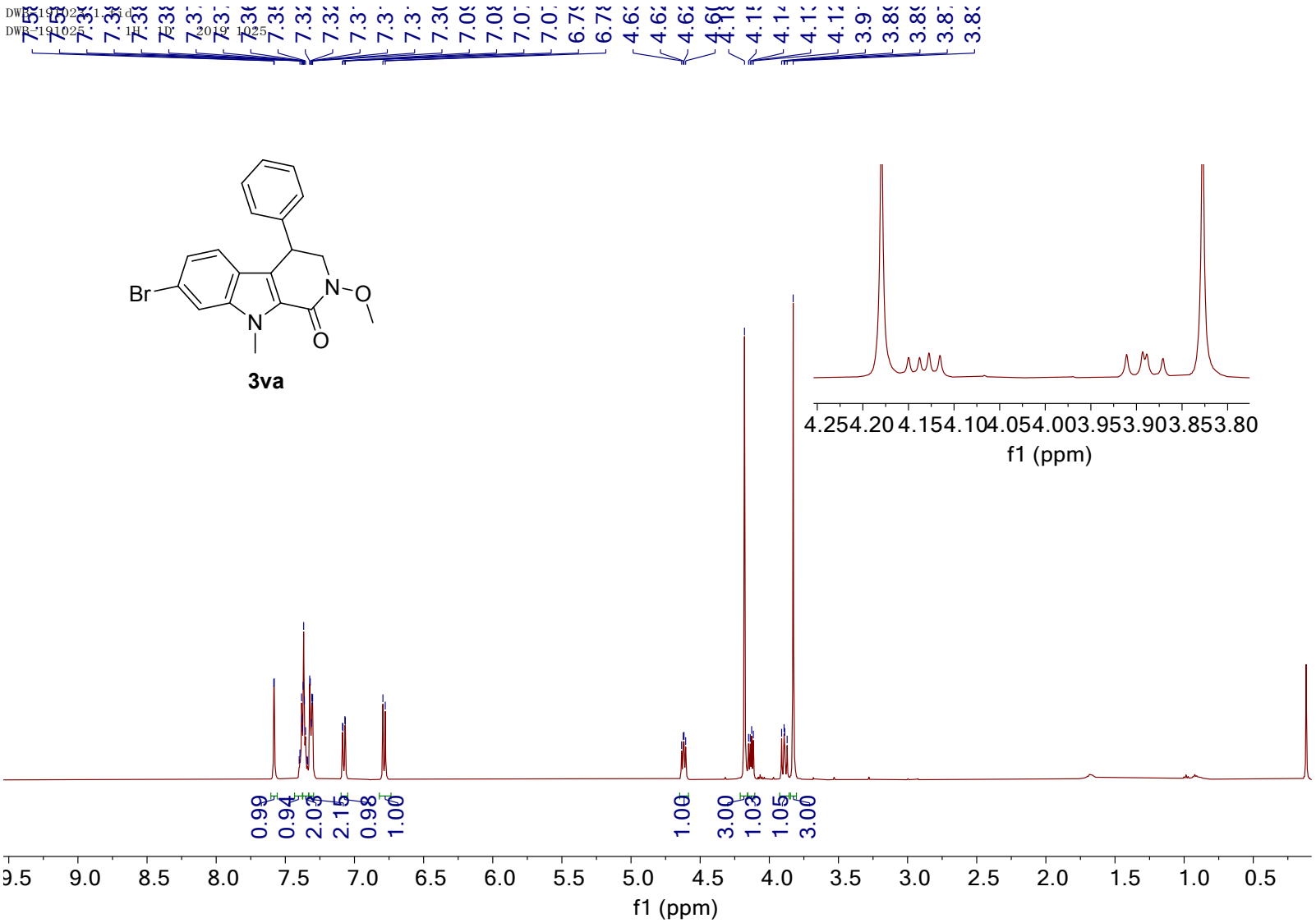

ZMH-20190319A.2.fid
ZMH-20190319A 13C 2019 03 24
152.3
140.5
134.9
132.6
130.6
128.7
127.5
127.4
124.3
122.9
119.2
117.7
115.7
77.3
77.0
76.7
62.3
55.1
38.7
5.4
4.9
4.5
N
N
OMe
O
3ta
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

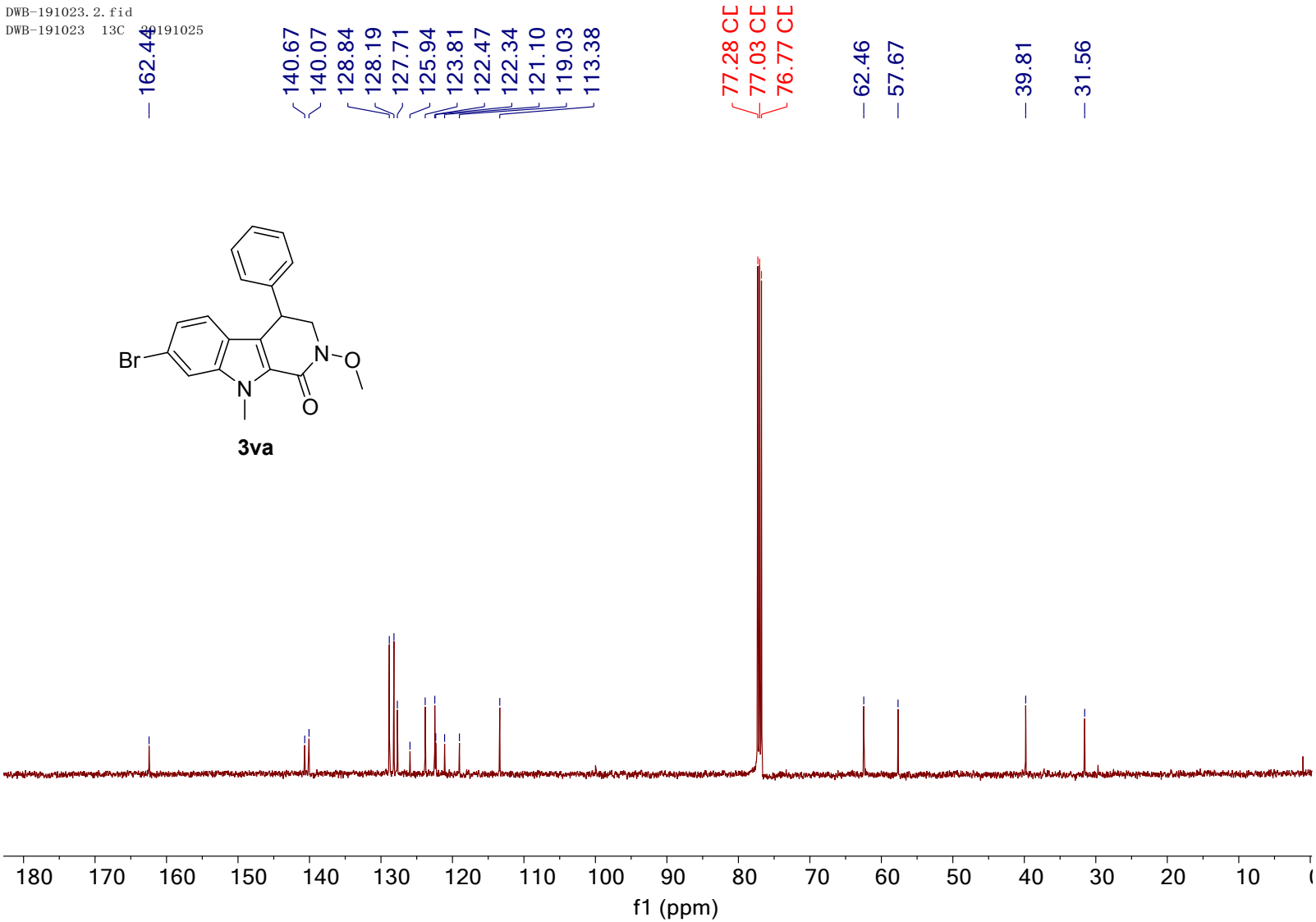

DWB-191018-Y-1.fid
DWB-191018-Y 1H 1D 2019_10_22
N
O
N
O
1ua
4.2
4.1
4.0
3.9
3.8
3.7
f1 (ppm)
1.12
6.24
2.06
1.00
2.99
1.14
1.06
3.03
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


DWB-191018-X.2.fid
DWB-191018-X 13C 191023
162.86
140.47
140.05
128.74
128.22
127.52
125.42
125.02
123.54
121.25
120.97
120.27
110.30
100.00
77.28 CD
77.02 CD
76.77 CD
62.42
57.81
39.87
31.41
N
O
N
O
1ua
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

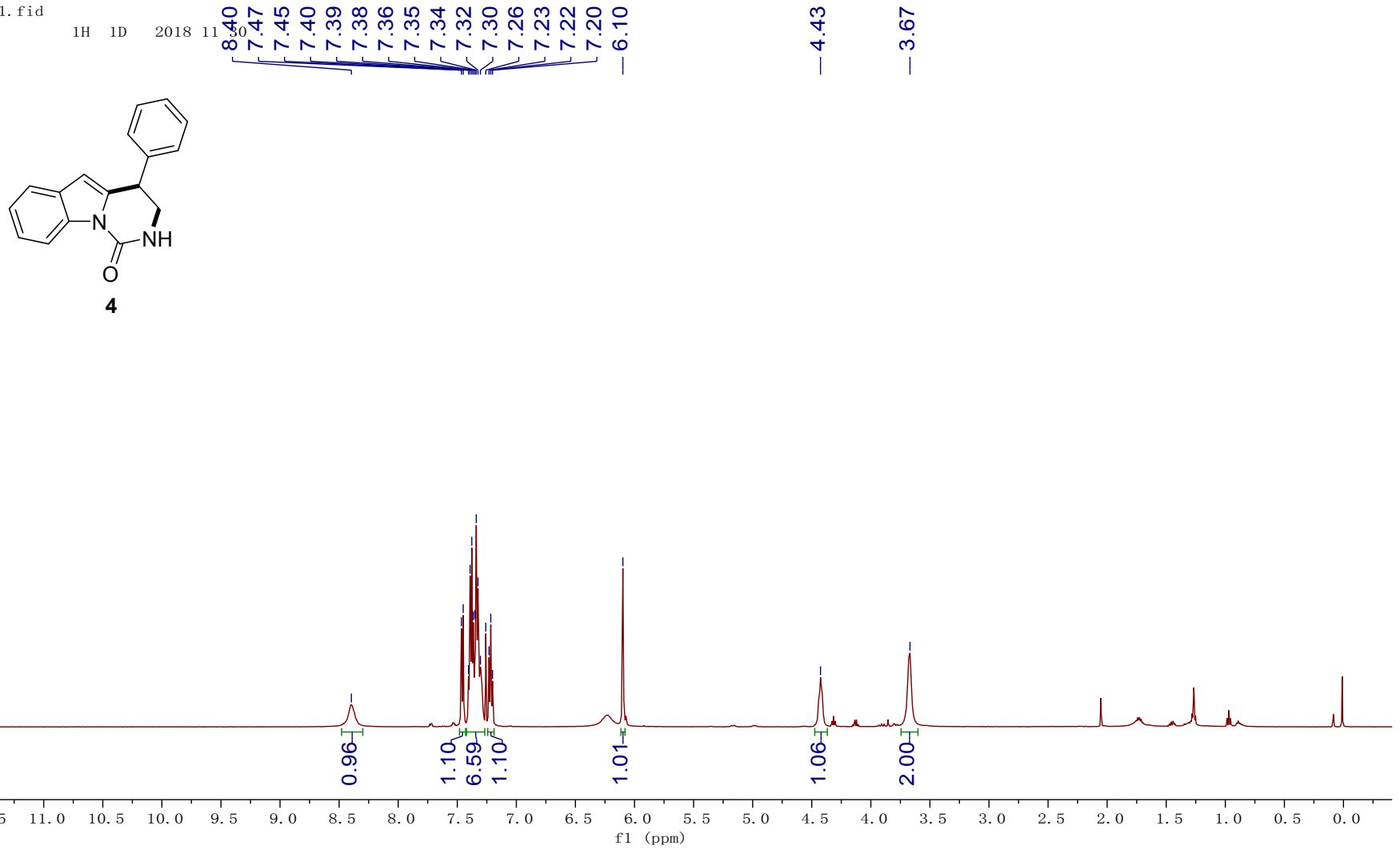

1ua
7.50 7.45 7.40 7.35 7.30 7.25 7.20 7.15 7.10
f1 (ppm)
3.60 3.55 3.50 3.45 3.40
f1 (ppm)
1.09 3.16 3.19 0.98 1.09 1.02 2.98 2.99 1.11 1.10
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)


DWB-191018-S.2.fid
DWB-191018-S 13C 1H 0 23
163.68
139.94
139.71
128.50
127.95
127.09
125.14
123.94
120.34
120.25
116.84
110.33
77.27 CDCl3
77.02 CDCl3
76.76 CDCl3
65.41
63.36
31.36
29.56
N
O
N
O
1ua'
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


Br
N
O
N
O
3va
4.254.20 4.154.10 4.054.00 3.953.90 3.853.80
f1 (ppm)
0.99
0.94
2.03
2.15
0.98
1.00
1.00
3.00
1.03
1.05
3.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

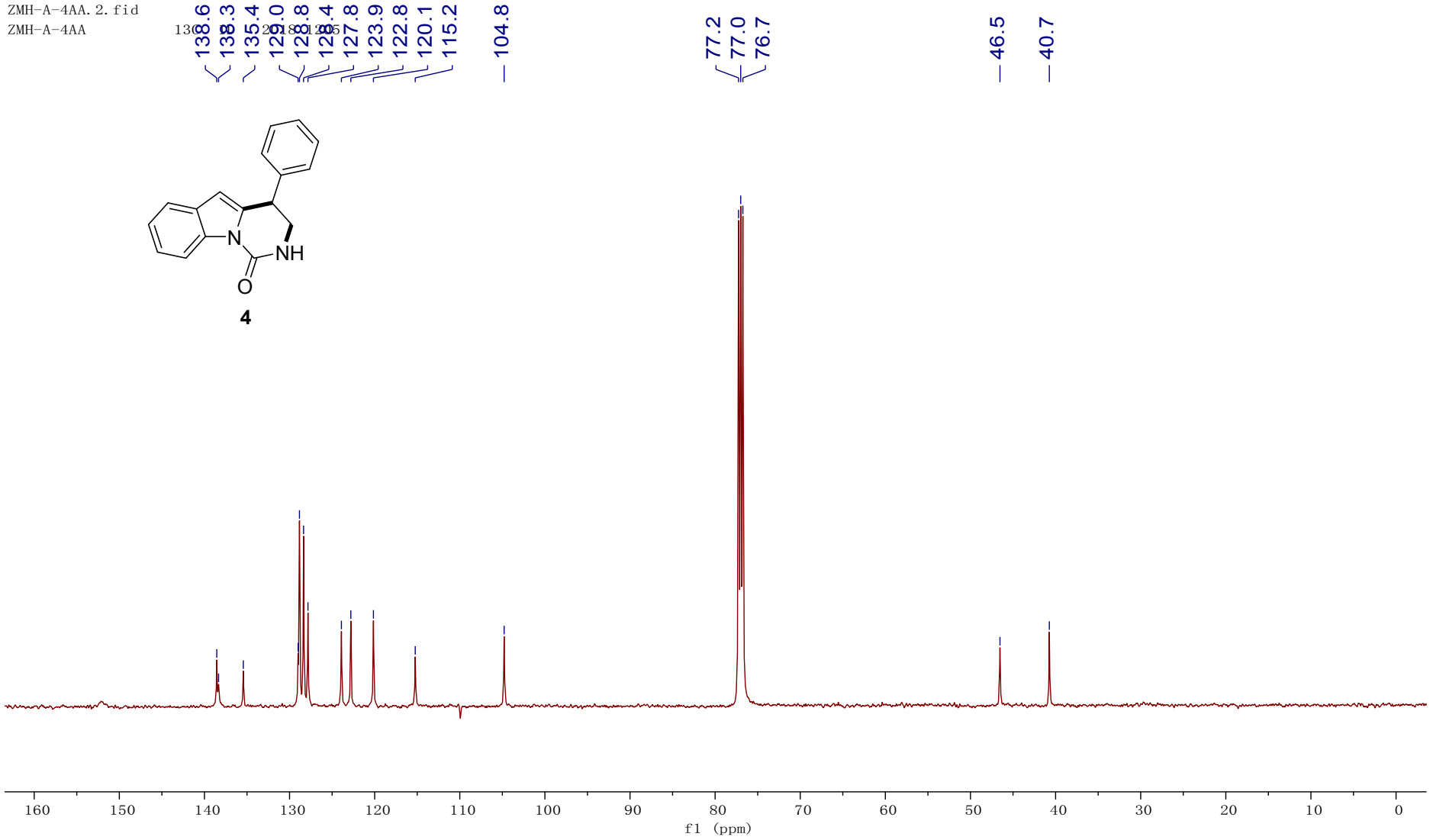

DWB-191023.2.fid
DWB-191023 13C 20191025
162.44
140.67
140.07
128.84
128.19
127.71
125.94
123.81
122.47
122.34
121.10
119.03
113.38
77.28 CDCl3
77.03 CDCl3
76.77 CDCl3
62.46
57.67
39.81
31.56
Br
N
O
N
O
3va
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

ZMH-A-4AA.1.fid
ZMH-A-4AA 1H 1D 2018 11 30



4

ZMH-A-4AA.2.fid
ZMH-A-4AA



References

[1] W. J. Kong, X. C. Chen, M. M. Wang, H. X. Dai and J.Q. Yu, *Org. Lett.* 2018**, 20**, 284-287.

[2] (a) J. Mo, T. Muller, J. C. A. Oliveira, S. Demeshko, F. Meyer and L. Ackermann, *Angew. Chem. Int. Ed.*, 2019, **58**, 12874 –12878; (b) Y. Aihara and N. Chatani, *Chem. Sci*., 2013, **4**, 664–670; (c) A. Rana, M. E. Cinar, D. Samanta and M. Schmittel, *Org. Lett.* 2016, **18**, 84−87.

---

[i] J. D. Chai and M. Head-Gordon, *Phys. Chem. Chem. Phys.* **2008**, *10*, 6615.

[ii] M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, Ö. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, D. J. Fox, Gaussian 09, Rev. D.01; Gaussian, Inc.: Wallingford, CT, **2013**.

[iii] P. J. Hay and W. R. Wadt, *J. Chem. Phys.* **1985**, *82*, 270.

[iv] W. R. Wadt and P. J. Hay, *J. Chem. Phys.* **1985**, *82*, 284.

[v] P. J. Hay and W. R. Wadt, *J. Chem. Phys.* **1985**, *82*, 299.

[vi] C. E. Check, T. O. Faust, J. M. Bailey, B. J. Wright, T. M. Gilbert and L. S. Sunderlin, *J. Phys. Chem. A* **2001**, *105*, 8111.

[vii] A. W. Ehlers, M. BÖhme, S. Dapprich, A. Gobbi, A. HÖllwarth, V. Jonas, K. F. KÖhler, R. Stegmann, A. Veldkamp and G. Frenking, *Chem. Phys. Lett.* **1993**, *208*, 111.

[viii] A. HÖllwarth, M. BÖhme, S. Dapprich, A. W. Ehlers, A. G. Obbi, V. Jonas, K. F. KÖhler, R. Stegmann, A. Veldkamp and G. Frenking, *Chem. Phys. Lett.* **1993**, *208*, 237.

[ix] P. C. Hariharan and J. A. Pople, *Theor. Chim. Acta* **1973**, *28*, 213.

[x] M. S. Gordon, *Chem. Phys. Lett.* **1980**, *76*, 163.

[xi] R. C. J. Binning and L. A. Curtiss, *J. Comput. Chem.* **1990**, *11*, 1206.

[xii] K. Fukui, *J. Phys. Chem.* **1970**, *74*, 4161.

[xiii] K. Fukui, *Acc. Chem. Res.* **1981**, *14*, 363.

- [xiv] (a) G. Y. Yin, I. Kalvet, U. Englertn and F. Schoenebeck, *J. Am. Chem. Soc.* **2015**, *137*, 4164. (b) G. Jindal and R. B. Sunoj, *J. Am. Chem. Soc.* **2014**, *136*, 15998. (c) Q. Q. Lu, H. Z. Yu and Y. Fu, *J. Am. Chem. Soc.* **2014**, *136*, 8252. (d) A. Fromm, C. V. Wüllen, D. Hackenberger and L. J. Gooßen, *J. Am. Chem. Soc.* **2014**, *136*, 10007. (e) G. J. Cheng, Y. F. Yang, P. Liu, P. Chen, T. Y. Sun, G. Li, X. H. Zhang, K. N. Houk, J. Q. Yu and Y. D. Wu, *J. Am. Chem. Soc.* **2014**, *136*, 894. (f) P. Liu, L. E. Sirois, P. H. Y. Cheong, Z. X. Yu, I. V. Hartung, H. Rieck, P. A. Wender and K. N. Houk, *J. Am. Chem. Soc.* **2010**, *132*, 10127. (g) S. F. Ni, L. Dang, *Phys. Chem. Chem. Phys.* **2016**, *18*, 4860. (h) S. F. Ni, T. L. Yang, L. Dang, *Organometallics*, **2017**, *36*, 2746. (h) L. B. Zhang, M. H. Zhu, S. F. Ni, L. R. Wen, M. Li, *ACS Catal*. **2019**, *9*,1680.

[xv] (a) J. D. Cox, D. D. Wagman, V.A. Medvedev, CODATA Key Values for Thermodynamics, Hemisphere Publishing Corp., New York, **1984**, 1. (b) P. Xiao, H. Y. Yuan, J. Q. Liu, Y. Y. Zheng, X. H. Bi, and J. P. Zhang, *ACS Catal.* **2015**, *5*, 6177. (c) J. Daru, Z. Benda, Á. Póti, Z. Novák, and A. Stirling, *Chem. Eur. J.* **2014**, *20*, 15395.