Chemistry 416 “Spectroscopy”
Fall Semester 1997
Dr. Rainer Glaser

*The **Final** Learning Experience*

Monday, December 15, 1997
3:00 - 5:00 pm

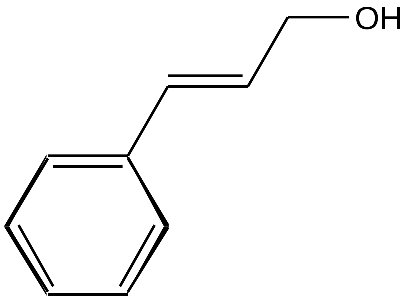
Name:
Answer Key

	Maximum	Earned
Question 1 (Combination I)	20	
Question 2 (Combination II)	20	
Question 3 (NOE)	20	
Question 4 (Natural Prod.)	40	
Total	100	
	X 2	

Question 1. Combination Problem I. (20 points)

Problem 21 given on the following page is taken from the book by Pavia, Lampman, and Kriz. In the space below, provide the structure of the unknown and argue for the structure you suggest. To provide the correct structure without any explanations will earn you only 10 points. Partial credit will be given for pieces of correct information deduced from the spectra.

trans 3-phenyl-2-propen-1-ol (*trans* cinnamyl alcohol)



The alcohol group stands out in the IR! Also broad NMR signal at 2.2 ppm.

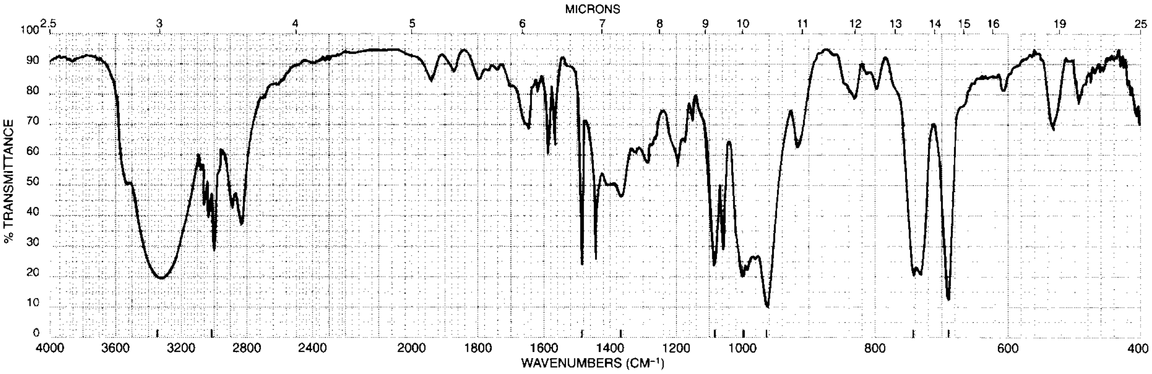
The olefinic region contains a doublet (15.9 Hz) and a dd (15.9 Hz, 5.7Hz).
The 15.9 Hz coupling constant shows that the -CH=CH- is *trans*.
The doublet shows exclusive coupling to the other olefinic H.
The dd also couples to an aliphatic H.

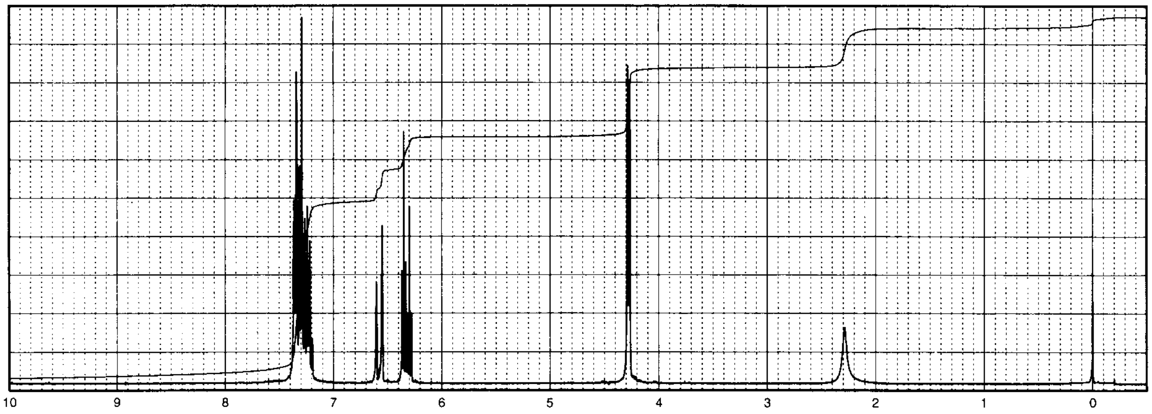
The signal at 4.3 ppm is the $C\underline{H}_2$-OH. The 5.7 Hz coupling shows up.
The 1.4 Hz coupling is the longer range coupling to CH that is farther away.

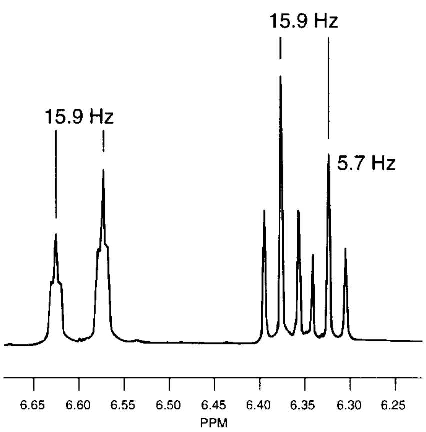
$-CH=CH-CH_2-OH$ identified, leaves $-C_6H_5$, a phenyl.

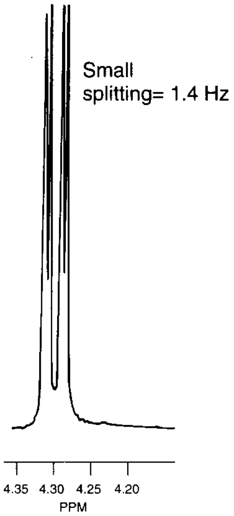
PROBLEM 21

This compound has the molecular formula $C_9H_{10}O$. We have supplied you with the IR and proton NMR spectra. The expansions of the interesting sets of peaks centering near 4.3, 6.35, and 6.6 ppm in the proton NMR are provided, as well. Do not attempt to interpret the messy pattern near 7.4 ppm for the aromatic protons. The broad peak at 2.3 ppm (one proton) is solvent- and concentration-dependent.





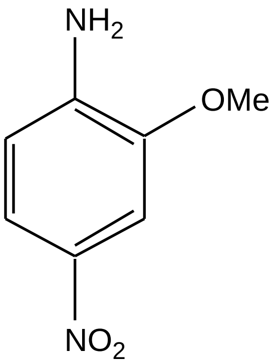




Question 2. Combination Problem II. (20 points)

Problem 23 given on the following page is taken from the book by Pavia, Lampman, and Kriz. In the space below, provide the structure of the unknown and argue for the structure you suggest. To provide the correct structure without any explanations will earn you only 10 points. Partial credit will be given for pieces of correct information deduced from the spectra.

2-Methoxy-4-nitroaniline



IR: Primary amine! Two sharp peaks > 3300 1/cm, no C=O.
Leaves C7H6NO3.

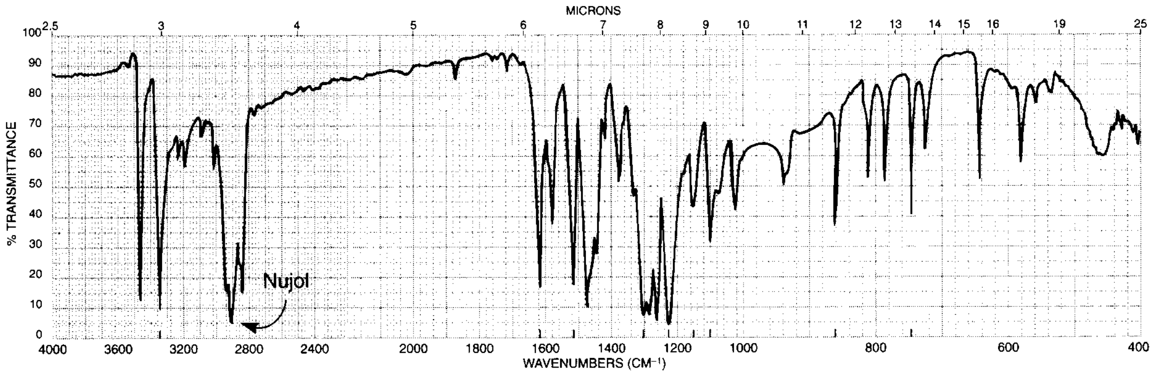
Singlet just below 4 ppm must be methyl attached to electronegative atom. Suggests methoxy. All carbonyl compounds are not possible, no esters ...

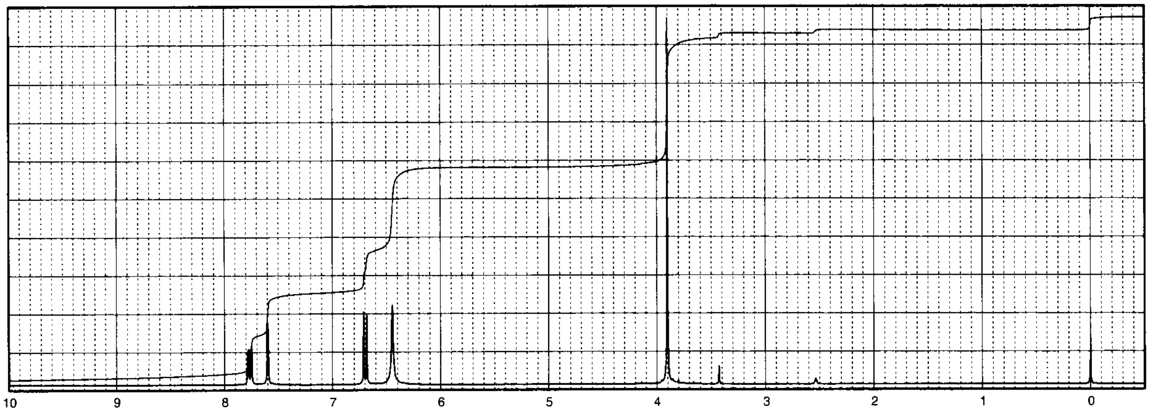
The NO2 group and its position are suggested by the UV/Vis. The 392 nm absorption indictes a dye. Using tables, this kind of absorption is only possible for para-donor-acceptor substituted systems.

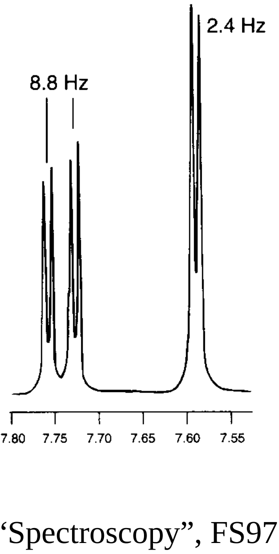
The position of the methoxy group can be either *ortho* to the amine or *ortho* to the nitro. It is *ortho* to amine. Two aromatic H at high chemical shift and they split each other (2.4 Hz). The 8.8 Hz coupling is between the CH hydrogens of the amino-C-CHCH-C-nitro.

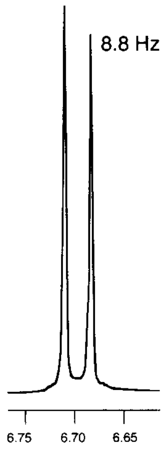
PROBLEM 23

This compound has the molecular formula $C_7H_8N_2O_3$. We have supplied you with the IR and proton NMR spectra (run in deuterated DMSO). The expansions of the interesting sets of peaks centering near 7.75, 7.6, and 6.7 ppm in the proton NMR are provided, as well. The peak at 6.45 ppm (two protons) is solvent- and concentration-dependent. The UV spectrum shows peaks at 204 nm (ϵ 1.68 $\times$ 10^4), 260 nm (ϵ 6.16 $\times$ 10^3), and 392 nm (ϵ 1.43 $\times$ 10^4). The presence of the intense band at 392 nm is an important clue as to the positions of groups on the ring. This band moves to a lower wavelength when acidified. The IR spectrum was determined in Nujol. The C—H bands for Nujol at about 2920 cm^{-1} obscure the C—H bands in the unknown compound.









Question 3. Discrimination Between Isomers Using NOE. (20 points)

Duddeck & Dietrich, *Structure Elucidation by Modern NMR*, Springer, 2nd ed., **1992**.

The acetate of a benzodiazepinone derivative has been nitrated. The question is whether the newly introduced nitro group is situated at position 7 or 8. This problem cannot be solved via chemical shift analysis because the other two substituents on the benzene ring both are acylated amines. This problem also cannot be solved by establishing the H,H connectivities since there are no detectable couplings between the aromatic and the aliphatic protons. However, the problem easily can be solved with an NOE experiment and the ^{1}H NMR spectrum and the NOE difference spectrum are shown below.

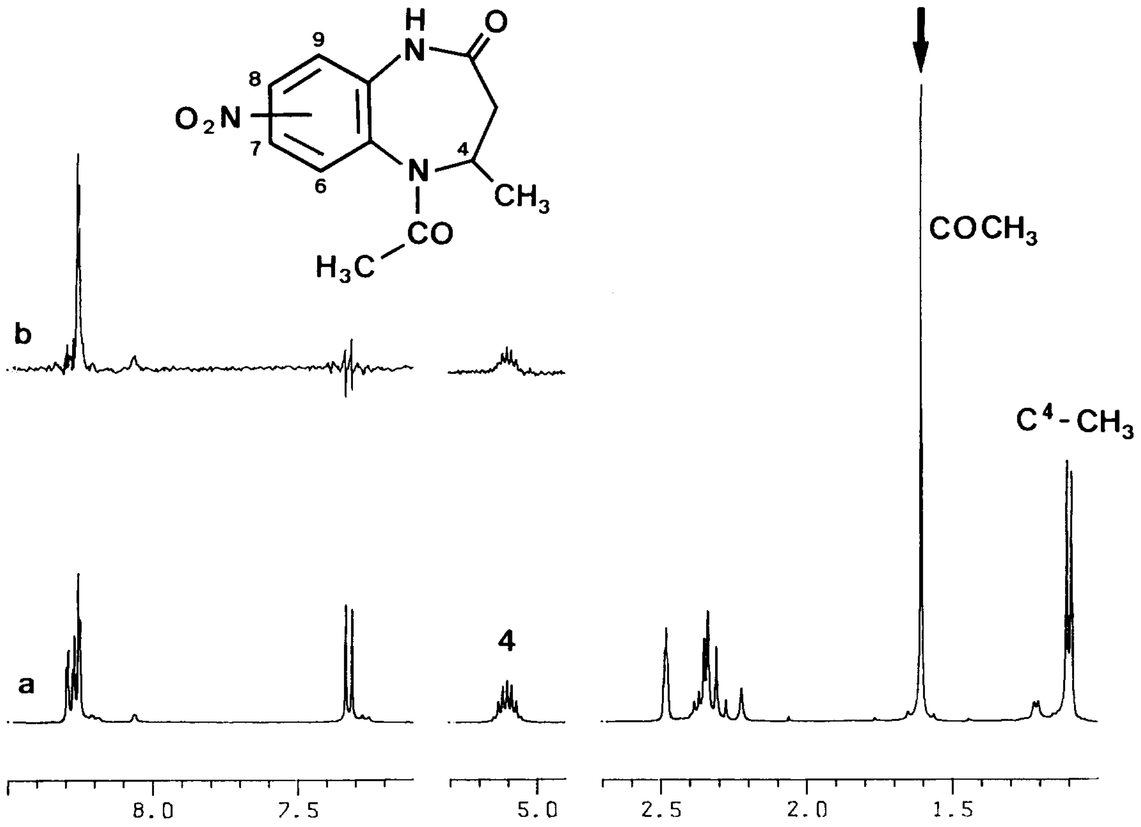


Fig. 2.3. 1a and b. NOE difference experiment with a nitrated benzodiazepinone derivative, in DMSO–d_6. **a** ^{1}H NMR spectrum; **b** NOE difference spectrum with irradiation at the position of the acetoxy methyl signal (marked by the arrow).

(a) Considering the NOE difference spectrum shown, state which two signals are significantly enhanced upon irradiation of the acetoxy methyl protons. For each enhanced signal, state the number of the C-atom to which the NOE enhanced H atom is attached and specify the chemical shift of that H. State whether the NOE difference spectrum show the NO_2 substituent to be in position 7 or 8 and explain your answer. (In your answer, you might also state what the other isomer's NOE difference spectrum would look like.) (12 points)

The H at C4 is enhanced. 5.1 ppm.
One of the aromatic H atoms is enhanced. 8.2 ppm.

The aromatic H that is enhanced can only be H6.
Since H6 shows up as a singlet, it cannot be coupled to a H at C7.
Thus, the nitro group must be at C7.

If the nitro group were attached to C8, then the NOE enhanced aromatic H would have been a doublet.

(b) Now consider the isomer that contains the NO_2 substituent in position 9. The three aromatic hydrogen in this isomer would constitute an ____**AMX**____ (AMX, ABC, AA'X, ...) spin system. State how many signals you would expect and what you expect their multiplicities to be (doublet, triplet, quartet, doublet of doublets, ...). (8 points)

Table of nitro group effects on the arom. H chem. shifts (Pretsch H255) suggests chemical shifts decrease in the order H(C8) (Z=0.95) > H(C6) (Z=0.38) > H(C7) (Z=0.26)

H(C8) a doublet (J), H(C7) dd (J and J'), and H(C6) a doublet (J').

Question 4. Natural Product Analysis. (40 points)

The following plots show the ^{1}H-NMR spectrum, the H,H COSY spectrum and the H,C COSY spectrum of the unknown compound "**8**". Compound **8** is a pleasant smelling liquid with molecular formula $C_{13}H_{20}O$. **We will conduct a guided solution of this problem**. The spectra all are taken from **Exercise 11** in the book by Duddeck & Dietrich.

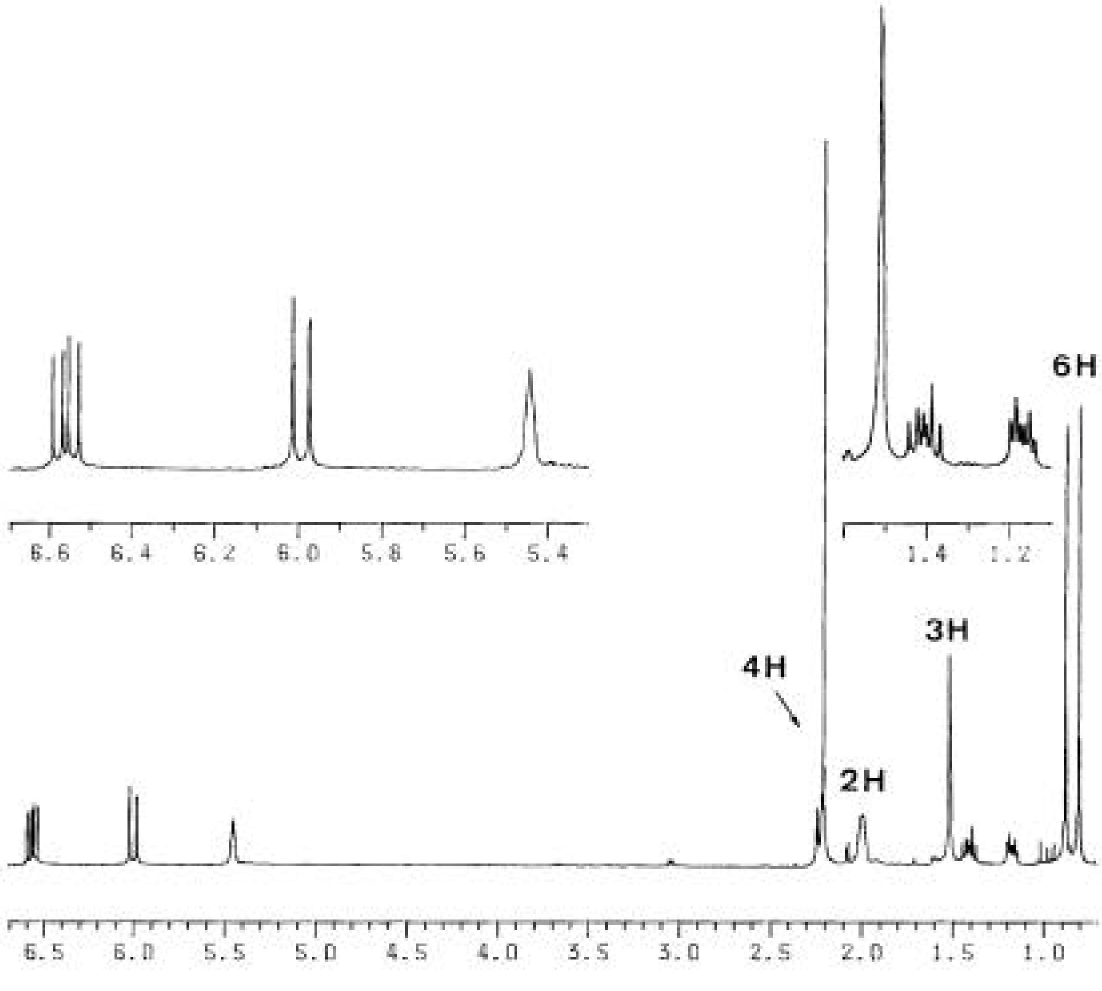


Fig. 3.11.1. ^{1}H NMR spectrum of **8**.

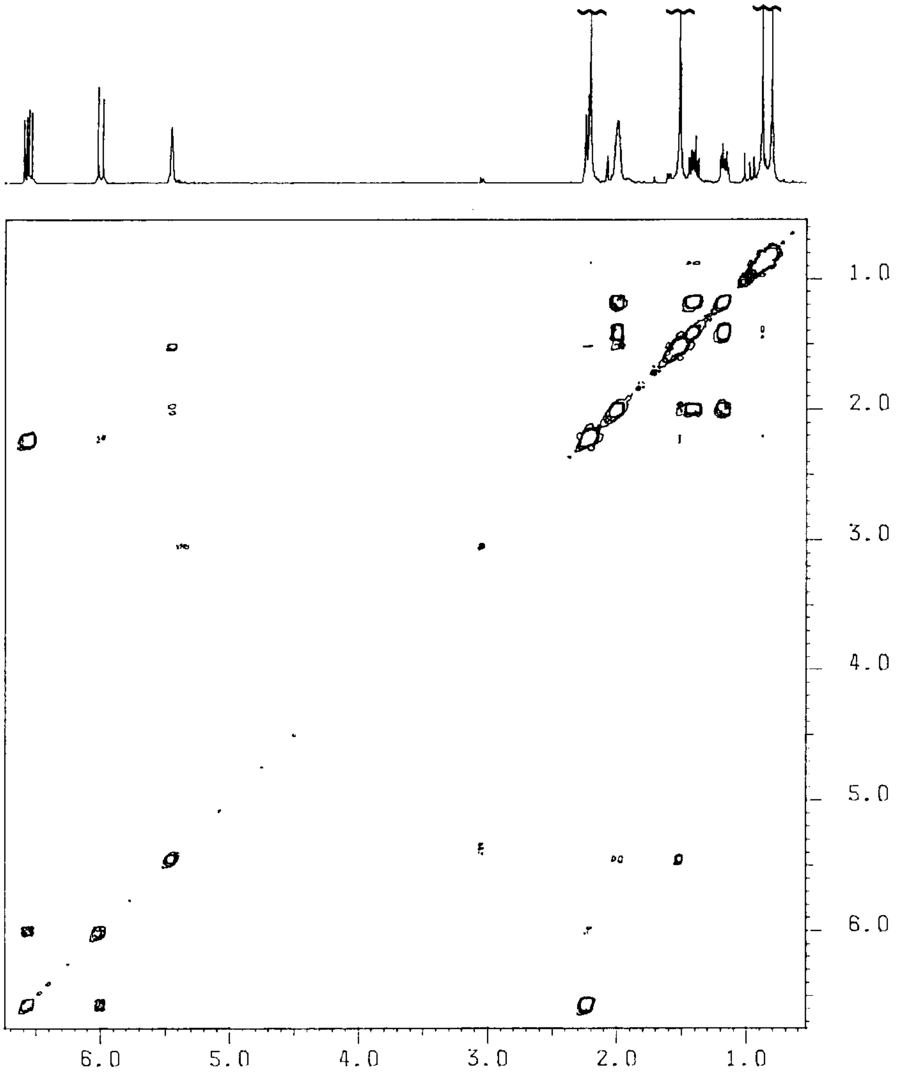


Fig. 3.11.2. H,H COSY spectrum of **8**.

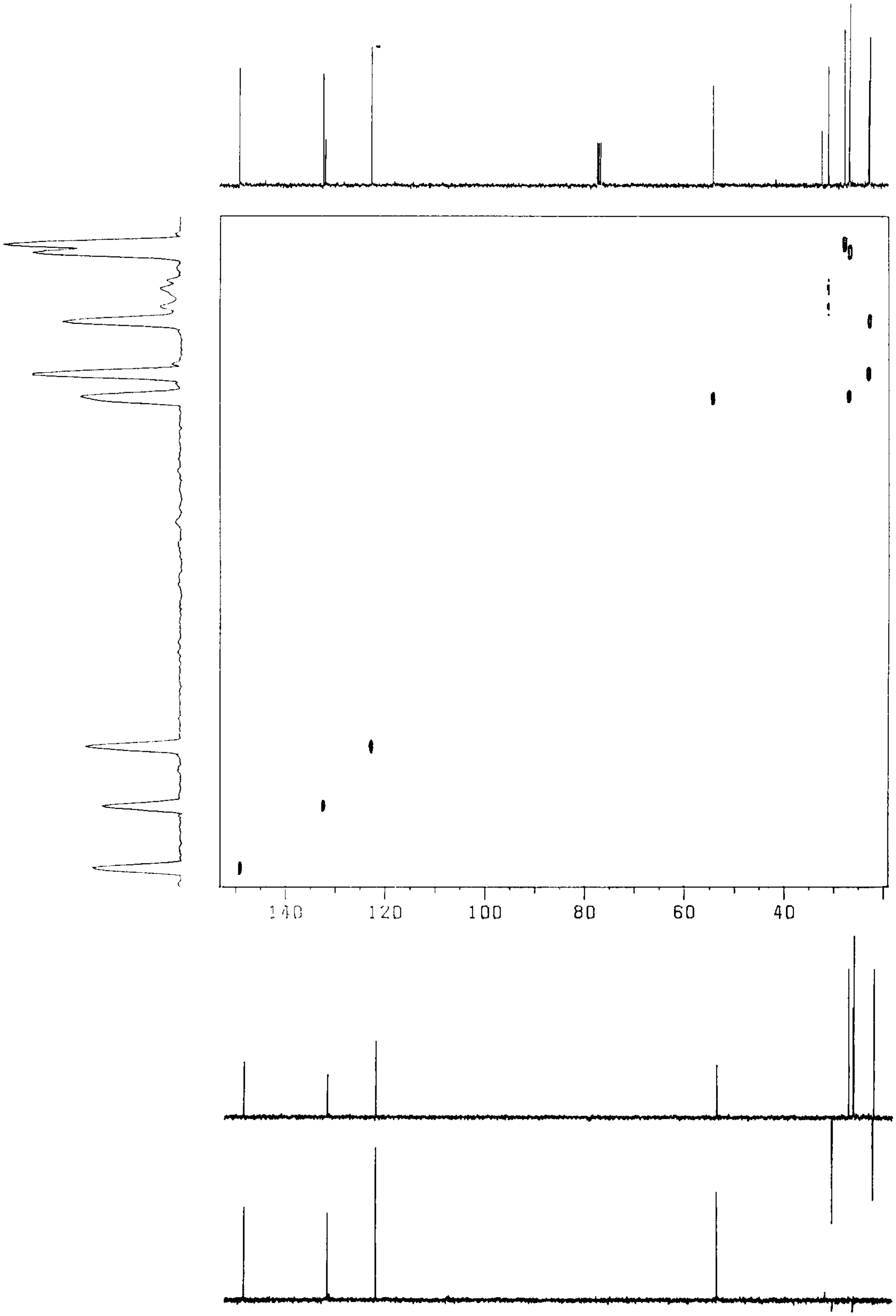


Fig. 3.11.3. H,C COSY and DEPT spectra of **8**; the ^{13}C NMR spectrum contains an additional signal at δ = 198.4 (C).

(a) Consider the regular C-NMR spectrum (given as part of the H,C COSY and **note** that a peak at 198.4 ppm exists but is not shown) and the two DEPT spectra on the bottom of that page. Based on this information, it is clear that there are __**3**_ quaternary C atoms, __**4**_ C atoms with one H attached, __**2**_ methylene groups, and **4** methyl groups. (Of course, the numbers you give should add up to 13.) (3 points)

(b) The olefinic region of the ^{1}H NMR spectrum contains three signals at δ = 6.56, 5.99, and 5.44 ppm. Based on the H,H COSY spectrum, clearly state whether these signals belong to the same double double bond or to different double bonds. For these couplings between the olefinic hydrogens, draw appropriate horizontal and vertical lines into the H,H COSY spectrum to connect cross-peaks with the diagonal peaks. (6 points)

Cross peaks show up only for the two Hs at 6.56 and 5.99 ppm.
These Hs are -CH=CH- connected.

The H at 5.44 belongs to a different double bond, -CH=C<.

(c) Draw appropriate horizontal and vertical lines in the H,C COSY spectrum to indicate which olefinic H atoms are connected to which olefinic C atoms. Considering the H,C COSY and the DEPT spectra, what can be deduced about the nature of the fourth olefinic C atom. (4 points)

Connect the three cross peaks in the lower left with the respective H and C signals.

One of the olefinic C must be quaternary.

(d) The multiplet centered at δ = 6.56 ppm is a doublet of doublets with coupling constants of J = 15.9 Hz and J' = 9.7 Hz. Which hydrogens (just give their chemical shifts for now) are responsible for this splitting to occur and clearly state which interaction goes with which coupling constant. Draw horizontal and vertical lines in the H,H COSY spectrum to indicate any cross-peaks that might be relevant to explaining the multiplet at δ = 6.56 ppm. Based on the coupling constants of this multiplet, can you make any statement as to the stereochemistry about the double bond? (6 points)

The -CHa=CHb- has an Ha,Hb coupling of 15.9 Hz. Must be trans.

The H at 6.56 ppm also couples to one aliphatic H.
The H,H COSY tells us that that H is at chemical shift 2.2 ppm.

(e) The molecule contains an **acetyl group**. List all the evidence in support of this statement. Which H-NMR (give chemical shift) and which two C-NMR signals (give chemical shifts) arise from this acetyl group? Draw a horizontal and a vertical line in the H,C COSY spectrum that shows which H-NMR and C-NMR are due to the methyl group of the acetyl group. (4 points)

Methyl C at 26.8 ppm.
Carbonyl C at 198.4 ppm.
Methyl H at 2.2 ppm. This singlet happens to overlap with a doublet due to C(1)-H.

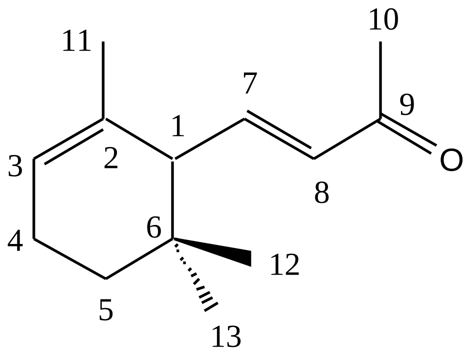
(f) The molecule contains an α,β-**unsaturated ketone**. List all evidence in support of the statement that the acetyl group is connected to an alkene. Do the chemical shifts tell us? If so, which ones? Is there any coupling information that would tell us? (4 points)

Txplains the absence of coupling other than the 15.9 Hz for H at C8.
The chem. shift of C8 fits that of a CH=CH-CMe=O. Pretch et al.

(g) There are **four methyl groups** in the molecule. The methyl group at δ = 2.2 ppm overlaps with a doublet signal of one H atom; this methyl signal __**does not**__ (does, does not) show any H,H coupling. The methyl group signal at δ = 1.5 ppm looks like a singlet; these methyl H atoms (i) are coupled to an olefinic H but the coupling constant is very small or (ii) is not coupled to any H atom. Based on the H,H COSY, it is clear that option ___**i**__ (i or ii) is correct. Considering the H,C COSY and the DEPT spectra, what can you say about the methyl groups at δ = 0.87 ppm and δ = 0.78 ppm? (4 points)

The methyls at 0.87 ppm and δ = 0.78 ppm are isolated.
Since we have 3 quat. C atoms, and only one is not accounted for by now
(one is C̲O, one is -CH=C̲Me-), it looks like we must have a >CMe_2 group.

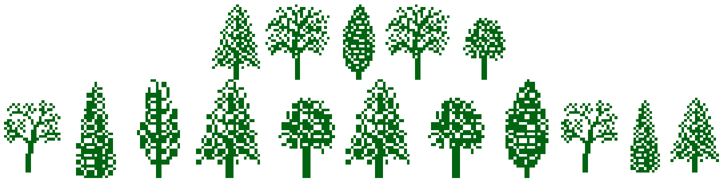
(h) Now put is all together and draw the natural product. Briefly state the pieces of evidence that allow you to connect the various fragments in the way you think they are connected. (9 points)



The COSY spectra shows that the methylene groups are connected.
The methylenes cannot be connected to the CH (H,H COSY, multiplicity)
The -CH= cannot be connected to the CH (H,H COSY, multiplicity)

The Final will be graded on Tuesday and I hope to be done in the early afternoon and the answer key, the performance histograms for the course and the final all will be posted on the Course Web Site at that time. I will inform you via email as to when you can pick up your final in my office.

Enjoy the break. Relax in a longitudinal fashion with T1 = 1 week!



Merry Christmas

The End