Midterm Exam 1

Please do not open or sign this packet until you are instructed to do so.

Please write all of your answers for this exam in this exam packet. Although you may use as many blue books for scratch work as you would like, the blue books will not be collected at the end of the exam or graded. Answer each question in the space provided if you can, but feel free to continue your answer on the back of the page if you need more room. (Please write a note by your answer pointing us to the continuation if you do this.) Feel free to remove the corner staple if this helps you analyze the spectra; you will have the opportunity to re-staple your exam at the end. The exam in this packet is designed to take 1 hour to complete. You will be given 2 hours total to finish the test.

This exam contains two problems, which are split into parts. Many of these parts can be answered independently. *Do not get stuck* on one part and then assume that you will be unable to answer the rest of the question—move on. In addition, partial credit will be given for incorrect but still plausible answers, so *guess* on problems you cannot answer perfectly.

At the end of the 2 hour exam period you will be asked to return your exam to the proctor. (You may, of course, also turn the packet in earlier if you choose.) You are allowed to use any materials you brought with you before the exam. However, we ask that you not bring any materials in or out of the room while you are taking the exam. Please do not take any part of the exam packet with you when you are done; everything will be returned to you after the exams are graded.

This packet should contain 24 pages, including this one. Please check to make sure that your packet contains 24 pages before beginning your exam.

Name: _____

Signature: _____

1. During a test oxidation reaction on linalool, Brian Eklov (Hoye Group) isolated the two diastereomeric, substituted tetrahydrofurans **1** and **2** and separated them by column chromatography. The ^{1}H NMR spectra of the two pure diastereomers were remarkably similar, and Brian found it impossible to distinguish relative stereochemistry at carbons 3 and 6 based on simple ^{1}H NMR analysis alone. In order to assign structures to **1** and **2**, he performed NOE irradiation experiments on each molecule.
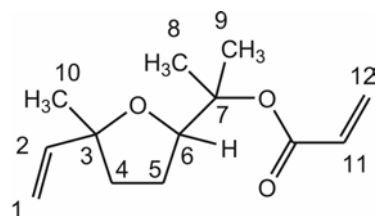

1 and **2**
(stereochemistry not assigned)
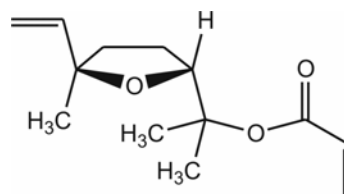
or
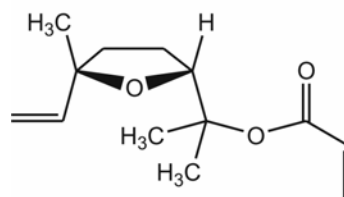
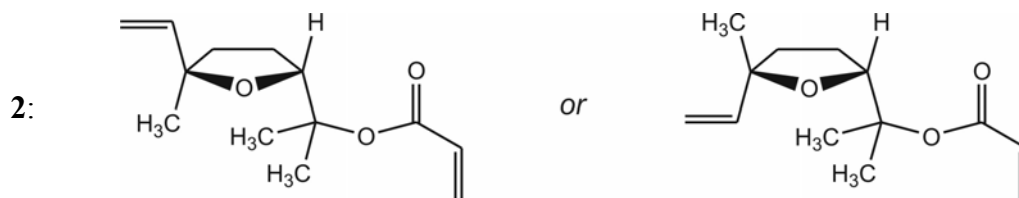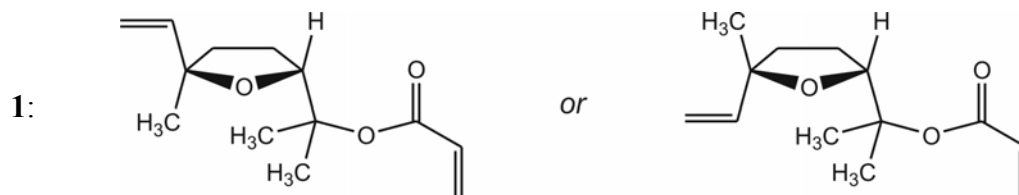| Page	Description
5	^{1}H NMR, **1**, 500 MHz, CDCl$_3$
6-8	Close-ups of page 5
9	[1]H NOE, **1**, irradiated at $\delta = 4.1$ ppm
10	^{1}H NMR, **2**, 500 MHz, CDCl$_3$
11	[1]H NOE, **2**, irradiated at $\delta = 4.1$ ppm

a. (21 pts) In the chart on the next page, assign chemical shifts, mulitplicities and coupling constants to some of the protons in **1**. Chemical shifts should be accurate within 0.01 ppm, and coupling constants should be accurate within 1 Hz.

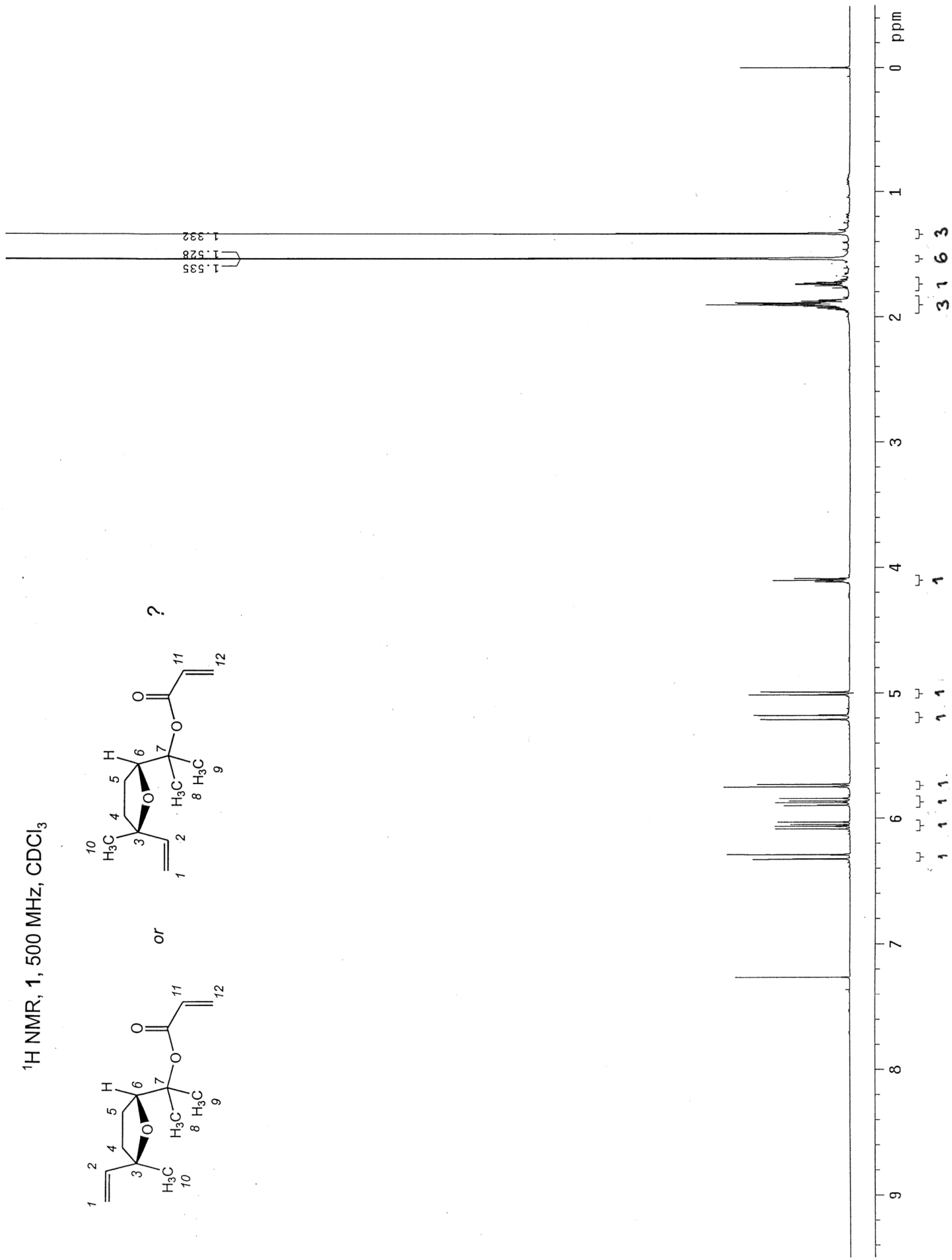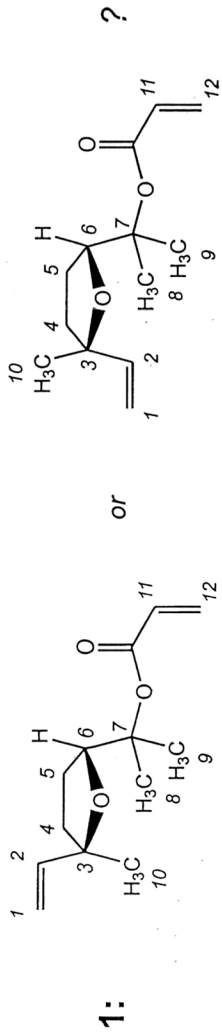Format for labeling double bonds:

R ＼ ＿ ／ H
Htrans ／ ＼ Hcis
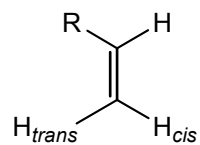
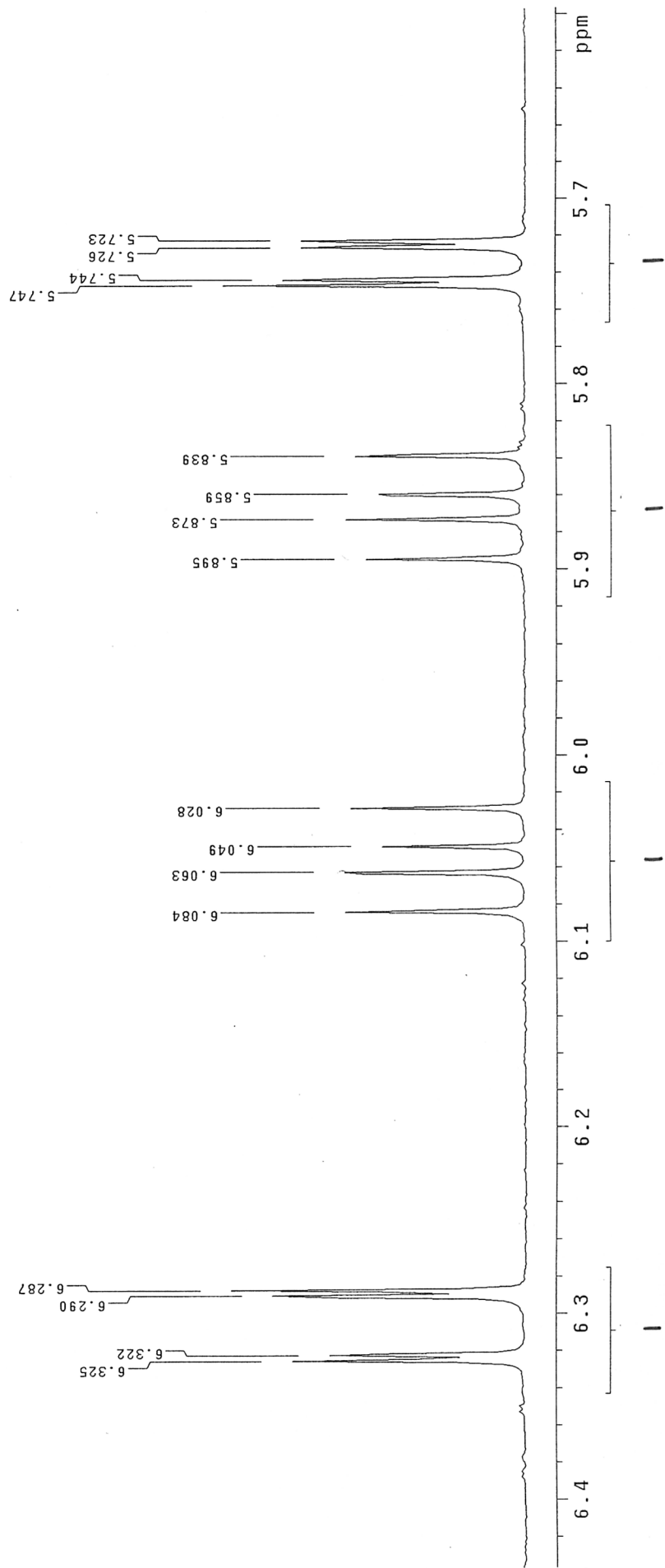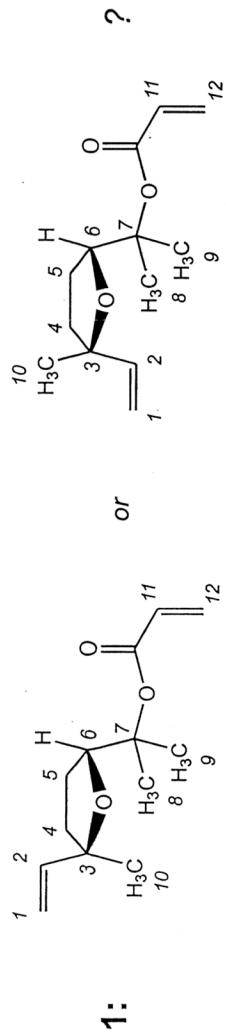| Proton	Chemical shift (δ, ppm)	Multiplicity (e.g., "dd")	Coupling partners, constants (e.g., "$J(H_4,H_5) = X$ Hz")
$H_{1,cis}$			
$H_{1,trans}$			
H_2			
H_6			
H_{11}			
$H_{12,cis}$			
$H_{12,trans}$			

b. (14 pts) On the structures below, indicate which diastereomer represents which molecule for **1** and **2** by drawing all of the NOE interactions observed for the correct structure with curved arrows. (If you like, draw an X through the incorrect diastereomeric structures.)
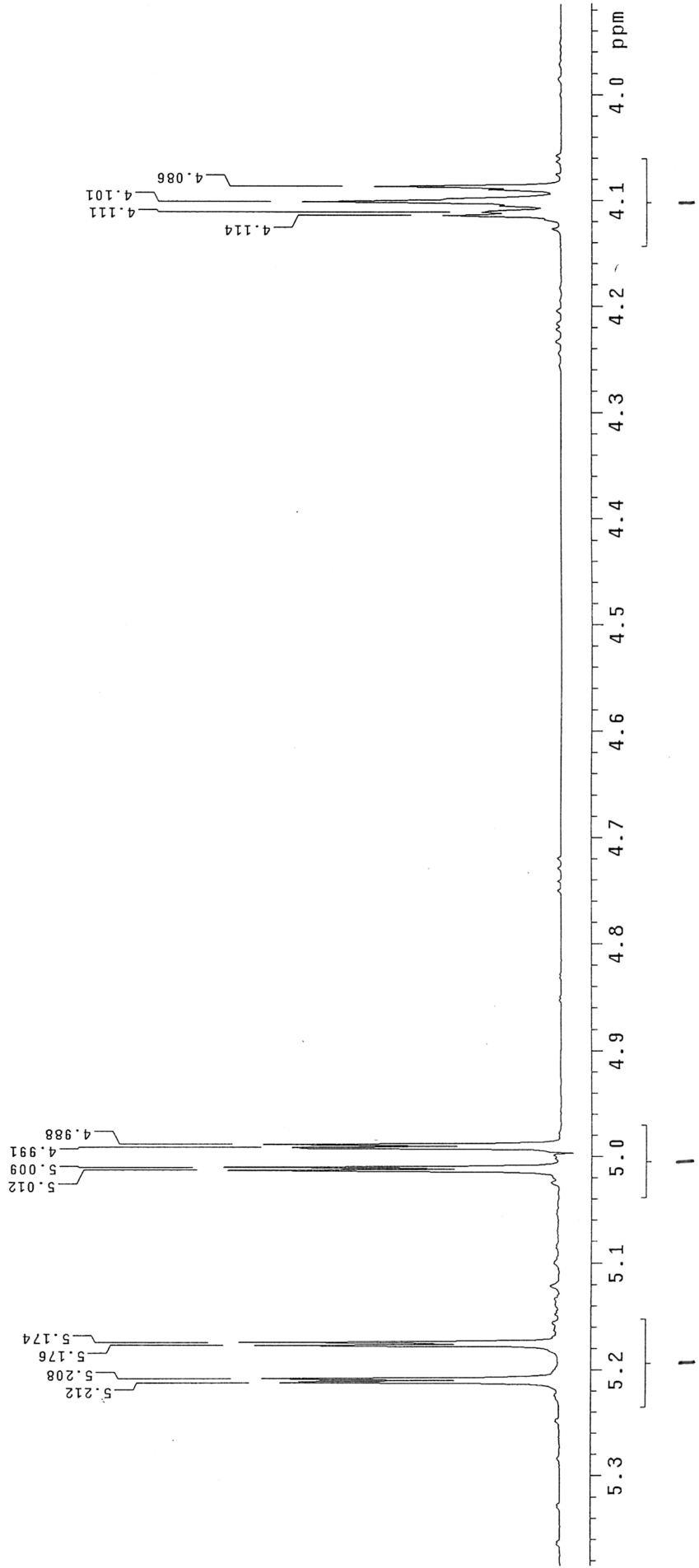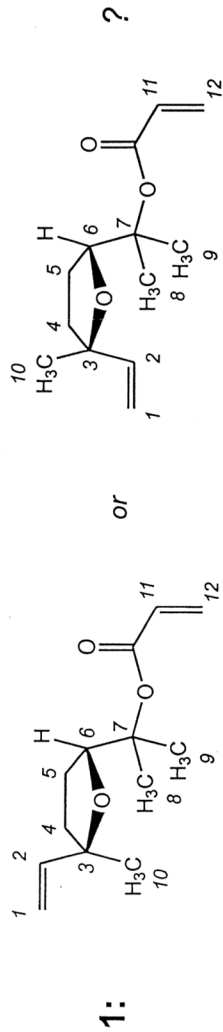
1:   *or*

2:   *or*
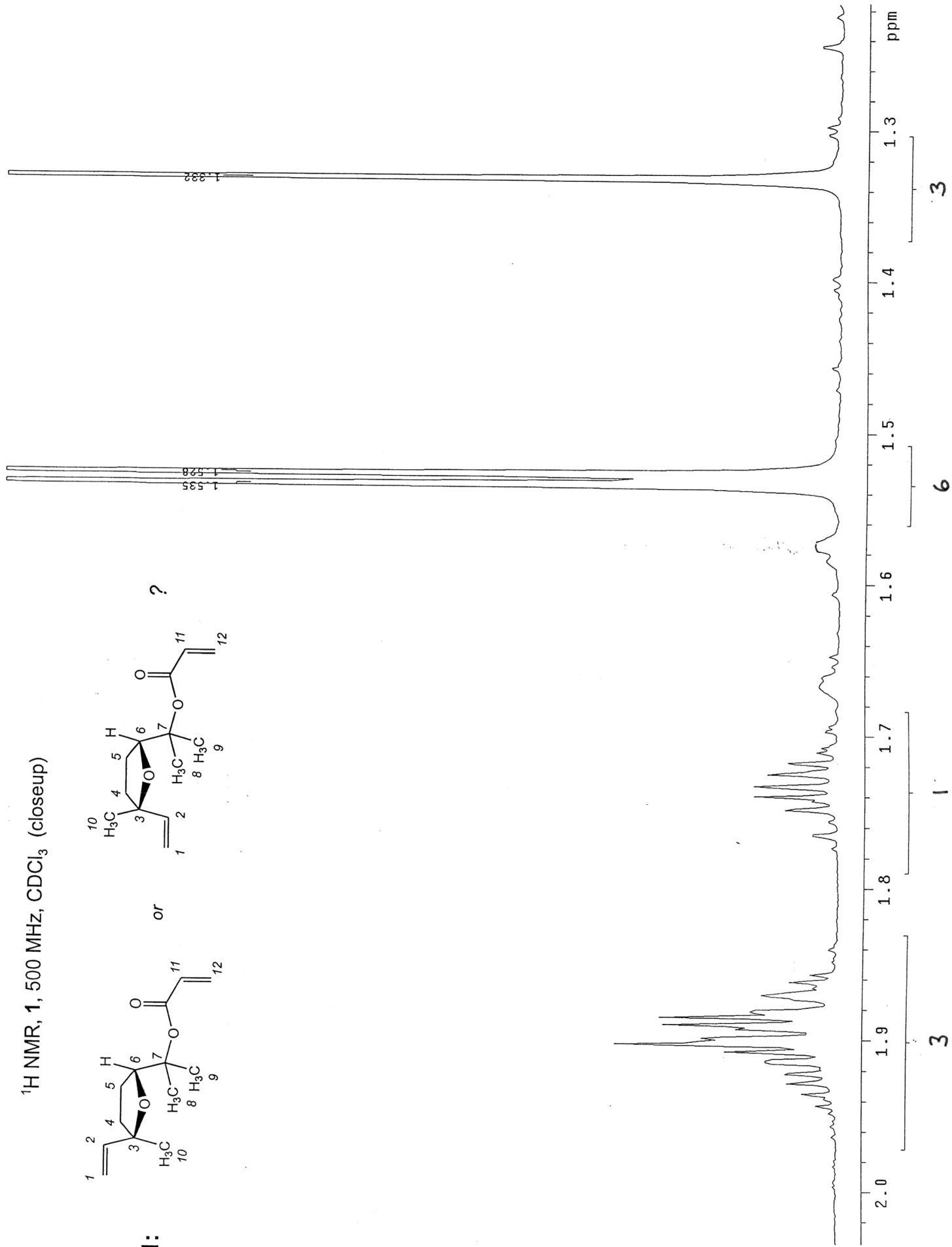
^{1}H NMR, **1**, 500 MHz, CDCl$_3$

1:

or

?

1.535
1.528
1.332

ppm
0   1   2   3   4   5   6   7   8   9

3 1 6 3

Structure labels: H$_3$C (10), 1, 2, 3, 4, 5, 6 H, 7, O, O, H$_3$C (8), H$_3$C (9), 11, 12

3   1   6   3   1   1   1   1   1   1   1   1

¹H NMR, **1**, 500 MHz, CDCl₃ (closeup)

1:

or

?

Peak labels (ppm):
- 5.723
- 5.726
- 5.744
- 5.747
- 5.839
- 5.859
- 5.873
- 5.895
- 6.028
- 6.049
- 6.063
- 6.084
- 6.287
- 6.290
- 6.322
- 6.325

x-axis: 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4 ppm

¹H NMR, **1**, 500 MHz, CDCl$_3$ (closeup)

1:

or

?

4.086
4.101
4.111
4.114

4.988
4.991
5.009
5.012

5.174
5.176
5.208
5.212

5.3   5.2   5.1   5.0   4.9   4.8   4.7   4.6   4.5   4.4   4.3   4.2   4.1   4.0   ppm

¹H NMR, **1**, 500 MHz, CDCl₃ (closeup)

1:

or

?

8

¹H NOE, 1, irradiated at δ = 4.1 ppm

1:

^{1}H NMR, **2**, 500 MHz, CDCl$_3$

2:

or

?

0.000

1.311
1.530
1.539
1.548

7.262

31 6 3

ppm

0 1 2 3 4 5 6 7 8 9

^{1}H NOE, **2**, irradiated at δ = 4.1 ppm

2:

or

?
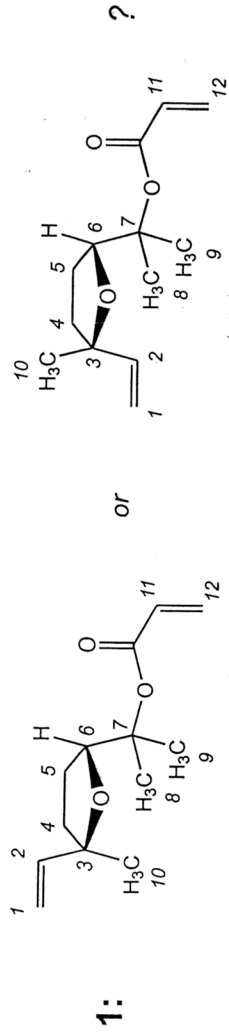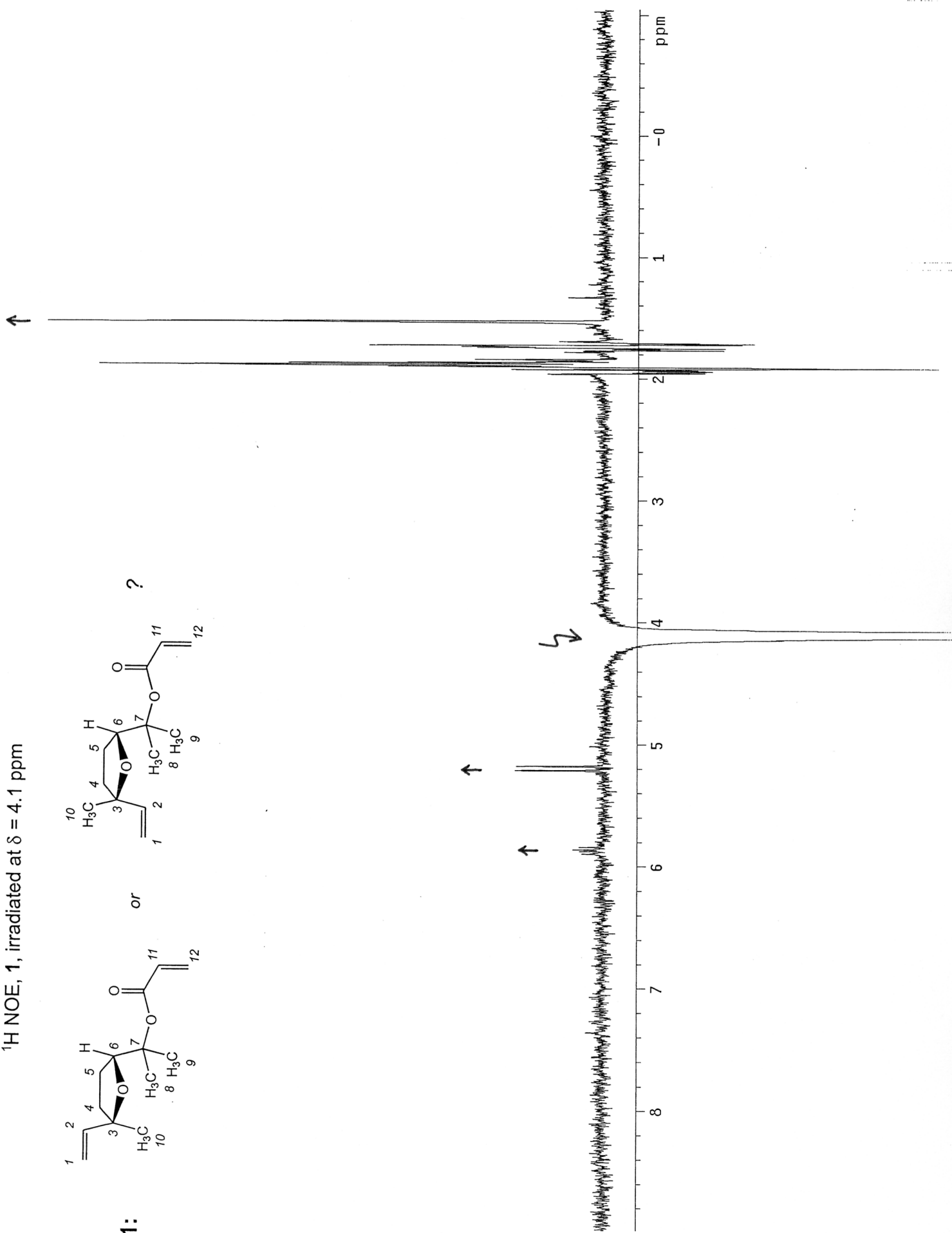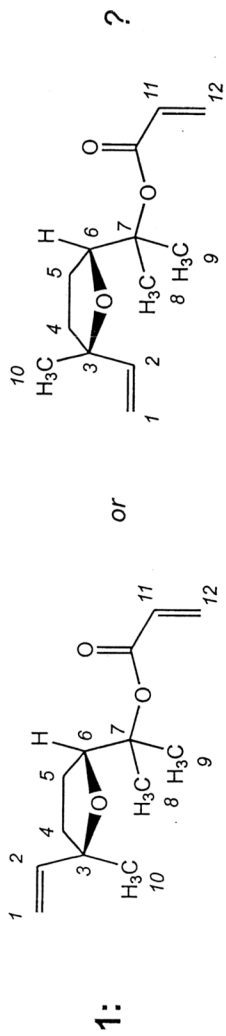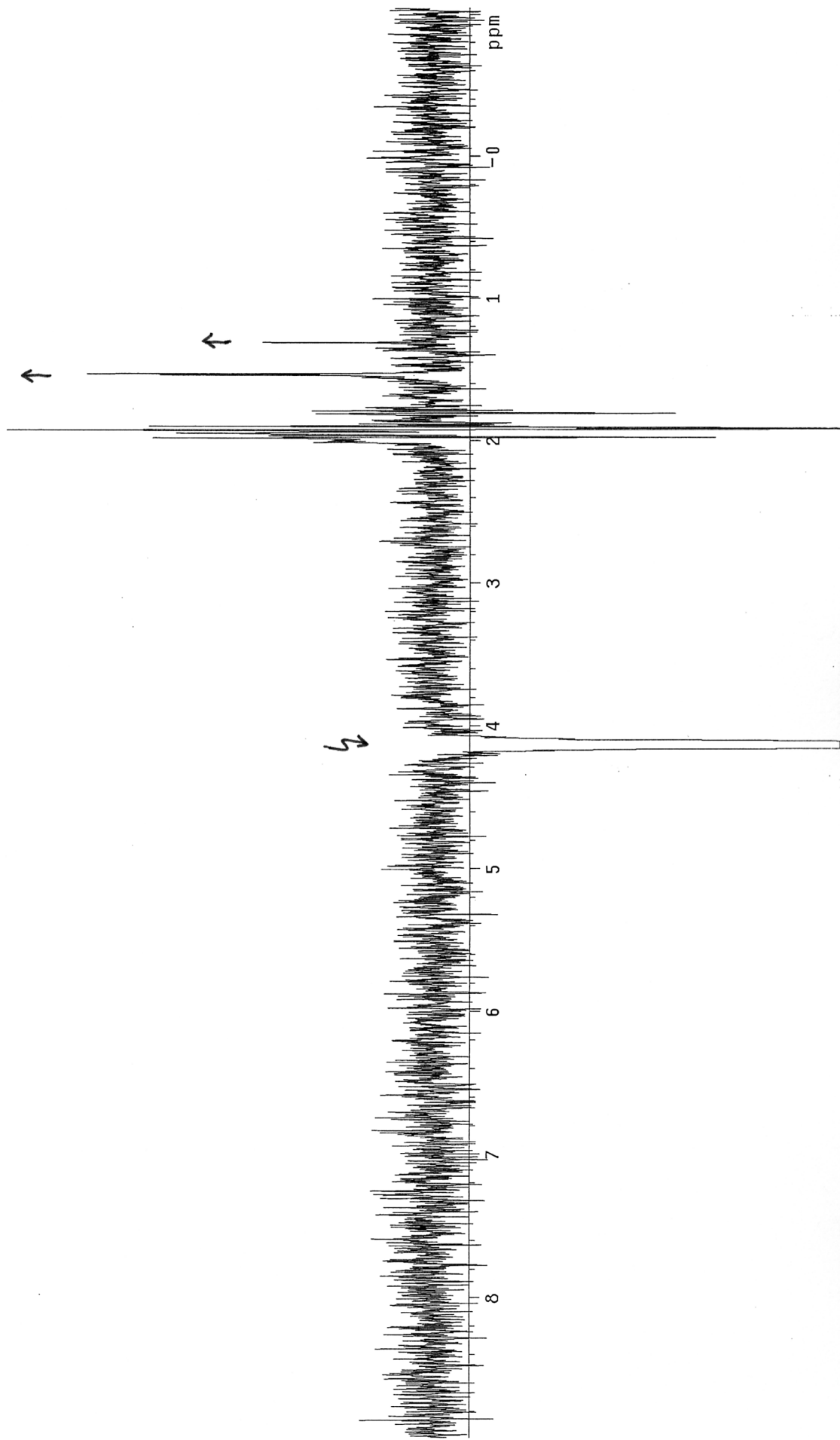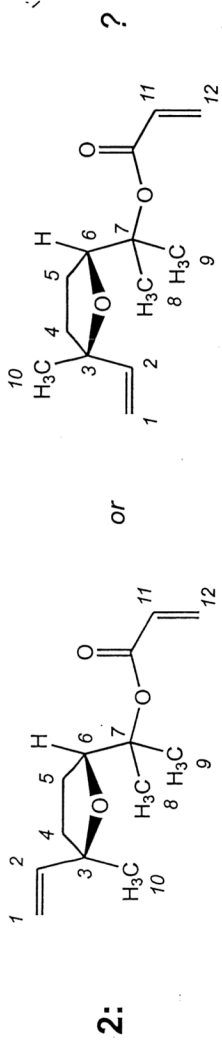
2. Chris Jeffrey, your intrepid TA, attempted a methallylation of **3** with the intention of synthesizing the methallyl ether **4**. Although the methallyl chloride reagent was consumed in the reaction, the primary product isolated was not **4**. In this problem, you will determine the structure of the unknown product **5**.
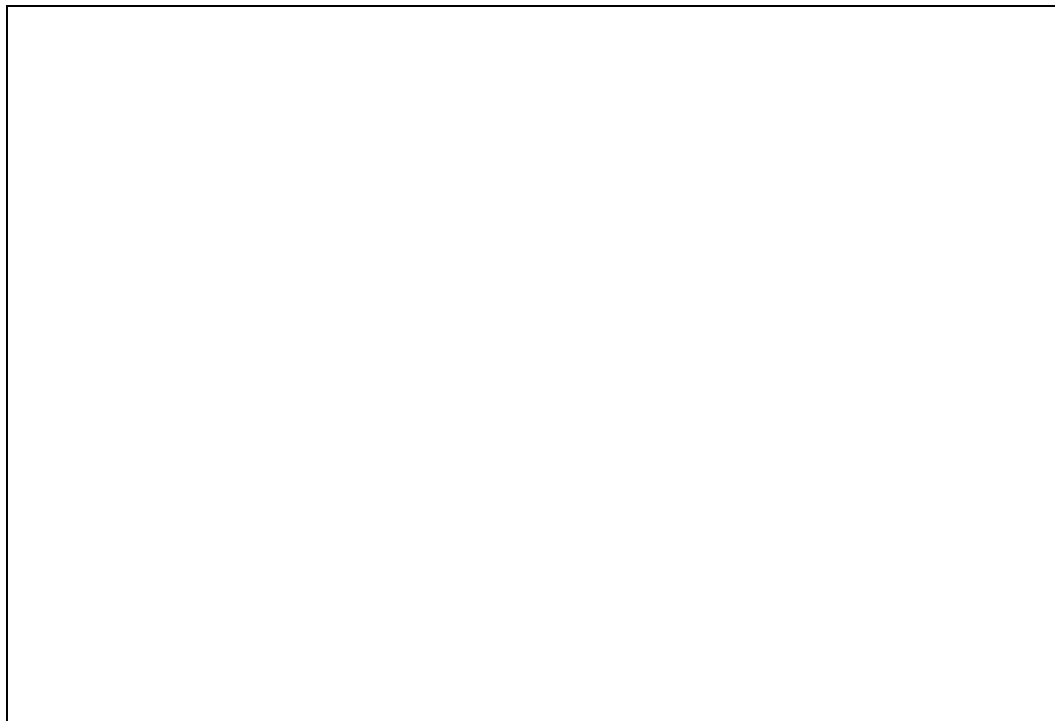

4 (not observed)
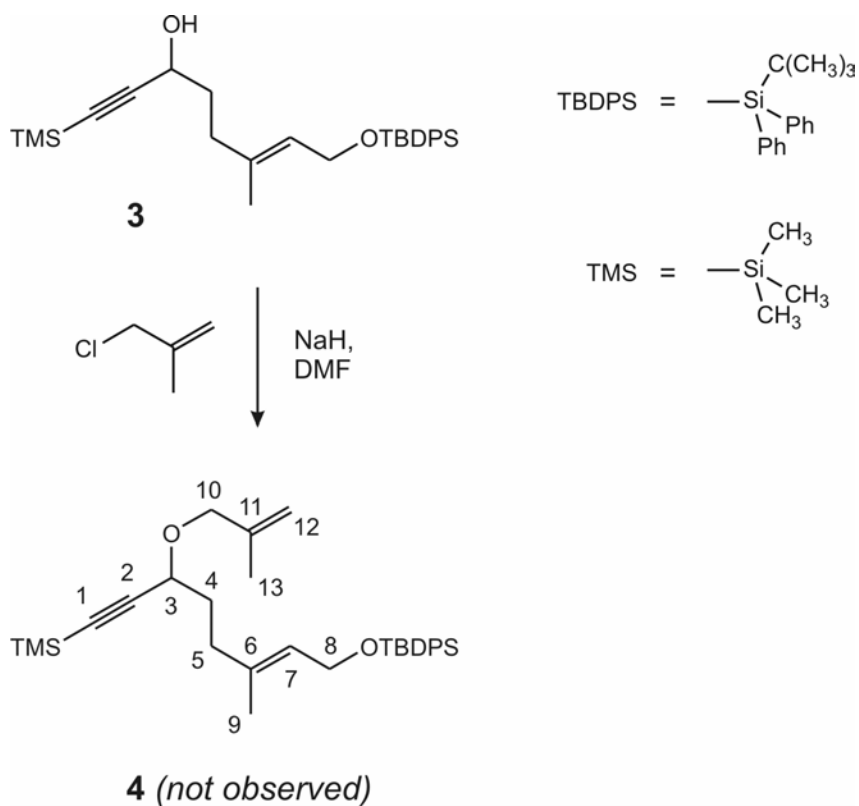
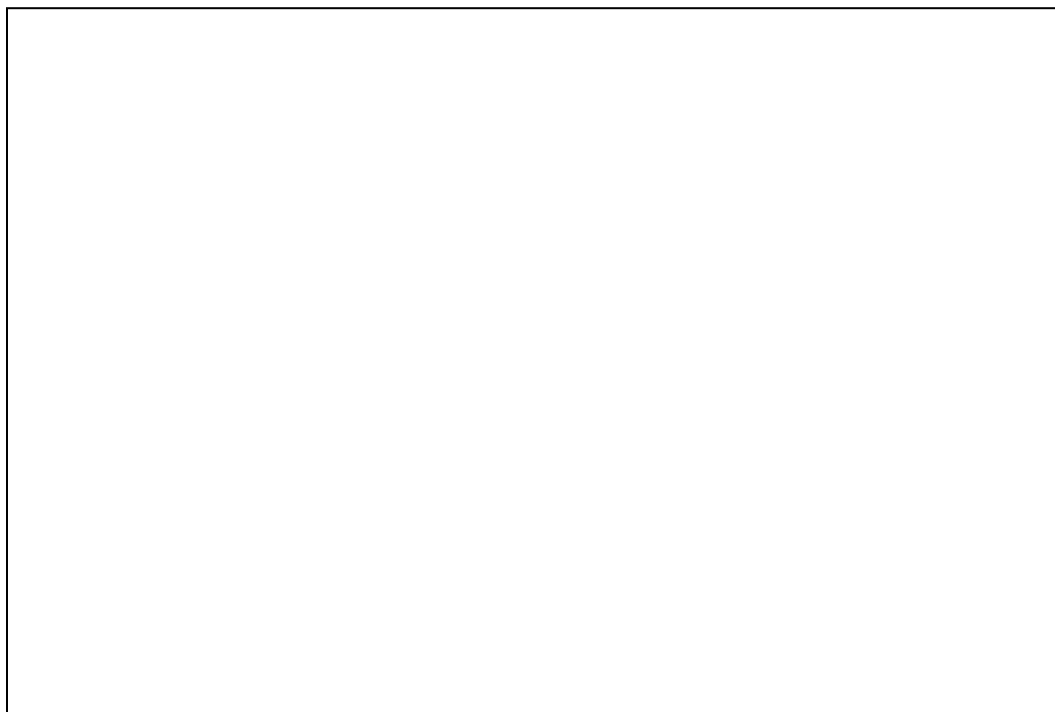| Page	Description
17	^{1}H NMR, **3**, 500 MHz, CDCl$_3$
18-19	Close-ups of page 17
20	^{1}H NMR, **5**, 500 MHz, CDCl$_3$
21-22	Close-ups of page 20
23	^{13}C NMR, **5**, 125 MHz, CDCl$_3$
24	DEPT-135/DEPT-90, **5**, 125 MHz, CDCl$_3$

a. (16 pts) Based on differences between the ^{1}H NMR spectra of **3** and **5**, Chris concluded that methallyl chloride had added to the alcohol group as planned, but that something about the rest of the molecule had changed. For each of the resonances listed on the chart below, either assign the resonances of **5** to a (numbered) proton that corresponds to one in the proposed structure **4**, or check the box that indicates that the proton does not correspond to any proton in structure **4**.

Chemical shift (δ, ppm), **5**	Assignment ("H$_N$")	OR	Does not correspond to proton in **4**
5.42		OR	
5.00		OR	
4.91		OR	
4.22		OR	
4.14		OR	
4.02		OR	
3.89		OR	
2.43		OR	

b. (11 pts) The splitting pattern of one coupled pair of multiplets in the table above is inconsistent with structure **4**. Which multiplets? How are they inconsistent?

c. (11 pts) Based on ^{1}H NMR data, propose a structure for **5**. Show how your proposed structure accounts for the splitting pattern and coupling constant(s) you described above.

d. (15 pts) The ^{13}C NMR of **5** has three groups of peaks: 110-145 ppm, 60-85 ppm, and 10-40 ppm. Does the number of peaks in each group correspond to the number of equivalent carbons in your proposed structure for **5**? In the chart below, draw your proposed structure and circle the carbons that you would expect to observe in each chemical shift range. Indicate where multiple carbons are equivalent.

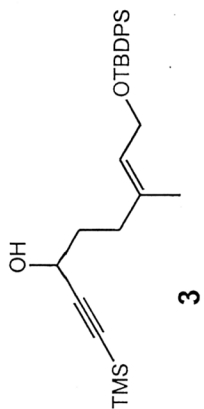| Chemical shift range (ppm)	Expected resonances from proposed structure of **5** (circle carbons)
110-145 number of peaks: 	 number of resonances expected:
60-85 number of peaks: 	 number of resonances expected:
10-40 number of peaks: 	 number of resonances expected:

e. (12 pts) One of the resonances in the ^{13}C DEPT spectra of **5** is inconsistent with the number of protons attached to the corresponding carbon. Which resonance? Which carbon in the structure of **5** does this resonance correspond to? Why is the DEPT intensity incorrect for this carbon?
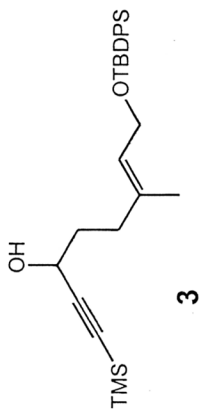
$\delta =$ [ ]
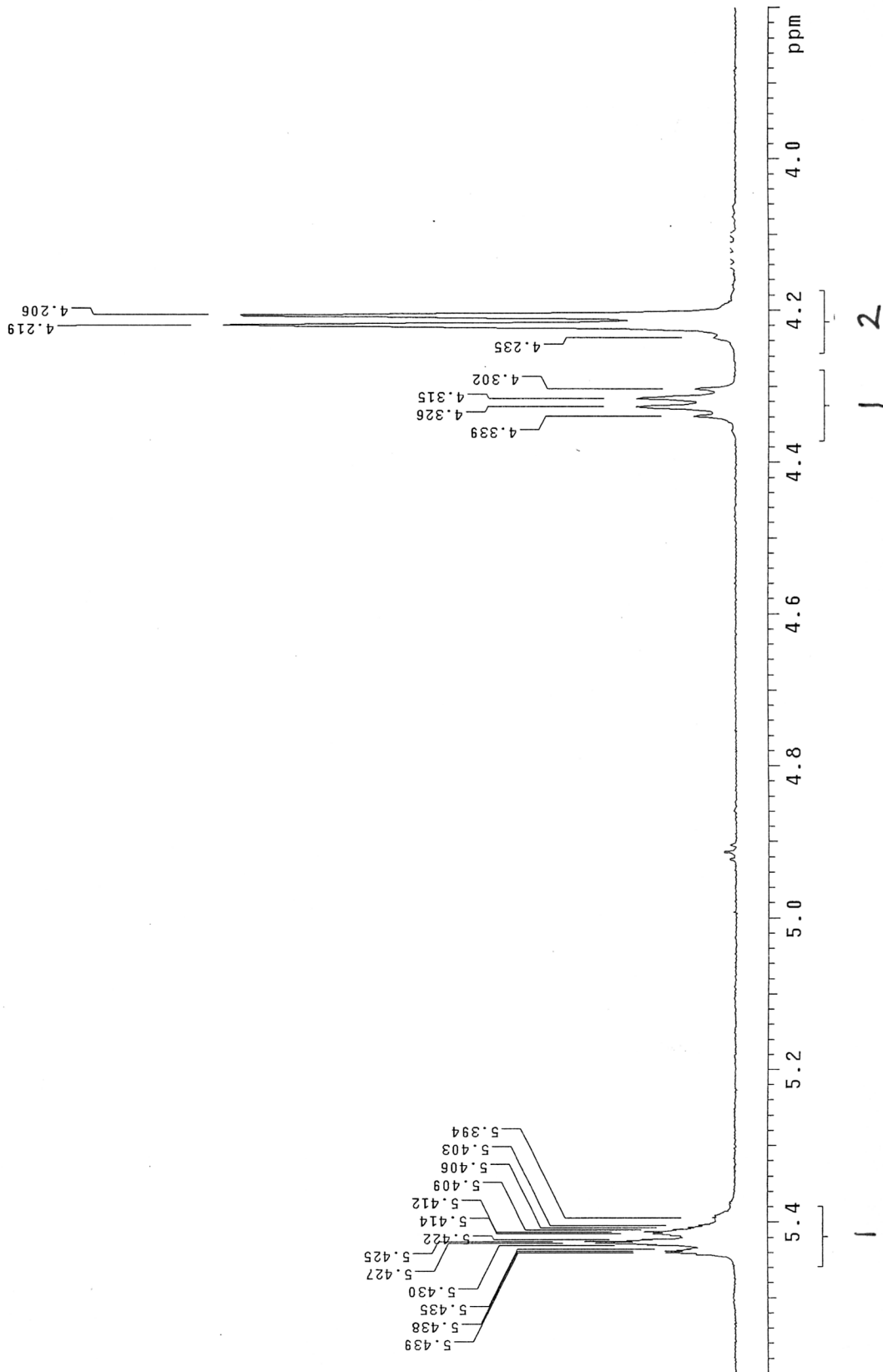
which carbon? (draw as substructure)
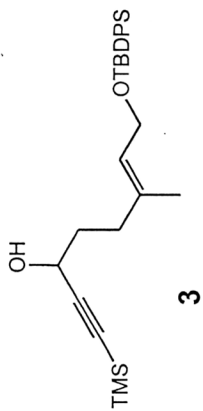
why?

¹H NMR, 3, 500 MHz, CDCl₃
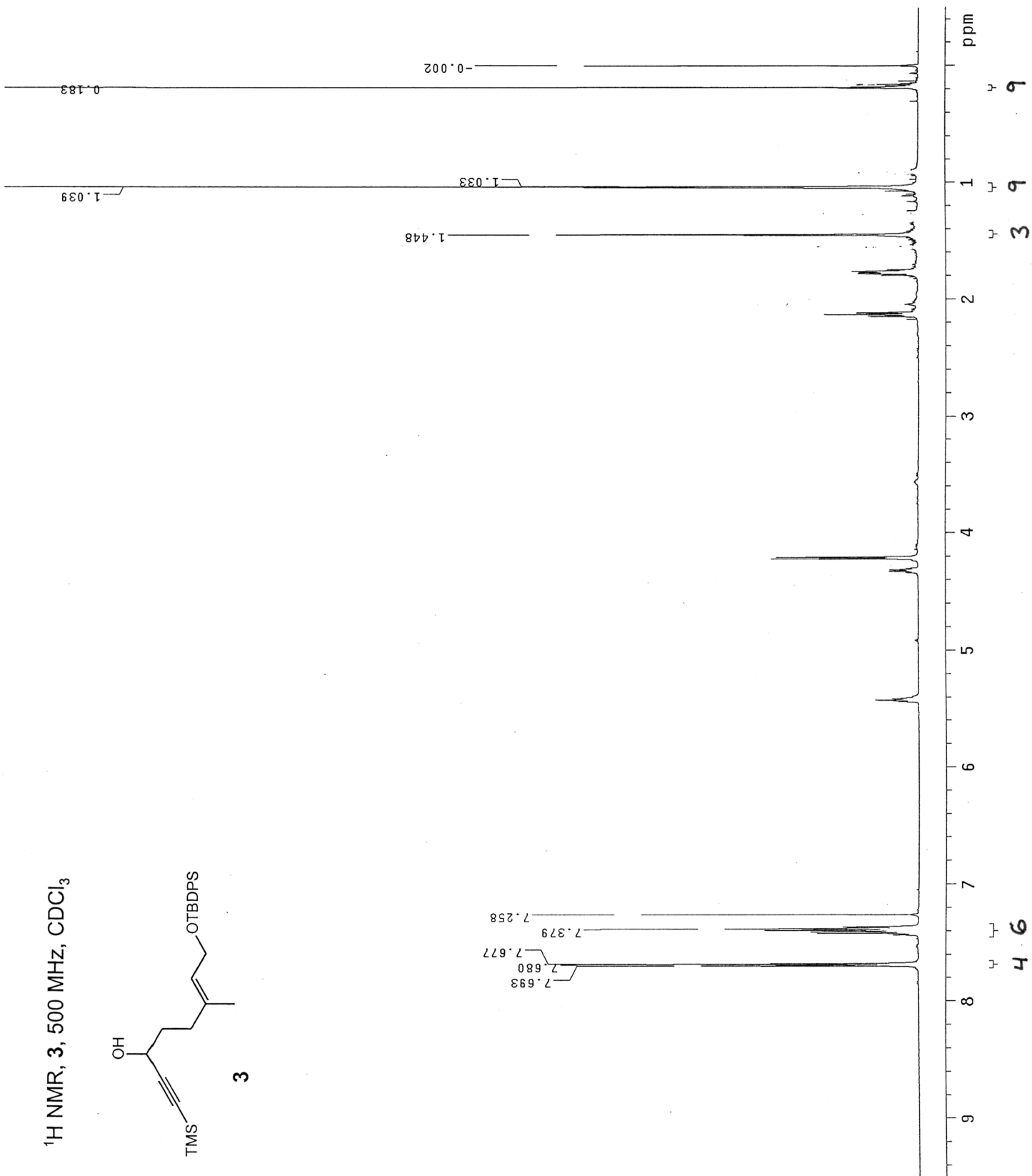
3

Structure: TMS–C≡C–CH(OH)–CH₂–CH₂–C(CH₃)=CH–CH₂–OTBDPS

Peaks:
- 7.693
- 7.680
- 7.677
- 7.379
- 7.258
- 1.448
- 1.039
- 1.033
- 0.183
- -0.002

^{1}H NMR, 3, 500 MHz, CDCl$_3$ (closeup)

3

TMS

HO

OTBDPS

5.394
5.403
5.406
5.409
5.412
5.414
5.422
5.425
5.427
5.430
5.435
5.438
5.439

4.206
4.219
4.235
4.302
4.315
4.326
4.339

ppm

4.0
4.2
4.4
4.6
4.8
5.0
5.2
5.4

1
2
1

^{1}H NMR, 3, 500 MHz, CDCl$_3$ (closeup)

Structure 3: TMS–C≡C–CH(OH)–CH$_2$–CH$_2$–C(CH$_3$)=CH–CH$_2$–OTBDPS

Peak labels: 1.748, 1.754, 1.762, 1.768, 1.771, 1.775, 1.780, 1.782, 1.784, 1.793, 1.798

2.116, 2.131, 2.146

Integration: 2, 2
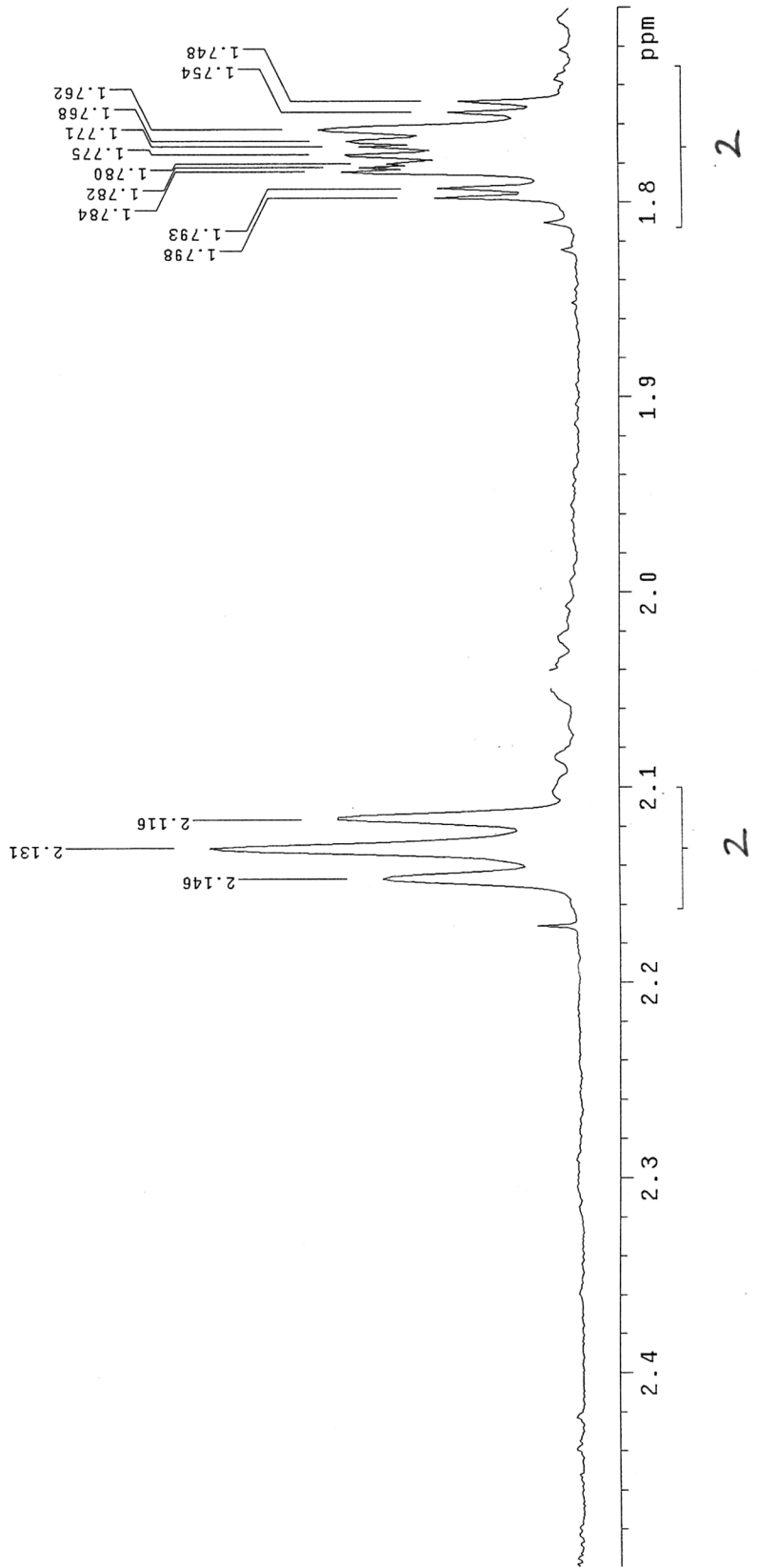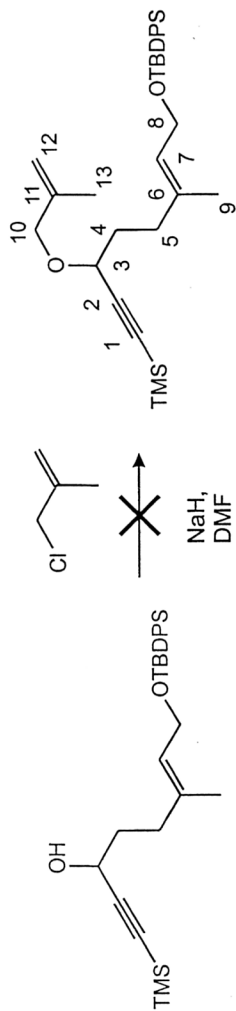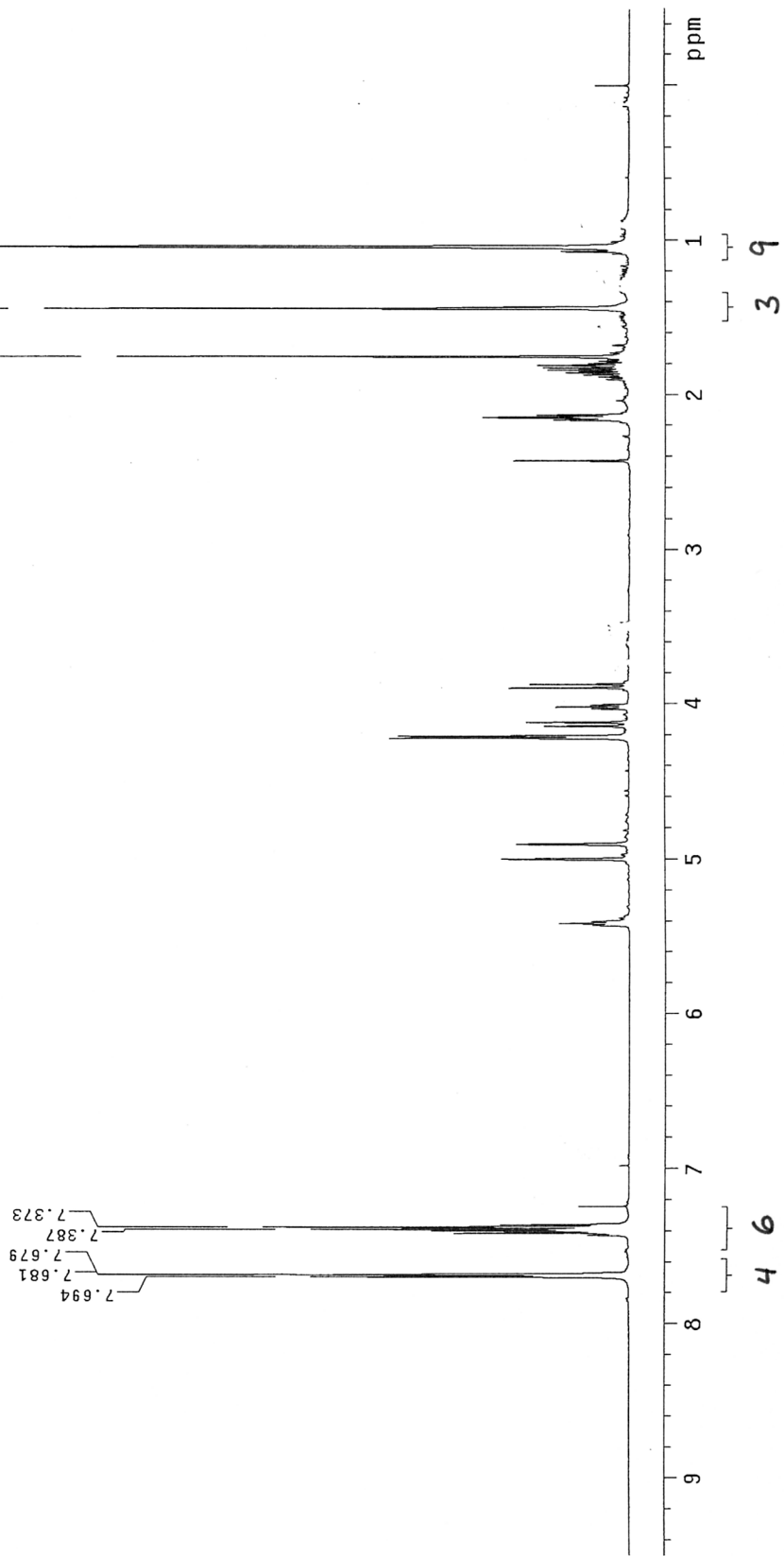
^{1}H NMR, **5**, 500 MHz, CDCl$_3$
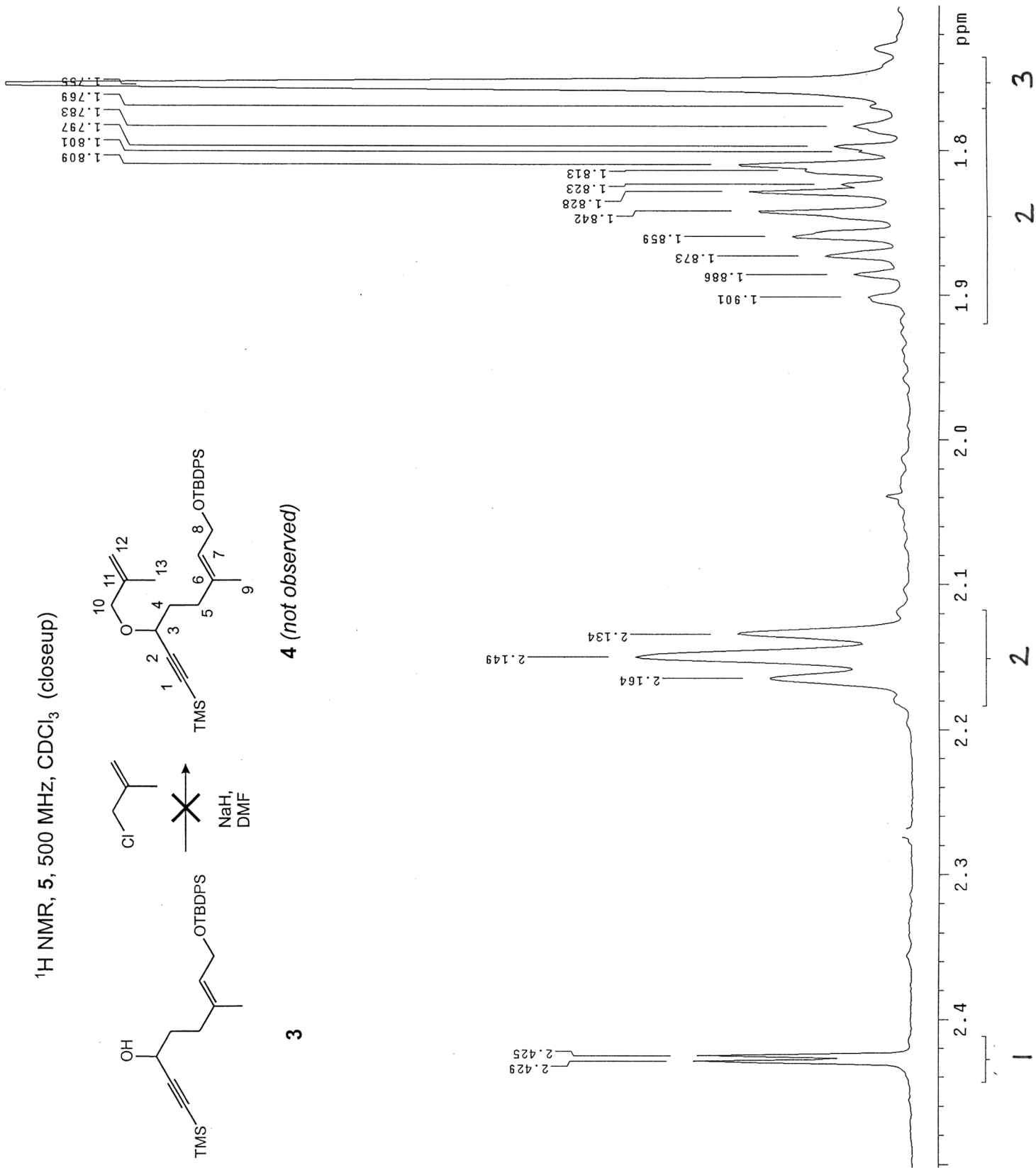

4 (not observed)
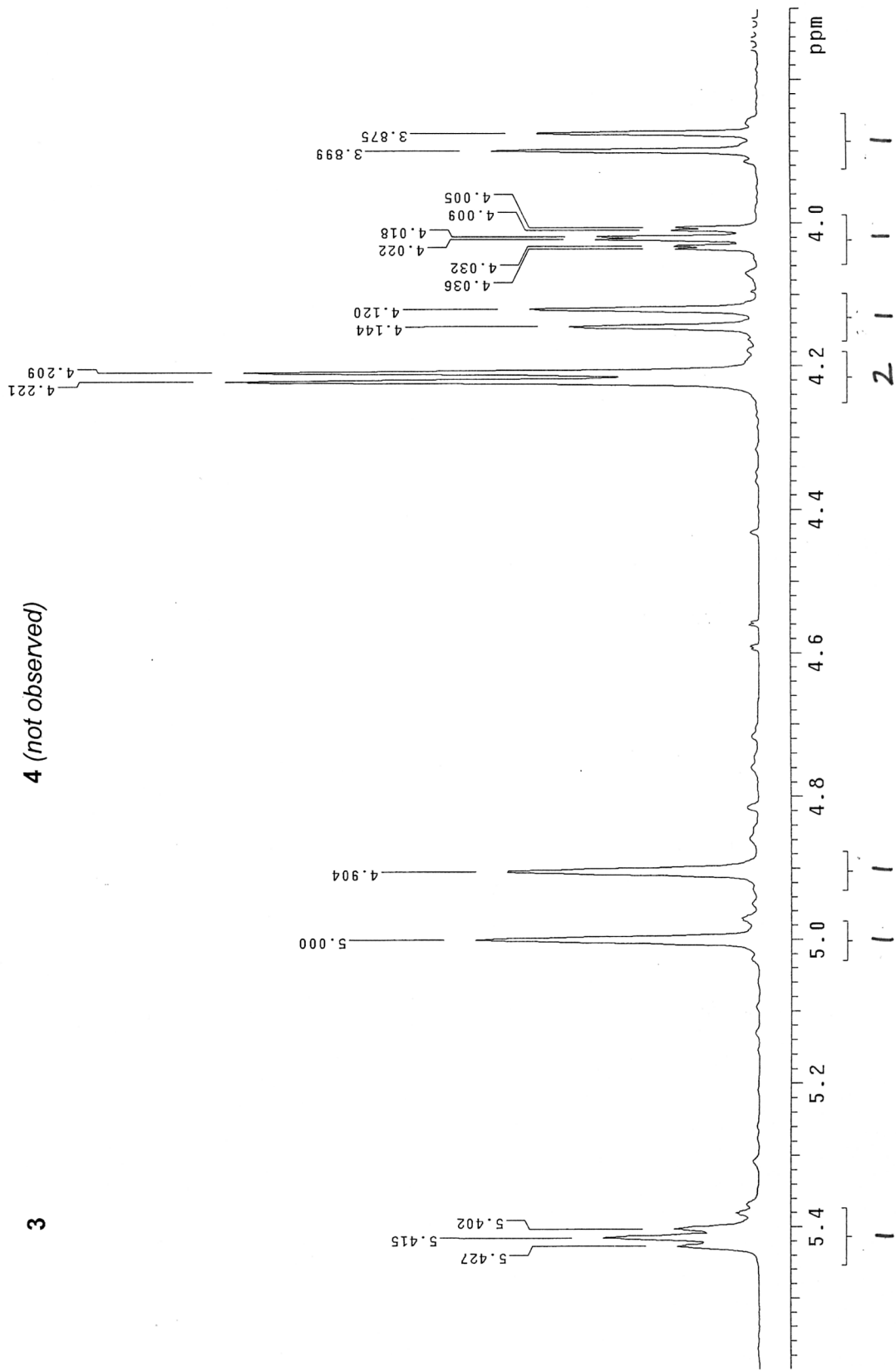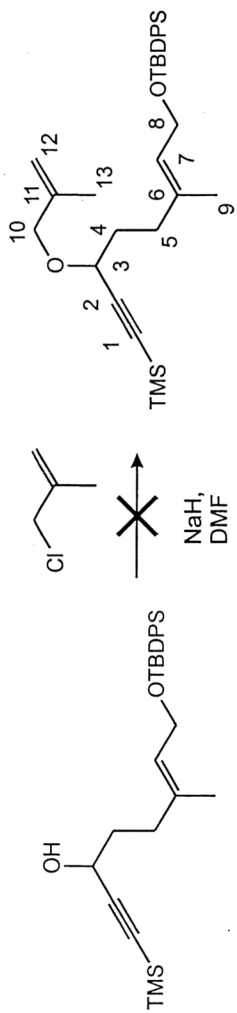
¹H NMR, **5**, 500 MHz, CDCl₃ (closeup)
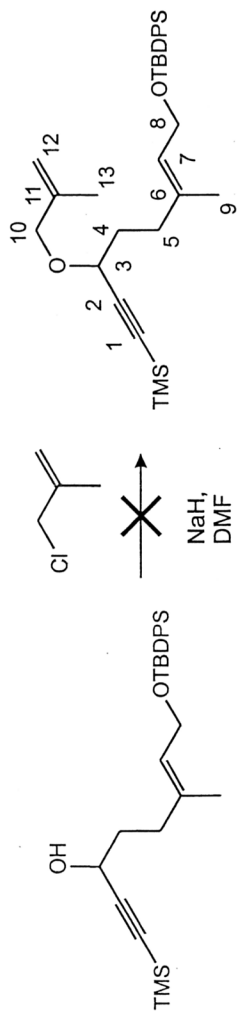
4 (not observed)

3

^{1}H NMR, **5**, 500 MHz, CDCl$_3$ (closeup)

4 (not observed)

3

ppm values:

1.755
1.769
1.783
1.797
1.801
1.809
1.813
1.823
1.828
1.842
1.859
1.873
1.886
1.901
2.134
2.149
2.164
2.425
2.429

^{13}C NMR, **5**, 125 MHz, CDCl$_3$

4 (not observed)

3

NaH,
DMF
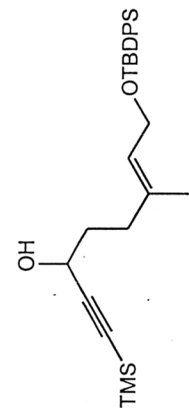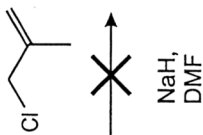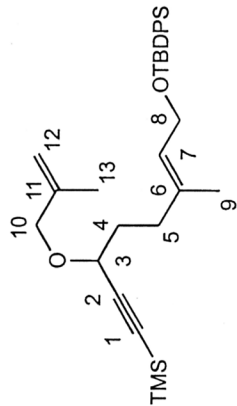
DEPT-135/DEPT-90, **5**, 500 MHz, CDCl$_3$

4 (not observed)