

Midterm Exam 2

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.

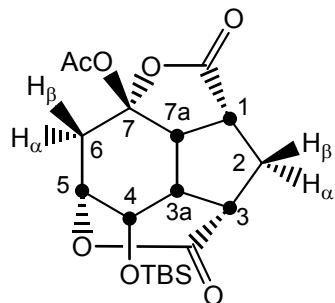
At the end of the 2 hour exam period you will be asked to return your exam to the proctor. (You may, of course, also turn the packet in earlier if you choose.) You are allowed to use any materials you brought with you before the exam. However, we ask that you not bring any materials in or out of the 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 18 pages, including this one. Please check to make sure that your packet contains 18 pages before beginning your exam.

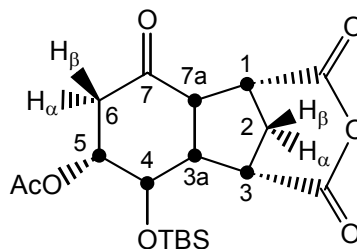
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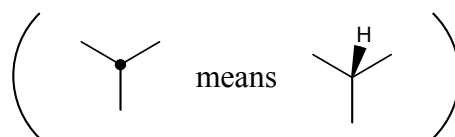
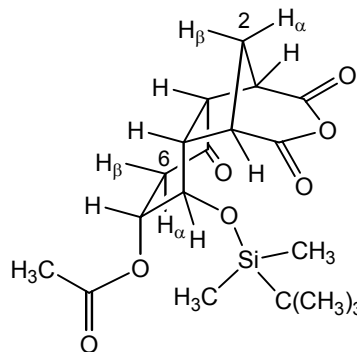
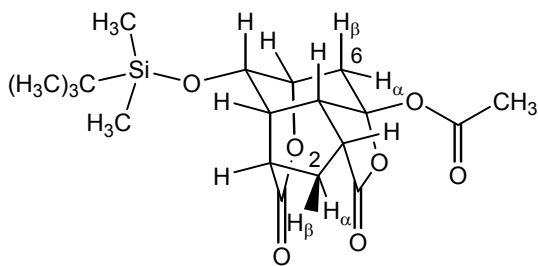
1. Andy Judd (Hoye Group) isolated a compound with chemical formula $C_{19}H_{28}SiO_7$ (formula obtained from high-resolution mass spectrometry), whose possible structure he narrowed down to two structural isomers:



1



2



Andy found it difficult to distinguish between these potential structures because the locations and connectivity for the protons in the two isomers are identical. (The fact that Andy had little material to analyze didn't help.) Andy performed a number of NMR experiments to try to elucidate the structure of his unknown compound.

<u>Page</u>	<u>Description</u>
6	^1H NMR, 1 or 2 , 500 MHz, CDCl_3
7-10	Close-ups of page 5
11	^1H - ^1H COSY, 1 or 2 , 500 MHz, CDCl_3
12	^1H - ^{13}C HMQC, 1 or 2 , 500/125 MHz, CDCl_3

- a. (5 pts) Both structures **1** and **2** have only two $\text{-CH}_2\text{-}$ carbons: C_2 and C_6 . Based on the HMQC data on page 12, what are the ^{13}C chemical shifts of these two carbons (to within 2 ppm)? (For this problem, there is no need to distinguish which carbon is which; simply give two chemical shifts that could be assigned to either carbon.)

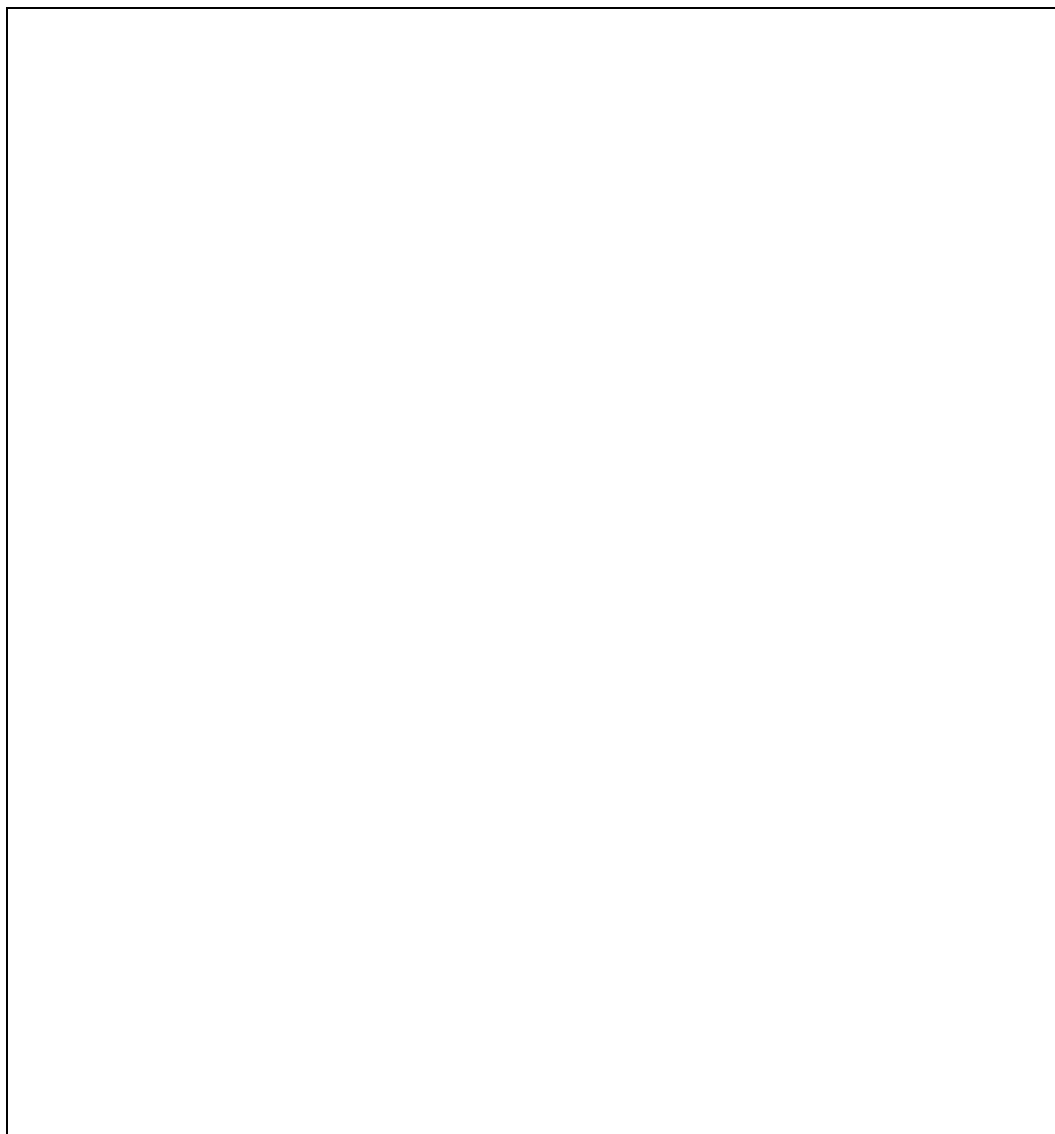
δ (^{13}C , ppm):

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- b. (30 pts) In the chart below, assign chemical shifts to protons in the bicyclic framework of Andy's unknown product. If any of the resonances cannot be precisely assigned (e.g., if a pair of resonances could be assigned to either of a pair of protons), indicate this ambiguity with double-headed arrows in the center of the table. Chemical shifts should be accurate to ± 0.01 ppm.

Proton	Chemical shift (δ , ppm)	Ambiguities? (Could any of these assignments be switched?)	Chemical shift (δ , ppm)	Proton
H_1				H_4
$\text{H}_{2\alpha}$				H_5
$\text{H}_{2\beta}$				$\text{H}_{6\alpha}$
H_3				$\text{H}_{6\beta}$
H_{3a}				H_{7a}

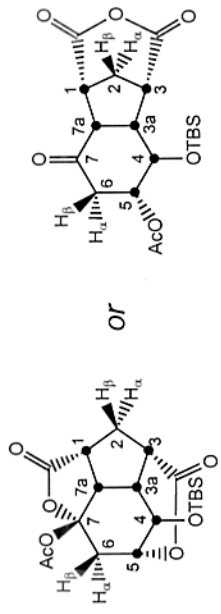
- c. (15 pts) Discuss one piece of evidence from the NMR data—a chemical shift, a coupling interaction, anything—that you feel points towards either structure **1** or **2** for the unknown. Describe not only how the evidence is consistent with the structure you think is correct, but also how the evidence would be different if the other structure were correct. (There are many potential answers to this question. The problem is intended to test your logic, and your structural assignment need not be correct.)



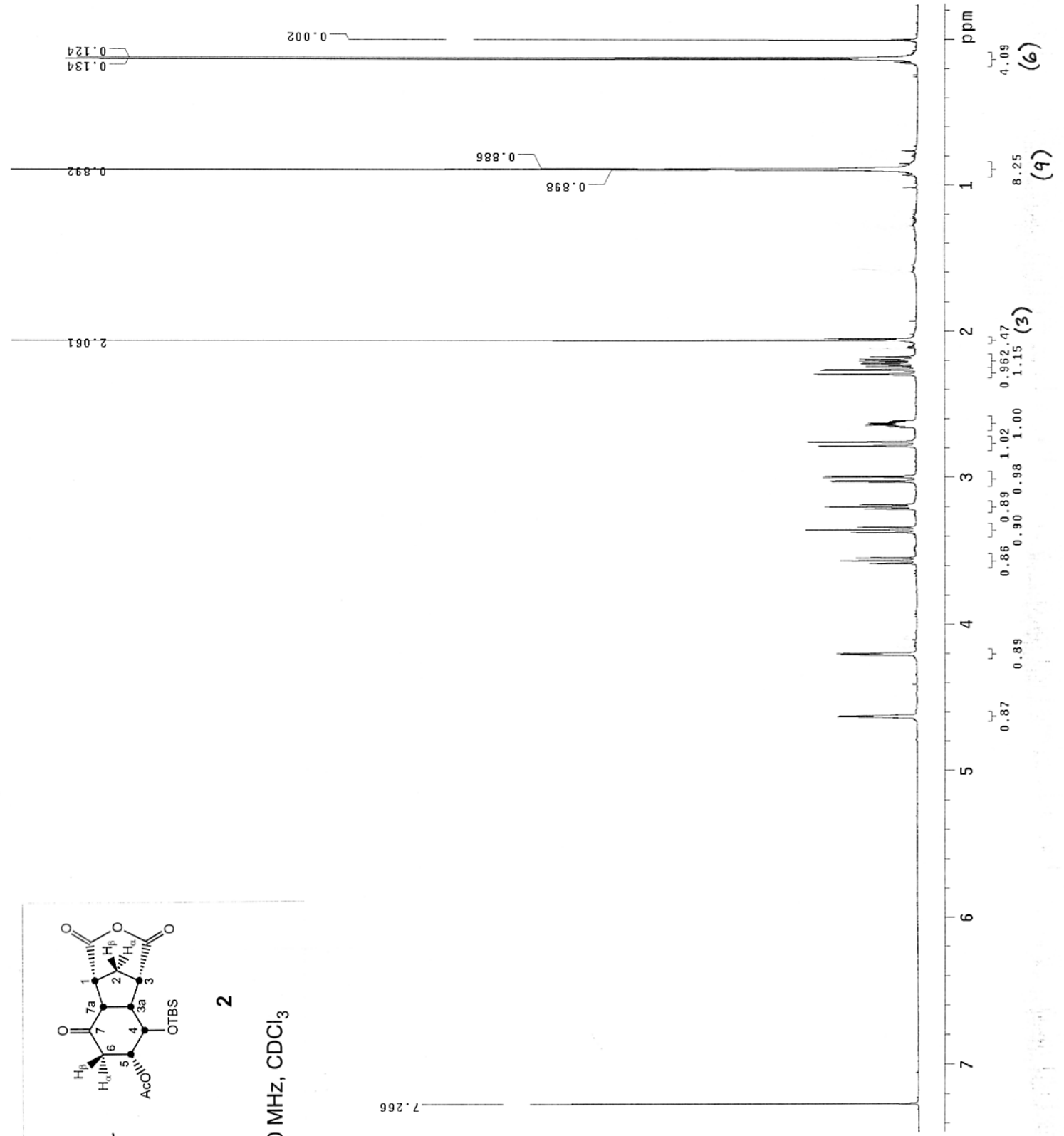
- d. (20 pts) Describe two additional spectroscopy experiments (other than the ones in this packet) that might help assign the structure of the unknown to **1** or **2**. Be specific; what particular pieces of data would you be looking for, and specifically how would that data distinguish between structural features of **1** and **2**?

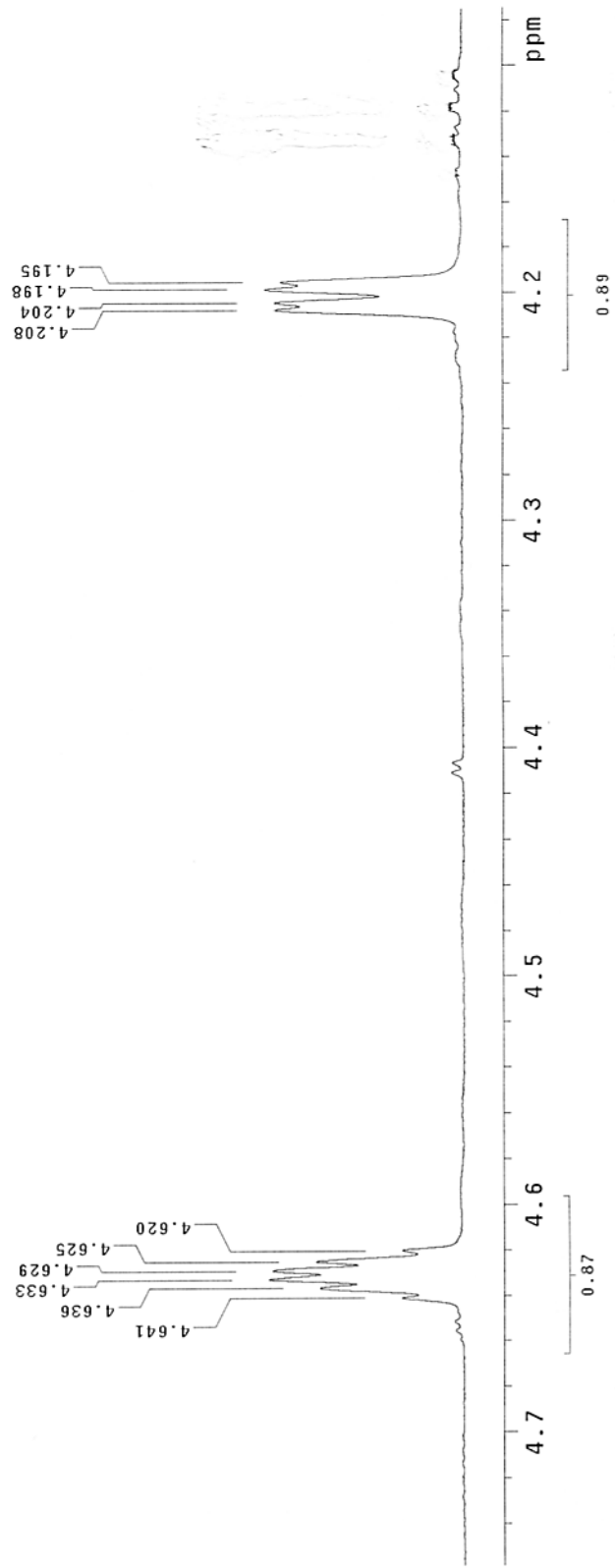
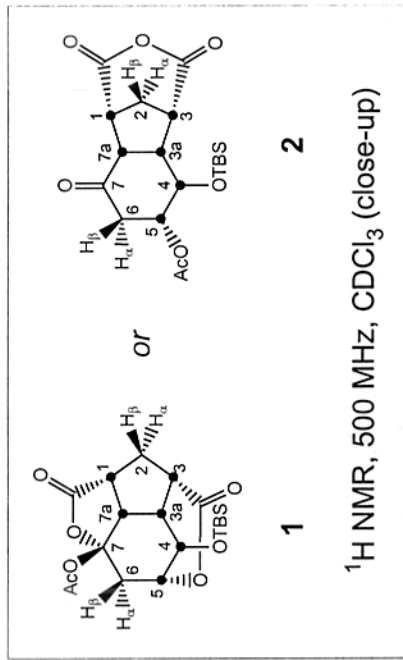
experiment 1:

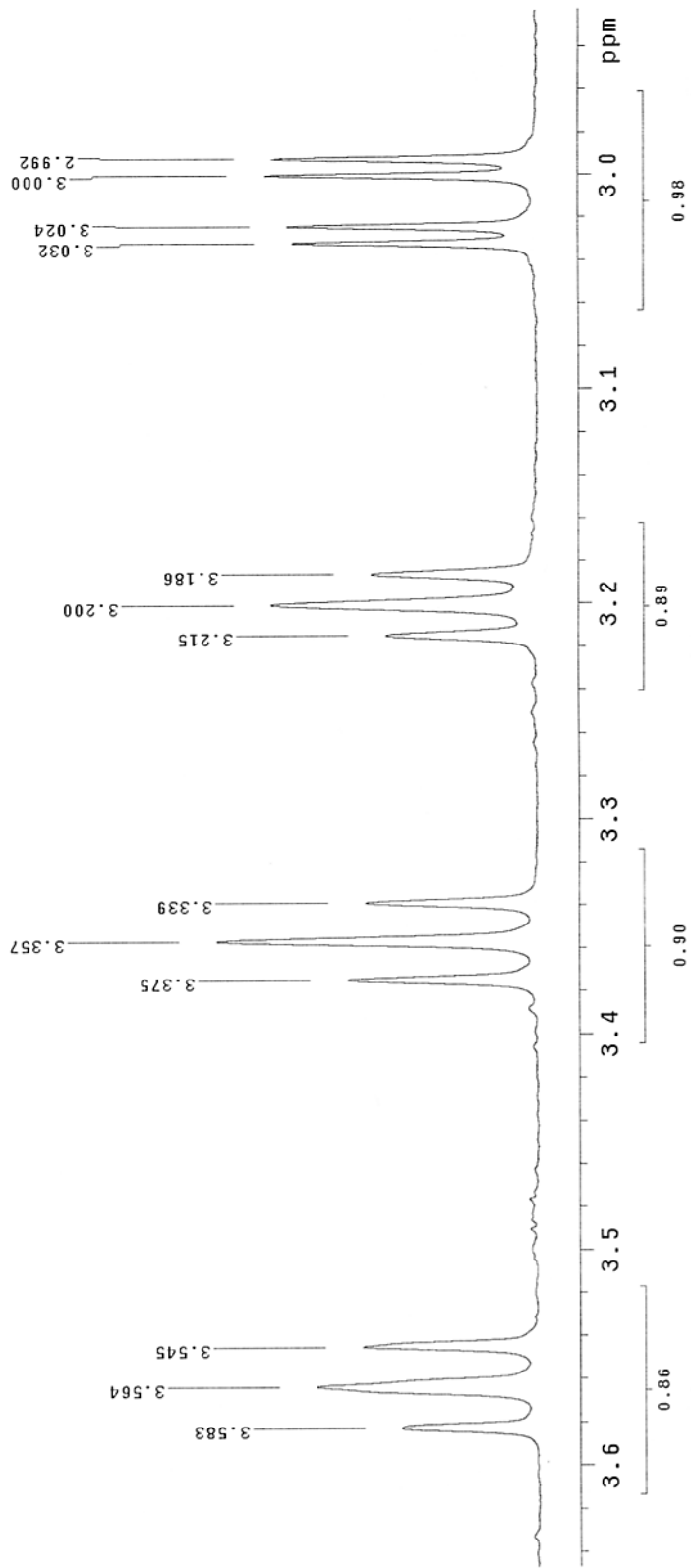
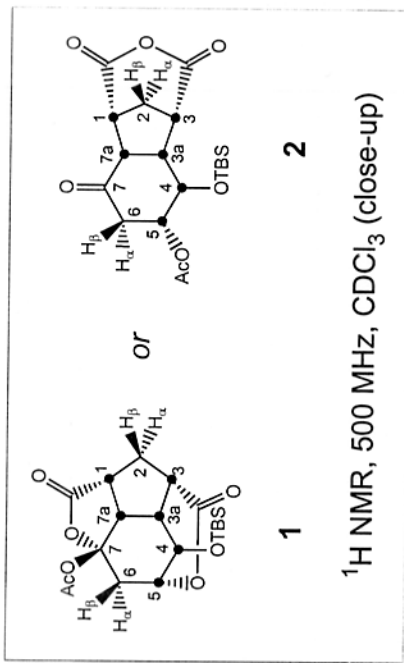
experiment 2:

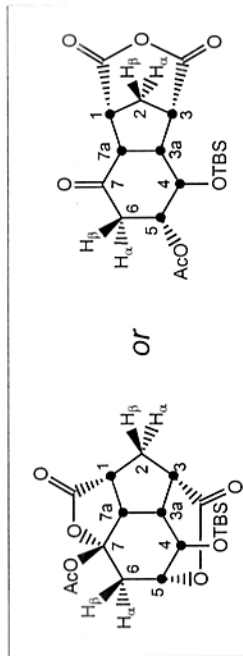


¹H NMR, 500 MHz, CDCl₃





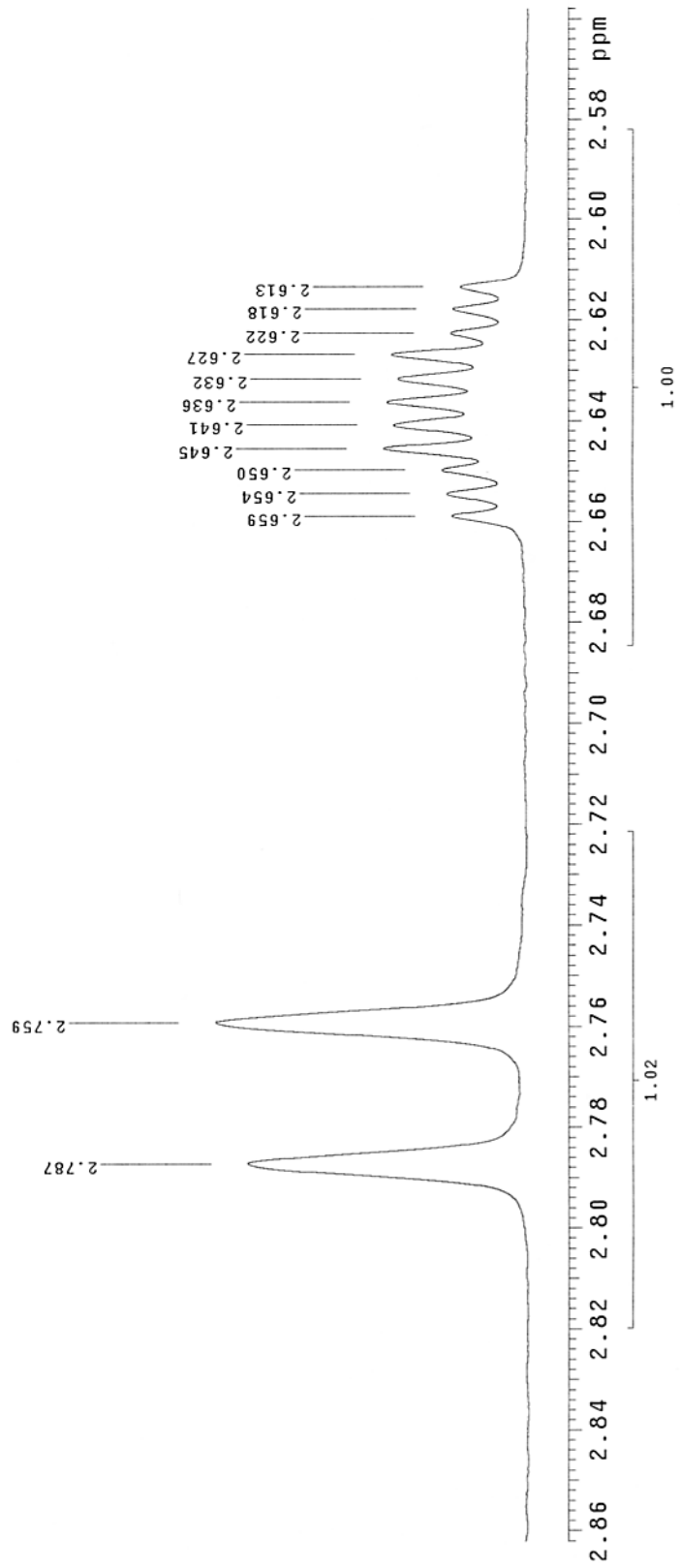


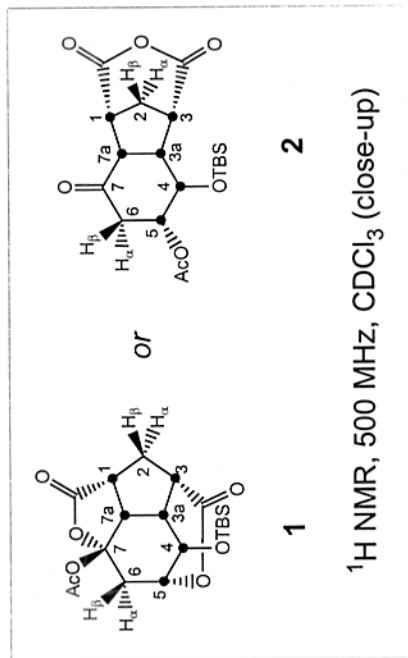


1

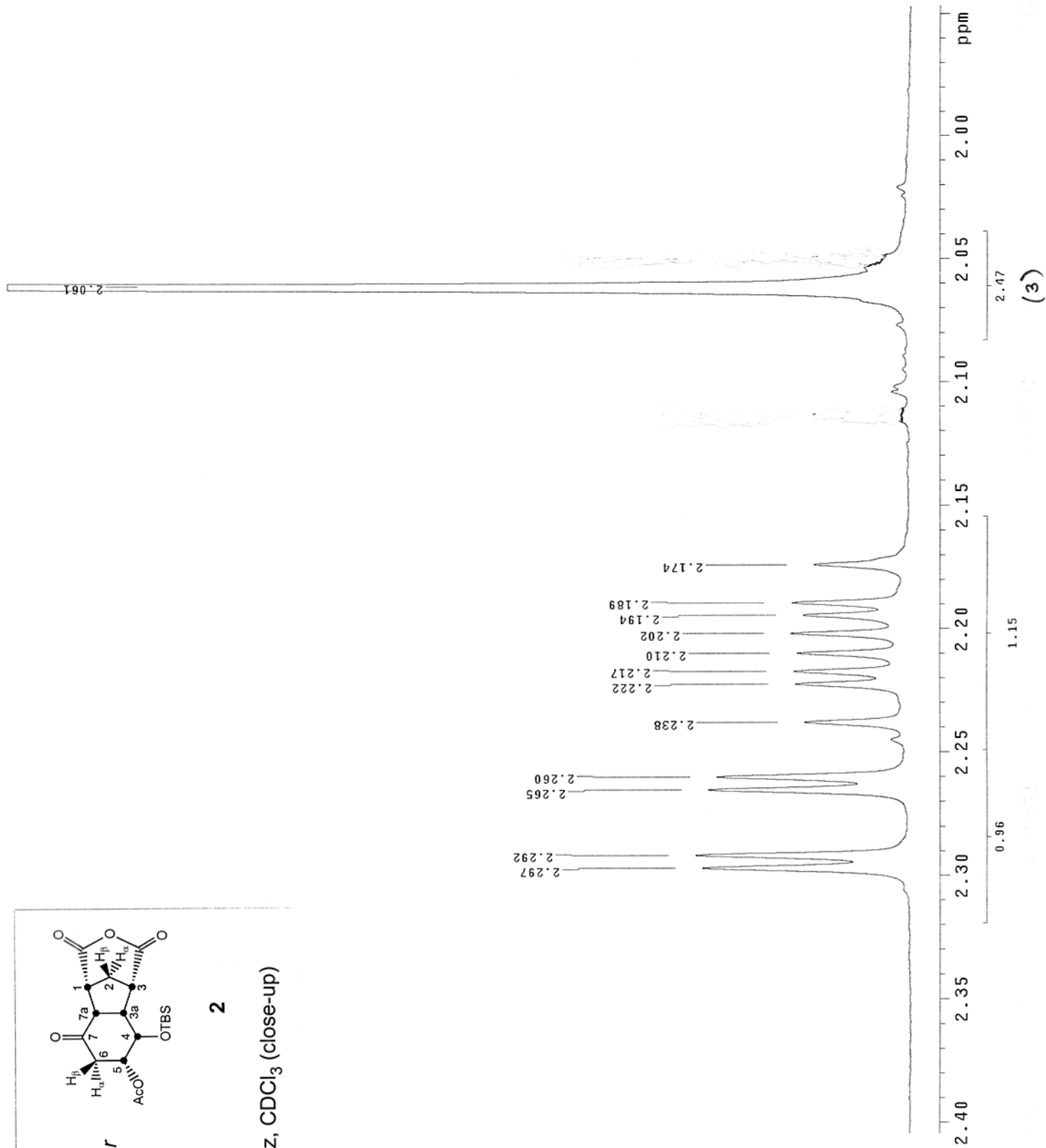
2

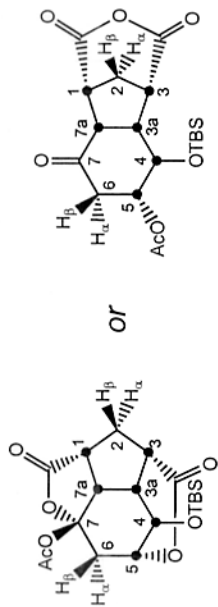
¹H NMR, 500 MHz, CDCl₃ (close-up)





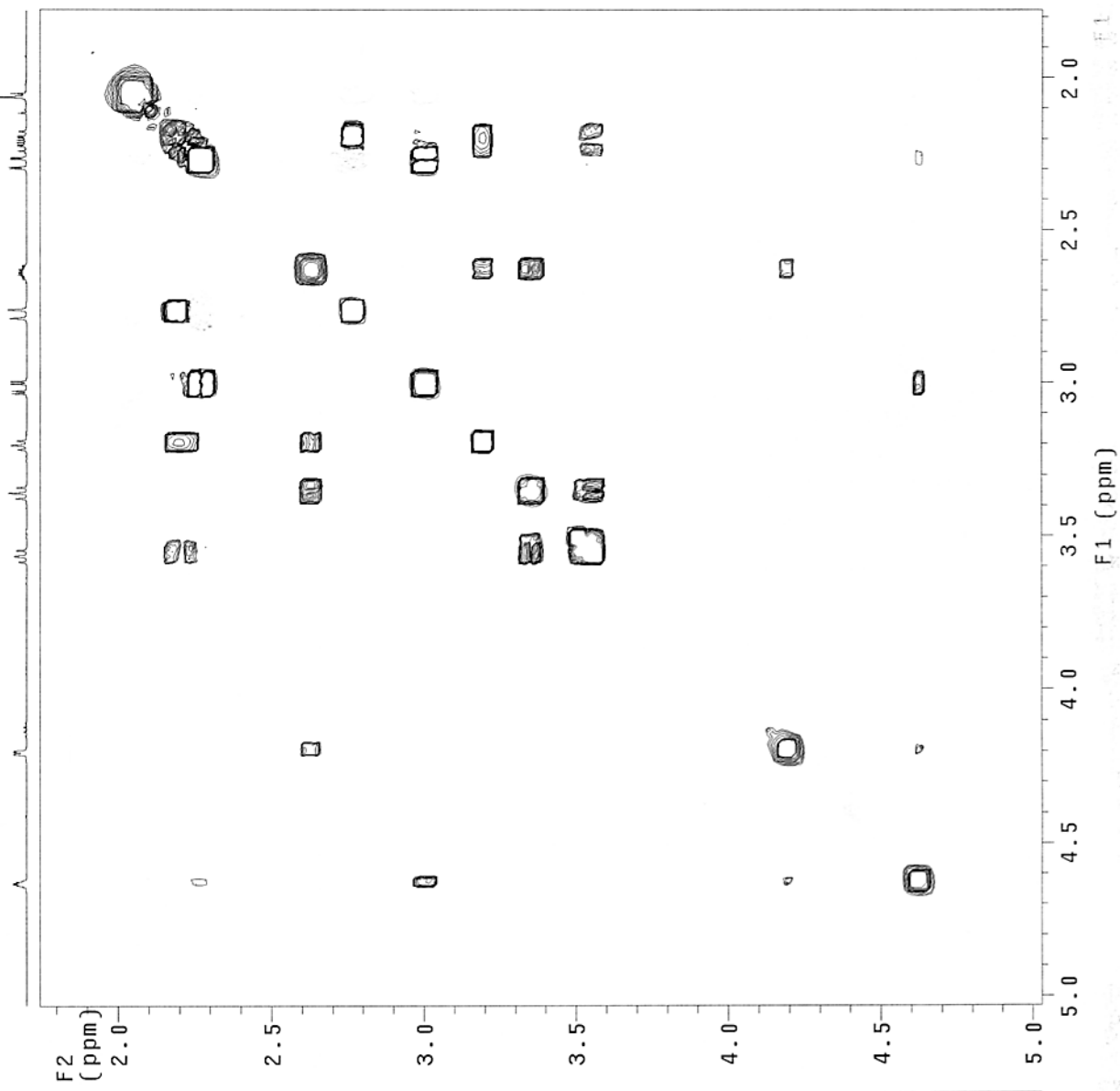
¹H NMR, 500 MHz, CDCl₃ (close-up)





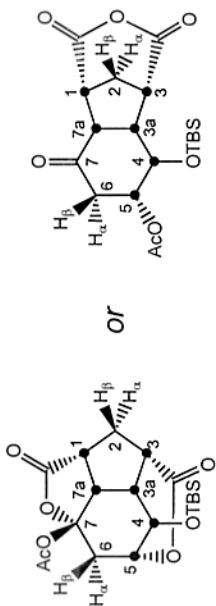
2

^1H - ^1H COSY, 500 MHz, CDCl_3



F1 (ppm)

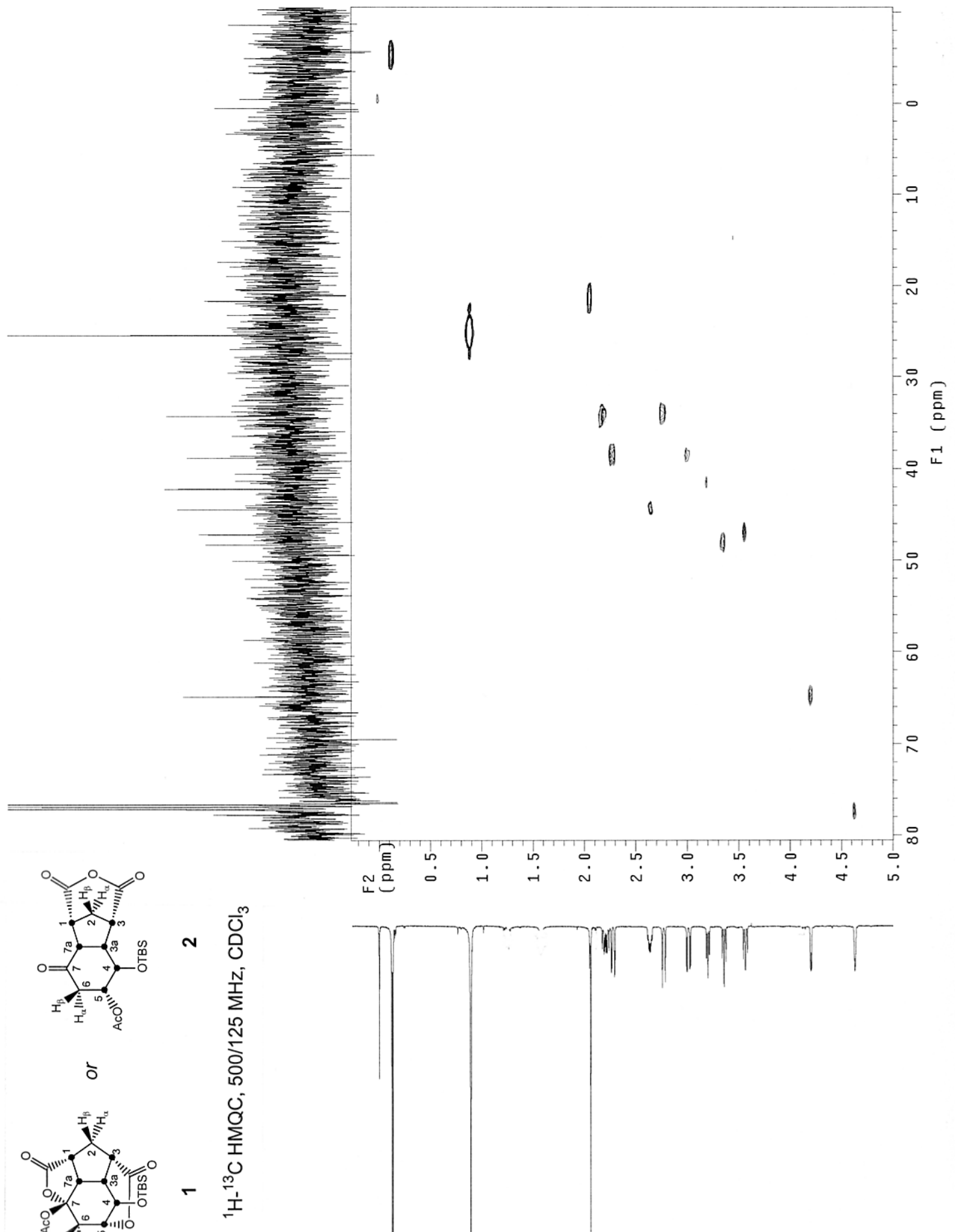
F2 (ppm)



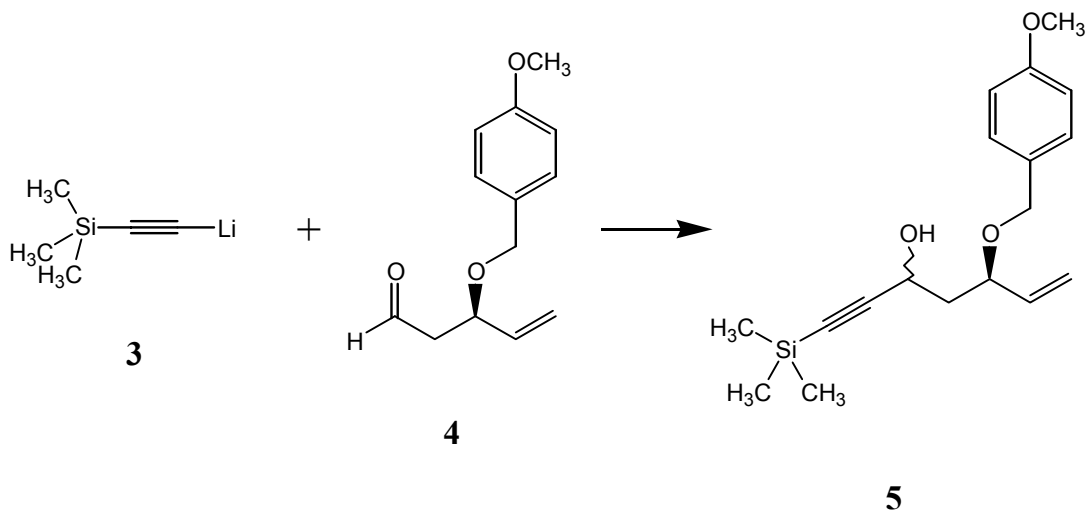
1

2

^1H - ^{13}C HMQC, 500/125 MHz, CDCl_3



2. Ed Luss (Forsyth Group) added the alkynyllithium reagent **3** to aldehyde **4** with the intention of forming two diastereomeric nucleophilic addition products **5**. Ed did in fact isolate and separate two products from the reaction, and subjected one of them to ^1H NMR, IR, and high-resolution mass spectral analysis. In this problem, you will determine whether this product had the structure **5**.



<u>Page</u>	<u>Description</u>
16	^1H NMR, product , 300 MHz, CDCl_3
17	FT-IR, product , NaCl plate
18	HR-ESI-MS (NH_3 reagent), product ; direct insertion, positive-ion mode

- a. (15 pts) In the high-resolution mass spectrum of the product, signals due to higher mass species were weak, but Ed did resolve a possible parent peak at $m/z = 336.2010$. For **5** ($\text{C}_{18}\text{H}_{26}\text{O}_3\text{Si}$), using the most abundant isotopes, Ed calculated an exact mass of 318.1651 amu.

The following page shows the output of a calculation of potential chemical formulae for exact mass 336.2010 amu. (Performed on the Elemental Composition Calculator, <http://medlib.med.utah.edu/masspec/elcomp.htm>.) For the calculation, the molecule was assumed to have chemical formula

$$\begin{aligned}
 &\text{C}_{18}\text{H}_m\text{N}_n\text{O}_p\text{Si}_q, \\
 &0 < m < 40, \\
 &0 < n < 1, \\
 &0 < p < 5, \\
 &0 < q < 1.
 \end{aligned}$$

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Elemental Composition Calculator v1.0

Calculations for : 336.2010 +/- 0.050 amu
monoisotopic mass

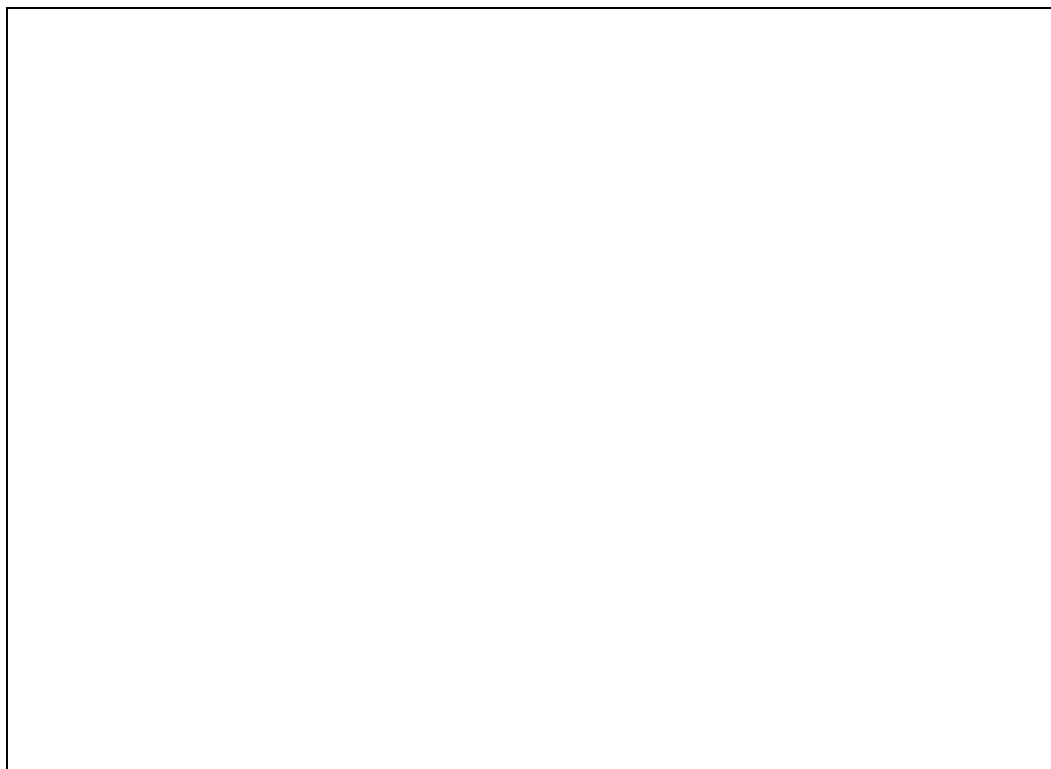
nucleus    mass    min    max

  C      12.0000    18    18
  H       1.0078     0    40
  N      14.0030     0     1
  O      15.9949     0     5
  Si     27.9769     0     1

  C   H   N   O   Si      mass      diff      ppm
18  26   1   5   0   336.1810   0.0199   59.2
18  30   1   3   1   336.1994   0.0015    4.4
18  28   0   4   1   336.1756   0.0253   75.3

Number of hits      :      3
Execution time      :      0.511 seconds
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Were these HR-MS results consistent or inconsistent with structure **5**? What could explain the difference between Ed's calculated exact mass for **5** and the observed parent mass?

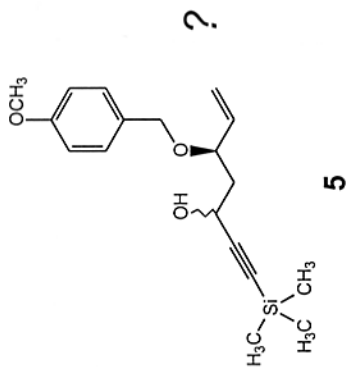


- b. (15 pts) Ed felt that many of the spectral features in the IR spectrum of his product matched structural elements of **5**. List three IR absorbances found in the IR spectrum of the product, and definitively assign them to functional groups or characteristics of structure **5**.

<i>IR frequency</i>	<i>functional group or characteristic of 5</i>
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<i>IR frequency</i>	<i>functional group or characteristic of 5</i>
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<i>IR frequency</i>	<i>functional group or characteristic of 5</i>
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^1H NMR, 300 MHz, CDCl_3

