C8953
NMR structural analysis seminar

Information about classes + 1D ^{1}H-NMR

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Information about classes

Credit:
- ▶ Max. 2 unexcused absences
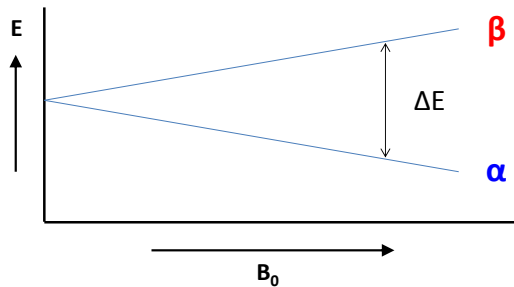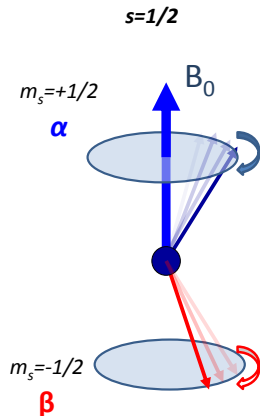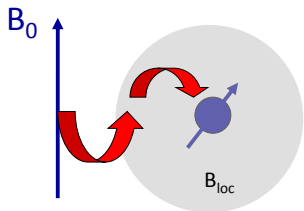- ▶ 2 successfully solved tests (midterm and final)

Study materials:
https://is.muni.cz/auth/el/1431/jaro2018/C8953/um
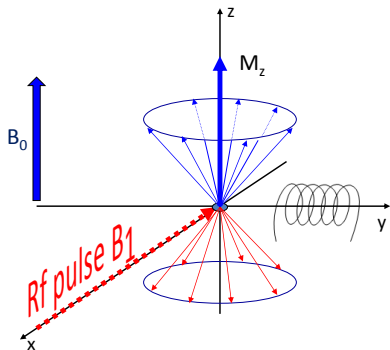
E-tests:
https://is.muni.cz/auth/el/1431/jaro2018/C8953/odp

Energy levels splitting

Behavior of nuclear spin after irradiation by RF pulse

B_0 induces local mag. field B_{loc}, which affects against B_0

↓

Nuclear shielding

|	
Precession frequency:	$\omega = -\gamma B_0$
Precession frequency affected by nuclear shielding:	$\omega = -(1+\sigma)B_0$
Chemical shift:	$\delta = \omega - \omega_{ref}$
Definition of th relative scale of the chemical shift:	$\delta = (\omega - \omega_{ref})/\omega_{ref}.10^6 ppm$

Characteristic intervals of chemical shifts values
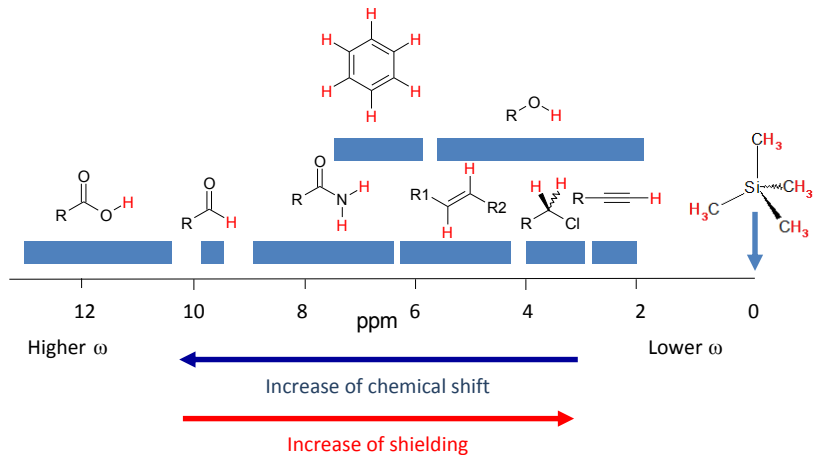
Trends in chemical shifts

- ▶ Electronegativity, inductive and mesomeric effects of substituents
- ▶ Hybridisation
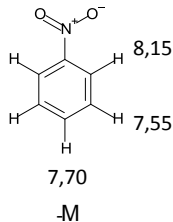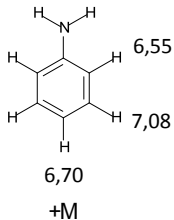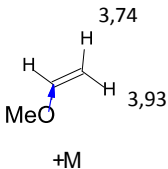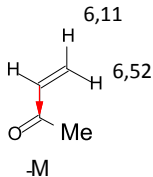- ▶ Relative position towards the ring, double bond

2,1 ppm   2,3 ppm   3 ppm   3,1 ppm   4,5 ppm
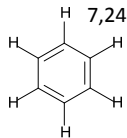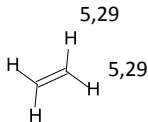
5,3 ppm

7,3 ppm
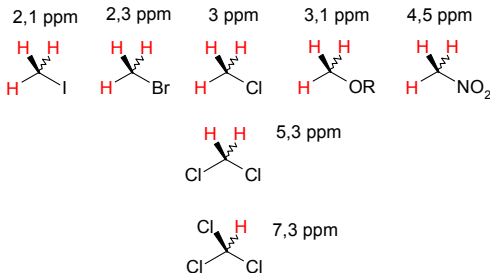
Substituents with -I effect

$=N^+R_2 > -N^+R_3 > -NO_2 > -NR_2$

$-SO_2R > -SO_3 > -SOR > -SR$

$-F > -OR > -NR_2 > -CR_3$

$-F > -Cl > -Br > -I$

$\equiv N > =NR > -NR_2$

$-C\equiv CH > -CH=CH_2 > -CH_2-CH_3$

Substituents with +I effects

$-N^- > -R > -O^- > -S^-$

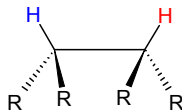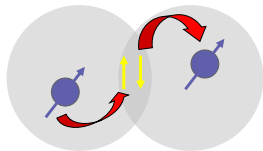$-C(CH_3)_3 > -CH(CH_3)_2 > -CH_2CH_3 > -CH_3$

metals

Mesomeric effect

Substituents with -M effects
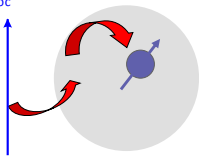-F, -Cl, -Br, -I, -OH, -OR, -NH₂, -NHR, -NR₂, -SH, -SR

Substituents with +M effect
-CH=O, -RC=O, -C(OH)=O, -C(OR)=O, -C(NH₂)=O, -NO₂, -SO₃H, -C≡N
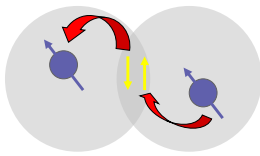
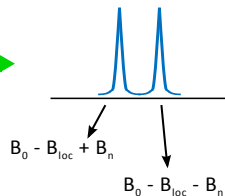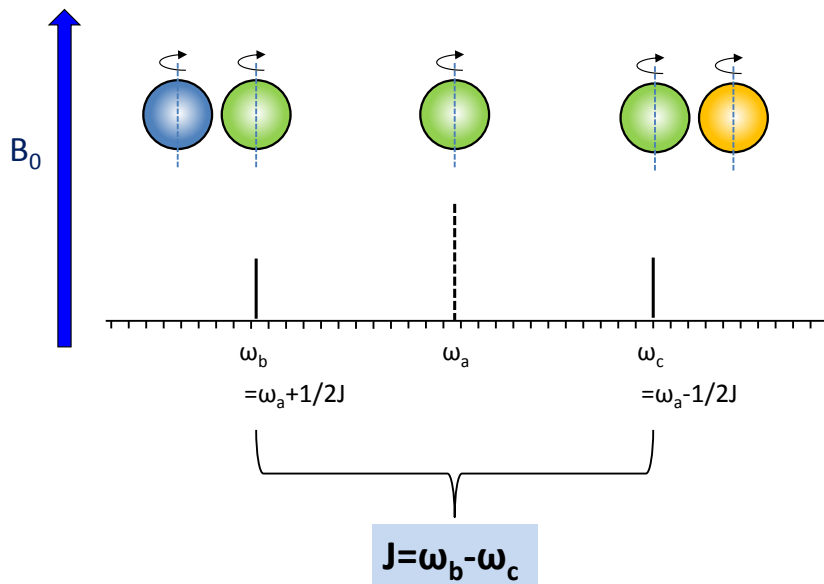# Spin-spin interaction, *J*-coupling

B_{loc}

H

$B_0 - B_{loc}$

H   H

Nucleus H: spin $\alpha \rightarrow -B_n$
spin $\beta \rightarrow +B_n$

$B_0 - B_{loc} + B_n$

$B_0 - B_{loc} - B_n$

Interaction constant *J*

Interaction constant J

$$- CH_2 - CH_3$$
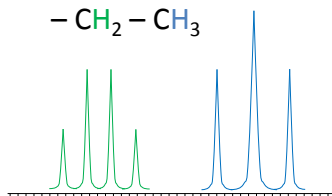
- ▶ Multiplicity of the nucleus I with the spin 1/2 is given by:
  $m = n + 1$, n = number of interacting nuclei with nucleus I
- ▶ Intensity of lines in multiplet follows Pascal's triangle

```
              1
           1     1
        1     2     1
     1     3     3     1
   1    4     6     4     1
 1   5    10    10     5    1
```

1D ^{1}H NMR spectrum

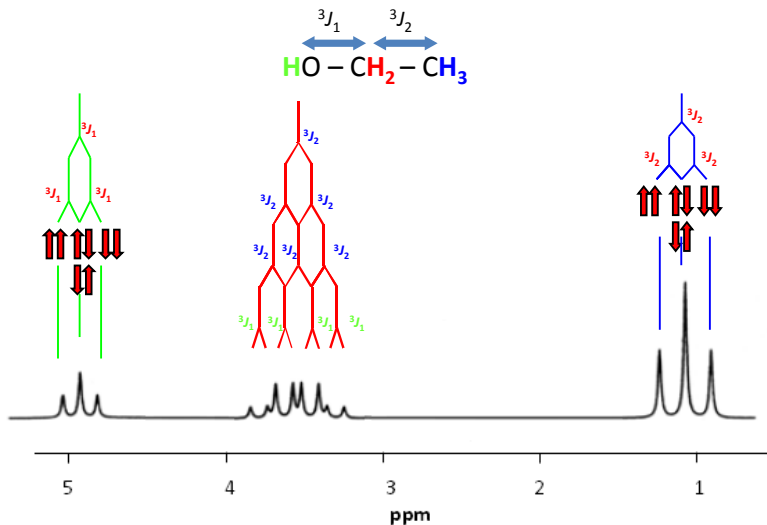# Values of *J*-constants - trends
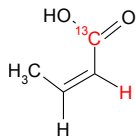
$^2J_{CH}$ = 3.1 Hz

$^3J_{HH}$ = 12 Hz
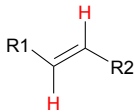
$^3J_{HH}$ = 13 - 18 Hz
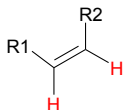
$^5J_{HH}$ = 7 - 12 Hz
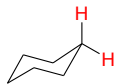
$^2J_{HH}$ = -12,5 Hz
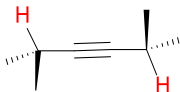
$^5J_{HH}$ = 2 - 3 Hz

$^1J_{CH}$ = 125 Hz

$^1J_{CH}$ = 160 Hz

$^1J_{CH}$ = 250 Hz

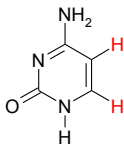# Values of *J*-constants - trends
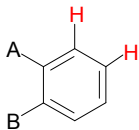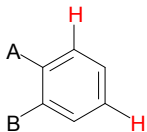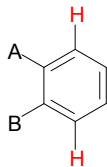
$^3J_{HH}$ = 7,5 Hz $^4J_{HH}$ = 1,5 Hz $^5J_{HH}$ = 0,7 Hz
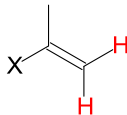
X=	Li	H	Cl	OMe	F
$^2J_{HH}$ (Hz)	7,1	2,5	-1,4	-2,0	-3,2

1D ^{1}H NMR spectroscopy

- ▶ the fastest measuring, the highest sensitivity
- ▶ complicated interpretation in case of more complex systems

We are looking for:

- ▶ position of the signal (ppm)
- ▶ multiplicity (^2J, ^3J, ^4J)
- ▶ intensity (integral)
- ▶ halfwidth

We are considering:

- ▶ chemical/magnetic equivalence
- ▶ enantiotopicity/diastereotopicity
- ▶ averaging of signals (dynamics, chemical exchange)

1D ^{1}H NMR spectrum of methyl-5-acetylsalicylate
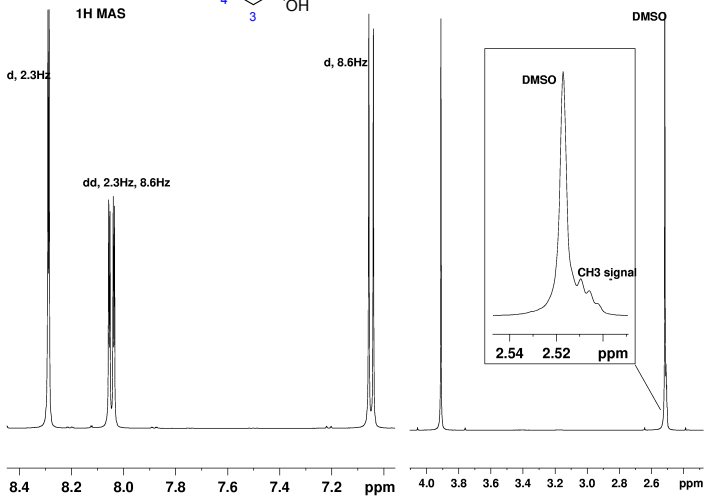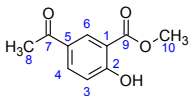
1D ^{1}H NMR spectrum of methyl-5-acetylsalicylate
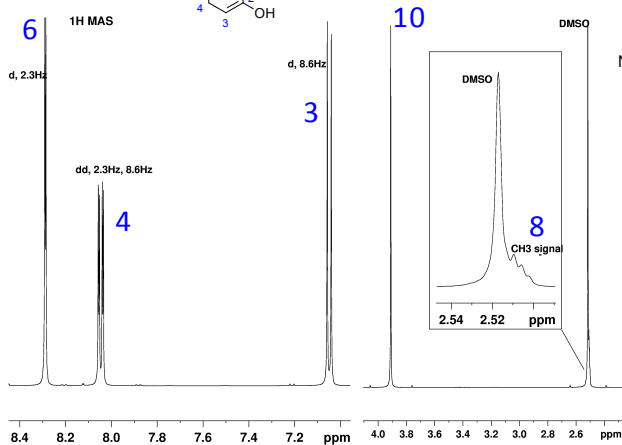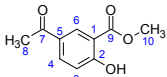
Notes:

- two singlets in the spectrum - two isolated groups in the structure - CH$_3$ groups; **Met-8** neighboring carbonyl has lowest shift than ester **Met-10**

- doublet of doublets (cca 8.0 ppm) - proton signal splitted by two neighbors - **H-4**

- two doublets in interaction with H-4 - based on the J-interaction: doublet with larger J-constant belongs to close proton - **H-3**, smaller J-constant - more distant proton - **H-6**

1D ^{1}H NMR spectrum of cinnamic acid

1H CINNAMIC ACID

1D ^{1}H NMR spectrum of cinnamic acid
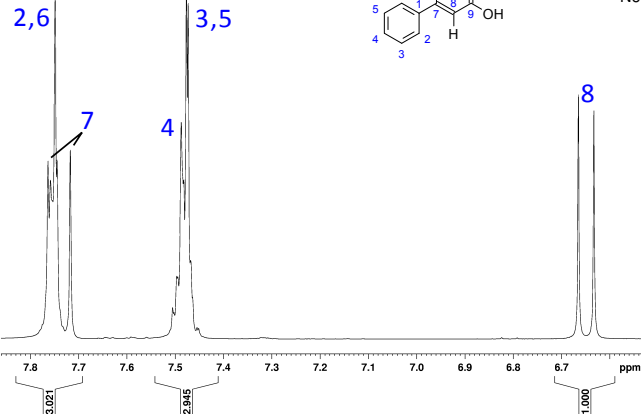
Notes:

- ▶ **H-8** - doublet with large coupling, in range of shifts of protons on double bond, integral = 1
- ▶ **H-7** - doublet with the same coupling like doublet H-8, deshielded due to -M effect of carboxyl and due to nearby aromatic ring
- ▶ more intensive signal between 7.7 and 7.8 ppm has integral: 3-1=2 protons - **H-2,6**, symmetrical, highest shift due to -M effect of substituent in *ortho* position on aromatic ring
- ▶ signal with integral = 3 around 7.5 ppm - less intensive signal - only one proton, highest shift due to -M effect of substituent in *para* position - **H-4**; more intensive signal with highest shift - **H-3,5**

Draw approximate 1D ^{1}H NMR spectrum of the following compound
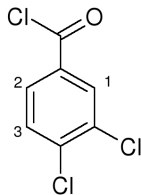
Draw approximate 1D ^{1}H NMR spectrum of the following compound
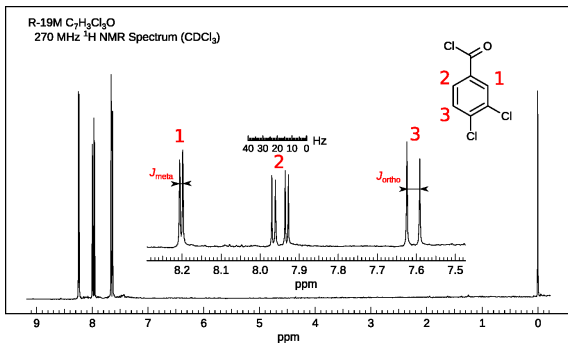
Notes:

- **H-2** - *meta*- and *ortho*- interaction with H-1 a H-3 - doublet of doublets
- **H-1** - only *meta*- interaction with H-2 - smaller coupling than **H-3** in *ortho*- interaction with H-2
- chemical shifts are result of overall effects of substituents on the aromatic ring

1D ^{1}H NMR spectrum of ethyl glutarate
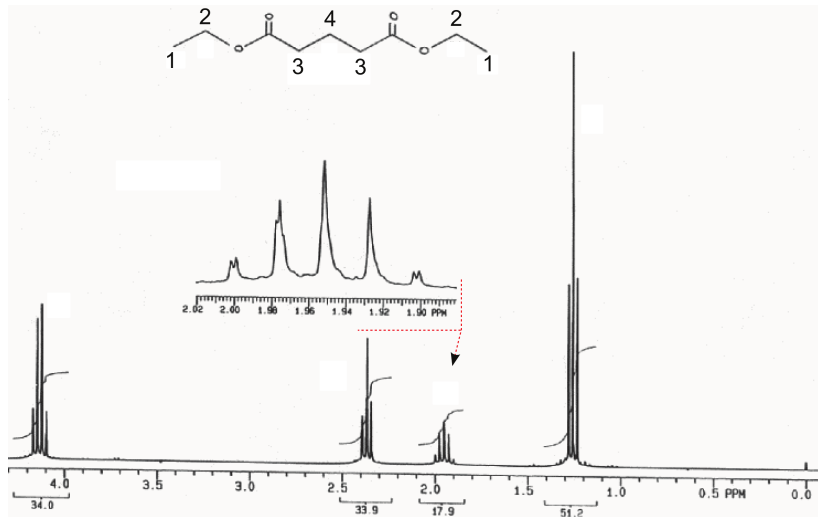
1D ^{1}H spectrum of ethyl glutarate
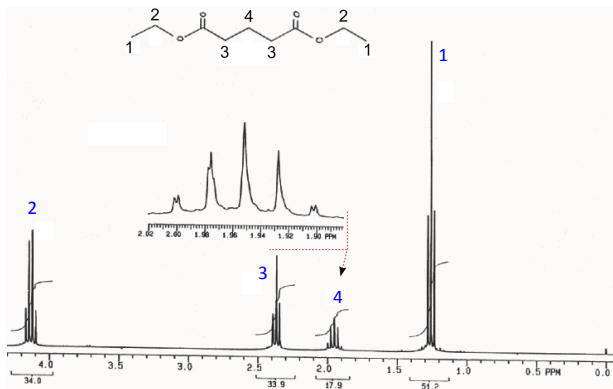
Notes:

- ▶ symmetrical molecule - equivalent groups will give rise to only one signal
- ▶ splitting corresponds to n+1 rule
- ▶ signal integrals correspond to number of protons in groups H-1:H-2:H-3:H-4 in the ratio 6:4:4:2
- ▶ chemical shifts depend on chemical environment of atoms

1D ^{1}H NMR spectrum of benzyl butyrate

1D ^{1}H NMR spektrum benzylbutyrátu

Notes

- highest shift - aromatic ring, which is flexible - **H-5**, **H-6**, **H-7** are under one signal, integral value corresponds to five protons
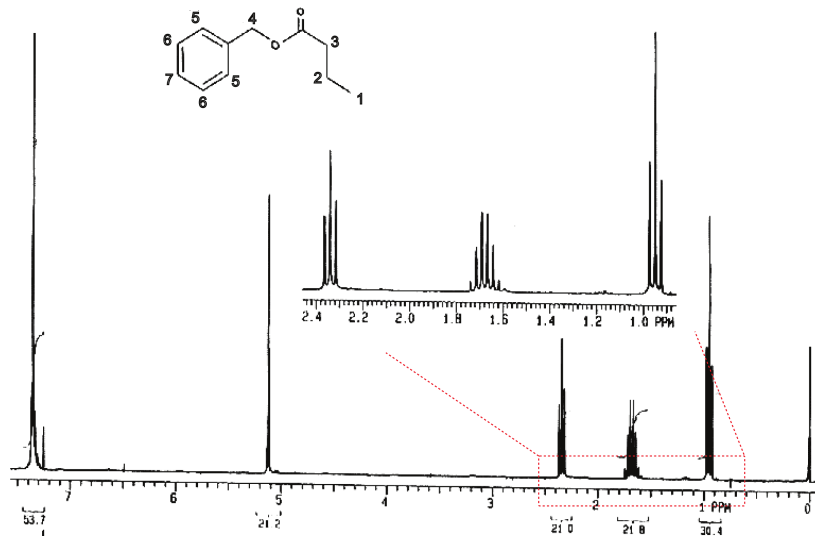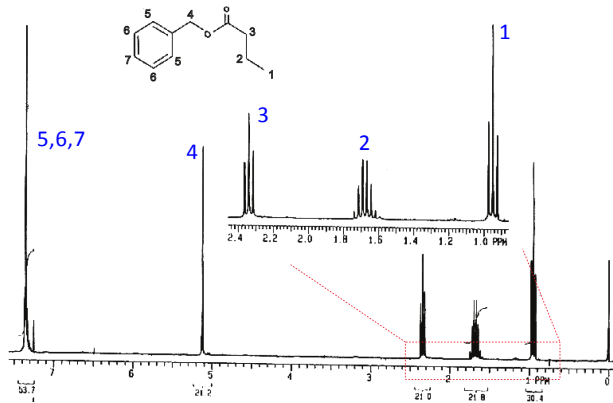- lowest shifts - alifatic chain H-1, H-2 a H-3: **H-1** - integral equals to three protons, splitted only by H-2 to triplet; **H-2** - integral equals to two protons, splitted by both H-1 and H-3 to triplet of quartets, which is due to similar *J*-coupling values fused into sextet; **H-3** - integral equals to two protons, splitted by H-2 to triplet
- **H-4** - integral equals to two protons, isolated signal - singlet, highest shift among all alifatic protons due to neighboring carboxyl and aromatic ring

1D ^{1}H NMR - methyl 2-acetoxy propanoate
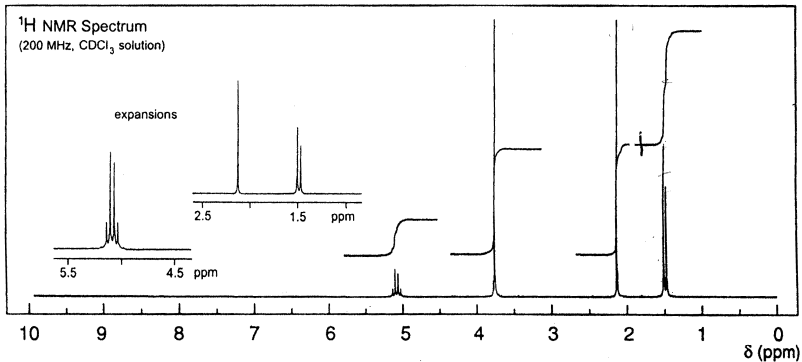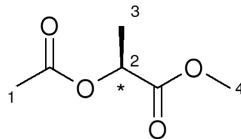
1D ^{1}H NMR - metyl 2-acetoxypropanoát

:
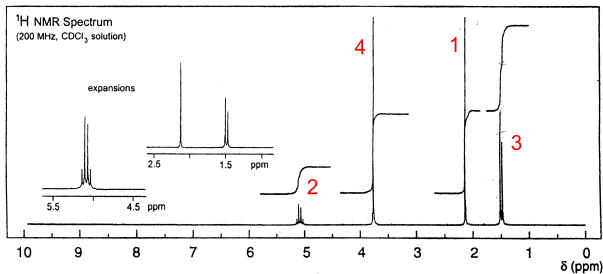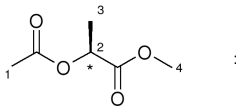
► lowest shift - methyl **H-3**, splitted due to neighboring stereogenic center C-2

► last splitted signal - **H-2** - splitted by H-3 to quartet, highest shift due to neighboring carboxyl groups

► two singlets - highest shift **H-4** next to carboxylic oxygen; lowest shift - **H-1** next to carboxylic carbon

► integrals corresponds to number of protons

1D ^{1}H NMR - ethyl 4-(methylamino)benzoate

^{1}H NMR Spectrum
(200 MHz, CDCl$_3$ solution)

expansion

7.6   7.0   ppm

exchanges
with D$_2$O on warming

TMS

10   9   8   7   6   5   4   3   2   1   0
δ (ppm)

1D ^{1}H NMR - etyl 4-(metylamino)benzoát
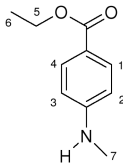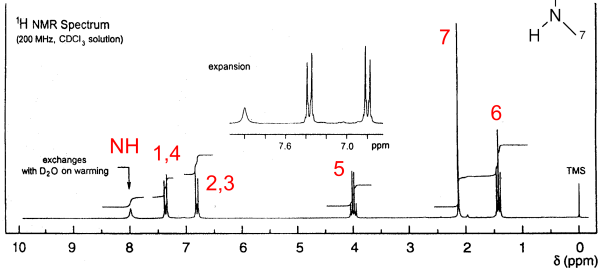
Notes:

► highest shift - **NH**, least intensive and broad signal because there is dynamical exchange of the proton with the solvent, it is visible in the spectrum thanks to $CDCl_3$ used as solvent

► lowest shifts - alifatics - signal at 1.5 ppm splitted to triplet - methyl **H-6** splitted by H-5; singlet around 2 ppm - methyl **H-7** - isolated, highest shift than H-6 thanks to nitrogen; quartet at 4 ppm - **H-5** - splitted by methyl H-6, highest shift thanks to oxygen

► two doublets in aromatic region around 7 ppm - **H-1,4** a **H-2,3** - symmetrical, shifts are resulting from effects of both substituents on aromatic ring

1D ^{1}H NMR spectrum of cartilagineal
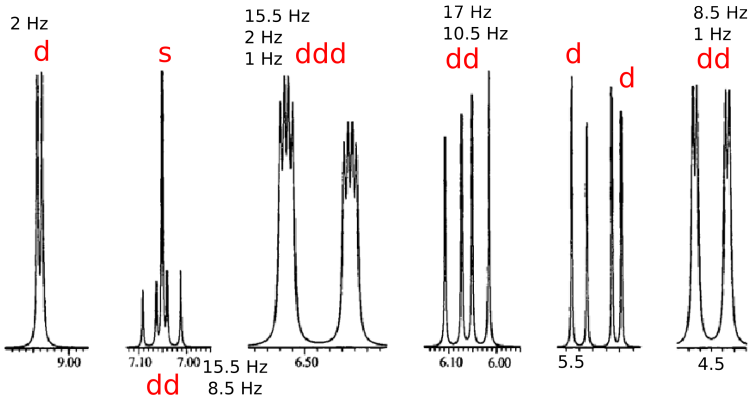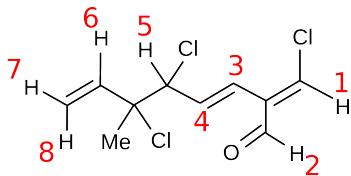
1D ^{1}H NMR spectrum - cartilagineal

1D ^{1}H NMR - cartilagineal
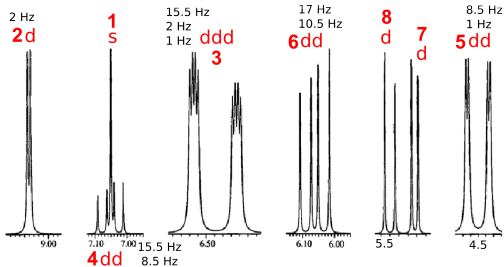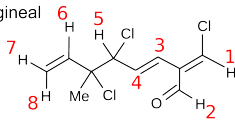
Notes:

- ► highest shift - **H-2** - proton of aldehydic group, splitted to doublet with $J = 2$ Hz (small value, interacting partner is relatively far away)

- ► the same $J = 2$ Hz belongs to doublet of doublets of doublets around 6.5 ppm, other Js: $J = 1$ Hz and $J = 15.5$ Hz - three J-constants - three partners - **H-3**

- ► large J-value 15.5 Hz suggests near neighbor - other signal with the same constant is doublet of doublets around 7 ppm - **H-4**

- ► last constant of multiplet at 6.5 ppm - $J = 1$ Hz - partner distant from H-3: either H-1 or H-5, the same J- constant belongs to doublet of doublets at 4,5 ppm - two constants, two partners which is not the case for H-1 - therefore signal at 4,5 ppm belongs to **H-5**

- ► just for check: both multiplets H-4 and H-5 are coupled with H-3 and with each other as well ($J = 8.5$ Hz)

- ► the only singlet in the spectrum is isolated **H-1**

- ► last unassigned doublet of doublets (6,1 ppm) must be **H-6** because it is the only proton from the trio H-6, H-7, H-8 with two unequivalent neighbors - larger coupling comes from interaction with **H-8** in *trans* position, smaller coupling comes from interaction with *cis* oriented **H-7**

- ► signal of the methyl group is not present in this spectrum

Next session:

1D ^{13}C-NMR spectra