Electronic Supplementary Information

A Concise Approach to 2-Pyrrolin-5-one Scaffold From α-Halohydroxamates and β-Keto Compounds

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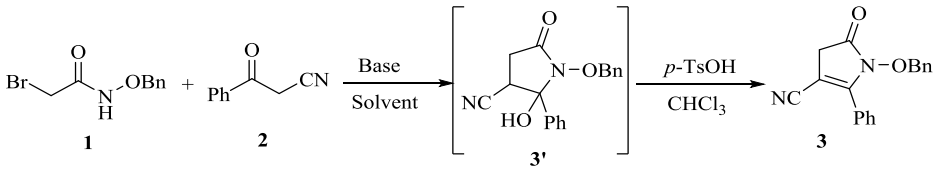
CONTENTS

1. Experimental Section

All solvents were purified and dried according to standard methods prior to use. Flash column chromatography was performed using Qingdao Haiyang flash silica gel (100–200 mesh). The ^{1}H, ^{13}C and ^{19}F NMR spectra were obtained in $CDCl_3$ using a Bruker-BioSpin AVANCE III HD NMR spectrometer at 500, 125 and 470 MHz, respectively. Chemical shifts are reported in parts per million (ävalue) calibrated against the residual solvent peak. The infrared spectra were recorded on a Bruker VERTEX 70 IR spectrometer as KBr pellets, with absorption reported in cm^{-1}. Mass spectra were obtained on Bruker APEX II FT-ICRMS mass spectrometer. Melting points were determined on a Stuard SMP3 melting point apparatus.

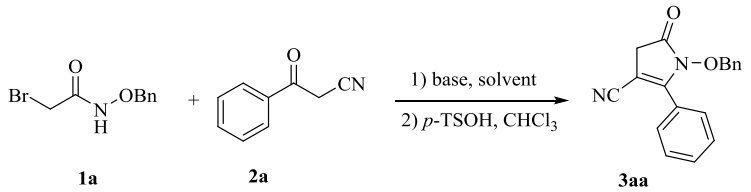
Table S1. The screening for the [3+2] annulation/elimination [a]



Entry	Base	Solvent	Time (h)	Yield(%)[b]
1	K_2CO_3	THF	24	36
2	Na_2CO_3	THF	24	trace
3	Cs_2CO_3	THF	24	46
4	**MeONa**	**THF**	**24**	**65**
5	EtONa	THF	48	54
6	^{t}BuONa	THF	48	15
7	NaOH	THF	48	n.d[c]
8	KOH	THF	24	n.d
9	Et_3N	THF	24	n.d
10	LDA	THF	24	n.d
11	MeONa	HFIP	24	n.d
12	MeONa	EtOH	24	55
13	MeONa	Et_2O	24	52
14	MeONa	$CHCl_3$	72	51
15	MeONa	CH_2Cl_2	72	48
16	MeONa	Toluene	72	43
17	MeONa	MeCN	48	50
18	MeONa	DMF	48	61
19	MeONa	Dioxane	48	46
20	MeONa	Acetone	48	59

[a]All reactions were performed using **1a** (0.3mmol, 1.5 equiv.), **2a**(0.2 mmol, 1.0equiv.) and different bases(0.4mmol, 2.0 equiv.) in different solvents at room temperature under N_2 atmosphere, the reaction process was monitored by TLC; [b] The isolated yield; [c] not detected the desired product.

Table S2. The screening for the amount of the base and the additives

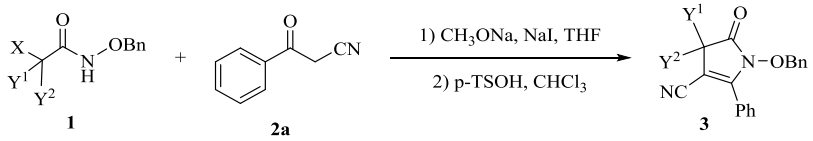


1a **2a** **3aa**

Entry	The ratio (**1a** : **2a** : CH_3ONa)	Additives	Temp.	Time (h)	Yield(%)
1	1.5 : 1 : 2	4Å MS	rt	24	66
2	1.5 : 1 : 2	NaI	rt	24	85
3	1.5 : 1 : 1.5	NaI	rt	24	57
4	**1.5 : 1 : 3**	**NaI**	**rt**	**24**	**92**
5	1.5 : 1 : 3	-	rt	48	72
6	1.5 : 1 : 4	NaI	rt	24	90
7	1.5 : 1 : 3	NaI	0	48	85
8	1.5 : 1 : 3	NaI	40	24	86
9	1 : 1.5 : 3	NaI	rt	24	62

[a]All reactions were performed in THF(2mL) under N_2 atmosphere using **2a** (0.2mmol), the other reagents were added according to the corresponding ratios shown in Table S2.

Table S3. The optimization for the different **α**-halohydroxamates

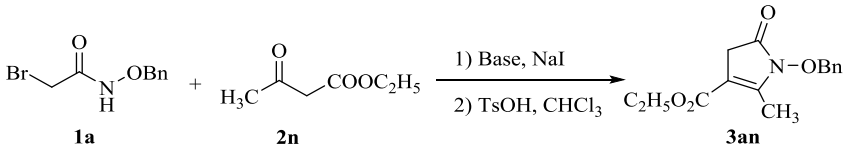


1 **2a** **3**

Entry	X	Y^1.	Y^2	Temp.	Time (h)	Yield(%)[b]
1	Cl	H	H	rt	48	75
2	Br	CH_3	H	rt~40	72	–
3	Br	CH_3	CH_3	rt~40	72	–
4	Cl	H	H	40	24	73

[a]All reactions were performed in THF(2 mL) under N_2 atmosphere using **1** (0.3 mmol), **2a** (0.2 mmol), CH_3ONa (0.6 mmol) and NaI (0.04 mmol), then *p*-TSOH(0.1mmol) in $CHCl_3$(2.0 mL); [b] The isolated yield of product **3**.

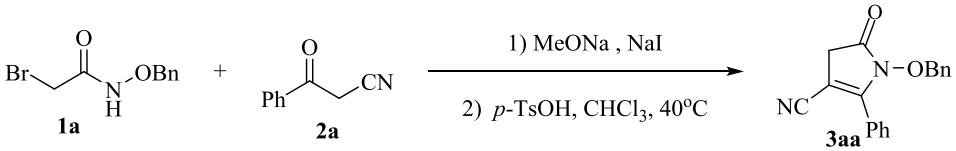
Table S4. The optimization for the reaction of *β*-keto ester with **α**-bromohydroxamates



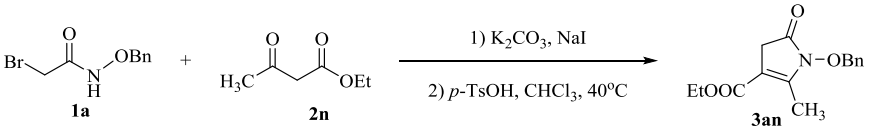
Entry	Base	Solvent	Temp.	Time (h)	Yield(%)[b]
1	CH_3ONa	THF	rt	24	37
2	C_2H_5ONa	THF	rt	24	34
3	^tBuOK	THF	rt	24	-
4	**K_2CO_3**	**THF**	**rt**	**24**	**82**
5	Na_2CO_3	THF	rt	24	60
6	Cs_2CO_3	THF	rt	24	38
7	K_2CO_3	CH_3CN	rt	48	51
8	K_2CO_3	C_2H_5OH	rt	48	-
9	K_2CO_3	HFIP	rt	48	-
10	K_2CO_3	$CHCl_3$	rt	48	25
11	K_2CO_3	DMF	rt	48	36

[a]All reactions were performed in THF under N_2 atmosphere using **1a**(0.3 mmol), **2a** (0.2mmol), base (0.6 mmol) and NaI(0.04mmol); [b]The isolated yield of product **3**.

2. General procedure for the optimal conditions:



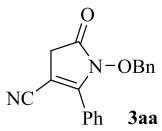
General procedure A: To a Schlenk tube were added compound **1a** (0.3 mmol, 1.5 eq.), **2a** (0.2 mmol, 1.0 eq.), MeONa (32 mg, 0.6 mmol, 3.0 eq.), NaI (6 mg, 0.04 mmol, 20 mol%) and THF (2.0 mL) under N_2, the mixture was stirred at room temperature until the reaction was completed(monitored by TLC). The reactant was filtered through celite plate, and the solvent was removed under vacuum, subsequently a solution of *p*-TsOH (19 mg, 0.1 mmol) in $CHCl_3$ (2 mL), was added and stirred at 40°C for 1h. After removing the solvent, the residue was purified by a flash column chromatography (Petroleum ether/ EtOAc = 5:1~3:1, V/V) to afford the product **3aa**.



General procedure B: To a Schlenk tube were added compound **1a** (0.3 mmol, 1.5 eq), **2n** (0.2 mmol, 1.0 eq), K_2CO_3 (82.8 mg, 0.6 mmol, 3.0 eq.), NaI (6 mg, 0.04 mmol, 20 mol%) and THF (2.0 mL) under N_2, the mixture was stirred at room temperature until the reaction was completed (monitored by TLC). The reactant was filtered through celite plate, the solvent was removed under vacuum, and a solution of *p*-TsOH (19 mg, 0.1 mmol) in $CHCl_3$ (2 mL) was added and stirred at 40°C for 1h. After removing the solvent, the residue was purified by a flash column chromatography (Petroleum ether/ EtOAc = 5:1~3:1, V/V) to afford the product **3an**.

3. Data for the products

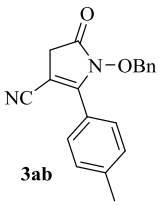
1-(benzyloxy)-5-oxo-2-phenyl-4,5-dihydro-1H-pyrrole-3-carbonitrile (3aa)



3aa

Following the **General procedure A**, **3aa** (53.3 mg) was isolated as a white solid in 92% yield, Mp: 137–139 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57–7.50 (m, 3H), 7.48–7.43 (m, 2H), 7.32–7.27 (m, 1H), 7.23–7.18 (m, 2H), 7.06 – 7.01 (m, 2H), 4.89 (s, 2H), 3.38 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.1, 156.6, 132.4, 131.5, 130.0, 129.4, 128.7, 128.6, 128.5, 125.6, 115.5, 79.5, 78.8, 35.3; HRMS ESI Calcd for $C_{18}H_{14}N_2NaO_2$ $[M+Na]^+$: 313.0947, Found: 313.0948. IR (KBr): 3027, 2923, 2852, 1745, 1598, 1494, 1454, 1341, 1165, 1091, 1038 cm^{-1}.

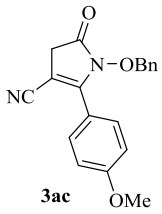
1-(benzyloxy)-5-oxo-2-(p-methyl phenyl)-4,5-dihydro-1H-pyrrole-3-carbonitrile (3ab)



3ab

Following the **General procedure A**, **3ab** (48.6 mg) was isolated as a white solid in 80% yield, Mp: 114–116 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50–7.46 (m, 2H), 7.33–7.26 (m, 3H), 7.24–7.20 (m, 2H), 7.10 –7.06 (m, 2H), 4.88 (s, 2H), 3.36 (s, 2H), 2.44 (s, 3H); ^{13}C NMR (125MHz, $CDCl_3$) δ 169.23, 156.61, 142.19, 132.54, 130.03, 129.50, 129.42, 128.51, 128.46, 122.79, 115.73, 78.77, 77.20, 35.25, 21.61. HRMS ESI Calcd for $C_{19}H_{16}N_2NaO_2$ $[M+Na]^+$: 327.1104, Found: 327.1103. IR (KBr): 3027, 2923, 2852, 1745, 1598, 1494, 1454, 1341, 1165, 1091, 1038 cm^{-1}.

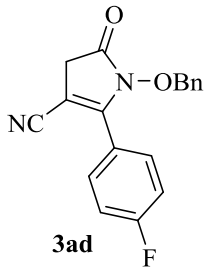
1-(benzyloxy)-5-oxo-2-(p-methoxy phenyl-4,5-dihydro-1H-pyrrole-3-carbonitrile (3ac)



3ac

Following the General procedure A, **3ac** (48.5 mg) was isolated as a white solid in 76% yield, Mp: 104–107 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58–7.53 (m, 2H), 7.33–7.29 (m, 1H), 7.25–7.21 (m, 2H), 7.11–7.06 (m, 2H), 6.99–6.94 (m, 2H), 4.88 (s, 2H), 3.88 (s, 3H), 3.34 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.3, 162.1, 156.2, 132.6, 130.4, 130.1, 129.5, 128.5, 118.0, 116.0, 114.2, 78.8, 77.8, 55.5, 35.2. HRMS ESI Calcd for $C_{19}H_{16}N_2NaO_3$ $[M+Na]^+$: 343.1053, Found: 343.1055. IR (KBr): 3027, 2923, 2852, 1745, 1598, 1494, 1454, 1341, 1165, 1091, 1038 cm^{-1}.

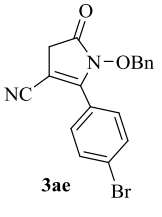
1-(benzyloxy)-5-oxo-2-(*p*-fluorophenyl)-4,5-dihydro-1H-pyrrole-3-carbonitrile (3ad)



3ad

Following the General procedure A, **3ad** (44.3 mg) was isolated as a white solid in 72% yield. Mp: 136–138 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53–7.48 (m, 2H), 7.33–7.28 (m, 1H), 7.24–7.19 (m, 2H), 7.16 – 7.11 (m, 2H), 7.05–7.01 (m, 2H), 4.91 (s, 2H), 3.38 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.0, 164.3 (d, *J* = 253.8 Hz), 155.7, 132.4, 131.0 (d, *J* = 8.7 Hz), 130.1, 129.60, 128.6, 121.8 (d, *J* = 3.4 Hz), 116.0 (d, *J* = 22.0 Hz), 115.4, 79.4, 78.9, 35.3. ^{19}F NMR (471 MHz, $CDCl_3$) δ -106.58. HRMS ESI Calcd for $C_{18}H_{13}FN_2NaO_2$ $[M+Na]^+$: 331.0853, Found: 331.0854. IR (KBr): 3027, 2923, 2852, 1745, 1598, 1494, 1454, 1341, 1165, 1091, 1038 cm^{-1}.

1-(4-bromobenzyloxy)-5-oxo-2-phenyl-4,5-dihydro-1H-pyrrole-3-carbonitrile (3ae)

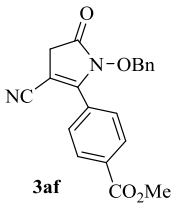


3ae

Following the General procedure A, **3ae** (53.8 mg) was isolated as a white solid in 73% yield. Mp: 134–136 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60–7.55 (m, 2H), 7.36–7.33 (m, 2H), 7.33–7.29 (m, 1H), 7.24–7.19 (m, 2H), 7.07 –7.00 (m, 2H), 4.92 (s, 2H), 3.36 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.9, 155.6, 132.3,

132.0, 130.1, 130.0, 129.6, 128.6, 126.2, 124.5, 115.2, 79.7, 78.9, 35.3. HRMS ESI Calcd for $C_{18}H_{13}BrN_2NaO_2$ $[M+Na]^+$: 391.0053, Found: 391.0052. IR (KBr): 3027, 2923, 2852, 1745, 1598, 1494, 1454, 1341, 1165, 1091, 1038 cm^{-1}.

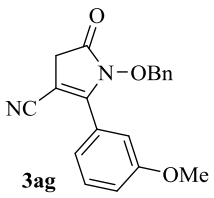
Methyl 4-(1-(benzyloxy)-3-cyano--5-oxo-4, 5-dihydro-1H-pyrrol-2-yl)benzoate



3af

Following the General procedure A, **3af** (48.7 mg) was isolated as a white solid in 70% yield. Mp: 121–123 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (d, *J* = 8.3 Hz, 1H), 7.55 (d, *J* = 8.3 Hz, 1H), 7.30 (t, *J* = 7.4 Hz, 1H), 7.18 (t, *J* = 7.6 Hz, 1H), 7.00 (d, *J* = 7.4 Hz, 1H), 4.93 (s, 1H), 3.98 (s, 2H), 3.40 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.92, 166.03, 155.74, 132.57, 132.32, 130.17, 129.76, 129.67, 129.65, 128.71, 128.63, 115.01, 80.77, 78.91, 52.55, 35.48. HRMS ESI Calcd for $C_{20}H_{16}N_2NaO_4$ $[M+Na]^+$: 371.1002, Found: 371.1000. IR (KBr): 2956, 2209, 1725, 1436, 1410, 1379, 1354, 1315, 1279, 1231, 1188, 1166, 1110, 772, 753, 701 cm^{-1}.

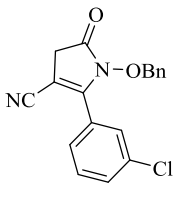
1-(benzyloxy)-5-oxo-2-(*m*-methoxyphenyl)-4,5-dihydro-1H-pyrrole-3-carbonitrile



3ag

Following the General procedure A, **3ag** (54.4 mg) was isolated as a white solid in 85% yield. Mp: 86–88 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (t, *J* = 8.0 Hz, 1H), 7.33–7.28 (m, 1H), 7.21 (t, *J* = 7.6 Hz, 2H), 7.15 (dt, *J* = 7.6, 1.2 Hz, 1H), 7.10–7.04 (m, 3H), 7.03 (t, *J* = 2.1 Hz, 1H), 4.89 (s, 2H), 3.79 (s, 3H), 3.37 (s, 2H).^{13}C NMR (125 MHz, $CDCl_3$) δ 169.1, 159.5, 156.4, 132.5, 130.1, 129.8, 129.4, 128.5, 126.6, 120.9, 117.9, 115.4, 113.4, 79.6, 78.9, 55.8, 35.3. HRMS ESI Calcd for $C_{19}H_{16}N_2NaO_3$ $[M+Na]^+$: 343.1053, Found: 343.1054. IR (KBr): 3027, 2923, 2852, 1745, 1598, 1494, 1454, 1341, 1165, 1091, 1038 cm^{-1}.

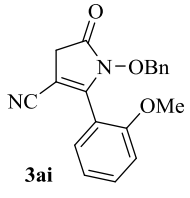
1-(benzyloxy)-5-oxo-2-(*m*-chlorophenyl)-4,5-dihydro-1H-pyrrole-3-carbonitrile



3ah

Following the General procedure A, **3ah** (46.0 mg) was isolated as a white solid in 71% yield. Mp: 94–96 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 (dt, *J* = 7.5, 1.9 Hz, 1H), 7.41–7.34 (m, 3H), 7.34–7.30 (m, 1H), 7.22–7.18 (m, 2H), 7.04–6.99 (m, 2H), 4.93 (s, 2H), 3.39 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.9, 155.3, 134.7, 132.3, 131.4, 130.2, 129.9, 129.6, 128.6, 128.5, 127.2, 126.8, 114.9, 80.3, 78.9, 35.4. HRMS ESI Calcd for $C_{18}H_{13}ClN_2NaO_2$ $[M+Na]^+$: 347.0558, Found: 347.0558. IR (KBr): 3027, 2923, 2852, 1745, 1598, 1494, 1454, 1341, 1165, 1091, 1038 cm^{-1}.

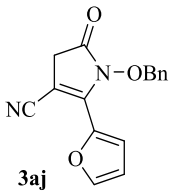
1-(benzyloxy)-5-oxo-2-(o-methoxyphenyl)-4,5-dihydro-1H-pyrrole-3-carbonitrile



3ai

Following the **General procedure A**, **3ai** (41.6 mg) was isolated as a white solid in 65% yield. Mp: 102–104 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (ddd, *J* = 8.8, 7.6, 1.7 Hz, 1H), 7.30–7.26 (m, 1H), 7.23–7.17 (m, 3H), 7.03–6.95 (m, 4H), 4.89 (s, 2H), 3.81 (s, 3H), 3.38 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.3, 157.4, 154.9, 133.1, 132.9, 130.9, 129.7, 129.1, 128.5, 120.6, 115.1, 115.0, 111.4, 81.9, 78.8, 55.6, 35.6. HRMS ESI Calcd for $C_{19}H_{16}N_2NaO_3$ $[M+Na]^+$: 343.1053, Found: 343.1057. IR (KBr): 3027, 2923, 2852, 1745, 1598, 1494, 1454, 1341, 1165, 1091, 1038 cm^{-1}.

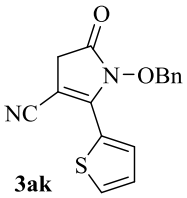
1-(benzyloxy)-5-oxo-2-(2-furyl)-4,5-dihydro-1H-pyrrole-3-carbonitrile



3aj

Following the General procedure A, **3aj** (43.6 mg) was isolated as a slightly yellow solid in 78% yield. Mp: 115–118 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (d, *J* = 1.6 Hz, 1H), 7.45 – 7.36 (m, 5H), 7.15 (d, *J* = 3.6 Hz, 1H), 6.57 (dd, *J* = 3.7, 1.8 Hz, 1H), 5.15 (s, 2H), 3.38 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.9, 146.0, 144.3, 140.9, 132.7, 129.9, 129.6, 128.7, 115.9, 115.6, 112.6, 79.3, 75.5, 35.3. HRMS ESI Calcd for $C_{16}H_{12}N_2NaO_3$ $[M+Na]^+$: 303.0740, Found: 303.0739. IR (KBr): 3027, 2923, 2852, 1745, 1598, 1494, 1454, 1341, 1165, 1091, 1038 cm^{-1}.

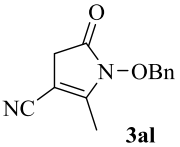
1-(benzyloxy)-5-oxo-2-(2-thiophenyl)-4,5-dihydro-1H-pyrrole-3-carbonitrile



3ak

Following the General procedure A, **3ak** (39.1 mg) was isolated as a slightly yellow solid in 66% yield. Mp: 138–140 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (d, *J* = 3.8 Hz, 1H), 7.64 (dd, *J* = 5.1, 1.0 Hz, 1H), 7.35 (qd, *J* = 8.3, 7.7, 4.6 Hz, 5H), 7.19 (dd, *J* = 5.0, 3.9 Hz, 1H), 5.10 (s, 2H), 3.39 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.8, 149.1, 132.4, 131.9, 131.4, 130.1, 129.6, 128.6, 127.9, 125.7, 116.2, 79.3, 76.1, 35.2. HRMS ESI Calcd for $C_{19}H_{16}N_2NaO_2S$ $[M+Na]^+$: 319.0512, Found: 319.0512. IR (KBr): 3027, 2923, 2852, 1745, 1598, 1494, 1454, 1341, 1165, 1091, 1038 cm^{-1}.

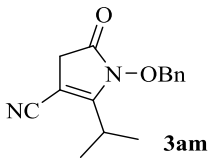
1-(benzyloxy)-2-methyl-5-oxo-4,5-dihydro-1H-pyrrole-3-carbonitrile



3al

Following the General procedure A, **3al** (36.9 mg) was isolated as a white solid in 81% yield. Mp: 90-92 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 – 7.34 (m, 5H), 5.09 (s, 2H), 3.21 (q, *J* = 2.4 Hz, 2H), 1.87 (t, *J* = 2.4 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.5, 157.0, 133.4, 130.1, 129.8, 128.9, 114.8, 79.2, 79.1, 34.8, 11.9. HRMS ESI Calcd for $C_{13}H_{12}N_2NaO_2$ $[M+Na]^+$: 251.0791, Found: 251.0791. IR (KBr): 3027, 2923, 2852, 1745, 1598, 1494, 1454, 1341, 1165, 1091, 1038 cm^{-1}.

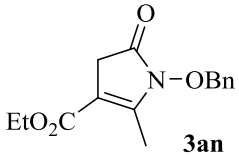
1-(benzyloxy)-2-isopropyl-5-oxo-4,5-dihydro-1H-pyrrole-3-carbonitrile



3am

Following the General procedure A, **3am** (39.4 mg) was isolated as a white solid in 77% yield. Mp: 218.5–219.5 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (s, 5H), 5.13 (s, 2H), 3.21 (s, 2H), 2.74 (hept, *J* = 7.0 Hz, 1H), 1.22 (d, *J* = 7.2 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.6, 165.1, 133.2, 129.9, 129.6, 128.8, 115.1, 78.8, 76.8, 35.3, 26.9, 19.8. HRMS ESI Calcd for $C_{15}H_{16}N_2NaO_2$ $[M+Na]^+$: 279.1104, Found: 279.1104. IR (KBr): 3027, 2923, 2852, 1745, 1598, 1494, 1454, 1341, 1165, 1091, 1038 cm^{-1}.

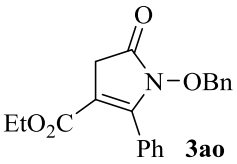
Ethyl 1-(benzyloxy)-2-methyl-5-oxo-4,5-dihydro-1H-pyrrole-3-carboxylate



3an

Following the General procedure B, **3an** (45.1 mg) was isolated as a white solid in 82% yield. Mp: 44–46 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48–7.35 (m, 5H), 5.10 (s, 2H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.24 (q, *J* = 2.4 Hz, 2H), 2.14 (t, *J* = 2.4 Hz, 3H), 1.27 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.9, 163.7, 153.2, 133.7, 130.0, 129.5, 128.7, 99.6, 78.9, 59.9, 34.5, 14.3, 11.0. HRMS ESI Calcd for $C_{15}H_{17}NNaO_4$ $[M+Na]^+$: 298.1050, Found: 298.1057. IR (KBr): 3027, 2923, 2852, 1745, 1598, 1494, 1454, 1341, 1165, 1091, 1038 cm^{-1}.

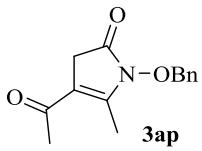
Ethyl 1-(benzyloxy)-2-phenyl-5-oxo-4,5-dihydro-1H-pyrrole-3-carboxylate



3ao

Following the General procedure B, **3ao** (32.4 mg) was isolated as a white solid in 45% yield. Mp: 69–71 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50–7.46 (m, 1H), 7.43–7.36 (m, 4H), 7.30–7.26 (m, 1H), 7.22–7.18 (m, 2H), 6.96–6.92 (m, 2H), 4.79 (s, 2H), 4.06 (q, *J* = 7.1 Hz, 2H), 3.43 (s, 2H), 1.10 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.7, 162.8, 152.9, 133.0, 130.1, 129.9, 129.8, 129.1, 128.4, 127.6, 127.2, 101.4, 78.7, 60.1, 35.1, 14.0. HRMS ESI Calcd for $C_{20}H_{19}NNaO_4$ $[M+Na]^+$: 360.1206, Found: 360.1201. IR (KBr): 3027, 2923, 2852, 1745, 1598, 1494, 1454, 1341, 1165, 1091, 1038 cm^{-1}.

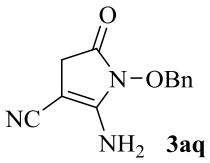
4-acetyl 1-(benzyloxy)-5-methyl-1, 3-dihydro-2H-pyrrol-2-one



3ap

Following the General procedure B, 3ap (35.3 mg) was isolated as a white solid in 72% yield. Mp: 106–108 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45–7.36 (m, 5H), 5.11 (s, 2H), 3.29 (q, *J* = 2.4 Hz, 2H), 2.19 (s, 3H), 2.16 (t, *J* = 2.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.3, 170.4, 152.6, 133.6, 130.0, 129.6, 128.8, 108.4, 79.0, 34.9, 29.0, 11.6. HRMS ESI Calcd for $C_{14}H_{15}NNaO_3$ $[M+Na]^+$: 268.0944, Found: 268.0945. IR (KBr): 3027, 2923, 2852, 1745, 1598, 1494, 1454, 1341, 1165, 1091, 1038 cm^{-1}.

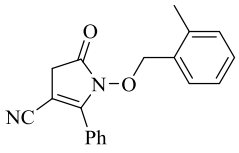
2-amino-1-(benzyloxy)-5-oxo-4,5-dihydro-1H-pyrrole-3-carbonitrile



3aq

Following the General procedure B, Compound 1 (0.2 mmol, 1.0 eq), malononitrile (0.3 mmol, 1.5 eq.) and K_2CO_3 (82.8 mg, 0.6 mmol, 3.0 eq), NaI (0.04mmol) and THF (2 mL), the crude product was purified by a flash column chromatography (Petroleum/ EtOAc = 3: 1) to obtain **3aq** (38.4mg) as a white solid in 84% yield. Mp: 110–112 °C. ^{1}H NMR (500 MHz, DMSO) δ 7.53 (d, *J* = 3.5 Hz, 2H), 7.41 (m, 5H), 5.02 (s, 2H), 3.18 (s, 2H). ^{13}C NMR (125 MHz, DMSO) δ 169.10, 155.52, 134.22, 130.49, 129.59, 128.79, 119.29, 79.05, 43.83, 32.35. HRMS ESI Calcd for $C_{12}H_{12}N_3O_2$ $[M+H]^+$: 230.0924, Found: 230.0925. IR (KBr): 3336, 3223, 2187, 1731, 1658, 1597, 1454, 1335, 1208, 1059, 909,732, 698, 670 cm^{-1}.

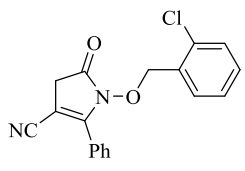
1-(o-methylbenzyloxy)- 5-oxo-2-phenyl-4,5-dihydro-1H-pyrrole-3-carbonitrile



3ba

Following the General procedure A, **3ba** (52.3 mg) was isolated as a white solid in 86% yield. Mp: 120–122 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (t, *J* = 7.3 Hz, 1H), 7.47 (d, *J* = 7.3 Hz, 2H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.20 (t, *J* = 7.5 Hz, 1H), 7.07 (t, *J* = 7.4 Hz, 1H), 6.96 (dd, *J* = 17.2, 7.5 Hz, 2H), 4.93 (s, 2H), 3.37 (s, 2H), 2.05 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.07, 156.87, 138.76, 131.35, 131.24, 130.71, 130.52, 129.86, 128.62, 128.46, 125.85, 125.57, 115.41, 79.45, 76.42, 35.32, 18.34. HRMS ESI Calcd for $C_{19}H_{16}N_2NaO_2$ $[M+Na]^+$: 327.1104, found: 327.1101. IR (KBr): 2952, 2903, 2207, 1735, 1446, 1377, 1355, 1321, 1228, 1186, 1165, 1057, 919, 762, 748, 693cm^{-1}.

1-(o-chlorobenzyloxy)- 5-oxo-2-phenyl-4,5-dihydro-1H-pyrrole-3-carbonitrile

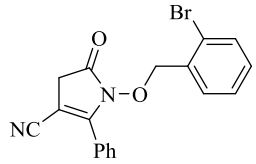


3ca

Following the General procedure A, 3ca (51.5 mg) was isolated as a white solid in 79% yield. Mp: 108-110 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 –

7.43 (m, 1H), 7.41 (t, *J* = 4.2 Hz, 2H), 7.40–7.34 (m, 2H), 7.22–7.15 (m, 2H), 7.09 (d, *J* = 7.1 Hz, 1H), 7.07–7.00 (m, 1H), 5.09 (s, 2H), 3.39 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.11, 156.79, 135.21, 132.34, 131.24, 130.87, 130.69, 129.56, 128.59, 128.44, 126.90, 125.41, 115.49, 79.42, 75.18, 35.37. HRMS ESI Calcd for $C_{18}H_{13}ClN_2NaO_2$ $[M+Na]^+$: 347.0558, found: 347.0558. IR (KBr): 3062, 2922, 2208, 1742, 1620, 1596, 1477, 1447, 1321, 1275, 1229, 1187, 1056, 910, 763, 695, 652, 606, 495, 408.cm^{-1}.

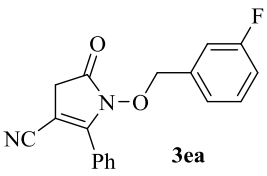
1-(o-bromobenzyloxy)- 5-oxo-2-phenyl-4,5-dihydro-1H-pyrrole-3-carbonitrile



3da

Following the General procedure A, 3da (64.9 mg) was isolated as a white solid in 88% yield. Mp: 118–120 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47–7.40 (m, 3H), 7.37 (t, *J* = 7.4 Hz, 3H), 7.14–7.04 (m, 3H), 5.08 (s, 2H), 3.39 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.08, 156.75, 132.83, 132.46, 132.28, 131.19, 130.91, 128.60, 128.44, 127.49, 125.42, 125.21, 115.44, 79.49, 77.48, 35.37. HRMS ESI Calcd for $C_{18}H_{13}BrN_2NaO_2$ $[M+Na]^+$: 391.0053, found: 391.0053. IR (KBr): 2956, 2917, 2207, 1735, 1446, 1379, 1354, 1321, 1228, 1186, 1165, 1058, 1030, 755, 734 , 693cm^{-1}.

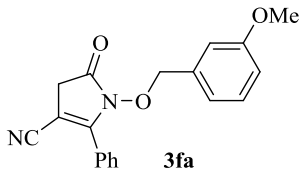
1-(m-flurobenzyloxy)- 5-oxo-2-phenyl-4,5-dihydro-1H-pyrrole-3-carbonitrile



3ea

Following the General procedure A, **3ea** (41.9 mg) was isolated as a white solid in 68% yield. Mp: 108–110 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (dd, *J* = 7.9, 0.7 Hz, 3H), 7.49 (dd, *J* = 8.0, 7.0 Hz, 2H), 7.23–7.18 (m, 1H), 7.00 (tdd, *J* = 8.5, 2.6, 0.9 Hz, 1H), 6.86 (d, *J* = 7.6 Hz, 1H), 6.71 (ddd, *J* = 9.2, 2.3, 1.8 Hz, 1H), 4.89 (s, 2H), 3.40 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.11, 163.48, 161.51, 156.42, 134.84, 134.77, 131.67, 130.11, 130.04, 128.81, 128.57, 125.51, 125.49, 125.46, 116.83, 116.66, 116.56, 116.39, 115.31, 79.75, 77.99, 35.31. ^{19}F NMR (471 MHz, CDCl3) δ -112.26. HRMS ESI Calcd for $C_{18}H_{13}FN_2NaO_2$ $[M+Na]^+$: 331.0853, found: 331.0853. IR (KBr): 3060, 2920, 2209, 1741, 1592, 1489, 1448, 1379, 1275, 1260, 1231, 1167, 1143, 1061, 792, 750.cm^{-1}.

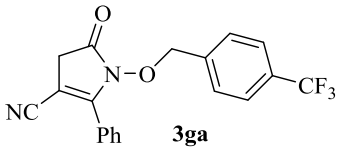
1-(m-methoxybenzyloxy)- 5-oxo-2-phenyl-4,5-dihydro-1H-pyrrole-3-carbonitrile



3fa

Following the General procedure A, **3fa** (51.8 mg) was isolated as a white solid in 81% yield. Mp:110–112 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58–7.48 (m, 3H), 7.48–7.40 (m, 2H), 7.16–7.09 (m, 1H), 6.83 (ddd, *J* = 8.3, 2.6, 0.7 Hz, 1H), 6.62 (d, *J* = 7.5 Hz, 1H), 6.56–6.48 (m, 1H), 4.87 (s, 2H), 3.66 (s, 3H), 3.37 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.09, 159.52, 156.64, 133.79, 131.39, 129.46, 128.62, 128.57, 125.66, 122.22, 115.42, 115.02, 79.44, 78.65, 55.04, 35.28. HRMS ESI Calcd for $C_{19}H_{16}N_2NaO_3$ $[M+Na]^+$: 343.1053, found: 343.1058. IR (KBr): 3055, 2950, 2830, 2207, 1735, 1597, 1491, 1447, 1378, 1355, 1267, 1229, 1187, 1052, 918, 790, 762, 693, 673, 652.cm^{-1}.

1-(p-trifluoromethylbenzyloxy)- 5-oxo-2-phenyl-4,5-dihydro-1H-pyrrole-3-carbonitrile

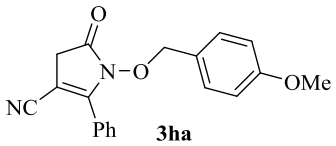


3ga

Following the General procedure A, 3**ga** (48 mg) was isolated as a white solid in 67% yield. Mp:106–108 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (t, *J* = 7.4 Hz, 1H), 7.50 (d, *J* = 7.4 Hz, 2H), 7.45

(t, *J* = 7.5 Hz, 4H), 7.16 (d, *J* = 8.0 Hz, 2H), 4.94 (s, 2H), 3.41 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.08, 156.24, 136.34, 131.60, 130.02, 128.80, 128.49, 125.47, 125.42, 125.39, 125.36, 125.34, 124.75, 115.20, 79.90, 77.91, 35.29. ^{19}F NMR (471 MHz, $CDCl_3$) δ -62.88. HRMS ESI Calcd for $C_{19}H_{13}F_3N_2NaO_2$ $[M+Na]^+$: 381.0821, found: 381.0821. IR (KBr):3007, 2990, 2210, 1738, 1321, 1275, 1260, 1229, 1162, 1112, 1019, 852, 827, 749, 694, 651, 910 cm^{-1}.

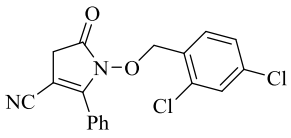
1-(*p*-methoxylbenzyloxy)- 5-oxo-2-phenyl-4,5-dihydro-1H-pyrrole-3-carbonitrile



3ha

Following the General procedure A, **3ha** (60.2 mg) was isolated as a white solid in 94% yield. Mp: 108–110 °C. ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 7.52 (t, *J* = 6.2 Hz, 3H), 7.48–7.42 (m, 2H), 6.93 (d, *J* = 8.5 Hz, 2H), 6.69 (d, *J* = 8.5 Hz, 2H), 4.82 (s, 2H), 3.77 (s, 3H), 3.37 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.13, 160.44, 156.73, 131.69, 131.41, 128.59, 125.72, 124.55, 115.53, 113.82, 79.26, 78.41, 55.21, 35.28. HRMS ESI Calcd for $C_{19}H_{16}N_2NaO_3$ $[M+Na]^+$: 343.1053, found: 343.1055. IR (KBr): 3005, 2989, 2208, 1740, 1611, 1514, 1447, 1356, 1275, 1260, 1175, 1030, 826, 759, 697 cm^{-1}.

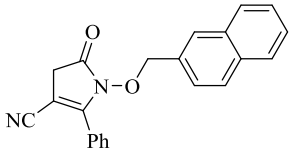
1-(2,4-dichlorobenzyloxy)- 5-oxo-2-phenyl-4,5-dihydro-1H-pyrrole-3-carbonitrile (3ia)



3ia

Following the General procedure A, **3ia** (50 mg) was isolated as a white solid in 70% yield. Mp: 108-110 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (dt, *J* = 8.3, 4.2 Hz, 1H), 7.40 (d, *J* = 4.4 Hz, 4H), 7.17 (d, *J* = 0.6 Hz, 1H), 6.99 (d, *J* = 1.6 Hz, 2H), 5.04 (s, 2H), 3.39 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.07, 156.63, 136.35, 135.89, 133.08, 131.40, 129.46, 129.39, 128.62, 128.43, 127.31, 125.42, 115.40, 79.68, 74.56, 35.40. HRMS ESI Calcd for $C_{18}H_{12}Cl_2N_2NaO_2$ $[M+Na]^+$: 381.0168, found: 381.0169. IR (KBr): 3070, 2915, 2208, 1739, 1589, 1475, 1447, 1382, 1256, 1275, 1228, 1186, 1104, 909, 869, 818, 694, 651 cm^{-1}.

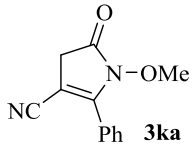
1-(2-naphthyloxy)- 5-oxo-2-phenyl-4, 5-dihydro-1H-pyrrole-3-carbonitrile (3ja)



3ja

Following the General procedure A, **3ja** (46.9 mg) was isolated as a white solid in 69% yield. Mp: 132–134 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (d, *J* = 7.9 Hz, 1H), 7.71 (d, *J* = 7.8 Hz, 1H), 7.65 (d, *J* = 8.4 Hz, 1H), 7.53 – 7.51 (m, 3H), 7.50 (d, *J* = 1.3 Hz, 1H), 7.46 (dd, *J* = 8.3, 1.3 Hz, 2H), 7.39 (dd, *J* = 10.8, 4.5 Hz, 2H), 7.10 (dd, *J* = 8.4, 1.7 Hz, 1H), 5.08 (s, 2H), 3.41 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.19, 156.71, 133.52, 132.83, 131.45, 129.95, 129.88, 128.62, 128.58, 128.29, 128.08, 127.63, 126.92, 126.87, 126.41, 125.63, 115.42, 79.45, 79.03, 35.34. HRMS ESI Calcd for $C_{22}H_{16}N_2NaO_2$ $[M+Na]^+$: 363.1104, found: 363.1105. IR (KBr): 3056, 2952, 2208, 1802, 1740, 1574, 1509, 1494, 1447, 1356, 1322, 1231, 1167, 1061, 949, 898, 857, 819, 762. cm^{-1}.

1-methoxy- 5-oxo-2-phenyl-4, 5-dihydro-1H-pyrrole-3-carbonitrile (3ka)

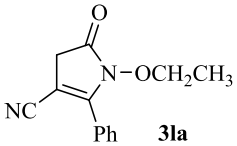


3ka

Following the General procedure A, **3ka** (36 mg) was isolated as a white solid in 84% yield. Mp: 45–47 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.2 Hz, 2H), 7.62–7.49 (m, 3H), 3.74 (s, 3H), 3.40 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.26, 155.68, 131.79, 129.00, 128.31, 125.40, 115.39, 80.12, 64.67,

35.35. HRMS ESI Calcd for $C_{12}H_{10}N_2NaO_2$ $[M+Na]^+$: 237.0634, found: 237.0634. IR (KBr): 2937, 2209, 1738, 1620, 1447, 1362, 1325, 1232, 1166, 958, 942, 764, 693, 667, 653, 618 cm^{-1}.

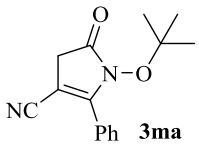
1-ethoxy- 5-oxo-2-phenyl-4, 5-dihydro-1H-pyrrole-3-carbonitrile (3la)



3la

Following the General procedure A, **3la** (37 mg) was isolated as a white solid in 81% yield;white solid, Mp: 81–83 ^oC. ^1H NMR (500 MHz, $CDCl_3$) δ 7.84–7.66 (m, 2H), 7.60–7.48 (m, 3H), 3.94 (q, *J* = 7.1 Hz, 2H), 3.40 (s, 2H), 1.13 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.29, 156.11, 131.73, 128.91, 128.41, 125.62, 115.51, 79.86, 73.31, 35.34, 13.08. IR: ν 3005, 2989, 2207, 1738, 1447, 1357, 1324, 1275, 1261, 1232, 1166, 1065, 1015, 749, 697. HRMS Calcd. For $C_{13}H_{12}N_2NaO_2$ $[M+Na]^+$:251.0791, found: 251.0791.

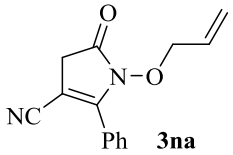
1-*tert*-butyloxy- 5-oxo-2-phenyl-4, 5-dihydro-1H-pyrrole-3-carbonitrile (3ma)



3ma

Following the General procedure A, **3ma** (37.9 mg) was isolated as a colorless oil in 74% yield. ^1H NMR (500 MHz, $CDCl_3$) δ 7.71–7.62 (m, 2H), 7.52 (t, *J* = 7.6 Hz, 3H), 3.41 (s, 2H), 1.06 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.28, 158.54, 131.23, 128.98, 128.64, 127.20, 115.58, 87.82, 80.52, 35.17, 27.14. HRMS ESI Calcd for $C_{15}H_{16}N_2NaO_2$ $[M+Na]^+$: 279.1104, found: 279.1104. IR (KBr): 2937, 2209, 1738, 1620, 1447, 1362, 1325, 1232, 1166, 958, 942, 764, 693, 667, 653, 618 cm^{-1}.

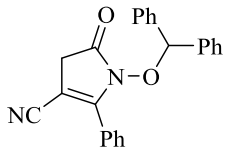
1-allyloxy- 5-oxo-2-phenyl-4, 5-dihydro-1H-pyrrole-3-carbonitrile (3na)



3na

Following the General procedure A, **3na** (34.6 mg) was isolated as a colorless oil in 72% yield. ^1H NMR (500 MHz, $CDCl_3$) δ 7.65 (d, *J* = 7.0 Hz, 2H), 7.52 – 7.44 (m, 3H), 5.58 (ddt, *J* = 17.0, 10.3, 6.8 Hz, 1H), 5.16 (t, *J* = 14.2 Hz, 2H), 4.29 (d, *J* = 6.8 Hz, 2H), 3.32 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.26, 155.68, 131.79, 129.00, 128.31, 125.40, 115.39, 80.12, 64.67, 35.35. HRMS ESI Calcd for $C_{14}H_{12}N_2NaO_2$ $[M+Na]^+$: 263.0791, found: 263.0792. IR (KBr): 2208, 1737, 1447, 1356, 1275, 1260, 1231, 1167, 1061, 942, 749, 696, 652. cm^{-1}.

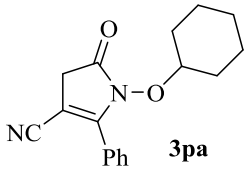
1-(benzhydryloxy)- 5-oxo-2-phenyl-4, 5-dihydro-1H-pyrrole-3-carbonitrile (3oa)



3oa

Following the General procedure A, **3oa** (44.7 mg) was isolated as a white solid in 63% yield. Mp: 141–143 ^oC. ^1H NMR (500 MHz, $CDCl_3$) δ 7.51 (t, *J* = 7.2 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 2H), 7.39 (d, *J* = 7.6 Hz, 2H), 7.28 (t, *J* = 3.6 Hz, 2H), 7.20 (t, *J* = 7.6 Hz, 4H), 7.10 (d, *J* = 7.6 Hz, 4H), 6.33 (s, 1H), 3.31 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) 168.88, 157.26, 136.66, 131.19, 128.76, 128.51, 128.29, 128.22, 128.18, 126.08, 115.47, 88.42, 79.11, 35.22. HRMS ESI Calcd for $C_{24}H_{18}N_2NaO_2$ $[M+Na]^+$: 389.1260, found: 389.1262. IR (KBr): 3005, 2989, 2208, 1735, 1495, 1448, 1365, 1334, 1285, 1260, 1232, 1167, 912, 749, 696, 605 cm^{-1}.

1-cyclohexyloxy- 5-oxo-2-phenyl-4, 5-dihydro-1H-pyrrole-3-carbonitrile (3pa)



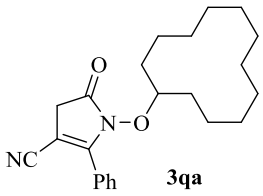
3pa

Following the General procedure A, **3pa** (47.9 mg) was isolated as a white solid in 85% yield.

Mp: 92–94 ^oC. ^1H NMR (500 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.2 Hz, 2H),

7.62–7.49 (m, 3H), 3.74 (s, 3H), 3.40 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.26, 155.68, 131.79, 129.00, 128.31, 125.40, 115.39, 80.12, 64.67, 35.35. HRMS ESI Calcd for $C_{12}H_{10}N_2NaO_2$ $[M+Na]^+$: 237.0634, found: 237.0634. IR (KBr): 2937, 2209, 1738, 1620, 1447, 1362, 1325, 1232, 1166, 958, 942, 764, 693, 667, 653, 618 cm^{-1}.

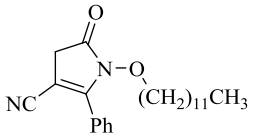
1-(cyclododecyloxy)- 5-oxo-2-phenyl-4, 5-dihydro-1H-pyrrole-3-carbonitrile (3qa)



3qa

Following the General procedure A, **3qa** (53.4 mg) was isolated as a white solid in 73% yield. Mp: 88–90 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (d, *J* = 7.5 Hz, 2H), 7.46 (dt, *J* = 14.4, 7.1 Hz, 3H), 3.95 (t, *J* = 4.5 Hz, 1H), 3.33 (s, 2H), 1.37 (dt, *J* = 13.6, 6.9 Hz, 2H), 1.31 (dd, *J* = 11.5, 6.4 Hz, 2H), 1.21–1.08 (m, 15H), 1.00 (d, *J* = 6.0 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.45, 157.21, 131.45, 128.77, 128.65, 126.11, 115.50, 85.50, 79.87, 35.29, 27.90, 24.05, 23.39, 23.25, 23.06, 20.74.HRMS ESI Calcd for $C_{23}H_{30}N_2NaO_2$ $[M+Na]^+$: 389.2199, found: 389.2199. IR (KBr): 3005, 2989, 2932, 2861, 2209, 1742, 1470, 1361, 1275, 1260, 1231, 1165, 896, 749, 418 cm^{-1}.

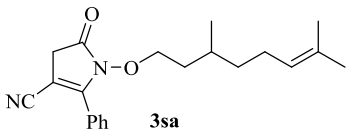
1-dodecyloxy- 5-oxo-2-phenyl-4, 5-dihydro-1H-pyrrole-3-carbonitrile (3ra)



3ra

Following the General procedure A, **3ra** (57.4 mg) was isolated as a white solid in 78% yield. Mp: 68–70 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76–7.68 (m, 2H), 7.59–7.47 (m, 3H), 3.85 (t, *J* = 6.5 Hz, 2H), 3.38 (s, 2H), 1.53–1.44 (m, 2H), 1.33–1.05 (m, 19H), 0.88 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.19, 156.23, 131.69, 128.86, 128.49, 125.57, 115.50, 79.83, 77.58, 35.36, 31.85, 29.55, 29.42, 29.29, 29.28, 29.02, 27.64, 25.41, 22.63, 14.07. HRMS ESI Calcd for $C_{23}H_{32}N_2NaO_2$ $[M+Na]^+$: 391.2356, found: 391.2357. IR (KBr): 2922, 2852, 2209, 1743, 1466, 1447, 1360, 1324, 1275, 1260, 1231, 1185, 1165, 1064, 763, 750 cm^{-1}.

1-(3,7-dimethyloct-8-en-1-yl)oxy-5-oxo-2-phenyl-4,5-dihydro-1H-pyrrole-3-carbonitrile (3sa)



3sa

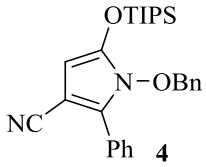
Following the General procedure A, **3sa** (50.7mg) was isolated as a colorless oil in 75% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.5 Hz, 2H), 7.54 (dt, *J* = 14.5, 7.0 Hz, 3H), 5.00 (t, *J* = 6.9 Hz, 1H), 3.98–3.82 (m, 2H), 3.39 (s, 2H), 1.93–1.76 (m, 2H), 1.67 (s, 3H), 1.62–1.49 (m, 4H), 1.41 (dt, *J* = 13.1, 6.6 Hz, 1H), 1.30 (dt, *J* = 14.0, 6.9 Hz, 1H), 1.17 (ddd, *J* = 15.4, 12.7, 5.9 Hz, 1H), 1.04 (dt, *J* = 14.1, 7.0 Hz, 1H), 0.70 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.16, 156.18, 131.69, 131.28, 128.86, 128.43, 125.56, 124.31, 115.46, 79.84, 75.95, 36.77, 35.34, 34.51, 28.94, 25.62, 25.17, 19.00, 17.56. HRMS ESI Calcd for $C_{21}H_{26}N_2NaO_2$ $[M+Na]^+$: 361.1886, found: 361.1886. IR (KBr): 3005, 2963, 2915, 2208, 1740, 1447, 1379, 1359, 1275, 1260, 1229, 1164, 1063, 943, 749, 694, 652 cm^{-1}.

Gram-scale reaction and further transformations

Gram-scale reaction: To a round-bottom flask were added compound **1a** (15 mmol, 1.5 eq.), **2a** (10 mmol, 1.0 eq.), MeONa (160 mg, 3.0 mmol, 3.0 eq.), NaI (30 mg, 0.2 mmol) and THF (10.0 mL) under N_2, the mixture was stirred for 24h at room temperature. The reactant was filtered through celite plate, and the solvent was removed under reduced pressure, subsequently a solution

of *p*-TsOH (100 mg, 0.5 mmol) in $CHCl_3$ (10 mL) was added and stirred at 40°C for 1h. After removing the solvent, the residue was purified by a flash column chromatography (Petroleum ether/ EtOAc = 5:1, V/V) to afford the product **3aa**(2.65g, 91%yield).

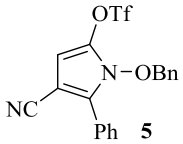
1-benzyloxy-2-phenyl-5-(triisopropylsilyl)oxy-1H-pyrrole-3-carbonitrile (4)



4

To a solution of **3aa**(0.1g, 0.345mmol) in dichloromethane(5mL) was added TIPSOTf (0.158g, 0.51mmol) by syringe slowly under nitrogen. The mixture was stirred for 2h. A saturated solution of brine was added, extracted with CH_2Cl_2 (5mL×3). The combined organic phase was dried over Na_2SO_4, concentrated and finally silica gel flash column chromatographed to give product **4** (132 mg, 86% yield) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62–7.58 (m, 2H), 7.39 (t, *J* = 7.4 Hz, 2H), 7.36–7.31 (m, 1H), 7.29 (dd, *J* = 8.3, 6.5 Hz, 1H), 7.21 (t, *J* = 7.6 Hz, 2H), 7.03 (d, *J* = 7.6 Hz, 2H), 5.55 (s, 1H), 4.85 (s, 2H), 1.35 (dt, *J* = 15.0, 7.5 Hz, 3H), 1.15 (d, *J* = 7.5 Hz, 18H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.30, 132.59, 129.89, 129.31, 129.26, 128.45, 128.36, 128.16, 127.91, 117.51, 88.91, 83.57, 80.58, 17.64, 12.18. HRMS ESI Calcd for $C_{27}H_{35}N_2O_2Si$ $[M+H]^+$: 447.2462, Found: 447.2464. IR (KBr): 2945, 2866, 2218, 1582, 1574, 1530, 1485, 1462, 1362, 1173, 996, 908, 845, 779, 737 cm^{-1}.

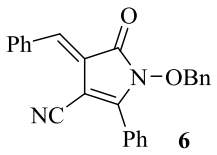
1-benzyloxy-4-cyano-5-phenyl-1H-pyrrol-2-yl trifluoromethanesulfonate



5

At 0℃, to a solution of **3aa**(58mg, 0.2mmol) and DIPEA(51.6mg, 0.4mmol) in dichloromethane(5mL) was added $(CF_3SO_2)_2O$ (84.6mg, 0.3mmol) by syringe slowly under nitrogen. The mixture was stirred at rt for 2h. A saturated solution of brine was added, extracted with CH_2Cl_2(5mL×3), dried over Na_2SO_4, concentrated and finally silica gel flash column chromatographed to give product **5** (61mg, 72%yield) as a light yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 7.73–7.63 (m, 1H), 7.53–7.45 (m, 3H), 7.35 (dd, *J* = 10.9, 4.0 Hz, 1H), 7.26 (t, *J* = 7.4 Hz, 2H), 7.06 (d, *J* = 7.8 Hz, 2H), 6.24 (d, *J* = 1.1 Hz, 1H), 4.84 (s, 2H).^{13}C NMR (125 MHz, $CDCl_3$) δ 133.40, 131.18, 130.30, 130.05, 129.90, 129.53, 128.99, 128.67, 128.47, 126.08, 122.41, 119.85, 117.29, 115.20, 114.73, 98.00, 85.76, 82.13. ^{19}F NMR (471 MHz, $CDCl_3$) *δ* -72.21. HRMS ESI Calcd for $C_{19}H_{14}F_3N_2O_4S$ $[M+H]^+$: 423.0621, Found: 423.0622. IR (KBr): 2959, 2227, 1569, 1524, 1434, 1371, 1246, 1216, 1131, 1115, 904, 869, 842, 792, 764 cm^{-1}.

4-benzylidene-1-benzyloxy-5-oxo-2-phenyl-4,5-dihydro-1H-pyrrole-3-carbonitrile

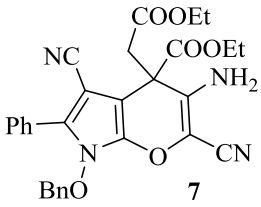


6

3aa(0.145g, 0.5mmol.) and piperydine (4.25mg, 0.05mmol) were added to a solution of benzaldehyde (63.6mg,0.6mmol) in ethanol (5 mL), and the mixture was stirred at reflux for 10 h. The mixture was concentrated under vacue, and the residue was poured into H_2O (10 mL), then extracted with CH_2Cl_2 (10mL×3), and the combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography on silica gel (Ethyl acetate/Petroleum ether= 1:4) to obtain the product (161mg, 85%yield) as a yellow solid. Mp: 124-126 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.35 (d, *J* = 3.6 Hz, 2H), 7.67 (d, *J* = 7.4 Hz, 2H), 7.59–7.43 (m, 6H), 7.37 (s, 2H), 7.29 (t, *J* = 7.3 Hz, 2H), 7.20 (t, *J* = 7.4 Hz, 2H), 7.10 (d, *J* = 7.3 Hz, 2H), 4.97 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.60, 150.30, 142.85, 133.19, 132.67, 132.45, 132.08, 131.47, 130.12, 129.36, 128.85, 128.74, 128.67, 128.47, 125.76, 123.60, 114.23,

84.04, 78.90. HRMS ESI Calcd for $C_{25}H_{19}N_2O_2$ $[M+H]^+$: 379.1441, Found: 379.1442. IR (KBr): 3065, 3027, 2211, 1712, 1614, 1594, 1571, 1491, 1447, 1389, 1155, 1067, 1037, 999 cm^{-1}.

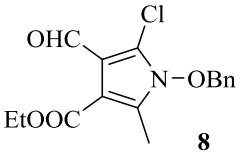
Ethyl 3-amino-7-(benzyloxy)-2,5-dicyano-4-(2-ethoxy-2-oxoethyl)-6-phenyl-4,7-Dihydro-pyrano[2,3-b]pyrrole-4-carboxylate



7

A solution of **3aa** (87mg. 0.3mmol), diethyl but-2-ynedioate (51mg, 0.3mmol) and malononitrile (19.8mg, 0.3mmol) in ethanol(5mL) was stirred at 50°C for 1h. After removing the solvent, H_2O(10mL) was added, and extracted with EtOAc (5mL×3). The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography on silica gel (Ethyl acetate/Petroleum ether= 1:1) to obtain the product (112mg, 71%yield) as a yellow solid. Mp: 154-156 °C.^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61–7.54 (m, 2H), 7.46–7.39 (m, 3H), 7.32 (d, *J* = 7.5 Hz, 1H), 7.23 (t, *J* = 7.6 Hz, 2H), 7.09–6.99 (m, 2H), 5.04 (s, 2H), 4.84 (d, *J* = 0.9 Hz, 2H), 4.36–4.26 (m, 2H), 4.10 (q, *J* = 7.1 Hz, 2H), 3.30 (dd, *J* = 40.3, 16.2 Hz, 2H), 1.37 (t, *J* = 7.1 Hz, 3H), 1.20 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.33, 169.13, 159.49, 133.90, 132.30, 131.82, 130.17, 129.81, 129.21, 128.70, 128.49, 128.39, 126.33, 117.62, 115.04, 94.91, 82.95, 81.81, 62.72, 61.31, 60.51, 44.89, 39.87, 14.03, 13.99. HRMS ESI Calcd. For $C_{29}H_{26}N_4NaO_6$ $[M+Na]^+$: 549.1745, found: 549.1746. IR (KBr): 3326, 2220, 2196, 1730, 1651, 1581, 1492, 1475, 1445, 1395, 1220, 1177, 1111, 1023, 914, 858, 749, 732, 694 cm^{-1}.

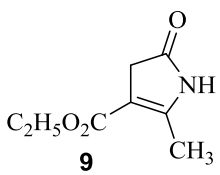
Ethyl 1-(benzyloxy)-5-chloro-4-formyl-2-methyl-1H-pyrrole-3-carboxylate



8

To pyrrolinone **3an** (55mg, 0.20 mmol) and DMF ((29.2 mg, 0.4mmol) was added $POCl_3$ (0.2 mL, 2.2mmol)) in a dropwise manner. The mixture was heated overnight at 100 °C and then poured on ice (8 mL). After 2 h stirring the suspension was extracted with ethyl acetate (5 mL×3). The organic phase was washed with brine and finally dried with sodium sulfate. The solvents were evaporated in vacuo and the residue was purified by flash chromatography on silica gel (CH_2Cl_2) to furnish the product **8** (44 mg, 68% yield) as brownish powder.Mp: 66-68 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.40 (s, 1H), 7.49–7.39 (m, 5H), 5.15 (s, 2H), 4.33 (q, *J* = 7.1 Hz, 2H), 2.36 (s, 3H), 1.36 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 186.95, 163.66, 133.79, 132.26, 130.04, 129.99, 128.96, 117.94, 115.60, 108.23, 81.59, 60.54, 14.34, 10.32. HRMS ESI Calcd for $C_{16}H_{16}ClNNaO_4$ $[M+Na]^+$: 344.0660, Found: 344.0659. IR (KBr): 2981, 2923, 1701, 1674, 1550, 1488, 1455, 1434, 1382, 1353, 1338, 1274, 1123, 1044, 1025 cm^{-1}.

Ethyl 2-methyl-5-oxo-4,5-dihydro-1H-pyrrole-3-carboxylate

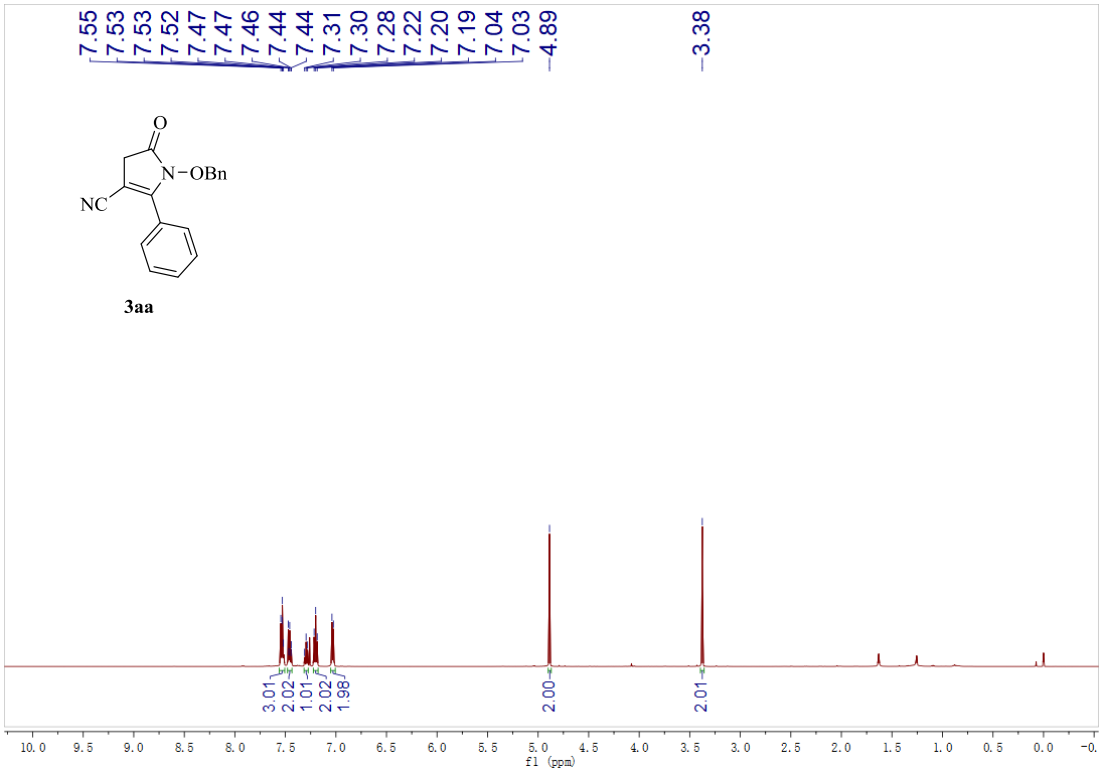


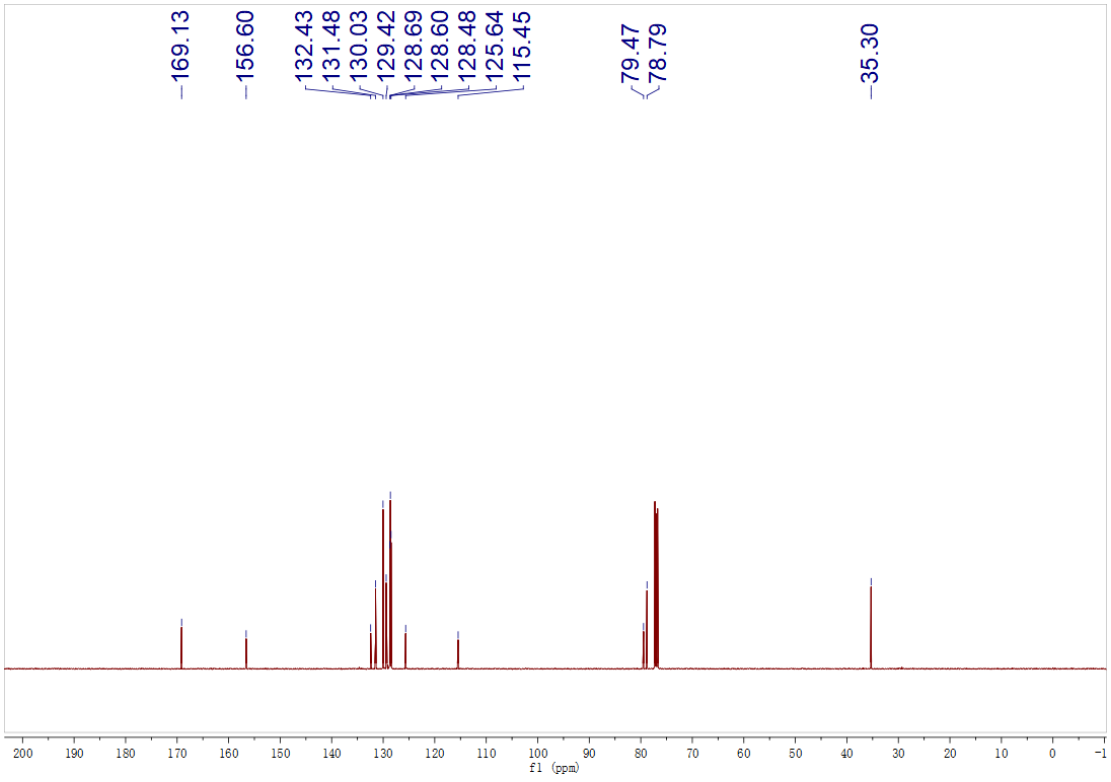
9

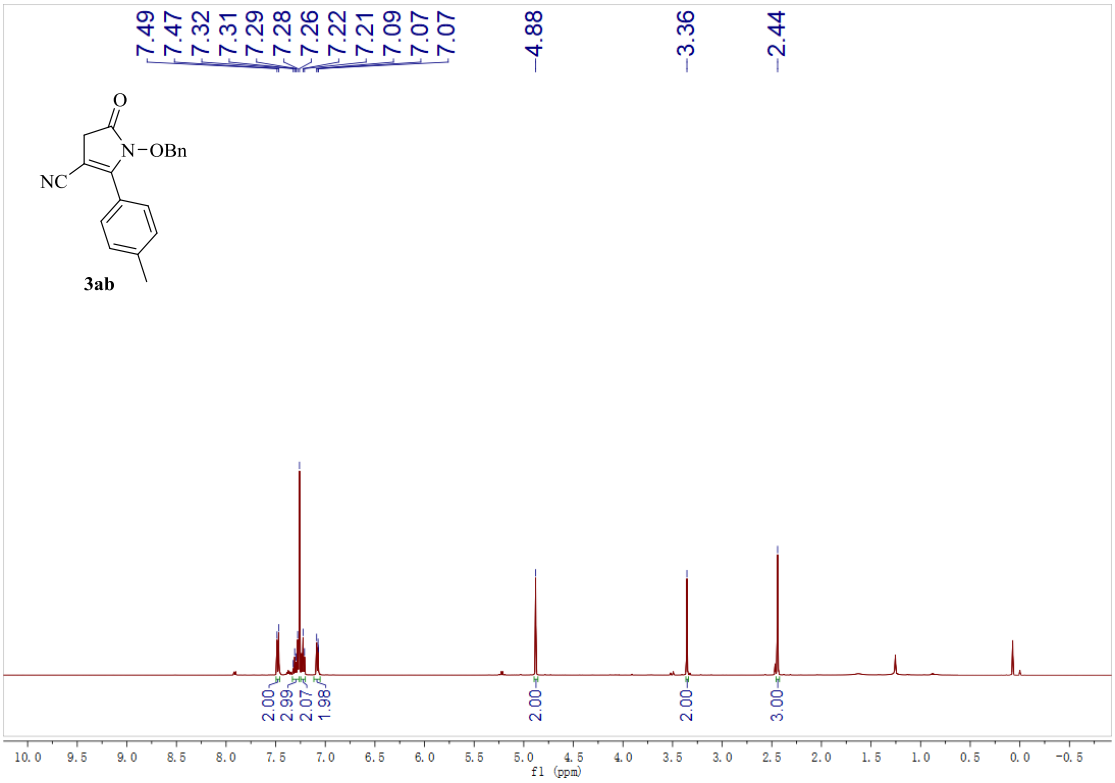
Under N_2 atmosphere Compound **3an** (55mg, 0.2 mmol) was dissolved in THF (3 mL) and then SmI_2 (0.1M, 6mL) was added dropwise by syringe. The reaction mixture was stirred for 12h at room temperature. After filtration through a plug of Celite, the filtrate was concentrated under reduced pressure and purified by flash chromatography on silica gel (Petroleum/EtOAc,1:1, V/V) to afford the product **9** as a pale white powder (29.5 mg, 88% yield).

Mp: 80-82 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.63 (s, 1H), 4.20 (q, *J* = 7.1 Hz, 1H), 3.30 (d, *J* = 2.3 Hz, 1H), 2.36 (t, *J* = 2.3 Hz, 1H), 1.30 (t, *J* = 7.1 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.17, 164.12, 151.49, 104.47, 59.85, 37.50, 14.40, 13.43. HRMS ESI Calcd for $C_8H_{12}NO_3$ $[M+H]^+$: 170.0812, Found: 170.0812. IR: ν 3171, 2987, 2921, 1711, 1690, 1639, 1452, 1372, 1313, 1201, 1121, 1073, 997, 755, 715 cm^{-1}.

4. ^{1}HNMR, ^{13}C NMR and ^{19}F NMR Spectrum for the Products



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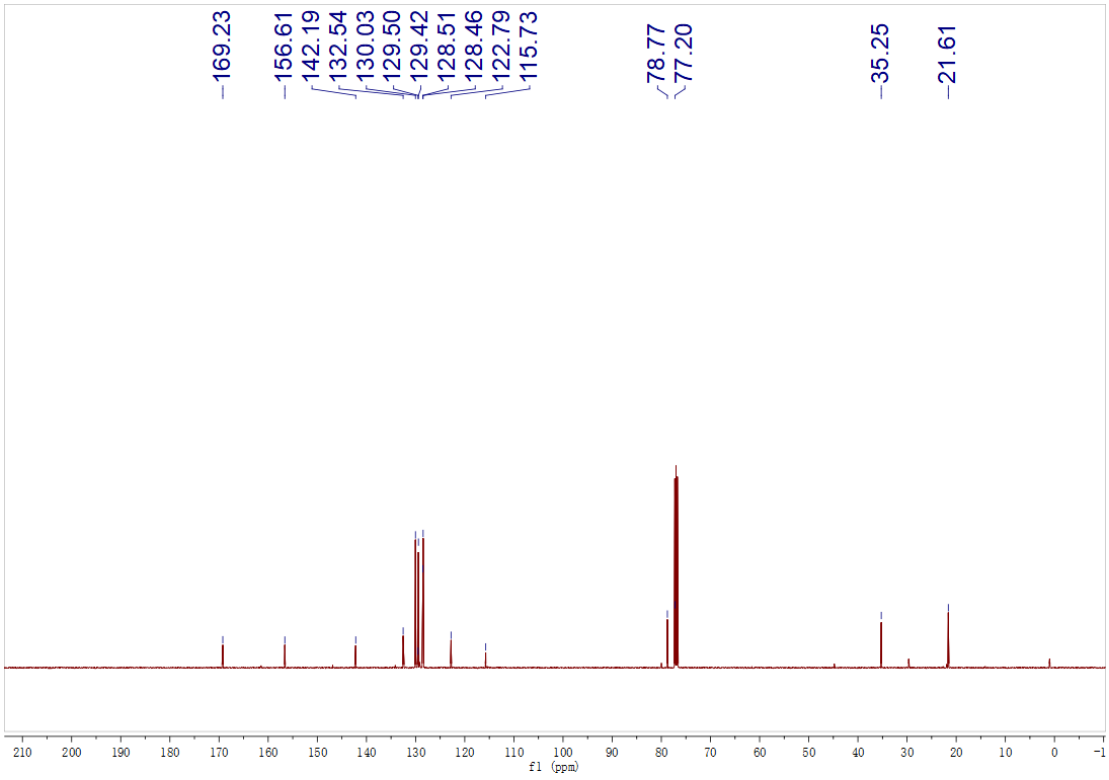
f1 (ppm)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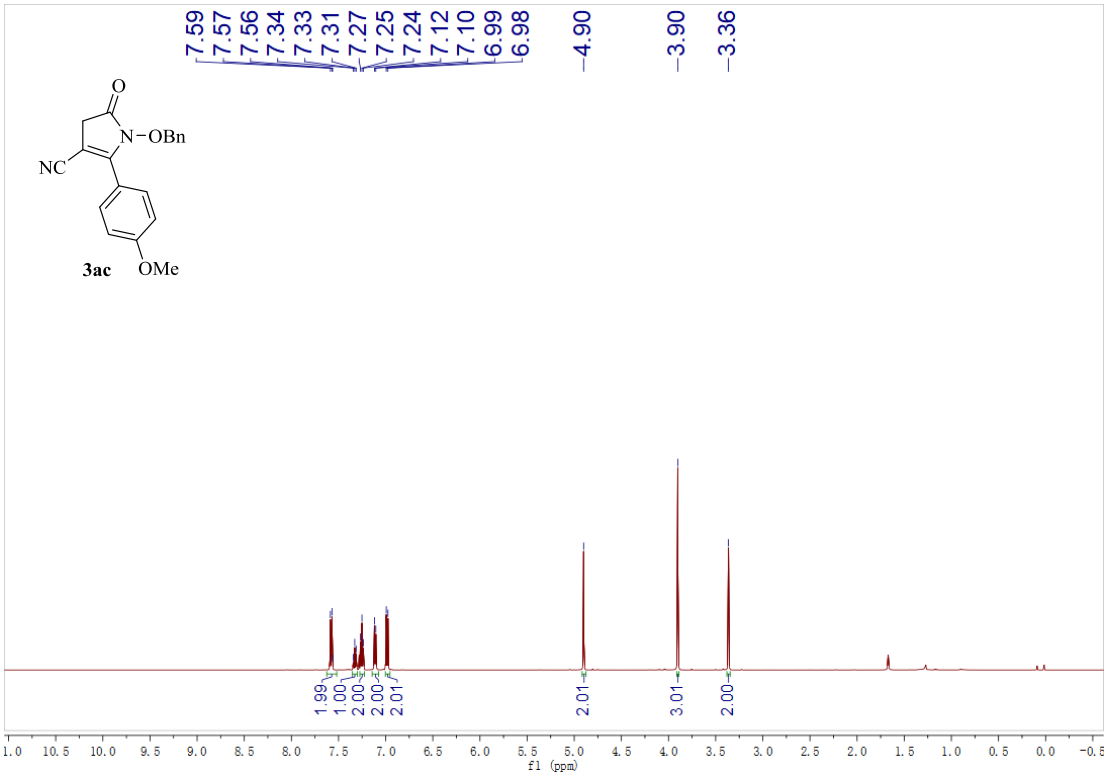
f1 (ppm)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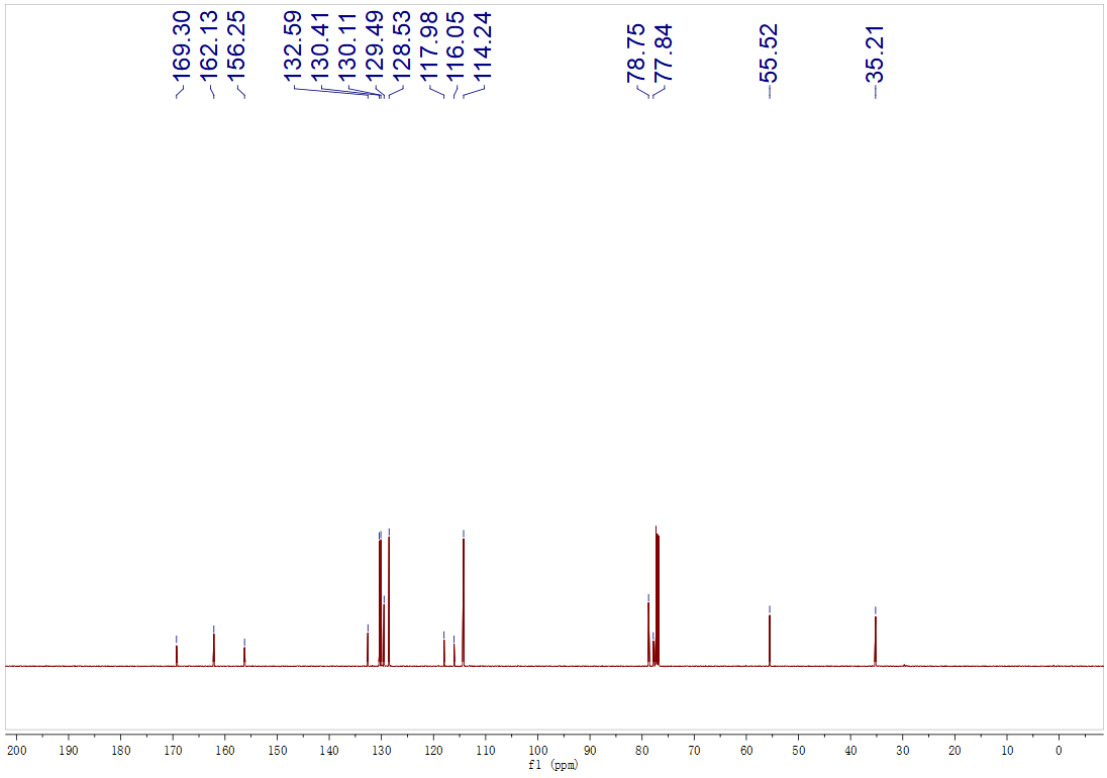
2.00
f1 (ppm)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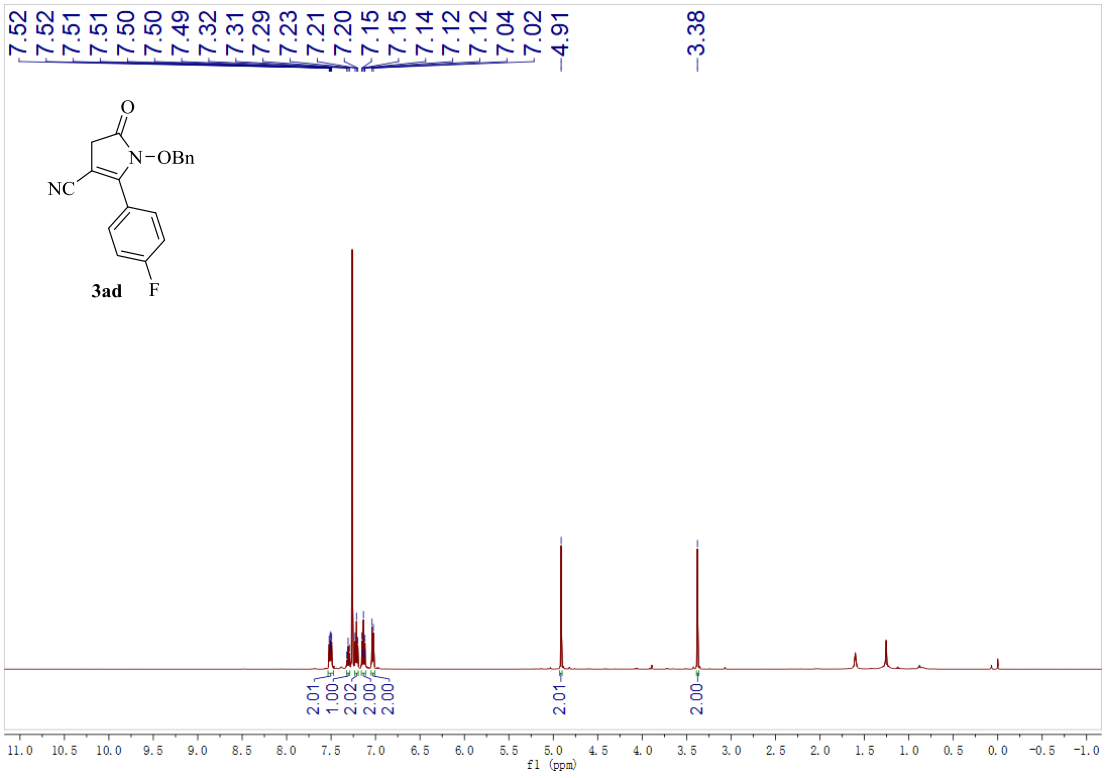
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7.12
7.04
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F
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1.00
2.02
2.00
2.00
2.01
2.00
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
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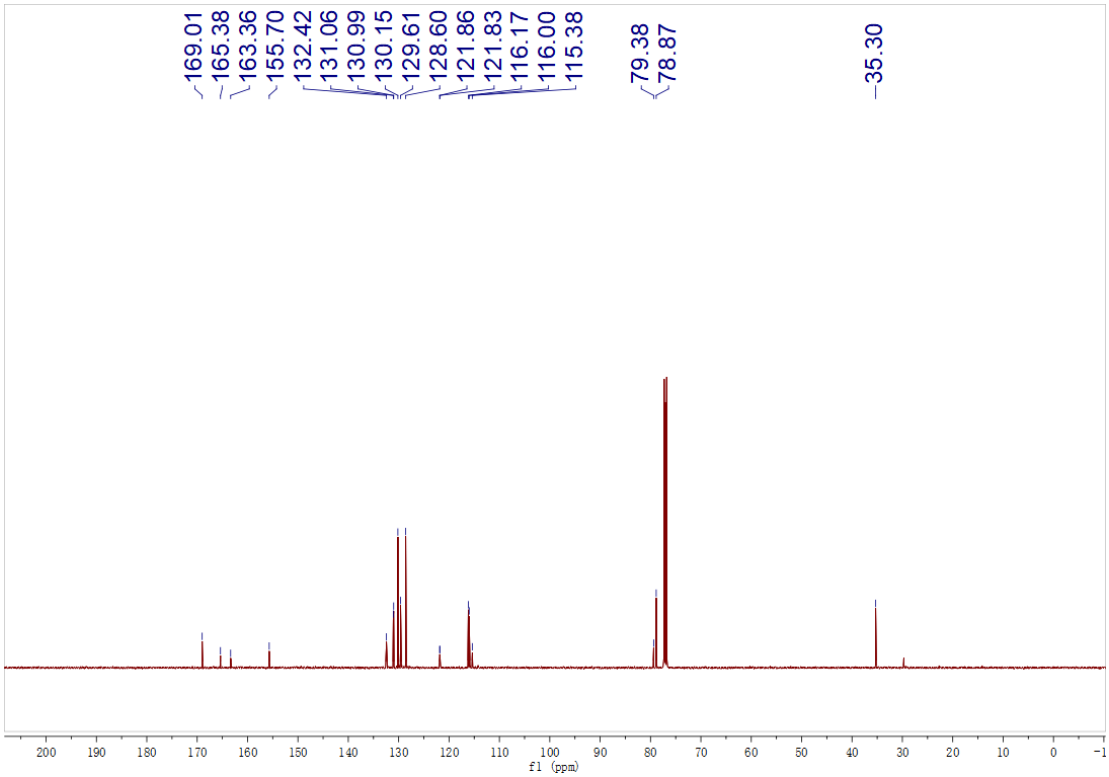
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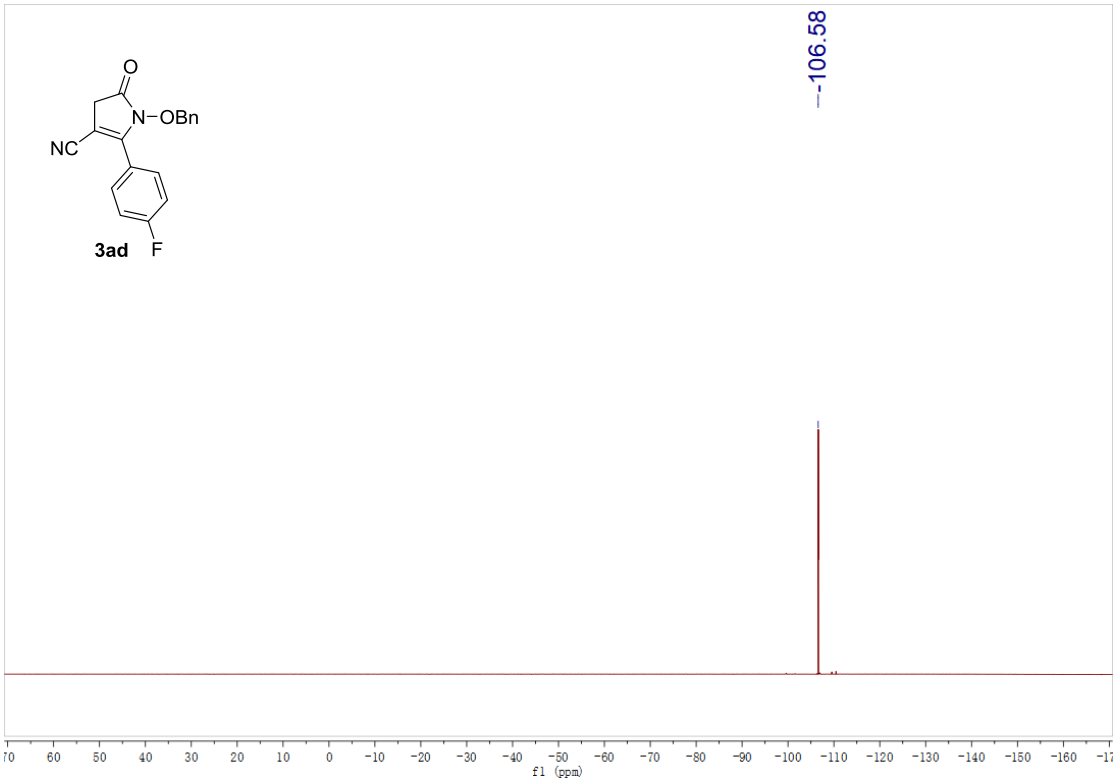
f1 (ppm)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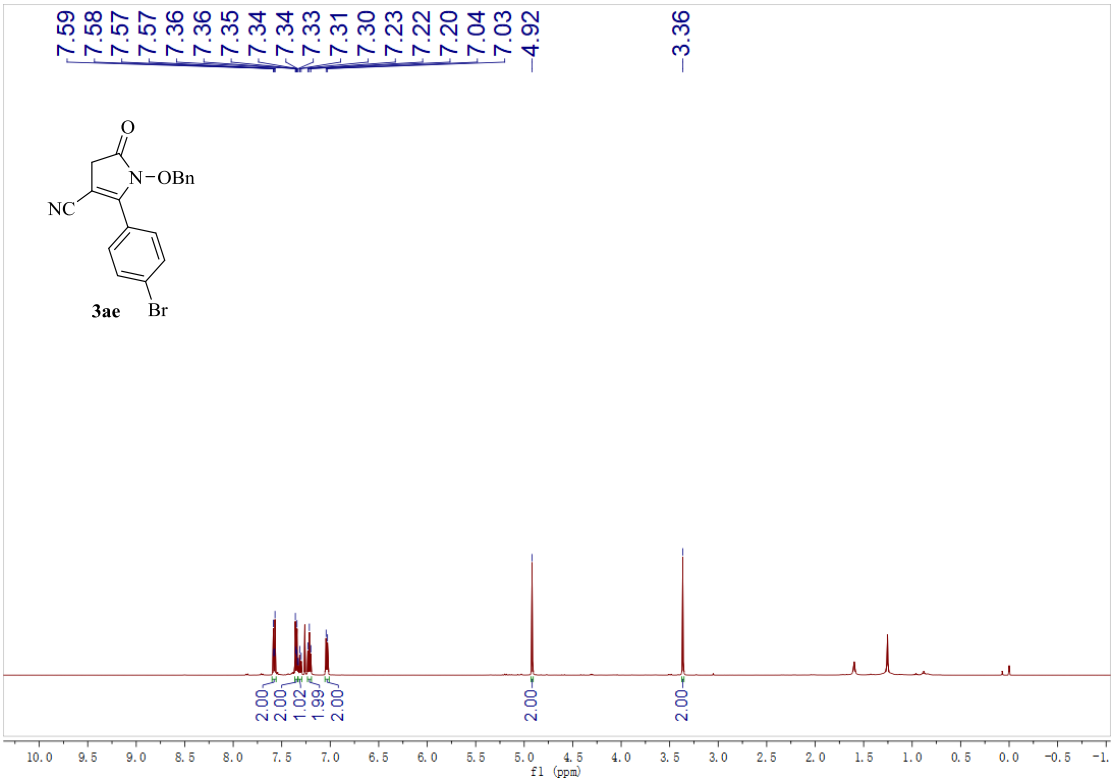
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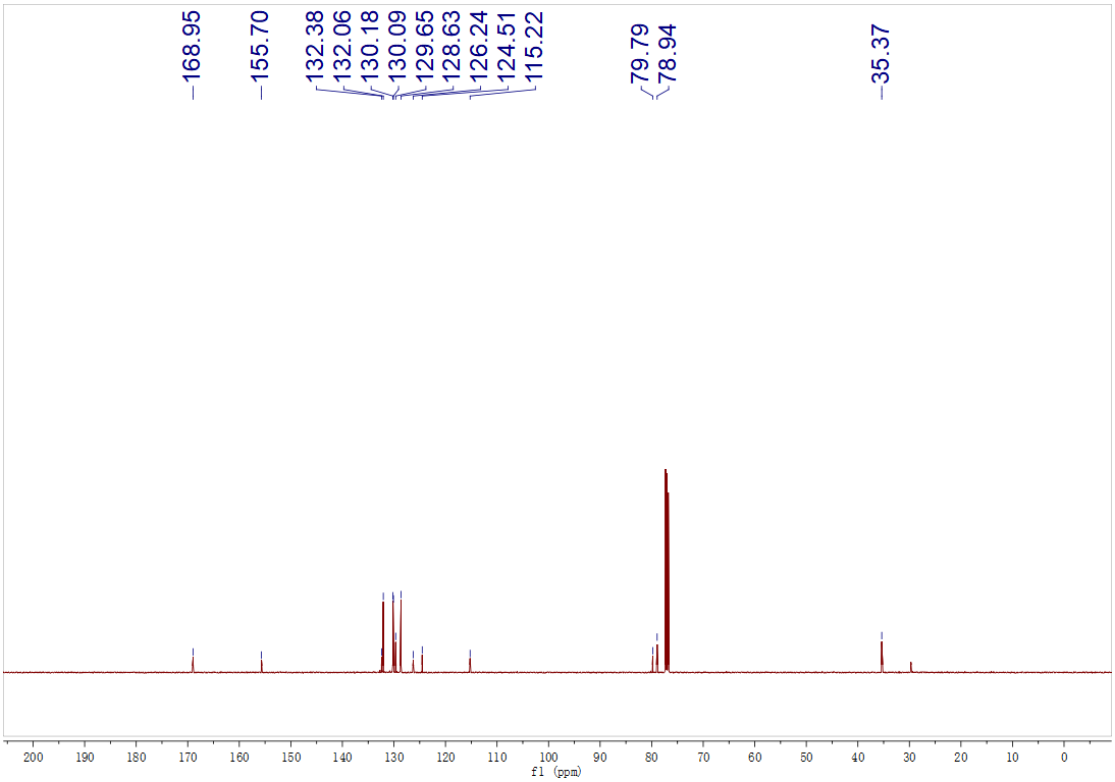
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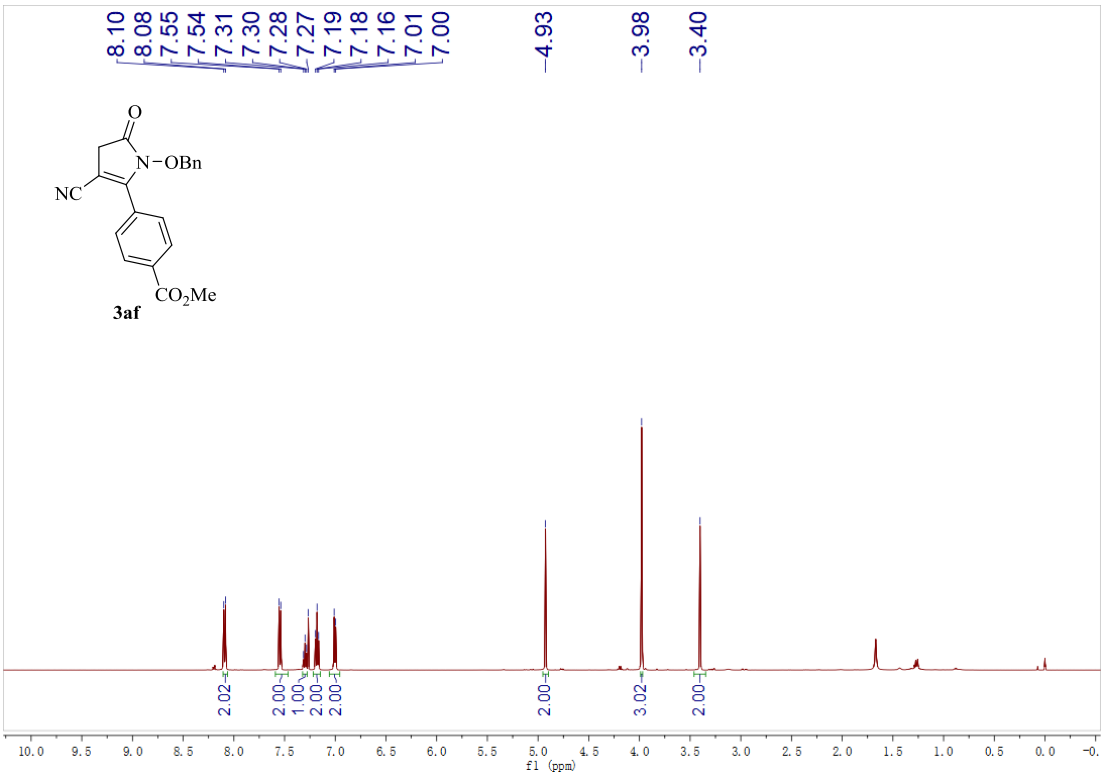
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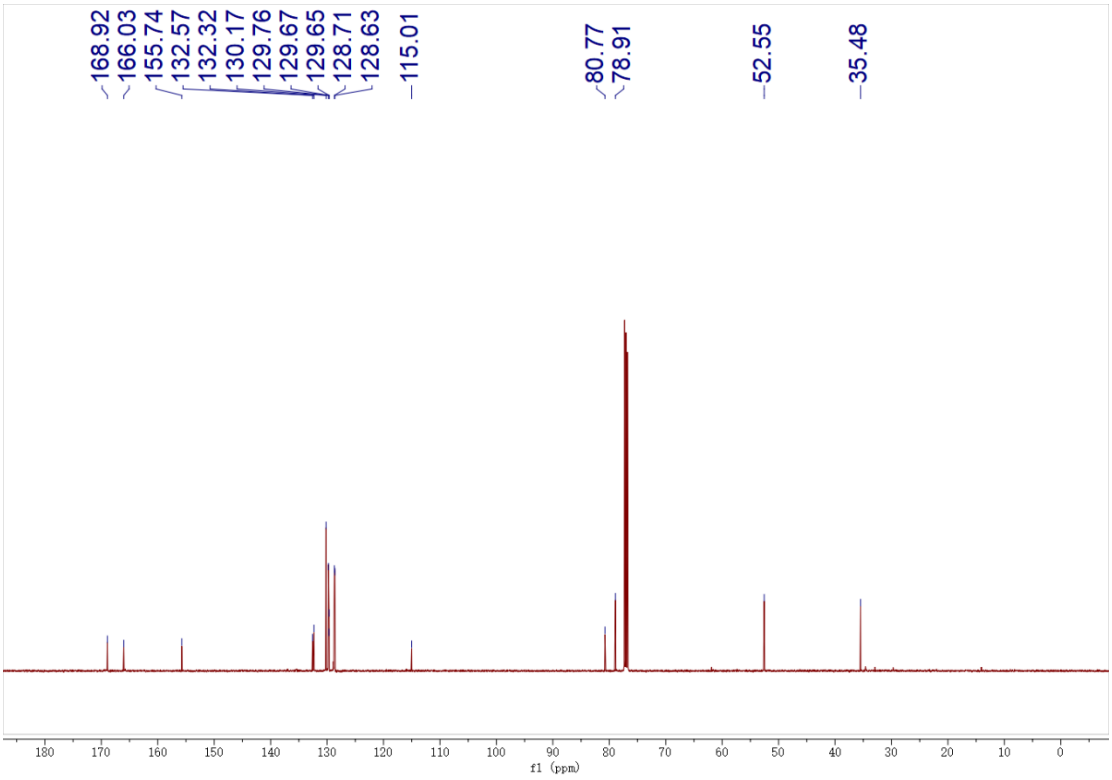
f1 (ppm)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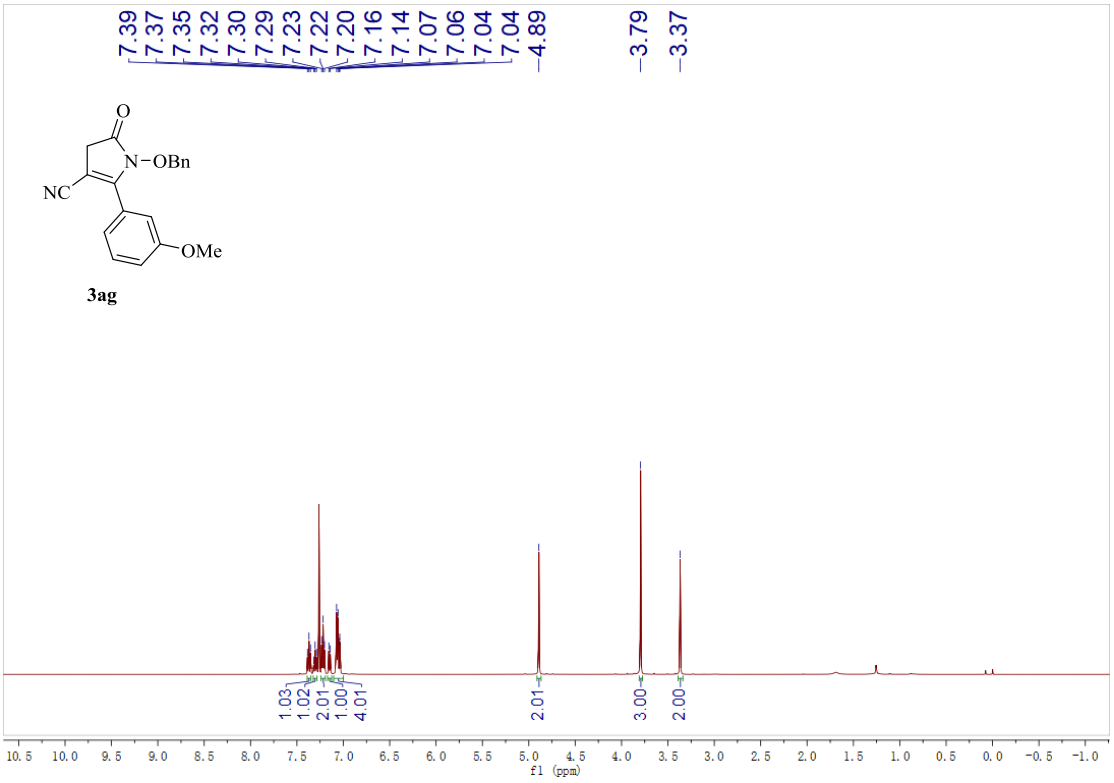
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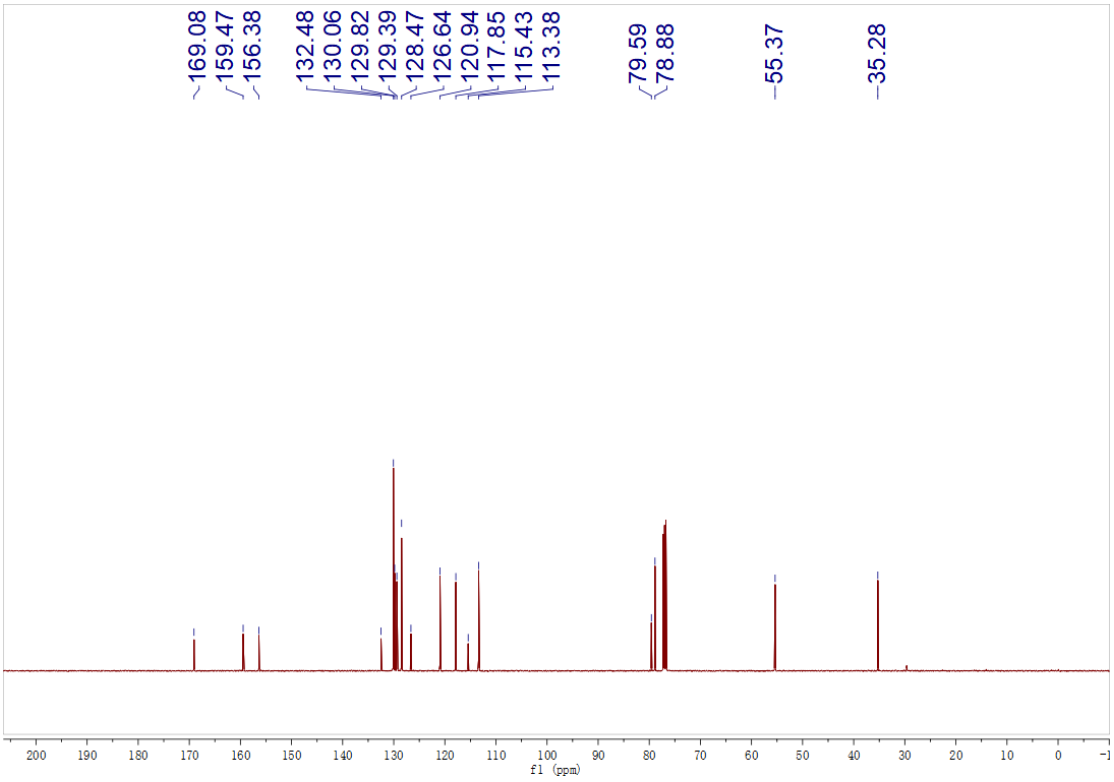
2.00
f1 (ppm)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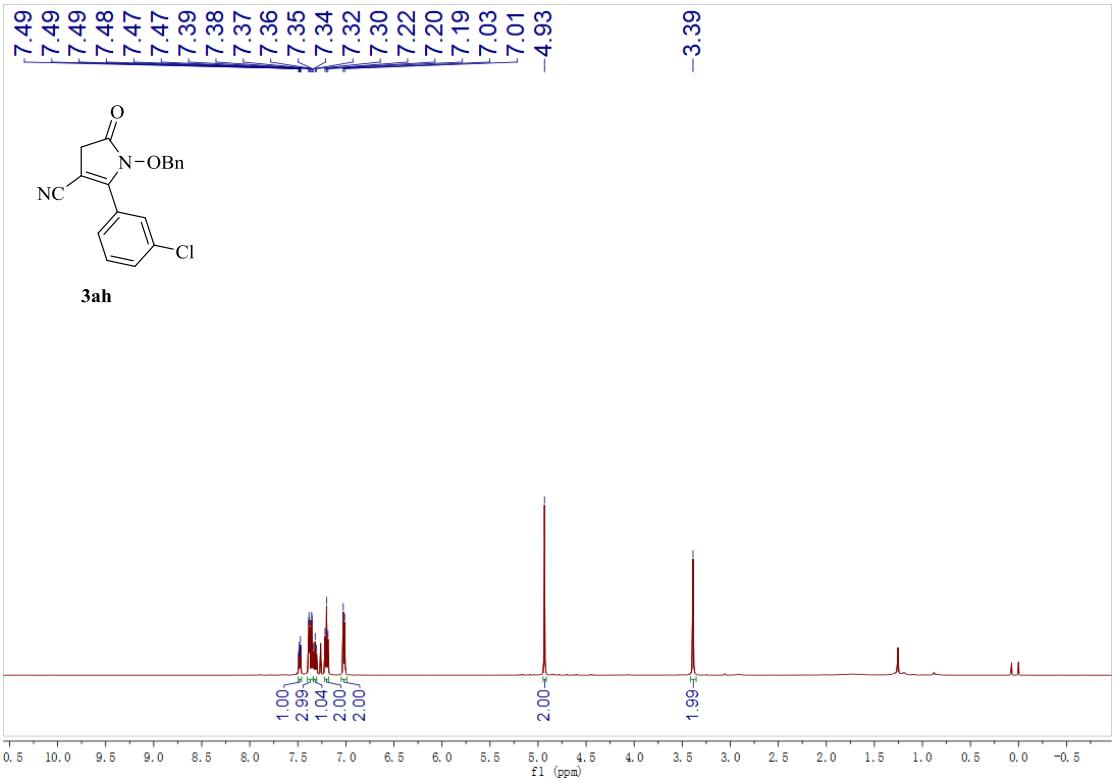
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7.19
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7.01
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Cl
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2.00
2.00
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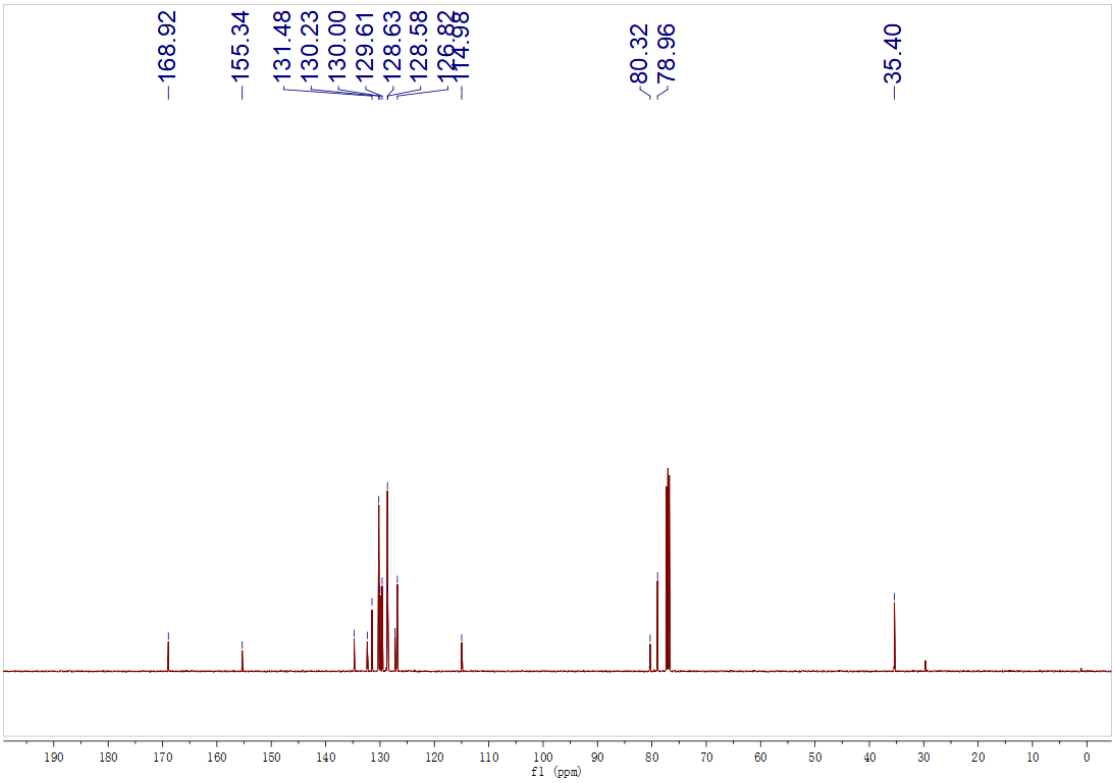
f1 (ppm)

3ah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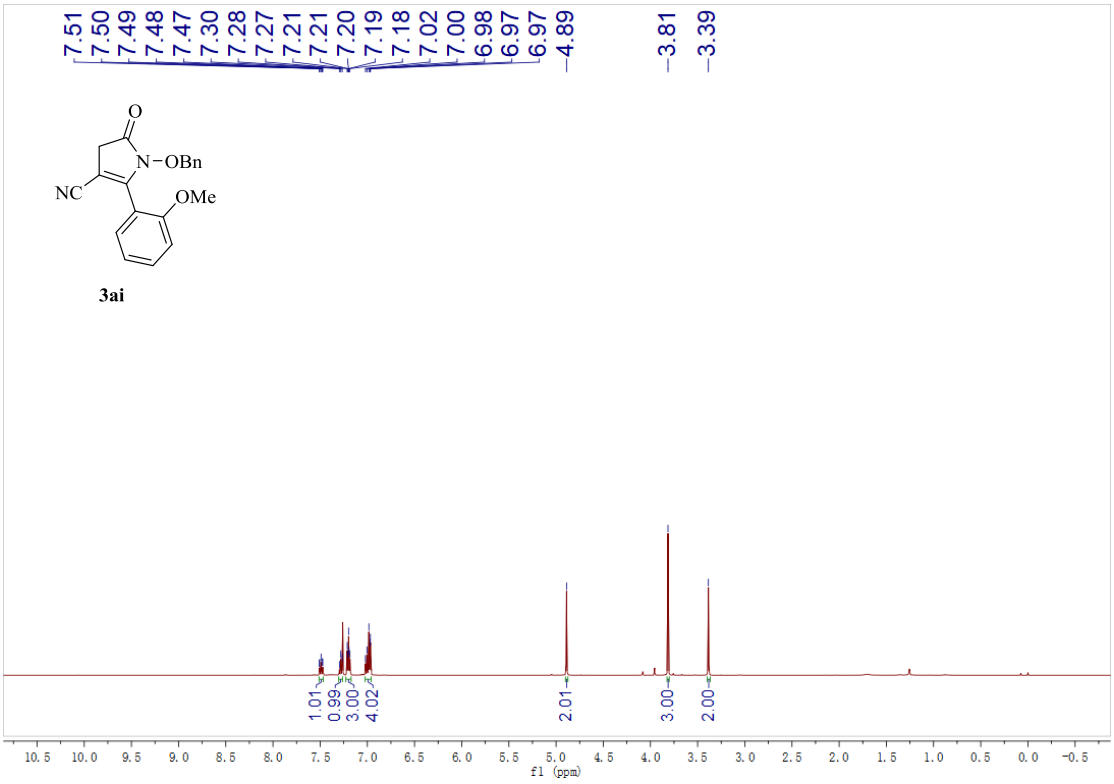
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6.97
6.97
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3.39
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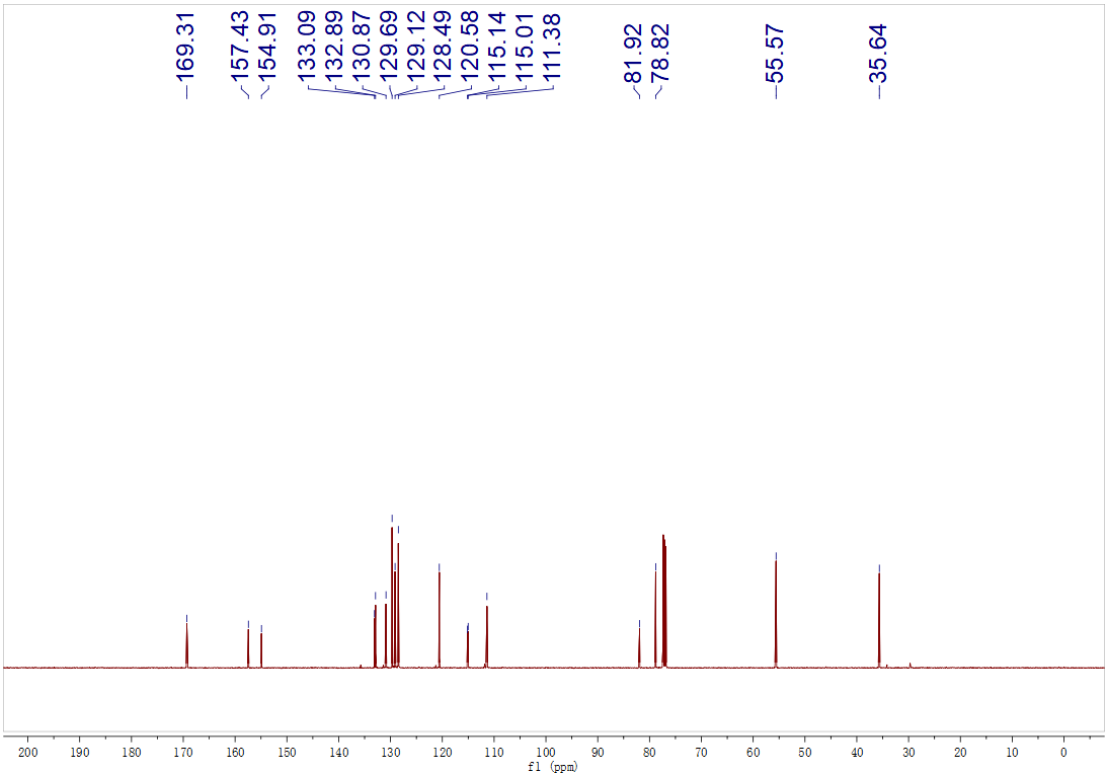
f1 (ppm)

3ai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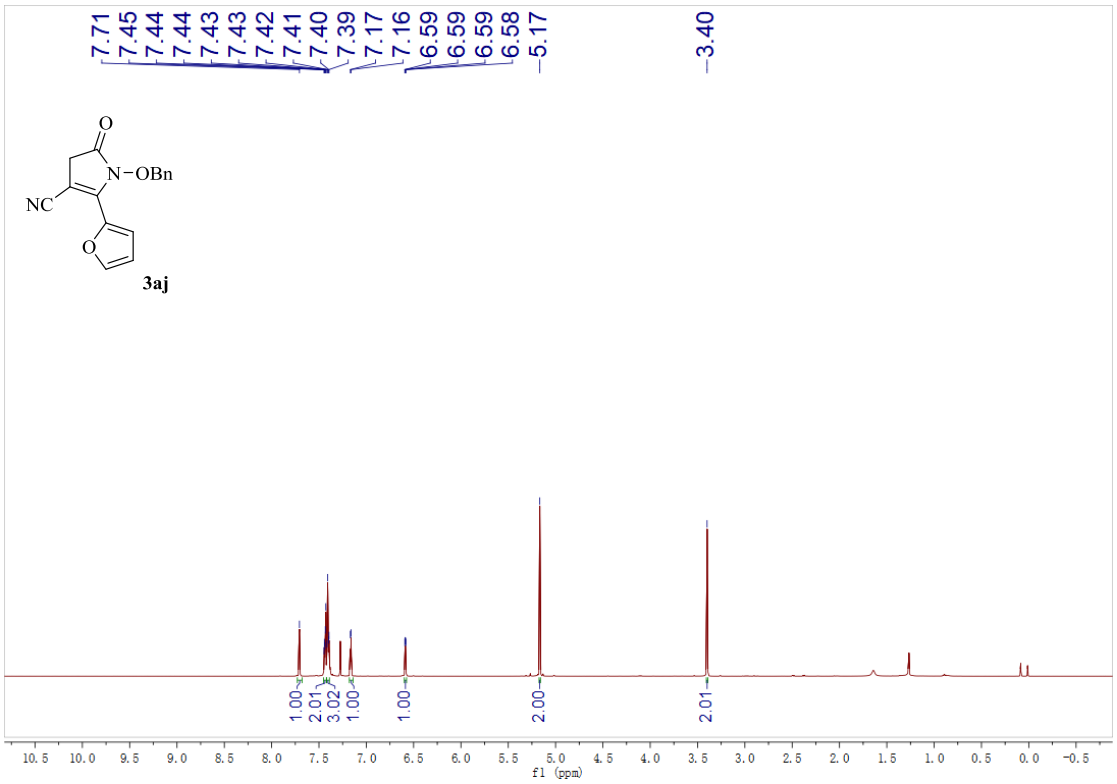
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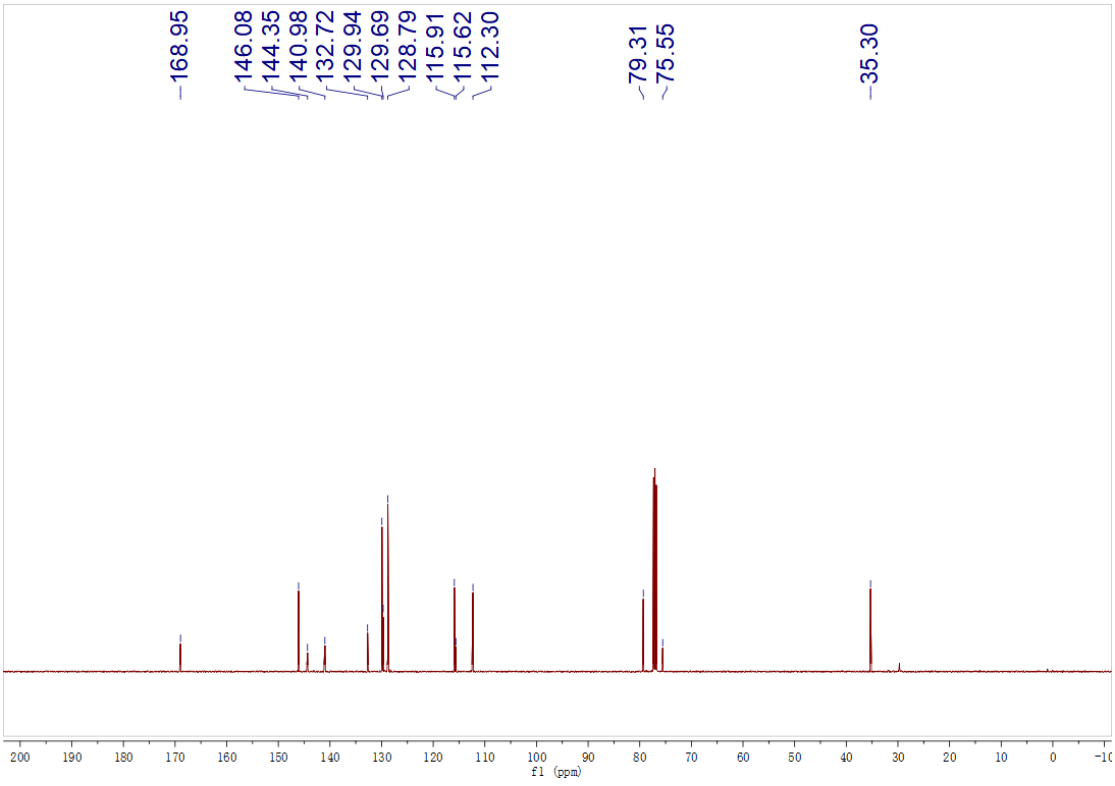
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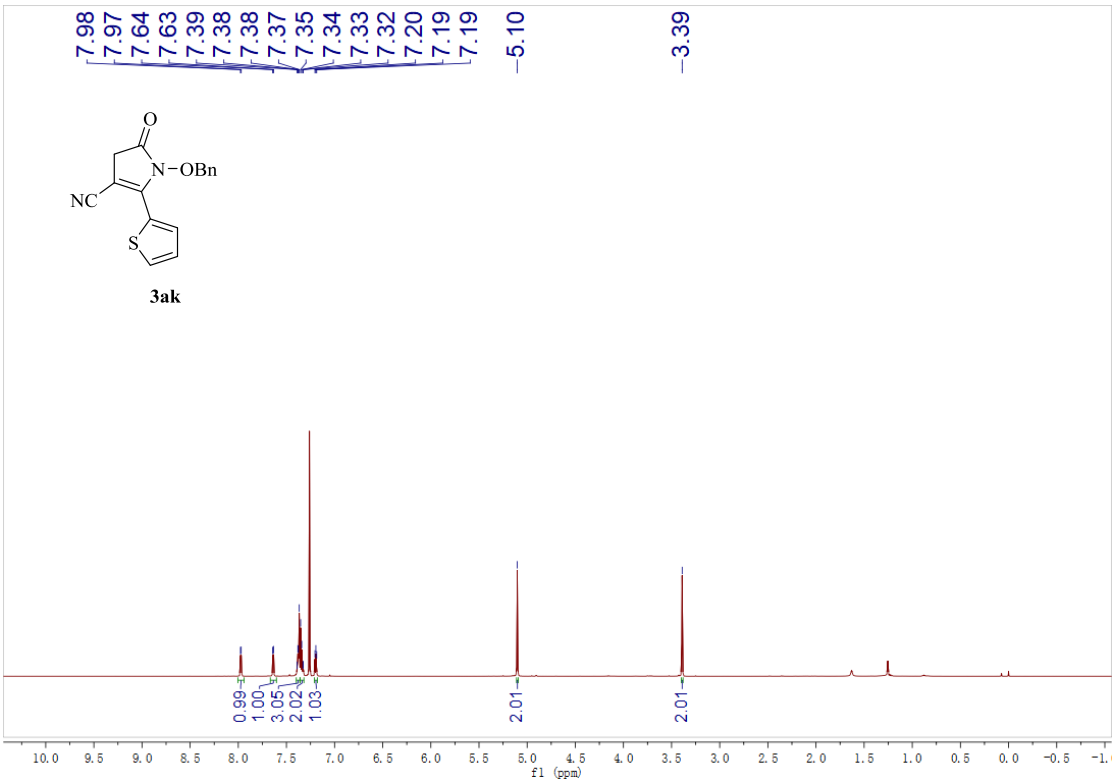
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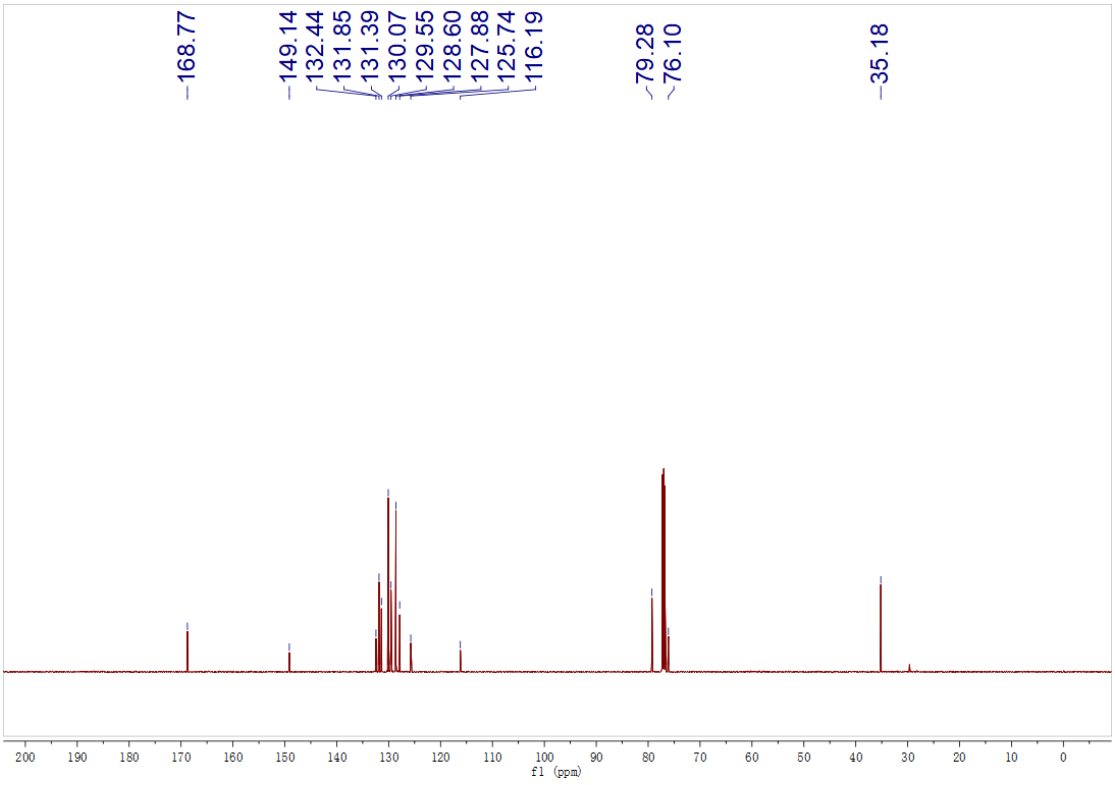
3ak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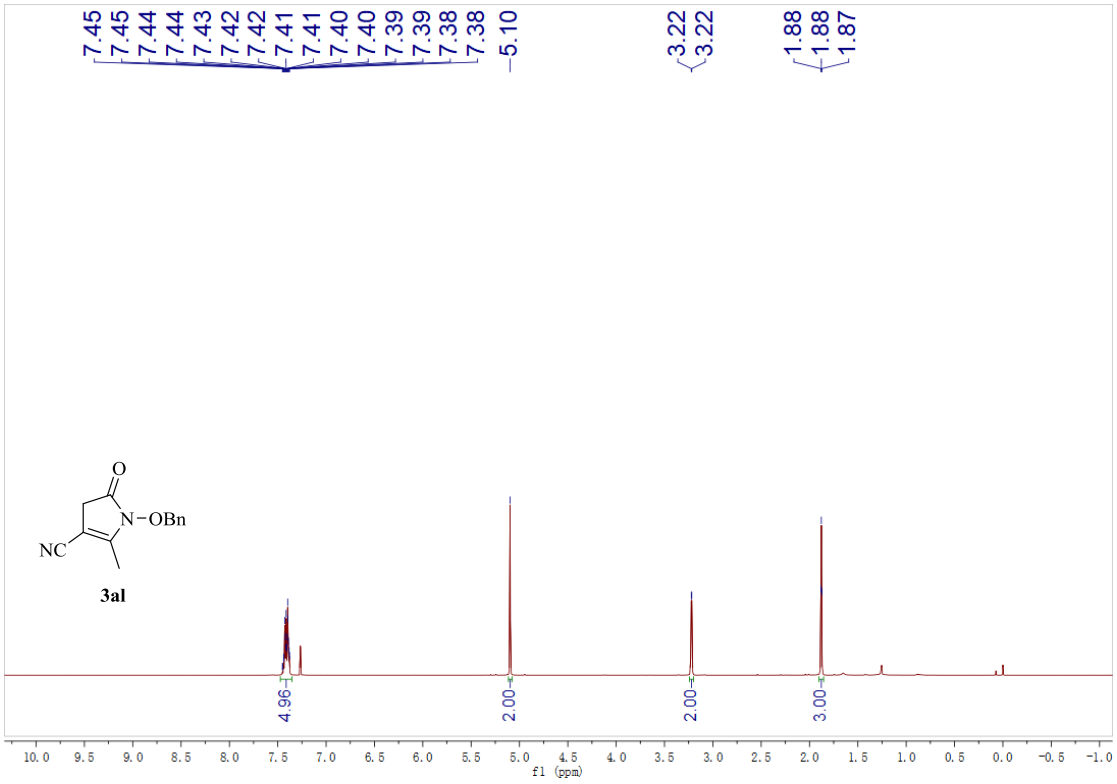
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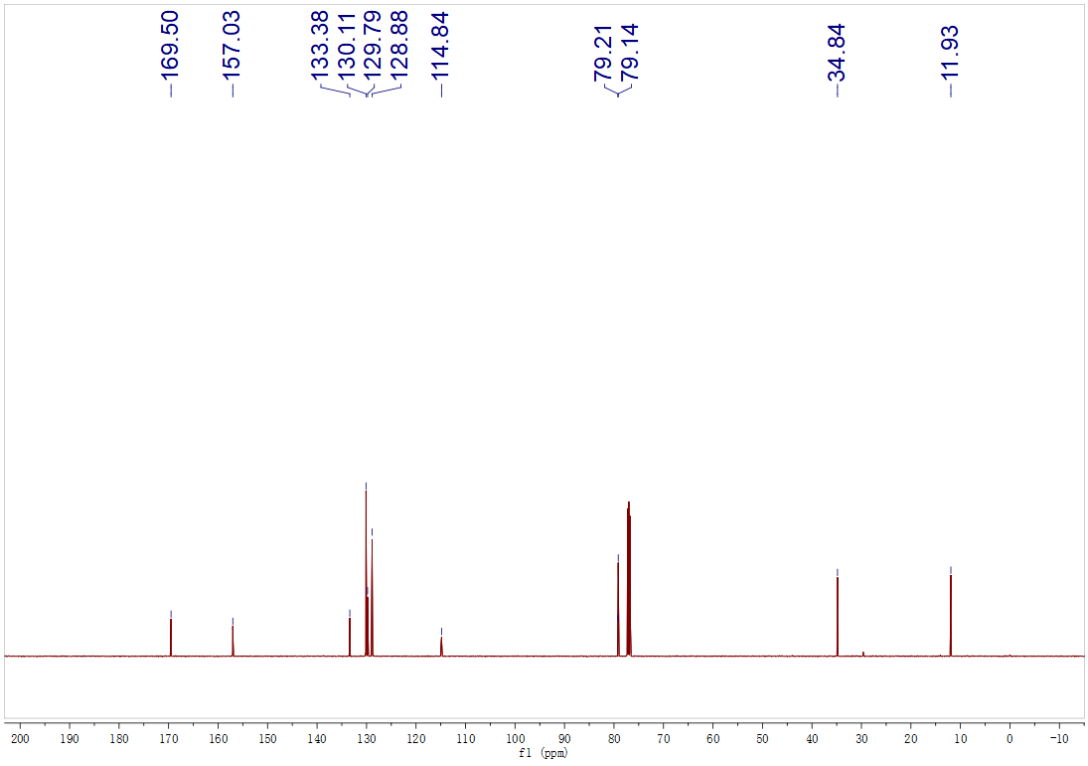
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11.93
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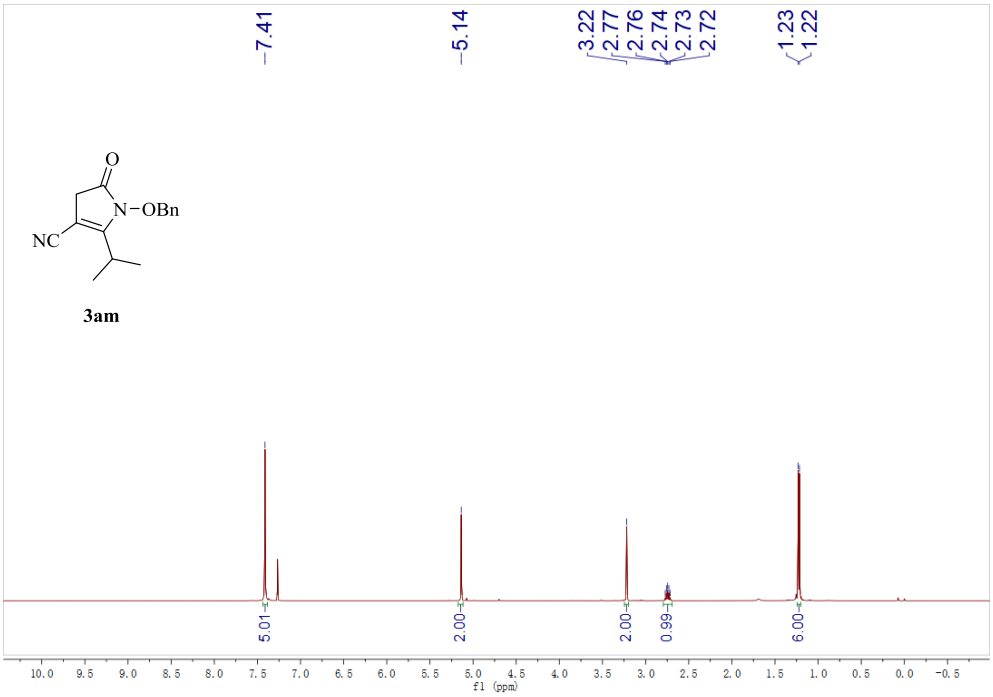
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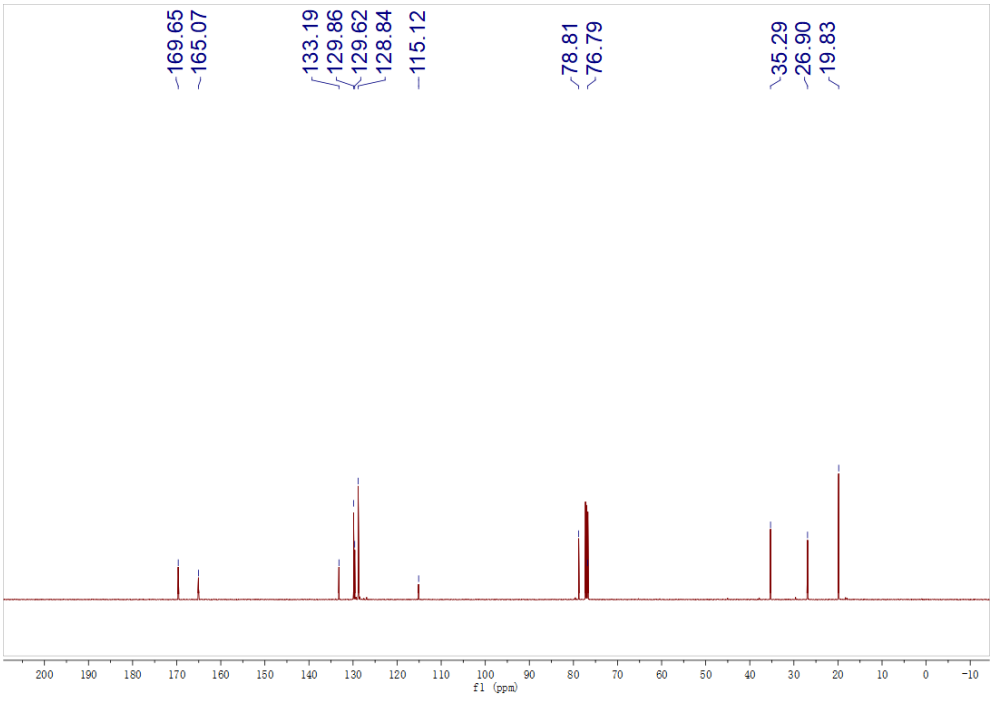
f1 (ppm)

3am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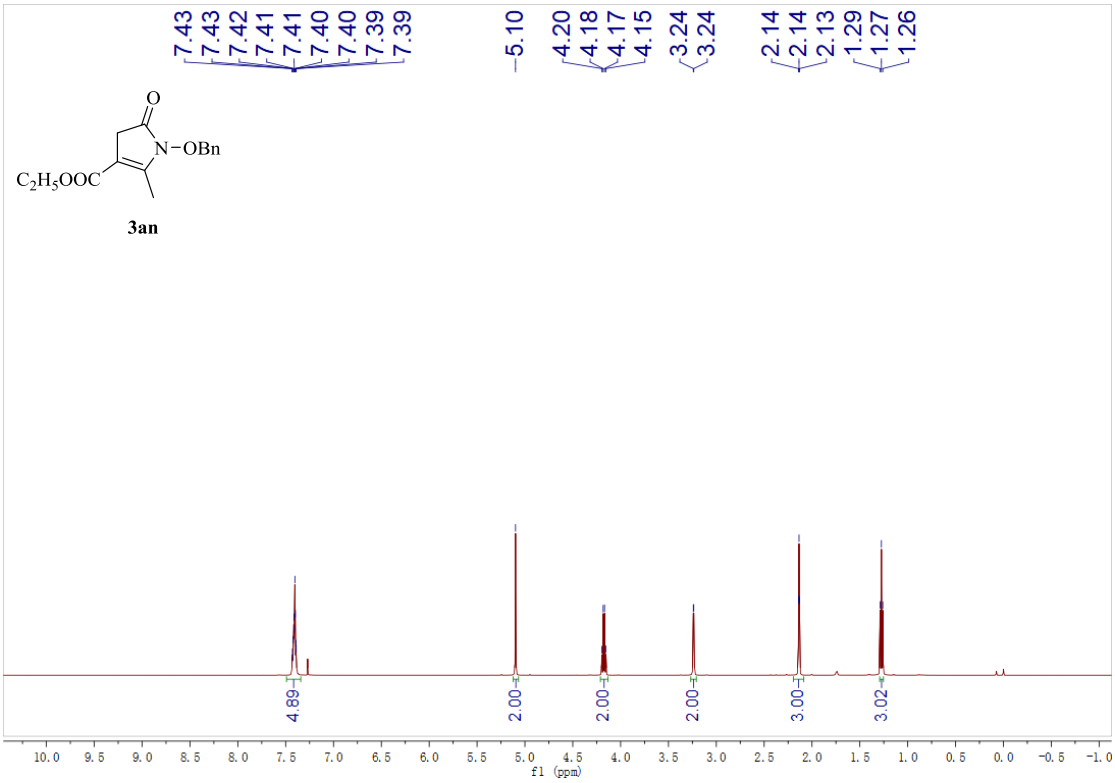
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1.29
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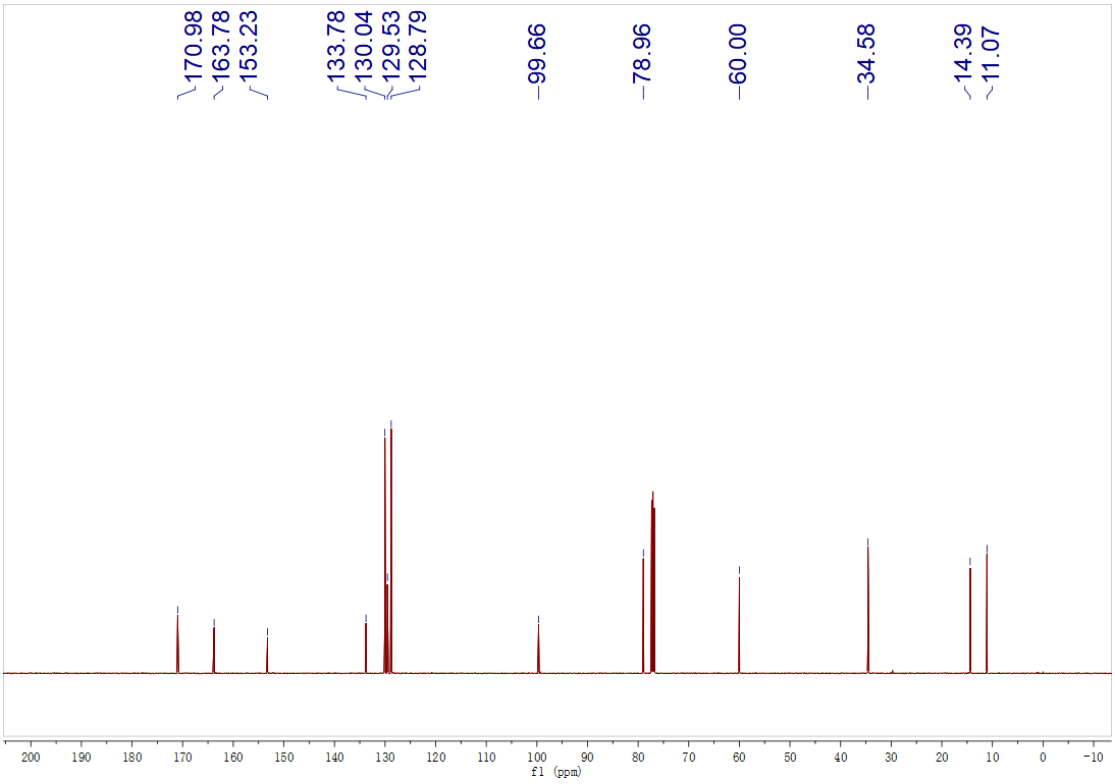
f1 (ppm)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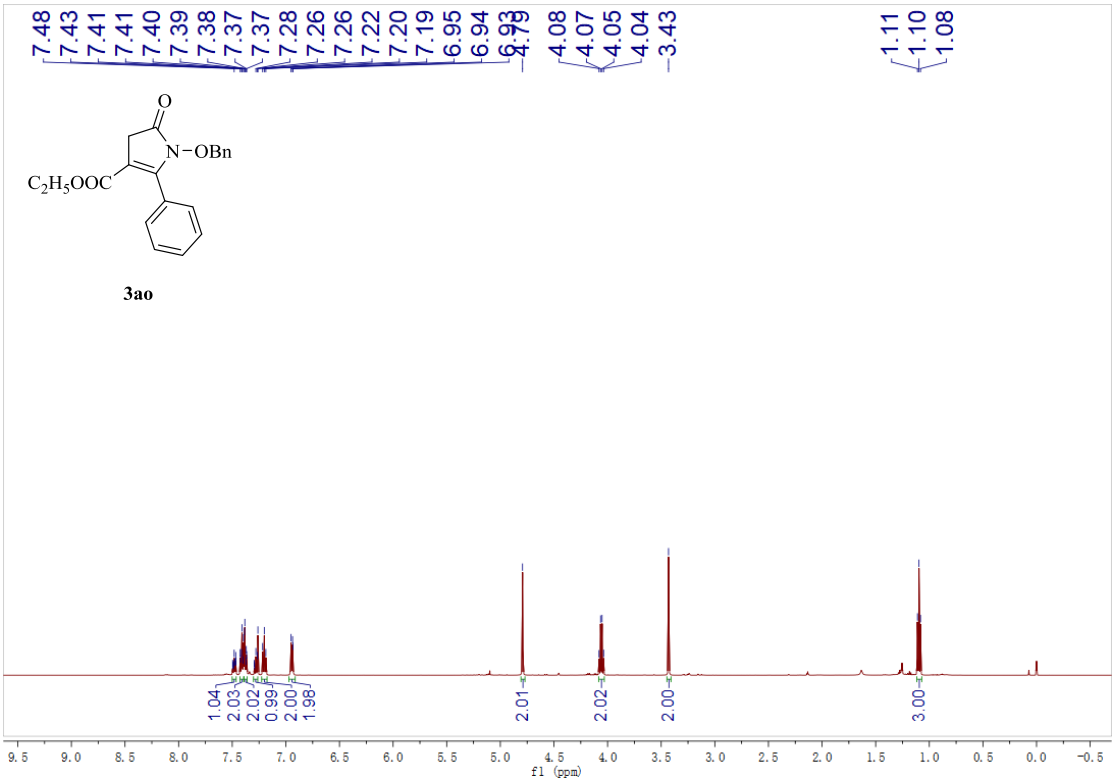
f1 (ppm)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7.39
7.38
7.37
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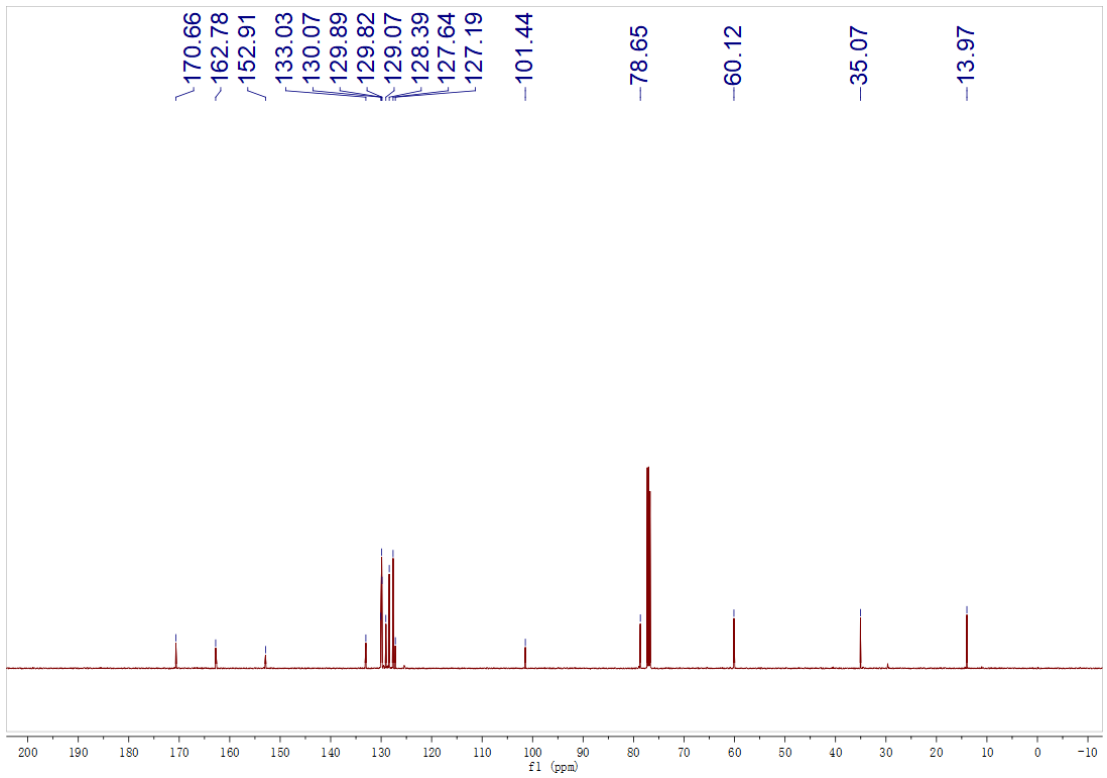
7.28
7.26
7.26
7.22
7.20
7.19
6.95
6.94
6.93
4.08
4.07
4.05
4.04
3.43
1.11
1.10
1.08
O
N−OBn
C2H5OOC
1.04
2.03
2.02
0.99
2.00
1.98
2.01
2.02
2.00
3.00
f1 (ppm)

3ao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129.07
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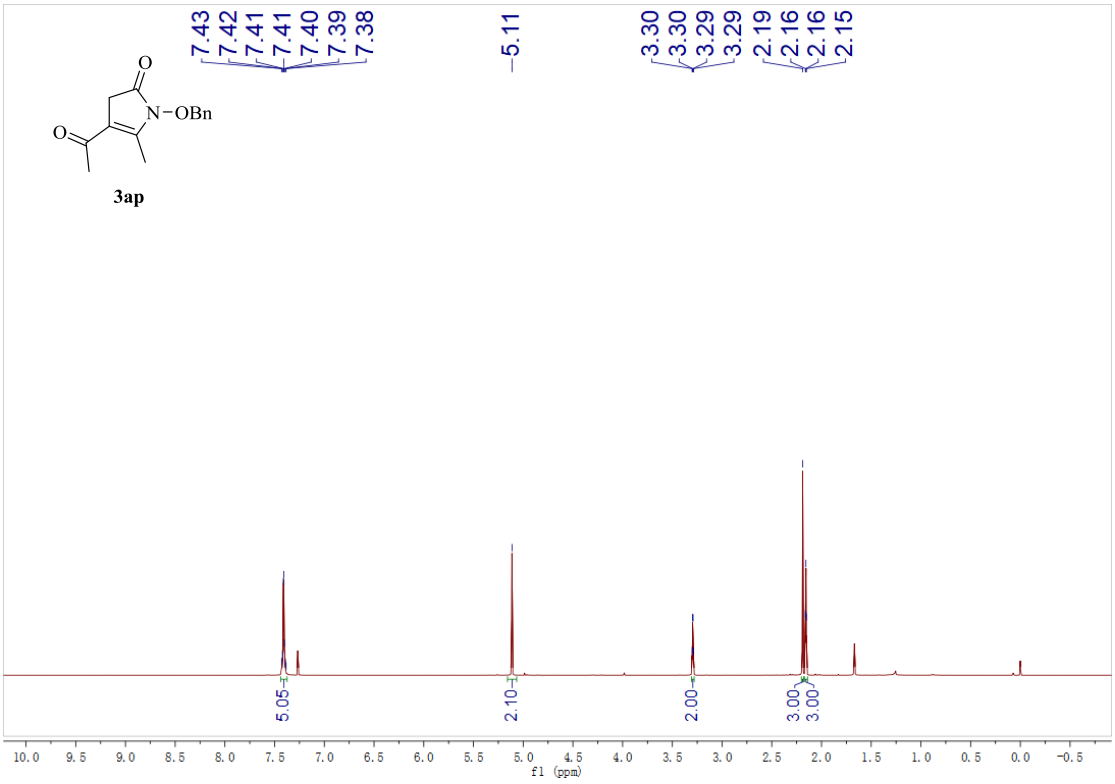
127.19
101.44
78.65
60.12
35.07
13.97
f1 (ppm)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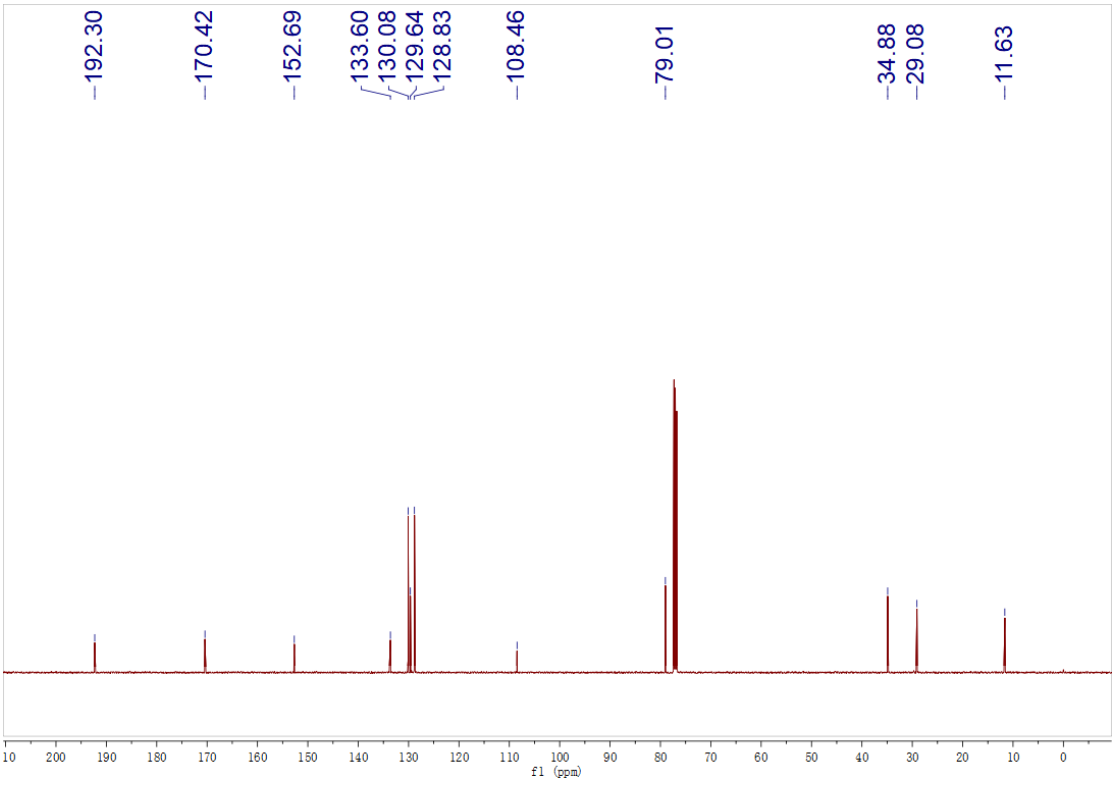
7.40
7.39
7.38
5.11
3.30
3.30
3.29
3.29
2.19
2.16
2.16
2.15
O
N−OBn
O
3ap
5.05
2.10
2.00
3.00
3.00
f1 (ppm)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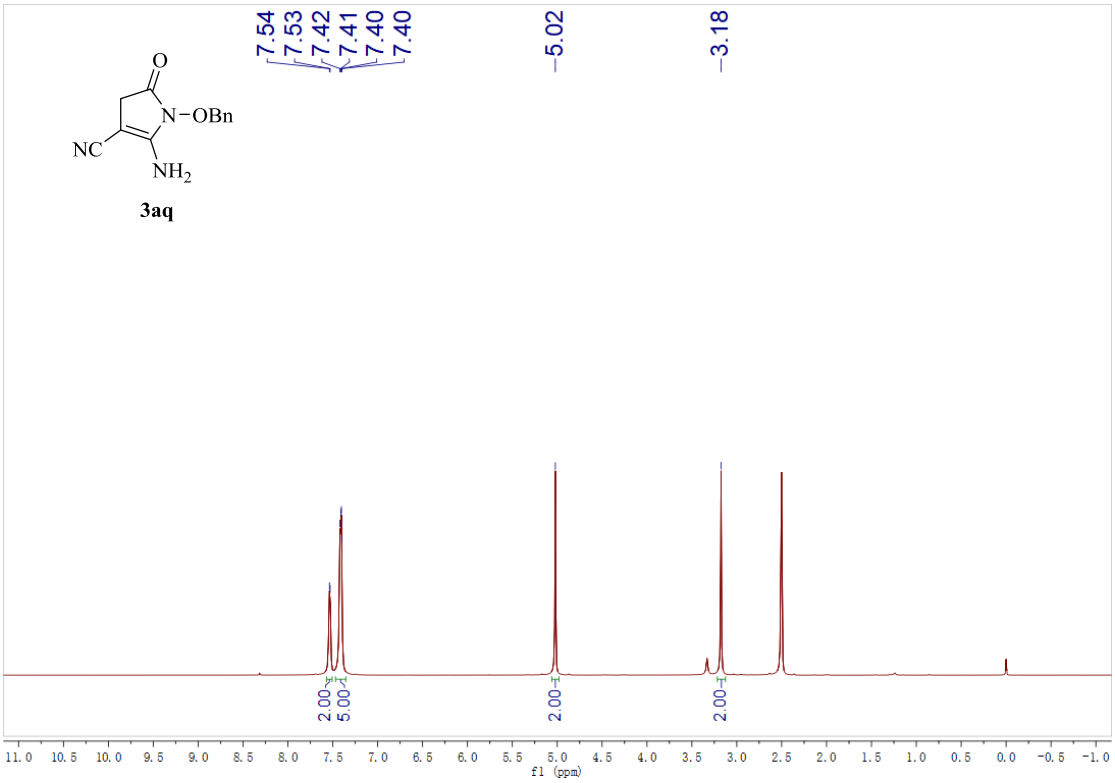
130.08
129.64
128.83
108.46
79.01
34.88
29.08
11.63
f1 (ppm)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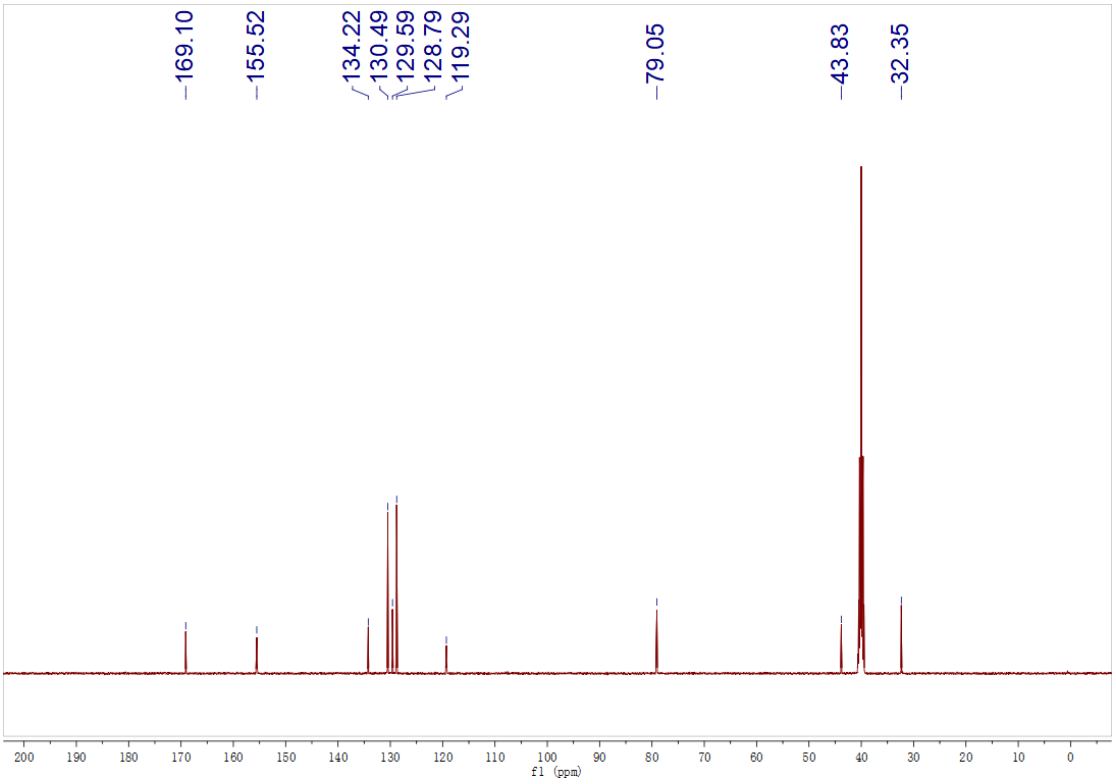
N−OBn
NC
NH2
3aq
2.00
5.00
2.00
2.00
f1 (ppm)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128.79
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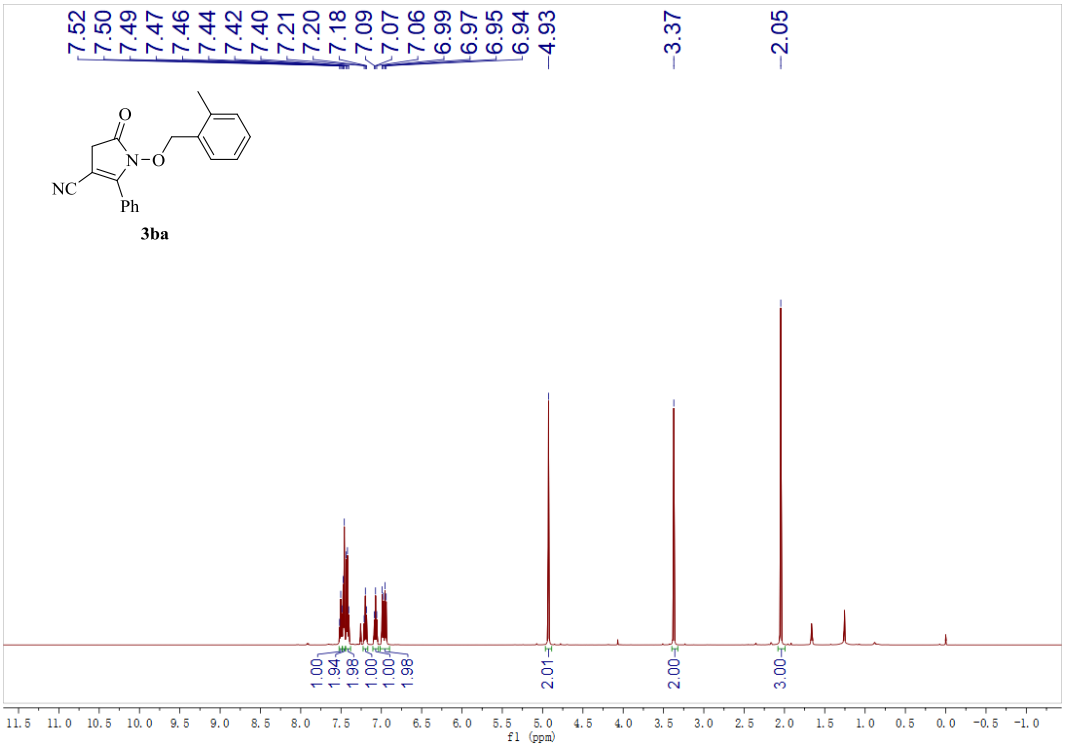
79.05
43.83
32.35
f1 (ppm)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7.40
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7.20
7.18
7.09
7.07
7.06
6.99
6.97
6.95
6.94
4.93
3.37
2.05
O
N–O
NC
Ph
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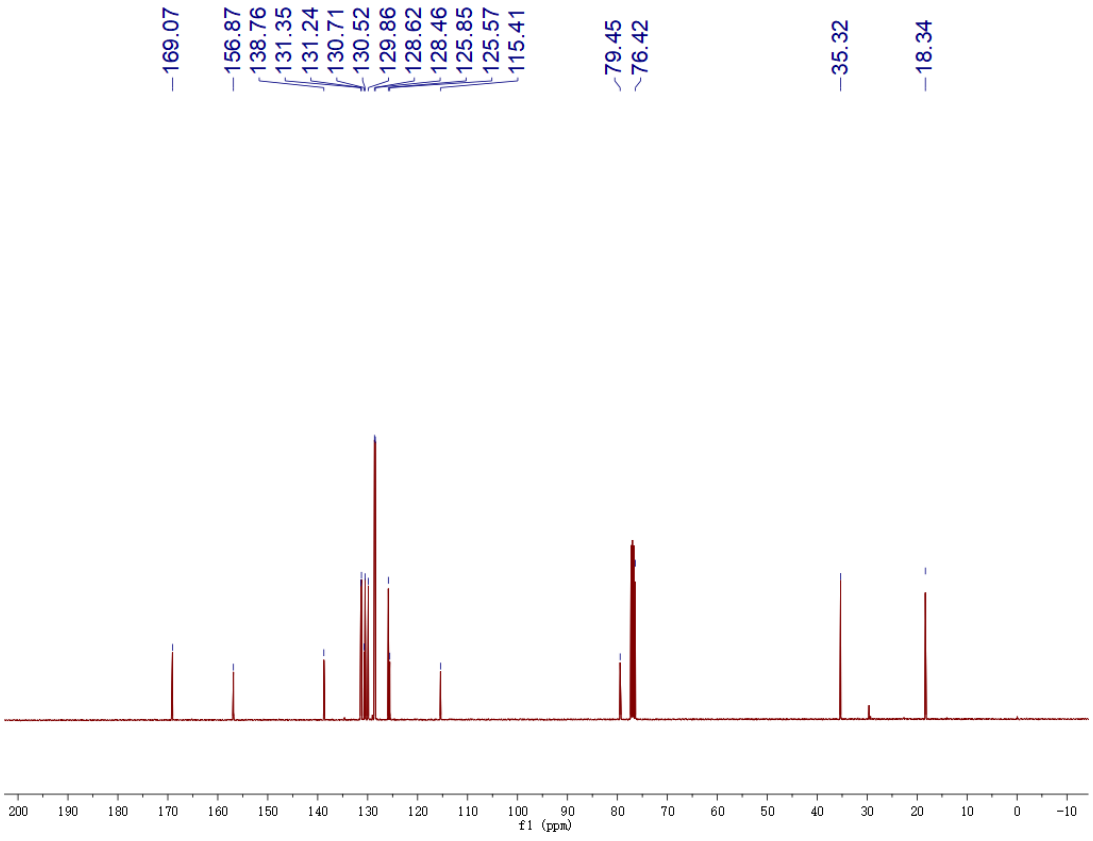
1.94
1.98
1.00
1.00
1.98
2.01
2.00
3.00
f1 (ppm)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125.57
115.41
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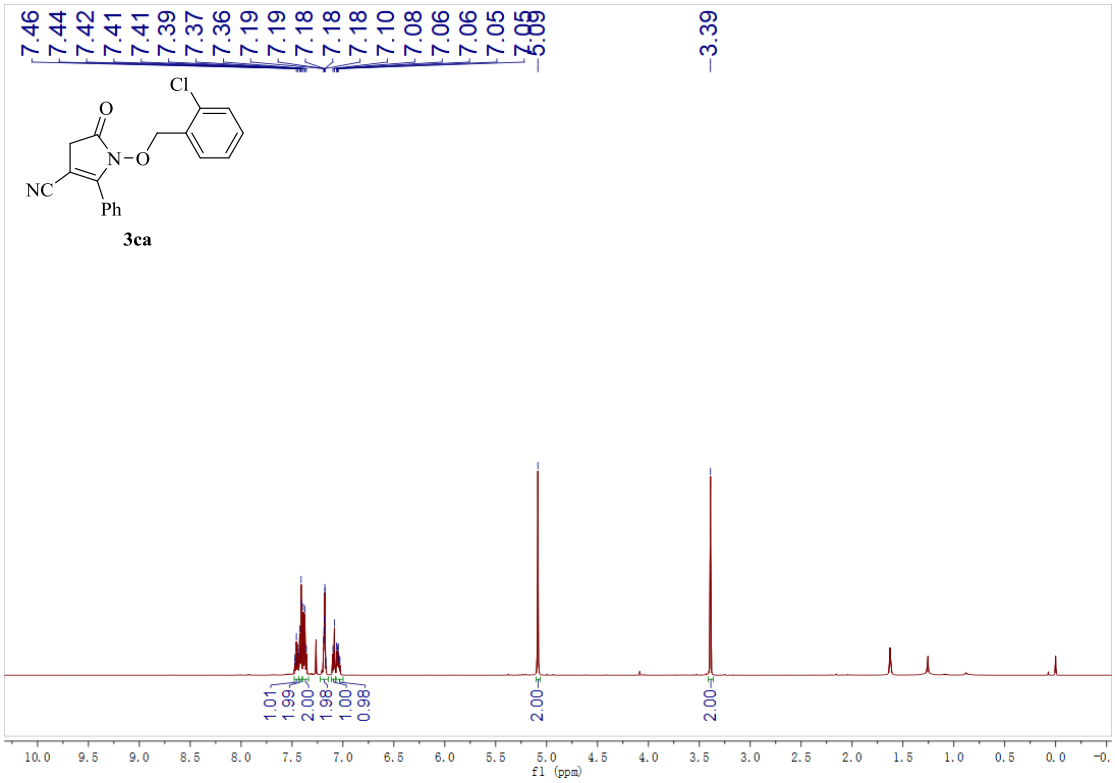
76.42
35.32
18.34
f1 (ppm)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7.19
7.19
7.18
7.18
7.18
7.10
7.08
7.06
7.06
7.05
7.05
5.09
3.39
Cl
O
N
O
NC
Ph
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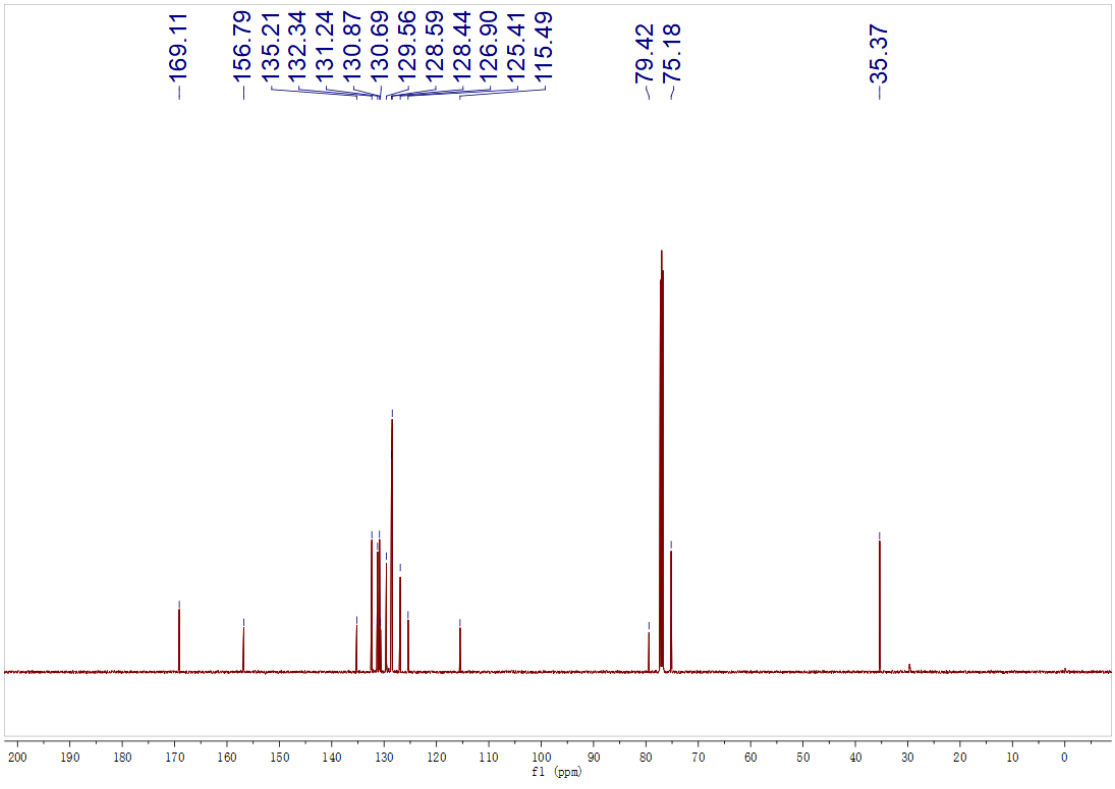
1.01
1.99
2.00
1.98
1.00
0.98
2.00
2.00
f1 (ppm)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156.79
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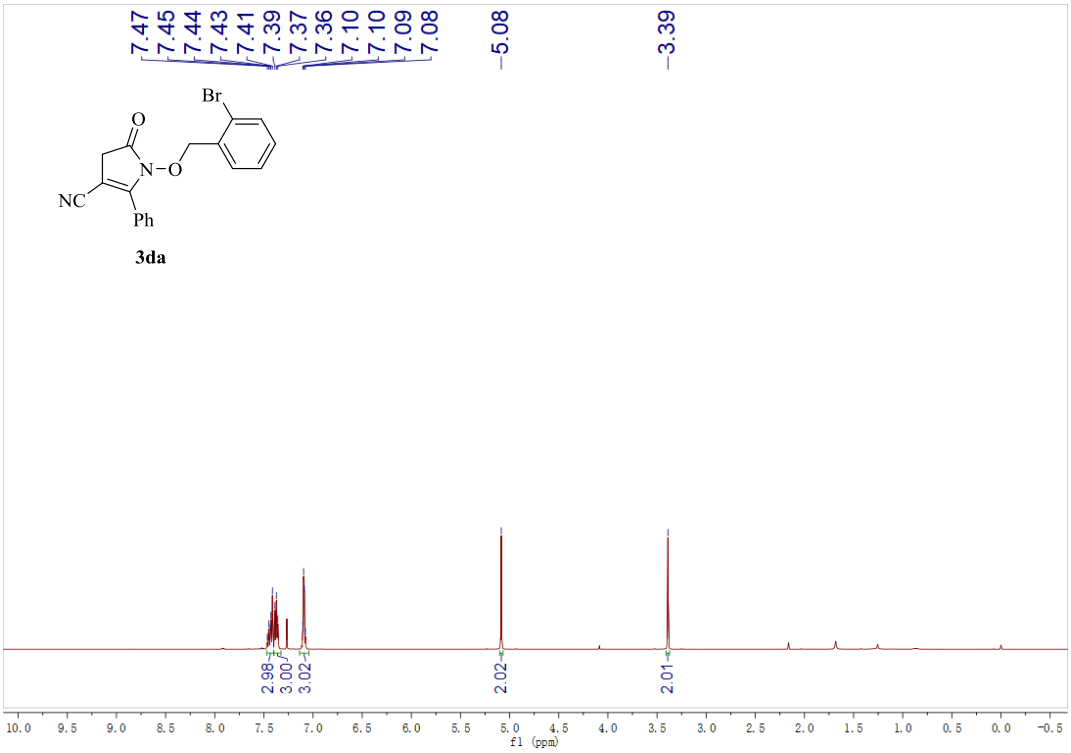
125.41
115.49
79.42
75.18
35.37
f1 (ppm)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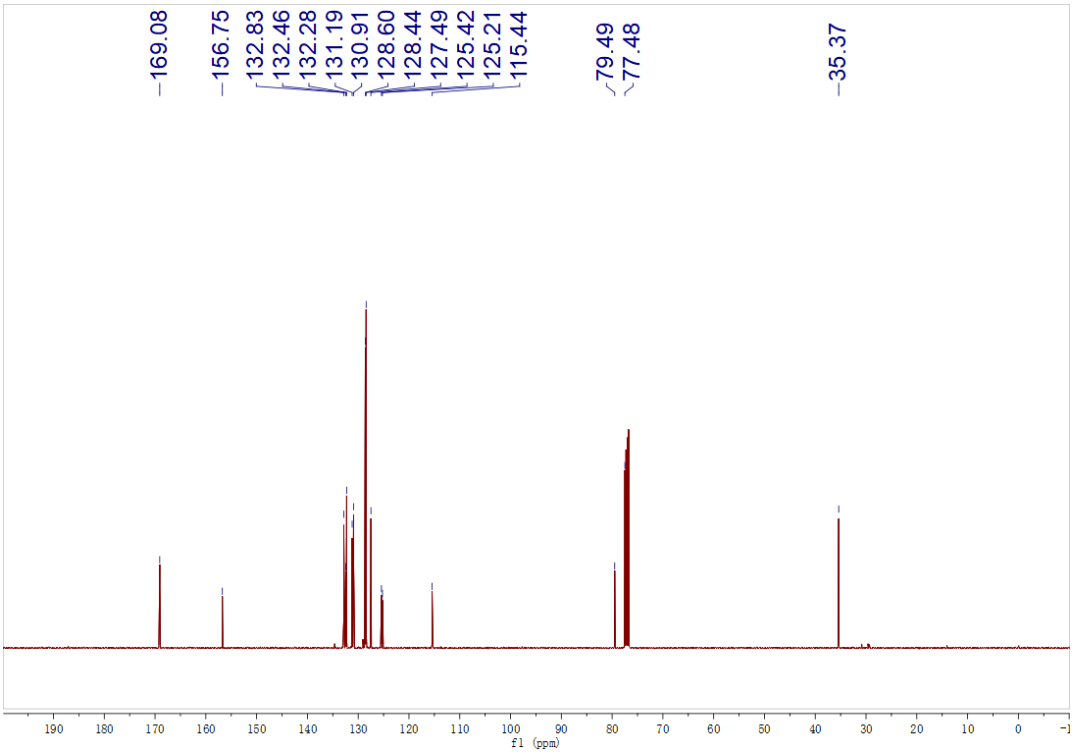
7.44
7.43
7.41
7.39
7.37
7.36
7.10
7.10
7.09
7.08
5.08
3.39
Br
O
N
O
NC
Ph
3da
2.98
3.00
3.02
2.02
2.01
f1 (ppm)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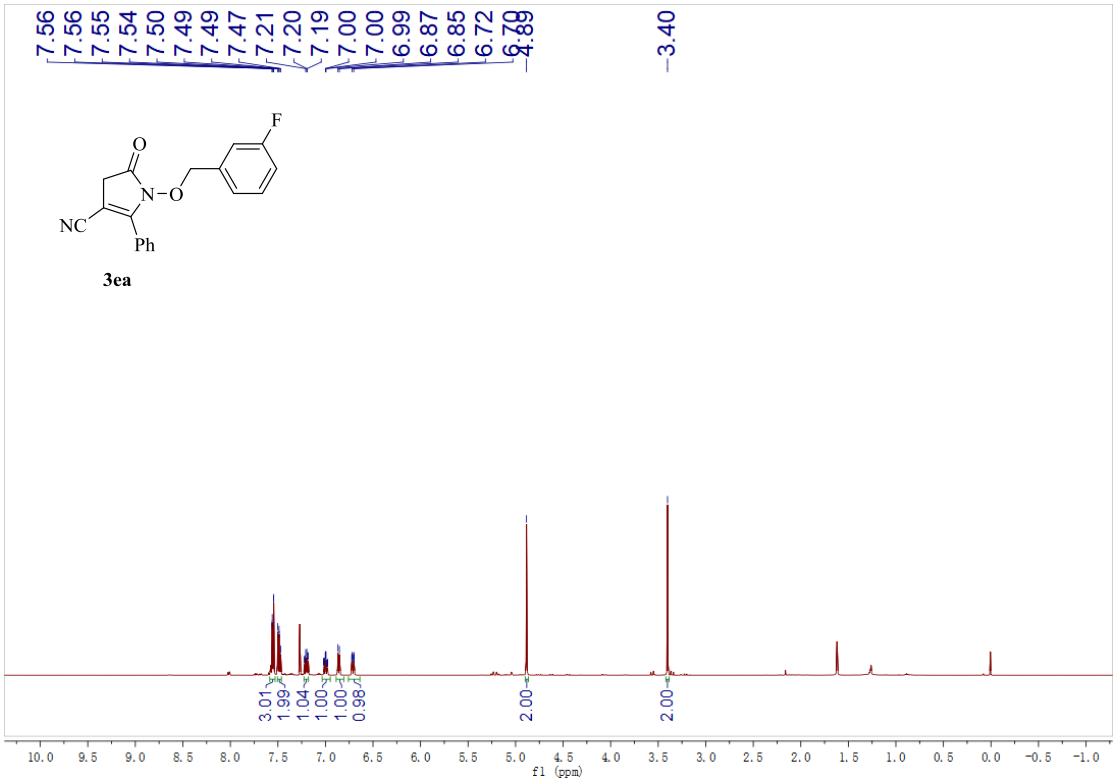
125.21
115.44
79.49
77.48
35.37
f1 (ppm)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7.19
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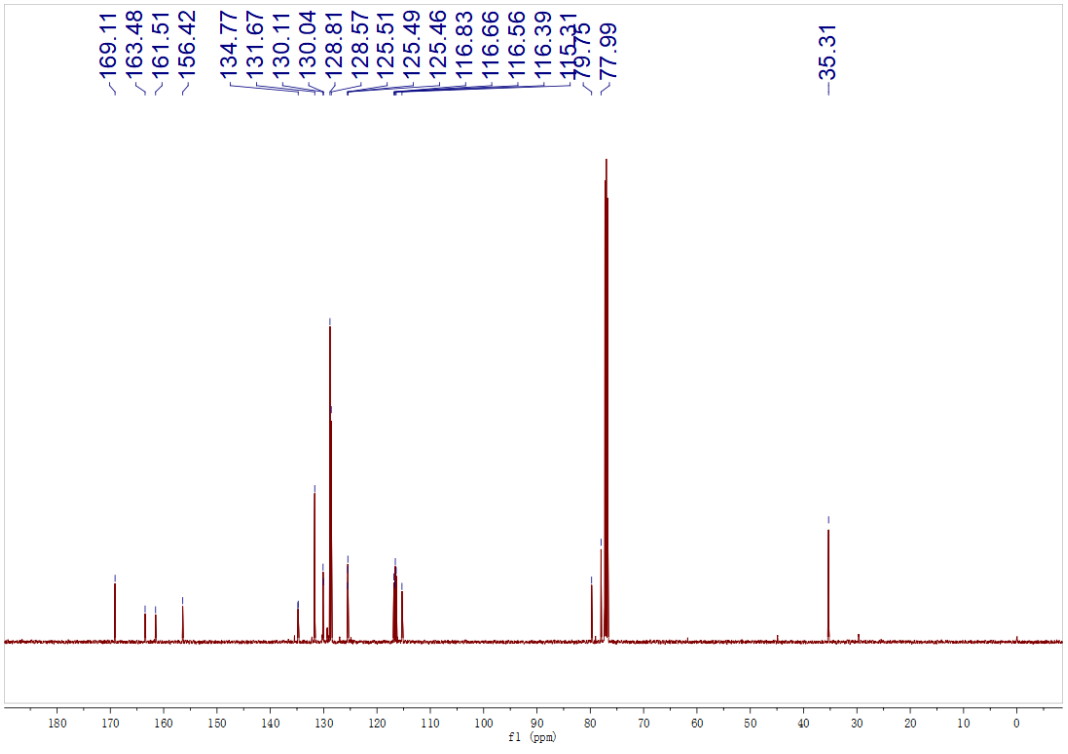
7.00
6.99
6.87
6.85
6.72
6.70
4.89
3.40
F
O
N
O
NC
Ph
3ea
3.01
1.99
1.04
1.00
1.00
0.98
2.00
2.00
f1 (ppm)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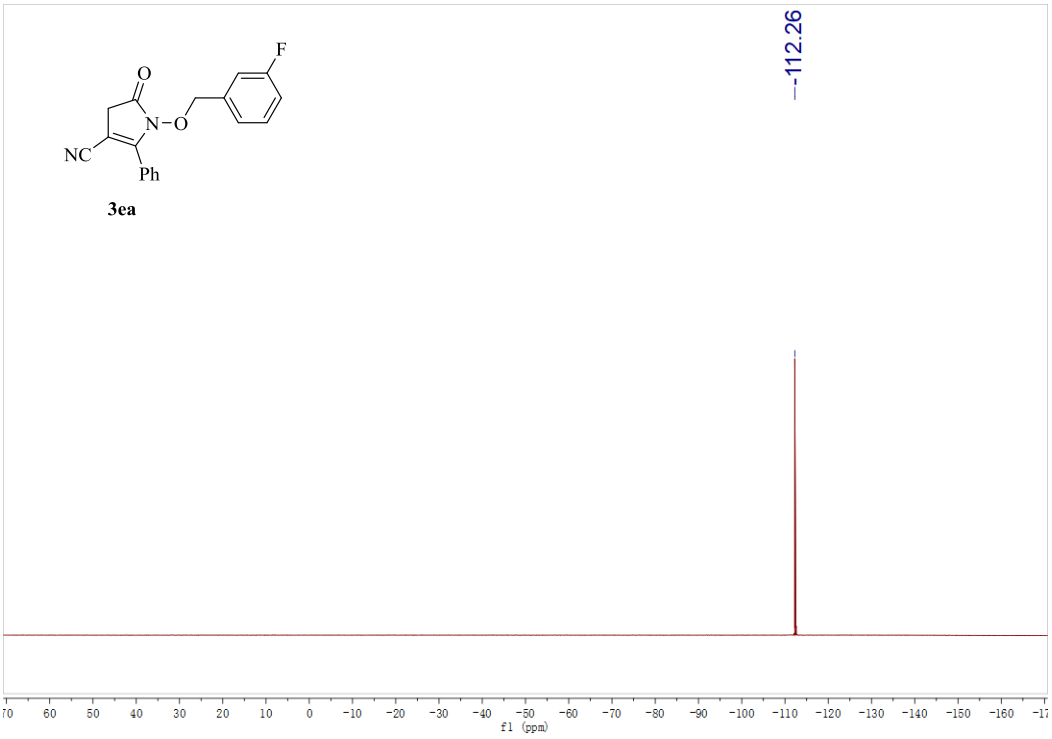
116.56
116.39
115.31
79.75
77.99
35.31
f1 (ppm)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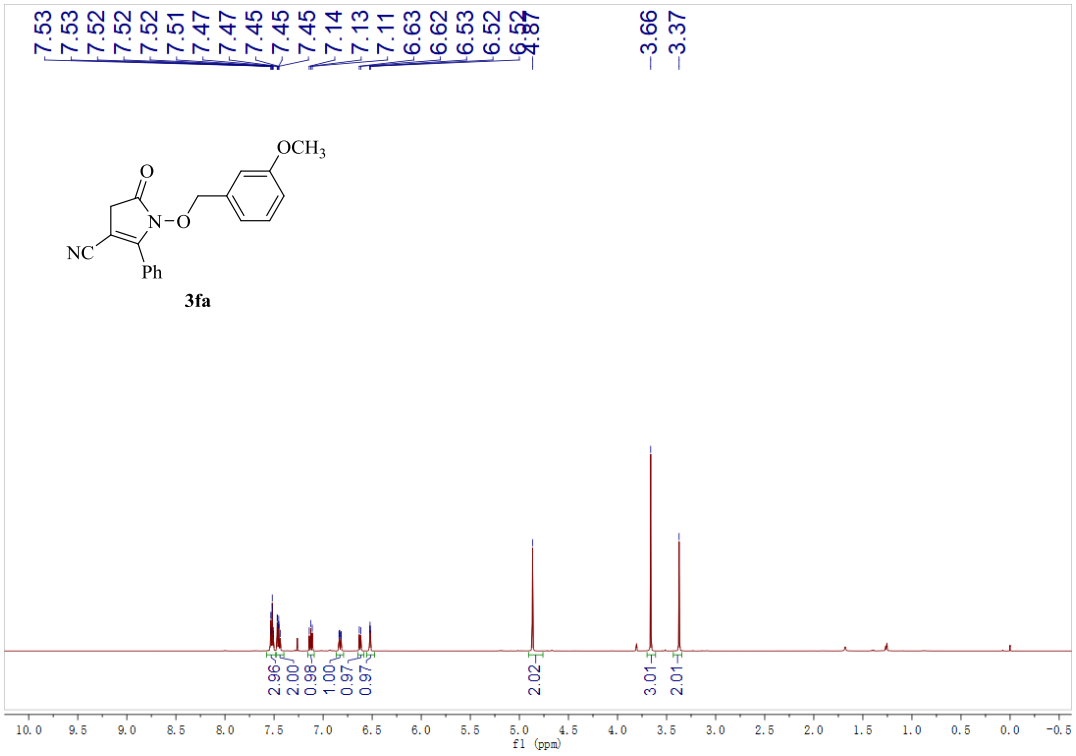
O
N
O
NC
Ph
-112.26
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -17
f1 (ppm)

3ea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7.52
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7.51
7.47
7.47
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7.45
7.45
7.14
7.13
7.11
6.63
6.62
6.53
6.52
6.52
4.87
3.66
3.37
OCH3
O
N
O
NC
Ph
2.96
2.00
0.98
1.00
0.97
0.97
2.02
3.01
2.01
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
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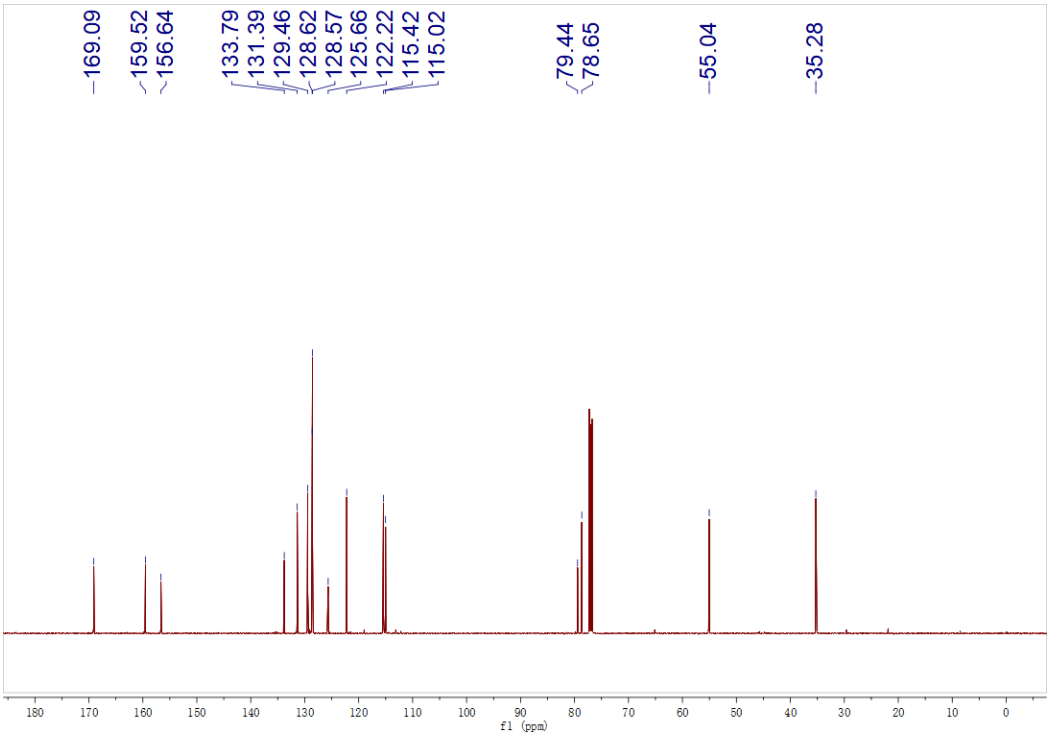
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

3fa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131.39
129.46
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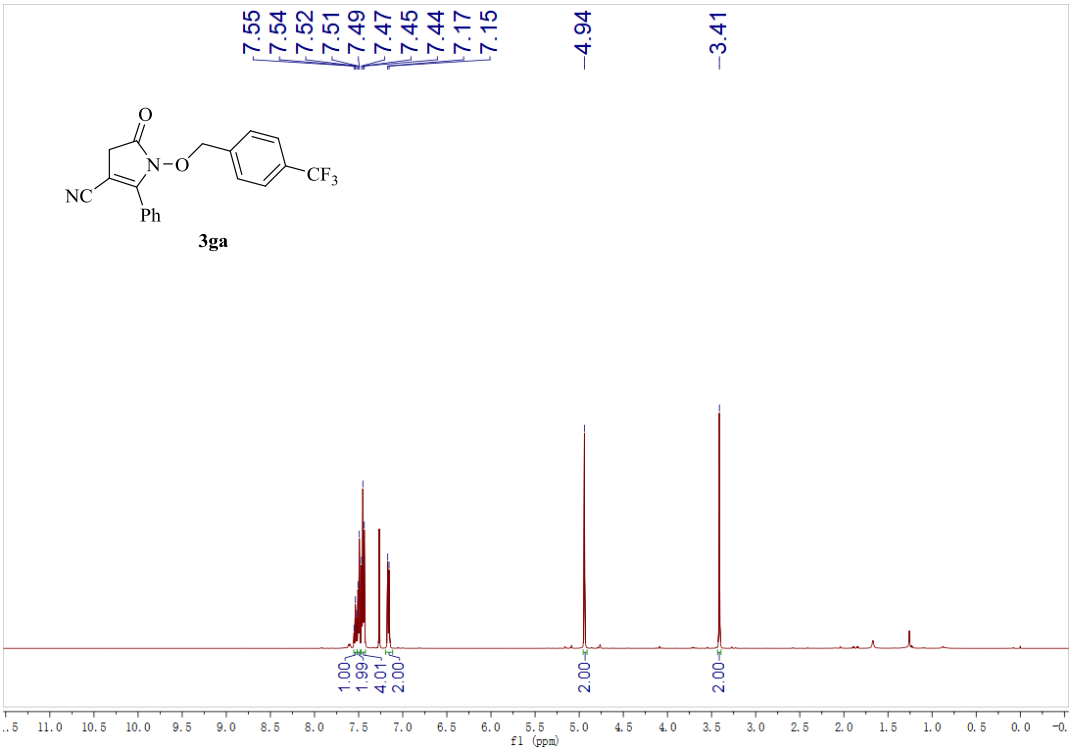
128.57
125.66
122.22
115.42
115.02
79.44
78.65
55.04
35.28
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.49
7.47
7.45
7.44
7.17
7.15
4.94
3.41
O
N
O
NC
Ph
CF3
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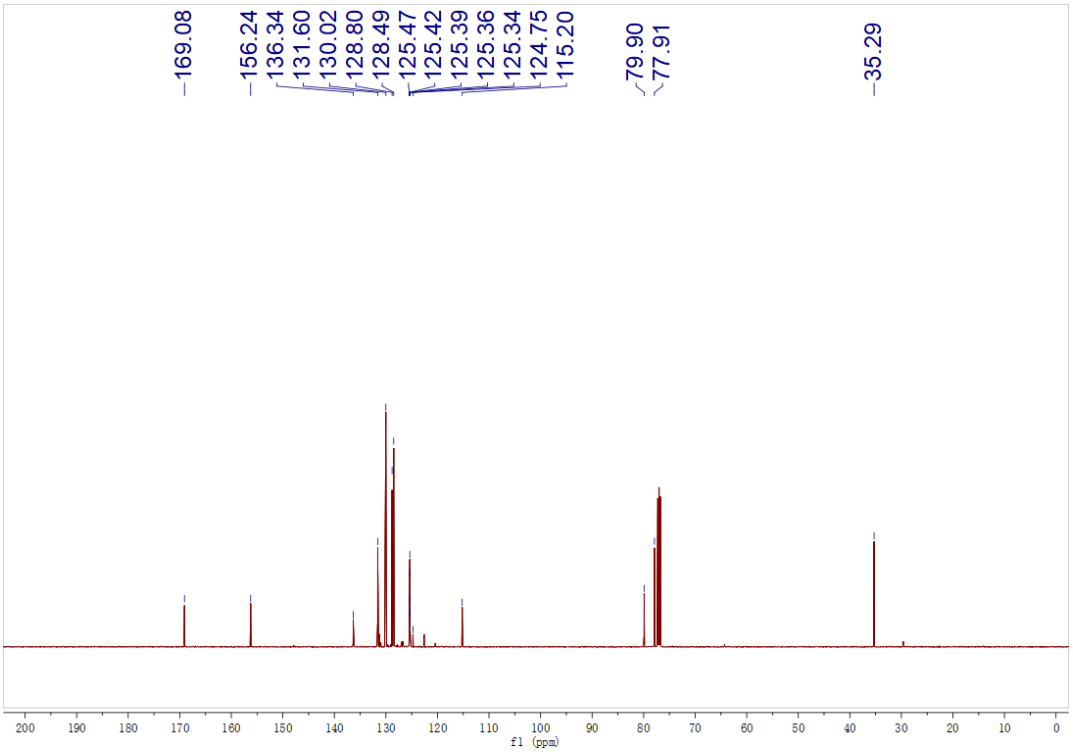
1.99
4.01
2.00
2.00
2.00
f1 (ppm)

3ga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136.34
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130.02
128.80
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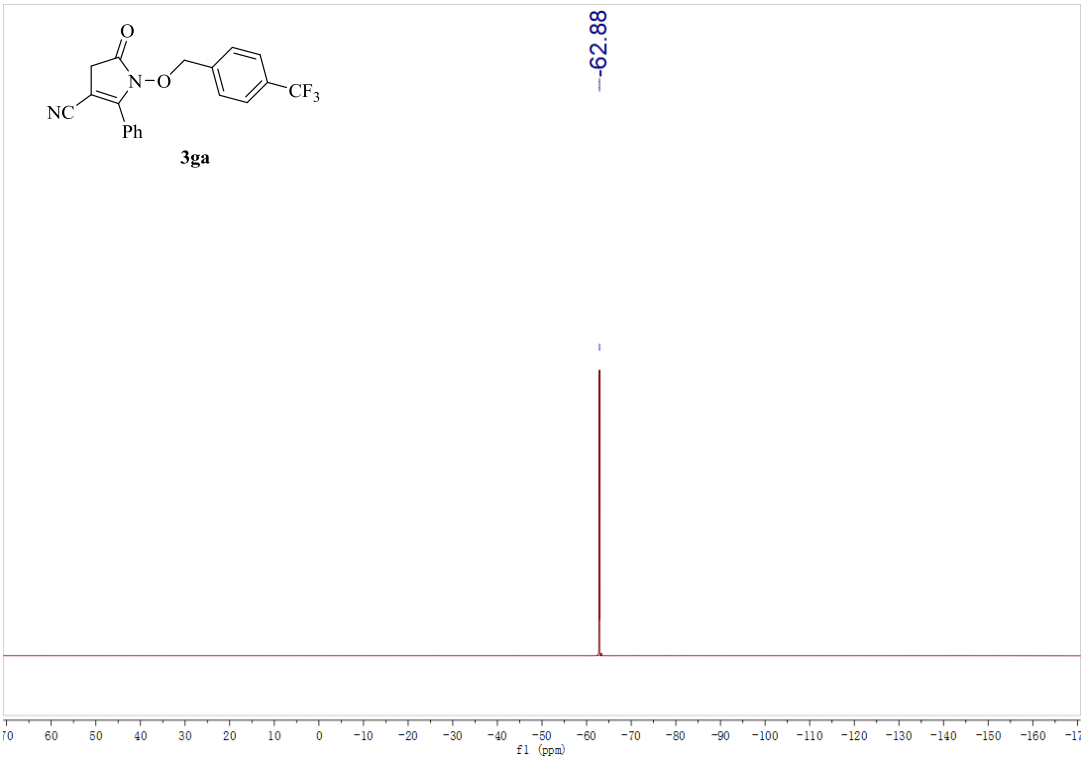
125.39
125.36
125.34
124.75
115.20
79.90
77.91
35.29
f1 (ppm)



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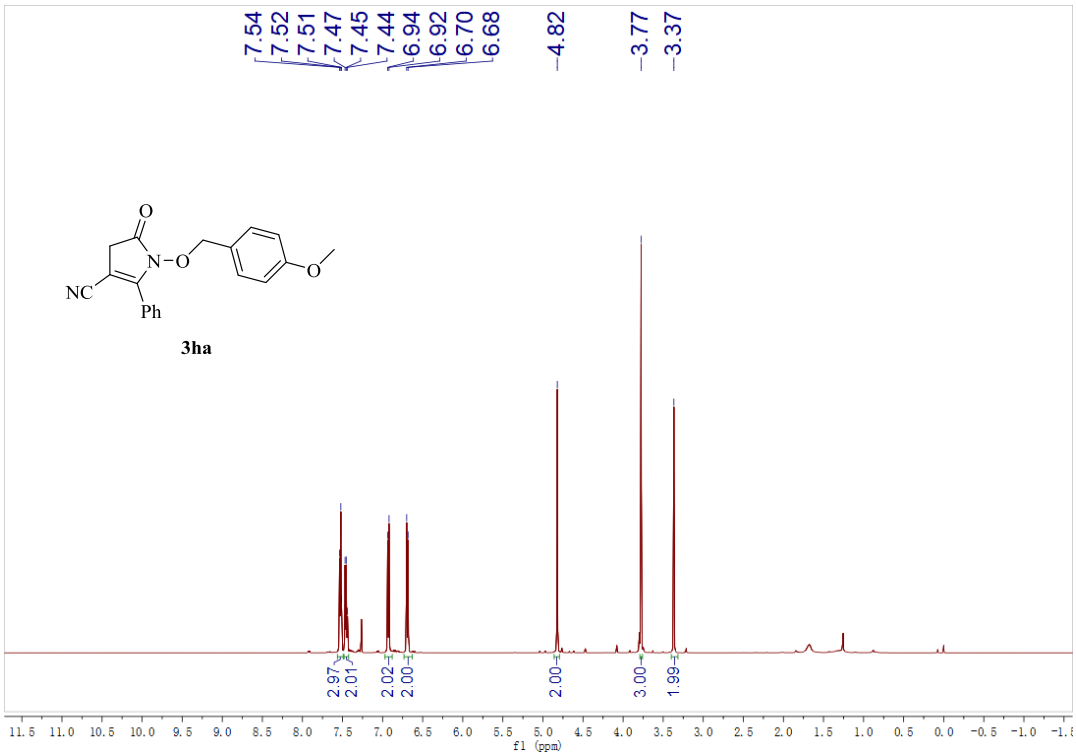
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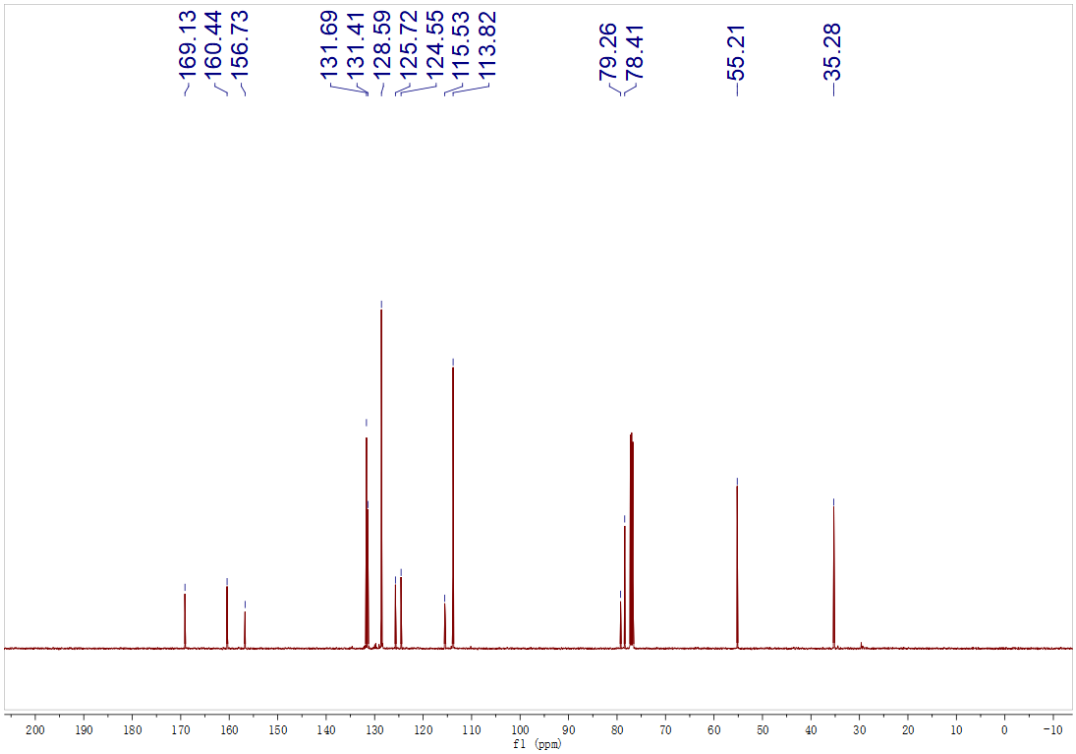
7.44
6.94
6.92
6.70
6.68
4.82
3.77
3.37
O
N
O
O
NC
Ph
2.97
2.01
2.02
2.00
2.00
3.00
1.99
f1 (ppm)

3ha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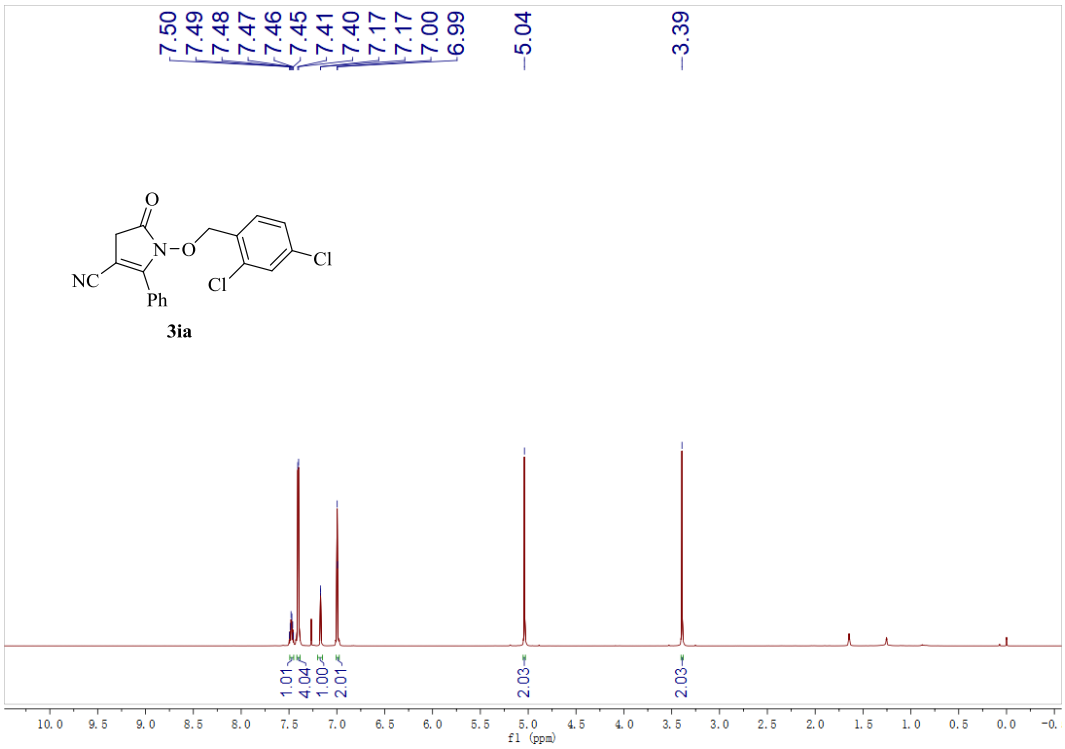
113.82
79.26
78.41
55.21
35.28
f1 (ppm)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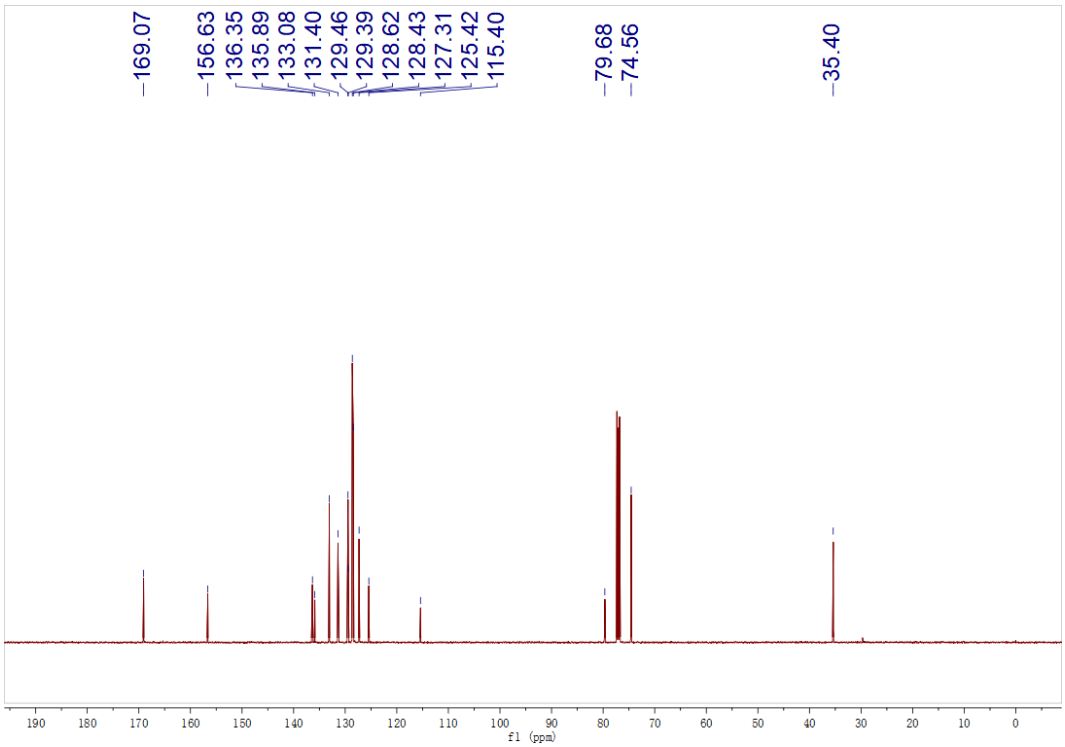
7.41
7.40
7.17
7.17
7.00
6.99
5.04
3.39
O
N
O
NC
Ph
Cl
Cl
1.01
4.04
1.00
2.01
2.03
2.03
f1 (ppm)

3ia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127.31
125.42
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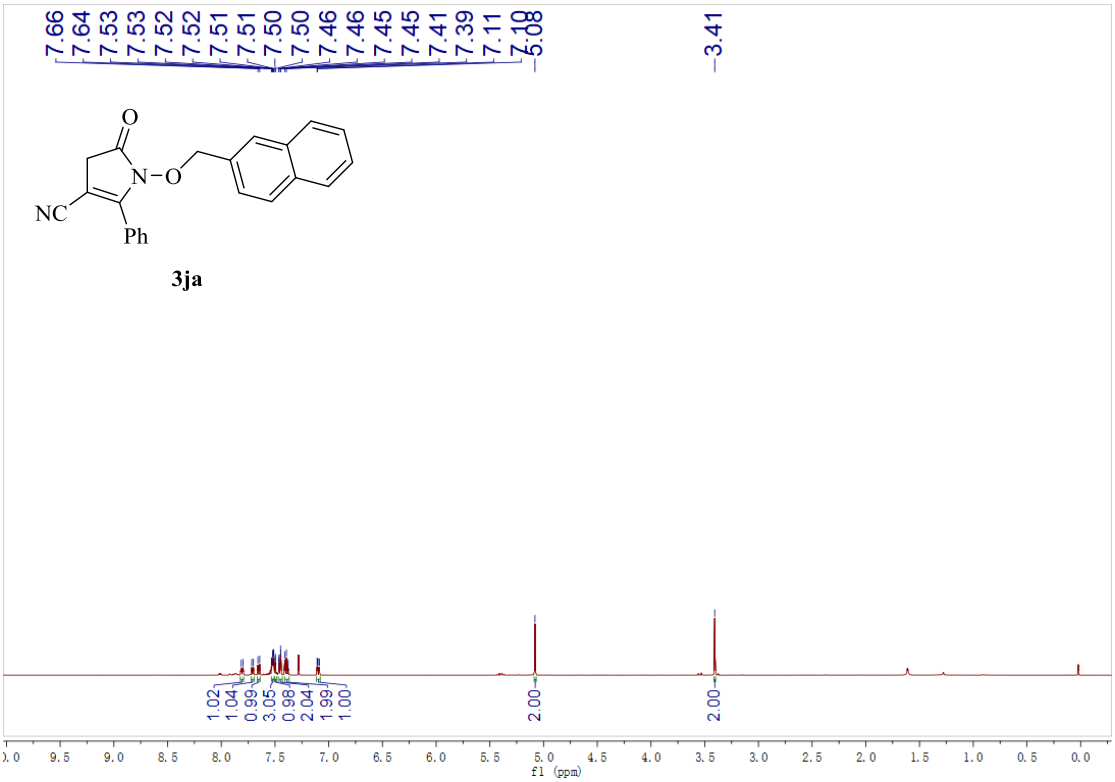
79.68
74.56
35.40
f1 (ppm)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7.51
7.51
7.50
7.50
7.46
7.46
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7.45
7.41
7.39
7.11
7.10
5.08
3.41
O
N–O
NC
Ph
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1.04
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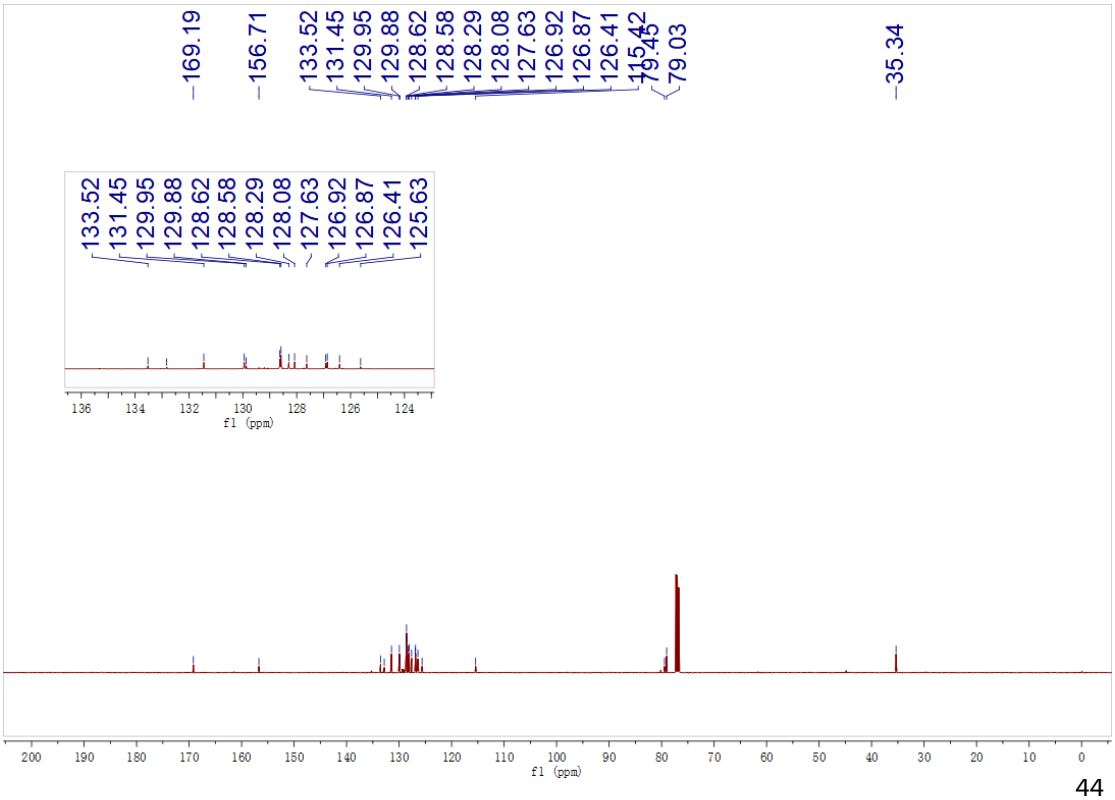
3.05
0.98
2.04
1.99
1.00
2.00
2.00
f1 (ppm)

3ja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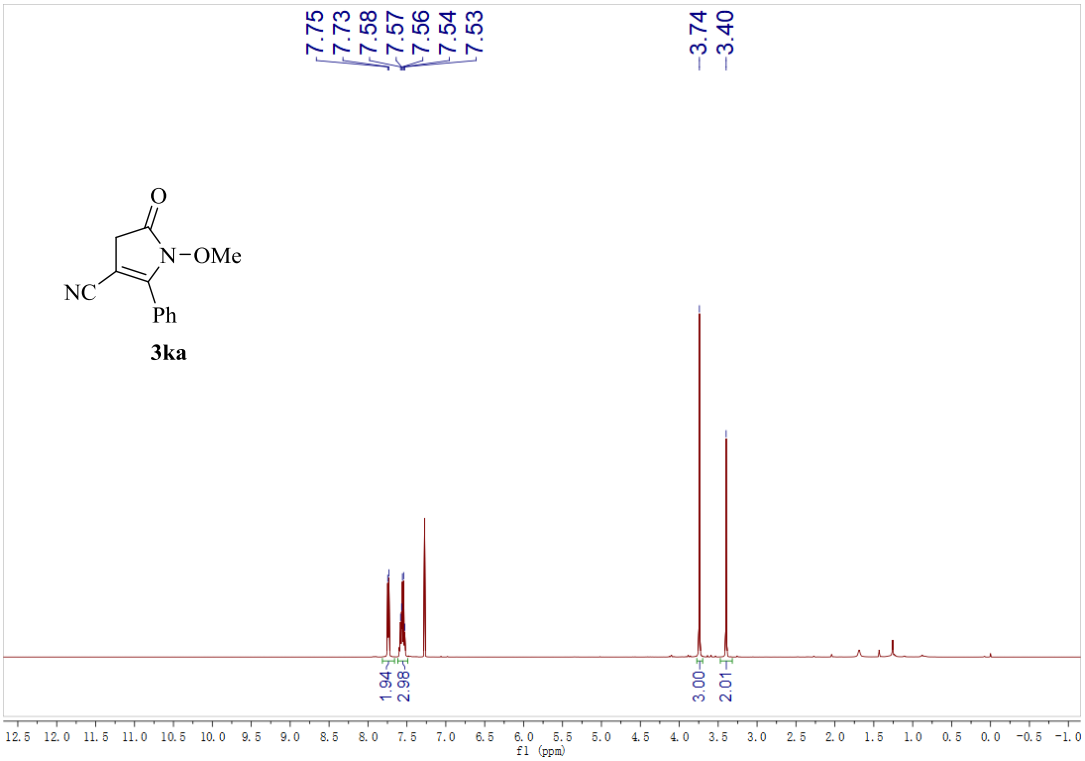
125.63
f1 (ppm)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N−OMe
NC
Ph
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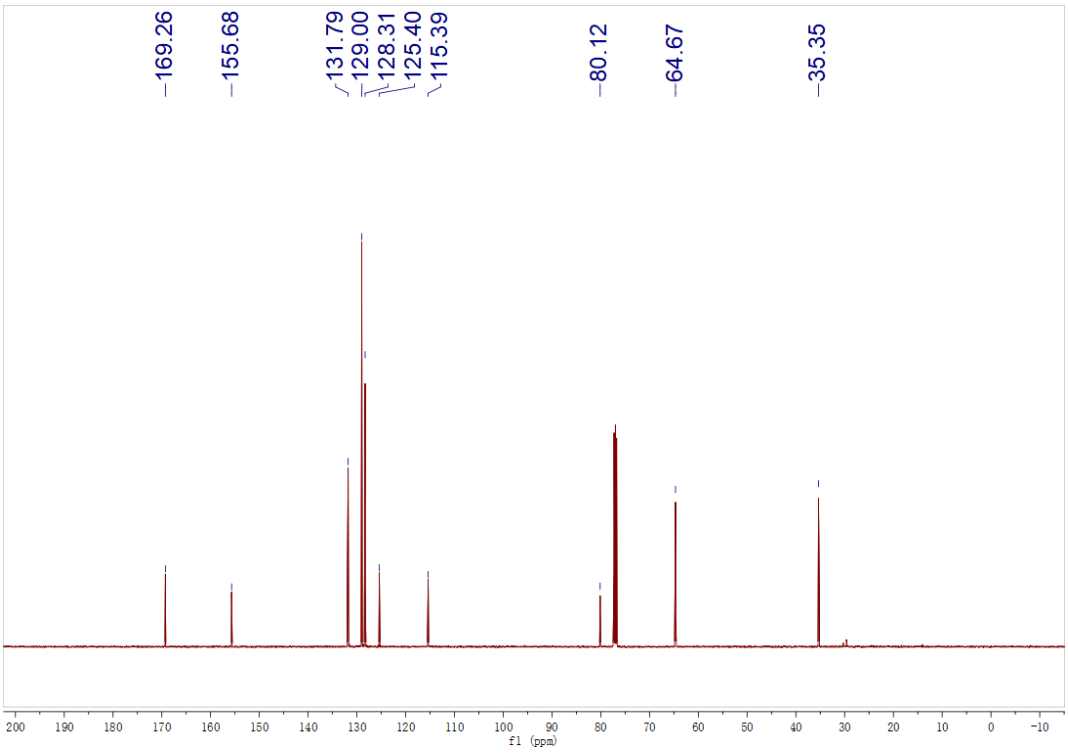
2.98
3.00
2.01
f1 (ppm)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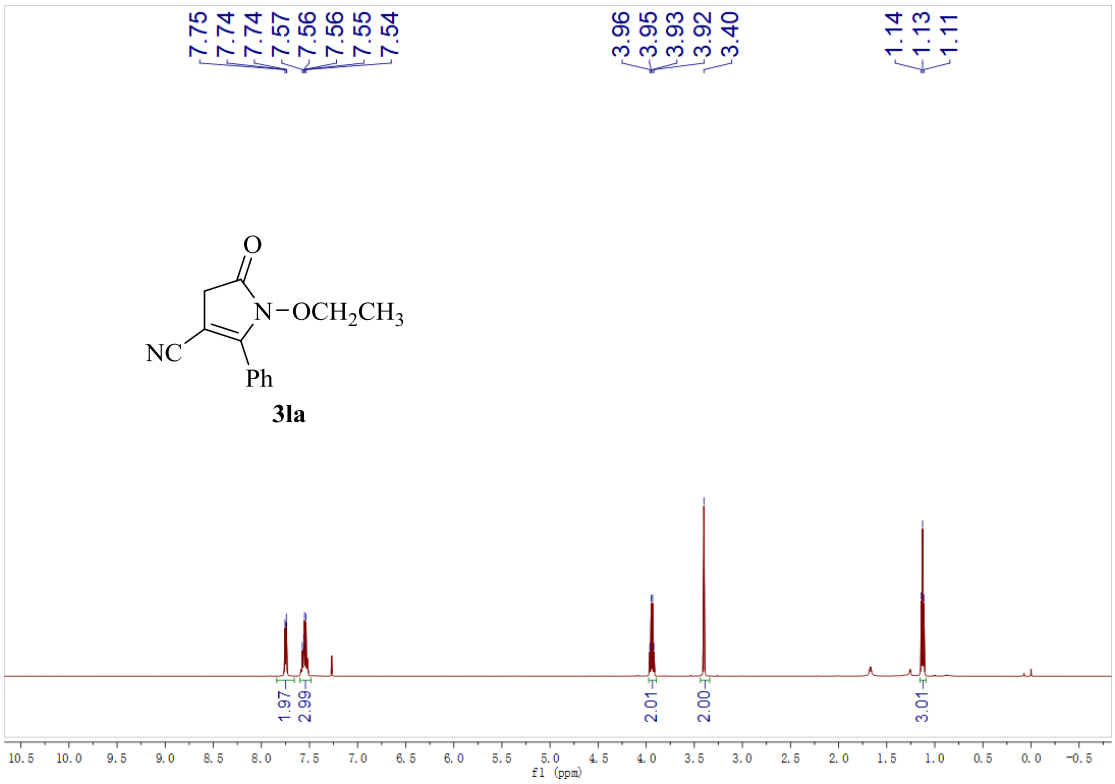
64.67
35.35
f1 (ppm)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3.95
3.93
3.92
3.40
1.14
1.13
1.11
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NC
Ph
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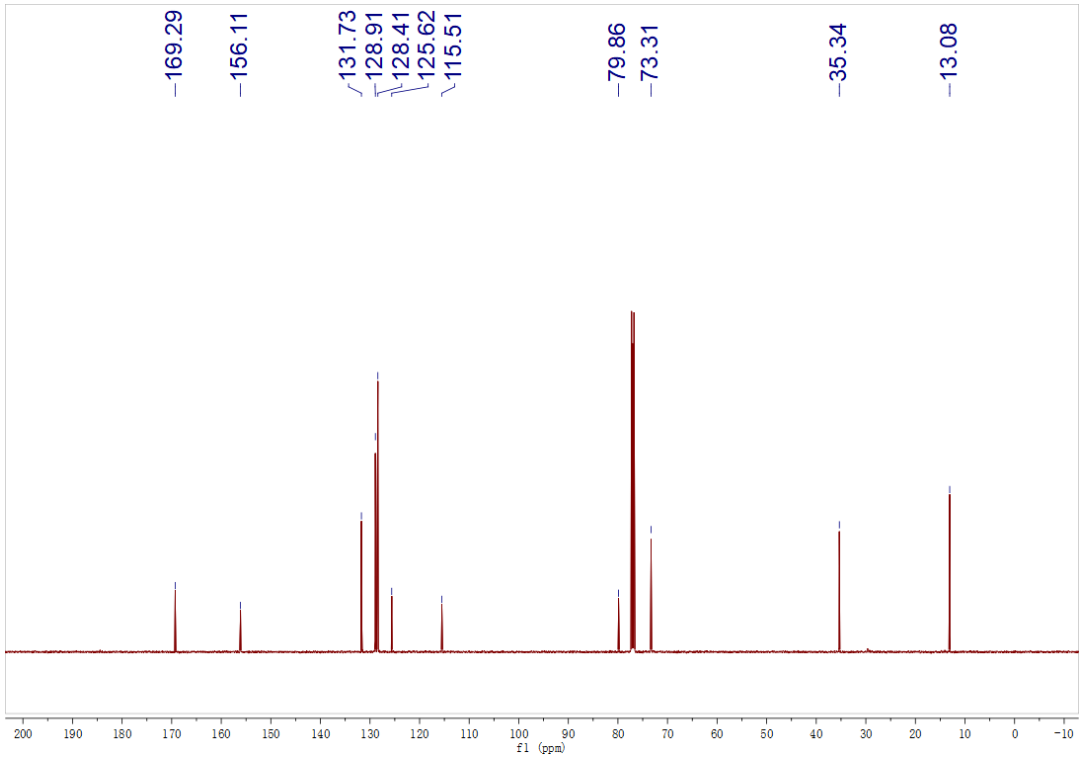
2.99
2.01
2.00
3.01
f1 (ppm)

3la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125.62
115.51
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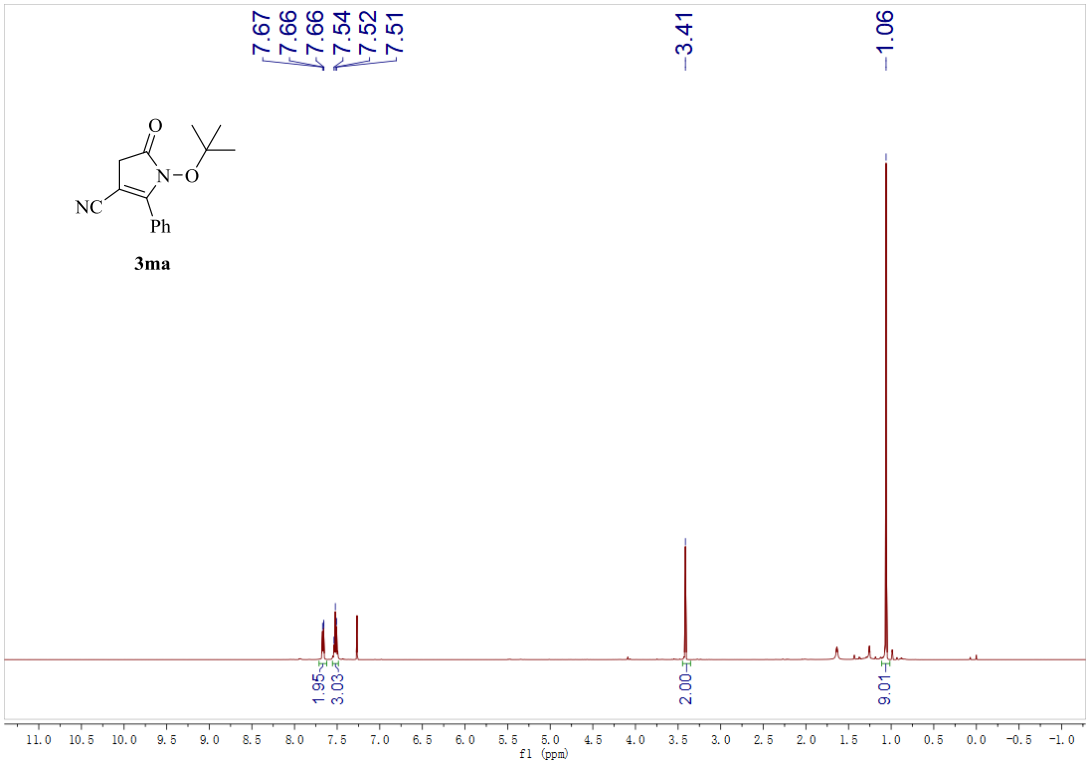
73.31
35.34
13.08
f1 (ppm)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O
N
O
NC
Ph
3ma
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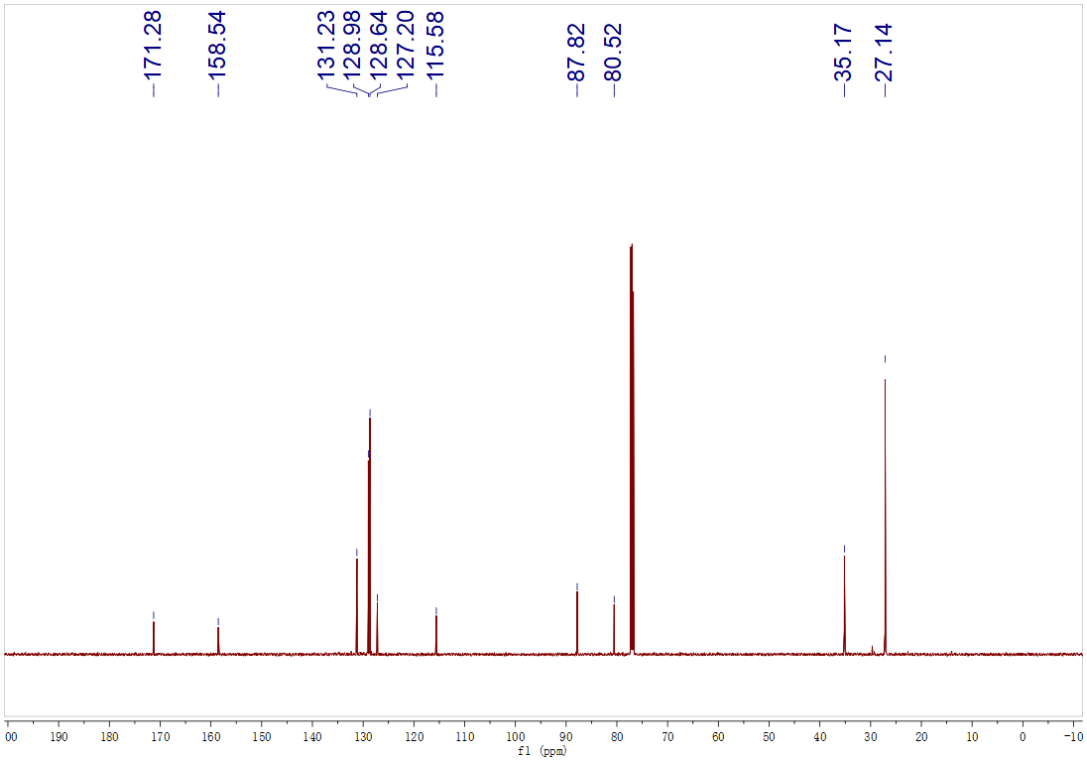
3.03
2.00
9.01
f1 (ppm)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115.58
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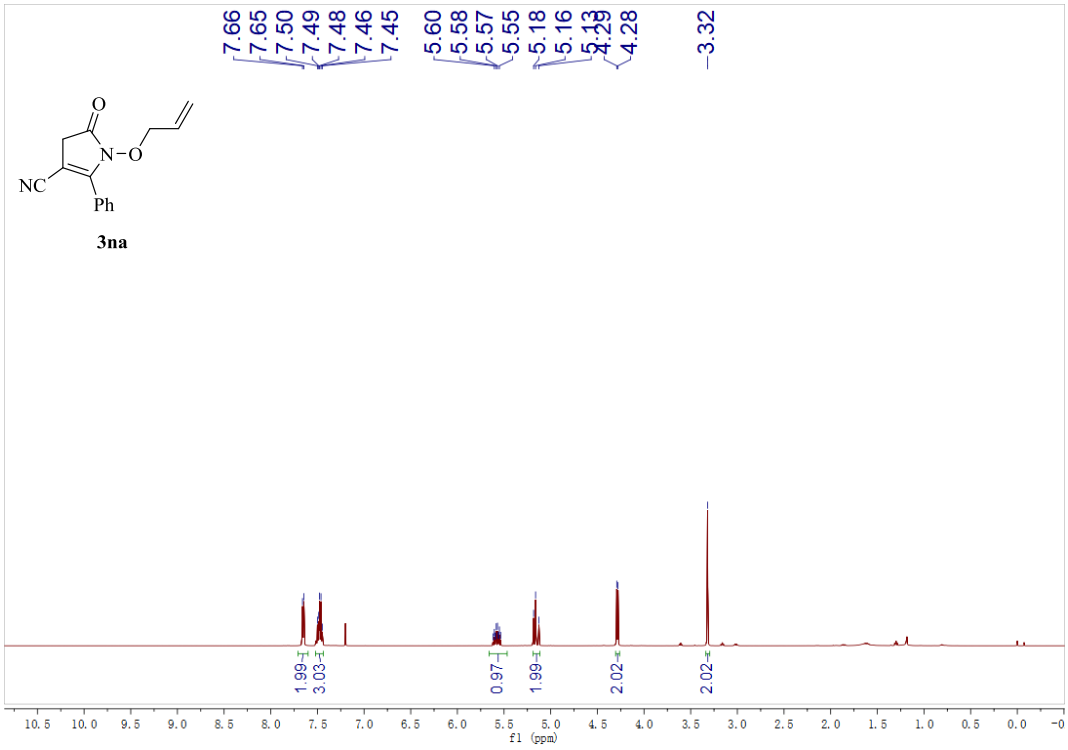
27.14
f1 (ppm)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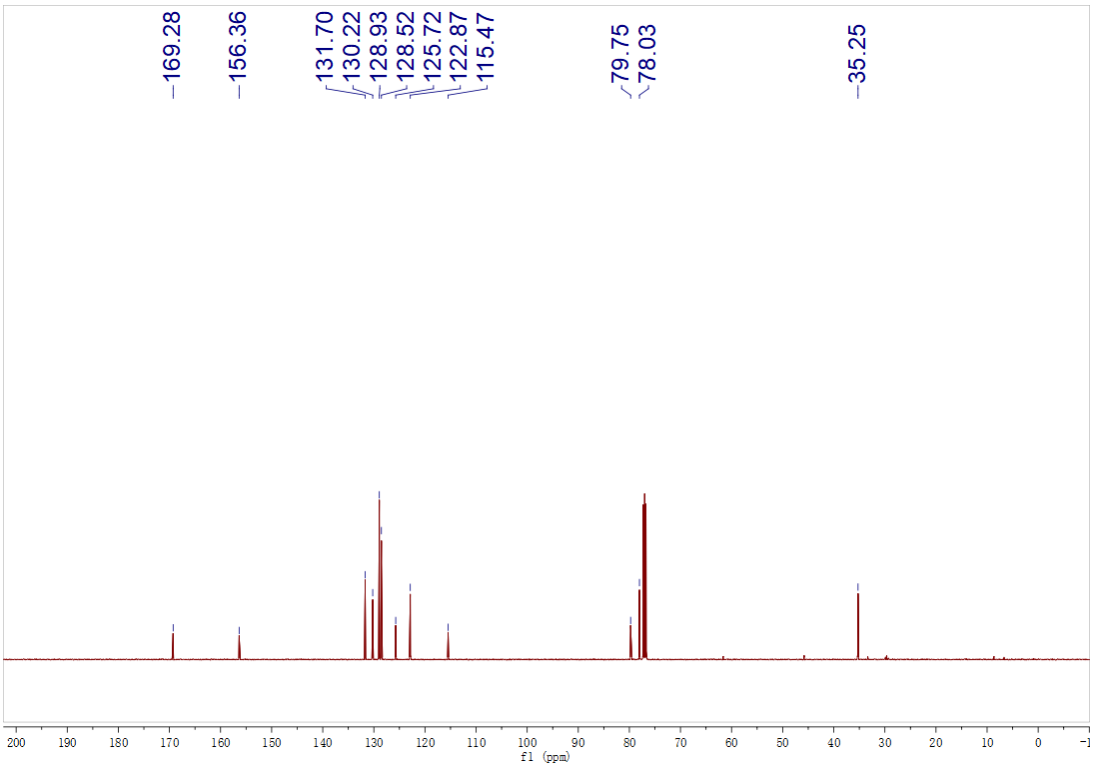
5.57
5.55
5.18
5.16
5.13
4.29
4.28
3.32
O
N–O
NC
Ph
3na
1.99
3.03
0.97
1.99
2.02
2.02
f1 (ppm)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128.52
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122.87
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79.75
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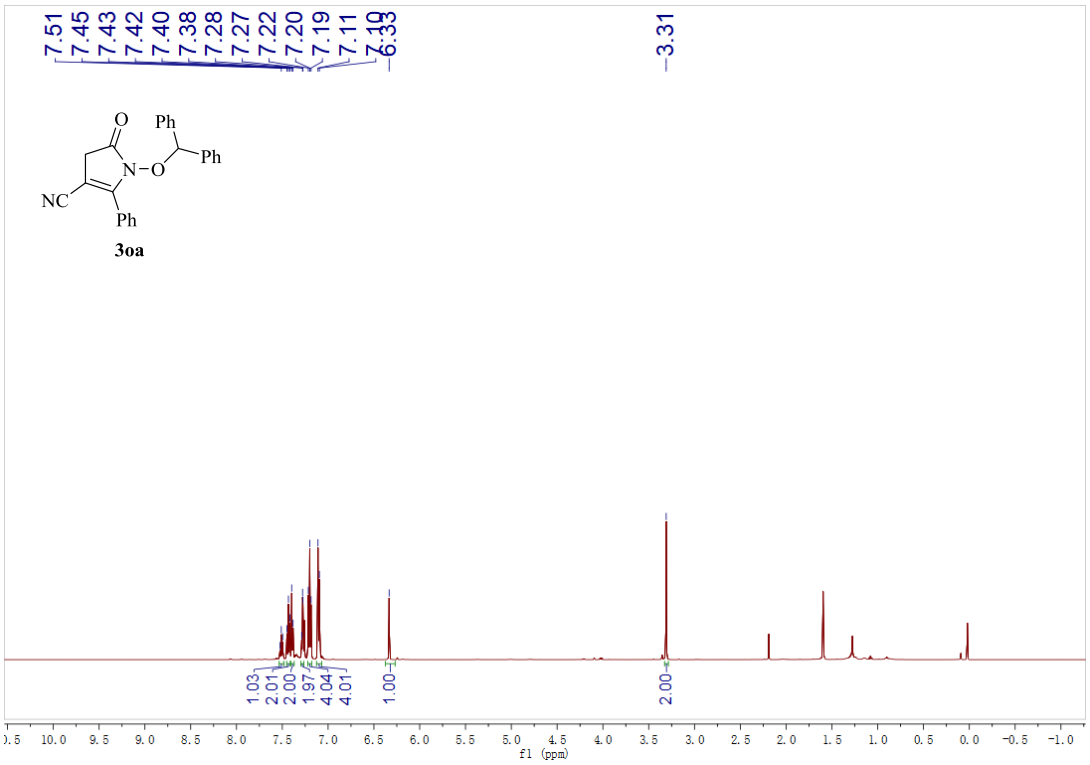
35.25
f1 (ppm)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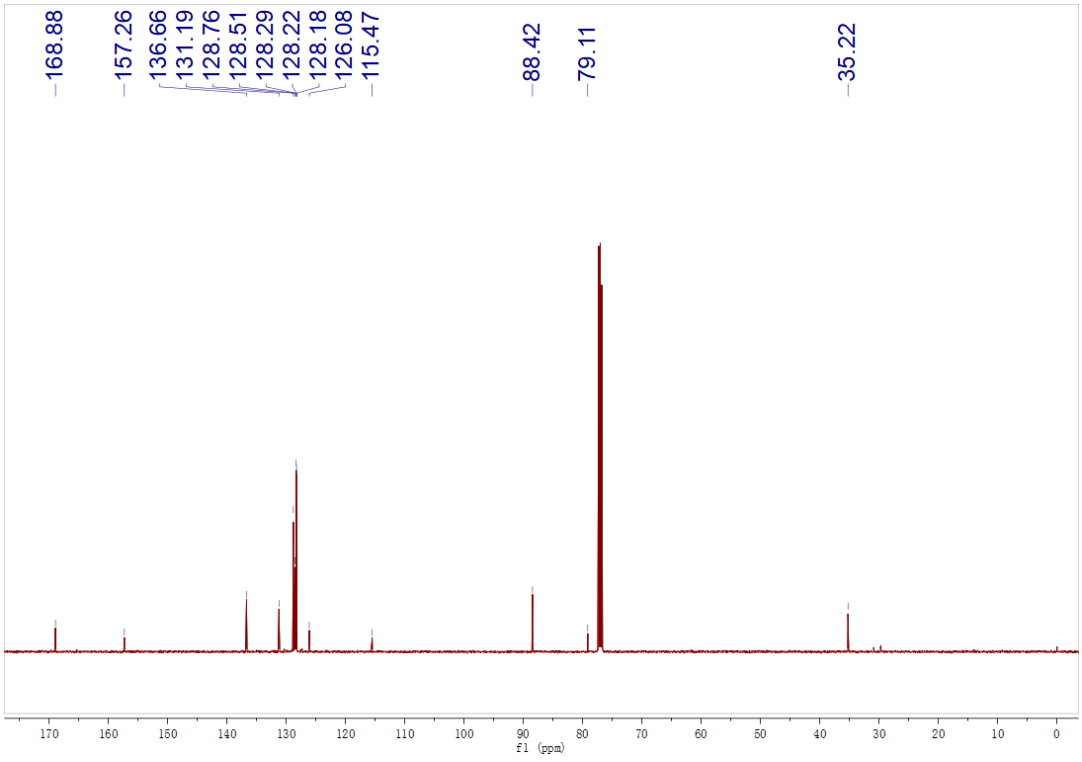
7.42
7.40
7.38
7.28
7.27
7.22
7.20
7.19
7.11
7.10
6.33
3.31
O
Ph
Ph
N−O
NC
Ph
3oa
1.03
2.01
2.00
1.97
4.04
4.01
1.00
2.00
f1 (ppm)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88.42
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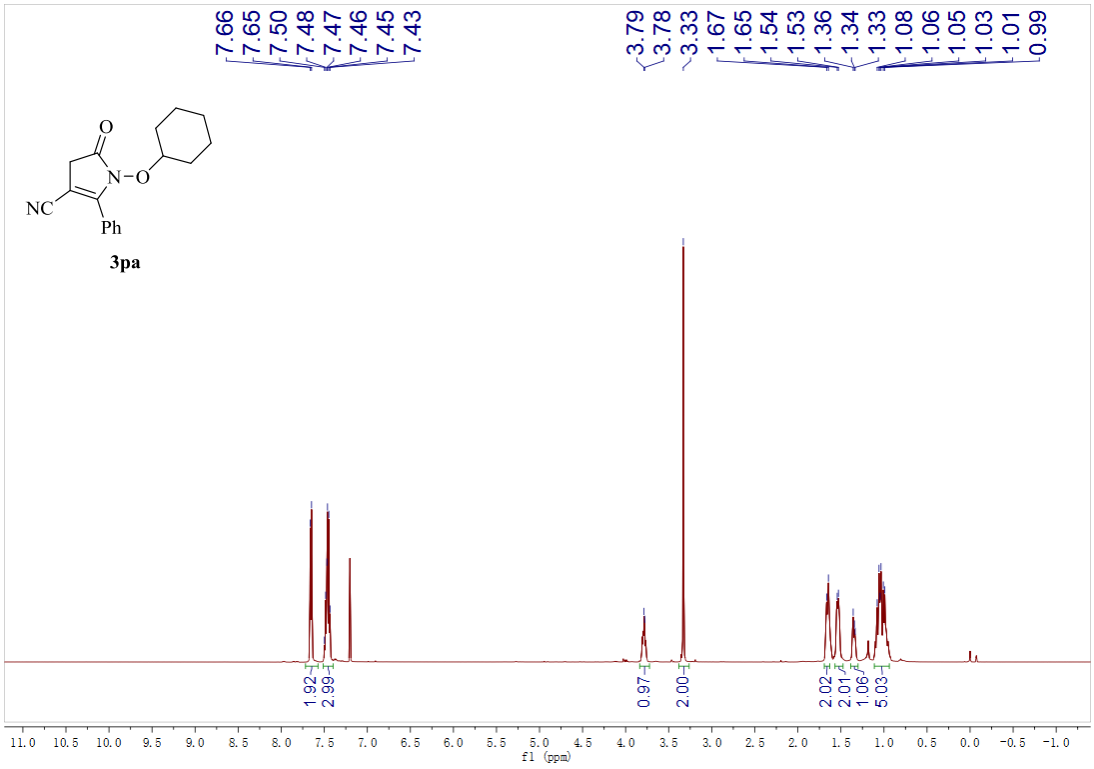
f1 (ppm)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7.45
7.43
3.79
3.78
3.33
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1.65
1.54
1.53
1.36
1.34
1.33
1.08
1.06
1.05
1.03
1.01
0.99
O
N
O
NC
Ph
3pa
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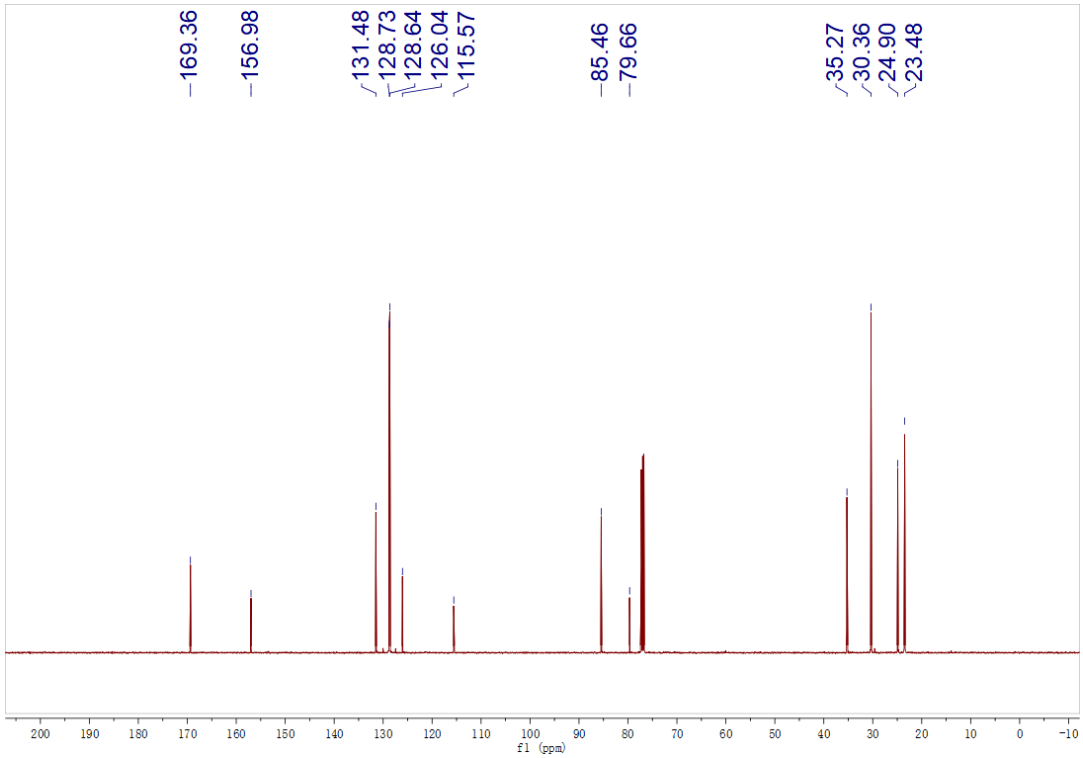
0.97
2.00
2.02
2.01
1.06
5.03
f1 (ppm)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85.46
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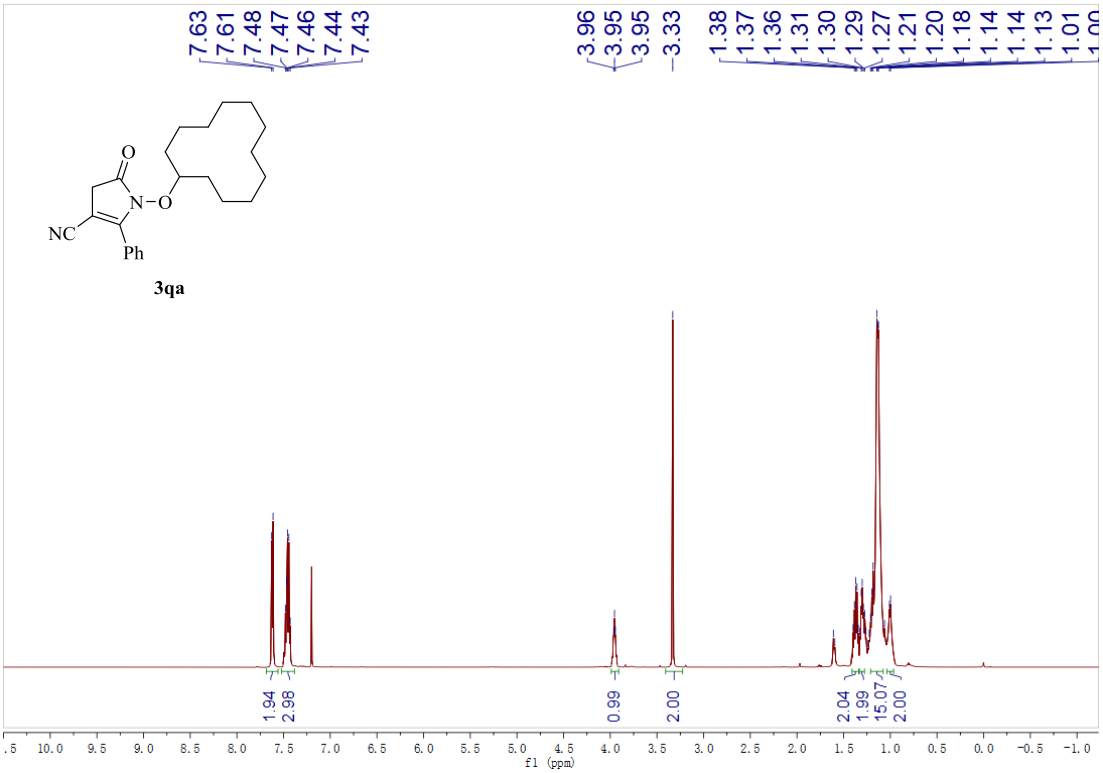
35.27
30.36
24.90
23.48
f1 (ppm)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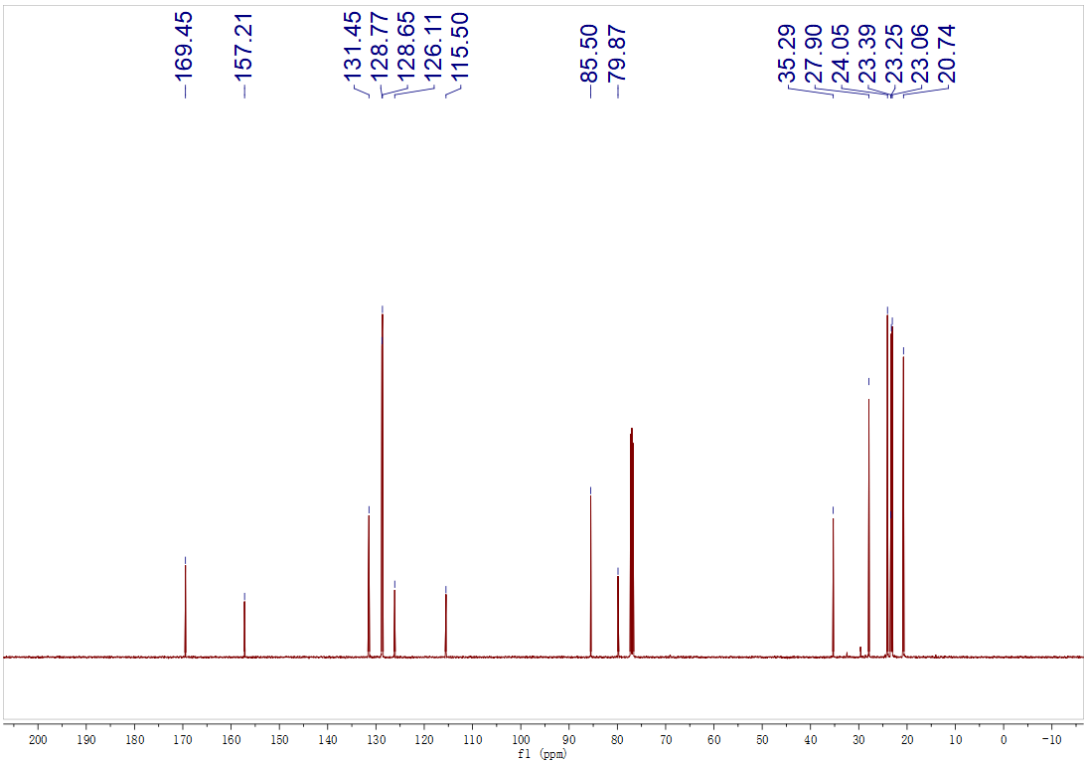
7.43
3.96
3.95
3.95
3.33
1.38
1.37
1.36
1.31
1.30
1.29
1.27
1.21
1.20
1.18
1.14
1.14
1.13
1.01
O
N
O
NC
Ph
1.94
2.98
0.99
2.00
2.04
1.99
15.07
2.00
f1 (ppm)

3qa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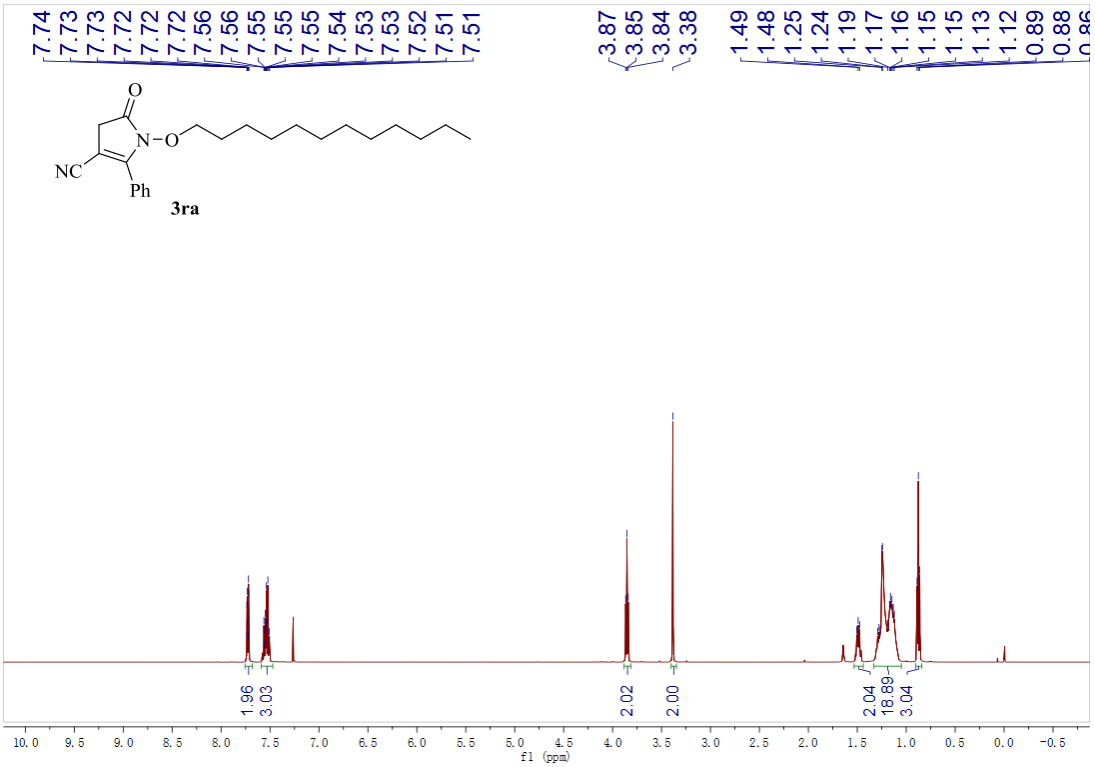
27.90
24.05
23.39
23.25
23.06
20.74
f1 (ppm)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7.56
7.55
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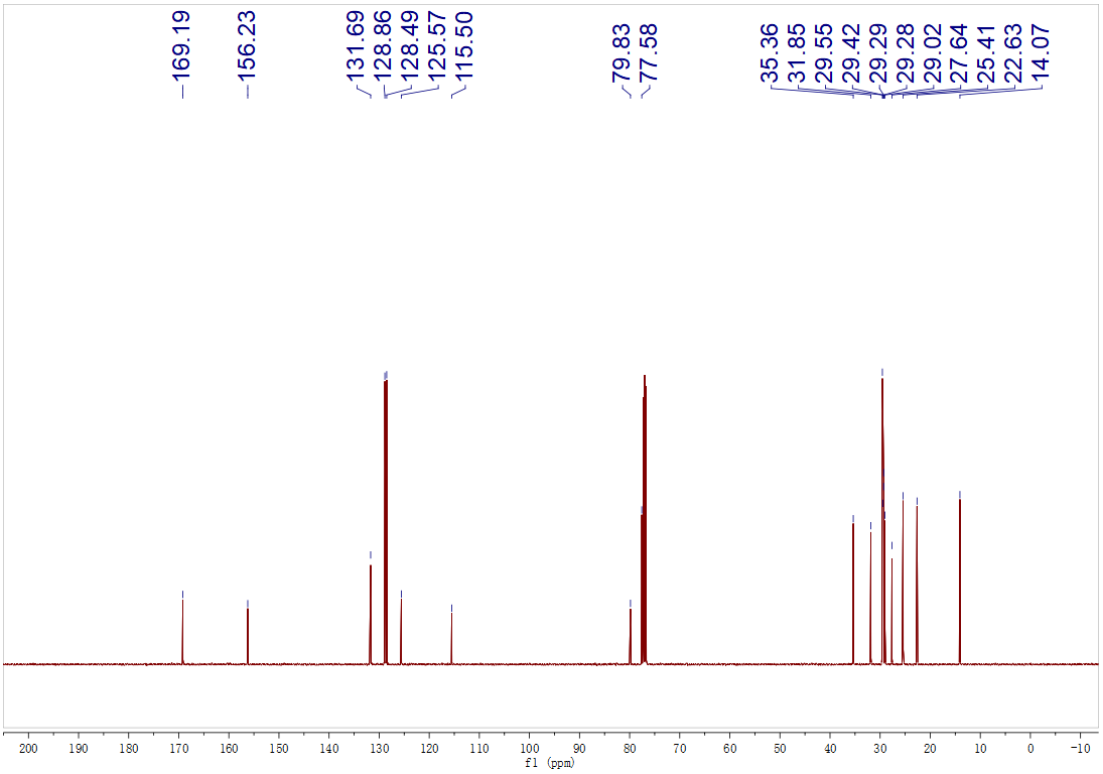
7.55
7.54
7.53
7.53
7.52
7.51
7.51
3.87
3.85
3.84
3.38
1.49
1.48
1.25
1.24
1.19
1.17
1.16
1.15
1.15
1.13
1.12
0.89
0.88
O
N
O
NC
Ph
3ra
1.96
3.03
2.02
2.00
2.04
18.89
3.04
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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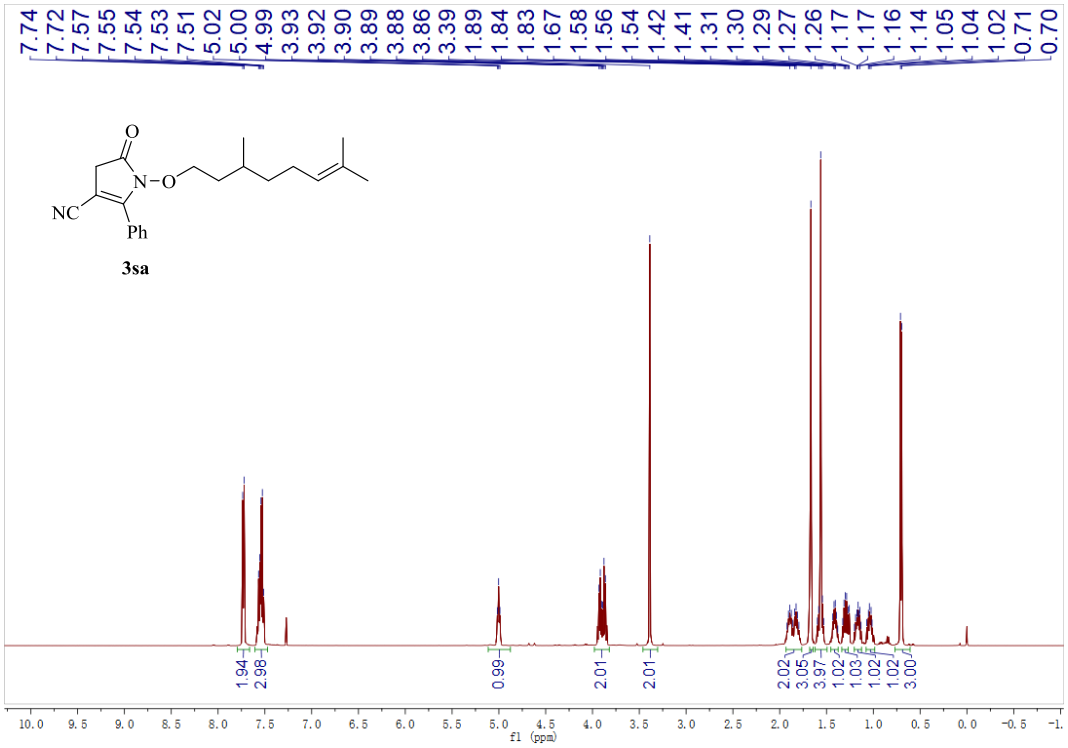
131.69
128.86
128.49
125.57
115.50
79.83
77.58
35.36
31.85
29.55
29.42
29.29
29.28
29.02
27.64
25.41
22.63
14.07
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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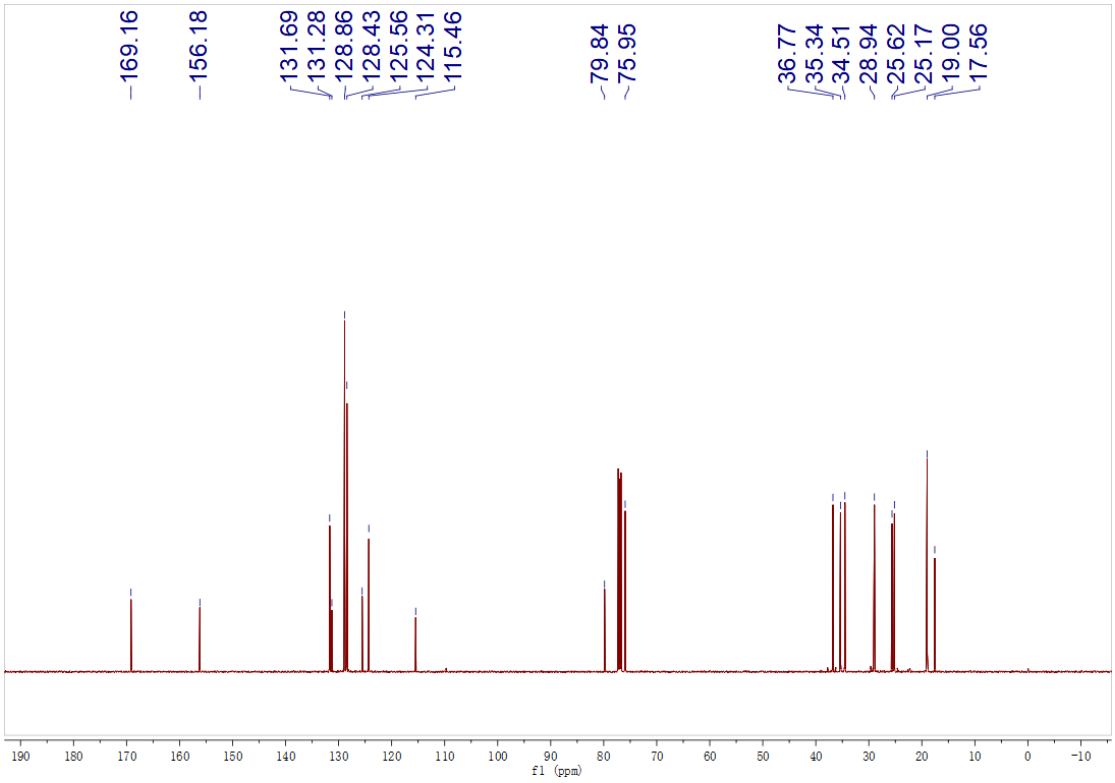
7.53
7.51
5.02
5.00
4.99
3.93
3.92
3.90
3.89
3.88
3.86
3.39
1.89
1.84
1.83
1.67
1.58
1.56
1.54
1.42
1.41
1.31
1.30
1.29
1.27
1.26
1.17
1.17
1.16
1.14
1.05
1.04
1.02
0.71
0.70
O
N
O
NC
Ph
3sa
1.94
2.98
0.99
2.01
2.01
2.02
3.05
3.97
1.02
1.03
1.02
1.02
3.00
f1 (ppm)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131.69
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128.86
128.43
125.56
124.31
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75.95
36.77
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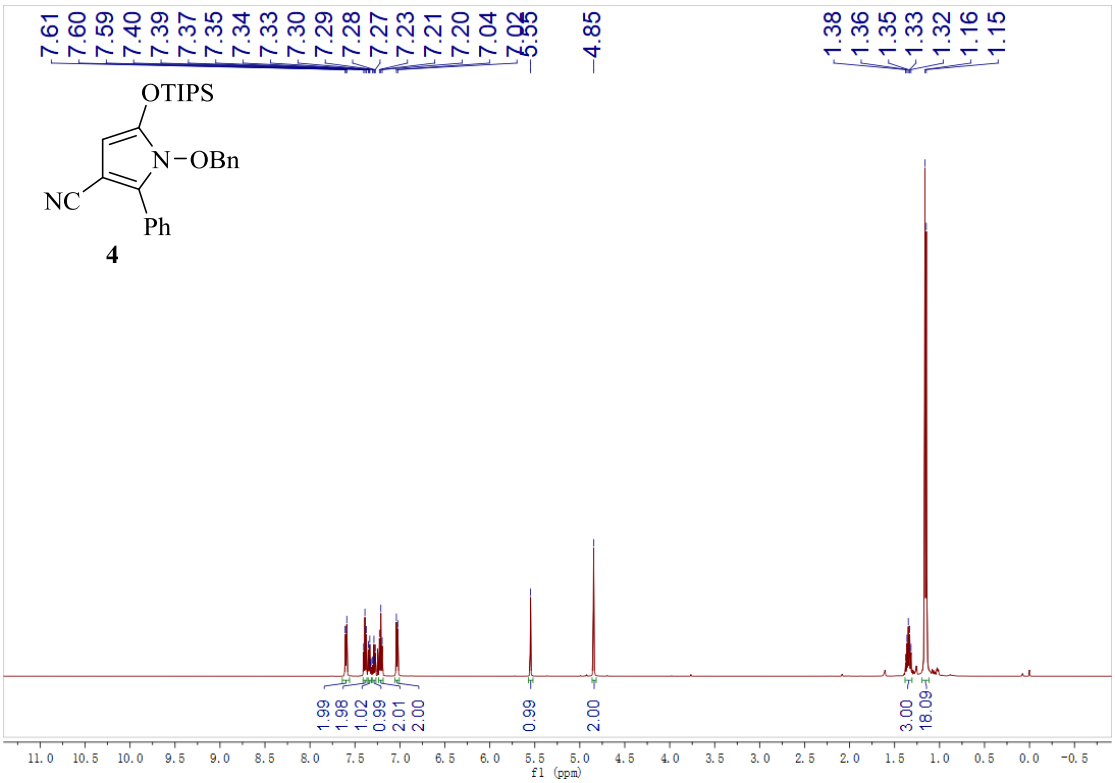
25.62
25.17
19.00
17.56
f1 (ppm)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7.34
7.33
7.30
7.29
7.28
7.27
7.23
7.21
7.20
7.04
5.55
4.85
1.38
1.36
1.35
1.33
1.32
1.16
1.15
OTIPS
N−OBn
NC
Ph
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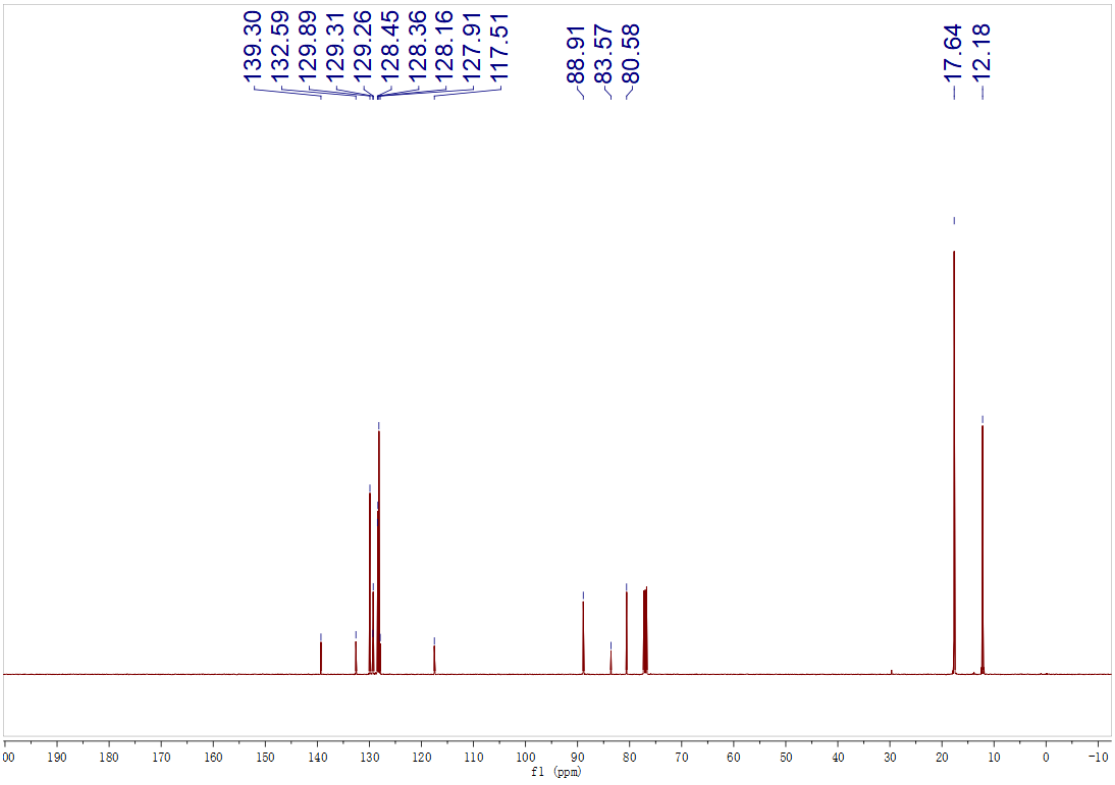
1.98
1.02
0.99
2.01
2.00
0.99
2.00
3.00
18.09
f1 (ppm)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129.89
129.31
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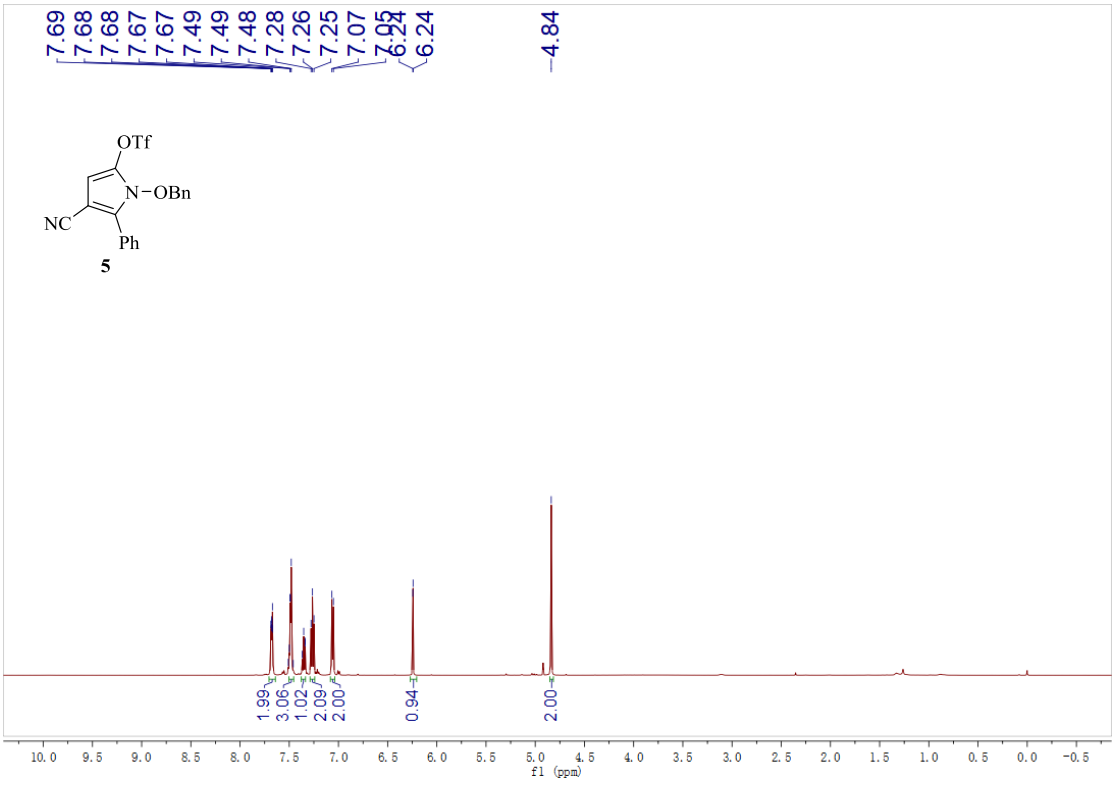
128.45
128.36
128.16
127.91
117.51
88.91
83.57
80.58
17.64
12.18
f1 (ppm)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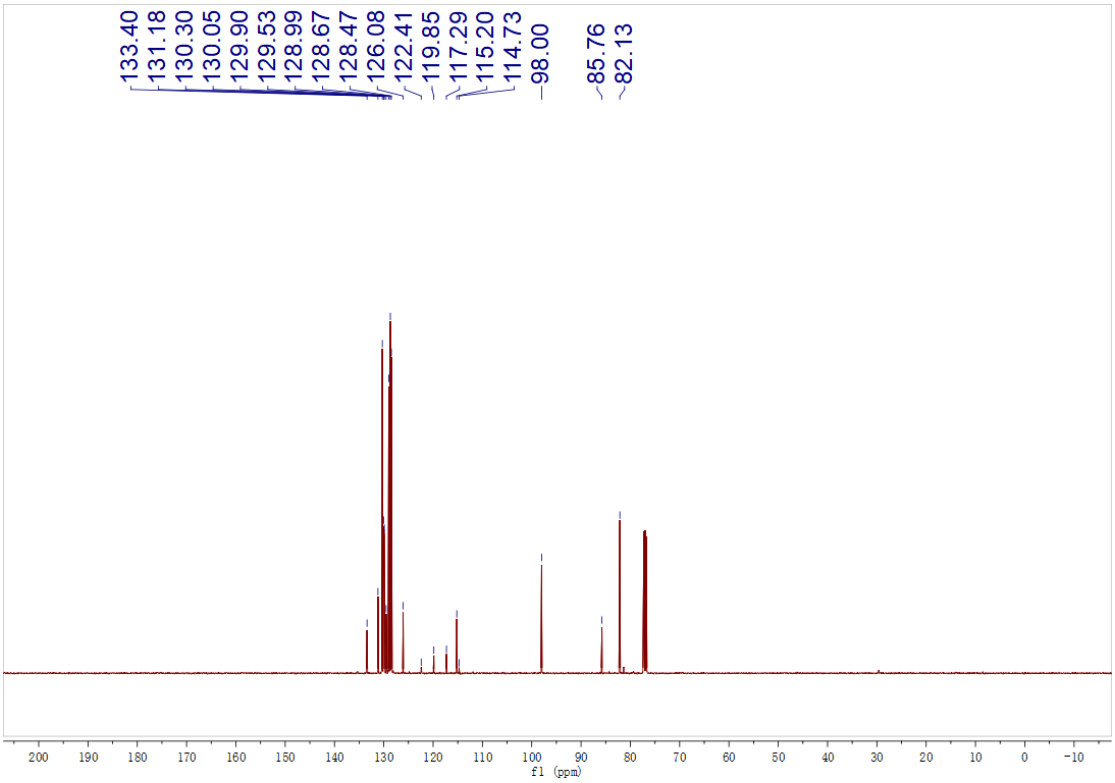
7.68
7.68
7.67
7.67
7.49
7.49
7.48
7.28
7.26
7.25
7.07
7.05
6.24
6.24
4.84
OTf
N−OBn
NC
Ph
5
1.99
3.06
1.02
2.09
2.00
0.94
2.00
f1 (ppm)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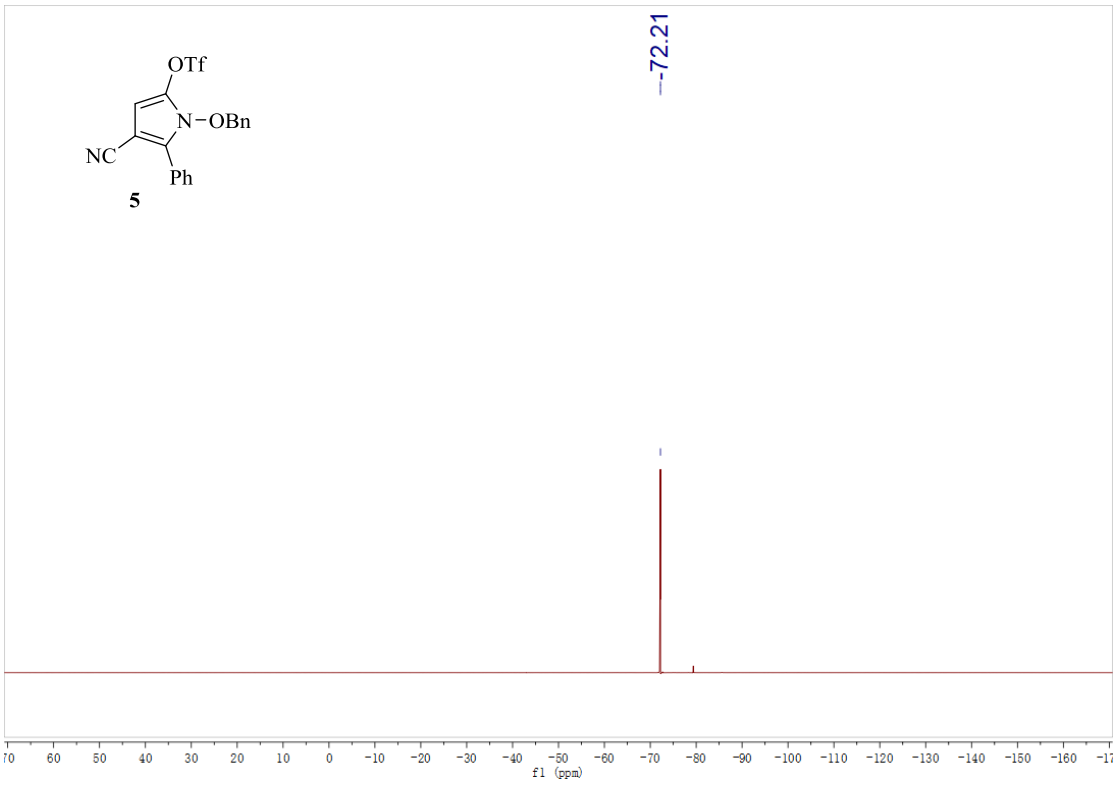
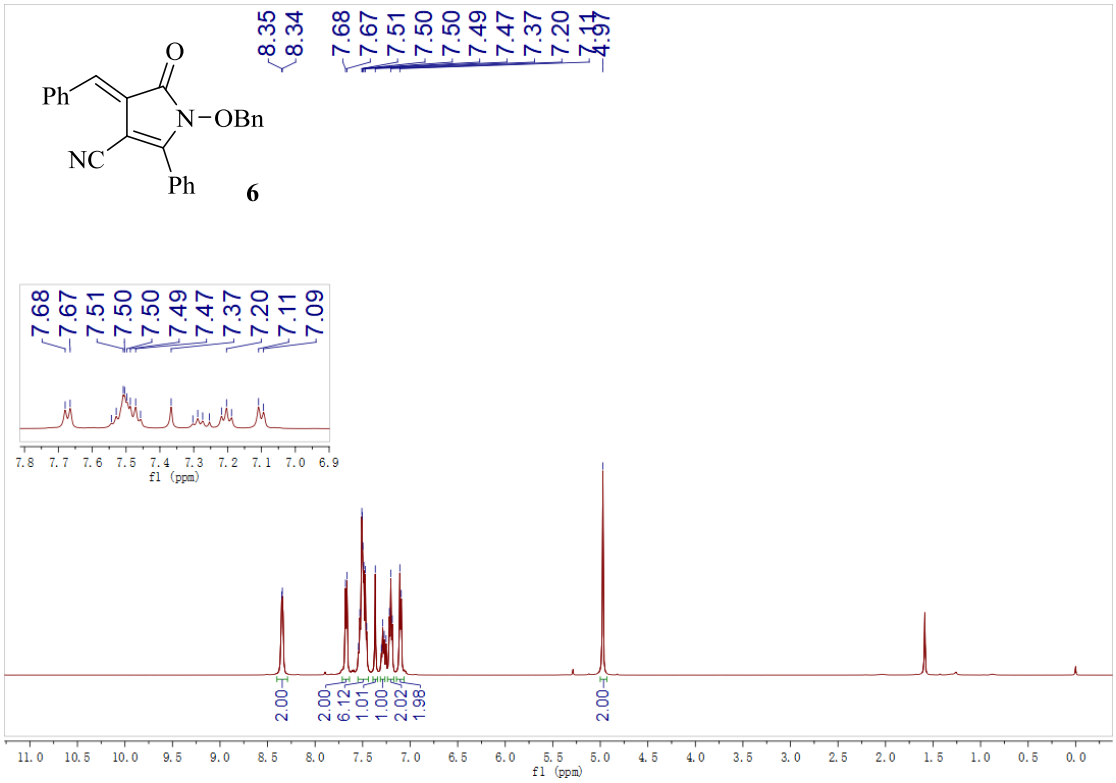
131.18
130.30
130.05
129.90
129.53
128.99
128.67
128.47
126.08
122.41
119.85
117.29
115.20
114.73
98.00
85.76
82.13
f1 (ppm)


OTf
N−OBn
NC
Ph
5
-72.21
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -17
f1 (ppm)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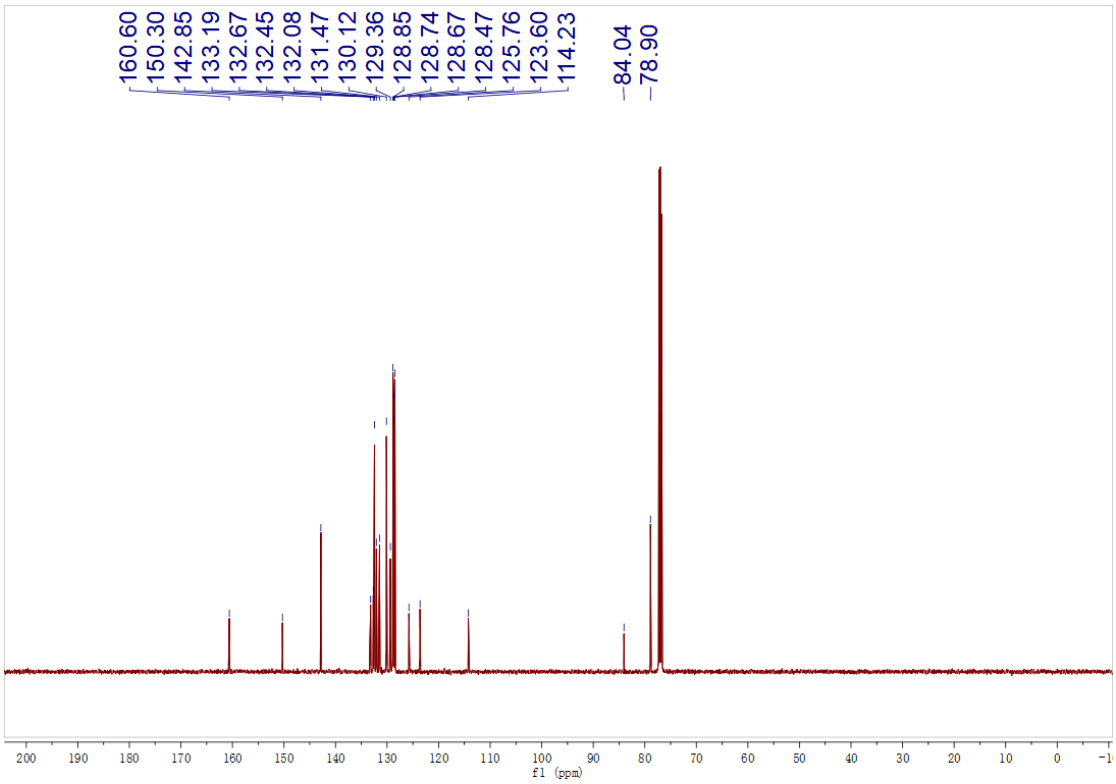
8.34
7.68
7.67
7.51
7.50
7.50
7.49
7.47
7.37
7.20
7.11
4.97
O
Ph
N−OBn
NC
Ph
6
7.68
7.67
7.51
7.50
7.50
7.49
7.47
7.37
7.20
7.11
7.09
7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9
f1 (ppm)
2.00
2.00
6.12
1.01
1.00
2.02
1.98
2.00
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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150.30
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133.19
132.67
132.45
132.08
131.47
130.12
129.36
128.85
128.74
128.67
128.47
125.76
123.60
114.23
84.04
78.90
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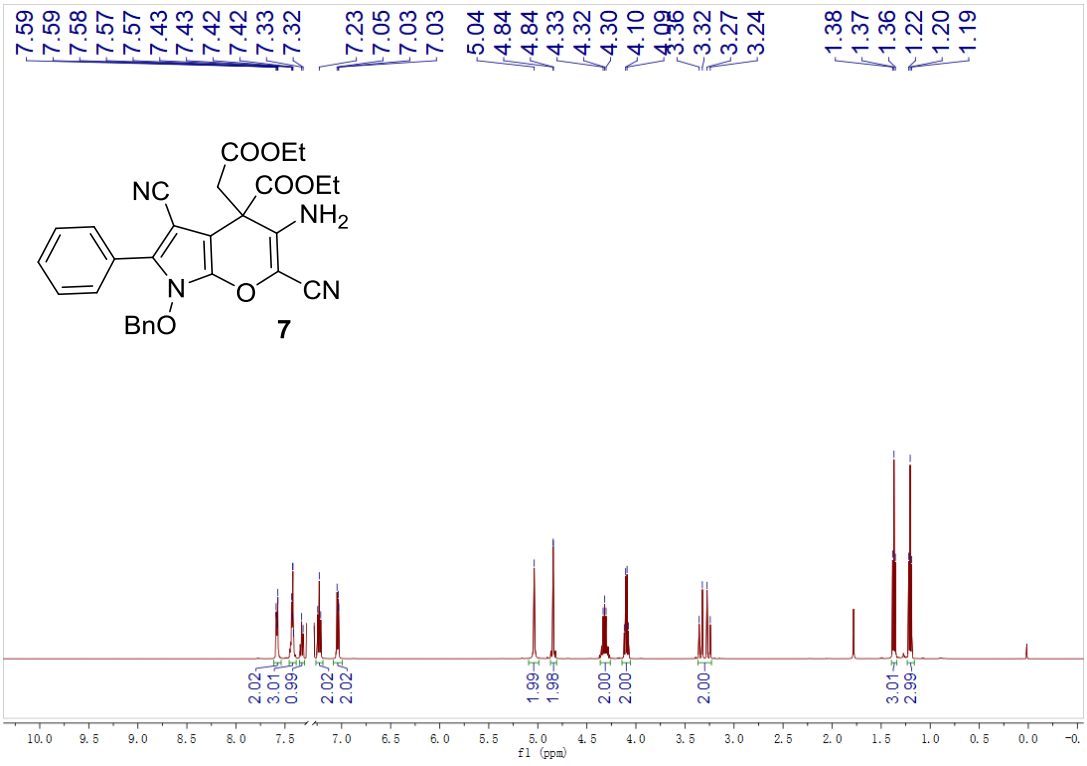
f1 (ppm)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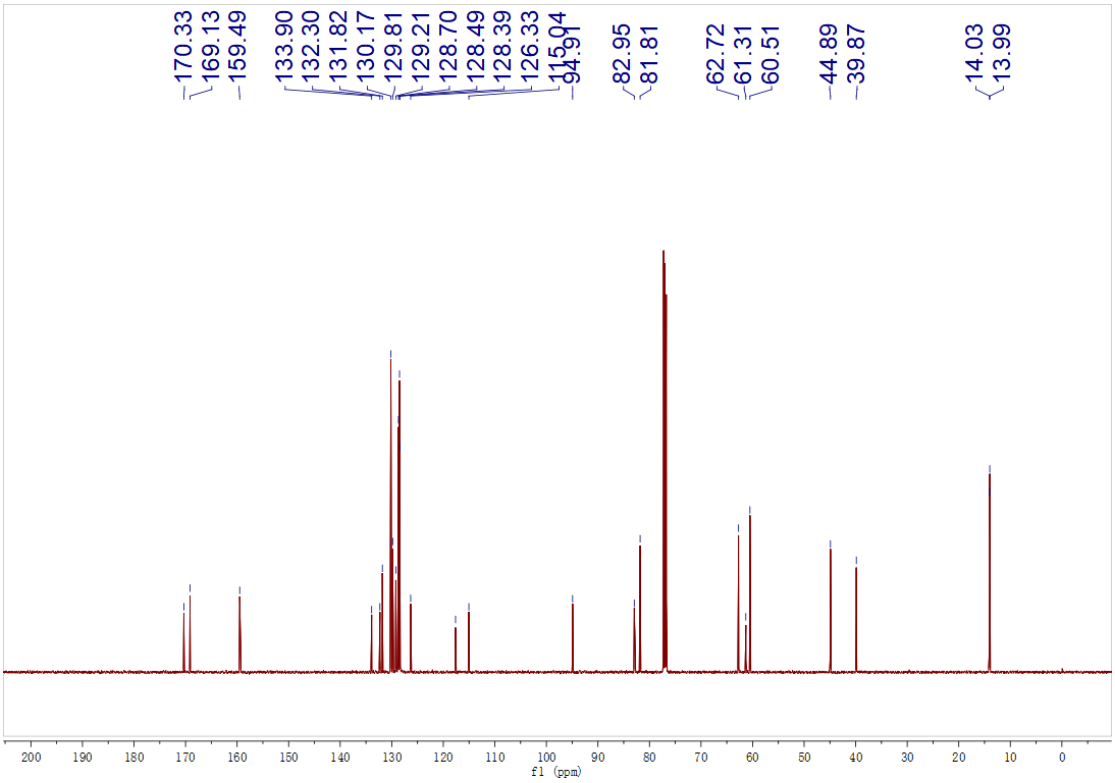
7.05
7.03
7.03
5.04
4.84
4.84
4.33
4.32
4.30
4.10
3.32
3.27
3.24
1.38
1.37
1.36
1.22
1.20
1.19
COOEt
COOEt
NC
NH2
N
O
CN
BnO
7
2.02
3.01
0.99
2.02
2.02
1.99
1.98
2.00
2.00
2.00
3.01
2.99
f1 (ppm)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133.90
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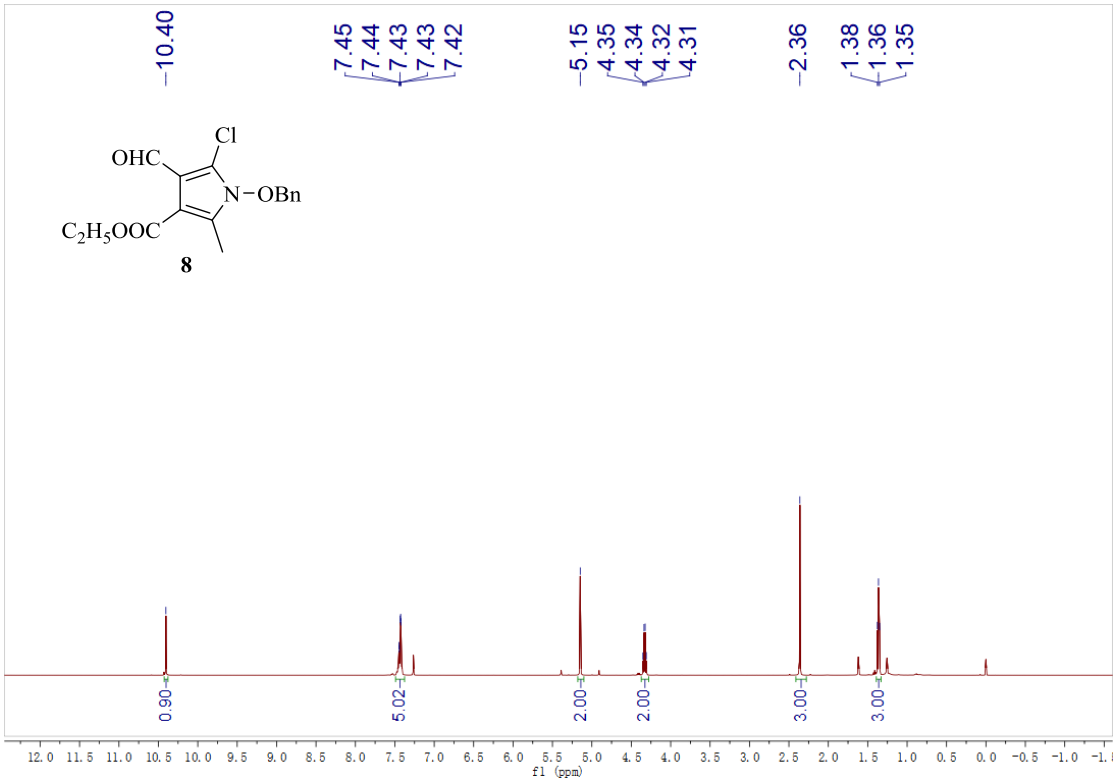
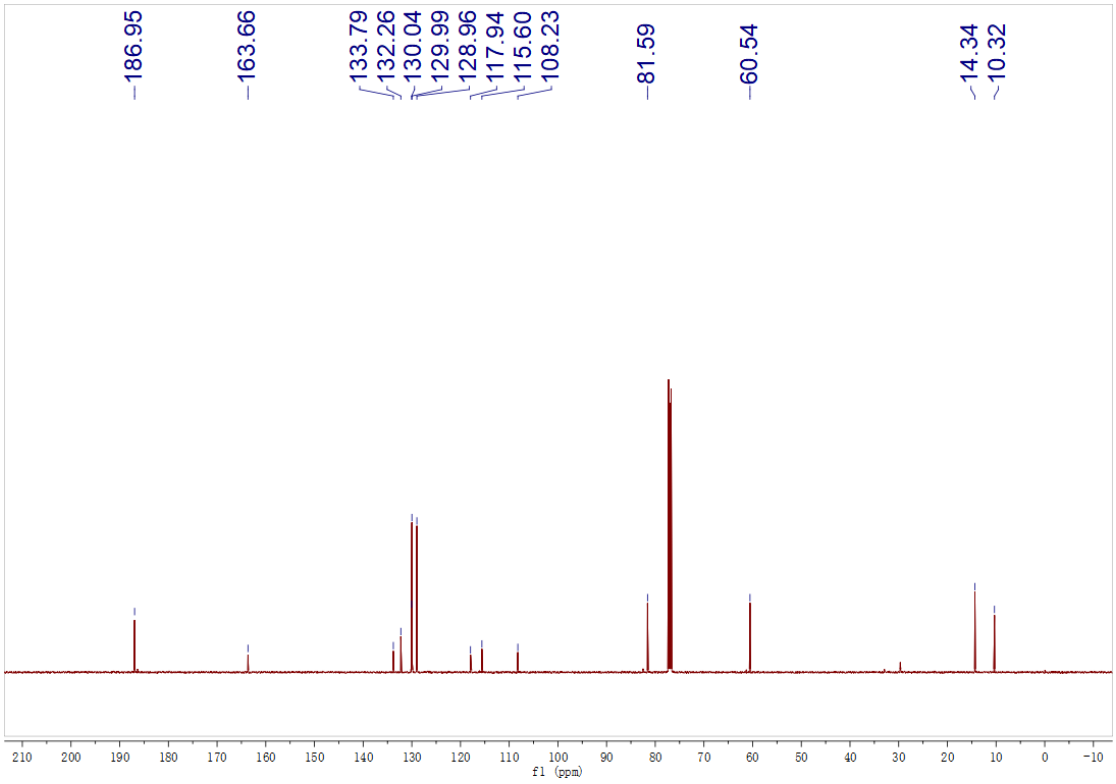
131.82
130.17
129.81
129.21
128.70
128.49
128.39
126.33
115.04
94.91
82.95
81.81
62.72
61.31
60.51
44.89
39.87
14.03
13.99
f1 (ppm)


10.40
7.45
7.44
7.43
7.43
7.42
5.15
4.35
4.34
4.32
4.31
2.36
1.38
1.36
1.35
Cl
OHC
N−OBn
C2H5OOC
8
0.90
5.02
2.00
2.00
3.00
3.00
f1 (ppm)


186.95
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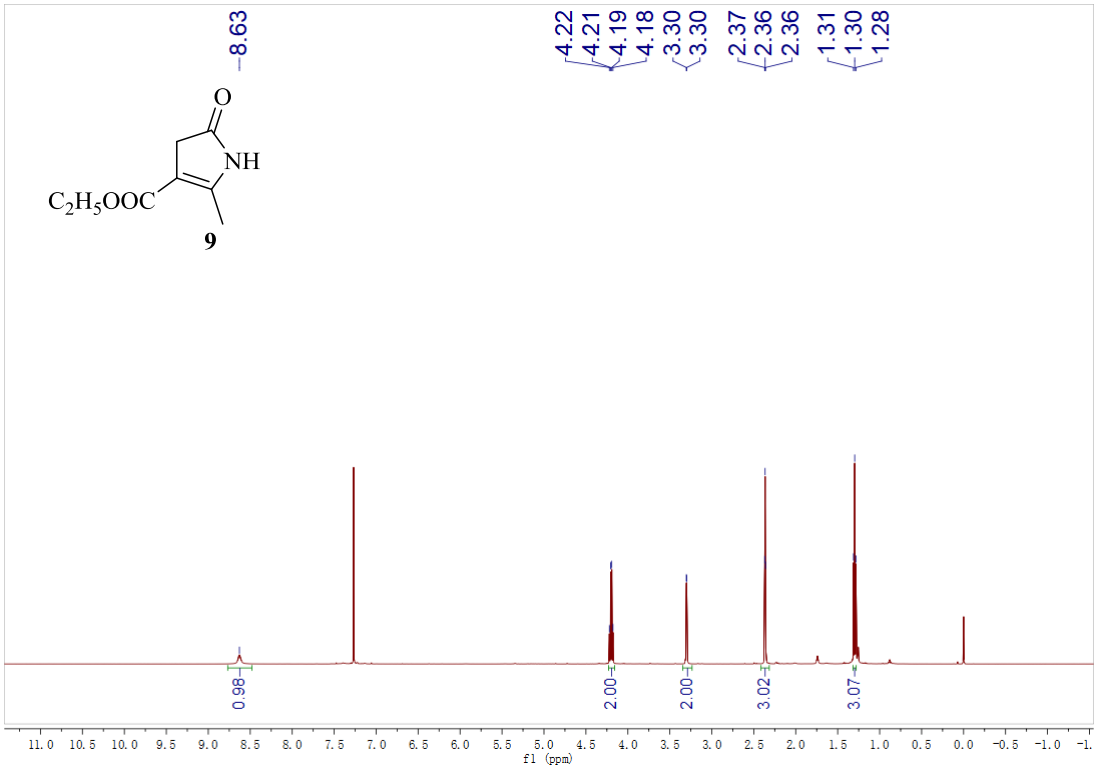
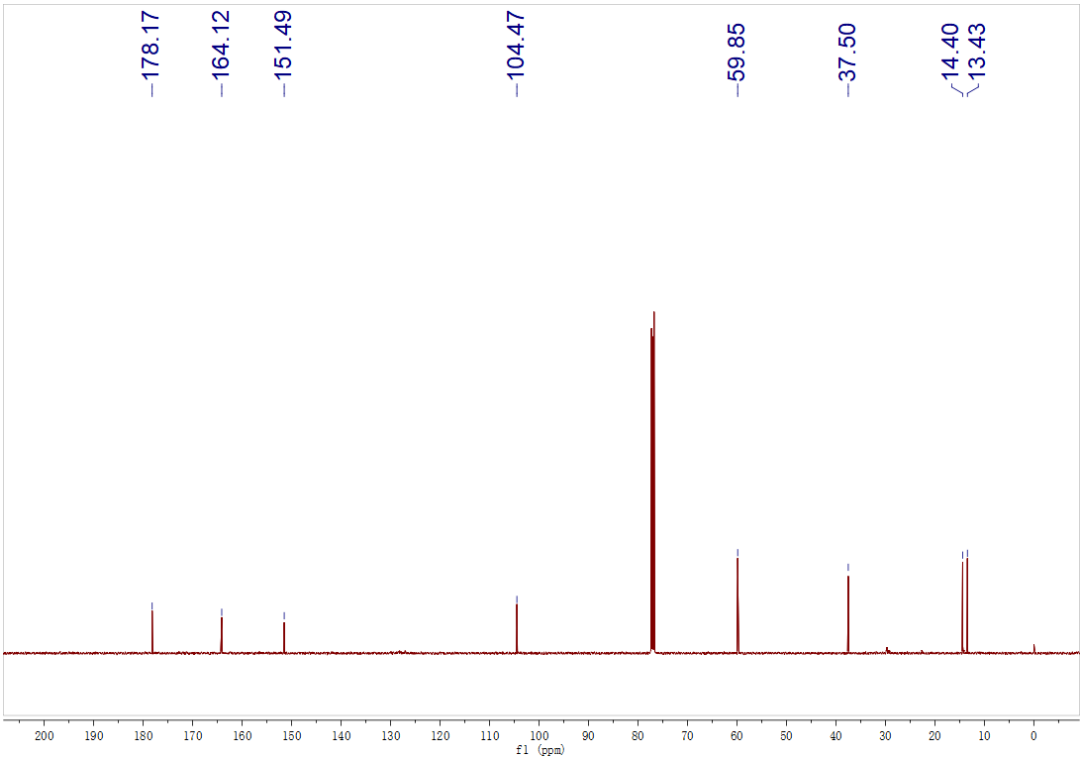
128.96
117.94
115.60
108.23
81.59
60.54
14.34
10.32
f1 (ppm)

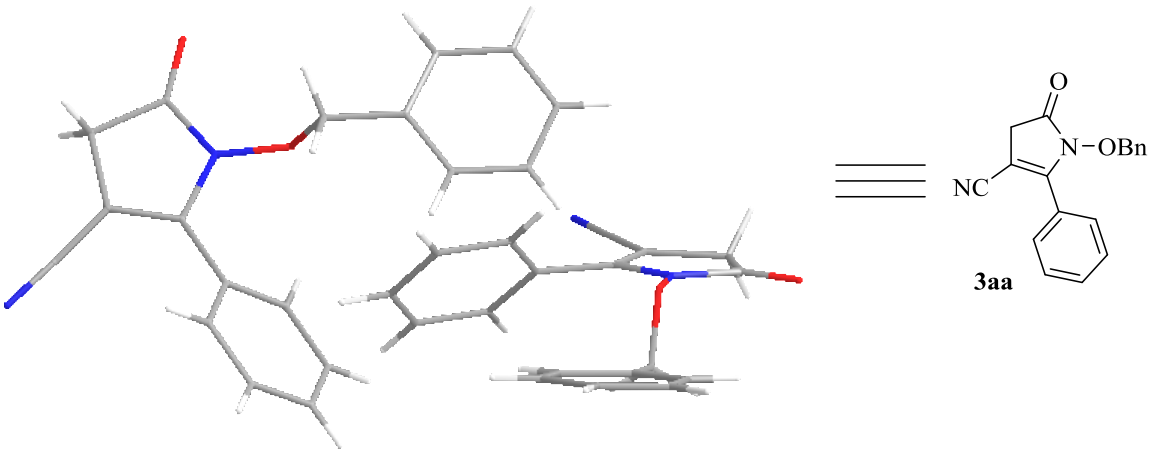

8.63
4.22
4.21
4.19
4.18
3.30
3.30
2.37
2.36
2.36
1.31
1.30
1.28
O
NH
C2H5OOC
9
0.98
2.00
2.00
3.02
3.07
f1 (ppm)


178.17
164.12
151.49
104.47
59.85
37.50
14.40
13.43
f1 (ppm)

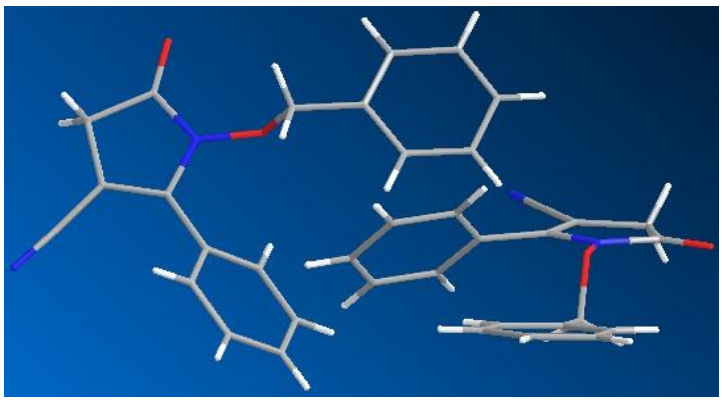
5. The crystal structure data of 3aa

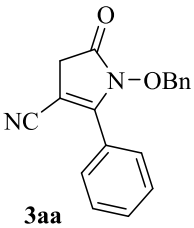
Table S5. Crystal data and structure refinement for**(3aa)**(**CCDC 2235249**)

Empirical formula	$C_{18}H_{14}N_2O_2$
Formula weight	290.31
Temperature / K	114.85(10)
Crystal system	monoclinic
Space group	Cc
a / Å, b / Å, c / Å	11.5249(9), 11.4884(10), 22.947(3)
α/°, β/°, γ/°	90.00, 98.346(8), 90.00
Volume / Å3	3006.1(5)
Z	8
ρ_{calc} / mg mm^{-3}	1.283
μ / mm^{-1}	0.085
F(000)	1216
Crystal size / mm^3	0.23 ×0.23 ×0.14
2Θ range for data collection	5.88 °to 51.98 °
Index ranges	-13 ≤ h ≤ 13, -13 ≤ k ≤ 14, -28 ≤ l ≤ 25
Reflections collected	6580
Independent reflections	4406[R(int) = 0.0462 (inf-0.9Å)]
Data/restraints/parameters	4406/2/397
Goodness-of-fit on F^2	1.023
Final R indexes [I>2σ (I) i.e. F_o>4σ (F_o)]	R_1 = 0.0551 wR_2 = 0.1118
Final R indexes [all data]	R_1 = 0.0710, wR_2 = 0.1253
Largest diff. peak/hole / e $Å^{-3}$	0.205/-0.259
Completeness	0.9968



3aa



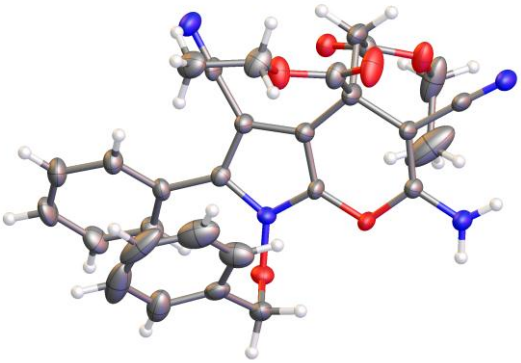


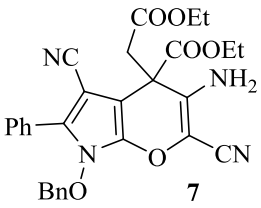
3aa

6. The crystal structure data of 7

Table S6. Crystal data and structure refinement for**(7)**(**CCDC 2267290**)

Empirical formula	$C_{29}H_{26}N_4O_6$
Formula weight	526.54
Temperature / K	118.25(10)
Crystal system	triclinic
Space group	P-1
a / Å, b / Å, c / Å	8.3944(5), 10.9479(8), 15.5175(9)
α/°, β/°, γ/°	76.896(6), 86.581(5), 70.851(6)
Volume / Å3	1311.91(14)
Z	2
ρ_{calc} / mg mm^{-3}	1.333
μ / mm^{-1}	0.095
F(000)	552
Crystal size / mm^3	0.35 ×0.33 ×0.11
2Θ range for data collection	5.84 °to 52 °
Index ranges	-7≤ h ≤ 10, -9 ≤ k ≤ 13, -19 ≤ l ≤ 19
Reflections collected	9361
Independent reflections	5020[R(int) = 0.0534]
Data/restraints/parameters	5020/2/354
Goodness-of-fit on F^2	1.021
Final R indexes [I>2σ (I) i.e. F_o>4σ (F_o)]	R_1 = 0.0764, wR_2 = 0.1665
Final R indexes [all data]	R_1 = 0.1261, wR_2 = 0.2052
Largest diff. peak/hole / e $Å^{-3}$	0.699/-0.334
Completeness	0.9981





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