Supporting Information

Flavin Nitroalkane Oxidase Mimics Compatibility with NOx/TEMPO Catalysis: Aerobic Oxidization of Alcohols, Diols, and Ethers

Pawan Thapa, Shan Hazoor, Bikash Chouhan, Thanh Thuy Vuong, and Frank W. Foss Jr.*

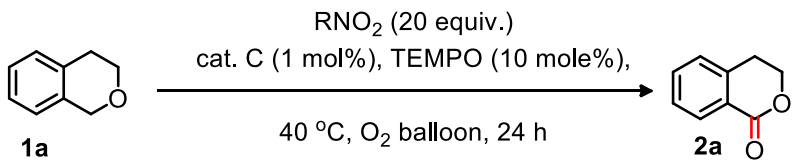
Department of Chemistry and Biochemistry

University of Texas at Arlington, Arlington, TX, 76019

*ffoss@uta.edu

Table of Contents:

A. Table S1: Optimization studies with Nitroalkane source[a]



Entry	Nitroalkane	Isolated yield
1	$MeNO_2$	94, 91[b]
2	$PhCH_2NO_2$	85
3	$MeCH_2NO_2$	42
4	$MeCH_2CH_2NO_2$	4
5	$(Me)_2CHNO_2$	9
6	CD_3NO_2	92, 5[b]

[a]Reaction conditions: **1a** (0.1 mmol), RNO_2 (20 equiv.), Catalyst C (1 mol%), TEMPO (10 mol%), 40 °C, O_2 balloon, 24 hours. [b]4-hour reaction.

B. General Procedure for measuring Kinetic Isotopic Effect:

0.6 mmol of each substrate **1a** and **1a-D$_2$** were added in two separate 1.5-dram vial. Each vial was added with a stir-bar and 0.6 mL of $MeNO_2$ at room temperature. The solution in each vial was divided equally into two 1.5-dram vial.

To get the NMR conversion, 25.0 µL of aliquot was taken from each vial at different time scale. Time t0 refers to solution before heating. Time t10, time t20, time t30, time t45, time t60, and time t75 refer to 10-minute, 20-minute, 30-minute, 45-minute, 60-minute, and 75-minute respectively. Each NMR sample was prepared by adding 25.0 µL aliquot with 0.6 mL of stock solution of $CDCl_3$ containing internal standard DMSO. The % NMR conversion for each aliquot was measured comparing integration value of peak at 2.8 ppm against internal standard peak at 2.5 ppm of DMSO.

A plot of % NMR conversion of starting material vs time was drawn which is as shown below:

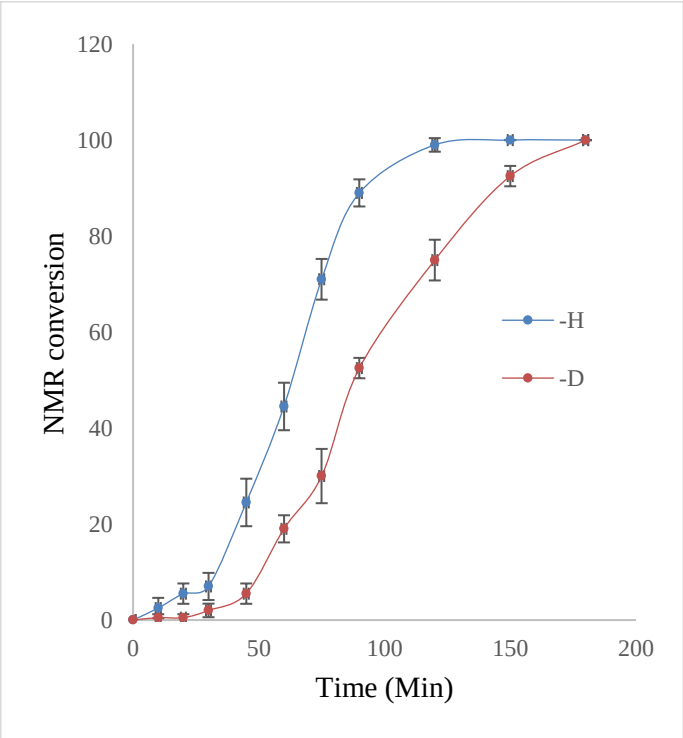


Figure S1: time(min) vs %NMR conversion plot for deuterated and non-deuterated isochroman substrate until full conversion

Time t0, t10, t20 and t30 data were selected for studying initial rate. KIE value was found from the ratio of slope of line 1 (H) to slope of line 2 (D). The plot for initial rate and slope for each line is shown below:

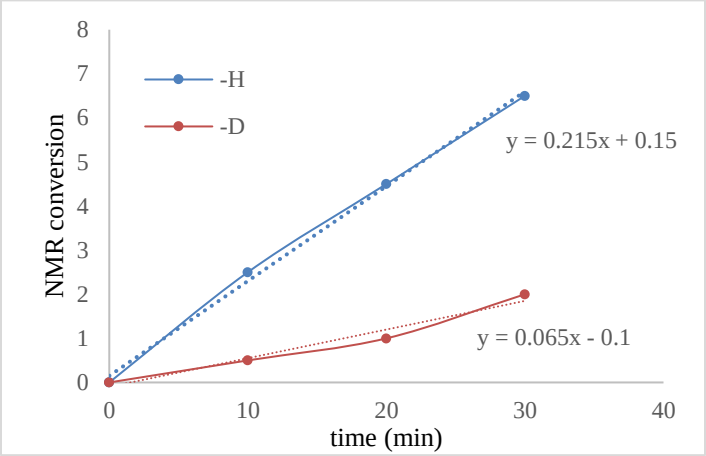


Figure S2: time(min) vs %NMR yield plot for deuterated and non-deuterated isochroman substrate until 30-minute reaction time

C. General Procedure for preparing samples for ion chromatography:

Flavin catalyst (1 mol%) and/or TEMPO (10 mol%) and/or isochroman (0.2 mmol) were added in an oven dried 2.0-dram vial fitted with septum and magnetic stirbar. The reaction vial was purged with O_2 before adding Nitromethane (0.1 mL). A separate vial with only Nitromethane was also prepared. The reaction vials were then heated in oil bath at temperature 40 °C for 2 hours. Then the solution from each vial was concentrated in rotary evaporator. Each vial was then reconstituted with 0.1 mL deionized water. A sample with only water was also evaluated as control sample.

Standard sample was prepared with 0.4 mM of nitrite, nitrate, chloride, and bromide each in deionized water.

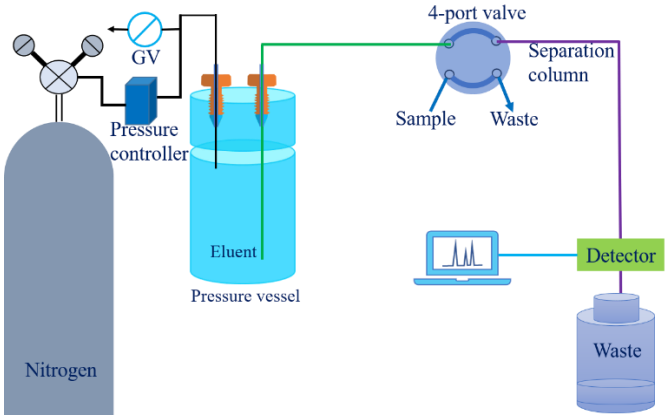


Figure S3: Open Tubular Ion Chromatography system. The solvent is pumped pneumatically.

Instrumental condition:

Open Tubular Ion Chromatographic Conditions are listed as follows. Column: AS 18 Anion Exchange latex coated silica columns (25 µm i.d., 360 µm o.d., Effective length: 40 cm); Eluent: 1 mM sodium benzoate; Injection volume: 4 nL; Flow rate: 150 nL/min; Detection: TraceDec Detector (Frequency: 150 KHz, Gain: 200%, Voltage: 0 dB, Offset: 0).

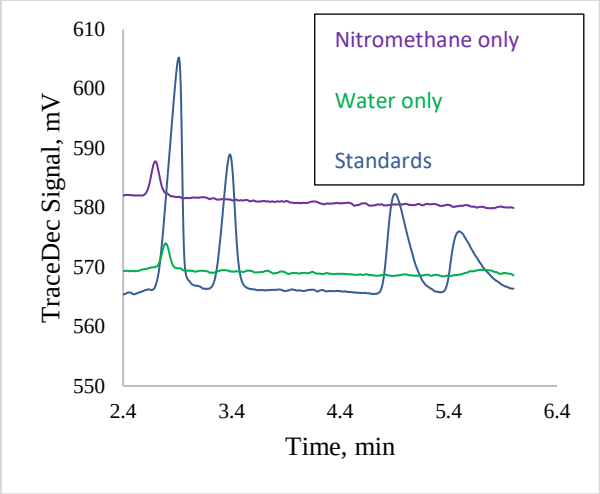


Figure S4: extracted ion chromatogram for control samples: nitromethane only (purple trace), water only (green trace) and standards (blue trace)

D. Crude NMR analysis of aldehyde product from the reaction of (nitromethyl)benzene with flavin catalyst A in the presence of TEMPO and *N*-phenyltetrahydroisoquinoline (N-PhTHIQ) as additives

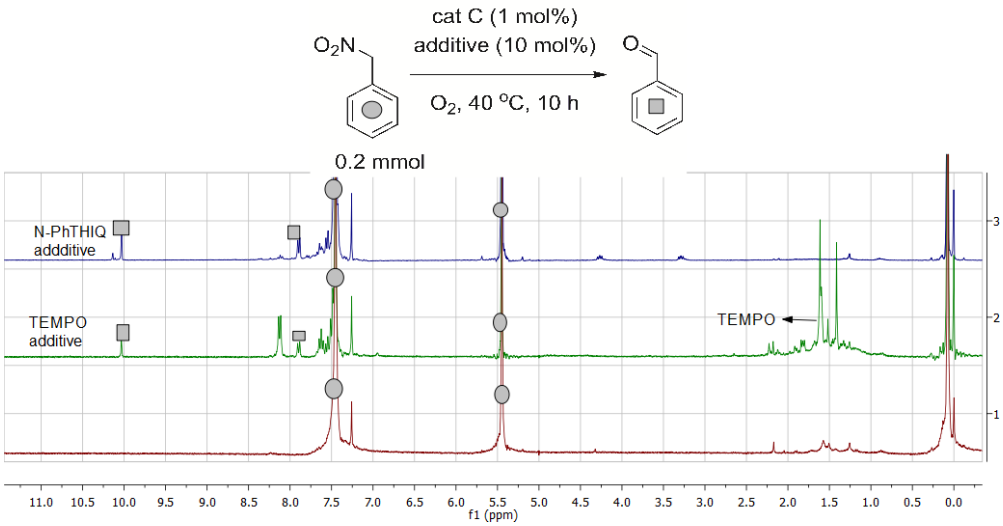
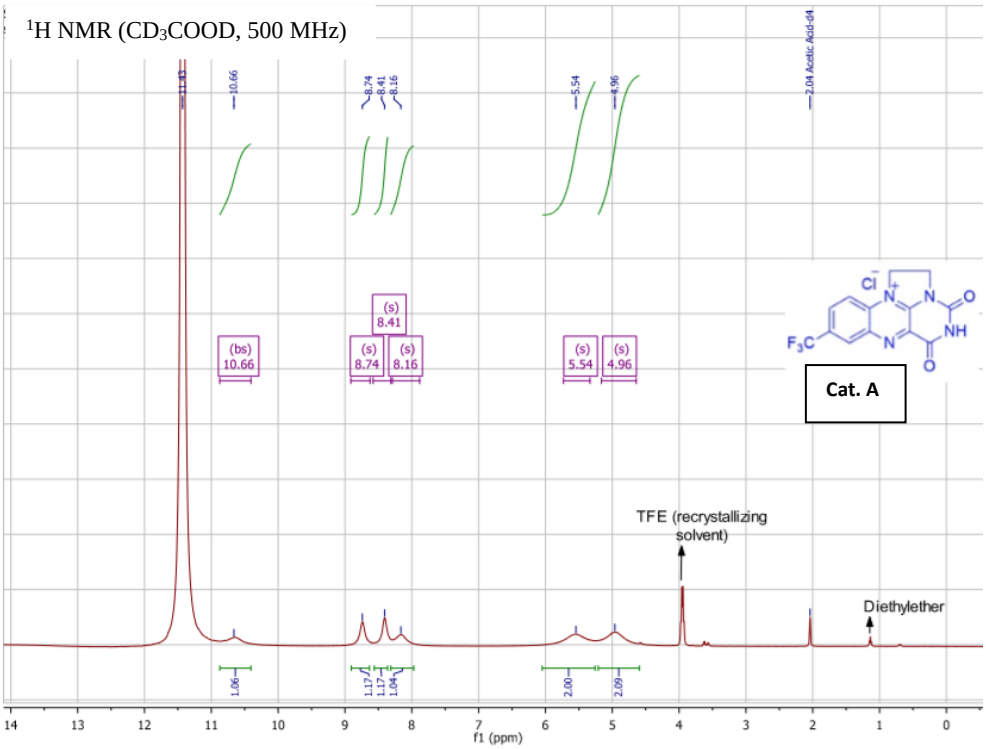
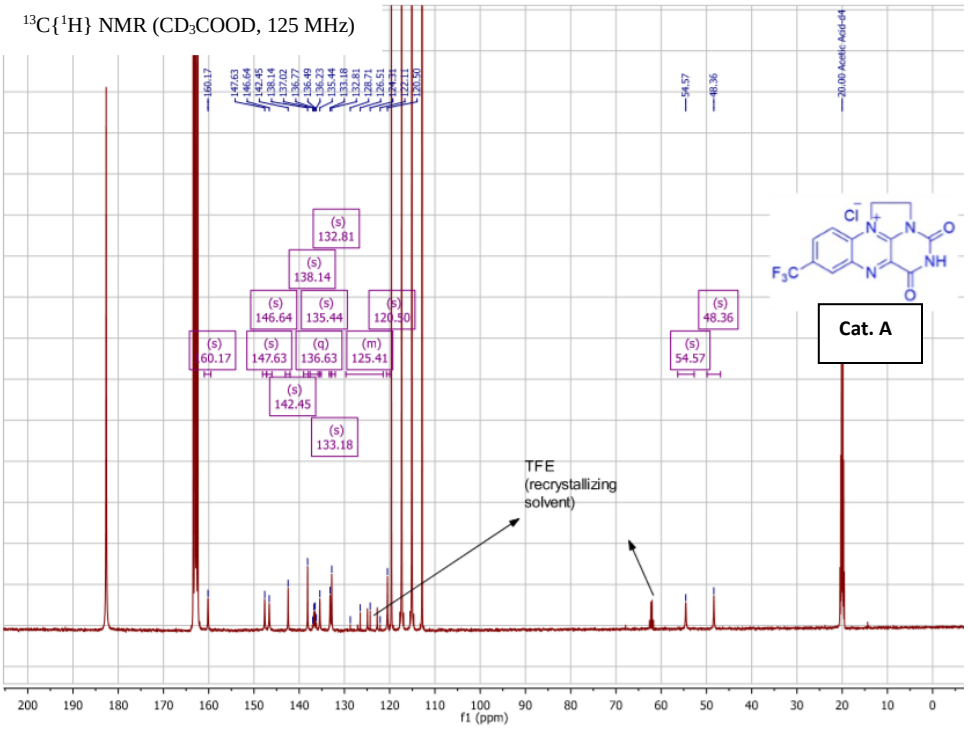


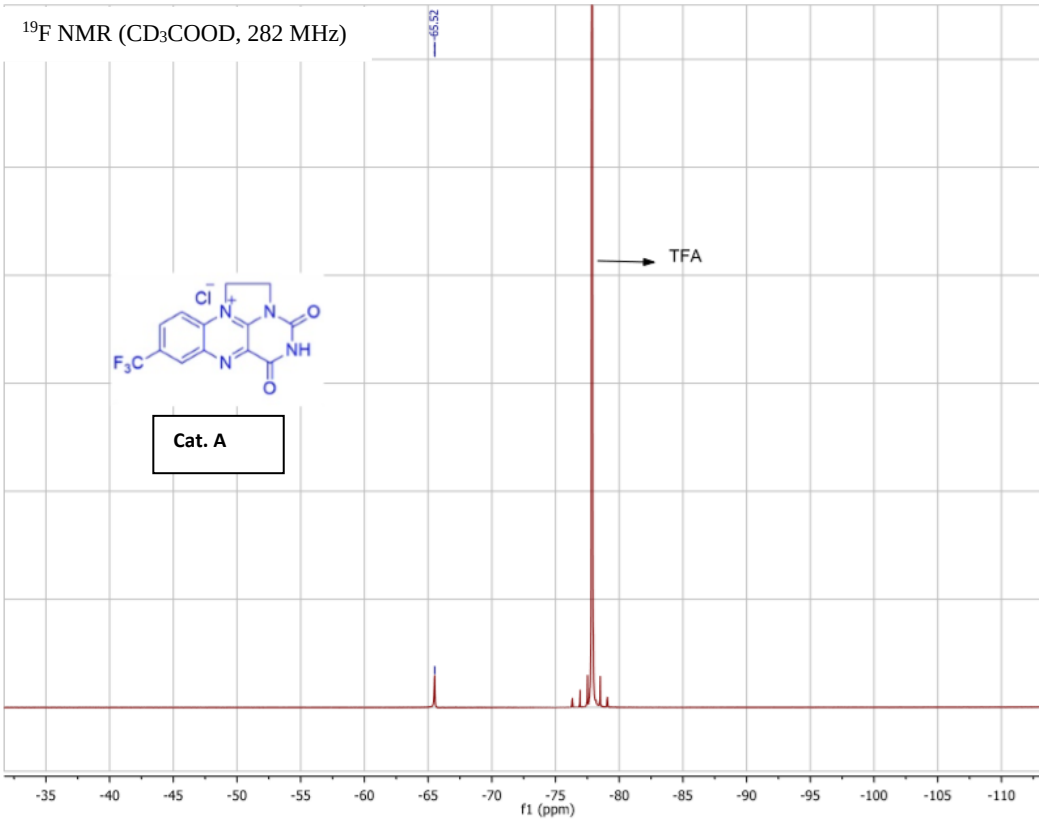
Figure S5: NMR spectral figure showing aldehyde formation in the presence of flavin and catalytic base (blue trace), flavin and TEMPO (green trace), and in the absence of additive and catalyst (red trace)

E. NMR spectral figure of catalysts:

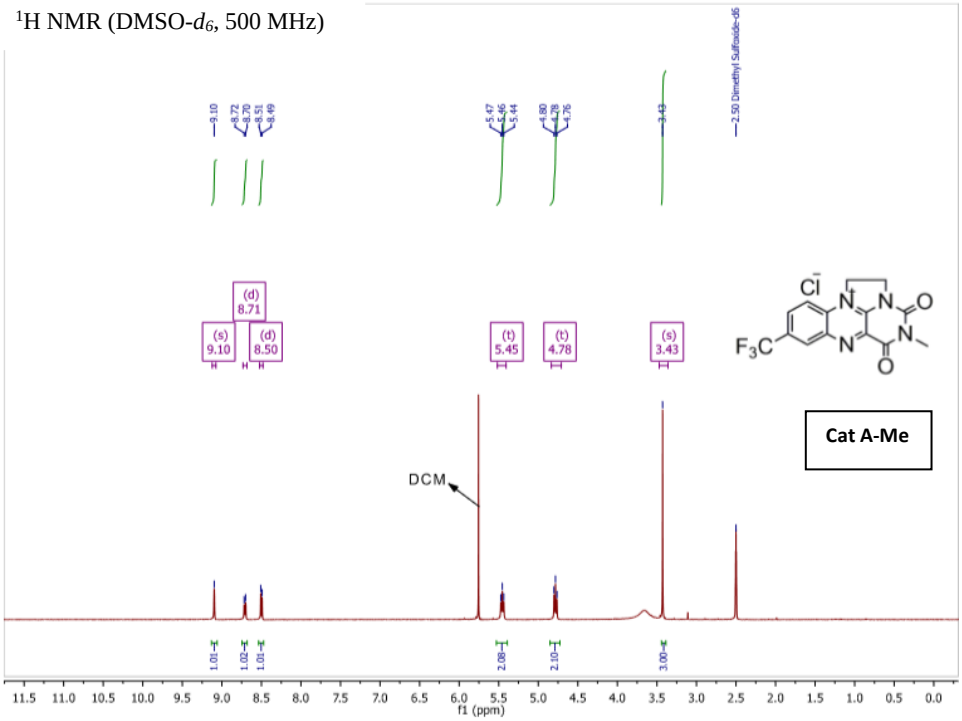




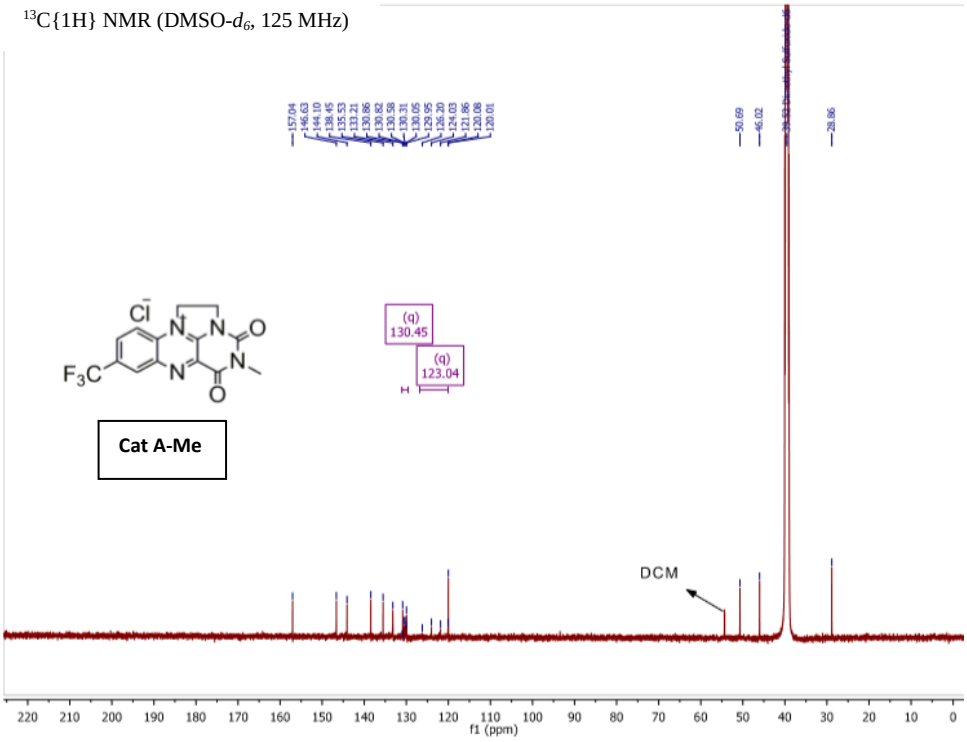
^{19}F NMR (CD_3COOD, 282 MHz)



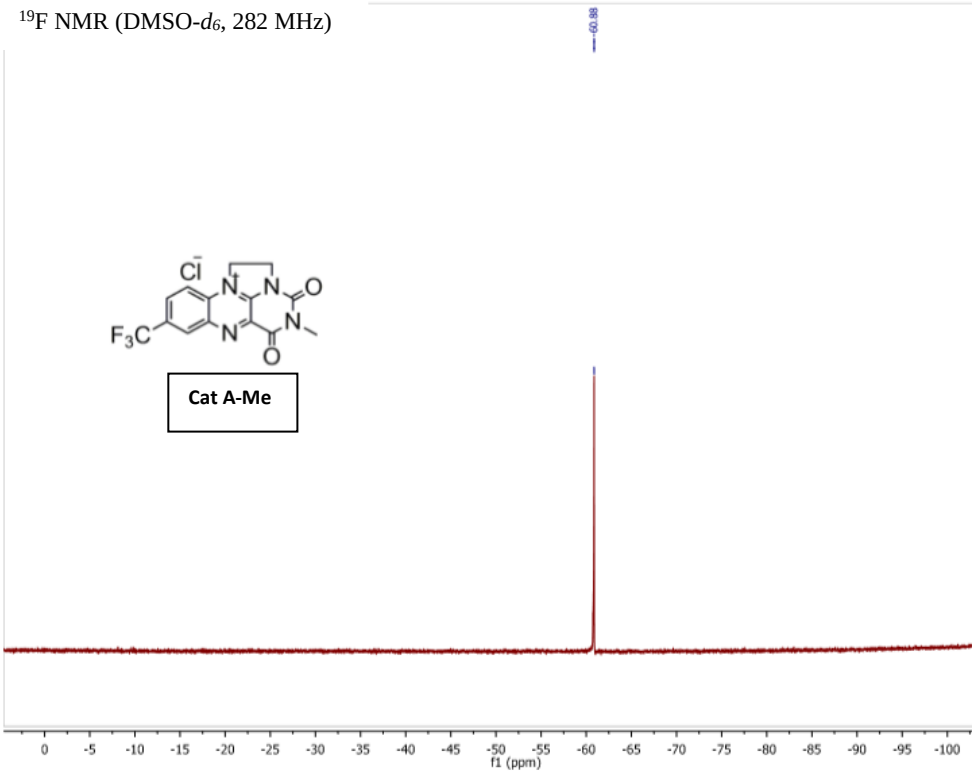
^{1}H NMR (DMSO-d_6, 500 MHz)



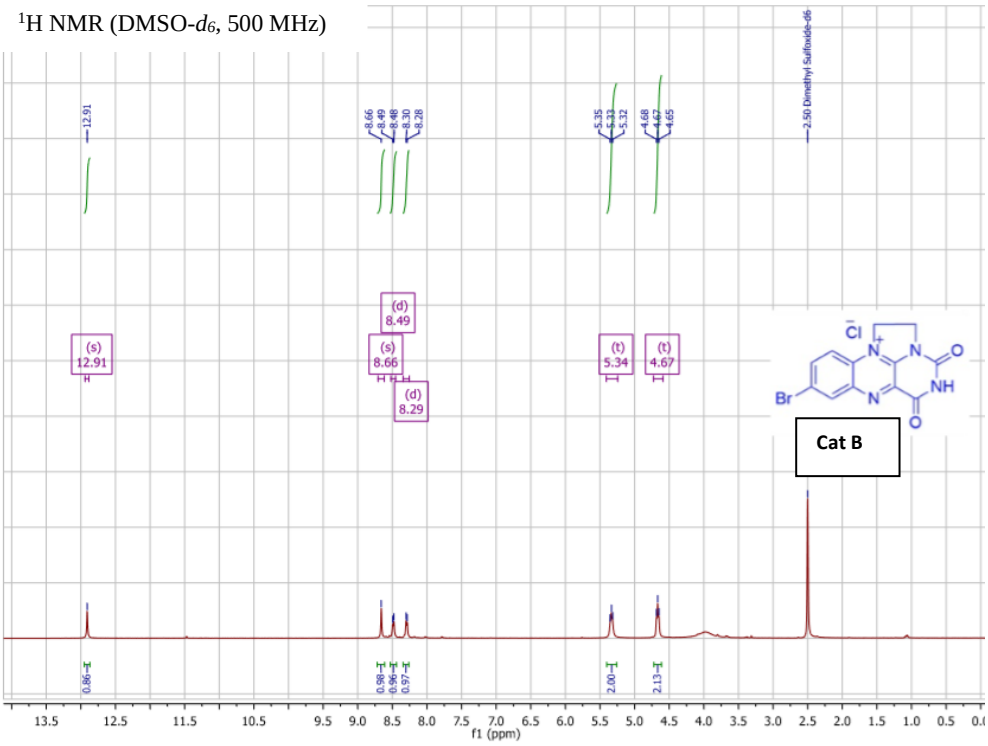
^{13}C{1H} NMR (DMSO-d_6, 125 MHz)



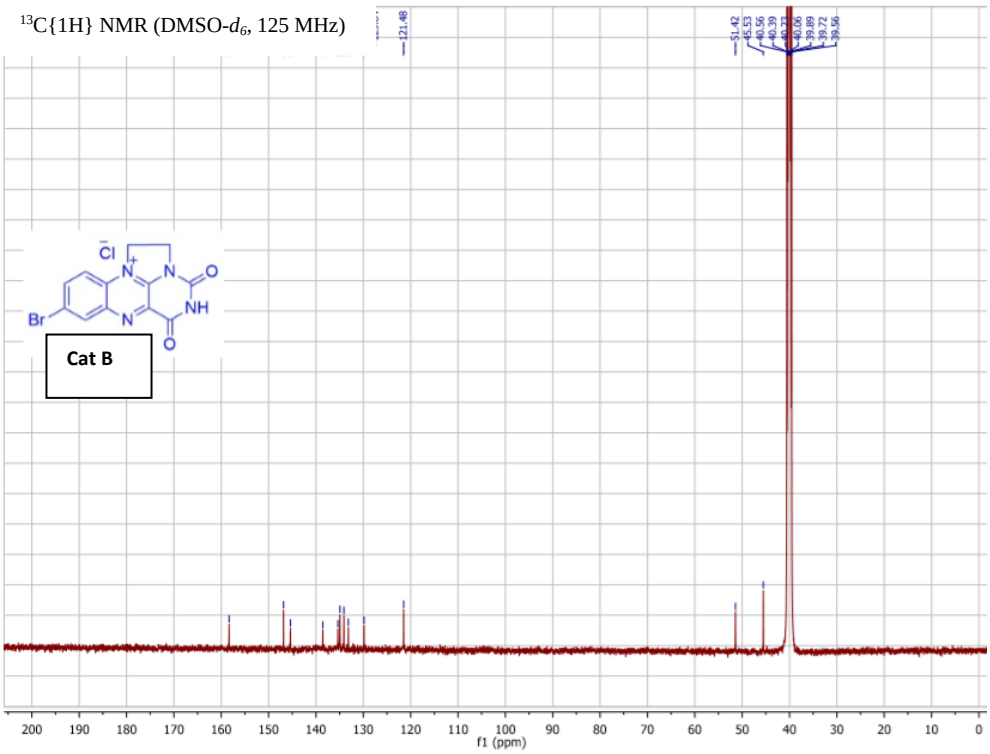
^{19}F NMR (DMSO-d_6, 282 MHz)



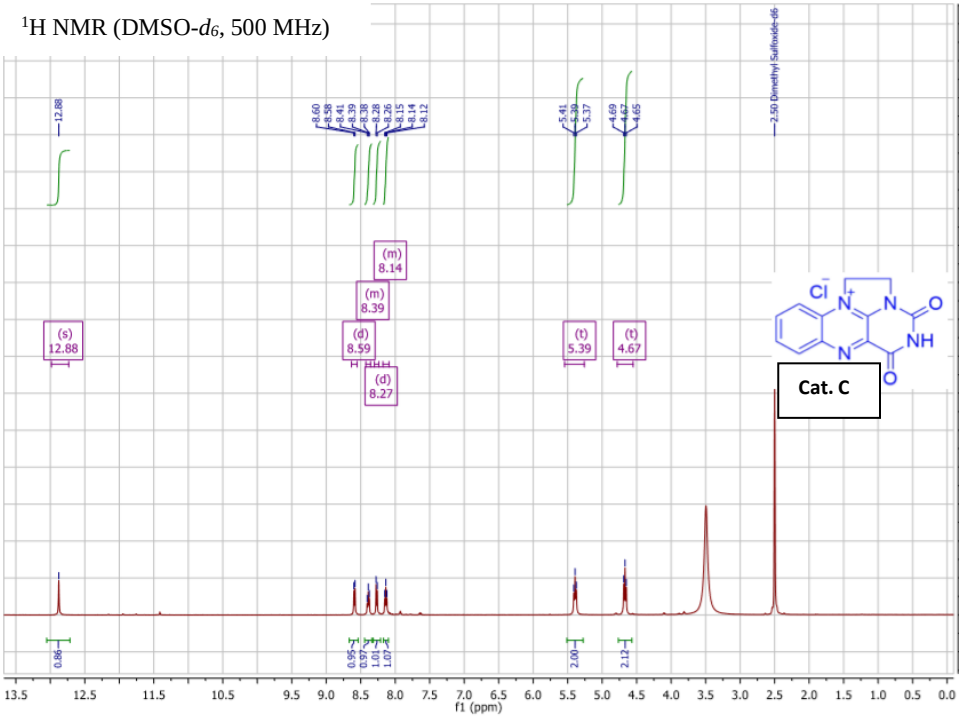
^{1}H NMR (DMSO-d_6, 500 MHz)



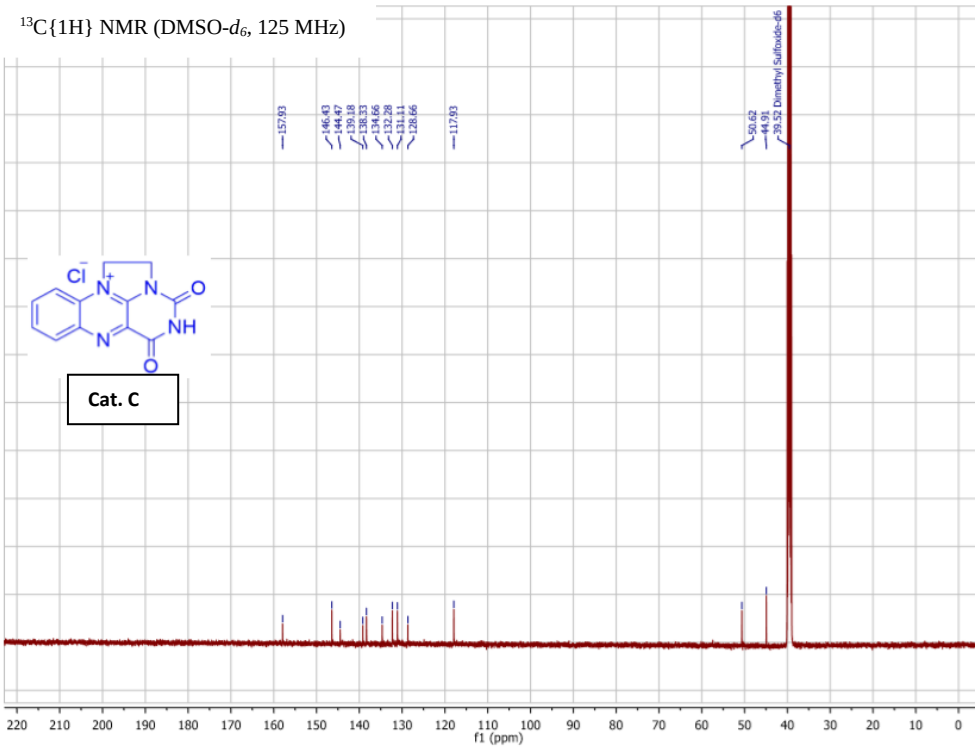
^{13}C{1H} NMR (DMSO-d_6, 125 MHz)



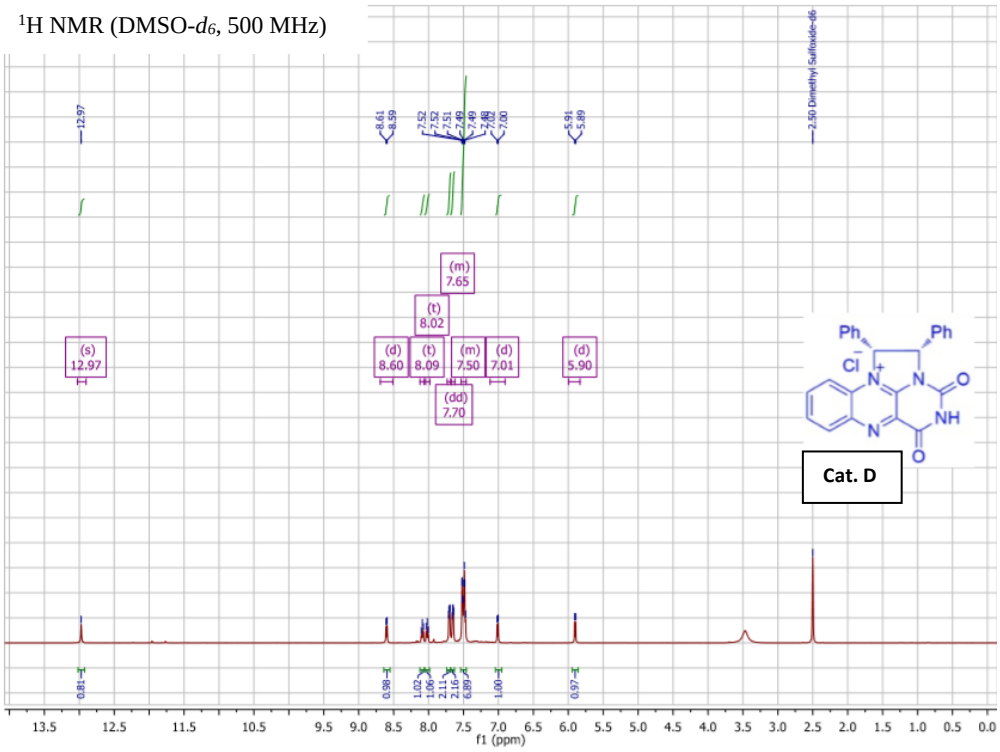
^{1}H NMR (DMSO-d_6, 500 MHz)



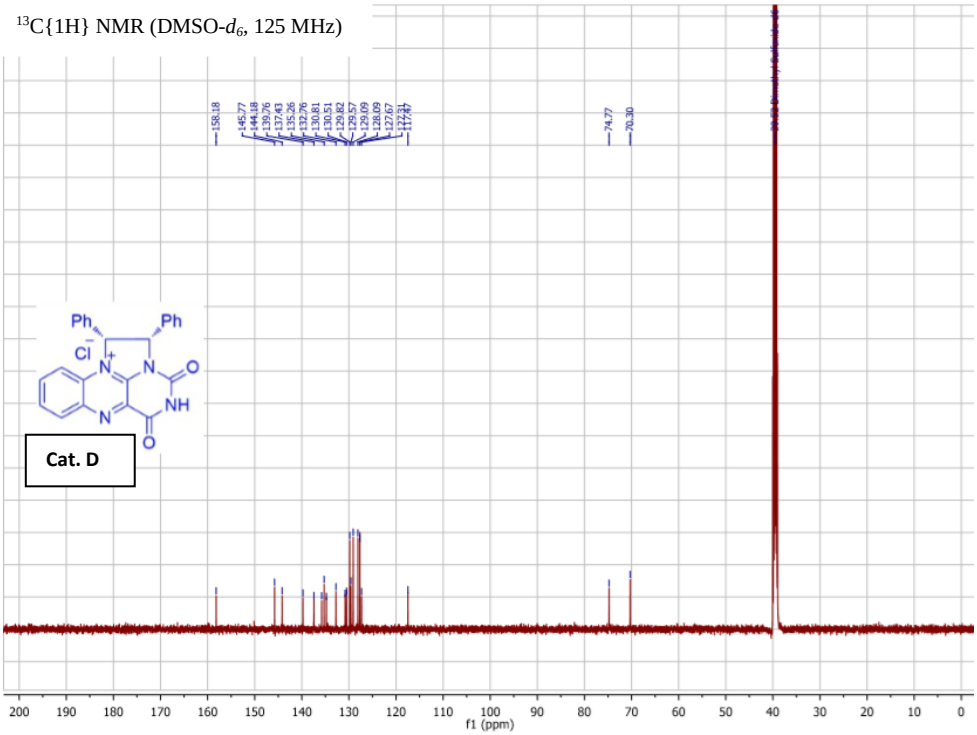
^{13}C{1H} NMR (DMSO-d_6, 125 MHz)



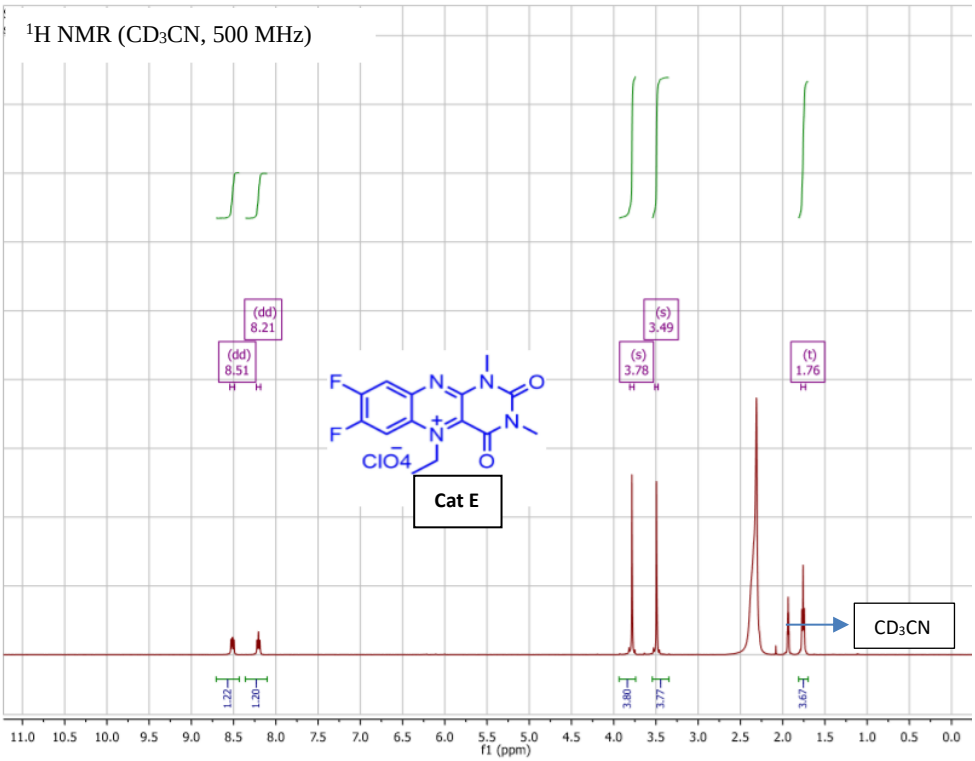
^{1}H NMR (DMSO-d_6, 500 MHz)



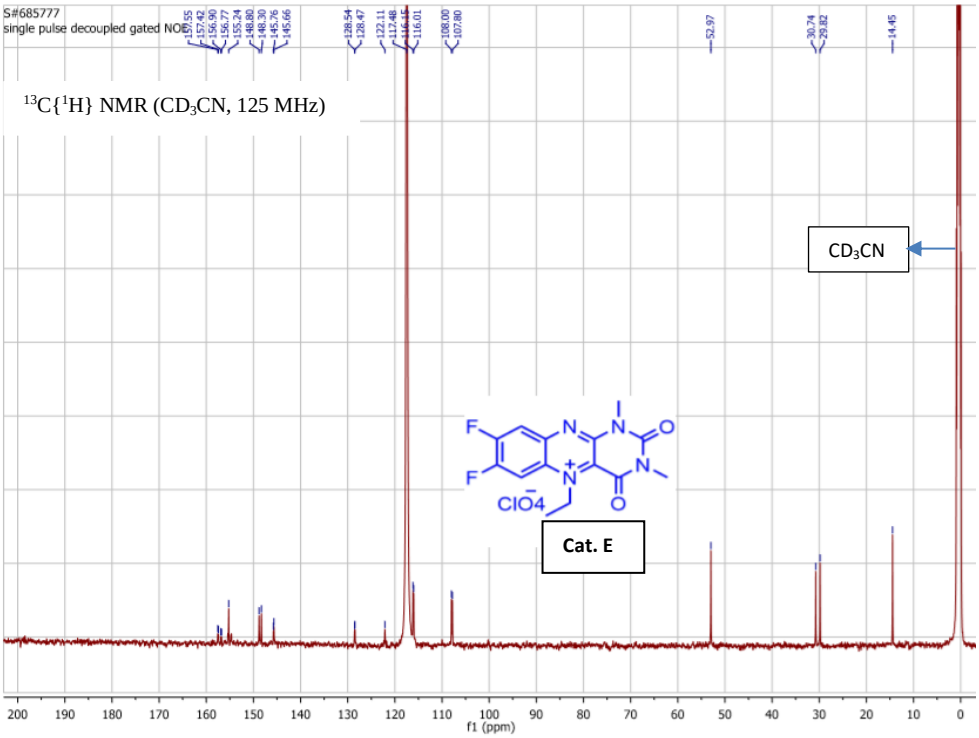
^{13}C{1H} NMR (DMSO-d_6, 125 MHz)



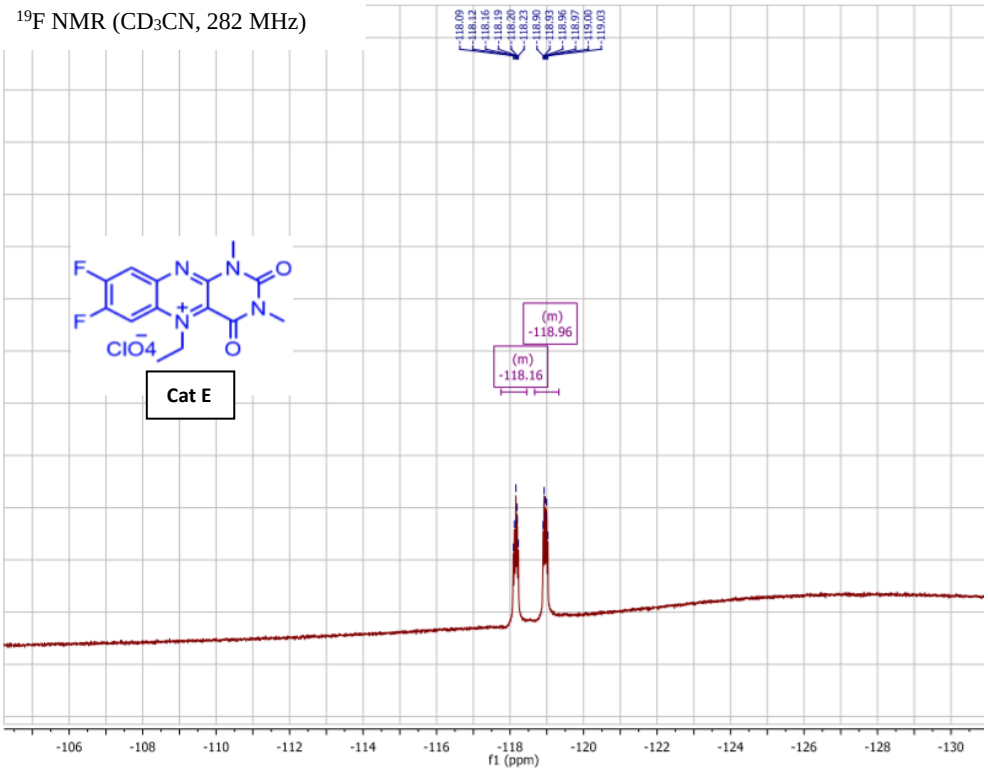
^{1}H NMR (CD_3CN, 500 MHz)



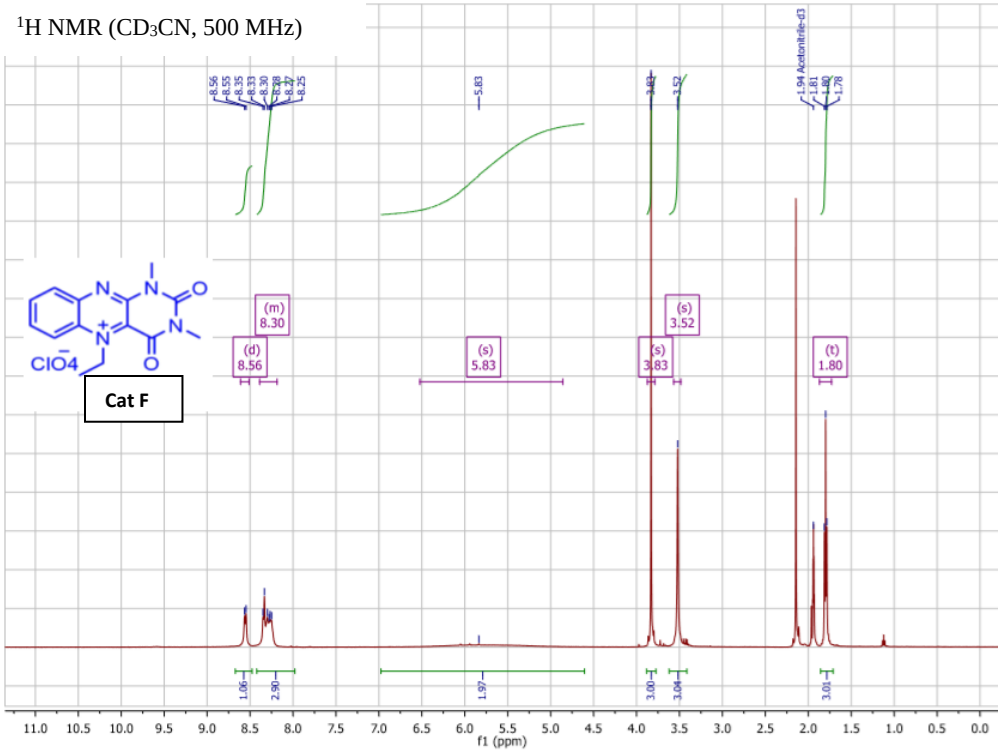
^{13}C{^{1}H} NMR (CD_3CN, 125 MHz)



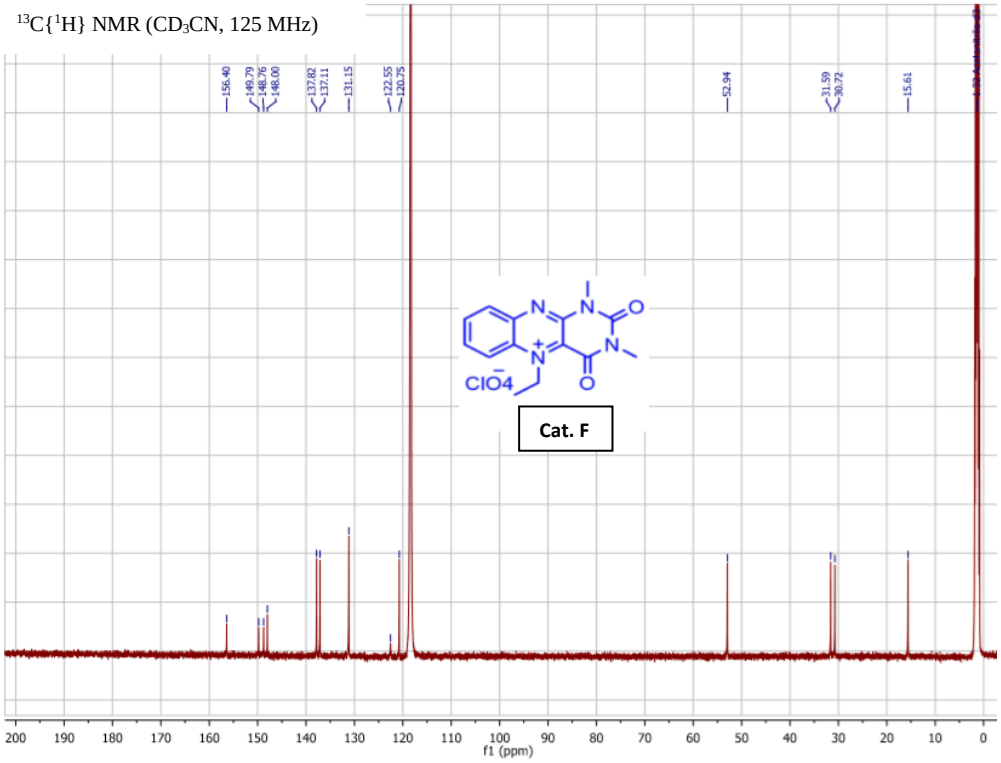
^{19}F NMR (CD_3CN, 282 MHz)



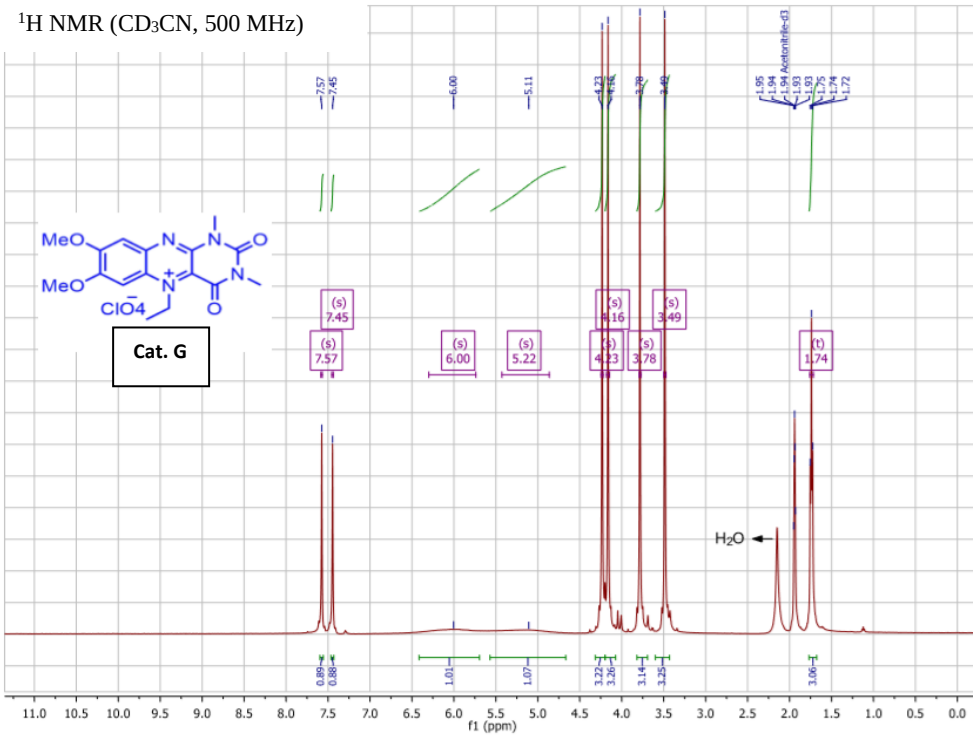
^{1}H NMR (CD_3CN, 500 MHz)



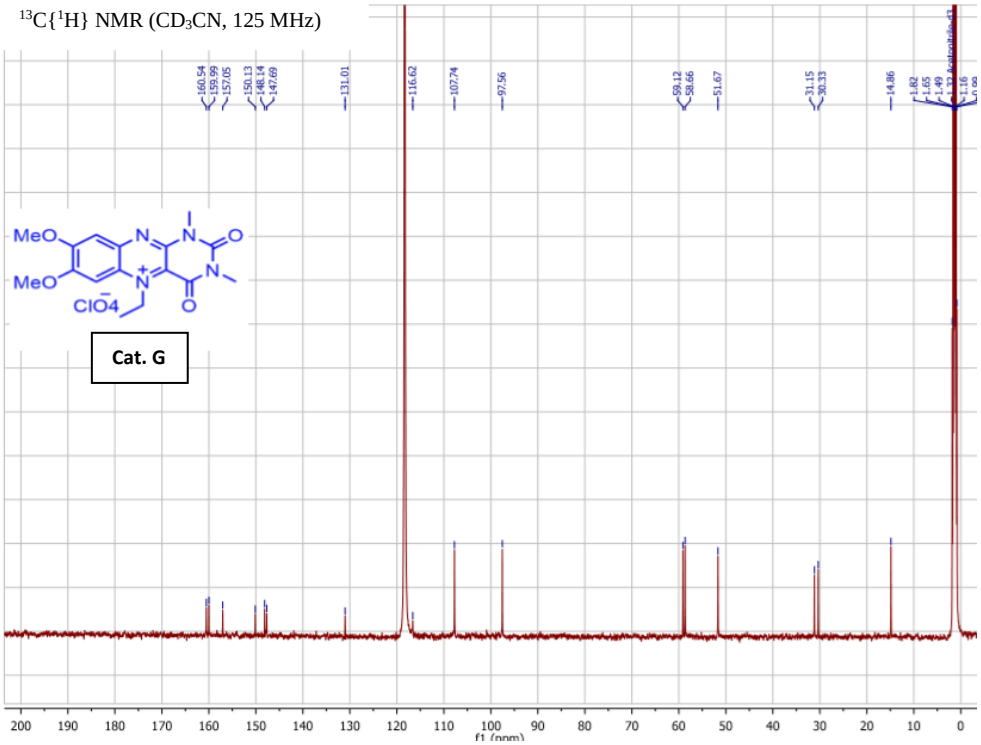
^{13}C{^{1}H} NMR (CD_3CN, 125 MHz)



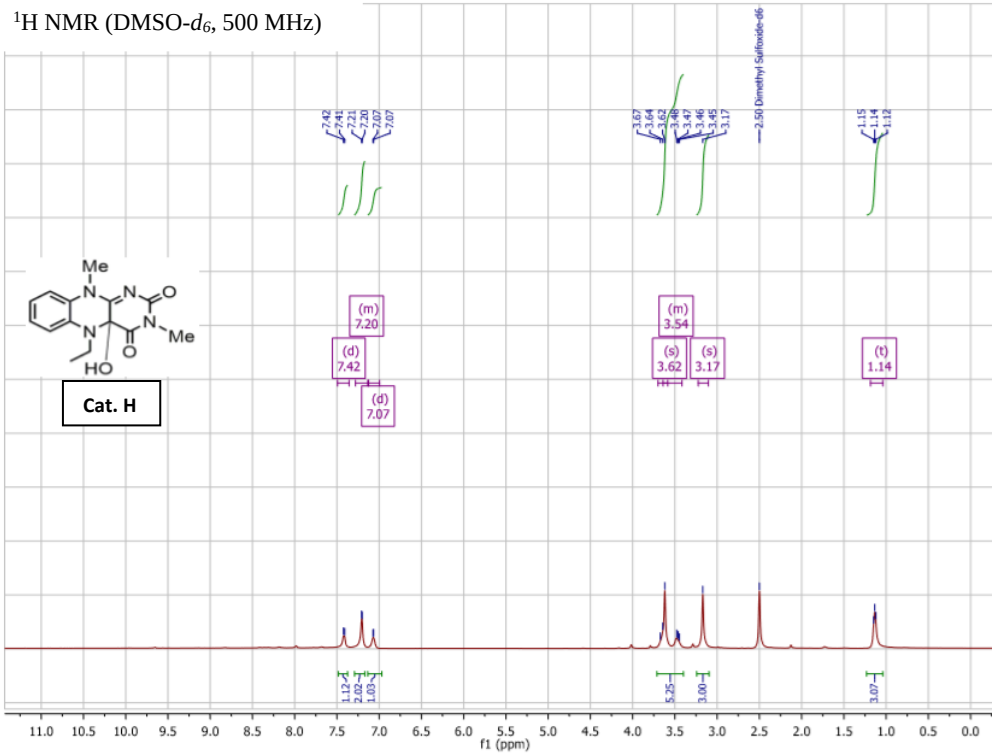
^{1}H NMR (CD_3CN, 500 MHz)



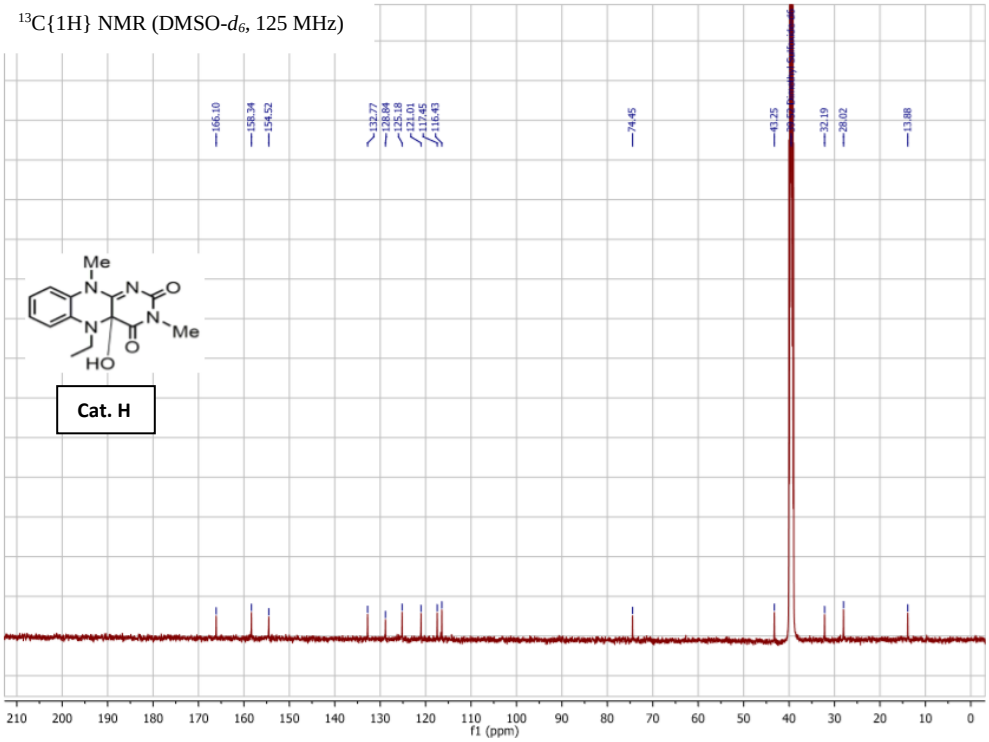
^{13}C{^{1}H} NMR (CD_3CN, 125 MHz)



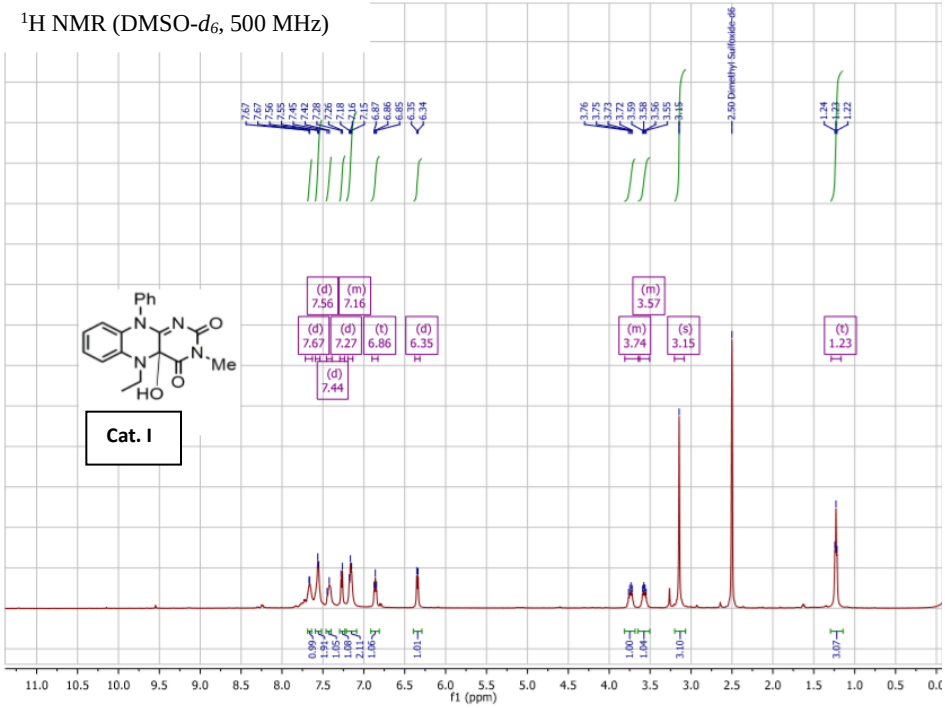
^{1}H NMR (DMSO-d_6, 500 MHz)



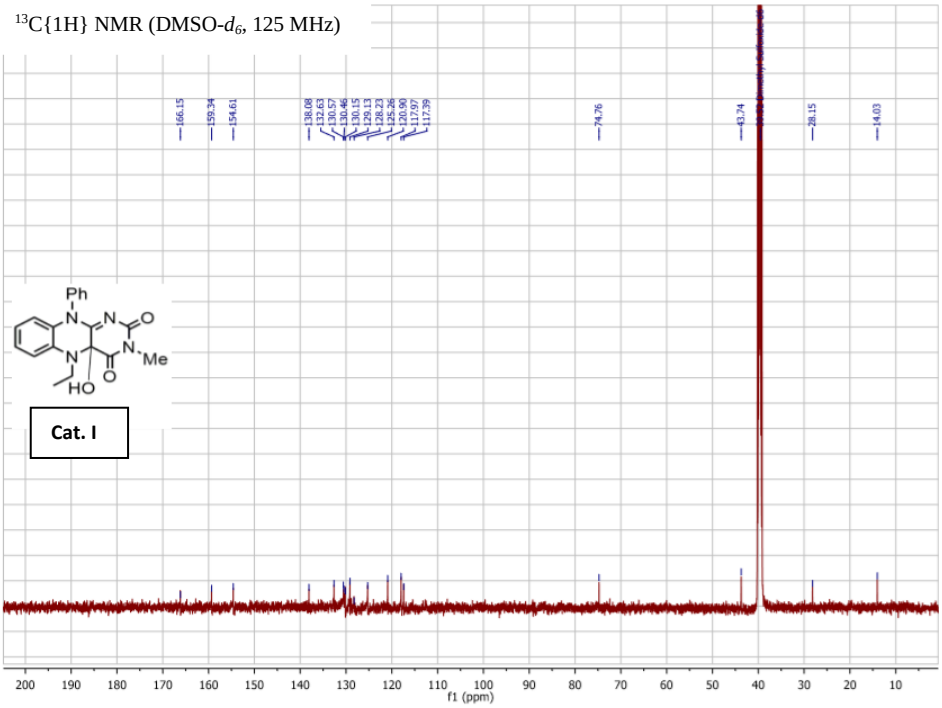
^{13}C{1H} NMR (DMSO-d_6, 125 MHz)



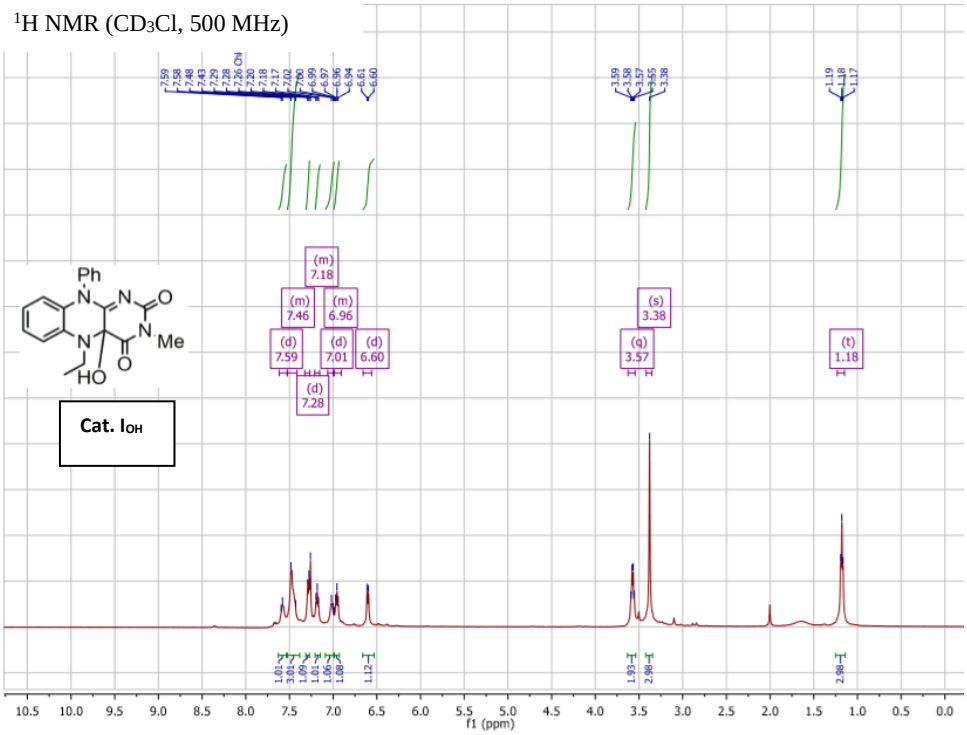
^{1}H NMR (DMSO-d_6, 500 MHz)



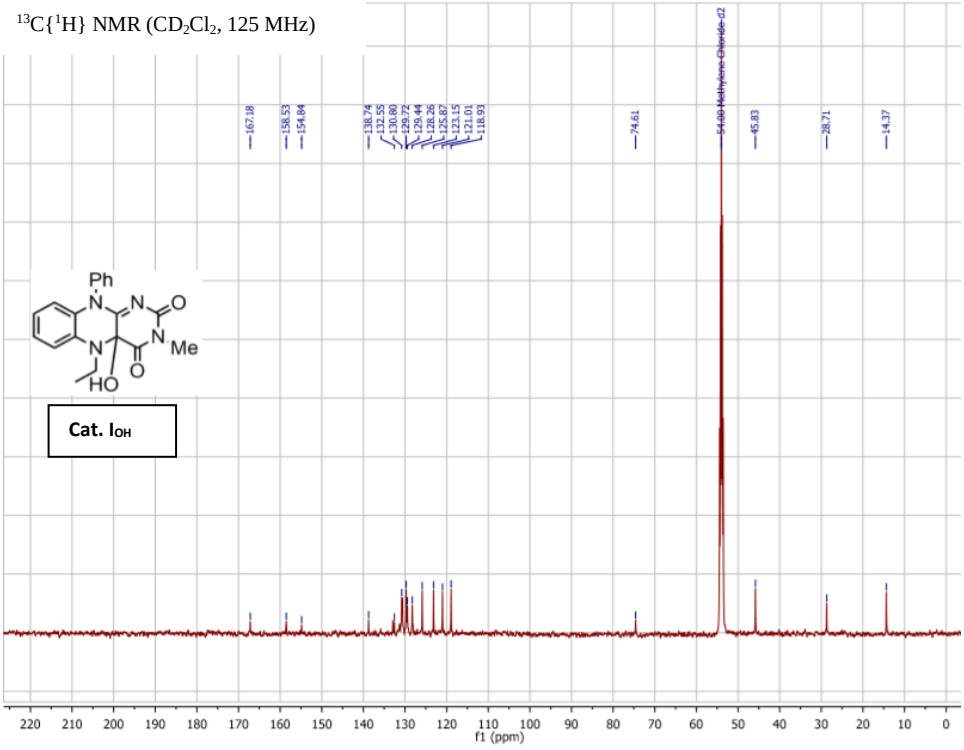
^{13}C{1H} NMR (DMSO-d_6, 125 MHz)



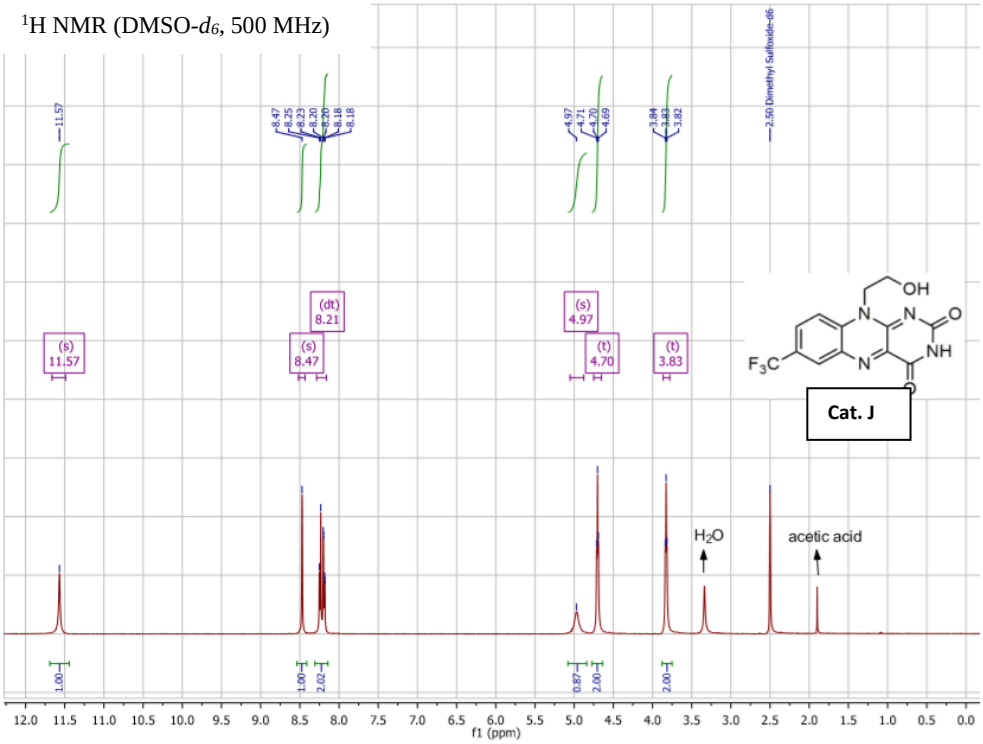
^{1}H NMR (CD_3Cl, 500 MHz)



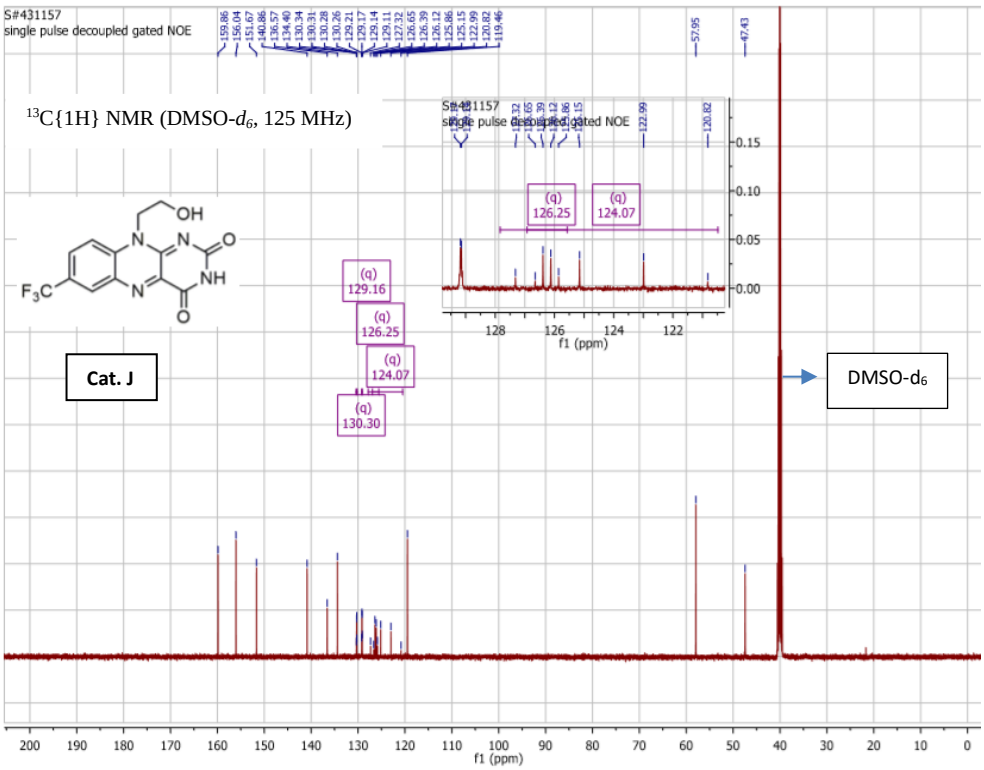
^{13}C{^{1}H} NMR (CD_2Cl_2, 125 MHz)



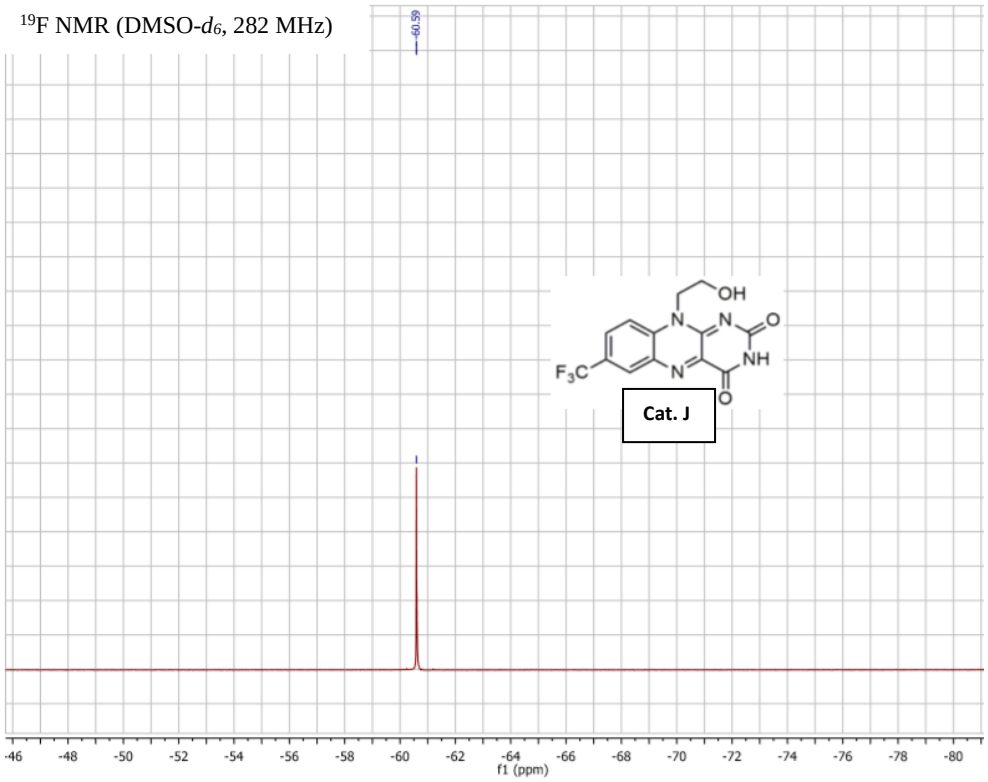
^{1}H NMR (DMSO-d_6, 500 MHz)



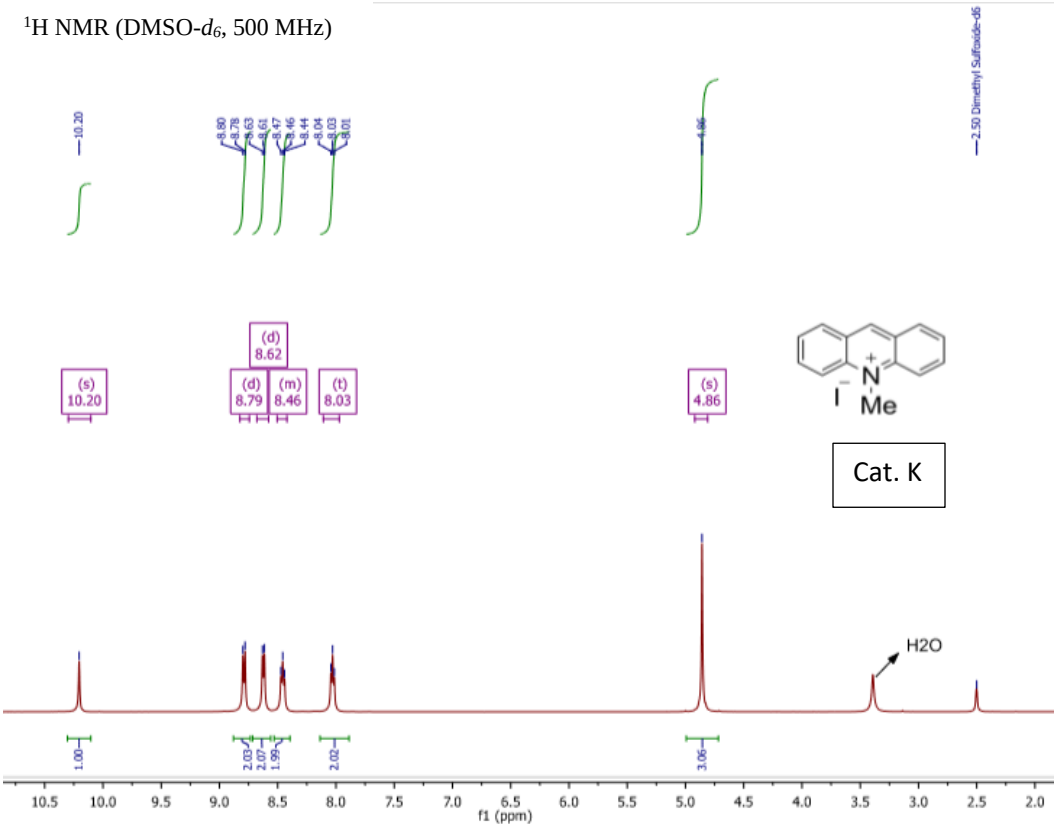
^{13}C{1H} NMR (DMSO-d_6, 125 MHz)



^{19}F NMR (DMSO-d_6, 282 MHz)

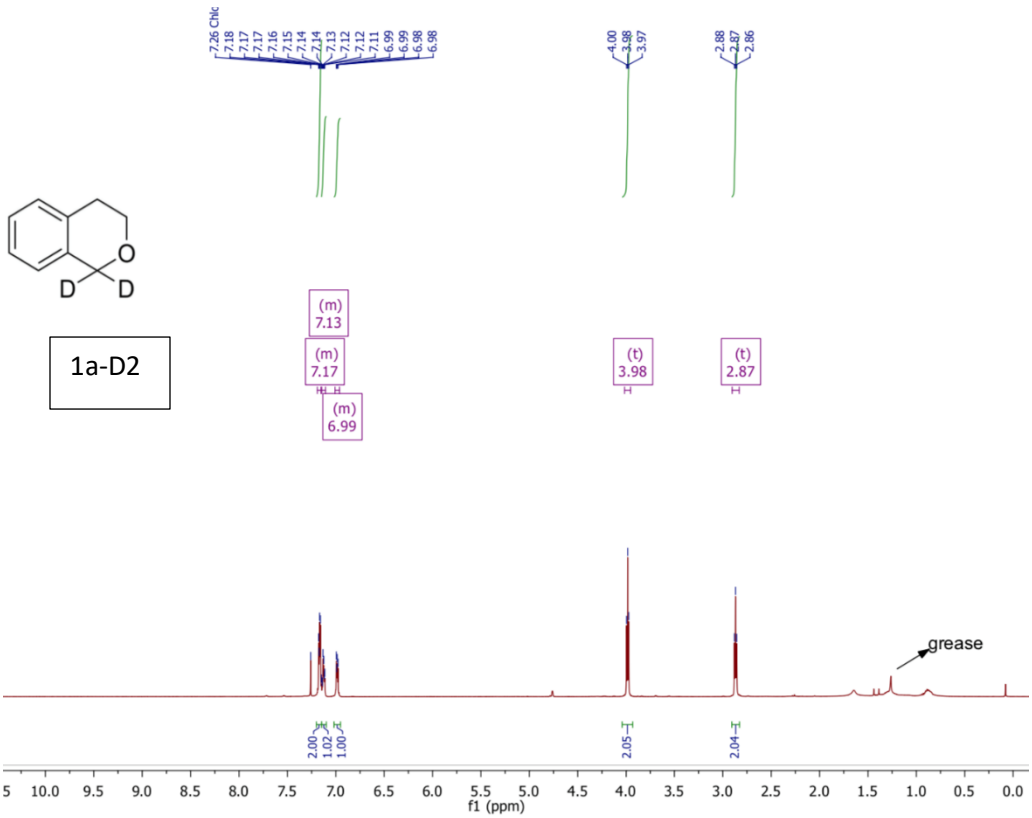


^{1}H NMR (DMSO-d_6, 500 MHz)

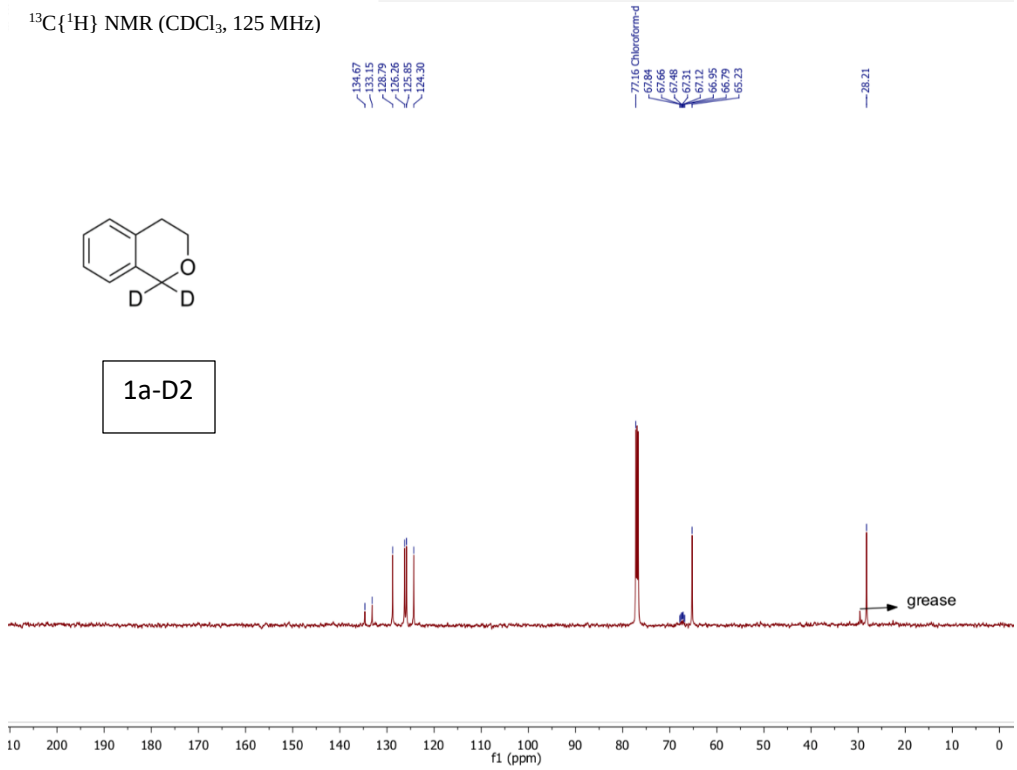


F. ^{1}H NMR spectral figures of starting materials:

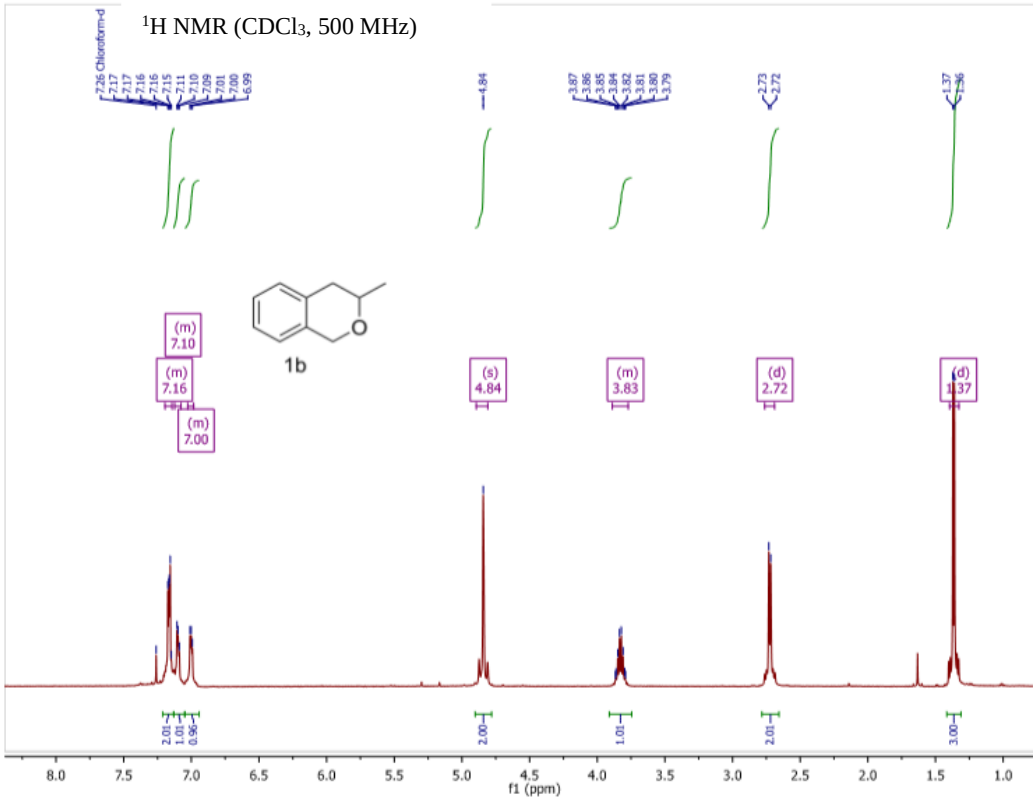
^{1}H NMR ($CDCl_3$, 500 MHz)



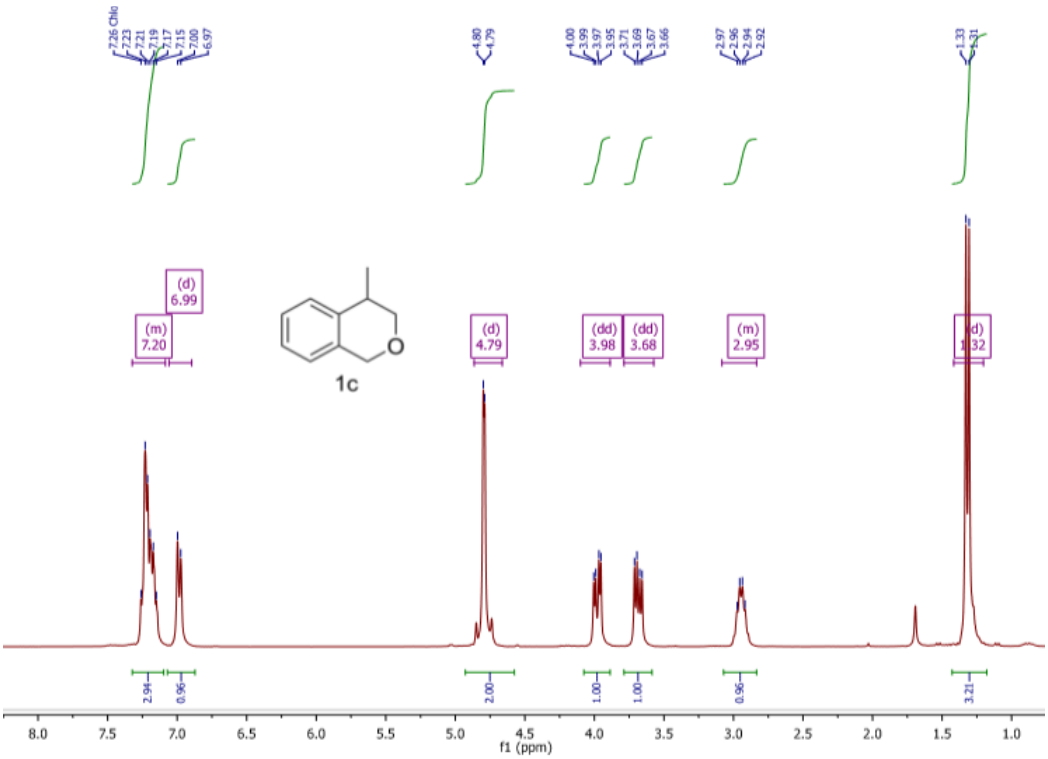
^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz)



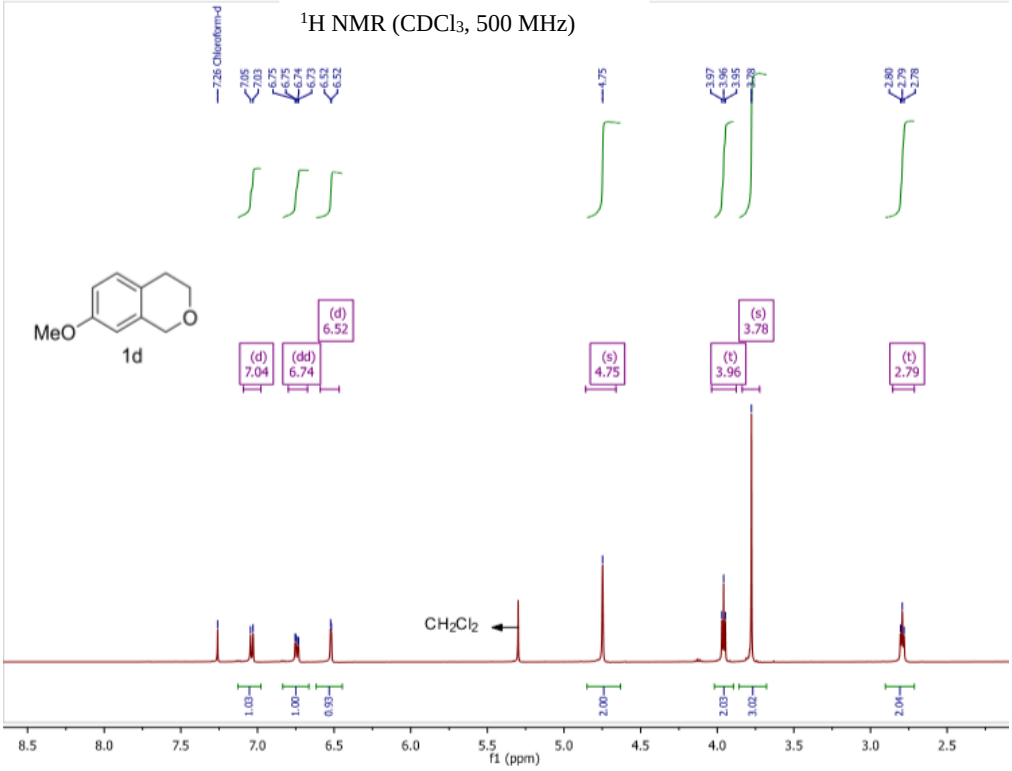
^{1}H NMR ($CDCl_3$, 500 MHz)



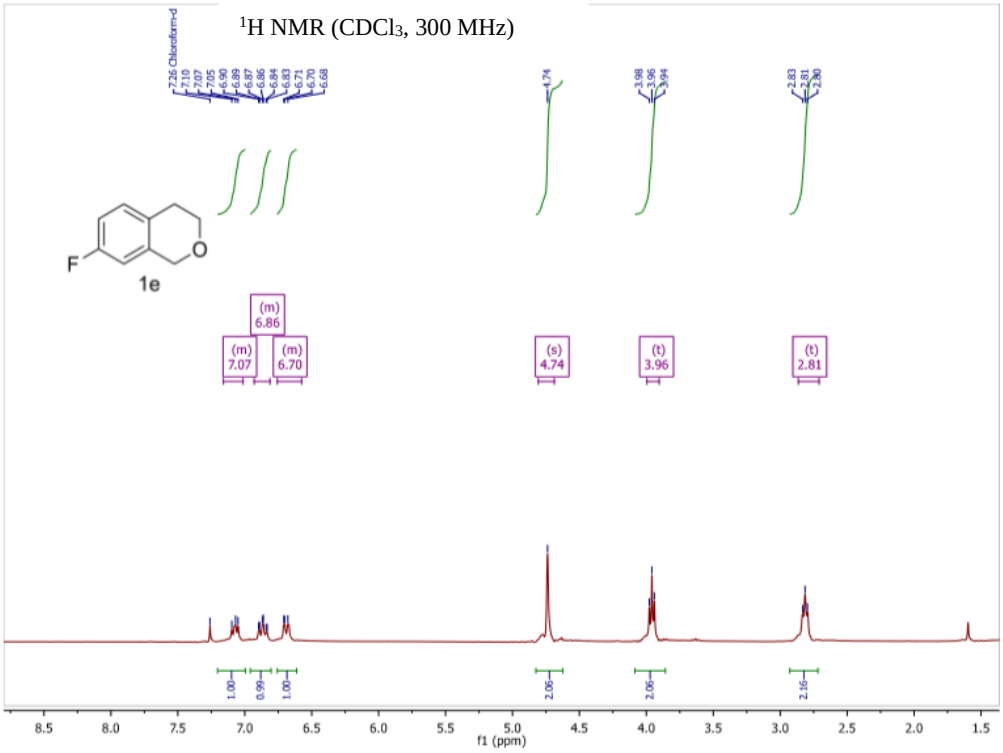
^{1}H NMR ($CDCl_3$, 300 MHz)



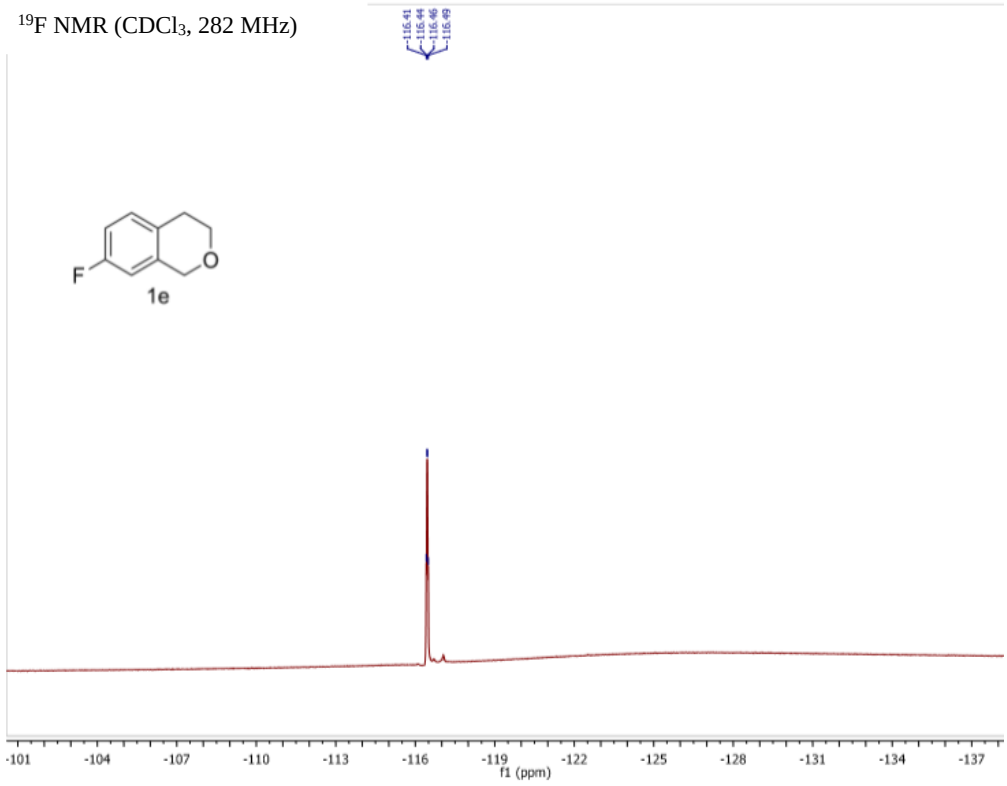
^{1}H NMR ($CDCl_3$, 500 MHz)



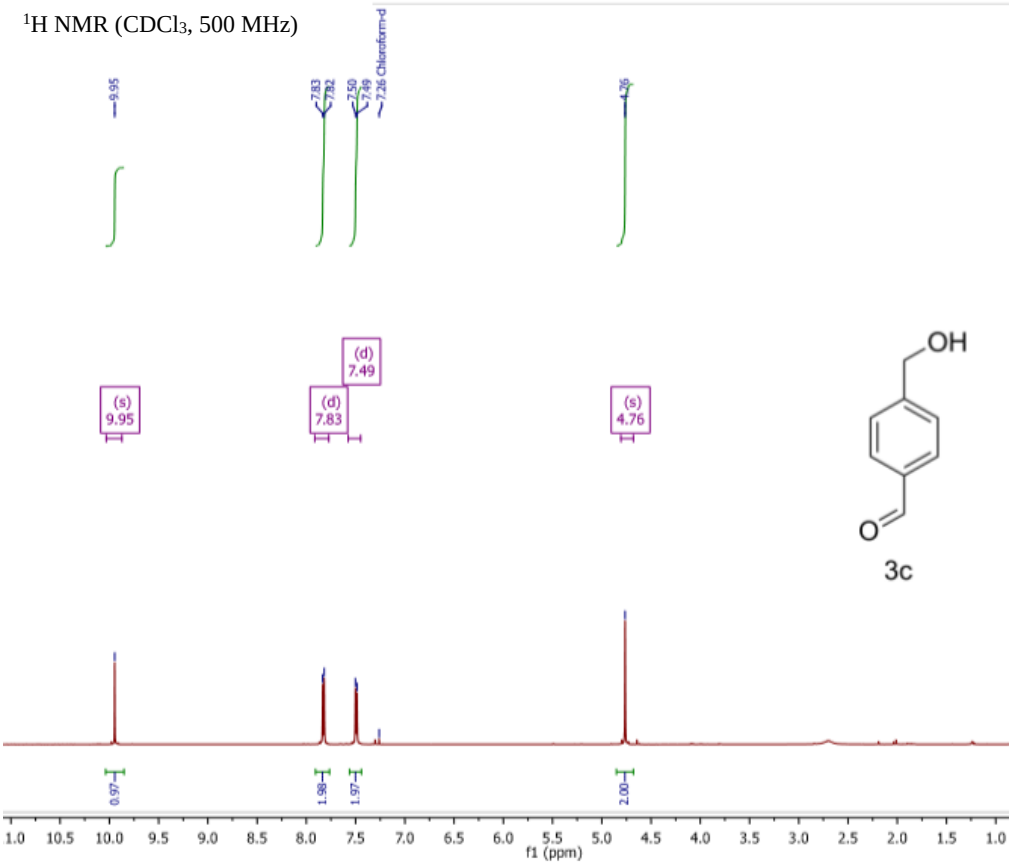
^{1}H NMR ($CDCl_3$, 300 MHz)



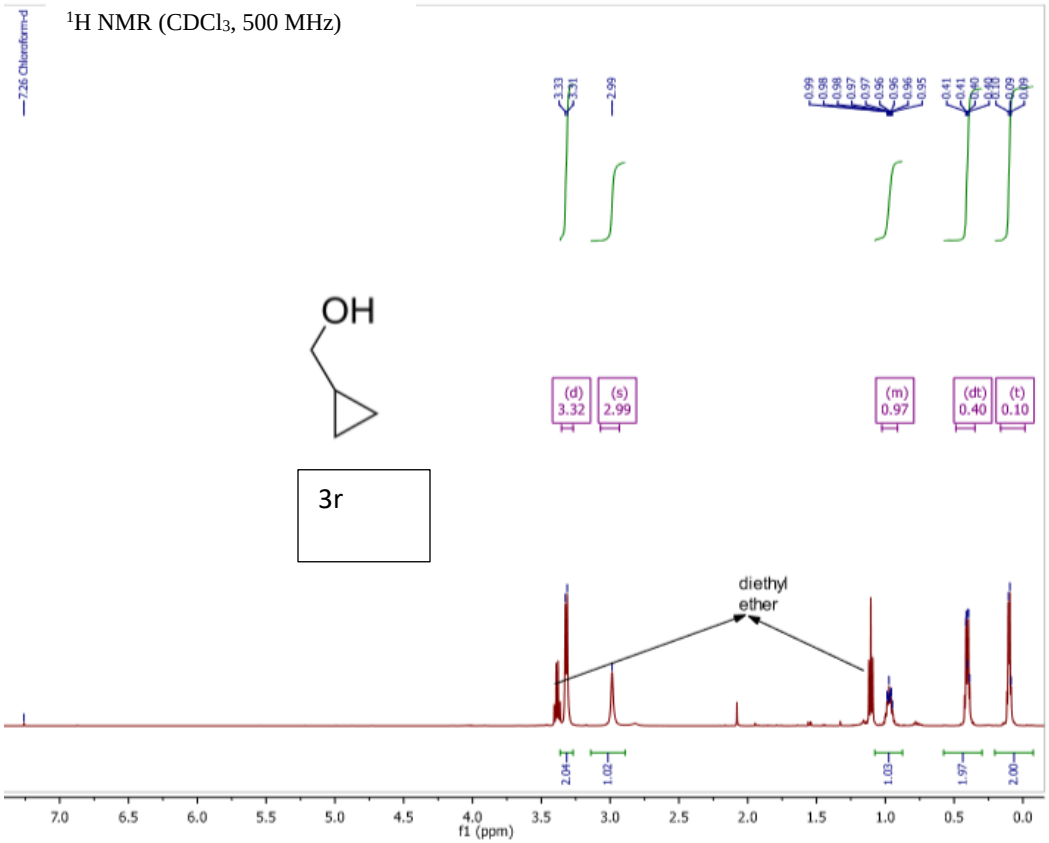
^{19}F NMR ($CDCl_3$, 282 MHz)



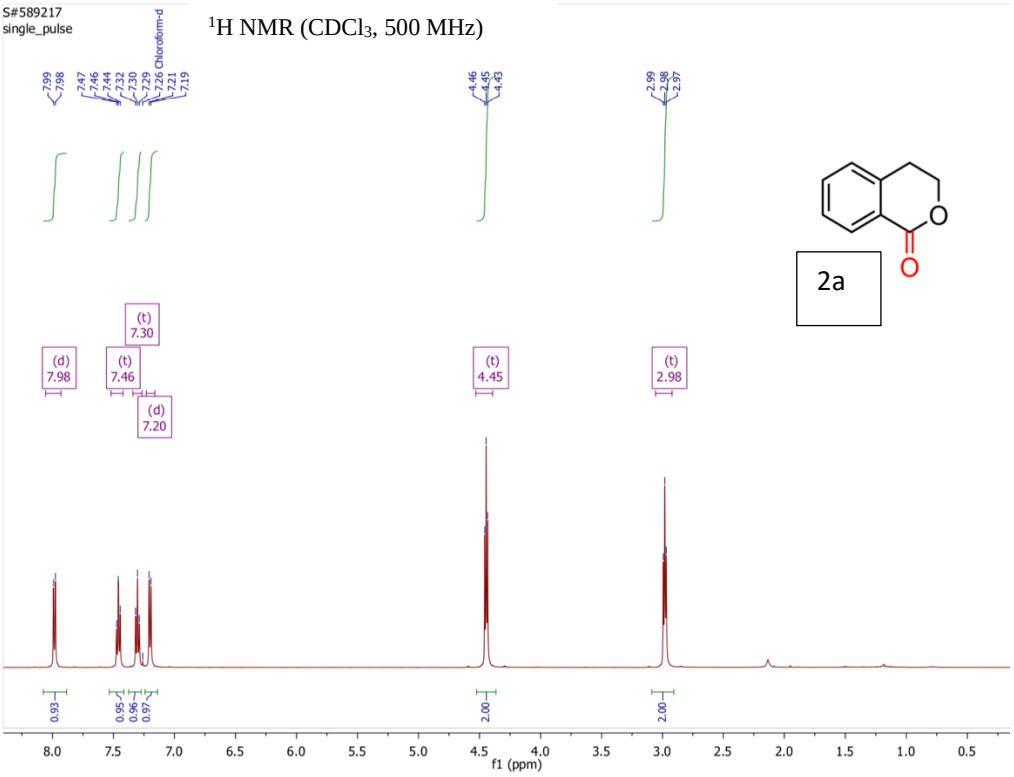
^{1}H NMR ($CDCl_3$, 500 MHz)

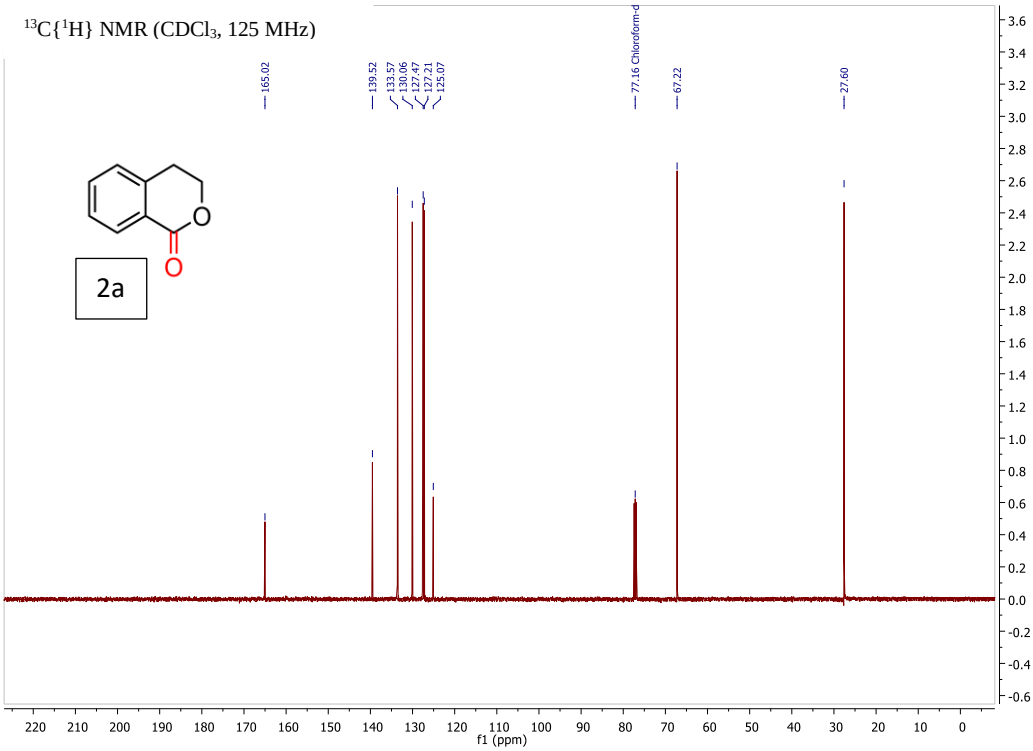


^{1}H NMR ($CDCl_3$, 500 MHz)

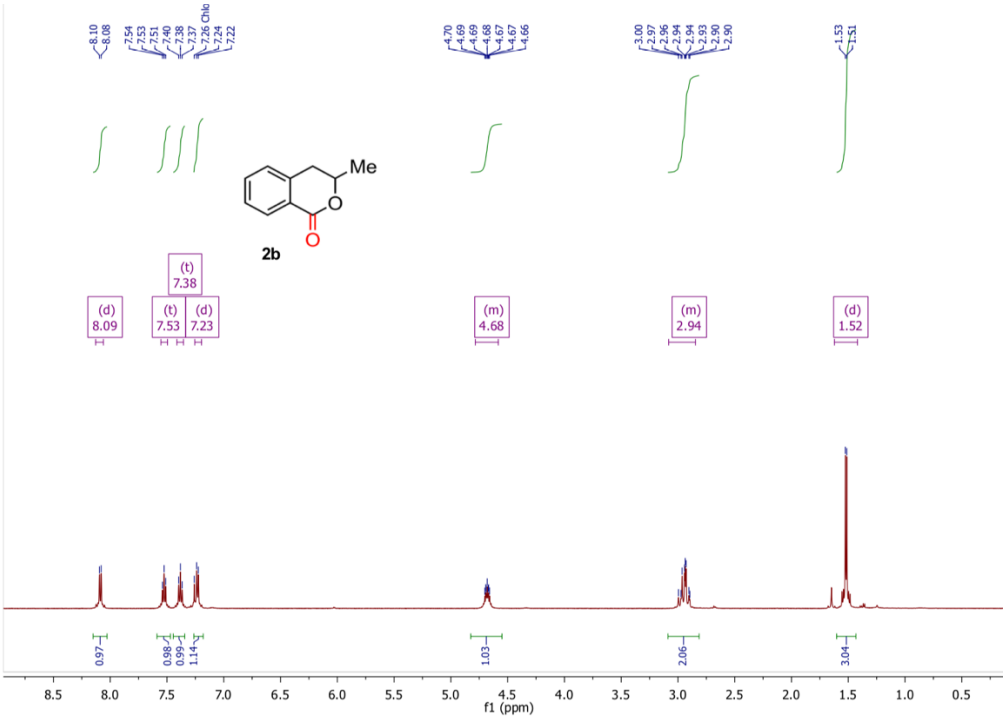


G. NMR spectral figure of products:

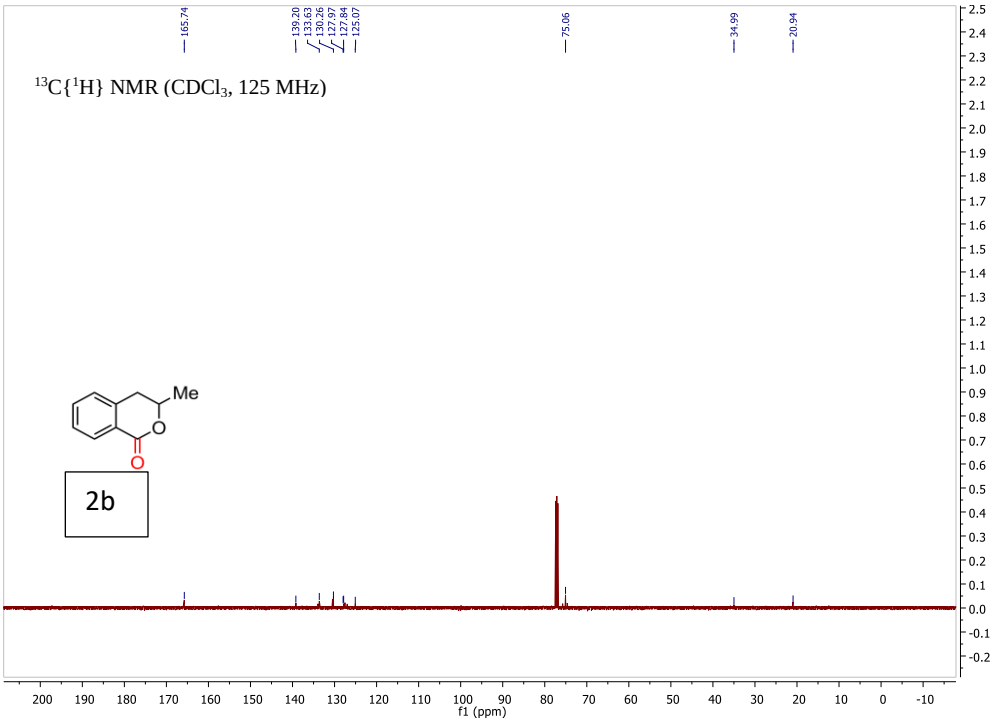




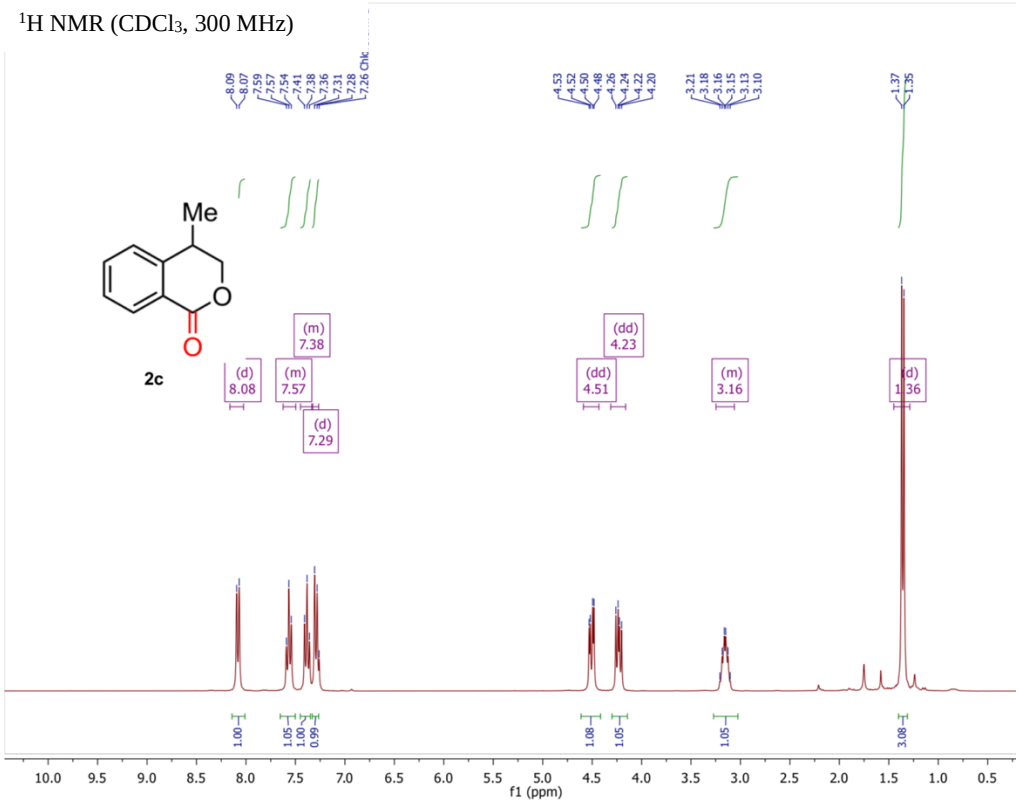
^{1}H NMR ($CDCl_3$, 500 MHz)



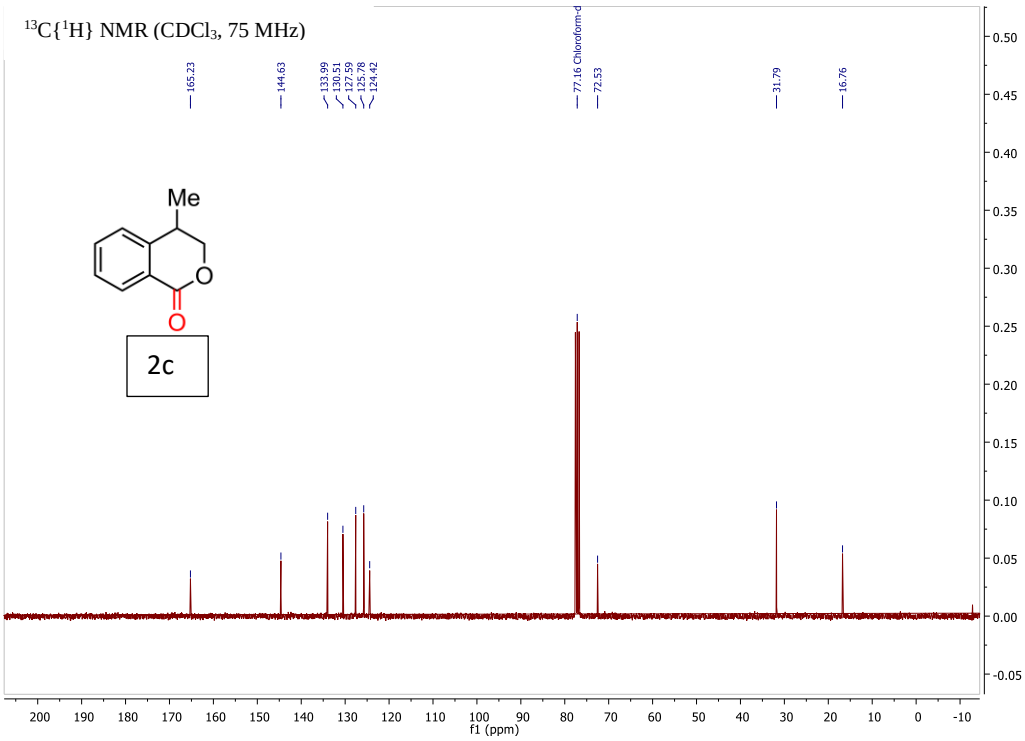
^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz)



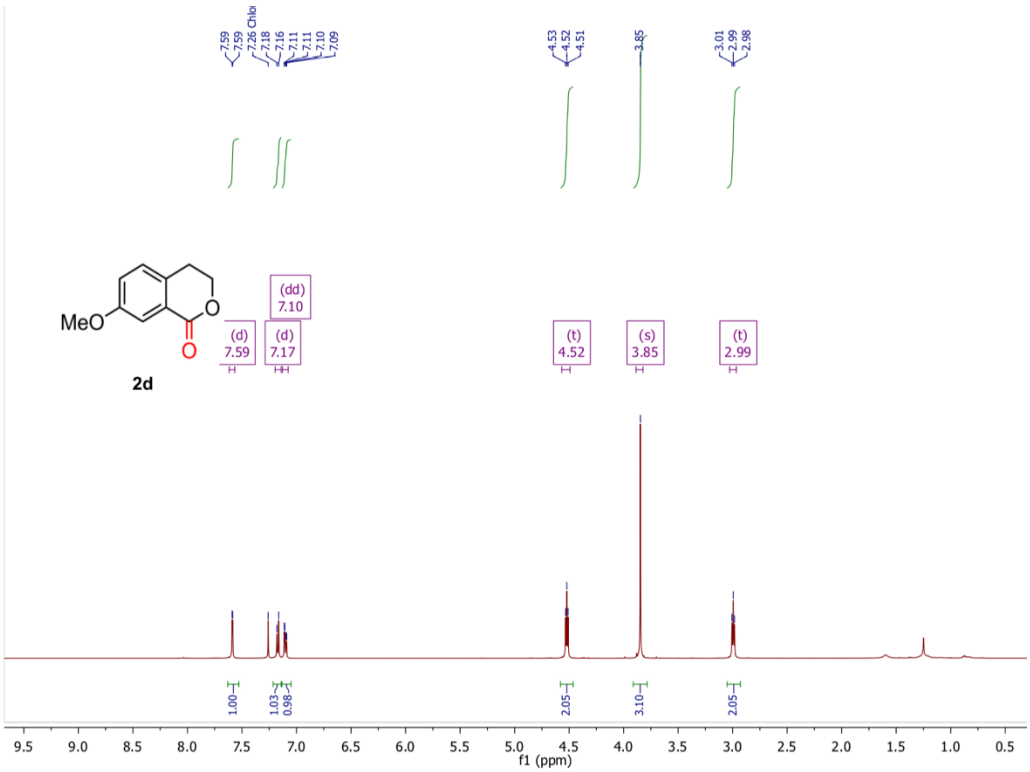
^{1}H NMR ($CDCl_3$, 300 MHz)



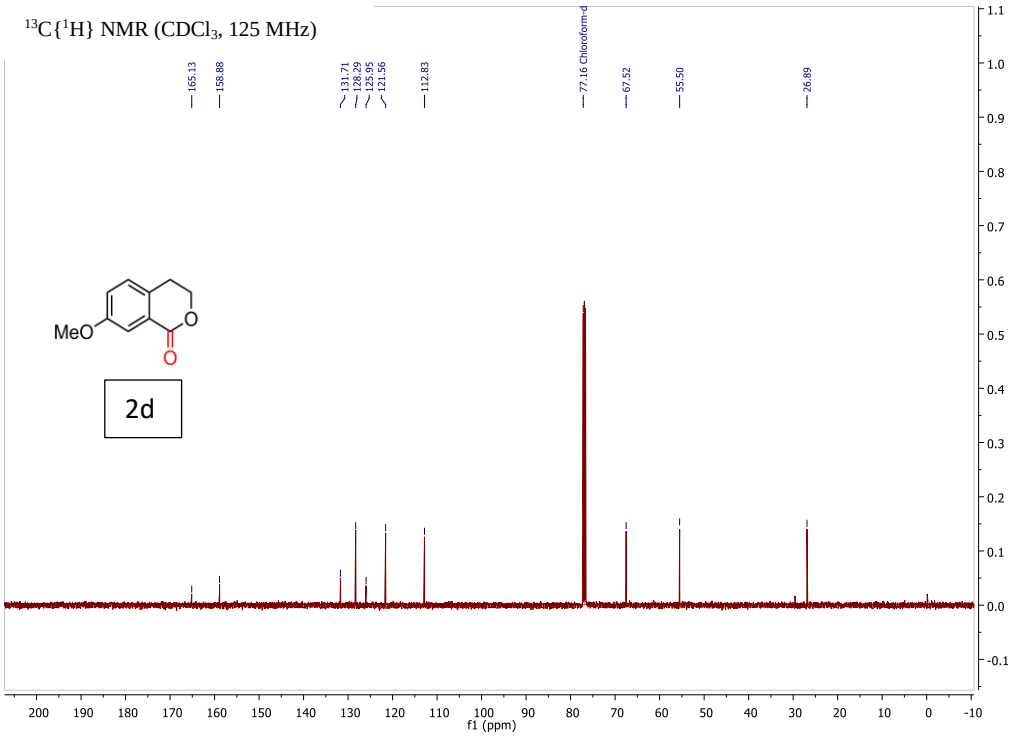
^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz)



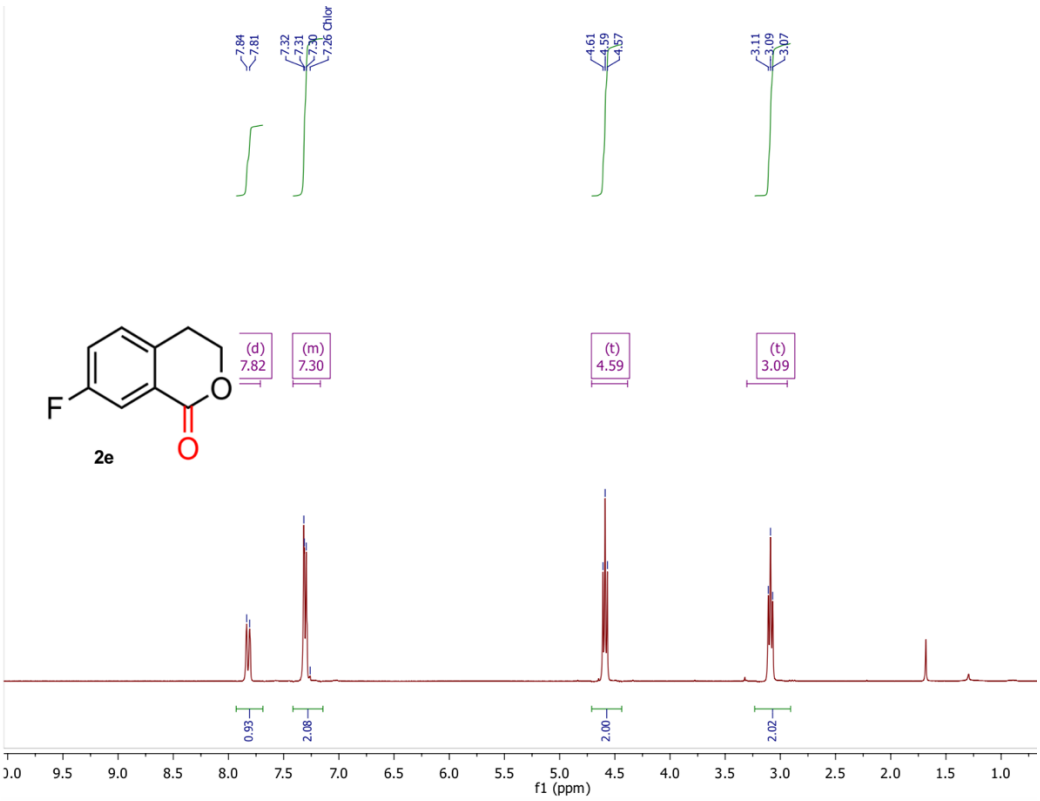
^{1}H NMR ($CDCl_3$, 500 MHz)



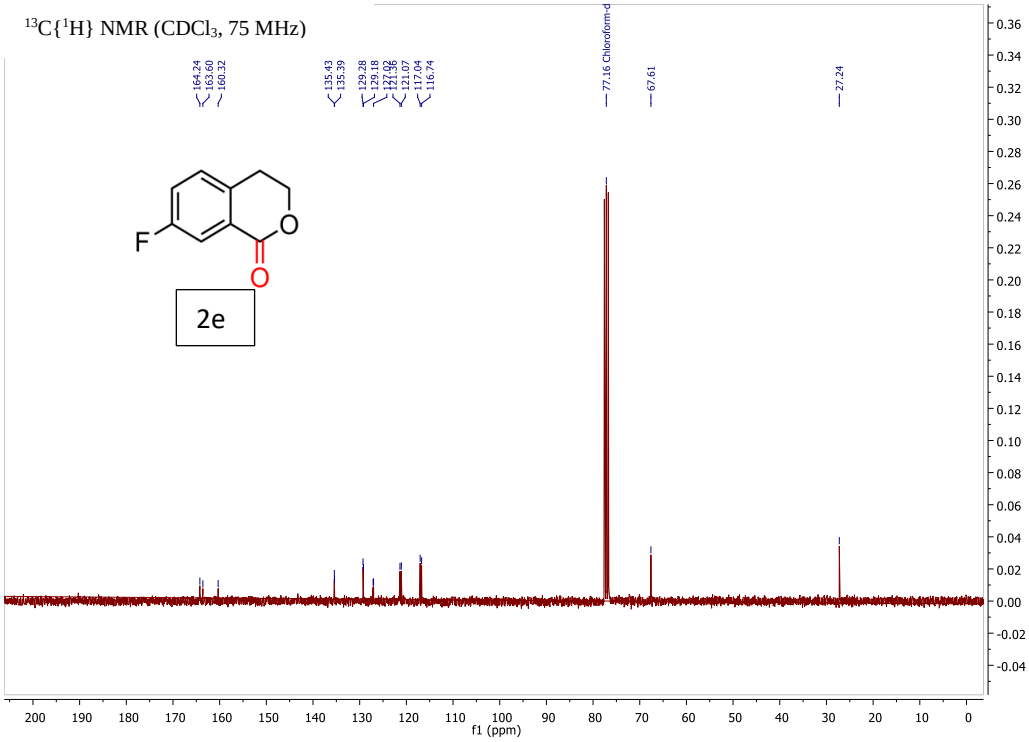
^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz)



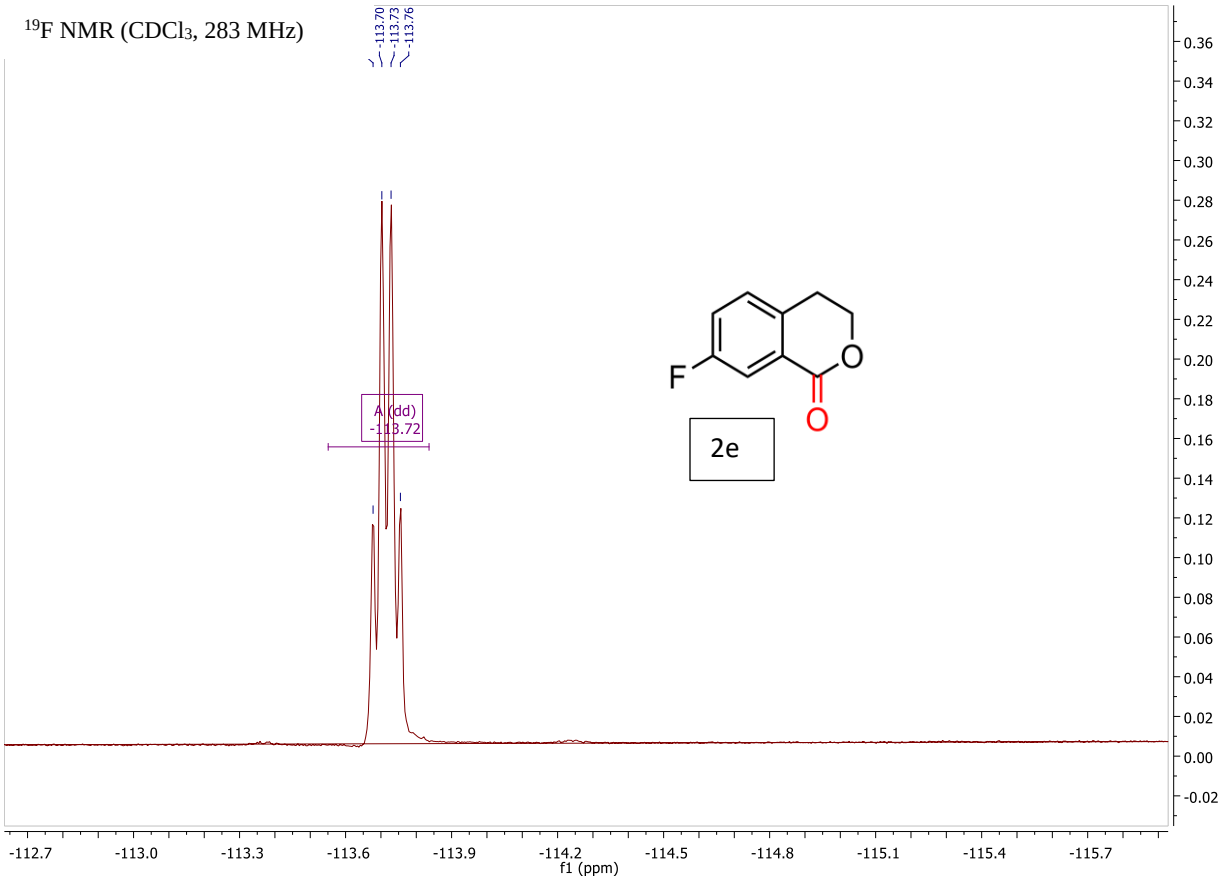
^{1}H NMR ($CDCl_3$, 300 MHz)



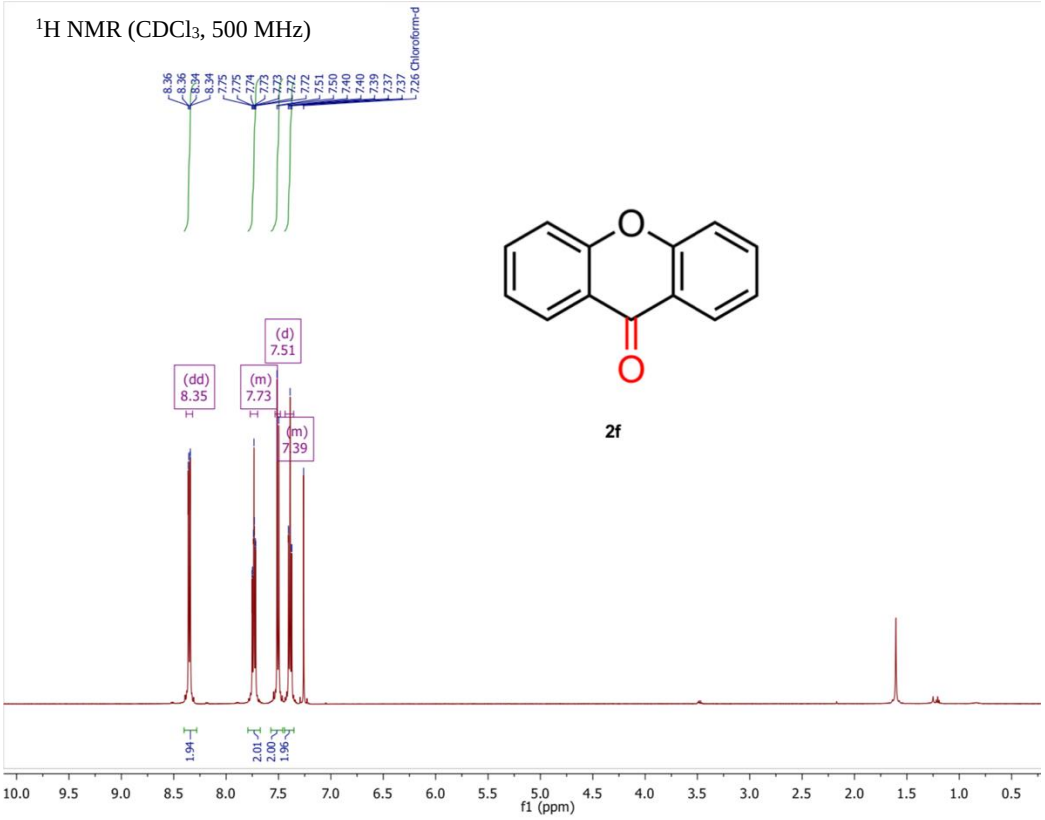
^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz)



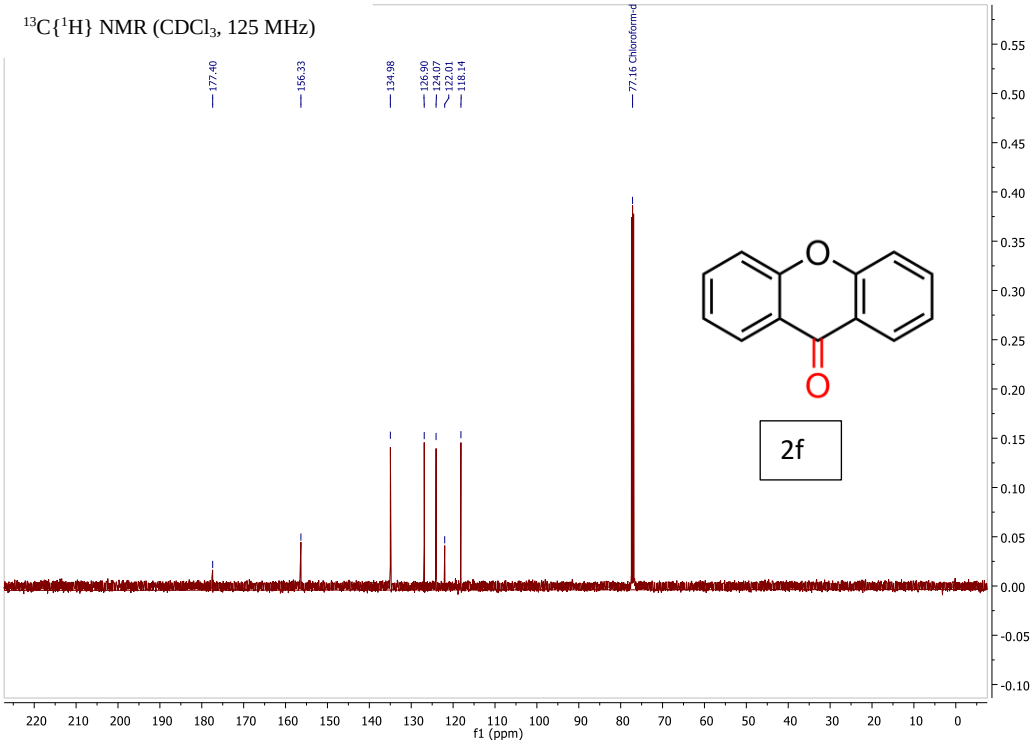
^{19}F NMR ($CDCl_3$, 283 MHz)

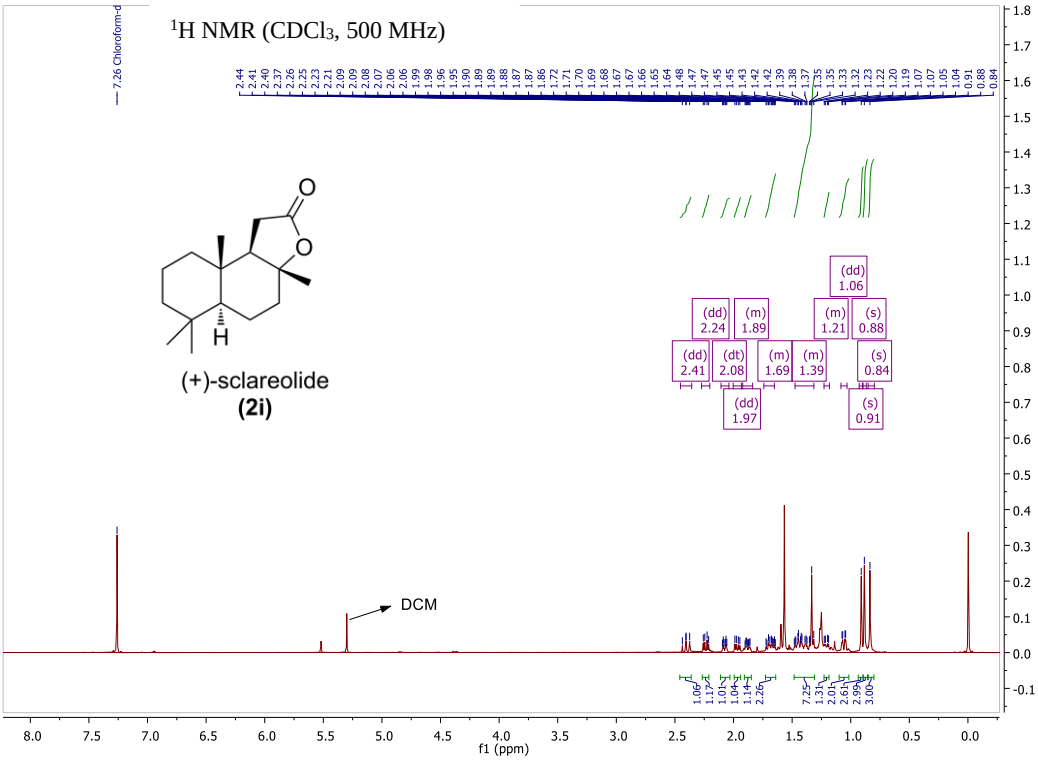


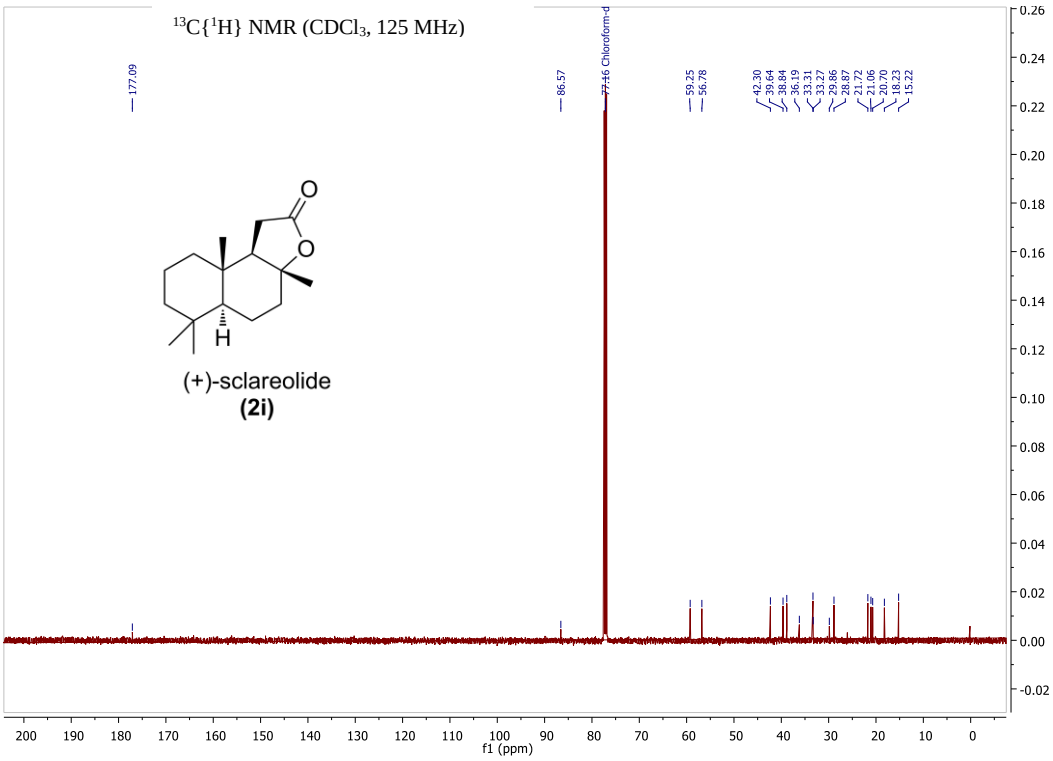
^{1}H NMR ($CDCl_3$, 500 MHz)



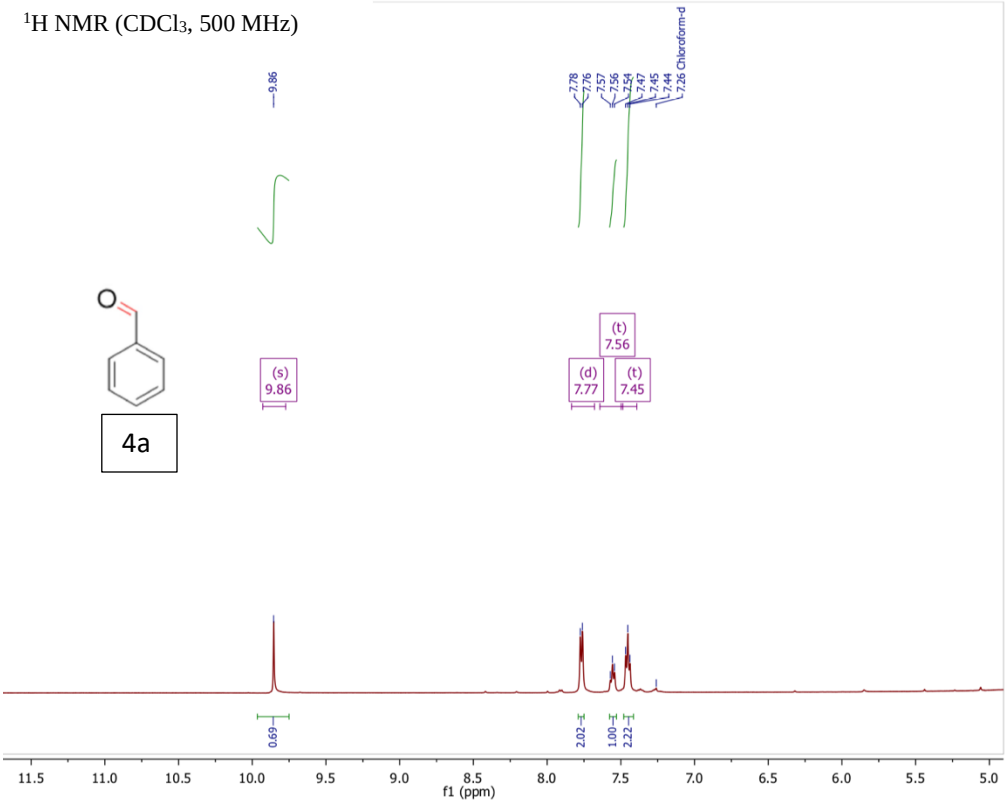
^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz)



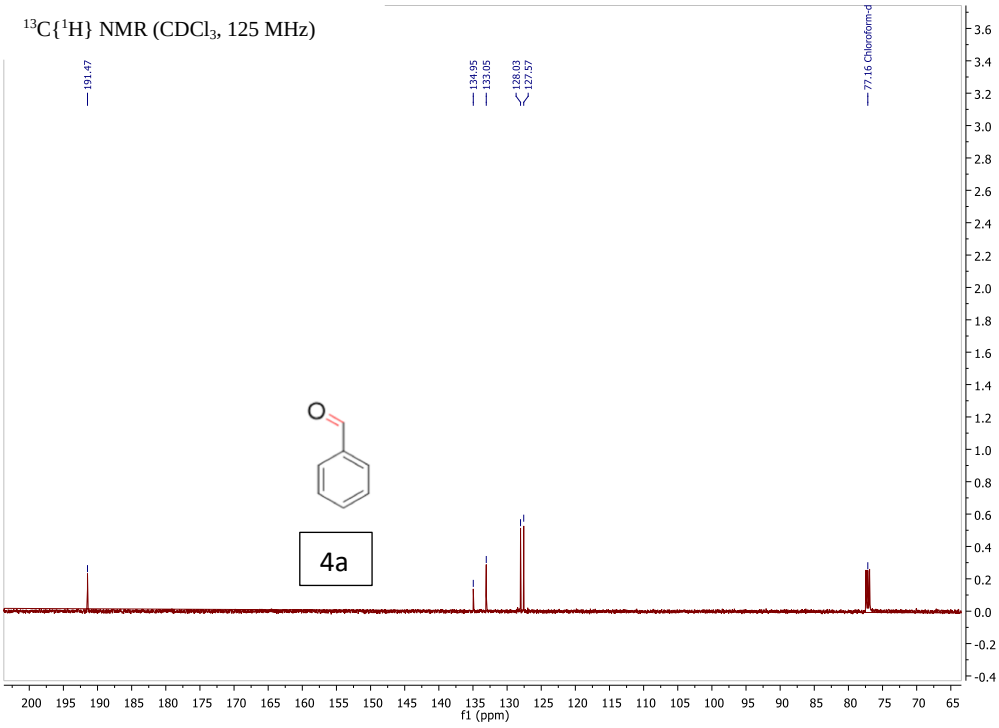

^{1}H NMR (CDCl$_3$, 500 MHz)
7.26 Chloroform-d
(+)-sclareolide
(2i)
(dd) 2.24
(m) 1.89
(dd) 2.41
(dt) 2.08
(m) 1.69
(dd) 1.97
(dd) 1.06
(m) 1.21
(s) 0.88
(m) 1.39
(s) 0.84
(s) 0.91
DCM
f1 (ppm)


^{13}C{^{1}H} NMR (CDCl$_3$, 125 MHz)
177.09
86.57
77.46 Chloroform-d
59.25
56.78
42.30
39.64
38.84
36.19
33.31
33.27
29.86
28.87
21.72
21.06
20.70
18.23
15.22
(+)-sclareolide
(2i)
f1 (ppm)

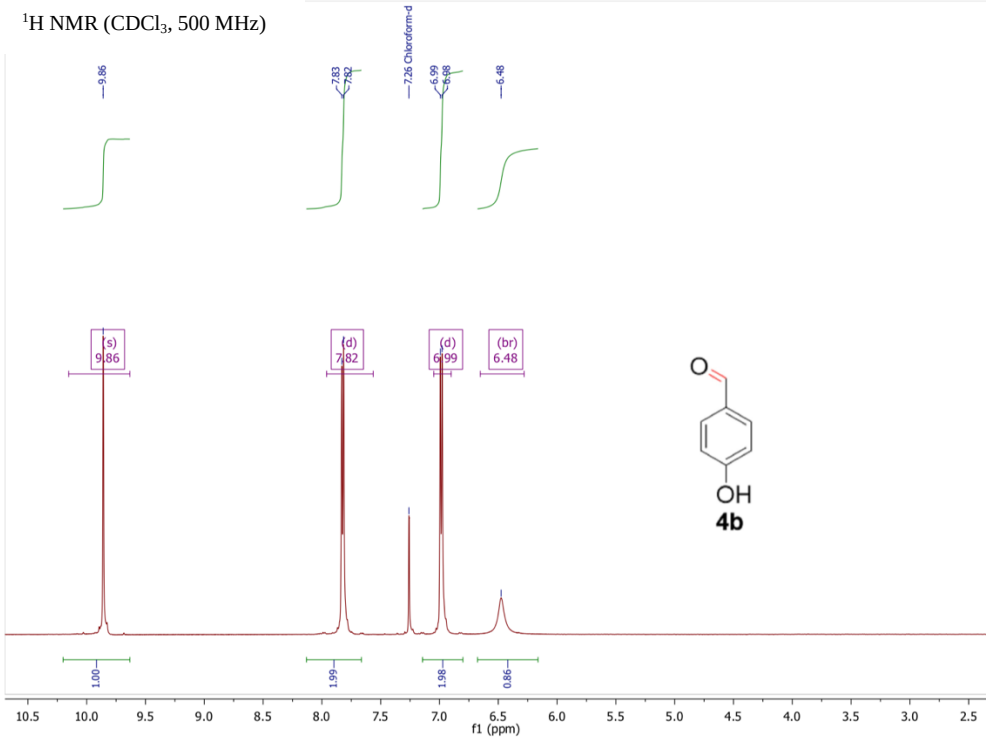
^{1}H NMR ($CDCl_3$, 500 MHz)



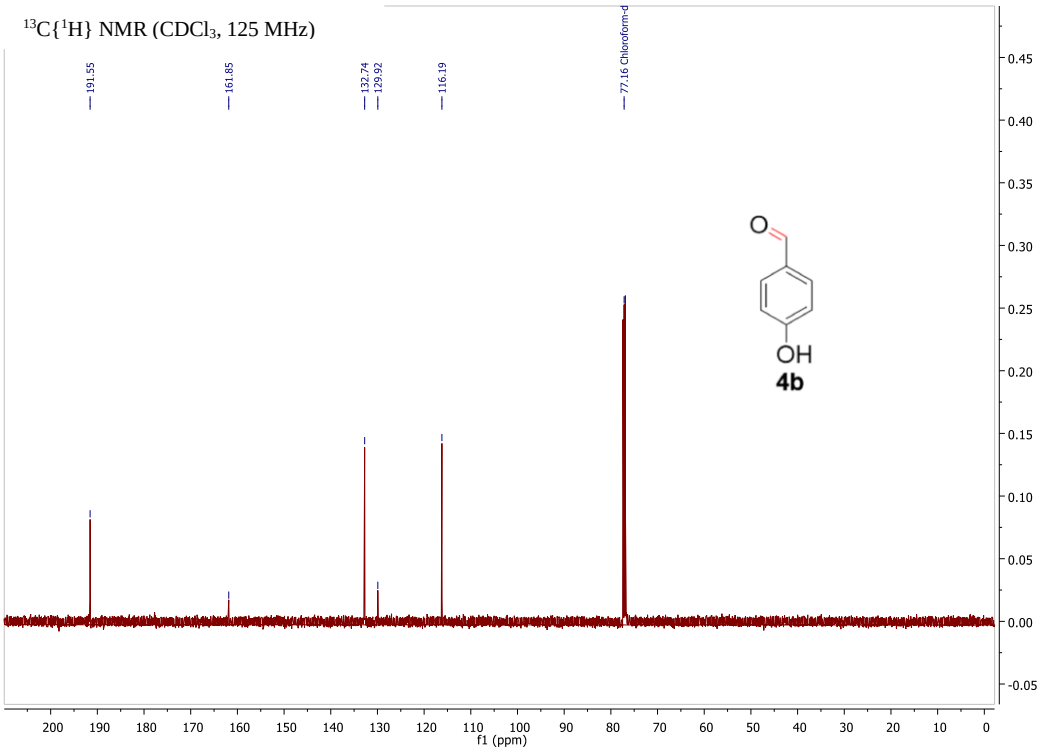
^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz)



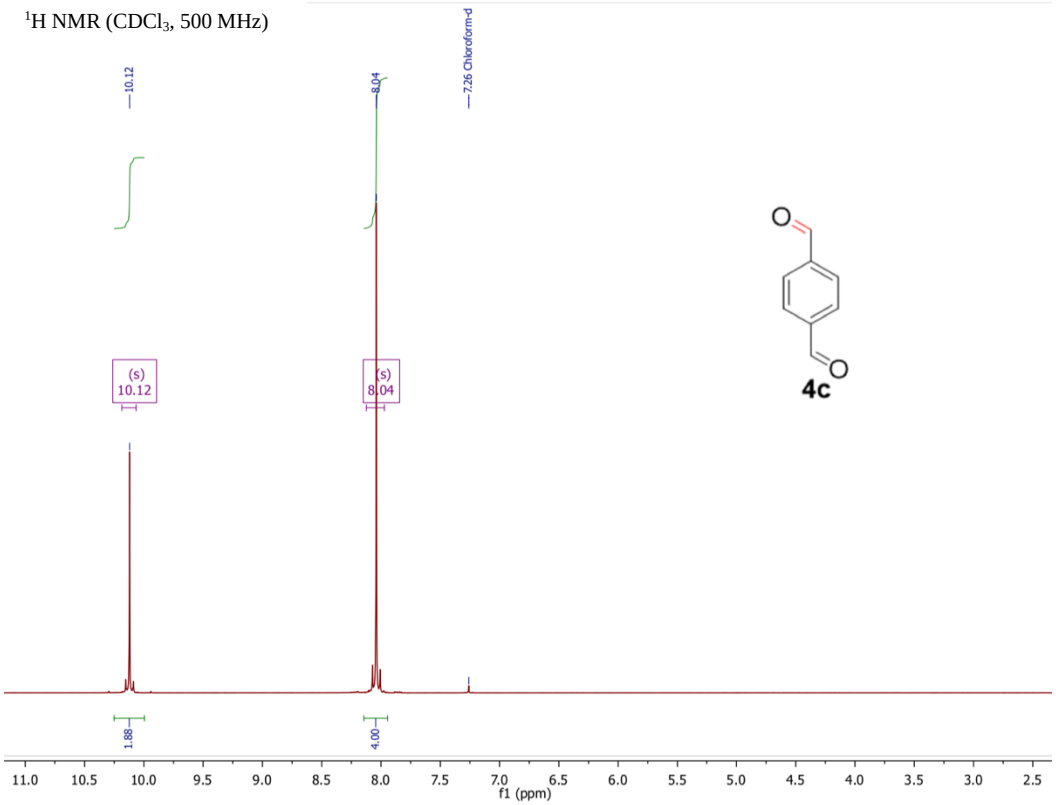
^{1}H NMR ($CDCl_3$, 500 MHz)



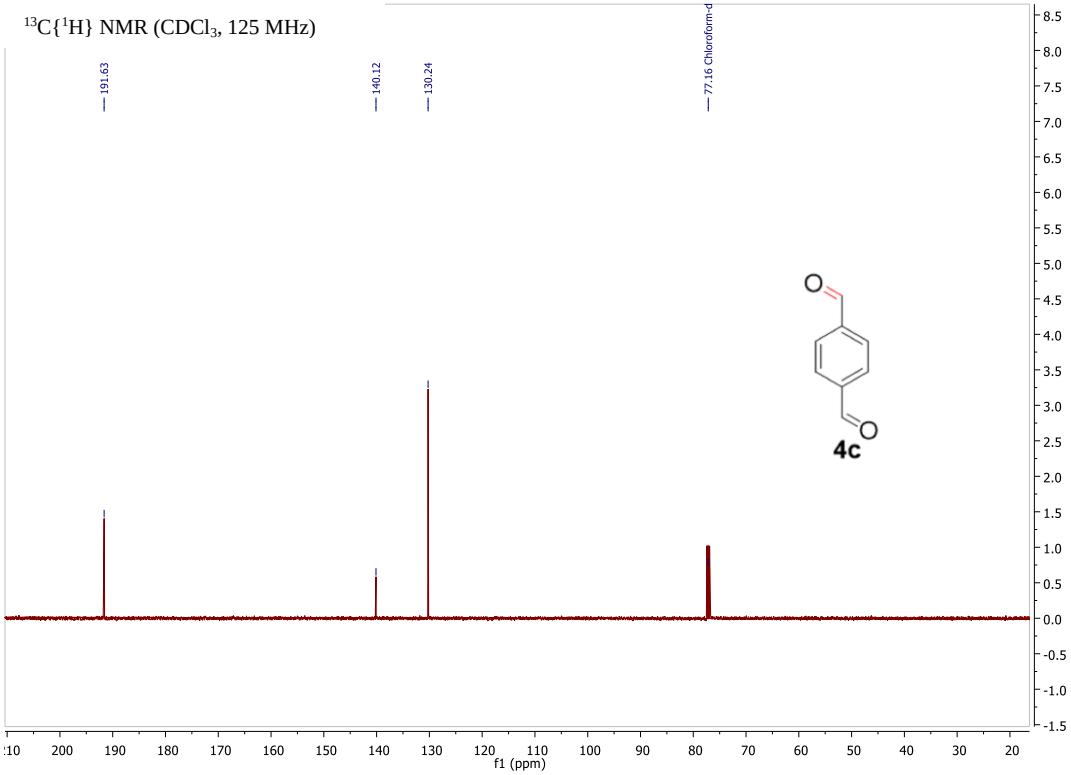
^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz)



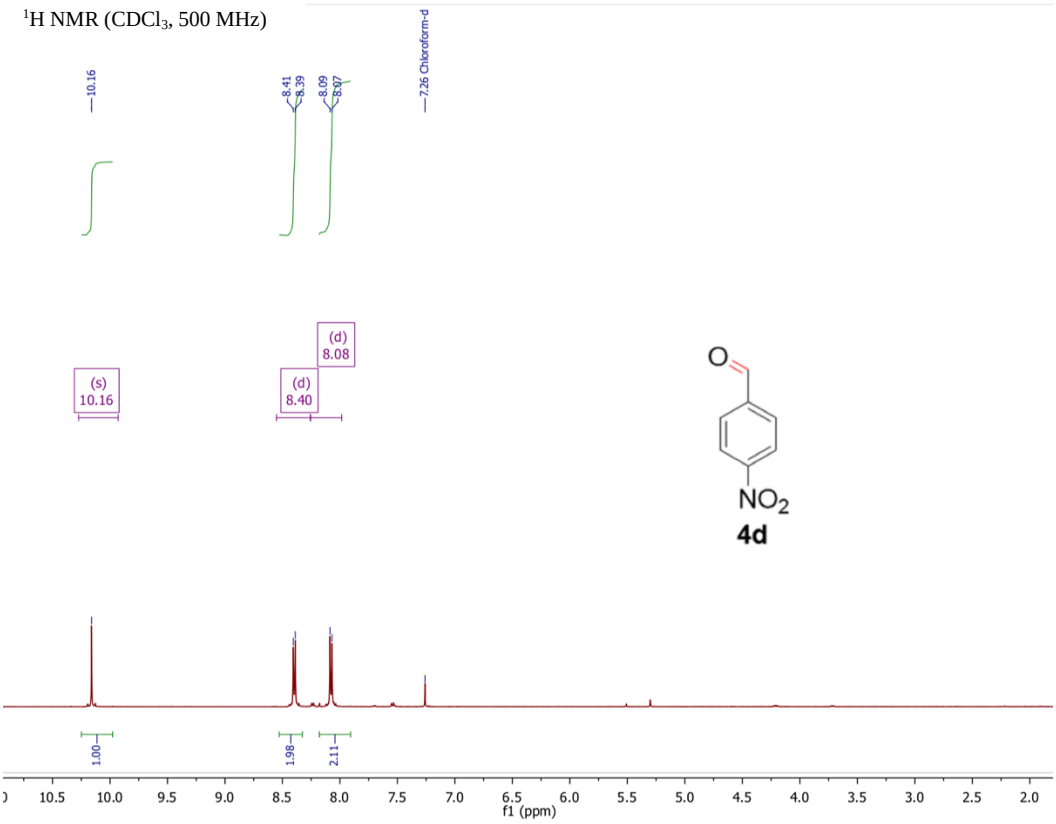
^{1}H NMR ($CDCl_3$, 500 MHz)



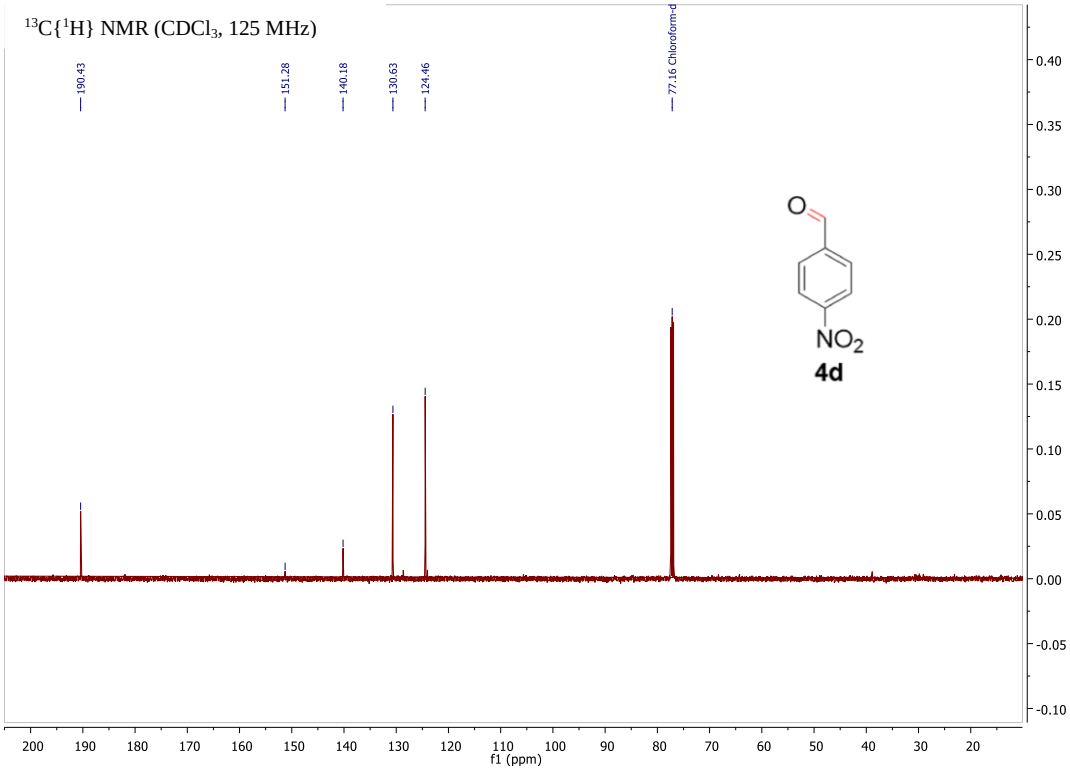
^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz)



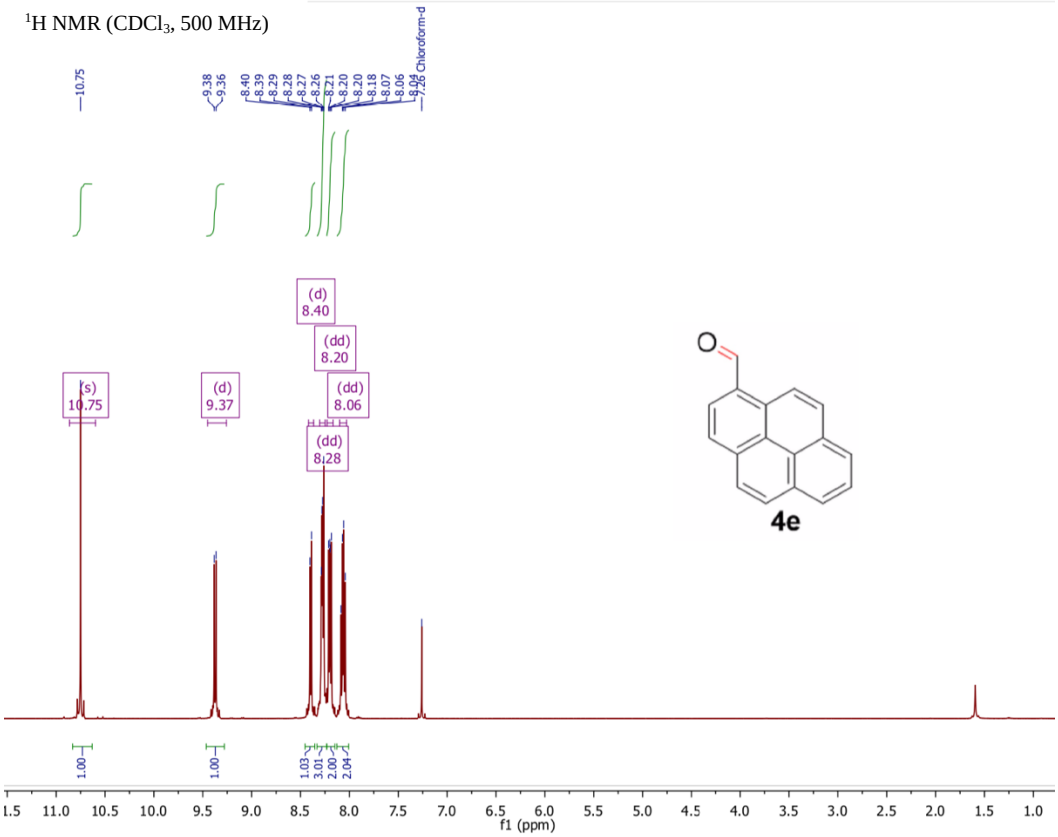
^{1}H NMR ($CDCl_3$, 500 MHz)



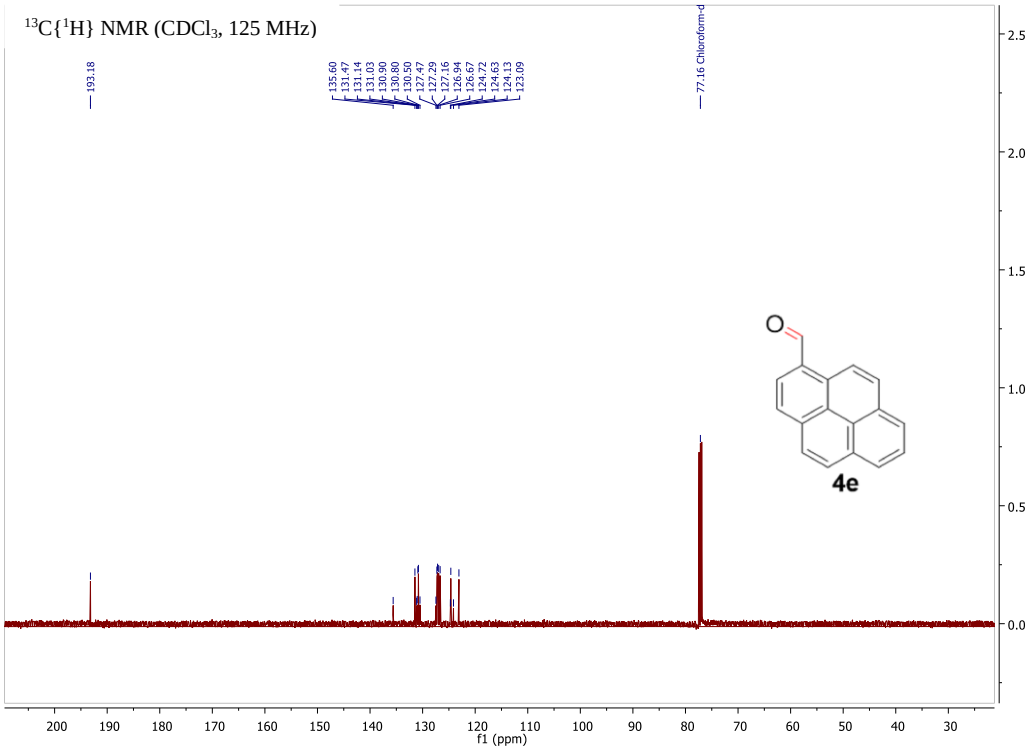
^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz)



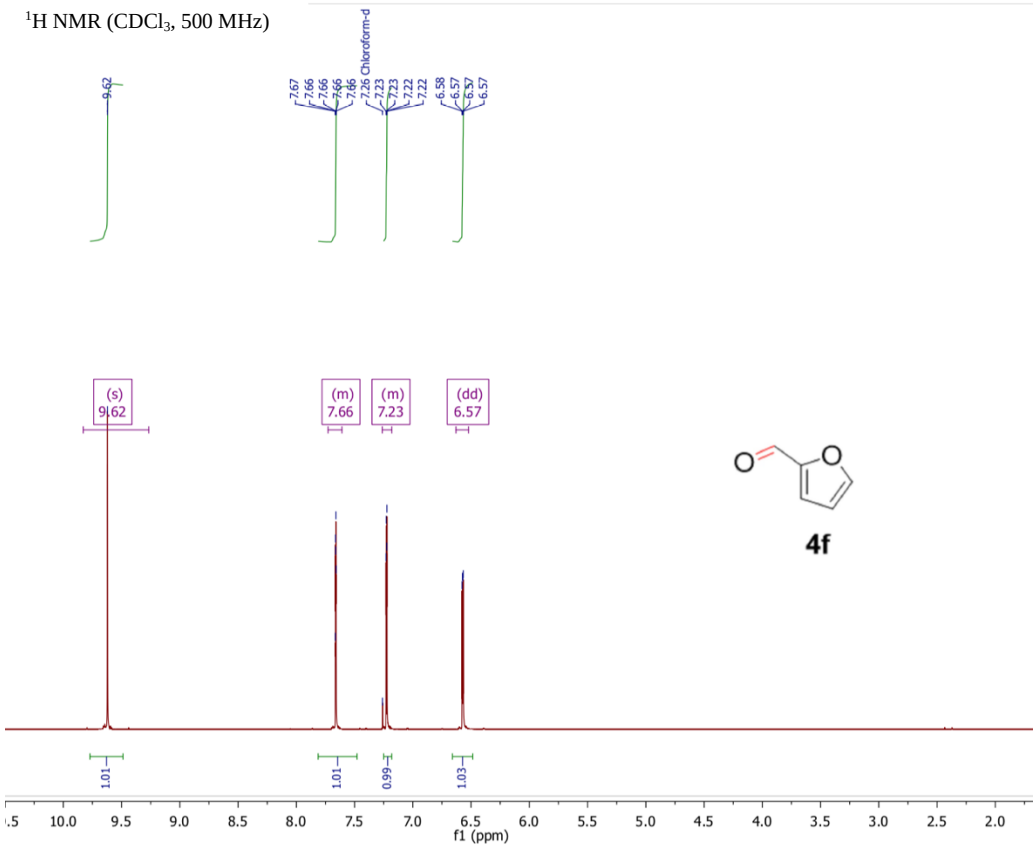
^{1}H NMR ($CDCl_3$, 500 MHz)



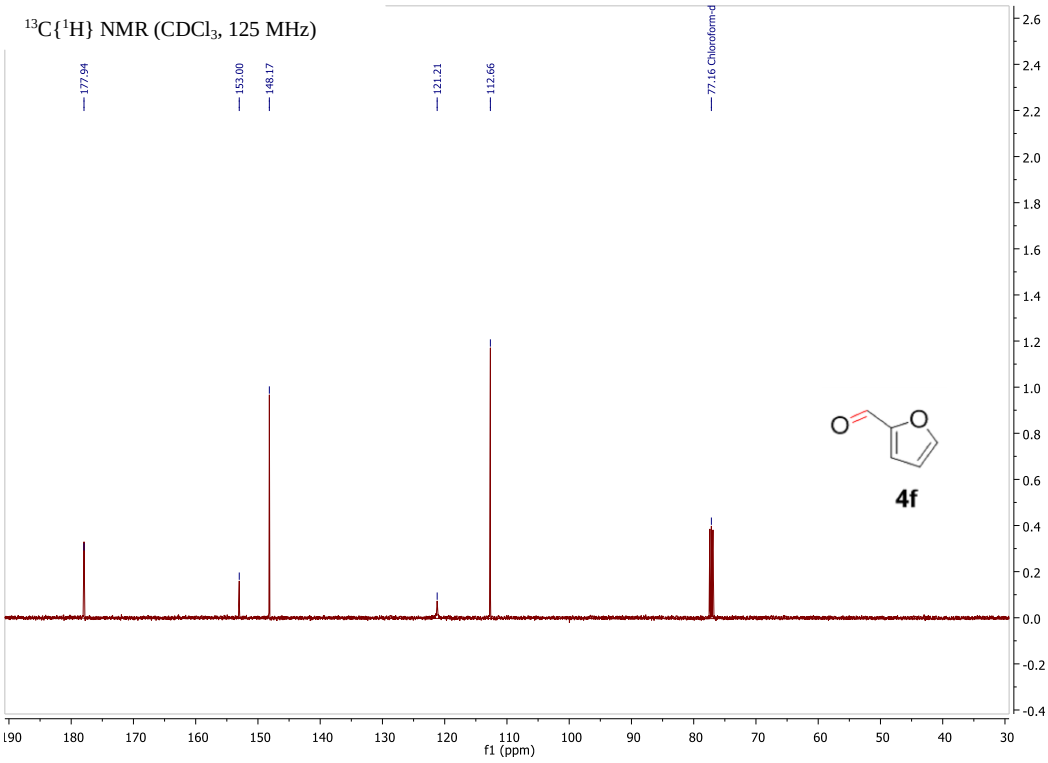
^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz)



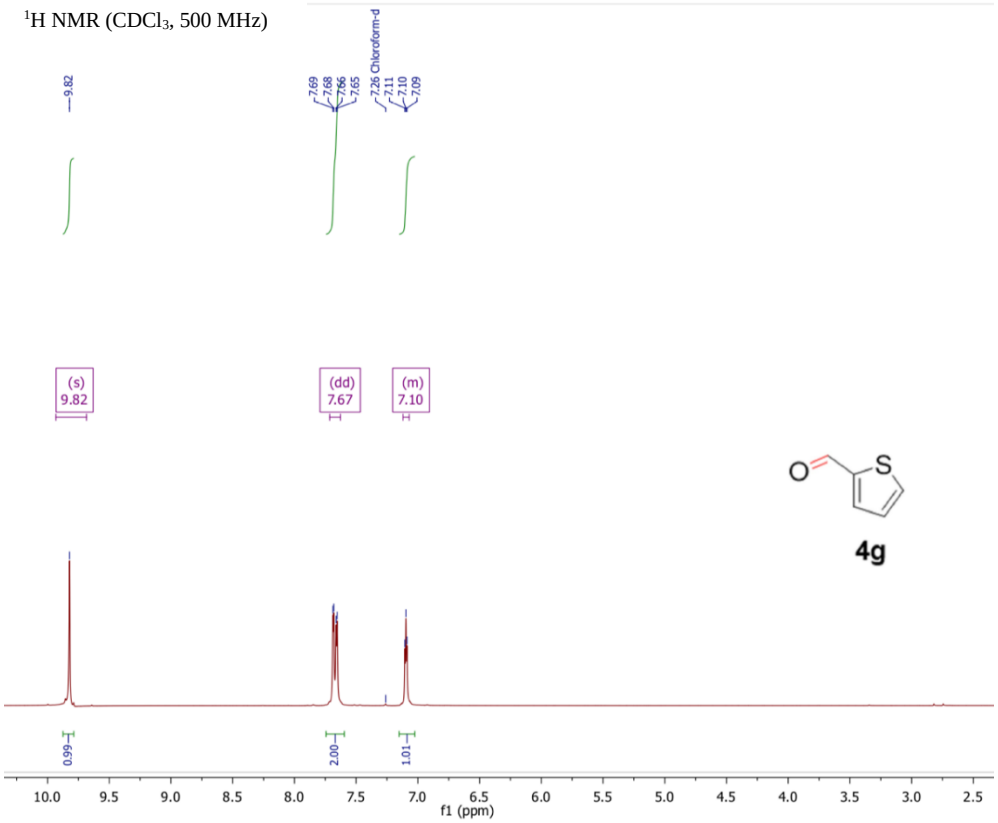
^{1}H NMR ($CDCl_3$, 500 MHz)



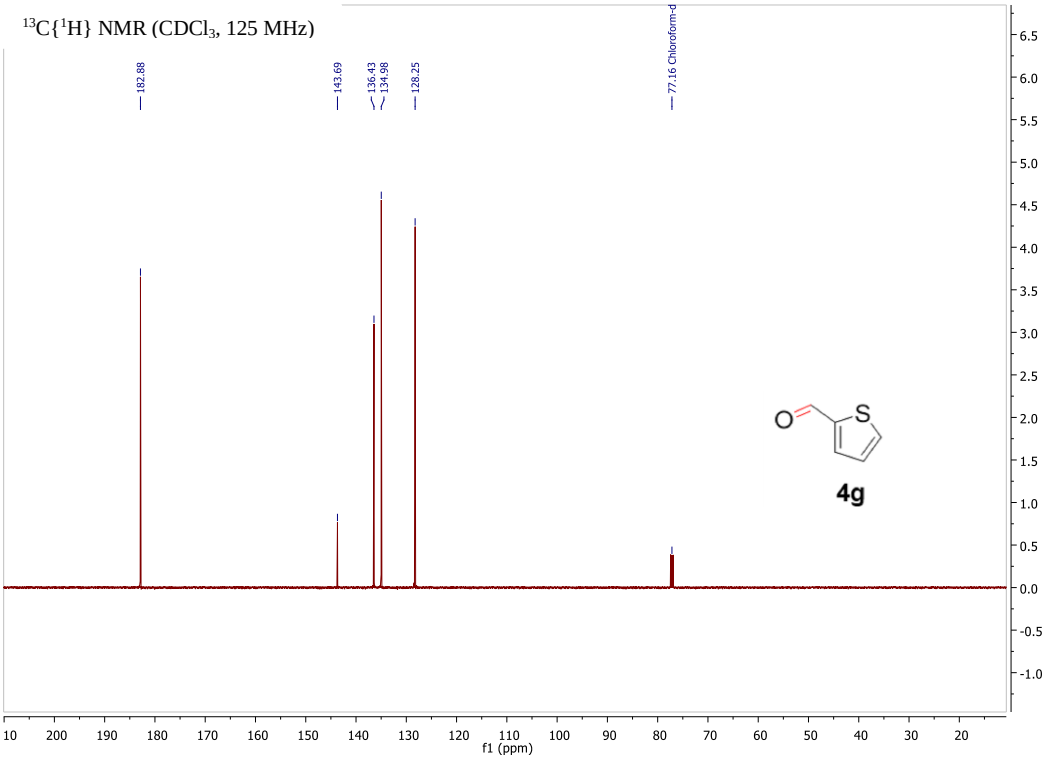
^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz)



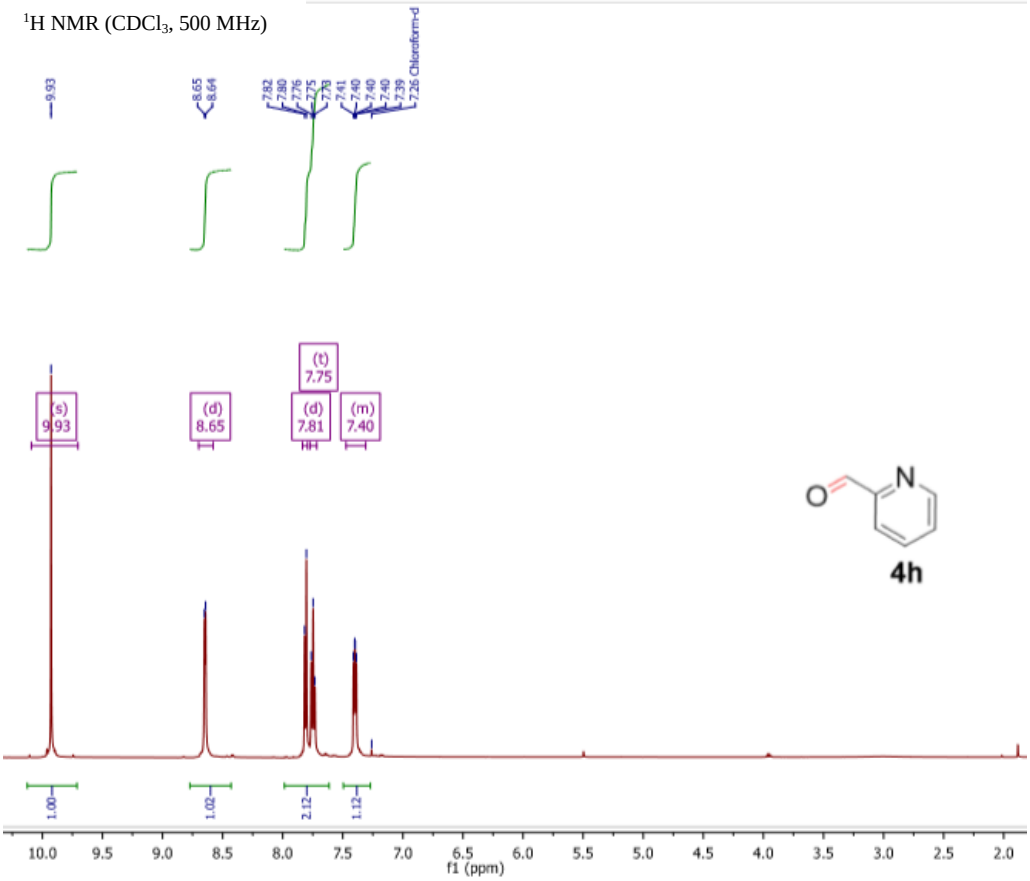
^{1}H NMR ($CDCl_3$, 500 MHz)

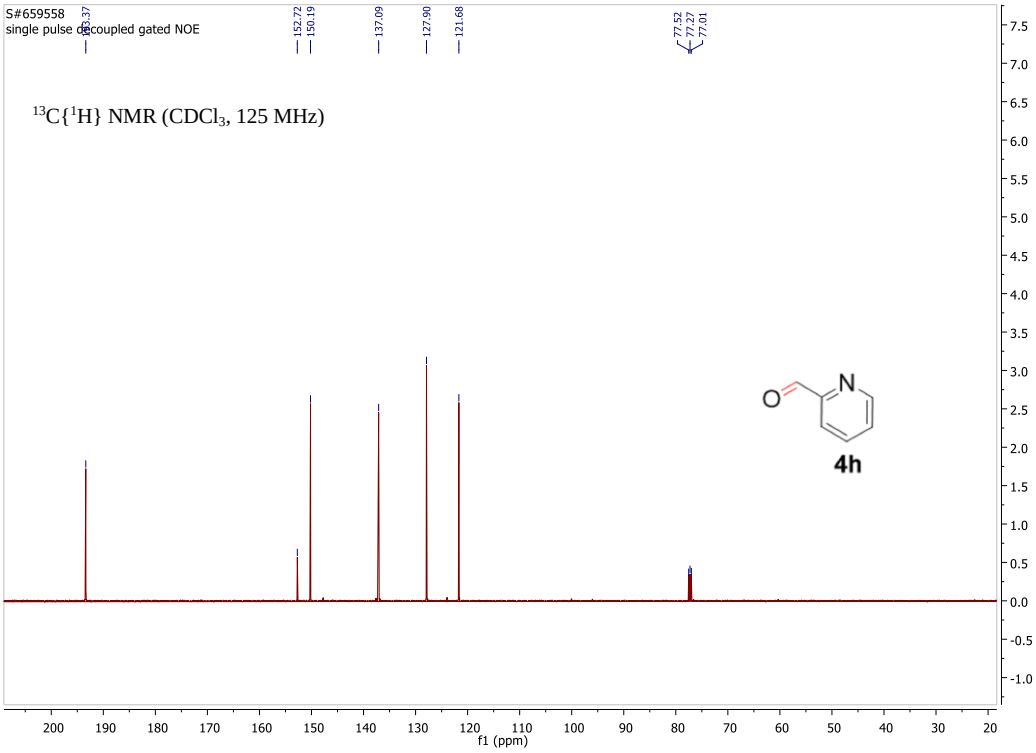


^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz)

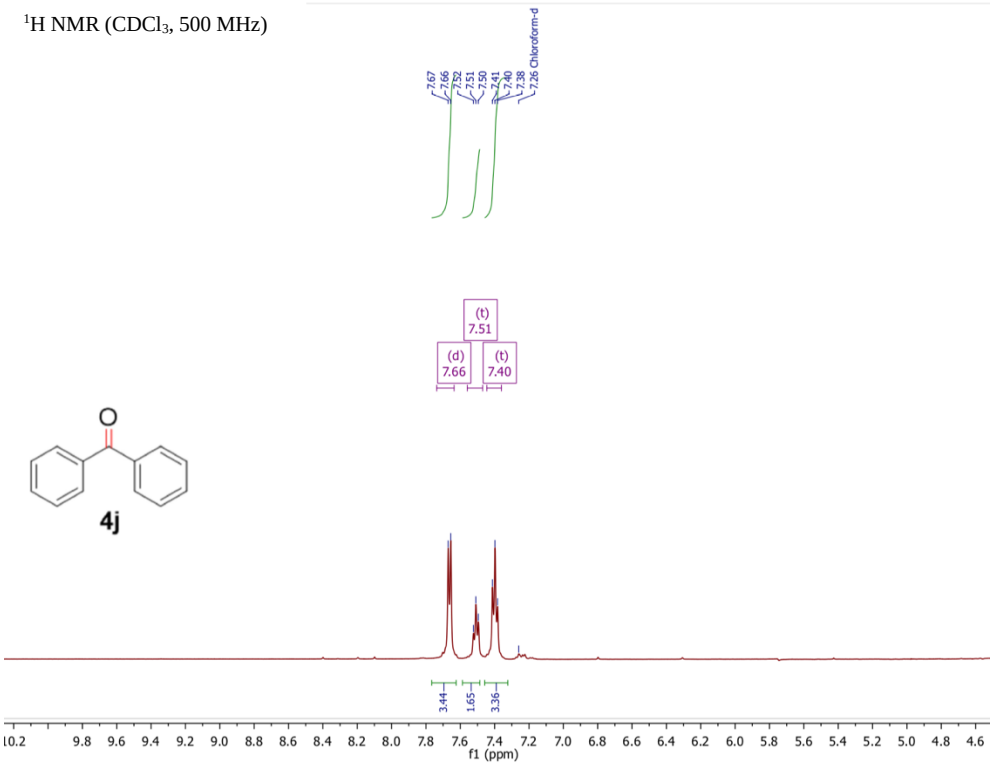


^{1}H NMR ($CDCl_3$, 500 MHz)

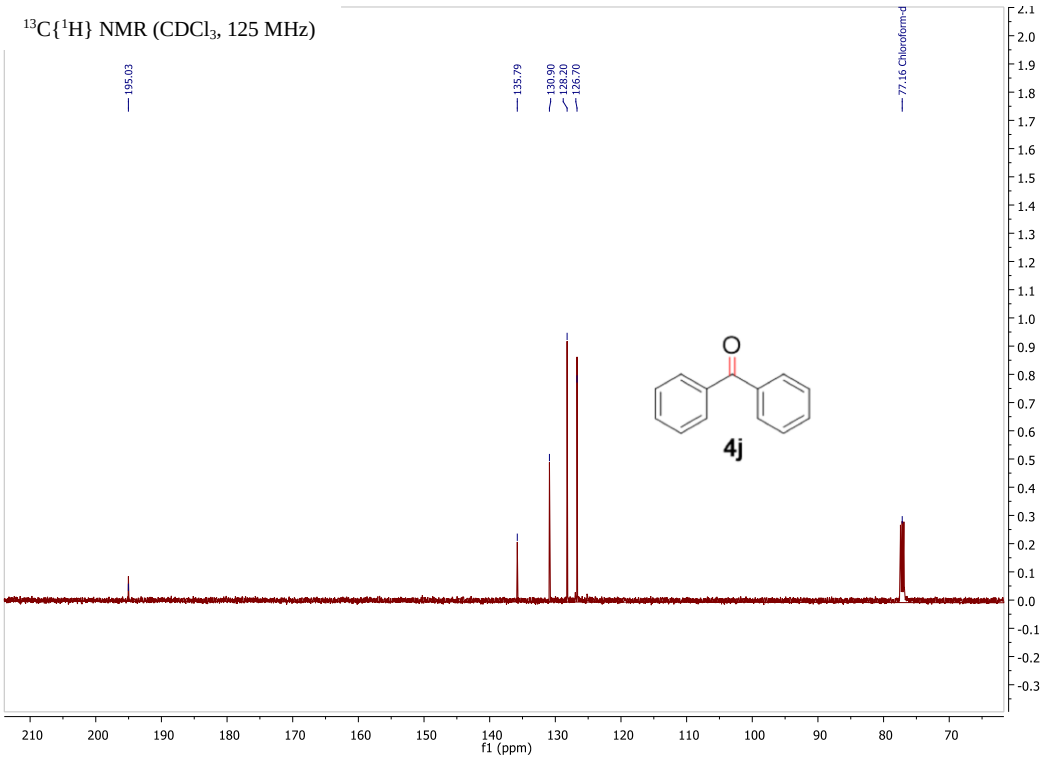




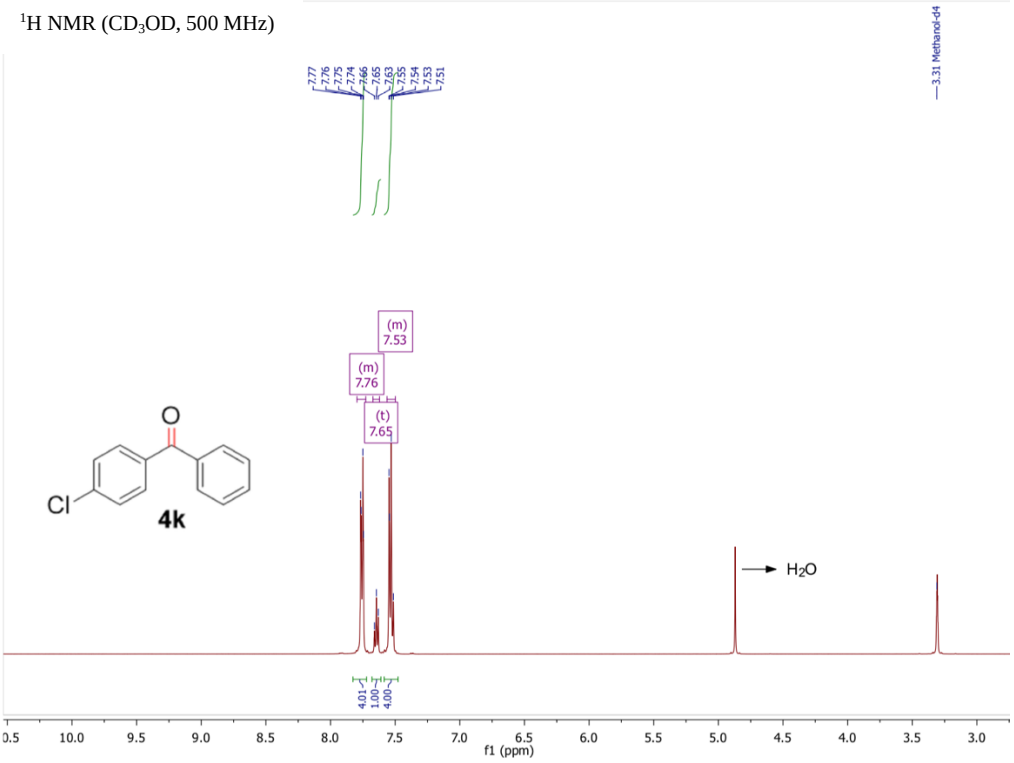
^{1}H NMR ($CDCl_3$, 500 MHz)



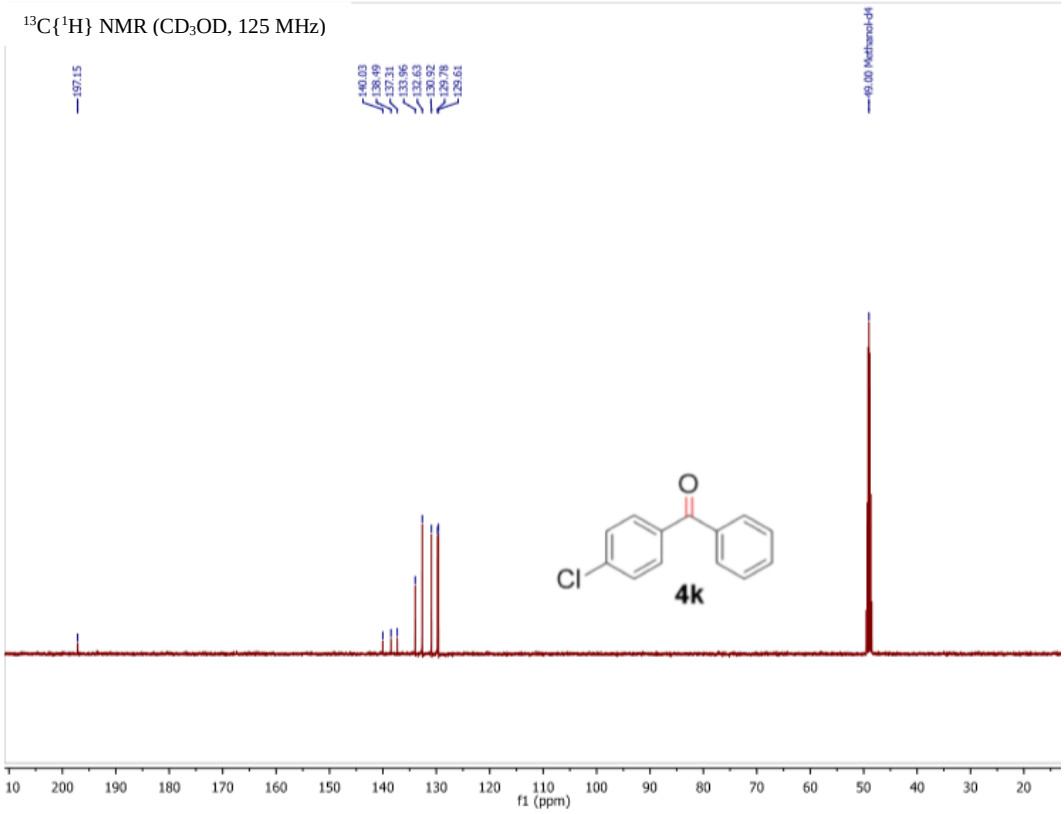
^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz)



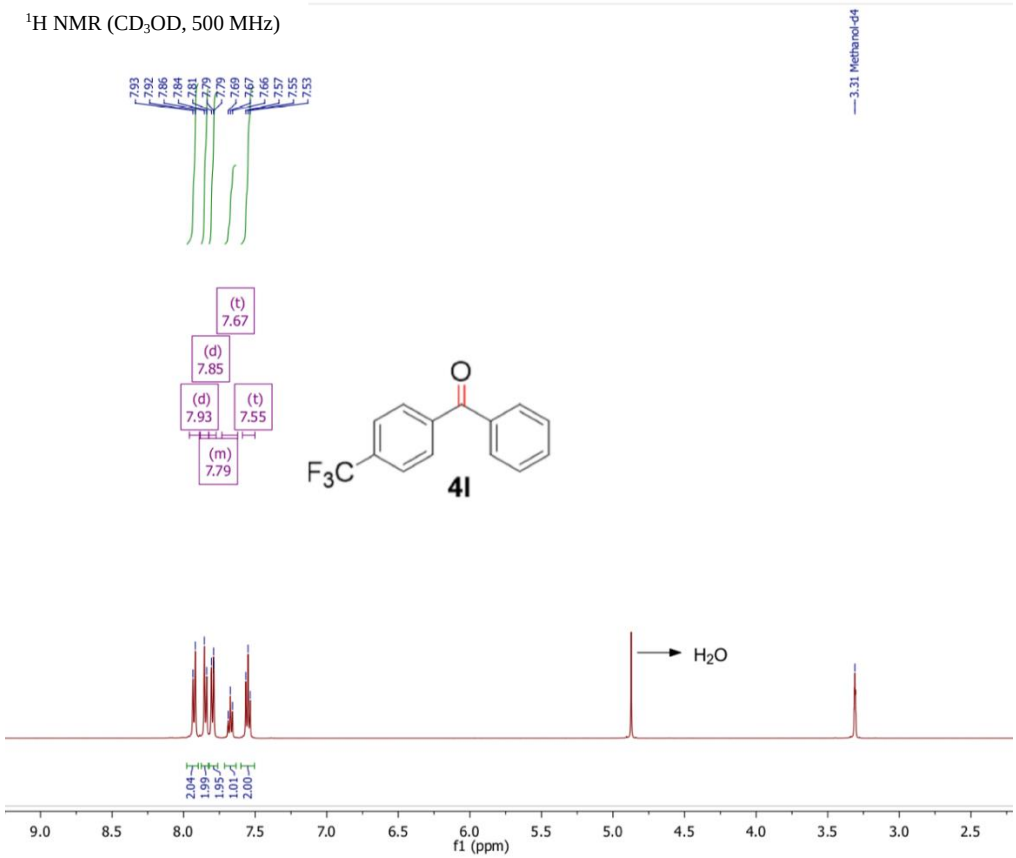
^{1}H NMR (CD_3OD, 500 MHz)



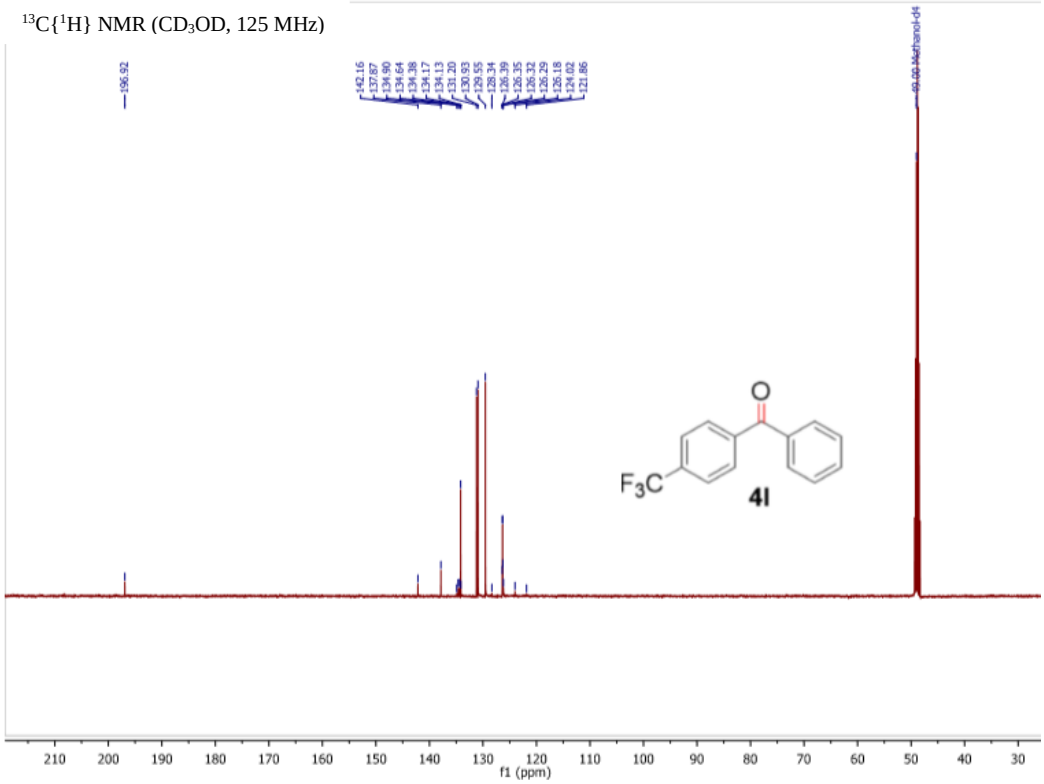
^{13}C{^{1}H} NMR (CD_3OD, 125 MHz)



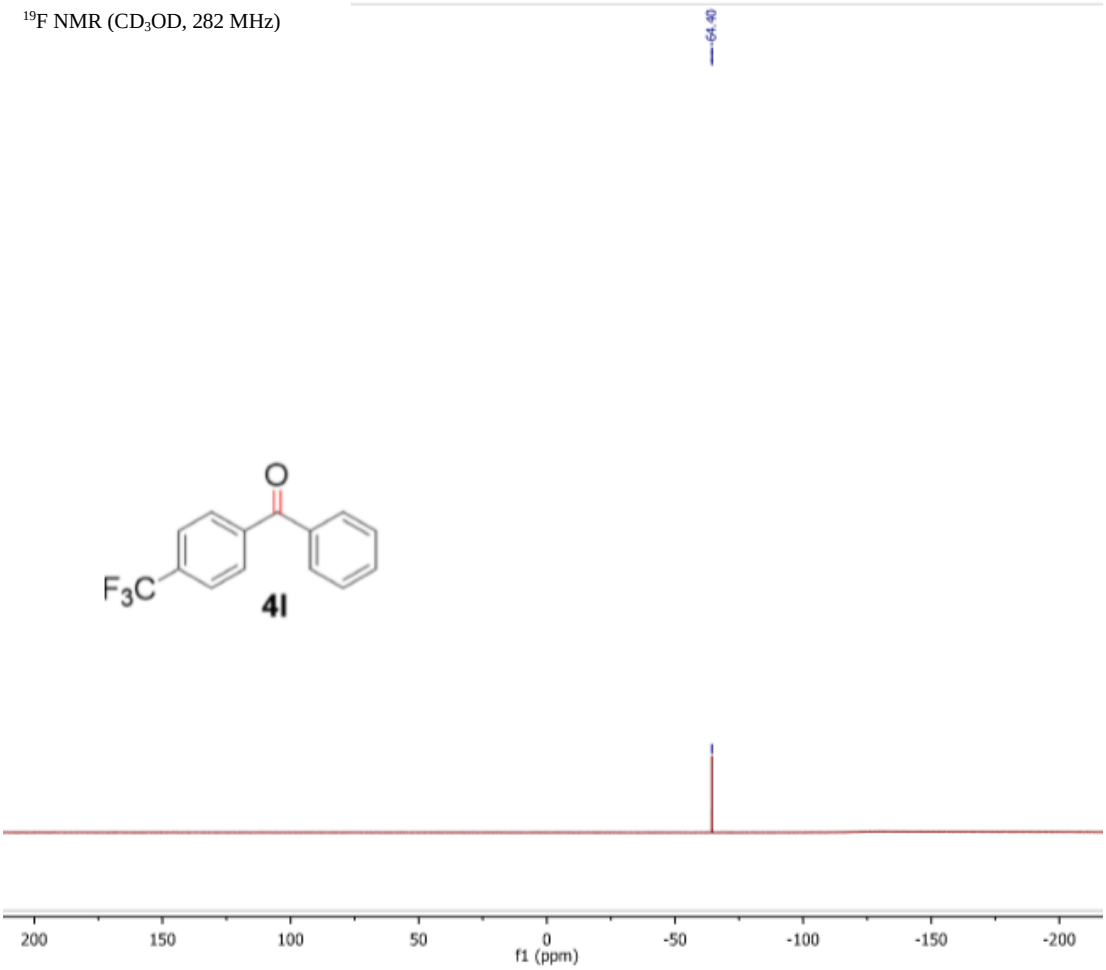
^{1}H NMR (CD_3OD, 500 MHz)



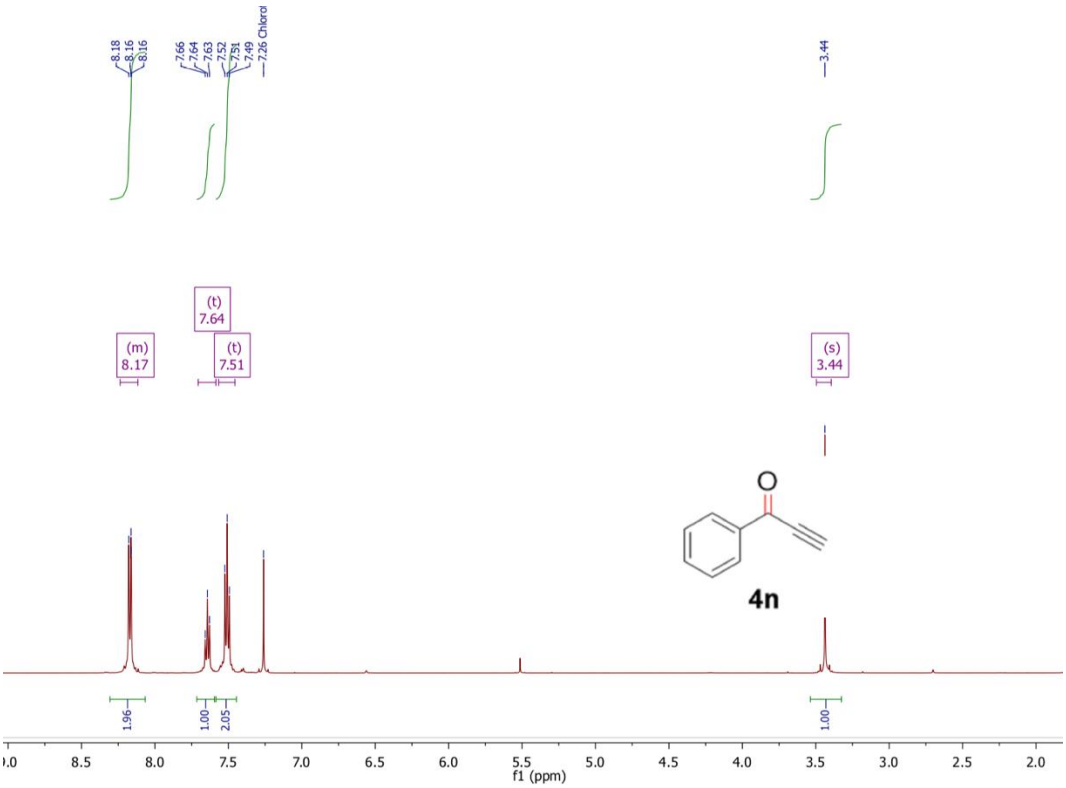
^{13}C{^{1}H} NMR (CD_3OD, 125 MHz)



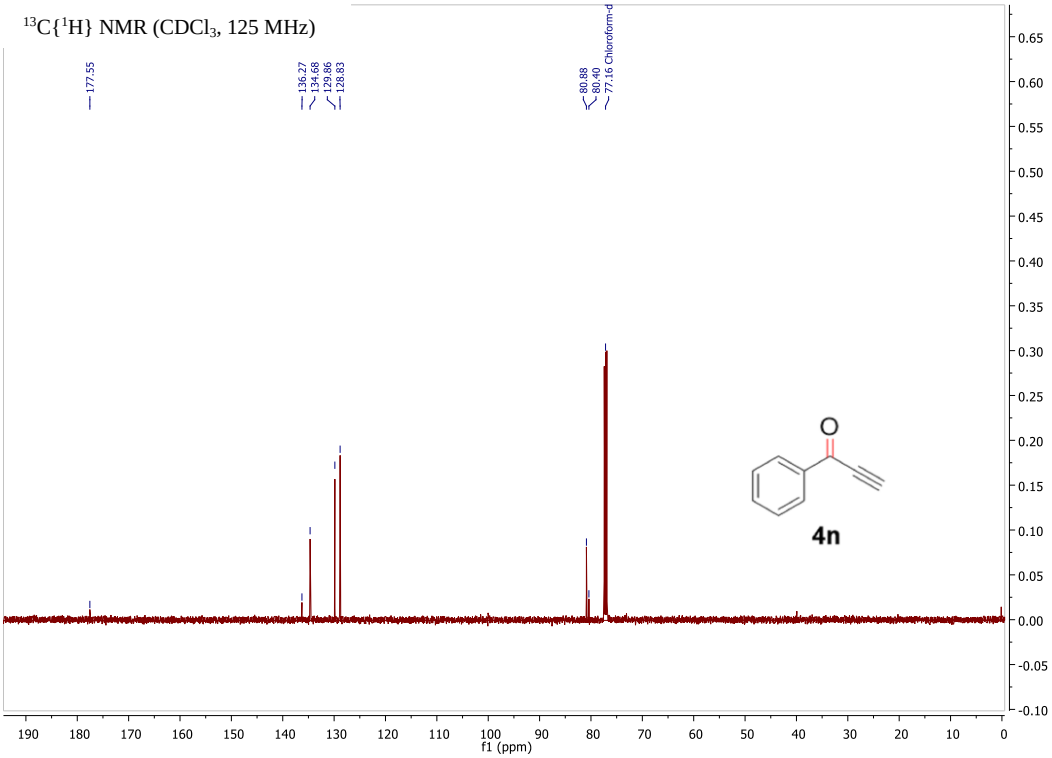
^{19}F NMR (CD_3OD, 282 MHz)



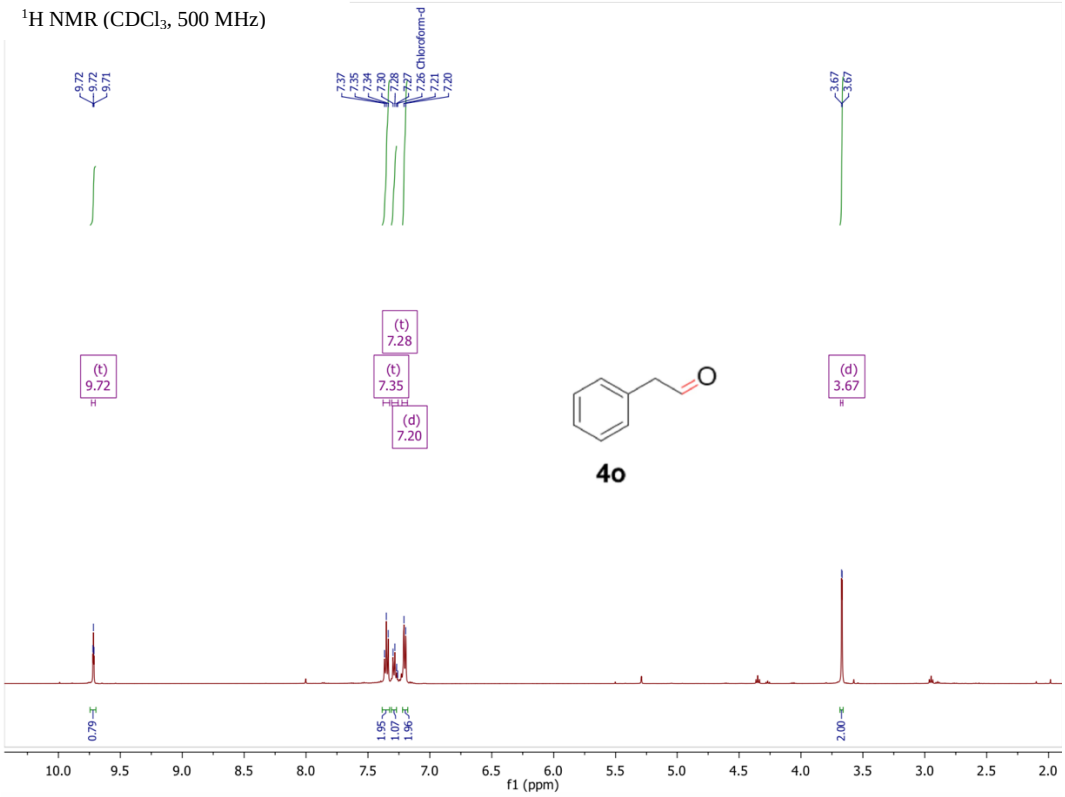
^{1}H NMR ($CDCl_3$, 500 MHz)



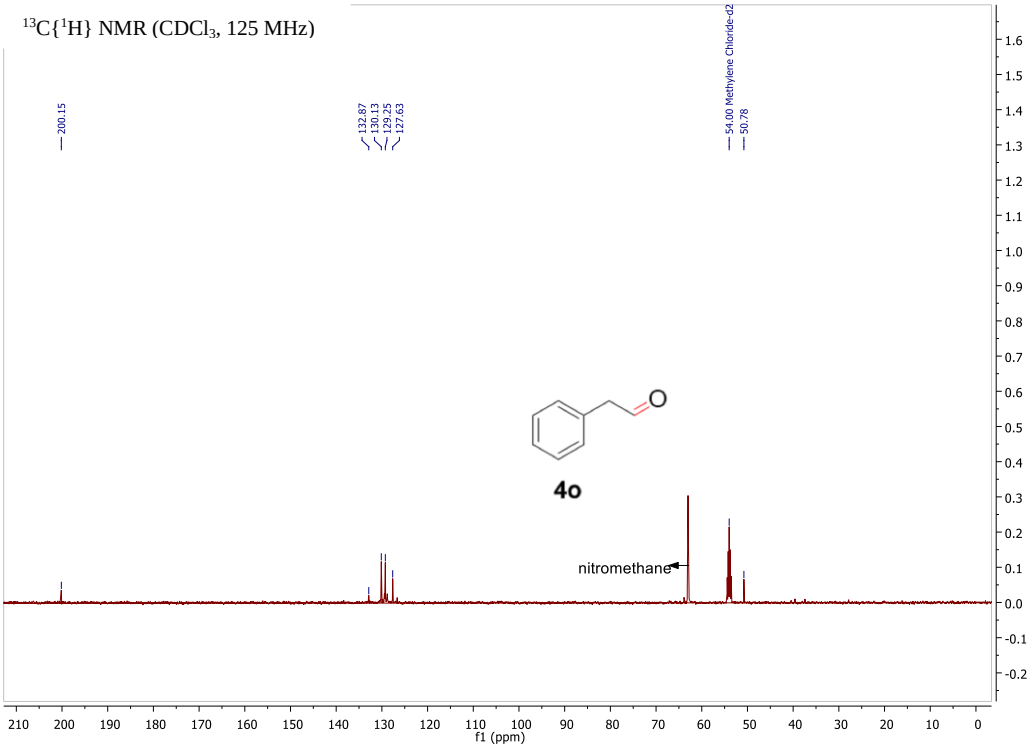
^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz)



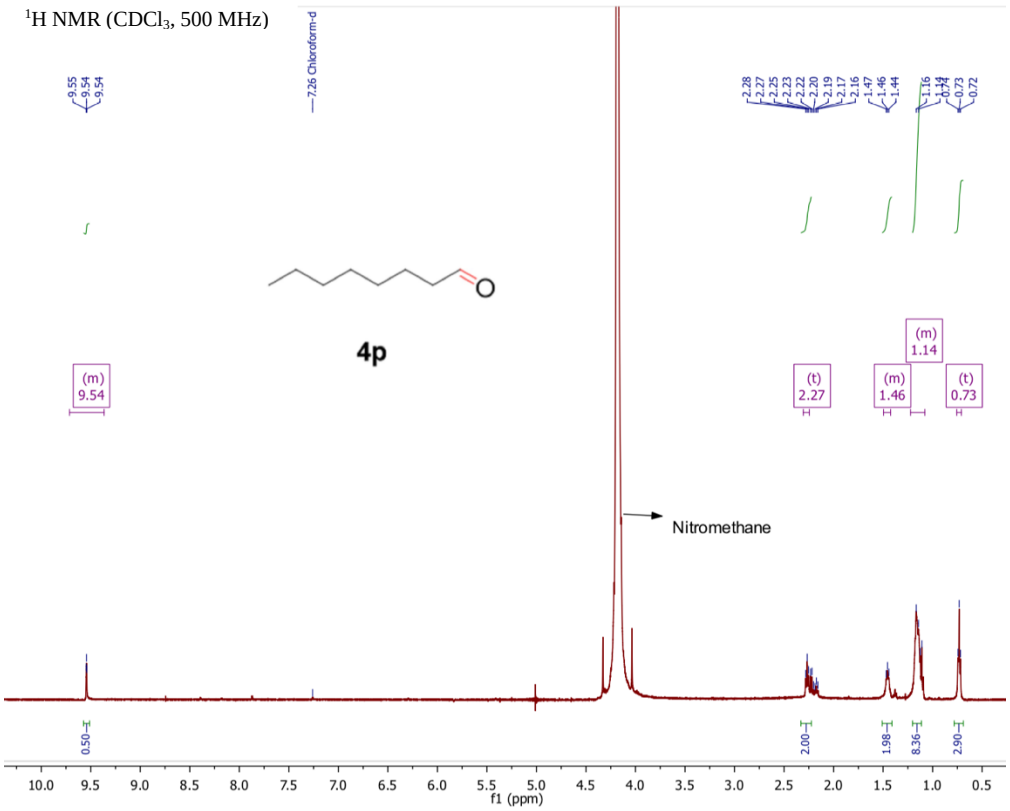
^{1}H NMR ($CDCl_3$, 500 MHz)



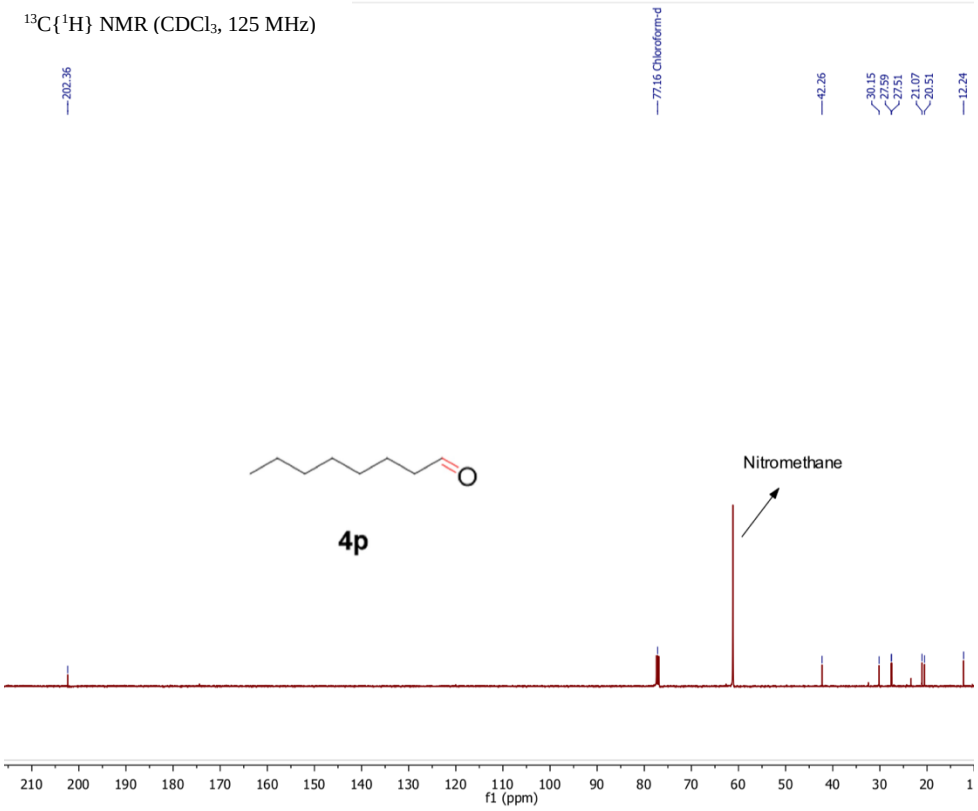
^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz)



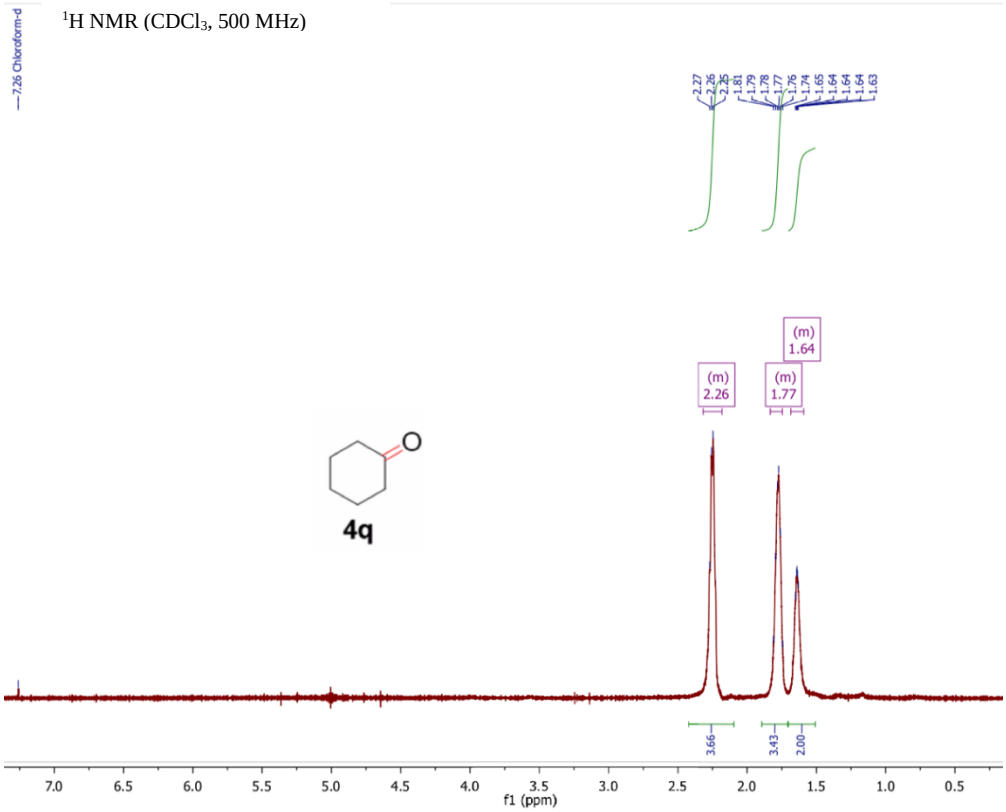
^{1}H NMR ($CDCl_3$, 500 MHz)



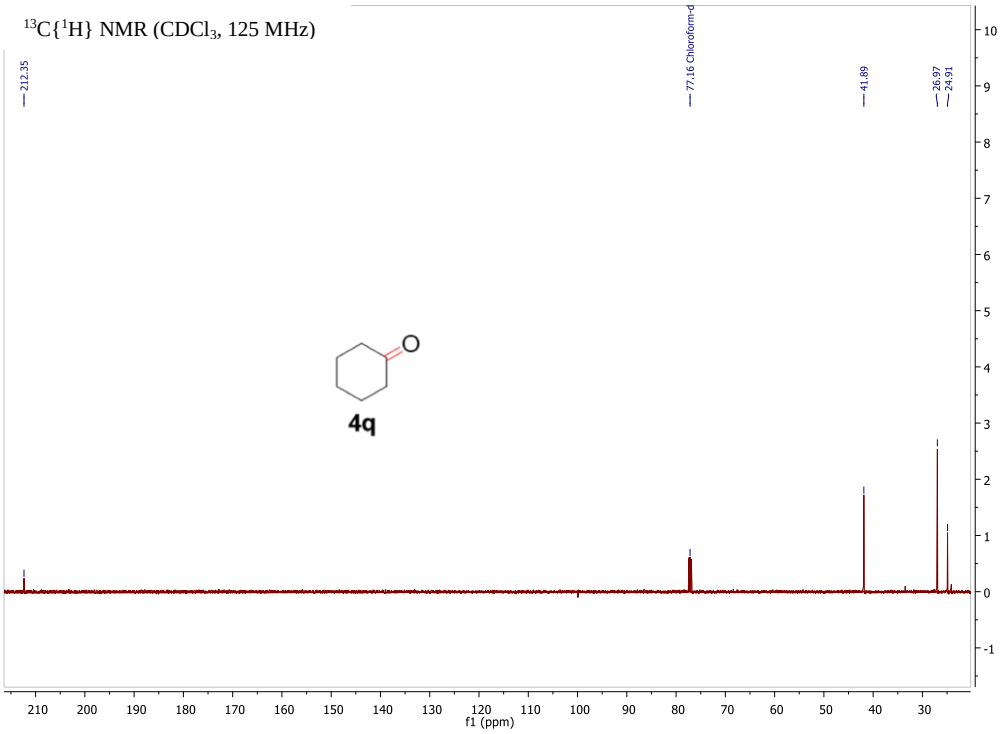
^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz)



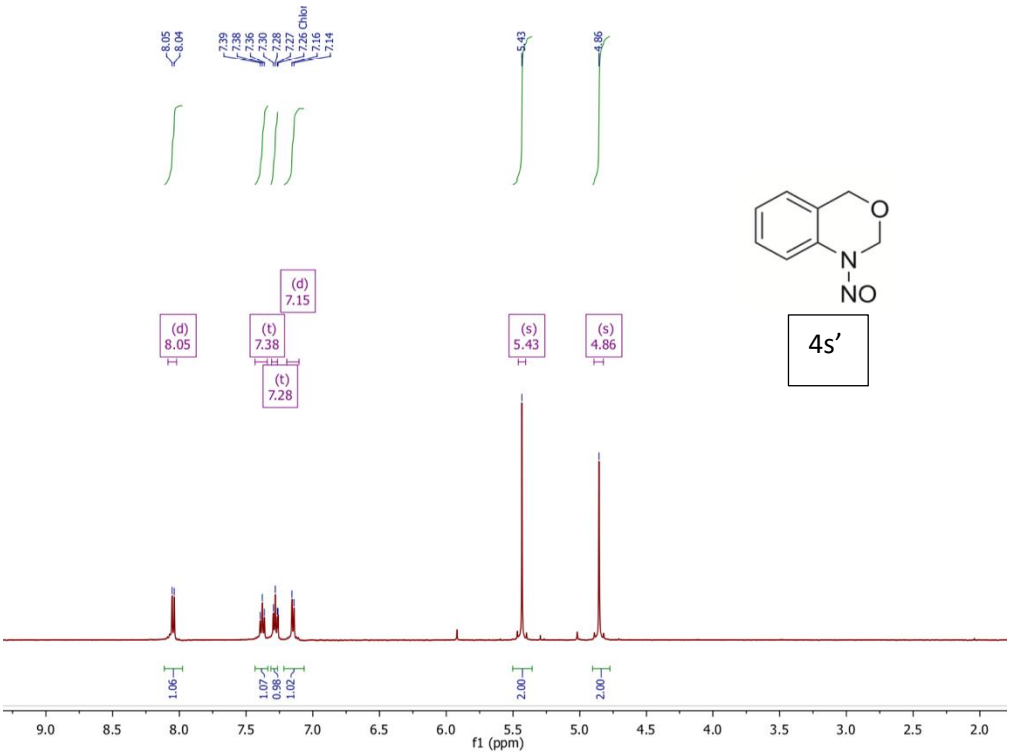
^{1}H NMR ($CDCl_3$, 500 MHz)



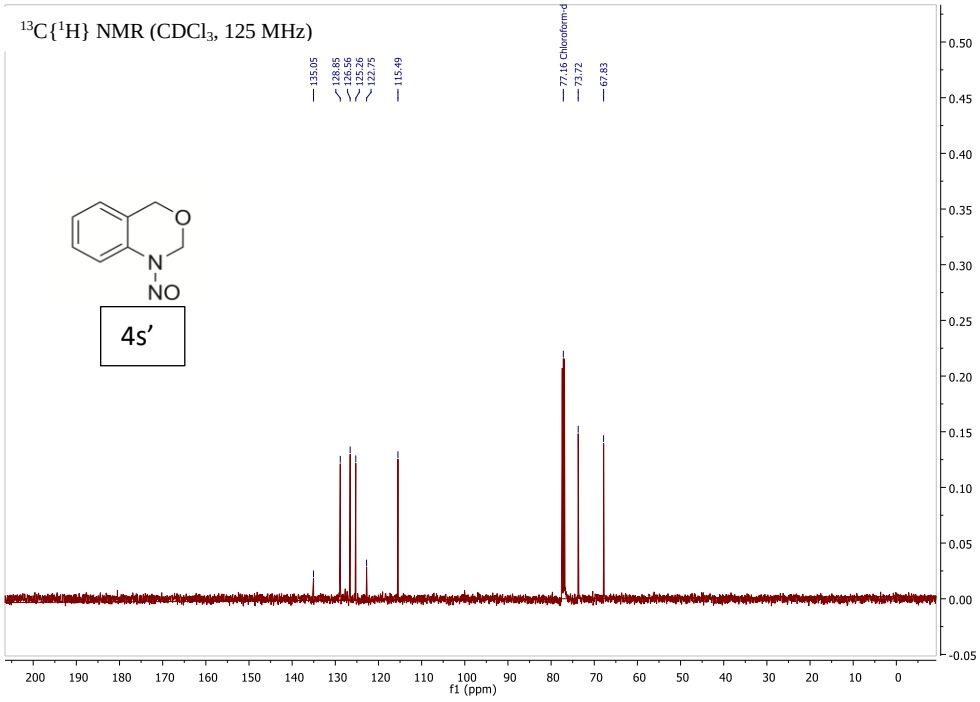
^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz)



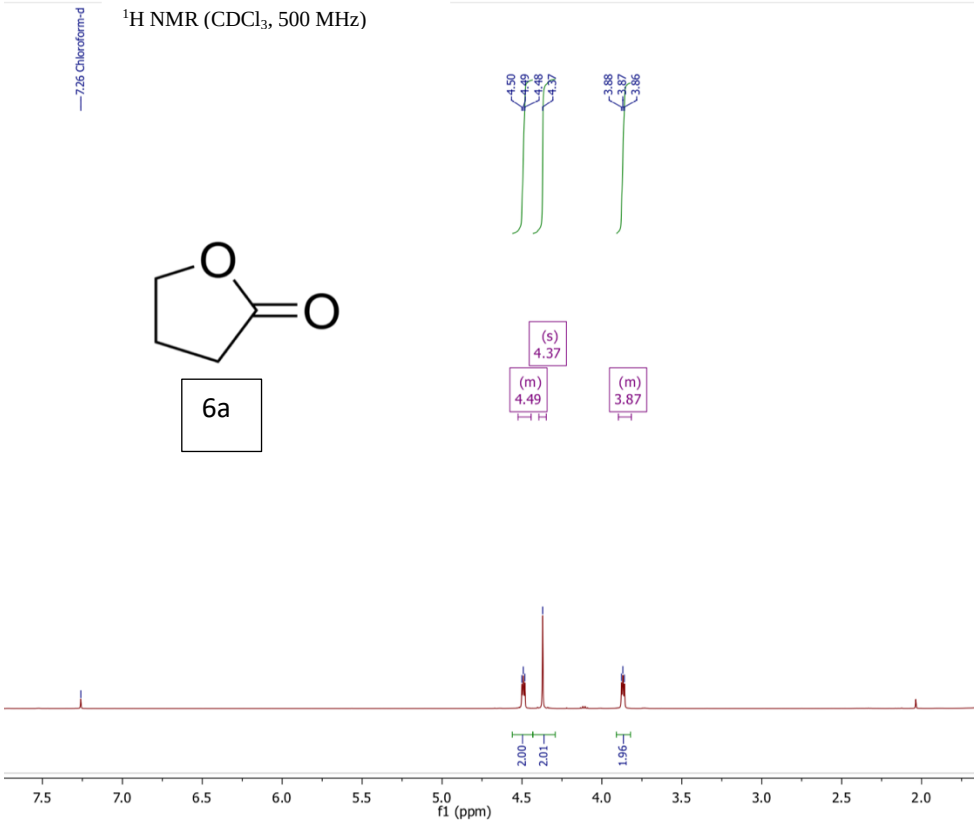
^{1}H NMR ($CDCl_3$, 500 MHz)



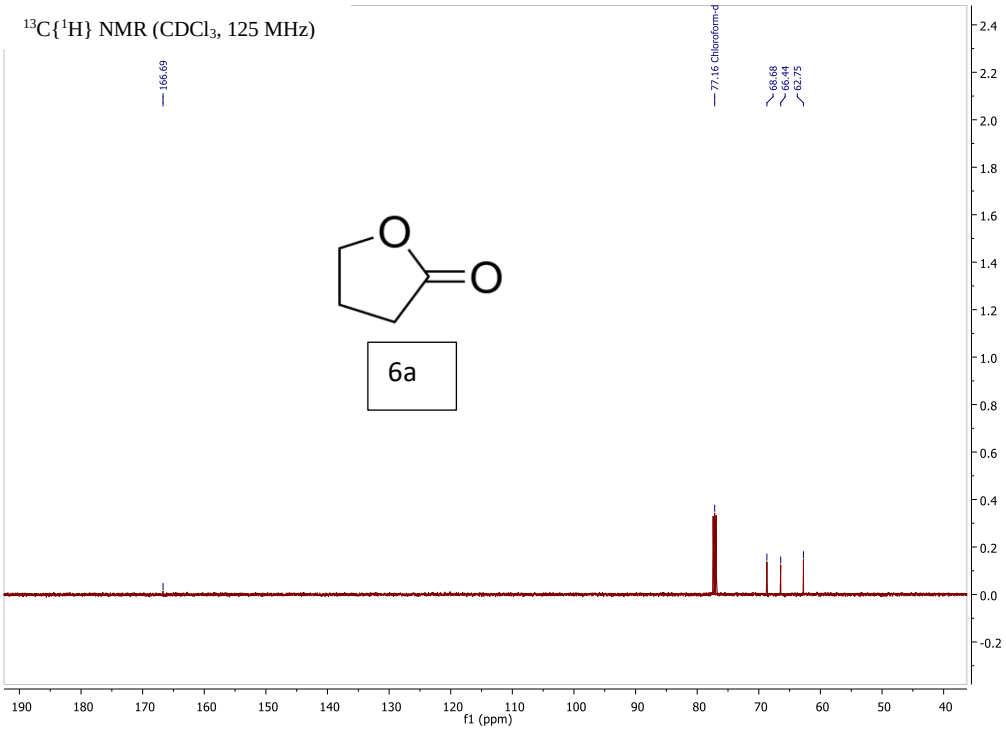
^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz)



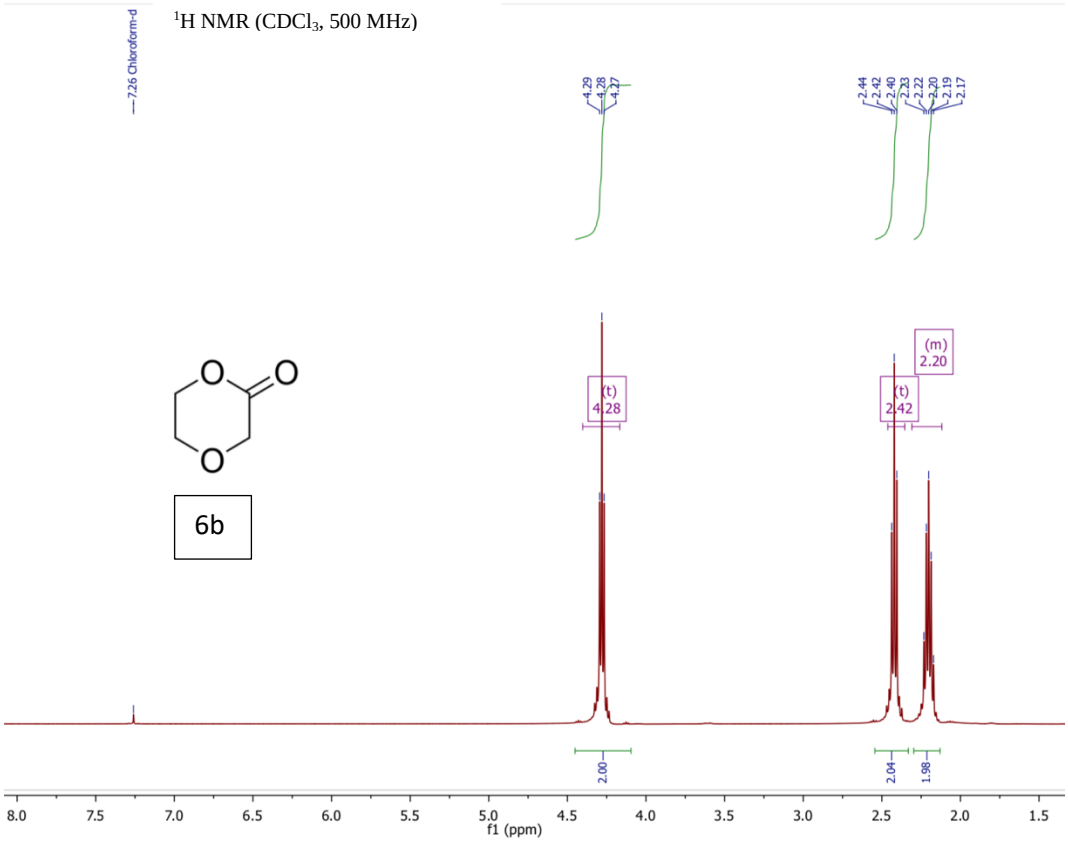
^{1}H NMR ($CDCl_3$, 500 MHz)



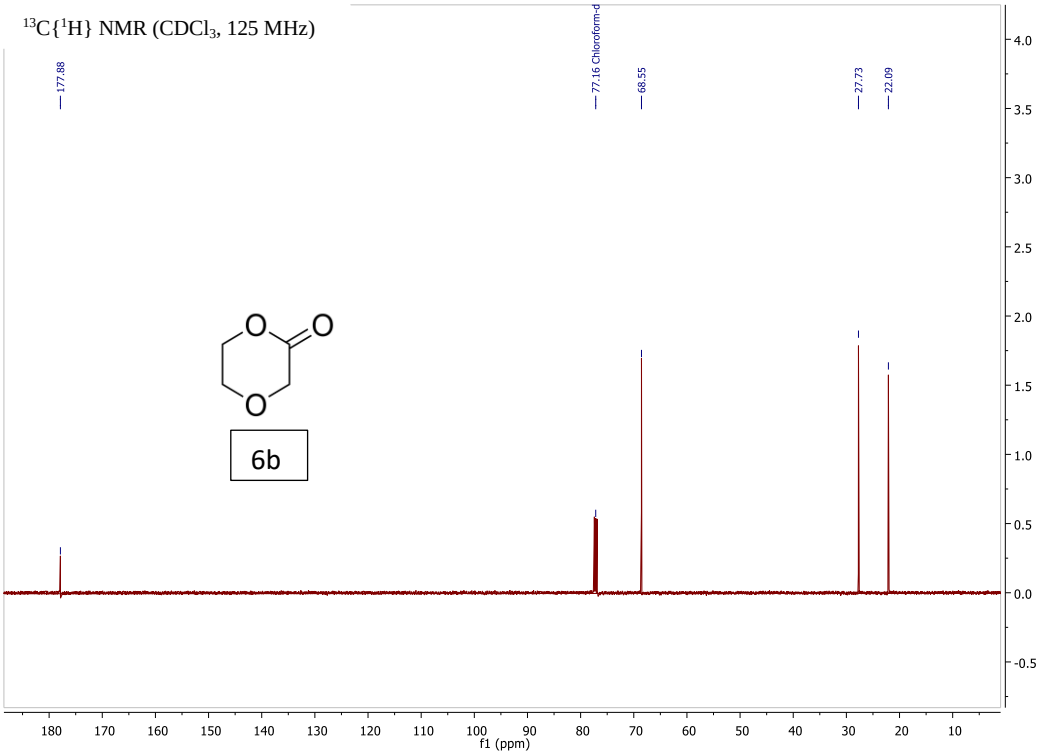
^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz)



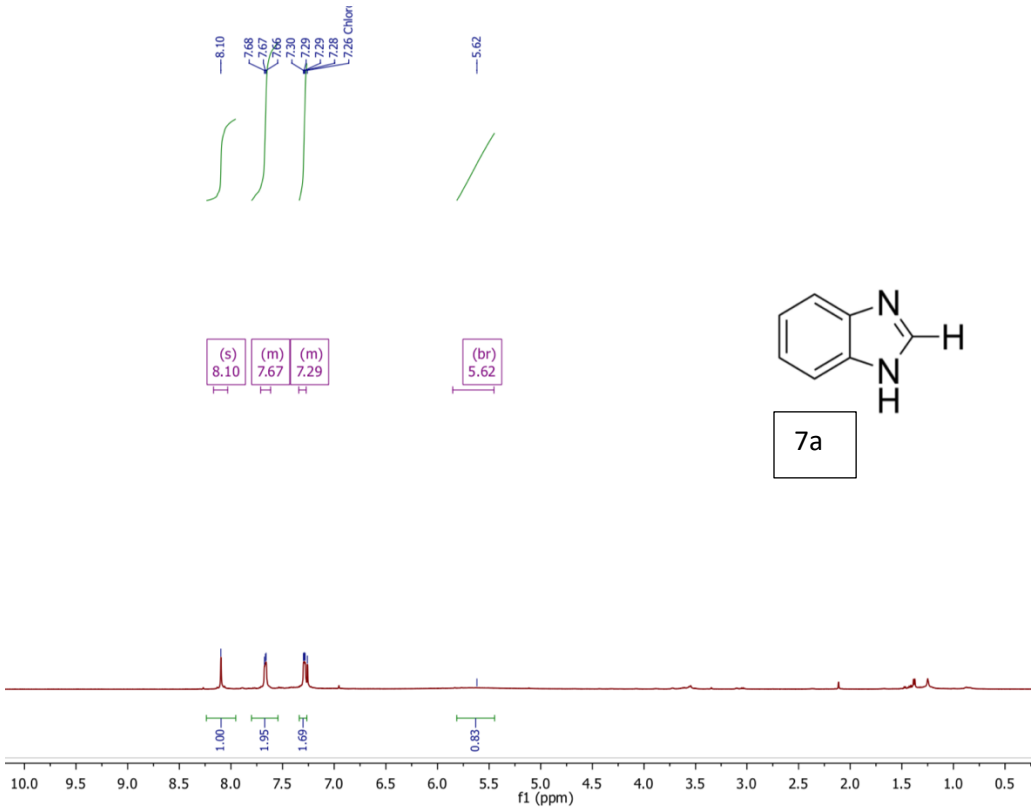
^{1}H NMR ($CDCl_3$, 500 MHz)



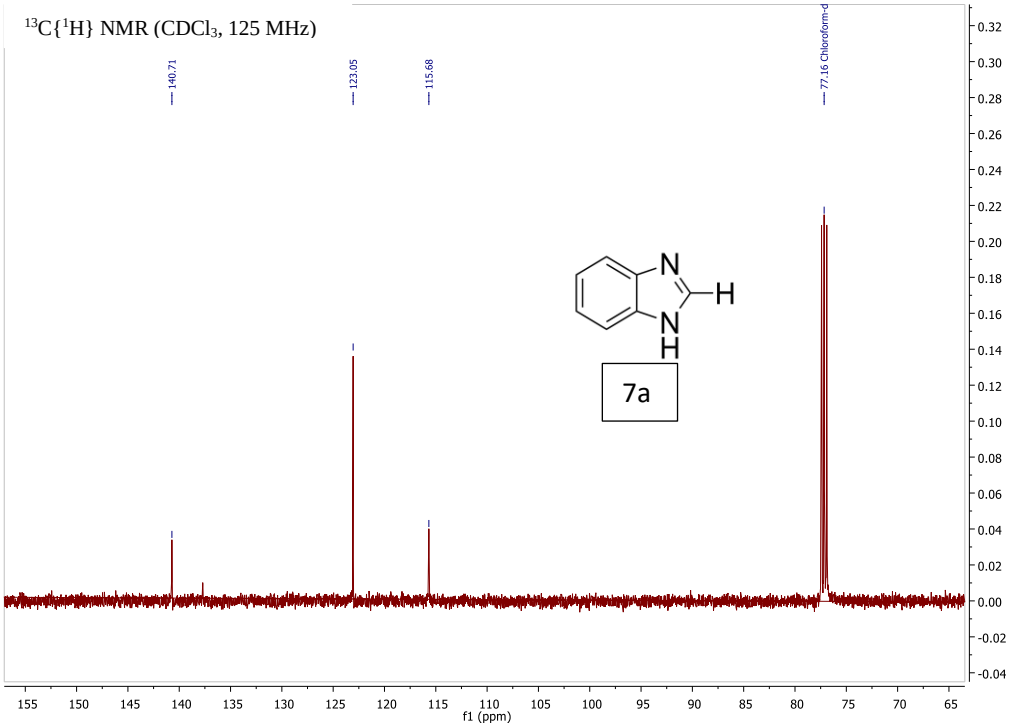
^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz)



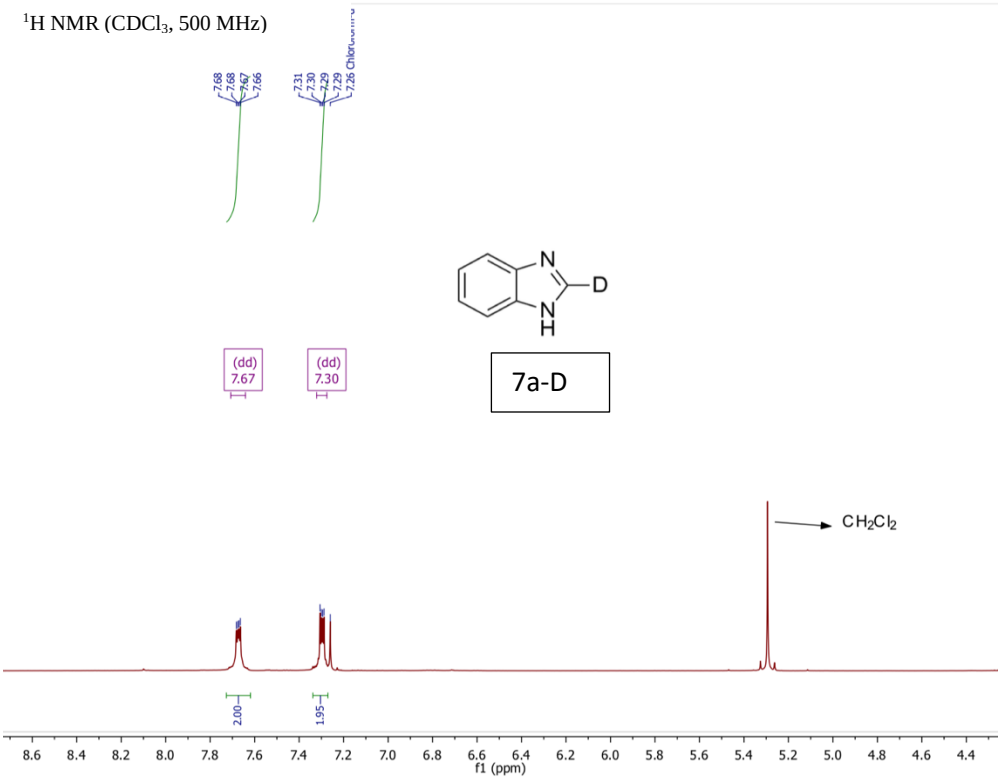
^{1}H NMR ($CDCl_3$, 500 MHz)



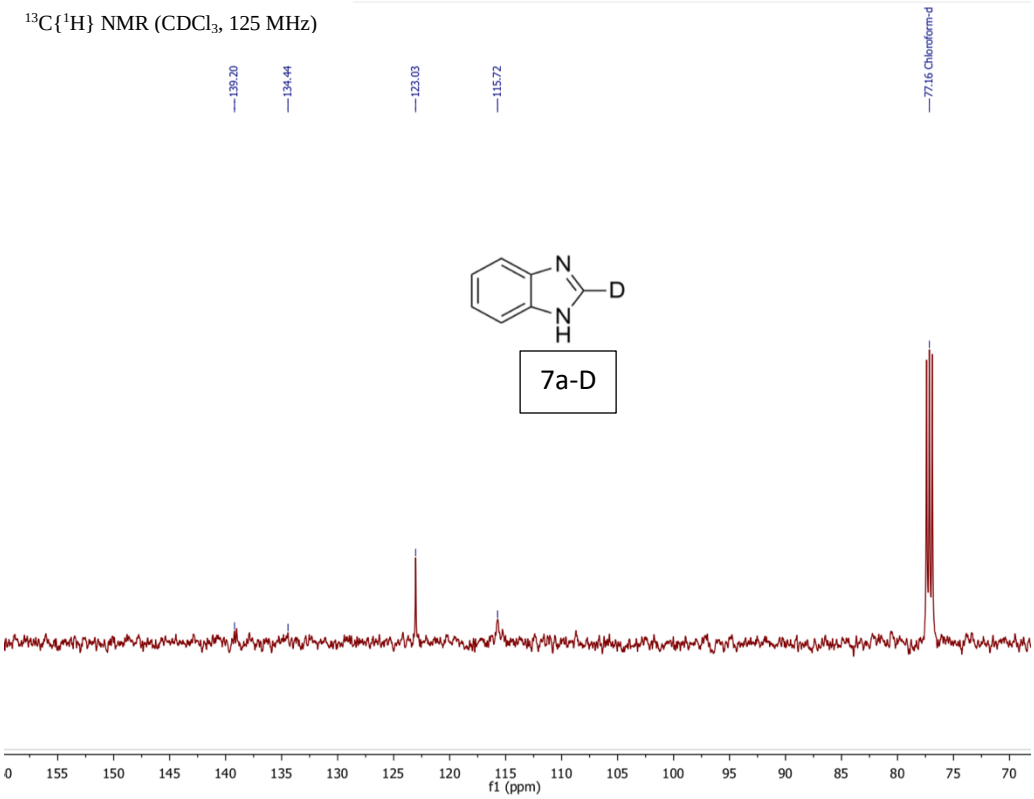
^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz)



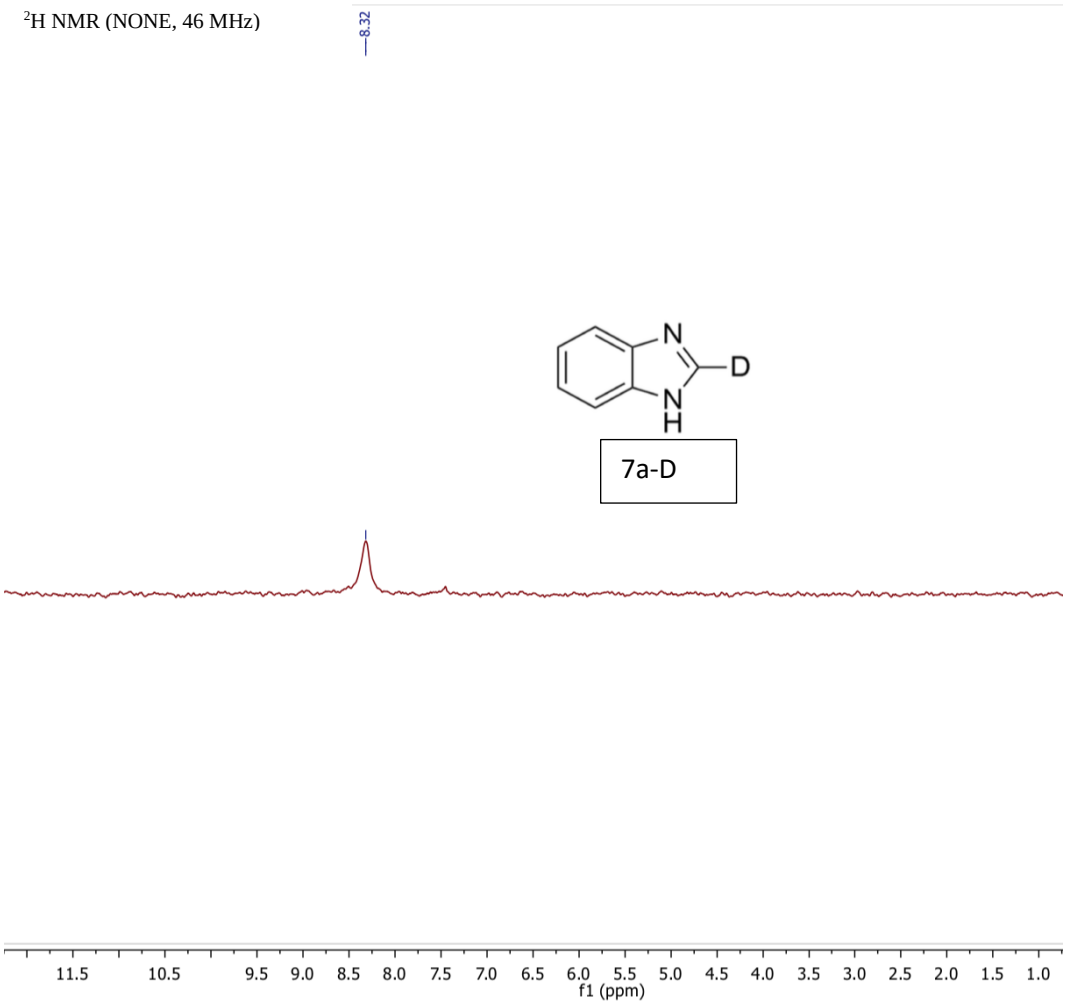
^{1}H NMR ($CDCl_3$, 500 MHz)



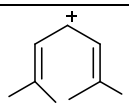
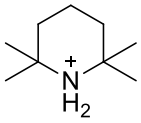
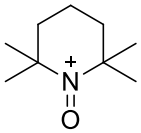
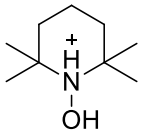
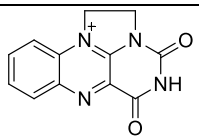
^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz)



^{2}H NMR (NONE, 46 MHz)



H. HRMS (IT-TOF) data representing different sample condition:

Fragments or Molecular ions					
m/z value	123	142	156	158	241

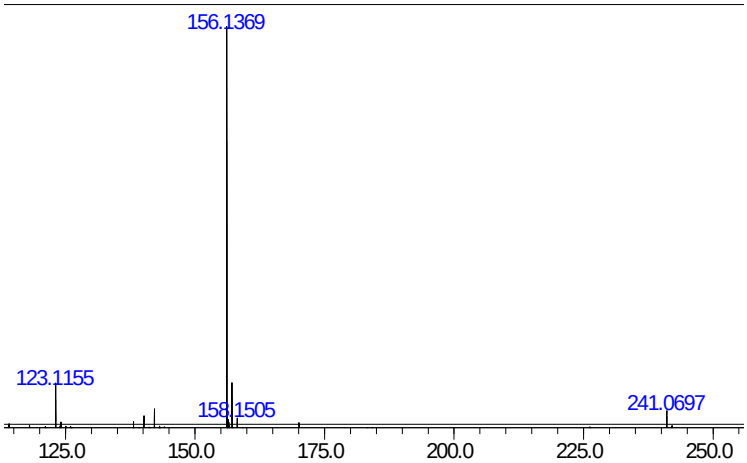


Figure S6: Mass spectrum of crude reaction mixture in the absence of Isochroman substrate after 2-hour reaction

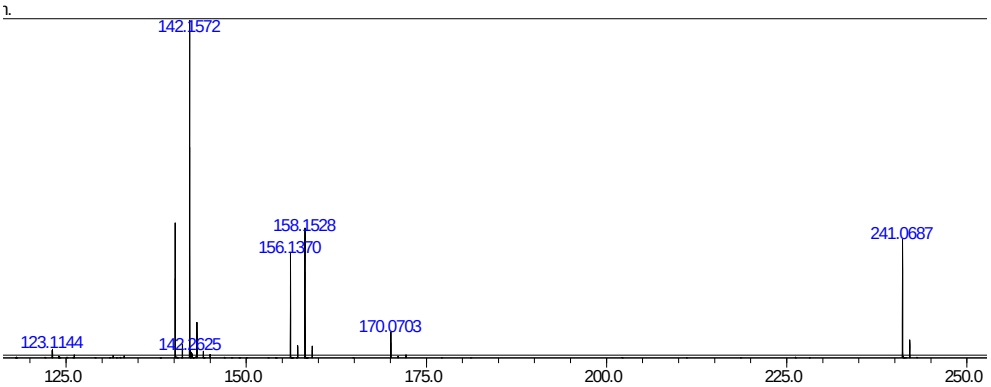


Figure S7: Mass spectrum of crude reaction mixture in the presence of Isochroman substrate after 2-hour reaction