

Copper(I)-catalyzed selective oxidation of hydrazones through C(sp³)-H functionalization

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P.R. China

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Supporting Information

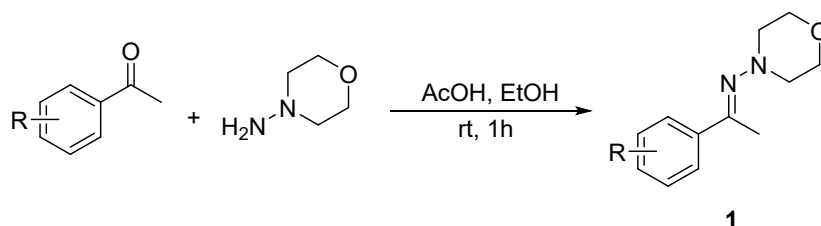
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1. Experimental Section

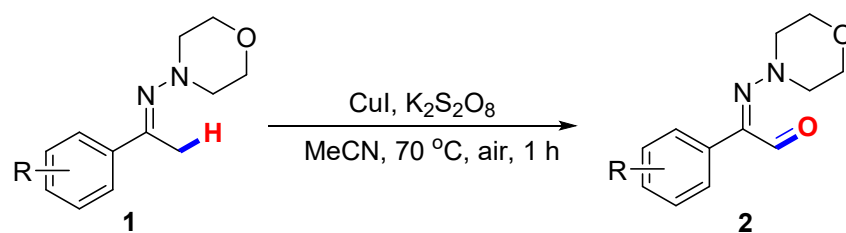
1.1 General procedure for the synthesis of **1**

A mixture of ketone (5.0 mmol, 1.0 equiv.), 4-aminomorpholine (5.5 mmol, 1.1 equiv.), acetic acid (5.5 mmol, 1.1 equiv.), and EtOH (15.0 mL) in a 25 mL flask was stirred at room temperature for 1 h. After completion of the reaction as indicated by TLC, purified water was added to the mixture to form the precipitate. The precipitate was washed with water and dried *in vacuo* to afford ketone hydrazone.

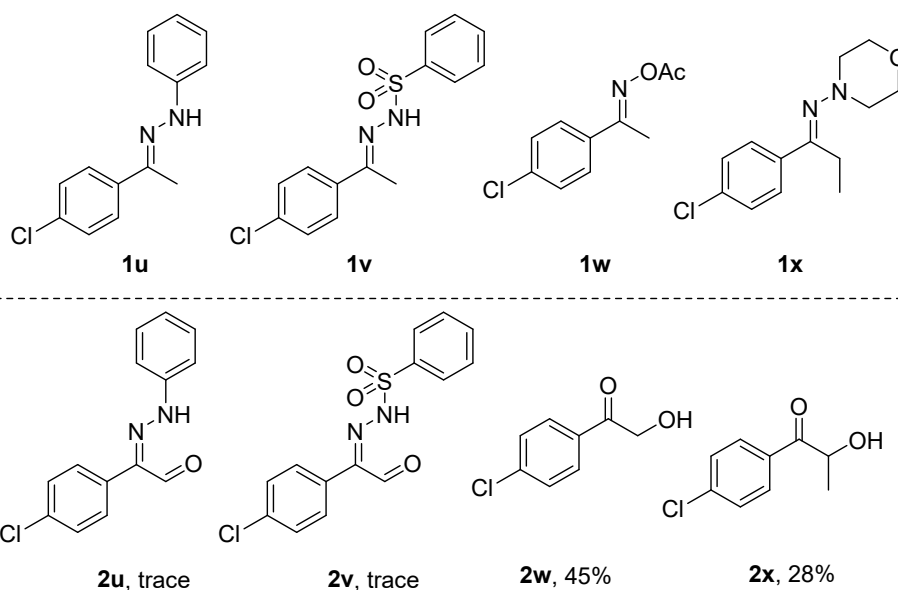


1.2 General procedure for oxidation of hydrazones

A mixture of **1** (0.2 mmol), $K_2S_2O_8$ (2.0 equiv.), CuI (5 mol %), dry MeCN (2.0 mL) in a 25 mL tube was stirred at 70 °C for 1 h. Then, the mixture was diluted with EtOAc and filtered through a pad of Celite gradually. The solvent was removed under reduced pressure. The gathered residue was then purified by silica gel column chromatography (200–300 mesh silica gel, PE/EA = 3:1).



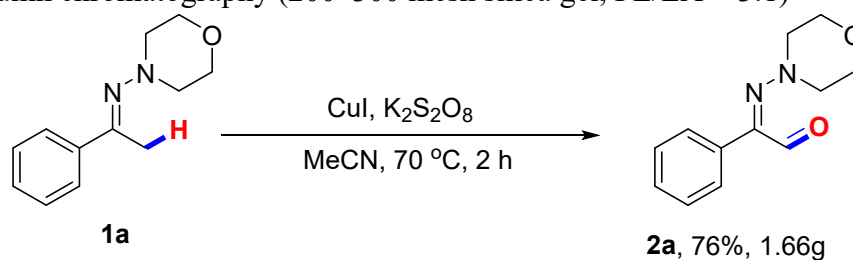
1.2.1 other protecting group screening



1.3 Gram-scale preparation

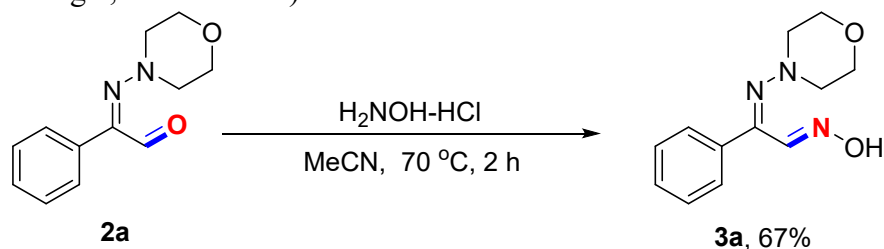
A mixture of **1** (10.0 mmol), $K_2S_2O_8$ (2.0 equiv.), CuI (5 mol %), dry MeCN (25

mL) in a 100 mL tube was stirred at 70 °C for 2 h. Then, the mixture was diluted with EtOAc and filtered through a pad of Celite gradually. The solvent was removed under reduced pressure. The gathered residue was then purified by silica gel column chromatography (200–300 mesh silica gel, PE/EA = 3:1)



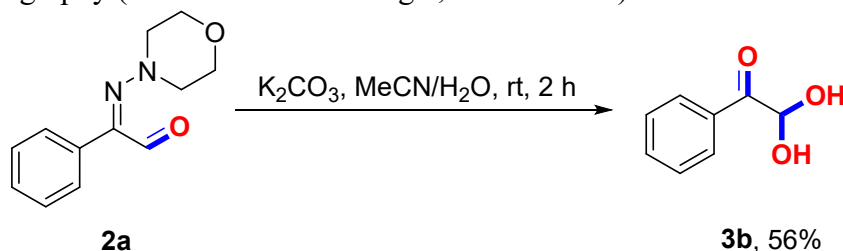
1.4 General procedure for the synthesis of 3a

A mixture of **2a** (0.2 mmol), $\text{NH}_2\text{OH}\cdot\text{HCl}$ (2.0 equiv.), dry MeCN (2.0 mL) in a 25 mL tube was stirred at 70 °C for 2 h. After completion of the reaction as indicated by TLC, the mixture was diluted with EtOAc and filtered through a pad of Celite gradually. The solvent was removed under reduced pressure. The gathered residue was then purified by silica gel column chromatography (200–300 mesh silica gel, PE/EA = 4:1).



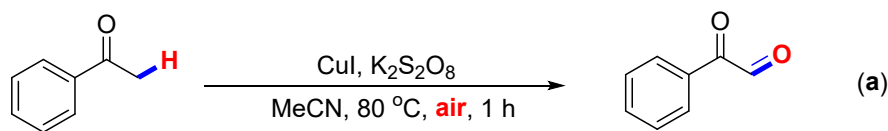
1.5 General procedure for the synthesis of 3b

A mixture of **2a** (0.2 mmol), K_2CO_3 (2.0 equiv.), MeCN/ H_2O (1:1, 2.0 mL) in a 25 mL tube was stirred at room temperature for 2 h. After completion of the reaction as indicated by TLC, the mixture was diluted with EtOAc and filtered through a pad of Celite gradually. The solvent was removed under reduced pressure. The gathered residue was then purified by silica gel column chromatography (200–300 mesh silica gel, PE/EA = 2:1).



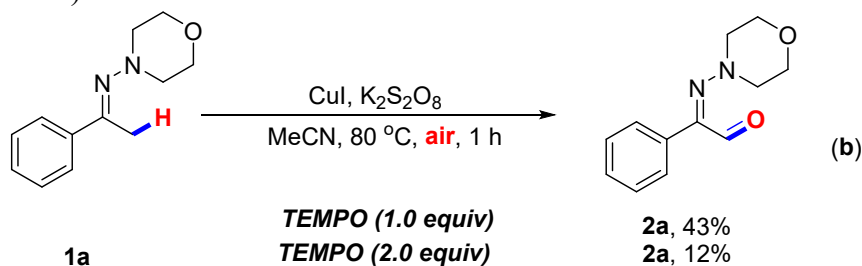
1.6 Control Experiments

(a) A mixture of acetophenone (0.2 mmol), $\text{K}_2\text{S}_2\text{O}_8$ (2.0 equiv.), CuI (5 mol %), dry MeCN (2.0 mL) in a 25 mL tube was stirred at 70 °C for 1 h. Only a trace amount of the product was detected.

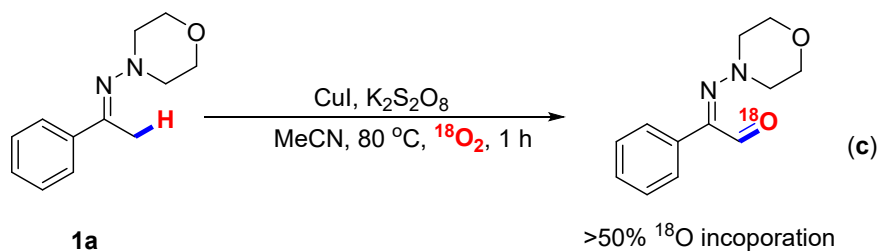


3c, trace

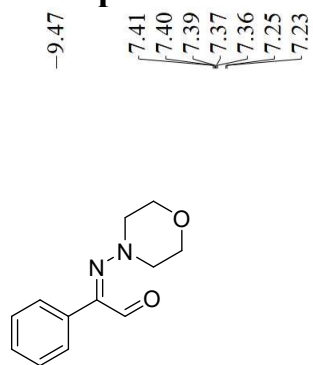
(b) A mixture of **1** (0.2 mmol), $\text{K}_2\text{S}_2\text{O}_8$ (2.0 equiv.), CuI (5 mol %), TEMPO (1.0 or 2.0 equiv.) dry MeCN (2.0 mL) in a 25 mL tube was stirred at 70 °C for 1 h. Then, the mixture was diluted with EtOAc and filtered through a pad of Celite gradually. The solvent was removed under reduced pressure. The gathered residue was then purified by silica gel column chromatography (200–300 mesh silica gel, PE/EA = 3:1).



(c) A mixture of **1** (0.2 mmol), $\text{K}_2\text{S}_2\text{O}_8$ (2.0 equiv.), CuI (5 mol %), dry MeCN (2.0 mL) in a 25 mL tube was stirred at 70 °C for 1 h under $^{18}\text{O}_2$ atmosphere. Then, the mixture was diluted with EtOAc and filtered through a pad of Celite gradually. The solvent was removed under reduced pressure. The gathered residue was then purified by silica gel column chromatography (200–300 mesh silica gel, PE/EA = 3:1).



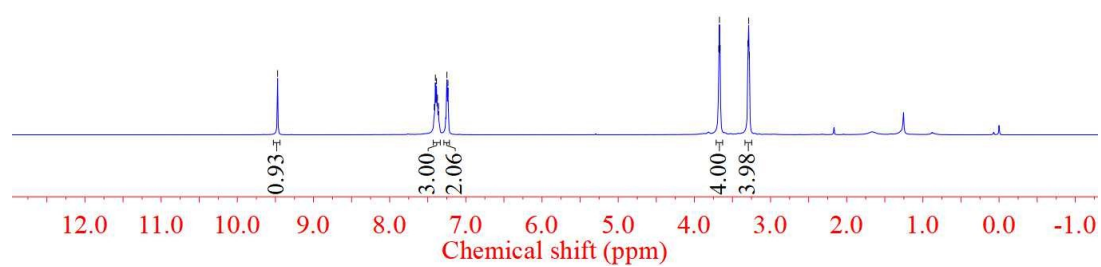
1. Copies of NMR Spectra



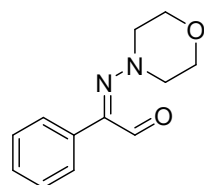
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3.28

9.47
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7.39
7.37
7.36
7.25
7.23

2a ¹H NMR (500 MHz, CDCl₃)



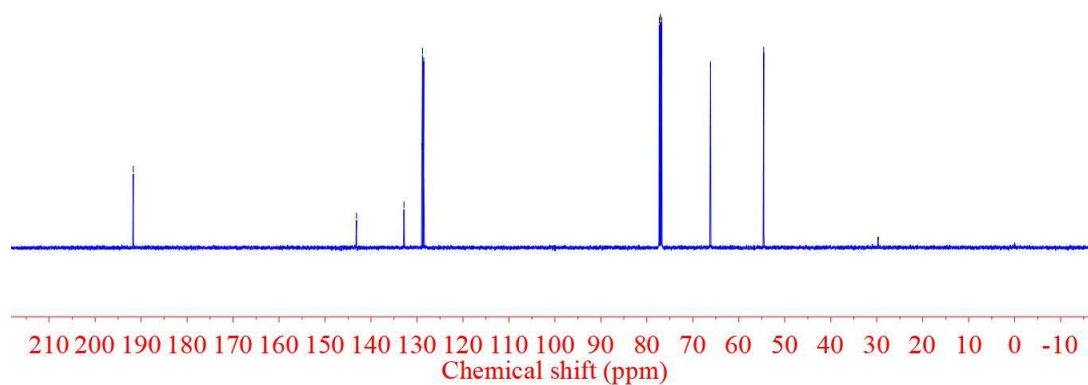
191.70

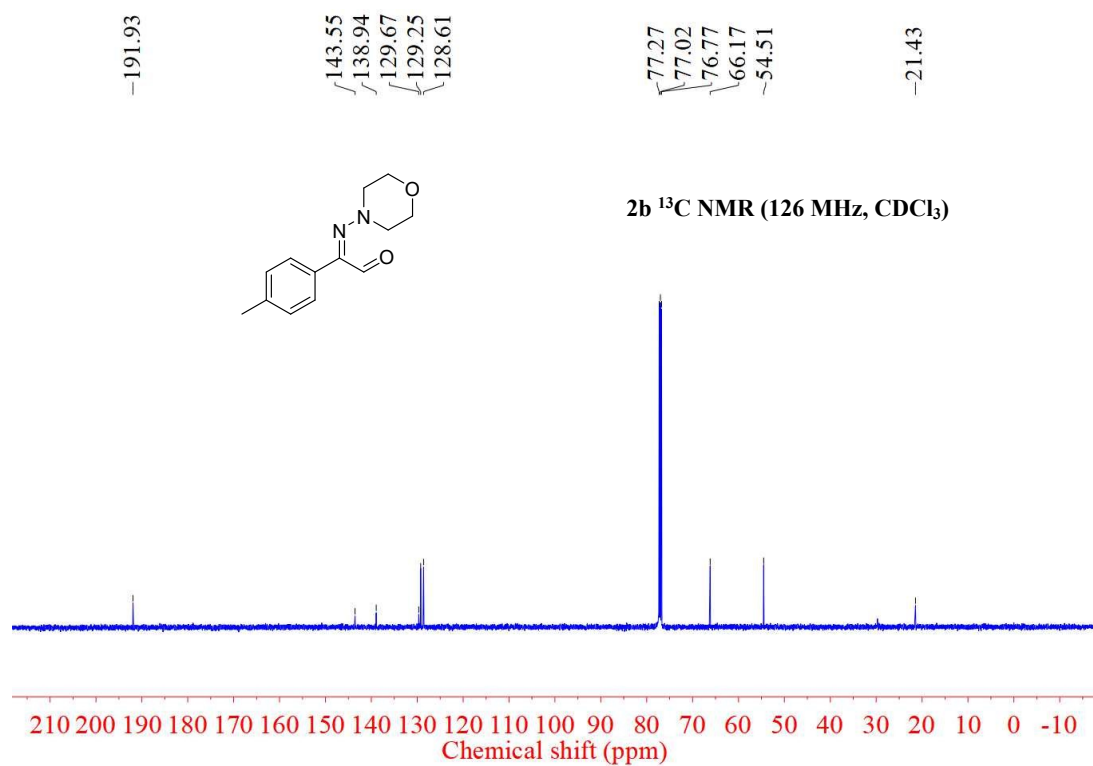
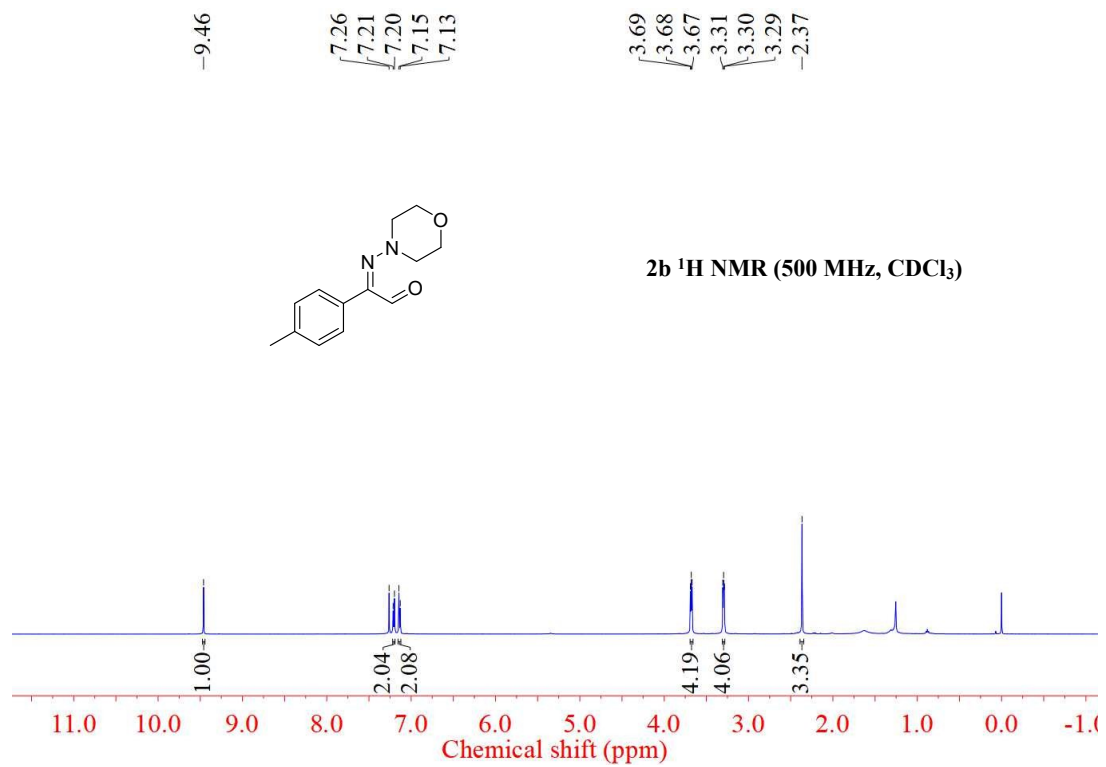


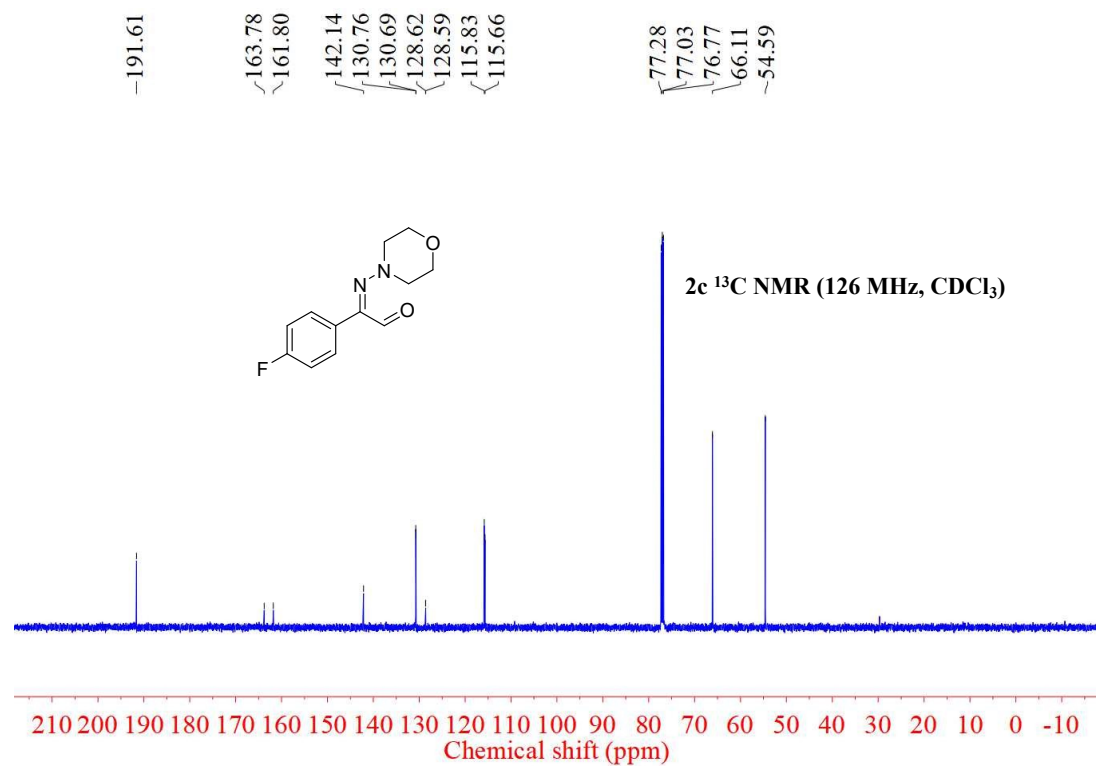
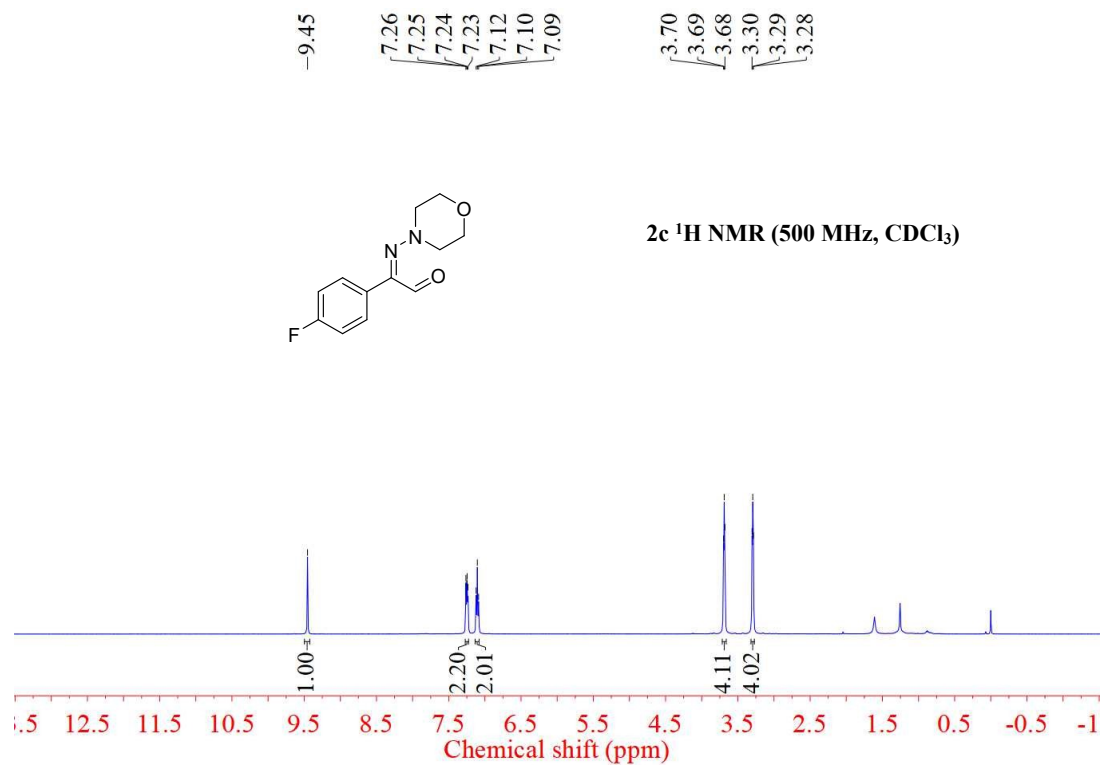
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76.79
66.15
54.59

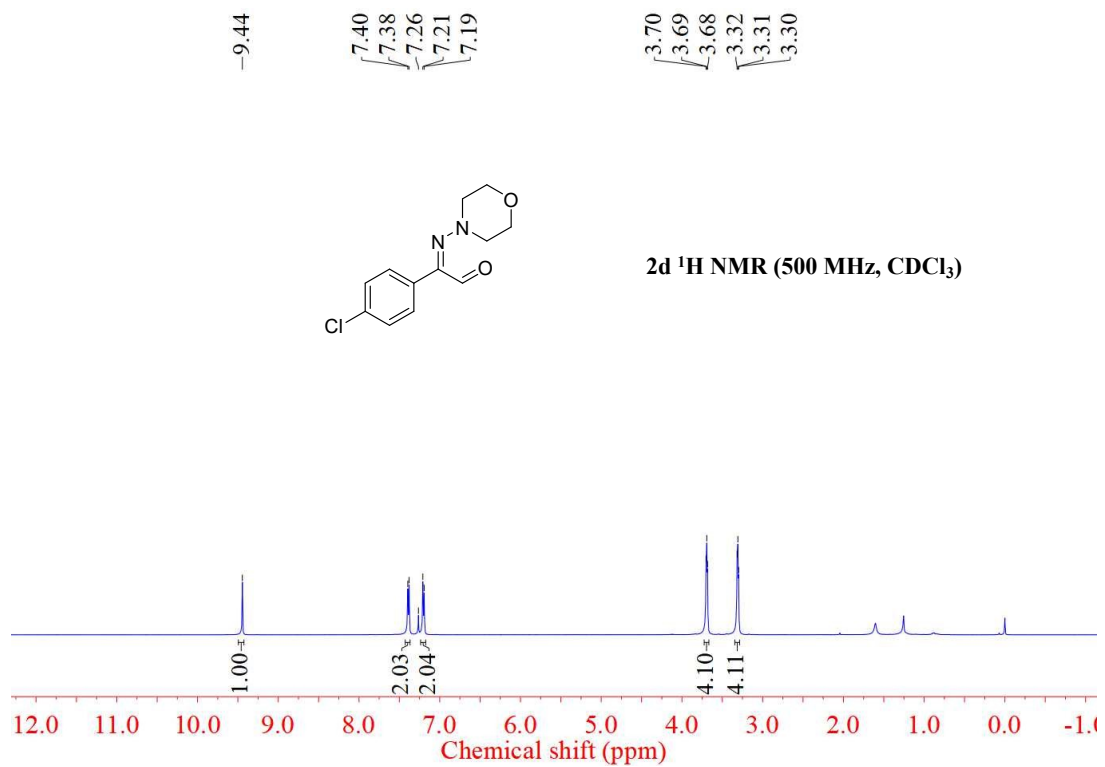
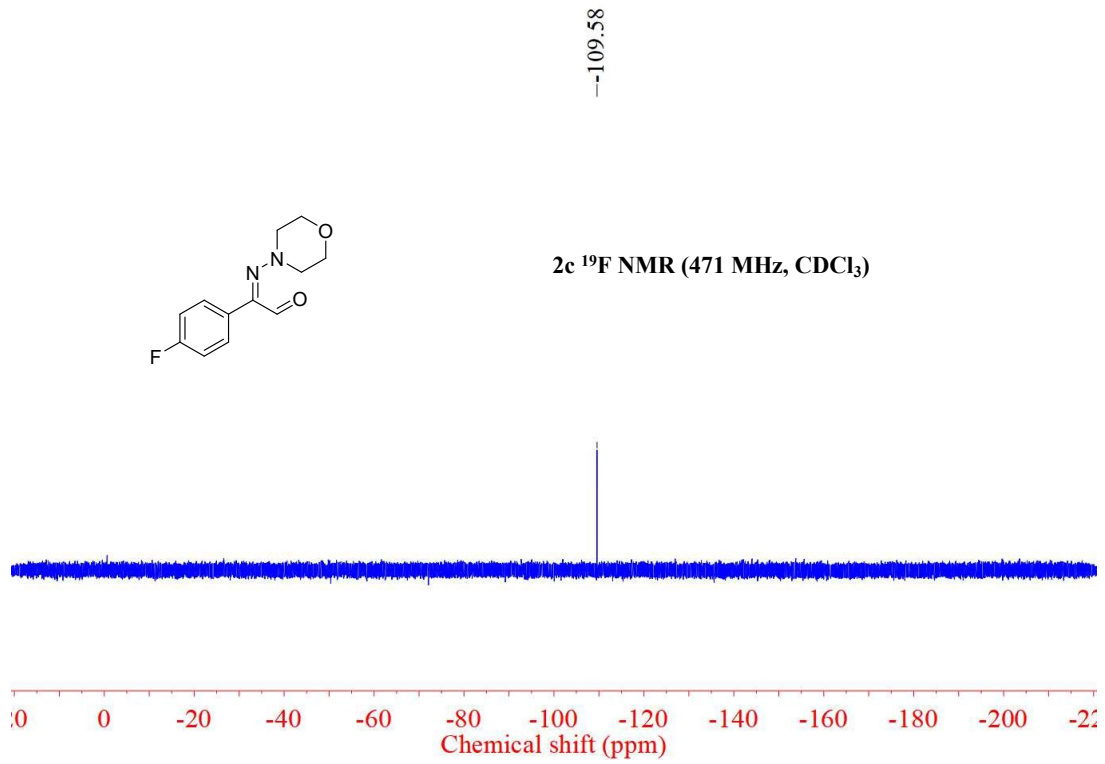
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128.79
128.52

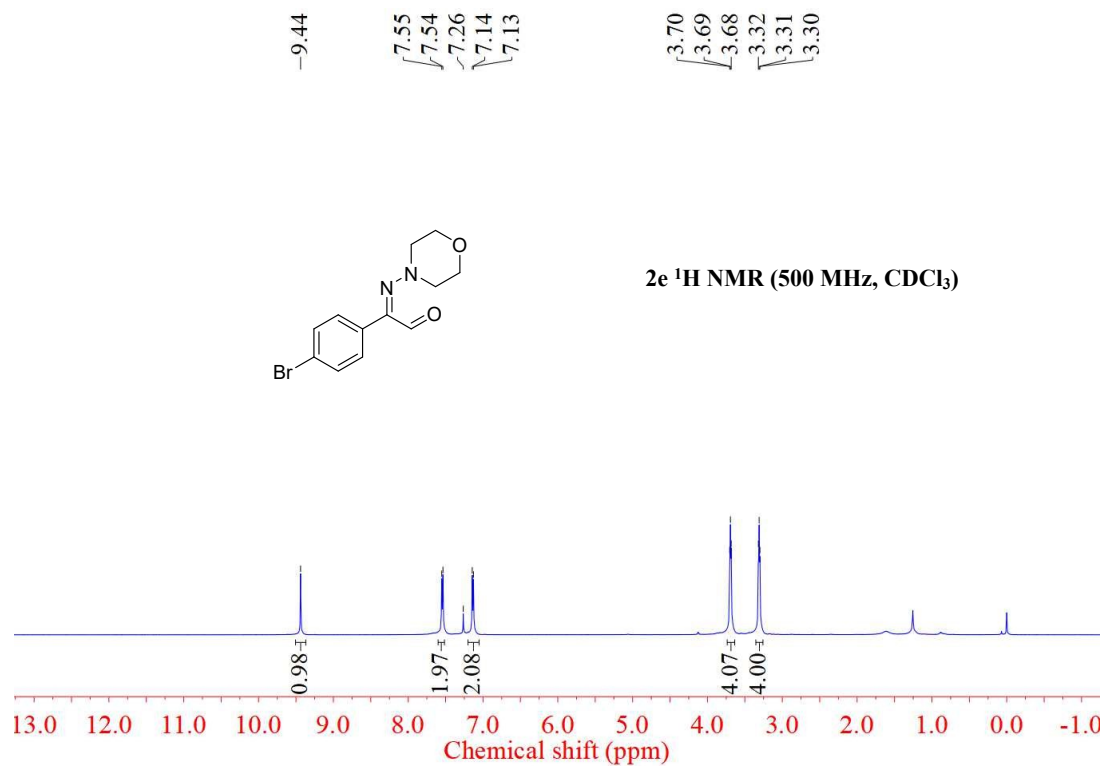
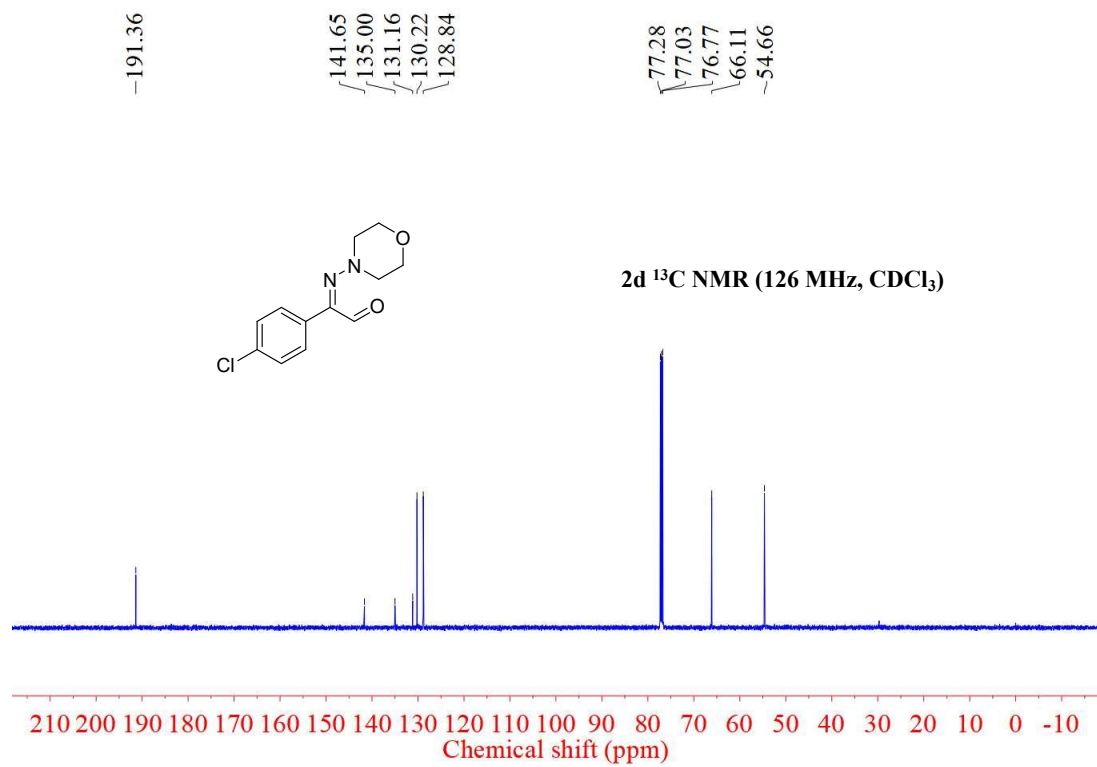
2a ¹³C NMR (126 MHz, CDCl₃)

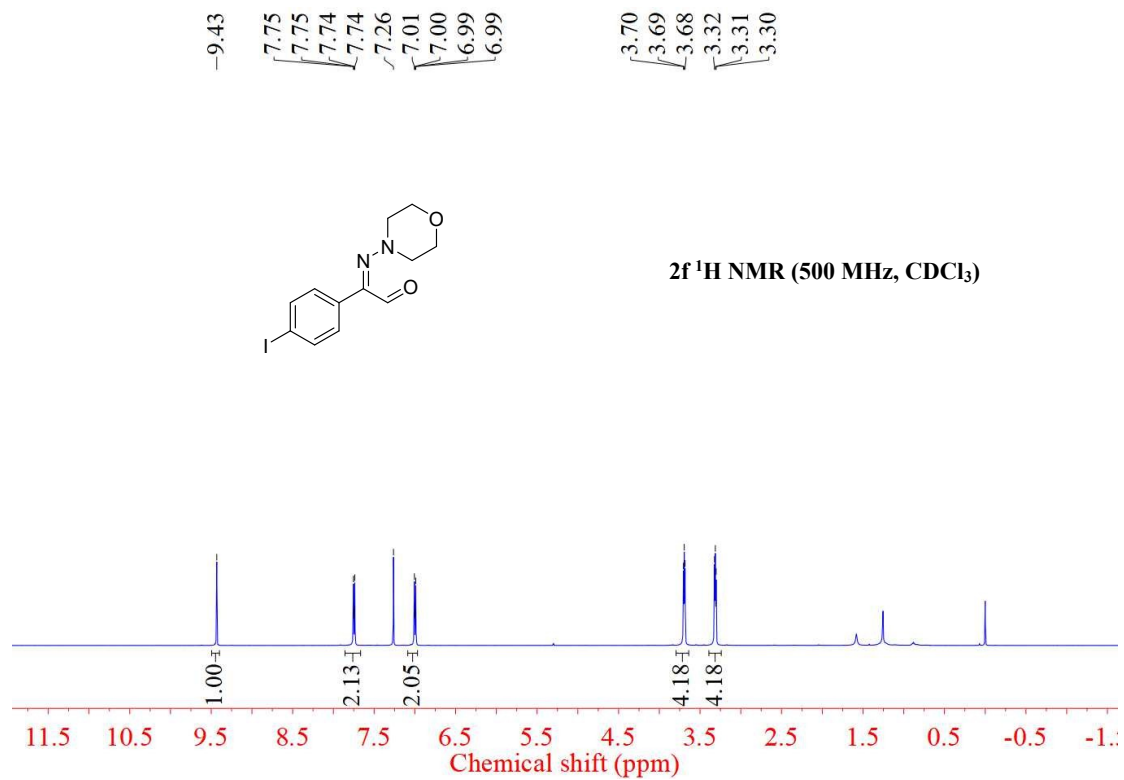
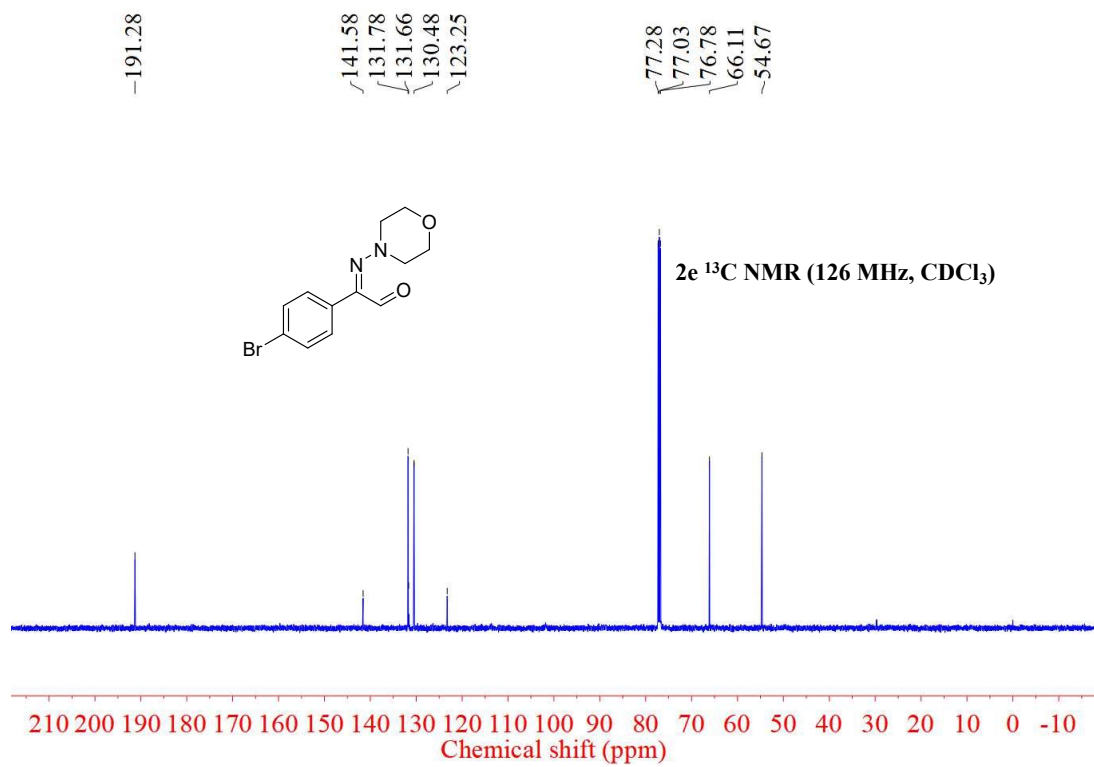


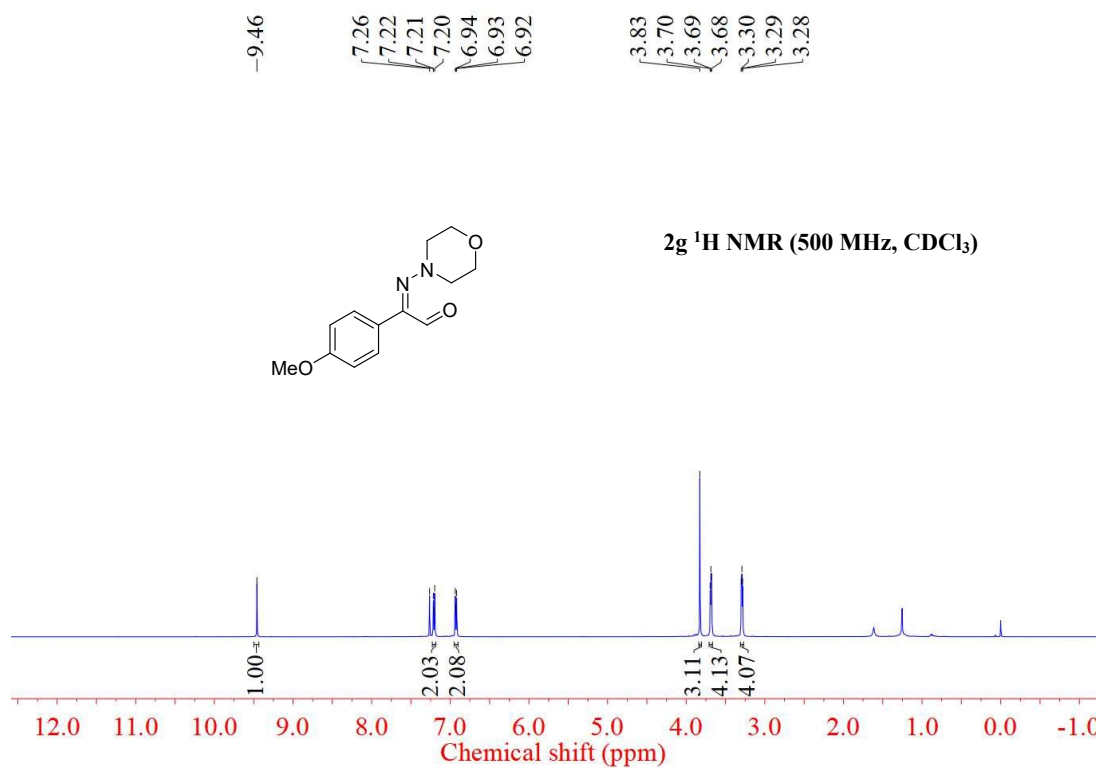
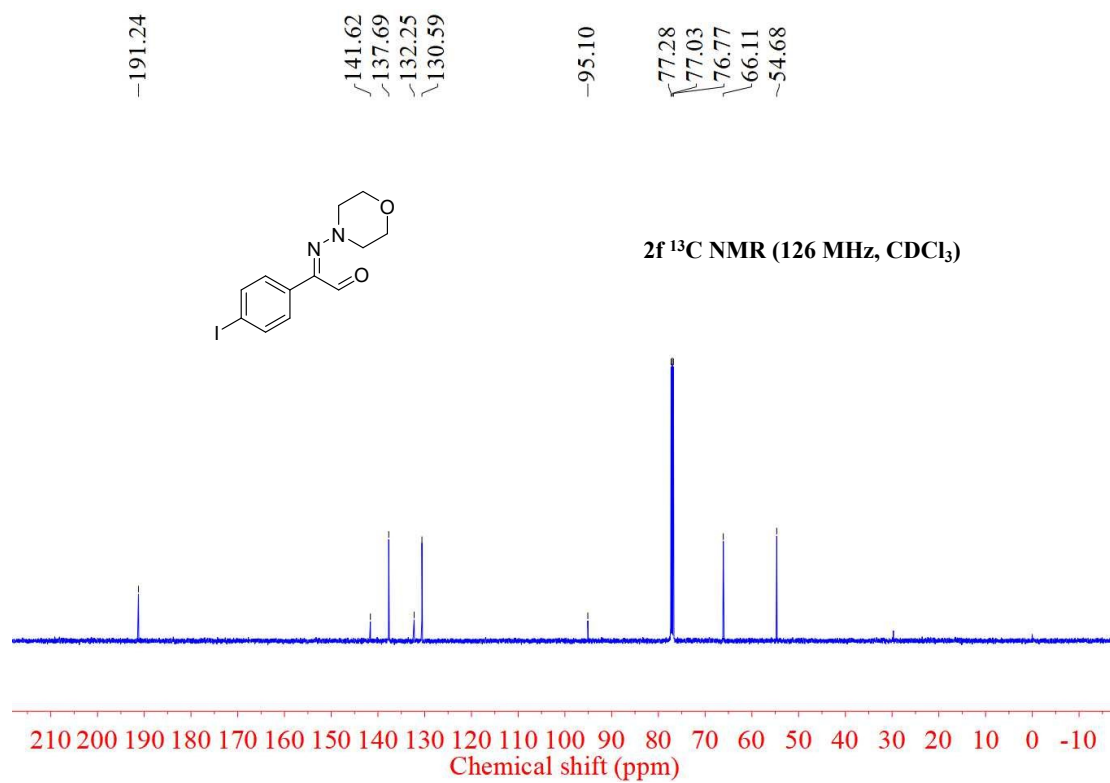


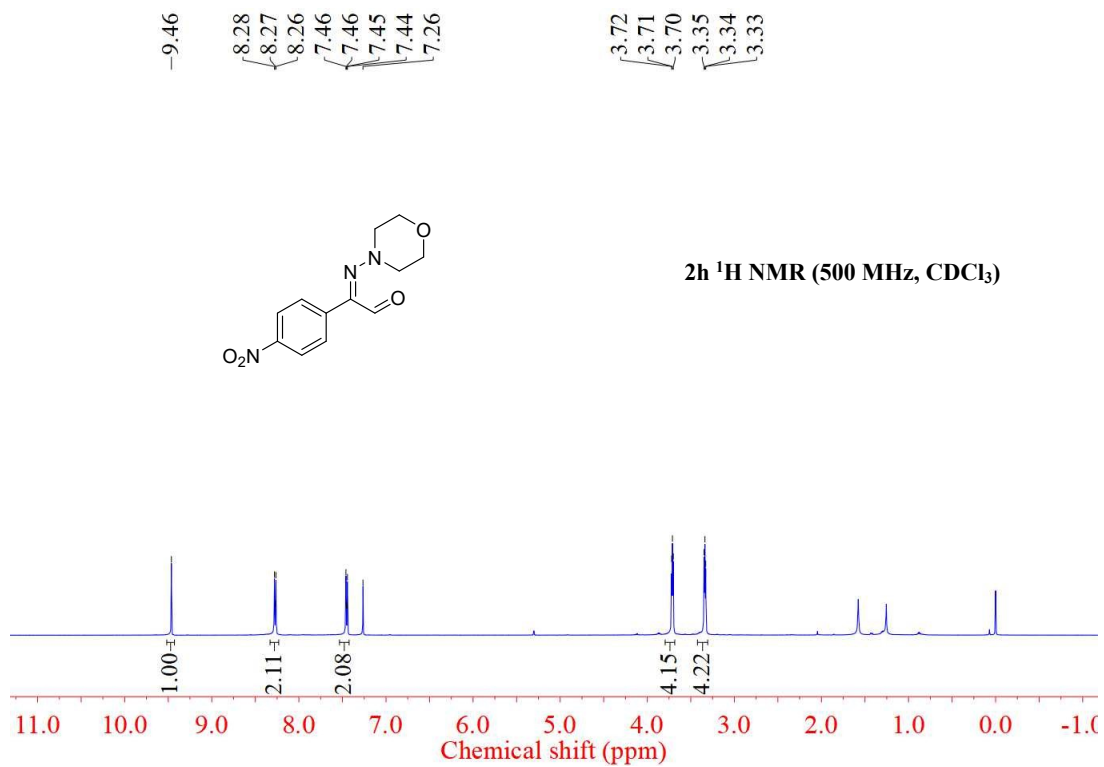
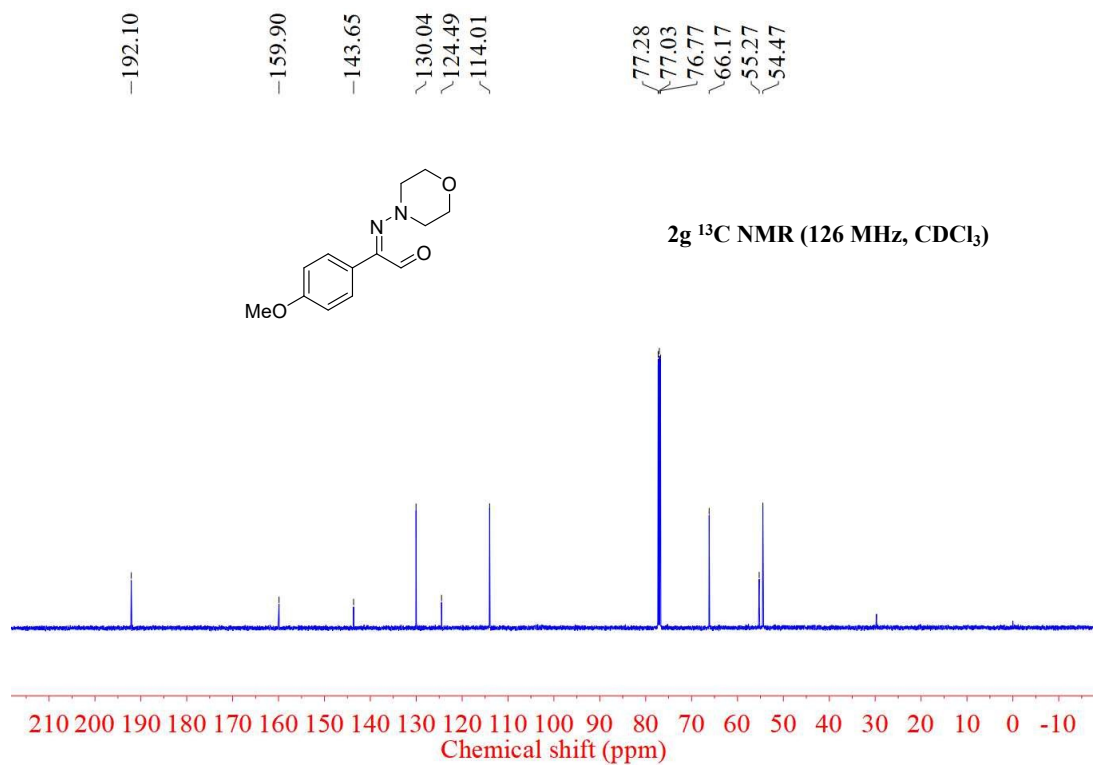


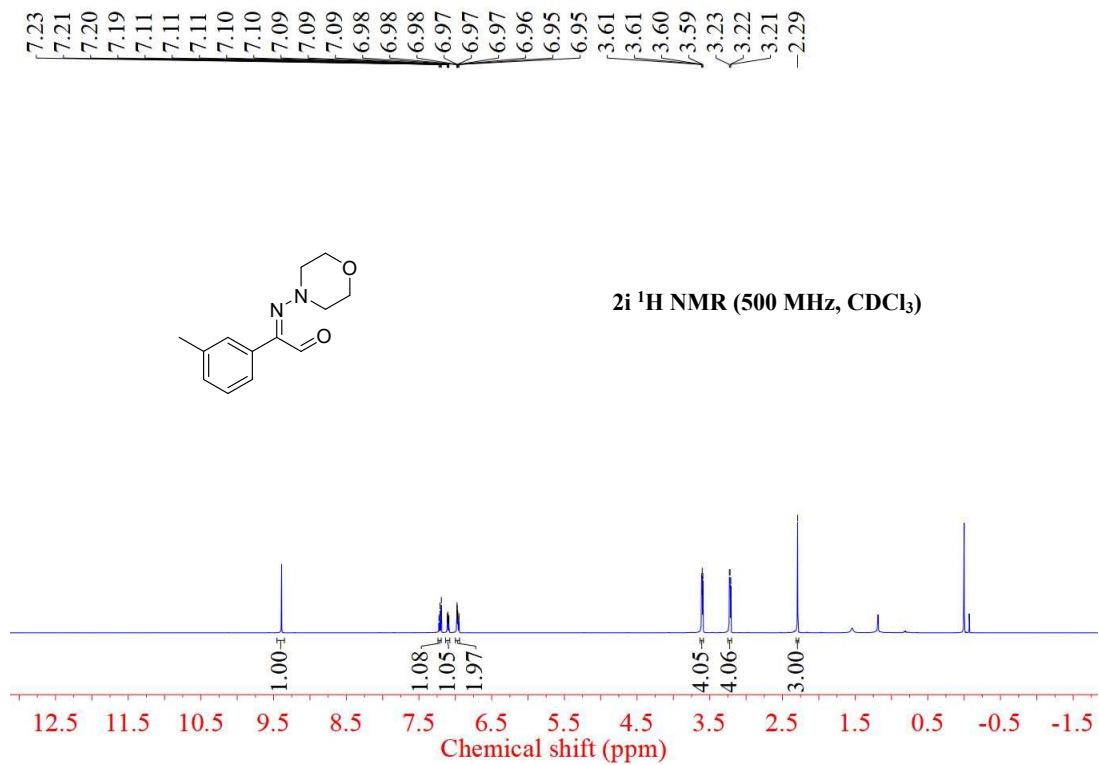
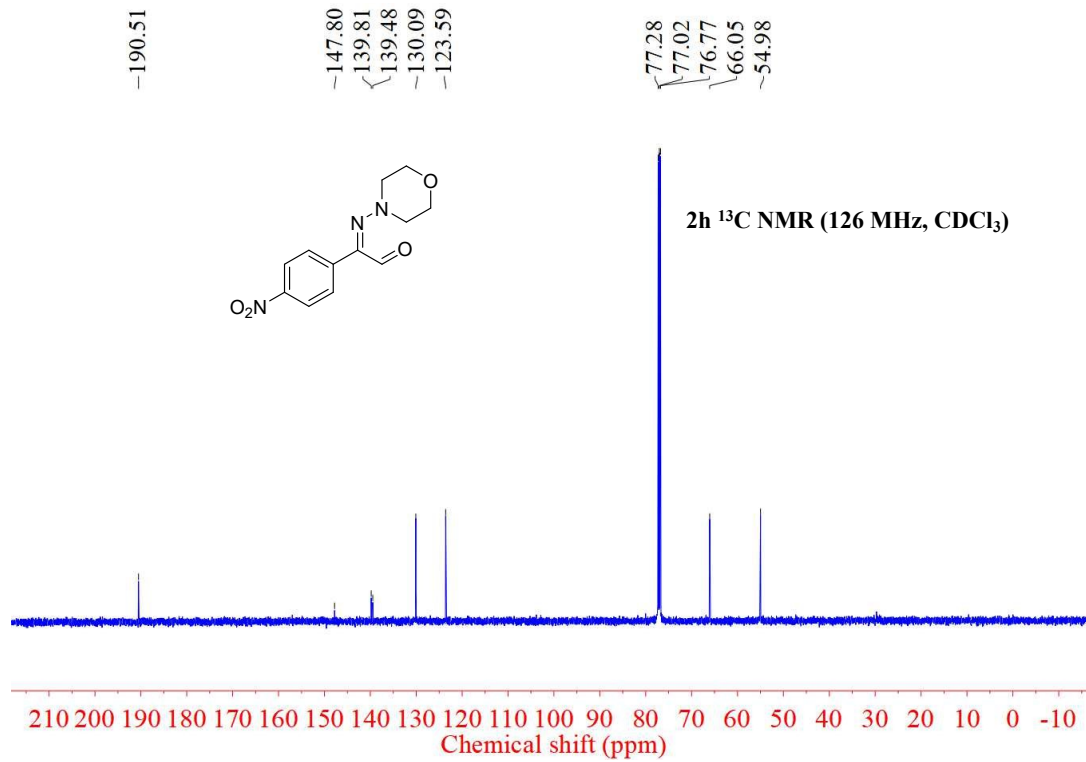


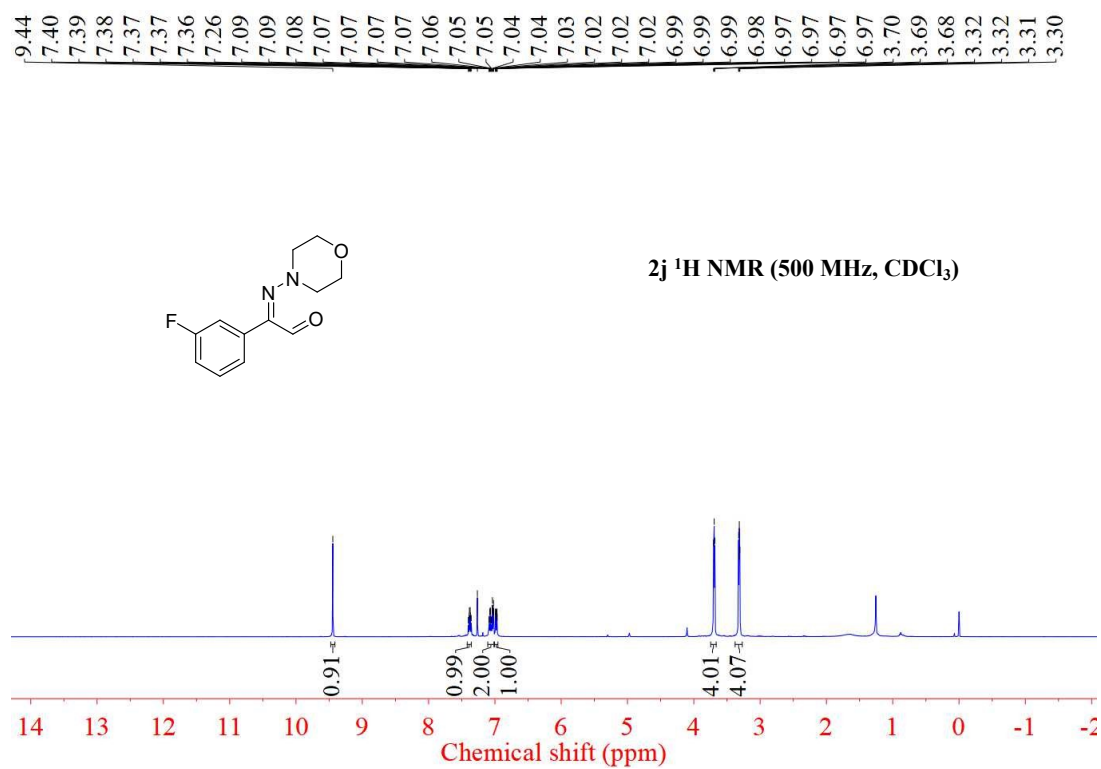
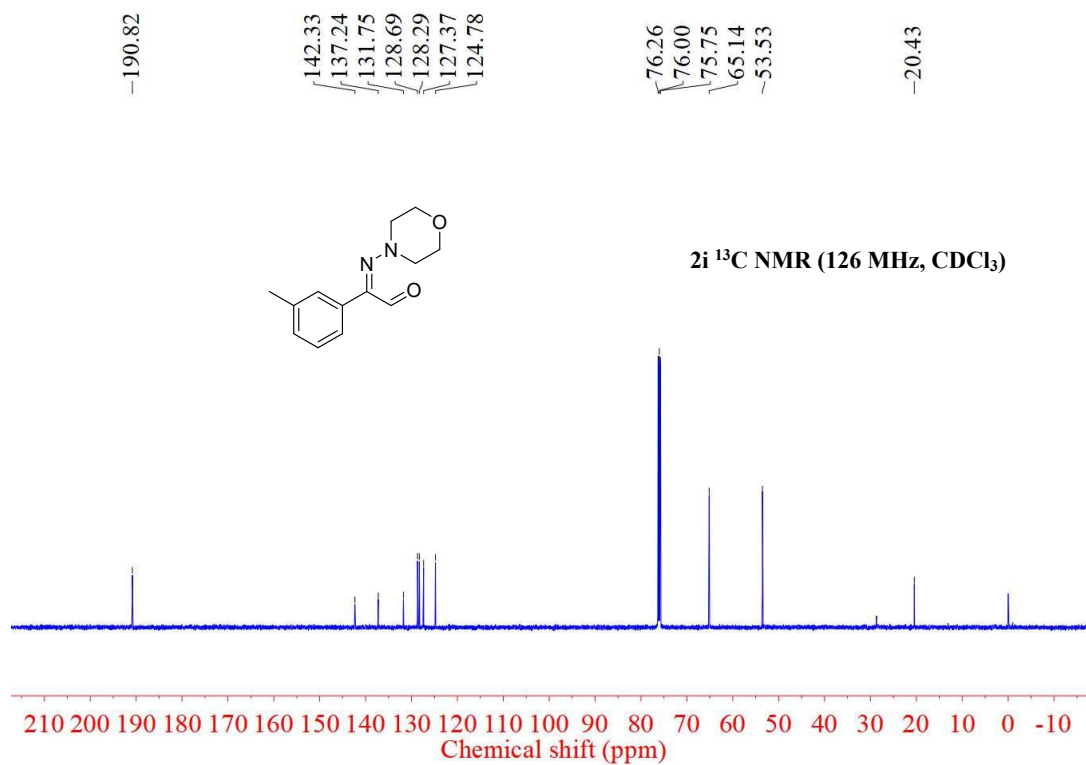


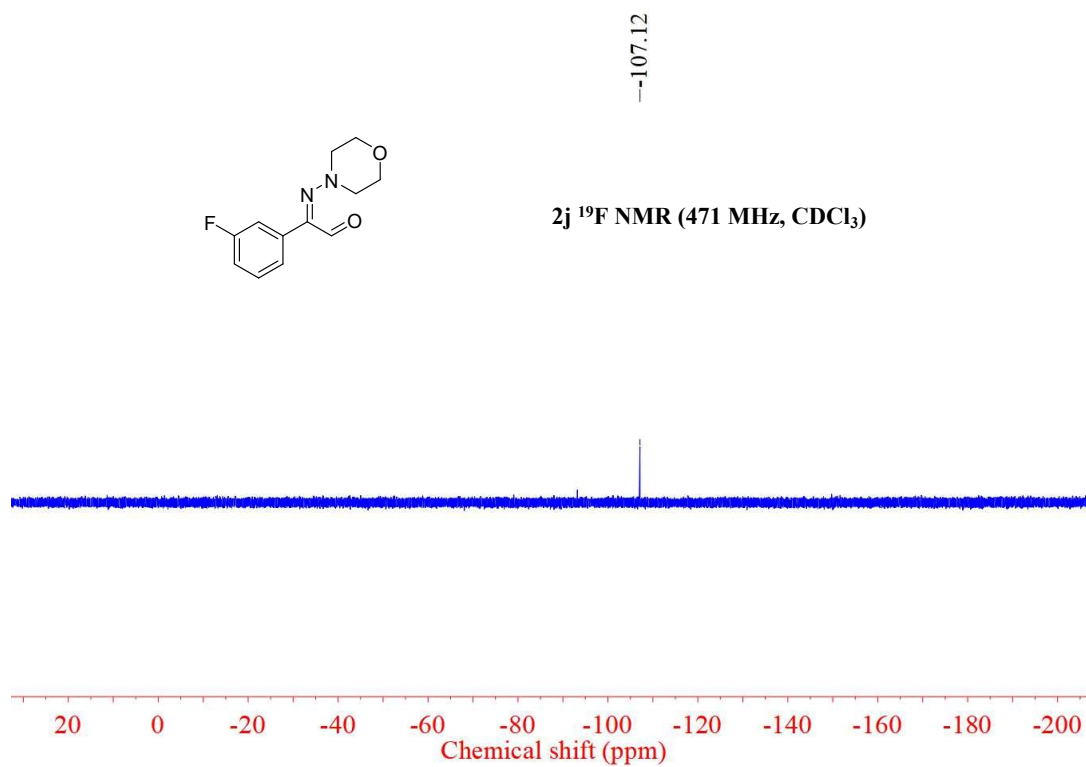
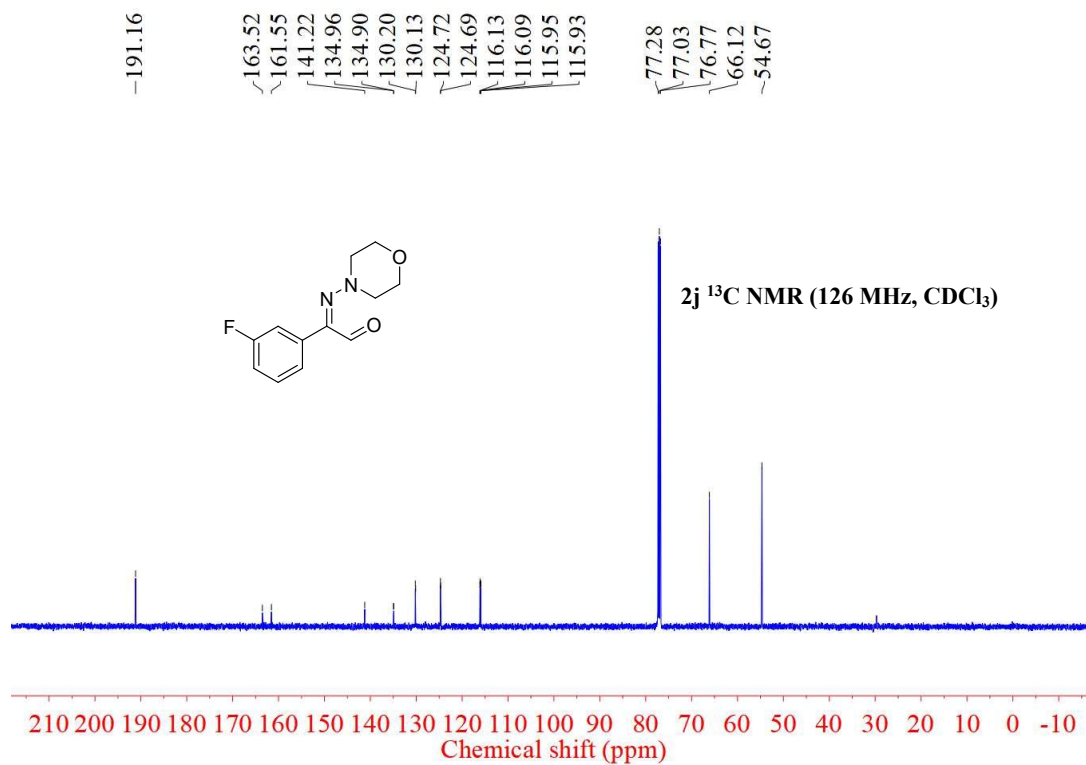


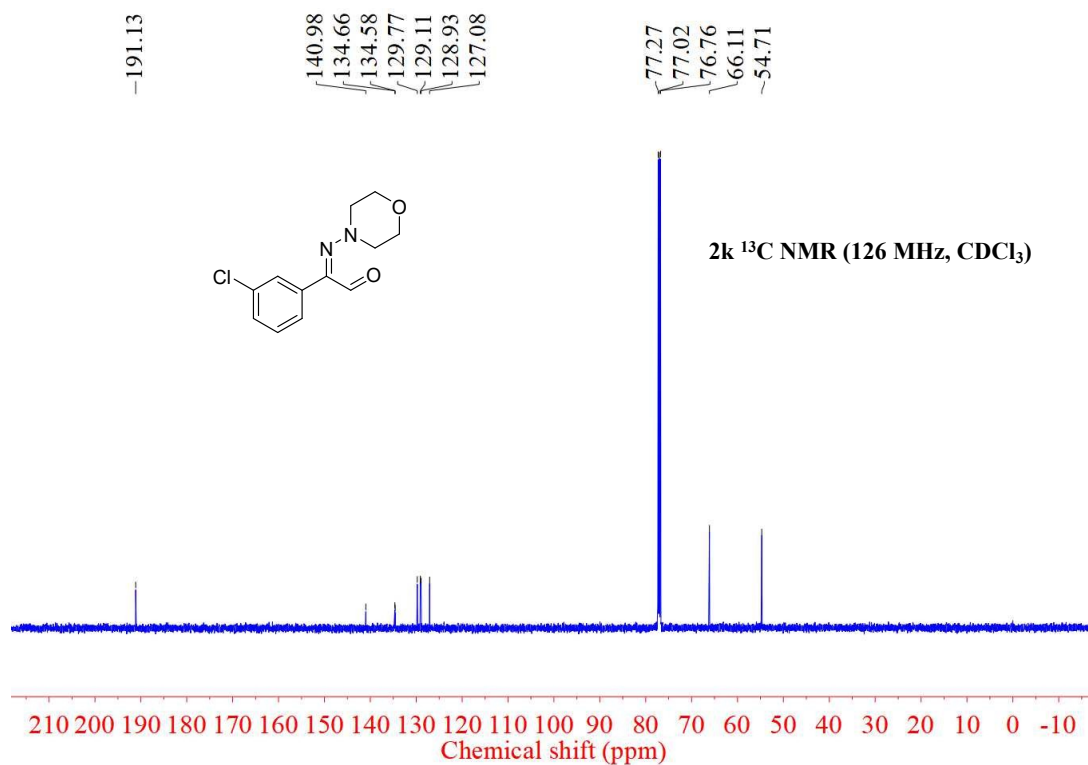
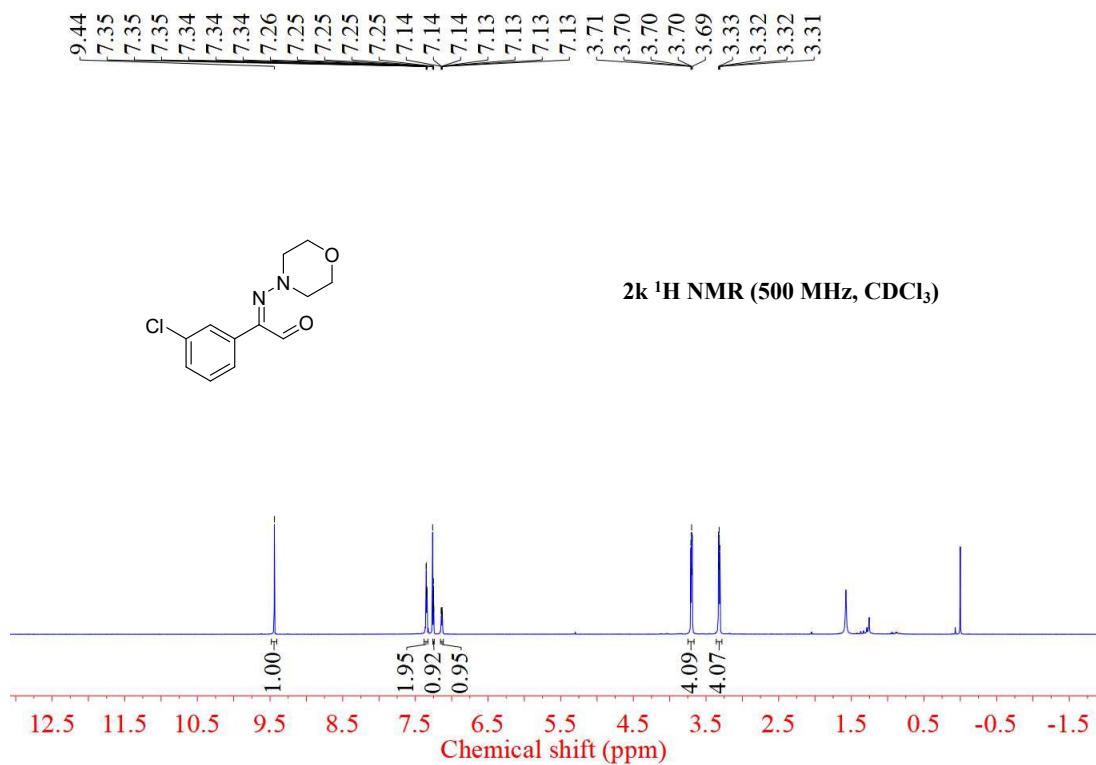


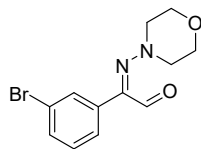




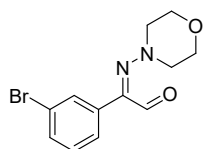
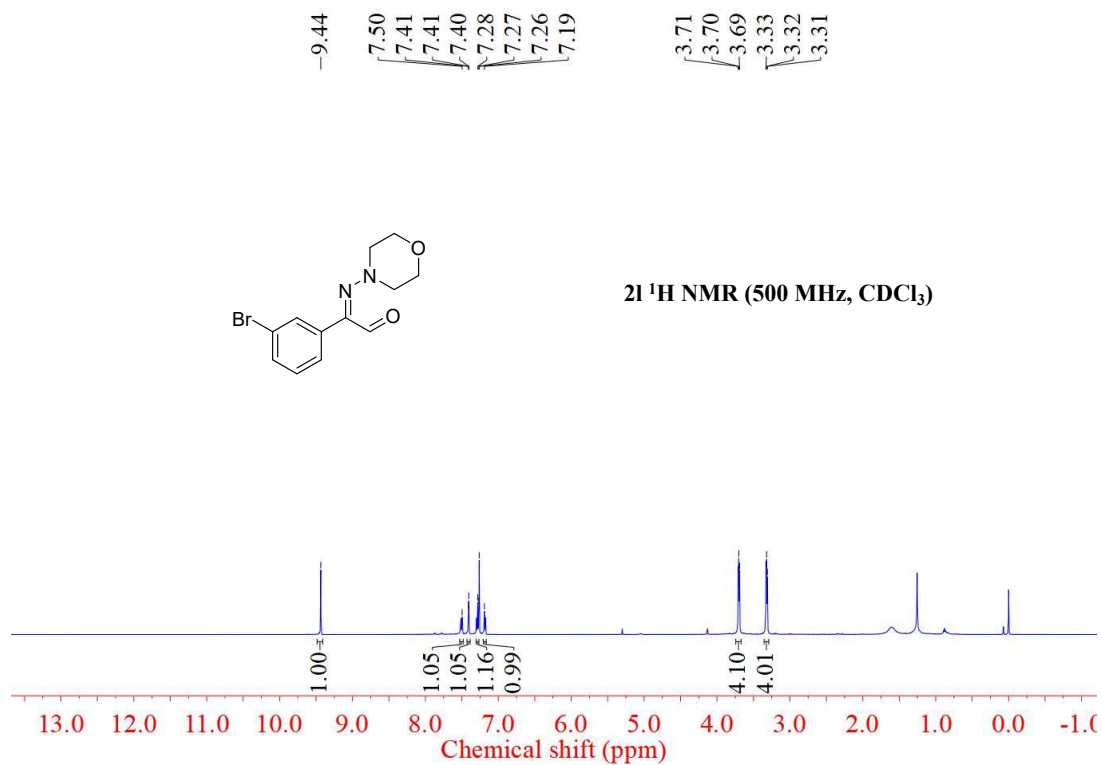




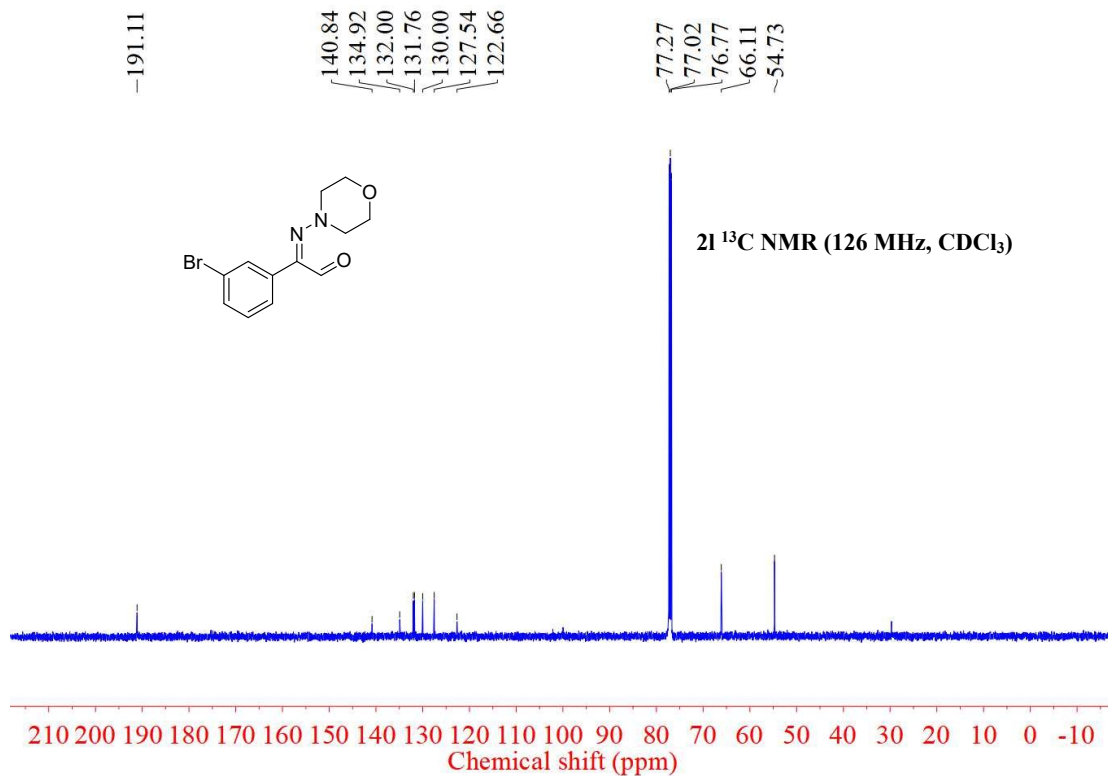




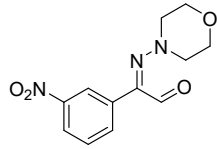
21 ¹H NMR (500 MHz, CDCl₃)



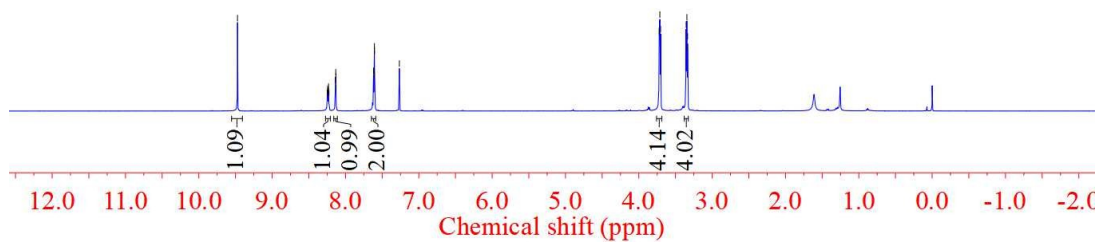
21 ¹³C NMR (126 MHz, CDCl₃)



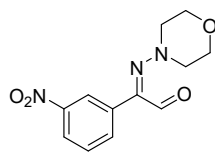
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3.34
3.33



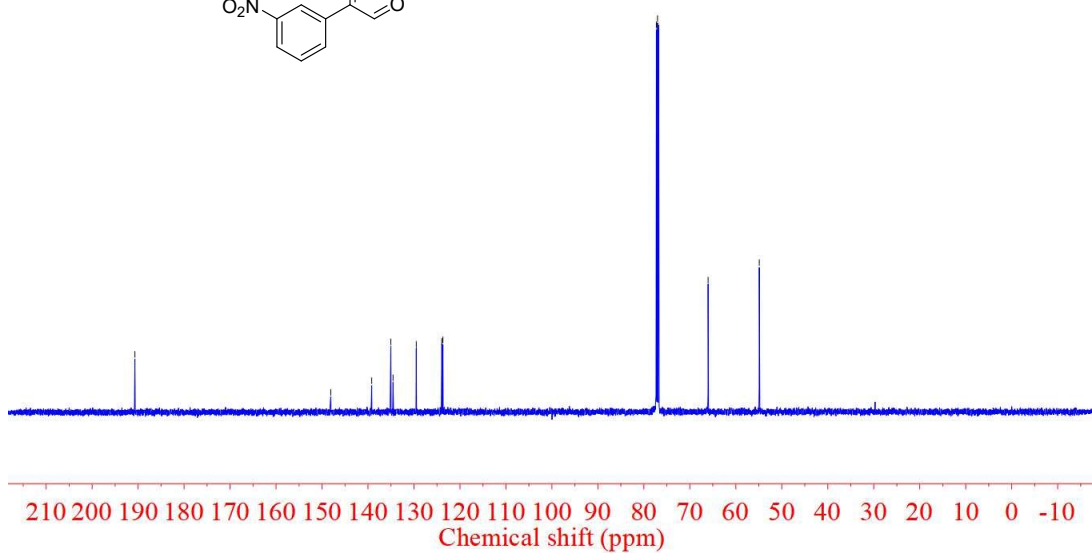
2m ¹H NMR (500 MHz, CDCl₃)



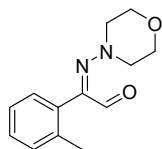
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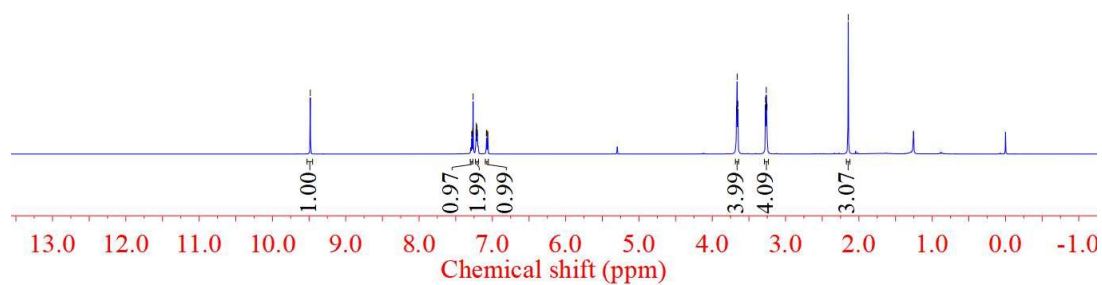
2m ¹³C NMR (126 MHz, CDCl₃)



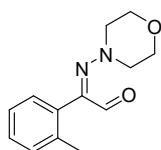
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3.27
3.26
3.26
3.25
-2.15



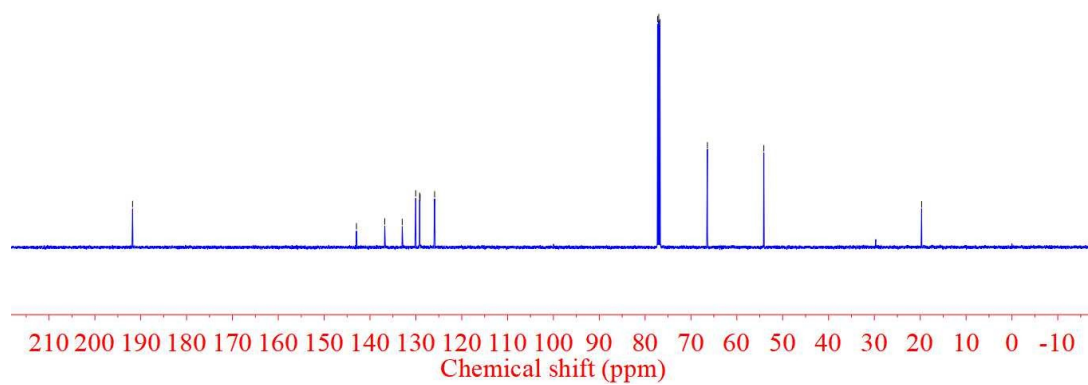
2n ¹H NMR (500 MHz, CDCl₃)



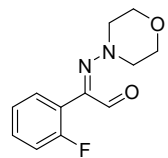
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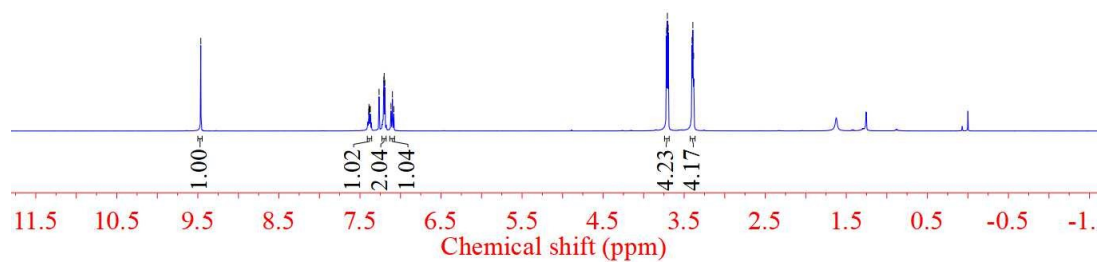
2n ¹³C NMR (126 MHz, CDCl₃)



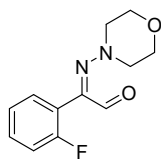
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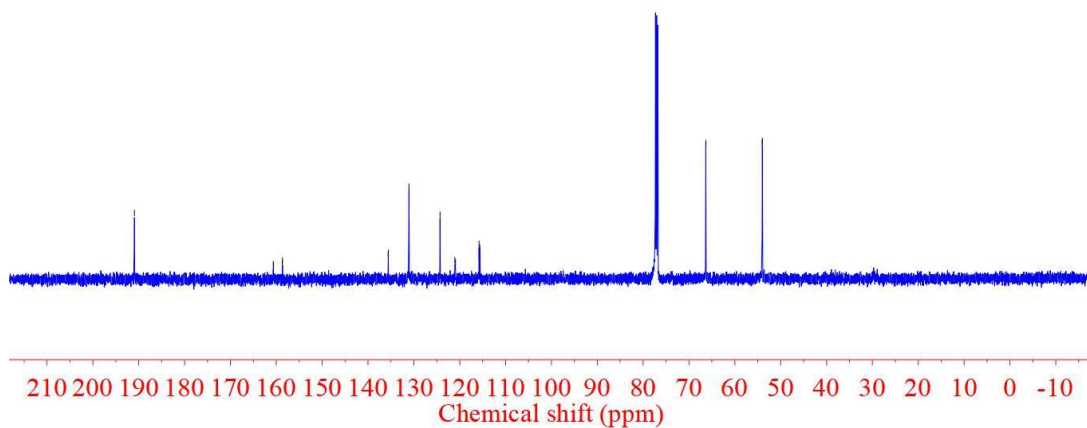
2o ¹H NMR (500 MHz, CDCl₃)



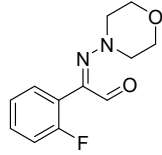
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66.30
54.03
53.99



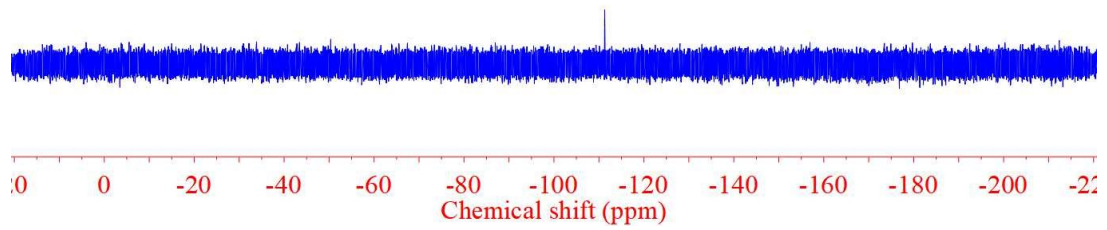
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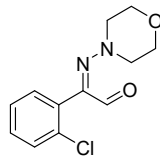
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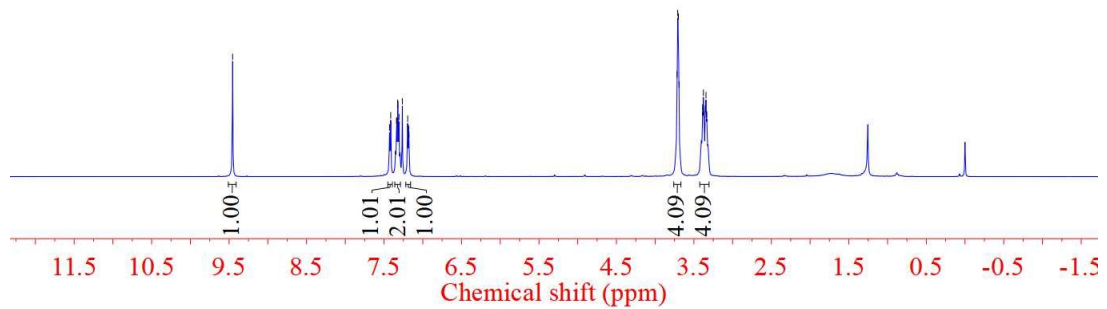
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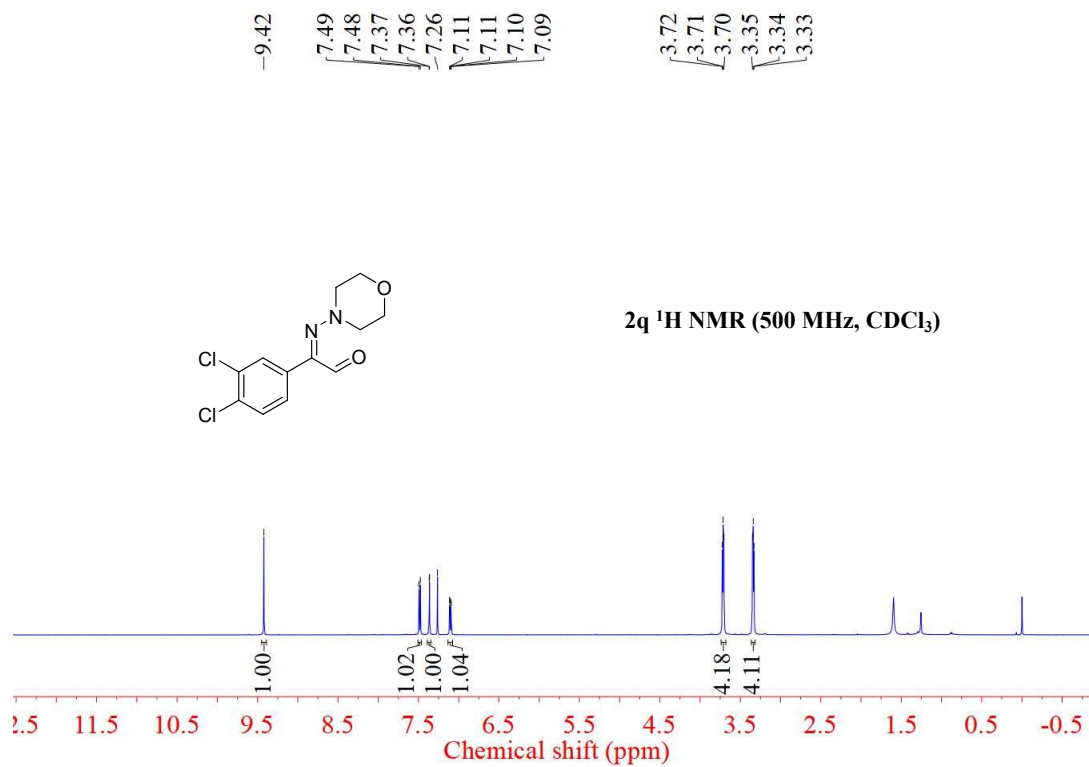
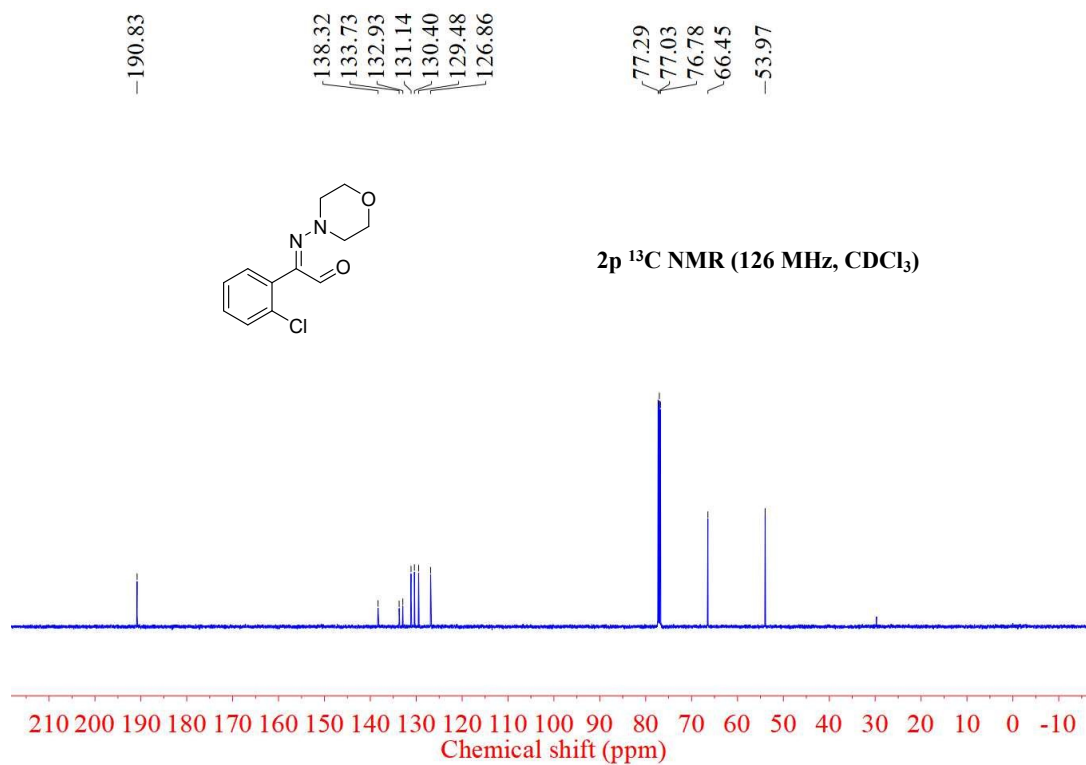


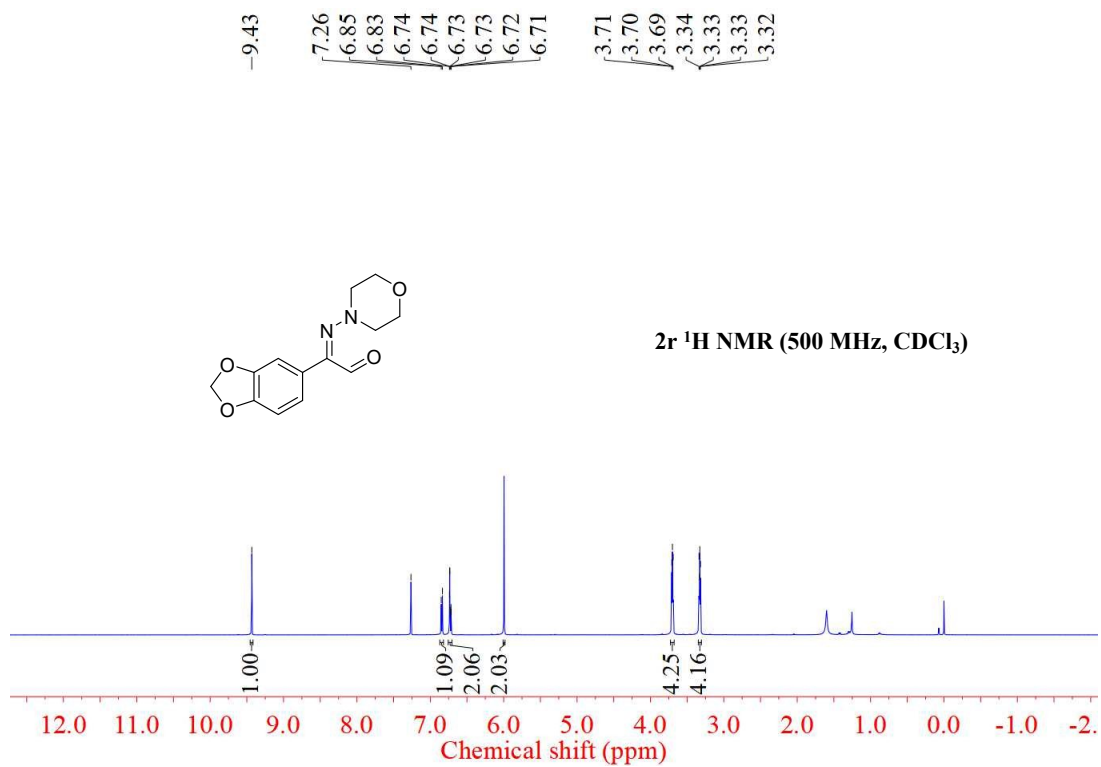
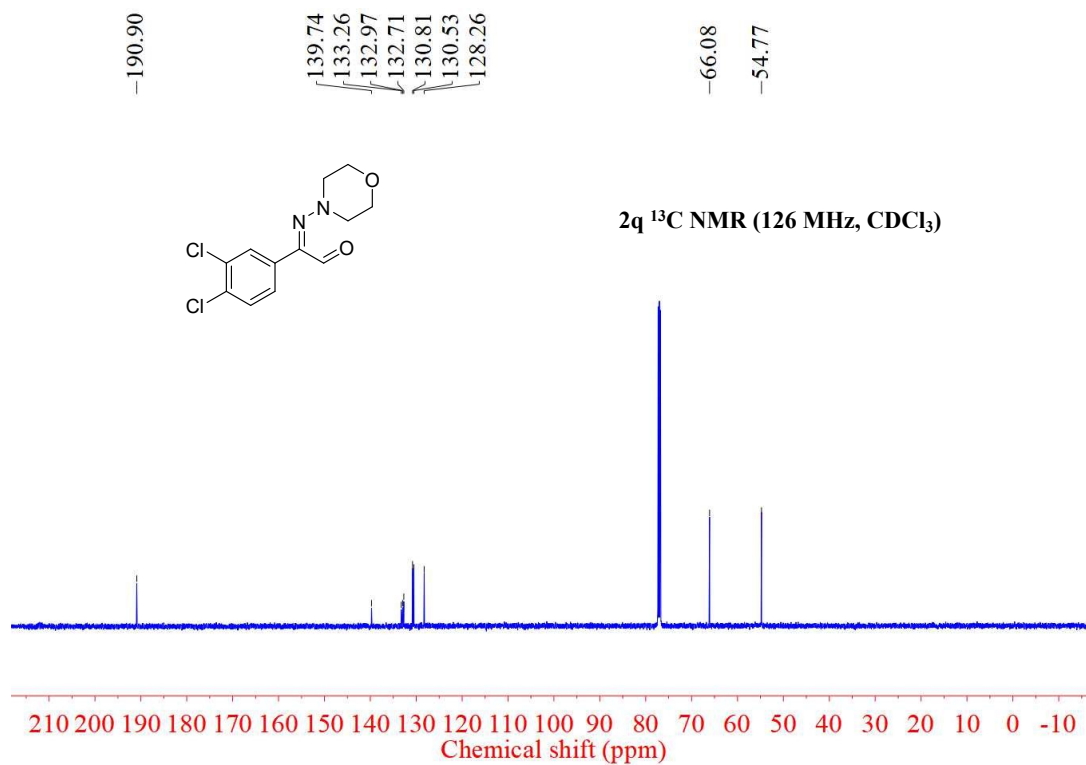
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3.34
3.33

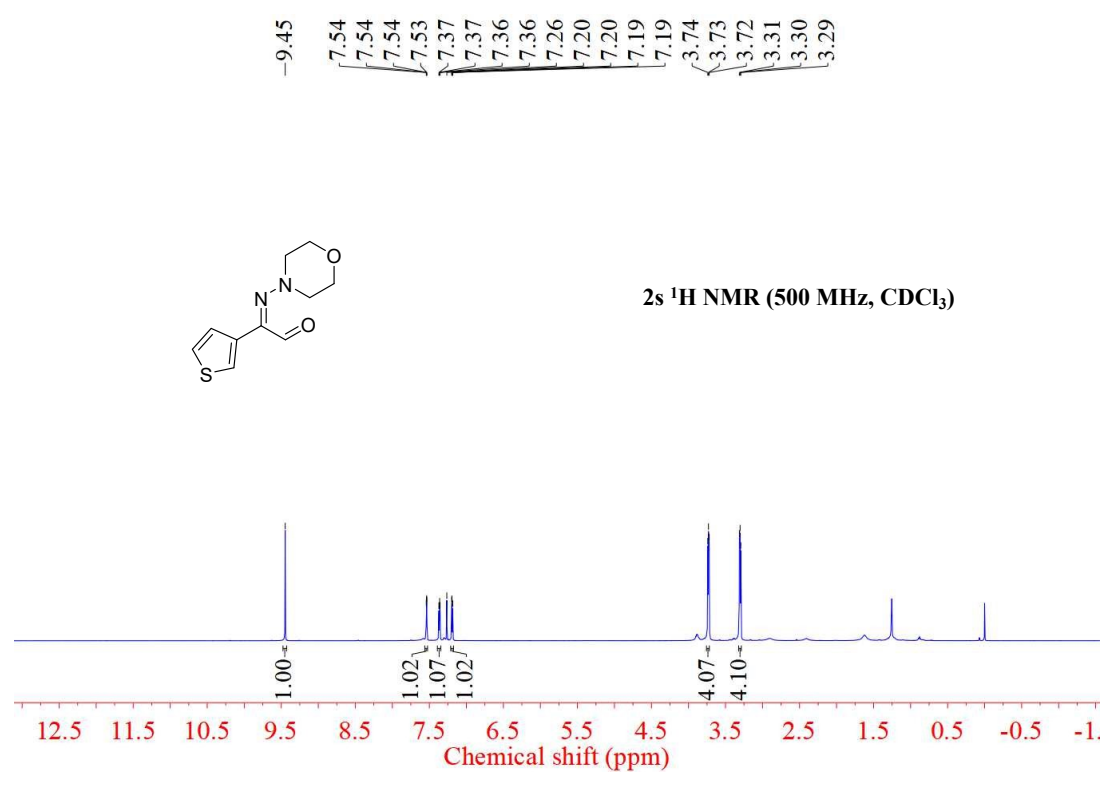
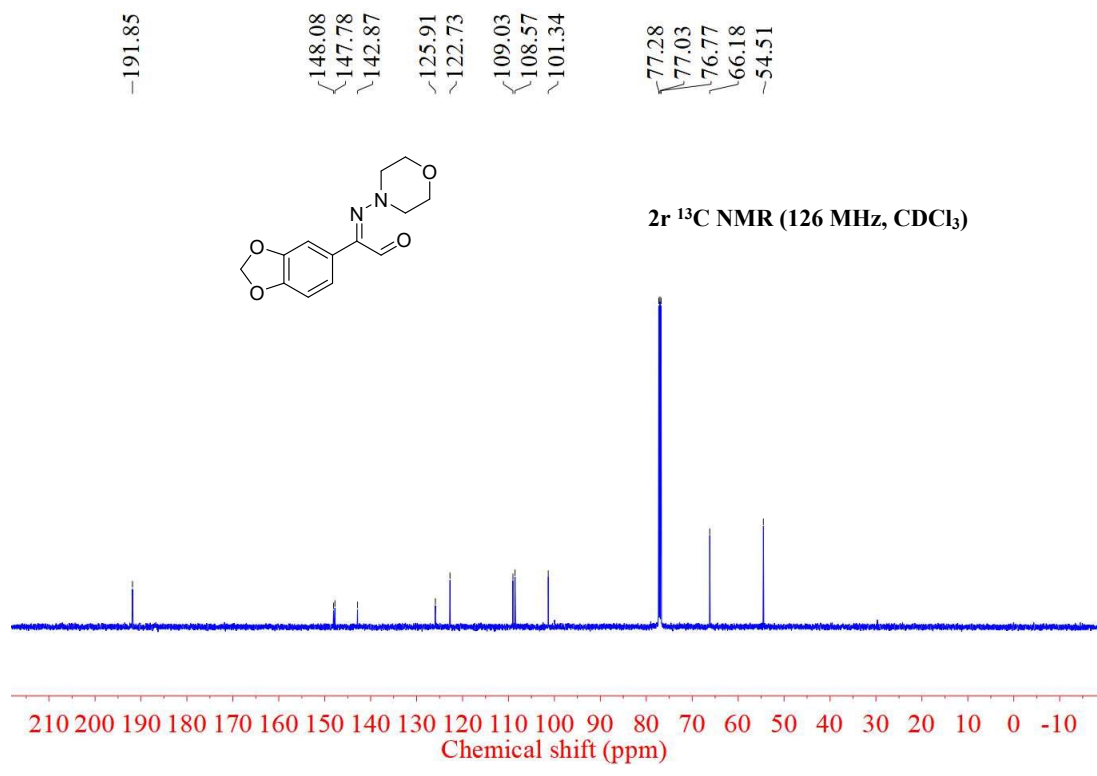


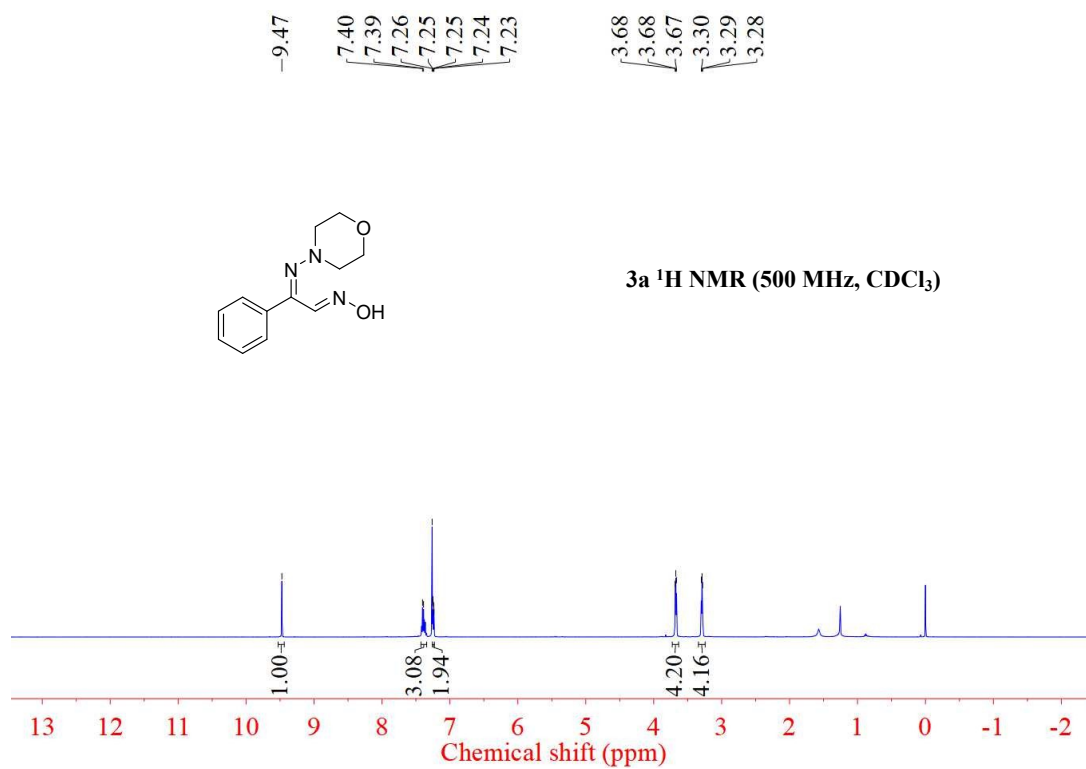
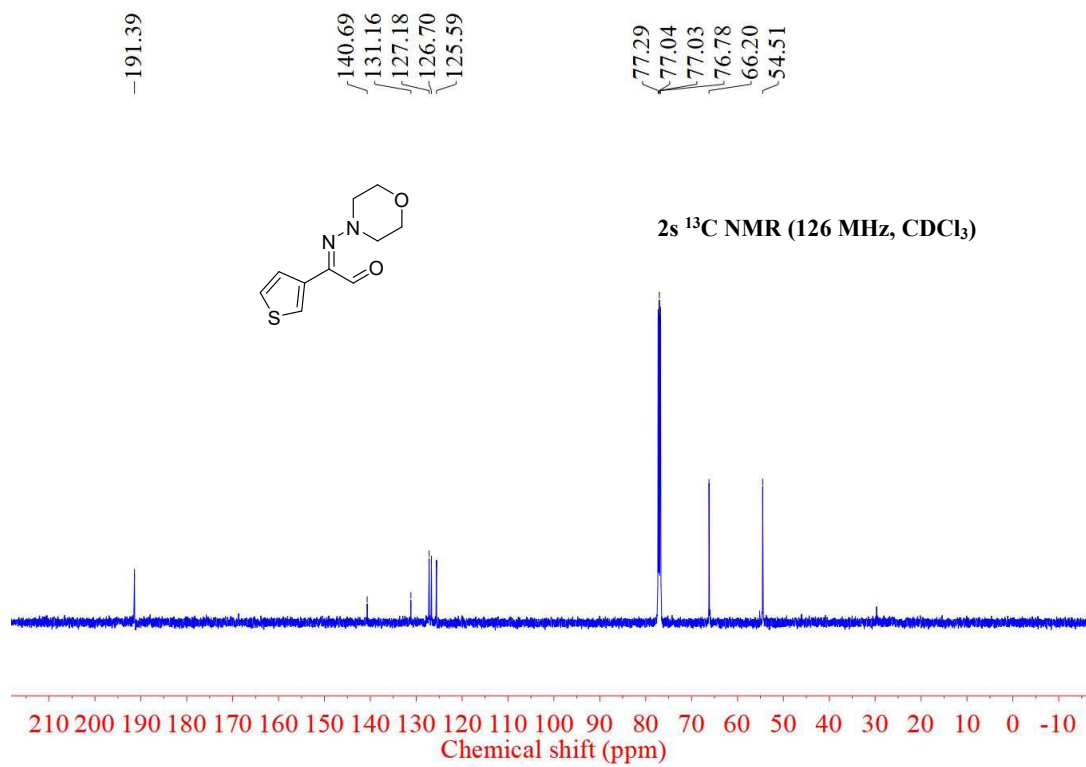
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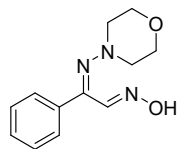




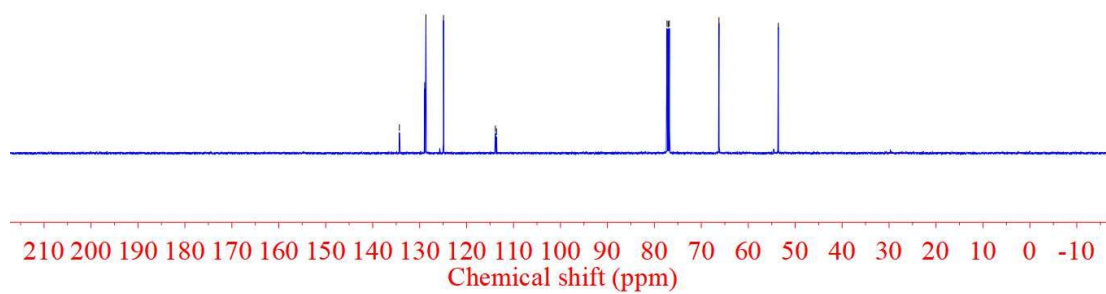


134.31
128.93
128.66
124.91
113.87
113.61

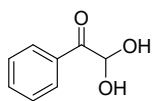
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66.23
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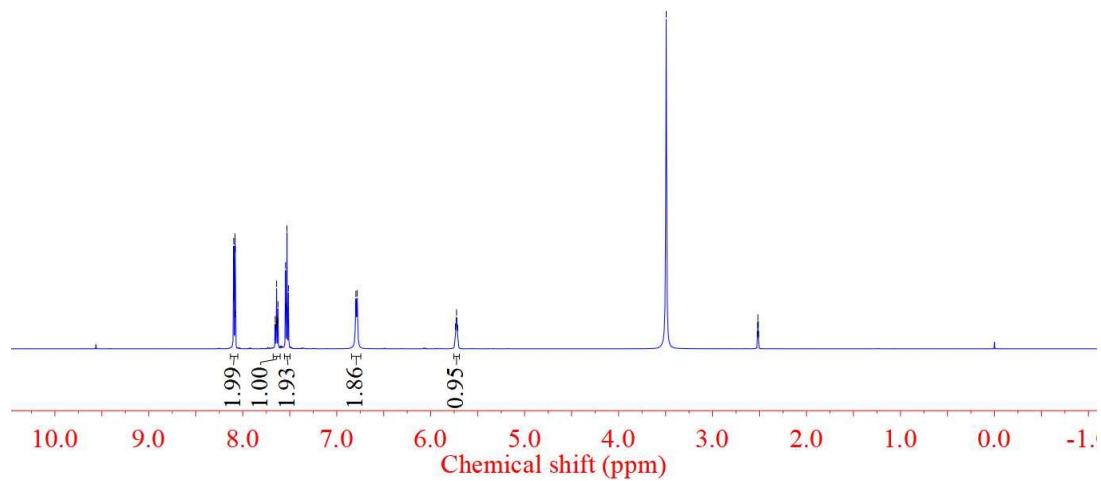
3a ¹³C NMR (126 MHz, CDCl₃)

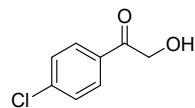


8.10
8.10
8.09
8.09
8.08
8.08
7.66
7.65
7.64
7.64
7.64
7.63
7.63
7.62
7.55
7.54
7.53
7.52
7.51
6.80
6.78
5.74
3.49
2.52
2.52
2.52
2.51
2.51

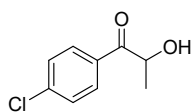
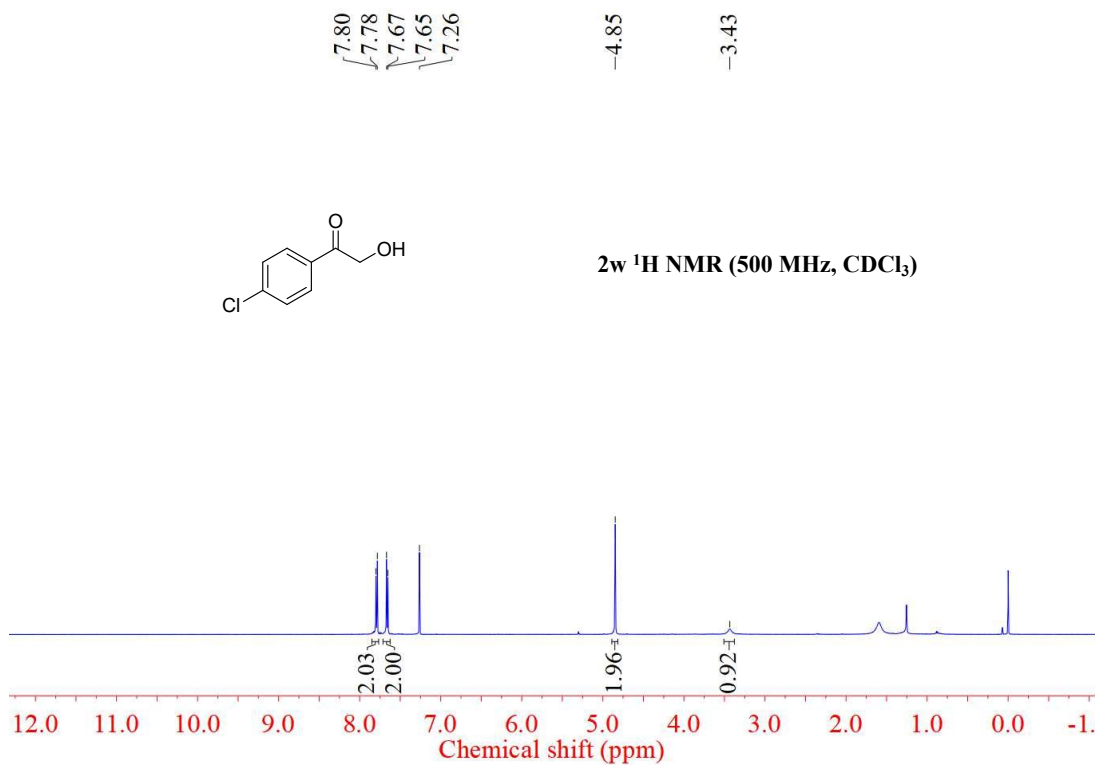


3b ¹H NMR (500 MHz, CDCl₃)

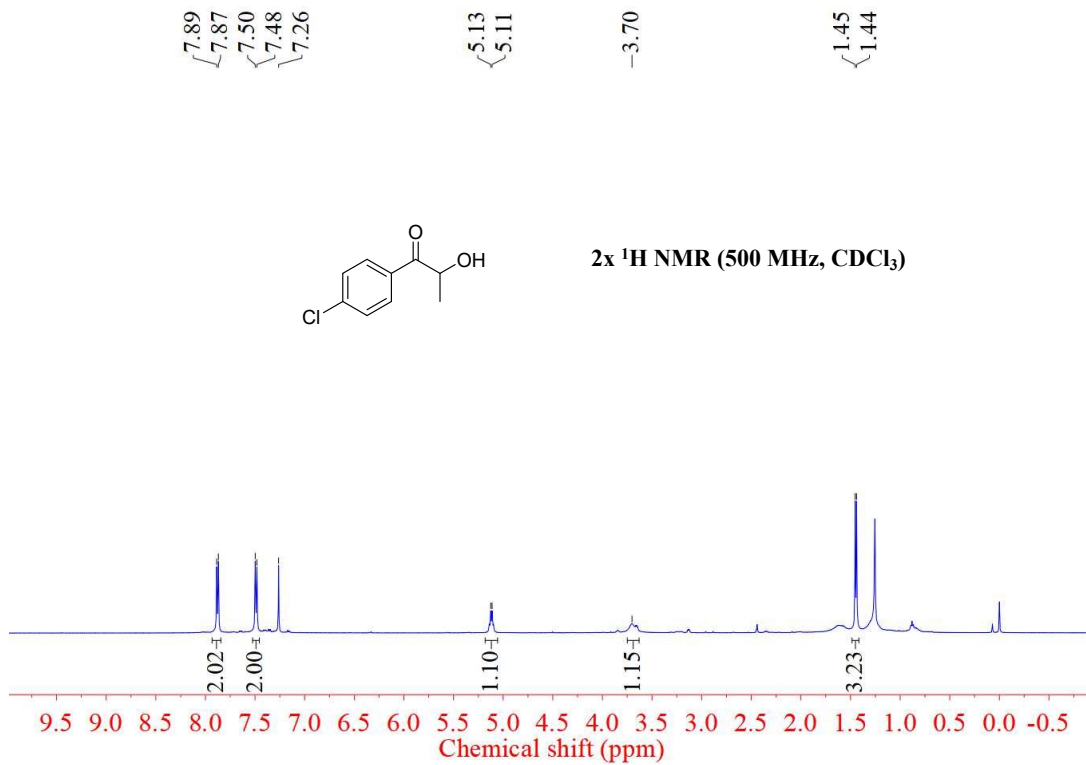




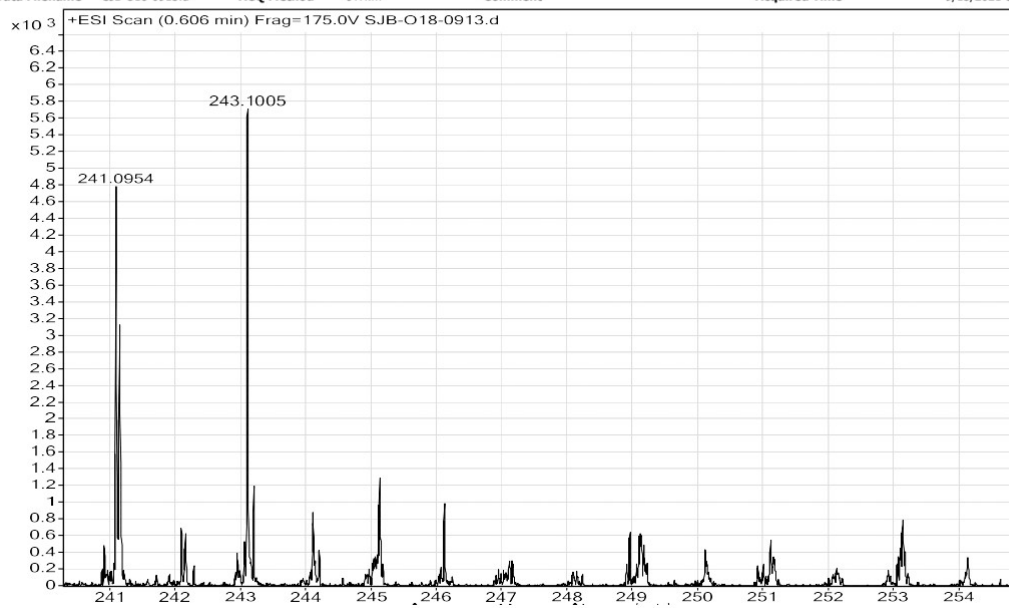
2w ¹H NMR (500 MHz, CDCl₃)



2x ¹H NMR (500 MHz, CDCl₃)



Sample Name	SJB-018	Position	P1-B1	Instrument Name	Instrument 1	User Name	
Inj Vol	5	InjPosition		SampleType	Sample	IRM Calibration Status	Success
Data Filename	SJB-018-0913.d	ACQ Method	JYH.m	Comment		Acquired Time	9/13/2021 6:50:11 PM



HRMS (ESI): [M+Na]⁺ Calculated for C₁₂H₁₄N₂O¹⁸ONa: 243.0995, Found 243.1005.