Experimental Report

07/07/2014

Proposal: **INTER-275** **Council:** 10/2012

Title: Internal time on D4

This proposal is a new proposal
Researh Area:

Main proposer: **TAVAGNACCO Letizia**

Experimental Team: TAVAGNACCO Letizia
MASON Philip

Local Contact: FISCHER Henry

Samples: 1,3,7-trimethylxanthine (caffeine) dissolved in D_2O
H_2O

Instrument	Req. Days	All. Days	From	To
D4	3	3	22/07/2013	25/07/2013

Abstract:

Experiment N°: INTER-275 **Instrument:** D4 **From :** 22/07/2013 **To :** 25/07/2013

Experimental team:
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Philip Mason, Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic

Local contact:
Henry Fischer

Caffeine aggregation in aqueous solution

Neutron diffraction with isotopic substitution experiments were performed to investigate the structure of caffeine solution with some model compounds. In particular the pyridine molecule and the tetrahydrofuran molecule were chosen. Their structures are displayed in Figure 1. Pyridine is an aromatic heterocycle that, unlike benzene, is soluble in water in all proportions. It has only one hydrogen bonding acceptor group. Tetrahydrofuran is a cyclic ether, very soluble in water which has one hydrogen bonding acceptor group. While the molecular structure of caffeine has some common features with pyrimidine bases, pyridine can resemble a purine base and tetrahydrofuran can be thought as a very simple model of a furanoside ring. Given the complexity of the interpretation of the structure factors produced by an NDIS experiment, the symmetric structure of these molecules, as well as the availability of isotopically substituted compounds, make them simple models suitable to be studied with these experiments.

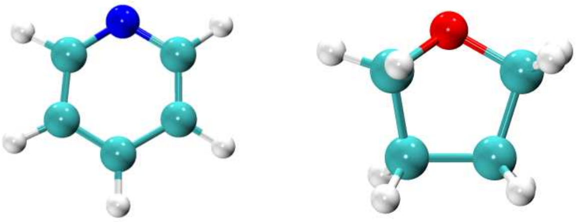

Figure 1 On the left, molecular structures of pyridine; on the right, molecular structure of tetrahydrofuran.

NDIS experiments were carried out on a caffeine pyridine solution with a caffeine concentration of 0.5 m and a pyridine concentration of 3 m and on a caffeine tetrahydrofuran solution with a caffeine concentration 0.5 m and a tetrahydrofuran concentration 3.3 m. The isotopic substitution was applied to the pyridine hydrogen atoms or to the tetrahydrofuran hydrogen atoms. Experiments were performed in heavy water at room temperature. Caffeine, natural abundance pyridine, deuterated pyridine-d_5 (>99% enrichment), natural abundance tetrahydrofuran and deuterated tetrahydrofuran-d_8 (>99% enrichment) were obtained from Sigma Aldrich.

To investigate caffeine-pyridine aqueous solutions four samples were prepared:

- 3 m natural abundance pyridine solution in D_2O;
- 3 m deuterated pyridine-d_5 solution in D_2O;
- 3 m natural abundance pyridine, 0.5 m caffeine solution in D_2O;
- 3m deuterated pyridine-d_5, 0.5 m caffeine solution in D_2O.

Similarly the caffeine-tetrahydrofuran system was characterized through the study of four samples:

- 3.3 m natural abundance tetrahydrofuran solution in D_2O;

- 3.3 m deuterated tetrahydrofuran-d_8 solution in D_2O;
- 3.3 m natural abundance tetrahydrofuran, 0.5 m caffeine solution in D_2O;
- 3.3 m deuterated tetrahydrofuran-$d_{5,}$ 0.5 m caffeine solution in D_2O.

Pyridine and tetrahydrofuran were previously dried using molecular sieves. The experiments were performed at 23°C. Samples were prepared by accurately weighting the components. Measurements were performed using cylindrical null scattering TiZr sample containers. The neutron incident beam had a wave length of 0.7 Å. Empty cell, empty belljar, a vanadium rod and detector efficiency were also measured to obtain the corrected structure factors. Diffraction data were collected for 8 hours for each sample. Raw data were corrected for multiple scattering, absorption and normalized to the vanadium using standard procedures. The second order difference method was applied.

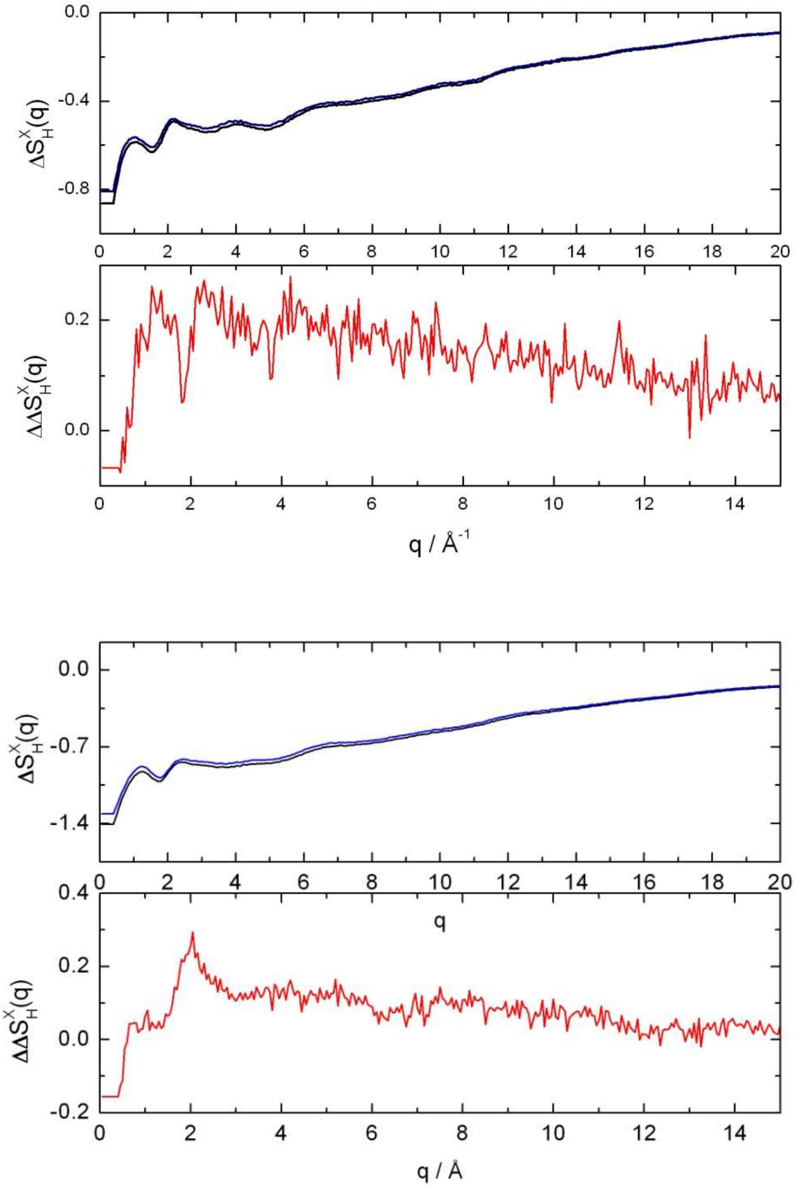

Figure 2 Above, in black first order difference $\Delta S_H^X(q)$ for 3 m pyridine; in blue first order difference $\Delta S_H^X(q)$ for 3 m pyridine and 0.5 m caffeine; in red second order difference $\Delta\Delta S_H^X(q)$. Below, in black first order difference $\Delta S_H^X(q)$ for 3.3 m tetrahydrofuran; in

blue first order difference $\Delta S_H^X(q)$ for 3.3 m tetrahydrofuran and 0.5 caffeine; in red second order difference $\Delta\Delta S_H^X(q)$.

The total structure measured in the NDIS experiments is the linear combination of the partial structure factors of all the pairs of atoms in the system:

$$F(Q) = \sum_\alpha \sum_\beta c_\alpha c_\beta b_\alpha b_\beta (S_{\alpha\beta}(Q) - 1)$$

where c_α is the atomic concentration of the species α and b_α is the coherent neutron scattering length of the species α, $S_{\alpha\beta}(Q)$ is the partial structure factor for the pair of atoms α and β and the sum is over all the pairs of atoms.

If we first consider the caffeine-pyridine aqueous solution, the system appears very complex, it is described by 45 partial structure factors.

Nonetheless the interpretation of the measured total structure factor can be simplified using the first and second order difference methods. In this approach the subtraction of the total structure factors measured for two identical samples with the exception of an atom isotopically substituted, eliminates any correlations that do not involve the labeled atom.

In this specific case, the first order difference method was first applied on the two solutions of 3 m natural and 3 m deuterated pyridine. The resulting first order difference ΔS_H^X is the summation of the 6 partial structure factors that involve the correlations of the pyridine hydrogen atoms. The first order difference method was then applied on the two solutions of 0.5 m caffeine and 3 m natural pyridine and 0.5 m caffeine and 3 m deuterated pyridine. In this second case the first order difference ΔS_H^X between the two total structure factors contains the 10 partial structure factors involving the pyridine hydrogen atoms. The difference between these two first order difference functions is the linear combination of the 4 partial structure factors that involve the correlations between the pyridine hydrogen atoms and the caffeine atoms. The results are displayed on the top of Figure 2. The second order difference function $\Delta\Delta S_H^X$ contains information on how caffeine and pyridine interact.

The same procedure was applied to the caffeine-tetrahydofuran systems. The results are shown in Figure 2. As can be seen, the second order difference function $\Delta\Delta S_H^X$ differs from the one determined for the caffeine-pyridine system, reflecting the specific solution structure.

To interpret these preliminary data, a comparison will be made to the results obtained from independent molecular dynamics simulations performed on the same systems.