

# Supporting Information

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

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### Instrumentation and Chemicals

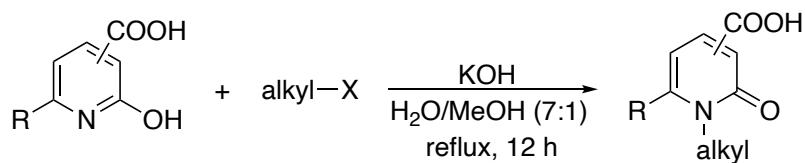
$^1\text{H}$ ,  $^{13}\text{C}\{^1\text{H}\}$ , and  $^{19}\text{F}\{^1\text{H}\}$  spectra were recorded at 400, 100, and 162 MHz, respectively, for  $\text{DMSO-}d_6$  and  $\text{CDCl}_3$  solutions. HRMS data were obtained by APCI using TOF or CI using a magnetic sector. GC analysis was carried out 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 60F<sub>254</sub>. 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  $\mu\text{m}$ ) (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.<sup>S1</sup> 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.<sup>S2</sup> 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**)



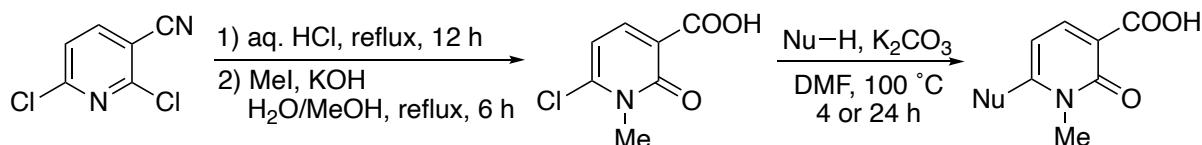
The above mentioned C6-substituted *N*-methyl-2-pyridone-3-carboxylic acid substrates were prepared from corresponding C6-substituted 3-cyano-2-pyridones (prepared according to literature report<sup>S3</sup>) in two steps.

In the first step, a mixture of suitable C6-substituted 3-cyano-2-pyridone (4.0 mmol), K<sub>2</sub>CO<sub>3</sub> (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 CHCl<sub>3</sub> (3 x 30 mL). The combined organic layers were washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>, 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  $\text{CHCl}_3$  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  $\text{K}_2\text{CO}_3$  (5.0 mmol) in DMF 10.0 mL was heated at 100 °C for 4 or 24 h under  $\text{N}_2$  (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  $\text{CHCl}_3$  (3 x 30 mL), and combined organic layers washed with brine, dried over  $\text{Na}_2\text{SO}_4$ , 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),  $[\text{Cp}^*\text{RhCl}_2]_2$  (3.2 mg 0.005 mmol),  $\text{Cu}(\text{OAc})_2 \bullet \text{H}_2\text{O}$  (40.0 mg, 0.2 mmol),  $\text{K}_4\text{P}_2\text{O}_7$  (132 mg, 0.4 mmol), and molecular sieves 4A (100 mg) were placed in a 20 mL screw vial. The reaction vessel was vacuumed and refilled with dry  $\text{N}_2$ . Toluene (1.0 mL) and styrene (**2a**) (69  $\mu\text{L}$ , 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  $\text{CHCl}_3$  (10.0 mL), filtered through a short celite pad, and washed three times (3 x 25.0 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  $\text{EtOAc}/\text{Hexane}/\text{Et}_3\text{N}$  = 1/5/0.05 to  $\text{EtOAc}/\text{CHCl}_3/\text{Et}_3\text{N}$  = 1/1/0.05 (v/v/v) to get **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),  $[\text{Cp}^*\text{RhCl}_2]_2$  (16 mg 0.025 mmol),  $\text{Cu}(\text{OAc})_2 \bullet \text{H}_2\text{O}$  (200.0 mg, 1.0 mmol),  $\text{K}_4\text{P}_2\text{O}_7$  (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  $\text{N}_2$ . 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  $\text{CHCl}_3$  (30.0 mL) and filtered through a short celite pad, washed three times (3 x 50.0 mL  $\text{MeOH}/\text{CHCl}_3$  = 1/1). The combined organic layers were evaporated, 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 **3aa** (145.6 mg, 69% yield) as an off white solid.

### Procedure for conversion of **3da** to **4** via hydrogenation in $\text{AcOH}$ (Scheme 4)

(*E*)-1-Benzyl-4-styrylpyridin-2(*1H*)-one (**3da**; 57.4 mg, 0.2 mmol) was dissolved in  $\text{AcOH}$  (6.0 mL) in a 25.0 mL round-bottom flask.  $\text{Pd}(\text{OH})_2$  (10 mol%) was added. The round bottom flask was evacuated and filled with  $\text{H}_2$  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  $\text{EtOAc}/\text{Hexane}/\text{Et}_3\text{N}$  = 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)<sub>2</sub> (10 mol %) was added. The round bottom flask was evacuated, and filled with H<sub>2</sub> 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/Et<sub>3</sub>N = 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 N<sub>2</sub>. 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\*RhCl<sub>2</sub>]<sub>2</sub> (3.2 mg 0.005 mmol), Cu(OAc)<sub>2</sub>•H<sub>2</sub>O (40.0 mg, 0.2 mmol), K<sub>2</sub>HPO<sub>4</sub> (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 N<sub>2</sub>. 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<sub>3</sub> (10.0 mL), filtered through a short celite pad, and washed three times (3 x 25.0 mL MeOH/CHCl<sub>3</sub> = 1/1). The combined organic layers were evaporated, and the residue was subjected to silica gel column chromatography using EtOAc/Hexane/Et<sub>3</sub>N = 1/5/0.05 to EtOAc/CHCl<sub>3</sub>/Et<sub>3</sub>N = 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-dihdropyridine-3-carboxylic acid (**9a**; 30.6 mg, 0.2 mmol),  $[\text{Cp}^*\text{RhCl}_2]_2$  (3.2 mg 0.005 mmol),  $\text{Cu}(\text{OAc})_2 \bullet \text{H}_2\text{O}$  (40.0 mg, 0.2 mmol),  $\text{K}_2\text{HPO}_4$  (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  $\text{N}_2$ . Toluene (1.0 mL) and cyclohexyl acrylate (**2o**; 94  $\mu\text{L}$ , 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  $\text{CHCl}_3$  (10.0 mL), filtered through a short celite pad, and washed three times (3 x 25.0 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  $\text{EtOAc}/\text{Hexane}/\text{Et}_3\text{N} = 1/5/0.05$  to  $\text{EtOAc}/\text{CHCl}_3/\text{Et}_3\text{N} = 1/1/0.05$  (v/v/v) 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-dihdropyridine-2-carboxylic acid (**13a**; 30.6 mg, 0.2 mmol),  $[\text{Cp}^*\text{RhCl}_2]_2$  (3.2 mg 0.005 mmol),  $\text{Cu}(\text{OAc})_2 \bullet \text{H}_2\text{O}$  (40.0 mg, 0.2 mmol),  $\text{K}_2\text{HPO}_4$  (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  $\text{N}_2$ . Toluene (1.0 mL) and styrene (**2a**; 69  $\mu\text{L}$ , 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  $\text{CHCl}_3$  (10.0 mL), filtered through a short celite pad, and washed three times (3 x 25.0 mL  $\text{MeOH}/\text{CHCl}_3 = 1/1$ ). The combined organic layers were evaporated, 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 **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-2*H*-[1,2'-bipyridine]-3-carboxylate (**15**, 46 mg, 0.2 mmol),<sup>54</sup>  $\text{PhBF}_3\text{K}$  (110 mg, 0.6 mmol),  $[\text{Cp}^*\text{RhCl}_2]_2$  (6.2 mg, 0.01 mmol),  $\text{AgSbF}_6$  (13.7 mg, 0.04 mmol), and  $\text{Ag}_2\text{O}$  (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  $\text{CHCl}_3$  (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  $\text{CH}_3\text{CN}$  in a 25 mL round-bottom flask, filled with nitrogen.  $\text{MeOTf}$  (66  $\mu\text{L}$ , 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  $\text{NaBH}_4$  (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  $\text{Na}_2\text{SO}_4$ , 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.  $\text{NaOH}$  (2 M, 3.0 mL) and  $\text{MeOH}$  (3.0 mL) was heated at 50 °C for 5 h. Acidification with aq.  $\text{HCl}$  (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),  $\text{Cu}(\text{OAc})_2 \bullet \text{H}_2\text{O}$  (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  $\text{N}_2$ . Toluene (1.0 mL) and styrene (**2a**) (69  $\mu\text{L}$ , 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  $\text{CHCl}_3$  (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

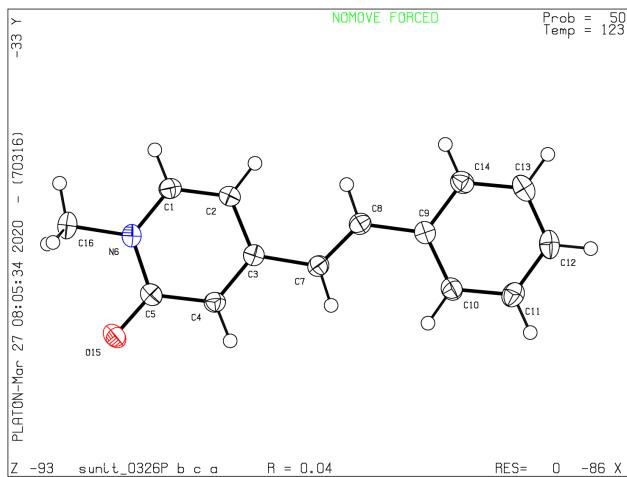
$\text{EtOAc/Hexane/Et}_3\text{N} = 1/5/0.05$  to  $\text{EtOAc/CHCl}_3/\text{Et}_3\text{N} = 1/1/0.05$  (v/v/v) to form **3ha** in 61% yield (35.1 mg, 0.12 mmol) as off white solid.

**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  $\text{Na}_2\text{SO}_4$ , filtered, and concentrated in vacuo. The residue was purified by silica gel column chromatography using  $\text{EtOAc/Hexane/Et}_3\text{N} = 1/1/0.05$  to  $\text{EtOAc/Et}_3\text{N} = 1/0.05$  (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.



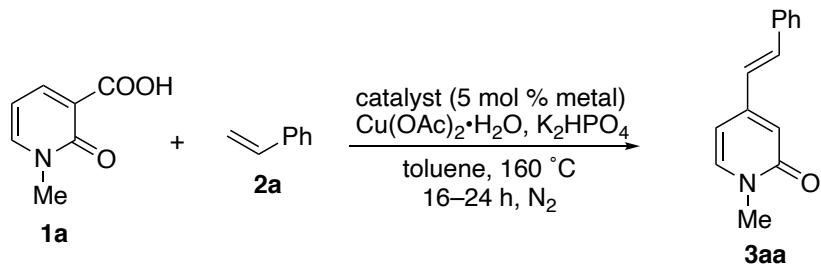
**Figure S1.** ORTEP drawing of **3aa** (CCDC 2032339, 50% thermal probability).

**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

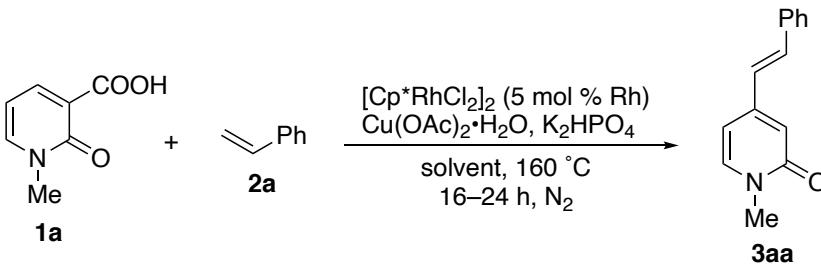
**Table S2.** Optimization Studies for Decarboxylative C4-Selective C–H Alkenylation of **1a** with **2a**: Catalyst Screening<sup>[a]</sup>



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

[a] Reaction conditions: **1a** (0.20 mmol), **2a** (0.40 mmol), catalyst (5 mol % on metal), Cu(OAc)<sub>2</sub>·H<sub>2</sub>O (0.20 mmol), K<sub>2</sub>HPO<sub>4</sub> (0.40 mmol), toluene (1.0 mL), 160 °C, 16–24 h, N<sub>2</sub>. [b] Estimated by <sup>1</sup>H NMR using CH<sub>2</sub>Br<sub>2</sub> as the internal standard.

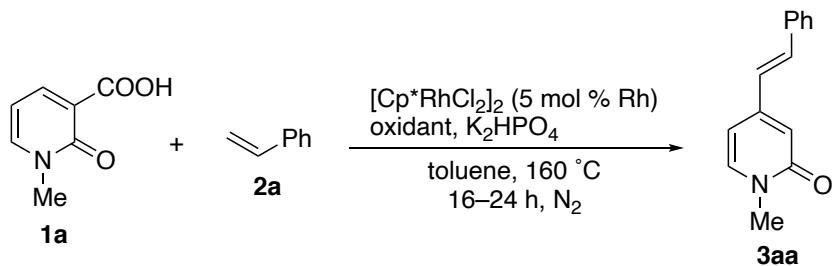
**Table S3.** Optimization Studies for Decarboxylative C4-Selective C–H Alkenylation of **1a** with **2a**: Solvent Screening<sup>[a]</sup>



entry	solvent	yield (%) <sup>[b]</sup>	entry	catalyst	yield (%) <sup>[b]</sup>
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\*RhCl<sub>2</sub>]<sub>2</sub> (0.0050 mmol), Cu(OAc)<sub>2</sub>·H<sub>2</sub>O (0.20 mmol), K<sub>2</sub>HPO<sub>4</sub> (0.40 mmol), solvent (1.0 mL), 160 °C, 16–24 h, N<sub>2</sub>. [b] Estimated by <sup>1</sup>H NMR using CH<sub>2</sub>Br<sub>2</sub> as the internal standard.

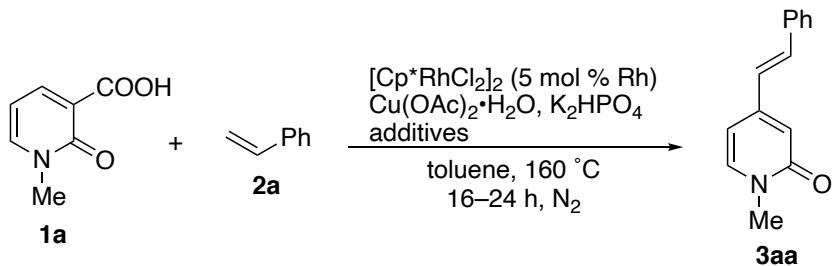
**Table S4.** Optimization Studies for Decarboxylative C4-Selective C–H Alkenylation of **1a** with **2a**: Oxidant Screening<sup>[a]</sup>



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

[a] Reaction conditions: **1a** (0.20 mmol), **2a** (0.40 mmol),  $[\text{Cp}^*\text{RhCl}_2]_2$  (0.0050 mmol), oxidant (0.20 mmol),  $\text{K}_2\text{HPO}_4$  (0.40 mmol), toluene (1.0 mL), 160 °C, 16–24 h,  $\text{N}_2$ . [b] Estimated by  $^1\text{H}$  NMR using  $\text{CH}_2\text{Br}_2$  as the internal standard. [c] In 1,4-dioxane.

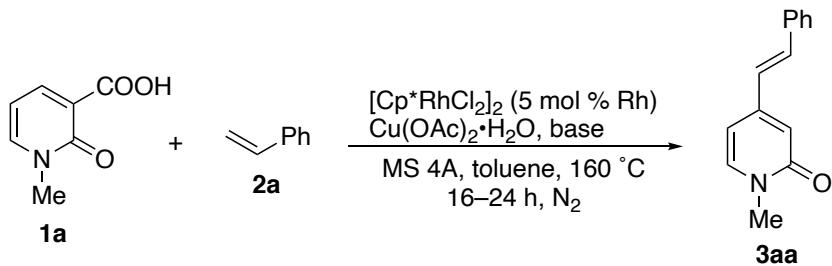
**Table S5.** Optimization Studies for Decarboxylative C4-Selective C–H Alkenylation of **1a** with **2a**: Additive Screening<sup>[a]</sup>



entry	additives	yield (%) <sup>[b]</sup>	entry	additives	yield (%) <sup>[b]</sup>
1	none	43	4 <sup>[d]</sup>	MS 4A (30 mg)	60
2	$\text{AgSbF}_6$ (10 mol %)	26	5 <sup>[d,e]</sup>	MS 4A (30 mg)	34
3 <sup>[c]</sup>	$\text{AgSbF}_6$ (10 mol %) $\text{NaOAc}$ (100 mol %)	21	6 <sup>[d]</sup>	<b>MS 4A (100 mg)</b>	<b>66</b>

[a] Reaction conditions: **1a** (0.20 mmol), **2a** (0.40 mmol),  $[\text{Cp}^*\text{RhCl}_2]_2$  (0.0050 mmol),  $\text{Cu(OAc)}_2\text{•H}_2\text{O}$  (0.20 mmol),  $\text{K}_2\text{HPO}_4$  (0.40 mmol), additives, toluene (1.0 mL), 160 °C, 16 h,  $\text{N}_2$ . [b] Estimated by  $^1\text{H}$  NMR using  $\text{CH}_2\text{Br}_2$  as the internal standard. [c] With 0.040 mmol of  $\text{Cu(OAc)}_2\text{•H}_2\text{O}$ . [d] With 0.60 mmol of **2a**. [e] With potassium salt of **1a** instead of free carboxylic acid **1a**.

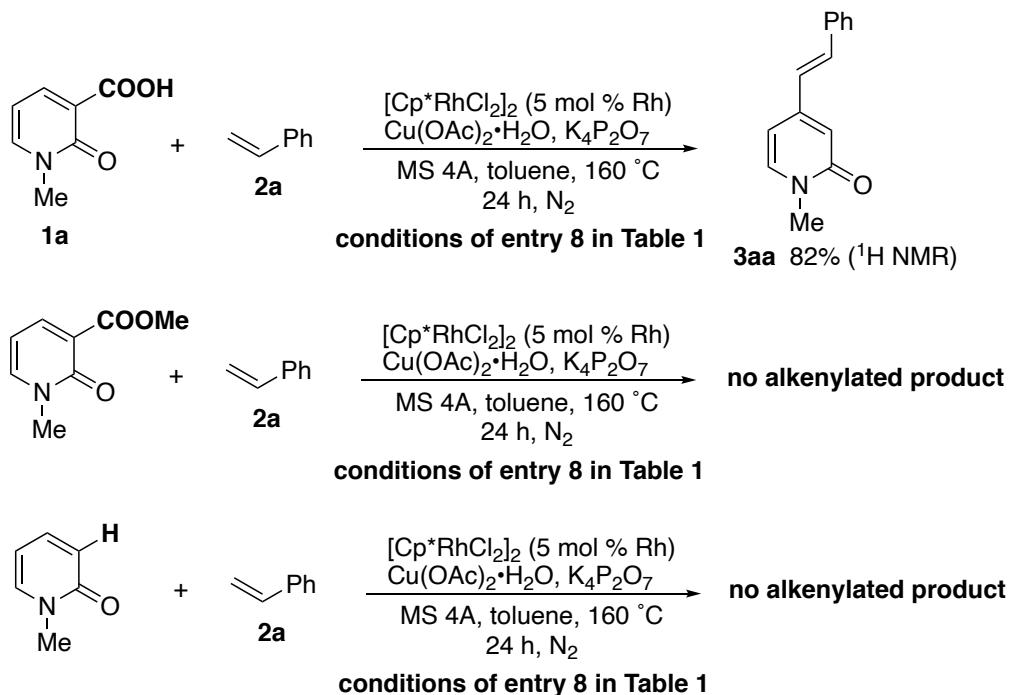
**Table S6.** Optimization Studies for Decarboxylative C4-Selective C–H Alkenylation of **1a** with **2a**: Base Screening<sup>[a]</sup>



entry	base	yield (%) <sup>[b]</sup>	entry	base	yield (%) <sup>[b]</sup>
1	none	5	6	NaHCO <sub>3</sub>	23
2	K <sub>2</sub> HPO <sub>4</sub>	66	7	KHCO <sub>3</sub>	25
3	Na <sub>2</sub> CO <sub>3</sub>	26	8	<b>K<sub>4</sub>P<sub>2</sub>O<sub>7</sub></b>	<b>82 (78)</b>
4	K <sub>2</sub> CO <sub>3</sub>	11	9 <sup>[c]</sup>	K <sub>4</sub> P <sub>2</sub> O <sub>7</sub>	45
5	Cs <sub>2</sub> CO <sub>3</sub>	0	10 <sup>[d]</sup>	K <sub>4</sub> P <sub>2</sub> O <sub>7</sub>	0

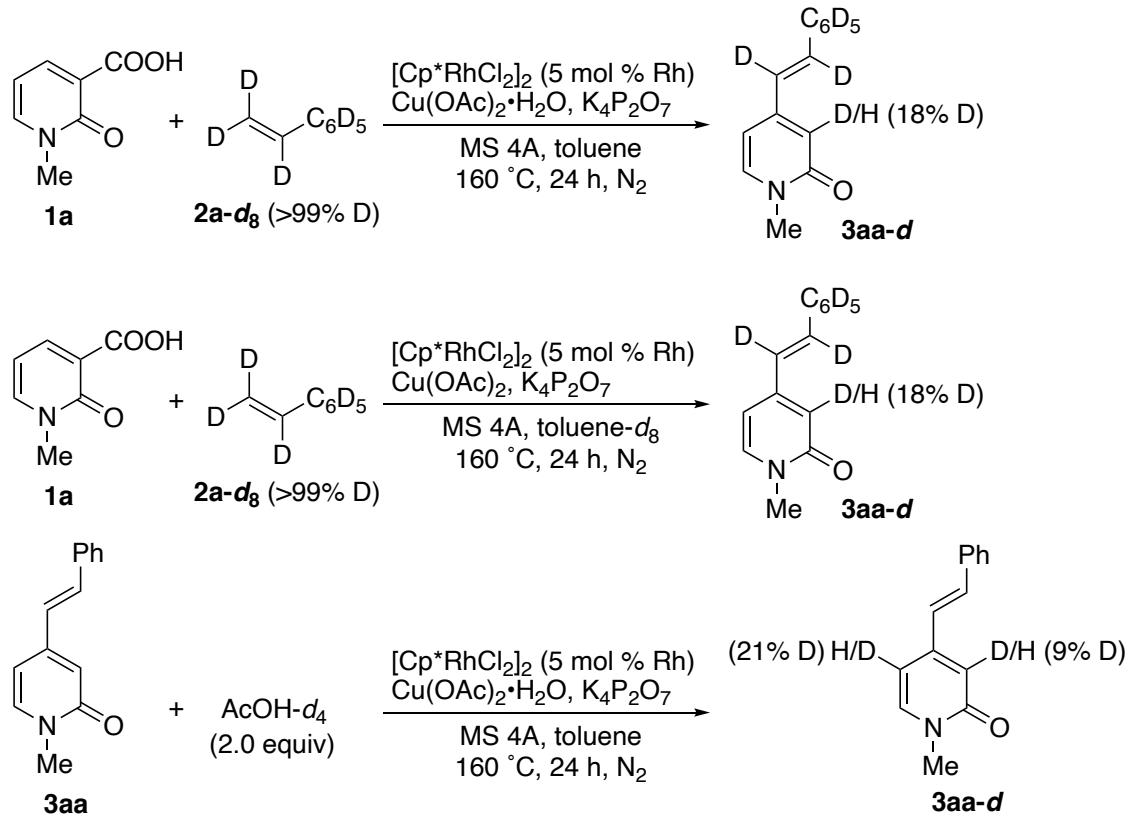
[a] Reaction conditions: **1a** (0.20 mmol), **2a** (0.60 mmol), [Cp\*RhCl<sub>2</sub>]<sub>2</sub> (0.0050 mmol), Cu(OAc)<sub>2</sub>·H<sub>2</sub>O (0.20 mmol), base (0.40 mmol), MS 4A (100 mg), toluene (1.0 mL), 160 °C, 16 h, N<sub>2</sub>. [b] Estimated by <sup>1</sup>H NMR using CH<sub>2</sub>Br<sub>2</sub> 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

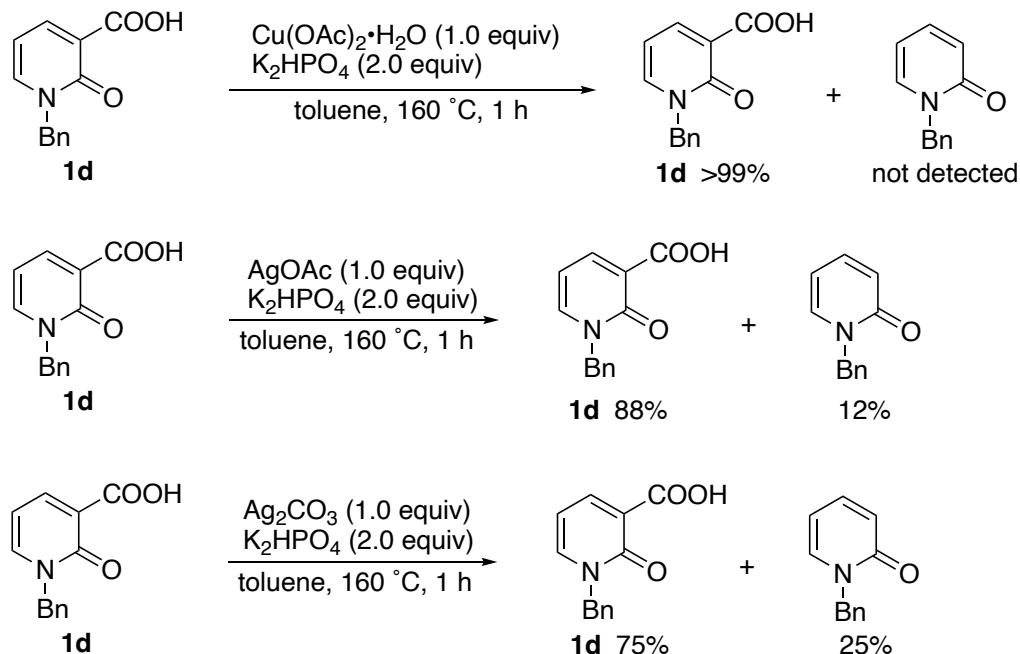
**Scheme S2.** Deuterium Incorporation Tests.



### Protoprocarboxylation Tests

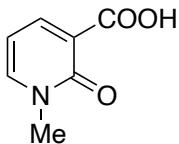
To compare the activity of  $\text{Cu}(\text{OAc})_2$ ,  $\text{AgOAc}$ , and  $\text{Ag}_2\text{CO}_3$  in the nonproductive protoprocarboxylation of **1d**, we performed the following experiments (Scheme S3).

**Scheme S3.** Protoprocarboxylation Tests.



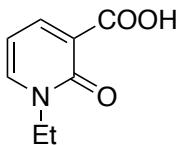
## Characterization Data for Products

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



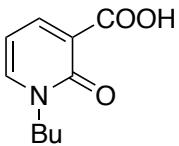
### 1-Methyl-2-oxo-1,2-dihydropyridine-3-carboxylic acid (1a)

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.<sup>S2</sup> 176-177 °C).  $^1\text{H}$  NMR (DMSO- $d_6$ , 400 MHz)  $\delta$  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)  $\delta$  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)

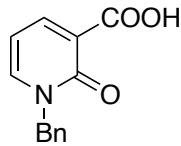
The compound was prepared according to general procedure **A** using 2-hydroxynicotinic acid and ethyl iodide (10.0 equiv.) and purified by recrystallization from chloroform. white solid, 492 mg, yield 59%. m.p. 177-179 °C.  $^1\text{H}$  NMR (DMSO- $d_6$ , 400 MHz)  $\delta$  14.72 (s, 1H), 8.38 (dd,  $J$  = 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)  $\delta$  165.3, 164.0, 145.6, 145.2, 116.8, 109.1, 45.8, 14.7. HRMS (APCI) m/z ([M+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)

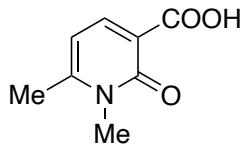
The compound was prepared according to general procedure **A** using 2-hydroxynicotinic acid and butyl iodide (5.0 equiv.) and purified by recrystallization chloroform. white solid, 555 mg, yield 57%. m.p. 103-105 °C.  $^1\text{H}$  NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  14.41(s, 1H), 8.51 (dd,  $J$  = 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).  $^{13}\text{C}\{\text{H}\}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  165.6, 164.1, 145.4, 142.7, 118.2, 108.3, 50.9, 31.2, 19.8, 13.6. HRMS (APCI) m/z ([M+H] $^+$ ) calcd for  $\text{C}_{10}\text{H}_{14}\text{NO}_3$  196.0968, found 196.0975.



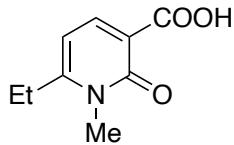
**1-Benzyl-2-oxo-1,2-dihydropyridine-3-carboxylic acid (1d)**

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.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  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).  $^{13}\text{C}\{\text{H}\}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  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 ([M+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)**

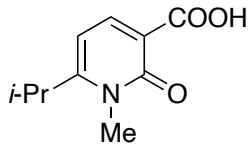
The compound was prepared according to general procedure **A** using 2-hydroxy-6-methylnicotinic acid and methyl iodide (10.0 equiv.) and purified by recrystallization from chloroform. white solid, 509 mg, yield 61%. m.p. 172-174 °C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  14.39 (s, 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).  $^{13}\text{C}\{\text{H}\}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  165.9, 165.2, 153.1, 144.5, 114.8, 109.3, 32.2, 21.7. HRMS (APCI) m/z ([M+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)**

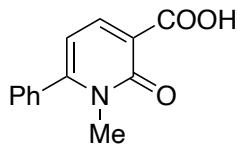
Prepared according to general procedure **B** from 6-ethyl-2-oxo-1,2-dihydropyridine-3-carbonitrile and used directly without further purification. white solid, 154 mg, yield 76% (over two steps). m.p.

146-148 °C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  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).  $^{13}\text{C}\{\text{H}\}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  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  $\text{C}_9\text{H}_{12}\text{NO}_3$  182.0812, found 182.0793.



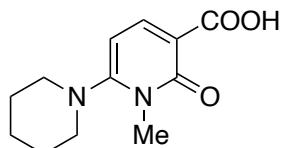
**6-Isopropyl-1-methyl-2-oxo-1,2-dihydropyridine-3-carboxylic acid (1g)**

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.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  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).  $^{13}\text{C}\{\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  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  $\text{C}_{10}\text{H}_{14}\text{NO}_3$  196.0968, found 196.0970.



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

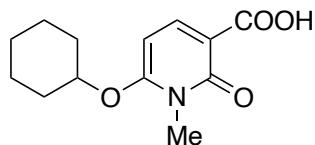
Prepared according to general procedure **B** from 2-oxo-6-phenyl-1,2-dihydropyridine-3-carbonitrile and used directly without further purification. white solid, 206 mg, yield 72% (over two steps). m.p. 209-211 °C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  14.45 (bs, 1H), 8.50 (d,  $J$  = 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).  $^{13}\text{C}\{\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  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  $\text{C}_{13}\text{H}_{12}\text{NO}_3$  230.0812, found 230.0795.



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

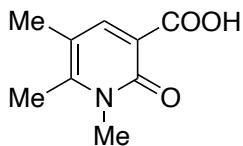
Prepared according to general procedure **C** from

6-chloro-1-methyl-2-oxo-1,2-dihdropyridine-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. <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 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). <sup>13</sup>C{<sup>1</sup>H} NMR (DMSO-*d*<sub>6</sub>, 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]<sup>+</sup>) calcd for C<sub>12</sub>H<sub>17</sub>N<sub>2</sub>O<sub>3</sub> 237.1234, found 237.1229.



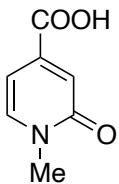
**6-(Cyclohexyloxy)-1-methyl-2-oxo-1,2-dihdropyridine-3-carboxylic acid (1j)**

Prepared according to general procedure C from 6-chloro-1-methyl-2-oxo-1,2-dihdropyridine-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. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 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). <sup>13</sup>C{<sup>1</sup>H} NMR (100 MHz, CDCl<sub>3</sub>) 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]<sup>+</sup>) calcd for C<sub>13</sub>H<sub>18</sub>NO<sub>4</sub> 252.1230, found 252.1234.



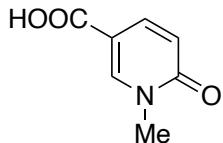
**1,5,6-Trimethyl-2-oxo-1,2-dihdropyridine-3-carboxylic acid (1k)**

Prepared according to general procedure B from 1,5,6-trimethyl-2-oxo-1,2-dihdropyridine-3-carbonitrile and used directly without further purification. White solid, 163 mg, yield 72% (over two steps). m.p. 196-198 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 14.63 (s, 1H), 8.32 (s, 1H), 3.71 (s, 3H), 2.46 (s, 3H), 2.23 (s, 3H). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 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]<sup>+</sup>) calcd for C<sub>9</sub>H<sub>12</sub>NO<sub>3</sub> 182.0812, found 182.0785.



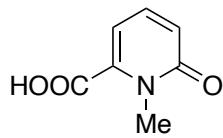
**1-Methyl-2-oxo-1,2-dihydropyridine-4-carboxylic acid (7a)**

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. <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 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). <sup>13</sup>C{<sup>1</sup>H} NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ 166.3, 162.1, 142.0, 141.0, 120.5, 103.7, 37.4. HRMS (APCI) m/z ([M+H]<sup>+</sup>) calcd for C<sub>7</sub>H<sub>8</sub>NO<sub>3</sub> 154.0499, found 154.0504.



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

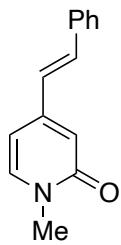
The compound was prepared in similar method as described in general procedure A using 6-hydroxynicotinic acid (3.0 mmol) and methyl iodide (10.0 equiv.) and purified by recrystallization from ethyl acetate-hexane. Pinkish white solid, 474 mg, yield 63%. m.p. 247-249 °C. <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 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). <sup>13</sup>C{<sup>1</sup>H} NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ 165.8, 162.5, 145.4, 139.3, 118.5, 109.4, 37.7. HRMS (APCI) m/z ([M+H]<sup>+</sup>) calcd for C<sub>7</sub>H<sub>8</sub>NO<sub>3</sub> 154.0499, found 154.0513.



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

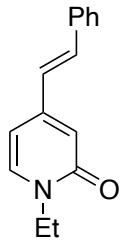
The compound was prepared in similar method as described in general procedure A using 6-hydroxypicolinic acid (3.0 mmol) and methyl iodide (10.0 equiv.) and used without further purification. Pinkish white solid, 474 mg, yield 63%. m.p. 248-250 °C. <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ 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). <sup>13</sup>C{<sup>1</sup>H} NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ 163.7, 161.8, 140.3, 138.4,

122.7, 108.8, 33.1. HRMS (APCI) m/z ([M+H]<sup>+</sup>) calcd for C<sub>7</sub>H<sub>8</sub>NO<sub>3</sub> 154.0499, found 154.0510.



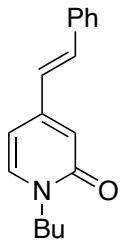
**(E)-1-Methyl-4-styrylpyridin-2(1H)-one (3aa)**

Purified by silica gel column chromatography using EtOAc/Hexane/Et<sub>3</sub>N = 1/5/0.05 to EtOAc/CHCl<sub>3</sub>/Et<sub>3</sub>N = 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. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 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). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 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]<sup>+</sup>) calcd for C<sub>14</sub>H<sub>14</sub>NO 212.1070, found 212.1080.



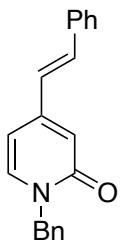
**(E)-1-Ethyl-4-styrylpyridin-2(1H)-one (3ba)**

Purified by silica gel column chromatography using EtOAc/Hexane/Et<sub>3</sub>N = 1/5/0.05 to EtOAc/CHCl<sub>3</sub>/Et<sub>3</sub>N = 1/1/0.05 (v/v/v). off white solid, 28.4 mg, yield 63%. m.p. 164-166 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 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). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 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]<sup>+</sup>) calcd for C<sub>15</sub>H<sub>16</sub>NO 226.1226, found 226.1215.



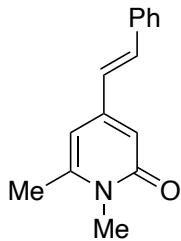
**(E)-1-Butyl-4-styrylpyridin-2(1H)-one (3ca)**

Purified by silica gel column chromatography using EtOAc/Hexane/Et<sub>3</sub>N = 1/5/0.05 to EtOAc/CHCl<sub>3</sub>/Et<sub>3</sub>N = 1/1/0.05 (v/v/v). off white solid, 28.4 mg, yield 57%. m.p. 164-166 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 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 H<sub>2</sub>O peak m, 2H), 1.43-1.34 (m, 2H), 0.96 (t, *J* = 7.4 Hz, 3H). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 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]<sup>+</sup>) calcd for C<sub>17</sub>H<sub>20</sub>NO 254.1539, found 254.1559.



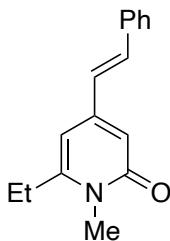
**(E)-1-Benzyl-4-styrylpyridin-2(1H)-one (3da)**

Purified by silica gel column chromatography using EtOAc/Hexane/Et<sub>3</sub>N = 1/5/0.05 to EtOAc/CHCl<sub>3</sub>/Et<sub>3</sub>N = 1/1/0.05 (v/v/v). off white solid. 47.1 mg, yield 82%. m.p. 102-104 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 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). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 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]<sup>+</sup>) calcd for C<sub>20</sub>H<sub>18</sub>NO 288.1383, found 288.1383.



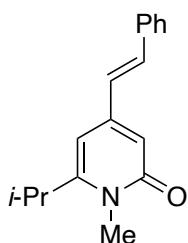
**(E)-1,6-Dimethyl-4-styrylpyridin-2(1H)-one (3ea)**

Purified by silica gel column chromatography using EtOAc/Hexane/Et<sub>3</sub>N = 1/5/0.05 to EtOAc/CHCl<sub>3</sub>/Et<sub>3</sub>N = 1/1/0.05 (v/v/v). off white solid, 37.9 mg, yield 84%. m.p. 159-161 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 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). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 100 MHz) 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]<sup>+</sup>) calcd for C<sub>15</sub>H<sub>16</sub>NO 226.1226, found 226.1236.



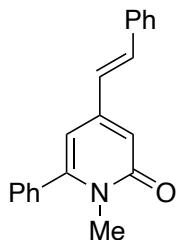
**(E)-6-Ethyl-1-methyl-4-styrylpyridin-2(1H)-one (3fa)**

Purified by silica gel column chromatography using EtOAc/Hexane/Et<sub>3</sub>N = 1/5/0.05 to EtOAc/CHCl<sub>3</sub>/Et<sub>3</sub>N = 1/1/0.05 (v/v/v). off white solid, 29.7 mg, yield 62%. m.p. 118-120 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 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). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 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]<sup>+</sup>) calcd for C<sub>16</sub>H<sub>18</sub>NO 240.1383, found 240.1394.



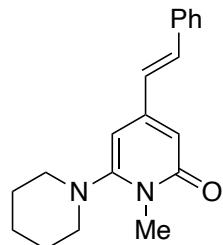
**(E)-6-Isopropyl-1-methyl-4-styrylpyridin-2(1H)-one (3ga)**

Purified by silica gel column chromatography using EtOAc/Hexane/Et<sub>3</sub>N = 1/5/0.05 to EtOAc/CHCl<sub>3</sub>/Et<sub>3</sub>N = 1/1/0.05 (v/v/v). Light brown gummy liquid. 26.8 mg, yield 53%. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 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). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 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]<sup>+</sup>) calcd for C<sub>17</sub>H<sub>20</sub>NO 254.1539, found 254.1527.



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

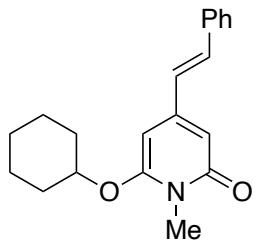
Purified by silica gel column chromatography using EtOAc/Hexane/Et<sub>3</sub>N = 1/5/0.05 to EtOAc/CHCl<sub>3</sub>/Et<sub>3</sub>N = 1/1/0.05 (v/v/v). off white solid, 35.1 mg, yield 61%. m.p. 126-128 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 7.51-7.48 (m, 5H), 7.40-7.35 (m, 4H), 7.33-7.30 (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). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 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]<sup>+</sup>) calcd for C<sub>20</sub>H<sub>18</sub>NO 288.1383, found 288.1383.



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

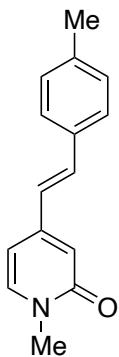
Purified by silica gel column chromatography using EtOAc/Hexane/Et<sub>3</sub>N = 1/5/0.05 to EtOAc/CHCl<sub>3</sub>/Et<sub>3</sub>N = 1/1/0.05 (v/v/v). Yellow gummy liquid, 33.6 mg, yield 57%. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 7.53-7.50 (m, 2H), 7.40-7.37 (m, 2H), 7.33-7.29 (m, 1H), 7.13 (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  $\text{H}_2\text{O}$  peak).  $^{13}\text{C}\{\text{H}\}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  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  $\text{C}_{19}\text{H}_{23}\text{N}_2\text{O}$  295.1805, found 295.1799.



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

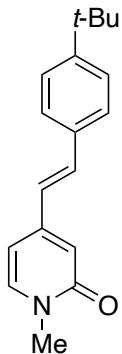
Purified by silica gel column chromatography using  $\text{EtOAc}/\text{Hexane}/\text{Et}_3\text{N} = 1/5/0.05$  to  $\text{EtOAc}/\text{CHCl}_3/\text{Et}_3\text{N} = 1/1/0.05$  (v/v/v). Light yellow gummy liquid. 39 mg, yield 63%.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.53-7.51 (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  $\text{H}_2\text{O}$  peak, m, 10H).  $^{13}\text{C}\{\text{H}\}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  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  $\text{C}_{20}\text{H}_{24}\text{NO}_2$  310.1802, found 310.1818.



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

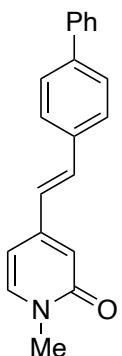
Purified by silica gel column chromatography using  $\text{EtOAc}/\text{Hexane}/\text{Et}_3\text{N} = 1/5/0.05$  to  $\text{EtOAc}/\text{CHCl}_3/\text{Et}_3\text{N} = 1/1/0.05$  (v/v/v). off white solid, 21.2 mg, yield 47%. m.p. 194-196 °C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.40 (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).  $^{13}\text{C}\{\text{H}\}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  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]<sup>+</sup>) calcd for C<sub>15</sub>H<sub>16</sub>NO 226.1226, found 226.1233.



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

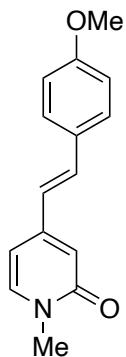
Purified by silica gel column chromatography using EtOAc/Hexane/Et<sub>3</sub>N = 1/5/0.05 to EtOAc/CHCl<sub>3</sub>/Et<sub>3</sub>N = 1/1/0.05 (v/v/v). off white solid, 27.8 mg, yield, 52%. m.p. 162-164 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 7.46-7.39 (m, 4H), 7.23 (d, *J* = 7.1 Hz, 1H), 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). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 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]<sup>+</sup>) calcd for C<sub>18</sub>H<sub>22</sub>NO 268.1696, found 268.1719.



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

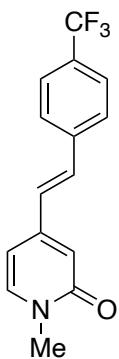
Purified by silica gel column chromatography using EtOAc/Hexane/Et<sub>3</sub>N = 1/5/0.05 to EtOAc/CHCl<sub>3</sub>/Et<sub>3</sub>N = 1/1/0.05 (v/v/v). off white solid, 22.4 mg, yield 39%. m.p. 241-243 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 7.64-7.58 (m, 6H), 7.48-7.43 (m, 2H), 7.39-7.34 (m, 1H), 7.25 (merged with CDCl<sub>3</sub>, 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). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 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]<sup>+</sup>) calcd for C<sub>20</sub>H<sub>18</sub>NO 288.1383, found 288.1366.



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

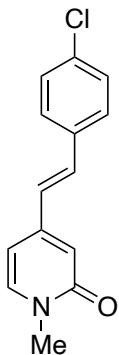
Purified by silica gel column chromatography using EtOAc/Hexane/Et<sub>3</sub>N = 1/5/0.05 to EtOAc/CHCl<sub>3</sub>/Et<sub>3</sub>N = 1/1/0.05 (v/v/v). off white solid, 26.5 mg, yield 55%. m.p. 207-209 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 7.47-7.44 (m, 2H), 7.22 (d, *J* = 7.1 Hz, 1H), 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). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 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]<sup>+</sup>) calcd for C<sub>15</sub>H<sub>16</sub>NO<sub>2</sub> 242.1176, found 242.1166.



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

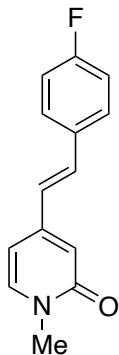
Purified by silica gel column chromatography using EtOAc/Hexane/Et<sub>3</sub>N = 1/5/0.05 to EtOAc/CHCl<sub>3</sub>/Et<sub>3</sub>N = 1/1/0.05 (v/v/v). solid, 26.3 mg, yield 47%. m.p. 177-179 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 7.64-7.59 (m, 4H), 7.27 (merged with CDCl<sub>3</sub>, d, *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). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 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,  $\text{CDCl}_3$ )  $\delta$  -62.65. HRMS (APCI) m/z ([M+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(1H)-one (3ag)**

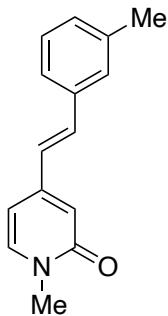
Purified by silica gel column chromatography using  $\text{EtOAc}/\text{Hexane}/\text{Et}_3\text{N} = 1/5/0.05$  to  $\text{EtOAc}/\text{CHCl}_3/\text{Et}_3\text{N} = 1/1/0.05$  (v/v/v). off white solid, 21.1 mg, yield 43%. m.p. 182-184 °C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.45-7.42 (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 ( $\text{CDCl}_3$ , 100 MHz)  $\delta$ . 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 ([M+H] $^+$ ) calcd for  $\text{C}_{14}\text{H}_{13}\text{ClNO}$  246.0680, found 246.0669.



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

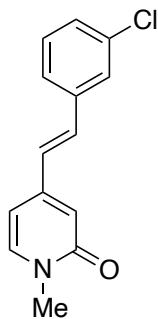
Purified by silica gel column chromatography using  $\text{EtOAc}/\text{Hexane}/\text{Et}_3\text{N} = 1/5/0.05$  to  $\text{EtOAc}/\text{CHCl}_3/\text{Et}_3\text{N} = 1/1/0.05$  (v/v/v). off white solid, 28.9 mg, yield 63%. m.p. 157-159 °C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.50-7.45 (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 ( $\text{CDCl}_3$ , 100 MHz)  $\delta$ . 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.  $^{19}\text{F}\{\text{H}\}$  (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -111.95. HRMS (APCI) m/z ([M+H] $^+$ ) calcd for  $\text{C}_{14}\text{H}_{13}\text{FNO}$  230.0976, found 230.0957.



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

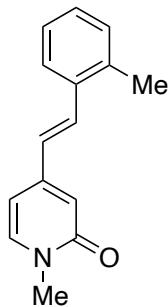
Purified by silica gel column chromatography using  $\text{EtOAc}/\text{Hexane}/\text{Et}_3\text{N} = 1/5/0.05$  to  $\text{EtOAc}/\text{CHCl}_3/\text{Et}_3\text{N} = 1/1/0.05$  (v/v/v). off white solid, 27.9 mg, yield 62%. m.p. 121-123°C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.33-7.23 (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).  $^{13}\text{C}\{\text{H}\}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  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 ([M+H] $^+$ ) calcd for  $\text{C}_{15}\text{H}_{16}\text{NO}$  226.1226, found 226.1233.



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

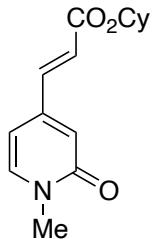
Purified by silica gel column chromatography using  $\text{EtOAc}/\text{Hexane}/\text{Et}_3\text{N} = 1/5/0.05$  to  $\text{EtOAc}/\text{CHCl}_3/\text{Et}_3\text{N} = 1/1/0.05$  (v/v/v). off white solid, 30.5 mg, yield, 62%. m.p. 136-138°C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.50-7.49 (m, 1H) 7.39-7.36 (m, 1H), 7.33-7.26 (merged with  $\text{CDCl}_3$ , m, 2H), 7.25 (merged with  $\text{CDCl}_3$ , 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).  $^{13}\text{C}\{\text{H}\}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$

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]<sup>+</sup>) calcd for C<sub>14</sub>H<sub>13</sub>ClNO 246.0680, found 246.0685.



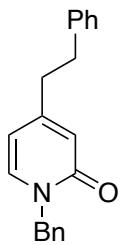
**(E)-1-Methyl-4-(2-methylstyryl)pyridin-2(1H)-one (3ak)**

Purified by silica gel column chromatography using EtOAc/Hexane/Et<sub>3</sub>N = 1/5/0.05 to EtOAc/CHCl<sub>3</sub>/Et<sub>3</sub>N = 1/1/0.05 (v/v/v). Off white solid, 15.8 mg, yield 35%. m.p. 103-105°C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 7.59-7.56 (m, 1H), 7.40 (d, *J* = 16.1 Hz, 1H), 7.26-7.18 (merged with CDCl<sub>3</sub>, 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). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 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]<sup>+</sup>) calcd for C<sub>15</sub>H<sub>16</sub>NO 226.1226, found 226.1232.



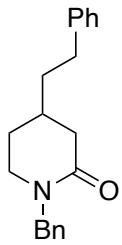
**Cyclohexyl (E)-3-(1-methyl-2-oxo-1,2-dihdropyridin-4-yl)acrylate (3al)**

Purified by silica gel column chromatography using EtOAc/Hexane/Et<sub>3</sub>N = 1/5/0.05 to EtOAc/CHCl<sub>3</sub>/Et<sub>3</sub>N = 1/1/0.05 (v/v/v) followed by GPC (EtOAc). Light yellow gummy liquid, 11.5 mg, yield 22%. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 7.39 (d, *J* = 16.0 Hz, 1H), 7.27 (merged with CDCl<sub>3</sub>, 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). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 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]<sup>+</sup>) calcd for C<sub>15</sub>H<sub>20</sub>NO<sub>3</sub> 262.1438, found 262.1413.



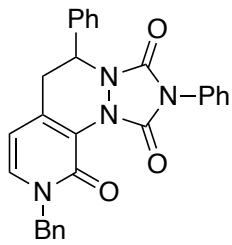
**1-Benzyl-4-phenethylpyridin-2(1H)-one (4)**

Purified by silica gel column chromatography using EtOAc/Hexane/Et<sub>3</sub>N = 1:1:0.05 (v/v/v) to EtOAc. Colorless liquid, 46.9 mg, yield 81%. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 7.36-7.25 (merged with CDCl<sub>3</sub>, 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). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 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]<sup>+</sup>) calcd for C<sub>20</sub>H<sub>20</sub>NO 290.1539, found 290.1542.



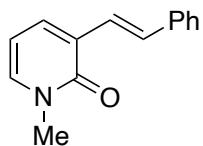
**1-Benzyl-4-phenethylpiperidin-2-one (5)**

Purified by silica gel column chromatography using EtOAc/Hexane/Et<sub>3</sub>N = 1:1:0.05 (v/v/v) to EtOAc. Colorless liquid, 49.9 mg, yield 85%. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 7.34-7.23 (merged with CDCl<sub>3</sub>, 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 H<sub>2</sub>O peak, m, 2H), 1.66-1.60 (m, 2H), 1.5-1.41 (m, 1H). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 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]<sup>+</sup>) calcd for C<sub>20</sub>H<sub>24</sub>NO 294.1852, found 294.1854.



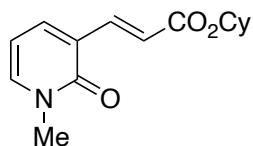
**9-Benzyl-2,5-diphenyl-5,6-dihydro-1*H*-pyrido[3,4-*c*][1,2,4]triazolo[1,2-*a*]pyridazine-1,3,10(2*H*,9*H*)-trione (6)**

Purified by GPC (EtOAc). Yellow gummy liquid, 56.4 mg, yield 61%. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  7.62-7.60 (m, 2H), 7.47-7.43 (m, 2H), 7.37-7.29 (merged with CDCl<sub>3</sub>, 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). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  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 ([M+H]<sup>+</sup>) calcd for C<sub>28</sub>H<sub>23</sub>N<sub>4</sub>O<sub>3</sub> 463.1765, found 463.1770.



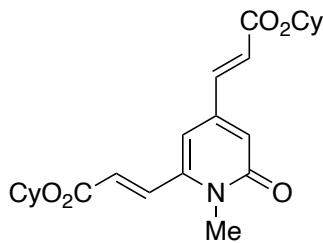
**(E)-1-Methyl-3-styrylpyridin-2(1*H*)-one (8aa)**

Purified by silica gel column chromatography using EtOAc/Hexane/Et<sub>3</sub>N = 1/5/0.05 to EtOAc/CHCl<sub>3</sub>/Et<sub>3</sub>N = 1/1/0.05 (v/v/v). Light yellow solid, 22.4 mg, yield 53%. m.p. 104-106°C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  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<sub>3</sub>, m, 3H), 6.22 (t, *J* = 14.4 Hz, 1H), 3.60 (s, 3H). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  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 ([M+H]<sup>+</sup>) calcd for C<sub>14</sub>H<sub>14</sub>NO 212.1070, found 212.1079.



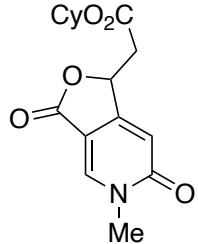
**Cyclohexyl (E)-3-(1-methyl-2-oxo-1,2-dihydropyridin-3-yl)acrylate (8al)**

Purified by silica gel column chromatography using EtOAc/Hexane/Et<sub>3</sub>N = 1/5/0.05 to EtOAc/CHCl<sub>3</sub>/Et<sub>3</sub>N = 1/1/0.05 (v/v/v). yellow liquid, 26.7 mg, yield 51%. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  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<sub>2</sub>O peak, m, 10H). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  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 ([M+H]<sup>+</sup>) calcd for C<sub>15</sub>H<sub>20</sub>NO<sub>3</sub> 262.1438, found 262.1418.



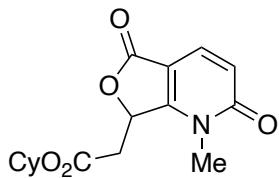
**Dicyclohexyl 3,3'-(1-methyl-6-oxo-1,6-dihdropyridine-2,4-diyl)(2E,2'E)-diacrylate (10al)**

Purified by silica gel column chromatography using EtOAc/Hexane/Et<sub>3</sub>N = 1/5/0.05 to EtOAc/CHCl<sub>3</sub>/Et<sub>3</sub>N = 1/1/0.05 (v/v/v), followed by GPC (EtOAc). Yellow liquid, 33.1 mg, yield 40%. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 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). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 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]<sup>+</sup>) calcd for C<sub>24</sub>H<sub>32</sub>NO<sub>5</sub> 414.2275, found 414.2305.



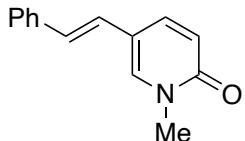
**Cyclohexyl 2-(5-methyl-3,6-dioxo-1,3,5,6-tetrahydrofuro[3,4-c]pyridin-1-yl)acetate (11al)**

Purified by silica gel column chromatography using EtOAc/Hexane/Et<sub>3</sub>N = 1/5/0.05 to EtOAc/CHCl<sub>3</sub>/Et<sub>3</sub>N = 1/1/0.05 (v/v/v), followed by GPC (EtOAc). Colorless gummy liquid, 6.1 mg, yield 10%. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 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). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 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]<sup>+</sup>) calcd for C<sub>16</sub>H<sub>20</sub>NO<sub>5</sub> 306.1336, found 306.1335.



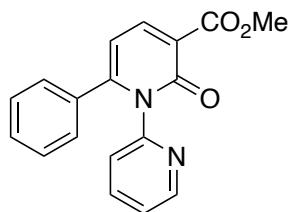
**Cyclohexyl 2-(1-methyl-2,5-dioxo-1,2,5,7-tetrahydrofuro[3,4-b]pyridin-7-yl)acetate (12al)**

Purified by silica gel column chromatography using EtOAc/Hexane/Et<sub>3</sub>N = 1/5/0.05 to EtOAc/CHCl<sub>3</sub>/Et<sub>3</sub>N = 1/1/0.05 (v/v/v), followed by GPC (EtOAc). Colorless gummy liquid, 3.1 mg, yield 5%. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 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 H<sub>2</sub>O peak, m, 10H). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 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]<sup>+</sup>) calcd for C<sub>16</sub>H<sub>20</sub>NO<sub>5</sub> 306.1336, found 306.1339.



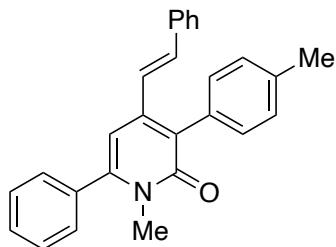
**(E)-1-Methyl-5-styrylpyridin-2(1H)-one (14aa)**

Purified by silica gel column chromatography using EtOAc/Hexane/Et<sub>3</sub>N = 1/5/0.05 to EtOAc/CHCl<sub>3</sub>/Et<sub>3</sub>N = 1/1/0.05 (v/v/v). Light yellow solid, 25.4 mg, yield 60%. m.p. 154-156°C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 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 CDCl<sub>3</sub>, 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). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 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]<sup>+</sup>) calcd for C<sub>14</sub>H<sub>14</sub>NO 212.1070, found 212.1077.



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

Purified by silica gel column chromatography using EtOAc/Hexane/Et<sub>3</sub>N = 1/5/0.05 to EtOAc/CHCl<sub>3</sub>/Et<sub>3</sub>N = 1/1/0.05 (v/v/v). Colorless liquid, 47.8 mg, yield 78%. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  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). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  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]<sup>+</sup>) calcd for C<sub>18</sub>H<sub>15</sub>N<sub>2</sub>O<sub>3</sub> 307.1077, found 307.1066.



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

Purified by silica gel column chromatography using EtOAc/Hexane/Et<sub>3</sub>N = 1/5/0.05 to EtOAc/CHCl<sub>3</sub>/Et<sub>3</sub>N = 1/1/0.05 (v/v/v) followed by GPC (EtOAc). Yellow gummy liquid, 39.3 mg, yield 52%. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  7.54-7.43 (m, 5H), 7.33-7.25 (merged with CDCl<sub>3</sub>, 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). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  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]<sup>+</sup>) calcd for C<sub>27</sub>H<sub>24</sub>NO 378.1852, found 378.1851.

## References

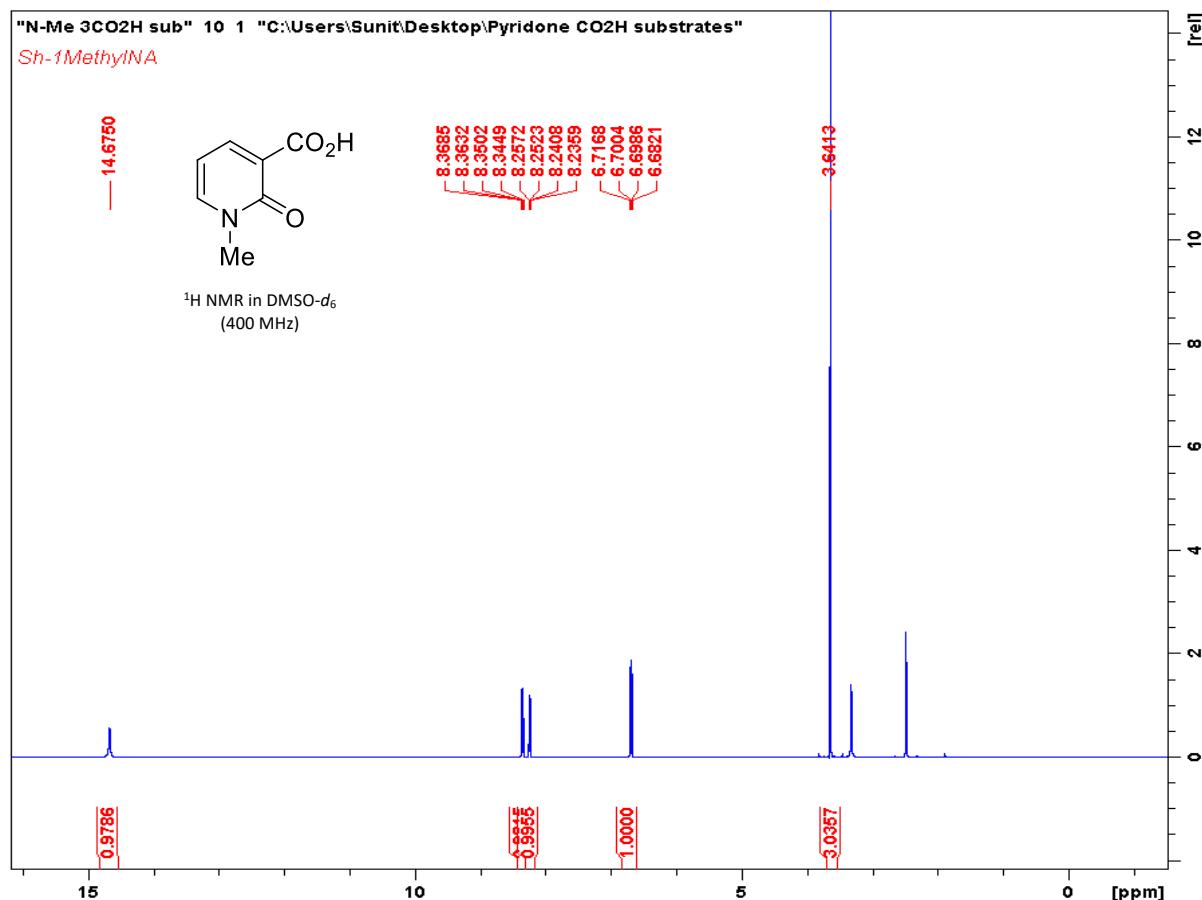
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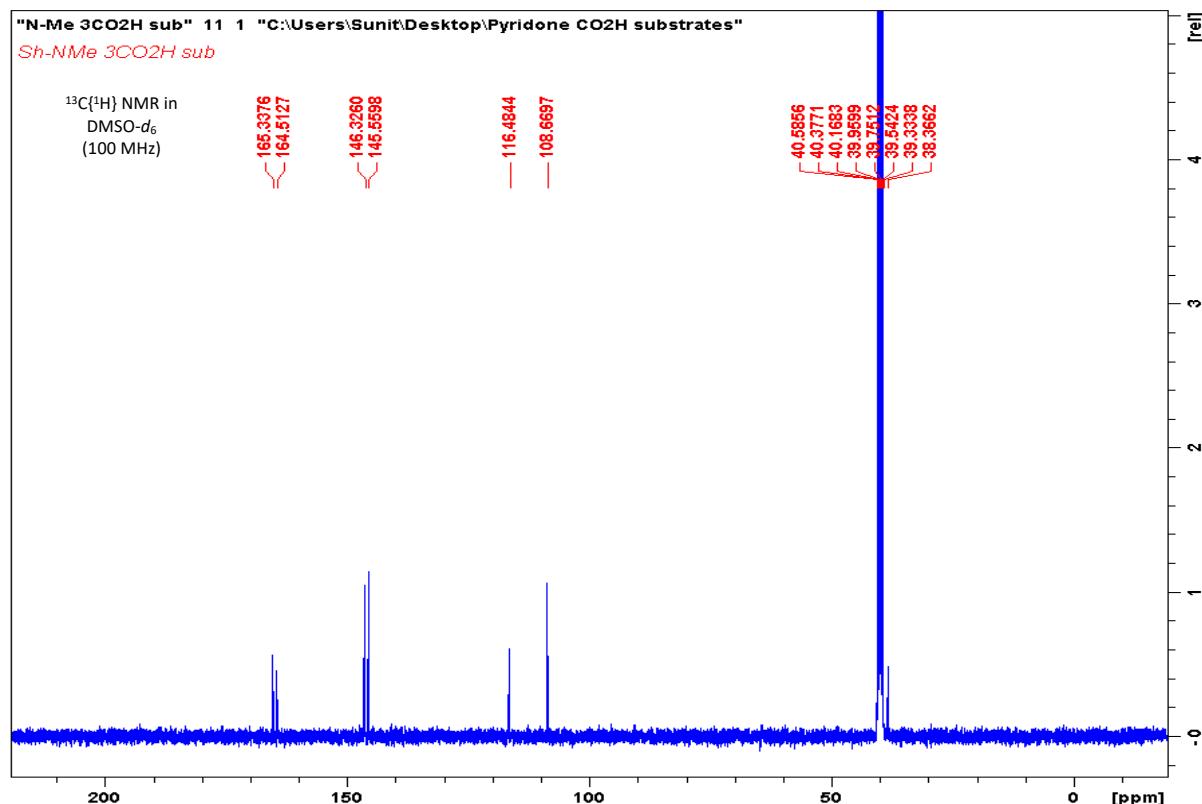
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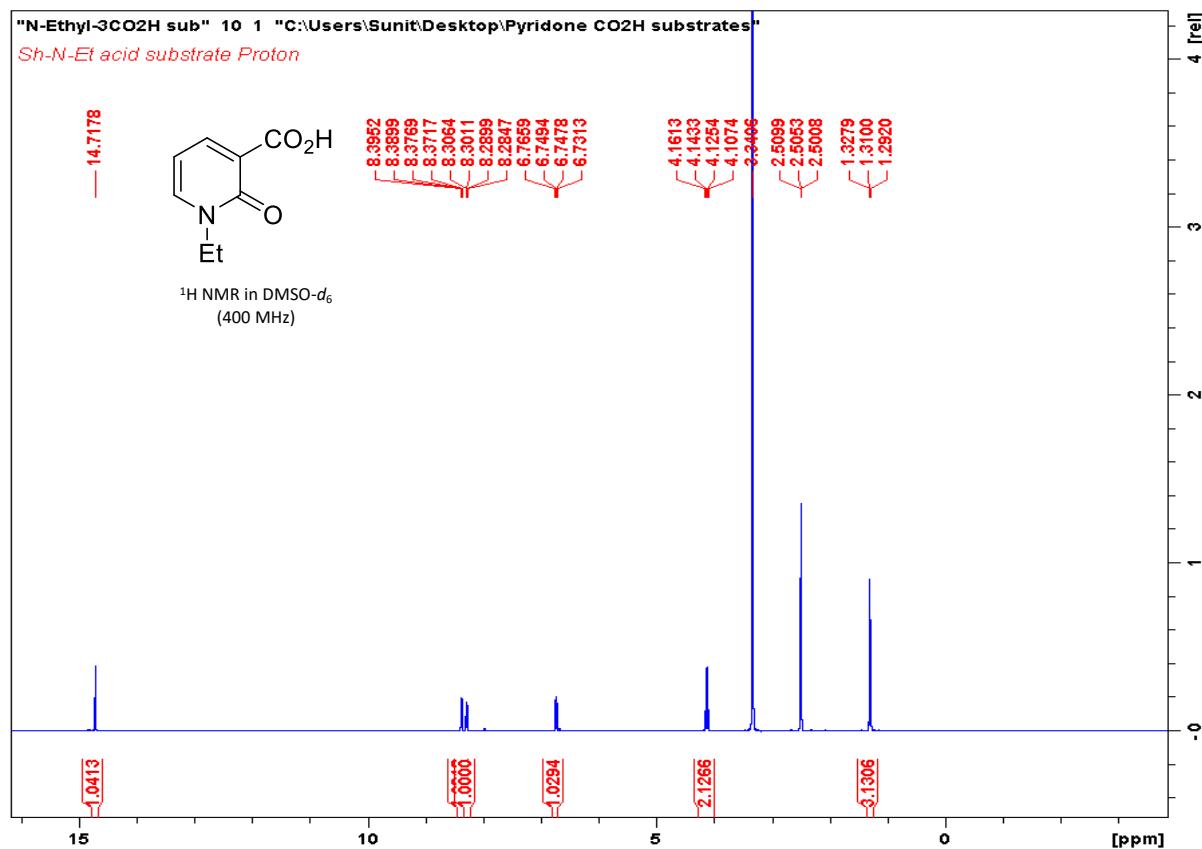
<sup>1</sup>H NMR of compound **1a** in DMSO-*d*<sub>6</sub> (400 MHz)



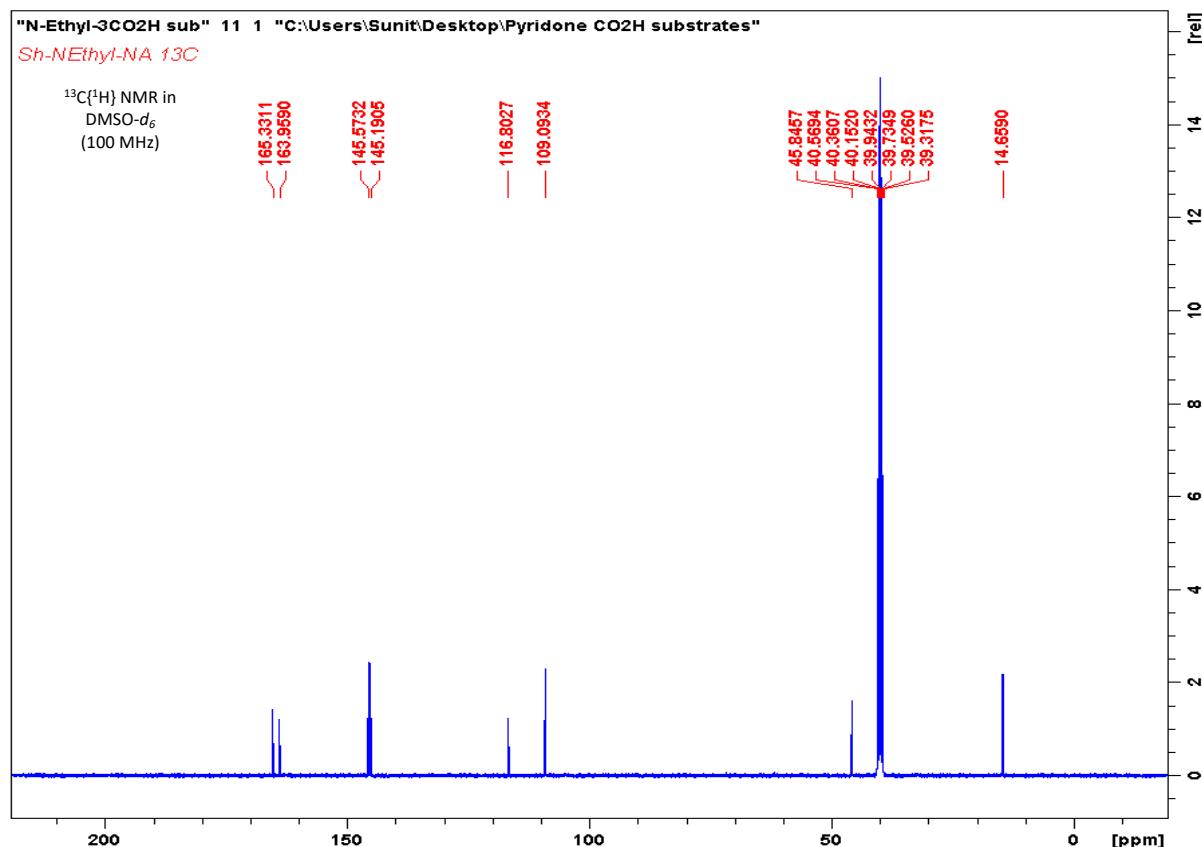
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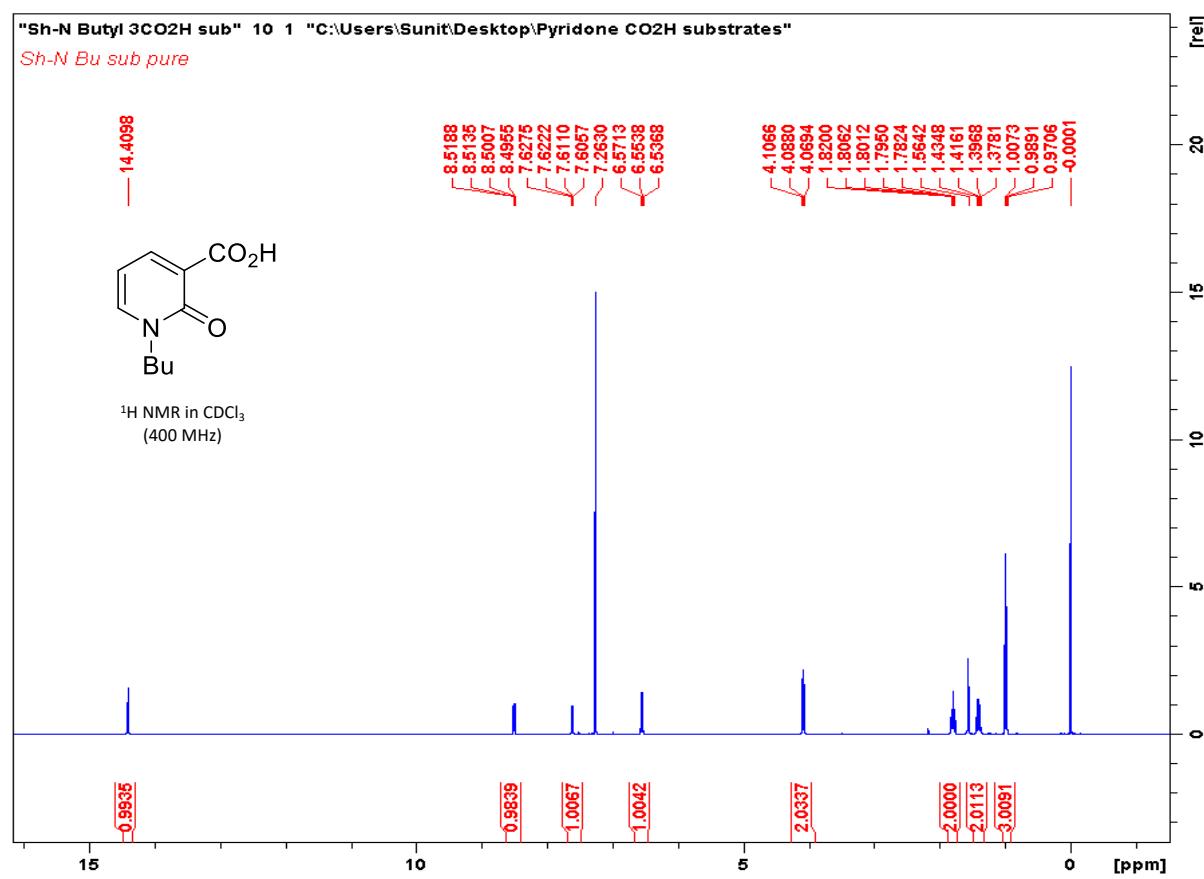
<sup>1</sup>H NMR of compound **1b** in DMSO-*d*<sub>6</sub> (400 MHz)



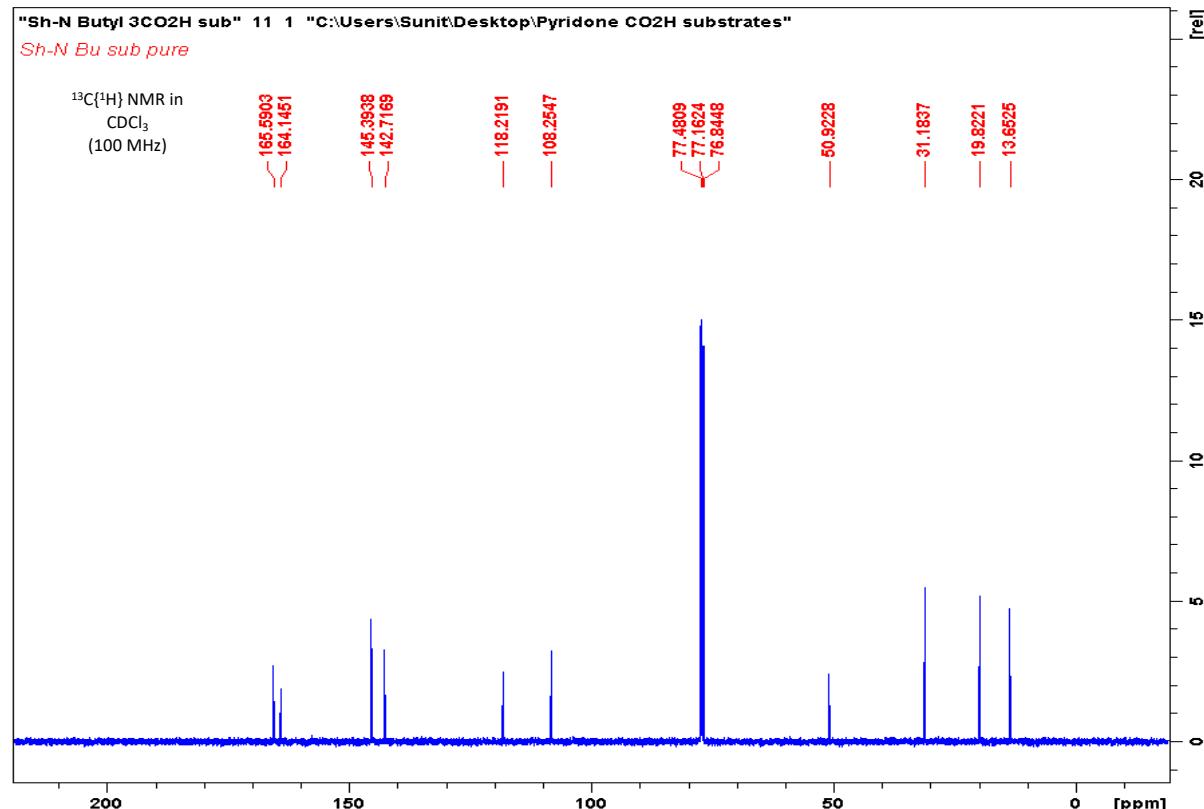
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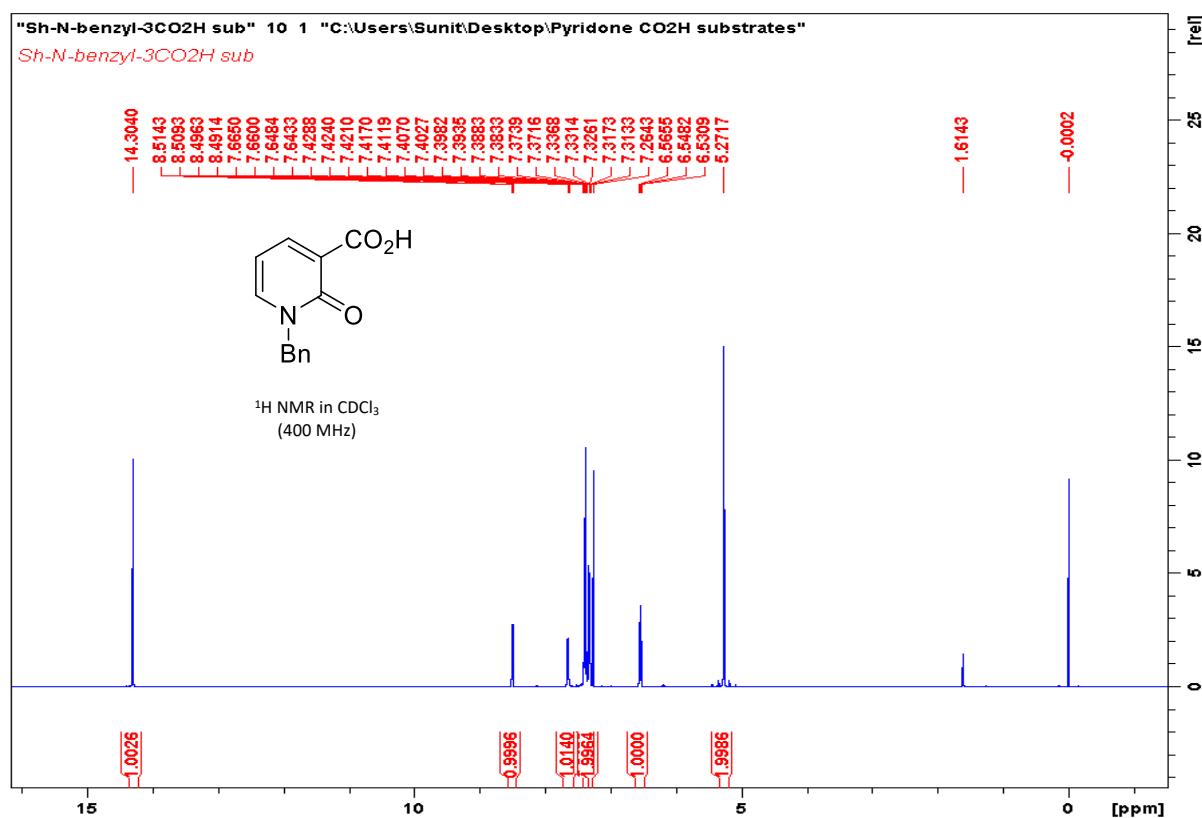
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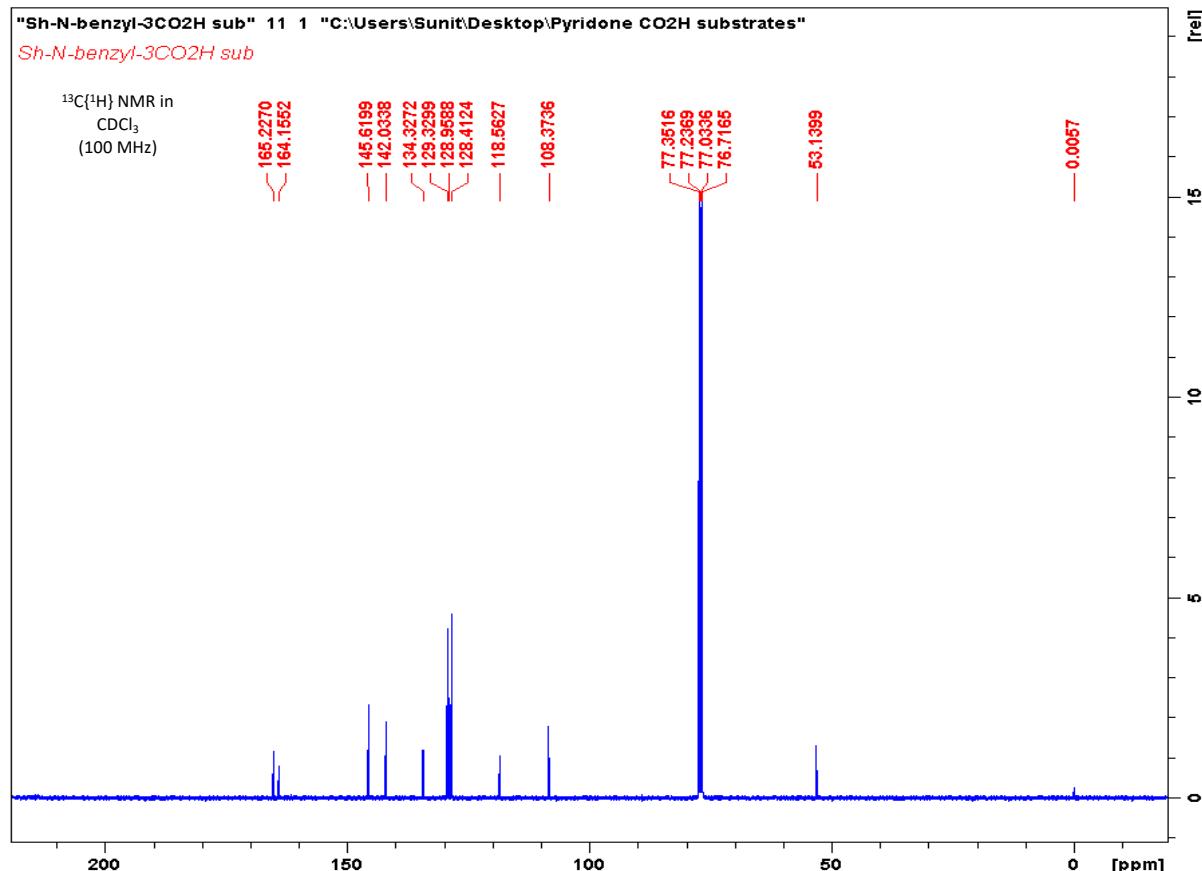
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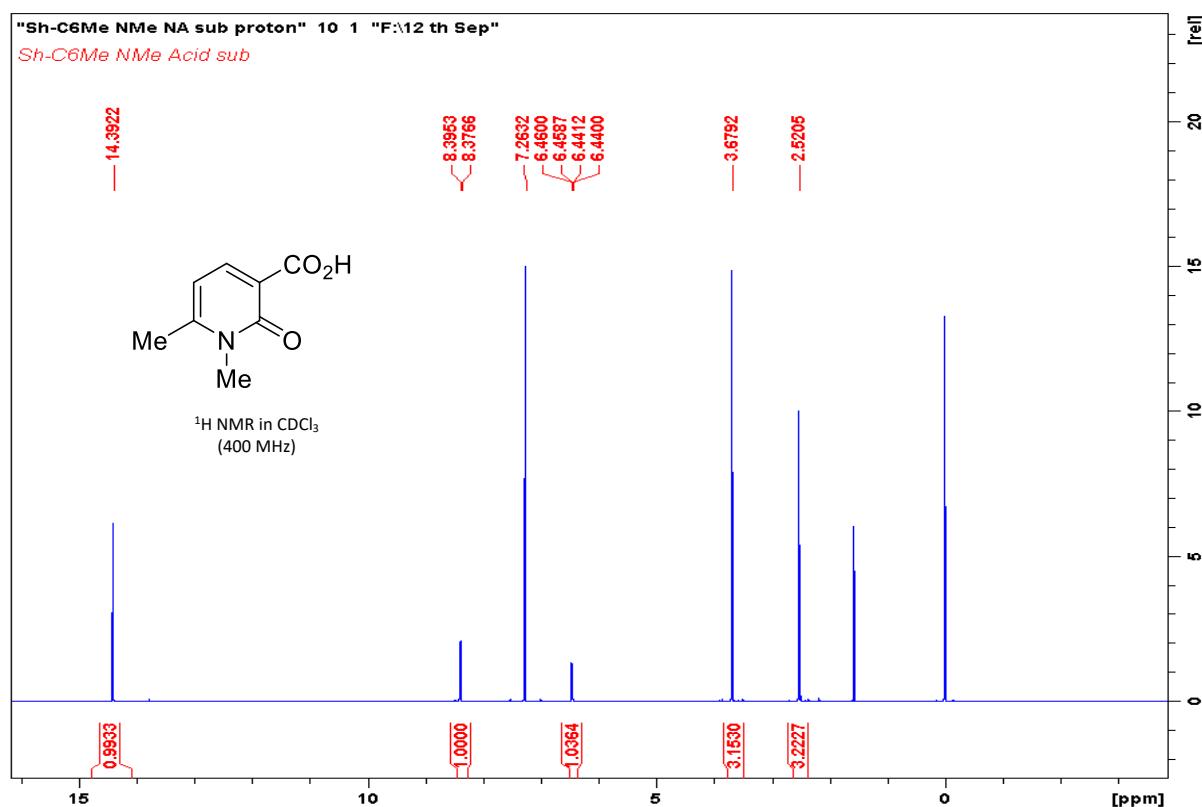
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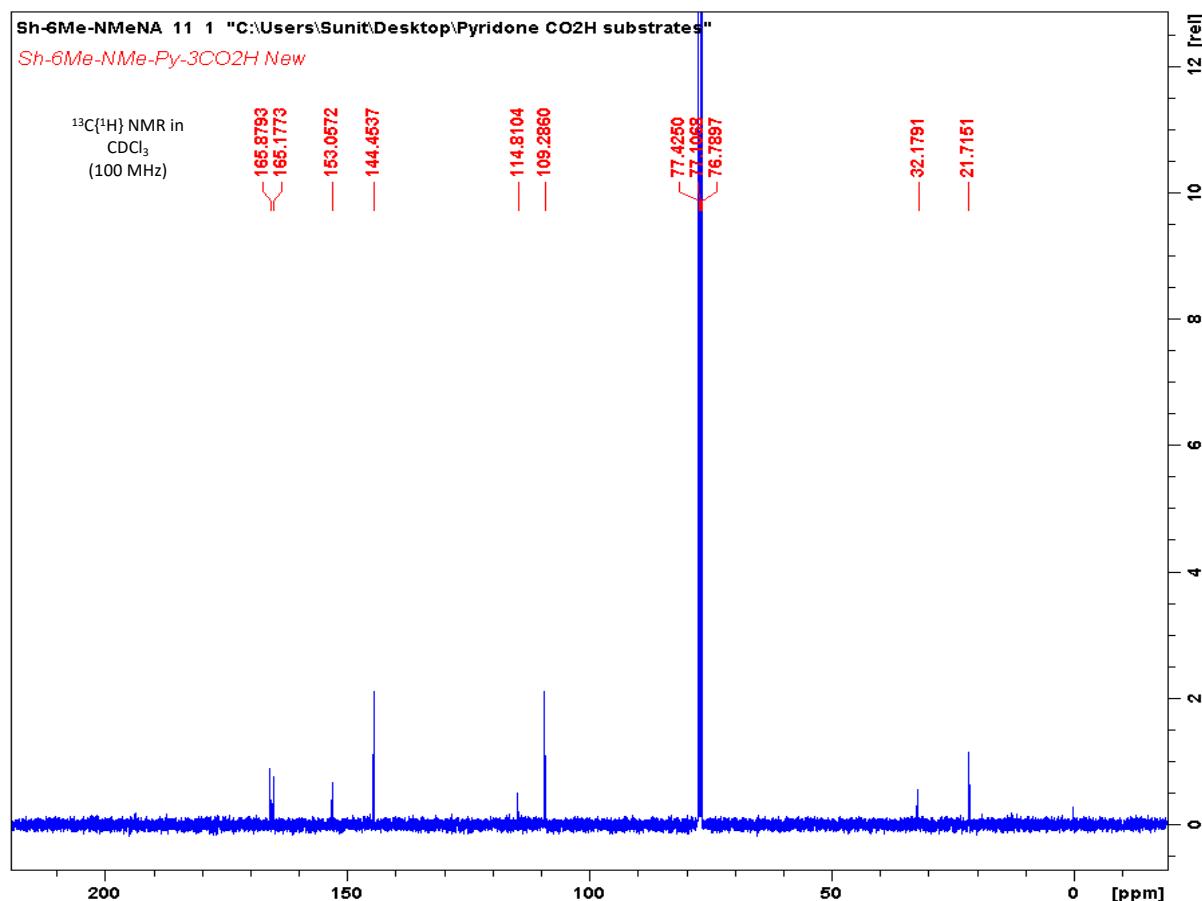
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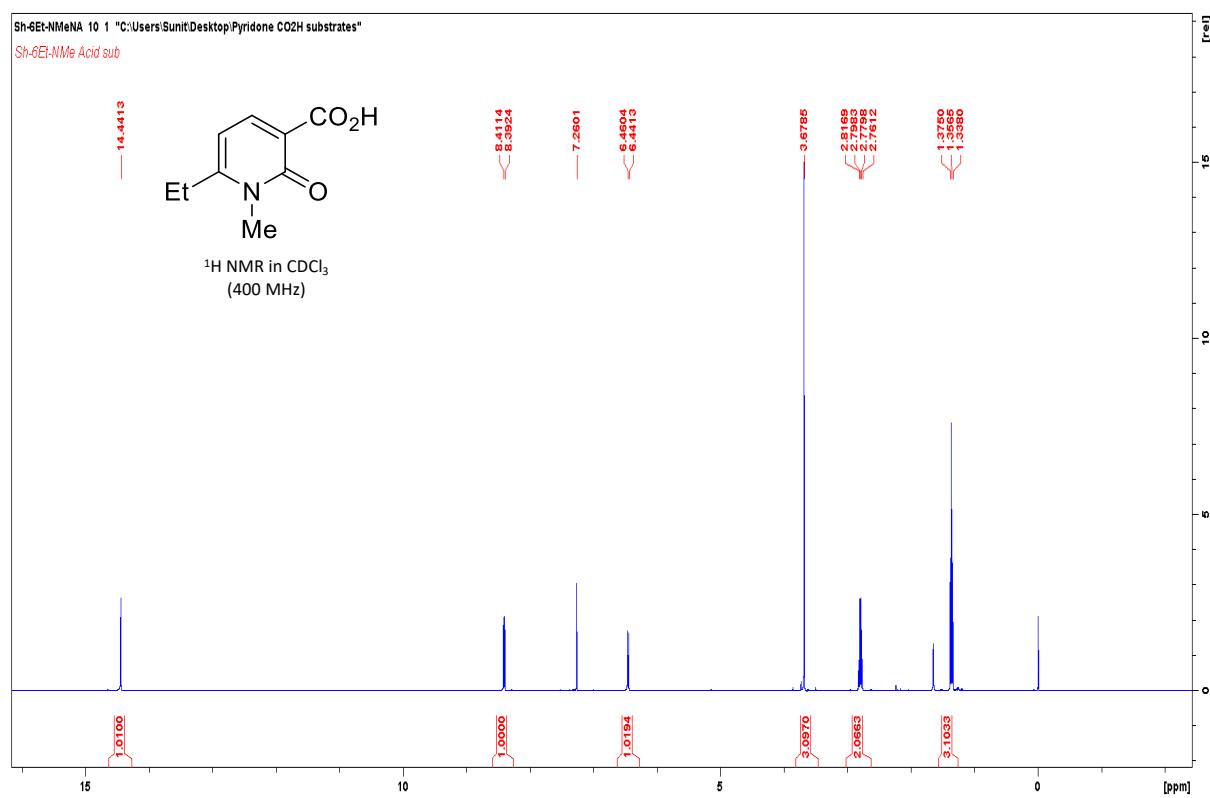
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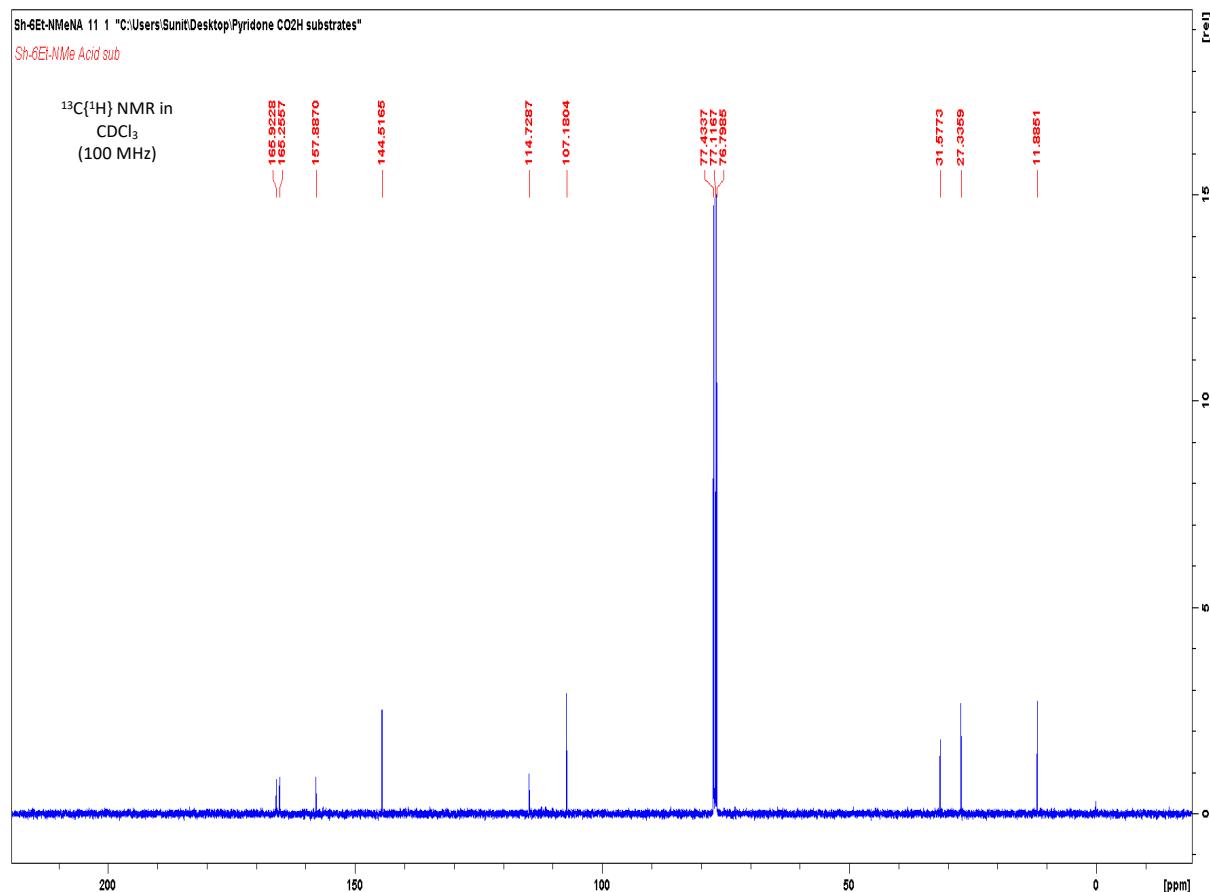
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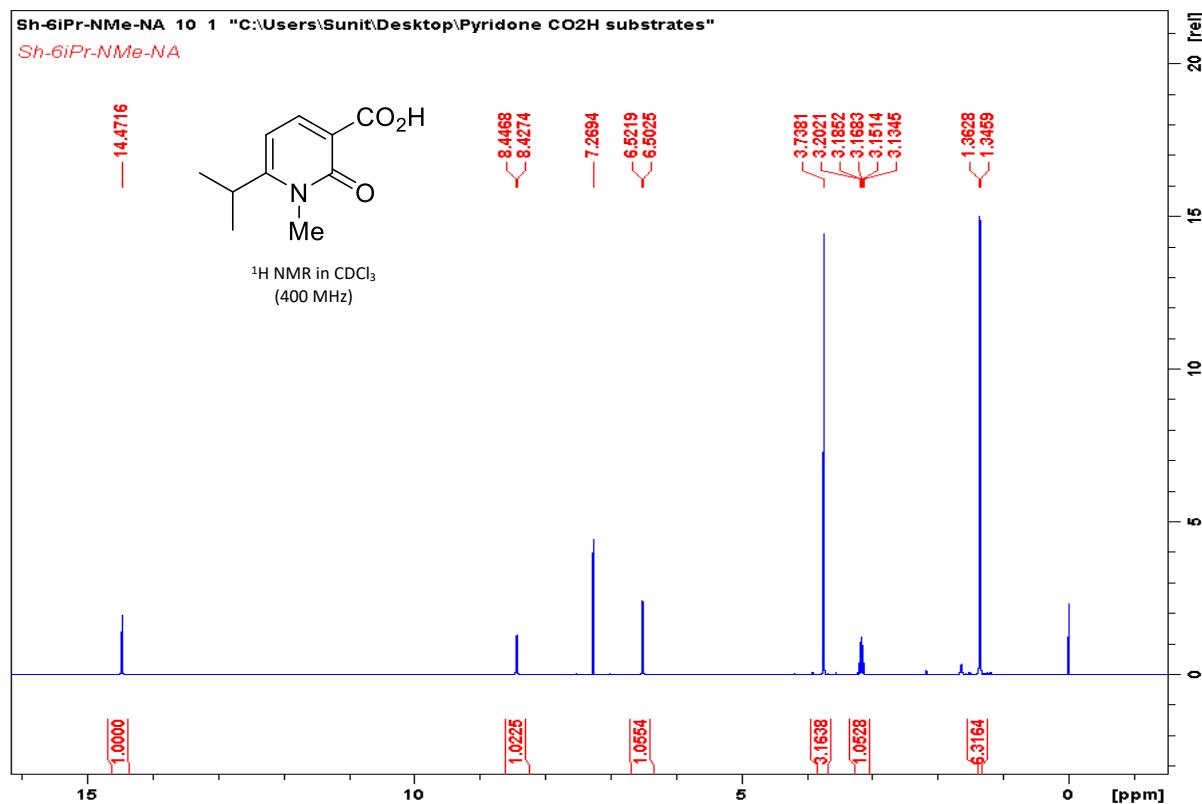
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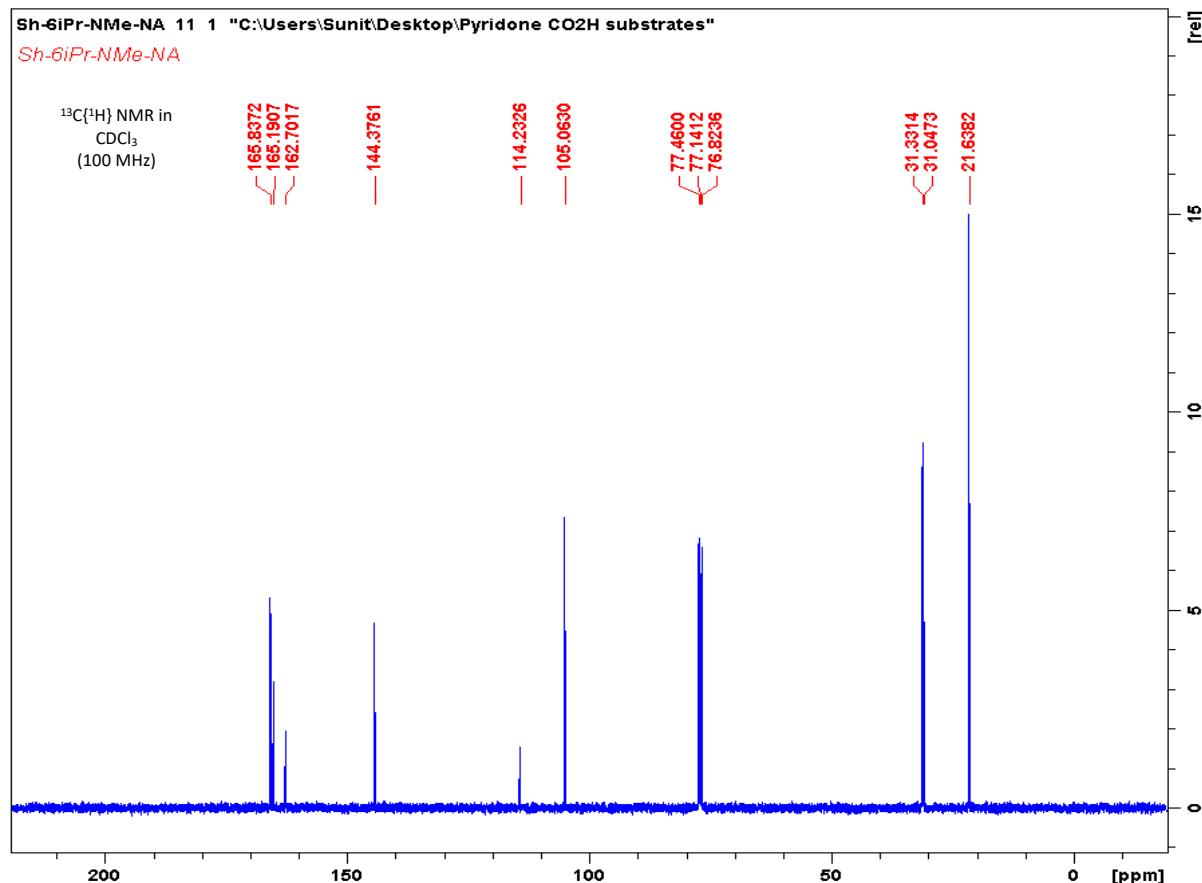
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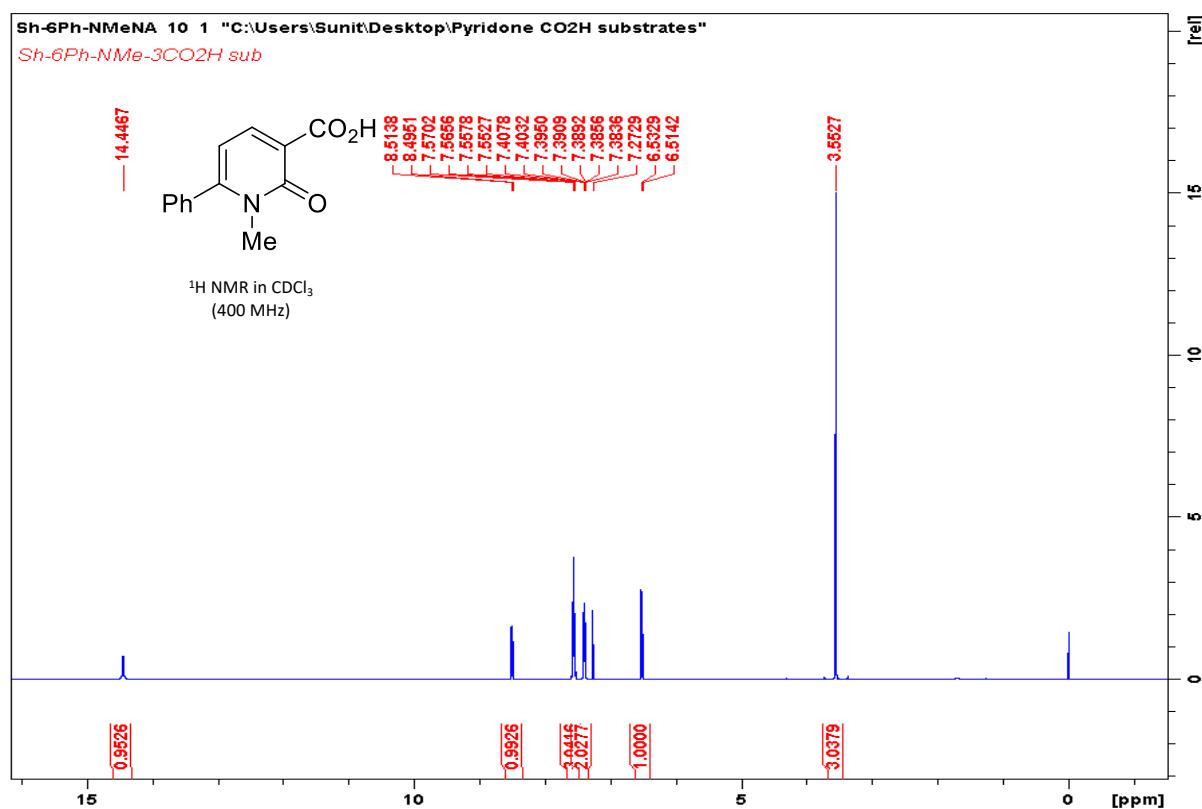
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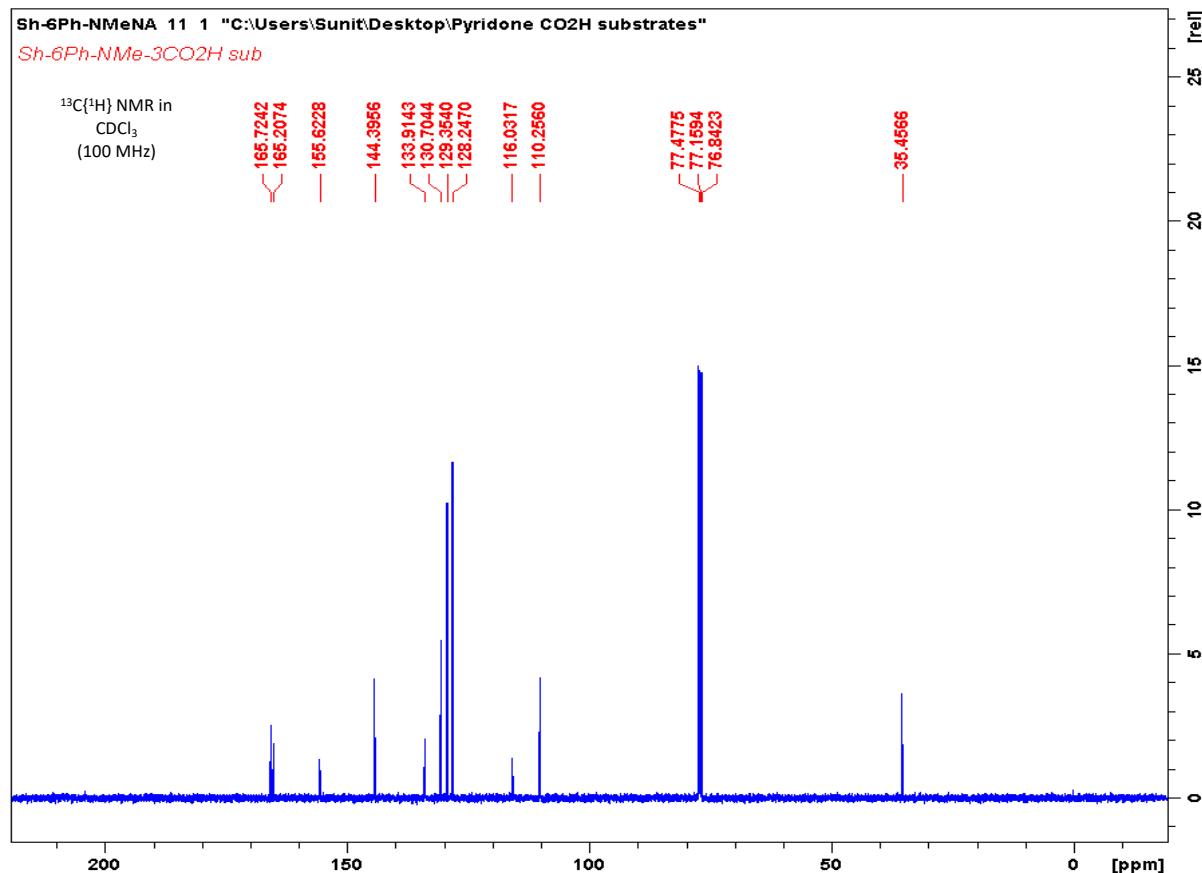
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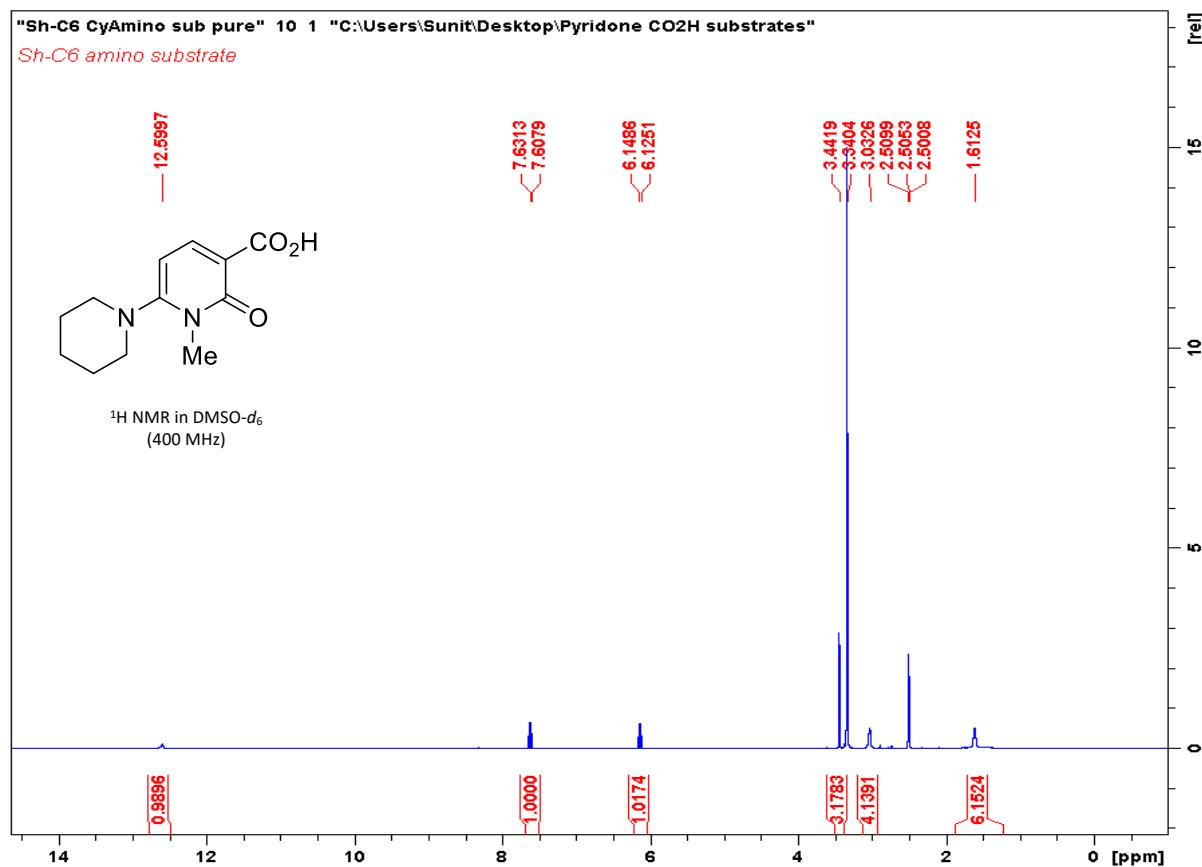
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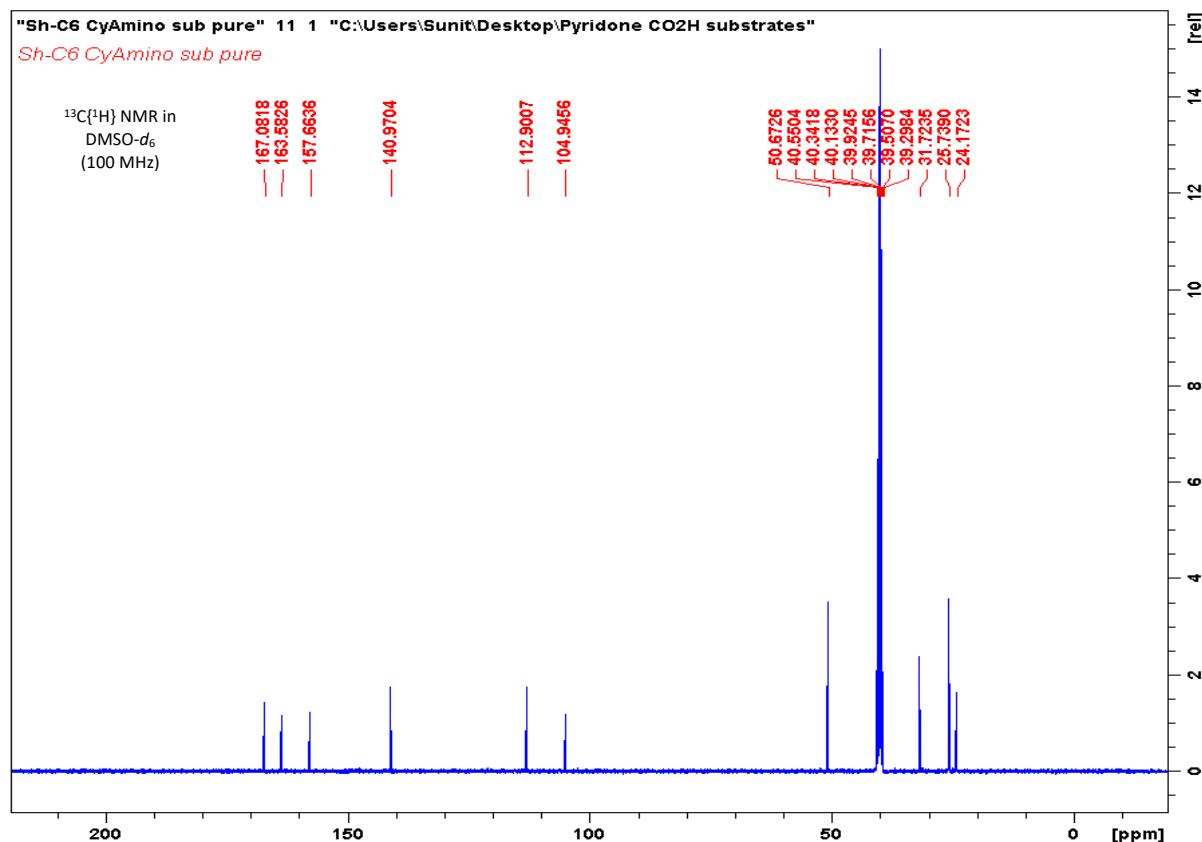
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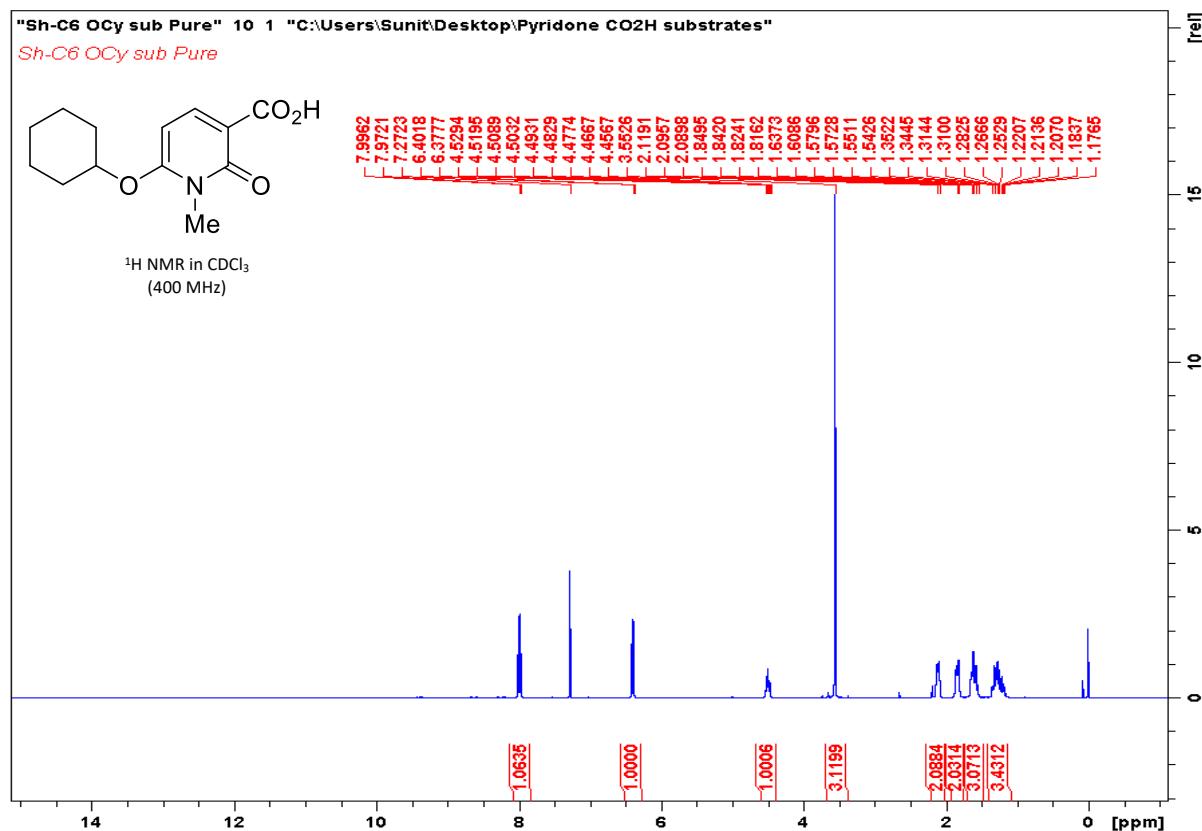
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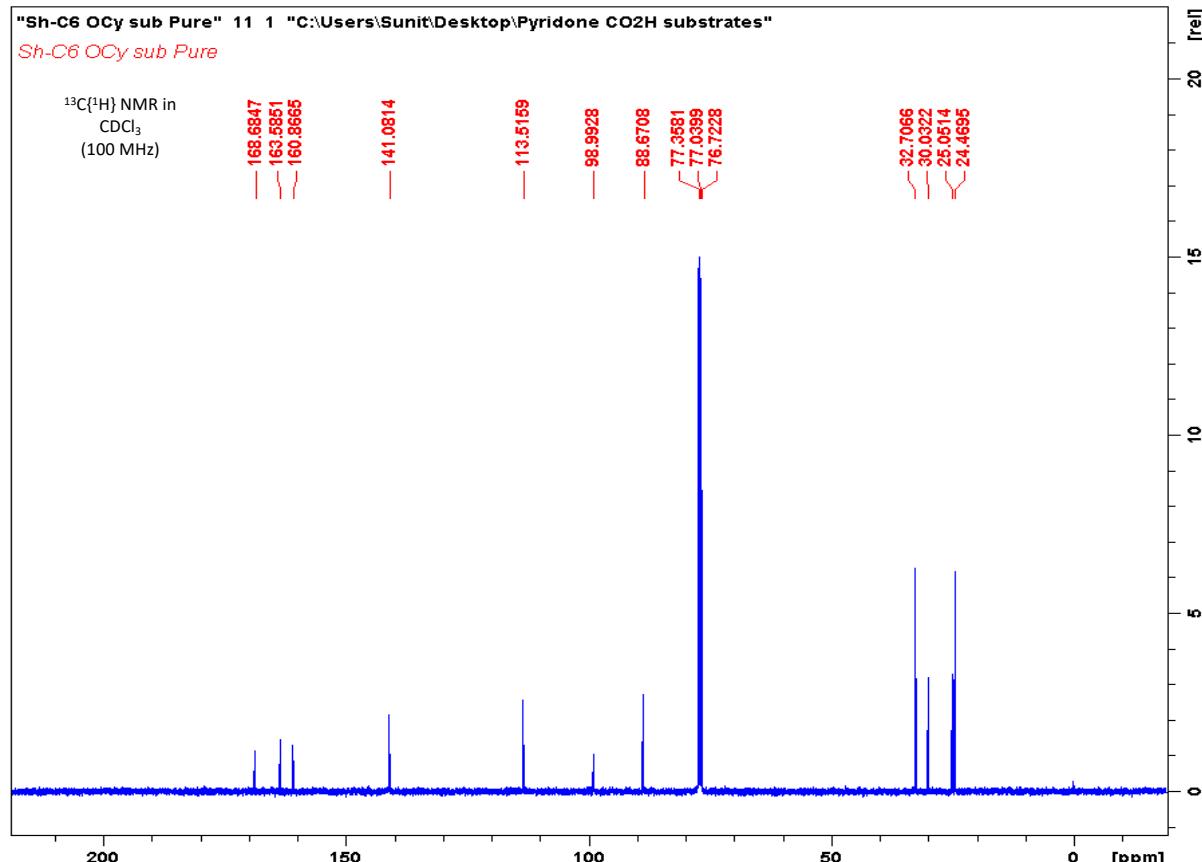
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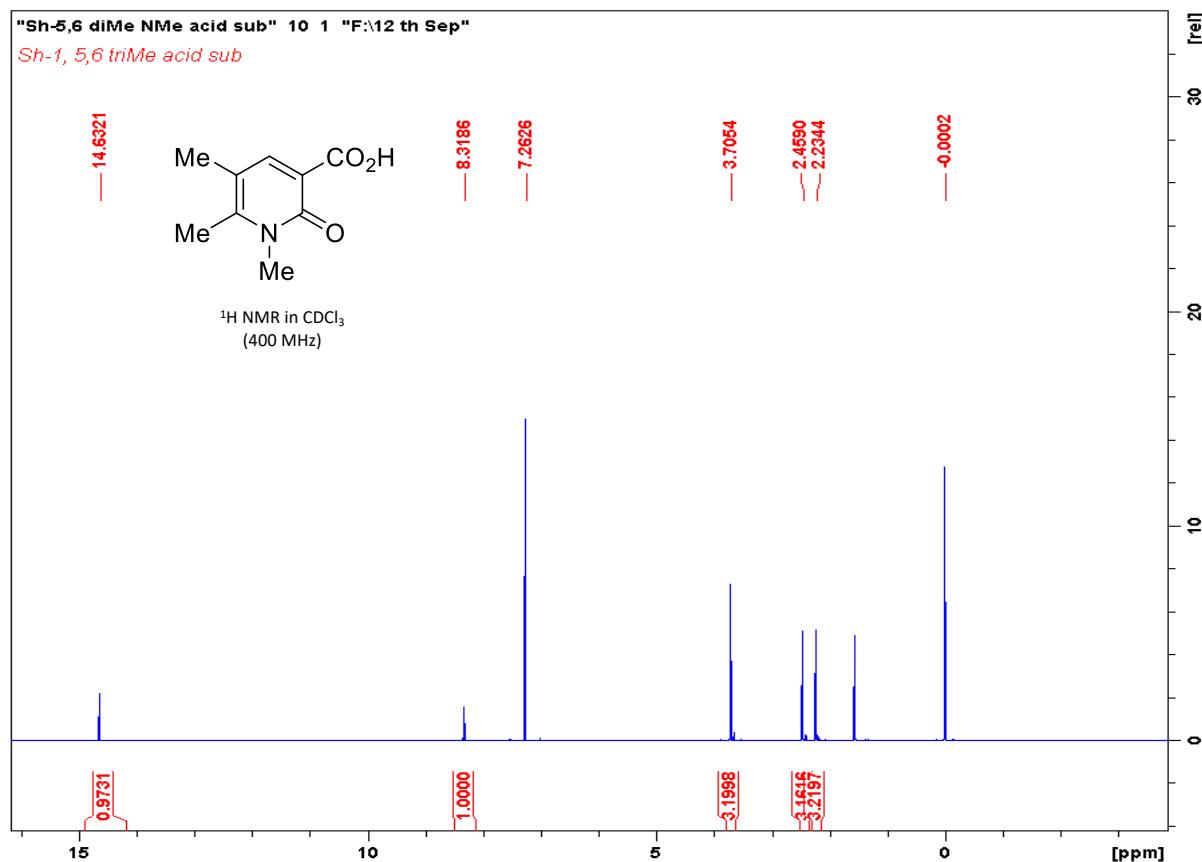
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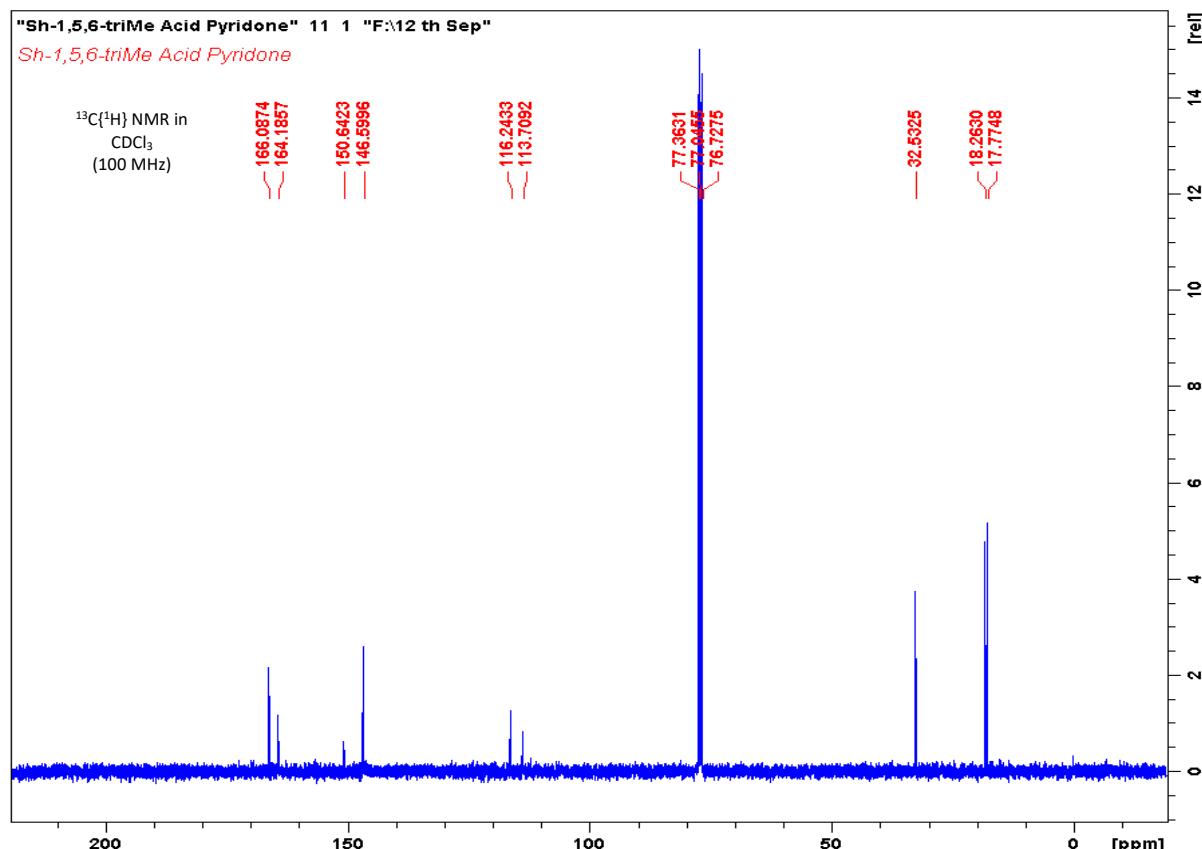
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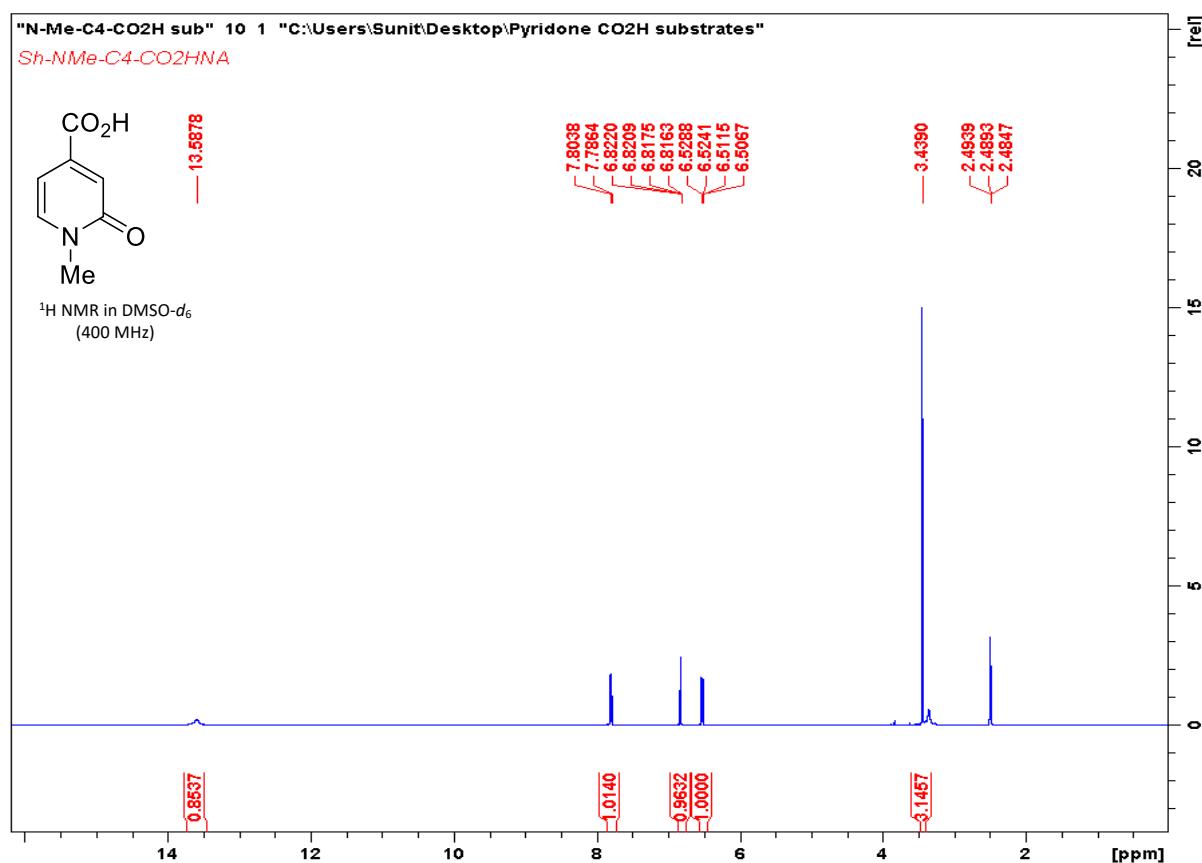
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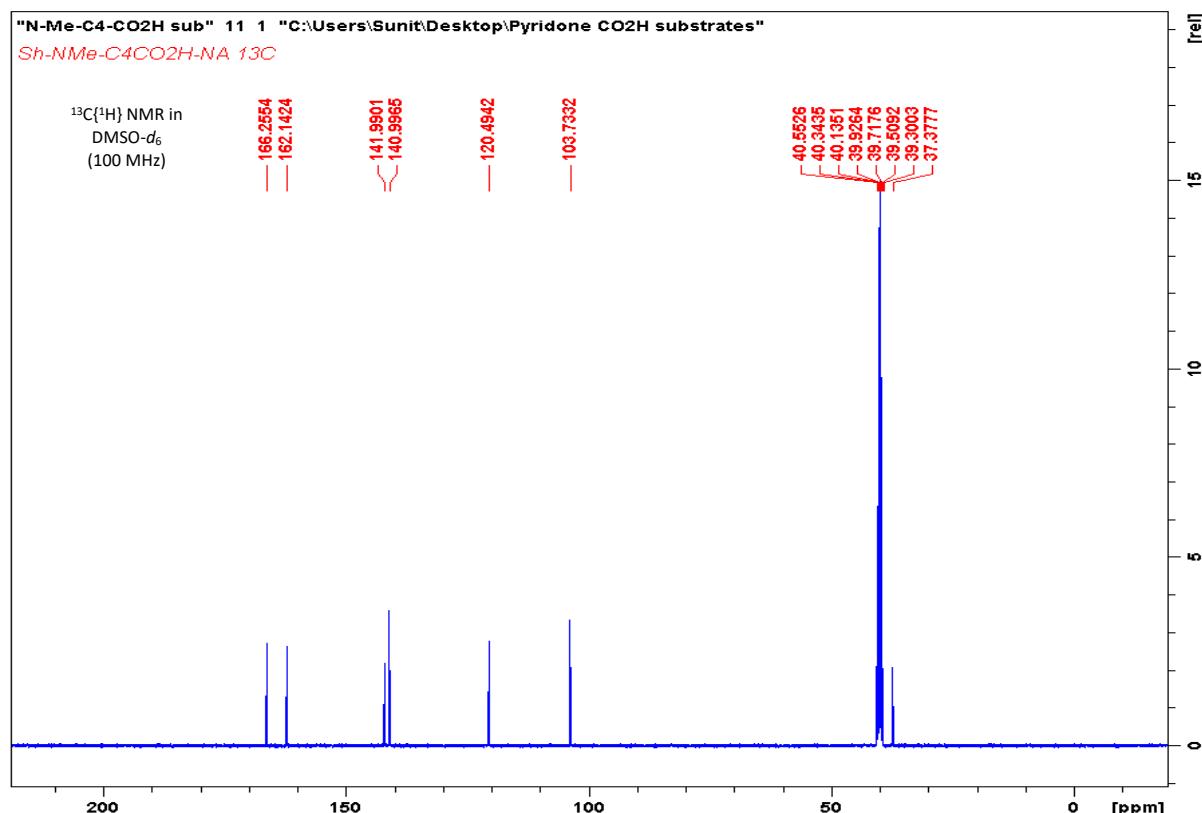
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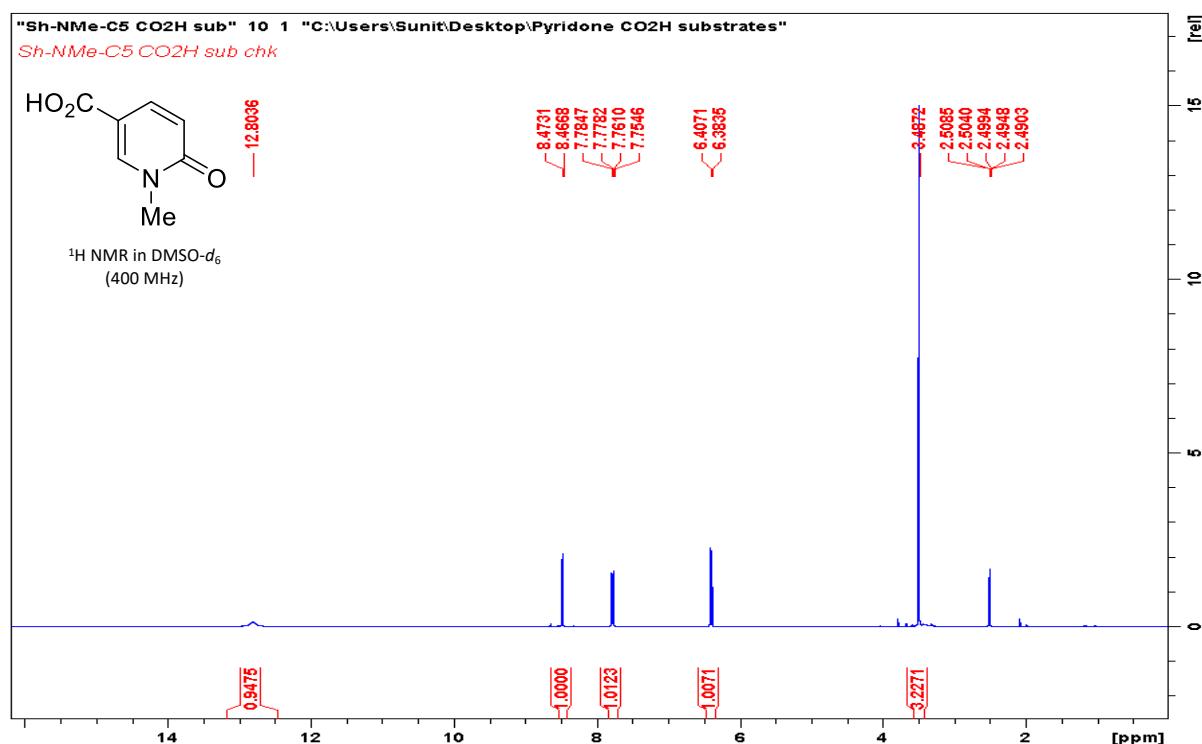
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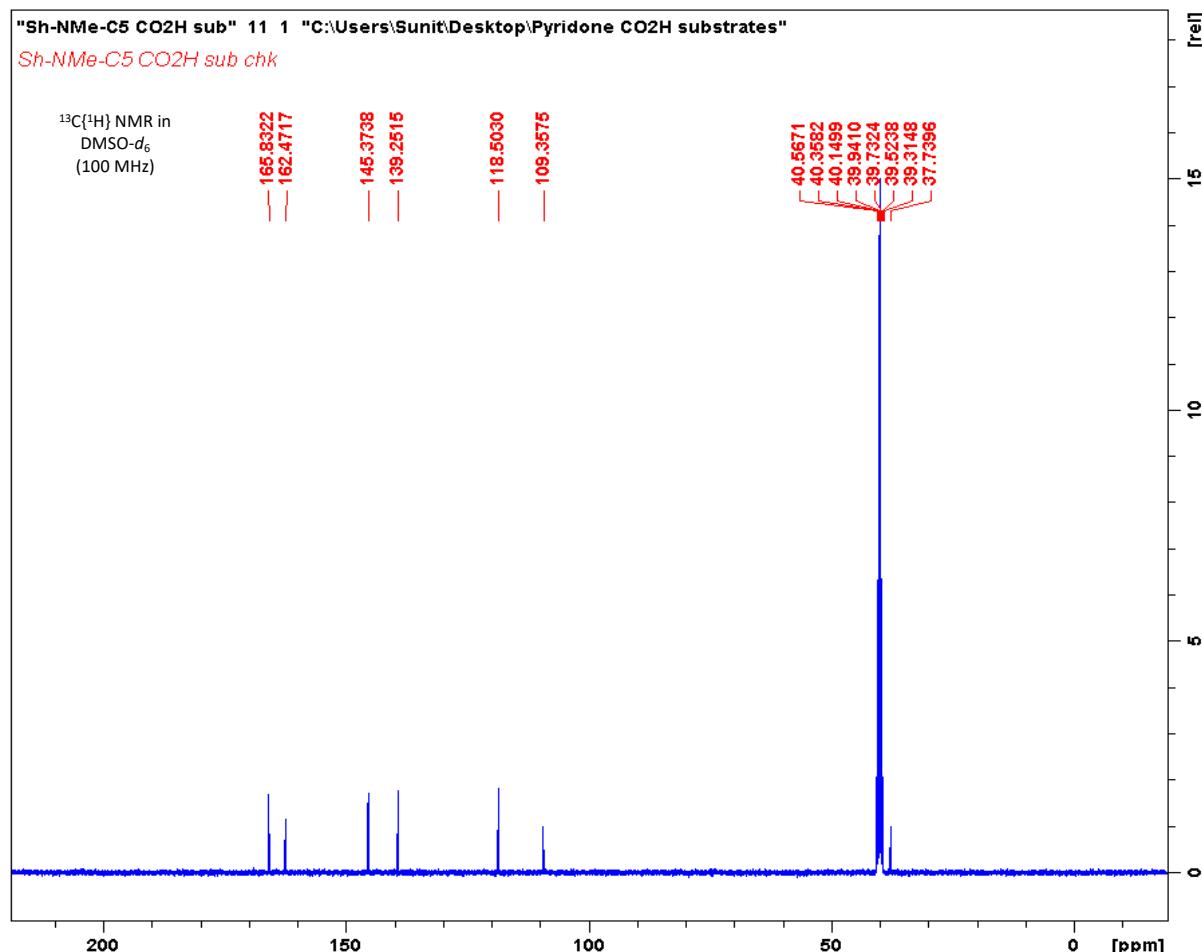
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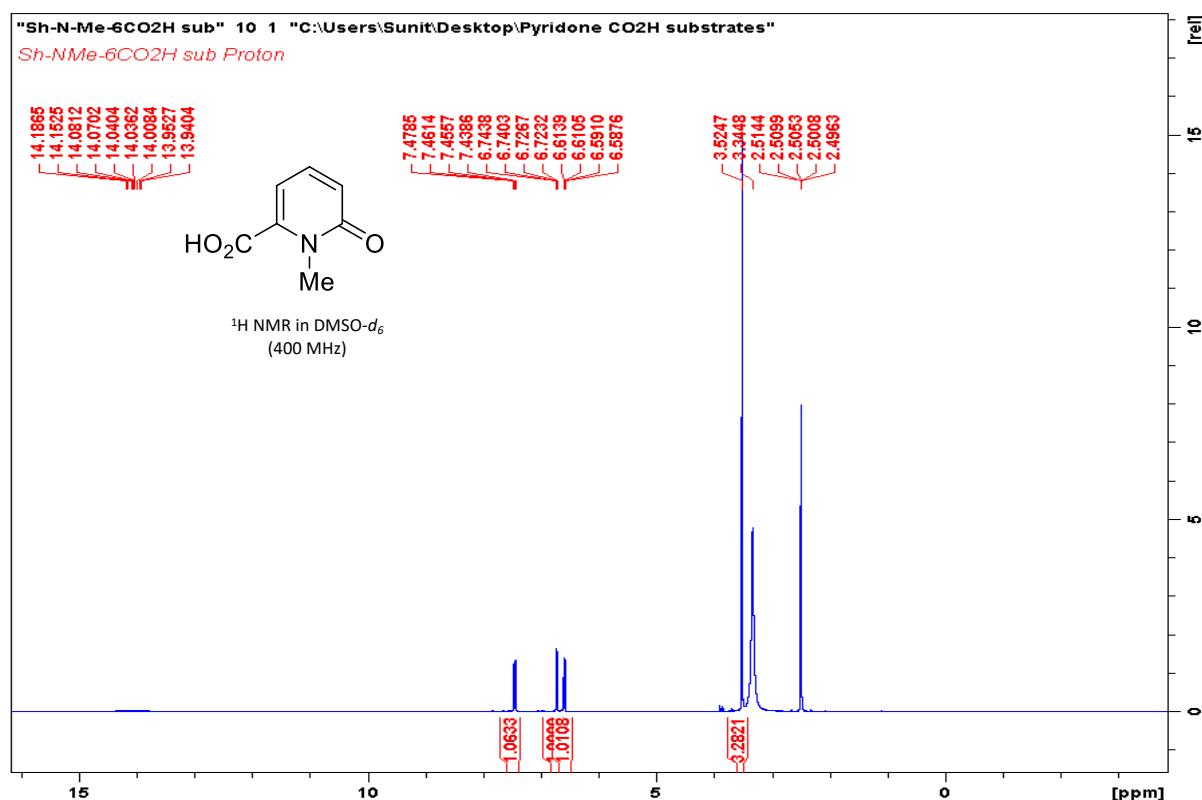
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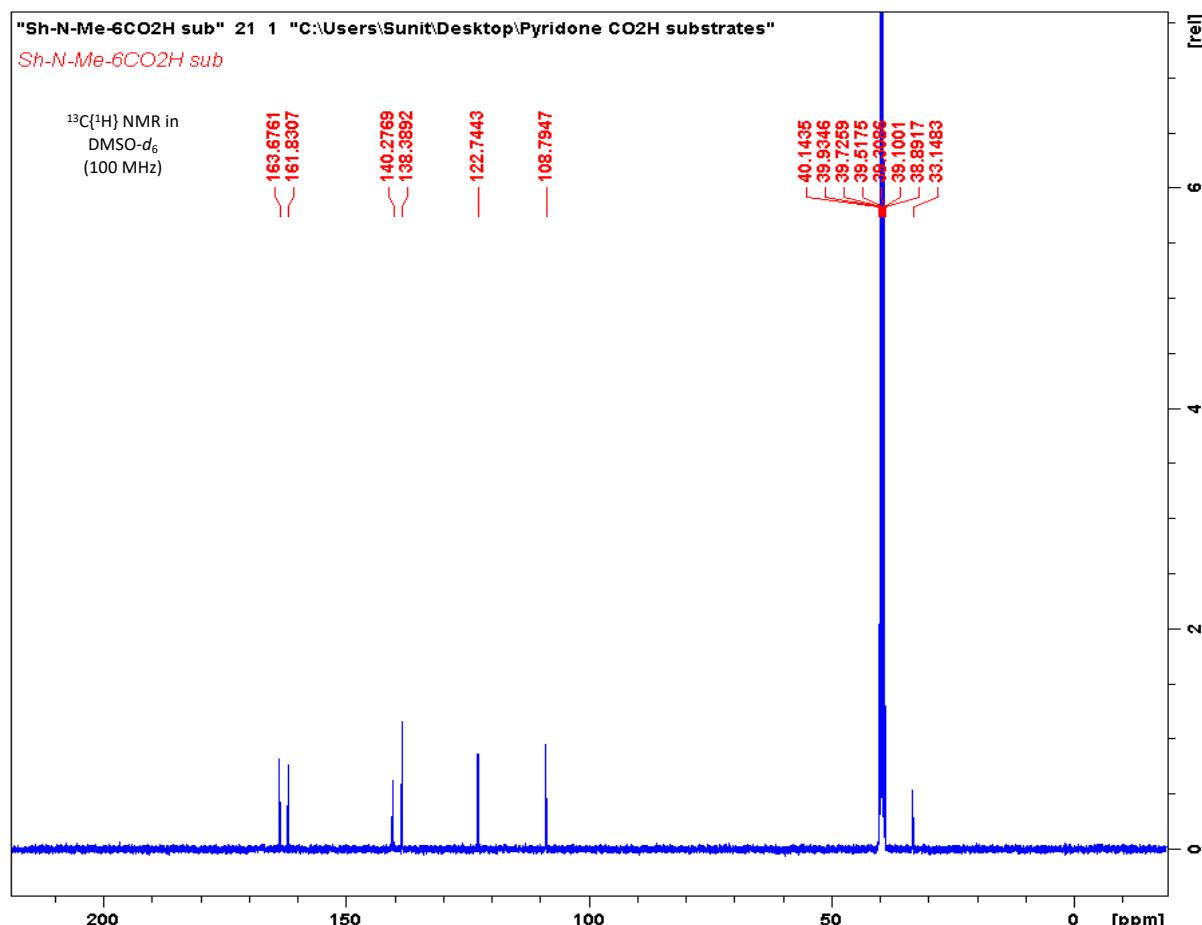
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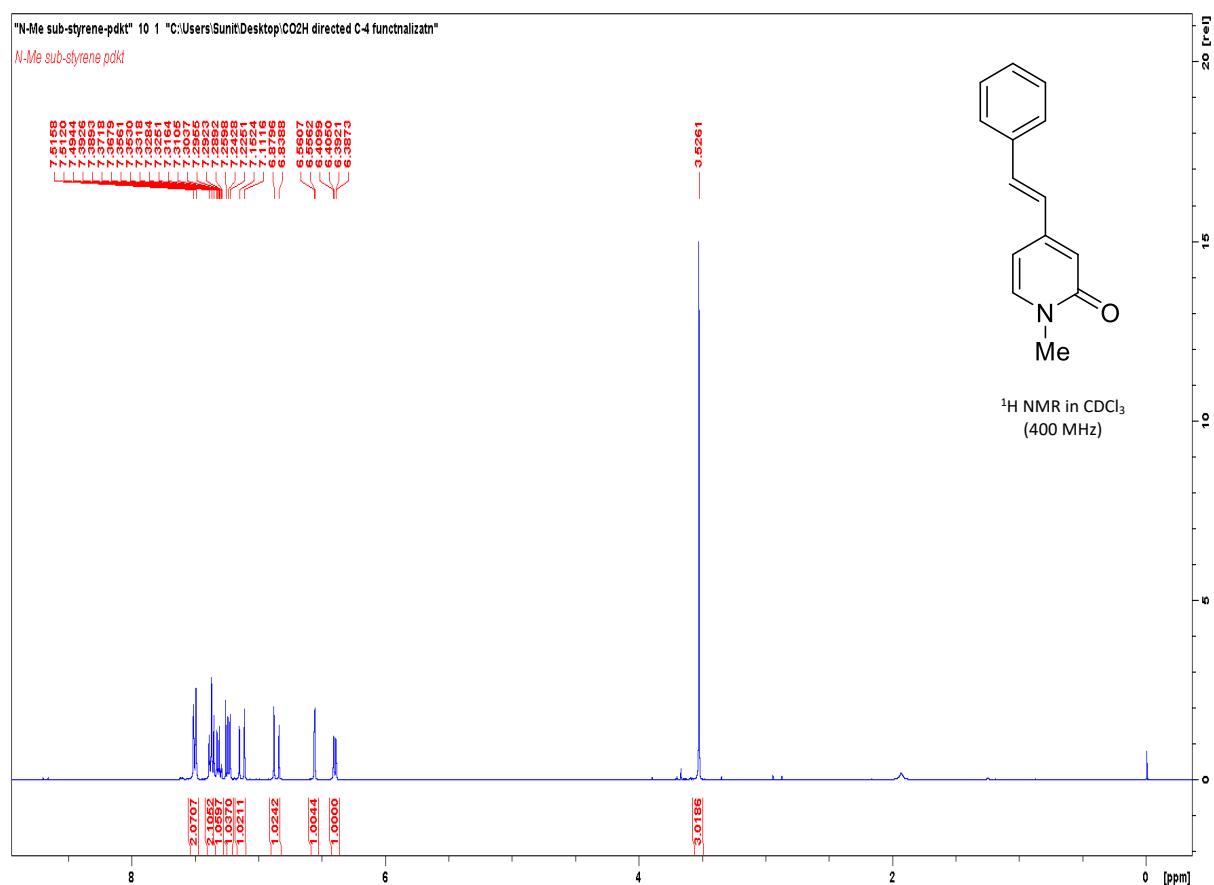
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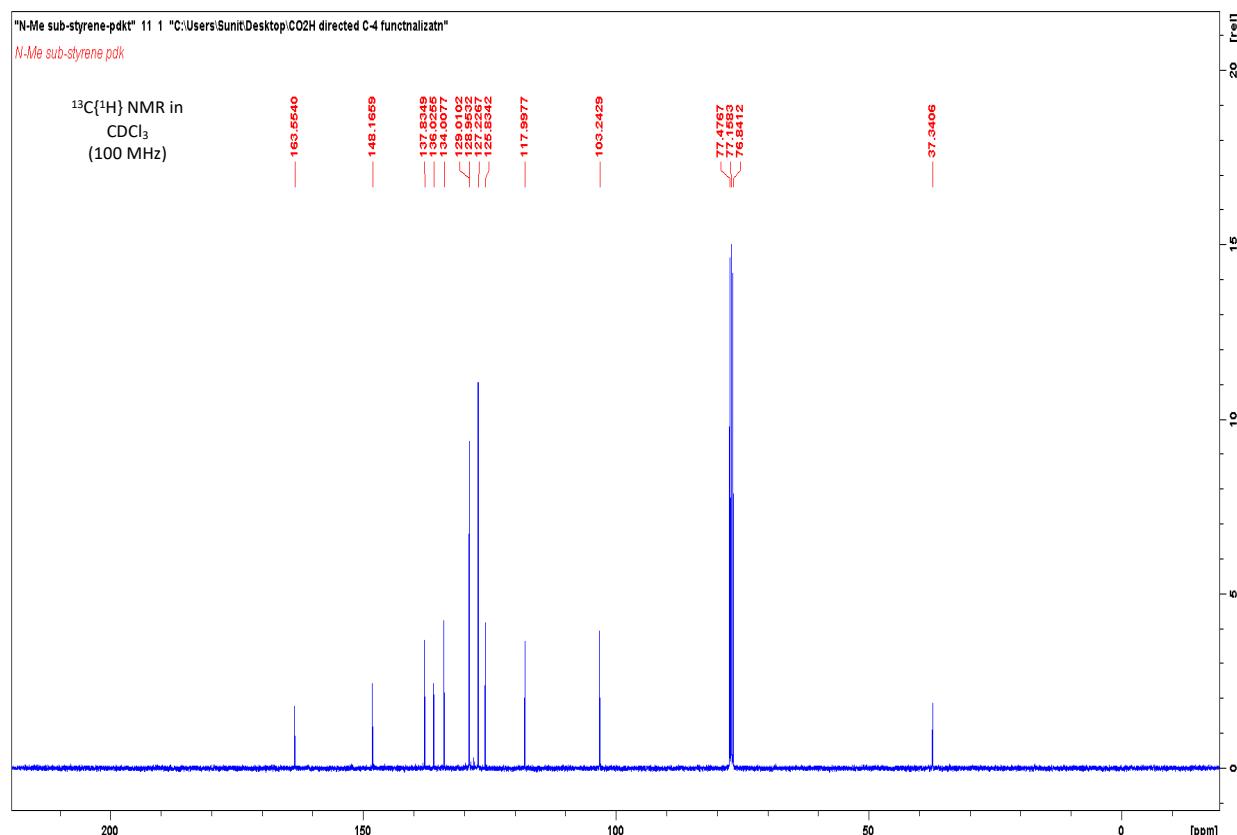
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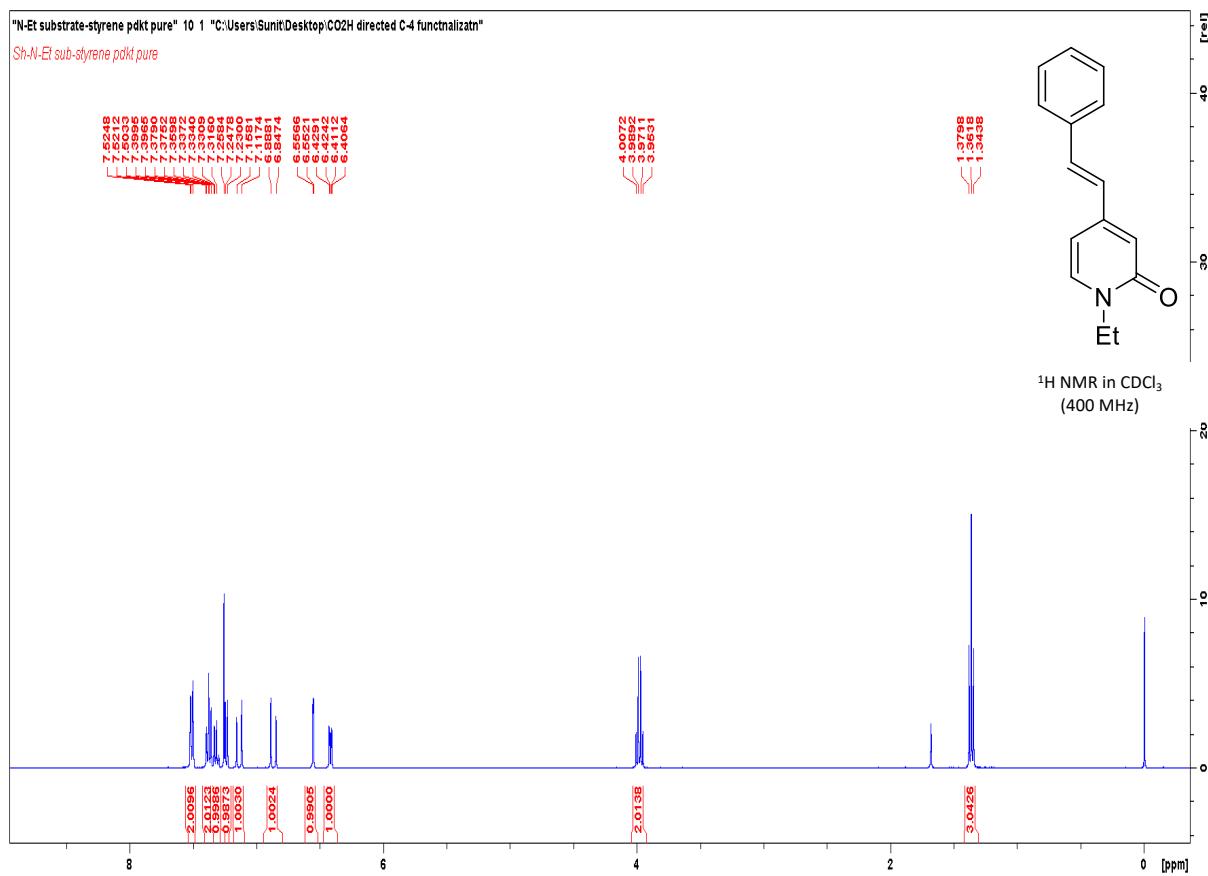
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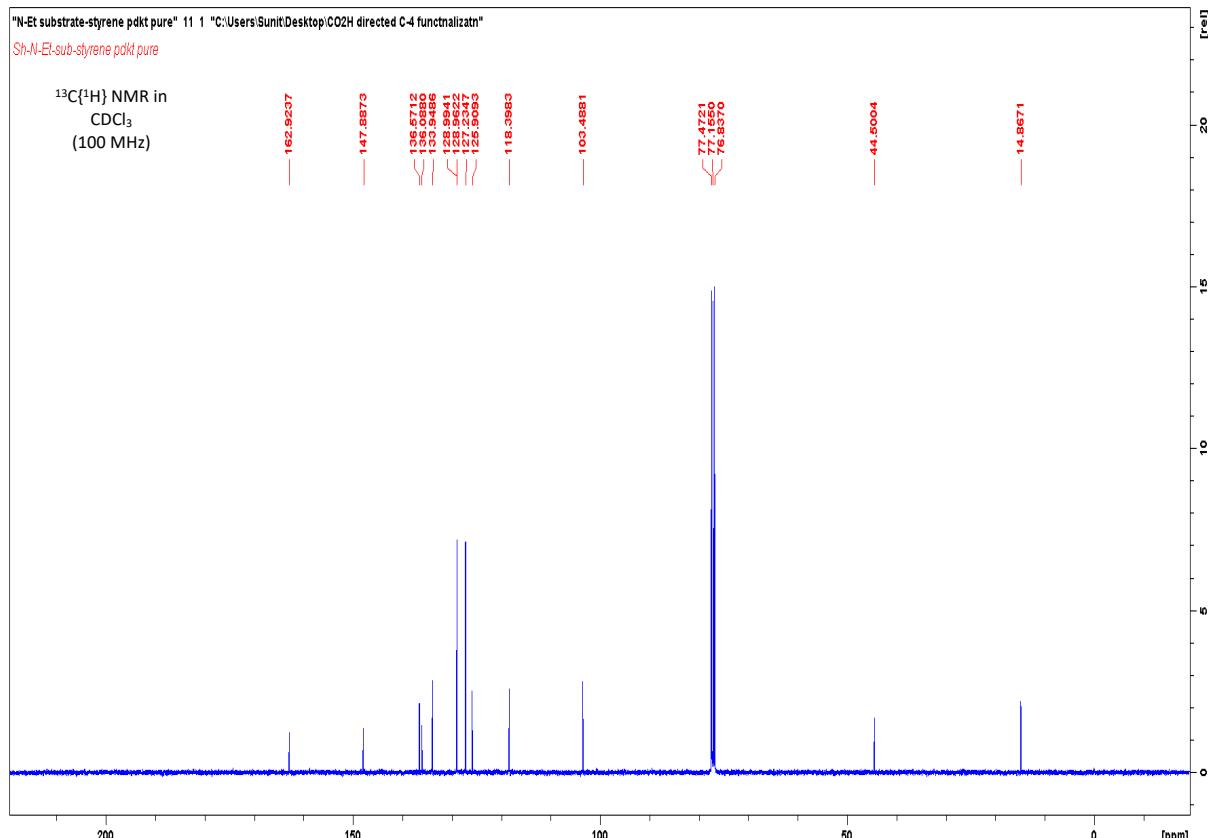
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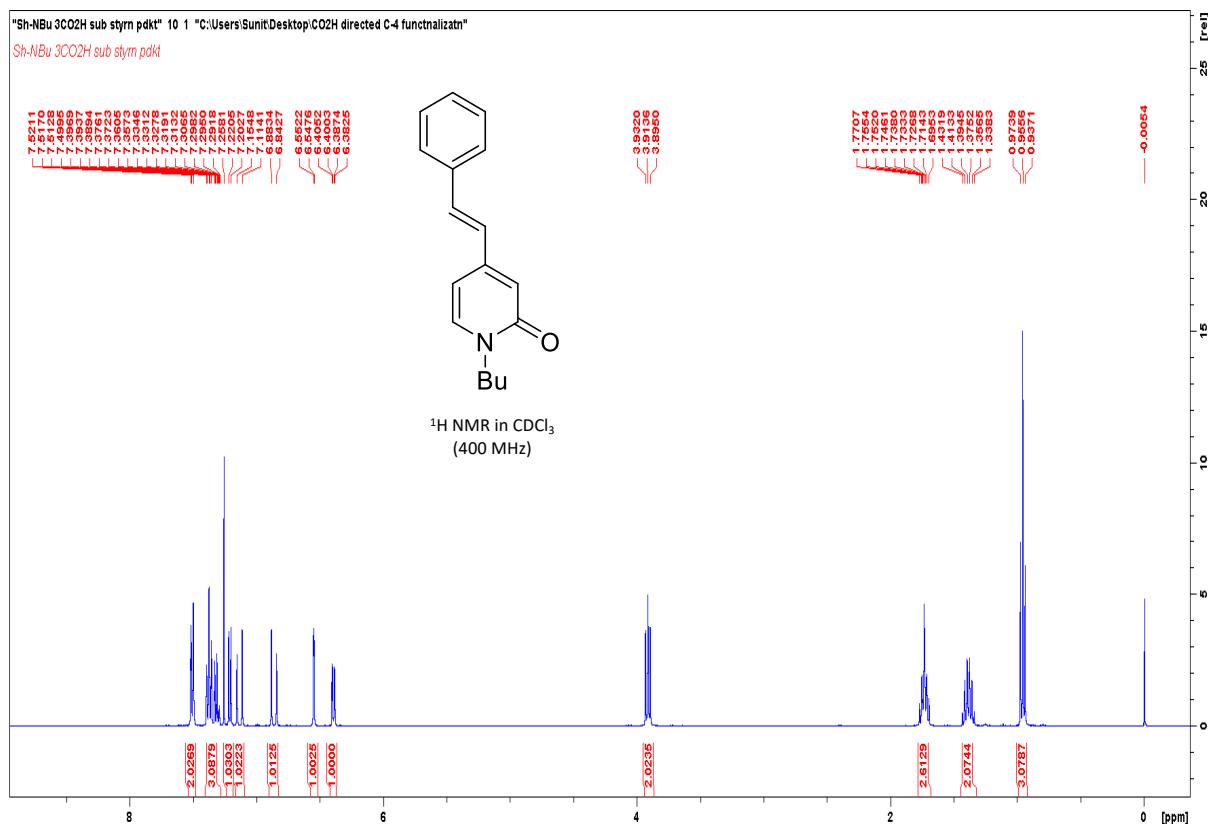
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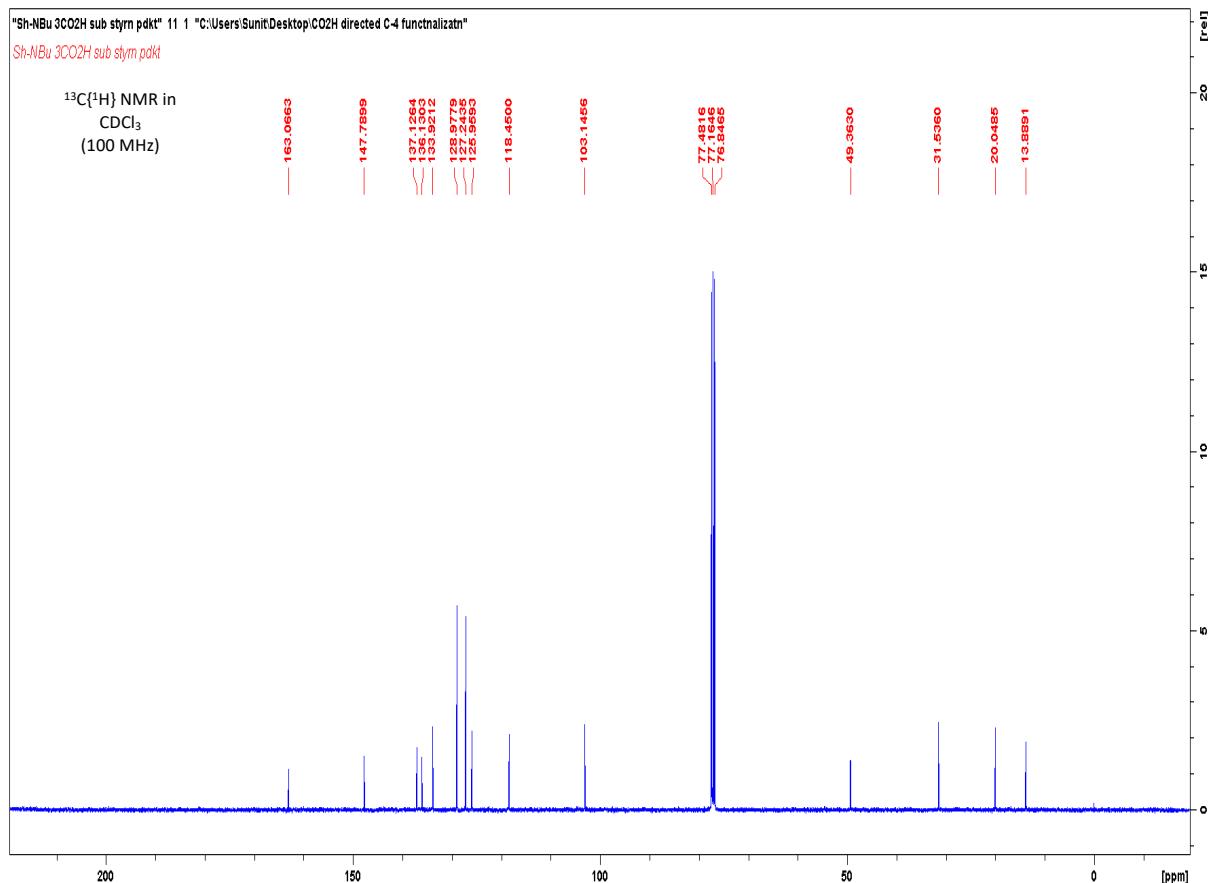
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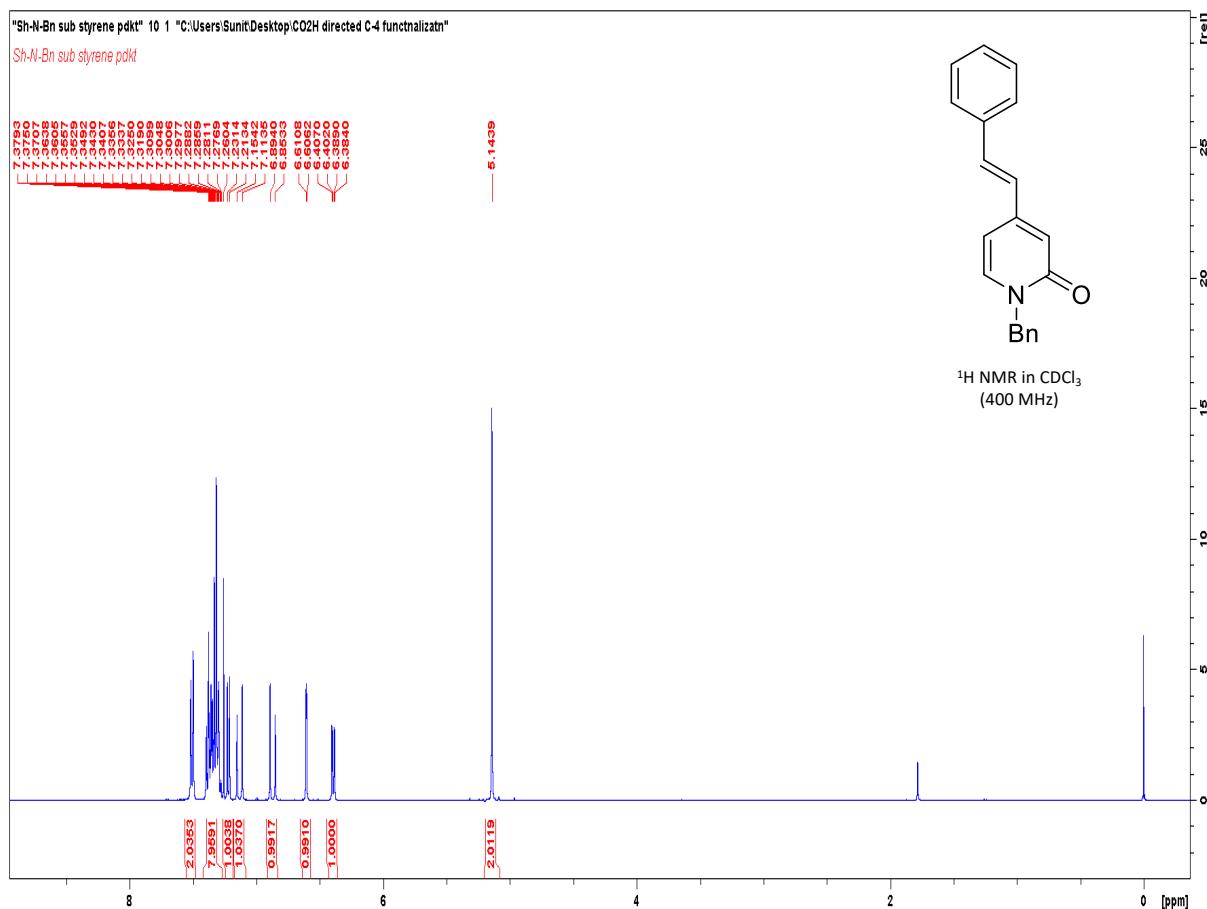
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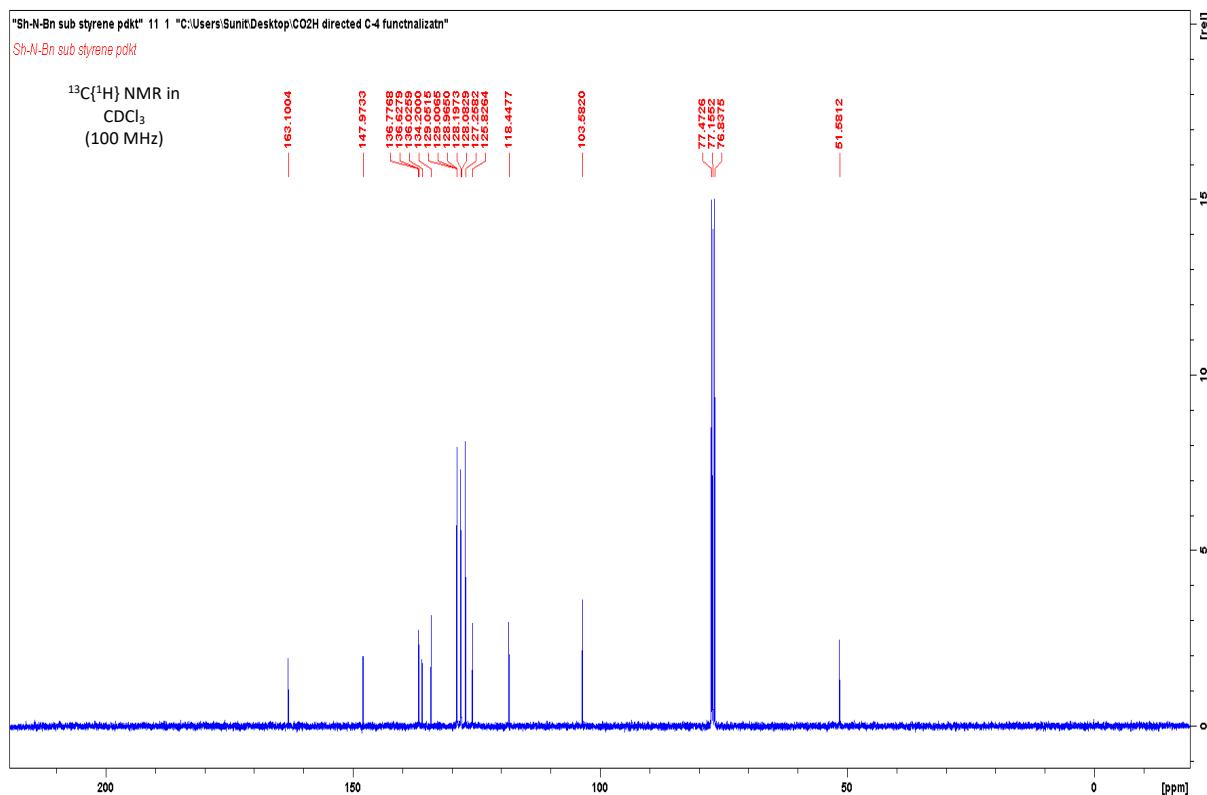
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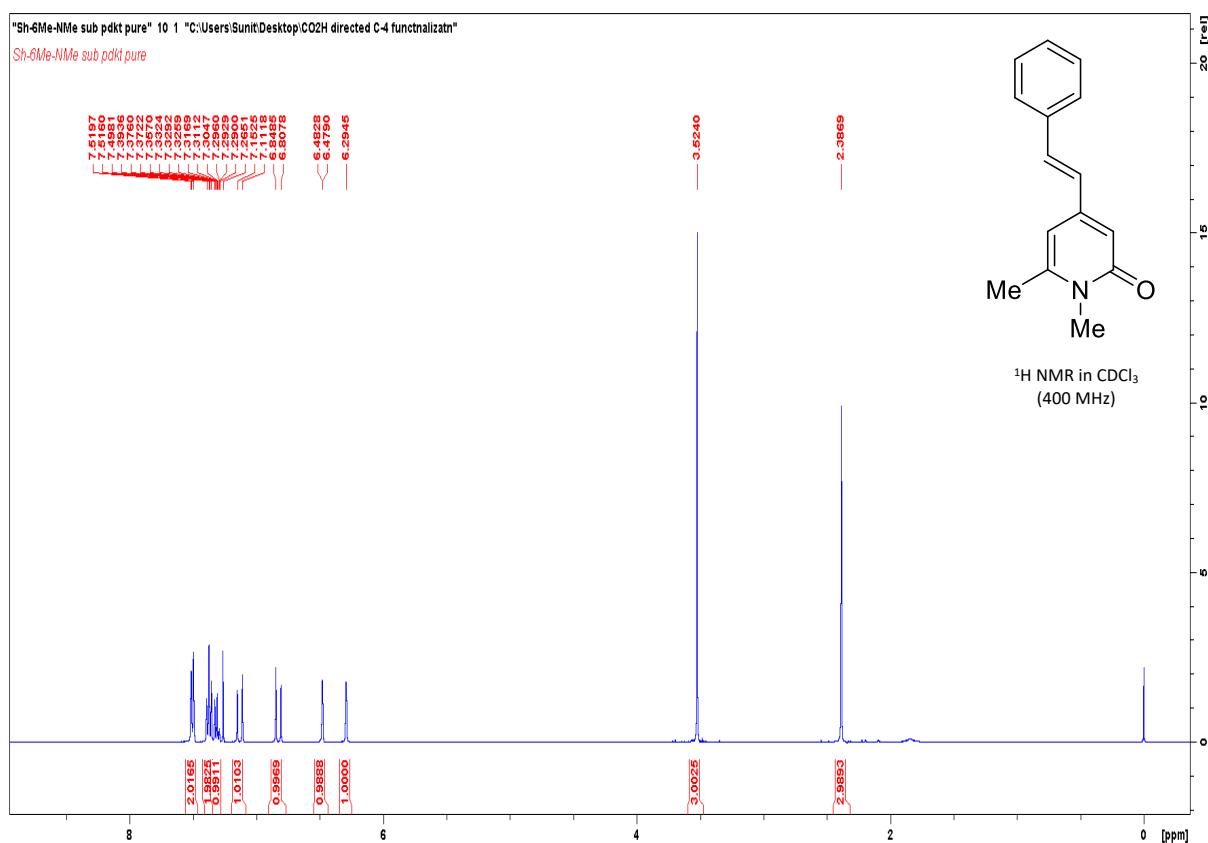
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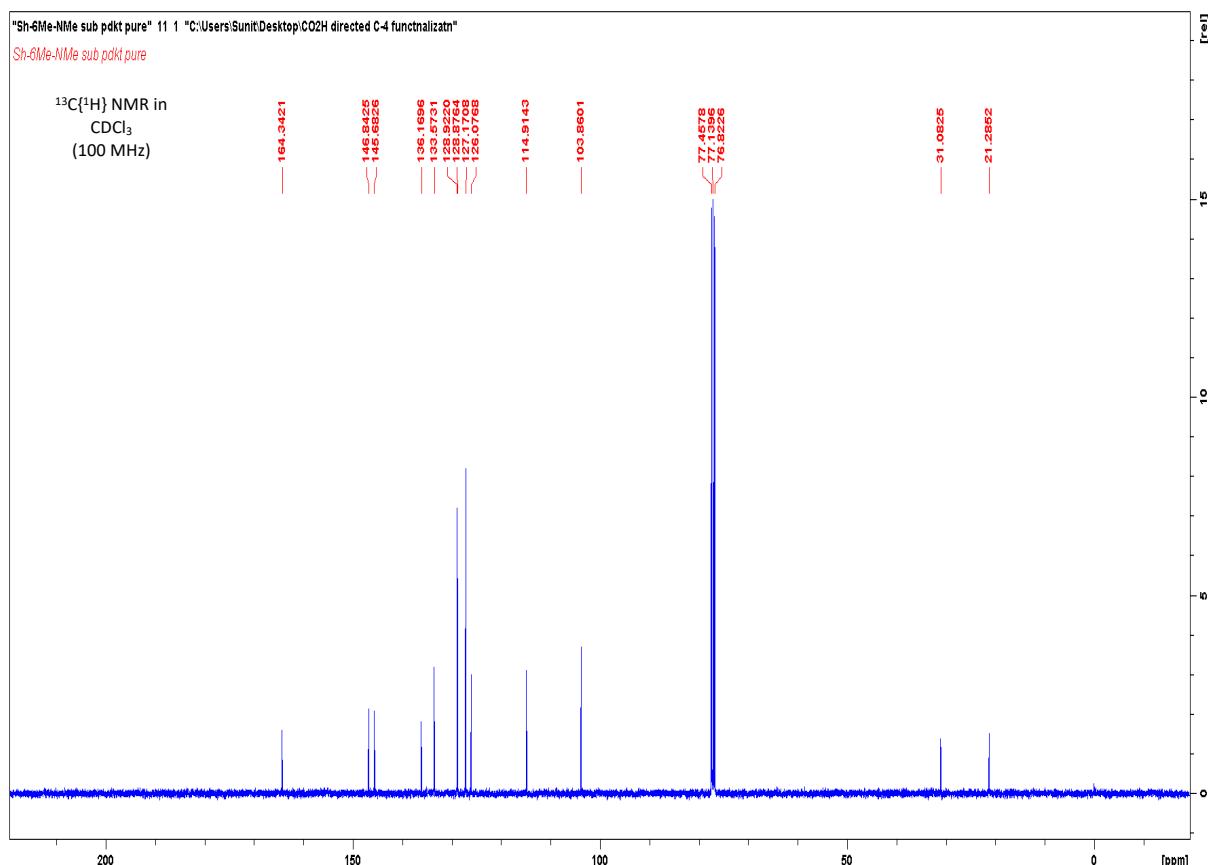
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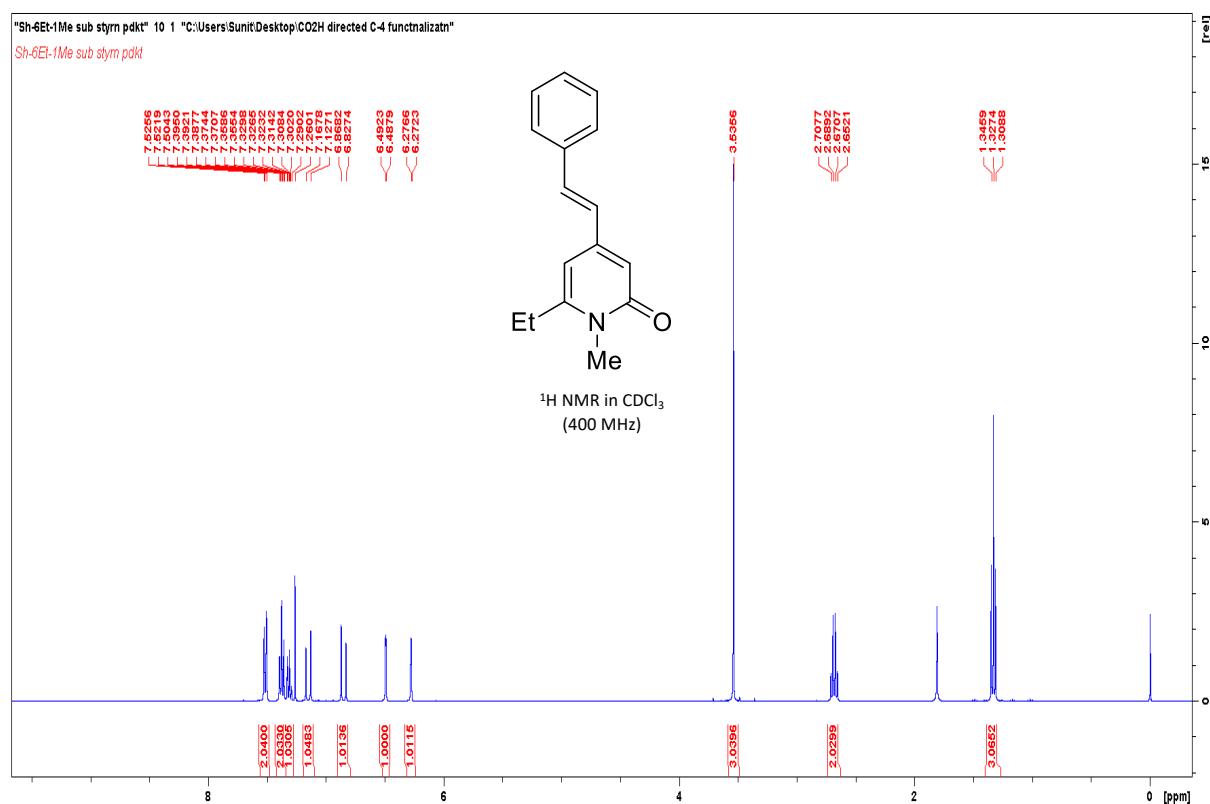
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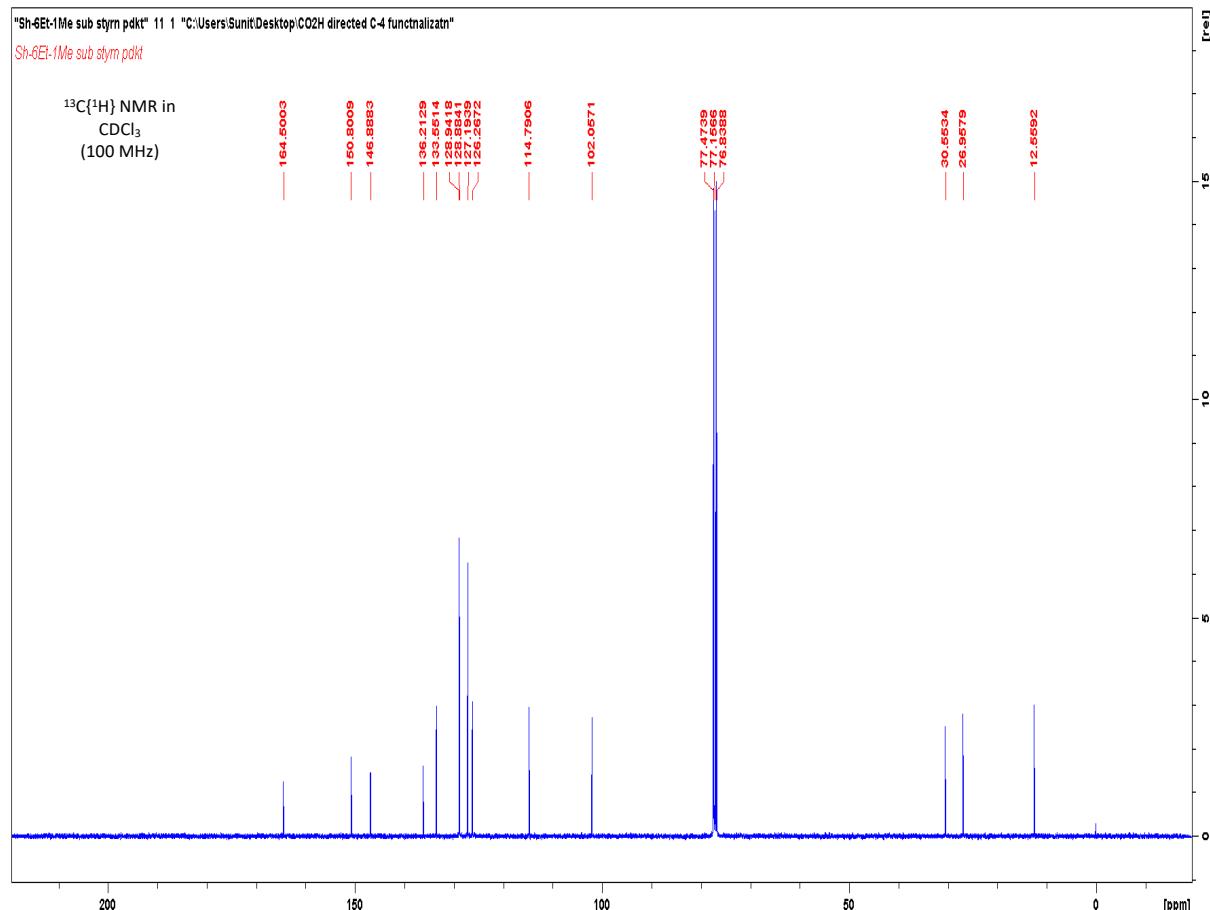
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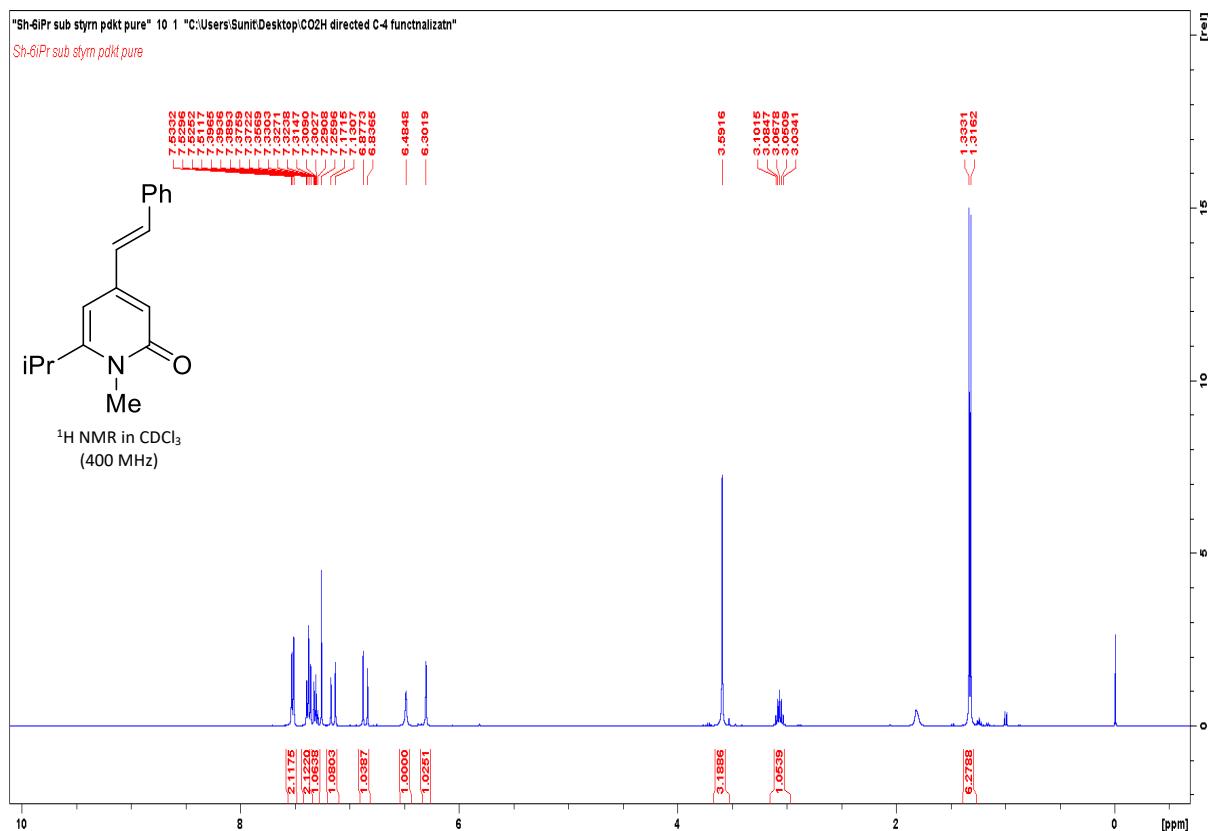
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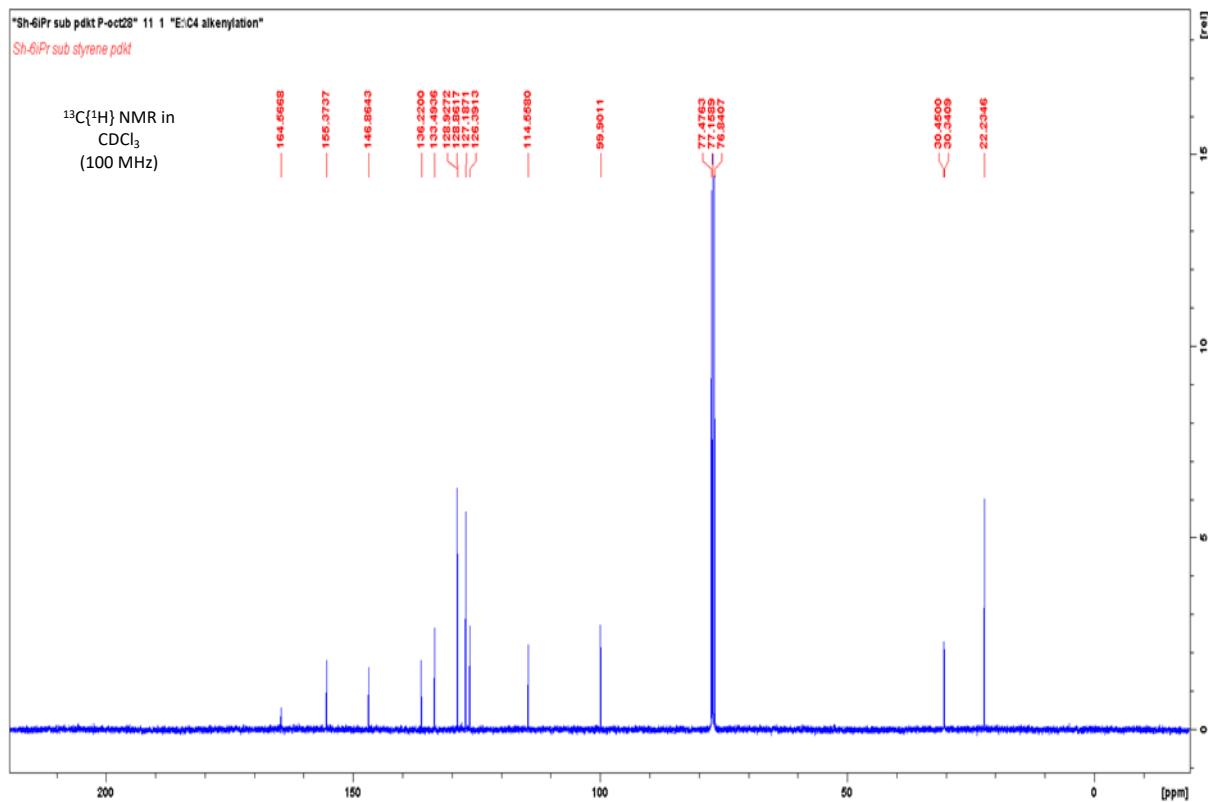
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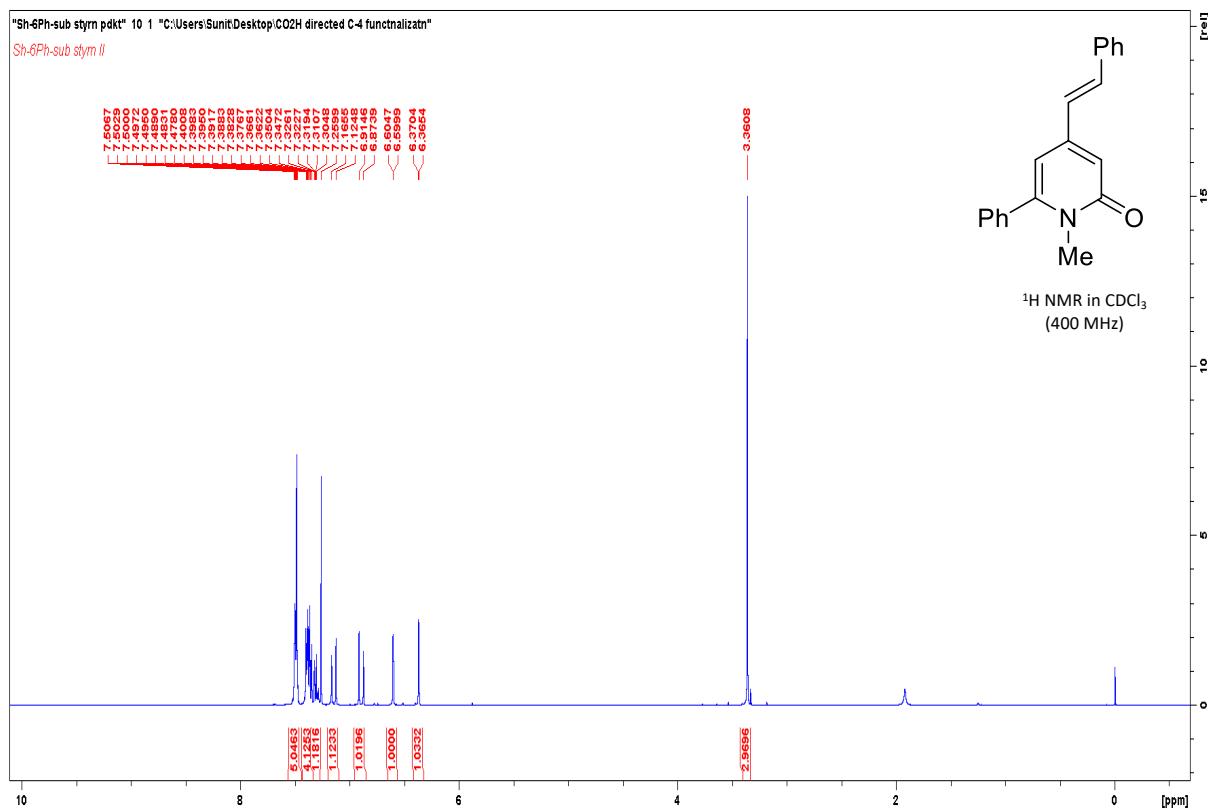
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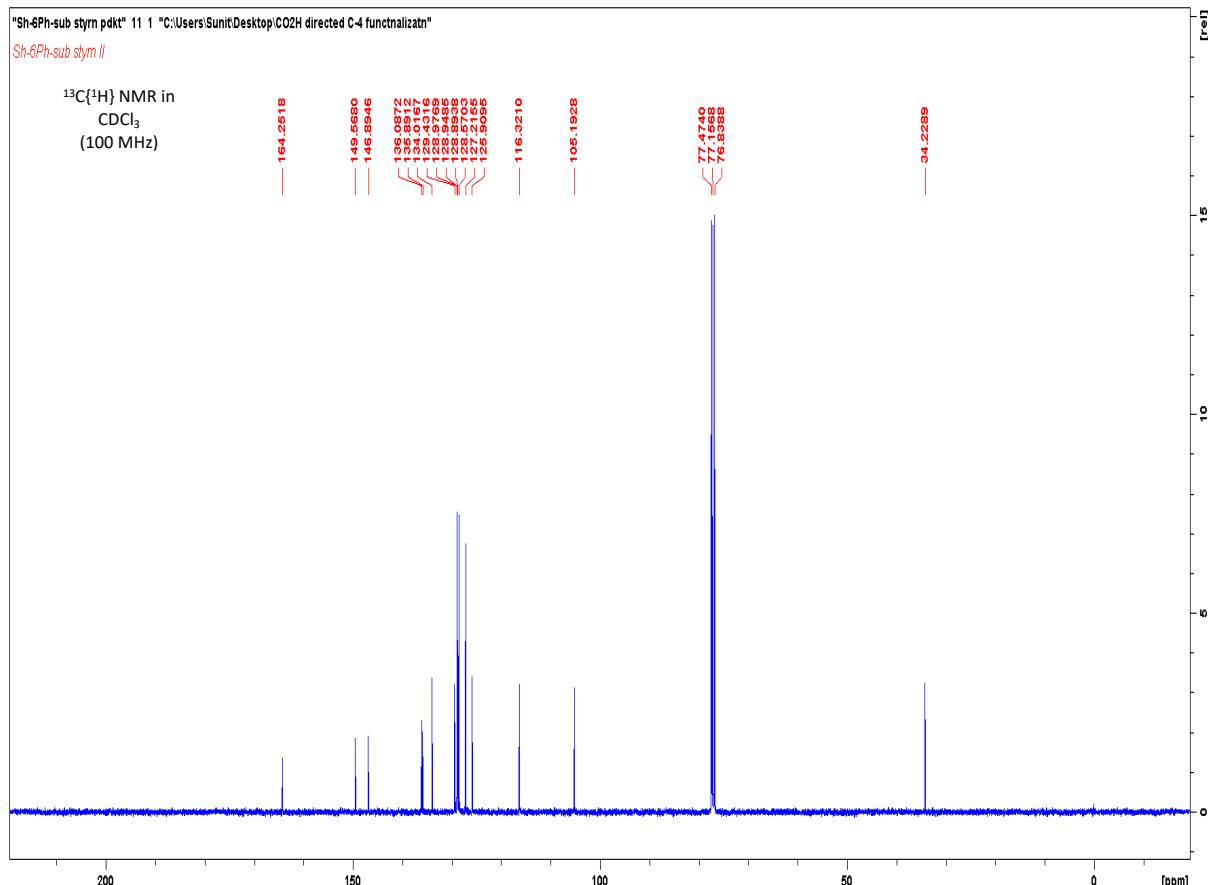
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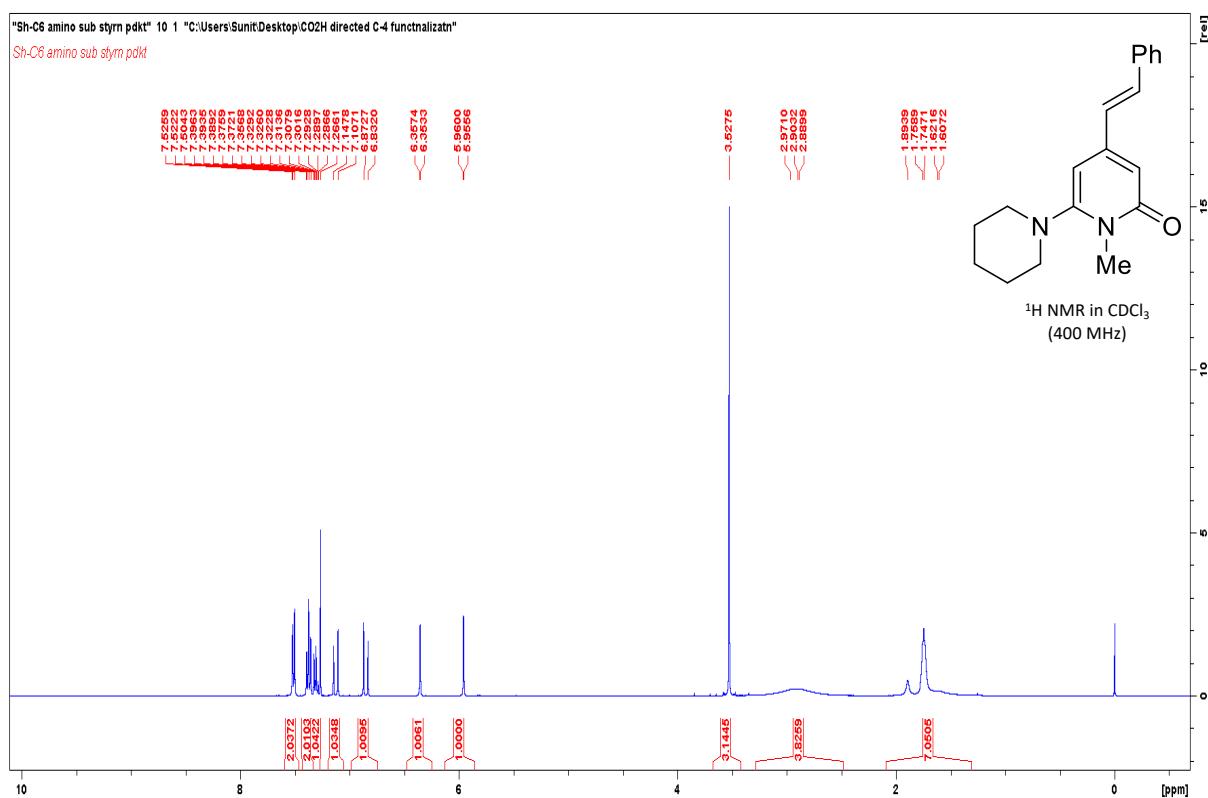
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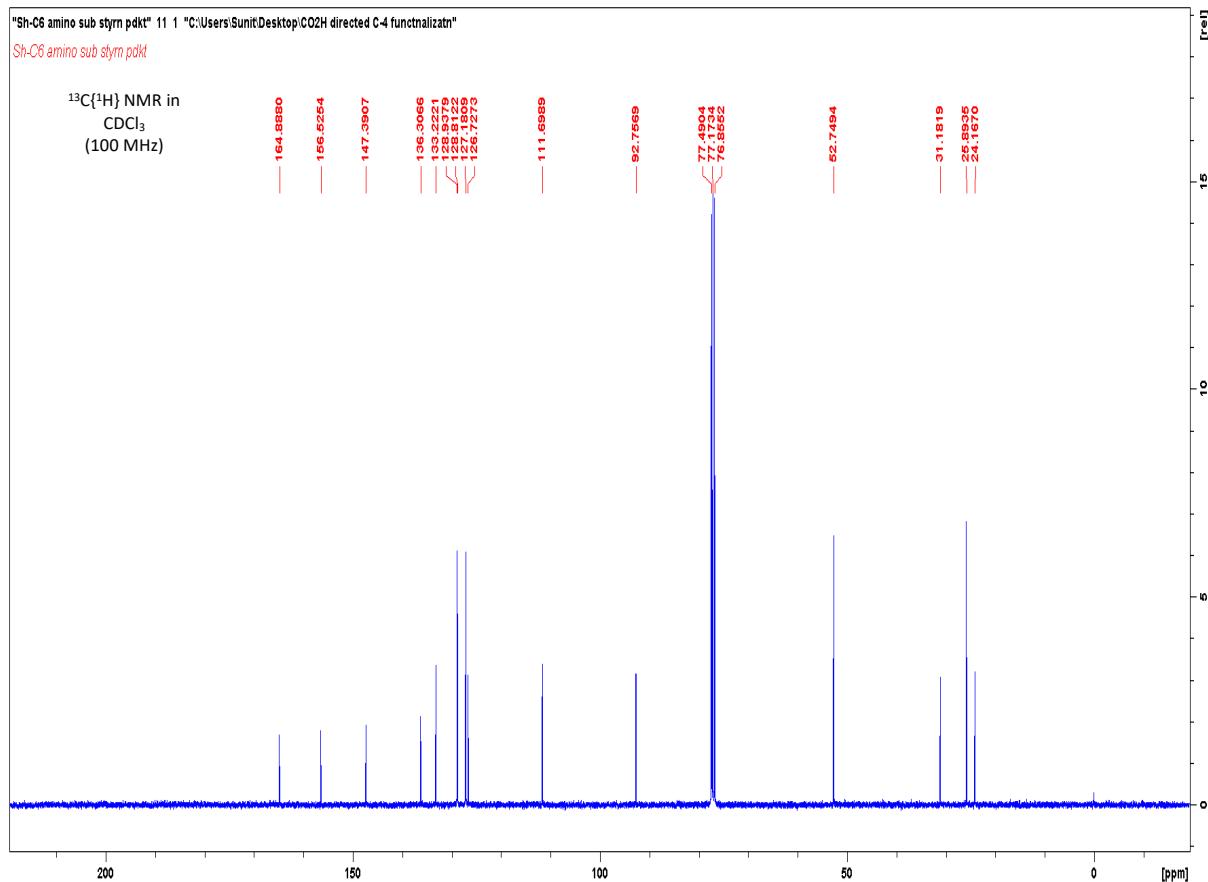
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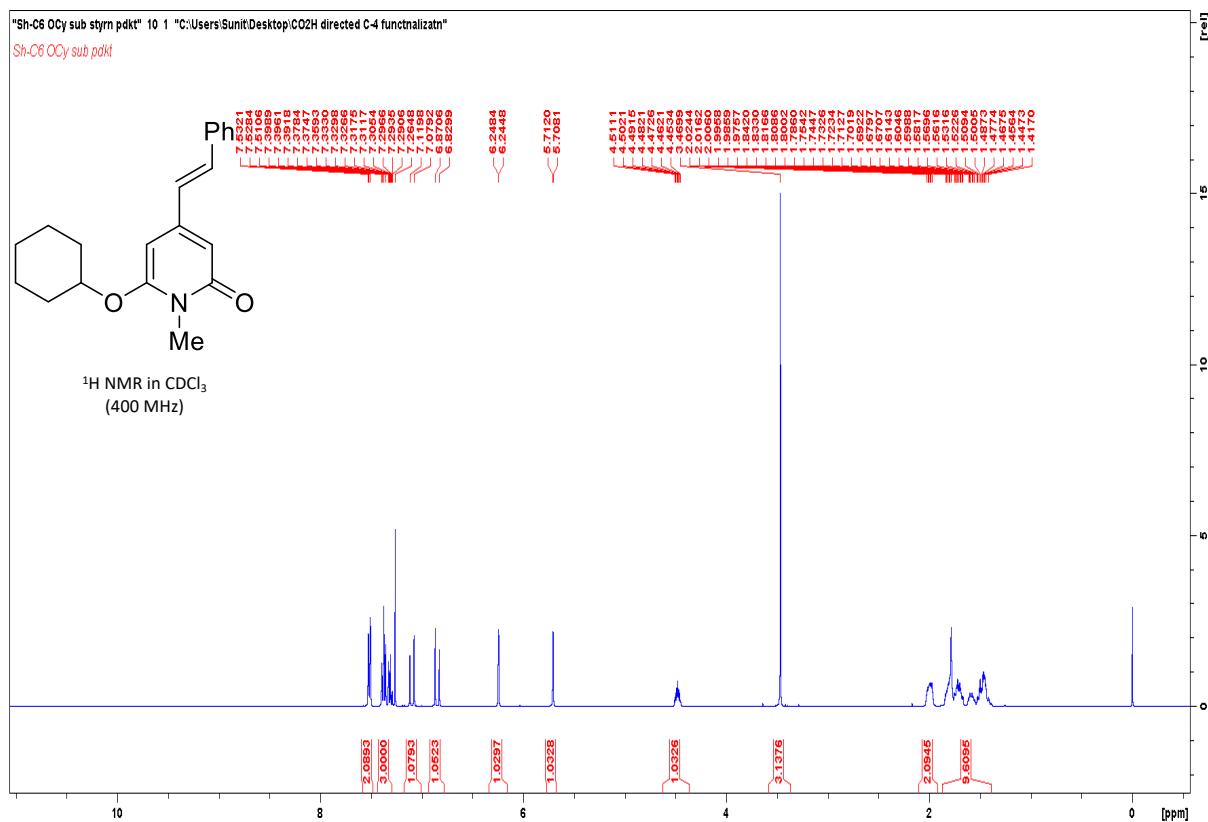
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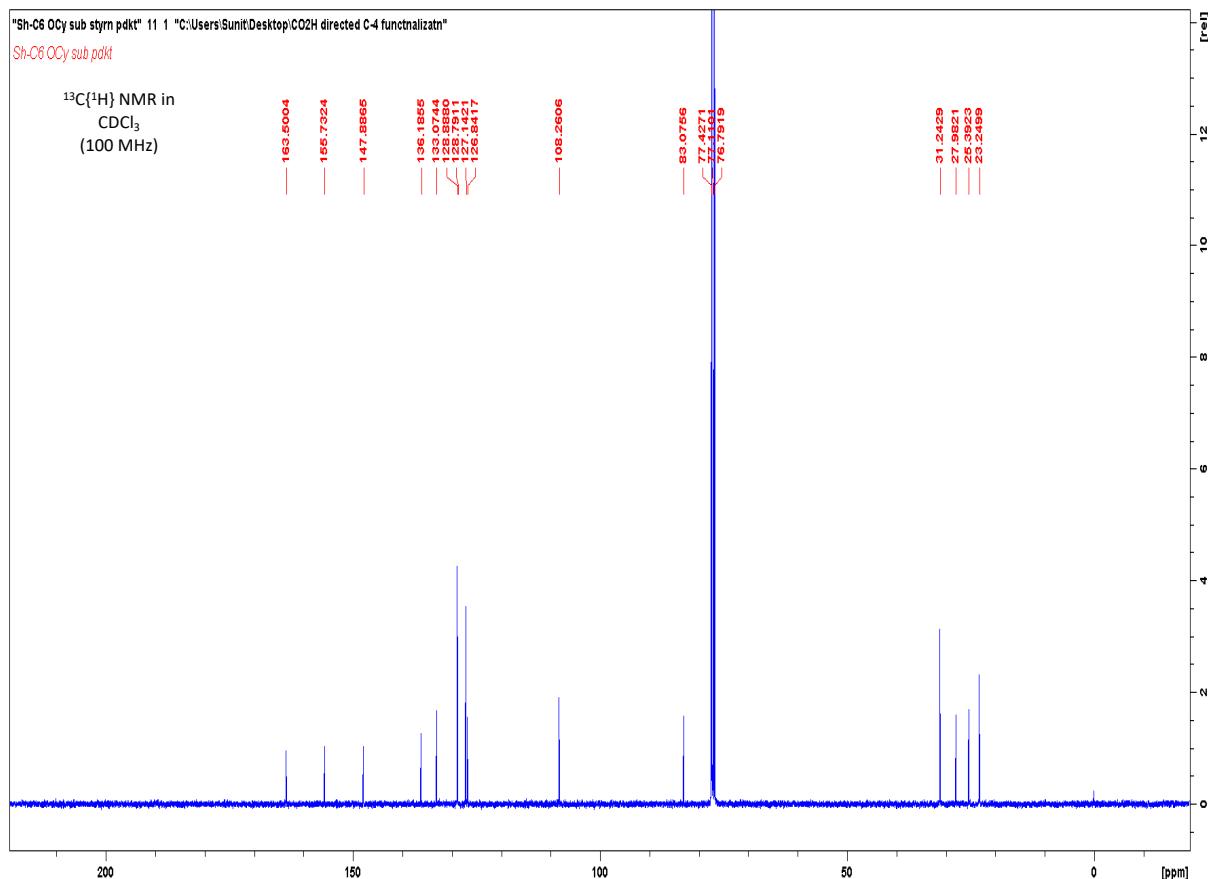
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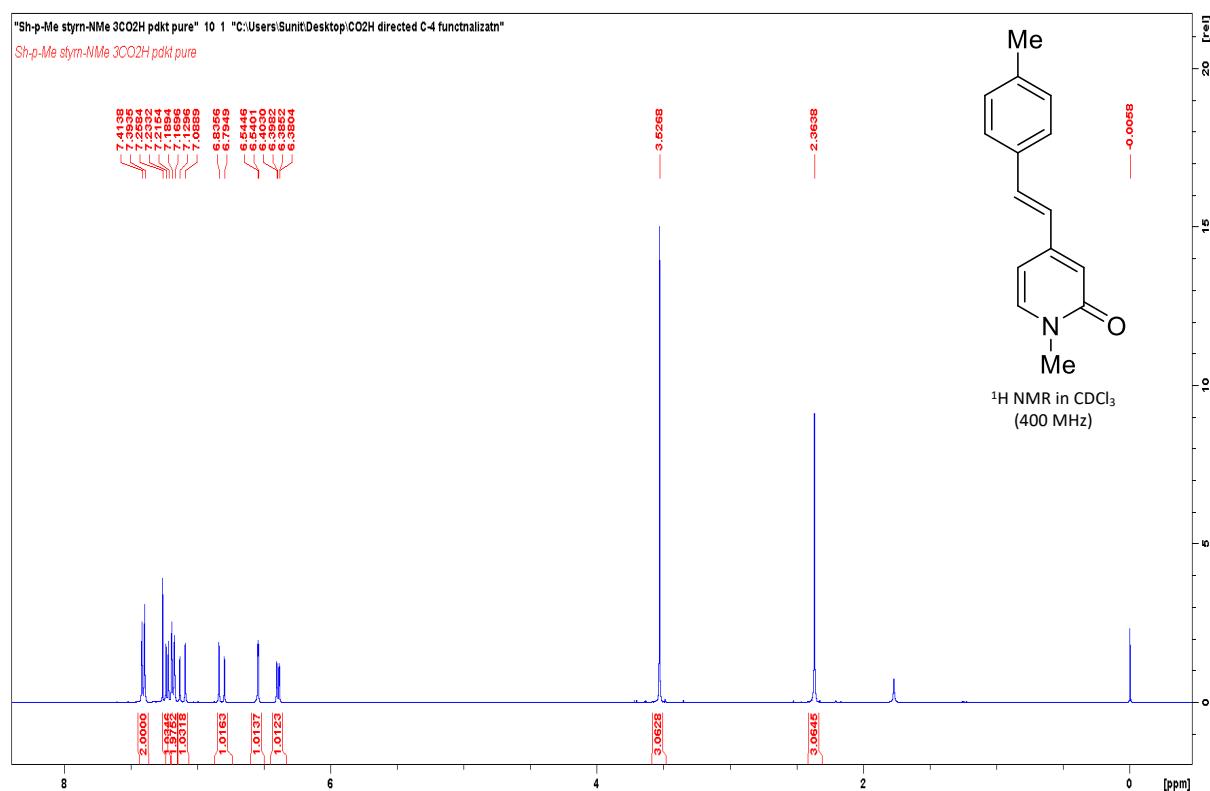
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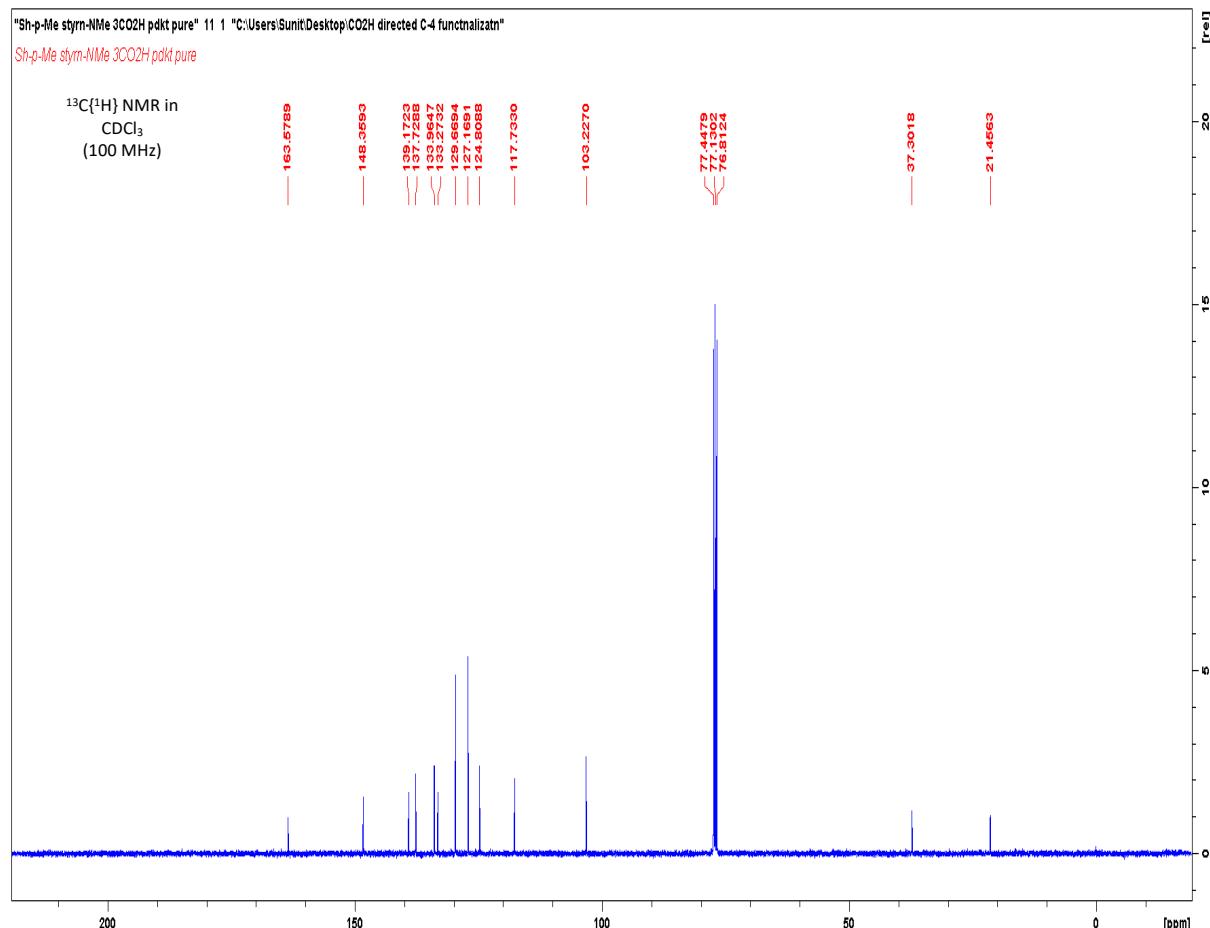
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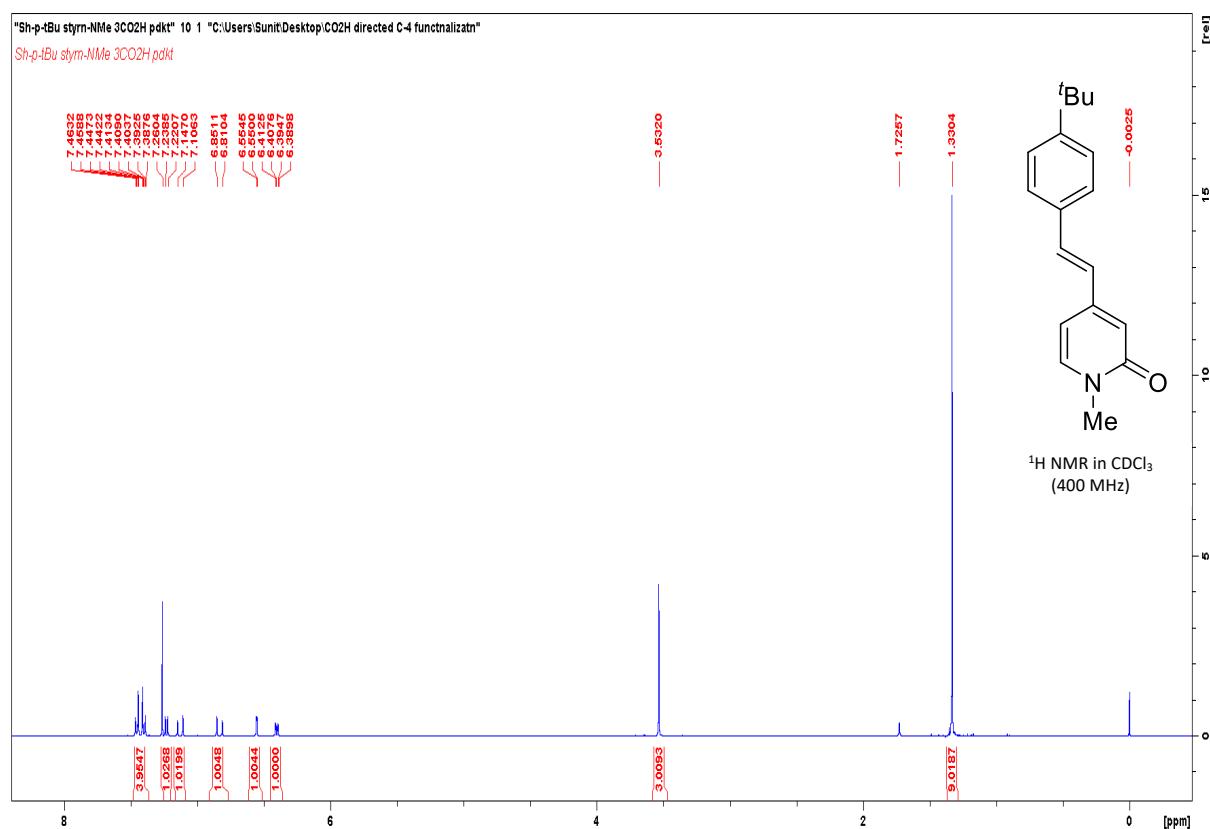
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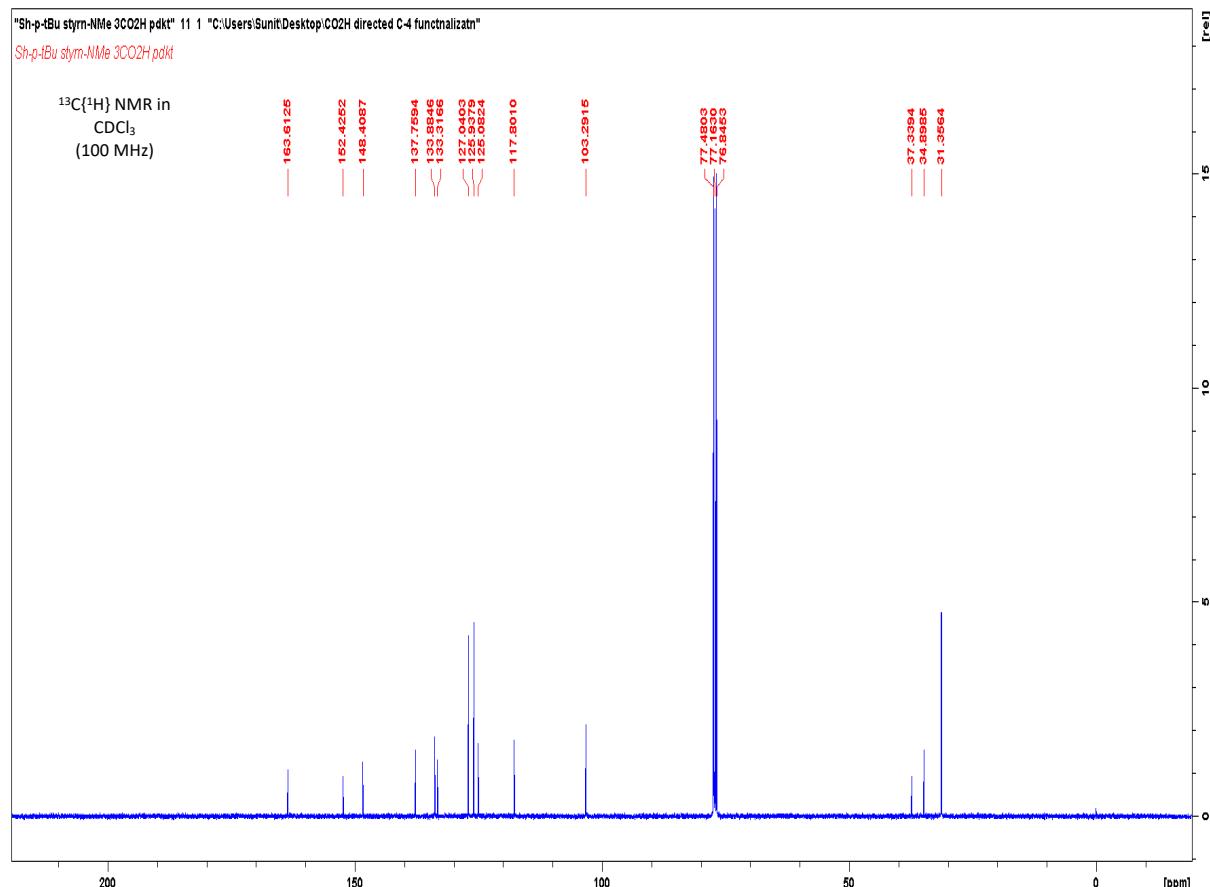
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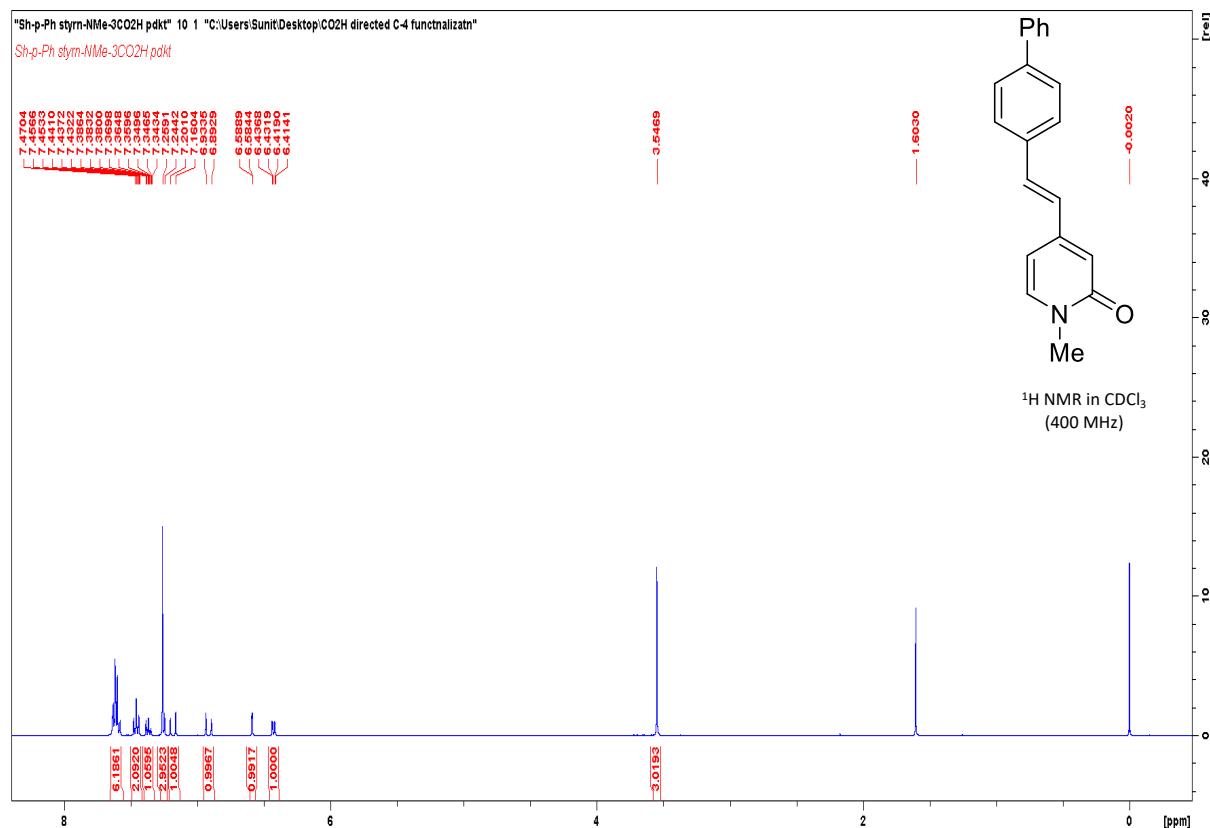
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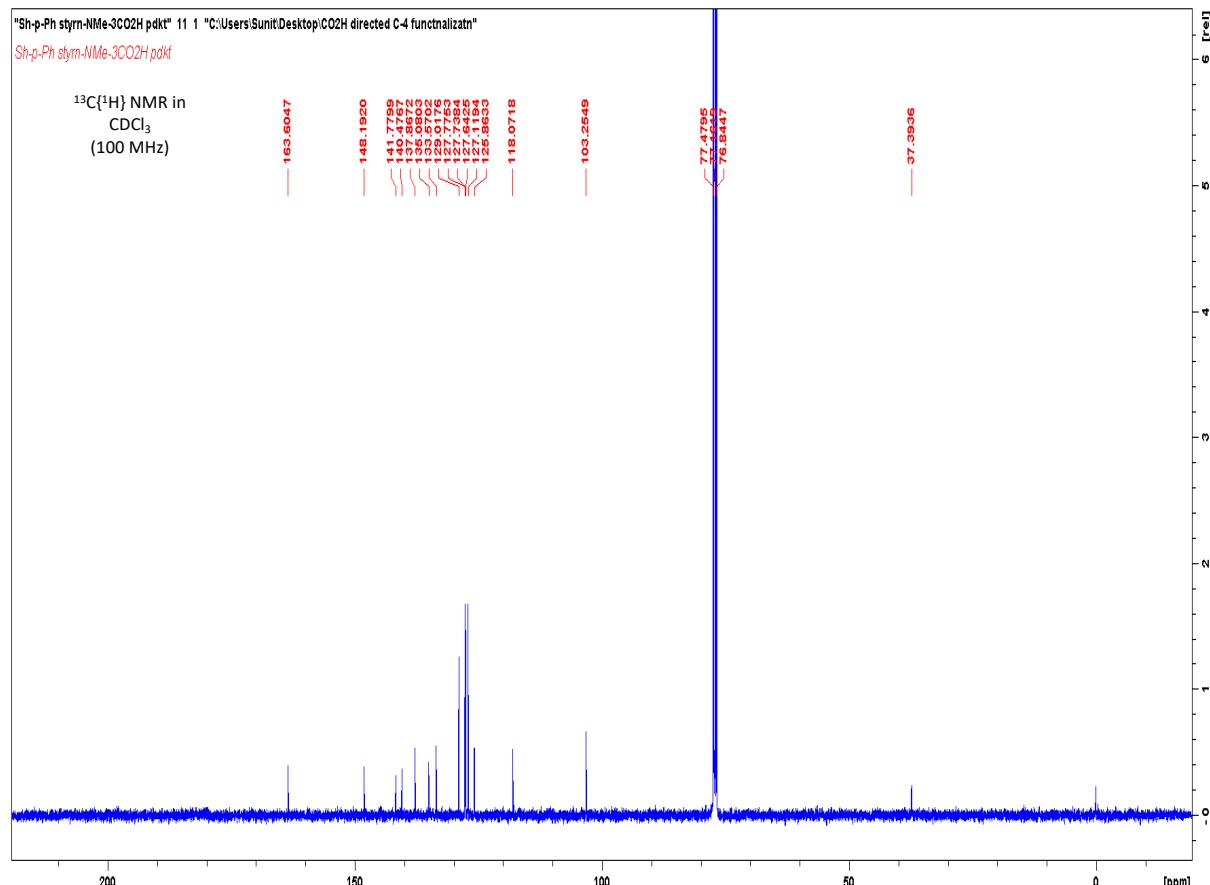
<sup>13</sup>C{<sup>1</sup>H} NMR of compound **3ac** in CDCl<sub>3</sub> (100 MHz)



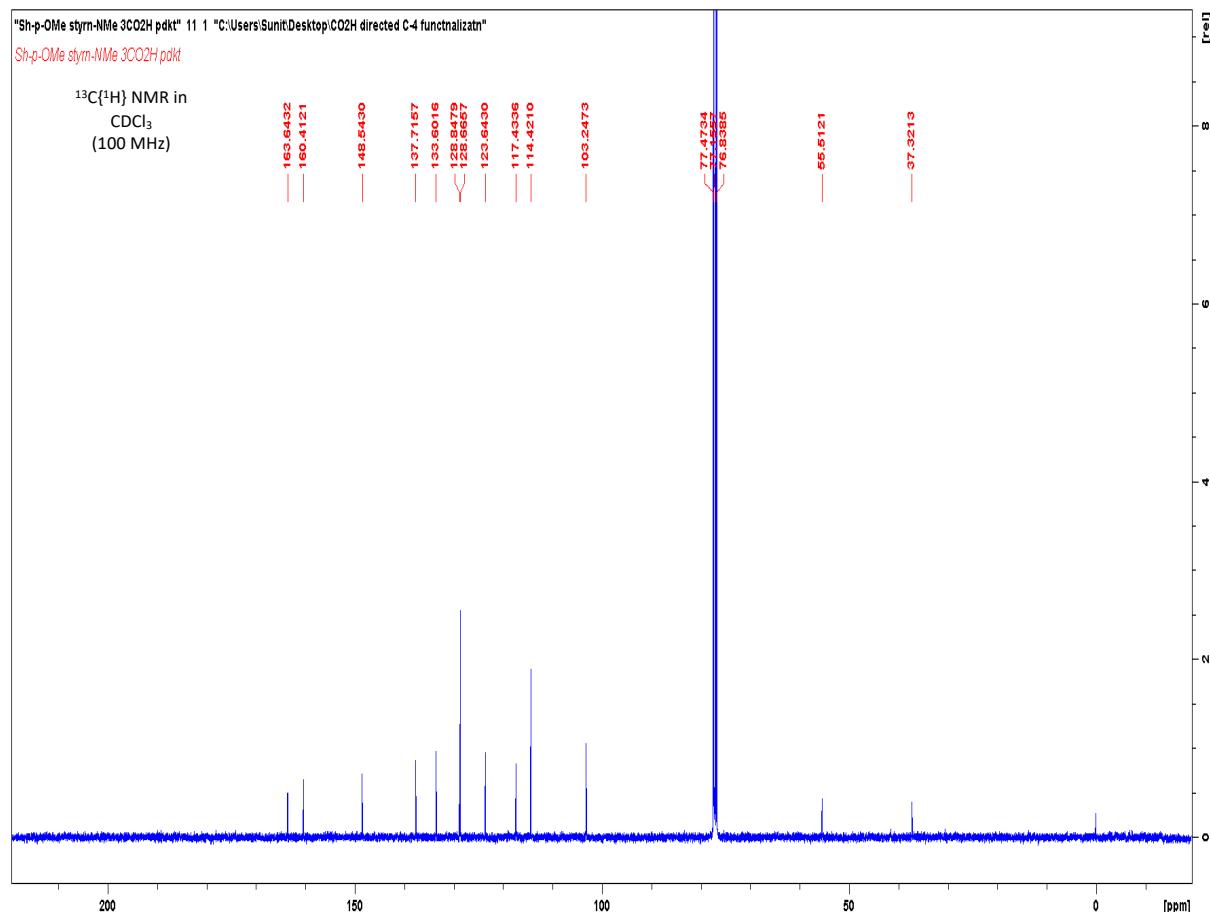
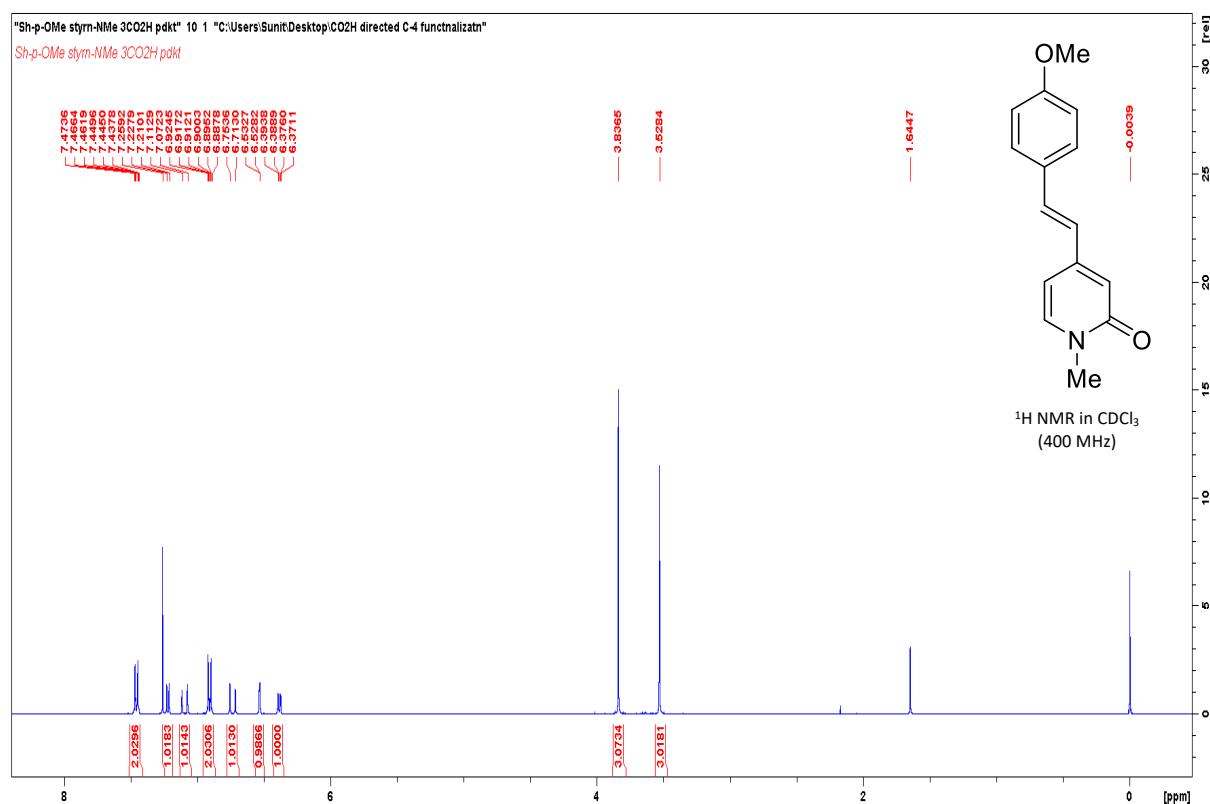
<sup>1</sup>H NMR of compound **3ad** in CDCl<sub>3</sub> (400 MHz)



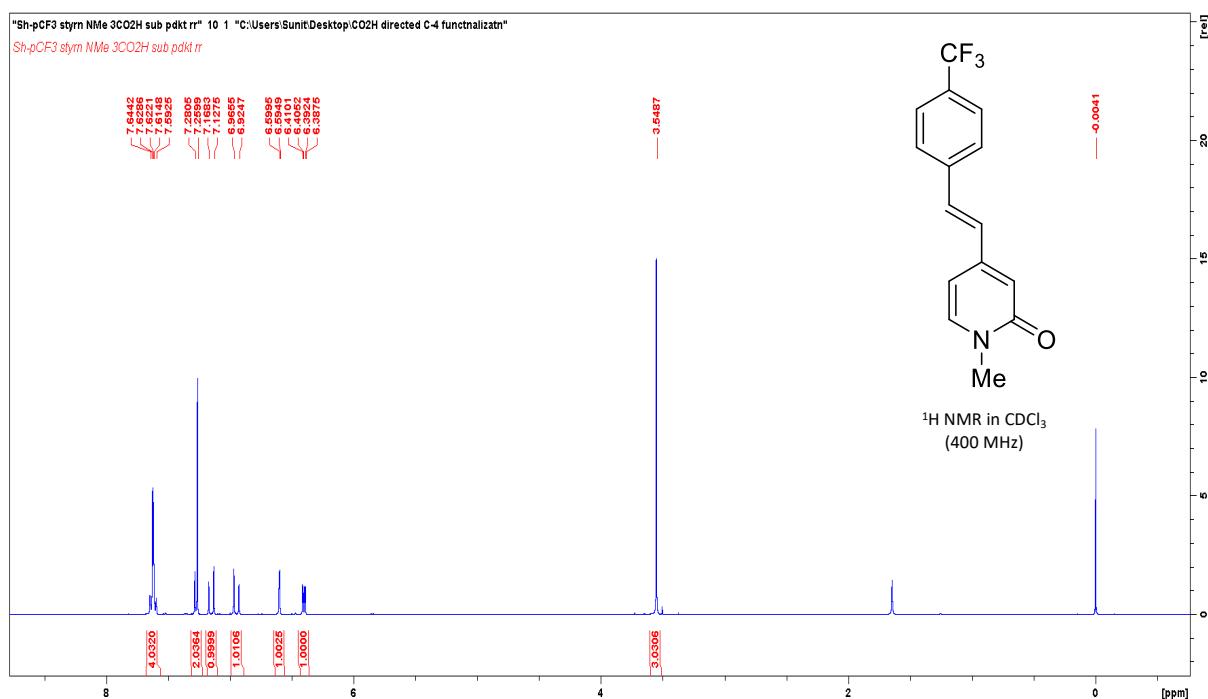
<sup>13</sup>C{<sup>1</sup>H} NMR of compound **3ad** in CDCl<sub>3</sub> (100 MHz)



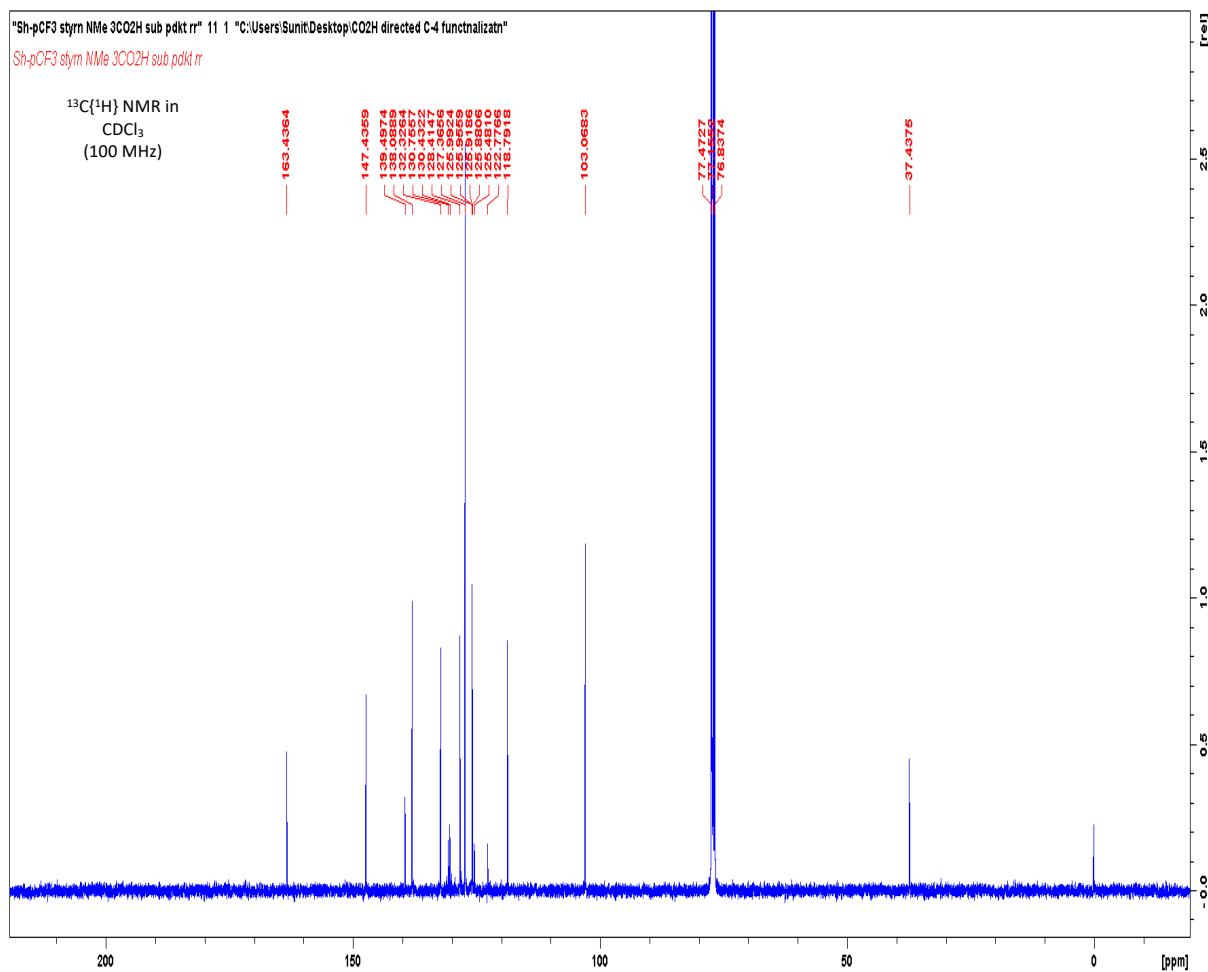
<sup>1</sup>H NMR of compound **3ae** in CDCl<sub>3</sub> (400 MHz)



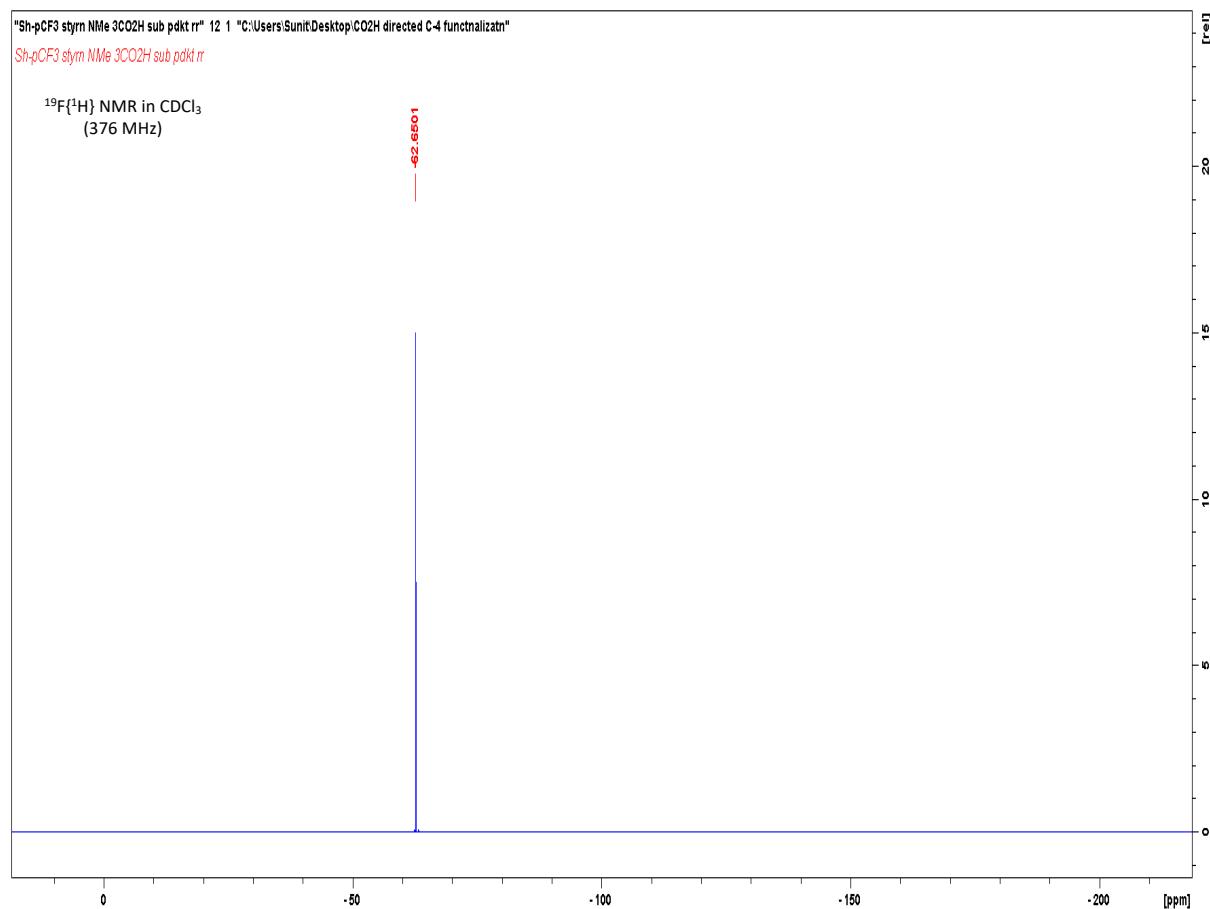
<sup>1</sup>H NMR of compound **3af** in CDCl<sub>3</sub> (400 MHz)



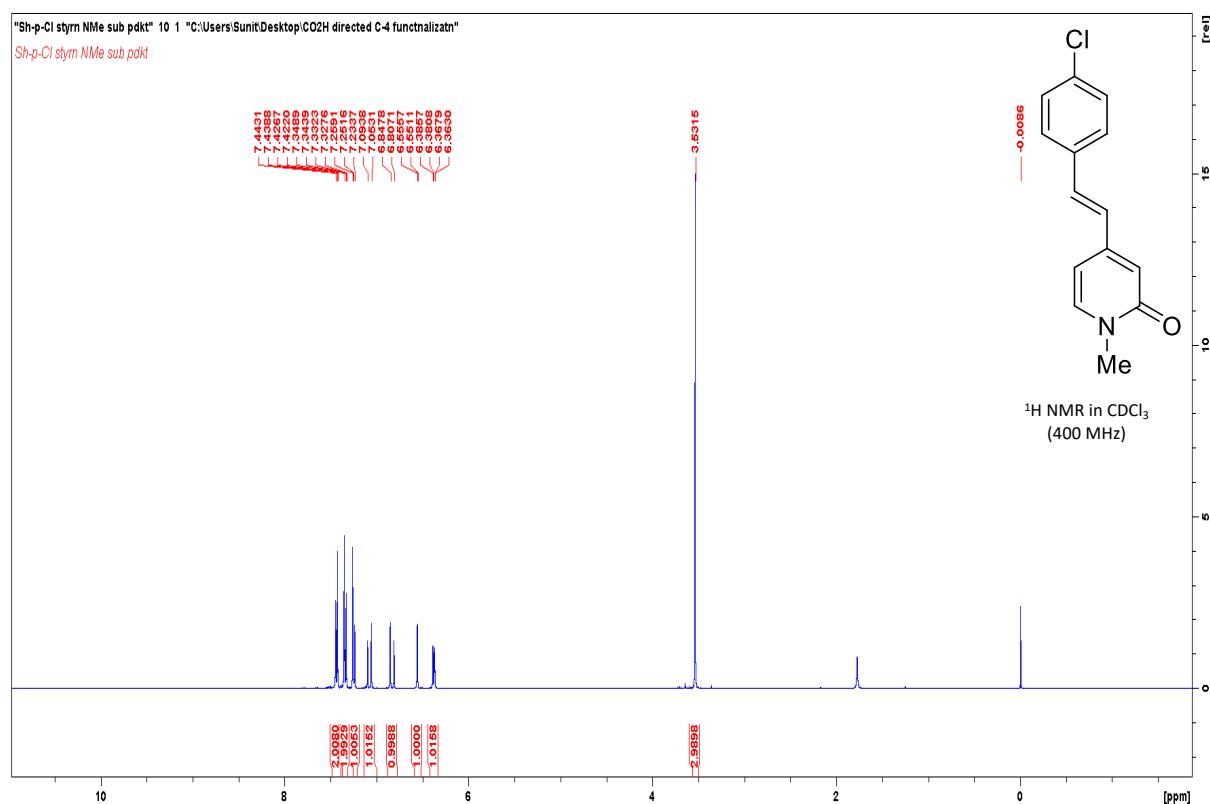
<sup>13</sup>C{<sup>1</sup>H} NMR of compound **3af** in CDCl<sub>3</sub> (100 MHz)



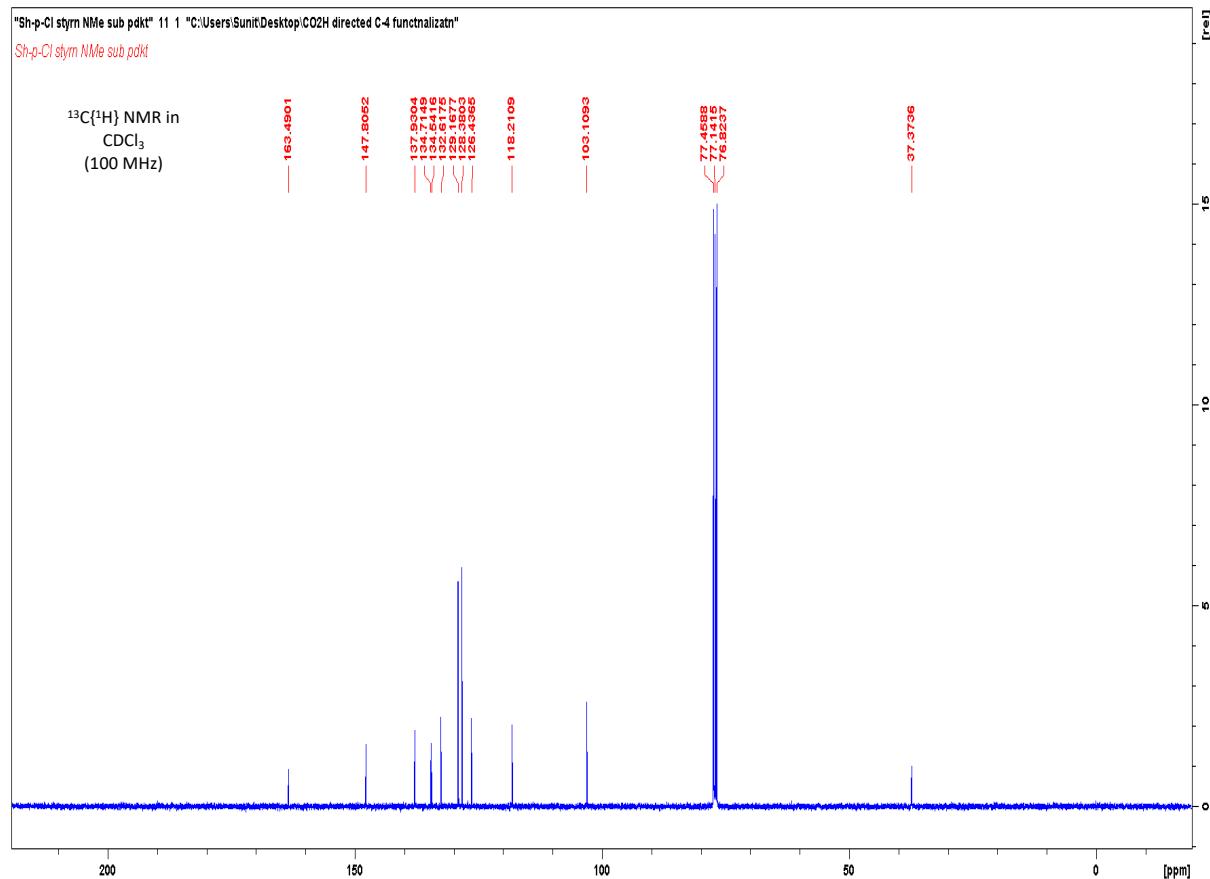
$^{19}\text{F}\{^1\text{H}\}$  NMR of compound **3af** in  $\text{CDCl}_3$  (376 MHz)



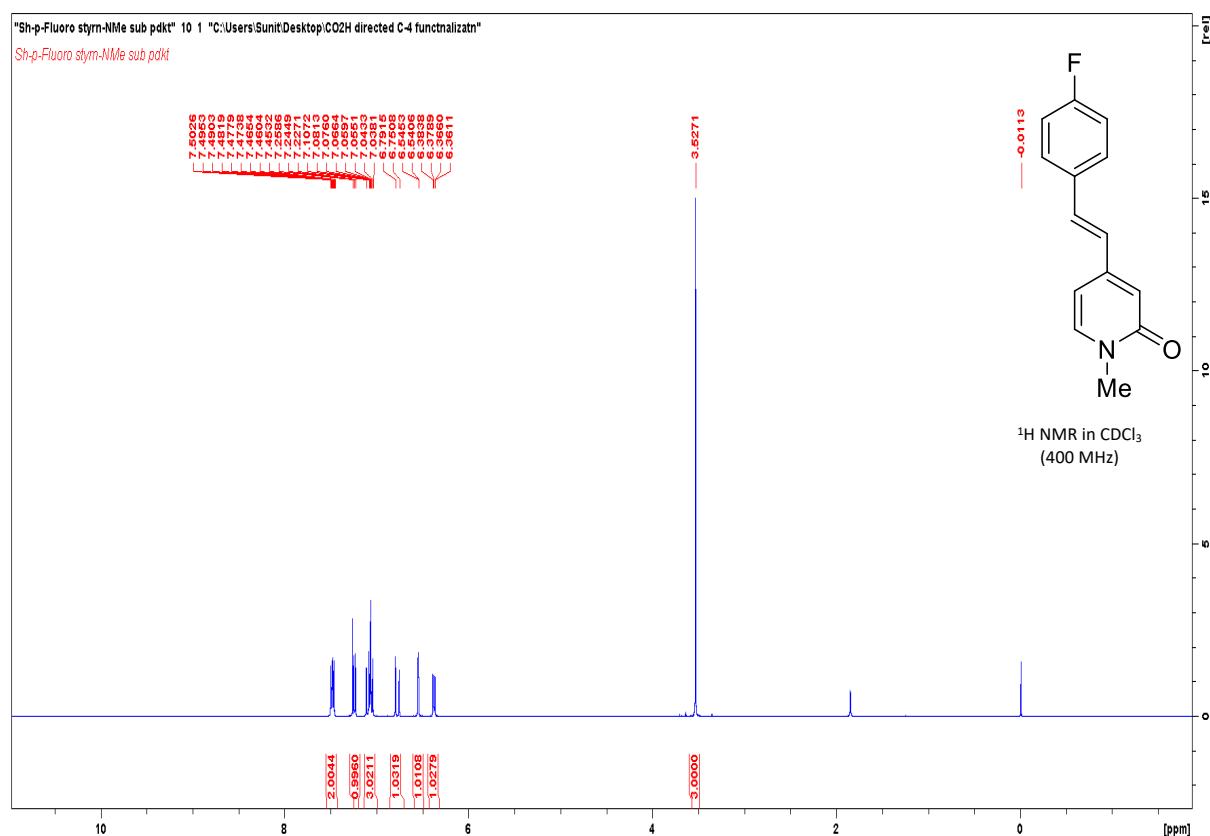
<sup>1</sup>H NMR of compound **3ag** in CDCl<sub>3</sub> (400 MHz)



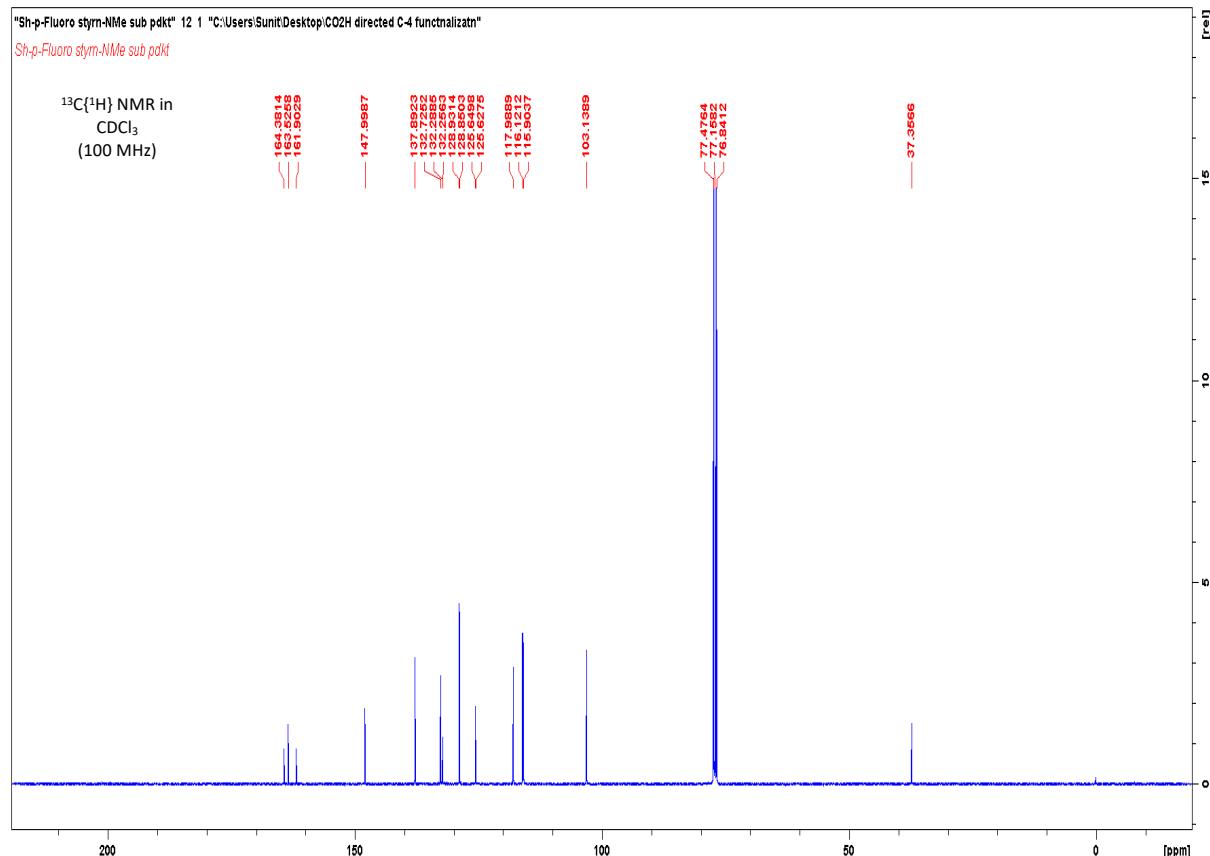
<sup>13</sup>C NMR of compound **3ag** in CDCl<sub>3</sub> (100 MHz)



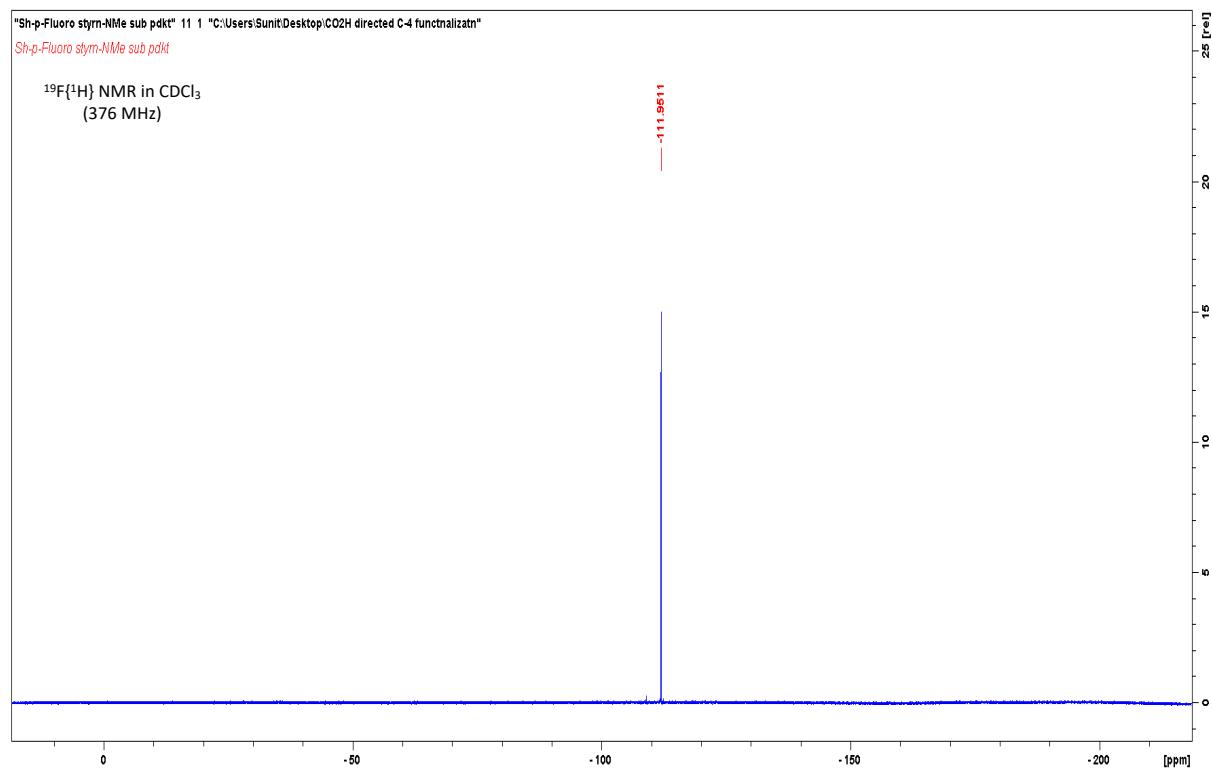
<sup>1</sup>H NMR of compound **3ah** in CDCl<sub>3</sub> (400 MHz)



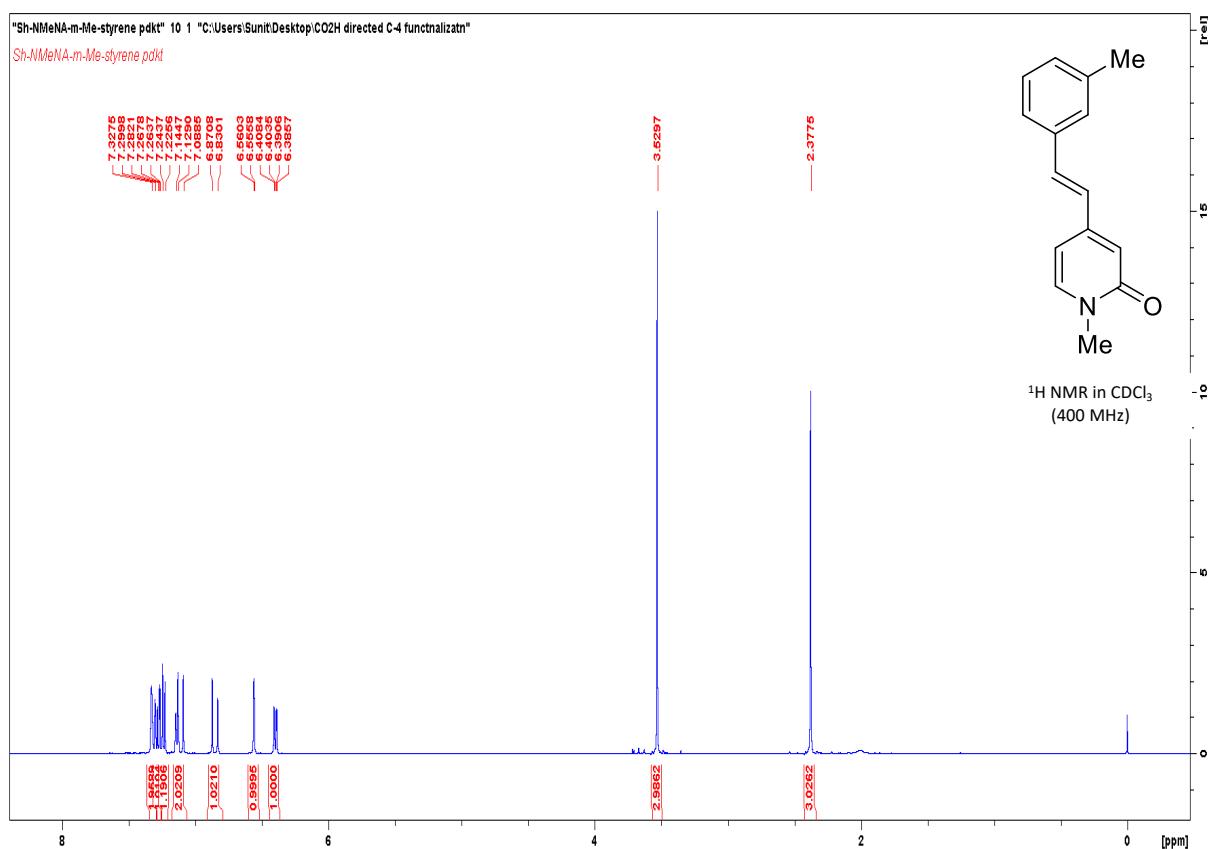
<sup>13</sup>C{<sup>1</sup>H} NMR of compound **3ah** in CDCl<sub>3</sub> (100 MHz)



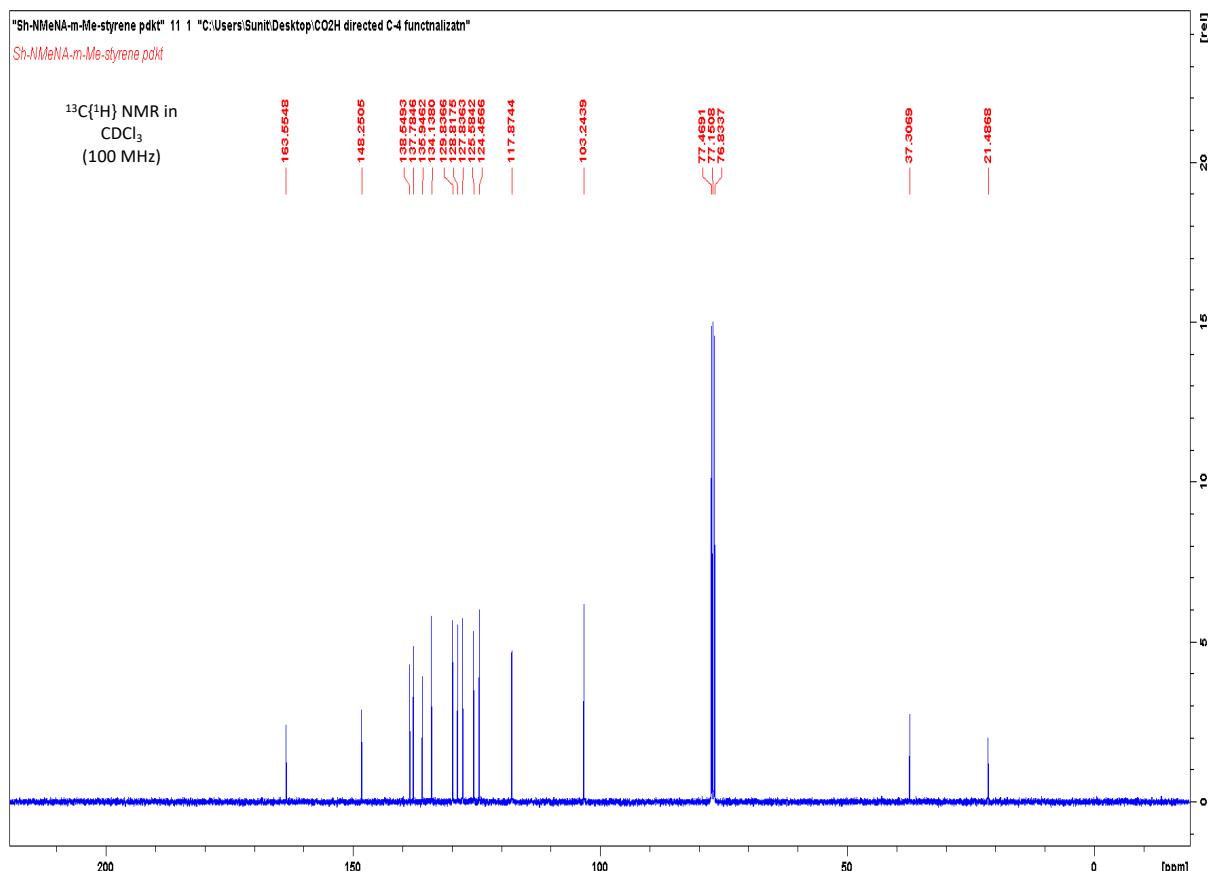
$^{19}\text{F}\{^1\text{H}\}$  NMR of compound **3ah** in  $\text{CDCl}_3$  (376 MHz)



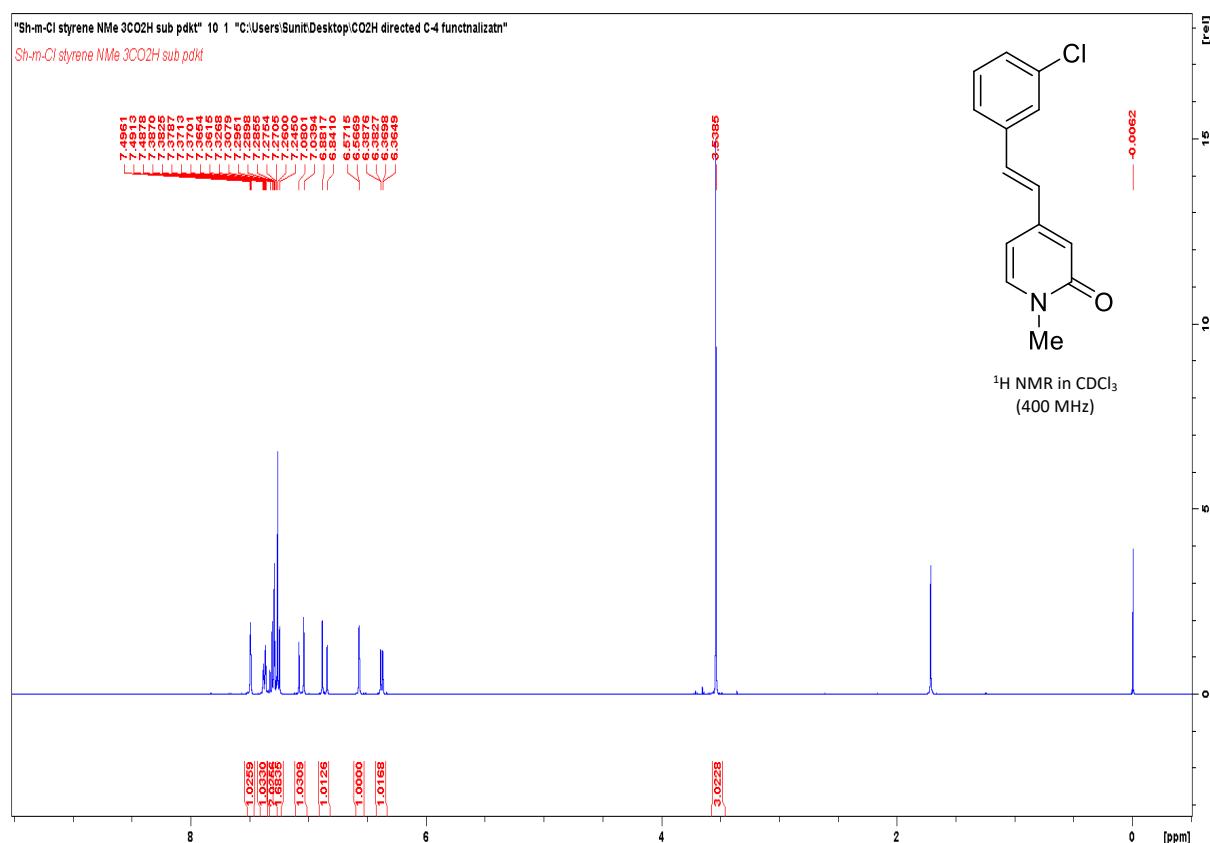
<sup>1</sup>H NMR of compound **3ai** in CDCl<sub>3</sub> (400 MHz)



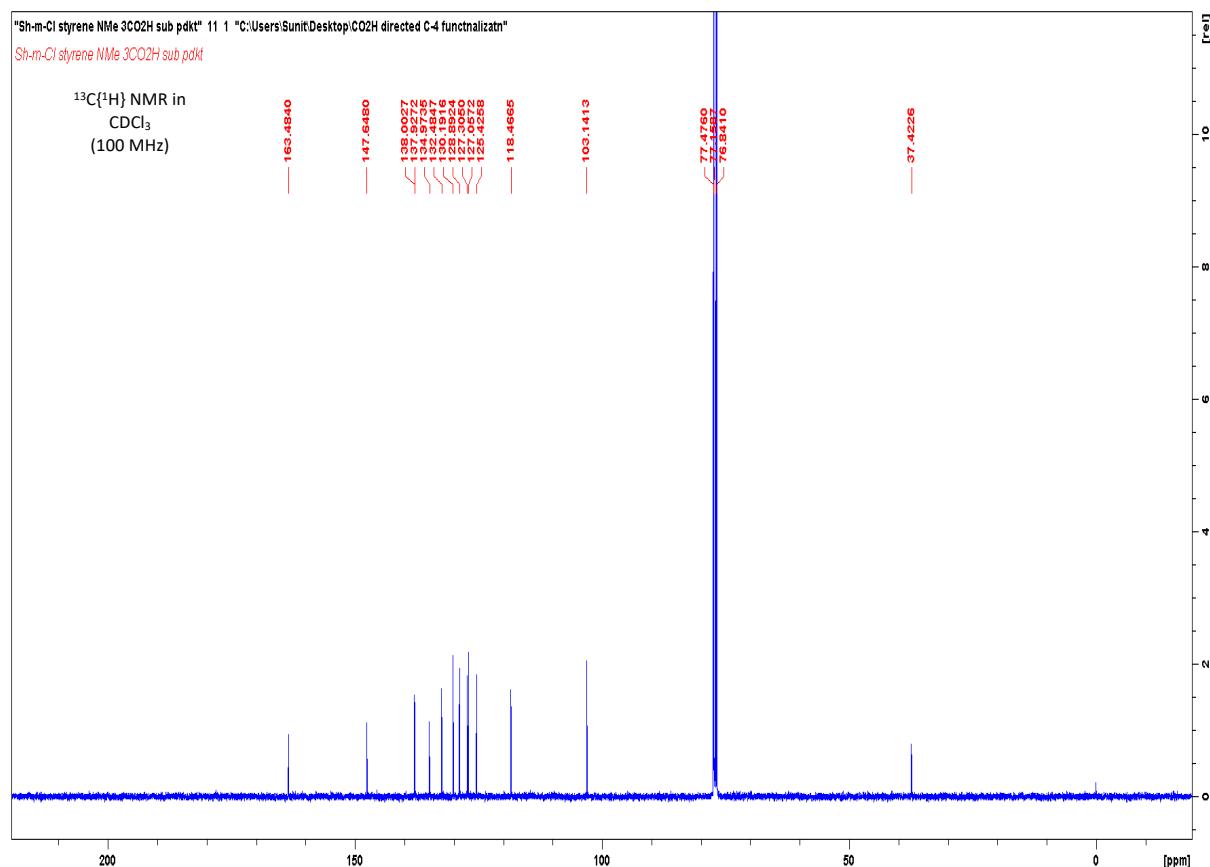
<sup>13</sup>C{<sup>1</sup>H} NMR of compound **3ai** in CDCl<sub>3</sub> (100 MHz)



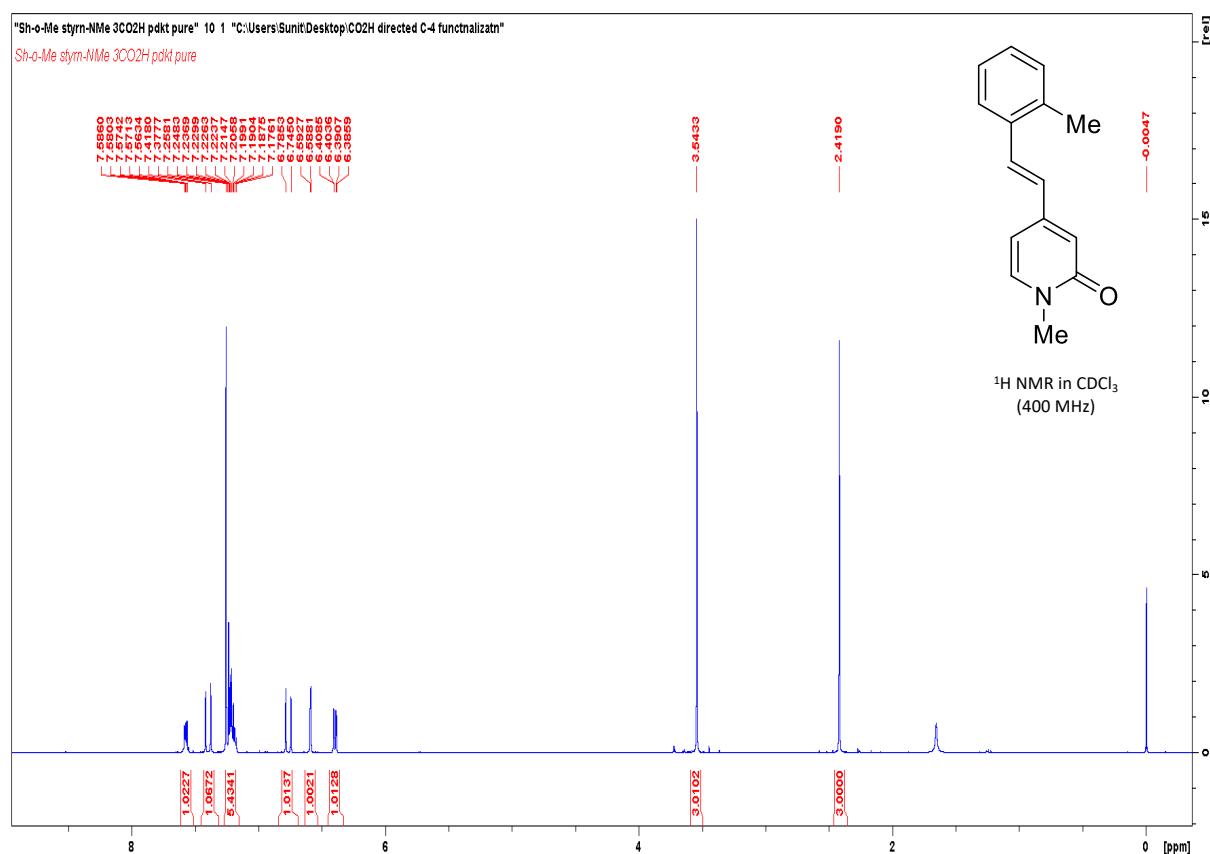
<sup>1</sup>H NMR of compound **3aj** in CDCl<sub>3</sub> (400 MHz)



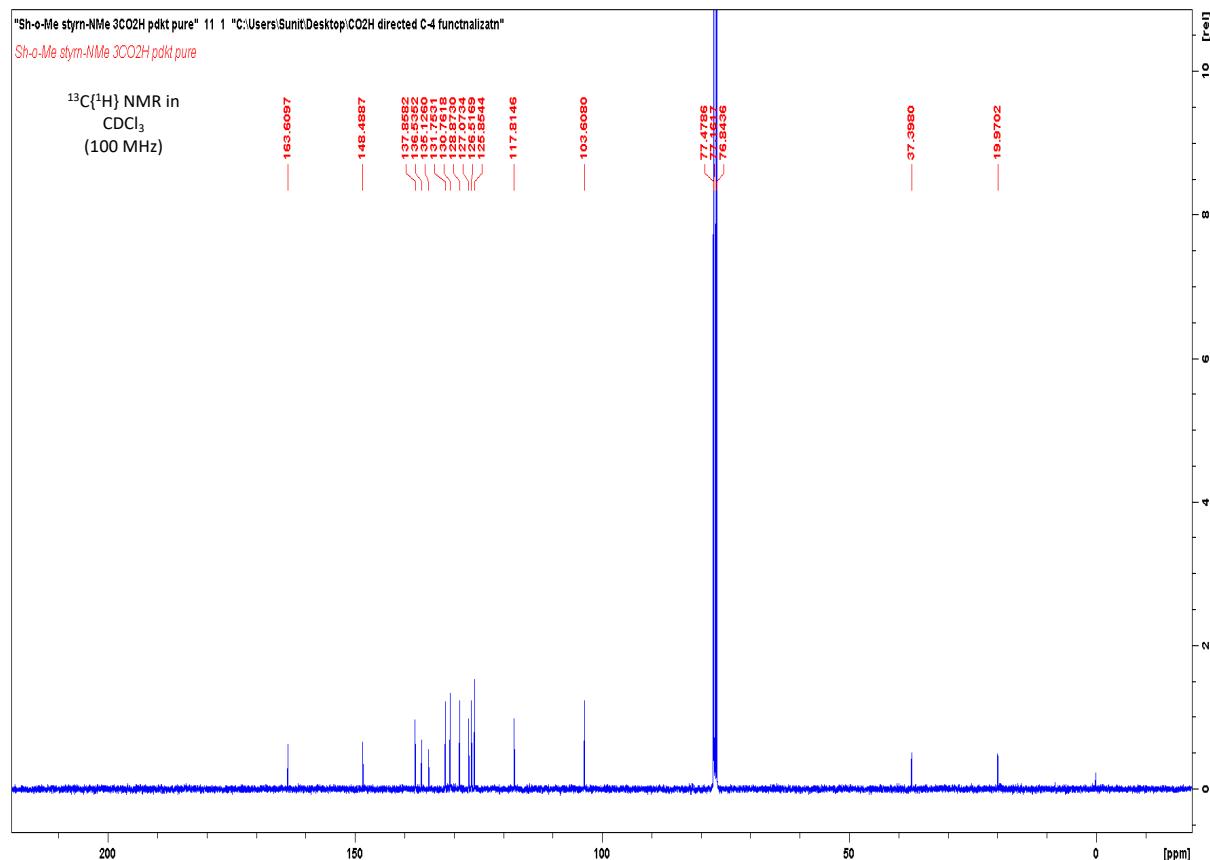
<sup>13</sup>C{<sup>1</sup>H} NMR of compound **3aj** in CDCl<sub>3</sub> (100 MHz)



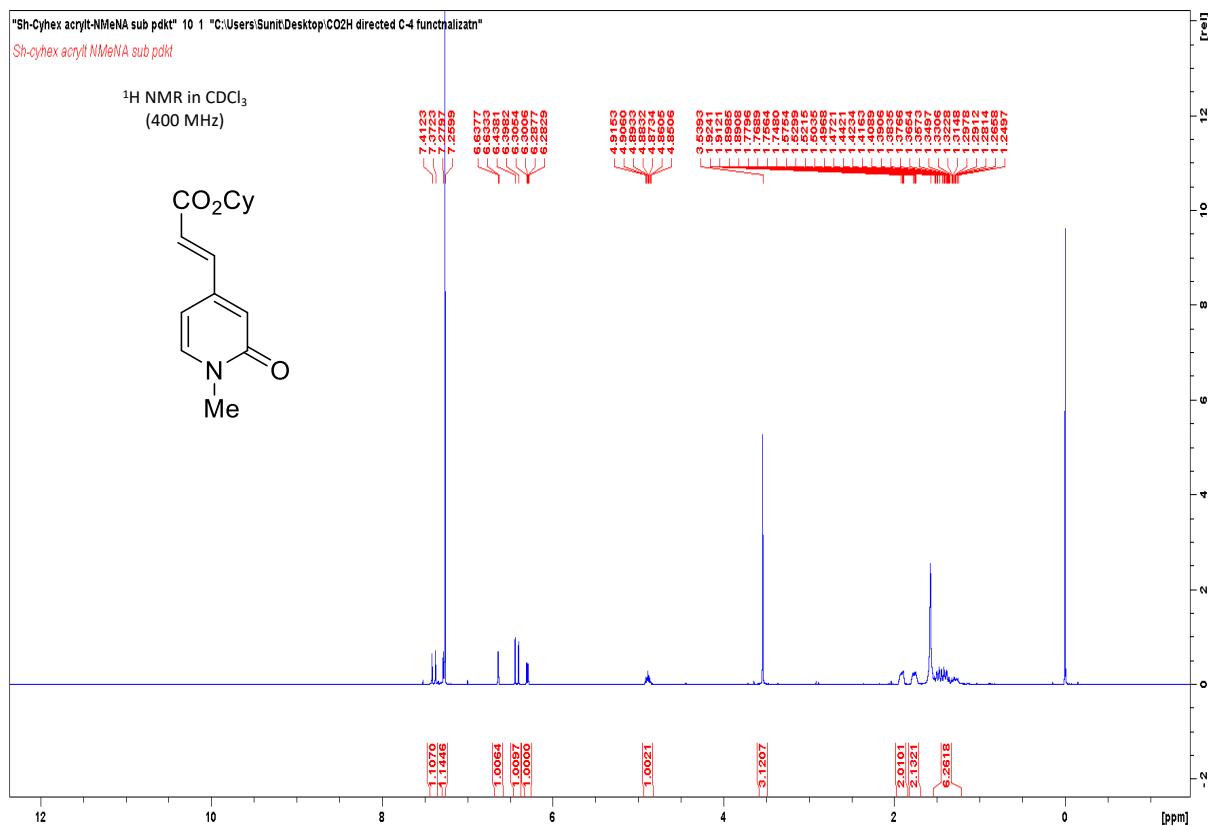
<sup>1</sup>H NMR of compound **3ak** in CDCl<sub>3</sub> (400 MHz)



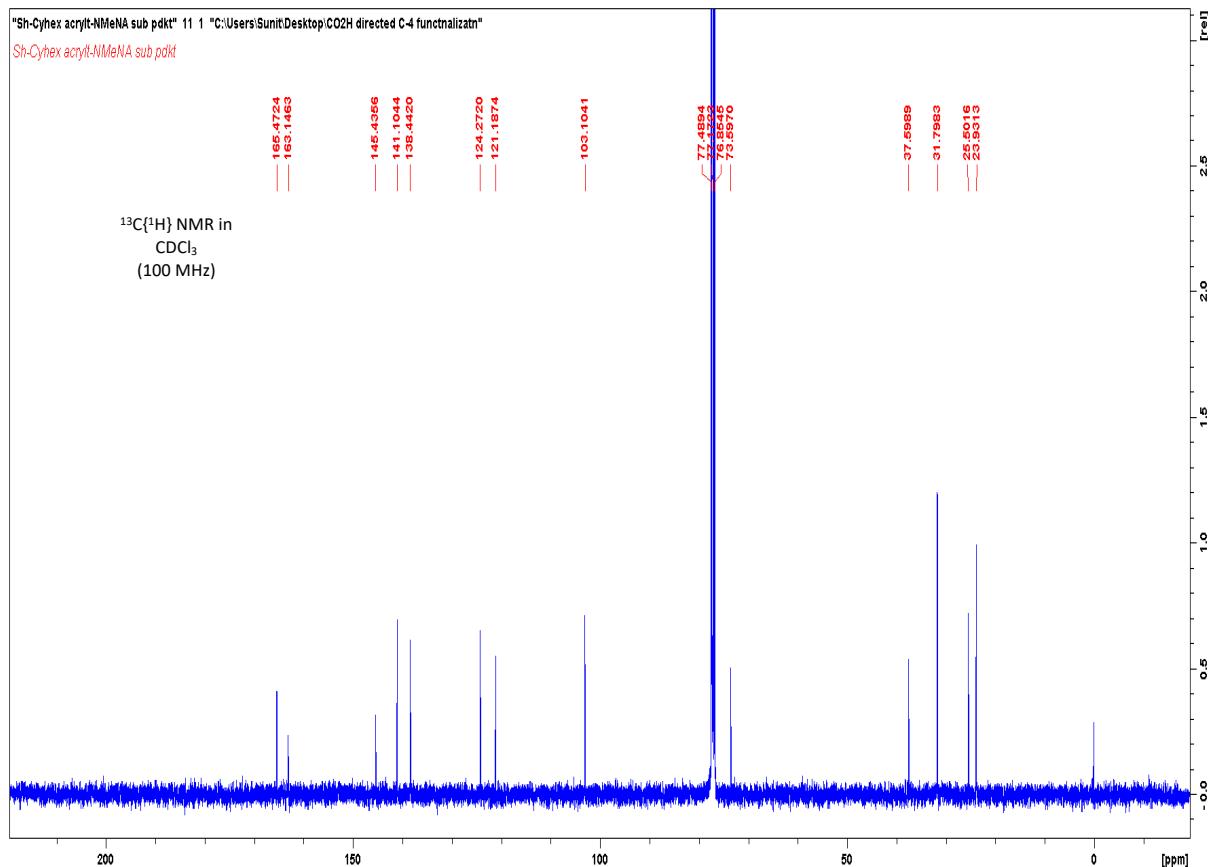
<sup>13</sup>C{<sup>1</sup>H} NMR of compound **3ak** in CDCl<sub>3</sub> (100 MHz)



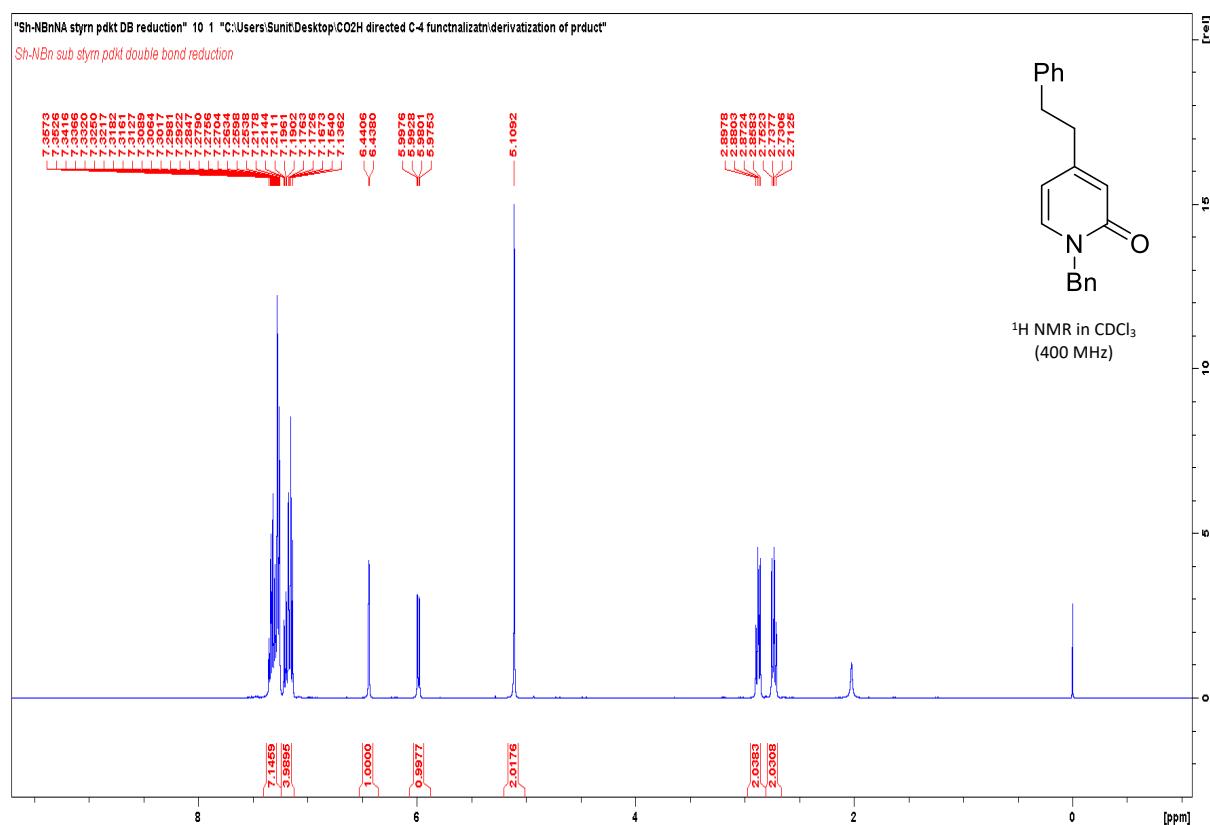
<sup>1</sup>H NMR of compound **3al** in CDCl<sub>3</sub> (400 MHz)



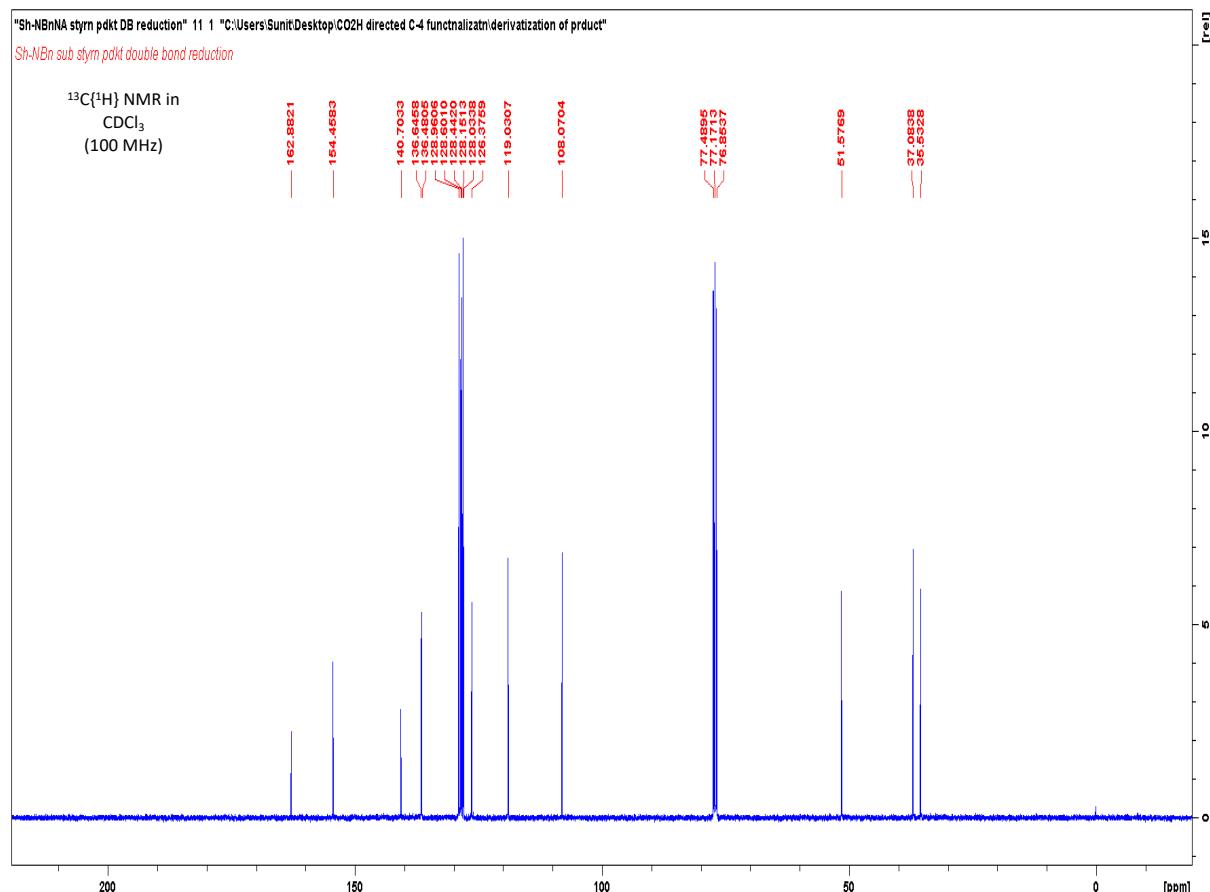
<sup>13</sup>C{<sup>1</sup>H} NMR of compound **3aI** in CDCl<sub>3</sub> (100 MHz)



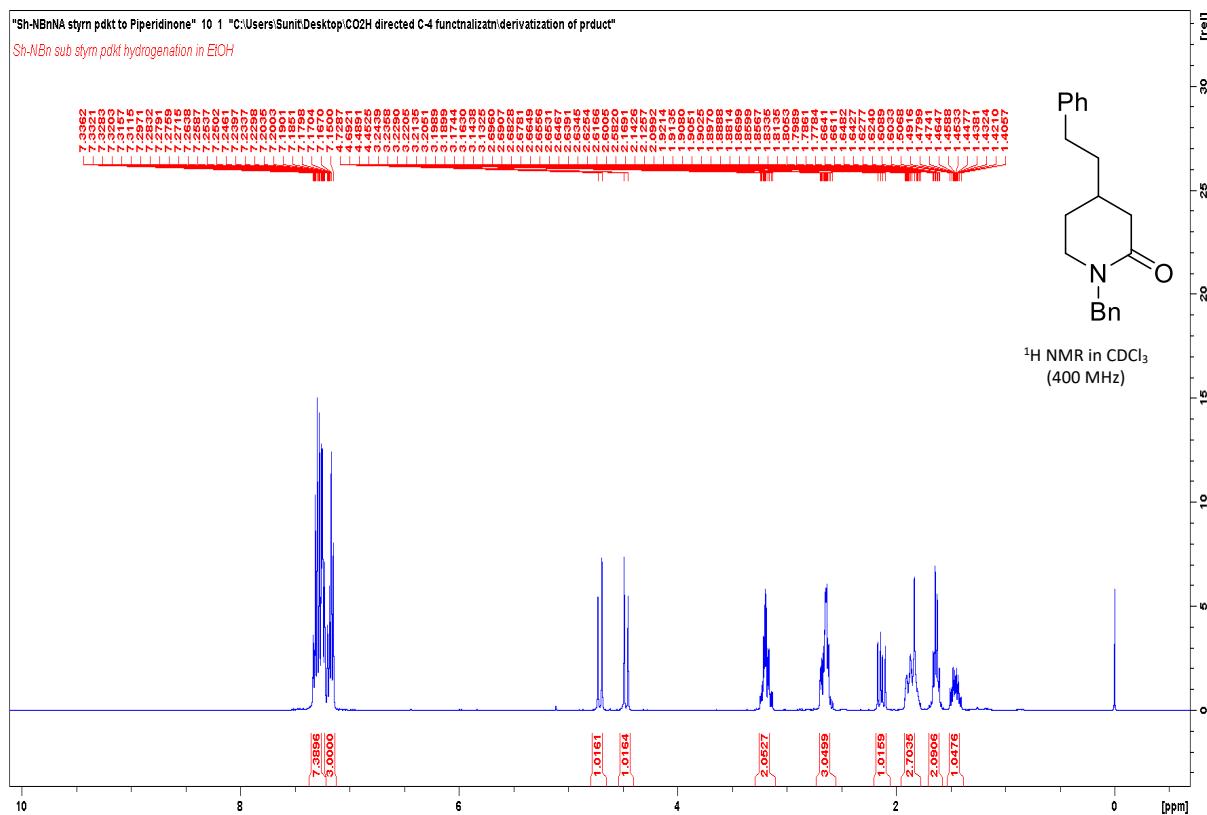
<sup>1</sup>H NMR of compound **4** in CDCl<sub>3</sub> (400 MHz)



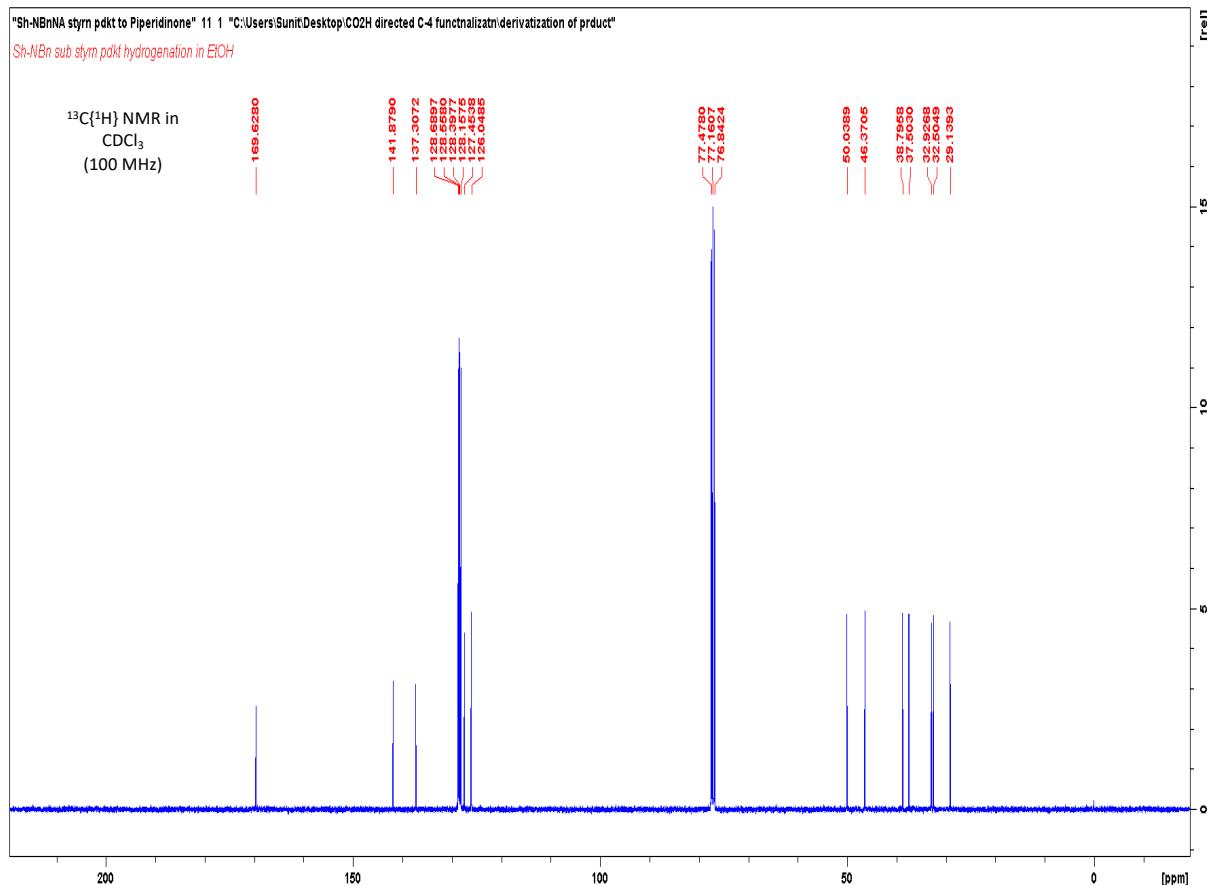
<sup>13</sup>C{<sup>1</sup>H} NMR of compound **4** in CDCl<sub>3</sub> (100 MHz)



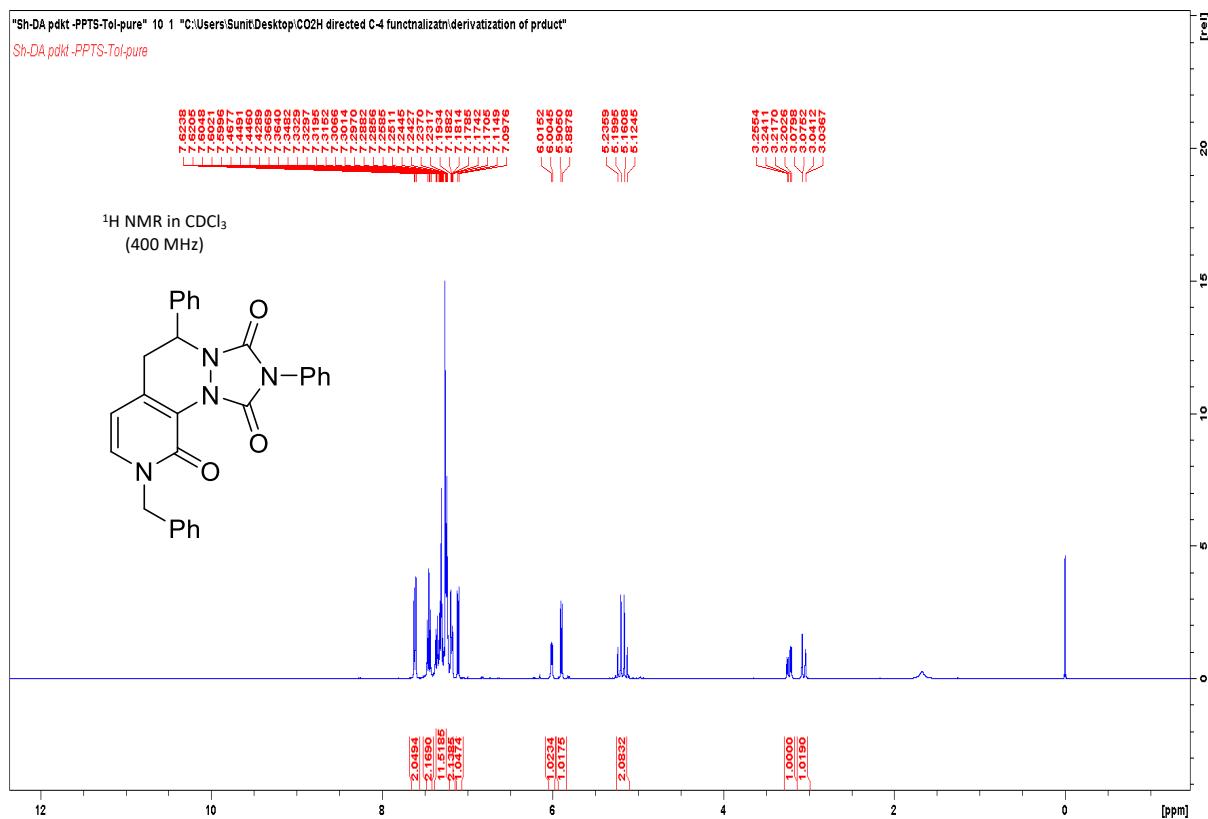
<sup>1</sup>H NMR of compound 5 in CDCl<sub>3</sub> (400 MHz)



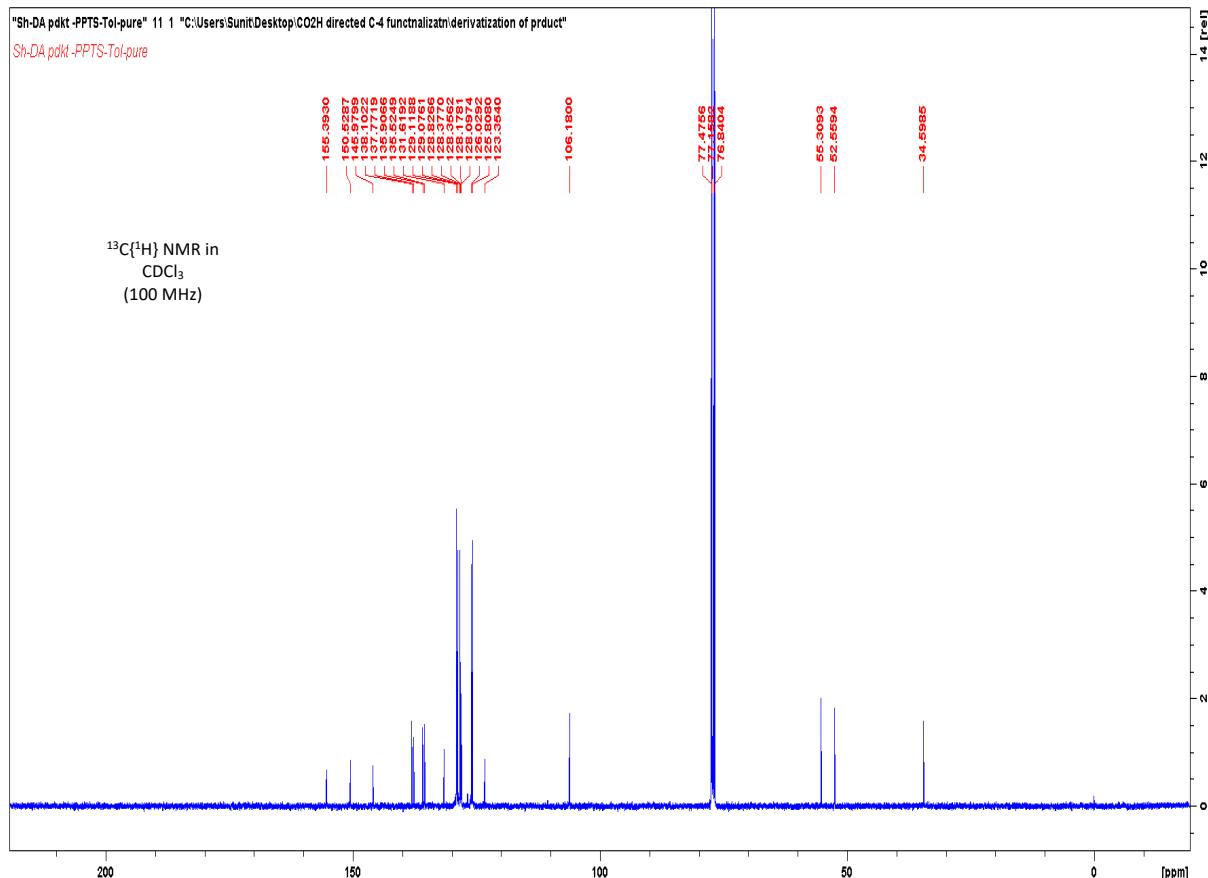
<sup>13</sup>C{<sup>1</sup>H} NMR of compound **5** in CDCl<sub>3</sub> (100 MHz)



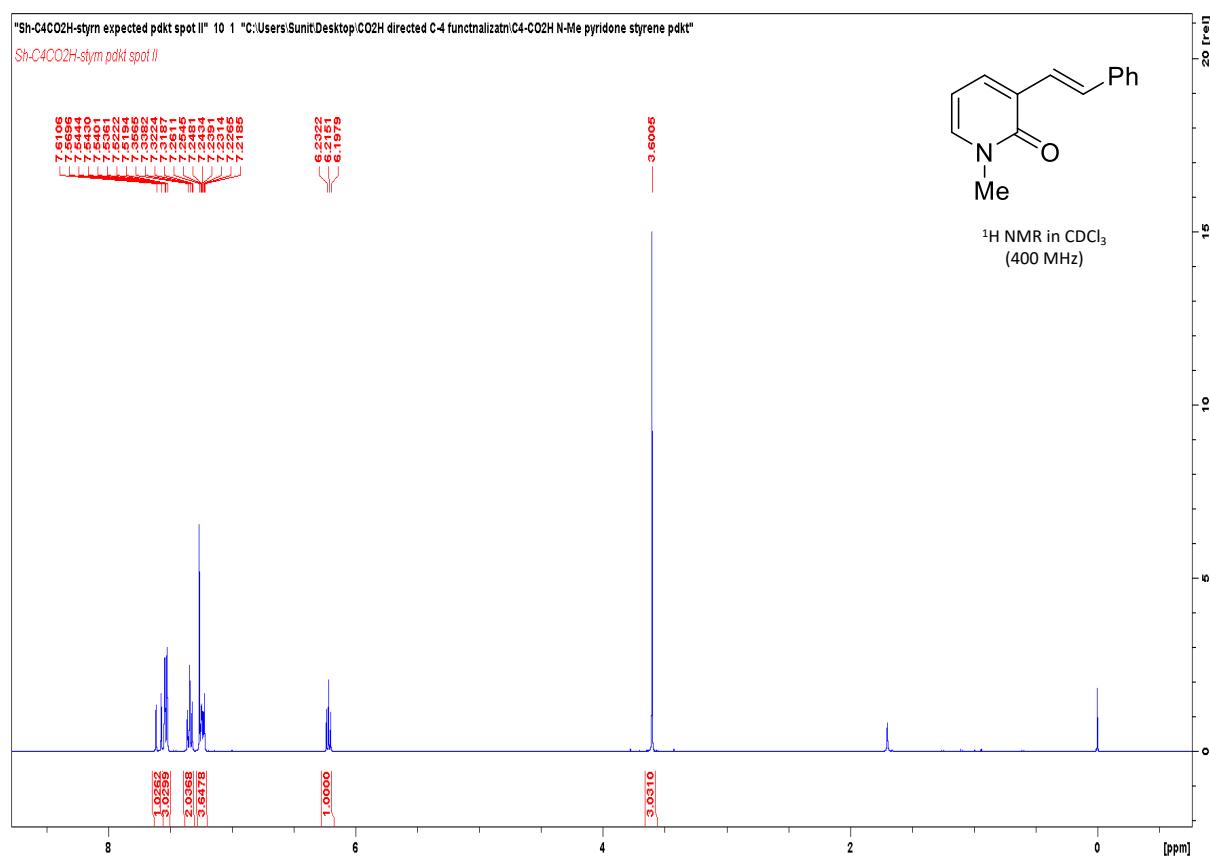
<sup>1</sup>H NMR of compound **6** in CDCl<sub>3</sub> (400 MHz)



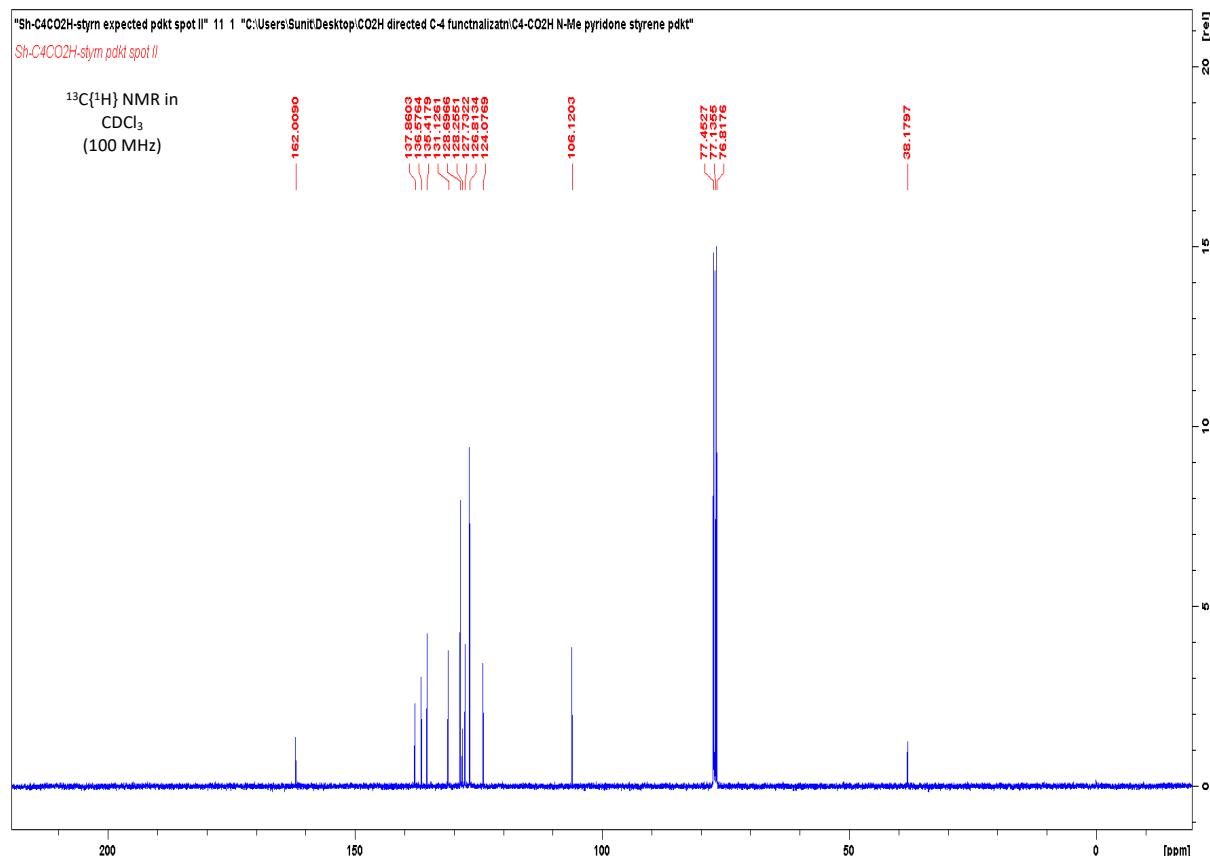
<sup>13</sup>C{<sup>1</sup>H} NMR of compound **6** in CDCl<sub>3</sub> (100 MHz)



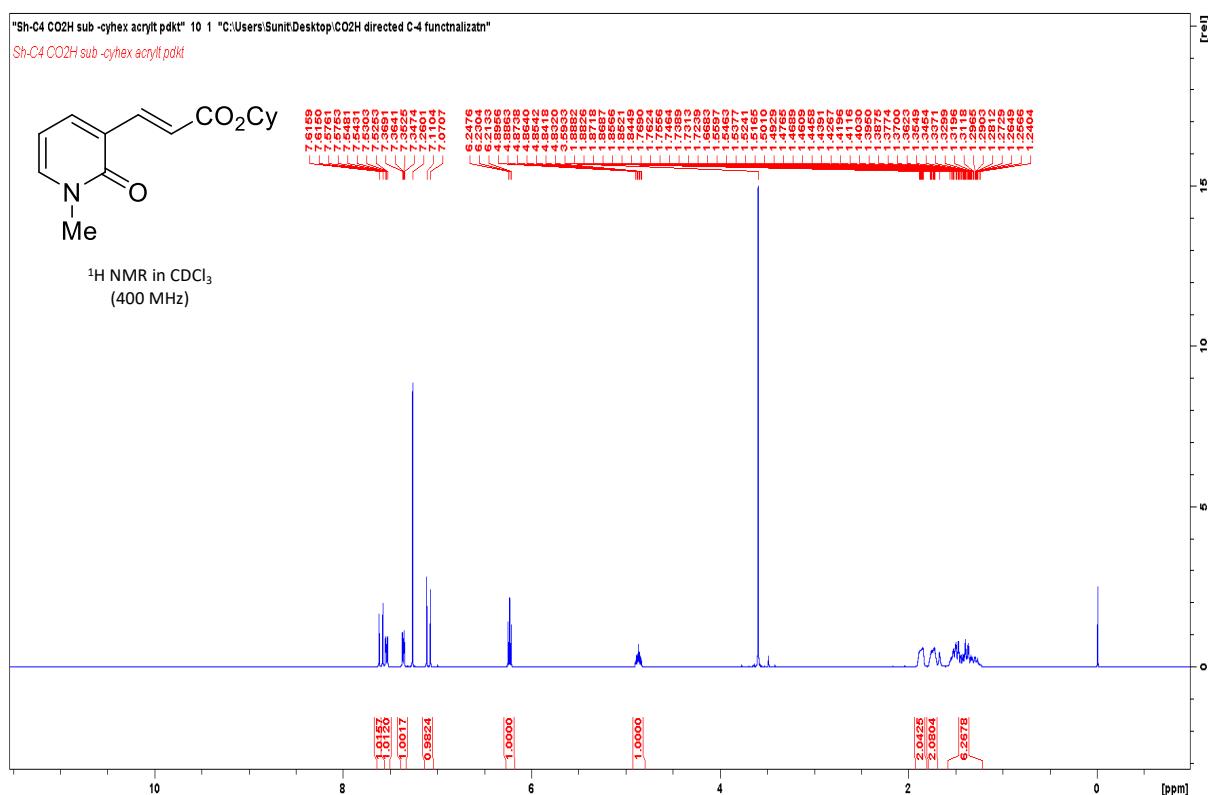
<sup>1</sup>H NMR of compound **8aa** in CDCl<sub>3</sub> (400 MHz)



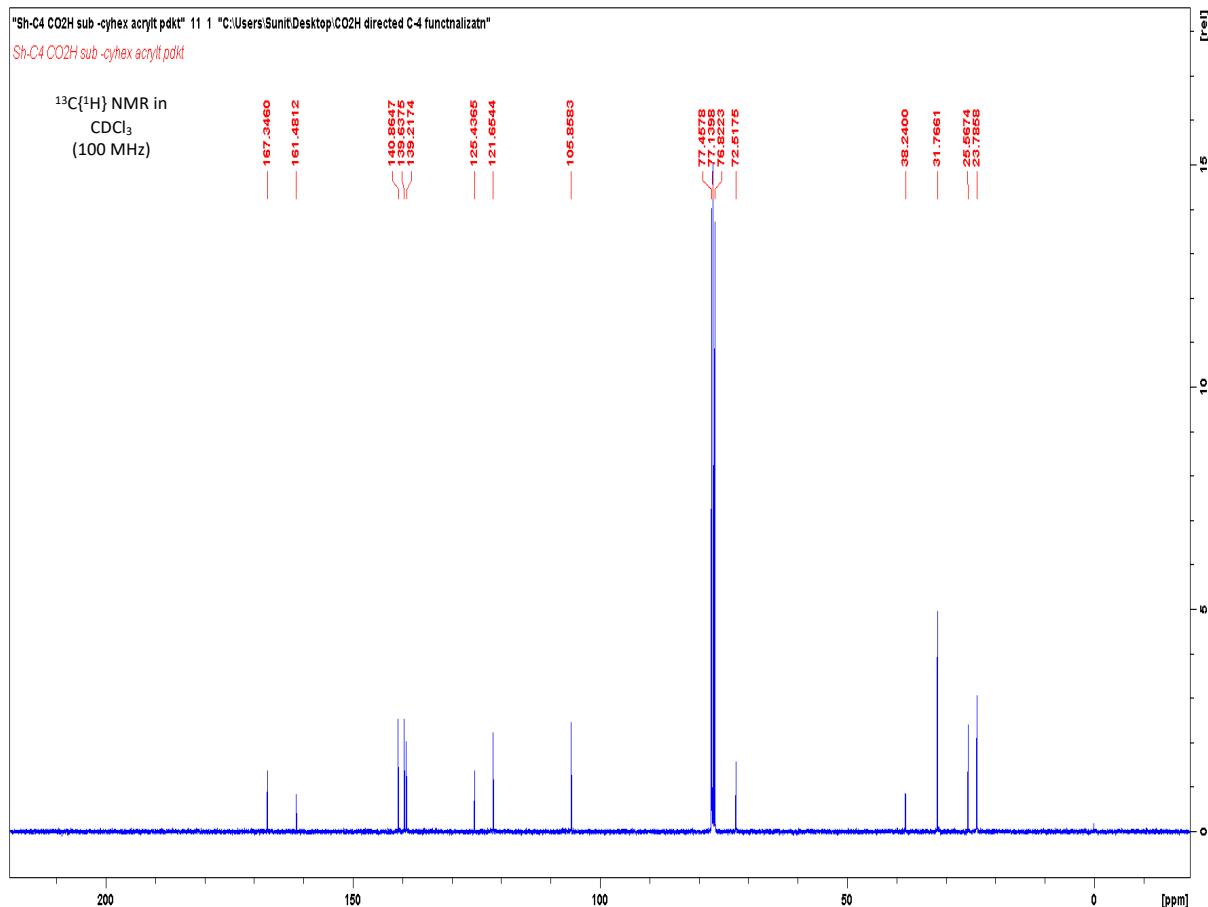
<sup>13</sup>C{<sup>1</sup>H} NMR of compound **8aa** in CDCl<sub>3</sub> (100 MHz)



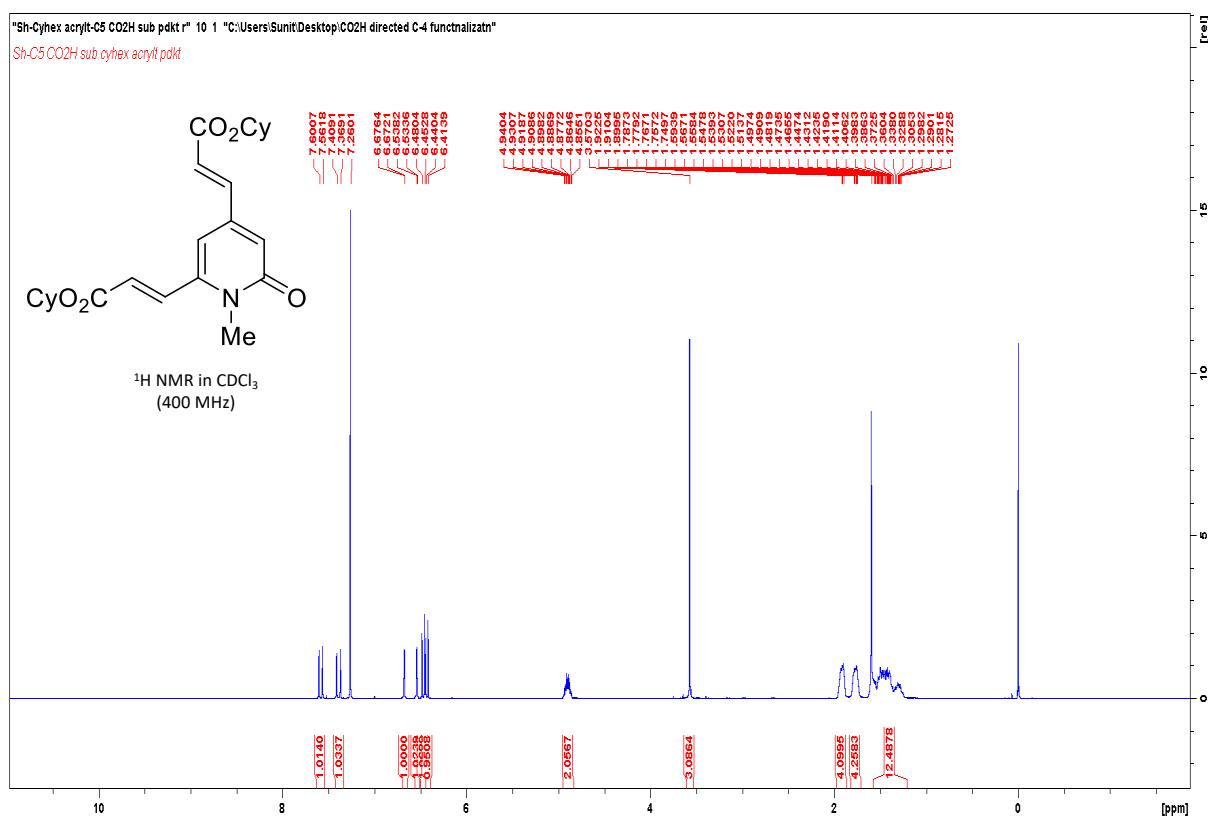
<sup>1</sup>H NMR of compound **8al** in CDCl<sub>3</sub> (400 MHz)



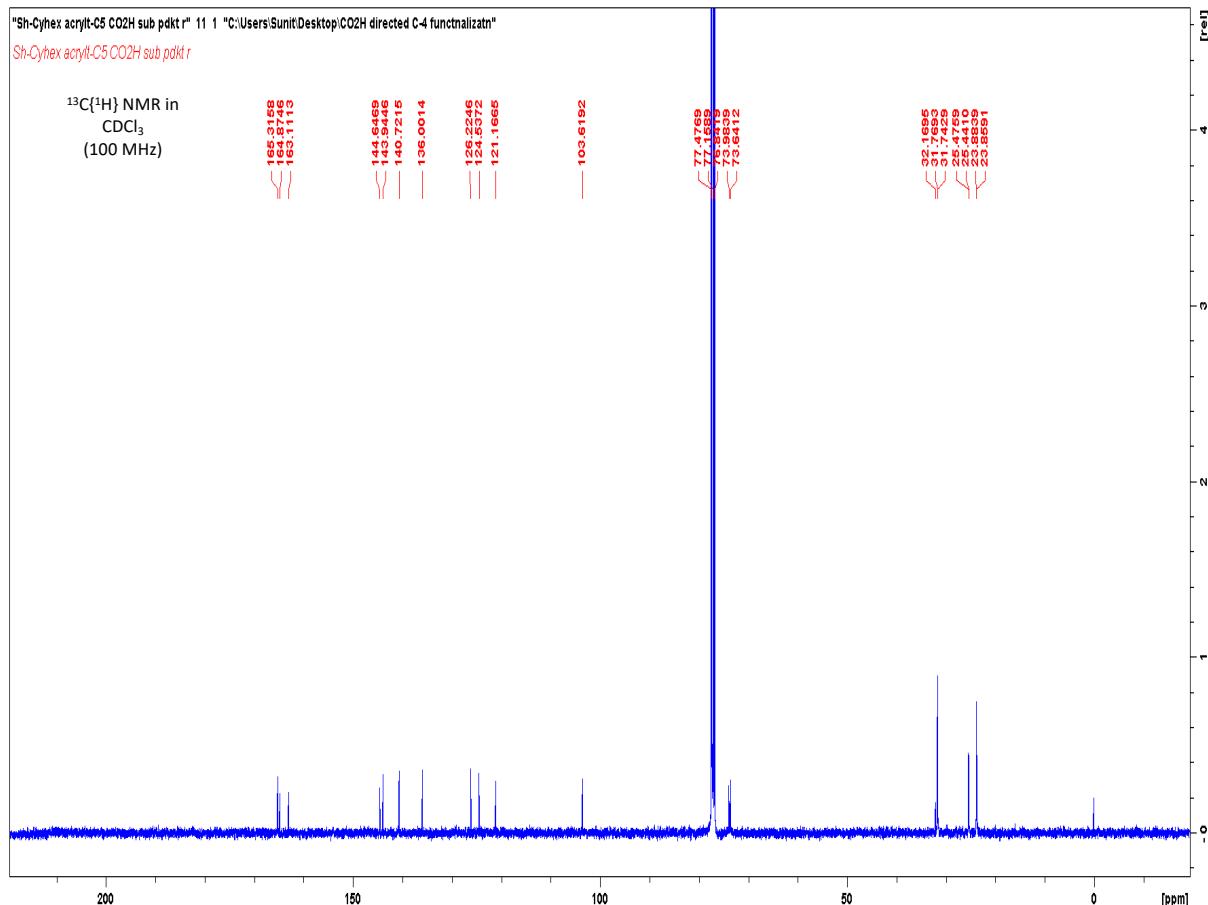
$^{13}\text{C}\{^1\text{H}\}$  NMR of compound **8aI** in  $\text{CDCl}_3$  (100 MHz)



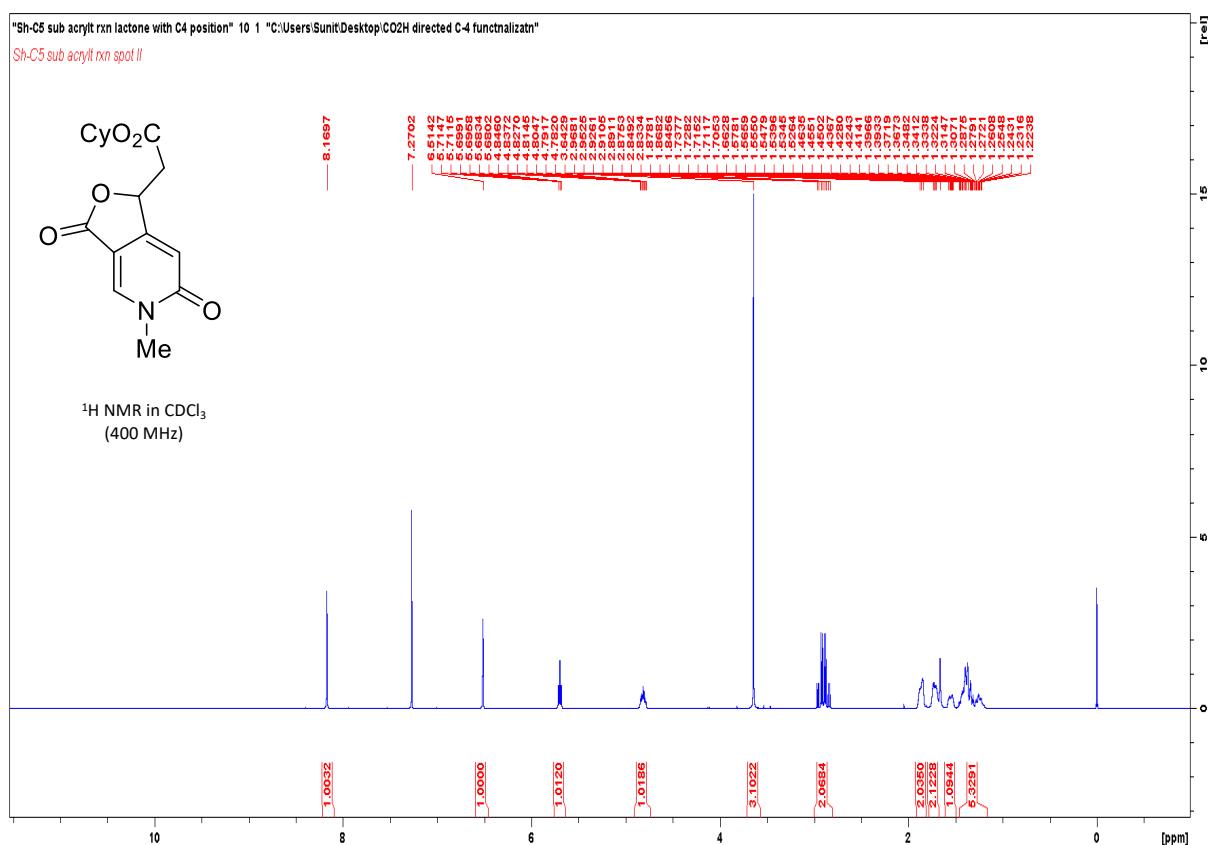
<sup>1</sup>H NMR of compound **10al** in CDCl<sub>3</sub> (400 MHz)



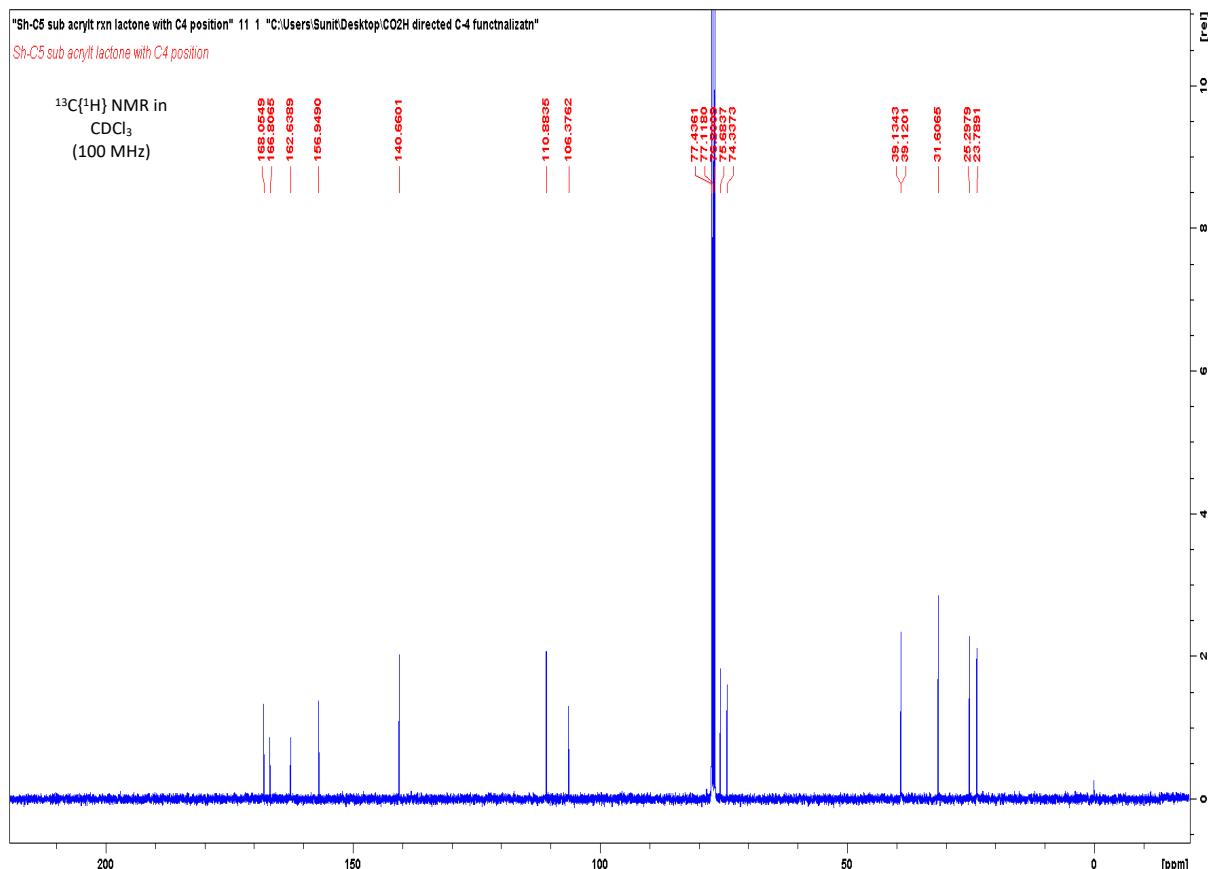
<sup>13</sup>C{<sup>1</sup>H} NMR of compound **10al** in CDCl<sub>3</sub> (100 MHz)



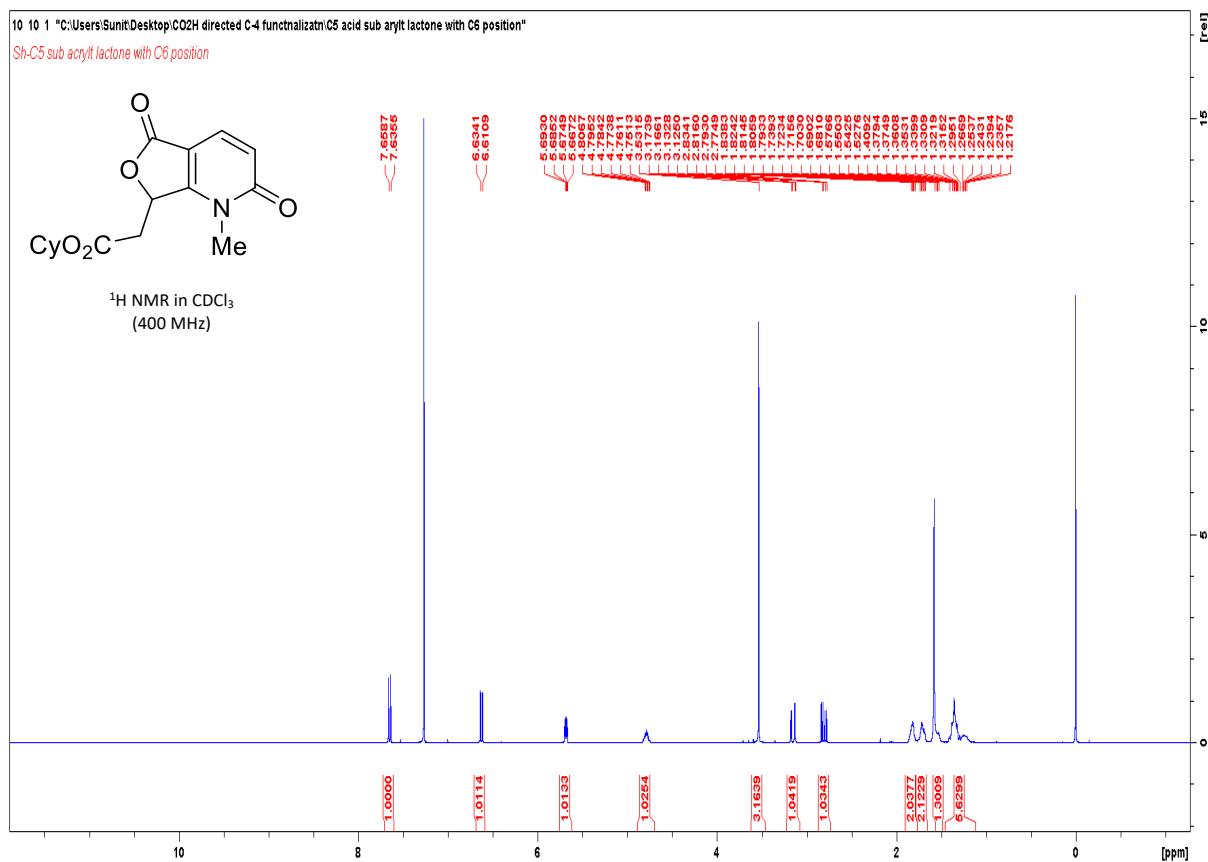
<sup>1</sup>H NMR of compound **11al** in CDCl<sub>3</sub> (400 MHz)



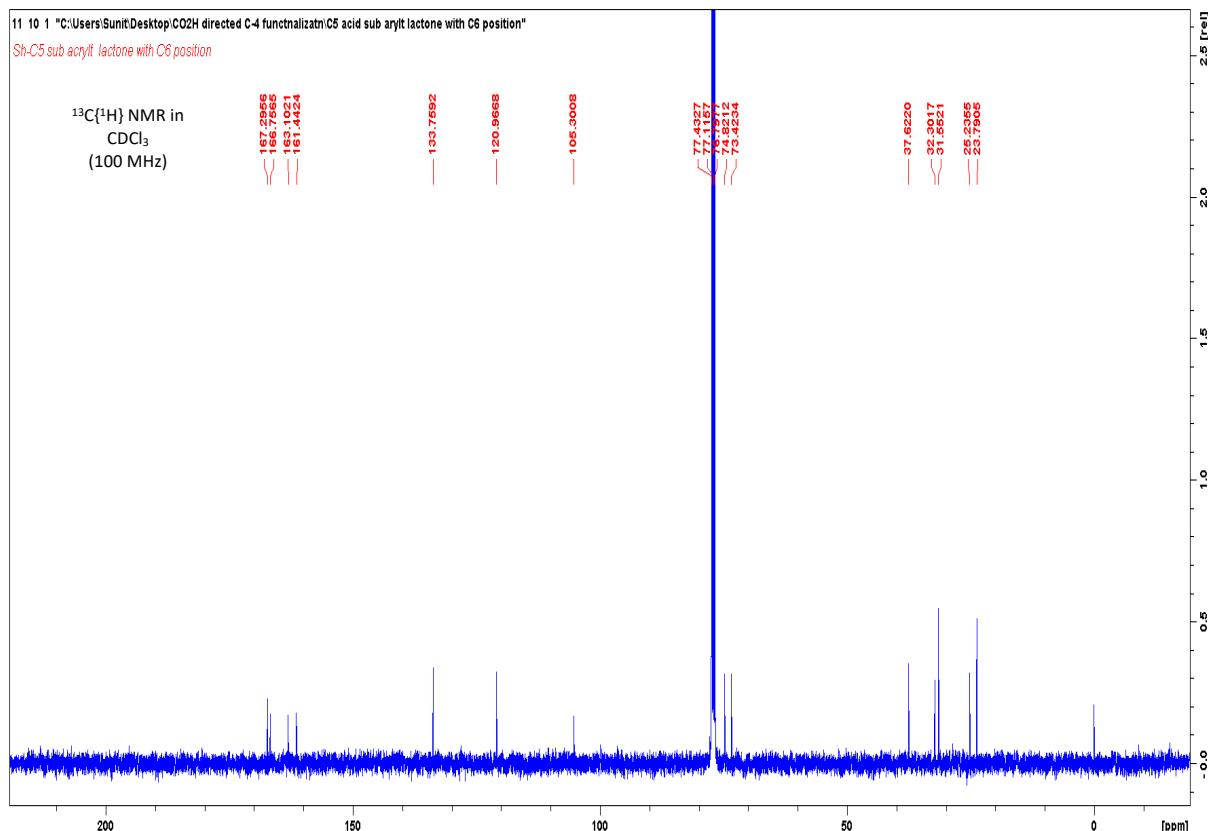
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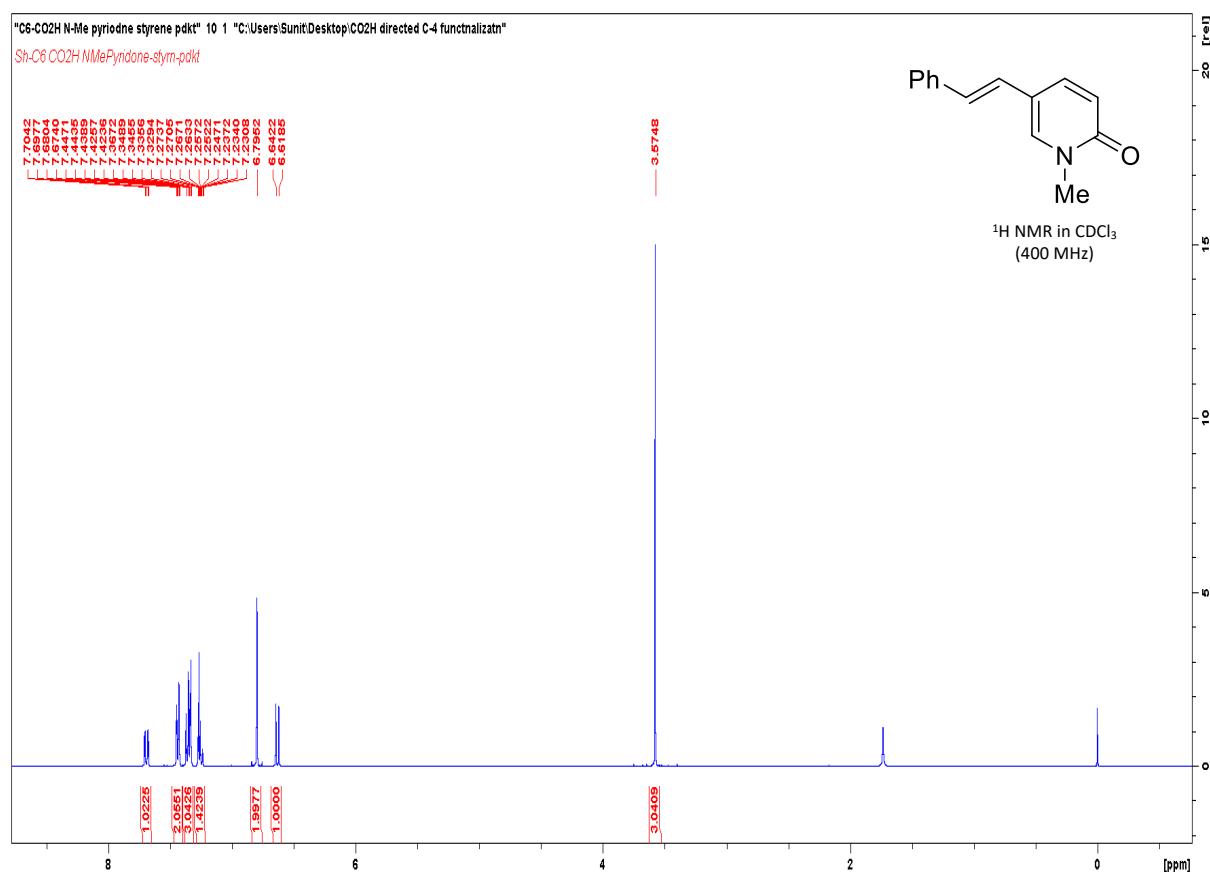
<sup>1</sup>H NMR of compound **12al** in CDCl<sub>3</sub> (400 MHz)



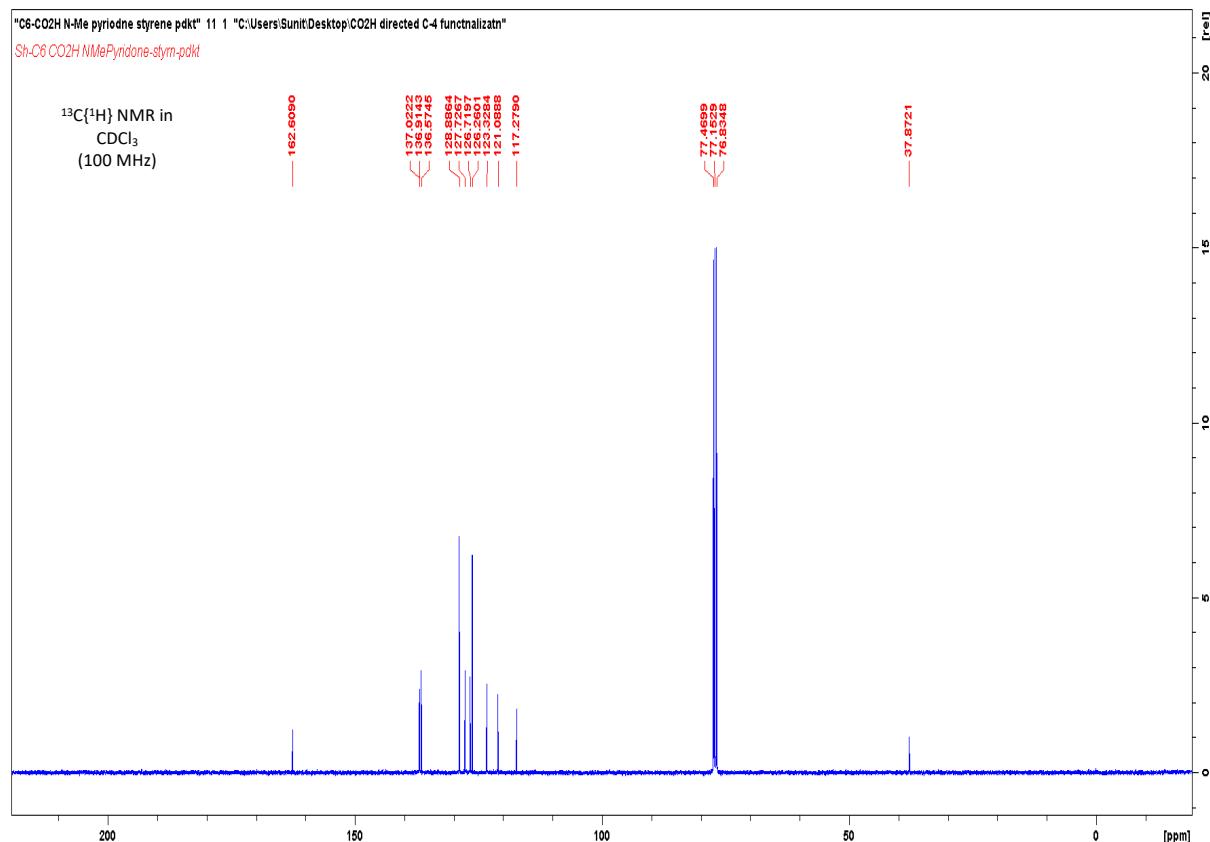
<sup>13</sup>C{<sup>1</sup>H} NMR of compound **12al** in CDCl<sub>3</sub> (100 MHz)



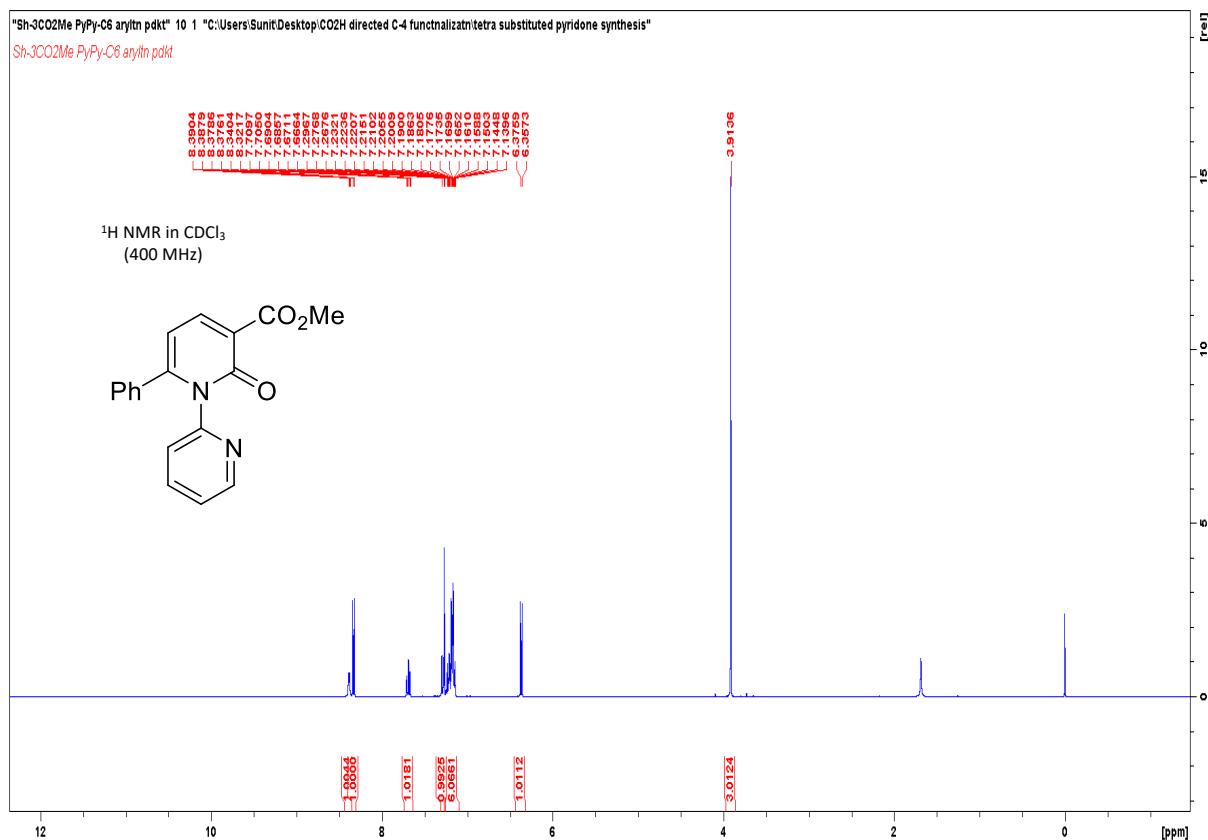
<sup>1</sup>H NMR of compound **14aa** in CDCl<sub>3</sub> (400 MHz)



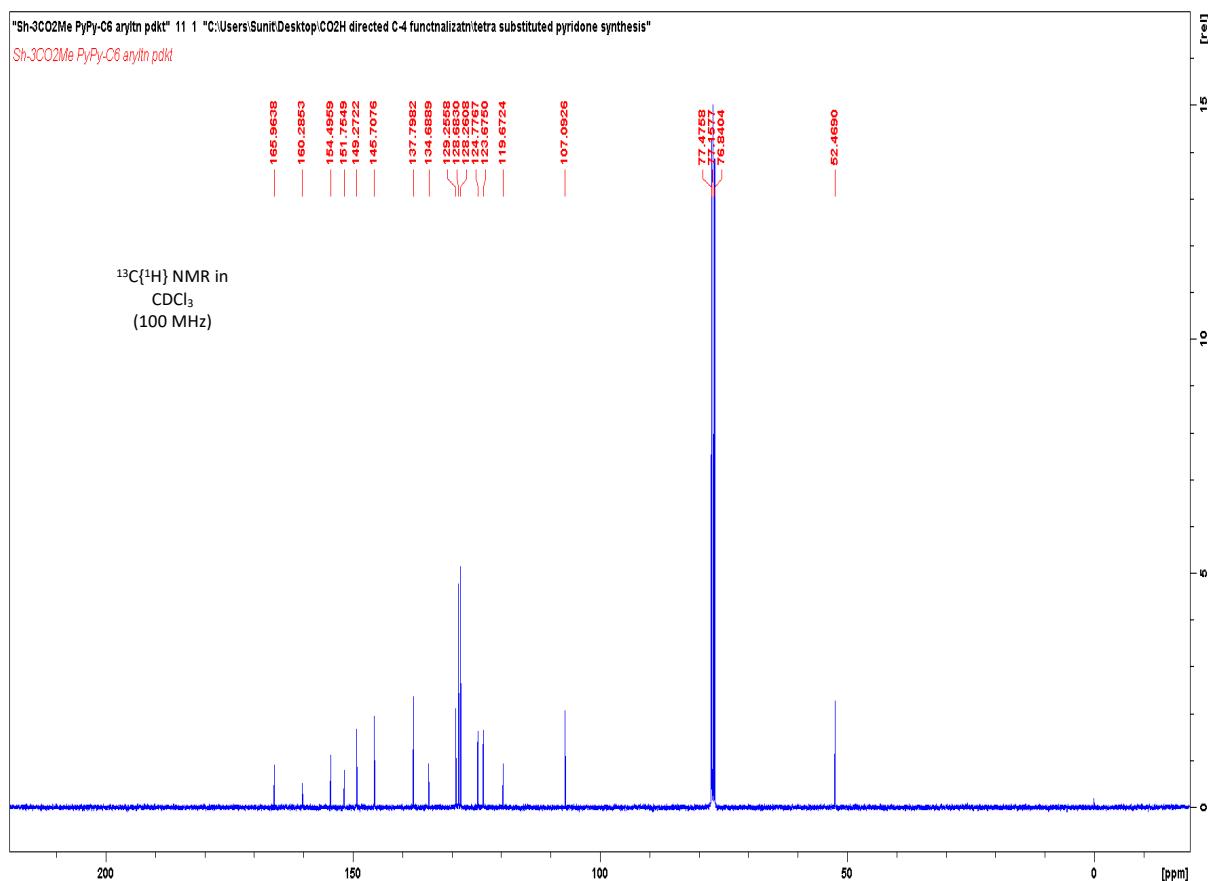
<sup>13</sup>C{<sup>1</sup>H} NMR of compound **14aa** in CDCl<sub>3</sub> (100 MHz)



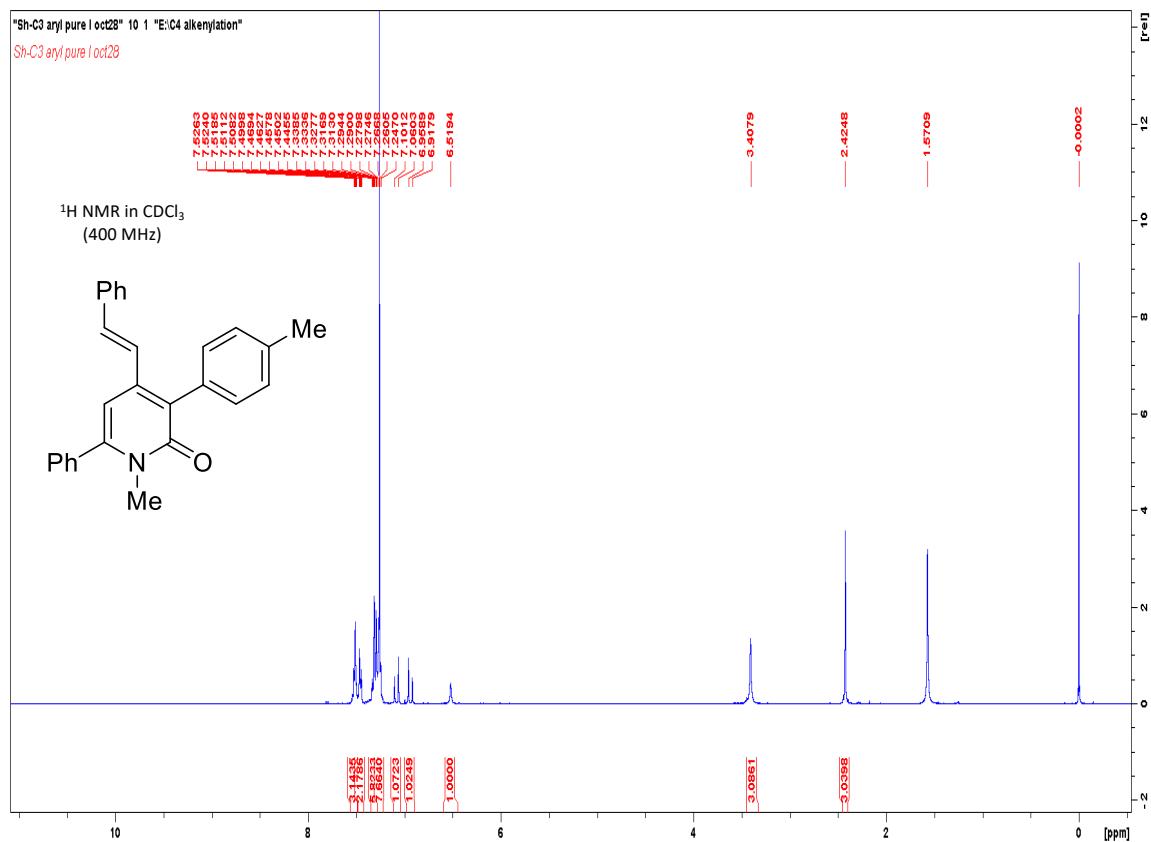
<sup>1</sup>H NMR of compound **16** in CDCl<sub>3</sub> (400 MHz)



<sup>13</sup>C{<sup>1</sup>H} NMR of compound **16** in CDCl<sub>3</sub> (100 MHz)



<sup>1</sup>H NMR of compound **17** in CDCl<sub>3</sub> (400 MHz)



<sup>13</sup>C{<sup>1</sup>H} NMR of compound **17** in CDCl<sub>3</sub> (100 MHz)

