Synthesis of Continuously Substituted Quinolines from *o*-Alkenyl Aromatic Isocyanides by Palladium-Catalyzed Intramolecular Imidoylative 6-*endo* Cyclization

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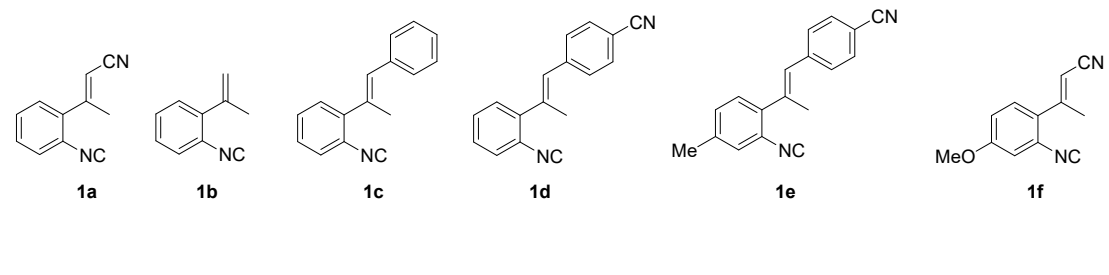
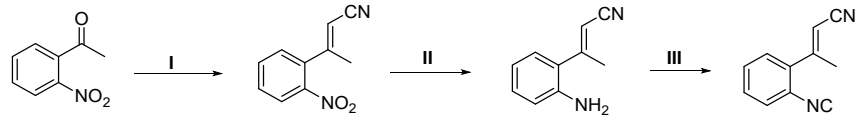
1. General Information

NMR spectra were recorded on a Bruker AM 400 MHz or 600 MHz spectrometer and calibrated using residual undeuterated solvent as an internal reference ($CDCl_3$ (^1H): δ = 7.24 ppm; $CDCl_3$ (^{13}C): δ = 77.23 ppm. High-resolution mass analysis was performed using a Thermo Scientific™ Q Exactive™ Hybrid Quadrupole-Orbitrap Mass Spectrometer. Melting points were determined on a Stanford Research Systems OptiMelt apparatus. The infrared (IR) spectra were acquired as thin films using a universal ATR sampling accessory on a Bruker Vertex 80 FT-IR spectrometer and the absorption frequencies are reported in cm^{-1}. Flash chromatography separations were carried out using silica gel columns. Isocyanides **1b**,[1] **1c**[2] and **1k**[1] were prepared according to literature procedure. All reagents and solvents were obtained from commercial sources and used as is without further purification. All new compounds were characterized by ^1H NMR, ^{13}C NMR, HRMS, and IR.

2. Preparation of *o*-alkenylaryl isocyanides



2.1 Preparation of 1a, 1b and 1f



I can refer to the Ref 3.

To a solution of 2'-nitroacetophenone (8.0 mmol, 1.0 equiv.) and LiOH (9.6 mmol, 1.2 equiv.) in THF (80.0 mL), was added diethyl cyanomethylphosphonate (1.56 g, 8.8 mmol, 1.1 equiv.). The reaction mixture was stirred at room temperature overnight. The completed reaction was diluted with ethyl acetate (30 mL), washed with water (30 mL) and brine (30 mL), dried (anhydrous Na_2SO_4) and concentrated. The residue was purified by column chromatography (Silica Gel, PE/EtOAc) to afford (*E*)-3-(2-nitrophenyl)but-2-enenitrile.

II can refer to the Ref 3

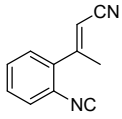
To a solution of (*E*)-3-(2-nitrophenyl)but-2-enenitrile (7.6 mmol, 1.0 equiv.) and Zinc (7.4 g, 114 mmol, 15.0 equiv.) in DCM (80.0 mL, 0.1 M), was added acetic acid (13.1 mL, 30.0 equiv.) dropwise over 10 min. The reaction mixture was stirred at room temperature overnight. The completed reaction was diluted with ethyl acetate (30 mL), washed with water (30 mL) and saturated $NaHCO_3$ (30 mL), dried (anhydrous Na_2SO_4) and concentrated. The residue was purified by column chromatography (Silica Gel, PE/EtOAc) to afford (*E*)-3-(2-aminophenyl)but -2-enenitrile.

III can refer to the Ref 4.

To a solution of (*E*)-3-(2-aminophenyl)but-2-enenitrile (2.0 mmol, 1.0 equiv.) in THF (4.0 mL, 0.50 M), was added acetic formic anhydride (6.0 mmol, 3.0 equiv.) dropwise at 0 °C. The resulting mixture was stirred at room temperature for 1 h. The completed reaction was quenched with water (15 mL) and extracted with DCM (20 mL x 3), The combined organic phase was washed with saturated $NaHCO_3$ (30 mL), dried (anhydrous Na_2SO_4) and concentrated. The residue was purified by column chromatography (Silica Gel, PE/EtOAc) to afford (*E*)-*N*-(2-(1-cyanoprop-1-en-2-yl) phenyl)formamide.

To a solution of (*E*)-*N*-(2-(1-cyanoprop-1-en-2-yl)phenyl)formamide (2.0 mmol, 1.0 equiv.) and Et_3N (12 mmol, 6.0 equiv.) in THF (10.0 mL, 0.2 M), was added $POCl_3$ (3.0 equiv.) dropwise at 0 °C. The resulting mixture was warmed up to room temperature and stirred for 6 hours. The completed reaction was quenched with water (15 mL) and extracted with DCM (30 mL x 3). The combined organic phase was dried (anhydrous Na_2SO_4) and concentrated. The residue was purified by column chromatography (Silica Gel, PE/EtOAc) to afford **1**.

(*E*)-3-(2-isocyanophenyl)but-2-enenitrile (1a):

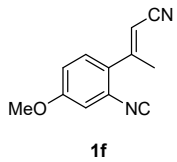


1a

Flash chromatography (Silica Gel, PE/EtOAc) afforded **1a** (0.242 g, 72%) as a light-yellow oil; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.49 – 7.40 (m,

3H), 7.29 – 7.26 (m, 1H), 5.50 (d, *J* = 1.3 Hz, 1H), 2.49 (d, *J* = 1.2 Hz, 3H); ^{13}C NMR (151 MHz, Chloroform-*d*) δ 169.1, 157.7, 137.3, 130.2, 129.9, 128.4, 128.3, 125.6, 116.1, 101.7, 21.9; IR (neat): 2883, 2218, 2119, 1514, 754 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{11}H_9N_2^+$ 169.0760, found 169.0763.

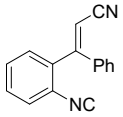
(*E*)-3-(2-isocyano-4-methoxyphenyl)but-2-enenitrile (1f)



1f

Flash chromatography (Silica Gel, PE/EtOAc) afforded **1f** (0.322 g, 81%) as a colorless oil; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.19 (d, *J* = 8.4 Hz, 1H), 6.96 (m, 2H), 5.49 (s, 1H), 3.84 (s, 3H), 2.46 (s, 3H); ^{13}C NMR (151 MHz, Chloroform-*d*) δ 168.8, 160.4, 157.0, 129.4, 129.1, 124.3, 116.3, 115.9, 113.3, 100.6, 55.7, 21.7; IR (neat): 2881, 2208, 2113, 1508, 736 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{12}H_{11}N_2O^+$ 199.0866, found 199.0872.

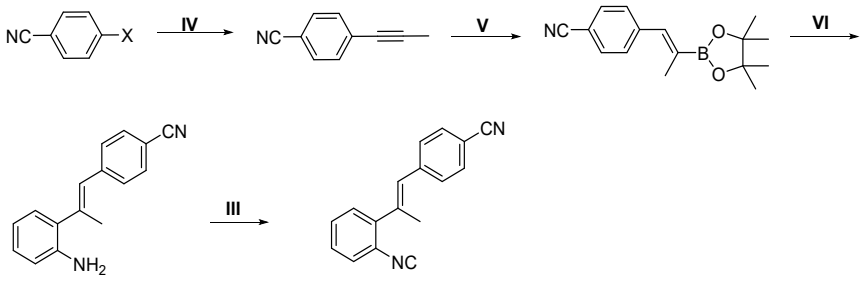
(*E*)-3-(2-isocyanophenyl)-3-phenylacrylonitrile (1k)



1k

Flash chromatography (Silica Gel, PE/EtOAc) afforded **1k** (0.418 g, 91%) as a yellow solid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.51 – 7.41 (m, 8H), 7.38 – 7.32 (m, 1H), 5.68 (s, 1H).^{13}C NMR (101 MHz, Chloroform-*d*) δ 169.2, 158.7, 136.7, 135.9, 130.9, 130.7, 130.6, 129.7, 129.0, 128.9, 128.2, 116.9, 99.3 (one carbon missing due to overlap); HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{16}H_{11}N_2^+$ 231.0917, found 231.0908.

2.2 Preparation of 1d-e and 1g-1l



IV can refer to the Ref 5.

To a solution of 4-Iodobenzonitrile (3.0 mmol, 1.0 equiv.), $PdCl_2(PPh_3)_2$ (0.06 mmol, 0.02 equiv.) and CuI (0.12 mmol, 0.04 equiv.) in Et_3N (9.0 mL, 0.3 M) was added terminal alkyne (4.5 mmol, 1.5 equiv.). The reaction mixture was heated in a 55 °C oil bath under argon for 5 h. After cooling to room temperature, the completed reaction was diluted with ethyl acetate (30 mL), washed with water (30 mL) and brine (30 mL), dried (anhydrous Na_2SO_4) and concentrated. The residue was purified by column chromatography (Silica Gel, PE/EtOAc) to afford 4-alkynylbenzonitrile.

V can refer to the Ref. 6.

To an oven dried schlenk tube equipped with a stir bar were added CuCl (0.15 mmol, 0.05 equiv.), NaO*t*-Bu (0.6 mmol, 0.2 equiv.), tri-*p*-tolylphosphine (0.3 mmol,

0.1 equiv.) and THF (2.4 mL) under nitrogen. After the mixture was stirred at room temperature for 30 min, bis(pinacolato)diboron (3.3 mmol, 1.1 equiv.) dissolved in THF (1.8 mL) was added. The reaction mixture was stirred for 10 min. Then, internal alkyne (3.0 mmol) was added followed by MeOH (6 mmol, 2.0 equiv.). The reaction was washed with THF (1.8 mL), sealed, and stirred until no starting material was detected by TLC. The reaction mixture was filtered through a pad of Celite and concentrated. The product was purified by column chromatography (Silica Gel, PE/EtOAc) to afford (*Z*)-4-(2-(4,4,5,5- tetramethyl-1,3,2-dioxaborolan-2-yl)prop-1-en -1-yl)benzonitrile.

VI can refer to the Ref. 7.

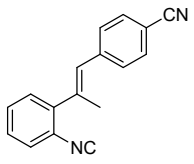
To a solution of (*Z*)-4-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)prop- 1-en-1-yl)benzonitrile (3.0 mmol, 1.0 equiv.) and 2-bromoaniline (3.0 mmol, 1.0 equiv.) in DMF (5.0 mL, 0.6 M) was added $Pd(PPh_3)_4$ (0.15 mmol, 5 mol %) and Na_2CO_3 (2.0 M in H_2O, 3.0 equiv.) under argon atmosphere. The reaction mixture was heated in an oil bath at 80 °C under argon atmosphere overnight. After cooling to room temperature, the completed reaction was diluted with ethyl acetate (30 mL), washed with water (30 mL) and brine (30 mL), dried (anhydrous Na_2SO_4) and concentrated. The residue was purified by column chromatography (Silica Gel, PE/EtOAc) to afford (*E*)-4-(2-(2-aminophenyl)prop-1-en-1-yl)benzonitrile.

III can refer to the Ref 4.

To a solution of (*E*)-3-(2-aminophenyl)but-2-enenitrile (2.0 mmol, 1.0 equiv.) in THF (4.0 mL, 0.50 M), was added acetic formic anhydride (6.0 mmol, 3.0 equiv.) dropwise at 0 °C. The resulting mixture was stirred at room temperature for 1 h. The completed reaction was quenched with water (15 mL) and extracted with DCM (20 mL x 3), The combined organic phase was washed with saturated $NaHCO_3$ (30 mL), dried (anhydrous Na_2SO_4) and concentrated. The residue was purified by column chromatography (Silica Gel, PE/EtOAc) to afford (*E*)-*N*-(2-(1-cyanoprop-1-en-2-yl) phenyl)formamide.

To a solution of (*E*)-*N*-(2-(1-cyanoprop-1-en-2-yl)phenyl)formamide (2.0 mmol, 1.0 equiv.) and Et_3N (12 mmol, 6.0 equiv.) in THF (10.0 mL, 0.2 M), was added $POCl_3$ (3.0 equiv.) dropwise at 0 °C. The resulting mixture was warmed up to room temperature and stirred for 6 hours. The completed reaction was quenched with water (15 mL) and extracted with DCM (30 mL x 3). The combined organic phase was dried (anhydrous Na_2SO_4) and concentrated. The residue was purified by column chromatography (Silica Gel, PE/EtOAc) to afford **1**.

(*E*)-4-(2-(2-isocyanophenyl)prop-1-en-1-yl)benzonitrile (1d)

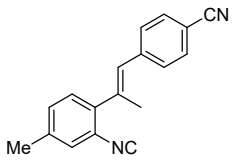


1d

Flash chromatography (Silica Gel, PE/EtOAc) afforded **1d** (0.316 g, 65%) as a light yellow solid; m.p.: 93-94 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.68 (d, *J* = 8.3 Hz, 2H), 7.49 (d, *J* = 8.3 Hz, 2H), 7.46 – 7.39 (m, 2H), 7.39 – 7.32 (m, 2H), 6.59 (s, 1H), 2.28 (d, *J* = 1.5 Hz, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.0, 142.2,

141.8, 137.8, 132.2, 130.3, 129.7, 129.6, 129.0, 128.4, 127.7, 124.3, 119.0, 110.6, 19.1; IR (neat): 2877, 2223, 2119, 1508, 752 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calculated for $C_{17}H_{13}N_2^+$ 245.1073, found 245.1076.

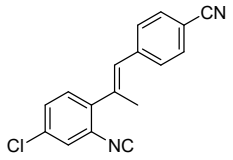
(*E*)-4-(2-(2-isocyano-4-methylphenyl)prop-1-en-1-yl)benzonitrile (1e)



1e

Flash chromatography (Silica Gel, PE/EtOAc) afforded **1e** (0.397 g, 77%) as a light yellow solid; m.p.: 87-88 ℃. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.69 (d, *J* = 8.1 Hz, 2H), 7.51 (d, *J* = 8.0 Hz, 2H), 7.24-7.28 (m, 3H), 6.60 (s, 1H), 2.40 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (151 MHz, Chloroform-*d*) δ 160.8, 148.4, 146.4, 143.3, 139.7, 135.1, 132.2, 131.5, 129.7, 128.3, 126.5, 126.2, 120.3, 111.8，16.8 (one carbon missing due to overlap); IR (neat): 2879, 2225, 2117, 1508, 729 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{18}H_{15}N_2^+$ 259.1230, found 259.1932.

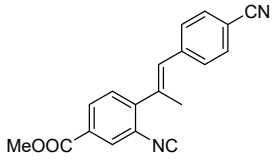
(*E*)-4-(2-(4-chloro-2-isocyanophenyl)prop-1-en-1-yl)benzonitrile (1g)



1g

Flash chromatography (Silica Gel, PE/EtOAc) afforded **1g** (0.40 g, 53%) as a light yellow solid. m.p.: 104-105 ℃. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.68 (d, *J* = 8.1 Hz, 2H), 7.48 (d, *J* = 8.0 Hz, 2H), 7.45 – 7.38 (m, 2H), 7.31 (d, *J* = 8.3 Hz, 1H), 6.59 (s, 1H), 2.26 (d, *J* = 1.4 Hz, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 168.7, 141.5, 140.7, 136.7, 133.8, 132.3, 130.9, 130.2, 130.0, 129.4, 127.6, 125.1, 118.9, 110.9, 19.0; IR (neat): 2882, 2223, 2119, 1512, 727 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{17}H_{12}ClN_2^+$ 279.0689, found 279.0685.

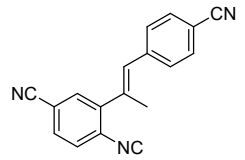
Methyl (*E*)-4-(1-(4-cyanophenyl)prop-1-en-2-yl)-3-isocyanobenzoate (1h)



1h

Flash chromatography (Silica Gel, PE/EtOAc) afforded **1h** (0.428 g, 71%) as a light yellow solid; m.p.: 179-180 ℃; ^1H NMR (400 MHz, Chloroform-*d*) δ 8.09 (s, 1H), 8.07 (d, *J* = 8.0 Hz, 1H), 7.69 (d, *J* = 8.1 Hz, 2H), 7.50 (d, *J* = 8.1 Hz, 2H), 7.45 (d, *J* = 8.0 Hz, 1H), 6.64 (s, 1H), 3.96 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 168.4, 165.2, 146.3, 141.4, 137.0, 132.3, 131.2, 130.6, 129.8, 129.4, 128.9, 124.6, 118.9, 111.0, 52.8, 18.9 (one carbon missing due to overlap); IR (neat): 2884, 2220, 2117, 1514, 748 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{19}H_{15}N_2O_2^+$ 303.1128, found 303.1141.

(*E*)-3-(1-(4-cyanophenyl)prop-1-en-2-yl)-4-isocyanobenzonitrile (1i)

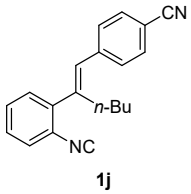


1i

Flash chromatography (Silica Gel, PE/EtOAc) afforded **1i** (0.242 g, 45%) as a light yellow solid. m.p.: 138-139 ℃; ^1H NMR (600 MHz, Chloroform-*d*) δ 7.73 – 7.68 (m, 3H), 7.66 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.55 (d, *J* = 8.2 Hz, 1H), 7.49 (d, *J* = 8.1 Hz, 2H), 6.63 (s, 1H), 2.28 (d, *J* = 1.5 Hz, 3H); ^{13}C NMR (151 MHz, Chloroform-*d*) δ 143.4, 140.9, 135.7, 133.1, 132.4, 132.0, 129.8, 128.7, 125.5, 118.8, 117.2, 113.8, 111.4, 18.9 (two carbon missing due to overlap); IR (neat): 2884, 2227, 2119, 1512, 729 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{18}H_{12}N_3^+$ 270.1026;

found 270.1041.

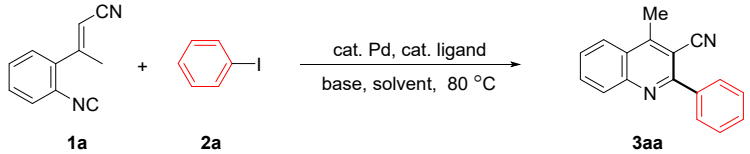
(*E*)-4-(2-(2-isocyanophenyl)hex-1-en-1-yl)benzonitrile (1j)



1j

Flash chromatography (Silica Gel, PE/EtOAc) afforded **1j** (0.314 g, 55%) as colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.67 (d, *J* = 8.1 Hz, 2H), 7.48 – 7.39 (m, 4H), 7.38 – 7.31 (m, 2H), 6.53 (s, 1H), 2.66 (t, *J* = 7.3 Hz, 2H), 1.24-1.29 (m, 4H), 0.80 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (151 MHz, Chloroform-*d*) δ 166.8, 142.7, 142.0, 140.8, 132.3, 130.2, 129.6, 129.5, 129.4, 128.3, 127.6, 124.9, 119.0, 110.7, 31.4, 30.5, 22.7, 13.9; IR (neat): 2954, 2225, 2119, 1508, 752 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{20}H_{19}N_2^+$ 287.1543, found 287.1542.

3. Reaction conditions optimization[a]



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

entry	Catalyst (mol%)	Ligand (mol%)	Base (equiv.)	Solvent	Addition of **1a**	Yield (%)
1	$Pd(OAc)_2$ (10)	PPh_3 (20)	CsOPiv (1.2)	Toluene	1.0 mL over 1 h	24
2	$Pd(dba)_2$ (10)	PPh_3 (20)	CsOPiv (1.2)	Toluene	1.0 mL over 1 h	24
3	$Pd(dba)_2$ (10)	PPh_3 (40)	CsOPiv (1.2)	Toluene	1.0 mL over 1 h	37
4	$Pd_2(dba)_3$ (5)	PPh_3 (40)	CsOPiv (1.2)	Toluene	1.0 mL over 1 h	21
5	$Pd(PPh_3)_4$ (10)	-	CsOPiv (1.2)	Toluene	1.0 mL over 1 h	44
6	$Pd(dba)_2$ (10)	P(*o*-tol)$_3$ (40)	CsOPiv (1.2)	Toluene	1.0 mL over 1 h	trace
7	$Pd(dba)_2$ (10)	RuPhos (20)	CsOPiv (1.2)	Toluene	1.0 mL over 1 h	trace
8	$Pd(dba)_2$ (10)	Ad_2Pn-Bu (0.4)	CsOPiv (1.2)	Toluene	1.0 mL over 1 h	29
10	$Pd(dba)_2$ (10)	BINAP (20)	CsOPiv (1.2)	Toluene	1.0 mL over 1 h	trace
11	$Pd(dba)_2$ (10)	dppm (20)	CsOPiv (1.2)	Toluene	1.0 mL over 1 h	11
12	$Pd(dba)_2$ (10)	DPEphos (20)	CsOPiv (1.2)	Toluene	1.0 mL over 1 h	25
13	$Pd(dba)_2$ (10)	Xantphos (20)	CsOPiv (1.2)	Toluene	1.0 mL over 1 h	trace
14	$Pd(dba)_2$ (10)	dppe (20)	CsOPiv (1.2)	Toluene	1.0 mL over 1 h	trace
15	$Pd(dba)_2$ (10)	dppp (20)	CsOPiv (1.2)	Toluene	1.0 mL over 1 h	9
16	$Pd(dba)_2$ (10)	dppb (20)	CsOPiv (1.2)	Toluene	1.0 mL over 1 h	trace
17	$Pd(dba)_2$ (10)	dppf (20)	CsOPiv (1.2)	Toluene	1.0 mL over 1 h	N.R.
20[b]	$Pd(PPh_3)_4$ (10)	-	CsOPiv (1.2)	Toluene	1.0 mL over 1 h	35
21[c]	$Pd(PPh_3)_4$ (10)	-	CsOPiv (1.2)	Toluene	1.0 mL over 1 h	30
22	$Pd(PPh_3)_4$ (10)	-	CsOPiv (1.2)	Toluene	one portion	trace
23	$Pd(PPh_3)_4$ (10)	-	CsOPiv (1.2)	Toluene	1.0 mL over 2 h	62
24	$Pd(PPh_3)_4$ (10)	-	CsOPiv (1.2)	Toluene	2.0 mL over 2 h	48
25	$Pd(PPh_3)_4$ (10)	-	CsOPiv (1.2)	Toluene	1.0 mL over 3 h	68
26	$Pd(PPh_3)_4$ (10)	-	CsOPiv (1.2)	Toluene	2.0 mL over 4 h	56
27	$Pd(PPh_3)_4$ (10)	-	CsOPiv (1.2)	Toluene	1.0 mL over 3.5 h	45
29	$Pd(PPh_3)_4$ (10)	-	CsOPiv (1.2)	dioxane	1.0 mL over 3 h	31

30	$Pd(PPh_3)_4$ (10)	-	CsOPiv (1.2)	DMF	1.0 mL over 3 h	22
31	$Pd(PPh_3)_4$ (10)	-	CsOPiv (1.2)	DCE	1.0 mL over 3 h	13
32	$Pd(PPh_3)_4$ (10)	-	CsOPiv (1.2)	DMSO	1.0 mL over 3 h	36
33	$Pd(PPh_3)_4$ (10)	-	CsOPiv (1.2)	MeCN	1.0 mL over 3 h	19
34	$Pd(PPh_3)_4$ (10)	-	CsOPiv (1.2)	NMP	1.0 mL over 3 h	13
35	$Pd(PPh_3)_4$ (10)	-	CsOPiv (1.2)	Toluene: MeCN 1:1	1.0 mL over 3 h	26
36	$Pd(PPh_3)_4$ (10)	-	CsOPiv (1.2)	Toluene:DMSO1:1	1.0 mL over 3 h	28
37[d]	$Pd(PPh_3)_4$ (10)	-	CsOPiv (1.2)	Toluene	1.0 mL over 3 h	49
38[e]	$Pd(PPh_3)_4$ (10)	-	CsOPiv (1.2)	Toluene	1.0 mL over 3 h	51
39[f]	$Pd(PPh_3)_4$ (10)	-	CsOPiv (1.2)	Toluene	1.0 mL over 3 h	43
40	$Pd(PPh_3)_4$ (5)	-	CsOPiv (1.2)	Toluene	1.0 mL over 3 h	31
41	$Pd(PPh_3)_4$ (10)	-	Na_2CO_3 (1.2)	Toluene	1.0 mL over 3 h	trace
42	$Pd(PPh_3)_4$ (10)	-	Cs_2CO_3 (1.2)	Toluene	1.0 mL over 3 h	trace
43	$Pd(PPh_3)_4$ (10)	-	NaOAc (1.2)	Toluene	1.0 mL over 3 h	trace
44	$Pd(PPh_3)_4$ (10)	-	Et_3N (1.2)	Toluene	1.0 mL over 3 h	trace
45	$Pd(PPh_3)_4$ (10)	-	Cs_2CO_3 (0.6) /PivOH (1.2)	Toluene	1.0 mL over 3 h	67
46[g]	$Pd(PPh_3)_4$ (10)	-	Cs_2CO_3 (0.6) /TMCA (1.2)	Toluene	1.0 mL over 3 h	95

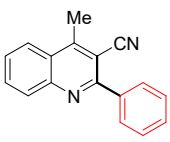
[a]Reaction conditions: to a solution of **2a** (1.5 equiv.), Pd catalyst, ligand and base in solvent (1.0 mL) at 80 °C under Ar, was added a solution of **1a** (0.2 mmol) in solvent as indicated by using a syringe pump. [b]100 °C. [c]60 °C. [d]2.0 equiv. of **2a**. [e]2.0 equiv. of **2a**. [f]0.83 equiv. of **2a**. [g]2,2,3,3-tetramethylcyclo propanecarboxylic acid (TMCA).

4. Preparation of Quinolines

4.1 from aryl iodides

To a 20 mL vial was added $Pd(PPh_3)_4$ (0.0236 g, 0.02 mmol, 0.1 equiv.), Cs_2CO_3 (0.0391 g, 0.12 mmol, 0.6 equiv.), TMCA (2,2,3,3-tetramethylcyclopropane carboxylic acid) (0.0341 g, 0.24 mmol, 1.2 equiv.) and a solution of aryl iodide (0.3 mmol, 1.5 equiv.) in toluene (1 mL) under argon. The resulting mixture was heated at 80 °C heating block for 30 min. Then a solution of isocyanide (0.2 mmol, 1.0 equiv.) in toluene (1 mL) was added to the reaction mixture dropwise over 3 h using a syringe pump. After further 1 h, the completed reaction was diluted with DCM (20 mL) and washed with satd. $NaHCO_3$ (20 mL x 2). The combined aqueous phase was back extracted with DCM (15 mL x 2). The combined organic phase was dried (anhydrous Na_2SO_4) and concentrated. The residue was purified by column chromatography (Silica Gel, PE/EtOAc) to afford the quinoline product **3**.

4-Methyl-2-phenylquinoline-3-carbonitrile (3aa)

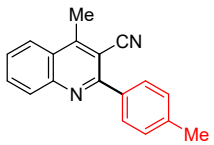


3aa

Flash chromatography (Silica Gel, PE/EtOAc) afforded **3aa** (0.046 g, 95%) as a light yellow solid; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.20 (d, *J* = 8.4 Hz, 1H), 8.11 (dd, *J* = 8.3, 1.3 Hz, 1H), 7.98 – 7.91 (m,

2H), 7.90 – 7.83 (m, 1H), 7.73 – 7.64 (m, 1H), 7.61 – 7.49 (m, 3H), 3.05 (s, 3H).^{13}C NMR (101 MHz, Chloroform-*d*) δ 158.9, 153.3, 148.4, 132.8, 131.2, 130.4, 129.7, 129.1, 128.3, 125.7, 124.8, 117.9, 18.2 (two carbon missing due to overlap); The spectroscopic data are in accordance with those reported in literature.[8]

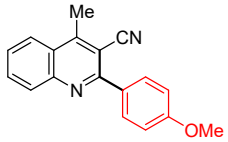
4-Methyl-2-(*p*-tolyl)quinoline-3-carbonitrile (3ab)



3ab

Flash chromatography (Silica Gel, PE/EtOAc) afforded **3ab** (0.046 g, 89%) as light yellow solid; m.p.: 136-139 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.12 (d, *J* = 8.4 Hz, 1H), 8.04 (d, *J* = 8.5 Hz, 1H), 7.83 – 7.76 (m, 3H), 7.65 – 7.56 (m, 1H), 7.30 (d, *J* = 7.9 Hz, 2H), 2.98 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.6 , 153.0 , 148.1, 140.3, 135.7, 132.6, 130.7, 129.5, 129.3, 127.8, 125.2, 124.5, 117.8, 106.5, 21.7, 18.0; IR (neat): 2924, 2210, 1584, 1341; HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{18}H_{15}N_2^+$ 259.1230, found 259.1230.

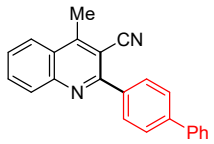
2-(4-Methoxyphenyl)-4-methylquinoline-3-carbonitrile (3ac)



3ac

Flash chromatography (Silica Gel, PE/EtOAc) afforded **3ac** (0.023 g, 41%) as light yellow solid; m.p.: 182-183 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.10 (d, *J* = 8.5 Hz, 1H), 8.02 (d, *J* = 8.9 Hz, 1H), 7.88 (d, *J* = 8.7 Hz, 2H), 7.78 – 7.75 (m, 1H), 7.63 – 7.54 (m, 1H), 7.01 (d, *J* = 8.8 Hz, 2H), 3.84 (s, 3H), 2.97 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.2, 158.1, 153.1, 148.1, 132.6, 130.9, 130.6, 127.7, 125.1, 124.5, 118.0, 114.2, 106.3, 55.6, 18.0 (one carbon missing due to overlap); IR (neat) : 3060, 2240, 1551, 1495, 1380 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{18}H_{15}N_2O^+$ 275.1179, found 275.1179.

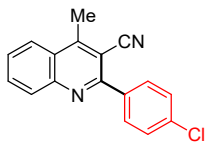
2-([1,1'-biphenyl]-4-yl)-4-methylquinoline-3-carbonitrile (3ad)



3ad

Flash chromatography (Silica Gel, PE/EtOAc) afforded **3ad** (0.057 g, 89%) as a white solid; m.p.: 145-146 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.21 (d, *J* = 7.9 Hz, 1H), 8.11 (d, *J* = 8.5 Hz, 1H), 8.05 (d, *J* = 8.3 Hz, 2H), 7.91 – 7.84 (m, 1H), 7.79 (d, *J* = 8.3 Hz, 2H), 7.73 – 7.64 (m 2H), 7.52 – 7.44 (m, 2H), 7.43 – 7.36 (m, 1H), 3.06 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 158.0, 153.0, 148.0, 142.8, 140.5, 137.2, 132.5, 130.7, 129.7, 128.9 , 127.8, 127.8, 127.4, 127.3, 125.2, 124.4, 117.6, 106.3, 17.9; IR (neat): 2922, 2218, 1490, 1272, 846, 740; HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{23}H_{17}N_2^+$ 321.1386, found 321.1391.

2-(4-chlorophenyl)-4-methylquinoline-3-carbonitrile (3ae)

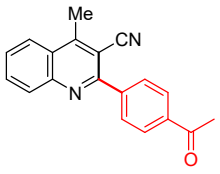


3ae

Flash chromatography (Silica Gel, PE/EtOAc) afforded **3ae** (0.041 g, 74%) as a white solid; m.p.: 190-191 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.17 (d, *J* = 8.5 Hz, 1H), 8.11 (d, *J* = 8.5 Hz, 1H), 7.94 – 7.83 (m, 3H), 7.72 – 7.66 (m, 1H), 7.53 (d, *J* = 8.6 Hz, 2H), 3.04 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 156.9, 152.9, 147.6, 136.4, 136.1, 132.4, 130.4, 128.7, 127.9, 125.0, 124.2, 117.1, 105.9, 17.7 (one

carbon missing due to overlap); IR (neat): 2900, 2360, 1514, 1269, 1095, 740; HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{17}H_{12}ClN_2^+$ 279.0684, found 279.0680.

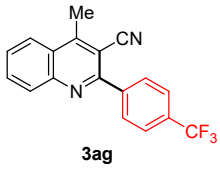
2-(4-acetylphenyl)-4-methylquinoline-3-carbonitrile (3af)



3af

Flash chromatography (Silica Gel, PE/EtOAc) afforded **3af** (0.045 g, 79%) as a white solid; m.p.: 196-197 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.20 (d, *J* = 8.5 Hz, 1H), 8.12-8.16 (m, 3H), 8.05 (d, *J* = 8.1 Hz, 2H), 7.93 – 7.86 (m, 1H), 7.75 – 7.69 (m, 1H), 3.06 (s, 3H), 2.69 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 197.8, 157.3, 153.3, 147.9, 142.6, 137.9, 132.8, 130.8, 129.7, 128.7, 128.4, 125.5, 124.5, 117.3, 106.3, 27.0, 18.0; IR (neat): 2910, 2362, 1745, 1513, 1274, 738; HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{19}H_{15}N_2O^+$ 287.1179, found 287.1176.

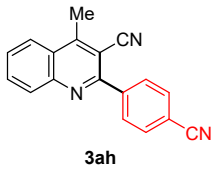
4-methyl-2-(4-(trifluoromethyl)phenyl)quinoline-3-carbonitrile (3ag)



3ag

Flash chromatography (Silica Gel, PE/EtOAc) afforded **3ag** (0.057 g, 91%) as a white solid; m.p.: 151-152 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.20 (d, *J* = 8.5 Hz, 1H), 8.14 (d, *J* = 8.5 Hz, 1H), 8.07 (d, *J* = 8.1 Hz, 2H), 7.94 – 7.86 (m, *J* = 7.7 Hz, 1H), 7.82 (d, *J* = 8.0 Hz, 2H), 7.76 – 7.69 (m, 1H), 3.07 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 157.0, 153.4, 147.9, 141.7, 132.9, 132.1 (q, *J* = 33 Hz), 130.8, 129.8, 128.5, 125.7 (q, *J* = 4.0 Hz), 125.5, 124.5, 117.3, 106.2, 18.0 (one carbon missing); ^{19}F NMR (377 MHz, $CDCl_3$) δ -62.74; IR (neat): 2917, 2221, 1546, 1325, 1114, 846; HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{18}H_{12}F_3N_2^+$ 313.0947, found 313.0947.

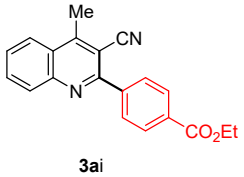
2-(4-cyanophenyl)-4-methylquinoline-3-carbonitrile (3ah)



3ah

Flash chromatography (Silica Gel, PE/EtOAc) afforded **3ah** (0.033 g, 62%) as a white solid; m.p.: 223-224 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.19 (d, *J* = 8.4 Hz, 1H), 8.14 (d, *J* = 8.5 Hz, 1H), 8.08 (d, *J* = 8.3 Hz, 2H), 7.96 – 7.89 (m, 1H), 7.86 (d, *J* = 8.3 Hz, 2H), 7.78 – 7.70 (m, 1H), 3.07 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 156.3, 153.6, 147.9, 142.5, 133.1, 132.5, 130.8, 130.1, 128.7, 125.6, 124.6, 118.6, 117.1, 113.7, 106.0, 18.1; IR (neat): 2898, 2358, 1507, 1269, 732; HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{18}H_{12}N_3^+$ 270.1026, found 270.1031.

ethyl 4-(3-cyano-4-methylquinolin-2-yl)benzoate (3ai)

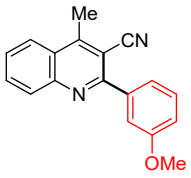


3ai

Flash chromatography (Silica Gel, PE/EtOAc) afforded **3ai** (0.039 g, 62%) as a white solid; m.p.: 148-149 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.20-8.24 (m, 3H), 8.13 (d, *J* = 8.5 Hz, 1H), 8.01 (d, *J* = 8.5 Hz, 2H), 7.92 – 7.85 (m, 1H), 7.74 – 7.67 (m, 1H), 4.43 (q, *J* = 7.1 Hz, 2H), 3.06 (s, 3H), 1.43 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.5, 157.6, 153.4, 148.1, 142.5, 133.0, 131.8, 131.0, 130.1, 129.5, 128.5, 125.6, 124.7, 117.5, 106.5, 61.5, 18.2, 14.6; IR

(neat): 2904, 2210, 1714, 1514, 1272, 744; HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{20}H_{17}N_2O_2^+$ 317.1285, found 317.1281.

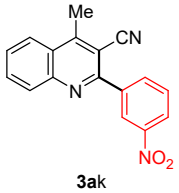
2-(3-methoxyphenyl)-4-methylquinoline-3-carbonitrile (3aj)



3aj

Flash chromatography (Silica Gel, PE/EtOAc) afforded **3aj** (0.035 g, 63%) as a white solid; m.p.: 129-130 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.20 (d, *J* = 8.4 Hz, 1H), 8.11 (d, *J* = 8.4 Hz, 1H), 7.90 – 7.84 (m, 1H), 7.72 – 7.65 (m, 1H), 7.54 – 7.50 (m, 1H), 7.50 – 7.41 (m, 2H), 7.07 (ddd, *J* = 8.2, 2.6, 1.1 Hz, 1H), 3.91 (s, 3H), 3.05 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 159.5, 158.0, 152.7, 147.6, 139.3, 132.3, 130.4, 129.5, 127.7, 125.0, 124.1, 121.4, 117.2, 116.0, 114.0, 106.2, 55.3, 17.7; The spectroscopic data is in accordance with those reported in literature.[9]

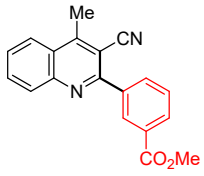
4-Methyl-2-(3-nitrophenyl)quinoline-3-carbonitrile (3ak)



3ak

Flash chromatography (Silica Gel, PE/EtOAc) afforded **3ak** (0.036 g, 62%) as a white solid; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.87 – 8.83 (m, 1H), 8.46 – 8.35 (m, 1H), 8.32 (d, *J* = 7.7 Hz, 1H), 8.21 (d, *J* = 8.4 Hz, 1H), 8.15 (d, *J* = 8.4 Hz, 1H), 7.96 – 7.89 (m, 1H), 7.79 – 7.71 (m, 2H), 3.08 (s, 3H); The spectroscopic data is in accordance with those reported in literature.[9]

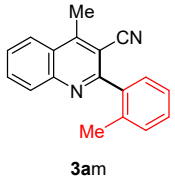
Methyl 3-(3-cyano-4-methylquinolin-2-yl)benzoate (3al)



3al

Flash chromatography (Silica Gel, PE/EtOAc) afforded **3al** (0.040 g, 66%) as a white solid; m.p.: 174-175 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.62 (s, 1H), 8.26 – 8.17 (m, 2H), 8.17 – 8.09 (m, 2H), 7.92 – 7.85 (m, 1H), 7.76 – 7.67 (m, 1H), 7.67 – 7.61 (m, 1H), 3.96 (s, 3H), 3.05 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.7, 157.4, 153.2, 147.9, 138.7, 133.5, 132.7, 131.0, 130.8, 130.7, 130.6, 128.9, 128.2, 125.4, 124.5, 117.3, 106.3, 52.5, 18.0; IR (neat): 2898, 2216, 1718, 1570, 1276, 752; HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{19}H_{15}N_2O_2^+$ 303.1128, found 303.1131.

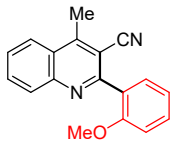
4-Methyl-2-(*o*-tolyl)quinoline-3-carbonitrile (3am)



3am

Flash chromatography (Silica Gel, PE/EtOAc) afforded **3am** (0.021 g, 40%) as a white solid; m.p.: 147-148 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.18 (d, *J* = 8.4 Hz, 1H), 8.13 (d, *J* = 8.4 Hz, 1H), 7.92 – 7.84 (m, 1H), 7.71 (dd, *J* = 8.5, 7.1 Hz, 1H), 7.44 – 7.37 (m, 2H), 7.32-7.37 (m, 2H), 3.04 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 160.1 , 152.1, 147.7, 138.3, 136.1, 132.5, 130.9, 130.7, 129.6, 129.2, 128.0, 126.1, 125.3, 124.5, 116.8, 108.3, 19.8, 17.8; IR (neat): 2914, 2220, 1589, 1344, 721; HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{18}H_{15}N_2^+$ 259.1230, found 259.1230.

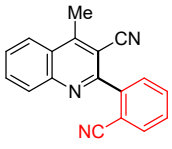
2-(2-Methoxyphenyl)-4-methylquinoline-3-carbonitrile (3an)



3an

Flash chromatography (Silica Gel, PE/EtOAc) afforded **3an** (0.035 g, 64%) as a white solid; m.p.: 219-220 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.19 (d, *J* = 9.2 Hz, 1H), 8.10 (d, *J* = 8.5 Hz, 1H), 7.88 – 7.80 (m, 1H), 7.71 – 7.64 (m, 1H), 7.55 – 7.44 (m, 2H), 7.16 – 7.10 (m, 1H), 7.06 (d, *J* = 8.6 Hz, 1H), 3.88 (s, 3H), 3.01 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 157.8, 157.3, 151.3, 148.3, 132.3, 131.6, 131.0, 130.8, 128.2, 128.0, 125.6, 124.6, 121.4, 117.5, 111.6, 109.5, 55.7, 18.0; IR (neat): 2902, 2358, 1558, 1257, 752; HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{18}H_{15}N_2O^+$ 275.1179, found 275.1182.

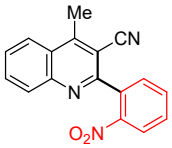
2-(2-Cyanophenyl)-4-methylquinoline-3-carbonitrile (3ao)



3ao

Flash chromatography (Silica Gel, PE/EtOAc) afforded **3ao** (0.038 g, 71%) as a white solid; m.p.: 212-213 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.23 (d, *J* = 7.3 Hz, 1H), 8.15 (d, *J* = 7.2 Hz, 1H), 7.96 – 7.86 (m, 2H), 7.86 – 7.71 (m, 3H), 7.68 – 7.60 (m, 1H), 3.07 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 155.6, 153.4, 147.7, 141.7, 134.2 , 133.2, 132.9, 131.0, 130.5, 130.2, 129.0, 125.9, 124.7, 117.8, 116.7, 113.0, 107.1, 18.2; IR (neat): 2892, 2225, 1570, 1271, 779; HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{18}H_{12}N_3^+$ 270.1026, found 270.1030.

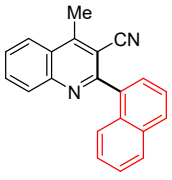
4-Methyl-2-(2-nitrophenyl)quinoline-3-carbonitrile (3ap)



3ap

Flash chromatography (Silica Gel, PE/EtOAc) afforded **3ap** (0.036 g, 62%) as a white solid; m.p.: 200-201 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.27 (d, *J* = 8.2 Hz, 1H), 8.17 – 8.07 (m, 2H), 7.91 – 7.85 (m, *J* = 7.6 Hz, 1H), 7.85 – 7.78 (m, 1H), 7.77 – 7.68 (m, 2H), 7.65 (d, *J* = 7.6 Hz, 1H), 3.03 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 156.7, 152.1, 148.0, 147.6, 134.2, 133.9, 132.8, 131.8, 130.7, 130.6, 128.5, 125.6, 125.2, 124.6, 116.4, 107.4, 17.9; IR (neat): 2910, 2216, 1516, 1338, 750; HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{17}H_{12}N_3O_2^+$ 290.0924, found 290.0921.

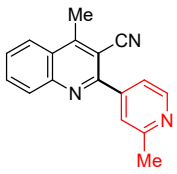
4-Methyl-2-(naphthalen-1-yl)quinoline-3-carbonitrile (3aq)



3aq

Flash chromatography (Silica Gel, PE/EtOAc) afforded **3aq** (0.031 g, 52%) as a white solid; m.p.: 136-137 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.23 (d, *J* = 8.4 Hz, 1H), 8.19 (d, *J* = 8.5 Hz, 1H), 8.02 (d, *J* = 8.1 Hz, 1H), 7.98 – 7.88 (m, 2H), 7.78 – 7.72 (m, 1H), 7.71 – 7.60 (m, 3H), 7.56 – 7.49 (m, 1H), 7.48 – 7.42 (m, 1H), 3.08 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 159.1, 152.4, 147.8, 135.9, 134.2, 132.7, 131.5, 130.8, 130.2, 128.7, 128.2, 127.8, 127.0, 126.4, 125.5, 125.2, 124.5, 116.8, 109.0, 17.9 (one carbon missing due to overlap); IR (neat): 2916, 2216, 1514, 1309, 727; HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{21}H_{15}N_2^+$ 295.1230, found 295.1231.

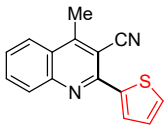
4-Methyl-2-(2-methylpyridin-4-yl)quinoline-3-carbonitrile (3ar)



3ar

Flash chromatography (Silica Gel, PE/EtOAc) afforded **3ar** (0.034 g, 65%) as a white solid; m.p.: 178-179 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.70 (d, *J* = 5.1 Hz, 1H), 8.20 (d, *J* = 8.5 Hz, 1H), 8.14 (d, *J* = 8.4 Hz, 1H), 7.94 – 7.87 (m, 1H), 7.78 – 7.68 (m, 2H), 7.65 (d, *J* = 5.3 Hz, 1H), 3.06 (s, 3H), 2.70 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 159.2, 156.1, 153.4, 149.6, 147.8, 145.8, 132.9, 130.7, 128.6, 125.6, 124.5, 122.9, 120.5, 116.9, 106.0, 24.7, 17.9; IR (neat): 2912, 2214, 1525, 1446, 1309, 750; HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{17}H_{14}N_3^+$ 260.1182, found 260.1182.

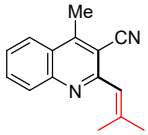
4-Methyl-2-(thiophen-2-yl)quinoline-3-carbonitrile (3as)



3as

Flash chromatography (Silica Gel, PE/EtOAc) afforded **3as** (0.020 g, 40%) as a white solid; m.p.: 142-143 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.31 (d, *J* = 3.8 Hz, 1H), 8.09 (d, *J* = 9.1 Hz, 1H), 8.03 (d, *J* = 8.4 Hz, 1H), 7.85 – 7.78 (m, 1H), 7.65 – 7.58 (m, 1H), 7.56 (d, *J* = 5.1 Hz, 1H), 7.22 – 7.18 (m, 1H), 3.01 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 153.6, 150.7, 148.0, 142.9, 132.8, 130.6, 130.5, 129.4, 128.8, 127.8, 125.2, 124.6, 118.0, 103.8, 18.0; IR (neat): 2883, 2358, 1525, 1461, 1311, 719; HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{15}H_{11}N_2S^+$ 251.0638, found 251.0649.

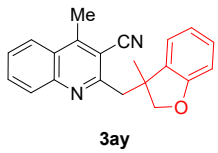
4-Methyl-2-(2-methylprop-1-en-1-yl)quinoline-3-carbonitrile (3at)



3at

Flash chromatography (Silica Gel, PE/EtOAc) afforded **3at** (0.020 g, 46%) as a light-yellow oil; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.07 (d, *J* = 8.4 Hz, 1H), 8.01 (d, *J* = 9.4 Hz, 1H), 7.82 – 7.75 (m, 1H), 7.63 – 7.54 (m, 1H), 7.25 (s, 1H), 6.75 (s, 1H), 2.94 (d, *J* = 2.6 Hz, 3H), 2.22 (s, 3H), 2.07 (s, 3H); ^{13}C NMR (151 MHz, Chloroform-*d*) δ 155.2, 150.2, 146.6, 146.4, 130.9, 129.1, 126.1, 123.4, 123.2, 120.5, 115.9, 106.5, 26.6, 19.4, 16.5; IR (neat): 2896, 2356, 1774, 1514, 1309, 727; HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{15}H_{15}N_2^+$ 223.1230, found 223.1225.

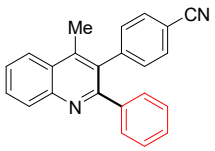
4-Methyl-2-((3-methyl-2,3-dihydrobenzofuran-3-yl)methyl)quinoline-3-carbonitrile (3ay)



3ay

Flash chromatography (Silica Gel, PE/EtOAc) afforded **3ay** (0.034 g, 54%) as a yellow oil; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.10 – 8.00 (m, 2H), 7.87 – 7.79 (m, 1H), 7.69 – 7.59 (m, 1H), 7.19 (d, *J* = 7.4 Hz, 1H), 7.14 (dd, *J* = 7.6, 7.6 Hz, 1H), 6.94 – 6.87 (m, 1H), 6.78 (d, *J* = 8.0 Hz, 1H), 5.09 (d, *J* = 9.0 Hz, 1H), 4.34 (d, *J* = 9.0 Hz, 1H), 3.64 (d, *J* = 14.5 Hz, 1H), 3.43 (d, *J* = 14.5 Hz, 1H), 2.92 (s, 3H), 1.48 (s, 3H); ^{13}C NMR (151 MHz, Chloroform-*d*) δ 159.3, 157.8, 151.3, 147.4, 134.6, 132.1, 130.1, 128.4, 127.4, 124.8, 124.2, 123.2, 120.5, 117.0, 109.7, 108.4, 82.2, 46.4, 46.2, 24.8, 17.5; IR (neat): 2920, 2218, 1548, 1307, 825, 752; HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{21}H_{19}N_2O^+$ 315.1492, found 315.1490.

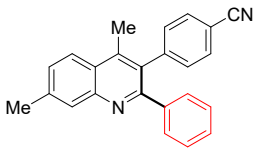
4-(4-methyl-2-phenylquinolin-3-yl)benzonitrile (3da)



3da

Flash chromatography (Silica Gel, PE/EtOAc) afforded **3da** (0.051 g, 79%) as a white solid; m.p.: 264-265 ℃; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.21 (dd, *J* = 8.5, 1.2 Hz, 1H), 8.10 (dd, *J* = 8.5, 1.3 Hz, 1H), 7.82 – 7.75 (m, 1H), 7.68 – 7.62 (m, 1H), 7.59 (d, *J* = 8.2 Hz, 2H), 7.26 – 7.20 (m, 7H), 2.53 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 158.1, 147.2, 144.4, 142.2, 140.7, 132.2, 131.8, 131.7, 130.5, 129.7, 129.6, 127.9, 126.9, 126.8, 124.1, 118.6, 111.1, 16.3 (one carbon missing due to overlap); IR (neat): 2914, 2220, 1506, 1309, 729; HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{23}H_{17}N_2^+$ 321.1386, found 321.1389.

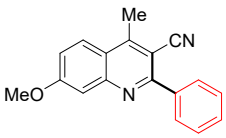
4-(4,7-Dimethyl-2-phenylquinolin-3-yl)benzonitrile (3ea)



3ea

Flash chromatography (Silica Gel, PE/EtOAc) afforded **3ea** (0.036 g, 54%) as a colorless oil; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.98 (d, *J* = 8.9 Hz, 2H), 7.58 (d, *J* = 8.0 Hz, 2H), 7.47 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.26 – 7.18 (m, 7H), 2.60 (s, 3H), 2.50 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 158.1, 147.4, 144.6, 141.9, 140.8, 140.1, 131.8, 131.8, 131.4, 129.6, 129.4, 129.2, 127.83 , 127.8, 124.8, 123.8, 118.7, 111.0, 21.7, 16.2; IR (neat): 2918, 2223, 1506, 1276, 702; HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{24}H_{19}N_2^+$ 335.1543, found 335.1536.

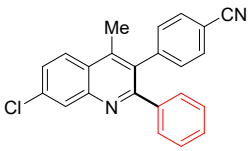
7-methoxy-4-methyl-2-phenylquinoline-3-carbonitrile (3fa)



3fa

Flash chromatography (Silica Gel, PE/EtOAc) afforded **3fa** (0.029 g, 52%) as a colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.99 (d, *J* = 9.2 Hz, 1H), 7.91 (dd, *J* = 7.9, 1.7 Hz, 2H),, 7.58 – 7.51 (m, 3H), 7.49 (d, *J* = 2.5 Hz, 1H), 7.30 (dd, *J* = 9.2, 2.6 Hz, 1H), 3.98 (s, 3H), 2.99 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 163.0, 159.3, 152.0, 150.2, 138.5, 129.8, 129.1, 128.5, 125.6, 120.9, 120.4, 117.7, 108.5, 104.2, 55.8, 17.6; IR (neat): 2887, 2356, 1514, 1311, 728; HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{18}H_{15}N_2O^+$ 275.1179, found 275.1180.

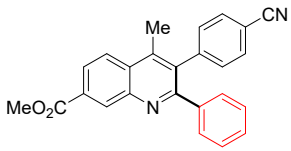
4-(7-Chloro-4-methyl-2-phenylquinolin-3-yl)benzonitrile (3ga)



3ga

Flash chromatography (Silica Gel, PE/EtOAc) afforded **3ga** (0.053 g, 79%) as a colorless oil; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.24 (d, *J* = 2.1 Hz, 1H), 8.06 (d, *J* = 9.0 Hz, 1H), 7.66 – 7.59 (m, 3H), 7.25-7.31 (m, 7H), 2.55 (s, 3H); ^{13}C NMR (151 MHz, Chloroform-*d*) δ 159.1, 147.5, 143.8, 142.4, 140.1, 135.6, 132.3, 131.8, 131.5, 129.5, 129.1, 128.0, 127.9, 127.7, 125.5, 125.2, 118.5, 111.1, 16.3; IR (neat): 2883, 1512, 1311, 1101, 669; HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{23}H_{16}ClN_2^+$ 355.0997, found 335.1000.

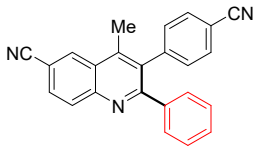
Methyl 3-(4-cyanophenyl)-4-methyl-2-phenylquinoline-7-carboxylate (3ha)



3ha

Flash chromatography (Silica Gel, PE/EtOAc) afforded **3ha** (0.039 g, 52%) as a white solid; m.p.: 151-152 °C; ^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.92 (d, *J* = 1.4 Hz, 1H), 8.21 (dd, *J* = 8.7, 1.4 Hz, 1H), 8.13 (d, *J* = 8.7 Hz, 1H), 7.60 (d, *J* = 8.1 Hz, 2H), 7.26 – 7.20 (m, 7H), 4.00 (s, 3H), 2.54 (s, 3H); ^{13}C NMR (151 MHz, Chloroform-*d*) δ 166.8, 159.2, 146.6, 144.0, 142.4, 140.3, 133.9, 133.0, 132.1, 131.6, 131.3, 129.7, 129.5, 128.3, 128.1, 126.5, 124.7, 118.7, 111.4, 52.6, 16.6; IR (neat): 2908, 1714, 1523, 1309, 678; HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{25}H_{19}N_2O_2^+$ 379.1441, found 379.1442.

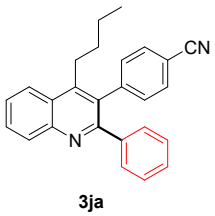
3-(4-cyanophenyl)-4-methyl-2-phenylquinoline-6-carbonitrile (3ia)



3ia

Flash chromatography (Silica Gel, PE/EtOAc) afforded **3ia** (0.049 g, 71%) as a white solid; m.p.: 149-150 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.50 (d, *J* = 1.7 Hz, 1H), 8.28 (d, *J* = 8.7 Hz, 1H), 7.92 (dd, *J* = 8.7, 1.8 Hz, 1H), 7.62 (d, *J* = 8.3 Hz, 2H), 7.28 – 7.22 (m, 7H), 2.56 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 161.2 , 148.3 , 143.5 , 143.2 , 133.9 , 132.2, 131.9, 131.6, 131.0, 130.6, 129.7, 128.7, 128.2, 119.0, 118.6, 111.8, 110.6, 16.6 (two carbon missing due to overlap); IR (neat): 2908, 2223, 1514, 1309, 736; HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{24}H_{16}N_3^+$ 346.1339, found 346.1340.

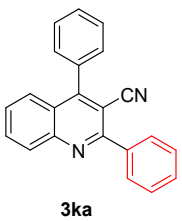
4-(4-Butyl-2-phenylquinolin-3-yl)benzonitrile (3ja)



3ja

Flash chromatography (Silica Gel, PE/EtOAc) afforded **3ja** (0.035 g, 49%) as a colorless oil; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.22 (d, *J* = 8.4 Hz, 1H), 8.10 (d, *J* = 8.5 Hz, 1H), 7.81 – 7.73 (m, 1H), 7.67 – 7.61 (m, 1H), 7.60 – 7.56 (m, 2H), 7.31 – 7.26 (m, 2H), 7.25 – 7.17 (m, 5H), 2.96 – 2.84 (m, 2H), 1.66 – 1.49 (m, 3H), 1.36 – 1.28 (m, 3H), 0.85 – 0.78 (m, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 158.2, 147.7, 147.0, 144.3, 140.8, 131.8, 131.7, 131.6, 130.6, 129.62, 129.59, 127.83, 127.80, 126.9, 125.9, 124.1, 118.6, 111.4, 33.0, 29.2, 23.0, 13.6; IR (neat): 2866, 2223, 1506, 730; HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{26}H_{23}N_2^+$ 363.1856, found 363.1865.

2,4-Diphenylquinoline-3-carbonitrile (3ka)



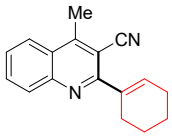
3ka

Flash chromatography (Silica Gel, PE/EtOAc) afforded **3ka** (0.038 g, 63%) as a white solid; ^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.26 (d, *J* = 8.4 Hz, 1H), 8.00 (dd, *J* = 8.0, 1.3 Hz, 2H), 7.90 – 7.85 (m, 1H), 7.70 (d, *J* = 8.4 Hz, 1H), 7.64 – 7.59 (m, 3H), 7.59 – 7.52 (m, 6H).^{13}C NMR (151 MHz, Chloroform-*d*) δ 158.7, 156.6, 148.7, 138.3, 134.8, 132.7, 130.3, 130.1, 129.9, 129.6, 129.5, 129.0, 128.8, 128.0, 127.0, 124.9, 117.4, 105.8; HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{22}H_{15}N_2^+$ 307.1230, found 307.1222.

4.2 from vinyl triflates

To a 20 mL vial was added $Pd(PPh_3)_4$ (0.0236 g, 0.02 mmol, 0.1 equiv.), Cs_2CO_3 (0.0391 g, 0.12 mmol, 0.6 equiv.) TMCA (2,2,3,3-tetramethylcyclopropane carboxylic acid) (0.0341 g, 0.24 mmol, 1.2 equiv.) and a solution of vinyl triflate (0.3 mmol, 1.5 equiv.) in toluene (1 mL) under argon. The resulting mixture was heated at 60 °C heating block for 30 min. Then a solution of isocyanide (0.2 mmol, 1.0 equiv.) in toluene (1 mL) was added to the reaction mixture dropwise over 3 h using a syringe pump. After further 1 h, the completed reaction was diluted with DCM (20 mL) and washed with satd. $NaHCO_3$ (20 mL x 2). The combined aqueous phase was back extracted with DCM (15 mL x 2). The combined organic phase was dried (anhydrous Na_2SO_4) and concentrated. The residue was purified by column chromatography (Silica Gel, PE/EtOAc) to afford the quinoline product **3**.

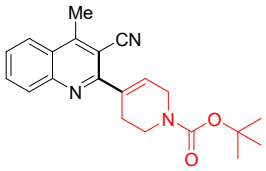
2-(Cyclohex-1-en-1-yl)-4-methylquinoline-3-carbonitrile (3av)



3av

Flash chromatography (Silica Gel, PE/EtOAc) afforded **3av** (0.026 g, 53%) as a light-yellow oil; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.09 (d, *J* = 8.4 Hz, 1H), 8.03 (d, *J* = 8.5 Hz, 1H), 7.84 – 7.77 (m, 1H), 7.65 – 7.57 (m, 1H), 6.37 (tt, *J* = 3.9, 1.7 Hz, 1H), 2.97 (s, 3H), 2.66 – 2.59 (m, 2H), 2.36 – 2.29 (m, 2H), 1.84-1.88 (m, 2H), 1.82 – 1.72 (m, 2H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 160.8, 152.1, 147.3, 136.8, 132.8, 131.9, 130.1, 127.1, 124.9, 124.0, 117.3, 105.9, 27.3, 25.5, 22.4, 21.5, 17.5; IR (neat): 3039, 2931, 2223, 1554, 1444, 754; HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{17}H_{17}N_2^+$ 249.1386, found 249.1394.

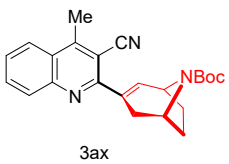
***tert*-butyl 4-(3-cyano-4-methylquinolin-2-yl)-3,6-dihydropyridine-1(2*H*)-carboxylate (3aw)**



3aw

Flash chromatography (Silica Gel, PE/EtOAc) afforded **3aw** (0.032 g, 46%) as a yellow oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.10 – 8.00 (m, 2H),7.87 – 7.78 (m, 1H), 7.86 – 7.78 (m, 1H), 6.54 – 6.33 (m, 1H), 4.19 (s, 2H), 3.72 (s, 2H), 2.97 (s, 3H), 2.79 (s, 2H), 1.50 (s, 9H); ^{13}C NMR (151 MHz, Chloroform-*d*) δ 158.4, 154.7 (br), 152.6, 147.3, 135.4 (br), 132.3, 130.2, 128.9 (br), 127.6, 125.1, 124.2, 117.2, 105.4, 79.7, 43.2 (br), 40.1 (br), 28.40, 27.4 (br), 17.6; HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{21}H_{24}N_3O_2^+$ 350.1863, found 350.1869.

***tert*-butyl 3-(3-cyano-4-methylquinolin-2-yl)-8-azabicyclo[3.2.1]oct-2-ene-8-carboxylate (3ax)**



3ax

Flash chromatography (Silica Gel, PE/EtOAc) afforded **3ax** (0.033 g, 44% yield) as a yellow oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.08 – 8.00 (m, 2H), 7.83 – 7.77 (m, 1H), 7.65 – 7.58 (m, 1H), 6.79 (s, 1H), 4.74 – 4.42 (m, 2H), 3.26-3.23 (m, 1H), 2.96 (s, 3H), 2.62 (d, *J* = 17.5 Hz, 1H), 2.26 (d, *J* = 10.6 Hz, 1H), 2.09 (s, 2H), 1.88 – 1.92 (m, 1H), 1.49 (s, 9H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ

158.1, 154.2, 152.7, 147.6, 136.9, 134.2, 132.3, 130.6, 127.8, 125.3, 124.4, 117.5, 105.8, 79.8, 53.8, 52.1, 35.8, 34.8, 29.6, 28.6, 17.9; IR (neat): 2914, 2356, 2214, 1523, 1315, 746; HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{23}H_{26}N_3O_2^+$ 376.2020, found 376.2024.

5. Scale up of 3aa

To a 100 mL RBF was added $Pd(PPh_3)_4$ (0.118 g, 0.1 mmol, 0.1 equiv.), Cs_2CO_3 (0.195 g, 0.6 mmol, 0.6 equiv.) TMCA (2,2,3,3-tetramethylcyclopropane carboxylic acid) (0.171 g, 1.2 mmol, 1.2 equiv.) and a solution of phenyl iodide (1.5 mmol, 1.5 equiv.) in toluene (5.0 mL) under argon. The resulting mixture was heated at 80 °C in an oil bath for 30 min. Then a solution of (*E*)-3-(2-isocyanophenyl)but-2-enenitrile (1.0 mmol, 1.0 equiv.) in toluene (5 mL) was added to the reaction dropwise over 3 h using a syringe pump. After a further 1 h, the completed reaction was diluted with DCM (50 mL) and washed with satd. $NaHCO_3$ (50 mL x 2). The combined aqueous phase was back extracted with DCM (30 mL x 2). The combined organic phase was dried (anhydrous Na_2SO_4) and concentrated. The residue was purified by column chromatography (Silica Gel, PE/EtOAc) to afford the quinoline **3** (0.22 g, 90%).

6. References

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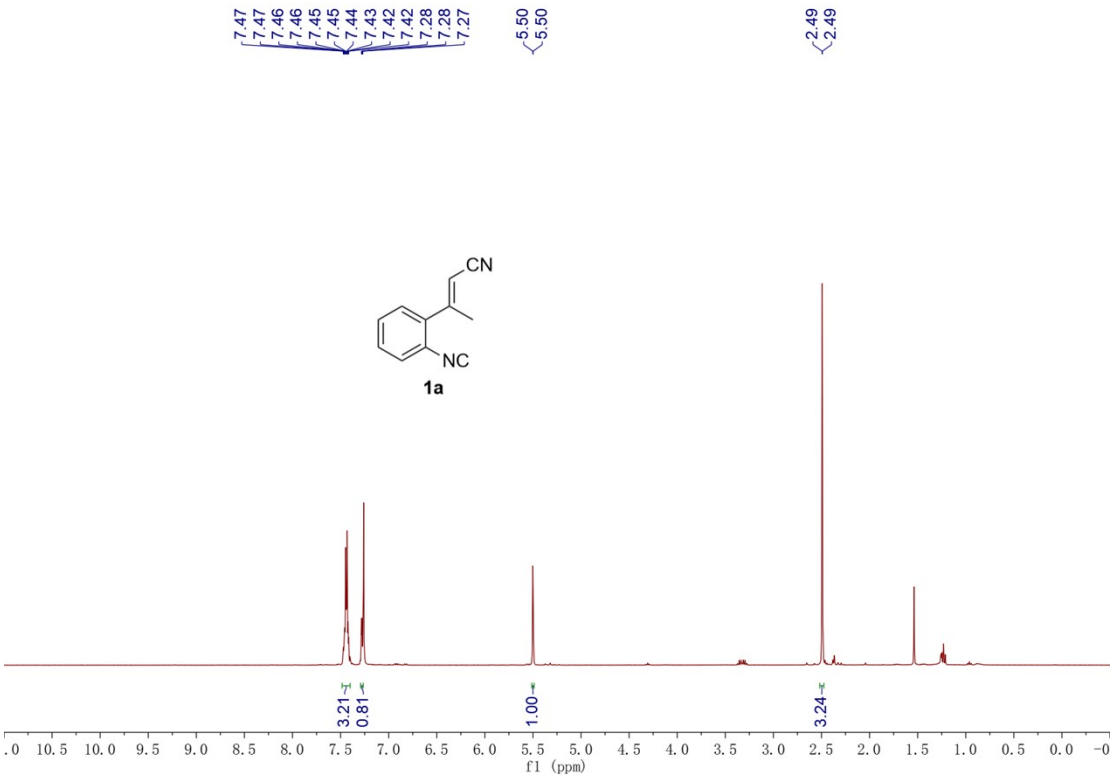
9. Kumar, M.; Goswami, A. *Org. Lett*. **2023**, *25*, 3254-3259.

7. Copies of NMR Spectroscopies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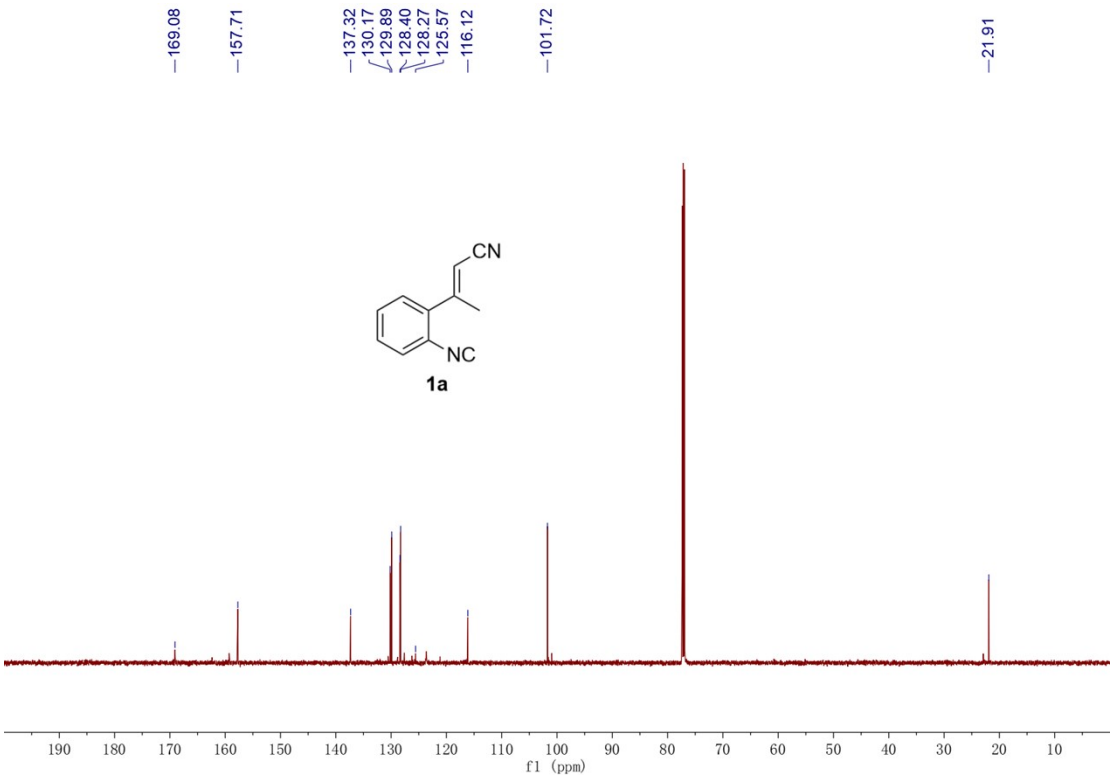
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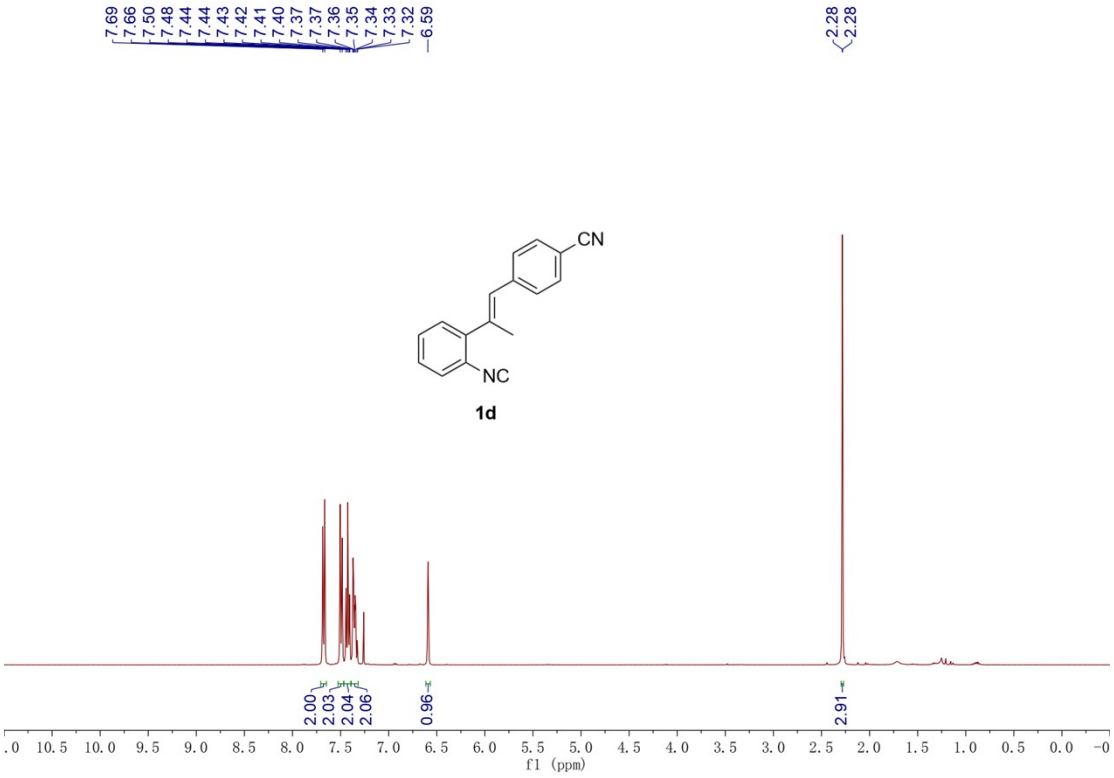
f1 (ppm)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7.37
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7.34
7.33
7.32
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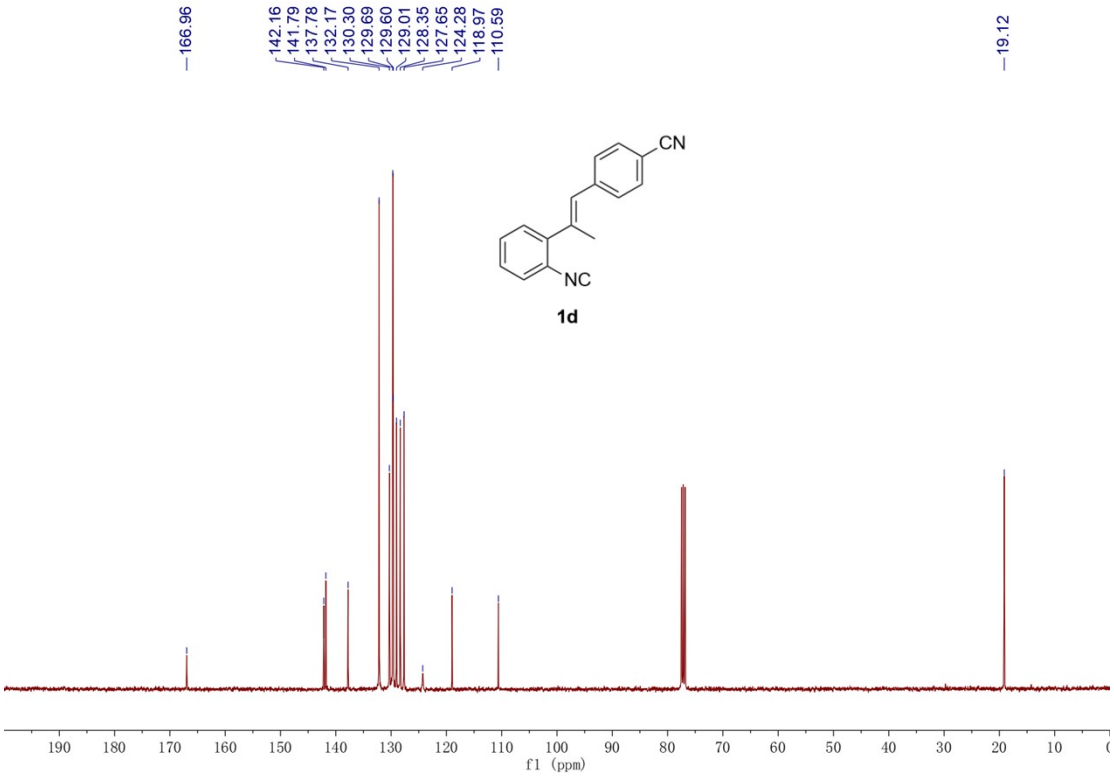
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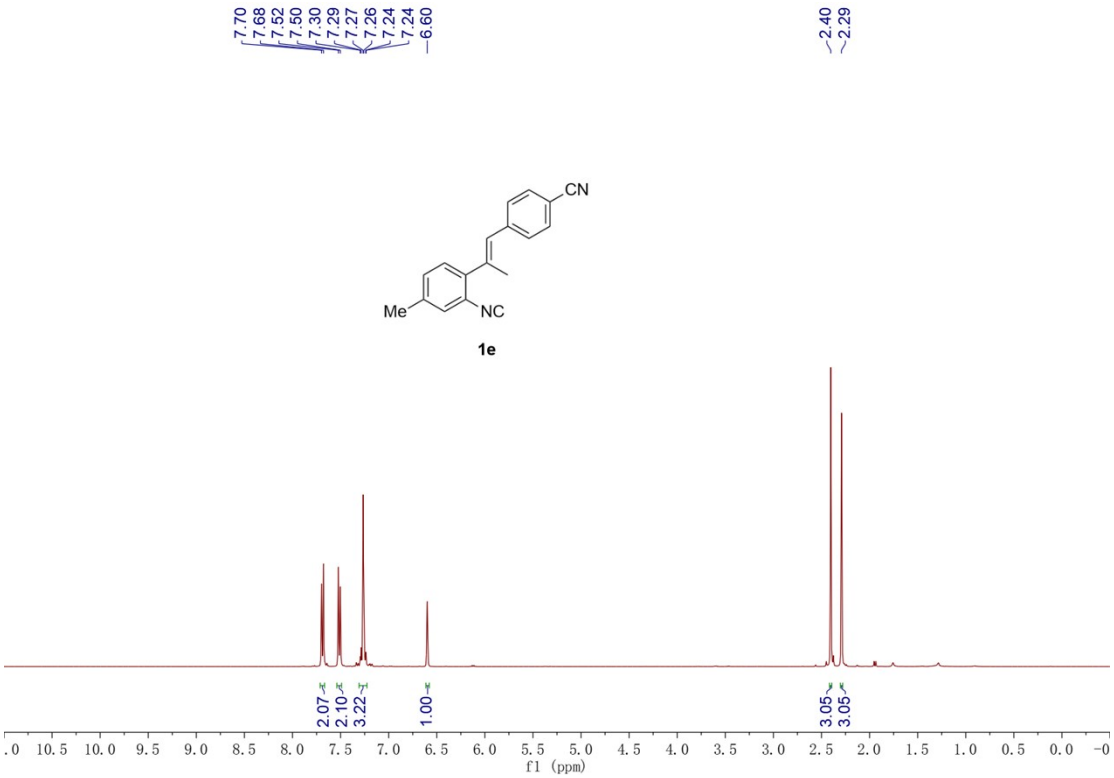
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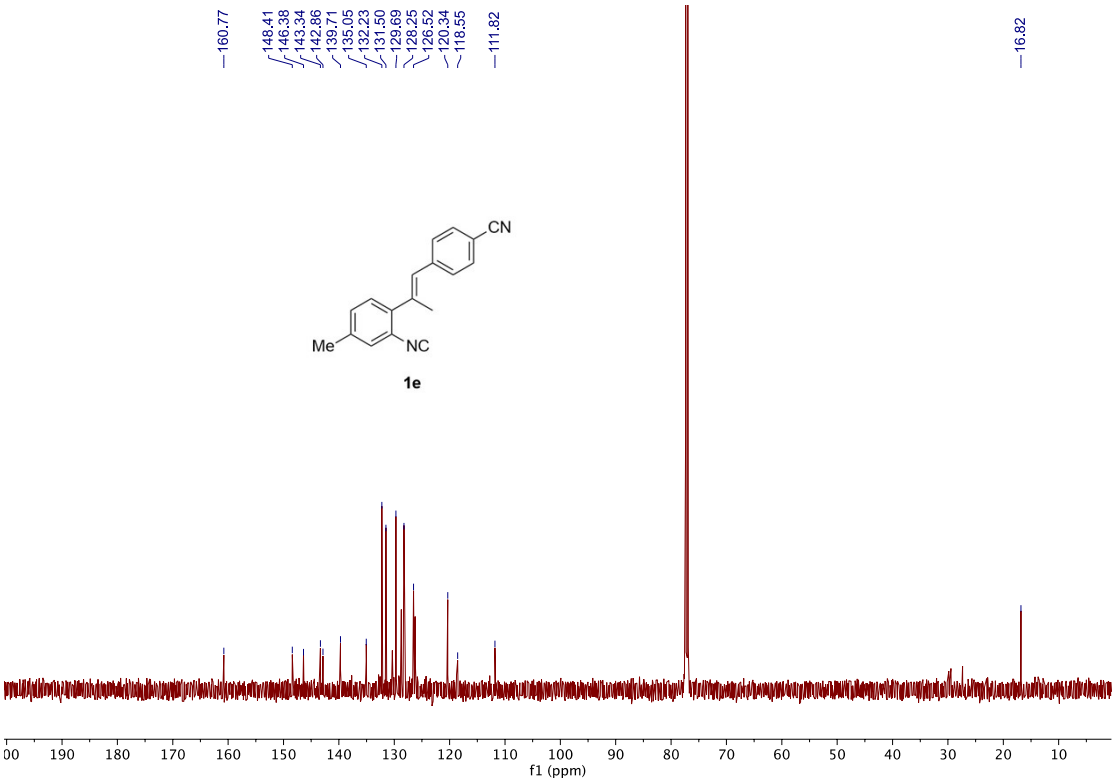
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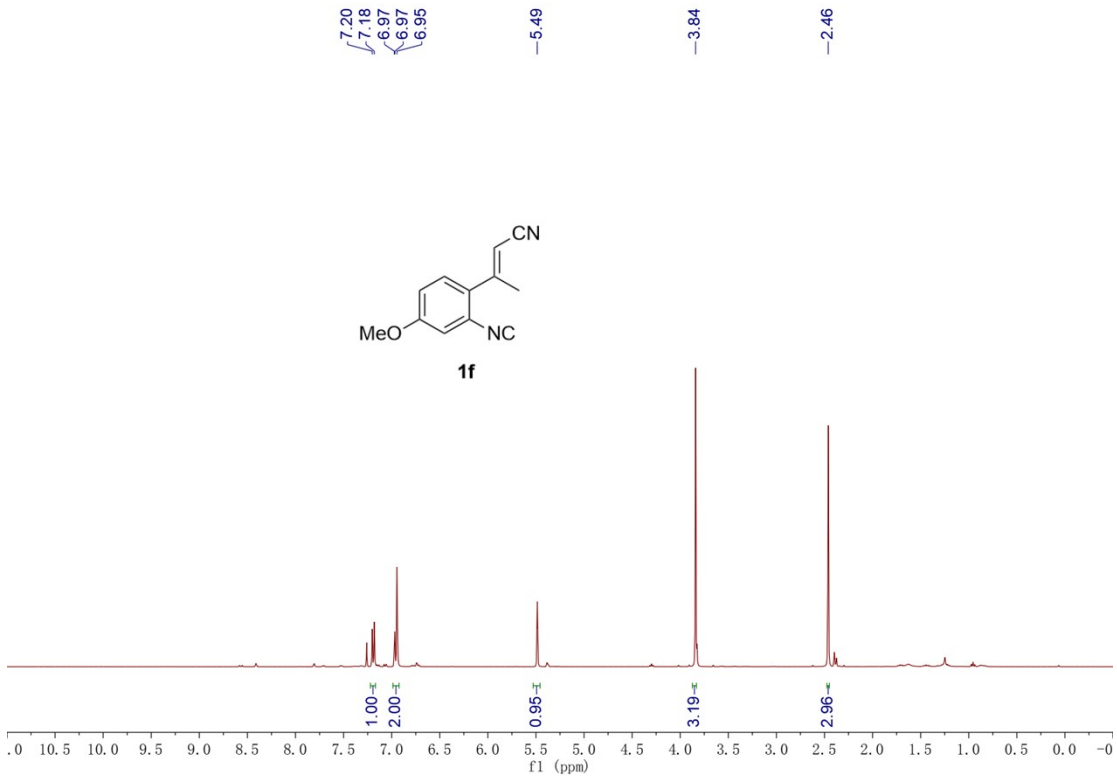
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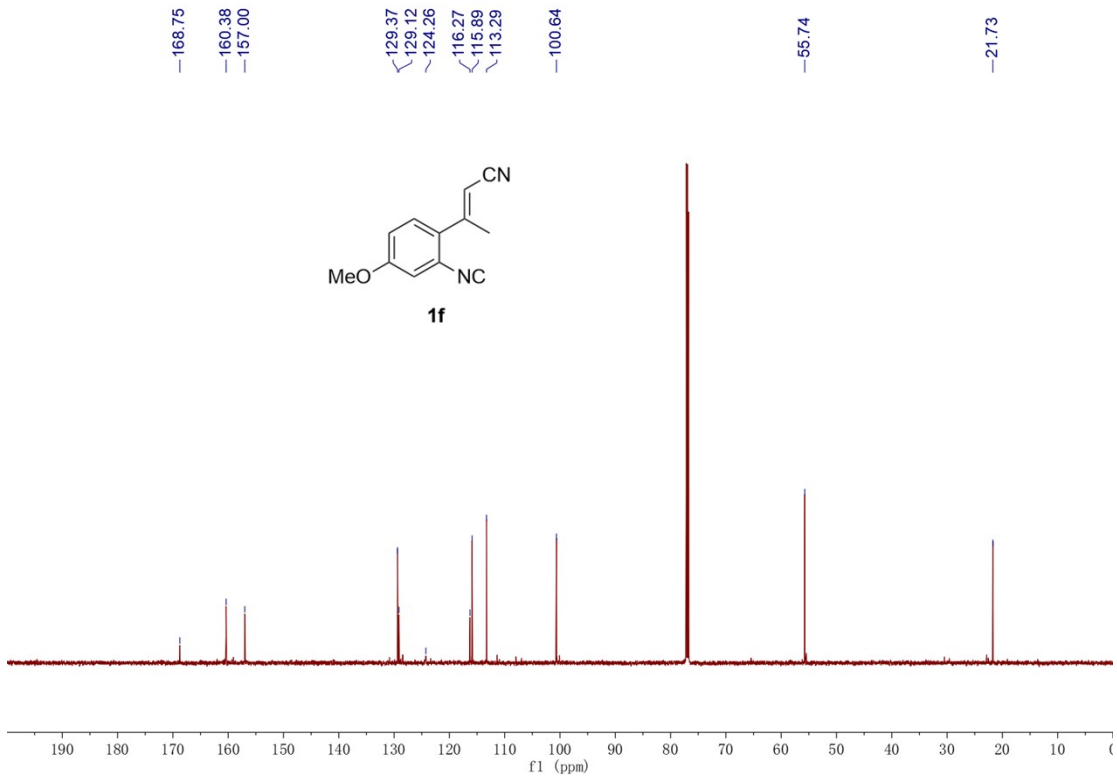
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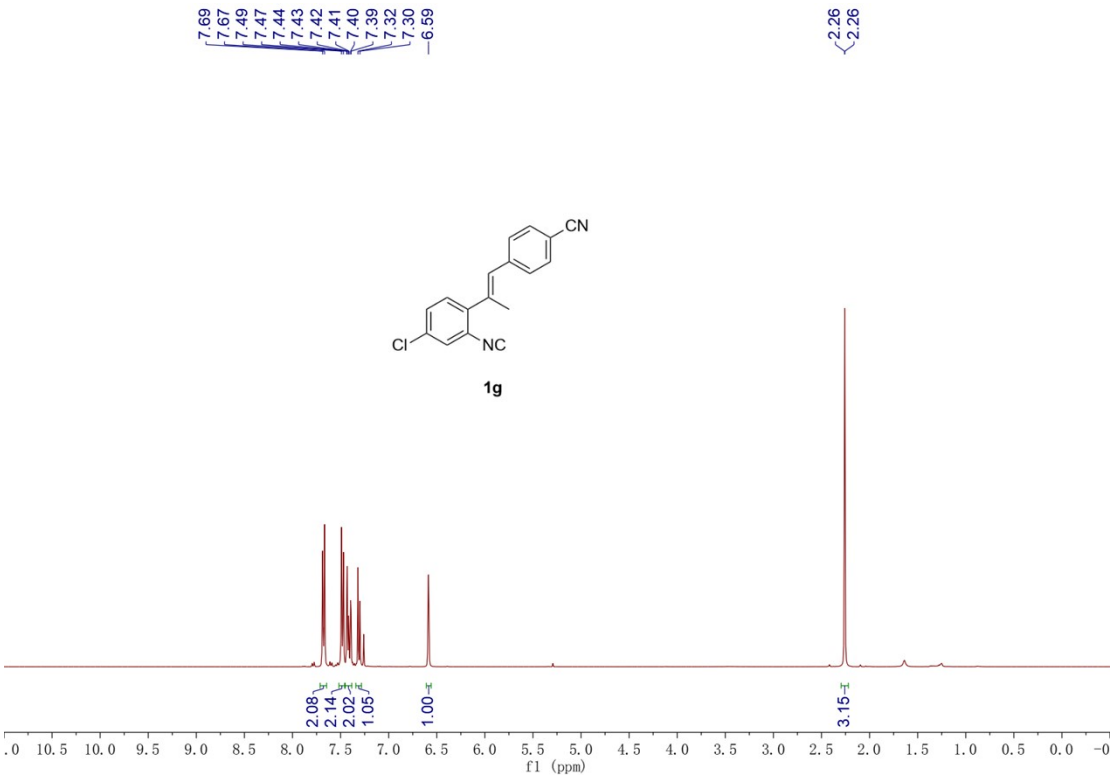
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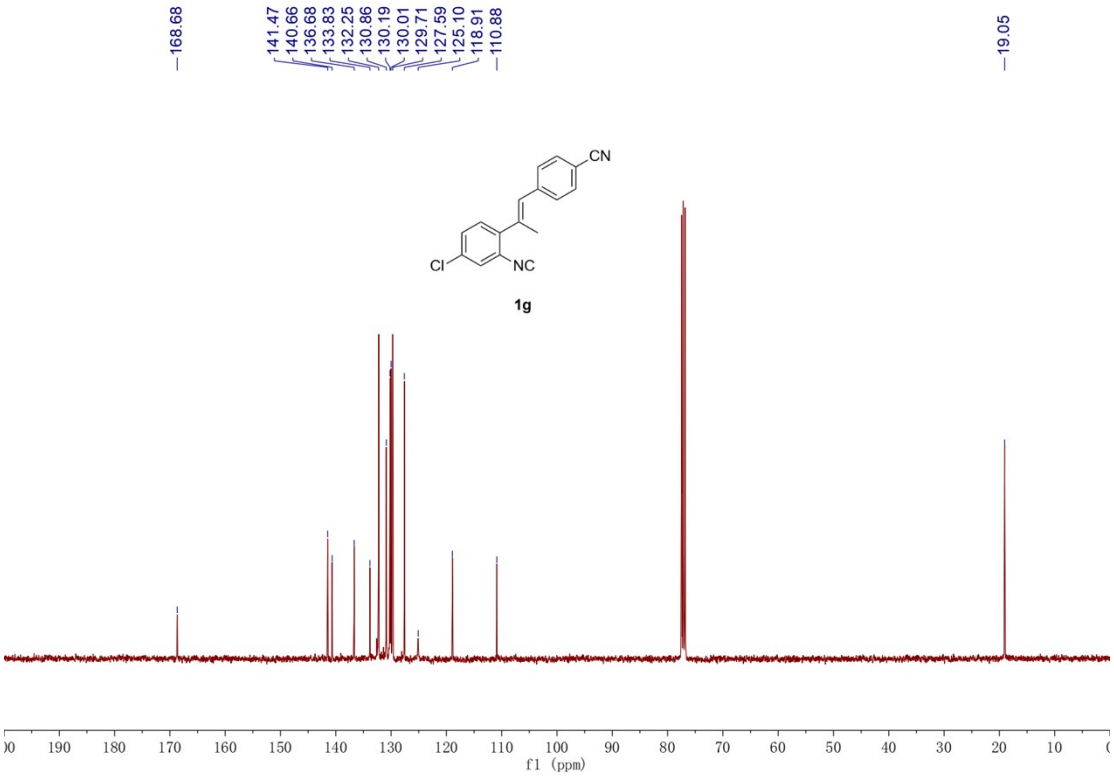
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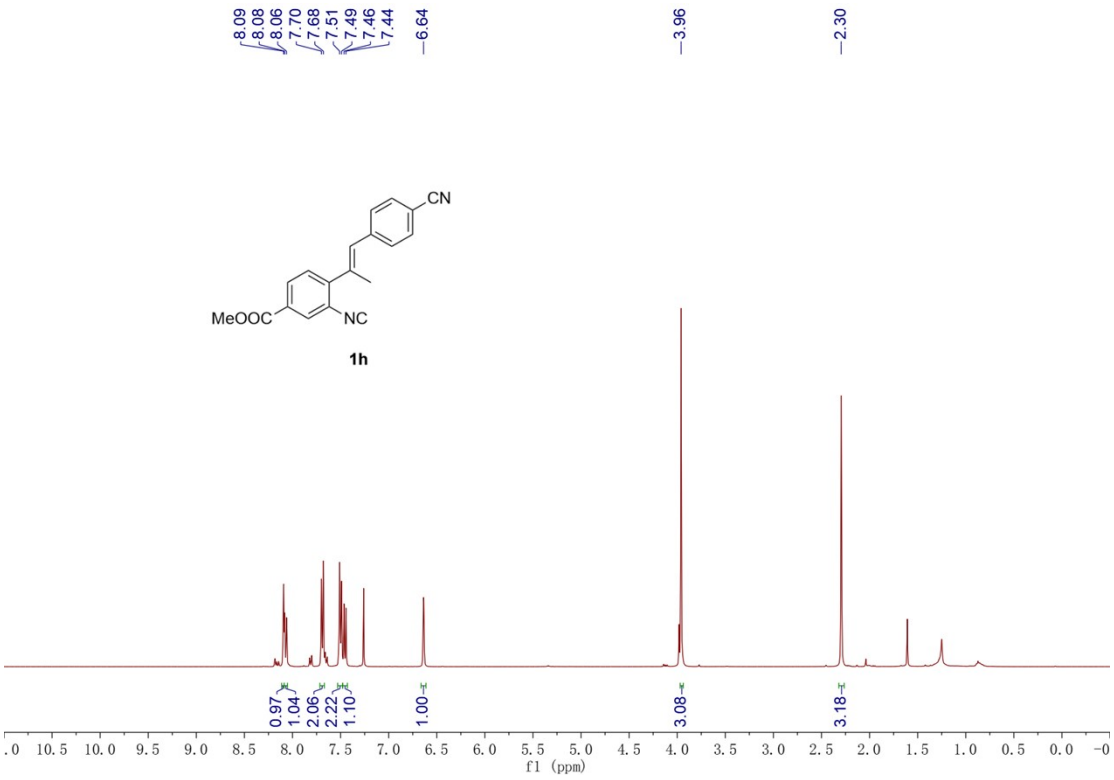
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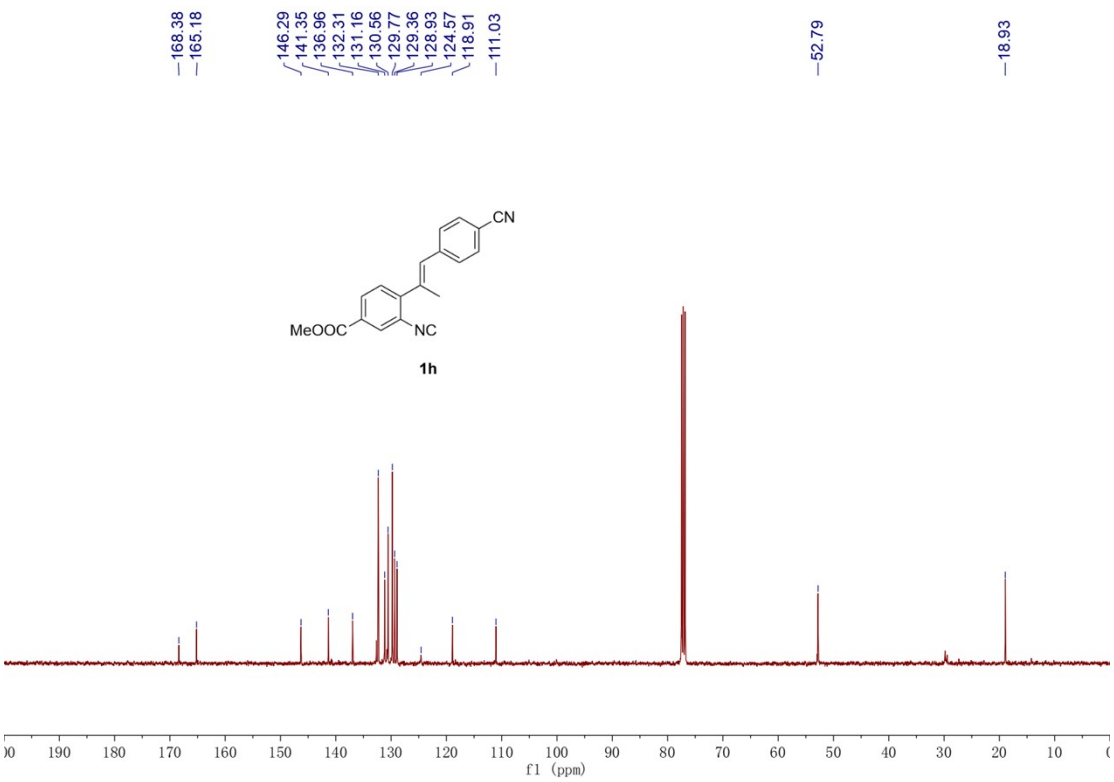
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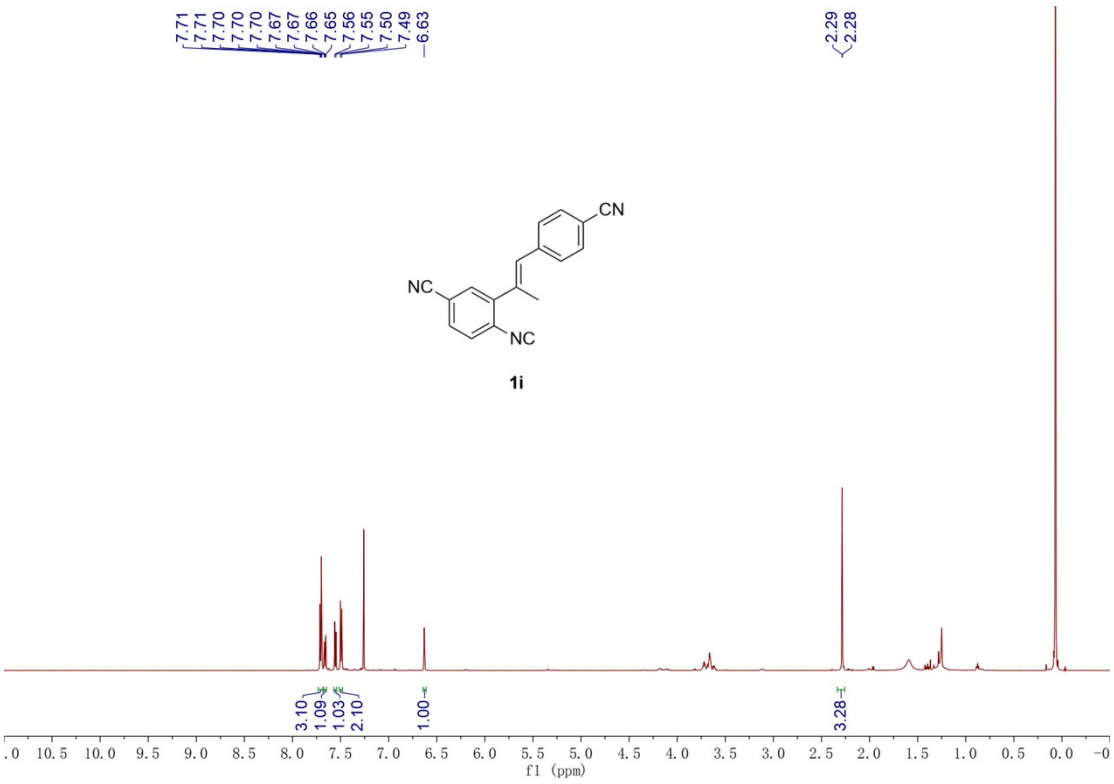
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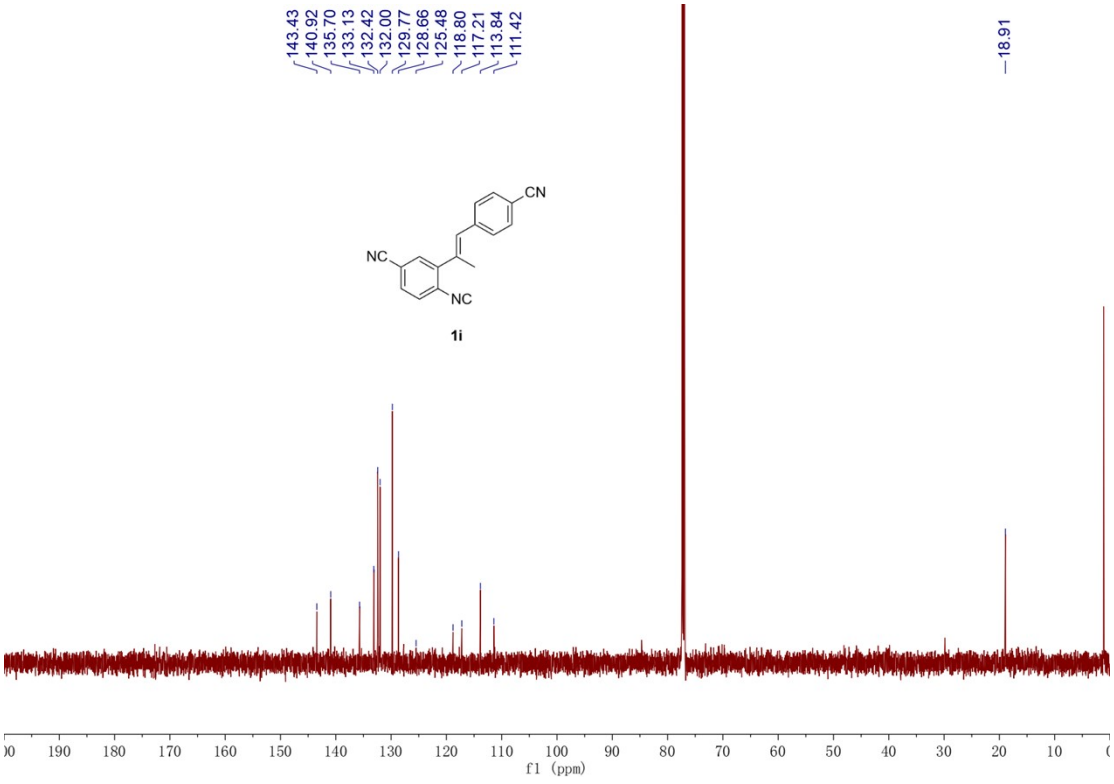
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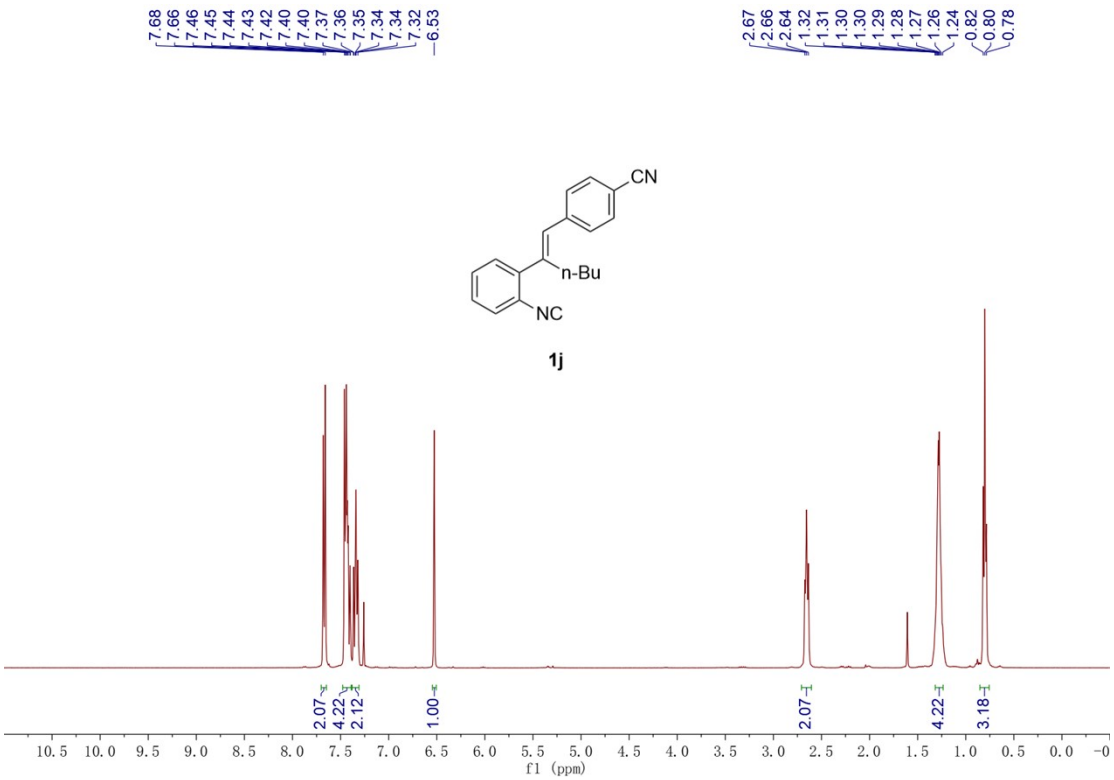
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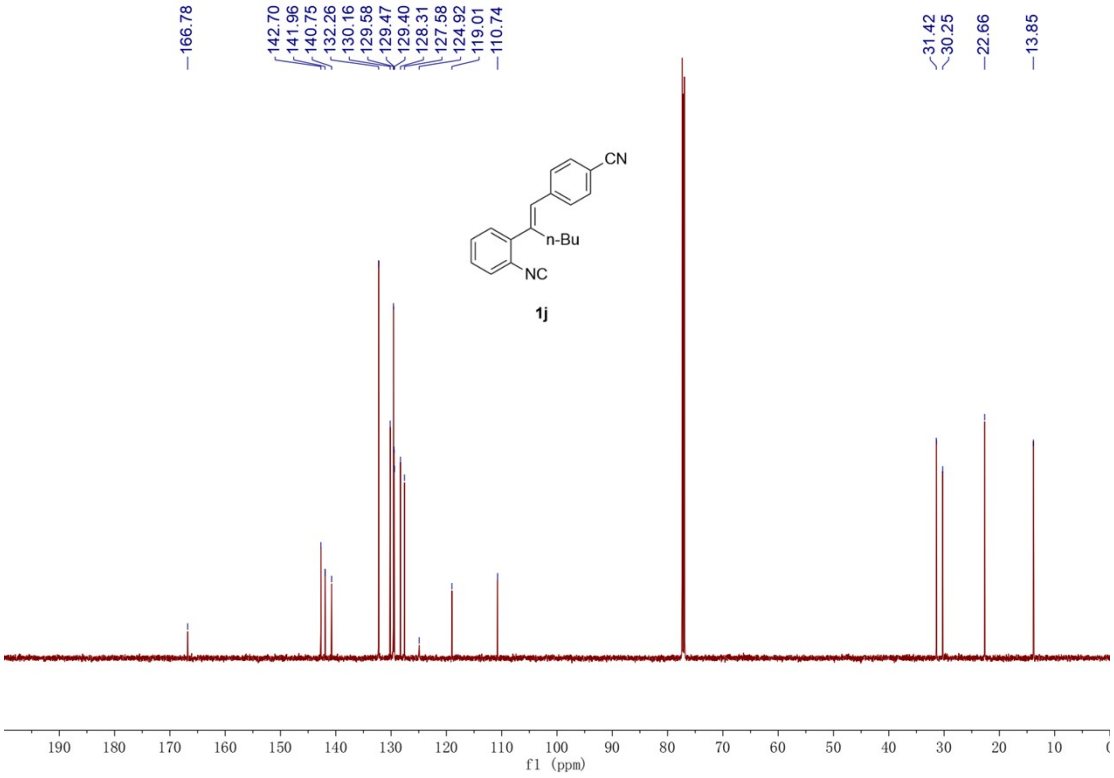
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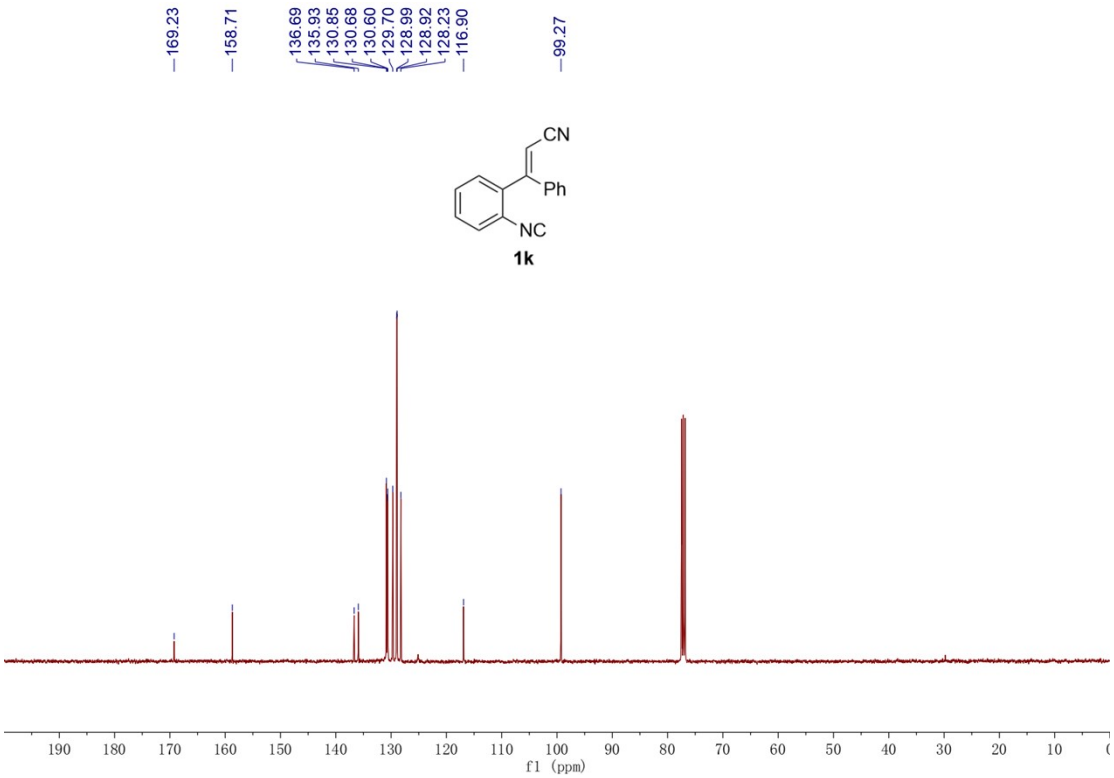
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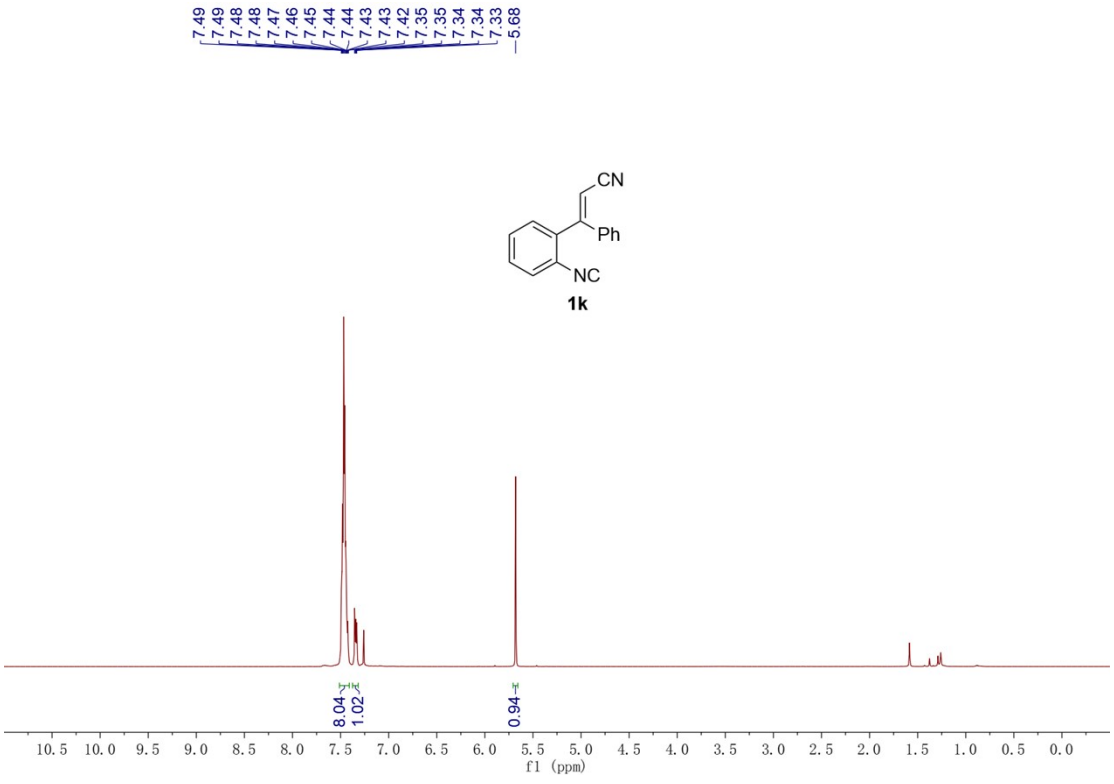
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Ph
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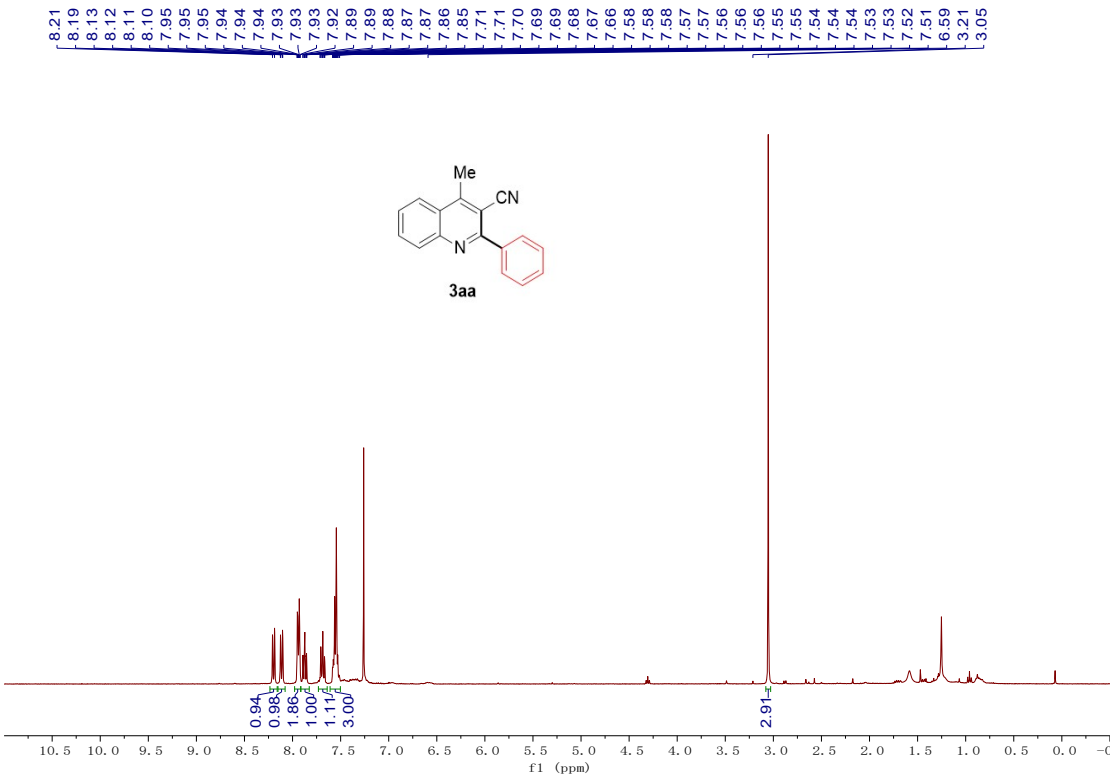
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Me
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N
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0.94 0.98 1.86 1.00 1.11 3.00 2.91
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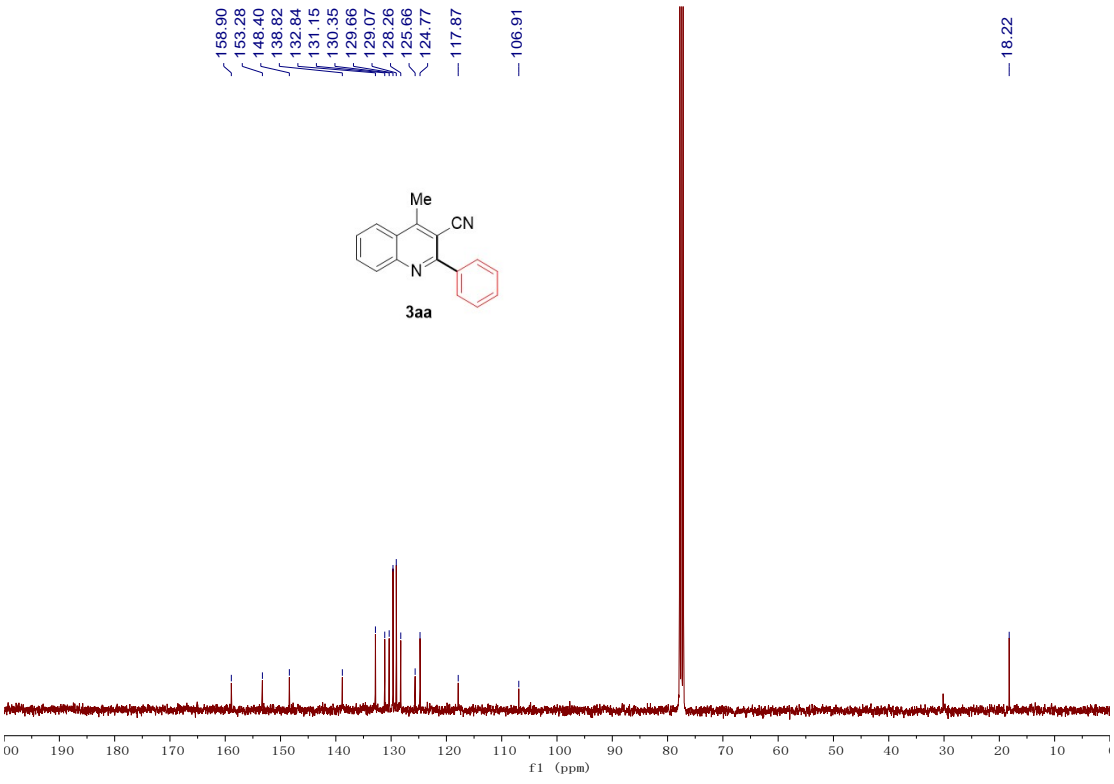
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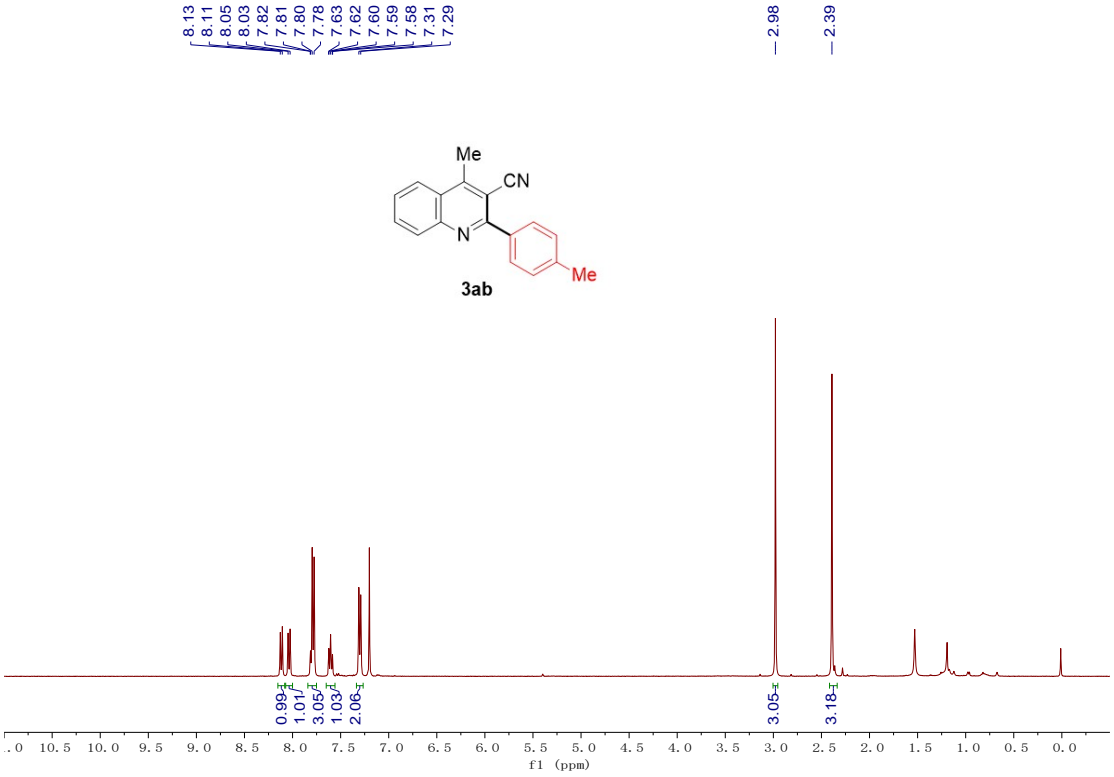
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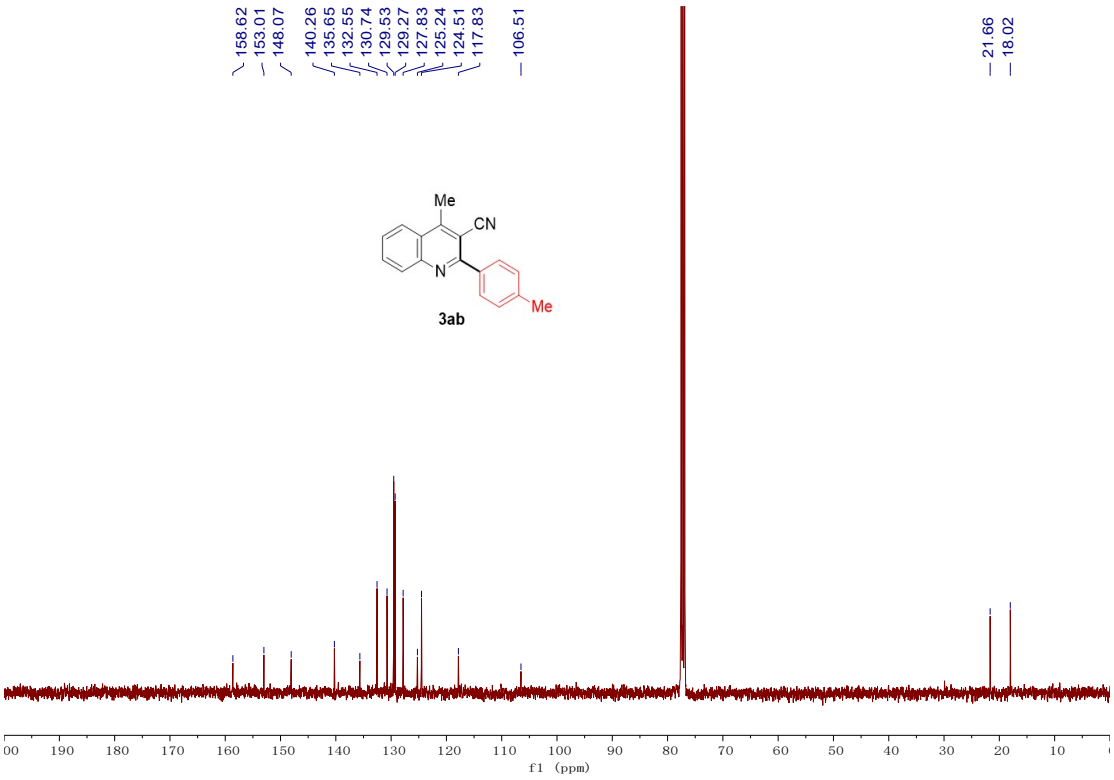
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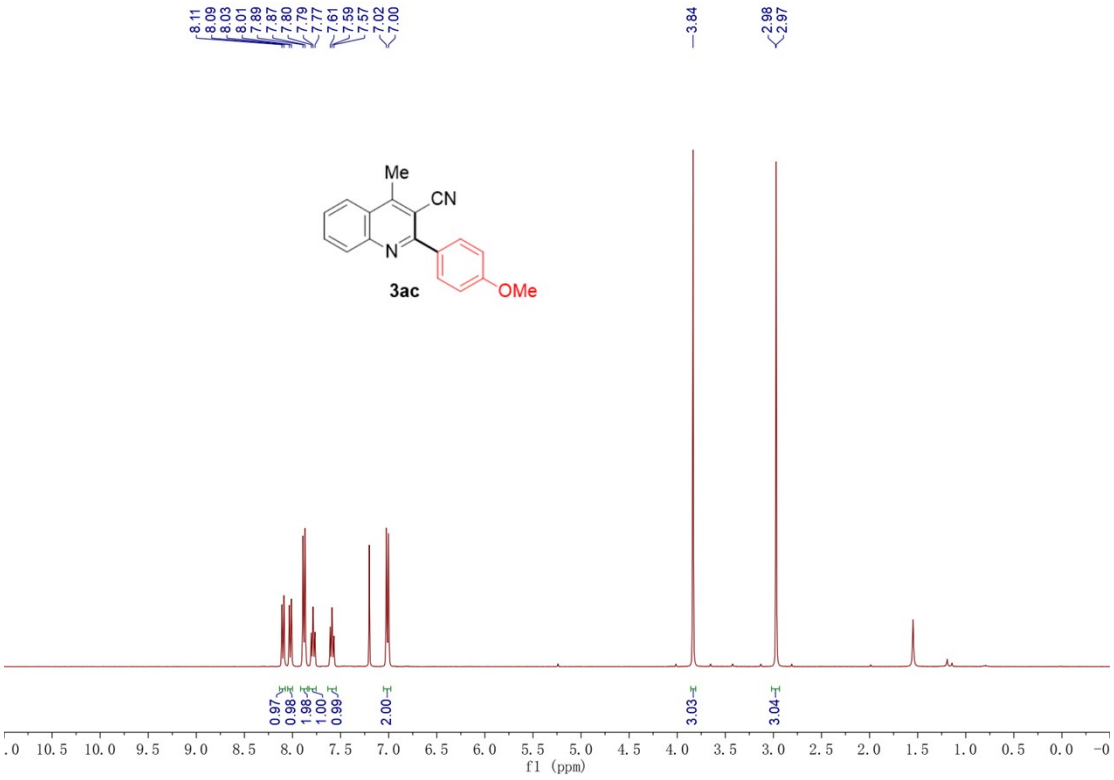
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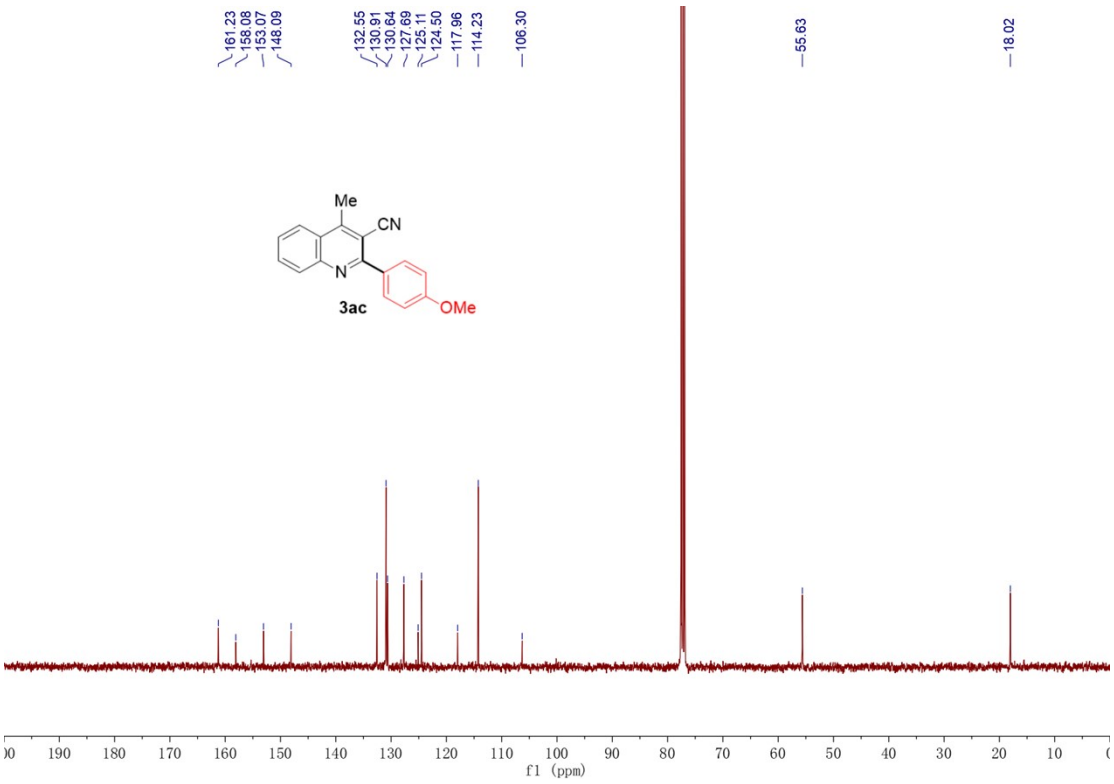
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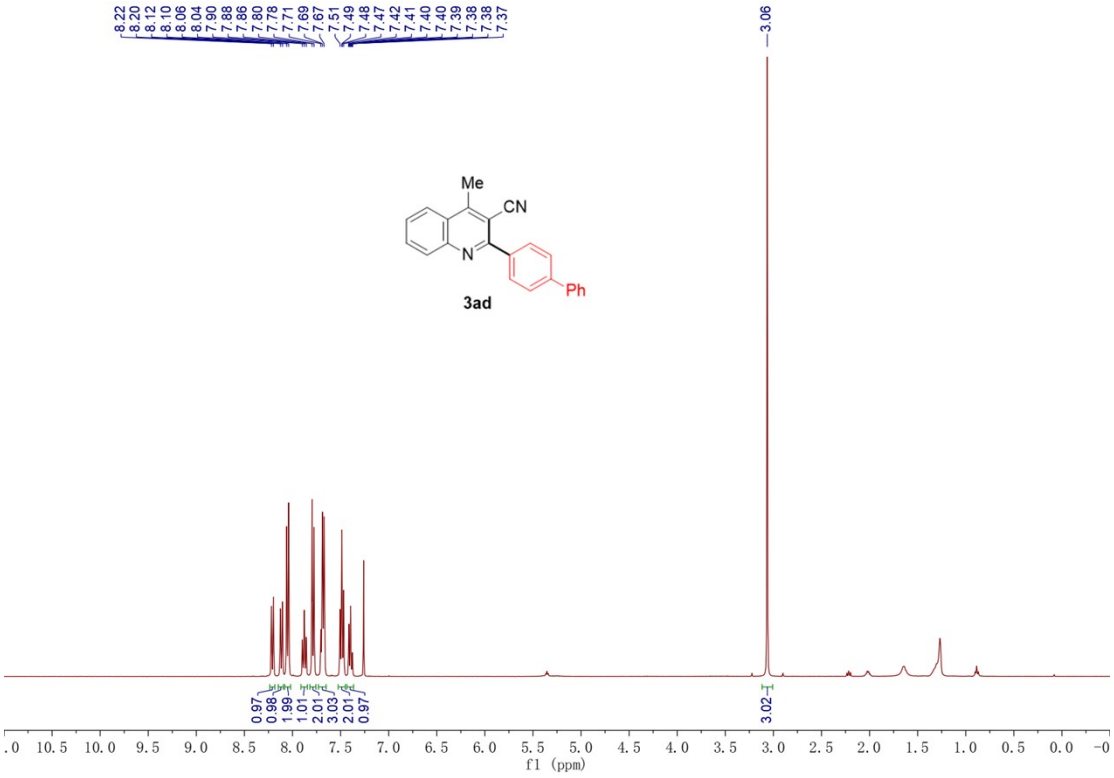
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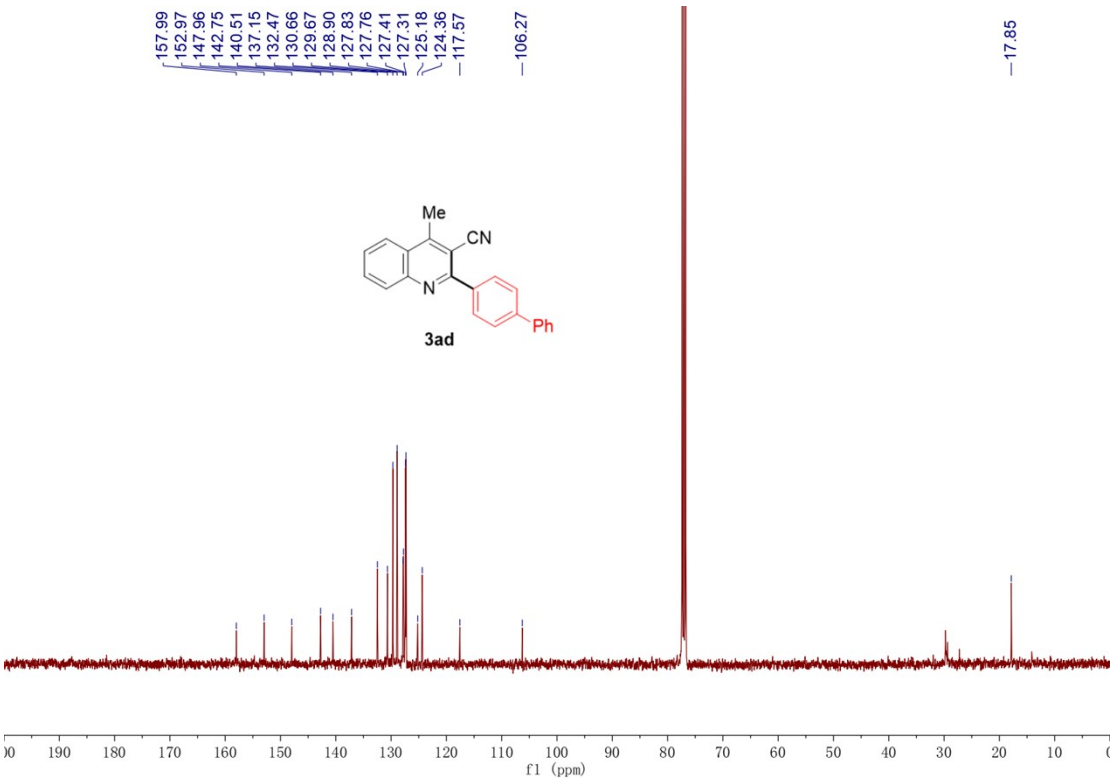
f1 (ppm)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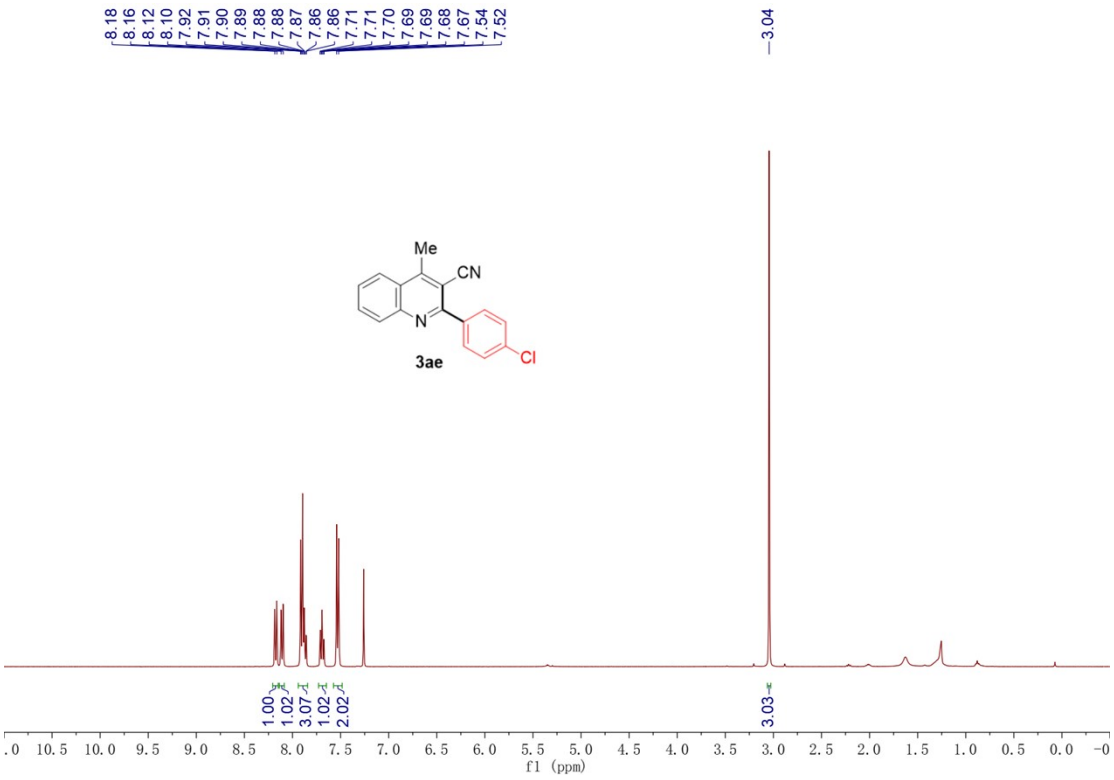
124.36
117.57
106.27
17.85
Me
CN
N
Ph
3ad
f1 (ppm)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7.86
7.86
7.71
7.71
7.70
7.69
7.69
7.68
7.67
7.54
7.52
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CN
N
Cl
3ae
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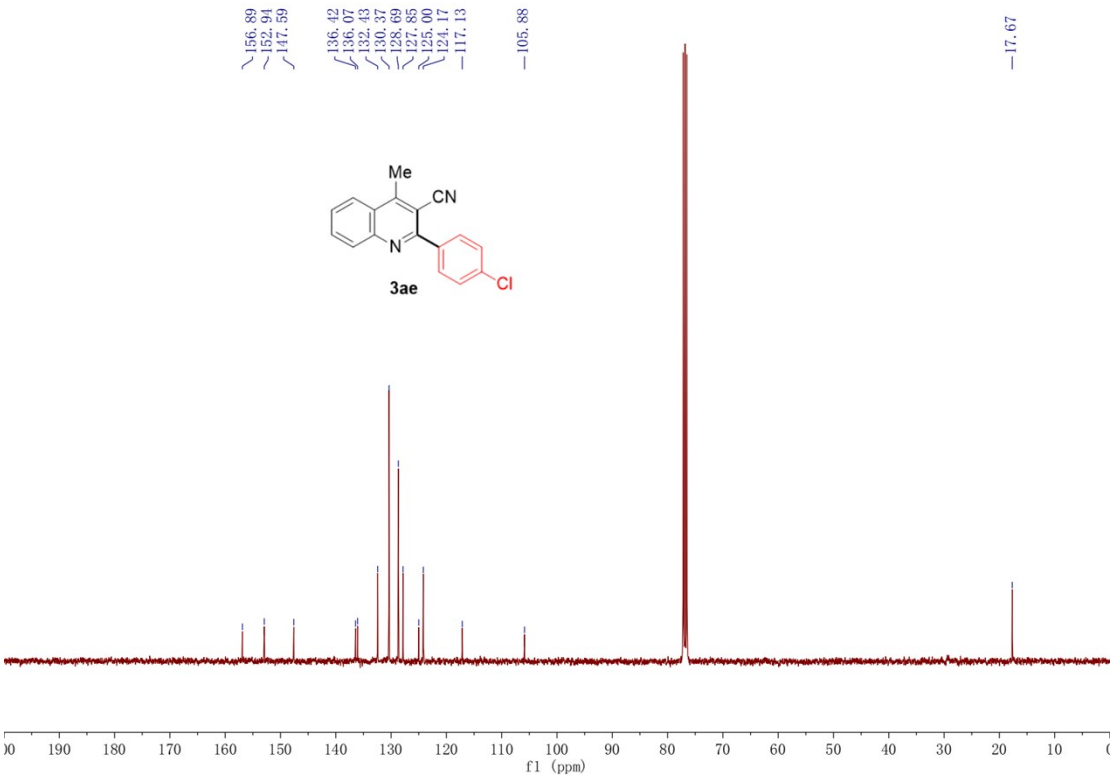
1.02
3.07
1.02
2.02
3.03
f1 (ppm)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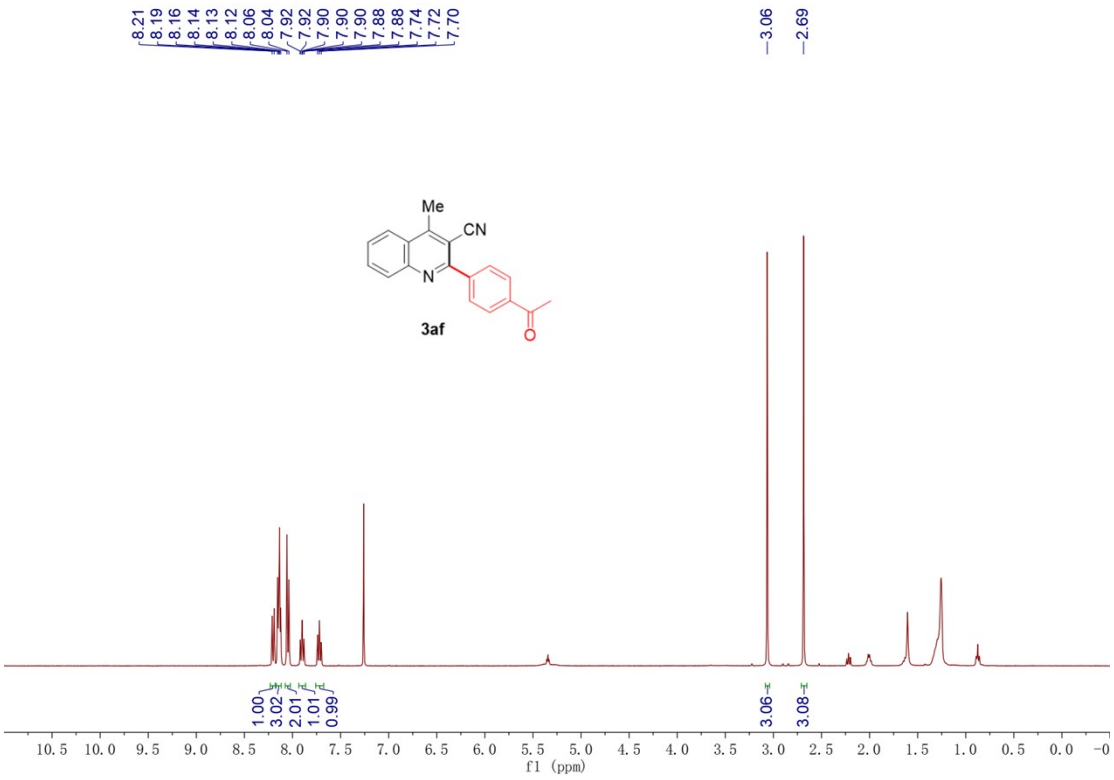
Me
CN
N
Cl
3ae
f1 (ppm)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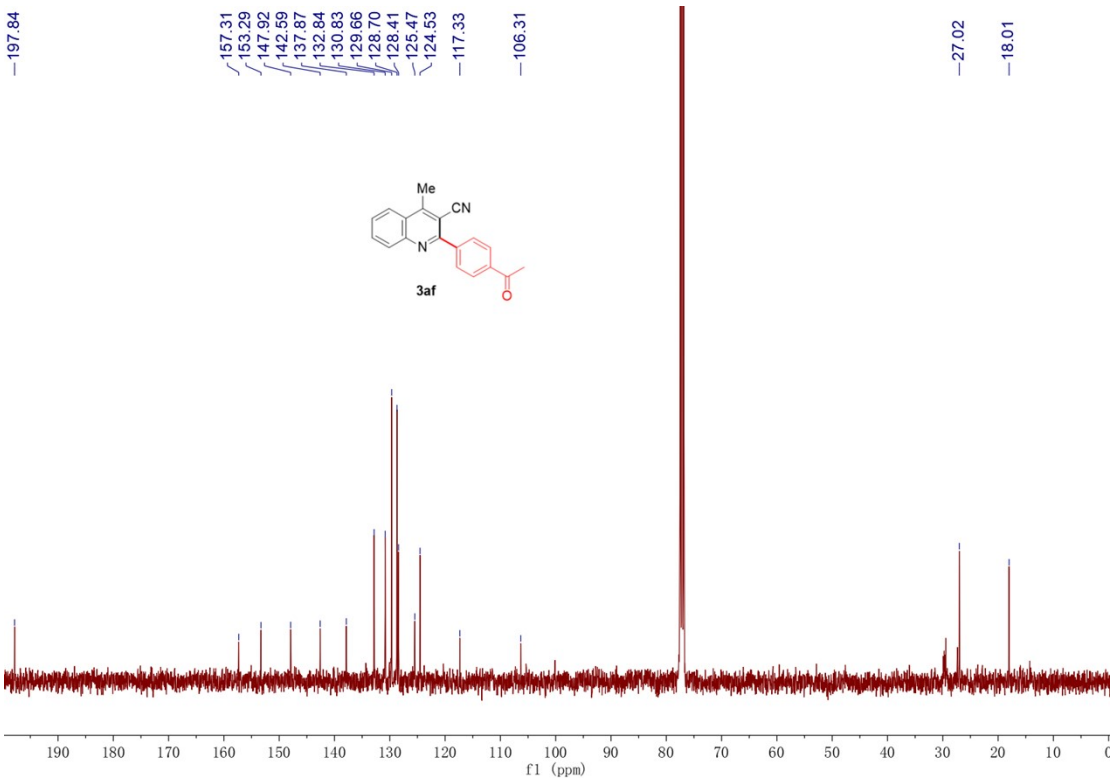
7.88
7.74
7.72
7.70
3.06
2.69
Me
CN
N
O
3af
1.00
3.02
2.01
1.01
0.99
3.06
3.08
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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124.53
117.33
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18.01
Me
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N
O
3af
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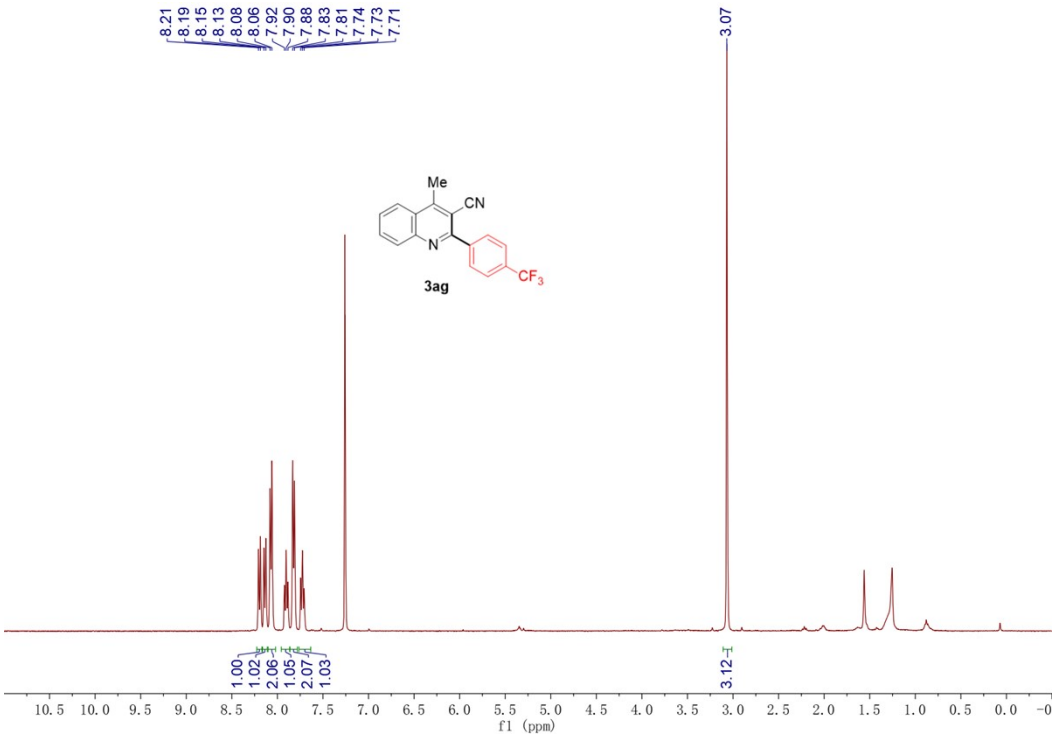
f1 (ppm)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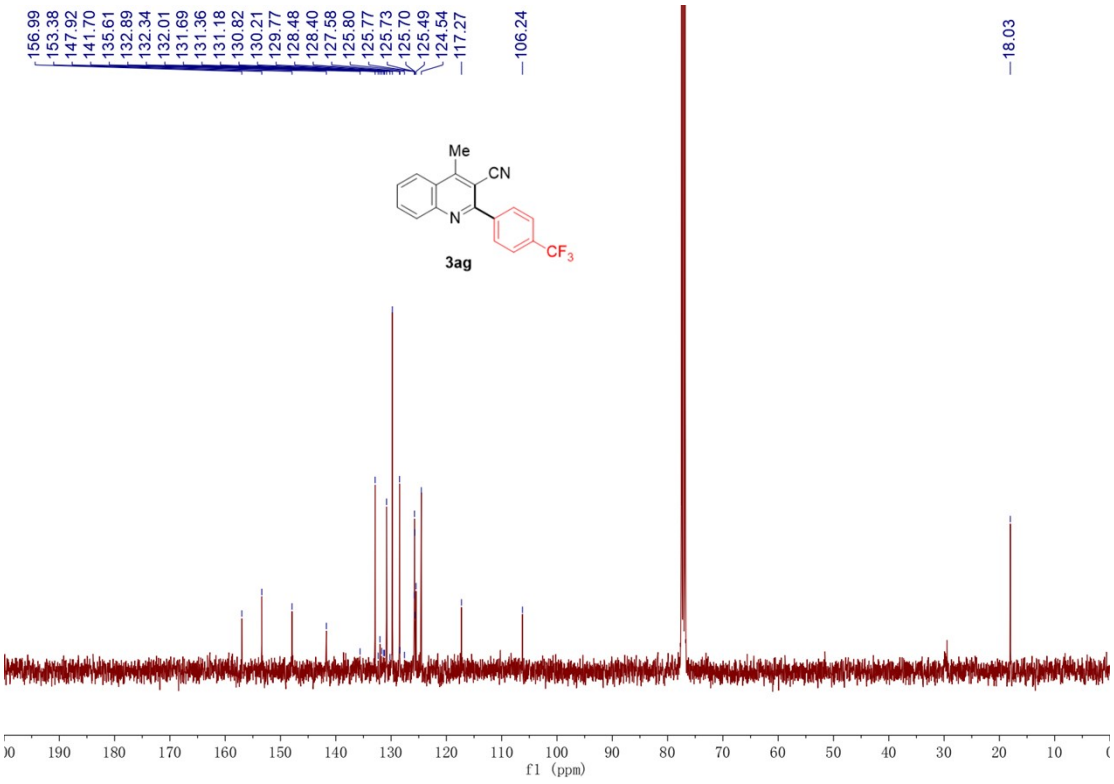
7.74
7.73
7.71
3.07
Me
CN
N
CF3
3ag
1.00
1.02
2.06
1.05
2.07
1.03
3.12
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0
f1 (ppm)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128.48
128.40
127.58
125.80
125.77
125.73
125.70
125.49
124.54
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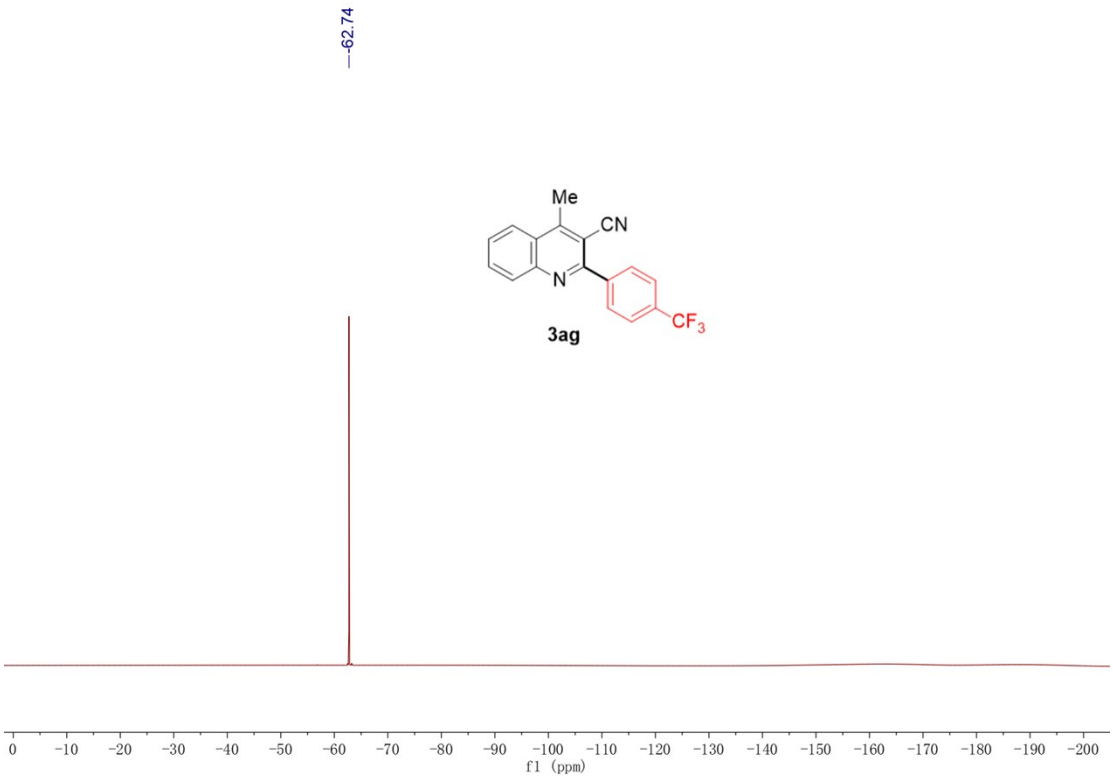
Me
CN
N
CF3
3ag
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)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-40
-50
-60
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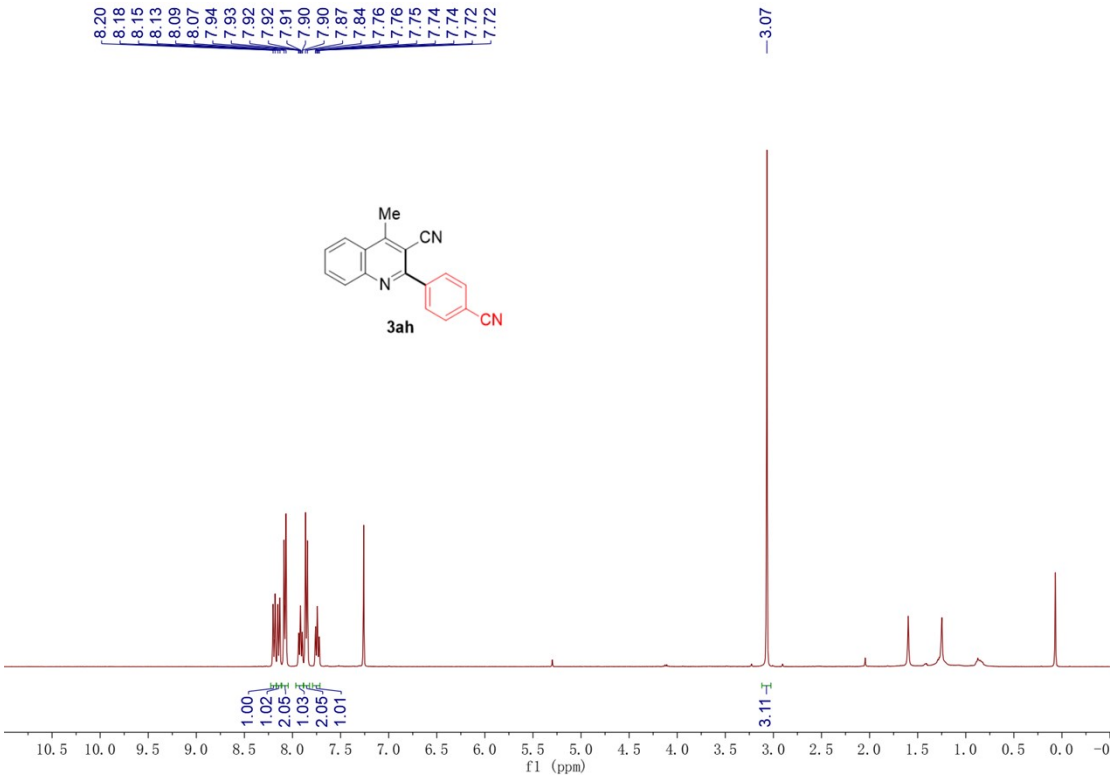
-160
-170
-180
-190
-200
f1 (ppm)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7.91
7.90
7.90
7.87
7.84
7.76
7.76
7.75
7.74
7.74
7.72
7.72
3.07
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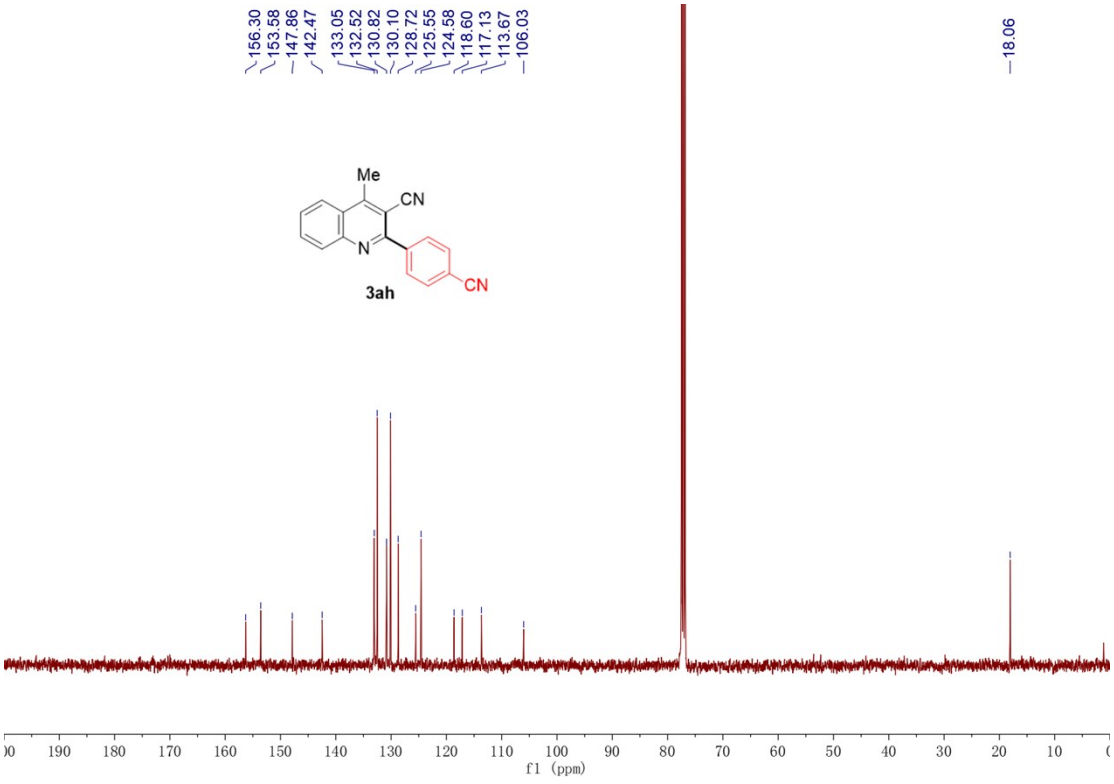
CN
N
CN
3ah
1.00
1.02
2.05
1.03
2.05
1.01
3.11
f1 (ppm)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106.03
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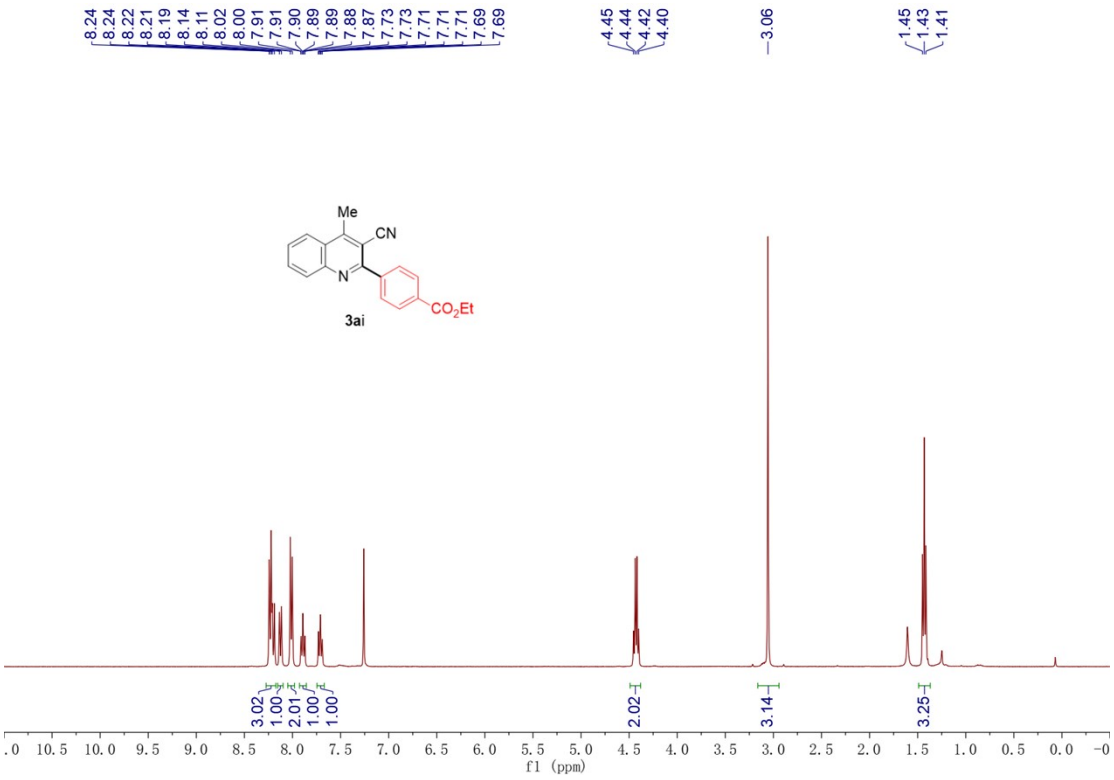
Me
CN
N
CN
3ah
f1 (ppm)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7.71
7.71
7.69
7.69
4.45
4.44
4.42
4.40
3.06
1.45
1.43
1.41
Me
CN
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CO2Et
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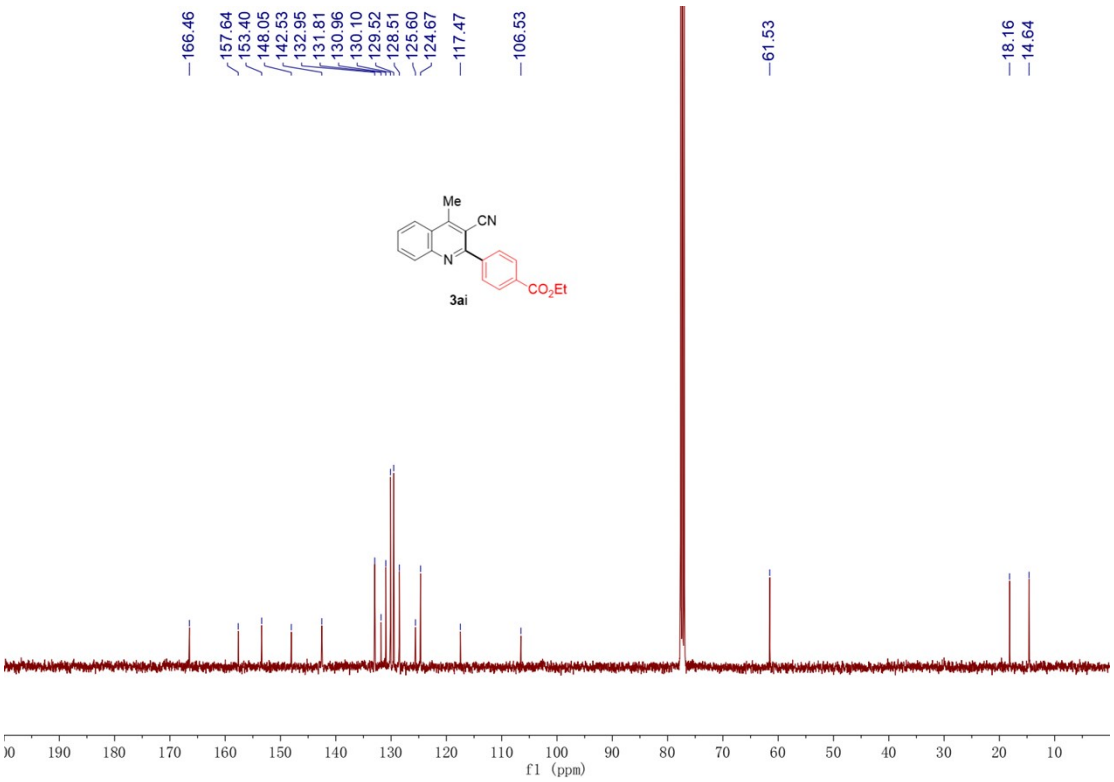
3.02
1.00
2.01
1.00
1.00
2.02
3.14
3.25
f1 (ppm)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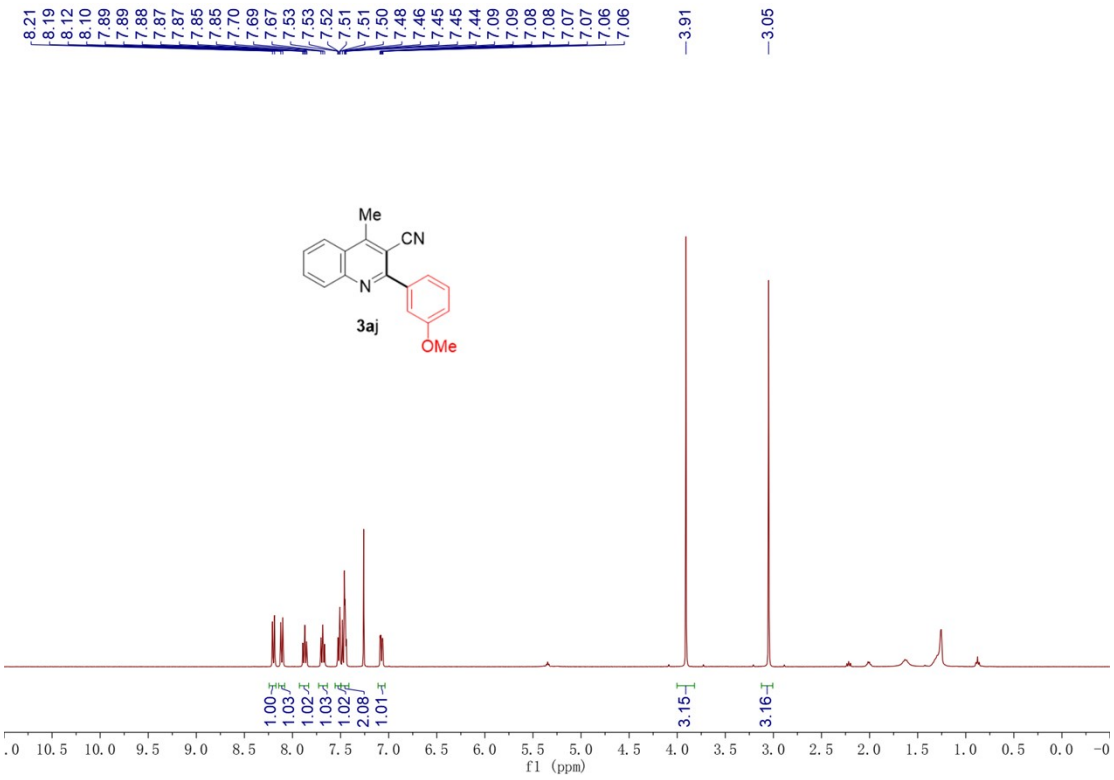
106.53
61.53
18.16
14.64
Me
CN
N
CO2Et
3ai
f1 (ppm)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7.51
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7.50
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7.46
7.45
7.45
7.44
7.09
7.09
7.08
7.08
7.07
7.07
7.06
7.06
3.91
3.05
Me
CN
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1.03
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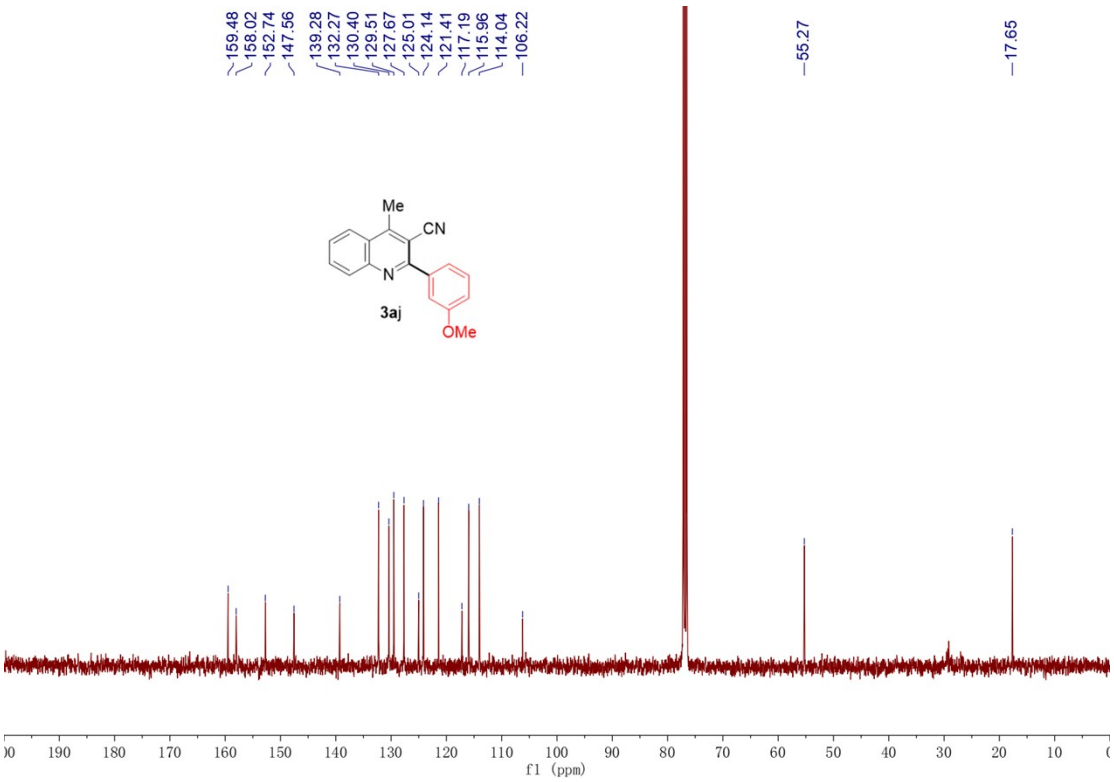
1.03
1.02
2.08
1.01
3.15
3.16
f1 (ppm)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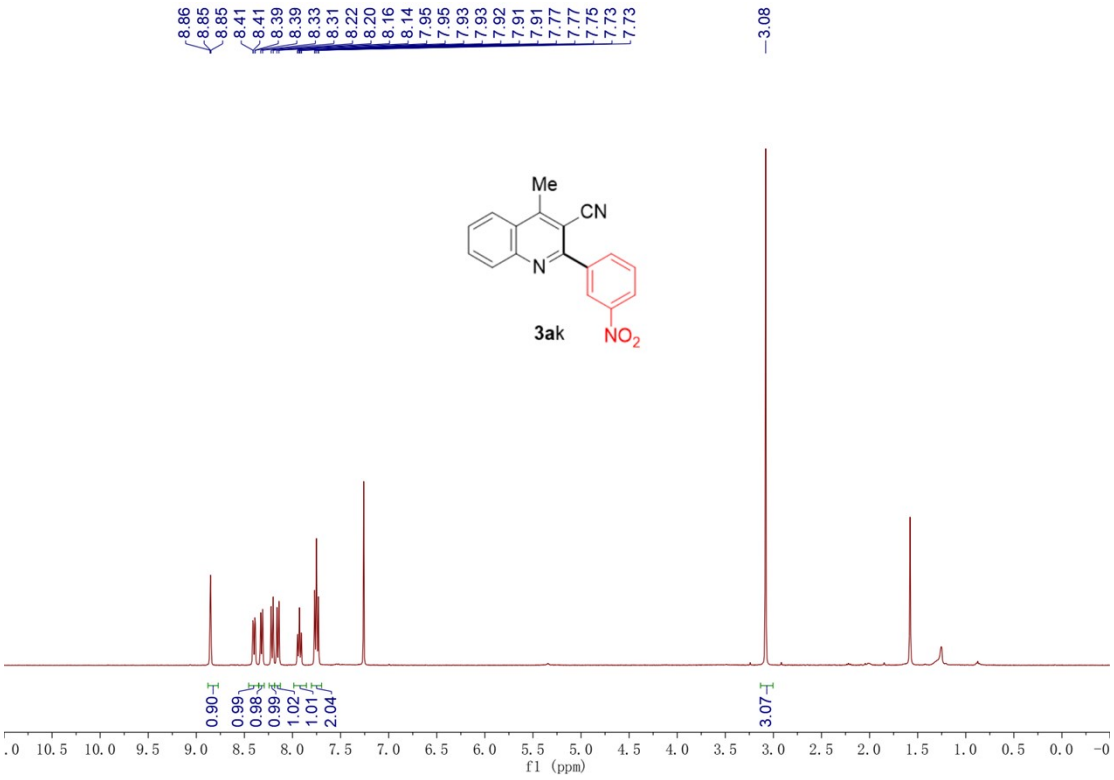
N
OMe
3aj
f1 (ppm)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7.93
7.92
7.91
7.91
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7.77
7.75
7.73
7.73
3.08
Me
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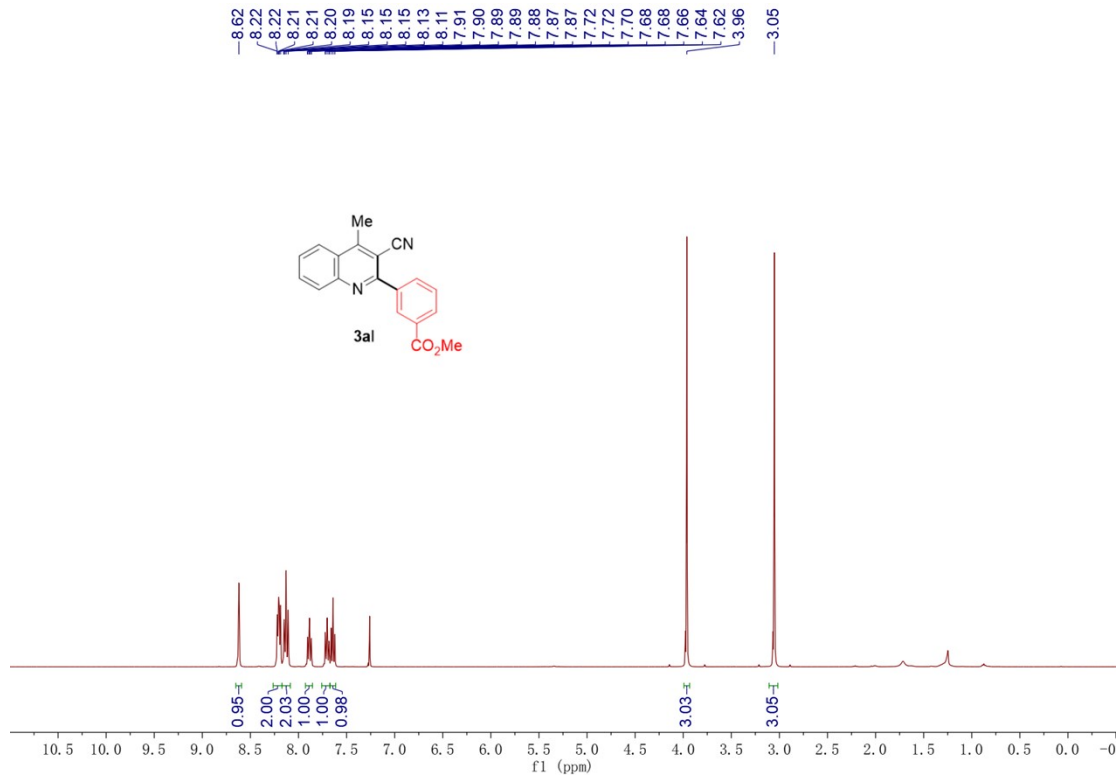
3.07
f1 (ppm)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7.68
7.66
7.64
7.62
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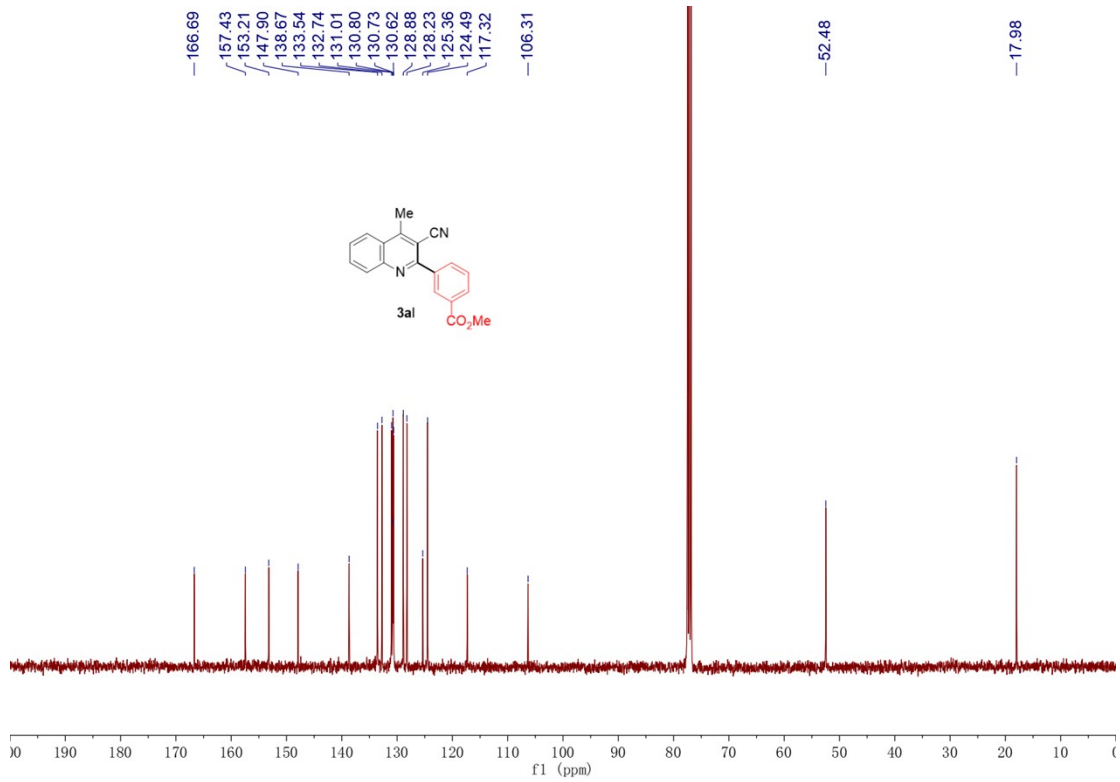
3.05
f1 (ppm)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N
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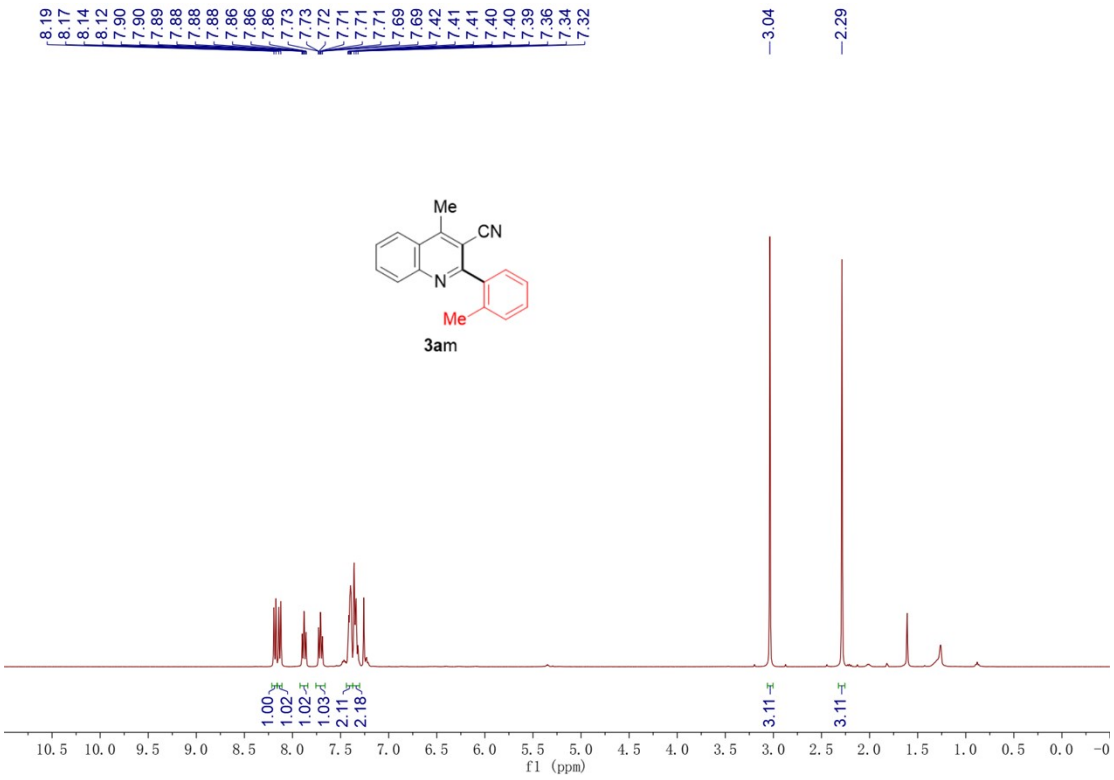
CO2Me
f1 (ppm)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7.32
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1.02
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2.18
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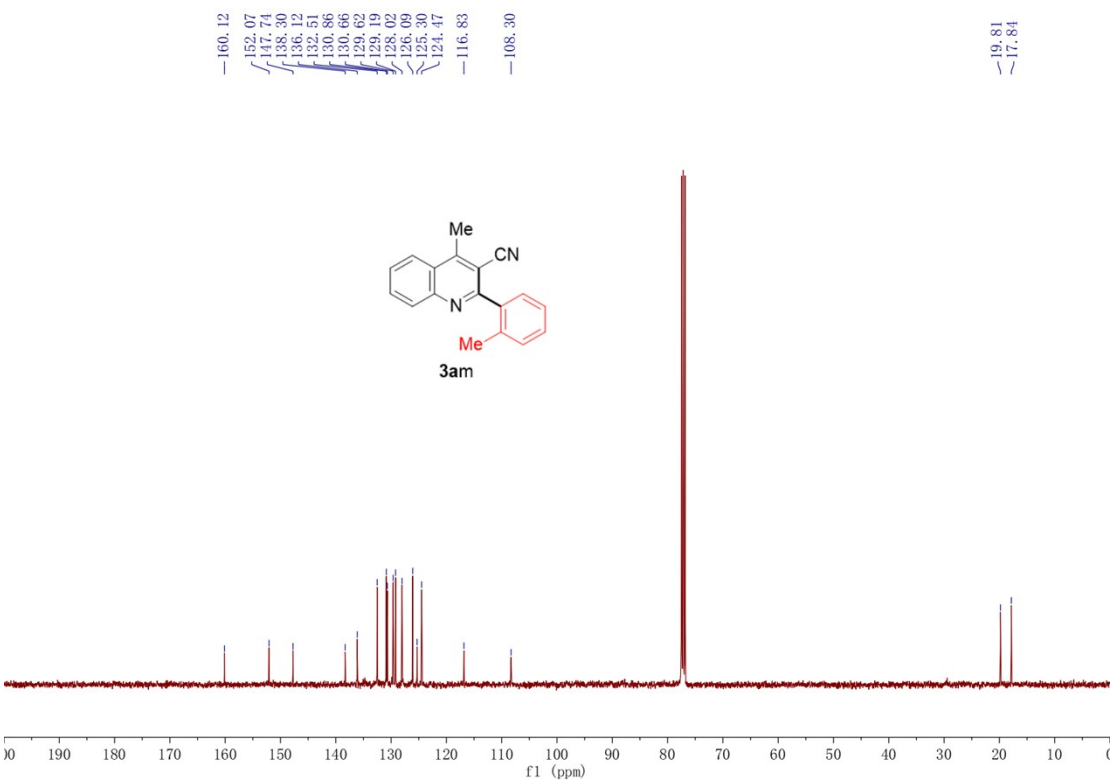
3.11
f1 (ppm)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116.83
108.30
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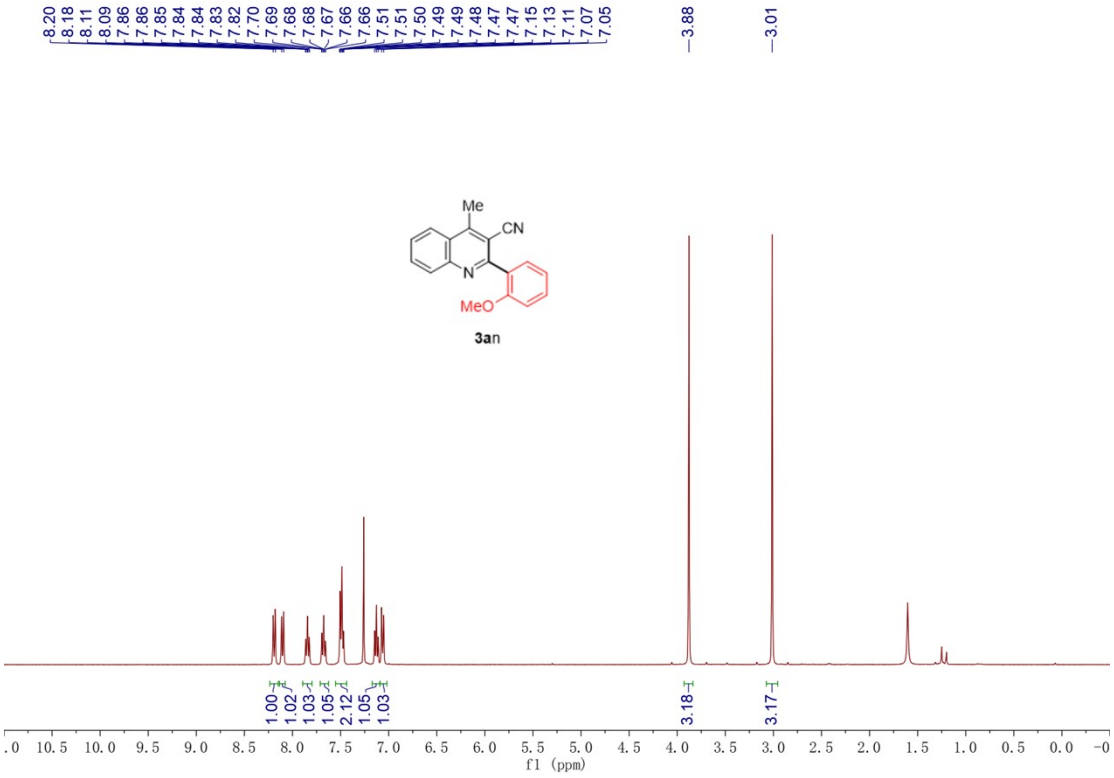
CN
N
Me
3am
f1 (ppm)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7.48
7.47
7.47
7.15
7.13
7.11
7.07
7.05
3.88
3.01
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CN
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1.05
2.12
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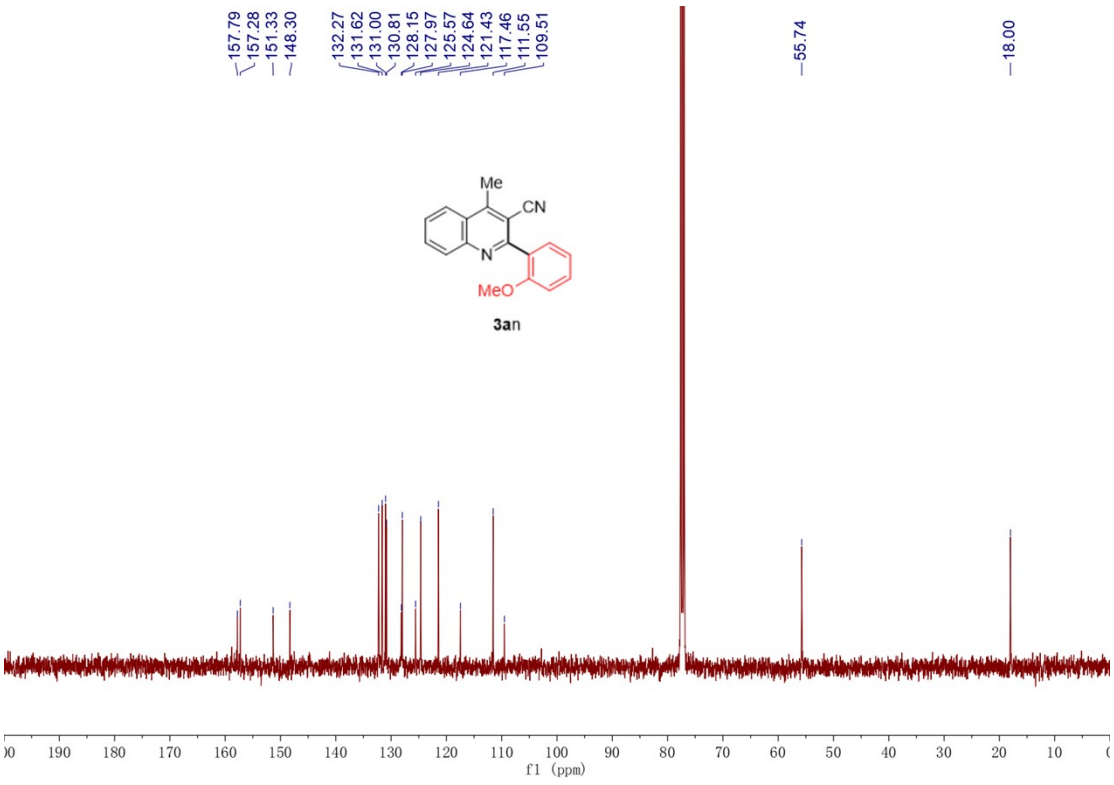
3.17
f1 (ppm)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18.00
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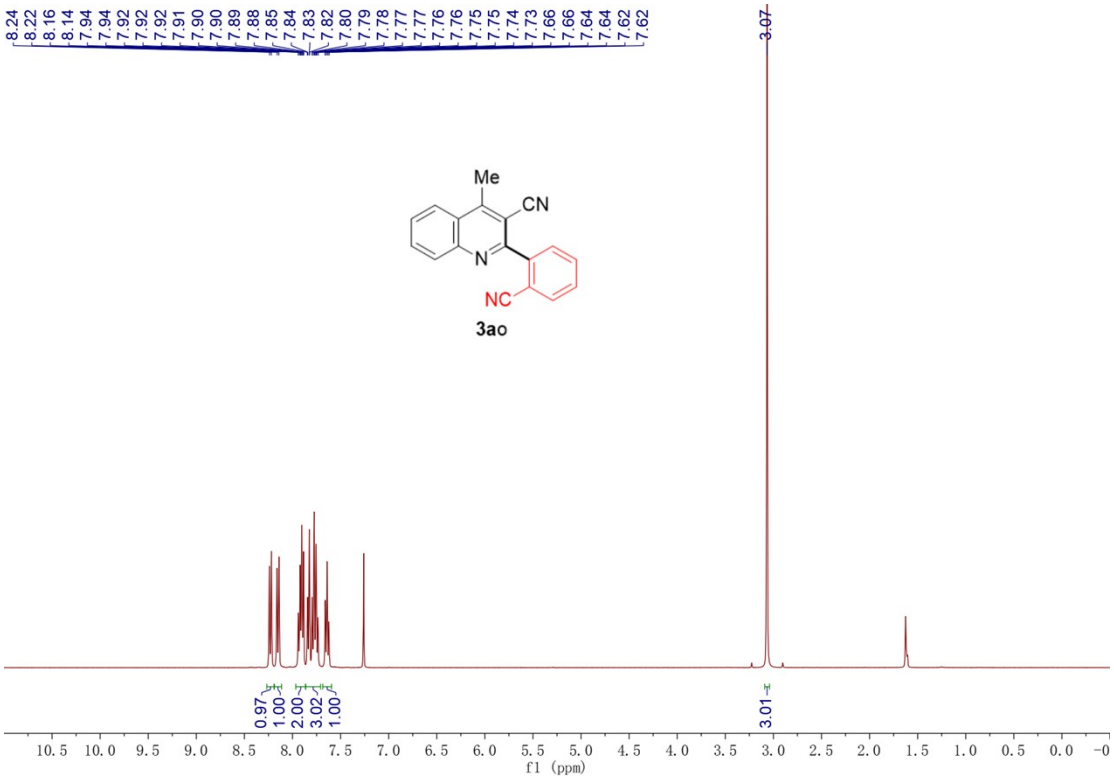
CN
N
MeO
3an
f1 (ppm)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7.74
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7.62
3.07
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2.00
3.02
1.00
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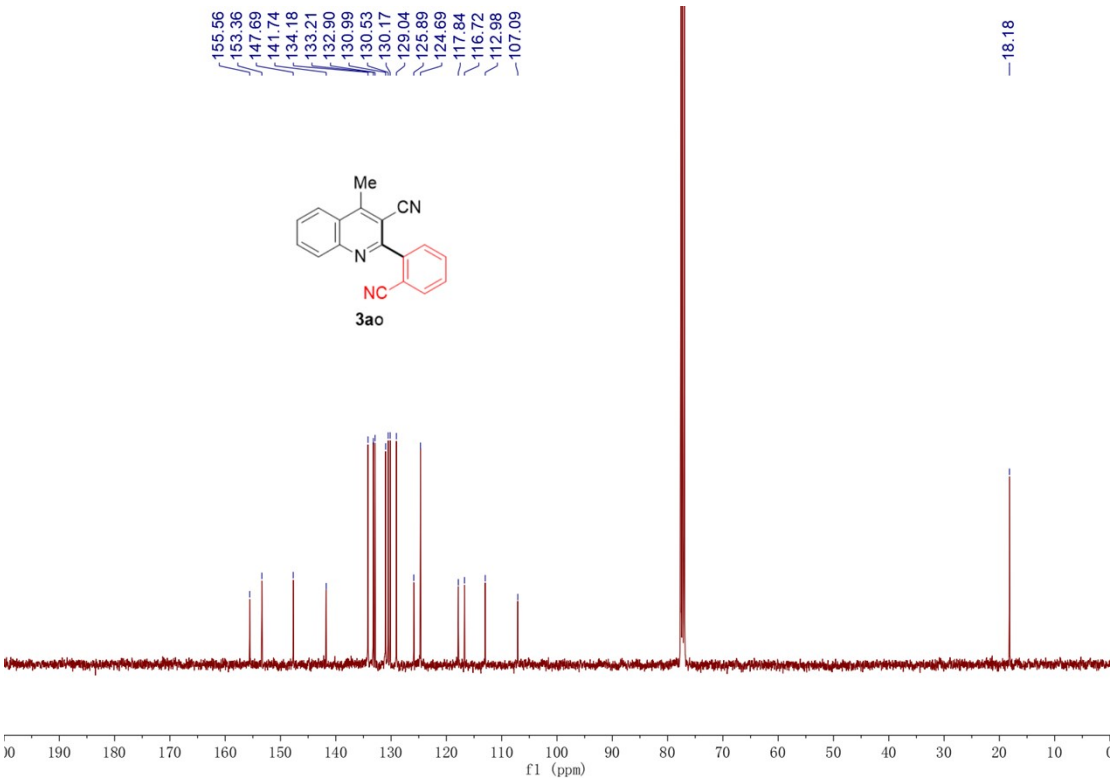
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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117.84
116.72
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18.18
Me
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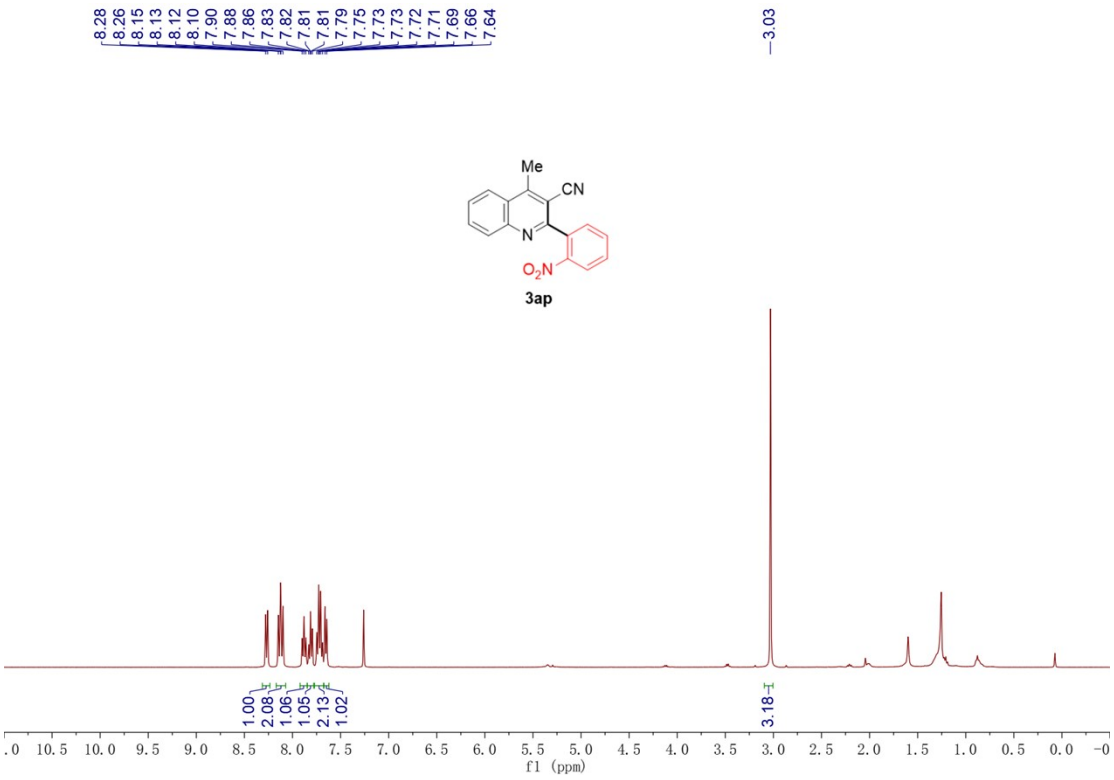
N
NC
3ao
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)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7.81
7.79
7.75
7.73
7.73
7.72
7.71
7.69
7.66
7.64
3.03
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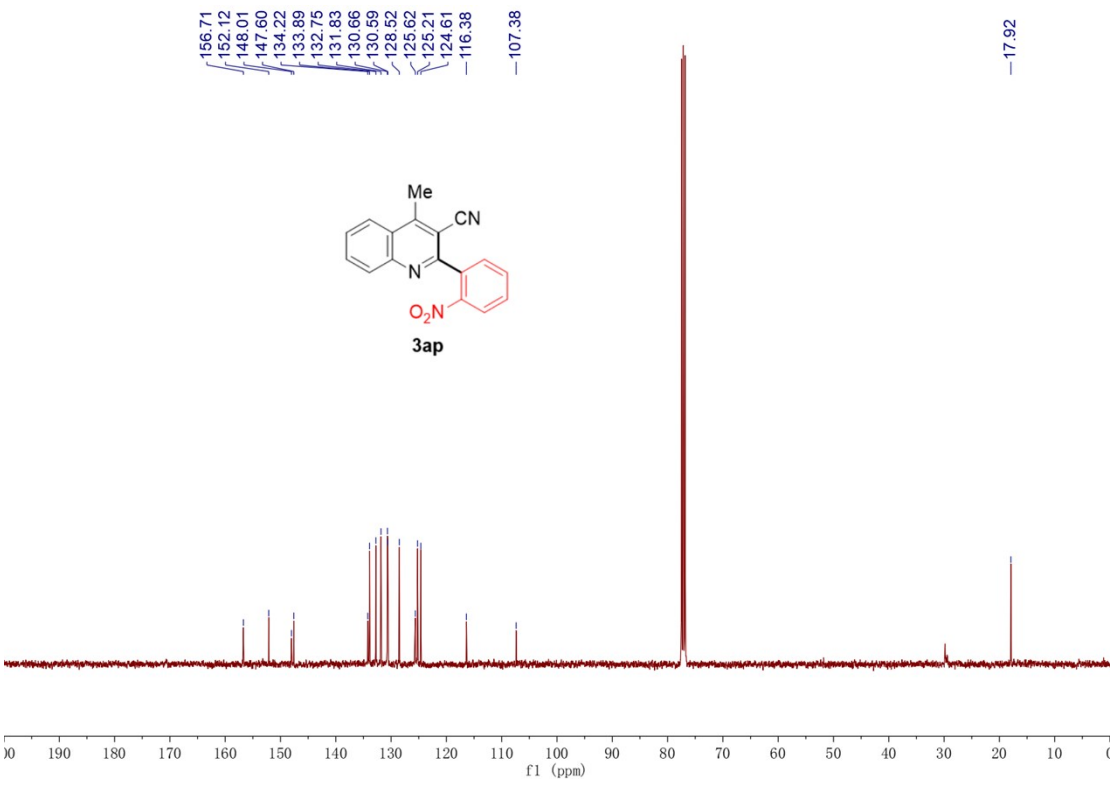
1.06
1.05
2.13
1.02
3.18
f1 (ppm)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124.61
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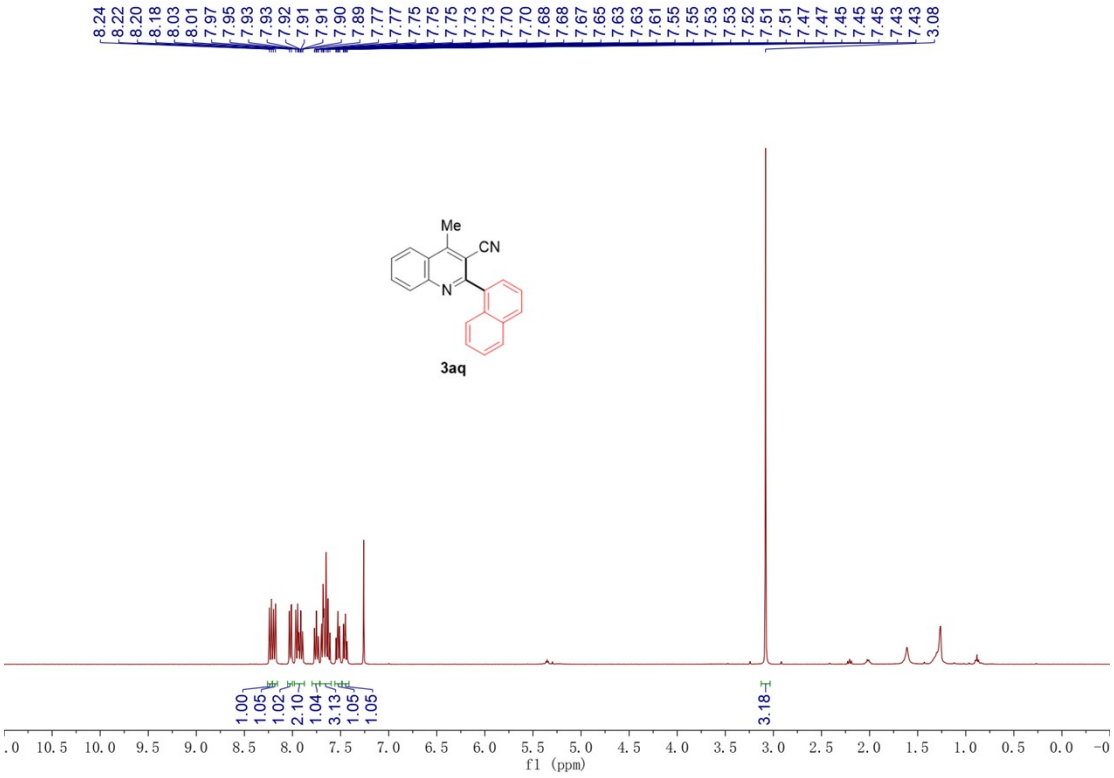
CN
N
O2N
3ap
f1 (ppm)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7.45
7.45
7.43
7.43
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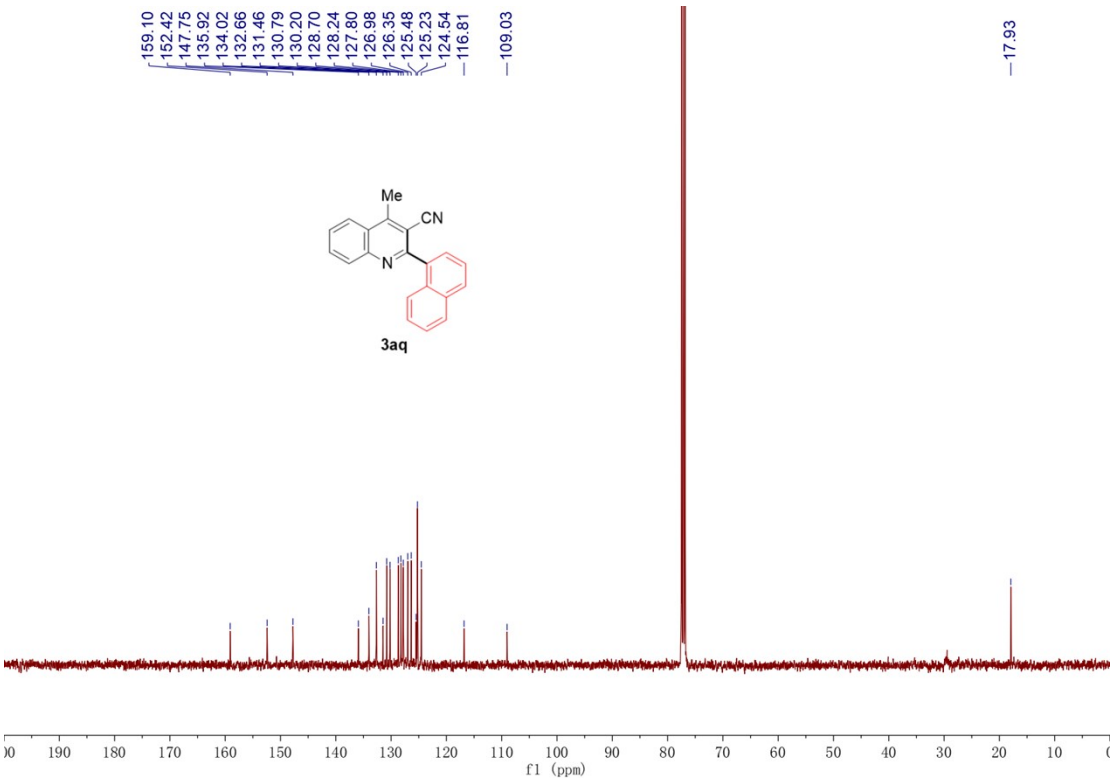
1.05
1.05
3.18
f1 (ppm)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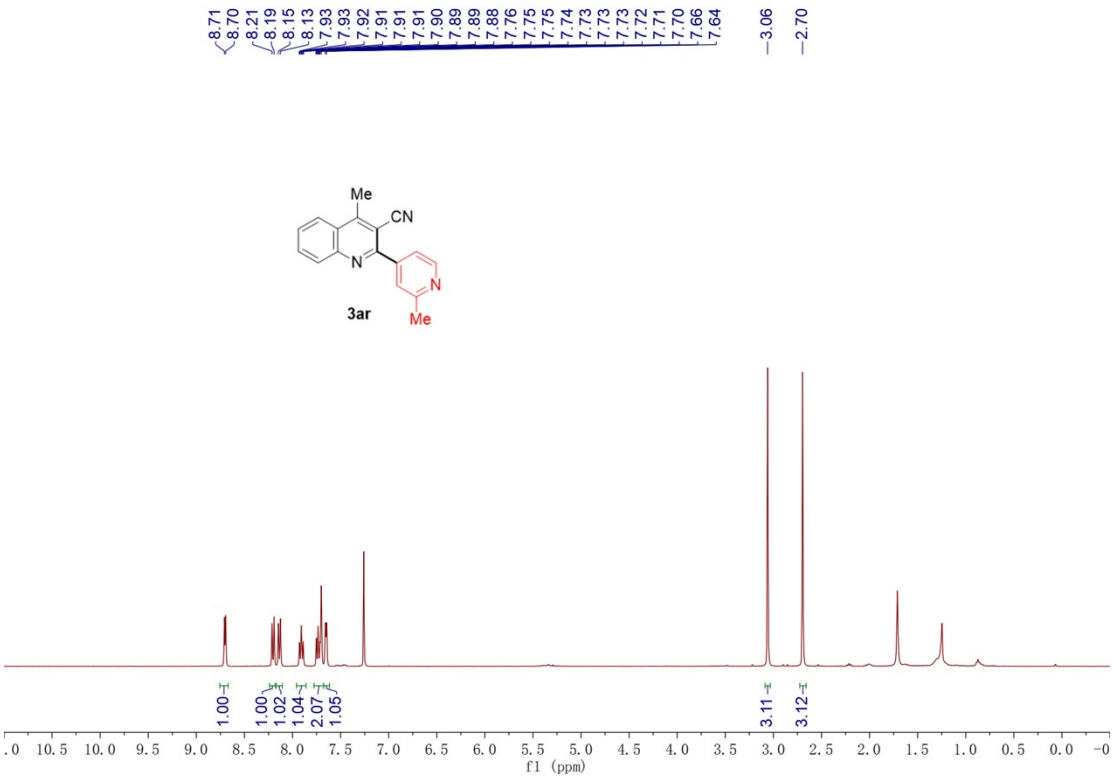
126.35
125.48
125.23
124.54
116.81
109.03
17.93
Me
CN
N
3aq
f1 (ppm)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7.89
7.89
7.88
7.76
7.75
7.75
7.74
7.73
7.73
7.73
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7.71
7.70
7.66
7.64
3.06
2.70
Me
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1.05
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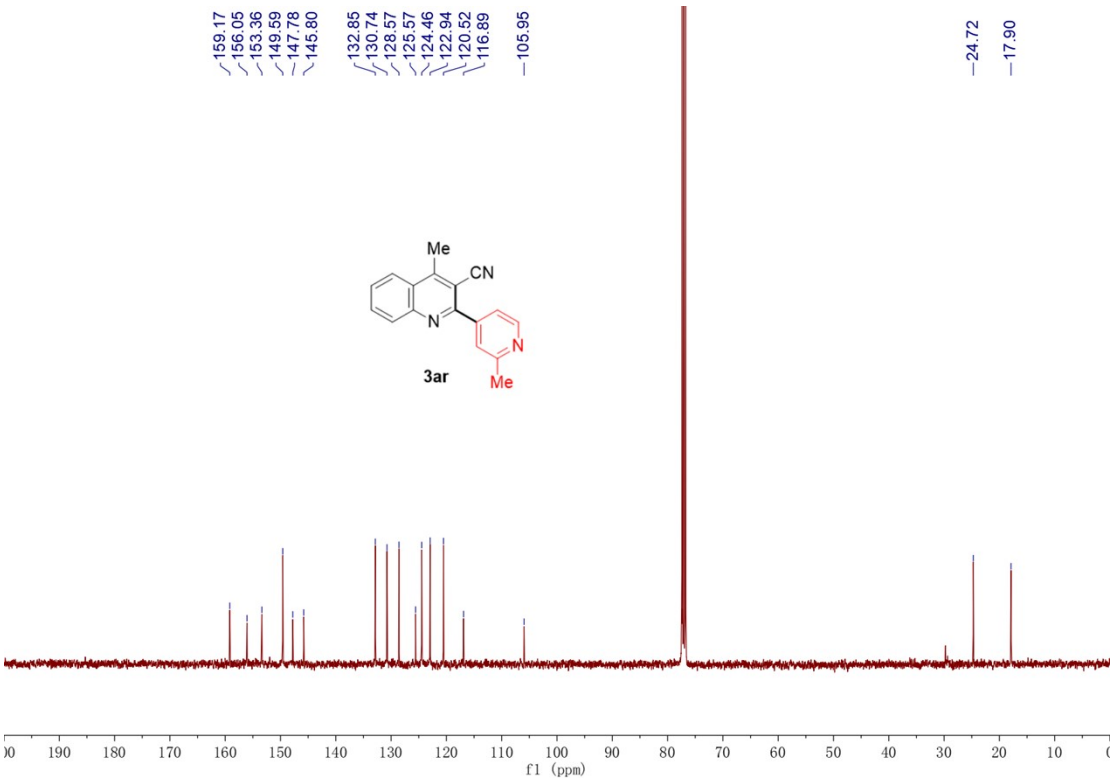
3.12
f1 (ppm)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CN
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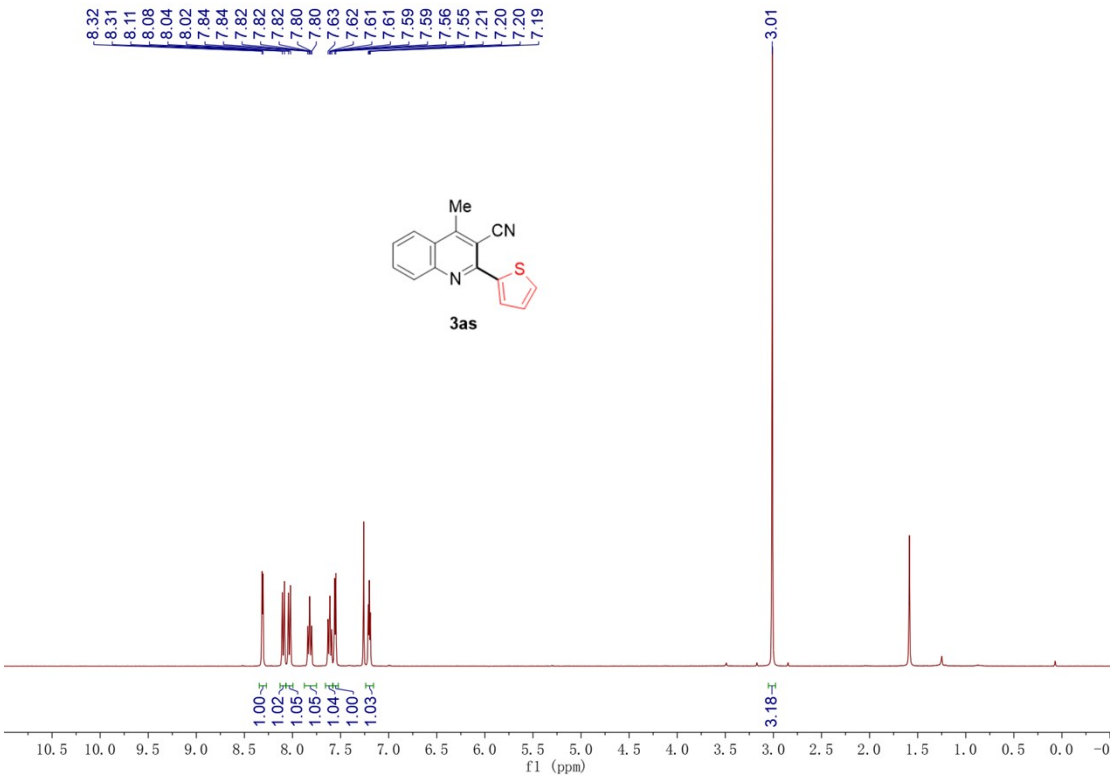
N
Me
3ar
f1 (ppm)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7.62
7.61
7.61
7.59
7.59
7.56
7.55
7.21
7.20
7.20
7.19
3.01
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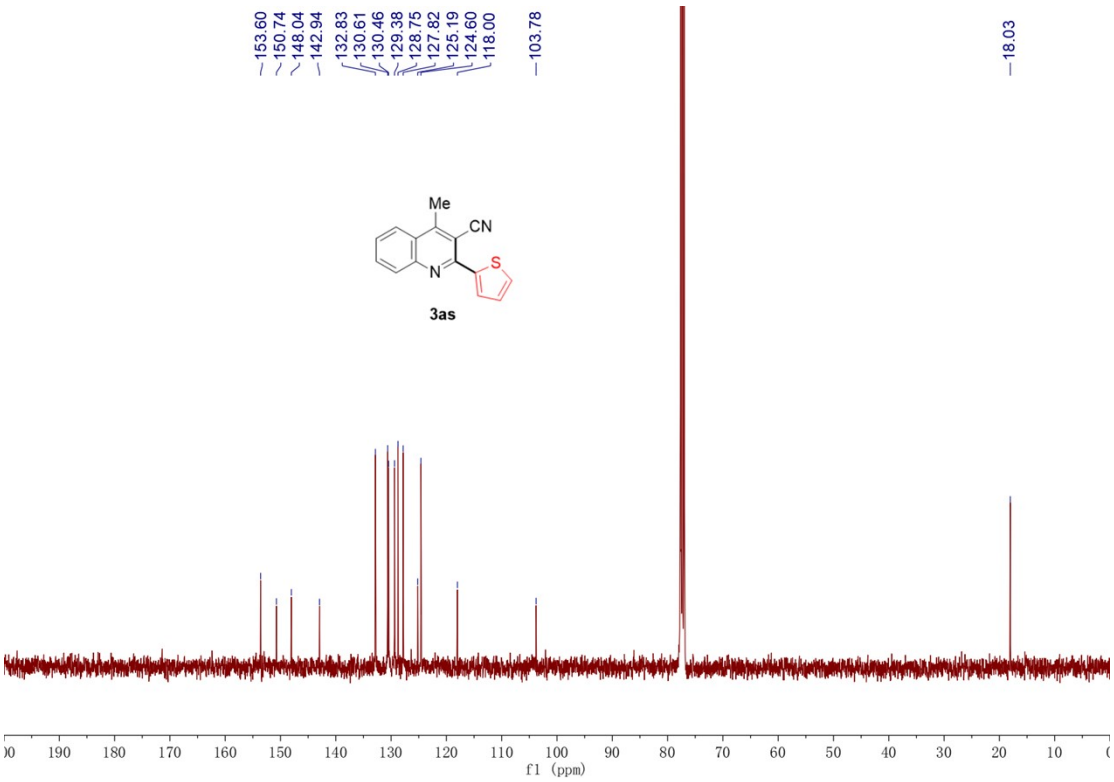
1.04
1.00
1.03
3.18
f1 (ppm)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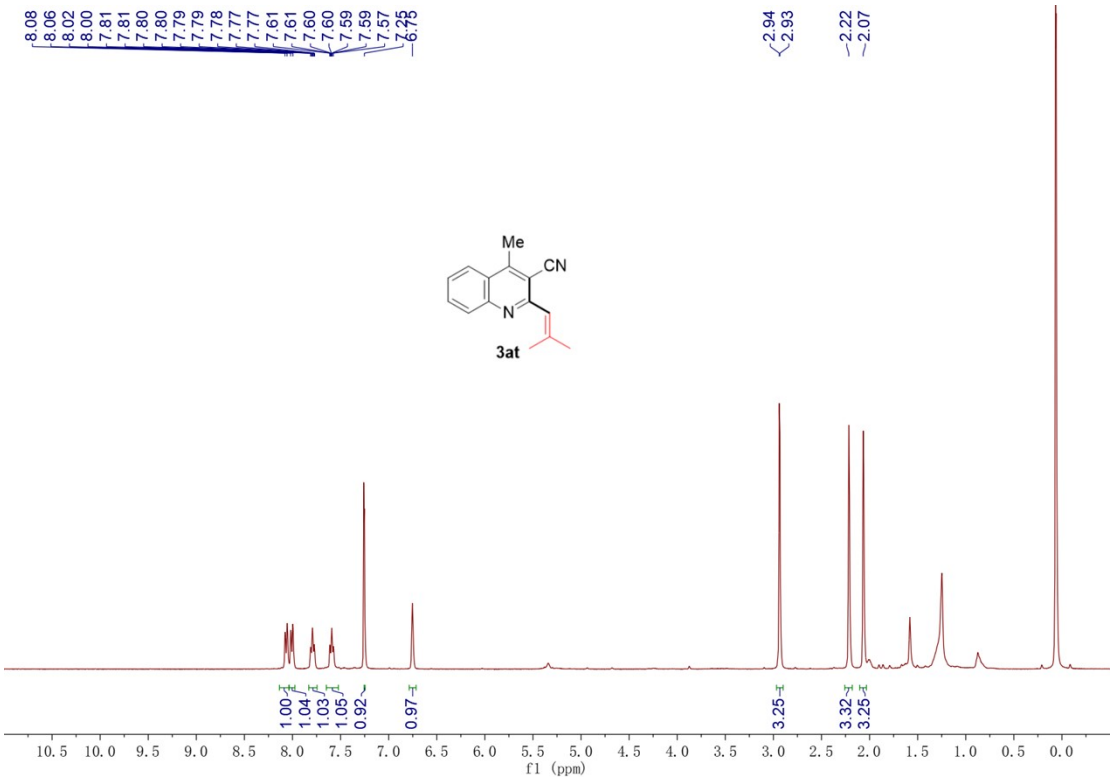
N
S
3as
f1 (ppm)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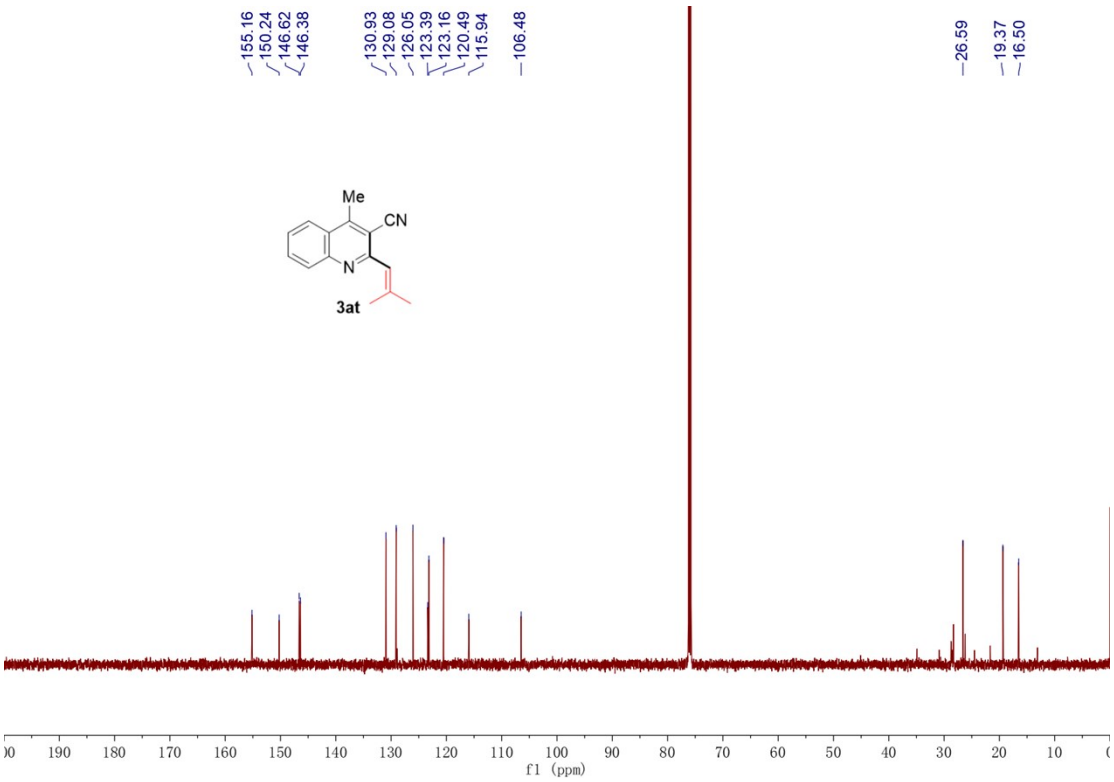
6.75
2.94
2.93
2.22
2.07
Me
CN
N
3at
1.00
1.04
1.03
1.05
0.92
0.97
3.25
3.32
3.25
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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120.49
115.94
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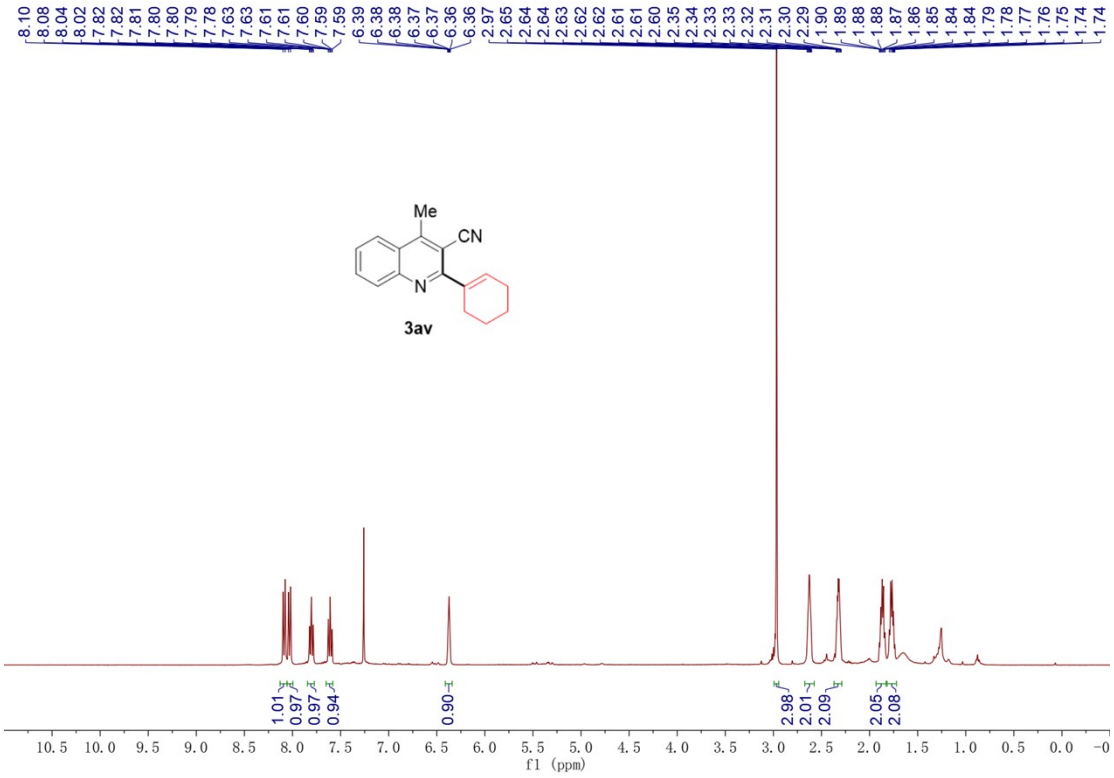
19.37
16.50
Me
CN
N
3at
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)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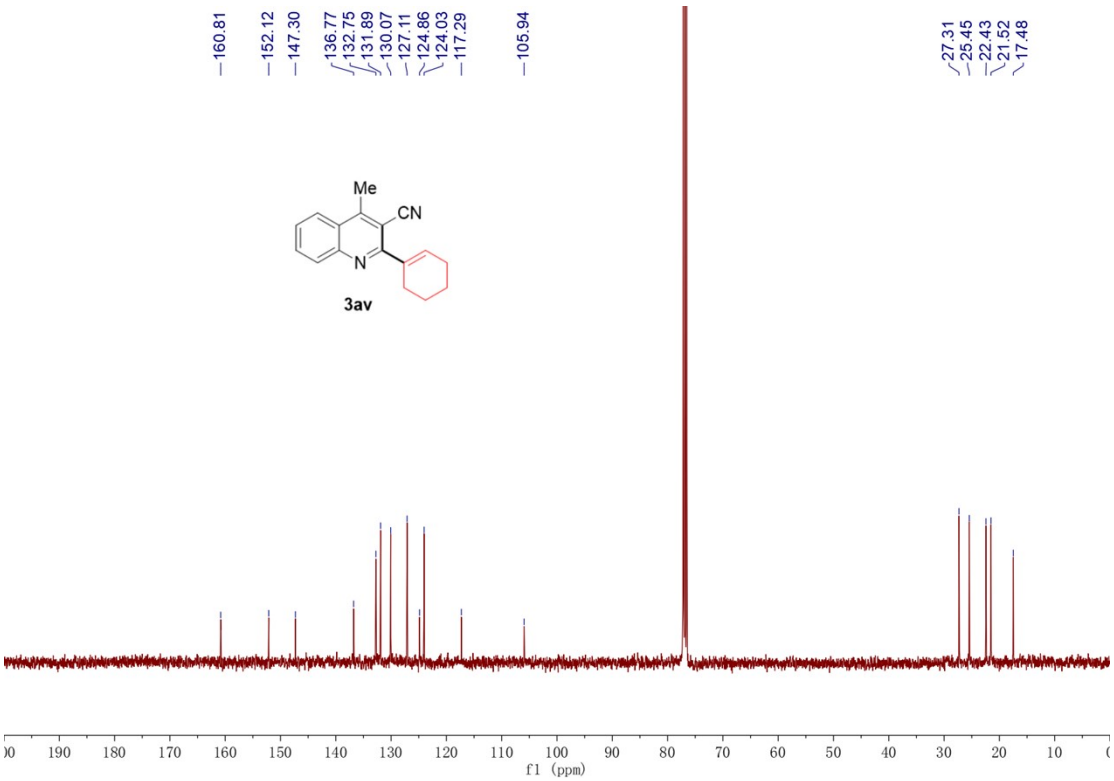
Me
CN
N
3av
1.01 0.97 0.97 0.94 0.90 2.98 2.01 2.09 2.05 2.08
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


160.81 152.12 147.30 136.77 132.75 131.89 130.07 127.11 124.86 124.03 117.29 105.94 27.31 25.45 22.43 21.52 17.48
Me
CN
N
3av
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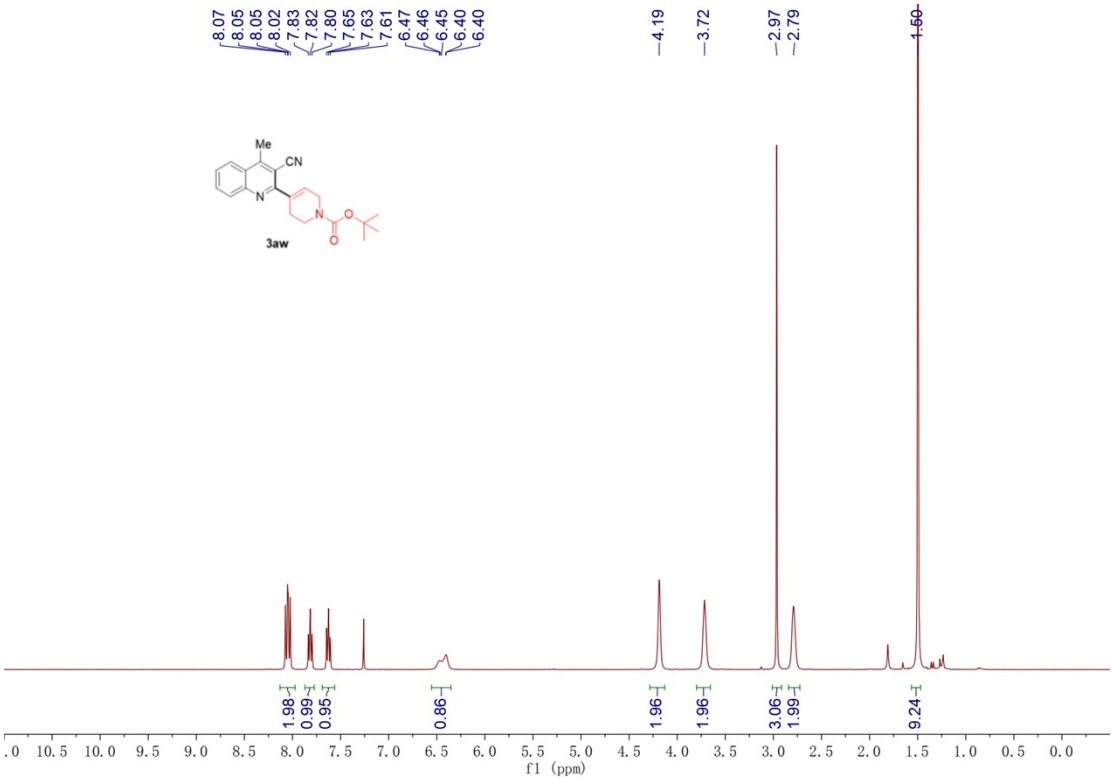
f1 (ppm)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7.82
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7.63
7.61
6.47
6.46
6.45
6.40
6.40
4.19
3.72
2.97
2.79
1.60
Me
CN
N
N
O
O
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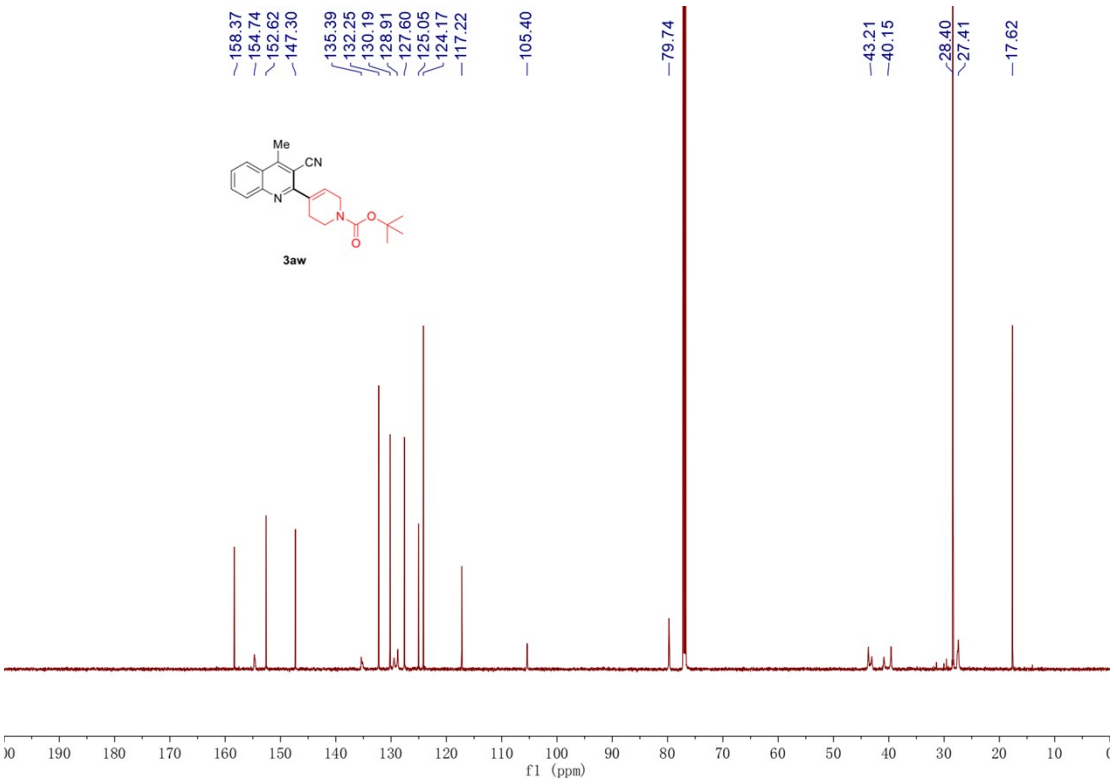
0.99
0.95
0.86
1.96
1.96
3.06
1.99
9.24
f1 (ppm)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117.22
105.40
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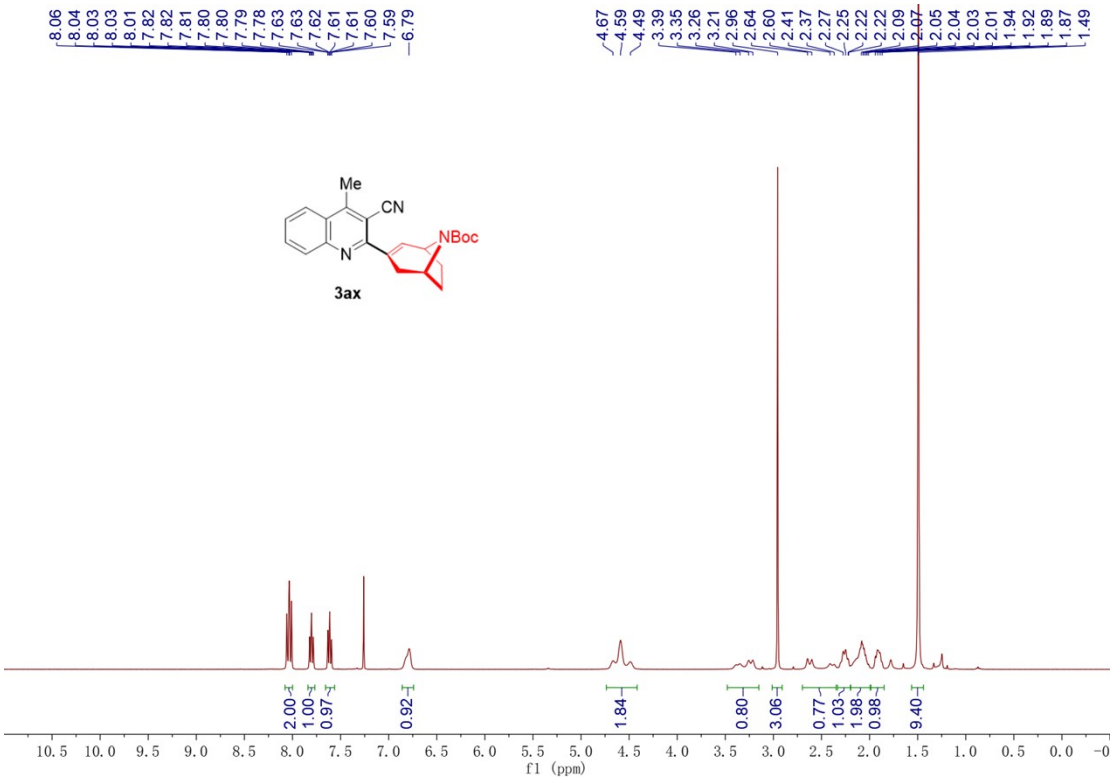
17.62
Me
CN
N
N
O
O
3aw
f1 (ppm)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7.63
7.62
7.61
7.61
7.60
7.59
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2.27
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2.07
2.05
2.04
2.03
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1.87
1.49
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CN
NBoc
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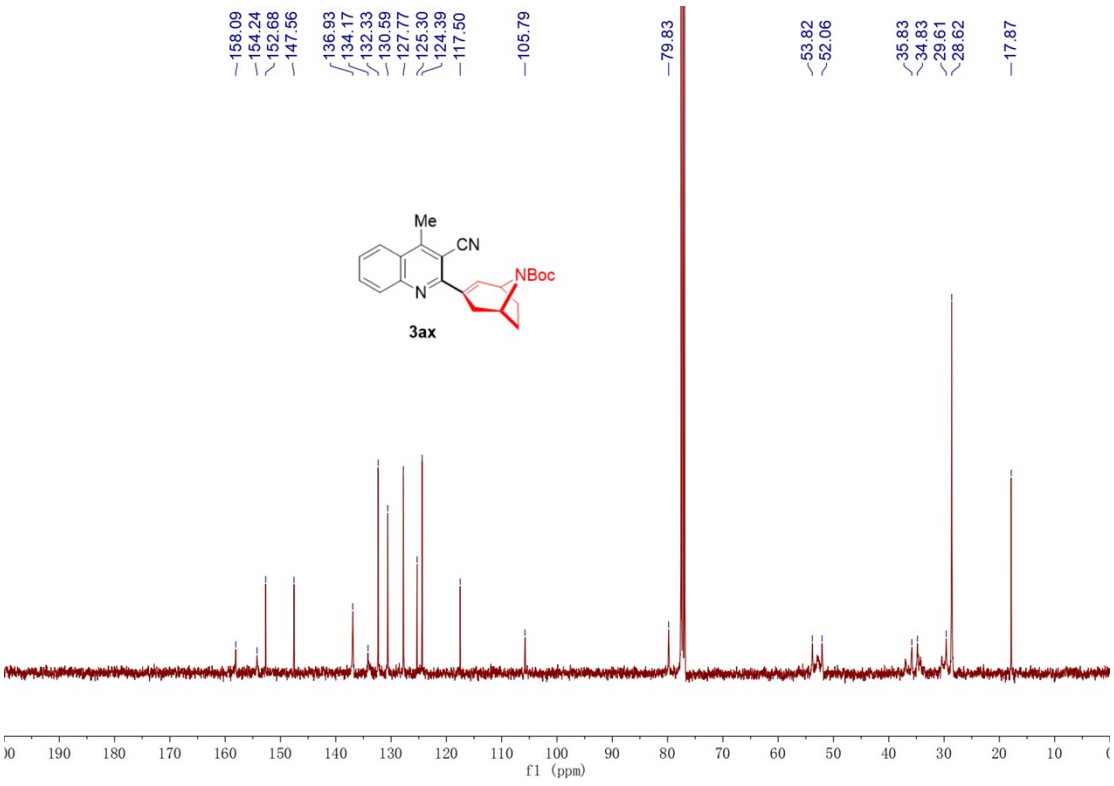
f1 (ppm)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124.39
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105.79
79.83
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34.83
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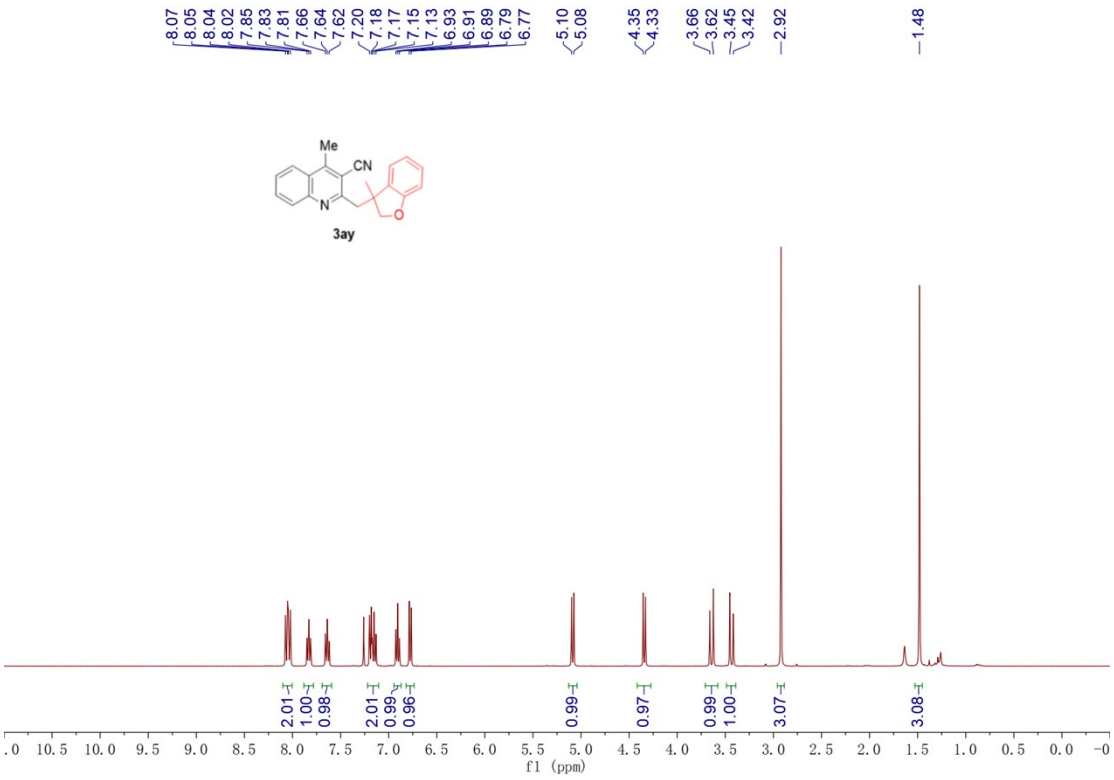
28.62
17.87
Me
CN
NBoc
N
3ax
f1 (ppm)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7.13
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6.91
6.89
6.79
6.77
5.10
5.08
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4.33
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3.42
2.92
1.48
Me
CN
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O
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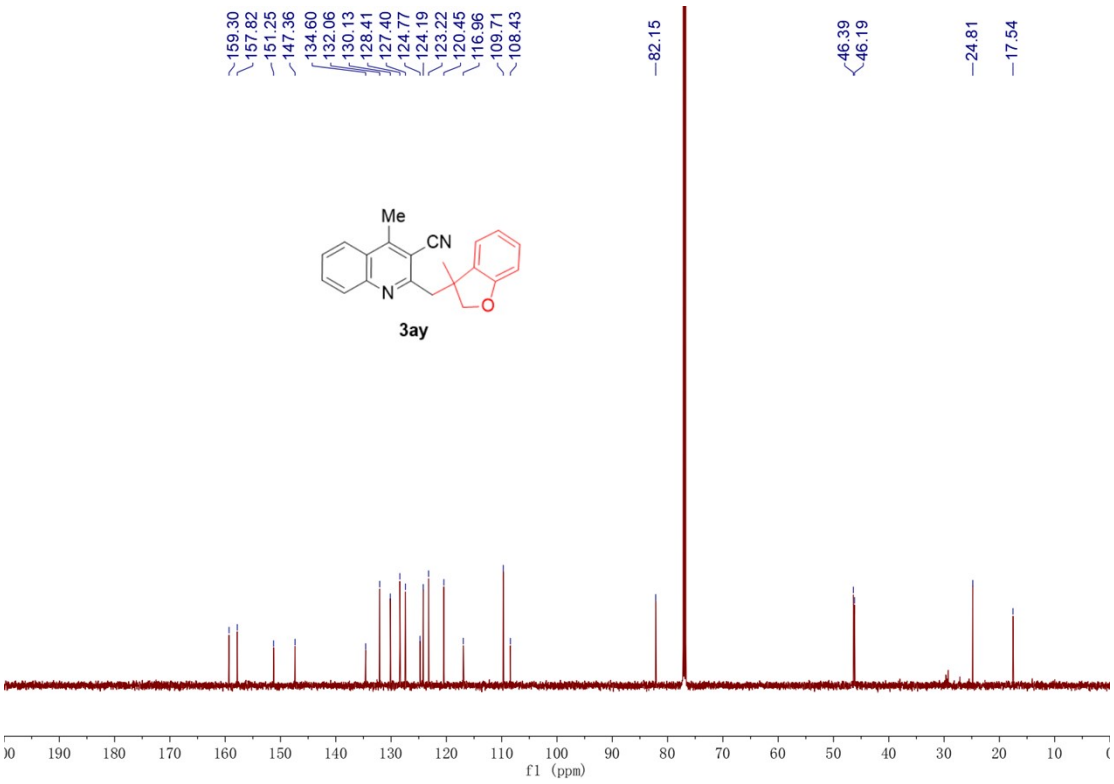
0.96
0.99
0.97
0.99
1.00
3.07
3.08
f1 (ppm)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123.22
120.45
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46.19
24.81
17.54
Me
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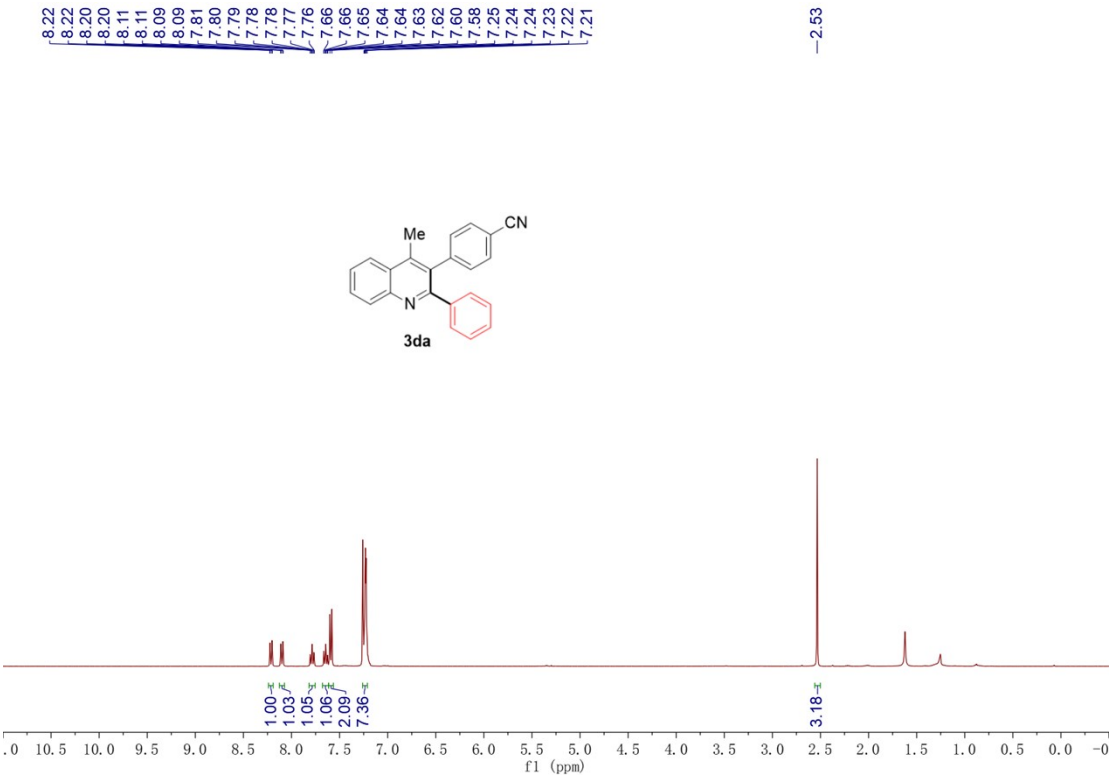
N
O
3ay
f1 (ppm)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7.64
7.64
7.63
7.62
7.60
7.58
7.25
7.24
7.24
7.23
7.22
7.21
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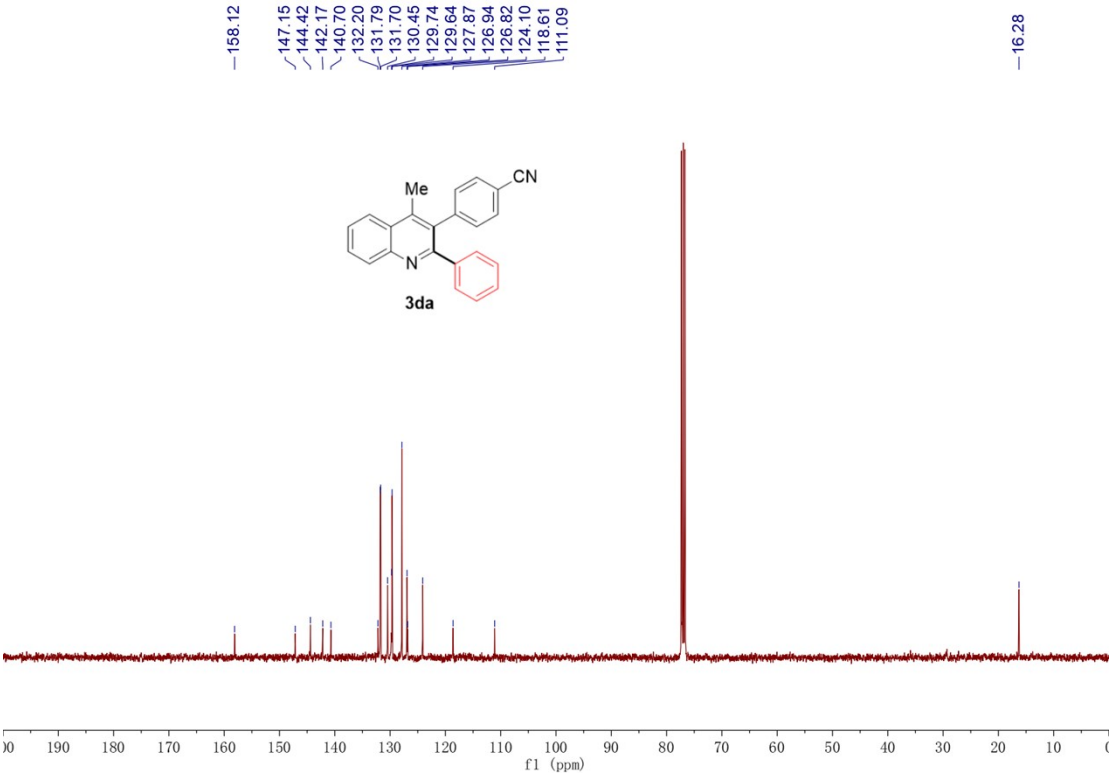
3.18
f1 (ppm)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N
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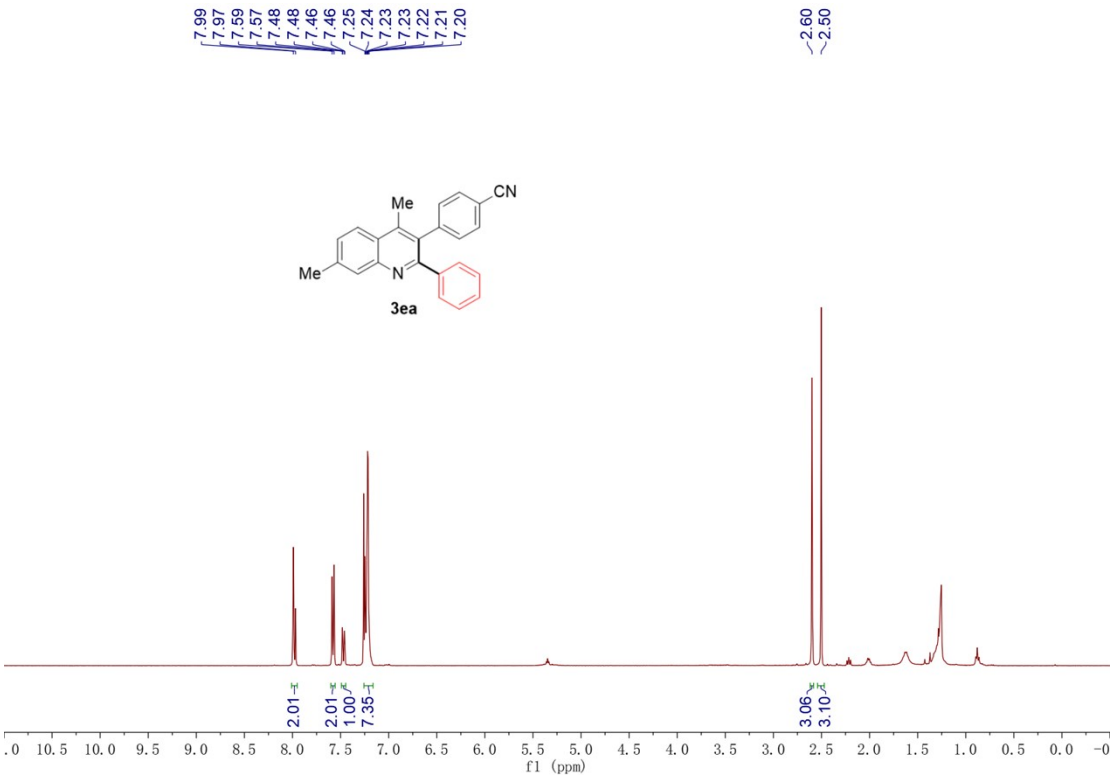
f1 (ppm)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7.20
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N
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2.01
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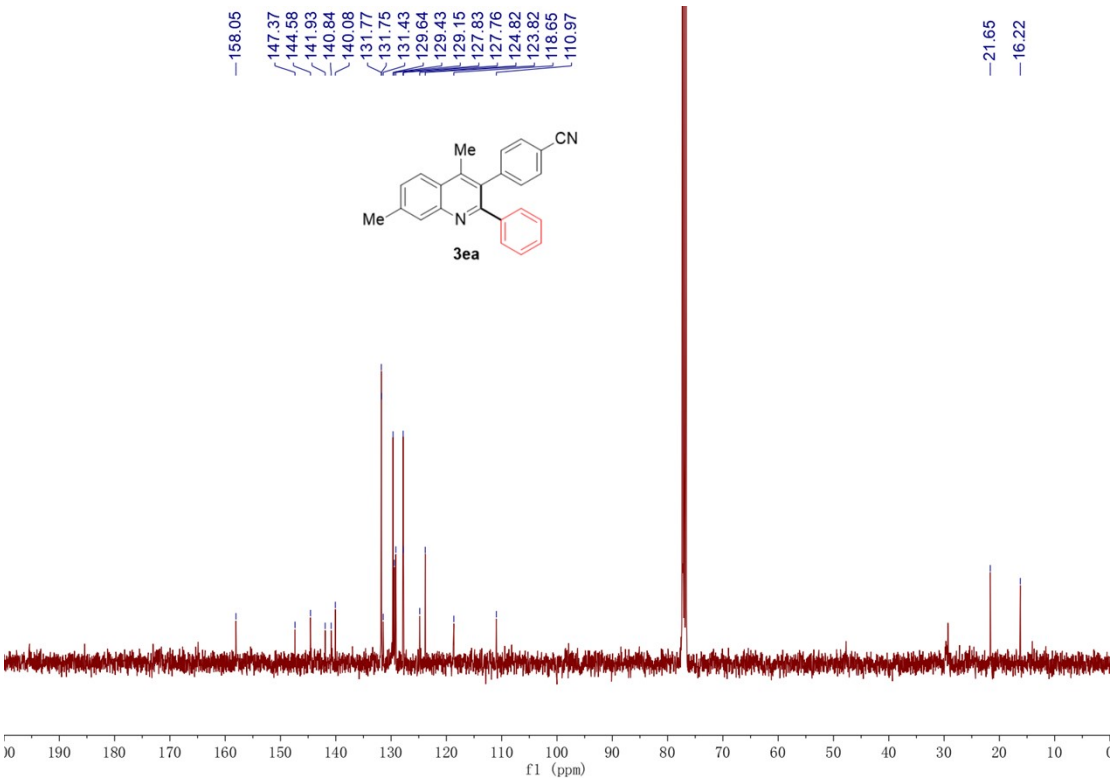
3.10
f1 (ppm)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123.82
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110.97
21.65
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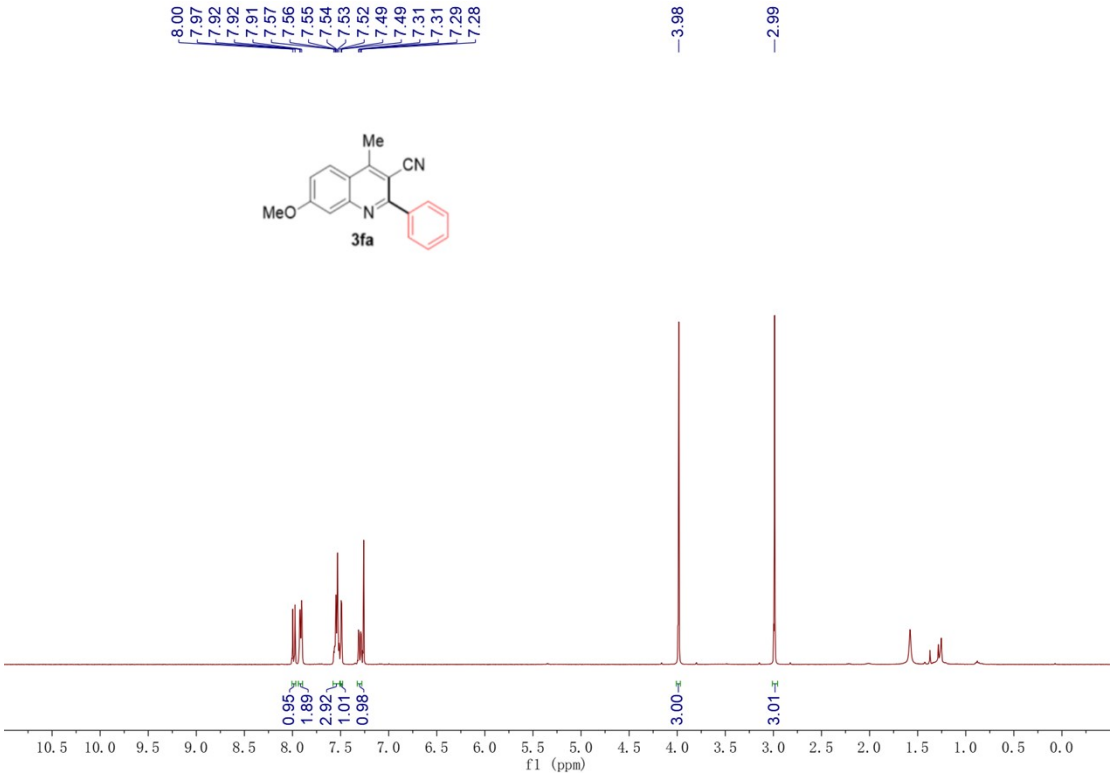
Me
CN
Me
N
3ea
f1 (ppm)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7.52
7.49
7.49
7.31
7.31
7.29
7.28
3.98
2.99
Me
CN
MeO
N
3fa
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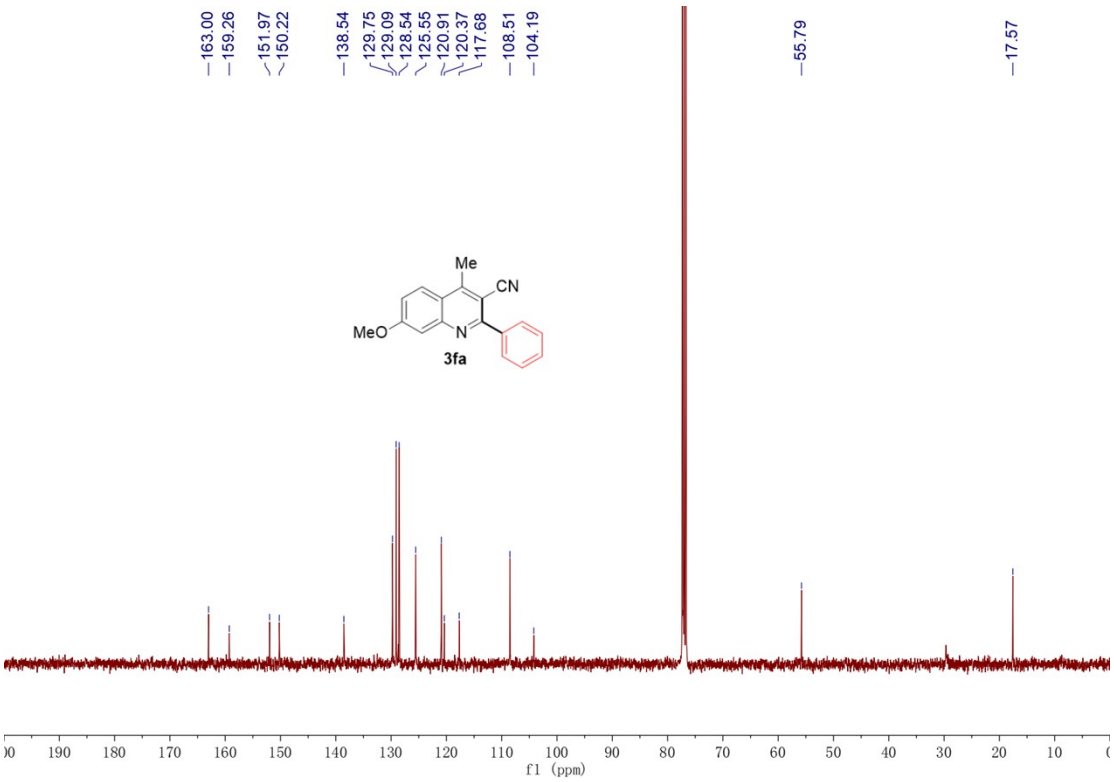
1.89
2.92
1.01
0.98
3.00
3.01
f1 (ppm)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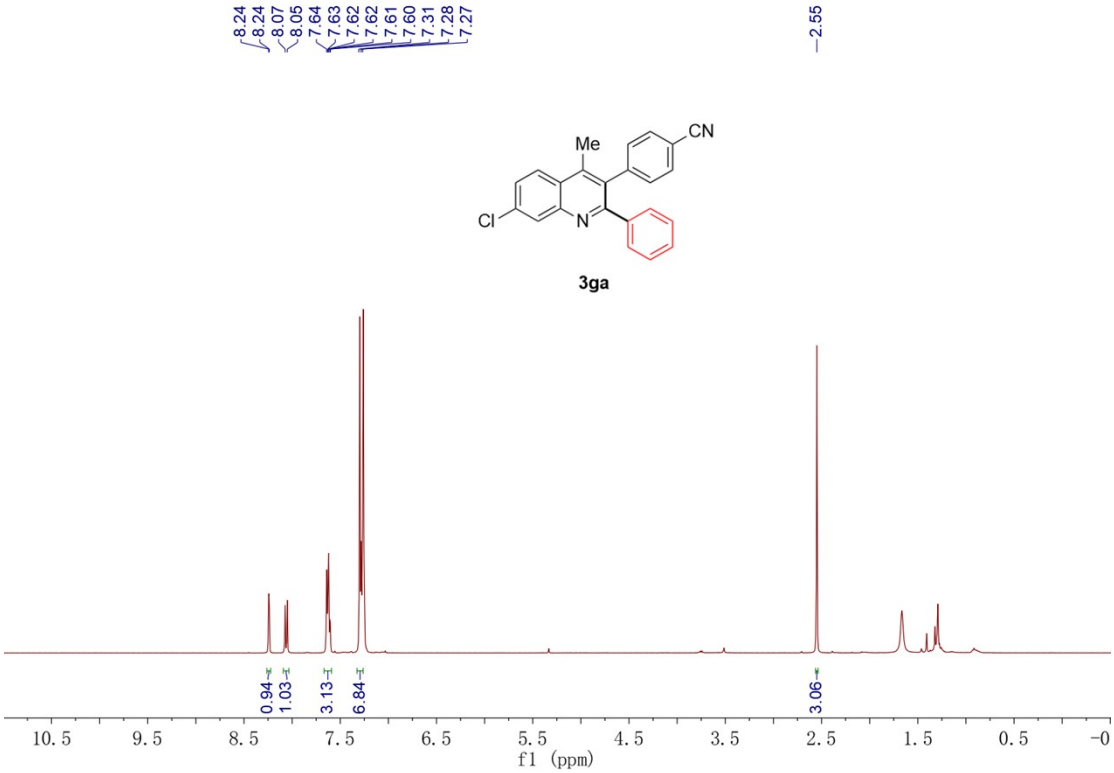
117.68
108.51
104.19
55.79
17.57
Me
CN
MeO
N
3fa
f1 (ppm)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7.60
7.31
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7.27
2.55
Me
CN
Cl
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3.13
6.84
3.06
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7.5
6.5
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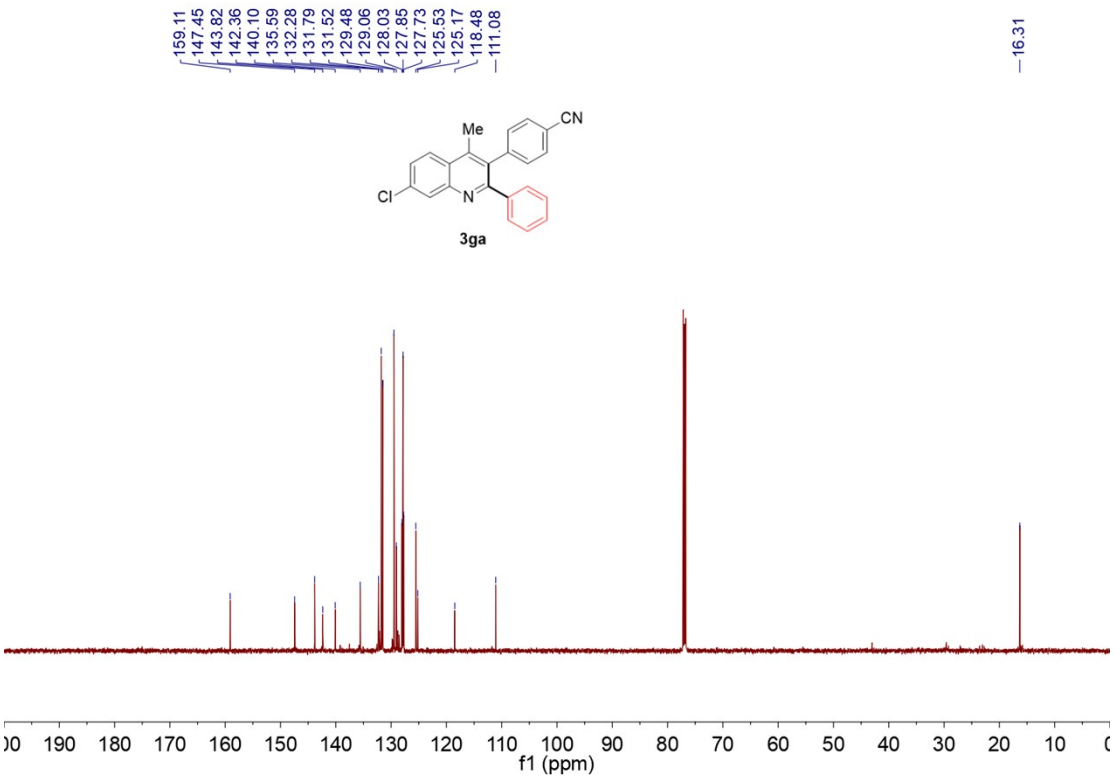
4.5
3.5
2.5
1.5
0.5
f1 (ppm)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127.85
127.73
125.53
125.17
118.48
111.08
16.31
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CN
Cl
N
3ga
190
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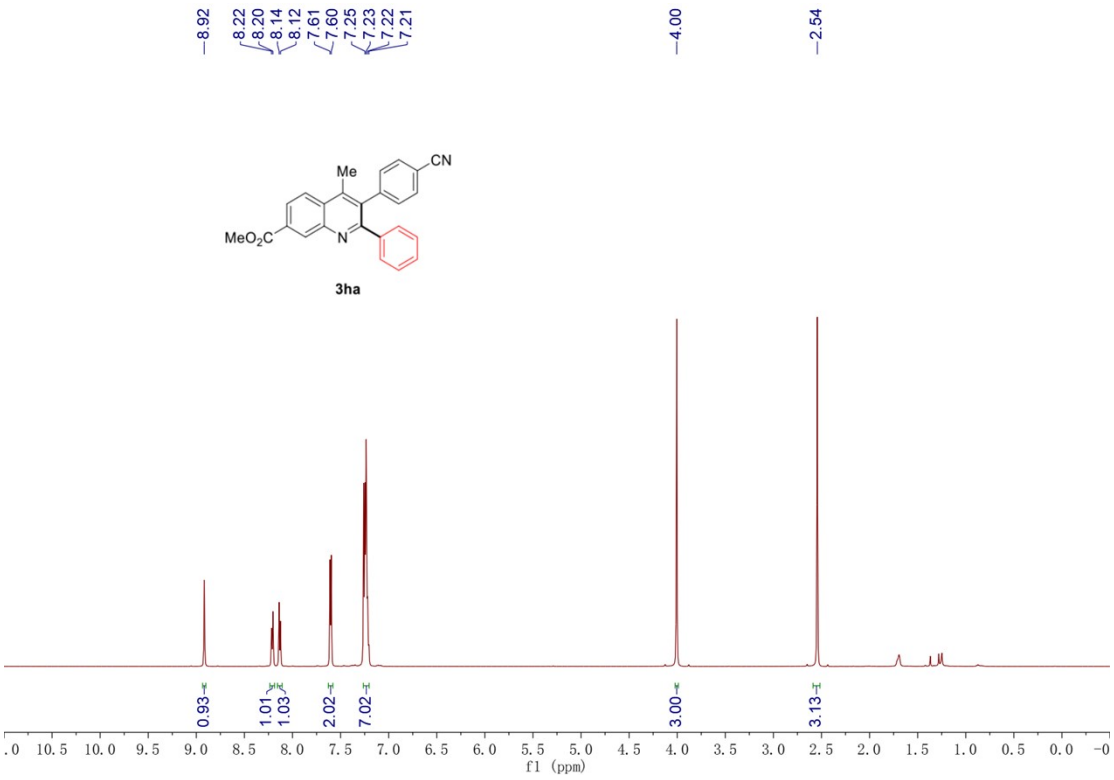
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)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7.22
7.21
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2.54
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MeO2C
N
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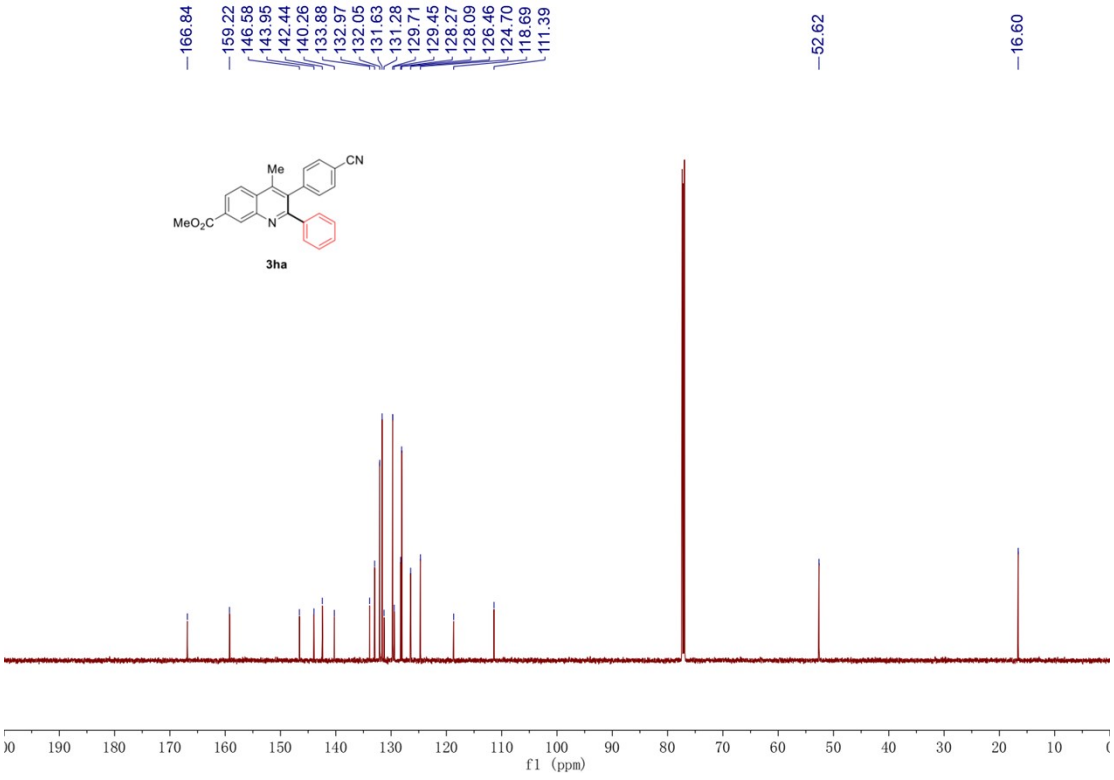
1.03
2.02
7.02
3.00
3.13
f1 (ppm)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129.45
128.27
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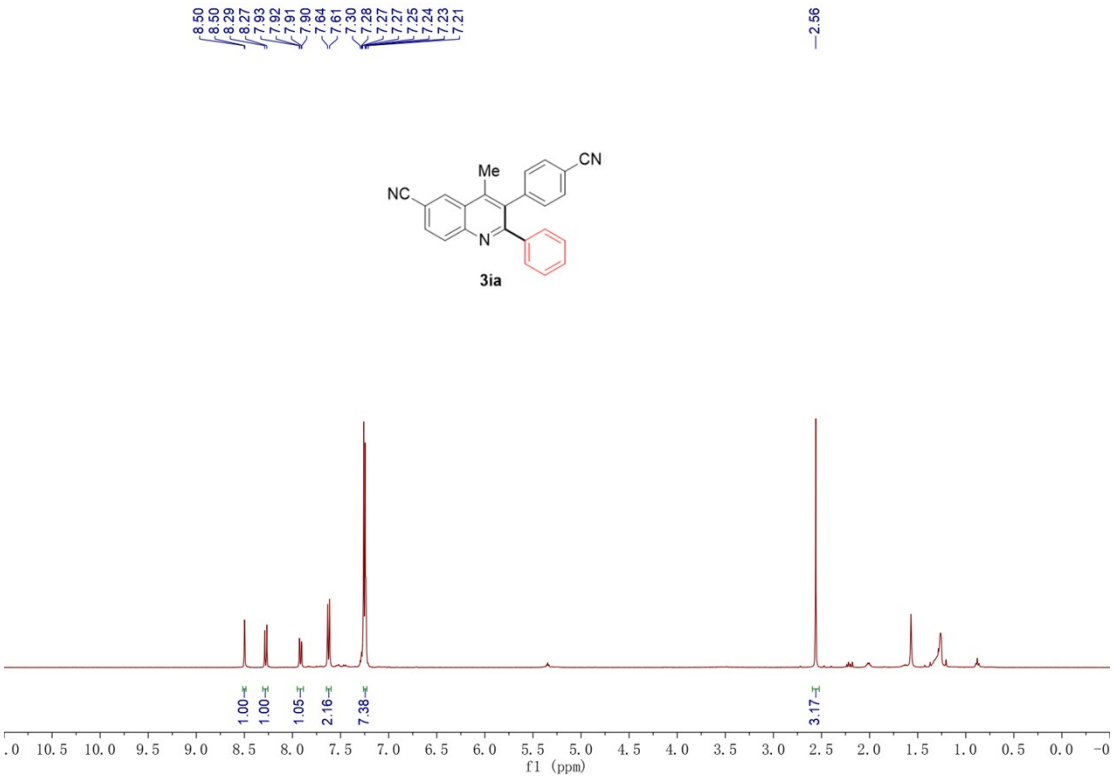
52.62
16.60
Me
CN
MeO2C
N
3ha
f1 (ppm)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7.90
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7.27
7.27
7.25
7.24
7.23
7.21
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CN
NC
N
3ia
1.00
1.00
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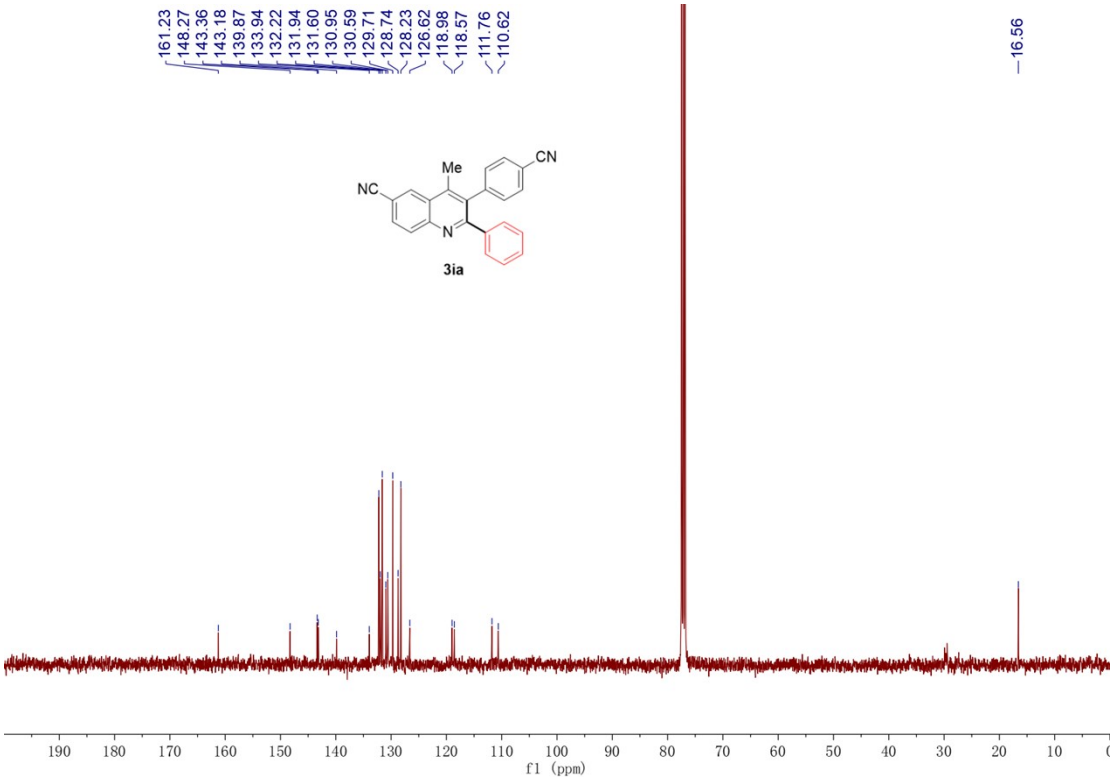
2.16
7.38
3.17
f1 (ppm)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111.76
110.62
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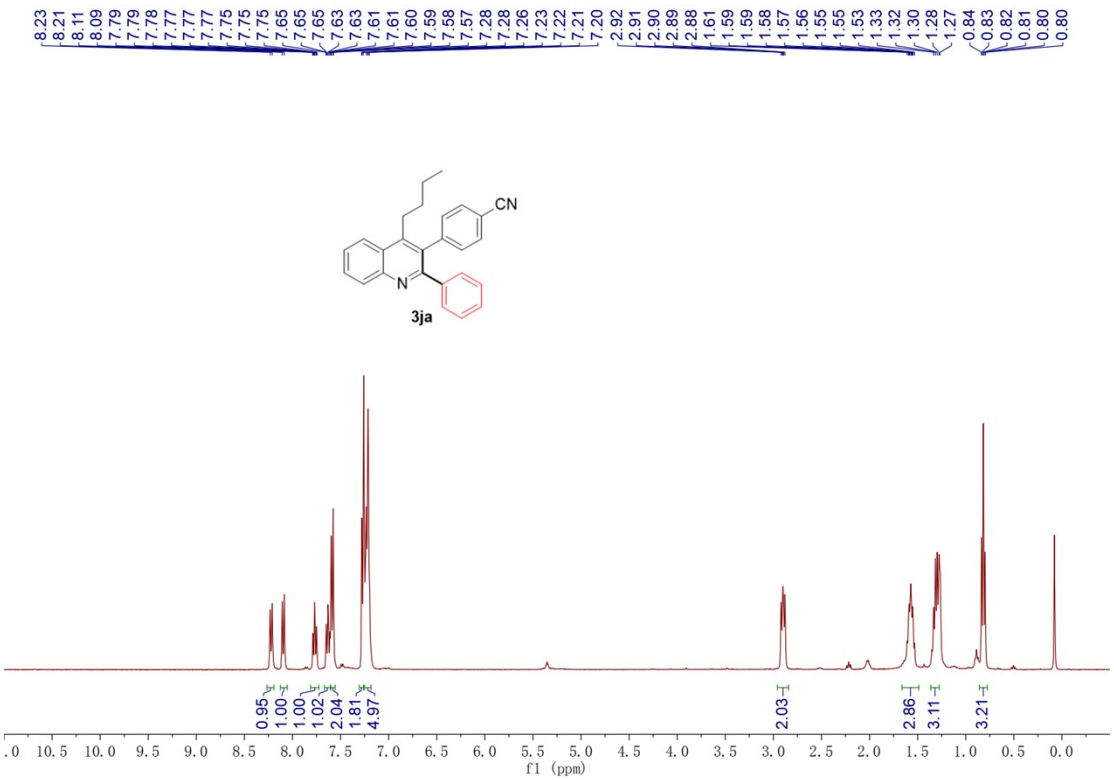
Me
CN
NC
N
3ia
f1 (ppm)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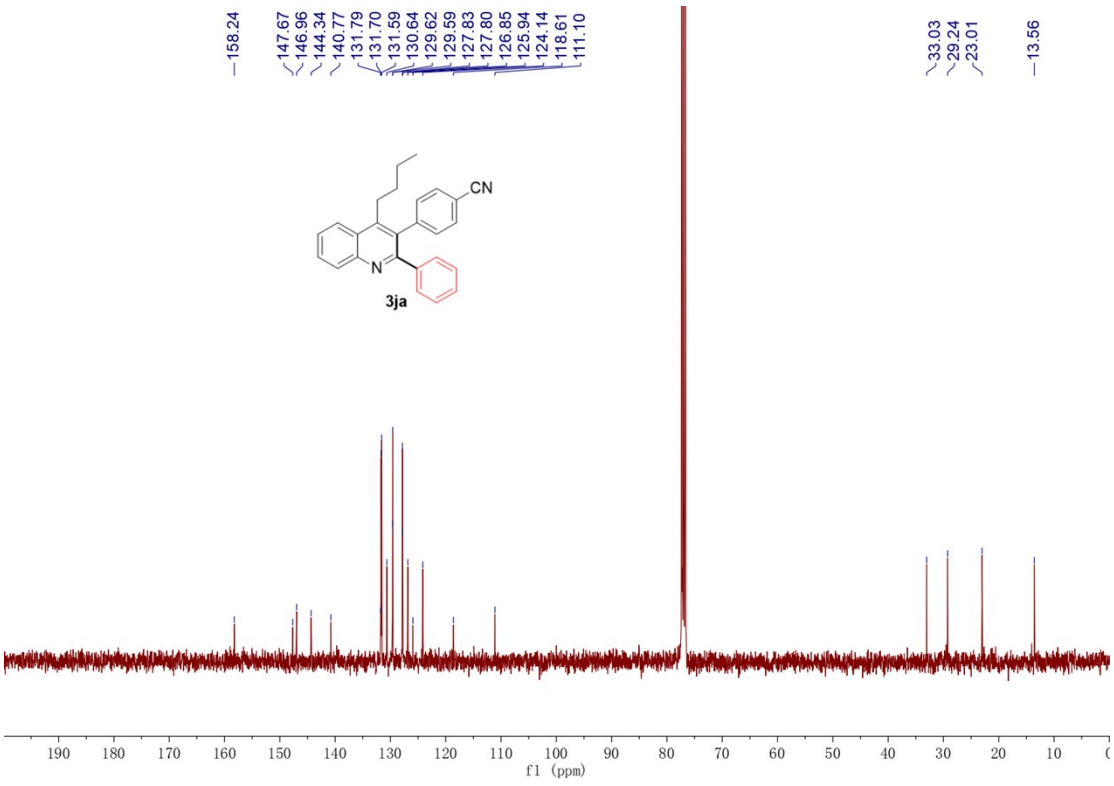
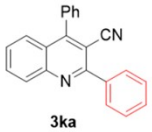
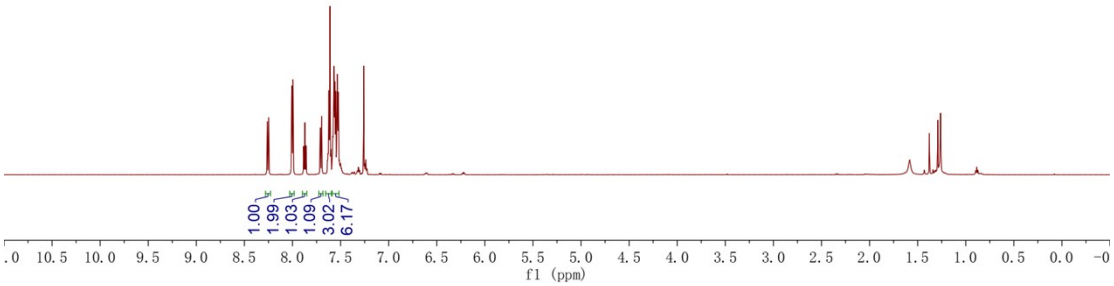
1.00
1.02
2.04
1.81
4.97
2.03
2.86
3.11
3.21
f1 (ppm)

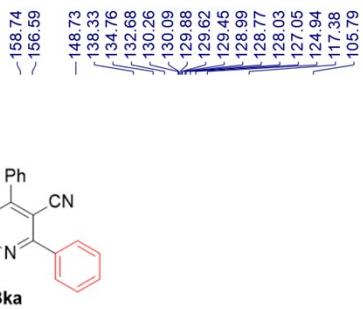

158.24
147.67
146.96
144.34
140.77
131.79
131.70
131.59
130.64
129.62
129.59
127.83
127.80
126.85
125.94
124.14
118.61
111.10
33.03
29.24
23.01
13.56
CN
N
3ja
f1 (ppm)


8.26
8.25
8.01
8.01
8.00
7.99
7.88
7.88
7.87
7.86
7.71
7.70
7.64
7.63
7.62
7.61
7.60
7.58
7.58
7.58
7.57
7.56
7.56
7.55
7.54
7.53
7.52
7.52


Ph
CN
N

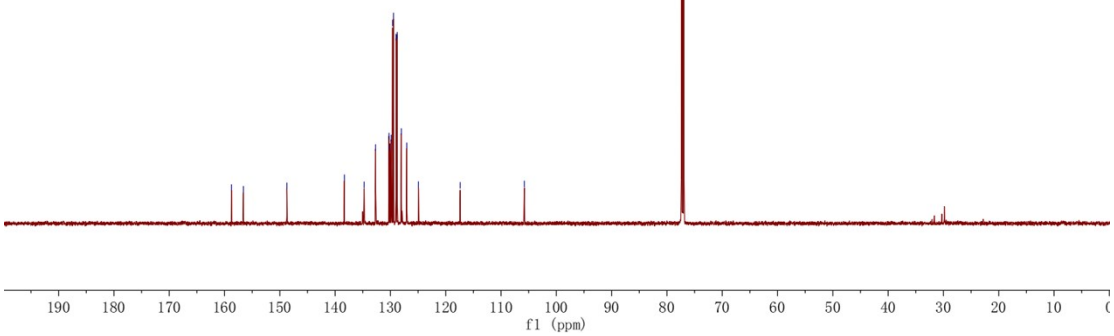
3ka


1.00
1.99
1.03
1.09
3.02
6.17
f1 (ppm)


158.74
156.59
148.73
138.33
134.76
132.68
130.26
130.09
129.88
129.62
129.45
128.99
128.77
128.03
127.05
124.94
117.38
105.79

Ph
CN
N

3ka


f1 (ppm)