New Friedel-Crafts strategy of preparing 3-acylindoles

Lian-Hua Li, Zhi-Jie Niu, Yong-Min Liang*

State Key Laboratory of Applied Organic Chemistry, College of Chemistry and Chemical Engineering, Lanzhou University,
Lanzhou, 730000, People's Republic of China
Fax: +86-931-8912582; e-mail: liangym@lzu.edu.cn

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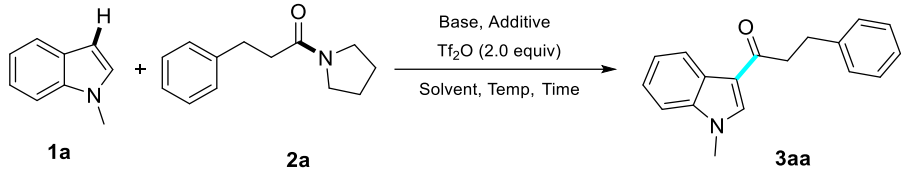
General information

Column chromatography was carried out on silica gel. **^{1}H NMR** spectra were recorded on 400 MHz in $CDCl_3$ and DMSO-d_6. **^{13}C NMR** spectra were recorded on 100 MHz in $CDCl_3$ and DMSO-d_6. Chemical shifts (ppm) were recorded with tetramethylsilane (TMS) and DMSO-d_6 as the internal reference standard. Multiplicities are given as s (singlet), d (doublet), t (triplet), dd (doublet of doublets), q (quartet), or m (multiplet). Their **^{1}H NMR** and **^{13}C NMR** spectra are provided in the Supporting Information. The **HRMS** was obtained using a Q-TOF instrument equipped with **ESI** source. Data collections for crystal structure were performed at room temperature (293 K) using Mo Kα radiation on a Bruker APEXII diffractometer. Melting points were measured with micro melting point apparatus.

The substituted amides were prepared according to the literature.[1] Trifluoromethanesulfonic anhydride (Tf_2O) was commercially available. Solvents were dried using standard methods. All commercially available reagents were used with further purification. The toluene was distilled over CaH_2.

Optimization of the reaction conditions

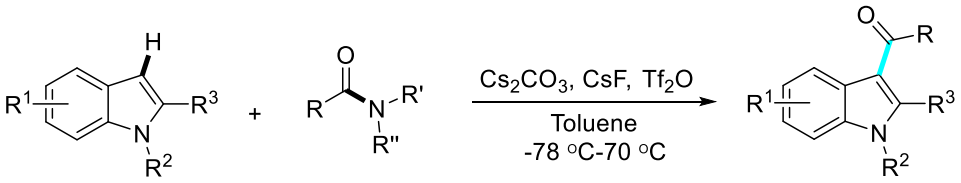
Table S1 Additional optimization of the reaction[a,b]



Entry	1a (X equiv.)	2a (Y equiv.)	Base (Z equiv.)	Additive (equiv.)	Temp (°C)	Time (h)	Solvent	Yield[d] (%)
1	1	1	2,6-lutidine (2.2)	-	-78-40	12	DCM	N.D
2	1	1	2,6-dichloropyridine (2.2)	-	-78-40	12	DCM	N.D
3	1	1	2-methypyridine (2.2)	-	-78-40	12	DCM	N.D
4	1	1	2-iodopyridine (2.2)	-	-78-40	12	DCM	N.D
5	1	1	NaH (2.2)	-	-78-40	12	DCM	<5%
6	1	1	NaOH (2.2)	-	-78-40	12	DCM	N.D
7	1	1	K_2CO_3 (2.2)	-	-78-40	12	DCM	N.D
8	1	1	Cs_2CO_3 (2.2)	-	-78-40	12	DCM	24
9	1.5	1	Cs_2CO_3 (2.2)	-	-78-40	12	DCM	28
10	1	1.5	Cs_2CO_3 (2.2)	-	-78-60	12	DCM	39
11	1	1.5	Cs_2CO_3 (2.2)	-	-78-70	12	DCM	47
12	1	1.5	Cs_2CO_3 (2.2)	-	-78-70	12	DCE	45
13	1	1.5	Cs_2CO_3 (2.2)	-	-78-70	12	toluene	60
14	1	1.5	Cs_2CO_3 (2.2)	-	-78-70	12	1,4-dioxane	N.D
15	1	1.5	Cs_2CO_3 (2.2)	-	-78-70	12	EtOAc	N.D
16	1	1.5	Cs_2CO_3 (2.2)	-	-78-70	12	CH_3OH	N.D
17	1	1.5	Cs_2CO_3 (2.2)	-	-78-70	12	CH_3NO_2	N.D
18	1	1.6	Cs_2CO_3 (2.2)	-	-78-70	12	toluene	63
19	1	1.8	Cs_2CO_3 (2.2)	-	-78-70	12	toluene	58
20	1	2.0	Cs_2CO_3 (2.2)	-	-78-70	12	toluene	63
21	1	1.6	Cs_2CO_3 (2.2)	-	-78-70	14	toluene	65
22	1	1.6	Cs_2CO_3 (2.0)	-	-78-70	14	toluene	63
23	1	1.6	Cs_2CO_3 (2.4)	-	-78-70	14	toluene	68
24	1	1.6	Cs_2CO_3 (2.6)	-	-78-70	14	toluene	72
25	1	1.6	Cs_2CO_3 (2.6)	-	-78-80	14	toluene	67
26	1	1.6	Cs_2CO_3 (2.6)	-	-78-90	14	toluene	52
27[c]	1	1.6	Cs_2CO_3 (2.6)	CsBr (0.5)	-78-70	14	toluene	83
28[c]	1	1.6	Cs_2CO_3 (2.6)	CsI (0.5)	-78-70	14	toluene	73
29[c]	**1**	**1.6**	**Cs_2CO_3 (2.6)**	**CsF (0.5)**	**-78-70**	**14**	**toluene**	**85**

[a] Reaction conditions: To a mixture of indole **1a** (X equiv.), amide **2a** (Y equiv.) and base (Z equiv.) in solvent (3.0 mL) was added Tf_2O (2.0 equiv.) at -78 °C under an Ar atmosphere. After 20 min, the reaction mixture was stirred at the reported temperature. [b] All reactions were carried out on 0.2 mmol scale. [C] The additive (0.5 equiv.) was added. [d] Isolated yields. DCM = dichloromethane, DCE = 1, 2-dichloroethane, Tf = trifluoromethanesulfonyl, TMS = trimethylsilyl.

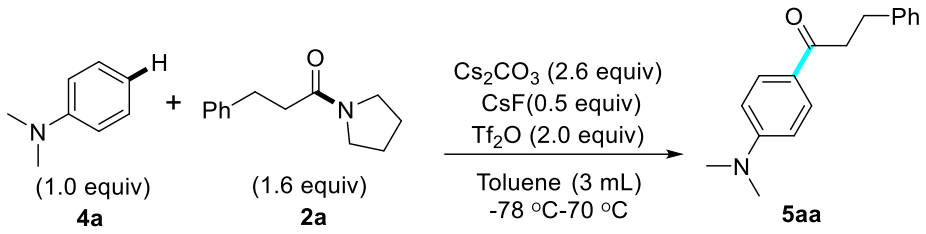
General procedure for the synthesis of desired 3-acylindoles



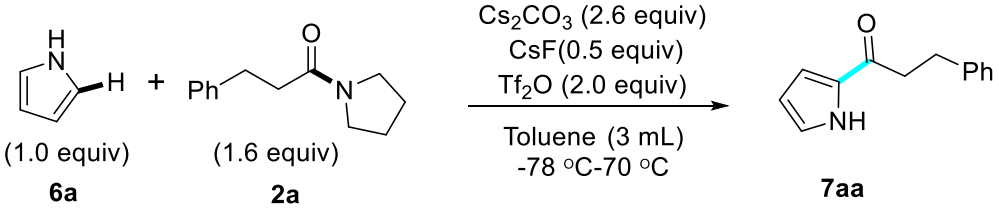
Indole **Amide** **3-acylindole**

The amide (0.32 mmol, 1.6 equiv.), Cs_2CO_3 (0.52 mmol) and CsF (0.1 mmol) were added to a dried round bottom flask and put under an Ar atmosphere. The indole (0.2 mmol, 1.0 equiv.), toluene (2.0 mL) were added and the solution was cooled to -78 °C, followed by addition of toluene (1.0 mL) solution of Tf_2O (0.4 mmol) via syringe. After 20 minutes, the reaction mixture was heated to 70 °C. After 14 hours, the mixture was quenched by the saturated $NaHCO_3$ solution and transferred to a separation funnel, diluted with DCM (15.0 mL) and the organic layer was washed with water (5.0 mL×2) and brine (5.0 mL), dried over anhydrous Na_2SO_4, concentrated in vacuum and subjected to column chromatography.

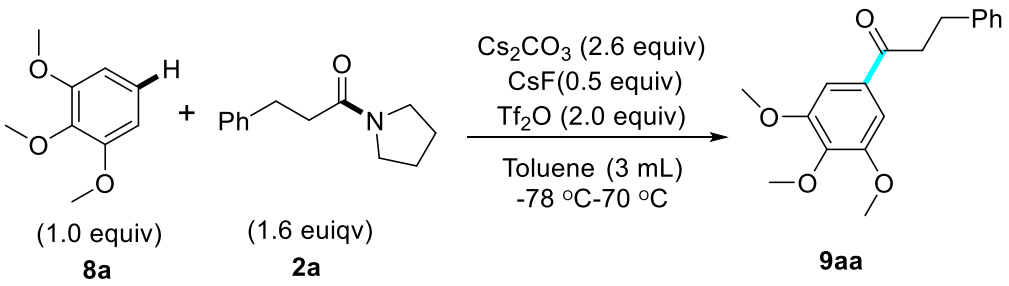
Further application



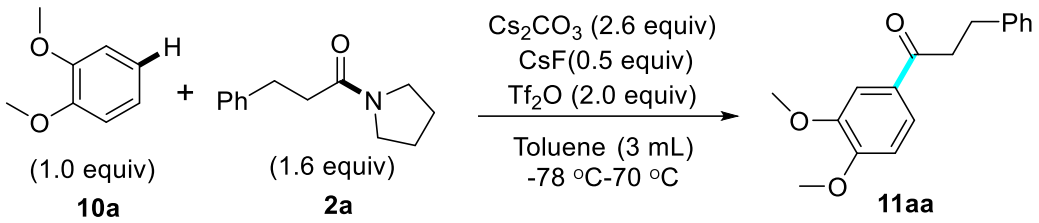
The amide **2a** (0.32 mmol, 1.6 equiv.), Cs_2CO_3 (0.52 mmol) and CsF (0.1 mmol) were added to a dried round bottom flask and put under an Ar atmosphere. The *N,N*-dimethyl aniline **4a** (0.2 mmol, 1.0 equiv.), toluene (2.0 mL) were added and the solution was cooled to -78 °C, followed by addition of toluene (1.0 mL) solution of Tf_2O (0.4 mmol) via syringe. After 20 minutes, the reaction mixture was heated to 70 °C. After 14 hours, the mixture was quenched by the saturated $NaHCO_3$ solution and transferred to a separation funnel, diluted with DCM (15.0 mL) and the organic layer was washed with water (5.0 mL×2) and brine (5.0 mL), dried over anhydrous Na_2SO_4, concentrated in vacuum and subjected to column chromatography, afforded acylated aniline **5aa** 7.59 mg in 15% isolated yield.



The amide **2a** (0.32 mmol, 1.6 equiv.), Cs_2CO_3 (0.52 mmol) and CsF (0.1 mmol) were added to a dried round bottom flask and put under an Ar atmosphere. The pyrrole **6a** (0.2 mmol, 1.0 equiv.), toluene (2.0 mL) were added and the solution was cooled to -78 °C, followed by addition of toluene (1.0 mL) solution of Tf_2O (0.4 mmol) via syringe. After 20 minutes, the reaction mixture was heated to 70 °C. After 14 hours, the mixture was quenched by the saturated $NaHCO_3$ solution and transferred to a separation funnel, diluted with DCM (15.0 mL) and the organic layer was washed with water (5.0 mL×2) and brine (5.0 mL), dried over anhydrous Na_2SO_4, concentrated in vacuum and subjected to column chromatography, afforded product **7aa** 22 mg in 55% isolated yield.



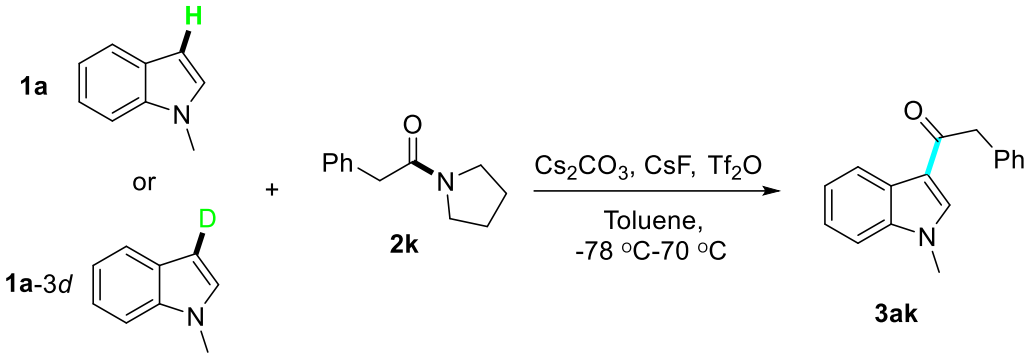
The amide **2a** (0.32 mmol, 1.6 equiv.), Cs_2CO_3 (0.52 mmol) and CsF (0.1 mmol) were added to a dried round bottom flask and put under an Ar atmosphere. The 1,2,3-trimethoxybenzene **8a** (0.2 mmol, 1.0 equiv.), toluene (2.0 mL) were added and the solution was cooled to -78 °C, followed by addition of toluene (1.0 mL) solution of Tf_2O (0.4 mmol) via syringe. After 20 minutes, the reaction mixture was heated to 70 °C. After 14 hours, the mixture was quenched by the saturated $NaHCO_3$ solution and transferred to a separation funnel, diluted with DCM (15.0 mL) and the organic layer was washed with water (5.0 mL×2) and brine (5.0 mL), dried over anhydrous Na_2SO_4, concentrated in vacuum and subjected to column chromatography, afforded product **9aa** 16.2 mg in 27% isolated yield.



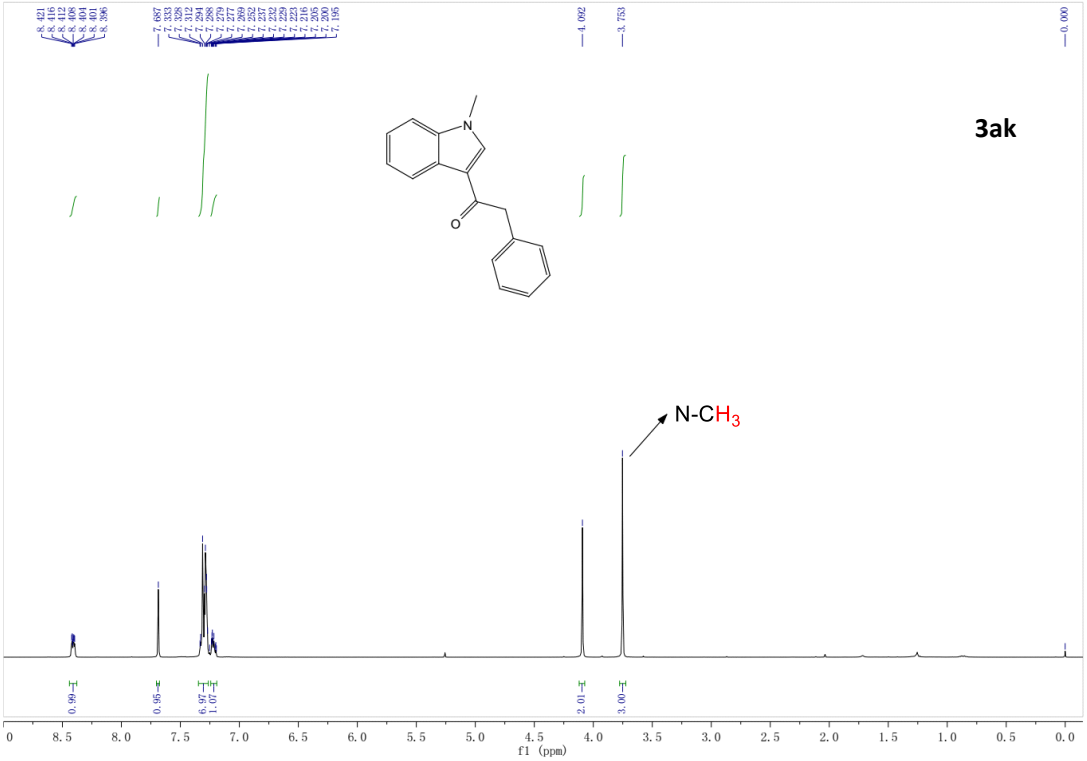
The amide **2a** (0.32 mmol, 1.6 equiv.), Cs_2CO_3 (0.52 mmol) and CsF (0.1 mmol) were added to a dried round bottom flask and put under an Ar atmosphere. The veratrole **10a** (0.2 mmol, 1.0 equiv.), toluene (2.0 mL) were added and the solution was cooled to -78 °C, followed by addition of toluene (1.0 mL) solution of Tf_2O (0.4 mmol) via syringe. After 20 minutes, the reaction mixture was heated to 70 °C. After 14 hours, the mixture was quenched by the saturated $NaHCO_3$ solution and transferred to a separation funnel, diluted with DCM (15.0 mL) and the organic layer was washed with water (5.0 mL×2) and brine (5.0 mL), dried over anhydrous Na_2SO_4, concentrated in vacuum and subjected to column chromatography, afforded product **11aa** 6.48 mg in 12% isolated yield.

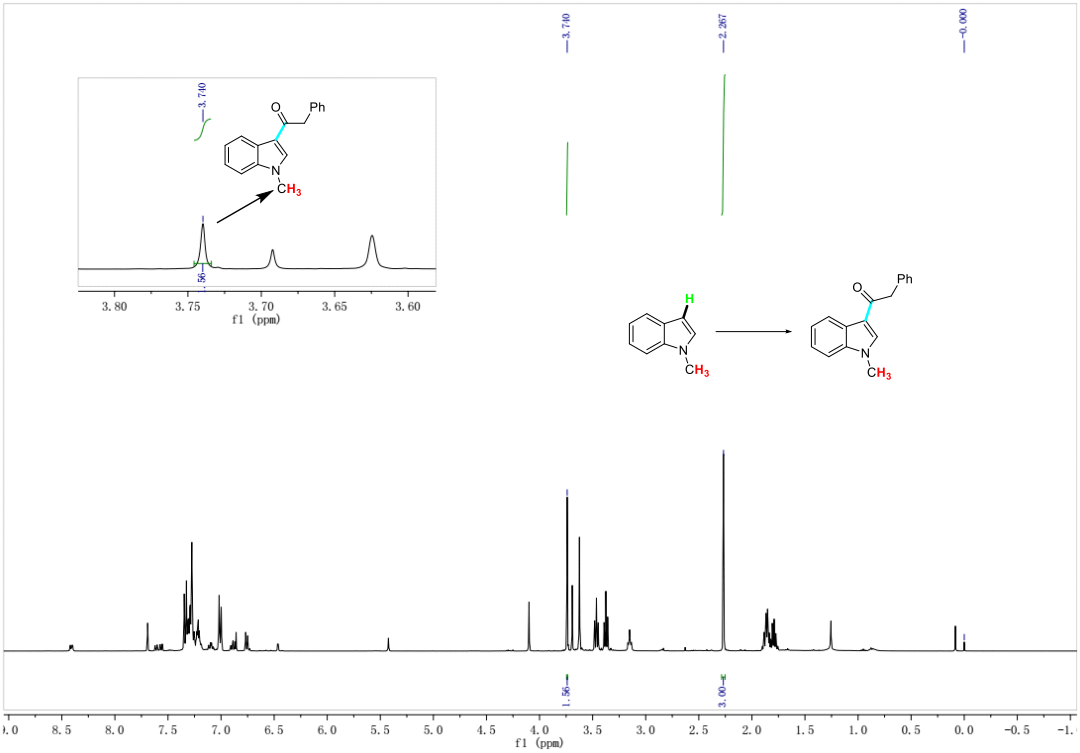
Mechanistic studies

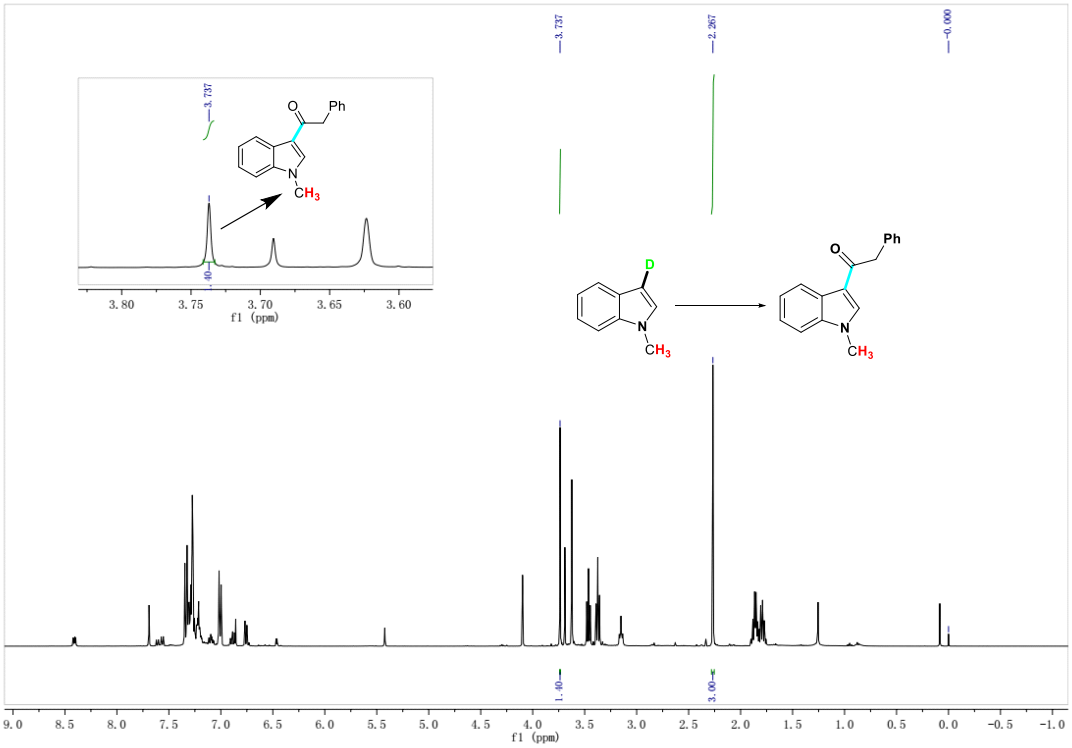
a) Deuterated labelling experiment



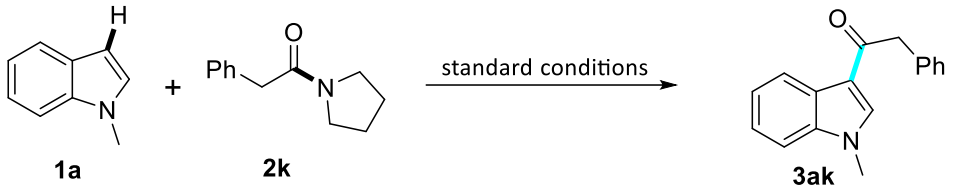
The amide **2k** (0.32 mmol, 1.6 equiv.), Cs_2CO_3 (0.52 mmol) and CsF (0.1 mmol) were added to a dried round bottom flask and put under an Ar atmosphere. The indole **1a** (0.2 mmol, 1 equiv.) or **1a**-3*d* (0.2 mmol, 1 equiv.), toluene (2.0 mL) were added and the solution was cooled to -78 °C, followed by addition of toluene (1.0 mL) solution of Tf_2O (0.4 mmol) via syringe. After 20 minutes, the reaction mixture was heated to 70 °C. After 30 minutes, the mixture was quenched by the saturated $NaHCO_3$ solution and transferred to a separation funnel, diluted with DCM (15.0 mL) and the organic layer was washed with water (5.0 mL×2) and brine (5.0 mL), dried over anhydrous Na_2SO_4, concentrated in vacuum and added *p*-bromotoluene (0.2 mmol) as internal standard, subjected to NMR tube. KIE value (k_H/k_D = 1.11) was determined by **^{1}H NMR** analysis (**400 MHz, $CDCl_3$**).




3.740
2.267
0.000
Ph
O
N
CH3
H
1.56
3.00
f1 (ppm)


3.737
2.267
0.000
Ph
O
N
CH3
D
1.40
3.00
f1 (ppm)

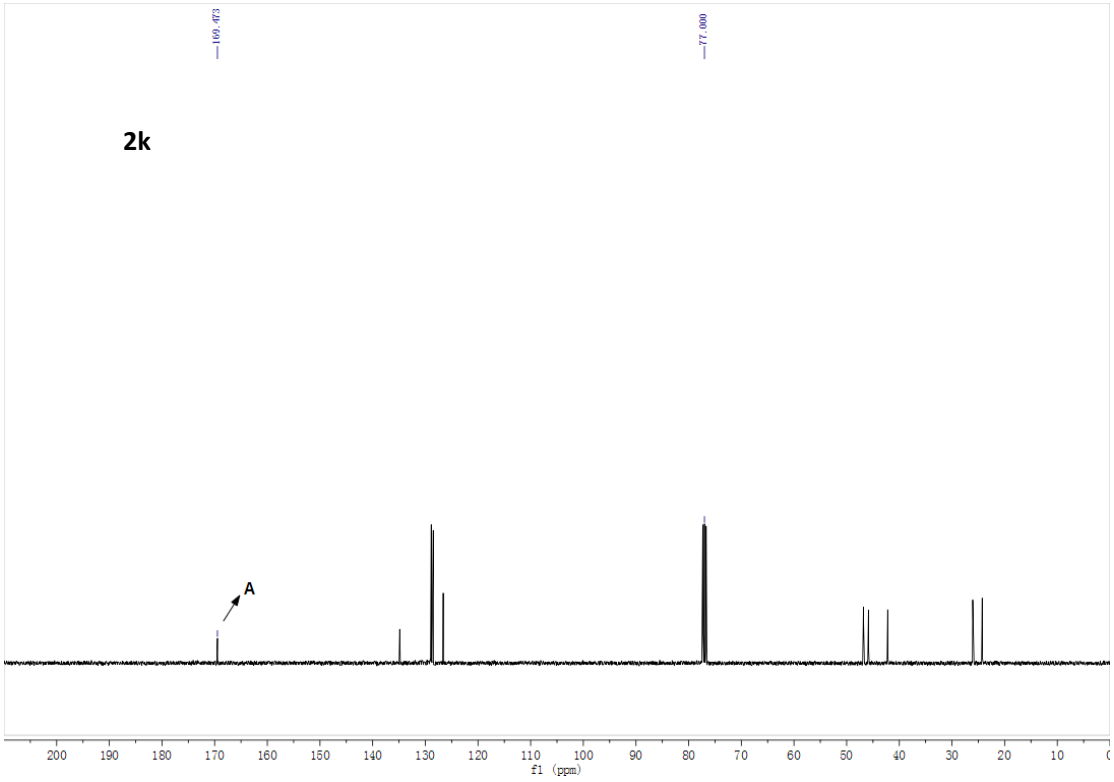
b) Monitoring experiment and NMR spectra

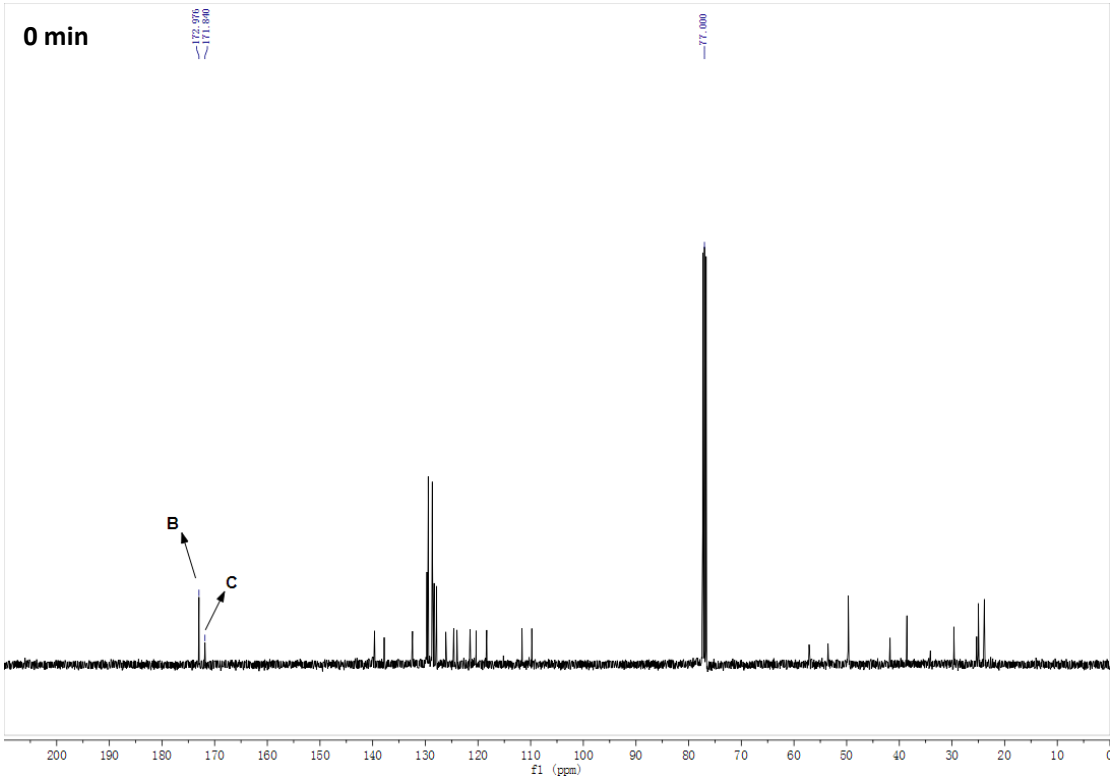


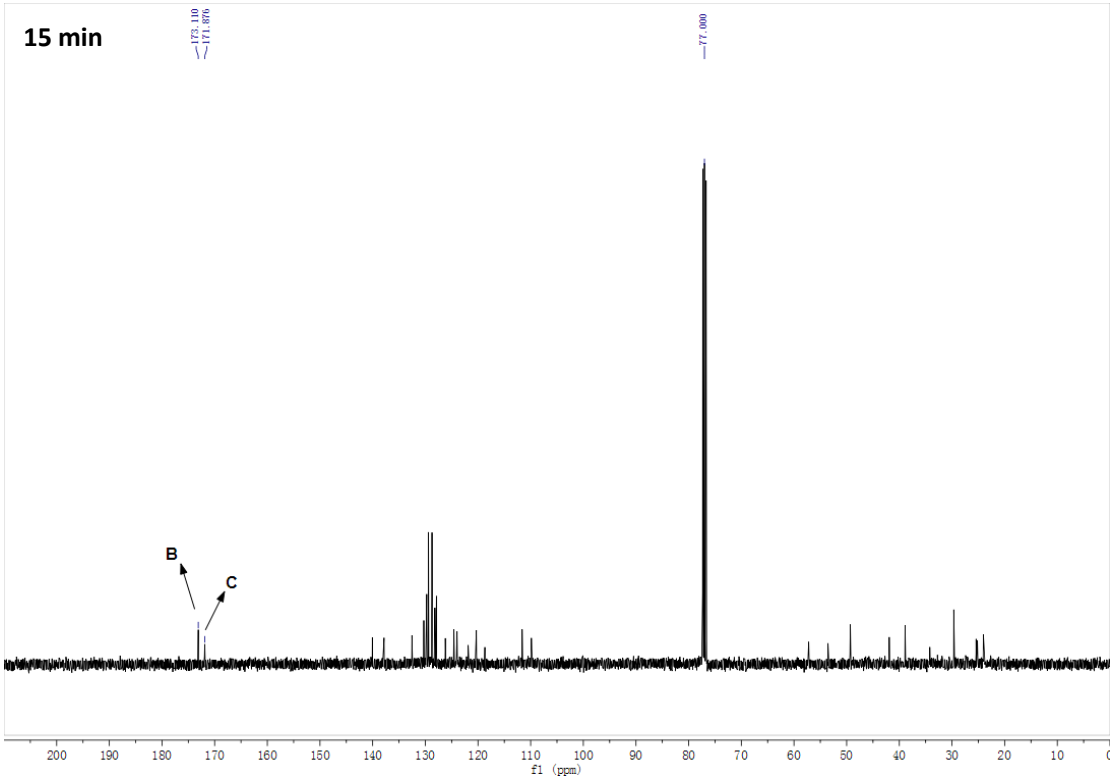
The first **^{13}C NMR** (**100MHz, $CDCl_3$**) was standard spectrum of substrate **2k**.

Four sets of the amide **2k** (0.32 mmol, 1.6 equiv.), Cs_2CO_3 (0.52 mmol), CsF (0.1 mmol) were added to four dried round bottom flasks and put under an Ar atmosphere, respectively. The indole **1a** (0.2 mmol, 1 equiv.), toluene (2.0 mL) were each added to four flasks and the solutions were cooled to -78 °C, followed by addition of toluene (1.0 mL) solution of Tf_2O (0.4 mmol) via syringe, respectively. All of four reactions kept under -78 °C for 20 minutes. Then, the first reaction was stopped without heating and concentrated in vacuum. The mixture was added to NMR tube and the second **^{13}C NMR** was acquired. The second reaction was heated at 70 °C for 15 minutes and stopped and concentrated in vacuum. The mixture was added to NMR tube and the third **^{13}C NMR** was acquired. The third reaction was heated for 1 hour and stopped and concentrated in vacuum. The mixture was added to NMR tube and the fourth **^{13}C NMR** was acquired. The fourth reaction was heated for 14 hours and stopped and concentrated in vacuum. The mixture was added to NMR tube and the fifth **^{13}C NMR** was acquired.

The sixth **^{13}C NMR** was standard spectrum of product **3ak**.




0 min
172.976
171.840
77.000
B
C
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


15 min
173.110
171.876
77.000
B
C
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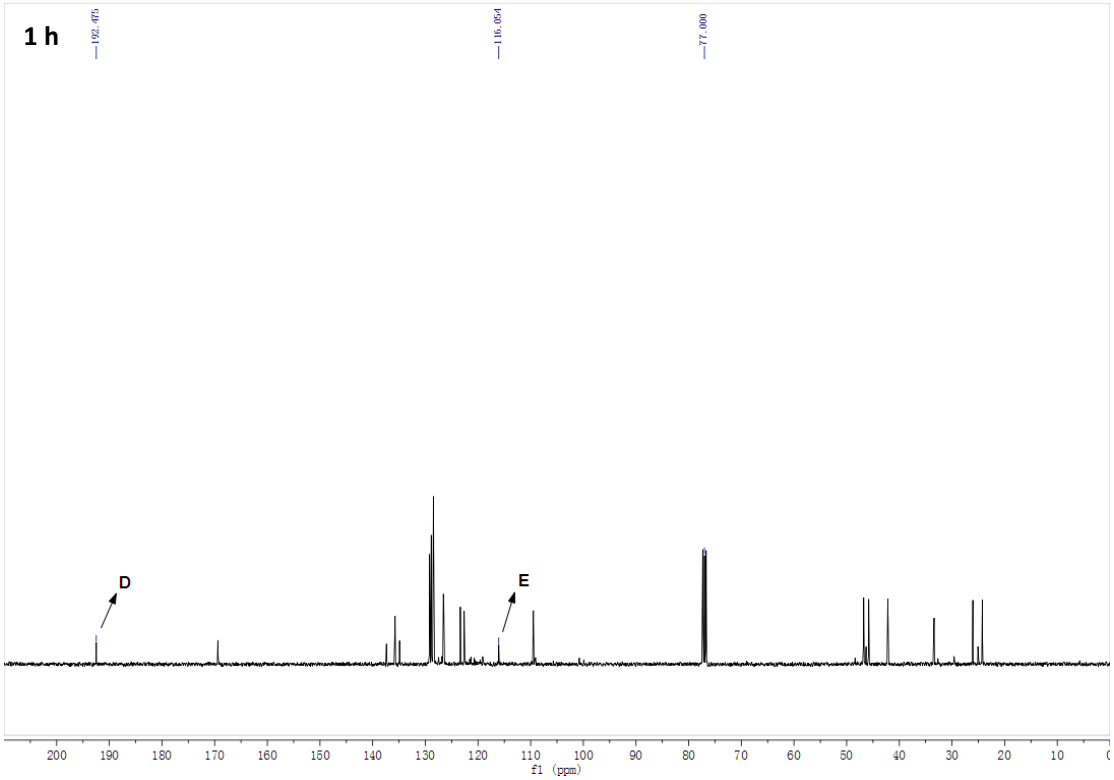
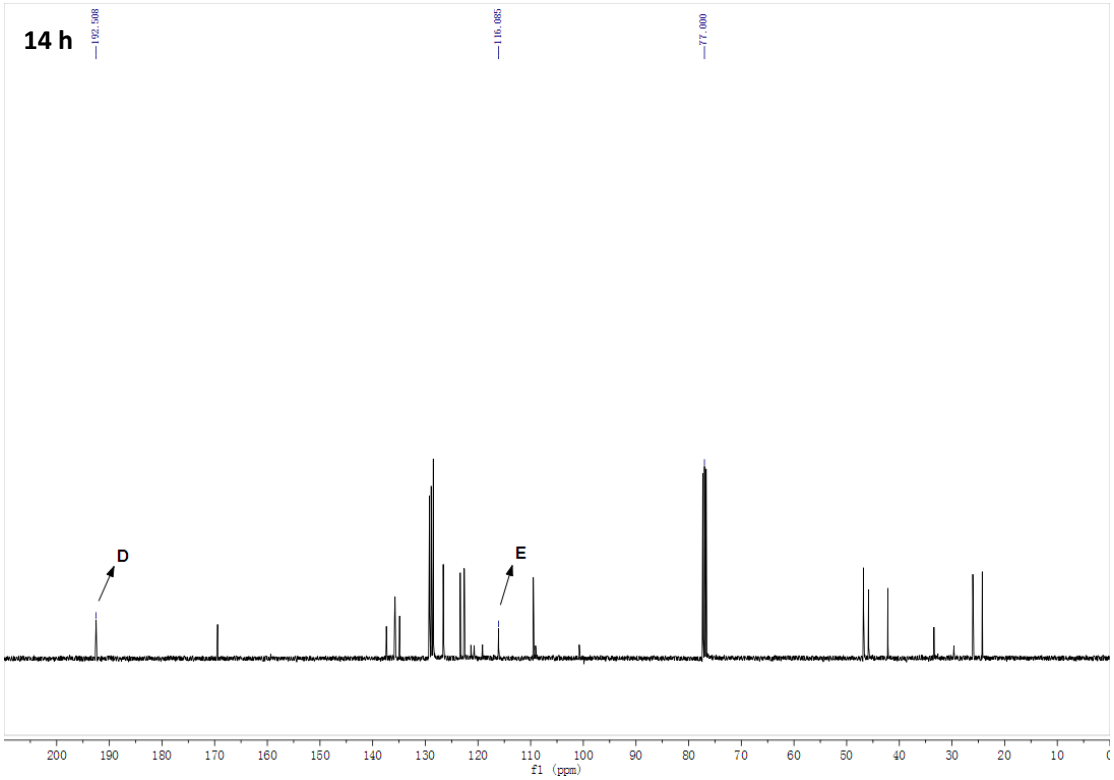
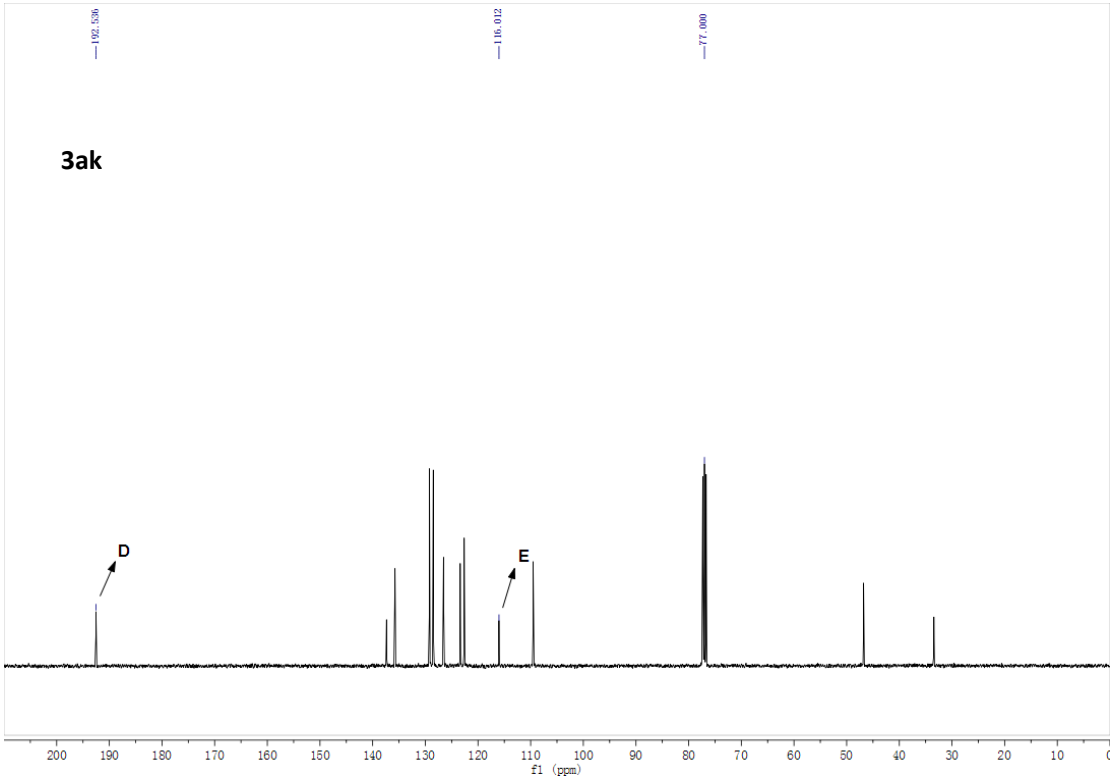
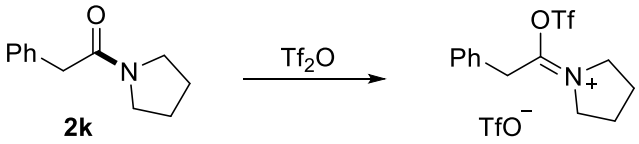
f1 (ppm)


1 h
192.475
116.054
77.000
D
E
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


14 h
192.508
116.085
77.000
D
E
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

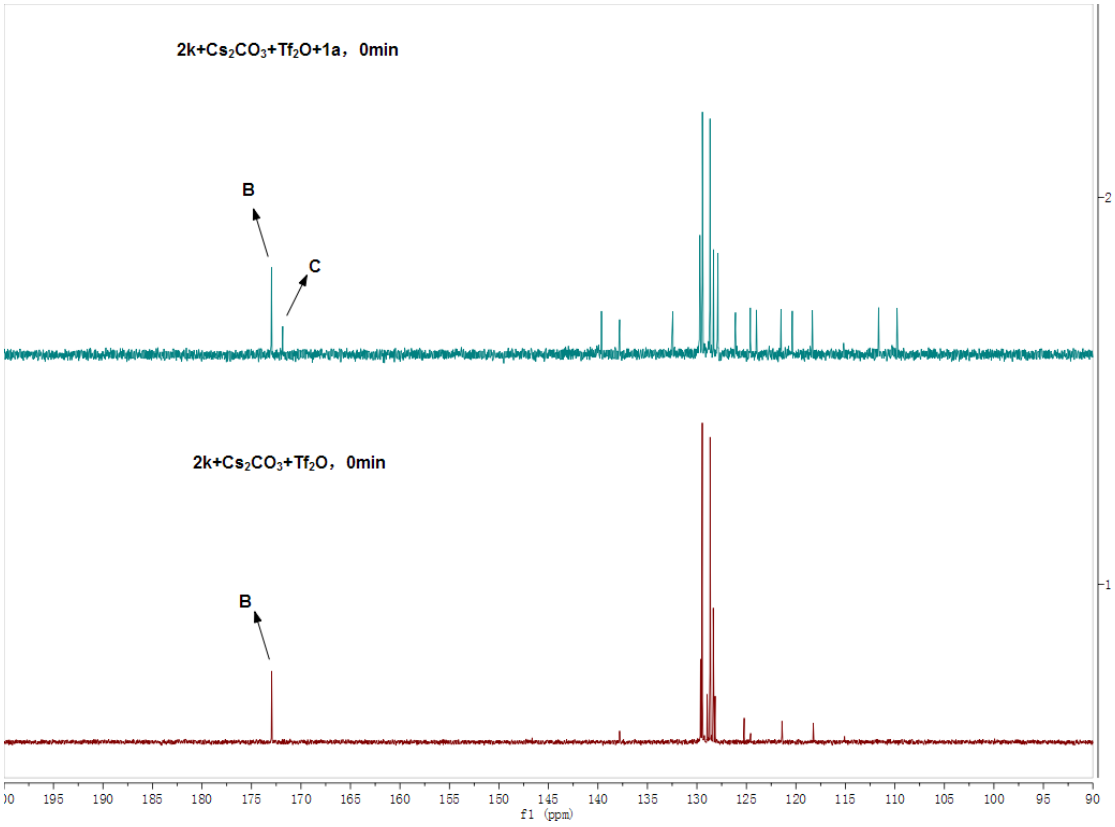


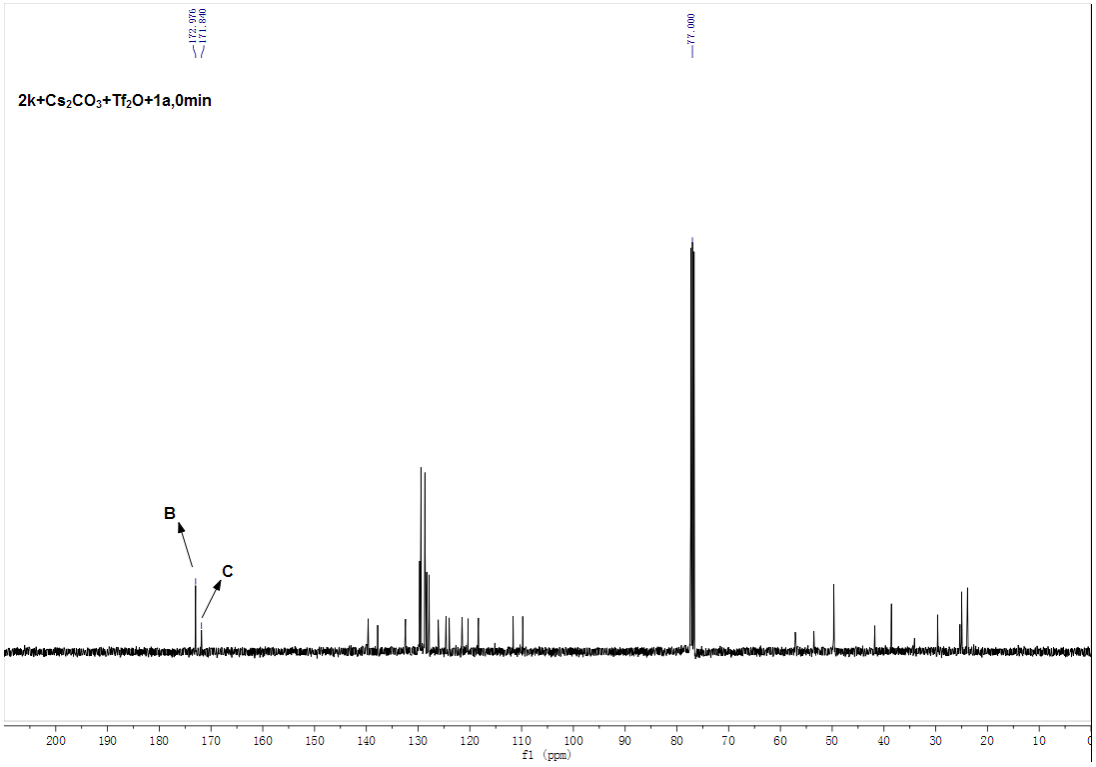
c) Survey of intermediate I and analysis

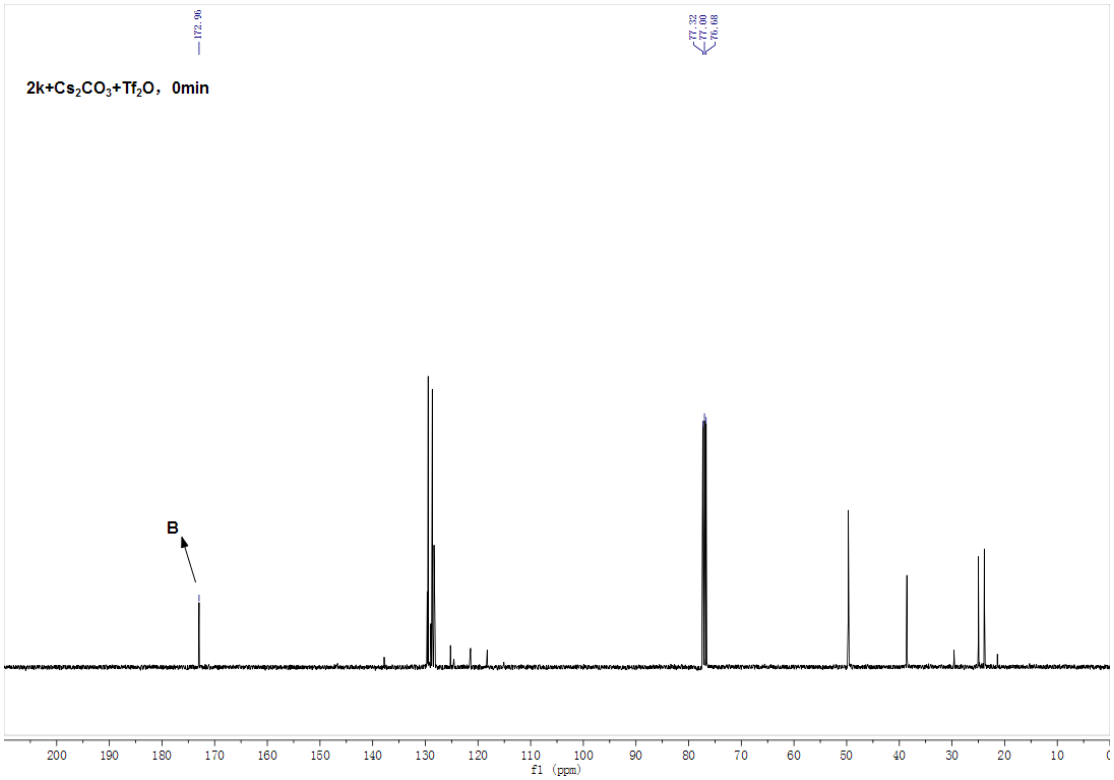


The amide **2k** (0.32 mmol, 1.6 equiv) and Cs_2CO_3 (0.52 mmol) were added to a dried round bottom flask and put under an Ar atmosphere. The toluene (2.0 mL) was added to the flask and the solution was cooled to -78 °C, followed by addition of toluene (1.0 mL) solution of Tf_2O (0.4 mmol) via syringe. The reaction kept under -78 °C for 20 minutes. Then, the reaction was warmed to the room temperature and concentrated in vacuum. The mixture was added to NMR tube and the **^{13}C NMR** and **^{19}F NMR** were acquired as **2k**+Tf_2O+Cs_2CO_3.

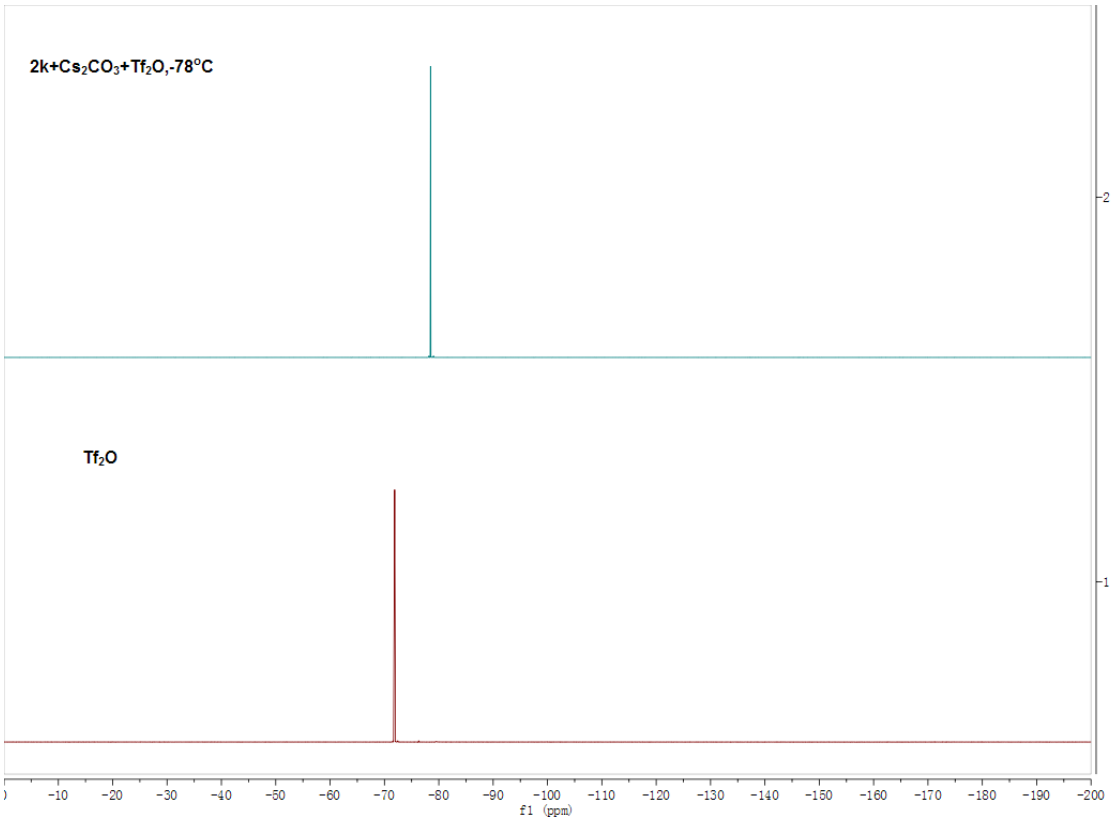
Analysis: Comparing the **^{13}C NMR** spectra of **2k**+Tf_2O+Cs_2CO_3+indole **1a** and **2k**+Tf_2O+Cs_2CO_3 at low temperature labeling as 0 min, it was noticed that when the amide was treated with Tf_2O and Cs_2CO_3 without indole, the system was detected out only **B** signal, and that could be assigned to intermediate **I**, and when the system was added indole, the intermediate **I** could be transferred into intermediate **II** by the attack of indole in short time. Therefore, the signals **B** and **C** are relevant **^{13}C NMR** signal.

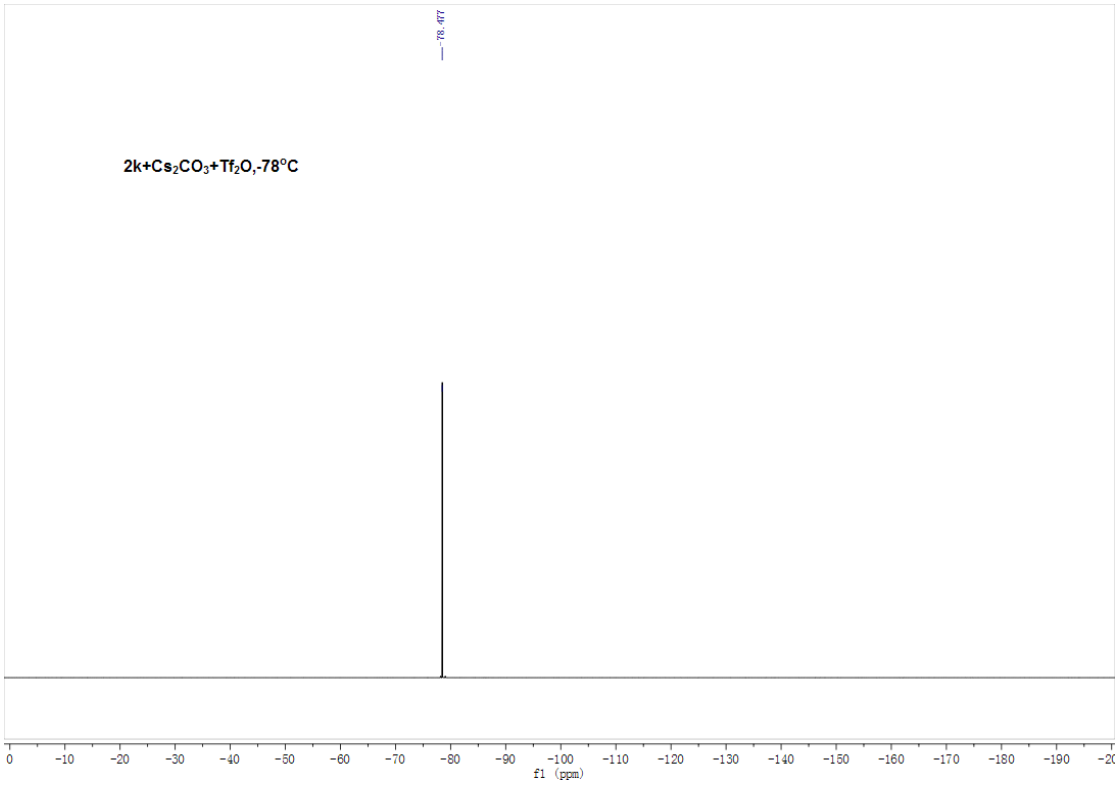

2k+Cs2CO3+Tf2O+1a，0min
B
C
2k+Cs2CO3+Tf2O，0min
B
f1 (ppm)

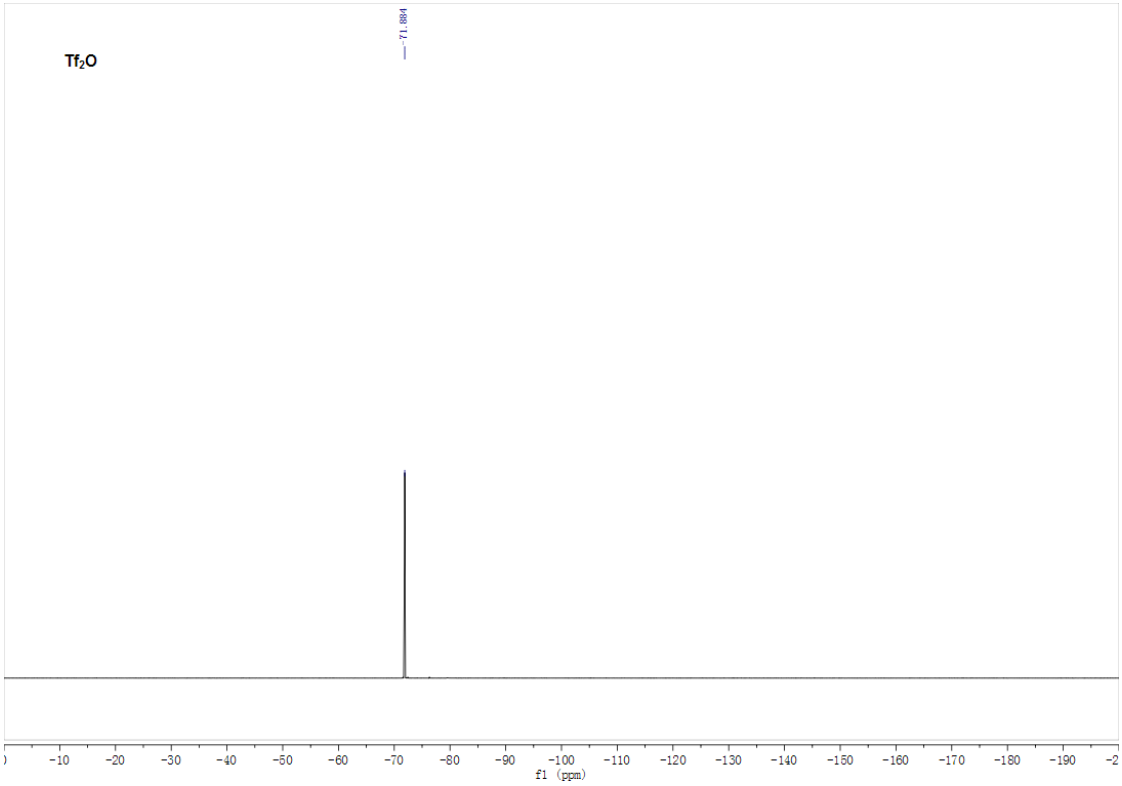

172.976
171.840
77.000
2k+Cs2CO3+Tf2O+1a,0min
B
C
f1 (ppm)



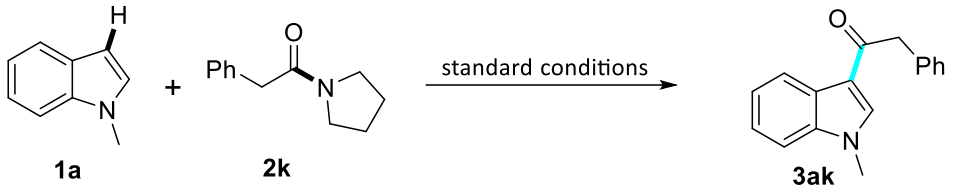
Analysis: Comparing the **^{19}F NMR** spectra of **2k**+Tf_2O+Cs_2CO_3 at low temperature and Tf_2O, it was confirmed that 2k could transfer into intermediate I.



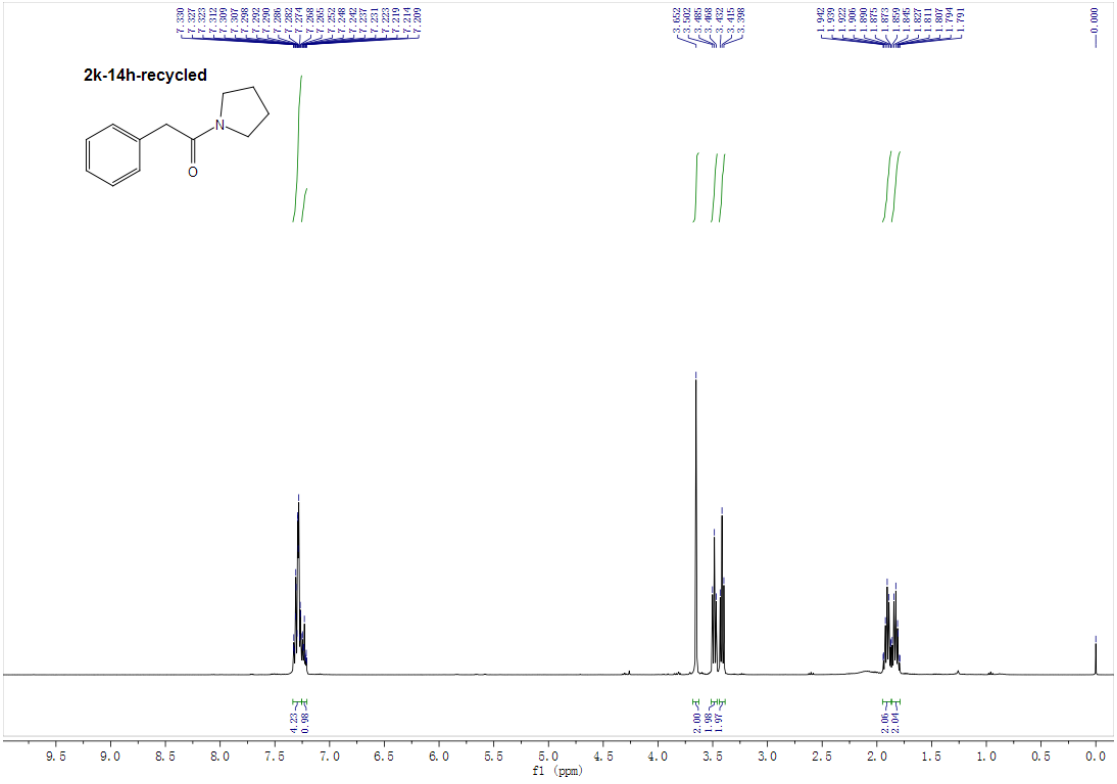

-78.477
2k+Cs2CO3+Tf2O,-78°C
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)


-71.884
Tf2O
-10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

d) Recycling experiment of starting material 2k



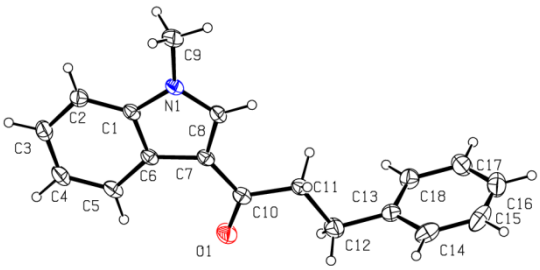
The amide **2k** (0.32 mmol, 1.6 equiv.), Cs_2CO_3 (0.52 mmol), CsF (0.1 mmol) were added to dried round bottom flask and put under an Ar atmosphere. The indole **1a** (0.2 mmol, 1 equiv.), toluene (2.0 mL) were added to the flask and the solution was cooled to -78 °C, followed by addition of toluene (1.0 mL) solution of Tf_2O (0.4 mmol) via syringe. The reaction kept under -78 °C for 20 minutes, and then heated to 70 °C. After 14 h, the reaction was quenched by the saturated $NaHCO_3$ solution and mixture was transferred to separation funnels, diluted with DCM (15.0 mL) and the organic layer was washed with water (5.0 mL×2) and brine (5.0 mL), dried over anhydrous Na_2SO_4, concentrated in vacuum and subjected to column chromatography, afforded product **3ak** 79% and recycled 47% of proportion of starting material **2k**.

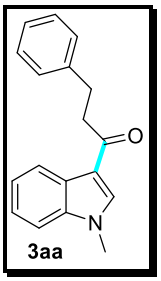


X-ray structures of Tetrazoles 3aa, 3al, 3ga, 3ua

The crystal structure of product 3aa

Crystallorgraphic data for compound **3aa** (CCDC-1857322) has been deposited with Crystallorgraphic Data Centre, Copies of the data can be obtained, free of charge, on application to CCDC (Email: deposit@ccdc.cam.ac.uk)





The ellipsoid contour percent probability level is 30% in the caption of the thermal ellipsoid plot.

Bond precision: C-C = 0.0020 A Wavelength=1.54184

Cell: a=22.0489(5) b=15.0516(3) c=18.1612(4)
alpha=90 beta=108.711(3) gamma=90

Temperature: 290 K

	Calculated	Reported
Volume	5708.6(2)	5708.6(2)
Space group	I 2/c	I 1 2/c 1
Hall group	-I 2yc	-I 2yc
Moiety formula	C18 H17 N O	C18 H17 N O
Sum formula	C18 H17 N O	C18 H17 N O
Mr	263.33	263.33
Dx,g cm-3	1.226	1.226
Z	16	16
Mu (mm-1)	0.590	0.590
F000	2240.0	2240.0
F000'	2246.16	
h,k,lmax	26,18,22	26,18,22
Nref	5402	5245
Tmin,Tmax	0.899,0.921	0.313,1.000
Tmin'	0.883	

Correction method= # Reported T Limits: Tmin=0.313 Tmax=1.000 AbsCorr = MULTI-SCAN

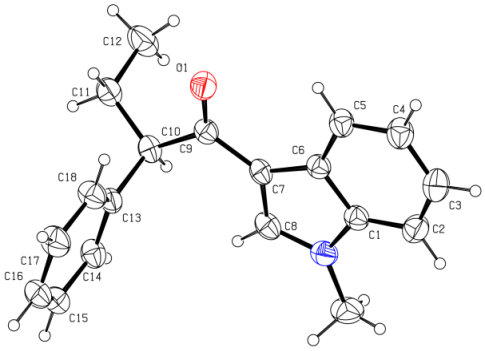
Data completeness= 0.971 Theta(max)= 69.960

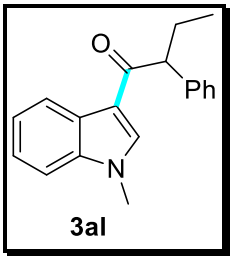
R(reflections)= 0.0416(4402) wR2(reflections)= 0.1155(5245)

S = 1.034 Npar= 363

The crystal structure of product 3al

Crystallorgraphic data for compound **3al** (CCDC-1857189) has been deposited with Crystallorgraphic Data Centre, Copies of the data can be obtained, free of charge, on application to CCDC (Email: deposit@ccdc.cam.ac.uk)





The ellipsoid contour percent probability level is 30% in the caption of the thermal ellipsoid plot.

Bond precision: C-C = 0.0051 A Wavelength=0.71073

Cell: a=9.2569(18) b=15.608(2) c=10.8924(18)
alpha=90 beta=105.432(19) gamma=90

Temperature: 232 K

	Calculated	Reported
Volume	1517.0(5)	1517.1(4)
Space group	P 21/n	P 1 21/n 1
Hall group	-P 2yn	-P 2yn
Moiety formula	C19 H19 N O	C19 H19 N O
Sum formula	C19 H19 N O	C19 H19 N O
Mr	277.35	277.35
Dx,g cm-3	1.214	1.214
Z	4	4
Mu (mm-1)	0.074	0.074
F000	592.0	592.0
F000'	592.23	
h,k,lmax	11,19,13	11,19,13
Nref	3000	2987
Tmin,Tmax	0.983,0.990	0.809,1.000
Tmin'	0.983	

Correction method= # Reported T Limits: Tmin=0.809 Tmax=1.000 AbsCorr = MULTI-SCAN

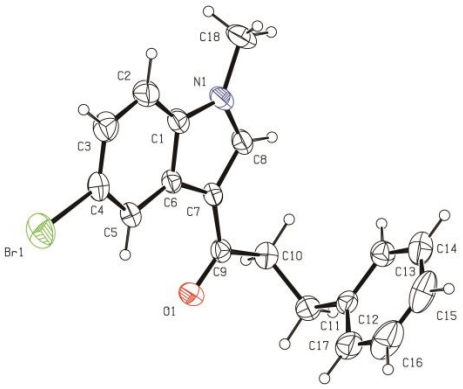
Data completeness= 0.996 Theta(max)= 26.020

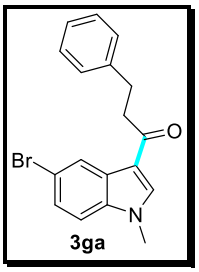
R(reflections)= 0.0812(1790) wR2(reflections)= 0.2195(2987)

S = 1.106 Npar= 192

The crystal structure of product 3ga

Crystallorgraphic data for compound **3ga** (CCDC-1857188) has been deposited with Crystallorgraphic Data Centre, Copies of the data can be obtained, free of charge, on application to CCDC (Email: deposit@ccdc.cam.ac.uk)





The ellipsoid contour percent probability level is 30% in the caption of the thermal ellipsoid plot.

Bond precision: C-C = 0.0046 A Wavelength=1.54184

Cell: a=8.4795(3) b=11.3762(4) c=16.2210(5)
alpha=90 beta=92.399(3) gamma=90

Temperature: 293 K

	Calculated	Reported
Volume	1563.38(9)	1563.38(9)
Space group	P 21/n	P 1 21/n 1
Hall group	-P 2yn	-P 2yn
Moiety formula	C18 H16 Br N O	C18 H16 Br N O
Sum formula	C18 H16 Br N O	C18 H16 Br N O
Mr	342.22	342.23
Dx,g cm-3	1.454	1.454
Z	4	4
Mu (mm-1)	3.558	3.558
F000	696.0	696.0
F000'	694.83	
h,k,lmax	10,13,19	10,13,19
Nref	2757	2685
Tmin,Tmax	0.808,0.867	0.896,1.000
Tmin'	0.780	

Correction method= # Reported T Limits: Tmin=0.896 Tmax=1.000 AbsCorr = MULTI-SCAN

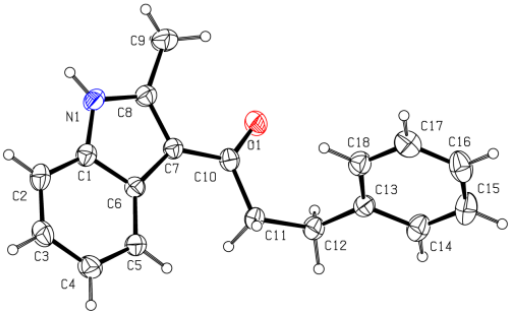
Data completeness= 0.974 Theta(max)= 66.590

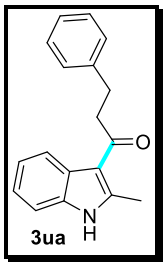
R(reflections)= 0.0430(2226) wR2(reflections)= 0.1183(2685)

S = 1.059 Npar= 191

The crystal structure of product 3ua

Crystallorgraphic data for compound **3ua** (CCDC-1857187) has been deposited with Crystallorgraphic Data Centre, Copies of the data can be obtained, free of charge, on application to CCDC (Email: deposit@ccdc.cam.ac.uk)





The ellipsoid contour percent probability level is 30% in the caption of the thermal ellipsoid plot.

Bond precision: C-C = 0.0034 A Wavelength=0.71073

Cell: a=9.6173(10) b=12.7178(10) c=11.2532(10)

alpha=90 beta=95.476(10) gamma=90

Temperature: 295 K

	Calculated	Reported
Volume	1370.1(2)	1370.1(2)
Space group	P 21/c	P 1 21/c 1
Hall group	-P 2ybc	-P 2ybc
Moiety formula	C18 H17 N O	C18 H17 N O
Sum formula	C18 H17 N O	C18 H17 N O
Mr	263.33	263.33
Dx,g cm-3	1.277	1.277
Z	4	4
Mu (mm-1)	0.079	0.079
F000	560.0	560.0
F000'	560.22	
h,k,lmax	11,15,13	11,15,13
Nref	2694	2690
Tmin,Tmax	0.987,0.991	0.627,1.000
Tmin'	0.987	

Correction method= # Reported T Limits: Tmin=0.627 Tmax=1.000 AbsCorr = MULTI-SCAN

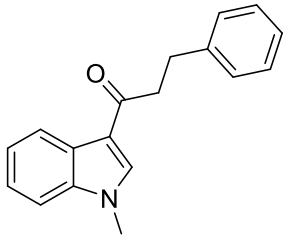
Data completeness= 0.999 Theta(max)= 26.020

R(reflections)= 0.0608(1744) wR2(reflections)= 0.1982(2690)

S = 1.041 Npar= 182

Characterization of compounds

(3aa) 1-(1-methyl-1H-indol-3-yl)-3-phenylpropan-1-one



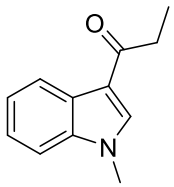
brownish red crystal, 44.7 mg, 85%, m.p. 57-59 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 – 8.38 (m, 1H), 7.64 (s, 1H), 7.34 – 7.25 (m, 7H), 7.23 – 7.16 (m, 1H), 3.79 (s, 3H), 3.19 – 3.14 (m, 2H), 3.14 – 3.07 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 194.4, 141.7, 137.3, 135.2, 128.4, 126.2, 125.9, 123.2, 122.5, 116.3, 109.5, 41.6, 33.4, 30.7.

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{18}H_{17}NO$) requires *m/z* 264.1383, found *m/z* 264.1383.

(3ab) 1-(1-methyl-1H-indol-3-yl)propan-1-one



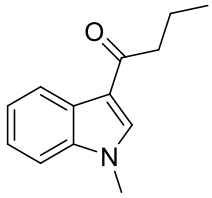
transparent crystal, 21.3 mg, 57%, m.p. 74-76 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 – 8.28 (m, 1H), 7.69 (s, 1H), 7.44 – 7.27 (m, 3H), 3.81 (s, 3H), 2.86 (q, *J* = 7.4 Hz, 2H), 1.25 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 196.3, 137.3, 134.9, 126.2, 123.1, 122.3, 116.1, 109.5, 33.4, 32.8, 8.9.

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{12}H_{13}NO$) requires *m/z* 188.1070, found *m/z* 188.1069.

(3ac) 1-(1-methyl-1H-indol-3-yl)butan-1-one



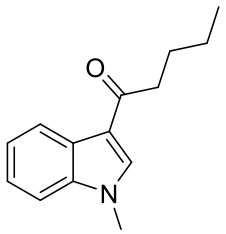
crimson oily liquid, 26.1 mg, 65%

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 – 8.37 (m, 1H), 7.68 (s, 1H), 7.33 – 7.27 (m, 3H), 3.80 (s, 3H), 2.79 (t, *J* = 7.2 Hz, 2H), 1.85 – 1.75 (m, 2H), 1.01 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 195.7, 137.3, 135.1, 126.2, 123.1, 122.5, 122.3, 116.5, 109.5, 41.8, 33.3, 18.6, 14.0.

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{13}H_{15}NO$) requires *m/z* 202.1226, found *m/z* 202.1225.

(3ad) 1-(1-methyl-1H-indol-3-yl)pentan-1-one



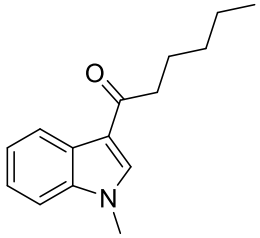
bright red liquid, 25.0 mg, 58%

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 – 8.36 (m, 1H), 7.69 (s, 1H), 7.33 – 7.27 (m, 3H), 3.82 (s, 3H), 2.82 (t, *J* = 8.0 Hz, 2H), 1.80 – 1.71 (m, 2H), 1.48 – 1.37 (m, 2H), 0.95 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 195.9, 137.4, 135.1, 126.3, 123.2, 122.6, 122.4, 116.5, 109.5, 39.6, 33.4, 27.3, 22.6, 13.9.

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{14}H_{17}NO$) requires *m/z* 216.1383, found *m/z* 216.1382.

(3ae) 1-(1-methyl-1H-indol-3-yl)hexan-1-one



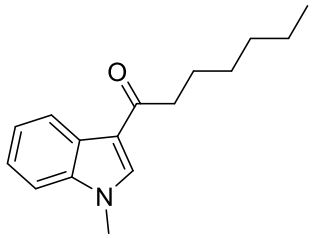
crimson liquid, 24.3 mg, 53%

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 – 8.37 (m, 1H), 7.70 (s, 1H), 7.30 (dt, *J* = 7.6, 2.4 Hz, 3H), 3.83 (s, 3H), 2.82 (t, *J* = 7.8 Hz, 2H), 1.82 – 1.73 (m, 2H), 1.42 – 1.32 (m, 4H), 0.95 – 0.87 (m, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 195.9, 137.4, 135.1, 126.3, 123.2, 122.6, 122.4, 116.5, 109.5, 39.9, 33.4, 31.7, 24.9, 22.5, 13.9.

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{15}H_{19}NO$) requires *m/z* 230.1539, found *m/z* 230.1539.

(3af) 1-(1-methyl-1H-indol-3-yl)heptan-1-one



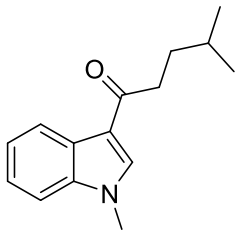
aubergine liquid, 27.7 mg, 57%

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 – 8.37 (m, 1H), 7.69 (s, 1H), 7.33 – 7.27 (m, 3H), 3.81 (s, 3H), 2.84 – 2.79 (m, 2H), 1.82 – 1.72 (m, 2H), 1.42 – 1.35 (m, 2H), 1.35 – 1.29 (m, 4H), 0.91 – 0.86 (m, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 195.9, 137.4, 135.1, 126.3, 123.1, 122.5, 122.4, 116.5, 109.5, 39.9, 33.4, 31.7, 29.2, 25.2, 22.5, 14.0.

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{16}H_{21}NO$) requires *m/z* 244.1696, found *m/z* 244.1696.

(3ag) 4-methyl-1-(1-methyl-1H-indol-3-yl)pentan-1-one



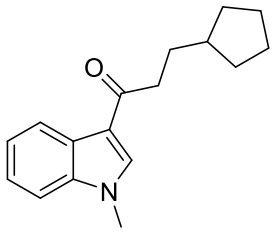
rufous liquid, 31.1 mg, 68%

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 – 8.37 (m, 1H), 7.68 (s, 1H), 7.32 – 7.27 (m, 3H), 3.81 (s, 3H), 2.85 – 2.79 (m, 2H), 1.70 – 1.63 (m, 3H), 0.95 (d, *J* = 6.0 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 196.1, 137.4, 135.1, 126.3, 123.2, 122.5, 122.4, 116.4, 109.5, 37.9, 34.1, 33.4, 27.9, 22.4.

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{15}H_{19}NO$) requires *m/z* 230.1539, found *m/z* 230.1539.

(3ah) 3-cyclopentyl-1-(1-methyl-1H-indol-3-yl)propan-1-one



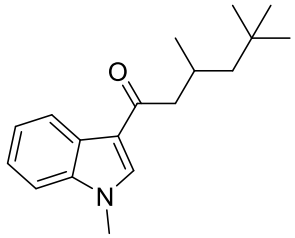
red liquid, 31.1 mg, 61%

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 – 8.37 (m, 1H), 7.69 (s, 1H), 7.33 – 7.27 (m, 3H), 3.82 (s, 3H), 2.86 – 2.80 (m, 2H), 1.87 – 1.74 (m, 5H), 1.68 – 1.46 (m, 4H), 1.20 – 1.10 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 196.0, 137.4, 135.1, 135.0, 126.3, 123.1, 122.6, 122.4, 116.4, 109.4, 39.9, 39.2, 33.4, 32.5, 31.5, 25.1.

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{17}H_{21}NO$) requires *m/z* 256.1696, found *m/z* 256.1696.

(3ai) 3,5,5-trimethyl-1-(1-methyl-1H-indol-3-yl)hexan-1-one



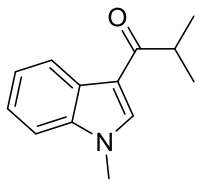
aubergine liquid, 35.2 mg, 65%

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 – 8.39 (m, 1H), 7.66 (s, 1H), 7.32 – 7.27 (m, 3H), 3.81 (s, 3H), 2.76 (dd, *J* = 14.8, 6.0 Hz, 1H), 2.66 (dd, *J* = 14.8, 8.0 Hz, 1H), 2.36 – 2.26 (m, 1H), 1.36 (dd, *J* = 14.0, 4.0 Hz, 1H), 1.17 (dd, *J* = 14.0, 6.4 Hz, 1H), 1.01 (d, *J* = 6.4 Hz, 3H), 0.92 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 195.5, 137.4, 135.2, 126.3, 123.2, 122.6, 122.4, 117.3, 109.4, 51.1, 49.5, 33.4, 31.1, 30.0, 27.0, 23.0.

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{18}H_{25}NO$) requires *m/z* 272.2009, found *m/z* 272.2009.

(3aj) 2-methyl-1-(1-methyl-1H-indol-3-yl)propan-1-one



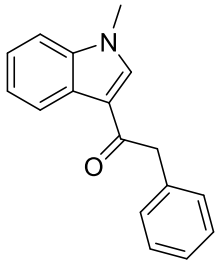
crimson liquid, 18.1 mg, 45%

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 – 8.31 (m, 1H), 7.73 (s, 1H), 7.40 – 7.27 (m, 3H), 3.84 (s, 3H), 3.31 (p, *J* = 6.8 Hz, 1H), 1.25 (d, *J* = 6.8 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 200.8, 137.4, 135.0, 126.5, 123.2, 123.2, 122.7, 122.4, 115.1, 109.4, 37.0, 33.4, 19.7.

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{13}H_{15}NO$) requires *m/z* 202.1226, found *m/z* 202.1226.

(3ak) 1-(1-methyl-1H-indol-3-yl)-2-phenylethan-1-one



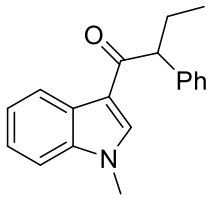
white crystal, 39.34 mg, 79%, m.p. 112-113 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 – 8.33 (m, 1H), 7.69 (s, 1H), 7.34 – 7.26 (m, 7H), 7.24 – 7.19 (m, 1H), 4.09 (s, 2H), 3.75 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 192.5, 137.3, 135.8, 135.7, 129.2, 128.5, 126.5, 126.5, 123.4, 122.6, 122.6, 116.0, 109.5, 46.8, 33.4.

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{17}H_{15}NO$) requires *m/z* 250.1226, found *m/z* 250.1225.

(3al) 1-(1-methyl-1H-indol-3-yl)-2-phenylbutan-1-one



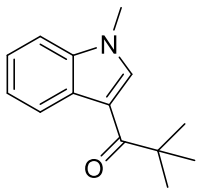
pink crystal, 35.0 mg, 63%, m.p. 166-168 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 – 8.44 (m, 1H), 7.69 (s, 1H), 7.39 (d, *J* = 8.0 Hz, 2H), 7.30 – 7.23 (m, 5H), 7.18 (t, *J* = 7.2 Hz, 1H), 4.17 (t, *J* = 7.3 Hz, 1H), 3.73 (s, 3H), 2.34 – 2.22 (m, 1H), 1.94 – 1.82 (m, 1H), 0.93 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 195.2, 141.1, 137.3, 135.5, 135.3, 128.5, 127.9, 123.3, 122.8, 122.5, 116.4, 109.3, 57.0, 33.4, 26.9, 12.5.

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{19}H_{19}NO$) requires *m/z* 278.1539, found *m/z* 278.1540.

(3am) 2,2-dimethyl-1-(1-methyl-1H-indol-3-yl)propan-1-one



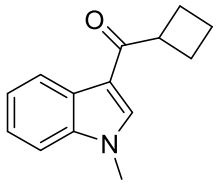
brown crystal, 11 mg, 25%, m.p. 115-116 °C

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.57 – 8.45 (m, 1H), 7.79 (s, 1H), 7.34 – 7.28 (m, 3H), 3.85 (s, 3H), 1.42 (s, 9H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 201.98 , 136.42 , 128.22 , 123.37 , 123.19 , 122.45 , 112.70 , 109.17 , 44.05 , 33.46 , 28.94 .

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{14}H_{17}NO$) requires *m/z* 216.1383, found *m/z* 216.1382.

(3an) cyclobutyl(1-methyl-1H-indol-3-yl)methanone



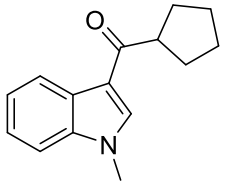
light red crystal, 28.5 mg, 67%, m.p. 89-90 °C

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.44 – 8.38 (m, 1H), 7.59 (s, 1H), 7.33 – 7.27 (m, 3H), 3.80 (s, 4H), 2.53 – 2.42 (m, 2H), 2.29 – 2.19 (m, 2H), 2.12 – 1.99 (m, 1H), 1.97 – 1.87 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) *δ* 196.6, 137.3, 134.9, 126.4, 123.1, 122.5, 122.3, 114.7, 109.4, 43.0, 33.4, 25.2, 18.3.

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{14}H_{15}NO$) requires *m/z* 214.1226, found *m/z* 214.1227.

(3ao) cyclopentyl(1-methyl-1H-indol-3-yl)methanone



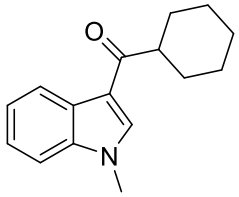
dark brown liquid, 24.5 mg, 54%

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.45 – 8.40 (m, 1H), 7.70 (s, 1H), 7.34 – 7.26 (m, 3H), 3.82 (s, 3H), 3.54 – 3.46 (m, 1H), 2.03 – 1.85 (m, 4H), 1.83 – 1.73 (m, 2H), 1.69 – 1.60 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) *δ* 198.5, 137.4, 135.1, 126.5, 123.1, 122.6, 122.4, 116.2, 109.4, 47.8, 33.4, 30.5, 26.3.

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{15}H_{17}NO$) requires *m/z* 228.1383, found *m/z* 228.1379.

(3ap) cyclohexyl(1-methyl-1H-indol-3-yl)methanone



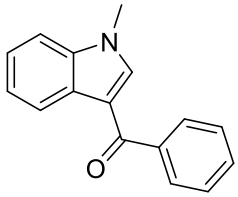
aubergine crystal, 24.1 mg, 50%, m.p. 133-135 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 – 8.36 (m, 1H), 7.73 (s, 1H), 7.35 – 7.27 (m, 3H), 3.83 (s, 3H), 3.06 – 2.97 (m, 1H), 1.94 – 1.82 (m, 4H), 1.77 – 1.70 (m, 1H), 1.68 – 1.56 (m, 2H), 1.45 – 1.25 (m, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 199.4, 137.5, 134.9, 126.5, 123.2, 122.69, 122.44, 115.39, 109.49, 47.78, 33.46, 33.40, 29.8, 26.0, 25.9.

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{16}H_{19}NO$) requires *m/z* 242.1539, found *m/z* 242.1539.

(3aq) (1-methyl-1H-indol-3-yl)(phenyl)methanone



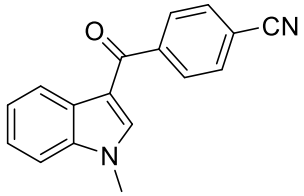
light red crystal, 18.3 mg, 39%, m.p. 108-109 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 – 8.39 (m, 1H), 7.82 (s, 1H), 7.80 (s, 1H), 7.57 – 7.44 (m, 4H), 7.39 – 7.32 (m, 3H), 3.83 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 190.8, 140.8, 137.9, 137.9, 137.4, 131.0, 128.6, 128.2, 127.1, 123.6, 122.6, 115.4, 109.5, 33.5.

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{16}H_{13}NO$) requires *m/z* 236.1070, found *m/z* 236.1069.

(3ar) 4-(1-methyl-1H-indole-3-carbonyl)benzonitrile



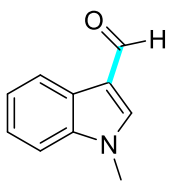
brownish crystal, 14.6 mg, 28%, m.p. 204-206 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 – 8.36 (m, 1H), 7.89 – 7.84 (m, 2H), 7.79 – 7.74 (m, 2H), 7.47 (s, 1H), 7.42 – 7.35 (m, 3H), 3.87 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 188.6, 144.6, 137.9, 137.6, 132.8, 129.0, 126.8, 124.1, 123.2, 122.6, 118.3, 115.1, 114.4, 109.8, 33.7.

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{17}H_{12}N_2O$) requires *m/z* 261.1022, found *m/z* 261.1025.

(3as)1-methyl-1H-indole-3-carbaldehyde



brownish crystal, 25 mg, 79%, m.p. 71-73 °C

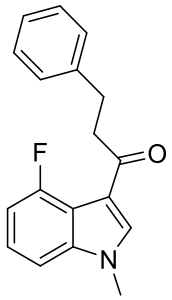
^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.95 (s, 1H), 8.32 – 8.27 (m, 1H), 7.62 (s, 1H), 7.36 – 7.29 (m, 3H), 3.83 (s, 3H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 184.3, 139.2, 137.8, 125.2, 123.9, 122.8, 121.9, 117.9, 109.8,

33.6.

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{10}H_9NO$) requires *m*/*z* 160.0757, found *m*/*z* 160.0759.

(3ba) 1-(4-fluoro-1-methyl-1H-indol-3-yl)-3-phenylpropan-1-one



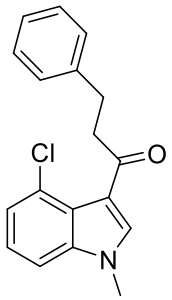
brownish red crystal, 25.9 mg, 46%, m.p. 80-82 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (s, 1H), 7.31 – 7.26 (m, 4H), 7.25 – 7.15 (m, 2H), 7.11 (d, *J* = 8.0 Hz, 1H), 6.99 – 6.93 (m, 1H), 3.80 (s, 3H), 3.31 – 3.25 (m, 2H), 3.12 – 3.07 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 193.6, 157.6, 155.1, 141.8, 140.3 (d, *J* = 11.0 Hz), 135.8, 128.4 (d, *J* = 8.0 Hz), 125.8, 123.8 (d, *J* = 8.0 Hz), 116.3 (d, *J* = 5.0 Hz), 113.8 (d, *J* = 20.0 Hz), 108.1 (d, *J* = 22.0 Hz), 105.9 (d, *J* = 4.0 Hz), 42.5 (d, *J* = 7.0 Hz), 33.8, 30.7.

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{18}H_{16}FN_5O$) requires *m*/*z* 282.1289, found *m*/*z* 282.1288.

(3ca) 1-(4-chloro-1-methyl-1H-indol-3-yl)-3-phenylpropan-1-one



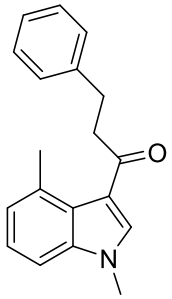
light yellow crystal, 42.1 mg, 71%, m.p. 82-84 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (s, 1H), 7.29 – 7.22 (m, 5H), 7.20 – 7.14 (m, 3H), 3.72 (s, 3H), 3.20 – 3.13 (m, 2H), 3.12 – 3.04 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 193.7, 141.6, 139.1, 135.7, 128.4, 128.8, 127.2, 125.9, 123.7, 123.6, 123.3, 117.4, 108.3, 43.5, 33.5, 30.9.

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{18}H_{16}ClNO$) requires *m*/*z* 298.0993, found *m*/*z* 298.0993.

(3da) 1-(1,4-dimethyl-1H-indol-3-yl)-3-phenylpropan-1-one



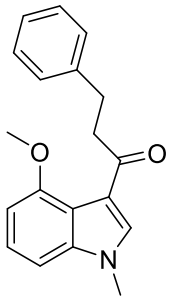
light yellow crystal, 31.1 mg, 56%, m.p. 95-96 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (s, 1H), 7.31 – 7.28 (m, 1H), 7.27 – 7.23 (m, 3H), 7.22 – 7.16 (m, 2H), 7.10 (d, *J* = 8.0 Hz, 1H), 7.04 (d, *J* = 7.2 Hz, 1H), 3.72 (s, 3H), 3.18 – 3.12 (m, 2H), 3.11 – 3.05 (m, 2H), 2.85 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 193.5, 141.7, 138.2, 136.1, 133.6, 128.4, 125.9, 125.0, 124.3, 123.5, 118.2, 107.0, 42.3, 33.4, 31.2, 23.0.

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{18}H_{17}NO$) requires *m/z* 278.1539, found *m/z* 278.1539.

(3ea) 1-(4-methoxy-1-methyl-1H-indol-3-yl)-3-phenylpropan-1-one



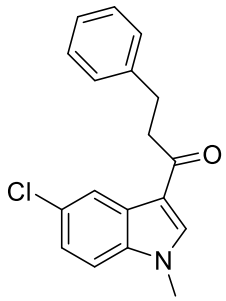
gray white crystal, 26.4 mg, 45%, m.p. 81-82 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (s, 1H), 7.30 – 7.22 (m, 5H), 7.20 – 7.15 (m, 1H), 6.95 – 6.91 (m, 1H), 6.68 (d, *J* = 7.6 Hz, 1H), 3.91 (s, 3H), 3.74 (s, 3H), 3.42 – 3.37 (m, 2H), 3.10 – 3.04 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 196.2, 153.9, 142.1, 139.3, 134.4, 128.3, 128.3, 125.7, 123.8, 118.0, 115.1, 103.0, 102.5, 55.3, 43.6, 33.5, 31.1.

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{19}H_{19}NO_2$) requires *m/z* 294.1489, found *m/z* 294.1485.

(3fa) 1-(5-chloro-1-methyl-1H-indol-3-yl)-3-phenylpropan-1-one



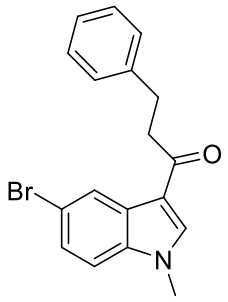
rufous crystal, 33.3 mg, 56%, m.p. 130-132 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 – 8.36 (m, 1H), 7.55 (d, *J* = 2.8 Hz, 1H), 7.31 – 7.28 (m, 1H), 7.27 – 7.23 (m, 3H), 7.21 – 7.16 (m, 2H), 7.16 – 7.12 (m, 1H), 3.73 (s, 3H), 3.11 – 3.05 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 194.0, 141.5, 135.9, 135.6, 128.4, 128.4, 127.1, 126.0, 123.5, 121.9, 115.7, 110.5, 41.3, 33.5, 30.5.

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{18}H_{16}ClNO$) requires *m/z* 298.0993, found *m/z* 298.0991.

(3ga) 1-(5-bromo-1-methyl-1H-indol-3-yl)-3-phenylpropan-1-one



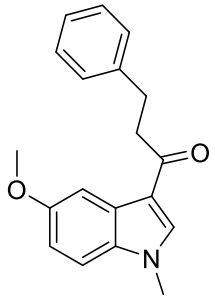
light pink crystal, 46.4 mg, 68%, m.p. 142-144 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 – 8.50 (m, 1H), 7.50 (d, *J* = 4.8 Hz, 1H), 7.33 – 7.27 (m, 2H), 7.27 – 7.23 (m, 3H), 7.21 – 7.16 (m, 1H), 7.09 – 7.04 (m, 1H), 3.71 (s, 3H), 3.09 – 3.05 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 193.9, 141.5, 135.7, 128.4, 127.6, 125.0, 124.9, 116.1, 115.66, 110.98, 41.31, 33.5, 30.5.

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{18}H_{16}BrNO$) requires *m/z* 342.0488, found *m/z* 342.0486.

(3ha) 1-(5-methoxy-1-methyl-1H-indol-3-yl)-3-phenylpropan-1-one



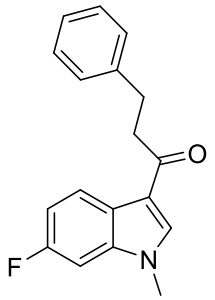
dark red crystal, 32.3 mg, 55%, m.p. 72-74 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 2.8 Hz, 1H), 7.56 (s, 1H), 7.30 – 7.25 (m, 4H), 7.21 – 7.16 (m, 2H), 6.93 (dd, *J* = 8.8, 2.8 Hz, 1H), 3.89 (s, 3H), 3.74 (s, 3H), 3.15 – 3.07 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 194.4, 156.4, 141.7, 135.3, 132.3, 128.4, 127.1, 125.8, 115.9, 113.9, 113.8, 110.4, 110.3, 103.6, 55.6, 41.3, 33.7, 30.7.

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{19}H_{19}NO_2$) requires *m/z* 294.1482, found *m/z* 294.1490.

(3ia) 1-(6-fluoro-1-methyl-1H-indol-3-yl)-3-phenylpropan-1-one



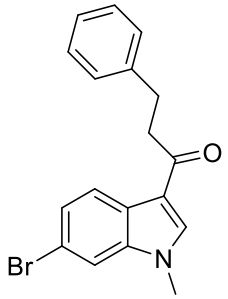
dark red crystal, 37.1 mg, 66%, m.p. 82-84 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (dd, *J* = 8.8, 5.6 Hz, 1H), 7.56 (s, 1H), 7.31 – 7.22 (m, 4H), 7.21 – 7.16 (m, 1H), 7.06 – 7.00 (m, 1H), 6.94 (dd, *J* = 9.2, 2.0 Hz, 1H), 3.70 (s, 3H), 3.14 – 3.04 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 194.2, 161.5, 159.1, 141.61, 137.5 (d, *J* = 12.0Hz), 135.44, 128.4 (d, *J* = 4.0 Hz), 125.9, 123.6 (d, *J* = 10.0 Hz), 122.6, 116.4, 110.9 (d, *J* = 24.0 Hz), 96.2 (d, *J* = 26.0 Hz), 41.3, 33.4, 30.6.

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{18}H_{16}FN_5O$) requires *m/z* 282.1289, found *m/z* 282.1290.

(3ja) 1-(6-bromo-1-methyl-1H-indol-3-yl)-3-phenylpropan-1-one



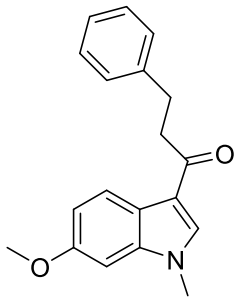
pink crystal, 52.5 mg, 77%, m.p. 127-128 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J* = 8.4 Hz, 1H), 7.55 (s, 1H), 7.43 (d, *J* = 1.6 Hz, 1H), 7.37 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.31 – 7.23 (m, 4H), 7.21 – 7.16 (m, 1H), 3.72 (s, 3H), 3.15 – 3.10 (m, 2H), 3.10 – 3.05 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 194.2, 141.5, 138.1, 135.4, 128.4, 128.4, 126.0, 125.7, 125.0, 123.8, 116.9, 116.4, 112.7, 41.5, 33.5, 30.6.

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{18}H_{16}BrNO$) requires *m/z* 342.0488, found *m/z* 342.0486.

(3ka) 1-(6-methoxy-1-methyl-1H-indol-3-yl)-3-phenylpropan-1-one



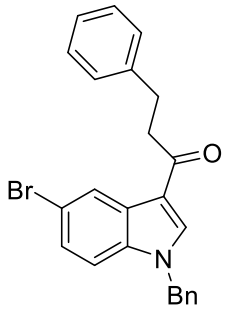
crimson liquid, 20.0 mg, 34%

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (dd, *J* = 8.8, 0.4 Hz, 1H), 7.52 (d, *J* = 1.2 Hz, 1H), 7.31 – 7.28 (m, 1H), 7.27 – 7.24 (m, 3H), 7.21 – 7.16 (m, 1H), 6.94 (dd, *J* = 8.8, 2.0 Hz, 1H), 6.74 (d, *J* = 2.0 Hz, 1H), 3.86 (s, 3H), 3.72 (s, 3H), 3.15 – 3.05 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 194.5, 157.3, 141.9, 138.4, 134.5, 128.5, 126.0, 123.4, 120.5, 116.5, 111.9, 93.4, 55.8, 41.5, 33.5, 31.0.

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{19}H_{19}NO_2$) requires *m/z* 294.1489, found *m/z* 294.1485.

(3la) 1-(1-benzyl-5-bromo-1H-indol-3-yl)-3-phenylpropan-1-one



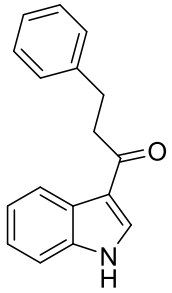
nacarat oil, 27.5 mg, 33%

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (d, *J* = 1.6 Hz, 1H), 7.63 (s, 1H), 7.34 – 7.26 (m, 5H), 7.26 – 7.22 (m, 3H), 7.20 – 7.15 (m, 1H), 7.12 – 7.07 (m, 3H), 5.26 (s, 2H), 3.15 – 3.10 (m, 2H), 3.10 – 3.05 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 194.2, 141.5, 135.6, 135.2, 135.1, 129.1, 128.4, 128.3, 128.0, 126.9, 126.5, 126.0, 125.3, 116.4, 111.5, 50.9, 41.5, 30.6.

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{24}H_{20}BrNO$) requires *m*/*z* 418.0801, found *m*/*z* 418.0802.

(3ma) 1-(1H-indol-3-yl)-3-phenylpropan-1-one



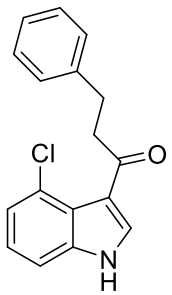
rufous powder, 21.4 mg, 43%, m.p. 157-159 °C

^{1}H NMR (400 MHz, DMSO-d_6) δ 11.90 (s, 1H), 8.35 (d, *J* = 3.2 Hz, 1H), 8.22 – 8.19 (m, 1H), 7.47 – 7.44 (m, 1H), 7.32 – 7.24 (m, 4H), 7.23 – 7.14 (m, 3H), 3.22 – 3.16 (m, 2H), 3.00 – 2.95 (m, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 194.3, 141.7, 136.7, 133.9, 128.4, 128.3, 125.8, 125.4, 122.7, 121.7, 121.4, 116.3, 112.1, 30.4.

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{17}H_{15}NO$) requires *m*/*z* 250.1226, found *m*/*z* 250.1225.

(3na) 1-(4-chloro-1H-indol-3-yl)-3-phenylpropan-1-one



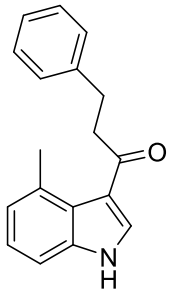
dark red liquid, 27.7 mg, 49%

^{1}H NMR (400 MHz, DMSO-d_6) δ 12.16 (s, 1H), 8.37 (d, *J* = 3.1 Hz, 1H), 7.46 – 7.41 (m, 1H), 7.31 – 7.24 (m, 4H), 7.20 – 7.14 (m, 3H), 3.26 – 3.20 (m, 2H), 2.99 – 2.92 (m, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 192.9, 141.6, 138.8, 134.7, 128.5, 128.3, 125.8, 125.7, 123.6, 122.9, 122.5, 117.3, 111.2, 42.0, 30.4.

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{17}H_{14}ClNO$) requires *m/z* 284.0837, found *m/z* 284.0844.

(3oa) 1-(4-methyl-1H-indol-3-yl)-3-phenylpropan-1-one



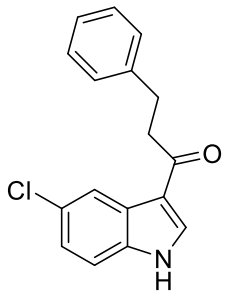
brown powder, 27.3 mg, 52%, m.p. 110-112 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.87 (s, 1H), 7.30 – 7.22 (m, 5H), 7.21 – 7.13 (m, 3H), 7.03 – 7.00 (m, 1H), 3.18 – 3.13 (m, 2H), 3.11 – 3.05 (m, 2H), 2.82 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 194.9, 141.5, 137.3, 133.2, 132.0, 128.5, 128.4, 126.0, 124.4, 124.1, 123.9, 119.7, 109.0, 42.4, 31.2, 23.0.

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{18}H_{17}NO$) requires *m/z* 264.1383, found *m/z* 264.1381.

(3pa) 1-(5-chloro-1H-indol-3-yl)-3-phenylpropan-1-one



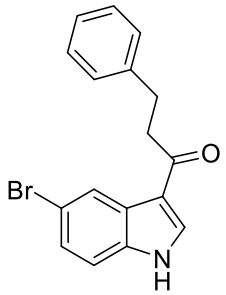
brown yellow powder, 26.6 mg, 47%, m.p. 188-189 °C

^{1}H NMR (400 MHz, DMSO-d_6) δ 12.10 (s, 1H), 8.43 (d, *J* = 2.8 Hz, 1H), 8.19 (d, *J* = 2.0 Hz, 1H), 7.48 (d, *J* = 8.8 Hz, 1H), 7.31 – 7.24 (m, 4H), 7.24 – 7.20 (m, 1H), 7.19 – 7.13 (m, 1H), 3.22 – 3.17 (m, 2H), 3.00 – 2.94 (m, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 194.4, 141.6, 135.3, 135.2, 128.4, 128.3, 126.6, 126.5, 125.8, 122.8, 120.5, 115.9, 113.8, 39.0, 30.2.

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{17}H_{14}ClNO$) requires *m/z* 284.0837, found *m/z* 284.0835.

(3qa) 1-(5-bromo-1H-indol-3-yl)-3-phenylpropan-1-one



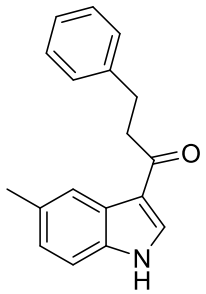
brownish powder, 35.9 mg, 55%, m.p. 182-183 °C

^{1}H NMR (400 MHz, DMSO-d_6) δ 12.11 (s, 1H), 8.41 (d, *J* = 2.8 Hz, 1H), 8.36 (d, *J* = 2.0 Hz, 1H), 7.44 (d, *J* = 8.4 Hz, 1H), 7.34 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.31 – 7.24 (m, 4H), 7.19 – 7.13 (m, 1H), 3.19 (t, *J* = 7.6 Hz, 2H), 2.96 (t, *J* = 7.6 Hz, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 194.4, 141.6, 135.4, 135.1, 128.4, 128.2, 127.2, 125.8, 125.3, 123.5, 115.79, 114.5, 114.2, 38.9, 30.2.

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{17}H_{14}BrNO$) requires *m*/*z* 328.0332, found *m*/*z* 328.0344.

(3ra) 1-(5-methyl-1H-indol-3-yl)-3-phenylpropan-1-one



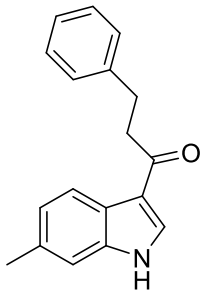
white powder, 20.0 mg, 38%, m.p. 208-210 °C

^{1}H NMR (400 MHz, DMSO-d_6) δ 11.79 (s, 1H), 8.28 (d, *J* = 3.1 Hz, 1H), 8.02 (s, 1H), 7.33 (d, *J* = 8.0 Hz, 1H), 7.31 – 7.24 (m, 4H), 7.19 – 7.14 (m, 1H), 7.02 (dd, *J* = 8.4, 2.0 Hz, 1H), 3.20 – 3.14 (m, 2H), 2.99 – 2.94 (m, 2H), 2.40 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 194.2, 141.7, 135.0, 133.9, 130.4, 128.4, 128.2, 125.8, 125.7, 124.2, 121.2, 115.9, 111.7, 30.4, 21.4.

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{18}H_{17}NO$) requires *m*/*z* 264.1383, found *m*/*z* 264.1386.

(3sa) 1-(6-methyl-1H-indol-3-yl)-3-phenylpropan-1-one



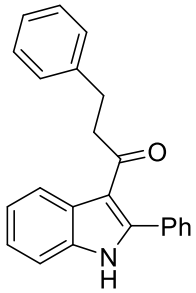
dark red oily liquid, 36.8 mg, 70%

^{1}H NMR (400 MHz, DMSO-d_6) δ 11.77 (s, 1H), 8.27 (d, J = 3.2 Hz, 1H), 8.07 (d, J = 8.0 Hz, 1H), 7.32 – 7.23 (m, 5H), 7.19 – 7.13 (m, 1H), 7.02 – 6.99 (m, 1H), 3.20 – 3.14 (m, 2H), 3.00 – 2.93 (m, 2H), 2.40 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 194.1, 141.8, 137.1, 132.0, 128.4, 128.3, 125.8, 123.3, 121.1, 116.3, 111.8, 38.0, 30.4, 21.3.

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{18}H_{17}NO$) requires m/z 264.1383, found m/z 264.1383.

(3ta) 3-phenyl-1-(2-phenyl-1H-indol-3-yl)propan-1-one



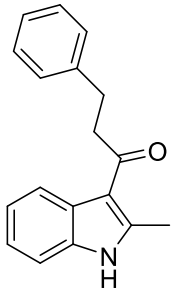
celadon crystal, 29.9 mg, 46%, m.p. 187-188 °C

^{1}H NMR (400 MHz, DMSO-d_6) δ 12.09 (s, 1H), 8.22 – 8.18 (m, 1H), 7.62 – 7.58 (m, 2H), 7.56 – 7.51 (m, 3H), 7.45 – 7.42 (m, 1H), 7.26 – 7.15 (m, 4H), 7.13 – 7.08 (m, 1H), 6.99 – 6.94 (m, 2H), 2.84 – 2.78 (m, 2H), 2.76 – 2.71 (m, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 195.7, 144.5, 141.4, 135.5, 132.8, 129.9, 129.3, 128.5, 128.2, 128.1, 127.1, 125.7, 122.9, 121.8, 121.6, 113.9, 111.7, 42.7, 30.4.

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{23}H_{19}NO$) requires m/z 326.1539, found m/z 326.1540.

(3ua) 1-(2-methyl-1H-indol-3-yl)-3-phenylpropan-1-one



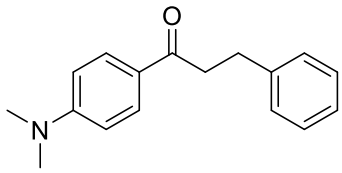
pink crystal, 41.0 mg, 78%, m.p. 141-142 °C

^{1}H NMR (400 MHz, DMSO-d_6) δ 11.83 (s, 1H), 8.02 – 7.96 (m, 1H), 7.39 – 7.34 (m, 1H), 7.20 – 7.10 (m, 3H), 3.21 (t, J = 7.2 Hz, 2H), 2.98 (t, J = 7.2 Hz, 2H), 2.68 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 194.5, 144.1, 142.0, 134.8, 128.4, 126.7, 125.7, 121.7, 121.3, 120.6, 113.1, 111.2, 43.4, 29.7, 15.3.

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{18}H_{17}NO$) requires m/z 264.1383, found m/z 264.1387.

(5aa) 1-(4-(dimethylamino)phenyl)-3-phenylpropan-1-one



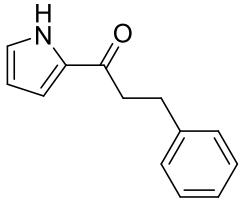
transparent crystal, 7.59 mg, 15%, m.p. 76-78 °C

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.91 – 7.85 (m, 2H), 7.32 – 7.23 (m, 4H), 7.22 – 7.16 (m, 1H), 6.66 – 6.61 (m, 2H), 3.22 – 3.17 (m, 2H), 3.04 (s, 8H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 197.3, 153.3, 141.8, 130.2, 128.4, 125.9, 124.9, 110.6, 39.9, 39.7, 30.7.

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{17}H_{19}NO$) requires *m/z* 254.1539, found *m/z* 254.1538.

(7aa) 3-phenyl-1-(1H-pyrrol-2-yl)propan-1-one



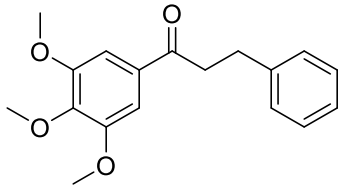
light yellow solid, 22 mg, 55%, m.p 54-56 °C

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.77 (s, 1H), 7.32 – 7.22 (m, 4H), 7.22 – 7.17 (m, 1H), 6.92 – 6.89 (m, 1H), 6.28 – 6.23 (m, 1H), 3.15 – 3.01 (m, 4H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 189.7, 141.2, 131.7, 128.4, 126.1, 124.7, 116.2, 110.5, 39.57, 30.7.

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{13}H_{13}NO$) requires *m/z* 200.1070, found *m/z* 200.1070.

(9aa) 3-phenyl-1-(3,4,5-trimethoxyphenyl)propan-1-one



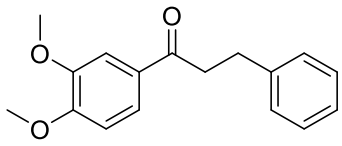
transparent liquid, 16.2 mg, 27%

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.48 (d, *J* = 8.8 Hz, 1H), 7.32 – 7.22 (m, 4H), 7.22 – 7.16 (m, 1H), 6.71 (d, *J* = 8.9 Hz, 1H), 3.92 (s, 3H), 3.90 (s, 3H), 3.86 (s, 3H), 3.32 – 3.25 (m, 2H), 3.06 – 2.99 (m, 2H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 199.9, 157.2, 153.9, 142.0, 141.6, 128.4, 125.9, 125.5, 107.1, 61.4, 60.8, 56.1, 44.6, 30.5.

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{18}H_{20}O$) requires *m/z* 301.1434, found *m/z* 301.1433.

(11aa) 1-(3,4-dimethoxyphenyl)-3-phenylpropan-1-one



light yellow liquid, 6.48 mg, 12%

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.58 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.53 (d, *J* = 1.9 Hz, 1H), 7.33 – 7.24 (m, 5H), 7.24 – 7.18 (m, 1H), 6.87 (d, *J* = 8.4 Hz, 1H), 3.94 (s, 3H), 3.93 (s, 3H), 3.29 – 3.24 (m, 2H), 3.09 – 3.04 (m, 2H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 197.8, 153.2, 149.0, 141.4, 130.1, 128.5, 126.1, 122.6, 110.1, 109.9, 56.0, 40.0, 30.4.

HRMS (ESI+): exact mass calculated for $[M+H]^+$ ($C_{17}H_{18}O_3$) requires *m/z* 271.1329, found *m/z* 271.1331.

Separate characterization of 3aa of table 4

2A ⟶ 3aa

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.42 – 8.37 (m, 1H), 7.55 (s, 1H), 7.30 – 7.23 (m, 7H), 7.20 – 7.15 (m, 1H), 3.71 (s, 3H), 3.15 – 3.05 (m, 4H).

2B ⟶ 3aa

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.41 – 8.37 (m, 1H), 7.56 (s, 1H), 7.31 – 7.23 (m, 7H), 7.21 – 7.15 (m, 1H), 3.72 (s, 3H), 3.15 – 3.05 (m, 4H).

2C ⟶ 3aa

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.41 – 8.36 (m, 1H), 7.55 (s, 1H), 7.31 – 7.23 (m, 7H), 7.22 – 7.15 (m, 1H), 3.71 (s, 3H), 3.15 – 3.04 (m, 4H).

2D ⟶ 3aa

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.41 – 8.36 (m, 1H), 7.56 (s, 1H), 7.31 – 7.22 (m, 7H), 7.20 – 7.15 (m, 1H), 3.72 (s, 3H), 3.15 – 3.05 (m, 4H).

2E ⟶ 3aa

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.41 – 8.36 (m, 1H), 7.55 (s, 1H), 7.30 – 7.22 (m, 7H), 7.20 – 7.15 (m, 1H), 3.71 (s, 3H), 3.15 – 3.05 (m, 4H).

2F ⟶ 3aa

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.42 – 8.37 (m, 1H), 7.65 (s, 1H), 7.34 – 7.25 (m, 7H), 7.22 – 7.16 (m, 1H), 3.80 (s, 3H), 3.23 – 3.08 (m, 4H).

2G ⟶ 3aa

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.41 – 8.36 (m, 1H), 7.54 (s, 1H), 7.30 – 7.23 (m, 7H), 7.20 – 7.15 (m, 1H), 3.70 (s, 3H), 3.15 – 3.05 (m, 4H).

2H ⟶ 3aa

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.42 – 8.37 (m, 1H), 7.64 (s, 1H), 7.33 – 7.25 (m, 7H), 7.22 – 7.16 (m, 1H), 3.79 (s, 3H), 3.19 – 3.07 (m, 4H).

2I ⟶ 3aa

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.42 – 8.37 (m, 1H), 7.64 (s, 1H), 7.34 – 7.25 (m, 7H), 7.22 – 7.17 (m, 1H), 3.80 (s, 3H), 3.19 – 3.07 (m, 4H).

2J ⟶ 3aa

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.42 – 8.37 (m, 1H), 7.62 (s, 1H), 7.33 – 7.25 (m, 7H), 7.22 – 7.16 (m, 1H), 3.78 (s, 3H), 3.18 – 3.07 (m, 4H).

2K ⟶ 3aa

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.41 – 8.37 (m, 1H), 7.61 (s, 1H), 7.32 – 7.24 (m, 7H), 7.21 – 7.16 (m, 1H), 3.77 (s, 3H), 3.18 – 3.07 (m, 4H).

2L ⟶ 3aa

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.42 – 8.37 (m, 1H), 7.57 (s, 1H), 7.31 – 7.23 (m, 7H), 7.20 – 7.15 (m, 1H), 3.73 (s, 3H), 3.16 – 3.05 (m, 4H).

2M⟶ 3aa

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.41 – 8.37 (m, 1H), 7.57 (s, 1H), 7.31 – 7.23 (m, 7H), 7.20 – 7.15 (m, 1H), 3.74 (s, 3H), 3.16 – 3.05 (m, 4H).

2N ⟶ 3aa

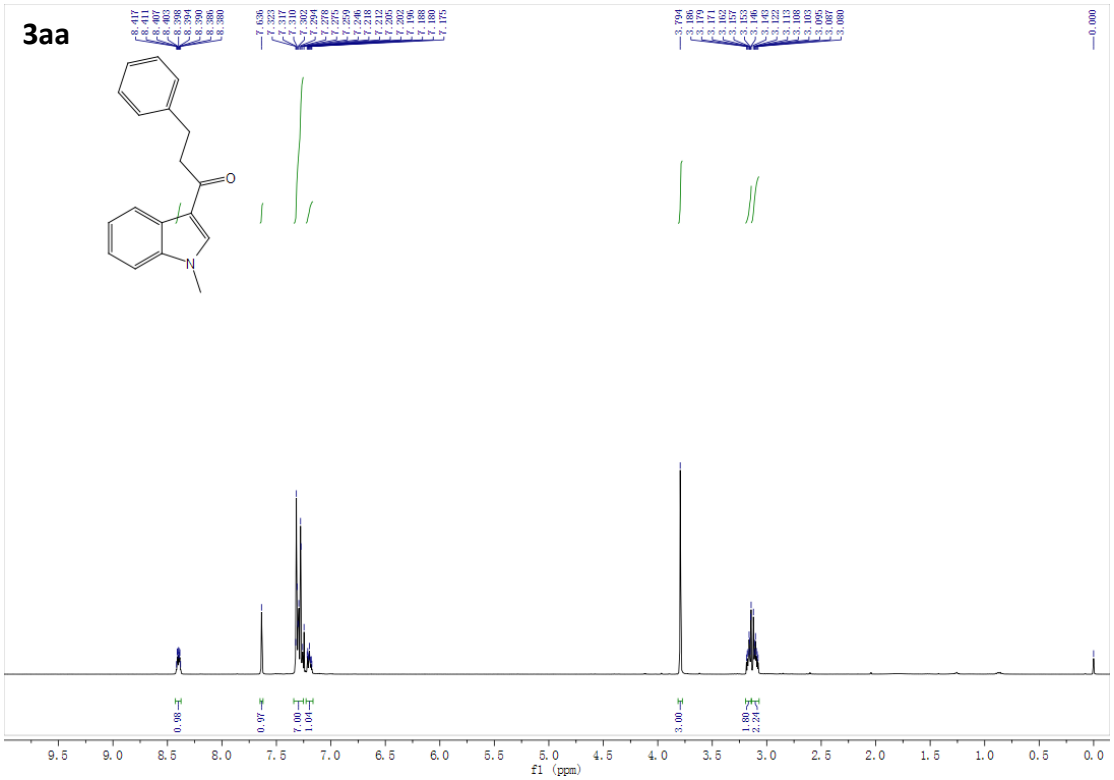
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.42 – 8.37 (m, 1H), 7.63 (s, 1H), 7.34 – 7.26 (m, 7H), 7.22 – 7.17 (m, 1H), 3.79 (s, 3H), 3.20 – 3.08 (m, 4H).

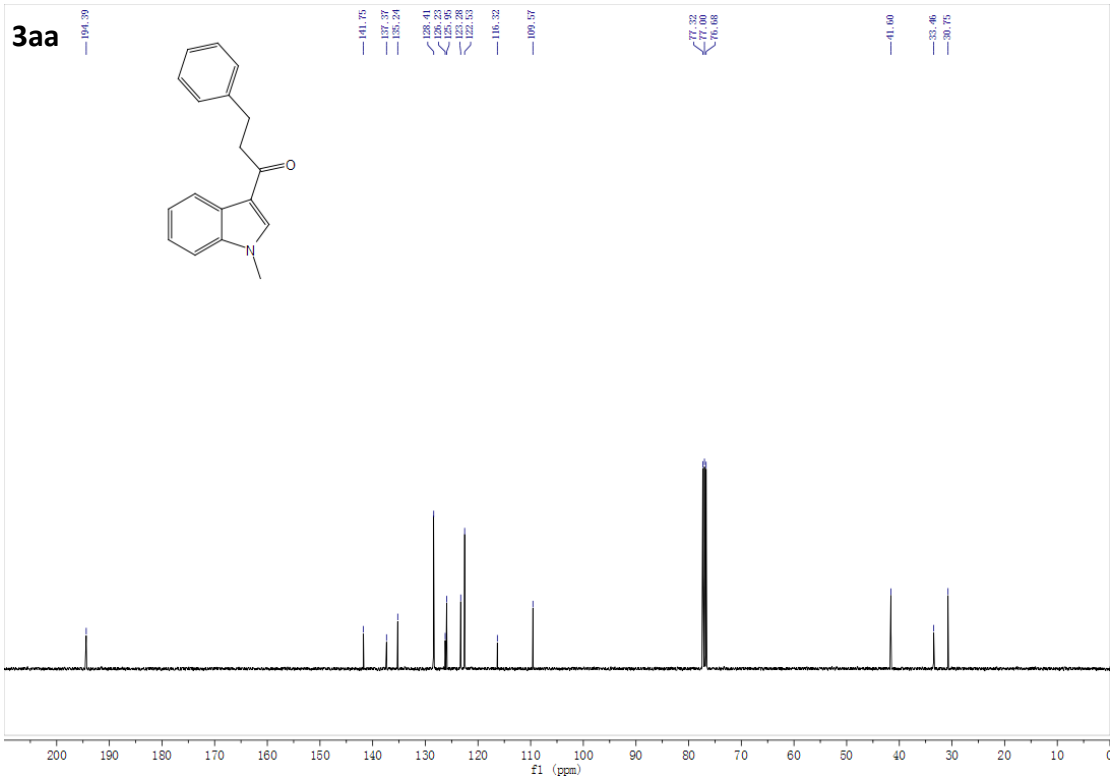
Recycling experiment characterization

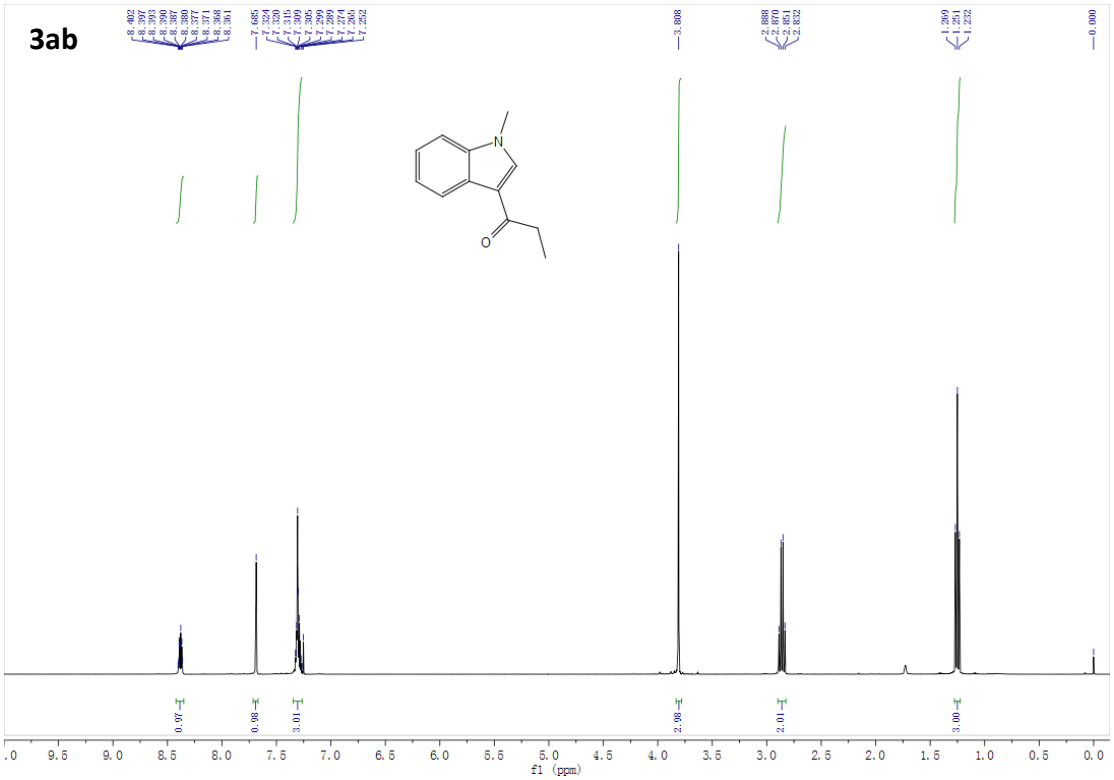
2k-recycled

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.34 – 7.26 (m, 4H), 7.25 – 7.21 (m, 1H), 3.65 (s, 2H), 3.49 (t, *J* = 6.8 Hz, 2H), 3.41 (t, *J* = 6.8 Hz, 2H), 1.95 – 1.87 (m, 2H), 1.87 – 1.79 (m, 2H).

Copies of NMR Spectra



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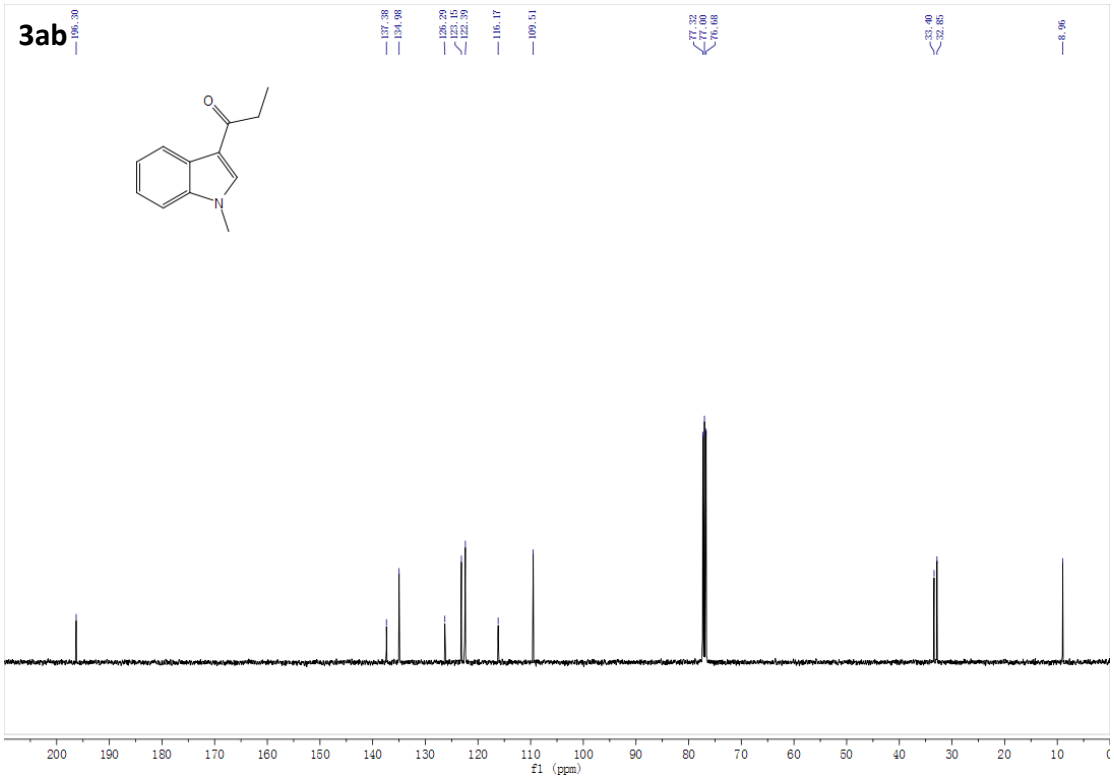
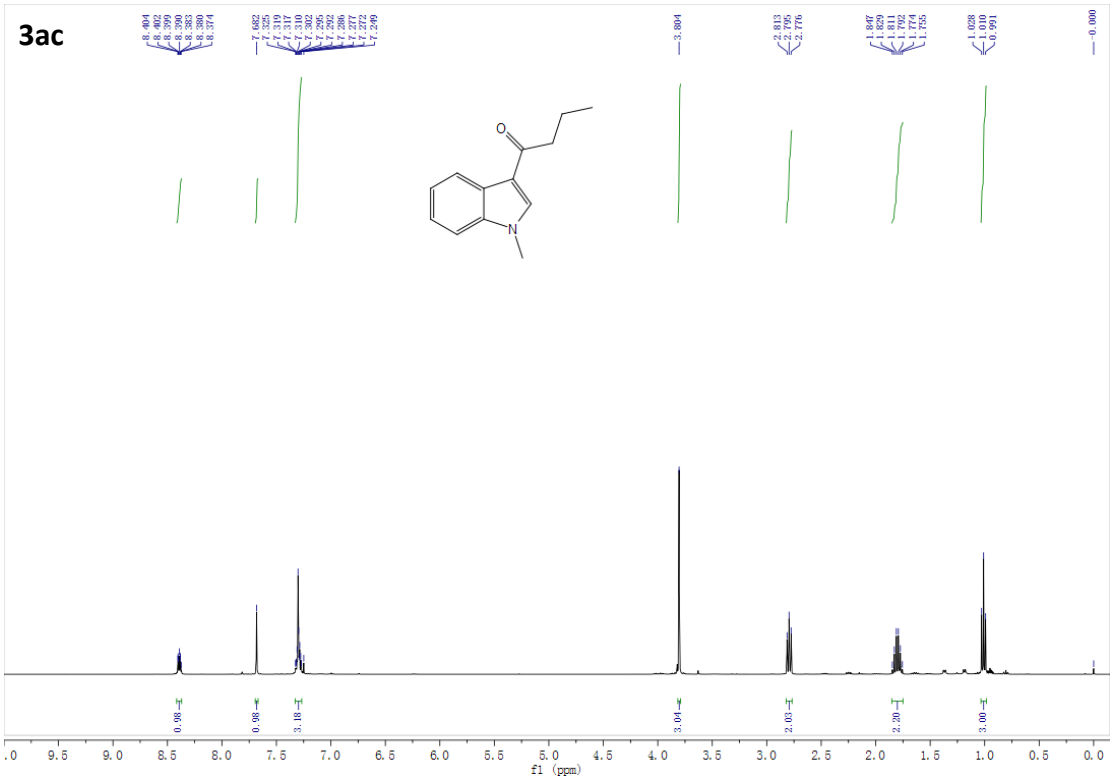
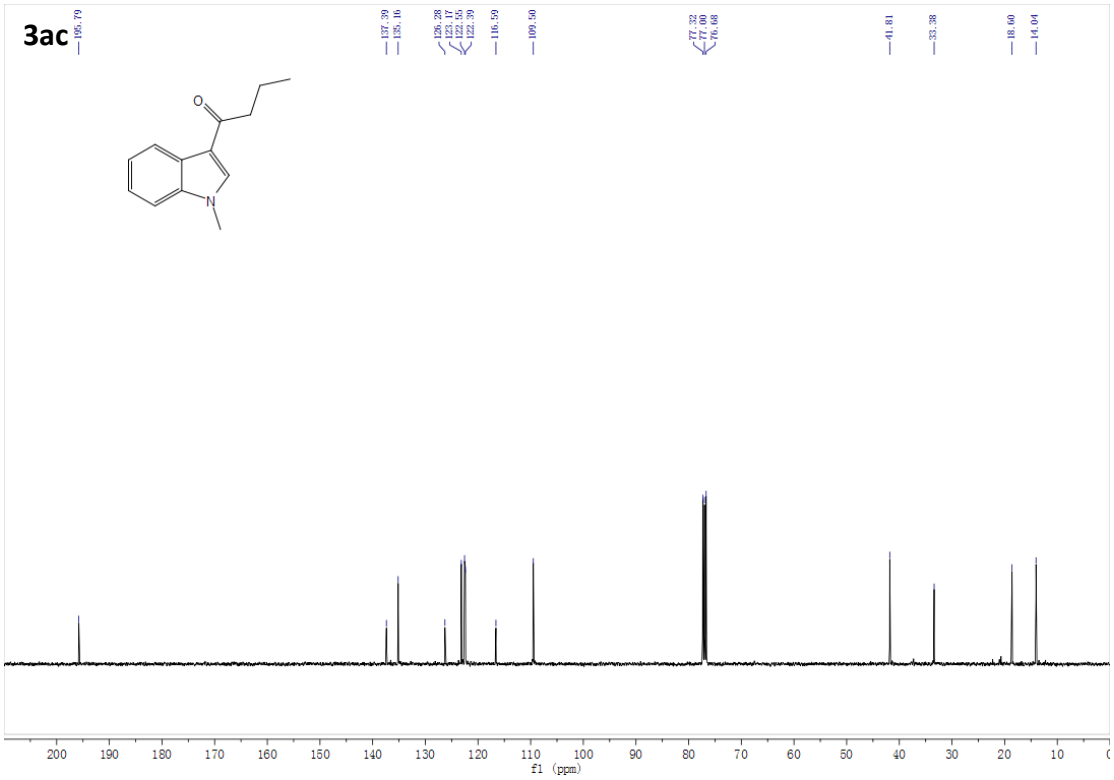
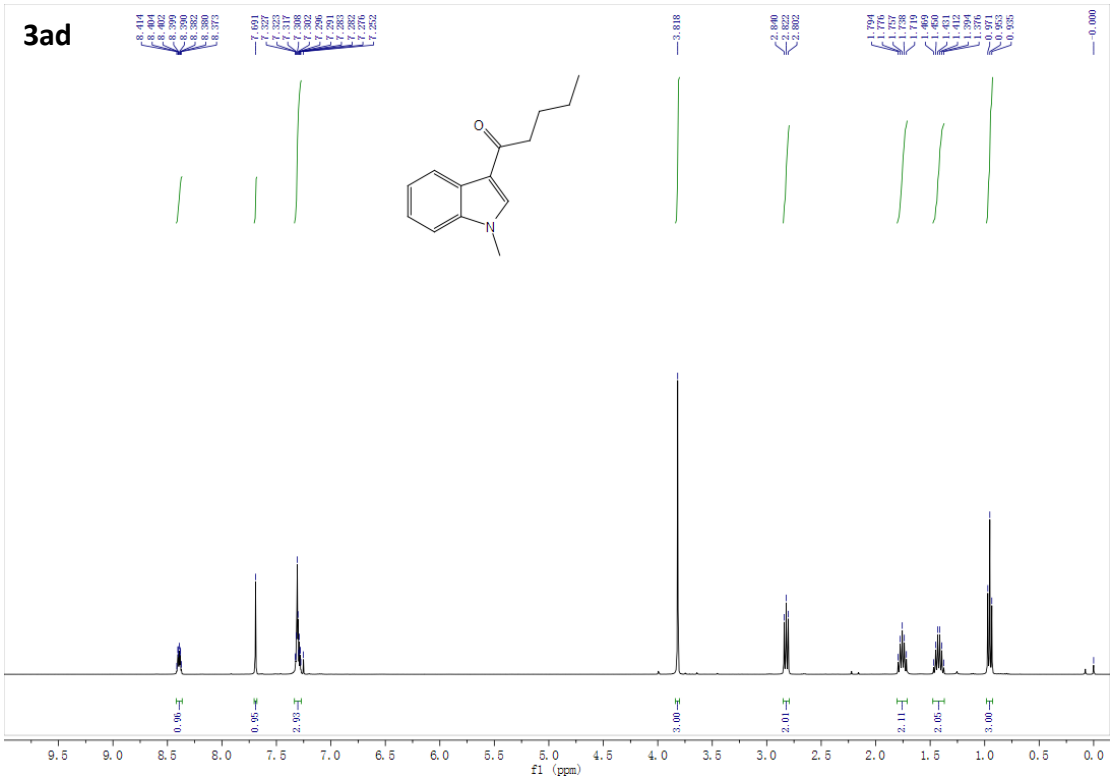
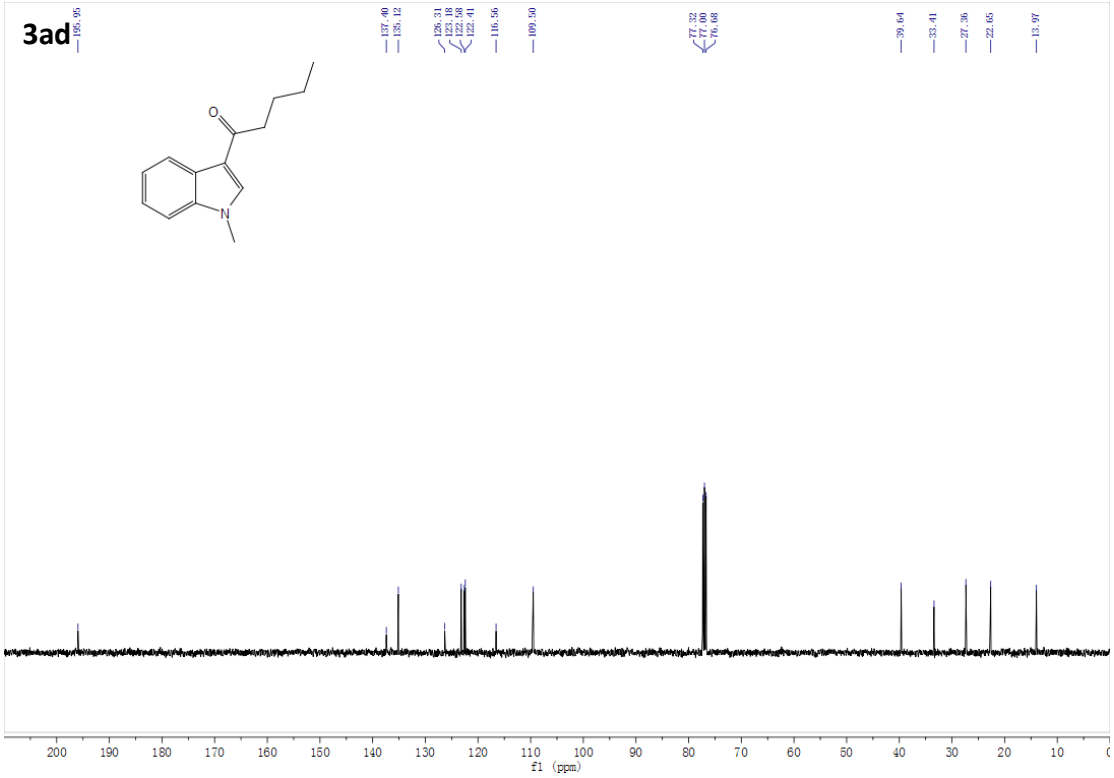
2.870
2.851
2.832
1.260
1.251
1.232
0.000
0.97
0.98
3.01
2.98
2.01
3.00
f1 (ppm)

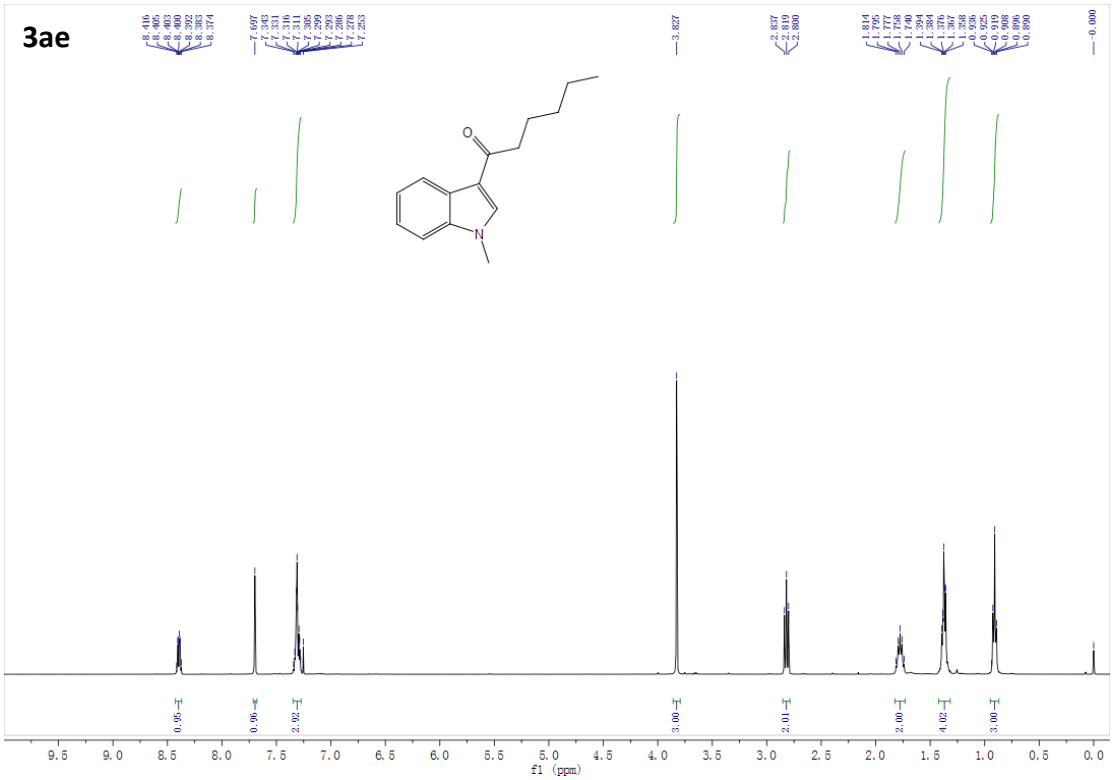

3ab
196.30
137.38
134.98
126.29
123.15
122.39
116.17
109.51
77.32
77.00
76.68
33.40
32.85
8.96
f1 (ppm)

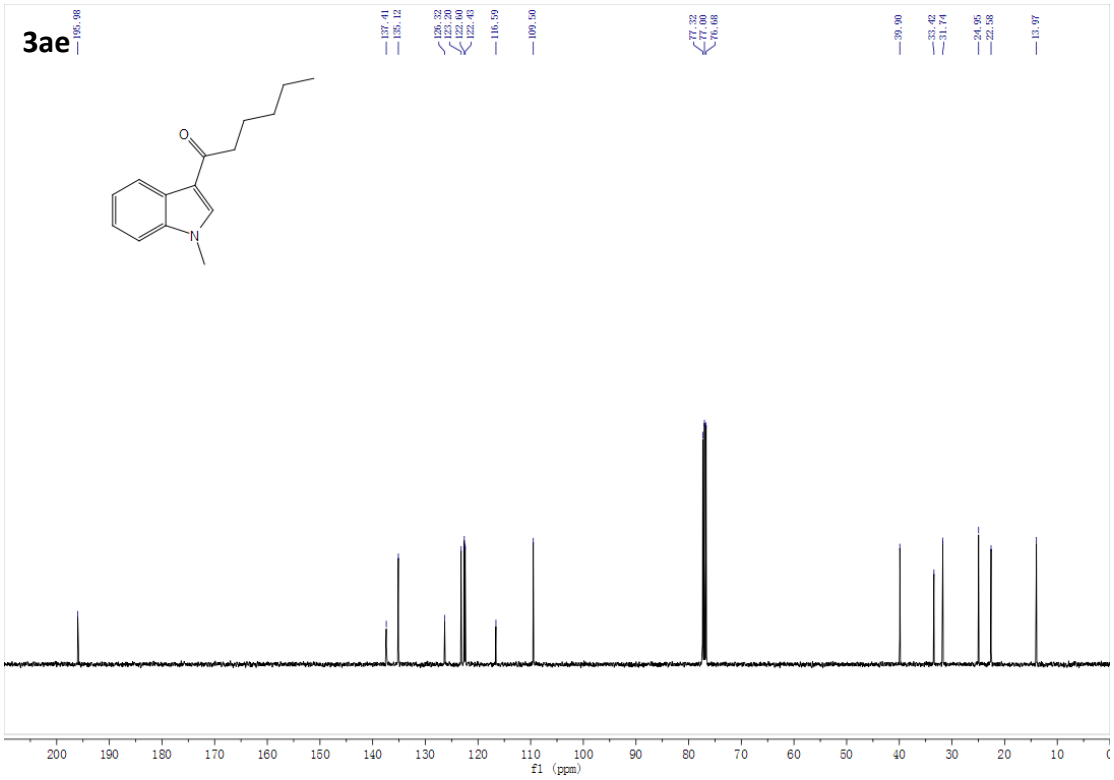

3ac
8.404
8.402
8.392
8.390
8.383
8.380
8.374
7.682
7.325
7.319
7.317
7.310
7.302
7.295
7.292
7.286
7.277
7.272
7.249
3.804
2.813
2.795
2.776
1.847
1.829
1.811
1.792
1.774
1.755
1.028
1.010
0.991
0.000
O
N
0.98
0.98
3.18
3.04
2.03
2.20
3.00
f1 (ppm)


3ac
195.79
137.39
135.16
126.28
123.17
122.55
122.39
116.59
109.50
77.32
77.00
76.68
41.81
33.38
18.60
14.04
O
N
f1 (ppm)

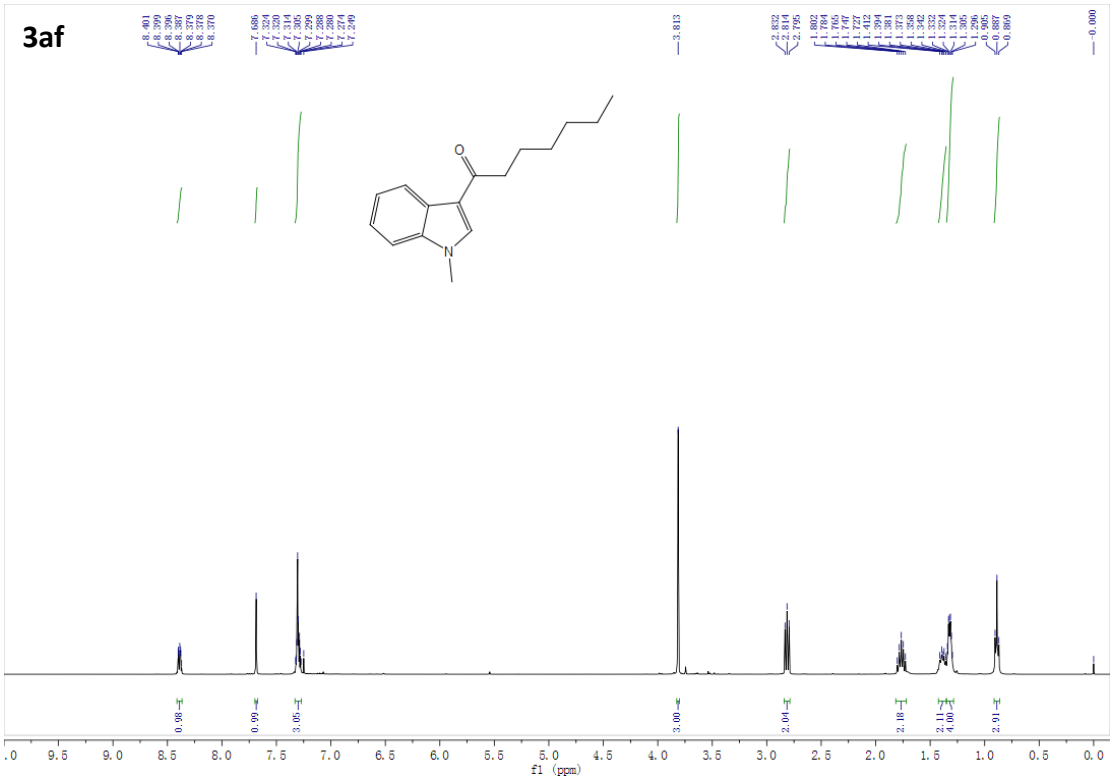

3ad
8.414
8.404
8.402
8.399
8.390
8.382
8.380
8.373
7.691
7.327
7.323
7.317
7.308
7.302
7.296
7.291
7.283
7.282
7.276
7.252
3.818
2.840
2.822
2.802
1.794
1.776
1.757
1.738
1.719
1.702
1.469
1.431
1.412
1.394
1.376
0.971
0.953
0.935
0.000
0.96
0.95
2.93
3.00
2.01
2.11
2.05
3.00
9.5
9.0
8.5
8.0
7.5
7.0
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
0.0
f1 (ppm)


3ad
195.95
137.40
135.12
126.31
123.18
122.58
122.41
116.56
109.50
77.32
77.00
76.68
39.64
33.41
27.36
22.65
13.97
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

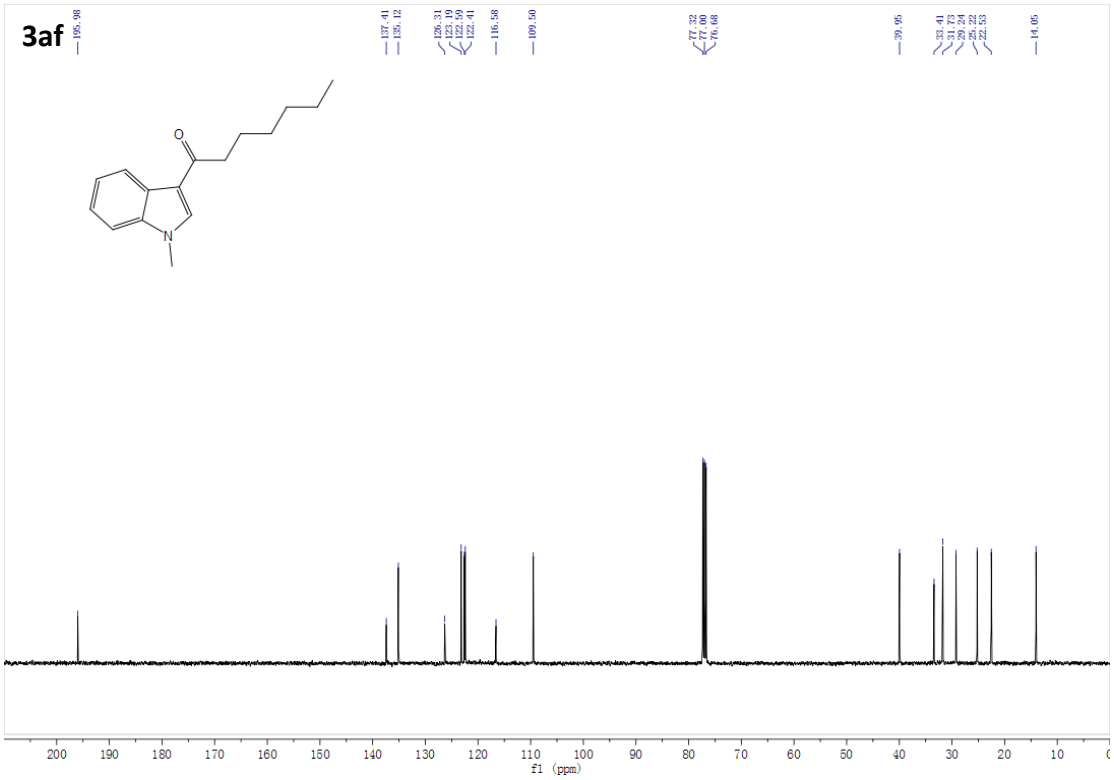

3ae
8.416
8.405
8.403
8.400
8.392
8.393
8.374
7.697
7.343
7.331
7.316
7.311
7.305
7.299
7.293
7.286
7.278
7.253
3.827
2.837
2.819
2.800
1.814
1.795
1.777
1.758
1.740
1.394
1.384
1.376
1.367
1.358
0.936
0.925
0.919
0.908
0.896
0.890
0.000
O
N
0.95
0.96
2.92
3.00
2.01
2.00
4.02
3.00
9.5 9.0 8.5 8.0 7.5 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 0.0
f1 (ppm)

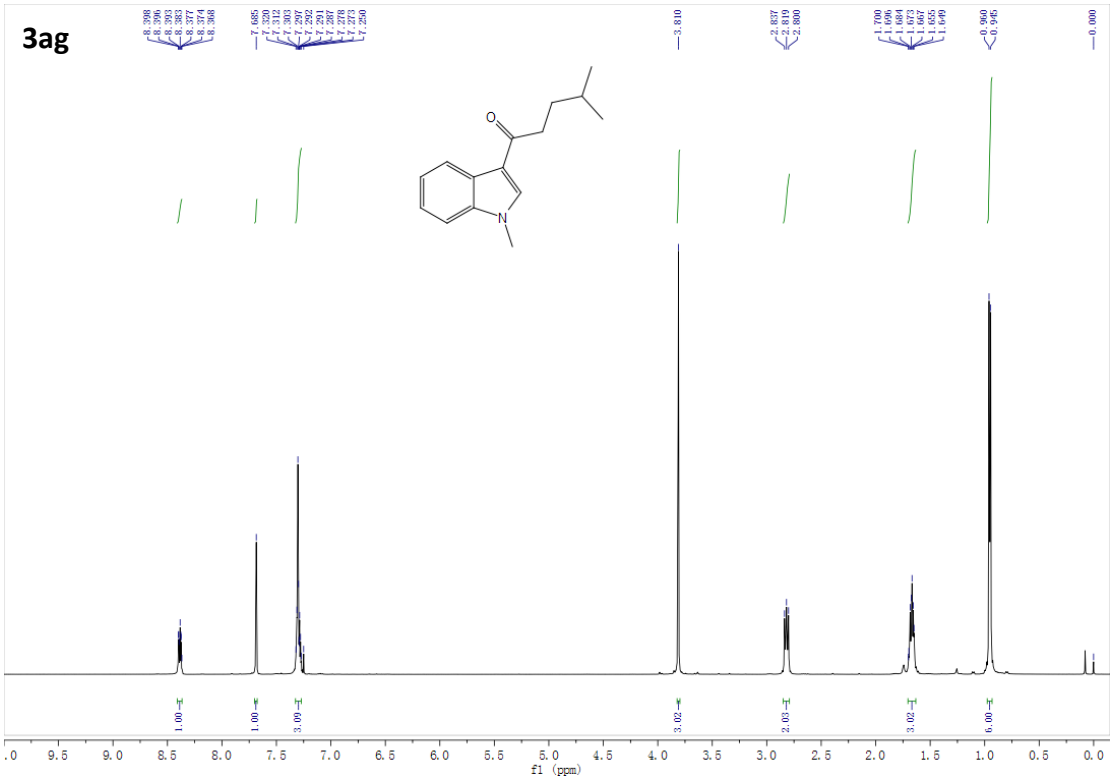

3ae
195.98
137.41
135.12
126.32
125.30
122.60
122.43
116.59
109.50
77.32
77.00
76.68
39.90
33.42
31.74
24.95
22.58
13.97
O
N
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

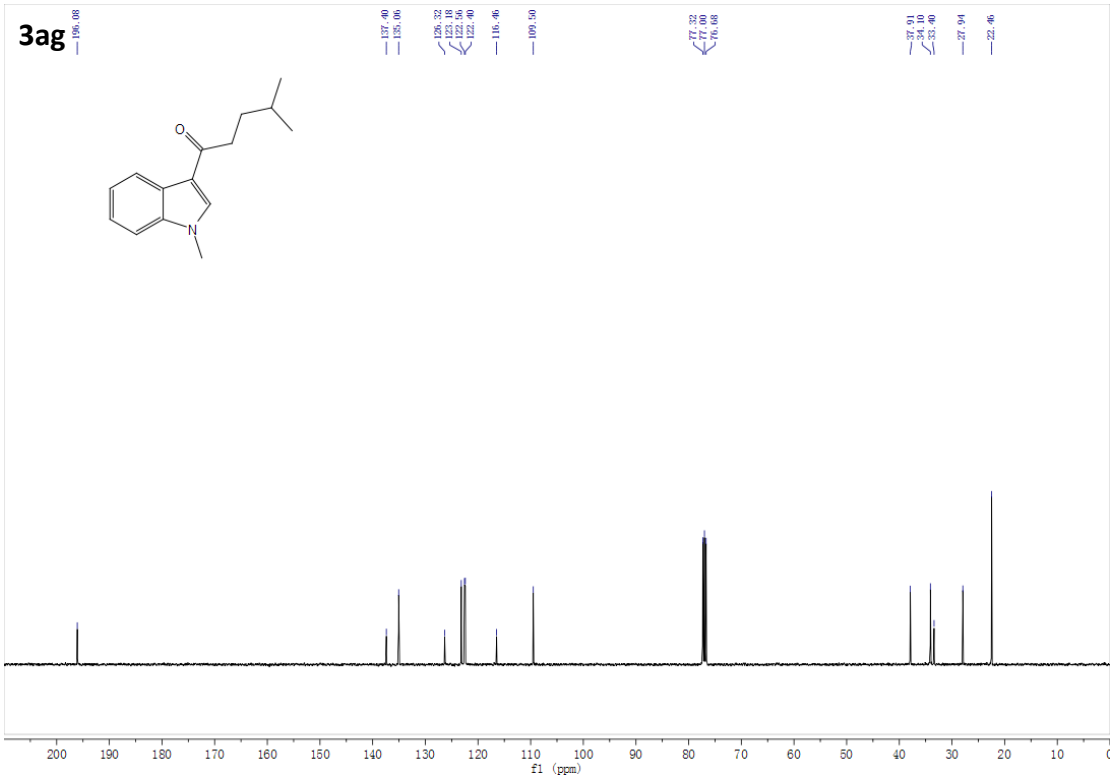
3af


8.401
8.399
8.396
8.387
8.379
8.378
8.370
7.686
7.354
7.320
7.314
7.305
7.299
7.288
7.280
7.274
7.249
3.813
2.832
2.814
2.795
1.802
1.784
1.765
1.747
1.727
1.412
1.394
1.381
1.373
1.358
1.342
1.332
1.324
1.314
1.305
1.296
0.905
0.887
0.869
0.000
O
N
0.98
0.99
3.05
3.00
2.04
2.18
2.11
4.00
2.91
f1 (ppm)

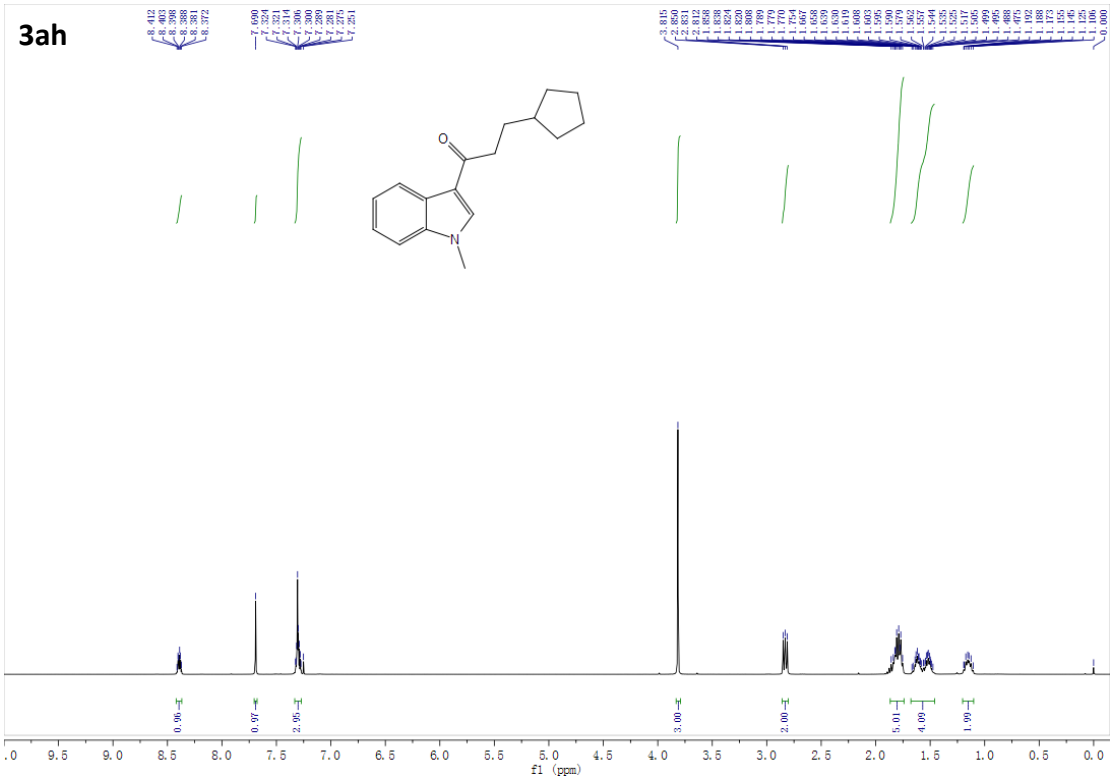
3af


195.98
137.41
135.12
125.31
123.19
122.59
122.41
116.58
109.50
77.32
77.00
76.68
39.95
33.41
31.73
29.24
25.22
22.53
14.05
O
N
f1 (ppm)

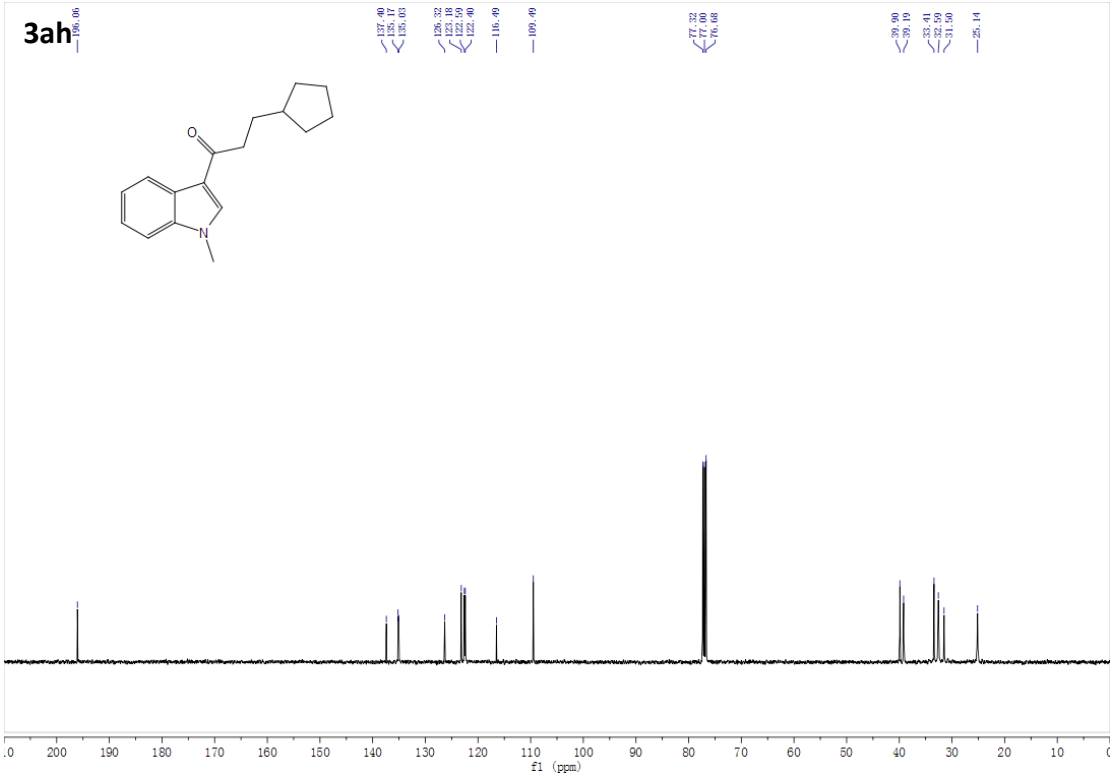

3ag
8.398
8.396
8.393
8.383
8.377
8.374
8.368
7.685
7.330
7.312
7.303
7.297
7.292
7.291
7.287
7.278
7.277
7.273
7.259
3.810
2.837
2.819
2.800
1.700
1.696
1.694
1.683
1.667
1.655
1.649
0.960
0.945
0.000
O
N
1.00
1.00
3.09
3.02
2.03
3.02
6.00
f1 (ppm)

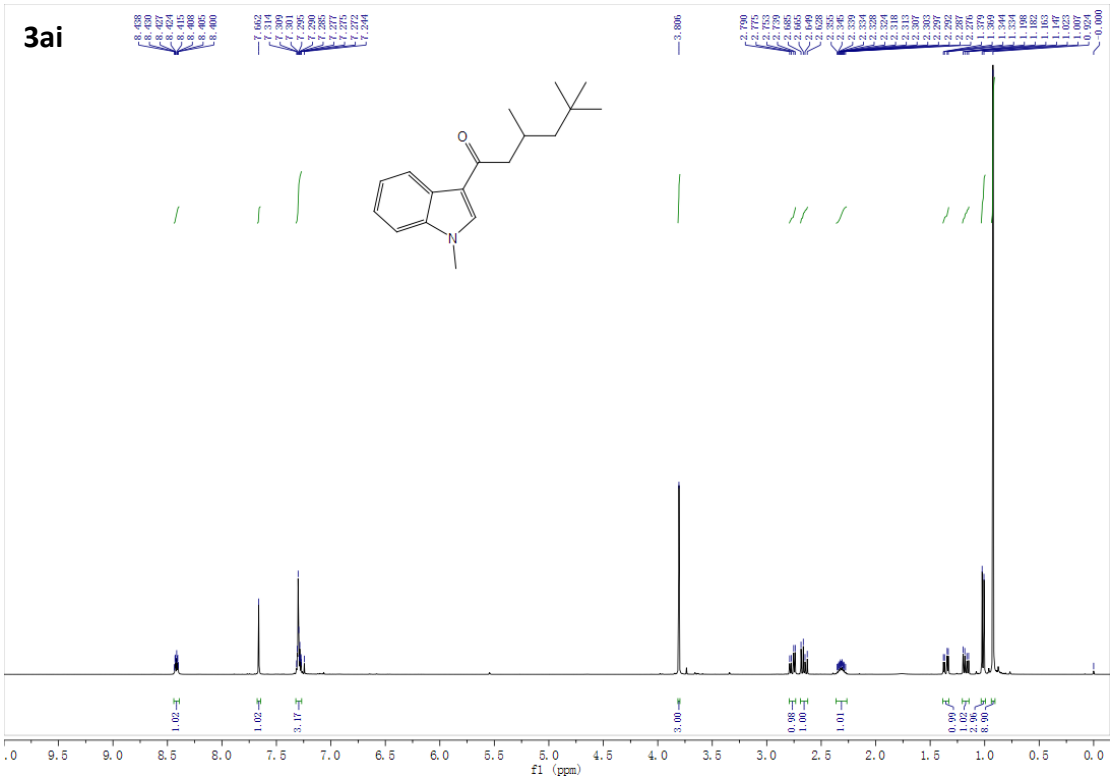

3ag
196.08
137.40
135.06
125.32
123.18
122.56
122.40
116.46
109.50
77.32
77.00
76.68
37.91
34.10
33.40
27.94
22.46
O
N
f1 (ppm)

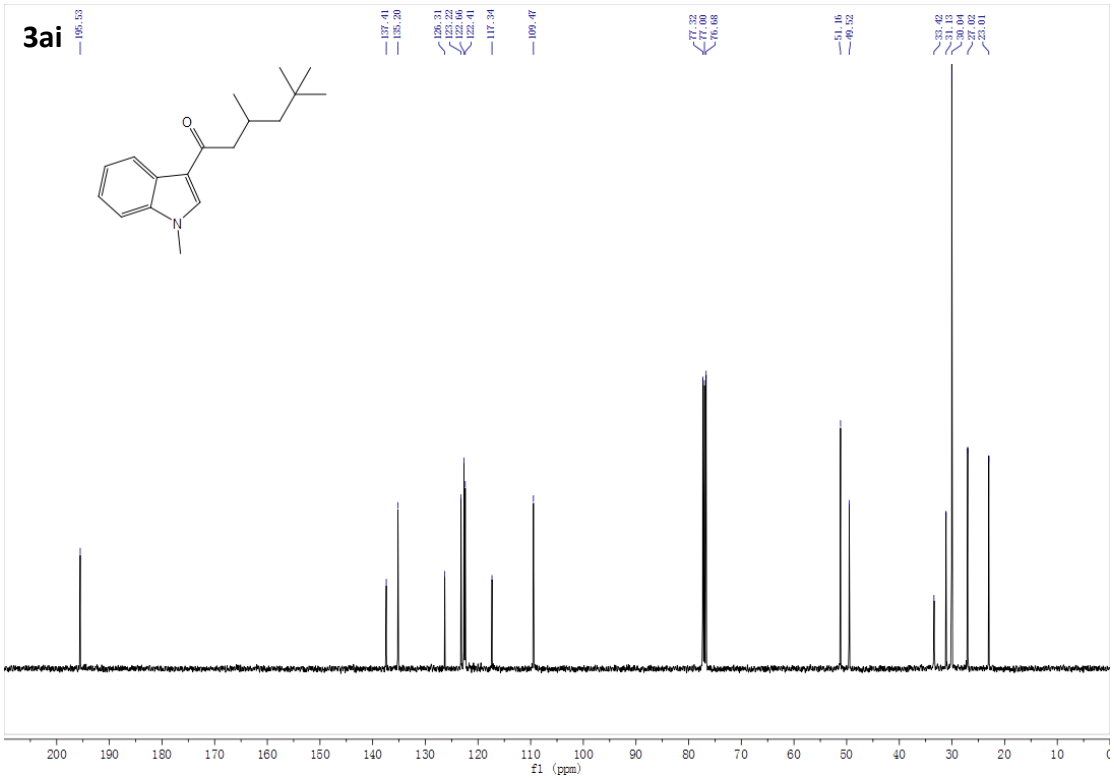
3ah

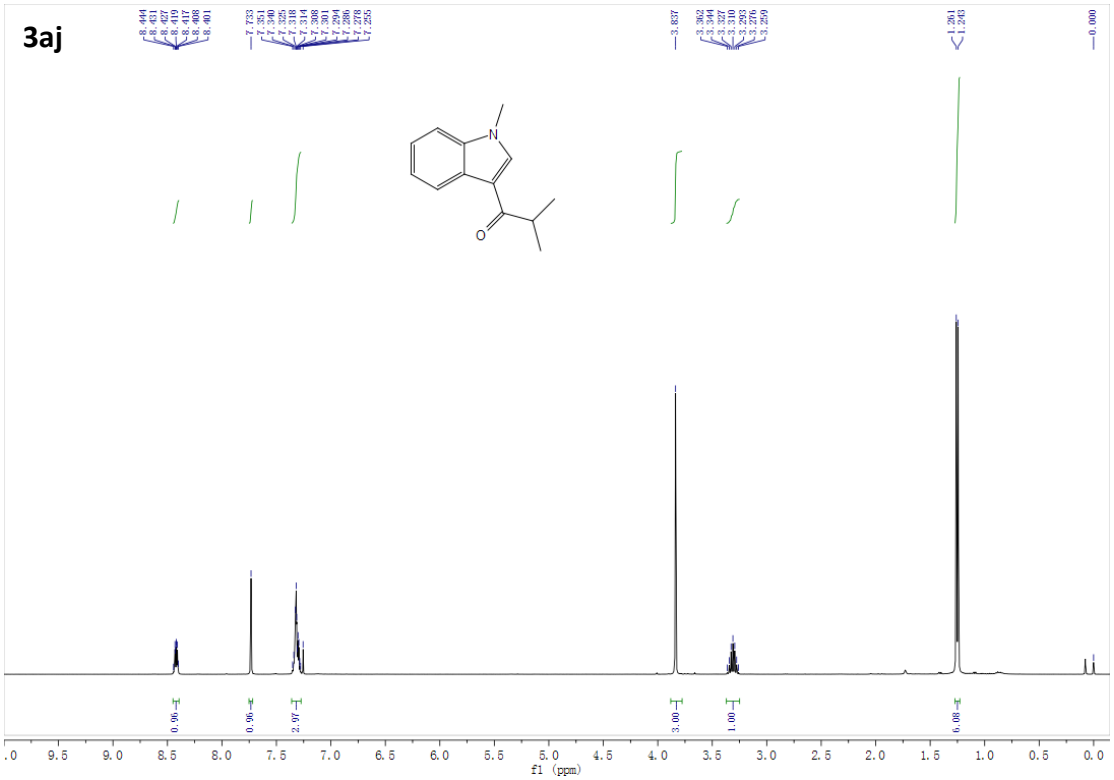


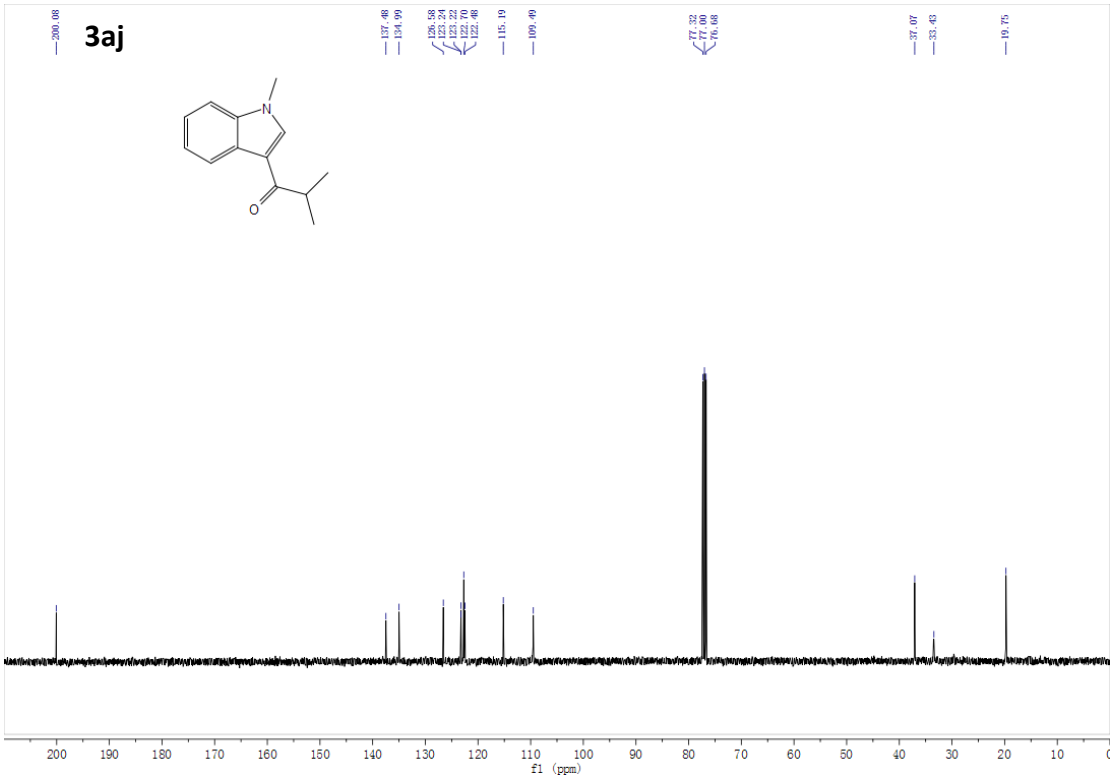
3ah

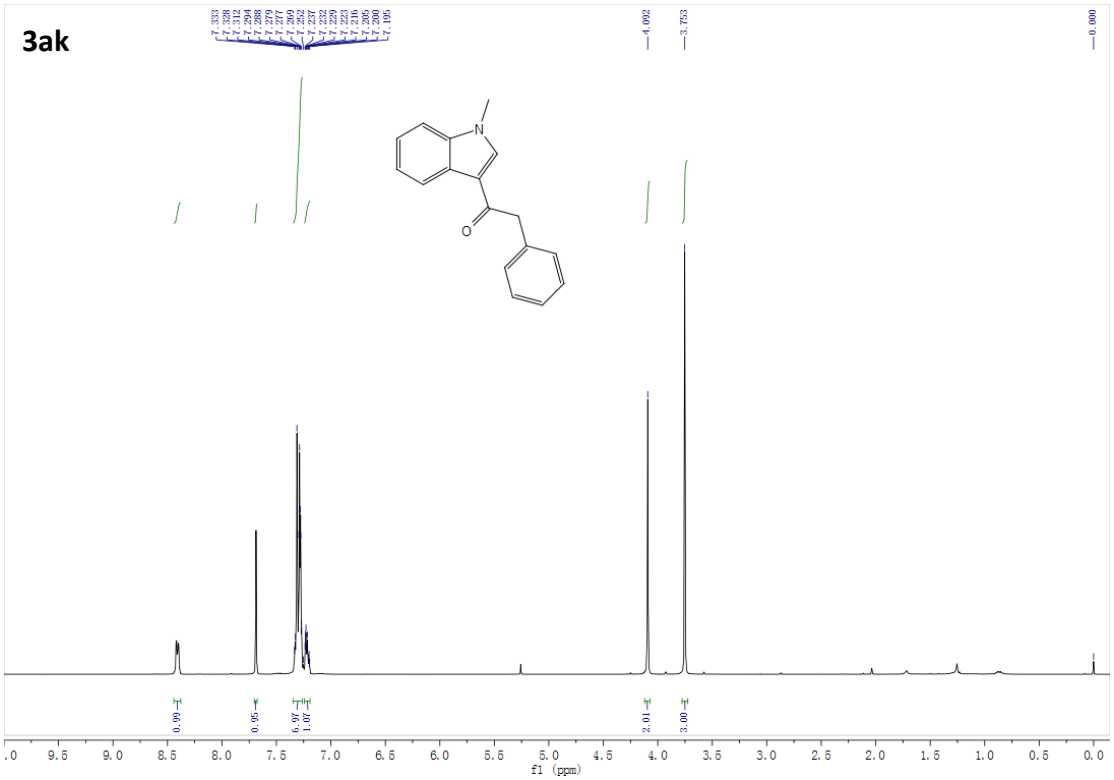


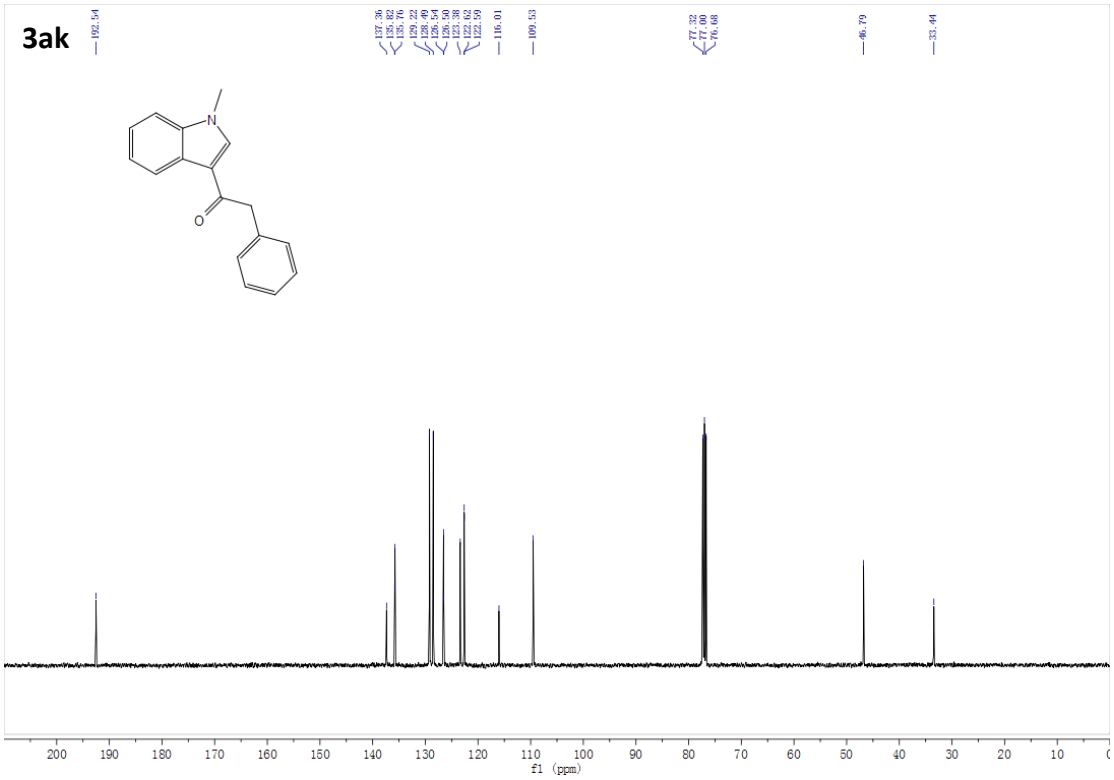

3ai
f1 (ppm)


3ai
f1 (ppm)

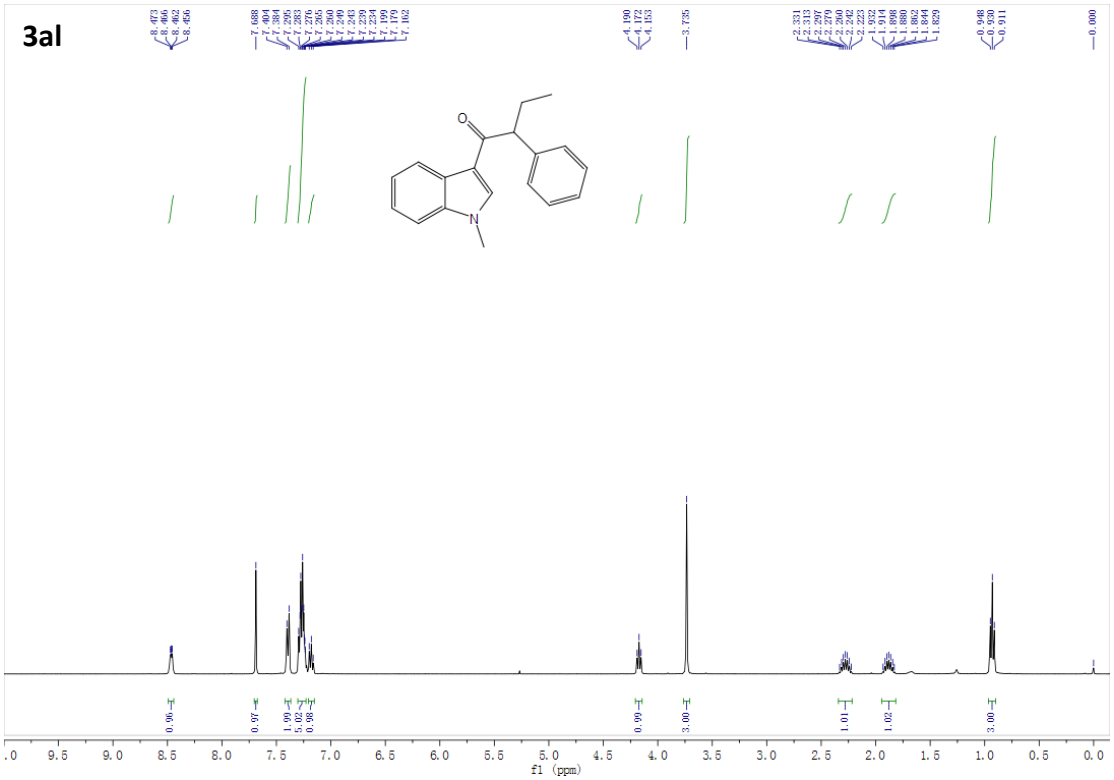

3aj
8.444
8.431
8.427
8.419
8.417
8.408
8.401
7.733
7.351
7.340
7.335
7.318
7.314
7.308
7.301
7.294
7.286
7.278
7.255
3.837
3.362
3.344
3.327
3.310
3.293
3.276
3.259
1.261
1.243
0.000
0.96
0.96
2.97
3.00
1.00
6.08
f1 (ppm)


3aj
200.08
137.48
134.99
126.58
123.24
123.22
122.70
122.48
115.19
109.49
77.32
77.00
76.68
37.07
33.43
19.75
f1 (ppm)

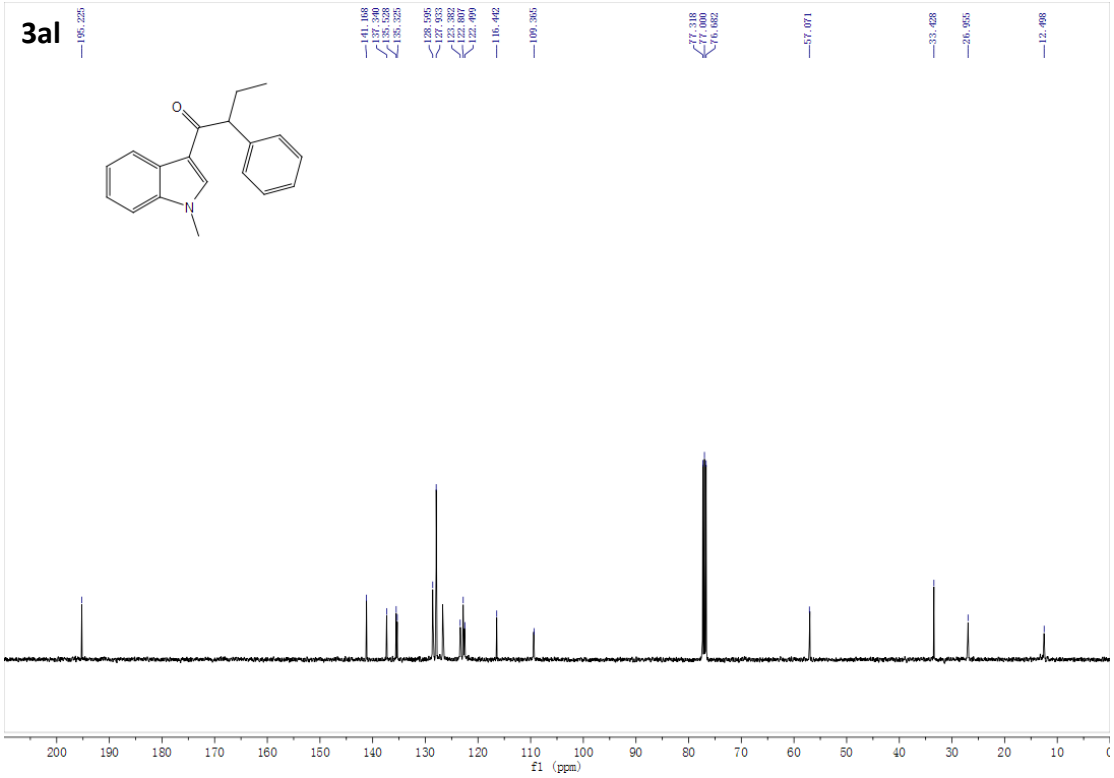

3ak
7.333
7.313
7.294
7.288
7.277
7.260
7.252
7.237
7.232
7.223
7.216
7.205
7.195
4.092
3.753
0.000
0.99
0.95
6.97
1.07
2.01
3.00
f1 (ppm)

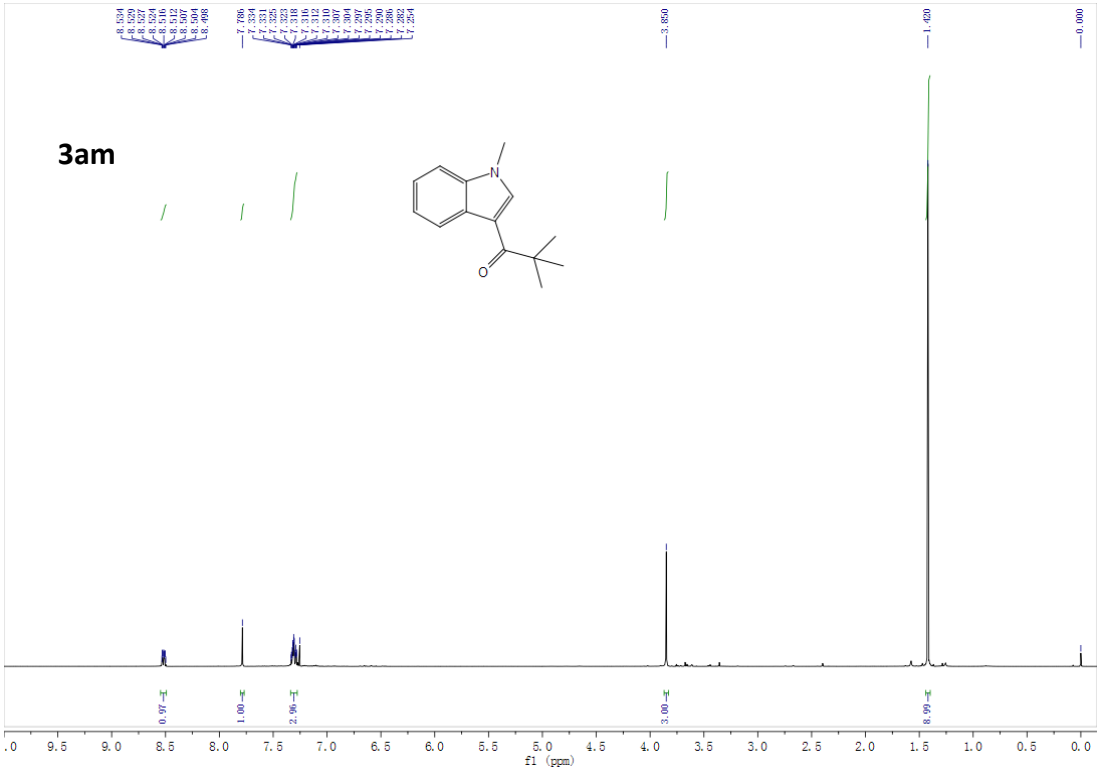

3ak
192.54
137.36
135.82
135.76
129.22
128.49
126.54
126.50
123.38
122.62
122.19
116.01
109.53
77.32
77.00
76.68
46.79
33.44
f1 (ppm)

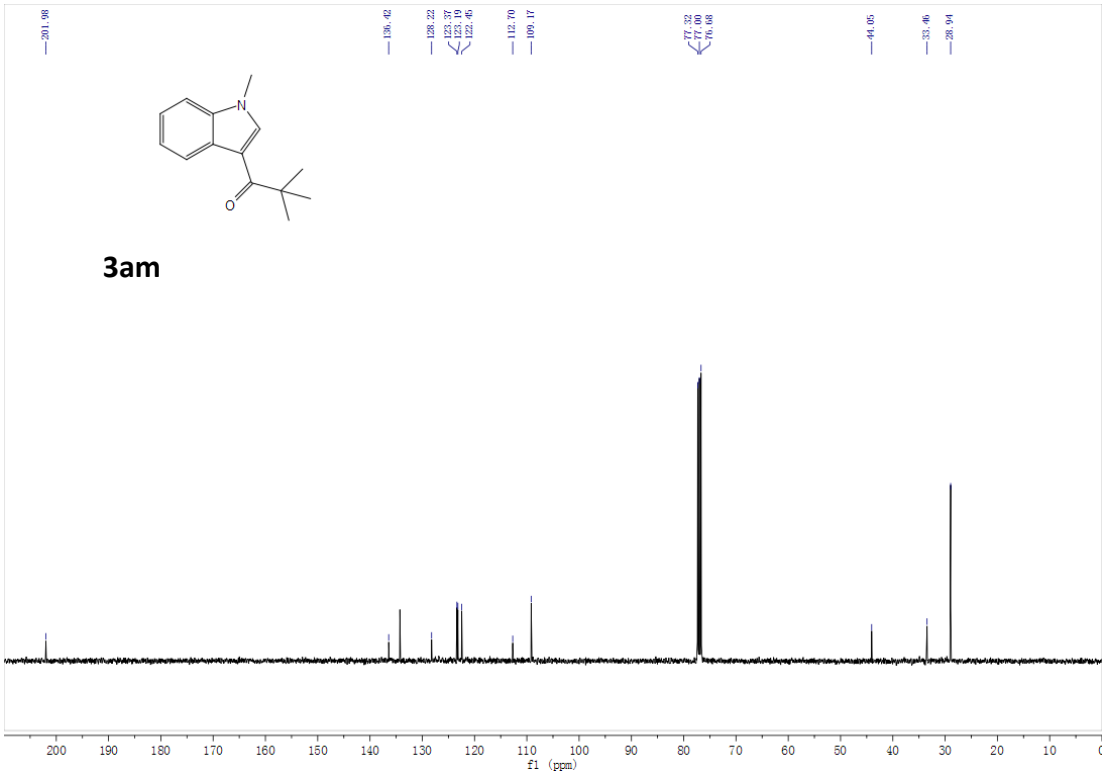
3al

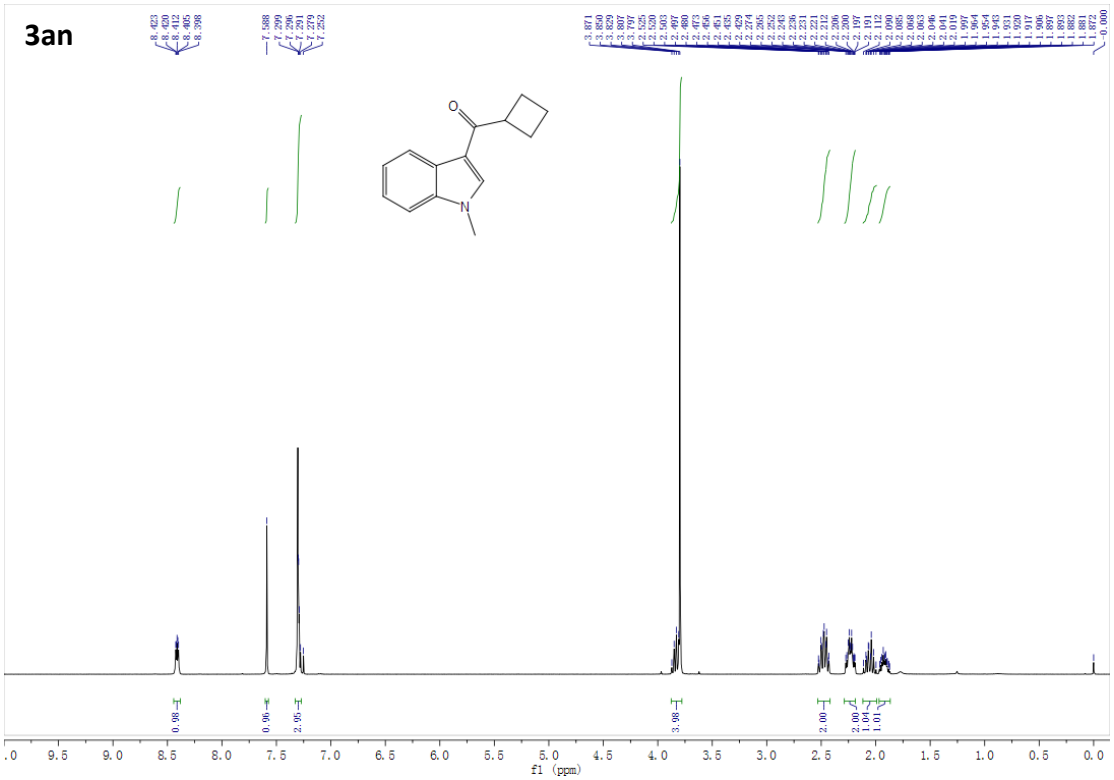

8.473
8.466
8.462
8.456
7.688
7.404
7.394
7.295
7.283
7.276
7.265
7.260
7.249
7.245
7.239
7.234
7.199
7.179
7.162
4.190
4.172
4.153
3.735
2.331
2.313
2.297
2.279
2.260
2.242
2.223
1.932
1.914
1.898
1.880
1.862
1.844
1.829
0.948
0.930
0.911
0.000
O
N
0.96
0.97
1.99
5.02
0.98
0.99
3.00
1.01
1.02
3.00
f1 (ppm)

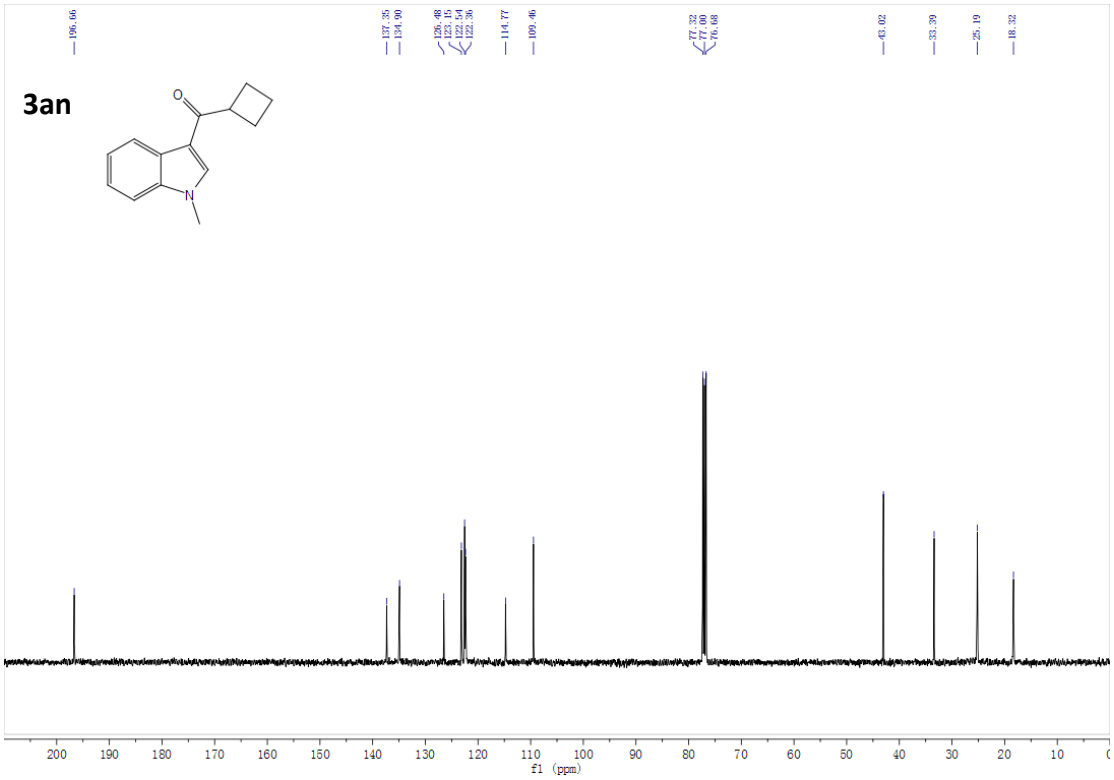
3al

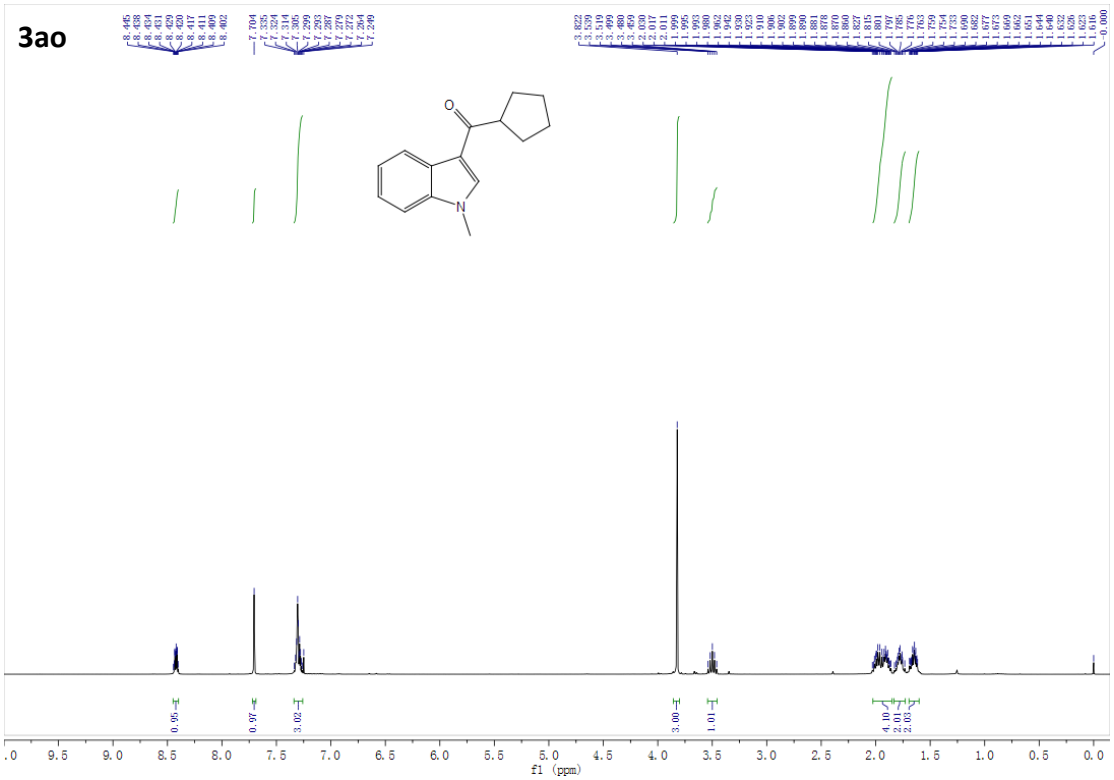

195.225
141.168
137.340
135.528
135.325
128.595
127.933
125.382
123.807
122.499
116.442
109.365
77.318
77.000
76.682
57.071
33.428
26.955
12.498
O
N
f1 (ppm)

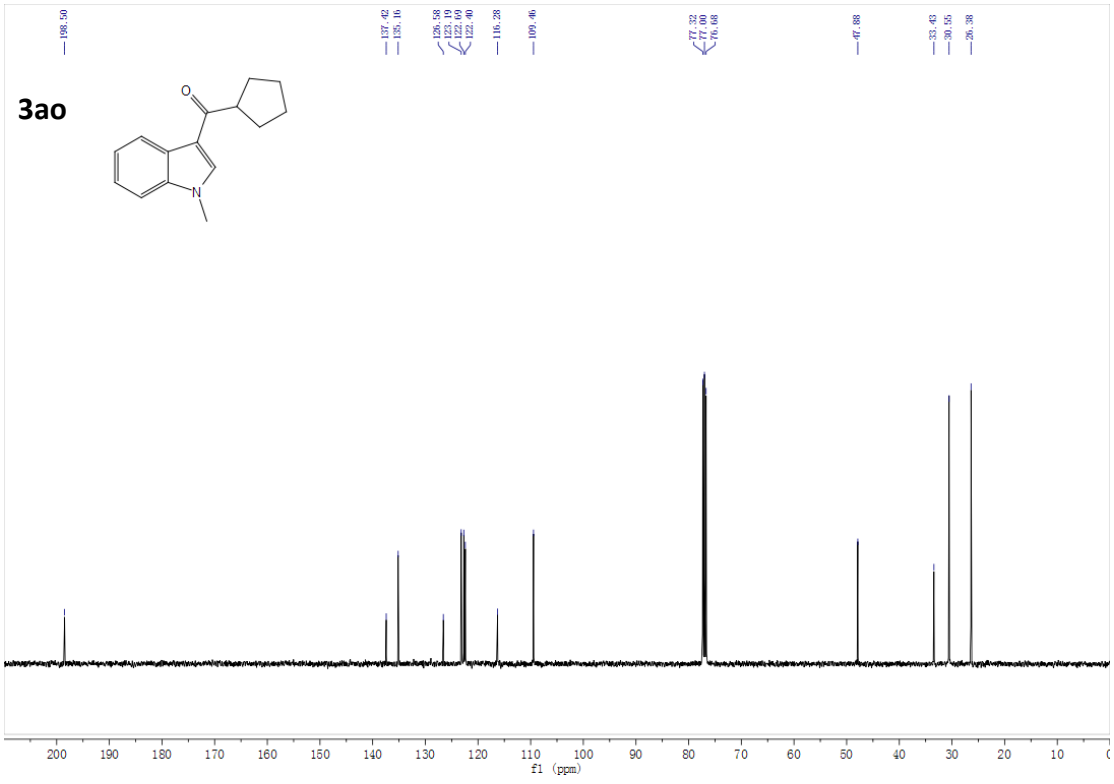

3am
8.534
8.529
8.527
8.524
8.516
8.512
8.507
8.504
8.498
7.706
7.334
7.331
7.325
7.323
7.318
7.316
7.312
7.310
7.307
7.304
7.297
7.295
7.290
7.286
7.282
7.254
3.850
1.420
0.000
0.97
1.00
2.96
3.00
8.99
f1 (ppm)

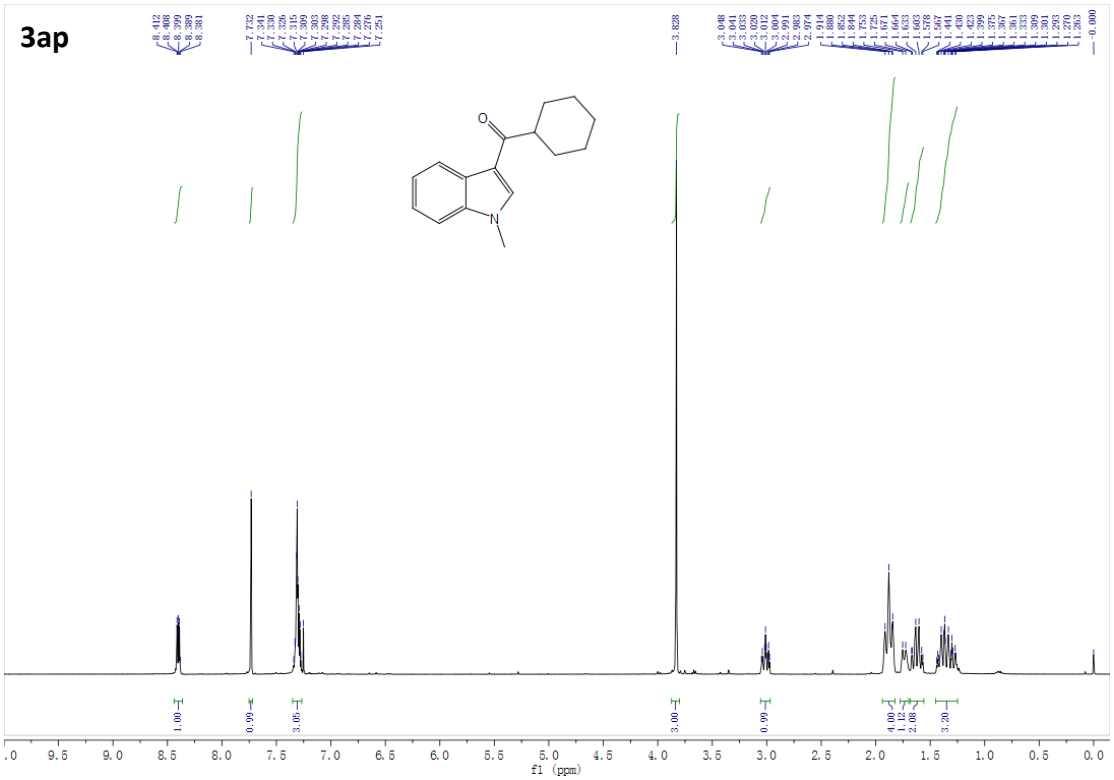

3am
201.98
136.42
128.22
123.37
123.19
122.45
112.70
109.17
77.32
77.00
76.68
44.65
33.46
28.94
f1 (ppm)

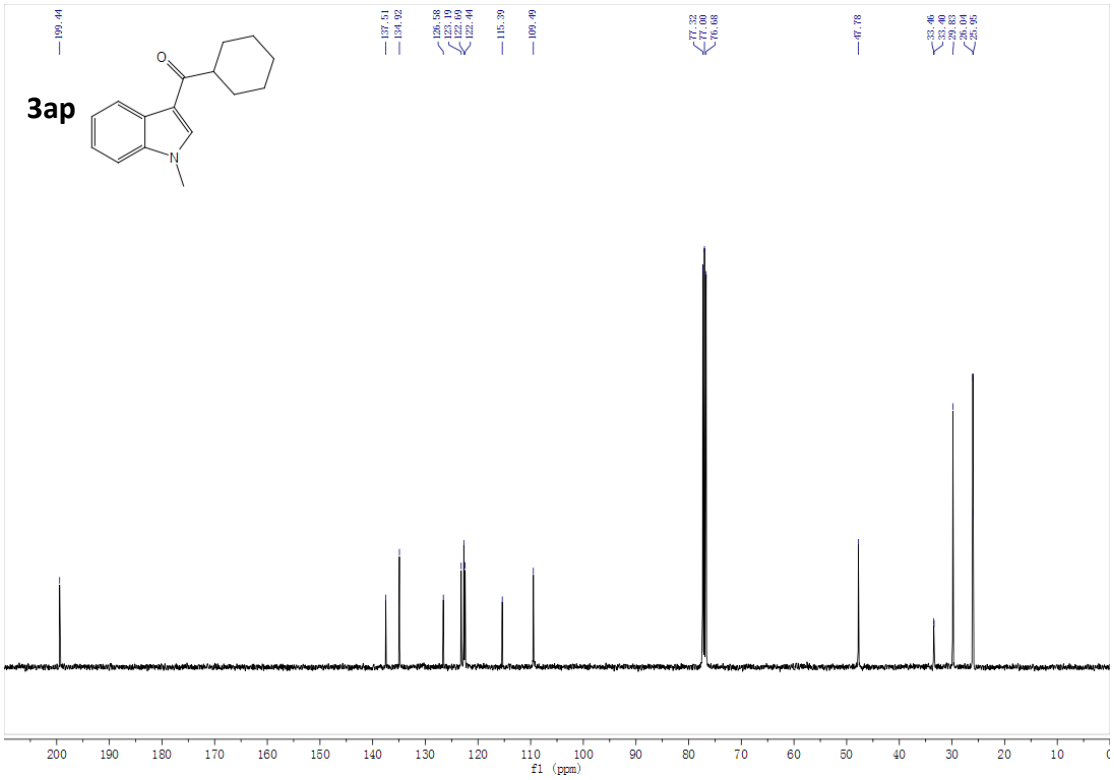

3an
8.423
8.420
8.412
8.405
8.398
7.588
7.299
7.296
7.291
7.279
7.272
7.222
3.871
3.850
3.829
3.807
3.797
2.525
2.520
2.503
2.497
2.489
2.473
2.456
2.451
2.435
2.429
2.274
2.265
2.252
2.243
2.236
2.231
2.221
2.212
2.206
2.200
2.197
2.191
2.112
2.090
2.085
2.068
2.063
2.046
2.041
2.019
1.997
1.964
1.954
1.945
1.931
1.920
1.917
1.906
1.897
1.893
1.882
1.881
1.877
-0.000
O
N
0.98
0.96
2.95
3.98
2.00
2.00
1.04
1.01
f1 (ppm)

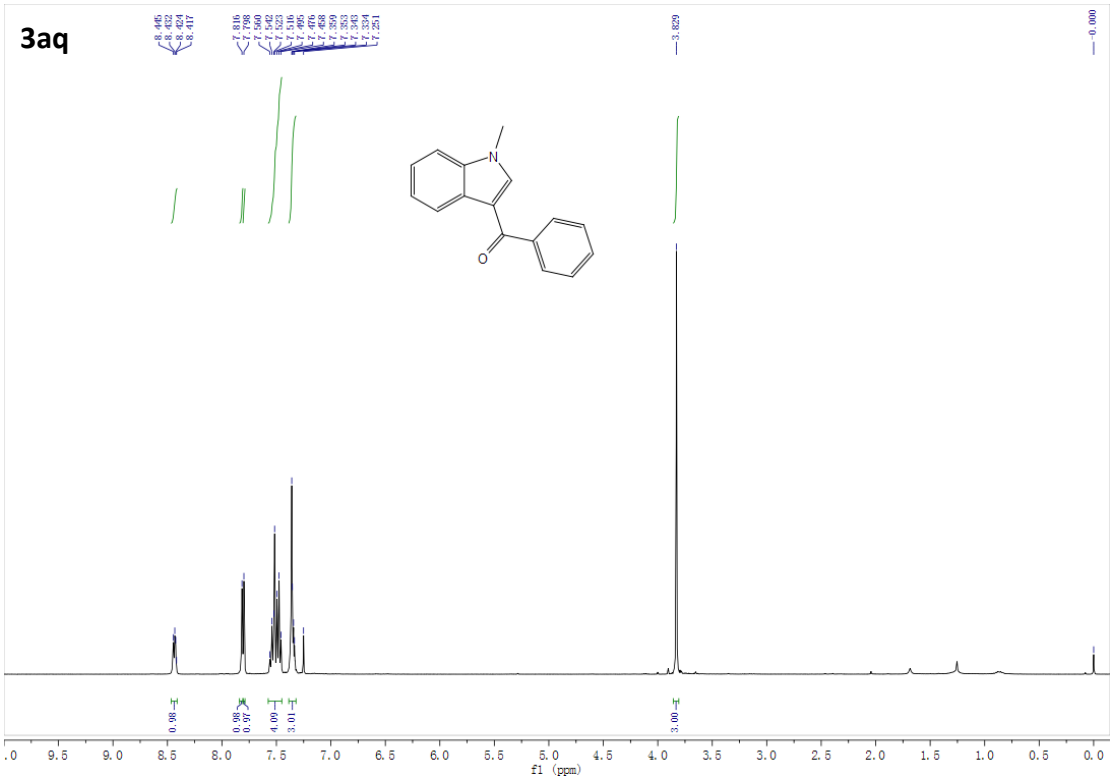

3an
196.66
137.35
134.90
125.48
123.15
122.54
122.36
114.77
109.46
77.32
77.00
76.68
63.02
33.39
25.19
18.32
O
N
f1 (ppm)

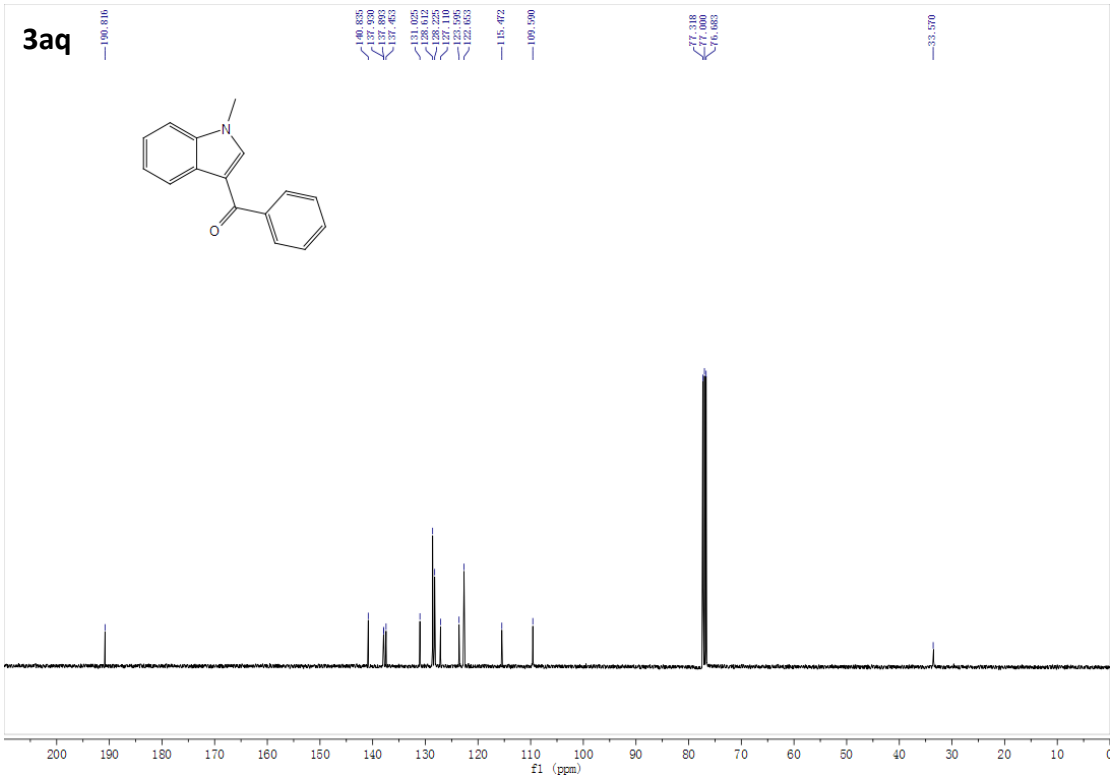

3ao
f1 (ppm)

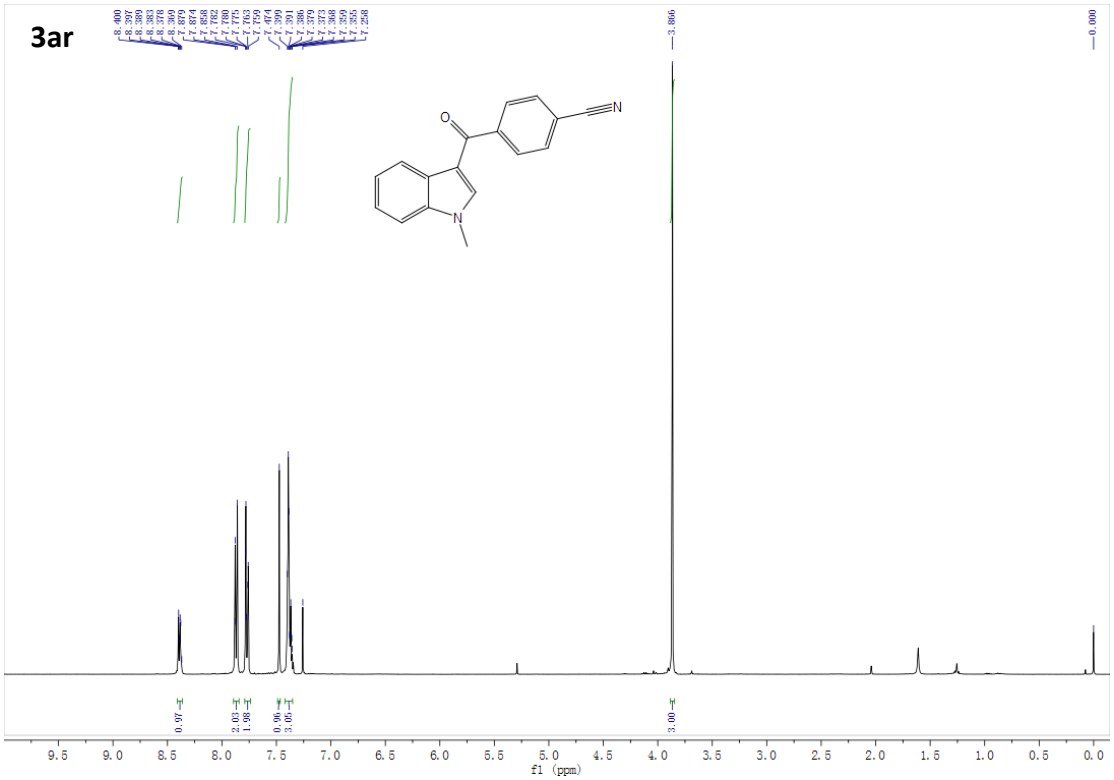

3ao
f1 (ppm)

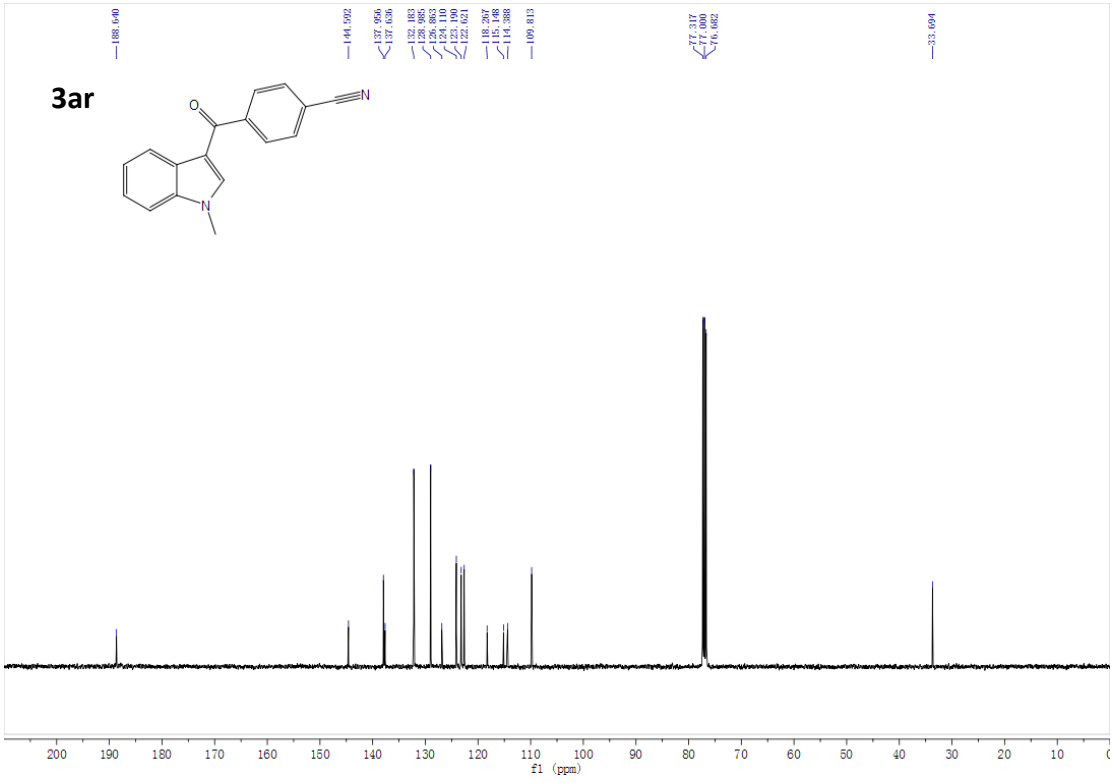

3ap
f1 (ppm)

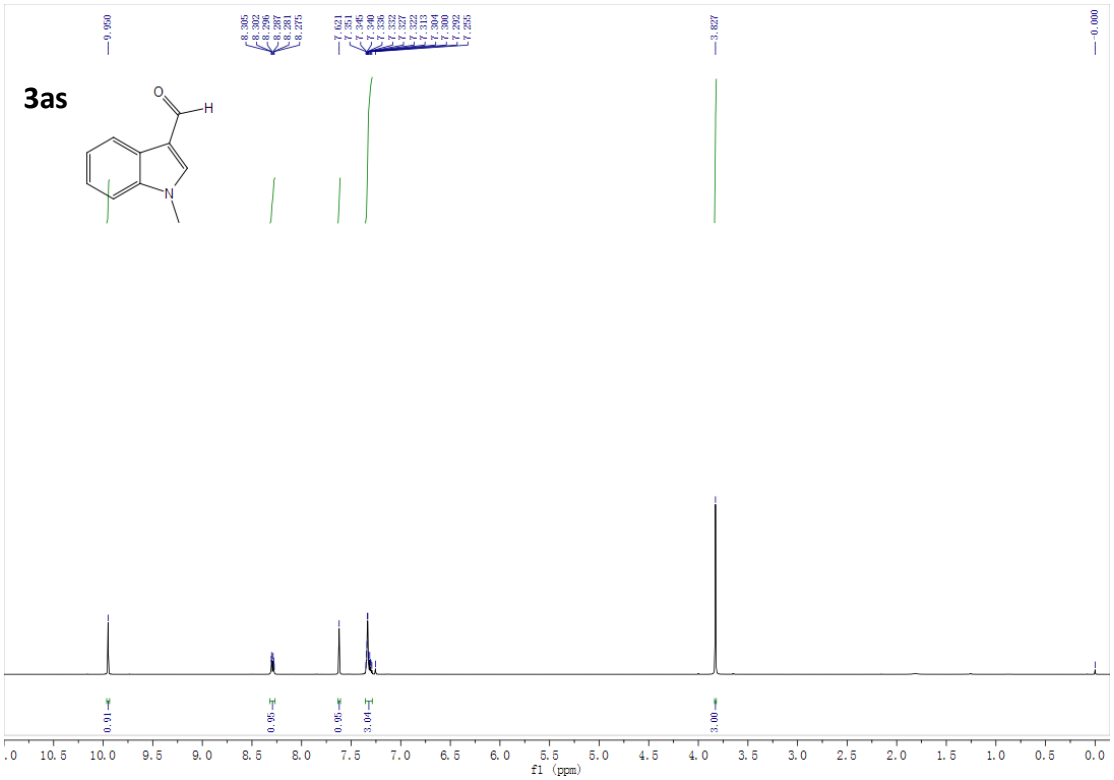

3ap
f1 (ppm)

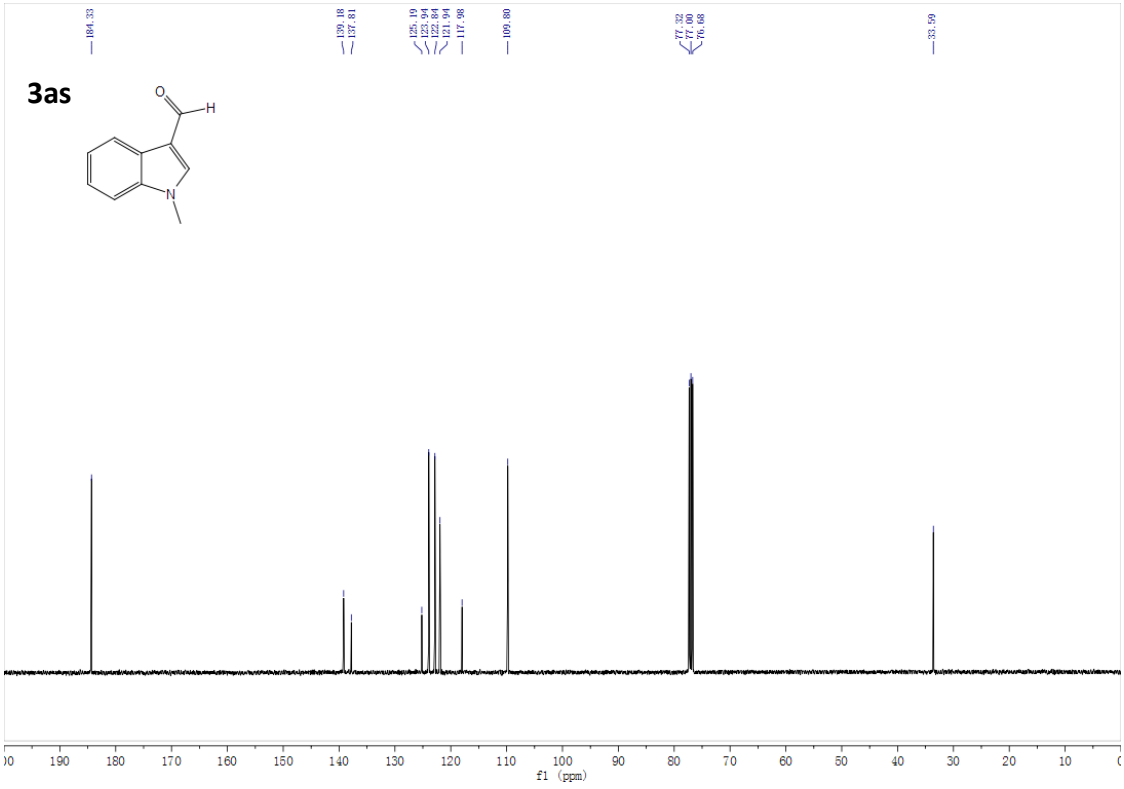

3aq
8.485
8.477
8.424
8.417
7.816
7.798
7.560
7.542
7.535
7.516
7.495
7.476
7.468
7.459
7.353
7.345
7.304
7.251
3.829
0.000
0.98
0.98
0.97
4.09
3.01
3.00
f1 (ppm)

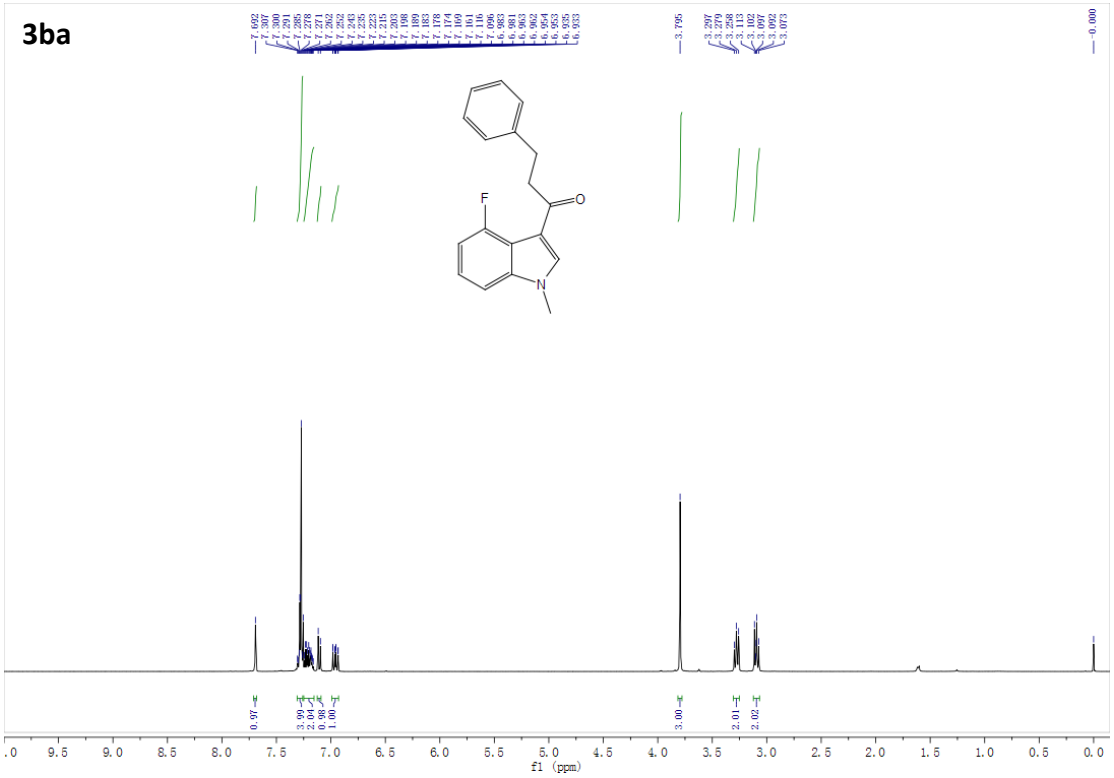

3aq
190.816
140.835
137.930
137.893
137.653
131.025
128.612
128.275
127.110
123.595
122.653
115.472
109.590
77.318
77.000
76.685
33.570
f1 (ppm)

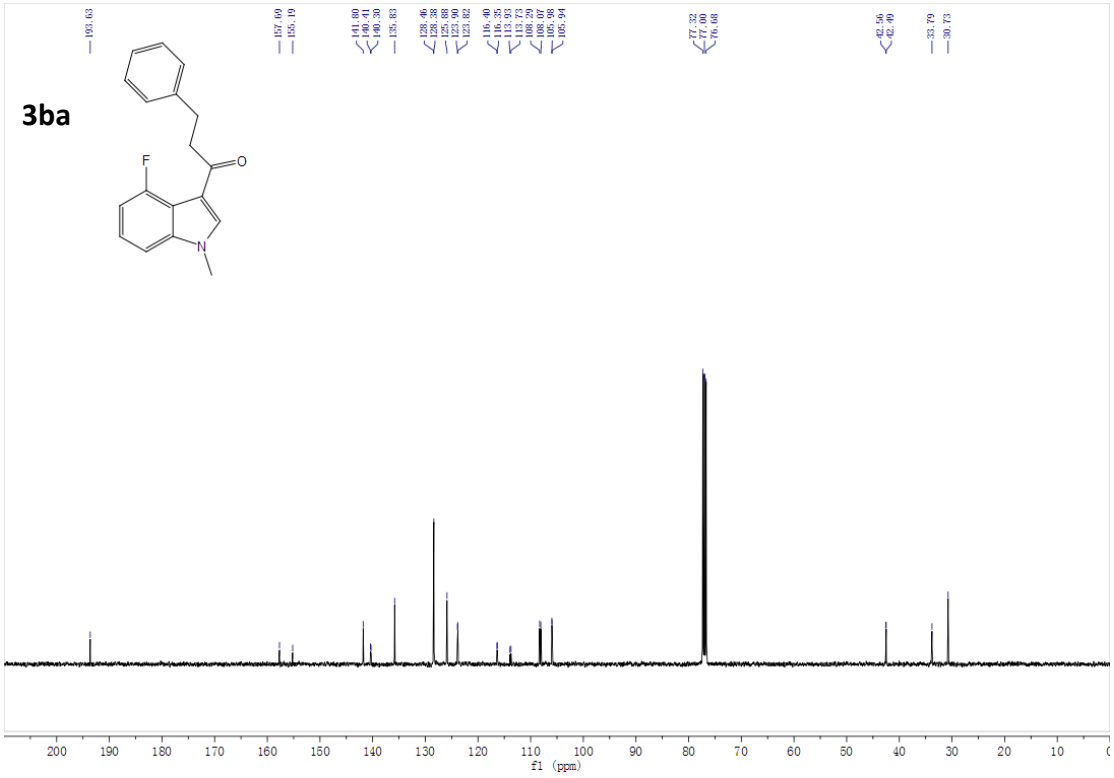

3ar
8.400
8.397
8.389
8.383
8.378
8.369
8.365
7.874
7.858
7.782
7.780
7.775
7.763
7.759
7.464
7.399
7.391
7.386
7.379
7.373
7.368
7.359
7.355
7.298
3.866
0.000
0.97
2.03
1.98
0.96
3.05
3.00
O
N
N
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

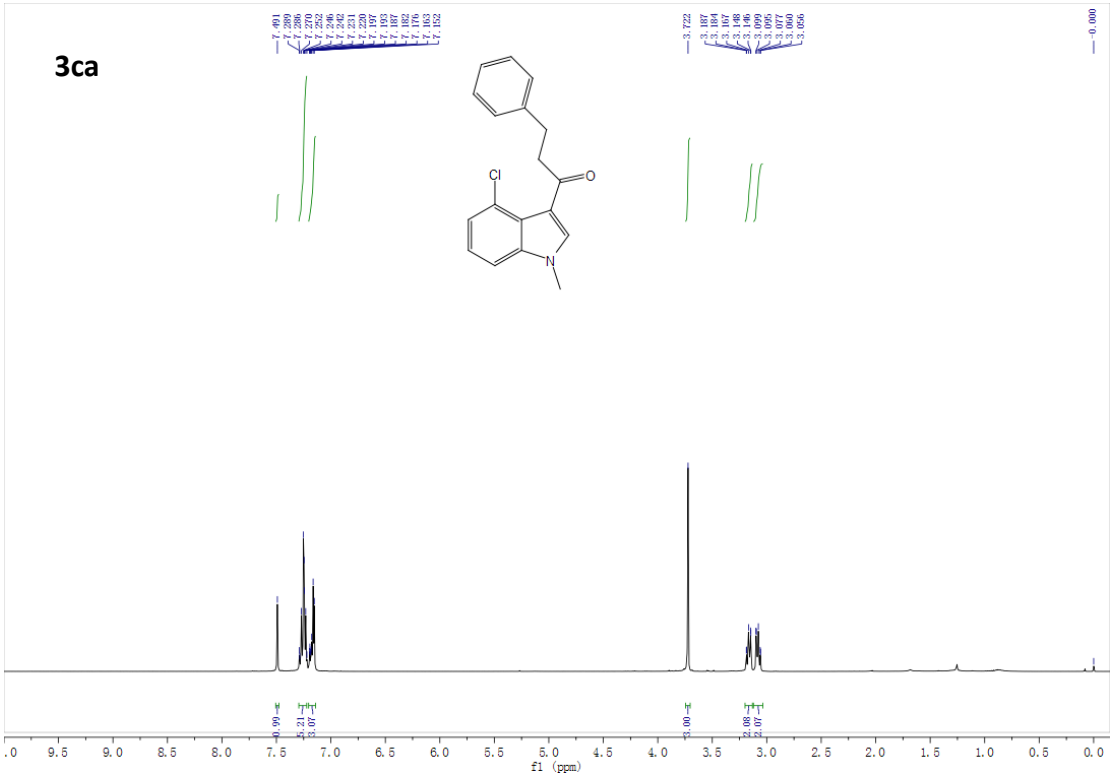

188.640
144.592
137.956
137.636
132.183
128.985
126.863
124.110
123.190
122.621
118.267
115.148
114.388
109.813
77.317
77.000
76.682
33.694
3ar
O
N
N
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

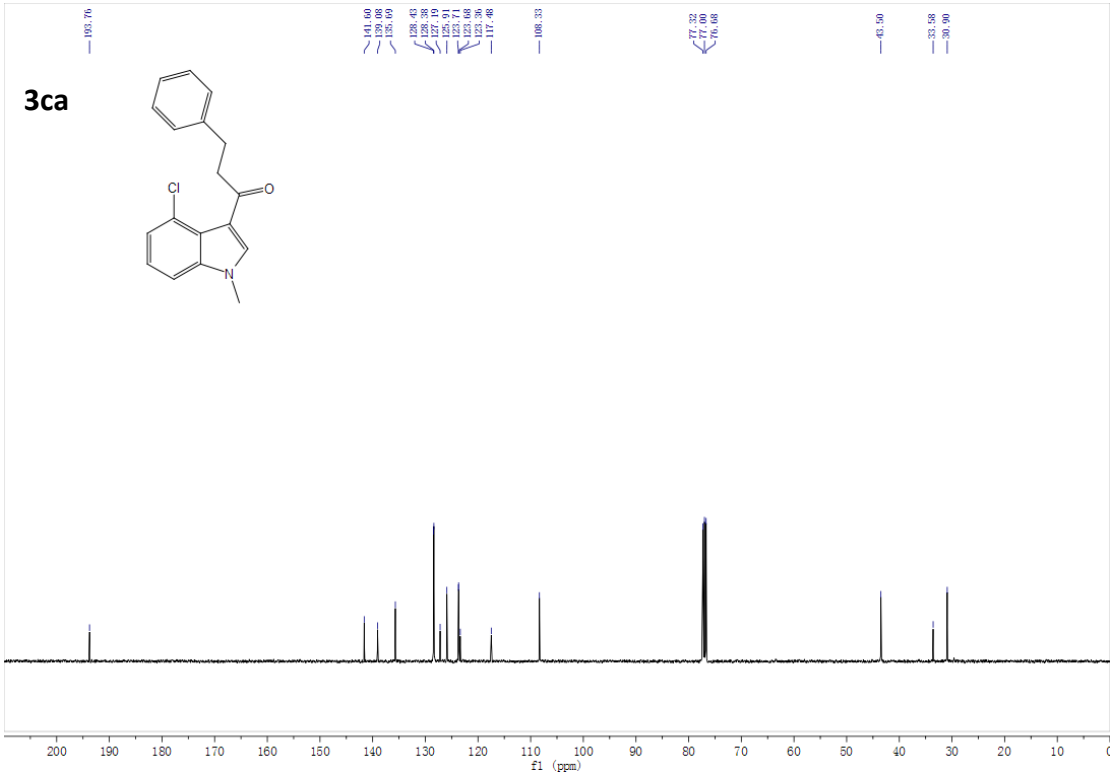

3as
9.950
8.305
8.302
8.299
8.297
8.281
8.275
7.621
7.351
7.345
7.340
7.339
7.332
7.327
7.322
7.313
7.304
7.300
7.292
7.255
3.827
0.000
0.91
0.95
0.95
3.04
3.00
f1 (ppm)

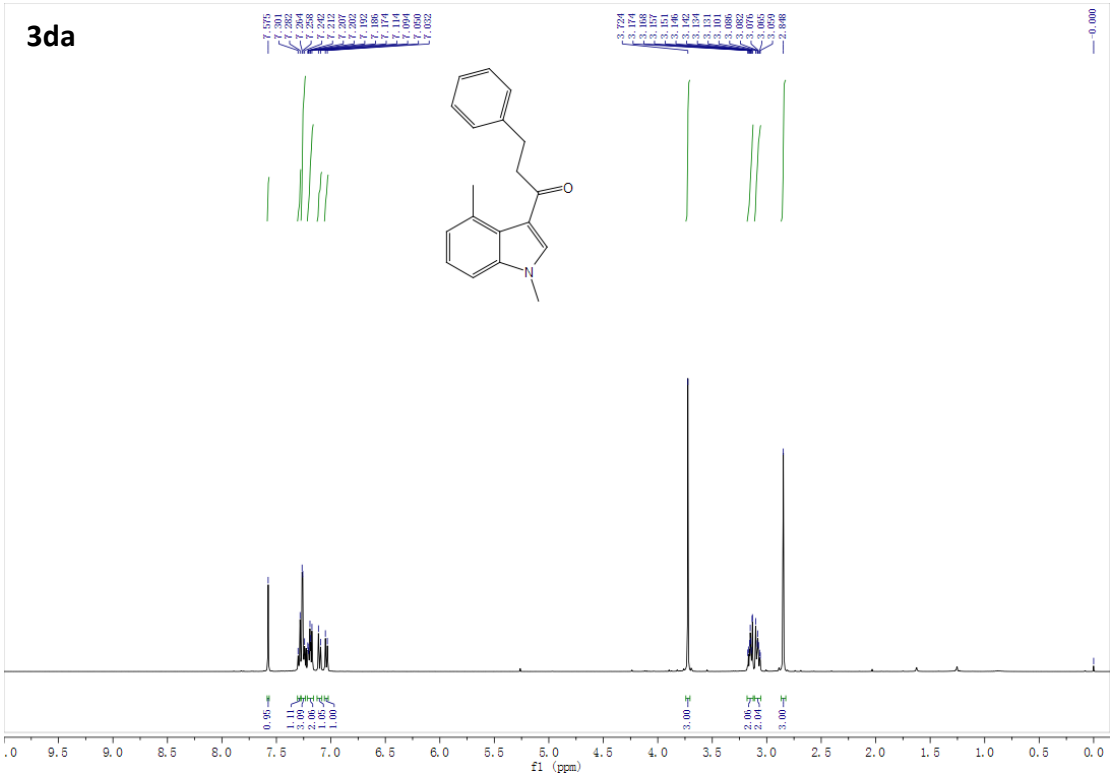

3as
184.33
139.18
137.81
125.19
123.94
122.84
121.94
117.98
109.80
77.32
77.00
76.68
33.59
f1 (ppm)


3ba
F
O
N
f1 (ppm)


3ba
F
O
N
f1 (ppm)


3ca
Cl
O
N
f1 (ppm)


3ca
Cl
O
N
f1 (ppm)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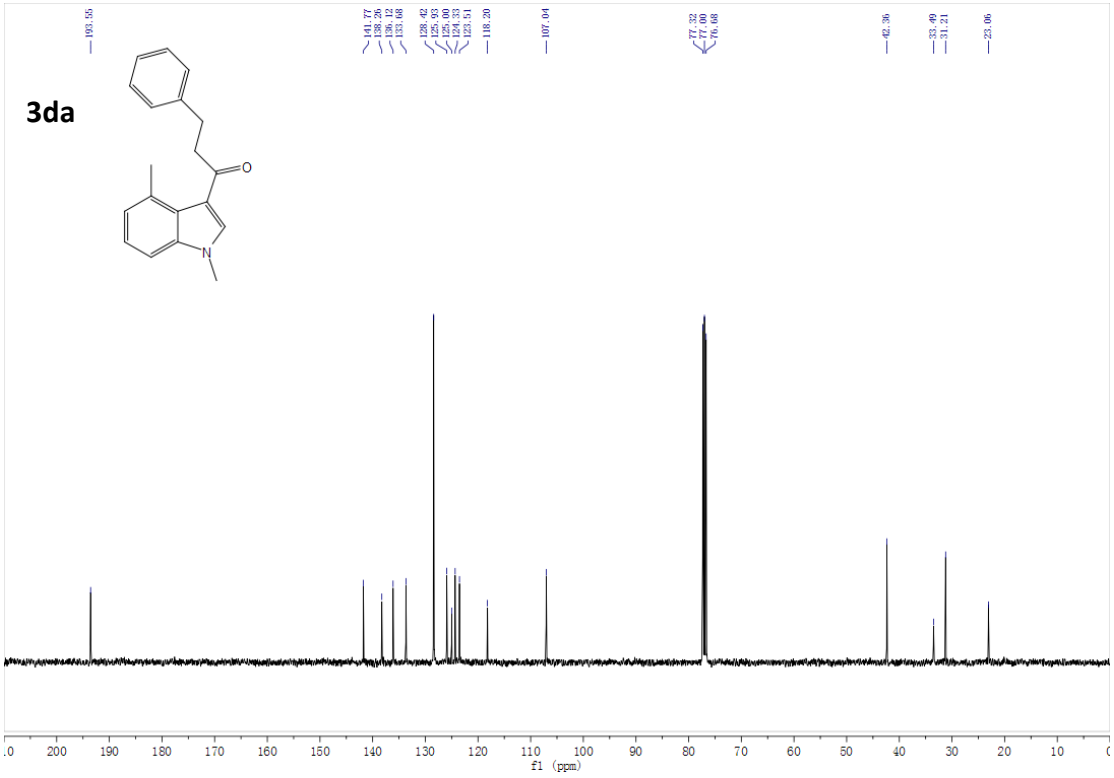
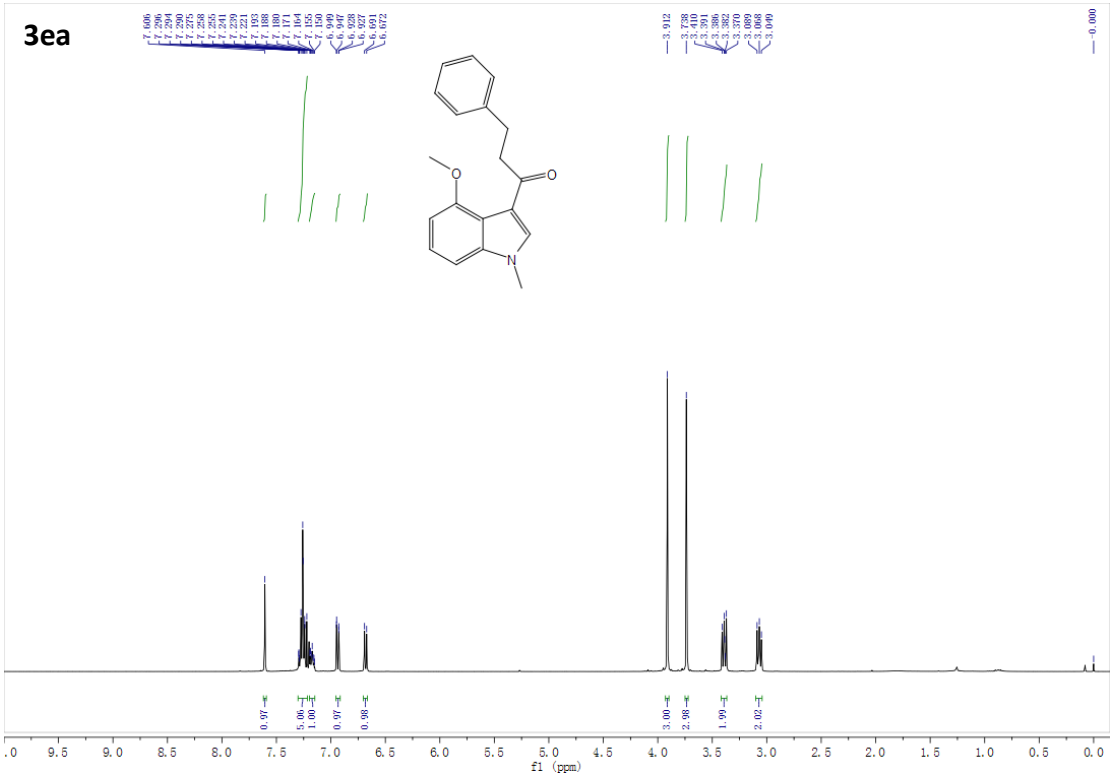
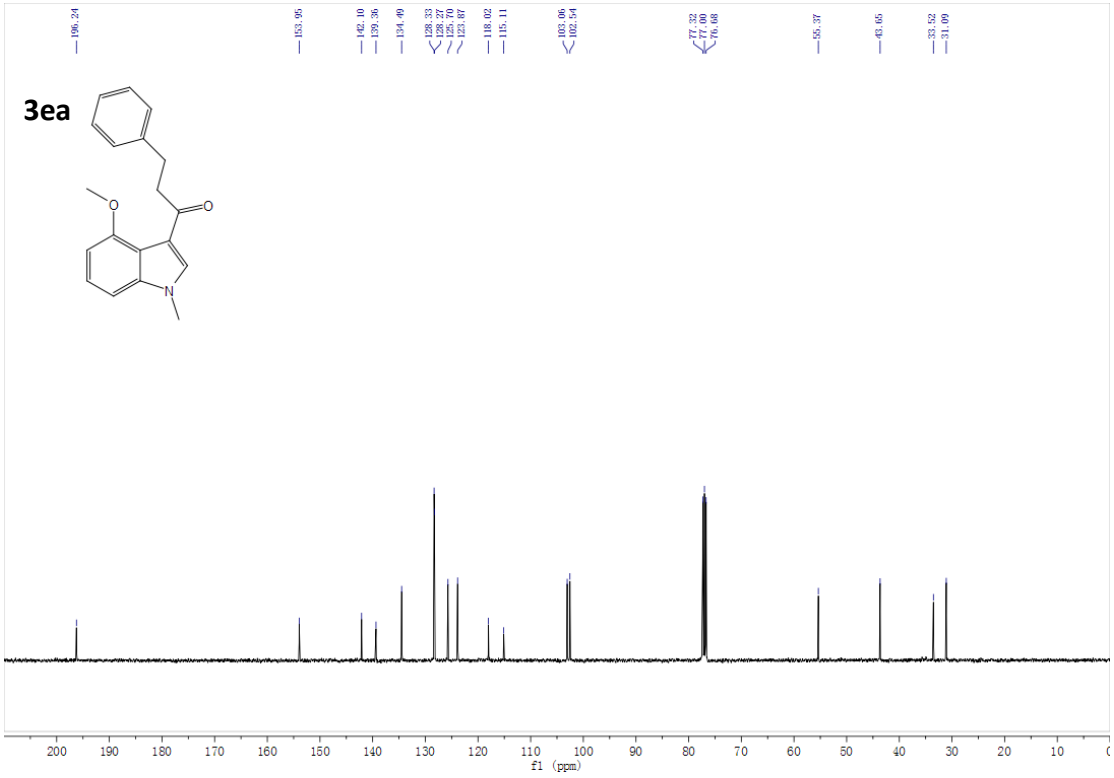
7.282
7.264
7.258
7.242
7.212
7.207
7.202
7.195
7.186
7.174
7.114
7.094
7.060
7.032
3.724
3.174
3.168
3.157
3.151
3.146
3.142
3.134
3.131
3.101
3.086
3.082
3.076
3.065
3.059
2.848
-0.000
0.95
1.11
3.09
2.06
1.05
1.00
3.00
2.00
2.04
3.00
f1 (ppm)


3da
193.55
141.77
138.25
136.12
133.68
128.42
127.55
125.00
124.33
123.51
118.20
107.04
77.32
77.00
76.68
42.36
33.49
31.21
23.06
f1 (ppm)


3ea
7.606
7.296
7.294
7.290
7.275
7.258
7.255
7.241
7.239
7.221
7.195
7.188
7.180
7.171
7.164
7.155
7.150
6.949
6.947
6.939
6.927
6.691
6.672
3.912
3.738
3.410
3.391
3.386
3.382
3.370
3.089
3.064
3.049
0.000
0.97
5.06
1.00
0.97
0.98
3.00
2.98
1.99
2.02
f1 (ppm)


3ea
196.24
153.95
142.10
139.36
134.49
128.33
128.27
125.70
123.87
118.02
115.11
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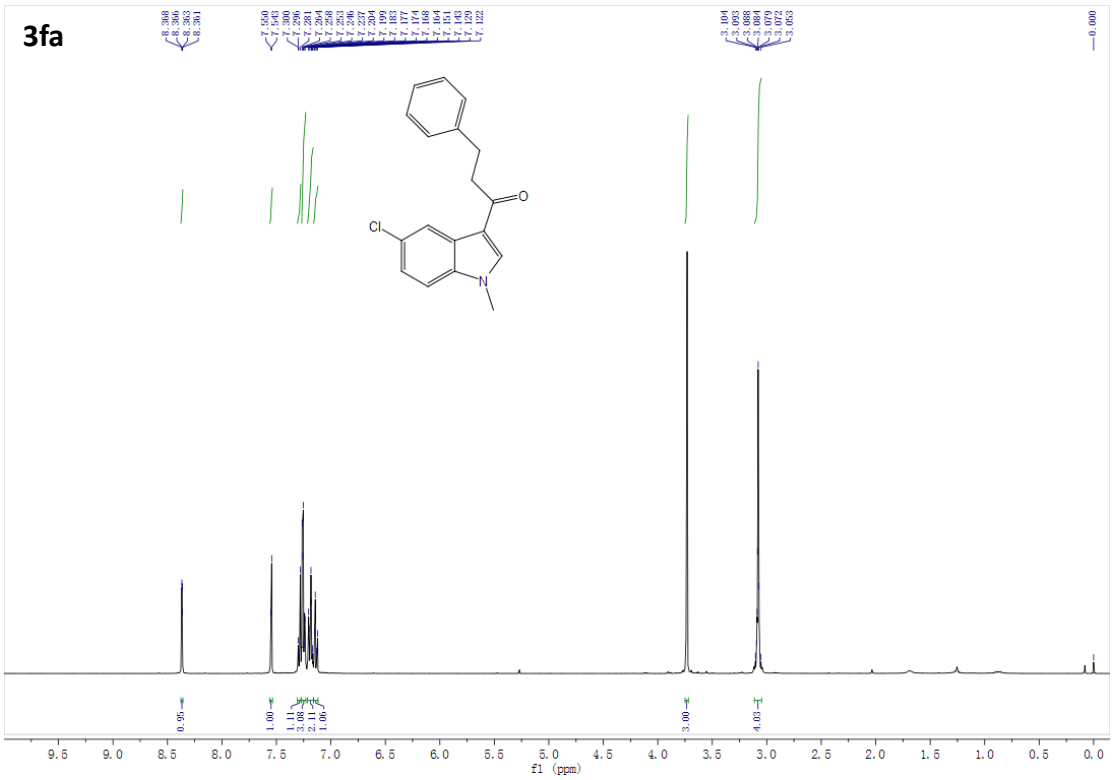
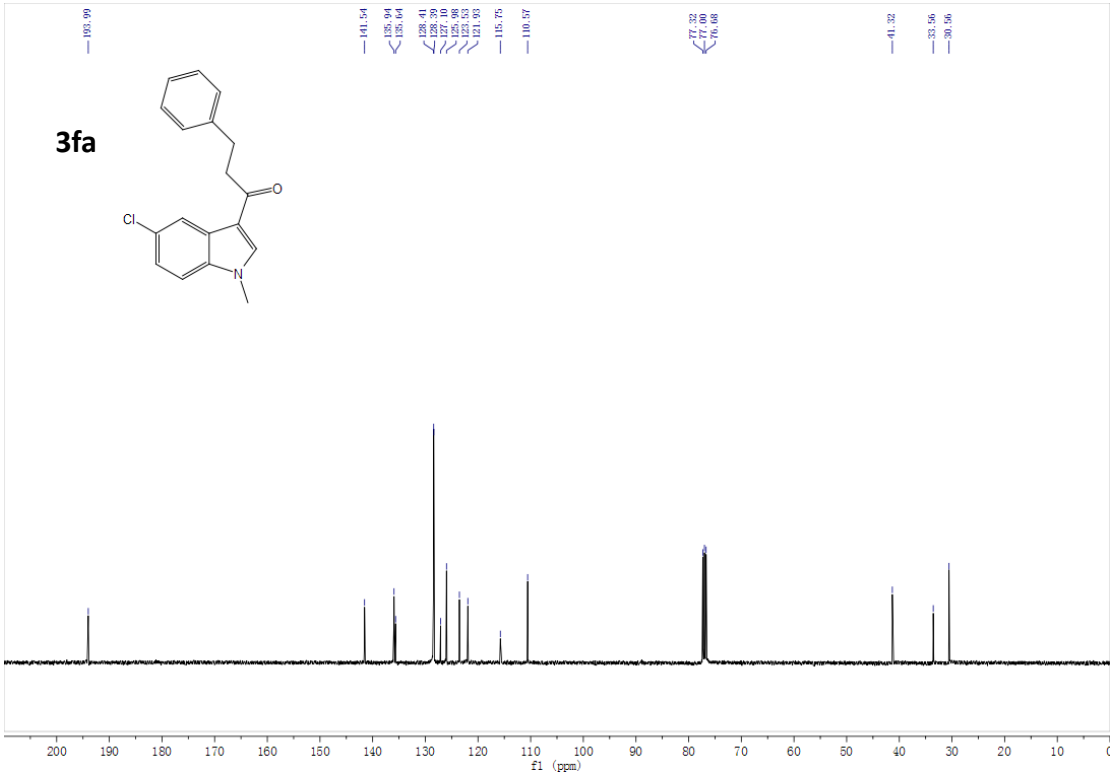
55.37
43.65
33.52
31.09
f1 (ppm)


3fa
Cl
O
N
f1 (ppm)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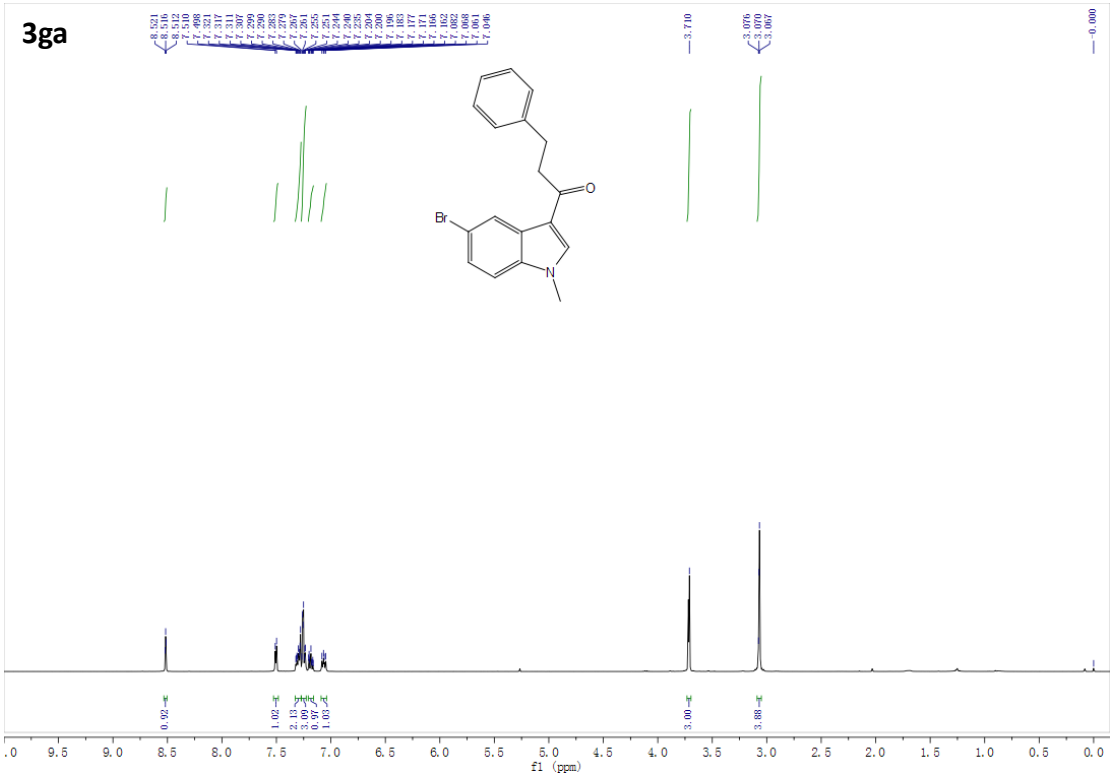
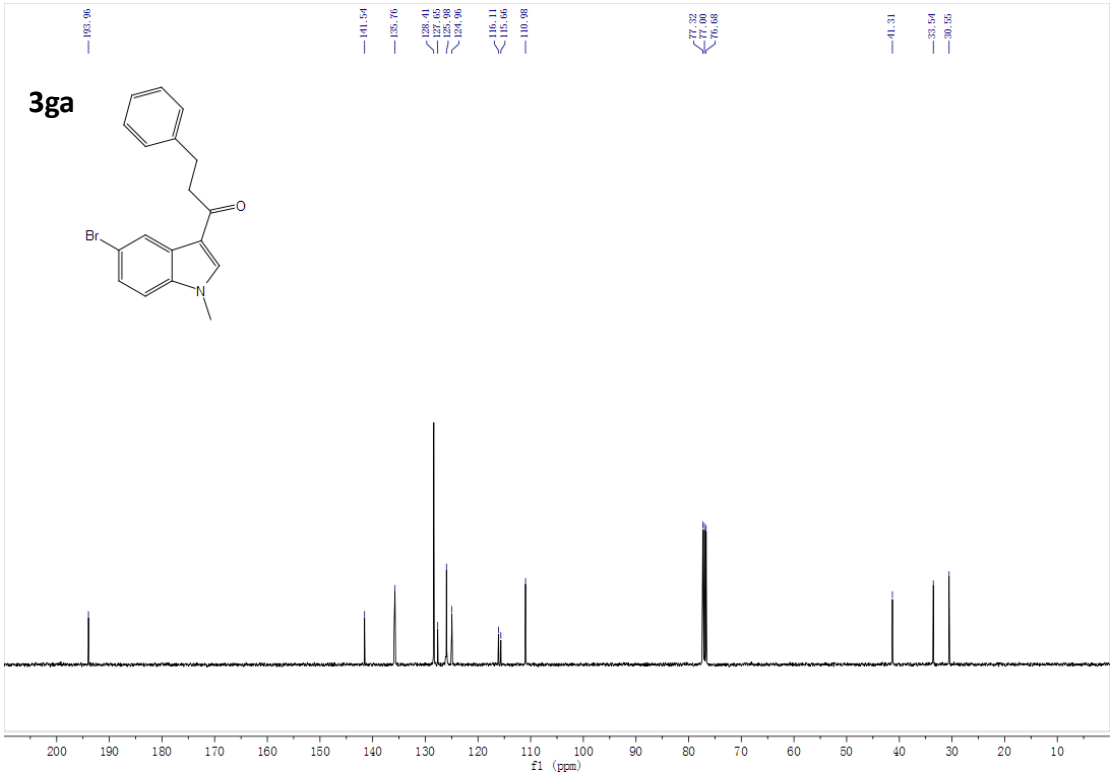
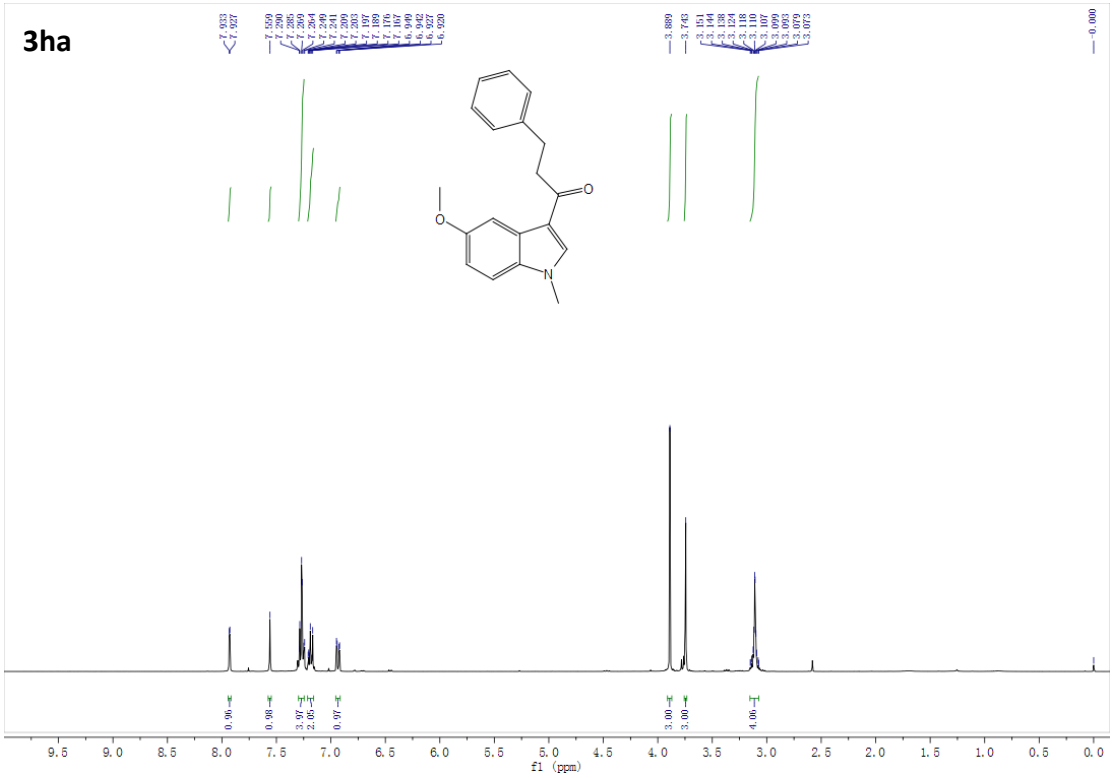
Cl
O
N
f1 (ppm)

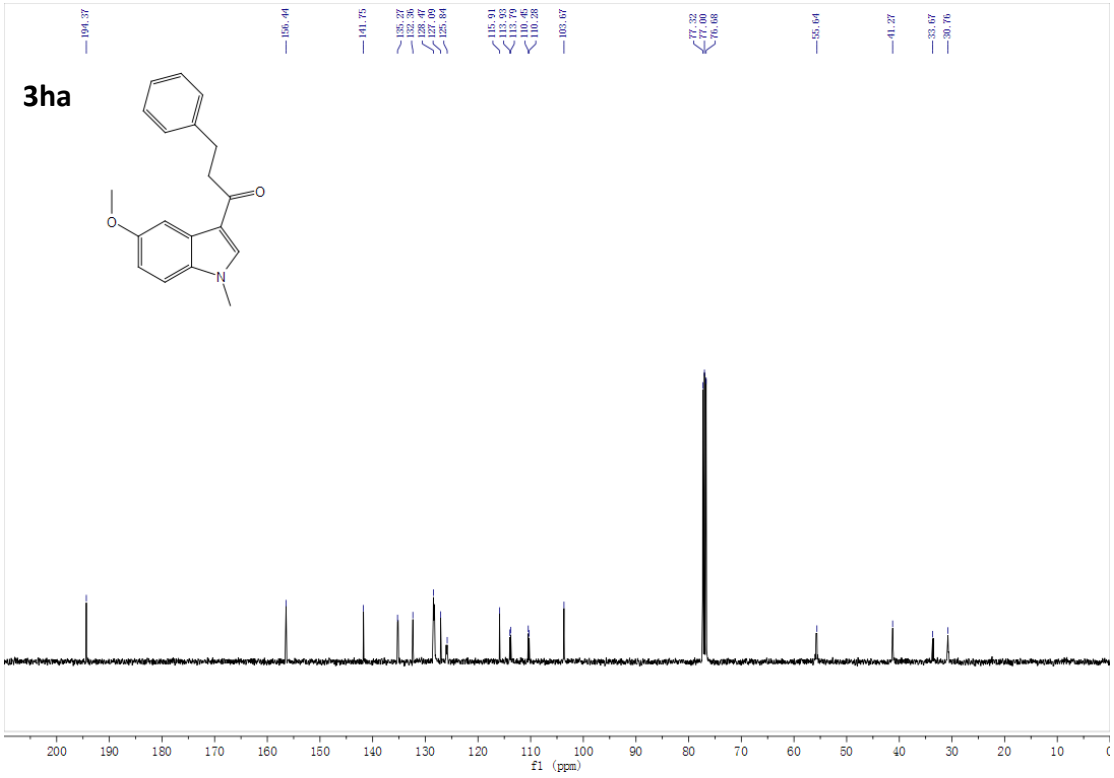

3ga
Br
O
N
f1 (ppm)

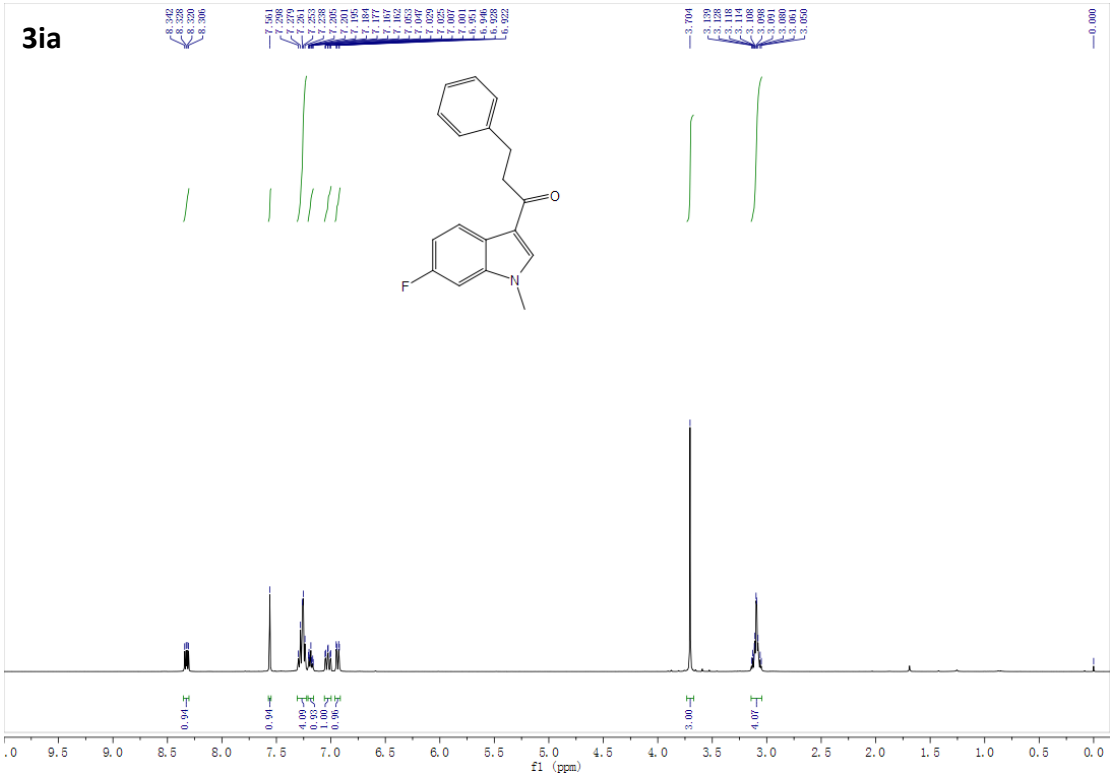

3ga
Br
O
N
f1 (ppm)

3ha



3ha




3ia
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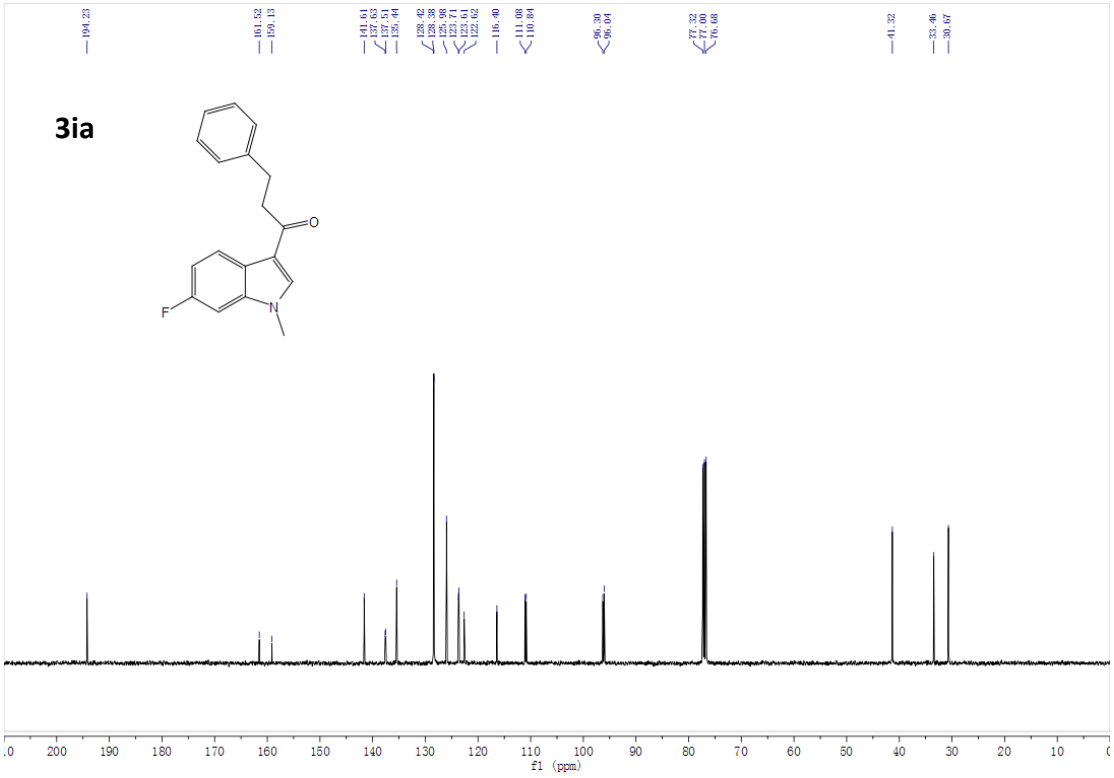
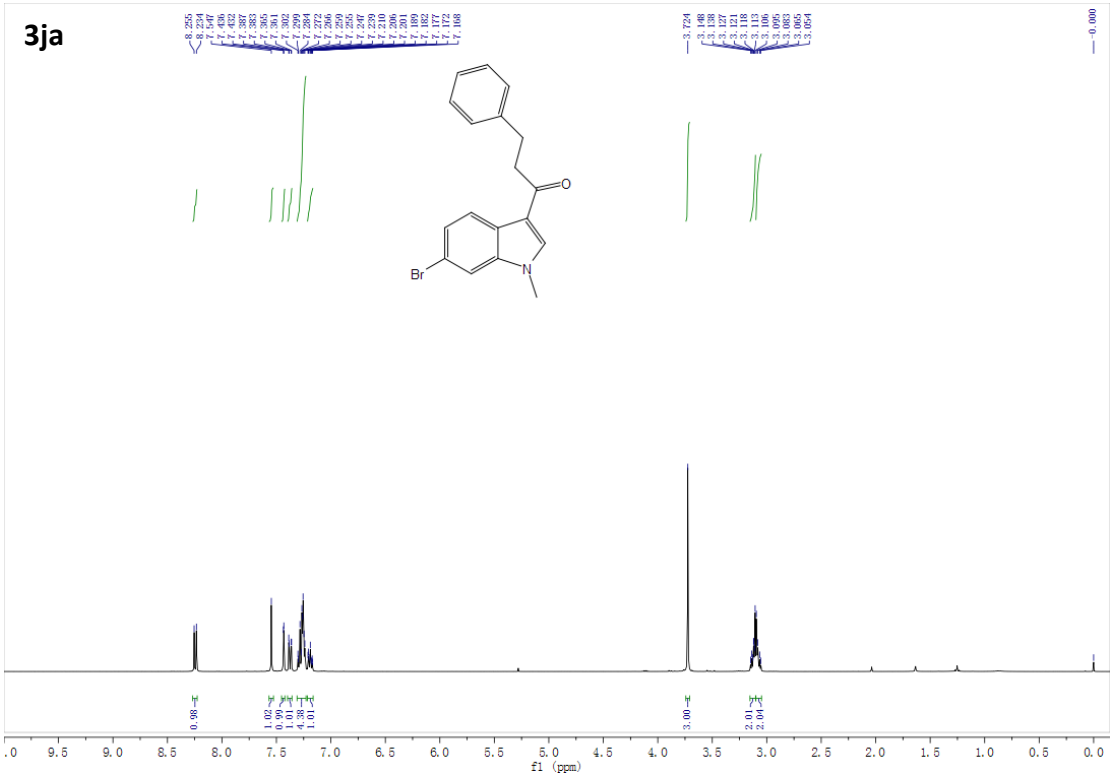
7.561
7.298
7.270
7.261
7.253
7.238
7.205
7.201
7.195
7.189
7.177
7.167
7.162
7.057
7.047
7.029
7.025
7.007
7.001
6.951
6.946
6.928
6.922
3.704
3.139
3.128
3.118
3.114
3.108
3.098
3.090
3.080
3.061
3.050
0.000
O
F
N
0.94
0.94
4.09
0.93
1.00
0.96
3.00
4.07
f1 (ppm)


3ia
194.23
161.52
159.13
141.61
137.63
137.51
135.44
128.42
128.38
125.98
123.71
123.64
122.62
116.40
111.08
110.84
96.30
96.04
77.32
77.00
76.68
41.32
33.46
30.67
O
F
N
f1 (ppm)

3ja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7.432
7.387
7.383
7.365
7.301
7.302
7.299
7.294
7.272
7.266
7.259
7.255
7.247
7.239
7.210
7.206
7.201
7.189
7.182
7.177
7.172
7.168
3.724
3.148
3.138
3.127
3.121
3.118
3.113
3.106
3.095
3.085
3.065
3.054
0.000
Br
N
O
0.98
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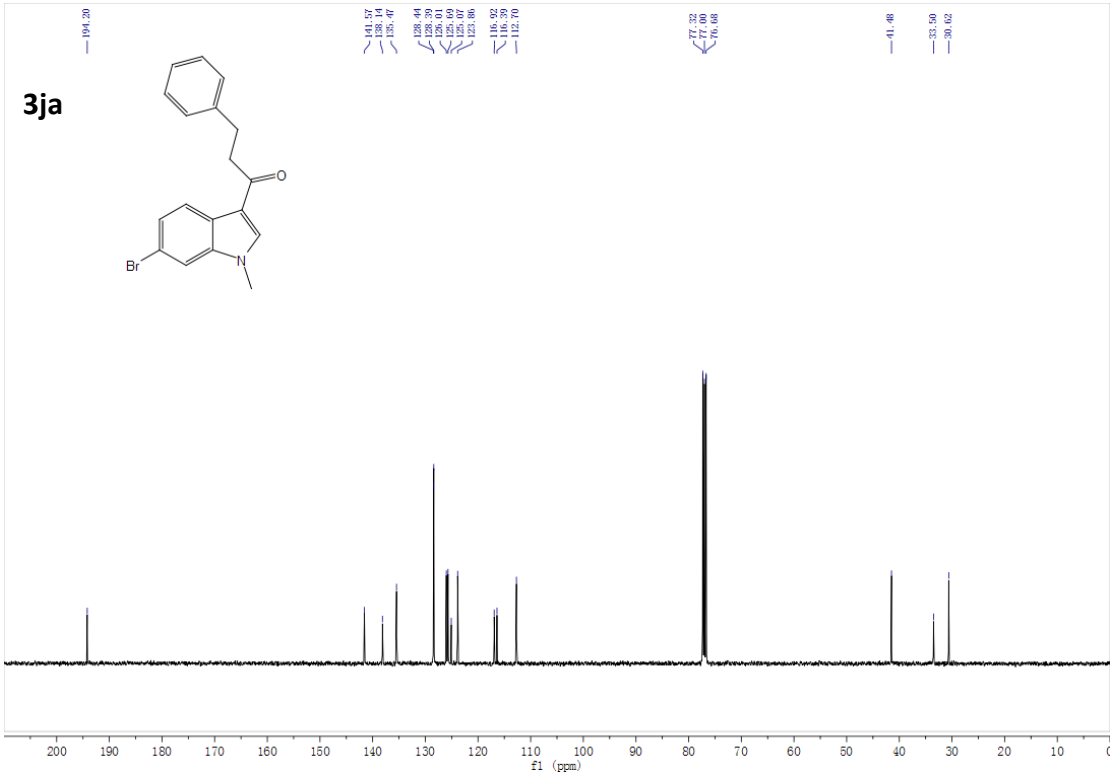
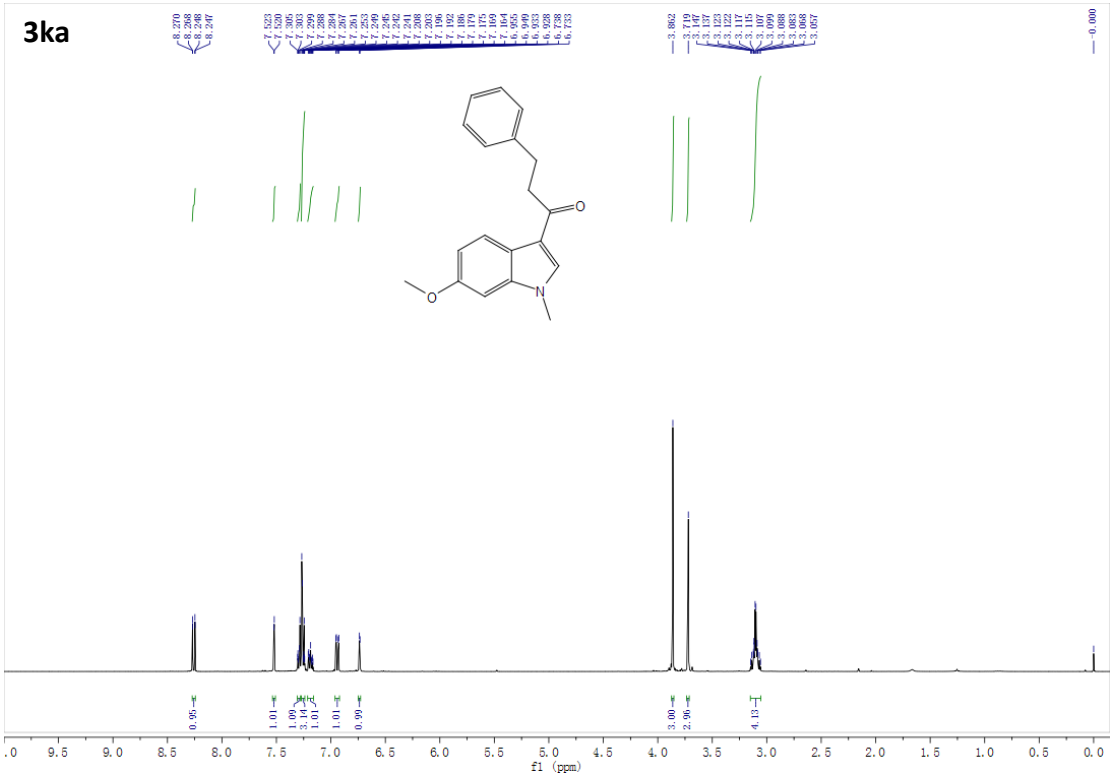
0.99
1.01
4.38
1.01
3.00
2.01
2.04
f1 (ppm)

3ja


194.30
141.57
138.14
135.47
128.44
128.39
126.01
125.69
125.07
123.86
116.32
116.28
112.70
77.32
77.00
76.68
41.48
33.50
30.62
Br
N
O
f1 (ppm)


3ka
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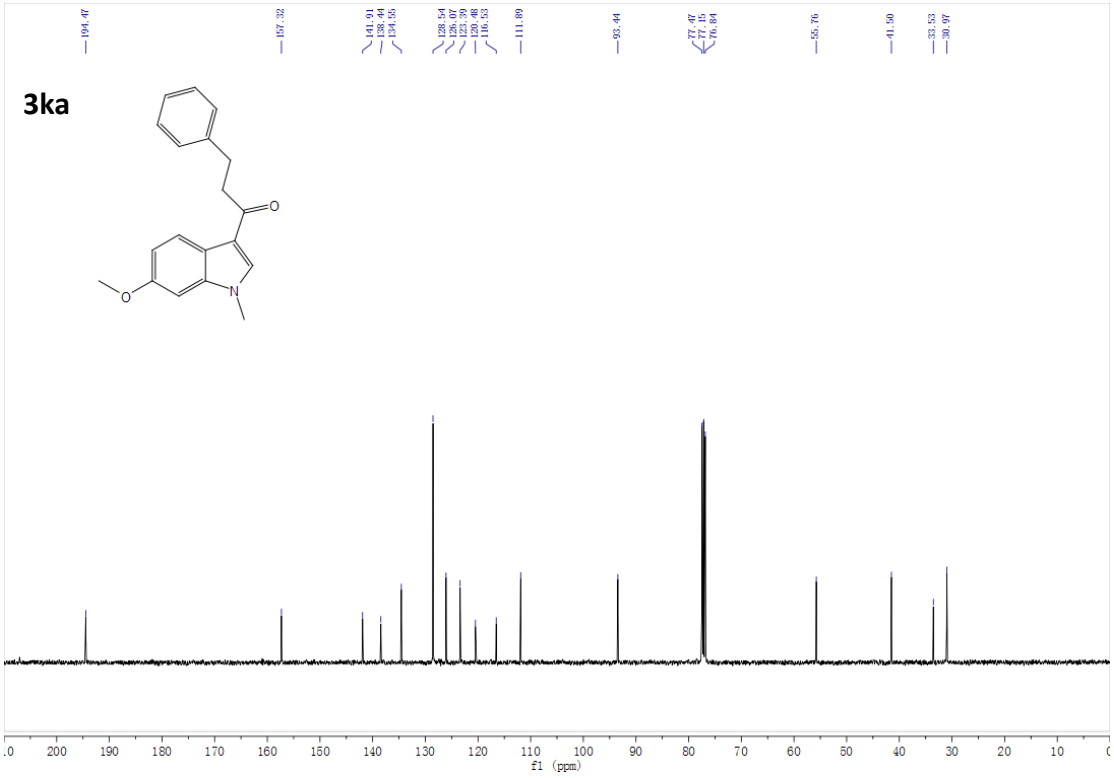
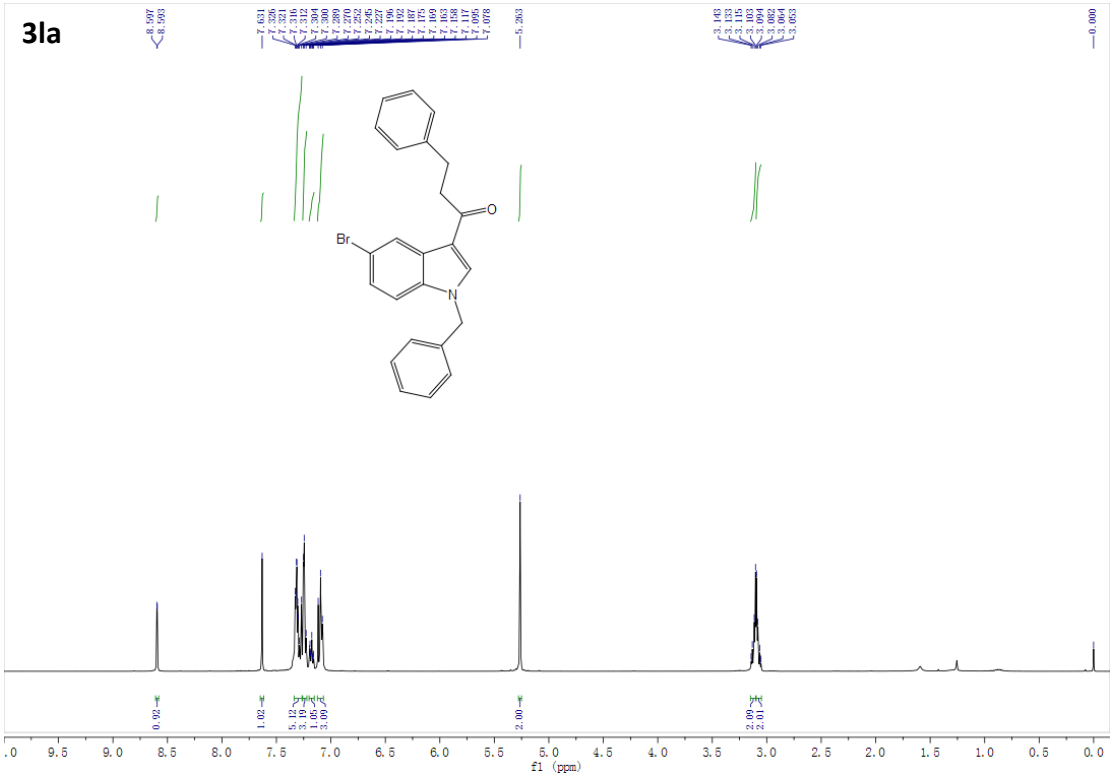
8.268
8.266
8.247
7.533
7.520
7.305
7.303
7.299
7.298
7.294
7.287
7.281
7.253
7.249
7.245
7.242
7.241
7.208
7.203
7.196
7.195
7.186
7.179
7.175
7.169
7.164
6.955
6.949
6.933
6.928
6.926
6.738
6.733
3.862
3.719
3.147
3.137
3.123
3.122
3.117
3.115
3.107
3.099
3.088
3.083
3.068
3.057
-0.000
0.95
1.01
1.09
3.14
1.01
1.01
0.99
3.00
2.96
4.13
f1 (ppm)


194.47
157.32
141.91
138.44
134.55
128.54
126.07
123.39
120.48
116.53
111.89
93.44
77.47
77.15
76.84
55.76
41.50
33.53
30.97
3ka
f1 (ppm)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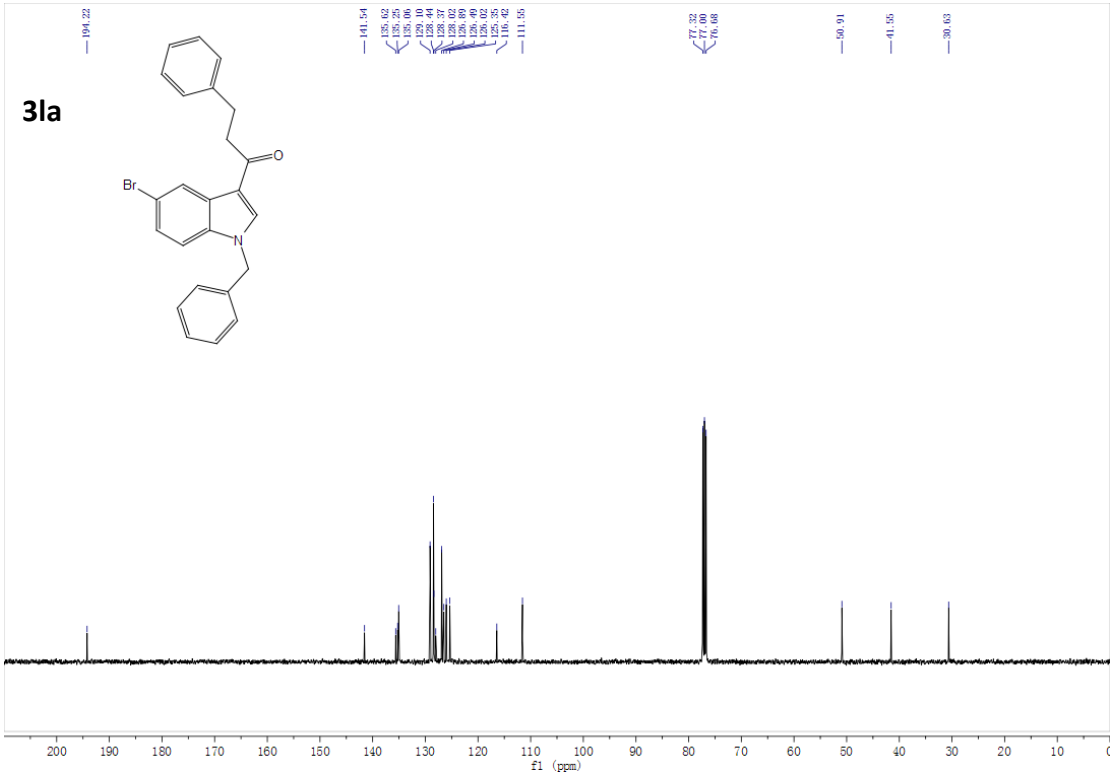
Br
O
N
f1 (ppm)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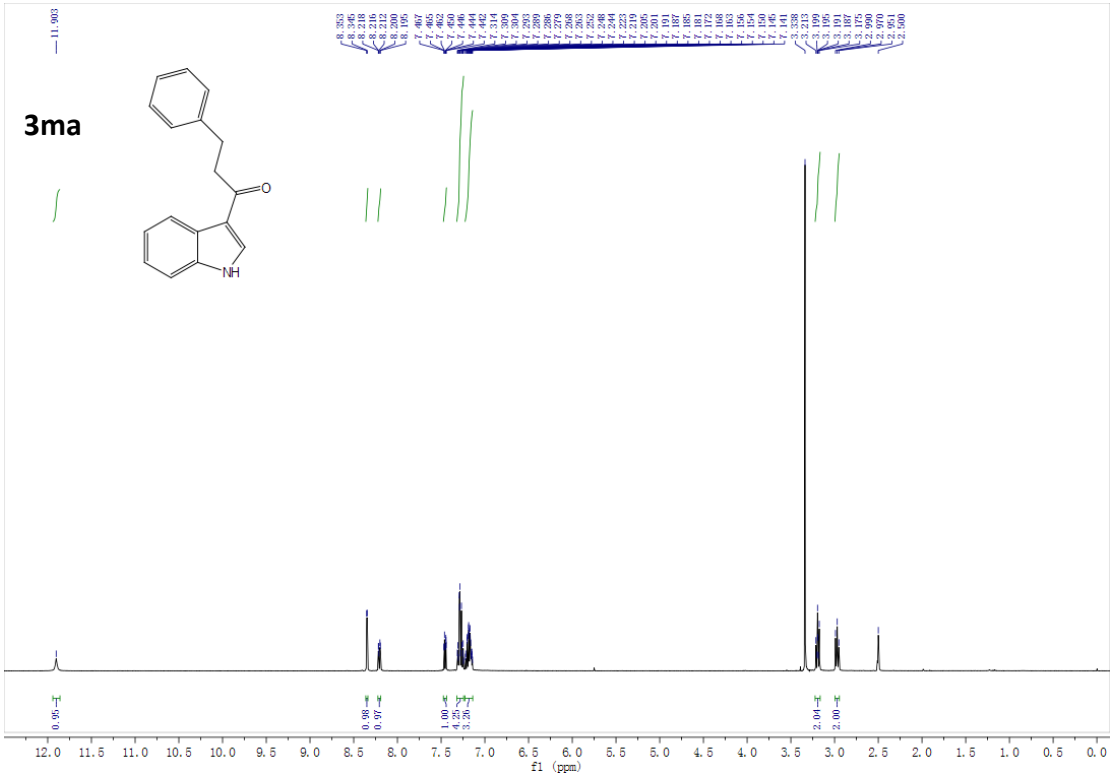
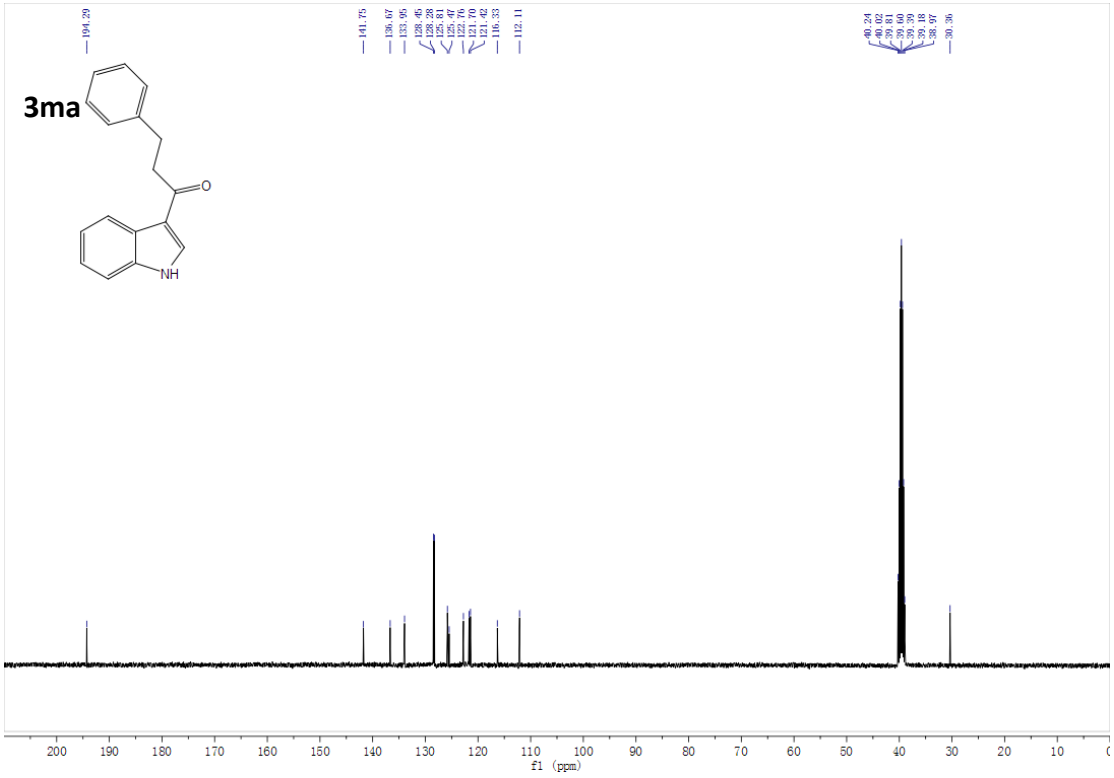
Br
O
N
f1 (ppm)


3ma
O
NH
f1 (ppm)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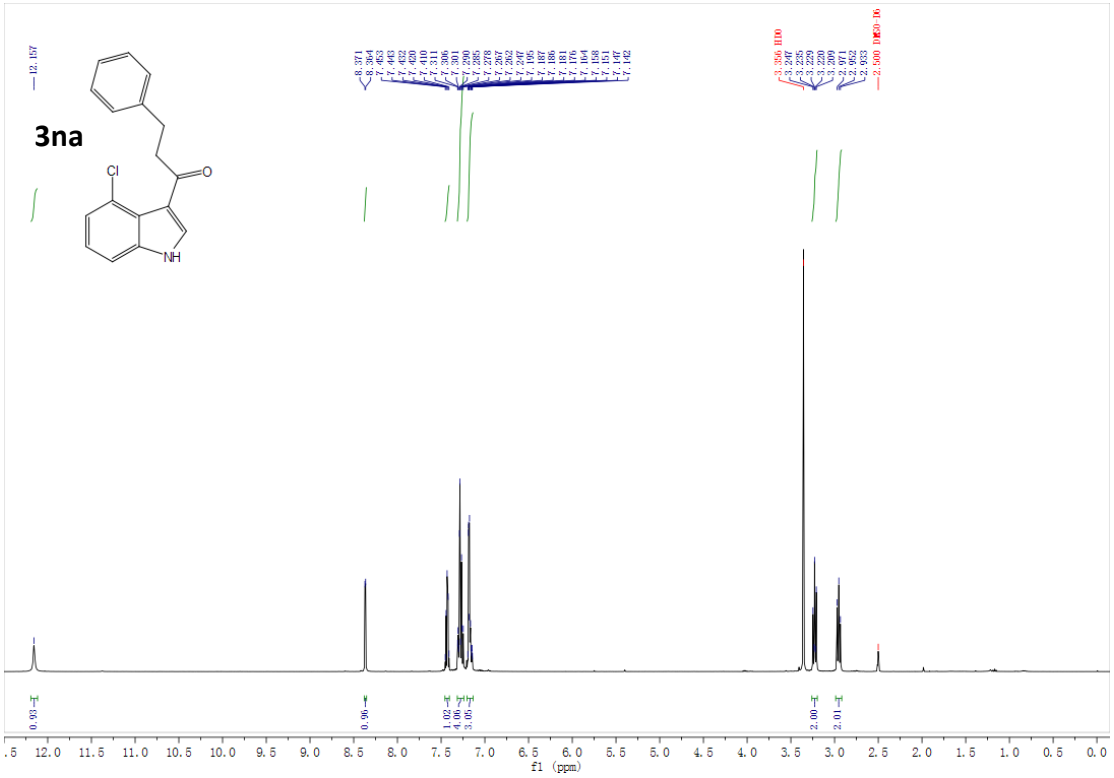
O
NH
f1 (ppm)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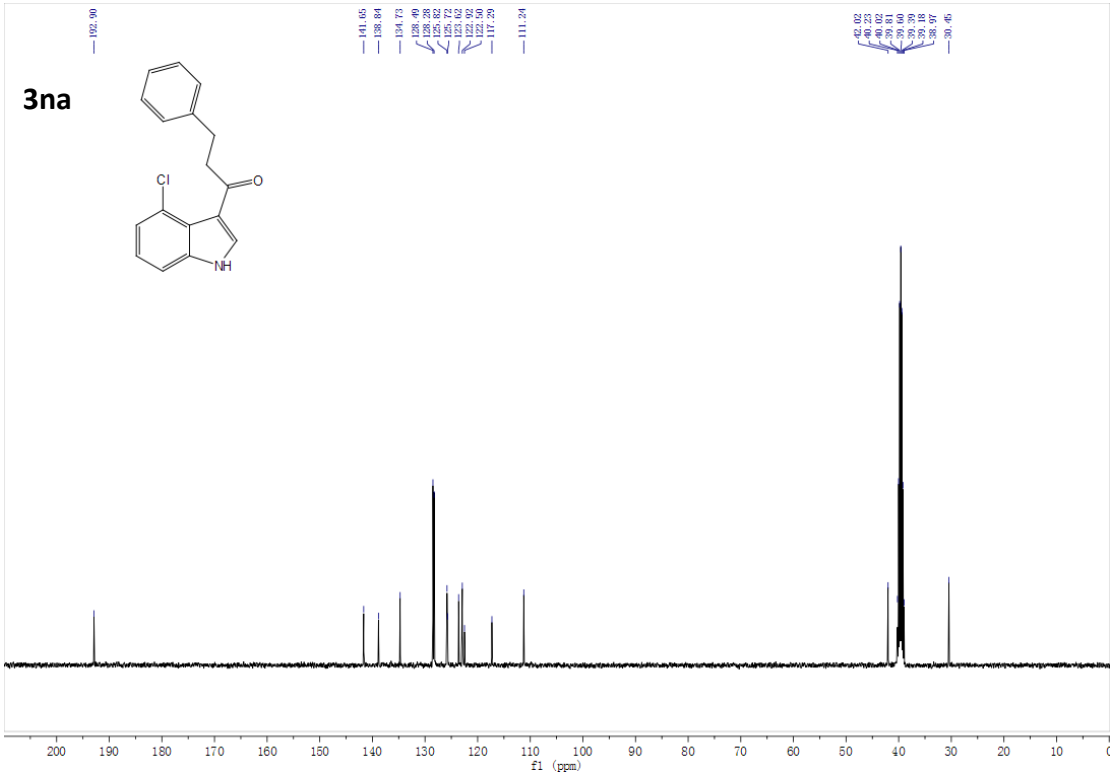
Cl
O
NH
f1 (ppm)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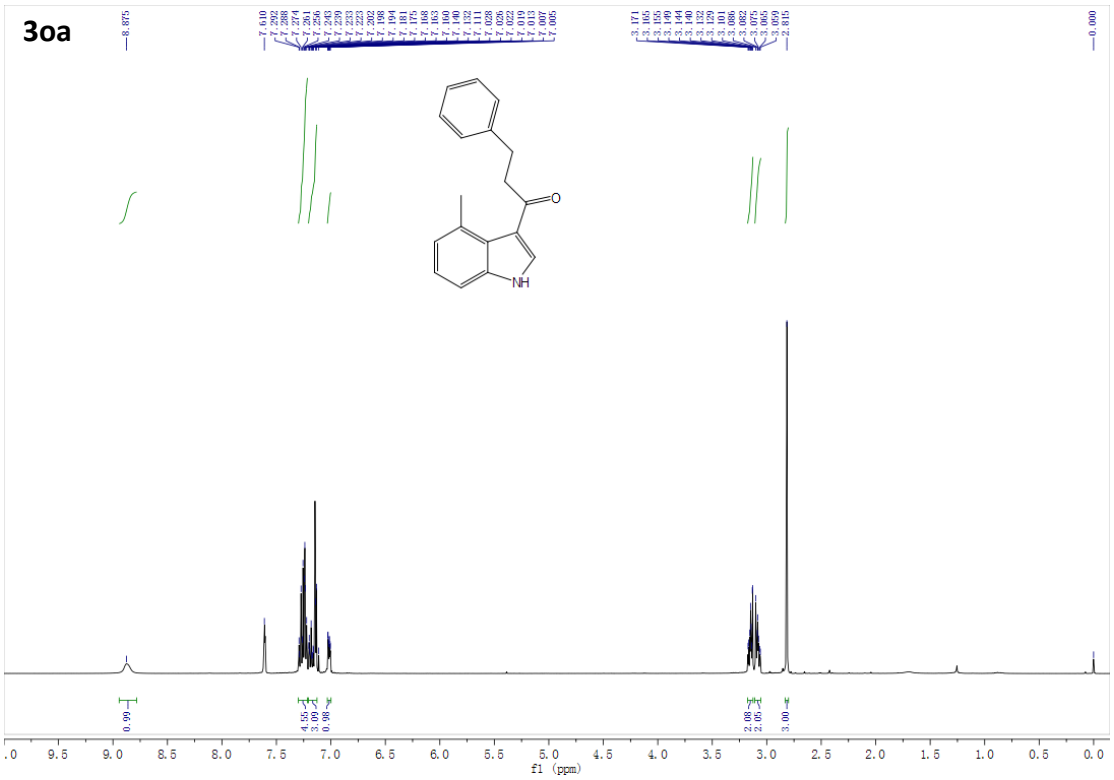
Cl
O
NH
f1 (ppm)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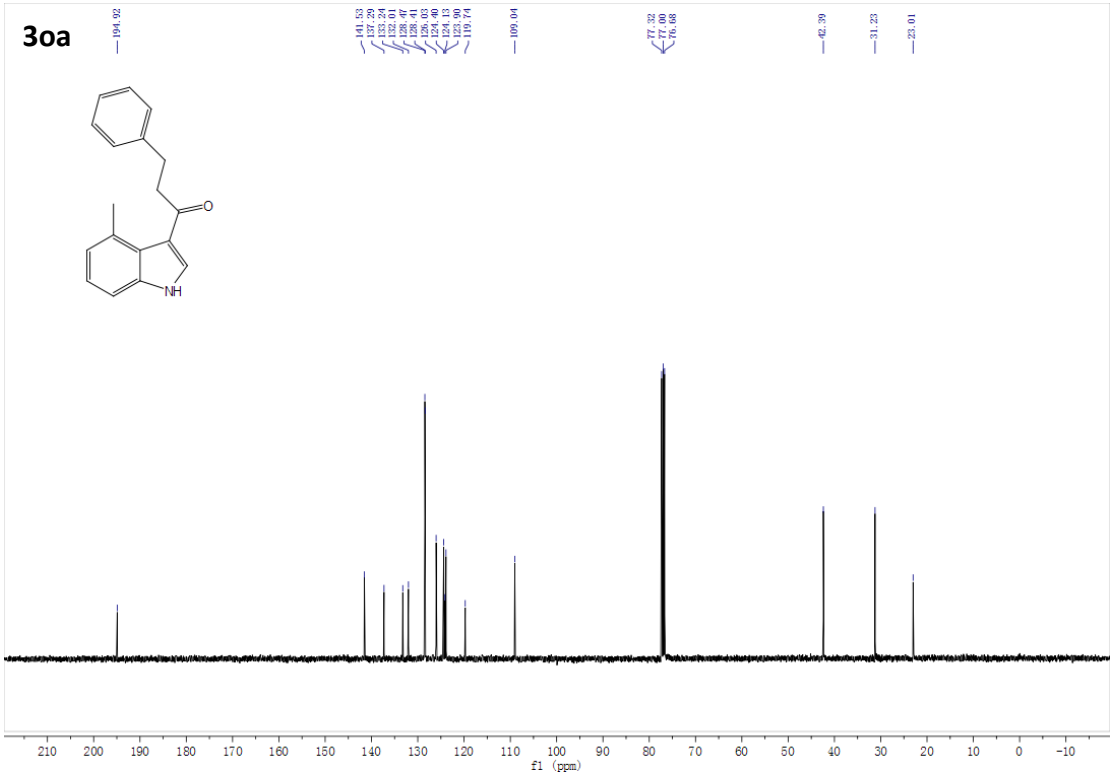
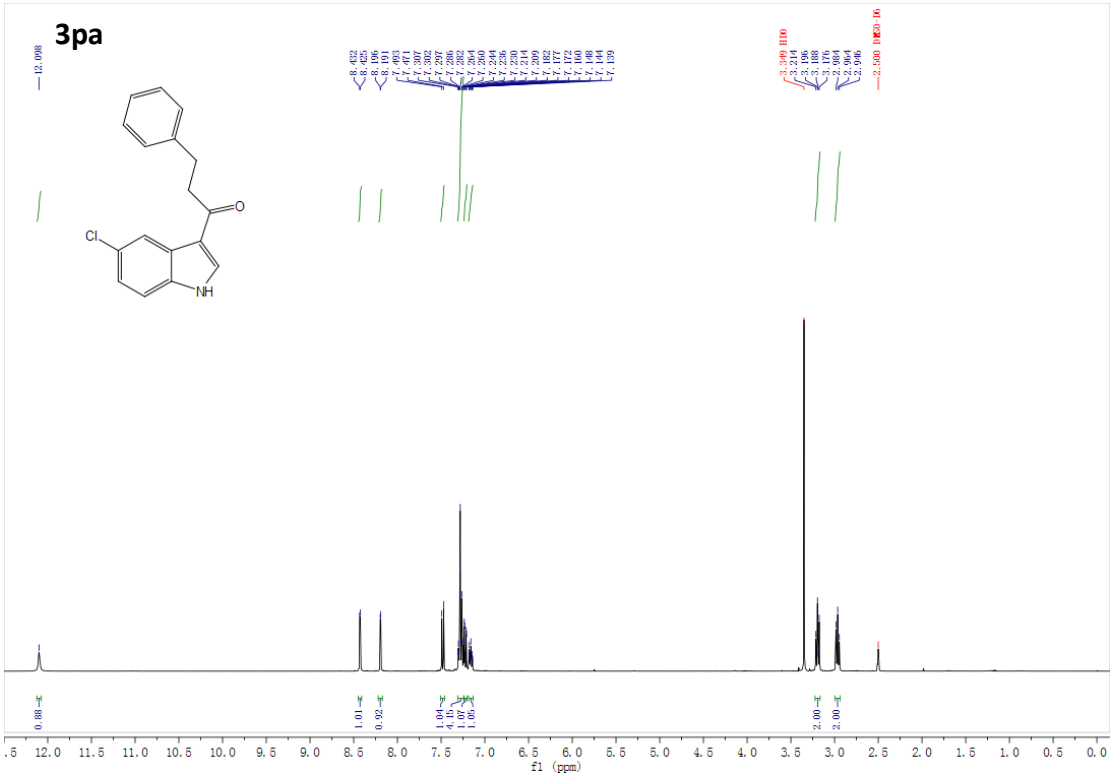
O
NH
f1 (ppm)


3oa
O
NH
f1 (ppm)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Cl
O
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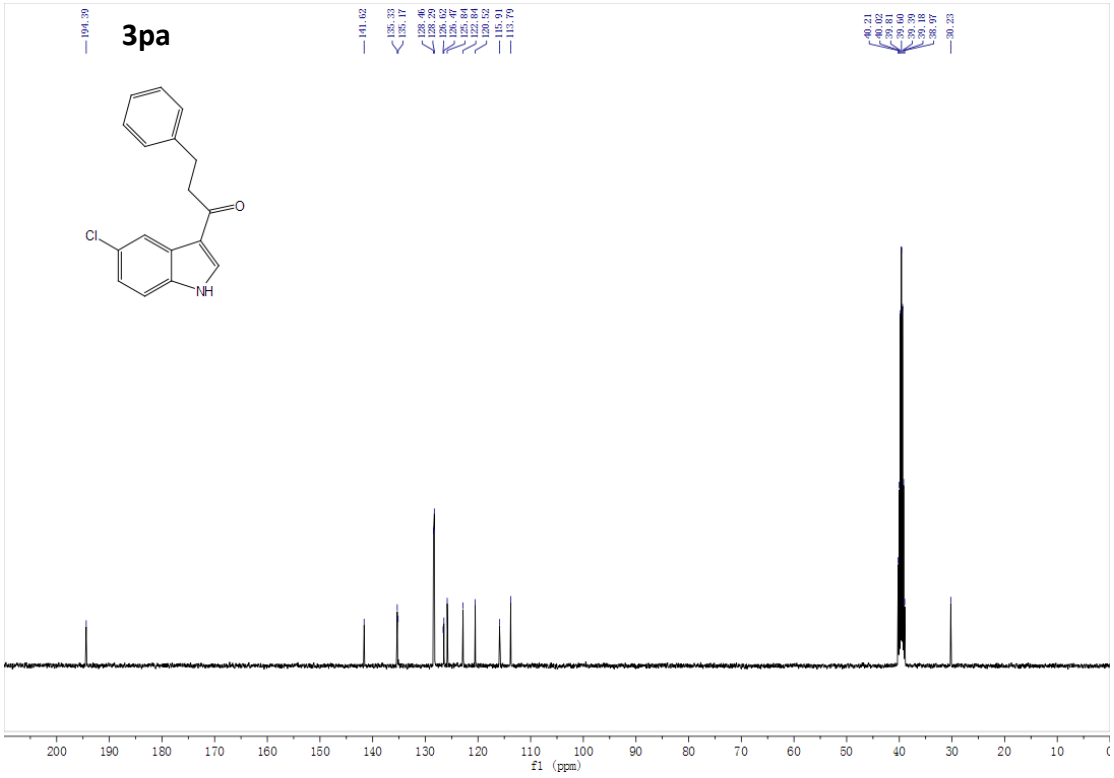
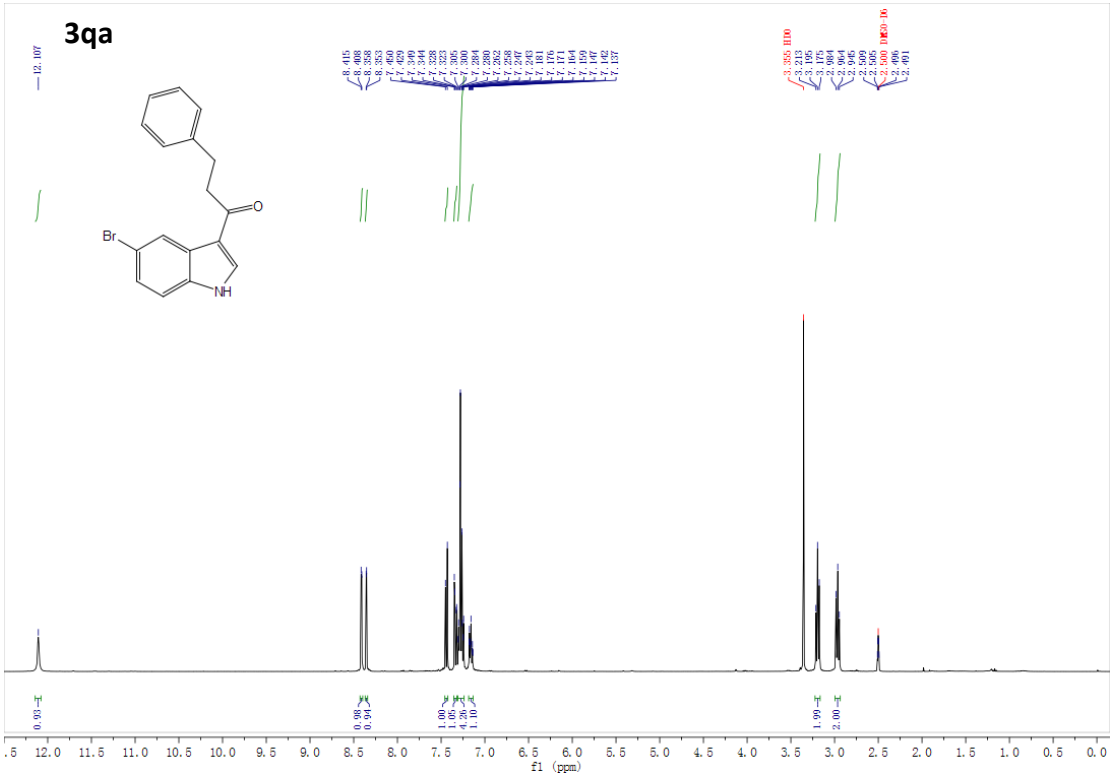
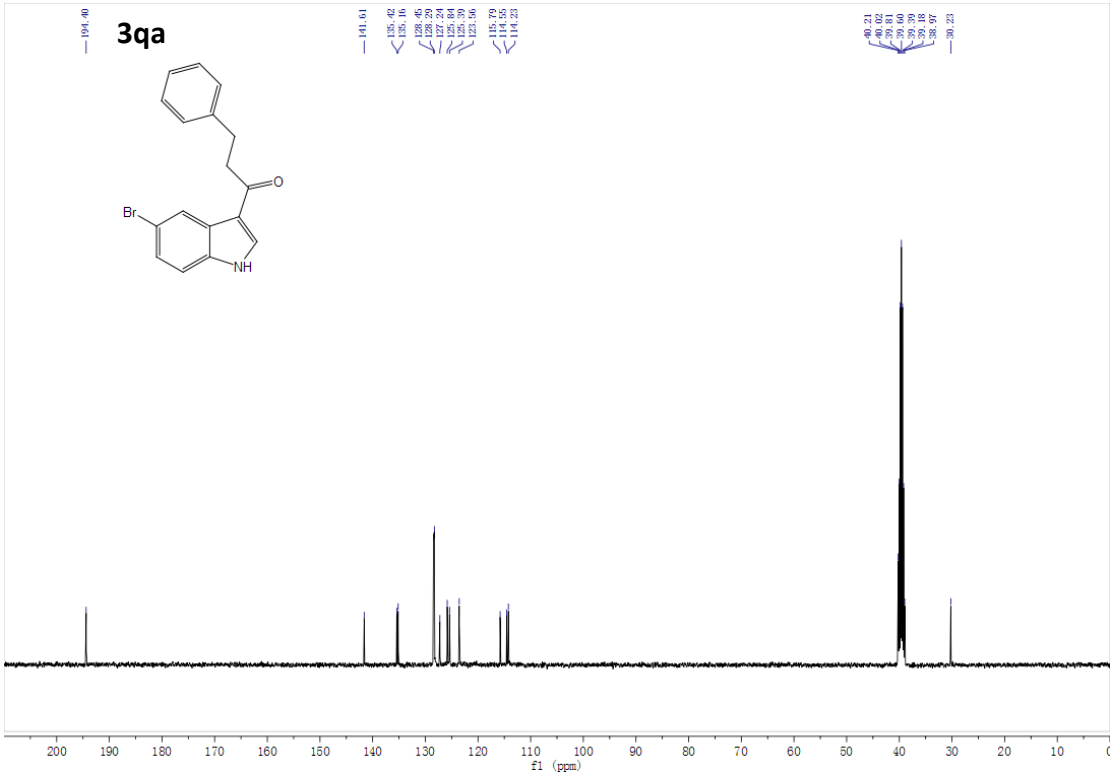
f1 (ppm)


3pa
Cl
O
NH
f1 (ppm)


3qa
Br
O
NH
f1 (ppm)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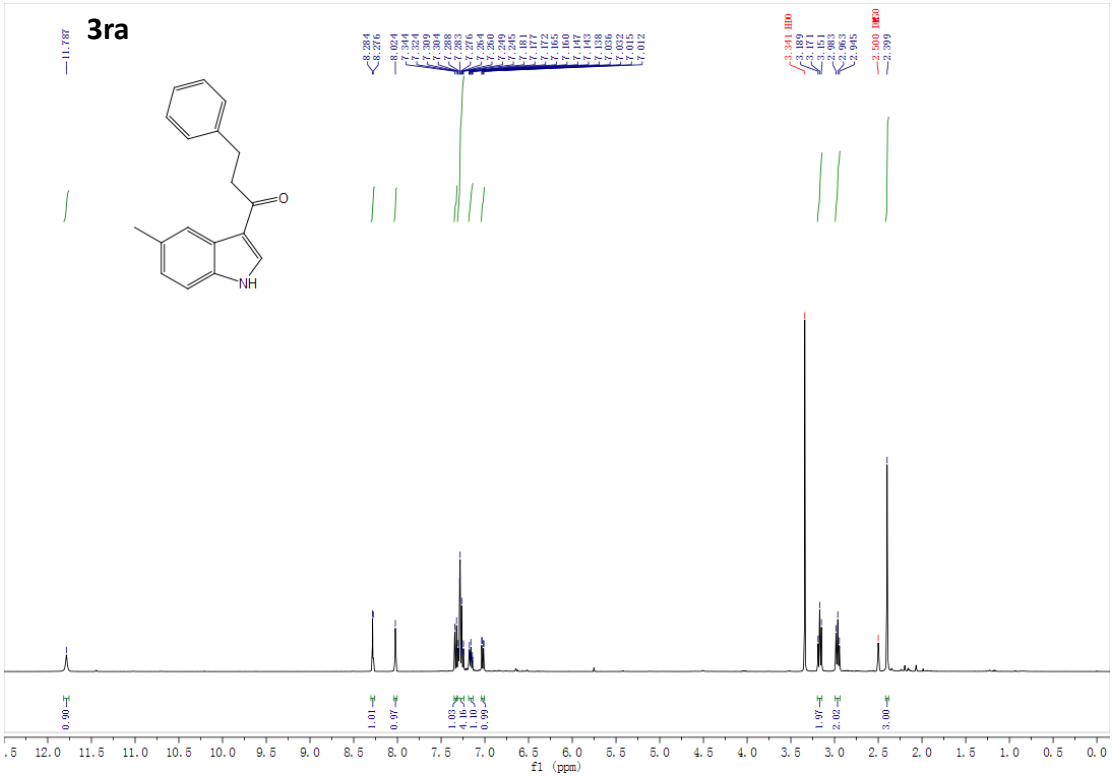
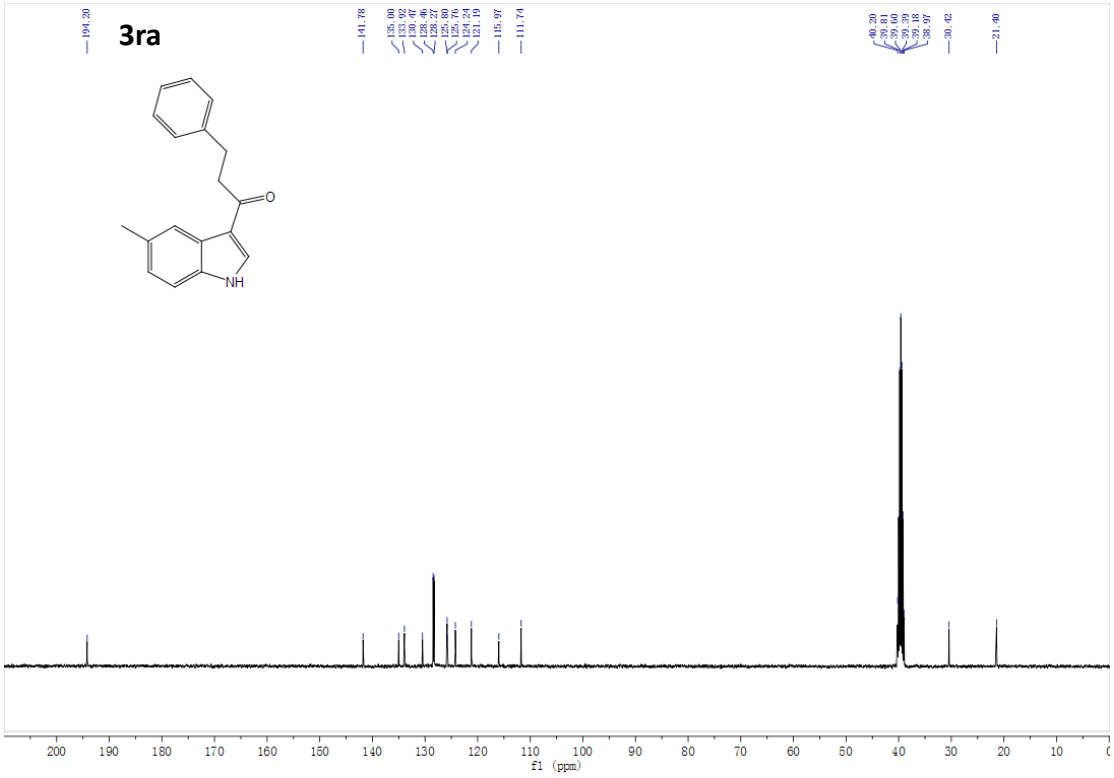
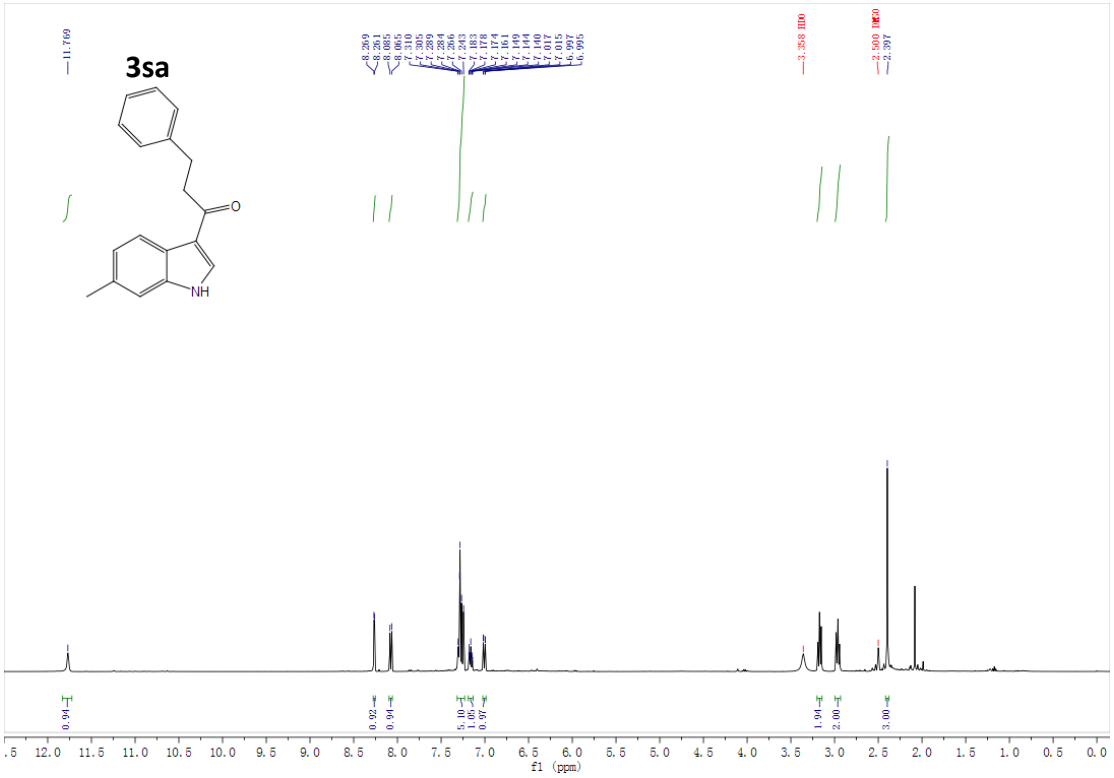
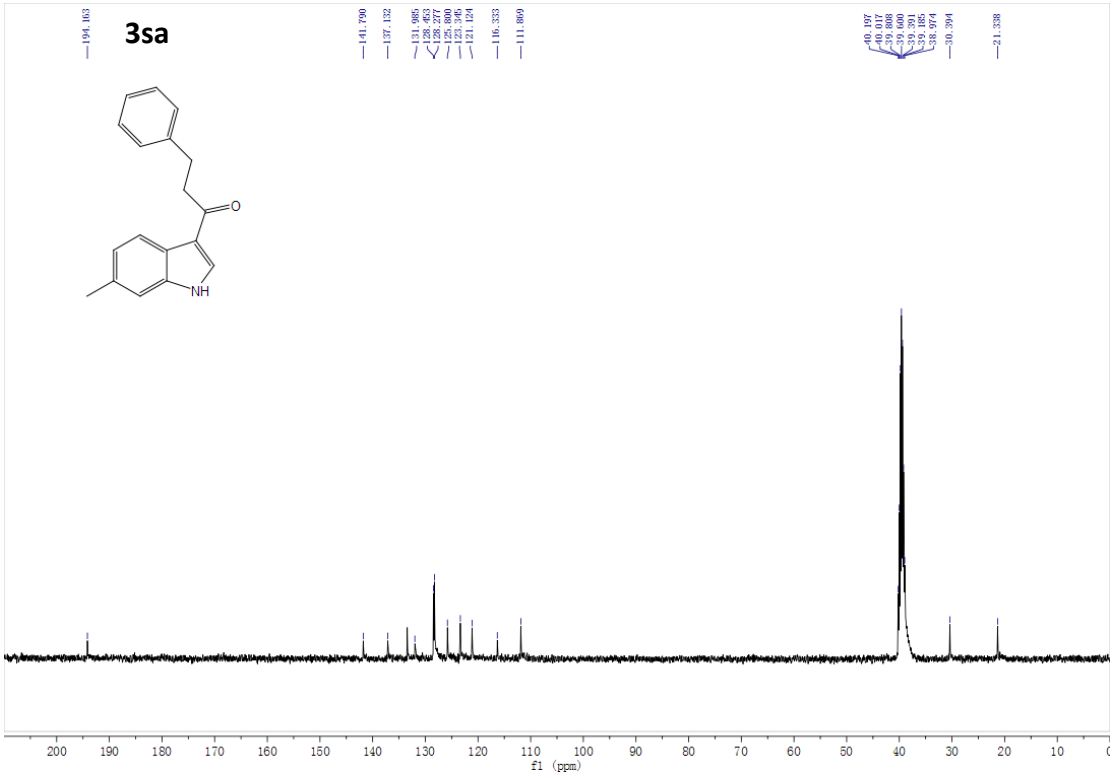
Br
O
NH
f1 (ppm)


3ra
O
NH
f1 (ppm)


3ra
O
NH
f1 (ppm)


3sa
O
NH
f1 (ppm)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O
NH
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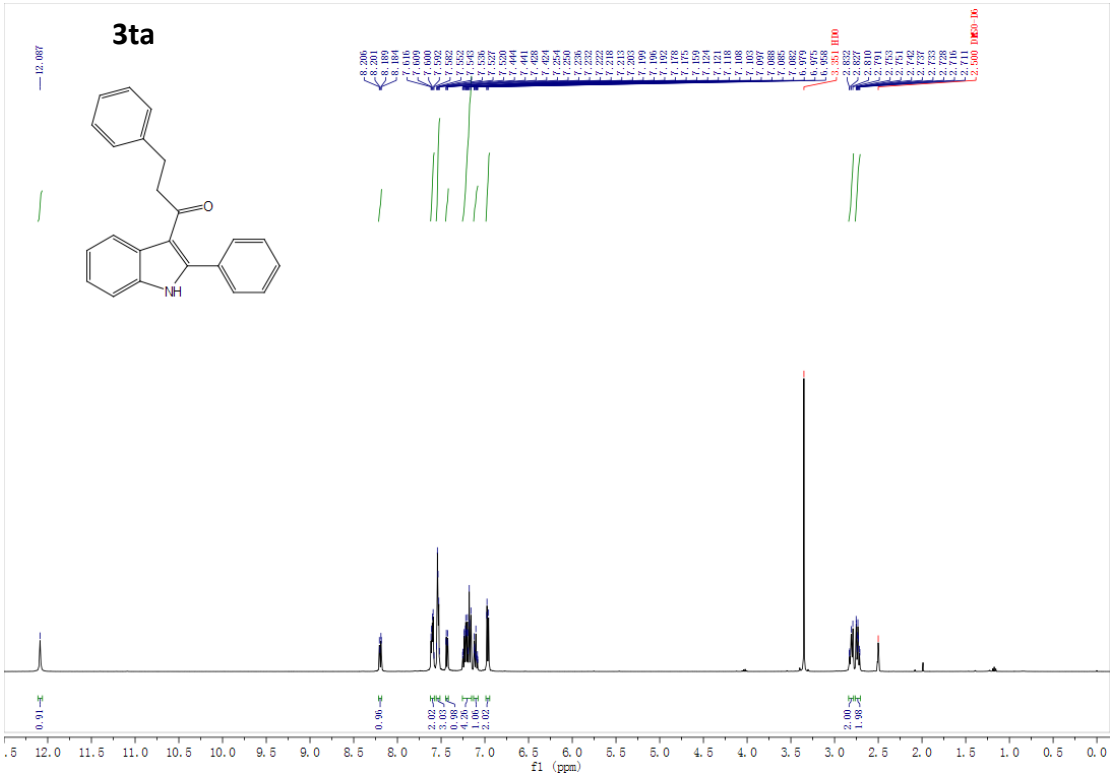
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O
NH
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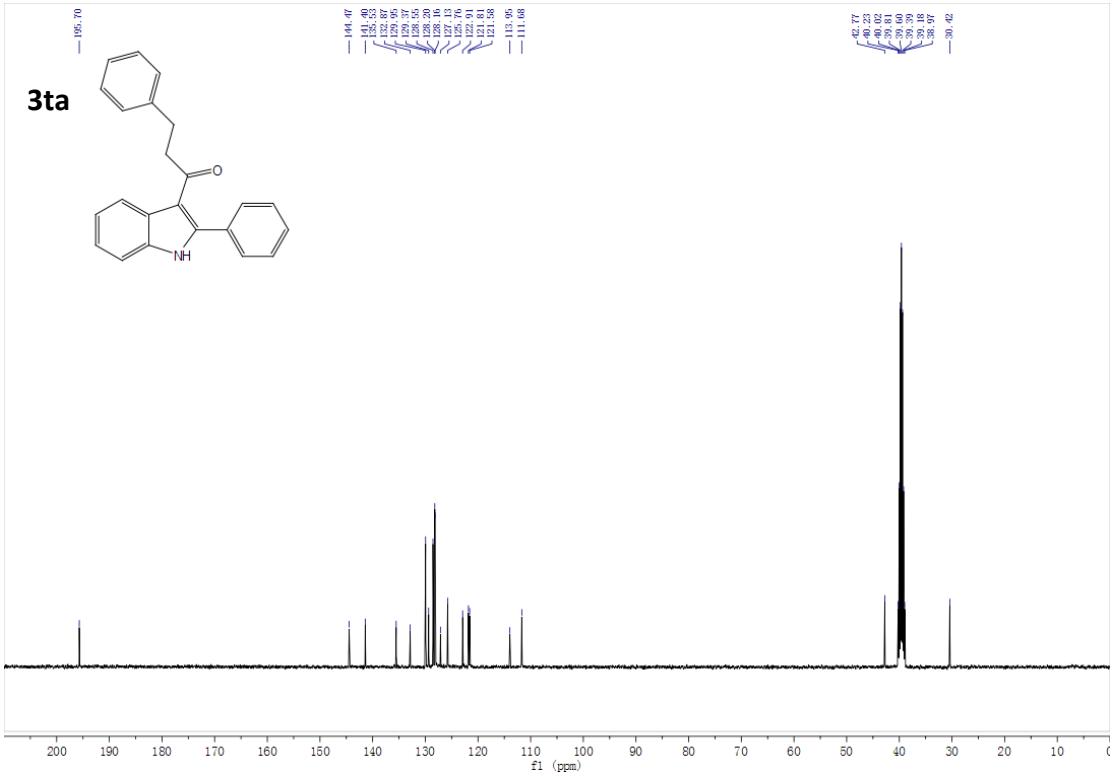
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O
NH
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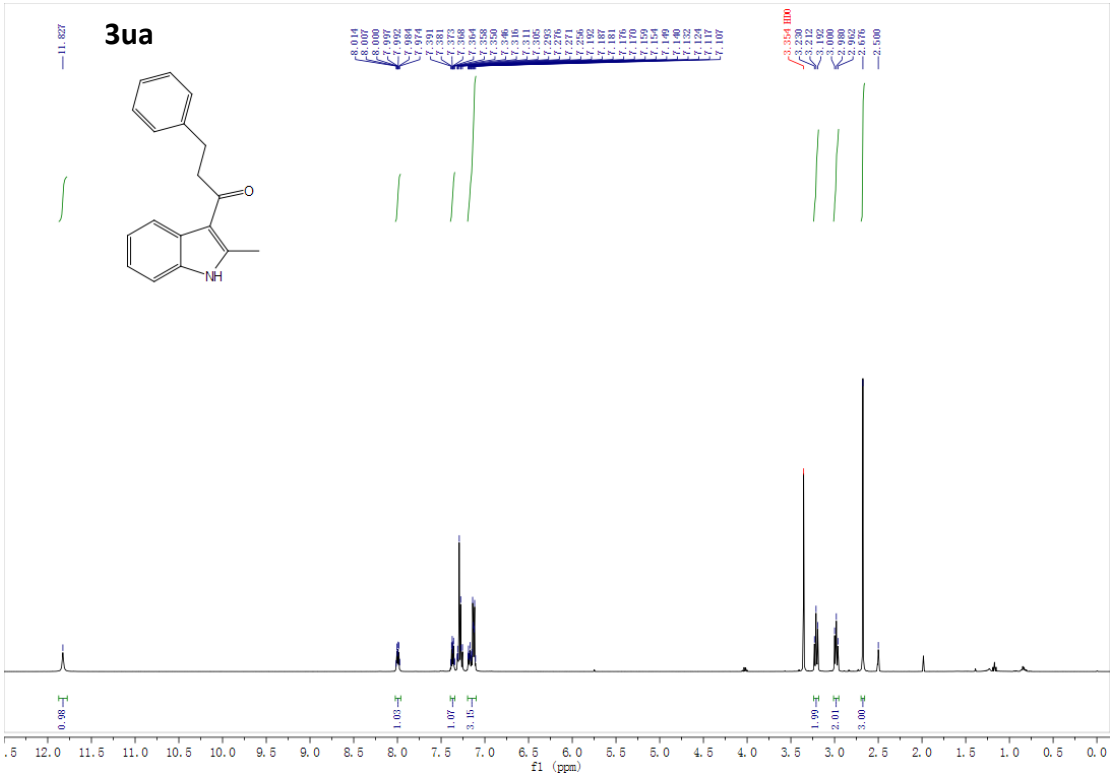
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O
NH
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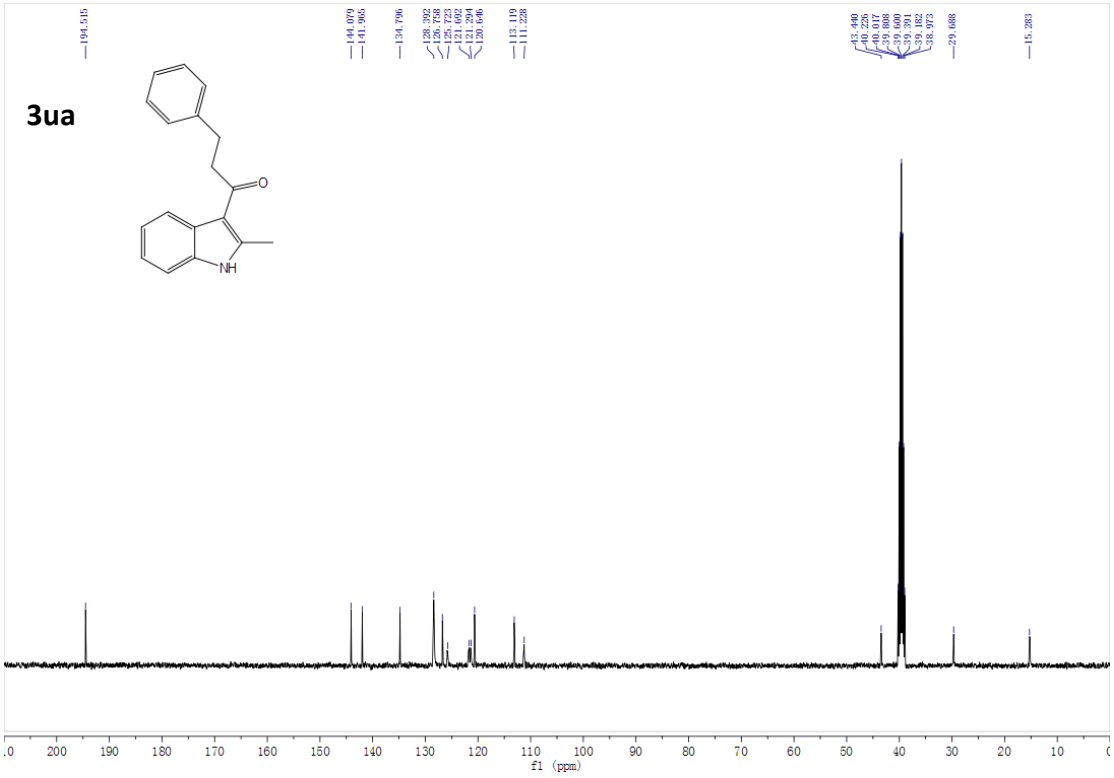
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NH
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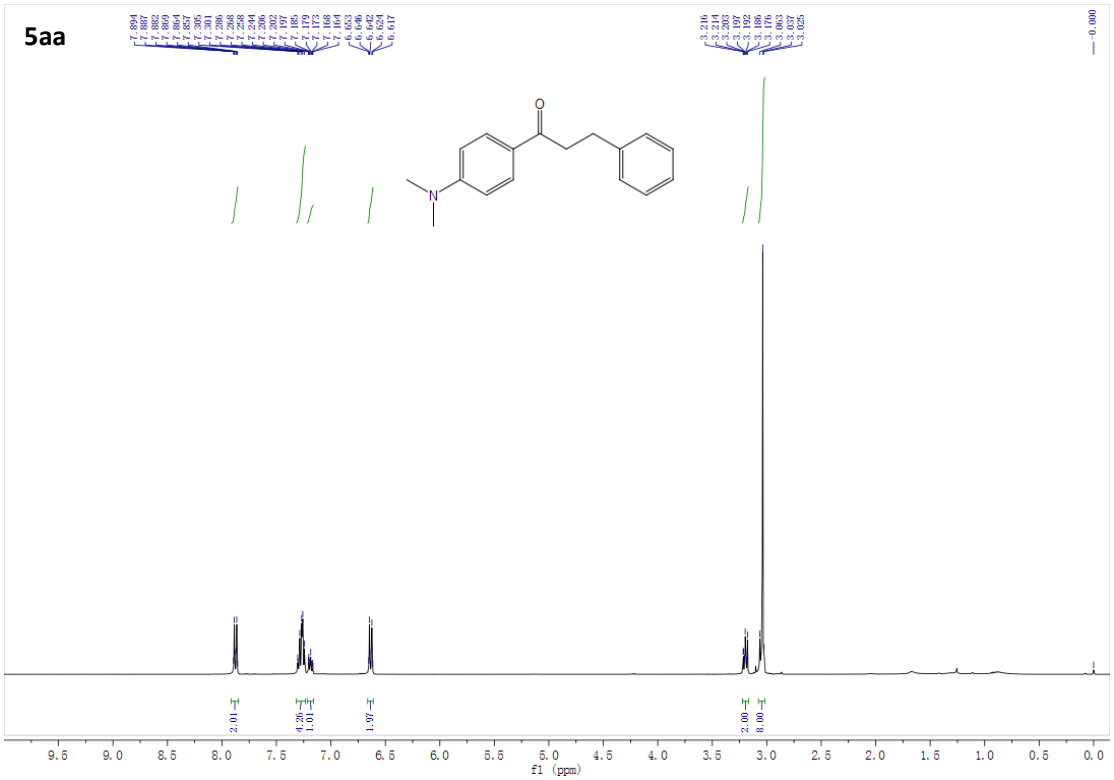
5aa
O
N
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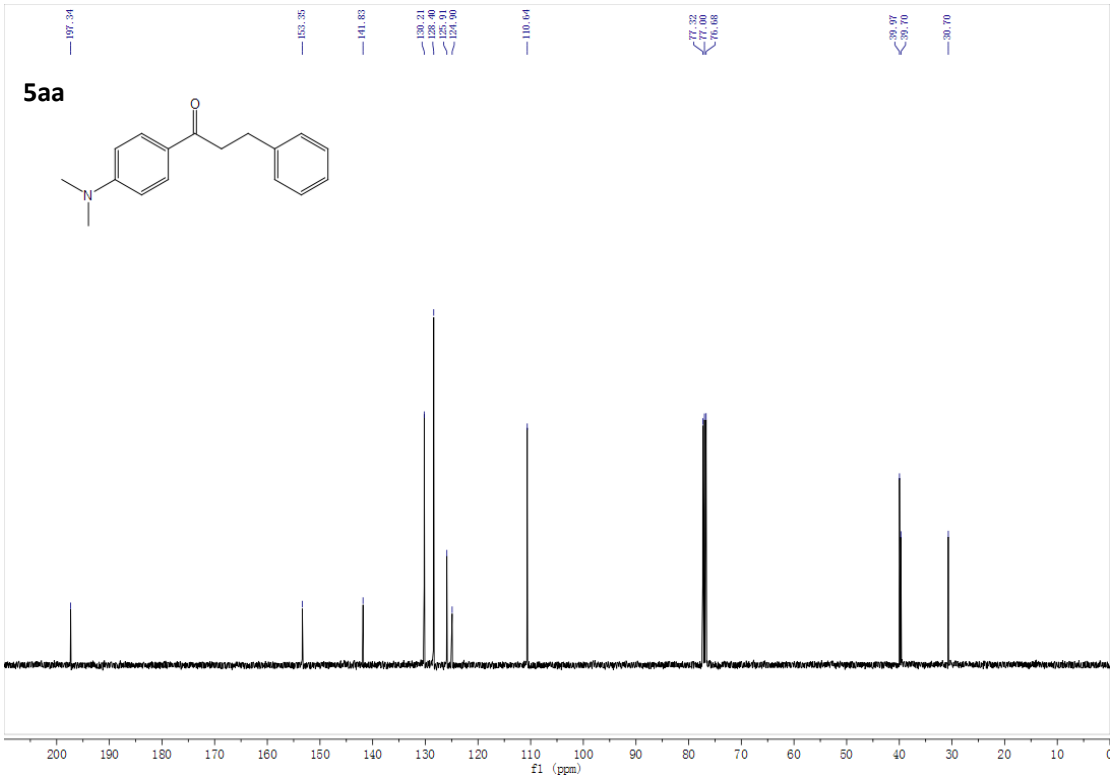
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O
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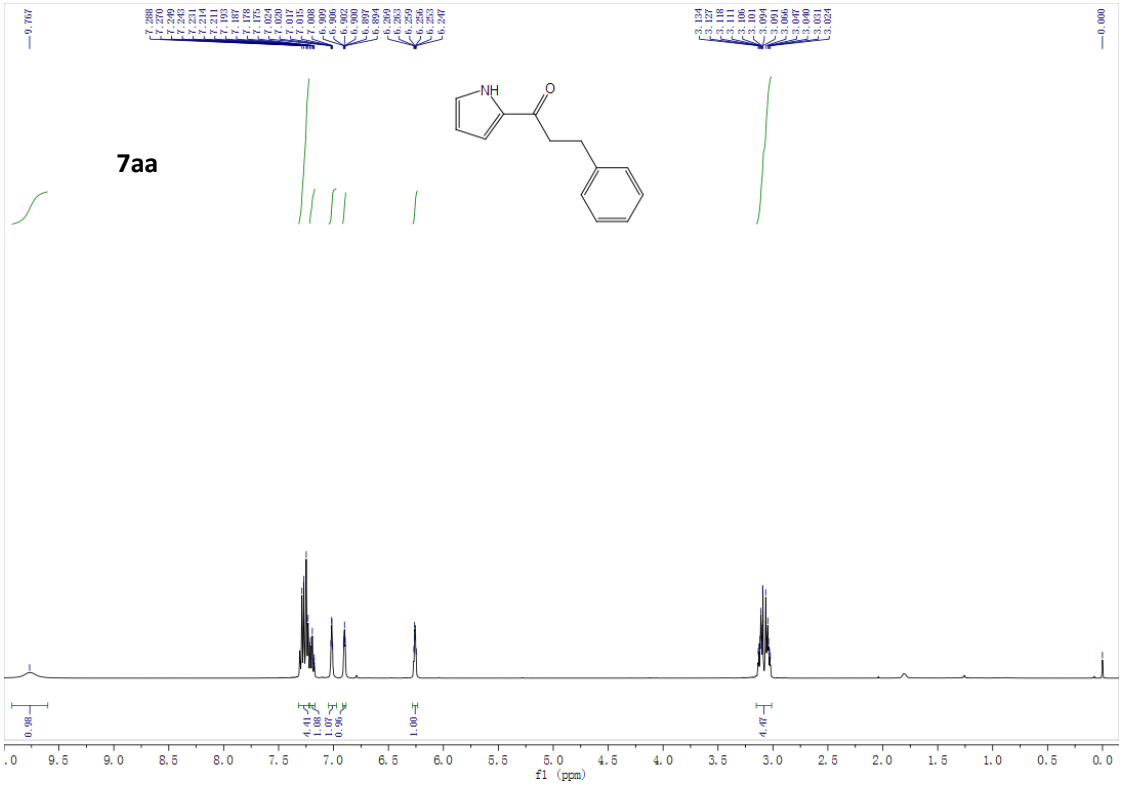
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NH
O
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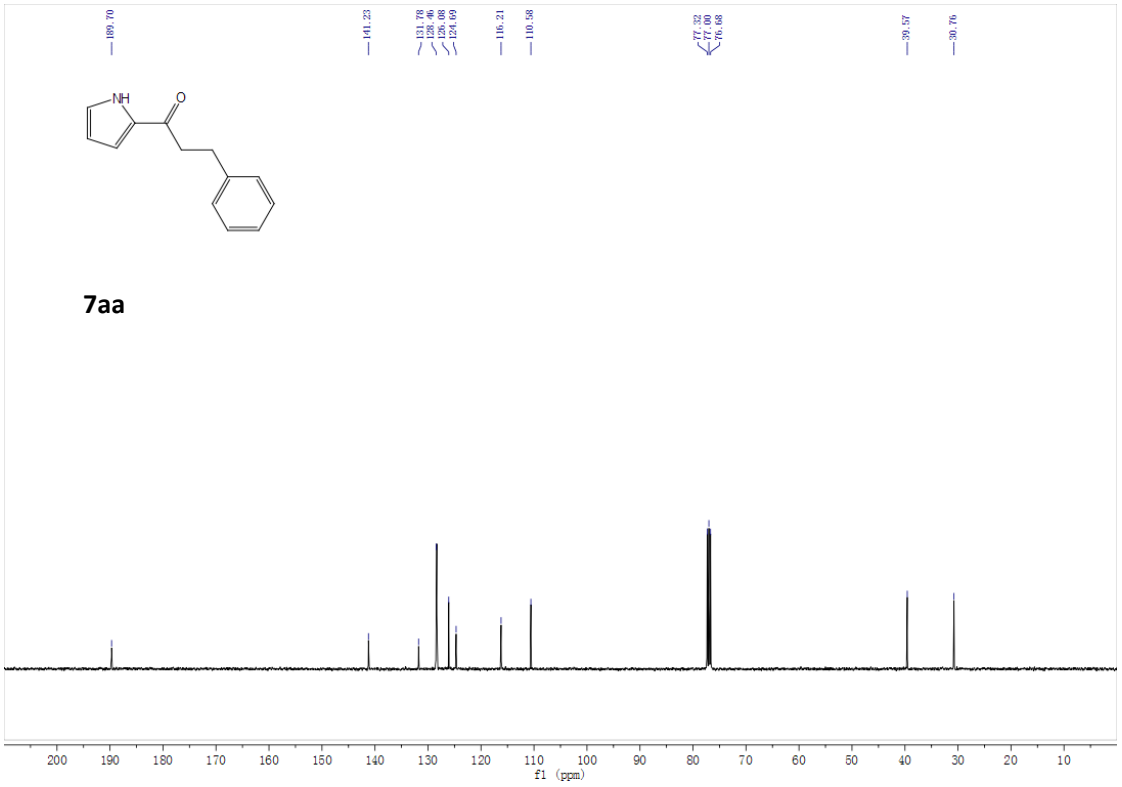
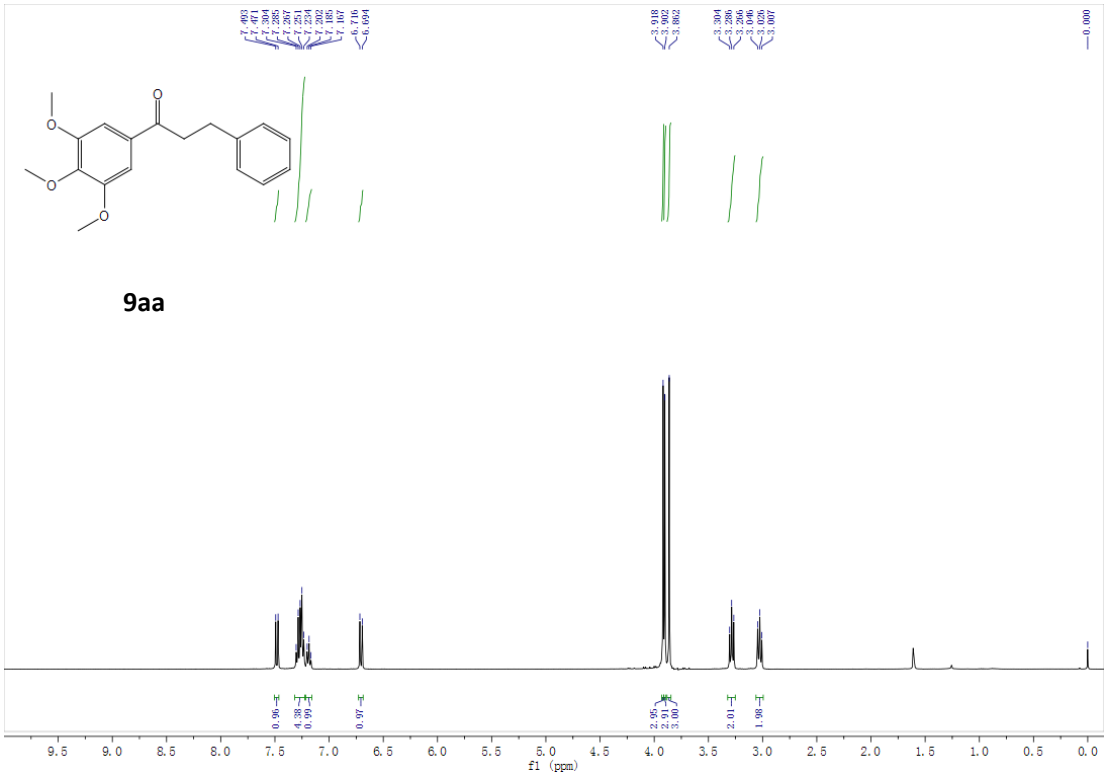
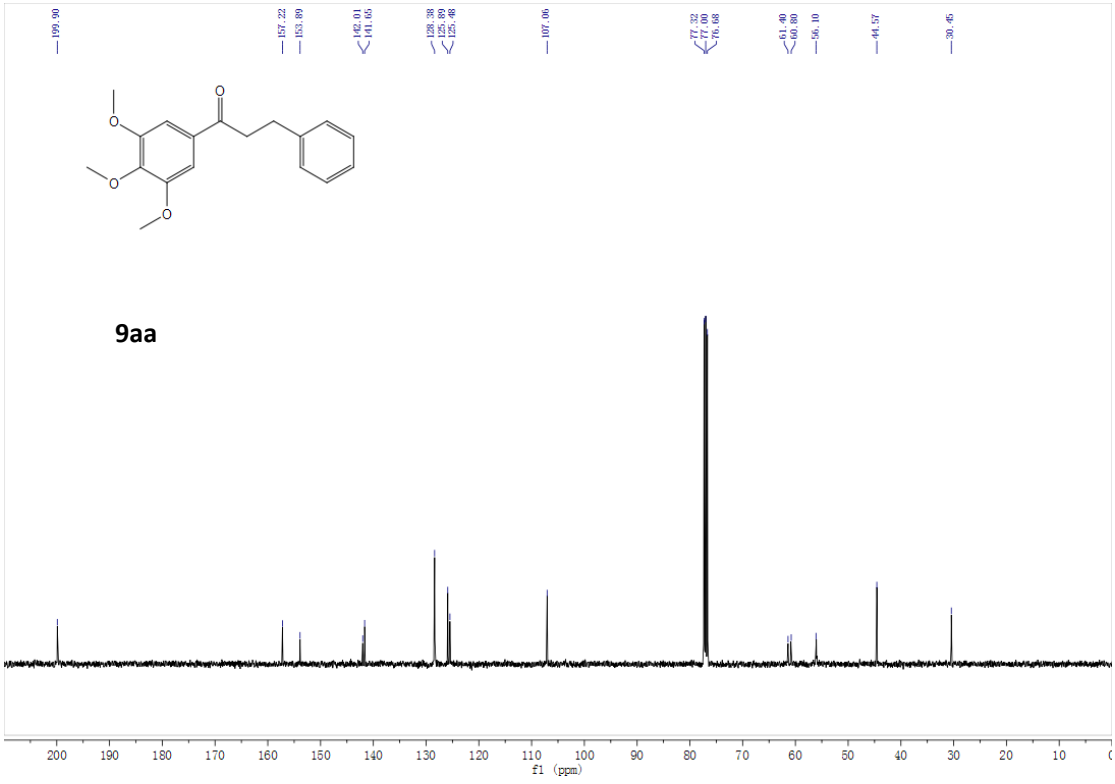

7aa
NH
O
f1 (ppm)


9aa
f1 (ppm)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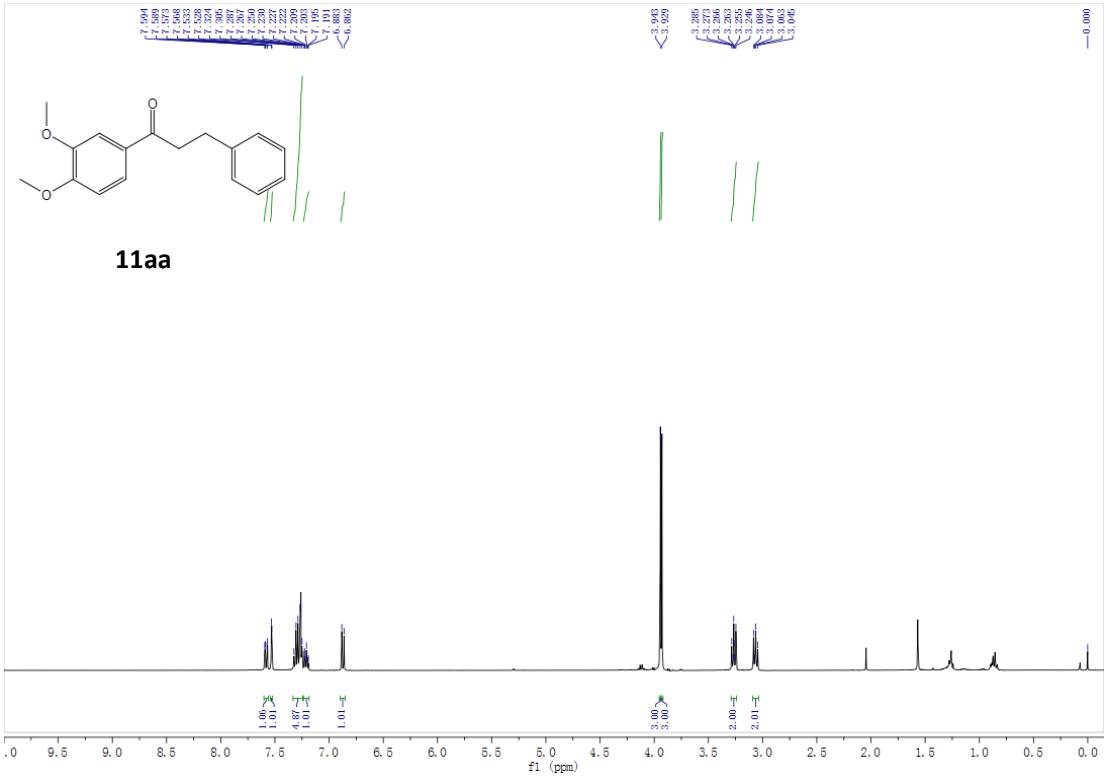
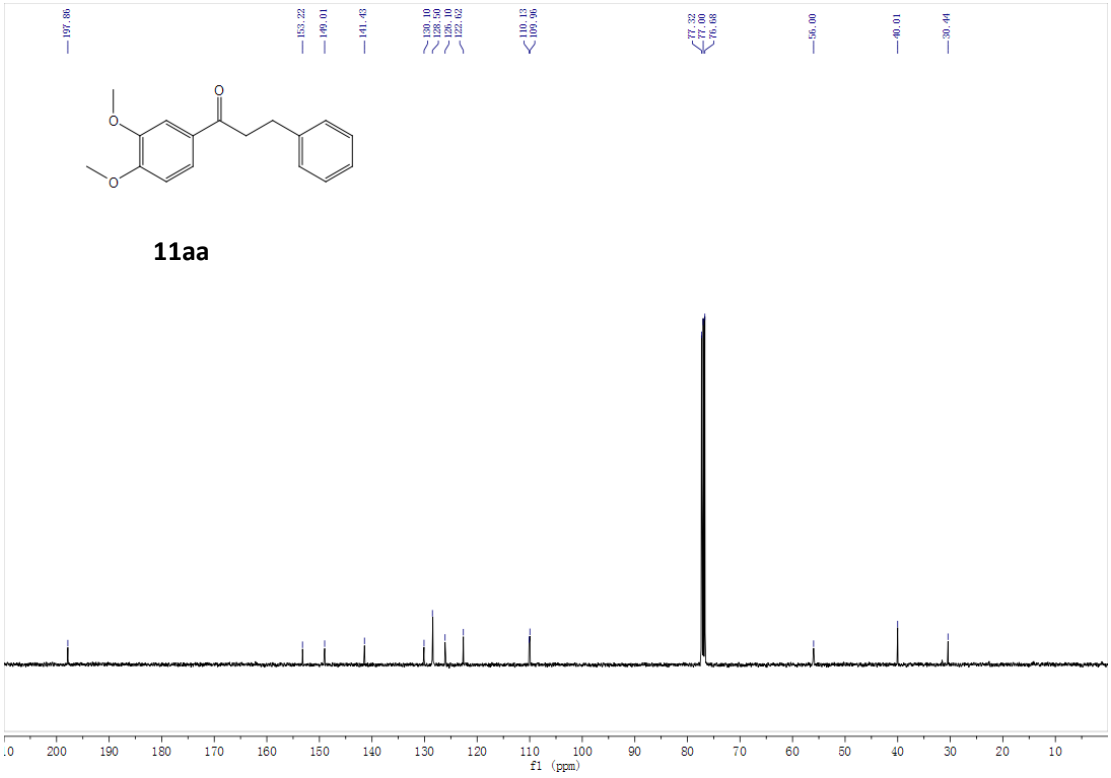
f1 (ppm)

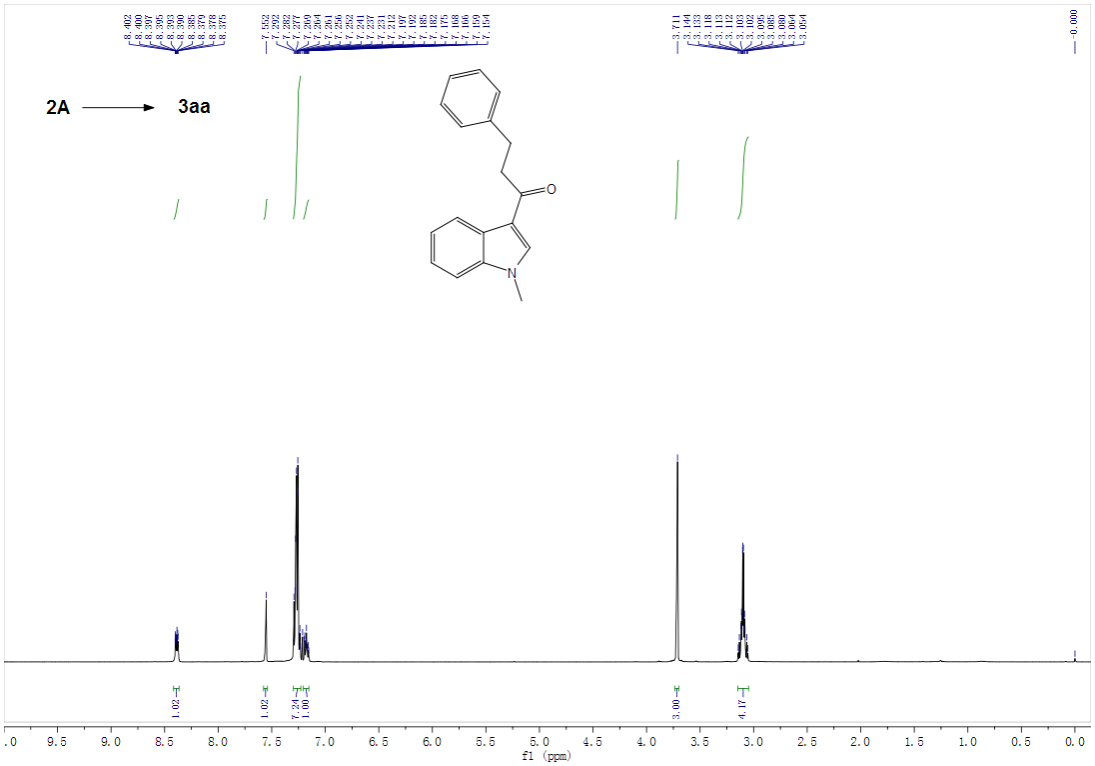


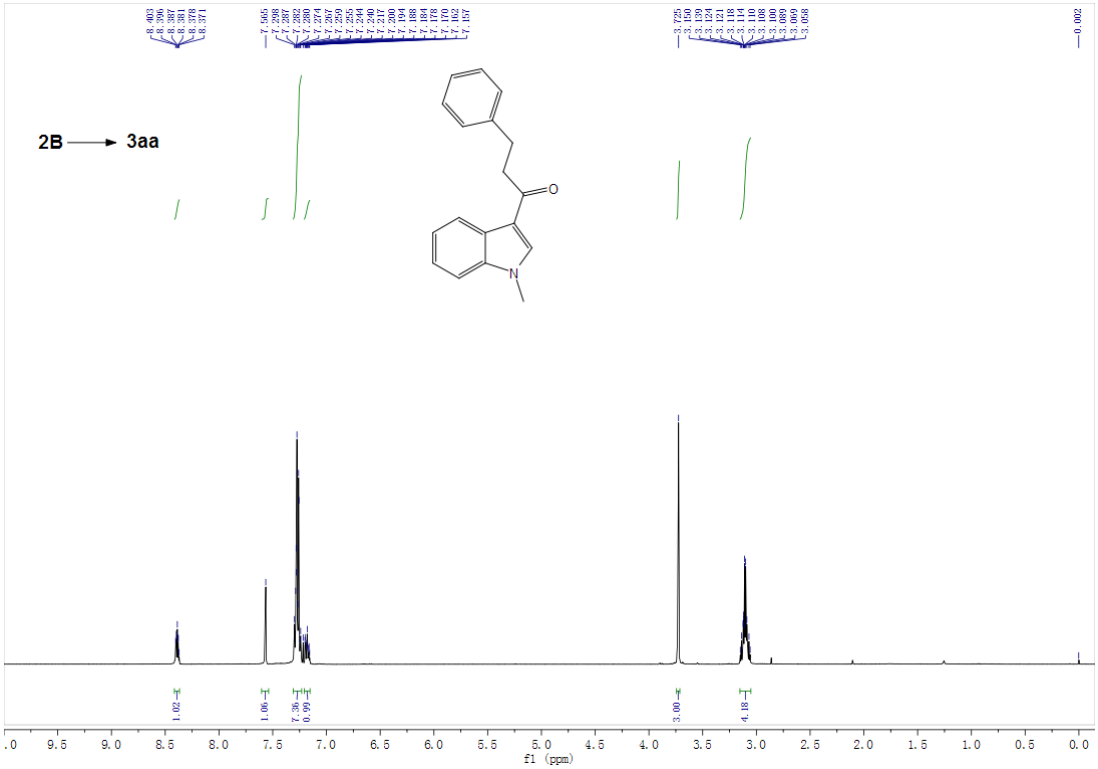
11aa

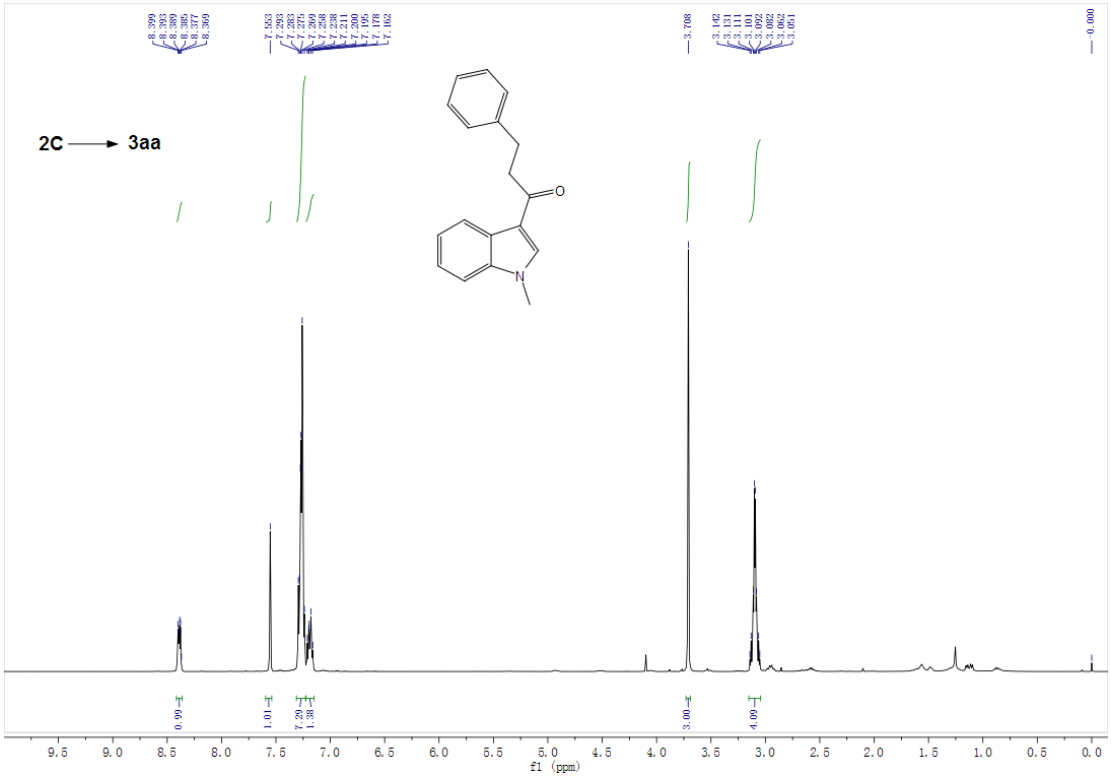


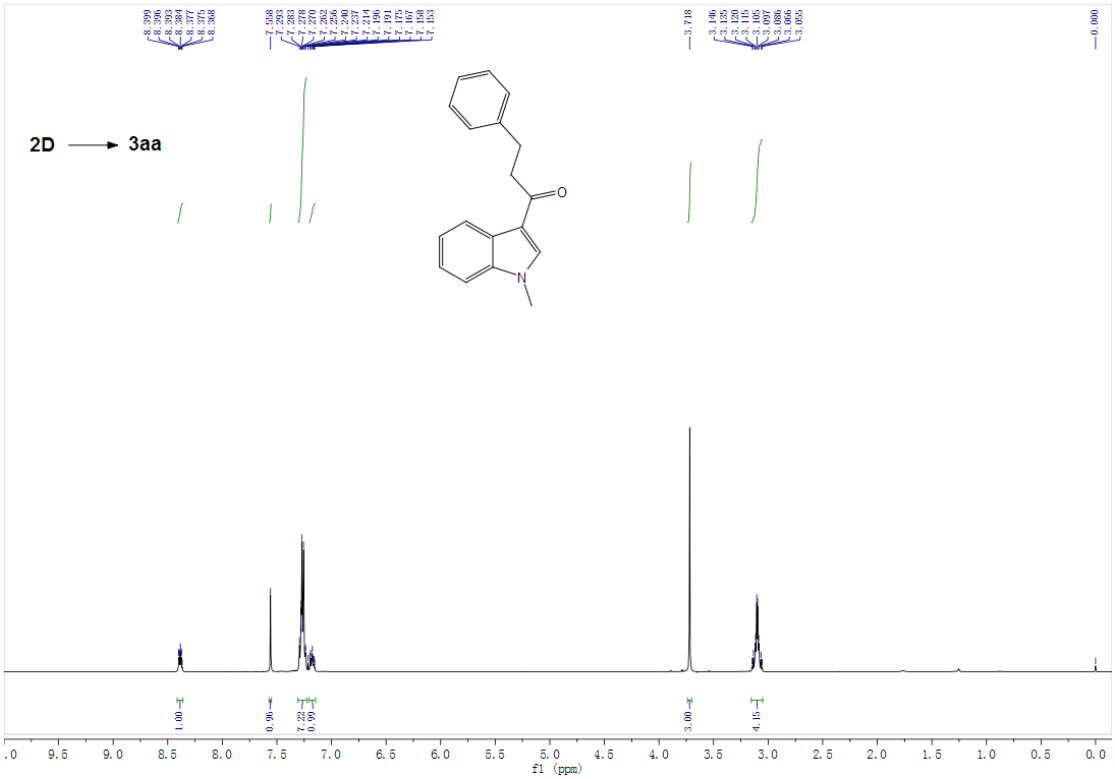
11aa

Separate copies of ^{1}H NMR spectra of 3aa of table 4






2C ⟶ 3aa
O
N
f1 (ppm)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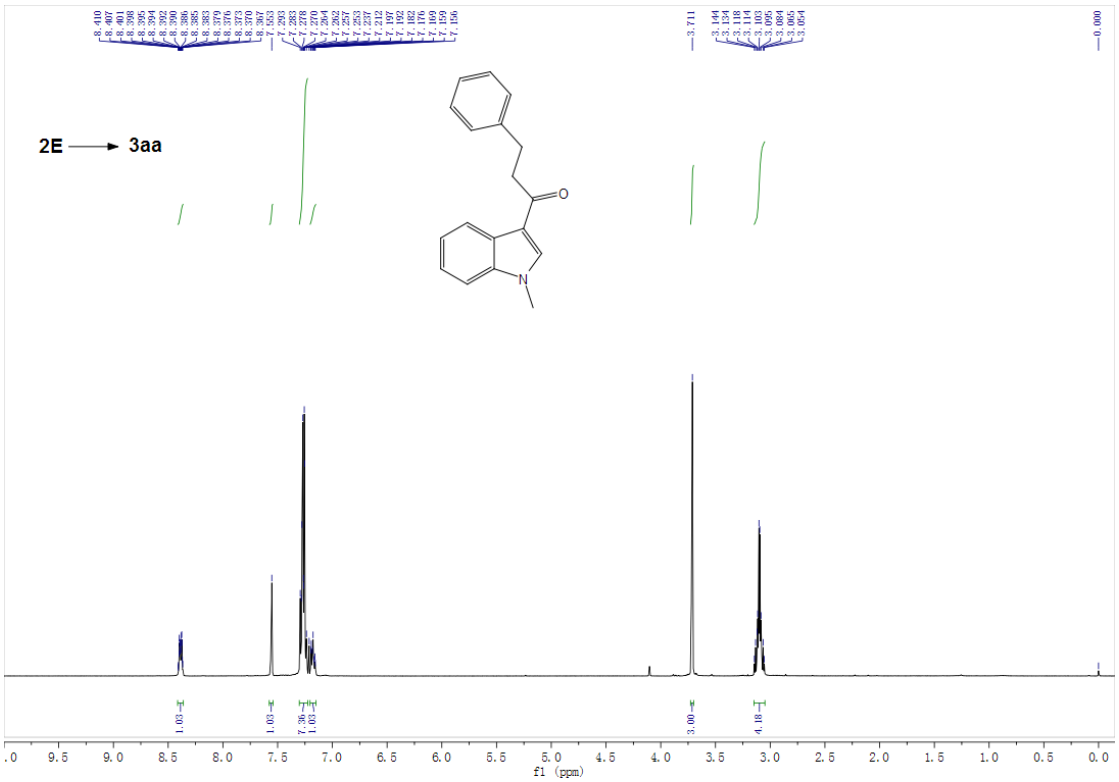
N
f1 (ppm)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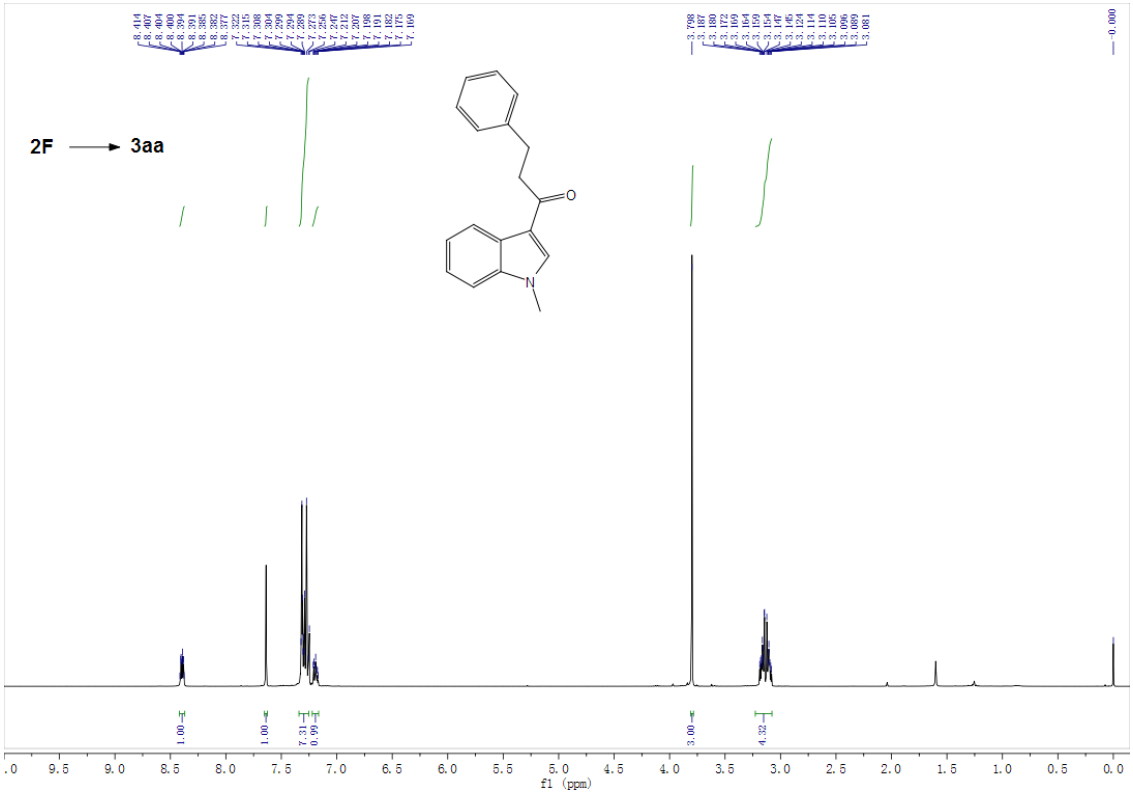
O
N
f1 (ppm)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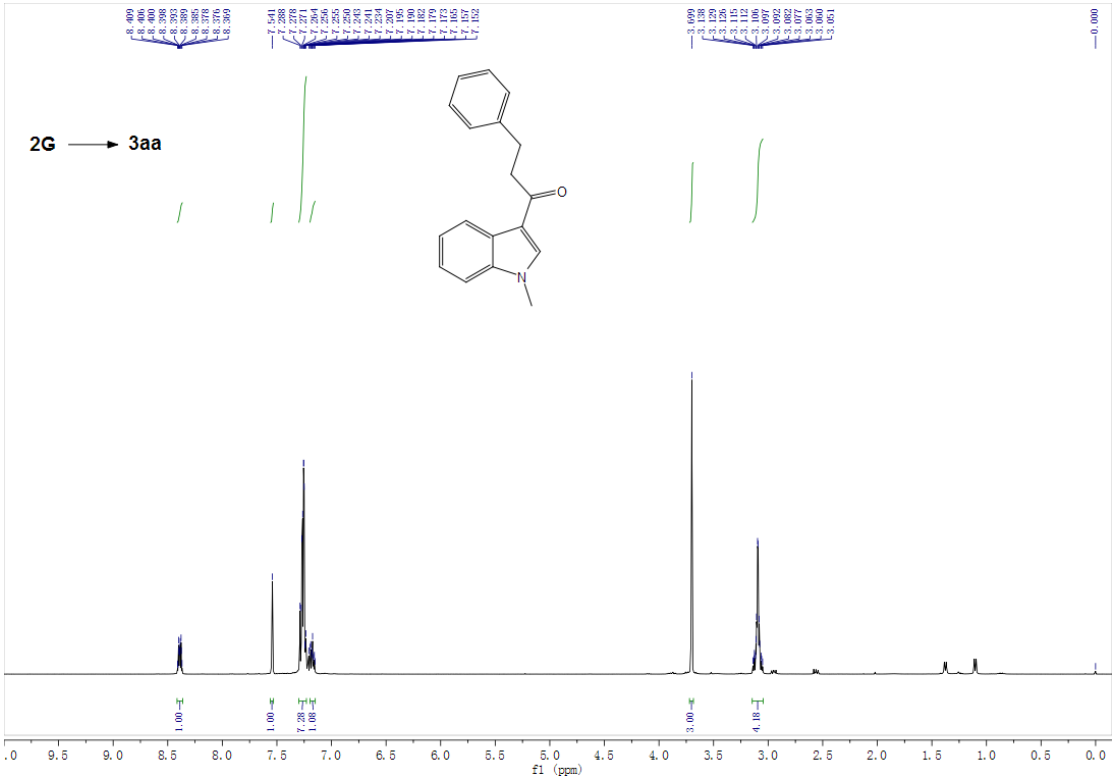
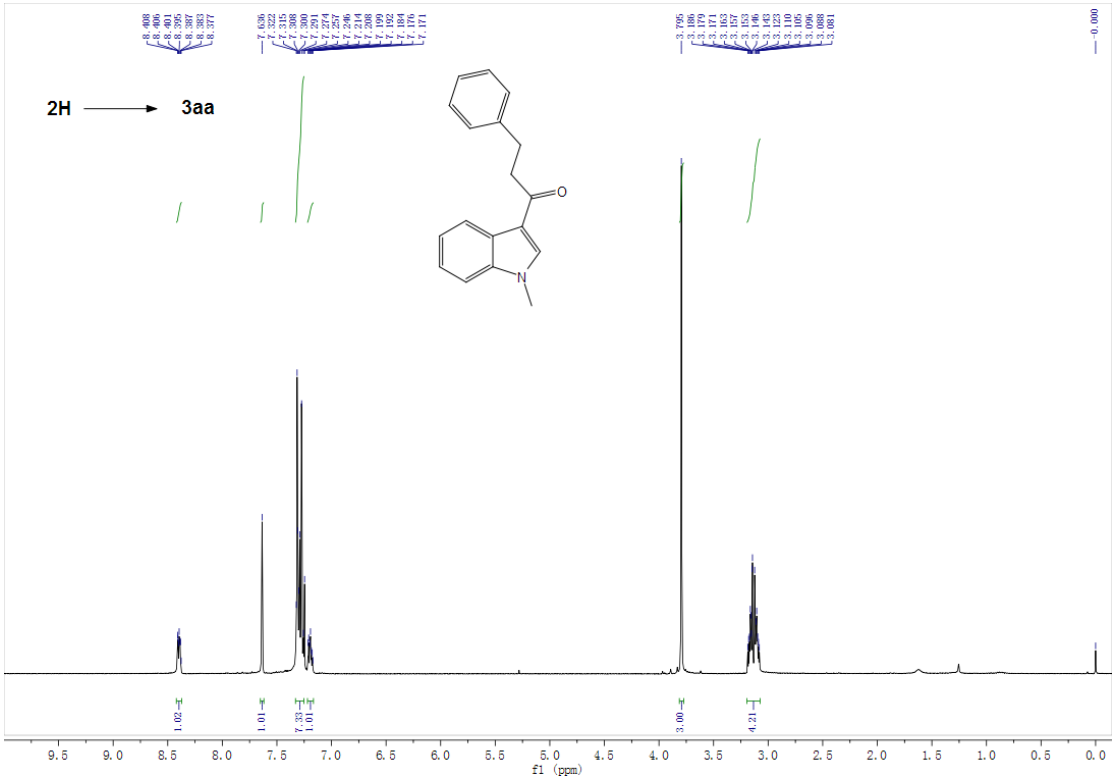
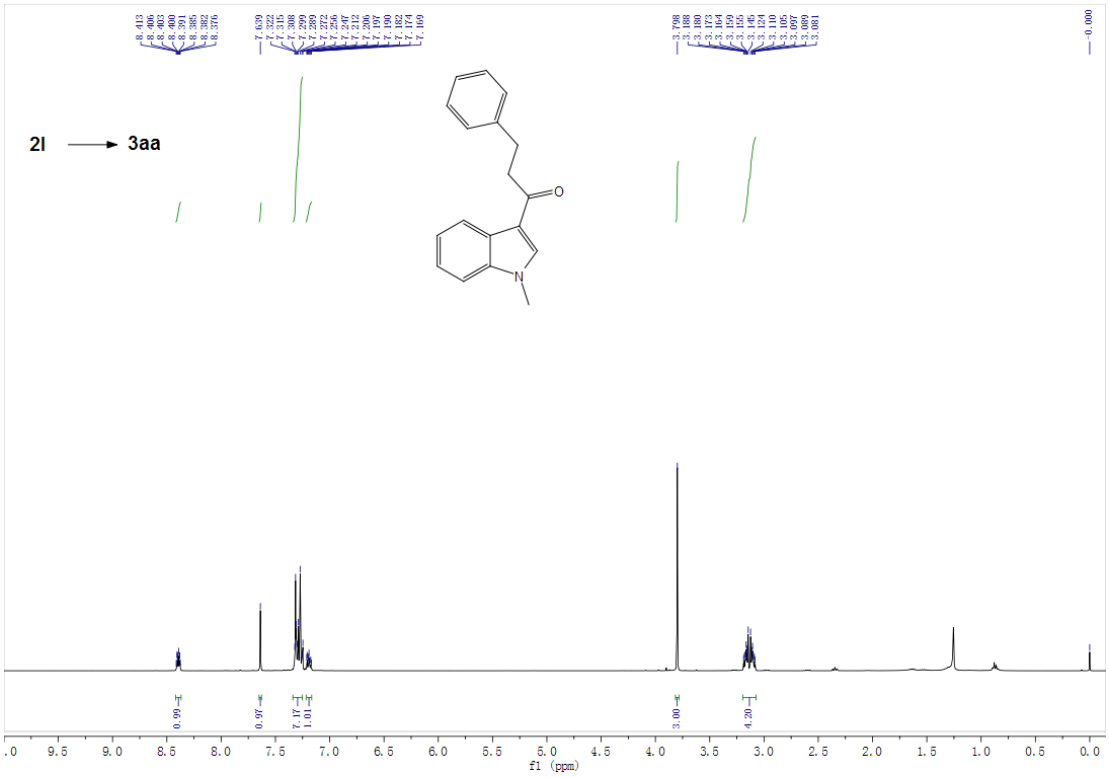
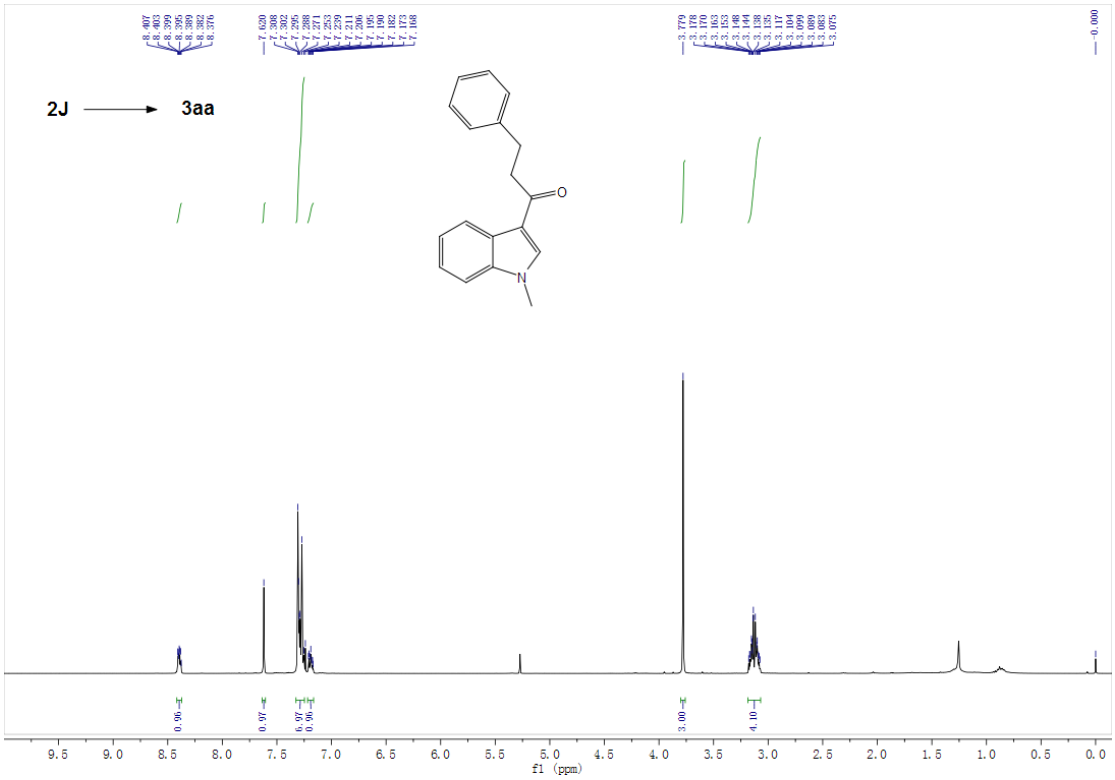
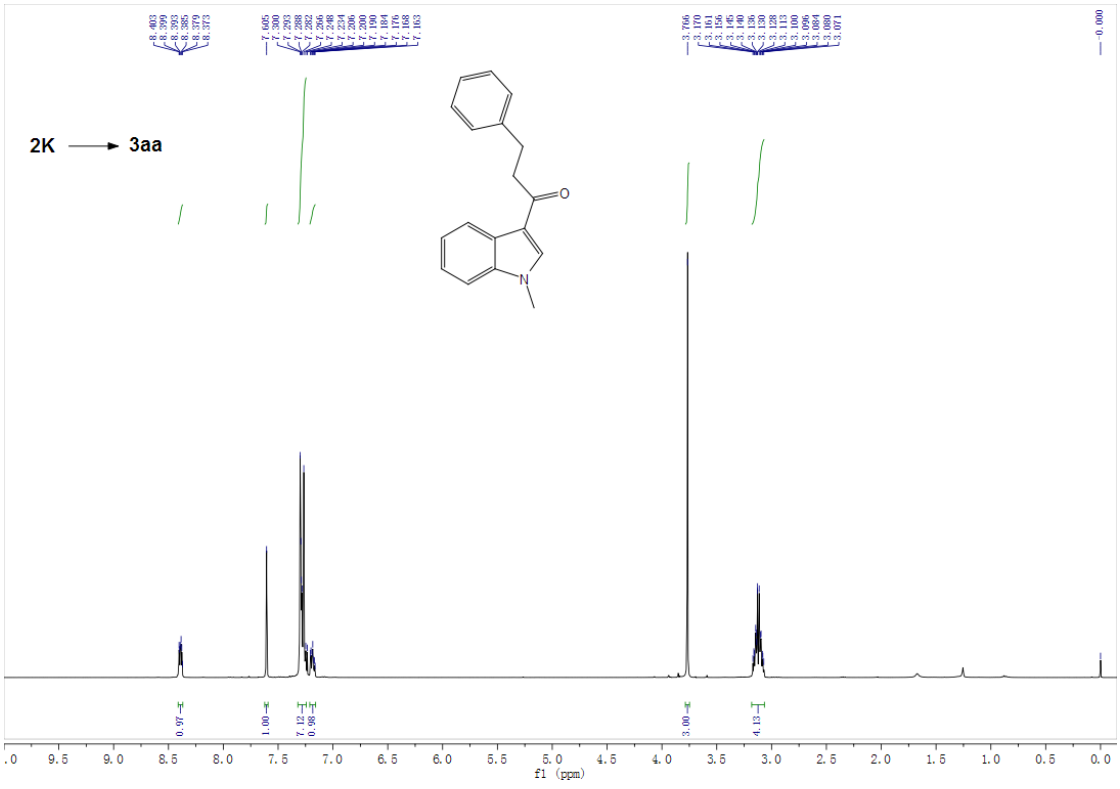
O
N
f1 (ppm)


2G ⟶ 3aa
O
N
f1 (ppm)


2H ⟶ 3aa
O
N
f1 (ppm)


2l ⟶ 3aa
O
N
f1 (ppm)


2J ⟶ 3aa
O
N
f1 (ppm)


2K ⟶ 3aa
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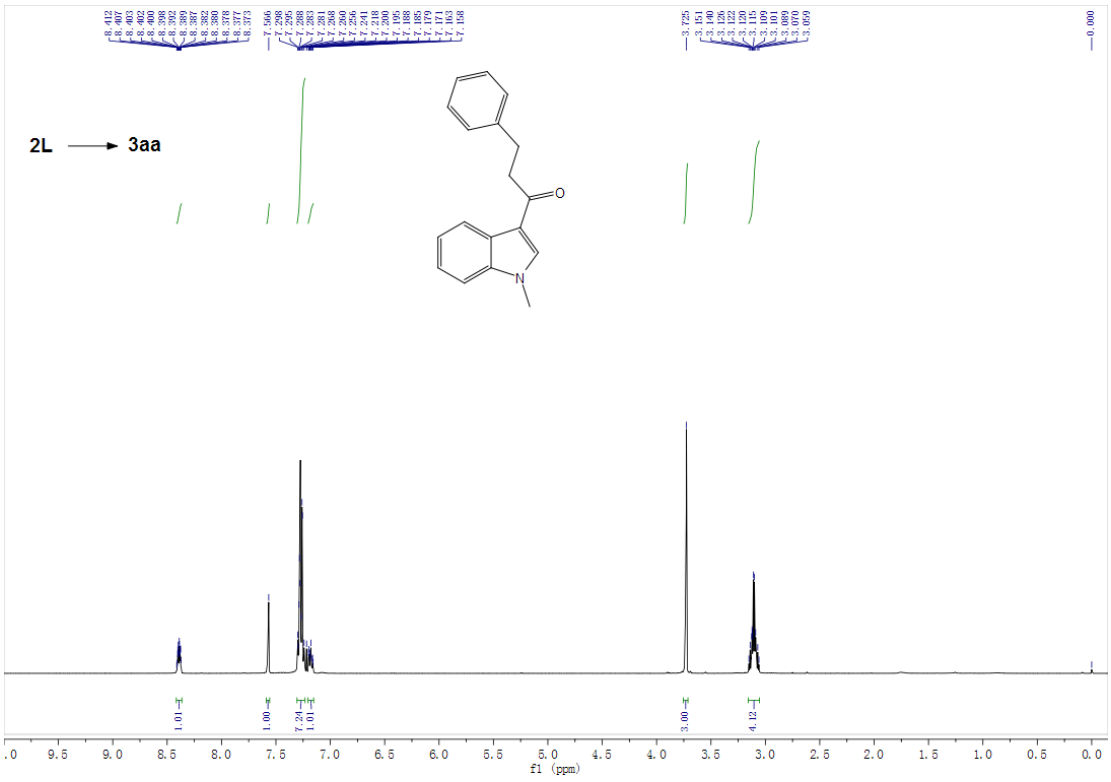
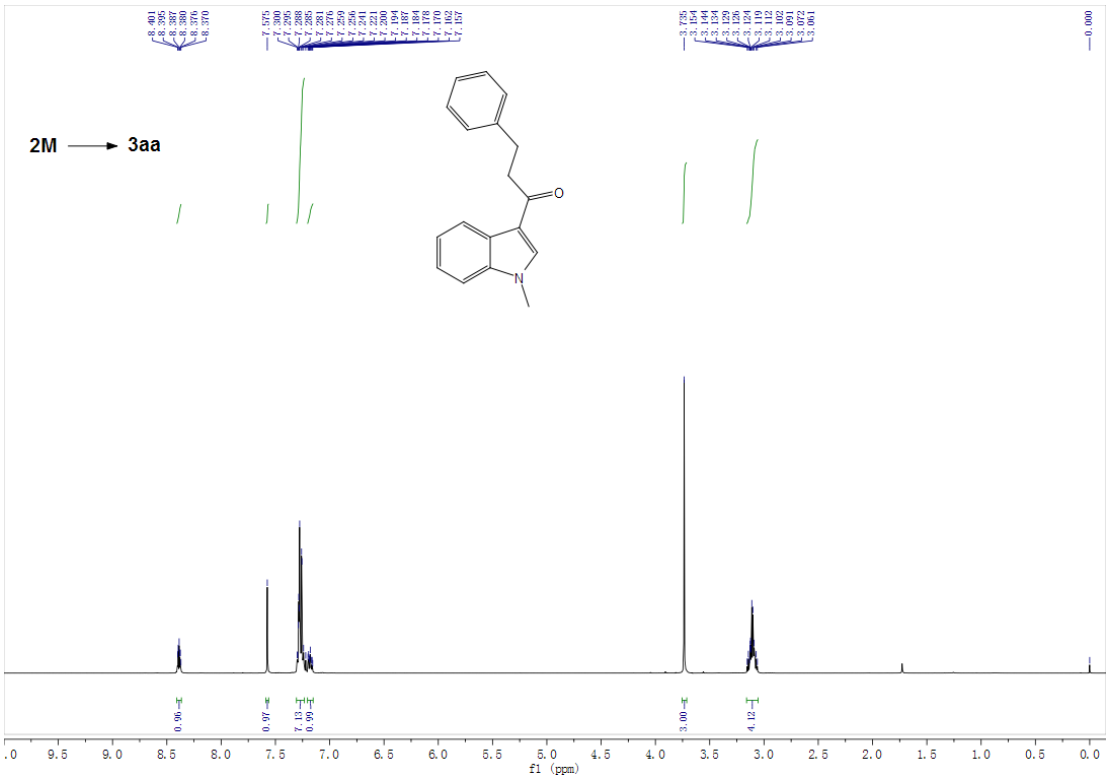
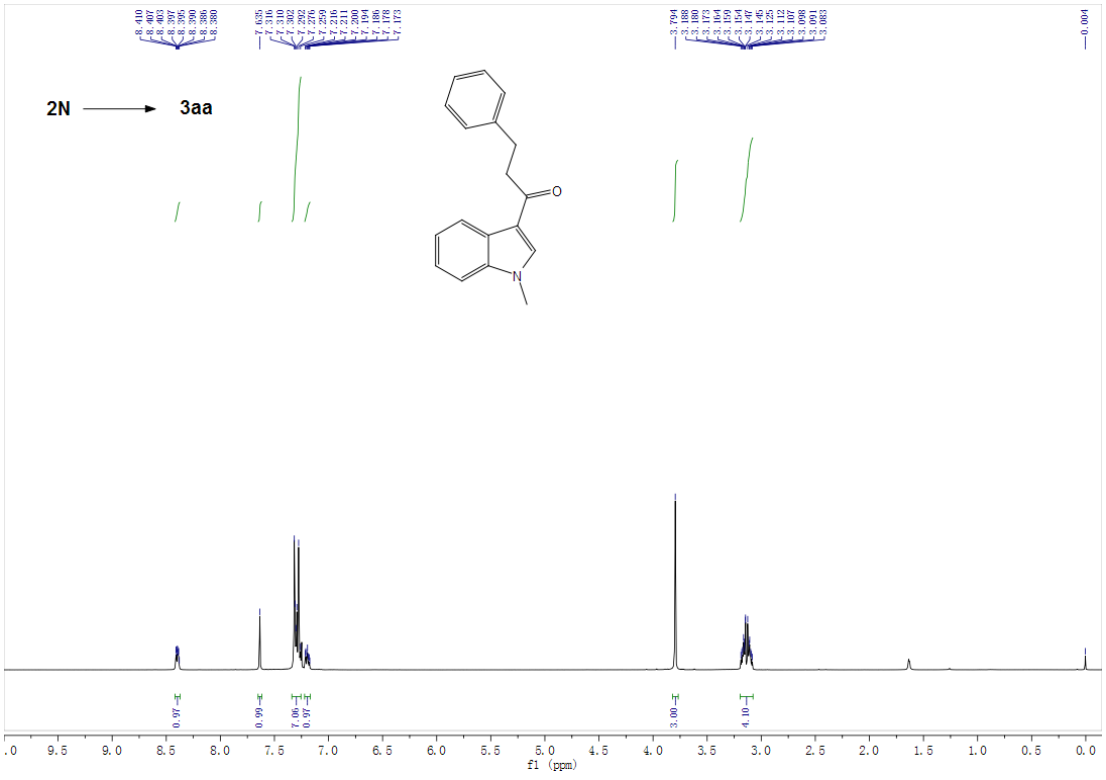

2L ⟶ 3aa
f1 (ppm)


2M ⟶ 3aa
O
N
f1 (ppm)


2N ⟶ 3aa
O
N
f1 (ppm)

References

1. J. Deruiter, B. E. Swearingen, V. Wandrekar, C. A. Mayfield, J. Med. Chem. 1989, 32, 1033.