Supporting Information

Decarboxylative C-4 Alkylation of Pyridines Enabled by Ground-state Hantzsch Ester

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Table of Contents

1. General information

General analytical information

^{1}H NMR spectra were recorded on Bruker Avance III HD 600 or Avance 400 MHz spectrometer at ambient temperature. Chemical shifts are recorded in ppm relative to tetramethylsilane (TMS, 0.00 ppm) and with the solvent resonance as the internal standard. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, m = multiplet, dd = doublet of doublets, dt = doublet of triplets, td = triplet of doublets, and br = broad signal), coupling constants (Hz), and integration.

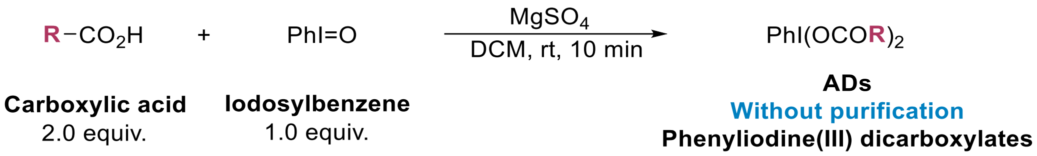
^{13}C NMR data were collected on Bruker Avance III HD 150 or Avance 100 MHz spectrometer. Chemical shifts are reported in ppm from the TMS with the solvent resonance as internal standard. High-resolution mass spectra (HRMS) were recorded on an ABI/Sciex QStar Mass Spectrometer (ESI).

General manipulation considerations

Flash column chromatography was performed using silica gel (Silicycle Inc, ultra-pure grade). The eluents for column chromatography were presented as ratios of solvent volumes. Yields reported in the publication are of isolated materials unless otherwise noted. All new products were characterized by ^{1}H, ^{13}C and ^{19}F NMR spectroscopy as well as high-resolution mass spectrometry (HRMS), and reported with physical state and the eluents for column chromatography were presented as ratios of solvent volumes. All known products were characterized by ^{1}H, ^{13}C and ^{19}F NMR spectroscopies and the spectra were compared with the reported data. All regents and solvents were purchased from commercial source.

2. General procedure

Preparation of phenyliodine(III) dicarboxylates

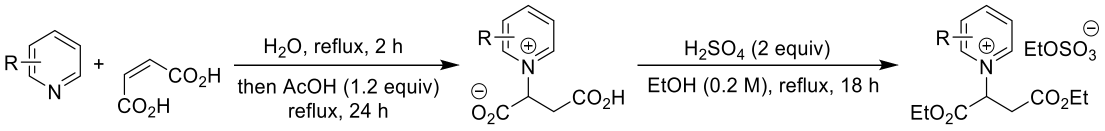


Following the literature procedure,[1] a 100 mL round bottom flask was charged with iodosylbenzene (1.32 g, 6.0 mmol, 1.0 equiv), carboxylic acid (12.0 mmol, 2.0 equiv), DCM (50 mL) and anhydrous $MgSO_4$ (2 g). The mixture was stirred at room temperature for 10 min, filtered and the solvent removed under reduced pressure (the vacuum ~ 0.1 MPa), yielding desired phenyliodine(III) dicarboxylate.

The products are typically generated in >99% yield. These phenyliodine(III) dicarboxylates can be directly used in the decarboxylative functionalization reactions without purification.

Iodosylbenzene (PhI=O) can be readily synthesized using the procedure described in *Org. Synth.*, **1963**, *43*, 60.

General procedure for pyridinium feedstock synthesis

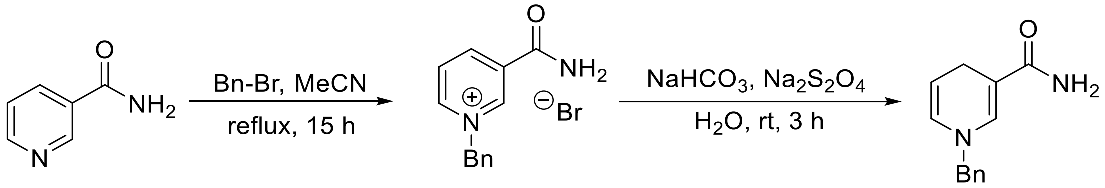


Following the literature procedure :[2]

Step 1: A solution of maleic acid (1.16 g, 10.0 mmol) and substituted pyridine (1.0 equiv, 10.0 mmol) in H_2O (5 mL) was stirred at 90 °C for 2 h. After a crystalline solid appeared in reaction mixture, acetic acid (686 μL, 1.2 equiv, 12.0 mmol) was added. The solution was kept in suspension with stirring at the same temperature for 24 h. The crude reaction mixture was cooled down to room temperature, filtered, washed with small amount of MeOH and EtOAc. The resulting white solid was dried under reduced pressure by rotary evaporator and high vacuum for overnight. The product was obtained and used for next step without further purification.

Step 2: A solution of pyridinium carboxylate salt (2.5 mmol, 1.0 equiv) in EtOH (12.5 mL, 0.2 M) with concentrated sulfuric acid (2.0 equiv, 5.0 mmol, 260 μL) was stirred at 90 °C for 18 h. Upon completion, the solvent (EtOH) was evaporated under reduced pressure. The concentrated crude mixture was diluted in dichloromethane (15 mL) and H_2O (2 mL) and extracted by dichloromethane monitoring by TLC both aqueous and organic phase until no desired product in the aqueous phase was observed. The combined organic phase was dried by anhydrous Na_2SO_4, filtered, concentrated under reduced pressure. The resulting colorless liquid was used for next step without further purification.

General procedure for the synthesis of BNAH (3b)

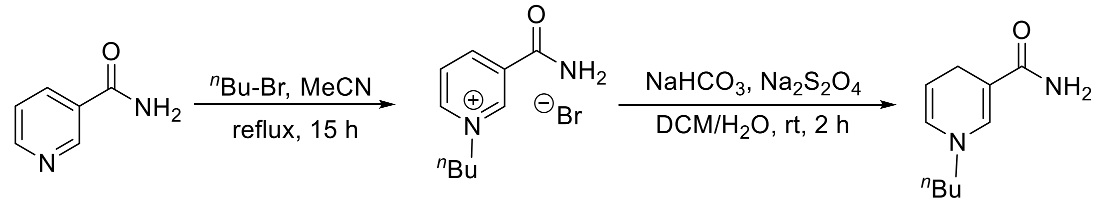


Following the literature procedure:[3]

Step 1: Nicotinamide (4.88 g, 40.0 mmol) was dissolved in MeCN (40 mL) and benzyl bromide (4.75 mL, 40.0 mmol) was added. The reaction mixture was refluxed for 15 h, after which time a precipitate was observed. The solution was cooled and diethyl ether (50 mL) was added to further precipitate the final product. After filtering and washing with diethyl ether (3 × 10 mL), the bromide salt l-benzyl-3-carbamoylpyridiumbromide was obtained as a white powder (10.8 g, 92%).

Step 2: Under nitrogen atmosphere,1-benzyl-carbamoylpyridinium bromide (2.93 g, 10.0 mmol) was dissolved in distilled H_2O (60 mL), and $NaHCO_3$ (4.20 g, 50.0 mmol) was added. Sodium dithionite $Na_2S_2O_4$ (8.71 g, 50.0 mmol) was then added in small portions and the reaction mixture was stirred at room temperature for 3 h in the dark, during which time the solution turned from orange to yellow as the yellow product precipitated. The solid was filtered, washed with cold water (3 × 10 mL) and dried over phosphorus pentoxide under vacuum to afford product 1-benzyl-1,4-dihydronicotinamide as a bright yellow powder (1.65 g, 77.9%).

General procedure for the synthesis of BuNAH (3c):

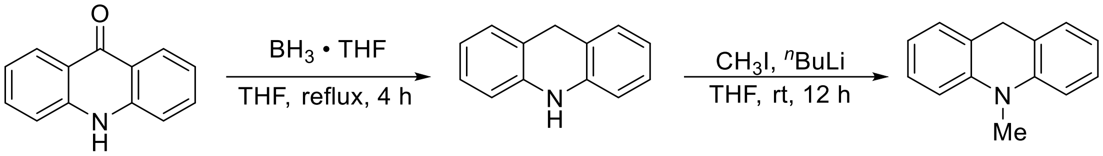


Following the literature procedure:[3]

Step 1: Nicotinamide (4.88 g, 40.0 mmol) was dissolved in MeCN (40 mL) and butyl bromide (4.72 mL, 44.0 mmol) was added. The reaction mixture was refluxed for 15 h, after which time the solution was cooled and diethyl ether (50 mL) was added to precipitate the final product. After filtering and washing with diethyl ether (3 × 10mL), the bromide salt was obtained as a white powder (8.3 g, 81%).

Step 2: Under nitrogen atmosphere, 1-butyl-3-carbamoylpyridinium bromide (2.58 g, 10.0 mmol) was dissolved in H_2O/DCM (200 mL/100 mL) at 0 °C, and $NaHCO_3$ (5.04 g, 60.0 mmol) was added. Sodium dithionite (6.97 g, 40.0 mmol) was then added in small portions over a period of 10 min and the reaction mixture was stirred at 0 °C for 2 h in the dark. The organic phase was separated, washed with cold water (3 × 10 mL), dried over anhydrous Na_2SO_4, and the solvent was evaporated under reduced pressure to afford product as a bright yellow powder (0.63 g, 35%), which was recrystallized from MeOH-H_2O.

General procedure for the synthesis of AcrH$_2$ (3d):

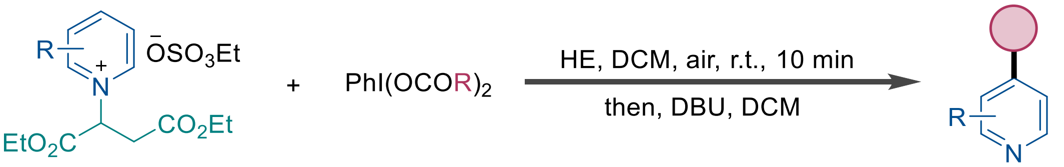


Following the literature procedure:[4]

Step 1: A 250 mL round bottom flask was charged with acridin-9(10*H*)-one (3.9 g, 20.0 mmol) and THF (80 mL), the flask was placed under vacuum and backfilled with nitrogen three times. Then, BH_3•THF solution (1.0 M in THF; 40 mL, 40.0 mmol) was added dropwise to the mixture. After that, the mixture was refluxed for 4 h under nitrogen atmosphere. On completion (checked by TLC) the mixture was cooled to 0 – 5 °C and brine (80 mL) was cautiously added followed by 2 M aq. NaOH (20 mL). The organic layer was separated, and the aqueous layer was extracted with Et_2O (1 × 40 mL). The collected organic layers were washed with sat. aq. $NaHCO_3$ (1 × 40 mL), dried over anhydrous Na_2SO_4 and evaporated. The crude product was purified by column chromatography on silica gel (PE/DCM = 10/1) to afford 9,10-dihydroacridine as a light yellowish powder (3.17 g, 81% yield).

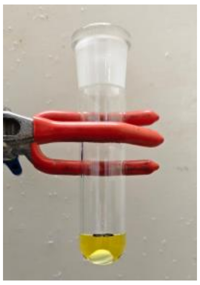
Step 2: A Schlenk-tube equipped with a magnetic stirrer was evacuated and refilled with N_2, then wise at 0 – 5 °C and the mixture stirred for 60 minutes, followed by the addition of methyliodide (3.0 mmol) in THF (2 mL). The mixture was then stirred at -5 °C for additional 2 h and then at room temperature overnight. The reaction was quenched by pouring on H_2O (30 mL), and the product was extracted with EtOAc (3 × 30 mL). The organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated to dryness in vacuo. The residue was purified by column chromatography on silica gel (PE/EA = 10/1) to afford the purified product (0.785 g, 75%). (Note: This compound easily turns brown on air and may be stored under nitrogen at -18 °C in a refrigerator).

General procedure (GP-A):



Fumarate-Pyr **ADs**

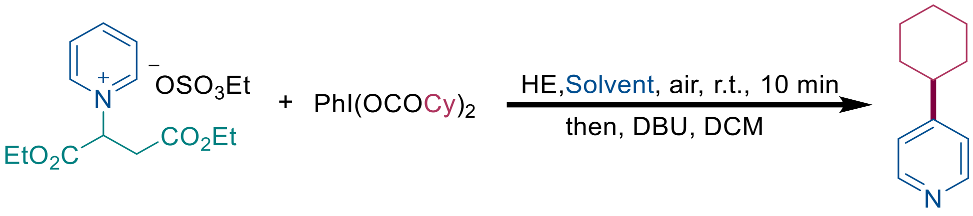
Under air atmosphere, fumarate-derived pyridinium salt (**Fumarate-Pyr**, 0.2 mmol), **ADs** (0.4 mmol), **HE** (0.2 mmol, 50.6 mg), DCM (2 mL) were sequentially added to a test tube. The mixture was stirred at room temperature for 10 min. Then, DBU (3 equiv., 0.6 mmol, 90 μL) was added to the mixture, and the reaction mixture was stirred at room temperature for another 30 min. The crude product residue was purified by column chromatography on silica gel or thin layer chromatography (PE/EA = 30/1 ~ 10/1) to afford the purified product.

The solvent evaporation during the reaction		
		
Stir for 0 min	Stir for 10 min	Stir for 40 min

NOTE: When the reaction is stirred open to air at 25 °C, solvent loss over the reaction period is minimal.

3. Condition optimization

Table S1: The screen of solvents[a]



1a **2a** **23**

Entry	Solvent	Time	Yield[b] (%)
1	DCM	10 min	47
2	DCE	10 min	35
3	$CHCl_3$	10 min	21
4	DMSO	10 min	30
5	DMF	10 min	42
6	THF	10 min	28
7	EA	10 min	n.d.
8	MeCN	10 min	42

[a]Reaction conditions: **1a** (0.2 mmol, 75.4 mg), **AD-1** (0.2 mmol, 91.7 mg) and **HE** (0.2 mmol, 50.6 mg) in solvent (2 mL) under air at room temperature. [b]The yield was determined by ^{1}H NMR analysis using CH_2Br_2 as the internal standard.

Note:

(1) For reactions conducted in DCM, deprotection step was performed by direct addition of DBU to the reaction mixture.

(2) For reactions conducted in high-boiling solvents (DMF or DMSO), deprotection step was performed by direct addition of DBU to the reaction mixture.

(3) For reactions conducted in other low-boiling solvents (e.g., DCE, $CHCl_3$, or THF), the solvent was first removed under reduced pressure; DCM (2 mL) was then added, followed by DBU.

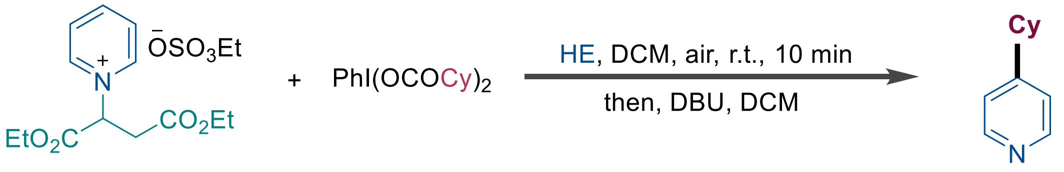
Procedure for ^{1}H NMR Yield Measurement

Low-boiling solvents: Upon completion of the reaction, the reaction mixture was concentrated under reduced pressure to remove the solvent (30 °C, 0.1 MPa). CH_2Br_2 (0.2 mmol, 14 μL) was then added as an internal standard, followed by $CDCl_3$ for ^{1}H NMR analysis.

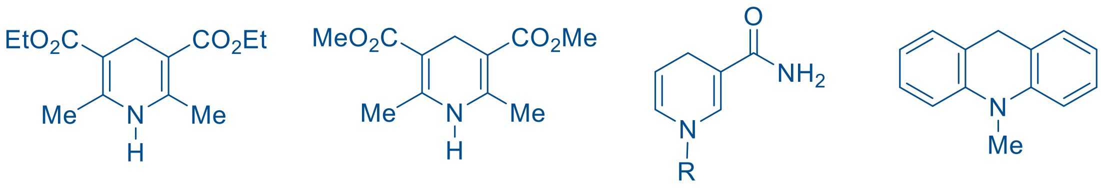
DMSO: After the reaction is complete using deuterated DMSO as the solvent, CH_2Br_2 (0.2 mmol, 14 µL) was added directly as an internal standard, followed by $CDCl_3$ for ^1H NMR analysis.

DMF: Upon completion of the reaction, the mixture was extracted once with EA/saturated NaCl solution (10 mL / 10 mL). The aqueous layer was re-extracted with EA (10 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure (30 °C, 0.1 MPa). CH_2Br_2 (0.2 mmol, 14 µL) was then added as an internal standard, followed by $CDCl_3$ for ^1H NMR analysis.

Table S2: The screen of NADH analogues[a]



1a **2a** **23**

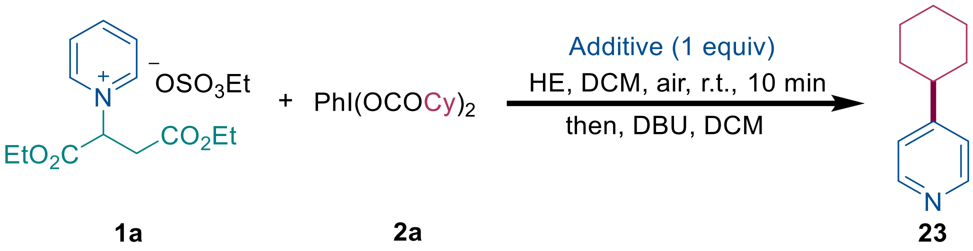


3a (HE) **3b** (Me-HE) **3c** (R = ^{t}Bu, BuNAH) **3d** (R = Bn, BNAH) **3e** ($AcrH_2$)

Entry	NADH Analogues	Time	Yield[c] (%)
1	**3a**	10 min	47
2	**3a**	30 min	47
4	**3b**	10 min	45
5	**3c**	10 min	40
6	**3d**	10 min	33
7	**3e**	10 min	n.d

[a] Reaction conditions: **1a** (0.2 mmol, 75.4 mg), **2a** (0.2 mmol, 91.7 mg) and **NADH Analogue** (0.2 mmol) in DCM (2 mL) under air at room temperature. [b] DBU = 1,8-Diazabicyclo[5.4.0]undecane-7-ene, $AcrH_2$ = N-Methyl-9,10-dihydroacridine. BNAH = N-benzyl-dihydronicotinamide, BuNAH = N-butyl-dihydronicotinamide. [c] The yield was determined by ^1H NMR analysis using CH_2Br_2 as the internal standard.

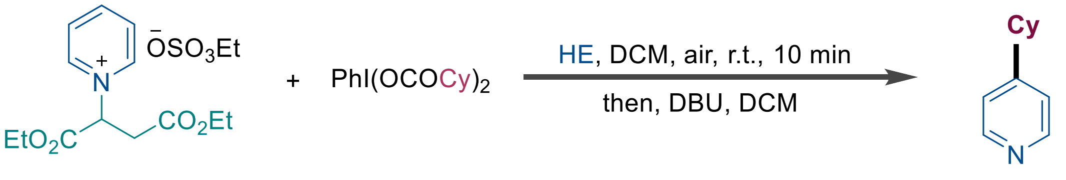
Table S3: The Effects of Additives[a]



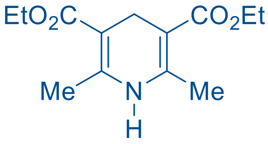
Entry	NADH Analogues	Additive (1.0 equiv)	Time	Solvent	Yield[b] (%)
1	**HE**	none	10 min	DCM	47
2	**HE**	DIPEA	10 min	DCM	42
3	**HE**	Et_3N	10 min	DCM	39
4	**HE**	K_2CO_3	10 min	DCM	46
5	**HE**	Cs_2CO_3	10 min	DCM	31

[a]Reaction conditions: **2** (0.2 mmol, 75.4 mg), **2a** (0.2 mmol, 91.7 mg) and **HE** (0.2 mmol, 50.6 mg) in DCM (2 mL) under air at room temperature. [b]The yield was determined by ^{1}H NMR analysis using CH_2Br_2 as the internal standard.

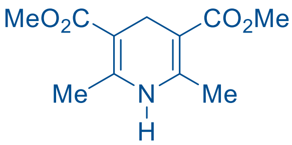
Table S4: Full optimization[a]



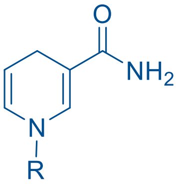
1a **2a** **23**



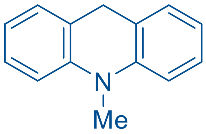
3a (HE)



3b (Me-HE)



3c (R = ^{t}Bu, BuNAH)
3d (R = Bn, BNAH)



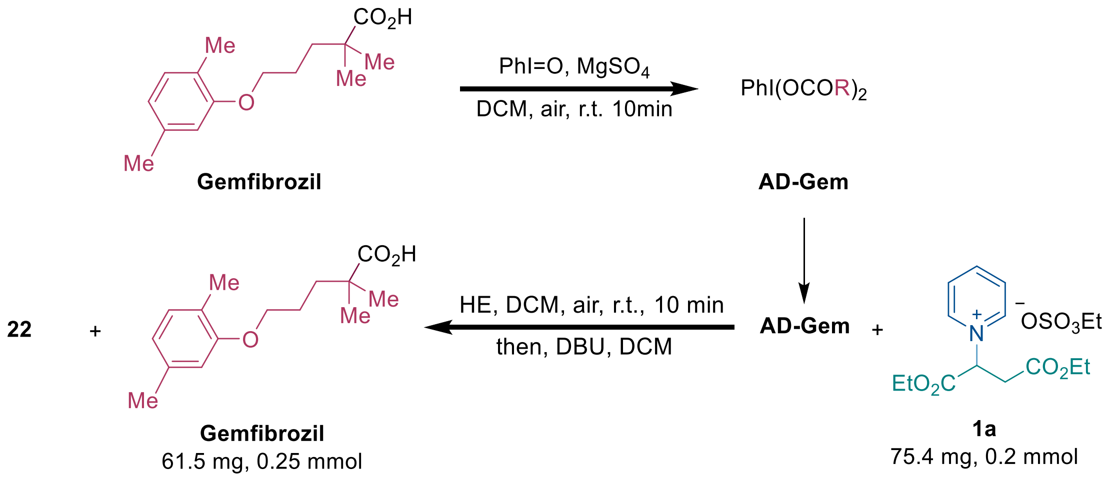
3e ($AcrH_2$)

Entry	Variation	Yield[b] (%)
1	none	47
2	30 min	47
3	with blue LEDs	46
4	**3b** instead of HE	45
5	**3c** instead of HE	40
6	**3d** instead of HE	33
7	**3e** instead of HE	N.R.[c]
8	DMF instead of DCM	42
9	DCE instead of DCM	35
10	adding K_2CO_3 (1.0 equiv.)	46
11	adding DIPEA (1.0 equiv.)	42
12	increasing **2a** to 2.0 equiv.	79
13	increasing **2a** to 2.0 equiv. sealed	78
14	increasing **2a** to 2.0 equiv., under dark	79

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.2 mmol) and HE (0.2 mmol) in DCM (2 mL) under ambient, open-air conditions. [b] Yields were determined by ^{1}H NMR analysis using CH_2Br_2 as the internal standard. [c] N.R.: No reaction. HE = Hantzsch ester; BNAH = 1-Benzyl-1,4-dihydronicotinamide; BuNAH = 1-Butyl-1,4-dihydronicotinamide; $AcrH_2$ = N-methyl-9,10-dihydroacridine, DIPEA = N,N-Diisopropylethylamine.

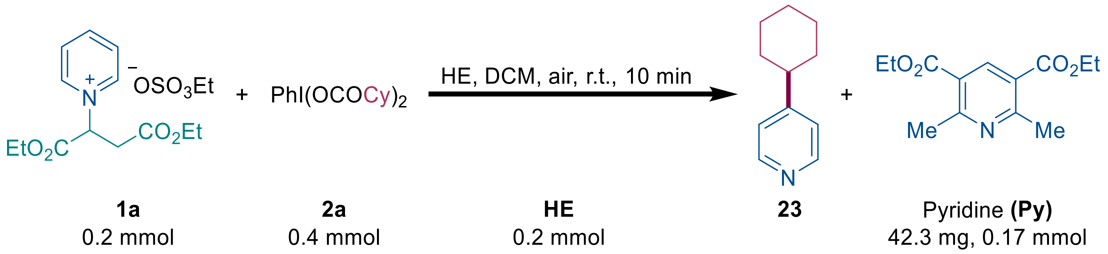
4. Recovery of by-products

4.1 The recovery of carboxylic acids



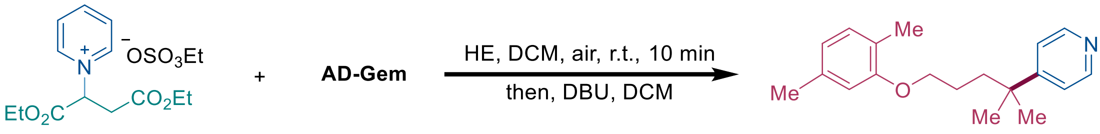
After the reaction was completed under the standard reaction conditions (Page S7, **GP-A**)，the generated Gemfibrozil could be isolated by column chromatography on silica gel or thin layer chromatography (PE/EA = 4/1 ~ 3/1), yielding 61.5 mg.

4.2 Procedure for the recovery of pyridine



After the thiolation under the standard reaction conditions (Page S7, **GP-A**), the **Py** can be separated on silica gel chromatography (PE/EA = 10/1), yielding 42.3 mg.

5. Gram-scale experiments



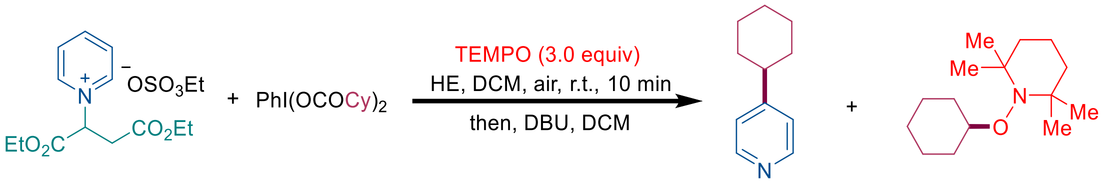
1a
0.943 g, 2.5 mmol

22
from Gemfibrozil
0.566 g, 80%

Under ambient and open-air conditions, **1a** (2.5 mmol, 0.943 g), **AD-Gem** (5.0 mmol, 3.513 g), **HE** (2.5 mmol, 0.633 g), and DCM (25 mL) were added in a test tube. The mixture was stirred at room temperature for 10 min. The crude material was used next step without further purification. The crude alkylated product was added DBU (3 equiv, 7.5 mmol, 1.120 mL) and the reaction mixture was stirred at room temperature for 30 min. The crude product residue was purified by column chromatography on silica gel (PE/EA = 10/1) to afford the following purified product: Product **22**, 0.566 g, 80% yield.

6. Mechanistic experiments

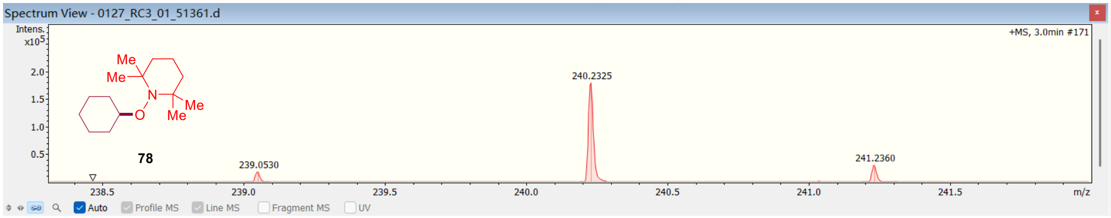
6.1 Radical trapping experiment



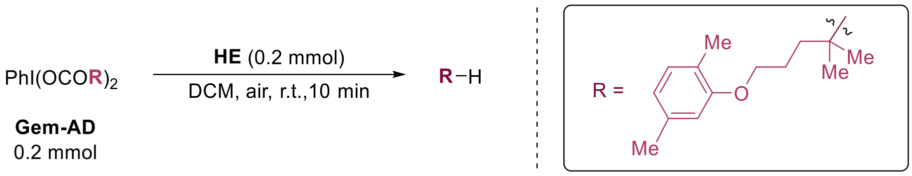
1a **2a** **23** not detected **78** (HRMS)

Procedure: Under air atmosphere, **1a** (0.2 mmol, 75.4 mg), **2a** (0.4 mmol, 183.3 mg), **HE** (0.2 mmol, 50.6 mg), TEMPO (0.6 mmol, 93.8 mg) and DCM (2 mL) were added in a test tube. The mixture was stirred at room temperature for 10 min. The crude alkylated product was added DBU (3 equiv, 0.6 mmol) and the reaction mixture was stirred at room temperature for 30 min. Under such conditions, the corresponding product **23** was not detected. The corresponding TEMPO-adduct **78** was characterized by HRMS (ESI).

HRMS (ESI) *m/z*: Calculated for $C_{15}H_{30}NO^+$ $[M+H]^+$ 240.2322. Found 240.2325.

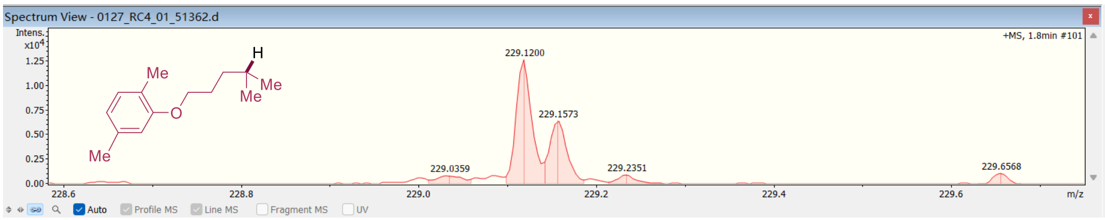


6.2 The evidence of HAT pathway



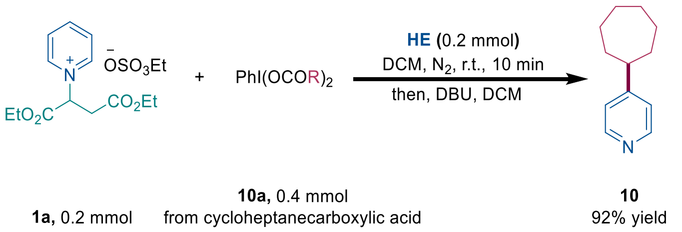
Procedure: Under air atmosphere, **Gem-AD** (0.2 mmol, 140.5 mg), **HE** (0.2 mmol, 50.6 mg) and DCM (2 mL) were added in a test tube. The mixture was stirred at room temperature for 10 min. The corresponding hydrogenation product **R**–H was characterized by HRMS (ESI) and NMR.

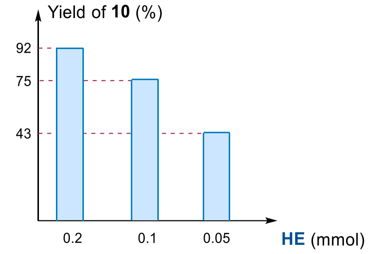
HRMS (ESI) *m/z*: Calculated for $C_{14}H_{22}NaO^+$ $[M+Na]^+$ 229.1563. . Found 229.1573.



NOTE: At the standard 10-minute reaction time, the yield of R–H is below 5%. To obtain sufficient material for NMR characterization, the reaction was extended to 1 hour, affording R–H in 10.3% isolated yield.

6.3 Pathway of radical generation[b]





Entry	1a (mmol)	10a (mmol)	HE (mmol)	10 (mmol)	Yield[a] (%)
1	0.2	0.4	0.2	0.184	92
2	0.2	0.4	0.1	0.15	75
3	0.2	0.4	0.05	0.086	43
4	0.2	0.4	0.2	0.184	92
5	0.2	0.3	0.2	0.156	78
6	0.2	0.2	0.2	0.126	63

[a]The yield was determined by ^1H NMR analysis using CH_2Br_2 as the internal standard.

[b] To exclude any potential contribution of atmospheric O_2 to the oxidative rearomatization step, the reaction was conducted under a nitrogen atmosphere.

Result:

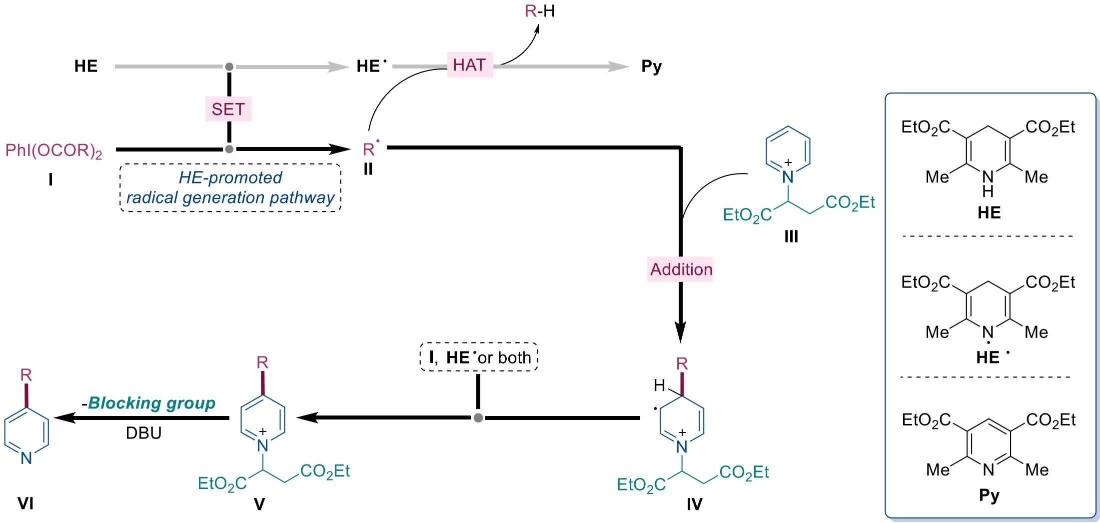
If the aryliodine(III) dicarboxylate were reduced exclusively by HE to generate the alkyl radical, the theoretical yield of product **10** would be limited by stoichiometry:

- Entry 2: Maximum 50% (0.10 mmol). The observed 75% yield exceeds this limit.
- Entry 3: Maximum 25% (0.05 mmol). The observed 43% yield exceeds this limit.

In both cases, the experimental results surpass the theoretical maximums, providing ~~strong~~ evidence for an additional radical-generation pathway operating in concert with HE reduction.

For precedents of aryliodine(III) reagents serving as oxidants in oxidative rearomatization, see: *Org. Lett.* **2018**, *20*, 4686.

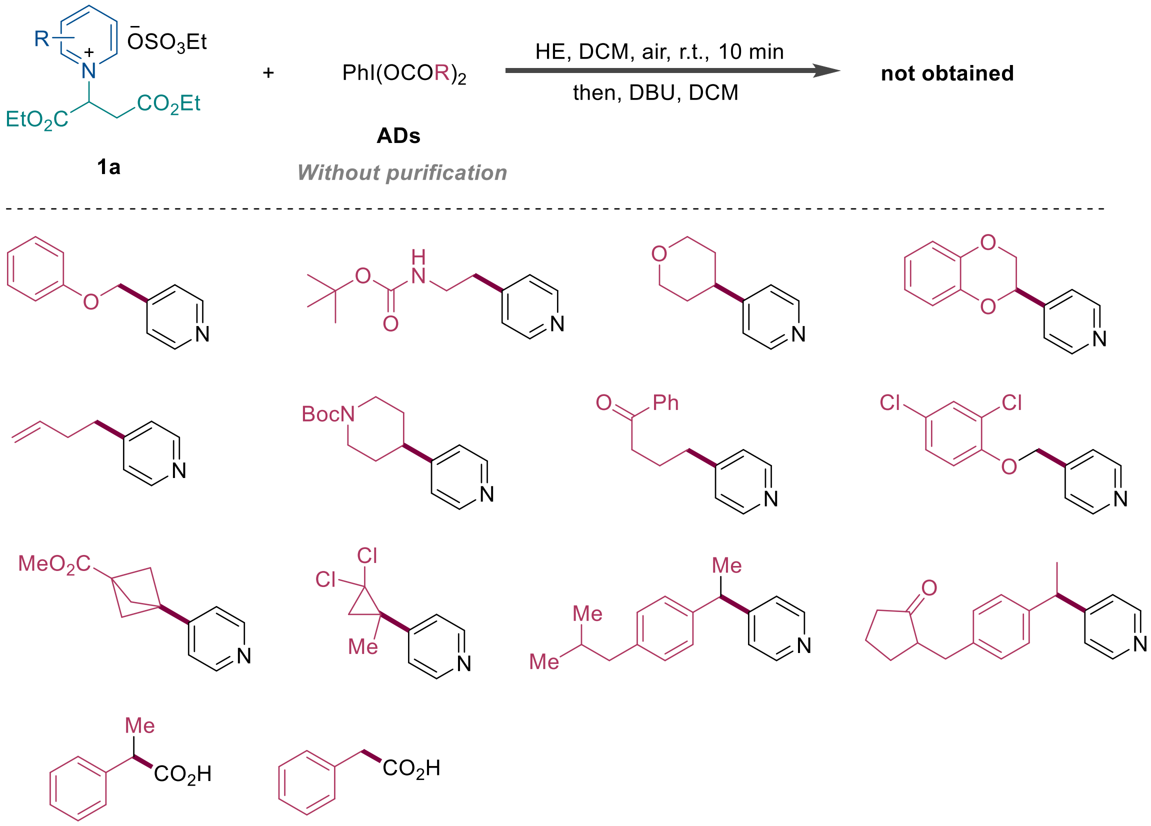
6.4 Proposed mechanism



The reaction is proposed to begin with single-electron transfer (SET) from the Hantzsch ester (**HE**) to phenyliodine(III) dicarboxylate **I**, generating radical **II** and **HE**$^{\bullet}$, and a proton (which is immediately captured by the in situ-formed carboxylate). A portion of **II** undergoes hydrogen-atom transfer (HAT) with **HE**$^{\bullet}$ to afford the HAT byproduct (**R–H**) and the corresponding pyridine (**Py**). Subsequently, radical **II** adds to pyridinium species **III** to give radical cation **IV**. Then, this intermediate is oxidized via another SET step mediated by phenyliodine(III) dicarboxylate **I, HE**$^{\bullet}$ or both, affording intermediate **V** after deprotonation. Finally, DBU-mediated removal of the blocking group furnishes product **VI**.

NOTE: Previous studies indicate that a proton-coupled electron transfer (PCET) is unlikely to occur in the HE-promoted radical generation process (for more details, see https://doi.org/10.1002/anie.202415131, SI, Page S23).

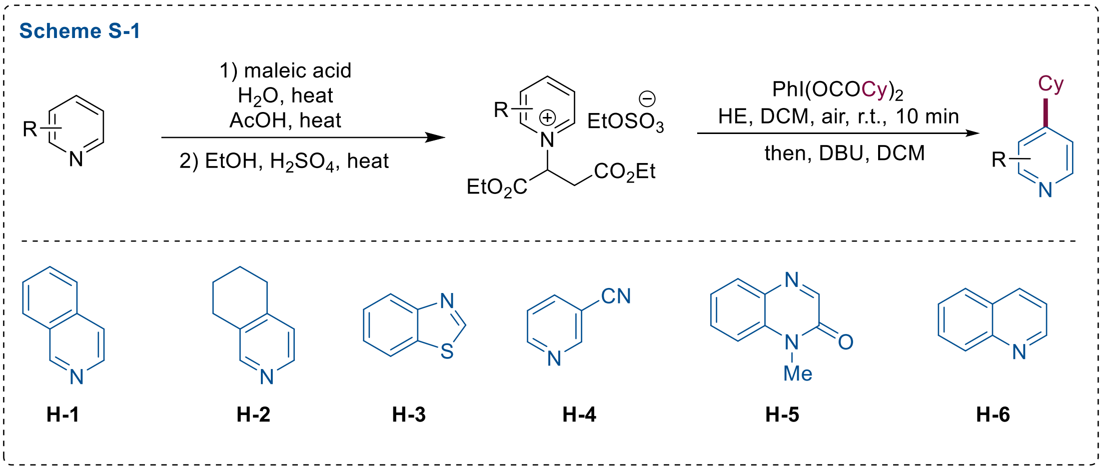
7. Unsuccessful examples



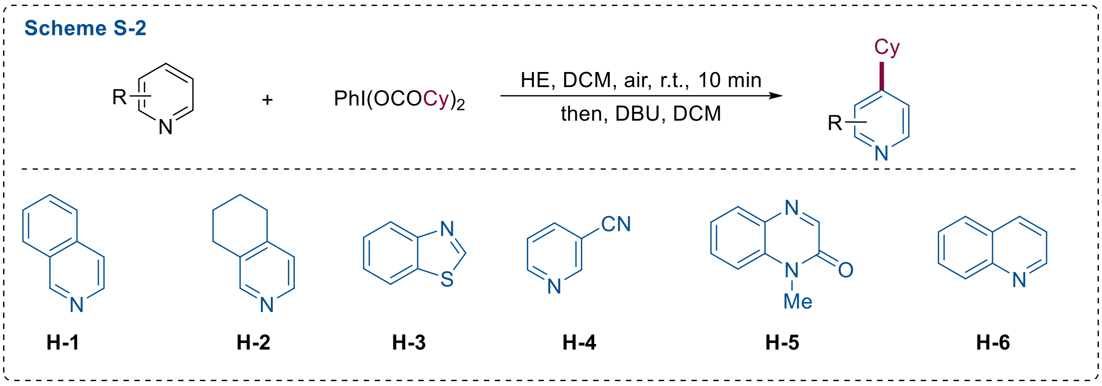
Under air atmosphere, fumarate-derived pyridinium salt (**Fumarate-Pyr**, 0.2 mmol), **ADs** (0.4 mmol), **HE** (0.2 mmol, 50.6 mg), DCM (2 mL) were sequentially added to a test tube. The mixture was stirred at room temperature for 10 min. Then, DBU (3 equiv, 0.6 mmol, 90 μL) was added to the mixture, and the reaction mixture was stirred at room temperature for another 30 min.

NOTE: Using these above **ADs**, we were unable to obtain the desired product.

Scheme S-1



Scheme S-2



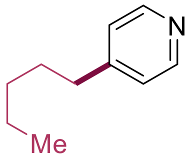
Scheme S-1 (Activation Followed by Alkylation)**:** The reaction was carried out according to the General Procedure for Pyridinium Feedstock Synthesis (Page S4). Arene **H-1** and **H-2** were converted into the corresponding salts following the procedure reported in the literature (Ref. 2). Then, **H1** or **H2** (0.2 mmol), **ADs** (0.4 mmol, 183.3 mg), **HE** (0.2 mmol, 50.6 mg), and DCM (2 mL) were added, and the mixture was stirred at room temperature for 10 minutes. DBU (3 equiv, 0.6 mmol, 90 μL) was subsequently added, and the reaction was stirred at room temperature for an additional 30 minutes.

H-3 to **H-6** could not be converted into the corresponding salts following the procedure reported in Ref. 2, and therefore were not subjected to the subsequent alkylation reaction step.

Scheme S-2 (Direct Alkylation of Arenes): Under air atmosphere, electron-deficient arenes (**H-1** to **H-6**, 0.2 mmol), **ADs** (0.4 mmol, 183.3 mg), **HE** (0.2 mmol, 50.6 mg), DCM (2 mL) were sequentially added to a test tube. The mixture was stirred at room temperature for 10 minutes.

8. Characterization of compounds

4-Pentylpyridine (1)



Prepared according to **GP-A** [**Table 1,** footnote **c**]. The crude product purified by flash column chromatography, using PE / EA = 5 / 1 to 3 / 1 (v / v) as an eluent, to yield the title compound **1** (12.8 mg) in 43% isolated yield.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.47 (d, *J* = 5.2 Hz, 2H), 7.10 (d, *J* = 6.0Hz, 2H), 2.62 – 2.56 (m, 2H), 1.62 (p, *J* = 7.6 Hz, 2H), 1.36 – 1.28(m, 4H), 0.89 (t, *J* = 6.8 Hz, 3H).

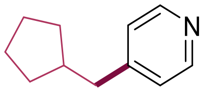
^{13}C NMR (101 MHz, Chloroform-*d*) δ 151.84, 149.56, 123.94, 35.22, 31.35, 29.98, 22.44, 13.96.

Physical State: orange oil

R$_f$ = 0.5 (PE / EA = 1 : 1)

HRMS (ESI) *m/z*: Calculated for $C_{10}H_{16}N^+$ [M+H]$^+$ 150.1277 . Found 150.1279.

4-(Cyclopentylmethyl)pyridine (2)



Prepared according to **GP-A**. The crude product purified by flash column chromatography, using PE / EA = 5 / 1 to 3 / 1 (v / v) as an eluent, to yield the title compound **2** (15.5 mg) in 48% isolated yield.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.46 (d, *J* = 4.0 Hz, 2H), 7.08 (d, *J* = 5.2 Hz, 2H), 2.59 (d, *J* = 7.6 Hz, 2H), 2.13 – 2.03 (m, 1H), 1.75 – 1.59 (m, 4H), 1.58 – 1.47 (m, 2H), 1.23 – 1.11 (m, 2H).

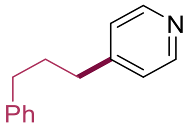
^{13}C NMR (101 MHz, Chloroform-*d*) δ 151.23, 149.52, 124.29, 41.42, 41.02, 32.45, 24.89.

Physical State: yellow solid

R$_f$ = 0.3 (PE / EA = 3 : 1)

HRMS (ESI) *m/z*: Calculated for $C_{11}H_{16}N^+$ [M+H]$^+$ 162.1277 . Found 162.1279.

4-Phenylpropylpyridine (3)



Prepared according to **GP-A** [**Table 1,** footnote **c**]. The crude product purified by flash column chromatography, using PE / EA = 5 / 1 to 3 / 1 (v / v) as an eluent, to yield the title compound **3** (14.6 mg) in 37% isolated yield.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.49 (d, *J* = 5.6 Hz, 2H), 7.30 (t, *J* = 7.2 Hz, 2H), 7.23 – 7.15 (m, 3H), 7.10 (d, *J* = 6.0 Hz, 2H), 2.65 (q, *J* = 8.0 Hz, 4H), 2.02 – 1.92 (m, 2H).

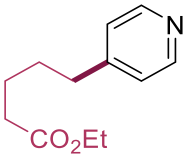
^{13}C NMR (101 MHz, Chloroform-*d*) δ 151.19, 149.70, 141.62, 128.44, 126.00, 123.94, 35.28, 34.64, 31.77.

Physical State: yellow oil

R$_f$ = 0.3 (PE / EA = 3 : 1)

HRMS (ESI) *m/z*: Calculated for $C_{14}H_{16}N^+$ $[M+H]^+$ 198.1277 . Found 198.1270.

Ethyl 5-(pyridin-4-yl)pentanoate (4)



Prepared according to **GP-A**. The crude product purified by flash column chromatography, using PE / EA = 5 / 1 to 3 / 1 (v / v) as an eluent, to yield the title compound **4** (12.4 mg) in 30% isolated yield.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.47 (d, *J* = 5.8 Hz, 2H), 7.10 (d, *J* = 6.0 Hz, 2H), 4.15 – 4.08 (m, 2H), 2.62 (t, *J* = 7.1 Hz, 2H), 2.32 (t, *J* = 7.1 Hz, 2H), 1.70 – 1.62 (m, 4H), 1.24 (t, *J* = 7.1 Hz, 3H).

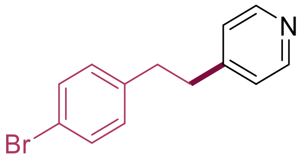
^{13}C NMR (101 MHz, Chloroform-*d*) δ 173.40, 151.05, 149.66, 123.87, 60.34, 34.88, 34.01, 29.65, 24.45, 14.24.

Physical State: yellow oil

R$_f$ = 0.3 (PE / EA = 3 : 1)

HRMS (ESI) *m/z*: Calculated for $C_{12}H_{18}NO_2^+$ $[M+H]^+$ 208.1332 . Found 208.1338.

4-(4-Bromophenethyl)pyridine (5)



Prepared according to **GP-A** The crude product purified by flash column chromatography, using PE / EA = 3 / 1 to 1 / 1 (v / v) as an eluent, to yield the title compound **5** (13.6 mg) in 26% isolated yield.

Prepared according to **GP-A** [**Table 1,** footnote **c**]. The crude product purified by flash column chromatography, using PE / EA = 3 / 1 to 1 / 1 (v / v) as an eluent, to yield the title compound **5** (16.7 mg) in 32% isolated yield.

^{1}**H NMR** (400 MHz, Chloroform-*d*) δ 8.49 – 8.46 (m, 2H), 7.40 – 7.36 (m, 2H), 7.06 – 7.03 (m, 2H), 7.01 – 6.97 (m, 2H), 2.88 (s, 4H).

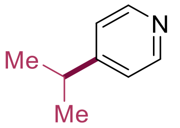
^{13}**C NMR** (101 MHz, Chloroform-*d*) δ 149.99, 149.76, 139.56, 131.54, 130.19, 123.92, 120.06, 36.81, 35.93.

Physical State: yellow solid

R$_f$ = 0.3 (PE / EA = 3 : 1)

HRMS (ESI) *m/z*: Calculated for $C_{13}H_{13}BrN^+$ [M+H]$^+$ 262.0226 . Found 262.0229.

4-Isopropylpyridine (6)



Prepared according to **GP-A**. The crude product purified by flash column chromatography, using PE / EA = 5 / 1 to 3 / 1 (v / v) as an eluent, to yield the title compound **6** (17.4 mg) in 72% isolated yield.

^{1}**H NMR** (400 MHz, Chloroform-*d*) δ 8.49 (d, *J* = 5.6 Hz, 2H), 7.14 (d, *J* = 6.0 Hz, 2H), 2.88 (p, *J* = 6.8 Hz, 1H), 1.26 (d, *J* = 6.9 Hz, 6H). *[Caution: this compound was quite volatile, all of the solvent evaporating step was performed below 40 °C, above 100 mbar]*

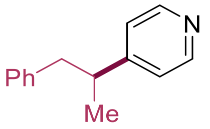
^{13}**C NMR** (101 MHz, Chloroform-*d*) δ 157.61, 149.68, 122.03, 33.57, 23.09.

Physical State: yellow oil

R$_f$ = 0.3 (PE / EA = 3 : 1)

HRMS (ESI) *m/z*: Calculated for $C_8H_{12}N^+$ [M+H]$^+$ 122.0964 . Found 122.0967.

4-(1-Phenylpropan-2-yl)pyridine (7)



Prepared according to **GP-A**. The crude product purified by flash column chromatography, using PE / EA = 5 / 1 to 3 / 1 (v / v) as an eluent, to yield the title compound **7** (22.1 mg) in 56% isolated yield.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.47 (d, *J* = 6.0 Hz, 2H), 7.25 – 7.14 (m, 3H),7.08 – 7.02 (m, 4H), 2.99 (q, *J* = 7.2 Hz, 1H),2.93 – 2.86 (m, 1H),2.84 – 2.77 (m, 1H), 1.26 (d, *J* = 6.8 Hz, 3H).

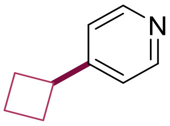
^{13}C NMR (101 MHz, Chloroform-*d*) δ 155.62, 149.71, 139.69, 129.08, 128.27, 126.20, 122.63, 44.15, 41.36, 20.52.

Physical State: yellow oil

R$_f$ = 0.3 (PE / EA = 3 : 1)

HRMS (ESI) *m/z*: Calculated for $C_{14}H_{16}N^+$ $[M+H]^+$ 198.1277 . Found 198.1278.

4-Cyclobutylpyridine (8)



Prepared according to **GP-A**. The crude product purified by flash column chromatography, using PE / EA = 5 / 1 to 3 / 1 (v / v) as an eluent, to yield the title compound **8** (14.9 mg) in 56% isolated yield.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.48 (d, *J* = 4.4 Hz, 2H), 7.11 (d, *J* = 5.6 Hz, 2H), 3.52 (p, *J* = 8.8 Hz, 1H), 2.40 – 2.32 (m, 2H), 2.18 – 2.02 (m, 3H), 1.92 – 1.85 (m, 1H).

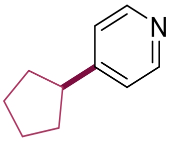
^{13}C NMR (101 MHz, Chloroform-*d*) δ 154.96, 149.54, 121.73, 39.33, 28.92, 18.35.

Physical State: yellow oil

R$_f$ = 0.5 (PE / EA = 3 : 1)

HRMS (ESI) *m/z*: Calculated for $C_9H_{12}N^+$ $[M+H]^+$ 134.0964 . Found 134.0964.

4-Cyclopentylpyridine (9)



Prepared according to **GP-A**. The crude product purified by flash column chromatography, using PE / EA = 5 / 1 to 3 / 1 (v / v) as an eluent, to yield the title compound **9** (19.1 mg) in 65% isolated yield.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.47 (d, *J* = 5.6 Hz, 2H), 7.14 (d, *J* = 5.6 Hz, 2H), 2.97 (p, *J* = 9.2 Hz, 1H), 2.14 – 2.02 (m, 2H), 1.87 – 1.76 (m, 2H), 1.76 – 1.64 (m, 2H), 1.64 – 1.53 (m, 2H).

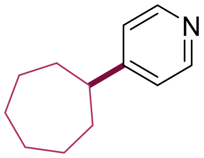
^{13}C NMR (101 MHz, Chloroform-*d*) δ 155.56, 149.62, 122.63, 45.13, 33.92, 25.52.

Physical State: yellow oil

R$_f$ = 0.5 (PE / EA = 3 : 1)

HRMS (ESI) *m/z*: Calculated for $C_{10}H_{14}N^+$ $[M+H]^+$ 148.1121 . Found 148.1122.

4-Cycloheptylpyridine (10)



Prepared according to **GP-A**. The crude product purified by flash column chromatography, using PE / EA = 5 / 1 to 3 / 1 (v / v) as an eluent, to yield the title compound **10** (32.2mg) in 92% isolated yield.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.45 (d, *J* = 6.0 Hz, 2H), 7.08 (d, *J* = 6.0 Hz, 2H), 2.67 – 2.58 (m, 1H), 1.91 – 1.84 (m, 2H), 1.82 – 1.74 (m, 2H), 1.73 – 1.64 (m, 2H), 1.63 – 1.48 (m, 6H).

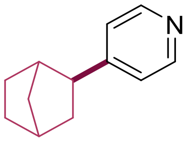
^{13}C NMR (101 MHz, Chloroform-*d*) δ 158.35, 149.73, 122.23, 46.23, 35.90, 27.85, 27.06.

Physical State: yellow oil

R$_f$ = 0.4 (PE / EA = 3 : 1)

HRMS (ESI) *m/z*: Calculated for $C_{12}H_{18}N^+$ $[M+H]^+$ 176.1434 . Found 176.1434.

4-(Bicyclo[2.2.1]heptan-2-yl)pyridine (11)



Prepared according to **GP-A**. The crude product purified by flash column chromatography, using PE / EA = 5 / 1 to 3 / 1 (v / v) as an eluent, to yield the title compound **11** (27.7 mg) in 80% isolated yield.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.47 – 8.41 (m, 2H), 7.09 (d, *J* = 6.0 Hz, 2H), 2.70 – 2.64 (m, 1H), 2.39 – 2.30 (m, 2H), 1.80 – 1.73 (m, 1H), 1.65 – 1.50 (m, 3H), 1.43 (d, *J* = 10.0 Hz, 1H), 1.37 – 1.15 (m, 3H).

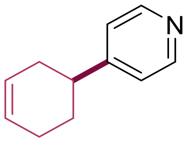
^{13}C NMR (101 MHz, Chloroform-*d*) δ 156.39, 149.51, 122.53, 46.67, 42.25, 38.52, 36.79, 36.16, 30.35, 28.73.

Physical State: yellow oil

R$_f$ = 0.4 (PE / EA = 3 : 1)

HRMS (ESI) *m/z*: Calculated for $C_{12}H_{16}N^+$ $[M+H]^+$ 174.1277 . Found 174.1278.

4-(Cyclohex-3-en-1-yl)pyridine (12)



Prepared according to **GP-A**. The crude product purified by flash column chromatography, using PE / EA = 5 / 1 to 3 / 1 (v / v) as an eluent, to yield the title compound **12** (21.3 mg) in 67% isolated yield.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.49 (d, *J* = 5.6 Hz, 2H), 7.13 (d, *J* = 6.0 Hz, 2H), 5.76 (d, *J* = 2.4 Hz, 2H), 2.84 – 2.74 (m, 1H), 2.28 (m, 1H), 2.21 – 2.07 (m, 3H), 1.97 – 1.88 (m, 1H), 1.80 – 1.68 (m, 1H).

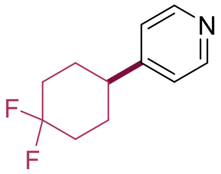
^{13}C NMR (101 MHz, Chloroform-*d*) δ 155.87, 149.80, 127.11, 126.02, 122.40, 39.40, 32.26, 28.82, 25.31.

Physical State: yellow oil

R$_f$ = 0.5 (PE / EA = 3 : 1)

HRMS (ESI) *m/z*: Calculated for $C_{11}H_{14}N^+$ [M+H]$^+$ 160.1121 . Found 160.1122.

4-(4,4-Difluorocyclohexyl)pyridine (13)



Prepared according to **GP-A**. The crude product purified by flash column chromatography, using PE / EA = 5 / 1 to 3 / 1 (v / v) as an eluent, to yield the title compound **13** (19.3 mg) in 49% isolated yield.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.52 (d, *J* = 5.2 Hz, 2H), 7.14 (d, *J* = 6.0 Hz, 2H), 2.60 (t, *J* = 9.6 Hz, 1H), 2.26 – 2.19 (m, 2H), 1.96 – 1.91 (m, 3H), 1.88 – 1.77 (m, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 153.88 (d, *J* = 2.1 Hz), 149.97, 122.71 (dd, *J* = 240.5, 240.4 Hz), 122.23, 41.75, 33.78 (dd, *J* = 23.3, 23.0 Hz), 29.49 (d, *J* = 10.1 Hz)

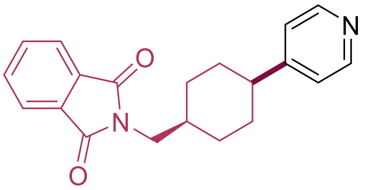
^{19}F NMR (377 MHz, Chloroform-*d*) δ -94.62 (d, *J* =237.5 Hz), -105.06 (d, *J* =237.1 Hz)

Physical State: yellow oil

R$_f$ = 0.4 (PE / EA = 1 : 1)

HRMS (ESI) *m/z*: Calculated for $C_{11}H_{14}F_2N^+$ [M+H]$^+$ 198.1089 . Found 198.1089.

2-((4-(Pyridin-4-yl)cyclohexyl)methyl)isoindoline-1,3-dione (14)



Prepared according to **GP-A**. The crude product purified by flash column chromatography, using PE / EA = 5 / 1 to 3 / 1 (v / v) as an eluent, to yield the title compound **14** (33.9 mg) in 53% isolated yield.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.48 (m, 2.32H), 7.86 – 7.82 (m, 2.31H), 7.71 (m, 2.36H), 7.19 (d, *J* = 6.0 Hz, 0.4H), 7.08 (d, *J* = 6.0 Hz, 2H), 3.74 (d, *J* = 8.0 Hz, 0.4H), 3.58 (d, *J* = 6.8 Hz, 2H), 2.60 (t, *J* = 4.0 Hz, 0.22H), 2.46 (t, *J* = 12.0 Hz, 1H), 2.24 (m, 1H), 1.94 – 1.81 (m, 6H), 1.74 (d, *J* = 4.0 Hz, 0.47H), 1.65 – 1.60 (m, 0.8H), 1.46 – 1.35 (m, 2H), 1.26 – 1.18 (m, 2H).

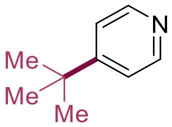
^{13}C NMR (101 MHz, Chloroform-*d*) δ 168.67, 155.77, 149.74, 133.98, 132.02, 123.26, 122.32, 43.86, 43.43, 36.63, 32.62, 30.64.

Physical State: yellow solid

R$_f$ = 0.3 (PE / EA = 1 : 1)

HRMS (ESI) *m/z*: Calculated for $C_{20}H_{21}N_2O_2{}^+$ $[M+H]^+$ 321.1598 . Found 321.1601.

4-(Tert-butyl)pyridine (15)



Prepared according to **GP-A**. The crude product purified by flash column chromatography, using PE / EA = 5 / 1 to 3 / 1 (v / v) as an eluent, to yield the title compound **15** (23.2 mg) in 86% isolated yield.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.50 (d, *J* = 6.0 Hz, 2H), 7.29 – 7.26 (m, 2H), 1.32 (s, 9H).

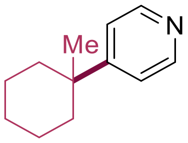
^{13}C NMR (101 MHz, Chloroform-*d*) δ 160.02, 149.59, 120.76, 34.66, 30.50.

Physical State: yellow oil

R$_f$ = 0.4 (PE / EA = 3 : 1)

HRMS (ESI) *m/z*: Calculated for $C_9H_{14}N^+$ $[M+H]^+$ 136.1121 . Found 136.1121.

4-(1-Methylcyclohexyl)pyridine (16)



Prepared according to **GP-A**. The crude product purified by flash column chromatography, using PE / EA = 5 / 1 to 3 / 1 (v / v) as an eluent, to yield the title compound **16** (27.3 mg) in 78% isolated yield.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.50 (d, *J* = 4.8 Hz, 2H), 7.25 – 7.20 (m, 2H), 2.00 – 1.90 (m, 2H), 1.60 – 1.50 (m, 4H), 1.44 – 1.32 (m, 4H), 1.15 (s, 3H).

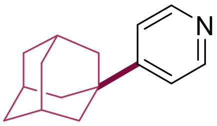
^{13}C NMR (101 MHz, Chloroform-*d*) δ 159.01, 149.81, 121.41, 38.04, 37.15, 30.00, 26.12, 22.47.

Physical State: orange oil

R$_f$ = 0.4 (PE / EA = 1 : 1)

HRMS (ESI) *m/z*: Calculated for $C_{12}H_{18}N^+$ [M+H]$^+$ 176.1434 . Found 176.1434.

4-(Adamantan-1-yl)pyridine (17)



Prepared according to **GP-A**. The crude product purified by flash column chromatography, using PE / EA = 5 / 1 to 3 / 1 (v / v) as an eluent, to yield the title compound **17** (34.6 mg) in 81% isolated yield.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.51 (d, *J* = 6.4 Hz, 2H), 7.25 – 7.22 (m, 2H), 2.11 (s, 3H), 1.89 (d, *J* = 2.8 Hz, 6H), 1.78 (q, *J* = 12.0 Hz, 6H).

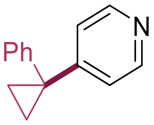
^{13}C NMR (101 MHz, Chloroform-*d*) δ 159.89, 149.65, 120.36, 42.34, 36.57, 36.22, 28.62.

Physical State: yellow solid

R$_f$ = 0.4 (PE / EA = 3 : 1)

HRMS (ESI) *m/z*: Calculated for $C_{15}H_{20}N^+$ [M+H]$^+$ 214.1590 . Found 214.1595.

4-(1-Phenylcyclopropyl)pyridine (18)



Prepared according to **GP-A**. The crude product purified by flash column chromatography, using PE / EA = 5 / 1 to 3 / 1 (v / v) as an eluent, to yield the title compound **18** (16.4 mg) in 42% isolated yield.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.34 (d, *J* = 6.0 Hz, 2H), 7.29 – 7.18 (m, 5H), 6.87 – 6.84 (m, 2H), 1.37 – 1.34 (m, 2H), 1.29 – 1.26 (m, 2H).

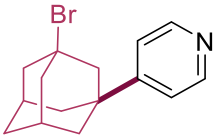
^{13}C NMR (101 MHz, Chloroform-*d*) δ 155.55, 149.45, 143.02, 129.81, 128.63, 126.96, 121.80, 29.13, 17.72.

Physical State: brown oil

R$_f$ = 0.3 (PE / EA = 3 : 1)

HRMS (ESI) *m/z*: Calculated for $C_{14}H_{14}N^{+}$ $[M+H]^{+}$ 196.1121 . Found 196.1124.

4-(3-Bromoadamantan-1-yl) pyridine (19)



Prepared according to **GP-A**. The crude product purified by flash column chromatography, using PE / EA = 5 / 1 to 3 / 1 (v / v) as an eluent, to yield the title compound **19** (43.1 mg) in 74% isolated yield.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.52 (d, *J* = 6 Hz, 2H), 7.20 (d, *J* = 6.0 Hz, 2H), 2.45 (s, 2H), 2.42 – 2.34 (m, 4H), 2.33 – 2.26 (m, 2H), 1.88 (d, *J* = 2.0 Hz, 4H), 1.80 – 1.68 (m, 2H).

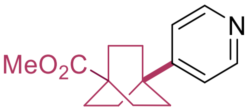
^{13}C NMR (101 MHz, Chloroform-*d*) δ 157.17, 149.96, 120.12, 64.56, 53.25, 48.14, 40.96 40.48, 34.50, 32.29.

Physical State: yellow solid

R$_f$ = 0.3 (PE / EA = 3 : 1)

HRMS (ESI) *m/z*: Calculated for $C_{15}H_{19}BrN^{+}$ $[M+H]^{+}$ 292.0695 . Found 292.0698.

Methyl 4-(pyridin-4-yl)bicyclo[2.2.2]octane-1-carboxylate (20)



Prepared according to **GP-A**. The crude product purified by flash column chromatography, using PE / EA = 5 / 1 to 3 / 1 (v / v) as an eluent, to yield the title compound **20** (38.2 mg) in 78% isolated yield.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.47 – 8.45 (m, 2H), 7.18 – 7.15 (m, 2H), 3.64 (s, 3H), 1.91 – 1.87 (m, 6H), 1.83 – 1.78 (m, 6H).

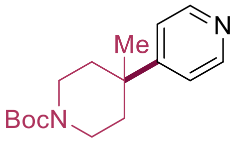
^{13}C NMR (101 MHz, Chloroform-*d*) δ 177.95, 157.99, 149.63, 120.93, 51.76, 39.01, 34.70, 31.06, 28.43.

Physical State: yellow oil

R$_f$ = 0.4 (PE / EA = 1 : 1)

HRMS (ESI) *m/z*: Calculated for $C_{15}H_{20}NO_2{}^+$ [M+H]$^+$ 246.1489 . Found 246.1487.

Tert-butyl 4-methyl-4-(pyridin-4-yl)piperidine-1-carboxylate (21)



Prepared according to **GP-A**. The crude product purified by flash column chromatography, using PE / EA = 3 / 1 to 1 / 1 (v / v) as an eluent, to yield the title compound **21** (23.8 mg) in 43% isolated yield.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.55 – 8.51 (m, 2H), 7.24 – 7.17 (m, 2H), 3.50 – 3.42 (m, 2H), 3.41 – 3.32 (m, 2H), 2.05 – 1.95 (m, 2H), 1.73 – 1.62 (m, 2H), 1.43 (s, 9H), 1.24 (s, 3H).

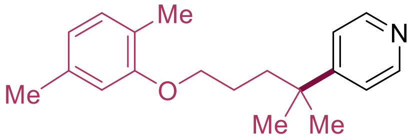
^{13}C NMR (101 MHz, Chloroform-*d*) δ 157.32, 154.84, 150.09, 121.11, 79.54, 36.55, 36.06, 28.44, 28.13.

Physical State: yellow oil

R$_f$ = 0.3 (PE / EA = 1 : 1)

HRMS (ESI) *m/z*: Calculated for $C_{16}H_{24}N_2NaO_2{}^+$ [M+Na]$^+$ 299.1730 . Found 299.1731.

4-(5-(2,5-Dimethylphenoxy)-2-methylpentan-2-yl)pyridine (22)



Prepared according to **GP-A**. The crude product purified by flash column chromatography, using PE / EA = 5 / 1 to 3 / 1 (v / v) as an eluent, to yield the title compound **22** (43.6 mg) in 77% isolated yield.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.52 (d, *J* = 6.0 Hz, 2H), 7.27 – 7.23 (m, 2H), 6.99 (d, *J* = 7.6 Hz, 1H), 6.64 (d, *J* = 7.6 Hz, 1H), 6.54 (s, 1H), 3.84 (d, *J* = 6.4 Hz, 2H), 2.28 (s, 3H), 2.17 (s, 3H), 1.85 – 1.79 (m, 2H), 1.59 – 1.48 (m, 2H), 1.33 (s, 6H).

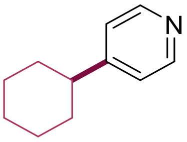
^{13}C NMR (101 MHz, Chloroform-*d*) δ 158.29, 156.91, 149.74, 136.48, 130.33, 123.46, 121.35, 120.74, 111.87 , 67.85, 39.99, 37.61, 28.29, 24.89, 21.42, 15.83.

Physical State: yellow oil

R_f = 0.3 (PE / EA = 3 : 1)

HRMS (ESI) *m/z*: Calculated for $C_{19}H_{26}NO^{+}$ $[M+H]^{+}$ 284.2009 . Found 284.2006.

4-Cyclohexylpyridine (23)



Prepared according to **GP-A**. The crude product purified by flash column chromatography, using PE / EA = 5 / 1 to 3 / 1 (v / v) as an eluent, to yield the title compound **23** (24.5 mg) in 76% isolated yield.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.46 (d, *J* = 6.0 Hz, 2H), 7.11 – 7.07 (m, 2H), 2.51 – 2.41 (m, 1H), 1.84 (m, 4H), 1.78 – 1.69 (m, 1H), 1.37 (m, 4H), 1.24 (m, 6.5 Hz, 1H).

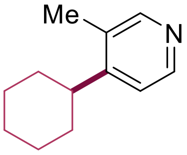
^{13}C NMR (101 MHz, Chloroform-*d*) δ 156.62, 149.64, 122.38, 43.82, 33.51, 26.52, 25.93.

Physical State: yellow oil

R_f = 0.4 (PE / EA = 3 : 1)

HRMS (ESI) *m/z*: Calculated for $C_{11}H_{16}N^{+}$ $[M+H]^{+}$ 162.1277 . Found 162.1282.

4-Cyclohexyl-3-methylpyridine (24)



Prepared according to **GP-A**. The crude product purified by flash column chromatography, using PE / EA = 5 / 1 to 3 / 1 (v / v) as an eluent, to yield the title compound **24** (22.1 mg) in 63% isolated yield.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.34 (d, *J* = 4.8 Hz, 1H), 8.30 (s, 1H), 7.07 (d, *J* = 5.2 Hz, 1H), 2.69 – 2.63 (m 1H), 2.27 (s, 3H), 1.92 – 1.70 (m, 5H), 1.47 – 1.33 (m, 4H), 1.32 – 1.24 (m, 1H).

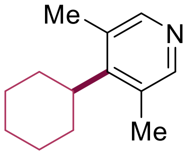
^{13}C NMR (101 MHz, Chloroform-*d*) δ 154.40, 150.69, 147.78, 130.68, 120.33, 39.78, 32.74, 26.76, 26.10, 16.01.

Physical State: yellow oil

R_f = 0.4 (PE / EA = 3 : 1)

HRMS (ESI) *m/z*: Calculated for $C_{12}H_{18}N^{+}$ $[M+H]^{+}$ 176.1434 . Found 176.1434.

4-Cyclohexyl-3,5-dimethylpyridine (25)



Prepared according to **GP-A**. The crude product purified by flash column chromatography, using PE / EA = 5 / 1 to 3 / 1 (v / v) as an eluent, to yield the title compound **25** (18.9 mg) in 50% isolated yield.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.13 (s, 2H), 2.96 – 2.86 (m, 1H), 2.33 (s, 5H), 1.89 – 1.75 (m, 5H), 1.66 – 1.60 (m, 2H), 1.42 – 1.20 (m, 4H).

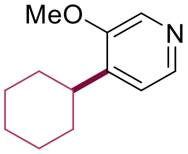
^{13}C NMR (101 MHz, Chloroform-*d*) δ 151.43, 149.76, 130.80, 41.59, 29.71, 27.27, 26.19, 18.31.

Physical State: yellow oil

R_f = 0.3 (PE / EA = 3 : 1)

HRMS (ESI) *m/z*: Calculated for $C_{13}H_{20}N^+$ $[M+H]^+$ 190.1590 . Found 190.1590.

4-Cyclohexyl-3-methoxypyridine (26)



Prepared according to **GP-A**. The crude product purified by flash column chromatography, using PE / EA = 5 / 1 to 3 / 1 (v / v) as an eluent, to yield the title compound **26** (19.1 mg) in 50% isolated yield.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.19 – 8.16 (m, 2H), 7.08 (d, *J* = 5.2 Hz, 1H), 3.90 (s, 3H), 2.97 – 2.87 (m, 1H), 1.87 – 1.72 (m, 4H), 1.48 – 1.22 (m, 6H).

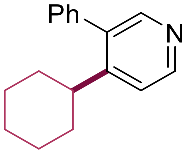
^{13}C NMR (101 MHz, Chloroform-*d*) δ 153.23, 144.56, 142.86, 132.80, 121.19, 55.98, 36.41, 32.34, 26.72, 26.20.

Physical State: yellow oil

R_f = 0.3 (PE / EA = 3 : 1)

HRMS (ESI) *m/z*: Calculated for $C_{12}H_{18}NO^+$ $[M+H]^+$ 192.1383 . Found 192.1383.

4-Cyclohexyl-3-phenylpyridine (27)



Prepared according to **GP-A** [**Table 1,** footnote **c**]. The crude product purified by flash column chromatography, using PE / EA = 30/ 1 to 10 / 1 (v / v) as an eluent, to yield the title compound **27** (23.7 mg) in 50% isolated yield.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.43 (d, *J* = 4.8 Hz, 1H), 8.32 (s, 1H), 7.40 – 7.32 (m, 3H), 7.22 – 7.18 (m, 3H), 2.64 – 2.55 (m, 1H), 1.71 – 1.57 (m, 5H), 1.35 (q, *J* = 12.4, 10.8 Hz, 2H), 1.20 – 1.06 (m, 3H).

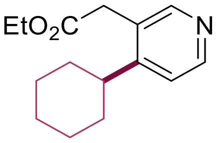
^{13}C NMR (101 MHz, Chloroform-*d*) δ 153.95, 150.32, 148.64, 138.06, 136.98, 129.44, 128.34, 127.51, 121.24, 39.63, 33.79, 26.39, 25.93.

Physical State: yellow oil

R_f = 0.3 (PE / EA = 10 : 1)

HRMS (ESI) *m/z*: Calculated for $C_{17}H_{20}N^+$ $[M+H]^+$ 238.1590 . Found 238.1589.

Ethyl 2-(4-cyclohexylpyridin-3-yl)acetate (28)



Prepared according to **GP-A** [**Table 1,** footnote **c**]. The crude product purified by flash column chromatography, using PE / EA = 5 / 1 to 3 / 1 (v / v) as an eluent, to yield the title compound **28** (22.8 mg) in 46% isolated yield.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.41 (d, *J* = 5.2 Hz, 1H), 8.36 (s, 1H), 7.15 (d, *J* = 5.2 Hz, 1H), 4.13 (q, *J* = 6.8 Hz, 2H), 3.64 (s, 2H), 2.70 – 2.60 (m, 1H), 1.89 – 1.68 (m, 5H), 1.45 – 1.31 (m, 4H), 1.23 (t, *J* = 7.2 Hz, 4H).

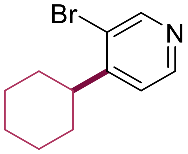
^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.97, 155.20, 151.23, 148.88, 127.70, 121.25, 61.15, 39.89, 36.15, 33.26, 26.64, 25.97, 14.15.

Physical State: yellow oil

R_f = 0.3 (PE / EA = 3 : 1)

HRMS (ESI) *m/z*: Calculated for $C_{15}H_{22}NO_2^+$ $[M+H]^+$ 248.1645 . Found 248.1647.

3-Bromo-4-cyclohexylpyridine (29)



Prepared according to **GP-A**. Upon completion, concentrate the reaction solution under reduced pressure. Then absolute ethanol (4 mL) and H_2O (4 mL) was added, together by NaOH (8.0 equiv, 1.6 mmol, 64 mg) and reflux at 80°C for 4 hours. After the reaction, the aqueous phase was extracted with dichloromethane (3 × 8 mL) and the combined organic layers were dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product purified by flash column chromatography, using PE / EA = 30 / 1 to 10 / 1 (v / v) as an eluent, to yield the title compound **29** (24.9 mg) in 52% isolated yield.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.63 (s, 1H), 8.40 (d, *J* = 5.2 Hz, 1H), 7.15 (d, *J* = 4.8 Hz, 1H), 2.96 – 2.86 (m, 1H), 1.92 – 1.83 (m, 4H), 1.78 (d, *J* = 12.8 Hz, 1H), 1.47 – 1.23 (m, 5H).

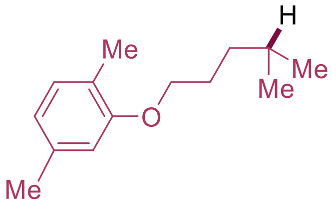
^{13}C NMR (101 MHz, Chloroform-*d*) δ 154.92, 151.87, 148.44, 123.03, 122.40, 42.86, 32.30, 26.47, 25.97.

Physical State: yellow oil

R$_f$ = 0.4 (PE / EA = 10 : 1)

HRMS (ESI) *m/z*: Calculated for $C_{11}H_{15}BrN^+$ [M+H]$^+$ 240.0382 . Found 240.0382.

1,4-Dimethyl-2-((4-methylpentyl)oxy)benzene (Gem-H)



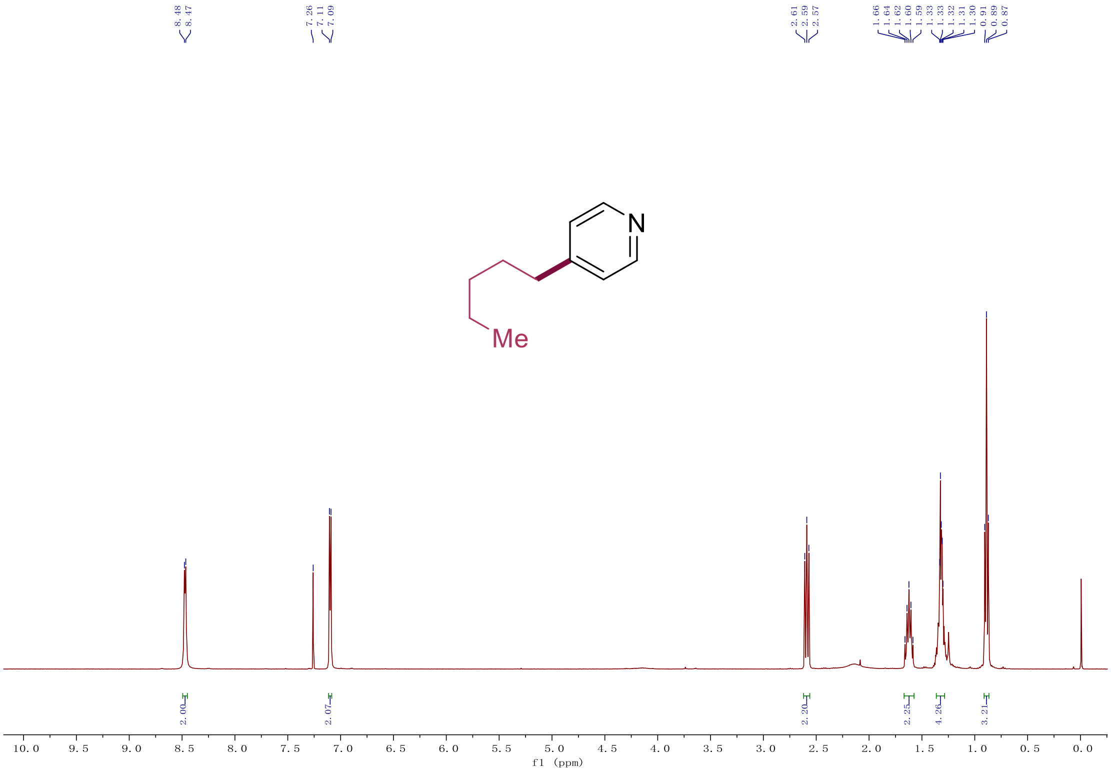
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.02 (d, *J* = 7.2 Hz, 1H), 6.70 – 6.64 (m, 2H), 3.95 (t, *J* = 5.2 Hz, 2H), 2.33 (s, 3H), 2.20 (s, 3H), 1.87 – 1.78 (m, 2H), 1.64 (m, 1H), 1.42 – 1.34 (m, 2H), 0.95 (d, *J* = 6.4 Hz, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 157.17, 137.52, 136.45, 130.28, 123.67, 120.58, 112.04, 68.20, 35.35, 27.82, 27.33, 22.62, 21.44, 15.82.

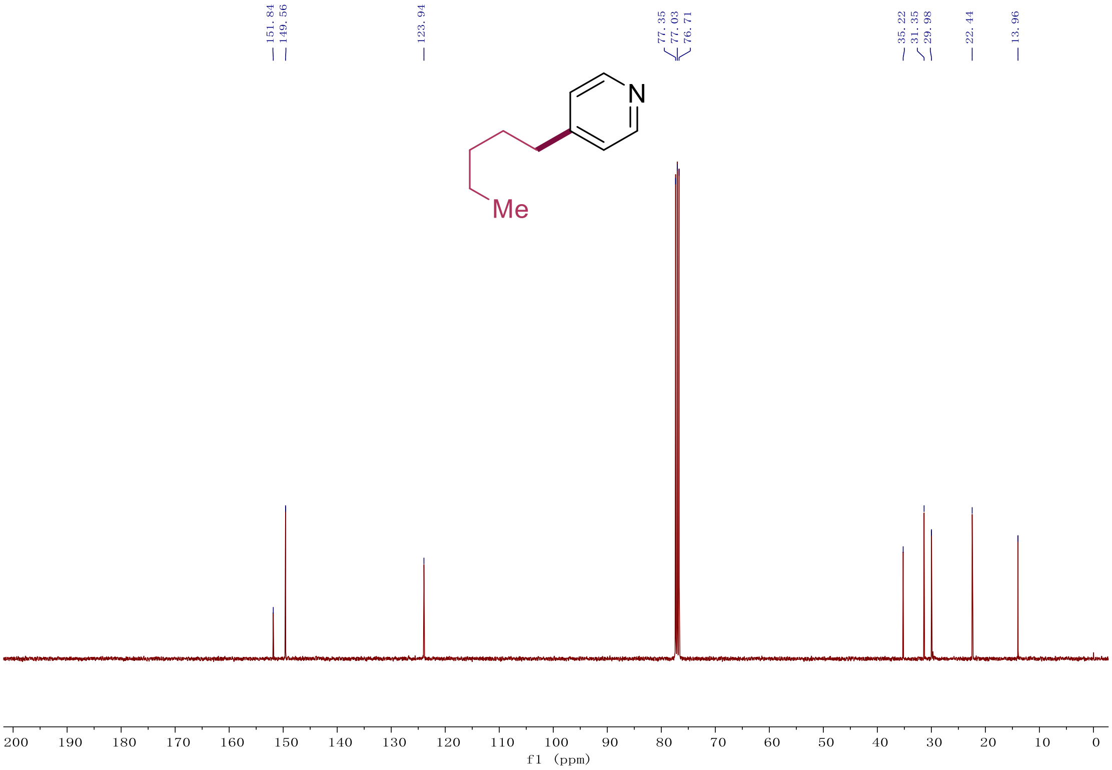
HRMS (ESI) *m/z*: Calculated for $C_{14}H_{22}NaO^+$ [M+Na]$^+$ 229.1563. . Found 229.1573.

9. Copies of ^{1}H, ^{13}C and ^{19}F NMR spectra

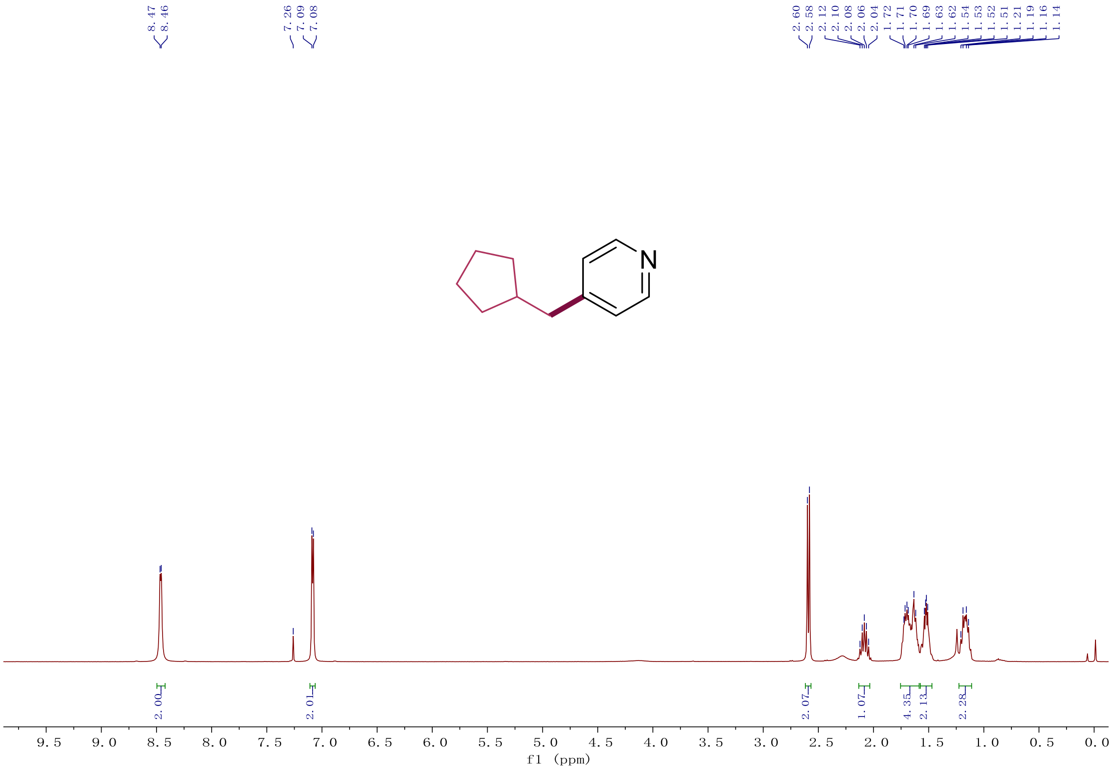
^{1}H NMR of 1 (400 MHz, CDCl$_3$)



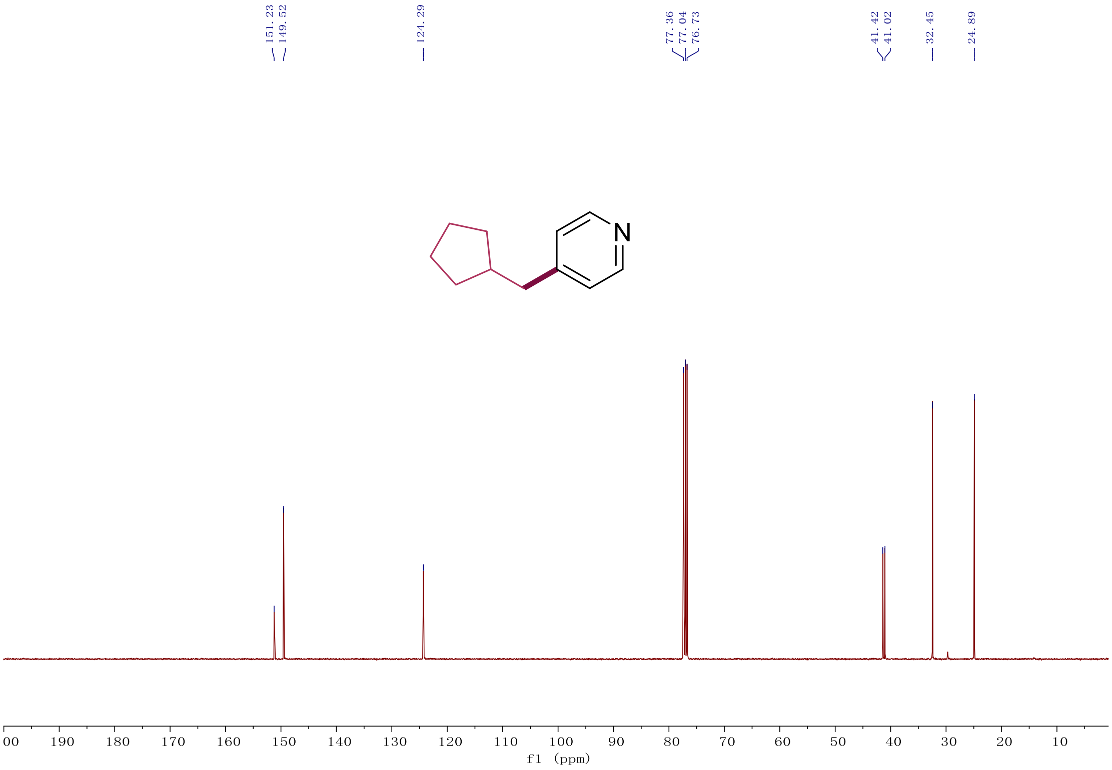
^{13}C NMR of 1 (101 MHz, CDCl$_3$)



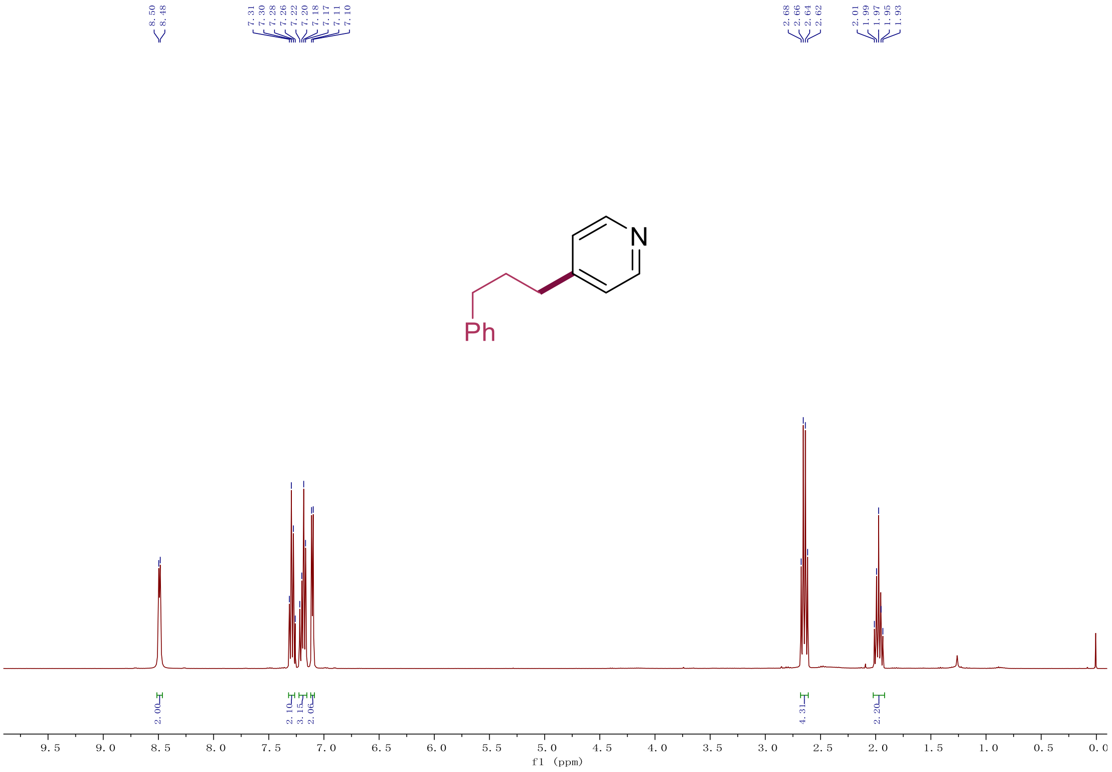
^{1}H NMR of 2 (400 MHz, CDCl$_3$)



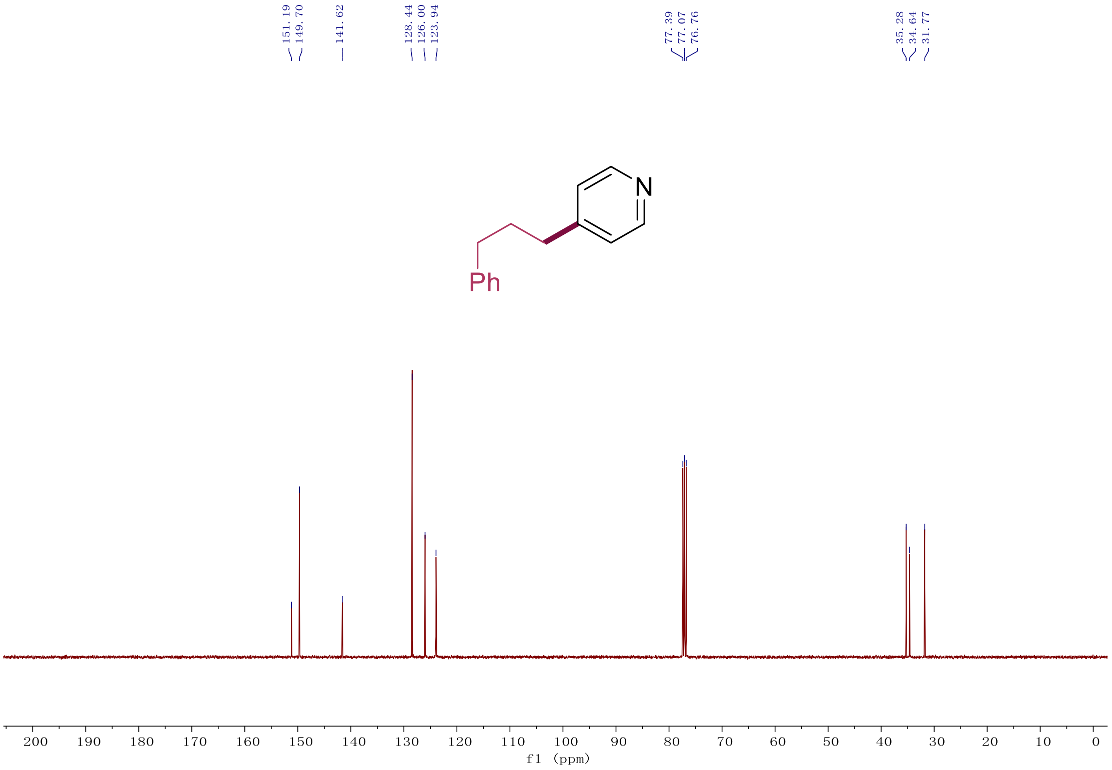
^{13}C NMR of 2 (101 MHz, CDCl$_3$)



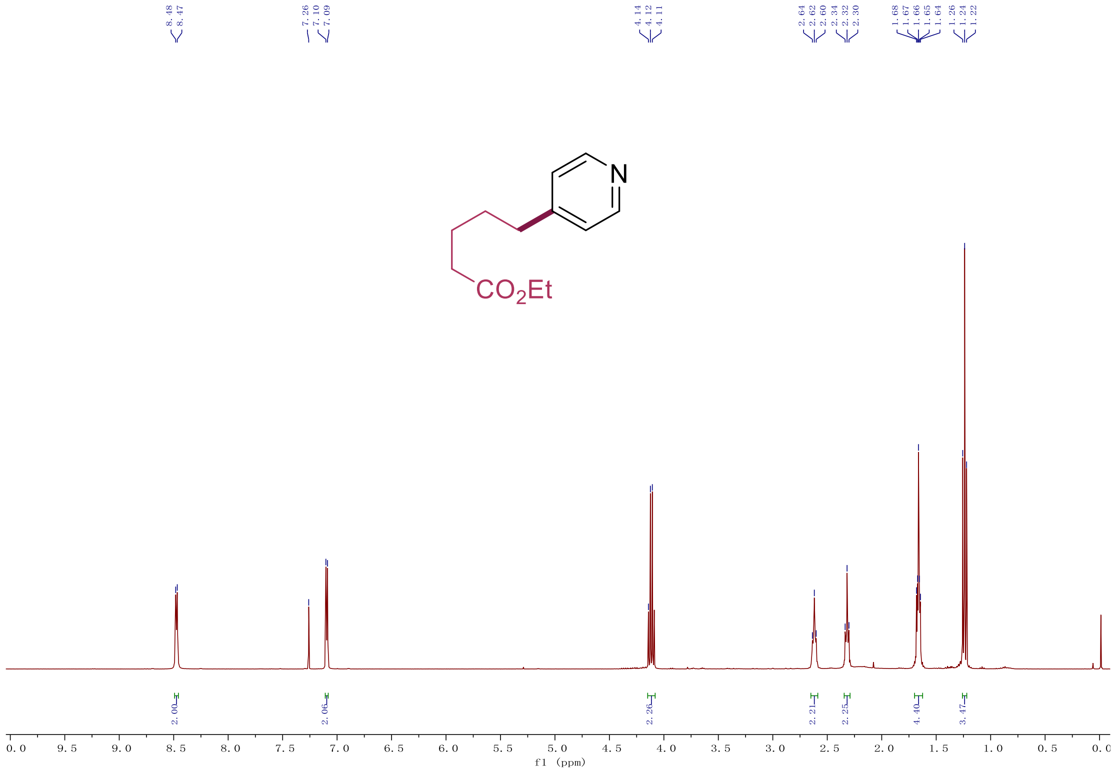
^{1}H NMR of 3 (400 MHz, $CDCl_3$)



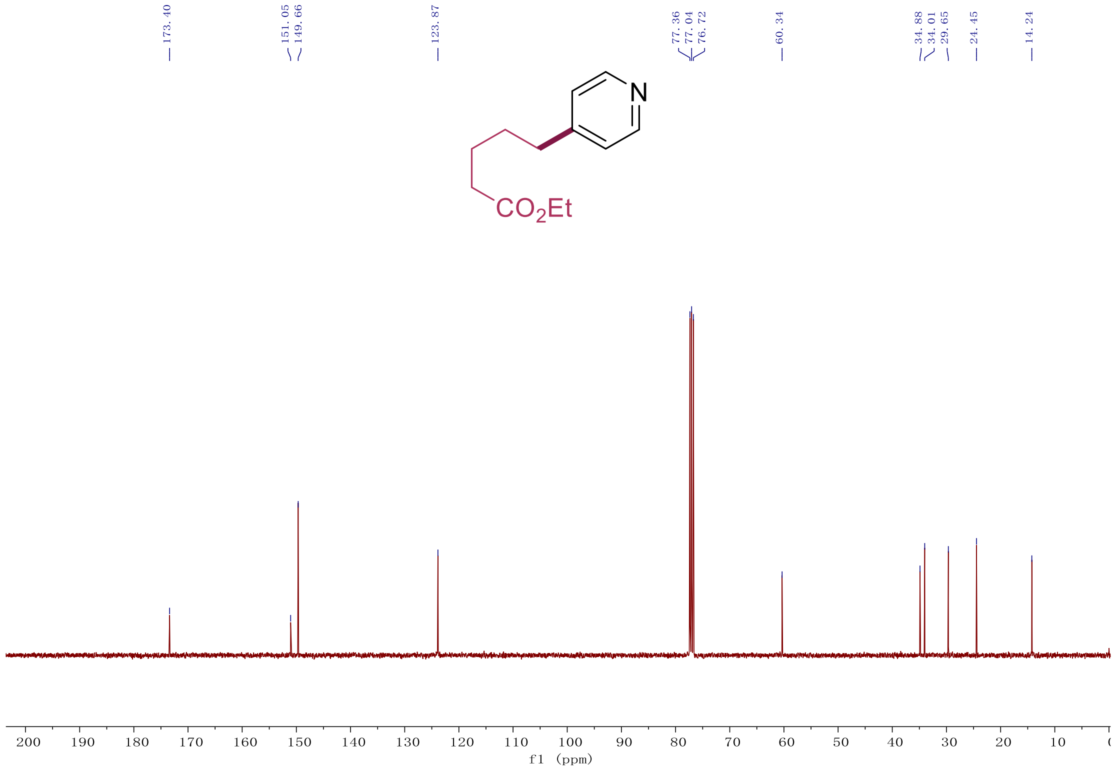
^{13}C NMR of 3 (101 MHz, $CDCl_3$)



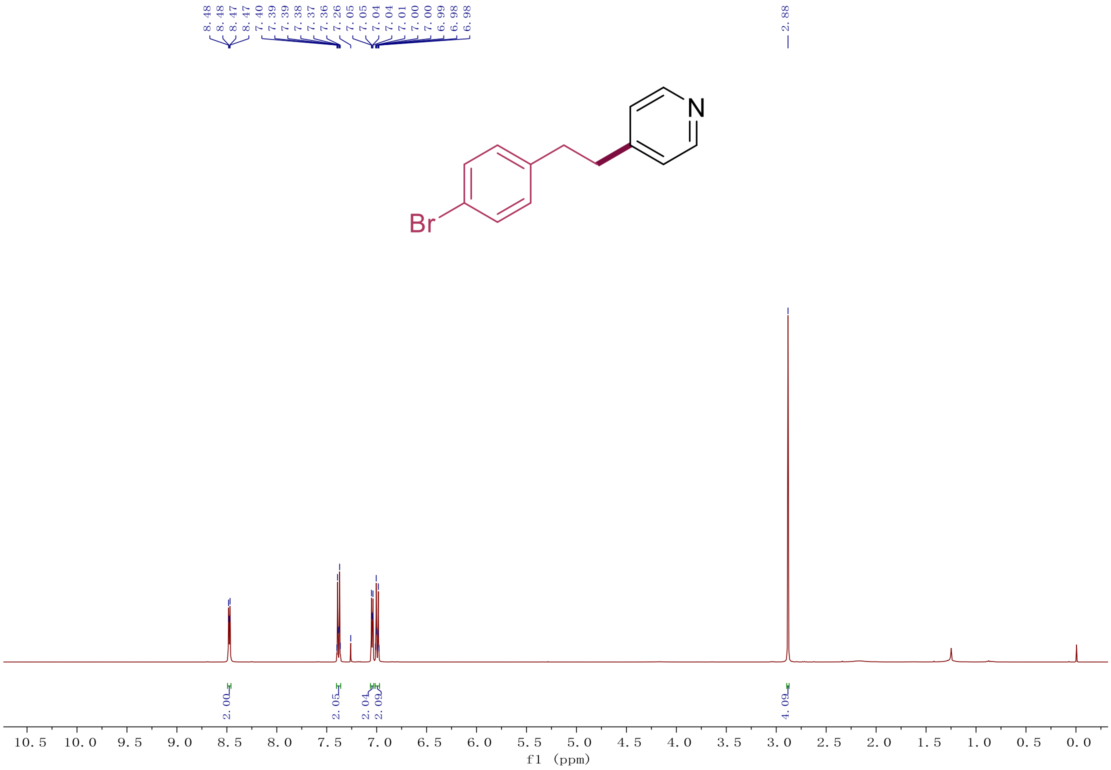
^{1}H NMR of 4 (400 MHz, CDCl$_3$)



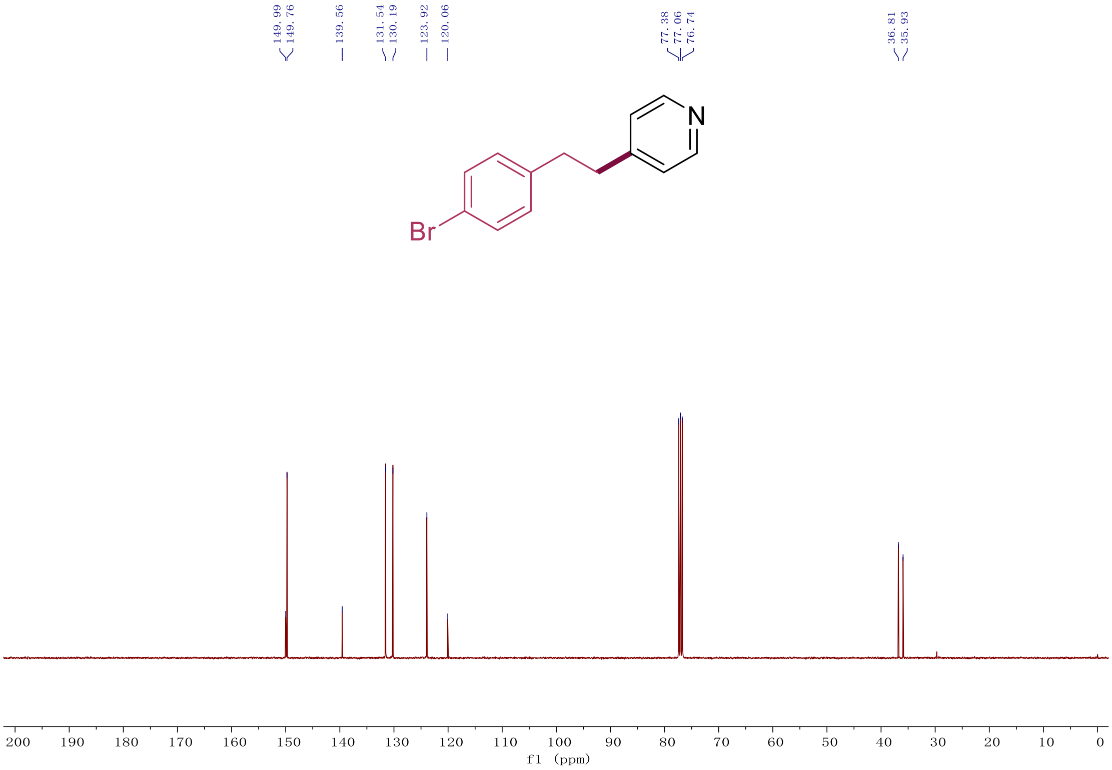
^{13}C NMR of 4 (101 MHz, CDCl$_3$)



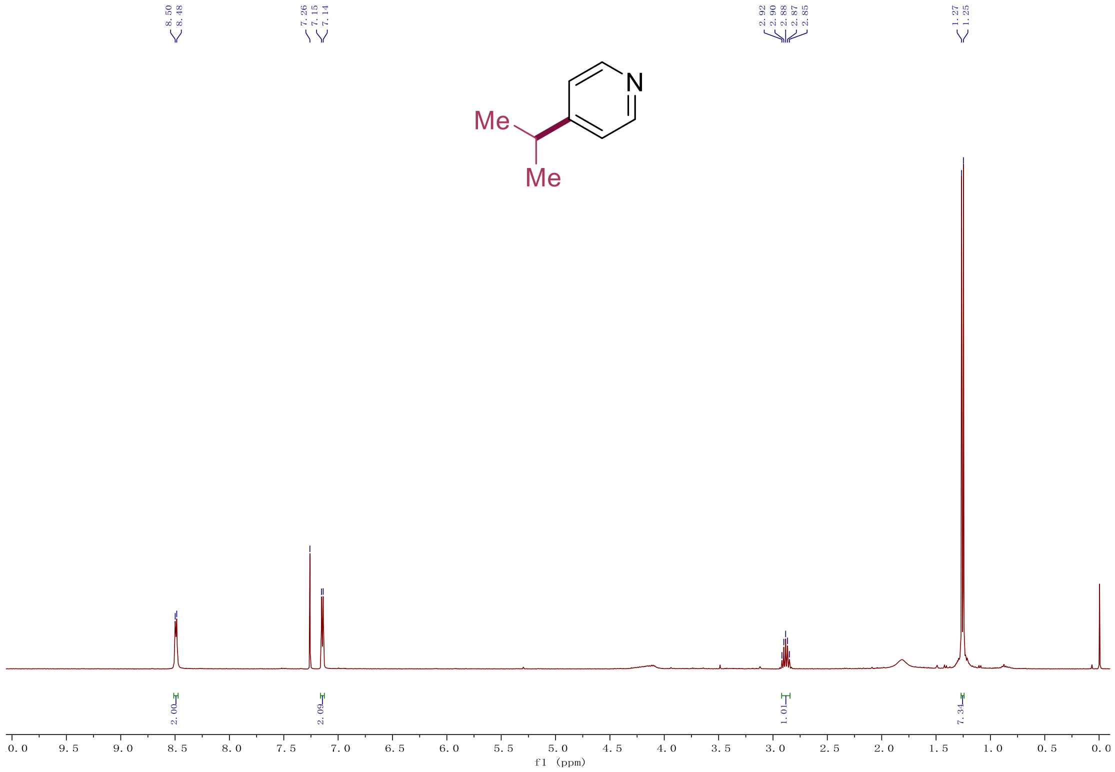
^{1}H NMR of 5 (400 MHz, CDCl$_3$)



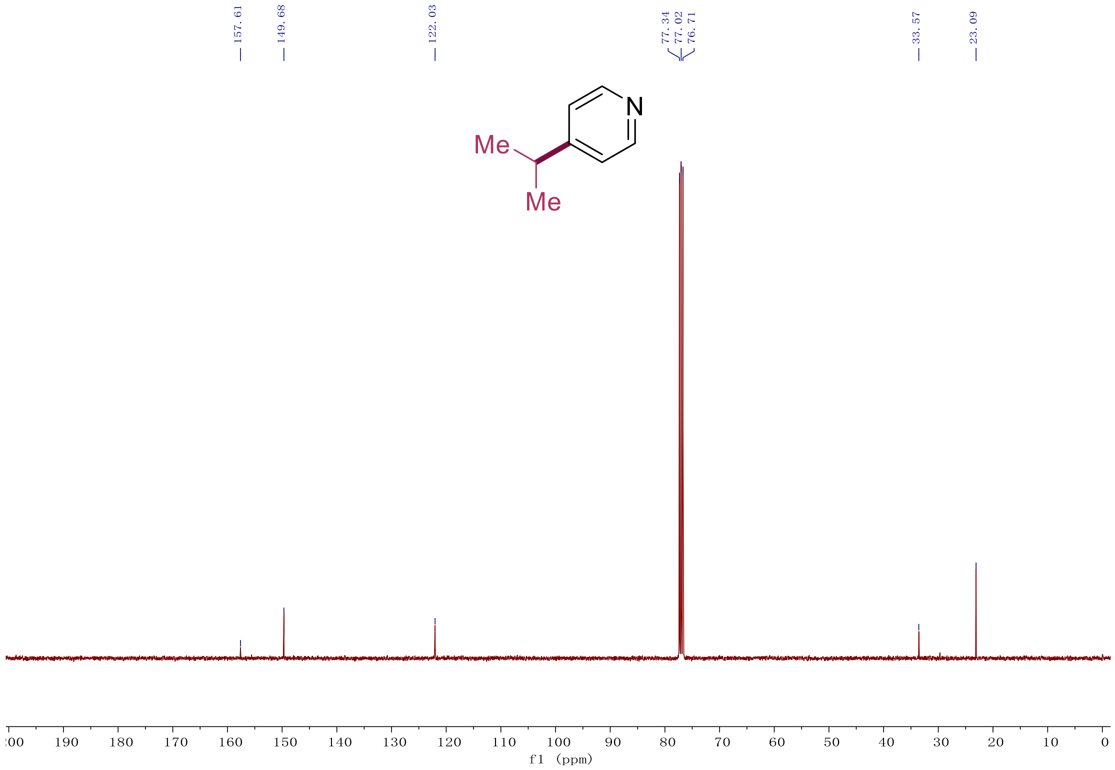
^{13}C NMR of 5 (101 MHz, CDCl$_3$)



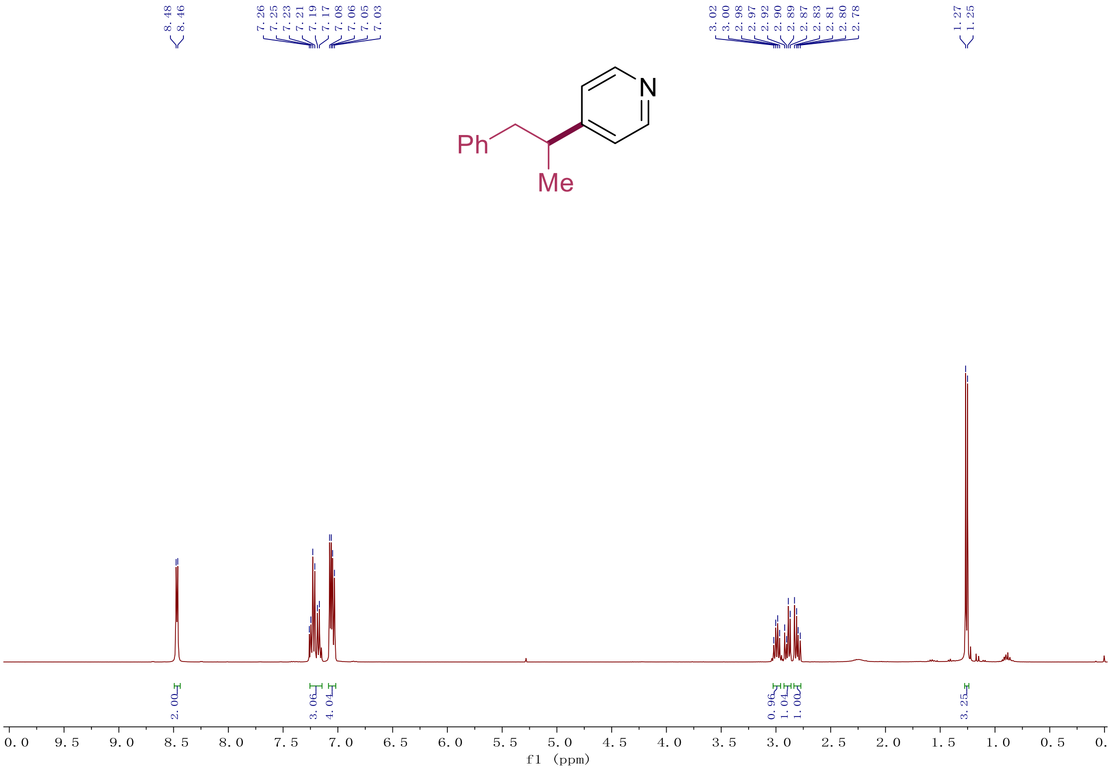
^{1}H NMR of 6 (400 MHz, CDCl$_3$)



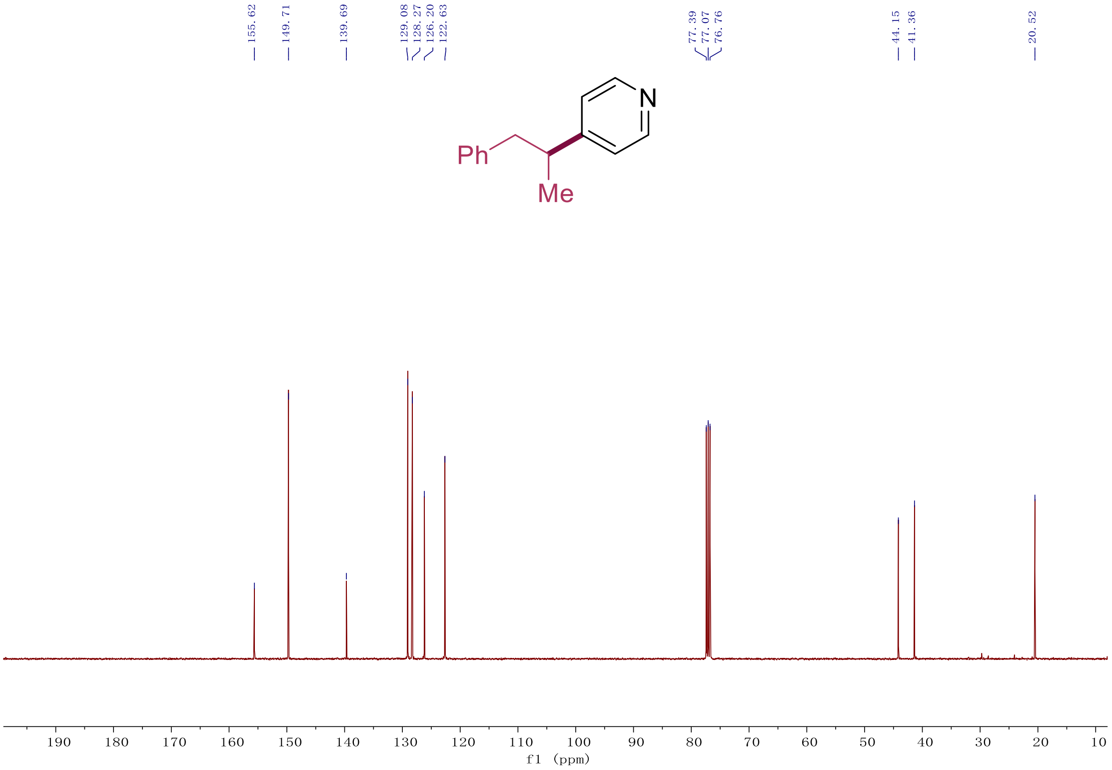
^{13}C NMR of 6 (101 MHz, CDCl$_3$)



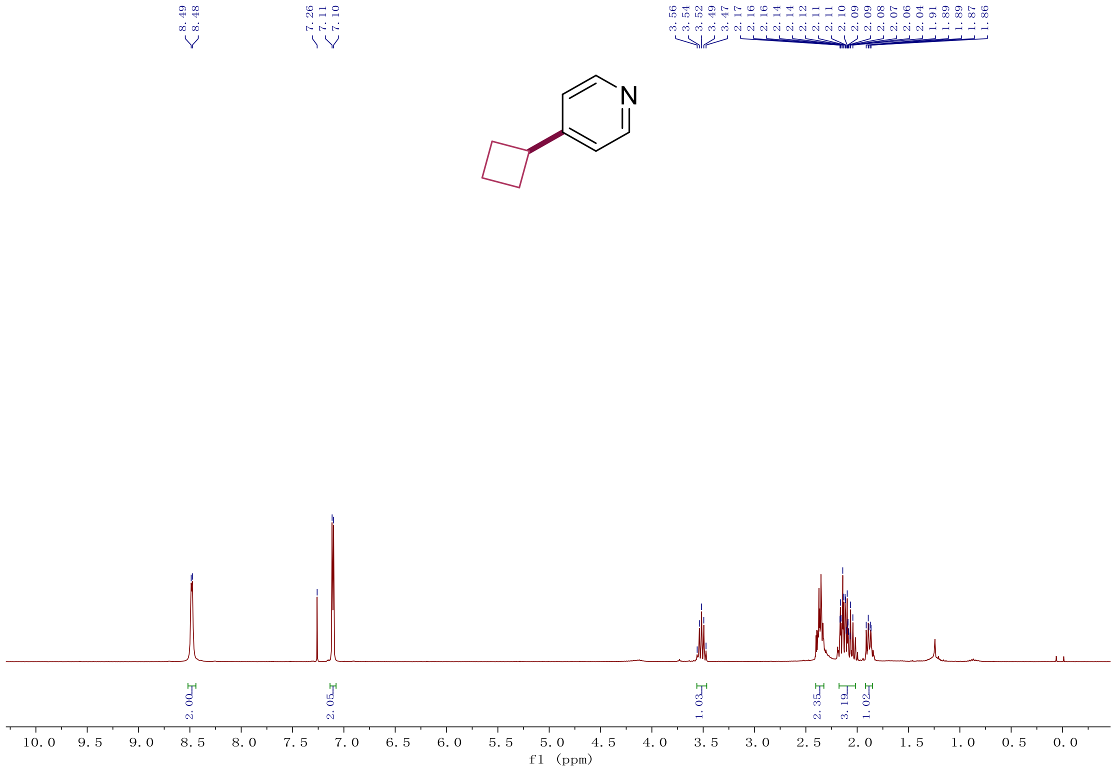
^{1}H NMR of 7 (400 MHz, CDCl$_3$)



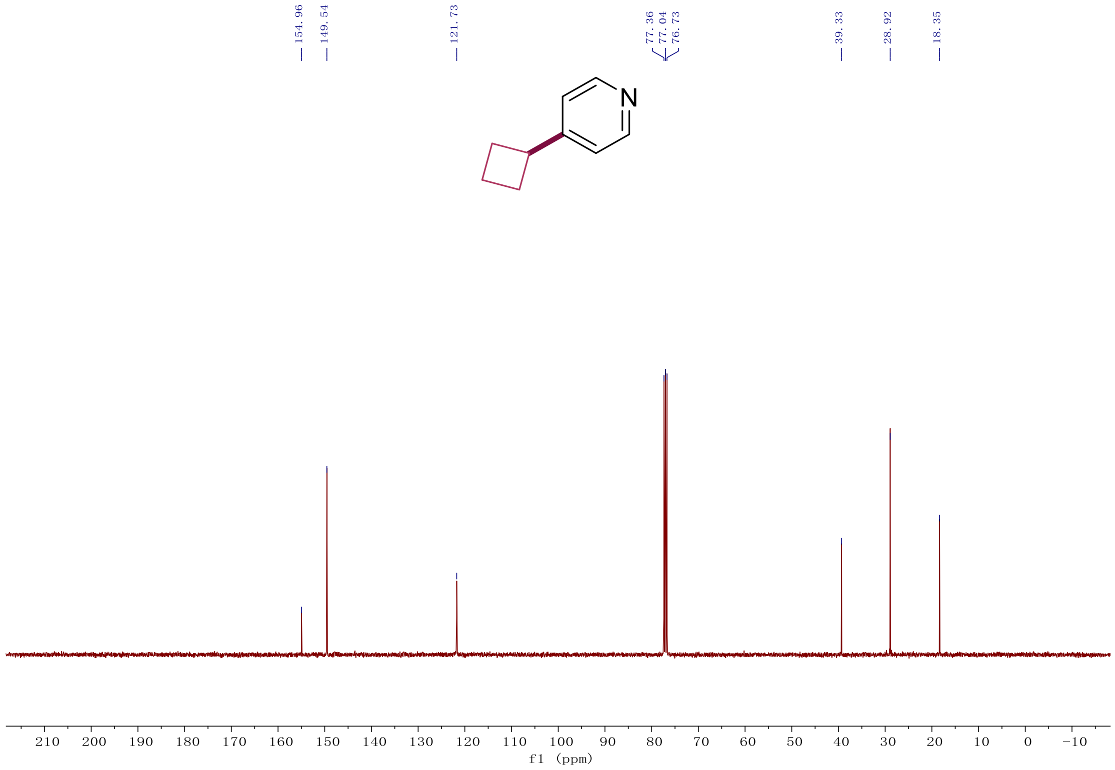
^{13}C NMR of 7 (101 MHz, CDCl$_3$)



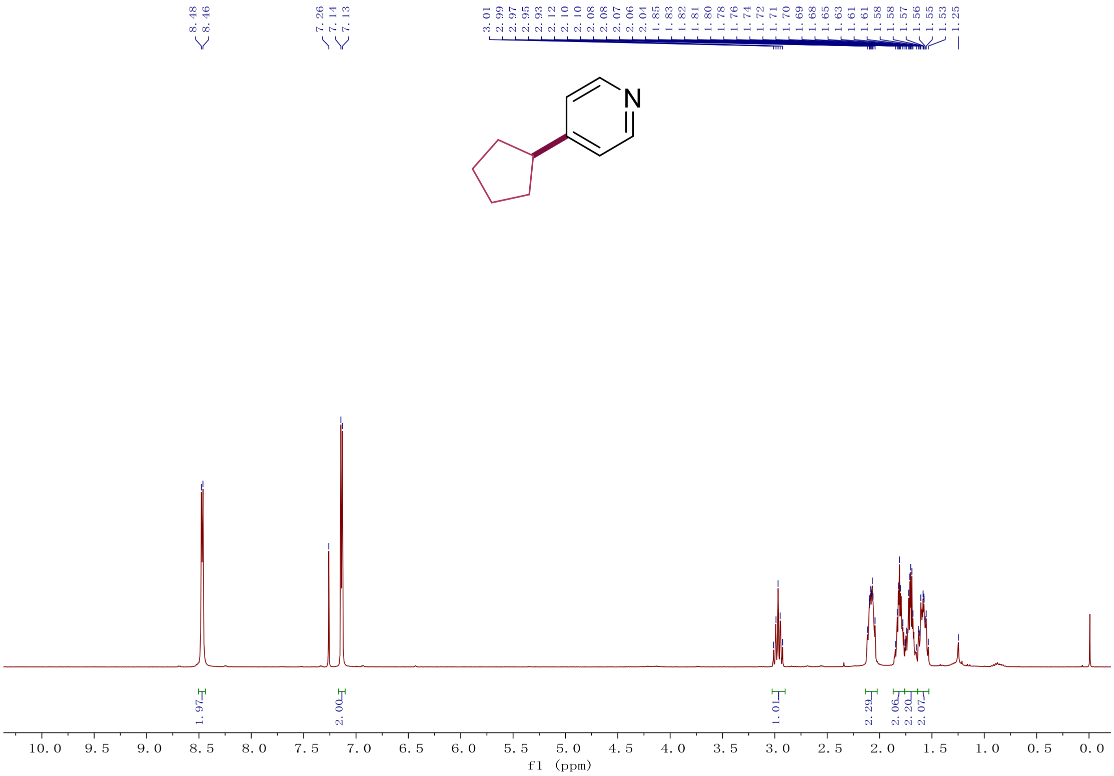
^{1}H NMR of 8 (400 MHz, $CDCl_3$)



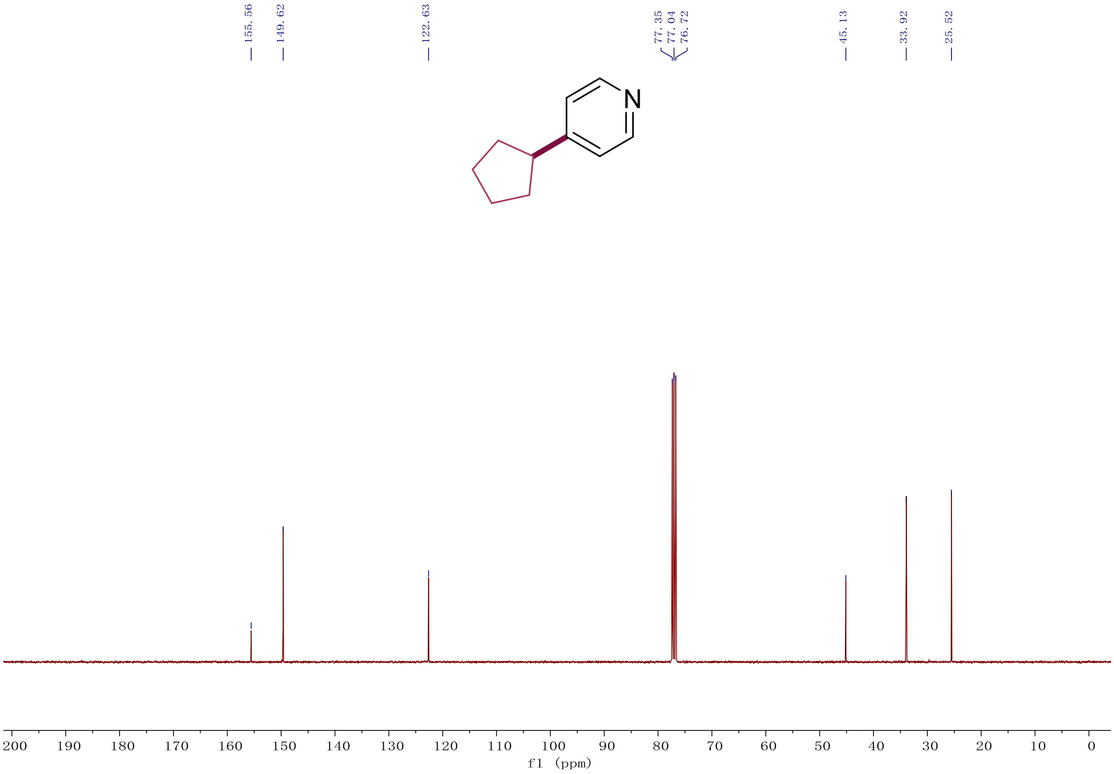
^{13}C NMR of 8 (101 MHz, $CDCl_3$)



^{1}H NMR of 9 (400 MHz, CDCl$_3$)



^{13}C NMR of 9 (101 MHz, CDCl$_3$)



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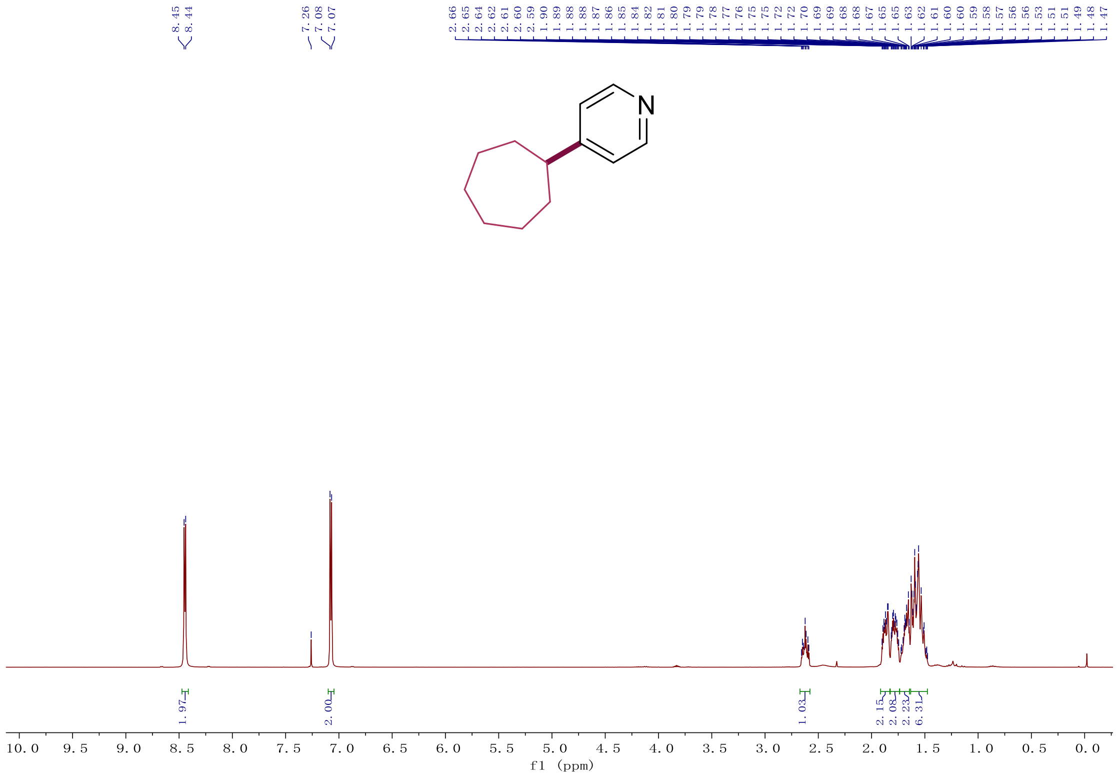

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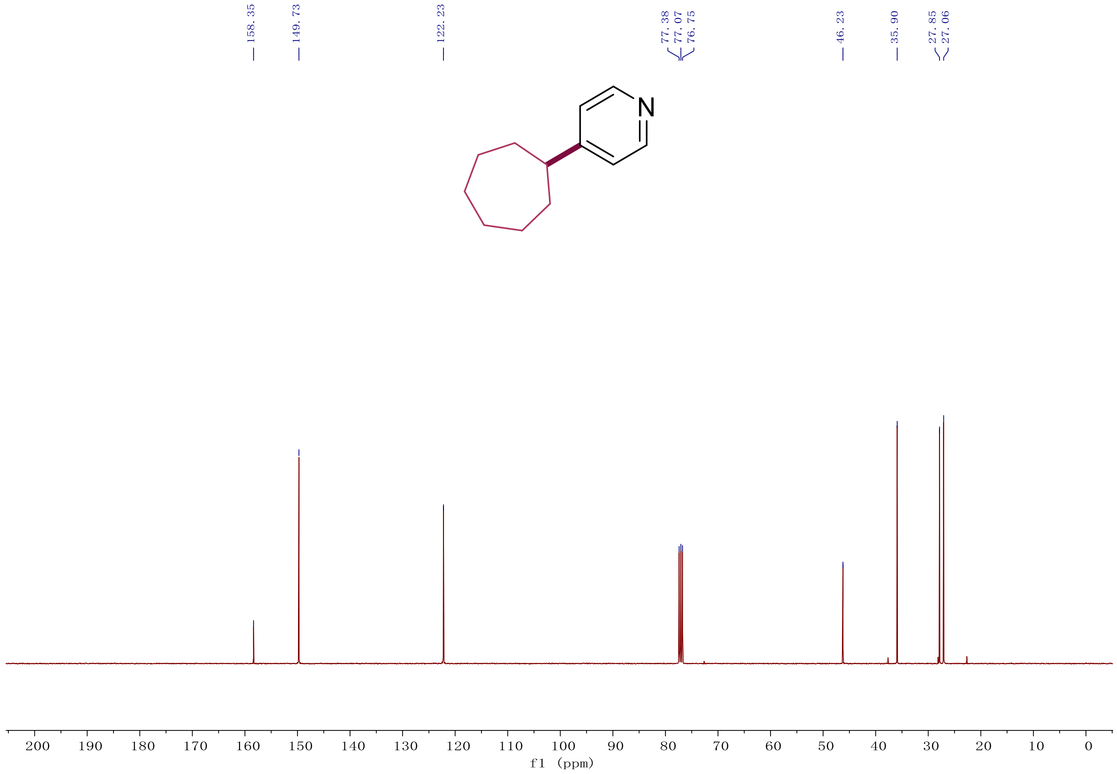
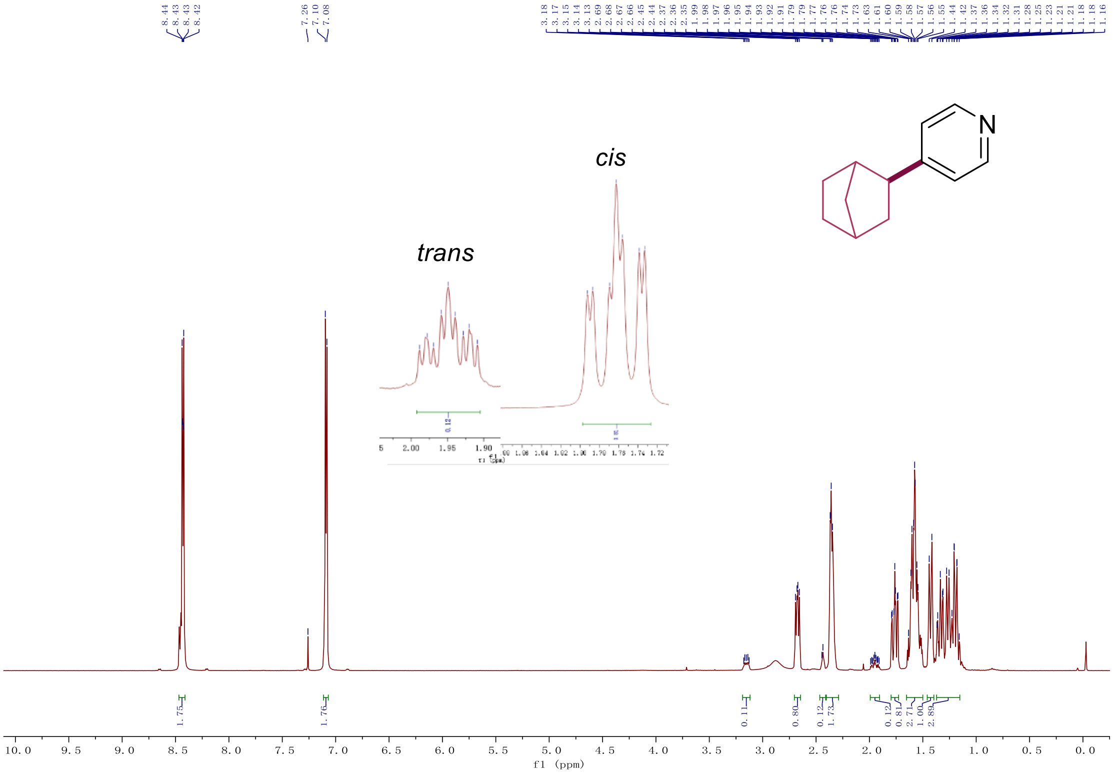


^{1}H NMR of 11 (400 MHz, CDCl$_3$)



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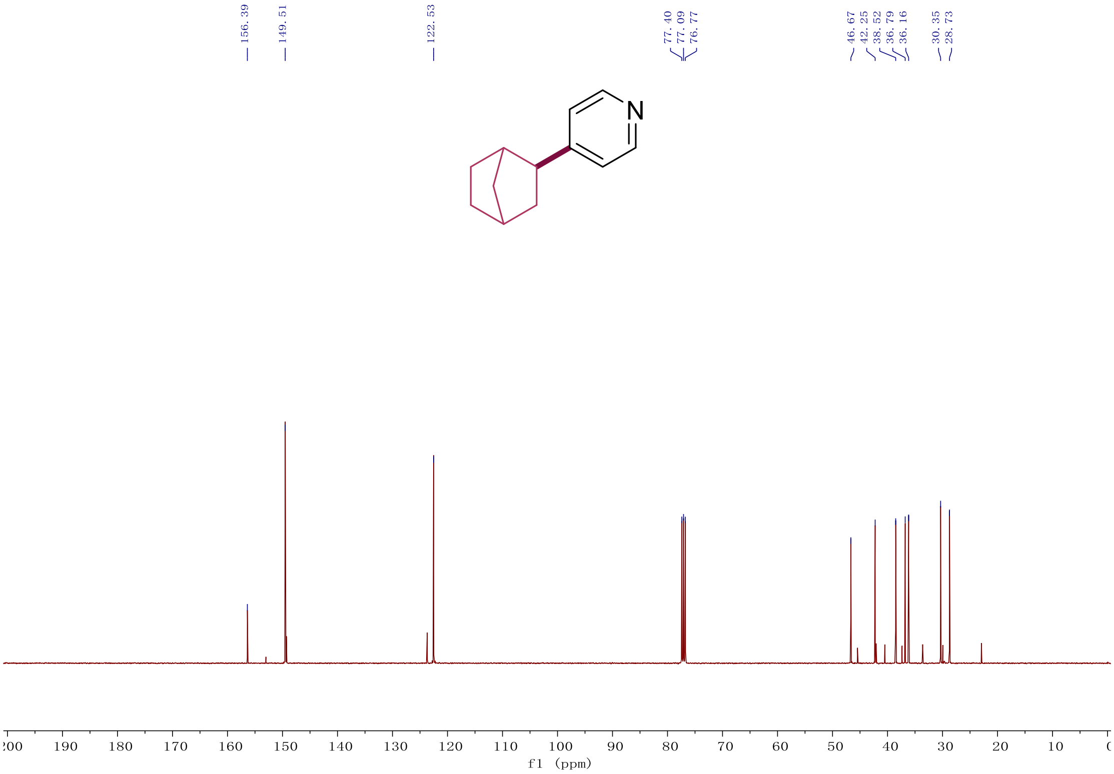
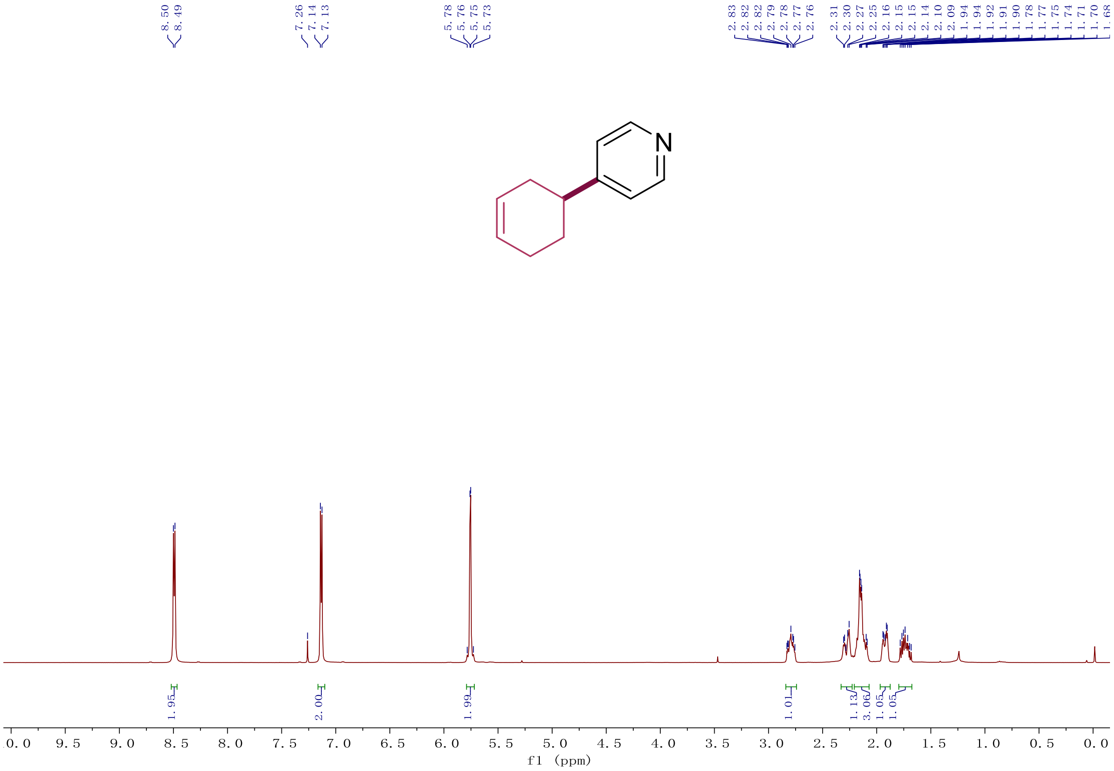
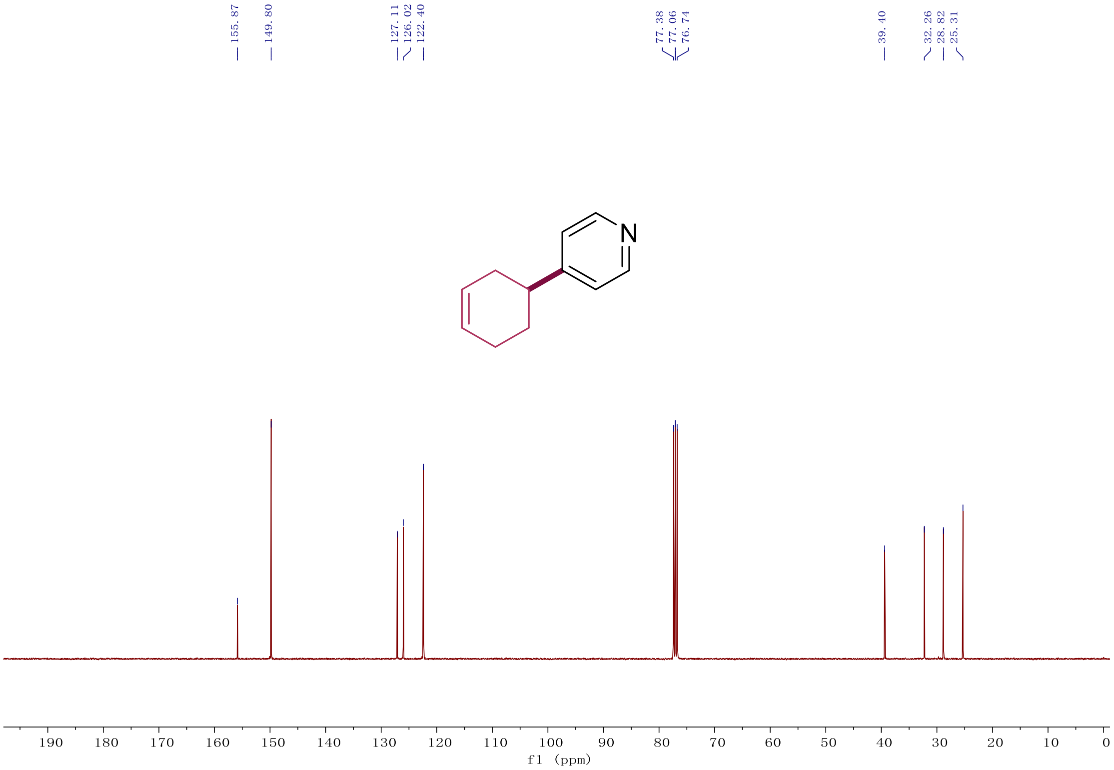
^{13}C NMR of 11 (101 MHz, CDCl$_3$)



^{1}H NMR of 12 (400 MHz, CDCl$_3$)



^{13}C NMR of 12 (101 MHz, CDCl$_3$)



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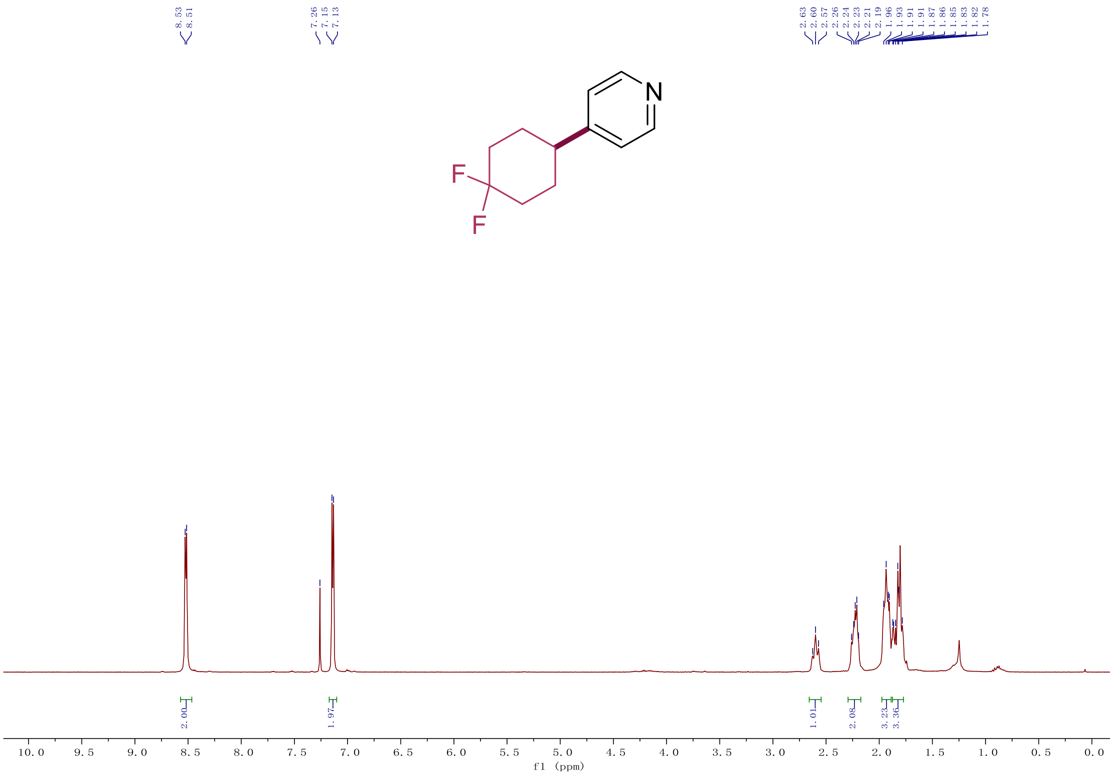

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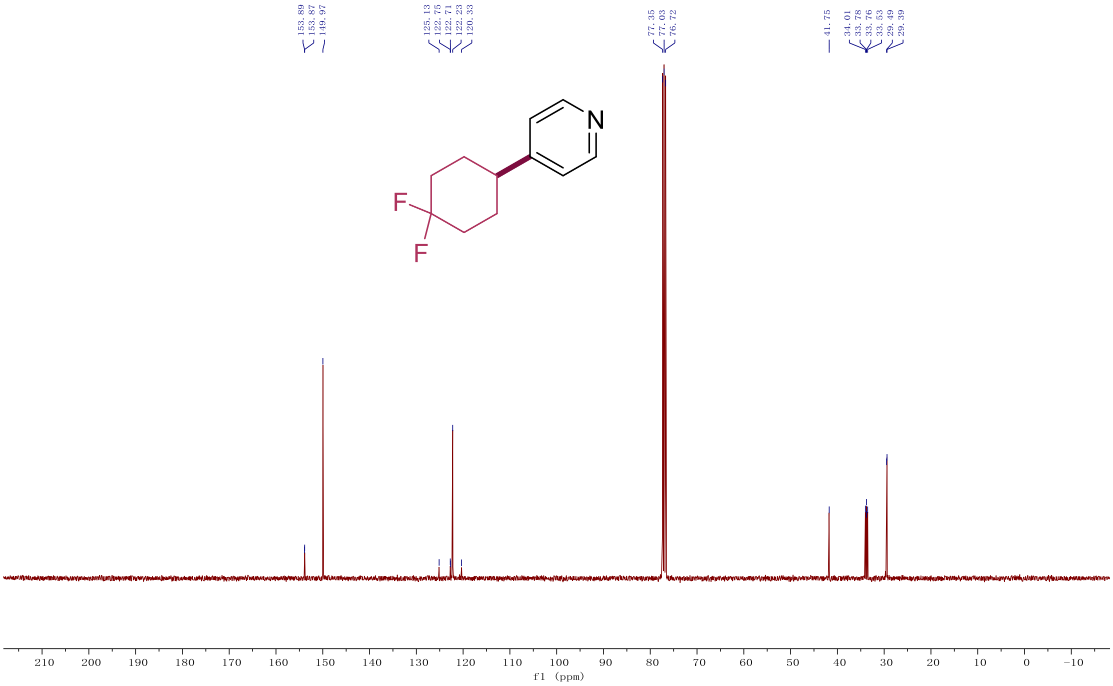
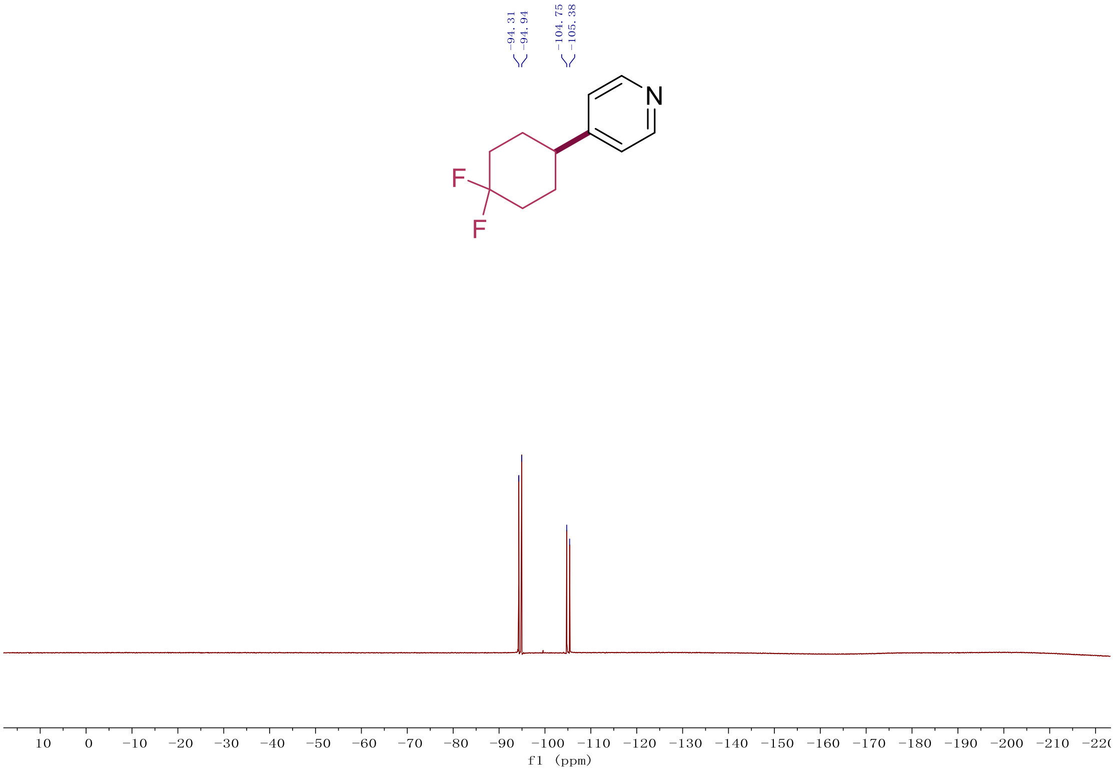
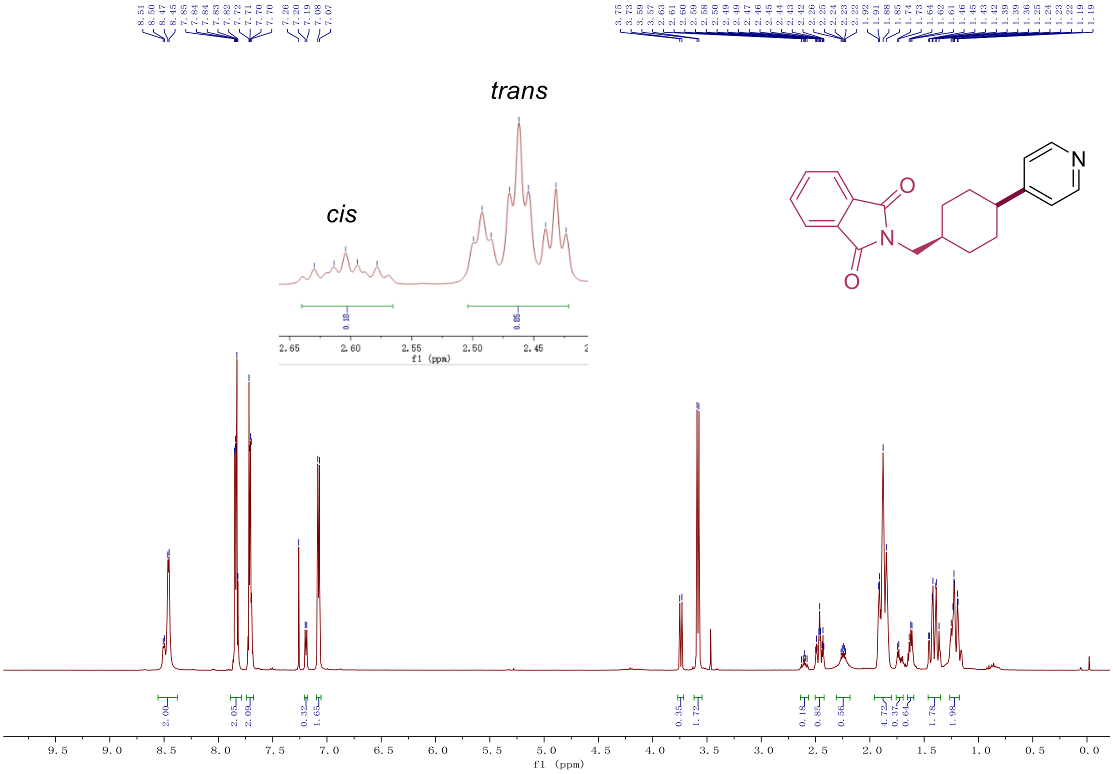


^{19}F NMR of 13 (377 MHz, $CDCl_3$)



^{1}H NMR of 14 (400 MHz, CDCl$_3$)



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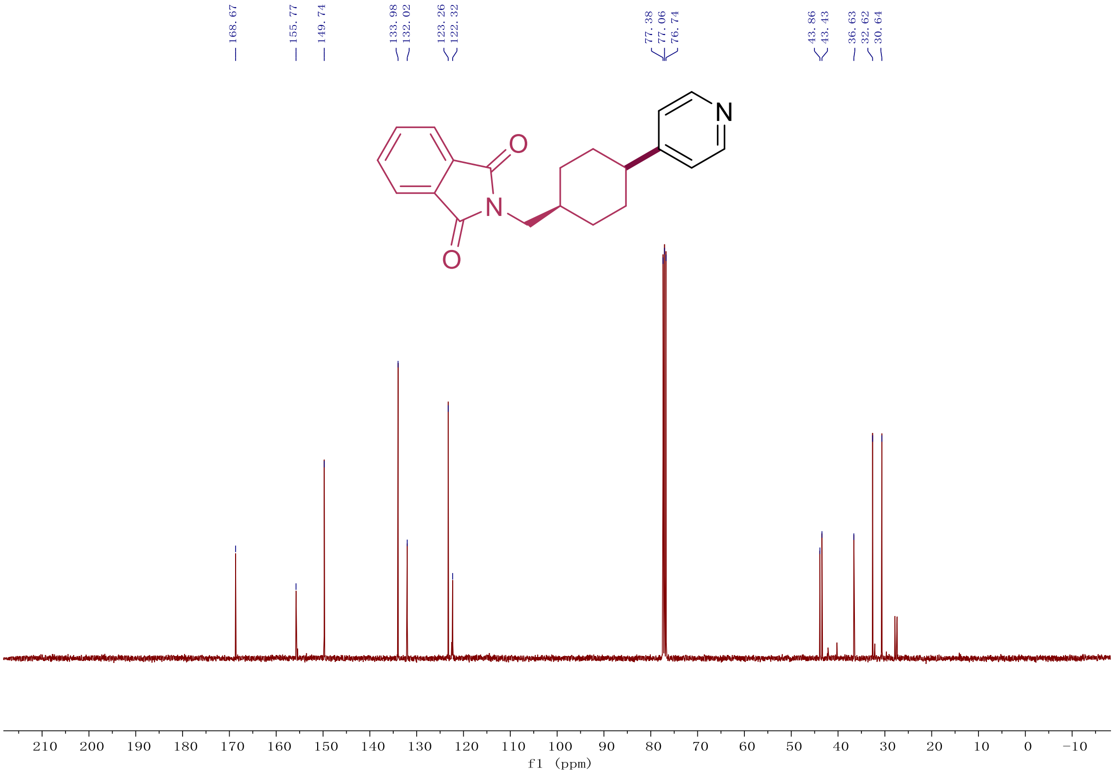
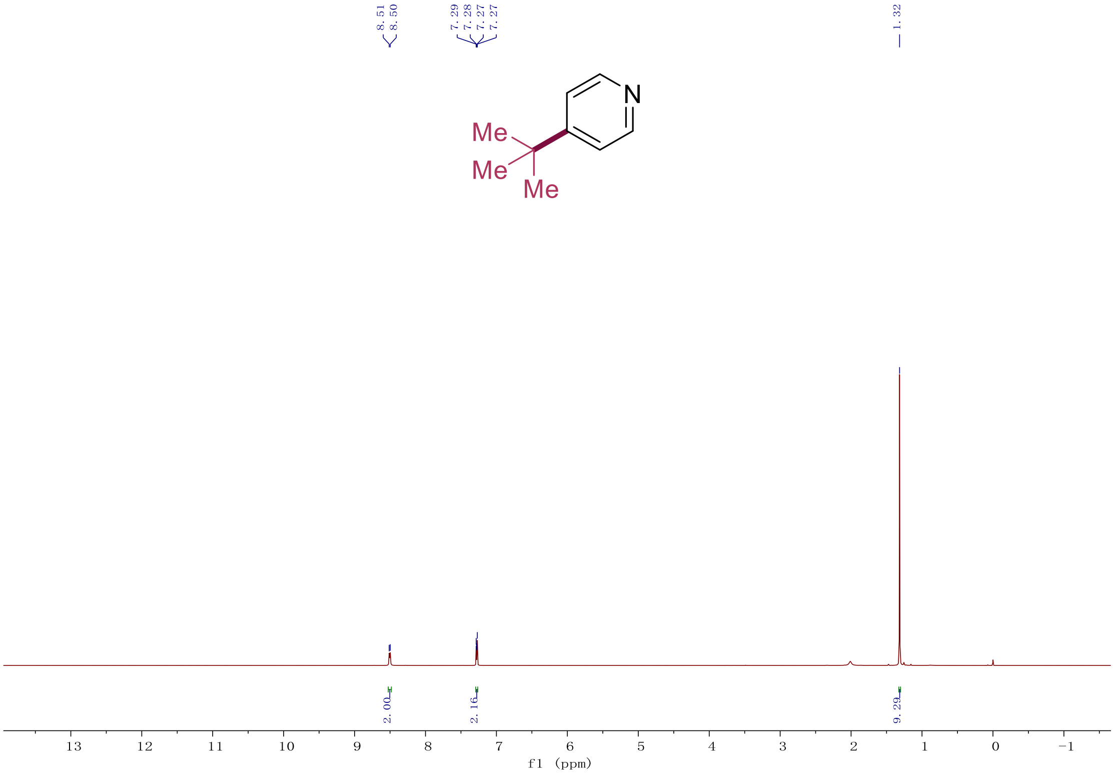
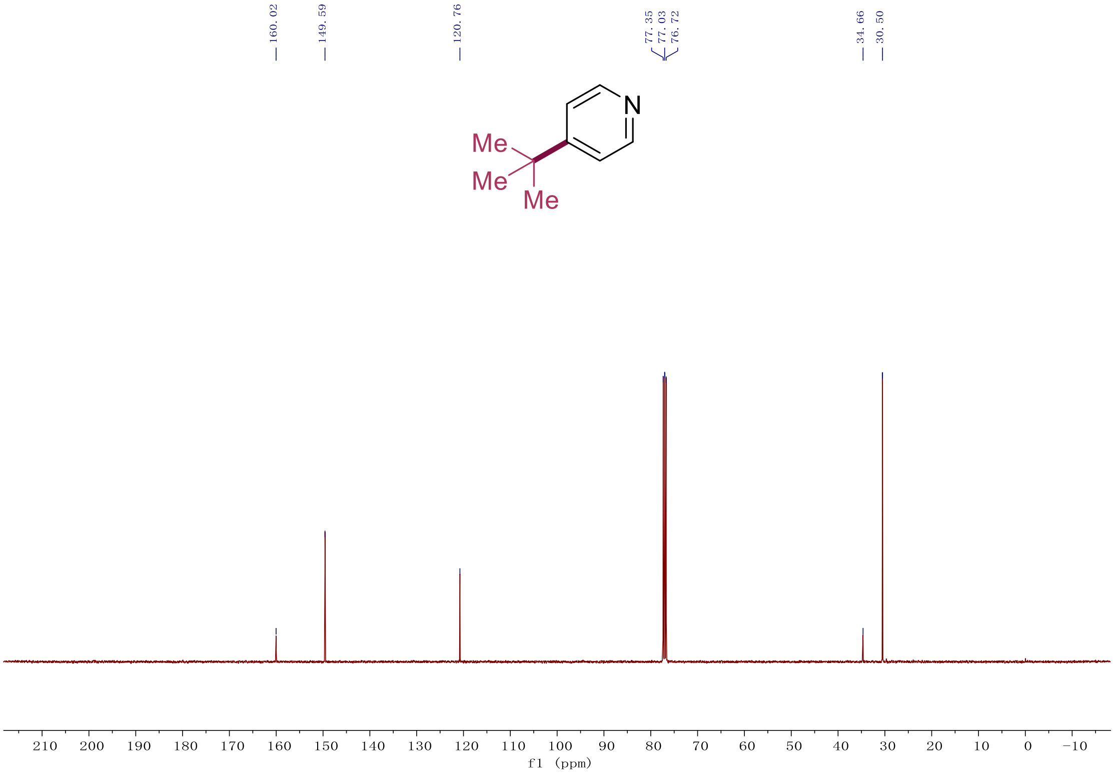
^{13}C NMR of 14 (101 MHz, CDCl$_3$)



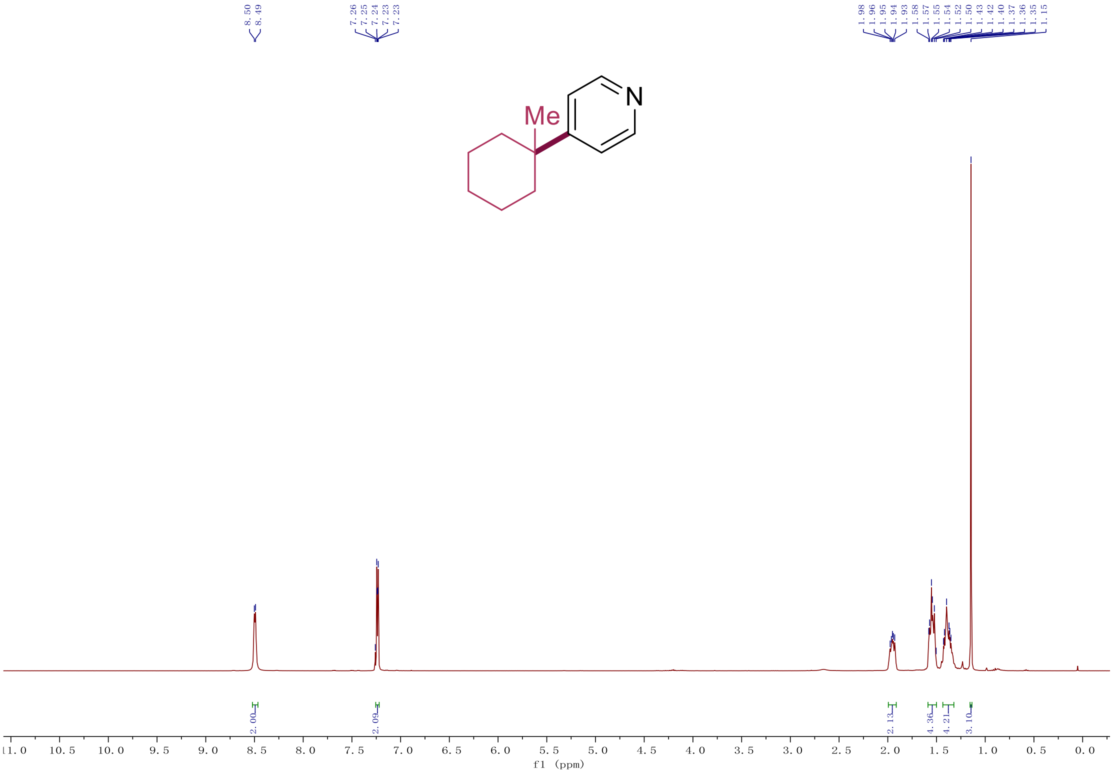
^{1}H NMR of 15 (400 MHz, CDCl$_3$)



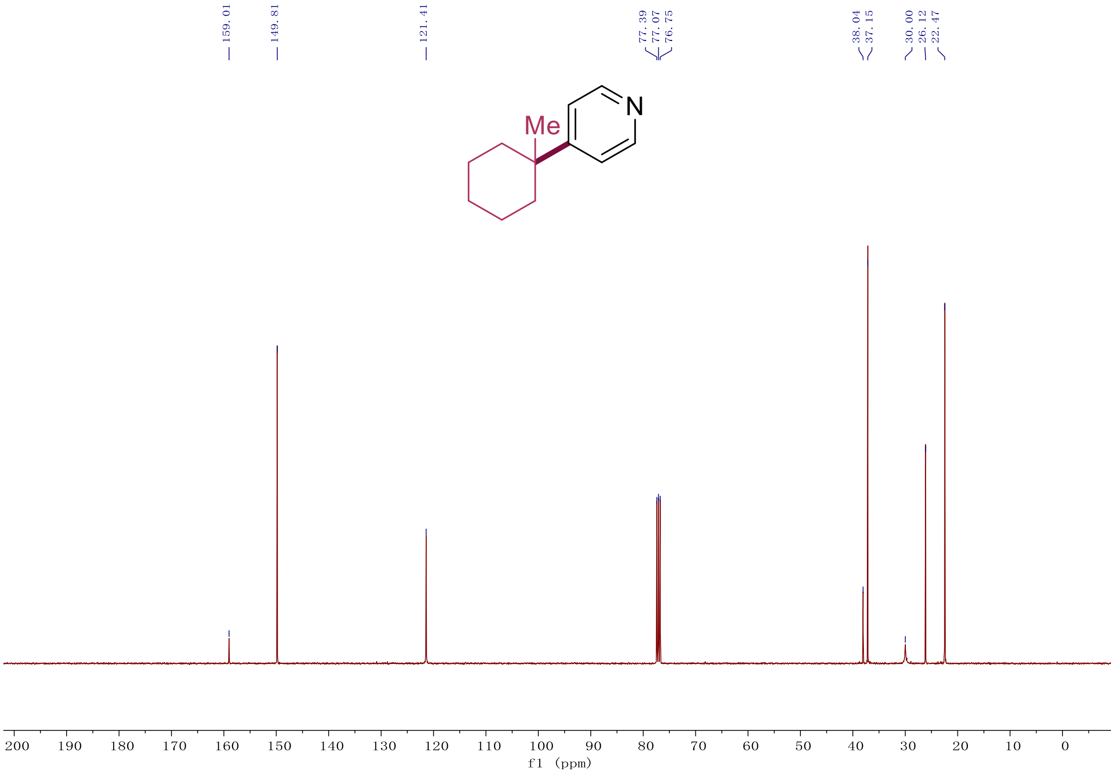
^{13}C NMR of 15 (101 MHz, CDCl$_3$)



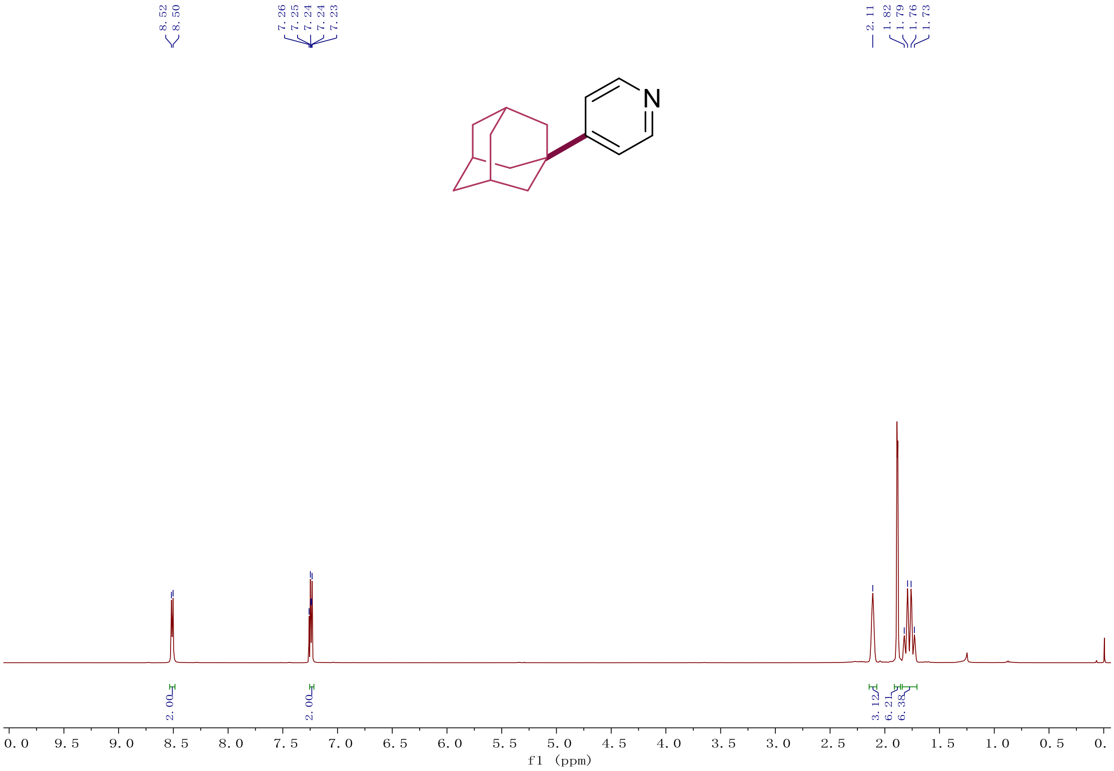
^{1}H NMR of 16 (400 MHz, $CDCl_3$)



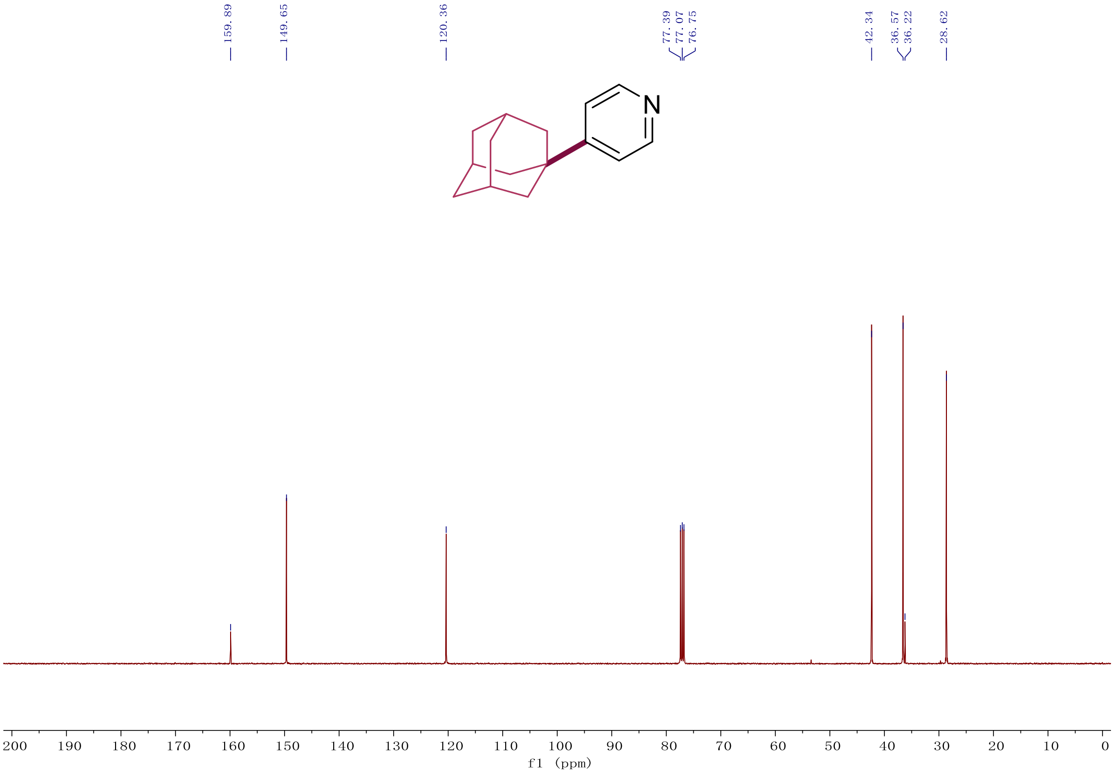
^{13}C NMR of 16 (101 MHz, $CDCl_3$)



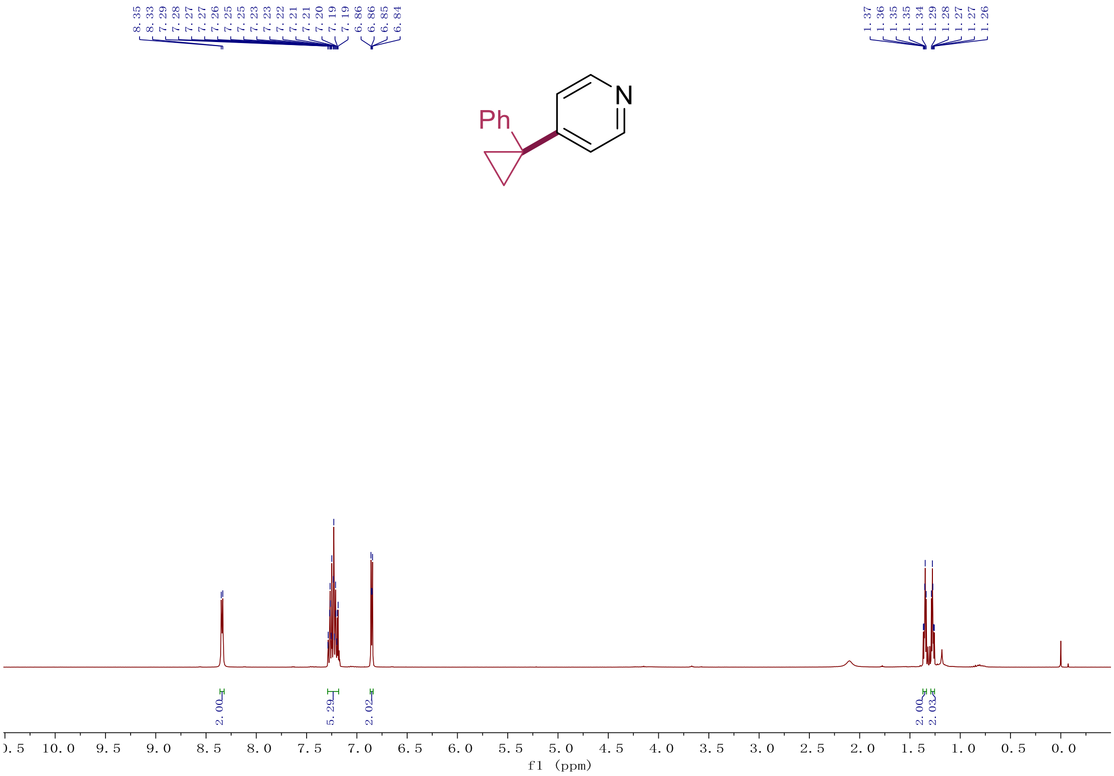
^{1}H NMR of 17 (400 MHz, $CDCl_3$)



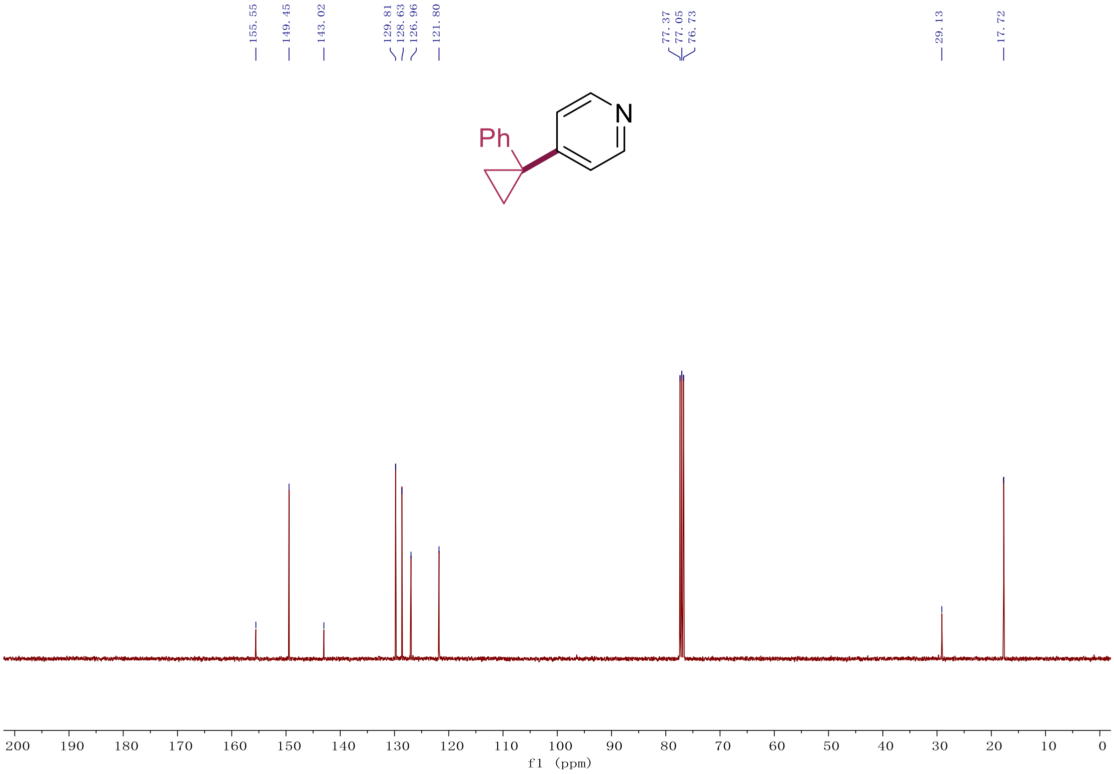
^{13}C NMR of 17 (101 MHz, $CDCl_3$)



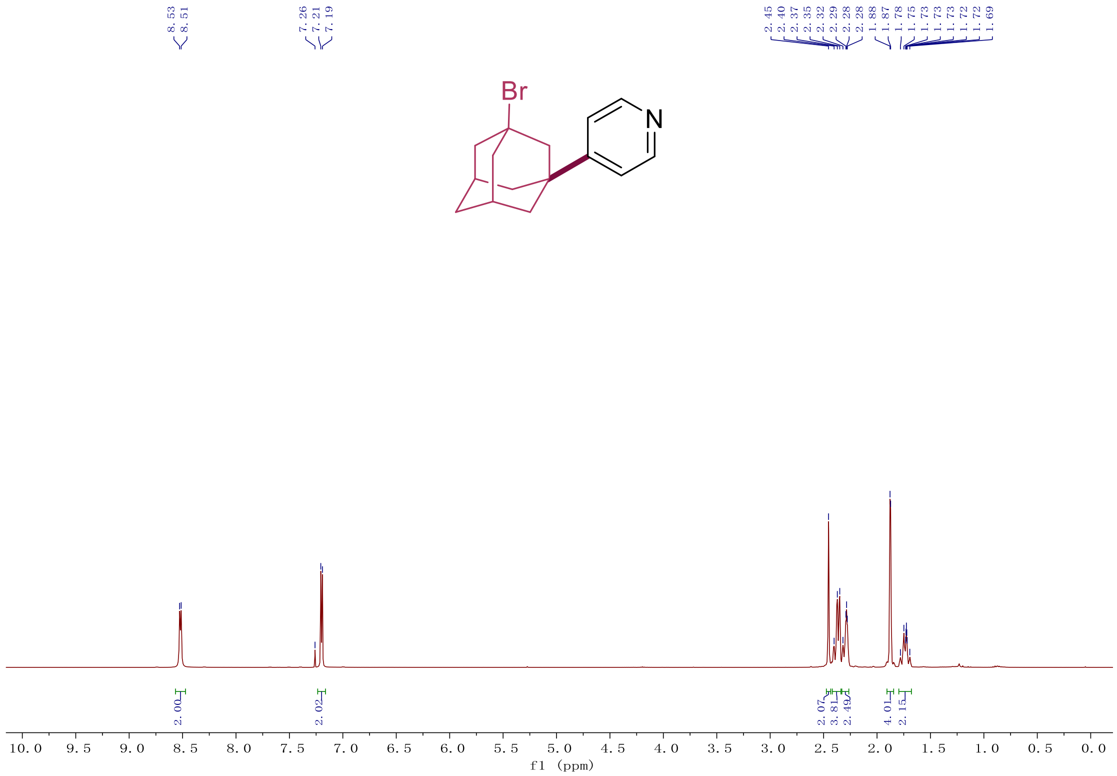
^{1}H NMR of 18 (400 MHz, $CDCl_3$)



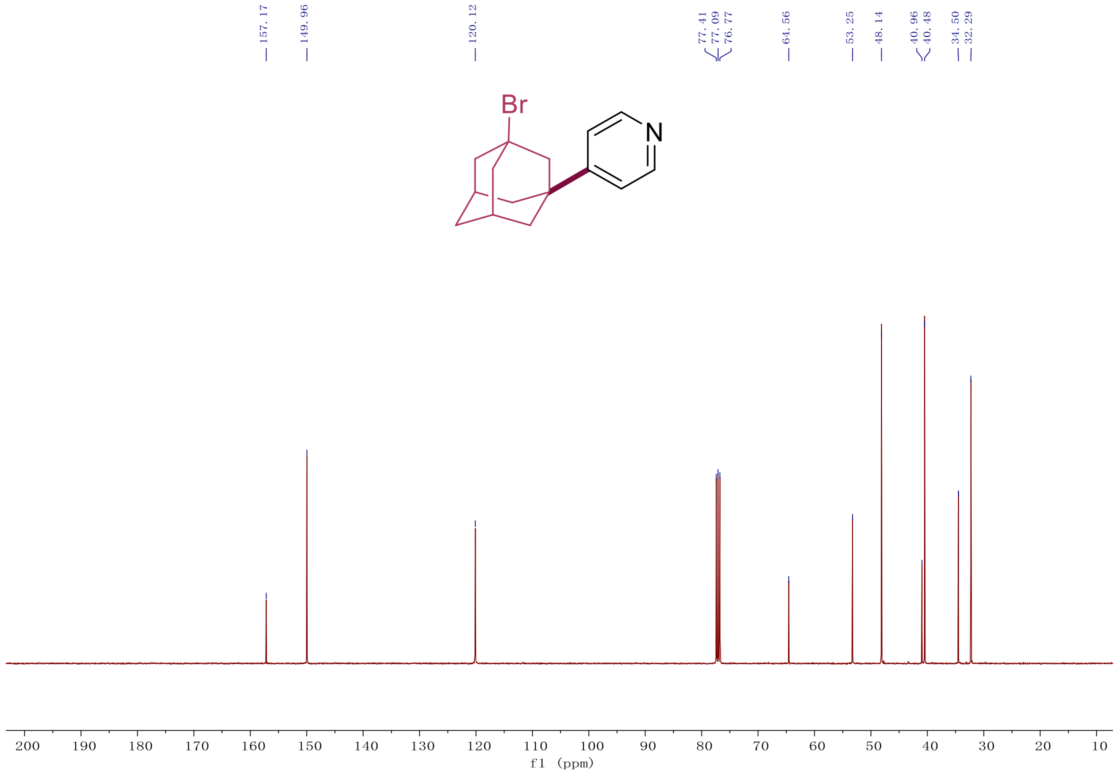
^{13}C NMR of 18 (101 MHz, $CDCl_3$)



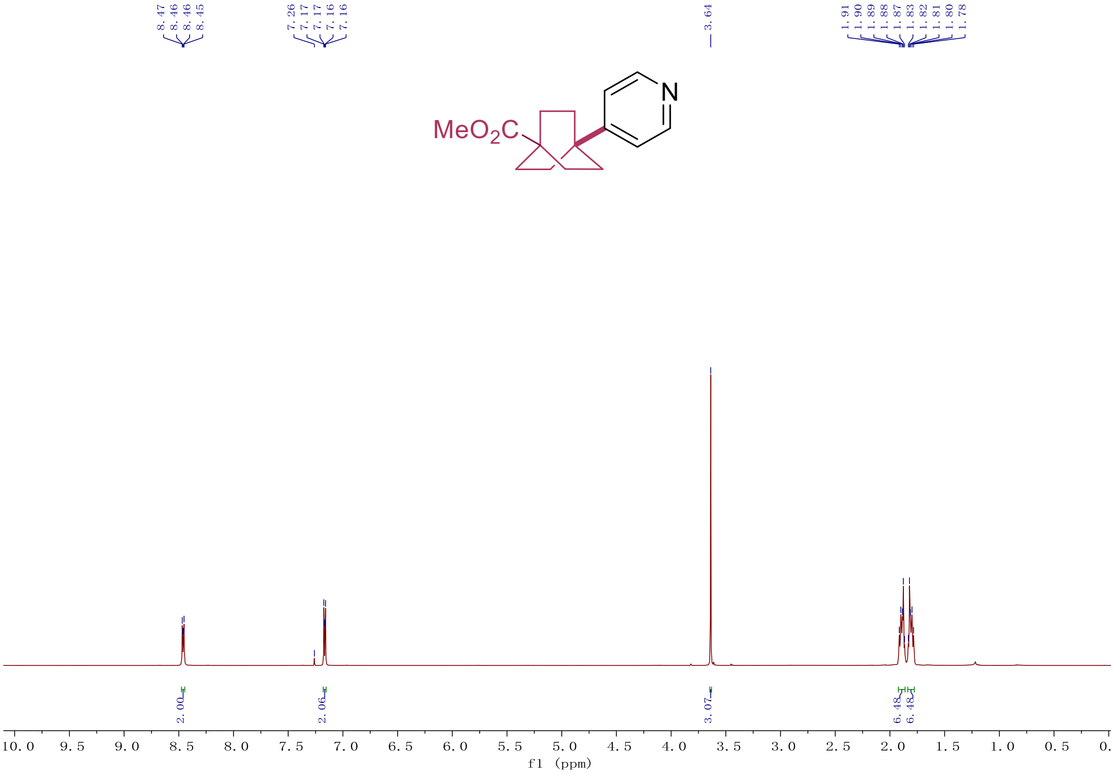
^{1}H NMR of 19 (400 MHz, CDCl$_3$)



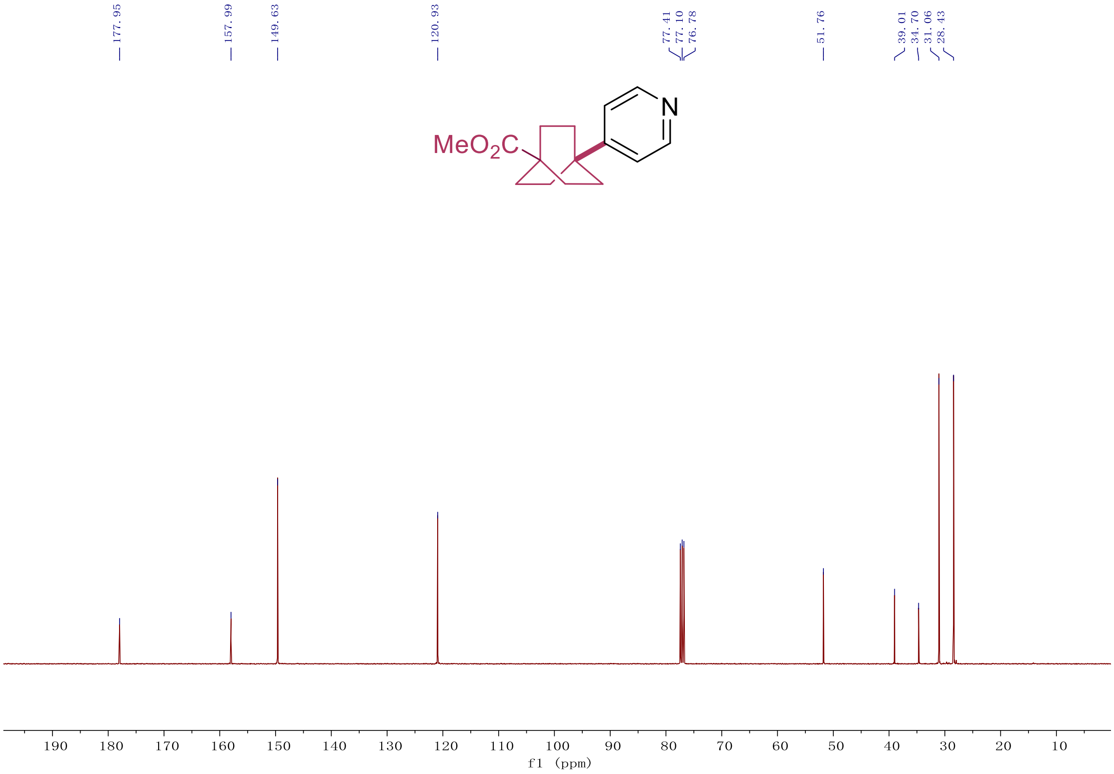
^{13}C NMR of 19 (101 MHz, CDCl$_3$)



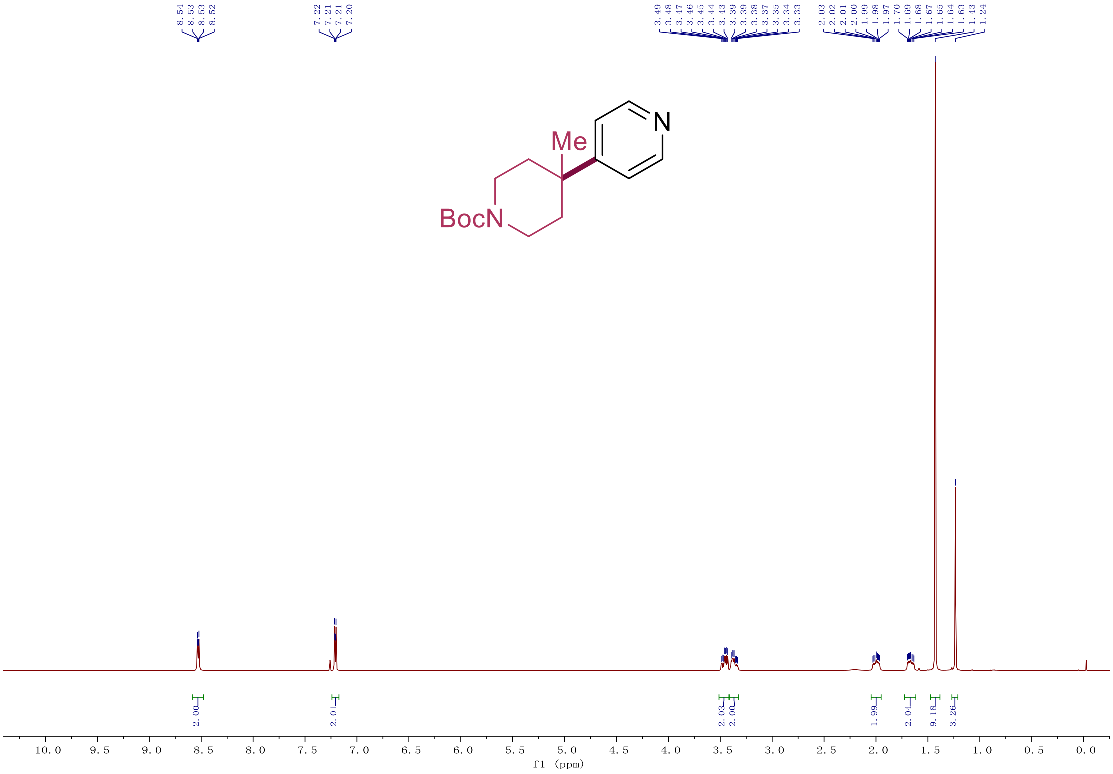
^{1}H NMR of 20 (400 MHz, $CDCl_3$)



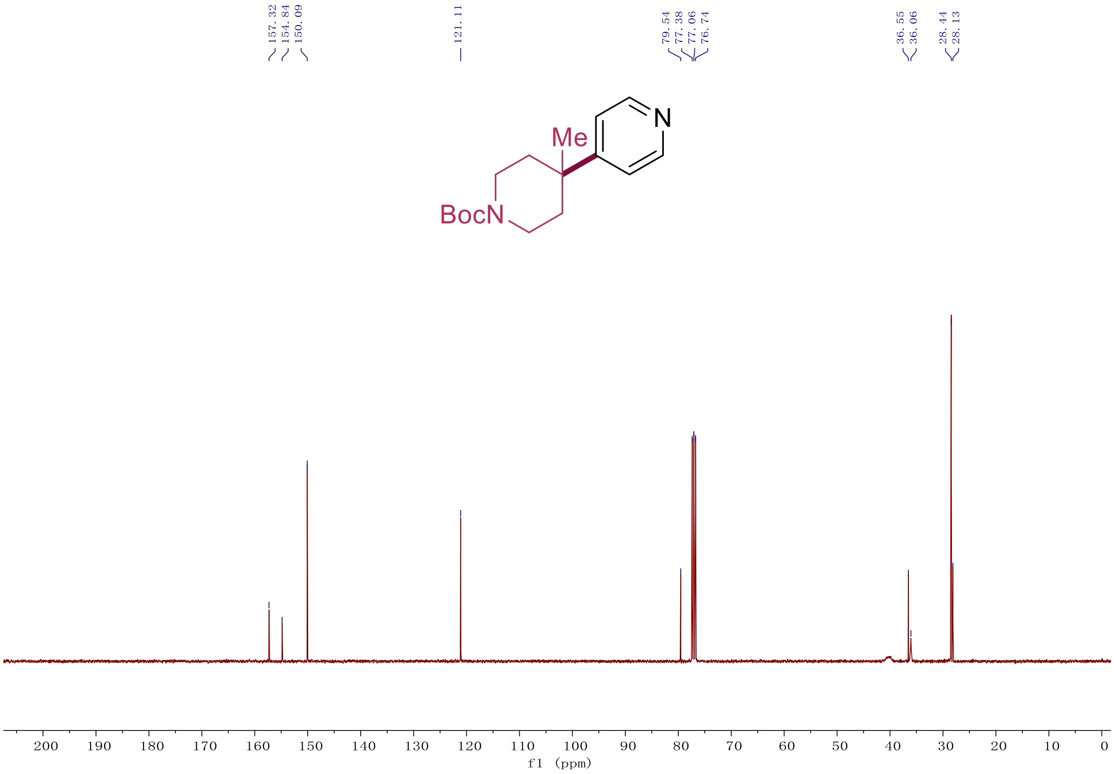
^{13}C NMR of 20 (101 MHz, $CDCl_3$)



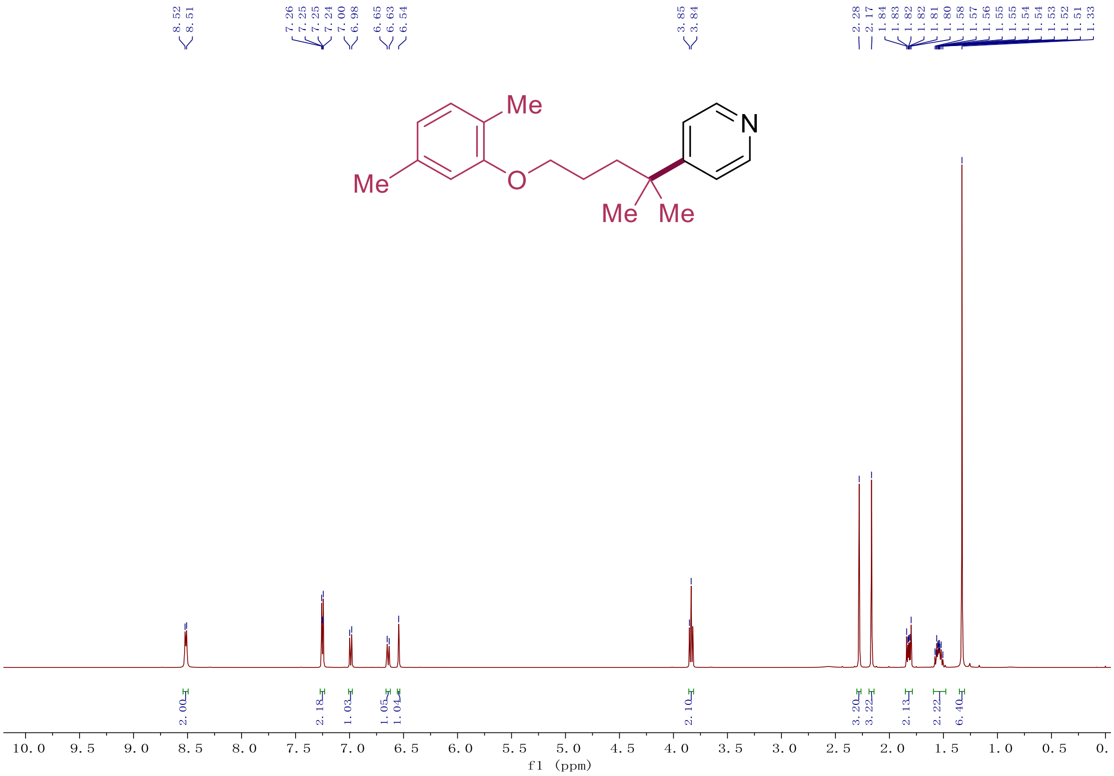
^{1}H NMR of 21 (400 MHz, CDCl$_3$)



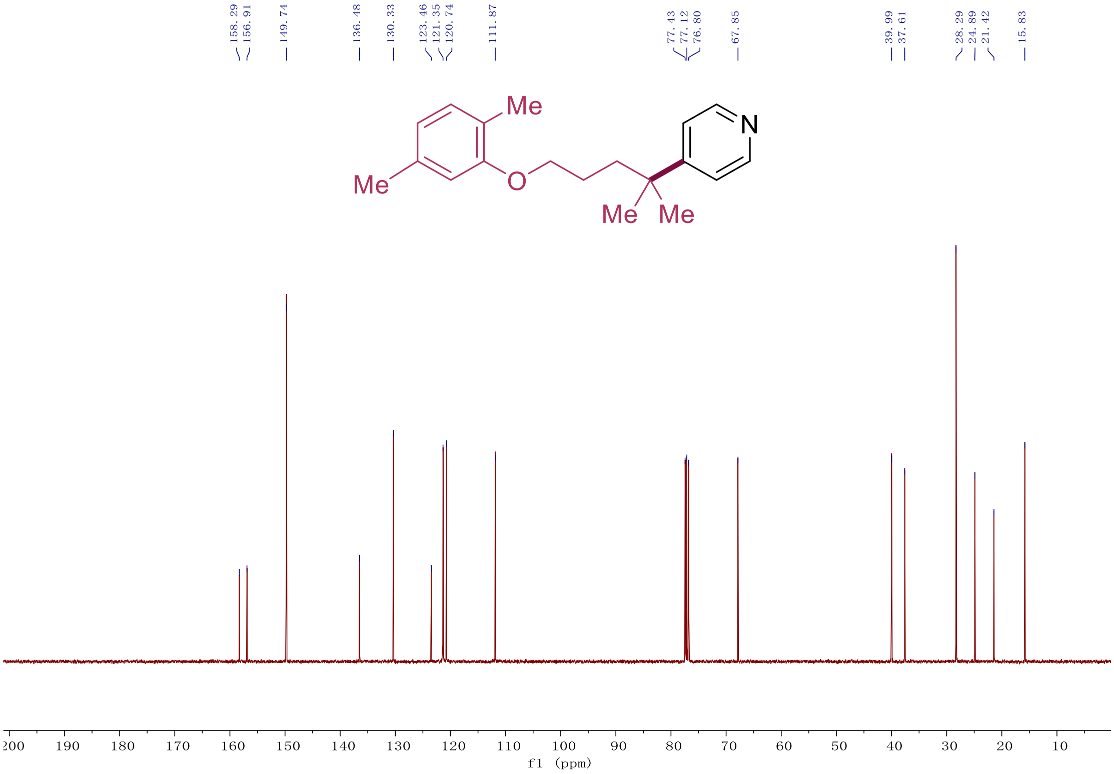
^{13}C NMR of 21 (101 MHz, CDCl$_3$)



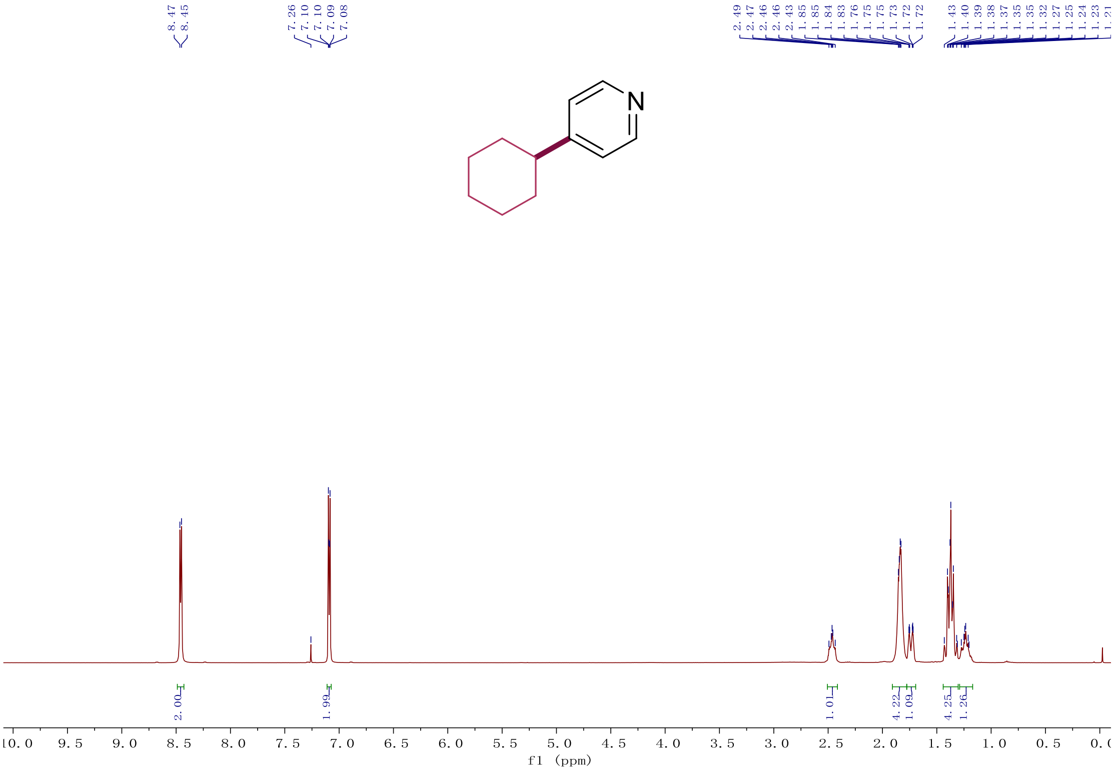
^{1}H NMR of 22 (400 MHz, CDCl$_3$)



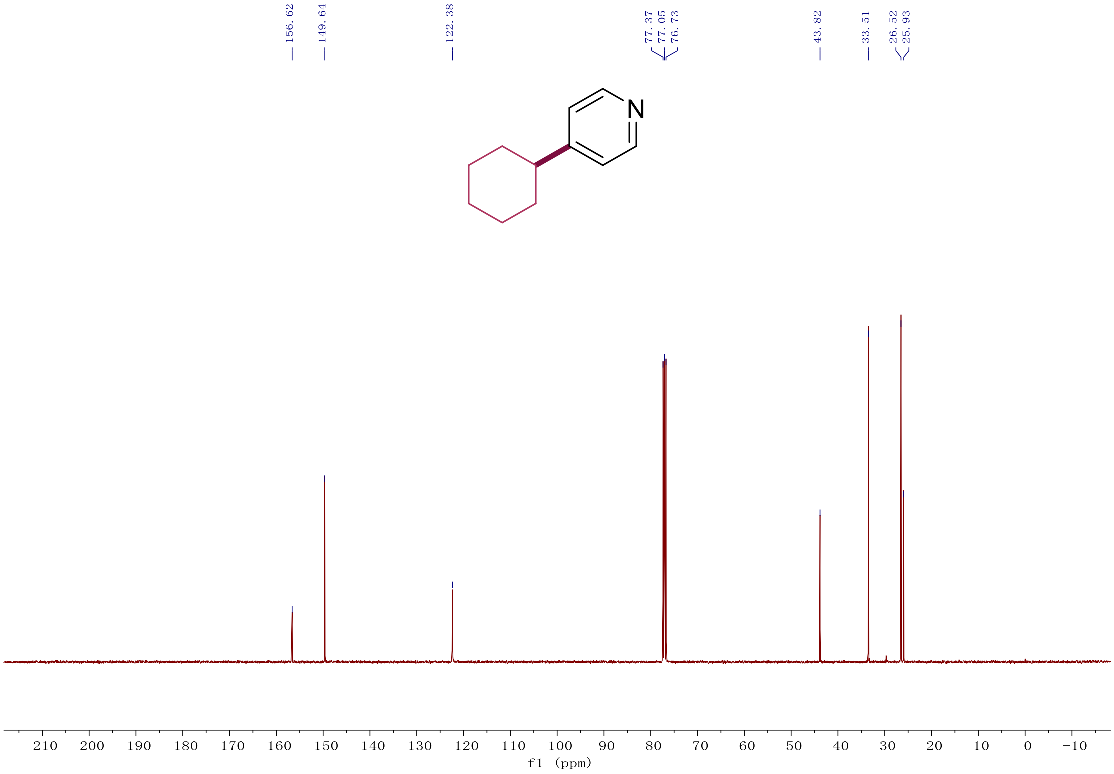
^{13}C NMR of 22 (101 MHz, CDCl$_3$)



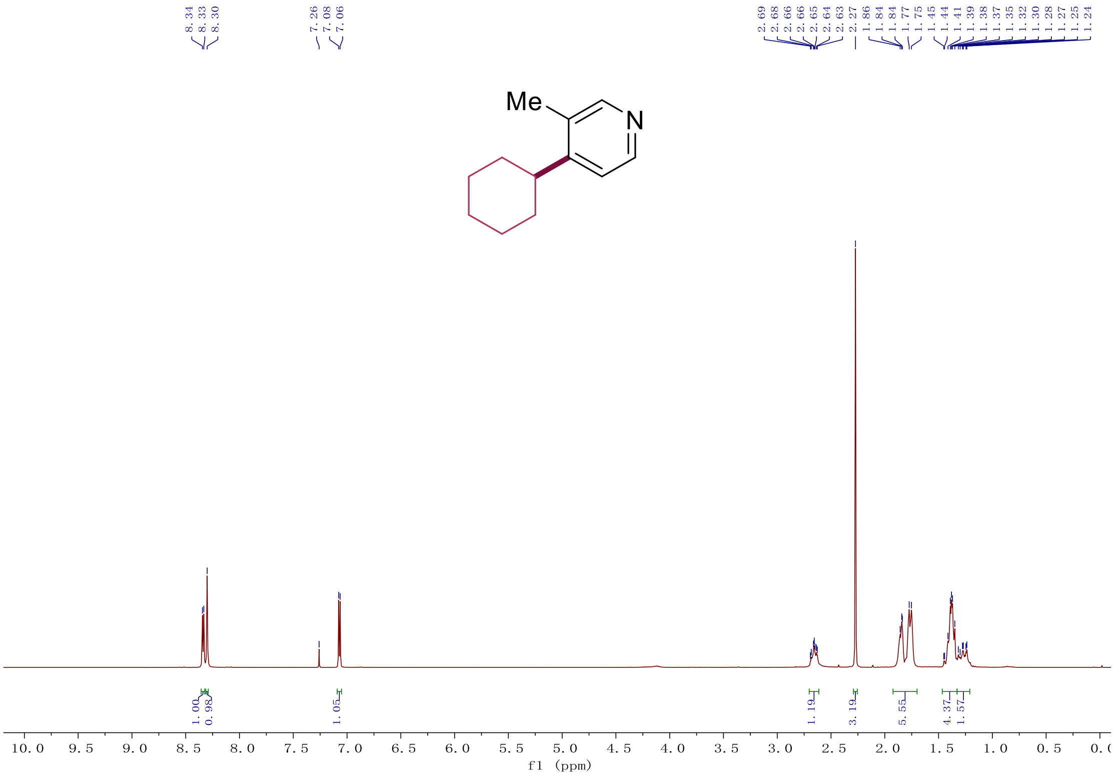
^{1}H NMR of 23 (400 MHz, CDCl$_3$)



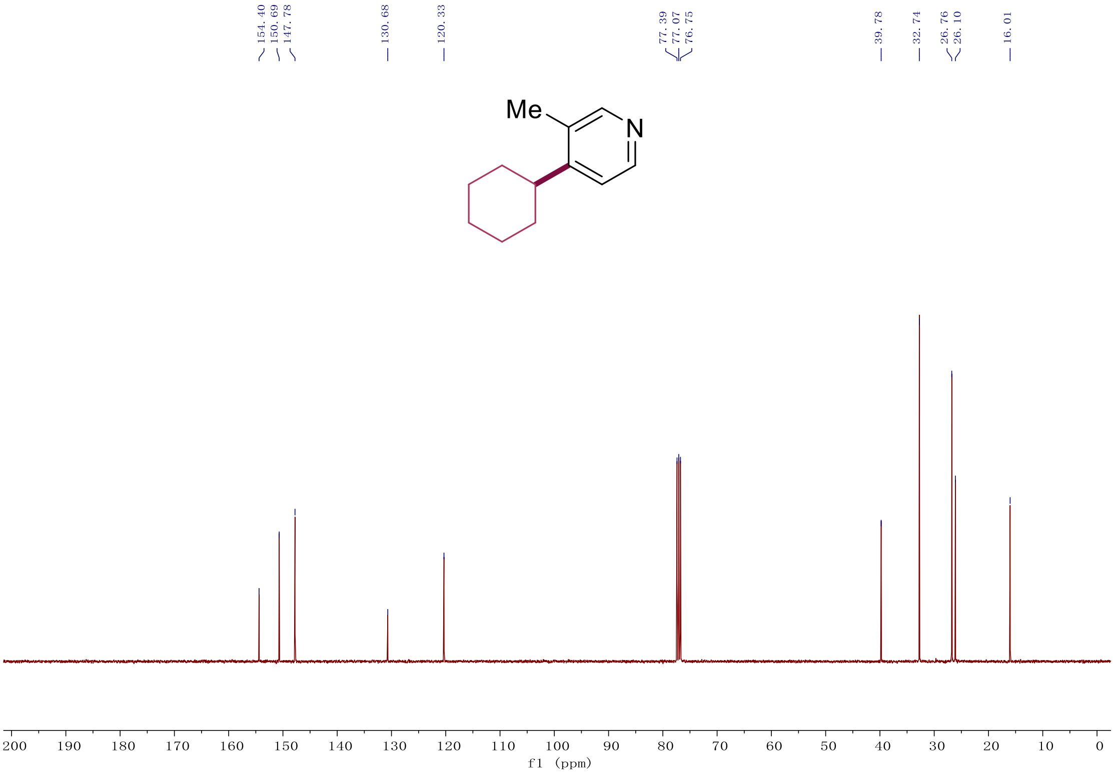
^{13}C NMR of 23 (101 MHz, CDCl$_3$)



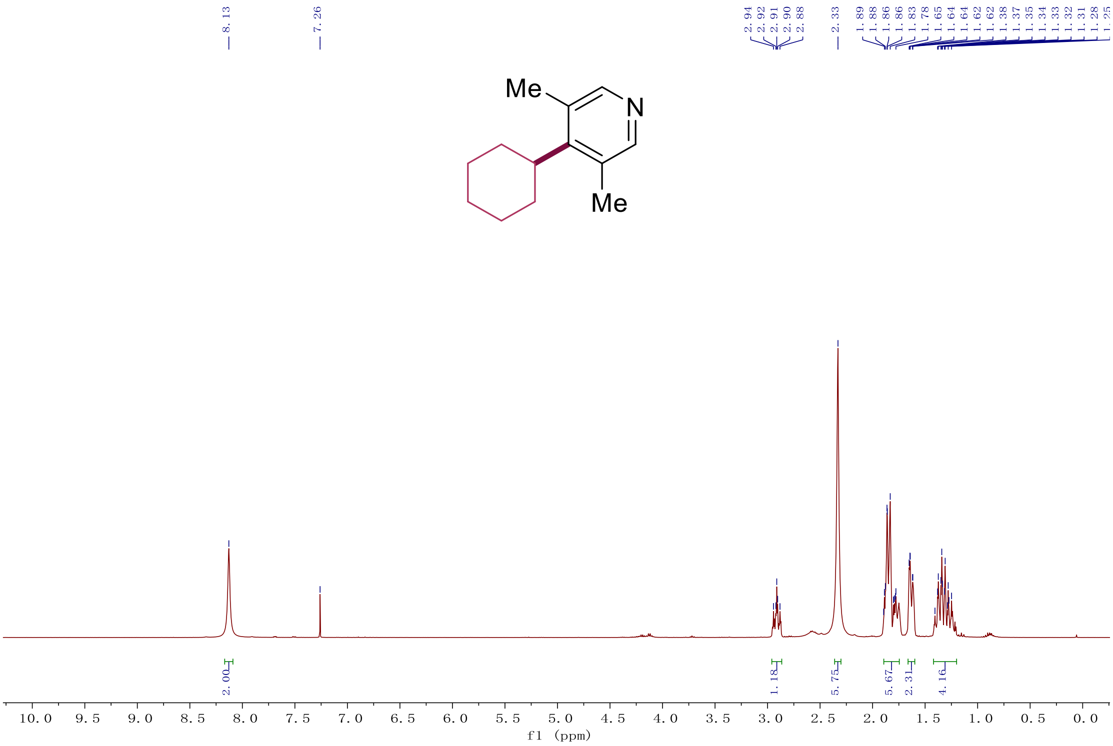
^{1}H NMR of **24** (400 MHz, CDCl$_3$)



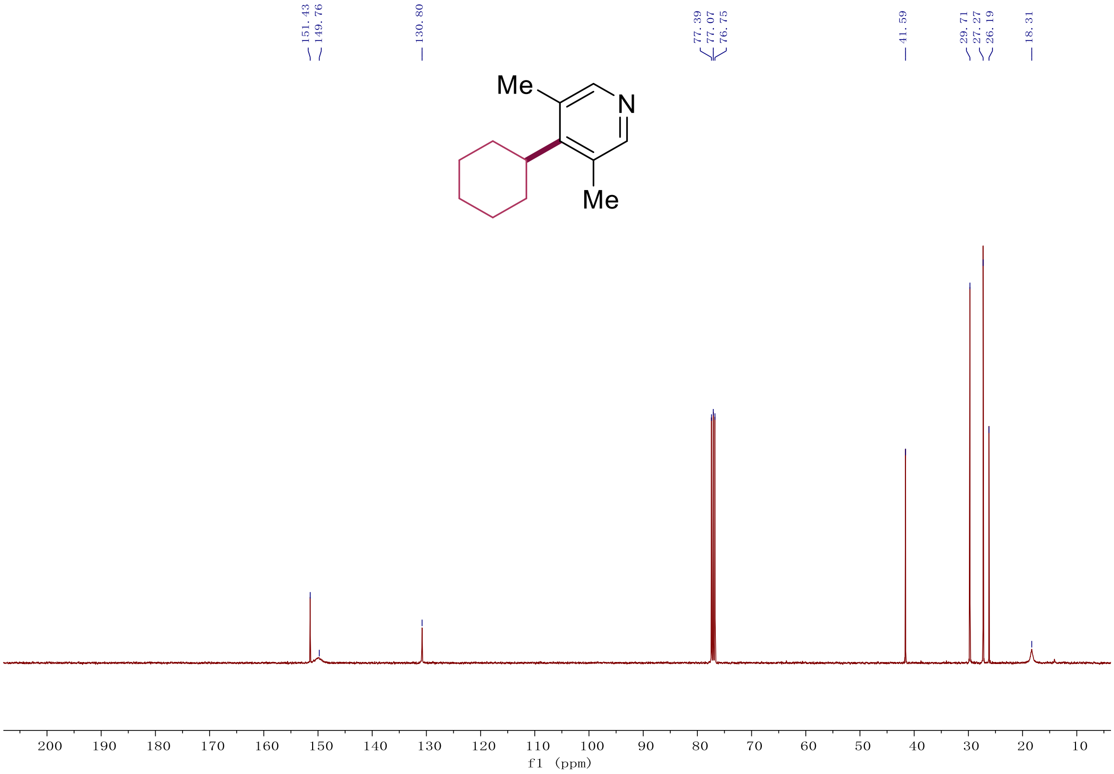
^{13}C NMR of **24** (101 MHz, CDCl$_3$)



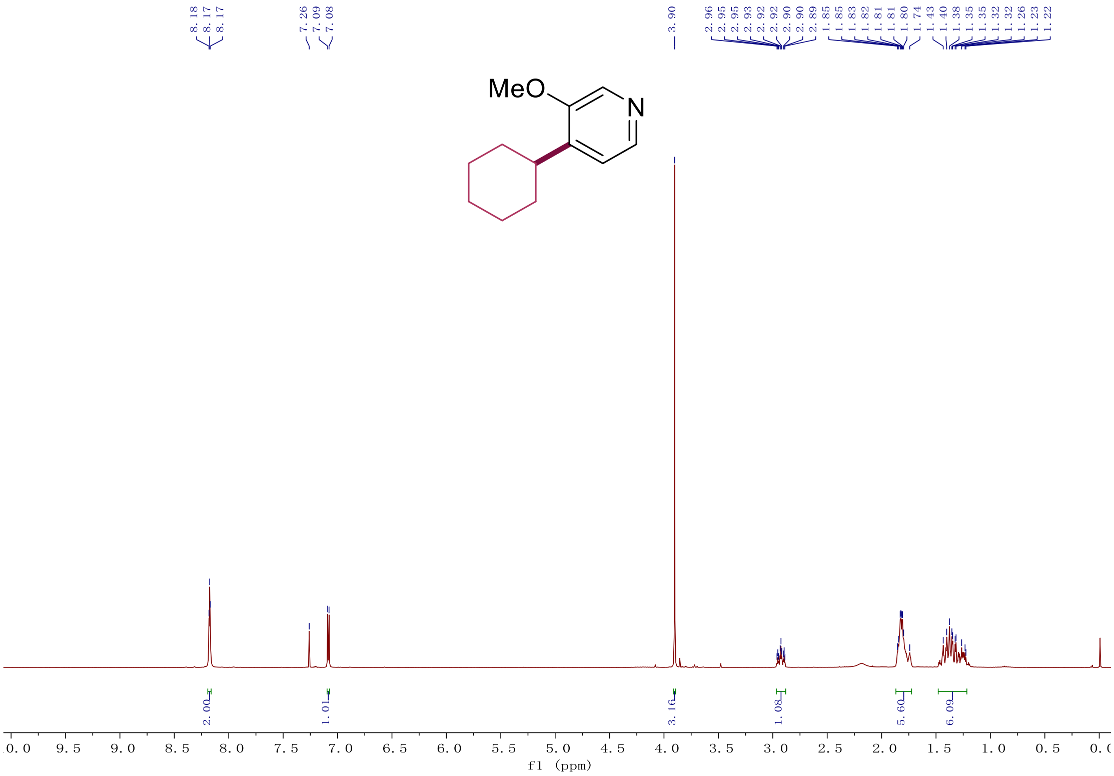
^{1}H NMR of 25 (400 MHz, CDCl$_3$)



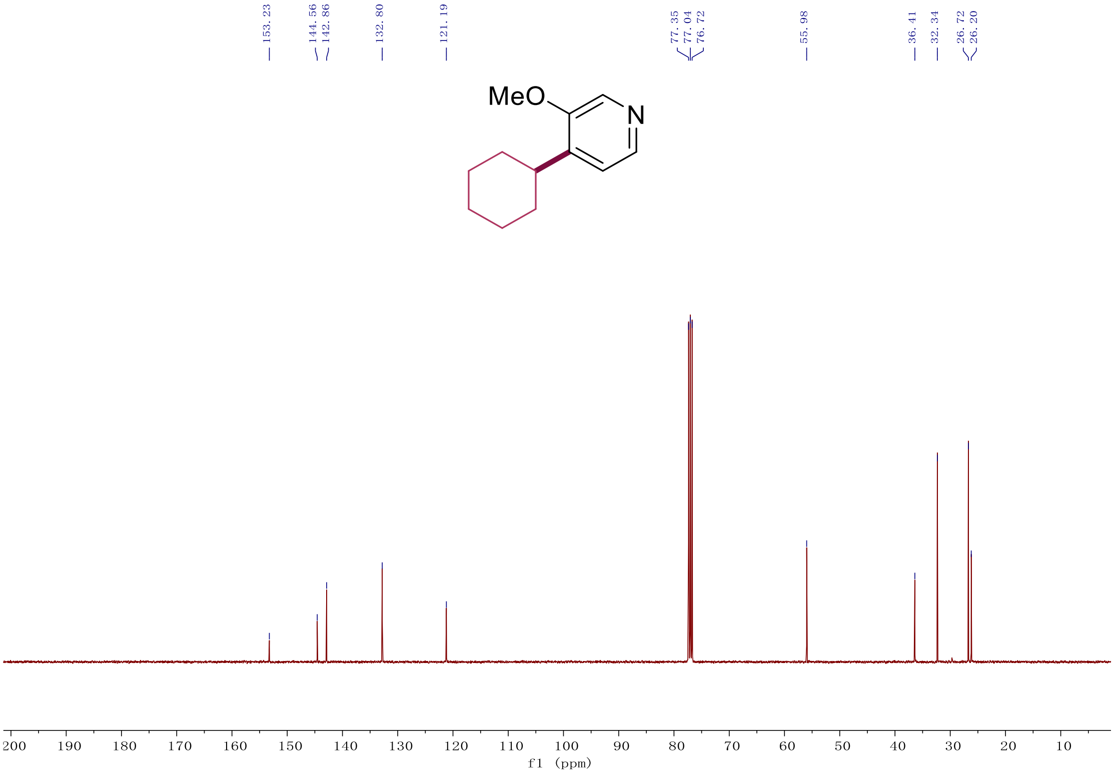
^{13}C NMR of 25 (101 MHz, CDCl$_3$)



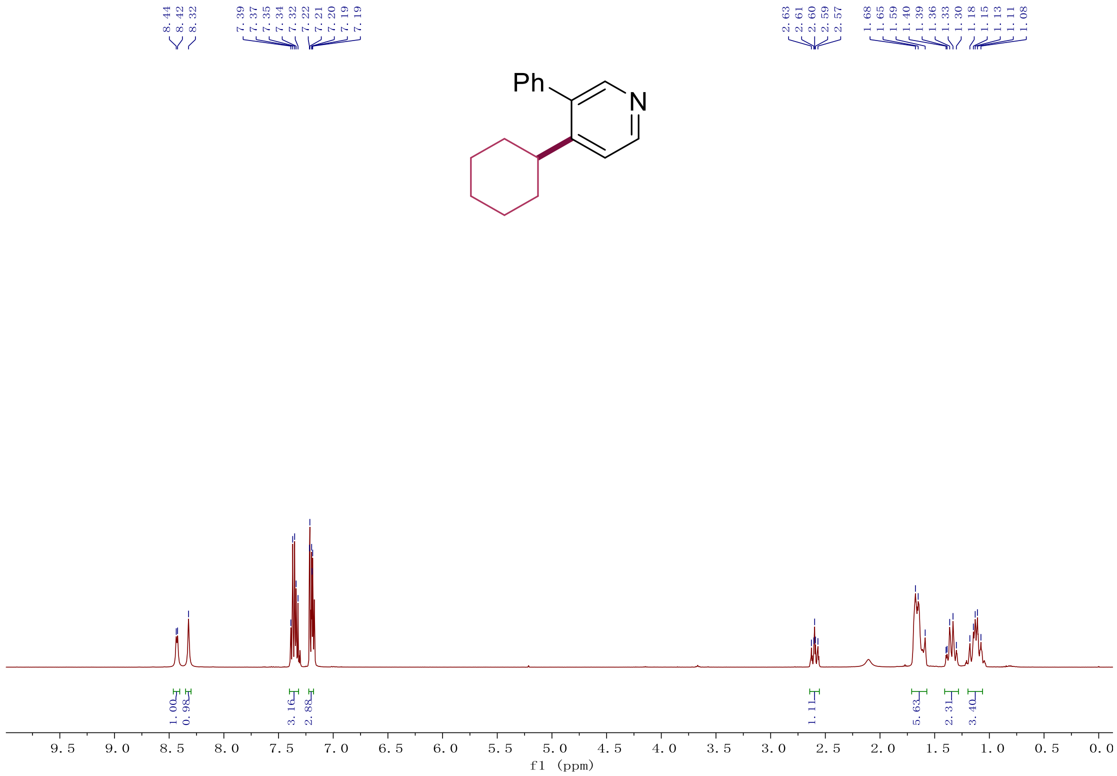
^{1}H NMR of 26 (400 MHz, CDCl$_3$)



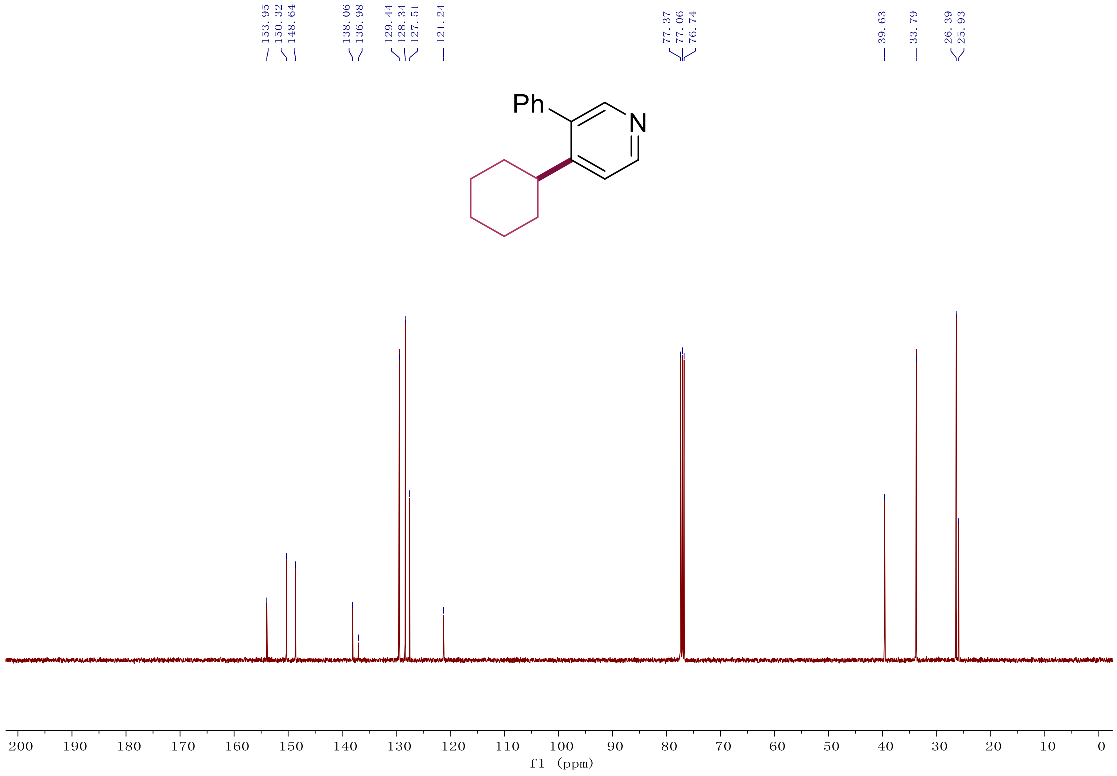
^{13}C NMR of 26 (101 MHz, CDCl$_3$)



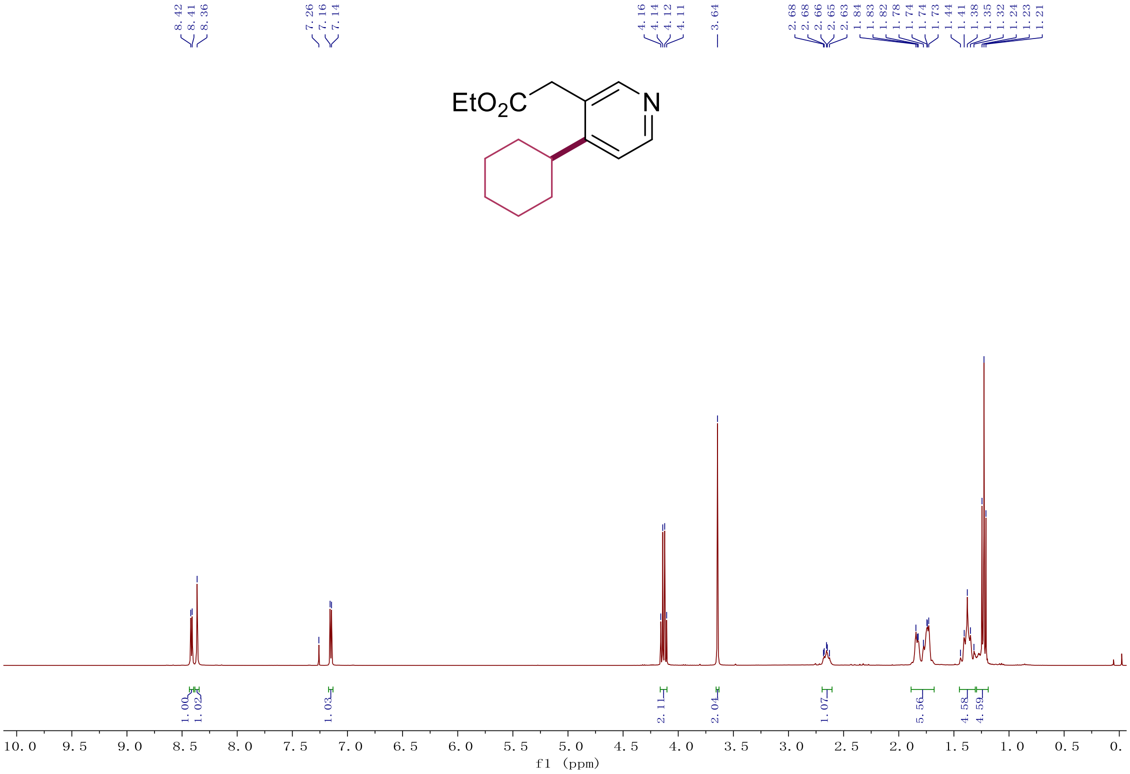
^{1}H NMR of 27 (400 MHz, $CDCl_3$)



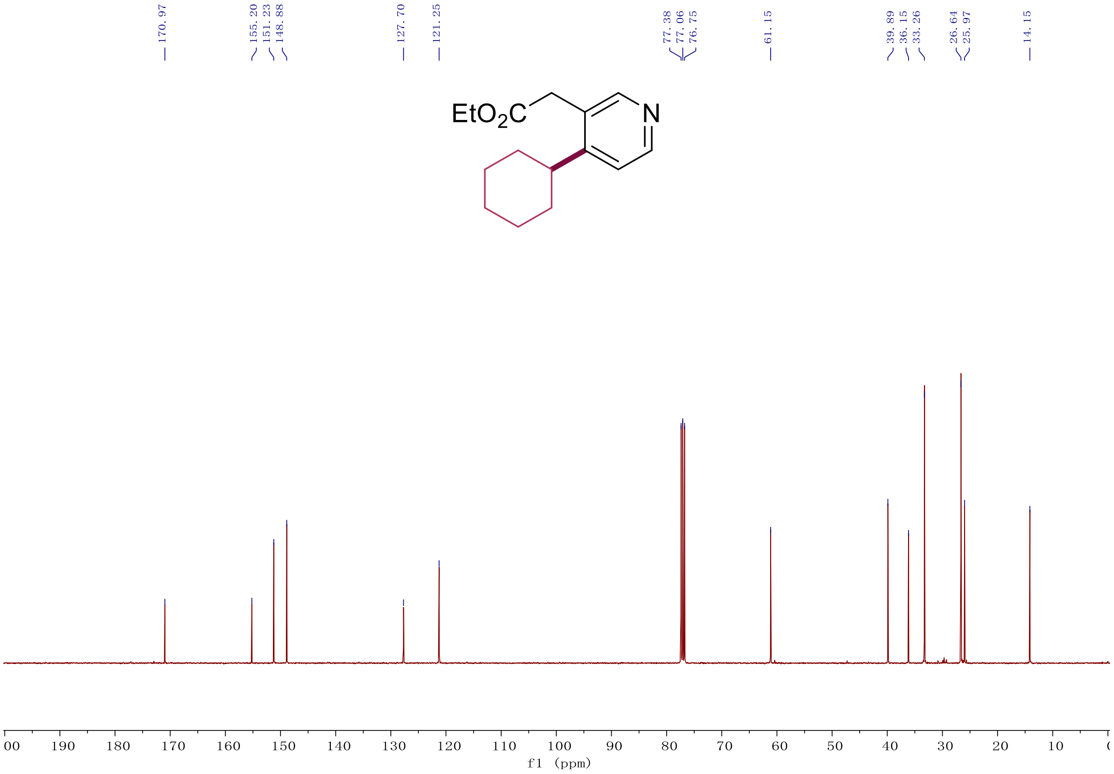
^{13}C NMR of 27 (101 MHz, $CDCl_3$)



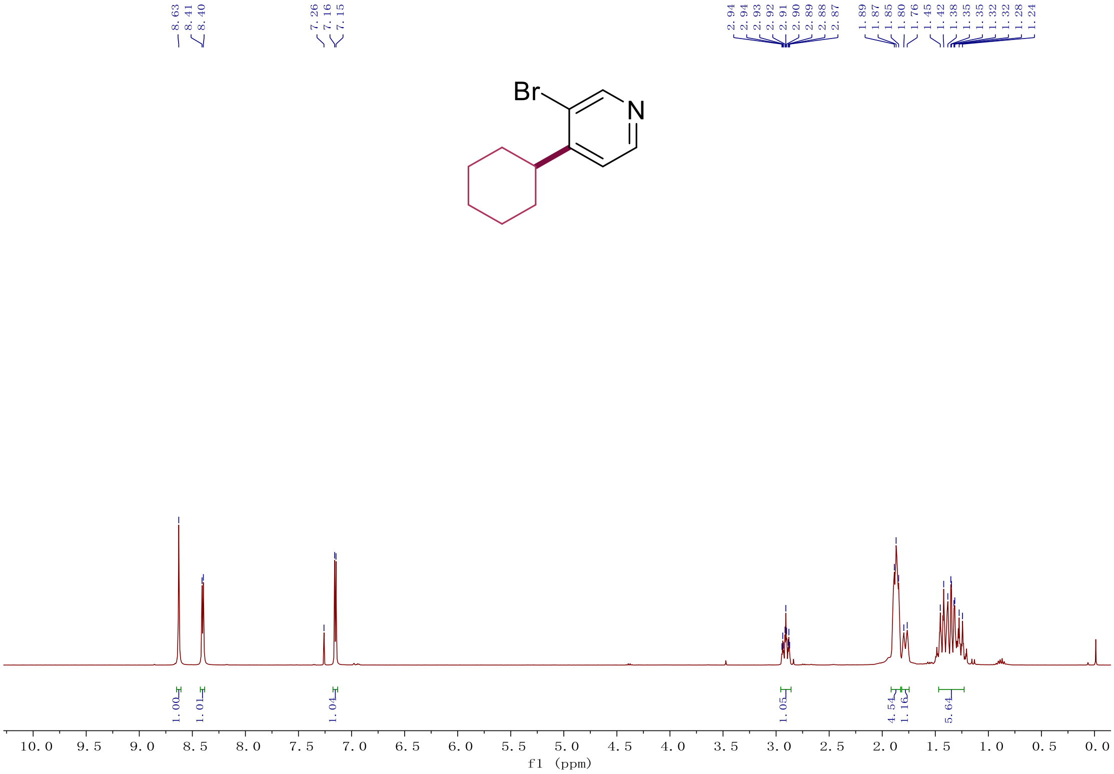
^{1}H NMR of 28 (400 MHz, CDCl$_3$)



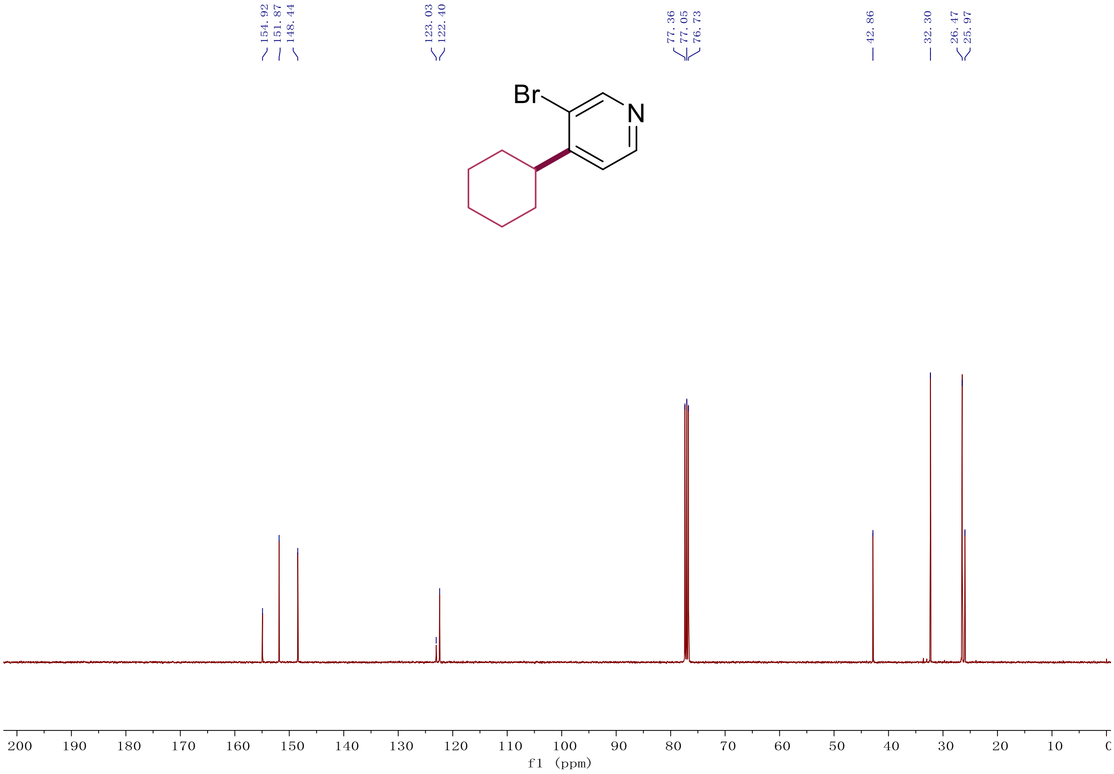
^{13}C NMR of 28 (101 MHz, CDCl$_3$)



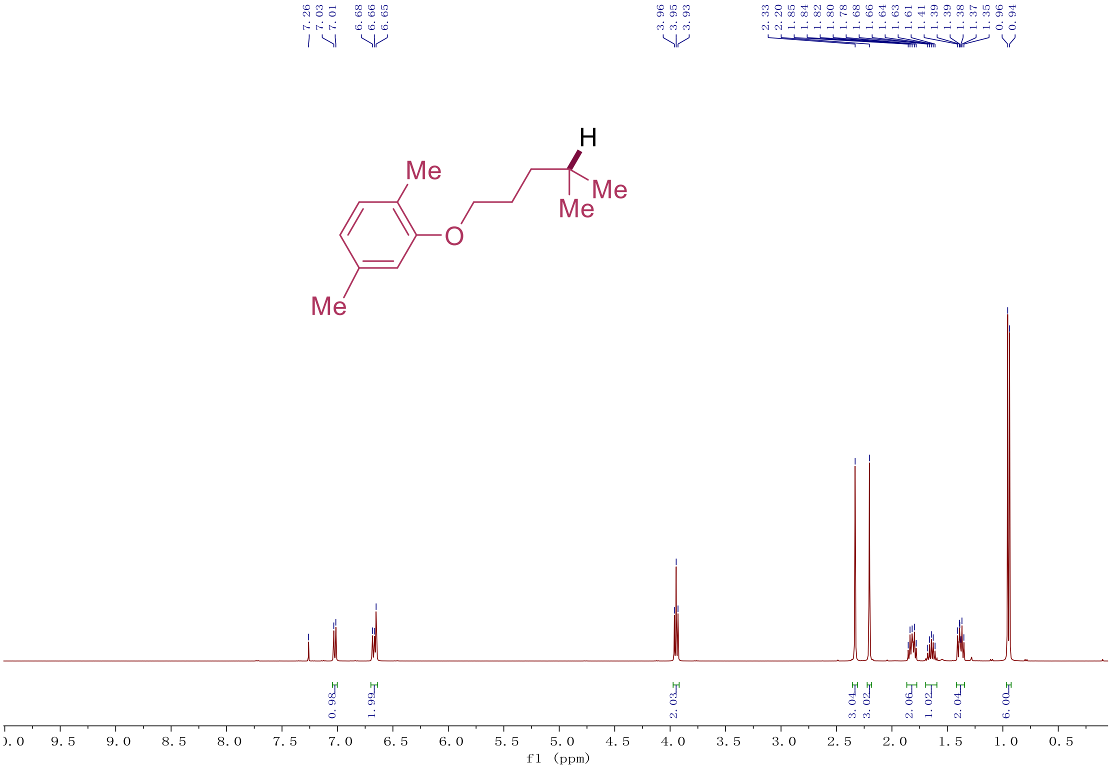
^{1}H NMR of 29 (400 MHz, $CDCl_3$)



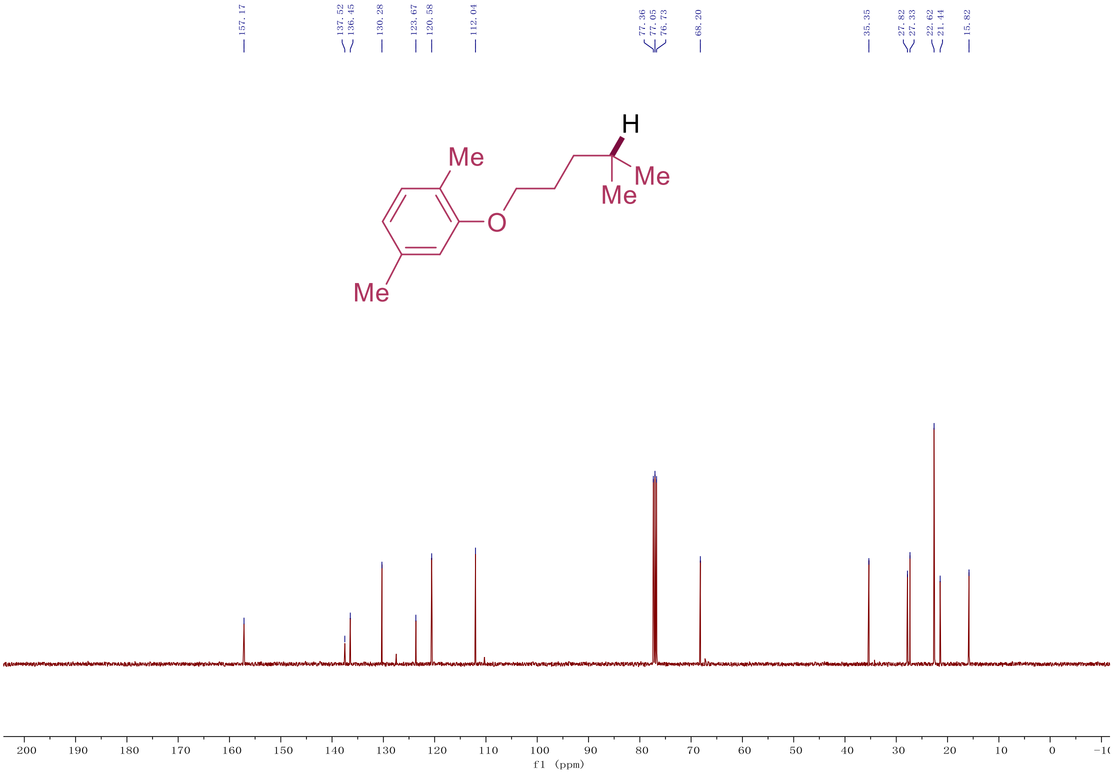
^{13}C NMR of 29 (101 MHz, $CDCl_3$)



^{1}H NMR of Gem-H (400 MHz, CDCl$_3$)



^{13}C NMR of Gem-H (101 MHz, CDCl$_3$)



10. Reference

[1] Tsymbal, A. V.; Bizzini, L. D.; MacMillan, D. W. J. J. o. t. A. C. S., Nickel catalysis via SH2 homolytic substitution: the double decarboxylative cross-coupling of aliphatic acids. *J. Am. Chem. Soc.* **2022,** *144*, 21278-21286.

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[3] Paul, C. E.; Gargiulo, S.; Opperman, D. J.; Lavandera, I.; Gotor-Fernández, V.; Gotor, V.; Taglieber, A.; Arends, I. W.; Hollmann, F. J. O. l., Mimicking Nature: Synthetic Nicotinamide Cofactors for C=C Bioreduction Using Enoate Reductases. *Org. Lett.* **2013,** *15*, 180-183.

[4] Song, Q.; Zhao, H.; Sun, Y.; Jiang, H.; Zhang, M. J. C. J. o. C., Direct C (sp^3)–H Sulfonylation of Xanthene Derivatives with Sodium Sulfinates by Oxidative Copper Catalysis. *Chin. J. Chem.* **2022,** *40.*

[5] H. Shinkai, M. Nishikawa, Y. Sato, K. Toi, I. Kumashiro, Y. Seto, M. Fukuma, K. Dan, S. Toyoshima, *J. Med. Chem.* **1989**, 32, 1436–1441.