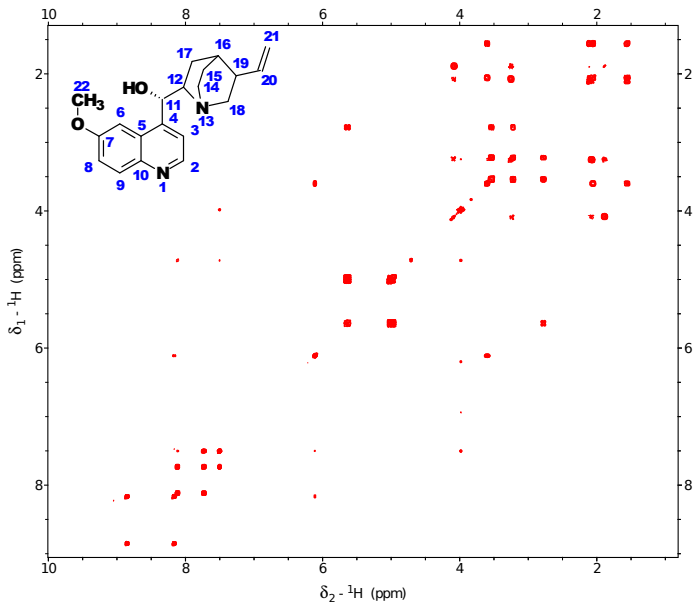


C8953  
NMR strukturní analýza  
seminář  
COSY & NOESY

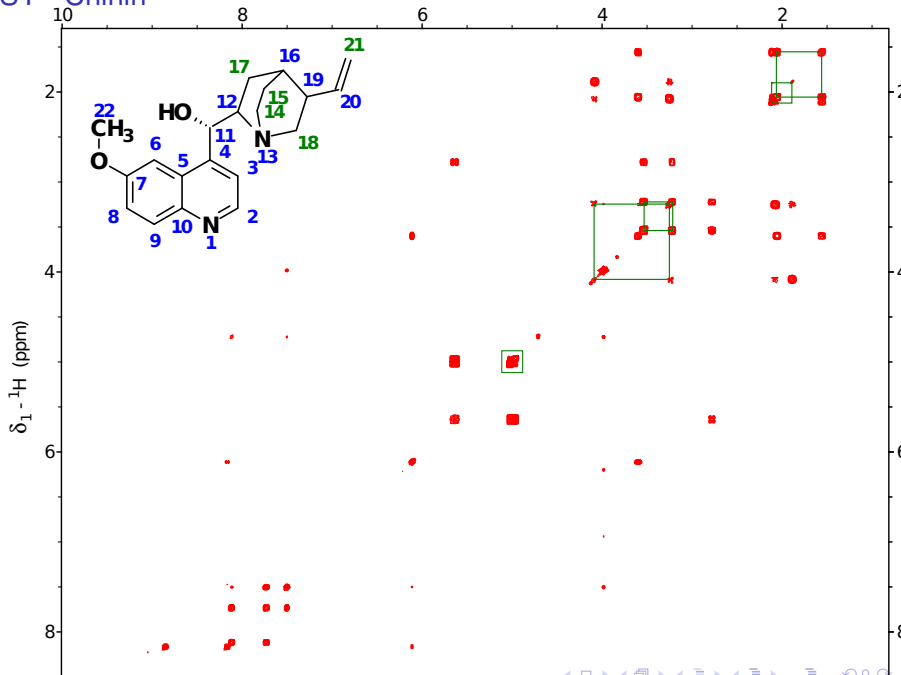
Jan Novotný, Kateřina Peterková  
176003@is.muni.cz

March 27, 2019

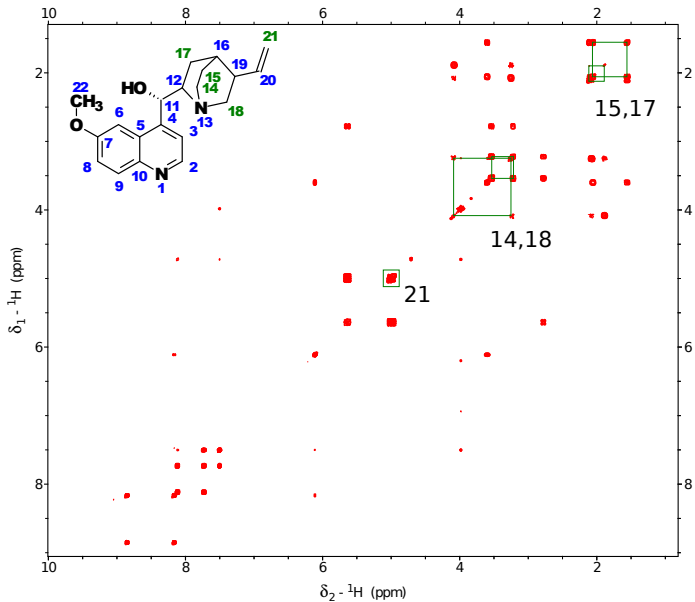
# COSY - Chinin



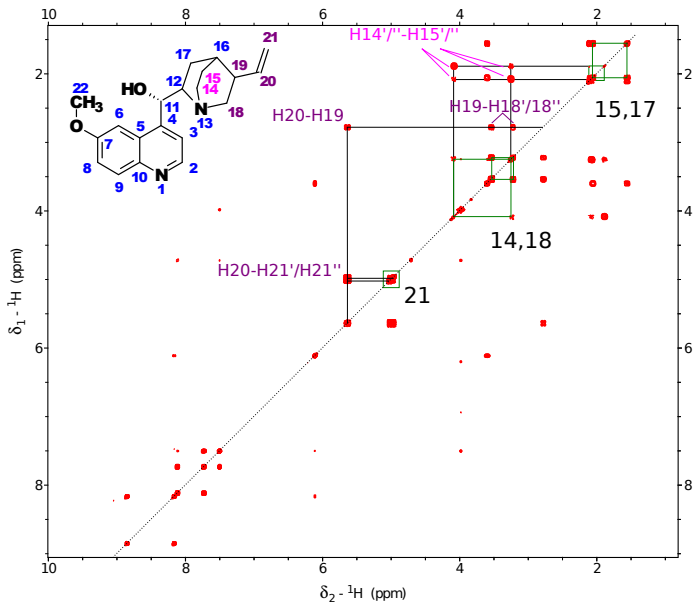
# COSY - Chinin



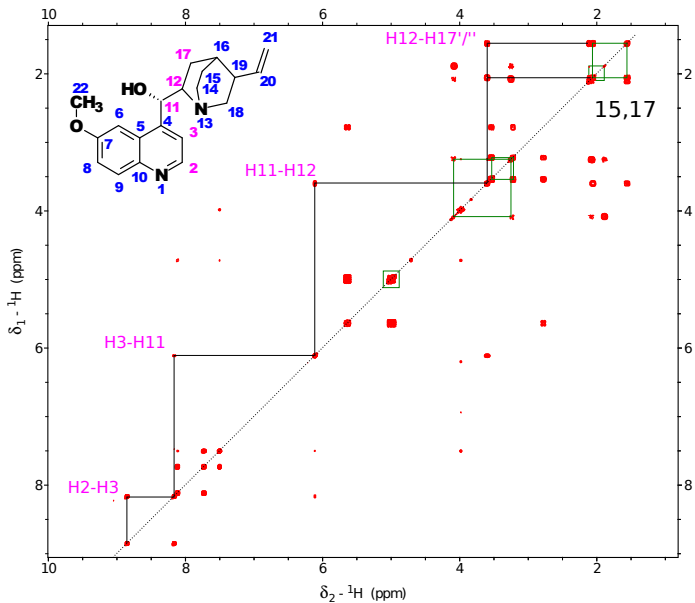
# COSY - Chinin



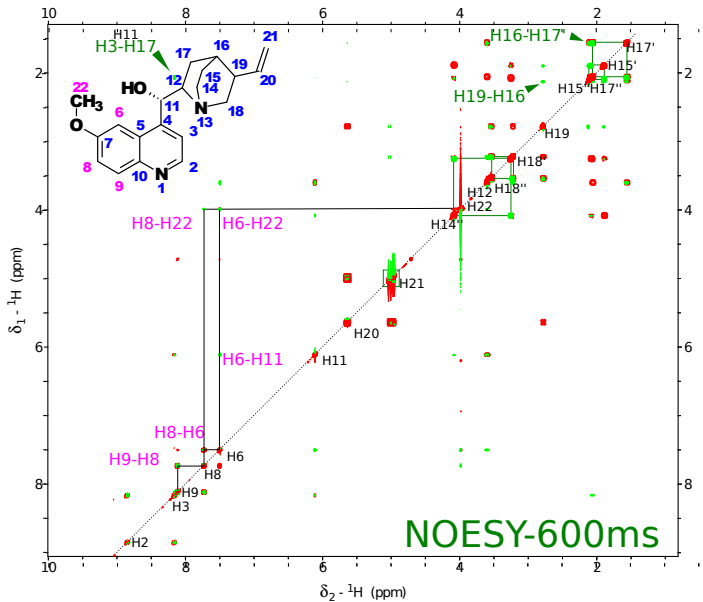
# COSY - Chinin



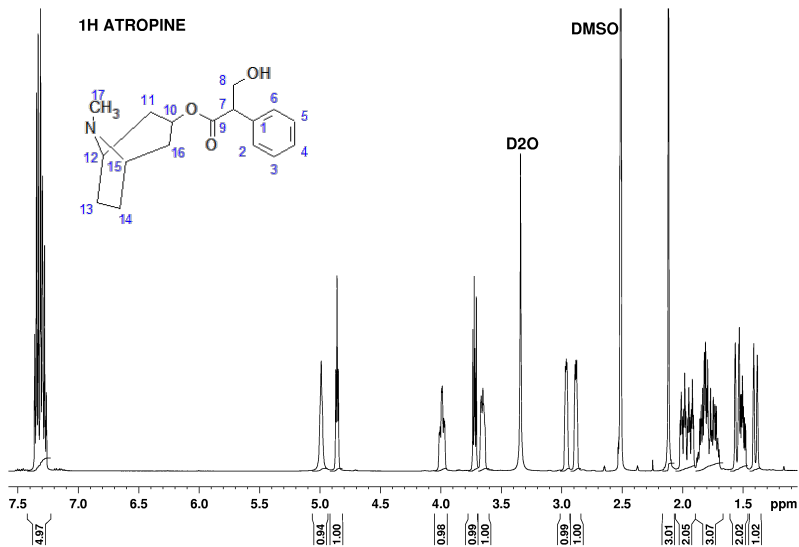
# COSY - Chinin



# COSY - Chinin

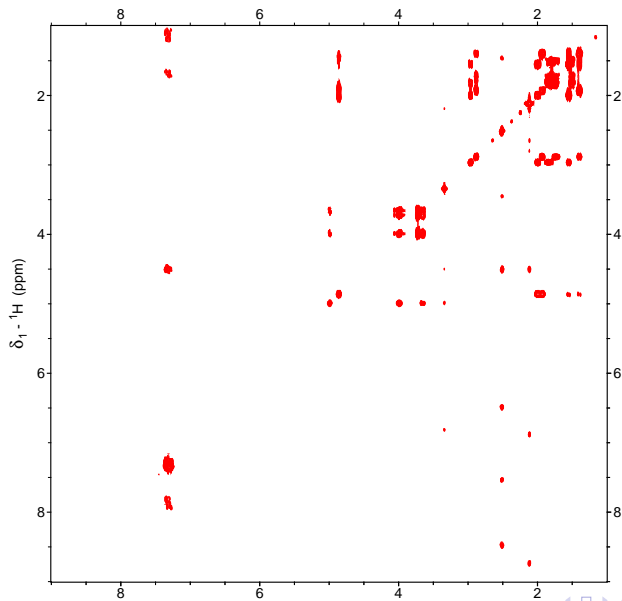
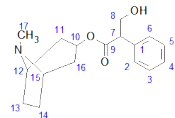


# COSY : Atropine

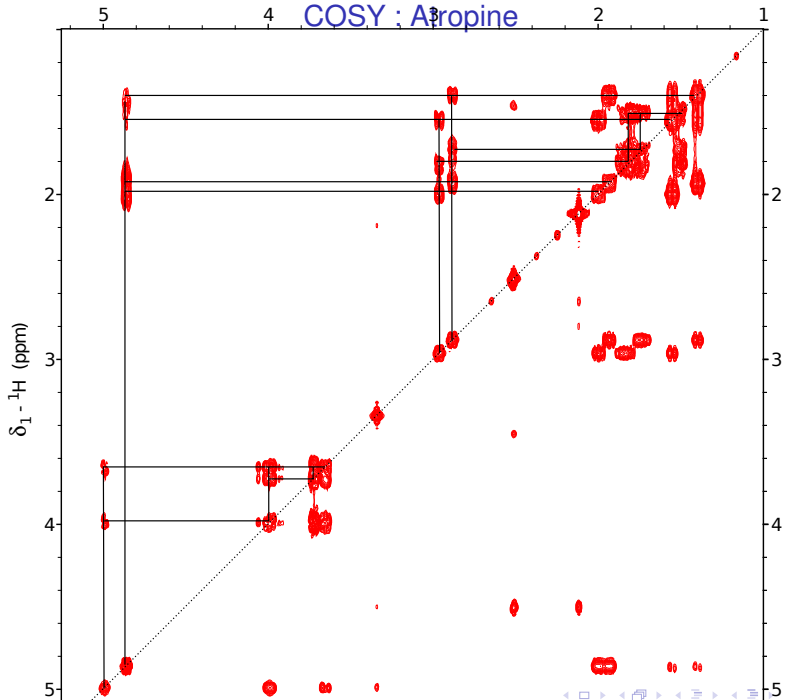


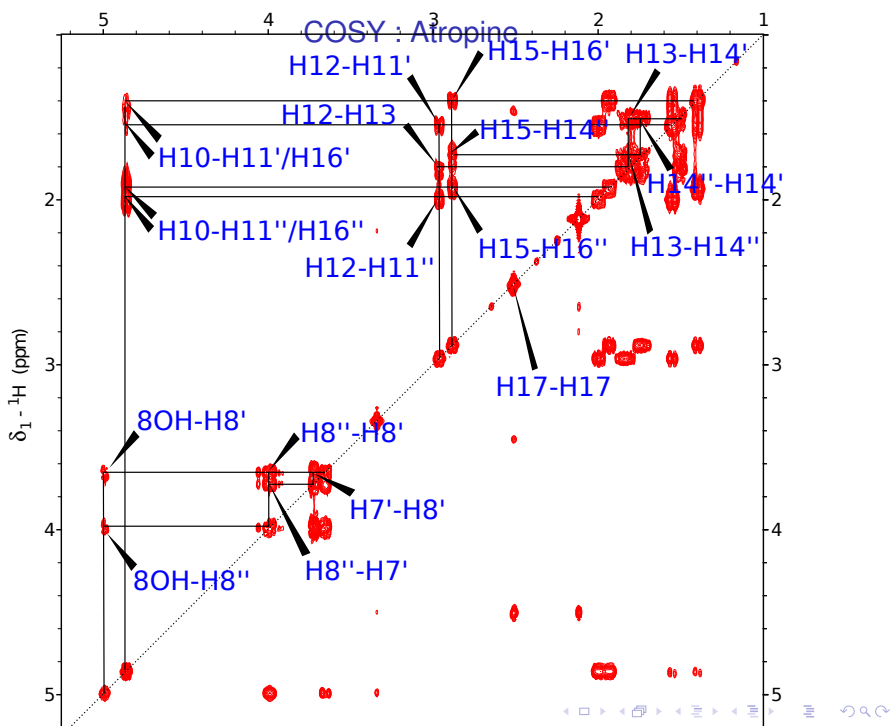


# COSY : Atropine



# COSY : Aropine





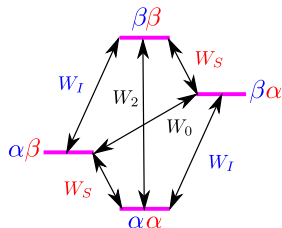
# NOESY - introduction

## Nuclear Overhauser effect

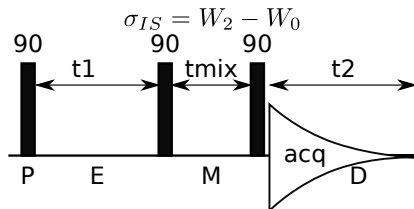
- ▶ dipol-dipol interaction
- ▶ magnetisation transfer THROUGH SPACE as a consequence of cross-relaxation

## NOESY

- ▶ correlates nuclei if their distance is **smaller than 5 Å**



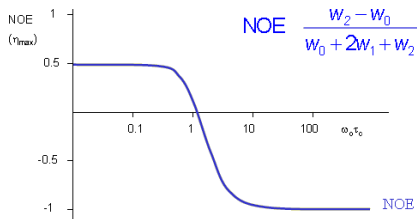
$$\frac{d\Delta I_z}{dt} = -\rho_I(I_z - I_z^0) - \sigma_{IS}(S_z - S_z^0)$$



# NOE vs. size of a molecule

## Correlation time $\tau_C$

- ▶  $\omega_0 \tau_C < 1 \Leftrightarrow \omega_0 \frac{1}{f} < 1 \Leftrightarrow \omega_0 < f$  (small molecules  $\ll 1$  kDa)
  - ▶ **fast molecular motion**,  $\beta\beta \rightarrow \alpha\alpha$  dominates  $\Rightarrow W_2 > W_0$
  - ▶ positive NOE
  - ▶ crosspeaks have opposite phase relative to diagonal
- ▶  $\omega_0 \tau_C > 1$  (large molecules  $\gg 1$  kDa)
  - ▶ **slow molecular motion**,  $\alpha\beta \rightarrow \beta\alpha$  dominates  $\Rightarrow W_0 > W_2$
  - ▶ negative NOE
  - ▶ crosspeaks have the same phase
- ▶  $\omega_0 \tau_C \approx 1$  (cca 1 kDa)
  - ▶  $\text{NOE} \approx 0$  - no crosspeaks
  - ▶ ROESY



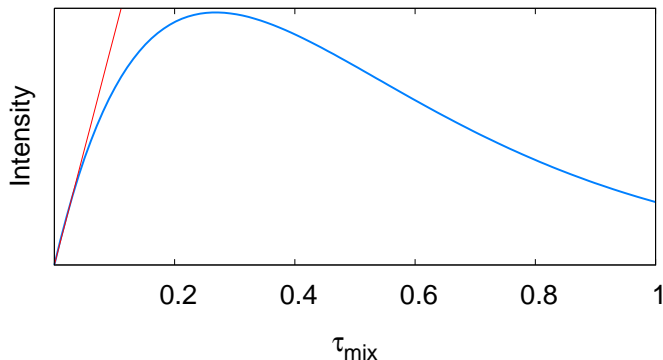
# Application of NOESY

## Mixing time $\tau_{\text{mix}}$

- ▶ small molecules  $\tau_{\text{mix}} \approx 500 - 800$  ms
- ▶ biomolecules  $\tau_{\text{mix}} \approx 50 - 300$  ms

## approximative determination of interatomic distances ( $< 5 \text{ \AA}$ )

- ▶ at short  $\tau_{\text{mix}}$
- ▶  $r_{ij} \approx A \times I_{ij}$

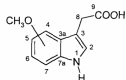


# NOE differential experiment

## PROBLEM 4

### NOE- Difference Spectroscopy

Figure 4.1 shows the  $^1\text{H}$  NMR and a  $^1\text{H}$  NOE difference spectrum of a 3-indolylacetic acid derivative **13** bearing a methoxy group at the benzenic ring.



What is the position of the methoxy group?

(400 MHz  $^1\text{H}$ )

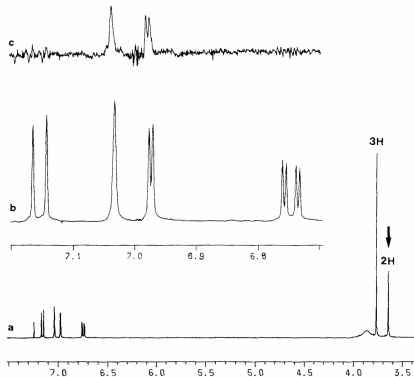


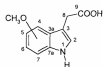
Fig. 4.1. 400 MHz  $^1\text{H}$  NMR spectrum of **13** in a mixture of  $\text{CDCl}_3$  and  $\text{CD}_3\text{OD}$ . a Full spectrum; b expanded section of the aromatic proton signals; c  $^1\text{H}$  NOE difference spectrum, same section as in b, irradiation position at  $\delta = 3.64$ .

# NOE differential experiment

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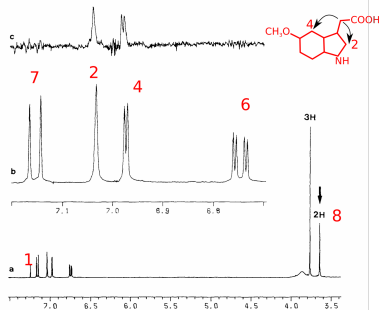
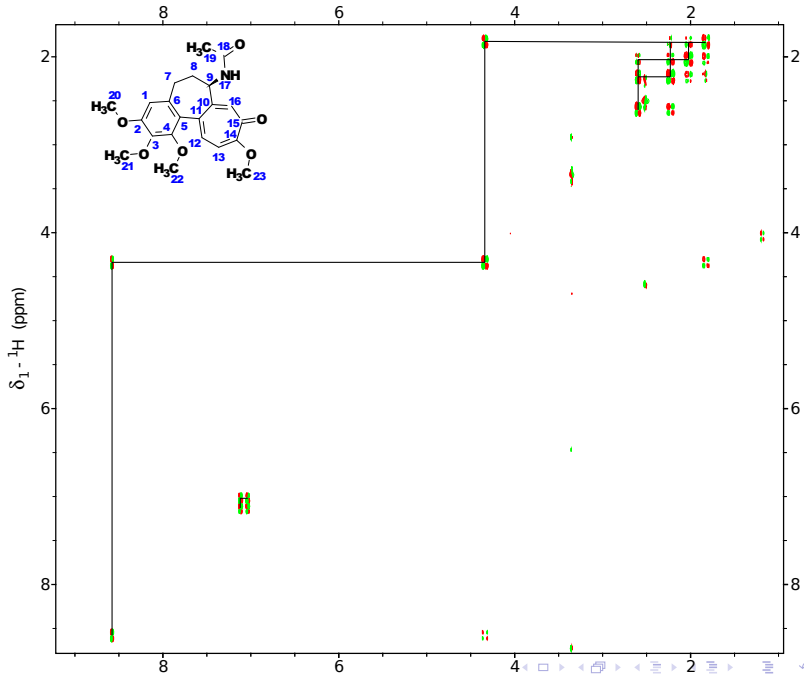


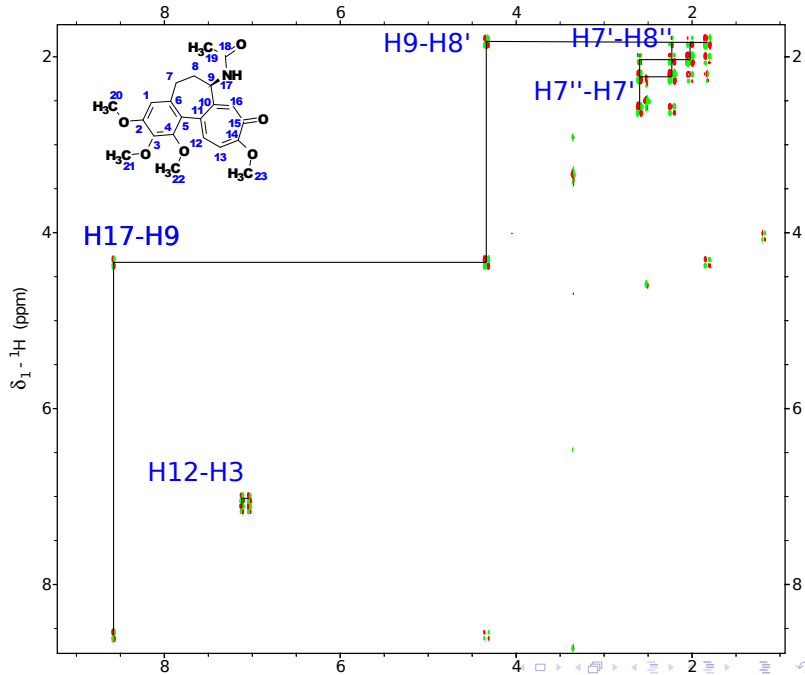
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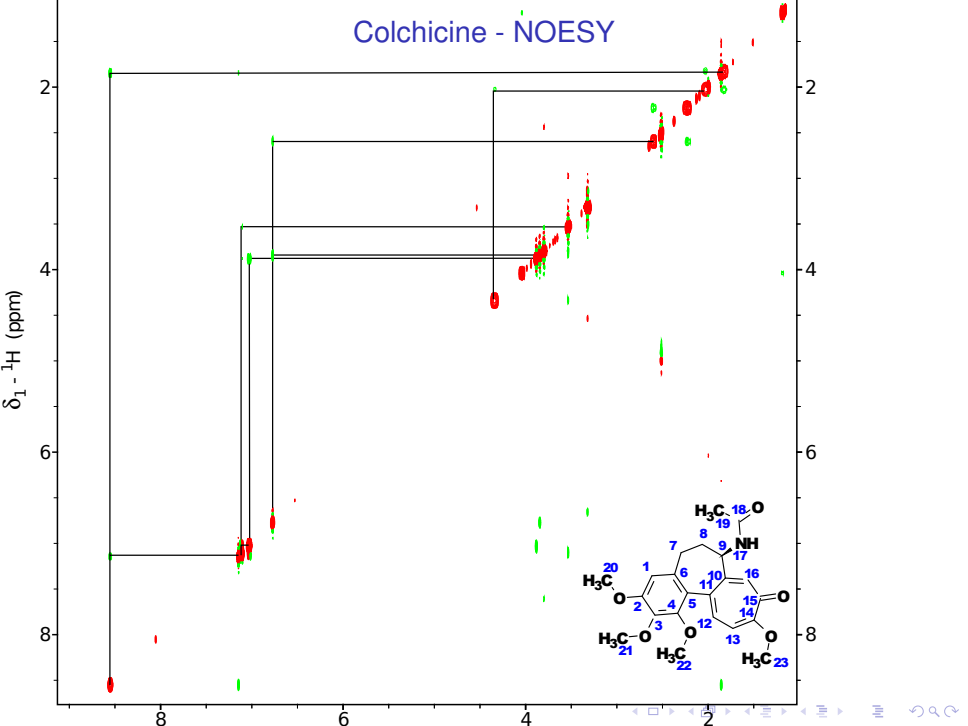
## Colchicine - DQF-COSY



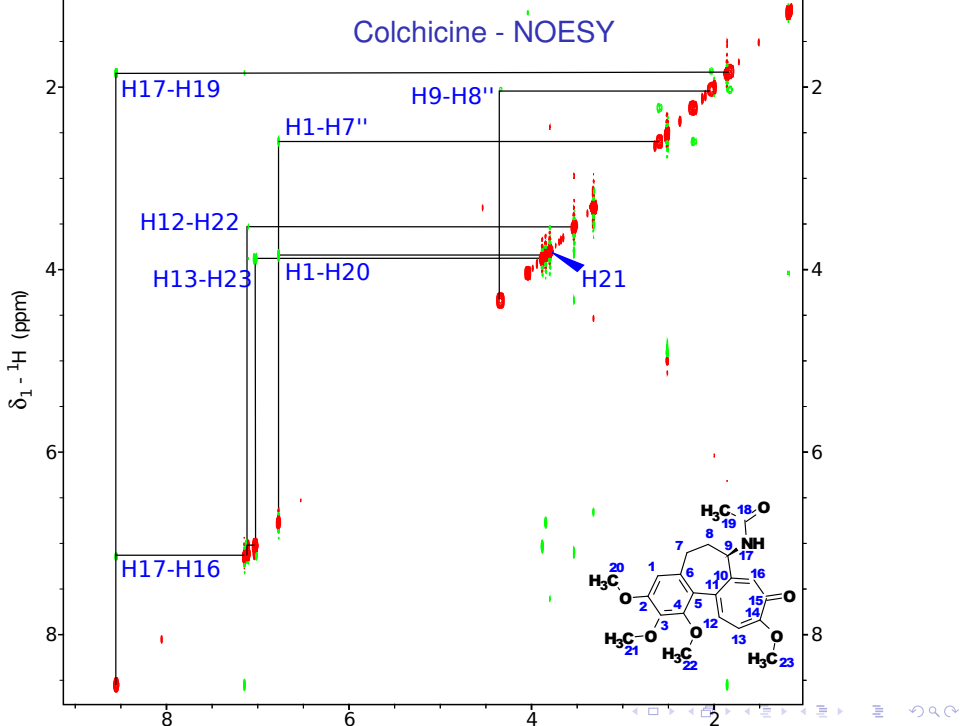
## Colchicine - DQF-COSY



## Colchicine - NOESY



## Colchicine - NOESY



Next session:

MIDTERM TEST, H-H CORRELATIONS USING SPIN LOCK