

Supporting Information

Rhodium-Catalyzed C4-Selective C–H Alkenylation of 2-Pyridones by Traceless Directing Group Strategy

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Instrumentation and Chemicals

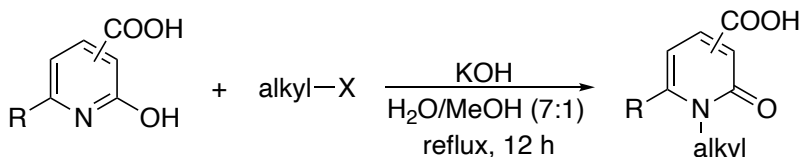
^1H , $^{13}\text{C}\{^1\text{H}\}$, and $^{19}\text{F}\{^1\text{H}\}$ spectra were recorded at 400, 100, and 162 MHz, respectively, for DMSO- d_6 and CDCl_3 solutions. HRMS data were obtained by APCI using TOF or CI using a magnetic sector. GC analysis was carried out using a silicon OV-17 column (i. d. 2.6 mm x 1.5 m) or CBP capillary column (i. d. 0.5 mm x 25 m). TLC analyses were performed on commercial glass plates bearing 0.25-mm layer of Merck Silica gel 60F₂₅₄. Gel permeation chromatography (GPC) was performed by LC-20AR (pump, SHIMADZU, 7.5 mL/min) and SPD-20A (UV detector, SHIMADZU, 254 nm) with two in-line YMC-GPC T2000 (20 x 600 mm, particle size: 10 μm) (preparative columns, YMC).

Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. $[\text{Cp}^*\text{RhCl}_2]_2$ was prepared according to the literature procedure.^{S1} Toluene was dried on a Glass Contour Solvent dispensing system (Nikko Hansen & Co., Ltd.) prior to use. All reactions were carried out under nitrogen atmosphere unless otherwise noted.

Experimental Procedures

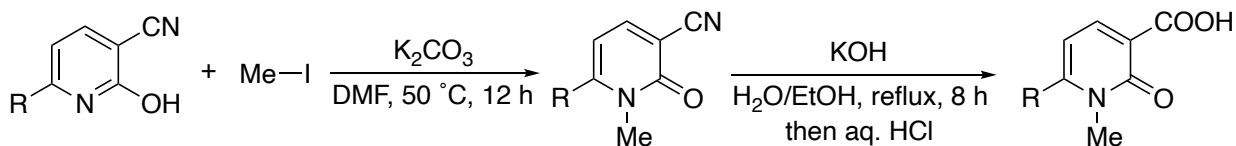
Preparation of Substrates

General procedure A for preparation of 2-oxo-1,2-dihydropyridine-3-carboxylic acids (**1a-e**) and regioisomers (**7a**, **9a**, and **13a**):



The starting carboxylic acids **1a-e**, **7a**, **9a**, and **13a** were prepared by following a modified literature report.^{S2} A mixture of 2-hydroxynicotinic acid or its derivative (5.0 mmol), potassium hydroxide (10.0 mmol), methanol (2.0 mL), and water (14.0 mL) was warmed to dissolve the acid salt. Alkyl halide (alkyl-X; 5-10 equiv.) was then added into the solution, and the mixture was refluxed for 12 h (oil bath). The reaction mixture was then cooled, concentrated under reduced pressure to half-volume, washed with ethyl acetate, and acidified to pH 1.0 with 3 M aq. HCl at 0 °C (ice bath). The formed solid was collected by filtration and dried to get the corresponding compound. An analytically pure compound was obtained by additional recrystallization.

General procedure B for preparation of C6-functionalized 1-methyl-2-oxo-1,2-dihydropyridine-3-carboxylic acids (**1f-h** and **1k**)



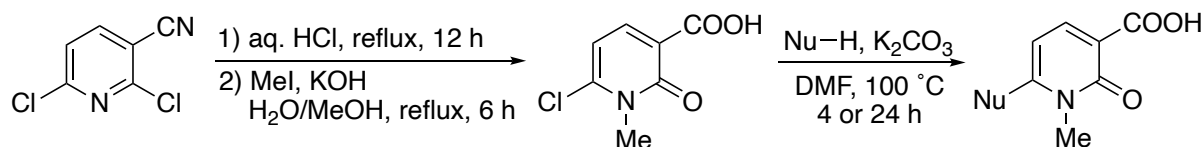
The above mentioned C6-substituted *N*-methyl-2-pyridone-3-carboxylic acid substrates were prepared from corresponding C6-substituted 3-cyano-2-pyridones (prepared according to literature report^{S3}) in two steps.

In the first step, a mixture of suitable C6-substituted 3-cyano-2-pyridone (4.0 mmol), K₂CO₃ (8.0 mmol), and MeI (8.0 mmol) in 15 mL DMF was heated at 50 °C in a 50 mL two-neck round bottom flask equipped with a reflux condenser under nitrogen for 12 h (oil bath). The reaction mixture was then diluted with water (50 mL) and extracted with CHCl₃ (3 x 30 mL). The combined organic layers were washed with brine, dried over Na₂SO₄, and concentrated under reduced pressure to get the

corresponding C6-substituted *N*-methyl-3-cyanopyridone which was used for next step without purification.

In the second step, a mixture of C6-substituted *N*-methyl-3-cyano-2-pyridone (1.0 mmol) and potassium hydroxide (8.0 mmol) in water/ethanol (10 mL, 4:1) was heated at reflux for 8 h (oil bath). The mixture was allowed to cool to room temperature and diluted with water. The aqueous layer was washed with CHCl₃ and then acidified to pH 1.0 with 3 M aq. HCl at 0 °C (ice bath). The formed solid was collected by filtration and dried to get the corresponding C6-substituted *N*-methyl-2-pyridone-3-carboxylic acid in a pure form.

General procedure C for preparation of 6-amino- and 6-alkoxy-1-methyl-2-oxo-1,2-dihydropyridine-3-carboxylic acid (**1i** and **1j**)



The substrate was prepared in two steps from 2,6-dichloronicotinic acid. In the first step 2,6-dichloronicotinic acid (15 mmol) was refluxed in 30 mL 6 M aq. HCl for 12 h (oil bath). After cooling, the product was precipitated out, which was collected by filtration, washed with cold water, and dried to get 1.04 g (yield 40%) of 6-chloro-2-hydroxynicotinic acid and directly used for the next step.

In the second step, 6-chloro-2-hydroxynicotinic acid was converted to 6-chloro-1-methyl-2-oxo-1,2-dihydropyridine-3-carboxylic acid following the general procedure A using 10 equivalent of iodomethane.

In the final step, a mixture of 6-chloro-1-methyl-2-oxo-1,2-dihydropyridine-3-carboxylic acid (1.0 mmol), corresponding nucleophile (amine or alcohol) (5.0 mmol), and K₂CO₃ (5.0 mmol) in DMF 10.0 mL was heated at 100 °C for 4 or 24 h under N₂ (oil bath). The reaction mixture was then cooled to room temperature, diluted with 50.0 mL water. The aqueous layer was washed with ethyl acetate and then acidified with 3 M aq. HCl at 0 °C. Finally, the acidified aqueous mixture was extracted with CHCl₃ (3 x 30 mL), and combined organic layers washed with brine, dried over Na₂SO₄, and concentrated under reduced pressure to get the compound.

Typical procedure for Rh-catalyzed C4-alkenylation of **1** with styrenes **2** in Toluene (Scheme 3)

0.20 mmol scale: 1-Methyl-2-oxo-1,2-dihydropyridine-3-carboxylic acid (**1a**; 30.6 mg, 0.2 mmol), [Cp*RhCl₂]₂ (3.2 mg 0.005 mmol), Cu(OAc)₂•H₂O (40.0 mg, 0.2 mmol), K₄P₂O₇ (132 mg, 0.4 mmol), and molecular sieves 4A (100 mg) were placed in a 20 mL screw vial. The reaction vessel was vacuumed and refilled with dry N₂. Toluene (1.0 mL) and styrene (**2a**) (69 µL, 0.6 mmol) were added via syringe, and the resulting mixture was stirred at 160 °C for 24 h (heat block). After cooling to room temperature, the reaction mixture was diluted with CHCl₃ (10.0 mL), filtered through a short celite pad, and washed three times (3 x 25.0 mL MeOH/CHCl₃ = 1/1). The combined organic layers were evaporated, and the residue was subjected to silica gel column chromatography using EtOAc/Hexane/Et₃N = 1/5/0.05 to EtOAc/CHCl₃/Et₃N = 1/1/0.05 (v/v/v) to get **3aa** (33 mg, 78% yield) as an off white solid.

1.0 mmol scale: 1-Methyl-2-oxo-1,2-dihydropyridine-3-carboxylic acid (**1a**; 150.3 mg, 1.0 mmol), [Cp*RhCl₂]₂ (16 mg 0.025 mmol), Cu(OAc)₂•H₂O (200.0 mg, 1.0 mmol), K₄P₂O₇ (660 mg, 2.0 mmol) and molecular sieves 4A (500 mg) were placed in a 20.0 mL screw vial. The reaction vessel was vacuumed and refilled with dry N₂. Toluene (5.0 mL) and styrene (**2a**, 0.35 mL, 3.0 mmol) were added via syringe, and the resulting mixture was stirred at 160 °C for 24 h (heat block). After cooling to room temperature, the reaction mixture was diluted with CHCl₃ (30.0 mL) and filtered through a short celite pad, washed three times (3 x 50.0 mL MeOH/CHCl₃ = 1/1). The combined organic layers were evaporated, the residue was subjected to silica gel column chromatography using EtOAc/Hexane/Et₃N = 1/5/0.05 to EtOAc/CHCl₃/Et₃N = 1/1/0.05 (v/v/v) to get **3aa** (145.6 mg, 69% yield) as an off white solid.

Procedure for conversion of **3da** to **4** via hydrogenation in AcOH (Scheme 4)

(*E*)-1-Benzyl-4-styrylpyridin-2(1*H*)-one (**3da**; 57.4 mg, 0.2 mmol) was dissolved in AcOH (6.0 mL) in a 25.0 mL round-bottom flask. Pd(OH)₂ (10 mol%) was added. The round bottom flask was evacuated and filled with H₂ gas (1atm, balloon). After being stirred for 10 h at room temperature, the reaction mixture was filtered through a celite pad and washed with 3 x 20 mL of methanol. The combined organic layers were evaporated, and the residue was purified by silica gel column chromatography using EtOAc/Hexane/Et₃N = 1/1/0.05 (v/v/v) to give **4** (46.9 mg, 81% yield) as a colorless liquid.

Procedure for conversion of **3da** to **5** via hydrogenation in EtOH (Scheme 4)

(*E*)-1-Benzyl-4-styrylpyridin-2(1*H*)-one (**3da**; 57.4 mg, 0.2 mmol) was dissolved in EtOH (6.0 mL) in a 25.0 mL round bottom flask. Pd(OH)₂ (10 mol %) was added. The round bottom flask was evacuated, and filled with H₂ gas (1atm, balloon). After being stirred for 18 h at room temperature, the reaction mixture was filtered through a celite pad and washed with 3 x 20 mL of methanol. The combined organic layers were evaporated, and the residue was purified by silica gel column chromatography using EtOAc/Hexane/Et₃N = 1/1/0.05 (v/v/v) to give **5** (49.9 mg, 85% yield) as a colorless liquid.

Procedure for conversion of **3da** to **6** via Diels-Alder reaction (Scheme 4)

(*E*)-1-Benzyl-4-styrylpyridin-2(1*H*)-one (**3da**, 57.4 mg, 0.2 mmol) was dissolved in acetone (5.0 mL) in a 25.0 mL round bottom flask under N₂. The mixture was cooled to 0 °C, and 4-phenyl-3*H*-1,2,4-triazole-3,5(4*H*)-dione (52.5 mg, 0.3 mmol) was added. The reaction mixture was allowed to come to room temperature and stirred for 24 h. The solvent was then evaporated, and the residue was then purified by GPC (EtOAc) to form a mixture of the Diels-Alder adduct and **6** as yellow gummy liquid.

The above mixture was dissolved in toluene (3.0 mL) in a screw cap vial, and PPTS (10.0 mg, 0.04 mmol) was added. The vial was capped under air, and the mixture was heated at 80 °C for 16 h. The reaction mixture was then cooled to room temperature, and solvent was evaporated. The residue was purified by GPC (EtOAc) to get compound **6** (56.4 mg, 61% yield) as yellow gummy liquid.

Procedure for Rh-catalyzed C3-alkenylation of **7a** with styrene (**2a**) in Toluene (Scheme 6)

1-Methyl-2-oxo-1,2-dihydropyridine-4-carboxylic acid (**7a**; 30.6 mg, 0.2 mmol), [Cp*RhCl₂]₂ (3.2 mg 0.005 mmol), Cu(OAc)₂•H₂O (40.0 mg, 0.2 mmol), K₂HPO₄ (70 mg, 0.4 mmol), and molecular sieves 4A (100 mg) were placed in a 20 mL screw vial. The reaction vessel was vacuumed and refilled with dry N₂. Toluene (1.0 mL) and styrene (**2a**) (69 µL, 0.6 mmol) were added via syringe, and the resulting mixture was stirred at 160 °C for 24 h (heat block). After cooling to room temperature, the reaction mixture was diluted with CHCl₃ (10.0 mL), filtered through a short celite pad, and washed three times (3 x 25.0 mL MeOH/CHCl₃ = 1/1). The combined organic layers were evaporated, and the residue was subjected to silica gel column chromatography using EtOAc/Hexane/Et₃N = 1/5/0.05 to EtOAc/CHCl₃/Et₃N = 1/1/0.05 (v/v/v) to get **8aa** (22.4 mg, 53% yield) as a light yellow solid.

Procedure for Rh-catalyzed C4- and C6-dialkenylation of **9a** with cyclohexyl acrylate **2o** in Toluene (Scheme 6)

1-Methyl-6-oxo-1,6-dihydropyridine-3-carboxylic acid (**9a**; 30.6 mg, 0.2 mmol), [Cp*RhCl₂]₂ (3.2 mg 0.005 mmol), Cu(OAc)₂•H₂O (40.0 mg, 0.2 mmol), K₂HPO₄ (70 mg, 0.4 mmol), and molecular sieves 4A (100 mg) were placed in a 20 mL screw vial. The reaction vessel was vacuumed and refilled with dry N₂. Toluene (1.0 mL) and cyclohexyl acrylate (**2o**; 94 µL, 0.6 mmol) were added via syringe, and the resulting mixture was stirred at 160 °C for 24 h (heat block). After cooling to room temperature, the reaction mixture was diluted with CHCl₃ (10.0 mL), filtered through a short celite pad, and washed three times (3 x 25.0 mL MeOH/CHCl₃ = 1/1). The combined organic layers were evaporated, and the residue was subjected to silica gel column chromatography using EtOAc/Hexane/Et₃N = 1/5/0.05 to EtOAc/CHCl₃/Et₃N = 1/1/0.05 (v/v/v) followed by GPC (EtOAc) to get **8** (33.1 mg, 40% yield) as a yellow gummy liquid. The two lactones **11ao** and **12ao** were also isolated in 10% and 5%, respectively, as colorless gummy liquids.

Procedure for Rh-catalyzed C5-alkenylation of **13a** with styrene **2a** in Toluene (Scheme 6)

1-Methyl-6-oxo-1,6-dihydropyridine-2-carboxylic acid (**13a**; 30.6 mg, 0.2 mmol), [Cp*RhCl₂]₂ (3.2 mg 0.005 mmol), Cu(OAc)₂•H₂O (40.0 mg, 0.2 mmol), K₂HPO₄ (70 mg, 0.4 mmol), and molecular sieves 4A (100 mg) were placed in a 20.0 mL screw vial. The reaction vessel was vacuumed and refilled with dry N₂. Toluene (1.0 mL) and styrene (**2a**; 69 µL, 0.6 mmol) were added via syringe, and the resulting mixture was stirred at 160 °C for 24 h (heat block). After cooling to room temperature, the reaction mixture was diluted with CHCl₃ (10.0 mL), filtered through a short celite pad, and washed three times (3 x 25.0 mL MeOH/CHCl₃ = 1/1). The combined organic layers were evaporated, the residue was subjected to silica gel column chromatography using EtOAc/Hexane/Et₃N = 1/5/0.05 to EtOAc/CHCl₃/Et₃N = 1/1/0.05 (v/v/v) to get **14aa** (26 mg, 60% yield) as a light yellow solid.

Procedure for synthesis of multiply substituted 2-pyridone **17** via site-selective C–H activation cascade (Scheme 7)

Step 1) C6-selective C–H arylation

Methyl 2-oxo-2H-[1,2'-bipyridine]-3-carboxylate (**15**, 46 mg, 0.2 mmol),^{S4} PhBF₃K (110 mg, 0.6 mmol), [Cp*RhCl₂]₂ (6.2 mg, 0.01 mmol), AgSbF₆ (13.7 mg, 0.04 mmol), and Ag₂O (69.5 mg, 0.3 mmol) were dissolved in DCE (2 mL) in a pressure tube. The mixture was stirred at 100 °C under nitrogen atmosphere for 24 h (heat block). After cooling to room temperature, the reaction mixture

was diluted with CHCl_3 (10mL), filtered through a short celite pad, and washed three times $\text{MeOH}/\text{CHCl}_3$ (1/1, 3 x 25 mL). The combined organic layers were evaporated, and the residue was subjected to silica gel column chromatography using $\text{EtOAc}/\text{Hexane}/\text{Et}_3\text{N} = 1/5/0.05$ to $\text{EtOAc}/\text{CHCl}_3/\text{Et}_3\text{N} = 1/1/0.05$ (v/v/v) to get **16** (47.8 mg, 78% yield) as colorless liquid.

Step 2) N-substituent switch and hydrolysis

Methyl 2-oxo-6-phenyl-2*H*-[1,2'-bipyridine]-3-carboxylate (**16**, 122.5 mg, 0.4 mmol) was dissolved in 5.0 mL of CH_3CN in a 25 mL round-bottom flask, filled with nitrogen. MeOTf (66 μL , 0.6 mmol) was then added at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 20 h. Volatile materials were evaporated under high vacuum. The residue was dissolved in 5.0 mL of methanol and cooled to 0 °C, and NaBH_4 (60.6 mg, 1.6 mmol) was added. The flask was filled with nitrogen again, and the reaction mixture was allowed to warm to room temperature and stirred for 6 h. The reaction mixture was quenched with water and extracted with ethyl acetate (3 x 25 mL). The combined organic layers were dried over Na_2SO_4 , filtered, and concentrated in vacuo. The residue was purified by silica gel column chromatography using $\text{EtOAc}/\text{Hexane}/\text{Et}_3\text{N} = 1/1/0.05$ to $\text{EtOAc}/\text{CHCl}_3/\text{Et}_3\text{N} = 1/1/0.05$ (v/v/v) to get the corresponding N-H pyridone as white solid.

A solution of the methyl ester obtained above (229.2 mg, 1.0 mmol) in aq. NaOH (2 M, 3.0 mL) and MeOH (3.0 mL) was heated at 50 °C for 5 h. Acidification with aq. HCl (3 M) at 0 °C (ice bath) promoted precipitation. The resulting solid was collected by filtration, washed with cold water, and dried. The formed free carboxylic acid was directly used for the next final step.

In the final step, **1h** (yield 54%, over four steps) was prepared according to general procedure **A** using methyl iodide (10.0 equiv.) and purified by recrystallization from chloroform.

Step 3) C4-selective C–H alkenylation

1-Methyl-2-oxo-6-phenyl-1,2-dihydropyridine-3-carboxylic acid (**1h**; 45.8 mg, 0.2 mmol), $[\text{Cp}^*\text{RhCl}_2]_2$ (3.2 mg 0.005 mmol), $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$ (40.0 mg, 0.2 mmol), $\text{K}_4\text{P}_2\text{O}_7$ (132 mg, 0.4 mmol), and molecular sieves 4Å (100 mg) were placed in a 20 mL screw vial. The reaction vessel was vacuumed and refilled with dry N_2 . Toluene (1.0 mL) and styrene (**2a**) (69 μL , 0.6 mmol) were added via syringe, and the resulting mixture was stirred at 160 °C for 24 h (heat block). After cooling to room temperature, the reaction mixture was diluted with CHCl_3 (10mL), filtered through a short silica gel, and washed three times (3 x 25 mL $\text{MeOH}/\text{CHCl}_3 = 1/1$). The combined organic layers were evaporated, and the residue was subjected to silica gel column chromatography using

EtOAc/Hexane/Et₃N = 1/5/0.05 to EtOAc/CHCl₃/Et₃N = 1/1/0.05 (v/v/v) to form **3ha** in 61% yield (35.1 mg, 0.12 mmol) as off white solid.

Step 4) C3-selective C–H arylation

A solution of **3ha** (57.4 mg, 0.2 mmol), *p*-tolylhydrazine hydrochloride (38.1 mg, 0.24 mmol), and potassium carbonate (82.8 mg, 0.6 mmol) in dimethyl sulfoxide (3.0 mL) was stirred under ambient conditions for 16 h. The reaction was then diluted with water (50 mL), and the aqueous layer was extracted with ethyl acetate (3 x 25 mL). The combined organic layer was dried over Na₂SO₄, filtered, and concentrated in vacuo. The residue was purified by silica gel column chromatography using EtOAc/Hexane/Et₃N = 1/1/0.05 to EtOAc/Et₃N = 1/0.05 (v/v/v) followed by GPC (EtOAc) to get **17** as yellow gummy liquid (39.3 mg, yield 52%).

X-Ray Analysis

The single X-ray quality crystals of **3aa** were grown from THF by slow evaporation at room temperature. The structure was refined by full-matrix least-squares method using SHELXL-2017/1.

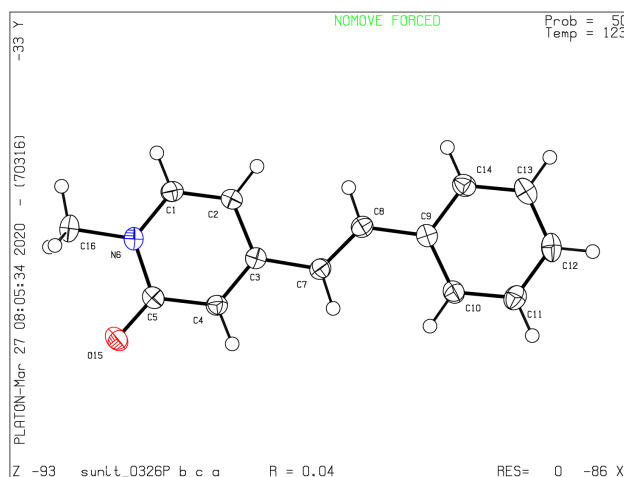


Figure S1. ORTEP drawing of **3aa** (CCDC 2032339, 50% thermal probability).

Table S1. Crystal Data for **3aa**

Crystal system	orthorhombic
Space group IT number	61
Space group name H-M alt	P b c a
Space group name Hall	-P 2ac 2ab
Cell length a	9.8273(3)
Cell length b	8.0689(3)
Cell length c	27.3707(11)
Cell angle alpha	90
Cell angle beta	90
Cell angle gamma	90
Cell volume	2170.37(14)
Cell formula units Z	8
Refine ls R factor all	0.0513
Refine ls R factor gt	0.0403
Refine ls wR factor gt	0.1016
Refine ls wR factor ref	0.1093
Refine ls goodness of fit ref	1.046

Detailed Optimization Studies

Table S2. Optimization Studies for Decarboxylative C4-Selective C–H Alkenylation of **1a** with **2a**: Catalyst Screening^[a]

Reaction scheme showing the decarboxylative C4-selective C–H alkenylation of **1a** with **2a** to form **3aa**. Conditions: catalyst (5 mol % metal), Cu(OAc)₂·H₂O, K₂HPO₄, toluene, 160 °C, 16–24 h, N₂.

entry	catalyst	yield (%) ^[b]	entry	catalyst	yield (%) ^[b]
1	[Cp*RhCl ₂] ₂	43	4	[Ru(<i>p</i> -cymene)Cl ₂] ₂	0
2	[Cp*IrCl ₂] ₂	0	5	Pd(OAc) ₂	0
3	Cp*Co(CO)I ₂	0	6	Cp*Rh(SbF ₆) ₂ (MeCN) ₃	15

[a] Reaction conditions: **1a** (0.20 mmol), **2a** (0.40 mmol), catalyst (5 mol % on metal), Cu(OAc)₂·H₂O (0.20 mmol), K₂HPO₄ (0.40 mmol), toluene (1.0 mL), 160 °C, 16–24 h, N₂. [b] Estimated by ¹H NMR using CH₂Br₂ as the internal standard.

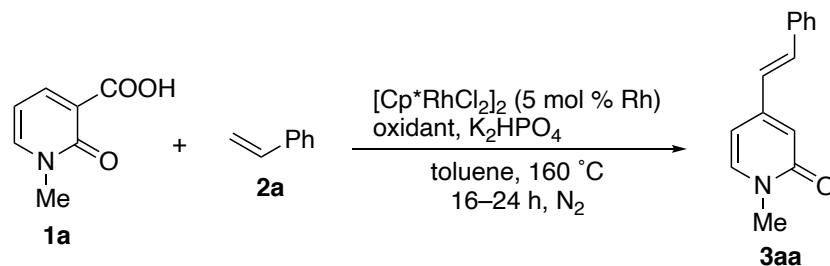
Table S3. Optimization Studies for Decarboxylative C4-Selective C–H Alkenylation of **1a** with **2a**: Solvent Screening^[a]

Reaction scheme showing the decarboxylative C4-selective C–H alkenylation of **1a** with **2a** to form **3aa**. Conditions: [Cp*RhCl₂]₂ (5 mol % Rh), Cu(OAc)₂·H₂O, K₂HPO₄, solvent, 160 °C, 16–24 h, N₂.

entry	solvent	yield (%) ^[b]	entry	catalyst	yield (%) ^[b]
1	toluene	43	5	<i>t</i> -AmOH	34
2	1,4-dioxane	23	6	MeCN	40
3	DMF	10	7	DCE	5
4	PhCl	21	8	xylene	0

[a] Reaction conditions: **1a** (0.20 mmol), **2a** (0.40 mmol), [Cp*RhCl₂]₂ (0.0050 mmol), Cu(OAc)₂·H₂O (0.20 mmol), K₂HPO₄ (0.40 mmol), solvent (1.0 mL), 160 °C, 16–24 h, N₂. [b] Estimated by ¹H NMR using CH₂Br₂ as the internal standard.

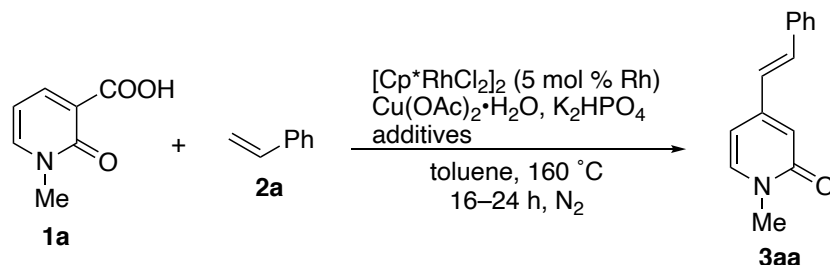
Table S4. Optimization Studies for Decarboxylative C4-Selective C–H Alkenylation of **1a** with **2a**: Oxidant Screening^[a]



entry	oxidant	yield (%) ^[b]	entry	catalyst	yield (%) ^[b]
1	<i>Cu(OAc)₂·H₂O</i>	43	4	Ag ₂ CO ₃	17
2	Cu ₂ O	40	5 ^[c]	Ag ₂ O	20
3	AgOAc	11			

[a] Reaction conditions: **1a** (0.20 mmol), **2a** (0.40 mmol), [Cp*RhCl₂]₂ (0.0050 mmol), oxidant (0.20 mmol), K₂HPO₄ (0.40 mmol), toluene (1.0 mL), 160 °C, 16–24 h, N₂. [b] Estimated by ¹H NMR using CH₂Br₂ as the internal standard. [c] In 1,4-dioxane.

Table S5. Optimization Studies for Decarboxylative C4-Selective C–H Alkenylation of **1a** with **2a**: Additive Screening^[a]



entry	additives	yield (%) ^[b]	entry	additives	yield (%) ^[b]
1	none	43	4 ^[d]	MS 4A (30 mg)	60
2	AgSbF ₆ (10 mol %)	26	5 ^[d,e]	MS 4A (30 mg)	34
3 ^[c]	AgSbF ₆ (10 mol %) NaOAc (100 mol %)	21	6^[d]	MS 4A (100 mg)	66

[a] Reaction conditions: **1a** (0.20 mmol), **2a** (0.40 mmol), [Cp*RhCl₂]₂ (0.0050 mmol), Cu(OAc)₂·H₂O (0.20 mmol), K₂HPO₄ (0.40 mmol), additives, toluene (1.0 mL), 160 °C, 16 h, N₂. [b] Estimated by ¹H NMR using CH₂Br₂ as the internal standard. [c] With 0.040 mmol of Cu(OAc)₂·H₂O. [d] With 0.60 mmol of **2a**. [e] With potassium salt of **1a** instead of free carboxylic acid **1a**.

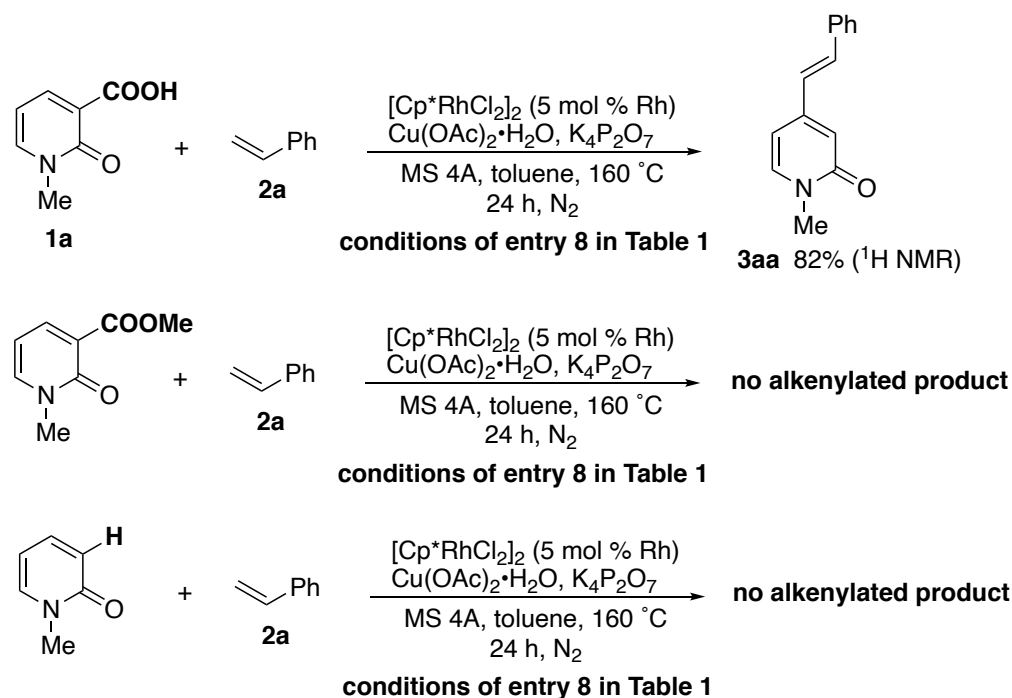
Table S6. Optimization Studies for Decarboxylative C4-Selective C–H Alkenylation of **1a** with **2a**: Base Screening^[a]

Reaction scheme showing the decarboxylative C4-selective C–H alkenylation of **1a** with **2a** to form **3aa**. Conditions: $[\text{Cp}^*\text{RhCl}_2]_2$ (5 mol % Rh), $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$, base, MS 4A, toluene, 160 °C, 16–24 h, N_2 .

entry	base	yield (%) ^[b]	entry	base	yield (%) ^[b]
1	none	5	6	NaHCO_3	23
2	K_2HPO_4	66	7	KHCO_3	25
3	Na_2CO_3	26	8	$\text{K}_4\text{P}_2\text{O}_7$	82 (78)
4	K_2CO_3	11	9 ^[c]	$\text{K}_4\text{P}_2\text{O}_7$	45
5	Cs_2CO_3	0	10 ^[d]	$\text{K}_4\text{P}_2\text{O}_7$	0

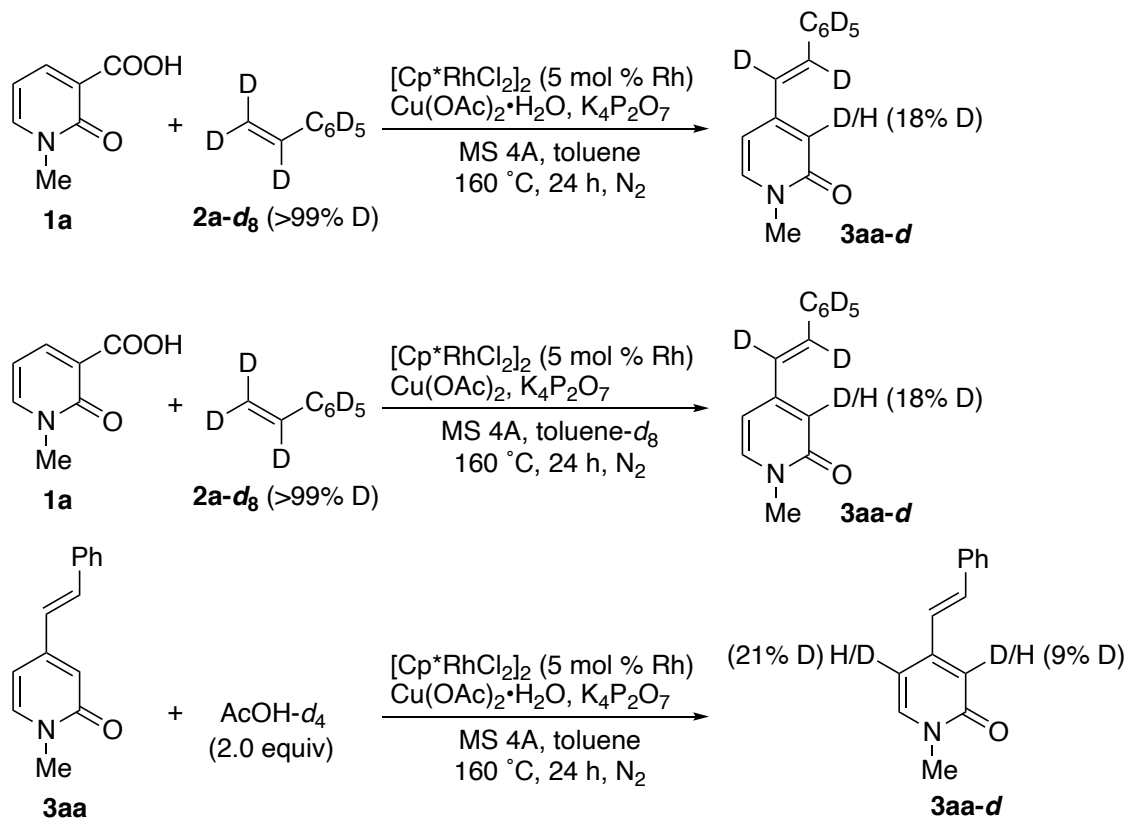
[a] Reaction conditions: **1a** (0.20 mmol), **2a** (0.60 mmol), $[\text{Cp}^*\text{RhCl}_2]_2$ (0.0050 mmol), $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$ (0.20 mmol), base (0.40 mmol), MS 4A (100 mg), toluene (1.0 mL), 160 °C, 16 h, N_2 . [b] Estimated by ^1H NMR using CH_2Br_2 as the internal standard. Isolated yield in parentheses. [c] Without MS 4A. [d] In mesitylene instead of toluene.

Scheme S1. Directing Effects of COOH under Optimal Conditions.



Deuterium Incorporation Tests

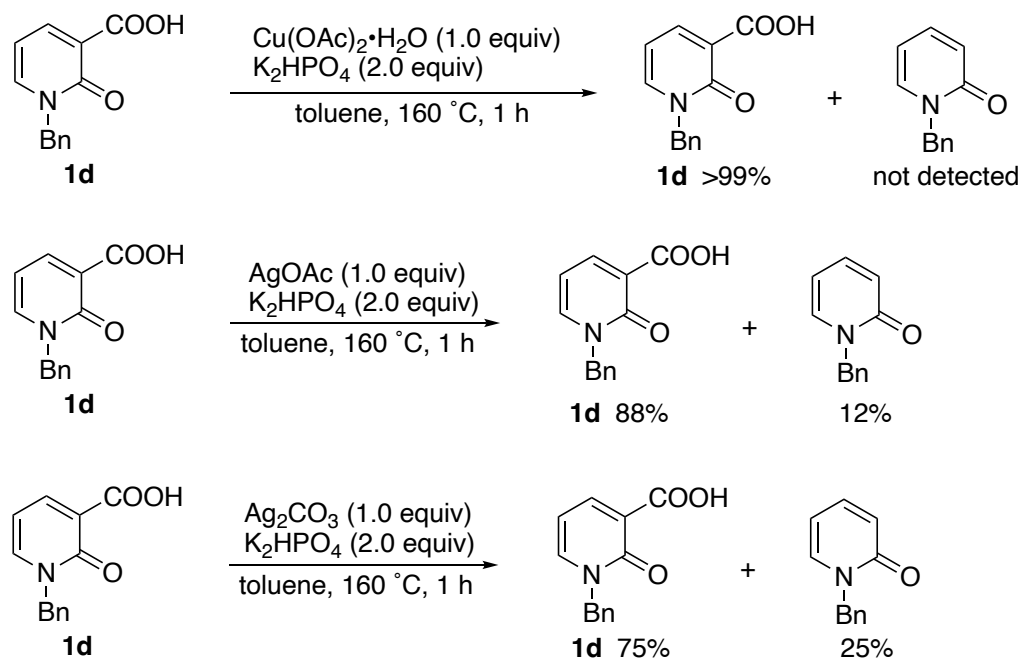
Scheme S2. Deuterium Incorporation Tests.



Protodecarboxylation Tests

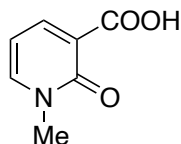
To compare the activity of $\text{Cu}(\text{OAc})_2$, AgOAc , and Ag_2CO_3 in the nonproductive protodecarboxylation of **1d**, we performed the following experiments (Scheme S3).

Scheme S3. Protodecarboxylation Tests.



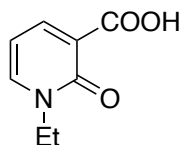
Characterization Data for Products

Copy of ^1H , $^{13}\text{C}\{^1\text{H}\}$, and $^{19}\text{F}\{^1\text{H}\}$ NMR spectra for all compounds are attached in the last part.



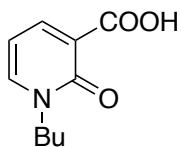
1-Methyl-2-oxo-1,2-dihydropyridine-3-carboxylic acid (1a)

The compound was prepared according to general procedure **A** using 2-hydroxynicotinic acid and methyl iodide (10.0 equiv.) and purified by recrystallization from chloroform. white solid, 498 mg, yield 65%. m.p. 181-182 °C (lit.^{S2} 176-177 °C). ^1H NMR (DMSO- d_6 , 400 MHz,) δ 14.68 (s, 1H), 8.36 (dd, J = 2.1, 7.3 Hz, 1H), 8.25 (dd, J = 2.0, 6.6 Hz, 1H) 6.70 (dd, J = 6.6, 7.3 Hz, 1H), 3.64 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (DMSO- d_6 , 100 MHz) δ 165.4, 164.5, 146.3, 145.6, 116.5, 108.7, 38.4.



1-Ethyl-2-oxo-1,2-dihydropyridine-3-carboxylic acid (1b)

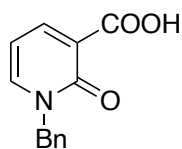
The compound was prepared according to general procedure **A** using 2-hydroxynicotinic acid and ethyl iodide (10.0 equiv.) and purified by recrystallization from chloroform. white solid, 492 mg, yield 59%. m.p. 177-179 °C. ^1H NMR (DMSO- d_6 , 400 MHz,) δ 14.72 (s, 1H), 8.38 (dd, J = 2.1, 7.3 Hz, 1H), 8.30 (dd, J = 2.1, 6.6 Hz, 1H), 6.75 (dd, J = 6.6, 7.3 Hz, 1H), 4.13, (q, J = 7.2 Hz, 2H), 1.31 (t, J = 7.2 Hz, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (DMSO- d_6 , 100 MHz) δ 165.3, 164.0, 145.6, 145.2, 116.8, 109.1, 45.8, 14.7. HRMS (APCI) m/z ($[\text{M}+\text{H}]^+$) calcd for $\text{C}_8\text{H}_{10}\text{NO}_3$ 168.0655, found 168.0656.



1-Butyl-2-oxo-1,2-dihydropyridine-3-carboxylic acid (1c)

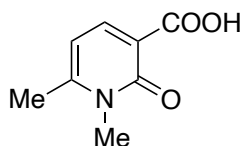
The compound was prepared according to general procedure **A** using 2-hydroxynicotinic acid and butyl iodide (5.0 equiv.) and purified by recrystallization chloroform. white solid, 555 mg, yield 57%. m.p. 103-105 °C. ^1H NMR (CDCl_3 , 400 MHz) δ 14.41(s, 1H), 8.51 (dd, J = 2.1, 7.2 Hz, 1H), 7.62 (dd, J = 2.1, 6.6 Hz, 1H), 6.55 (t, J = 6.8 Hz, 1H), 4.09, (t, J = 7.4 Hz, 2H), 1.82-1.78 (m, 2H), 1.43-1.38 (m,

2H), 0.99 (t, $J = 7.4$ Hz, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 100 MHz) δ 165.6, 164.1, 145.4, 142.7, 118.2, 108.3, 50.9, 31.2, 19.8, 13.6. HRMS (APCI) m/z ($[\text{M}+\text{H}]^+$) calcd for $\text{C}_{10}\text{H}_{14}\text{NO}_3$ 196.0968, found 196.0975.



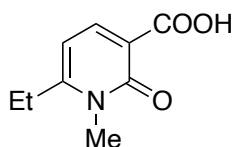
1-Benzyl-2-oxo-1,2-dihydropyridine-3-carboxylic acid (1d)

The compound was prepared according to general procedure **A** using 2-hydroxynicotinic acid and benzyl bromide (5.0 equiv.) and purified by recrystallization from ethyl acetate. white solid, 813 mg, yield 71%. m.p. 131-133 °C. ^1H NMR (CDCl_3 , 400 MHz) δ 14.3 (s, 1H), 8.50 (dd, $J = 2.0, 7.2$ Hz, 1H), 7.65 (dd, $J = 2.0, 6.7$ Hz, 1H), 7.43-7.37 (m, 3H), 7.34-7.31 (m, 2H), 6.55 (t, $J = 6.9$ Hz, 1H), 5.27 (s, 2H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 100 MHz) δ 165.2, 164.1, 145.6, 142.0, 134.3, 129.3, 129.0, 128.4, 118.6, 108.4, 53.1. HRMS (APCI) m/z ($[\text{M}+\text{H}]^+$) calcd for $\text{C}_{13}\text{H}_{12}\text{NO}_3$ 230.0812, found 230.0801.



1,6-Dimethyl-2-oxo-1,2-dihydropyridine-3-carboxylic acid (1e)

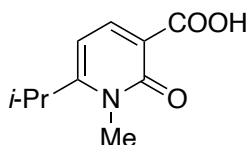
The compound was prepared according to general procedure **A** using 2-hydroxy-6-methylnicotinic acid and methyl iodide (10.0 equiv.) and purified by recrystallization from chloroform. white solid, 509 mg, yield 61%. m.p. 172-174 °C. ^1H NMR (CDCl_3 , 400 MHz) δ 14.39 (s, 1H), 8.39 (d, $J = 7.5$ Hz, 1H), 6.45 (dd, $J = 0.5, 7.5$ Hz, 1H), 3.68 (s, 3H), 2.52 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 100 MHz) δ 165.9, 165.2, 153.1, 144.5, 114.8, 109.3, 32.2, 21.7. HRMS (APCI) m/z ($[\text{M}+\text{H}]^+$) calcd for $\text{C}_8\text{H}_{10}\text{NO}_3$ 168.0655, found 168.0658.



6-Ethyl-1-methyl-2-oxo-1,2-dihydropyridine-3-carboxylic acid (1f)

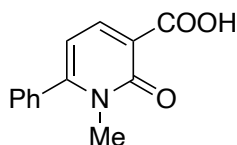
Prepared according to general procedure **B** from 6-ethyl-2-oxo-1,2-dihydropyridine-3-carbonitrile and used directly without further purification. white solid, 154 mg, yield 76% (over two steps). m.p.

146-148 °C. ¹H NMR (CDCl₃, 400 MHz) δ 14.43 (s, 1H), 8.43 (d, *J* = 7.6 Hz, 1H), 6.46 (d, *J* = 7.6 Hz, 1H), 3.69 (s, 3H), 2.79 (q, *J* = 7.2 Hz, 2H), 1.37 (t, *J* = 7.2 Hz, 3H). ¹³C{¹H} NMR (CDCl₃, 100 MHz) δ 165.9, 165.3, 157.9, 144.5, 114.7, 107.2, 31.6, 27.3, 11.9. HRMS (APCI) *m/z* ([M+H]⁺) calcd for C₉H₁₂NO₃ 182.0812, found 182.0793.



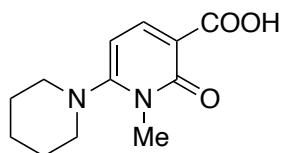
6-Isopropyl-1-methyl-2-oxo-1,2-dihydropyridine-3-carboxylic acid (1g)

Prepared according to general procedure **B** from 6-isopropyl-2-oxo-1,2-dihydropyridine-3-carbonitrile and used directly without further purification. white solid, 176 mg, yield (81% over two steps). m.p. 187-189 °C. ¹H NMR (CDCl₃, 400 MHz) δ 14.47 (s, 1H), 8.64 (d, *J* = 7.8 Hz, 1H), 6.51 (d, *J* = 7.8 Hz, 1H), 3.74 (s, 3H), 3.17 (septet, *J* = 8.8 Hz, 1H), 1.35 (d, *J* = 8.8 Hz, 6H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 165.8, 165.2, 162.7, 144.4, 114.2, 105.1, 31.3, 31.0, 21.6. HRMS (APCI) *m/z* ([M+H]⁺) calcd for C₁₀H₁₄NO₃ 196.0968, found 196.0970.



1-Methyl-2-oxo-6-phenyl-1,2-dihydropyridine-3-carboxylic acid (1h)

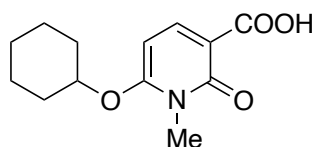
Prepared according to general procedure **B** from 2-oxo-6-phenyl-1,2-dihydropyridine-3-carbonitrile and used directly without further purification. white solid, 206 mg, yield 72% (over two steps). m.p. 209-211 °C. ¹H NMR (CDCl₃, 400 MHz) δ 14.45 (bs, 1H), 8.50 (d, *J* = 7.5 Hz, 1H), 7.57-7.55 (m, 3H), 7.41-7.38 (m, 2H), 6.52 (d, *J* = 7.5 Hz, 1H), 3.55 (s, 3H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 165.7, 165.2, 155.6, 144.4, 133.9, 130.7, 129.3, 128.2, 116.0, 110.3, 35.5. HRMS (APCI) *m/z* ([M+H]⁺) calcd for C₁₃H₁₂NO₃ 230.0812, found 230.0795.



1-Methyl-2-oxo-6-(piperidin-1-yl)-1,2-dihydropyridine-3-carboxylic acid (1i)

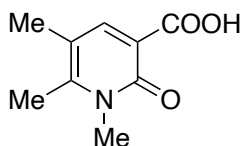
Prepared according to general procedure **C** from

6-chloro-1-methyl-2-oxo-1,2-dihydropyridine-3-carboxylic acid and piperidine at 100 °C for 4 h and used directly without further purification. Pinkish white solid, 196 mg, yield 83%. m.p. 159-161 °C. ¹H NMR (DMSO-*d*₆, 400 MHz) δ 12.60 (bs, 1H), 7.62 (d, *J* = 9.4 Hz, 1H), 6.14 (d, *J* = 9.4 Hz, 1H), 3.44 (s, 3H), 3.03 (broad multiplet, 4H), 1.61 (broad multiplet, 6H). ¹³C{¹H} NMR (DMSO-*d*₆, 100 MHz) δ 167.1, 163.6, 157.7, 141.0, 112.9, 104.9, 50.7, 31.7, 25.7, 24.2. HRMS (APCI) *m/z* ([M+H]⁺) calcd for C₁₂H₁₇N₂O₃ 237.1234, found 237.1229.



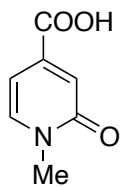
6-(Cyclohexyloxy)-1-methyl-2-oxo-1,2-dihydropyridine-3-carboxylic acid (1j)

Prepared according to general procedure **C** from 6-chloro-1-methyl-2-oxo-1,2-dihydropyridine-3-carboxylic acid and cyclohexanol at 100 °C for 24 h and then purified silica gel chromatography using chloroform as eluent. Light brown solid, 101 mg, yield 40%. m.p. 151-153 °C. ¹H NMR (CDCl₃, 400 MHz) δ Acidic OH peak missing, 7.98 (d, *J* = 9.6 Hz, 1H), 6.39 (d, *J* = 9.6 Hz, 1H), 4.53-4.46 (m, 1H), 3.55 (s, 3H), 2.12-2.09 (m, 2H), 1.85-1.82 (m, 2H), 1.64-1.54 (m, 3H), 1.35-1.18 (m, 3H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 168.7, 163.6, 160.9, 141.1, 113.5, 99.0, 88.7, 32.7, 30.0, 25.1, 24.5. HRMS (CI) *m/z* ([M+H]⁺) calcd for C₁₃H₁₈NO₄ 252.1230, found 252.1234.



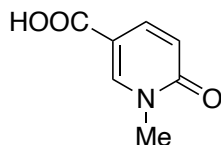
1,5,6-Trimethyl-2-oxo-1,2-dihydropyridine-3-carboxylic acid (1k)

Prepared according to general procedure **B** from 1,5,6-trimethyl-2-oxo-1,2-dihydropyridine-3-carbonitrile and used directly without further purification. White solid, 163 mg, yield 72% (over two steps). m.p. 196-198 °C. ¹H NMR (CDCl₃, 400 MHz) δ 14.63 (s, 1H), 8.32 (s, 1H), 3.71 (s, 3H), 2.46 (s, 3H), 2.23 (s, 3H). ¹³C{¹H} NMR (CDCl₃, 100 MHz) δ 166.1, 164.2, 150.6, 146.6, 116.2, 113.7, 32.5, 18.3, 17.8. HRMS (APCI) *m/z* ([M+H]⁺) calcd for C₉H₁₂NO₃ 182.0812, found 182.0785.



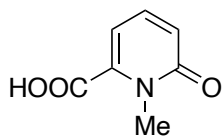
1-Methyl-2-oxo-1,2-dihydropyridine-4-carboxylic acid (7a)

The compound was prepared in similar method as described in general procedure **A** using 2-hydroxyisonicotinic acid (3.0 mmol) and methyl iodide (10.0 equiv.) and used without further purification. Yellowish white solid, 519 mg, yield 69%. m.p. 264-266 °C. ¹H NMR (DMSO-*d*₆, 400 MHz) δ 13.59 (bs, 1H), 7.80 (d, *J* = 7.0, Hz, 1H), 6.82 (dd, *J* = 0.5, 1.8 Hz, 1H), 6.52 (dd, *J* = 1.9, 7.0 Hz, 1H), 3.44, (s, 3H). ¹³C{¹H} NMR (100 MHz, DMSO-*d*₆) δ 166.3, 162.1, 142.0, 141.0, 120.5, 103.7, 37.4. HRMS (APCI) *m/z* ([*M*+*H*]⁺) calcd for C₇H₈NO₃ 154.0499, found 154.0504.



1-Methyl-6-oxo-1,6-dihydropyridine-3-carboxylic acid (9a)

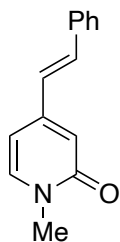
The compound was prepared in similar method as described in general procedure **A** using 6-hydroxynicotinic acid (3.0 mmol) and methyl iodide (10.0 equiv.) and purified by recrystallization from ethyl acetate-hexane. Pinkish white solid, 474 mg, yield 63%. m.p. 247-249 °C. ¹H NMR (DMSO-*d*₆, 400 MHz) δ 12.80 (bs, 1H), 8.47 (d, *J* = 2.5 Hz, 1H), 7.77 (dd, *J* = 2.6, 9.4 Hz, 1H), 6.40 (d, *J* = 9.4 Hz, 1H), 3.49, (s, 3H). ¹³C{¹H} NMR (100 MHz, DMSO-*d*₆) δ 165.8, 162.5, 145.4, 139.3, 118.5, 109.4, 37.7. HRMS (APCI) *m/z* ([*M*+*H*]⁺) calcd for C₇H₈NO₃ 154.0499, found 154.0513.



1-Methyl-6-oxo-1,6-dihydropyridine-2-carboxylic acid (13a)

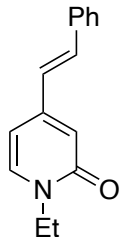
The compound was prepared in similar method as described in general procedure **A** using 6-hydroxypicolinic acid (3.0 mmol) and methyl iodide (10.0 equiv.) and used without further purification. Pinkish white solid, 474 mg, yield 63%. m.p. 248-250 °C. ¹H NMR (DMSO-*d*₆, 400 MHz) δ 14.04 (bs, acidic OH peak), 7.46 (dd, *J* = 6.8, 9.1 Hz, 1H), 6.73 (dd, *J* = 1.4, 6.8 Hz, 1H), 6.60 (dd, *J* = 1.4, 9.1 Hz, 1H), 3.52 (s, 3H). ¹³C{¹H} NMR (100 MHz, DMSO-*d*₆) δ 163.7, 161.8, 140.3, 138.4,

122.7, 108.8, 33.1. HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_7H_8NO_3$ 154.0499, found 154.0510.



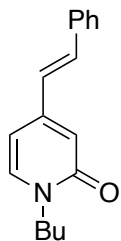
(E)-1-Methyl-4-styrylpyridin-2(1H)-one (3aa)

Purified by silica gel column chromatography using EtOAc/Hexane/ Et_3N = 1/5/0.05 to EtOAc/ $CHCl_3$ / Et_3N = 1/1/0.05 (v/v/v). off white solid, 33 mg, yield 78%. m.p. 164-166 °C. A suitable crystal was formed from THF for X-ray analysis. 1H NMR ($CDCl_3$, 400 MHz) δ 7.52-7.49 (m, 2H), 7.38-7.35 (m, 2H), 7.33-7.29 (m, 1H), 7.23 (d, J = 7.1 Hz, 1H), 7.13 (d, J = 16.3 Hz, 1H), 6.86 (d, J = 16.3 Hz, 1H), 6.56 (d, J = 1.8 Hz, 1H), 6.40 (dd, J = 1.8, 7.1 Hz, 1H), 3.53 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 1000 MHz) δ 163.6, 148.2, 137.8, 136.0, 134.0, 129.01, 128.95, 127.2, 125.8, 118.0, 103.2, 37.3. HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{14}H_{14}NO$ 212.1070, found 212.1080.



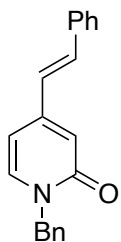
(E)-1-Ethyl-4-styrylpyridin-2(1H)-one (3ba)

Purified by silica gel column chromatography using EtOAc/Hexane/ Et_3N = 1/5/0.05 to EtOAc/ $CHCl_3$ / Et_3N = 1/1/0.05 (v/v/v). off white solid, 28.4 mg, yield 63%. m.p. 164-166 °C. 1H NMR ($CDCl_3$, 400 MHz) δ 7.52-7.50 (m, 2H), 7.40-7.36 (m, 2H), 7.34-7.29 (m, 1H), 7.24 (d, J = 7.2 Hz, 1H), 7.14 (d, J = 16.3 Hz, 1H), 6.87 (d, J = 16.3 Hz, 1H), 6.56 (d, J = 1.8 Hz, 1H), 6.42 (dd, J = 1.8, 7.2 Hz, 1H), 3.98 (q, J = 6.7 Hz, 2H), 1.36 (t, J = 6.7 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 162.9, 147.9, 136.6, 136.1, 133.9, 128.99, 128.96, 127.2, 125.9, 118.4, 103.5, 44.5, 14.9. HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{15}H_{16}NO$ 226.1226, found 226.1215.



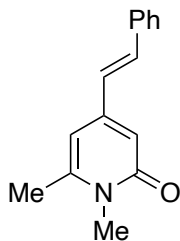
(E)-1-Butyl-4-styrylpyridin-2(1H)-one (3ca)

Purified by silica gel column chromatography using EtOAc/Hexane/Et₃N = 1/5/0.05 to EtOAc/CHCl₃/Et₃N = 1/1/0.05 (v/v/v). off white solid, 28.4 mg, yield 57%. m.p. 164-166 °C. ¹H NMR (CDCl₃, 400 MHz) δ 7.52-7.50 (m, 2H), 7.40-7.29 (m, 3H), 7.21 (d, *J* = 7.1 Hz, 1H), 7.13 (d, *J* = 16.3 Hz, 1H), 6.86 (d, *J* = 16.3 Hz, 1H), 6.55 (d, *J* = 1.8 Hz, 1H), 6.39 (dd, *J* = 1.8, 7.1 Hz, 1H), 3.91 (t, *J* = 7.4 Hz, 2H), 1.77-1.70 (merged with H₂O peak m, 2H), 1.43-1.34 (m, 2H), 0.96 (t, *J* = 7.4 Hz, 3H). ¹³C{¹H} NMR (CDCl₃, 100 MHz) δ 163.1, 147.8, 137.1, 136.1, 133.9, 129.0, 127.2, 126.0, 118.4, 103.1, 49.4, 31.5, 20.0, 13.9 (one carbon peak merged with another). HRMS (APCI) *m/z* ([M+H]⁺) calcd for C₁₇H₂₀NO 254.1539, found 254.1559.



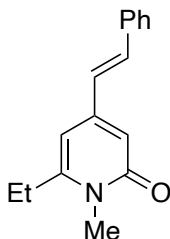
(E)-1-Benzyl-4-styrylpyridin-2(1H)-one (3da)

Purified by silica gel column chromatography using EtOAc/Hexane/Et₃N = 1/5/0.05 to EtOAc/CHCl₃/Et₃N = 1/1/0.05 (v/v/v). off white solid. 47.1 mg, yield 82%. m.p. 102-104 °C. ¹H NMR (CDCl₃, 400 MHz) δ 7.52-7.50 (m, 2H), 7.40-7.28 (m, 8H), 7.22 (d, *J* = 7.2 Hz, 1H), 7.13 (d, *J* = 16.3 Hz, 1H), 6.87 (d, *J* = 16.3 Hz, 1H), 6.61 (d, *J* = 1.8 Hz, 1H), 6.40 (dd, *J* = 1.8, 7.2 Hz, 1H), 5.14 (s, 2H). ¹³C{¹H} NMR (CDCl₃, 100 MHz) δ 163.1, 148.0, 136.8, 136.6, 136.0, 134.2, 129.05, 129.01, 128.96, 128.2, 128.1, 127.3, 125.8, 118.4, 103.6, 51.6. HRMS (APCI) *m/z* ([M+H]⁺) calcd for C₂₀H₁₈NO 288.1383, found 288.1383.



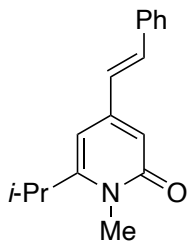
(E)-1,6-Dimethyl-4-styrylpyridin-2(1H)-one (3ea)

Purified by silica gel column chromatography using EtOAc/Hexane/Et₃N = 1/5/0.05 to EtOAc/CHCl₃/Et₃N = 1/1/0.05 (v/v/v). off white solid, 37.9 mg, yield 84%. m.p. 159-161 °C. ¹H NMR (CDCl₃, 400 MHz) δ 7.52-7.50 (m, 2H), 7.40-7.29 (m, 3H), 7.13 (d, *J* = 16.3 Hz, 1H), 6.83 (d, *J* = 16.3 Hz, 1H), 6.48 (d, *J* = 1.5 Hz, 1H), 6.29 (s, 1H), 3.52 (s, 3H), 2.39 (s, 3H). ¹³C{¹H} NMR (CDCl₃, 100MHz) δ 164.3, 146.8, 145.7, 136.2, 133.6, 128.92, 128.88, 127.2, 126.1, 114.9, 103.9, 31.1, 21.3. HRMS (APCI) *m/z* ([M+H]⁺) calcd for C₁₅H₁₆NO 226.1226, found 226.1236.



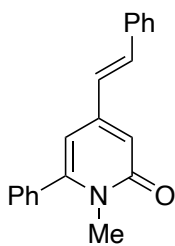
(E)-6-Ethyl-1-methyl-4-styrylpyridin-2(1H)-one (3fa)

Purified by silica gel column chromatography using EtOAc/Hexane/Et₃N = 1/5/0.05 to EtOAc/CHCl₃/Et₃N = 1/1/0.05 (v/v/v). off white solid, 29.7 mg, yield 62%. m.p. 118-120 °C. ¹H NMR (CDCl₃, 400 MHz) δ 7.53-7.50 (m, 2H), 7.40-7.36 (m, 2H), 7.33-7.29 (m, 1H), 7.15 (d, *J* = 16.3 Hz, 1H), 6.85 (d, *J* = 16.3 Hz, 1H), 6.49 (d, *J* = 1.8 Hz, 1H), 6.27 (d, *J* = 1.7 Hz, 1H), 3.54 (s, 3H), 2.68 (q, *J* = 7.4, 2H), 1.33 (t, *J* = 7.4 Hz, 3H). ¹³C{¹H} NMR (CDCl₃, 100 MHz) δ 164.5, 150.8, 146.9, 136.2, 133.6, 128.94, 128.88, 127.2, 126.3, 114.8, 102.1, 30.6, 27.0, 12.6. HRMS (APCI) *m/z* ([M+H]⁺) calcd for C₁₆H₁₈NO 240.1383, found 240.1394.



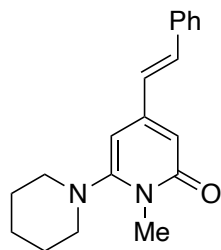
(E)-6-Isopropyl-1-methyl-4-styrylpyridin-2(1H)-one (3ga)

Purified by silica gel column chromatography using EtOAc/Hexane/Et₃N = 1/5/0.05 to EtOAc/CHCl₃/Et₃N = 1/1/0.05 (v/v/v). Light brown gummy liquid. 26.8 mg, yield 53%. ¹H NMR (CDCl₃, 400 MHz) δ 7.53-7.51 (m, 2H), 7.40-7.30 (m, 2H), 7.33-7.29 (m, 1H), 7.15 (d, *J* = 16.3 Hz, 1H), 6.86 (d, *J* = 15.5 Hz, 1H), 6.48 (s, 1H), 6.30 (s, 1H), 3.59 (s, 3H), 3.07 (septet, *J* = 6.8 Hz, 1H), 1.32 (d, *J* = 6.8 Hz, 6H). ¹³C{¹H} NMR (CDCl₃, 100 MHz) δ 164.5, 155.3, 146.8, 136.1, 133.4, 128.82, 128.76, 127.1, 126.3, 114.5, 99.8, 30.34, 30.23, 22.1. HRMS (APCI) *m/z* ([M+H]⁺) calcd for C₁₇H₂₀NO 254.1539, found 254.1527.



(E)-1-Methyl-6-phenyl-4-styrylpyridin-2(1H)-one (3ha)

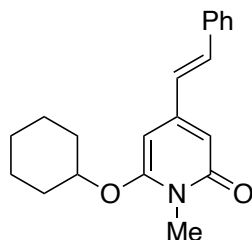
Purified by silica gel column chromatography using EtOAc/Hexane/Et₃N = 1/5/0.05 to EtOAc/CHCl₃/Et₃N = 1/1/0.05 (v/v/v). off white solid, 35.1 mg, yield 61%. m.p. 126-128 °C. ¹H NMR (CDCl₃, 400 MHz) δ 7.51-7.48 (m, 5H), 7.40-7.35 (m, 4H), 7.33-7.30 (m, 1H), 7.15 (d, *J* = 16.3 Hz, 1H), 6.89 (d, *J* = 16.3 Hz, 1H), 6.60 (d, *J* = 1.9 Hz, 1H), 6.37 (d, *J* = 2.0 Hz, 1H), 3.36 (s, 3H). ¹³C{¹H} NMR (CDCl₃, 100 MHz) δ 164.3, 149.6, 146.9, 136.1, 135.9, 134.0, 129.4, 129.0, 128.95, 128.89, 128.6, 127.2, 125.9, 116.3, 105.2, 34.2. HRMS (APCI) *m/z* ([M+H]⁺) calcd for C₂₀H₁₈NO 288.1383, found 288.1383.



(E)-1-Methyl-6-(piperidin-1-yl)-4-styrylpyridin-2(1H)-one (3ia)

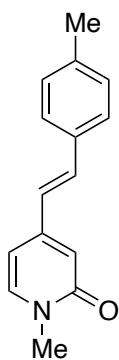
Purified by silica gel column chromatography using EtOAc/Hexane/Et₃N = 1/5/0.05 to EtOAc/CHCl₃/Et₃N = 1/1/0.05 (v/v/v). Yellow gummy liquid, 33.6 mg, yield 57%. ¹H NMR (CDCl₃, 400 MHz) δ 7.53-7.50 (m, 2H), 7.40-7.37 (m, 2H), 7.33-7.29 (m, 1H), 7.13 (d, *J* = 16.3 Hz, 1H), 6.85

(d, $J = 16.3$ Hz, 1H), 6.36 (d, $J = 1.6$ Hz, 1H), 5.96 (d, $J = 1.8$ Hz, 1H), 3.53 (s, 3H), 2.90 (broad multiplet, 4H), 1.74 (broad multiplet, 6H, merged with H₂O peak). ¹³C{¹H} NMR (CDCl₃, 100 MHz) δ 164.9, 156.5, 147.4, 136.3, 133.2, 128.9, 128.8, 127.2, 126.7, 111.7, 92.8, 52.7, 31.2, 25.9, 24.2. HRMS (APCI) m/z ([M+H]⁺) calcd for C₁₉H₂₃N₂O 295.1805, found 295.1799.



(*E*)-6-(Cyclohexyloxy)-1-methyl-4-styrylpyridin-2(1*H*)-one (3ja)

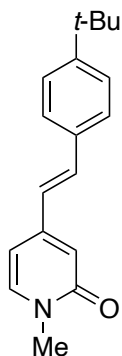
Purified by silica gel column chromatography using EtOAc/Hexane/Et₃N = 1/5/0.05 to EtOAc/CHCl₃/Et₃N = 1/1/0.05 (v/v/v). Light yellow gummy liquid. 39 mg, yield 63%. ¹H NMR (CDCl₃, 400 MHz) δ 7.53-7.51 (m, 2H), 7.40-7.29 (m, 3H), 7.10 (d, $J = 16.3$ Hz, 1H), 6.85 (d, $J = 16.3$ Hz, 1H), 6.25 (d, $J = 1.4$ Hz, 1H), 5.71 (d, $J = 1.6$ Hz, 1H), 4.51-4.45 (m, 1H), 3.47 (s, 3H), 2.02-1.42 (merged with H₂O peak, m, 10H). ¹³C{¹H} NMR (CDCl₃, 100 MHz) δ 163.5, 155.7, 147.9, 136.2, 133.1, 128.9, 128.8, 127.1, 126.8, 108.3, 83.1, 31.2, 28.0, 25.4, 23.2. (one carbon peak merged with another). HRMS (APCI) m/z ([M+H]⁺) calcd for C₂₀H₂₄NO₂ 310.1802, found 310.1818.



(*E*)-1-Methyl-4-(4-methylstyryl)pyridin-2(1*H*)-one (3ab)

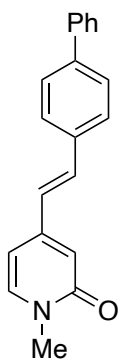
Purified by silica gel column chromatography using EtOAc/Hexane/Et₃N = 1/5/0.05 to EtOAc/CHCl₃/Et₃N = 1/1/0.05 (v/v/v). off white solid, 21.2 mg, yield 47%. m.p. 194-196 °C. ¹H NMR (CDCl₃, 400 MHz) δ 7.40 (d, $J = 8.1$ Hz, 2H), 7.22 (d, $J = 7.1$ Hz, 1H), 7.18 (d, $J = 7.9$ Hz, 2H), 7.11 (d, $J = 16.3$ Hz, 1H), 6.82 (d, $J = 16.3$ Hz, 1H), 6.54 (d, $J = 1.8$ Hz, 1H), 6.39 (dd, $J = 1.8, 7.14.5$ Hz, 1H), 3.53 (s, 3H), 2.36 (s, 3H). ¹³C{¹H} NMR (CDCl₃, 100 MHz) δ 163.6, 148.4, 139.2, 137.7, 134.0,

133.3, 129.7, 127.2, 124.8, 117.7, 103.2, 37.3, 21.5. HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{15}H_{16}NO$ 226.1226, found 226.1233.



(E)-4-(4-(*tert*-Butyl)styryl)-1-methylpyridin-2(1H)-one (3ac)

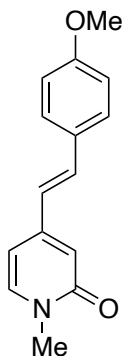
Purified by silica gel column chromatography using EtOAc/Hexane/ Et_3N = 1/5/0.05 to EtOAc/ $CHCl_3$ / Et_3N = 1/1/0.05 (v/v/v). off white solid, 27.8 mg, yield, 52%. m.p. 162-164 °C. 1H NMR ($CDCl_3$, 400 MHz) δ 7.46-7.39 (m, 4H), 7.23 (d, J = 7.1 Hz, 1H), 7.13 (d, J = 16.3 Hz, 1H), 6.83 (d, J = 16.3 Hz, 1H), 6.55 (d, J = 1.8 Hz, 1H), 6.40 (dd, J = 1.8, 7.1 Hz, 1H), 3.53 (s, 3H), 1.33 (s, 9H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 163.6, 152.4, 148.4, 137.8, 133.9, 133.3, 127.0, 125.9, 125.1, 117.8, 103.3, 37.3, 34.9, 31.4. HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{18}H_{22}NO$ 268.1696, found 268.1719.



(E)-4-(2-([1,1'-Biphenyl]-4-yl)vinyl)-1-methylpyridin-2(1H)-one (3ad)

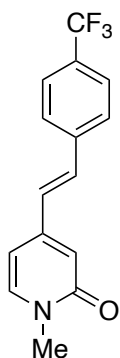
Purified by silica gel column chromatography using EtOAc/Hexane/ Et_3N = 1/5/0.05 to EtOAc/ $CHCl_3$ / Et_3N = 1/1/0.05 (v/v/v). off white solid, 22.4 mg, yield 39%. m.p. 241-243 °C. 1H NMR ($CDCl_3$, 400 MHz) δ 7.64-7.58 (m, 6H), 7.48-7.43 (m, 2H), 7.39-7.34 (m, 1H), 7.25 (merged with $CDCl_3$, d, J = 6.8 Hz, 1H), 7.18 (d, J = 16.2 Hz, 1H), 6.91 (d, J = 16.2 Hz, 1H), 6.59 (d, J = 1.8 Hz, 1H), 6.43 (dd, J = 1.8, 6.8 Hz, 1H), 3.55 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 163.6, 148.2, 141.8,

140.5, 137.9, 135.1, 133.6, 129.0, 127.8, 127.7, 127.6, 127.1, 125.9, 118.1, 103.3, 37.4. HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{20}H_{18}NO$ 288.1383, found 288.1366.



(*E*)-4-(4-Methoxystyryl)-1-methylpyridin-2(1*H*)-one (3ae)

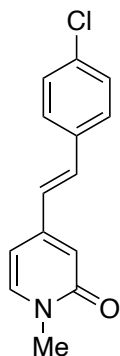
Purified by silica gel column chromatography using EtOAc/Hexane/ Et_3N = 1/5/0.05 to EtOAc/ $CHCl_3$ / Et_3N = 1/1/0.05 (v/v/v). off white solid, 26.5 mg, yield 55%. m.p. 207-209 °C. 1H NMR ($CDCl_3$, 400 MHz) δ 7.47-7.44 (m, 2H), 7.22 (d, J = 7.1 Hz, 1H), 7.09 (d, J = 16.2 Hz, 1H), 6.92-6.89 (m, 2H), 6.73 (d, J = 16.2 Hz, 1H), 6.53 (d, J = 1.8 Hz, 1H), 6.38 (dd, J = 1.8, 7.1 Hz, 1H), 3.84 (s, 3H), 3.53 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 400 MHz) δ 163.6, 160.4, 148.5, 137.7, 133.6, 128.8, 128.7, 123.6, 117.4, 114.4, 103.2, 55.5, 37.3. HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{15}H_{16}NO_2$ 242.1176, found 242.1166.



(*E*)-1-Methyl-4-(4-(trifluoromethyl)styryl)pyridin-2(1*H*)-one (3af)

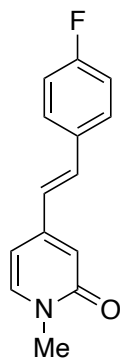
Purified by silica gel column chromatography using EtOAc/Hexane/ Et_3N = 1/5/0.05 to EtOAc/ $CHCl_3$ / Et_3N = 1/1/0.05 (v/v/v). solid, 26.3 mg, yield 47%. m.p. 177-179 °C. 1H NMR ($CDCl_3$, 400 MHz) δ 7.64-7.59 (m, 4H), 7.27 (merged with $CDCl_3$, d, J = 8.2 Hz, 1H), 7.15 (d, J = 16.3 Hz, 1H), 6.95 (d, J = 16.3 Hz, 1H), 6.60 (d, J = 1.2 Hz, 1H), 6.40 (dd, J = 1.2, 8.2 Hz, 1H), 3.55 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 163.4, 147.4, 139.5, 138.1, 132.3, 130.6 (q, J = 32.3 Hz), 128.4, 127.4,

125.9 (q, $J = 3.8$ Hz), 120.8 (q, $J = 266.3$ Hz), 118.8, 103.1, 37.4. $^{19}\text{F}\{^1\text{H}\}$ (376 MHz, CDCl_3) δ -62.65. HRMS (APCI) m/z ($[\text{M}+\text{H}]^+$) calcd for $\text{C}_{15}\text{H}_{13}\text{F}_3\text{NO}$ 280.0944, found 280.0938.



(*E*)-4-(4-Chlorostyryl)-1-methylpyridin-2(1*H*)-one (3ag)

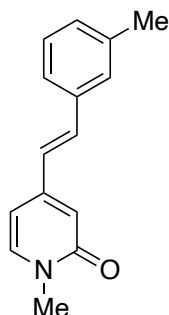
Purified by silica gel column chromatography using $\text{EtOAc/Hexane/Et}_3\text{N} = 1/5/0.05$ to $\text{EtOAc/CHCl}_3/\text{Et}_3\text{N} = 1/1/0.05$ (v/v/v). off white solid, 21.1 mg, yield 43%. m.p. 182-184 °C. ^1H NMR (CDCl_3 , 400 MHz) δ 7.45-7.42 (m, 2H), 7.35-7.32 (m, 2H), 7.24 (d, $J = 7.2$ Hz, 1H), 7.07 (d, $J = 16.3$ Hz, 1H), 6.83 (d, $J = 16.3$ Hz, 1H), 6.55 (d, $J = 1.8$ Hz, 1H), 6.37 (dd, $J = 1.8, 7.2$ Hz, 1H), 3.53 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 100 MHz) δ . 163.4, 147.8, 137.9, 134.7, 134.5, 132.6, 129.2, 128.4, 126.4, 118.2, 103.1, 37.4. HRMS (APCI) m/z ($[\text{M}+\text{H}]^+$) calcd for $\text{C}_{14}\text{H}_{13}\text{ClNO}$ 246.0680, found 246.0669.



(*E*)-4-(4-Fluorostyryl)-1-methylpyridin-2(1*H*)-one (3ah)

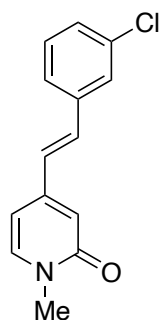
Purified by silica gel column chromatography using $\text{EtOAc/Hexane/Et}_3\text{N} = 1/5/0.05$ to $\text{EtOAc/CHCl}_3/\text{Et}_3\text{N} = 1/1/0.05$ (v/v/v). off white solid, 28.9 mg, yield 63%. m.p. 157-159 °C. ^1H NMR (CDCl_3 , 400 MHz) δ 7.50-7.45 (m, 2H), 7.24 (d, $J = 7.2$ Hz, 1H), 7.11-7.03 (m, 3H), 6.77 (d, $J = 16.3$ Hz, 1H), 6.54 (d, $J = 1.9$ Hz, 1H), 6.37 (dd, $J = 1.9, 7.2$ Hz, 1H), 3.53 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 100 MHz) δ . 163.5, 163.1 (d, $J = 247.8$ Hz), 148.0, 138.0, 132.7, 132.3 (d, $J = 3.2$ Hz), 128.9 (d, $J =$

8.1 Hz), 125.6 (d, $J = 2.2$ Hz), 118.0, 116.0 (d, $J = 21.7$ Hz), 103.1, 37.4. $^{19}\text{F}\{^1\text{H}\}$ (376 MHz, CDCl_3) δ -111.95. HRMS (APCI) m/z ($[\text{M}+\text{H}]^+$) calcd for $\text{C}_{14}\text{H}_{13}\text{FNO}$ 230.0976, found 230.0957.



(*E*)-1-Methyl-4-(3-methylstyryl)pyridin-2(1*H*)-one (3ai)

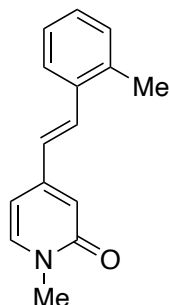
Purified by silica gel column chromatography using $\text{EtOAc/Hexane/Et}_3\text{N} = 1/5/0.05$ to $\text{EtOAc/CHCl}_3/\text{Et}_3\text{N} = 1/1/0.05$ (v/v/v). off white solid, 27.9 mg, yield 62%. m.p. 121-123°C. ^1H NMR (CDCl_3 , 400 MHz) δ 7.33-7.23 (m, 4H), 7.14 (d, $J = 6.3$ Hz, 1H), 7.11 (d, $J = 16.2$ Hz, 1H), 6.85 (d, $J = 16.3$ Hz, 1H), 6.56 (d, $J = 1.8$ Hz, 1H), 6.40 (dd, $J = 1.8, 6.3$ Hz, 1H), 3.53 (s, 3H), 2.38 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 100 MHz) δ 163.5, 148.3, 138.5, 137.8, 135.9, 134.1, 129.8, 128.8, 127.8, 125.6, 124.5, 117.9, 103.2, 37.3, 21.5. HRMS (APCI) m/z ($[\text{M}+\text{H}]^+$) calcd for $\text{C}_{15}\text{H}_{16}\text{NO}$ 226.1226, found 226.1233.



(*E*)-4-(3-Chlorostyryl)-1-methylpyridin-2(1*H*)-one (3aj)

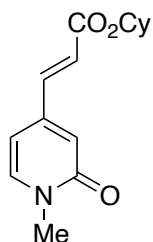
Purified by silica gel column chromatography using $\text{EtOAc/Hexane/Et}_3\text{N} = 1/5/0.05$ to $\text{EtOAc/CHCl}_3/\text{Et}_3\text{N} = 1/1/0.05$ (v/v/v). off white solid, 30.5 mg, yield, 62%. m.p. 136-138°C. ^1H NMR (CDCl_3 , 400 MHz) δ 7.50-7.49 (m, 1H), 7.39-7.36 (m, 1H), 7.33-7.26 (merged with CDCl_3 , m, 2H), 7.25 (merged with CDCl_3 , d, $J = 6.0$ Hz, 1H), 7.06 (d, $J = 16.3$ Hz, 1H), 6.86 (d, $J = 16.3$ Hz, 1H), 6.57 (d, $J = 1.8$ Hz, 1H), 6.38 (dd, $J = 2.0, 7.1$ Hz, 1H), 3.54 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 100 MHz) δ

163.5, 147.6, 138.0, 137.9, 135.0, 132.5, 130.2, 128.9, 127.3, 127.1, 125.4, 118.5, 103.1, 37.4. HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{14}H_{13}ClNO$ 246.0680, found 246.0685.



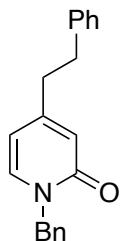
(*E*)-1-Methyl-4-(2-methylstyryl)pyridin-2(1*H*)-one (3ak)

Purified by silica gel column chromatography using EtOAc/Hexane/ Et_3N = 1/5/0.05 to EtOAc/ $CHCl_3$ / Et_3N = 1/1/0.05 (v/v/v). Off white solid, 15.8 mg, yield 35%. m.p. 103-105°C. 1H NMR ($CDCl_3$, 400 MHz) δ 7.59-7.56 (m, 1H), 7.40 (d, J = 16.1 Hz, 1H), 7.26-7.18 (merged with $CDCl_3$, m, 4H), 6.77 (d, J = 16.1 Hz, 1H), 6.59 (d, J = 1.8 Hz, 1H), 6.40 (dd, J = 1.8, 7.1 Hz, 1H), 3.54 (s, 3H), 2.42 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 163.6, 148.5, 137.9, 136.5, 135.1, 131.7, 130.8, 128.9, 127.1, 126.5, 125.9, 117.8, 103.6, 37.4, 20.0. HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{15}H_{16}NO$ 226.1226, found 226.1232.



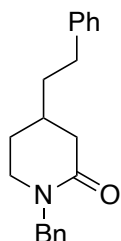
Cyclohexyl (*E*)-3-(1-methyl-2-oxo-1,2-dihydropyridin-4-yl)acrylate (3al)

Purified by silica gel column chromatography using EtOAc/Hexane/ Et_3N = 1/5/0.05 to EtOAc/ $CHCl_3$ / Et_3N = 1/1/0.05 (v/v/v) followed by GPC (EtOAc). Light yellow gummy liquid, 11.5 mg, yield 22%. 1H NMR ($CDCl_3$, 400 MHz) δ 7.39 (d, J = 16.0 Hz, 1H), 7.27 (merged with $CDCl_3$, d, J = 7.9 Hz, 1H), 6.64 (d, J = 1.8 Hz, 1H), 6.42 (d, J = 16.0 Hz, 1H), 6.29 (dd, J = 1.9, 7.1 Hz, 1H), 4.91-4.85, (m, 1H), 3.54 (s, 3H), 1.92-1.89 (m, 2H), 1.78-1.75 (m, 2H), 1.53-1.25 (m, 6H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 165.5, 163.1, 145.4, 141.1, 138.4, 124.3, 121.2, 103.1, 73.6, 37.6, 31.8, 25.5, 23.9. HRMS (APCI) m/z ($[M+H]^+$) calcd for $C_{15}H_{20}NO_3$ 262.1438, found 262.1413.



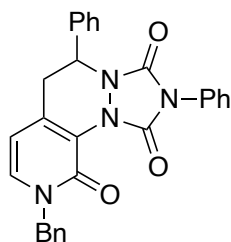
1-Benzyl-4-phenethylpyridin-2(1H)-one (4)

Purified by silica gel column chromatography using EtOAc/Hexane/Et₃N = 1:1:0.05 (v/v/v) to EtOAc. Colorless liquid, 46.9 mg, yield 81%. ¹H NMR (CDCl₃, 400 MHz) δ 7.36-7.25 (merged with CDCl₃, m, 7H), 7.22-7.14 (m, 4H), 6.44 (d, *J* = 0.5 Hz, 1H), 5.99 (dd, *J* = 2.5, 4.5 Hz, 1H), 5.11 (s, 2H), 2.90-2.86 (m, 2H), 2.75-2.71 (m, 2H). ¹³C{¹H} NMR (CDCl₃, 100 MHz) δ 162.9, 154.5, 140.7, 136.6, 136.5, 129.0, 128.6, 128.4, 128.2, 128.0, 126.4, 119.0, 108.1, 51.6, 37.1, 35.5. HRMS (APCI) *m/z* ([M+H]⁺) calcd for C₂₀H₂₀NO 290.1539, found 290.1542.



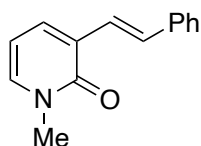
1-Benzyl-4-phenethylpiperidin-2-one (5)

Purified by silica gel column chromatography using EtOAc/Hexane/Et₃N = 1:1:0.05 (v/v/v) to EtOAc. Colorless liquid, 49.9 mg, yield 85%. ¹H NMR (CDCl₃, 400 MHz) δ 7.34-7.23 (merged with CDCl₃, m, 7H), 7.20-7.15 (m, 3H), 4.71 (d, *J* = 14.6 Hz, 1H), 4.47 (d, *J* = 14.6 Hz, 1H), 3.24-3.13 (m, 2H), 2.70-2.58 (m, 3H), 2.14 (dd, *J* = 10.6 17.4 Hz, 1H), 1.92-1.78 (merged with H₂O peak, m, 2H), 1.66-1.60 (m, 2H), 1.5-1.41 (m, 1H). ¹³C{¹H} NMR (CDCl₃, 100 MHz) δ 169.6, 141.9, 137.3, 128.7, 128.6, 128.4, 128.2, 127.5, 126.0, 50.0, 46.4, 38.8, 37.5, 32.9, 32.5, 29.1. HRMS (APCI) *m/z* ([M+H]⁺) calcd for C₂₀H₂₄NO 294.1852, found 294.1854.



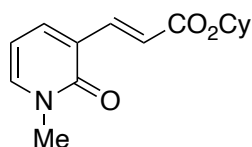
9-Benzyl-2,5-diphenyl-5,6-dihydro-1H-pyrido[3,4-c][1,2,4]triazolo[1,2-a]pyridazine-1,3,10(2H,9H)-trione (6)

Purified by GPC (EtOAc). Yellow gummy liquid, 56.4 mg, yield 61%. ^1H NMR (CDCl_3 , 400 MHz) δ 7.62-7.60 (m, 2H), 7.47-7.43 (m, 2H), 7.37-7.29 (merged with CDCl_3 , m 9H), 7.19-7.17 (m, 2H), 7.11 (d, J = 6.9 Hz, 1H), 6.01 (d, J = 4.3 Hz, 1H), 5.90 (dd, J = 6.9 Hz, 1H), 5.22 (d, J = 14.6 Hz, 1H), 5.14 (d, J = 14.6 Hz, 1H), 3.23 (dd, J = 5.7, 15.4 Hz, 1H), 3.06 (dd, J = 1.8, 15.4 Hz, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 100 MHz) δ 155.4, 150.5, 146.0, 138.1, 137.8, 135.9, 135.5, 131.6, 129.11, 129.08, 128.8, 128.38, 128.36, 128.2, 128.1, 126.0, 125.8, 123.4, 106.2, 55.3, 52.6, 34.6 HRMS (APCI) m/z ($[\text{M}+\text{H}]^+$) calcd for $\text{C}_{28}\text{H}_{23}\text{N}_4\text{O}_3$ 463.1765, found 463.1770.



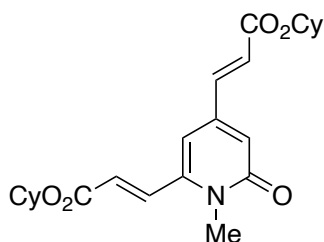
(E)-1-Methyl-3-styrylpyridin-2(1H)-one (8aa)

Purified by silica gel column chromatography using EtOAc/Hexane/ Et_3N = 1/5/0.05 to EtOAc/ CHCl_3 / Et_3N = 1/1/0.05 (v/v/v). Light yellow solid, 22.4 mg, yield 53%. m.p. 104-106°C. ^1H NMR (CDCl_3 , 400 MHz) δ 7.59 (d, J = 16.4 Hz, 1H), 7.54-7.52 (m, 3H), 7.36-7.32 (m, 2H), 7.26-7.22 (merged with CDCl_3 , m, 3H), 6.22 (t, J = 14.4 Hz, 1H), 3.60 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 100 MHz) δ 162.0, 137.9, 136.6, 135.4, 131.1, 129.7, 128.3, 127.3, 126.8, 124.1, 106.1, 37.2. HRMS (APCI) m/z ($[\text{M}+\text{H}]^+$) calcd for $\text{C}_{14}\text{H}_{14}\text{NO}$ 212.1070, found 212.1079.



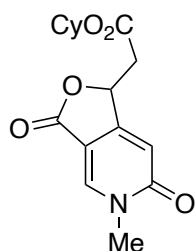
Cyclohexyl (E)-3-(1-methyl-2-oxo-1,2-dihydropyridin-3-yl)acrylate (8al)

Purified by silica gel column chromatography using EtOAc/Hexane/ Et_3N = 1/5/0.05 to EtOAc/ CHCl_3 / Et_3N = 1/1/0.05 (v/v/v). yellow liquid, 26.7 mg, yield 51%. ^1H NMR (CDCl_3 , 400 MHz) δ 7.61 (d, J = 16.0 Hz, 1H), 7.54 (d, J = 2.0, 7.1 Hz, 1H), 7.36 (dd, J = 2.0, 6.7 Hz, 1H), 7.09 (d, J = 15.6 Hz, 1H), 6.23 (t, J = 6.8 Hz, 1H), 4.83-4.90 (m, 1H), 3.59 (s, 3H), 1.89-1.24 (merged with H_2O peak, m, 10H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 100 MHz) δ 167.3, 161.5, 140.9, 139.6, 139.2, 125.4, 121.7, 105.9, 72.5, 38.2, 31.8, 25.6, 23.8. HRMS (APCI) m/z ($[\text{M}+\text{H}]^+$) calcd for $\text{C}_{15}\text{H}_{20}\text{NO}_3$ 262.1438, found 262.1418.



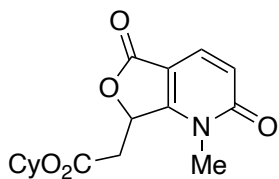
Dicyclohexyl 3,3'-(1-methyl-6-oxo-1,6-dihydropyridine-2,4-diyl)(2E,2'E)-diacrylate (10al)

Purified by silica gel column chromatography using EtOAc/Hexane/Et₃N = 1/5/0.05 to EtOAc/CHCl₃/Et₃N = 1/1/0.05 (v/v/v), followed by GPC (EtOAc). Yellow liquid, 33.1 mg, yield 40%. ¹H NMR (CDCl₃, 400 MHz) δ 7.58 (d, *J* = 16.0 Hz, 1H), 7.39 (d, *J* = 16.0 Hz, 1H), 6.67 (d, *J* = 1.8 Hz, 1H), 6.54 (d, *J* = 1.8 Hz, 1H), 6.47 (d, *J* = 11.0 Hz, 1H), 6.43 (d, *J* = 11.0 Hz, 1H), 4.94-4.86 (m, 2H), 3.57 (s, 3H), 1.92-1.90 (m, 4H), 1.79-1.75 (m, 4H), 1.59-1.27 (m, 12H). ¹³C{¹H} NMR (CDCl₃, 100 MHz) δ 165.3, 164.9, 163.1, 144.6, 143.9, 140.7, 136.0, 126.2, 124.5, 121.2, 103.6, 74.0, 73.6, 32.2, 31.77, 31.74, 25.48, 25.44, 23.88, 23.86. HRMS (APCI) *m/z* ([M+H]⁺) calcd for C₂₄H₃₂NO₅ 414.2275, found 414.2305.



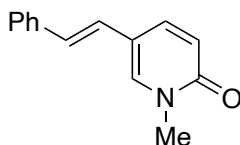
Cyclohexyl 2-(5-methyl-3,6-dioxo-1,3,5,6-tetrahydrofuro[3,4-c]pyridin-1-yl)acetate (11al)

Purified by silica gel column chromatography using EtOAc/Hexane/Et₃N = 1/5/0.05 to EtOAc/CHCl₃/Et₃N = 1/1/0.05 (v/v/v), followed by GPC (EtOAc). Colorless gummy liquid, 6.1 mg, yield 10%. ¹H NMR (CDCl₃, 400 MHz) δ 8.17 (s, 1H), 6.51 (s, 1H), 5.70 (dt, *J* = 1.3, 6.2 Hz, 1H), 4.85-4.78 (m, 1H), 3.64 (s, 3H), 2.94 (dd, *J* = 6.3, 13.6 Hz, 1H), 2.86 (dd, *J* = 6.3, 13.6 Hz, 1H), (these two peaks have overlapped with each other), 1.88-1.22 (m, 10H). ¹³C{¹H} NMR (CDCl₃, 100 MHz) δ 168.1, 166.8, 162.6, 156.9, 140.7, 110.9, 106.4, 75.7, 74.3, 39.13, 39.12, 31.6, 25.3, 23.8. HRMS (APCI) *m/z* ([M+H]⁺) calcd for C₁₆H₂₀NO₅ 306.1336, found 306.1335.



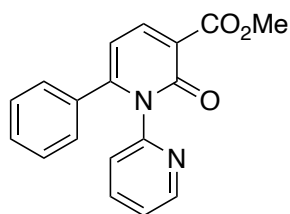
Cyclohexyl 2-(1-methyl-2,5-dioxo-1,2,5,7-tetrahydrofuro[3,4-*b*]pyridin-7-yl)acetate (12al)

Purified by silica gel column chromatography using EtOAc/Hexane/Et₃N = 1/5/0.05 to EtOAc/CHCl₃/Et₃N = 1/1/0.05 (v/v/v), followed by GPC (EtOAc). Colorless gummy liquid, 3.1 mg, yield 5%. ¹H NMR (CDCl₃, 400 MHz) δ 7.65 (d, *J* = 9.3 Hz, 1H), 6.62 (d, *J* = 9.3 Hz, 1H), 5.68 (dd, *J* = 3.1, 7.2 Hz, 1H), 4.81-4.75 (m, 1H), 3.53 (s, 3H), 3.15 (dd, *J* = 3.1, 16.4 Hz, 1H), 2.80 (dd, *J* = 7.2, 16.4 Hz, 1H), 1.84-1.22 (merged with H₂O peak, m, 10H). ¹³C{¹H} NMR (CDCl₃, 100 MHz) δ 167.3, 166.8, 163.1, 161.4, 133.8, 121.0, 105.3, 74.8, 73.4, 37.6, 32.3, 31.6, 25.2, 23.8. HRMS (APCI) *m/z* ([*M*+*H*]⁺) calcd for C₁₆H₂₀NO₅ 306.1336, found 306.1339.



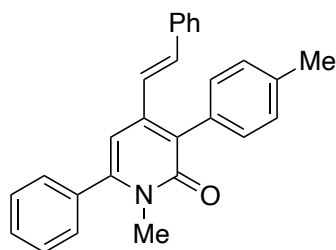
(*E*)-1-Methyl-5-styrylpyridin-2(1*H*)-one (14aa)

Purified by silica gel column chromatography using EtOAc/Hexane/Et₃N = 1/5/0.05 to EtOAc/CHCl₃/Et₃N = 1/1/0.05 (v/v/v). Light yellow solid, 25.4 mg, yield 60%. m.p. 154-156°C. ¹H NMR (CDCl₃, 400 MHz) δ 7.69 (dd, *J* = 2.5, 9.5 Hz, 1H), 7.45-7.42 (m, 2H), 7.37-7.33 (m, 3H), 7.27-7.23 (merged with CDCl₃, m, 1H), 6.80 (t, due to merging of two doublets, *J* = 17.0 Hz, 2H), 6.63 (d, *J* = 9.5 Hz, 1H), 3.57 (s, 3H). ¹³C{¹H} NMR (CDCl₃, 100 MHz) δ 162.6, 137.0, 136.9, 136.6, 128.9, 127.7, 126.7, 126.3, 123.3, 121.1, 117.3, 37.9. HRMS (APCI) *m/z* ([*M*+*H*]⁺) calcd for C₁₄H₁₄NO 212.1070, found 212.1077.



Methyl 2-oxo-6-phenyl-2*H*-[1,2'-bipyridine]-3-carboxylate (16)

Purified by silica gel column chromatography using EtOAc/Hexane/Et₃N = 1/5/0.05 to EtOAc/CHCl₃/Et₃N = 1/1/0.05 (v/v/v). Colorless liquid, 47.8 mg, yield 78%. ¹H NMR (CDCl₃, 400 MHz) δ 8.38 (dd, *J* = 1.0, 4.7 Hz, 1H), 8.33 (d, *J* = 1.0, 7.5 Hz, 1H), 7.69 (dt, *J* = 1.9, 7.7 Hz, 1H), 7.29 (d, *J* = 8.0 Hz, 1H), 7.23-7.14 (m, 6H), 6.37 (d, *J* = 7.4 Hz, 1H), 3.91 (s, 3H). ¹³C{¹H} NMR (CDCl₃, 100 MHz) δ 166.0, 160.3, 154.5, 151.8, 149.3, 145.7, 137.8, 134.7, 129.3, 128.7, 128.3, 124.8, 123.7, 119.7, 107.1, 52.5. HRMS (APCI) *m/z* ([M+H]⁺) calcd for C₁₈H₁₅N₂O₃ 307.1077, found 307.1066.



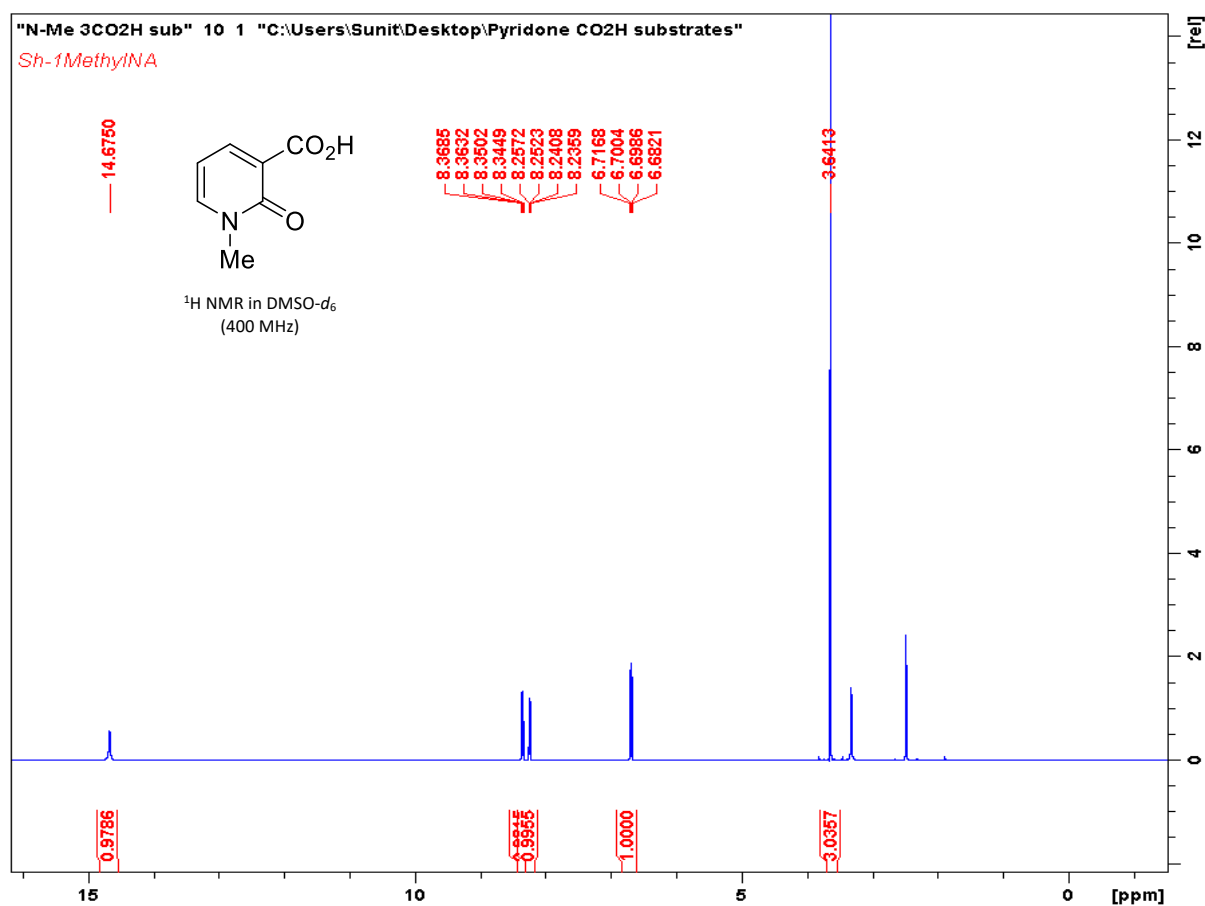
(*E*)-1-Methyl-6-phenyl-4-styryl-3-(p-tolyl)pyridin-2(1*H*)-one (17)

Purified by silica gel column chromatography using EtOAc/Hexane/Et₃N = 1/5/0.05 to EtOAc/CHCl₃/Et₃N = 1/1/0.05 (v/v/v) followed by GPC (EtOAc). Yellow gummy liquid, 39.3 mg, yield 52%. ¹H NMR (CDCl₃, 400 MHz) δ 7.54-7.43 (m, 5H), 7.33-7.25 (merged with CDCl₃, m, 9H), 7.08 (d, *J* = 16.4 Hz, 1H), 6.94 (d, *J* = 16.4 Hz, 1H), 6.52 (s, 1H), 3.41 (s, 3H), 2.42 (s, 3H). ¹³C{¹H} NMR (CDCl₃, 100 MHz) δ 163.5, 147.7, 142.7, 137.3, 136.6, 136.2, 133.1, 132.4, 131.0, 129.3, 128.91, 128.89, 128.85, 128.7, 128.59, 128.56, 127.2, 125.9, 104.9, 34.8, 21.5. HRMS (APCI) *m/z* ([M+H]⁺) calcd for C₂₇H₂₄NO 378.1852, found 378.1851.

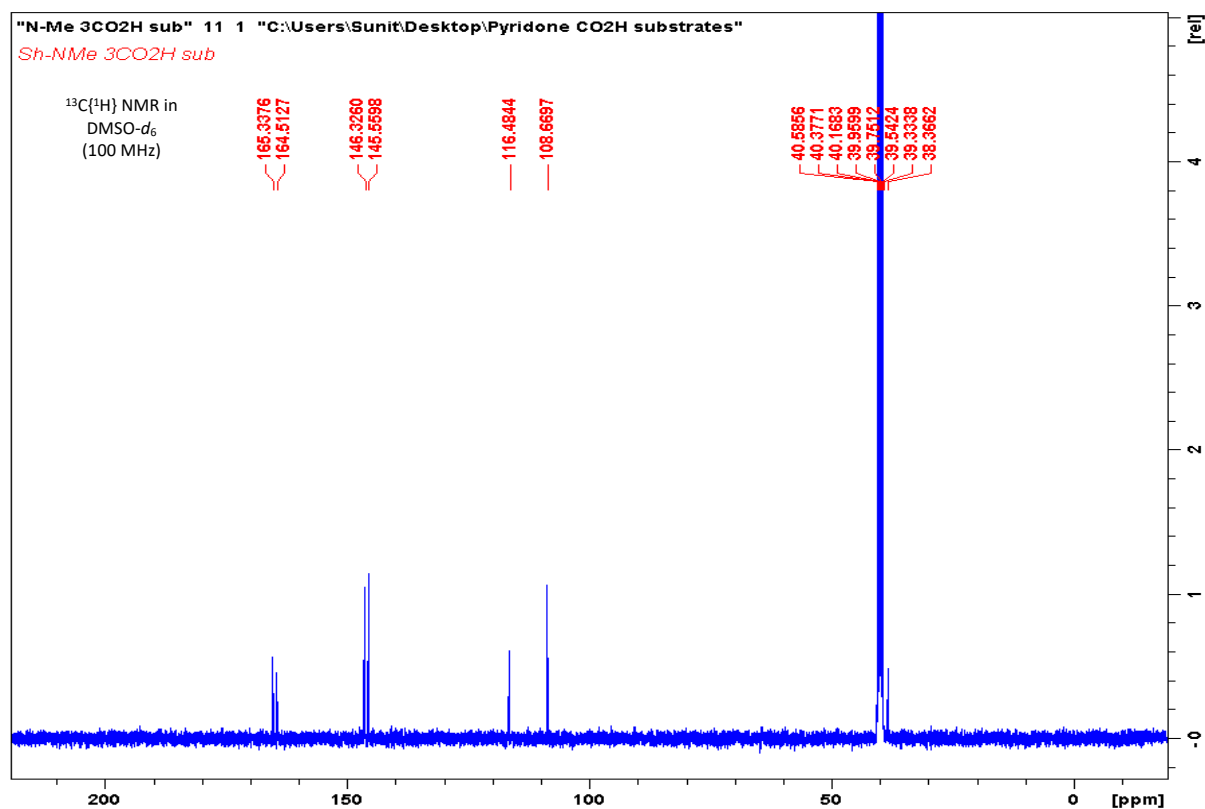
References

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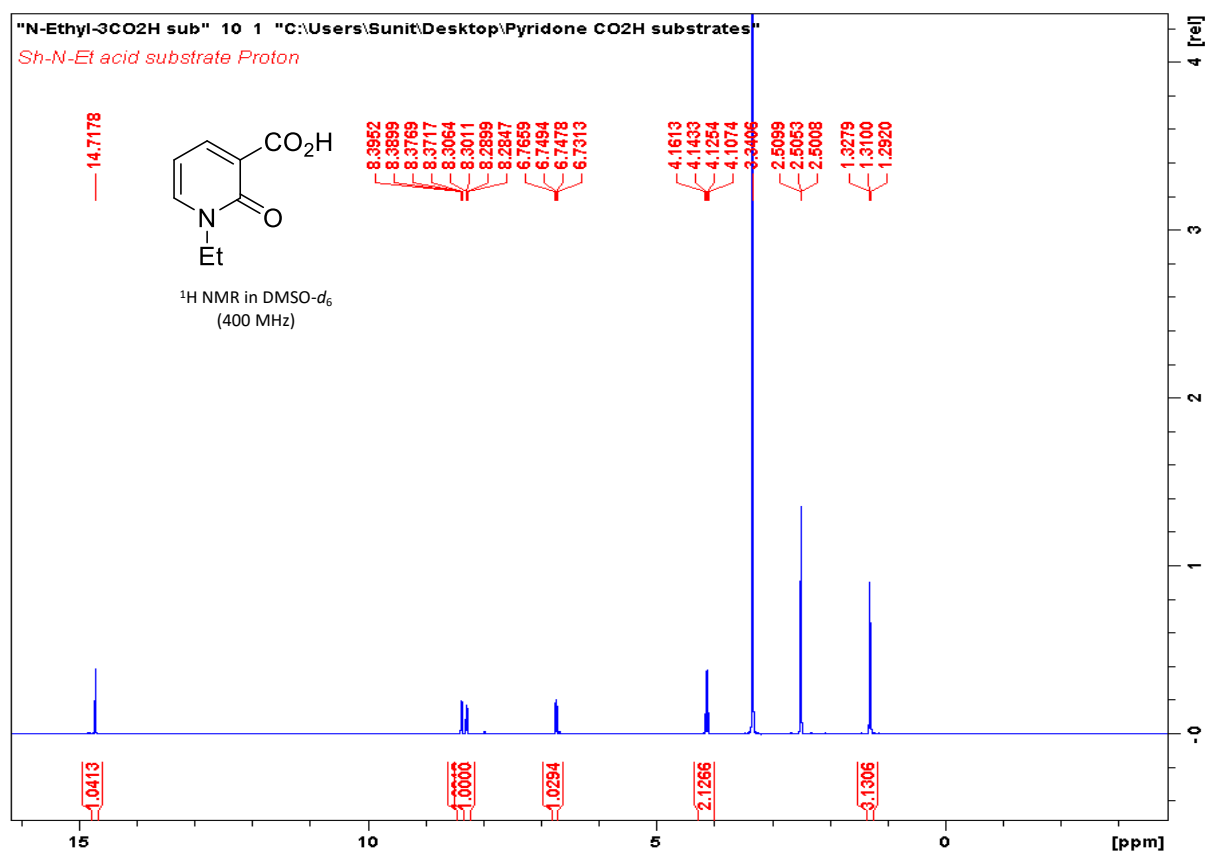
^1H NMR of compound **1a** in $\text{DMSO}-d_6$ (400 MHz)



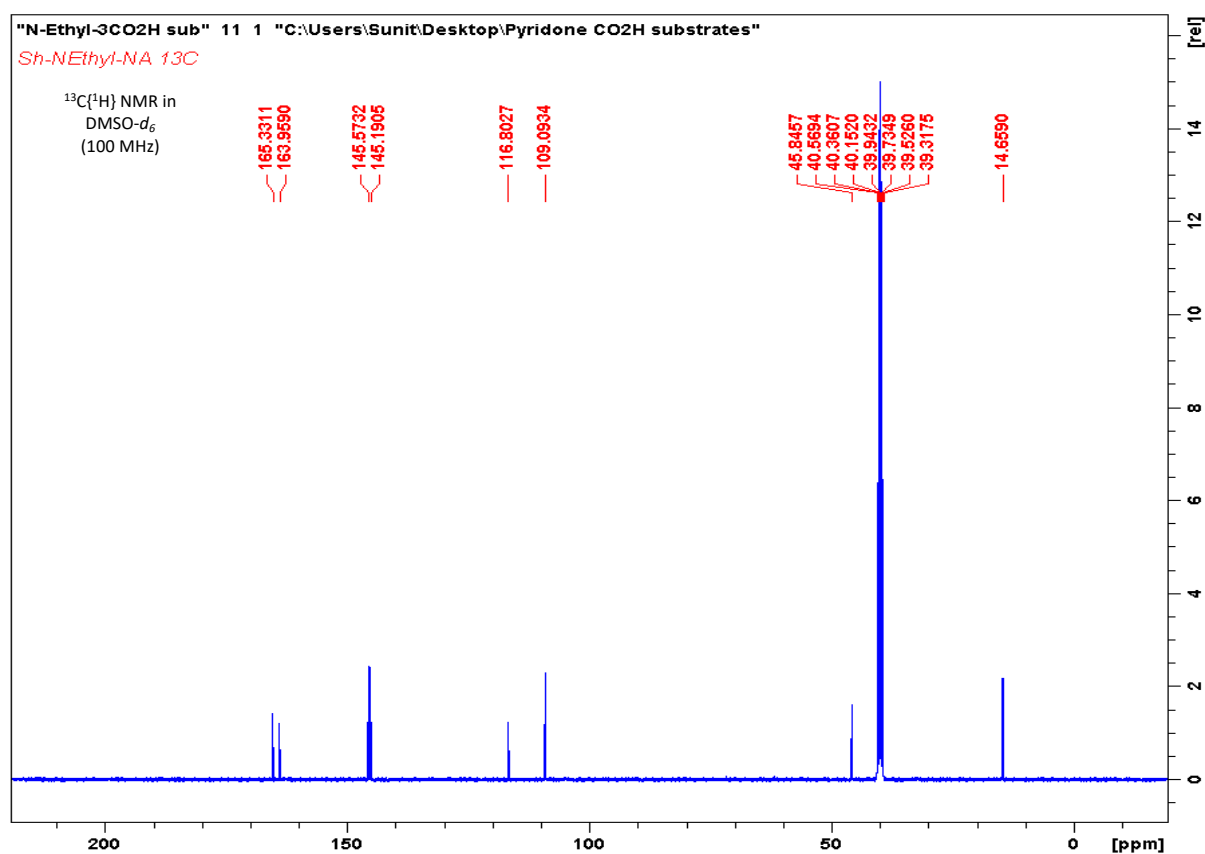
$^{13}\text{C}\{^1\text{H}\}$ NMR of compound **1a** in $\text{DMSO}-d_6$ (100 MHz)



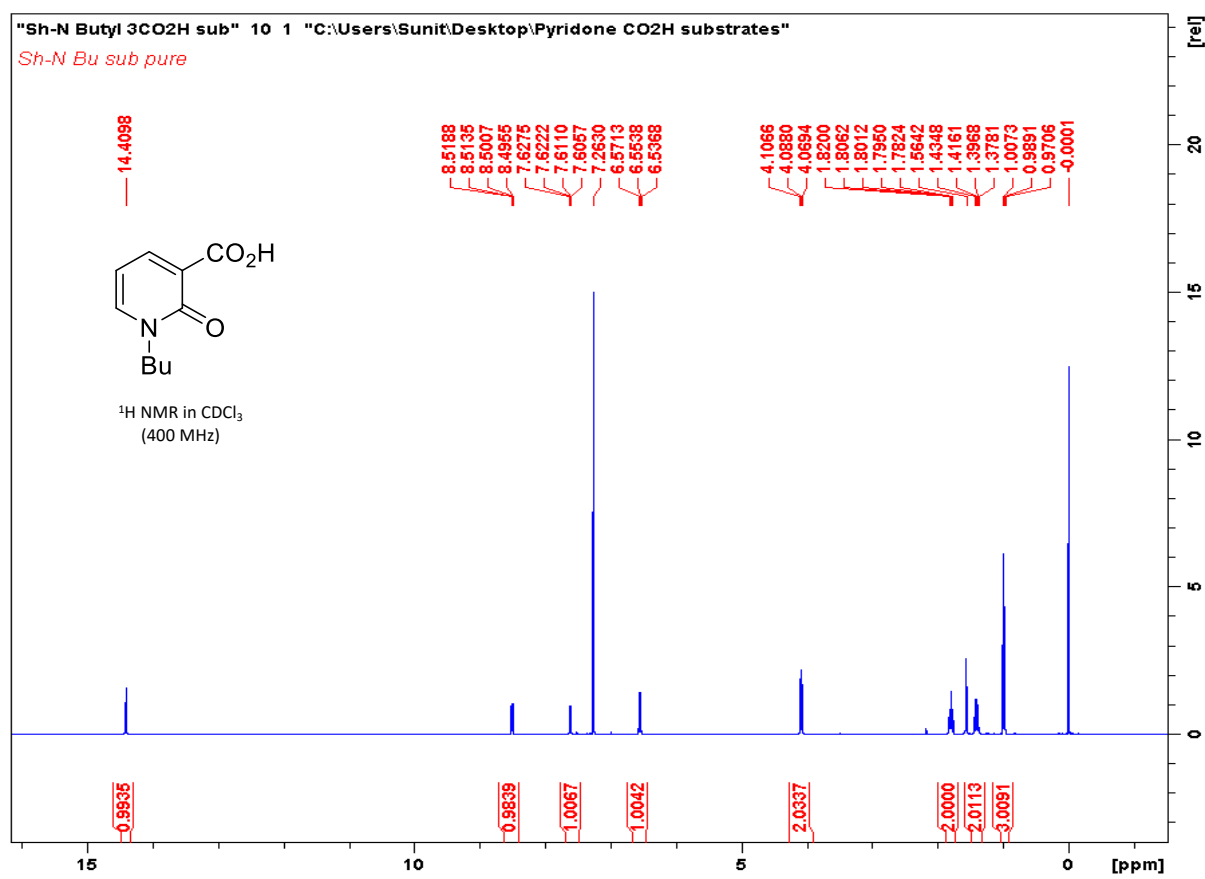
^1H NMR of compound **1b** in $\text{DMSO-}d_6$ (400 MHz)



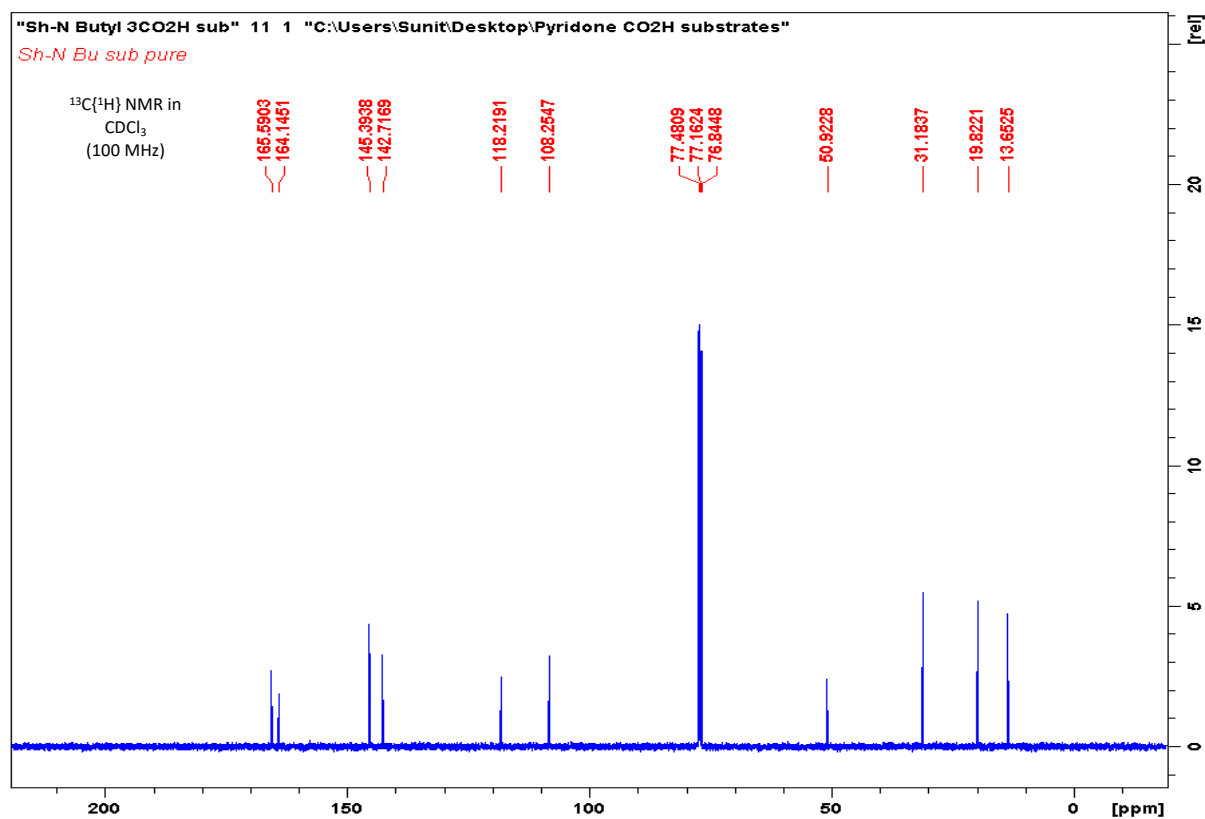
$^{13}\text{C}\{^1\text{H}\}$ NMR of compound **1b** in $\text{DMSO-}d_6$ (100 MHz)



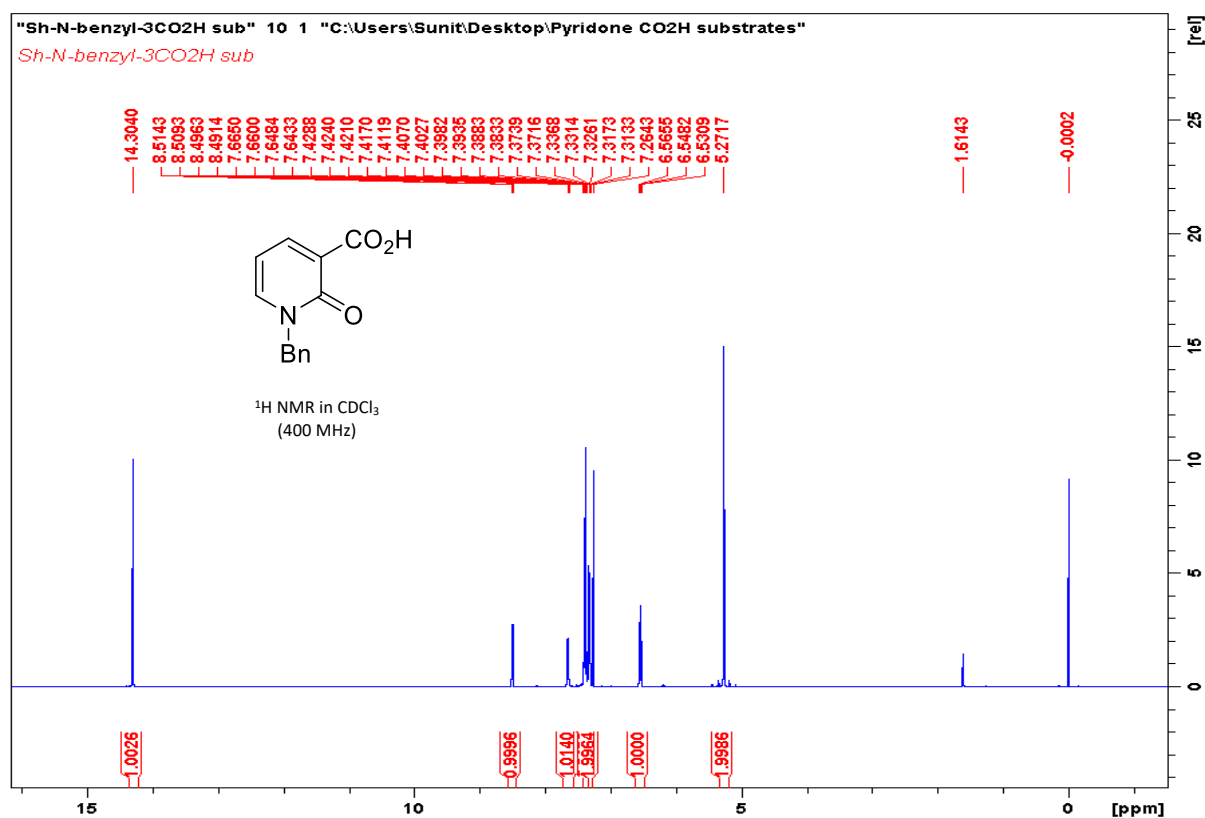
^1H NMR of compound **1c** in CDCl_3 (400 MHz)



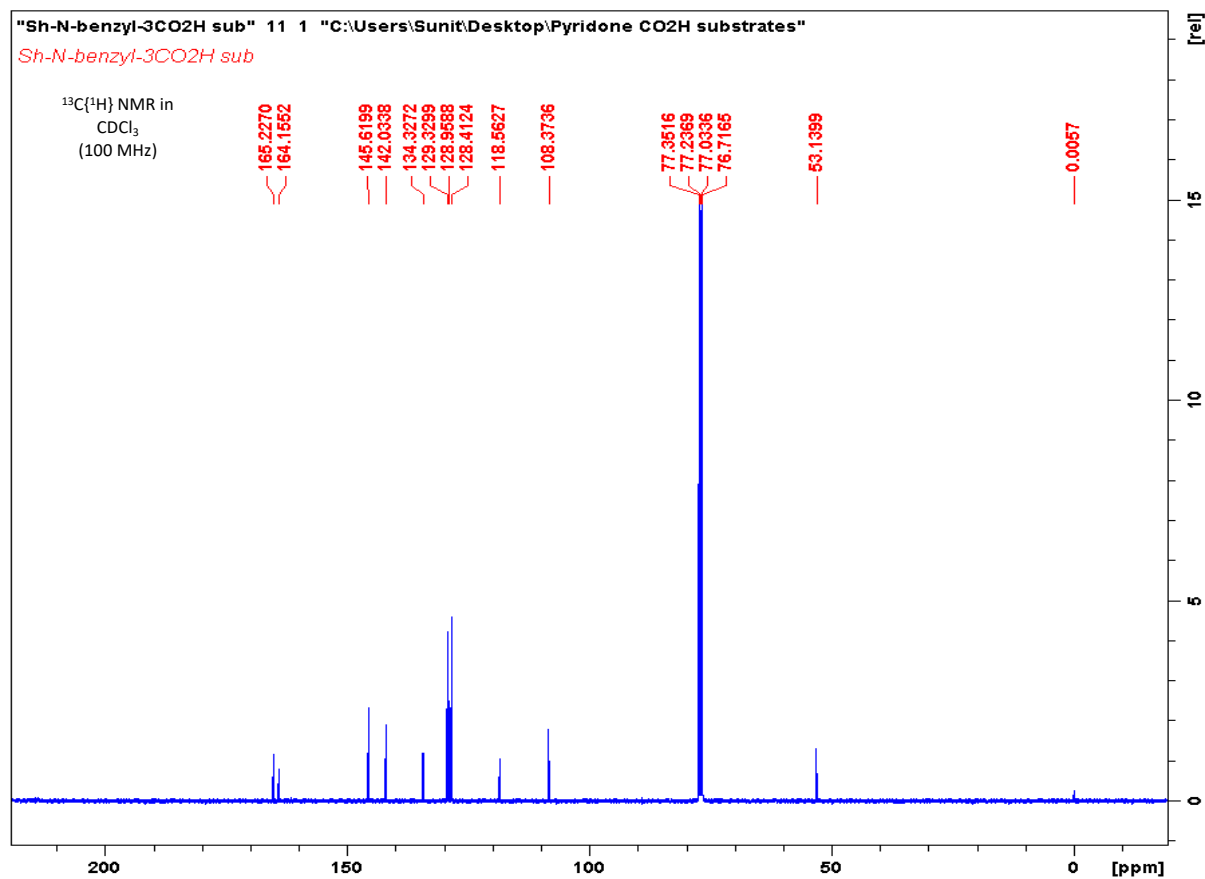
$^{13}\text{C}\{^1\text{H}\}$ NMR of compound **1c** in CDCl_3 (100 MHz)



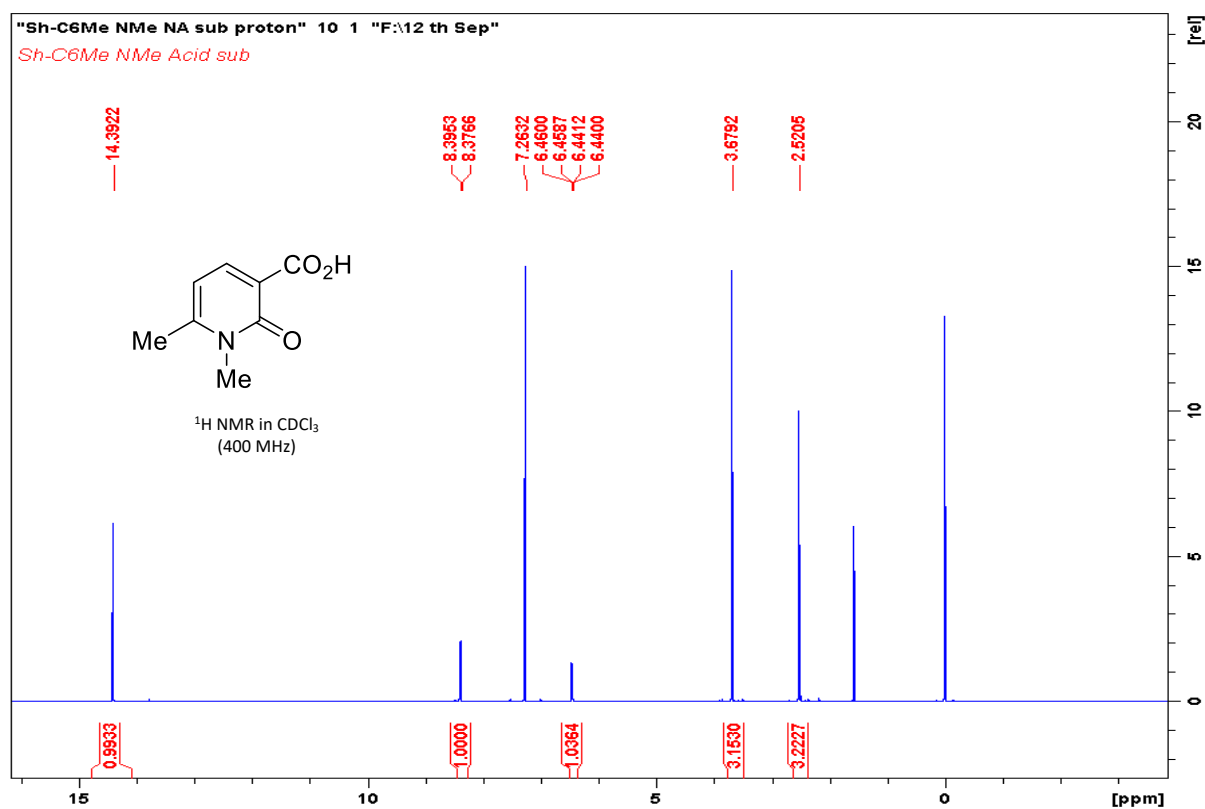
^1H NMR of compound **1d** in CDCl_3 (400 MHz)



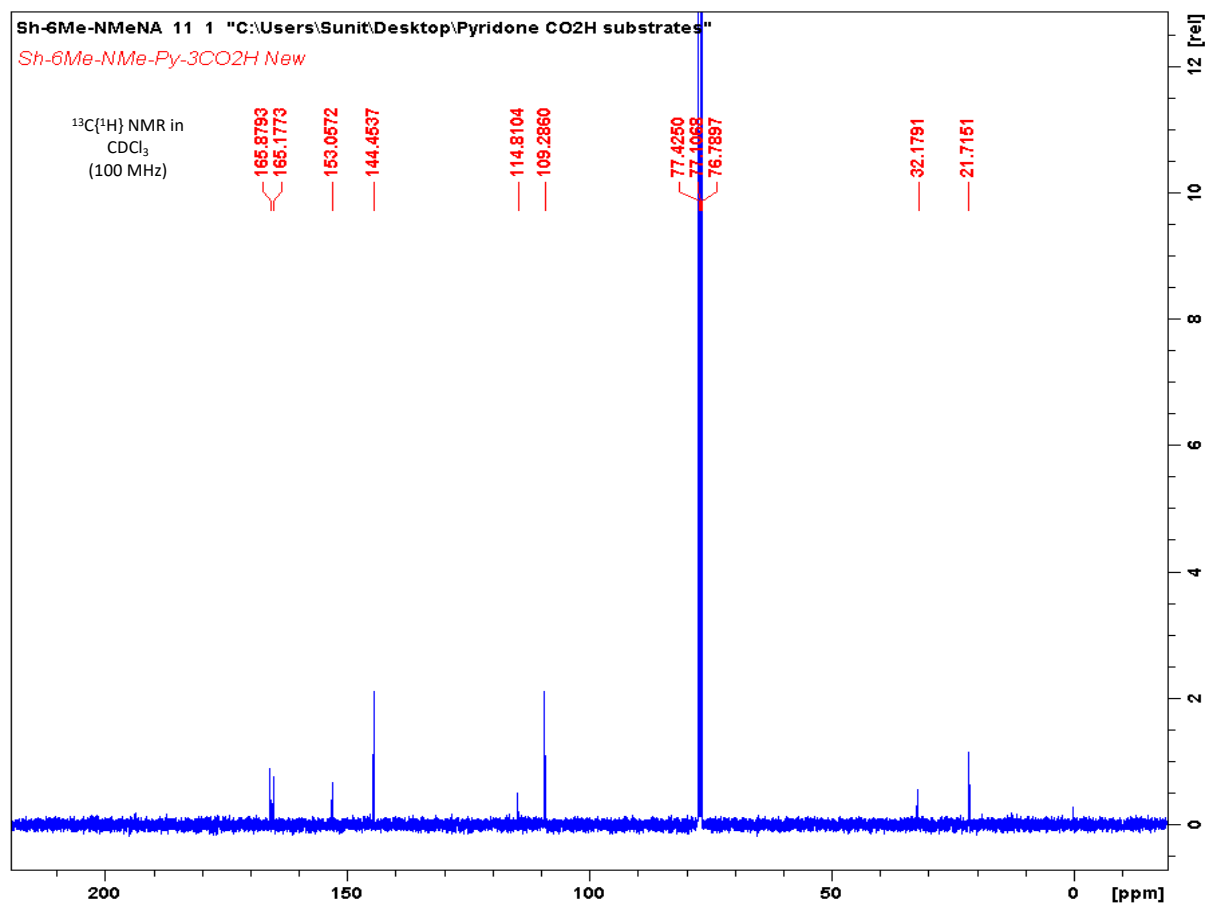
$^{13}\text{C}\{^1\text{H}\}$ NMR of compound **1d** in CDCl_3 (100 MHz)



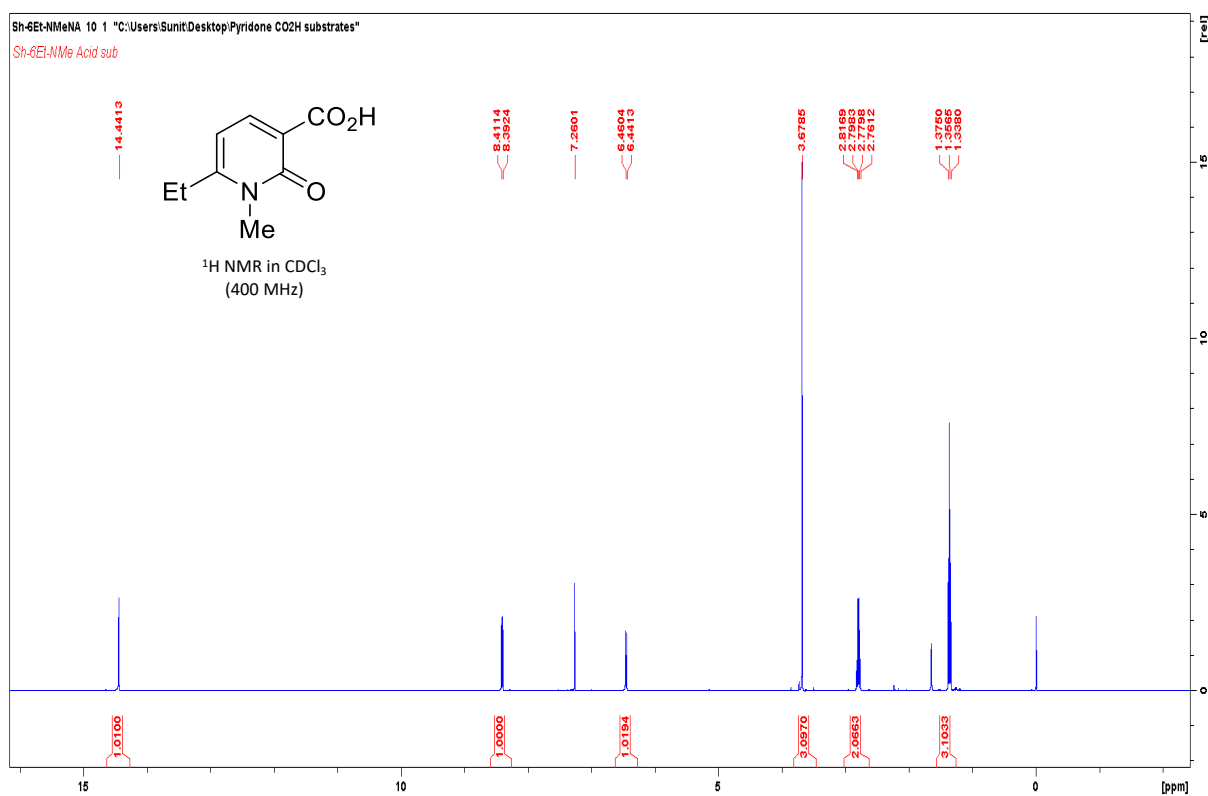
^1H NMR of compound **1e** in CDCl_3 (400 MHz)



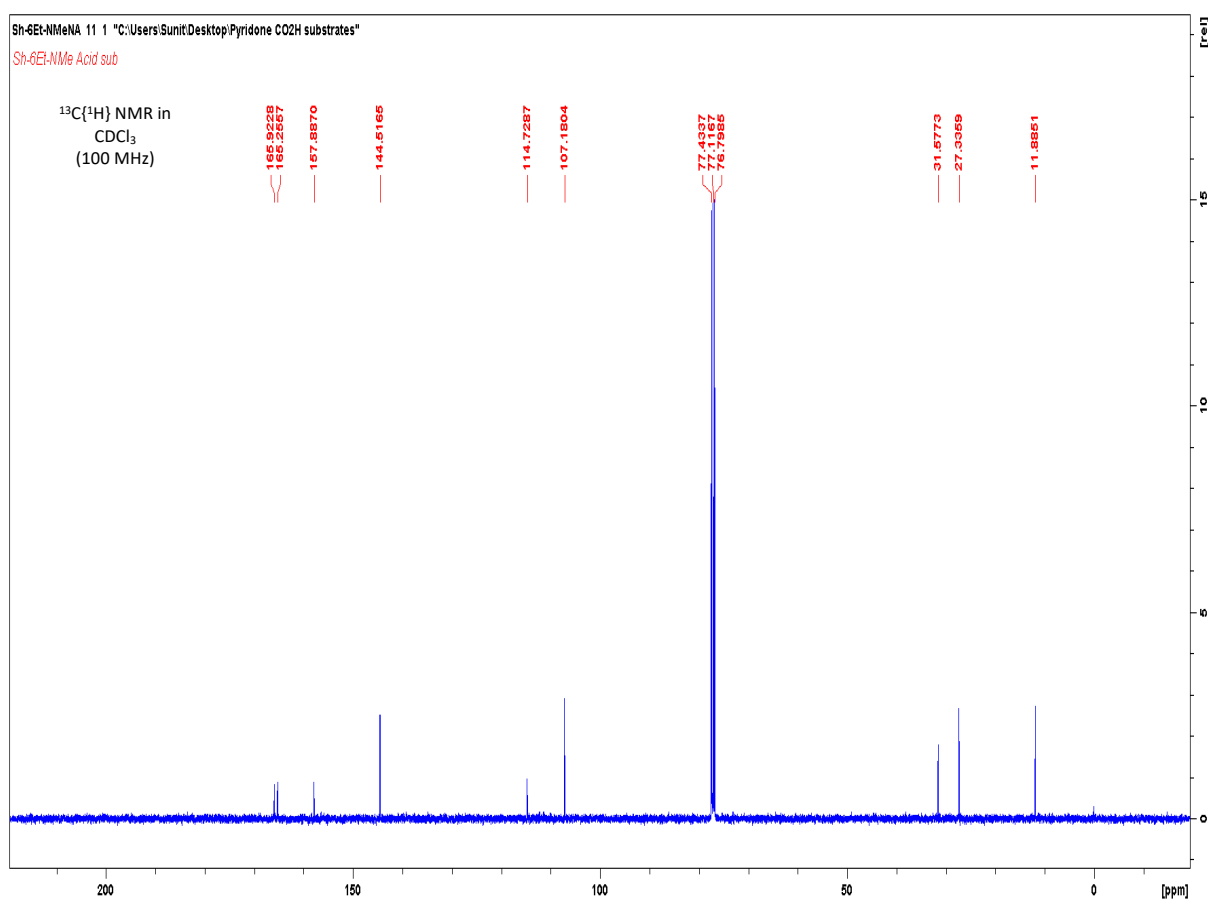
$^{13}\text{C}\{^1\text{H}\}$ NMR of compound **1e** in CDCl_3 (100 MHz)



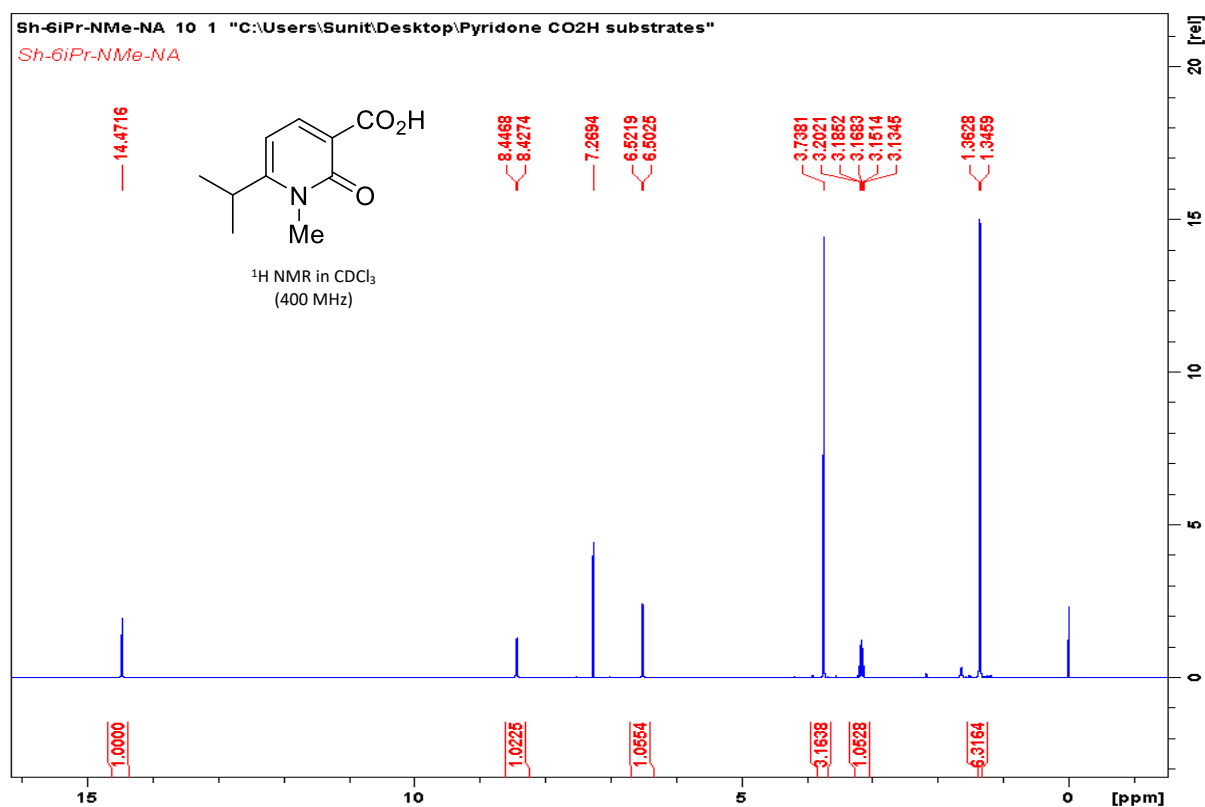
^1H NMR of compound **1f** in CDCl_3 (400 MHz)



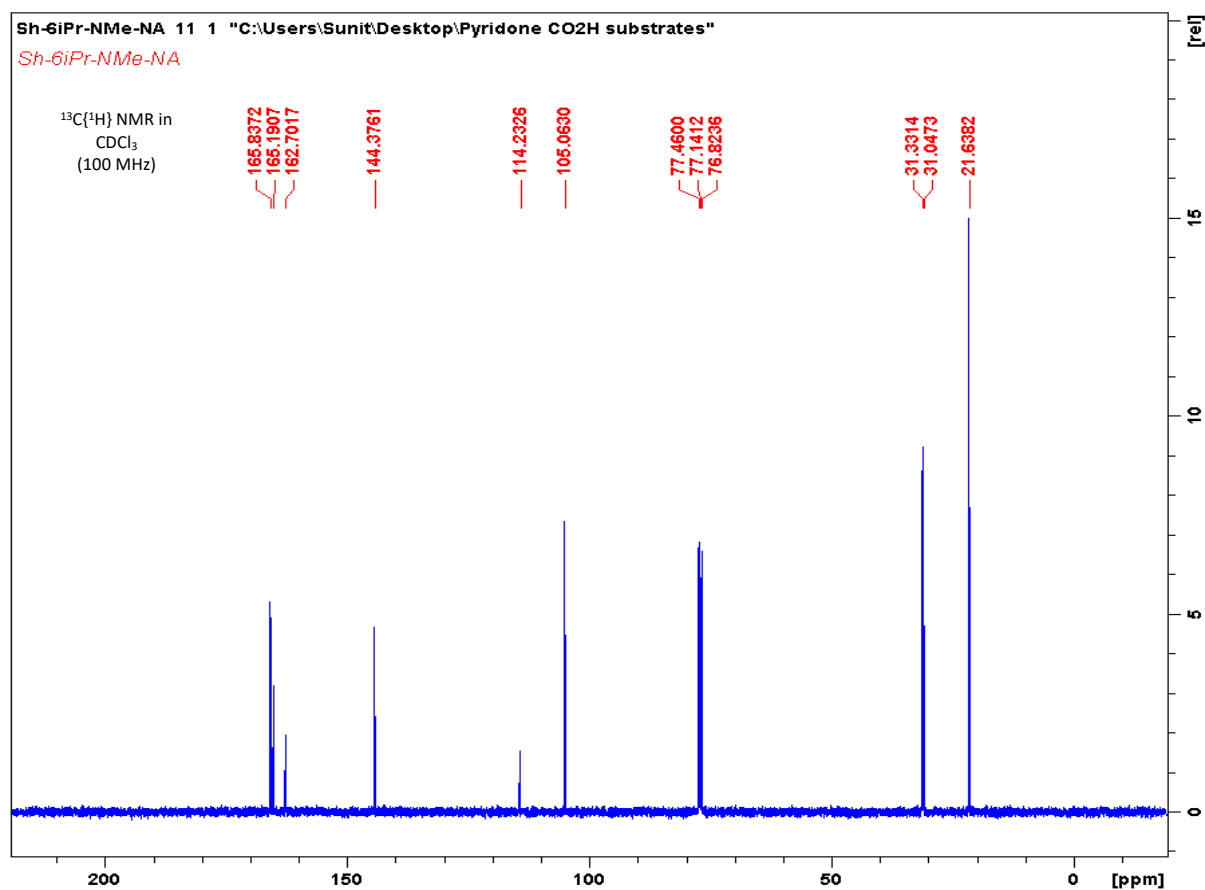
$^{13}\text{C}\{^1\text{H}\}$ NMR of compound **1f** in CDCl_3 (100 MHz)



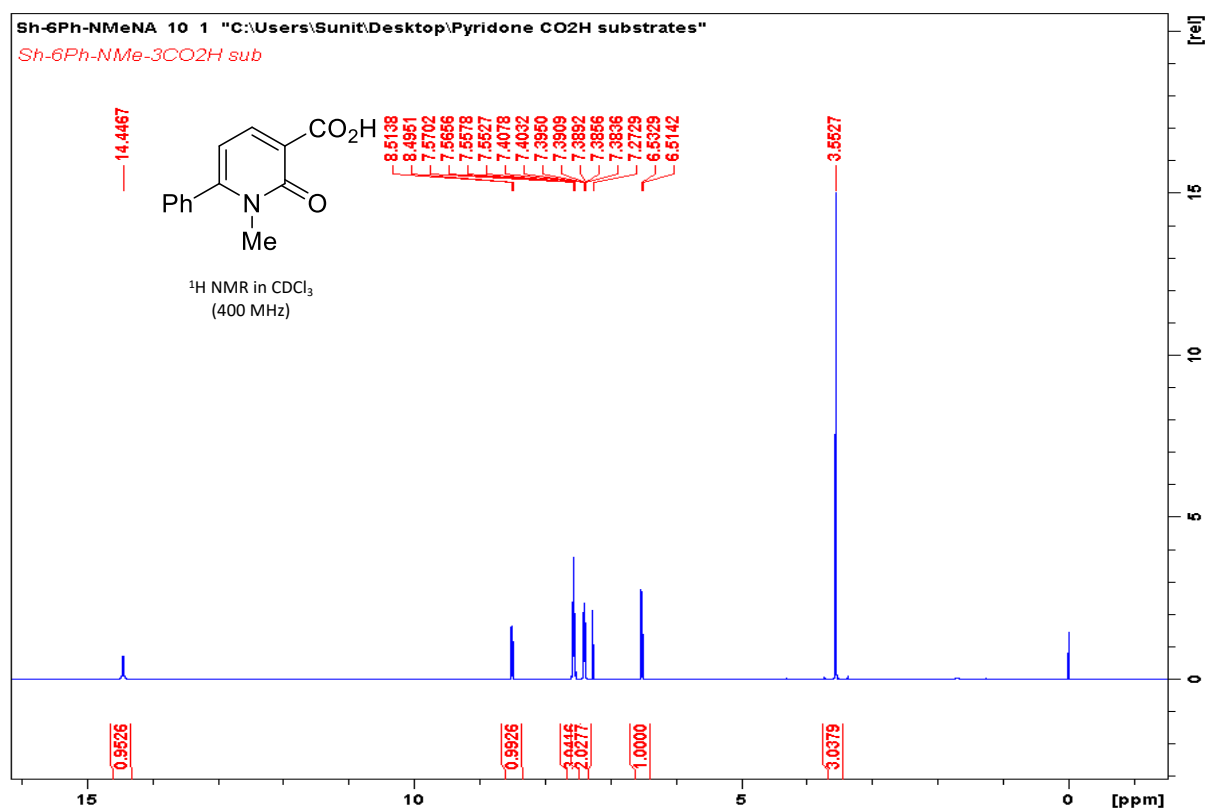
^1H NMR of compound **1g** in CDCl_3 (400 MHz)



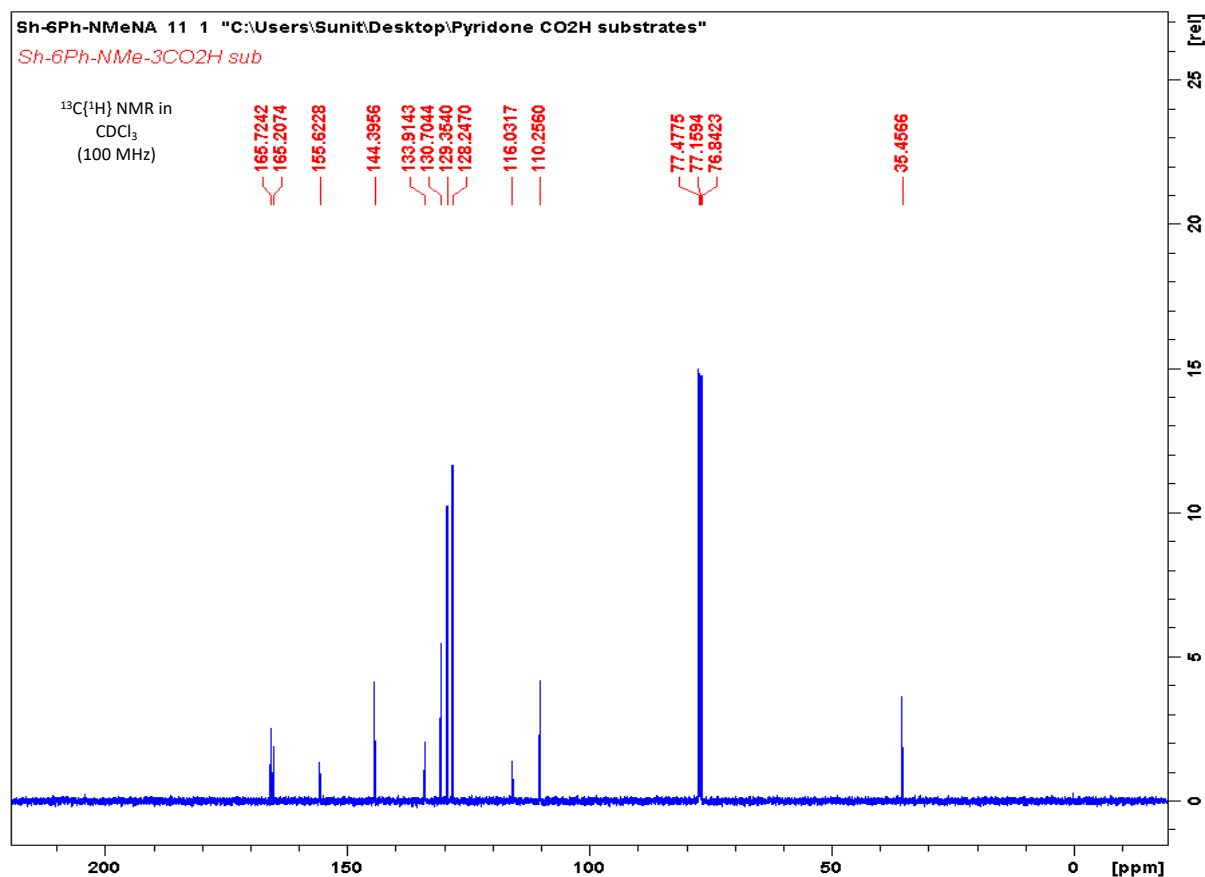
$^{13}\text{C}\{^1\text{H}\}$ NMR of compound **1g** in CDCl_3 (100 MHz)



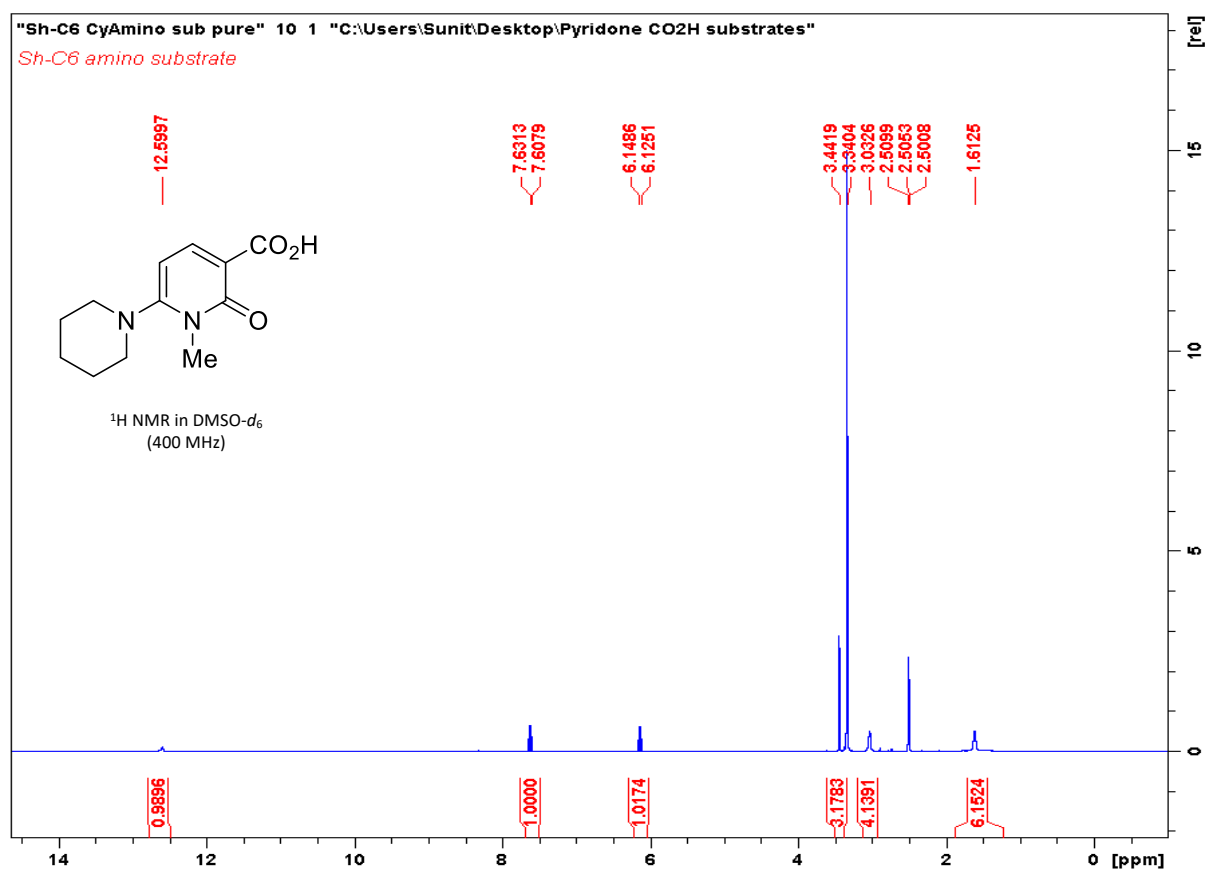
^1H NMR of compound **1h** in CDCl_3 (400 MHz)



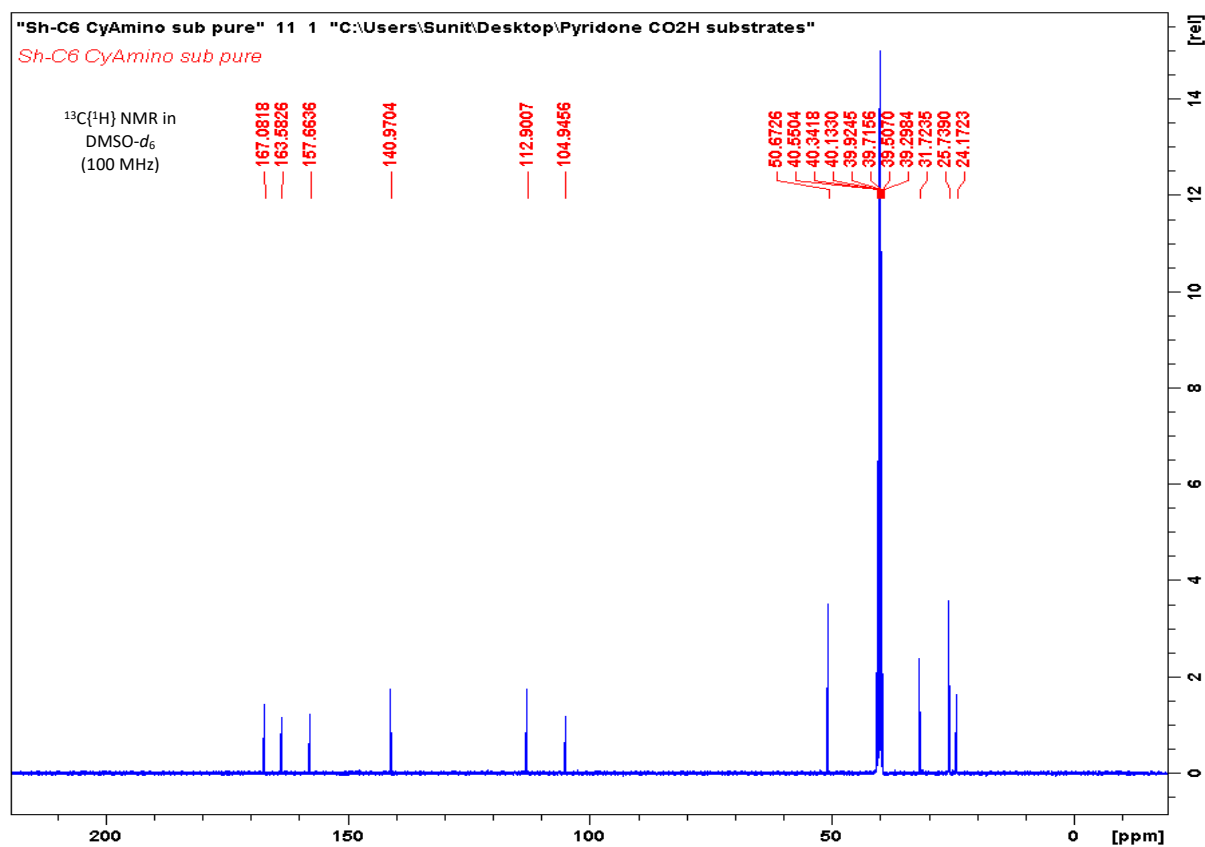
$^{13}\text{C}\{^1\text{H}\}$ NMR of compound **1h** in CDCl_3 (100 MHz)



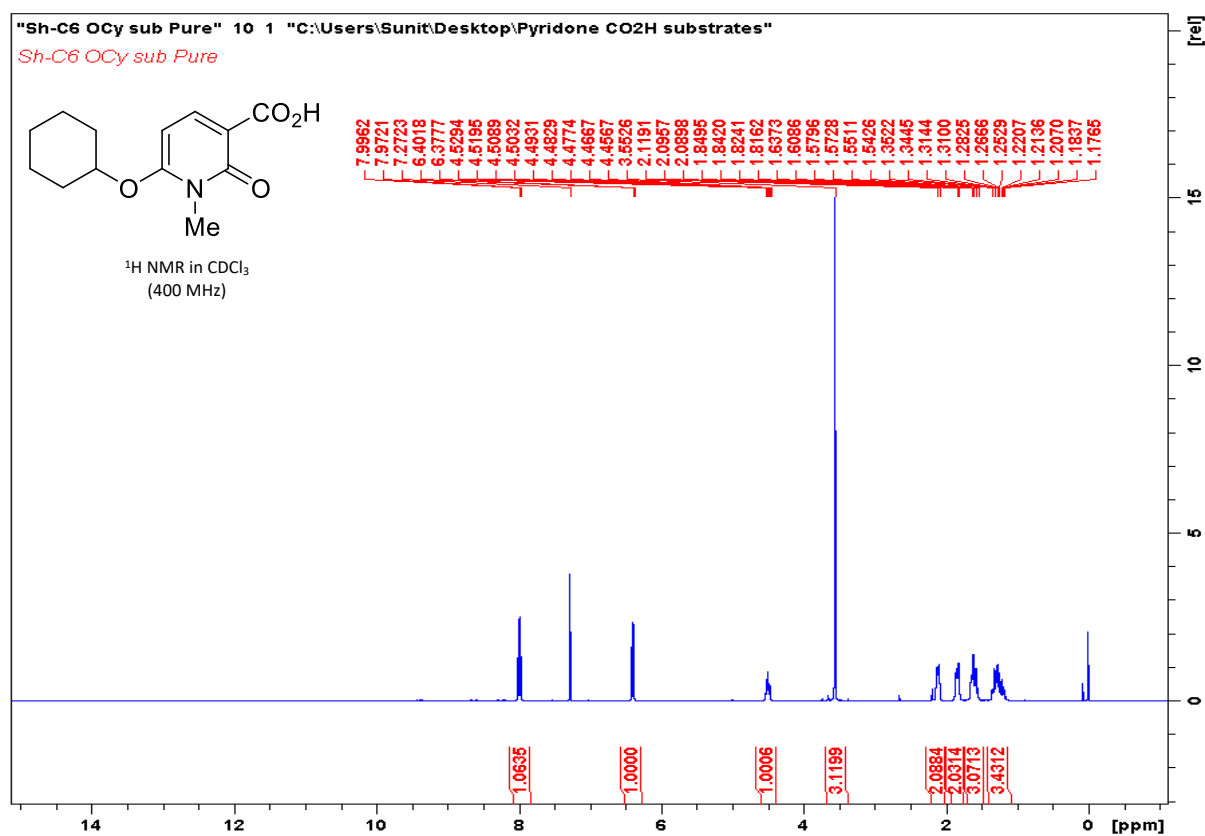
^1H NMR of compound **1i** in $\text{DMSO}-d_6$ (400 MHz)



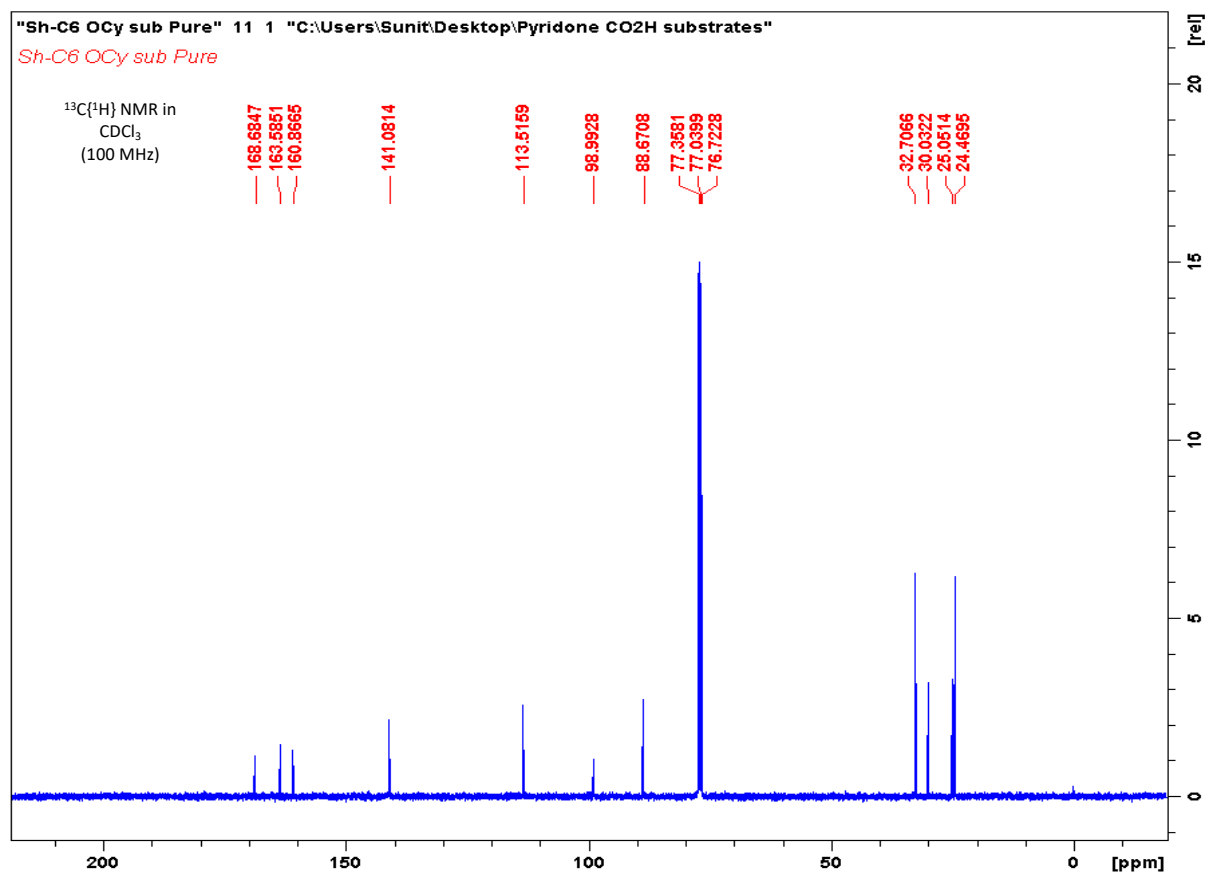
$^{13}\text{C}\{^1\text{H}\}$ NMR of compound **1i** in $\text{DMSO}-d_6$ (100 MHz)



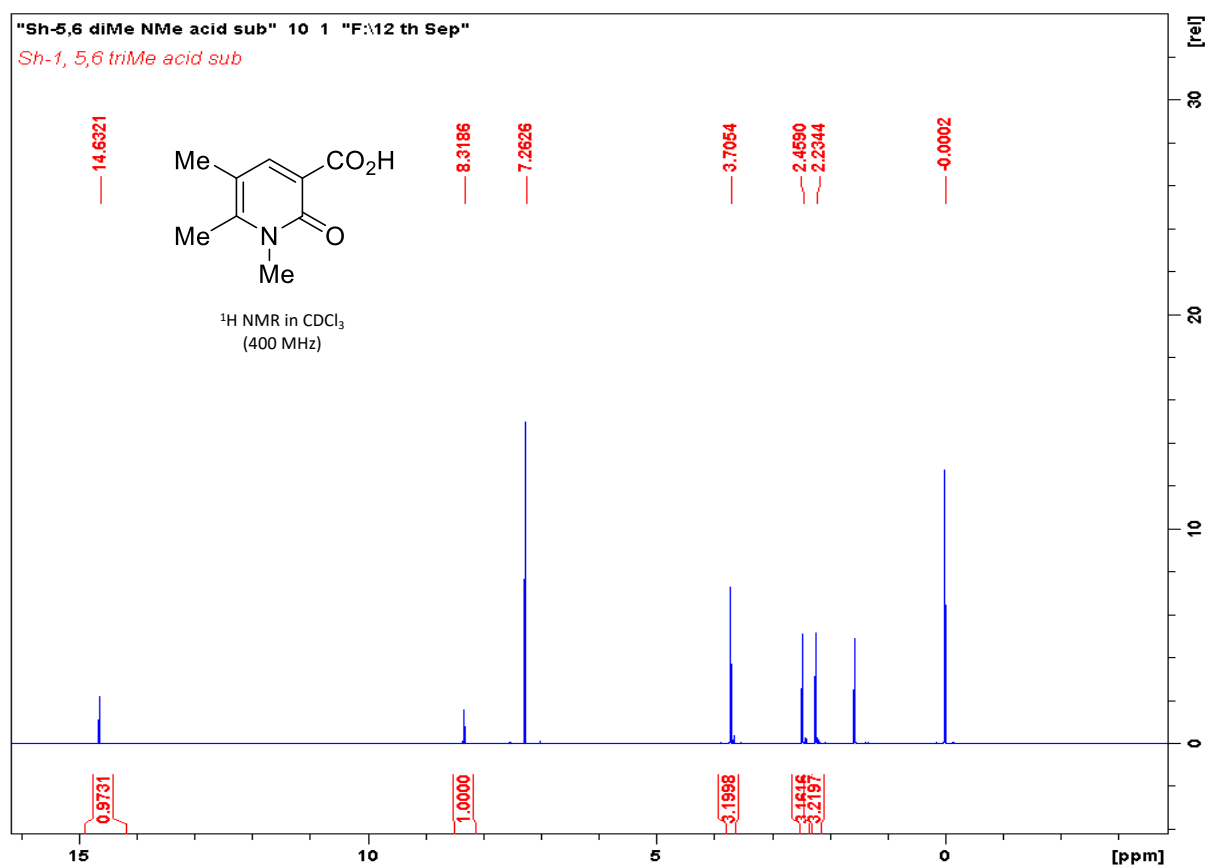
^1H NMR of compound **1j** in CDCl_3 (400 MHz)



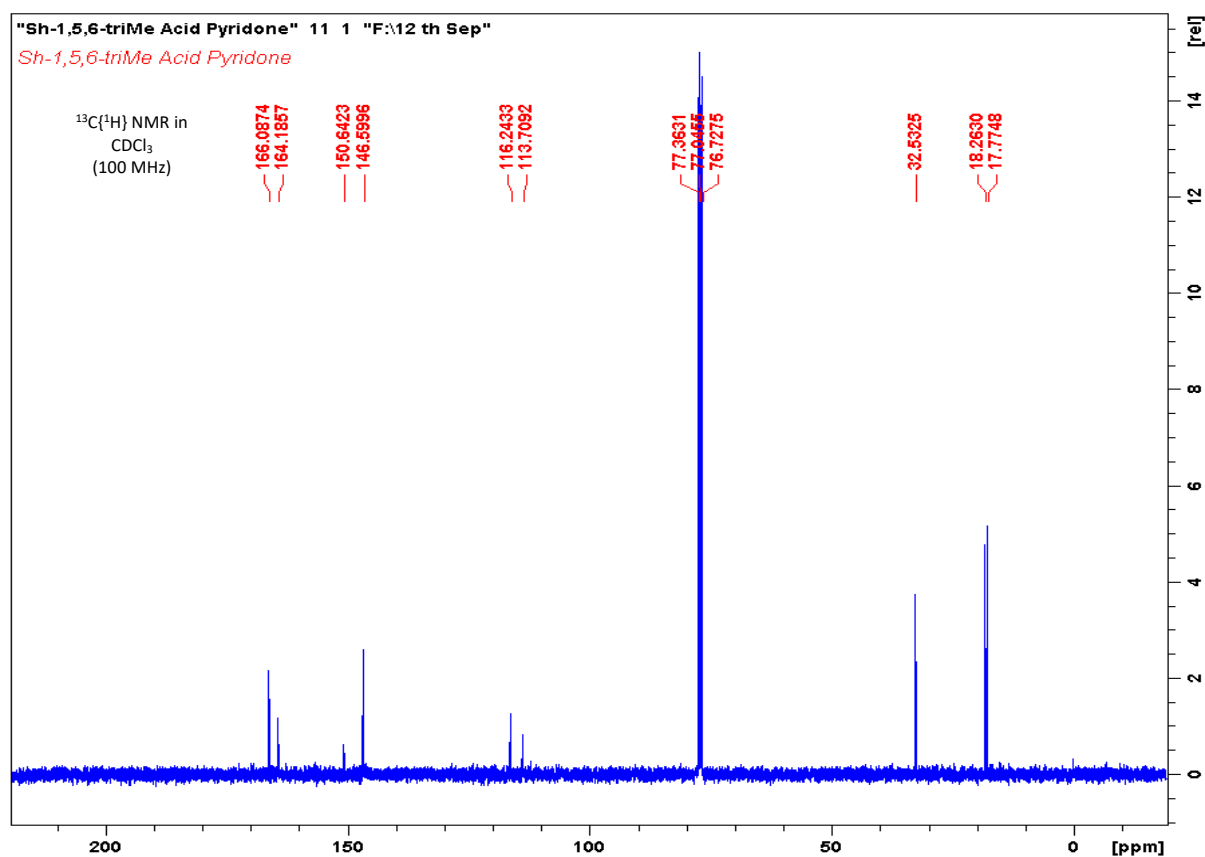
$^{13}\text{C}\{^1\text{H}\}$ NMR of compound **1j** in CDCl_3 (100 MHz)



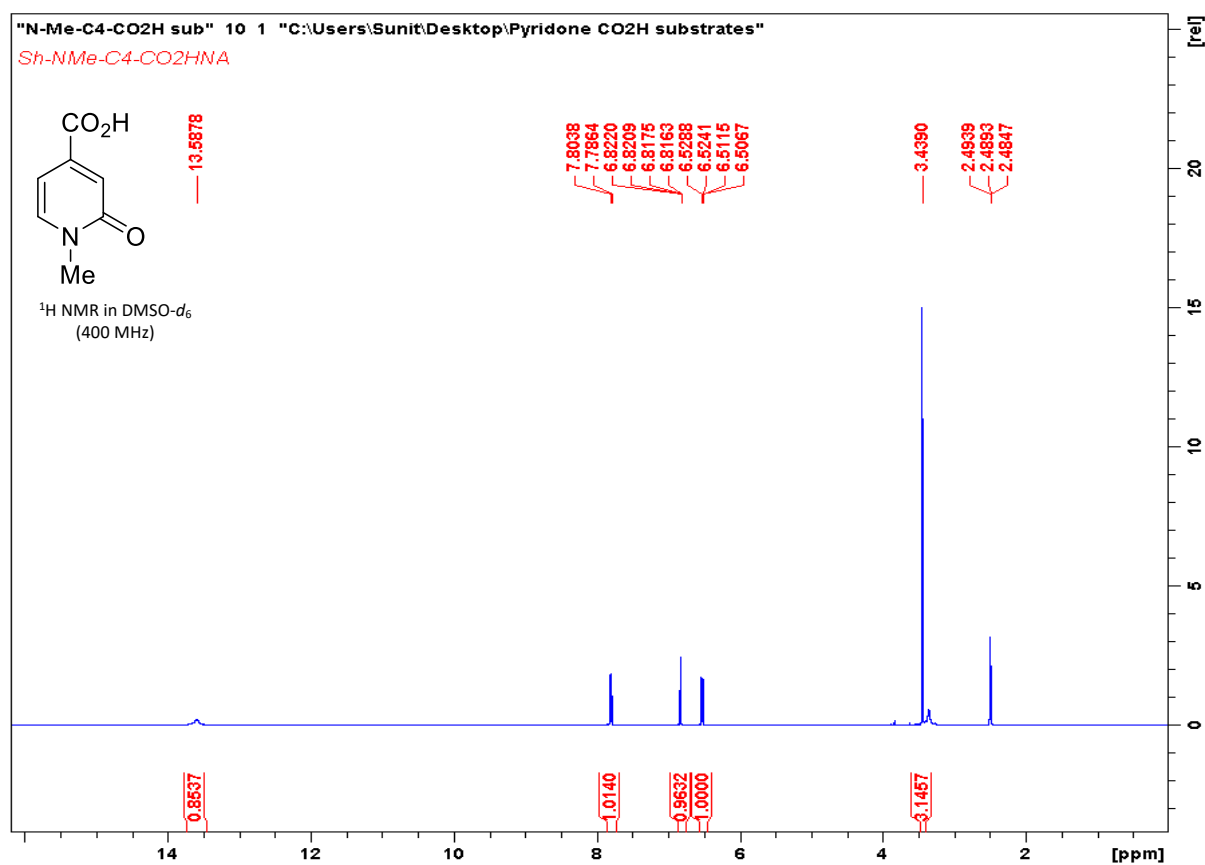
^1H NMR of compound **1k** in CDCl_3 (400 MHz)



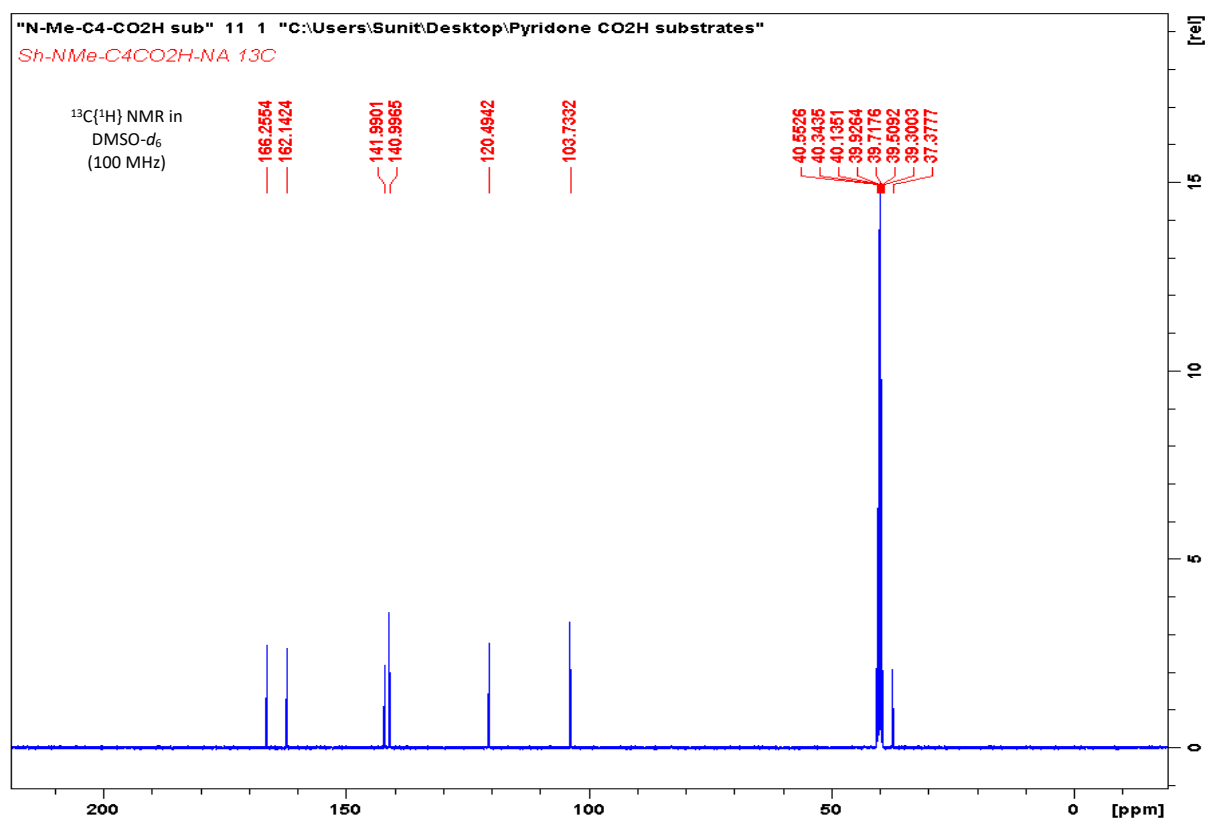
$^{13}\text{C}\{^1\text{H}\}$ NMR of compound **1k** in CDCl_3 (100 MHz)



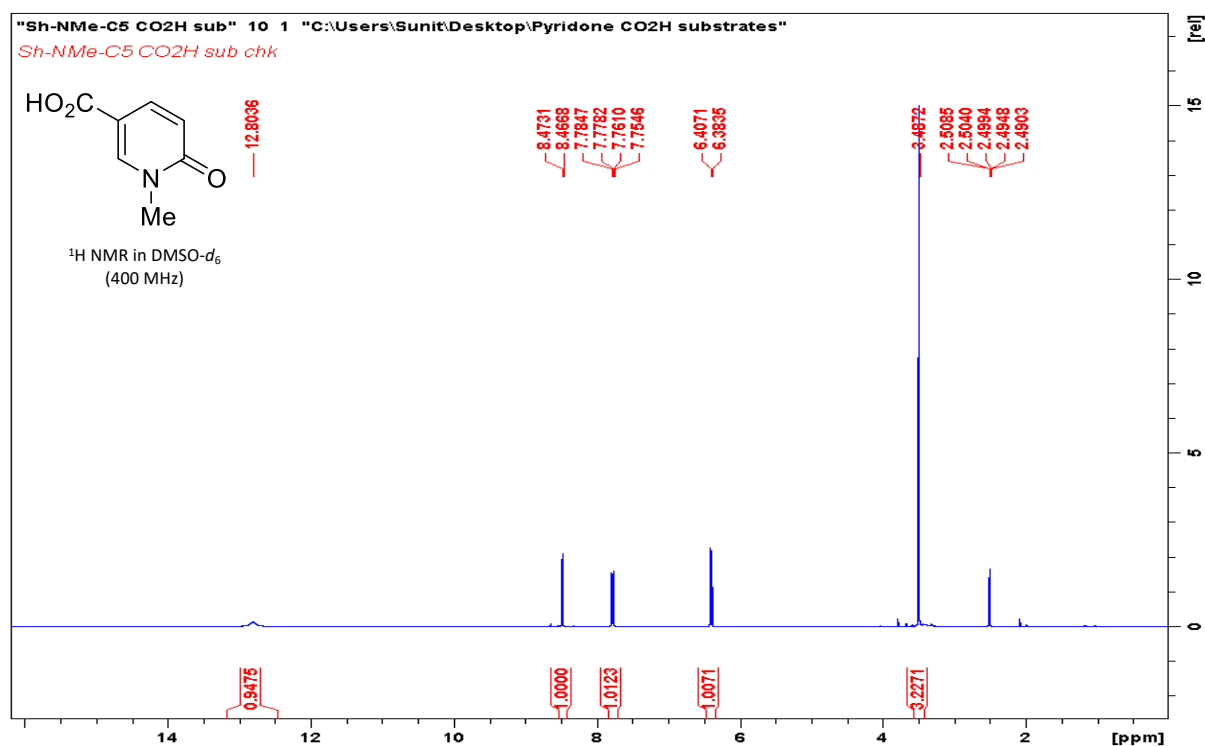
^1H NMR of compound **7a** in $\text{DMSO}-d_6$ (400 MHz)



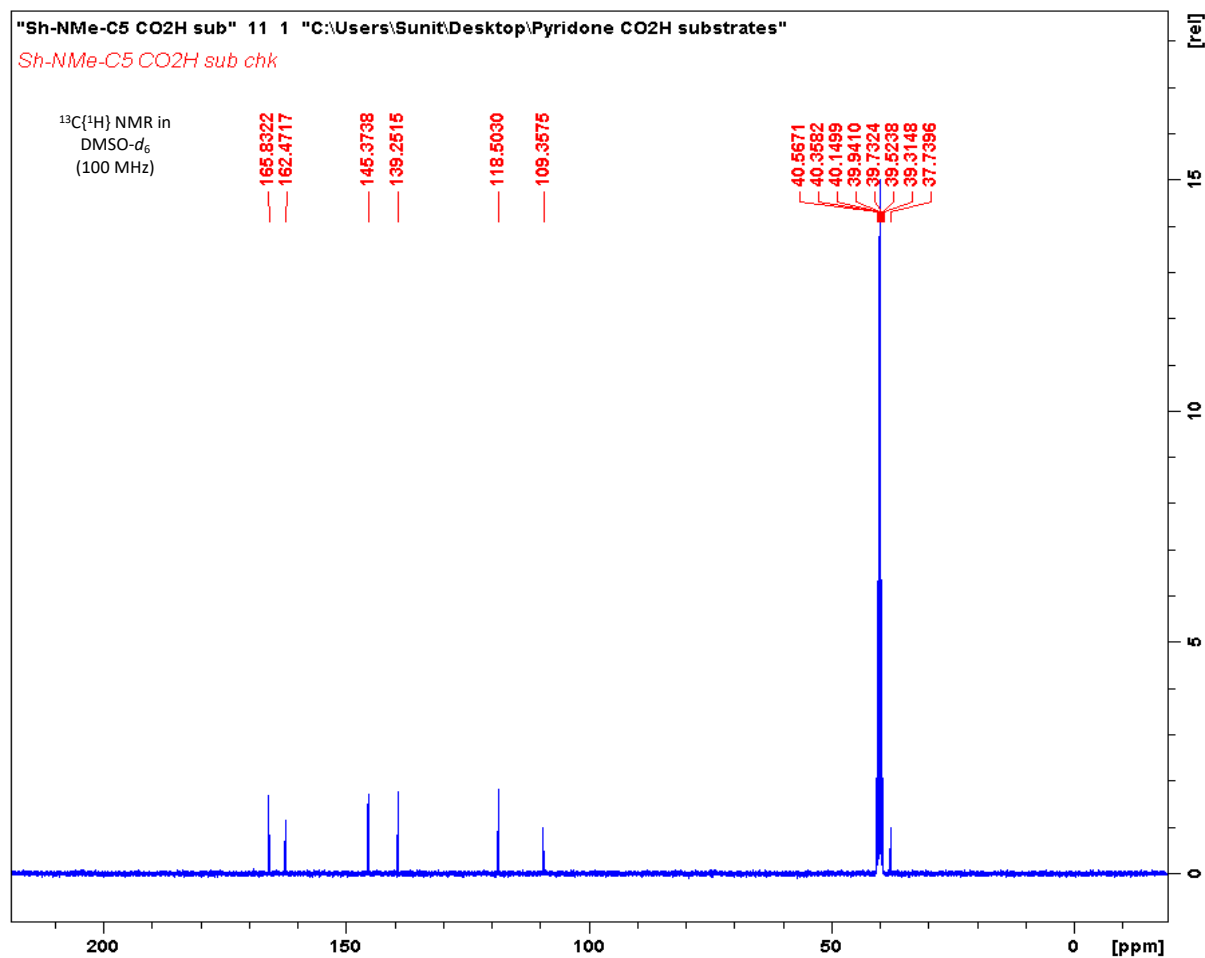
$^{13}\text{C}\{^1\text{H}\}$ NMR of compound **7a** in $\text{DMSO}-d_6$ (100 MHz)



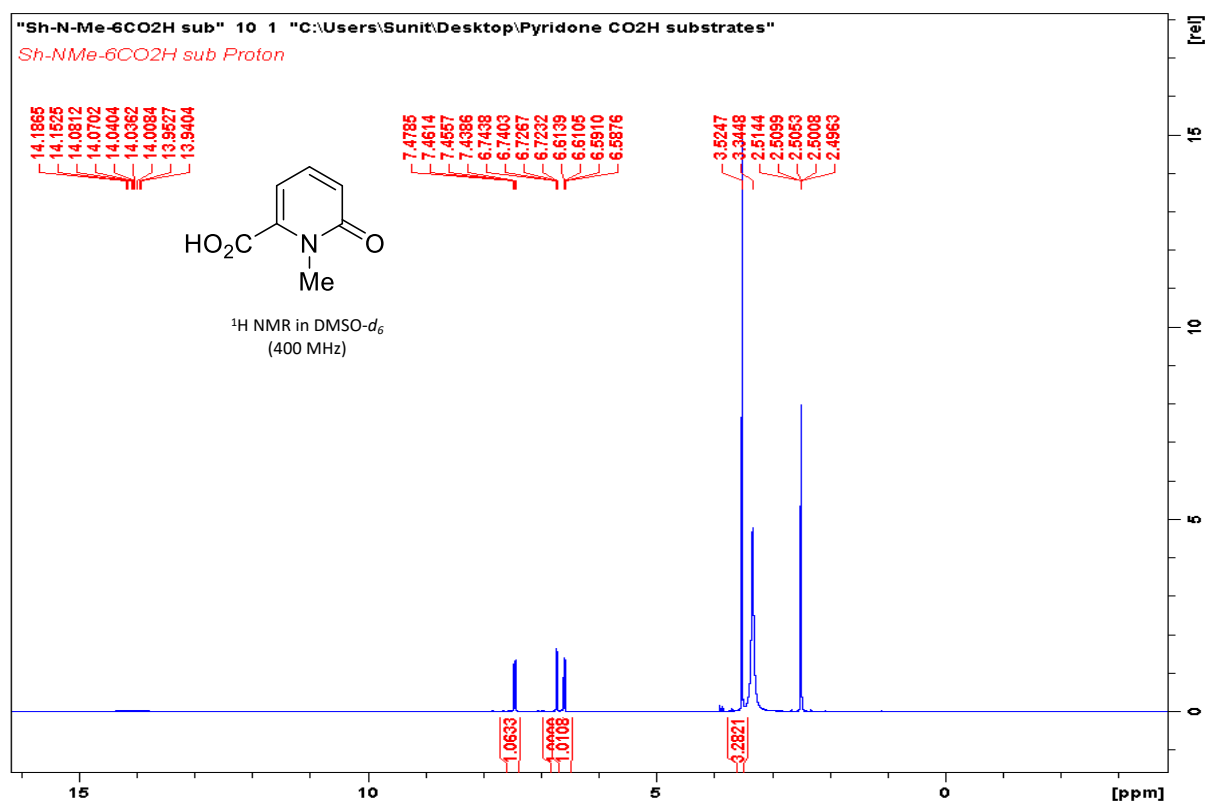
^1H NMR of compound **9a** in $\text{DMSO}-d_6$ (400 MHz)



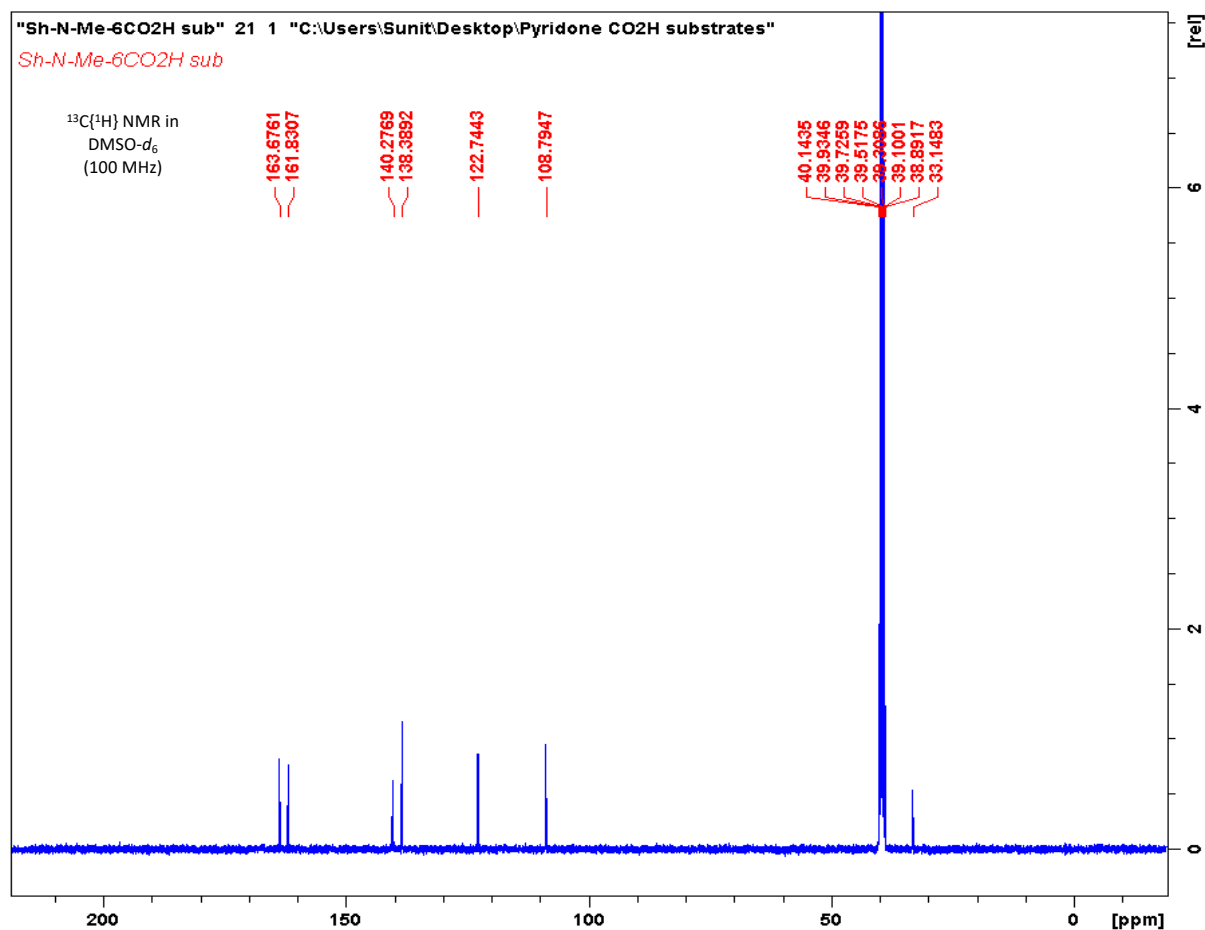
$^{13}\text{C}\{^1\text{H}\}$ NMR of compound **9a** in $\text{DMSO}-d_6$ (100 MHz)



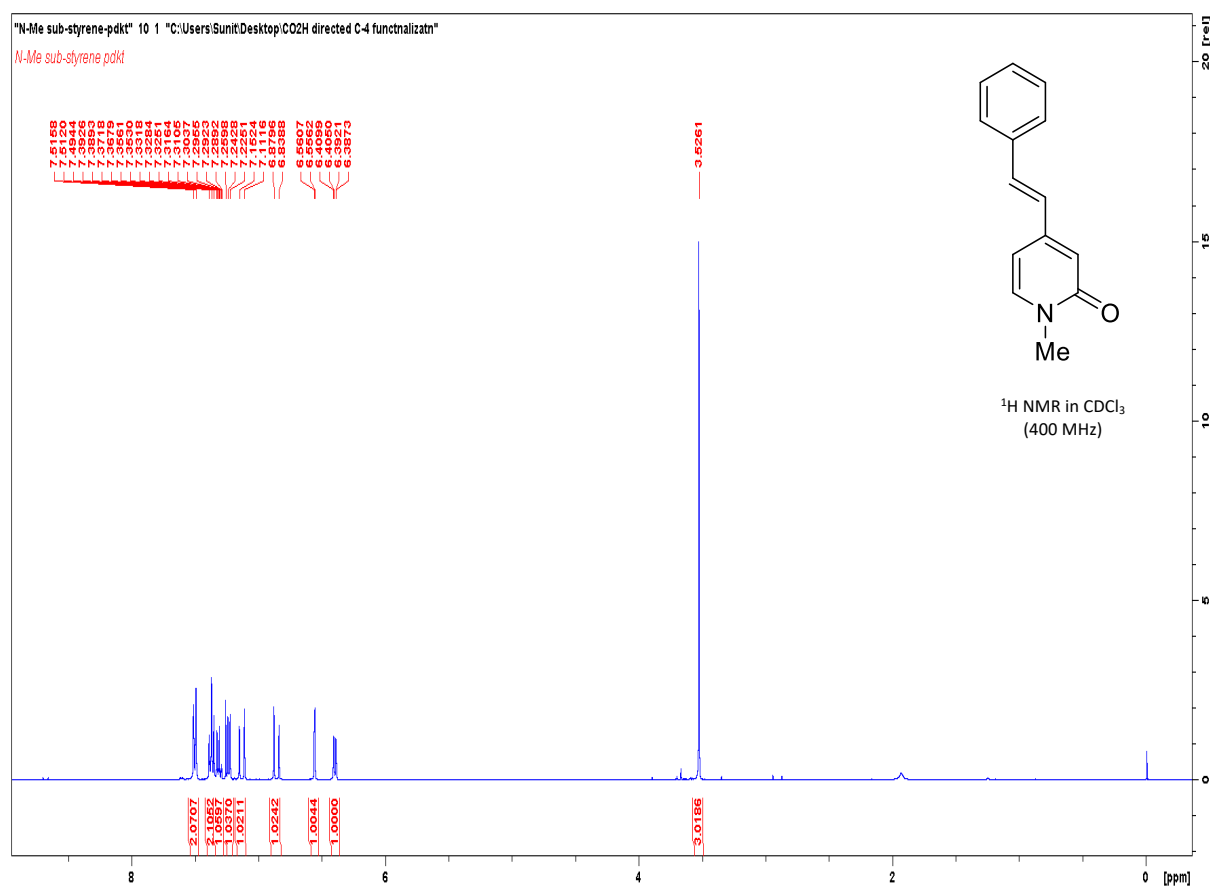
^1H NMR of compound **13a** in $\text{DMSO-}d_6$ (400 MHz)



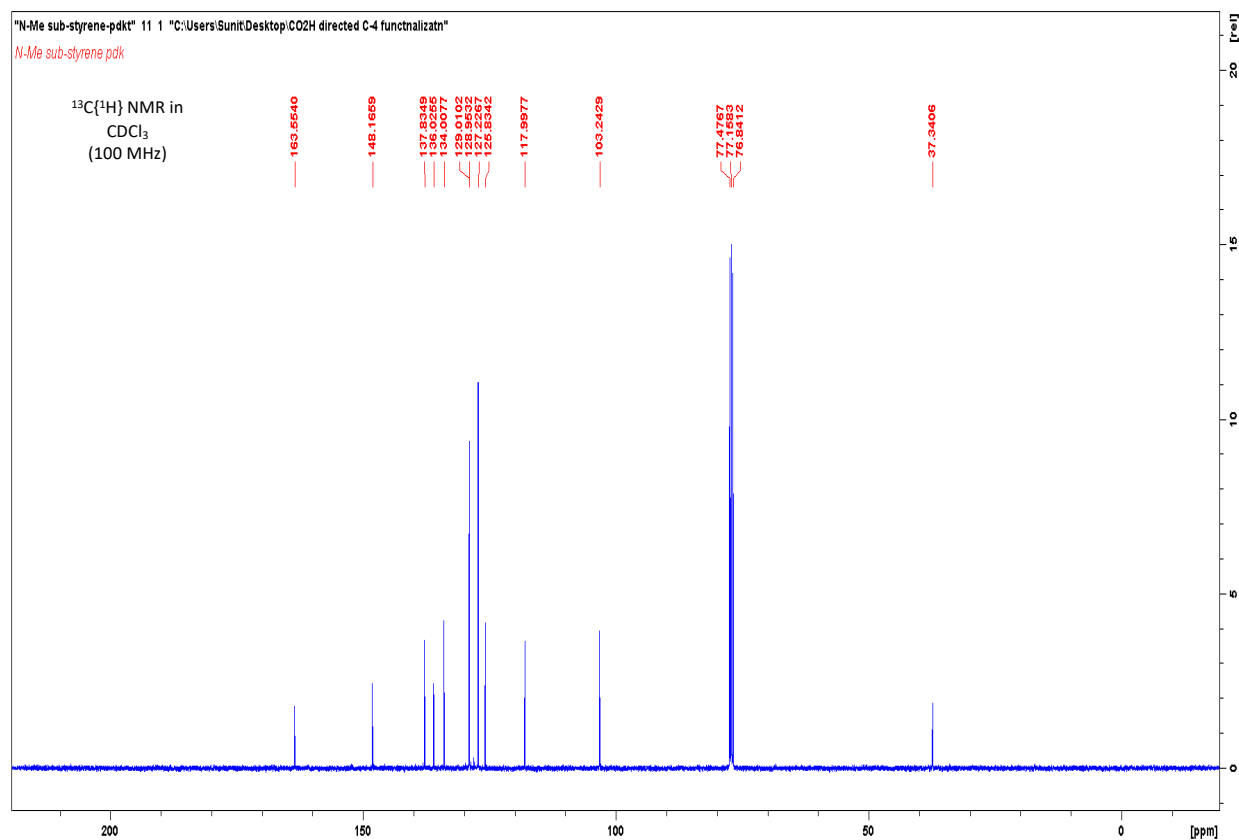
$^{13}\text{C}\{^1\text{H}\}$ NMR of compound **13a** in $\text{DMSO-}d_6$ (100 MHz)



¹H NMR of compound **3aa** in CDCl₃ (400 MHz)



¹³C{¹H} NMR of compound **3aa** in CDCl₃ (100 MHz)



"N-Et substrate-styrene pdkt pure" 10 1 "C:\Users\Sunit\Desktop\CO2H directed C-4 functnalizatr"

Sh-N-Et sub-styrene pdkt pure

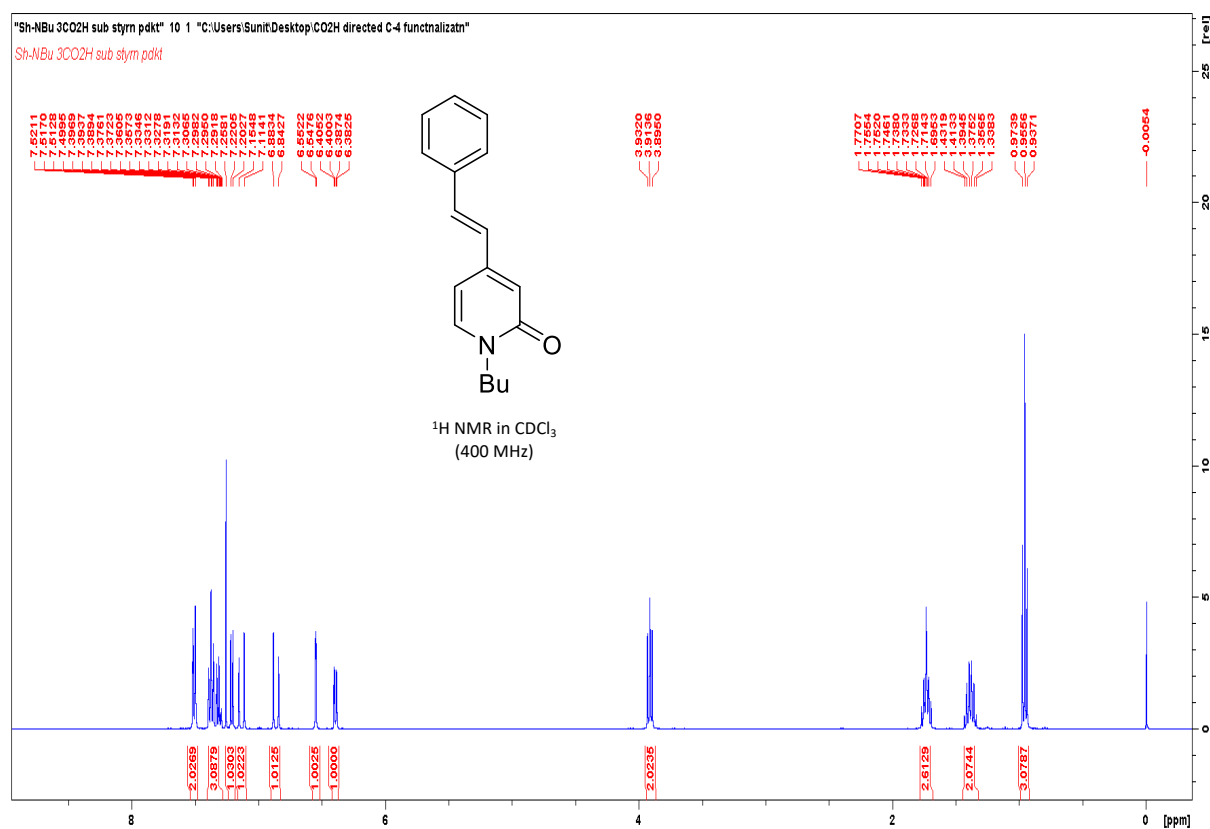
¹³C{¹H} NMR in CDCl₃ (100 MHz)

Sh-N-Et-sub-styrene pdkt pure

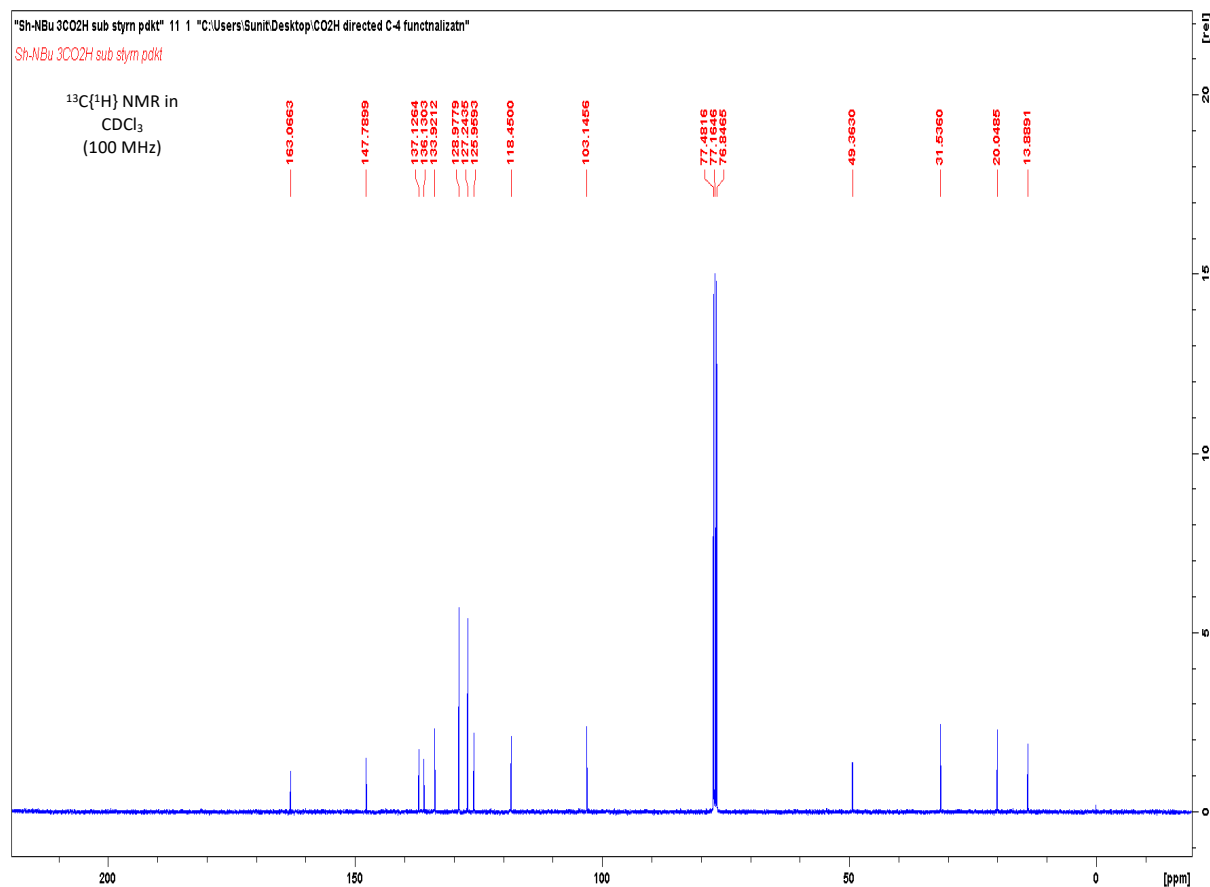
162.9237, 147.8873, 136.5712, 136.0980, 133.9486, 128.9941, 128.9871, 127.2347, 125.9053, 118.3983, 103.4881, 77.4261, 77.1650, 76.8370, 44.5004, 14.8671

ppm

^1H NMR of compound **3ca** in CDCl_3 (400 MHz)



$^{13}\text{C}\{^1\text{H}\}$ NMR of compound **3ca** in CDCl_3 (100 MHz)



¹H NMR sub styrene pdkt¹⁰ 10 1 "C:\Users\Sunit\Desktop\CO2H directed C-4 functionalizatn"

Sh-N-Bn sub styrene pdkt

¹H NMR in CDCl₃ (400 MHz)

Chemical structure of the compound: c1ccc(cc1)/C=C/c2ccc(cc2)C(=O)Nc3ccccc3

Integration values (from left to right): 2.0363, 7.9891, 1.0038, 1.0370, 0.9917, 0.9910, 1.0000, 2.0119, 5.1439.

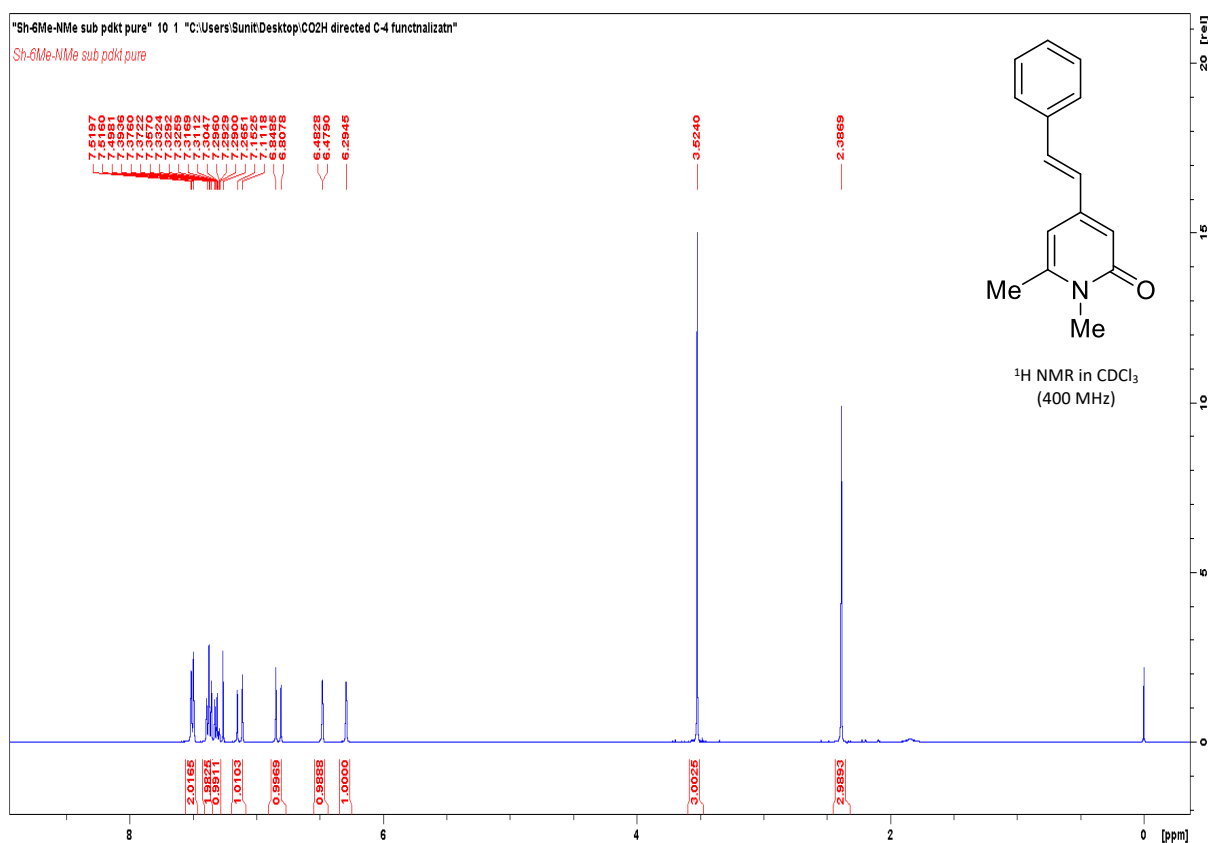
¹³C{¹H} NMR in CDCl₃ (100 MHz)

Sh-N-Bn sub styrene pdkt

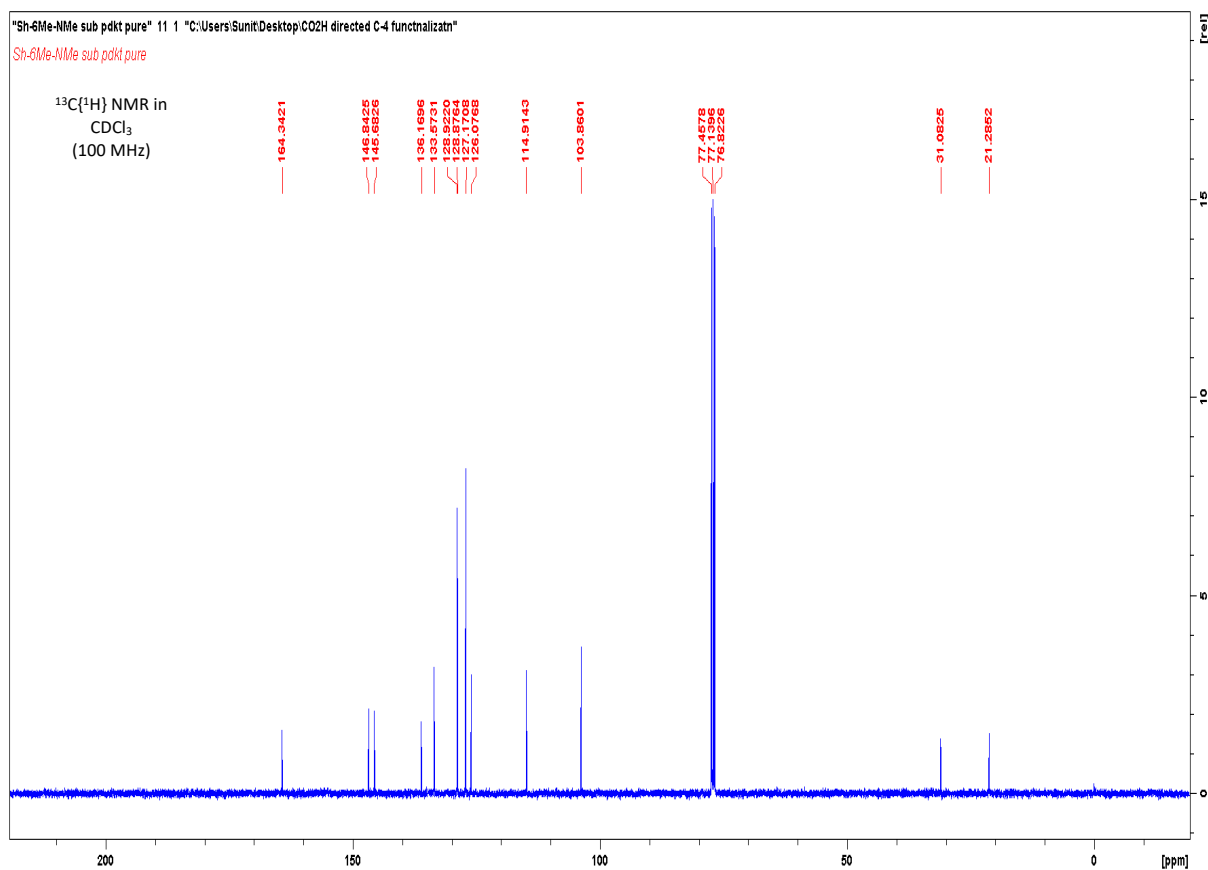
163.1004, 147.9733, 136.7768, 136.6279, 136.5279, 136.2000, 136.2000, 129.0115, 129.0085, 128.9690, 128.9690, 128.0629, 128.0629, 126.5284, 126.5284, 118.4477, 103.5820, 77.4783, 77.4783, 76.8375, 51.5812

ppm

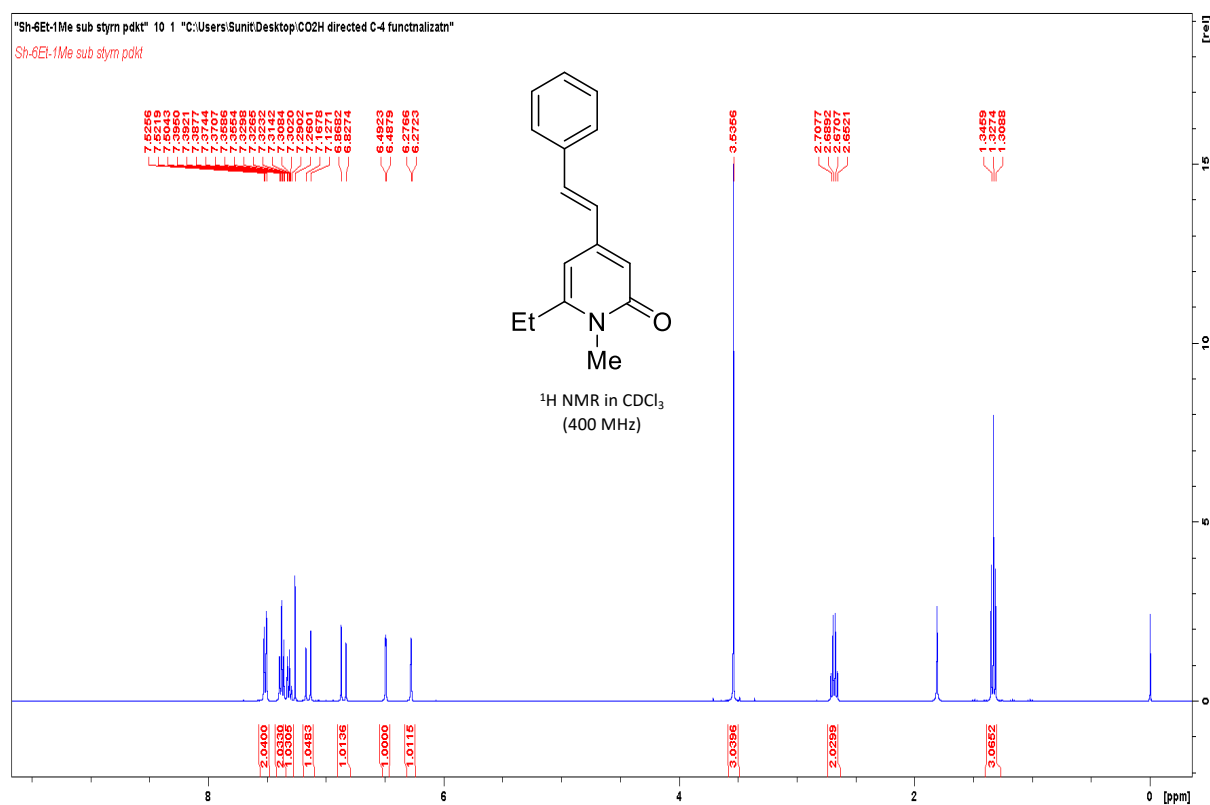
^1H NMR of compound **3ea** in CDCl_3 (400 MHz)



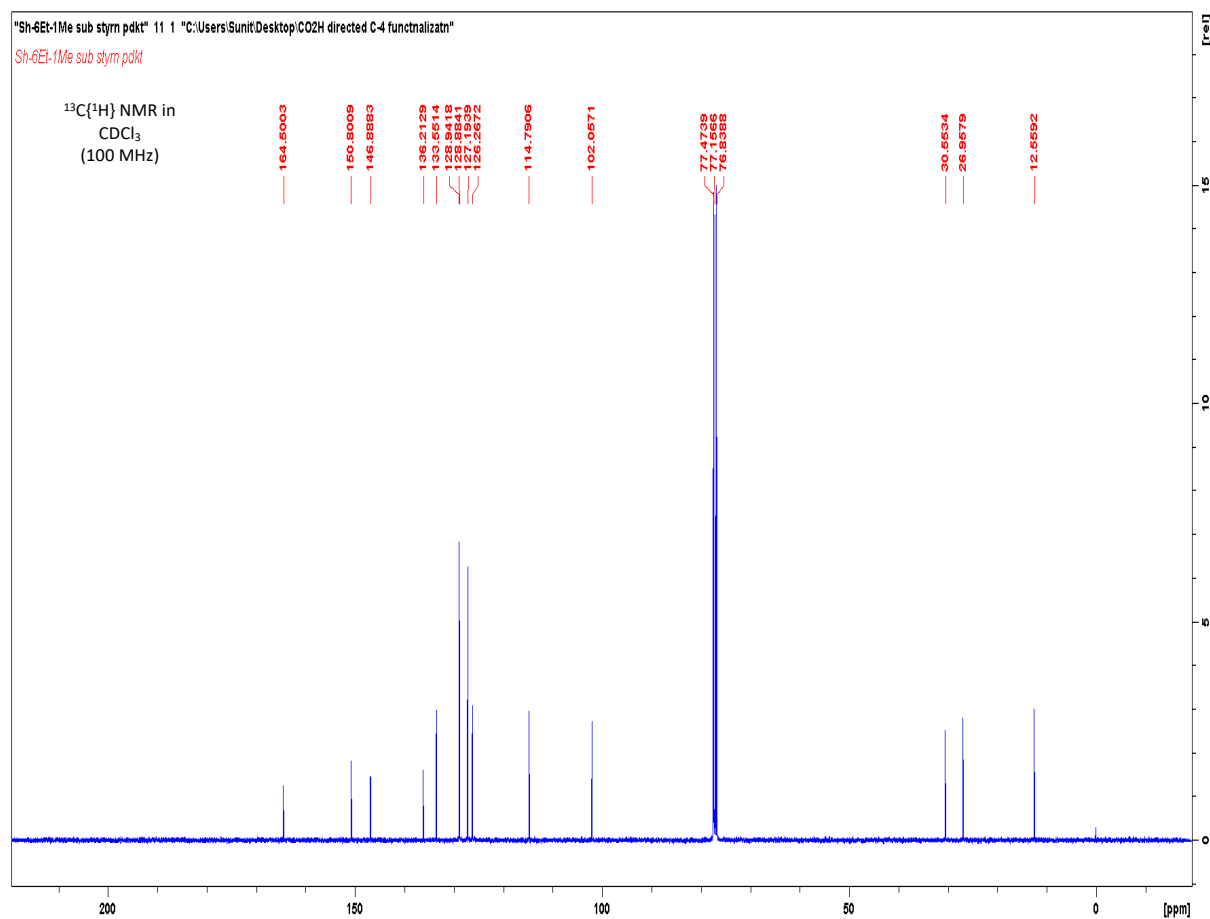
$^{13}\text{C}\{^1\text{H}\}$ NMR of compound **3ea** in CDCl_3 (100 MHz)



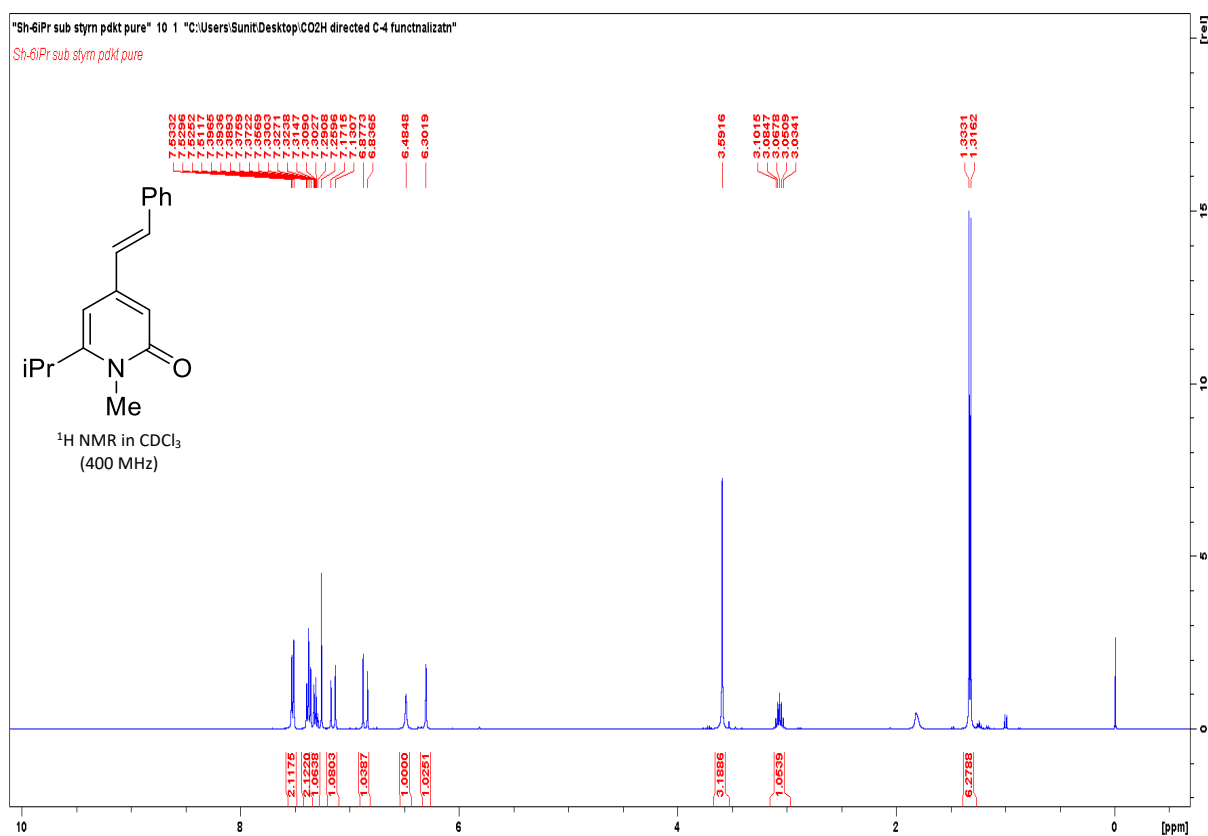
^1H NMR of compound **3fa** in CDCl_3 (400 MHz)



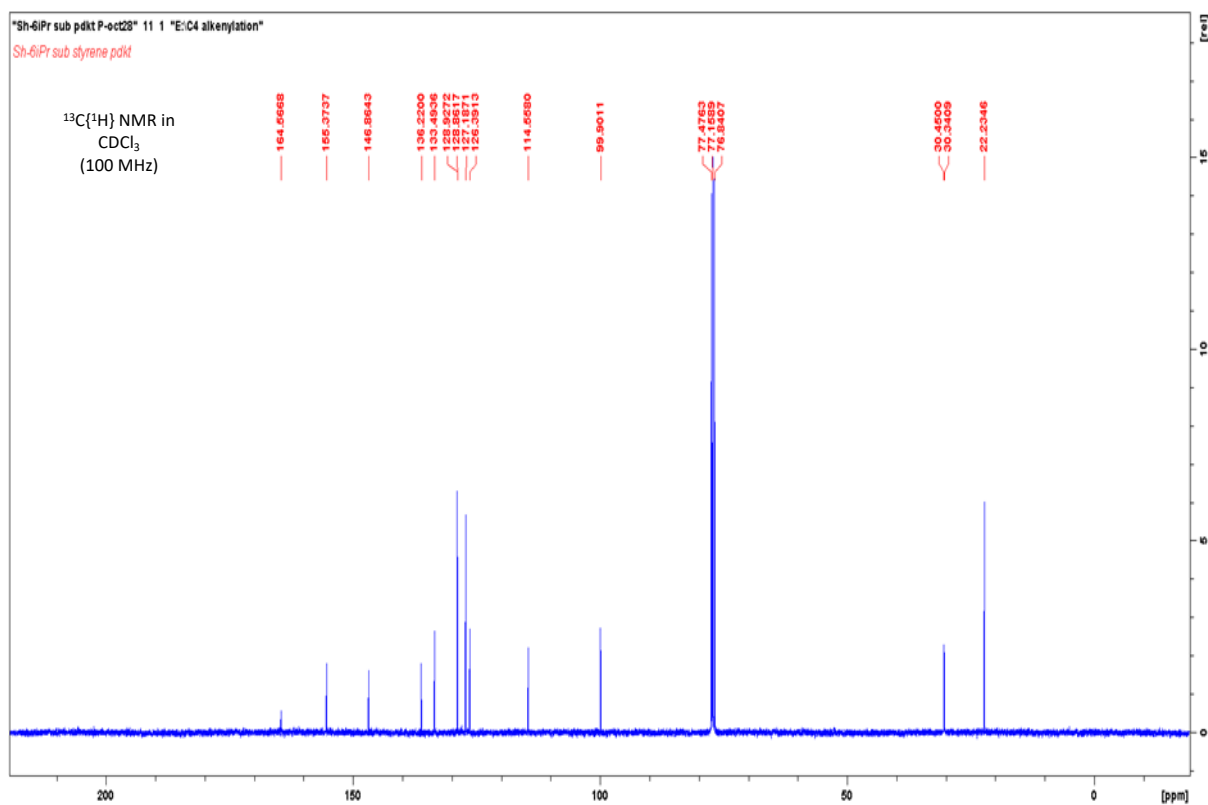
$^{13}\text{C}\{^1\text{H}\}$ NMR of compound **3fa** in CDCl_3 (100 MHz)



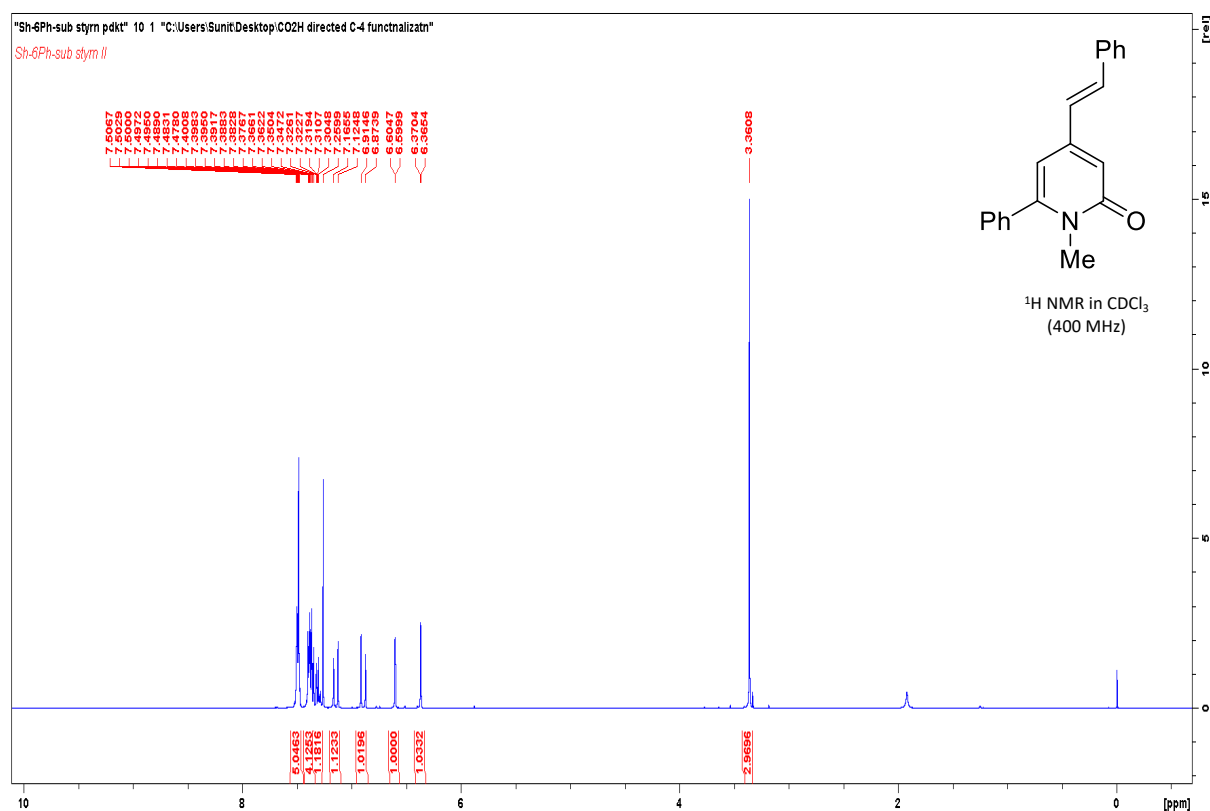
^1H NMR of compound **3ga** in CDCl_3 (400 MHz)



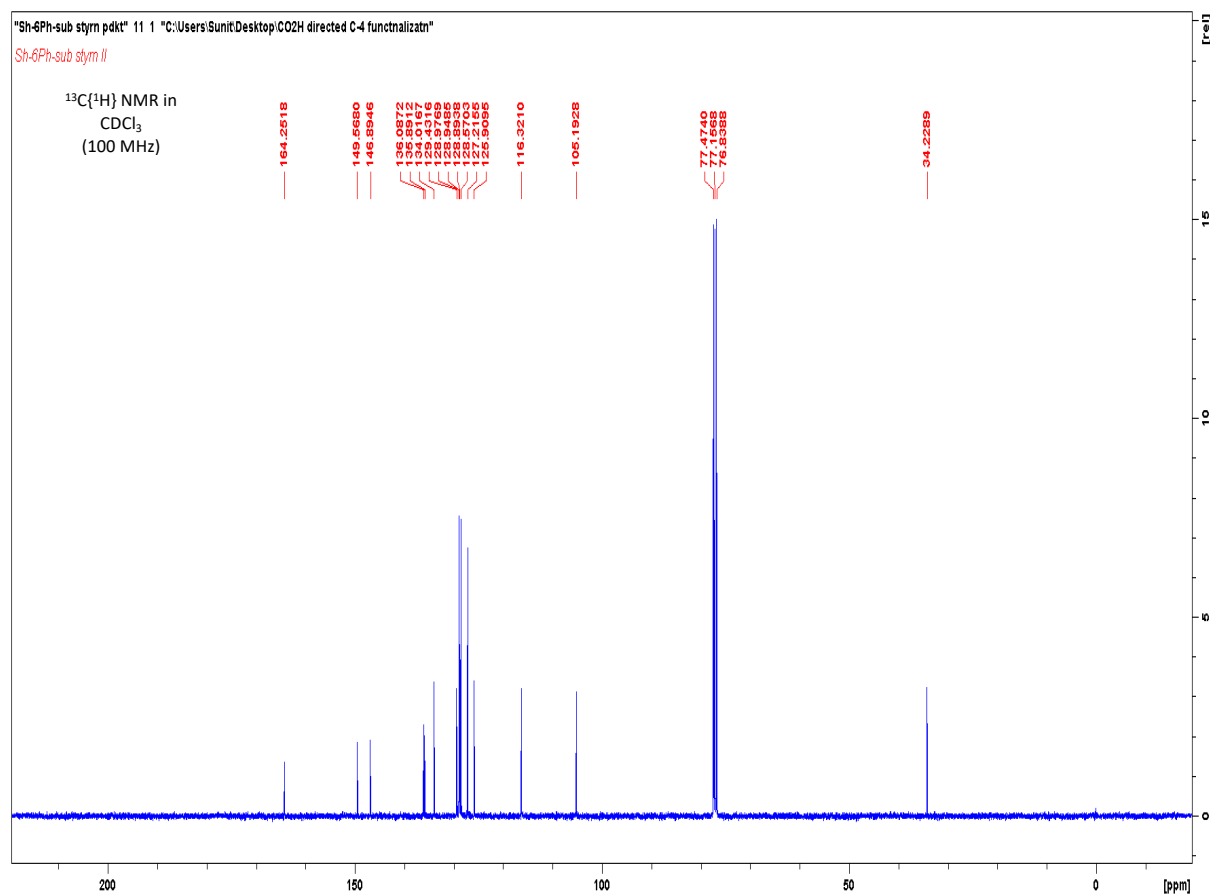
$^{13}\text{C}\{^1\text{H}\}$ NMR of compound **3ga** in CDCl_3 (100 MHz)



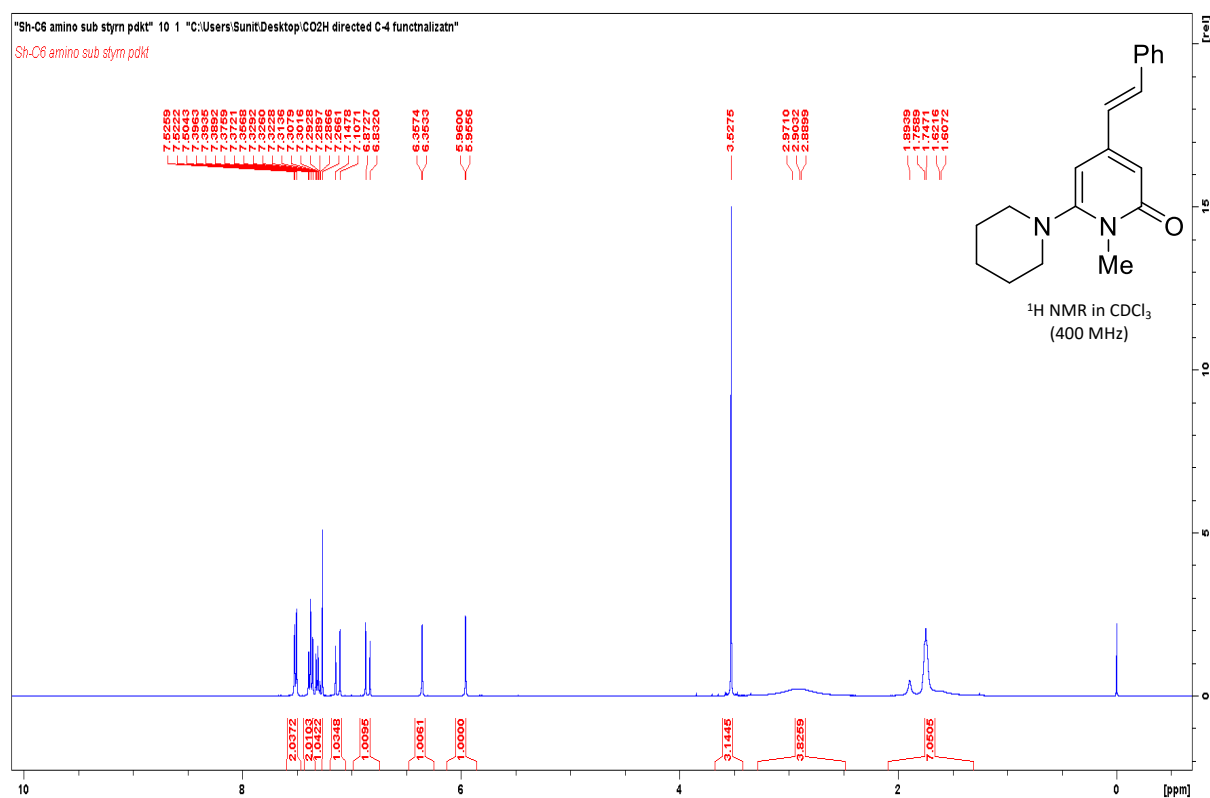
^1H NMR of compound **3ha** in CDCl_3 (400 MHz)



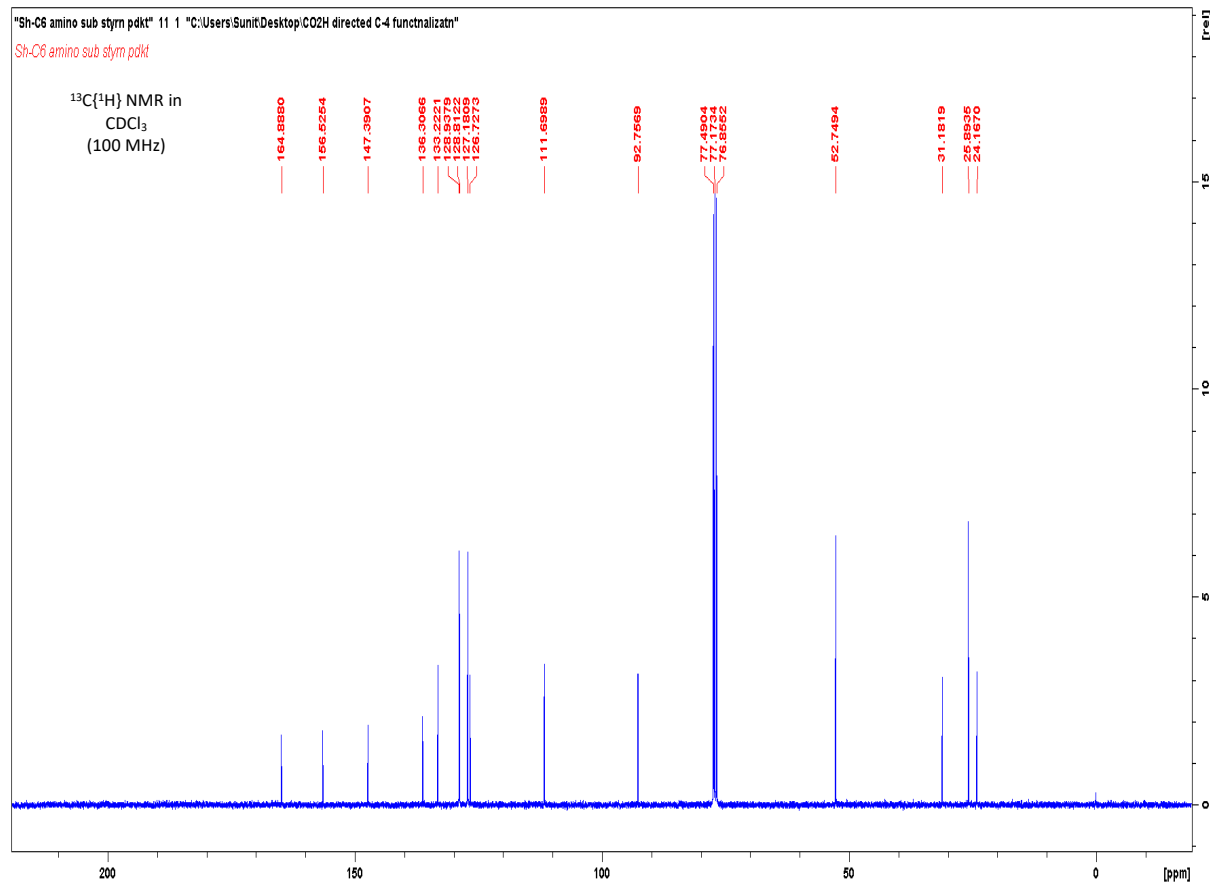
$^{13}\text{C}\{^1\text{H}\}$ NMR of compound **3ha** in CDCl_3 (100 MHz)



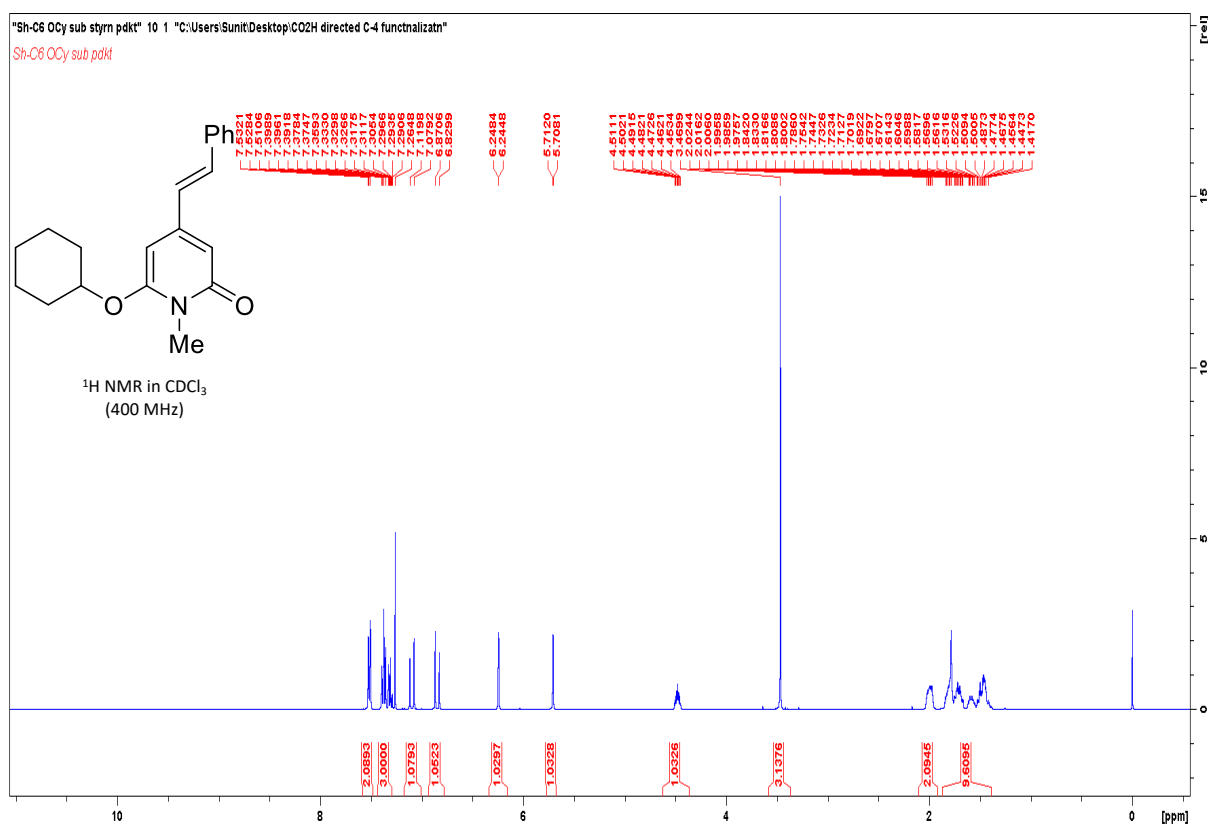
^1H NMR of compound **3ia** in CDCl_3 (400 MHz)



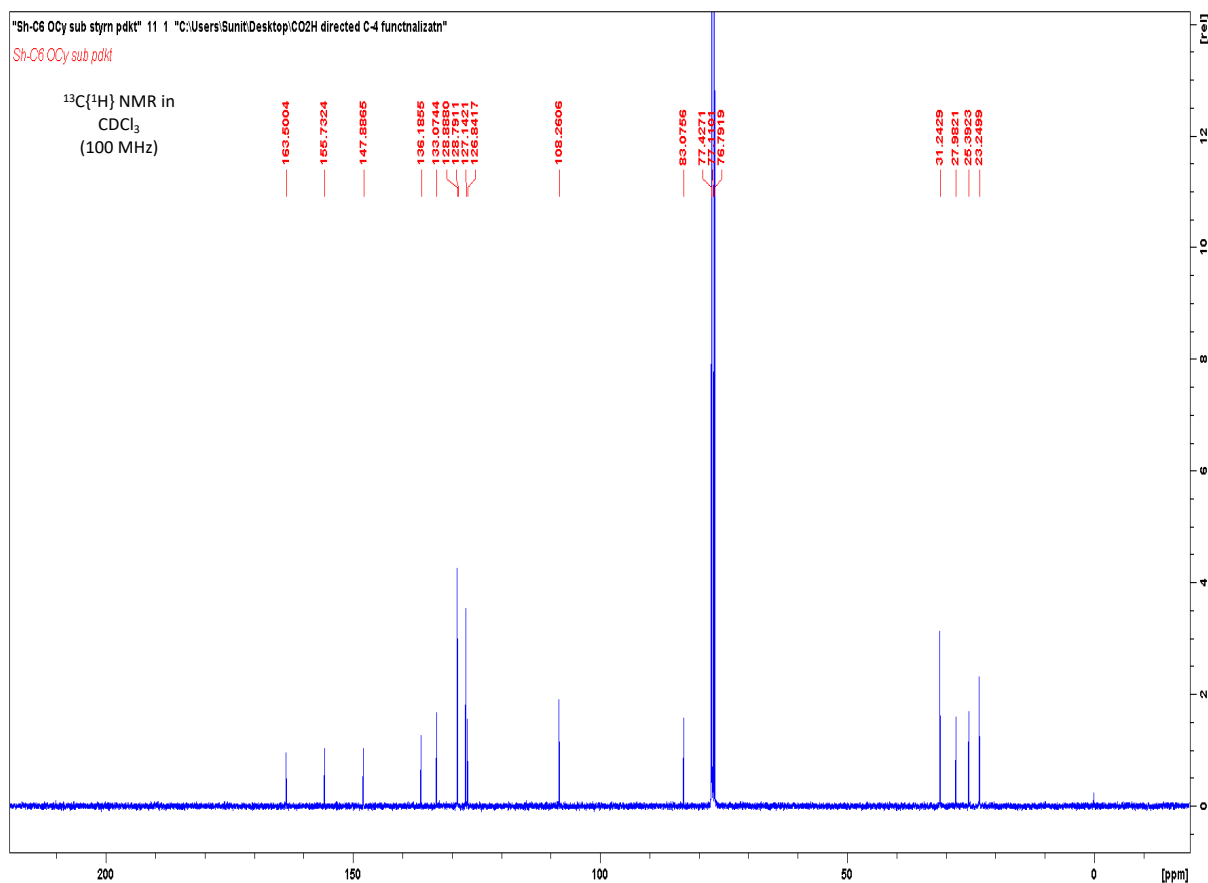
$^{13}\text{C}\{^1\text{H}\}$ NMR of compound **3ia** in CDCl_3 (100 MHz)



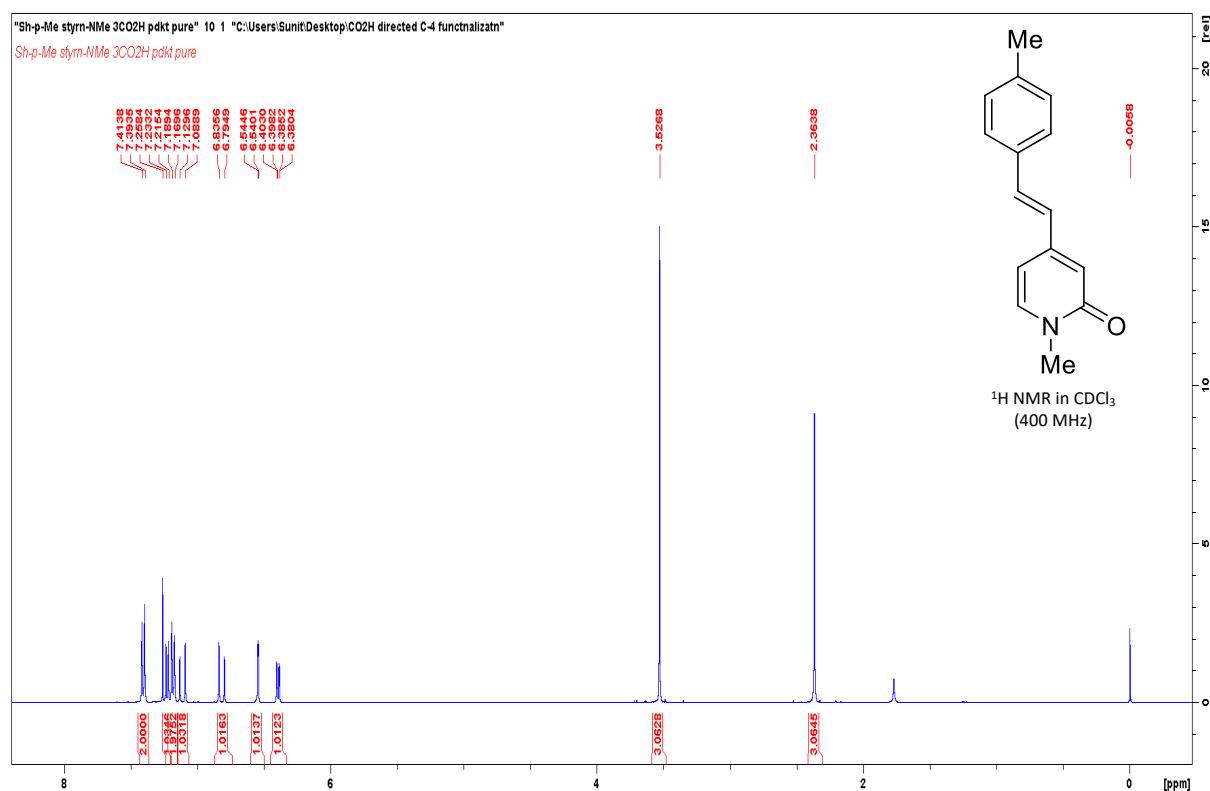
¹H NMR of compound **3ja** in CDCl₃ (400 MHz)



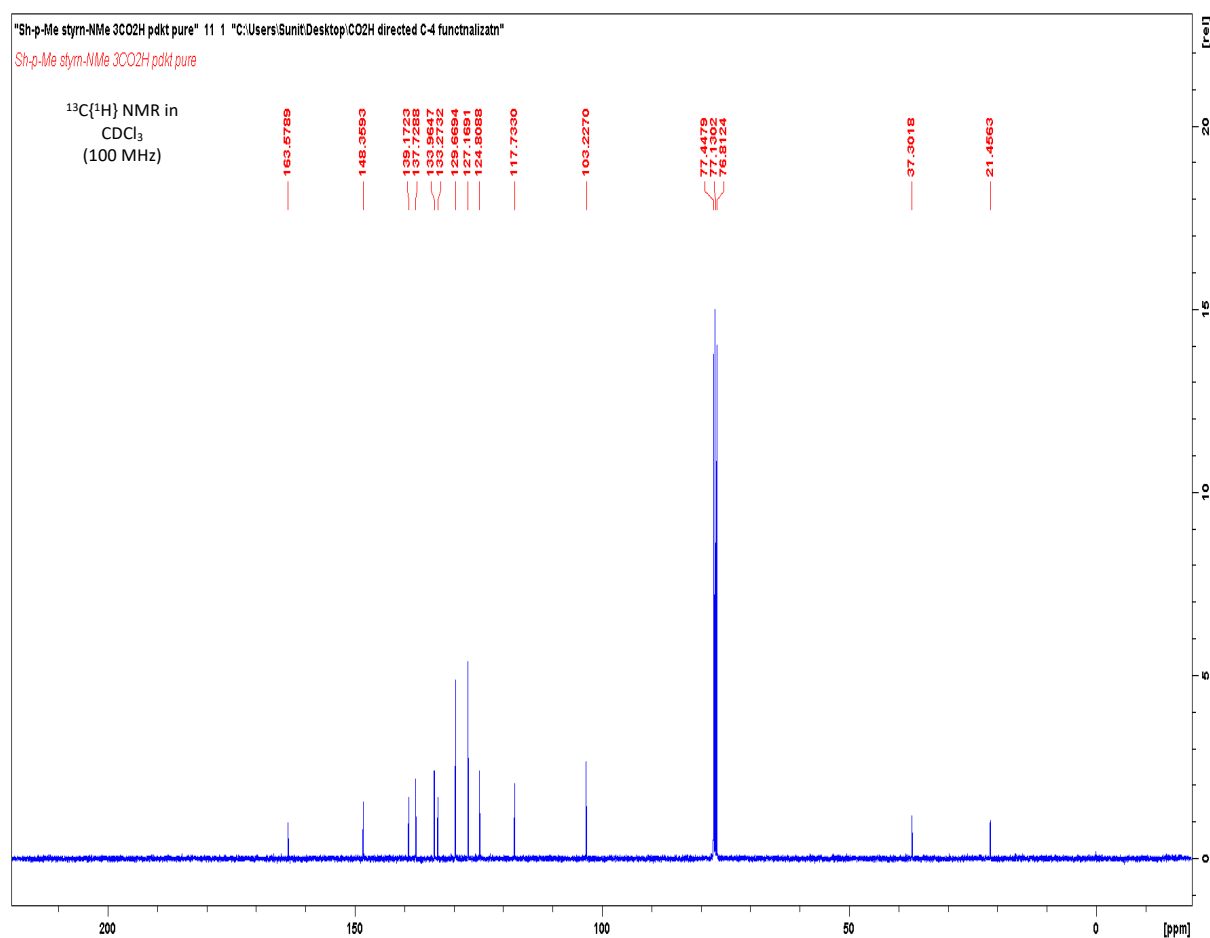
¹³C{¹H} NMR of compound **3ja** in CDCl₃ (100 MHz)



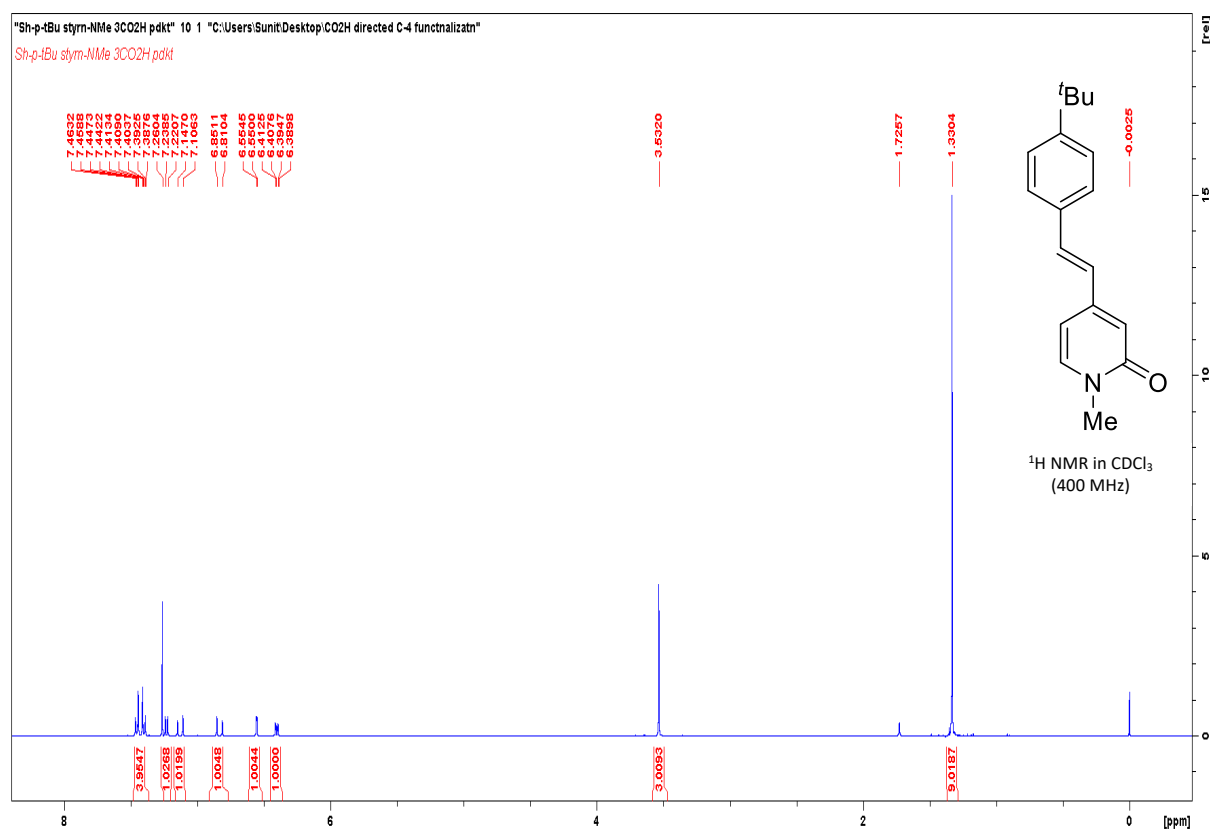
¹H NMR of compound **3ab** in CDCl₃ (400 MHz)



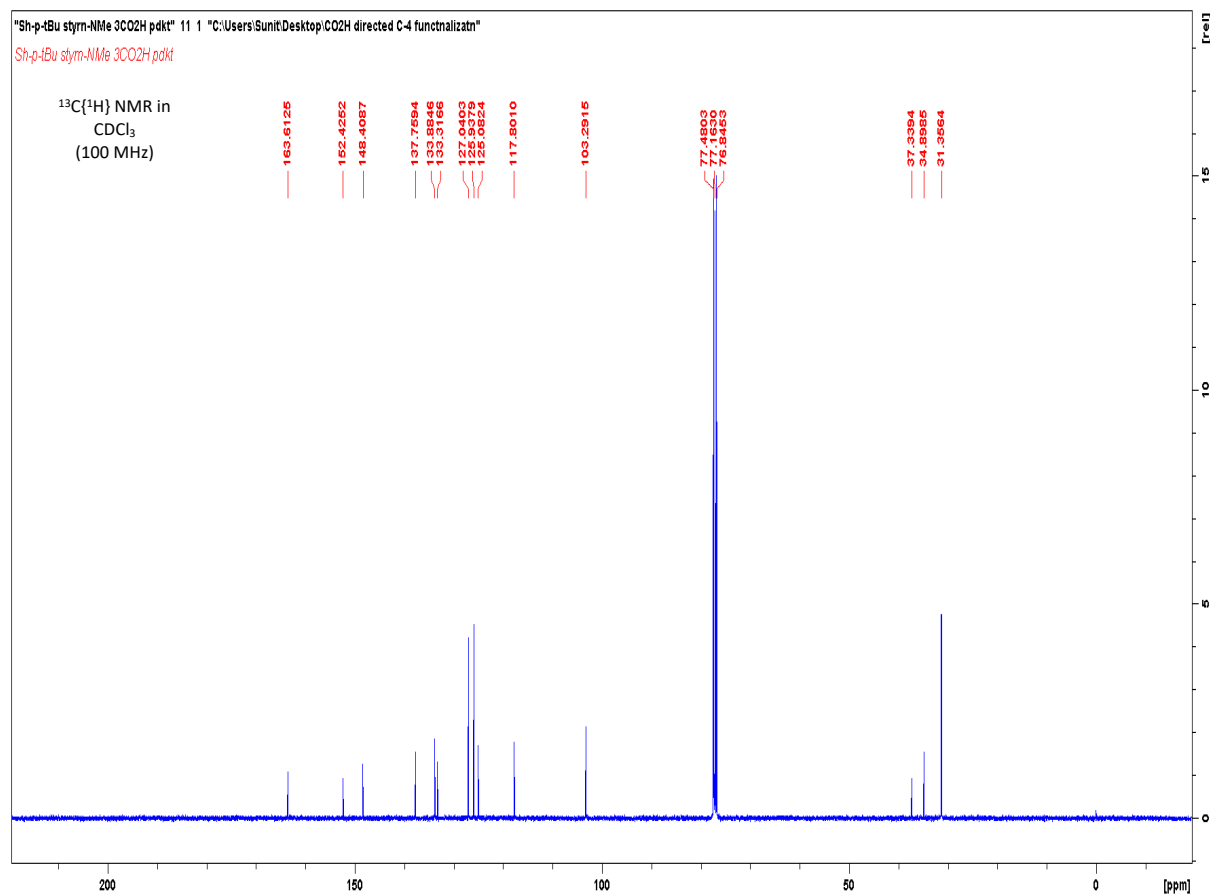
¹³C{¹H} NMR of compound **3ab** in CDCl₃ (100 MHz)



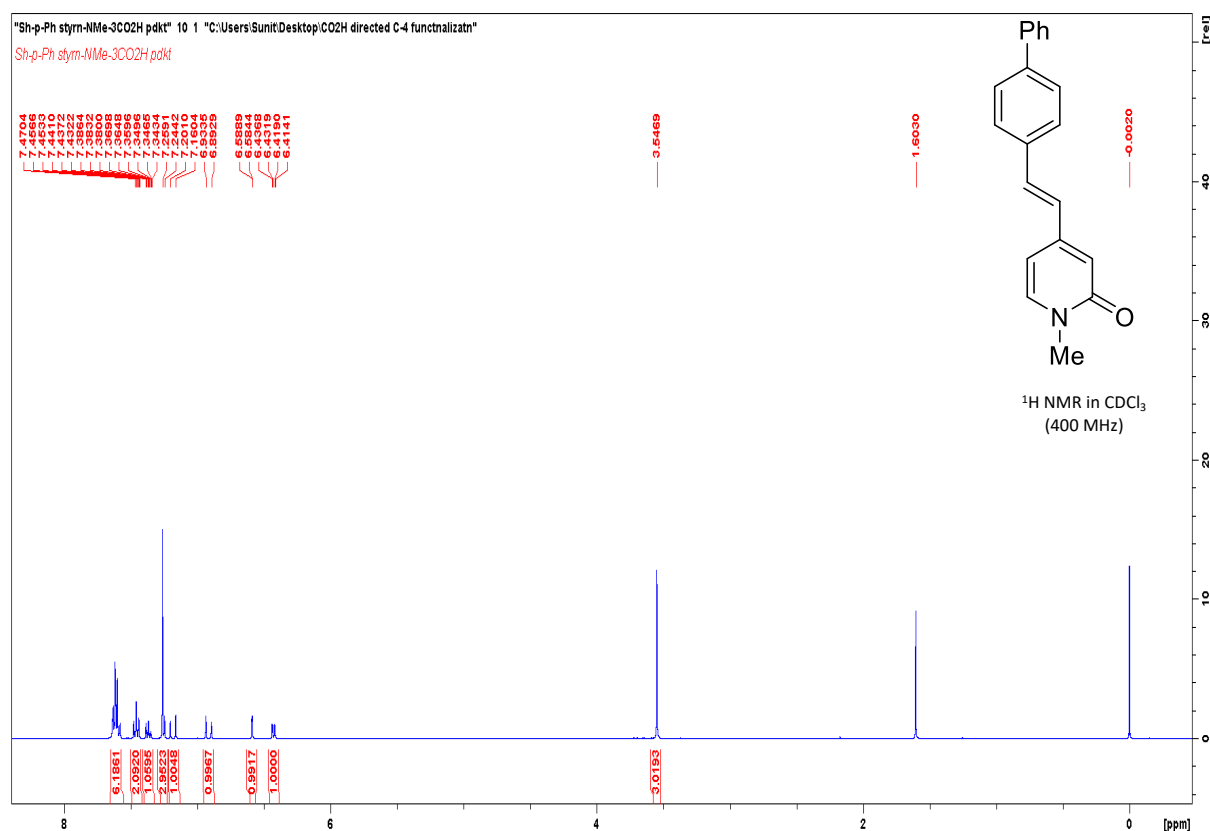
^1H NMR of compound **3ac** in CDCl_3 (400 MHz)



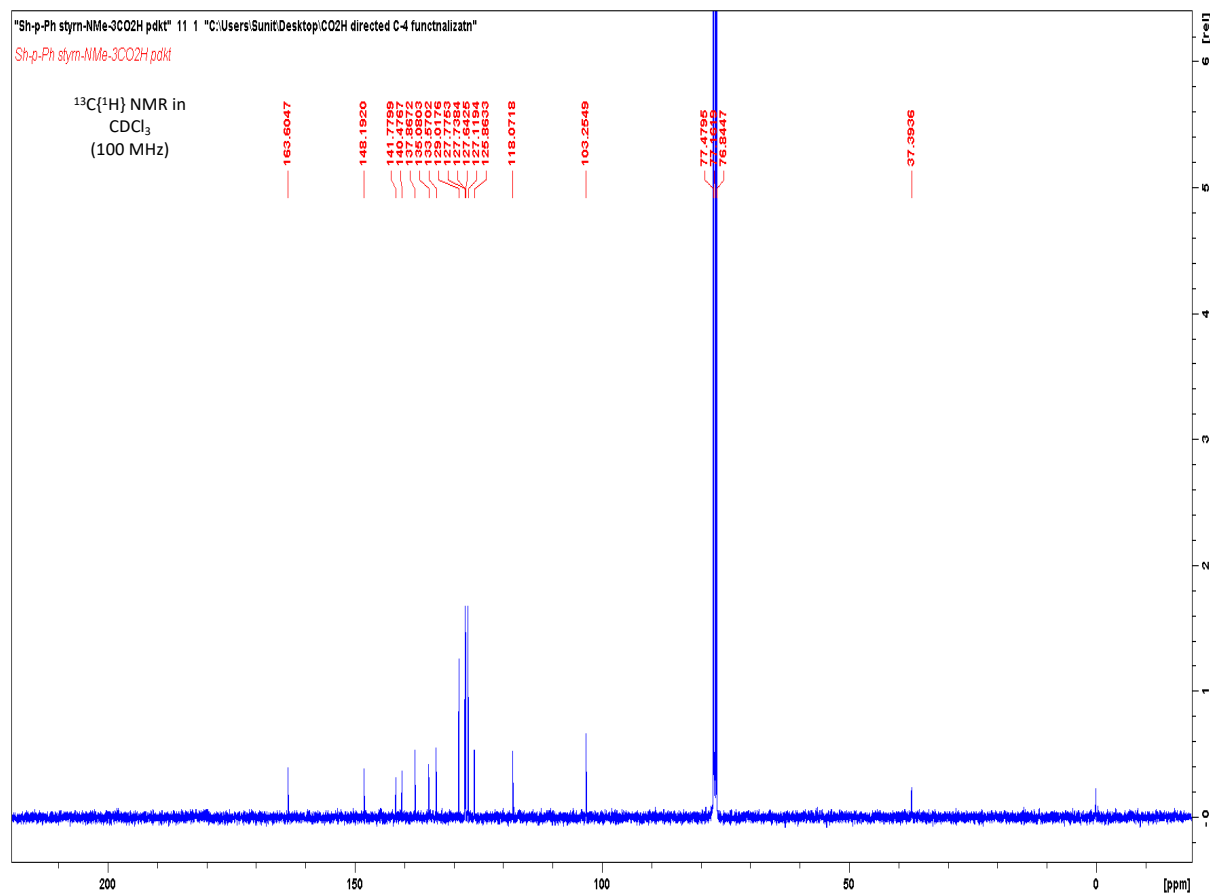
$^{13}\text{C}\{^1\text{H}\}$ NMR of compound **3ac** in CDCl_3 (100 MHz)



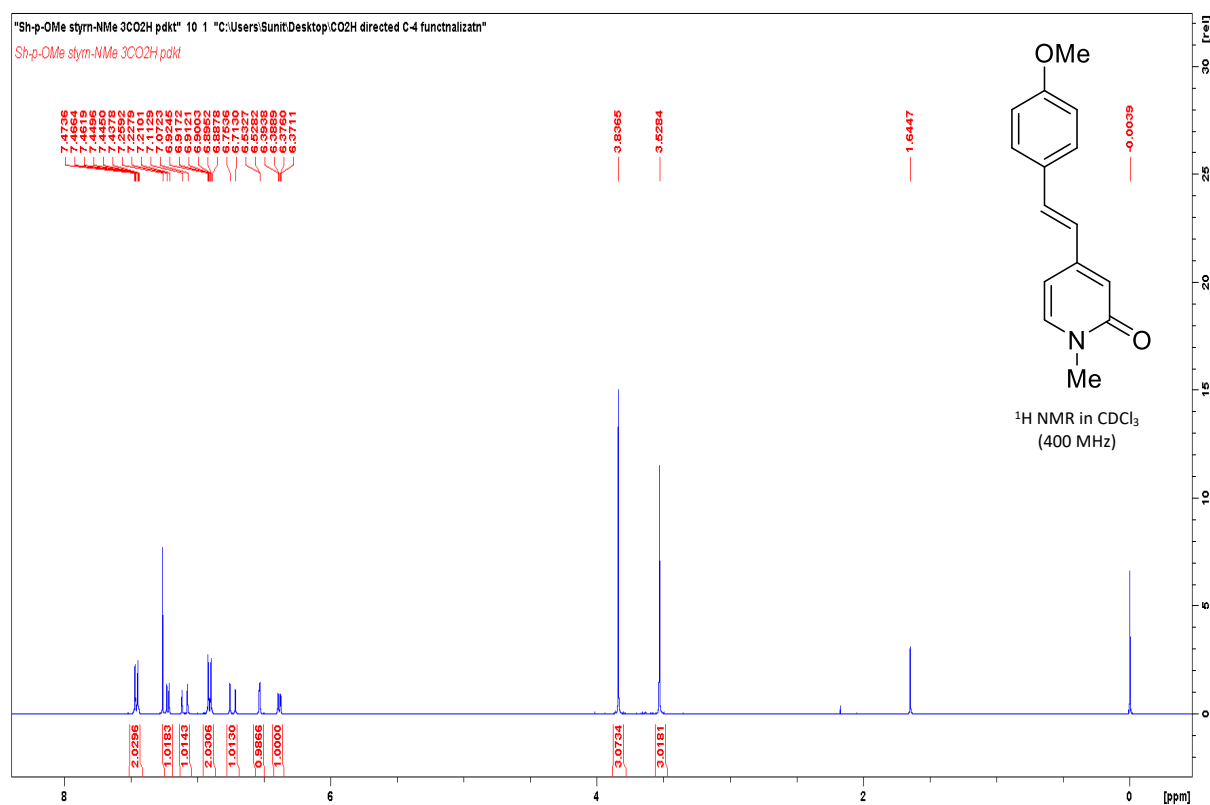
^1H NMR of compound **3ad** in CDCl_3 (400 MHz)



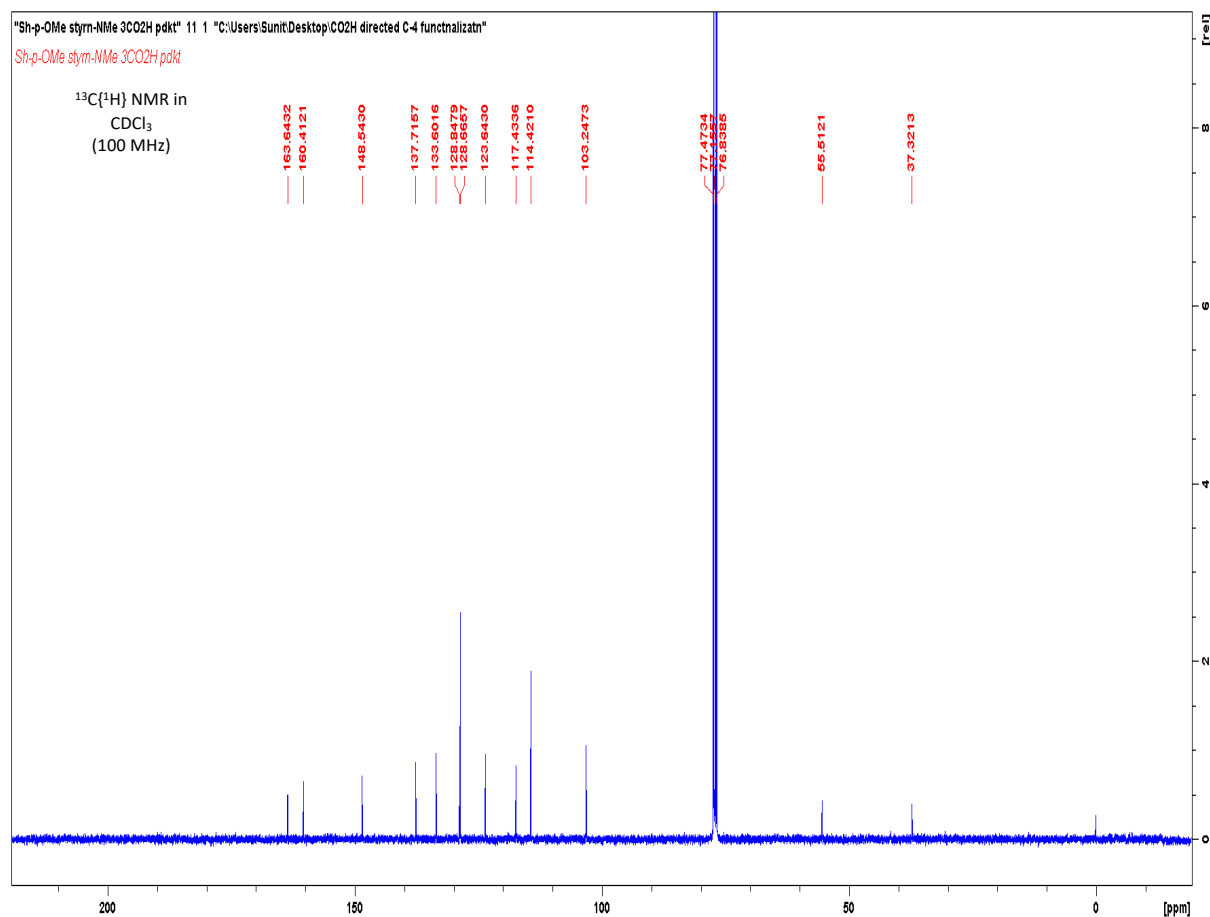
$^{13}\text{C}\{^1\text{H}\}$ NMR of compound **3ad** in CDCl_3 (100 MHz)



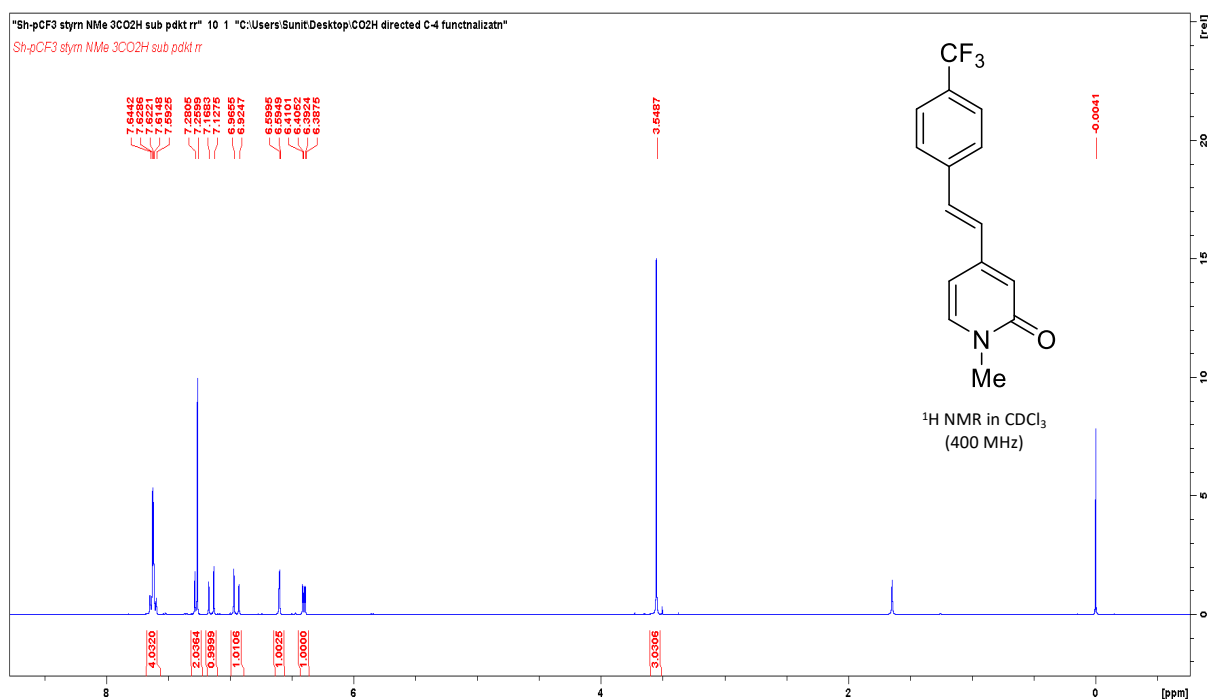
¹H NMR of compound **3ae** in CDCl₃ (400 MHz)



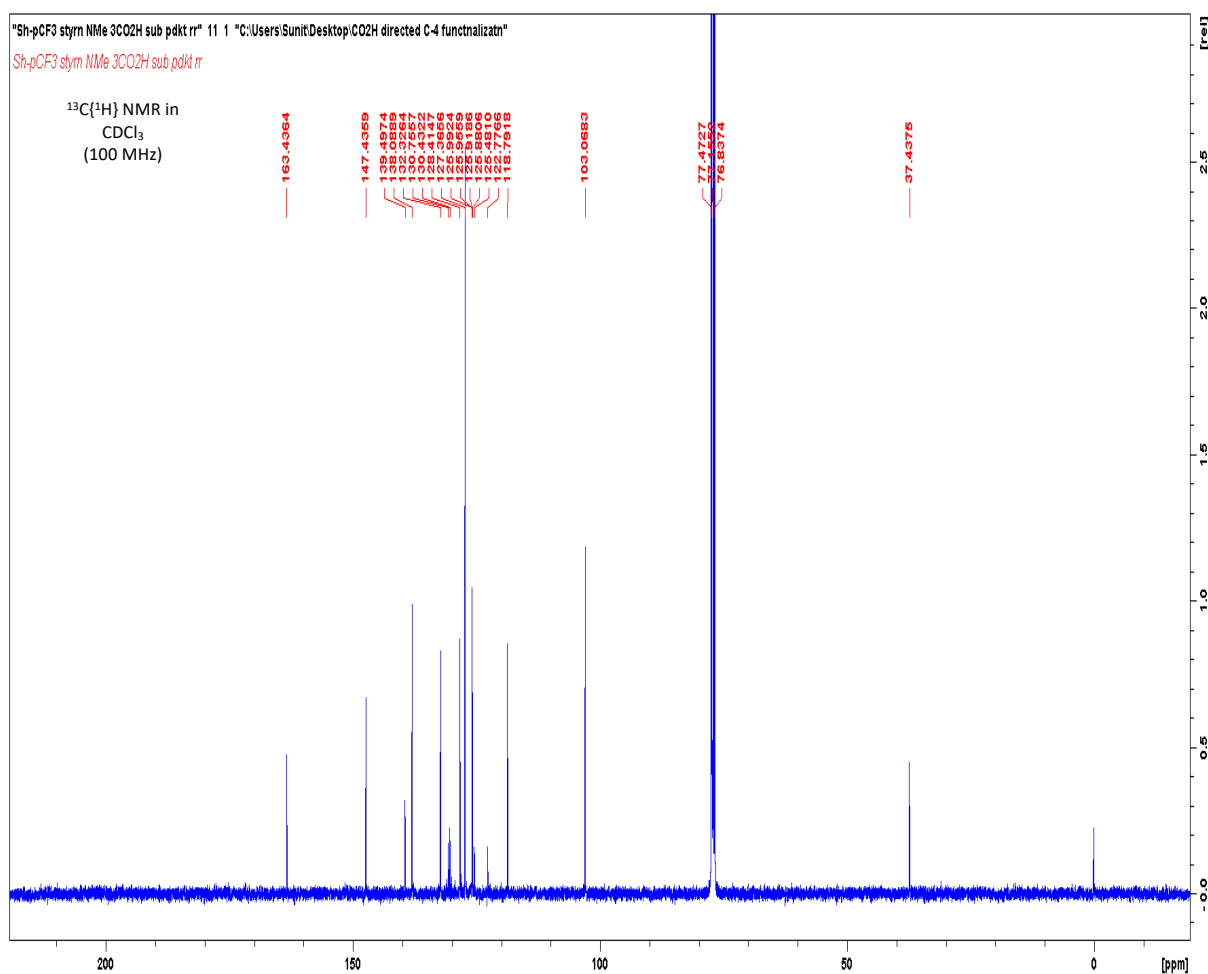
¹³C{¹H} NMR of compound **3ae** in CDCl₃ (100 MHz)



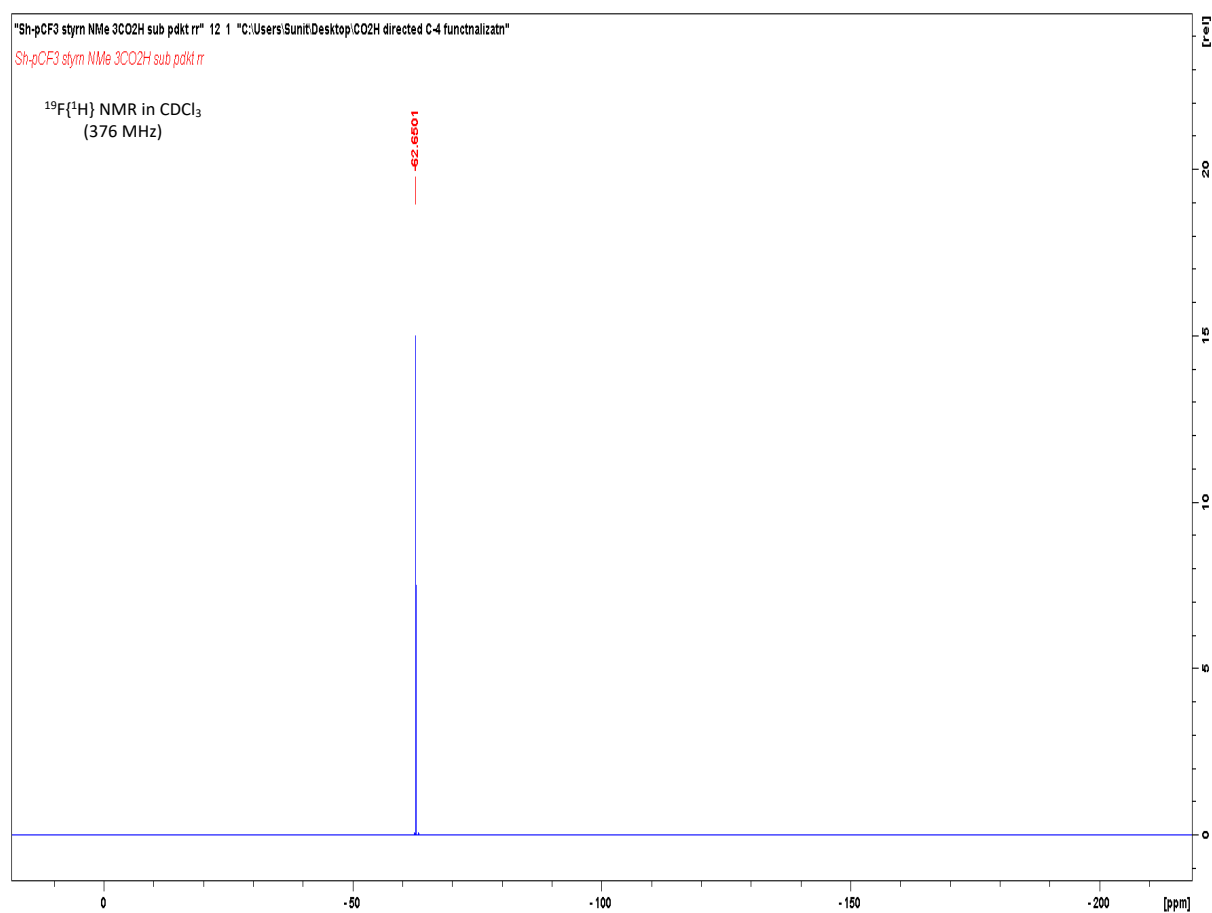
^1H NMR of compound **3af** in CDCl_3 (400 MHz)



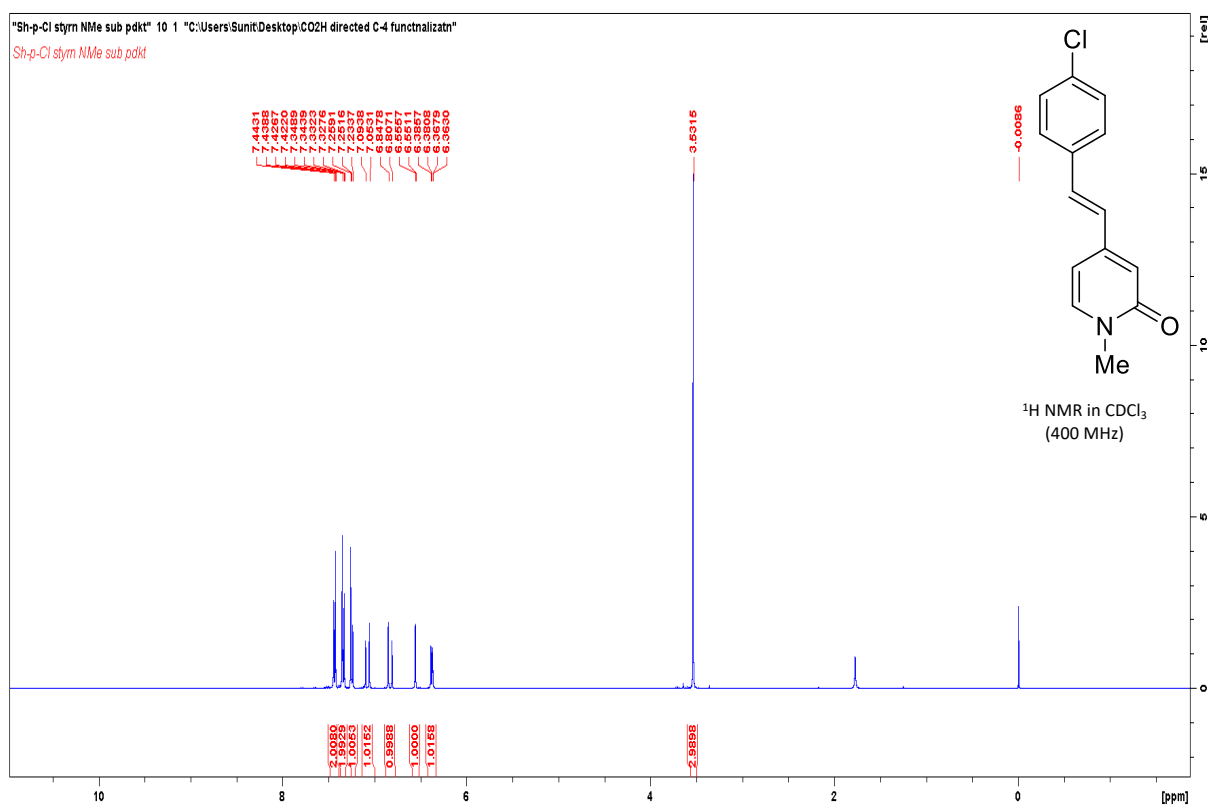
$^{13}\text{C}\{^1\text{H}\}$ NMR of compound **3af** in CDCl_3 (100 MHz)



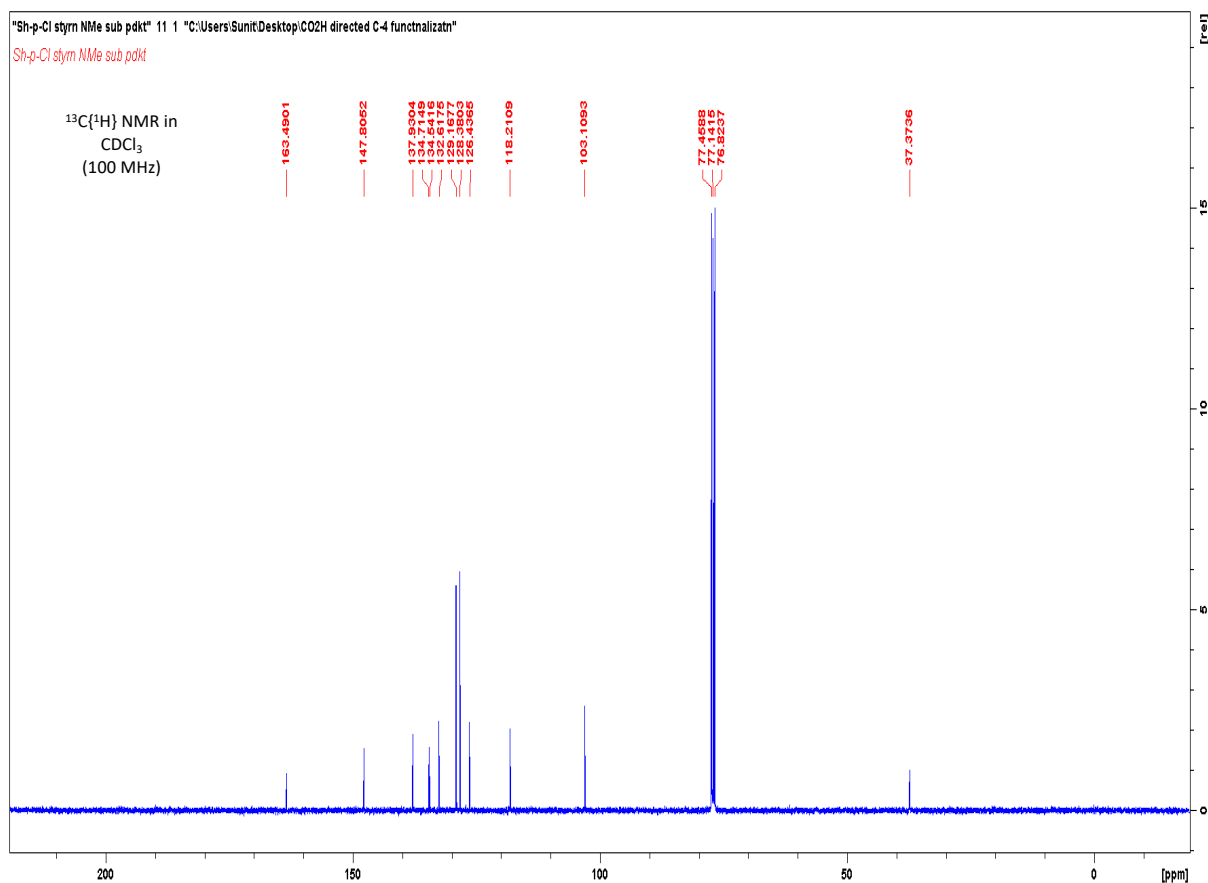
$^{19}\text{F}\{^1\text{H}\}$ NMR of compound **3af** in CDCl_3 (376 MHz)



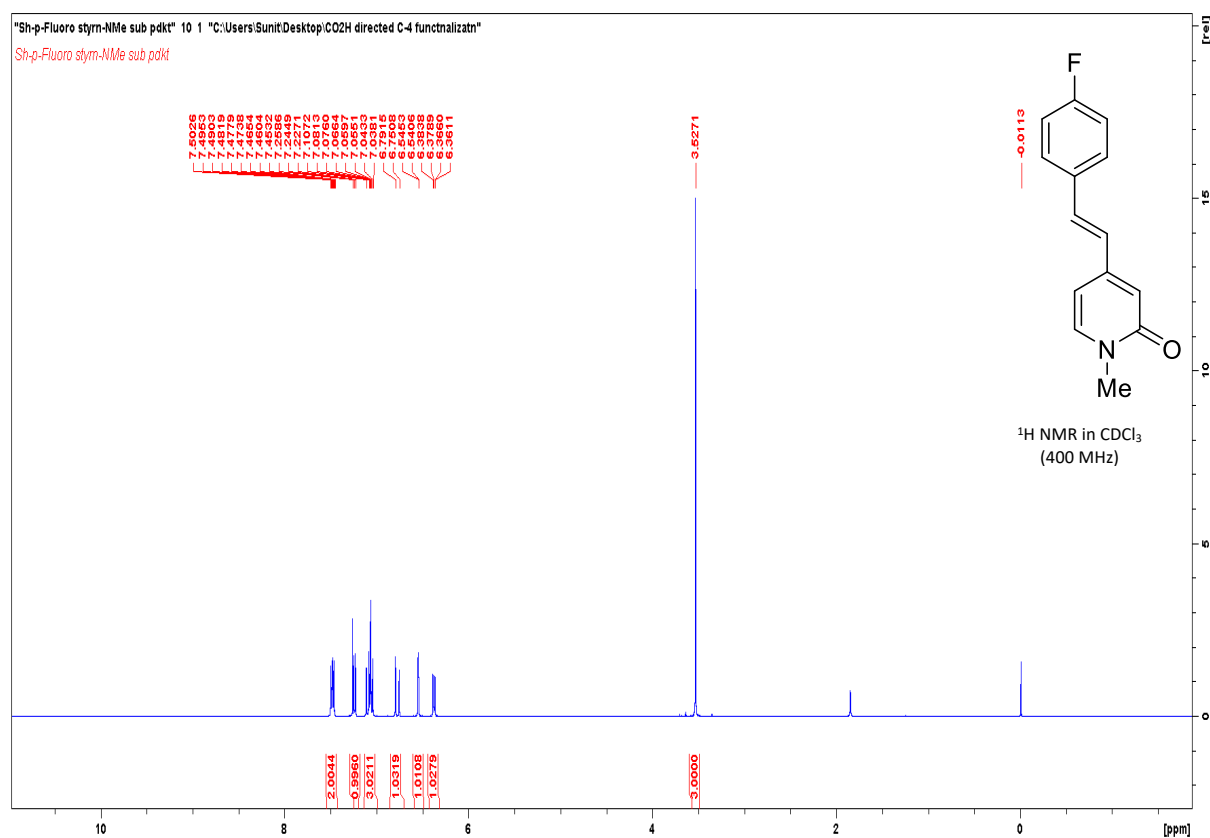
¹H NMR of compound **3ag** in CDCl₃ (400 MHz)



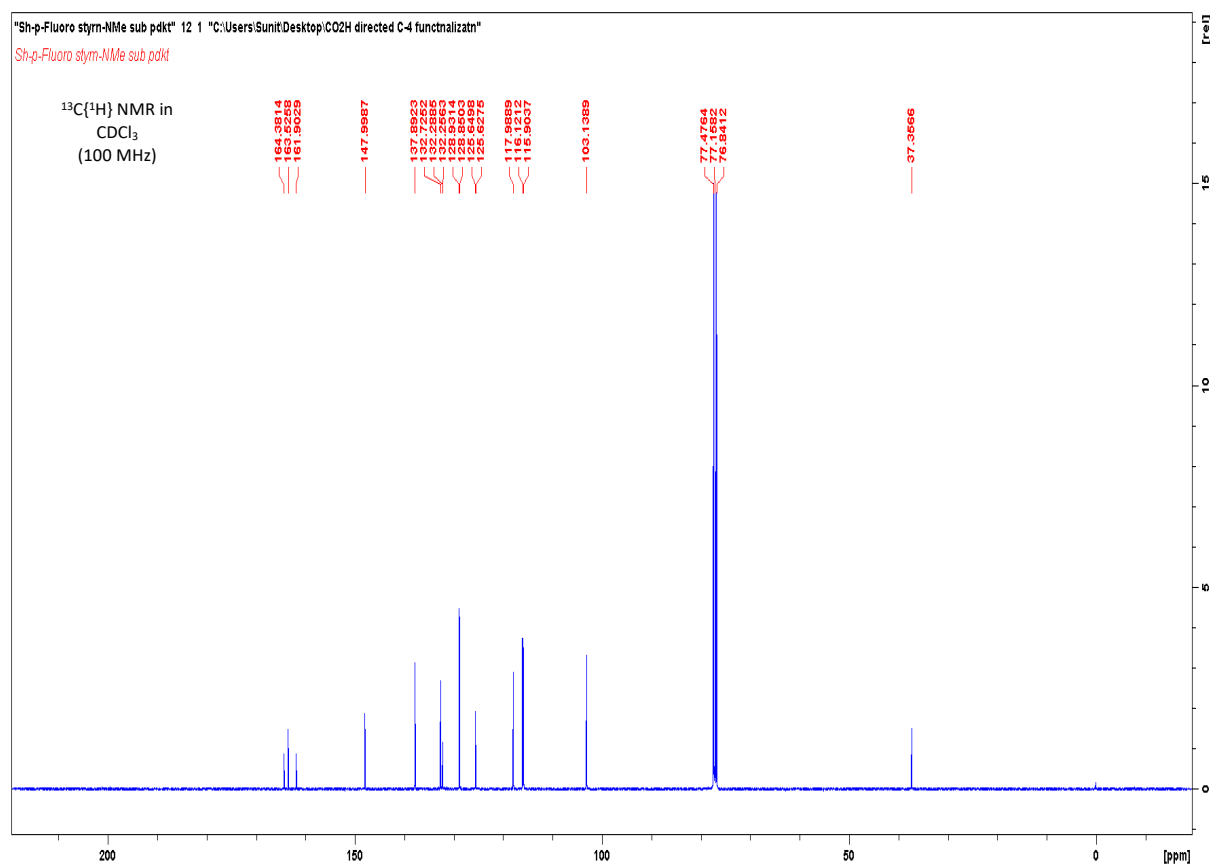
¹³C NMR of compound **3ag** in CDCl₃ (100 MHz)



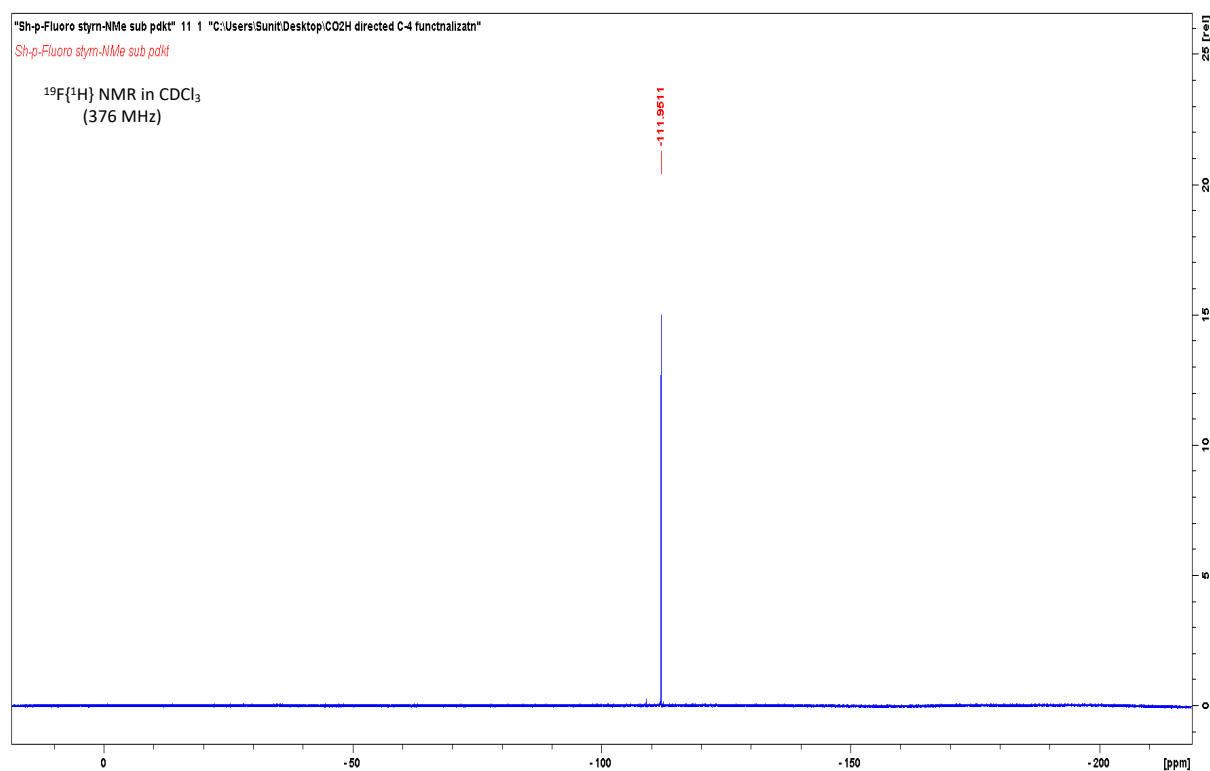
^1H NMR of compound **3ah** in CDCl_3 (400 MHz)



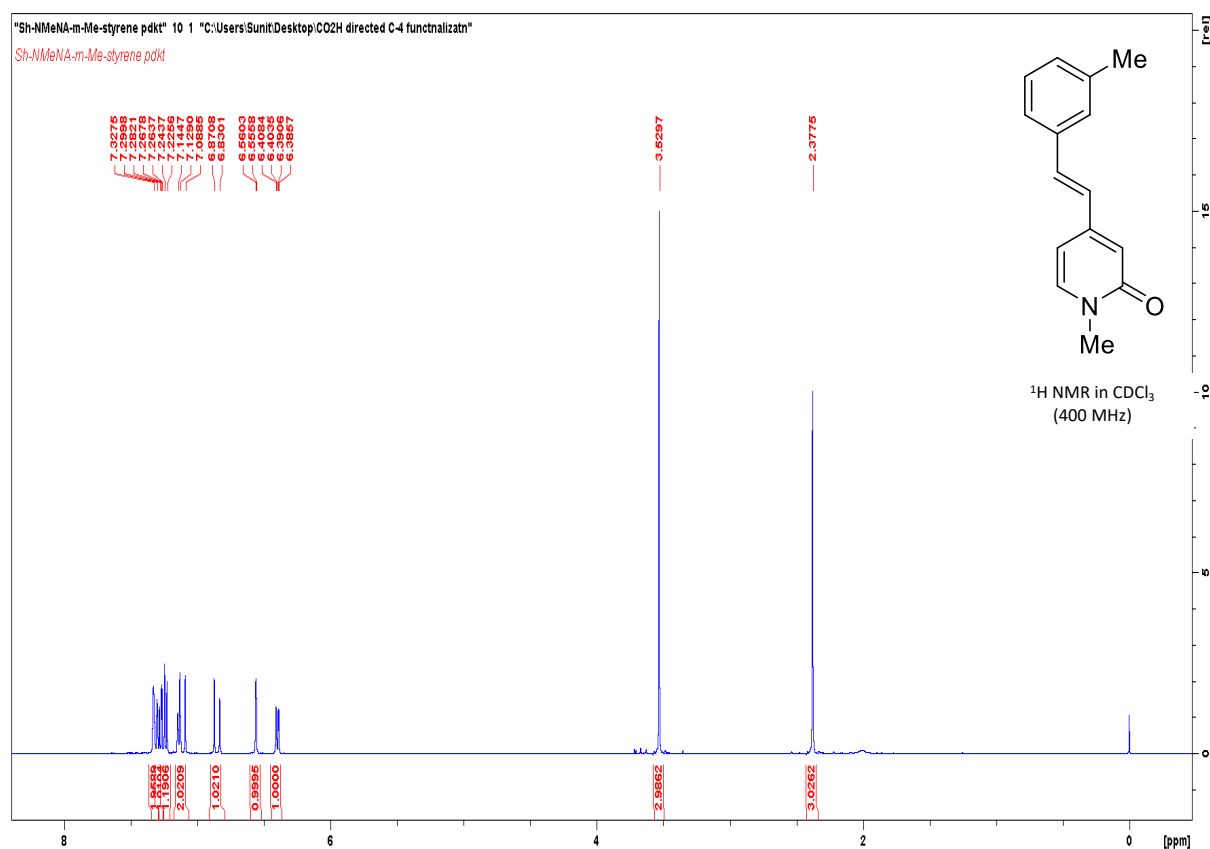
$^{13}\text{C}\{^1\text{H}\}$ NMR of compound **3ah** in CDCl_3 (100 MHz)



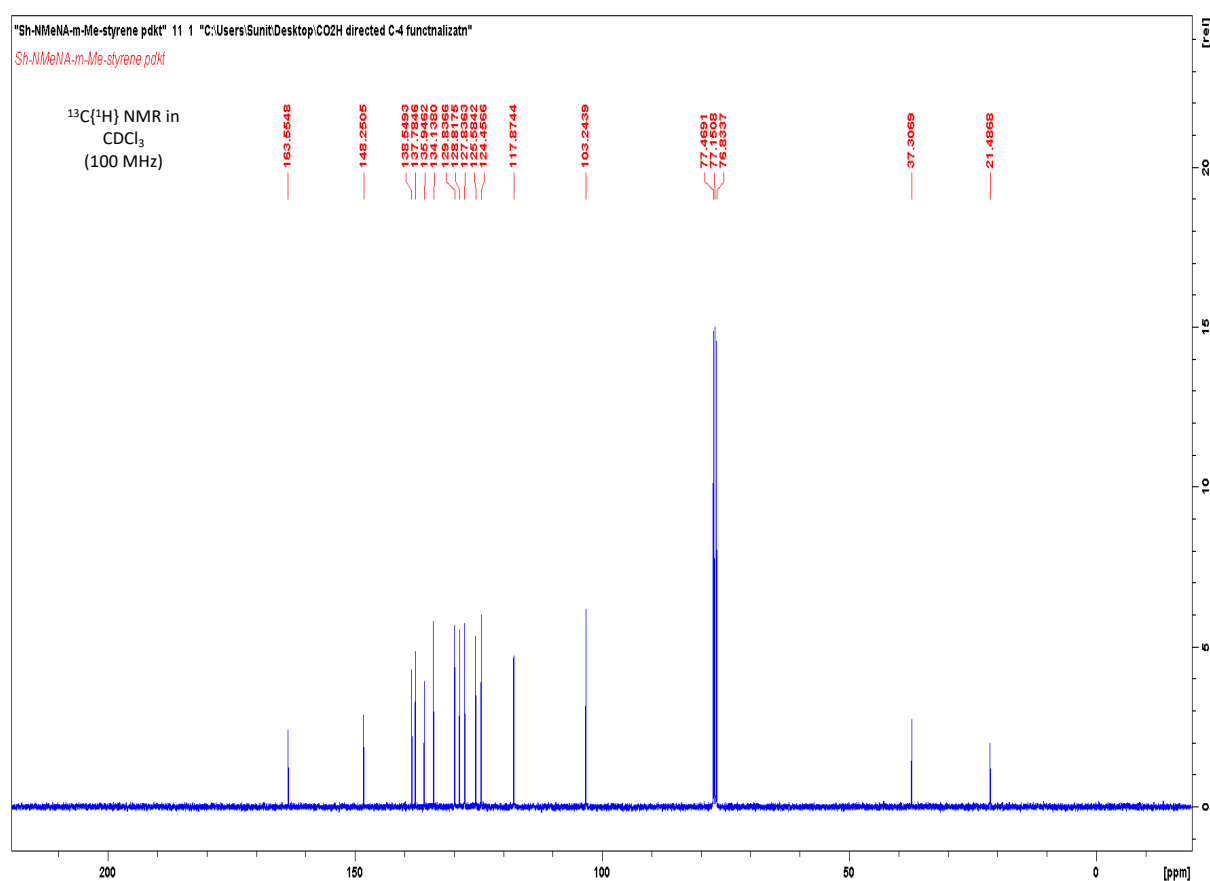
$^{19}\text{F}\{^1\text{H}\}$ NMR of compound **3ah** in CDCl_3 (376 MHz)



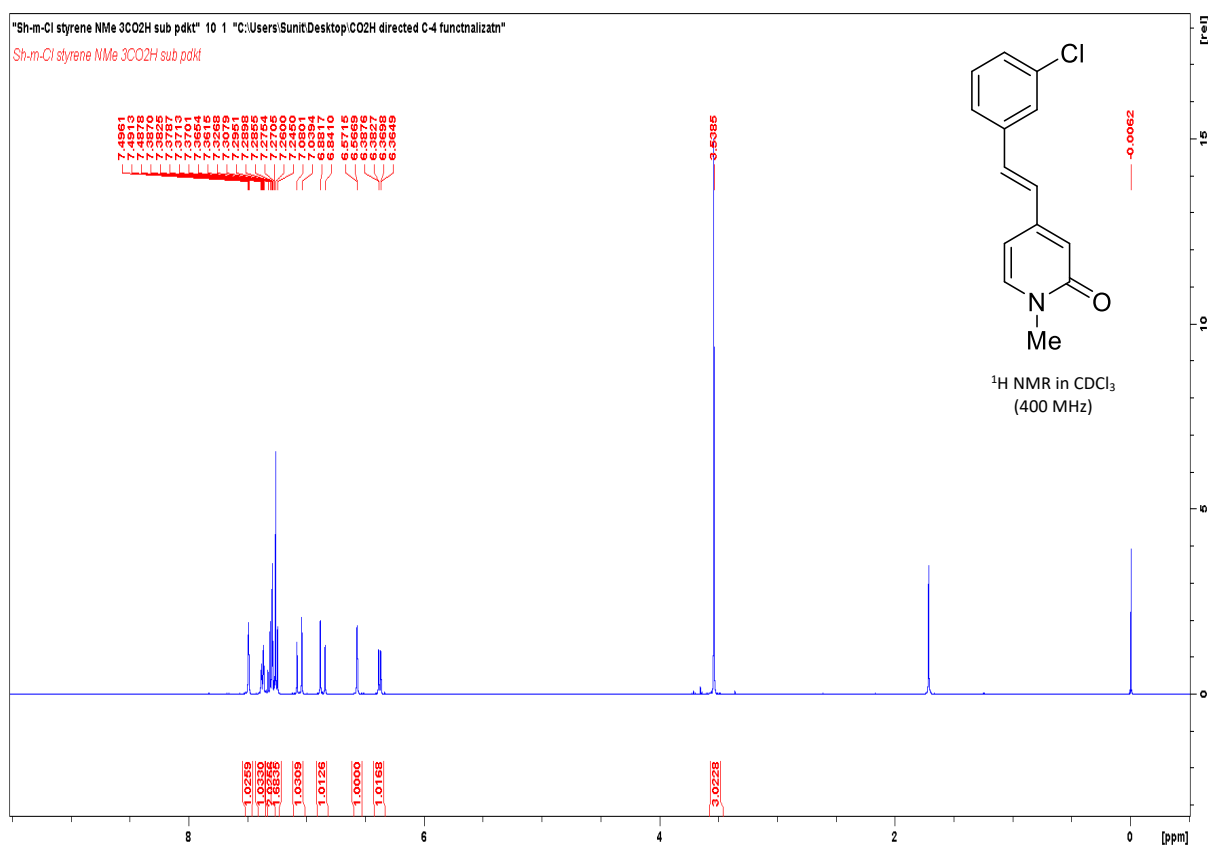
¹H NMR of compound **3ai** in CDCl₃ (400 MHz)



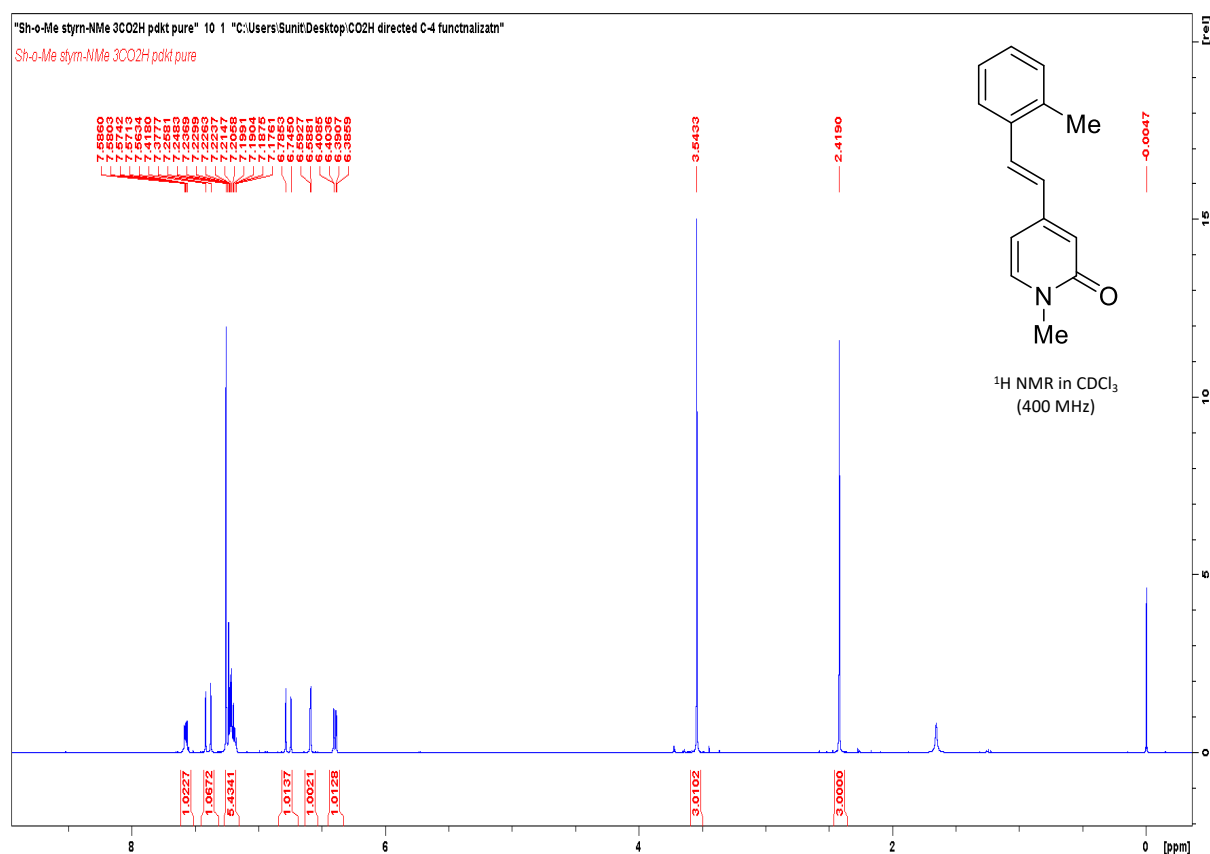
¹³C{¹H} NMR of compound **3ai** in CDCl₃ (100 MHz)



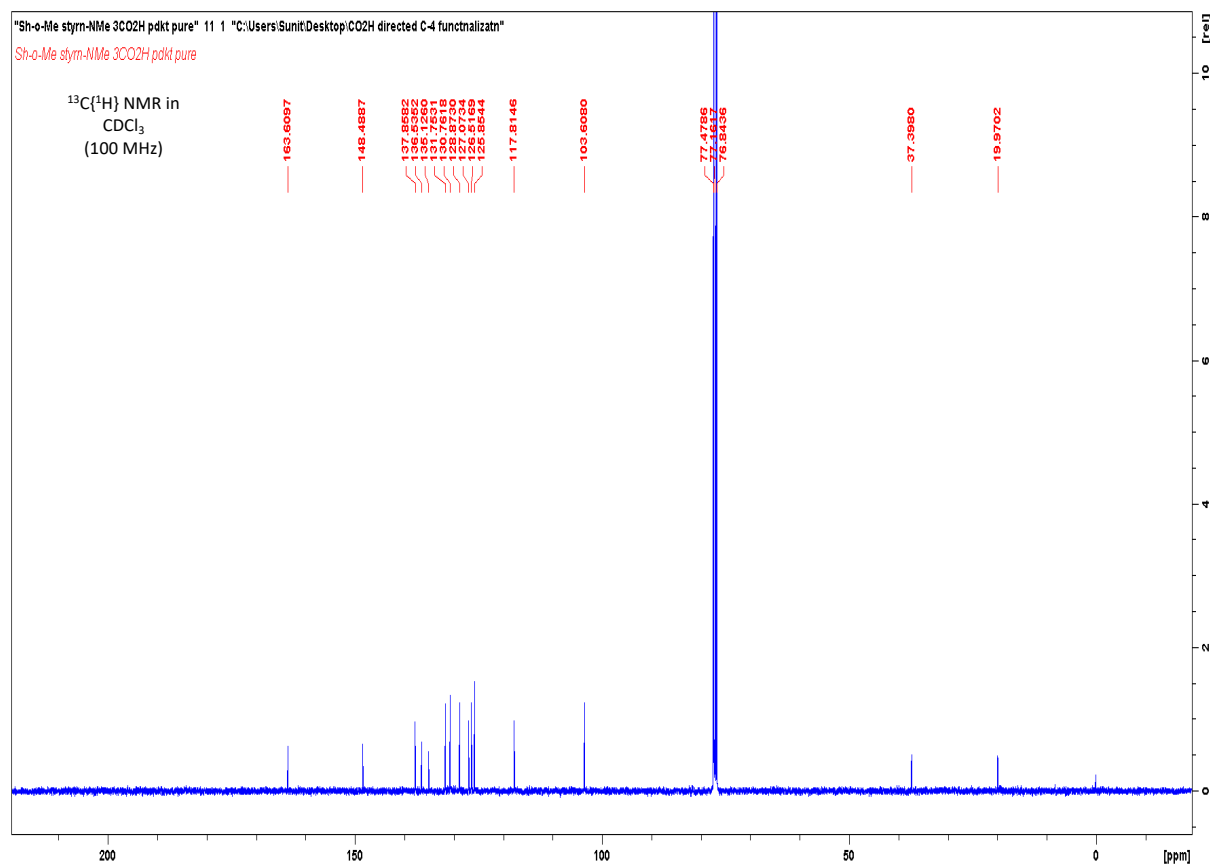
¹H NMR of compound **3aj** in CDCl₃ (400 MHz)



^1H NMR of compound **3ak** in CDCl_3 (400 MHz)



$^{13}\text{C}\{^1\text{H}\}$ NMR of compound **3ak** in CDCl_3 (100 MHz)



¹H NMR in CDCl₃ (400 MHz)

Sh-cyhex acrylyl NMeNA sub pdkt

CN1C=CC(=C(C=C1)C=C(C)OC(=O)C2CCCCC2)C(=O)O

Chemical structure: CN1C=CC(=C(C=C1)C=C(C)OC(=O)C2CCCCC2)C(=O)O

Integration values (from left to right): 1.1070, 1.1446, 1.0064, 1.0097, 1.0000, 1.0021, 3.1207, 2.0101, 2.1321, 6.2618.

"Sh-Cyhex acrylt-NMeNA sub pdkt" 11 1 "C:\Users\Sunit\Desktop\CD2H directed C-4 functionalizatzn"

Sh-Cyhex acrylt-NMeNA sub pdkt

$^{13}\text{C}\{^1\text{H}\}$ NMR in CDCl_3 (100 MHz)

Chemical shifts (ppm) labeled above the spectrum:

- 165.4724
- 163.1463
- 145.4356
- 141.1044
- 138.4420
- 124.2720
- 121.1874
- 103.1041
- 77.4924
- 77.4323
- 76.8646
- 75.5970
- 37.5989
- 31.7983
- 25.5016
- 23.9313

"Sh-NBnMA styryl pdkt DB reduction" 10 1 ¹³C:User\Sunit\Desktop\CO2H directed C-4 functionalization\derivatization of product"

Sh-NBn sub styryl pdkt double bond reduction

¹³C{¹H} NMR in CDCl₃ (100 MHz)

Chemical shift (ppm): 162.8821, 164.4583, 140.7033, 136.5453, 136.4808, 128.8606, 128.8110, 128.4420, 128.1120, 128.0538, 126.3759, 119.0307, 108.0704, 77.4395, 77.0611, 76.5637, 51.5759, 37.0838, 36.0629.

Chemical shift (ppm): 162.8821, 164.4583, 140.7033, 136.5453, 136.4808, 128.8606, 128.8110, 128.4420, 128.1120, 128.0538, 126.3759, 119.0307, 108.0704, 77.4395, 77.0611, 76.5637, 51.5759, 37.0838, 36.0629.

"Sh-NBnMA styren pdkt to Piperidinone" 10 ¹C:Users\Sunit\Desktop\CO2H directed C-4 functionalizatr\derivatization of product"

Sh-NBn sub styren pdkt hydrogenation in EtOH

Chemical Structure: c1ccc(cc1)CCN2CCCC(=O)C2

¹H NMR (400 MHz) in CDCl₃:

Peak list (ppm): 7.362, 7.359, 7.358, 7.357, 7.356, 7.355, 7.354, 7.353, 7.352, 7.351, 7.350, 7.349, 7.348, 7.347, 7.346, 7.345, 7.344, 7.343, 7.342, 7.341, 7.340, 7.339, 7.338, 7.337, 7.336, 7.335, 7.334, 7.333, 7.332, 7.331, 7.330, 7.329, 7.328, 7.327, 7.326, 7.325, 7.324, 7.323, 7.322, 7.321, 7.320, 7.319, 7.318, 7.317, 7.316, 7.315, 7.314, 7.313, 7.312, 7.311, 7.310, 7.309, 7.308, 7.307, 7.306, 7.305, 7.304, 7.303, 7.302, 7.301, 7.300, 7.299, 7.298, 7.297, 7.296, 7.295, 7.294, 7.293, 7.292, 7.291, 7.290, 7.289, 7.288, 7.287, 7.286, 7.285, 7.284, 7.283, 7.282, 7.281, 7.280, 7.279, 7.278, 7.277, 7.276, 7.275, 7.274, 7.273, 7.272, 7.271, 7.270, 7.269, 7.268, 7.267, 7.266, 7.265, 7.264, 7.263, 7.262, 7.261, 7.260, 7.259, 7.258, 7.257, 7.256, 7.255, 7.254, 7.253, 7.252, 7.251, 7.250, 7.249, 7.248, 7.247, 7.246, 7.245, 7.244, 7.243, 7.242, 7.241, 7.240, 7.239, 7.238, 7.237, 7.236, 7.235, 7.234, 7.233, 7.232, 7.231, 7.230, 7.229, 7.228, 7.227, 7.226, 7.225, 7.224, 7.223, 7.222, 7.221, 7.220, 7.219, 7.218, 7.217, 7.216, 7.215, 7.214, 7.213, 7.212, 7.211, 7.210, 7.209, 7.208, 7.207, 7.206, 7.205, 7.204, 7.203, 7.202, 7.201, 7.200, 7.199, 7.198, 7.197, 7.196, 7.195, 7.194, 7.193, 7.192, 7.191, 7.190, 7.189, 7.188, 7.187, 7.186, 7.185, 7.184, 7.183, 7.182, 7.181, 7.180, 7.179, 7.178, 7.177, 7.176, 7.175, 7.174, 7.173, 7.172, 7.171, 7.170, 7.169, 7.168, 7.167, 7.166, 7.165, 7.164, 7.163, 7.162, 7.161, 7.160, 7.159, 7.158, 7.157, 7.156, 7.155, 7.154, 7.153, 7.152, 7.151, 7.150, 7.149, 7.148, 7.147, 7.146, 7.145, 7.144, 7.143, 7.142, 7.141, 7.140, 7.139, 7.138, 7.137, 7.136, 7.135, 7.134, 7.133, 7.132, 7.131, 7.130, 7.129, 7.128, 7.127, 7.126, 7.125, 7.124, 7.123, 7.122, 7.121, 7.120, 7.119, 7.118, 7.117, 7.116, 7.115, 7.114, 7.113, 7.112, 7.111, 7.110, 7.109, 7.108, 7.107, 7.106, 7.105, 7.104, 7.103, 7.102, 7.101, 7.100, 7.099, 7.098, 7.097, 7.096, 7.095, 7.094, 7.093, 7.092, 7.091, 7.090, 7.089, 7.088, 7.087, 7.086, 7.085, 7.084, 7.083, 7.082, 7.081, 7.080, 7.079, 7.078, 7.077, 7.076, 7.075, 7.074, 7.073, 7.072, 7.071, 7.070, 7.069, 7.068, 7.067, 7.066, 7.065, 7.064, 7.063, 7.062, 7.061, 7.060, 7.059, 7.058, 7.057, 7.056, 7.055, 7.054, 7.053, 7.052, 7.051, 7.050, 7.049, 7.048, 7.047, 7.046, 7.045, 7.044, 7.043, 7.042, 7.041, 7.040, 7.039, 7.038, 7.037, 7.036, 7.035, 7.034, 7.033, 7.032, 7.031, 7.030, 7.029, 7.028, 7.027, 7.026, 7.025, 7.024, 7.023, 7.022, 7.021, 7.020, 7.019, 7.018, 7.017, 7.016, 7.015, 7.014, 7.013, 7.012, 7.011, 7.010, 7.009, 7.008, 7.007, 7.006, 7.005, 7.004, 7.003, 7.002, 7.001, 7.000, 6.999, 6.998, 6.997, 6.996, 6.995, 6.994, 6.993, 6.992, 6.991, 6.990, 6.989, 6.988, 6.987, 6.986, 6.985, 6.984, 6.983, 6.982, 6.981, 6.980, 6.979, 6.978, 6.977, 6.976, 6.975, 6.974, 6.973, 6.972, 6.971, 6.970, 6.969, 6.968, 6.967, 6.966, 6.965, 6.964, 6.963, 6.962, 6.961, 6.960, 6.959, 6.958, 6.957, 6.956, 6.955, 6.954, 6.953, 6.952, 6.951, 6.950, 6.949, 6.948, 6.947, 6.946, 6.945, 6.944, 6.943, 6.942, 6.941, 6.940, 6.939, 6.938, 6.937, 6.936, 6.935, 6.934, 6.933, 6.932, 6.931, 6.930, 6.929, 6.928, 6.927, 6.926, 6.925, 6.924, 6.923, 6.922, 6.921, 6.920, 6.919, 6.918, 6.917, 6.916, 6.915, 6.914, 6.913, 6.912, 6.911, 6.910, 6.909, 6.908, 6.907, 6.906, 6.905, 6.904, 6.903, 6.902, 6.901, 6.900, 6.899, 6.898, 6.897, 6.896, 6.895, 6.894, 6.893, 6.892, 6.891, 6.890, 6.889, 6.888, 6.887, 6.886, 6.885, 6.884, 6.883, 6.882, 6.881, 6.880, 6.879, 6.878, 6.877, 6.876, 6.875, 6.874, 6.873, 6.872, 6.871, 6.870, 6.869, 6.868, 6.867, 6.866, 6.865, 6.864, 6.863, 6.862, 6.861, 6.860, 6.859, 6.858, 6.857, 6.856, 6.855, 6.854, 6.853, 6.852, 6.851, 6.850, 6.849, 6.848, 6.847, 6.846, 6.845, 6.844, 6.843, 6.842, 6.841, 6.840, 6.839, 6.838, 6.837, 6.836, 6.835, 6.834, 6.833, 6.832, 6.831, 6.830, 6.829, 6.828, 6.827, 6.826, 6.825, 6.824, 6.823, 6.822, 6.821, 6.820, 6.819, 6.818, 6.817, 6.816,

¹³C{¹H} NMR in CDCl₃ (100 MHz)

Sh-NBn sub stym pdkt hydrogenation in EtOH

Chemical shift (ppm): 169.6280, 141.8790, 137.3072, 128.6897, 128.6320, 128.5977, 128.5776, 126.0485, 77.4780, 76.8424, 50.0389, 46.3705, 38.7958, 37.5030, 32.9268, 29.1389, 28.1393.

¹H NMR in CDCl₃ (400 MHz)

c1ccc(cc1)CN2C(=O)N(Cc3ccccc3)C(=O)N2C4=CC=CC=C4

Chemical structure of the compound is shown. The spectrum displays peaks corresponding to the structure, with integration values and chemical shifts (ppm) provided for each signal.

Integration values (from left to right): 2.0494, 2.1690, 2.1395, 2.0474, 1.0234, 1.0176, 2.0932, 1.0000, 1.0190.

Chemical shifts (ppm) (from left to right): 7.6238, 7.6206, 7.6021, 7.5877, 7.4951, 7.4889, 7.4860, 7.3640, 7.3482, 7.3297, 7.3182, 7.3066, 7.2970, 7.2876, 7.2856, 7.2696, 7.2445, 7.2370, 7.1534, 7.1882, 7.1785, 7.1725, 7.1705, 7.1489, 7.0378, 6.0152, 6.0045, 6.8050, 6.8078, 6.1359, 6.1352, 6.1608, 6.1248, 3.2854, 3.2111, 3.2171, 3.2026, 3.0762, 3.0532, 3.0467.

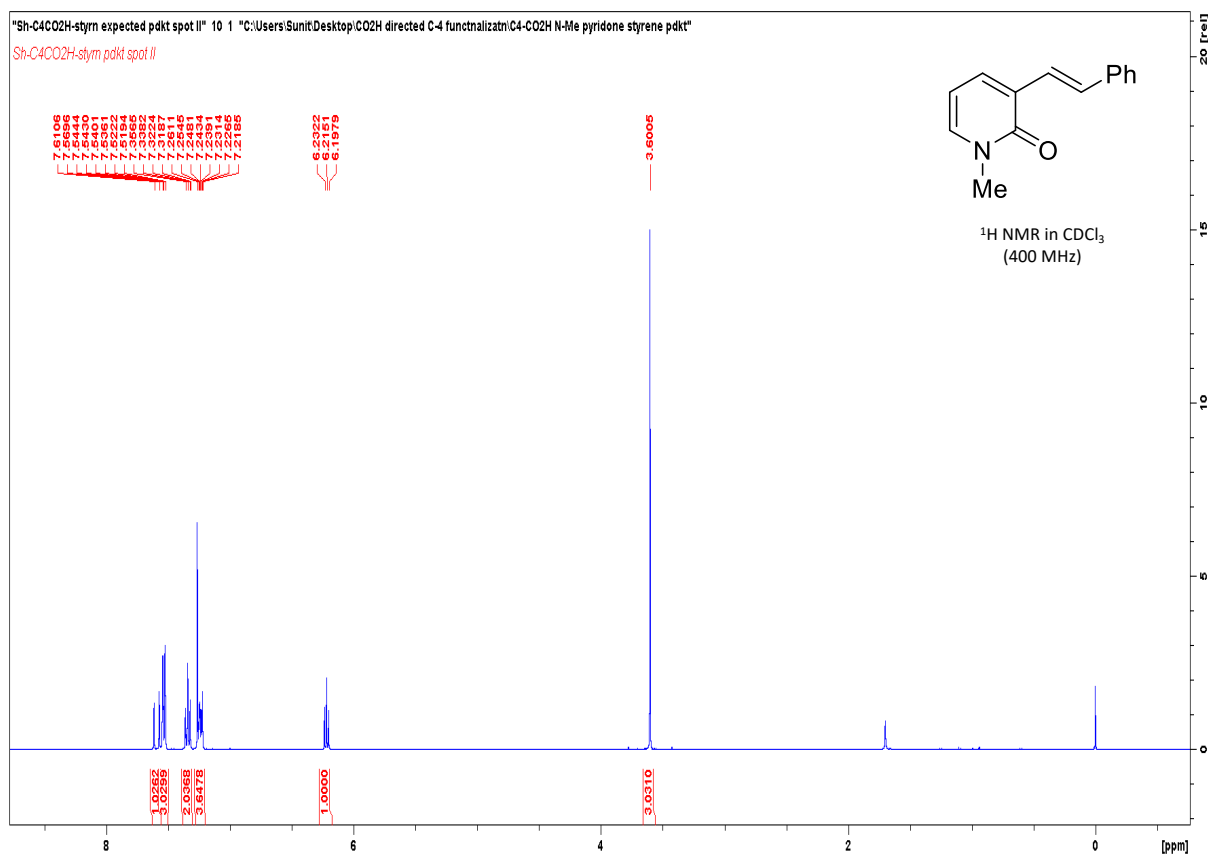
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Sh-DA.pdkt -PPTS-Tol-pure

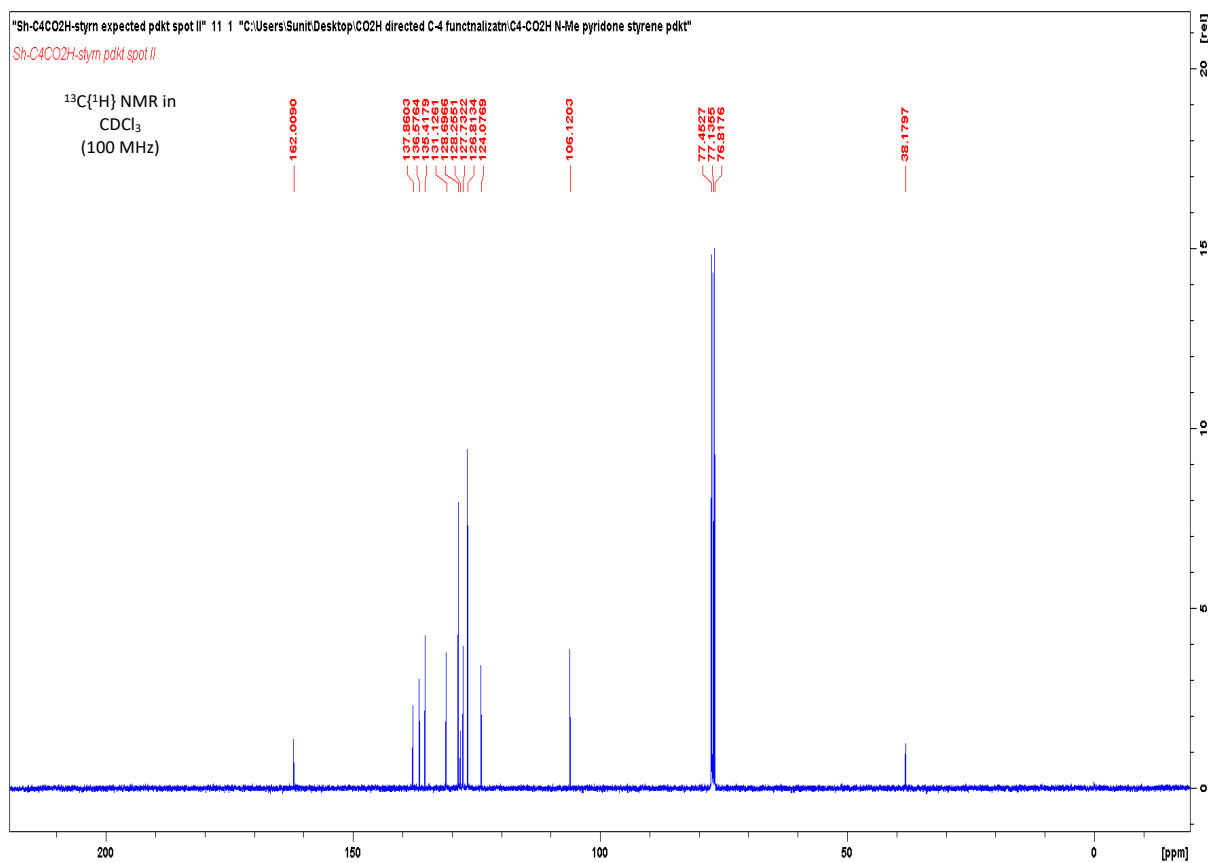
$^{13}\text{C}\{^1\text{H}\}$ NMR in CDCl_3 (100 MHz)

Chemical shifts (ppm): 155.3930, 150.5287, 145.9759, 137.7115, 135.1522, 135.5066, 131.6192, 129.1835, 129.0781, 128.8296, 128.3662, 128.1871, 128.0374, 126.0392, 123.3840, 106.1800, 77.4759, 76.8404, 55.3093, 52.6594, 34.5985.

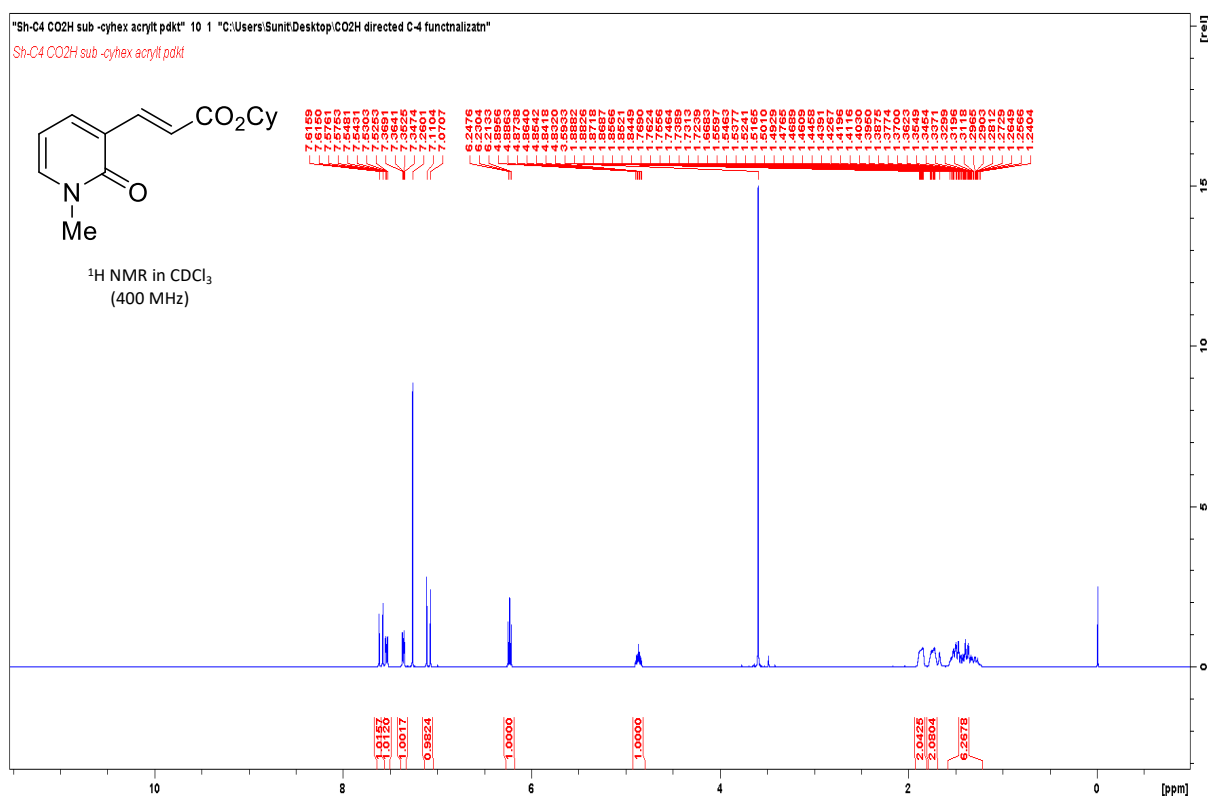
¹H NMR of compound **8aa** in CDCl₃ (400 MHz)



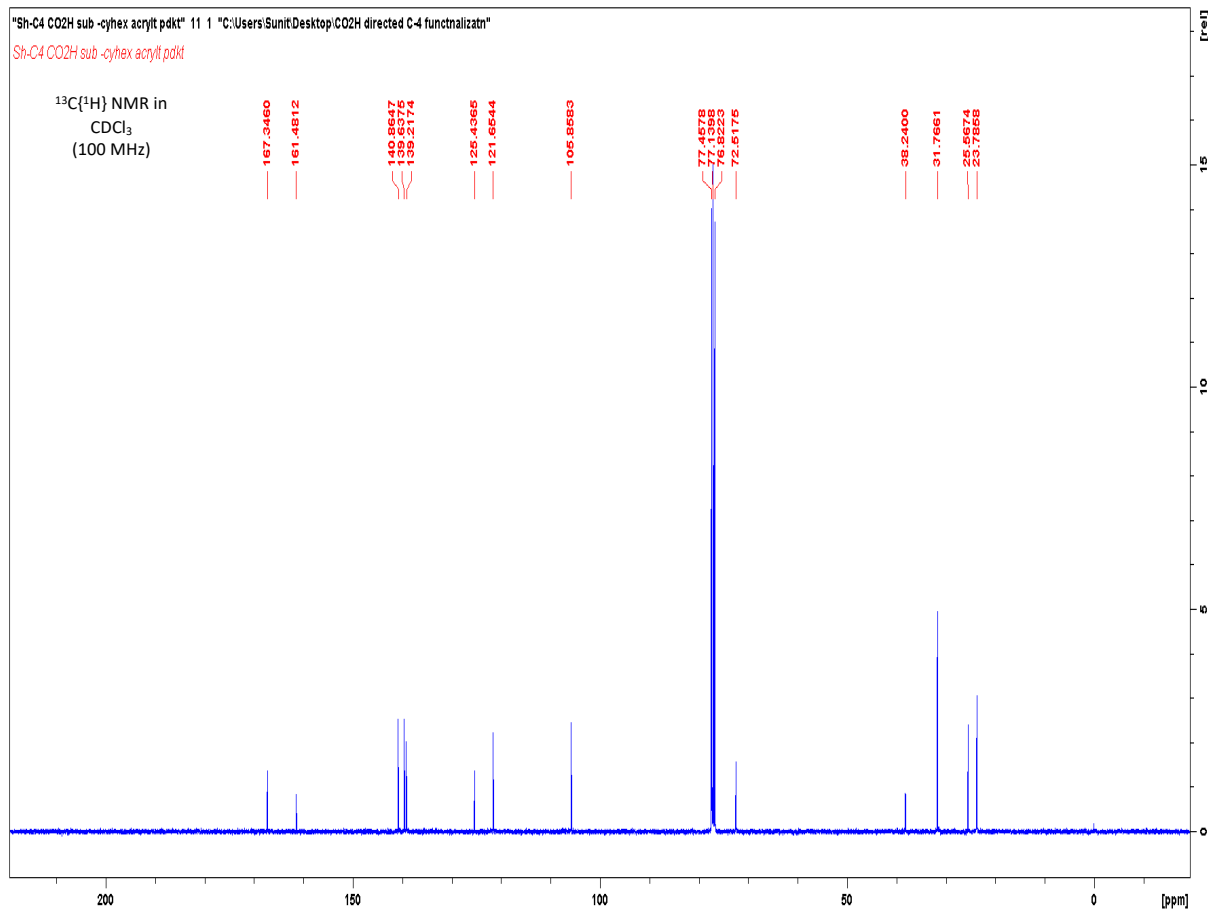
¹³C{¹H} NMR of compound **8aa** in CDCl₃ (100 MHz)



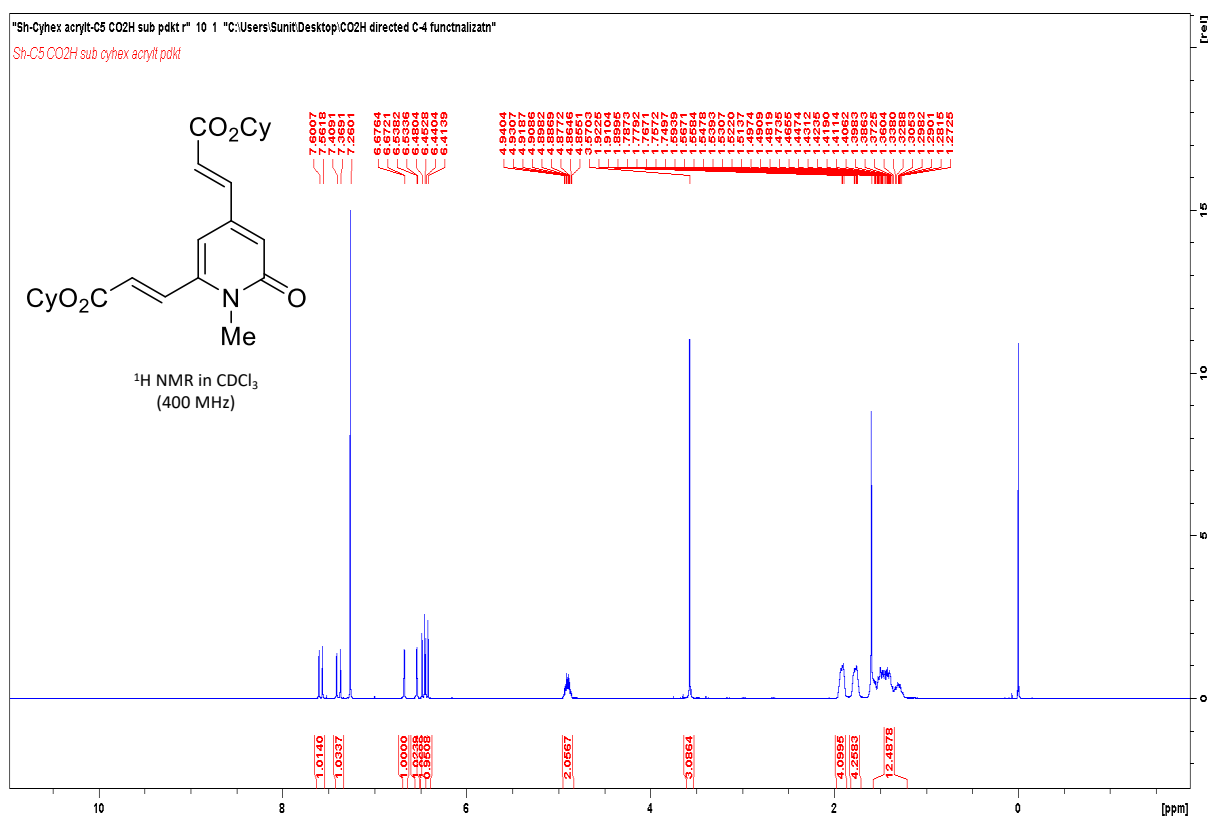
¹H NMR of compound **8al** in CDCl₃ (400 MHz)



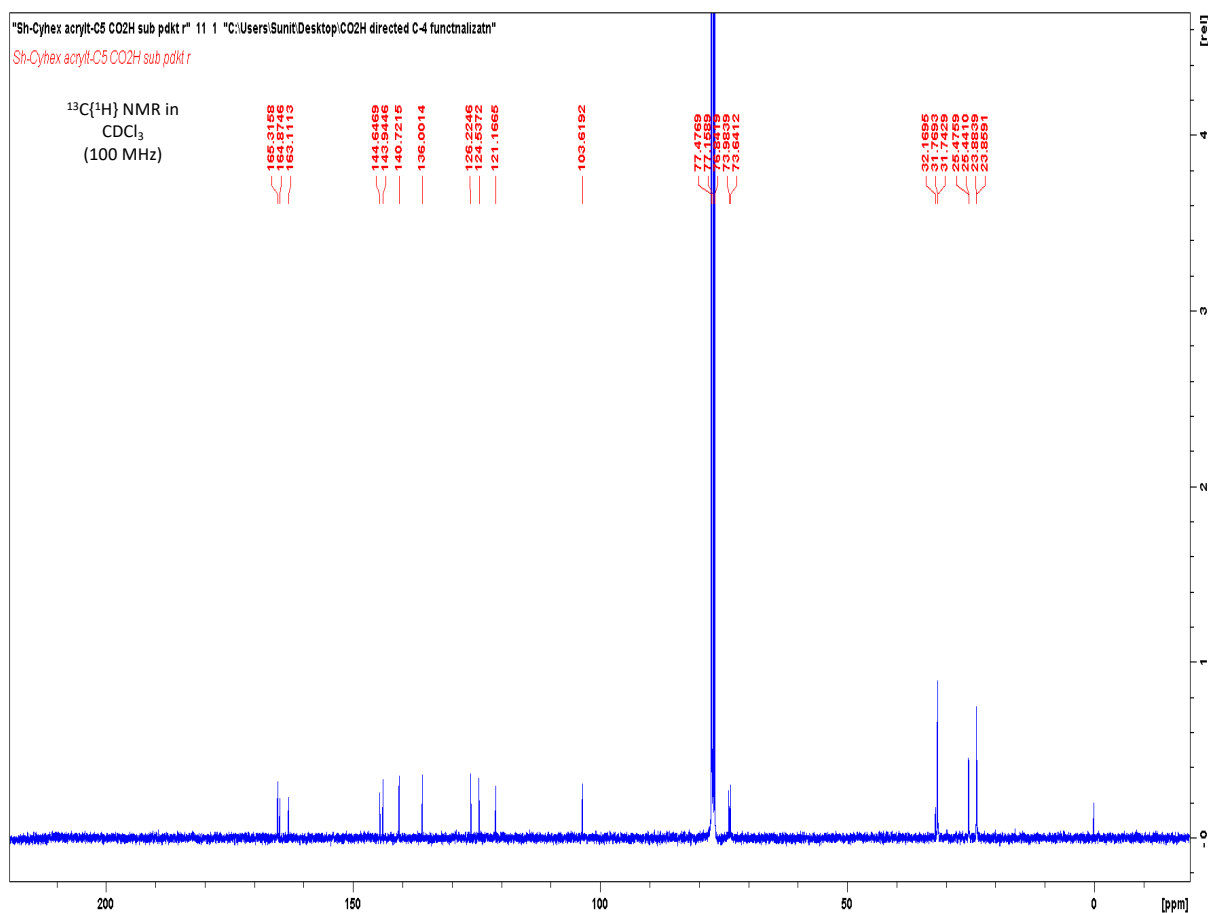
¹³C{¹H} NMR of compound **8al** in CDCl₃ (100 MHz)



^1H NMR of compound **10aI** in CDCl_3 (400 MHz)



$^{13}\text{C}\{^1\text{H}\}$ NMR of compound **10aI** in CDCl_3 (100 MHz)



CC1=CC(=C2C(=C1)C(=O)OC2C(CO2C)C)C(=O)N1C

¹H NMR in CDCl₃
 (400 MHz)

Integration values (from left to right): 1.0032, 1.0000, 1.0120, 1.0186, 3.1022, 2.0684, 2.0360, 2.1228, 1.0844, 5.3291.

Chemical shifts (ppm) listed on the right: 8.1697, 7.2702, 6.5142, 6.5116, 6.5116, 6.5098, 6.5098, 6.4834, 6.4834, 4.8400, 4.8270, 4.8045, 4.7917, 4.7810, 3.6429, 3.6251, 3.6251, 2.9261, 2.9261, 2.6334, 2.6334, 1.8682, 1.8682, 1.7375, 1.7375, 1.7282, 1.7117, 1.7117, 1.6928, 1.6928, 1.6781, 1.6781, 1.6560, 1.6560, 1.6346, 1.6346, 1.6336, 1.6336, 1.4502, 1.4502, 1.4367, 1.4367, 1.4243, 1.4243, 1.3946, 1.3946, 1.3933, 1.3933, 1.3673, 1.3673, 1.3412, 1.3412, 1.3398, 1.3398, 1.3147, 1.3147, 1.2876, 1.2876, 1.2721, 1.2721, 1.2608, 1.2608, 1.2431, 1.2431, 1.2316, 1.2316.

¹³C{¹H} NMR in CDCl₃ (100 MHz)

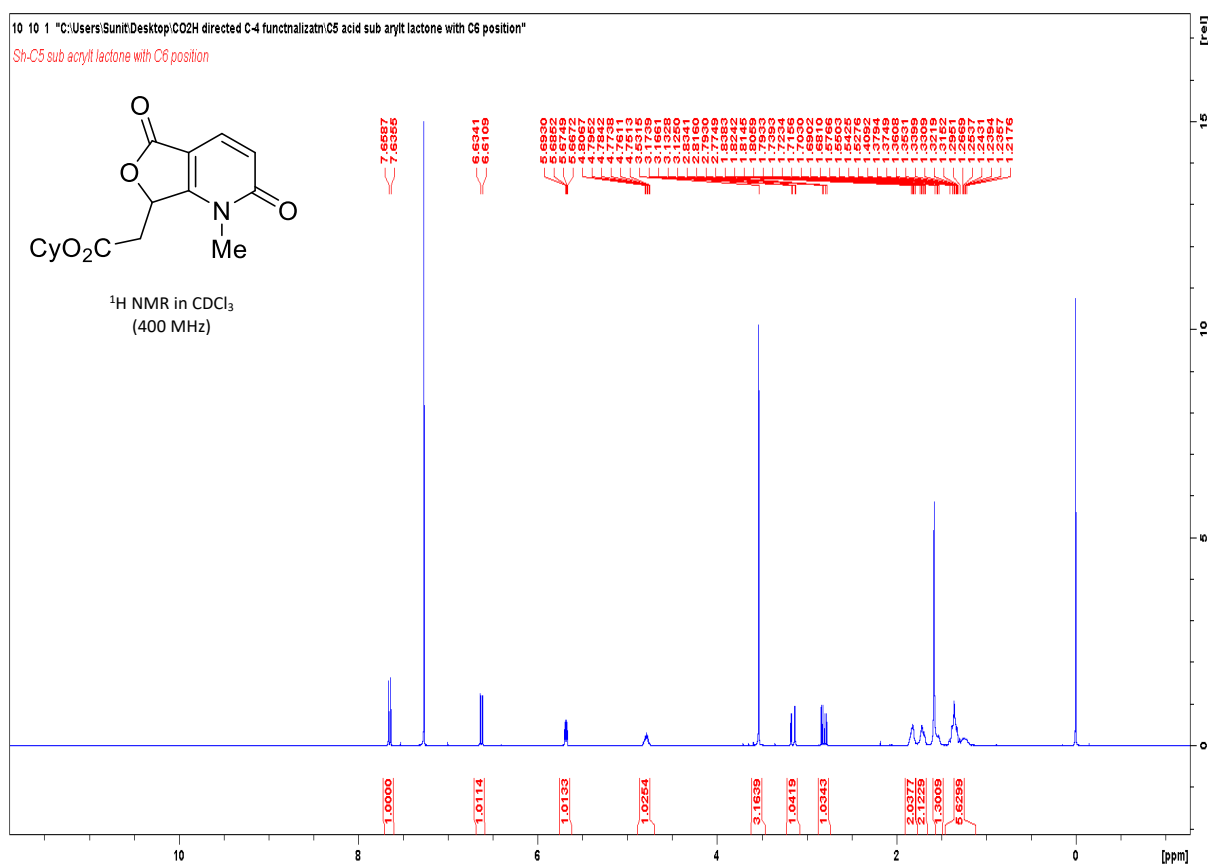
Sh-C5 sub acrylt lactone with C4 position

11 1 "C:\Users\Sunit\Desktop\CO2H directed C-4 functionalizatn"

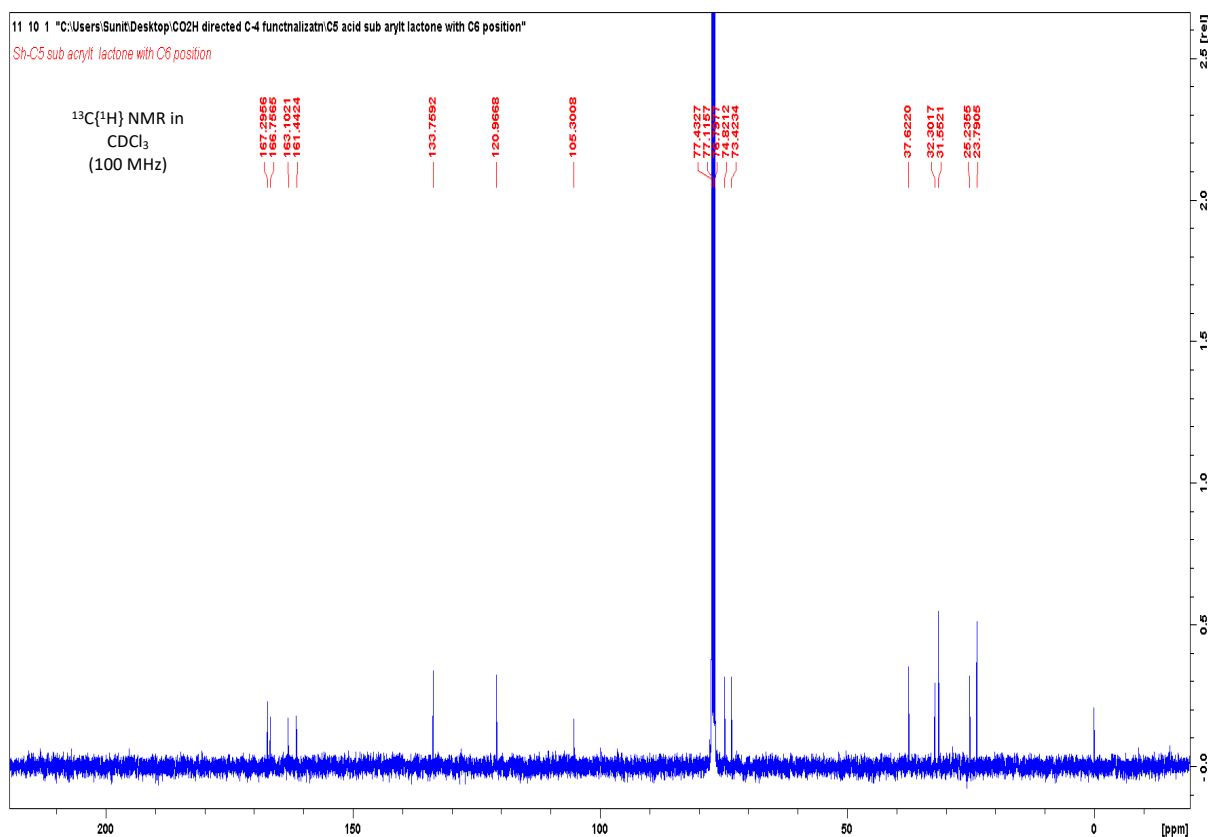
168.0649
166.8065
162.6389
156.9490
140.6601
110.8835
106.3762
77.4361
77.1180
76.8937
74.3373
39.1343
38.1201
31.6065
25.2879
23.7891

[ppm]

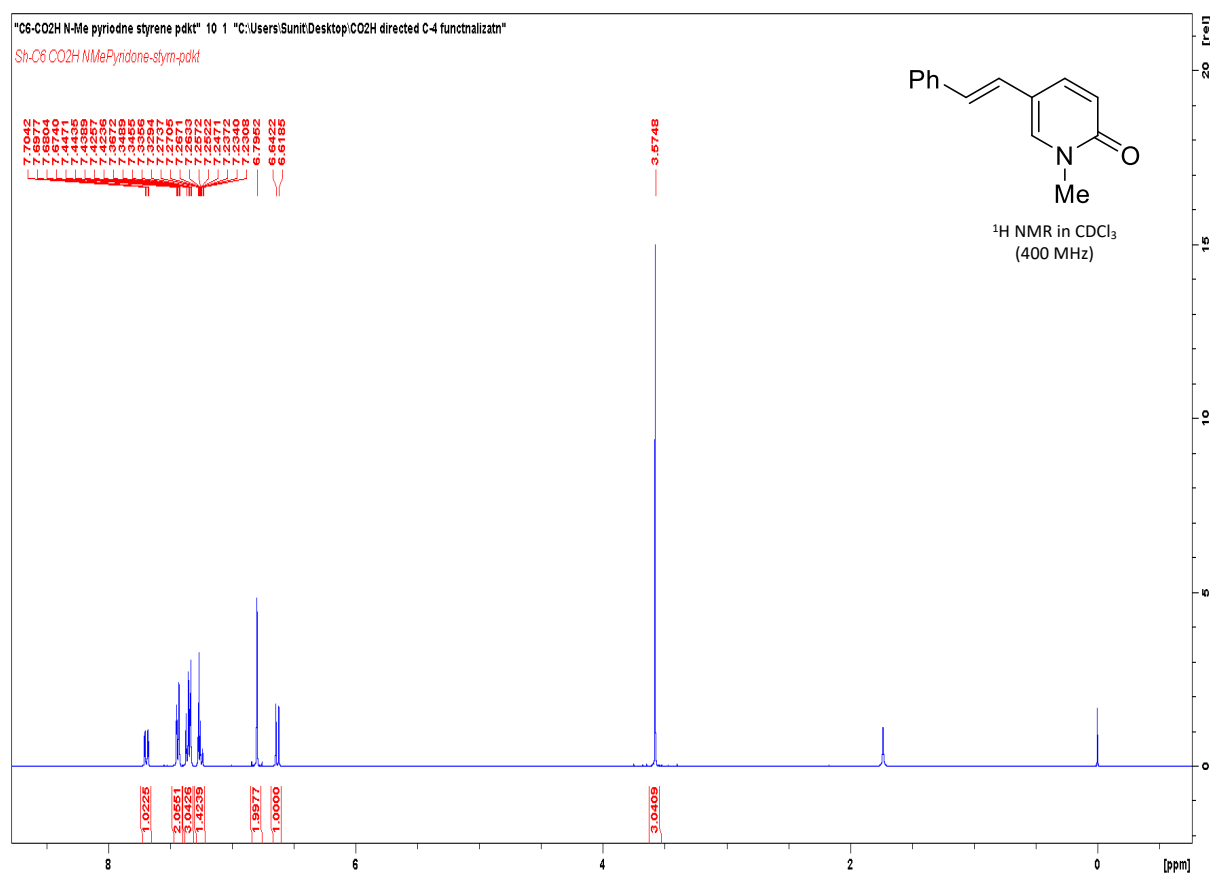
¹H NMR of compound **12aI** in CDCl₃ (400 MHz)



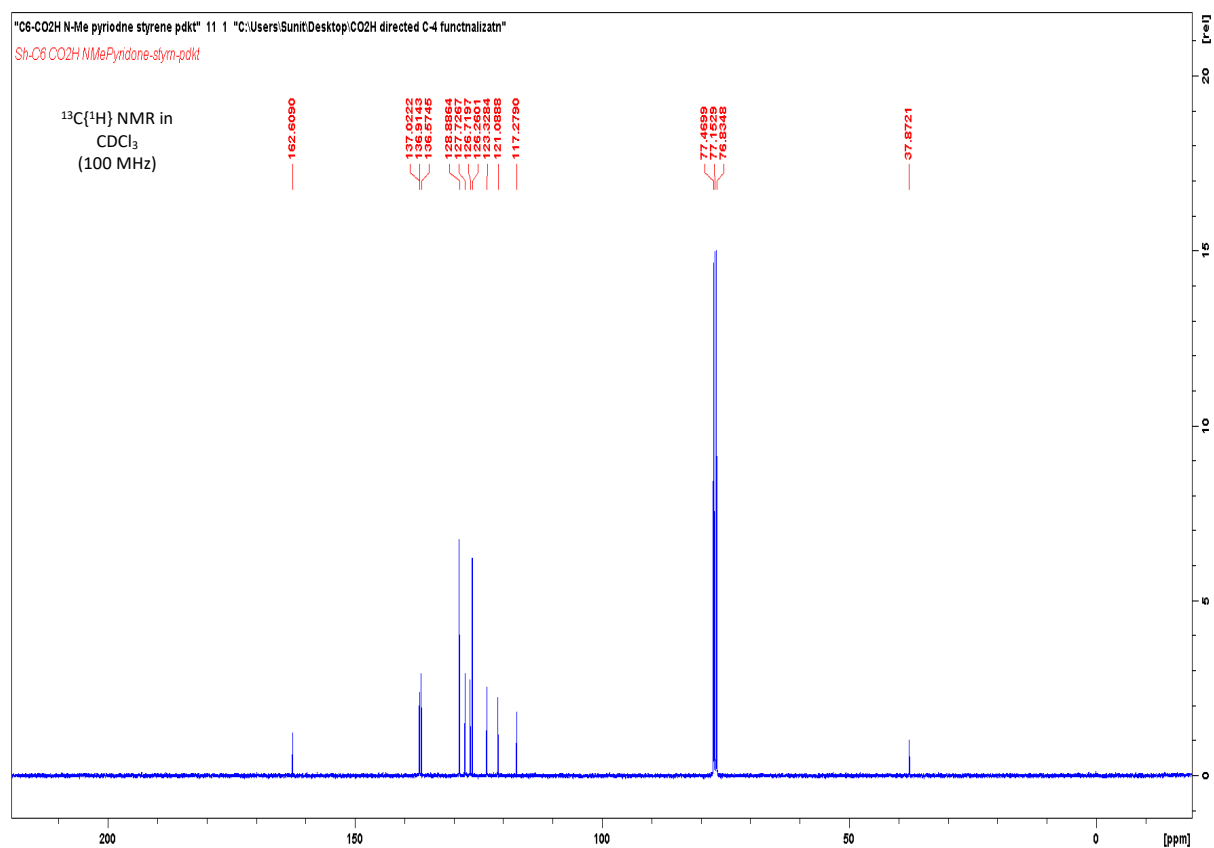
¹³C{¹H} NMR of compound **12aI** in CDCl₃ (100 MHz)



^1H NMR of compound **14aa** in CDCl_3 (400 MHz)



$^{13}\text{C}\{^1\text{H}\}$ NMR of compound **14aa** in CDCl_3 (100 MHz)



¹H NMR in CDCl₃ (400 MHz)

COC(=O)c1cc(C(=O)c2ccccc2)ccn1-c3ccccc3

Chemical structure of the compound: 1-(2-phenyl-6-methoxycarbonylpyridin-3-yl)pyrene.

¹H NMR spectrum (400 MHz, CDCl₃) showing peaks in the aromatic region (6.3-8.4 ppm) and a methoxy singlet (3.9 ppm). Integration values are provided below the baseline.

Chemical Shift (ppm)	Integration
8.3904, 8.3786, 8.3404, 8.3217, 7.7680, 7.7644, 7.6711, 7.6857, 7.6844, 7.5967, 7.5768, 7.5231, 7.5207, 7.5102, 7.5095, 7.1800, 7.1809, 7.1805, 7.1735, 7.1699, 7.1610, 7.1611, 7.1603, 7.1448, 7.1377, 6.3759, 6.3573	1.0044, 1.0006, 1.0181, 0.9826, 6.0661, 1.0112
3.9136	3.0124

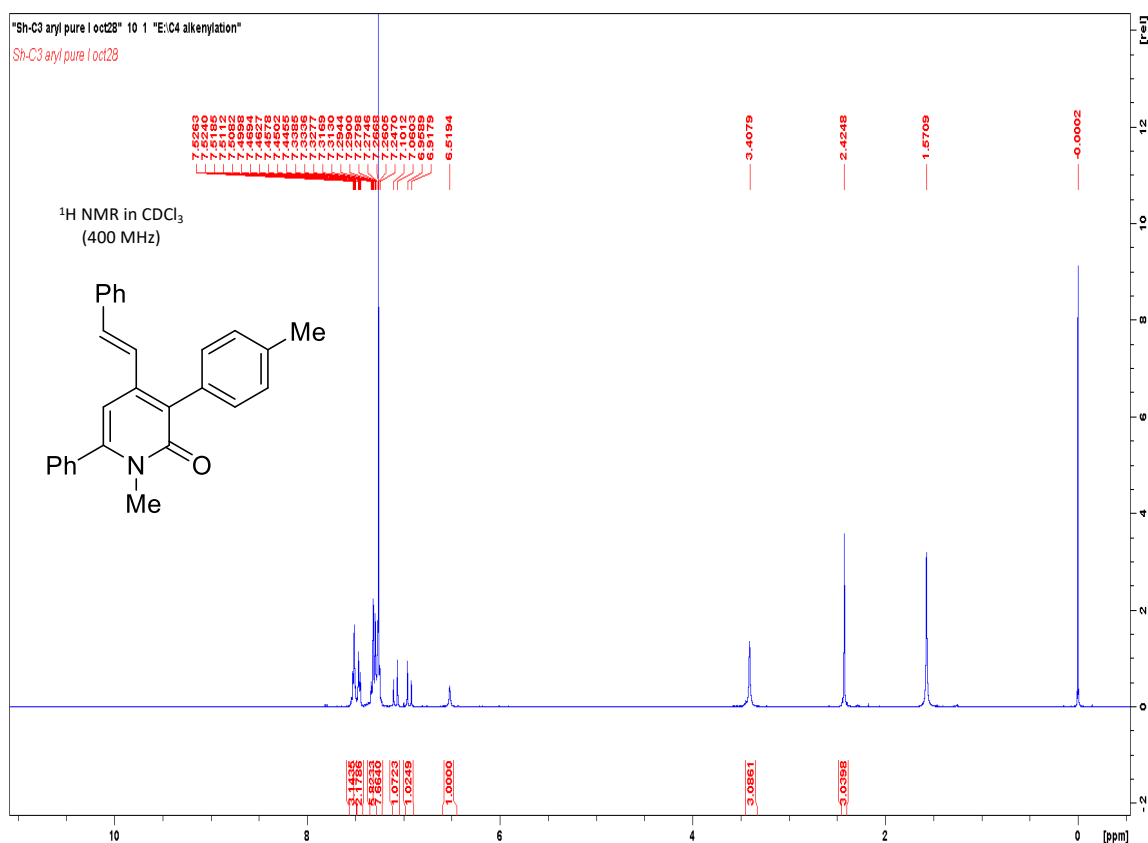
¹³C{¹H} NMR in CDCl₃ (100 MHz)

Sh-3CO2Me PyPy-C6 aryltn pdkt" 11 1 "C:\Users\Sunit\Desktop\CO2H directed C-4 functionalizatn/tetra substituted pyridone synthesis"

Sh-3CO2Me PyPy-C6 aryltn pdkt

Chemical shifts (ppm): 165.9638, 160.2853, 154.4369, 151.7549, 149.2722, 145.7076, 137.7982, 134.6889, 133.2598, 132.2608, 131.7531, 123.6750, 119.6724, 107.0926, 77.4759, 77.0, 76.8404, 52.4690.

¹H NMR of compound **17** in CDCl₃ (400 MHz)



¹³C{¹H} NMR of compound **17** in CDCl₃ (100 MHz)

