

C8953
NMR strukturní analýza
seminář
NOESY

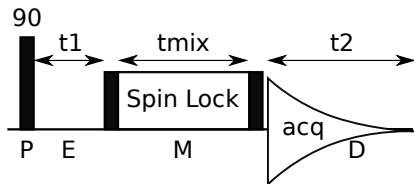
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April 7, 2021

TOCSY (Total Correlation SpectroscopY)

spin lock - isotropic mixing

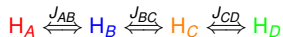
- ▶ series of short 180° pulses
- ▶ "lock-in" of spins in transversal plane
- ▶ higher power in case of TOCSY, offset set into the middle (on resonance)
- ▶ smaller power in case of ROESY, offset set into the edge (off resonance)
- ▶ crosstalk (ROE transfer in TOCSY, J -coupling in ROESY)



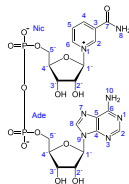
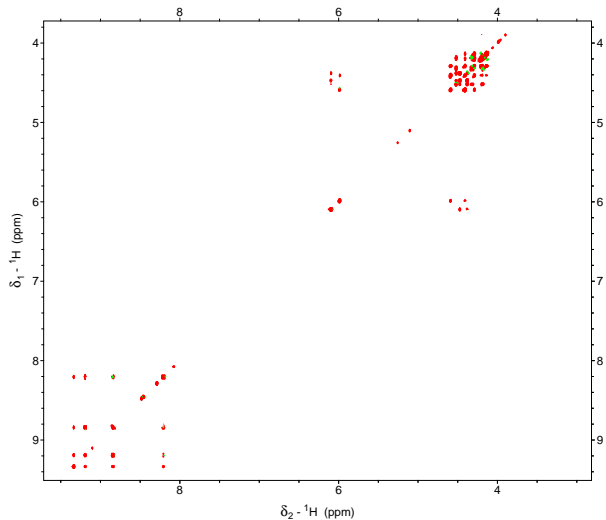
TOCSY (Total Correlation Spectroscopy)

correlation based on J

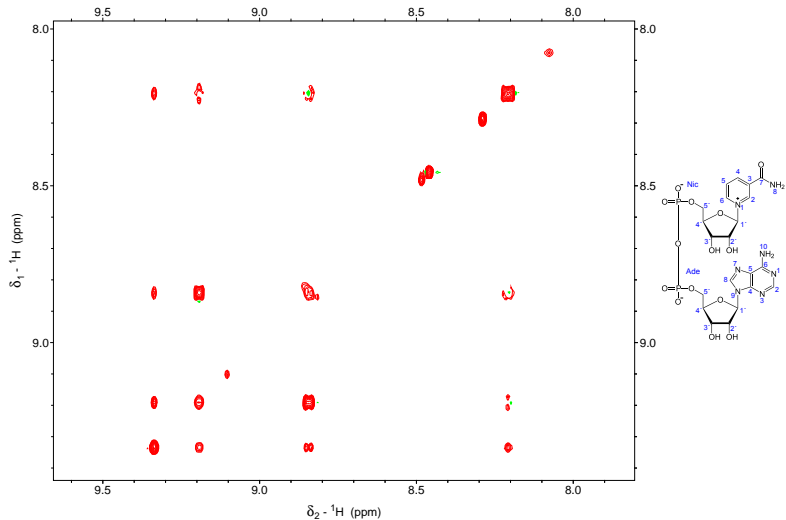
- ▶ mutual correlation of all protons in one spin system
- ▶ $\tau_{mix} \approx 20 - 120\text{ms}$
- ▶ crosspeak intensity depends on τ_{mix} a J value



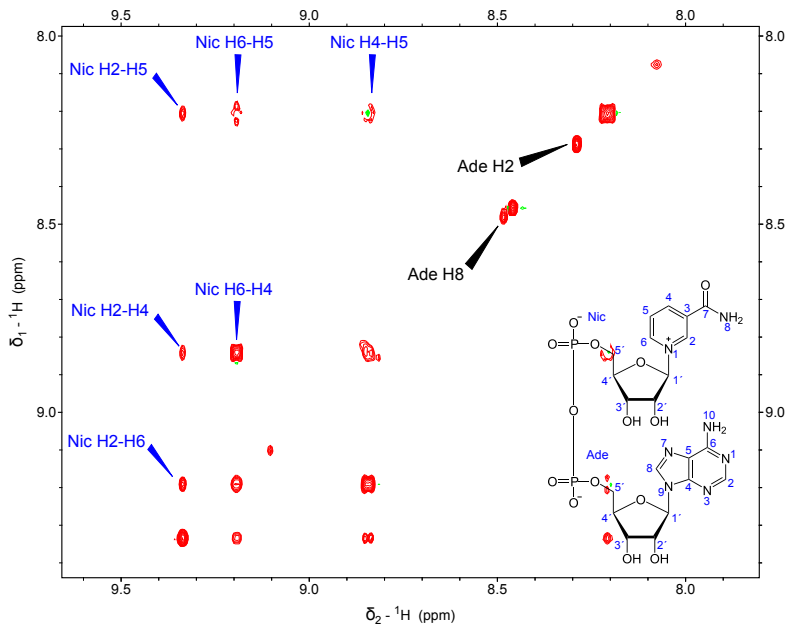
NAD⁺: TOCSY (40ms)



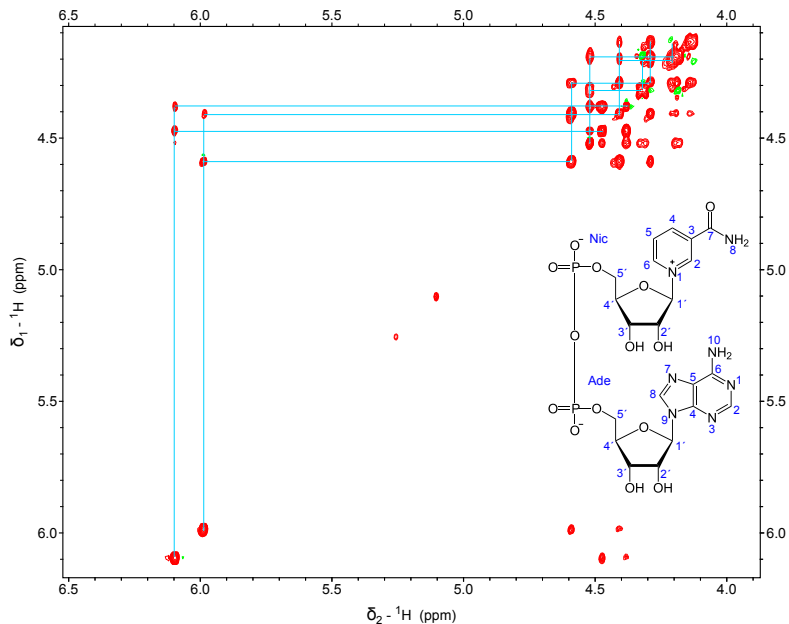
NAD⁺: TOCSY (40ms), detail of aromatics



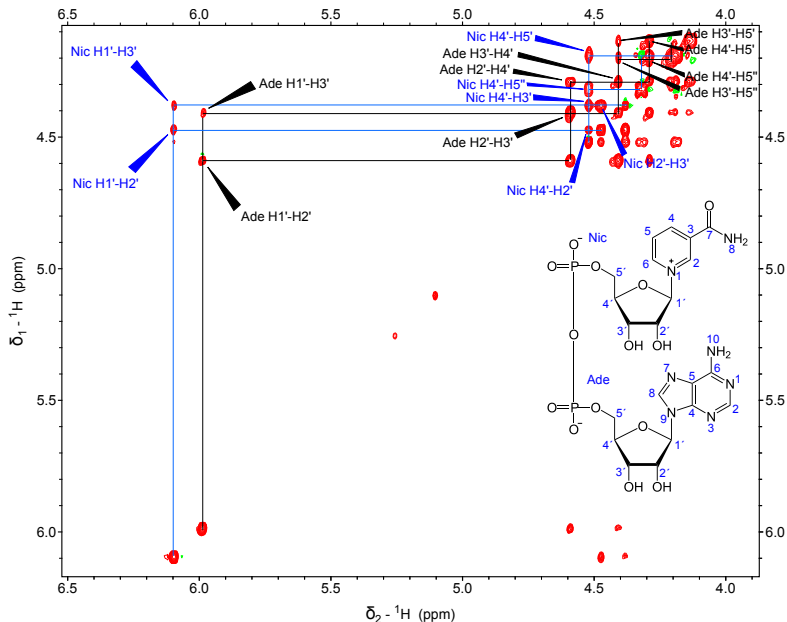
NAD⁺: TOCSY (40ms), detail of aromatics



NAD⁺: TOCSY (40ms), detail of aliphatics



NAD⁺: TOCSY (40ms), detail of aliphatics



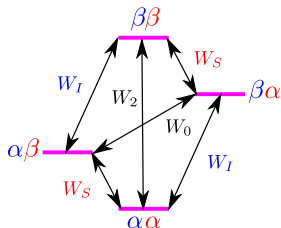
NOESY - introduction

Nuclear Overhauser effect

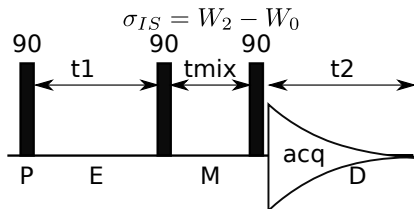
- ▶ dipol-dipol interaction
- ▶ magnetisation transfer THROUGH SPACE as a consequence of cross-relaxation

NOESY

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



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



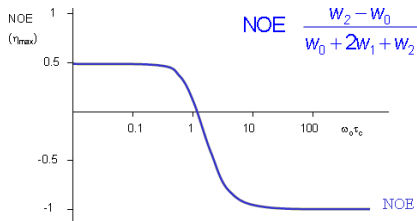
NOE vs. size of a molecule

NOE enhancement

$\frac{M_I^S - M_{0I}}{M_{0I}} \approx \frac{\sigma_{IS}}{\rho_I} = \frac{W_2 - W_0}{W_0 + 2W_1 + W_2}$, where M_I^S is magnetisation of I perturbed by saturation of S

Correlation time τ_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)
 - ▶ NOE ≈ 0 - no crosspeaks
 - ▶ ROESY is an alternative



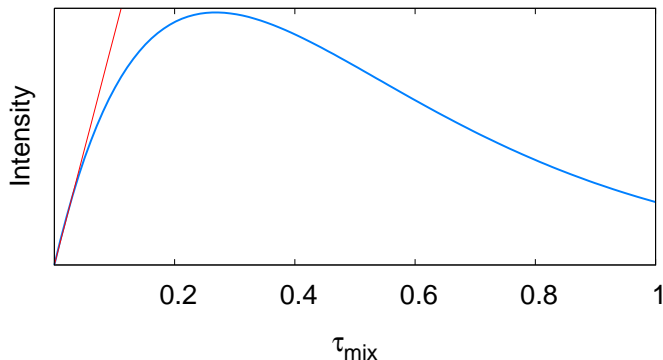
Application of NOESY

Mixing time τ_{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 τ_{mix}
- ▶ $r_{ij} \approx A \times I_{ij}$

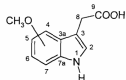


NOE differential experiment

PROBLEM 4

NOE- Difference Spectroscopy

Figure 4.1 shows the ^1H NMR and a ^1H 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 ^1H)

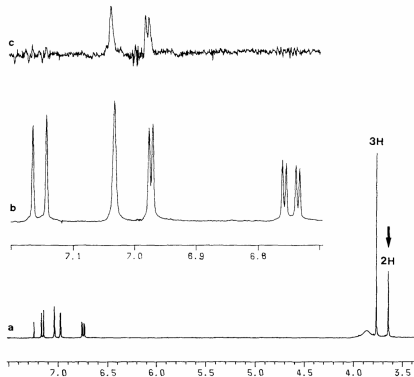


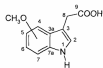
Fig. 4.1. 400 MHz ^1H NMR spectrum of **13** in a mixture of CDCl_3 and CD_3OD . a Full spectrum; b expanded section of the aromatic proton signals; c ^1H NOE difference spectrum, same section as in b, irradiation position at $\delta = 3.64$.

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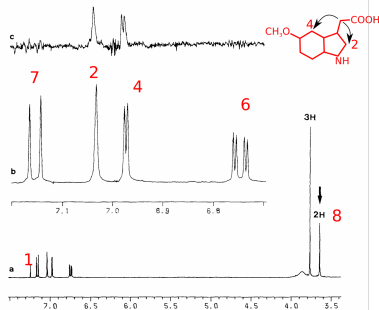
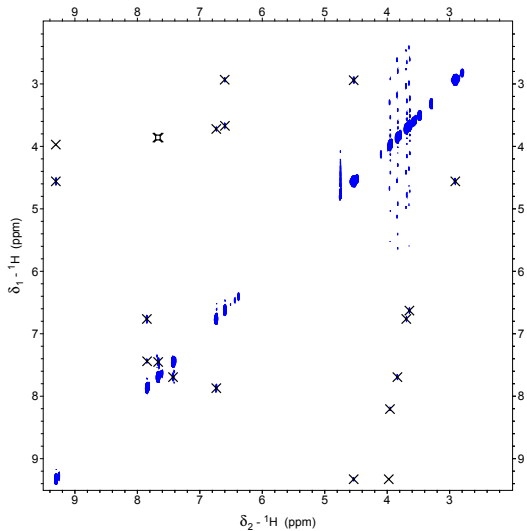
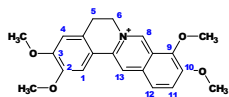
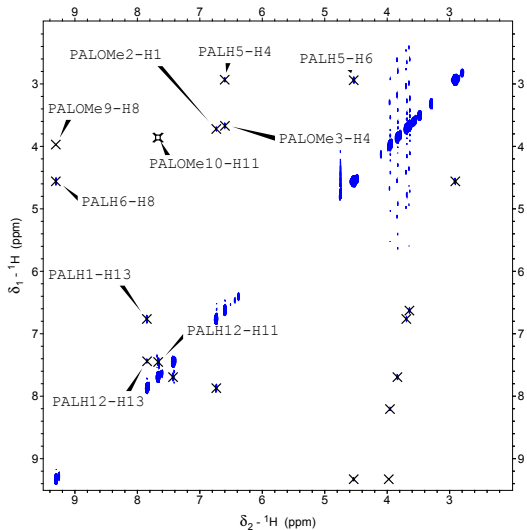
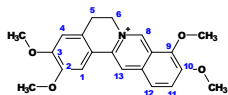


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NOESY - Palmatine

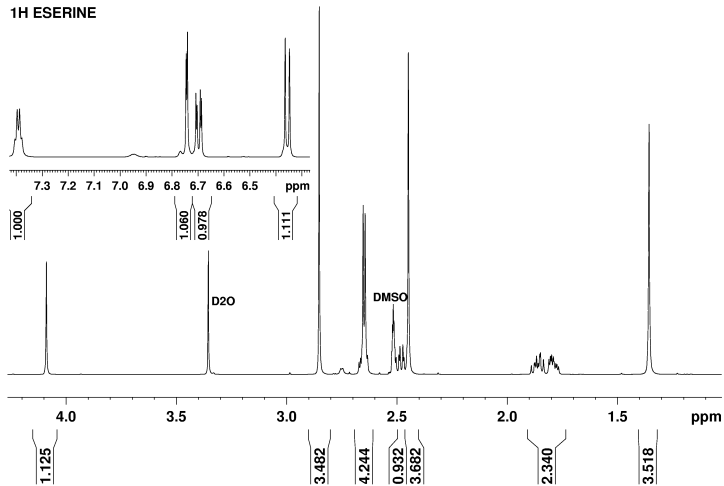


NOESY - Palmatine

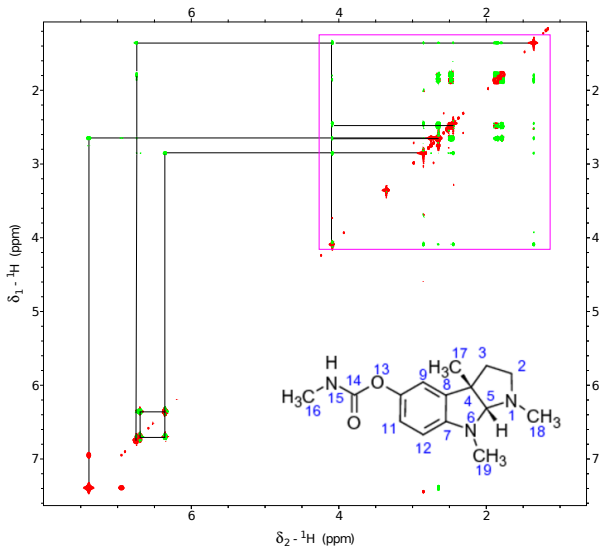


Eserine ^1H

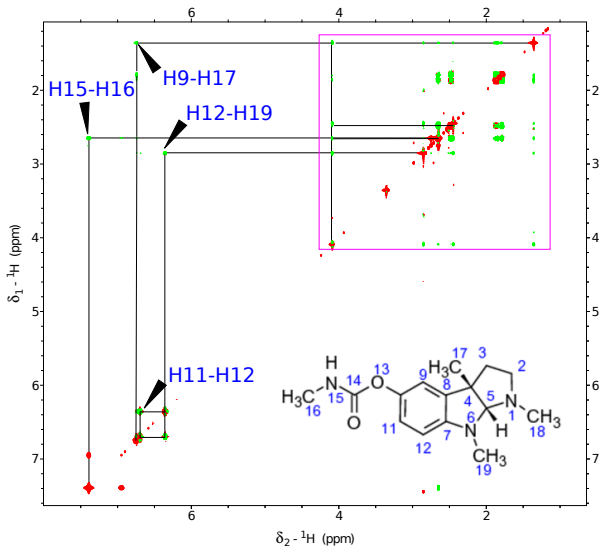
^1H ESERINE



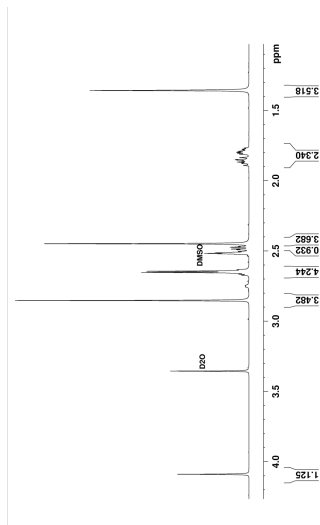
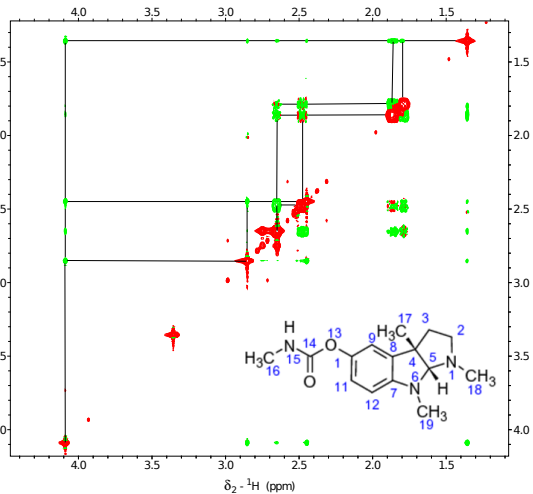
NOESY - Eserine in DMSO



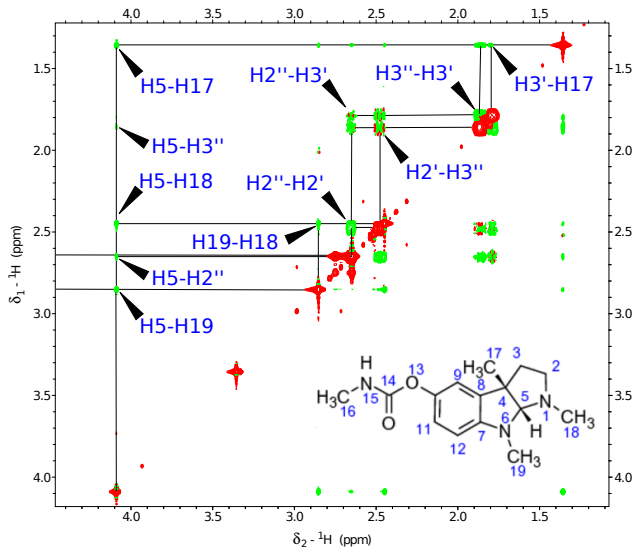
NOESY - Eserine in DMSO



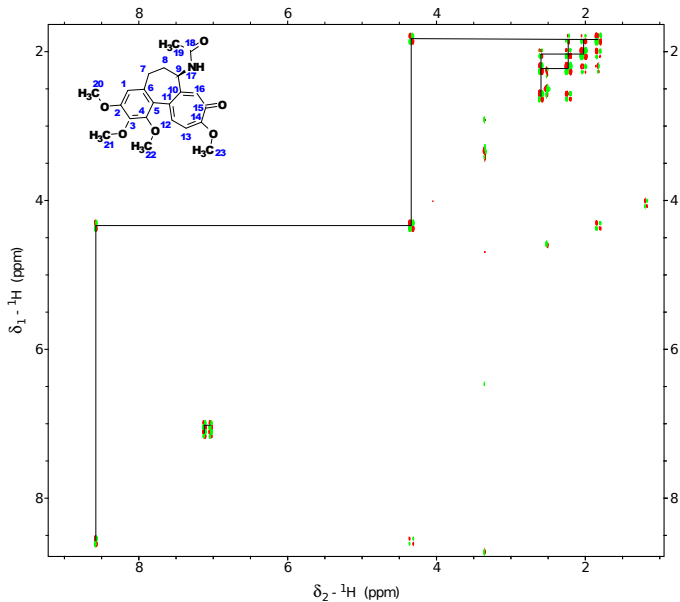
NOESY - Eserine



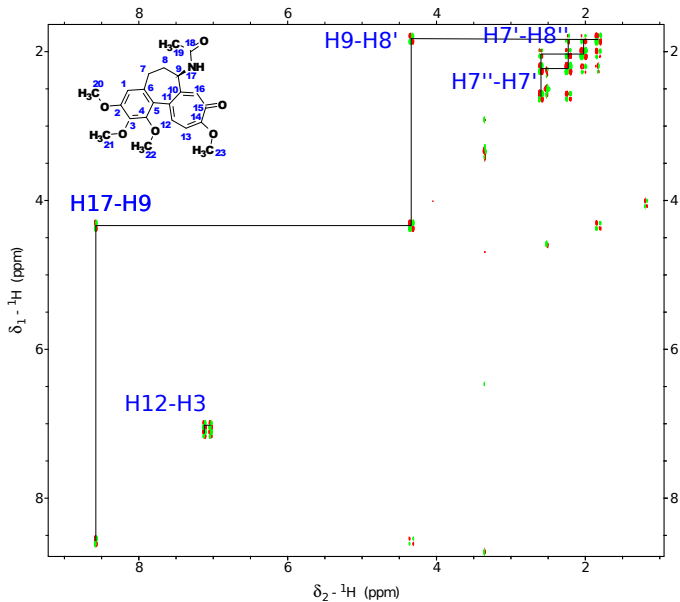
NOESY - Eserine



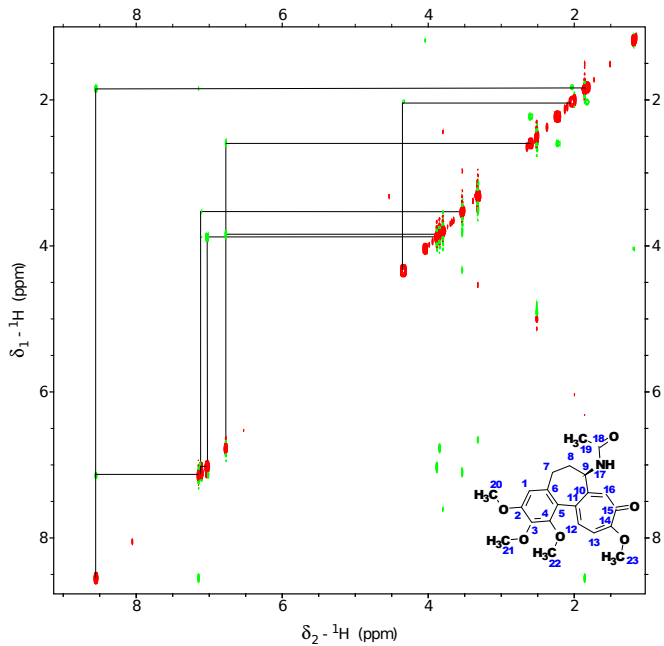
Colchicine - DQF-COSY



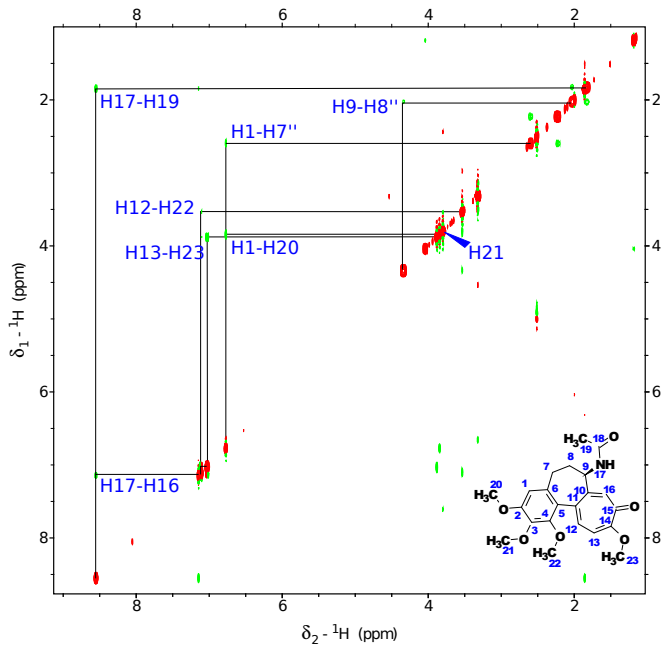
Colchicine - DQF-COSY



Colchicine - NOESY



Colchicine - NOESY



Next session:

Heteronuclear correlations