

C8953

NMR structural analysis seminar

Information about classes + 1D ^1H -NMR

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February 24, 2022

Information about classes

Credit:

- ▶ 3 homework tests + final exercise

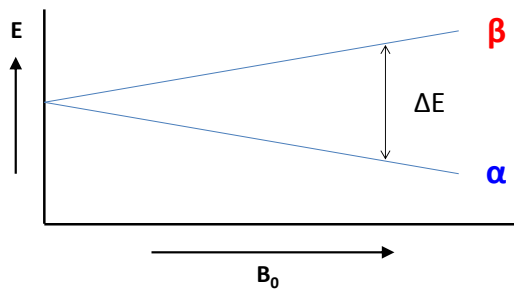
Study materials:

<https://is.muni.cz/auth/el/1431/jaro2021/C8953/um>

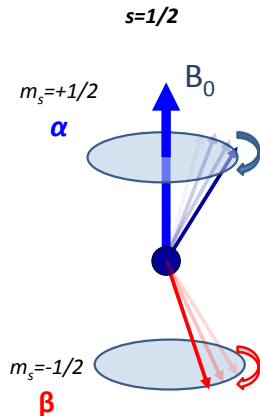
E-tests:

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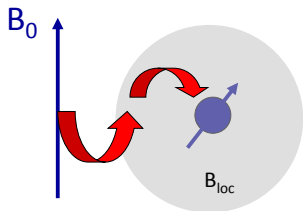
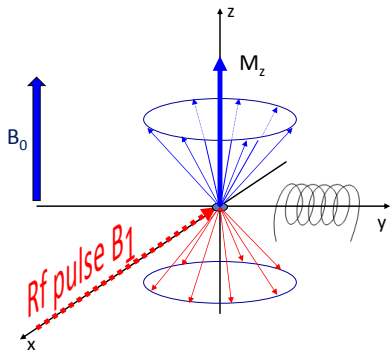
Energy levels splitting



$$N_\alpha > N_\beta$$



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:

Precession frequency affected by nuclear shielding:

Chemical shift:

Definition of the relative scale of the chemical shift:

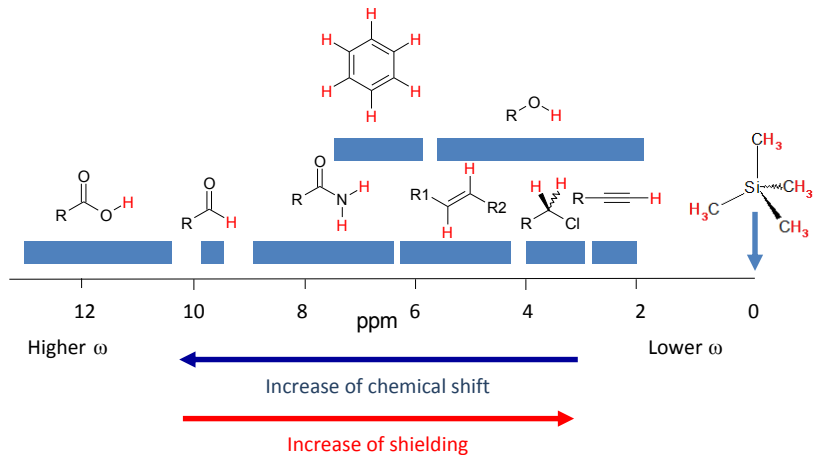
$$\omega = -\gamma B_0$$

$$\omega = -(1+\sigma)B_0$$

$$\delta = \omega - \omega_{ref}$$

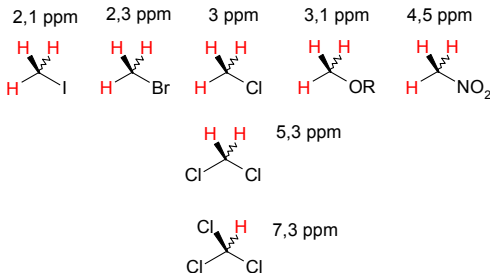
$$\delta = (\omega - \omega_{ref})/\omega_{ref} \cdot 10^6 \text{ppm}$$

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



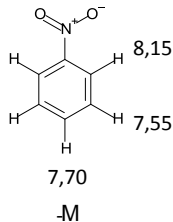
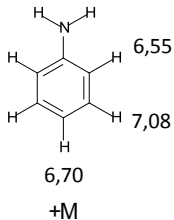
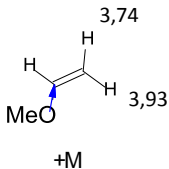
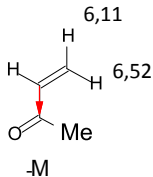
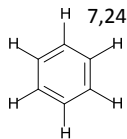
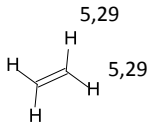
Substituents with -I effect

$=N^+R_2 > -N^+R_3 > -NO_2 > -NR_2$
 $-SO_2R > -SO_3 > -SOR > -SR$
 $-F > -OR > -NR_2 > -CR_3$
 $-F > -Cl > -Br > -I$
 $\equiv N > =NR > -NR_2$
 $-C\equiv CH > -CH=CH_2 > -CH_2-CH_3$

Substituents with +I effects

$-N-R > -O > -S-$
 $-C(CH_3)_3 > -CH(CH_3)_2 > -CH_2CH_3 > -CH_3$
metals

Mesomeric effect



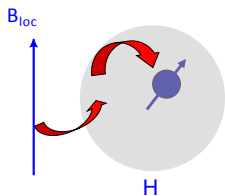
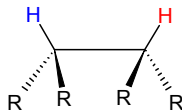
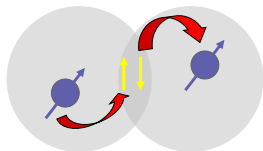
Substituents with $-M$ effects

$-\text{F}$, $-\text{Cl}$, $-\text{Br}$, $-\text{I}$, $-\text{OH}$, $-\text{OR}$, $-\text{NH}_2$, $-\text{NHR}$, $-\text{NR}_2$, $-\text{SH}$, $-\text{SR}$

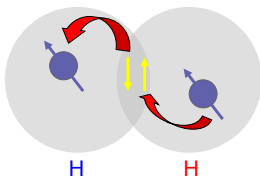
Substituents with $+M$ effect

$-\text{CH}=\text{O}$, $-\text{RC}=\text{O}$, $-\text{C}(\text{OH})=\text{O}$, $-\text{C}(\text{OR})=\text{O}$, $-\text{C}(\text{NH}_2)=\text{O}$, $-\text{NO}_2$, $-\text{SO}_3\text{H}$, $-\text{C}\equiv\text{N}$

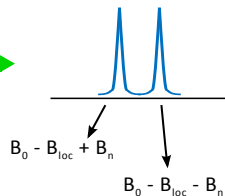
Spin-spin interaction, J -coupling



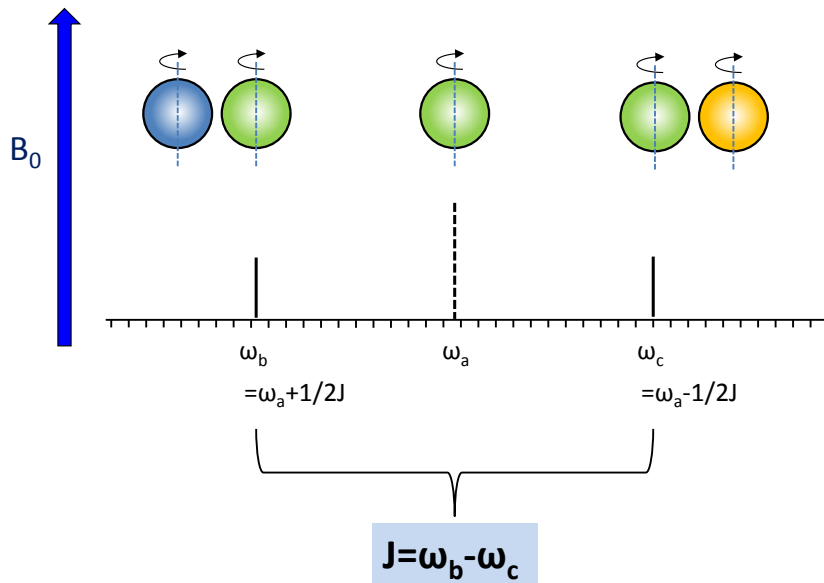
$$B_0 - B_{loc}$$



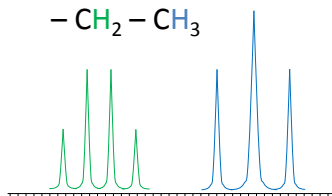
Nucleus H: spin $\alpha \rightarrow -B_n$
spin $\beta \rightarrow +B_n$



Interaction constant J



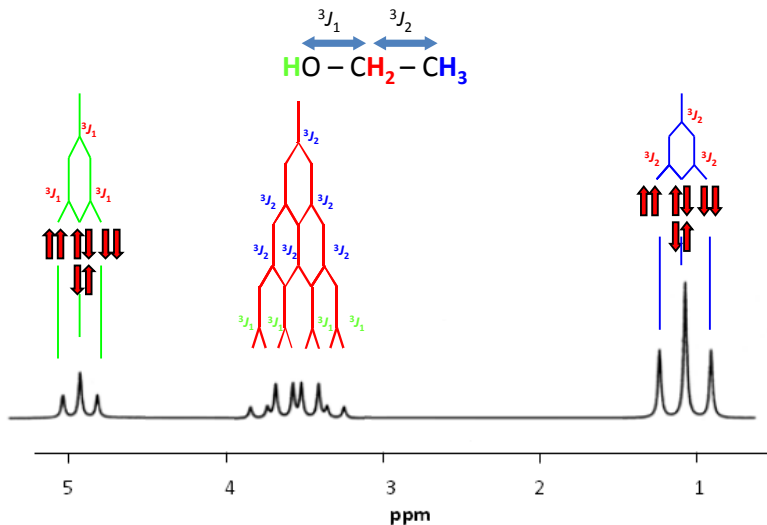
Interaction constant J



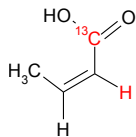
- ▶ Multiplicity of the nucleus I with the spin $1/2$ is given by:
 $m = n + 1$, $n =$ number of interacting nuclei with nucleus I
- ▶ Intensity of lines in multiplet follows Pascal's triangle

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

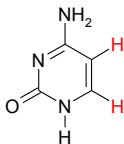
1D ^1H NMR spectrum



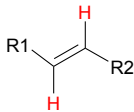
Values of J -constants - trends



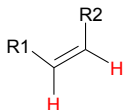
$${}^2J_{CH} = 3.1 \text{ Hz}$$



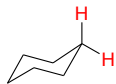
$${}^3J_{HH} = 12 \text{ Hz}$$



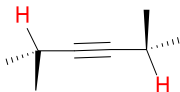
$${}^3J_{HH} = 13 - 18 \text{ Hz}$$



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



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



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



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

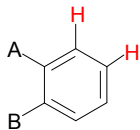


$${}^1J_{CH} = 160 \text{ Hz}$$

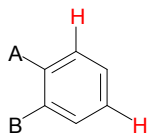


$${}^1J_{CH} = 250 \text{ Hz}$$

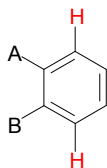
Values of J -constants - trends



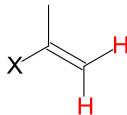
$${}^3J_{HH} = 7,5 \text{ Hz}$$



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



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



X=	Li	H	Cl	OMe	F
${}^2J_{HH}$ (Hz)	7,1	2,5	-1,4	-2,0	-3,2

1D ^1H NMR spectroscopy

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

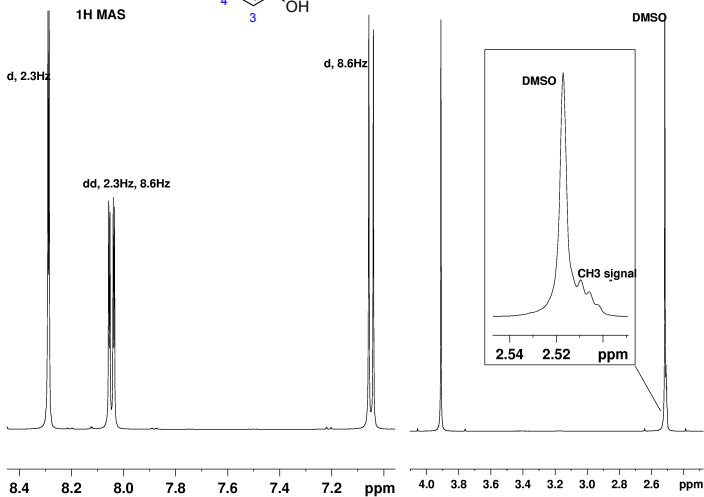
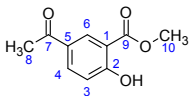
We are looking for:

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

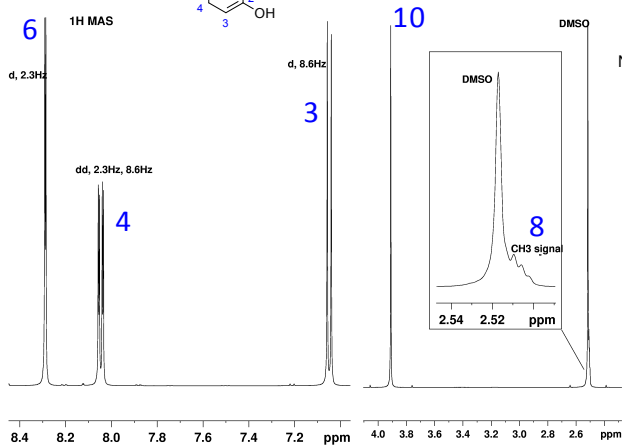
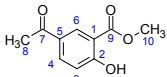
We are considering:

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

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



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

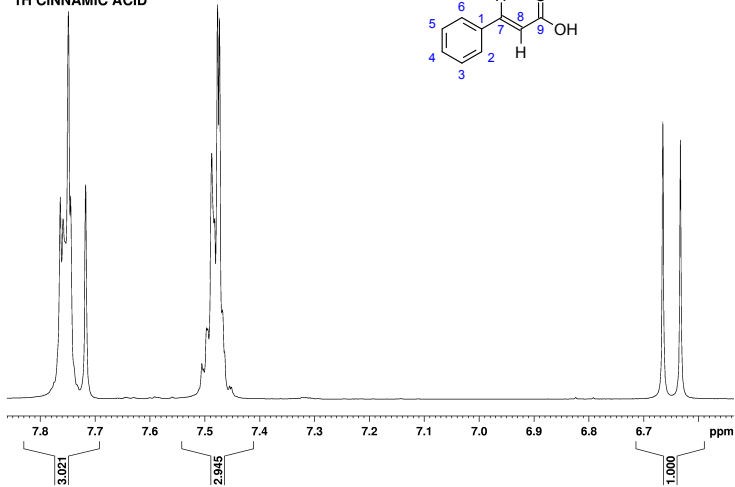
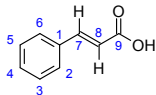


Notes:

- ▶ 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**

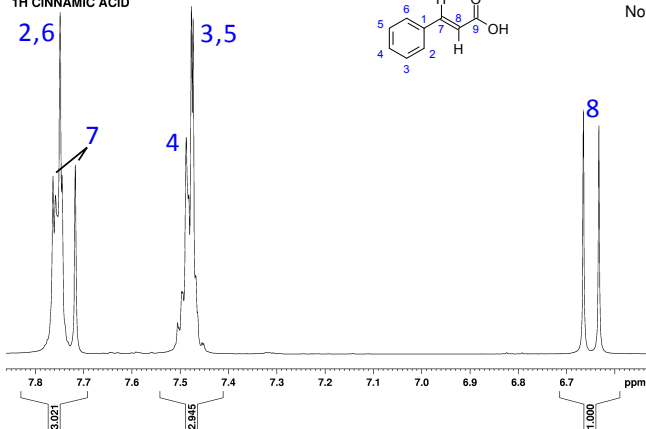
1D ^1H NMR spectrum of cinnamic acid

1H CINNAMIC ACID



1D ^1H NMR spectrum of cinnamic acid

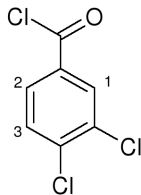
^1H CINNAMIC ACID



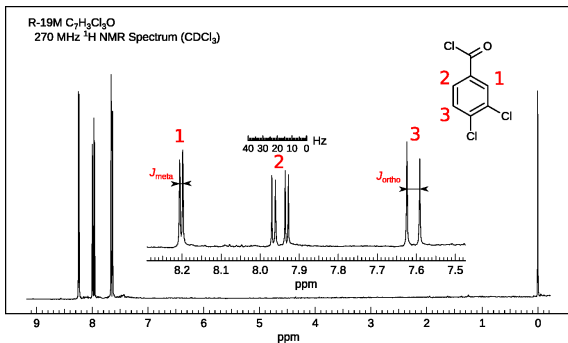
Notes:

- ▶ **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 ^1H NMR spectrum of the following compound



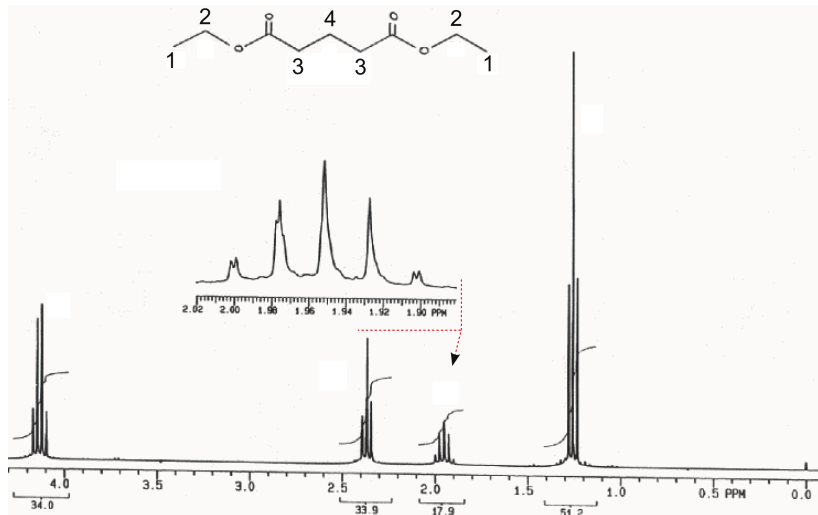
Draw approximate 1D ^1H NMR spectrum of the following compound



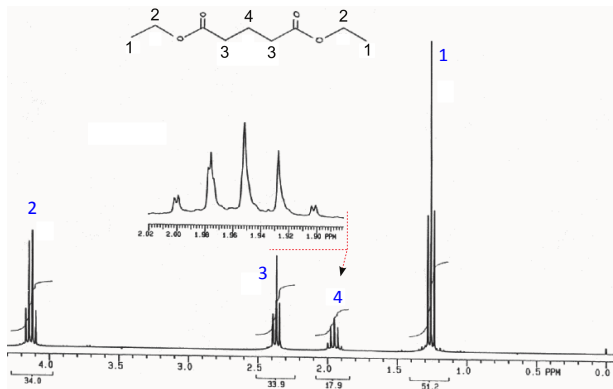
Notes:

- ▶ **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 ^1H NMR spectrum of ethyl glutarate



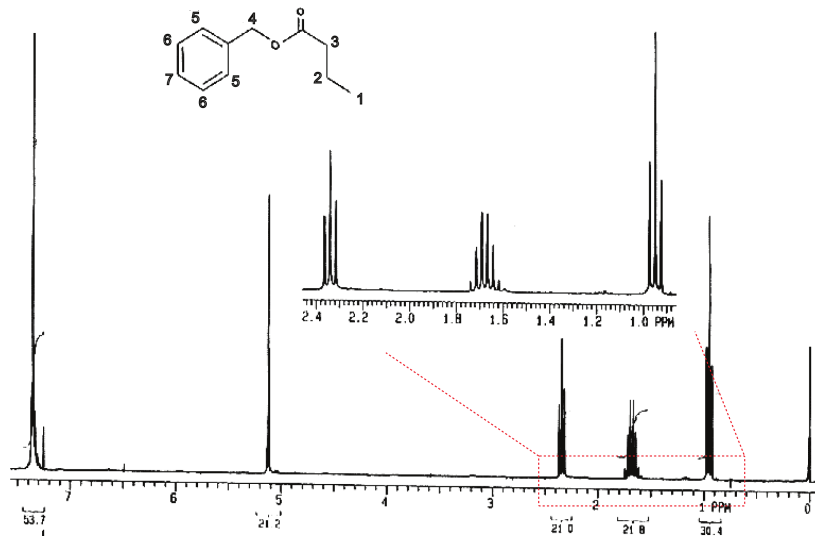
1D ^1H spectrum of ethyl glutarate



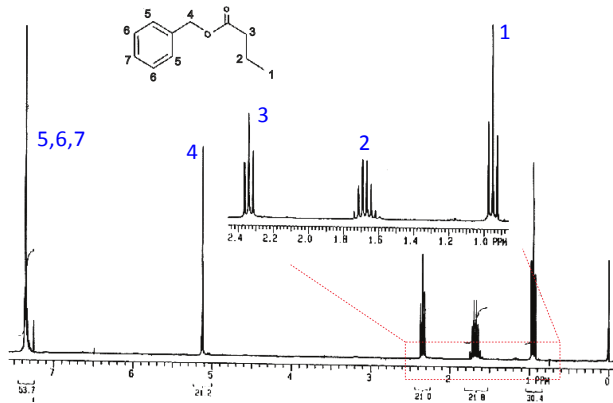
Notes:

- ▶ 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 ^1H NMR spectrum of benzyl butyrate



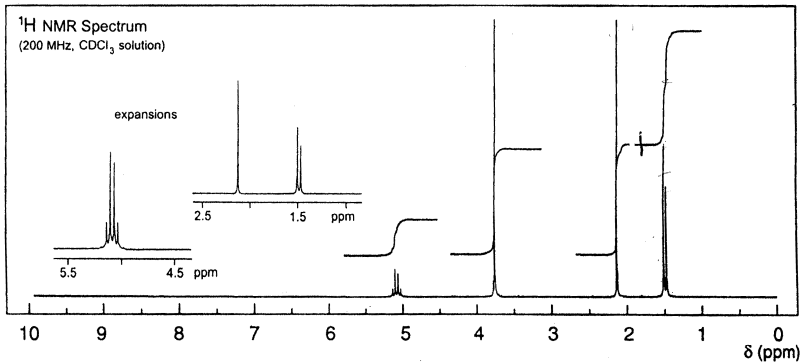
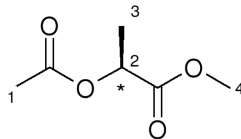
1D ^1H NMR spektrum benzylobutyrátu



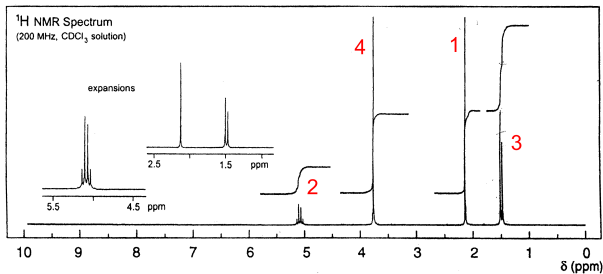
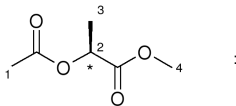
Notes

- ▶ 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 - aliphatic 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 aliphatic protons due to neighboring carboxyl and aromatic ring

1D ^1H NMR - methyl 2-acetoxy propanoate

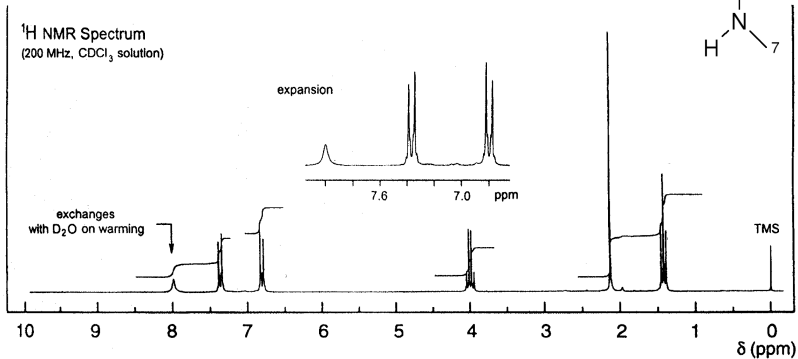
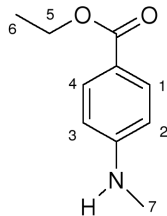


1D ^1H NMR - metyl 2-acetoxypropanoát

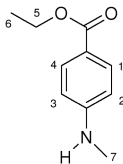
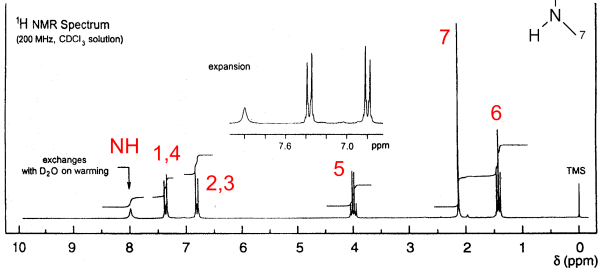


- ▶ lowest shift - methyl **H-3**, splitted due to neighboring stereogenic center C-2
- ▶ last splitted signal - **H-2** - splitted by H-3 to quartet, highest shift due to neighboring carboxyl groups
- ▶ two singlets - highest shift **H-4** next to carboxylic oxygen; lowest shift - **H-1** next to carboxylic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

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



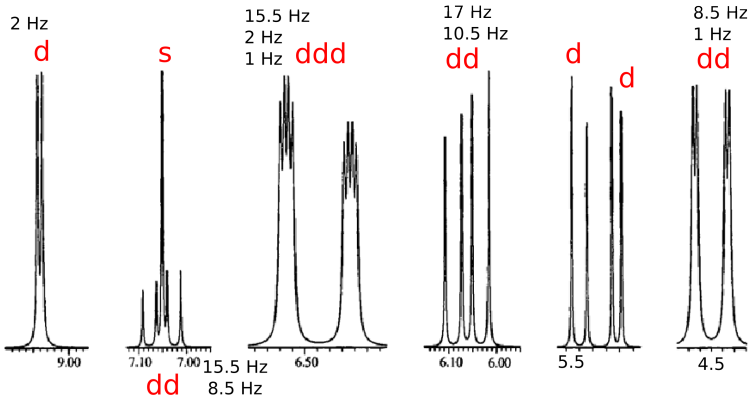
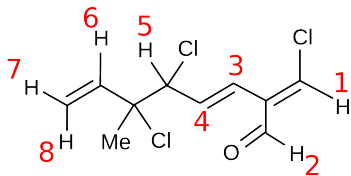
1D ¹H NMR - ethyl 4-(methylamino)benzoate



Notes:

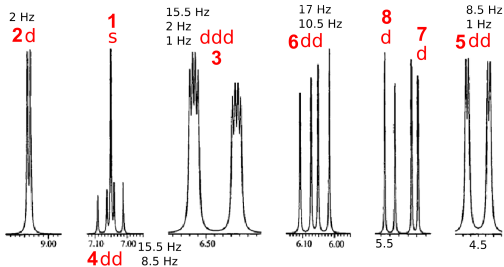
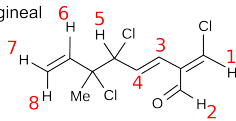
- ▶ highest shift - **NH**, least intensive and broad signal because there is dynamical exchange of the proton with the solvent, it is visible in the spectrum thanks to CDCl₃ used as solvent
- ▶ lowest shifts - alifatics - signal at 1.5 ppm splitted to triplet - methyl **H-6** splitted by H-5; singlet 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 ^1H NMR spectrum of cartilageneal



1D ^1H NMR spectrum - cartilagineal

1D ^1H 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 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