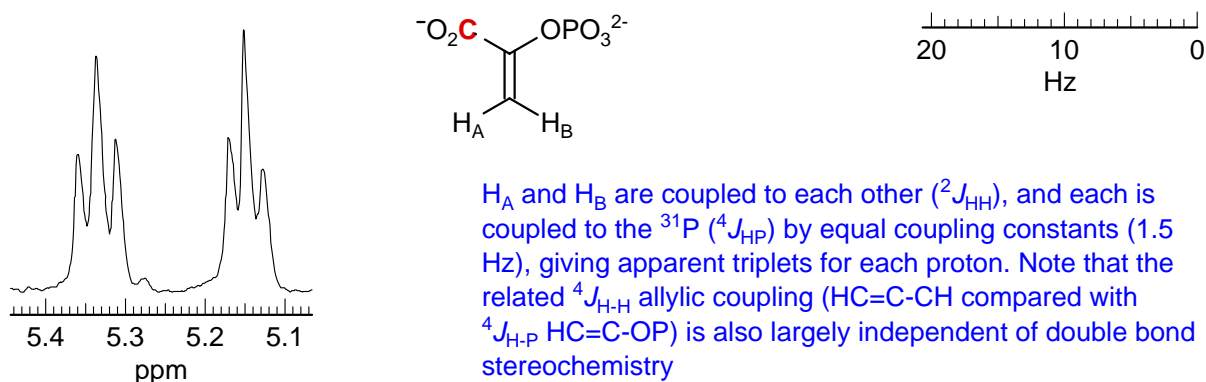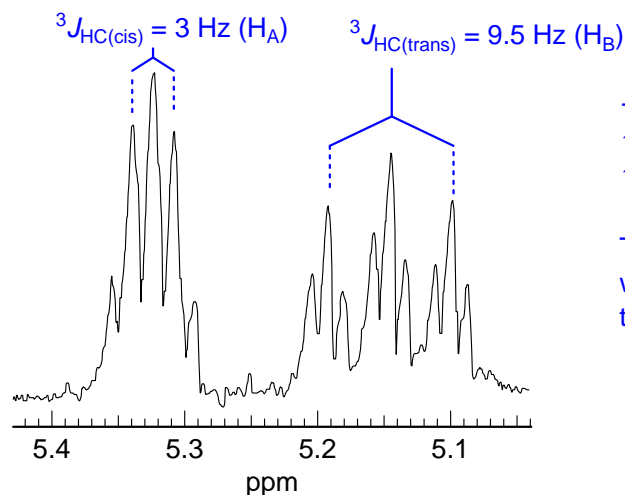# Problem Set 12

Problem R-85K (*J. Am. Chem. Soc.* **1970**, *92*, 4095)

(a) The 60 MHz ^{1}H NMR spectrum of phosphoenolpyruvate (PEP) is shown below. Analyze the multiplets and assign the couplings

H_A and H_B are coupled to each other ($^2J_{HH}$), and each is coupled to the ^{31}P ($^4J_{HP}$) by equal coupling constants (1.5 Hz), giving apparent triplets for each proton. Note that the related $^4J_{H-H}$ allylic coupling (HC=C-CH compared with $^4J_{H-P}$ HC=C-OP) is also largely independent of double bond stereochemistry

(b) The 100 MHz ^{1}H NMR spectrum of PEP labeled 60% with ^{13}C at the carboxyl carbon is shown below. Analyze the multiplets and assign the chemical shifts and couplings.

$^3J_{HC(cis)}$ = 3 Hz (H_A) $^3J_{HC(trans)}$ = 9.5 Hz (H_B)

The central peaks are from the 40% of the sample that has ^{12}C at the carboxyl carbon, the satellites are from the 60% ^{13}C.

This allows assignment of the two protons - the upfield one with the large $^3J_{HC}$ is trans to the carboxyl group (H_B) and the other H_A ($^3J_{HC}$(trans) is always larger than $^3J_{HC}$(cis))
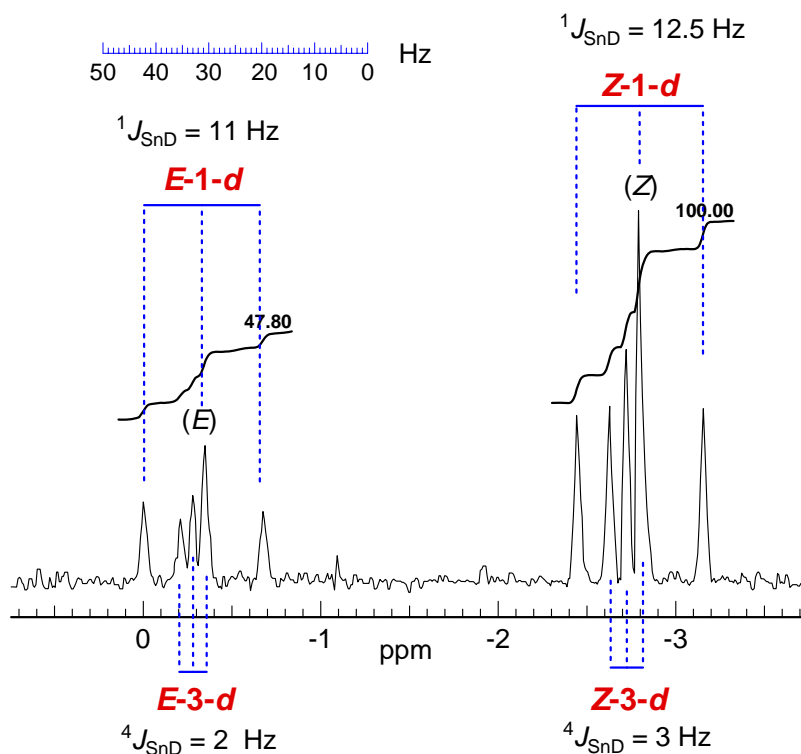
(c) The 60 MHz ^{1}H NMR spectrum of PEP labeled with one deuterium atom is shown below. Draw the structure of the compound, include stereochemistry.

H_A has been replaced by deuterium
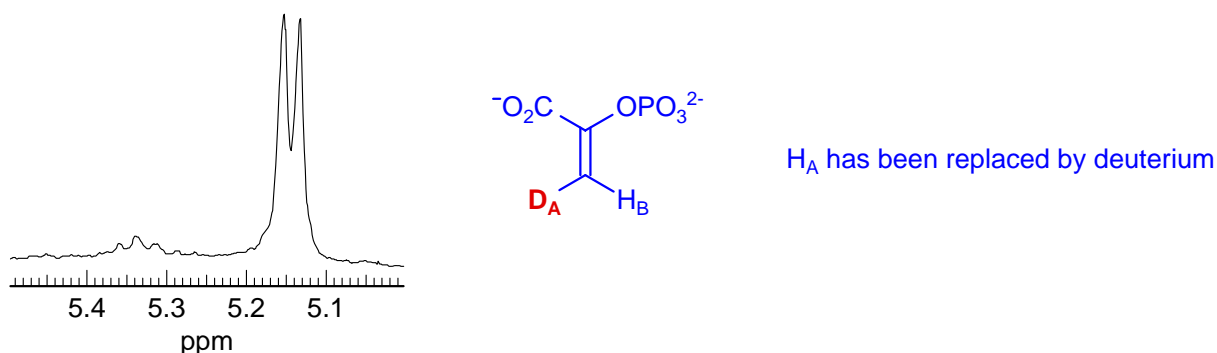
Problem R-306 ($C_{10}H_{20}Sn$). Below is the 33.54 MHz $^{119}Sn\{^1H\}$ NMR spectrum of a reaction product from the reaction shown (Quintard, J.-P.; Degueil-Castaing, M.; Dumartin, G.; Barbe, B.; Petraud, M. *J. Orgmet. Chem.* **1982**, *234*, 36):
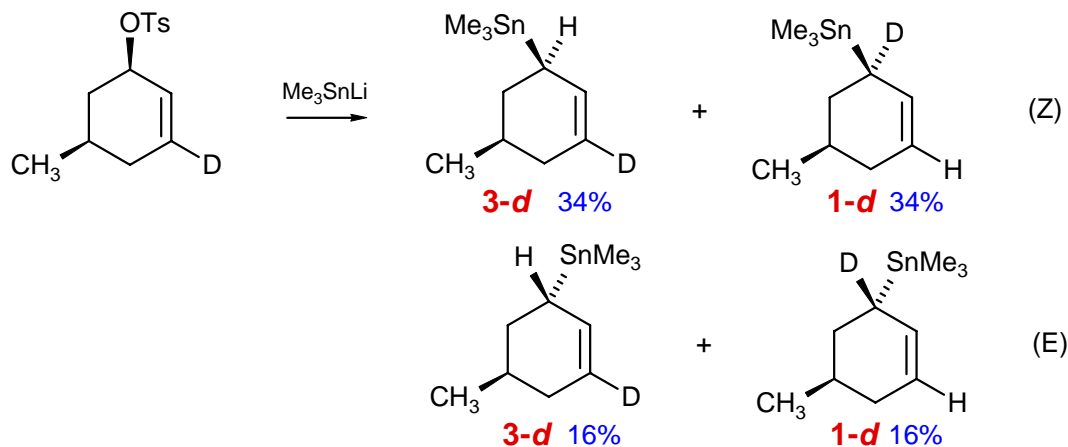
Estimate the ratio of the four isomeric products from the NMR spectrum. All materials are racemic.

$^1J_{SnD}$ = 12.5 Hz

Z-1-d

(Z)

100.00

$^1J_{SnD}$ = 11 Hz

E-1-d

47.80

(E)

E-3-d
$^4J_{SnD}$ = 2 Hz

Z-3-d
$^4J_{SnD}$ = 3 Hz

Each of the ^{119}Sn signals is coupled to the deuterium, to give overlapping 1:1:1 triplets

We would expect the $^2J_{SnD}$ (1-d) to be larger than $^4J_{SnD}$ (3-d).

The ratio of 3-d to 1-d is 1:1

The E to Z ratio is 48/100 (32/68)

This experiment was carried out to determine the mechanism of the nucleophilic substition at carbon. A direct S_N2 substitution would have given ony the E-3-d isomer (inversion at carbon), so either a carbonium ion (S_N1 through the allyl cation) or, more likely, a radical mechanism (S_{RN1} through the allyl radical) is involved.

Problem R-307 ($C_5H_5BF_4Se$). Shown below is the 15.17 MHz ^{77}Se NMR spectrum of selenapyrylium fluoroborate. Interpret the splitting pattern (Sandor, P.; Radics, L. *Org. Magn. Reson.* **1981**, *16*, 148).
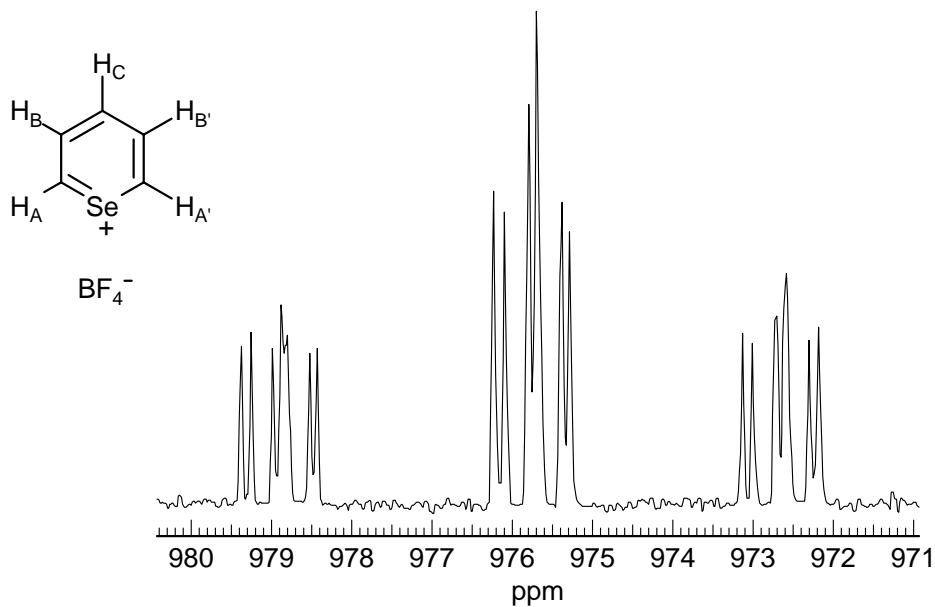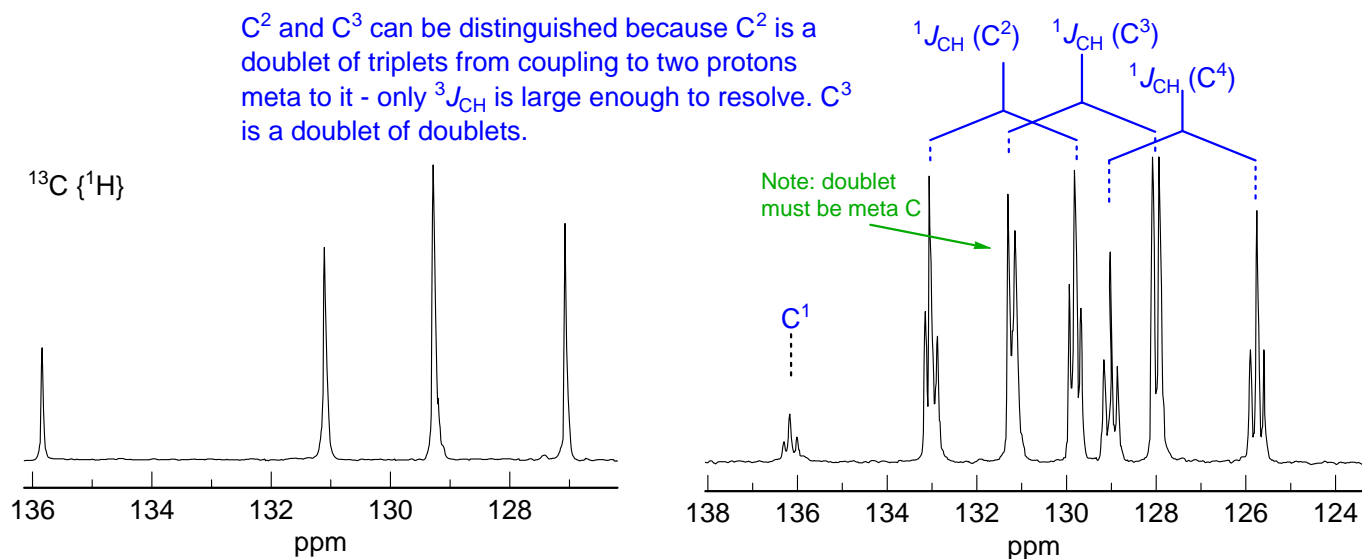

The ^{77}Se NMR signal is an apparent ttd, J = 47, 6, 3 Hz from coupling to H_A, H_B and H_C. The pattern is actually the X part of an AA'BB'CX spin system (X = Se), which is not strictly first order. Hence the somewhat irregular intensities of the peaks, and small additional splittings.
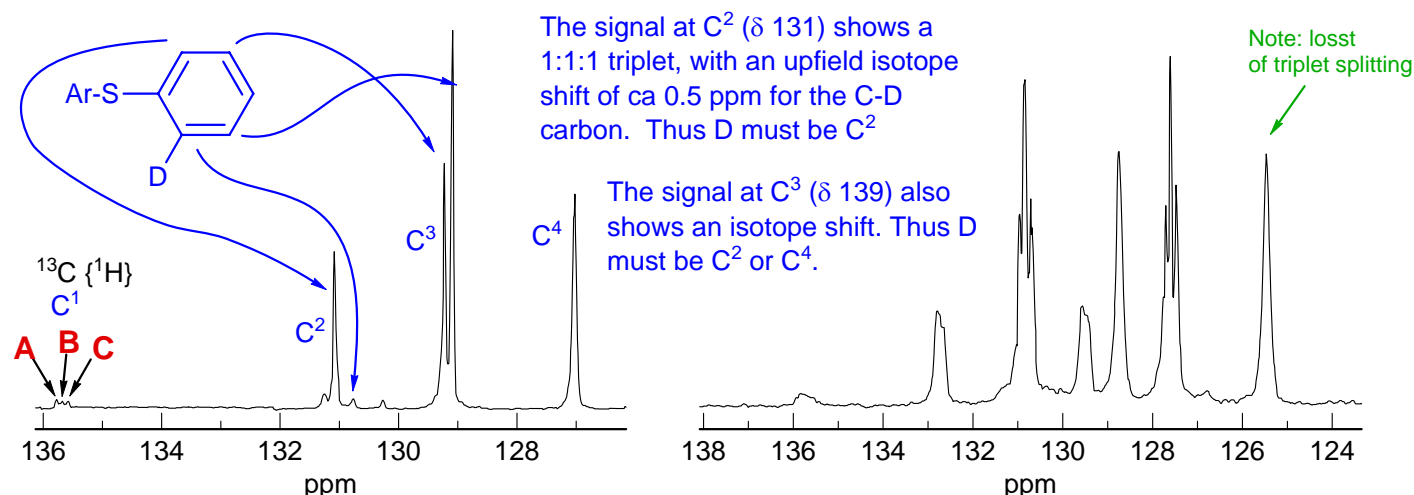
Problem R-64 ($C_{12}H_{10}S$). Below are four ^{13}C NMR spectra (50 MHz). The upper spectra are of diphenyl sulfide (Ph_2S). The lowerr spectra are of Ph_2S partially deuterated. The left set of spectra are proton-decoupled, the right set is fully coupled. Have PLT

(a) Assign the resonances in the unlabelled spectra (C^1, C^2, C^3, C^4).

C^2 and C^3 can be distinguished because C^2 is a doublet of triplets from coupling to two protons meta to it - only $^3J_{CH}$ is large enough to resolve. C^3 is a doublet of doublets.

$^1J_{CH}$ (C^2) $^1J_{CH}$ (C^3) $^1J_{CH}$ (C^4)

^{13}C {^1H}

Note: doublet must be meta C

C^1

136   134   132   130   128
ppm

138   136   134   132   130   128   126   124
ppm

(b) Assign the various peaks in the D-labelled spectra.

Ar-S—

D

The signal at C^2 (δ 131) shows a 1:1:1 triplet, with an upfield isotope shift of ca 0.5 ppm for the C-D carbon. Thus D must be C^2

The signal at C^3 (δ 139) also shows an isotope shift. Thus D must be C^2 or C^4.

Note: losst of triplet splitting

^{13}C {^1H}

C^1

A B C

C^2

C^3 C^4

136   134   132   130   128
ppm

138   136   134   132   130   128   126   124
ppm

(c) Determine the **position(s)** and roughly estimate the **extent** of deuteration indicated by the upper spectra. Briefly give your reasoning. Hint: calculate the expected C-D couplings and compare to the observed ones before assigning the signals.

Ar-S— **A**   Ar-S— **B**   Ar-S— **C**

$^1J_{CH}$ = 159 Hz

$^2J_{CH}$ = 1.0 Hz

$^3J_{CH}$ = 7.4 Hz

$^4J_{CH}$ = -1.1 Hz
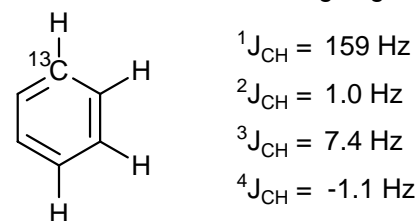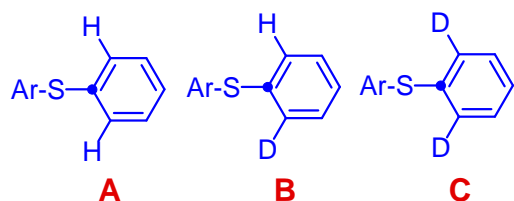
The three peaks for C^1 (labelled A, B, C) are separated by 6 Hz. These cannot be due to $^3J_{CD}$ since this would be at most 1/6 x 7.4 Hz (if D was meta), or to $^2J_{CD}$, if D was ortho (as it actually is) since it would be only 1/6 x 1.0 Hz.

The deuterium seems to be almost entirely at C^2 (this is the only carbon that shows $^1J_{CD}$). The best estimate of the level of labelling at C^2 is probably from the two peaks at C^3 (two-bond isotope shift), (60% D, 40% H). There must a significant amount of 2,6-dideutero, to account for peak C at C^1, and very little 2,6-diprotio (structure A), otherwise peak A at C^1 would be taller. Peaks B and C are vey weak because they would have long T_1 due to loss of $\underline{C}H$ DD relaxation, leading to saturation, and possible loss of NOE enhancement.
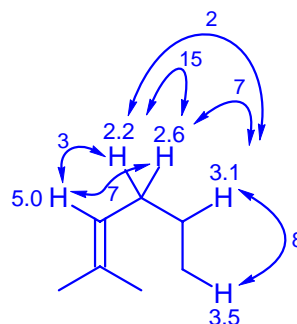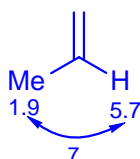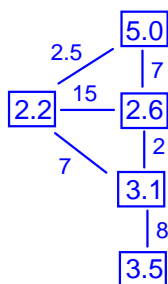
Problem R-84P. The compound $C_{17}H_{27}NO_3Si$ whose 270 MHz ^1H NMR spectrum (CDCl$_3$) is shown has part structures:

$-OSi(CH_3)_2C(CH_3)_3$
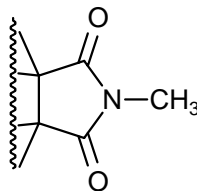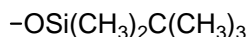
(a) DBE __6__

(b) Identify additional part structures from the NMR spectrum. Give chemical shifts and coupling constants.

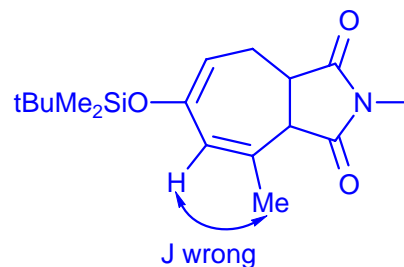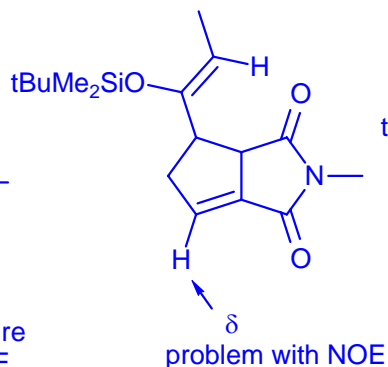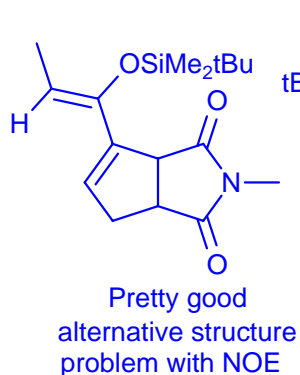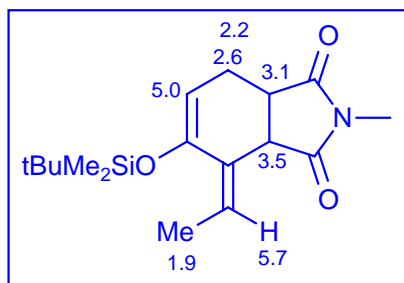|	δ	mult	J
CH$_3$ —	1.9	d	7
CH$_2$	2.2	ddd	15, 7, 2.5
	2.6	ddd	15, 7, 2
	3.1	ddd	8, 7, 2
	3.5	d	8.5
Vinyl-H	5.0	dd	7.5, 2.5
	5.7	q	7, 7, 7

2.2, 2.6 (15 Hz leaning)
3.2, 3.5 (8 Hz leaning)

(c) Give a complete structure of **R-84P** below and make a note of any additional structural ambiguities (if any) that remain. Assign signals.

Pretty good
alternative structure
problem with NOE

problem with NOE

J wrong

(d) Irradiation of the signal at δ 5.7 leads to an increase in area of the signal at δ 3.5 of 24%. However, irradiation of the signal at δ 1.9 leads to no change of the signal at δ 3.5. What experiment is being done here, and what does it tell you about the structure of **R-84P**?

This is a Nuclear Overhauser Effect (NOE) experiment. It tells us that the δ 5.7 and δ 3.5 protons are close in space (i.e., double bond stereochemistry is as shown), and that the proton at δ 5.7 causes a large part of the relaxation of δ 3.5. The protons at δ 1.9 are not very close to δ 3.5 proton.

Correct NOE

Incorrect

No NOE
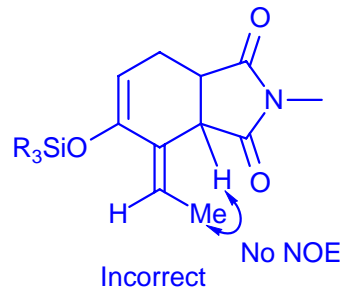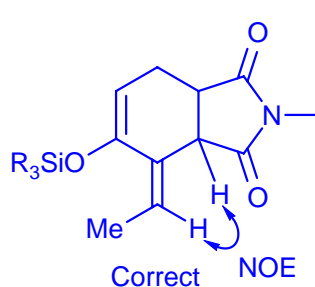
(e) Explain the origin of the closely spaced doublet at δ 0 (the sample contains no tetramethylsilane).

The molecule is chiral, and hence the gem-dimethyl groups on silicon are diastereotopic.
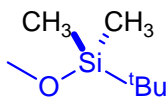
Problem R-84P ($C_{17}H_{27}NO_3Si$)

270 MHz ^{1}H NMR spectrum CDCl$_3$
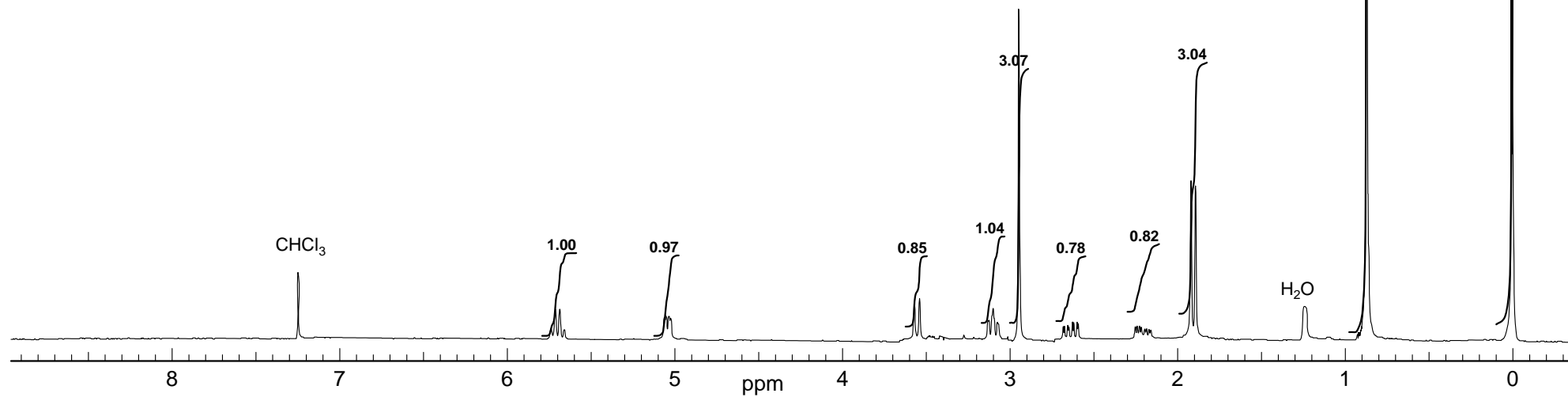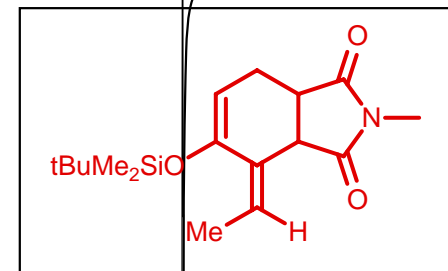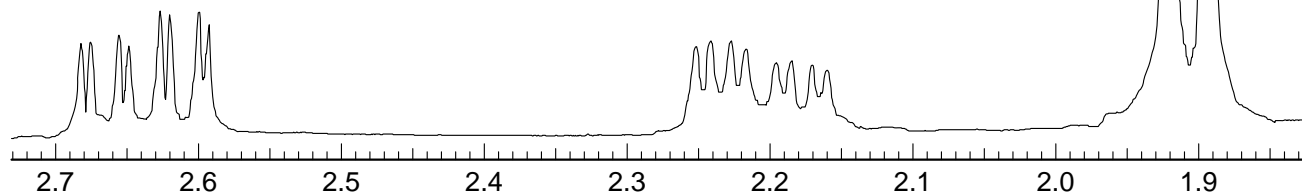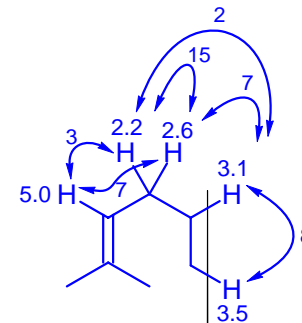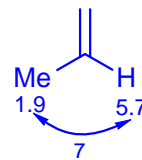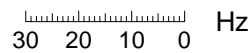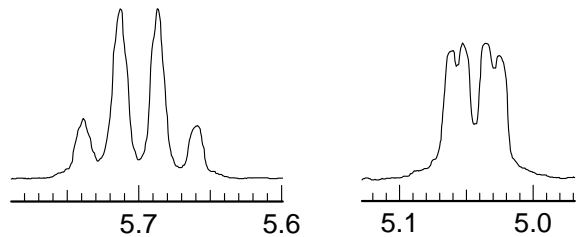
Source: Martha Kelly/Reich 9/14

δ	mult	J
CH$_3$ — 1.9	d	7
CH$_2$ [2.2	ddd	15, 7, 2.5
2.6	ddd	15, 7, 2
3.1	ddd	8, 7, 2
3.5	d	8.5
Vinyl-H [5.0	dd	7.5, 2.5
5.7	q	7, 7, 7

2.2, 2.6 (15 Hz leaning)

3.2, 3.5 (8 Hz leaning)

Hz 30 20 10 0

(c) Give a complete structure of **R-84P** below and make a note of any additional structural ambiguities (if any) that remain. Assign signals.

Molecular fragments (top row): vinyl fragment with H H, 3.1 H, 5.0 H, H; maleimide (succinimide) fragment O, N—, O; propenyl fragment Me, H; —OSiMe₂tBu

Boxed structure (R-84P): tBuMe₂SiO-substituted bicyclic imide
- 2.2
- 2.6 3.1
- 5.0
- N—
- 3.5
- Me H
- 1.9 5.7

Second structure: bicyclic imide with OSiMe₂tBu
Pretty good
alternative structure
problem with NOE

Third structure: tBuMe₂SiO-, H, N—, H
δ
problem with NOE

Fourth structure: tBuMe₂SiO-, cycloheptane-fused imide, H, Me
J wrong
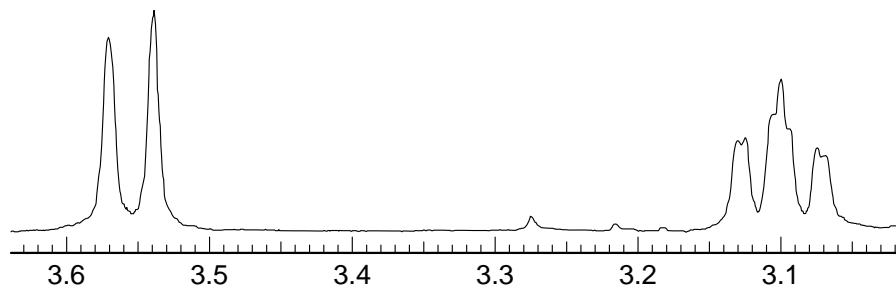
Problem R-28A (C$_{23}$H$_{26}$O$_5$)
  300 MHz ^{1}H COSY 2D NMR spectrum in CDCl$_3$
  512x128 FT'd to 512x512, sinebell-squared apodization symmetrized Source: Wilds/C. Fry
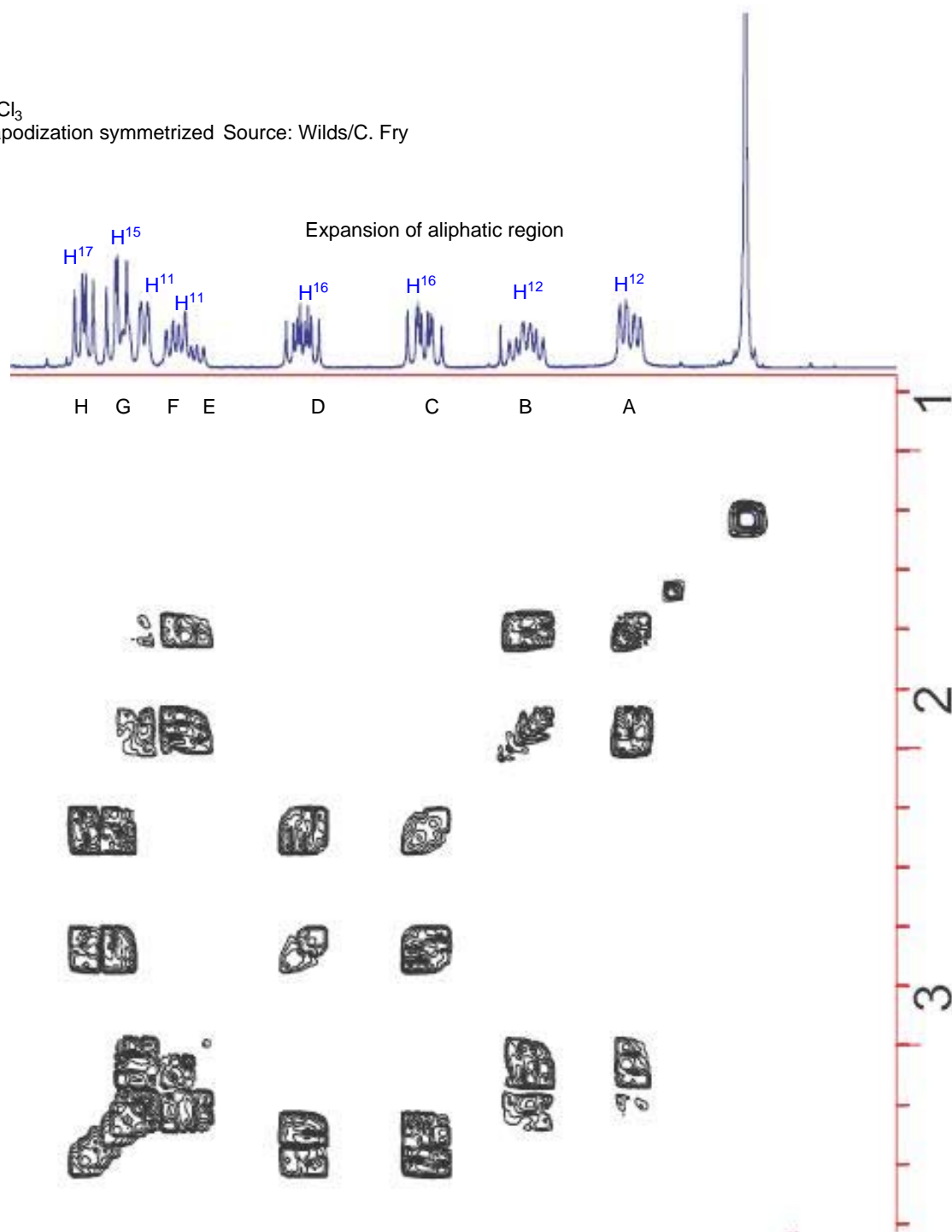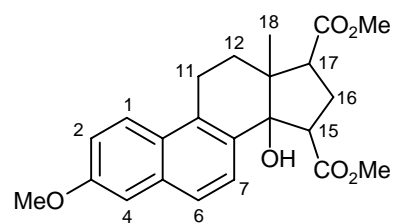
Problem R-28B (C$_{23}$H$_{26}$O$_5$)
600 MHz ^{1}H NMR in CDCl$_3$
Source: C. Fry/Wilds

Interpret the NOE difference experiments on the compound below shown
on the next two pages. The protons were partially assigned in Problem
R-28A. Use the information to complete the assignment and establish the
relative stereochemistry at the four asymmetric centers around the
cyclopentane ring. Are there any remaining ambiguities?

80 60 40 20 0   Hz

20 Hz/cm

ppm

Problem R-28B ($C_{23}H_{26}O_5$)
600 MHz ^{1}H NMR NOESY 1D in CDCl$_3$
Source: C. Fry/Wilds

Follow: ① ② etc

OH Stereochem up

⑤

17   11 up   H^{16} up 12

Irradiate H^{17} (up)

Irradiate H^{15} (down)

H^7

Irradiate H^{11} down

H^1

18
CO$_2$Me
12
11   17
                16
MeO   OH   15
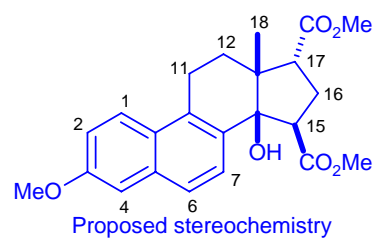   CO$_2$Me
4   6   7

Proposed stereochemistry

Irradiate H^{11} up

Irradiate H^{16} down

H^{16} up

Confirm H^{15} down

④
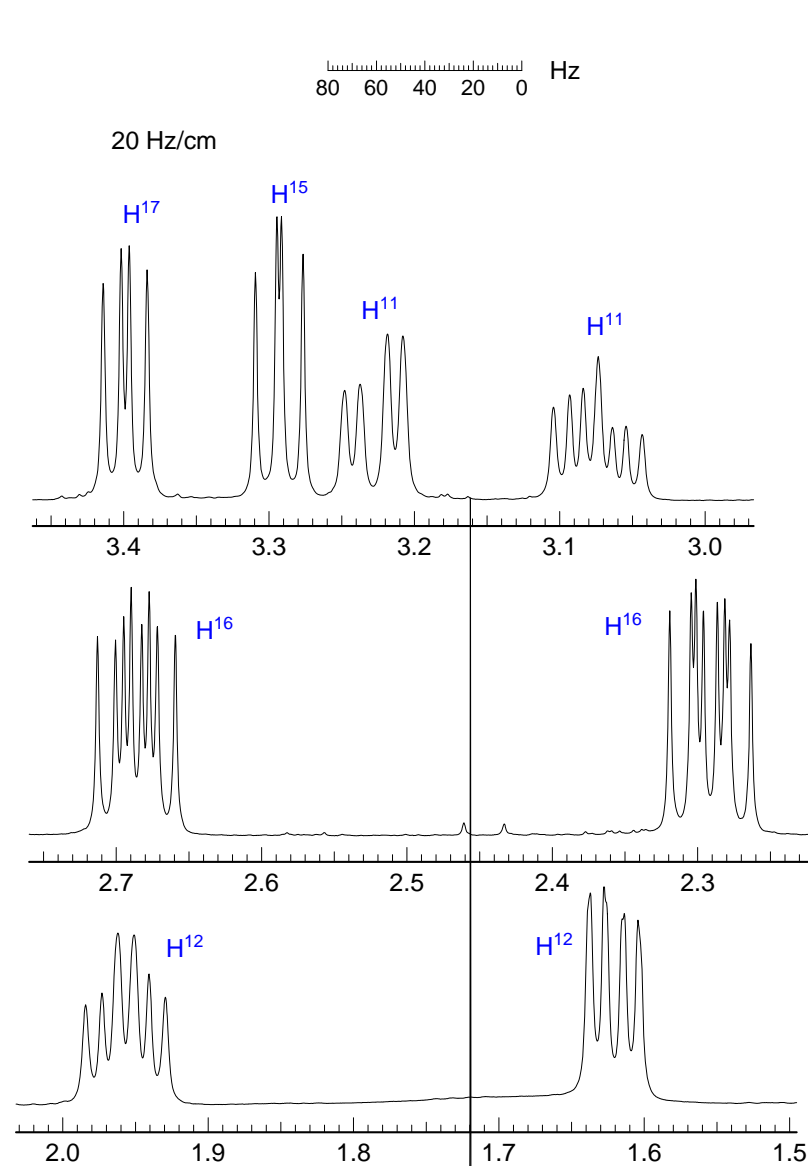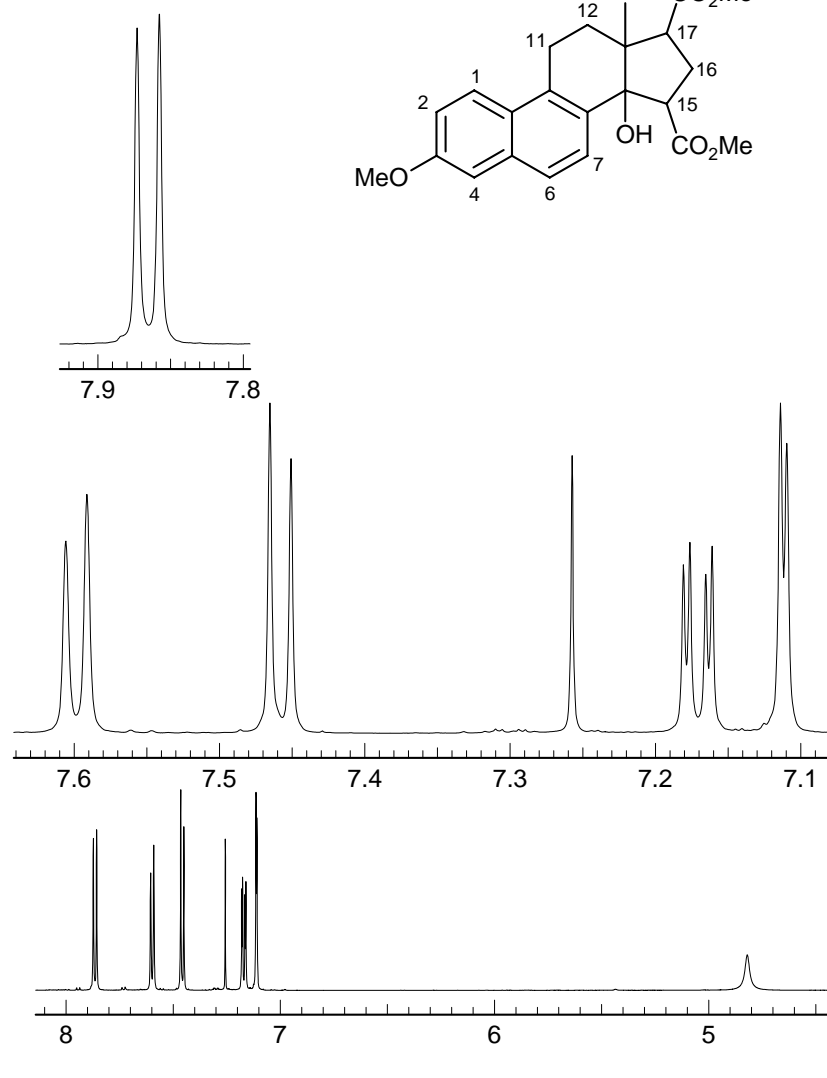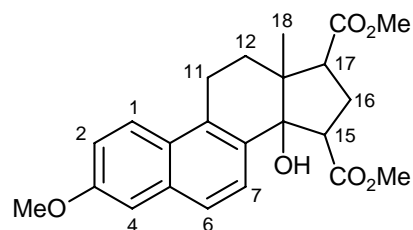
OH up?   Confirm H^{17} up   H^{16} down   Irradiate H^{16} up   ③

Irradiate H^{12} down

H^{15} down
H^{11} down   H^{16} down   H^{12} up   ②

H^{12} down   Irradiate H^{12} up

Start by arbitrarily assigning the Me the "up" stereochemistry, everything else will be relative to that

OH up?

H^{17} up   H^{11} up   H^{12} up   ①

Define Me = up

17-OMe
Ar-OMe   15-OMe
1   6   7   2   4   17   15   11   11   16   16   12   12   18

7   6   5   4   3   2   ppm

Problem R-28B ($C_{23}H_{26}O_5$)
NOESY 1D 600 MHz 06-06 Fry

H^6

H^4

Me / H

HO

H

E / 17 / E / 12 / H

15 / 16 / H

"trans" NOE
see #8

17

H^{11} down

H^{11} up

(10)

18 / CO$_2$Me

11 / 12 / 17

1

2 / 16

15

7

MeO / 4 / 6 / OH / CO$_2$Me

Proposed stereochemistry

H^7

Confirm OH Stereochem

Me up

Irradiate OH up

H^{17} up

H^{16} up

(6)

H^2

H^4

Irradiate Ar-OMe

Water peak? - saturation transfer

(7)

Irradiate 17-CO$_2$Me (down)

H^{12} up

?

H^{17} up

(8)

H^7

Irradiate 15-CO$_2$Me (up)

H^{15} down

(9)

8

14

20

1

6 / 7

2 / 4

17-OMe

15-OMe

Ar-OMe

17 / 15

11 / 11

16

16

12

12

18

7

6

5

4

3

2

ppm
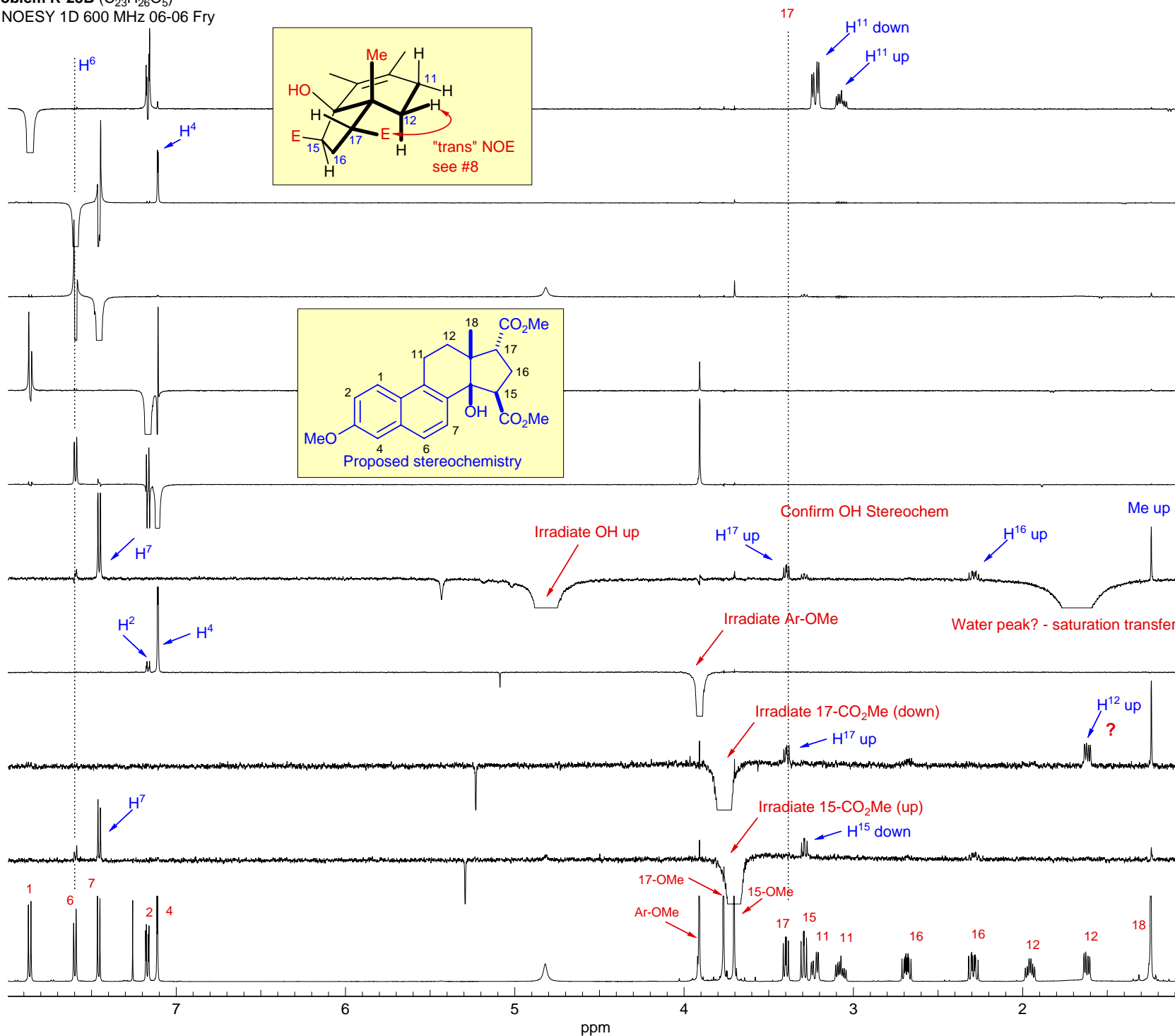
Problem R-28B (C₂₃H₂₆O₅)   **Answer**
600 MHz ¹H NMR in CDCl₃
Source: C. Fry (A18)/Wilds

Interpret the NOE difference experiments on the compound below shown
on the next two pages. The protons were partially assigned in Problem
R-28A. Use the information to complete the assignment and establish the
relative stereochemistry at the four asymmetric centers around the
cyclopentane ring. Are there any remaining ambiguities?