A Pd-catalyzed Miyaura Borylation/Suzuki cross-coupling cascade synthesis of tricyclic biaryls

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Supporting information

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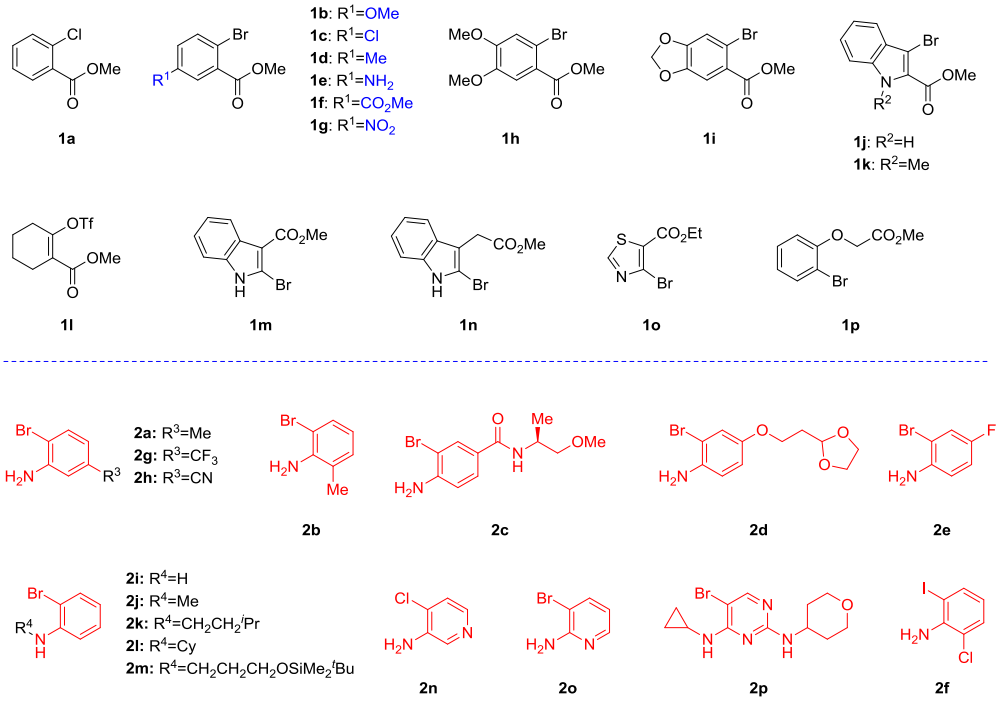
I. General Information

Glassware and stir bars were dried in an oven at 140 °C for at least 12 h and then cooled in a desiccator cabinet over Drierite prior to use. Optimization and substrate screens were performed in 20 mL tubes. All other reactions were performed in round-bottom flasks sealed with rubber septa. Plastic syringes or glass pipets were used to transfer liquid reagents. Reactions were stirred magnetically using Teflon-coated, magnetic stir bars.

All commercially available reagents were used without any further purification. Flash chromatography was carried out on pre-packed silica gel disposable columns. A gradient from 0% to 100% ethyl acetate (100% to 0% hexane) for nonpolar compounds and 20% methanol (100% to 80% CH_2Cl_2) for polar compounds were used as elutes. Analytical thin-layer chromatography (TLC) was performed with silica gel 60 F_{254}, 0.25 mm pre-coated TLC plates. TLC plates were visualized using UV_{254} and/or $KMnO_4$ stain or phosphomolybdic acid (PMA) with charring. All ^1H NMR spectra were obtained with a 400 MHz spectrometer and ^{13}C NMR spectra were obtained with a 100 MHz spectrometer. MS was performed using an analytical instrument with the UV detector set to 220 nm, 254 nm, and 280 nm, and a single quadrupole mass spectrometer using electrospray ionization (ESI) source. Samples were injected (2 μL) onto a 4.6 x 50 mm, 1.8 μM, C18 column at room temperature. A linear gradient from 10% to 100% B (MeOH + 0.1% acetic acid) in 5.0 min was followed by pumping 100% B for another 2 or 4 minutes with A being H_2O + 0.1% acetic acid. The flow rate was 1.0 mL/min. Infrared spectroscopic data are reported in wavenumbers (cm-1). High-resolution mass spectra were obtained using a liquid chromatography-electrospray ionization and time-of-flight mass spectrometer.

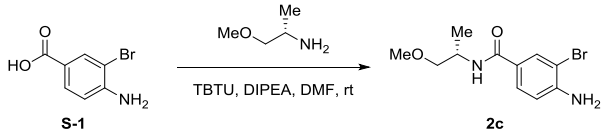
II. Synthesis of Starting materials

II-1. The structures of starting materials **1** and **2**: majority of starting material **1** and **2** were purchased from Aldrich, Alfa, Combi-Blocks, or Matrix. The synthesis of the ones that were not commercially available are in section II-2.



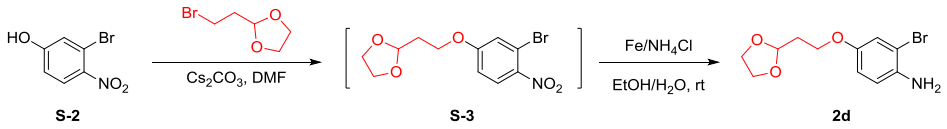
Scheme 1. Structures of starting materials **1** and **2**.

II-2. Synthesis of Starting materials



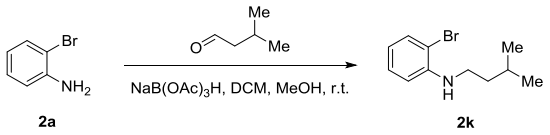
(*S*)-4-Amino-3-bromo-*N*-(1-methoxypropan-2-yl)benzamide (**2c**): To a mixture of 4-amino-3-bromobenzoic acid (**S-1**, 2.16g, 10.0 mmol, 1.0 equiv) and *O*-(benzotriazol-1-yl)-*N*,*N*,*N*′,*N*′-tetramethyluronium tetrafluoroborate (TBTU, 3.85 g, 12.0 mmol, 1.2 equiv) in 60 mL DMF was slowly added DIPEA (1.85 g, 15.0 mmol, 1.5 equiv) and (*S*)-1-methoxypropan-2-amine (1.07g, 12.0 mmol, 1.2 equiv) at room temperature. The reaction mixture was stirred at room temperature (rt) overnight. The solvents were removed under reduced pressure. The residue was purified by silica column to afford the desired product **2c** as brown oil (2.6 g, 91% yield). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.43 (d, J = 8.0 Hz, 1H), 7.21 (d, J = 4.0 Hz, 1H), 6.89 (dd, J_1 = 8.0 Hz, J_2 = 2.0 Hz, 1H), 6.58 (d, J = 8.0 Hz, 1H), 5.44 (br, 1H), 4.34-4.30 (m, 1H), 3.50 (dd, J_1 = 8.0 Hz, J_2 = 2.0 Hz, 1H), 3.42 (dd, J_1 = 8.0 Hz, J_2 = 4.0 Hz, 2H), 3.38 (s, 3H), 1.27 (d, J = 8.0 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): 166.7, 144.4, 134.8, 132.5, 116.8, 114.4, 112.3, 75.3, 59.1, 45.4, 17.6; **IR** (neat, cm^{-1}): 3411.5, 2956.3, 2918.7, 2869.6, 15968, 1509.0, 1457.0, 1428.0, 1320.0, 1161.9, 1018.2, 739.6;

HRMS-ESI (m/z): Calcd for $C_{11}H_{16}BrN_2O_2^+$ ([M+H]$^+$): 287.0390; found: 287.0390.

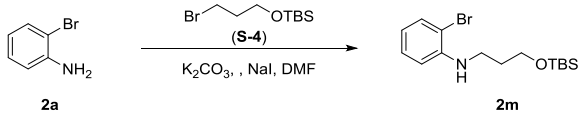


4-(2-(1,3-Dioxolan-2-yl)ethoxy)-2-bromoaniline (**2d**): To a mixture of 3-bromo-4-nitrophenol (**S-2**, 2.18 g, 10.0 mmol, 1.0 equiv) and cesium carbonate (Cs_2CO_3, 4.90 g, 15.0 mmol, 1.5 equiv) in 20mL dimethylformamide (DMF) was slowly added 2-(2-bromoethyl)-1,3-dioxolane (2.17 g, 12.0 mmol, 1.2 equiv). The reaction mixture was heated at 50℃ overnight (3-bromo-4-nitrophenol was consumed), diluted with ethyl acetate (EtOAc) (150 mL), washed with water (30 mL×2) and brine (30 mL), and dried (magnesium sulfate ($MgSO_4$)). After filtration and concentration, the crude product **S-3** was directly used in the next step without further purification.

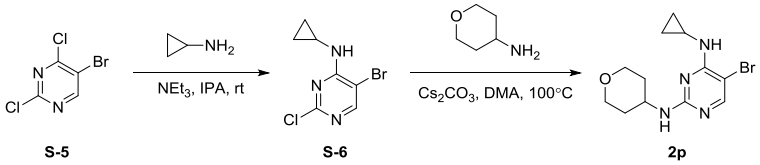
The crude product **S-3** and ammonium chloride (NH_4Cl, 530 mg, 10 mmol, 1.0 equiv) were dissolved in a mixture of ethanol (EtOH) and H_2O (3:1, 80 mL), followed by the addition of iron powder (2.8 g, 50 mmol, 5.0 equiv) at rt in the open air. The reaction mixture was heated at 60℃ for 6 h (the **S-3** was consumed). Then the reaction mixture was then cooled down to room temperature, filtered with celite and washed by methanol (MeOH). All the solvents were removed under the reduced pressure. The residue was purified by pre-packed silica gel column to afford the desired product **2d** (1.18 g, 41% yield for two steps). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.25 (d, J = 8.0 Hz, 1H), 6.33 (d, J = 2.0 Hz, 1H), 6.22 (dd, J_1 = 8.0 Hz, J_2 = 4.0 Hz, 1H), 5.06 (t, J = 4.0 Hz, 1H), 4.05 (t, J = 8.0 Hz, 2H), 4.04 (m, 1H), 4.01-3.97 (m, 2H), 3.89-3.86 (m, 2H), 2.15-2.10 (m, 2H); **^{13}C NMR** (100 MHz, DMSO-D_6): 158.7, 146.6, 132.4, 104.4, 101.2, 100.9, 98.7, 64.2, 63.2, 33.3; **IR** (neat, cm^{-1}): 3360.4, 2967.0, 2885.0, 1617.0, 1490.7, 1196.6, 1141.7, 1065.5, 1010.5, 917.0, 827.3; **HRMS-ESI** (m/z): Calcd for $C_{11}H_{15}BrNO_3^+$ ([M+H]$^+$): 288.0230; found: 288.0228; **m.p.** 83 ℃.



2-Bromo-*N*-isopentylaniline (**2k**) To a solution of **2a** (1.72 g, 10.0 mmol, 1.0 equiv) and 3-methylbutanal (860 mg, 10.0 mmol, 1.0 equiv) in a mixture of dichloromethane (DCM) and MeOH (5:1, 60 mL) was added sodium triacetoxyborohydride ($NaB(OAc)_3H$, 2.33 g 11.0 mmol, 1.1 equiv) at room temperature. The reaction mixture was stirred at rt overnight, diluted with EtOAc (100 mL), washed with H_2O (20 mL×2) and brine (20 mL), and dried ($MgSO_4$). After filtration and concentration, the residue was purified by pre-packed silica gel column (Hexane: EtOAc = 20:1) to afford the desired product **2k** (1.6 g, 66% yield) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.41 (dd, J_1 = 8.0 Hz, J_2 =2.0 Hz, 1H), 7.18 (td, J_1 = 8.0 Hz, J_2 = 4. Hz, 1H), 6.63 (d, J = 8.0 Hz, 1H), 6.55 (dt, J_1 = 8.0 Hz, J_2 =2.0 Hz, 1H), 4.22 (br, 1H), 3.19-3.14 (m, 2H), 1.78-1.71 (m, 1H), 1.60-1.57 (m, 2H), 0.97 (d, J = 8.0 Hz, 6H); **^{13}C NMR** (100 MHz, DMSO-D_6): 145.1, 132.3, 128.4, 117.3, 111.1, 109.6, 42.0, 38.2, 26.0, 22.6; **IR** (neat, cm^{-1}): 3648.7, 2947.7, 2874.4, 1652.7, 1595.8, 1508.1, 1099.2, 1012.5, 740.5; **HRMS-ESI** (m/z): Calcd for $C_{11}H_{17}BrN^+$ ([M+H]$^+$): 242.0539; found: 242.0542.



2-Bromo-*N*-(3-((tert-butyldimethylsilyl)oxy)propyl)aniline (**2m**) A solution of **2a** (1.72 g, 10.0 mmol, 1.0 equiv) in DMF (20 mL) was added potassium carbonate (K_2CO_3 , 2.76 g, 20.0 mmol, 2.0 equiv), sodium iodide (NaI, 450 mg, 3.0 mmol, 30 mol%) and (3-bromopropoxy)(*tert*-butyl)dimethylsilane (**S-4**, 2.53 g, 10.0 mmol, 1.0 equiv) at room temperature. The reaction mixture was heated at 50℃ for 24 h, diluted with EtOAc (150 mL) at room temperature, washed with H_2O (30 mL×4) and brine (30 mL), and dried ($MgSO_4$). After filtration and concentration, the residue was purified by pre-packed silica gel column (Hexane) to afford the desired product **2m** (509 mg, 15% yield, conversion<100%, not optimized) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.43 (d, *J* = 8.0 Hz, 1H), 7.19 (t, J_1 = 8.0 Hz, 1H), 6.75 (d, *J* = 8.0 Hz, 1H), 6.60 (t, *J* = 8.0 Hz, 1H), 4.68 (br, 1H), 3.78 (t, *J* = 8.0 Hz, 2H), 3.31 (t, *J* = 8.0 Hz, 2H),1.93-1.87 (m, 2H), 0.93 (s, 9H), 0.09 (s, 6H); **^{13}C NMR** (100 MHz, DMSO-D_6): 144.5, 132.4, 128.4, 118.1, 112.0, 110.0, 61.1, 41.7, 26.0, 18.4, 5.3; **IR** (neat, cm^{-1}): 3652.5, 2954.4, 2861.8, 1716.3, 1597.7, 1540.9, 1457.0, 1256.4, 1098.3, 836.0, 739.6; **HRMS-ESI** (m/z): Calcd for $C_{15}H_{27}BrNOSi^+$ ([M+H]$^+$): 344.1040; found: 344.1045.



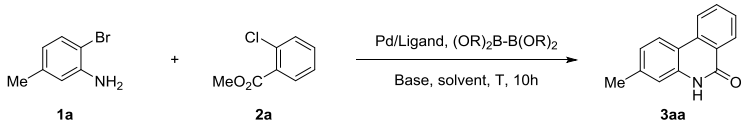
5-Bromo-N^4-cyclopropyl-N^2-(tetrahydro-2*H*-pyran-4-yl)pyrimidine-2,4-diamine (**2p**) A solution of 5-bromo-2,4-dichloropyrimidine (**S-5**, 6.81 g, 30 mmol, 1.0 equiv) in isopropanol (IPA) (70 mL) was slowly added a solution of cyclopropanamine (2.18 mL, 31.5 mmol, 1.05 equiv) and triethyl amine (NEt_3, 6.5 mL, 45 mmol, 1.5 equiv) in IPA (30 mL) at 0℃. The reaction mixture was warmed slowly to rt and stirred overnight (5-bromo-2,4-dichloropyrimidine was consumed (LC-MS)). The solvents were removed under the reduced pressure. The residue was dissolved in EtOAc (200 mL), washed by H_2O (50 mL), sodium bicarbonate ($NaHCO_3$, aq. 50 mL), and brine (50 mL), and dried ($MgSO_4$). After filtration and concentration, the crude product **S-6** was obtained as white solid (6.9 g, >90% purity in based LC), and was used as such in the next step.

A solution of **S-6** (1.23 g, 5.0 mmol, 1.0 equiv) in dimethylacetamide (DMA) (30 mL) was added Cs_2CO_3 (1.96 mg, 6.0 mmol, 1.2 equiv) and tetrahydro-2*H*-pyran-4-amine (606 mg, 6.0 mmol, 1.2 equiv) at room temperature. The reaction mixture was heated at 100℃ overnight. After filtration and concentration, the residue was purified by pre-packed silica gel column (Hexane: EtOAc = 1:1) to afford the desired product **2q** (765 mg, 49% yield) as a yellow solid. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.86 (s, 1H), 5.28 (br, 1H), 4.82 (d, *J* = 8.0 Hz, 1H), 4.01-3.96 (m, 2H), 3.51 (td, J_1 = 8.0 Hz, J_2 = 4.0 Hz, 2H), 2.78-2.74 (m, 1H), 2.08-2.03 (m, 1H), 1.59-1.49 (m, 2H), 0.83-0.78 (m, 2H), 0.59-0.55 (m, 2H); **^{13}C NMR** (100 MHz, DMSO-D_6): 160.1, 159.1 155.9, 155.8, 66.2, 47.1, 32.5, 24.0, 6.3; **IR** (neat, cm^{-1}): 3418.2, 3308.3, 3251.4, 2953.5, 2839.7, 1575.6, 1524.5, 1484.9, 1352.8, 1237.1, 1138.8, 781.0; **HRMS-ESI** (m/z): Calcd for $C_{12}H_{18}BrN_4O^+$ ([M+H]$^+$): 313.0659; found: 313.0659.

III. Optimization of Reaction Conditions

Compound **1a** and **2a** were used to optimize the reaction conditions. All the reactions were conducted at 0.2 mmol scale (**1a**) and the yields were determined by ^{1}H-NMR of crude reaction mixtures with DMF (15 μL) as the internal standard. All the starting materials, catalysts, ligands, base and solvents were purchased from Sigma Aldrich.

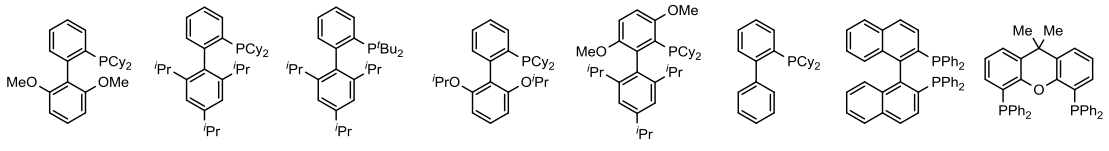
Table 1. Ligands screening



1a 0.2 mmol + **2a** → **3aa**

Entry	**1a** (equiv)	**2a** (equiv)	Pd(%)	Ligand (%)	$(OR)_2B$-$B(OR)_2$ (equiv)	Base (equiv)	Solvent[a]	T(°C)	yield(%)
1	1.0	1.0	$Pd_2(dba)_3$ (4)	PPh_3(10)	(Pin)B-B(Pin) (1.2)	K_3PO_4 (2.0)	n-BuOH	100	17
2	1.0	1.0	$Pd_2(dba)_3$ (4)	SPhos(10)	(Pin)B-B(Pin) (1.2)	K_3PO_4 (2.0)	n-BuOH	100	26
3	1.0	1.0	$Pd_2(dba)_3$ (4)	XPhos(10)	(Pin)B-B(Pin) (1.2)	K_3PO_4 (2.0)	n-BuOH	100	43
4	1.0	1.0	$Pd_2(dba)_3$ (4)	*rac*-BINAP (10)	(Pin)B-B(Pin) (1.2)	K_3PO_4 (2.0)	n-BuOH	100	N.O
5	1.0	1.0	$Pd_2(dba)_3$ (4)	^{t}BuXPhos(10)	(Pin)B-B(Pin) (1.2)	K_3PO_4 (2.0)	n-BuOH	100	52
6	1.0	1.0	$Pd_2(dba)_3$ (4)	BrettPhos(10)	(Pin)B-B(Pin) (1.2)	K_3PO_4 (2.0)	n-BuOH	100	36
7	1.0	1.0	$Pd_2(dba)_3$ (4)	RuPhos(10)	(Pin)B-B(Pin) (1.2)	K_3PO_4 (2.0)	n-BuOH	100	35
8	1.0	1.0	$Pd_2(dba)_3$ (4)	L1 (10)	(Pin)B-B(Pin) (1.2)	K_3PO_4 (2.0)	n-BuOH	100	26
9	1.0	1.0	$Pd_2(dba)_3$ (4)	L2(10)	(Pin)B-B(Pin) (1.2)	K_3PO_4 (2.0)	n-BuOH	100	40
10	1.0	1.0	$Pd_2(dba)_3$ (4)	L3 10)	(Pin)B-B(Pin) (1.2)	K_3PO_4 (2.0)	n-BuOH	100	N.O
11	1.0	1.0	$Pd_2(dba)_3$ (4)	XantPhos(10)	(Pin)B-B(Pin) (1.2)	K_3PO_4 (2.0)	n-BuOH	100	50
12	1.0	1.0	$Pd_2(dba)_3$ (4)	CyJohnPhos (10)	(Pin)B-B(Pin) (1.2)	K_3PO_4 (2.0)	n-BuOH	100	25
13	1.0	1.0	$Pd_2(dba)_3$ (4)	Q-Phos (10)	(Pin)B-B(Pin) (1.2)	K_3PO_4 (2.0)	n-BuOH	100	11
14	*1.0*	*1.0*	*$Pd_2(dba)_3$ (4)*	*PCy_3 (10)*	*(Pin)B-B(Pin) (1.2)*	*K_3PO_4 (2.0)*	*n-BuOH*	*100*	*82*
15	1.0	1.0	$Pd_2(dba)_3$ (4)	L4 (10)	(Pin)B-B(Pin) (1.2)	K_3PO_4 (2.0)	n-BuOH	100	<5
16	1.0	1.0	$Pd_2(dba)_3$ (4)	L5 (10)	(Pin)B-B(Pin) (1.2)	K_3PO_4 (2.0)	n-BuOH	100	25
17	1.0	1.0	$Pd_2(dba)_3$ (4)	L6 (10)	(Pin)B-B(Pin) (1.2)	K_3PO_4 (2.0)	n-BuOH	100	<5

[a] Aldrich, anhydrous BuOH.



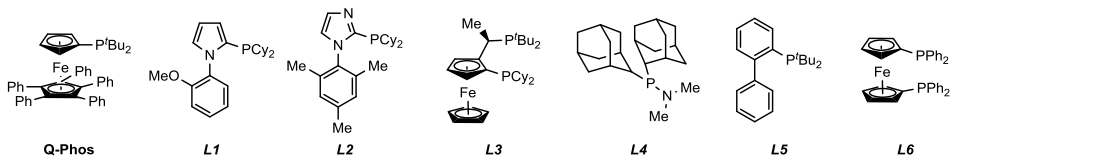
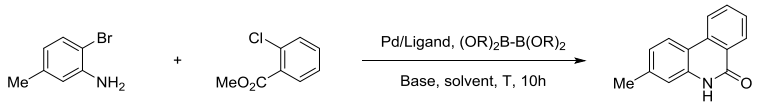


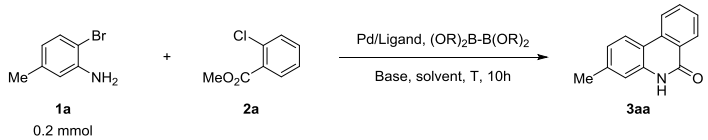
Table 2. Bases screening



Entry	**1a** (equiv)	**2a** (equiv)	Pd(%)	Ligand (%)	$(OR)_2B$-$B(OR)_2$ (equiv)	Base (equiv)	Solvent[a]	T(°C)	yield(%)
1	*1.0*	*1.0*	*$Pd_2(dba)_3$ (4)*	*PCy_3 (10)*	*(Pin)B-B(Pin) (1.2)*	*K_3PO_4 (2.0)*	*n-BuOH*	*100*	*82*
2	1.0	1.0	$Pd_2(dba)_3$ (4)	PCy_3 (10)	(Pin)B-B(Pin) (1.2)	K_2CO_3 (2.0)	n-BuOH	100	42
3	1.0	1.0	$Pd_2(dba)_3$ (4)	PCy_3 (10)	(Pin)B-B(Pin) (1.2)	Na_2CO_3 (2.0)	n-BuOH	100	68
4	1.0	1.0	$Pd_2(dba)_3$ (4)	PCy_3 (10)	(Pin)B-B(Pin) (1.2)	Cs_2CO_3 (2.0)	n-BuOH	100	25
5	1.0	1.0	$Pd_2(dba)_3$ (4)	PCy_3 (10)	(Pin)B-B(Pin) (1.2)	CsF (2.0)	n-BuOH	100	72
6	1.0	1.0	$Pd_2(dba)_3$ (4)	PCy_3 (10)	(Pin)B-B(Pin) (1.2)	NaOH (2.0)	n-BuOH	100	62
7	1.0	1.0	$Pd_2(dba)_3$ (4)	PCy_3 (10)	(Pin)B-B(Pin) (1.2)	Na^{t}OBu (2.0)	n-BuOH	100	33
8	1.0	1.0	$Pd_2(dba)_3$ (4)	PCy_3 (10)	(Pin)B-B(Pin) (1.2)	KOAc (2.0)	n-BuOH	100	35
9	1.0	1.0	$Pd_2(dba)_3$ (4)	PCy_3 (10)	(Pin)B-B(Pin) (1.2)	NaOAc (2.0)	n-BuOH	100	N.O

[a] Aldrich, anhydrous BuOH.

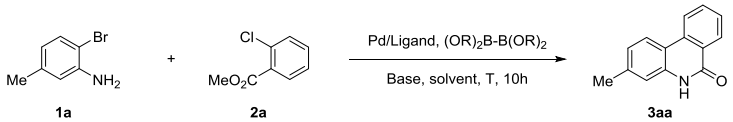
Table 3. Solvents screening



Entry	**1a** (equiv)	**2a** (equiv)	Pd(%)	Ligand (%)	$(OR)_2B$-$B(OR)_2$ (equiv)	Base (equiv)	Solvent	T(°C)	yield(%)
1	1.0	1.0	$Pd_2(dba)_3$ (4)	PCy_3 (10)	(Pin)B-B(Pin) (1.2)	K_3PO_4 (2.0)	n-BuOH(99.4%)	100	57
2	1.0	1.0	$Pd_2(dba)_3$ (4)	PCy_3 (10)	(Pin)B-B(Pin) (1.2)	K_3PO_4 (2.0)	*i*-BuOH[a]	100	48
3	*1.0*	*1.0*	*$Pd_2(dba)_3$ (4)*	*PCy_3 (10)*	*(Pin)B-B(Pin) (1.2)*	*K_3PO_4 (2.0)*	*2-ethoxylethnol[b]*	*100*	*76*
4	1.0	1.0	$Pd_2(dba)_3$ (4)	PCy_3 (10)	(Pin)B-B(Pin) (1.2)	K_3PO_4 (2.0)	1-PrOH[a]	100	57
5	1.0	1.0	$Pd_2(dba)_3$ (4)	PCy_3 (10)	(Pin)B-B(Pin) (1.2)	K_3PO_4 (2.0)	Dioxane[a]	100	35
6	1.0	1.0	$Pd_2(dba)_3$ (4)	PCy_3 (10)	(Pin)B-B(Pin) (1.2)	K_3PO_4 (2.0)	Dioxane/n-BuOH (4:1)[a]	100	36
7	1.0	1.0	$Pd_2(dba)_3$ (4)	PCy_3 (10)	(Pin)B-B(Pin) (1.2)	K_3PO_4 (2.0)	Dioxane/H_2O (10:1)	100	50
8	1.0	1.0	$Pd_2(dba)_3$ (4)	PCy_3 (10)	(Pin)B-B(Pin) (1.2)	K_3PO_4 (2.0)	DMF[a]	100	43
9	1.0	1.0	$Pd_2(dba)_3$ (4)	PCy_3 (10)	(Pin)B-B(Pin) (1.2)	K_3PO_4 (2.0)	DMSO[a]	100	35

[a] Aldrich, anhydrous solvents; [b] Aldrich, 99%.

Table 3. Pd catalysts screening

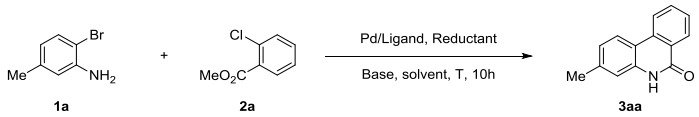


1a 0.2 mmol + **2a** → **3aa**

Entry	**1a** (equiv)	**2a** (equiv)	Pd(%)	Ligand (%)	$(OR)_2B\text{-}B(OR)_2$ (equiv)	Base (equiv)	Solvent[a]	T(°C)	yield(%)
1	1.0	1.0	$Pd_2(dba)_3$ (4)	PCy_3 (10)	(Pin)B-B(Pin) (1.2)	K_3PO_4 (2.0)	n-BuOH(99.4%)	100	54
2	1.0	1.0	$Pd(OAc)_3$ (4)	PCy_3 (10)	(Pin)B-B(Pin) (1.2)	K_3PO_4 (2.0)	n-BuOH(99.4%)	100	50
3	1.0	1.0	$PdCl_2$ (4)	PCy_3 (10)	(Pin)B-B(Pin) (1.2)	K_3PO_4 (2.0)	n-BuOH(99.4%)	100	50
4	1.0	1.0	$Pd(dppf)Cl_2$ (4)	N.O	(Pin)B-B(Pin) (1.2)	K_3PO_4 (2.0)	n-BuOH(99.4%)	100	27
5	1.0	1.0	$Pd_2(MeCN)Cl_2$ (4)	PCy_3 (10)	(Pin)B-B(Pin) (1.2)	K_3PO_4 (2.0)	n-BuOH(99.4%)	100	46
6	1.0	1.0	$Pd(PhCN)Cl_2$ (4)	PCy_3 (10)	(Pin)B-B(Pin) (1.2)	K_3PO_4 (2.0)	n-BuOH(99.4%)	100	52
7	1.0	1.0	$Pd(\pi\text{-cinnamyl})Cl_2$(4)	PCy_3 (10)	(Pin)B-B(Pin) (1.2)	K_3PO_4 (2.0)	n-BuOH(99.4%)	100	60

[a] Aldrich, 99.4%.

Table 5. Catalyst loading, substrate ration and reducing reagent loading screening

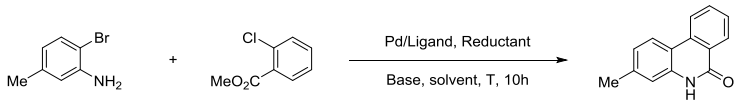


1a 0.2 mmol + **2a** → **3aa**

Entry	**1a** (equiv)	**2a** (equiv)	Pd(%)	Ligand (%)	Reductant (equiv)	Base (equiv)	Solvent[a]	T(°C)	yield(%)
1	1.0	1.0	$Pd_2(dba)_3$ (4)	PCy_3 (10)	(Pin)B-B(Pin) (1.2)	K_3PO_4 (2.0)	2-ethoxyethanol	100	72
2	1.0	1.0	$Pd_2(dba)_3$ (3)	PCy_3 (8)	(Pin)B-B(Pin) (1.2)	K_3PO_4 (2.0)	2-ethoxyethanol	100	17
3	1.0	1.0	$Pd_2(dba)_3$ (6)	PCy_3 15	(Pin)B-B(Pin) (1.2)	K_3PO_4 (2.0)	2-ethoxyethanol	100	72
4	1.0	1.0	$Pd_2(dba)_3$ (4)	PCy_3 (10)	(Pin)B-B(Pin) (1.2)	K_3PO_4 (1.0)	2-ethoxyethanol	100	79
5	1.0	1.0	$Pd_2(dba)_3$ (4)	PCy_3 (10)	(Pin)B-B(Pin) (1.2)	K_3PO_4 (3.0)	2-ethoxyethanol	100	80
6	1.0	1.0	$Pd_2(dba)_3$ (4)	PCy_3 (10)	(Pin)B-B(Pin) (1.2)	K_3PO_4 (2.0)	2-ethoxyethanol (1.0 mL)	100	62
7	1.0	1.0	$Pd_2(dba)_3$ (4)	PCy_3 (10)	(Pin)B-B(Pin) (1.2)	K_3PO_4 (2.0)	2-ethoxyethanol (3.0 mL)	100	48

[a] Aldrich, 99%.

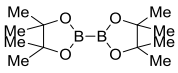
Table 6. Diboronic reagents screening



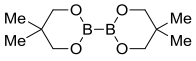
1a 0.2 mmol | **2a** | **3aa**

Entry	**1a** (equiv)	**2a** (equiv)	Pd(%)	Ligand (%)	Reductant (equiv)	Base (equiv)	Solvent[a]	T(°C)	yield(%)
1	1.0	1.0	$Pd_2(dba)_3$ (4)	PCy_3 (10)	(Pin)B-B(Pin) (1.2)	K_3PO_4 (2.0)	2-ethoxyethanol	100	72
2	1.0	1.0	$Pd_2(dba)_3$ (4)	PCy_3 (10)	(Neo)B-B(Neo) (1.2)	K_3PO_4 (2.0)	2-ethoxyethanol	100	66
3	1.0	1.0	$Pd_2(dba)_3$ (4)	PCy_3 (10)	$(OH)_2$B-B$(OH)_2$ (1.2)	K_3PO_4 (2.0)	2-ethoxyethanol	100	49
4	1.0	1.0	Pd(π-cinnamyl)Cl_2 (4)	PCy_3 (10)	(Pin)B-B(Pin) (1.2)	K_3PO_4 (2.0)	2-ethoxyethanol	100	66
5	1.5	1.0	$Pd_2(dba)_3$ (4)	PCy_3 (10)	(Pin)B-B(Pin) (1.8)	K_3PO_4 (3.0)	2-Ethoxyethanol	100	92
6	***1.0***	***1.5***	***$Pd_2(dba)_3$ (4)***	***PCy_3 (10)***	***(Pin)B-B(Pin) (1.8)***	***K_3PO_4 (3.0)***	***2-ethoxyethanol***	***100***	***96***

[a] Aldrich, 99%.



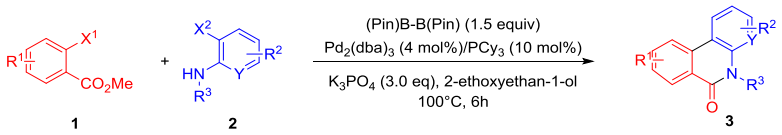
(Pin)B-B(Pin)



(Neo)B-B(Neo)

$(OH)_2$B-B$(OH)_2$

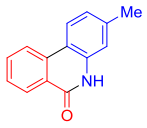
IV. **General Procedures and Product Spectra Data**



1 2 3

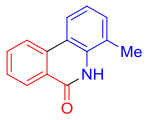
General procedure A. To a mixture of **1** (1.3 mmol, 1.3 equiv), **2** (1.0 mmol, 1.0 equiv), bis(pinacolato)diboron (1.5 mmol, 1.5 equiv), K_3PO_4 (3.0 mmol, 3.0 equiv), $Pd_2(dba)_3$ (36.6 mg, 4 mol%) and PCy_3 (28 mg, 10 mol%) was added 2-ethoxyethan-1-ol (10 mL, 0.1 M) at rt under N_2 atmosphere. The reaction mixture was quickly heated to 100℃ for 30 min to 5h and then cooled to room temperature. The reaction mixture was diluted with EtOAc (100 mL), washed with H_2O (20 mL), NaOH (2.0 M aq. 20 mL×2), and brine (20 mL), and dried ($MgSO_4$). After filtration and concentration under reduced pressure, the residue was purified by a prepacked silica gel column (Hexane: EtOAc = 10:1-7:3) to afford the desired product **3**.

General Procedure B. The reactions were conducted under the same conditions as general procedure A with 0.5 mmol of **2** (1.0 equiv).



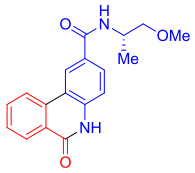
3aa

3-Methylphenanthridin-6(5*H*)-one (**3aa**)[1]: The title compound (152 mg, 73% yield) was prepared according to the general procedure A as a white solid. **^{1}H NMR** (400 MHz, DMSO-D_6): δ 11.61 (s, 1H), 8.45 (d, J = 8.0 Hz, 1H), 8.29 (d, J = 8.0 Hz, 1H), 8.26 (d, J = 8.0 Hz, 1H), 7.82 (dd, J_1 = 8.0 Hz, J_2 = 4.0 Hz, 1H), 7.60 (t, J = 8.0 Hz, 1H), 7.16 (s,1H), 7.09 (d, J = 8.0 Hz, 1H), 2.39 (s, 3H).



3ab

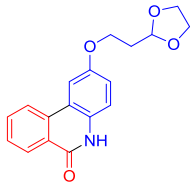
4-Methylphenanthridin-6(5*H*)-one (**3ab**)[2]: The title compound (164 mg, 78% yield) was prepared according to the general procedure A as a white solid. **^{1}H NMR** (400 MHz, DMSO-D_6): δ 10.68 (s, 1H), 8.51 (d, J = 8.0 Hz, 1H), 8.34 (dd, J_1 = 8.0 Hz, J_2 = 4.0 Hz, 1H), 8.26 (d, J = 8.0 Hz, 1H), 7.85 (dd, J_1 = 8.0 Hz, J_2 = 4.0 Hz, 1H), 7.64 (t, J = 8.0 Hz, 1H), 7.35 (d, J = 8.0 Hz, 1H), 7.18 (t, J = 8.0 Hz, 1H), 2.48 (s, 3H).



3ac

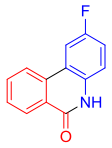
[1] Bhakuni, B. S.; Kumar, A.; Balkrishna, S. J.; Sheikh, J. A.; Konar, S.; Kumar, S. *Org. Lett*. **2012**, 2838-2841.
[2] Ferraccioli, R.; Carenzi, D.; Rombola, O.; Catellani, M. *Org. Lett*. **2004**, *6*, 4759-4762.

(*S*)-*N*-(1-Methoxypropan-2-yl)-6-oxo-5,6-dihydrophenanthridine-2-carboxamide (**3ac**): The title compound (206 mg, 66% yield) was prepared according to the general procedure A as a yellow solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.82 (br, 1H), 8.54 (d, *J* = 8.0 Hz, 1H), 8.30 (d, *J* = 8.0 Hz, 1H), 8.26 (d, *J* = 8.0 Hz, 1H), 7.84 (t, *J* = 8.0 Hz, 1H), 7.68-7.65 (m, 2H), 7.60 (d, *J* = 8.0 Hz, 1H), 6.50 (br, 1H), 4.45-4.39 (m, 1H), 3.56 (dd, J_1 = 8.0 Hz, J_2 = 4.0 Hz, 1H), 3.48 (dd, J_1 = 8.0 Hz, J_2 = 4.0 Hz, 1H), 3.43 (s, 3H), 1.35 (d, *J* = 4.0 Hz, 3H); **^{13}C NMR** (100 MHz, DMSO-D_6) 166.2, 160.8, 136.4, 135.6, 133.6, 132.9, 128.6, 127.5, 126.1, 123.22, 123.20, 120.5, 119.6, 115.8, 75.0, 58.1, 44.6, 17.3; **IR** (neat, cm^{-1}) 3268.8, 2871.5, 2821.4, 1673.0, 1632.7, 1546.6, 1357.6, 1137.8, 890.0; **HRMS-ESI** (m/z) Calcd for $C_{18}H_{19}N_2O_3^+$ ([M+H]$^+$): 311.1390; found: 311.1391; **m.p.** 245℃.



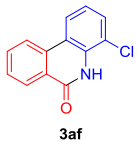
3ad

2-(2-(1,3-Dioxolan-2-yl)ethoxy)phenanthridin-6(5*H*)-one (**3ad**): The title compound (188 mg, 60% yield) was prepared according to the general procedure A as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.43 (br, 1H), 8.49 (d, *J* = 8.0 Hz, 1H), 8.10 (d, *J* = 8.0 Hz, 1H), 7.76 (t, *J* = 8.0 Hz, 1H), 7.63 (t, *J* = 8.0 Hz, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 6.70 (d, 1H), 5.14 (t, *J* = 8.0 Hz, 1H), 4.24 (t, *J* = 8.0 Hz, 2H), 4.03-4.01 (m, 2H), 3.93-3.91 (m, 2H), 2.25-2.20 (m, 2H); **^{13}C NMR** (100 MHz, DMSO-D_6) 161.1, 159.4, 138.0, 134.5, 132.8, 127.4, 126.8, 124.8, 124.3, 122.0, 111.2, 110.4, 109.6, 101.1, 100.1, 64.3, 63.7, 33.2; **IR** (neat, cm^{-1}) 2949.6, 2885.0, 1360.4, 1658.5, 16103, 1146.5, 764.6; **HRMS-ESI** (m/z) Calcd for $C_{18}H_{18}NO_4^+$ ([M+H]$^+$): 312.1230; found: 312.1233; **m.p.** 160℃.



3ae

2-Fluorophenanthridin-6(5*H*)-one (**3ae**)[3]: The title compound (112 mg, 53% yield) was prepared according to the general procedure A as a white solid. **^{1}H NMR** (400 MHz, DMSO-D_6) δ 11.73 (s, 1H), 8.62 (d, *J* = 8.0 Hz, 1H), 8.33 (d, *J* = 8.0 Hz, 1H), 8.27 (d, *J* = 8.0 Hz, 1H), 7.87 (dd, J_1 = 8.0 Hz, J_2 = 8.0 Hz, 1H), 7.68 (dd, J_1 = 8.0 Hz, J_2 = 8.0 Hz, 1H), 7.39-7.37 (m, 2H).



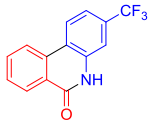
3af

4-Chlorophenanthridin-6(5*H*)-one (**3af**)[4]: The title compound (66 mg, 29% yield) was prepared according to the general procedure A as a white solid. **^{1}H NMR** (400 MHz, DMSO-D_6) δ 10.77 (s, 1H), 8.56 (d, *J* = 8.0 Hz, 1H), 8.43 (d, *J* = 8.0 Hz, 1H), 8.37 (d, *J* = 4.0 Hz, 1H), 7.91 (dd, J_1 = 8.0 Hz, J_2 = 4.0 Hz, 1H), 7.71 (t, *J*

[3] Yuan, M.; Chen, L.; Wang, J.; Chen, S.; Wang, K.; Xue, Y.; Yao, G.; Luo, Z.; Zhang, Y.; Yuan, M.; Chen, L.; Wang, J.; Chen, S.; Wang, K.; Xue, Y.; Yao, G.; Luo, Z.; Zhang, Y.; *Org. Lett.* **2015**, *17*, 346-349.

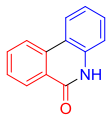
[4] Dubost, E.; Magnelli, R.; Cailly, T.; Legay, R.; Fabis, F.; Rault, S. *Tetrahedron*, **2010**, *66*, 5008-5016.

= 8.0 Hz, 1H), 7.67 (d, *J* = 8.0 Hz, 1H), 7.30 (t, *J* = 8.0 Hz, 1H).



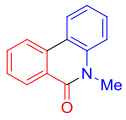
3ag

3-(Trifluoromethyl)phenanthridin-6(5*H*)-one (**3ag**)[3]: The title compound (100 mg, 38% yield) was prepared according to the general procedure A as a white solid. **^{1}H NMR** (400 MHz, DMSO-D_6) δ 12.01 (s, 1H), 8.74 (s, 1H), 8.69 (d, *J* = 8.0 Hz, 1H), 8.34 (dd, J_1 = 8.0 Hz, J_2 = 4.0 Hz, 1H), 7.90 (dd, J_1 = 8.0 Hz, J_2 = 8.0 Hz, 1H), 7.82 (dd, J_1 = 8.0 Hz, J_2 = 4.0 Hz, 1H), 7.72 (dd, J_1 = 8.0 Hz, J_2 = 8.0 Hz, 1H), 7.53 (d, *J* = 8.0 Hz, 1H).



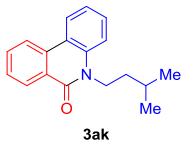
3ai

Phenanthridin-6(5*H*)-one (**3ai**)[5]: The title compound (98 mg, 50% yield) was prepared according to the general procedure A as a white solid. **^{1}H NMR** (400 MHz, DMSO-D_6) δ 11.68 (s, 1H), 8.51 (d, *J* = 8.0 Hz, 1H), 8.39 (d, *J* = 8.0 Hz, 1H), 8.32 (d, *J* = 8.0 Hz, 1H), 7.86 (dd, J_1 = 8.0 Hz, J_2 = 4.0 Hz, 1H), 7.64 (dd, J_1 = 8.0 Hz, J_2 = 8.0 Hz, 1H), 7.37 (d, *J* = 8.0 Hz, 1H), 7.27 (td, J_1 = 8.0 Hz, J_2 = 4.0 Hz, 1H).



3aj

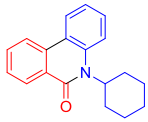
5-Methylphenanthridin-6(5*H*)-one (**3aj**)[6]: The title compound (85 mg, 81% yield) was prepared according to the general procedure A as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.56 (d, *J* = 8.0 Hz, 1H), 8.31-8.27 (m, 2H), 7.76 (t, *J* = 8.0 Hz, 1H), 7.59 (t, *J* = 8.0 Hz, 1H), 7.56 (t, *J* = 8.0 Hz, 1H), 7.43 (d, *J* = 8.0 Hz, 1H), 7.33 (t, *J* = 8.0 Hz, 1H), 3.83 (s, 3H).



3ak

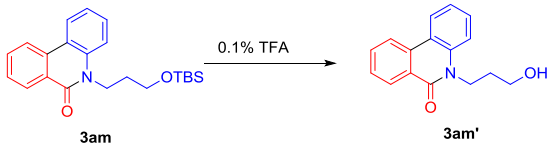
5-Isopentylphenanthridin-6(5*H*)-one (**3ak**): The title compound (247 mg, 93% yield) was prepared according to the general procedure A as a gel. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.56 (d, *J* = 8.0 Hz, 1H), 8.32-8.28 (m, 2H), 7.76 (t, *J* = 8.0 Hz, 1H), 7.61-7.53 (m, 2H), 7.42 (d, *J* = 8.0 Hz, 1H), 7.32 (t, *J* = 8.0 Hz, 1H), 4.42 (t, *J* = 8.0 Hz, 2H), 1.88-1.79 (m, 1H), 1.73-1.67 (m, 2H), 1.07 (d, *J* = 8.0 Hz, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$) 161.2, 137.0, 133.5, 132.3, 129.5, 128.7, 127.9, 125.5, 123.4, 122.2, 121.5, 119.5, 115.0, 41.4, 36.0, 26.6, 22.6; **IR** (neat, cm^{-1}) 3074.0, 2956.3, 2922.6, 2868.6, 1648.8, 1587.1, 1437.7, 1364.7, 1335.5, 1177.3 1116.6, 747.3; **HRMS-ESI** (m/z) Calcd for $C_{18}H_{20}NO^+$ ([M+H]$^+$): 266.1545; found: 266.1537.

[5] Bhakuni, B. S.; Kumar, A.; Balkrishna, S. J.; Sheikh, J. A.; Konar, S.; Kumar, S. *Org. Lett*. **2012**, 2838-2841.
[6] Feng, M.; Tang, B.; Xu, H-X.; Jiang, X. *Org. Lett*. **2016**, *18*, 4352-4355



3al

5-Cyclohexylphenanthridin-6(5*H*)-one (**3al**)[7]: The title compound (244 mg, 88% yield) was prepared according to the general procedure A as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.50 (d, *J* = 8.0 Hz, 1H), 8.28-8.22 (m, 2H), 7.73 (t, *J* = 8.0 Hz, 1H), 7.64 (m, 1H), 7.56 (t, *J* = 8.0 Hz, 1H), 7.49 (t, *J* = 8.0 Hz, 1H), 7.28 (t, *J* = 8.0 Hz, 1H), 4.79 (m, 1H), 2.74-2.72 (m, 2H), 1.98-1.94 (m, 2H), 1.87-1.83 (m, 2H), 1.79-1.75 (m, 1H), 1.55-1.36 (m, 3H).



3am 3am'

5-(3-((*tert*-Butyldimethylsilyl)oxy)propyl)phenanthridin-6(5H)-one (**3am**): The title compound (125 mg, 68% yield) was prepared according to the general procedure A as a colorless oil. However, **3am** was not stable under weak acidic conditions, thus unprotected **3am'** was prepared for the characterization.

5-(3-Hydroxypropyl)phenanthridin-6(5*H*)-one (**3am'**): **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.56 (d, *J* = 8.0 Hz, 1H), 8.35-8.29 (m, 2H), 7.79 (t, *J* = 8.0 Hz, 1H), 7.61 (t, *J* = 8.0 Hz, 1H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.50 (d, *J* = 8.0 Hz, 1H), 7.36 (t, *J* = 8.0 Hz, 1H), 4.60 (t, *J* = 8.0 Hz, 2H), 3.57-3.55 (t, *J* = 8.0 Hz, 2H), 2.09-2.06 (m, 2H); **^{13}C NMR** (100 MHz, DMSO-D_6) 162.7, 136.7, 133.7, 132.8, 129.7, 129.0, 128.1, 124.8, 123.6, 122.9, 121.6, 120.0, 115.2, 58.2, 39.2, 30.3; **IR** (neat, cm^{-1}) 3403.7, 2948.6, 1631.5, 1608.3, 1584.2, 1438.6, 1370.2, 1334.5, 1056.8, 749.2, 725.1; **HRMS-ESI** (m/z) Calcd for $C_{16}H_{16}NO_2^+$ ([M+H]$^+$): 254.1176; found: 254.1179; **m.p.** 103℃.

3an

Benzo[c][1,7]naphthyridin-6(5*H*)-one (**3an**)[8]: The title compound (90 mg, 63% yield) was prepared according to the general procedure A as a white solid. **^{1}H NMR** (400 MHz, DMSO-D_6) δ 12.03 (s, 1H), 8.71 (s, 1H), 8.65 (d, *J* = 8.0 Hz, 1H), 8.47-8.46 (m, 2H), 8.39 (dd, J_1 = 8.0 Hz, J_2 = 4.0 Hz, 1H), 7.97 (dd, J_1 = 8.0 Hz, J_2 = 8.0 Hz, 1H), 7.83 (td, dd, J_1 = 8.0 Hz, J_2 = 4.0 Hz, 1H).

3ao

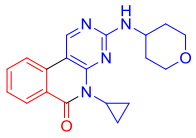
Benzo[c][1,8]naphthyridin-6(5*H*)-one (**3ao**)[9]: The title compound (124 mg, 63% yield) was prepared according to the general procedure A as a white solid. **^{1}H NMR** (400 MHz, DMSO-D_6) δ 12.03 (s, 1H),

[7] Lu, C.; Dubrovskiy, A. V.; Larock, R. C. *J. Org. Chem.* **2012**, *77*, 8648-8656

[8] Rocca, P.; Cochennec, C.; Marsais, F.; Thomas-dit-Dumont, L.; Mallet, M.; Godard, A.; Queguiner, G. *J. Org. Chem.* **1993**, *58*, 7832-7838.

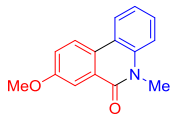
[9] Ferraris, D.; Ko, Y-S.; Pahutski, T.; Ficco, R. P.; Serdyuk, L.; Alemu, C.; Bradford, C.; Chiou, T.; Hoover, R.; Huang, S.; Lautar, S.; Liang, S.; Lin, Q.; Lu, M. X.-C.; Mooney, M.; Morgan, L.; Qian, Y.; Tran, S.; Williams, L.R.; Wu, Q. Y.; Zhang, J.; Zou, Y.; Kalish, V. *J. Med. Chem.* **2003**, *46*, 3138-3151.

8.82 (d, J = 8.0 Hz, 1H), 8.55 (d, J = 8.0 Hz, 1H), 8.50 (dd, J_1 = 8.0 Hz, J_2 = 4.0 Hz, 1H), 8.33 (d, J = 8.0 Hz, 1H), 7.90 (dd, J_1 = 8.0 Hz, J_2 = 8.0 Hz, 1H), 7.70 (dd, J_1 = 8.0 Hz, J_2 = 8.0 Hz, 1H), 7.34 (dd, J_1 = 8.0 Hz, J_2 = 8.0 Hz, 1H).



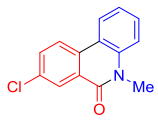
3ap

5-Cyclopropyl-3-((tetrahydro-2*H*-pyran-4-yl)amino)pyrimido[4,5-*c*]isoquinolin-6(5*H*)-one (**3ap**): The title compound (160 mg, 66% yield) was prepared according to the general procedure A as a yellow solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 10.06 (br, 1H), 8.72 (s, 1H), 8.39 (d, J = 8.0 Hz, 1H), 7.84-7.77 m, 2H), 7.61 (t, J = 8.0 Hz, 1H), 4.21-4.19 (m, 1H), 4.10-4.05 (m, 2H), 3.55 (t, J = 8.0 Hz, 2H), 2.99-2.96 (m, 1H), 2.09-2.07 (m, 2H), 1.92-1.86 (m, 2H), 1.37-1.32 (m, 2H), 0.94-0.90 (m, 2H); **^{13}C NMR** (100 MHz, DMSO-D_6) 163.1, 159.3, 158.1, 156.2, 153.2, 133.2, 131.8, 127.8, 126.7, 123.3, 120.3, 66.2, 53.1, 32.3, 25.3, 9.5; **IR** (neat, cm^{-1}) 3069.2, 2962.1, 2926.5, 2855.1, 1697.1, 1643.1, 1430.9, 1276.7, 1188.9, 1133.0, 786.8; **HRMS-ESI** (m/z) Calcd for $C_{19}H_{21}N_4O_2^+$ ([M+H]$^+$): 337.1659; found: 337.1661; **m.p.** 210℃.



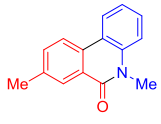
3bj

8-Methoxy-5-methylphenanthridin-6(5*H*)-one (**3bj**)[6]: The title compound (99 mg, 83% yield) was prepared according to the general procedure B as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.22-8.20 (m, 2H), 7.98 (s, 1H), 7.51 (t, J = 8.0 Hz, 1H), 7.42 (d, J = 8.0 Hz, 1H), 7.37-7.30 (m, 2H), 3.97 (s, 3H), 3.84 (s, 3H).



3cj

8-chloro-5-methylphenanthridin-6(5*H*)-one (**3cj**): The title compound (73 mg, 60% yield) was prepared according to the general procedure B as a light yellow solid. **^{1}H NMR** (400 MHz, CD_3OD) δ 8.53 (s, 1H), 8.25-8.21 (m, 2H), 7.70 (d, J = 8.0 Hz, 1H), 7.58 (d, J = 8.0 Hz, 1H), 7.41 (d, J = 8.0 Hz, 1H), 7.35 (t, J = 8.0 Hz, 1H), 3.82 (s, 3H); **^{13}C NMR** (100 MHz, CD_3OD) 155.8, 133.6, 129.4, 128.1, 127.6, 125.5, 123.6, 122.5, 119.2, 118.8, 118.1, 113.9, 110.7, 25.4; **IR** (neat, cm^{-1}) 3084.6, 1690.3, 1645.0, 1207.2, 1141.7, 746.3; **HRMS-ESI** (m/z) Calcd for $C_{14}H_{11}ClNO^+$ ([M+H]$^+$): 244.0524; found: 244.0526. **m.p.** 158℃.

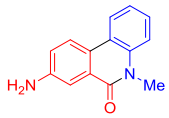


3dj

5,8-Dimethylphenanthridin-6(5*H*)-one (**3dj**)[10]: The title compound (92 mg, 82% yield) was prepared according to the general procedure B as a white solid. **^{1}H** NMR (400 MHz, $CDCl_3$) δ 8.36 (m, 1H), 8.26 (d,

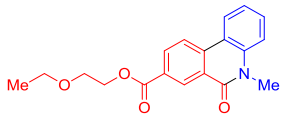
[10] Iwasaki, H.; Eguchi, T.; Tsutsui, N.; Ohno, H.; Tanaka, T. *J. Org. Chem.* **2008**, *73*, 7145-7152

J = 8.0 Hz, 1H), 8.18 (d, *J* = 8.0 Hz, 1H), 7.58 (d, *J* = 8.0 Hz, 1H), 7.53 (t, *J* = 8.0 Hz, 1H), 7.42 (d, *J* = 8.0 Hz, 1H), 7.32 (t, *J* = 8.0 Hz, 1H), 3.82 (s, 3H), 2.53 (s, 3H).



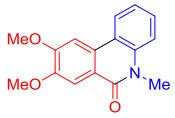
3ej

8-Amino-5-methylphenanthridin-6(5*H*)-one (**3ej**): The title compound (82 mg, 73% yield) was prepared according to the general procedure B as a yellow solid. **^{1}H NMR** (400 MHz, CD_3OD) δ 8.17 (d, *J* = 8.0 Hz, 1H), 8.11 (d, *J* = 8.0 Hz, 1H), 7.79 (d, *J* = 4.0 Hz, 1H), 7.47 (t, *J* = 8.0 Hz, 1H), 7.41 (d, *J* = 8.0 Hz, 1H), 7.30 (t, *J* = 8.0 Hz, 1H), 7.13 (dd, J_1 = 8.0 Hz, J_2 = 2.0 Hz), 3.83 (s, 3H); **^{13}C NMR** (100 MHz, DMSO-D_6) 160.3, 146.5, 136.1, 127.9, 126.1, 124.2, 123.8, 122.4, 122.2, 121.8, 119.2, 115.4, 112.3, 29.7; **IR** (neat, cm^{-1}) 3356.5, 2977.6, 2606.3, 1682.6, 1633.4, 1586.2, 1361.5, 1203.4, 1135.9, 755.0; **HRMS-ESI** (m/z) Calcd for $C_{14}H_{13}N_2O^+$ ([M+H]$^+$): 225.1022; found: 225.1023; **m.p.** 180℃.



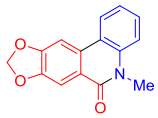
3fj

2-Ethoxyethyl 5-methyl-6-oxo-5,6-dihydrophenanthridine-8-carboxylate (**3fj**): The title compound (125 mg, 77% yield) was prepared according to the general procedure B as a colorless oil. **^{1}H NMR** (400 MHz, CD_3OD) δ 9.00 (s, 1H), 8.62 (d, *J* = 8.0 Hz, 1H), 8.40 (d, *J* = 8.0 Hz, 1H), 8.21 (d, *J* = 8.0 Hz, 1H), 7.60 (t, *J* = 8.0 Hz, 1H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.38 (t, *J* = 8.0 Hz, 1H), 4.57 (t, *J* = 8.0 Hz, 2H), 3.85-3.83 (m, 5H), 3.83 (q, *J* = 8.0 Hz, 2H), 1.27 (t, *J* = 8.0 Hz, 3H); **^{13}C NMR** (100 MHz, DMSO-D_6) 166.2, 159.7, 137.8, 133.3, 133.2, 130.6, 128.9, 127.9, 127.7, 123.6, 123.4, 122.9, 117.7, 115.8, 67.6, 66.6, 64.7, 29.9, 15.1; **IR** (neat, cm^{-1}) 3296.7, 2975.6, 2877.3, 1721.2, 1642.1, 1422.2, 1348.0, 1287.3, 1257.4, 1105.0, 1032.7, 743.4; **HRMS-ESI** (m/z) Calcd for $C_{19}H_{20}NO_4^+$ ([M+H]$^+$): 326.1387; found: 326.1385; **m.p.** 115℃.



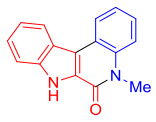
3hj

8,9-Dimethoxy-5-methylphenanthridin-6(5*H*)-one (**3hj**)[6]: The title compound (101 mg, 75% yield) was prepared according to the general procedure B as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 8.0 Hz, 1H), 7.94 (s, 1H), 7.60 (s, 1H), 7.52 (t, *J* = 8.0 Hz, 1H), 7.42 (d, *J* = 8.0 Hz, 1H), 7.32 (t, *J* = 8.0 Hz, 1H), 4.09 (s, 3H), 4.04 (s, 3H), 3.82 (s, 3H).



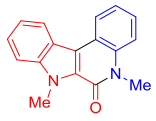
3ij

5-Methyl-[1,3]dioxolo[4,5-j]phenanthridin-6(5*H*)-one (**3ij, *N*-methylcrinasiadine**)[6]: The title compound (115 mg, 74% yield) was prepared according to the general procedure B as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.10 (d, *J* = 8.0 Hz, 1H), 7.92 (s, 1H), 7.63 (s, 1H), 7.52 (t, *J* = 8.0 Hz, 1H), 7.41 (d, *J* = 8.0 Hz, 1H), 7.31 (t, *J* = 8.0 Hz, 1H), 6.13 (s, 3H), 3.81 (s, 3H).



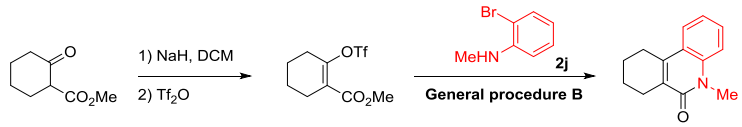
3jj

5-Methyl-5,7-dihydro-6H-indolo[2,3-*c*]quinolin-6-one (**3jj**)[11]: The title compound (110 mg, 89% yield) was prepared according to the general procedure B as a yellow solid. **^{1}H NMR** (400 MHz, CD_3OD) δ 9.89 (br, 1H), 8.48 (d, *J* = 8.0 Hz, 1H), 8.40 (d, *J* = 8.0 Hz, 1H), 7.67 (d, *J* = 4.0 Hz, 1H), 7.58-7.40 (m, 3H), 7.45 (t, *J* = 8.0 Hz, 1H), 7.38 (t, *J* = 8.0 Hz, 1H), 3.96 (s, 3H); **^{13}C NMR** (100 MHz, DMSO-D_6) 155.3, 139.0, 135.9, 127.0, 126.4, 125.7, 123.5, 122.7, 122.5, 122.1, 120.8, 118.9, 117.0, 115.7, 113.1, 29.3; **HRMS-ESI** (m/z) Calcd for $C_{16}H_{13}N_2O^+$ ([M+H]$^+$): 249.1022; found: 249.1024.



3kj

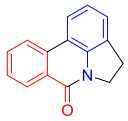
5,7-Dimethyl-5,7-dihydro-6H-indolo[2,3-*c*]quinolin-6-one (**3kj**): The title compound (125 mg, 95% yield) was prepared according to the general procedure B as a white solid. **^{1}H NMR** (400 MHz, CD_3OD) δ 8.50 (d, *J* = 8.0 Hz, 1H), 8.44 (d, *J* = 8.0 Hz, 1H), 7.59-7.47 (m, 4H), 7.43-7.36 (m, 2H), 4.42 (s, 3H), 3.89 (s, 3H); **^{13}C NMR** (100 MHz, DMSO-D_6) 155.9, 140.3, 135.9, 126.5, 126.0, 125.6, 123.5, 122.7, 122.6, 121.2, 121.0 118.6, 117.6, 115.6, 111.2, 31.4, 29.2; **IR** (neat, cm^{-1}) 3047.0, 1648.8, 1296.9, 1200.5, 726.1; **HRMS-ESI** (m/z) Calcd for $C_{17}H_{15}N_2O^+$ ([M+H]$^+$): 263.1179; found: 263.1181; **m.p.** 234℃.



S-7 1l 3lj

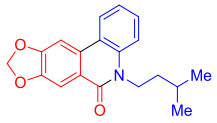
5-Methyl-7,8,9,10-tetrahydrophenanthridin-6(5*H*)-one (**3lj**): A solution of methyl 2-oxocyclohexane-1-carboxylate (**S-7**, 1.56 g, 10.0 mmol, 1.0 equiv) in anhydrous DCM (50 mL) was added NaH (60 wt%, 440 mg, 11.0 mmol, 1.1 equiv) in portions at 0℃ under nitrogen atmosphere. The reaction mixture was stirred at 0℃ for 30 min, then was added trifluoromethanesulfonic anhydride (Tf_2O, 2.82 g, 1.69 mL, 10.0 mmol, 1.0 equiv) dropwise. The resulting mixture was warmed to rt and stirred overnight, quenched with H_2O (0.5 mL), diluted with DCM (150 mL), washed with a saturated aqueous $NaHCO_3$ solution (50 mL× 2) and brine (50 mL), and dried ($MgSO_4$). After filtration and concentration to provide the crude product **1l** (2.6 g) as a green-dark liquid and used as such in next step. The title compound **3ij** (33 mg, 31% yield) was prepared according to the general procedure B from **1l** and **2j** as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.0 Hz, 1H), 7.50 (t, *J* = 8.0 Hz, 1H), 7.35 (d, *J* = 8.0 Hz, 1H), 7.23 (t, *J* = 8.0 Hz, 1H), 3.74 (s, 3H), 2.87-2.84 (m, 2H), 2.68-2.66 (m, 2H), 1.88-1.78 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$) 162.2, 141.7, 138.1, 129.0, 128.5, 123.5, 121.7, 121.2, 114.0, 29.6, 25.4, 24.6, 21.97, 21.96; **IR** (neat, cm^{-1}) 3074.0, 2956.3, 2868.6, 1648.8, 1608.3, 1587.1, 1437.7, 1364.7, 1335.5, 1313.3, 1177.3, 747.3; **HRMS-ESI** (m/z) Calcd for $C_{14}H_{16}NO^+$ ([M+H]$^+$): 214.1226; found: 214.1228.

[11] Li, Z.; Wang, W.; Zhang, X.; Hu, C.; Zhang, W. *Synlett*, **2013**, *24*, 73-78.



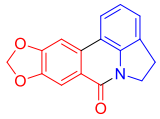
3aq

4,5-Dihydro-7*H*-pyrrolo[3,2,1-de]phenanthridin-7-one (**3aq**)[12]: The title compound (165 mg, 75% yield) was prepared according to the general procedure A as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.57 (d, *J* = 8.0 Hz, 1H), 8.22 (d, *J* = 8.0 Hz, 1H), 7.93 (d, *J* = 8.0 Hz, 1H), 7.76 (t, *J* = 8.0 Hz, 1H), 7.60 (t, *J* = 8.0 Hz, 1H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.23 (t, *J* = 8.0 Hz, 1H), 4.51 (t, *J* = 8.0 Hz, 2H), 3.45 (t, *J* = 8.0 Hz, 2H).



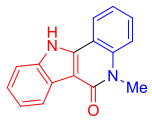
3ik

5-Isopentyl-[1,3]dioxolo[4,5-*j*]phenanthridin-6(5*H*)-one (**3ik**)[6]: The title compound (114 mg, 74% yield) was prepared according to the general procedure B as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.11 (d, *J* = 8.0 Hz, 1H), 7.91 (s, 1H), 7.63 (s, 1H), 7.51 (t, *J* = 8.0 Hz, 1H), 7.39 (d, *J* = 8.0 Hz, 1H), 7.28 (t, *J* = 8.0 Hz, 1H), 6.12 (s, 2H), 4.39 (t, *J* = 8.0 Hz, 2H), 1.88-1.78 (m, 1H), 1.71-1.66 (m, 2H), 1.06 (d, *J* = 8.0 Hz, 3H).



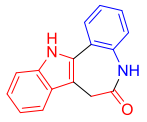
3iq

4,5-Dihydro-7*H*-[1,3]dioxolo[4,5-*j*]pyrrolo[3,2,1-*de*]phenanthridin-7-one (**3iq**)[11]: The title compound (46 mg, 35%yield) was prepared according to the general procedure B as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.78 (d, *J* = 8.0 Hz, 1H), 7.58 (s, 1H), 7.32 (d, *J* = 8.0 Hz, 1H), 7.23 (t, *J* = 8.0 Hz, 1H), 6.14 (s, 2H), 4.52 (t, *J* = 8.0 Hz, 2H), 3.46 (d, *J* = 8.0 Hz, 2H).



3mj

5-Methyl-5,11-dihydro-6*H*-indolo[3,2-*c*]quinolin-6-one (**3mj**)[13]: The title compound (110 mg, 89% yield) was prepared according to the general procedure B as a light yellow solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.89 (br, 1H), 8.50 (d, *J* = 4.0 Hz, 1H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.61 (t, *J* = 8.0 Hz, 1H), 7.55-7.52 (m, 2H), 7.43-7.33 (m, 3H), 3.88 (s, 3H); **^{13}C NMR** (100 MHz, DMSO-D_6) 159.0, 139.6, 138.7, 137.7, 129.6, 124.6, 124.1, 122.6, 121.7, 121.1 120.8, 115.7, 112.9, 111.7, 105.9, 28.5.



4ni

7,12-Dihydrobenzo[2,3]azepino[4,5-*b*]indol-6(5*H*)-one (**4ni**)[14]: The title compound (79 mg, 64% yield)

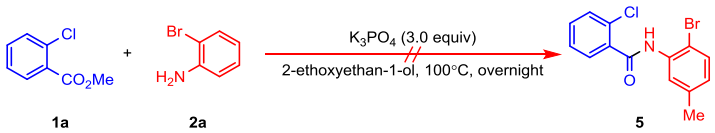
[12] S. De,; S. Ghosh,; S. Bhunia,; J. A. Sheikh,; A. Bisai, *Org. Lett.* **2012**. *14*, 4466-4469.
[13] Shi, Z.; Ren, Y.; Li, B.; Lu, S.; Zhang, W. *Chem. Comm.* **2010**, *46*, 3973–3975
[14] Stuart, D. R.; Alsabeh, P.; Kuhn, M.; Fagnou, K. *J. Am. Chem. Soc.* **2010**, *132*. 18326-18339

was prepared according to the general procedure B as a light yellow solid. **^{1}H NMR** (400 MHz, DMSO-D_6) δ 11.57 (s, 1H), 10.08 (s, 1H), 7.74 (d, J = 8.0 Hz, 1H), 7.66 (dd, J_1 = 8.0 Hz, J_2 = 8.0 Hz, 1H), 7.44 (d, J = 8.0 Hz, 1H), 7.36 (dd, J_1 = 8.0 Hz, J_2 = 8.0 Hz, 1H), 7.28 (d, J = 8.0 Hz, 1H), 7.25 (d, J = 8.0 Hz, 1H), 7.17 (dd, J_1 = 8.0 Hz, J_2 = 8.0 Hz, 1H), 7.07(dd, J_1 = 8.0 Hz, J_2 = 8.0 Hz, 1H), 3.50 (s, 3H).

V. Mechanism study

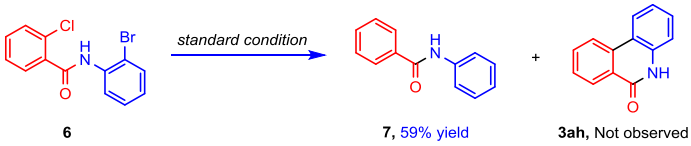
Part A: Control experiments

Control experiment A:



To a mixture of **1a** (1.3 mmol, 1.3 equiv), **2a** (1.0 mmol, 1.0 equiv), and K_3PO_4 (3.0 mmol, 3.0 equiv) was added 2-ethoxyethan-1-ol (10 mL) at rt under N_2 atmosphere. The reaction mixture was heated at 100℃ (monitored by TLC and LC-MS). No desired product **5** was observed after 24 h.

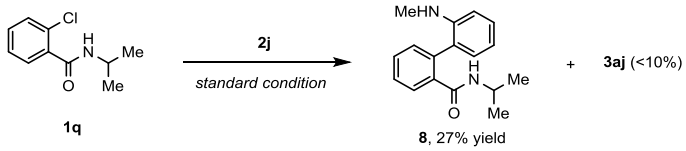
Control experiment B:



To a mixture of **6**[15] (1.0 mmol), $Pd_2(dba)_3$ (4 mol%), PCy_3 (10 mol%), $B_2(Pin)_2$ (1.3 equiv), and K_3PO_4 (3.0 equiv) was added 2-ethoxyethan-1-ol (10 mL) at rt under N_2 atmosphere. The reaction mixture was heated at 100℃ overnight. No desired product **3ah** was observed on LC-MS spectra, instead the reduced product **7** (pale yellow solid, 58 mg, 59% yield) was isolated as the major product. Minor dimer and trace amount of trimmer were also observed on LC-MS spectra.

***N*-Phenylbenzamide** (7, pale yellow solid, 58 mg, 59% yield)[16]: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.85 (d, J = 8.0 Hz, 2H), 7.81 (br, 1H), 7.63 (d, J = 8.0 Hz, 2H), 7.53 (dd, J_1 = 8.0 Hz, J_2 = 8.0 Hz, 1H), 7.47 (dd, J_1 = 8.0 Hz, J_2 = 8.0 Hz, 2H), 7.36 (dd, J_1 = 8.0 Hz, J_2 = 8.0 Hz, 2H), 7.14 (dd, J_1 = 8.0 Hz, J_2 = 8.0 Hz, 1H).

Control experiment C:



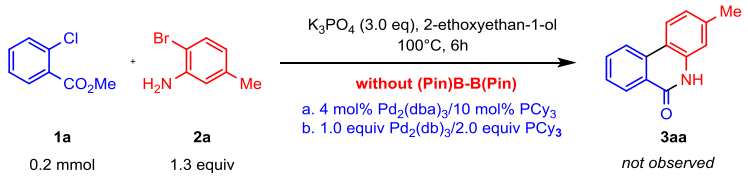
***N*-Isopropyl-2'-(methylamino)-[1,1'-biphenyl]-2-carboxamide** (**8**): To a mixture of **1q** (0.5 mmol, 1.0 equiv), **2j** (0.65 mmol, 1.3 equiv), bis(pinacolato)diboron (0.75 mmol, 1.5 equiv), K_3PO_4 (1.5 mmol, 3.0 equiv), $Pd_2(dba)_3$ (4 mol%) and PCy_3 (10 mol%) was added 2-ethoxyethan-1-ol (5.0 mL, 0.1 M) at rt under N_2 atmosphere. The reaction mixture was heated at 100℃ for 1.5 h, diluted with EtOAc (10 mL) at rt, filtrated through a pad of celite, and concentrated. The residue was purified by a prepacked silica gel

[15] Compound **6** was prepared according to reported literature: Lu, J.; Gong, X.; Yang, H.; Fu, H. *Chem.Comm.* **2010**, *46*, 4172-4174

[16] Zultanski, S. L.; Zhao, J.; Stahl, S. S. *J. Am. Chem. Soc*. **2016**, *138*, 6416-6419.

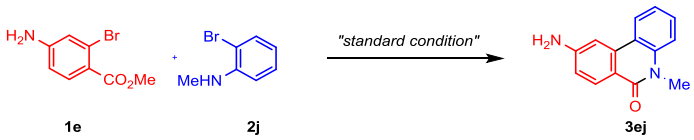
column (Hexane: EtOAc = 10:1-5:1) to afford the desired product **8** (36 mg, 27% yield) as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.91 (dd, J_1 = 8.0 Hz, J_2 = 4.0 Hz, 1H), 7.52-7.43 (m, 2H), 7.32 (t, J = 8.0 Hz, 1H), 7.22 (t, J = 8.0 Hz, 1H), 7.03 (dd, J_1 = 8.0 Hz, J_2 = 4.0 Hz, 1H), 6.80 (t, J = 8.0 Hz, 1H), 6.68 (d, J = 8.0 Hz, 1H), 5.92 (br, 1H), 3.98-3.89 (m, 1H), 3.55 (br, 1H), 2.77 (d, J = 4.0 Hz, 3H), 0.84 (d, J = 4.0 Hz, 3H), 0.75 (d, J = 4.0 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) 167.1, 146.3, 136.3, 135.9, 130.84, 130.75, 129.8, 129.5, 129.4, 128.3, 126.4, 117.4, 109.9, 41.3, 30.3, 22.0, 21.9; **IR** (neat, cm^{-1}) 3368.1, 3299.6, 3057.6, 2966.0, 1639.2, 1513.9, 1460.8, 1315.2, 1289.2, 1168.7, 746.3; **HRMS-ESI** (m/z) Calcd for ($C_{17}H_{21}N_2O^+$) ([M+H]$^+$): 269.1648; found: 269.1648; **m.p.** 109℃.

Control experiment D

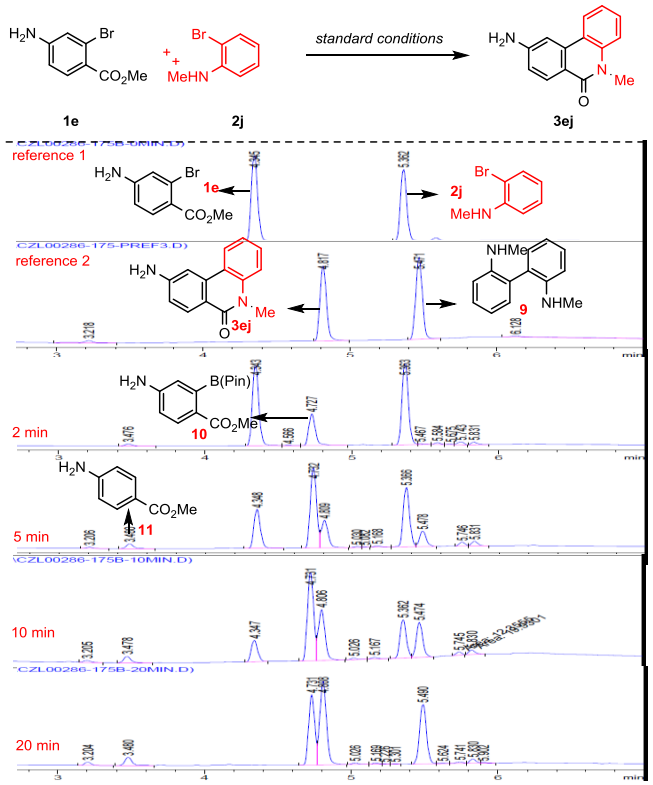


To a mixture of **1q** (0.5 mmol, 1.0 equiv), **2a** (0.65 mmol, 1.3 equiv), K_3PO_4 (1.5 mmol, 3.0 equiv), $Pd_2(dba)_3$ (a: 4 mol%; b: 1.0 equiv), and PCy_3 (a: 10 mol%, b: 2.0 equiv) was added 2-ethoxyethan-1-ol (5.0 mL 0,1 M) at rt under N_2 atmosphere. The reaction mixture was heated at 100℃ overnight. No desired product **3aa** was observed by LC-MS spectra.

Part B: Kinetic study

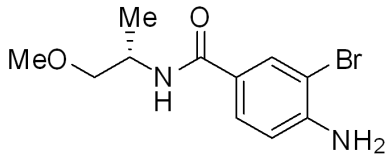


A kinetic study of the cascade reactions was also conducted at 0.2 mmol scale with substrates **1e** and **2j** which had strong signals in UV spectra and could be easily monitored by LC-MS spectra. Since the UV absorption was distinquisable for these compounds, we used a 1:1 mixture of **1e** and **2j** (ref 1) and a 1:1 mixture of **3ej** and home coupling product **9** of **2j** (ref 2) as references as shown in Scheme 7. After the reaction initiated, an aliquot was quenched by MeOH after 2, 5, 10, and 20 min and was detected by LC-MS. Interestingly, **1e** was partially converted to the boronic ester **10** after 2 min as shown in Scheme 2. The desired product **3ej** and side product **9** started to be observed at 5 min. At the same time, a small amount of **11**, the reduced product of **1e**, appeared in the reaction. At 20 min, both starting material **1e** and **2j** were consumed and the reaction was complete. Surprisingly, we didn't observed any homo-coupling product of **1e** and the boronic ester of **2j** although the homo-coupling product **9** of **2j** was gradually formed starting at 5 min. In addition, the direct product of the cross coupling reaction was not observed. This indicates that the ring closure reaction was not the rate-determining step. Instead the initial coupling intermediate was converted to the final product **3ej** spontaneously and did not accumulate.

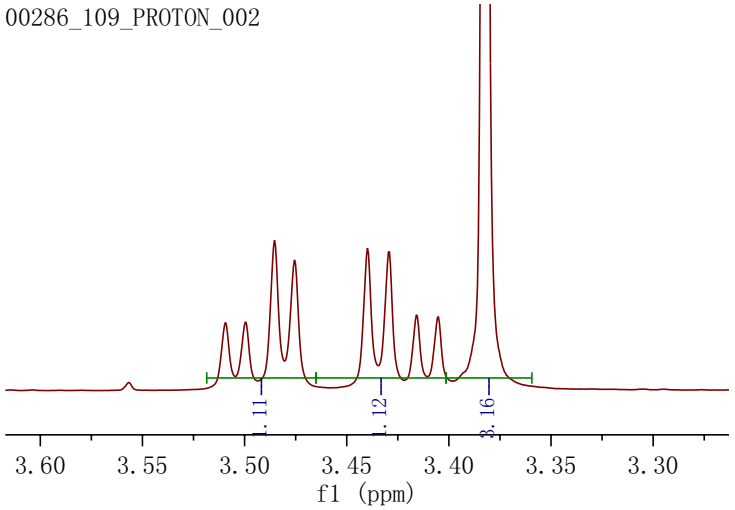


Scheme 2. Kinetic study of the reaction mechanism.

00286_109_PROTON_002

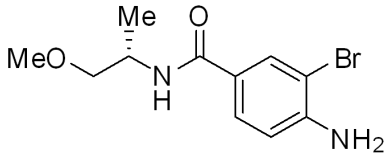


2c

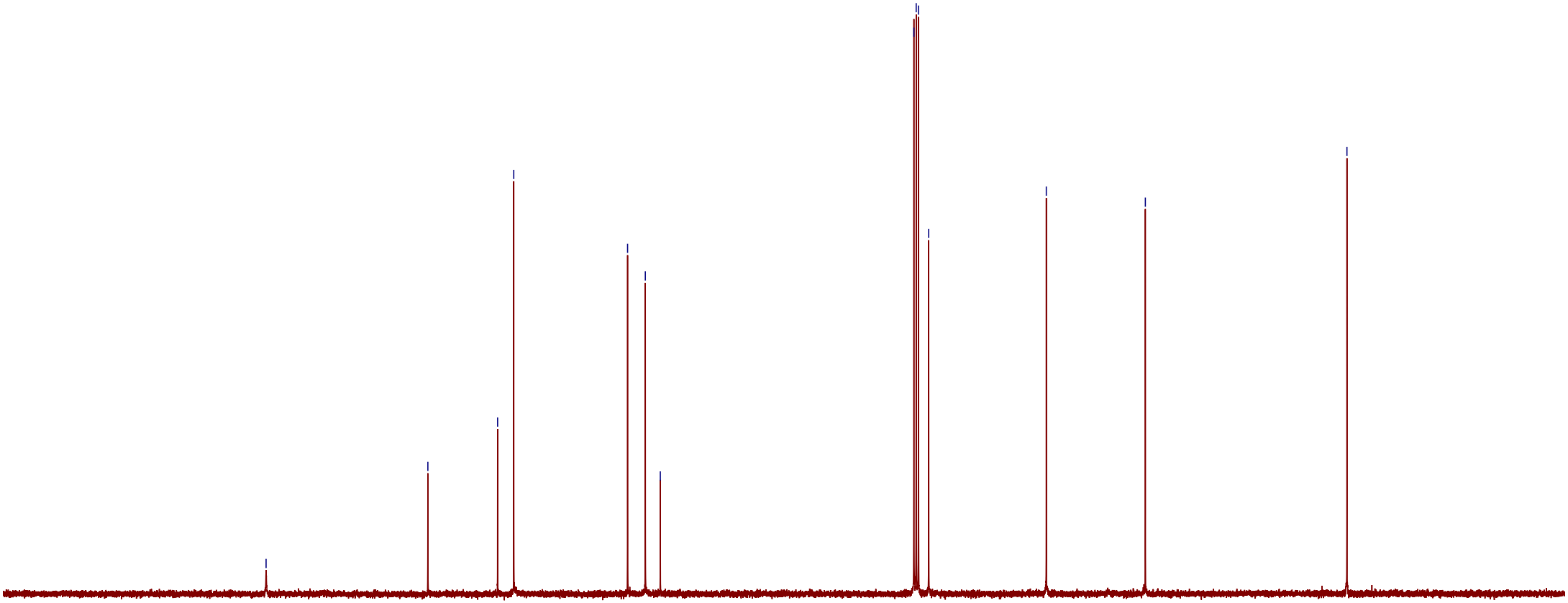


00286_109carbon_CARBON_001

166.69
144.37
134.75
132.52
116.82
114.37
112.30
77.32
77.00
76.68
75.27
59.05
45.39
17.57



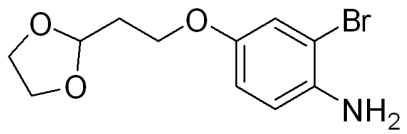
2c



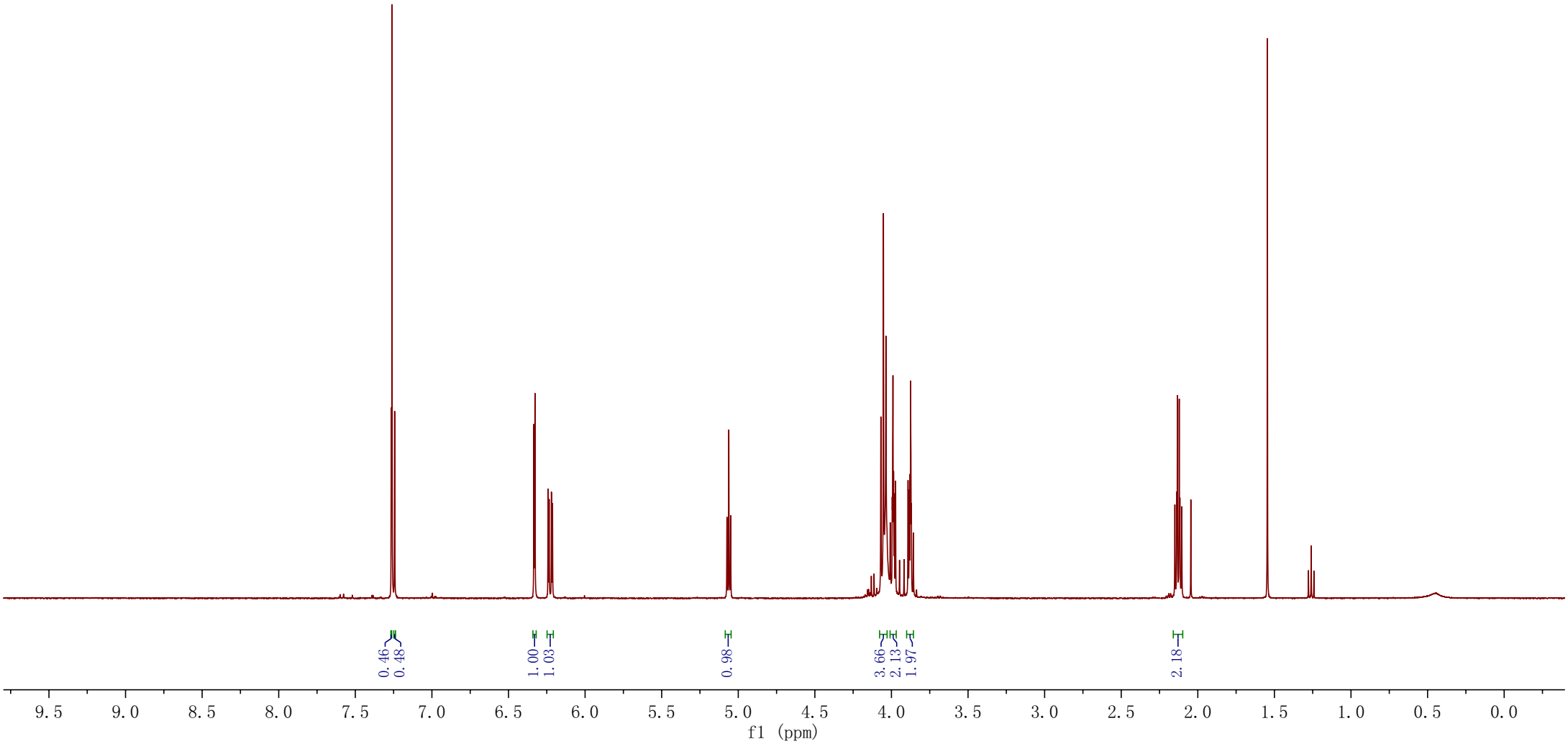
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

f1 (ppm)

00286_108_PROTON_001

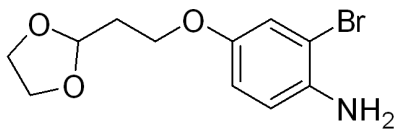


2d



00286_108_CARBON_001

158.68
146.57
104.38
101.15
100.90
98.74
64.24
63.32
40.15
39.94
39.73
39.52
39.31
39.10
38.89
33.26



2d

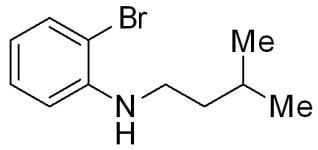
00286_108_CARBON_001

104.38
101.15
100.90
98.74

107 106 105 104 103 102 101 100 99 98 97
f1 (ppm)

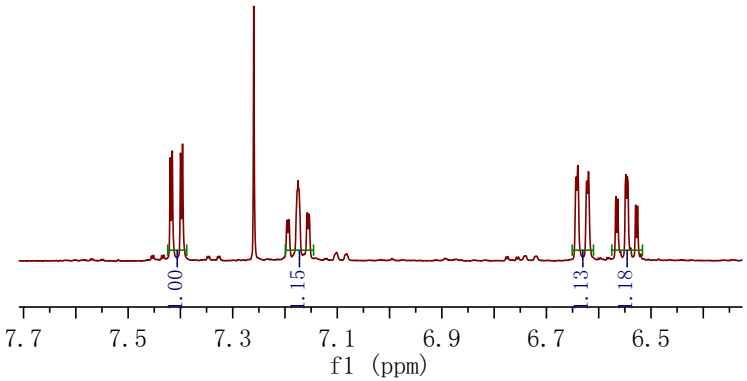
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

00286_092_PROTON_001

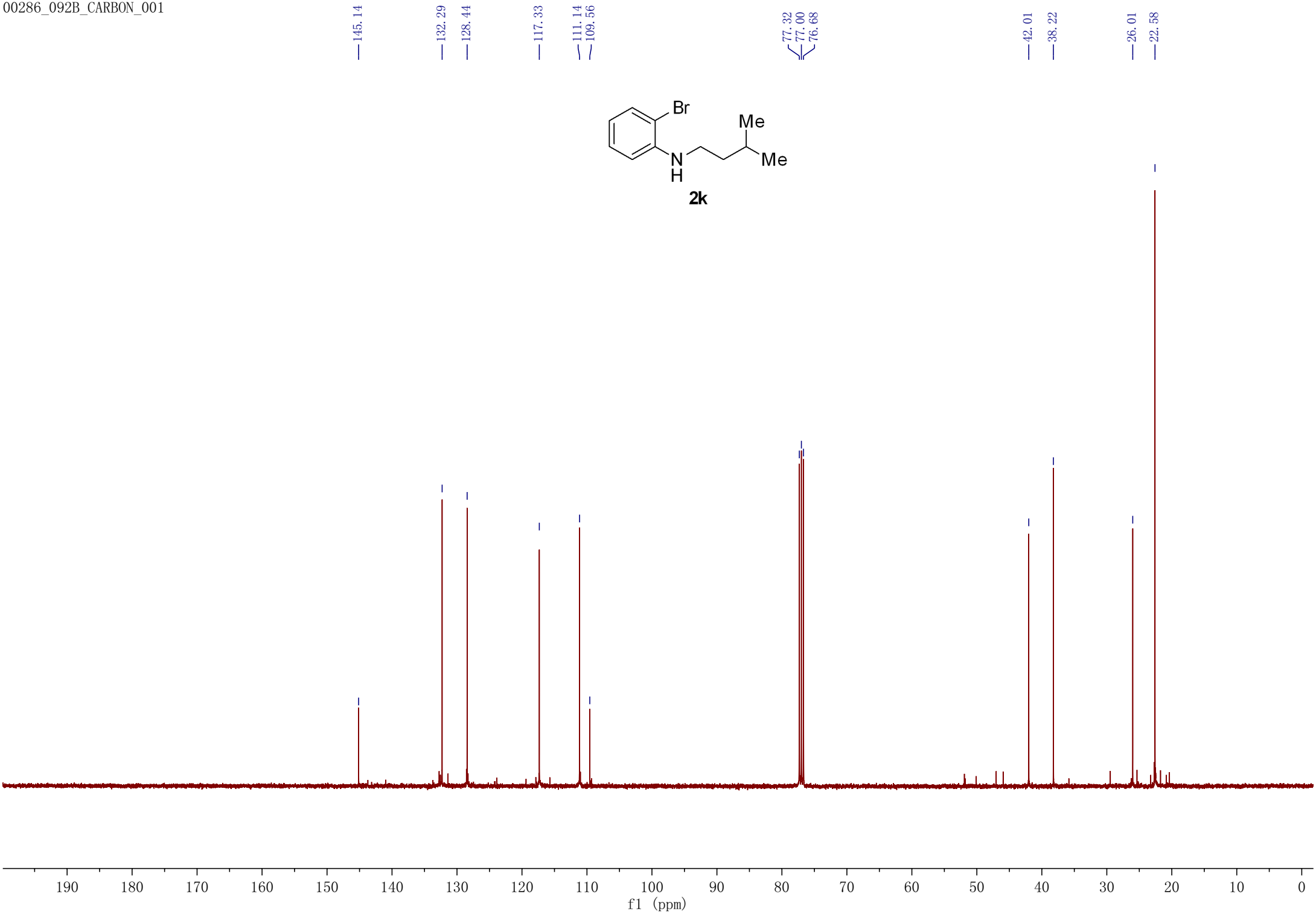


2k

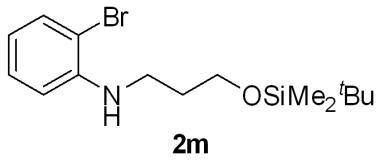
00286_092_PROTON_001



00286_092B_CARBON_001

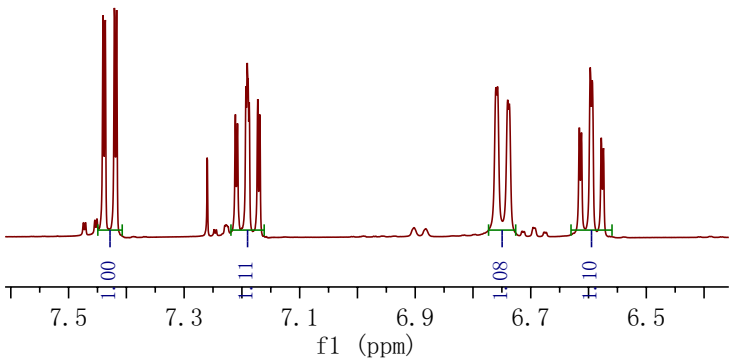


00286_121B_PROTON_001



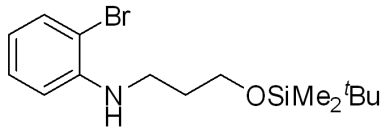
2m

00286_121B_PROTON_001

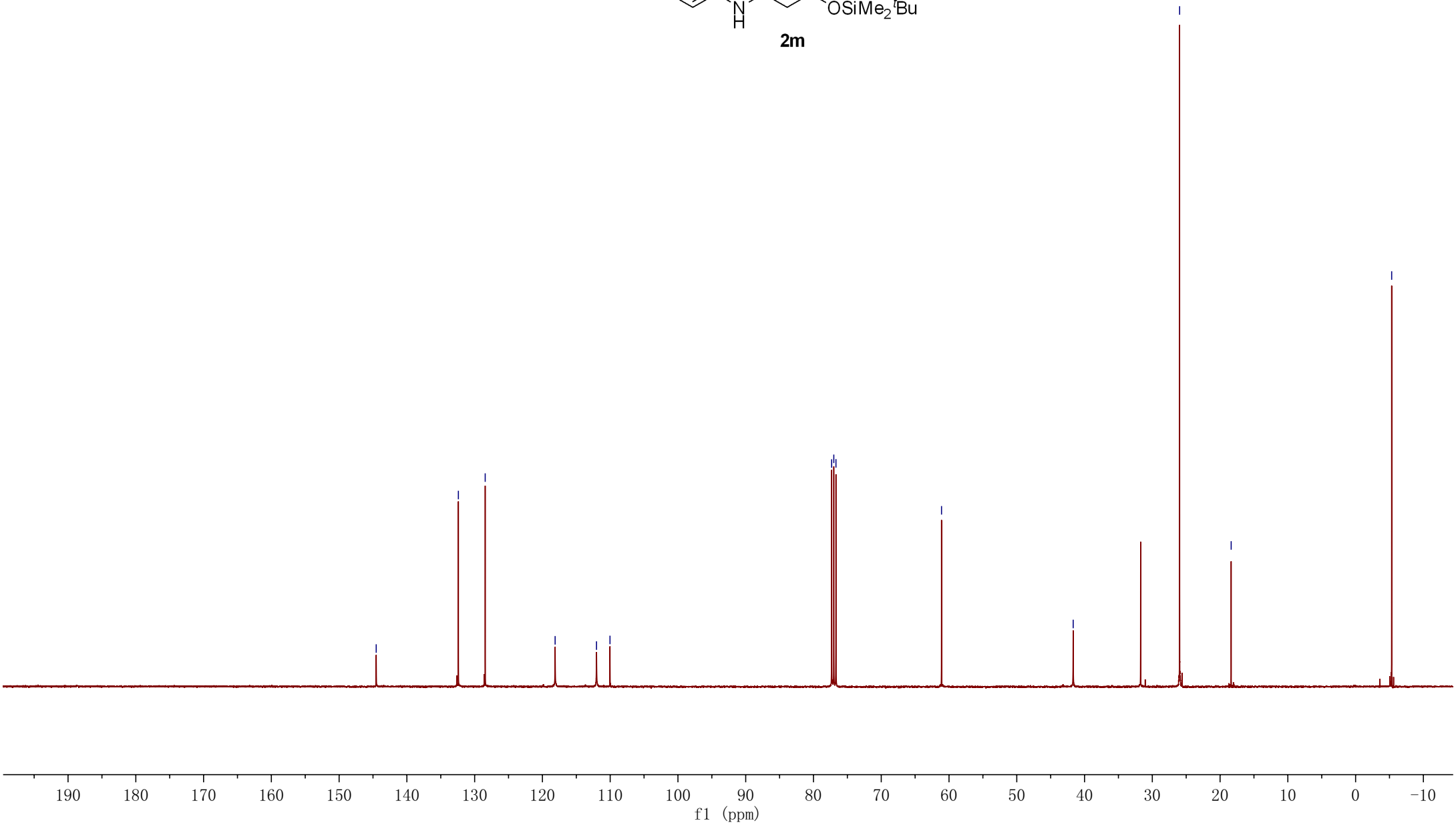


00286_121B_CARBON_001

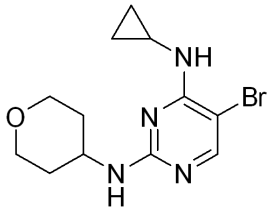
144.53
132.40
128.44
118.12
112.02
110.03
77.32
77.00
76.68
61.10
41.67
25.97
18.36
-5.32



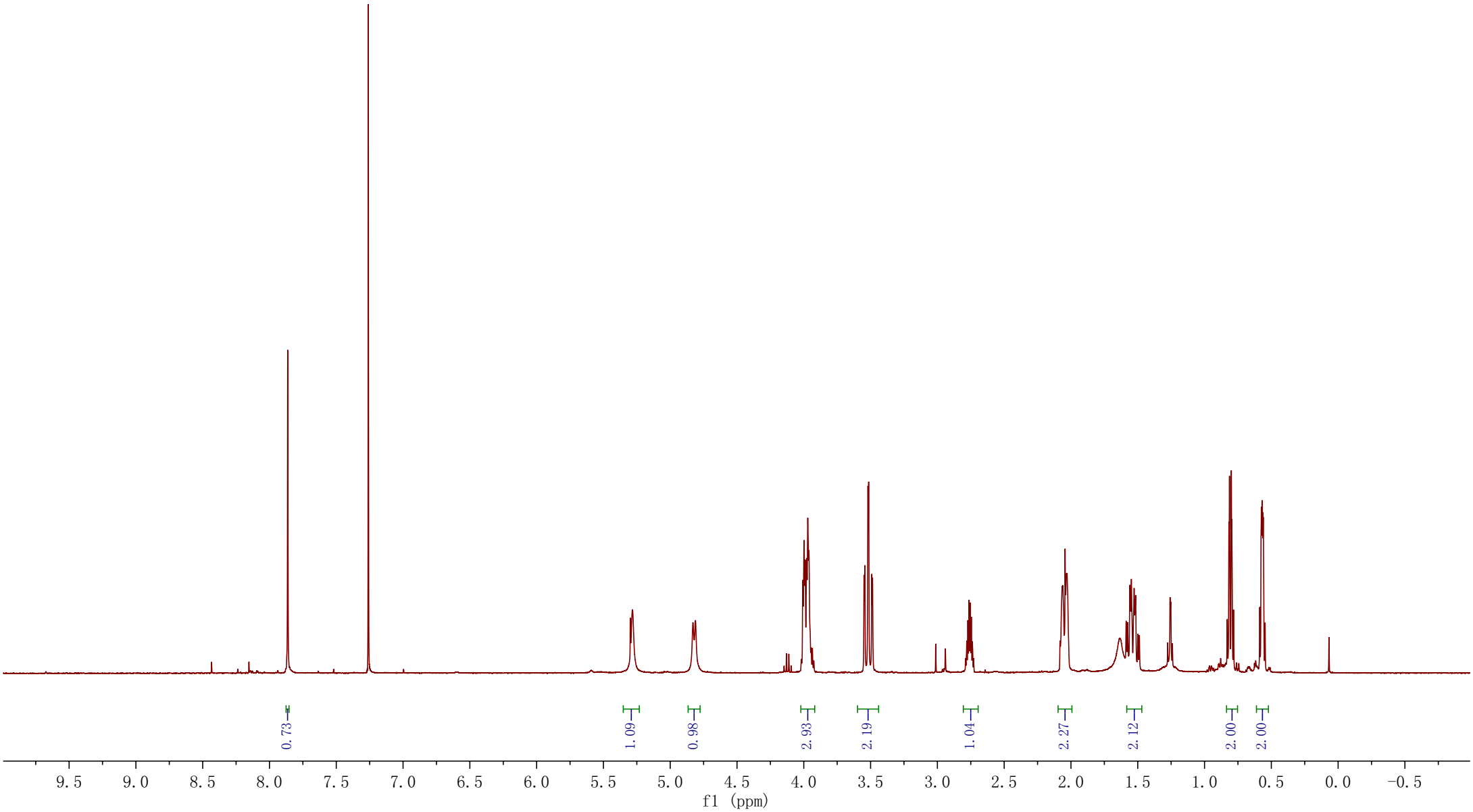
2m



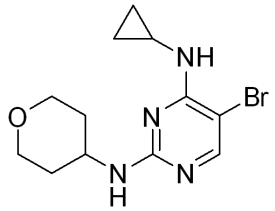
00286_107_PROTON_002



2p



00286_107carbon_CARBON_001

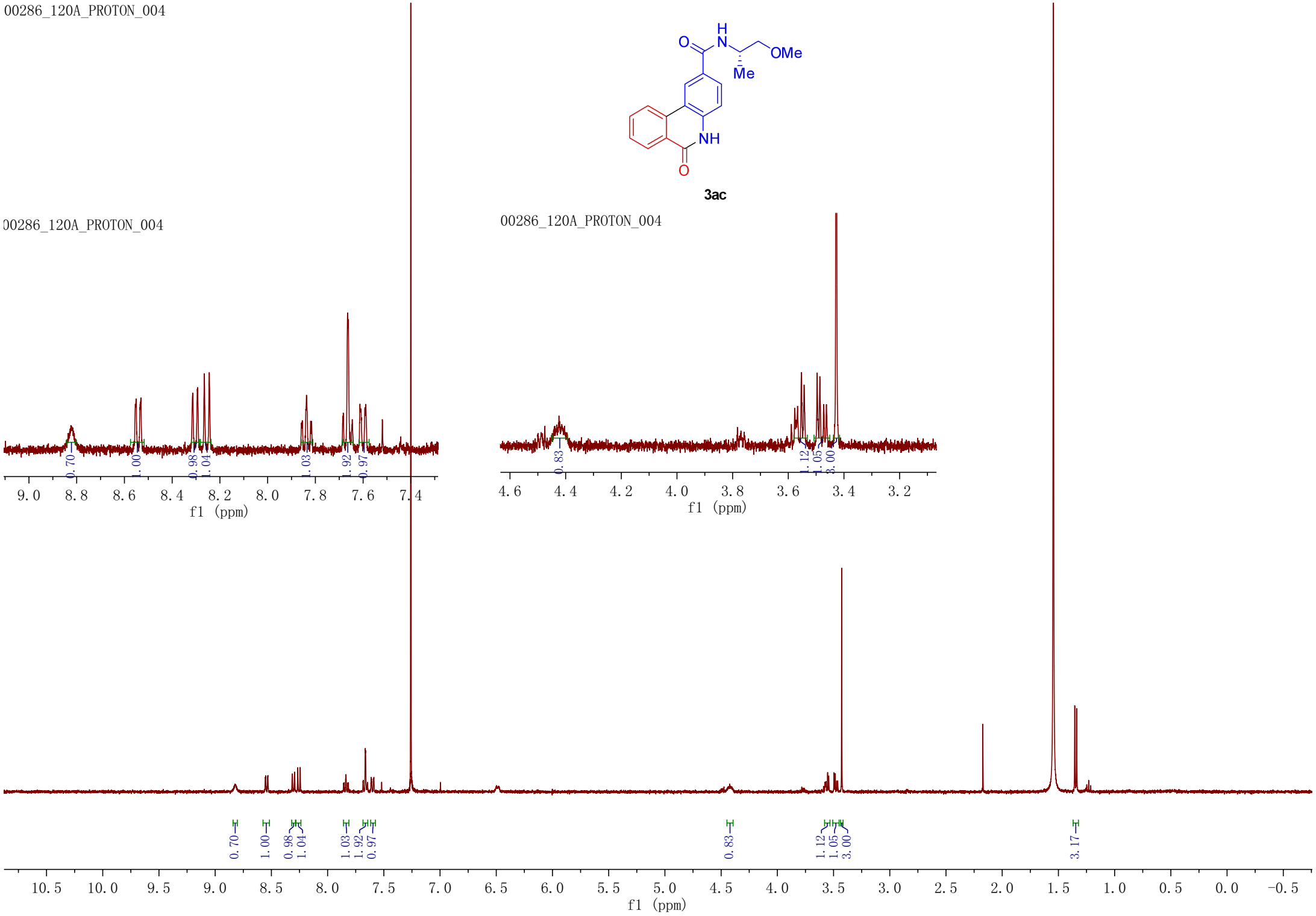


2p

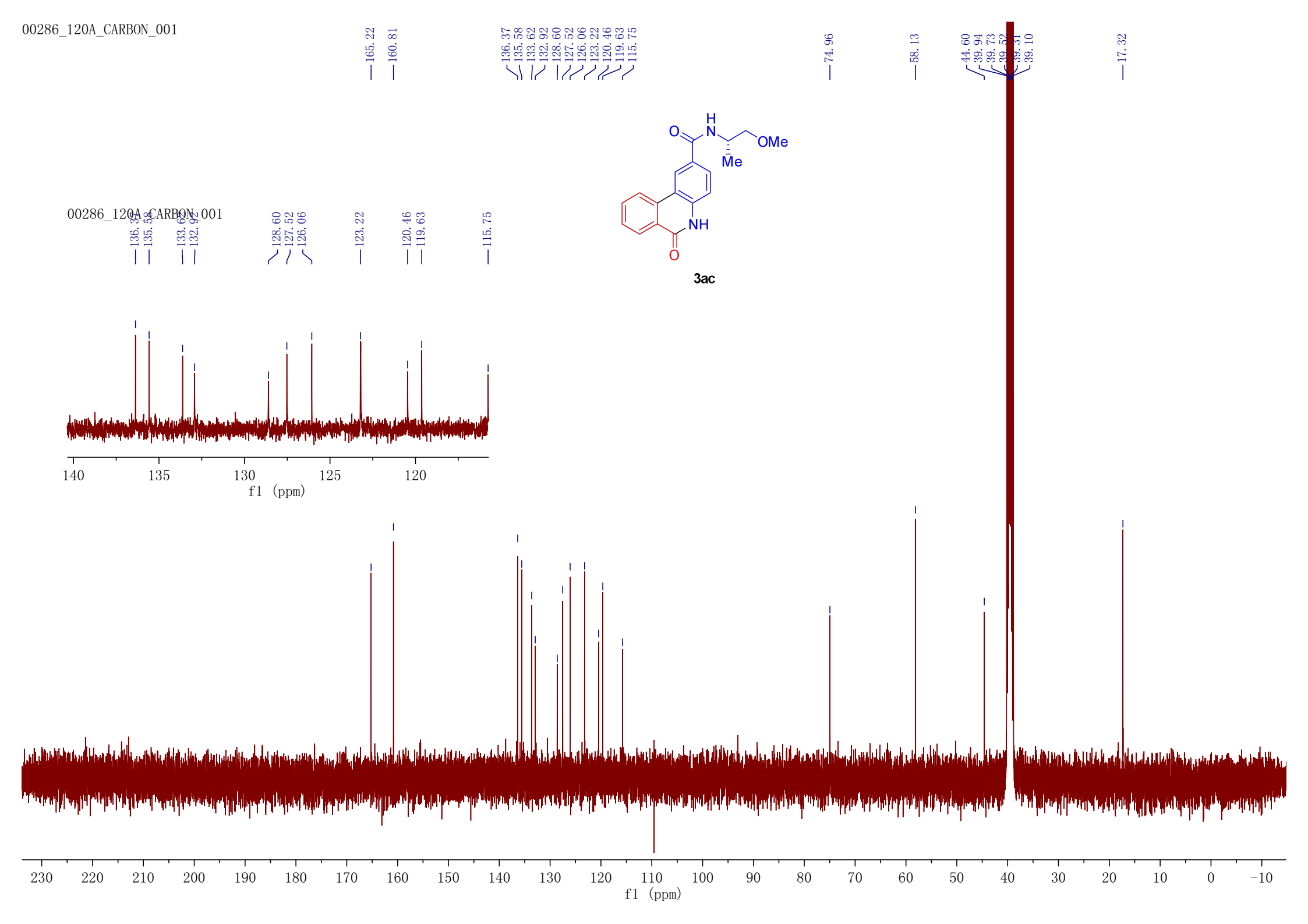
160.54
159.58
156.36
156.23
66.67
47.56
32.99
24.43
6.78

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

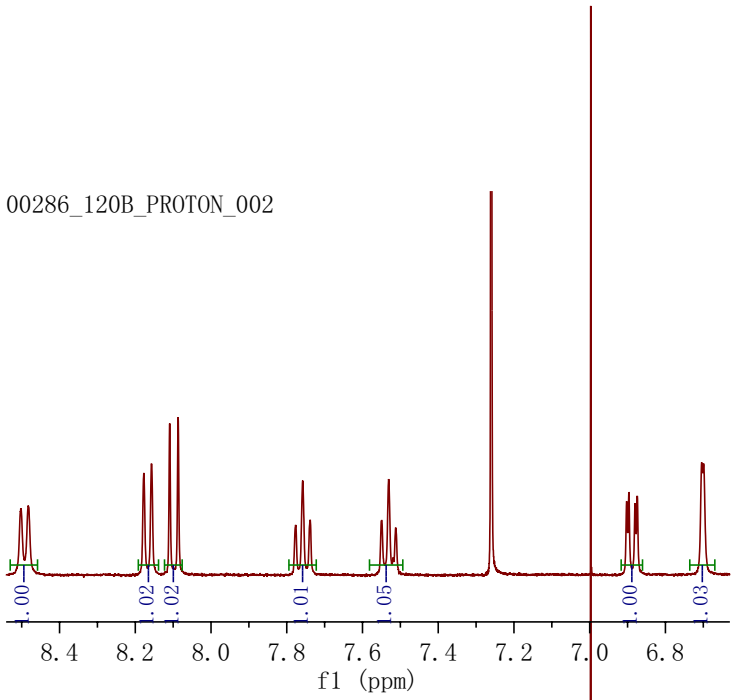
f1 (ppm)

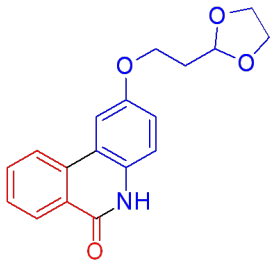

00286_120A_PROTON_004
H
N
O
OMe
Me
NH
O
3ac
00286_120A_PROTON_004
0.70
1.00
0.98
1.04
1.03
1.92
0.97
9.0
8.8
8.6
8.4
8.2
8.0
7.8
7.6
7.4
f1 (ppm)
00286_120A_PROTON_004
0.83
1.12
1.05
3.00
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
f1 (ppm)
0.70
1.00
0.98
1.04
1.03
1.92
0.97
0.83
1.12
1.05
3.00
3.17
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

00286_120A_CARBON_001

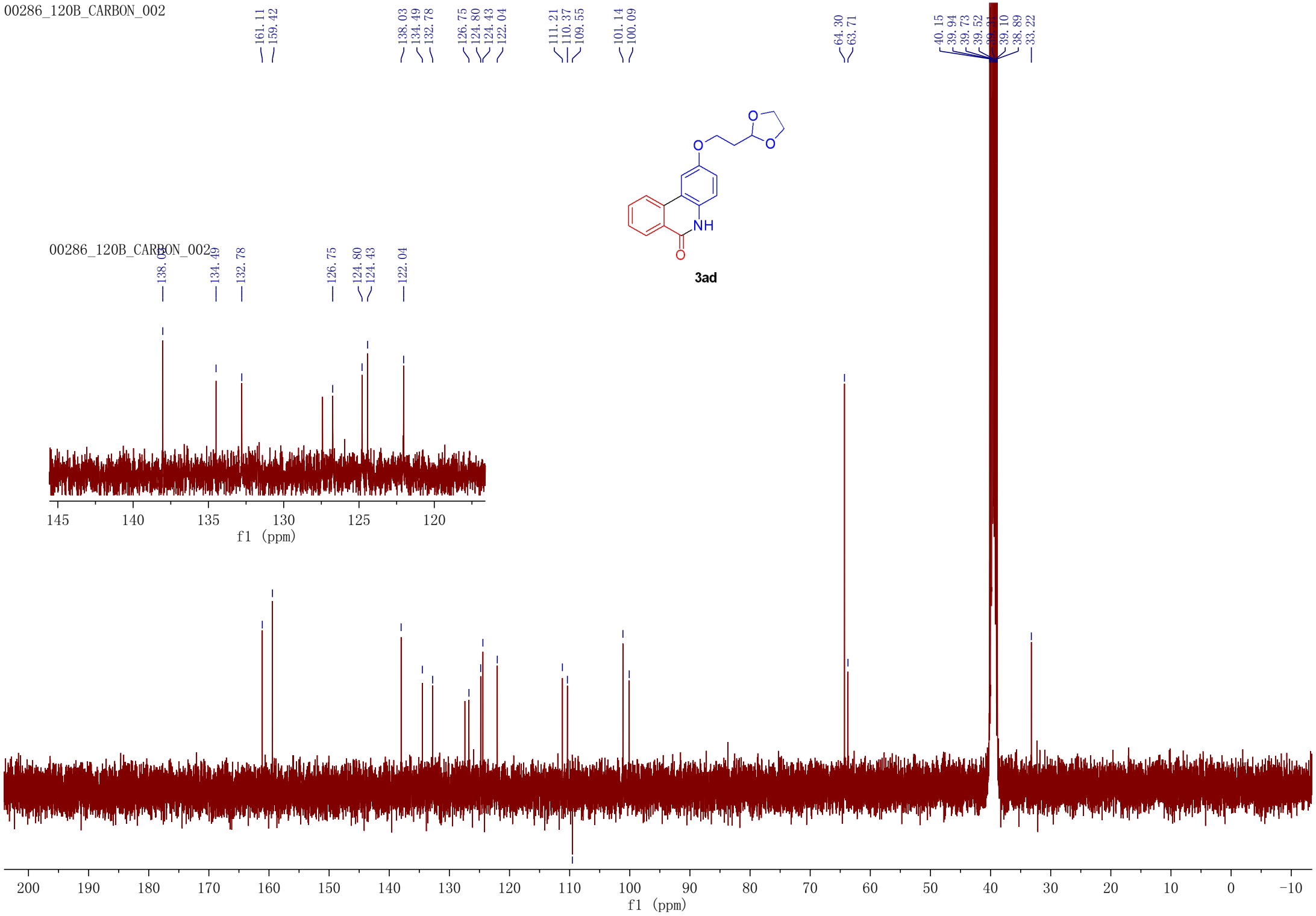


00286_120B_PROTON_002

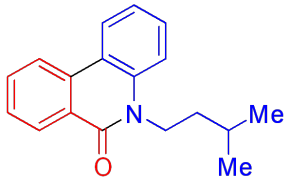




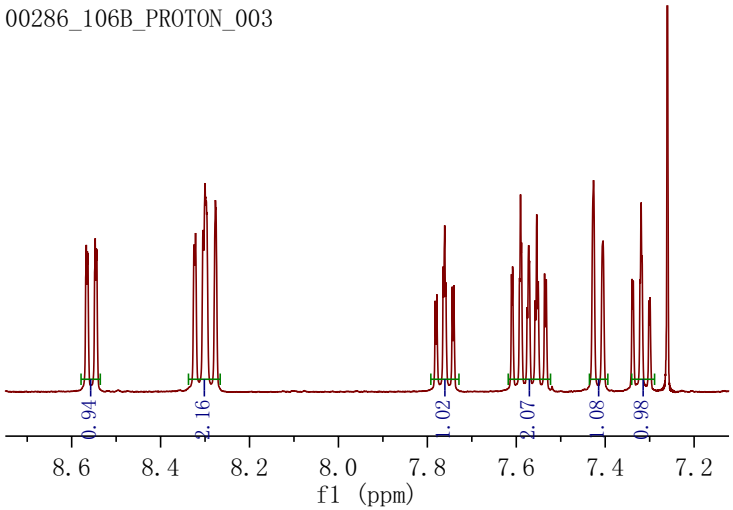
3ad


00286_120B_CARBON_002
161.11
159.42
138.03
134.49
132.78
126.75
124.80
124.43
122.04
111.21
110.37
109.55
101.14
100.09
64.30
63.71
40.15
39.94
39.73
39.52
39.31
39.10
38.89
33.22
O
O
O
NH
O
3ad
00286_120B_CARBON_002
138.03
134.49
132.78
126.75
124.80
124.43
122.04
145
140
135
130
125
120
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

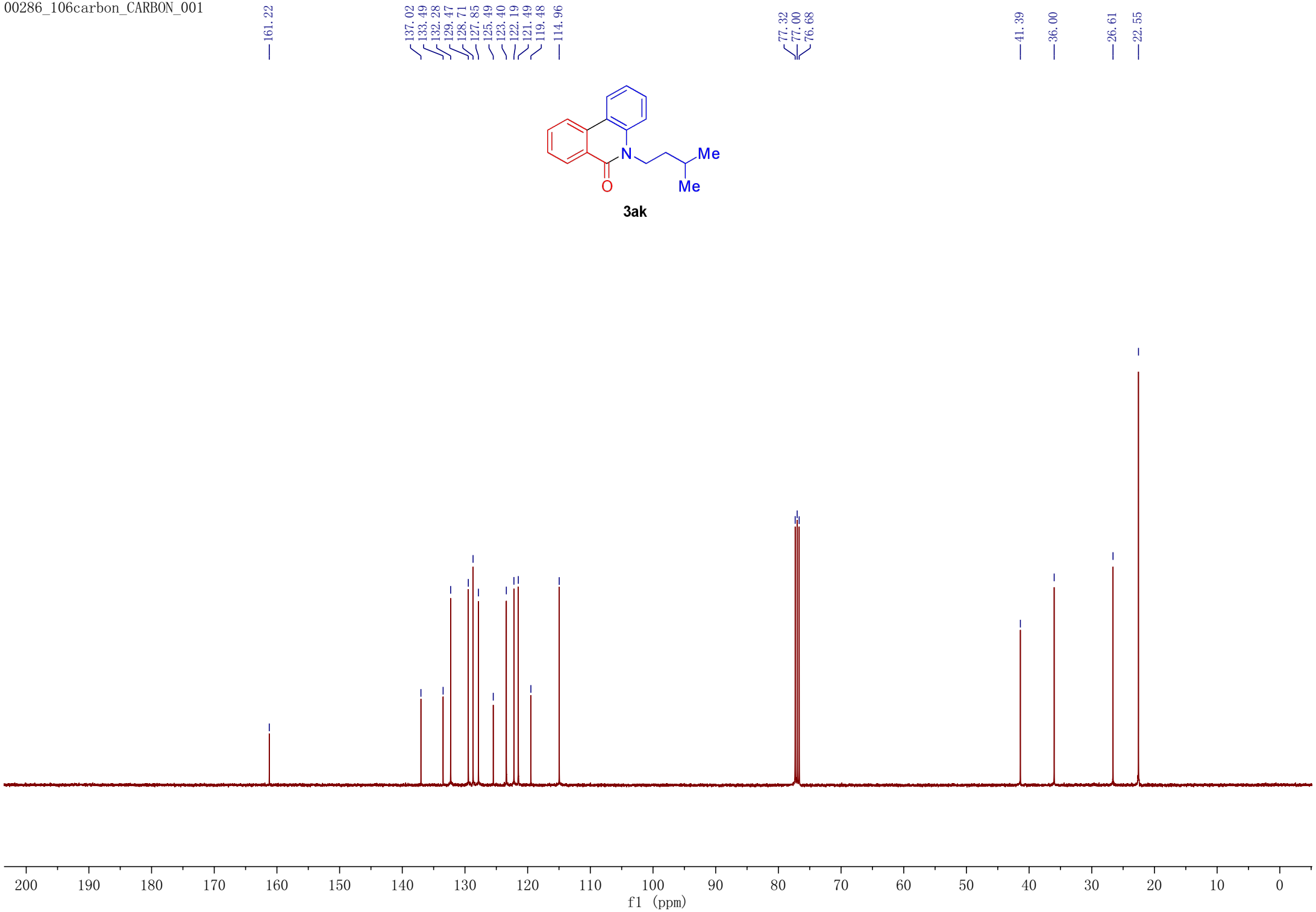
00286_106B_PROTON_003



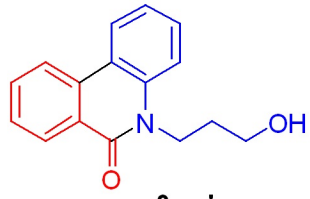
3ak



00286_106carbon_CARBON_001

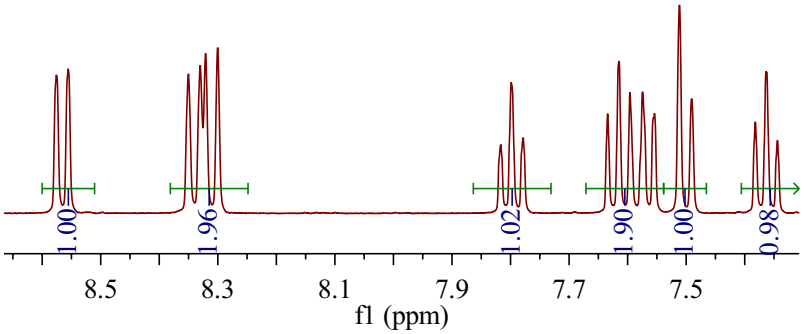


CZL00286_151_PROTON_001

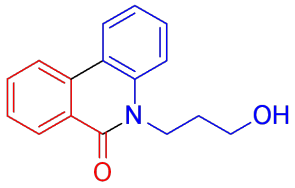


3am'

CZL00286_151_PROTON_001

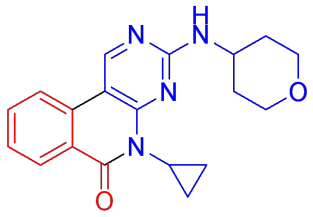


00286_151_CARBON_001



3am'

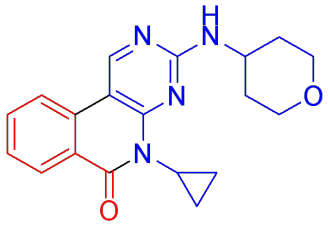
00286_120C_PROTON_002



3ap

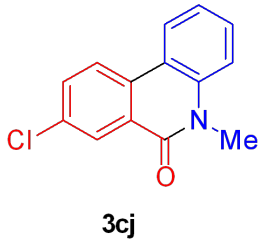
00286_120C-carbon_CARBON_001

163.14
159.34
158.13
156.23
153.20
133.17
131.84
127.84
126.70
123.33
120.30
66.17
53.14
40.15
39.94
39.73
39.52
39.31
39.10
38.89
32.30
25.28
9.47

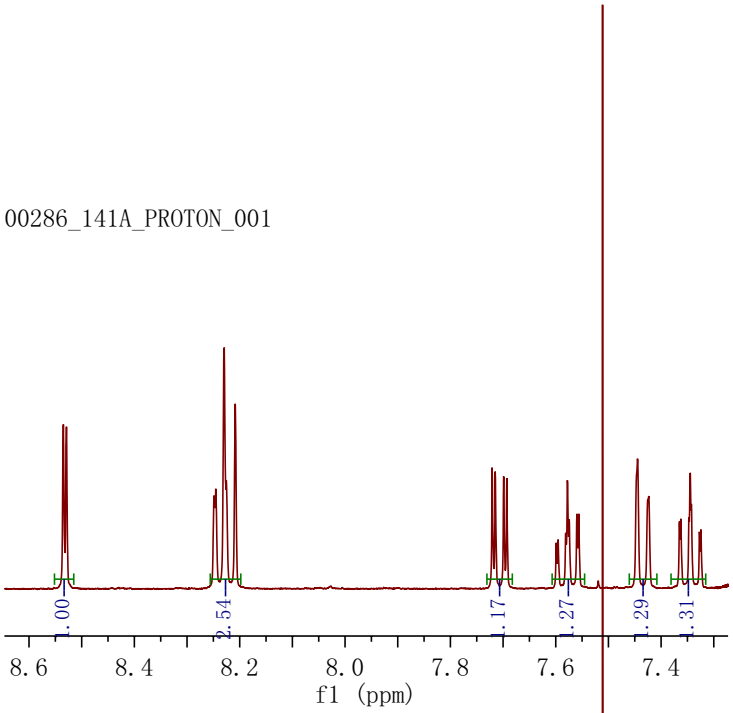


3ap

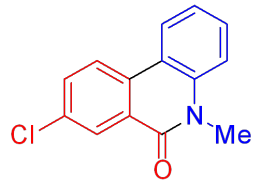
00286_141A_PROTON_001



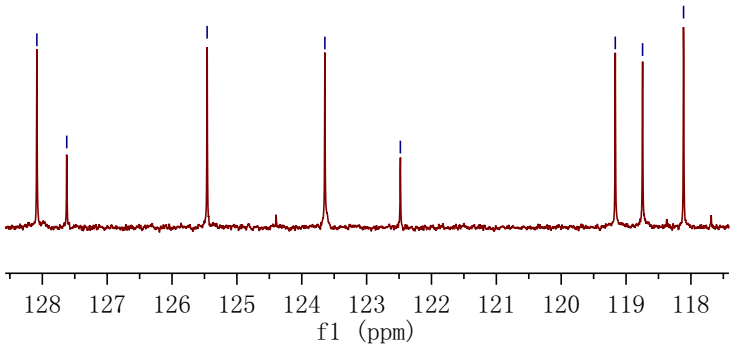
3cj



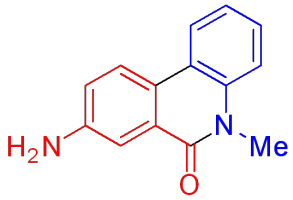
00286_141_CARBON_001



3cj

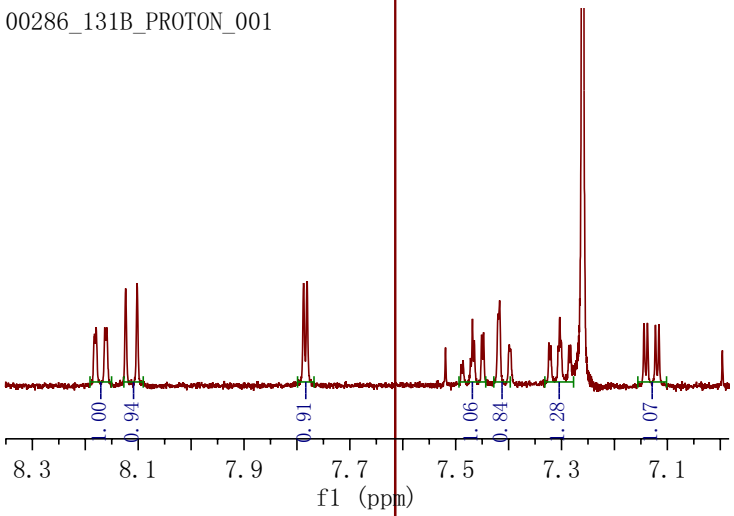


00286_131B_PROTON_001

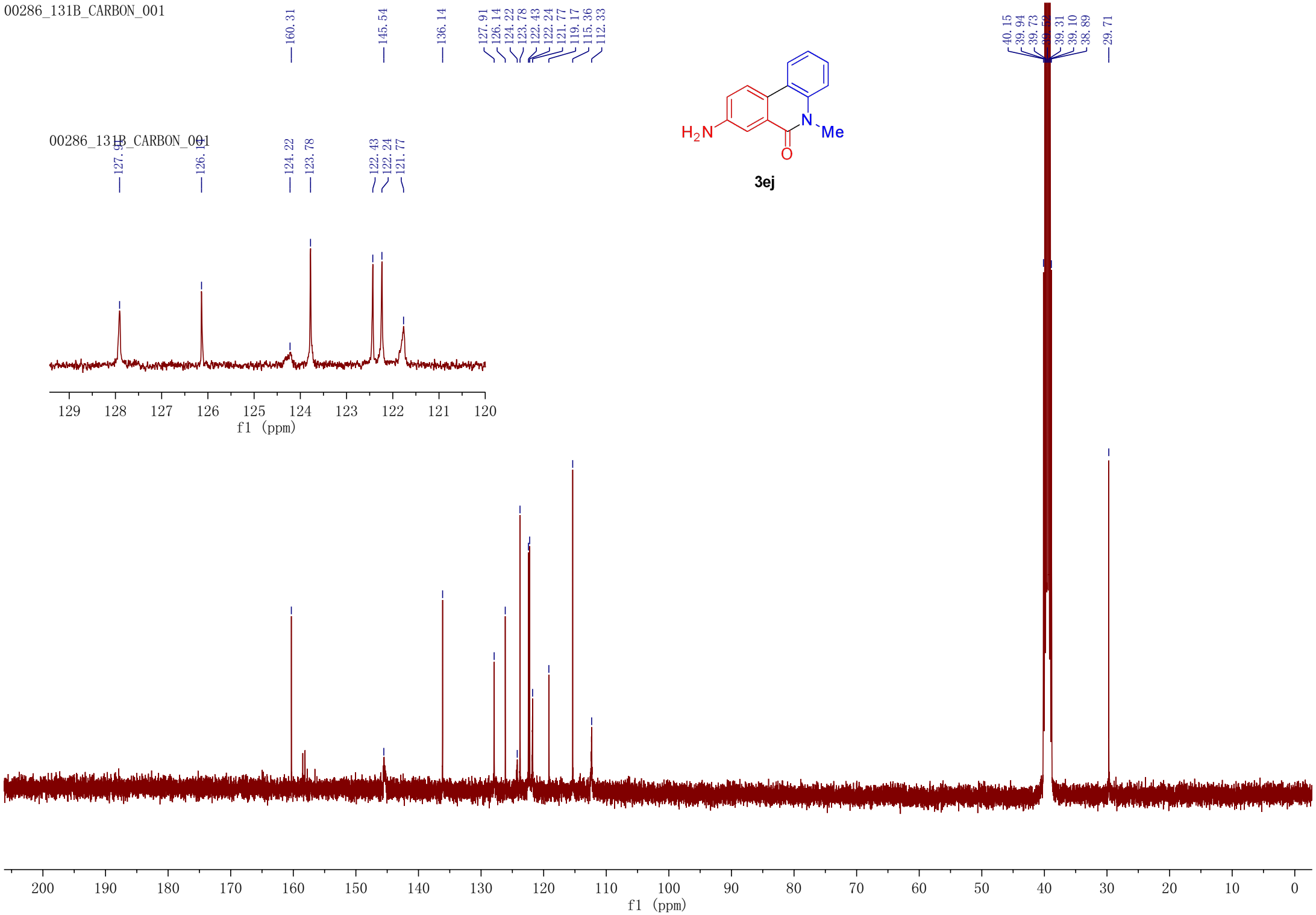


3ej

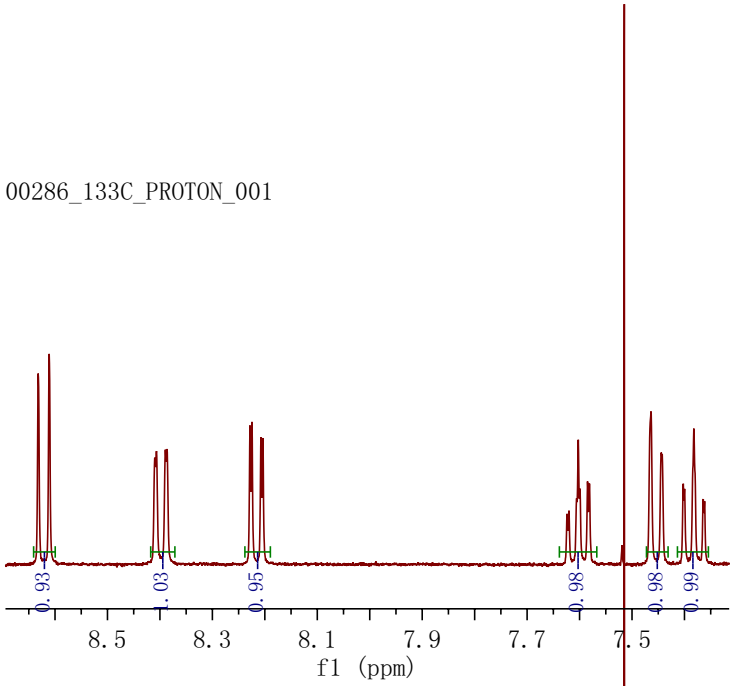
00286_131B_PROTON_001

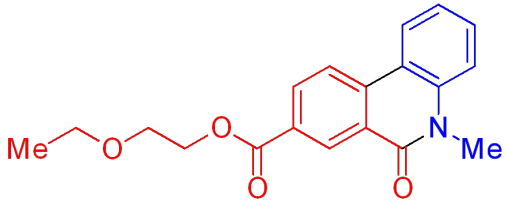


00286_131B_CARBON_001



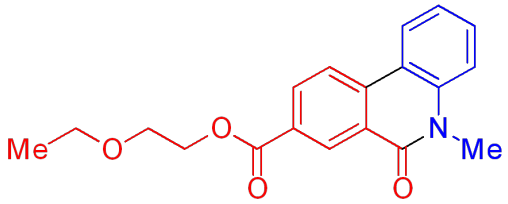
00286_133C_PROTON_001





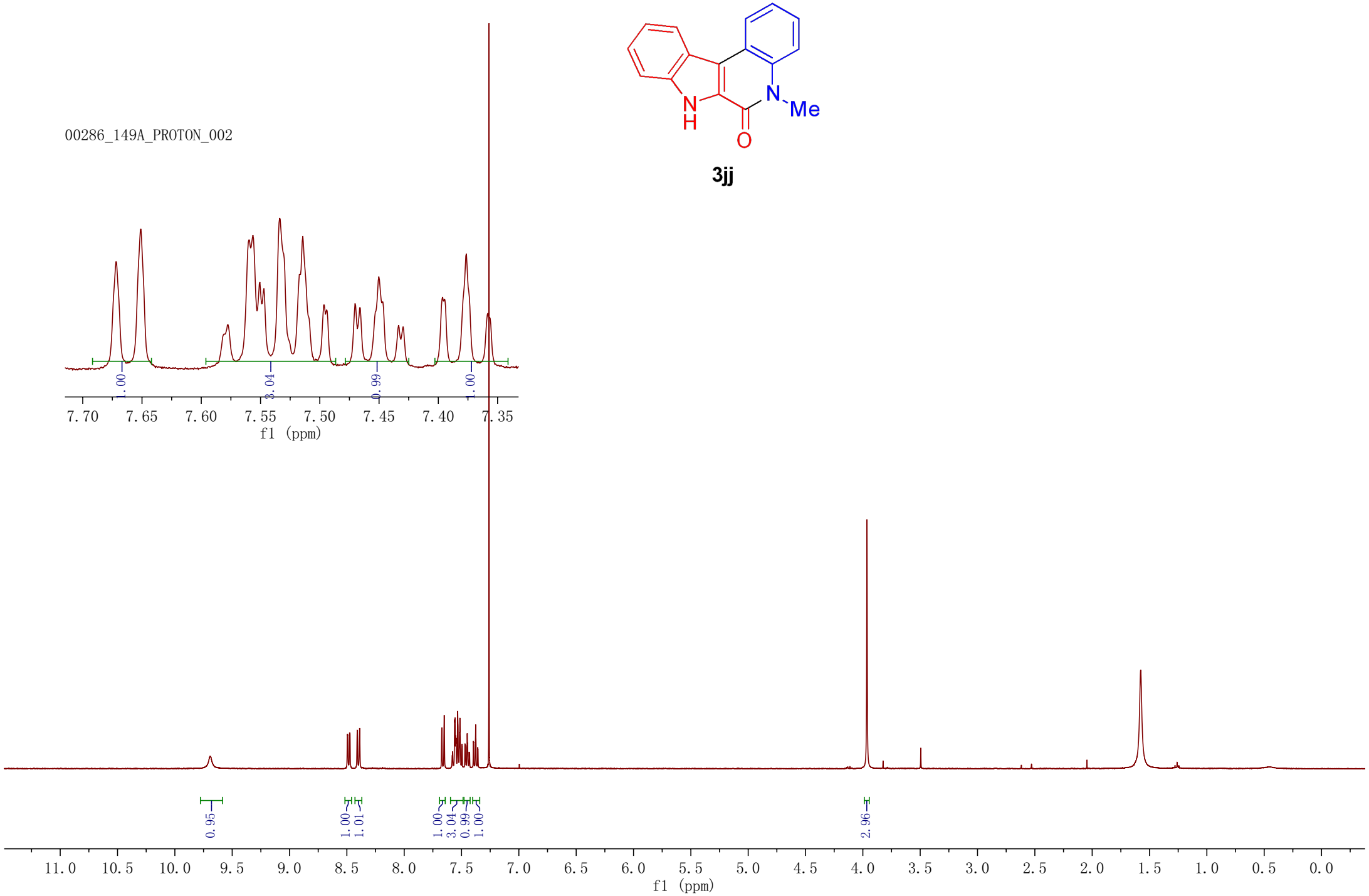
3fj

00286_133C-carbon_CARBON_001



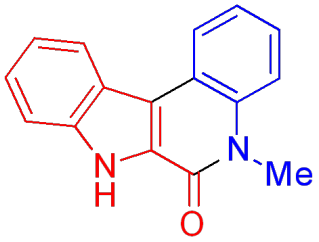
3fj

00286_149A_PROTON_002



3jj

00286-149_carbon_CARBON_001



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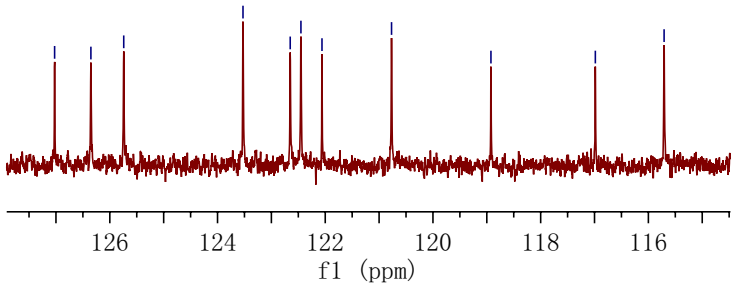
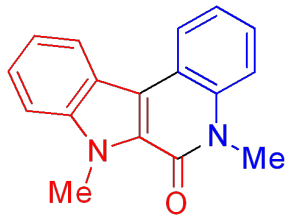
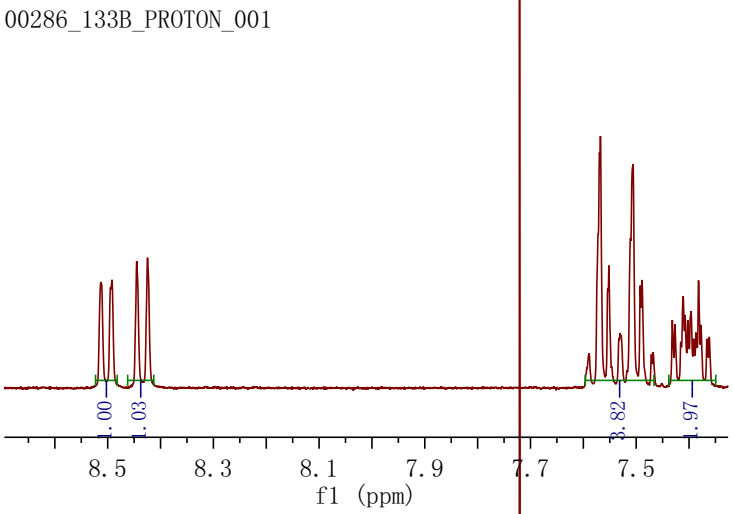


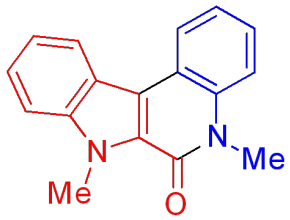
00286_133B_PROTON_001



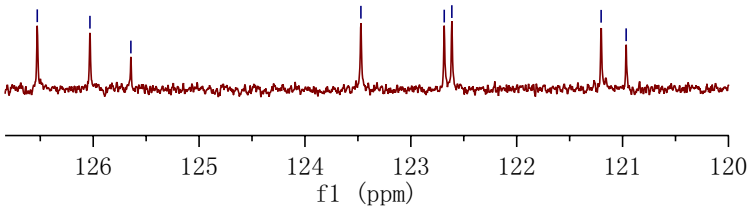
3kj



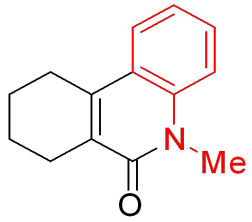
00286_133B-carbon_CARBON_001



3kj

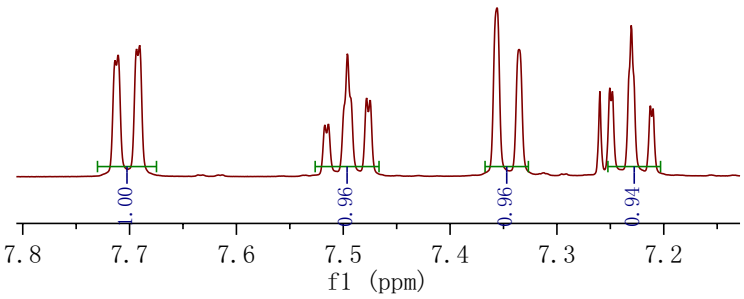


00286_172A_PROTON_002



3lj

00286_172A_PROTON_002



00286_172B_CARBON_001

162.18
141.72
138.07
128.96
128.52
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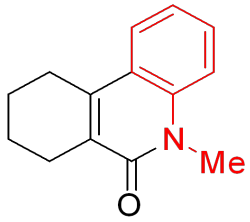
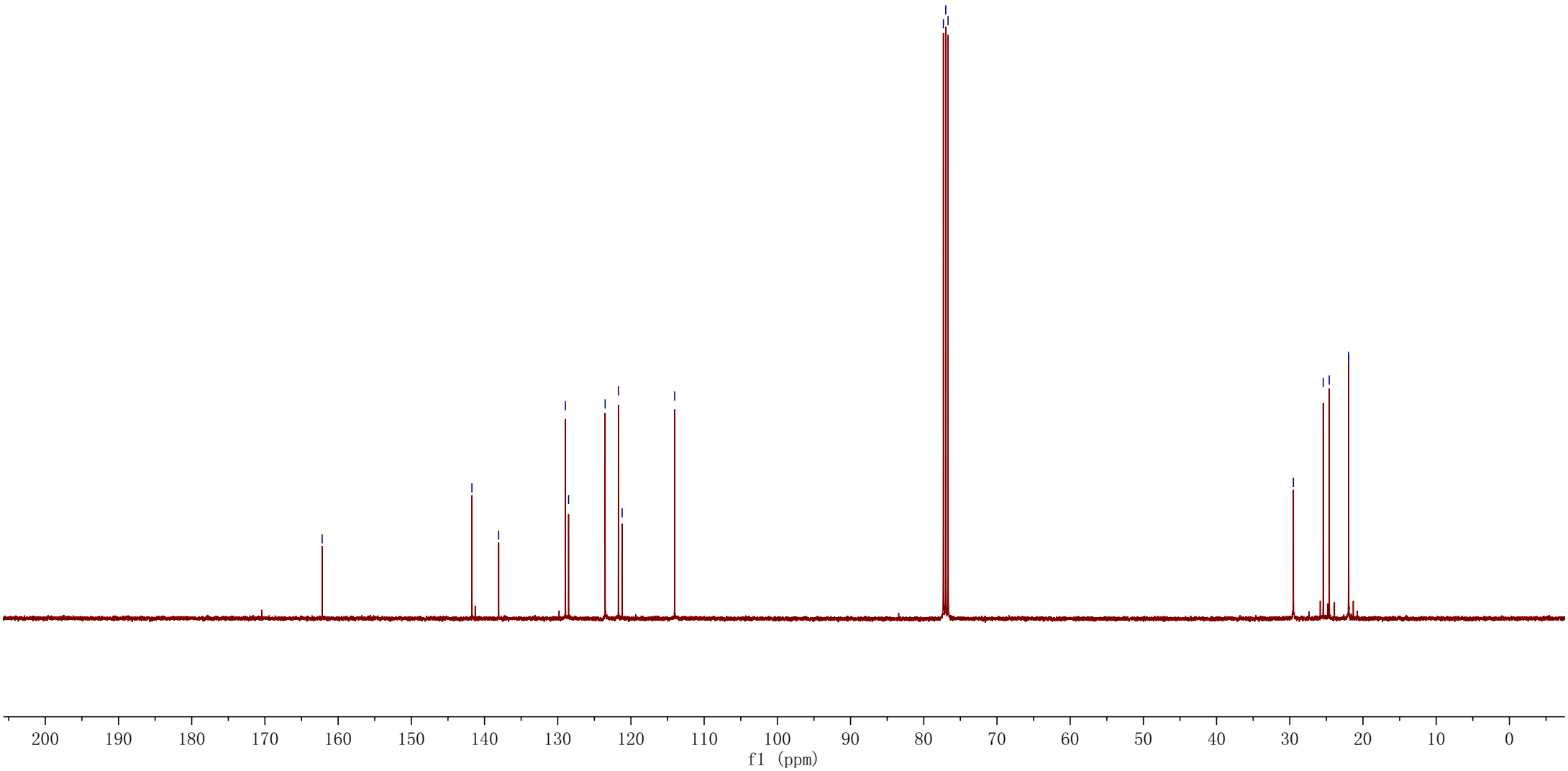
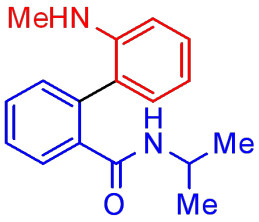
121.71
121.20
114.03
77.32
77.00
76.68
29.51
25.43
24.61
21.97
21.95



3lj



00286_169_PROTON_001

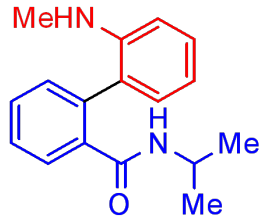


8

f1 (ppm)

00286_169_CARBON_001

167.06
146.26
136.26
135.86
130.84
130.76
129.75
129.53
129.41
128.28
117.43
109.91
77.32
77.00
76.68
41.29
30.32
21.97
21.92



8