Chemistry 5361/8361 Tuesday, December 16, 2003

Final Exam

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

Please write all of your answers for this exam 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 one problem, which is 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.

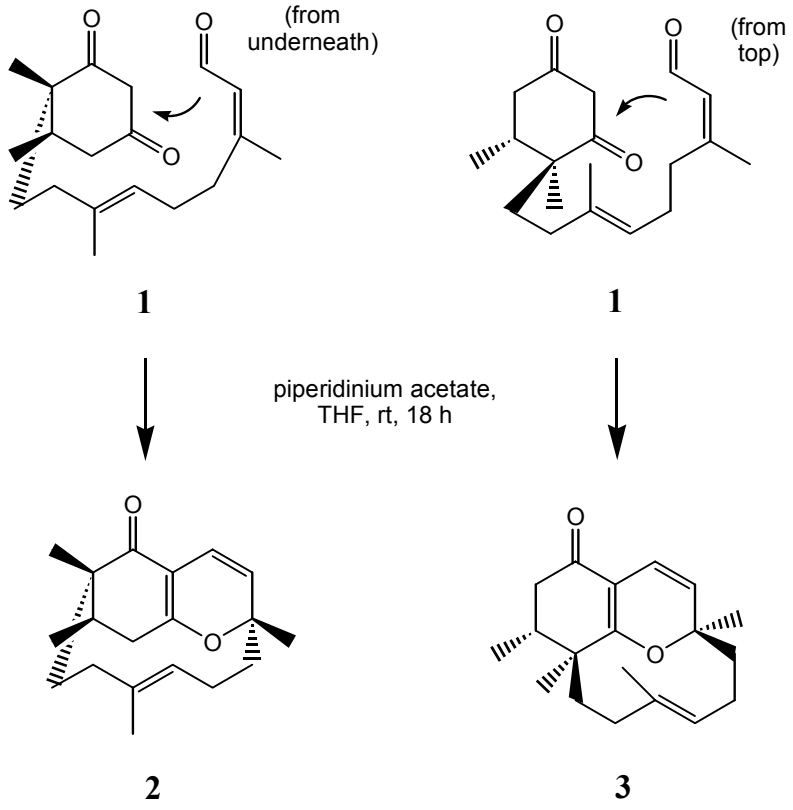
At the end of the 2 hour exam period you will be asked to return your exam to the proctor. (You may, of course, also turn the packet in earlier if you choose.) You are allowed to use any materials you brought with you before the exam. However, we ask that you not bring any materials in or out of the 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: _____

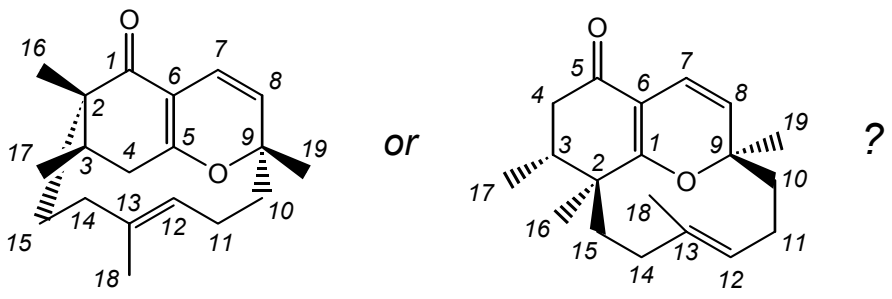
Kevin Cole (Hsung Group) recently reported that a synthetic precursor to phomactin A, an anti-inflammatory natural product, could be constructed using a tandem, intramolecular cyclization reaction. In this reaction scheme, the tethered α,β-unsaturated ketone portion of precursor **1** could add in one of two ways to the diketone portion, to give products **2** and **3**:



1 **1**

2 **3**

Kevin did in fact isolate two major products from his reaction mixture. In this problem, you will follow Kevin's attempts to identify which structure corresponded to one of his purified products. Throughout the problem, carbons will be numbered according to their position in the starting material:



2 **3**

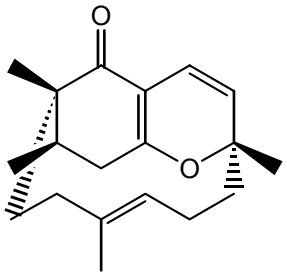
Page	Description
8	LR-ESI-MS, **product**; sample injected in MeOH/HCl/NaCl
9	FT-IR, **product**, NaCl plate
10	^{1}H NMR, **product**, 500 MHz, $CDCl_3$
11-14	close-ups of page 10
15	resolution-enhanced closeups of page 10
16	^{1}H-^{1}H COSY, **product**, 500 MHz, $CDCl_3$
17	close-up of page 16
18-21	^{1}H NOE, **product**, 500 MHz, $CDCl_3$
22	^{13}C NMR, **product**, 125 MHz, $CDCl_3$
23	^{1}H-^{13}C HMQC, **product**, 500/125 MHz, $CDCl_3$
24	^{1}H-^{13}C HMBC, **product**, 500/125 MHz, $CDCl_3$

a. (10 pts) Kevin expected to see (and did see) a peak at m/z = 287.2 for $[M+H]^+$ in the low-resolution ESI-MS, regardless of whether his pure product was **2** or **3**. However, he also observed much larger peaks at m/z = 309.2 and 595.4. Kevin was convinced that all of these peaks were still consistent with either **2** or **3**. What ionic species did these larger peaks correspond to? (You may either draw structures or use "M" notation (e.g., "$[M+H]^+$") to answer this question.)

m/z = 309.2

m/z = 595.4

b. (5 pts) In the IR spectrum of his product, Kevin expected the resonance at 1688 cm^{-1} to be much more intense than it was. What functional group in **2** and **3** should this resonance correspond to? Circle one functional group in each structure.



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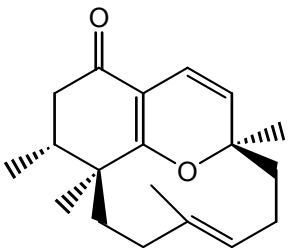


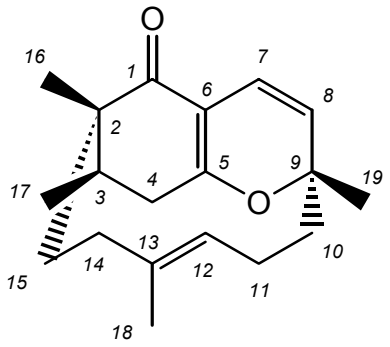
3

c. (45 pts) Based on the NMR data, complete the chart of chemical shifts and coupling constants below. Some of the assignments are easy and can be made from the 1-D ^{1}H NMR alone; others are harder, and will require you to use multiple spectra as references. There is no need to determine whether **2** or **3** is the correct structure for Kevin's unknown to answer this question—connectivity and expected chemical shifts for the two molecules are the same. There is also no need to define which of H_{4a} or H_{4b} is up or down.

proton	chemical shift (δ, ppm, +/-0.02 ppm)	$^{2}J_{H,H}/^{3}J_{H,H}$ coupling constants (Hz, +/-1 Hz)
H_3		$J(H_3,H_{4a})$ =
		$J(H_3,H_{4b})$ =
		$J(H_3, H_{17})$ =
H_{4a}		$J(H_{4a},H_{4b})$ =
H_{4b}		*see H_3, H_{4a}*
H_7		$J(H_7,H_8)$ =

proton	chemical shift (δ, ppm, +/-0.02 ppm)	$^{2}J_{H,H}/^{3}J_{H,H}$ coupling constants (Hz, +/-1 Hz)
H_8		*see H_7*
H_{12}		complex—please skip
H_{16}		no $^{2/3}J_{H,H}$ partners
H_{17}		*see H_3*
H_{18}		no $^{2/3}J_{H,H}$ partners
H_{19}		no $^{2/3}J_{H,H}$ partners

d. (6 pts) The ^{1}H-^{1}H COSY spectrum of Kevin's product showed an unexpected crosspeak at δ = (5.15, 1.38) ppm. In order to get a better look at this interaction, Kevin performed a resolution enhancement on these two resonances in the 1-D ^{1}H NMR spectrum (page 15), which brought out a small coupling constant between these peaks. Assuming this coupling occured regardless of whether Kevin's product were **2** or **3**, on each of the structures below, draw arrows that represent this interaction. Over how many bonds does this coupling occur?



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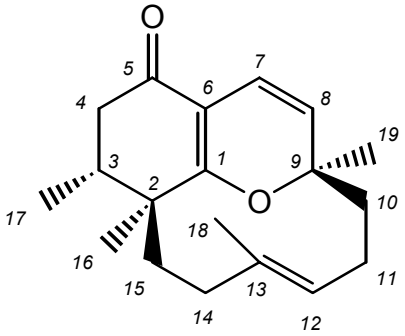

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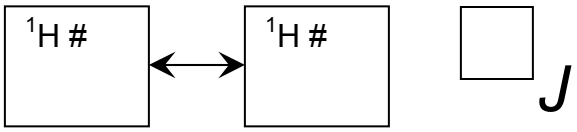
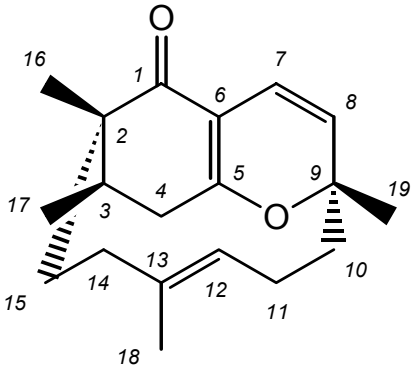


e. (12 pts) Assign the ^{13}C resonances in the chart to carbon atoms in the structures of **2** and **3**. Because the same carbons in the starting material sometimes end up in different places in **2** and **3**, the numbers you write in the two columns may or may not be the same for each ^{13}C resonance.

^{13}C chemical shift (δ, ppm)	carbon # (in **2**)	carbon # (in **3**)
198.6		
169.1		
125.3		
119.8		
118.0		
82.9		

f. (6 pts) In the ^{13}C spectrum, the peaks at δ = 198.6, 169.1 and 125.3 ppm are much taller than the peaks at δ = 125.3, 119.8 and 118.0 ppm. Why?

g. (12 pts) Kevin relied heavily on HMBC to assign the correct structure to his product; he found that HMBC gave a few ^{1}H-^{13}C correlations that were consistent with only one of the two possible structures. On one of the two structures below, draw two arrows that represent two ^{1}H-^{13}C correlations that could not be observed for the other structure. For clarity, also write the numbers of the interacting carbon and hydrogen atoms in the boxes below the appropriate structure. (Leave the boxes under the wrong structure blank.)



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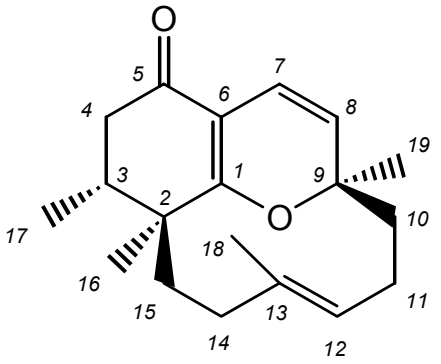


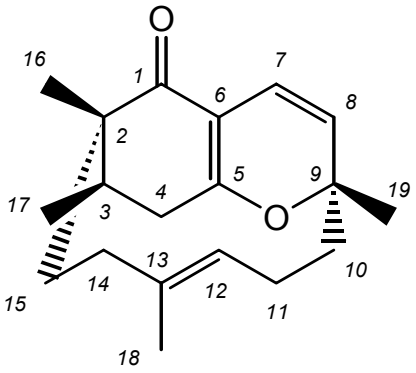
3

^{13}C #	↔	^{1}H #
^{13}C #	↔	^{1}H #

or

^{13}C #	↔	^{1}H #
^{13}C #	↔	^{1}H #

h. (4 pts) Kevin also found NOE interactions that were consistent with only one of the two structures. On one of the structures below, draw an arrow that represents one ^{1}H-^{1}H NOE interaction that could not be observed for the other structure. For clarity, also write the numbers of the interacting hydrogen atoms in the boxes below the appropriate structure. (Leave the boxes under the wrong structure blank.)



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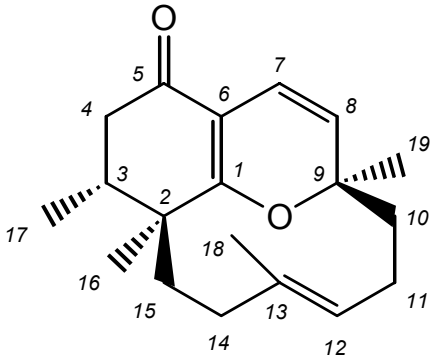

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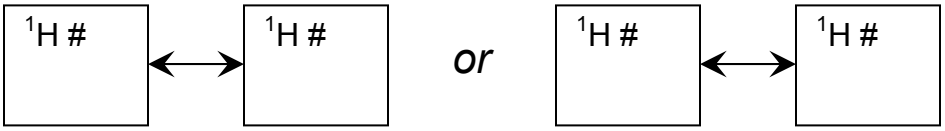

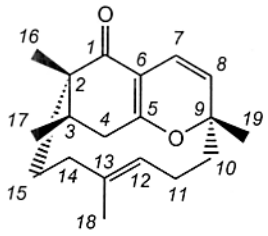

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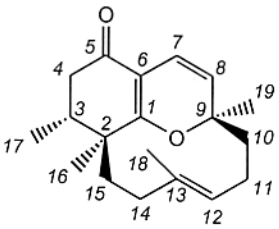
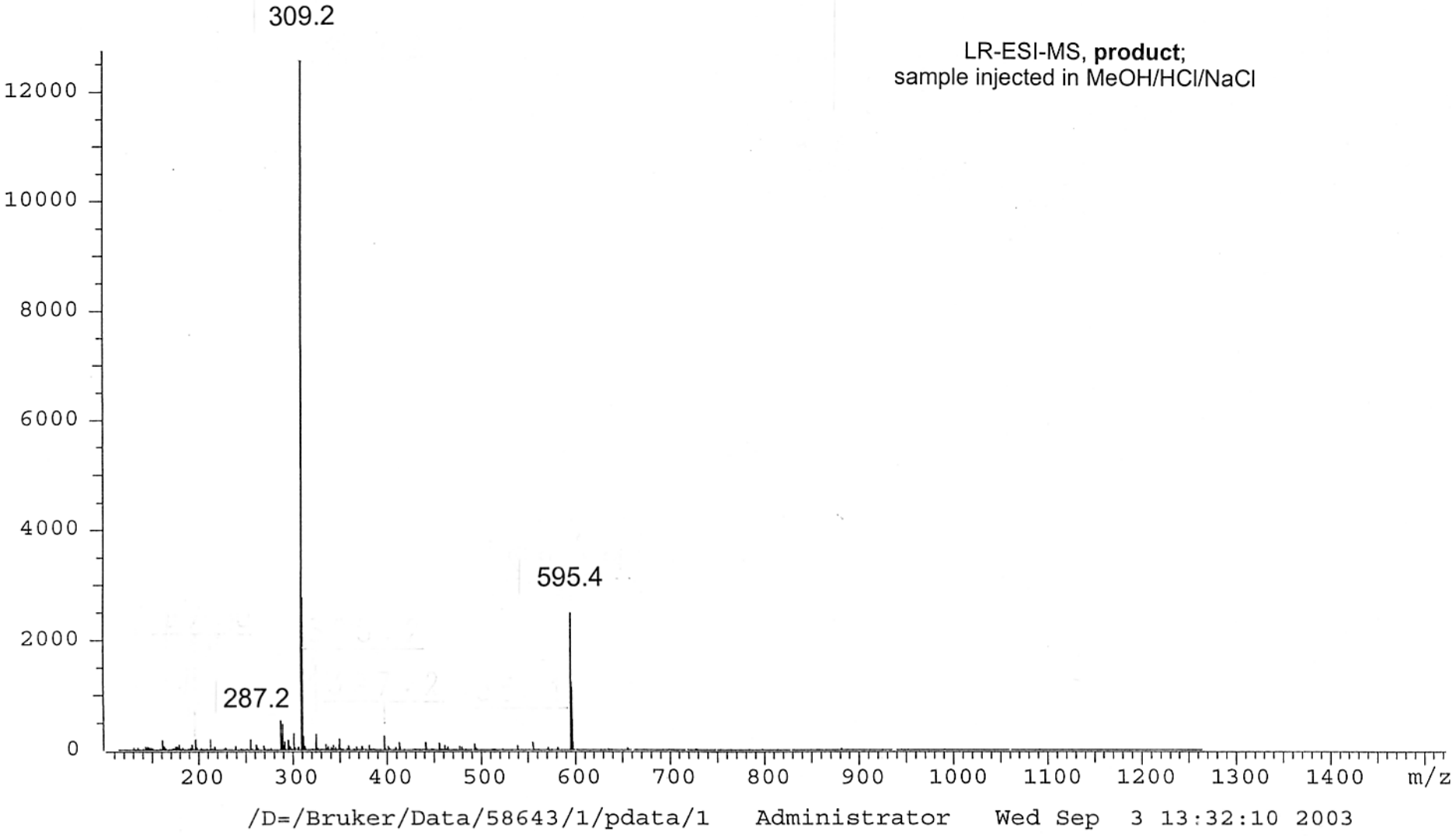
or

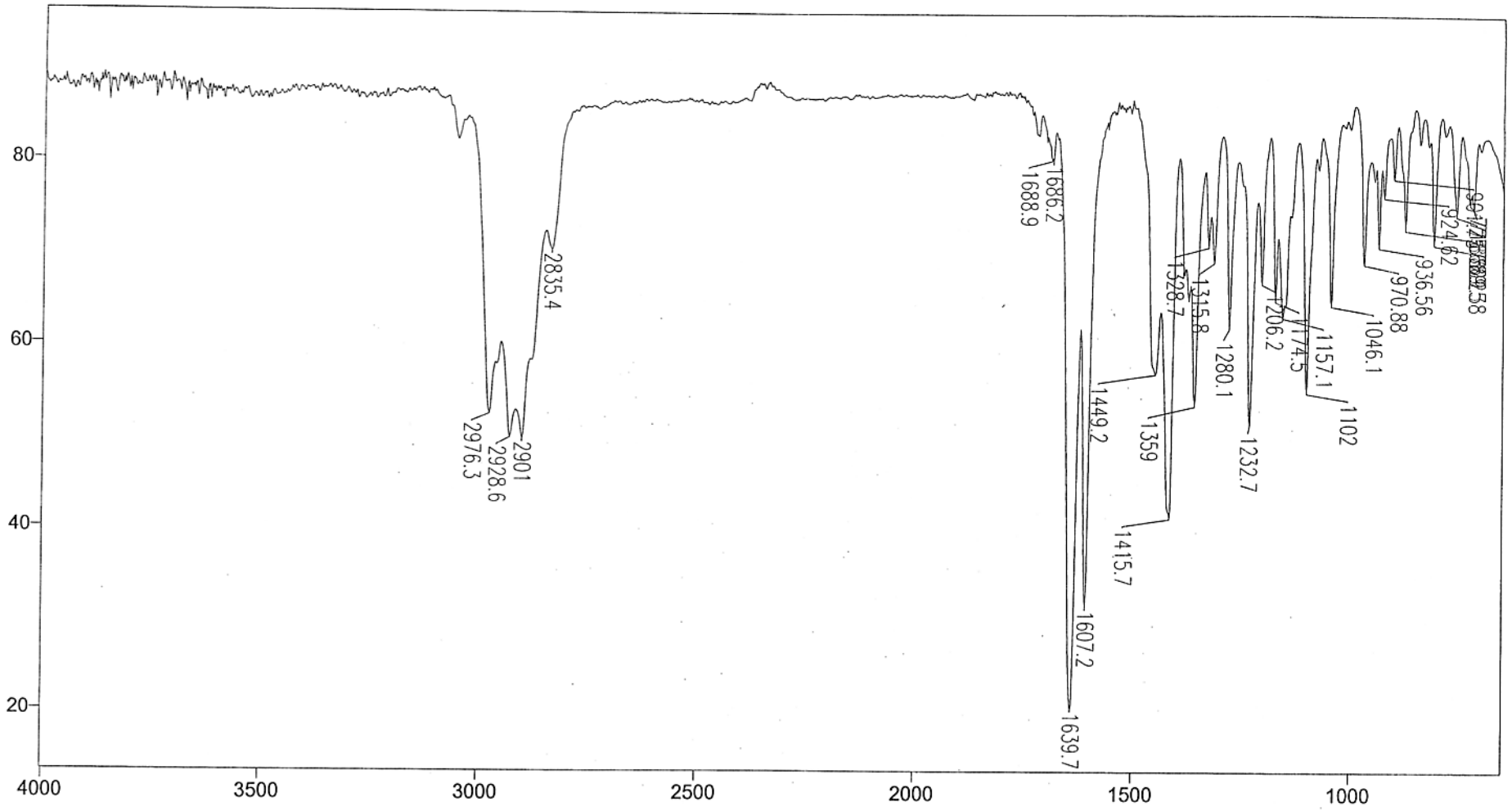


3

?

LR-ESI-MS, **product**;
sample injected in MeOH/HCl/NaCl

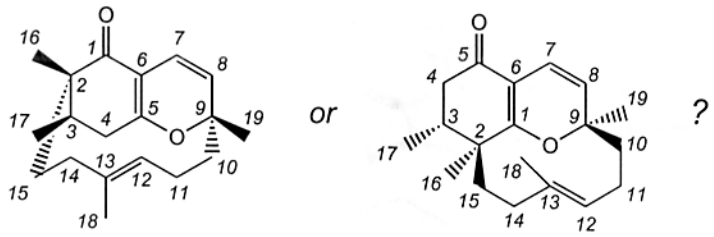




Transmission / Wavenumber (cm-1)

File # 1 = LAB2311

poly - dc



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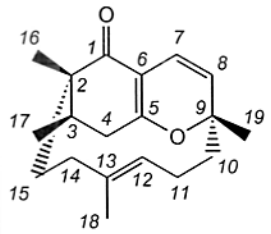
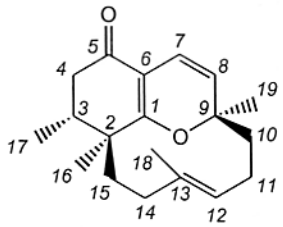
Paged X-Zoom CURSOR

9/3/2003 5:59 PM Res=4 cm-1

FT-IR, **product**, NaCl plate

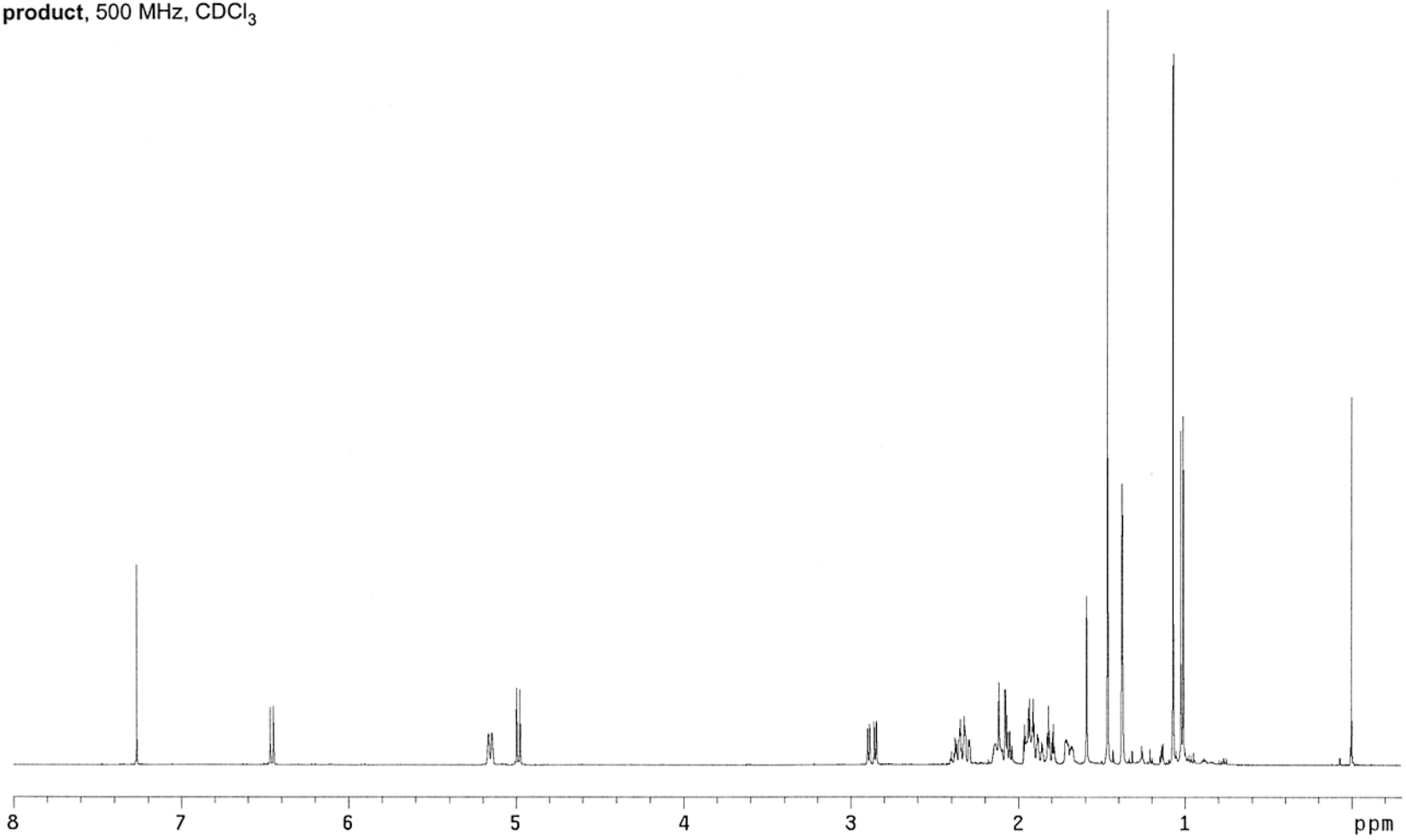


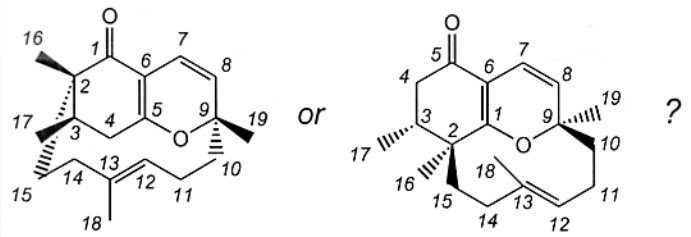
2 *or*



3 *?*

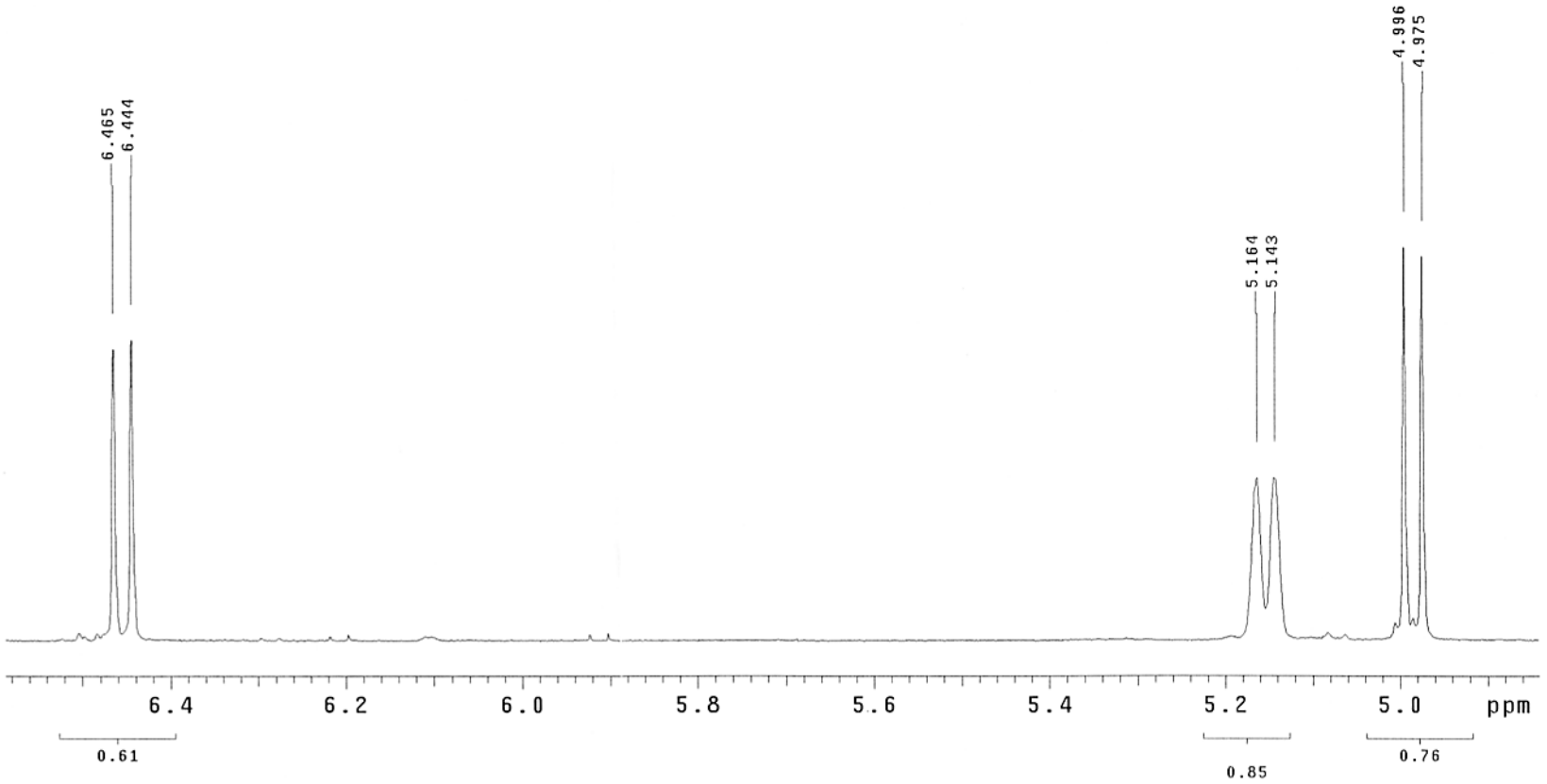
^{1}H NMR, **product**, 500 MHz, $CDCl_3$

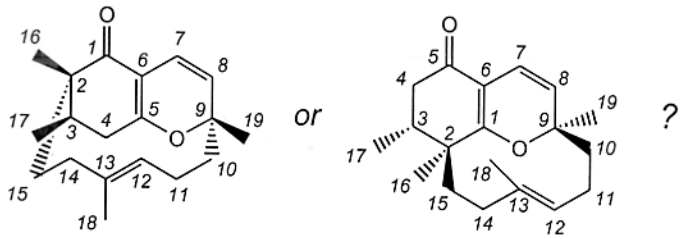




2 **3**

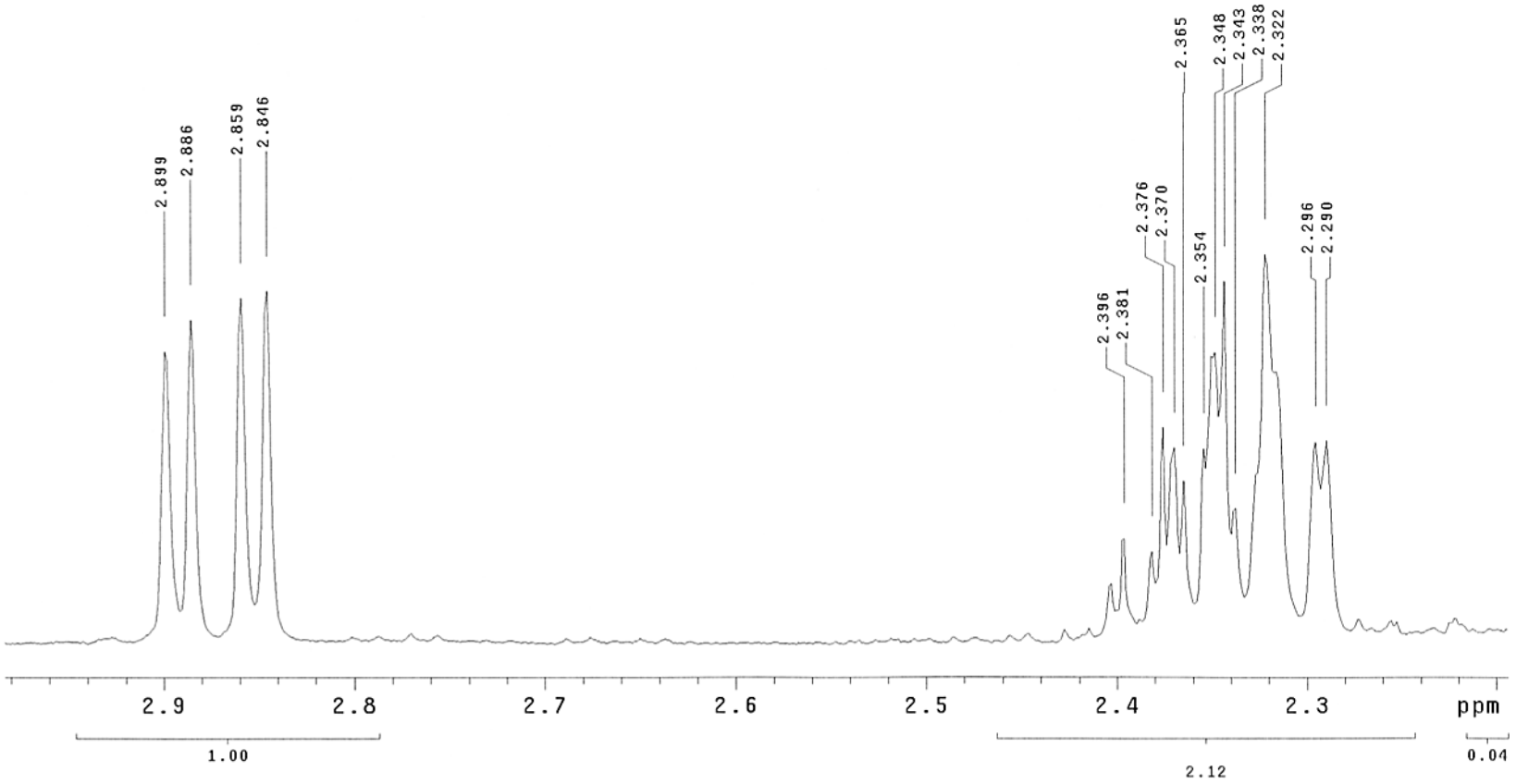
^{1}H NMR, **product**, 500 MHz, $CDCl_3$
(closeup)

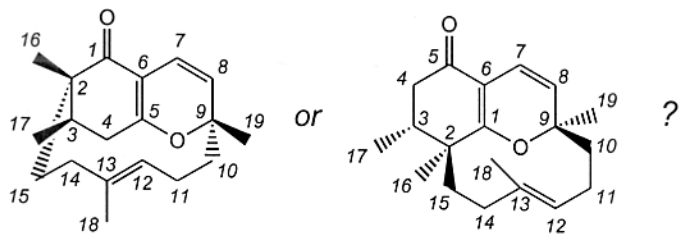




2 **3**

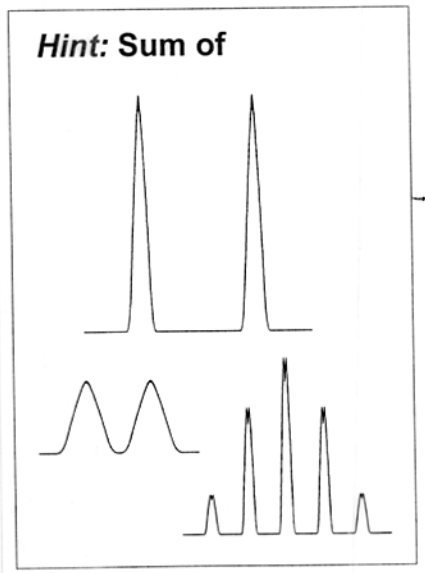
^{1}H NMR, **product**, 500 MHz, $CDCl_3$
(closeup)

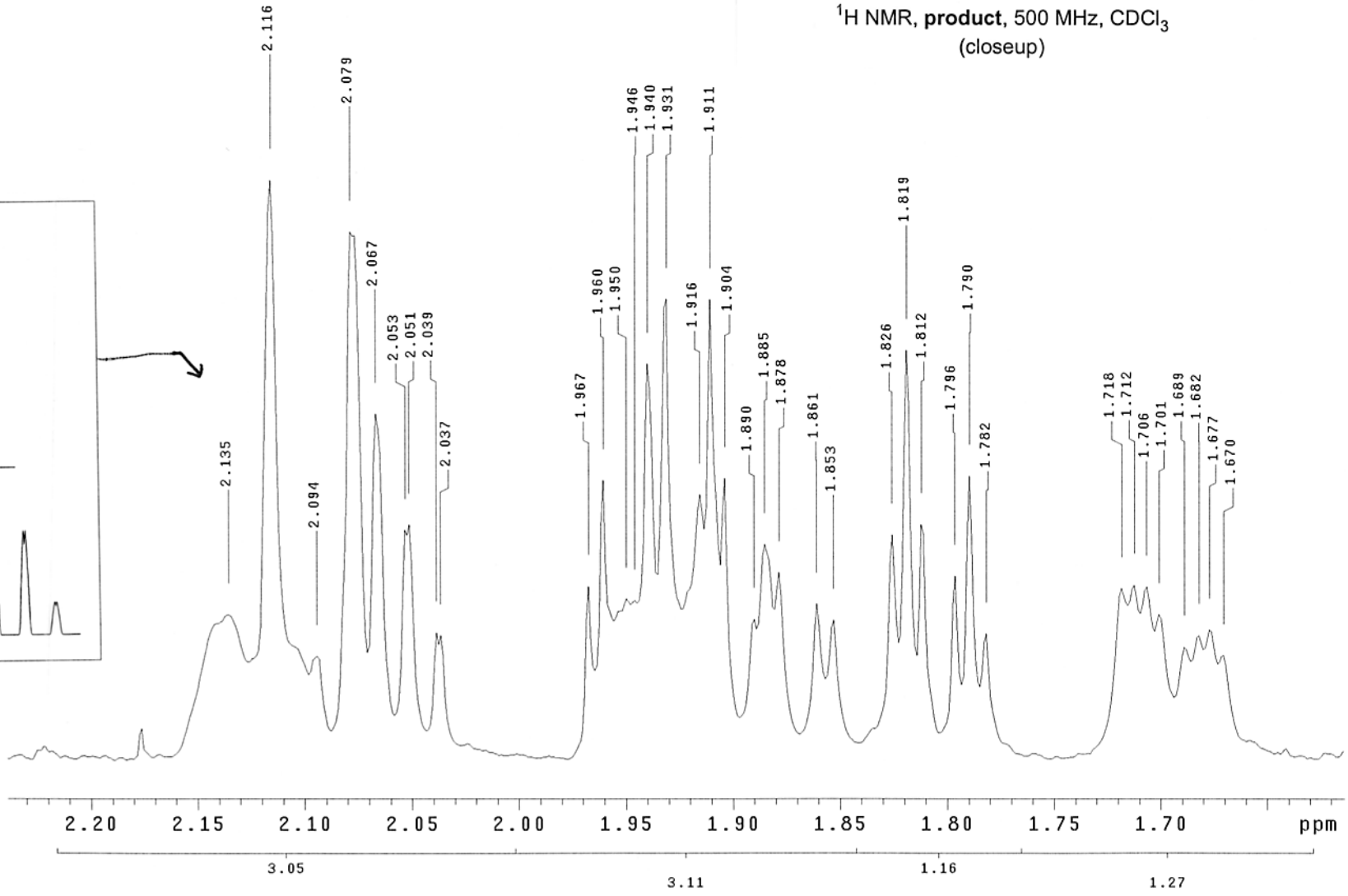


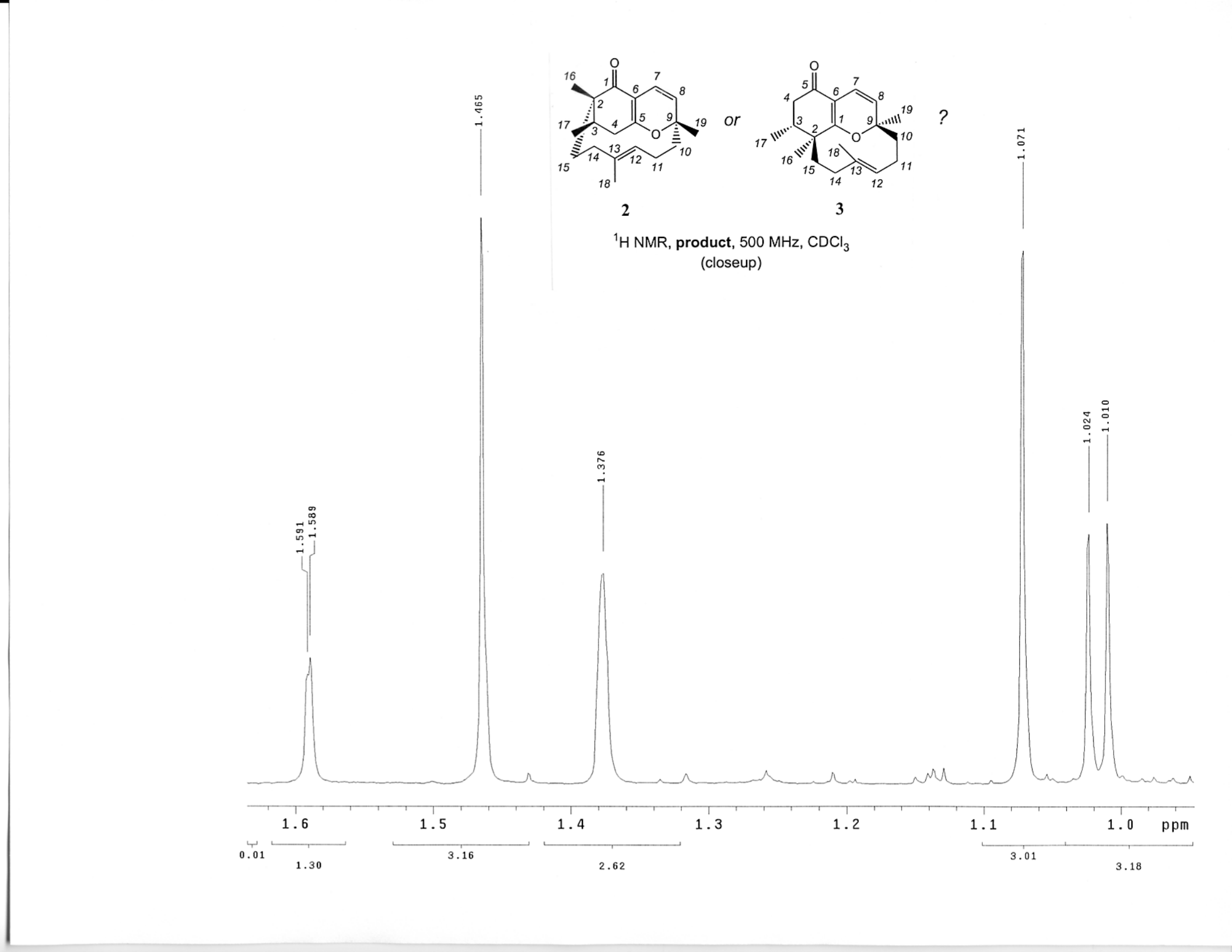


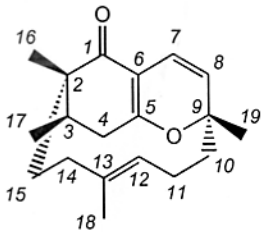
2 or 3 ?

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






or
?
2
3
1H NMR, product, 500 MHz, CDCl3
(closeup)
1.591
1.589
1.465
1.376
1.071
1.024
1.010
1.6
1.5
1.4
1.3
1.2
1.1
1.0
ppm
0.01
1.30
3.16
2.62
3.01
3.18



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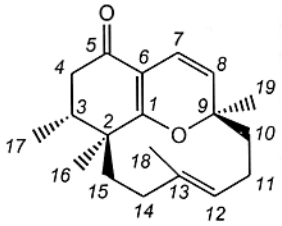
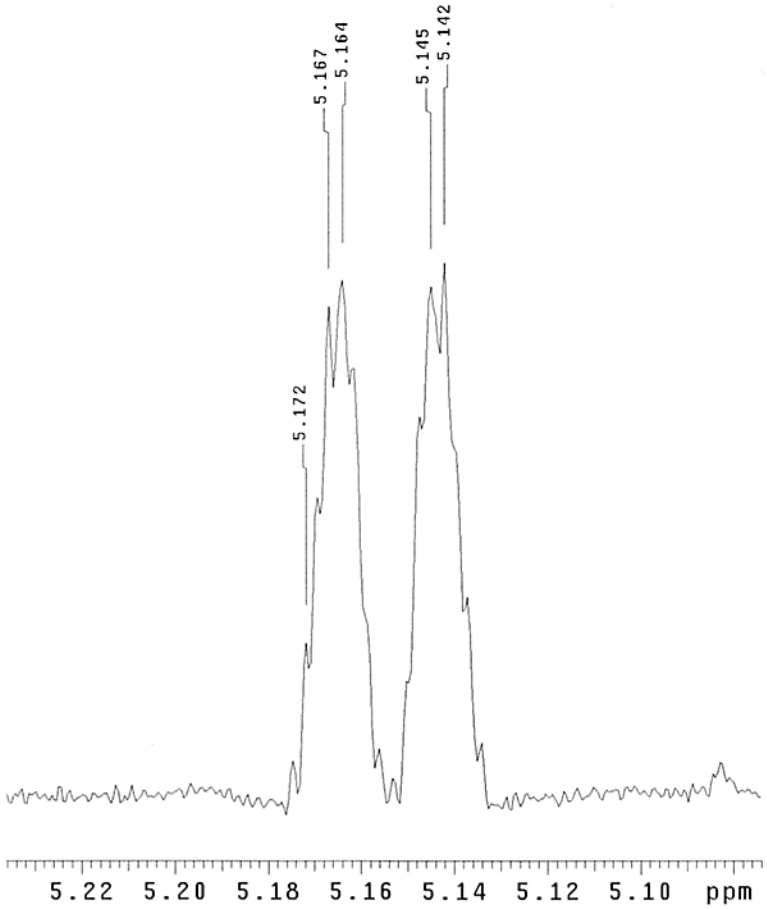
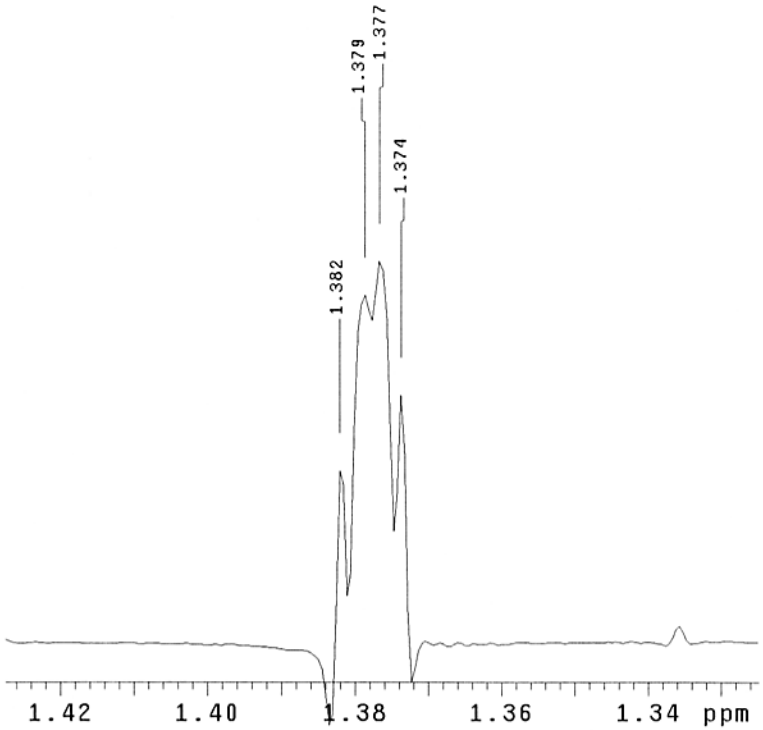


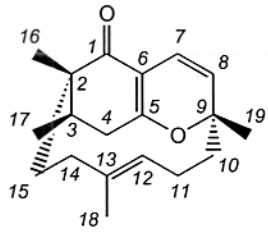
3

?

^{1}H NMR, **product**, 500 MHz, $CDCl_3$
(closeup, resolution-enhanced)







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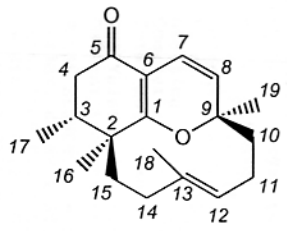
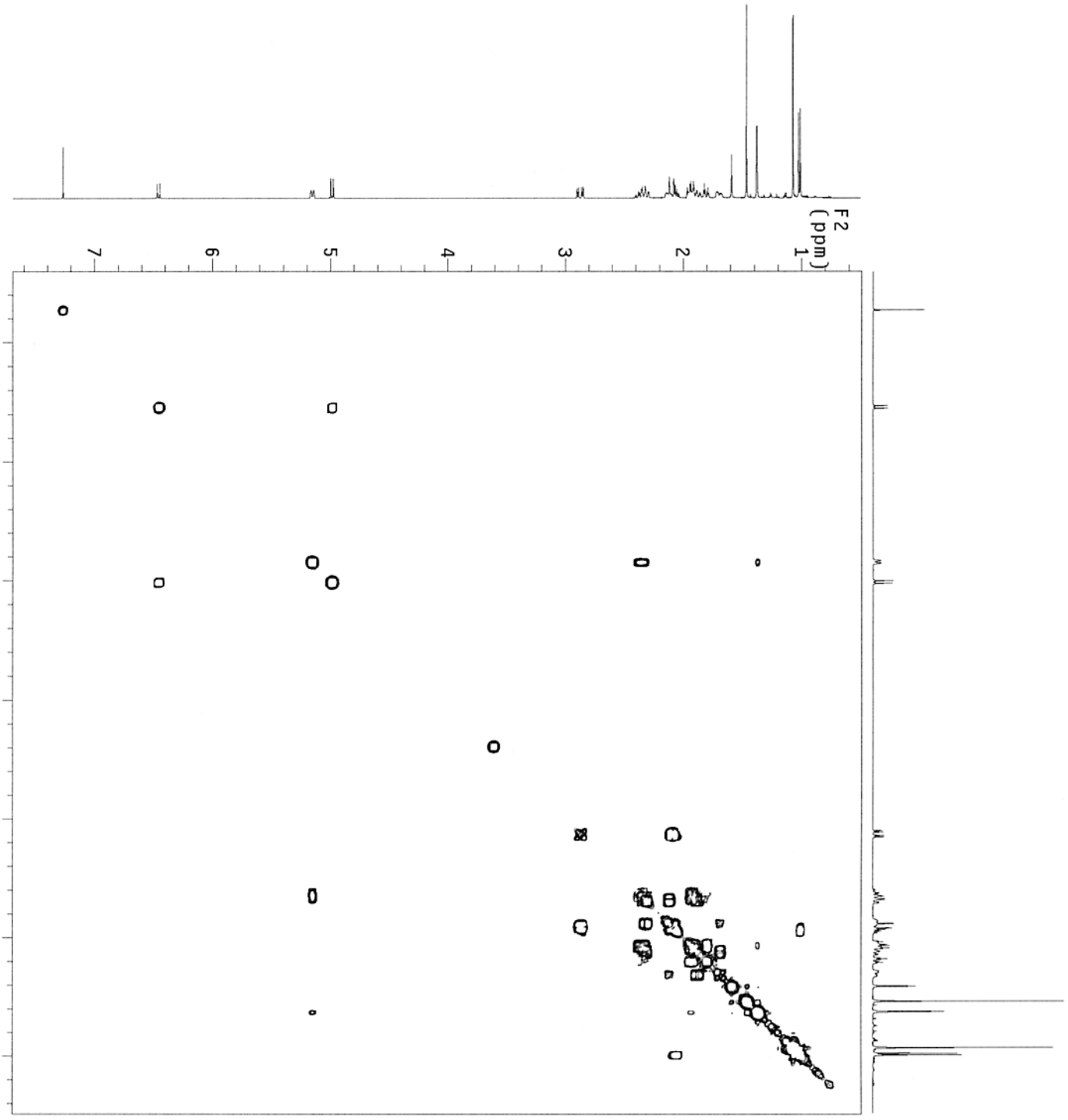
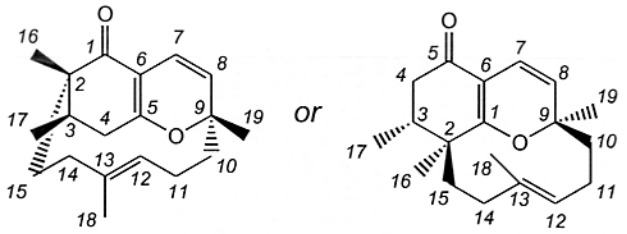


3

?

^{1}H-^{1}H COSY, **product**, 500 MHz, $CDCl_3$





or

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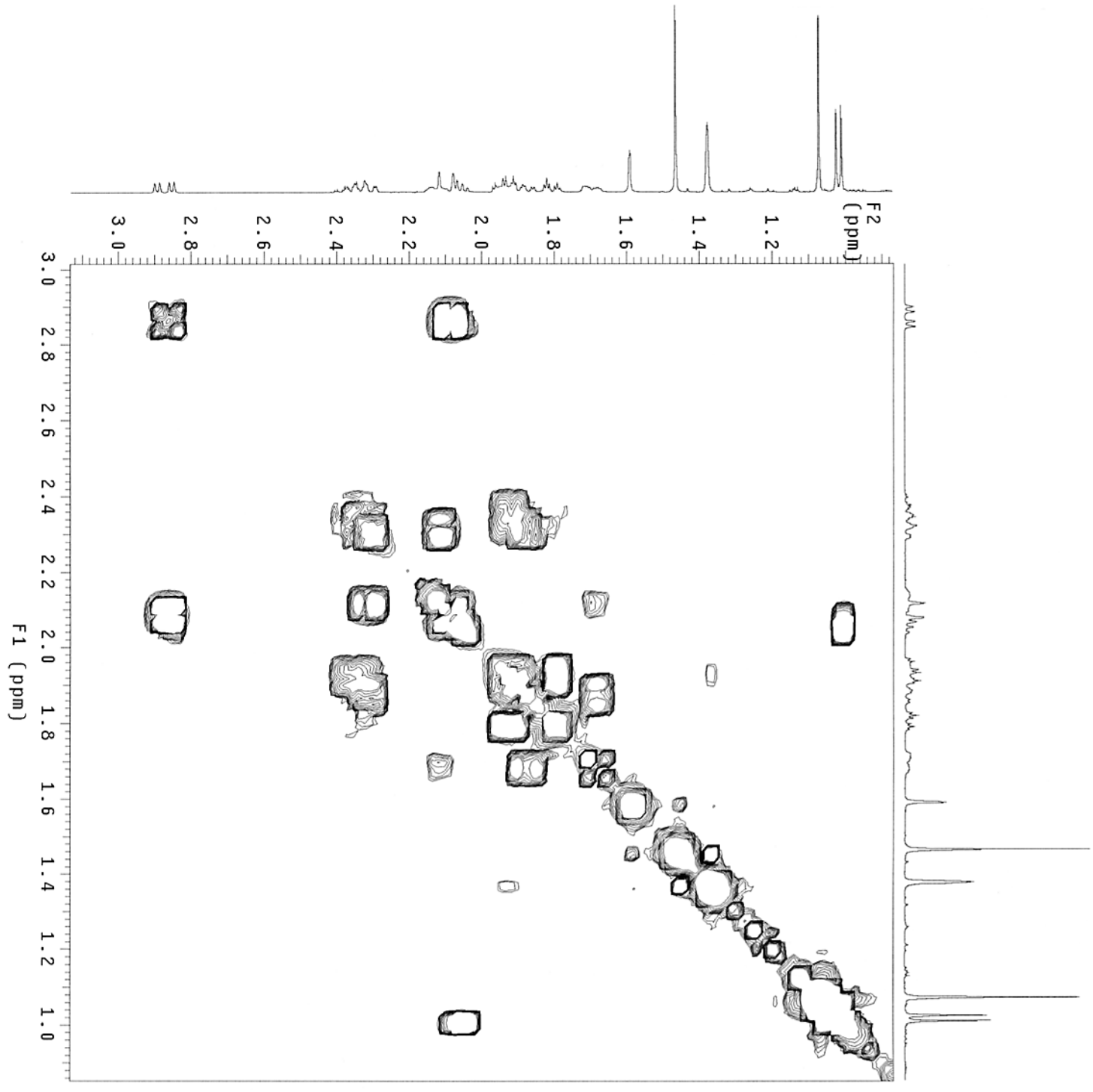
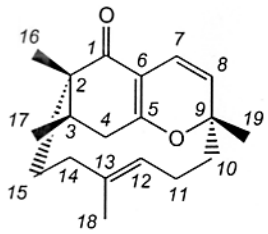
2 **3**

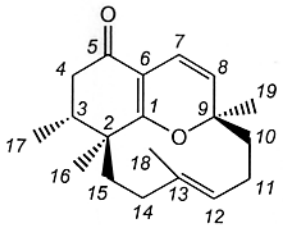
^{1}H-^{1}H COSY, **product**, 500 MHz, $CDCl_3$
(closeup)





2

or



3

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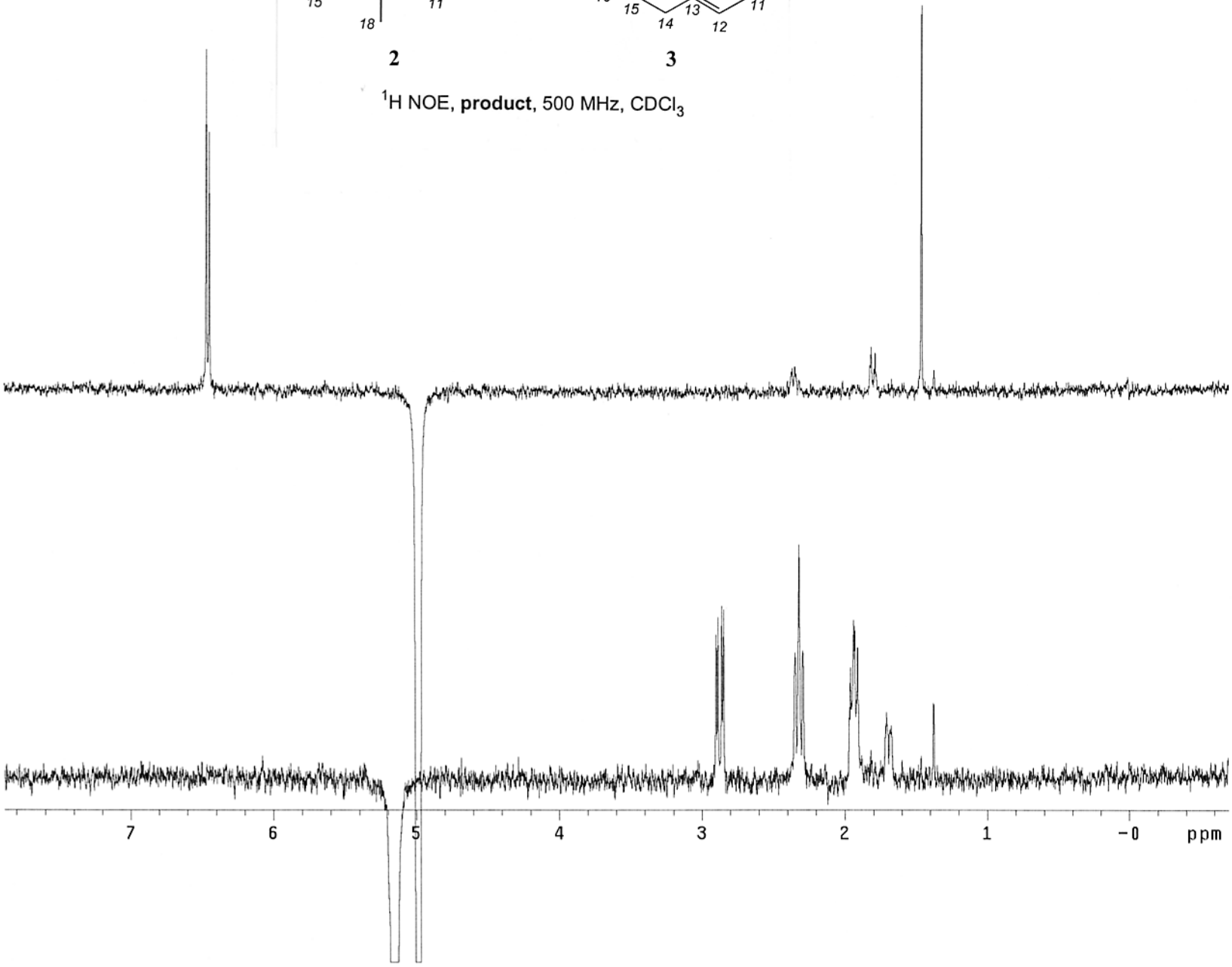
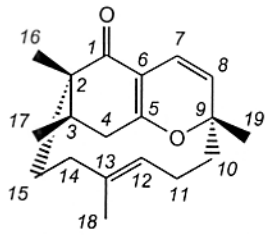
^{1}H NOE, **product**, 500 MHz, $CDCl_3$





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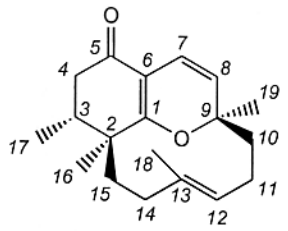
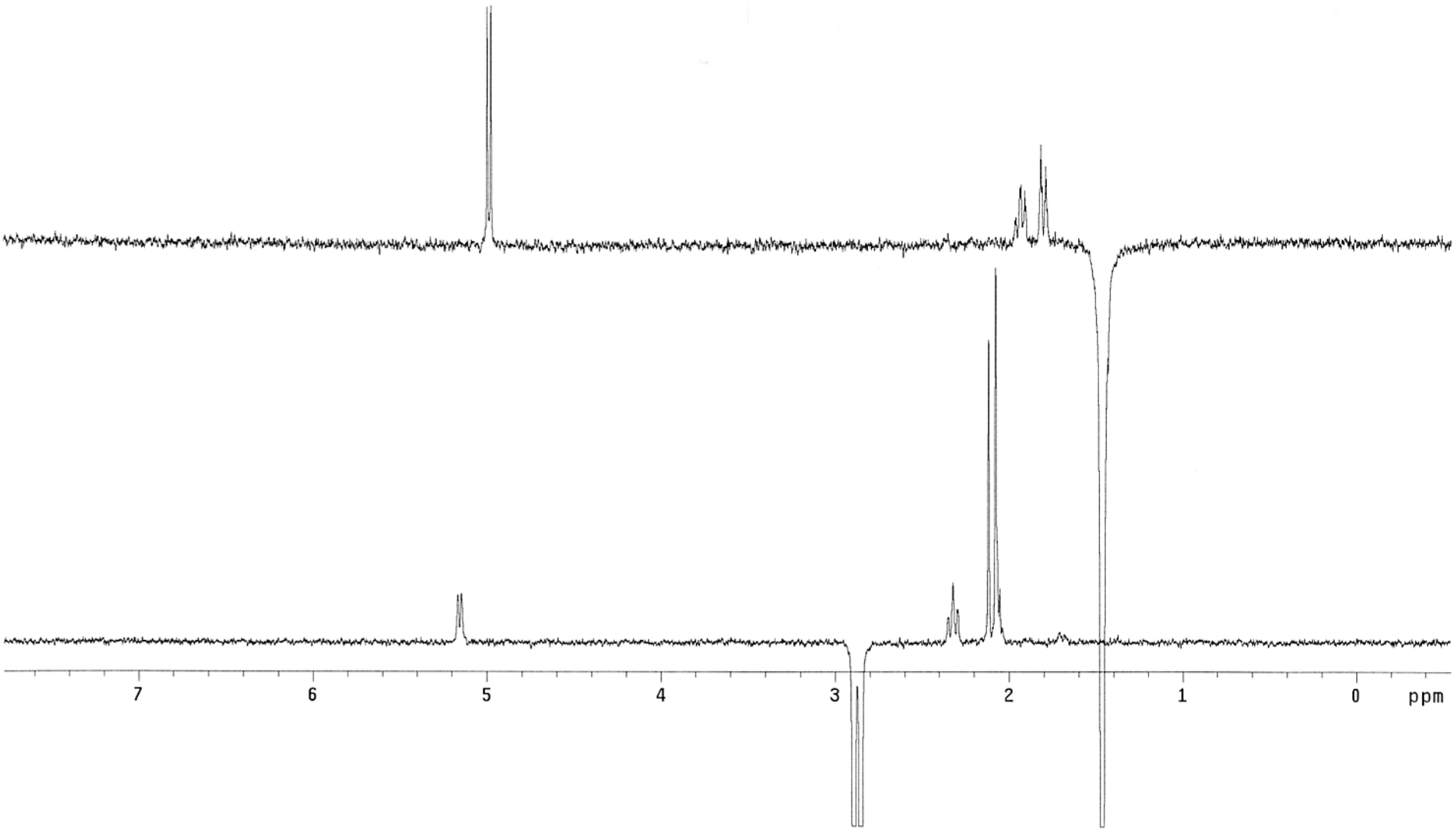
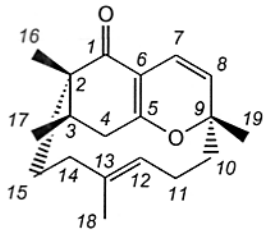


3

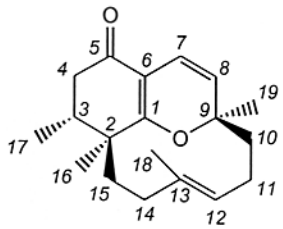
?

^{1}H NOE, **product**, 500 MHz, $CDCl_3$





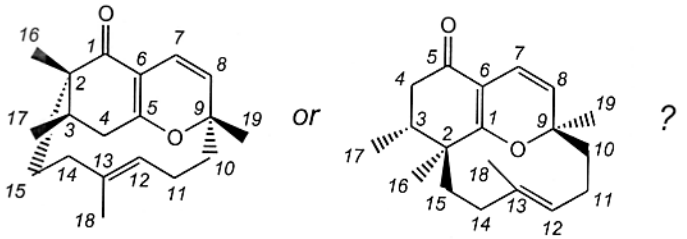
or



?

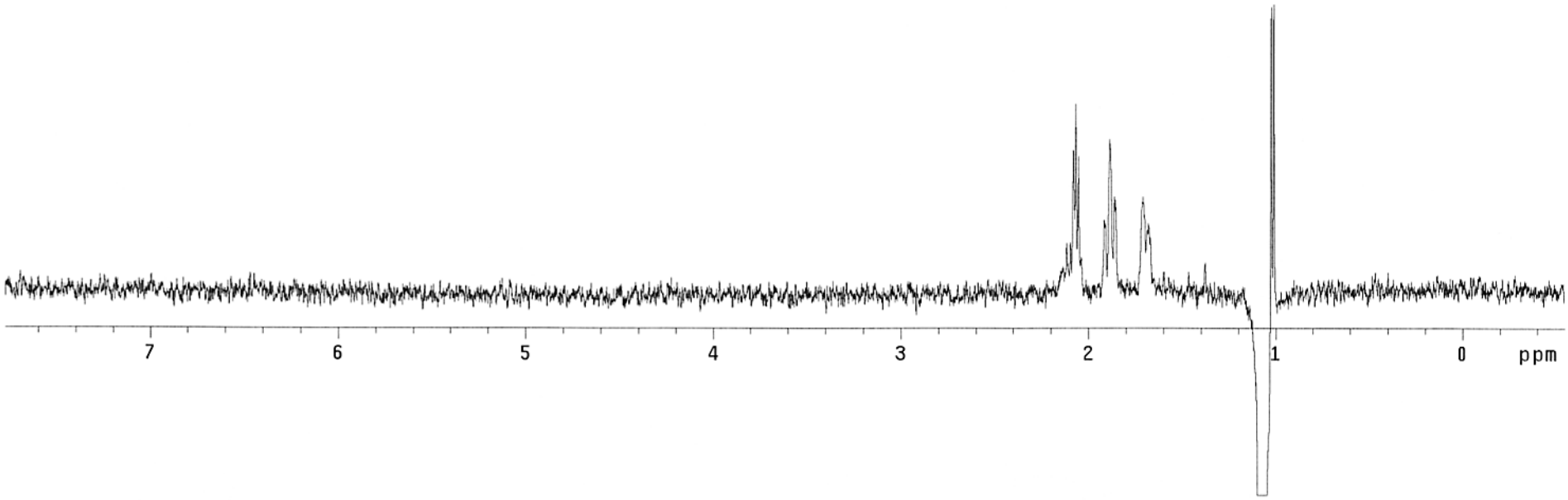
2 **3**

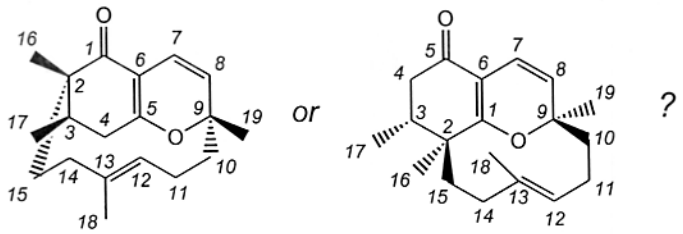
^{1}H NOE, **product**, 500 MHz, $CDCl_3$



2 **3**

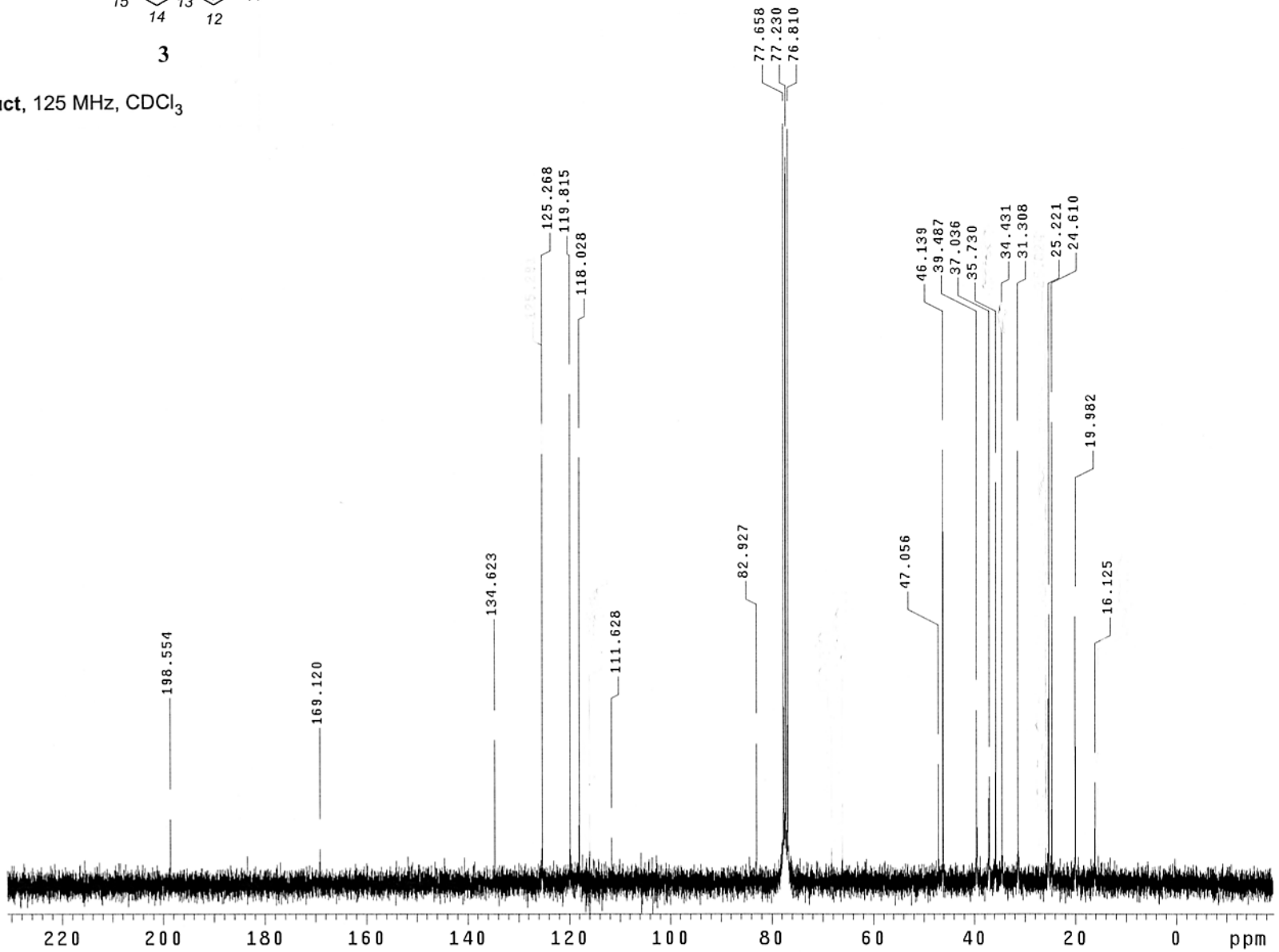
^{1}H NOE, **product**, 500 MHz, $CDCl_3$

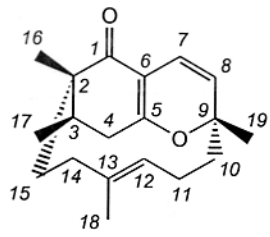




2 or 3 ?

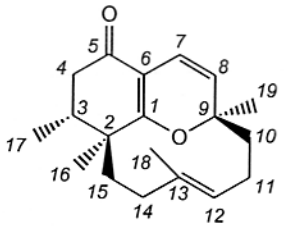
^{13}C NMR, **product**, 125 MHz, $CDCl_3$





2

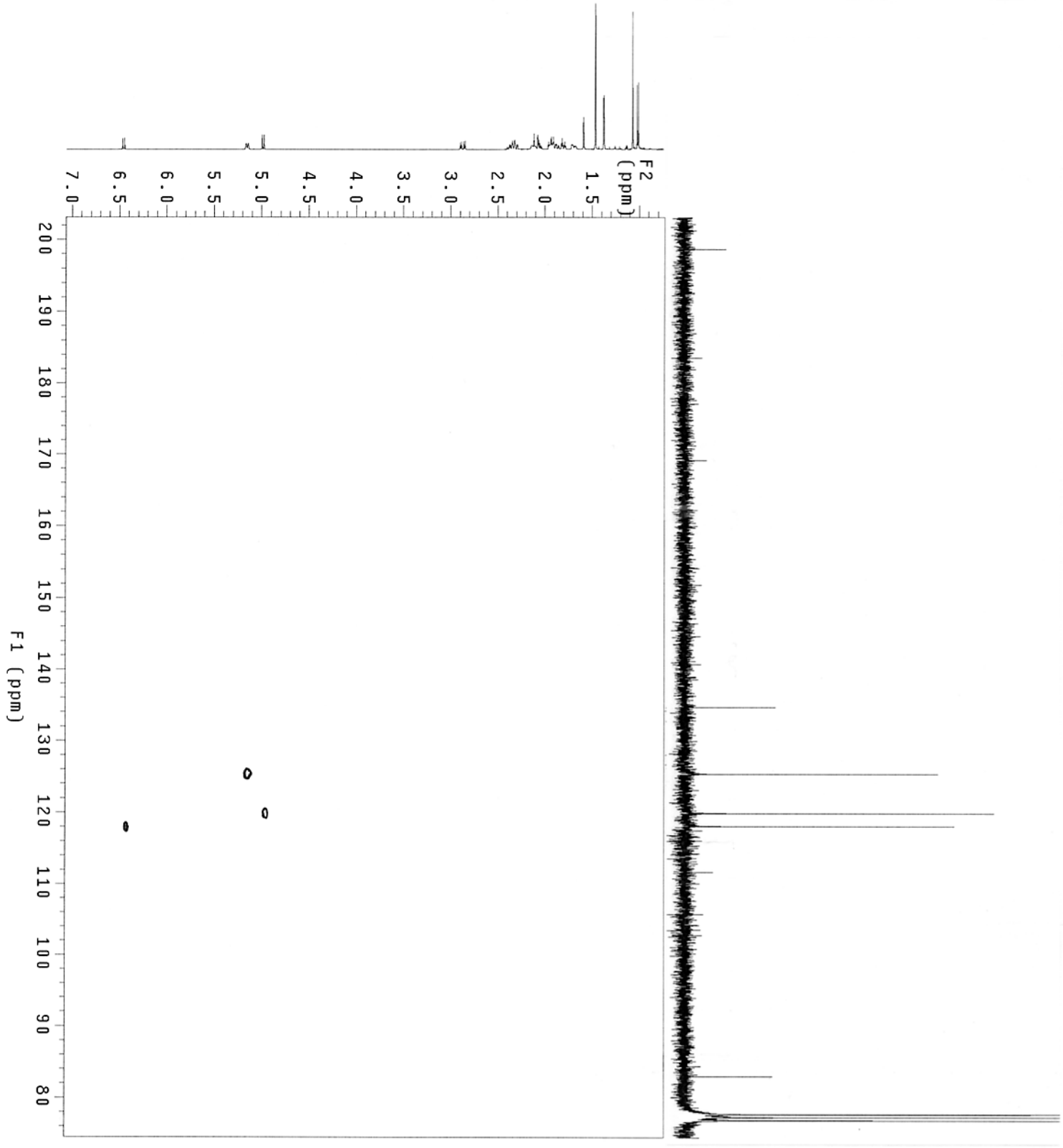
or

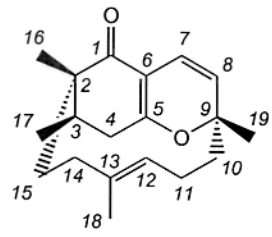


3

?

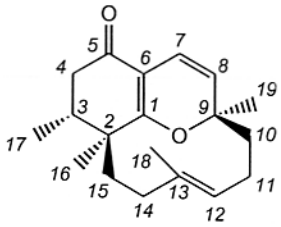
^{1}H-^{13}C HMQC, **product**, 500/125 MHz, $CDCl_3$





2

or



3

?

^{1}H-^{13}C HMBC, **product**, 500/125 MHz, $CDCl_3$