Department of Organic Chemistry

# To self-assemble or not to self-assemble: that is the question

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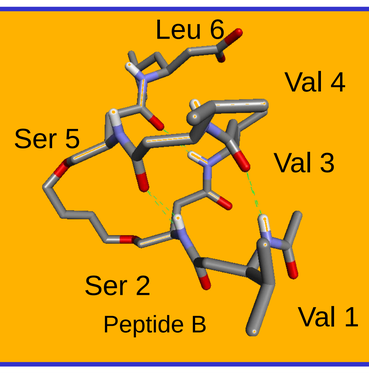
## Introduction

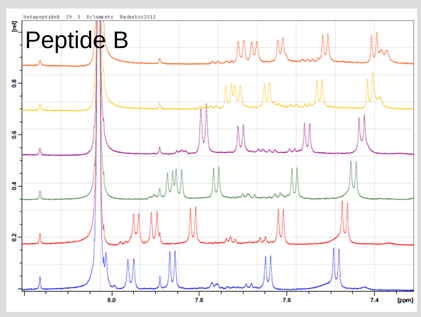
Molecular self-assembly is a process where molecules from a disordered state adopt a specific arrangement without any exterior influences. This concept was found in nature and can be used to develop new strategies in pharmaceutical applications. In this project the potential self-assembly of β³-peptides synthesized by Perlmutter et al was studied through NMR-spectroscopy. NMR-spectroscopy can provide knowledge about the nanotube structure, the self-assembly proces in solution and the β³ –amino acids present in the peptide. The spectra were obtained with a high field 700 MHz NMR Spectrometer.



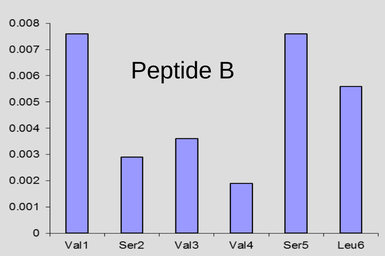

## 1. Temperature Study

To be able to make a decent analysis of the β³-peptide, the optimal temperature was to be found. In other words, the temperature where the peaks in NH region don't coincide.

If there are overlapping peaks, one can anticipate that by varying the temperature, different changes in chemical shifts will be observed for the inner (H-bond) and outer (solvent interactions) NH's, thus separating the peaks.

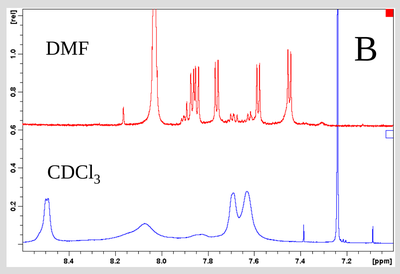


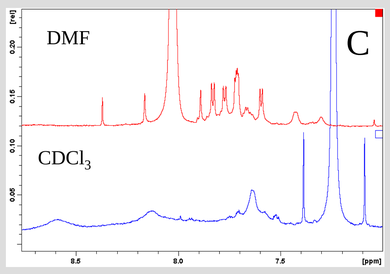

The figure on the right shows the temperature coefficients of the different amino acids that make up the peptide. The lower coefficients belong to amino acids which form intramolecular H-bonds, the higher coefficients correspond to amino acids that form intermolecular H-bonds.

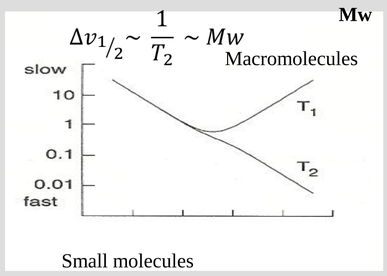



## 2. Effect of molecular weight on resonance broadening

Narrow resonances were detected in the DMF solvent, while in chloroform, broad resonances are visible. The line widths are inversely proportional to the $T_2$ relaxation time, and at the same time proportional to the molecular weights. This indicates that in chloroform, where the lines are much broader, high molecular weight entities are present.

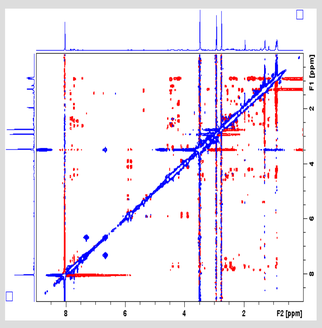


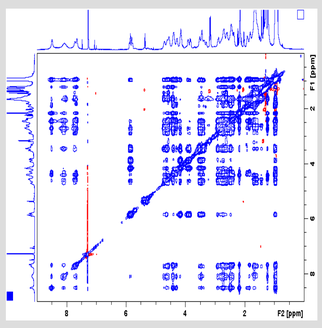




## 3. Effect of molecular weight on Nuclear Overhauser Effect (NOE)

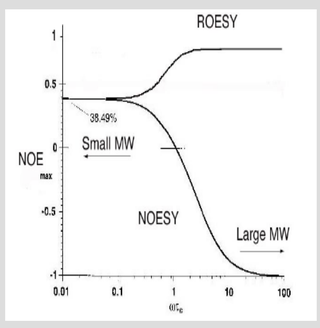
Weak positive peaks were detected in the NOESY spectra of peptide C in DMF, which are characteristic for small molecules tumbling fast in solution. On the other hand, in chloroform, intense negative peaks are seen which indicate larger molecular assemblies.



Peptide C in DMF



Peptide C in $CDCl_3$



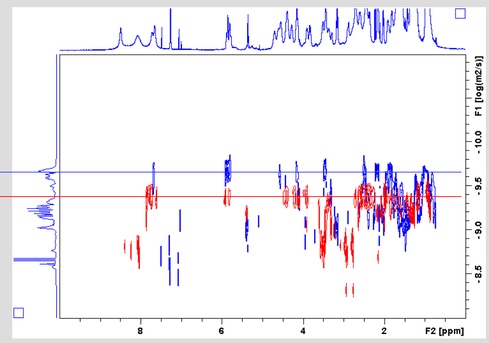

## 4. Translational diffusion on Diffusion Ordered Spectroscopy (DOSY )

Diffusion in chloroform occurs slower than in DMF. The diffusion constant depends on the size and shape of the molecule, temperature and viscosity of the solvent. According to the Stokes-Einstein equation, the larger the molecule, the smaller the diffusion constant. The smaller diffusion constant in chloroform indicates the presence of larger molecules.

$$D = \frac{k_b T}{c \pi \eta r_h}$$

Stokes-Einstein equation[1]

D = 2,1 x $10^{-10}$ $m^2s^{-1}$
Peptide C in $CDCl_3$
Peptide C in DMF
D = 4,2 x $10^{-10}$ $m^2s^{-1}$



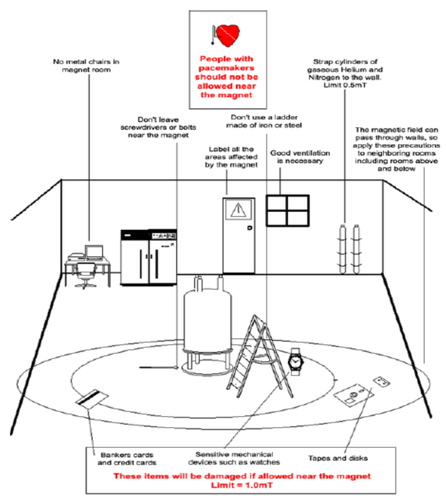

## 5. Conclusion

In our experiments, four effects were observed that could indicate the occurance of self-assembly in betapeptides in a non-hydrogen-bond-forming solvent (chloroform) compared to DMF: line broadening, negative NOE peaks, spin diffusion correlation and lower diffusion coefficients.

## 6. Safety issues[2]

The magnet is potentially dangerous due to its large attractive force on ferromagnetic objects. All metal objects near the magnet should be replaced by non-ferromagnetic objects or should be firmly attached. Pacemakers and mechanical watches as well as data-storage materials can be damaged by the magnetic field. The strength of the magnetic field increases with proximity, the 10 Gauss line is marked, so caution is advised upon crossing it.

The cryogenic fluids present danger as well. When the magnet experiences a sudden temperature rise, the cryogenic fluids will evaporate leading to a rapid pressure buildup and possible explosion.
When the magnet releases some of its evaporated cryogenic fluids it can lead to a sudden drop in oxygen level. Therefore the room should be well ventilated and the oxygen level must be monitored.




## 7. Key references

[1]A. Einstein, *Uber die von der Molekularkinetischen Theorie der Wärme Geforderten Bewegung von in Ruhenden Flüssigkeiten Suspendierten Teilchen* **1905**.
[2]S. J. Niles, *Site Planning for AVANCE Systems 300 - 700 MHz User Guide* **2008**.