Chemistry 5361/8361 Thursday, November 7, 2002

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 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.

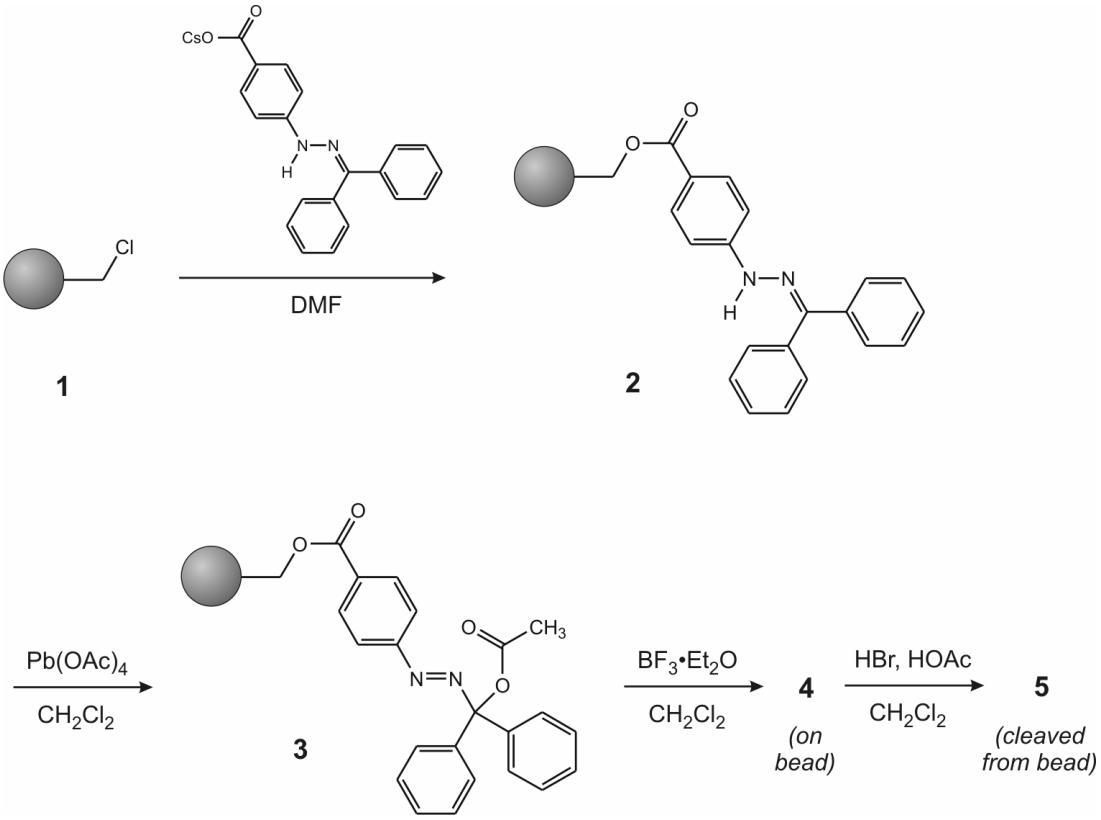
At the end of the 2 hour exam period you will be asked to return your exam to the proctor. (You may, of course, also turn the packet in earlier if you choose.) You are allowed to use any materials you brought with you before the exam. However, we ask that you not bring any materials in or out of the 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 21 pages, including this one. (The last page contains a chart of isotope ratios and exact atomic masses, and is not part of the graded exam.) Please check to make sure that your packet contains 21 pages before beginning your exam.

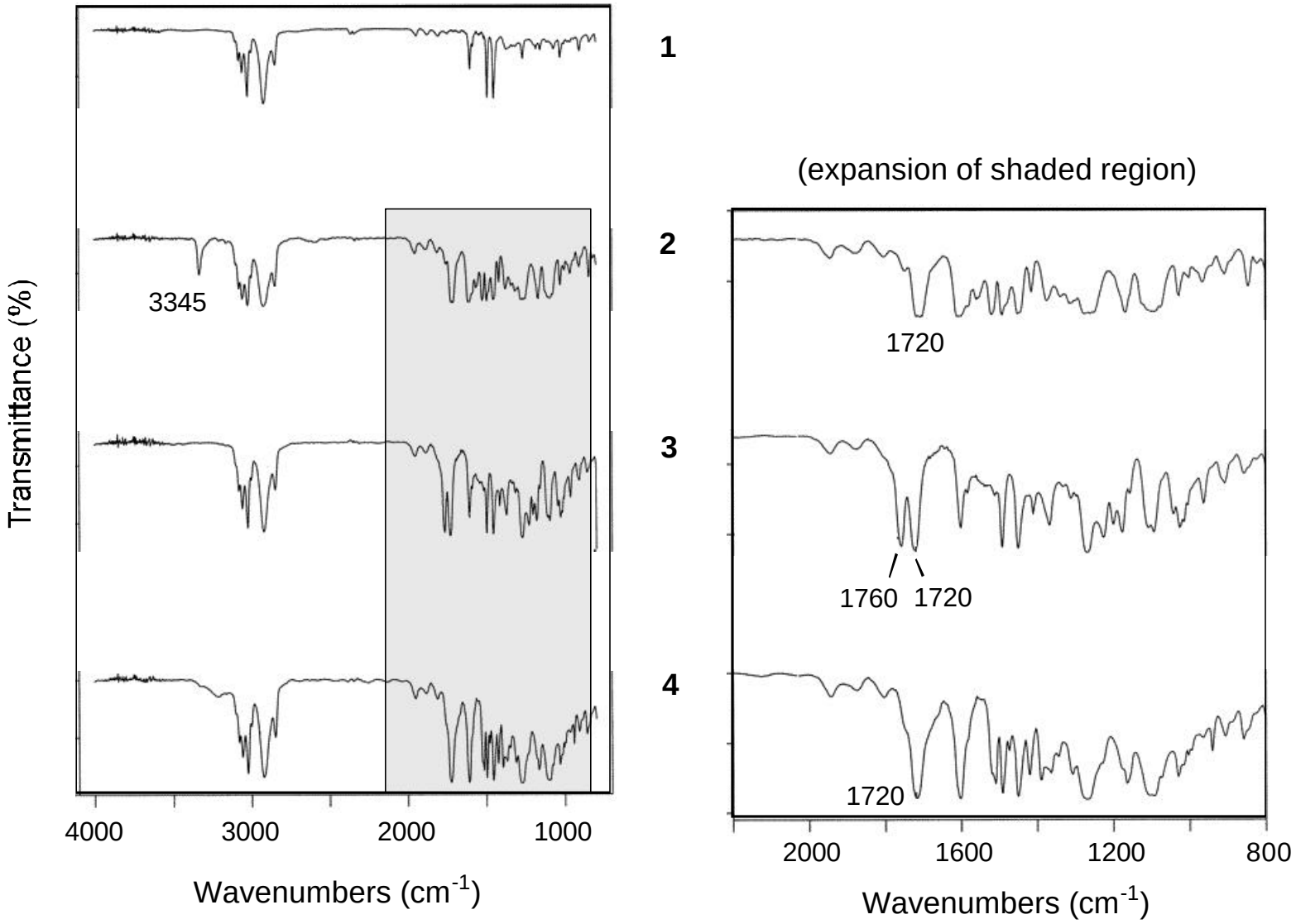
Name: _____

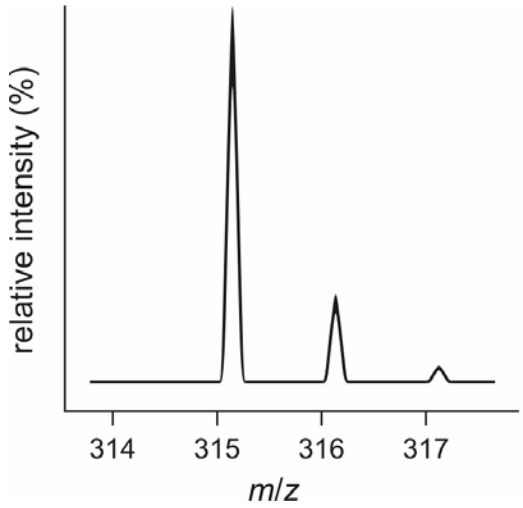
Signature: _____

1. One important recent development in IR spectroscopy of organic molecules has been on-bead, IR microspectroscopic characterization of combinatorial libraries. Bing Yan and coworkers at Novartis Pharmaceuticals reported the synthesis of a complex aromatic product **5** via surface reactions on chlorinated polystyrene (Merrifield) resin (**1**). Monitoring each step by IR spectroscopy meant that the product did not have to be cleaved from the resin for analysis until the very end of the synthesis.



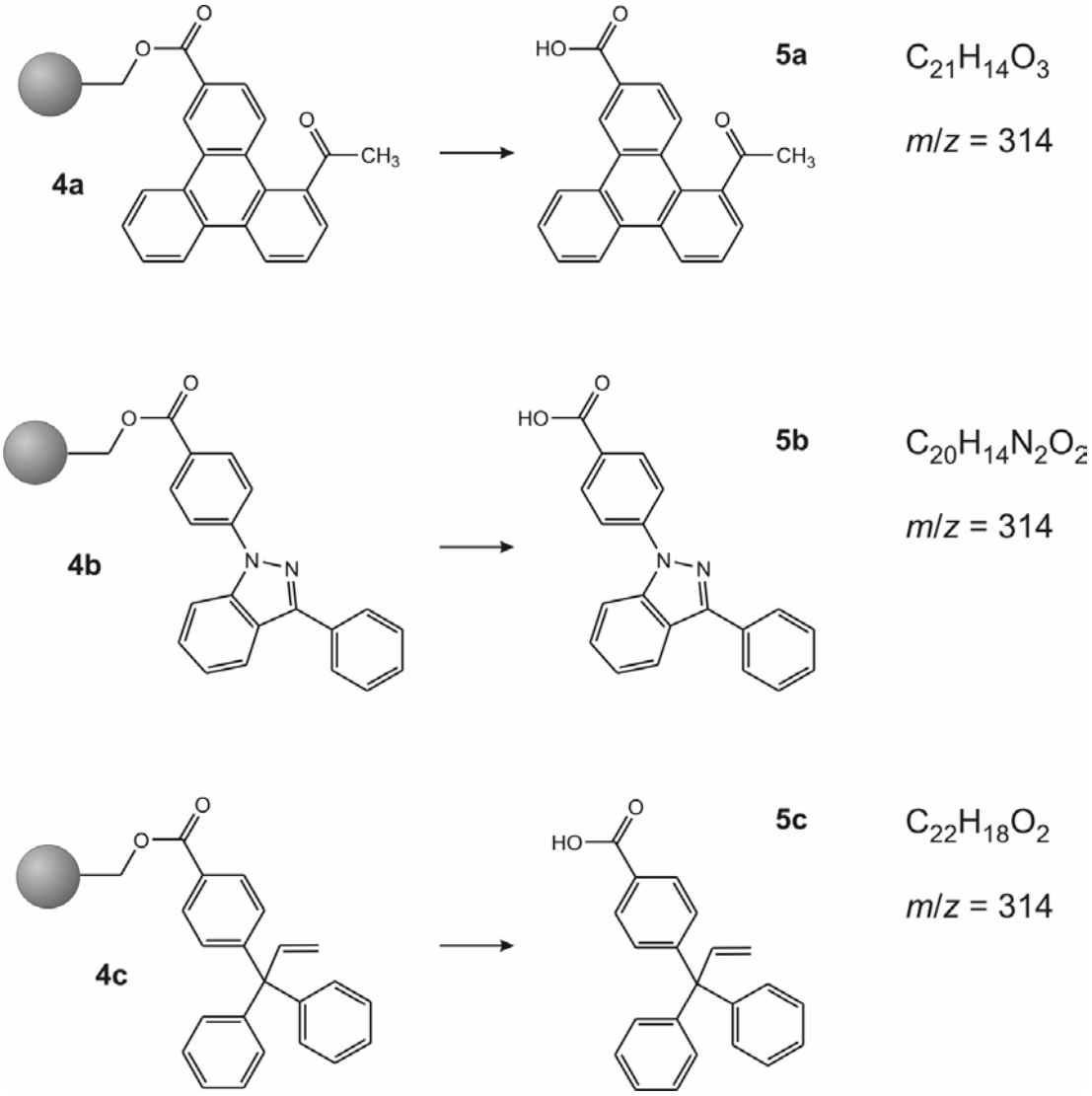
All steps between **1** and **4** were monitored by IR microspectroscopy, and the IR spectra obtained are shown on the next page. (Important peaks have been labeled.) Cleavage of the ester connection to the bead generated the product **5**, for which there was too little material to analyze by NMR. However, positive-ion-mode electrospray mass spectrometry (ESI-MS) gave the exact mass and isotopic pattern shown on page 4. Three candidate structures for **4** and **5** are also shown on page 4.


1
2
3
4
3345
(expansion of shaded region)
1720
1760
1720
1720
Transmittance (%)
4000
3000
2000
1000
Wavenumbers (cm-1)
2000
1600
1200
800
Wavenumbers (cm-1)

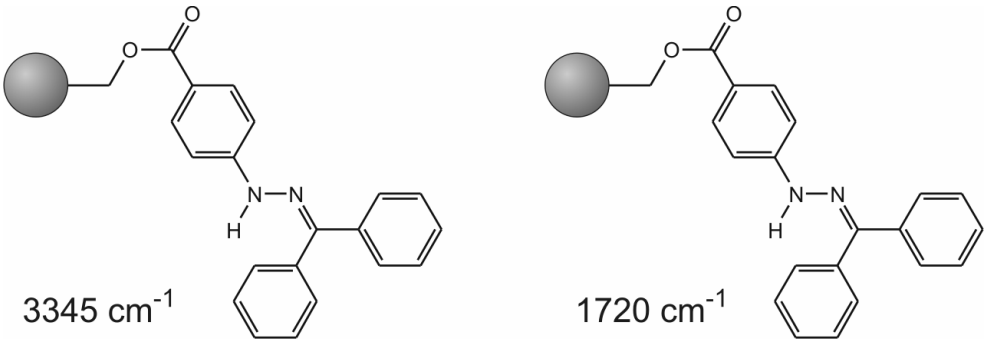


peak position (*m*/*z*)	relative intensity (%)
315.1138	100.0
316.1163	22.9
317.1156	2.5

Candidate structures for **4** and **5**:



a. (4 pts) In the structures of molecule **2** below, <u>circle</u> the structural features that are responsible for the IR absorbances observed at 3345 cm^{-1} and 1720 cm^{-1}.



b. (6 pts) How does the transformation from **2** to **3** change the IR spectrum? Why?

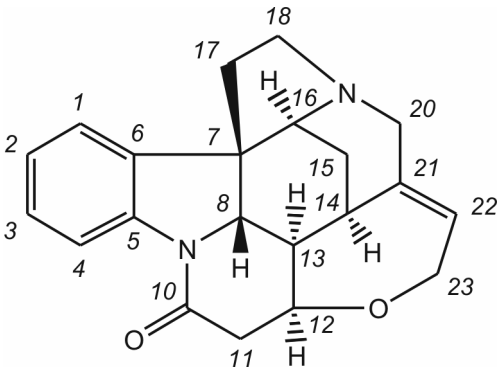
c. (8 pts) Yan considered **5a**, **5b**, and **5c** (m/z = 314) as potential candidate structures for **5**—but the parent peak he observed by mass spectrometry was one mass unit heavier (m/z = 315) than all of these. Explain why.

d. (20 pts) Based on the data at your disposal, which do you think is the correct structure of **5**—**5a**, **5b** or **5c**? Of the IR data, the exact mass peak positions, and the isotopic ratios, which were helpful to you in choosing the correct structure and which were not? Explain. (The tables on the last page of this exam will help you answer this question.)

Correct Structure:
(**5a**, **5b** or **5c**)

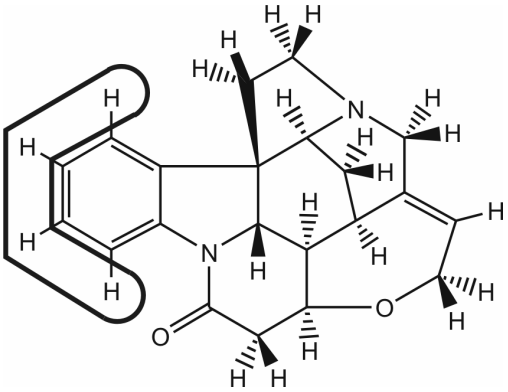
Explanation:

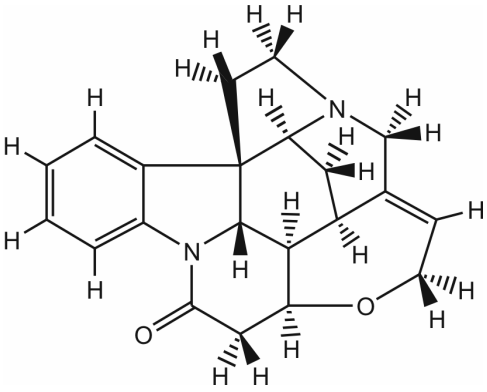
2. The spectra on pages 11-19 of this exam refer to strychnine, whose structure is given below:

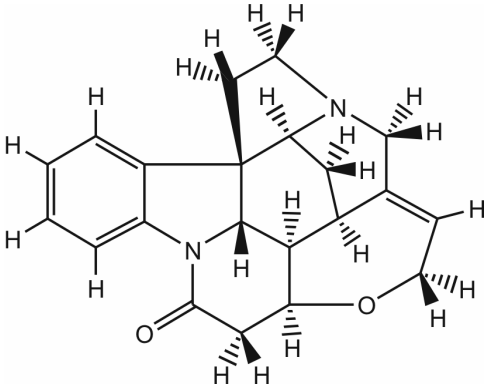


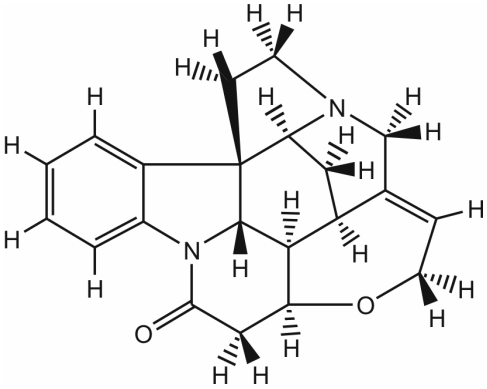
Page	Description
11	^{1}H NMR, 300 MHz, $CDCl_3$.
12-14	Close-ups of page 11, w/ integrations and peak labels.
15	^{1}H-^{1}H COSY, 300 MHz, $CDCl_3$.
16	Close-up of page 15.
17	^{1}H-^{13}C HMQC, 500 MHz, $CDCl_3$. *Writing on this page will be graded; see part c.*
18	Copy of page 17 (for scratch work). *Writing on this page will not be graded.*
19	^{1}H-^{1}H NOESY, 500 MHz, $CDCl_3$. *Writing on this page will be graded; see part d.*
20	Copy of page 18 (for scratch work). *Writing on this page will not be graded.*

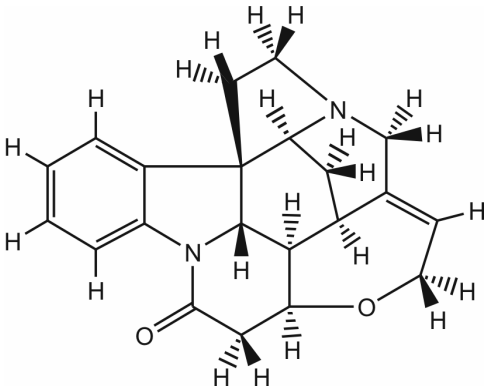
a. (4 pts) There are five, independent sets of coupled protons in the structure of strychnine. On the structures on the following page, circle each of these sets. (One of the sets has already been circled as an example.) *Every proton in strychnine belongs to a coupled set. Make sure you have not left any out.*











b. (26 pts) In the COSY spectra shown on pages 15-16, crosspeaks corresponding to the four simpler sets of coupled protons are shown in gray, and those corresponding to the most complicated set are in black. (Gray and black peaks that overlap are shown as black.) Based on the information in the ^{1}H-^{1}H COSY and ^{1}H-^{13}C HMQC NMR spectra, assign chemical shifts, within 0.05 ppm, to each of the protons in the chart below.

proton	δ (ppm)	
H_8		
H_{11} (x2)		
H_{12}		
H_{13}		
H_{14}		
H_{15} (x2)		
H_{16}		
H_{20} (x2)		
H_{23} (x2)		

c. (8 pts) The HMQC data can be used to verify your assignment of the paired protons (H_{11}, H_{15}, H_{20} and H_{23}) listed above. On the HMQC spectrum on page 17, **circle** each crosspeak that corresponds to these four pairs of protons, and **connect** each pair with arrows. (The identical HMQC spectrum on page 18 is for scratch work only. Marks on page 18 will not be graded.)

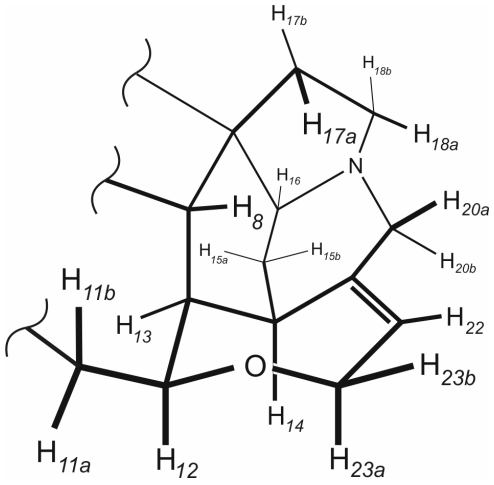
d. (12 pts) The four pairs of protons discussed above ($H_{11a/b}$, $H_{15a/b}$, $H_{20a/b}$ and $H_{23a/b}$) cannot be stereospecifically assigned from only the COSY data. However, the NOESY spectrum of strychnine allows for definitive assignment of all of these protons.

i) On the NOESY spectrum on page 19, circle **three** crosspeaks that help you assign at least one of these pairs. (The identical NOESY spectrum on page 20 is for scratch work only. Marks on page 19 will not be graded.) Label these circles **A**, **B** and **C**.

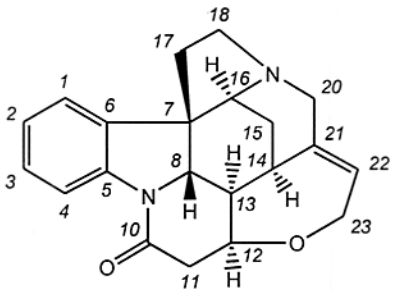
ii) Then, on the 3-dimensional structure at the top of page 19, show the NOE interaction responsible for each crosspeak you labeled with an arrow, and label the arrows **A**, **B** and **C** accordingly.

e. (12 pts) Given the information you discovered above, correctly assign **three** of the four pairs of protons from part b in the chart below. (Your choice which three. Please leave the fourth set blank.)

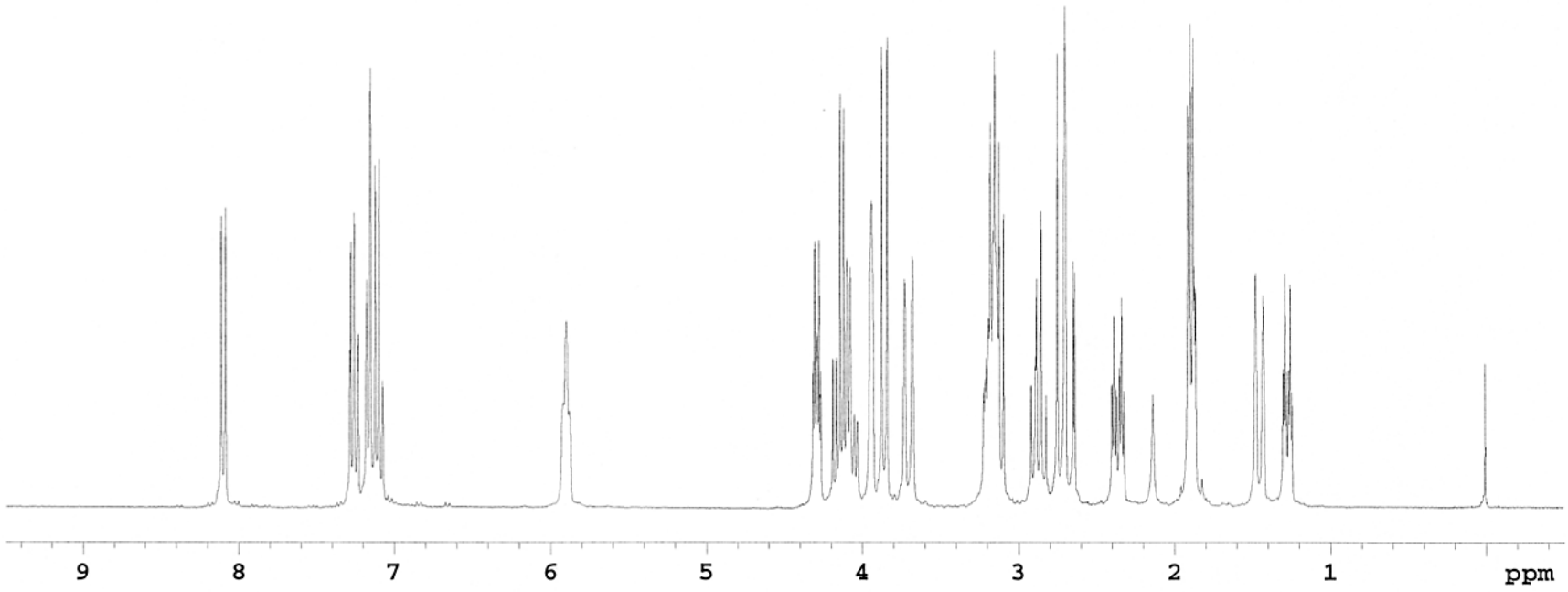
proton #	δ (ppm) for H_a	δ (ppm) for H_b
H_{11}		
H_{15}		
H_{20}		
H_{23}		

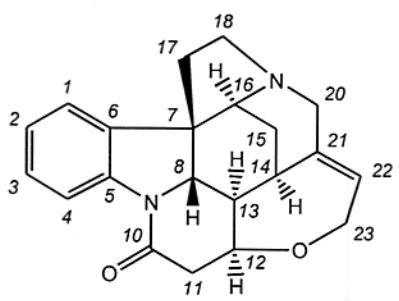


Thicker bonds and larger atom labels are closer to you; thinner bonds and smaller labels are receding into the page. This part of strychnine is shaped like a cup, with H_8, H_{17a} and O at the outer rim and $H_{15a/b}$ and H_{16} at the bottom.

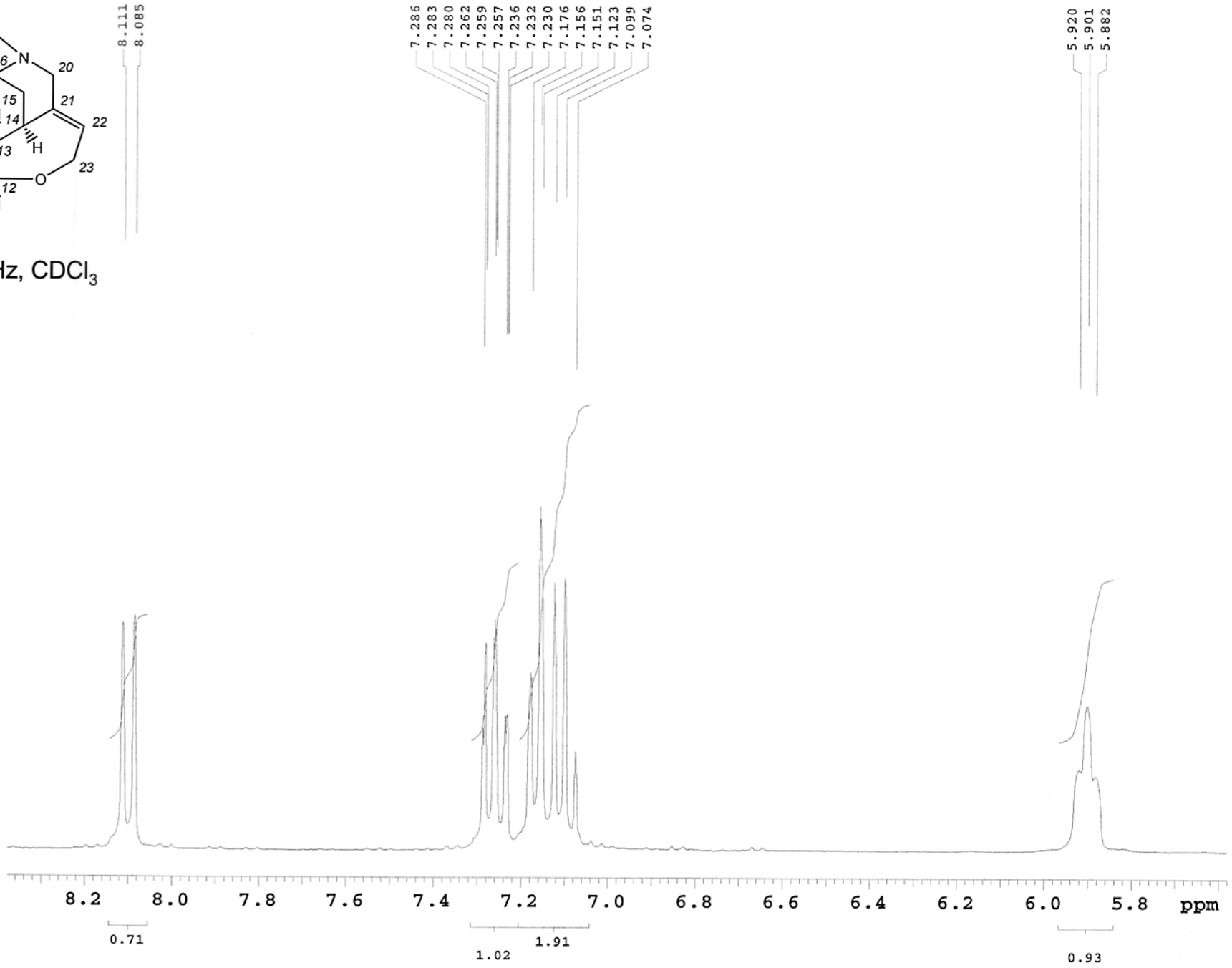


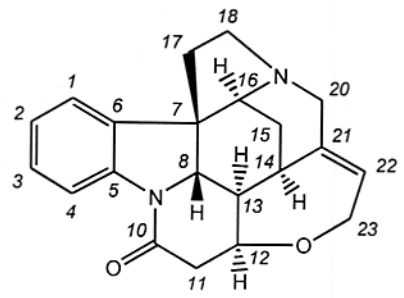
^{1}H NMR, 300 MHz, $CDCl_3$



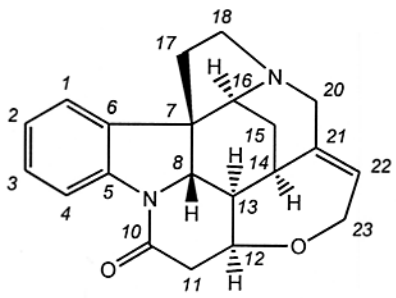


^{1}H NMR, 300 MHz, $CDCl_3$

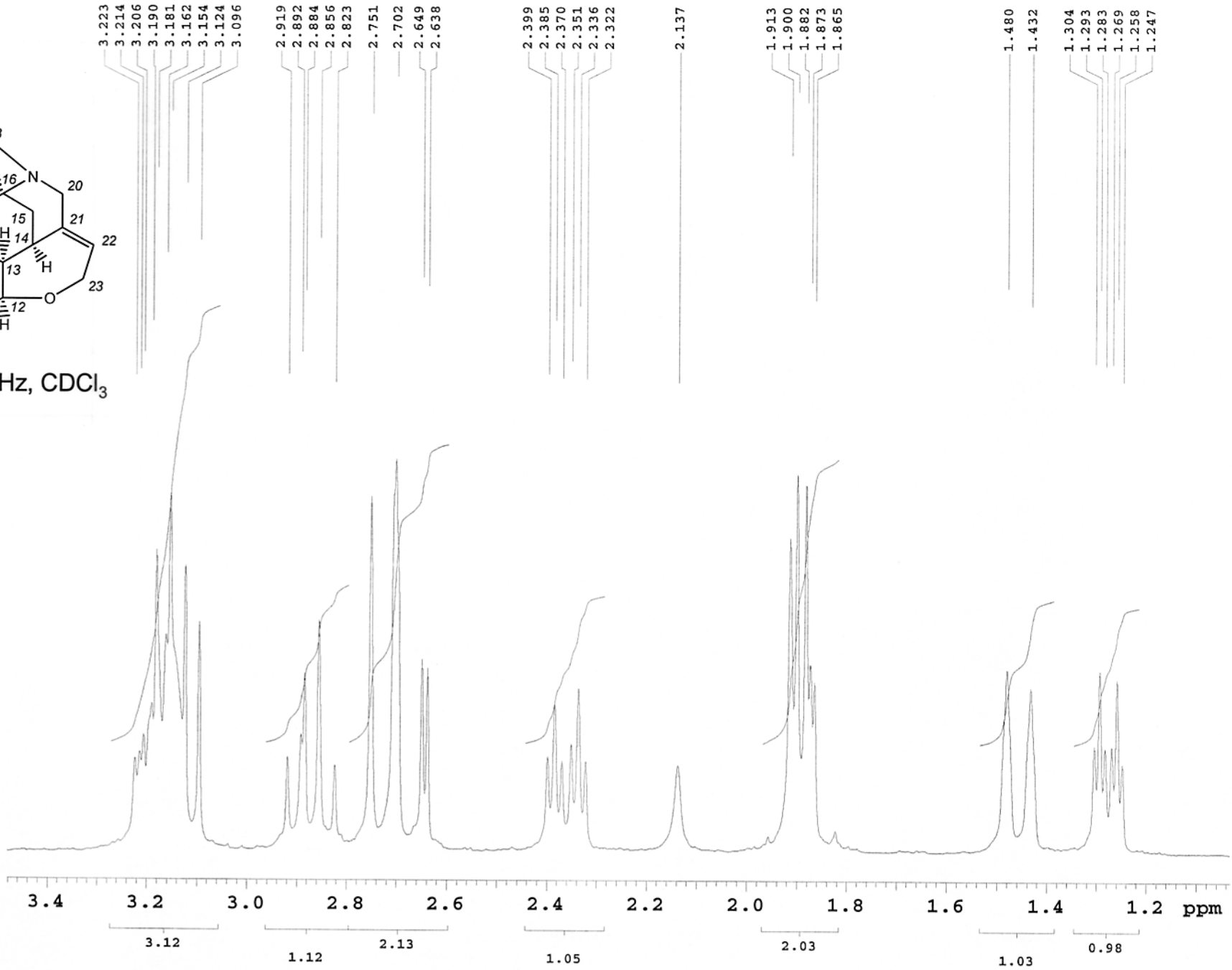




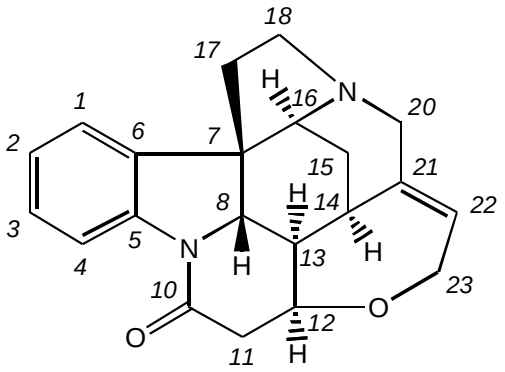
^{1}H NMR, 300 MHz, $CDCl_3$



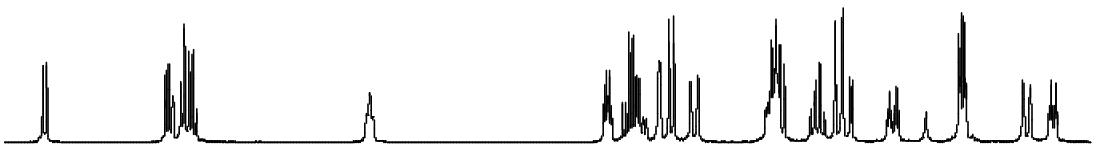
^{1}H NMR, 300 MHz, $CDCl_3$

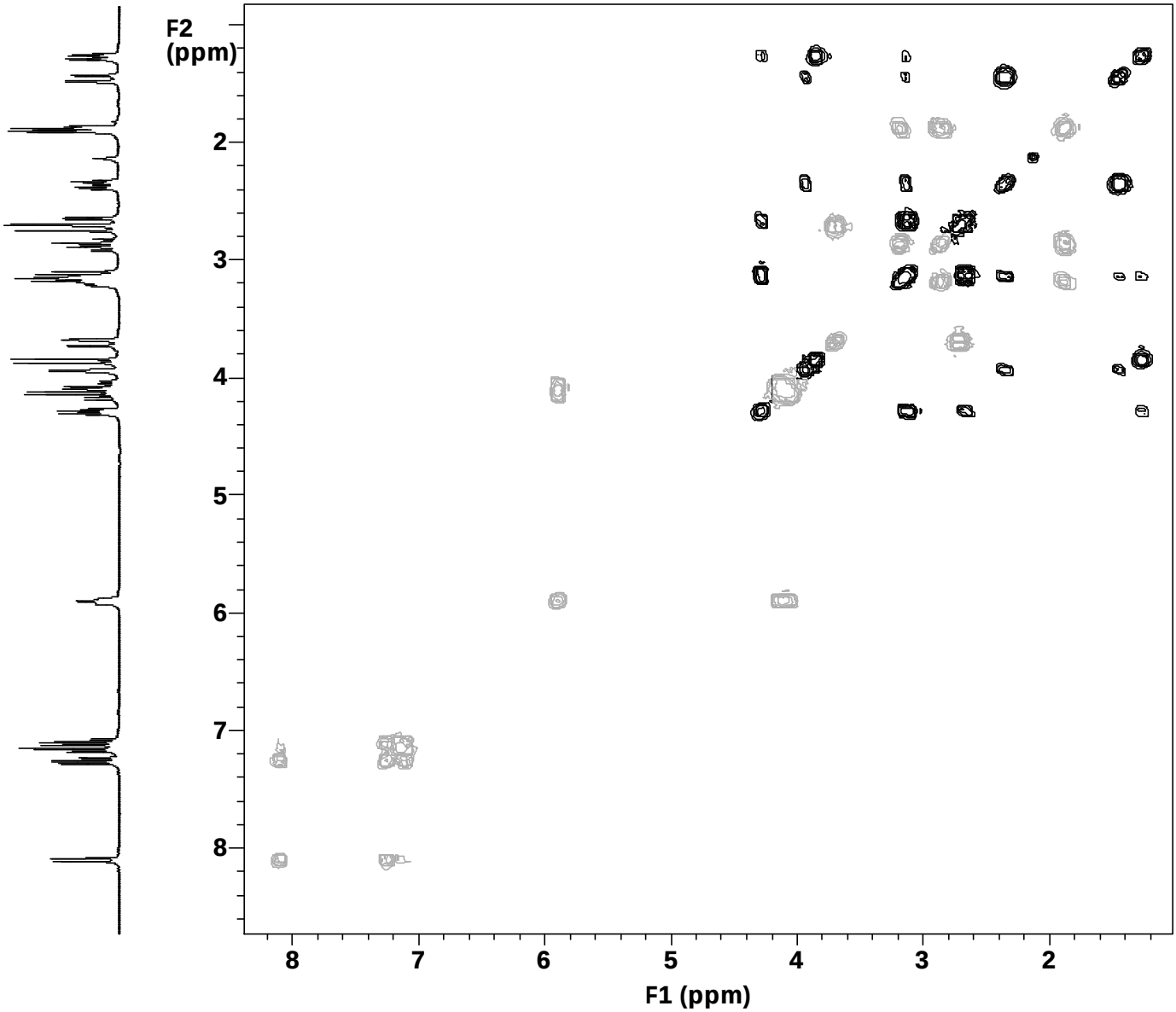


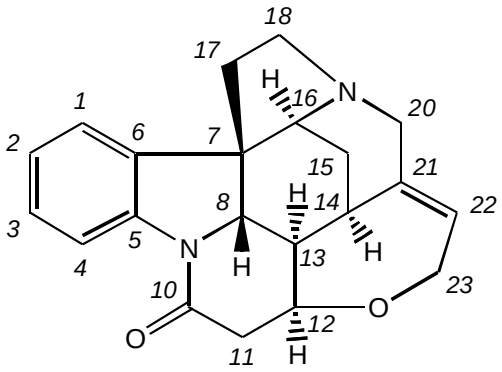
14



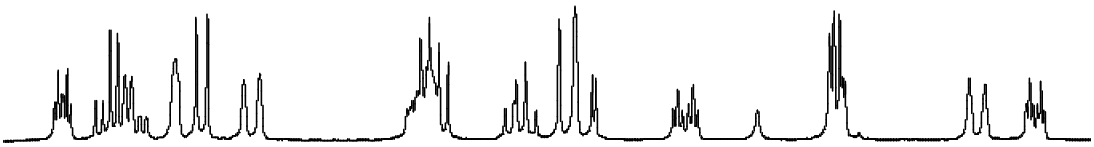
^{1}H-^{1}H COSY, 300 MHz, $CDCl_3$

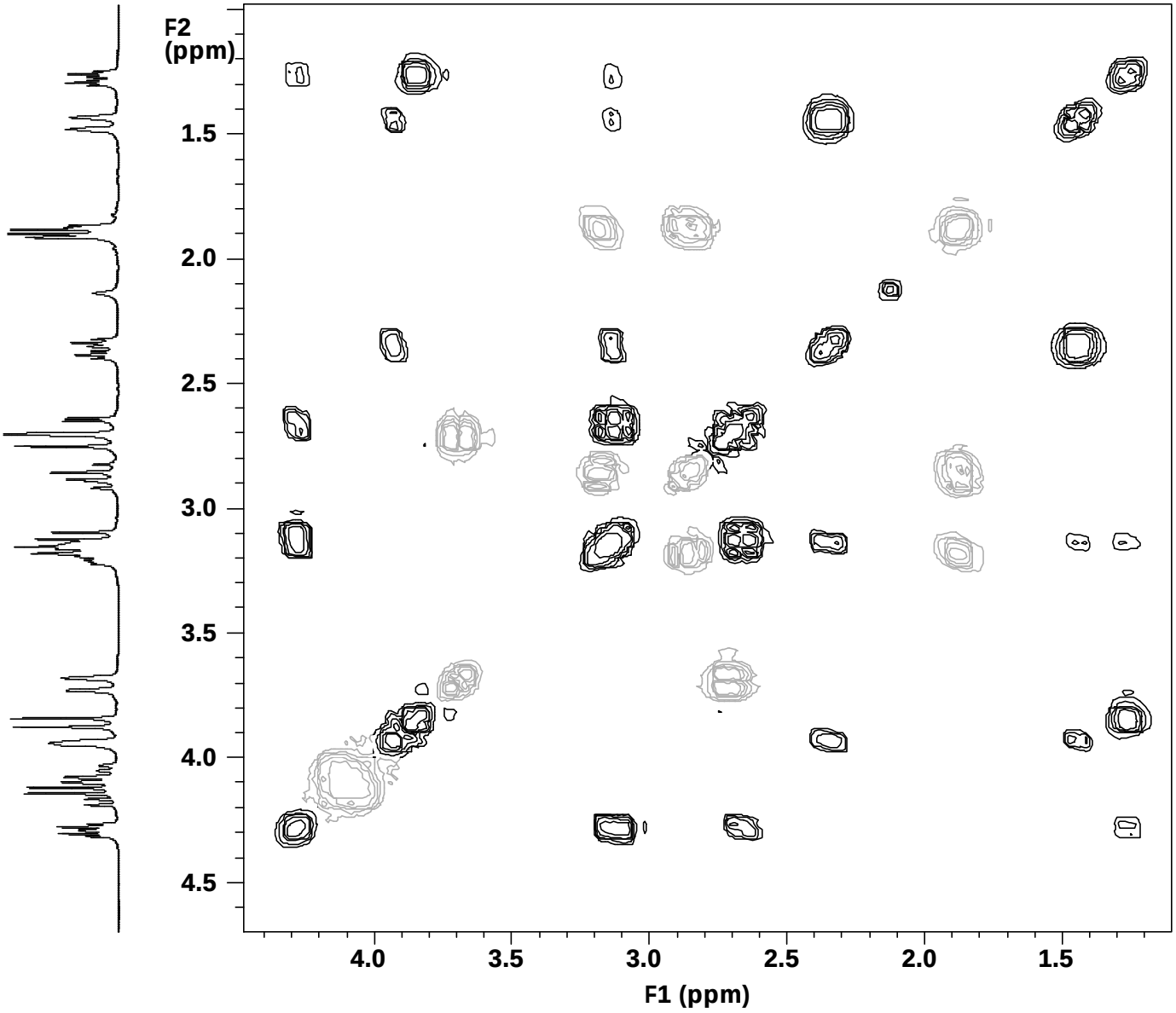






^{1}H-^{1}H COSY, 300 MHz, $CDCl_3$





Univ of Minnesota, VI-500

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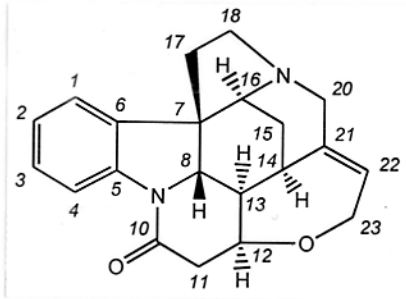
Date: Oct. 26, 2002
Solvent: cdcl3
File: strhmqc
Starting Time: 12:35:02
Completion Time: 12:40:23
Total acq. time 5 minutes

UNITYplus-500 "spectrum"
Temp. 23.0 C / 296.1 K

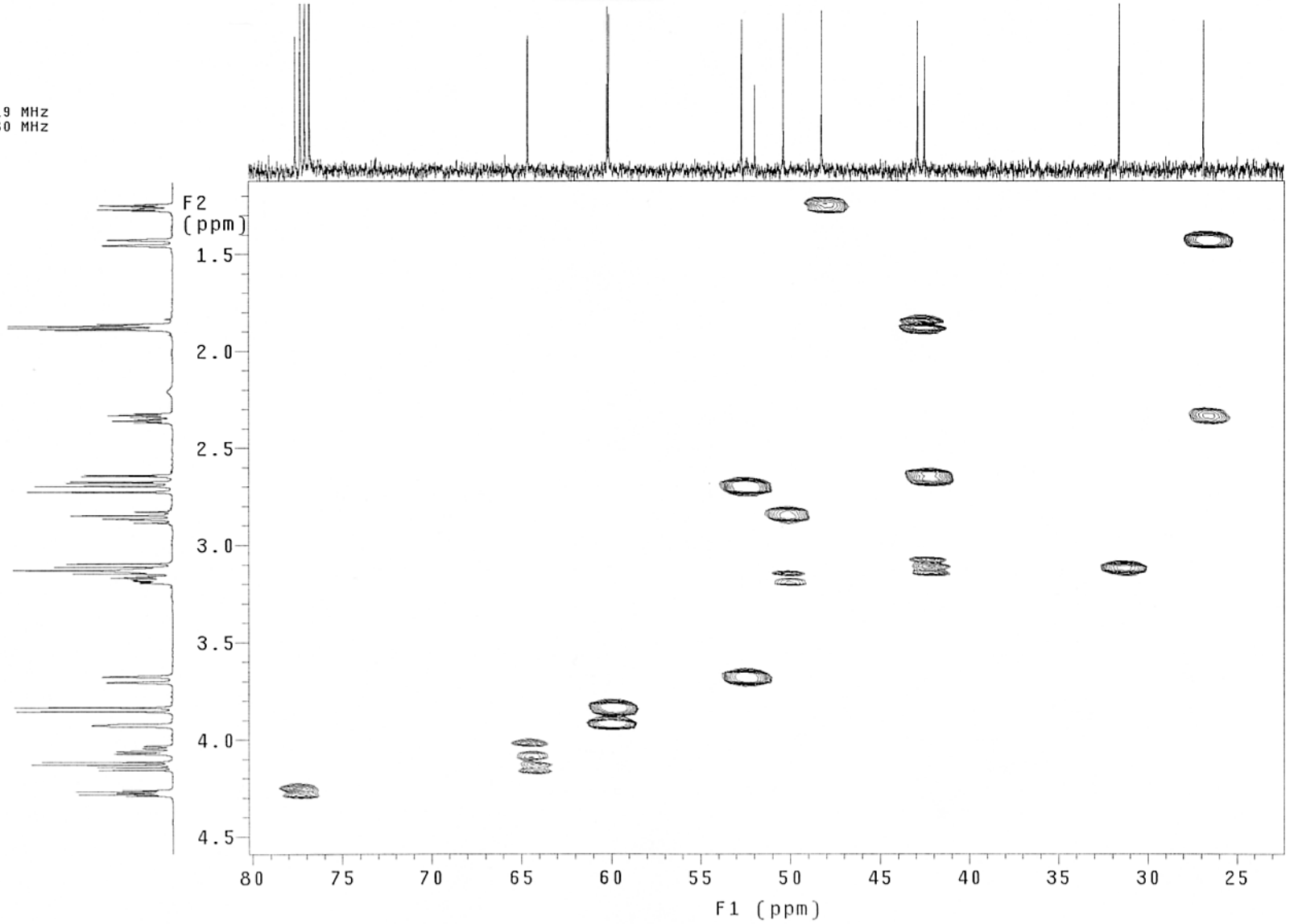
PULSE SEQUENCE: ghmqc
Relax. delay 1.388 sec
Acq. time 0.112 sec
Width 4559.4 Hz
2D Width 25798.1 Hz
Single scan
192 increments
OBSERVE H1, 499.8671219 MHz
DECOUPLE C13, 125.7039580 MHz
Power 47 dB
on during acquisition
off during delay
wurst modulated
DATA PROCESSING
Sine bell 0.056 sec
F1 DATA PROCESSING
Sine bell 0.004 sec
FT size 1024 x 1024



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

Writing on this page **will** *be graded.*

2 peaks



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Univ of Minnesota, VI-500

Pulse Sequence: ghmqc

User: 1-14-87
Date: Oct. 26, 2002
Solvent: cdcl3
File: strhmqc
Starting Time: 12:35:02
Completion Time: 12:40:23
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UNITYplus-500 "spectrum"
Temp. 23.0 C / 296.1 K

PULSE SEQUENCE: ghmqc
Relax. delay 1.388 sec
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Width 4559.4 Hz
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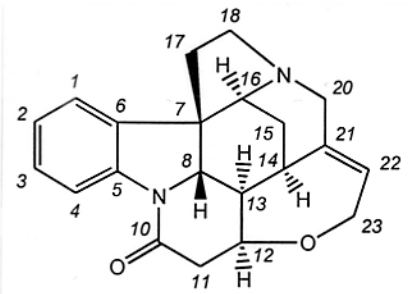
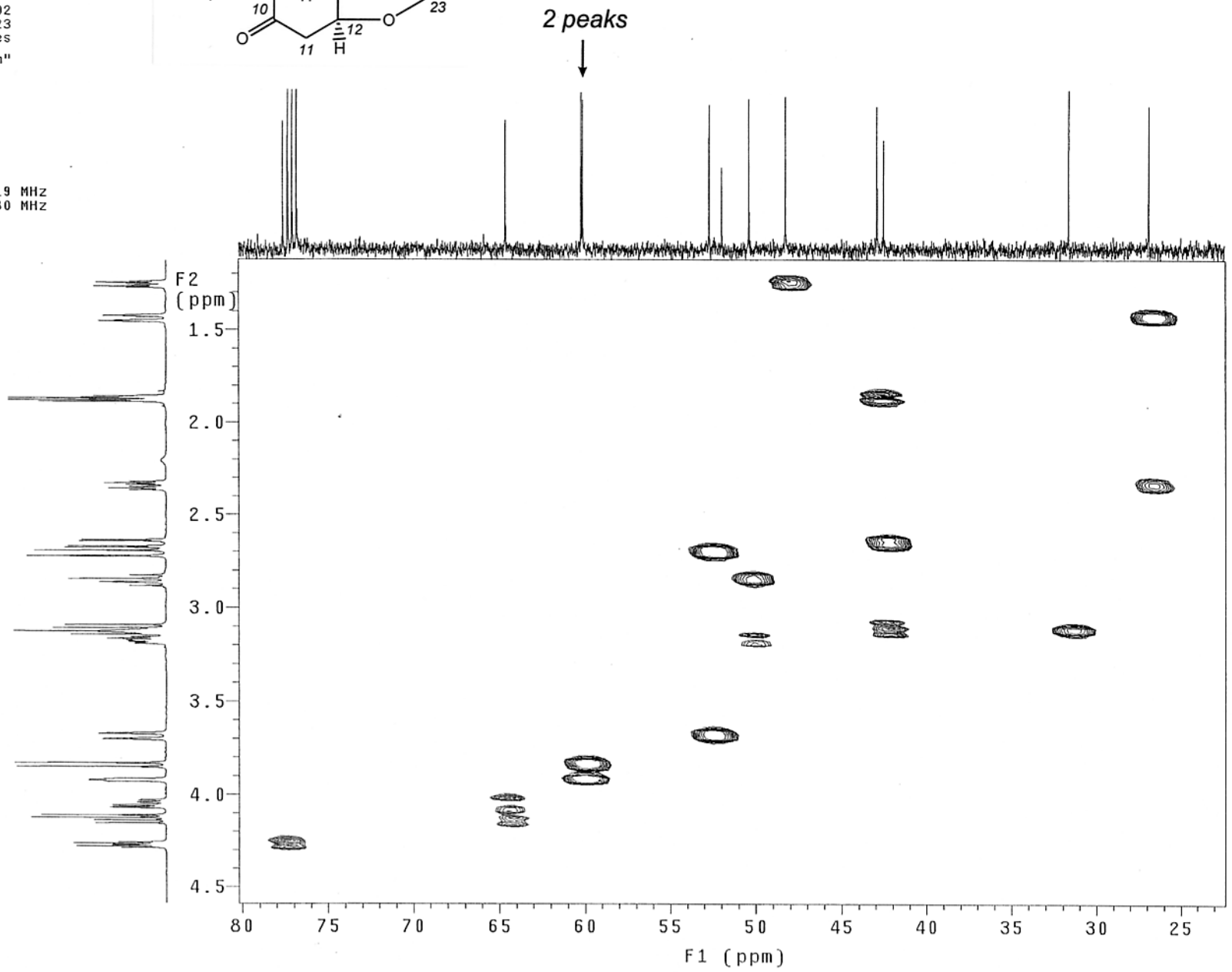
wurst modulated
DATA PROCESSING
Sine bell 0.056 sec
F1 DATA PROCESSING
Sine bell 0.004 sec
FT size 1024 x 1024



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

Writing on this page will **not** *be graded.*
Use this page for scratch work.



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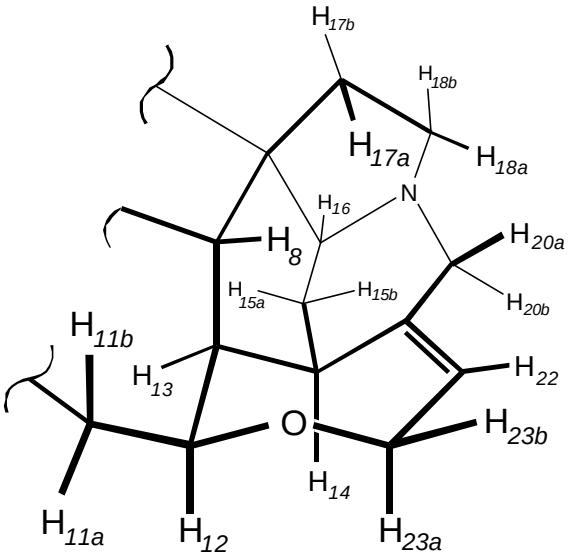

^{1}H-^{1}H NOESY, 500 MHz, $CDCl_3$

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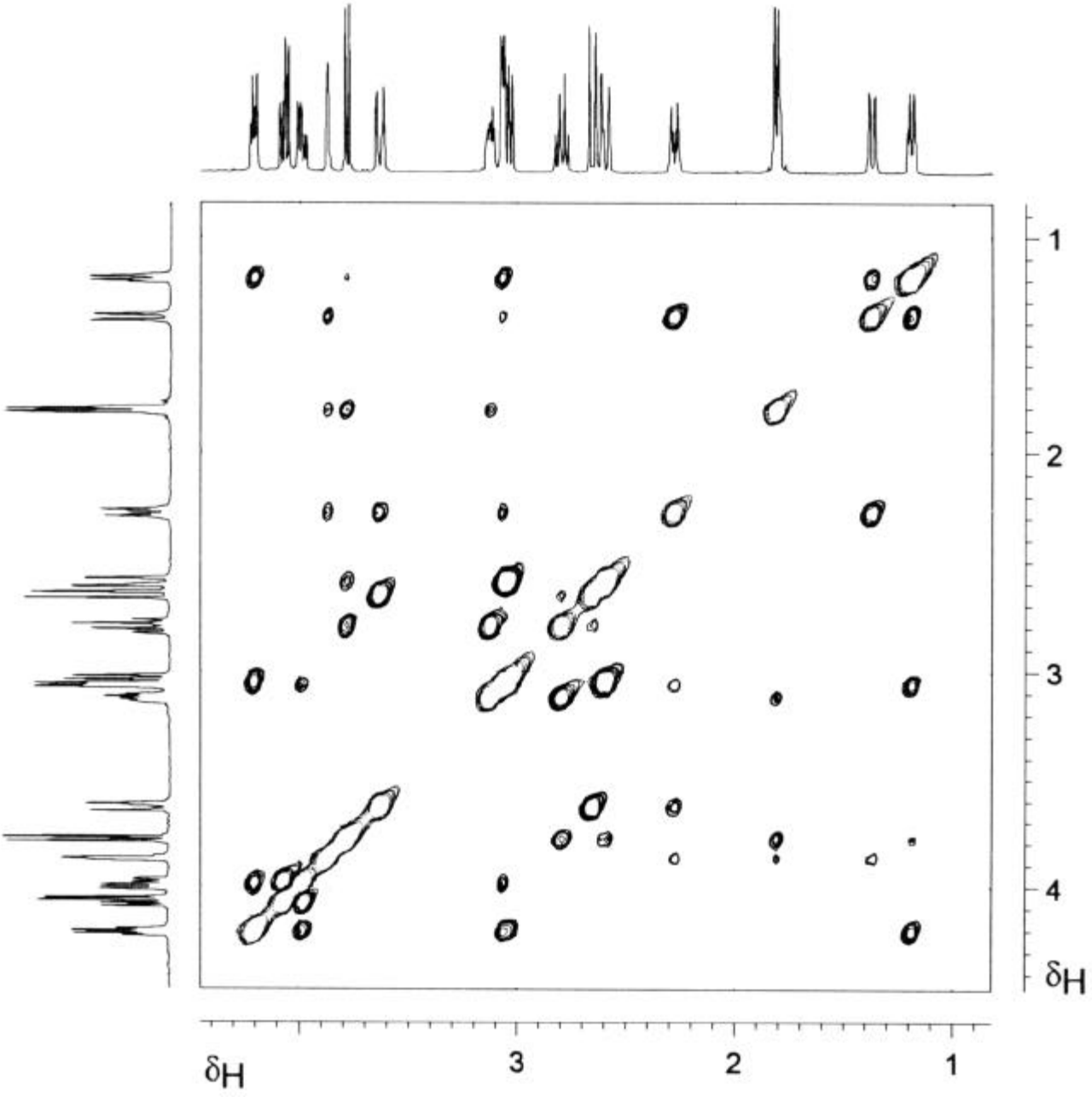
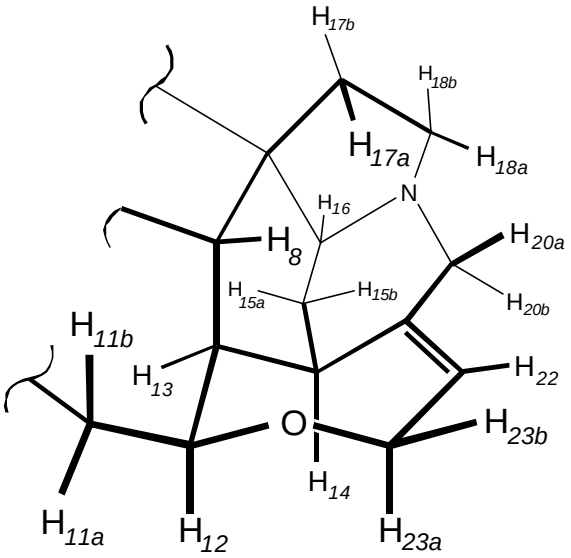
will *be graded.*





^{1}H-^{1}H NOESY, 500 MHz, $CDCl_3$

*Writing on this page will **not** be graded. Use this page for scratch work.*

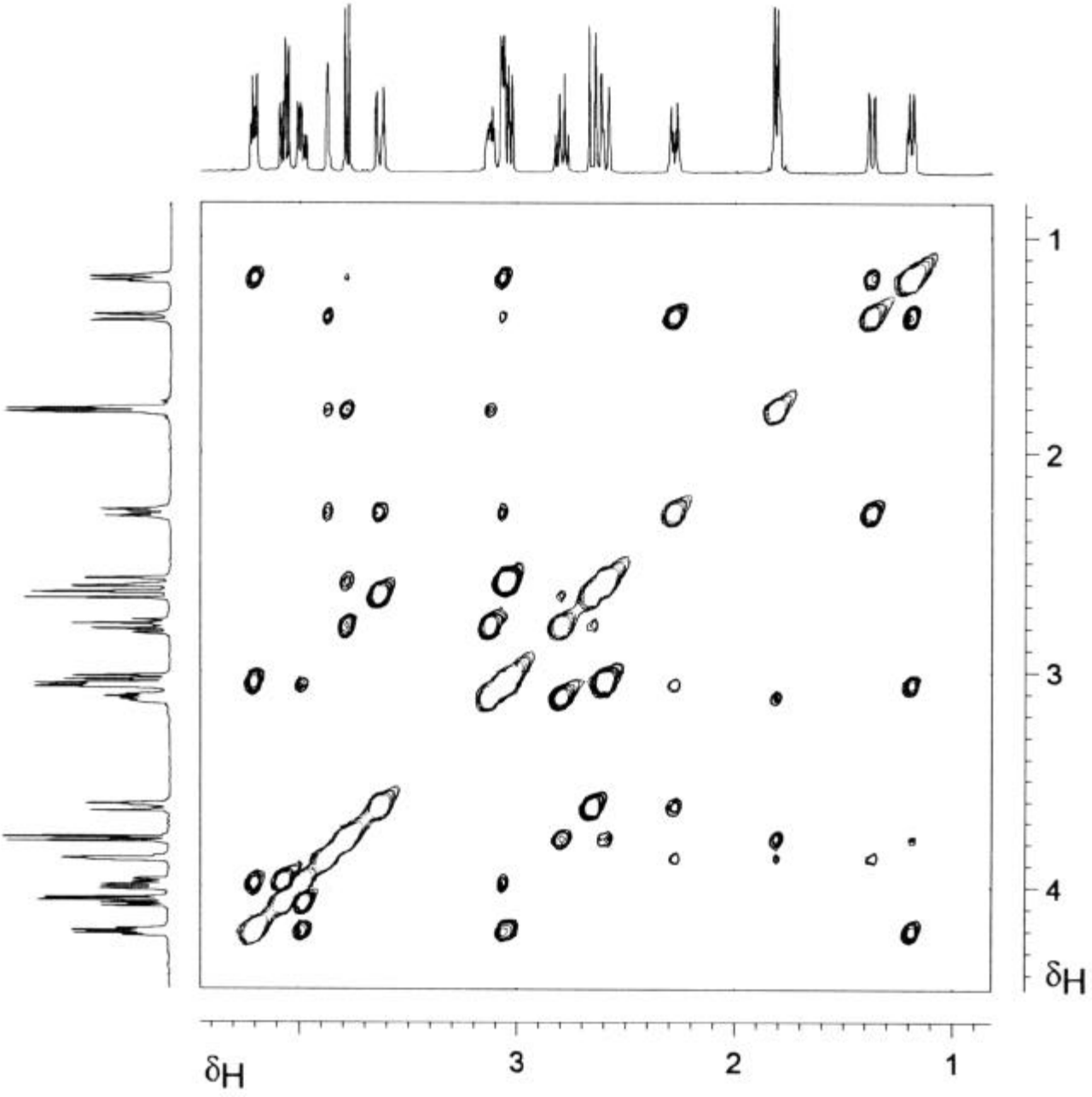


TABLE 6.1 Exact Isotope Masses for Calculating MS Molecular Weights of Important Elements[a]

Element	*Atomic Weight*	*Nuclide*	*Mass*	*Relative Abundance*
Hydrogen	1.00797	^{1}H	1.00783	100.0
		D(^{2}H)	2.01410	0.015
Carbon	12.01115	^{12}C	12.00000[b]	100.0
		^{13}C	13.00336	1.11
Nitrogen	14.0067	^{14}N	14.0031	100.0
		^{15}N	15.0001	0.37
Oxygen	15.9994	^{16}O	15.9949	100.0
		^{17}O	16.9991	0.04
		^{18}O	17.9992	0.20
Fluorine	18.9984	^{19}F	18.9984	100.0
Silicon	28.086	^{28}Si	27.9769	100.0
		^{29}Si	28.9765	5.06
		^{30}Si	29.9738	3.36
Phosphorus	30.974	^{31}P	30.9738	100.0
Sulfur	32.064	^{32}S	31.9721	100.0
		^{33}S	32.9715	0.79
		^{34}S	33.9679	4.43
Chlorine	35.453	^{35}Cl	34.9689	100.0
		^{37}Cl	36.9659	31.98
Bromine	79.909	^{79}Br	78.9183	100.0
		^{81}Br	80.9163	97.3
Iodine	126.904	^{127}I	126.9045	100.0

[a] Round-off to the nearest 0.0001 amu when analyzing high resolution data. Round-off to the nearest amu when examining low resolution data.
[b] Standard.

Table 2.2. *Isotopic contributions for carbon and hydrogen. If the abundance of the peak A is 100 (after correction for isotopic contributions to it), then its isotopic contributions will be:*

	(A + 1)	(A + 2)		(A + 1)	(A + 2)	(A + 3)
C_1	1.1	0.00	C_{16}	18	1.5	0.1
C_2	2.2	0.01	C_{17}	19	1.7	0.1
C_3	3.3	0.04	C_{18}	20	1.9	0.1
C_4	4.4	0.07	C_{19}	21	2.1	0.1
C_5	5.5	0.12	C_{20}	22	2.3	0.2
C_6	6.6	0.18	C_{22}	24	2.8	0.2
C_7	7.7	0.25	C_{24}	26	3.3	0.3
C_8	8.8	0.34	C_{26}	29	3.9	0.3
C_9	9.9	0.44	C_{28}	31	4.5	0.4
C_{10}	11.0	0.54	C_{30}	33	5.2	0.5
C_{11}	12.1	0.67	C_{35}	39	7.2	0.9
C_{12}	13.2	0.80	C_{40}	44	9.4	1.3
C_{13}	14.3	0.94	C_{50}	55	15	2.6
C_{14}	15.4	1.1	C_{60}	66	21	4.6
C_{15}	16.5	1.3	C_{100}	110	60	22

For each additional element present, add *per atom*:
(A + 1): N, 0.37; O, 0.04; Si, 5.1; S, 0.79.
(A + 2): O, 0.20; Si, 3.4; S, 4.4; Cl, 32.0; Br, 97.3.
Typical values for (A + 4): C_{25}, 0.02; C_{40}, 0.13; C_{100}, 5.7.