Spin Locking: Total Correlation Spectroscopy (TOCSY)

COSY

In an NMR experiment, magnetisations perpendicular to the static magnetic field B0 will rotate about the B0 field at its characteristic Larmor frequency, often referred to as chemical shift precession. In addition to the chemical shift precession the magnetisations will also evolve under the influence of the mutual coupling between the spins, the scalar or J-coupling. The chemical shift evolution accounts for the position of a particular resonance in the spectrum, while the J-coupling is the source of the peak splitting patterns. When the J-couplings are small in comparison to the difference between the resonance frequencies of the coupled spins, the evolution is dominated by the chemical shift. This may be true because the B0 field is high or because the pair of spins are separated in the molecule by several bonds producing a small coupling. In some experiments it is desirable to suppress the chemical shift evolution and allow the spin system to evolve under the J-coupling only. This is often referred to as isotropic mixing.

The suppression of the chemical shift evolution can be achieved by applying a strong RF pulse along a chosen direction keeping the magnetisations locked in alignment with the field. This is referred to as spin locking and the RF field as the spin lock field. There are a number of methods exploiting composite pulses designed to provide a spin lock where imperfections in the RF-pulse can be continually refocused to provide a clean spin lock. The two most common are the MLEV-17 [Bax, A and Davis, DG, Journal of Magnetic Resonance 65, 355-360, 1985] and DIPSI [Shaka, AJ, Lee, CJ, and Pines, A, Journal of Magnetic Resonance 77(2), 274-293, 1988].

TOCSY

Total correlation spectroscopy TOCSY, is a homonuclear 2D experiment similar to COSY (see application note 7) in which the J-coupling between two hydrogen nuclei manifests as a cross peak in the spectrum. Unlike COSY, however, the detection of the coupled spins is not limited to nearest neighbours. The TOCSY experiment exploits the isotropic mixing condition during spin locking to produce cross peaks between all hydrogen nuclei that form part of an unbroken chain of coupled spins.

Consider a chain of four hydrogens, labelled A, B, C and D, where hydrogen A is coupled to B which is coupled to C which, in turn, is coupled to D. In a COSY experiment we would expect to see a cross peak between hydrogen nuclei in the following pairs of positions, (A, B), (B,C) and (C,D). In contrast, the TOCSY spectrum of these hydrogens would show cross peaks between all pairs of nuclei (see Figure 1).

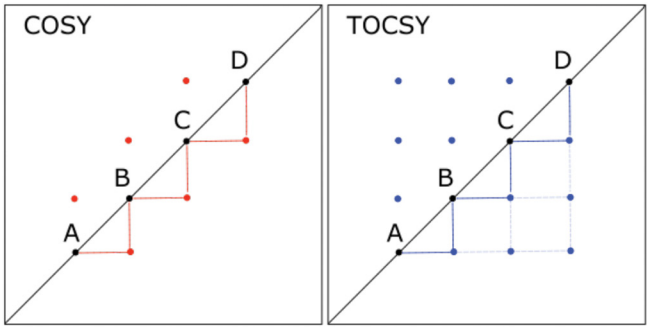


Figure 1: *Comparison of 2D COSY and 2D TOCSY spectra for a hypothetical molecule in which hydrogen A is coupled to hydrogen B, which is coupled to C, which in turn, is coupled to D. Lines are drawn to connect the peaks below the diagonal, illustrating the through-bond connectivity shown by each spectrum; heavier lines indicate couplings shown in both spectra, lighter lines indicate connectivity shown in the TOCSY spectrum but not the COSY.*

To further illustrate this concept, we consider the molecule trans-2-hexenoic acid shown in figure 2 (top). The 1D 1H NMR spectrum (figure 2 bottom) of this molecule shows six resonances, five which have been labelled A to E corresponding to hydrogens attached to the carbon backbone of the molecule and a sixth which corresponds to the –OH of the carboxylic acid group. The resonances A to E all show peak splitting corresponding to the manner in which they are coupled to the neighbouring hydrogens. The COSY spectrum (figure 3) reveals the coupling between A,B and B,C and C,D and D,E. It also shows the coupling between C and E, which might be expected because of the double bond between D and E resulting in a stronger coupling between C and E than D and B for instance.

The TOCSY spectrum (figure 4) shows the coupling between all pairs of hydrogen nuclei confirming the fact that resonances A to E comprise a single unbroken chain of coupled spins. If we compare figure 3 to the TOCSY spectrum of ethyl crotonate in figure 5 we can see that the ethyl crotonate comprises two separate chains of spins, the ethyl group, resonances A and C and the crotonyl group, resonances B, D and E. The lack of cross peaks between the two sets of spins confirms the presence of a nucle which effectively breaks the J-coupling chain. In this case the oxygen from the ester coupling.

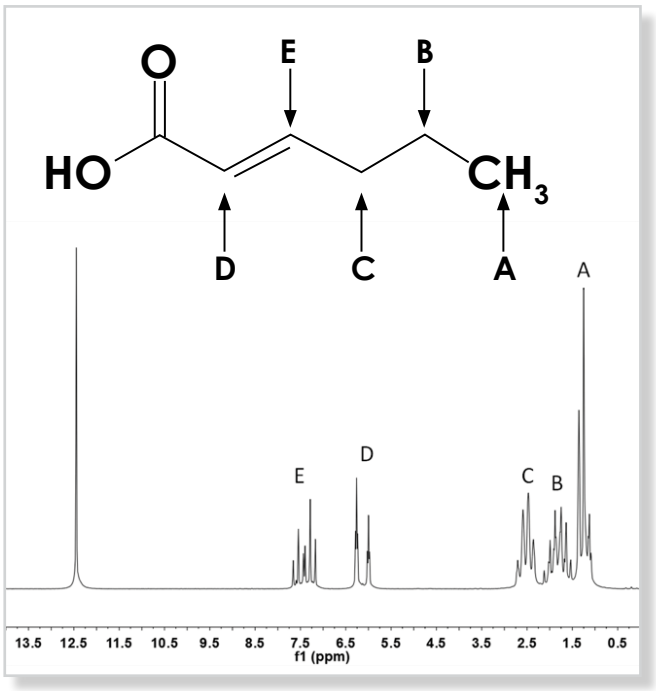


Figure 2: *The structure (top) and 1D 1H spectrum (bottom) of trans-2-hexenoic acid. Hydrogen positions on the carbon backbone are labelled A to E to identify the appropriate resonance in the spectrum. The unlabelled singlet ay 12.5 ppm corresponds to the –OH group of the carboxylic acid.*

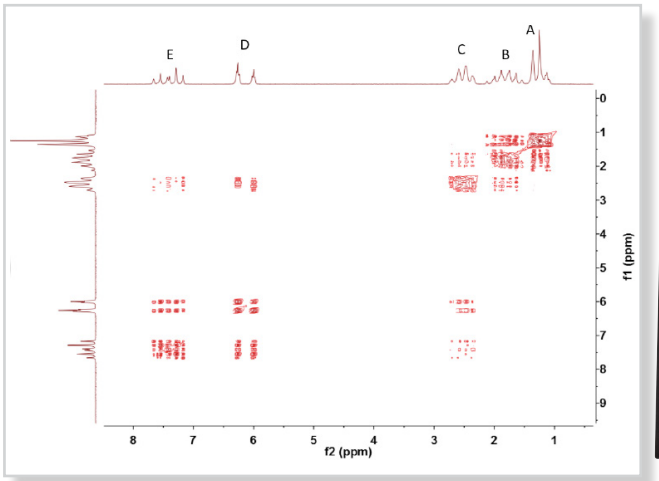


Figure 3: *COSY spectrum of trans-2-hexenoic acid*

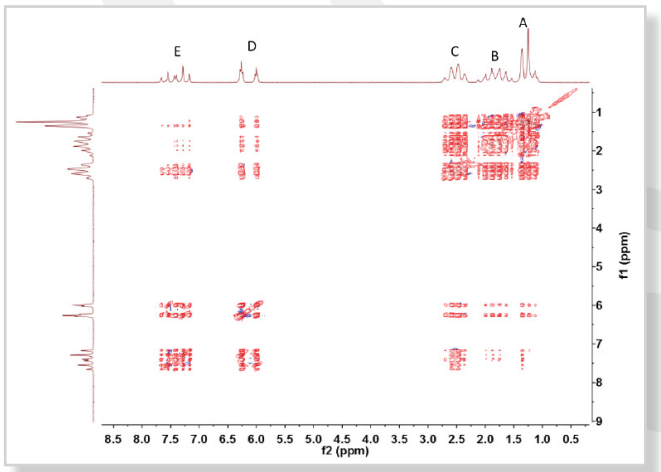


Figure 4:*. Spin lock was implemented using MLEV-17*

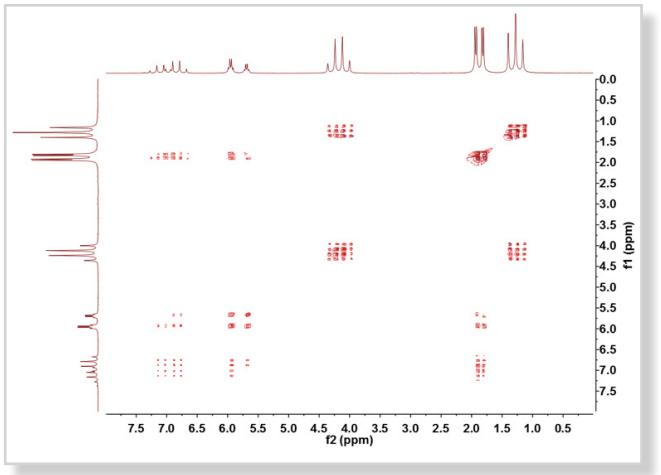
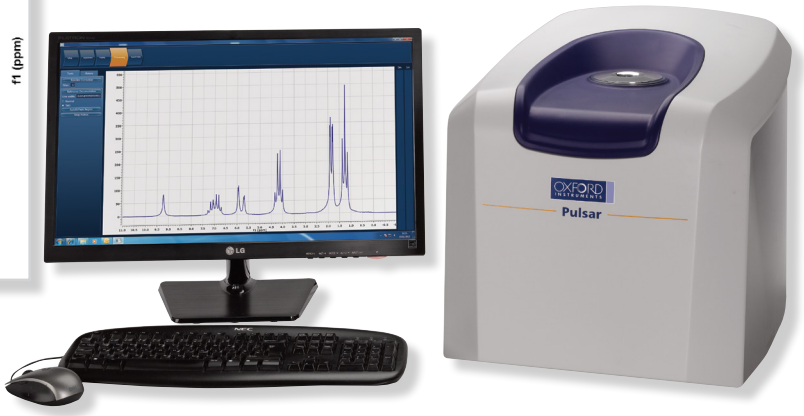


Figure 5: TOCSY spectrum of ethyl crotonate.



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