Nuclear magnetic resonance spectroscopy

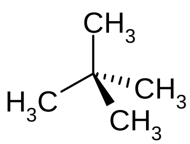
I. ^{1}H NMR

Reading:
Pavia
Chapter 5.8–5.19
Chapter 7.1-7.3, 7.5, 7.6, 7.7 A-C and F, 7.8-7.10
Chapter 8.1, 8.2 A and C

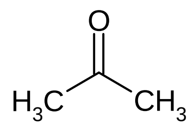
1. Chemical equivalence

- protons in chemically identical environments
  - are chemically equivalent
  - exhibit the same δ

- equivalence through symmetry considerations

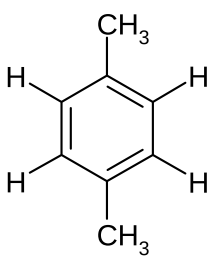


1 signal for 12 ^{1}H

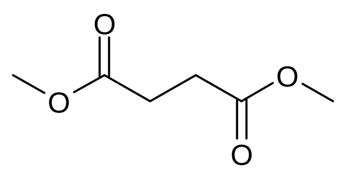


1 signal for 6 ^{1}H

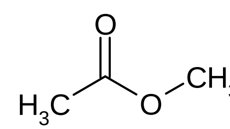
- obvious non-equivalence



2 sets:
1 signal for 6 ^{1}H in CH_3
1 signal for 4 ^{1}H in CH



2 sets:
1 signal for 6 ^{1}H in OCH_3
1 signal for 4 ^{1}H in CH_2

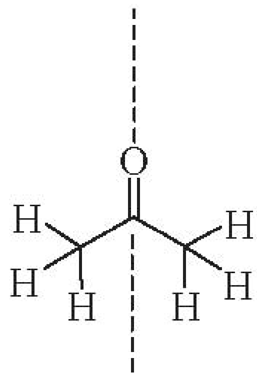


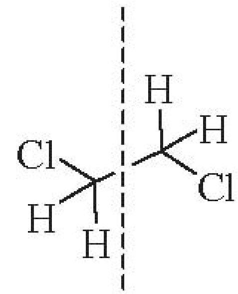
2 sets:
1 signal for 3 ^{1}H in CH_3
1 signal for 3 ^{1}H in OCH_3

Example

Chemical and magnetic equivalence: Proton signal is a singlet

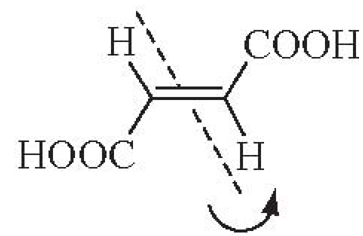
plane of symmetry



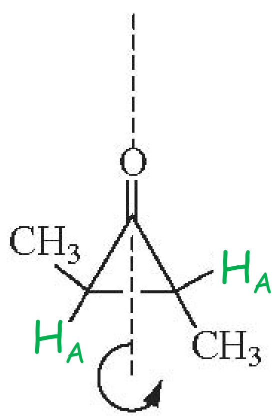


plane of symmetry

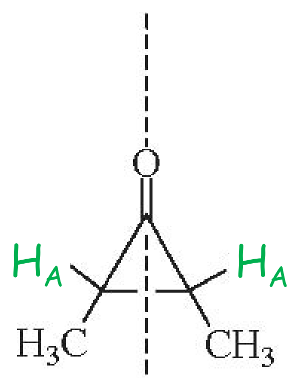
axis of symmetry



fumaric acid

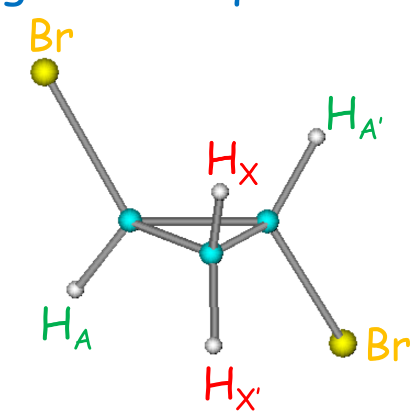


axis of symmetry



plane of symmetry

magnetic inequivalence:



complicated spectrum:
will not discuss!

1. Chemical equivalence continued

- spectral regions
  - chemical environment of the ^1H is important:
    - electronegativity effects
    - hybridization effects
    - H-bonding effects
    - magnetic anisotropy effects

often given as inset

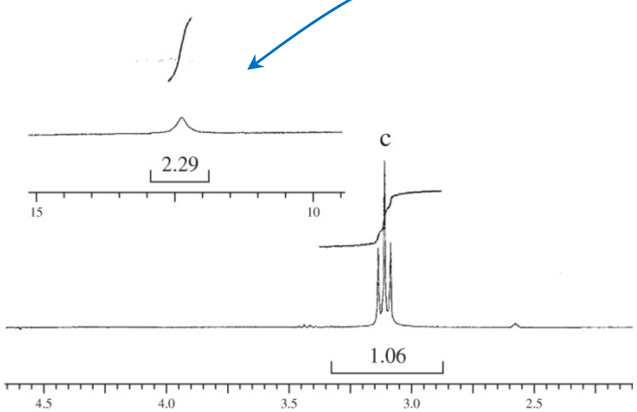


Fig. 5.49

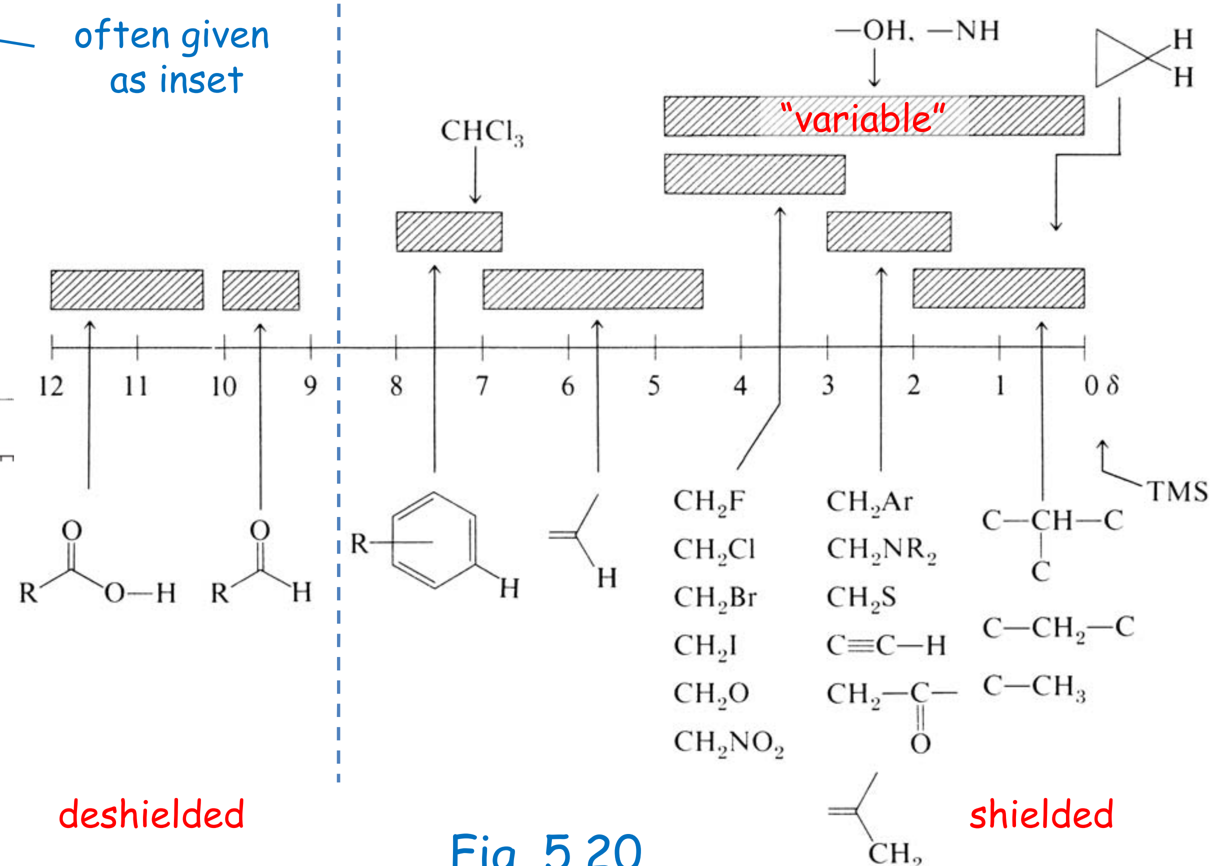
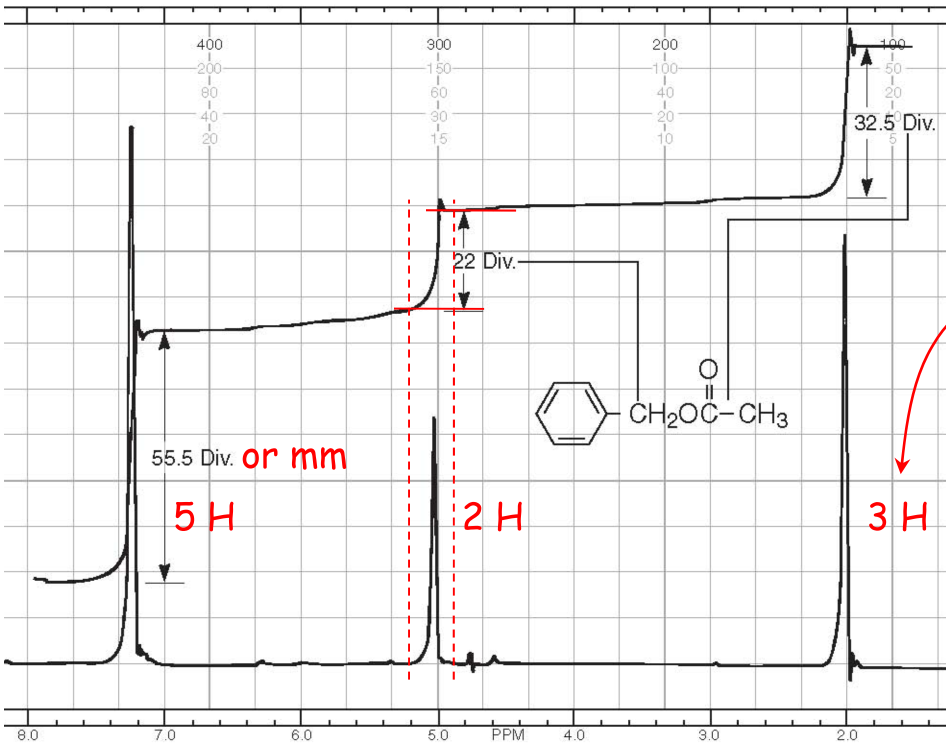


Fig. 5.20

see p. A-8 ff

2. Integration

- determines the number of equivalent ^1H for a signal
- determined through the area under the signal
    - given through a step trace (need a ruler!)
- provides first important label



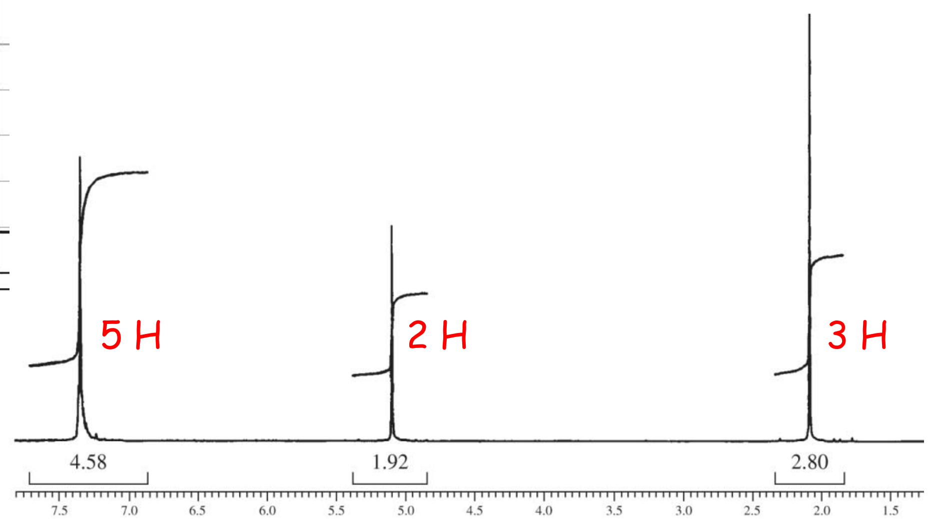
55.5 : 22 : 32.5

2.5 : 1 : 1.5

5 : 2 : 3

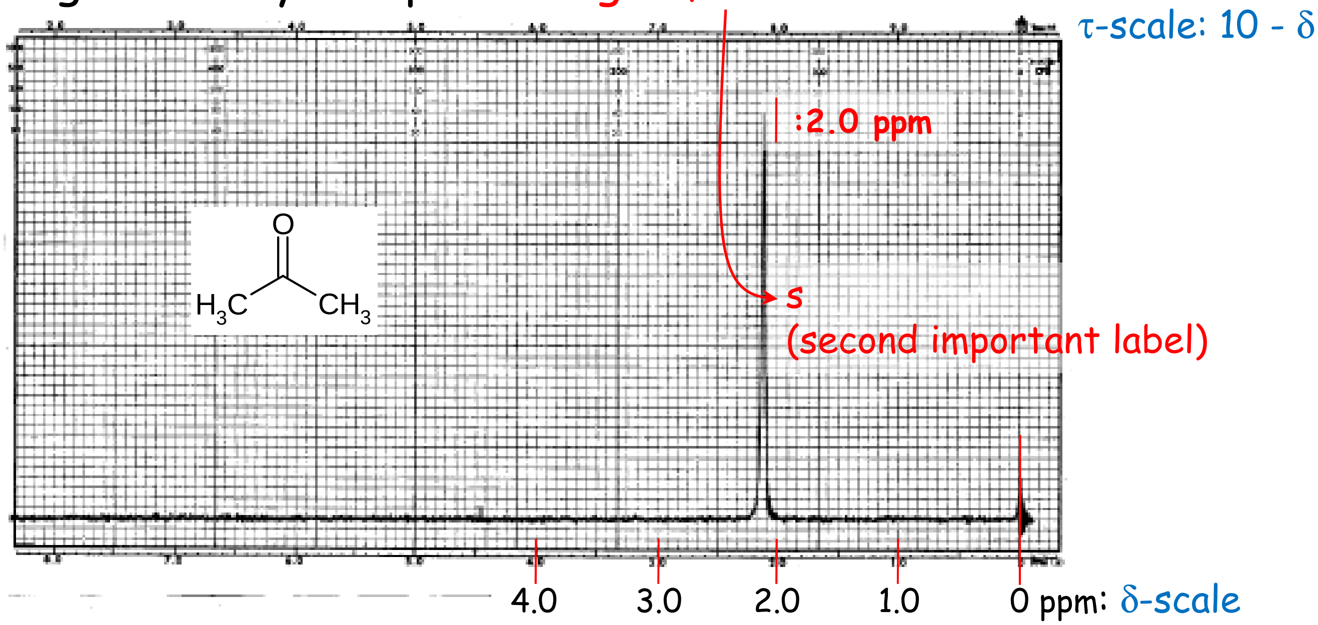
⇒ proton count:
total of 10 ^1H (at least)!

digital information:

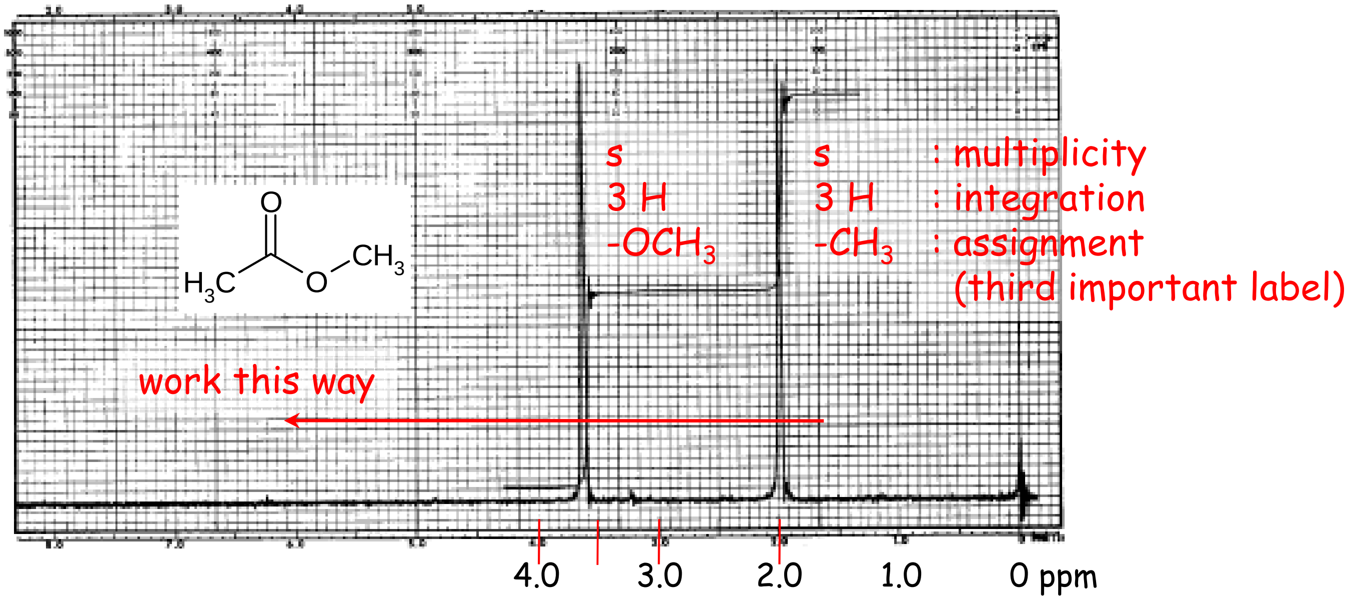


3. Simple (singlet) spectra

- signal is only one peak: singlet, s

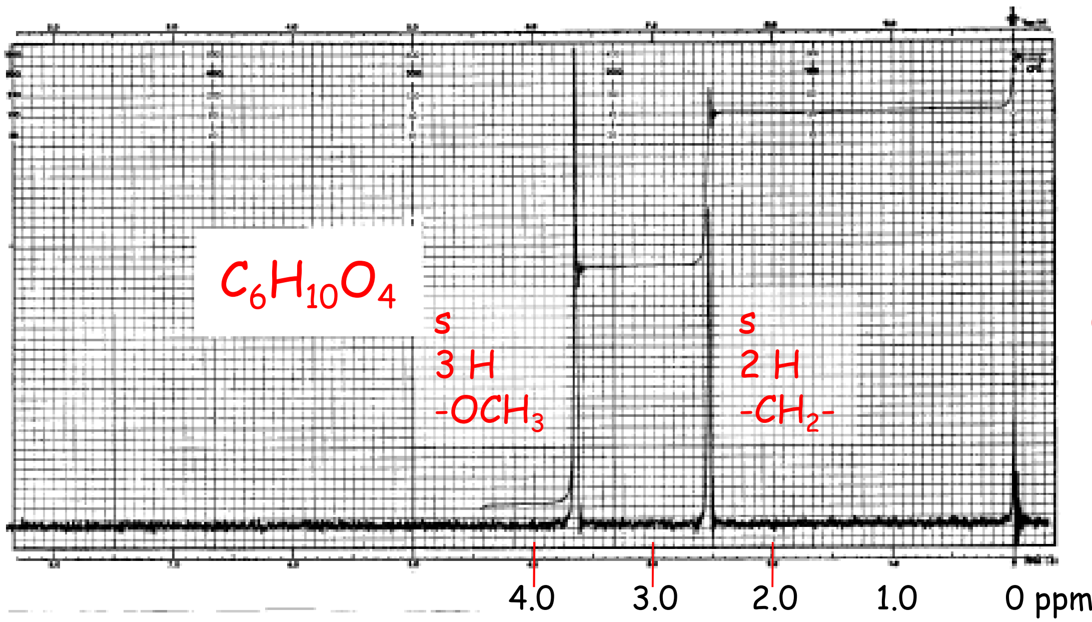


reported:
2.1 s (6H)
C_3H_6O



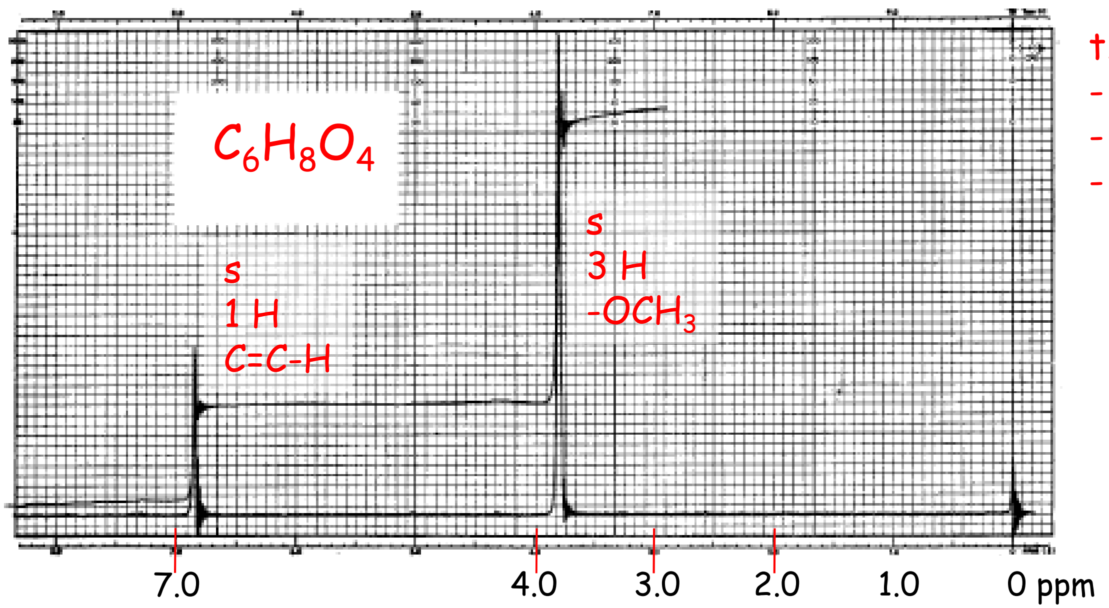
reported:
2.0 s (3H)
3.65 s (3H)
$C_3H_6O_2$

3. Simple spectra continued



integration:
1.5 : 1 or
3 : 2 or revised (!)
6 : 4

reported:
2.55 s 4H
3.65 s 6H
⇒ for a total of 10 ^1H



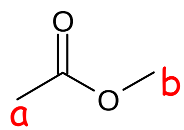
thoughts:
- aromatic?
- U?
- empirical formula?

reported:
3.8 s 6H
6.85 s 2H
⇒ for a total of 8 ^1H

4. Estimation of δ^1H

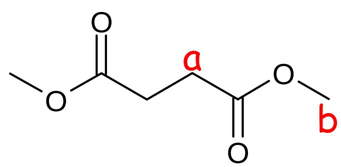
- from increment systems
  - for $X\text{-}CH_2\text{-}Y$ (and $X\text{-}CH_3$, where Y=H adds zero)

δ^1H (ppm) = 0.23 + increments for X and Y substituents see p. A-18



$$\delta^1H_a = 0.23 + \underbrace{1.55}_{COOR} + \underbrace{0}_{H} = 1.78 \text{ ppm (exp. 2.0 ppm)}$$ compare: ok

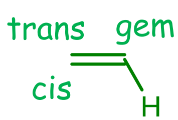
$$\delta^1H_b = 0.23 + \underbrace{3.13}_{OCOR} + \underbrace{0}_{H} = 3.36 \text{ ppm (exp. 3.65 ppm)}$$ ok



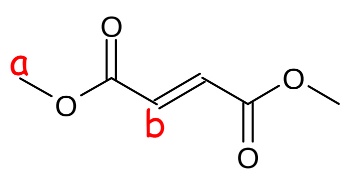
(appropriate?)

$$\delta^1H_a = 0.23 + \underbrace{1.55}_{COOR} + \underbrace{0.47^{?}}_{R} = 2.25 \text{ ppm (exp. 2.55 ppm)}$$ ok

$$\delta^1H_b = 0.23 + \underbrace{3.13}_{OCOR} + \underbrace{0}_{H} = 3.36 \text{ ppm (exp. 3.65 ppm)}$$ ok

- for 

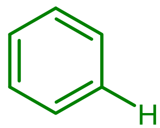
δ^1H (ppm) = 5.25 + increments for gem, trans and cis substituents see p. A-19



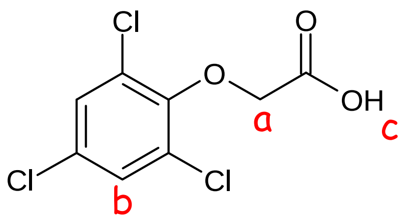
$$\delta^1H_a = 0.23 + \underbrace{3.13^{?}}_{OCOR} + \underbrace{0}_{H} = 3.36 \text{ ppm (exp. 3.8 ppm)}$$ not reliable

$$\delta^1H_b = 5.25 + \underbrace{0.84}_{\substack{gem\\COOR}} + \underbrace{1.15}_{\substack{cis\\COOR}} + \underbrace{0}_{\substack{trans\\H}} = 7.24 \text{ ppm (exp. 6.85 ppm)}$$ ok

4. Estimation of δ¹H continued

- from an increment system
  - for 

δ^1H (ppm) = 7.27 + increments for substituents see p. A-20

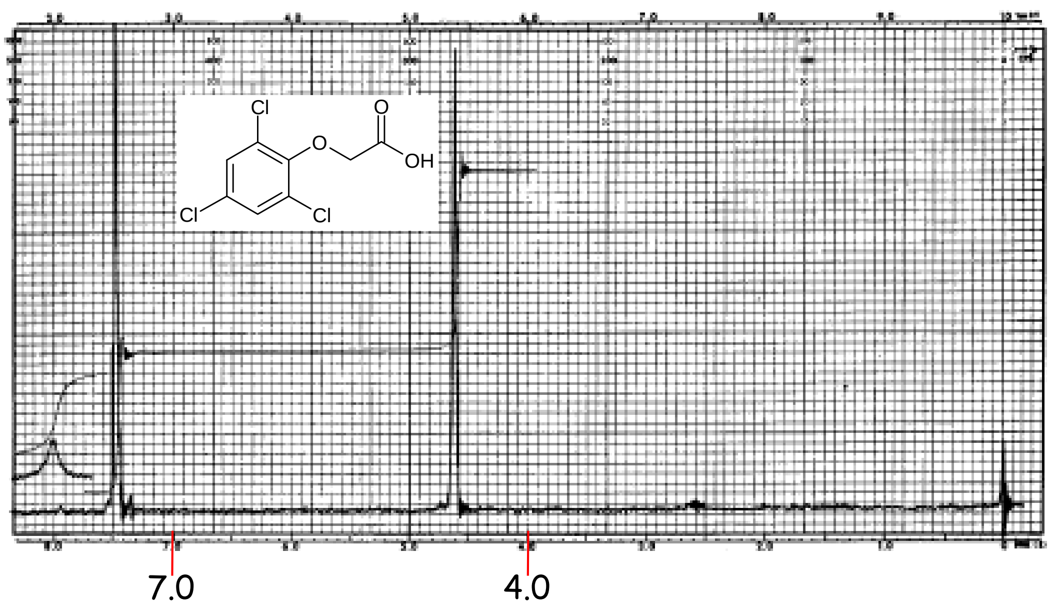


δ^1H_a = 0.23 + 1.55? + 3.23? = 5.01 ppm (exp. 4.6 ppm) ok?
(1.55: COOR; 3.23: OC_6H_5)

δ^1H_b = 7.27 + 2·0.03 + (-0.09) + (-0.09) = 7.15 ppm (exp. 7.5 ppm) ok?
(0.03: o-Cl; -0.09: p-Cl; -0.09: m-OR)

δ^1H_c = 11-12 ppm (no increments; from Table 5.4 or p. A-8)

inset;
problem:
no scale given! →

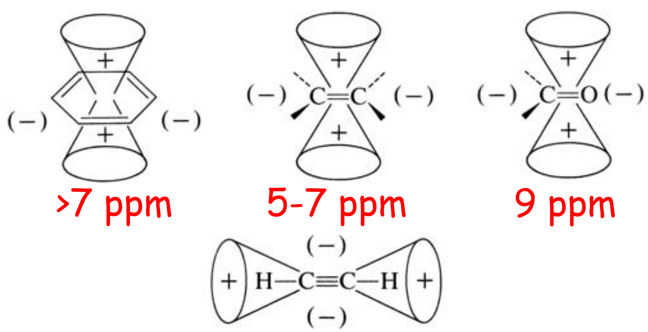


Not overly important for us

5. Magnetic anisotropy

- phenomenon observed for protons on or near π-systems
  - mobile π-electrons create local magnetic fields
  - shielding (+) and deshielding (-) regions
  - unusual chemical shifts

general shielding observations:



>7 ppm

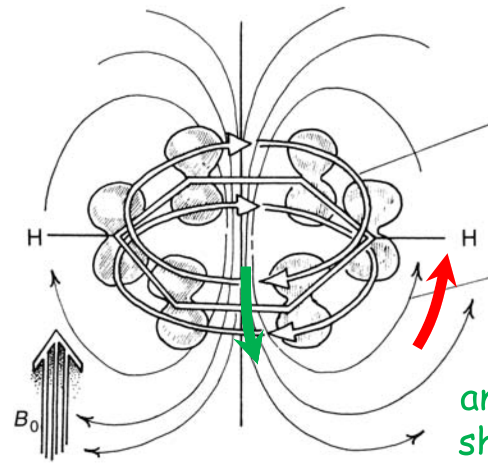
5-7 ppm

9 ppm

2-3 ppm

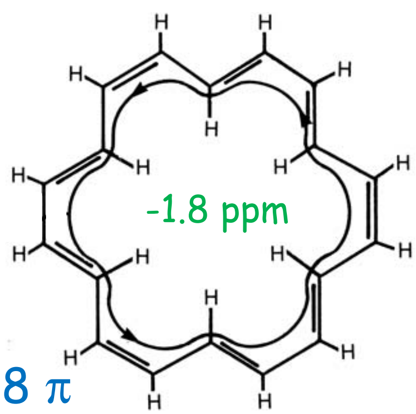
reasoning:

Fig. 5.21



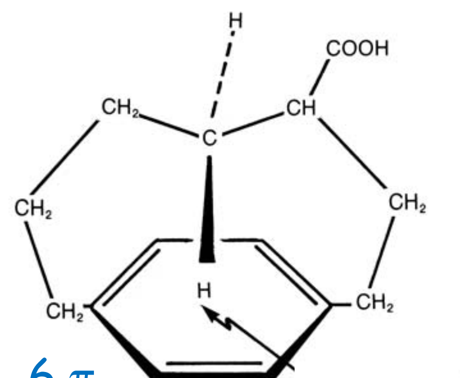
parallel:
deshielding (-)
stronger apparent B_0

antiparallel:
shielding (+)
weaker apparent B_0



-1.8 ppm

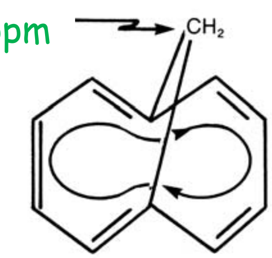
18 π



6 π

-1.4 ppm

-0.5 ppm

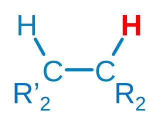


10 π

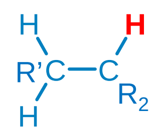
6. Spin-spin coupling

- between sets of chemically equivalent protons: signals are no longer singlets
- signal can be split into (use the red labels):
  - 2 lines: doublet, d
  - 3 lines: triplet, t
  - 4 lines, quartet, q
  - 5 lines, quintet, quint
  - 6 lines, sextet, sext
  - 7 lines, septet, sept

# of lines depends on the number of neighbouring ^1H:
n+1 rule:
n+1 lines in the signal for n equivalent neighbouring ^1H



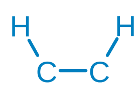
: d signal



: t signal

- protons can couple over
  - 2 bonds: ^2J coupling

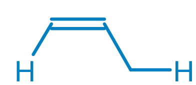
  - 3 bonds: ^3J coupling

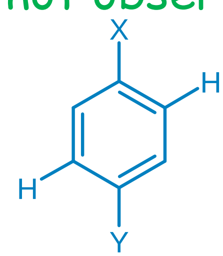


Will get back to this in detail later

  - 4 bonds or more: ^4J, ^5J coupling or "long-range" coupling (mostly not observed)

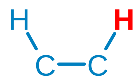
but observed across multiple bonds:





6. Spin-spin coupling continued

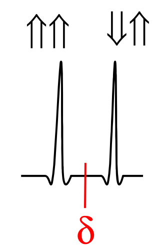
- signal multiplicity (number of lines) explained:



signal observed for this ¹H

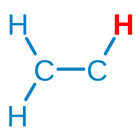
⇑ ⇑
⇓ ⇑

¹H sees ***one*** ¹H on the next carbon atom:
- total of 2 different spin situations: ⇑⇑ and ⇓⇑
- signal for ¹H splits into 2 lines: doublet



equal probability
⇒ same area/height
⇒ intensity ratio in signal 1:1

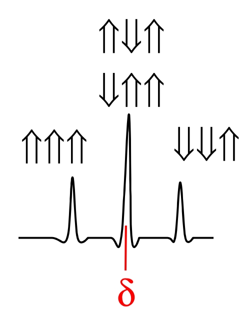
total spin observed by ¹H: $+\frac{1}{2}$ $-\frac{1}{2}$



signal observed for this ¹H

⇑⇑ ⇑
[⇑⇓ ⇑
[⇓⇑ ⇑
⇓⇓ ⇑

¹H sees ***two*** ¹H on the next carbon atom:
- total of 3 different spin situations
- signal for ¹H splits into 3 lines: triplet



⇒ intensity ratio in signal 1:2:1

total spin observed by ¹H: +1 0 -1

6. Spin-spin coupling continued

- for I = ½, intensities of the lines within a signal follow the binomial distribution
- Pascal's triangle (easily constructed)

1   one line only

1   1   two lines, equal intensities

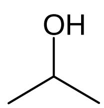
1   2   1   three lines, intensity ratio 1:2:1

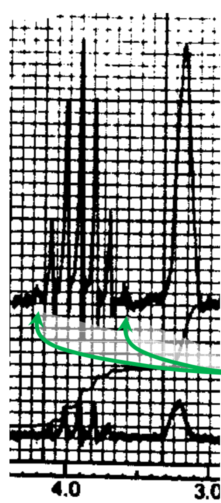
1   3   3   1

1   4   6   4   1

1   5   10   10   5   1

1   6   15   20   15   6   1   septet, outer lines often tough to detect!





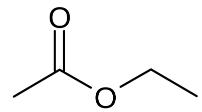
don't miss the outer lines!

looks like only 5 lines

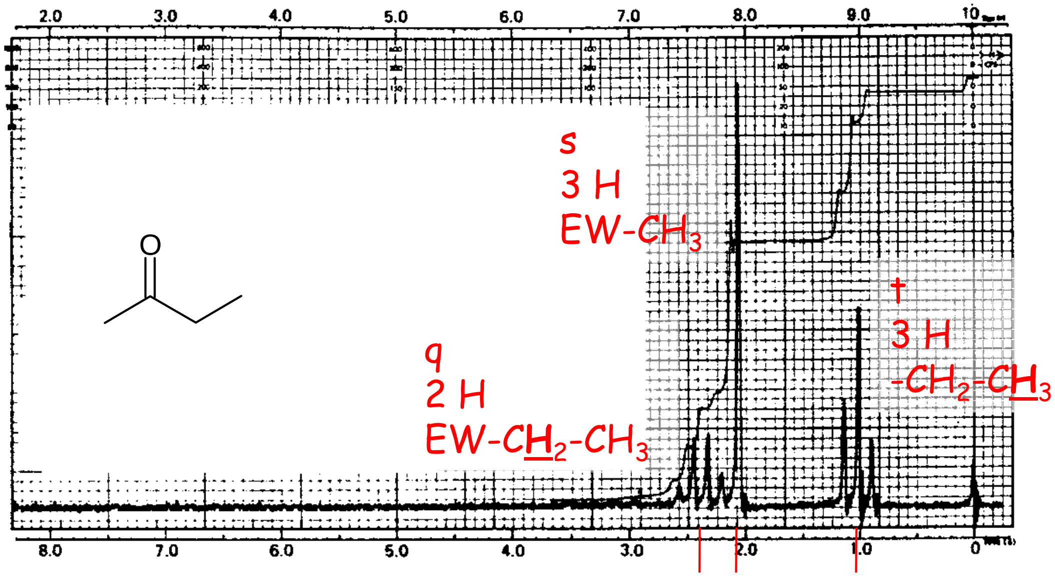
now we can predict ^{1}H spectra

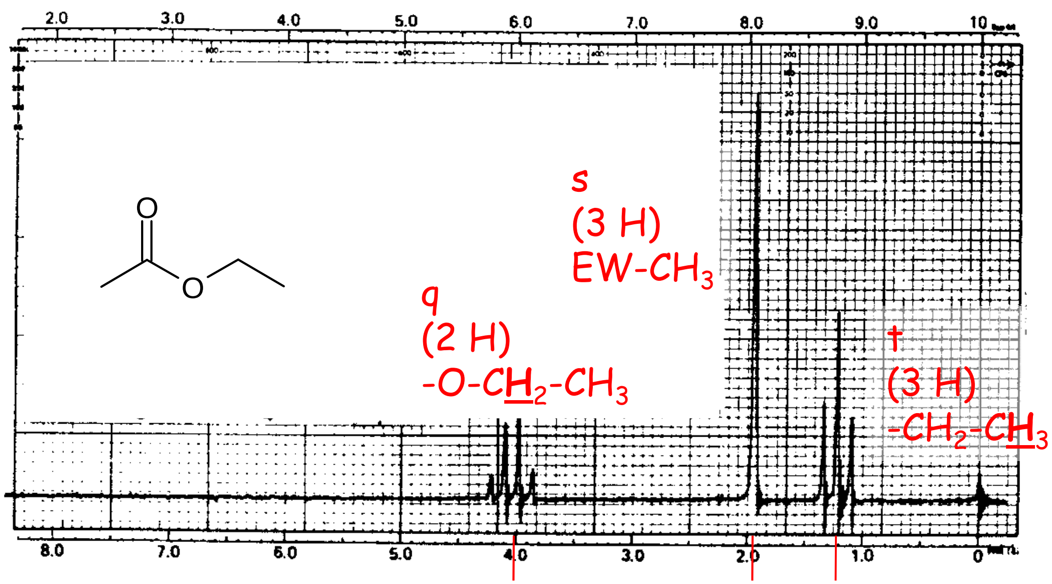
Example

Better than problem 5.13!

Predict (draw) the ^{1}H NMR spectrum for  .
First list (the calculated) δ, multiplicity and integration.

7. Spectra with simple multiplets





Do not forget that you need all three labels on a signal!

Table 5.8: examples of splitting patterns

7. Spectra with simple multiplets continued

- multiplet issues

I. Multiplicity

$ClCH_2CH_2CH_2CH_3$

quint sext

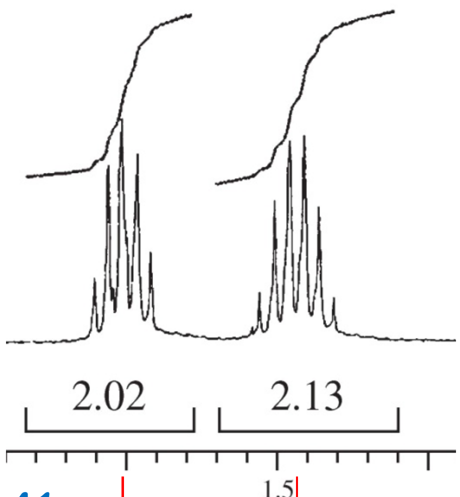


Fig. 5.41

Δδ 0.25 ppm

$CH_3OCH_2CH_2CH_2CH_3$

quint? sext?

Or both rather "mult"?

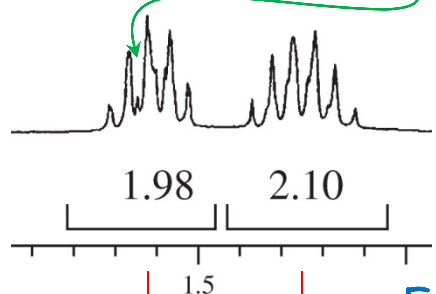


Fig. 5.43

Δδ 0.15 ppm

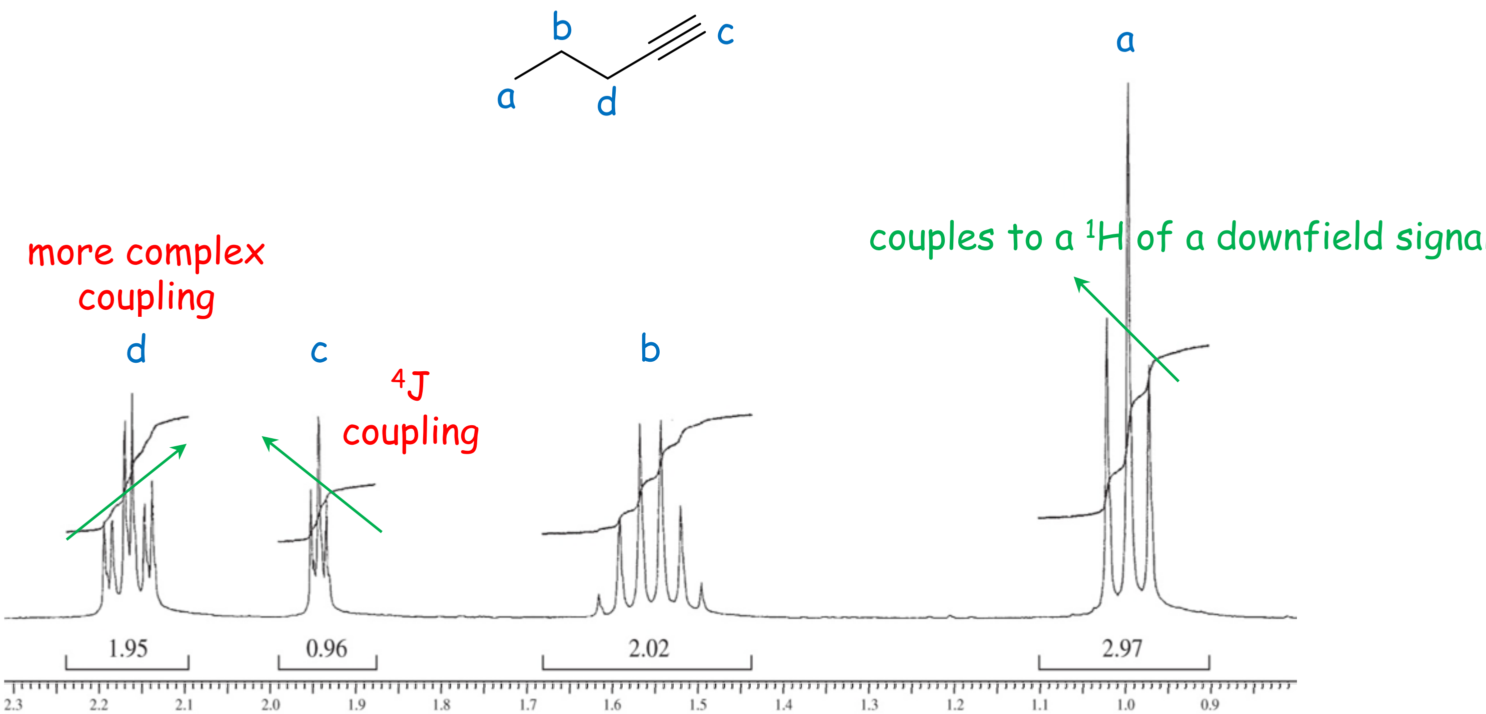
Will discuss later in more detail, but for our purposes, these are still quint and sext!

7. Spectra with simple multiplets continued

- multiplet issues

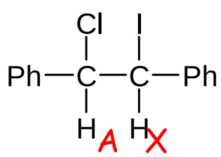
II. Skewing in multiplets

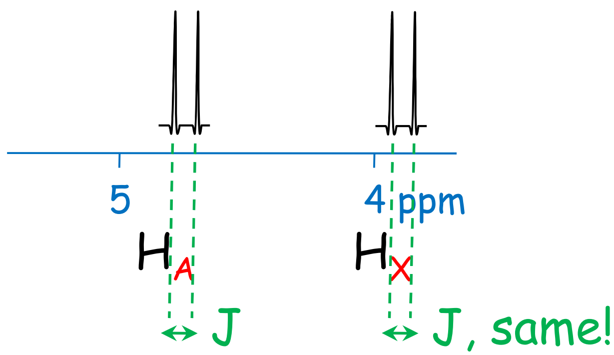
- first information on which protons are coupled



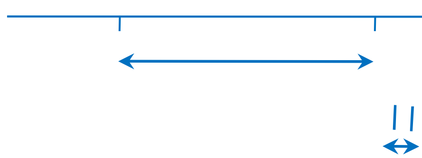
8. Coupling constant, J

- number assigned to the spread of the lines in a multiplet
  - more reliable information on which protons are coupled than skewing
  - for two multiplets from coupling protons, J is the same





if this spectrum was taken at 60 MHz:



1 ppm or 60 Hz

0.1 ppm $\Rightarrow$ ^3J 6 Hz

AX spin system:

- Pople notation for coupling protons
- two chemically different protons, $\Delta\delta$ is (relatively) large

8. Coupling constant, J, continued

ICH_2CH_3

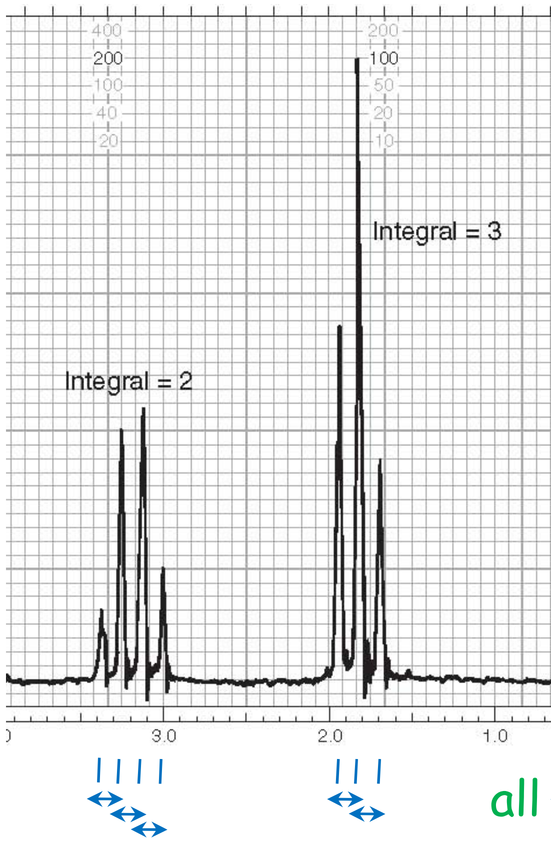


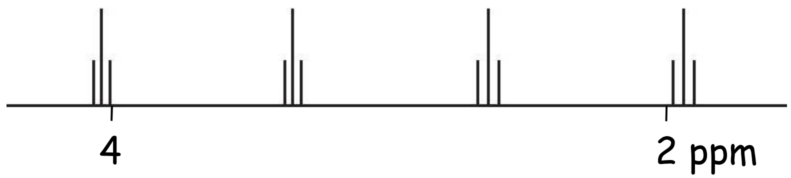
Table 5.9:
generalized J values
and
A-13 ff

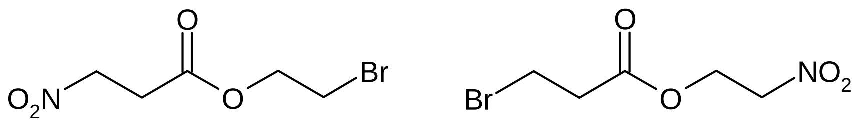
all ↔ spacings are the same,
^3J 7.5 Hz

A_2X_3 spin system:
- Pople notation
- two sets of chemically different protons, $\Delta\delta$ is (relatively) large

Example

Assuming that ^3J is greater upon Br-substitution, which structure is correct?





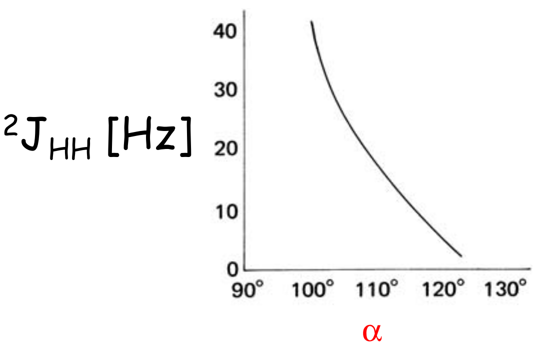
8. Coupling constant, J, continued

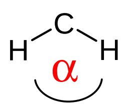
- origin of the coupling: via the electrons in the bonds

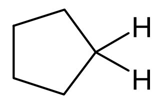
: interaction between spins of nuclei and electrons

size of J depends on the geometry:

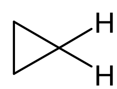
- ^2J depends on the HCH bond angle: larger J with smaller angle (better interaction of σ-orbitals)







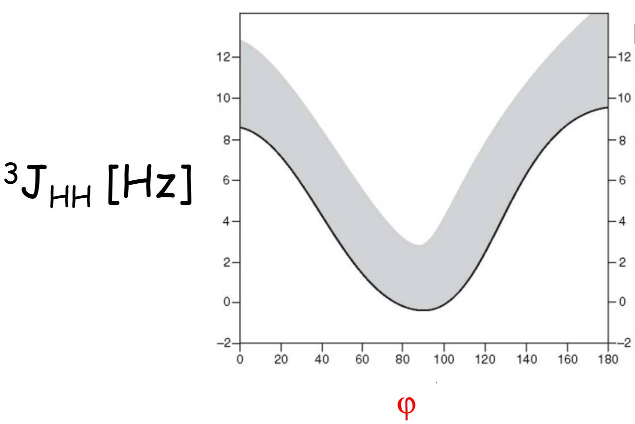
α 109°
^2J 12 Hz

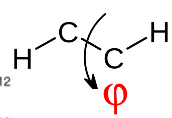


α 118°
^2J 5 Hz

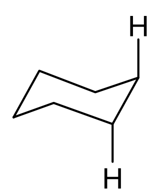
Fig. 7.4

- ^3J depends on the HCCH torsion angle: minimum function at 90° (no interaction of σ-orbitals)

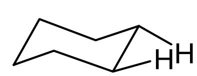




Karplus curve



φ 180°
^3J 12 Hz



φ 60°
^3J 4 Hz

Fig. 7.7

9. First and second order spectra

- Second-order spectra are found for sets of nuclei if $\Delta\nu/J$ is too small

both in Hz

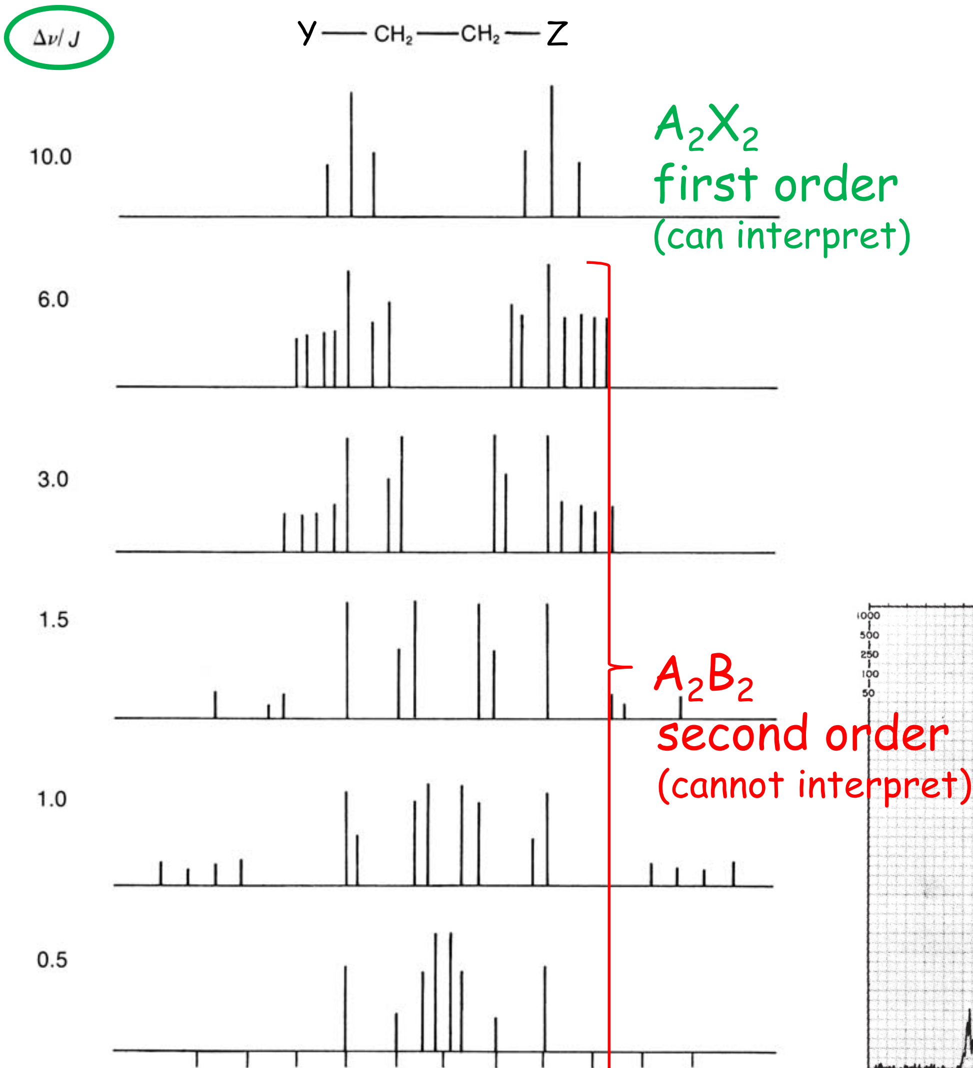


Fig. 7.44

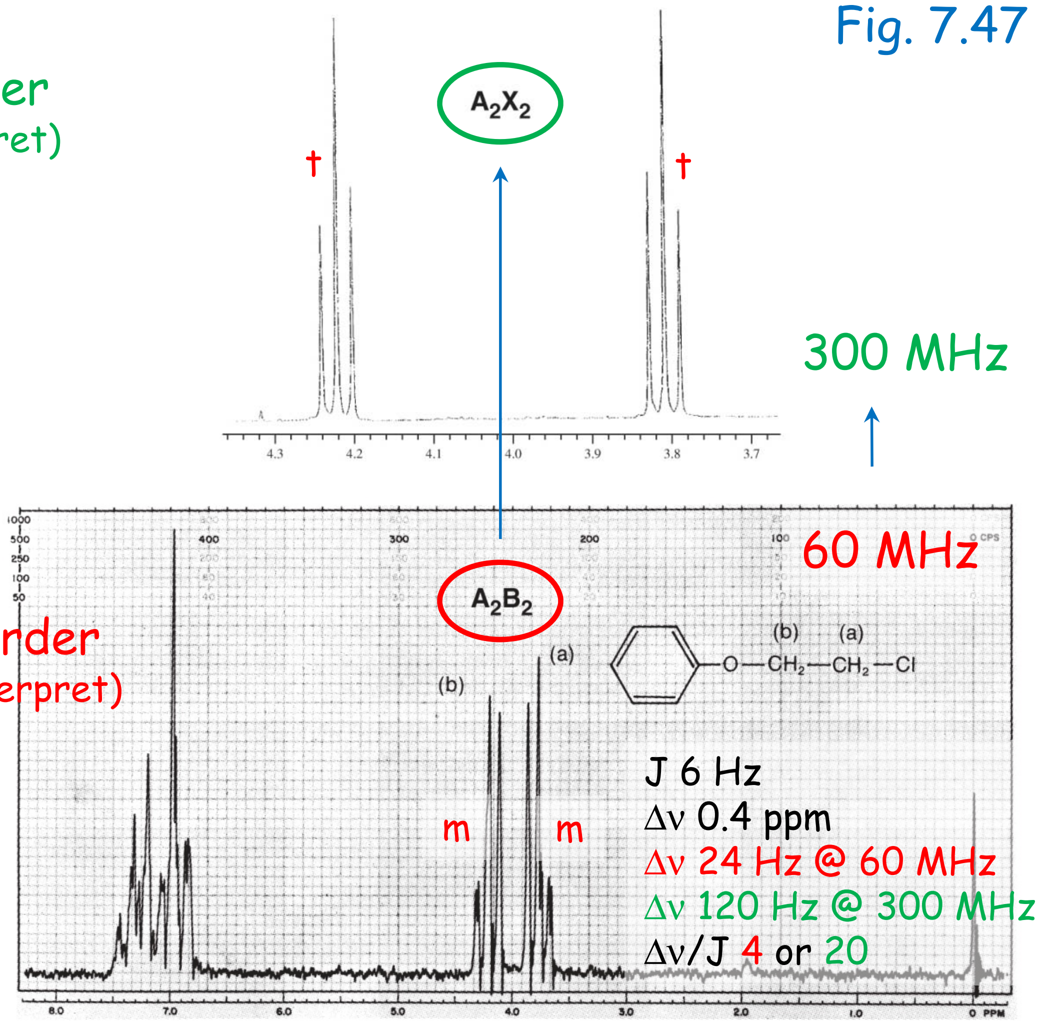
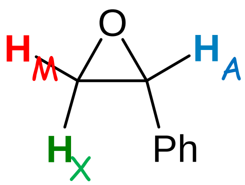


Fig. 7.47

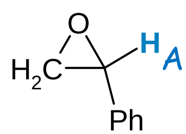
10. Non-equivalence within a group

- coupling within a group (CH_2, e.g.) when protons are ***not*** chemically equivalent



all three [1]H are chemically different

⇒ all will couple amongst each other

⇒this is ***not*** 

, H_A does ***not*** couple into a triplet!

- observed coupling here: $^3J_{AM} \neq {}^3J_{AX}$, $^2J_{MX}$
- we expect - three different coupling constants
  - signals of different multiplicity than so far

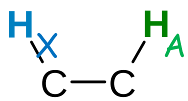
- we can analyse – coupling constants
  - appearance of a signal

  through tree-diagrams

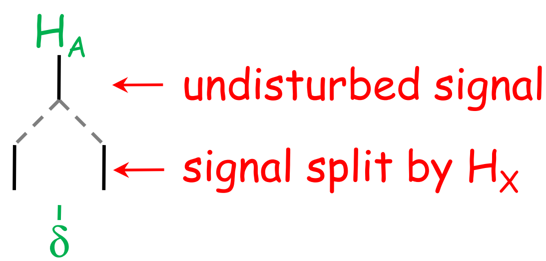
10. Non-equivalence within a group continued

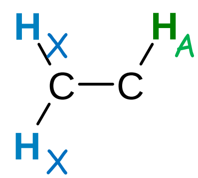
- analysis with a tree-diagram

simple system:
coupling to one type of ^{1}H

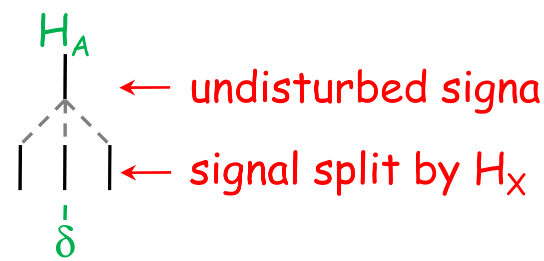


⇒ doublet for H_A

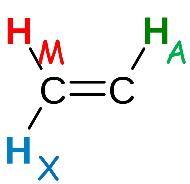




⇒ triplet for H_A



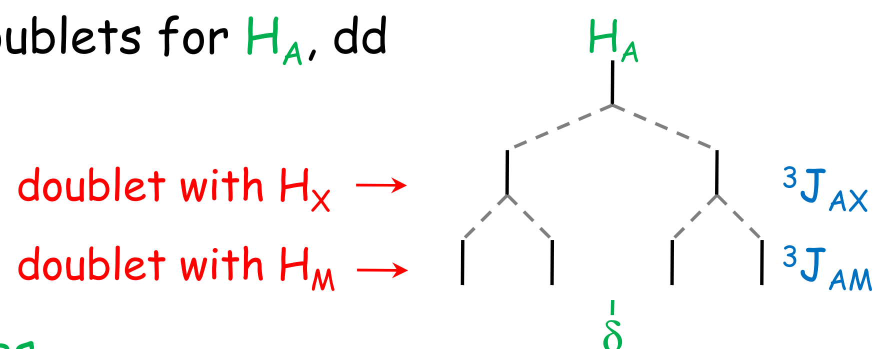
advanced system:
coupling to two types of ^{1}H



AMX system

⇒ one doublet for H_A with H_M, one doublet for H_A with H_X

⇒ doublet of doublets for H_A, dd



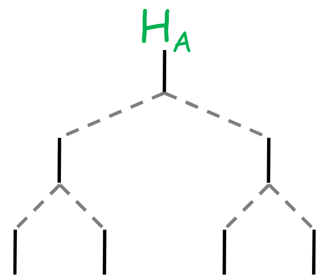
⇒ 1 signal, 4 lines

10. Non-equivalence within a group continued

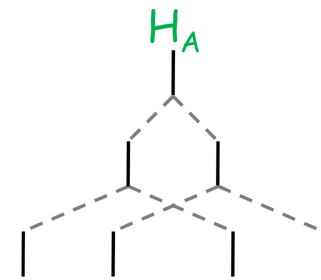
- two uses of a tree-diagram

towards a spectrum: what does the signal look like?

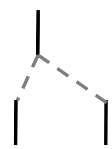
- use larger J first



not like this:



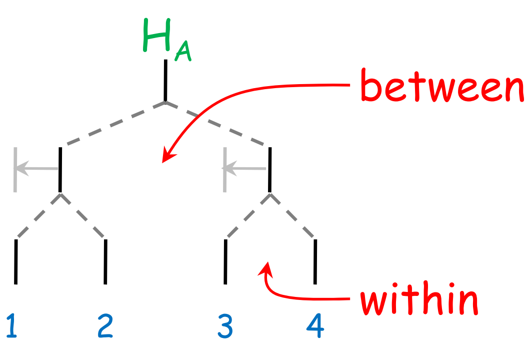
- stay symmetrical



: not like this, either!

from a spectrum: what are the coupling constants?

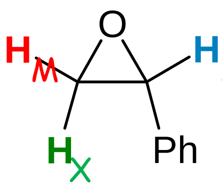
- take distance ***within*** and ***between*** the "sub-multiplets"



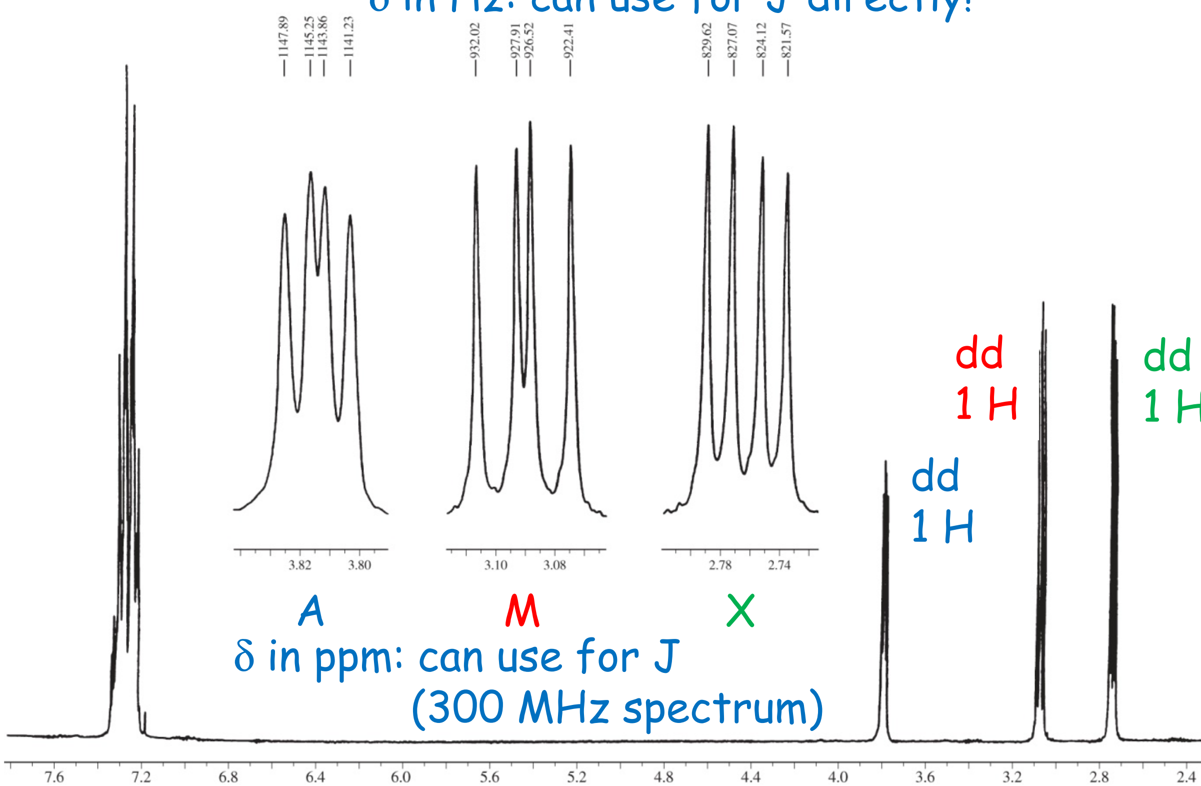
for a dd, measure
"within": distance of lines 1 and 2 or 3 and 4
"between": distance of lines 1 and 3 or 2 and 4

10. Non-equivalence within a group continued

- appearance of the spectrum



δ in Hz: can use for J directly!

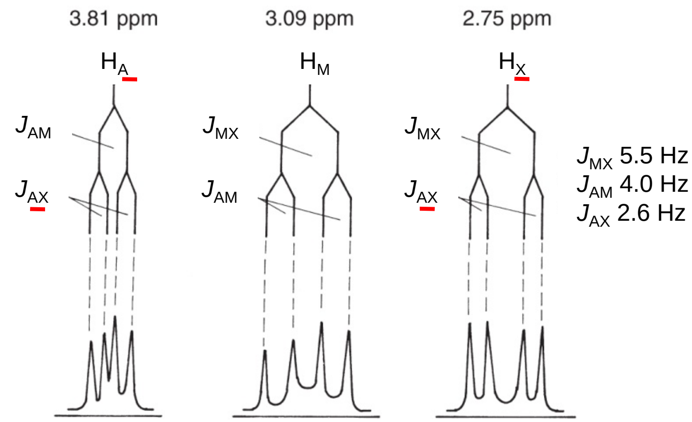


δ in ppm: can use for J

(300 MHz spectrum)

Fig. 7.31

tree-diagram analysis



example:

J_{AX} appears twice:

- in the signal for H_A
- in the signal for H_X

summarize as:

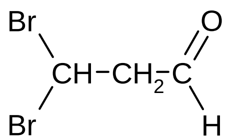
$^3J_{AX}$ 2.6 Hz

$^3J_{AM}$ 4.0 Hz

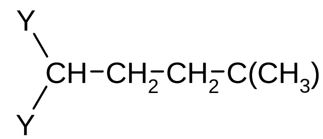
$^2J_{MX}$ 5.5 Hz

10. Non-equivalence within a group continued

- two practice patterns



spin system:



spin system:

multiplicities:

tree-diagram (assume $J_1 > J_2$):

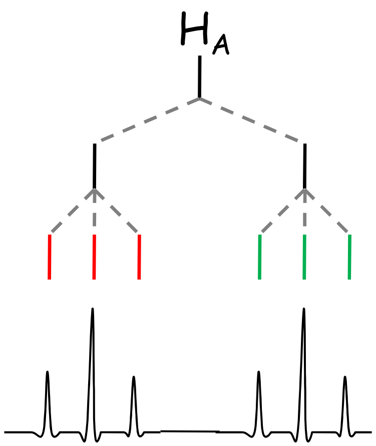
multiplicities:

tree-diagram:

How do you determine which J is which?

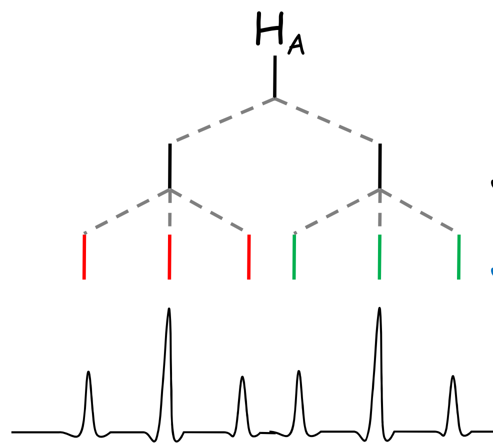
10. Non-equivalence within a group continued

- the appearance of a dt as J changes



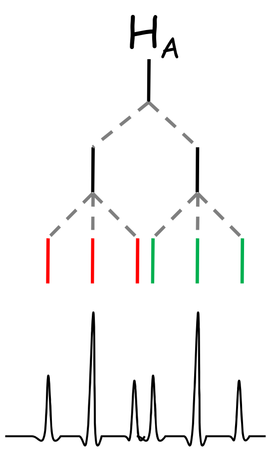
J_1 14 Hz

J_2 3 Hz



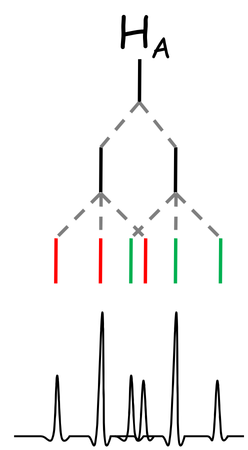
J_1 14 Hz

J_2 6 Hz



J_1 8 Hz

J_2 3 Hz

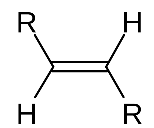


J_1 6 Hz (bit less)

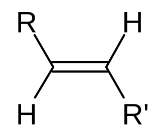
J_2 3 Hz

10. Non-equivalence within a group continued

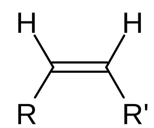
- coupling examples in alkenes



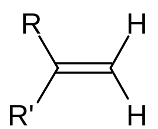
[1]H are chemically and magnetically equivalent
⇒ s, 2H, no splitting



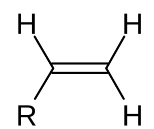
2 d, ^3J ~ 16 Hz (large)



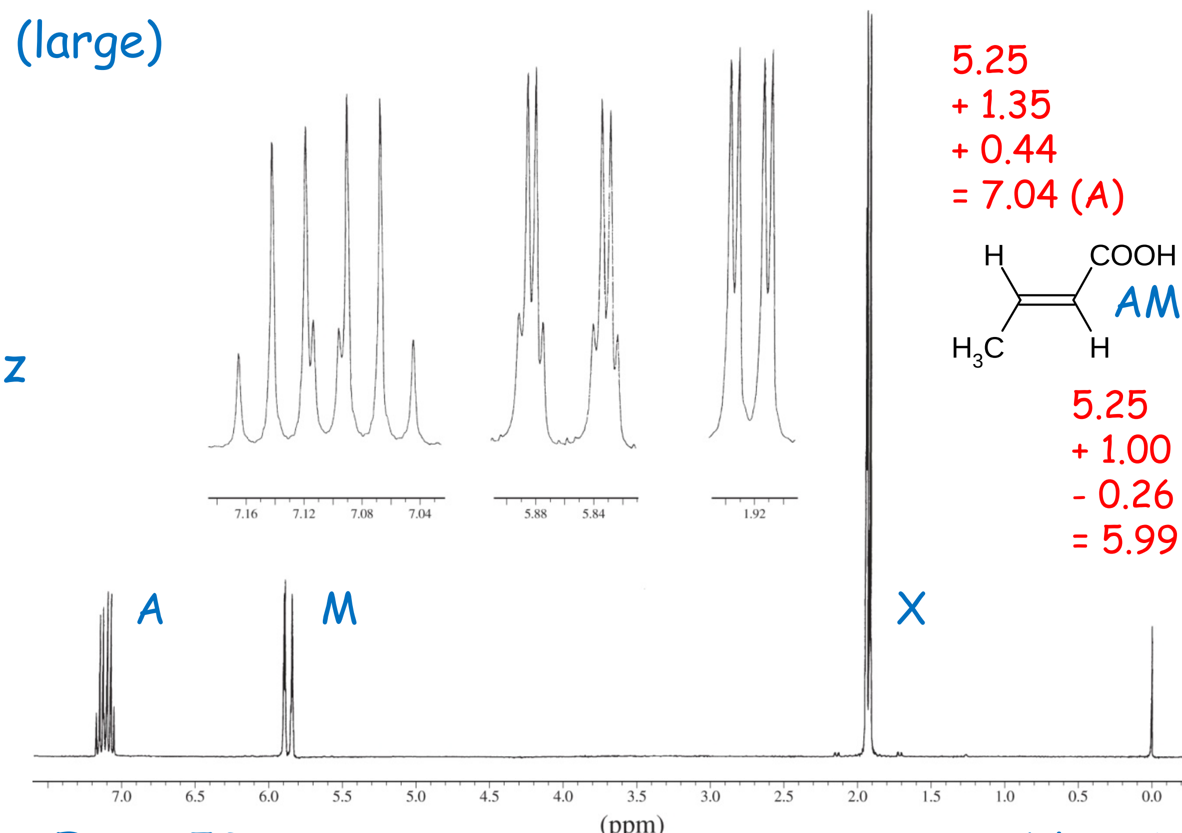
2 d, ^3J ~ 8 Hz



2 d, ^2J ~ 0-5 Hz



3 dd



5.25
+ 1.35
+ 0.44
= 7.04 (A)

H COOH
H_3C H

AMX$_3$

5.25
+ 1.00
- 0.26
= 5.99 (M)

Fig. 7.53

Table A6.2

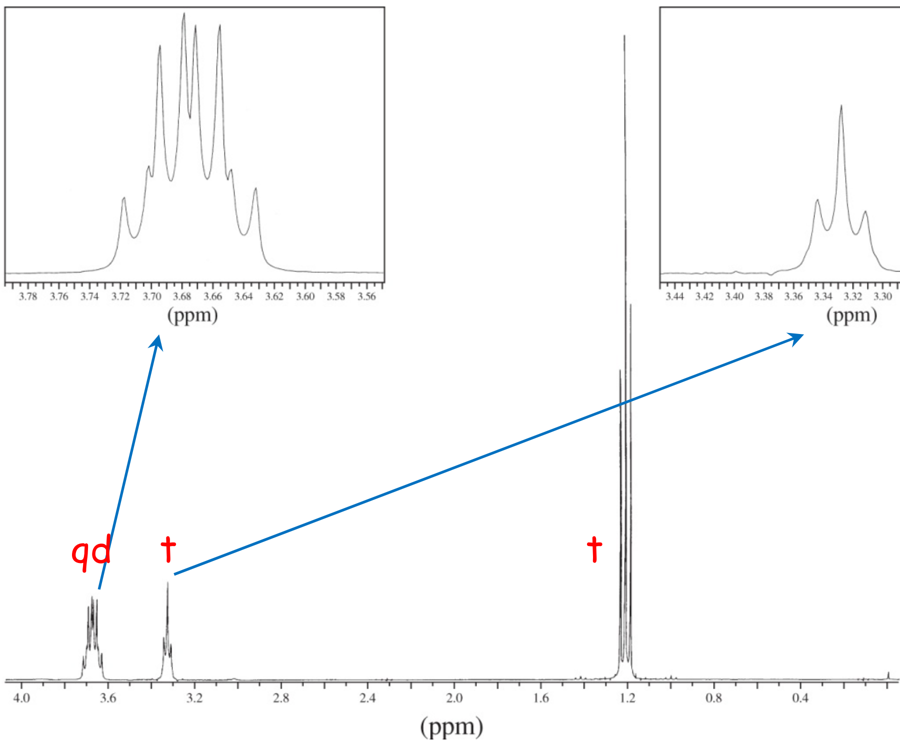
11. Protons on oxygen

- 2 issues

I. Lack of coupling

CH_3CH_2OH

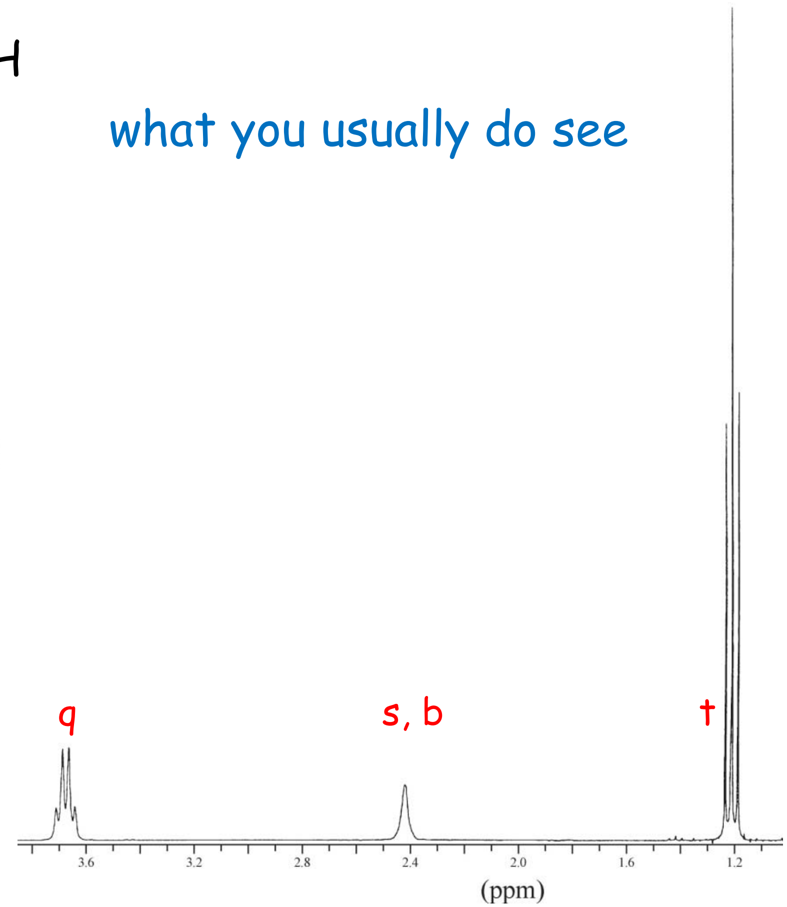
what you might expect to see



- ultrapure sample
- coupling to the OH proton observed

Fig. 8.3

what you usually do see



- ordinary sample
- coupling to the OH proton ***not*** observed

Fig. 8.2

11. Protons on oxygen continued

- Reason that coupling to protons on oxygen is not observed:
  - exchange takes place with other ROH, H_2O, traces of acid…
  - OH proton is not attached long enough for coupling to be recorded
  - rate of exchange is too great

Examples of fast exchange (high rate):

$CH_3OH + H_3O^+ \rightleftharpoons CH_3OH_2^+ + H_2O$ 10^8 L/mol·s

$RSH + R'S^- \rightleftharpoons RS^- + R'SH$ $6 \cdot 10^5$ L/mol·s

Example of a slow exchange (low rate):

$CH_3OH + H^*OH \rightleftharpoons CH_3OH^* + H_2O$ 3 L/mol·s

- for coupling to be observed,

  rate of exchange (1/s) ≈ coupling constant J (Hz)

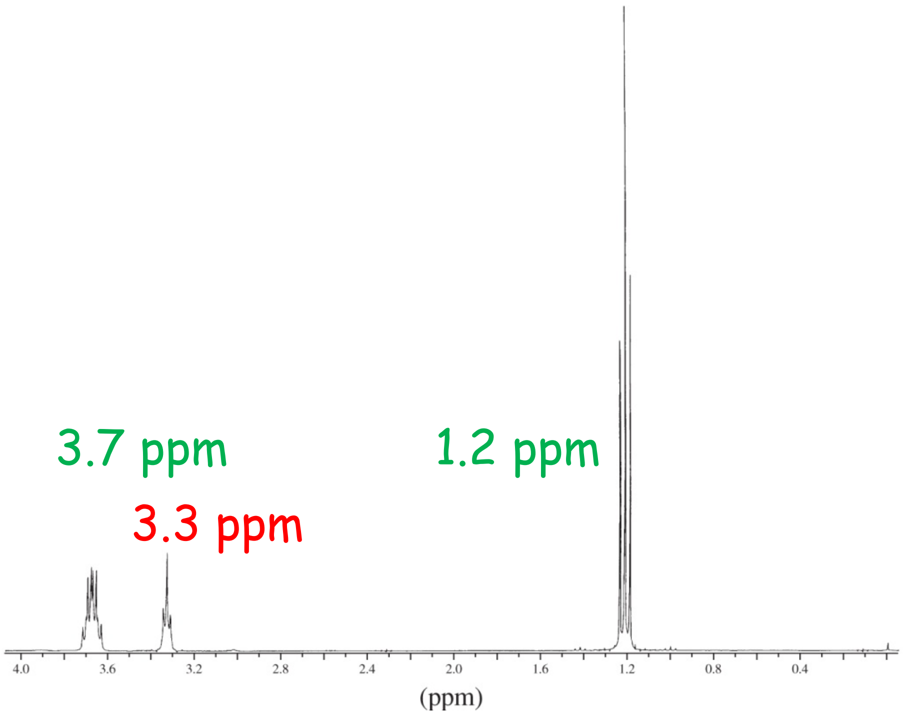
How would you slow down the rate of exchange?
Cooling?
H-bonding?

11. Protons on oxygen continued

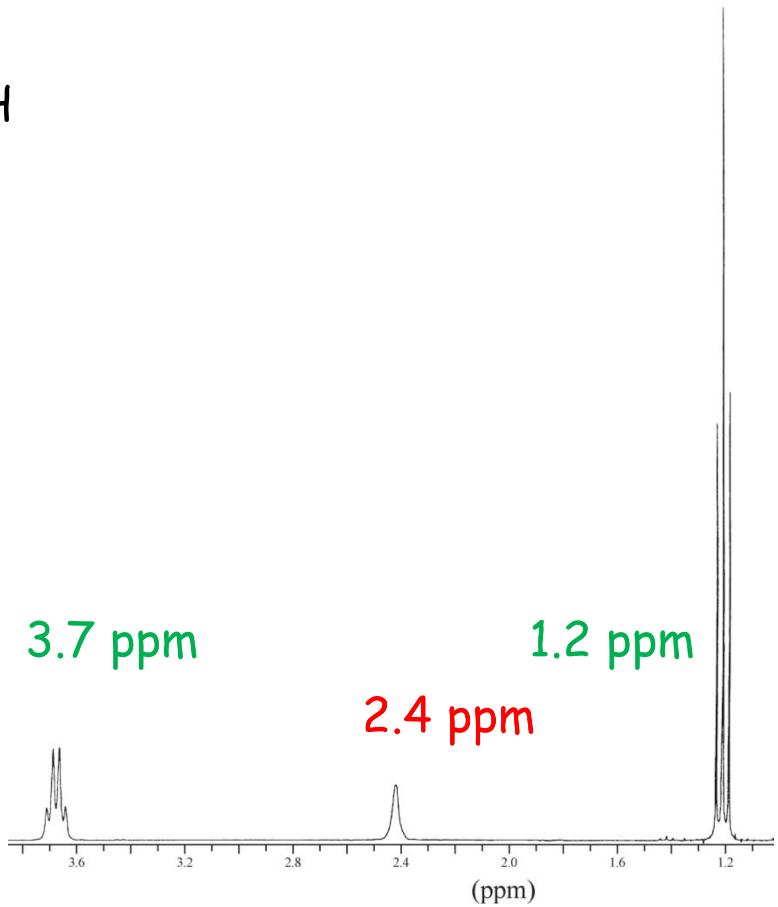
- 2 issues

II. Variability in δ

CH_3CH_2OH



- ultrapure sample



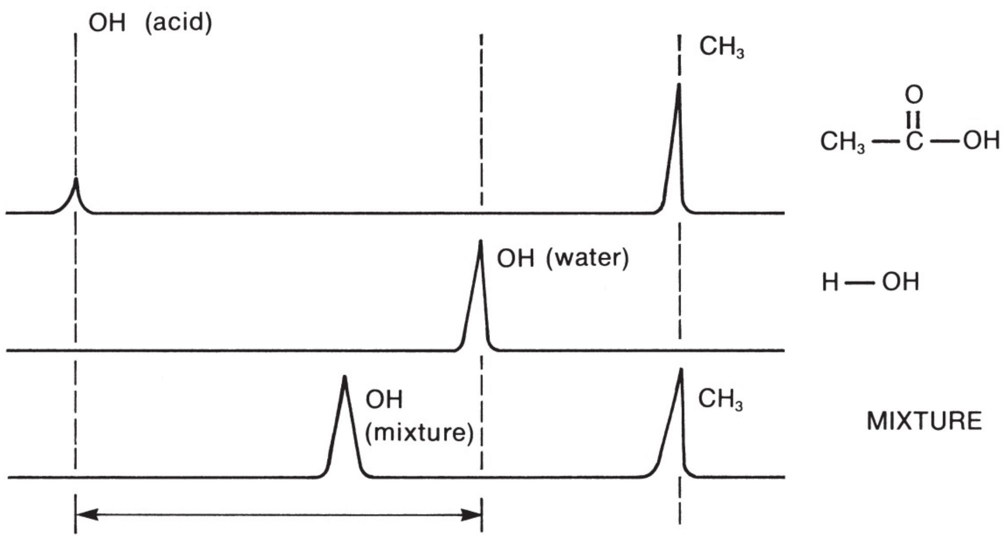
- ordinary sample

Fig. 8.3

Fig. 8.2

11. Protons on oxygen continued

- Reason for the variable δ:
  - rapid exchange with H_2O… (again)
  - OH signal position becomes the weighted average



exact position depends on the amount of water

Fig. 8.4