

Supplementary Materials

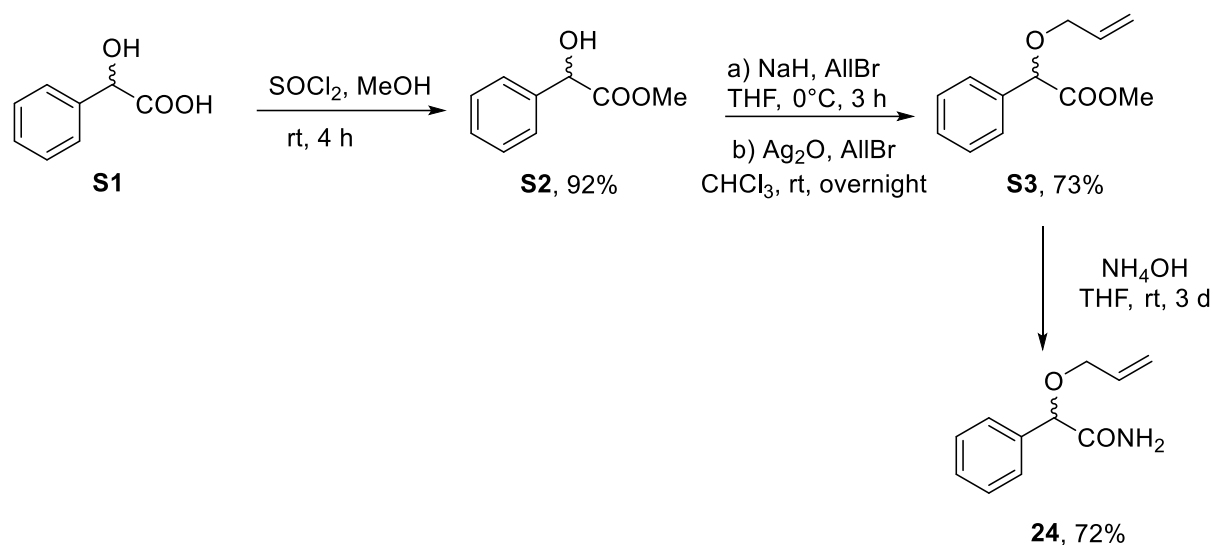
Glycopyranosylidene-Spiro-Morpholinones: Evaluation of the Synthetic Possibilities Based on Glyculosonamide Derivatives and a New Method for the Construction of the Morpholine Ring

Nándor Kánya, Sándor Kun and László Somsák *

Contents

Synthesis of 2-allyloxy-2-phenylacetamide (24).....	2
Attempted transformations of glucopyranosonamide 18.....	3
Copies of the ^1H and ^{13}C J-MOD NMR spectra	4

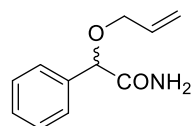
Synthesis of 2-allyloxy-2-phenylacetamide (24)



This synthesis was performed from racemic mandelic acid **S1** via the known intermediates **S2** and **S3** prepared according to a published procedure (Vink, M.K.S., PhD Thesis, University of Amsterdam, 2003).

<https://dare.uva.nl/search?identifier=7012b66e-2c8b-48f7-8258-d284d5e8ffde>

2-Allyloxy-2-phenylacetamide (24)



Methyl 2-(allyloxy)-2-phenylacetate (**S3**, 3.0 g, 14.5 mmol) was dissolved in THF (15 mL), and aqueous ammonia solution (25 w/w %, 25 mL) was added. The resulting two-phase system was stirred vigorously at room temperature for 2 days, after which TLC showed complete conversion. The mixture was diluted with water (40 mL), and the aqueous layer was extracted with ethyl acetate (3×20 mL), and the combined organic phases was dried on magnesium sulphate, filtered and concentrated. The crude product was used without further purification. Yield: 2.0 g (72 %), pale yellow oil. $R_f = 0.38$ (hexane/acetone 2:1). ^1H NMR (400 MHz CDCl_3) δ (ppm): 7.42-7.29 (5H, m, Ar), 6.72 (1H, brs, NH), 6.63 (1H, brs, NH), 5.89 (1H, dddd, $J = 17.2, 10.5, 6.0, 5.4$ Hz, $-\text{OCH}_2\text{-CH=CH}_2$), 5.26 (1H, dq, $J = 17.3, 1.6, 1.6$ Hz, $-\text{OCH}_2\text{-CH=CH}_2$), 5.21 (1H, dq, $J = 10.4, 1.2$ Hz, $-\text{OCH}_2\text{-CH=CH}_2$), 4.76 (1H, s, Ph-CH-O), 4.03 (1H, ddt, $J = 12.7, 5.2, 1.4$ Hz, $-\text{OCH}_2\text{-CH=CH}_2$), 3.94 (1H, ddt, $J = 12.8, 6.0, 1.3$ Hz, $-\text{OCH}_2\text{-CH=CH}_2$). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm): 174.0 (CONH_2), 137.0, 133.7, 128.6 (2), 128.6, 127.2 (2) (Ar, $-\text{OCH}_2\text{-CH=CH}_2$), 118.0 ($-\text{OCH}_2\text{-CH=CH}_2$), 81.1 (Ph-CH-O), 70.2 ($-\text{OCH}_2\text{-CH=CH}_2$).

Attempted transformations of glucopyranosonamide 18

Table S1. Attempted transformations of **18** with dielectrophiles

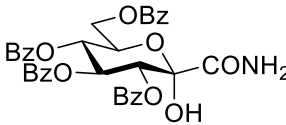
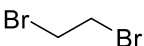
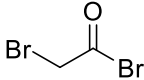
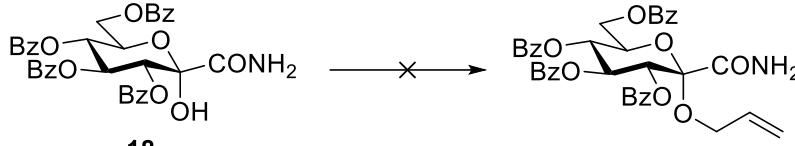
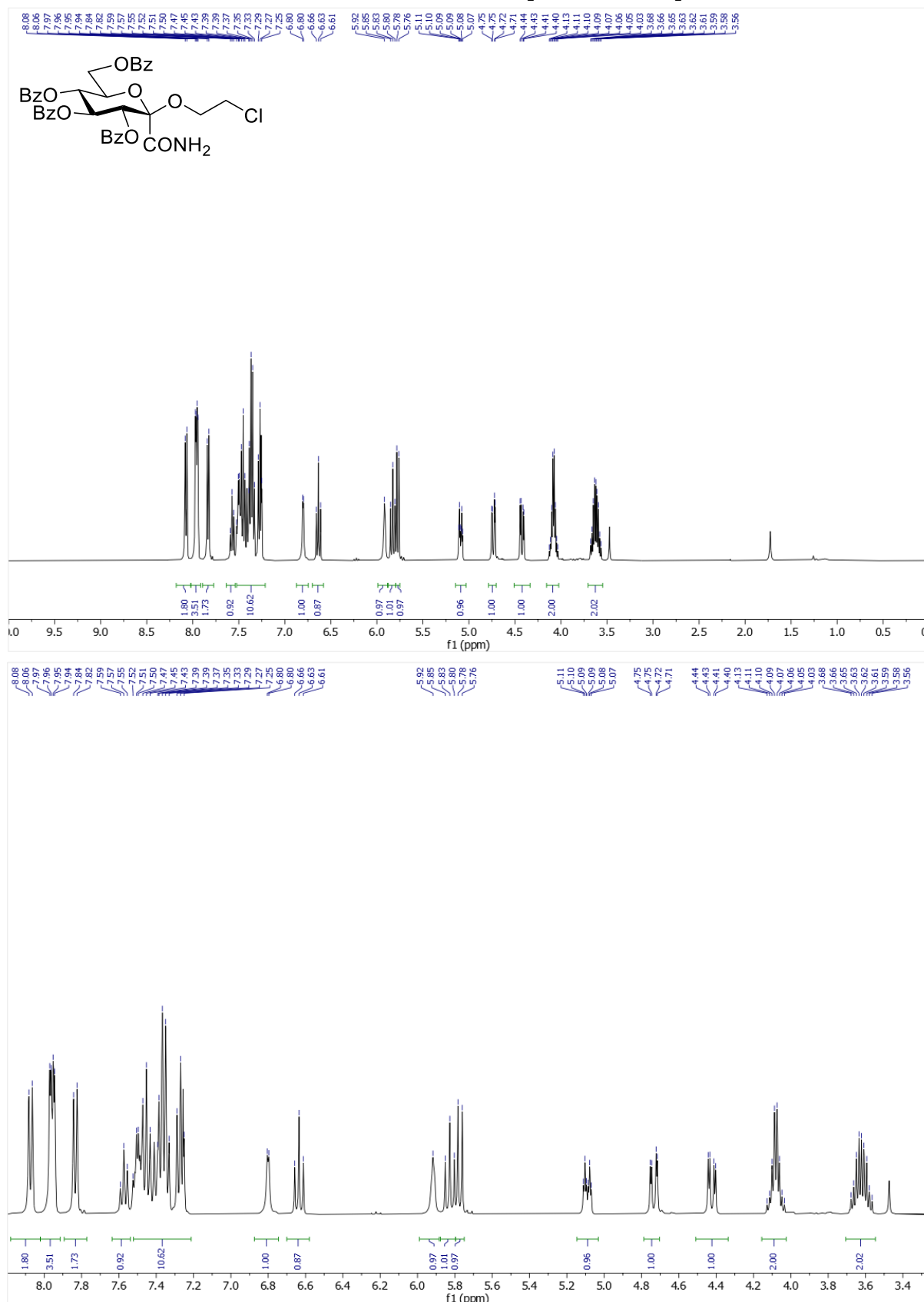
 18		
Reagent		
Conditions		
NaH/THF/25°C	Decomposition	Decomposition
K ₂ CO ₃ /MeCN/100°C	No reaction	No reaction
Pyridine/100°C	No reaction	No reaction

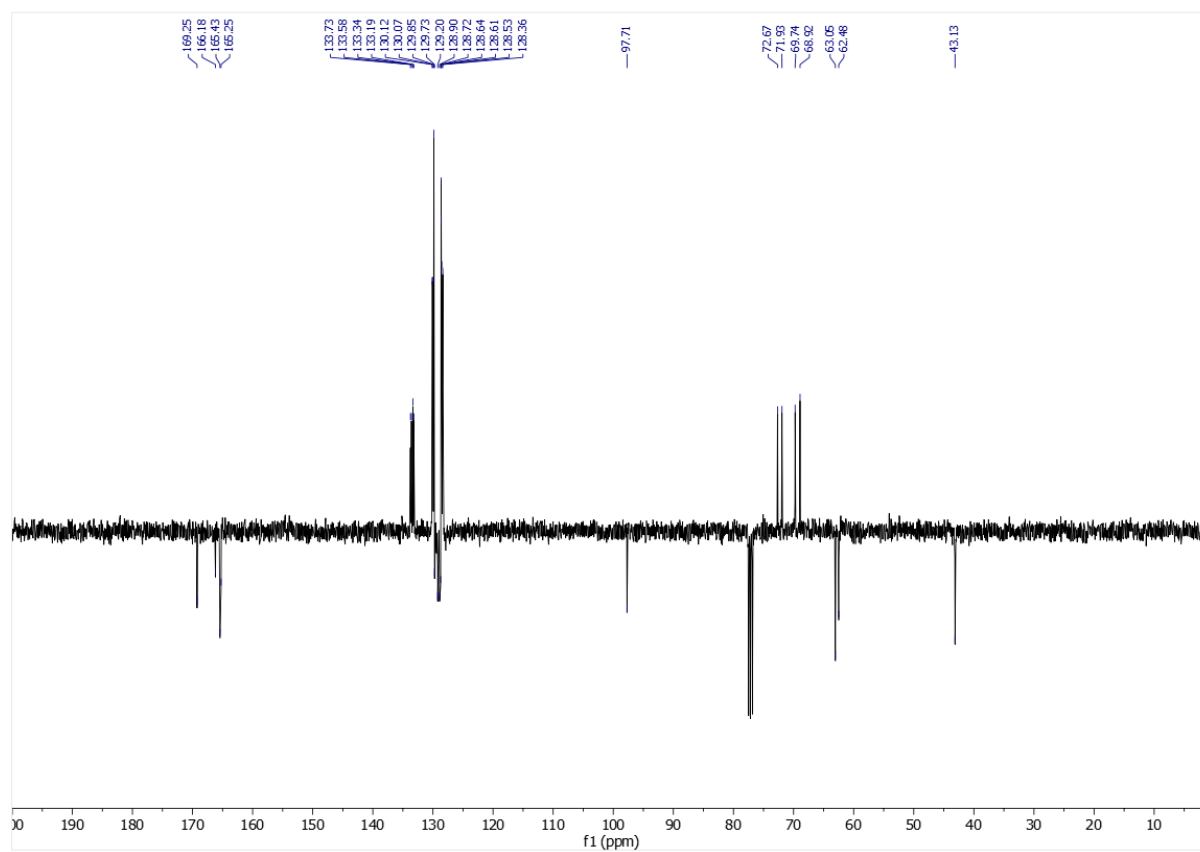
Table S2. Unsuccessful experiments for the allylation of **18**

 18	
Conditions	Observation
Allyl bromide/NaH//THF/0°C	Decomposition
1. Allyl alcohol + Tf ₂ O/0°C, 2. 18 + K ₂ CO ₃	No reaction
Allyl bromide + AgOTf/Et ₃ N/CHCl ₃ /25°C	No reaction
1. Allyl alcohol + Cl ₃ C-CN/NaH/Et ₂ O/0°C	No reaction
2. 18 + K ₂ CO ₃	
Allyl bromide + Pd(dba) ₃ /CHCl ₃ /25°C	No reaction
„Tsuji-Trost allylation” {Trost, 1996 #6396}	
1. Me ₃ Si-NEt ₂ , 2. Allyl-bromide +	No reaction
CsF/DMF/0°C {Suzuki, 2015 #6397}	

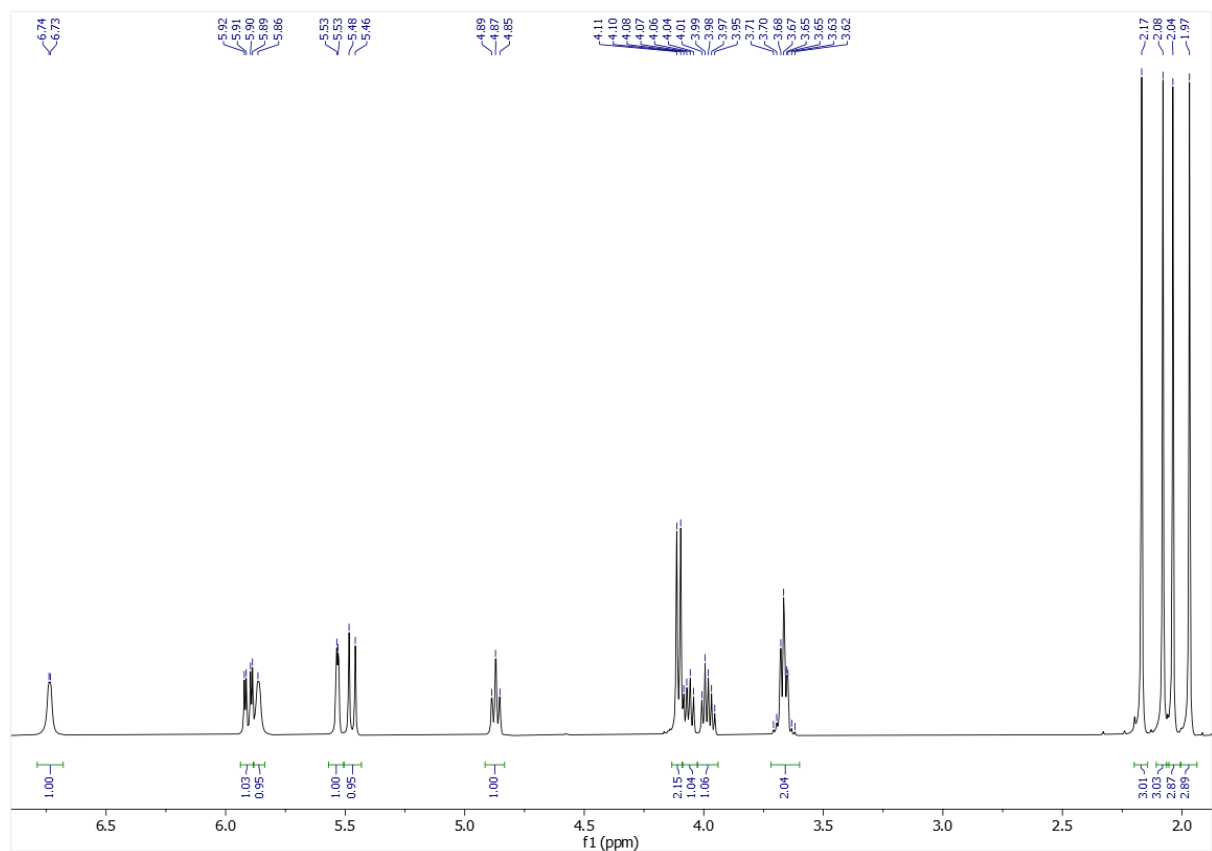
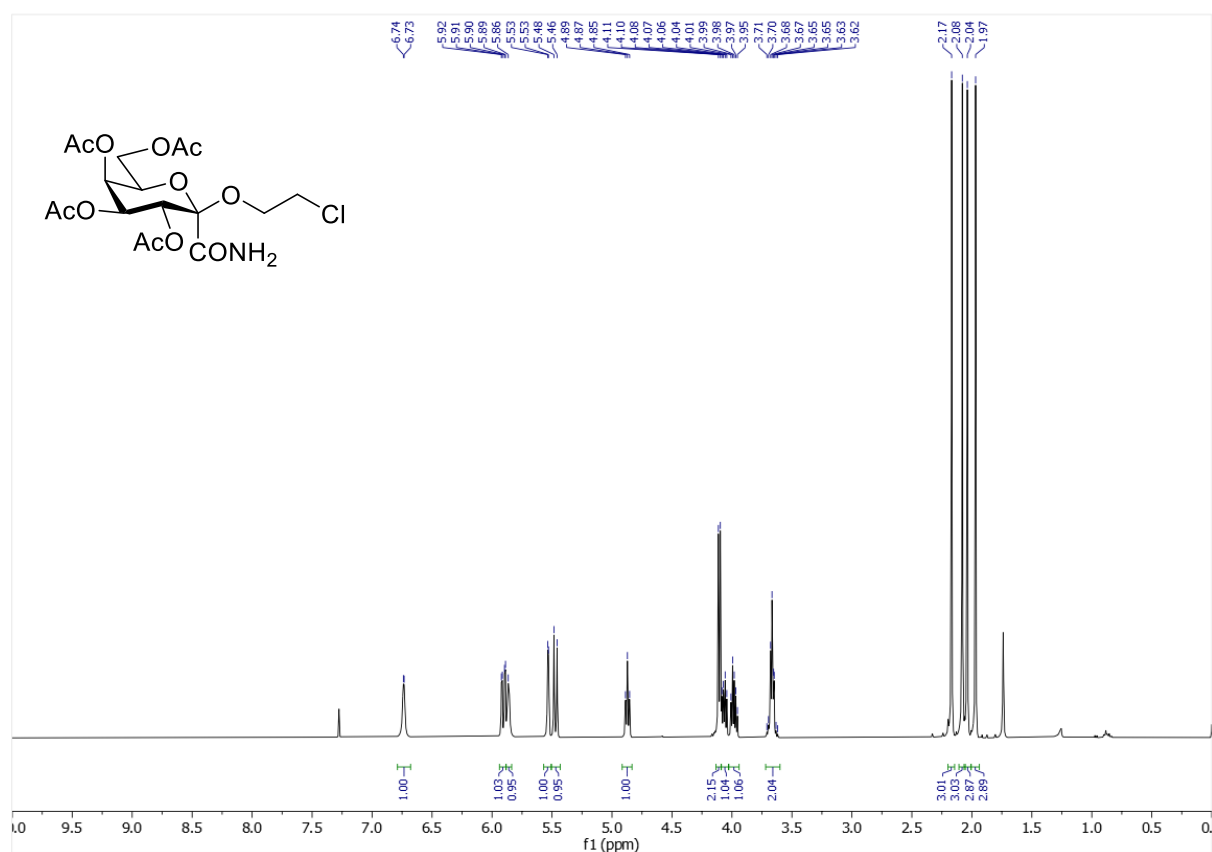
Copies of the ^1H and ^{13}C J-MOD NMR spectra

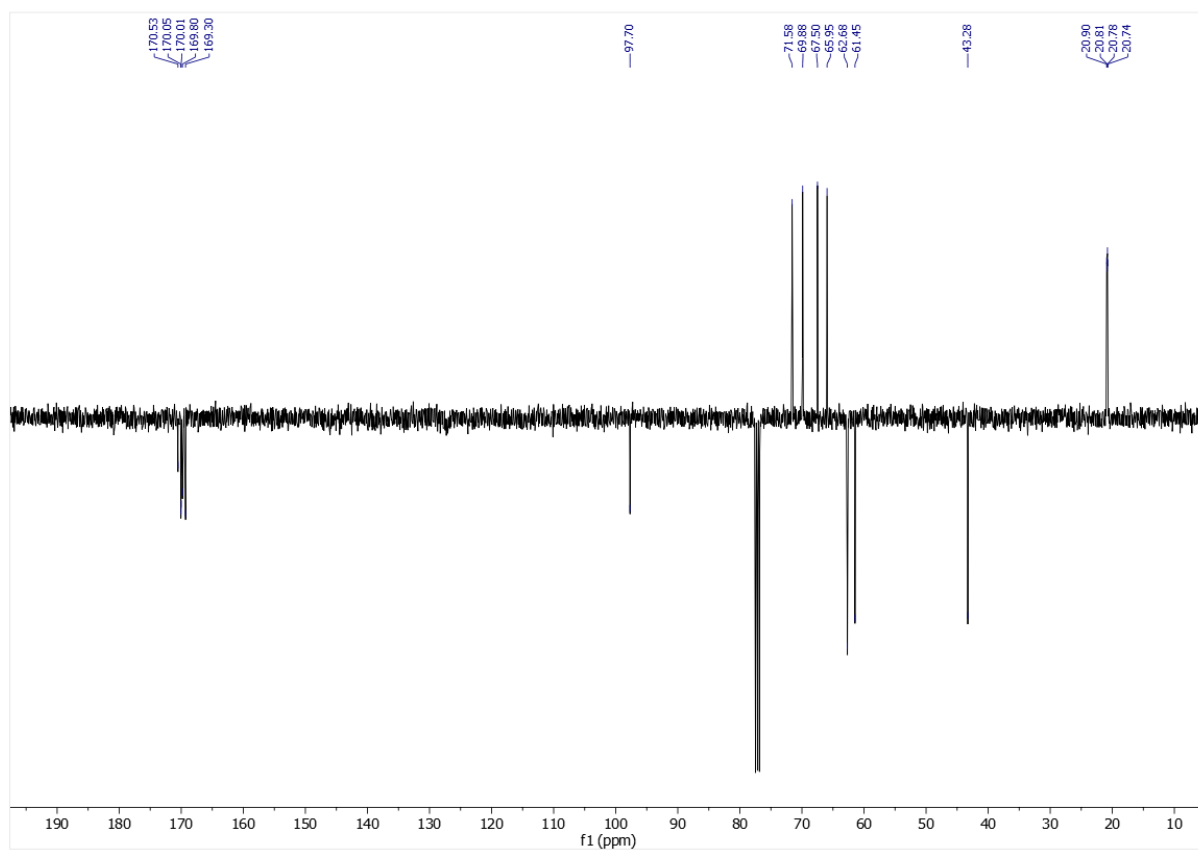
^1H (400 MHz) and ^{13}C J-MOD (100 MHz) NMR spectra of compound **11** in CDCl_3



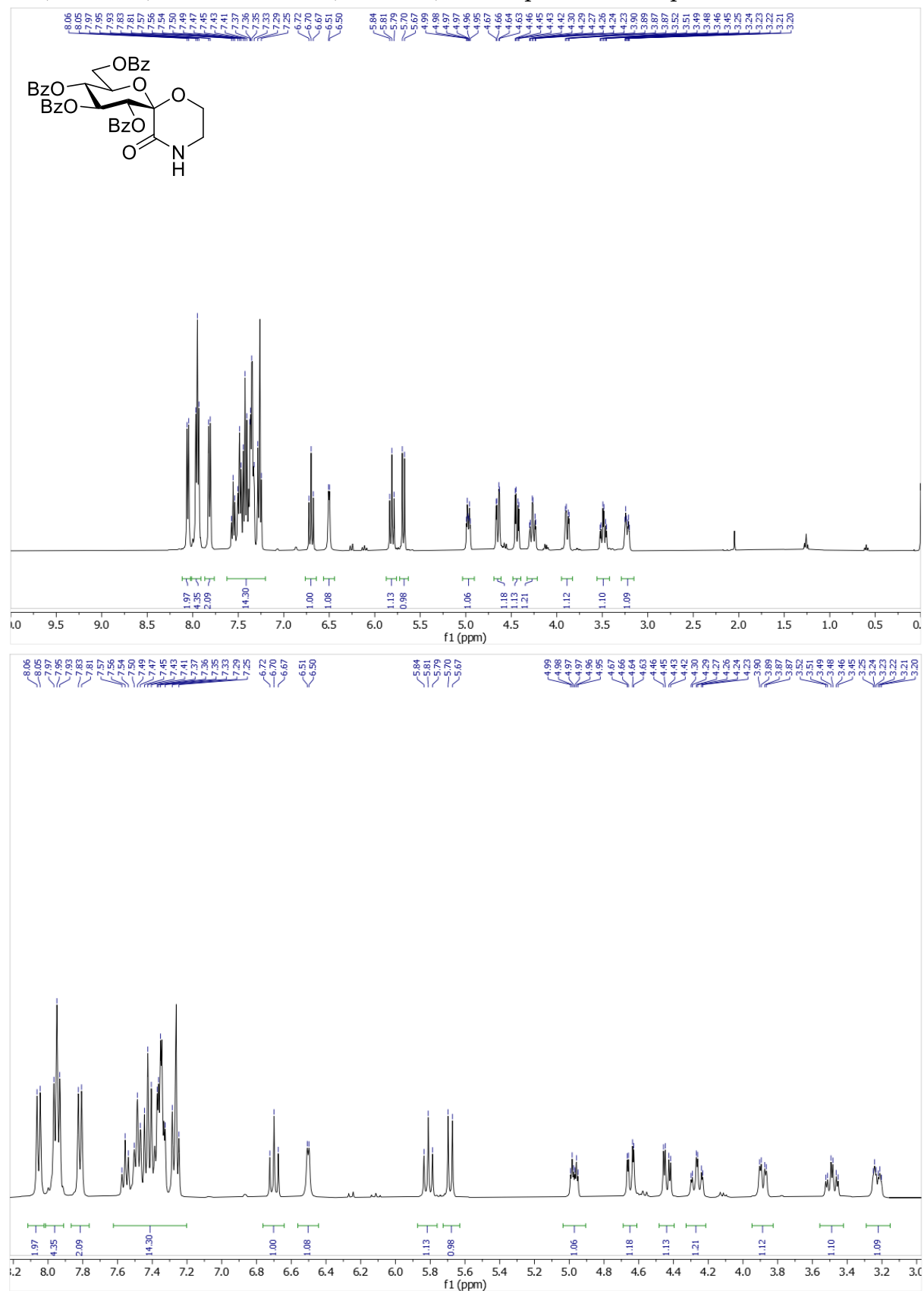


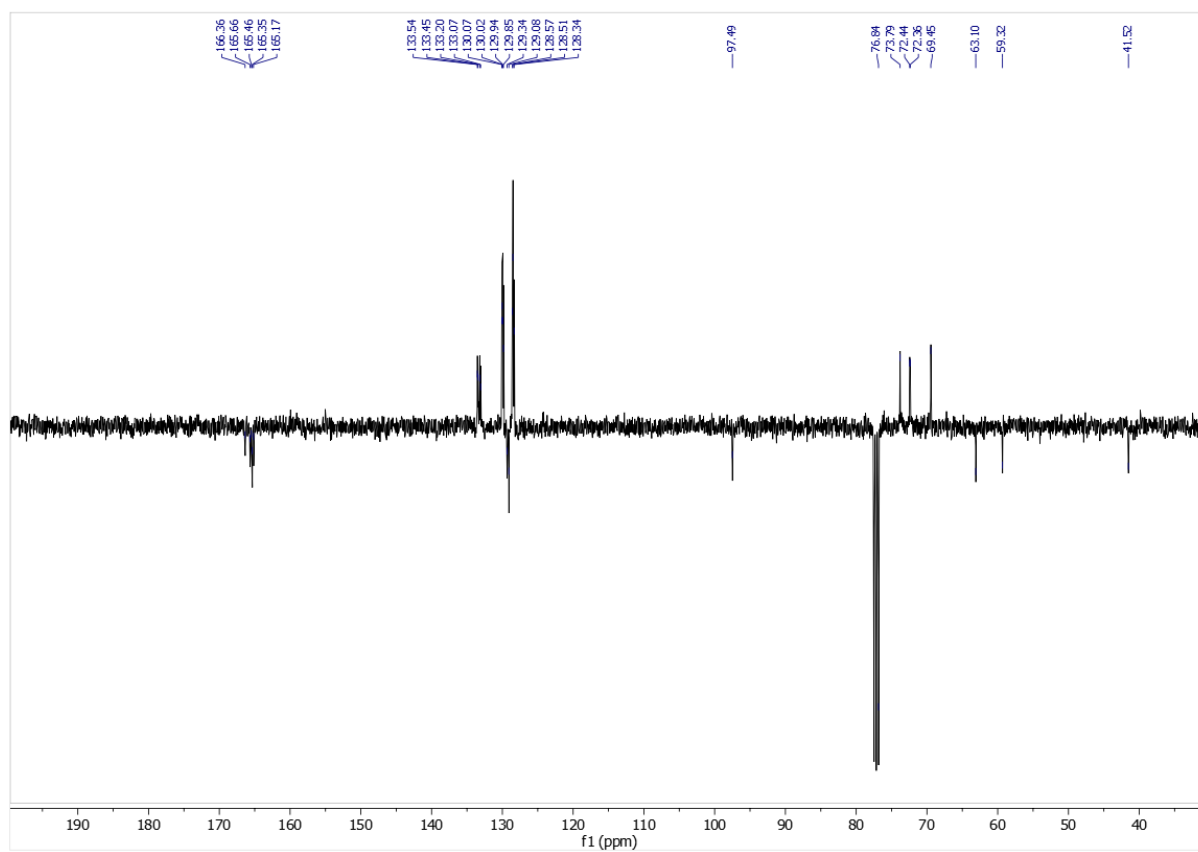
^1H (400 MHz) and ^{13}C J-MOD (100 MHz) NMR spectra of compound **12** in CDCl_3



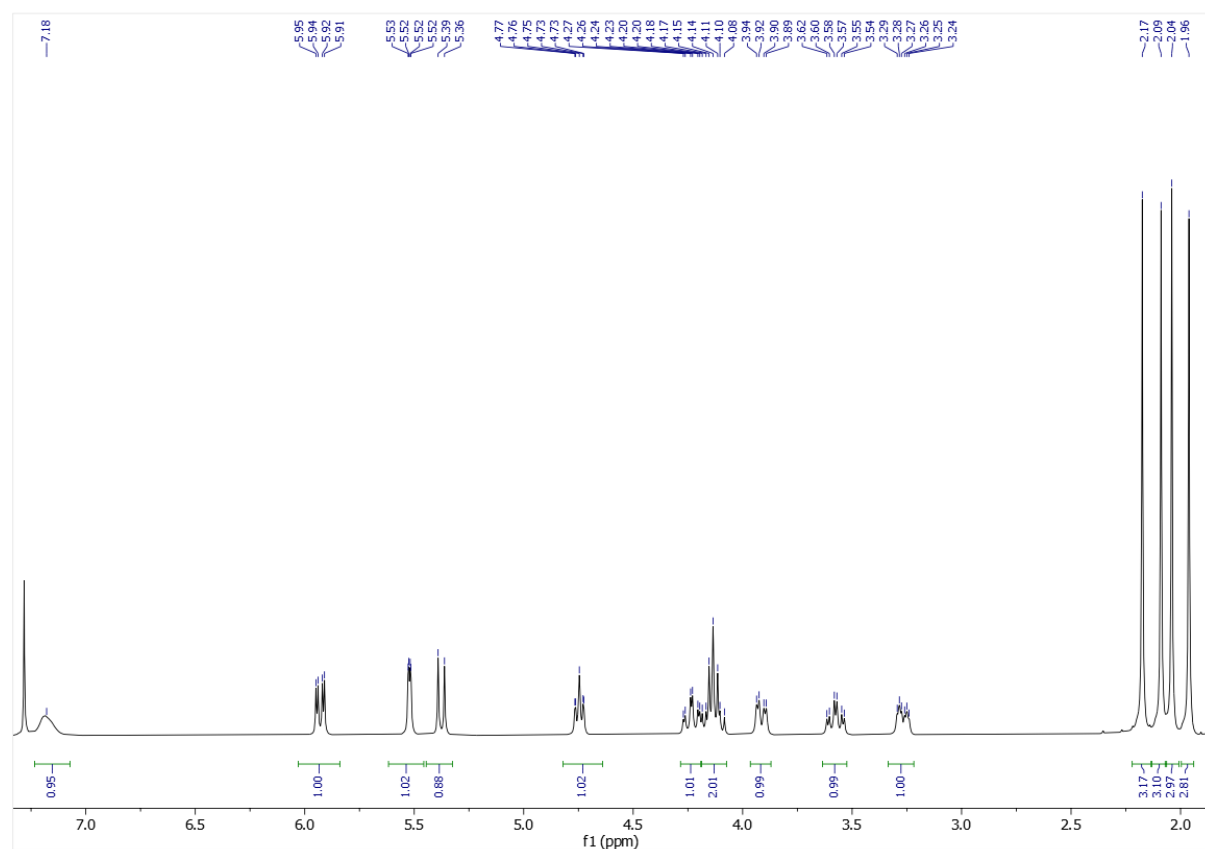
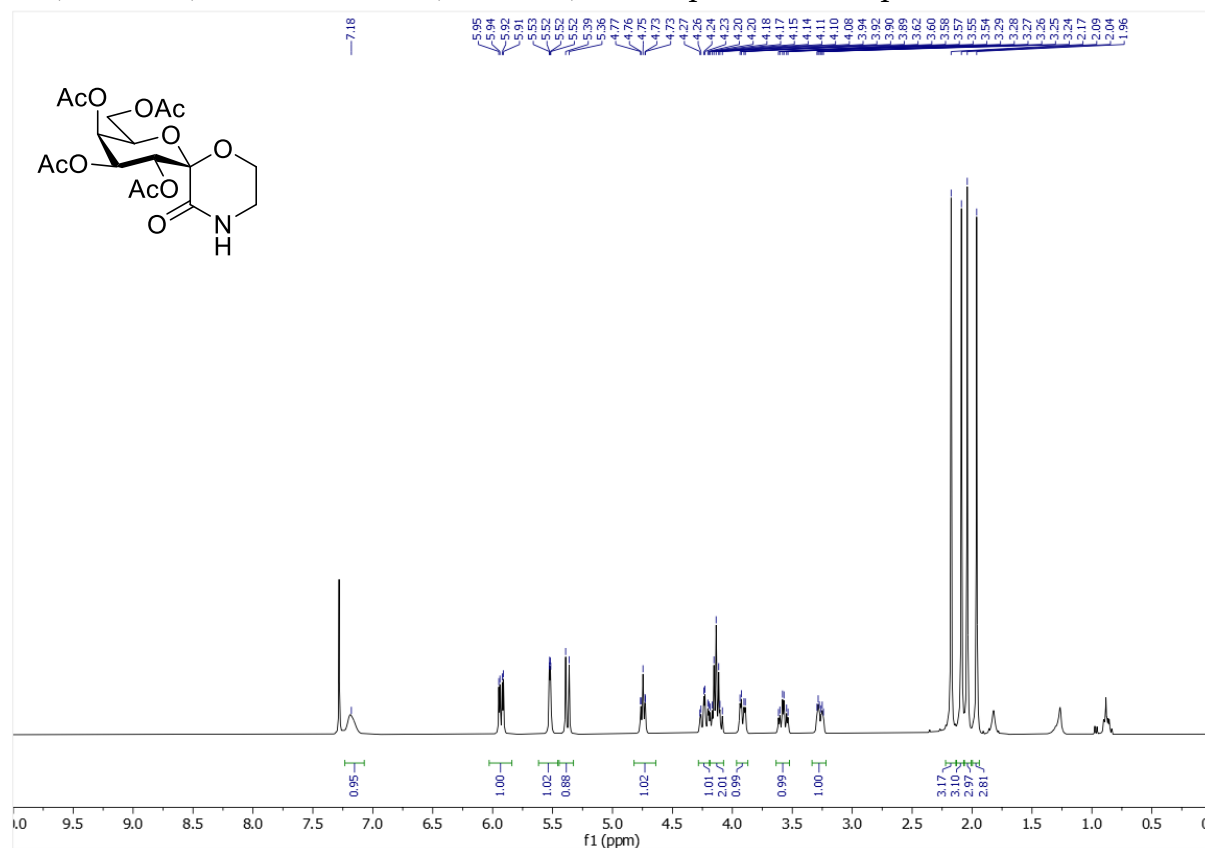


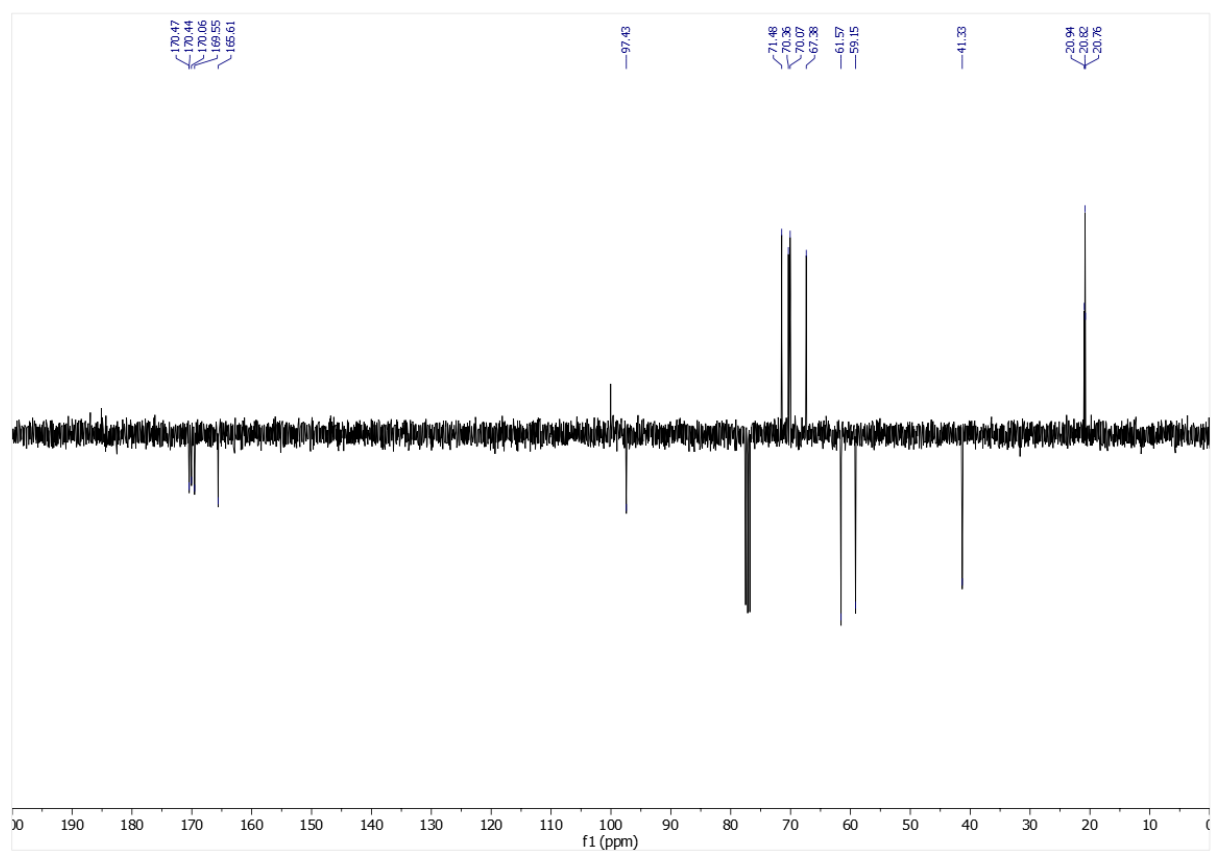
^1H (400 MHz) and ^{13}C J-MOD (100 MHz) NMR spectra of compound **13** in CDCl_3



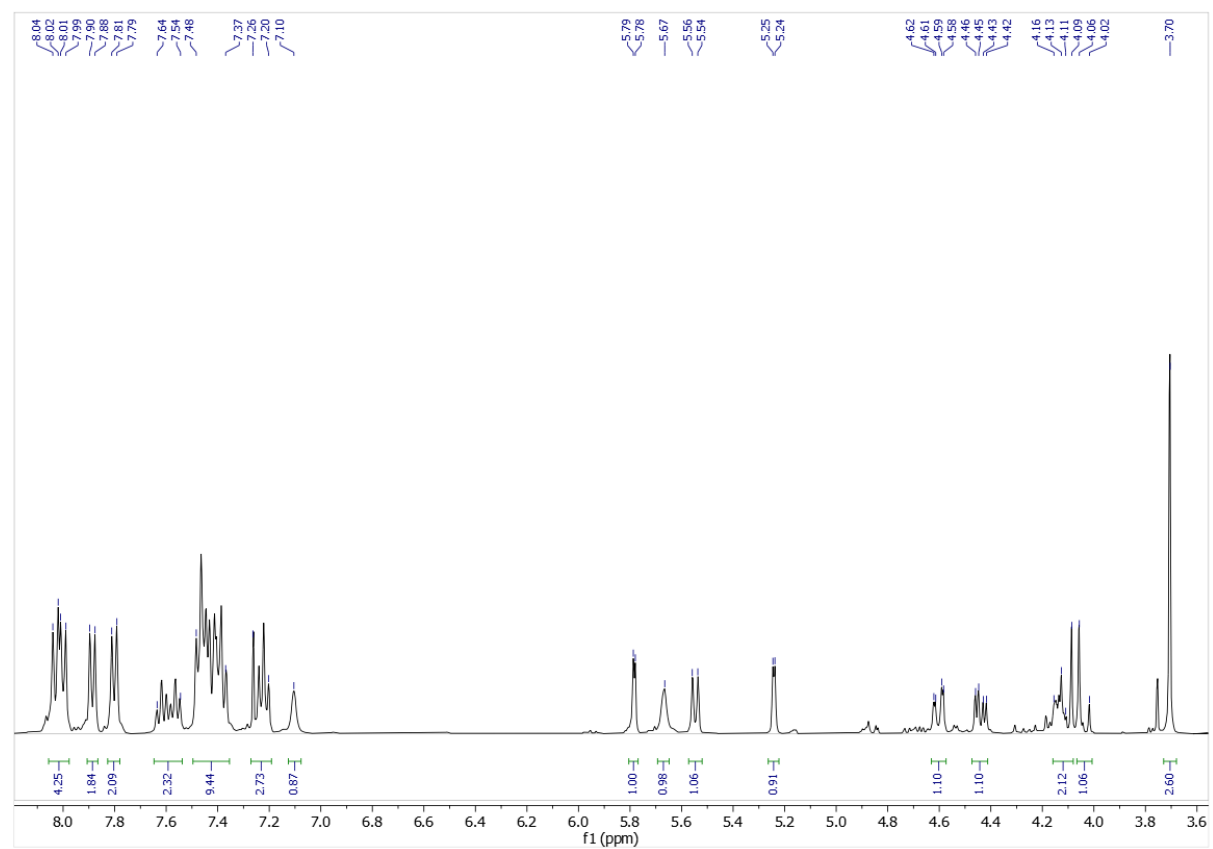
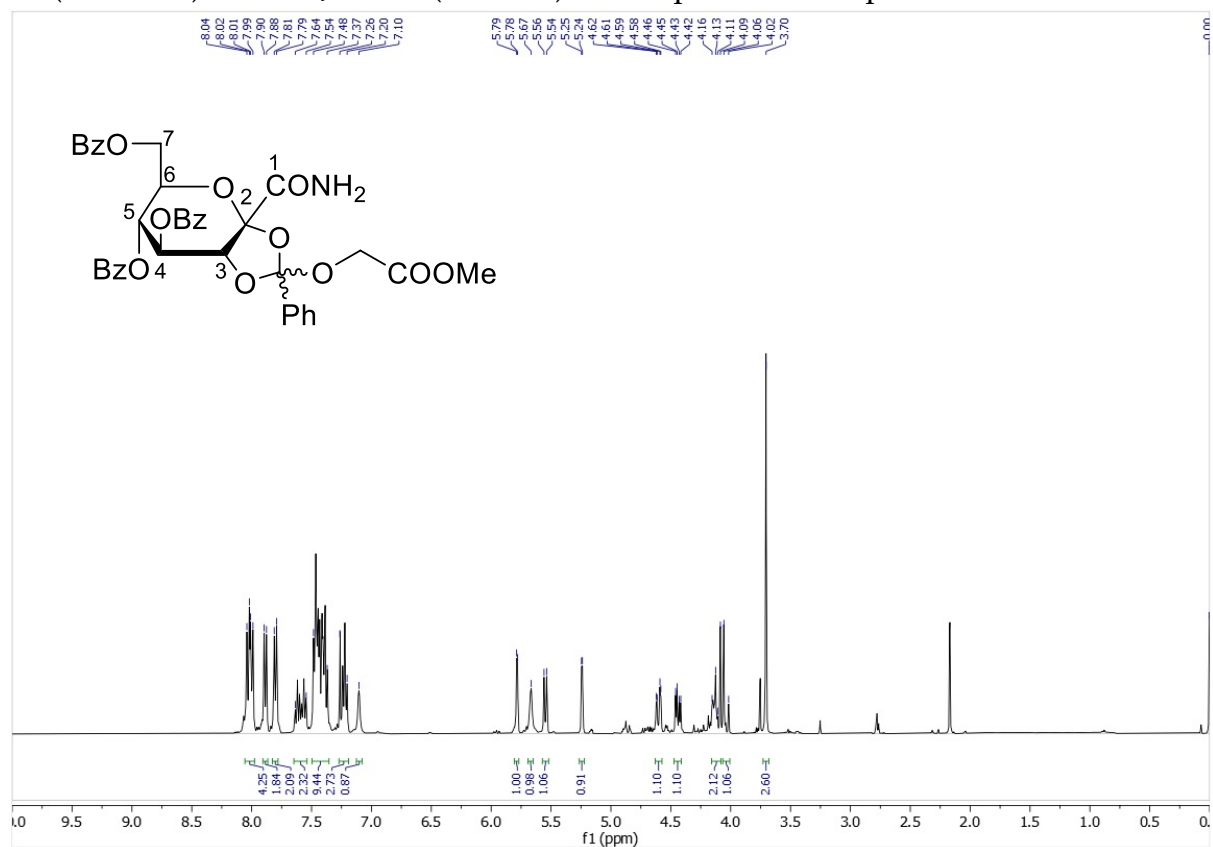


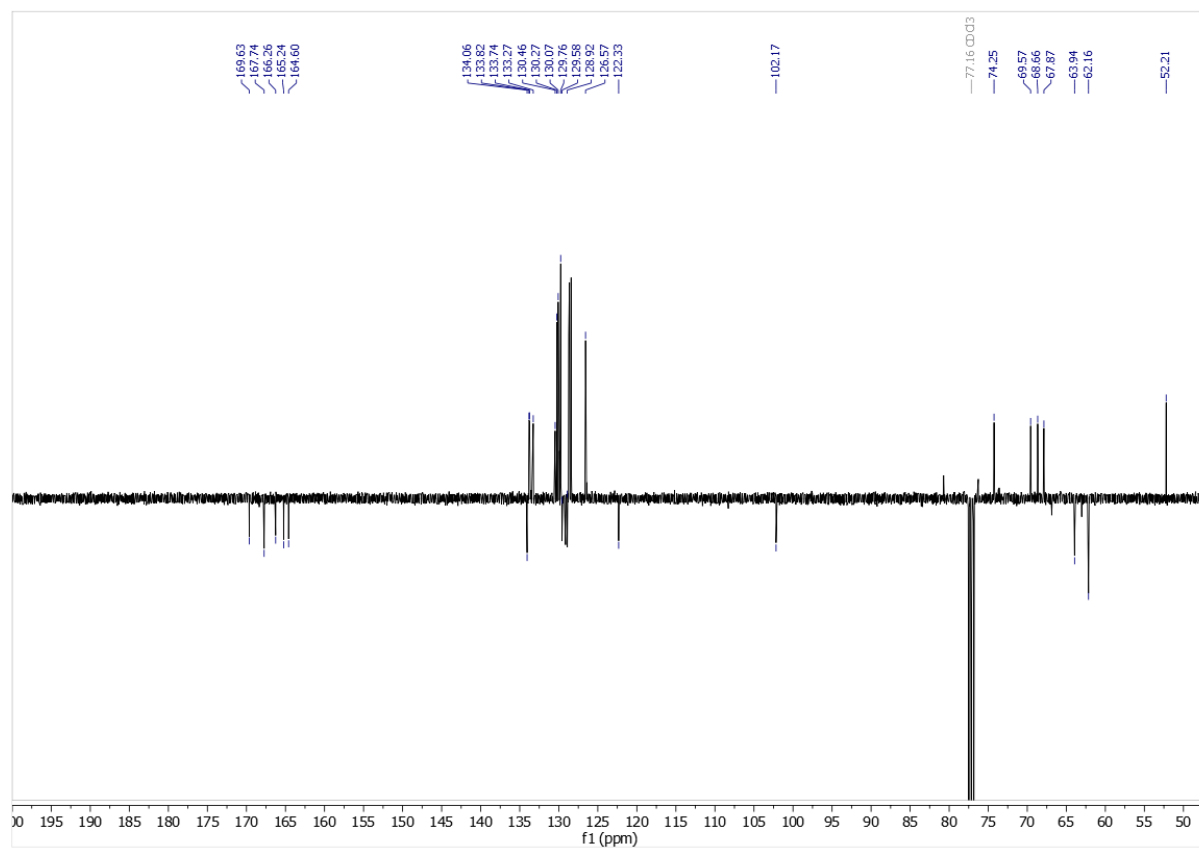
^1H (400 MHz) and ^{13}C J-MOD (100 MHz) NMR spectra of compound **14** in CDCl_3



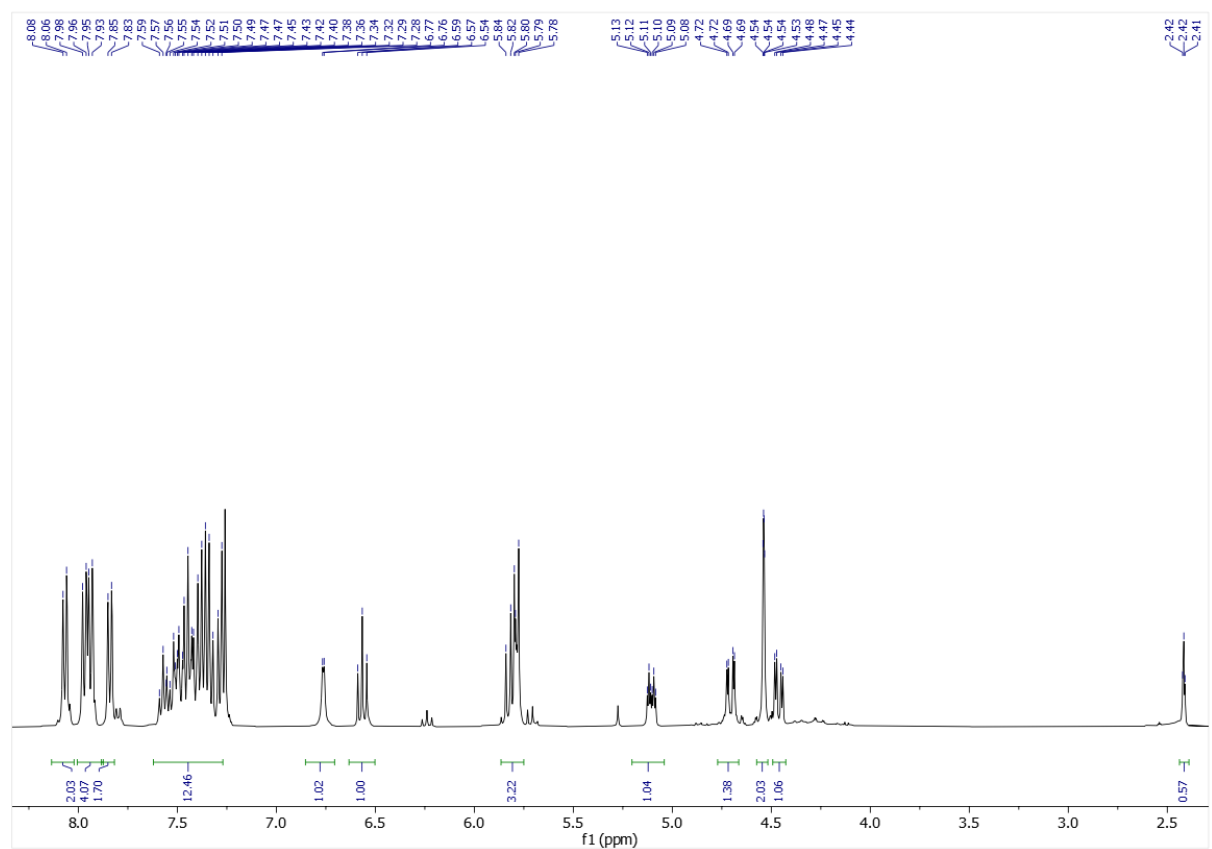
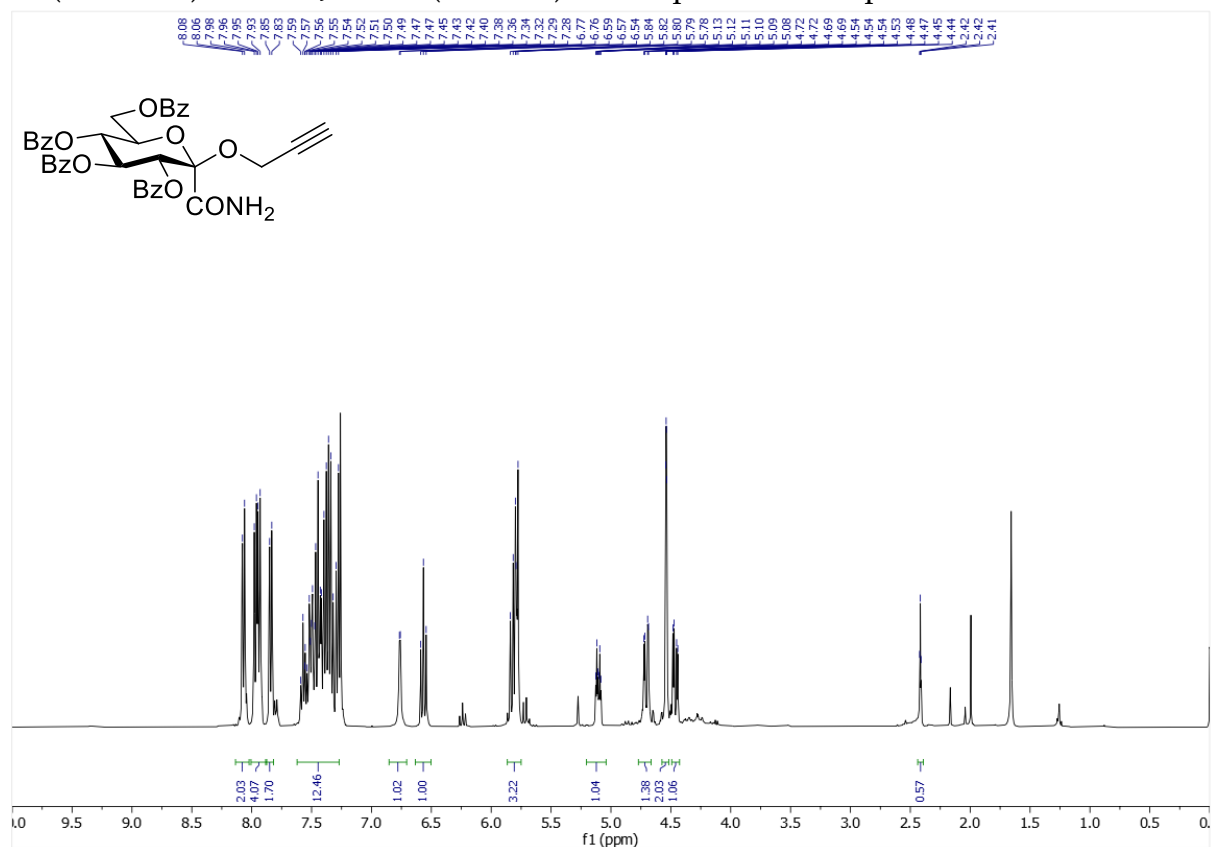


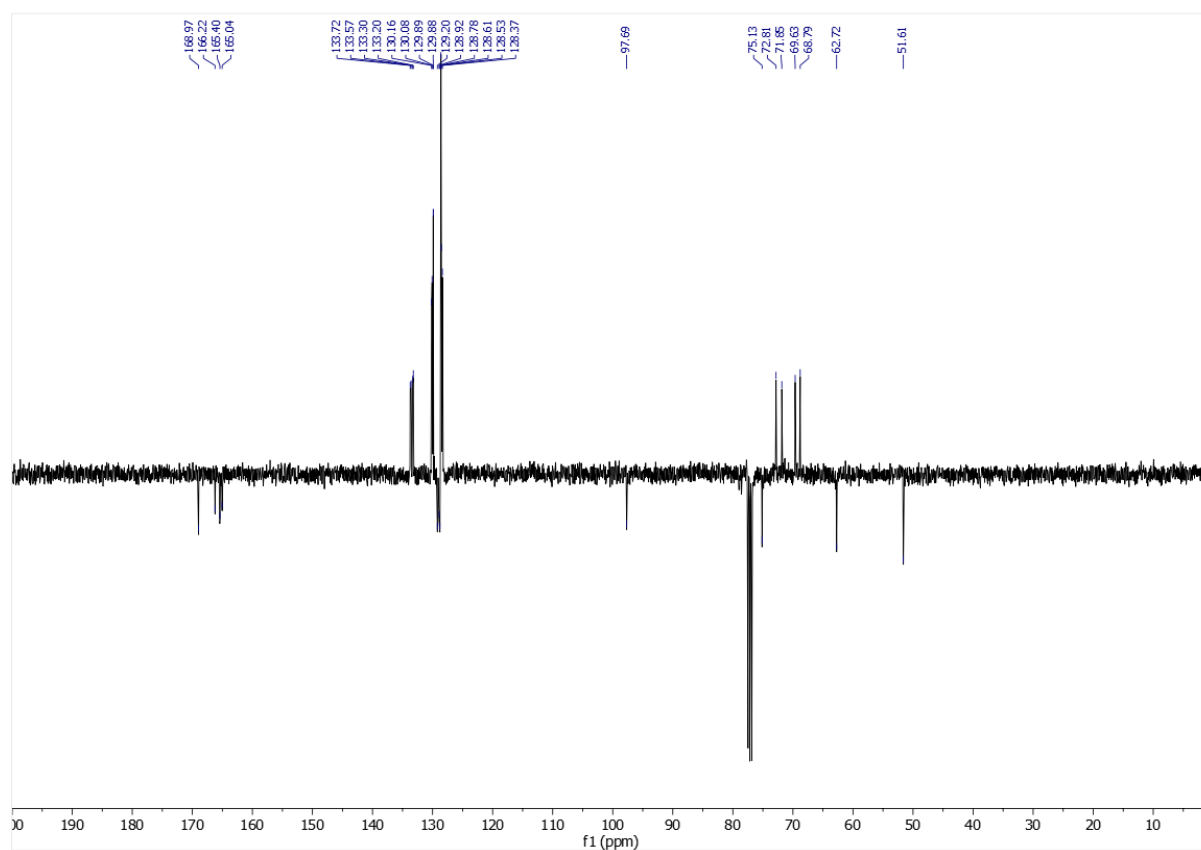
^1H (400 MHz) and ^{13}C J-MOD (90 MHz) NMR spectra of compound **17** in CDCl_3



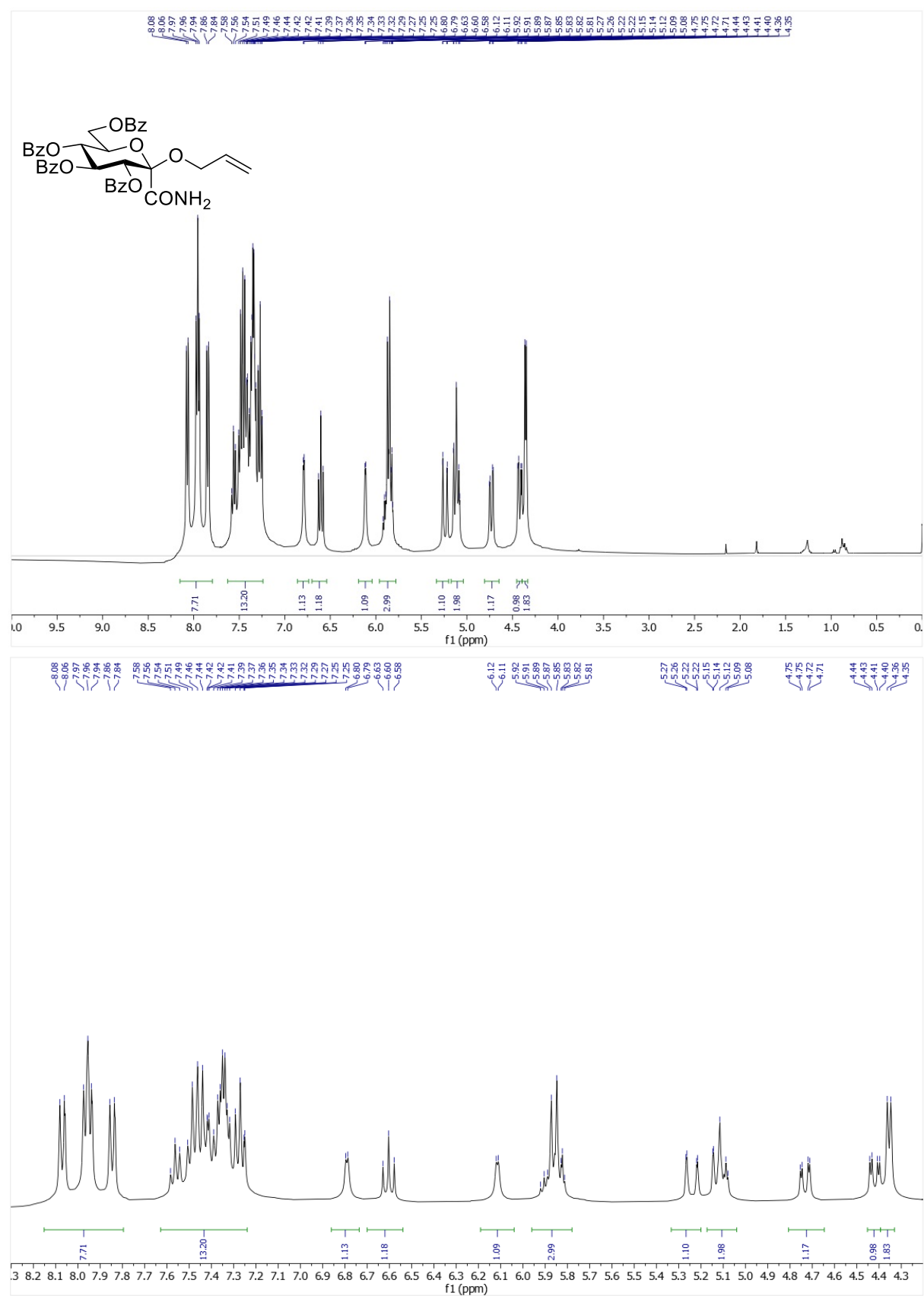


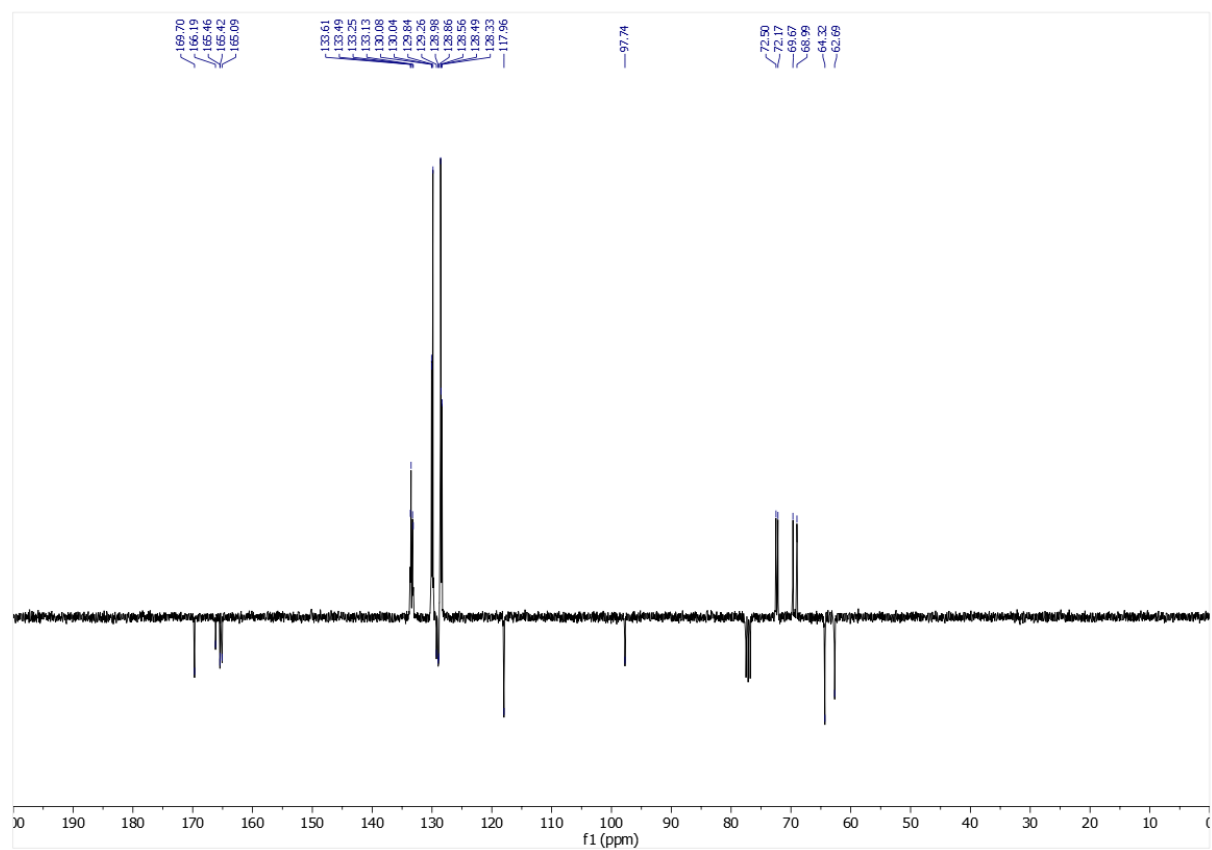
^1H (360 MHz) and ^{13}C J-MOD (90 MHz) NMR spectra of compound **19** in CDCl_3





^1H (360 MHz) and ^{13}C J-MOD (90 MHz) NMR spectra of compound **20** in CDCl_3

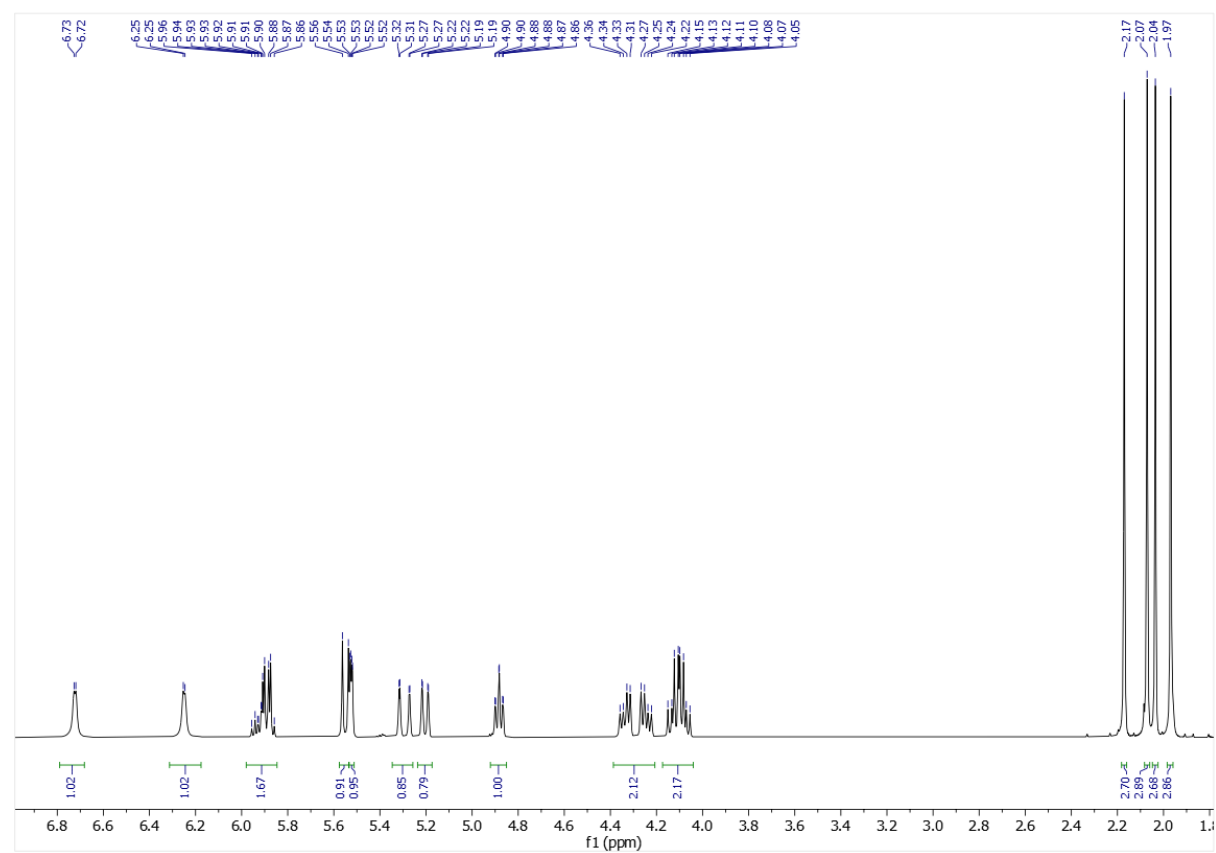


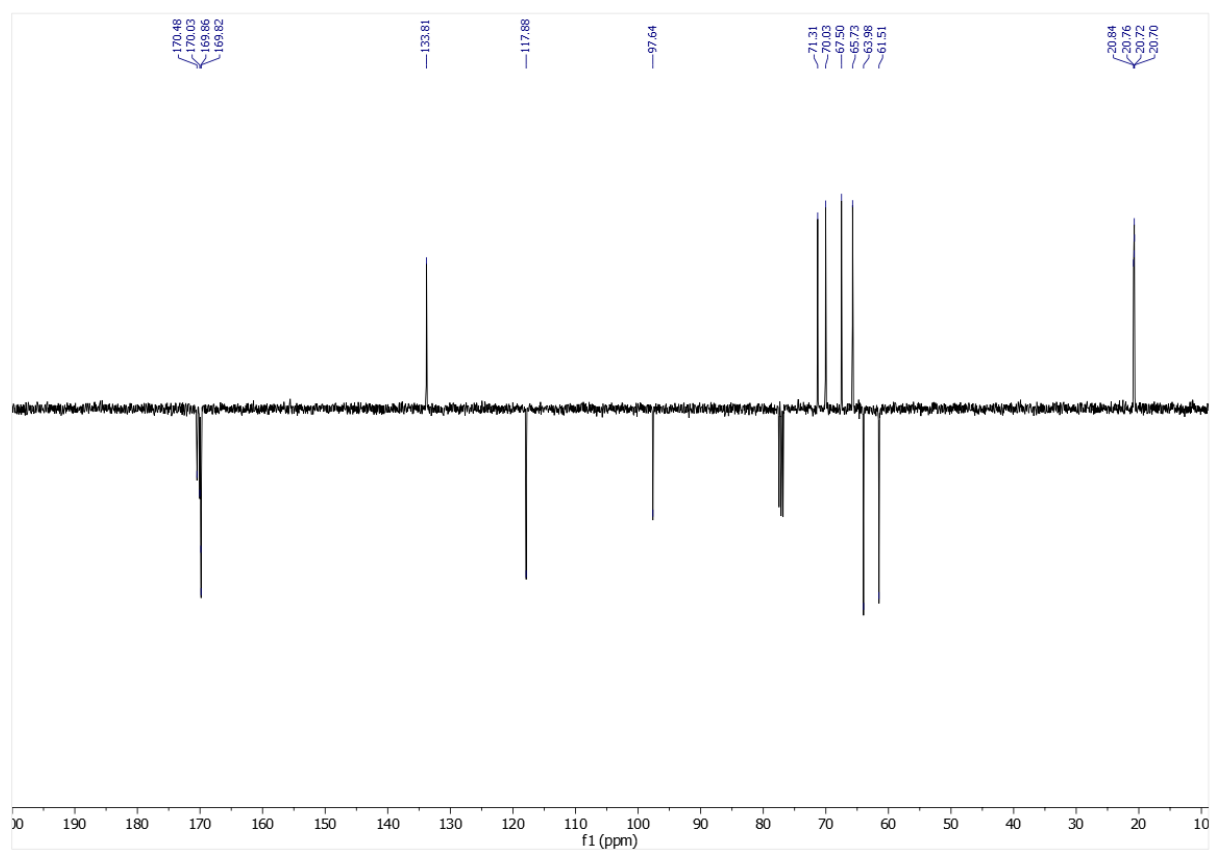


Chemical structure of compound 10 is shown in the top left corner. The structure is a cyclohexane ring with an acetate group (AcO) at C1, an allyloxy group (OCH₂CH=CH₂) at C2, an acetate group (AcO) at C3, an acetate group (AcO) at C4, and a primary amide group (CONH₂) at C5.

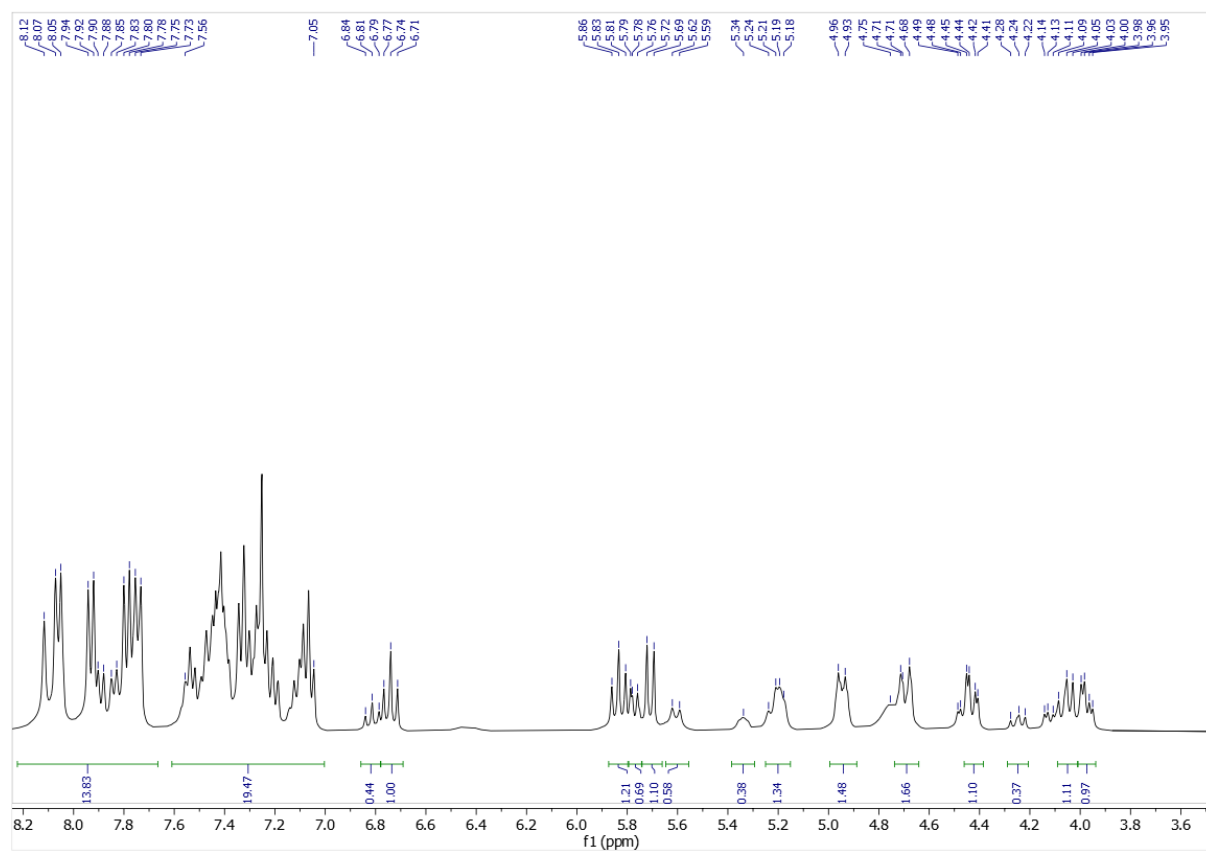
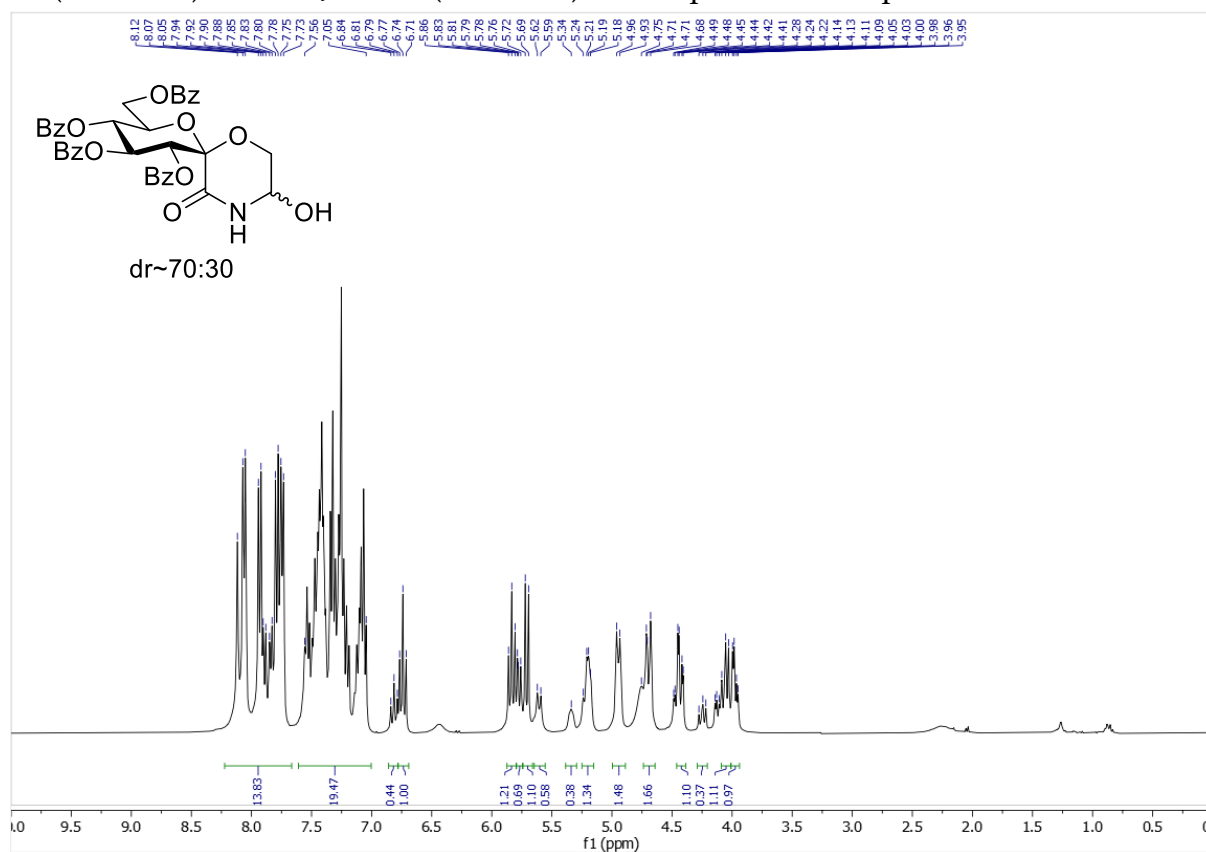
The ¹H NMR spectrum (CDCl₃) shows peaks from 0 to 10 ppm. The x-axis is labeled f1 (ppm). The spectrum displays several sharp peaks, including a broad peak around 6.7 ppm (NH₂), and a complex set of peaks between 4.0 and 6.0 ppm (ring protons and allyl group). Integration values are provided below the baseline for several peak regions.

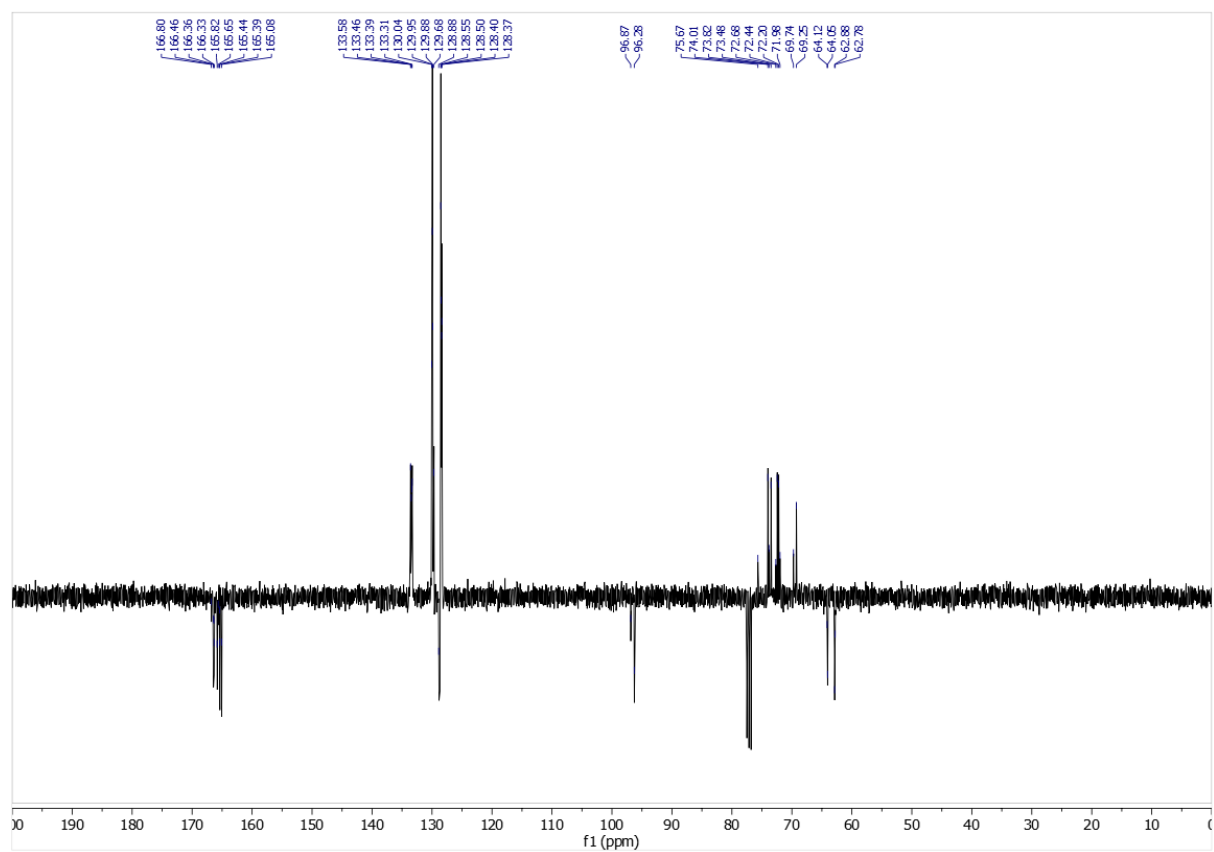
Integration values (from left to right): 1.02, 1.02, 1.67, 0.91, 0.95, 0.79, 1.00, 2.12, 2.17, 2.70, 2.69, 2.86.

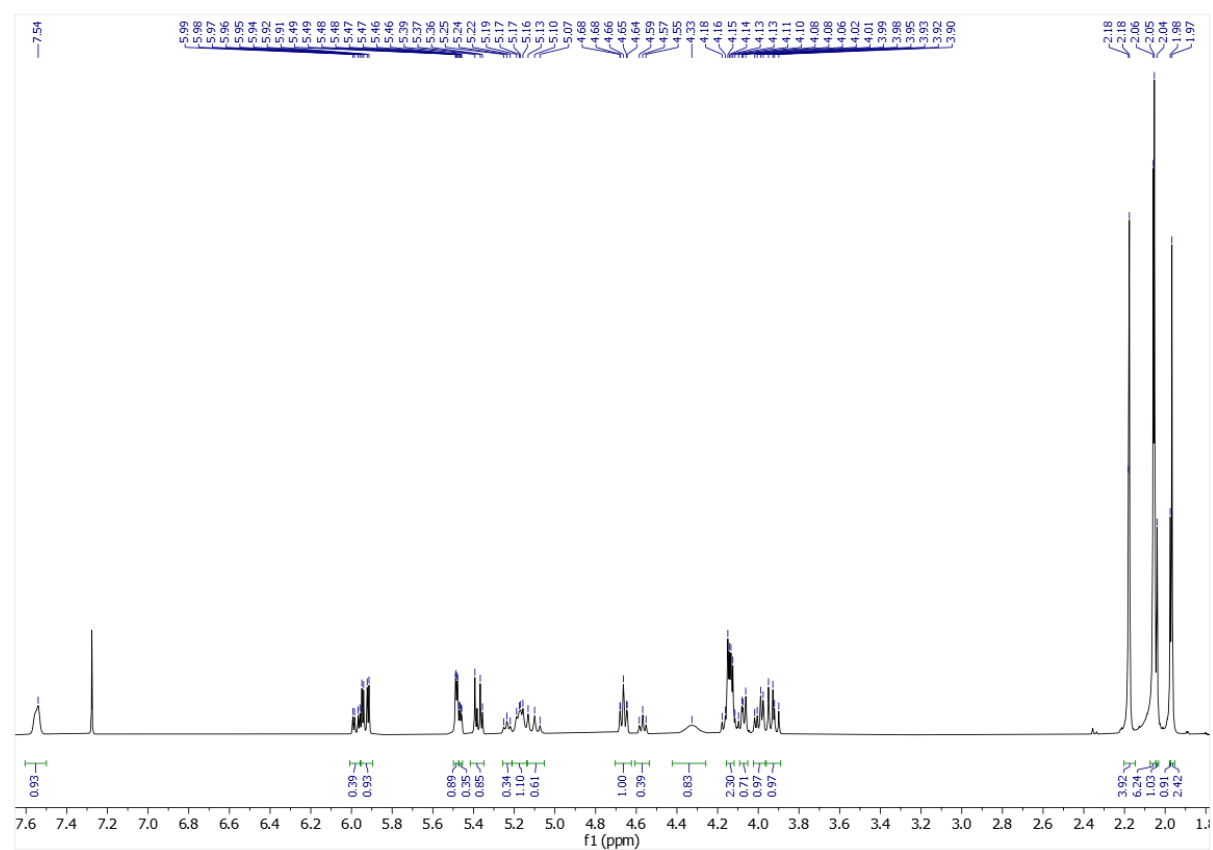
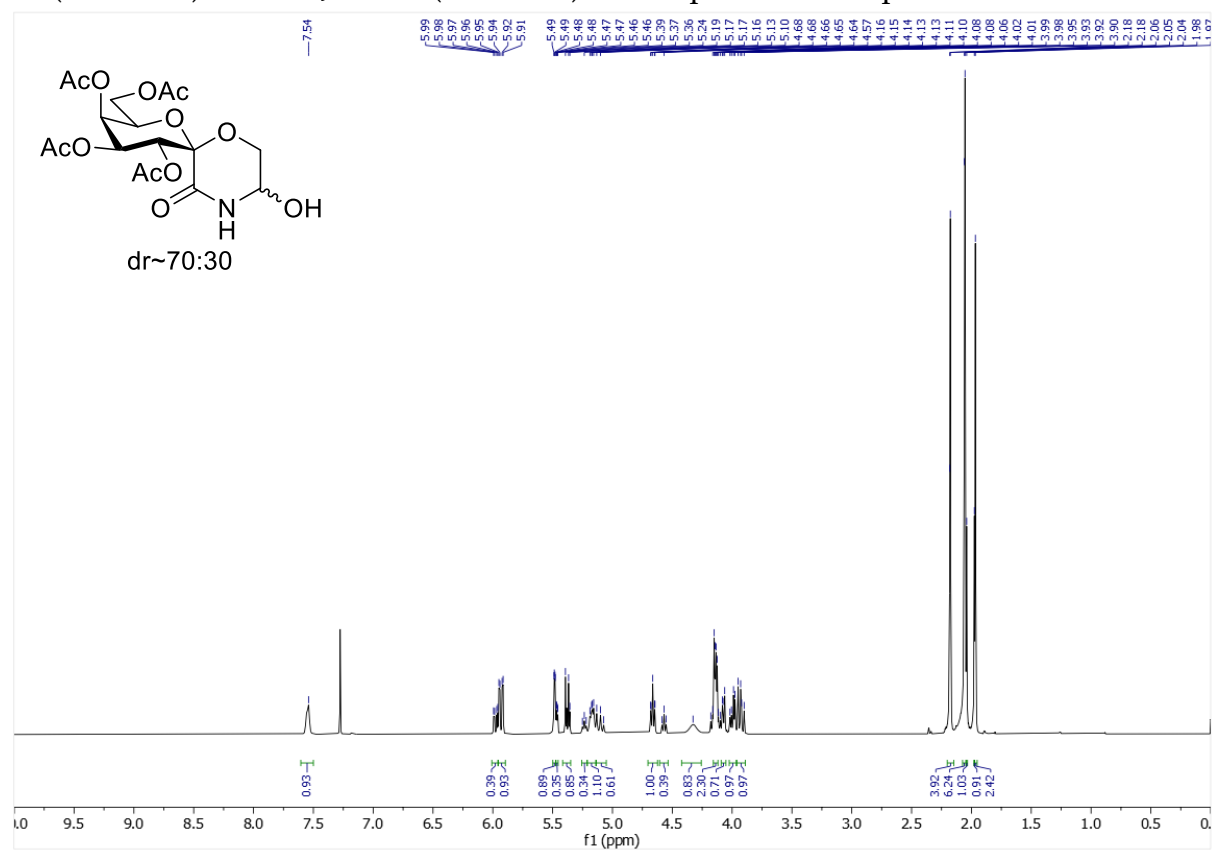


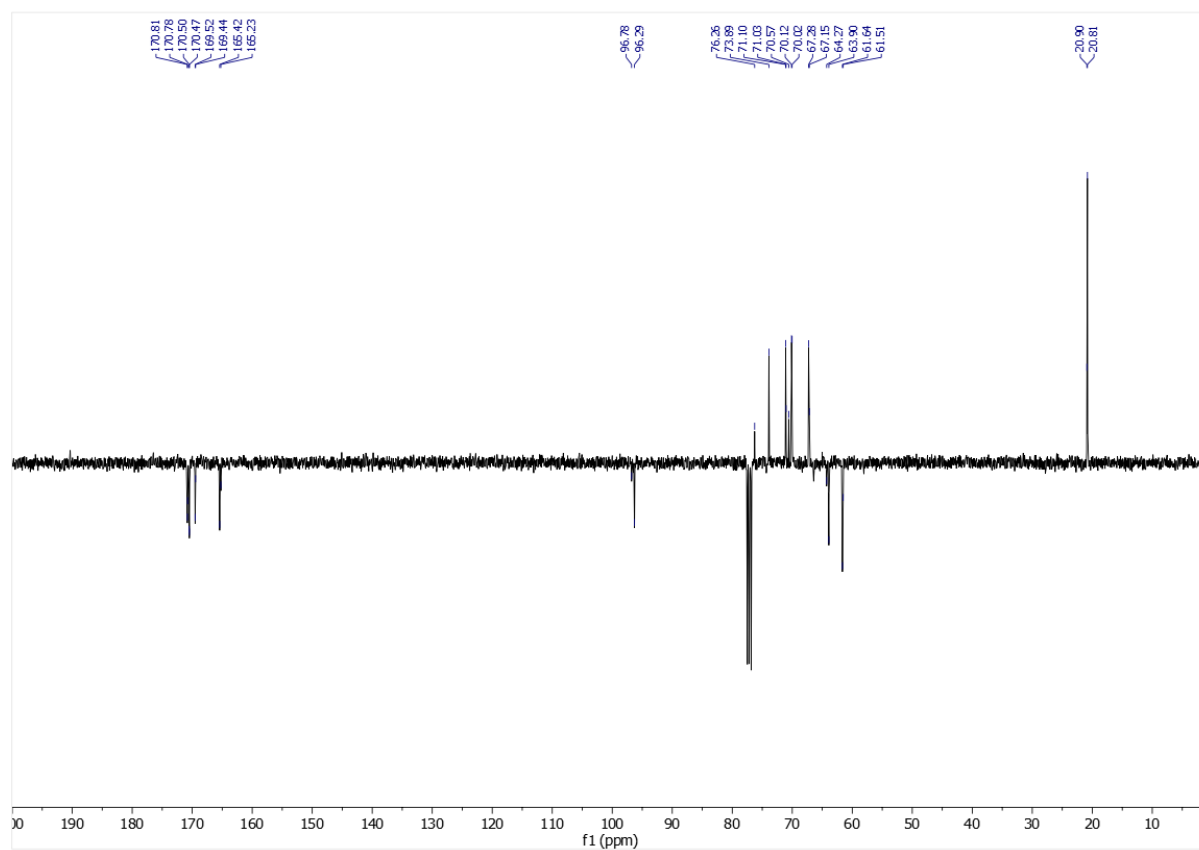


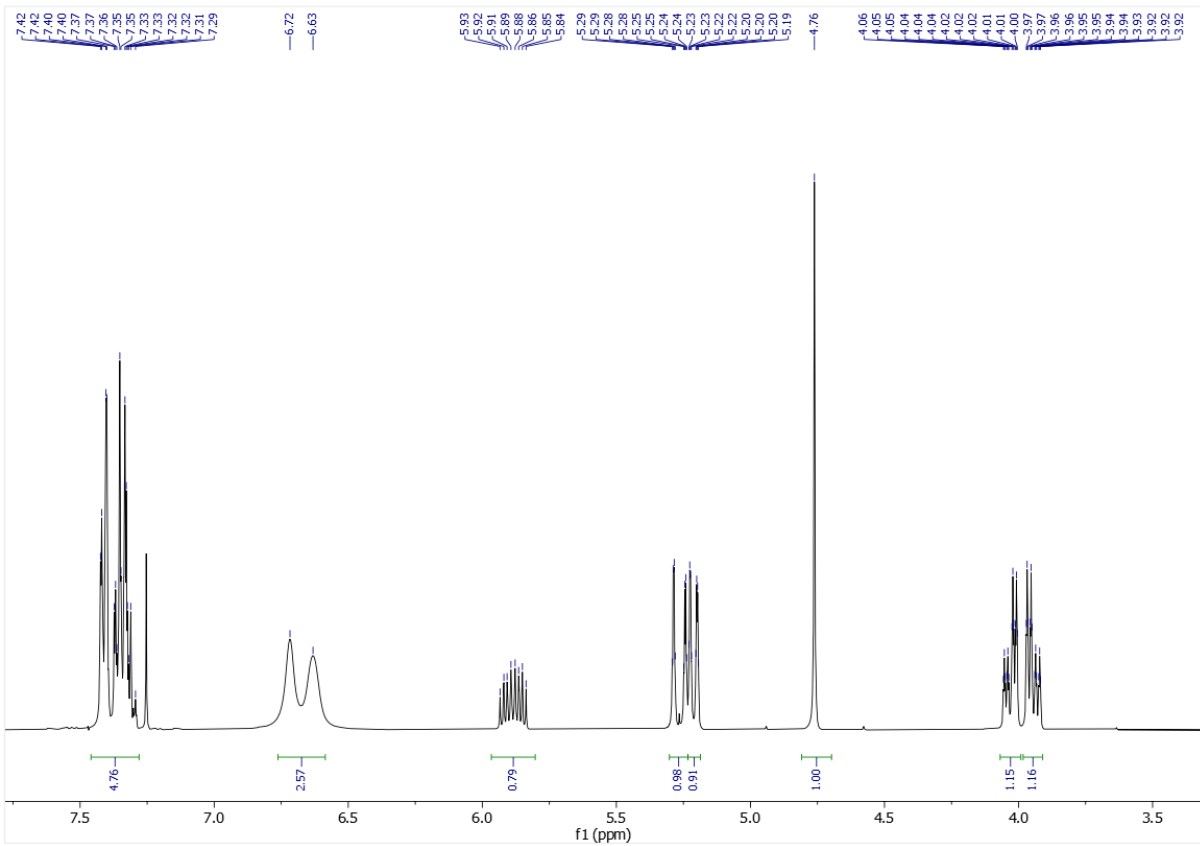
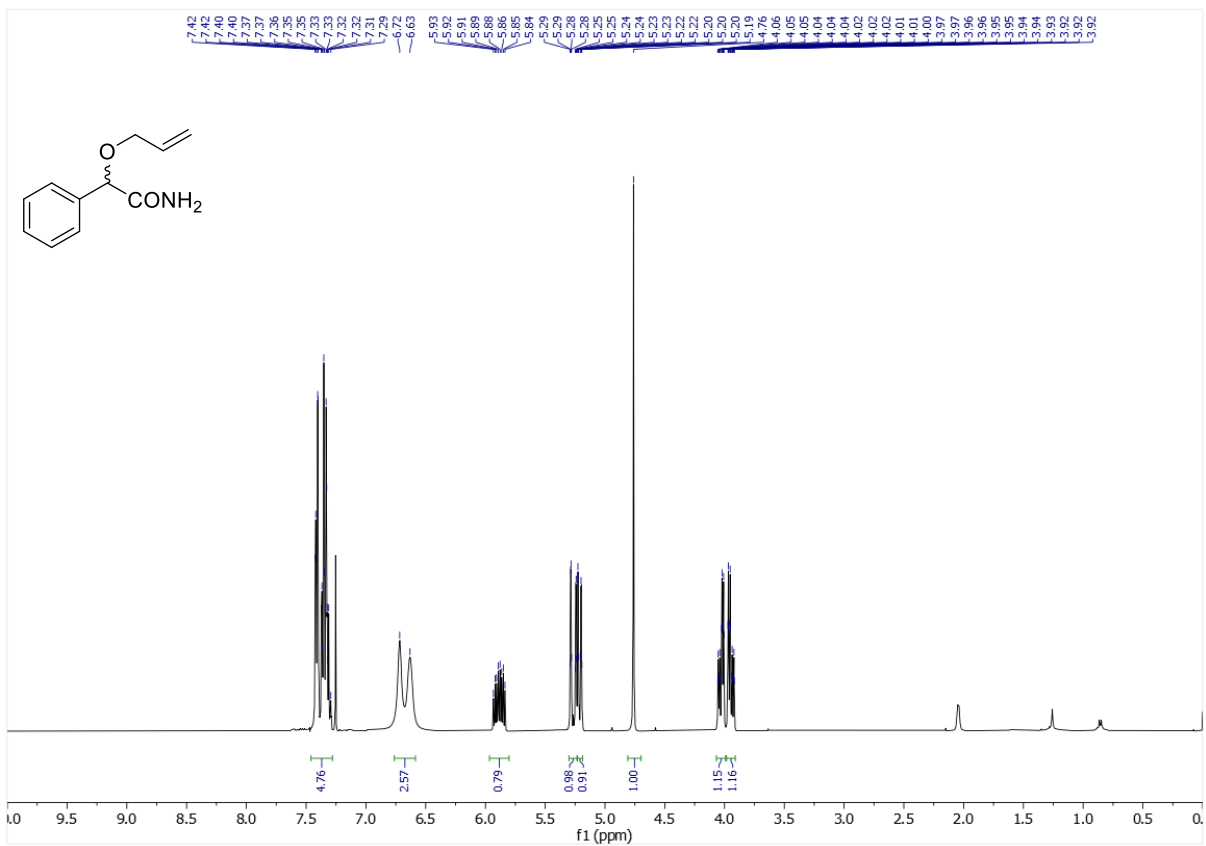
^1H (400 MHz) and ^{13}C J-MOD (100 MHz) NMR spectra of compound **22** in CDCl_3

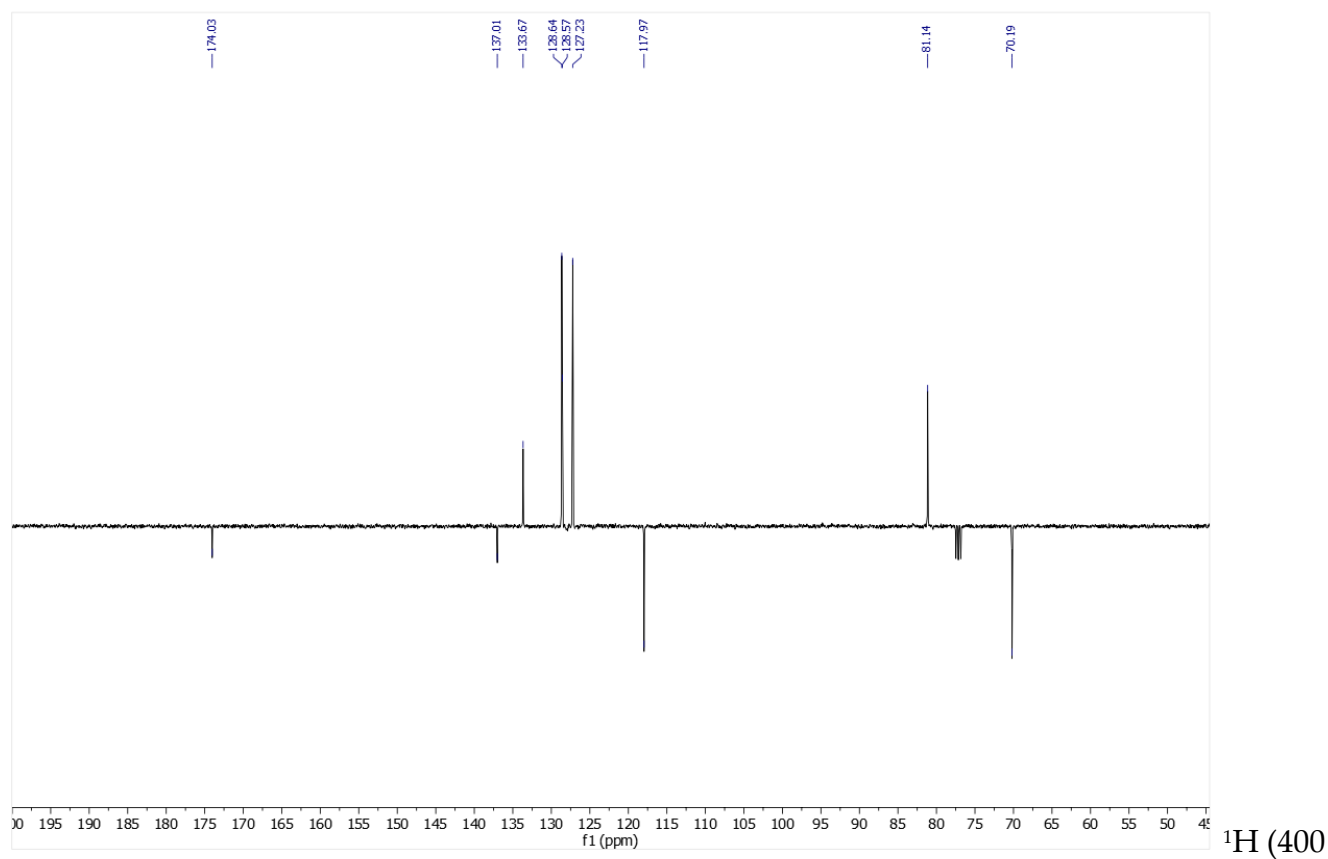




¹H (400 MHz) and ¹³C J-MOD (100 MHz) NMR spectra of compound **23** in CDCl₃

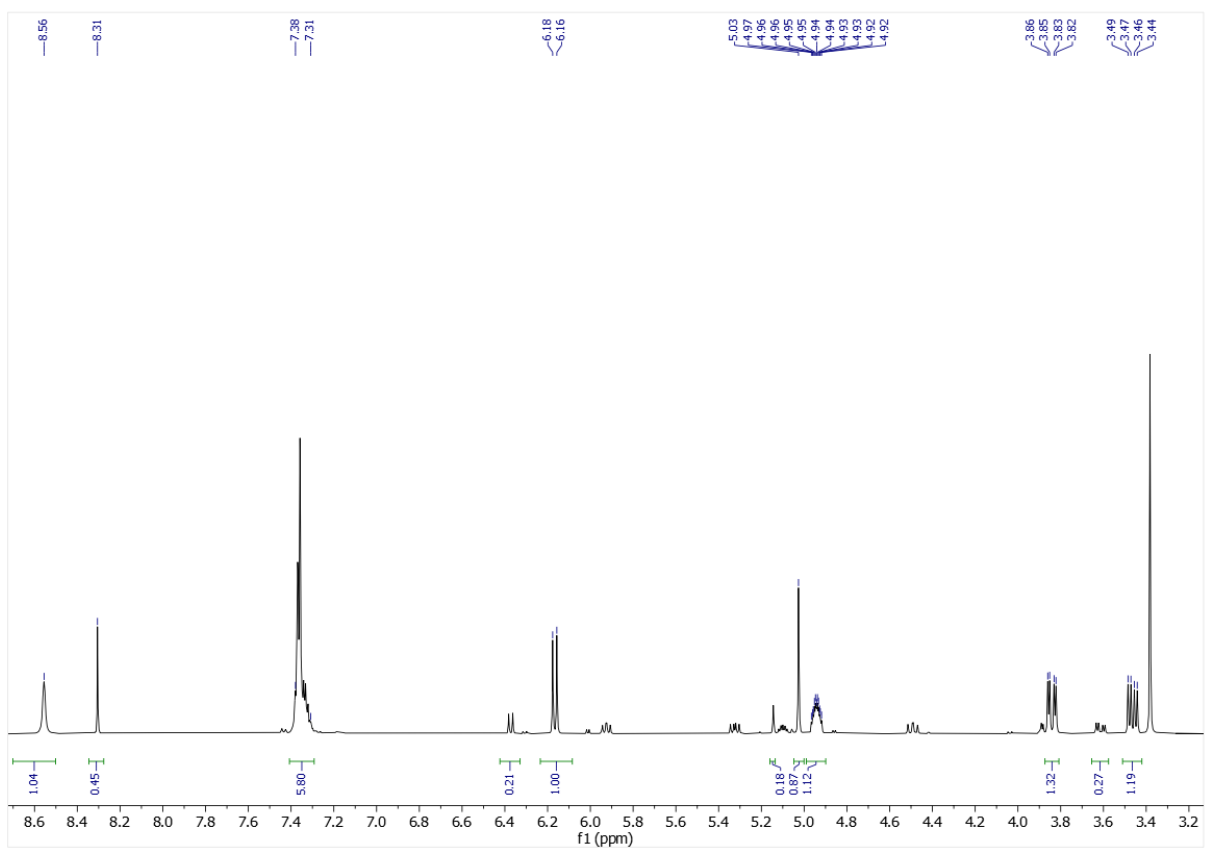
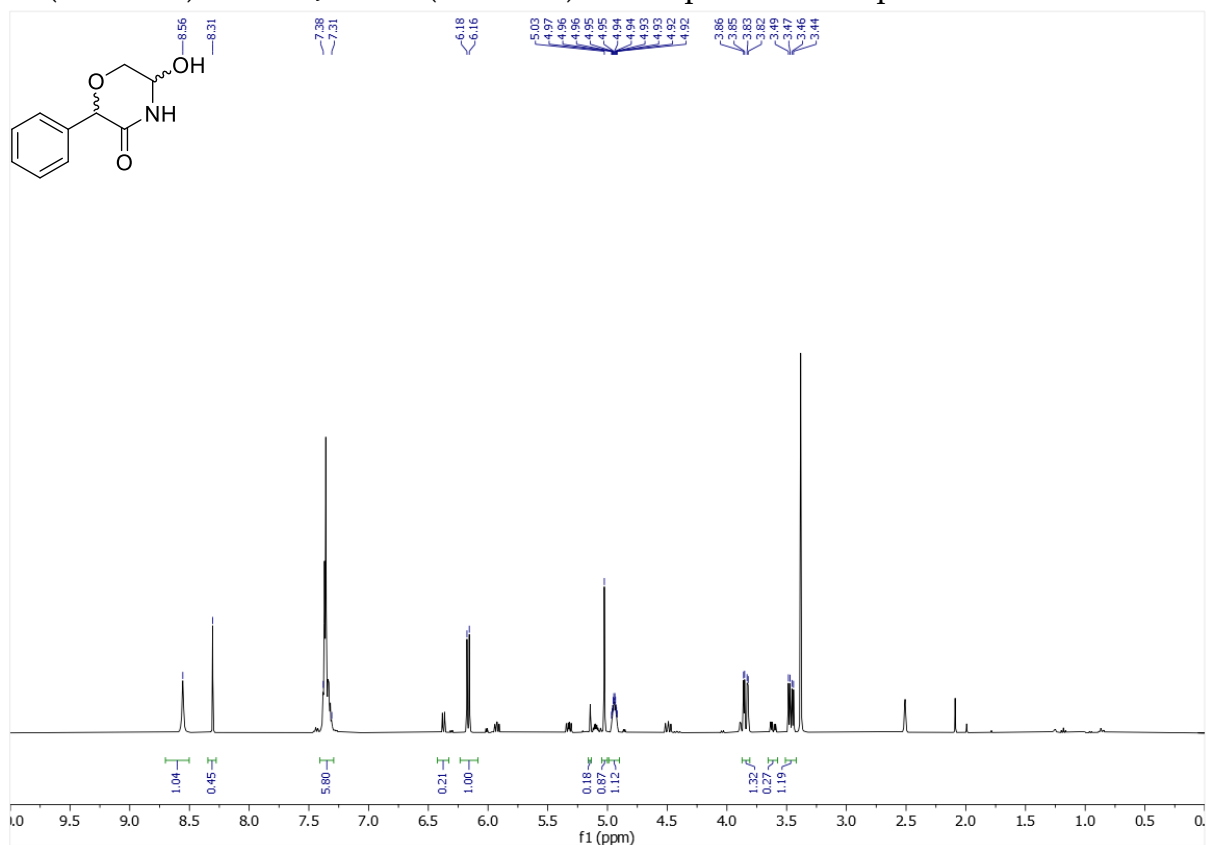


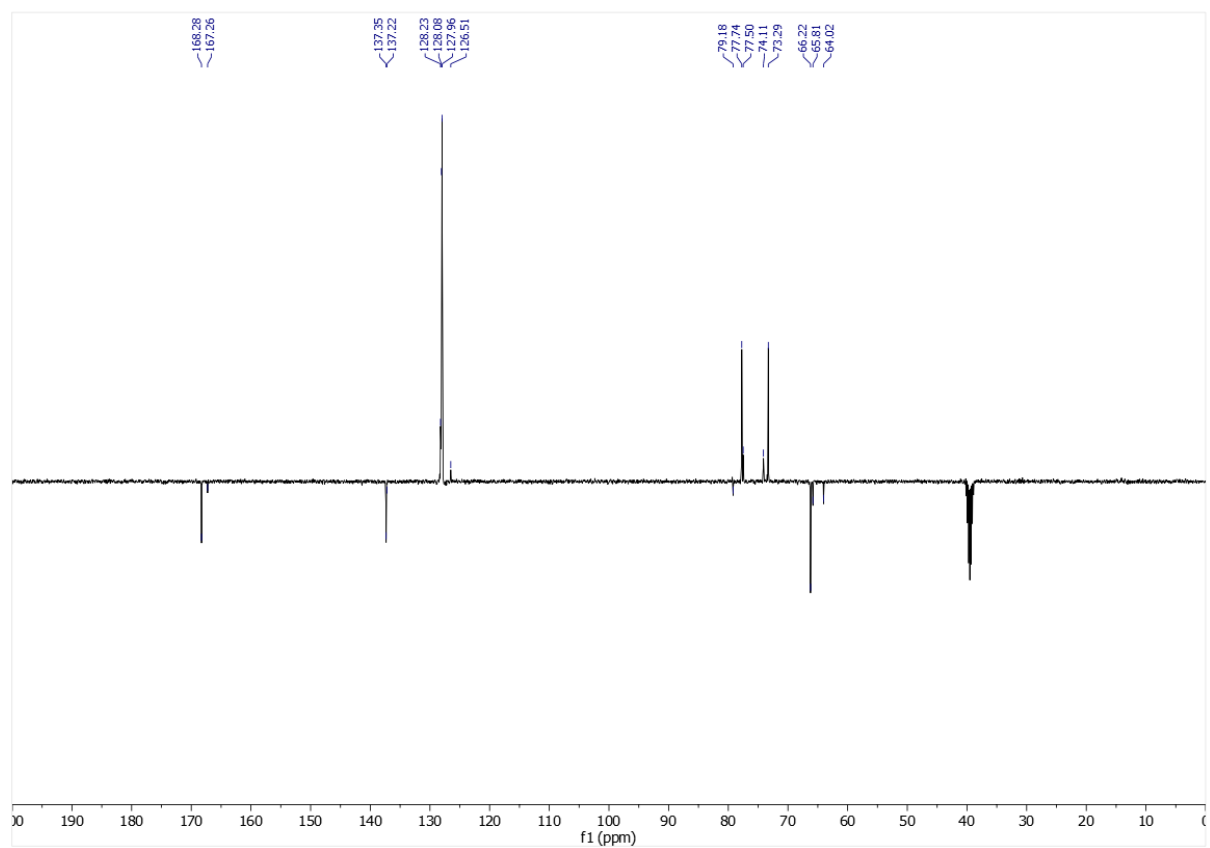




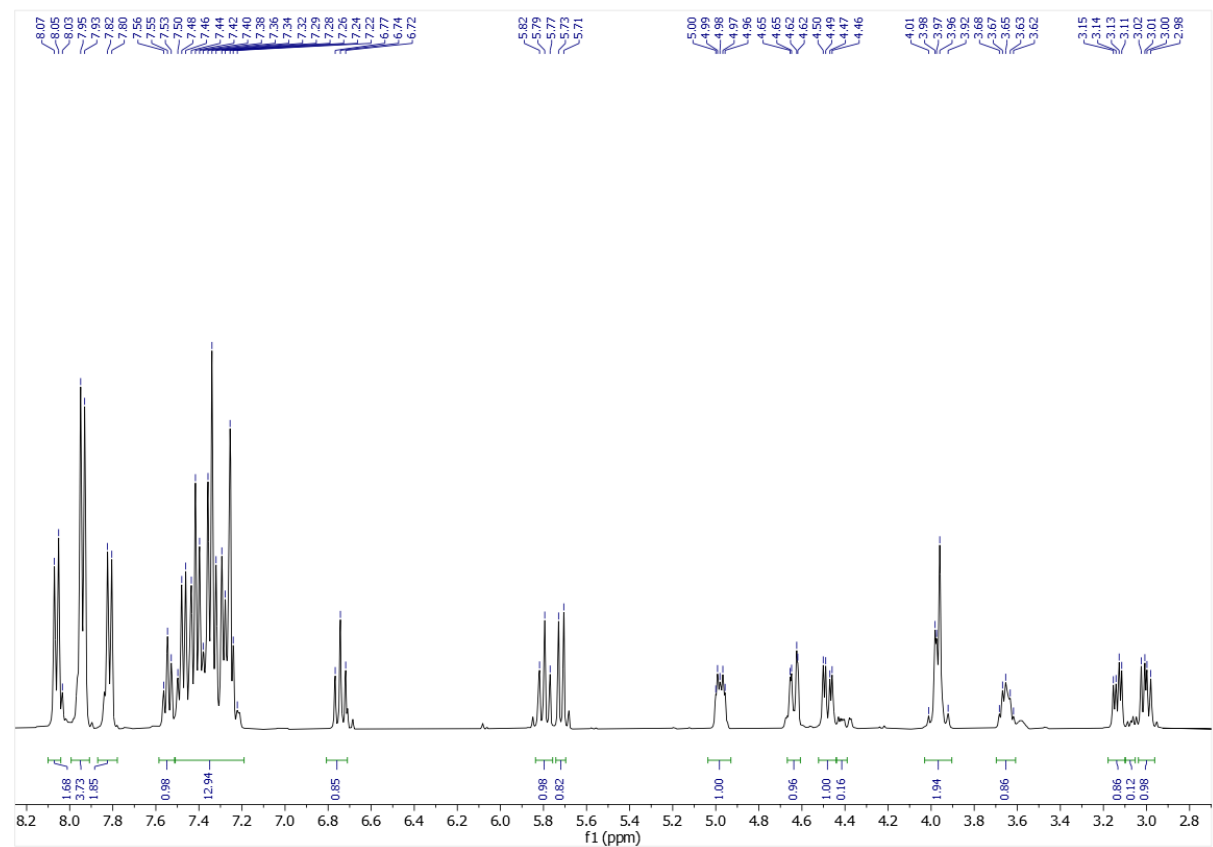
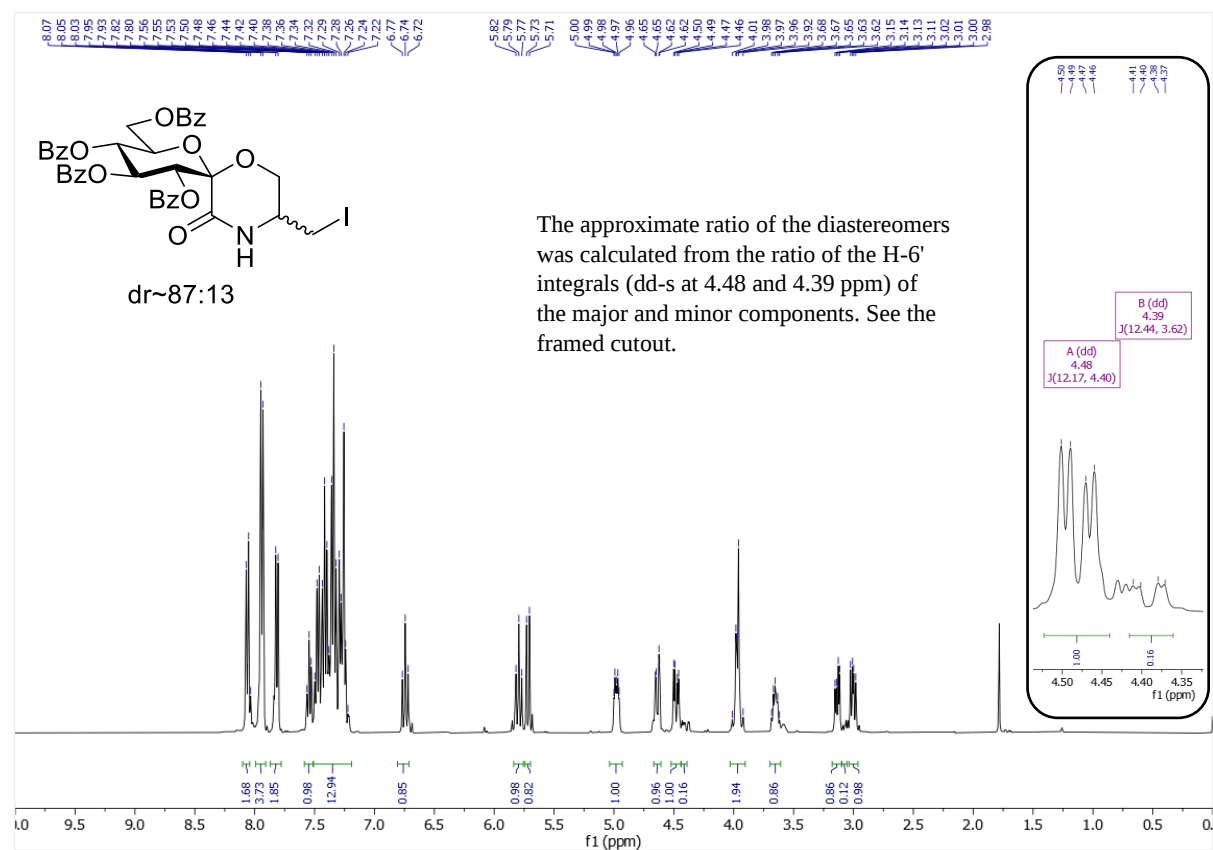
MHz) and ^{13}C J-MOD (100 MHz) NMR spectra of compound **24** in CDCl_3

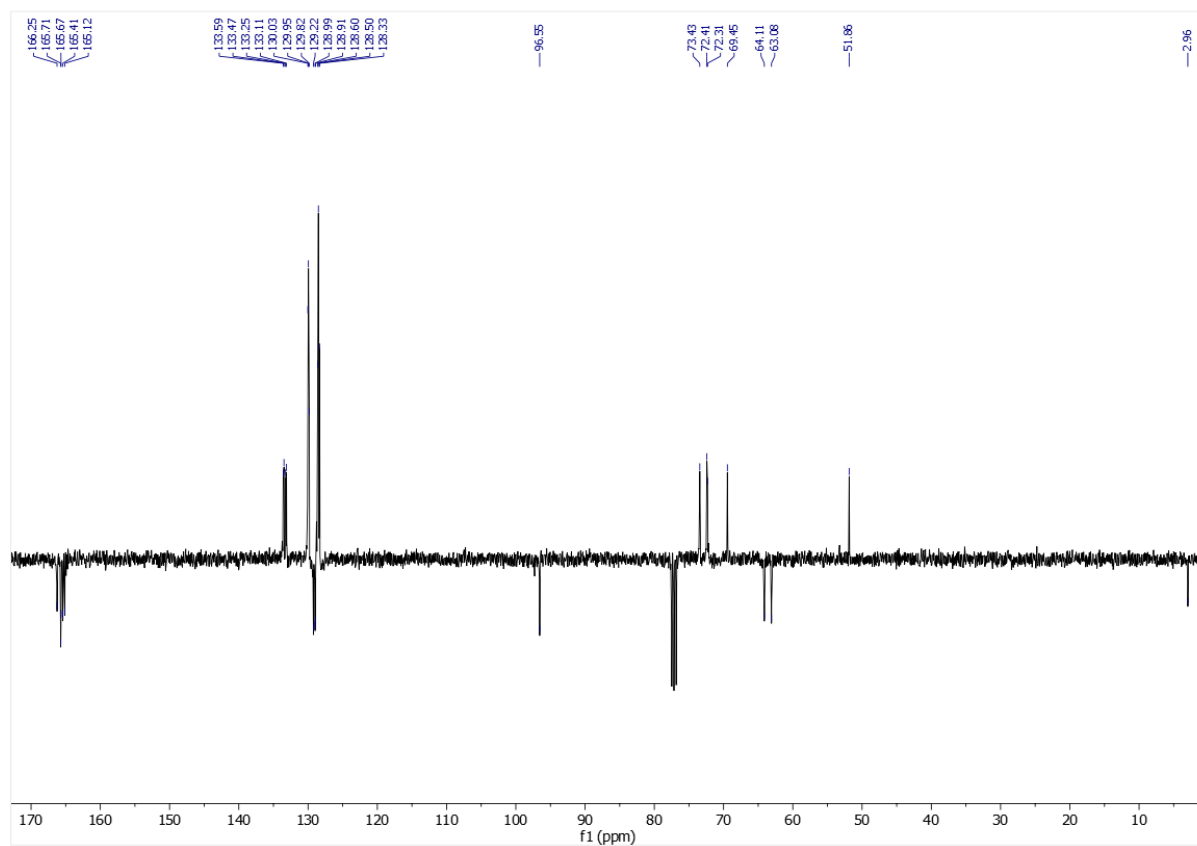
^1H (400 MHz) and ^{13}C J-MOD (100 MHz) NMR spectra of compound **25** in DMSO-d_6



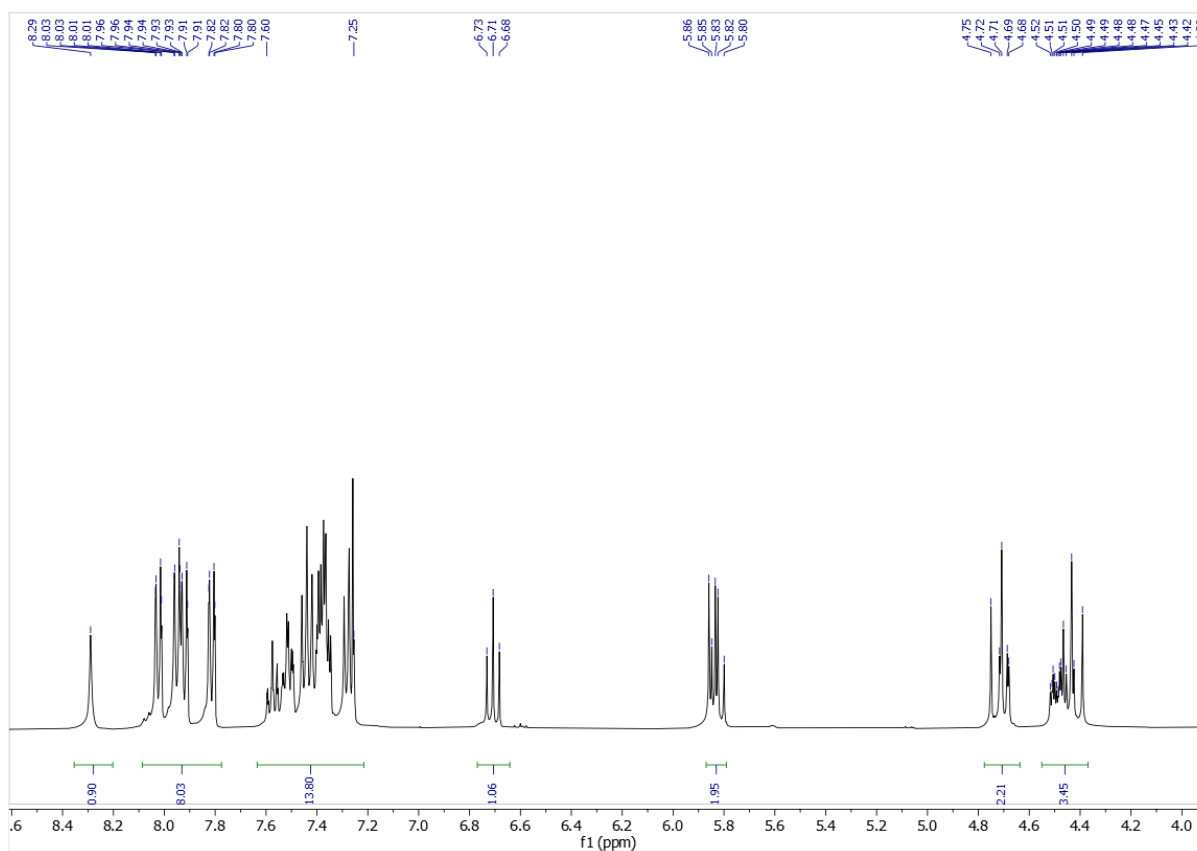
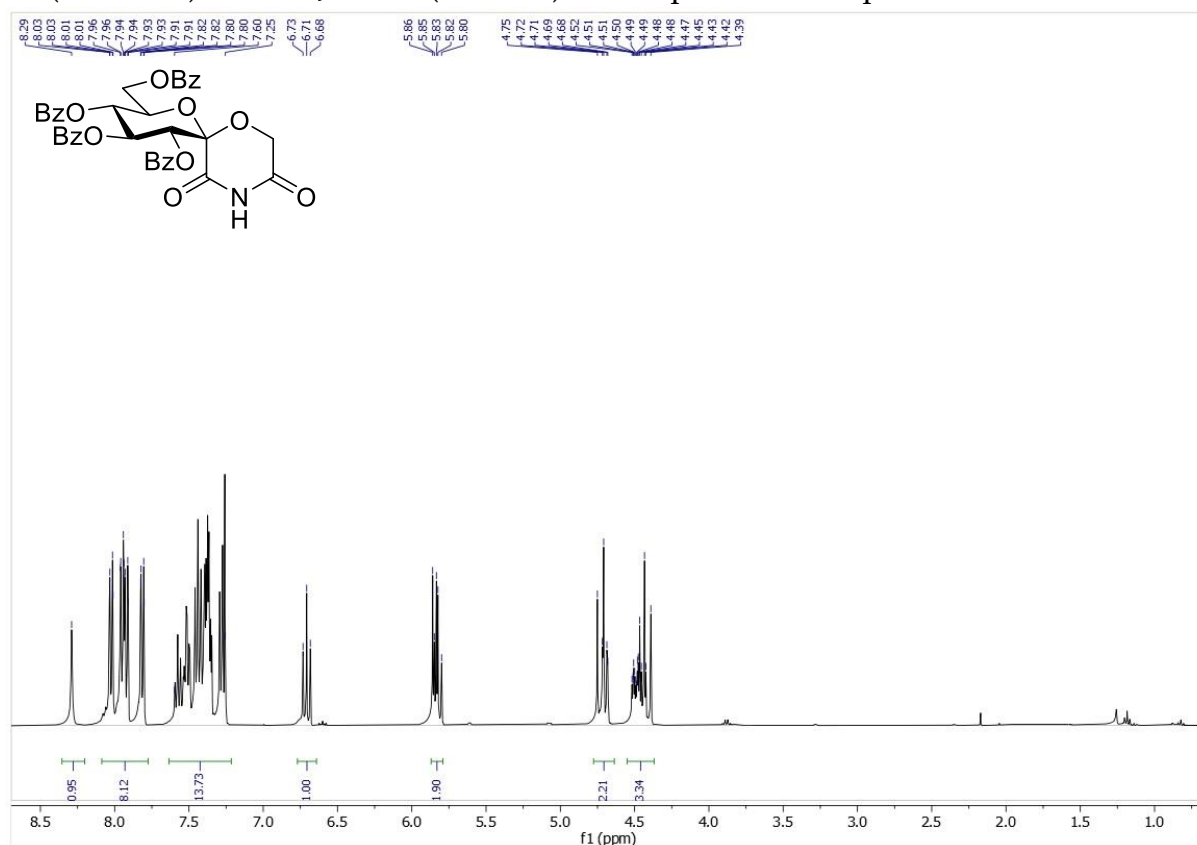


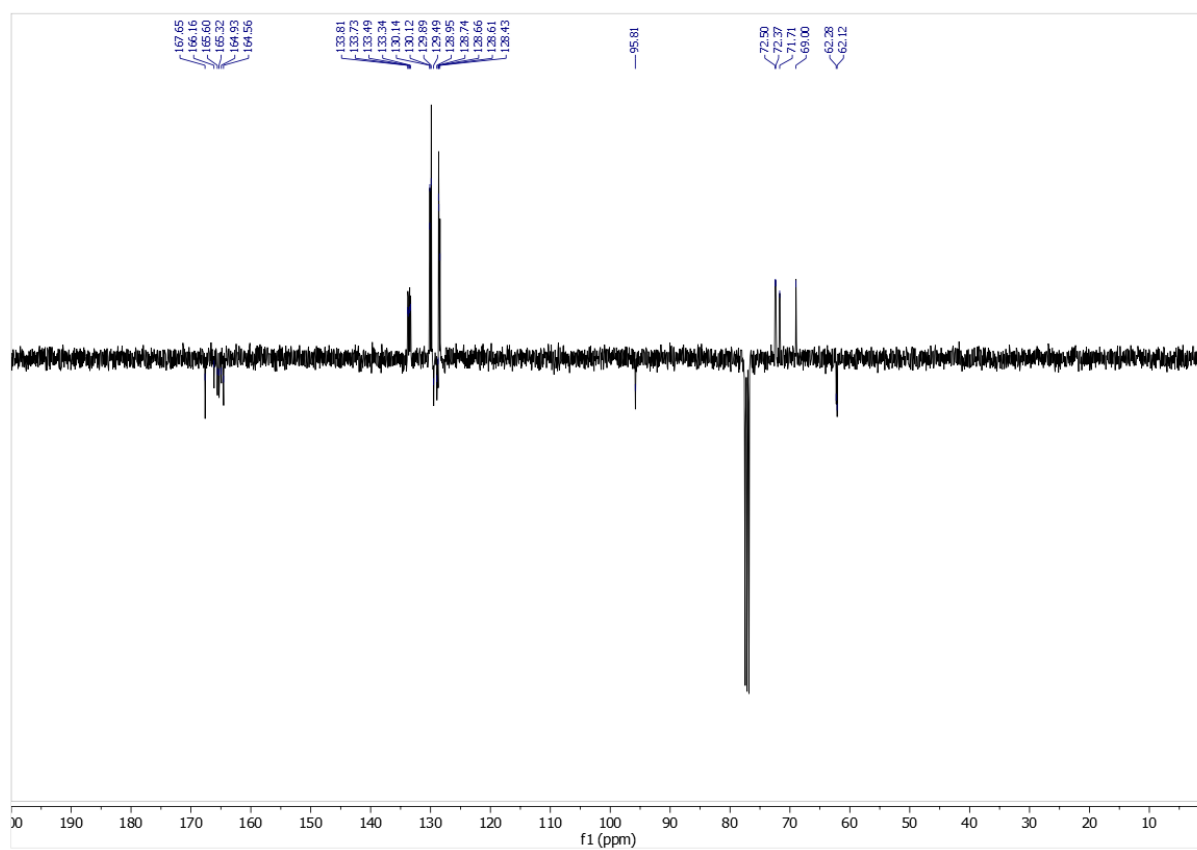
^1H (400 MHz) and ^{13}C J-MOD (100 MHz) NMR spectra of compound **26** in CDCl_3



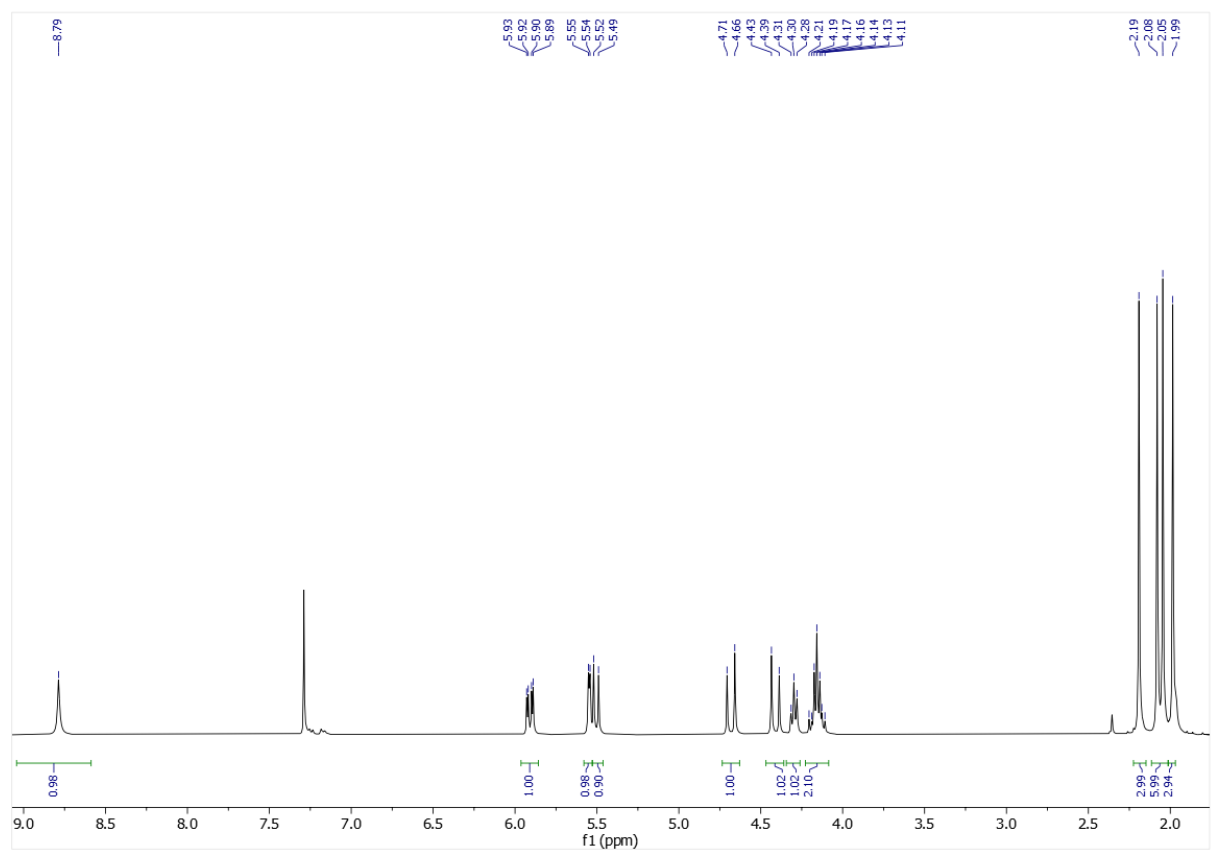
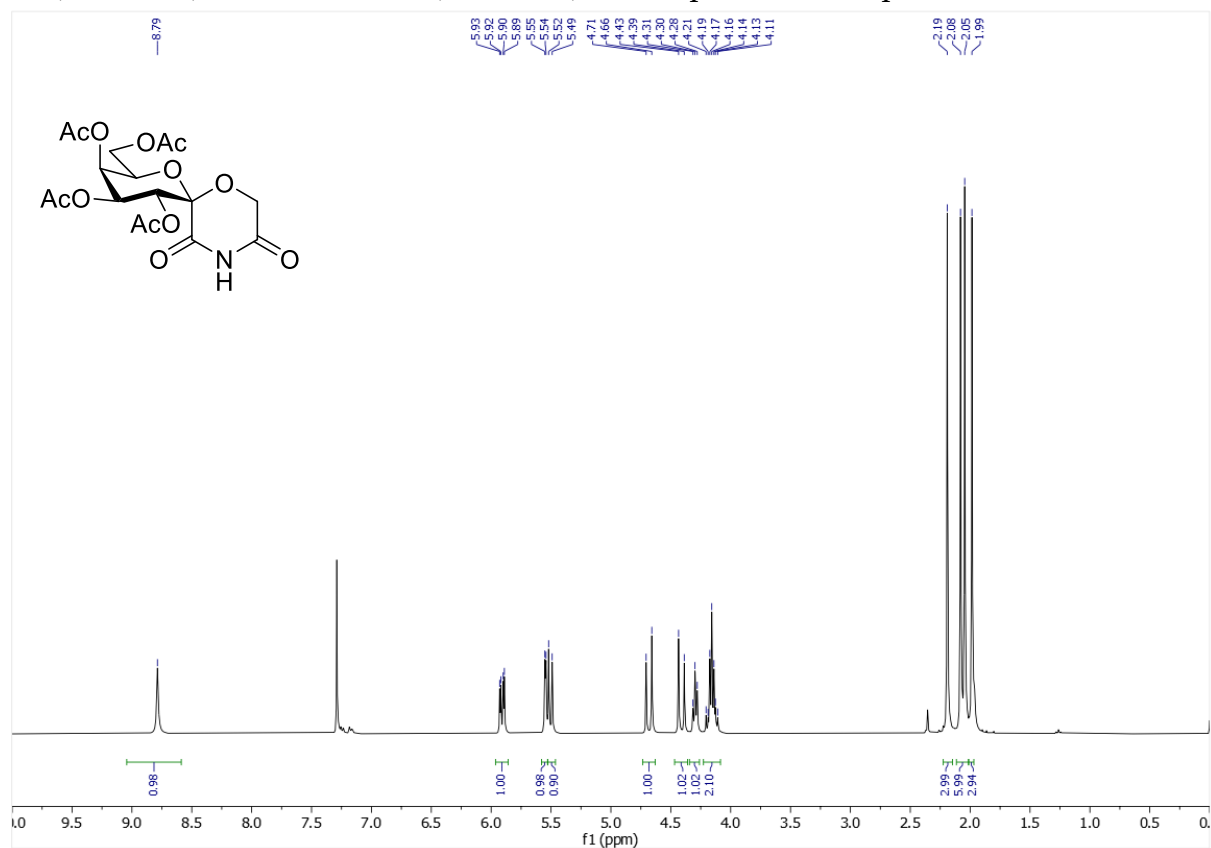


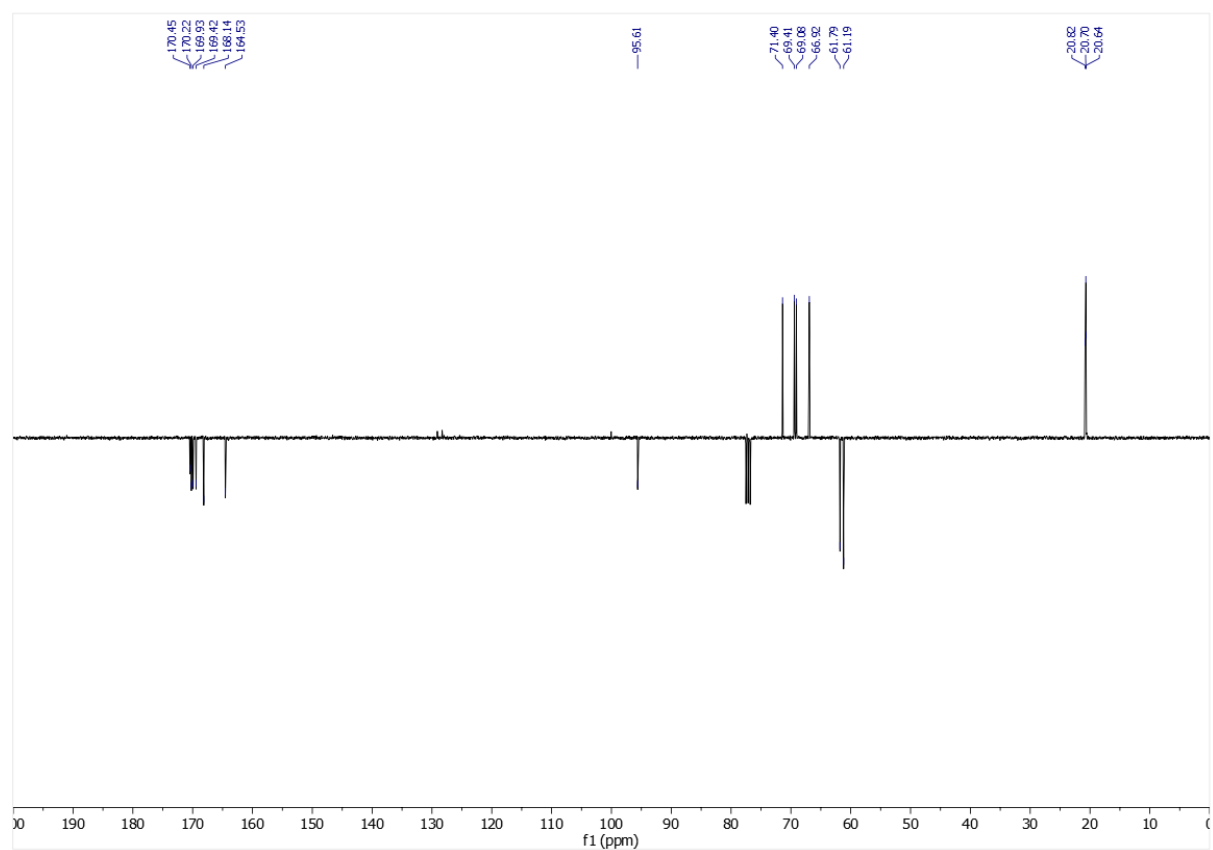
^1H (360 MHz) and ^{13}C J-MOD (90 MHz) NMR spectra of compound **27** in CDCl_3



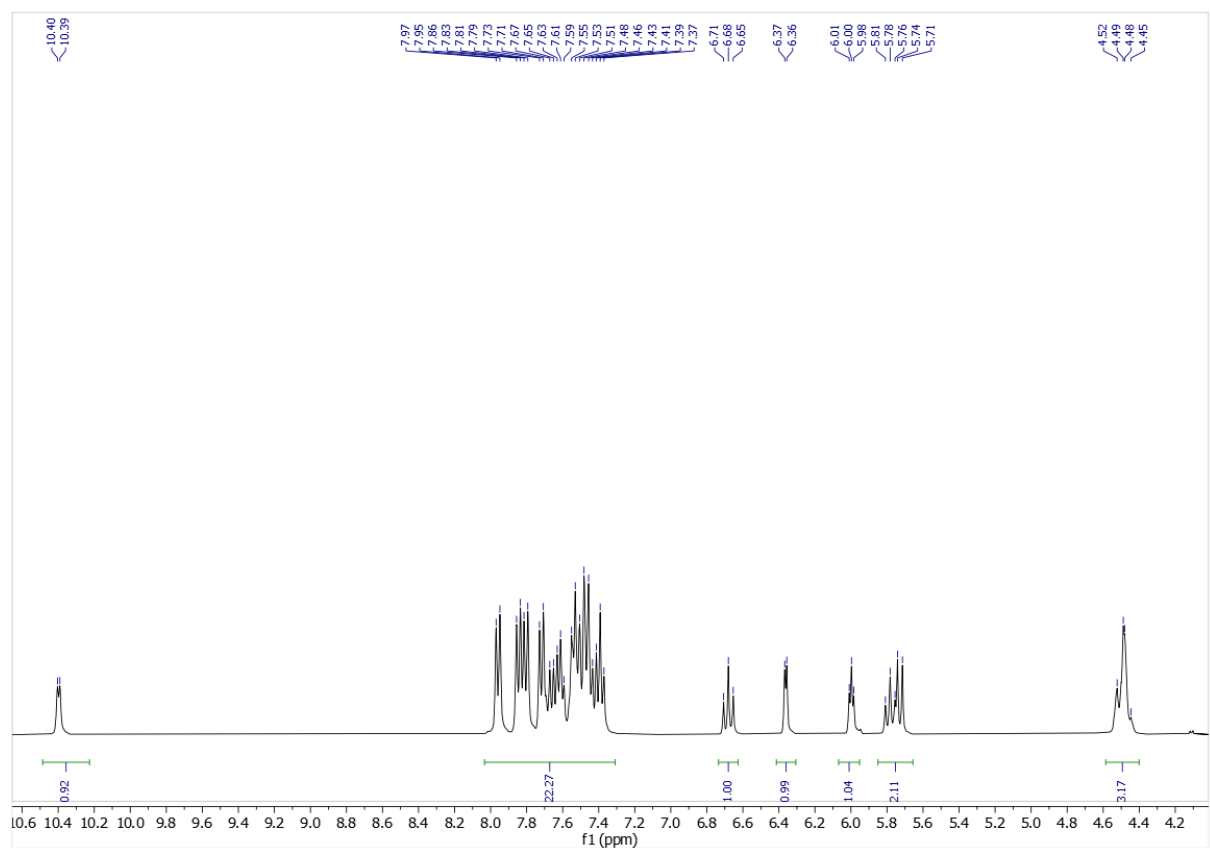
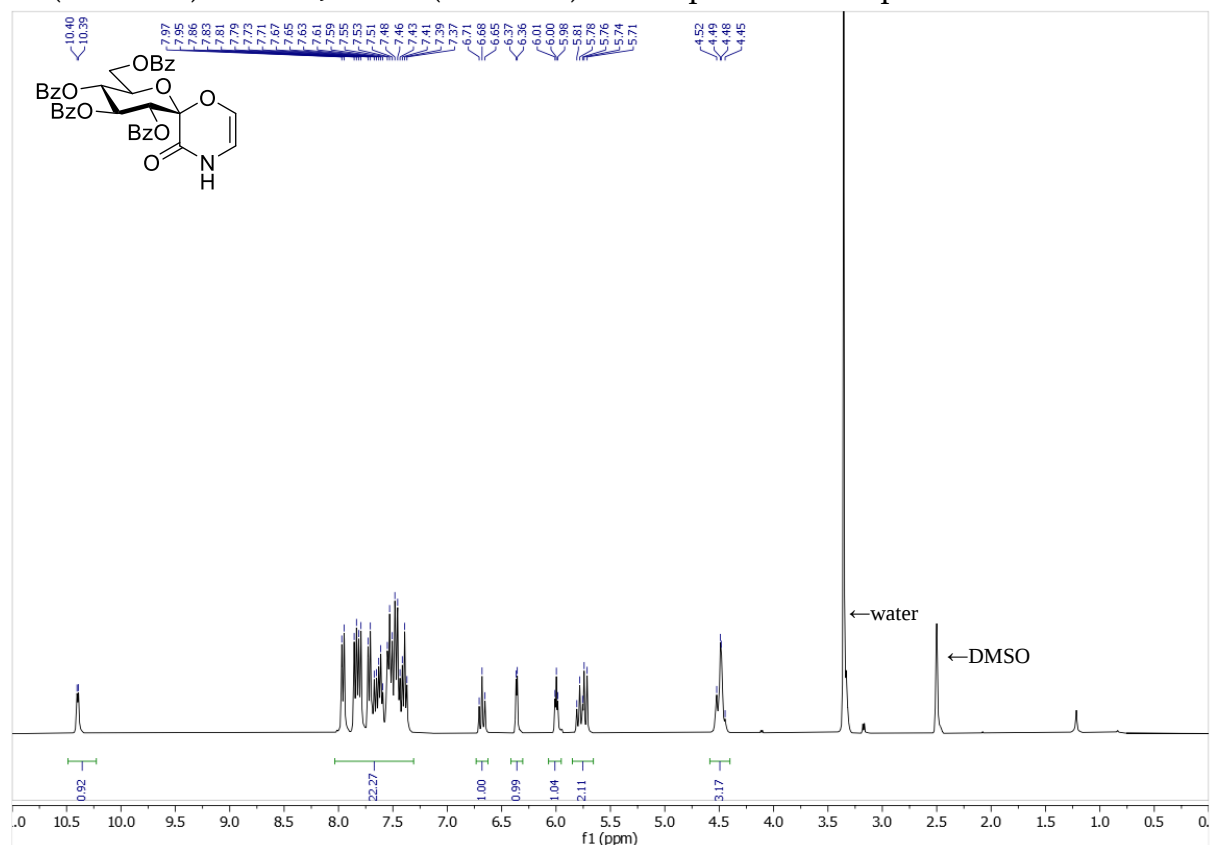


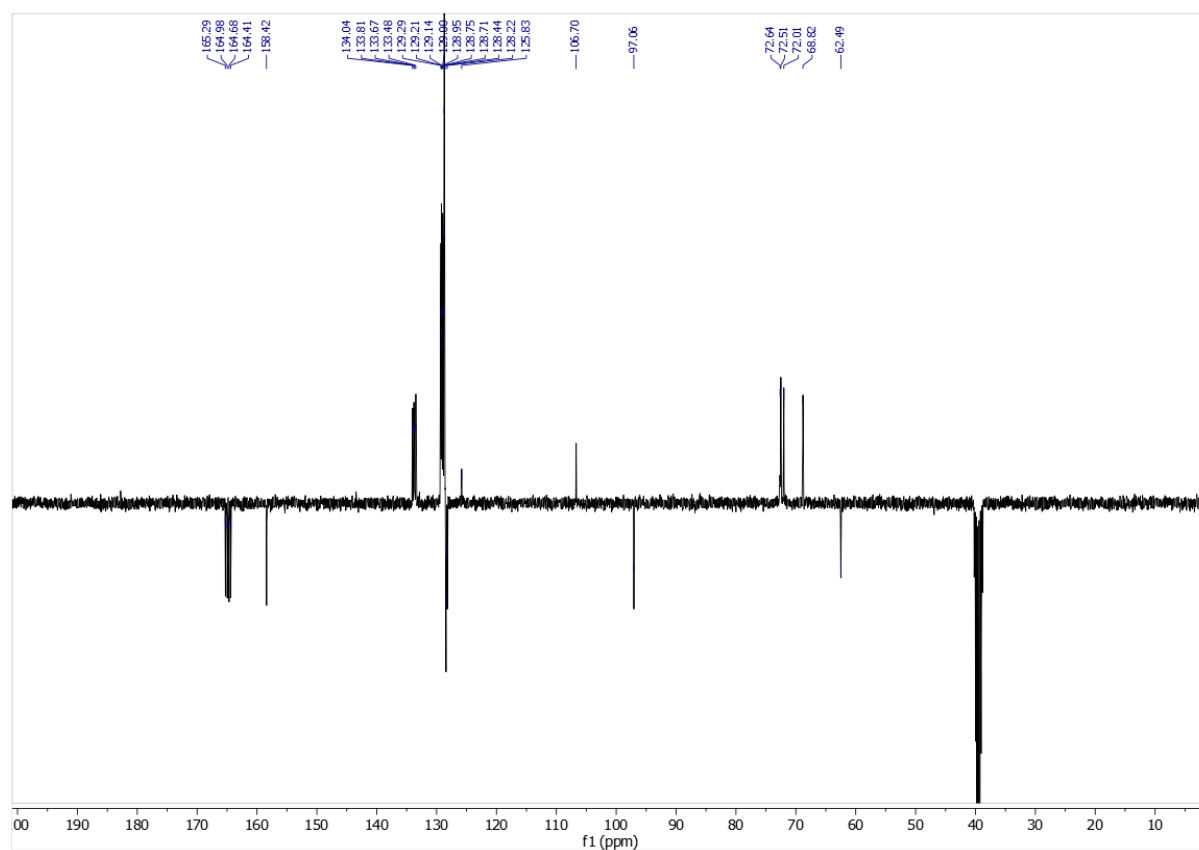
^1H (400 MHz) and ^{13}C J-MOD (100 MHz) NMR spectra of compound **28** in CDCl_3



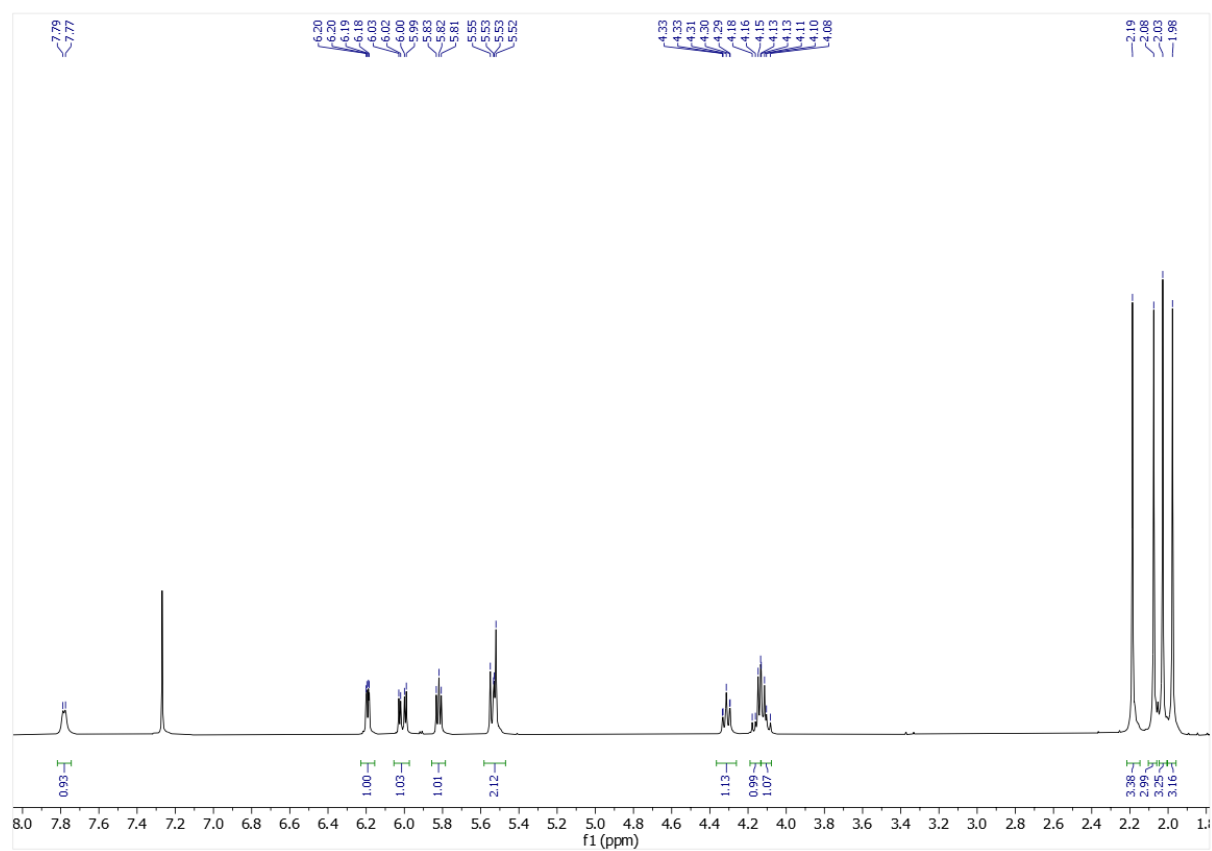
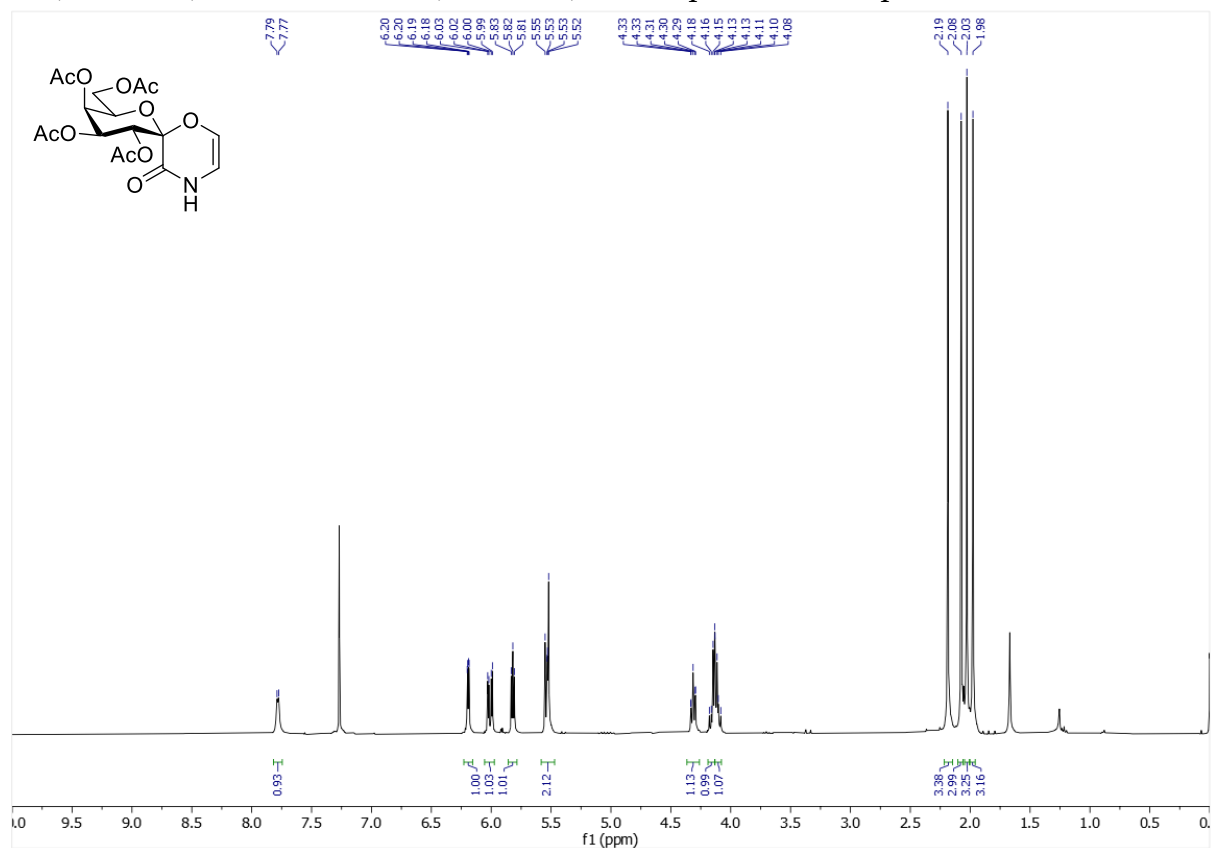


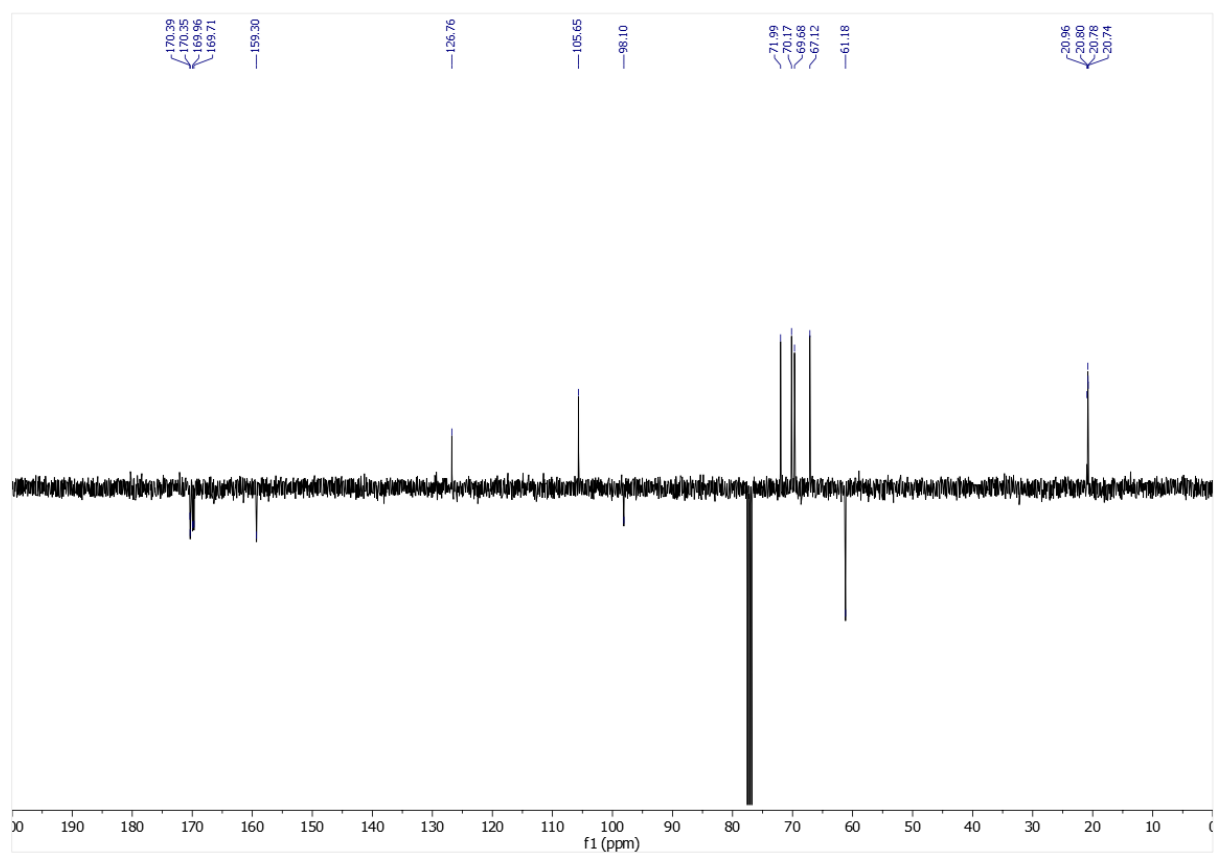
^1H (400 MHz) and ^{13}C J-MOD (100 MHz) NMR spectra of compound **29** in DMSO-d_6



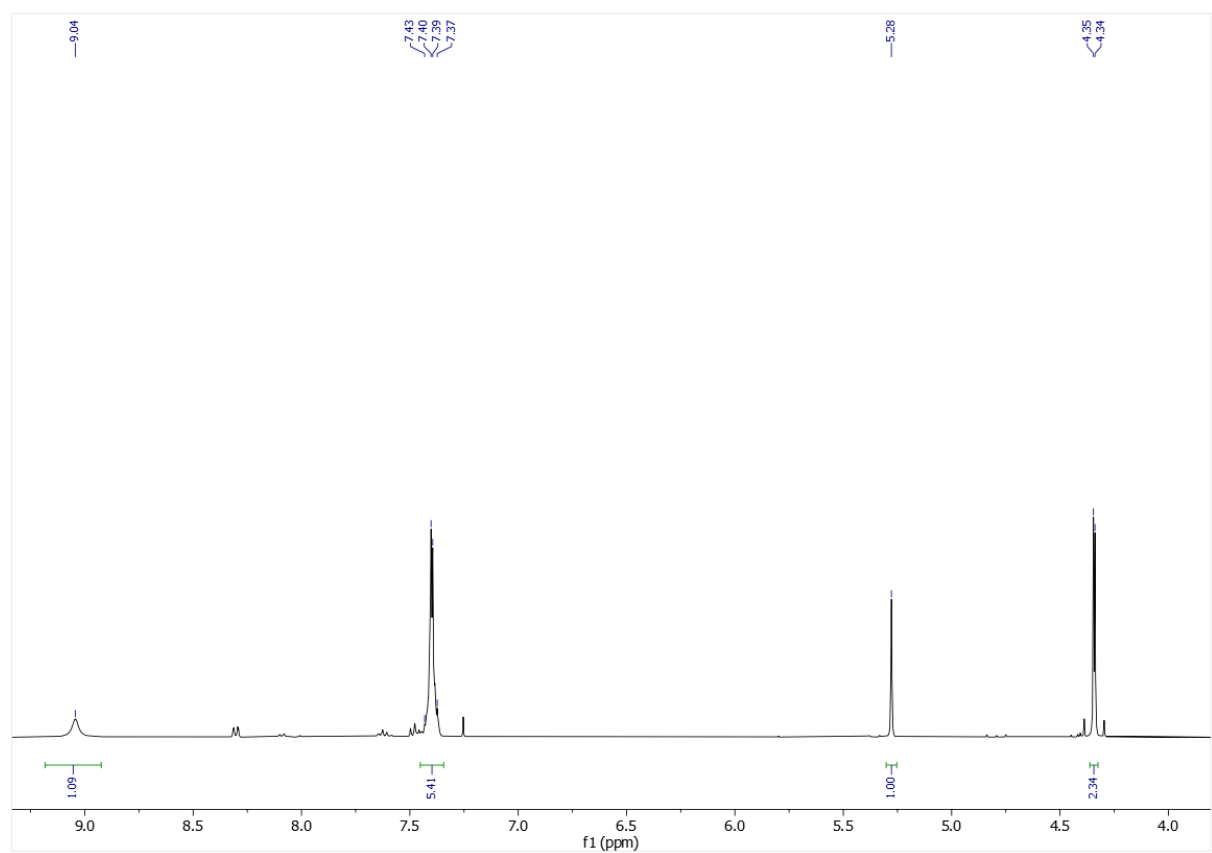
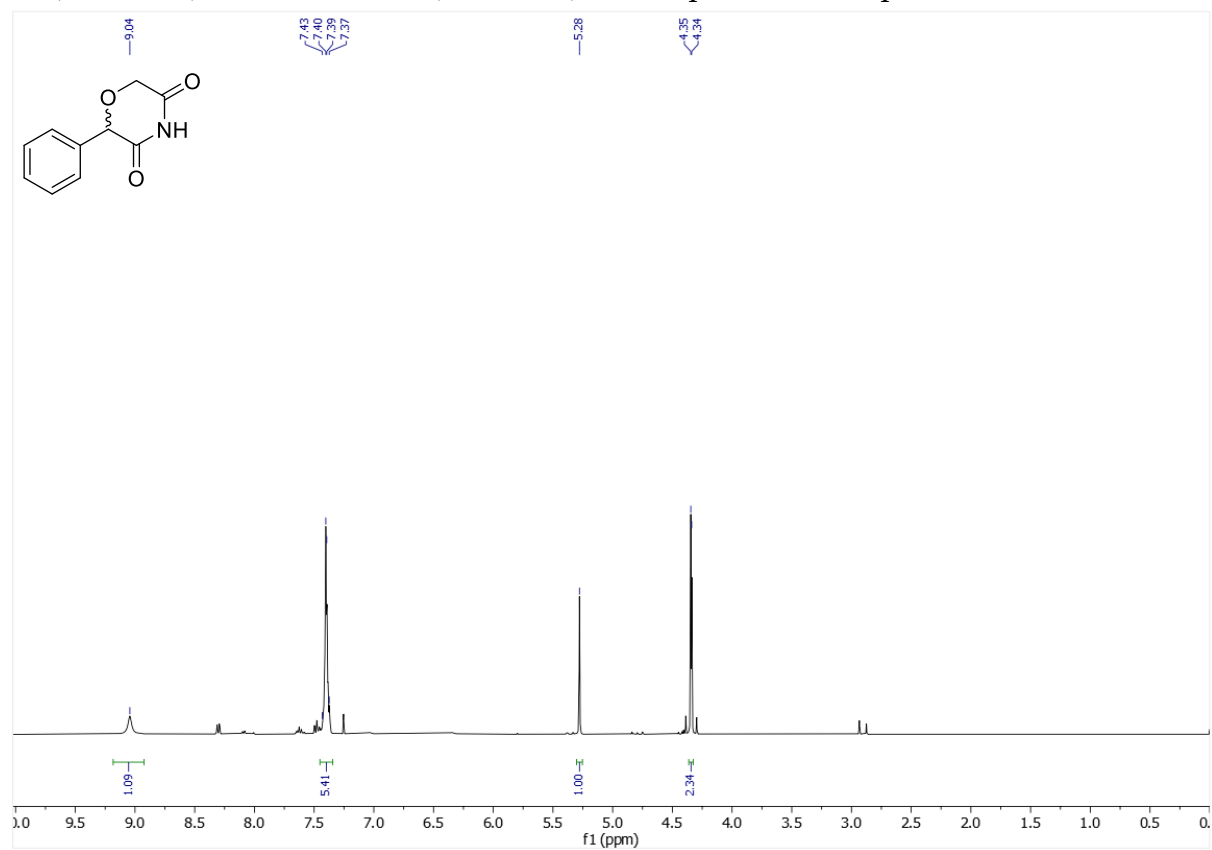


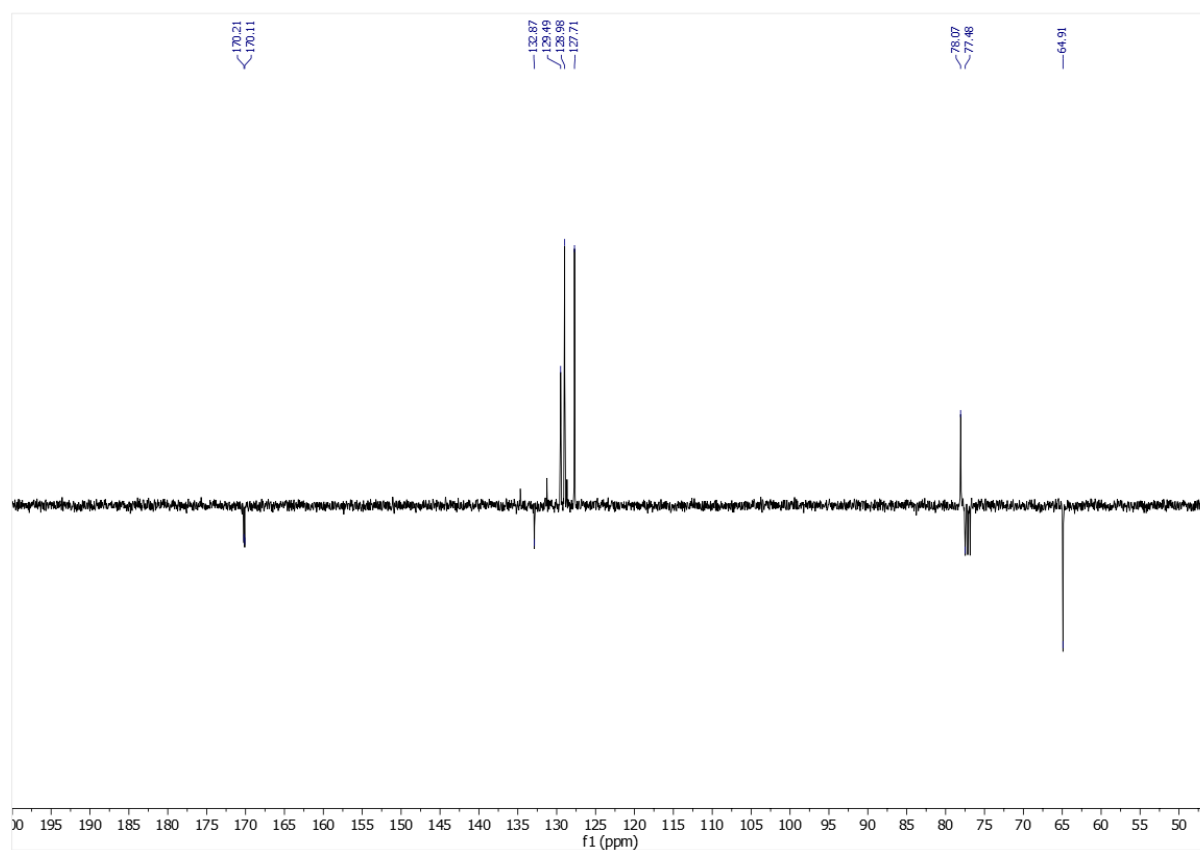
^1H (400 MHz) and ^{13}C J-MOD (100 MHz) NMR spectra of compound **30** in CDCl_3





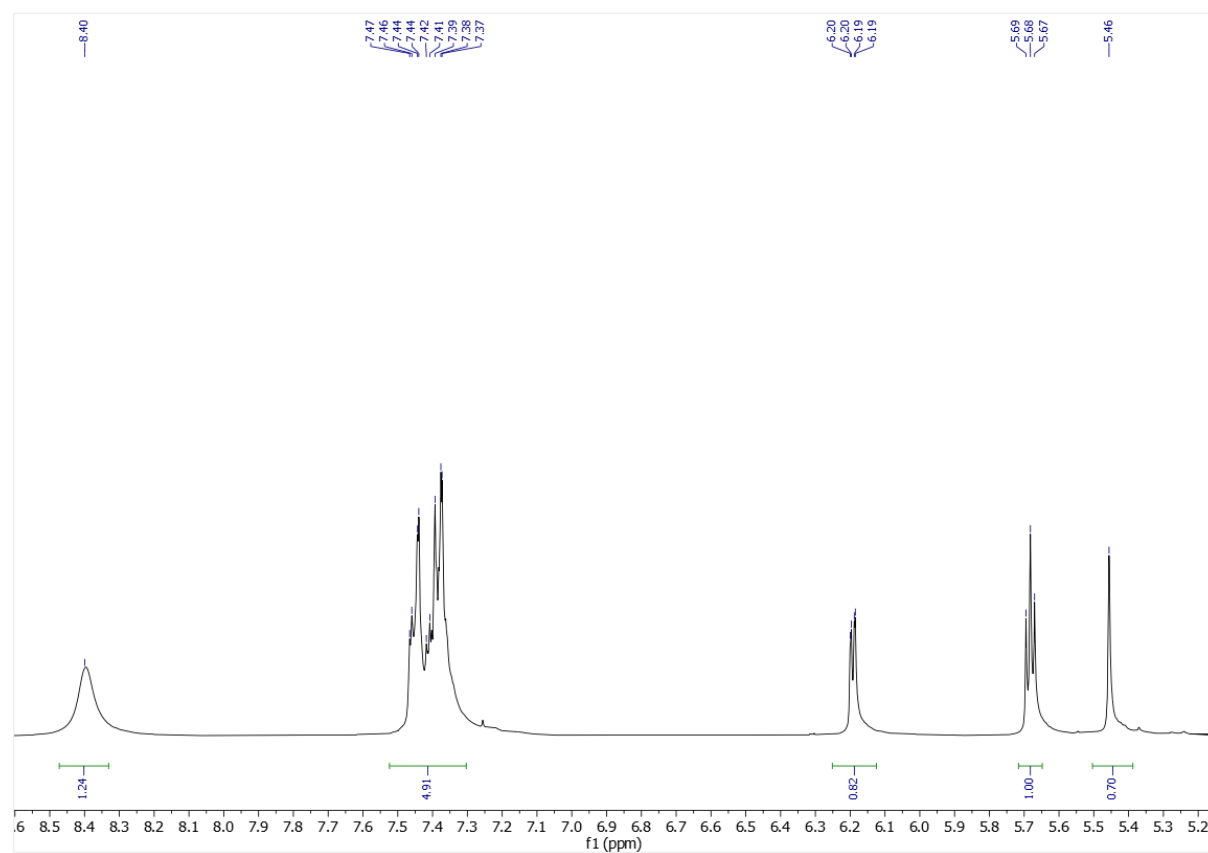
^1H (400 MHz) and ^{13}C J-MOD (100 MHz) NMR spectra of compound **31** in CDCl_3

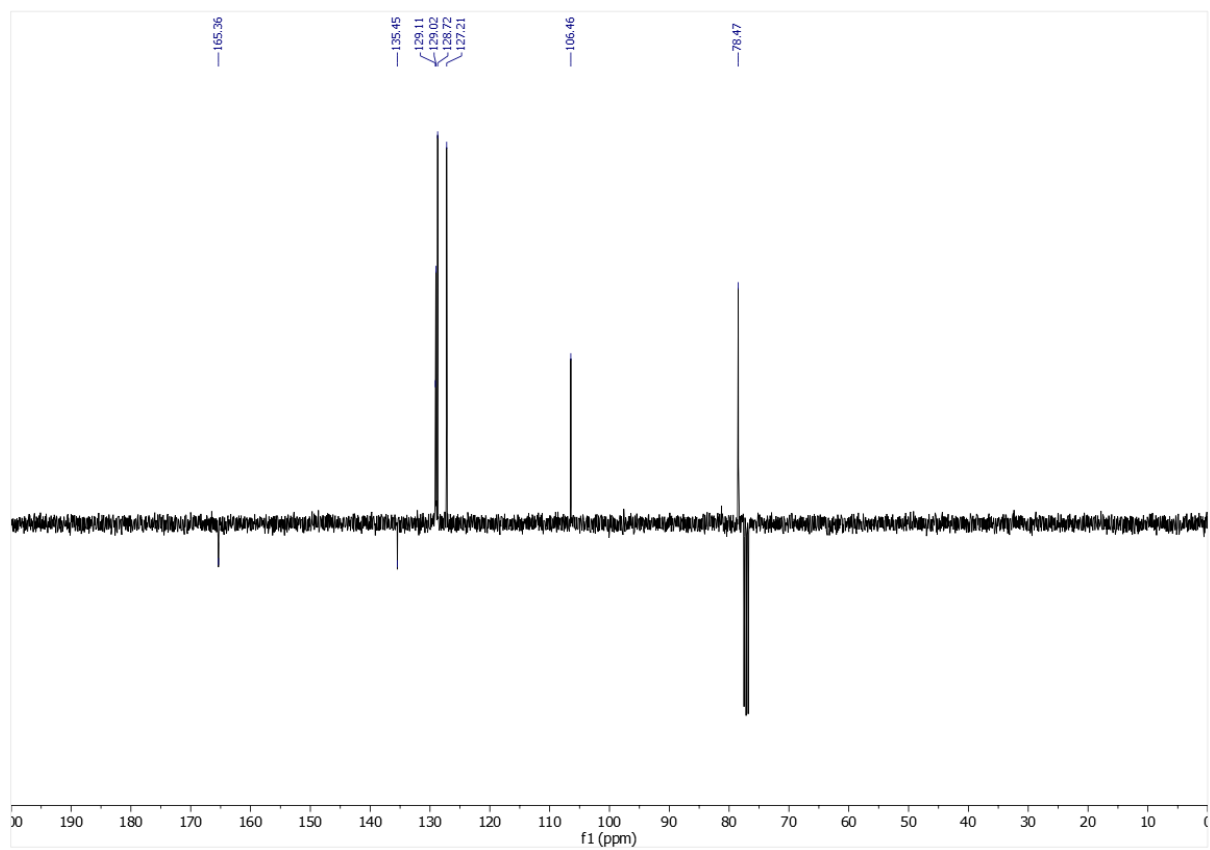




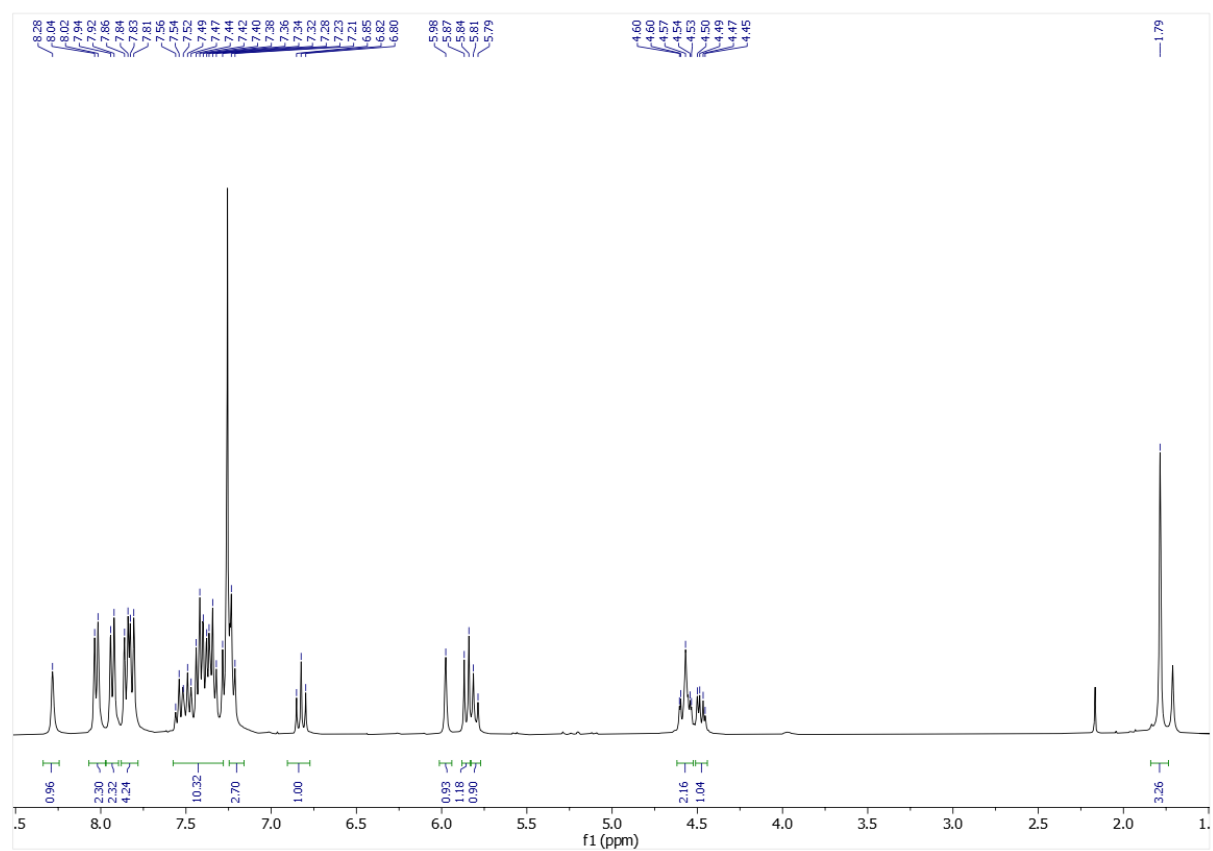
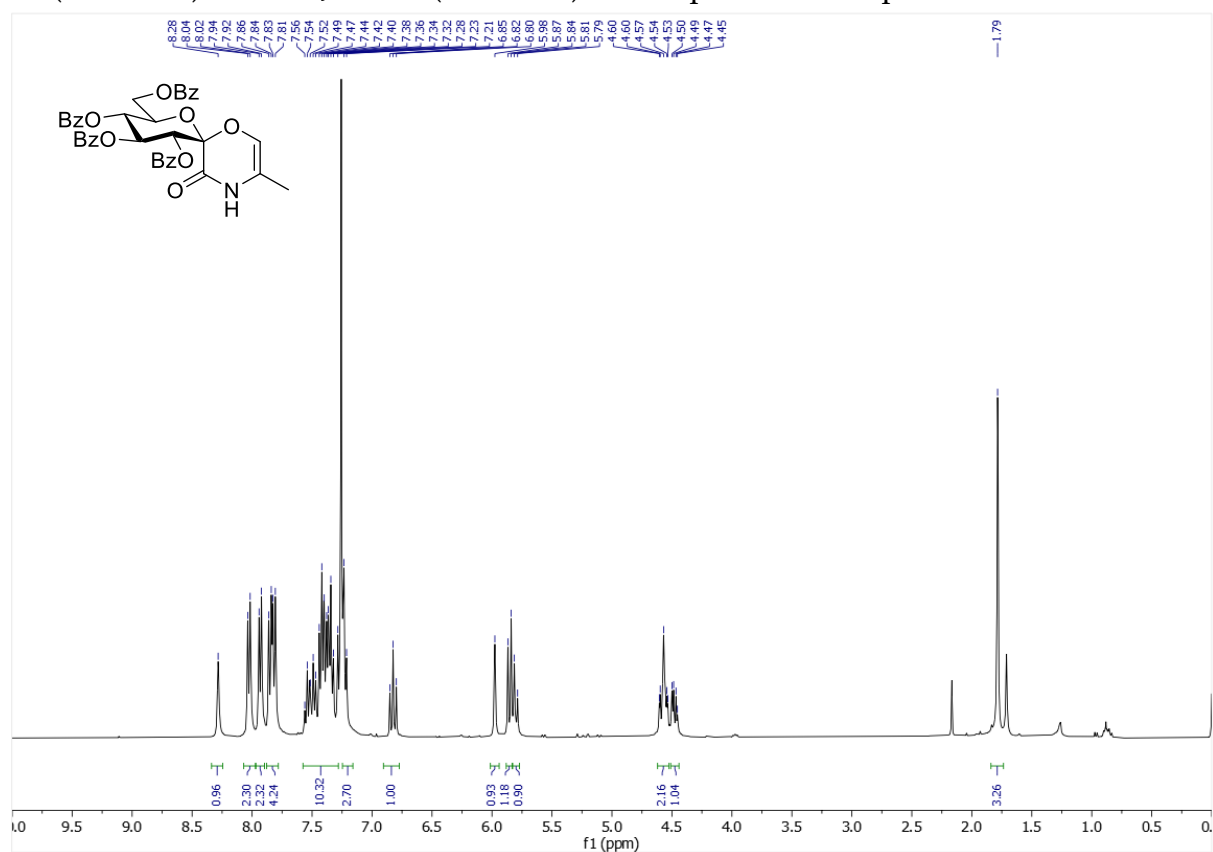
O=C1NC=CC1C2=CC=CC=C2

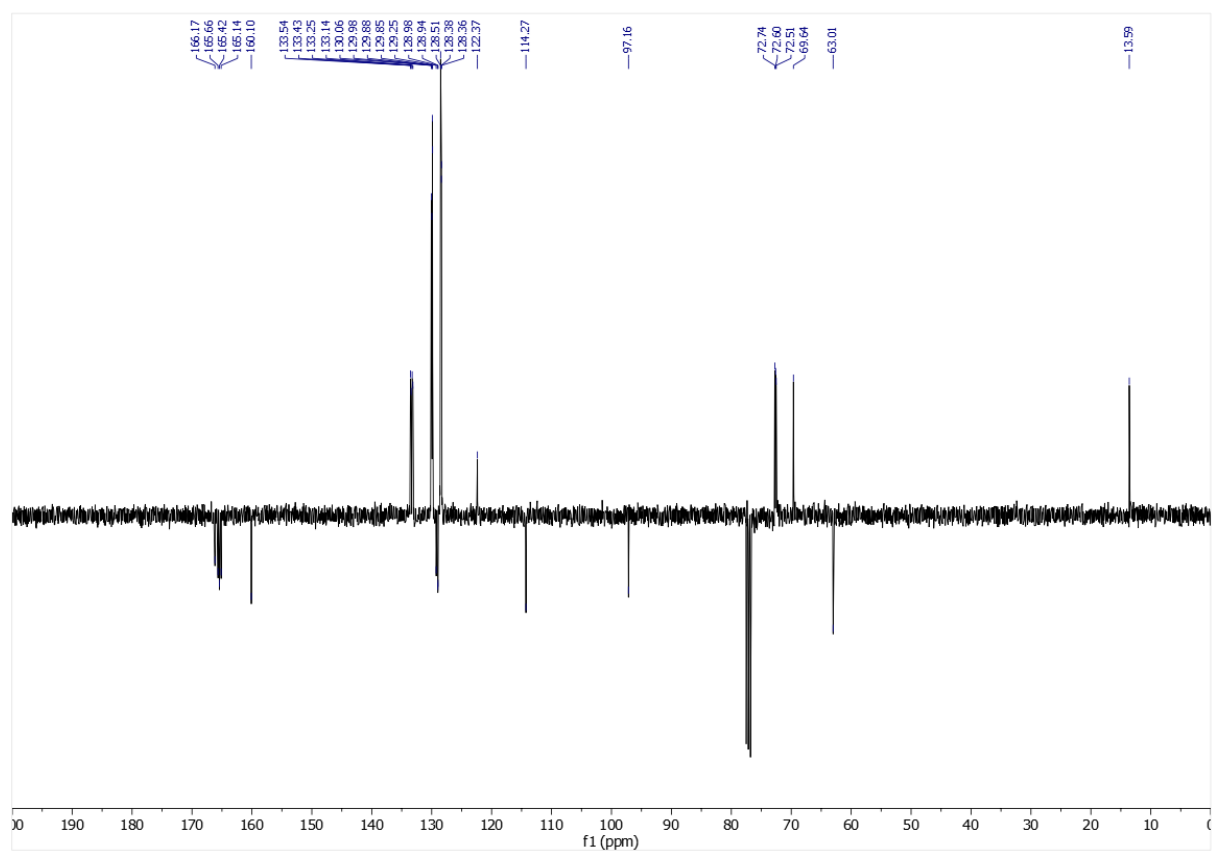
¹H NMR spectrum (400 MHz, CDCl₃) of 2-phenyl-2-oxo-1,3-dihydroisobenzofuran. The spectrum shows peaks at 8.40 (s, 1H), 7.47-7.37 (m, 4H), 6.20-6.19 (m, 2H), 5.69-5.46 (m, 2H), and 1.50 (s, 3H). Integration values are 1.24, 4.91, 0.82, 1.00, and 0.70 respectively.



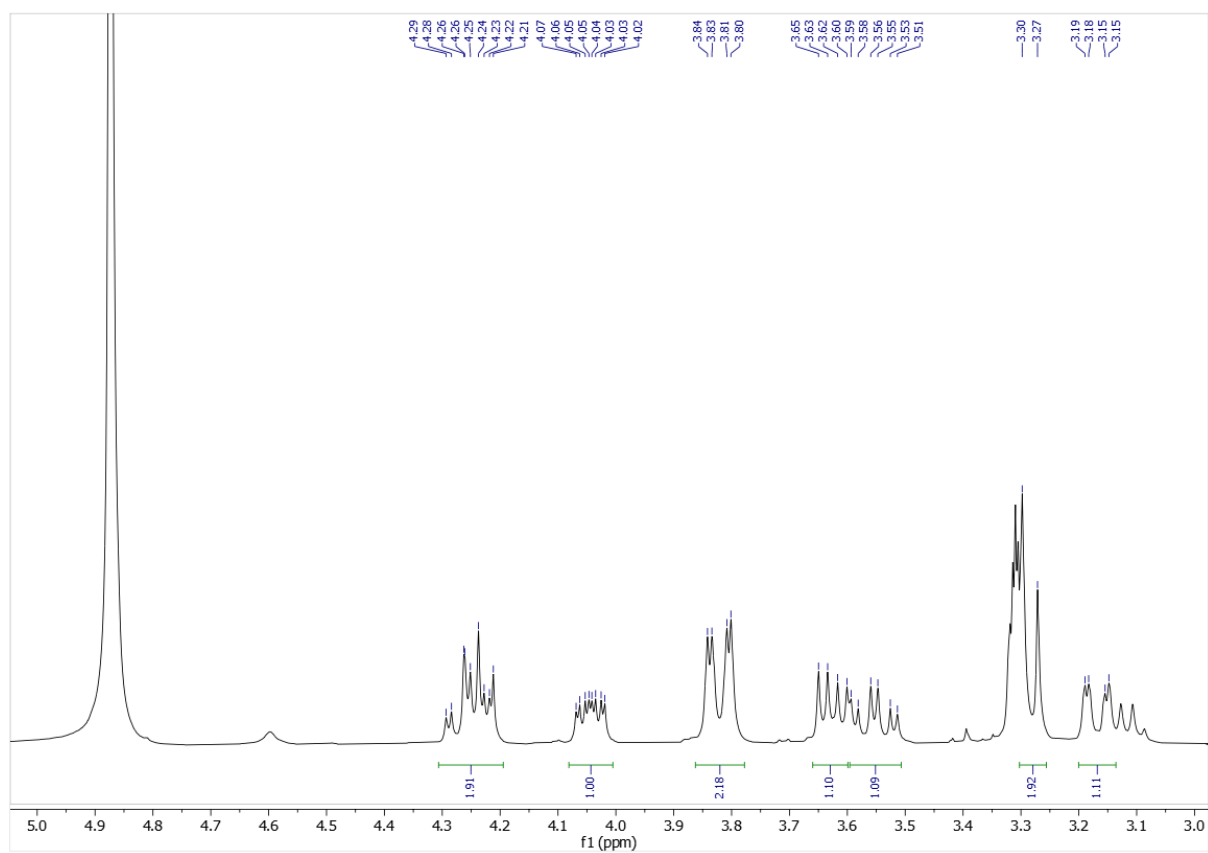
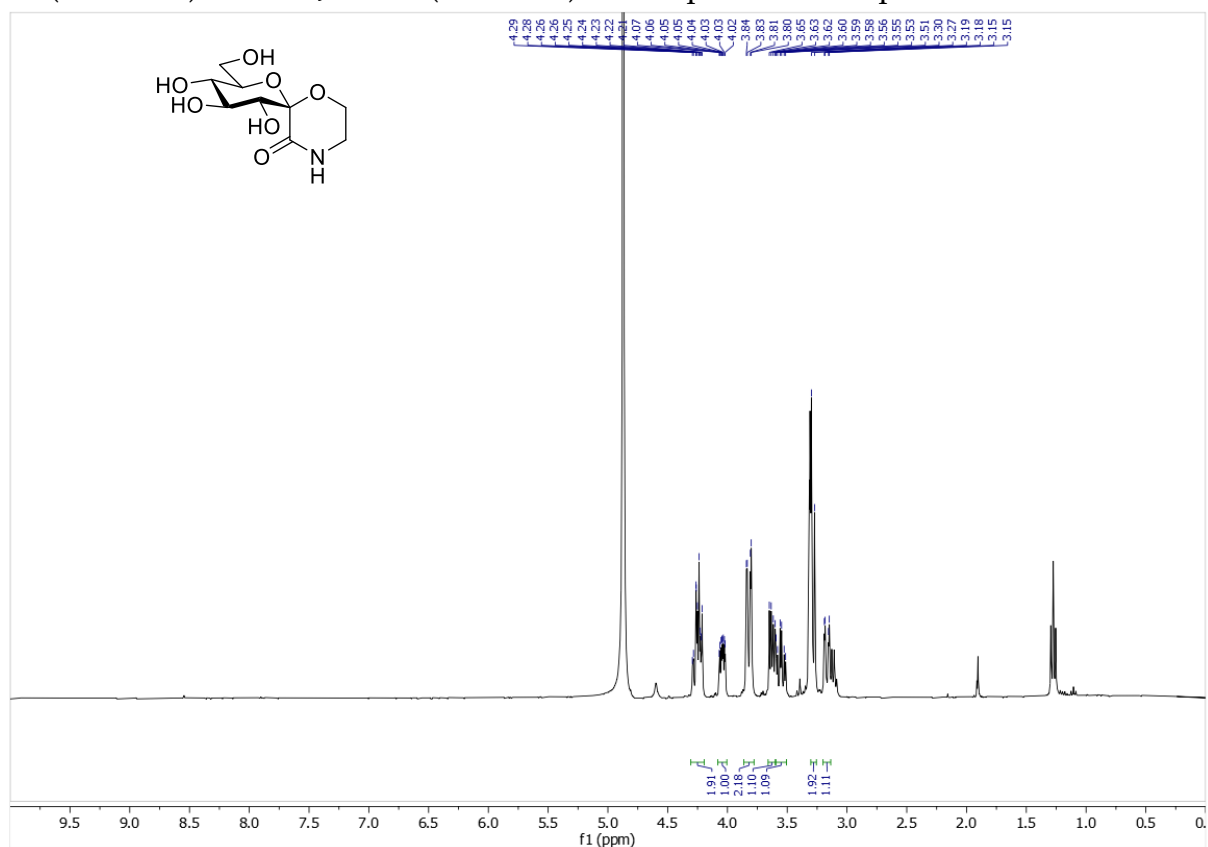


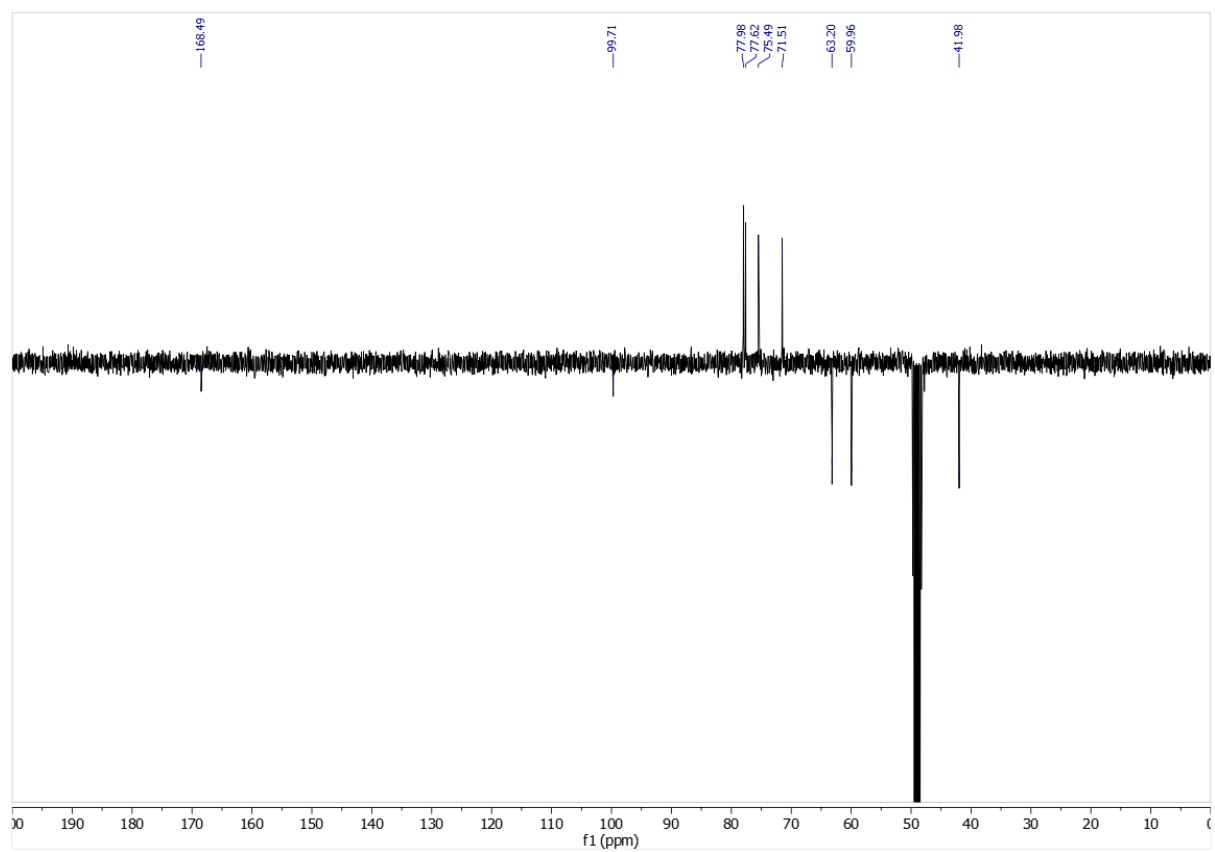
^1H (400 MHz) and ^{13}C J-MOD (100 MHz) NMR spectra of compound **33** in CDCl_3



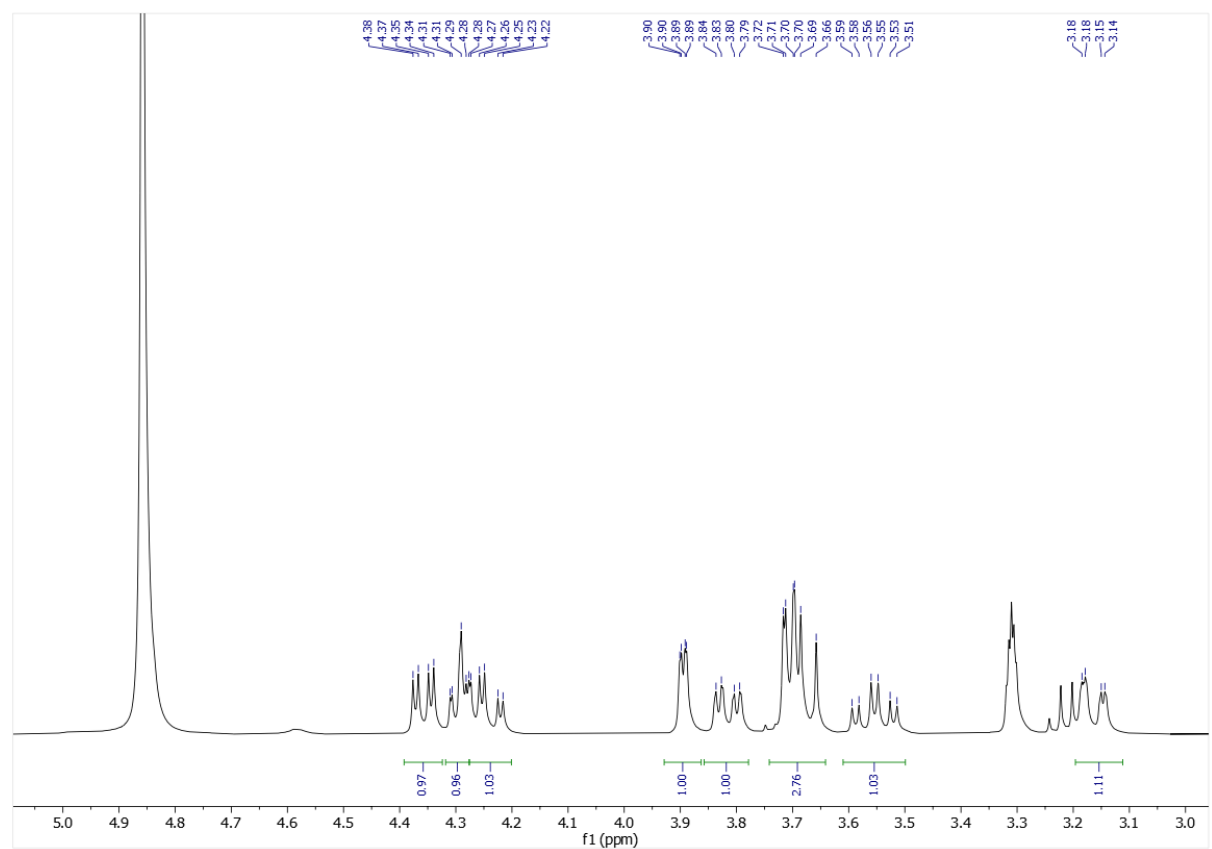
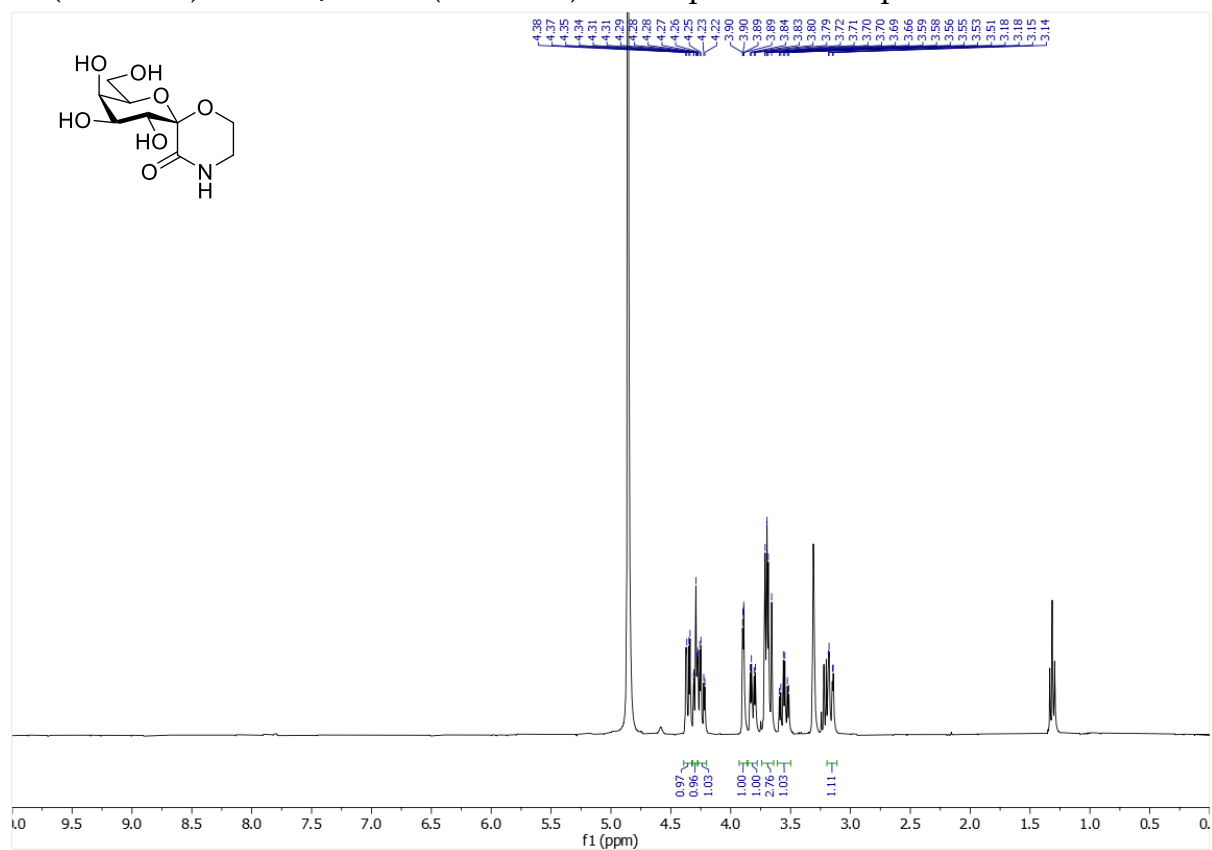


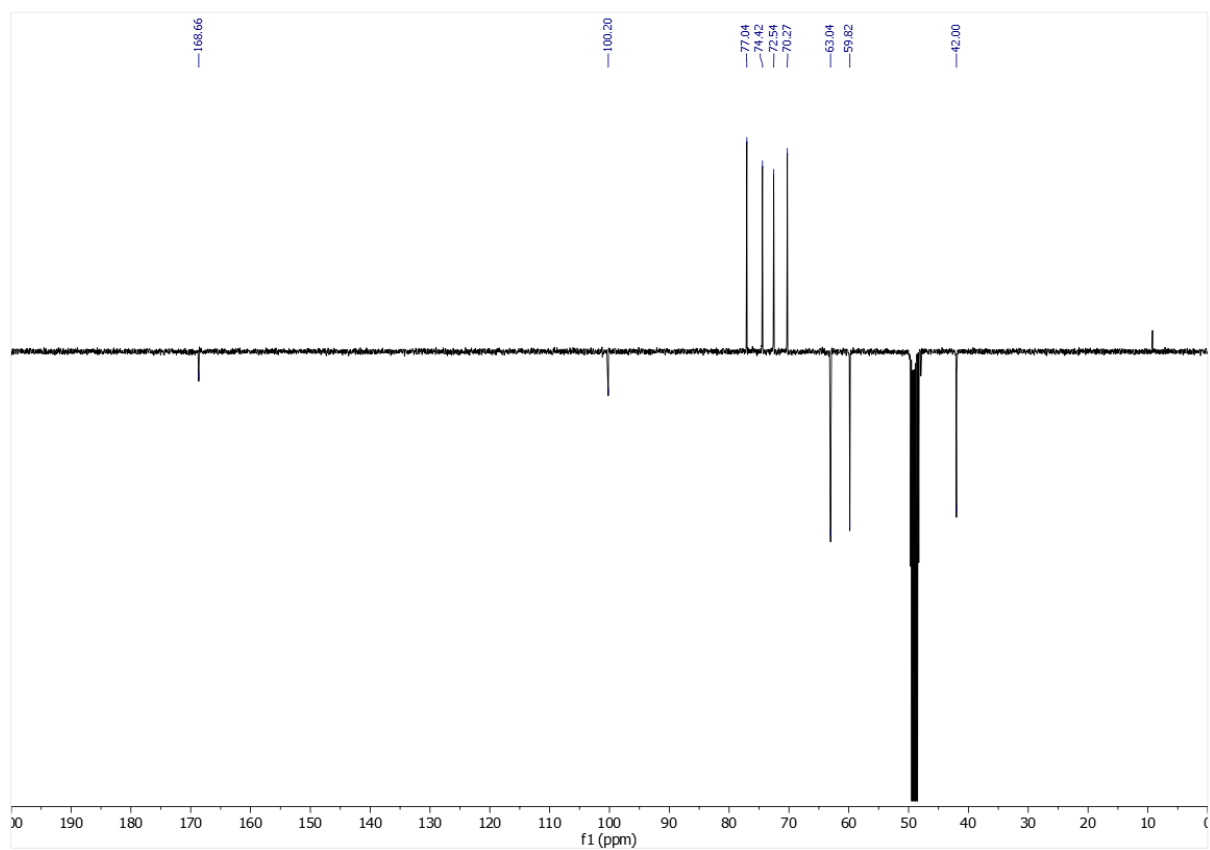
^1H (400 MHz) and ^{13}C J-MOD (100 MHz) NMR spectra of compound **34** in CD_3OD



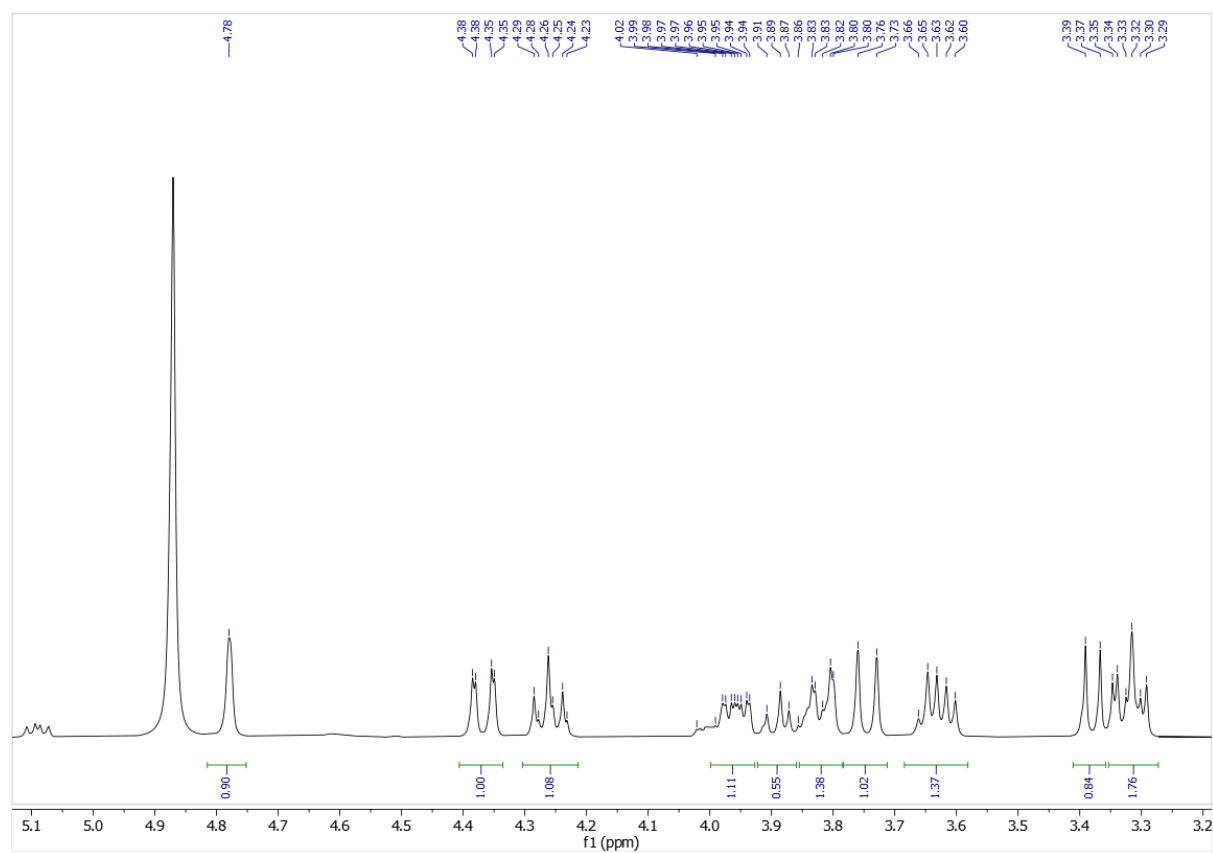
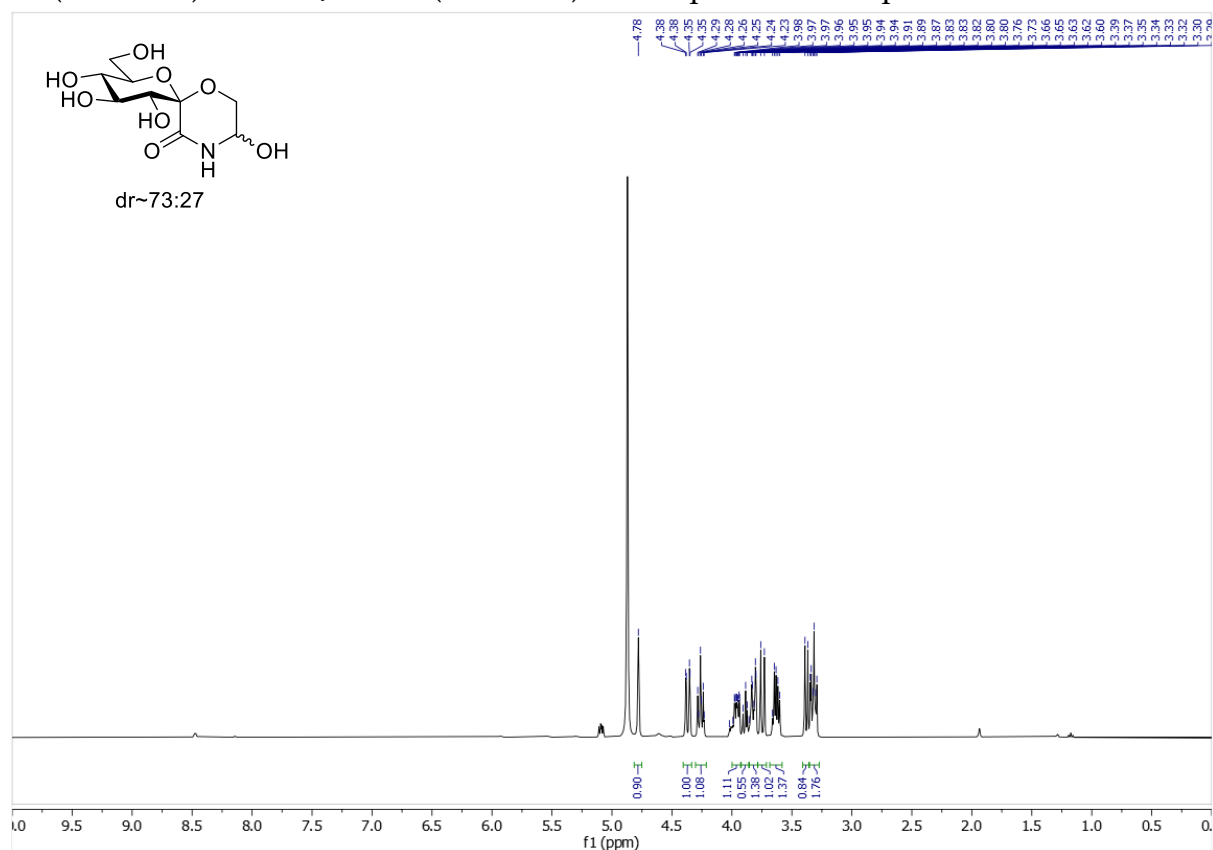


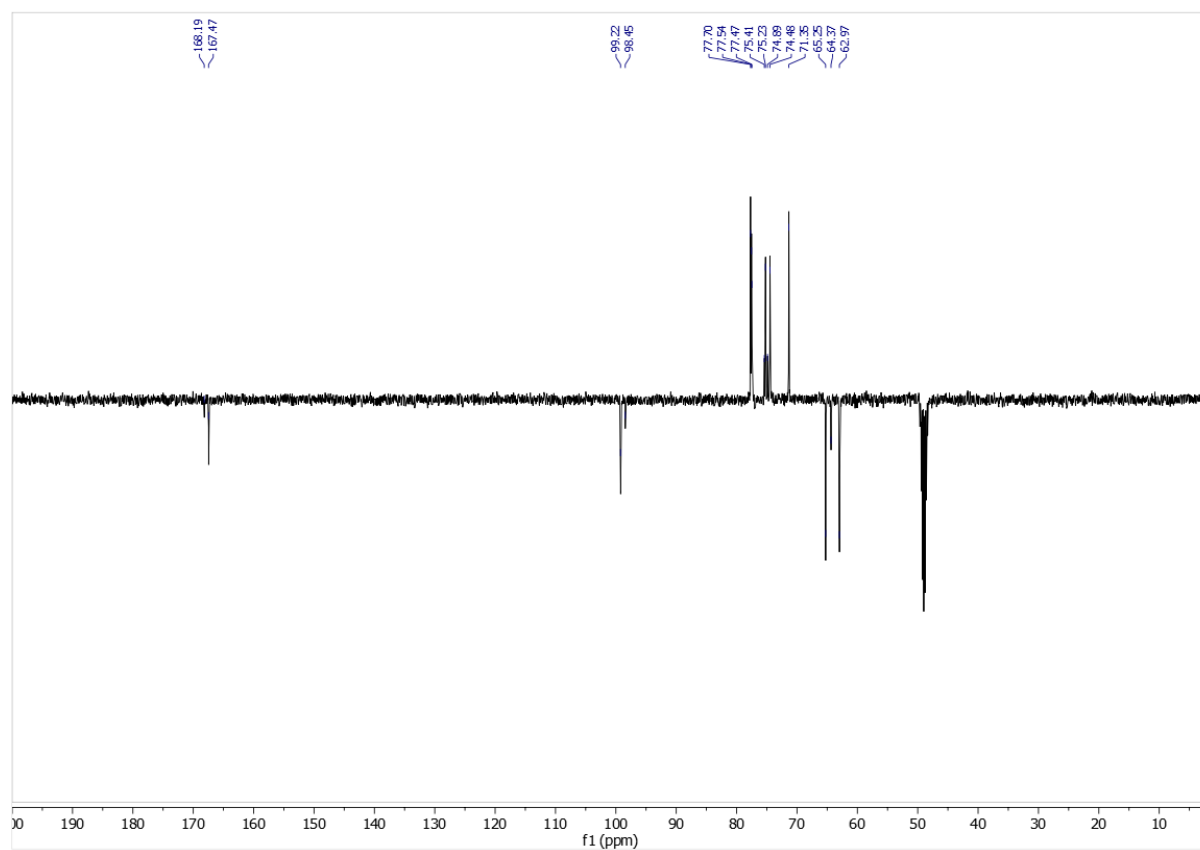
^1H (400 MHz) and ^{13}C J-MOD (100 MHz) NMR spectra of compound **35** in CD_3OD



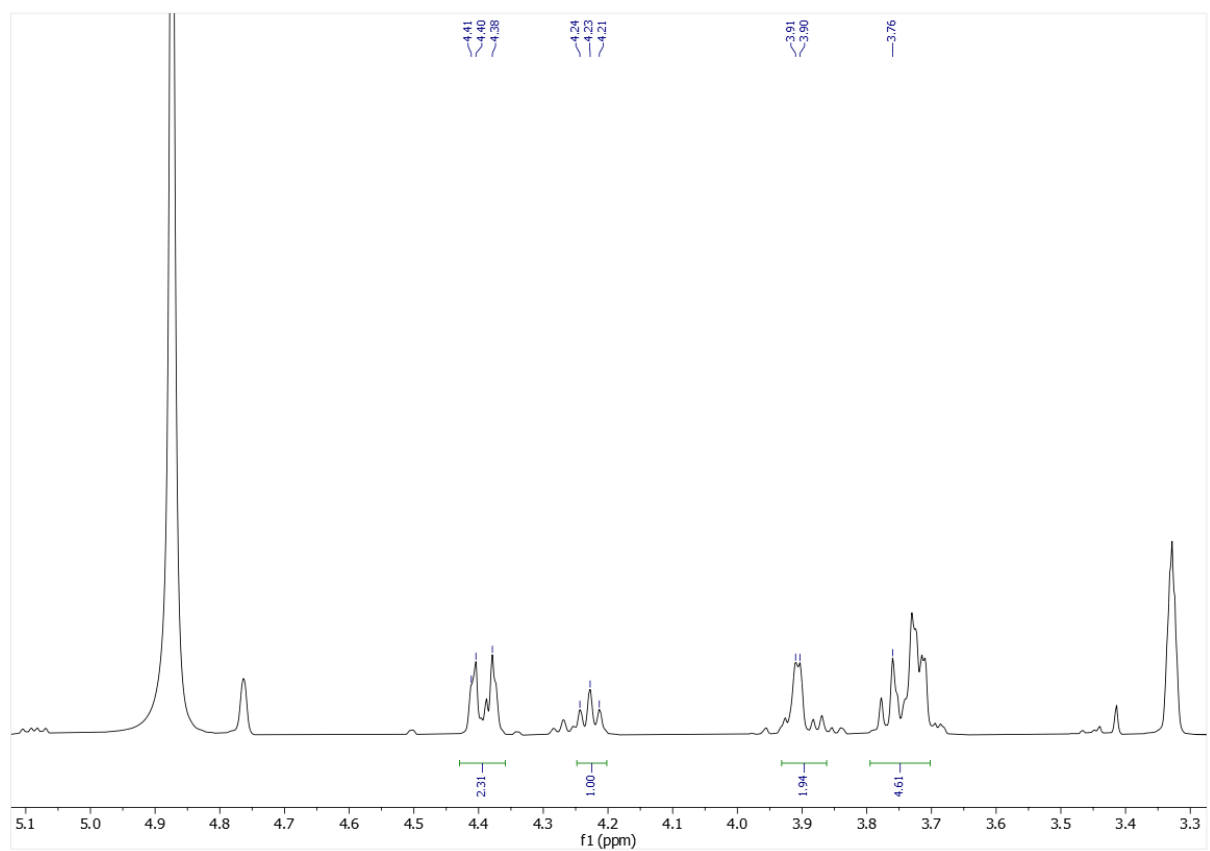
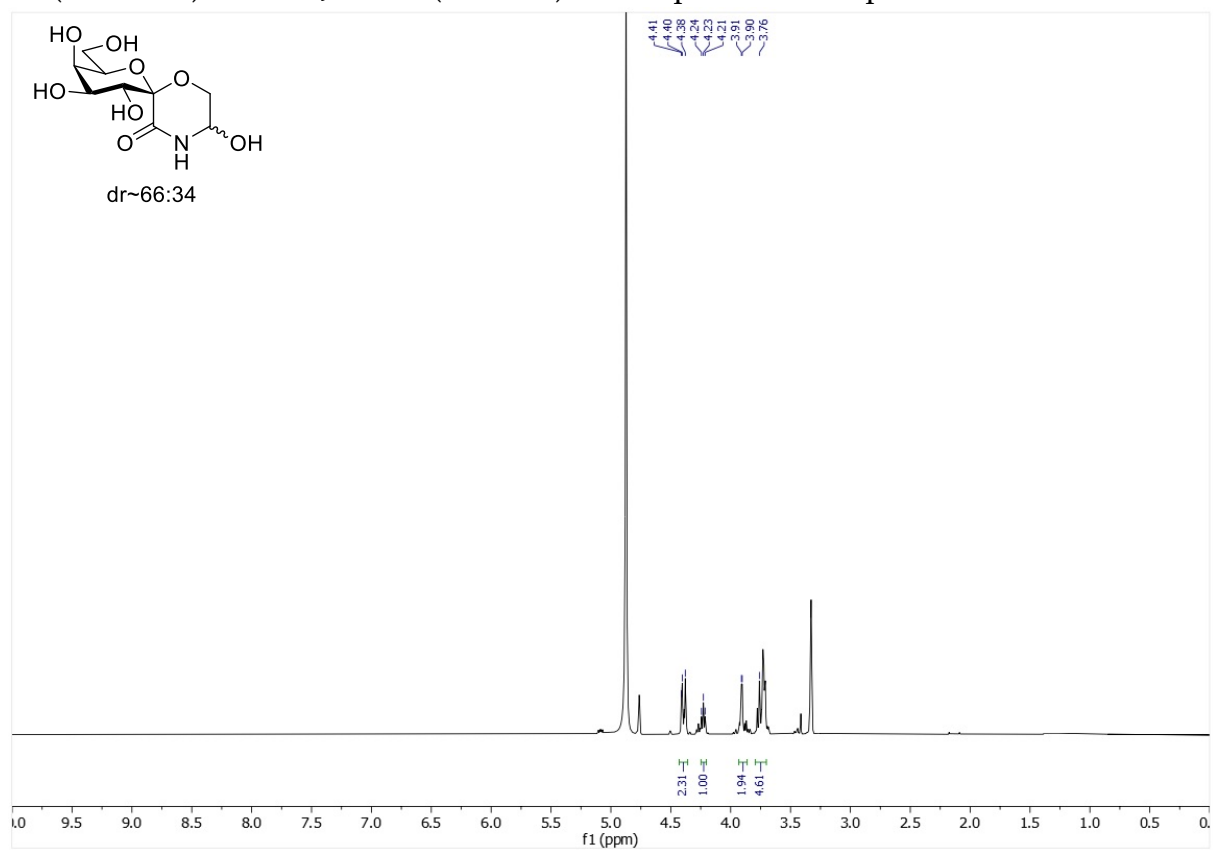


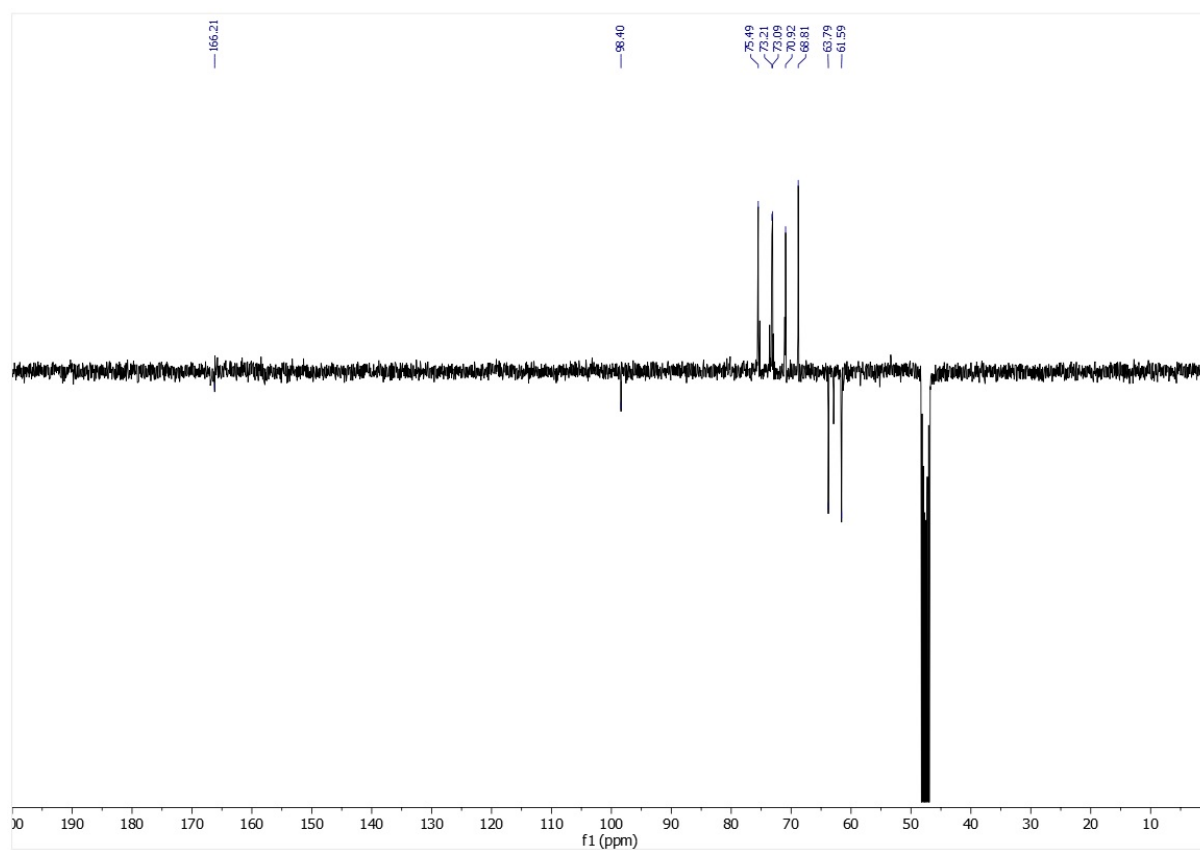
^1H (400 MHz) and ^{13}C J-MOD (100 MHz) NMR spectra of compound **36** in CD_3OD



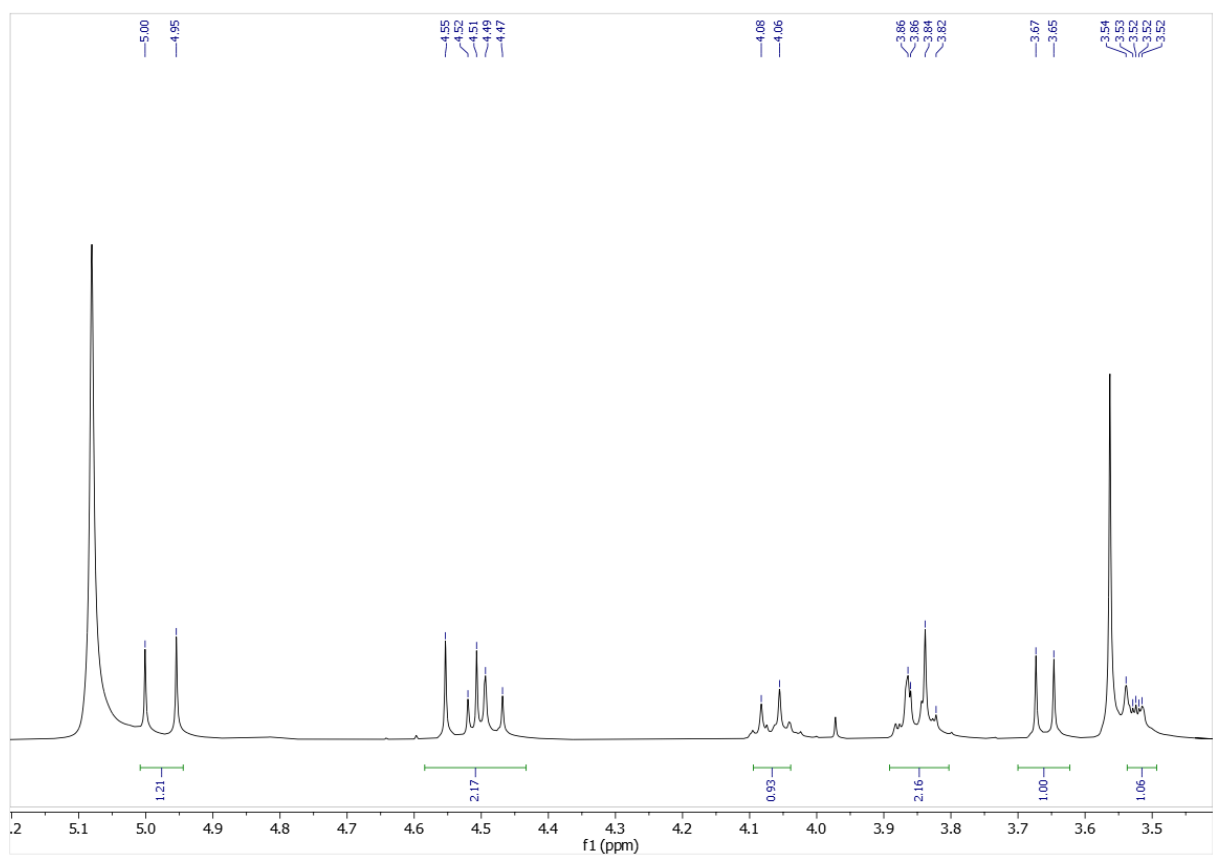
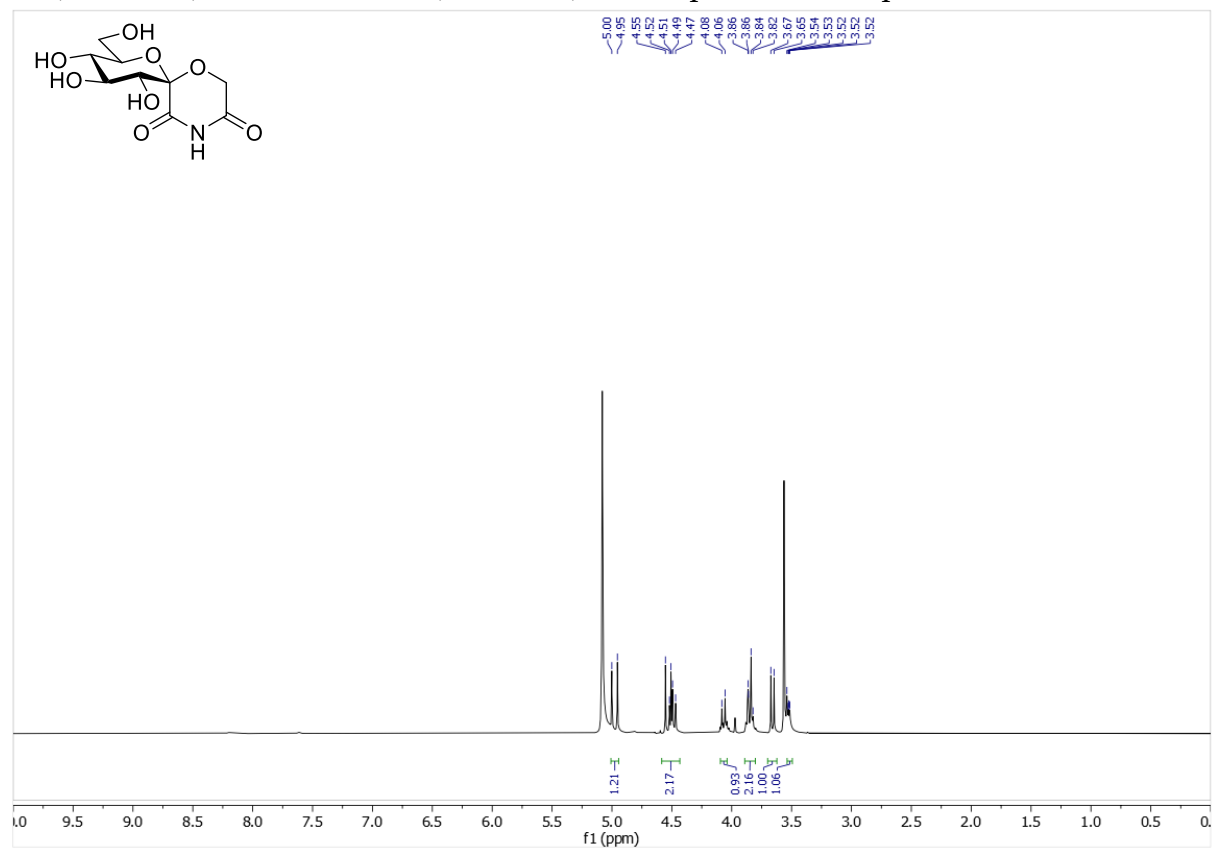


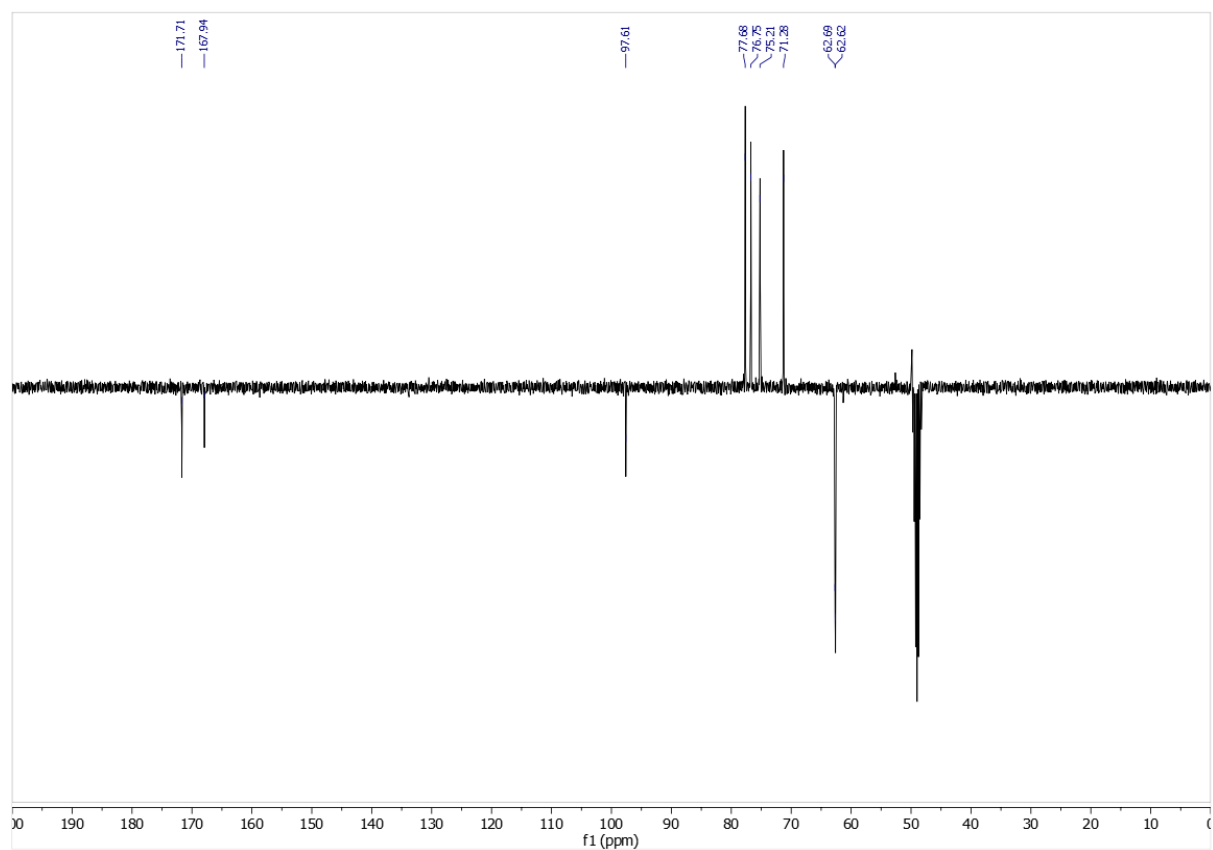
^1H (360 MHz) and ^{13}C J-MOD (90 MHz) NMR spectra of compound **37** in CD_3OD



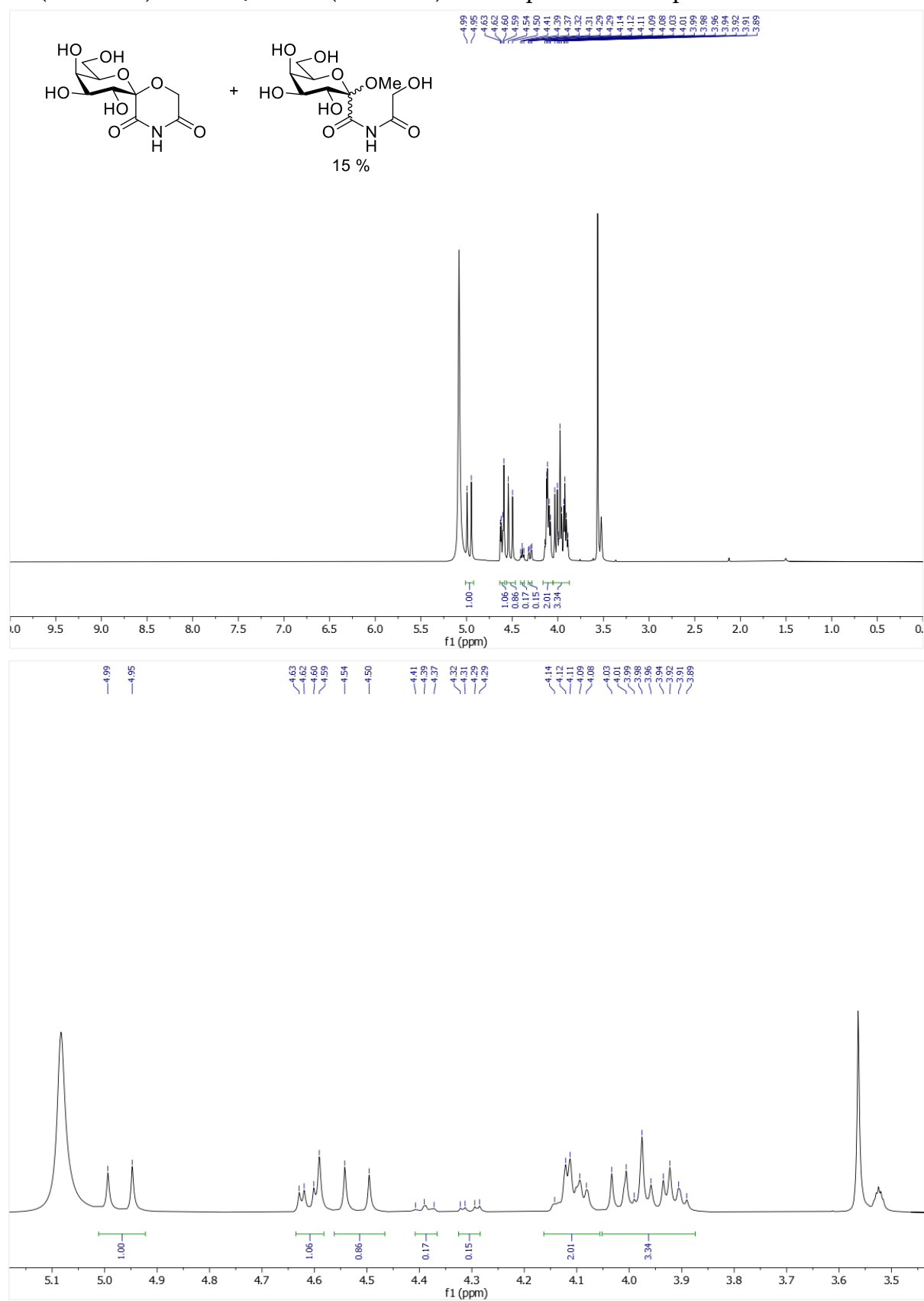


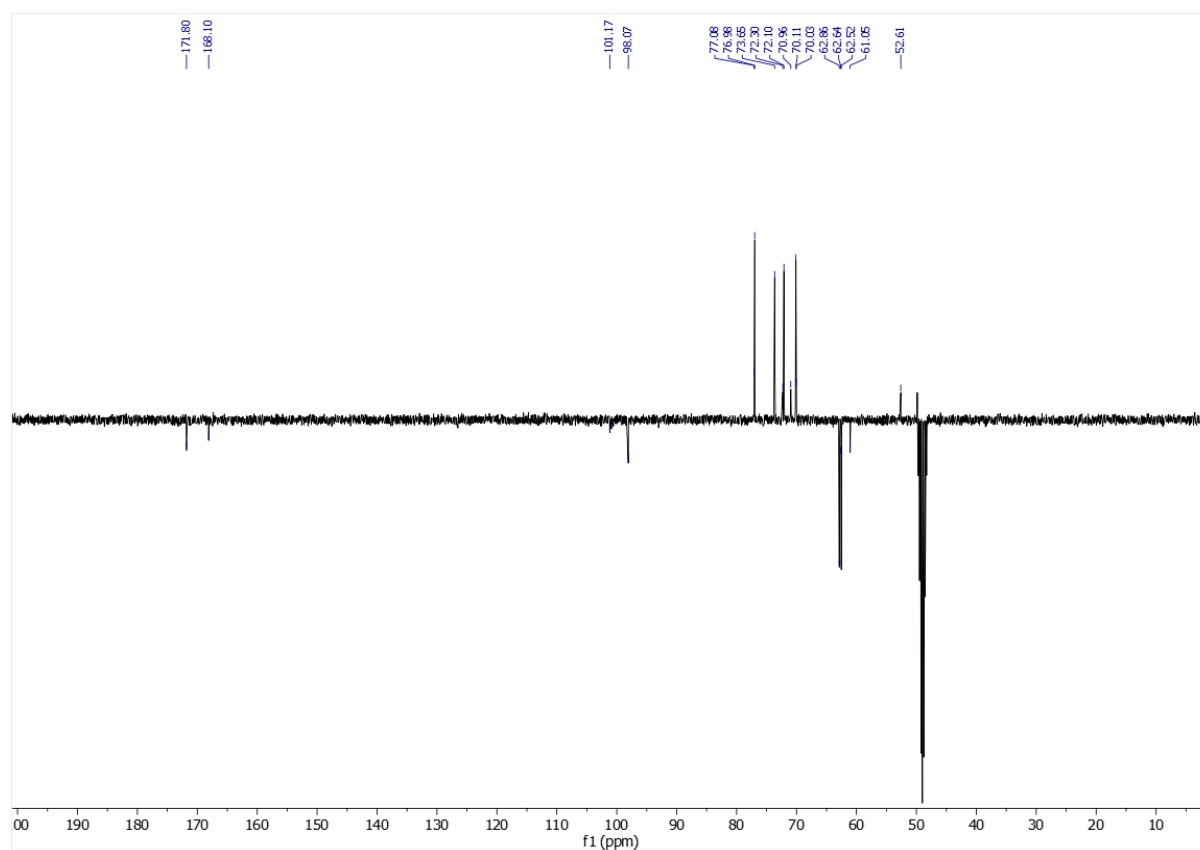
^1H (400 MHz) and ^{13}C J-MOD (100 MHz) NMR spectra of compound **38** in CD_3OD



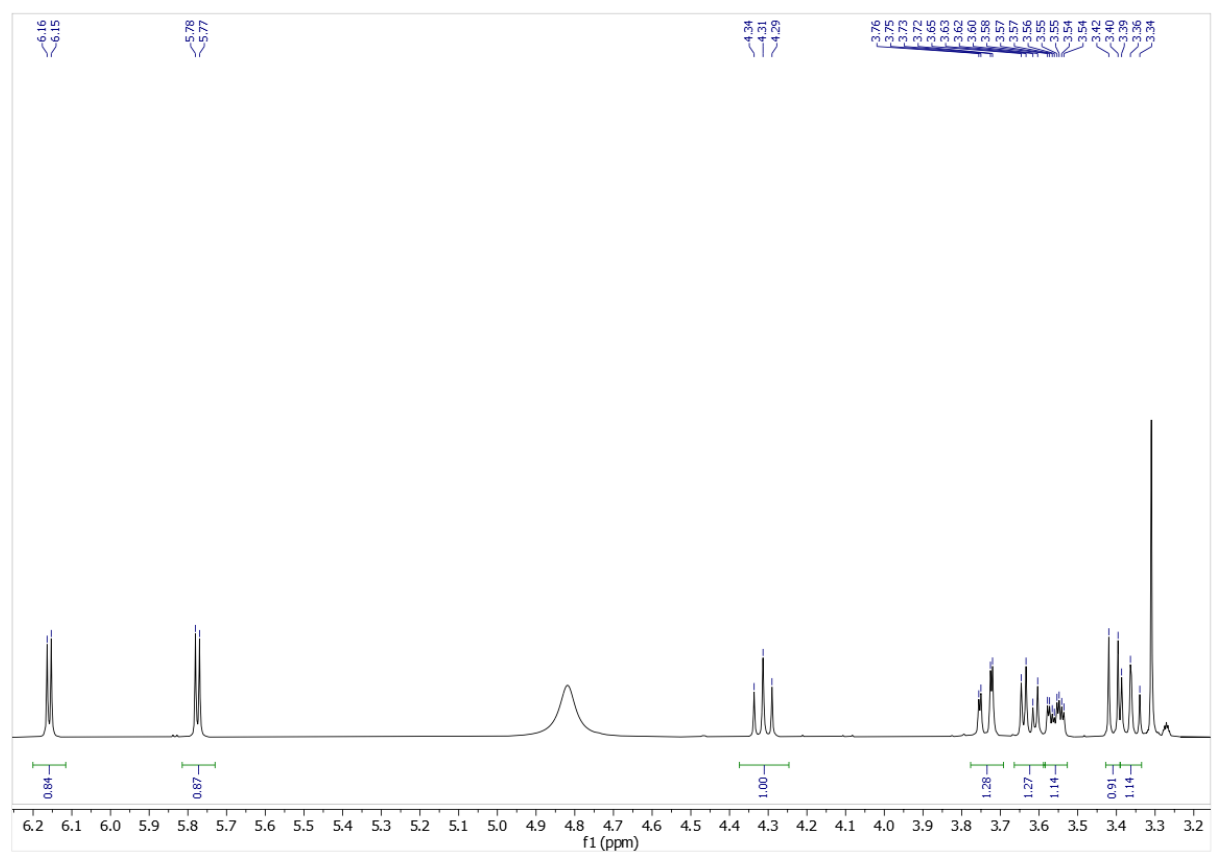
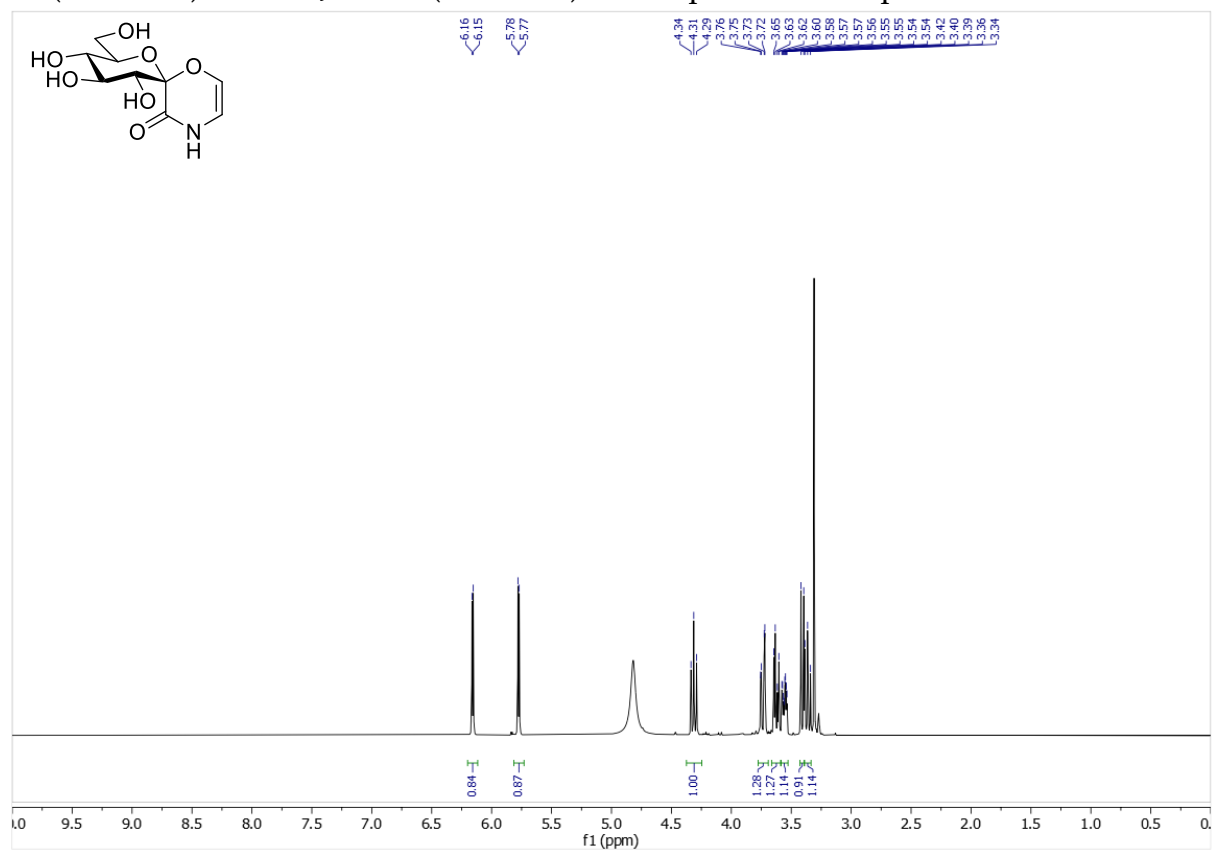


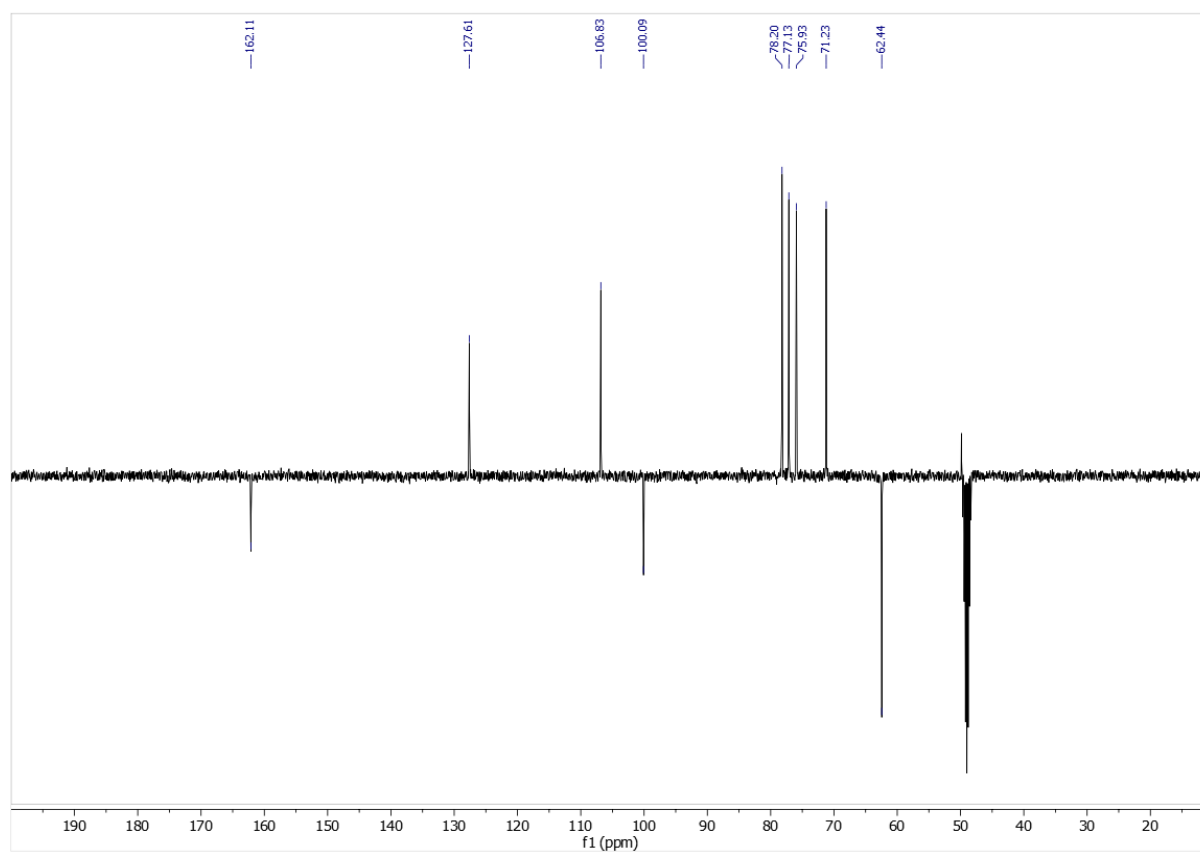
^1H (400 MHz) and ^{13}C J-MOD (100 MHz) NMR spectra of compound **39** in CD_3OD



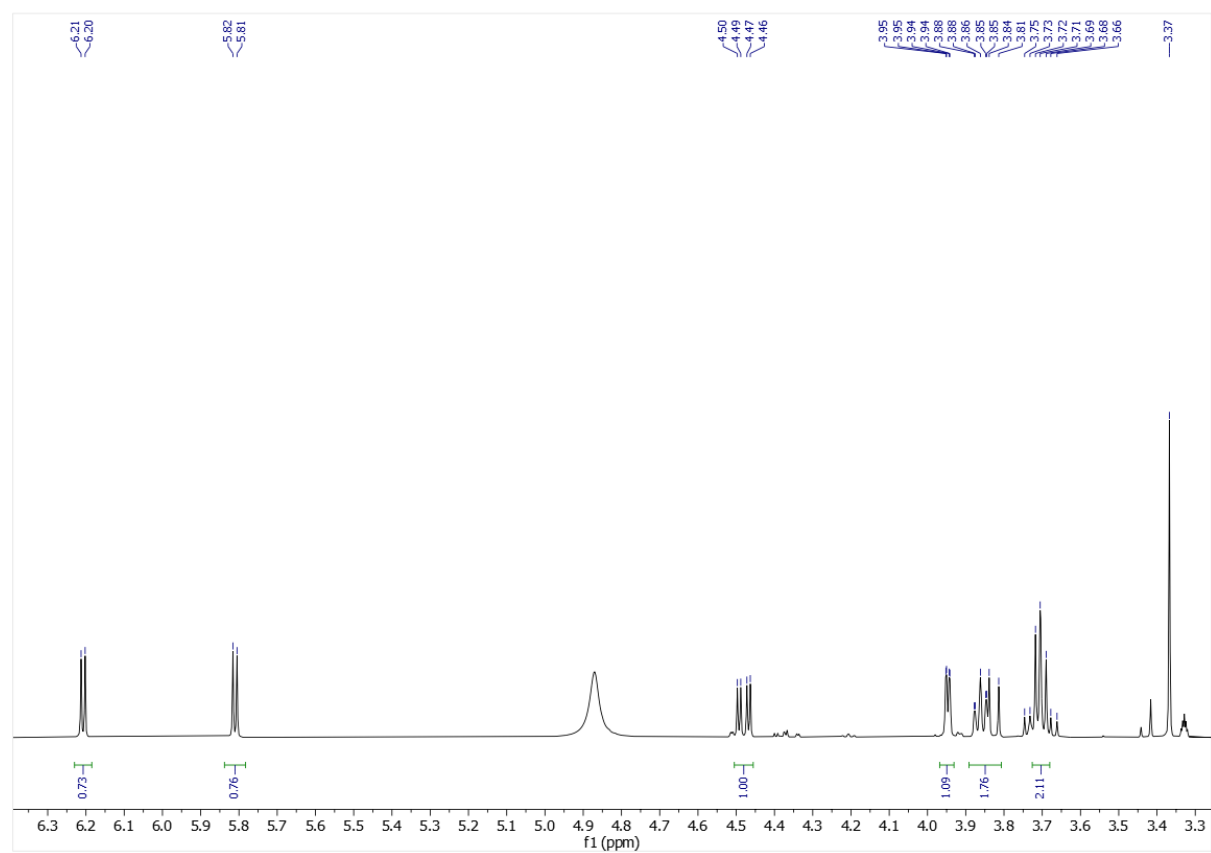
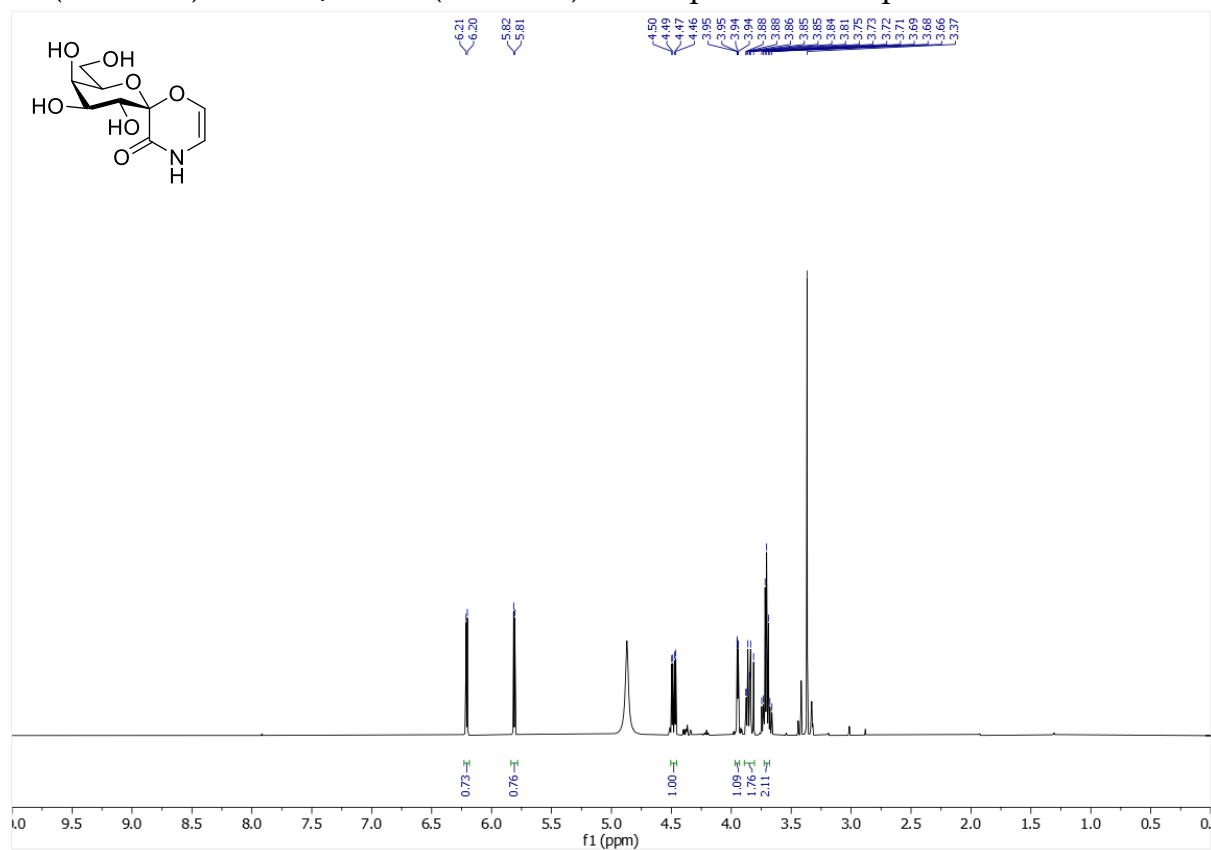


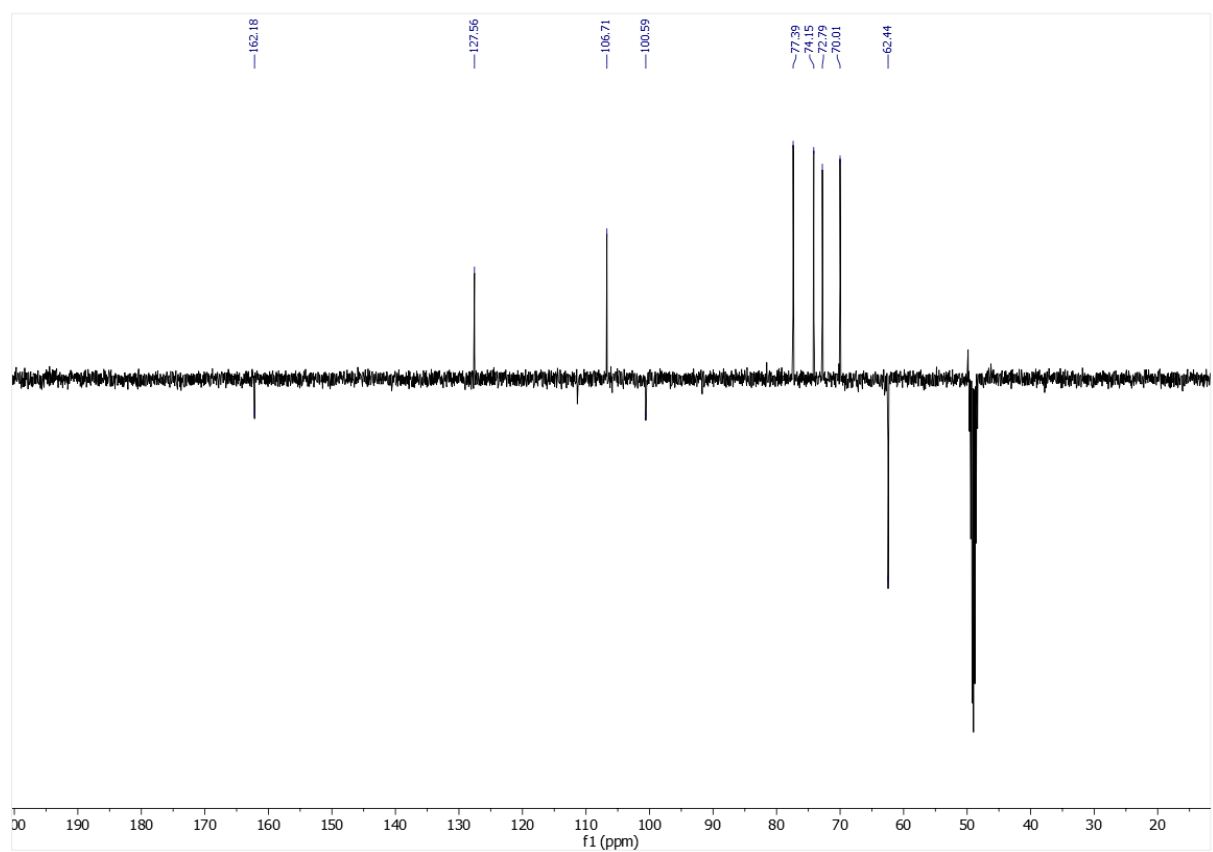
^1H (400 MHz) and ^{13}C J-MOD (100 MHz) NMR spectra of compound **40** in CD_3OD





^1H (400 MHz) and ^{13}C J-MOD (100 MHz) NMR spectra of compound **41** in CD_3OD





^1H (400 MHz in CD_3OD) and ^{13}C J-MOD (100 MHz in DMSO-d_6) NMR spectra of compound **42**

