

C8953  
NMR structural analysis  
seminar

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

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February 27, 2023

# Information about classes

## Credit:

- ▶ midterm test and final project

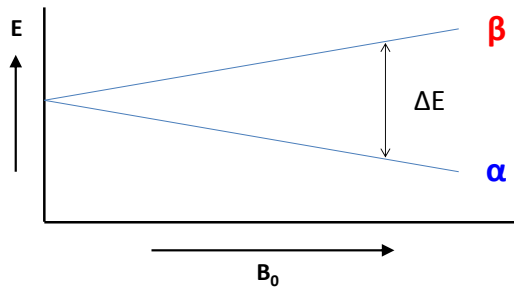
## Study materials:

<https://is.muni.cz/auth/el/1431/jaro2023/C8953/um>

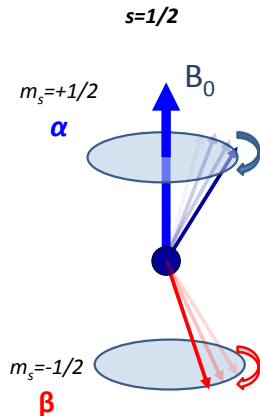
## E-tests:

<https://is.muni.cz/auth/el/1431/jaro2023/C8953/odp>

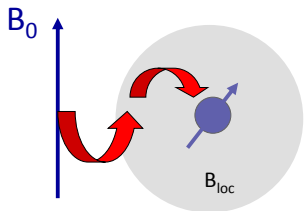
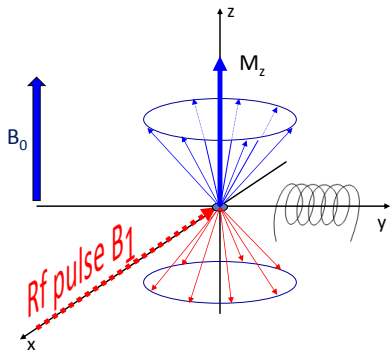
# Energy levels splitting



$$N_\alpha > N_\beta$$



# 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:

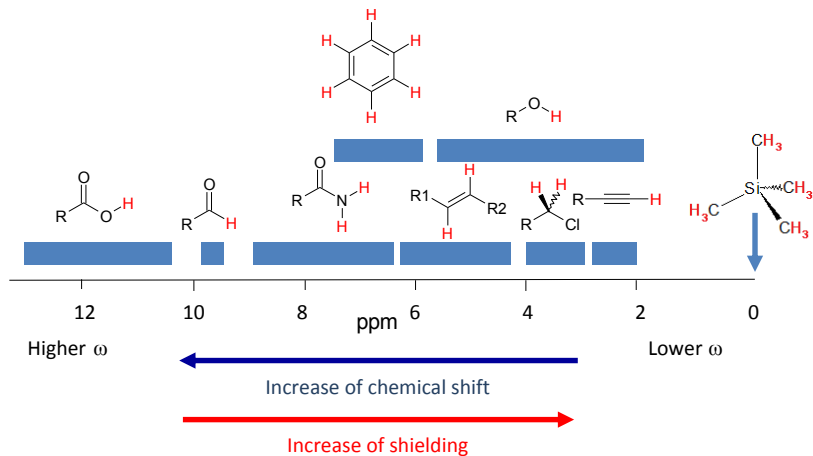
$$\omega = -\gamma B_0$$

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

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

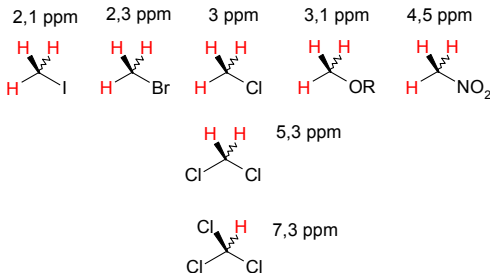
$$\delta = (\omega - \omega_{ref})/\omega_{ref} \cdot 10^6 \text{ppm}$$

# 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



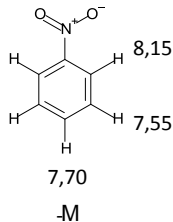
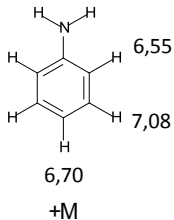
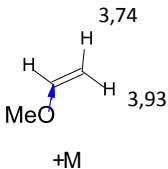
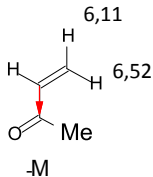
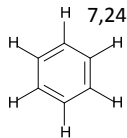
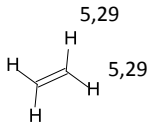
## Substituents with -I effect

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

## Substituents with +I effects

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

# Mesomeric effect



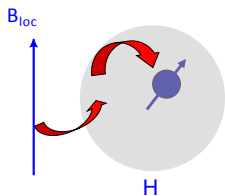
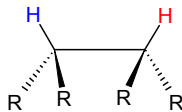
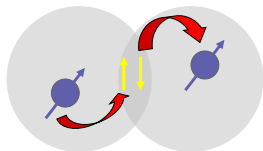
## Substituents with $-M$ effects

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

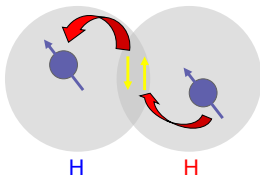
## Substituents with $+M$ effect

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

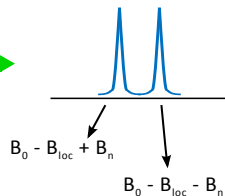
# Spin-spin interaction, $J$ -coupling



$$B_0 - B_{loc}$$

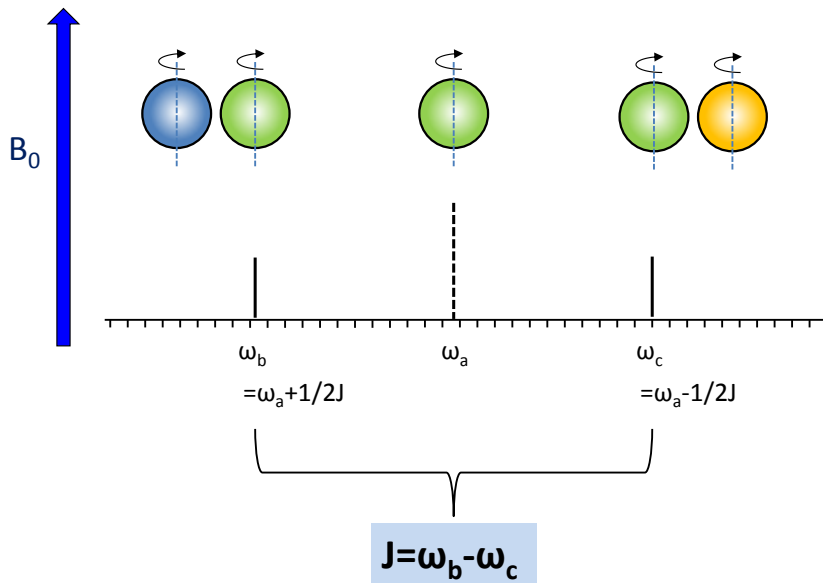


Nucleus H: spin  $\alpha \rightarrow -B_n$   
spin  $\beta \rightarrow +B_n$

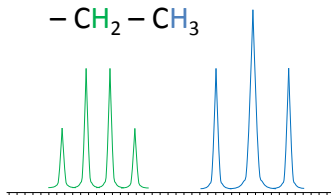




# Interaction constant $J$



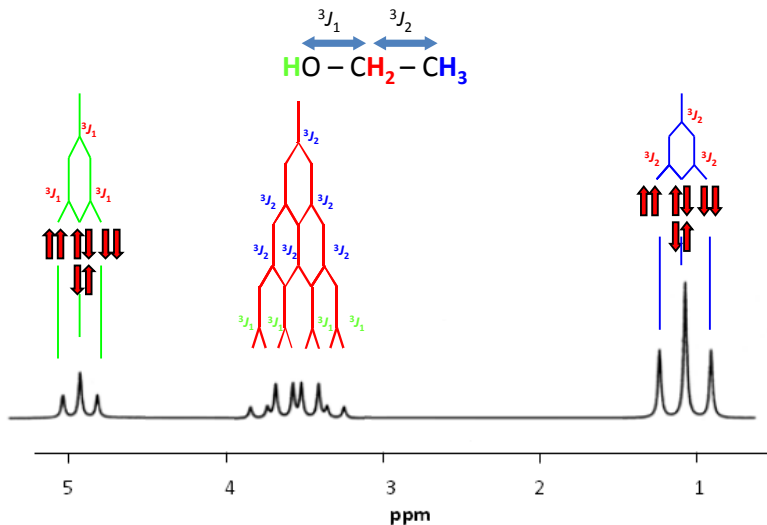
# Interaction constant $J$



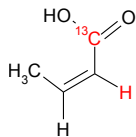
- ▶ Multiplicity of the nucleus I with the spin  $1/2$  is given by:  
 $m = n + 1$ ,  $n =$  number of interacting nuclei with nucleus I
- ▶ Intensity of lines in multiplet follows Pascal's triangle

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

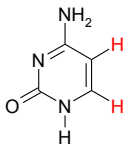
# 1D $^1\text{H}$ NMR spectrum



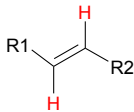
# Values of $J$ -constants - trends



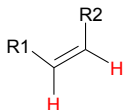
$$^2J_{\text{CH}} = 3.1 \text{ Hz}$$



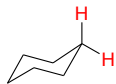
$$^3J_{\text{HH}} = 12 \text{ Hz}$$



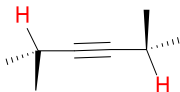
$$^3J_{\text{HH}} = 13 - 18 \text{ Hz}$$



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



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



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



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

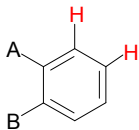


$$^1J_{\text{CH}} = 160 \text{ Hz}$$

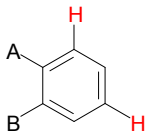


$$^1J_{\text{CH}} = 250 \text{ Hz}$$

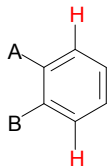
# Values of $J$ -constants - trends



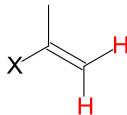
$${}^3J_{HH} = 7,5 \text{ Hz}$$



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



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



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

# 1D $^1\text{H}$ NMR spectroscopy

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

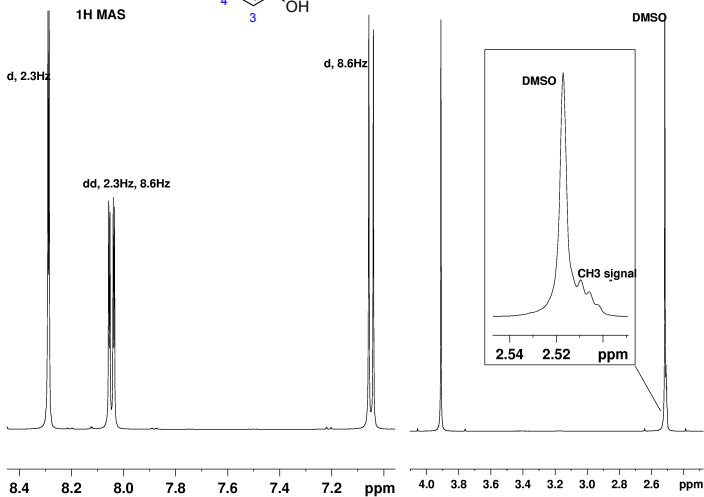
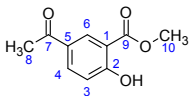
## We are looking for:

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

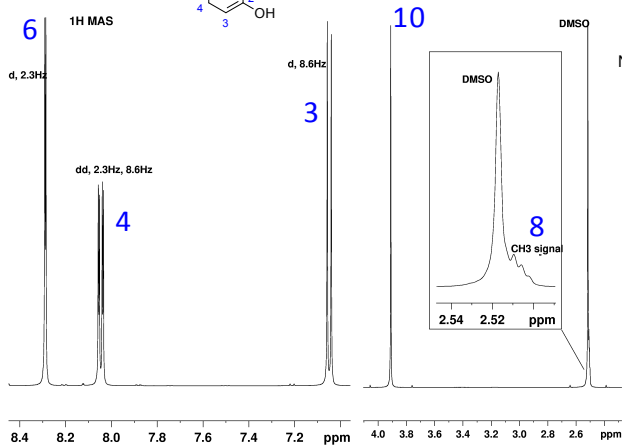
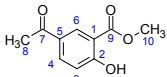
## We are considering:

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

# 1D $^1\text{H}$ NMR spectrum of methyl-5-acetylsalicylate



# 1D $^1\text{H}$ NMR spectrum of methyl-5-acetylsalicylate



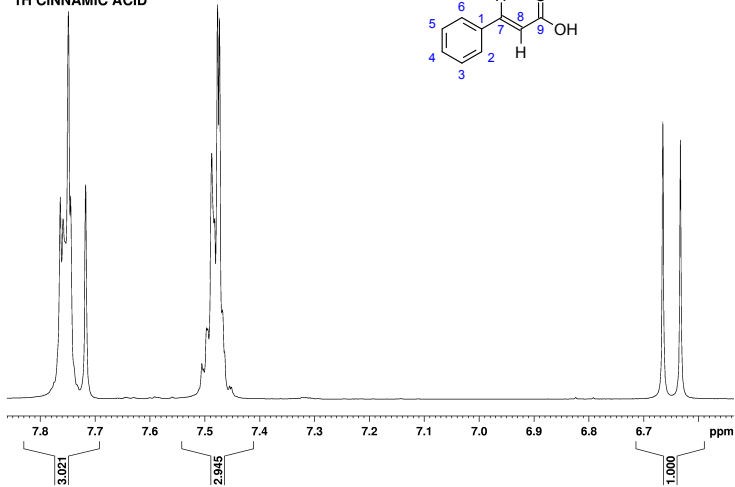
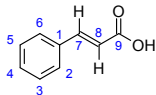
Notes:

- ▶ two singlets in the spectrum - two isolated groups in the structure - CH<sub>3</sub> 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**



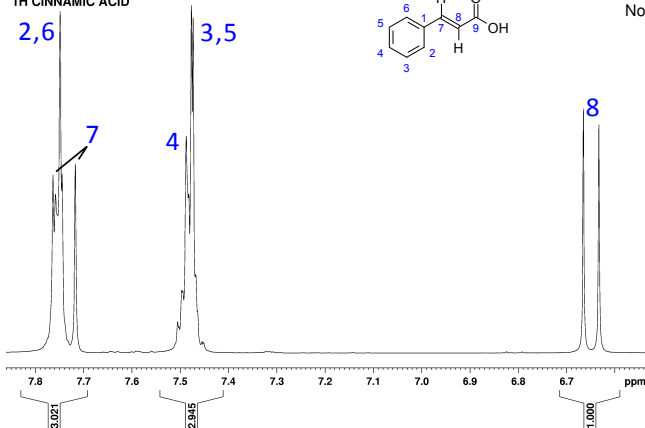
# 1D $^1\text{H}$ NMR spectrum of cinnamic acid

1H CINNAMIC ACID



# 1D $^1\text{H}$ NMR spectrum of cinnamic acid

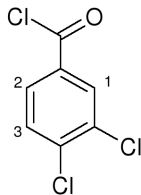
$^1\text{H}$  CINNAMIC ACID



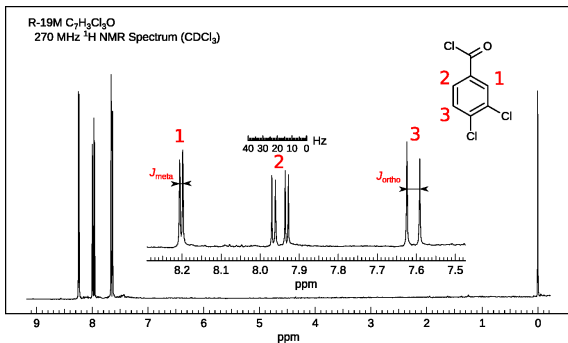
Notes:

- ▶ **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  $^1\text{H}$  NMR spectrum of the following compound



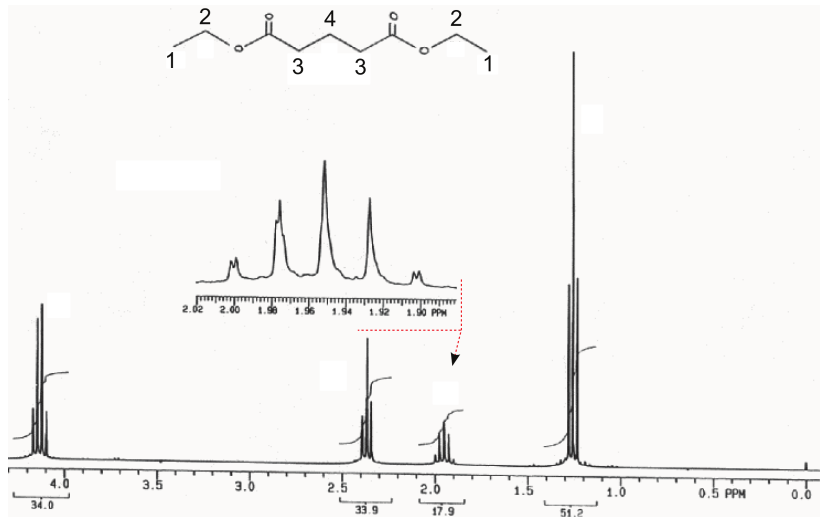
# Draw approximate 1D $^1\text{H}$ NMR spectrum of the following compound



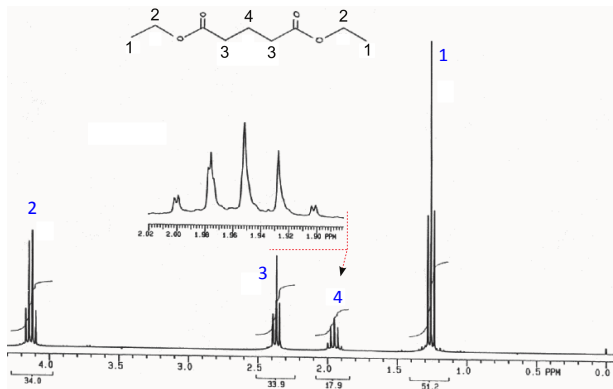
Notes:

- ▶ **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 $^1\text{H}$ NMR spectrum of ethyl glutarate



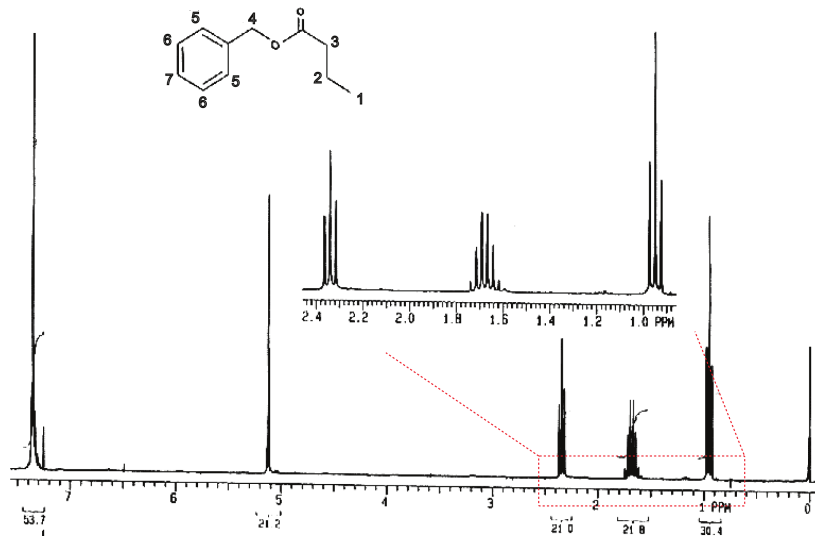
# 1D $^1\text{H}$ spectrum of ethyl glutarate



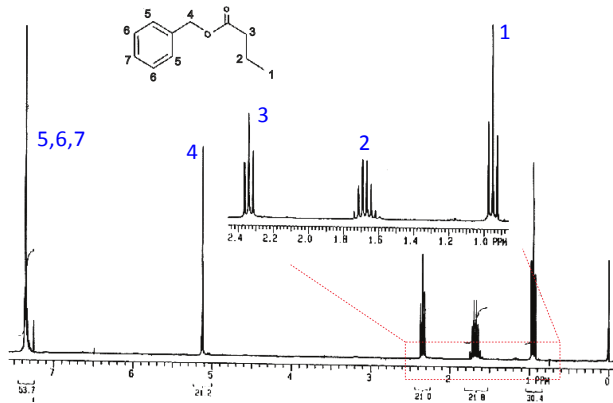
## Notes:

- ▶ 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 $^1\text{H}$ NMR spectrum of benzyl butyrate



# 1D $^1\text{H}$ NMR spektrum benzylobutyrátu

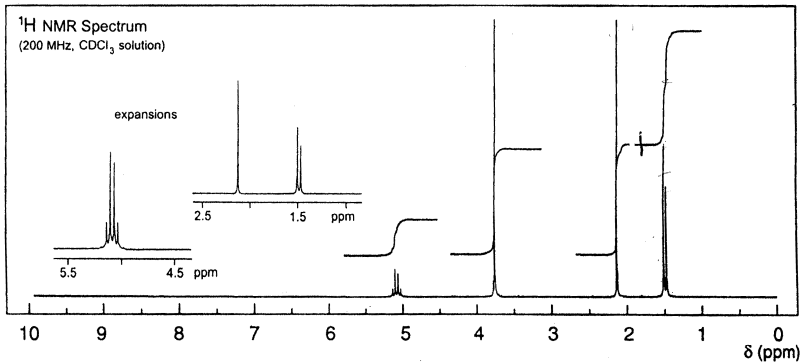
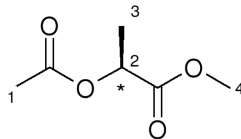


## Notes

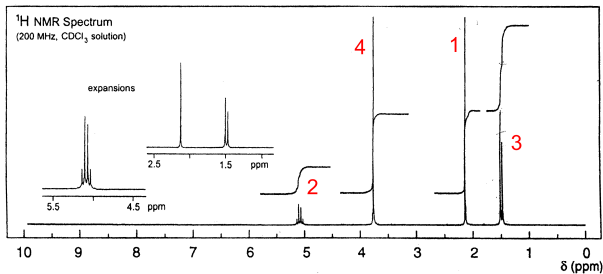
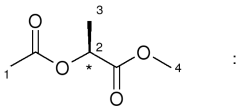
- ▶ highest shift - aromatic ring, which is flexible - **H-5, H-6, H-7** are under one signal, integral value corresponds to five protons
- ▶ lowest shifts - alifatic chain H-1, H-2 a H-3: **H-1** - integral equals to three protons, splitted only by H-2 to triplet; **H-2** - integral equals to two protons, 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 $^1\text{H}$ NMR - methyl 2-acetoxy propanoate

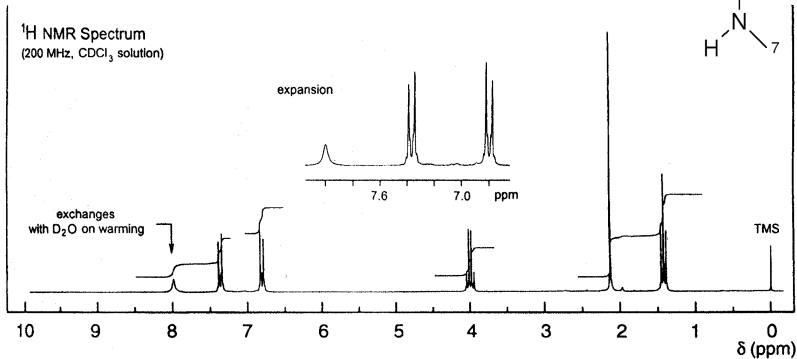
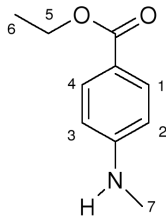


# 1D $^1\text{H}$ NMR - metyl 2-acetoxypropanoát

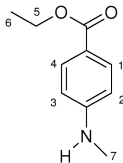
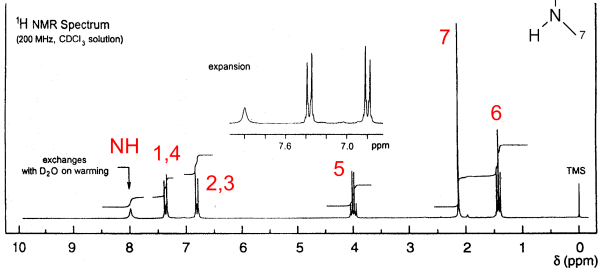


- ▶ lowest shift - methyl **H-3**, splitted due to neighboring stereogenic center C-2
- ▶ last splitted signal - **H-2** - splitted by H-3 to quartet, highest shift due to neighboring carboxyl groups
- ▶ two singlets - highest shift **H-4** next to carboxylic oxygen; lowest shift - **H-1** next to carboxylic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

# 1D $^1\text{H}$ NMR - ethyl 4-(methylamino)benzoate



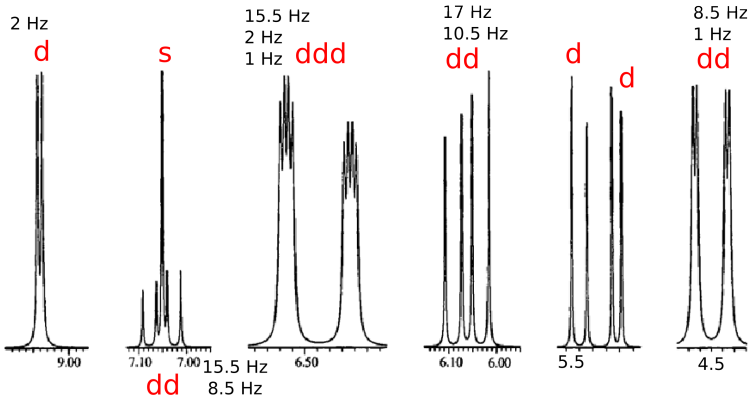
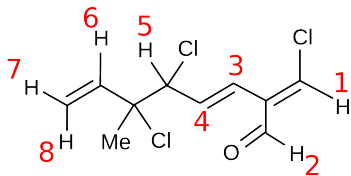
# 1D <sup>1</sup>H NMR - ethyl 4-(methylamino)benzoate



## Notes:

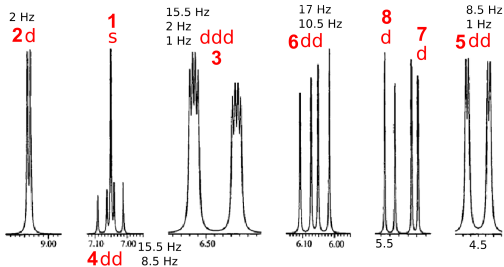
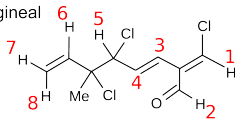
- ▶ highest shift - **NH**, least intensive and broad signal because there is dynamical exchange of the proton with the solvent, it is visible in the spectrum thanks to CDCl<sub>3</sub> used as solvent
- ▶ lowest shifts - alifatics - signal at 1.5 ppm splitted to triplet - methyl **H-6** splitted by 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 $^1\text{H}$ NMR spectrum of cartilageneal



# 1D $^1\text{H}$ NMR spectrum - cartilagineal

1D  $^1\text{H}$  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  $^{13}\text{C}$ -NMR spectra