C8953
NMR structural analysis seminar

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

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Information about classes

Credit:

- active attendance (2 absences tolerated)
- final project/test

Study materials:

`https://is.muni.cz/auth/el/1431/jaro2025/C8953/um`

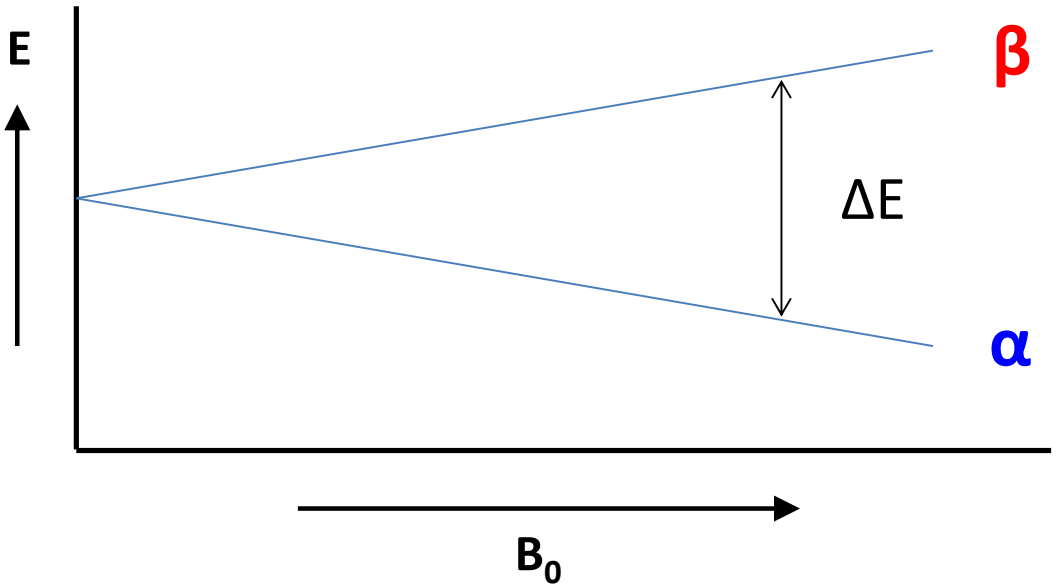
E-tests:

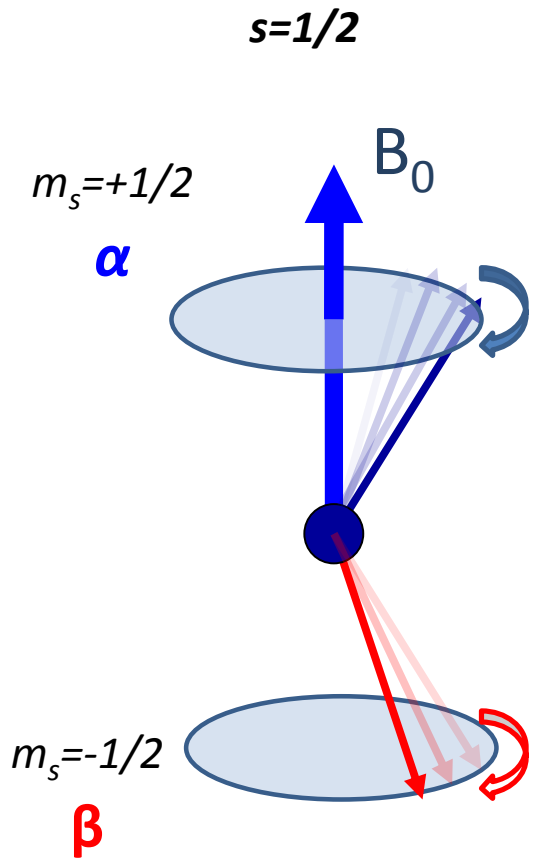
`https://is.muni.cz/auth/el/1431/jaro2025/C8953/odp`

NMR-challenge: on-line training of compound identification developed at IOCB Prague

`https://nmr-challenge.uochb.cas.cz/`

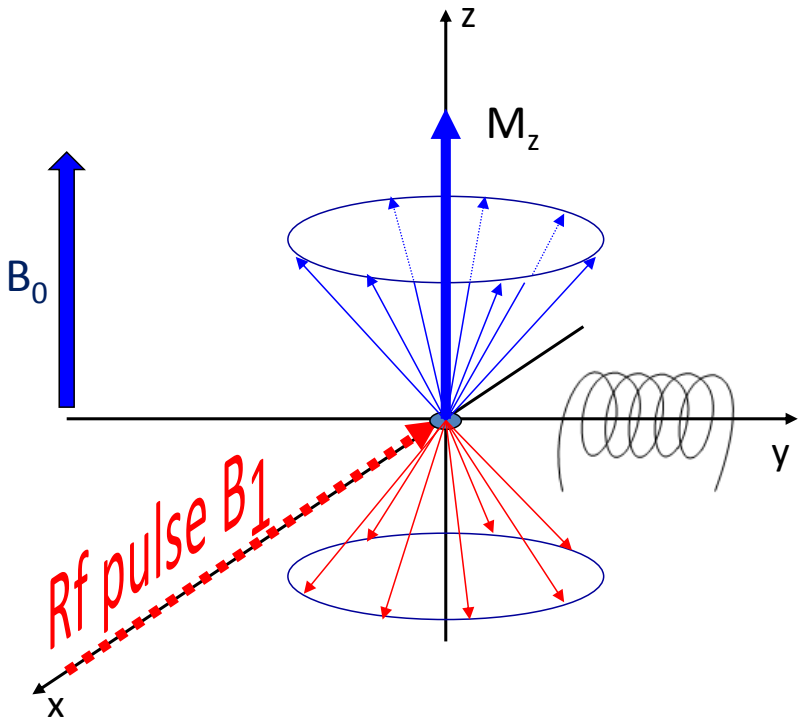
Energy levels splitting

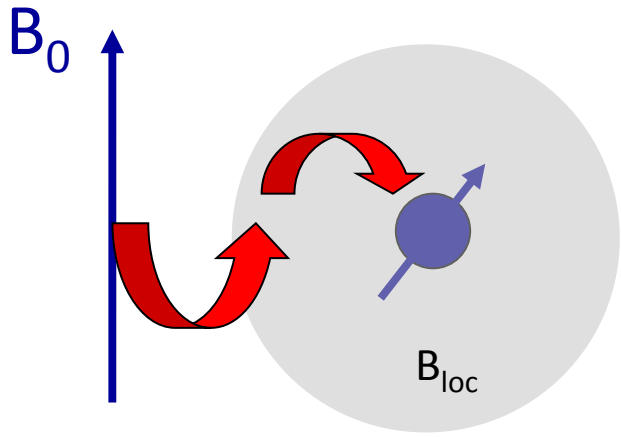




$N_{\alpha} > N_{\beta}$

Behavior of nuclear spin after irradiation by RF pulse





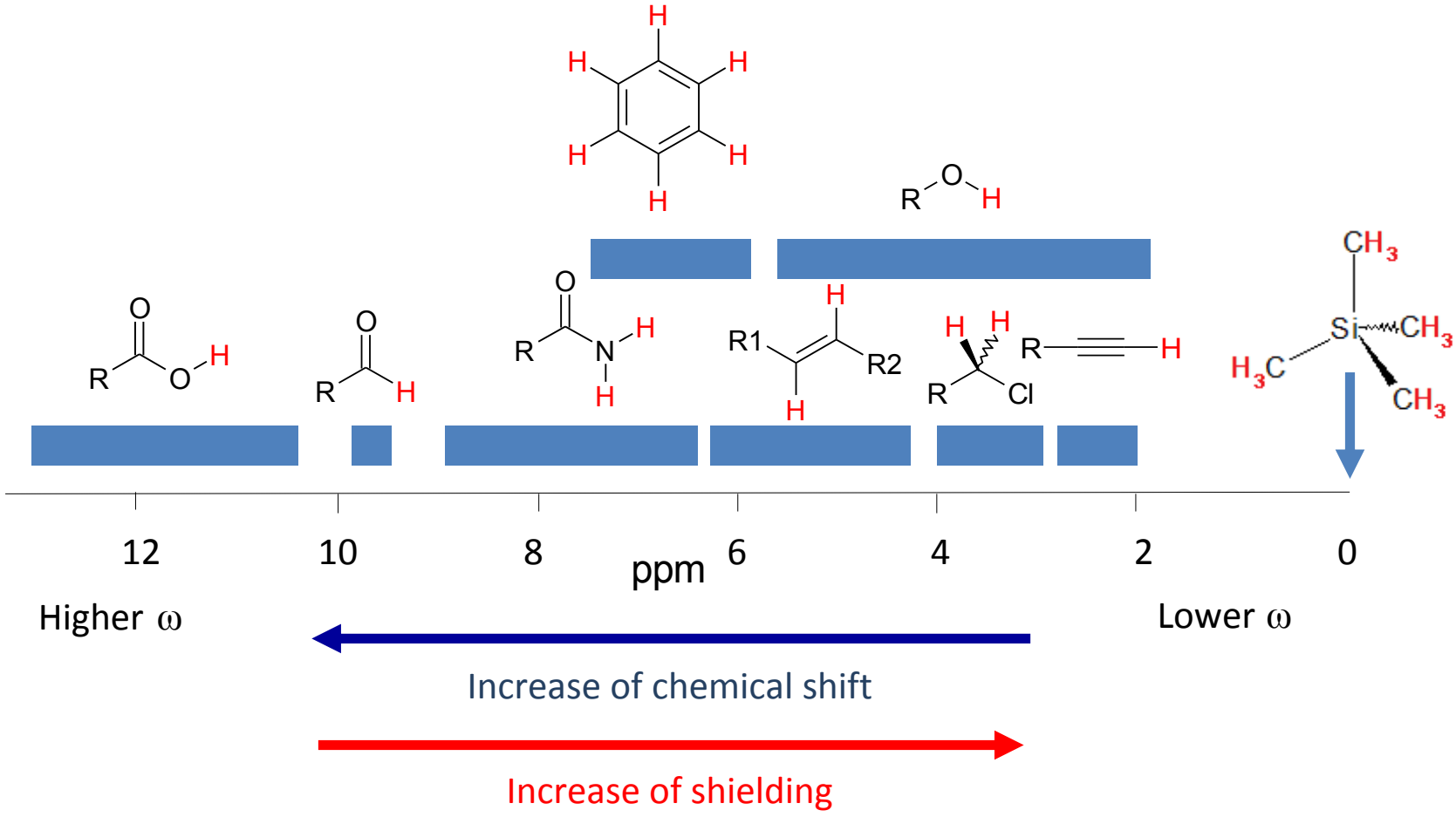
B_0 induces local mag. field B_{loc}, which affects against B_0

↓

Nuclear shielding

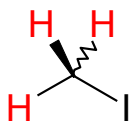
Precession frequency:	$\omega = -\gamma B_0$
Precession frequency affected by nuclear shielding:	$\omega = -(1+\sigma)B_0$
Chemical shift:	$\delta = \omega - \omega_{ref}$
Definition of th relative scale of the chemical shift:	$\delta = (\omega - \omega_{ref})/\omega_{ref}.10^6 ppm$

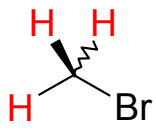
Characteristic intervals of chemical shifts values

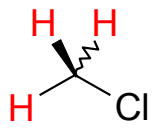


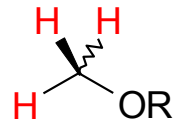
Trends in chemical shifts

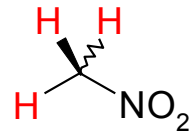
- Electronegativity, inductive and mesomeric effects of substituents
- Hybridisation
- Relative position towards the ring, double bond

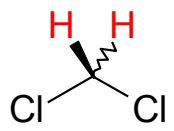
2,1 ppm 

2,3 ppm 

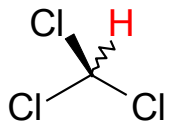
3 ppm 

3,1 ppm 

4,5 ppm 



5,3 ppm



7,3 ppm

Substituents with -I effect

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

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

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

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

$\equiv N>=NR>-NR_2$

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

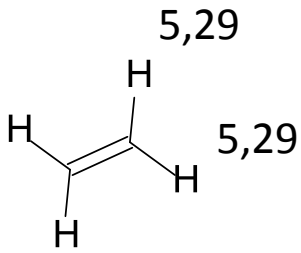
Substituents with +I effects

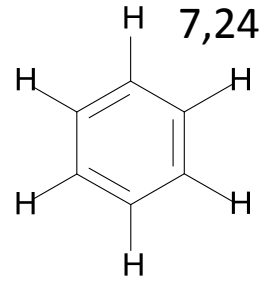
$-N-R>-O->S-$

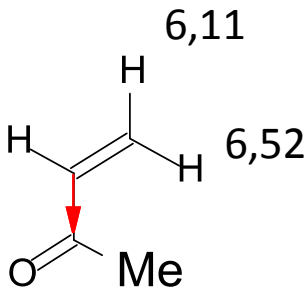
$-C(CH_3)_3>-CH(CH_3)_2>-CH_2CH_3>-CH_3$

metals

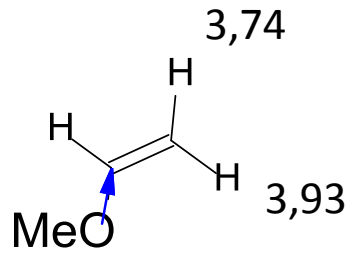
Mesomeric effect



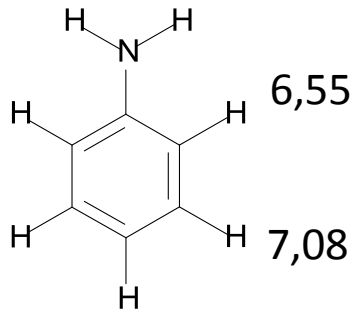




-M

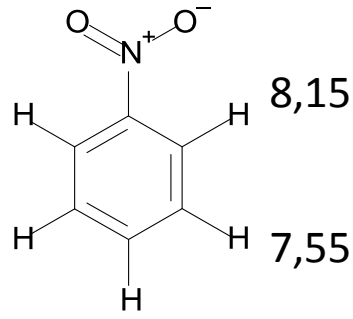


+M



6,70

+M



7,70

-M

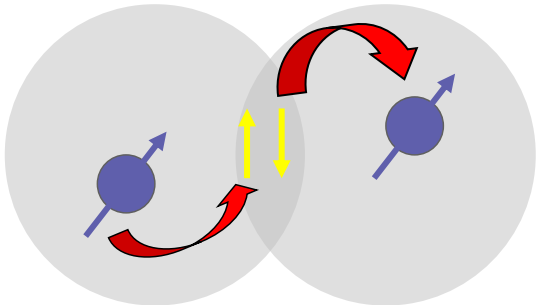
Substituents with -M effects

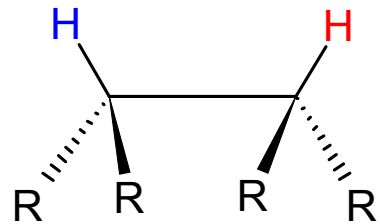
-F, -Cl, -Br, -I, -OH, -OR, -NH_2, -NHR, -NR_2, -SH, -SR

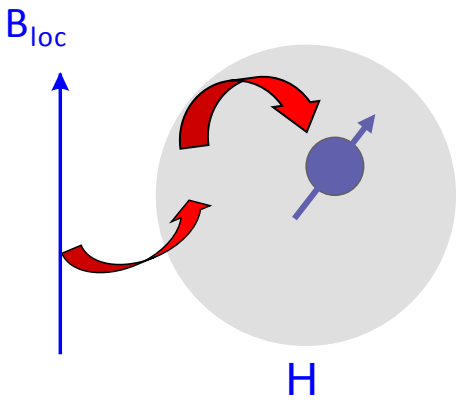
Substituents with +M effect

-CH=O, -RC=O, -C(OH)=O, -C(OR)=O, -C(NH_2)=O, -NO_2, -SO_3H, -C≡N

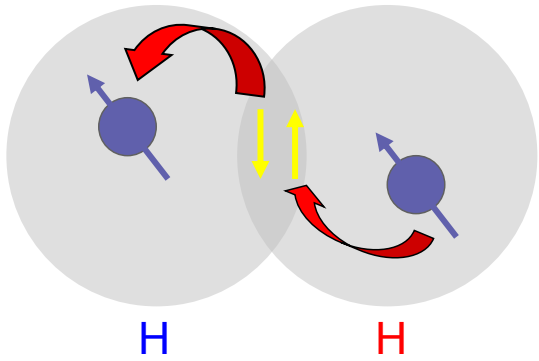
Spin-spin interaction, *J*-coupling





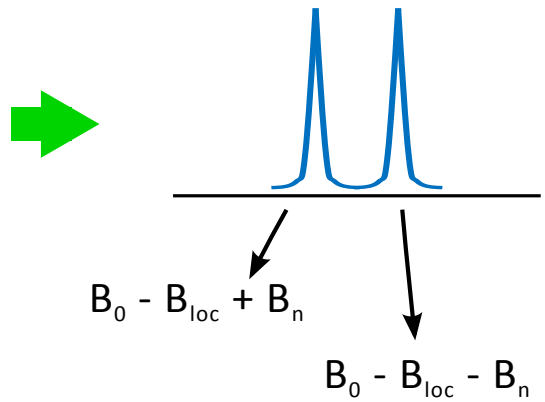


$B_0 - B_{loc}$

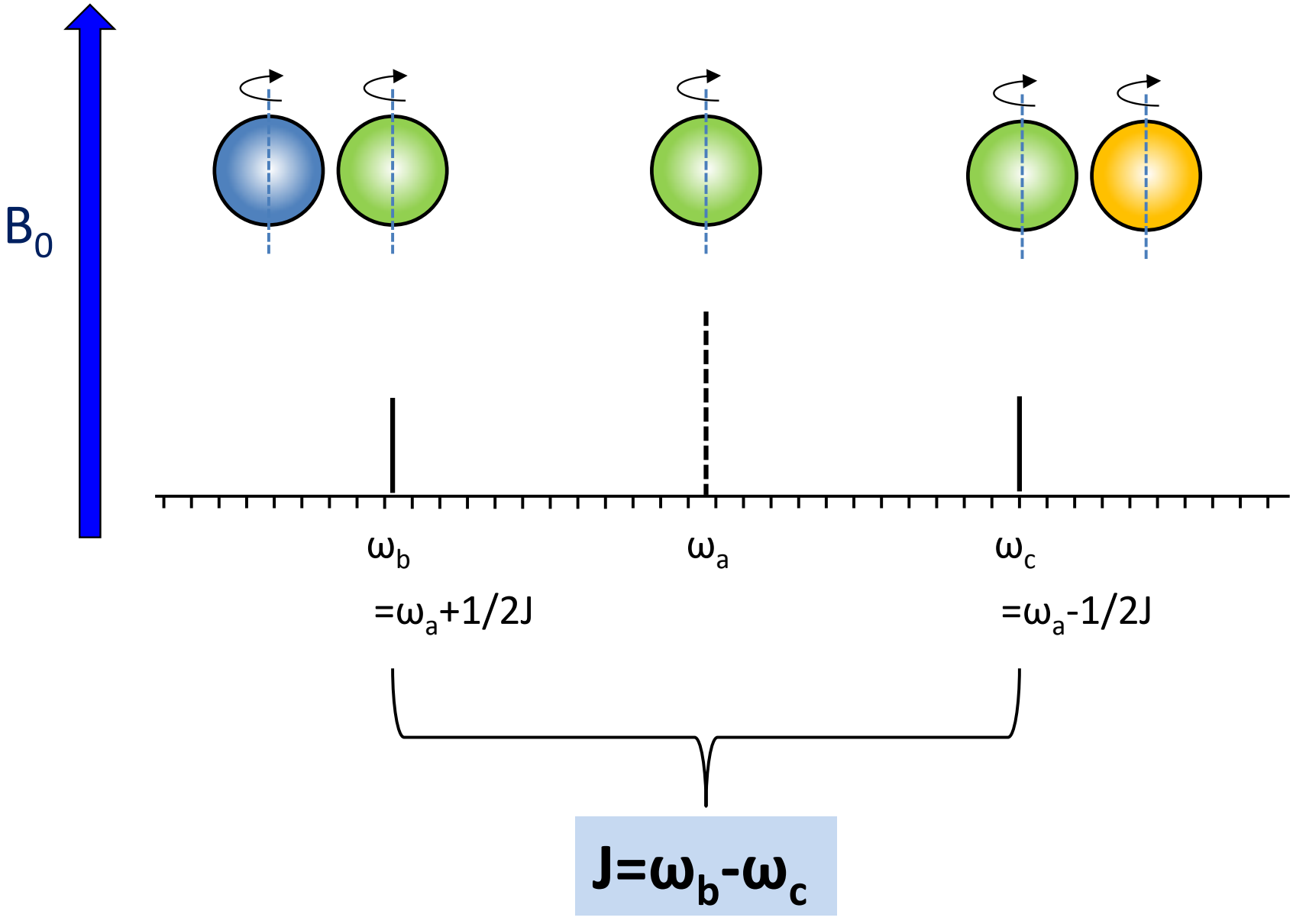


Nucleus H: spin α → $-B_n$

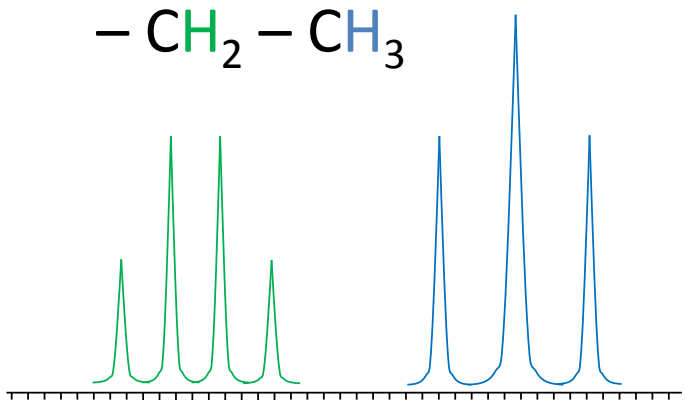
spin β → $+B_n$



Interaction constant *J*



Interaction constant *J*



- 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

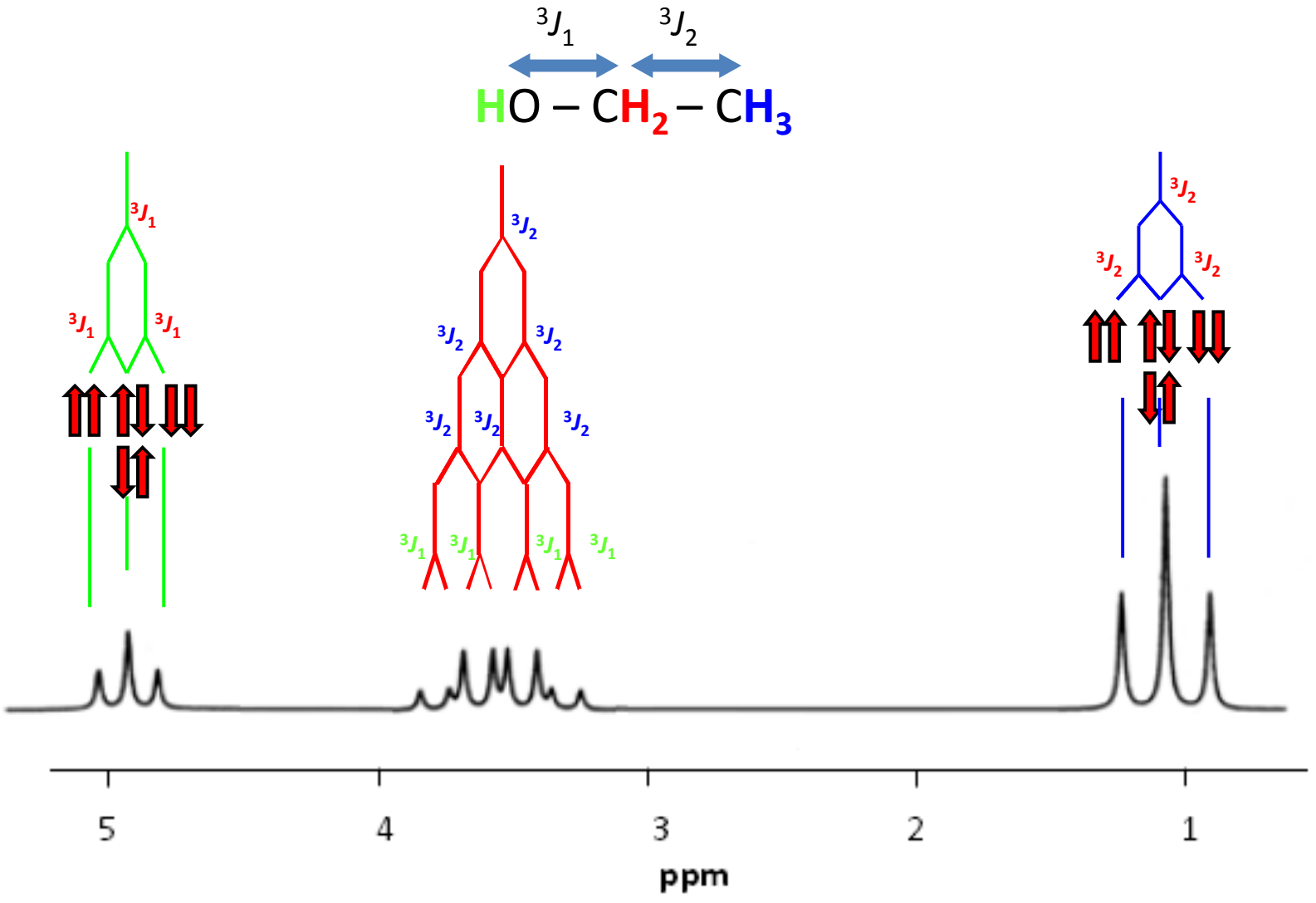
1 2 1

1 3 3 1

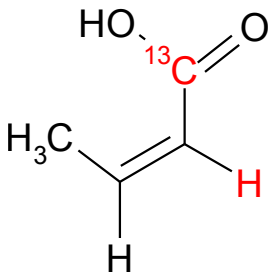
1 4 6 4 1

1 5 10 10 5 1

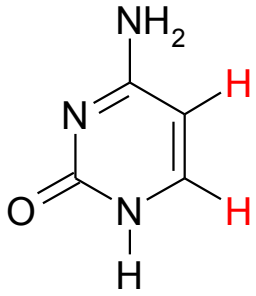
1D ^{1}H NMR spectrum



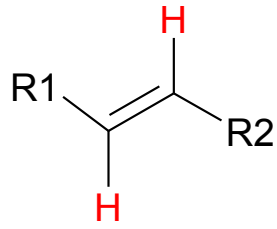
Values of *J*-constants - trends



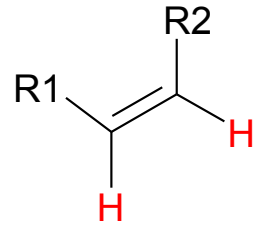
$^{2}J_{CH}$= 3.1 Hz



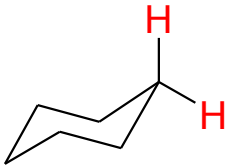
$^{3}J_{HH}$= 12 Hz



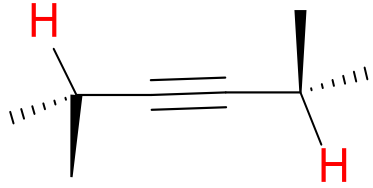
$^{3}J_{HH}$ = 13 - 18 Hz



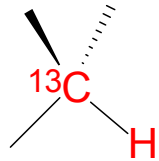
$^{5}J_{HH}$ = 7 - 12 Hz



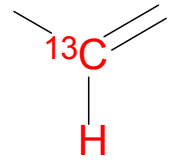
$^{2}J_{HH}$= -12,5 Hz



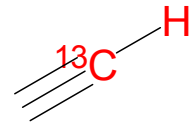
$^{5}J_{HH}$= 2 - 3 Hz



$^{1}J_{CH}$ = 125 Hz

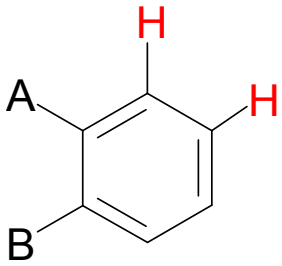


$^{1}J_{CH}$ = 160 Hz

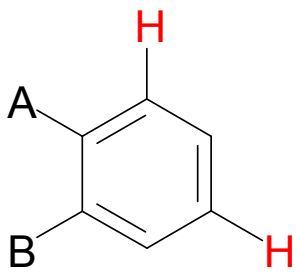


$^{1}J_{CH}$ = 250 Hz

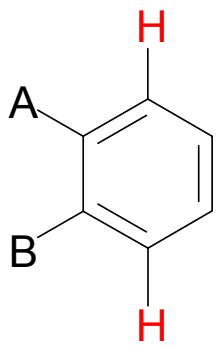
Values of *J*-constants - trends



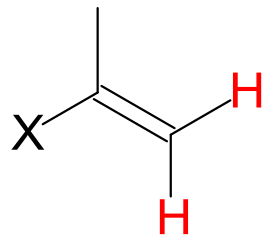
$^{3}J_{HH}$ = 7,5 Hz



$^{4}J_{HH}$ = 1,5 Hz



$^{5}J_{HH}$ = 0,7 Hz



X=	Li	H	Cl	OMe	F
$^{2}J_{HH}$ (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

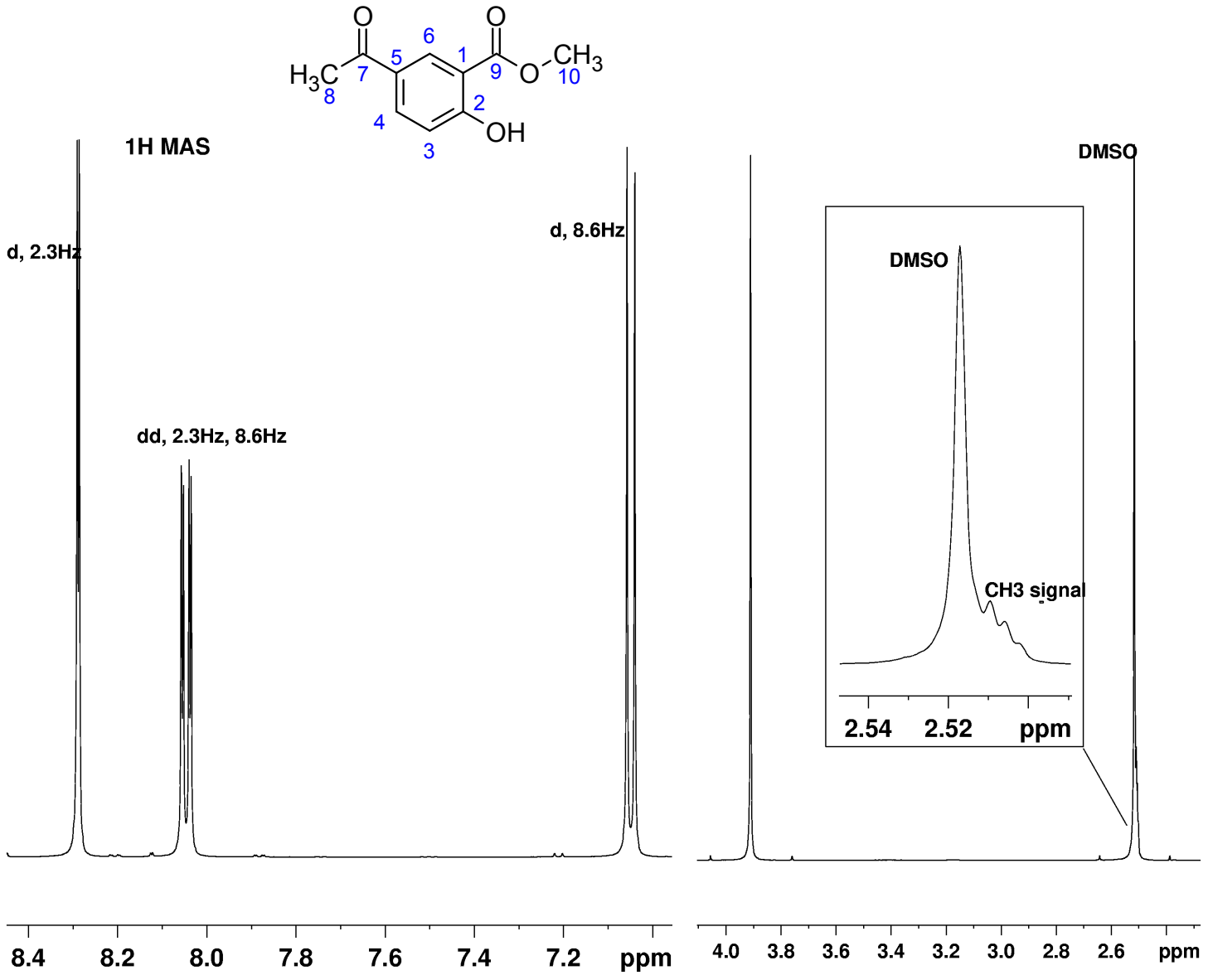
We are looking for:

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

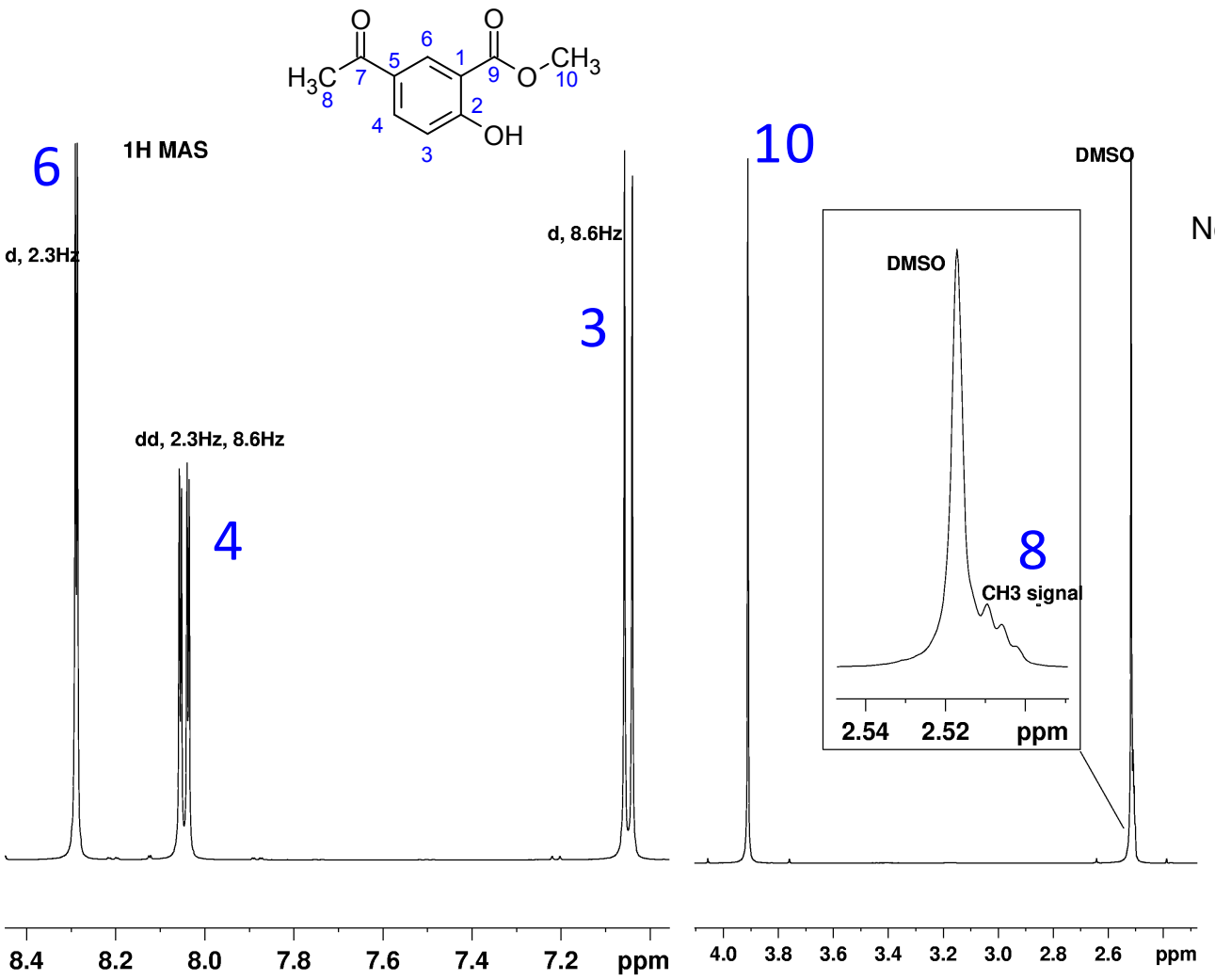
We are considering:

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

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



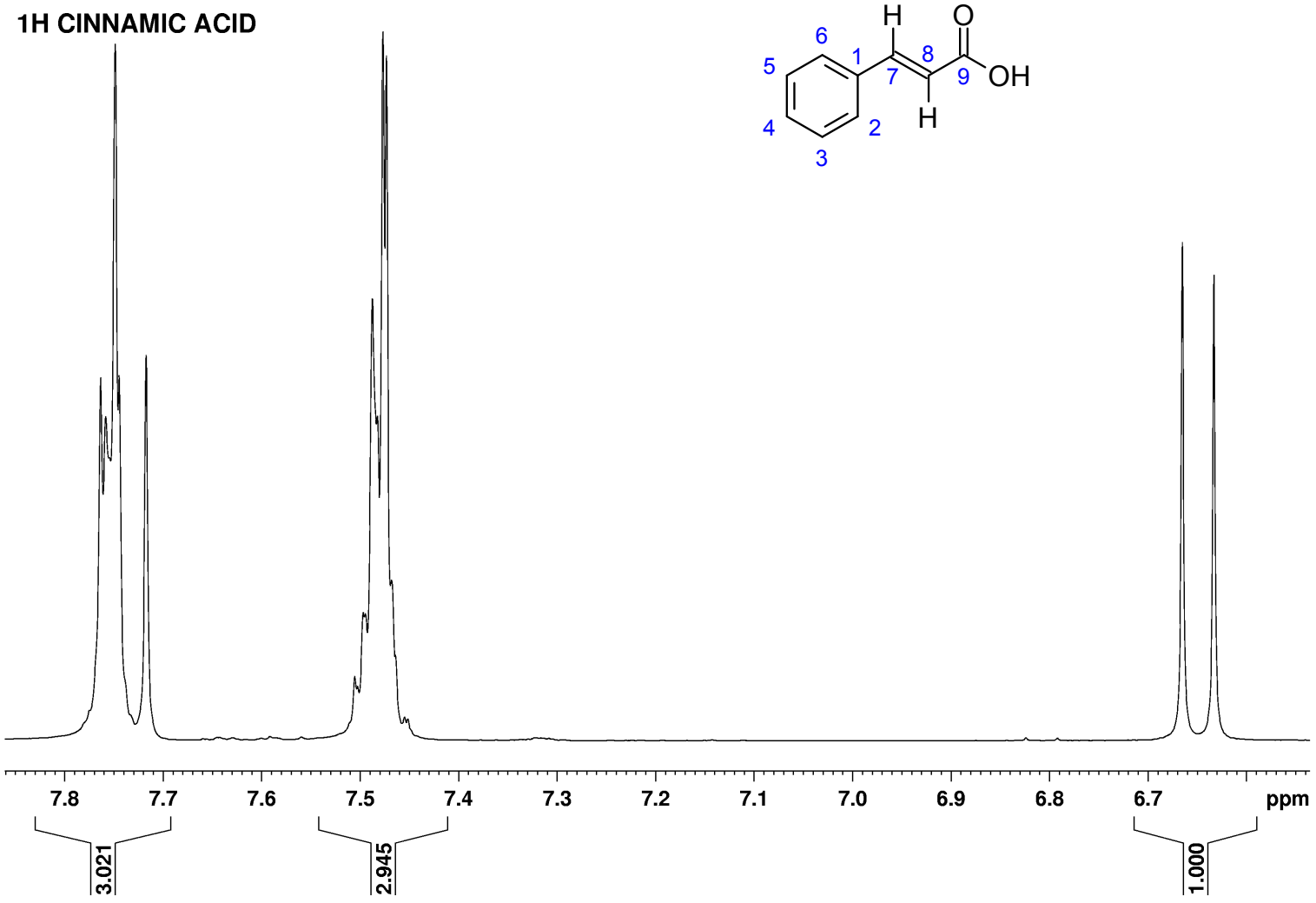
1D ^{1}H NMR spectrum of methyl-5-acetylsalicylate



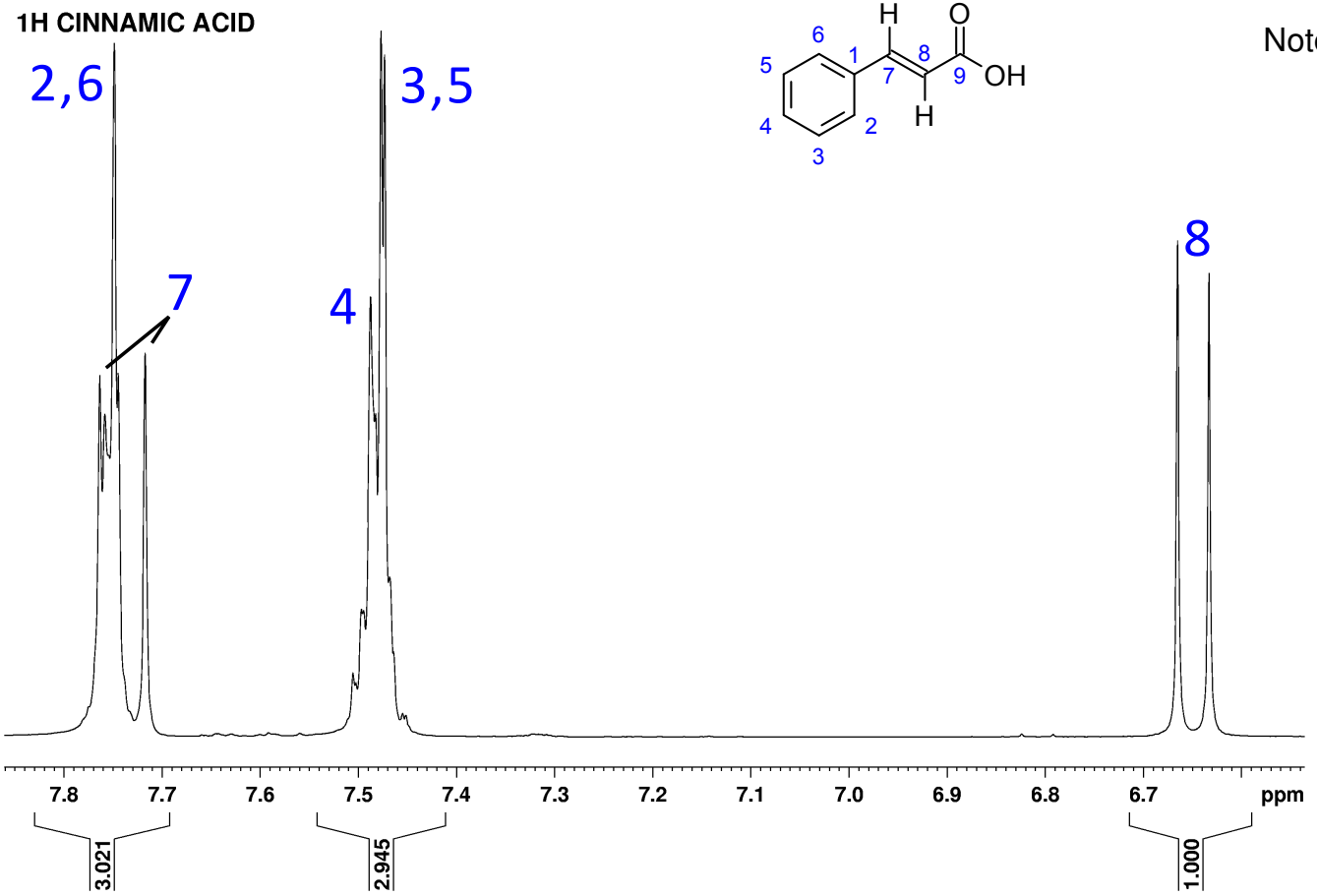
Notes:

- 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



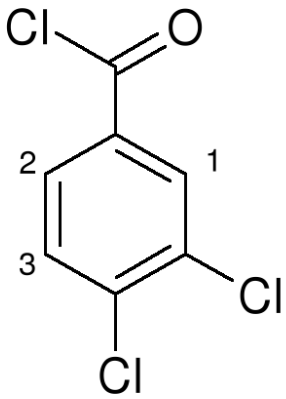
1D ^{1}H NMR spectrum of cinnamic acid



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



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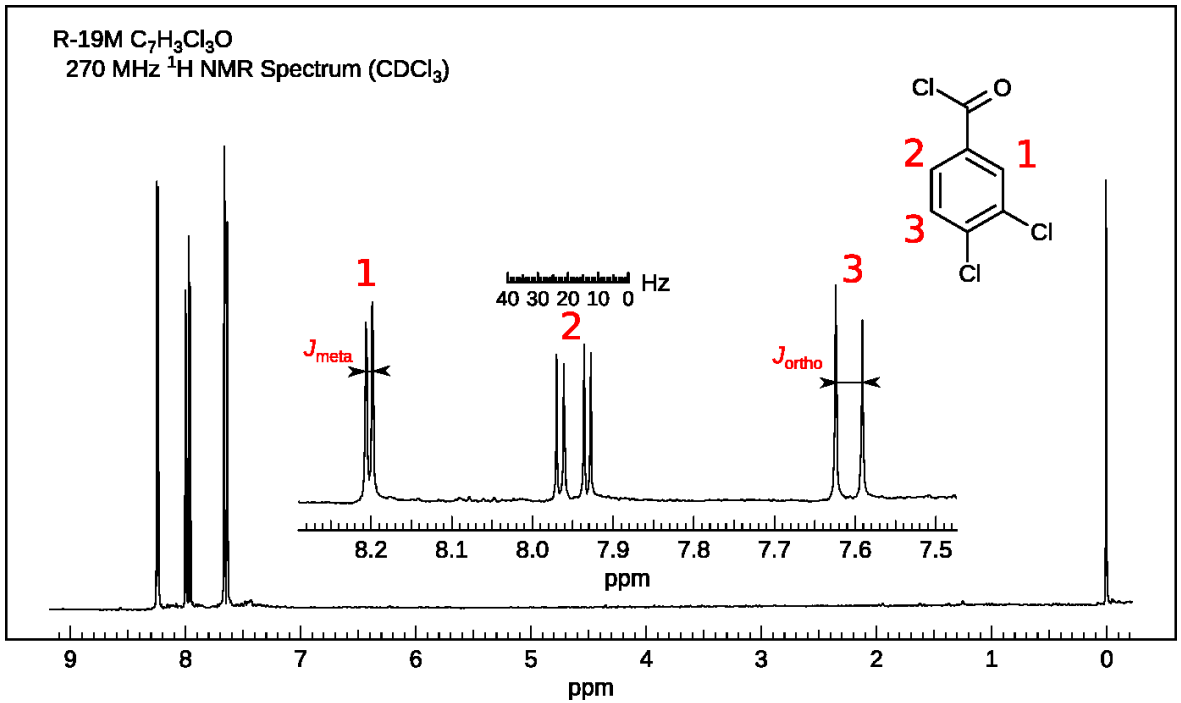
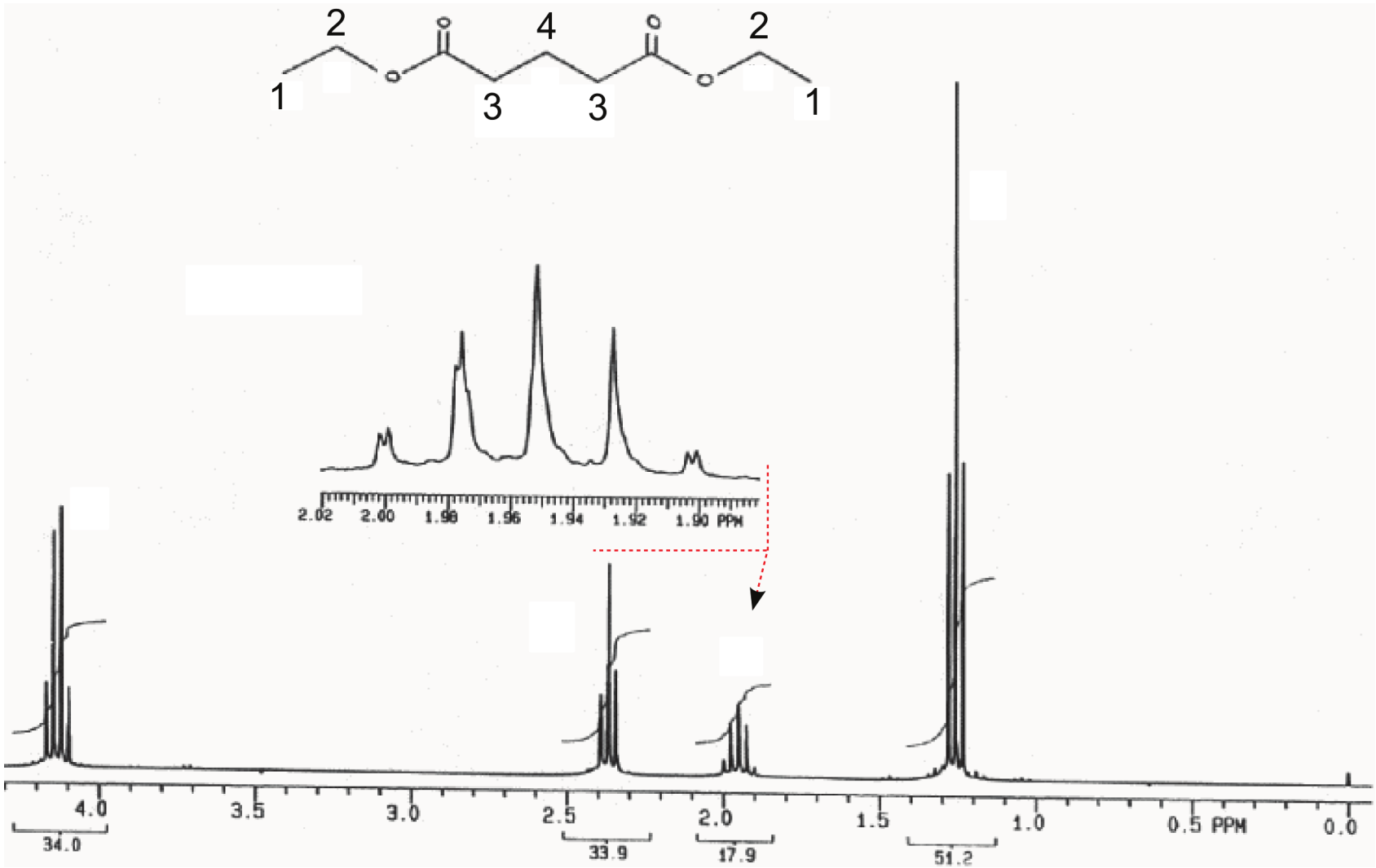


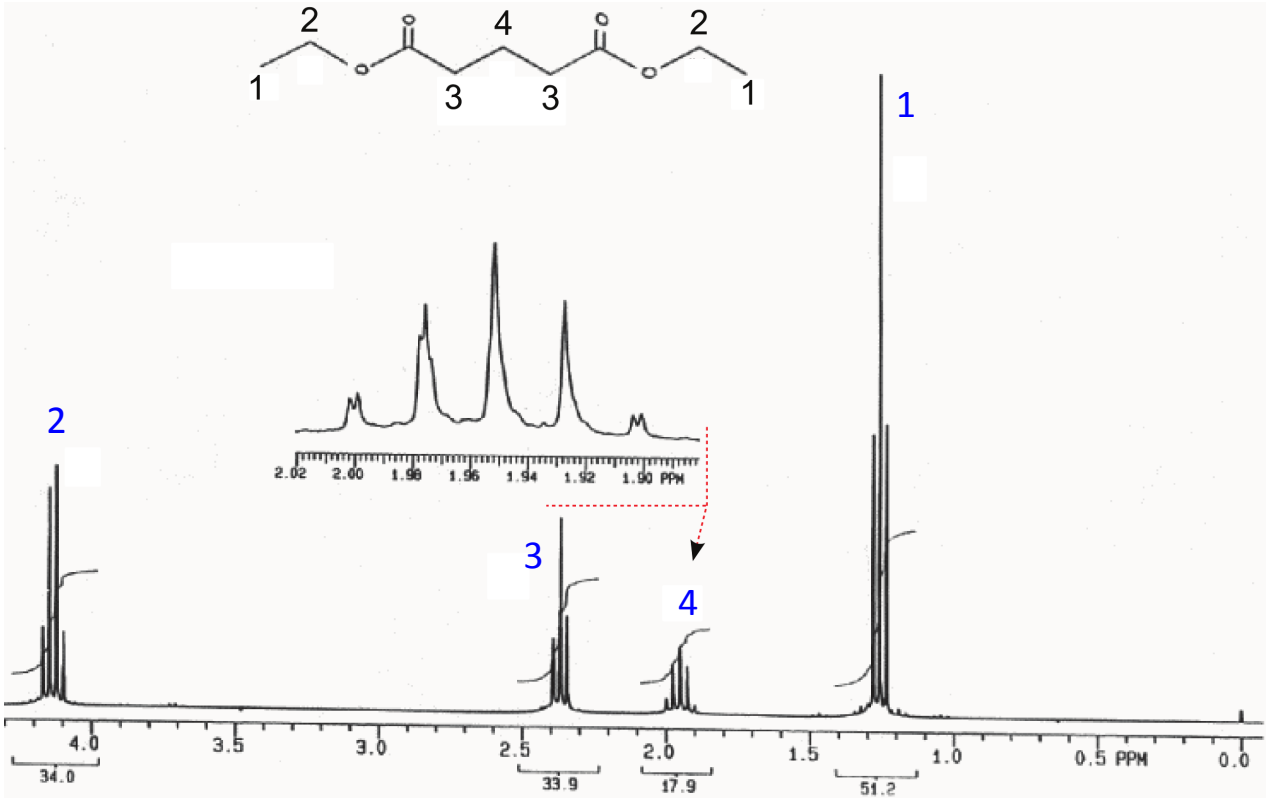
Notes:

- **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



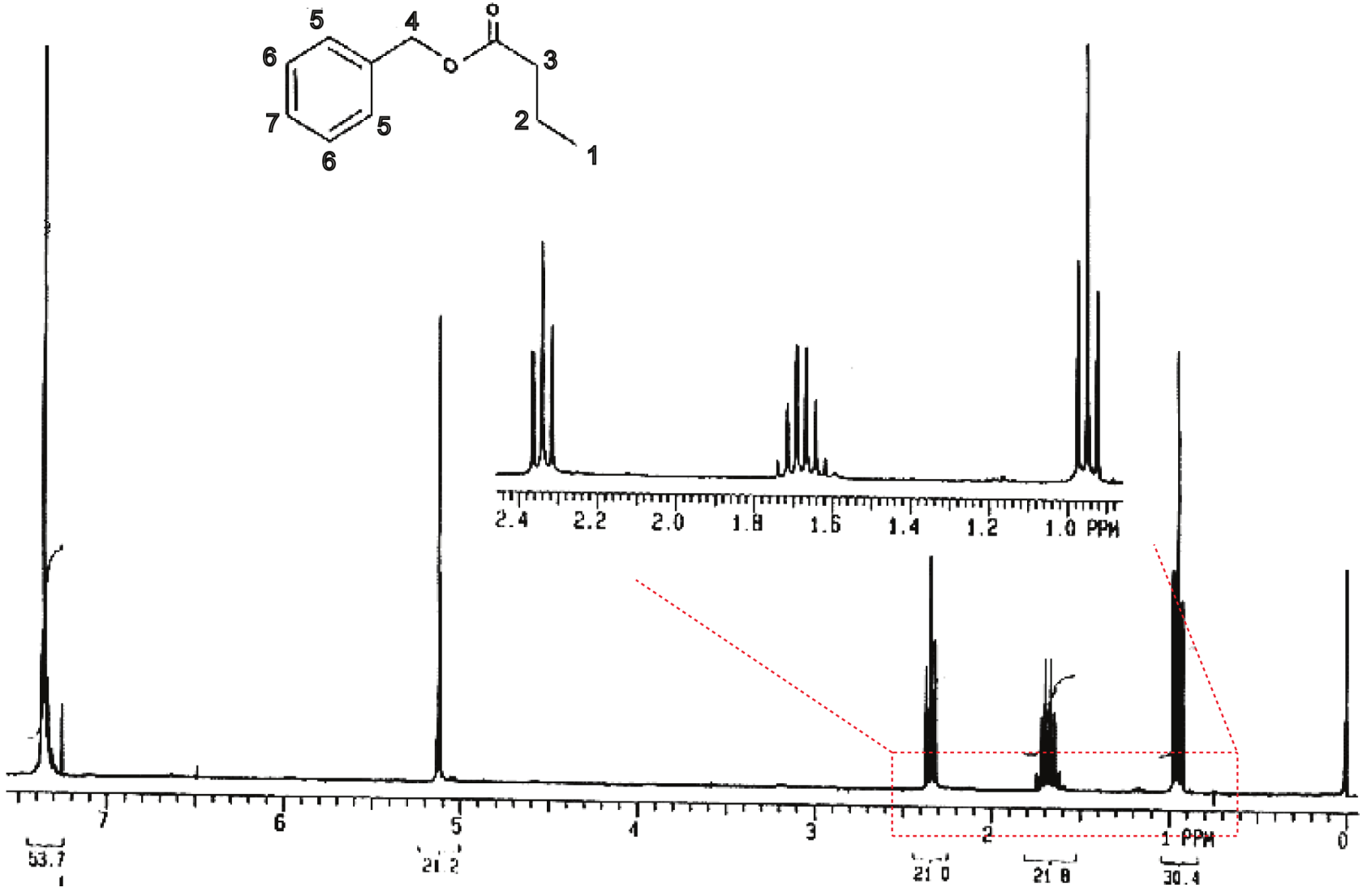
1D ^{1}H spectrum of ethyl glutarate



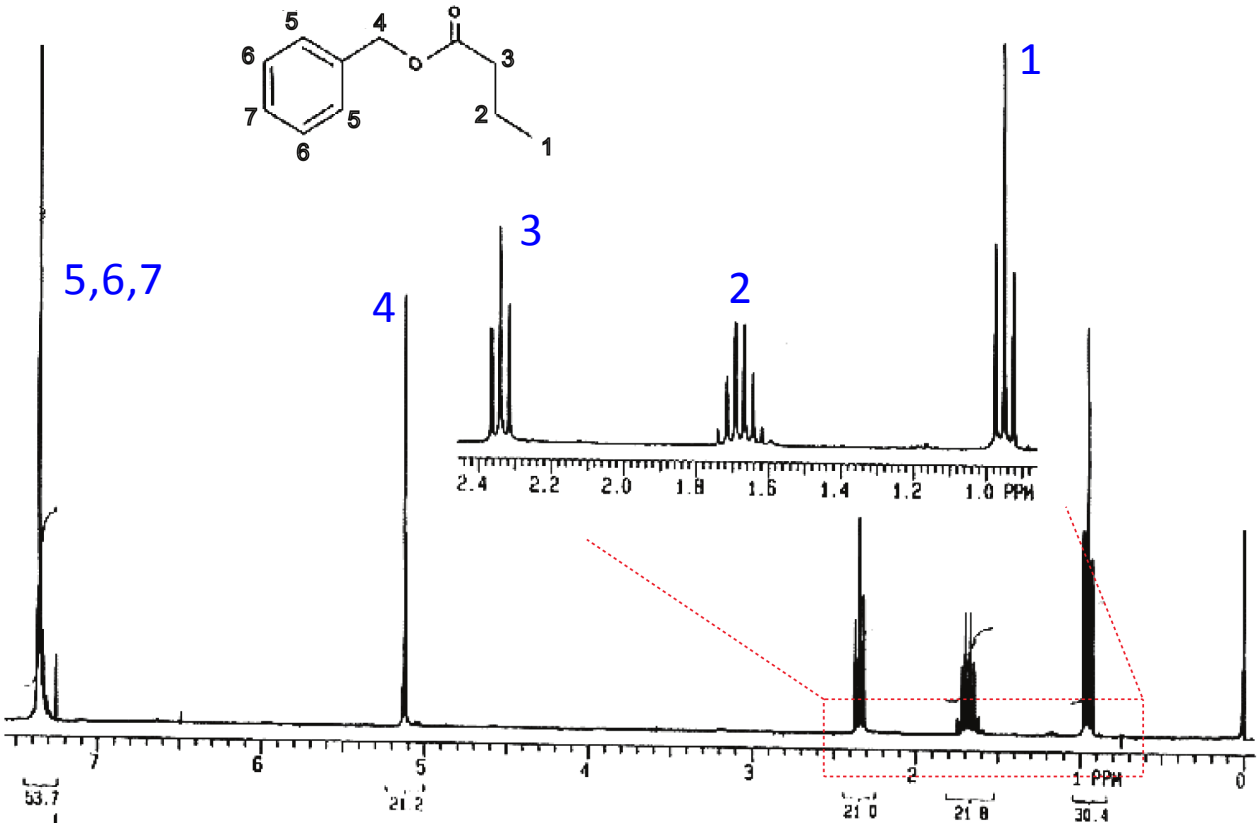
Notes:

- 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



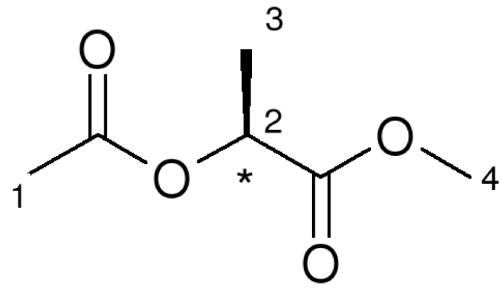
1D ^{1}H NMR spektrum benzylbutyrátu

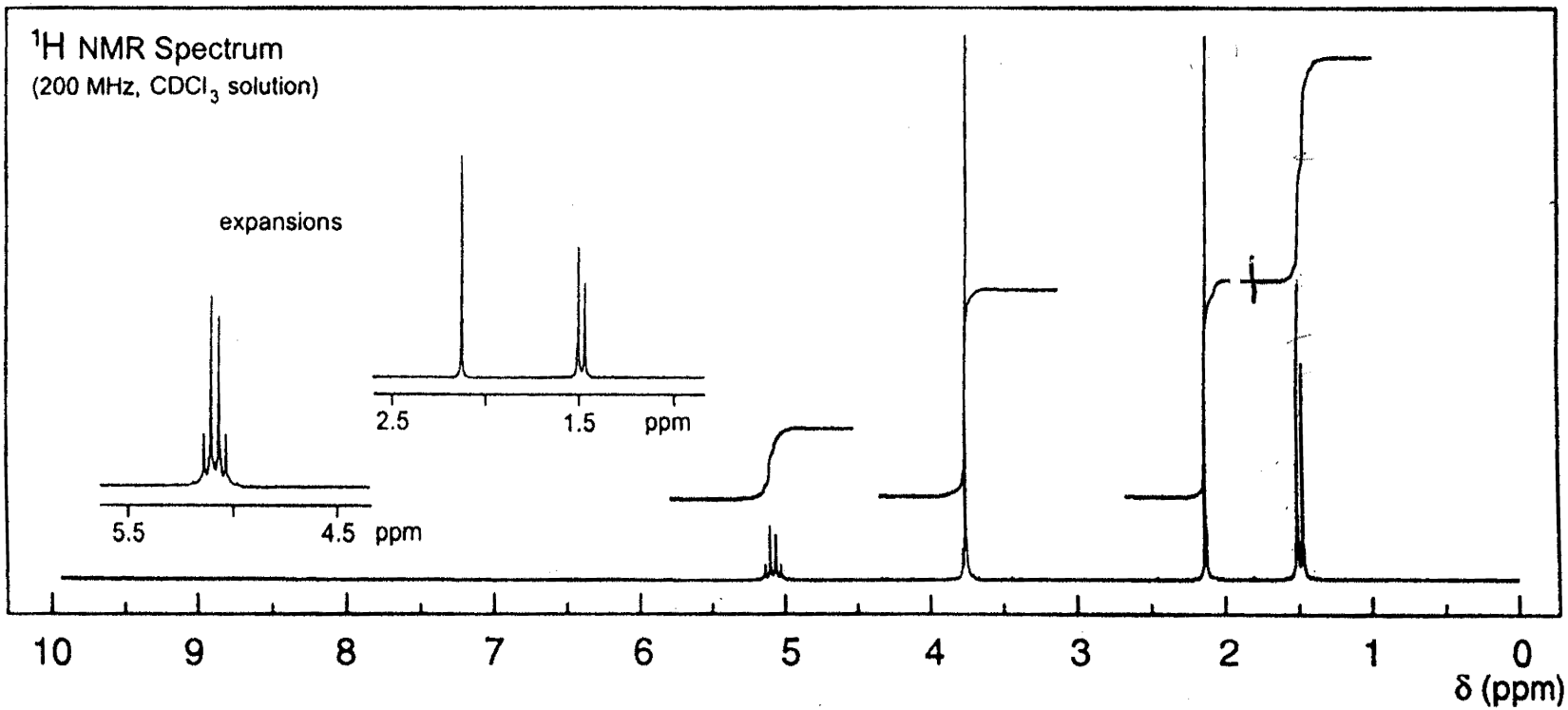


Notes

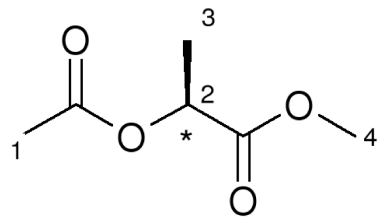
- highest shift - aromatic ring, which is flexible - **H-5**, **H-6**, **H-7** are under one signal, integral value corresponds to five protons
- lowest shifts - alifatic chain H-1, H-2 a H-3: **H-1** - integral equals to three protons, splitted only by H-2 to triplet; **H-2** - integral equals to two 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



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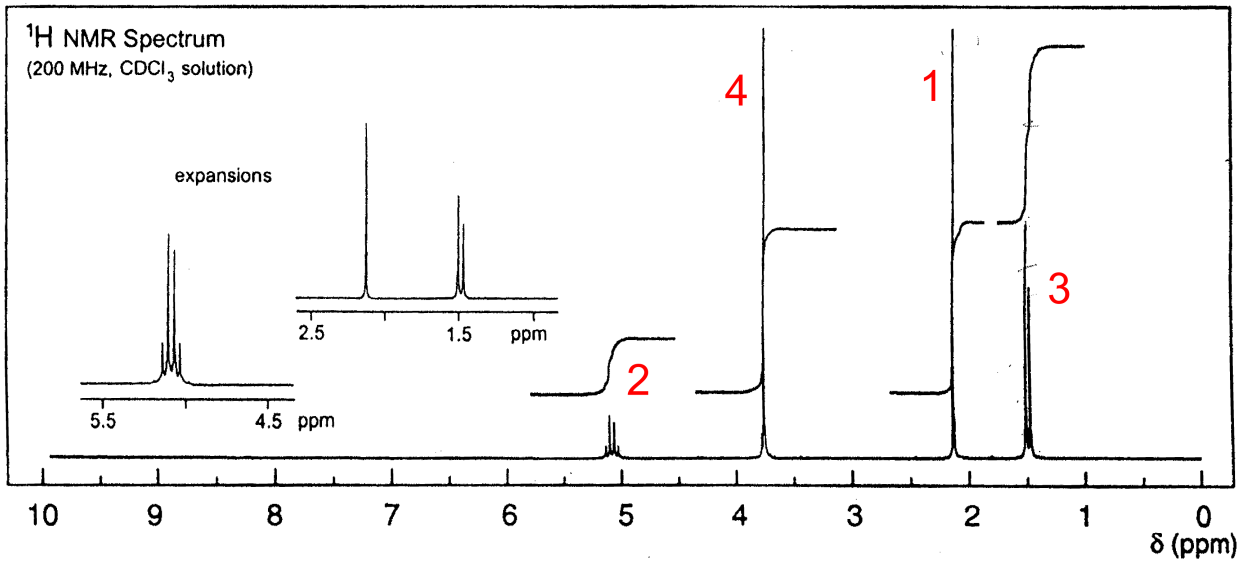
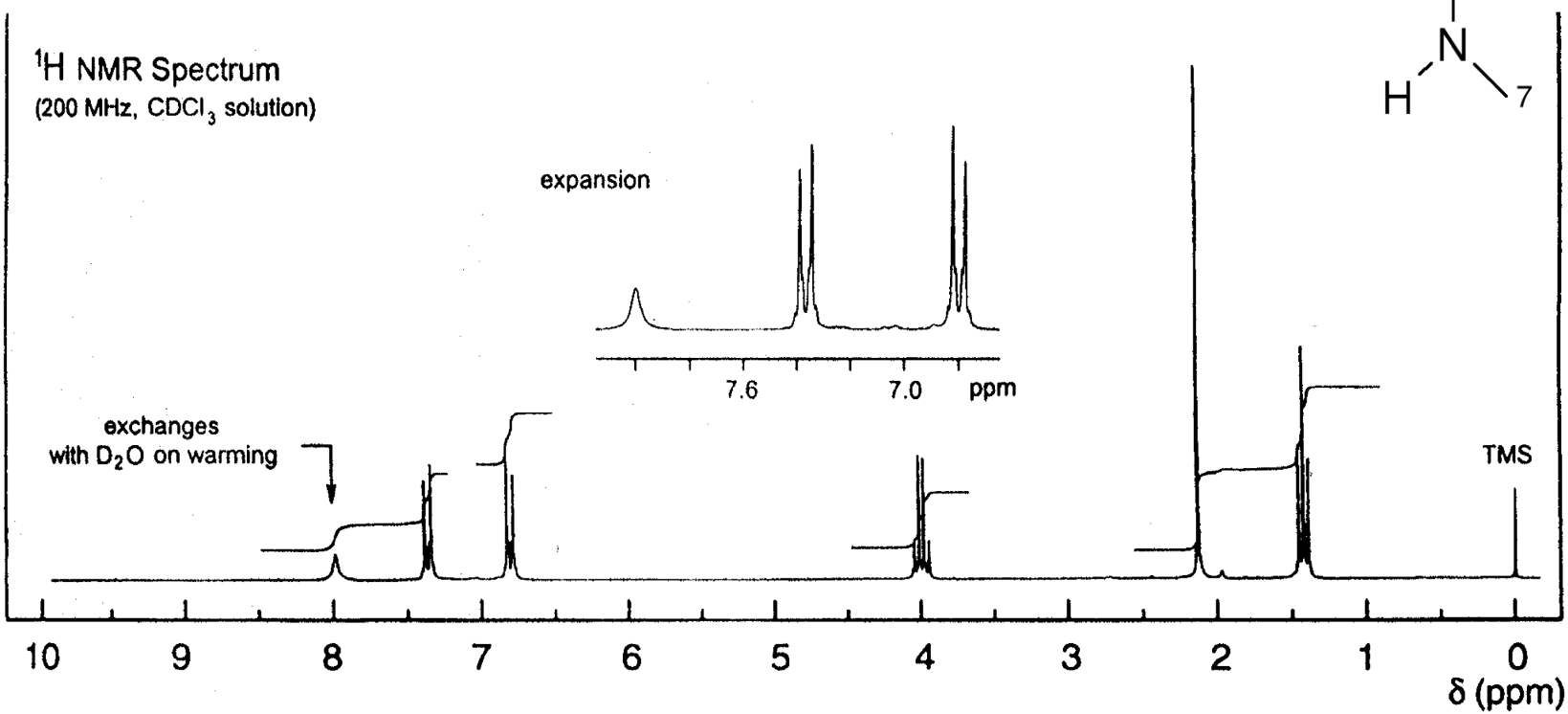
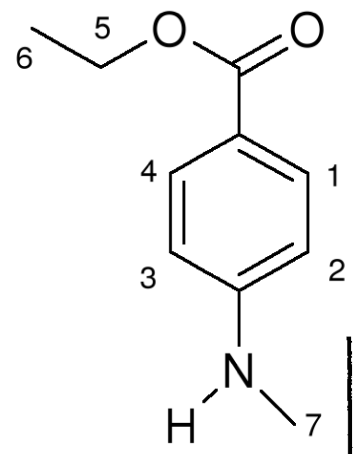


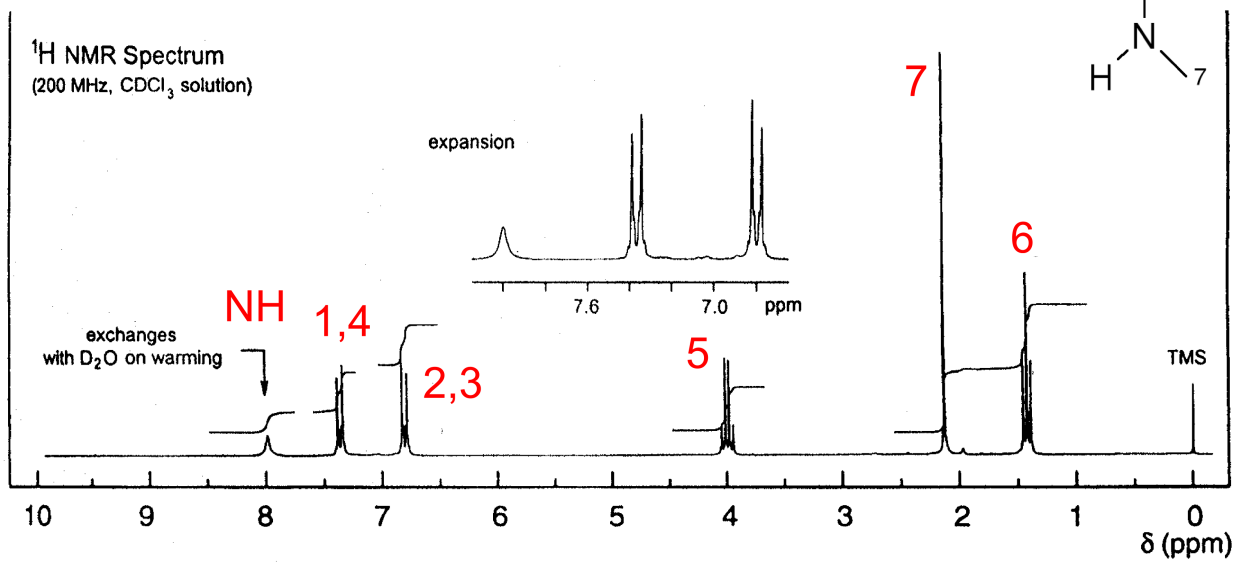
- lowest shift - methyl **H-3**, splitted due to neighboring stereogenic center C-2
- last splitted signal - **H-2** - splitted by H-3 to quartet, highest shift due to neighboring carboxyl groups
- two singlets - highest shift **H-4** next to carboxylic oxygen; lowest shift - **H-1** next to carboxylic carbon
- integrals corresponds to number of protons

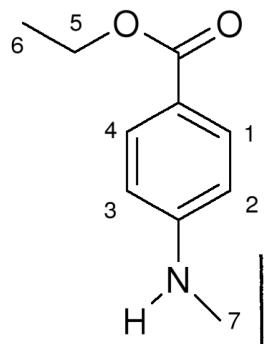
1D ^{1}H NMR - ethyl 4-(methylamino)benzoate





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

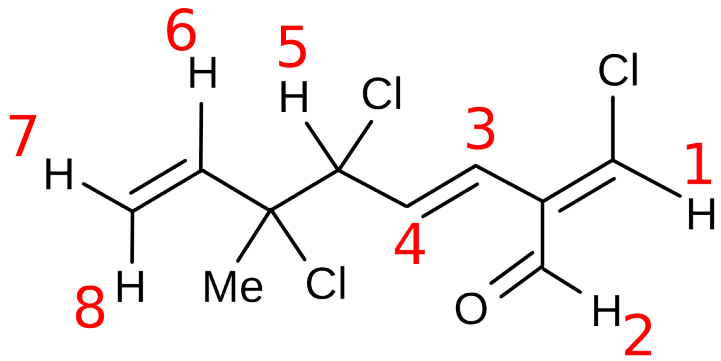


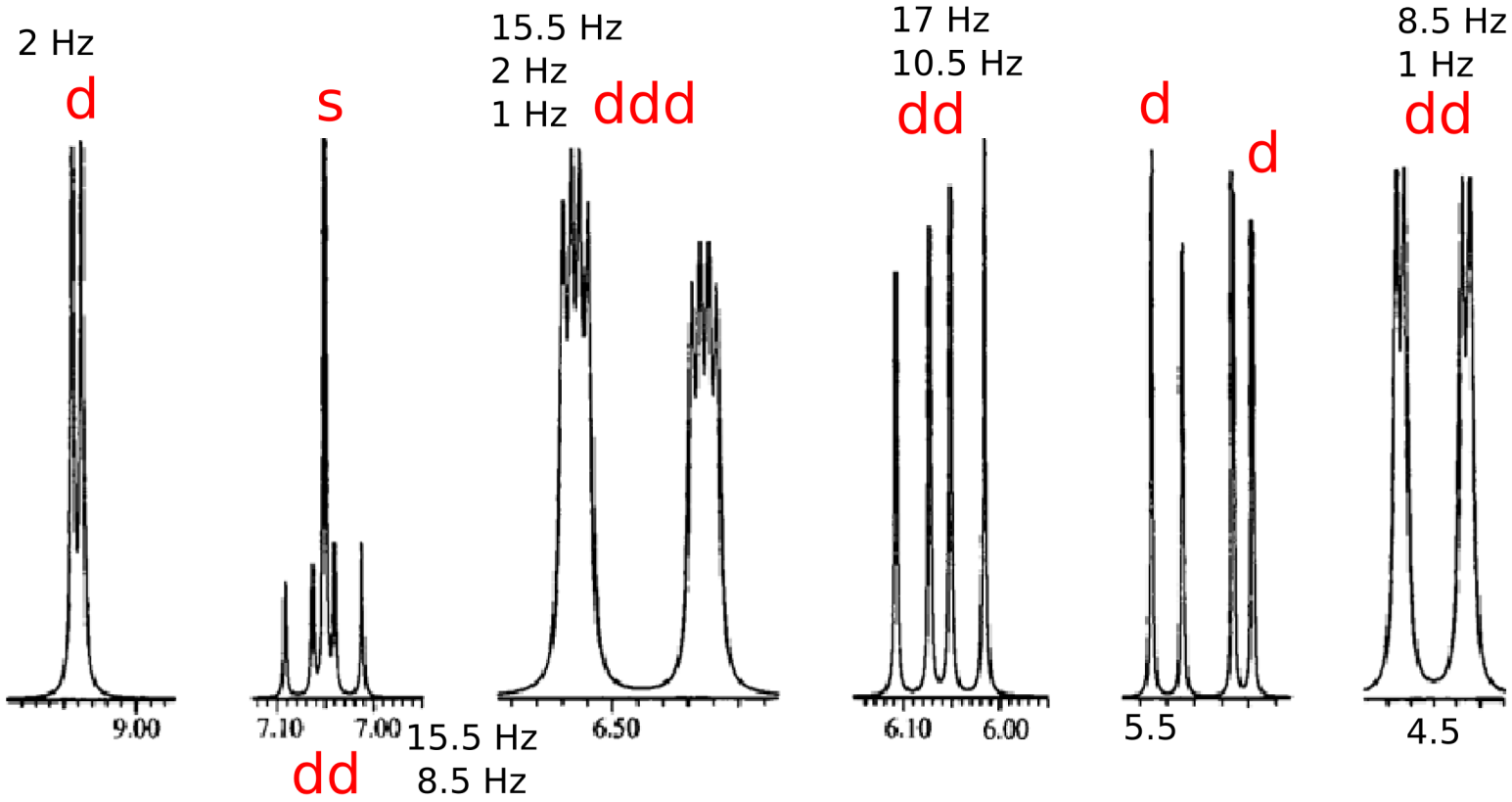


Notes:

- 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

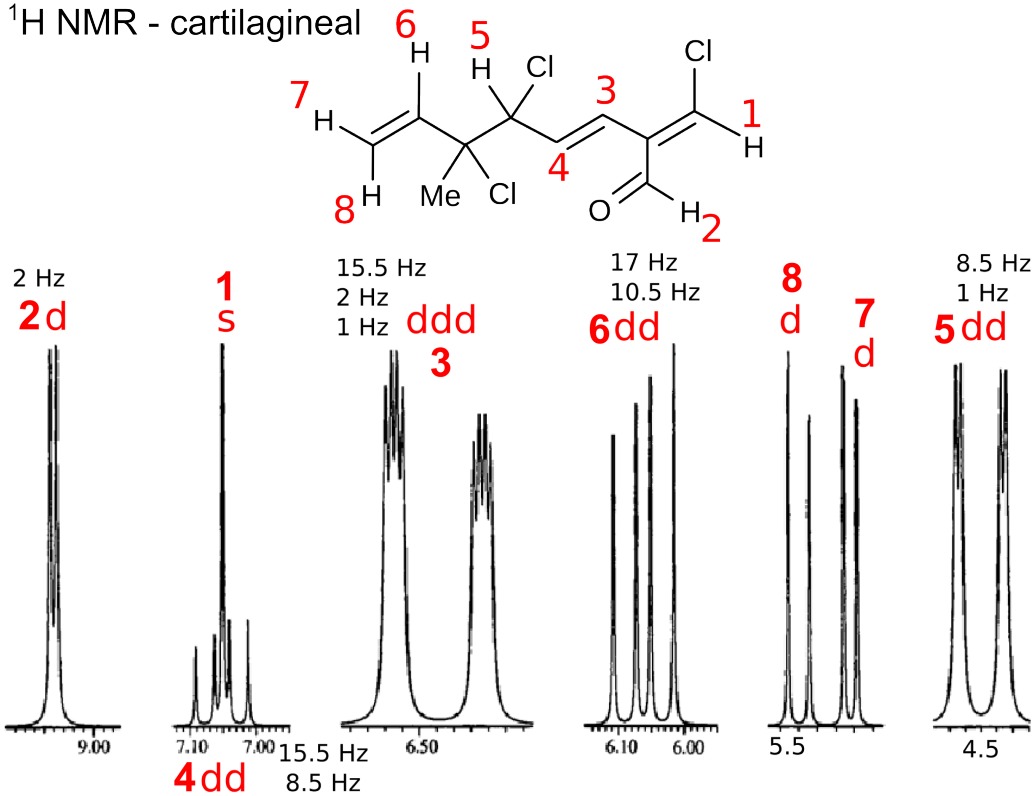
1D ^{1}H NMR spectrum of cartilagineal





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 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 unasigned 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