

NMR STRUCTURE ELUCIDATION OF SMALL ORGANIC MOLECULES

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NTNU NMR club, 03.03.2020

STRUCTURE ELUCIDATION OF UNKNOWN COMPOUNDS

○ Additional information

- How has the compound been obtained:
 - Natural product
 - Extraction and isolation procedure
 - Synthetic product
 - Synthesys pathway, work-up, purification
- MS spectra, molecular mass, molecular formula
- Physical constants and properties
 - m.p., b.p., solubility, polarity
- Mass and purity

USUAL SET OF NMR SPECTRA FOR STRUCTURE ELUCIDATION OF SMALL ORGANIC MOLECULES

- 1D proton
- 1D ^{13}C (BB) / DEPT?
- 2D HSQC/HMQC
- 2D COSY
- 2D HMBC
- 2D NOESY/ROESY
- 2D TOCSY/HSQC-TOCSY
- H2BC

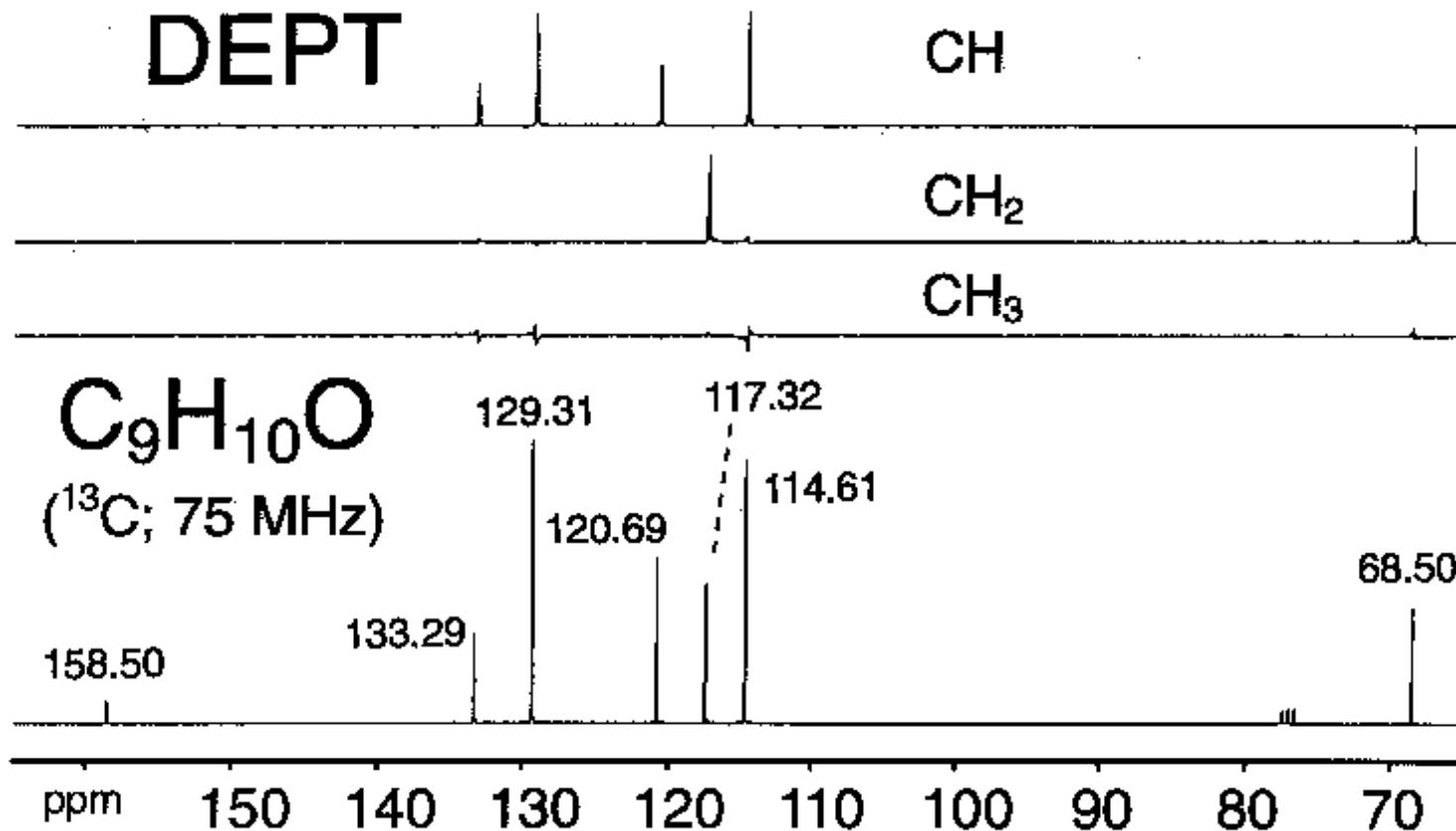
AVAILABLE INFORMATION FROM VARIOUS SPECTRA

- 1D proton:

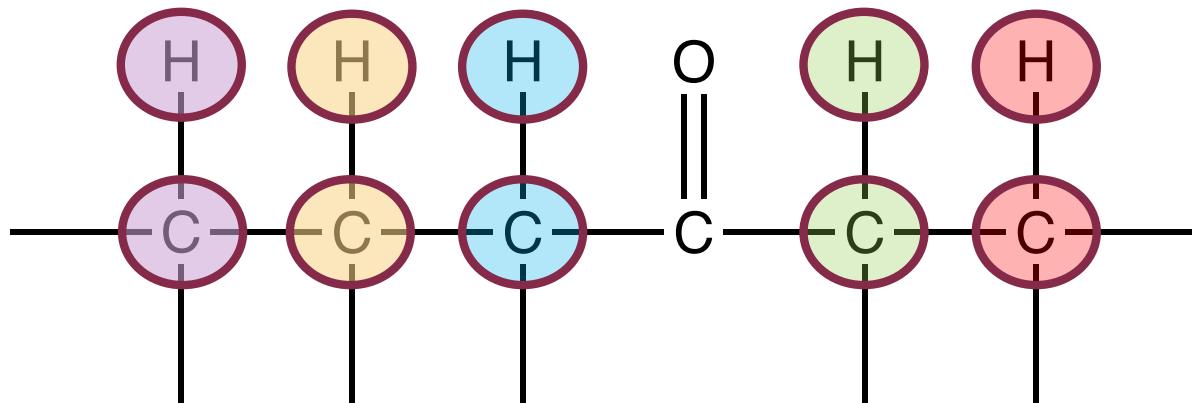
- Shifts
- Multiplicity, coupling constants
- Integrals

- 1D ^{13}C :

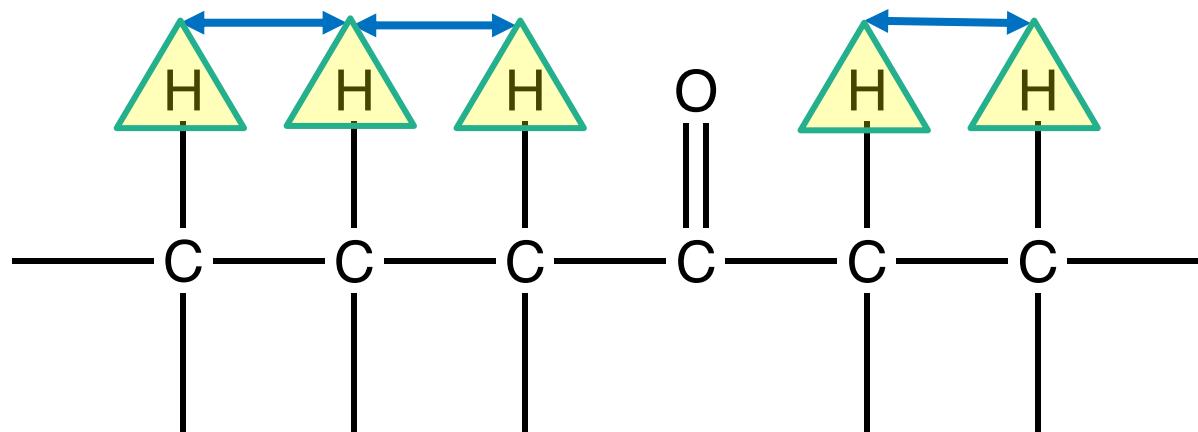
- Shifts
- No. of C-atoms (not always!)
- With DEPT: distinguishing of $\text{CH}_3/\text{CH}_2/\text{CH}$ carbons



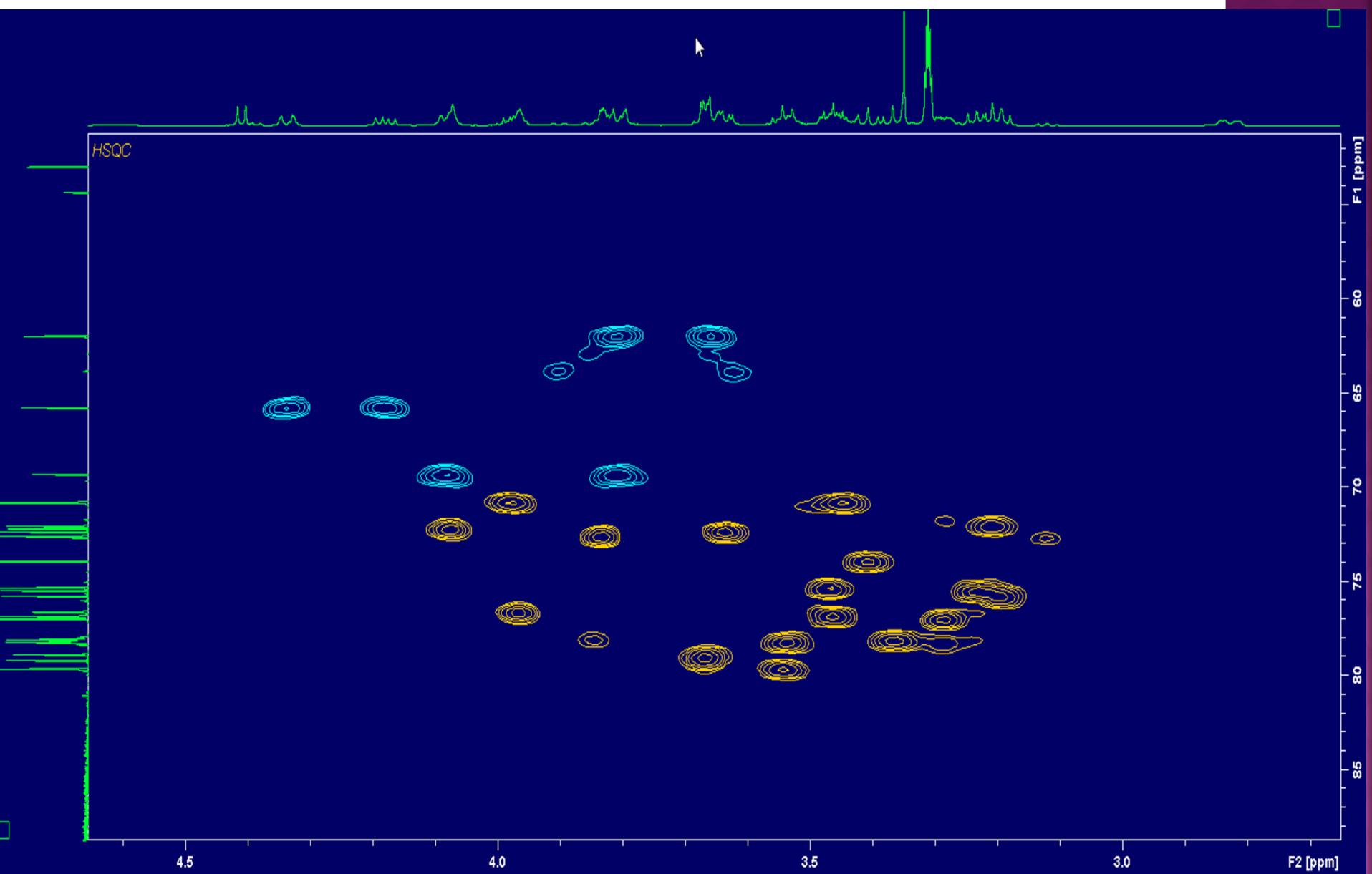
HSQC/HMQC



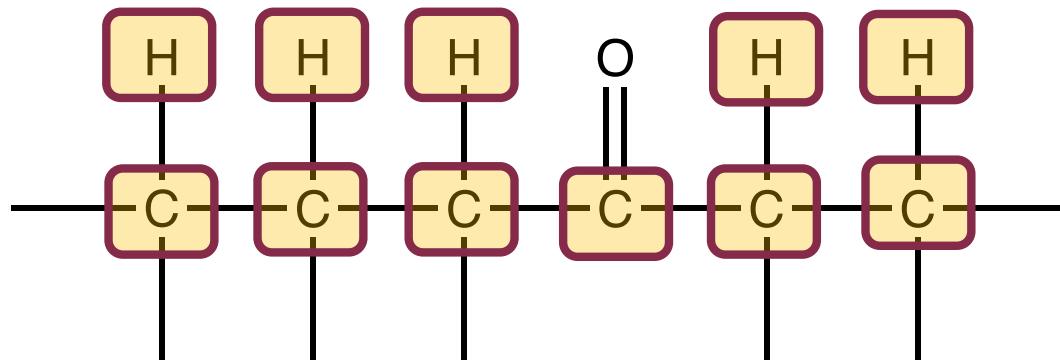
COSY



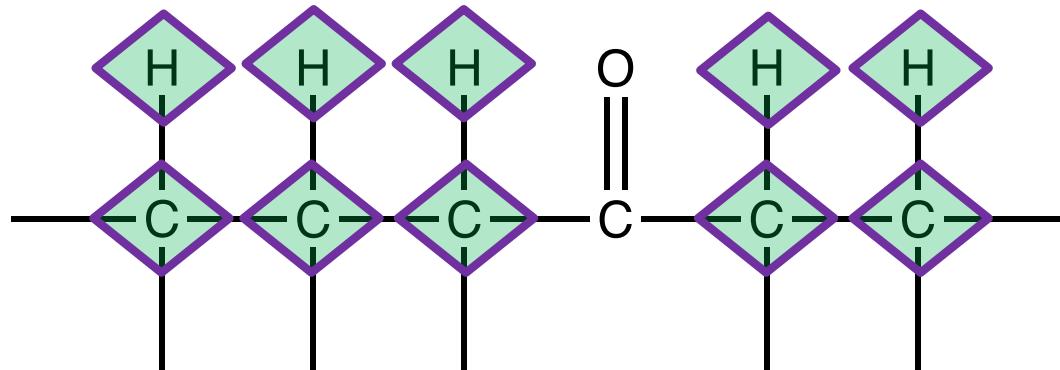
MULTIPLICITY EDITED HSQC

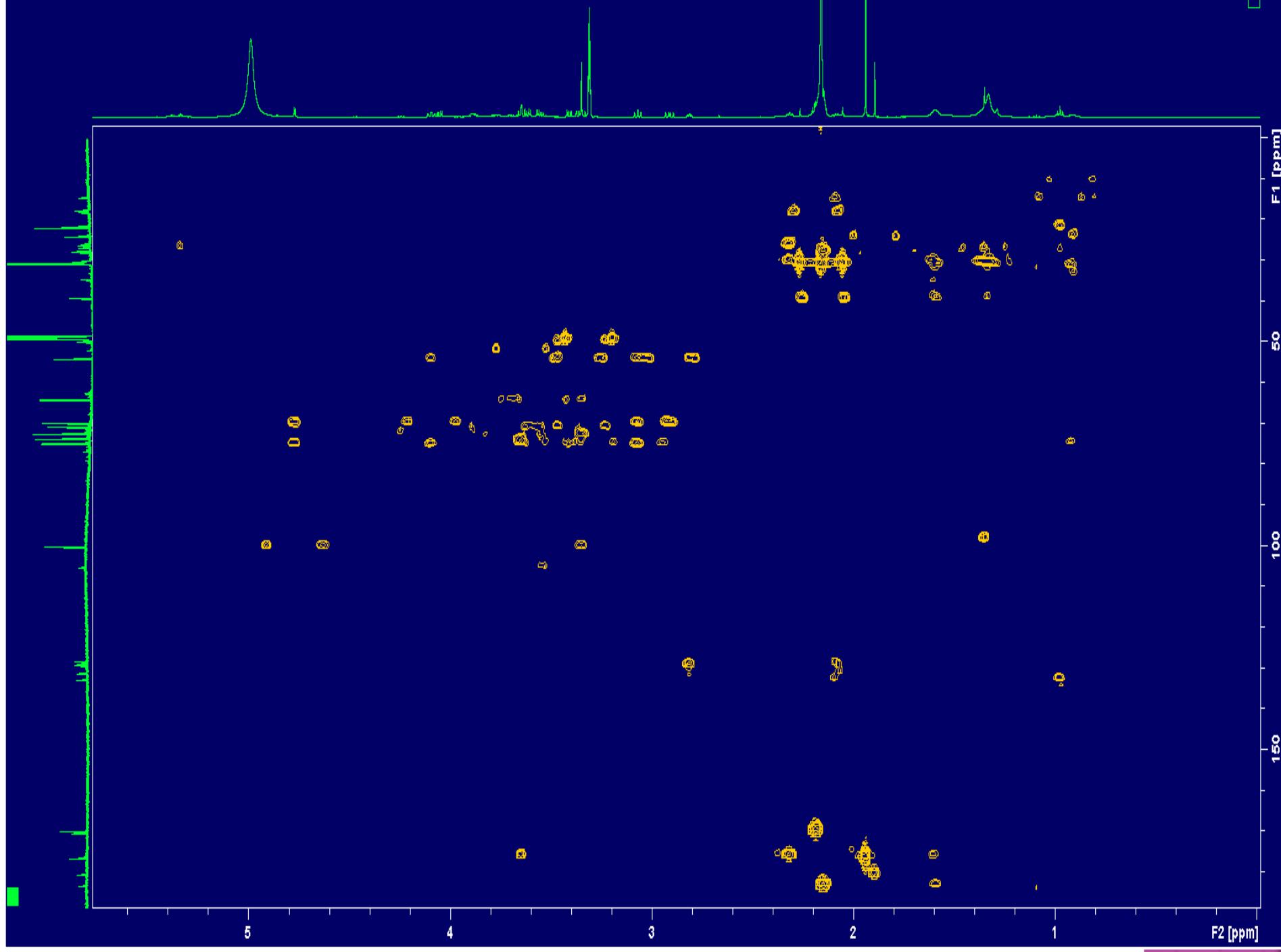


HMBC

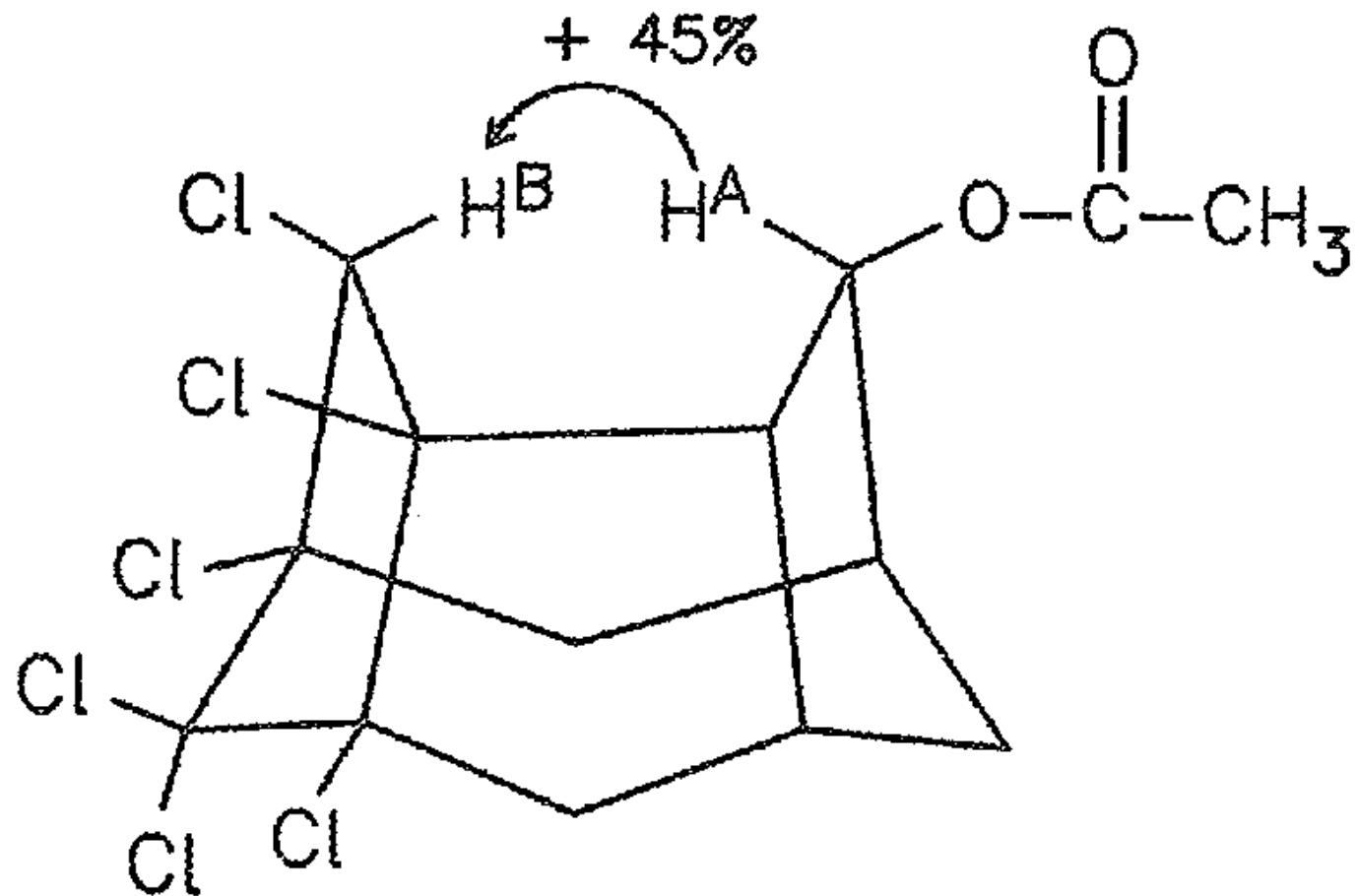


H2BC

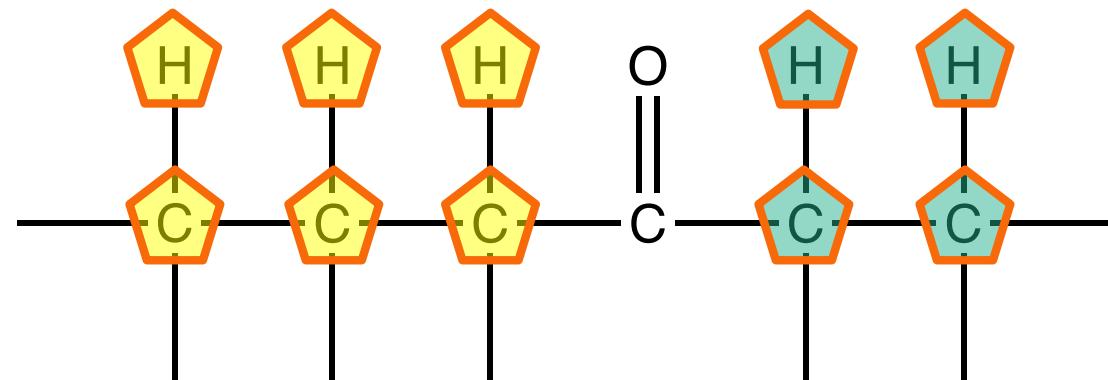


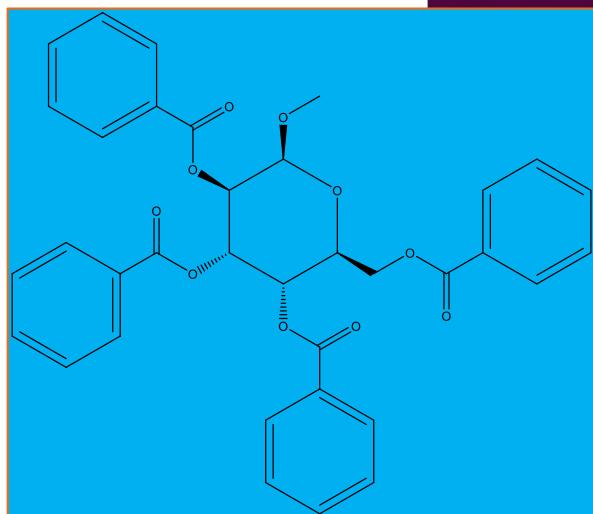
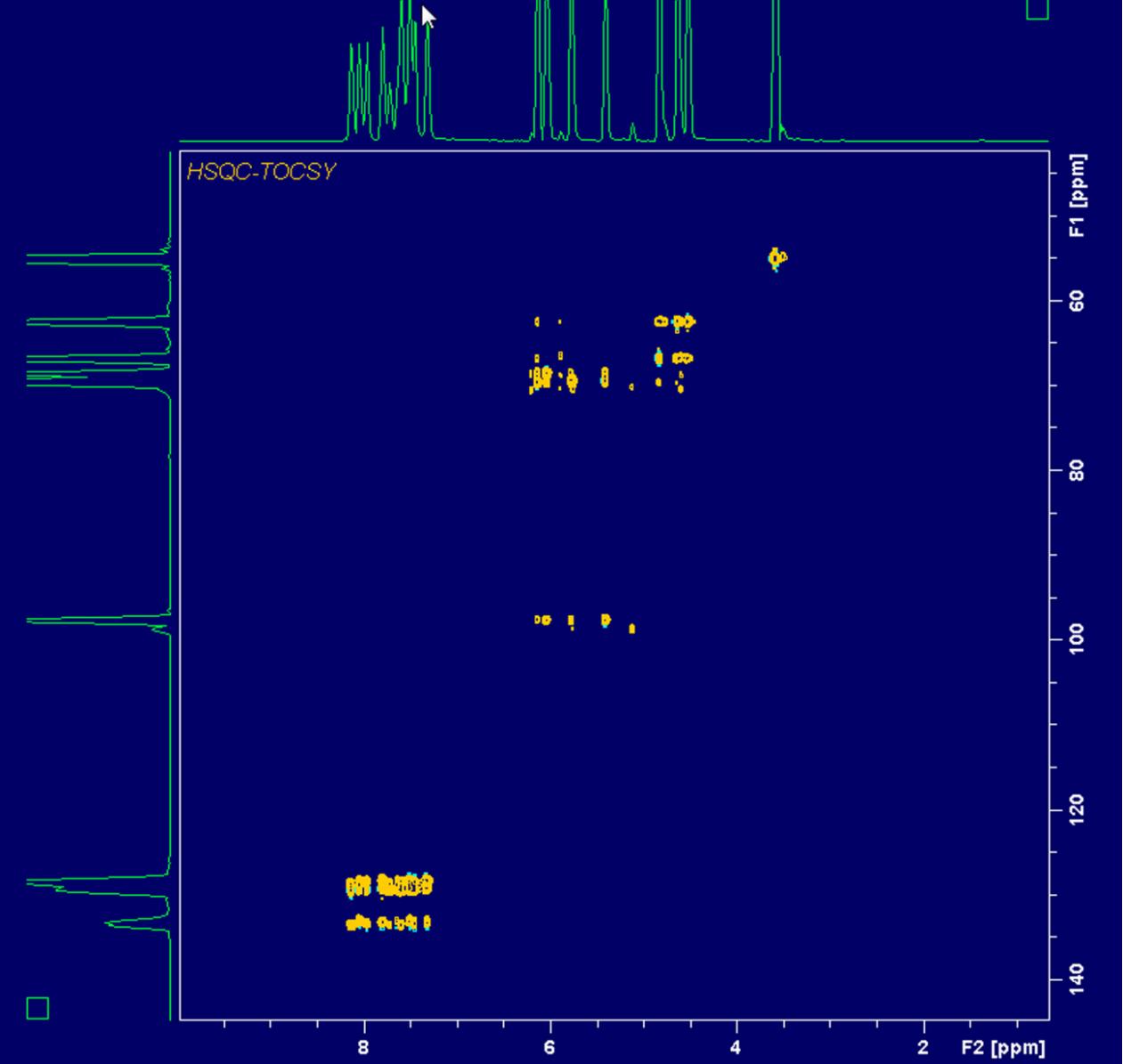


NOESY/ROESY

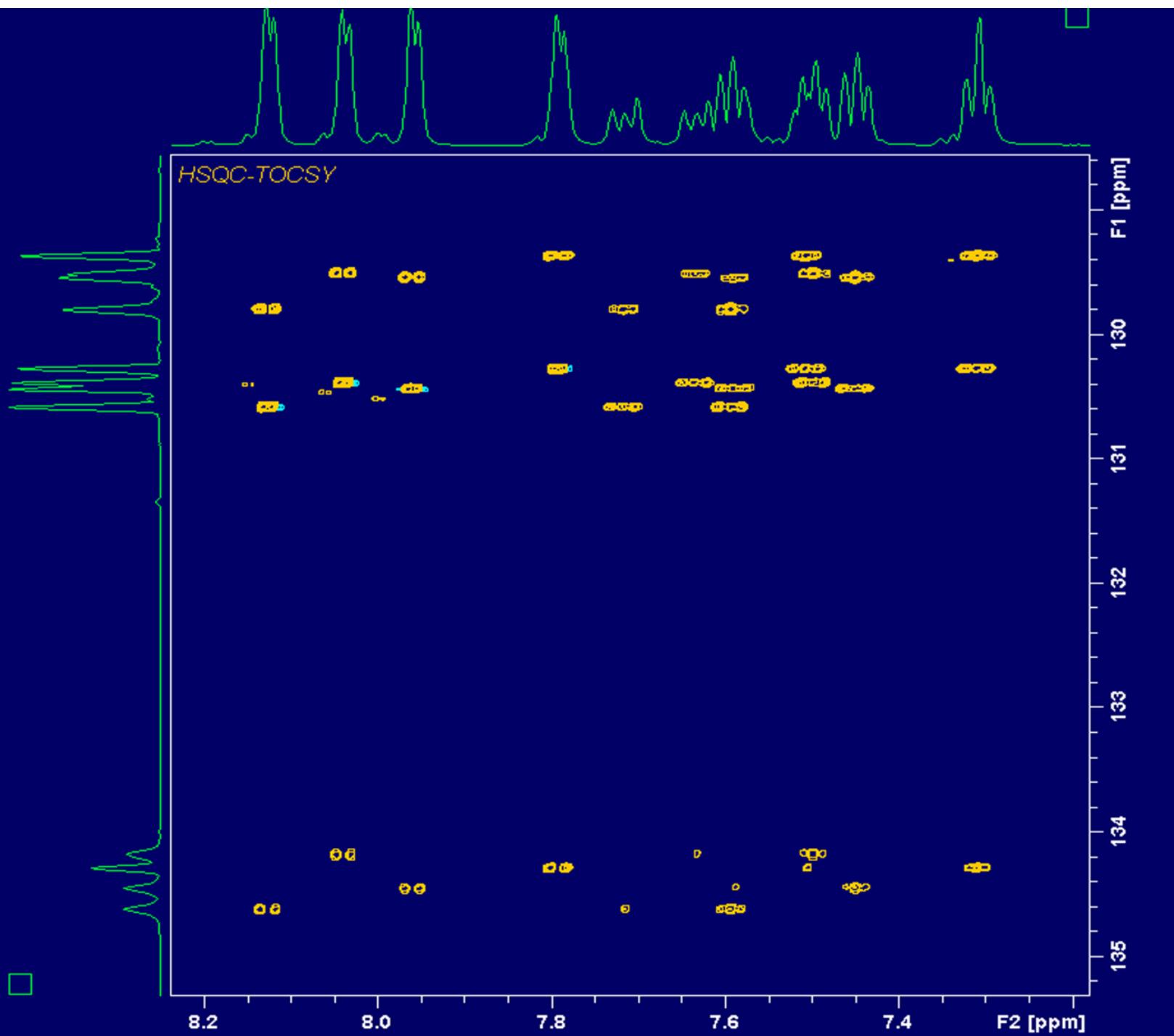


2D TOCSY / HSQC-TOCSY





A. Esmurziev, N. Simic, E. Sundby, B.H. Hoff, ¹H and ¹³C NMR Data of Methyl Tetra-O-Benzoyl-D-Pyranosides in Acetone-d₆, *Magnetic Resonance in Chemistry* 47(5) 449-452 (2009)



GENERAL REMARKS

- No general rule
- Still, some procedures proved to be efficient in practice
 - If a molecular formula is given, calculate first the HDI (hydrogen deficiency index)
 - Next, start with collecting primary data from
 - 1D ^1H spectrum
 - 1D ^{13}C and, if available, DEPT spectrum
 - 2D HSQC/HMQC/C,H-COSY spectrum

1D ^1H SPECTRUM

- ## ⦿ Make a table

1D ^1H SPECTRUM (CONT.)

δ ^1H (ppm)	Integral	Multiplicity	J (Hz)
0.83	3H	s	-
0.91	3H	s	-
1.20	1H	dtr	4.8/13.4
1.44	1H	m	8.2/13.4
1.54	3H	m	1.6/3.5
2.02	2H	m	-
2.23	3H	s	-
2.26	1H	d	10.0
5.48	1H	bs	-
6.03	1H	dd	0.5/15.8
6.59	1H	dd	9.7/15.8

1D ^{13}C SPECTRUM / DEPT

- Make a table - extract shifts

δ ^{13}C (ppm)	δ ^1H (ppm)	Remark
22.7		
23.0		
26.8		
26.9		
27.7		
31.2		
32.5		
54.3		
122.6		
131.9		
132.3		
149.0		
198.4		

HSQC

- Use the table from previous slide and complete it with data from HSQC

δ ^{13}C (ppm)	δ ^1H (ppm)	Remark
22.7	1.54	CH_3
23.0	2.02	CH_2
26.8	0.91	CH_3
26.9	2.23	CH_3
27.7	0.83	CH_3
31.2	1.20/1.44	CH_2
32.5	-	C_q
54.3	2.26	CH
122.6	5.48	CH
131.9	-	C_q
132.3	6.03	CH
149.0	6.59	CH
198.4	-	C_q

HSQC - MAKE INFORMATION EASY TO RETRIEVE

δ ^{13}C (ppm)	δ ^1H (ppm)	Remark
22.7	1.54	CH_3
23.0	2.02	CH_2
26.8	0.91	CH_3
26.9	2.23	CH_3
27.7	0.83	CH_3
31.2	1.20/1.44	CH_2
32.5	-	C_q
54.3	2.26	CH
122.6	5.48	CH
131.9	-	C_q
132.3	6.03	CH
149.0	6.59	CH
198.4	-	C_q

NOW, LET THE GAME BEGIN!

- What can you conclude from the HSQC table and the HDI? Any fragment to recognize?
- Choose a unique shift to start with
- Start from the end of the C-chain
- CH₃ group is usually the best to start with
- Here, for example, Me group at 0.83/27.7 ppm has a unique proton shift

HMBC

$\delta^{1}\text{H}$ (ppm) →	0.83	0.91	1.20	1.44	1.54	2.02	2.23	2.26	5.48	6.03	6.59
$\delta^{13}\text{C}$ (ppm) ↓											
22.7								*			
23.0			◻	◻							
26.8	•		◻	◻				*			
26.9										■	
27.7		◆	◻	◻							
31.2	•	◆				x		*			
32.5	•	◆	◻	◻		x		*			✓
54.26	•	◆	◻	◻	◆					■	✓
122.6				◆		x		*			
131.9				◆		x		*			✓
132.3						◻					
149.0						◻		*			
198.4						◻				■	✓

COSY

δ ^1H (ppm)	0.83	0.91	1.20	1.44	1.54	2.02	2.23	2.26	5.48	6.03	6.59
0.83											
0.91											
1.20				◆		●					
1.44			★			●					
1.54					●				■		
2.02			★	◆	○				■		
2.23											
2.26									✓	✗	
5.48					○	●					
6.03								X		✗	
6.59								X		✓	