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Fast-pulsing NMR techniques for the detection of weak interactions: successful natural abundance probe of hydrogen bonds in peptides

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Table 1: ^1H T_1 measurement with and without selective pulses

1/ Cyclosporin A in $CDCl_3$

	Abu (2)	**Ala (7)**	**Val (5)**	**D-Ala (8)**
T_1 hard (s)	0.86	0.78	0.98	1.18
T_1 selective (s)	0.73	0.69	0.83	1.00

2/ Octamer in pyridine-d_5

	2	**4**	**5,6**	**8**	**1**	**7,3**
T_1 hard (s)	1.82	1.36	1.52	1.63	1.75	1.58
T_1 selective (s)	1.24	0.99	0.85	0.83	0.87	0.89

Ernst angle optimization

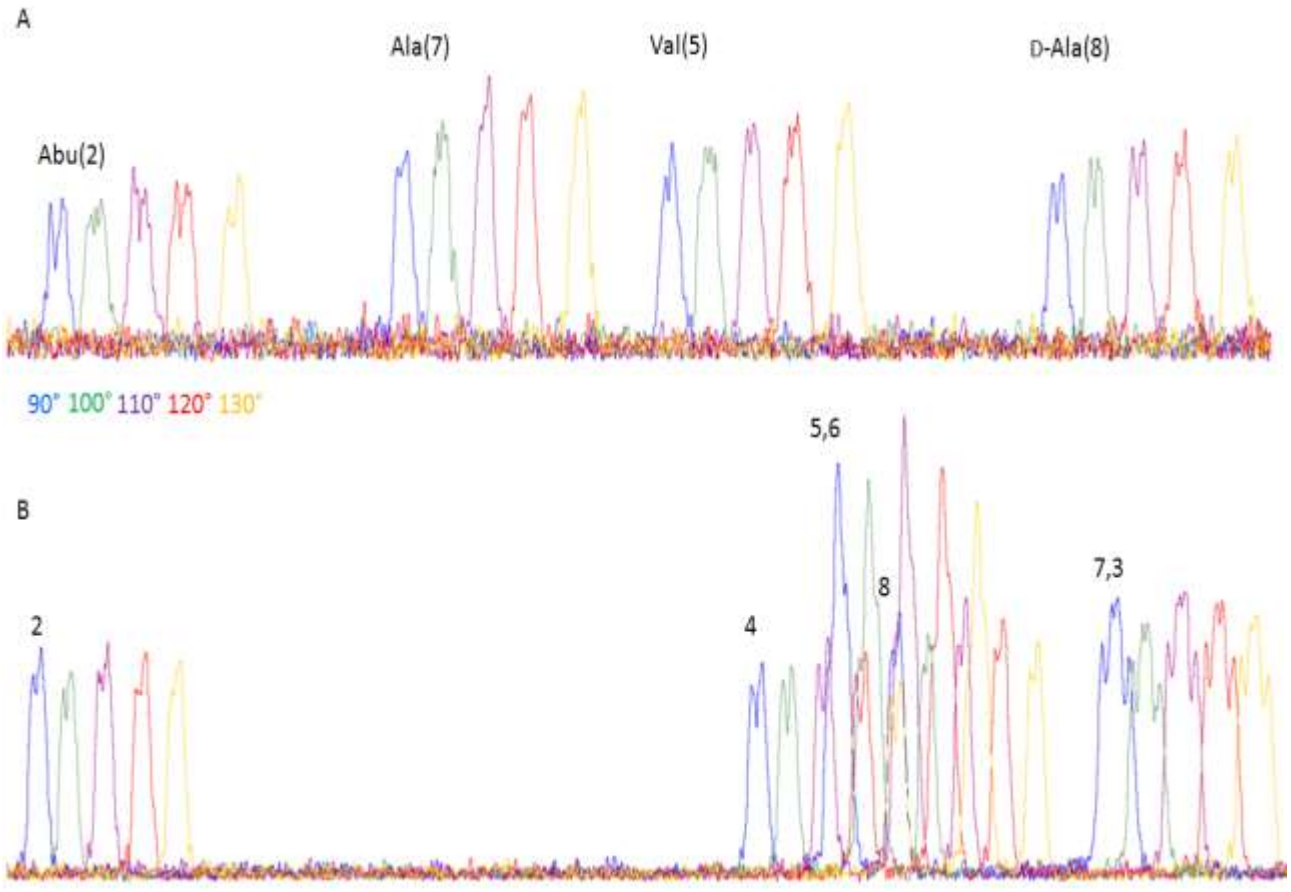

Figure SI-1 Comparison of different excitation angle (α) (90° to 130° from the left to the right) on the intensity of signals for the cyclosporin A (panel A) and the octamer (panel B) (see Figure 2). For each molecule an optimized excitation angle leading to the best sensitivity has been chosen to 110°.

Theoretical part on the calculation of the best excitation angle

Ernst *et al.* [1] have shown that the optimal flip angle can be predicted from equation 1:[1,2]

$$\cos(180 - \alpha) = \exp(-(aq + t_{rec})/T_1) \qquad \text{(eq. 1)}$$

Thus, the optimal excitation angle α^{opt} for the SOFAST HMBC can be expressed as following:

$$\alpha^{opt} = 180 - \text{Arccos}[\exp(-T_{rep}/T_1)] \qquad \text{(eq. 2)}$$

In Table 2 are compared theoretical and experimental values of the α angles for each compound. The experimentally optimized values from the most intense ^{1}H signals were collected. The error of about ± 10° for the experimental α angle (α^{exp}) comes mainly from errors on the 90° pulse calibration. Uncertainties of ± 5° on the calculated α angle (α^{th}) from equation 1 are due to errors on T_1 values (± 0.10 s) measured with the selective version of the inversion recovery. α^{exp} and α^{th} are in agreement by considering errors on their measurement and calculation, respectively.

Table 2: Comparison between experimental and theoretical α angle values

For the cyclosporin A

T_1 (H^N_2) (s)	T_{rep} (s)	α^{exp} (°)	α^{th} (°)
0.73 ± 0.10	0.43	110 ± 10 (see Fig.SI 1 A)	123 ± 5
T_1 (H^N_7) (s)	T_{rep} (s)	α^{exp} (°)	α^{th} (°)
0.69 ± 0.10	0.43	110 ± 10 (see Fig. SI 1 A)	122 ± 5
T_1 (H^N_5) (s)	T_{rep} (s)	α^{exp} (°)	α^{th} (°)
0.83 ± 0.10	0.43	130 ± 10 (see Fig.SI 1A)	126 ± 5
T_1 (H^N_8) (s)	T_{rep} (s)	α^{exp} (°)	α^{th} (°)
1.0 ± 0.10	0.43	120 ± 10 (see Fig. SI 1 A)	130 ± 5

For the β-peptide

T_1 (H^N_2) (s)	T_{rep} (s)	α^{exp} (°)	α^{th} (°)
1.24 ± 0.10	0.43	110 – 120 ± 10 (see Fig.SI 1 B)	135 ± 5
T_1 (H^N_4) (s)	T_{rep} (s)	α^{exp} (°)	α^{th} (°)
0.99 ± 0.10	0.43	110 – 120 ± 10 (see Fig. SI 1 B)	130 ± 5
T_1 (H^N_5) (s)	T_{rep} (s)	α^{exp} (°)	α^{th} (°)
0.85 ± 0.10	0.43	110 ± 10 (see Fig.SI 1 B)	127 ± 5
T_1 (H^N_6) (s)	T_{rep} (s)	α^{exp} (°)	α^{th} (°)
0.85 ± 0.10	0.43	110 ± 10 (see Fig. SI 1 B)	127 ± 5
T_1 (H^N_8) (s)	T_{rep} (s)	α^{exp} (°)	α^{th} (°)
0.83 ± 0.10	0.43	110 – 120 ± 10 (see Fig.SI 1 B)	126 ± 5
T_1 (H^N_7) (s)	T_{rep} (s)	α^{exp} (°)	α^{th} (°)
0.87 ± 0.10	0.43	110 - 120 ± 10 (see Fig. SI 1 B)	127 ± 5
T_1 (H^N_3) (s)	T_{rep} (s)	α^{exp} (°)	α^{th} (°)
0.87 ± 0.10	0.43	110 - 120 ± 10 (see Fig. SI 1 B)	127 ± 5

Effect of the signal truncation on the detection of H^N···OC H-bonds:

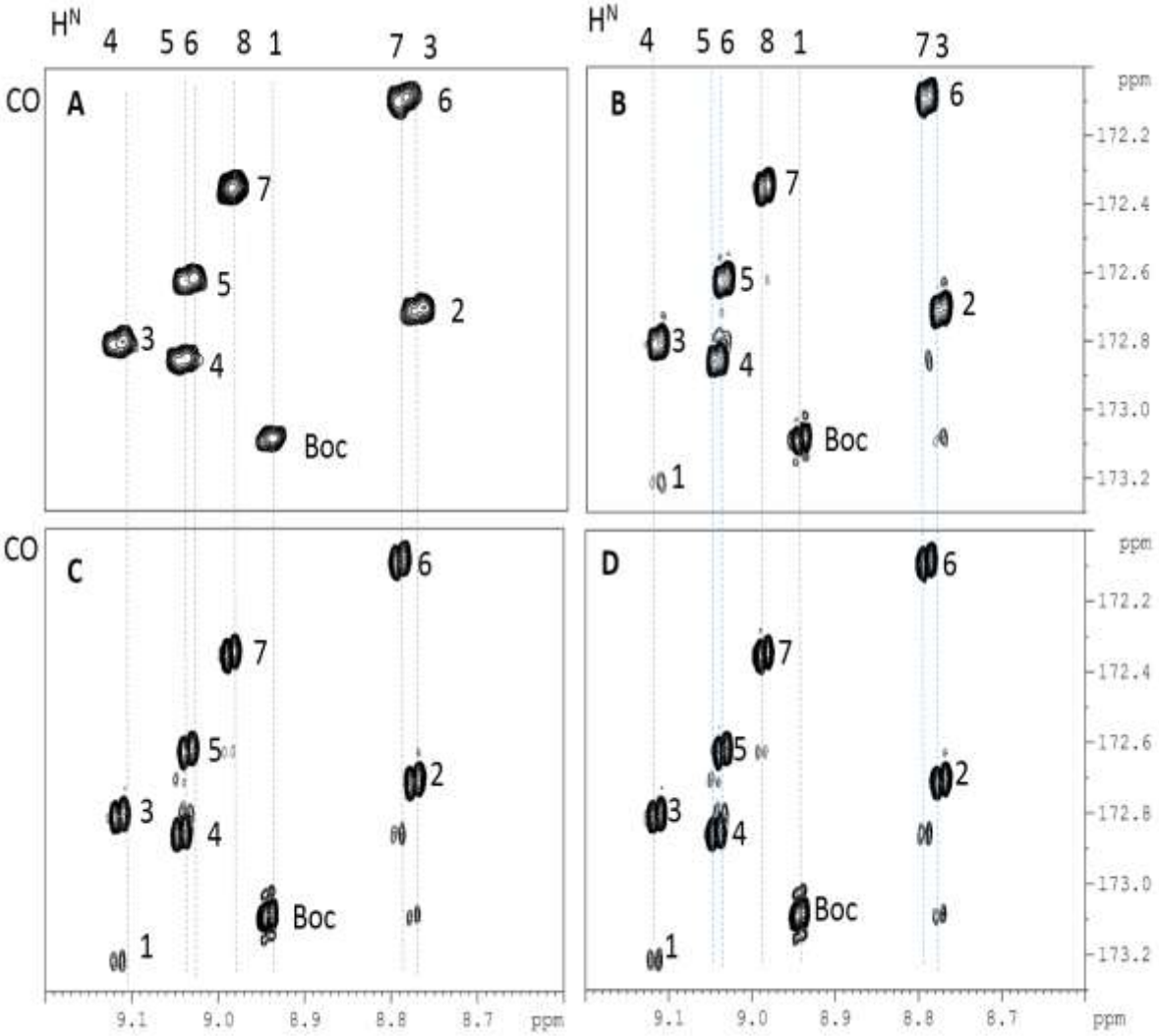

Figure SI-2 H^N-CO SOFAST HMBC recorded maps on the octamer (see Figure 2) in pyridine-d_5 with different truncation level corresponding to acquisition time (aq): A. 107 ms, B. 215 ms, C. 322 ms, D. 430 ms. A long range delay Δ of 200 ms was used for $^{h2}J_{NH\cdots OC}$ couplings to prevent lost in sensitivity due to the transverse relaxation. For aq=107 ms all correlation peaks due to $^{2}J_{HN-CO}$ are visible but not the ones coming from the evolution of $^{h2}J_{NH\cdots OC}$. For aq = 215 ms H^N(4)···CO(1), H^N(6)···OC(3), and H^N(3)···OC(Boc) start appearing. For aq = 322 ms, H^N(5)···CO(2), H^N(8)···CO(5) appear and other H^N···CO get a higher sensitivity. Finally the optimum aq = 430 ms allowed detecting all H bonds correlations.

References

1. R. Ernst and W. Anderson, *Rev. Sci. Instrum*. 1966, **37**, 93.
2. R., Ernst, G. Bodenhausen and A. Wokaun, *Principles of Nuclear Magnetic Resonances in One and Two Dimensions,* Oxford, Science Publications, 1987