PSYCHE pure shift NMR: spectral simplification and its applications

L. Castañar, M. Foroozandeh, G. Dal Poggetto, M. Nilsson and G. A. Morris

School of Chemistry, University of Manchester, Manchester, United Kingdom

laura.castanaracedo@manchester.ac.uk

Introduction

Resolution and sensitivity are essential for the analysis and interpretation of NMR spectra. In high-resolution ^{1}H NMR spectroscopy, because of the narrow range of chemical shifts and the many homonuclear couplings, multiplet overlap is very common and can severely complicate the analysis of spectra. Pure shift NMR techniques[1-3] have greatly improved signal resolution by removing homonuclear couplings, but at considerable cost in sensitivity. The most recent pure shift method, PSYCHE,[4] although it still sacrifices significant signal, typically offers almost an order of magnitude improvement over previous methods. We present three new pure shift experiments, implementing PSYCHE in selective 1D TOCSY, Oneshot DOSY, and the recently published CLIP-COSY experiment.[3]

Results

A new tool for NMR analysis of complex systems: selective 1D TOCSY-PSYCHE

Selective 1D TOCSY-PSYCHE experiment (Figure 1) combines selective 1D TOCSY with PSYCHE, yielding pure shift spectra of individual components in intact complex mixtures. The benefits of this method are shown in the analysis of a natural peppermint oil sample (Figure 2).

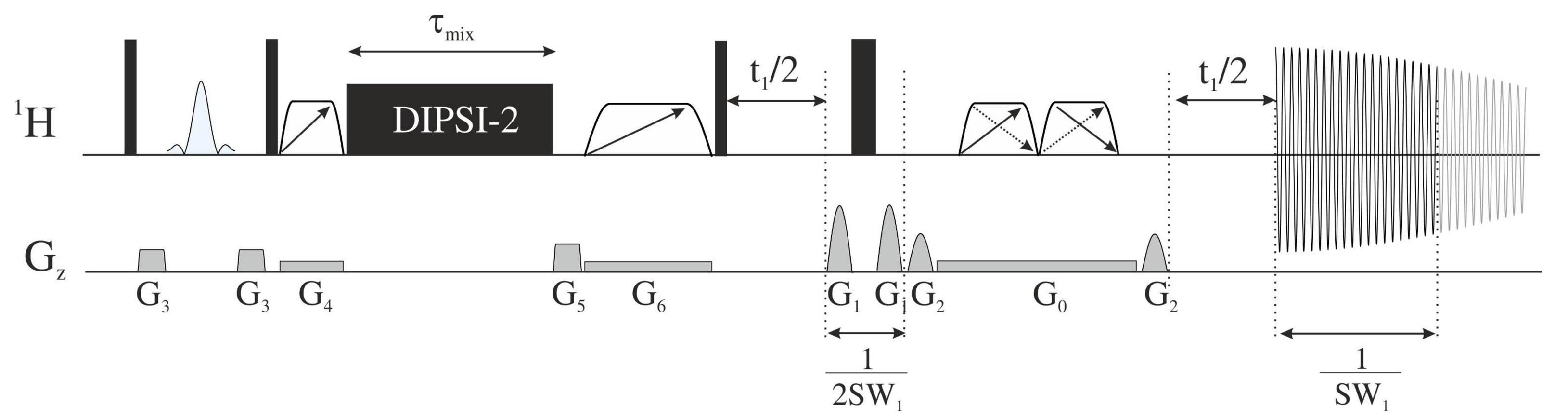

Figure 1. Pulse sequence for the selective 1D TOCSY-PSYCHE experiment. The narrow and wide filled rectangles denote hard 90° and 180° RF pulses, respectively. Trapezoids with cross-diagonal arrows are low-power chirp pulses of small flip angle β (β=20°) that sweep frequency simultaneously in opposite directions (saltire elements). Trapezoids on either side of the DIPSI-2 isotropic mixture element are low-power 180º chirp pulses used to suppress zero quantum coherences. G_1, G_2 and G_3 indicate pulsed field gradients for CTP selection, G_5 is a homospoil gradient pulse, and G_0, G_4, G_6 are weak rectangular gradient pulses applied during the double saltire chirp element and the two single chirp pulses, respectively. The first selective 180º pulse is applied to an isolated resonance; typically RSNOB or REBURP shapes are used.

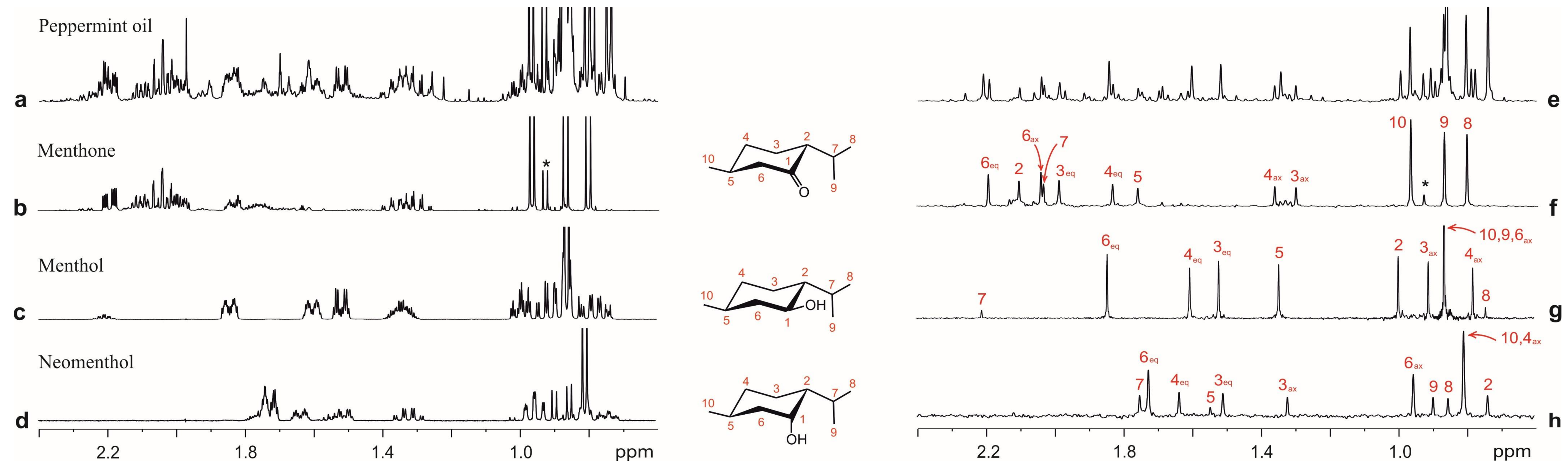

Figure 2. 500 MHz a) conventional, b-d) selective 1D TOCSY, e) PSYCHE, f-h) selective 1D TOCSY-PSYCHE ^{1}H NMR spectra from peppermint oil 25% (v/v) in DMSO-d_6. b,f) H_2 of menthone (2.10 ppm), c,g) H_1 of menthol (3.17 ppm), and d,h) H_1 of neomenthol (3.91 ppm) were selected using 70 ms RSNOB pulses; a 200 ms mixing period was used. All PSYCHE and selective 1D TOCSY-PSYCHE spectra were recorded with 50 t_1 increments (with a chunk duration of 11.3 ms).

Ultra-high resolution pure shift COSY: F_1-PSYCHE-CLIP-COSY

F_1-PSYCHE-CLIP-COSY experiment (Figure 3) is based on CLIP-COSY,[5] using the PSYCHE element in the middle of the evolution time to obtain pure shift signals in the indirect dimension. Used in combination with covariance processing, the result is an ultra-high resolution phase-sensitive COSY spectrum with singlets in both dimensions (Figure 4).

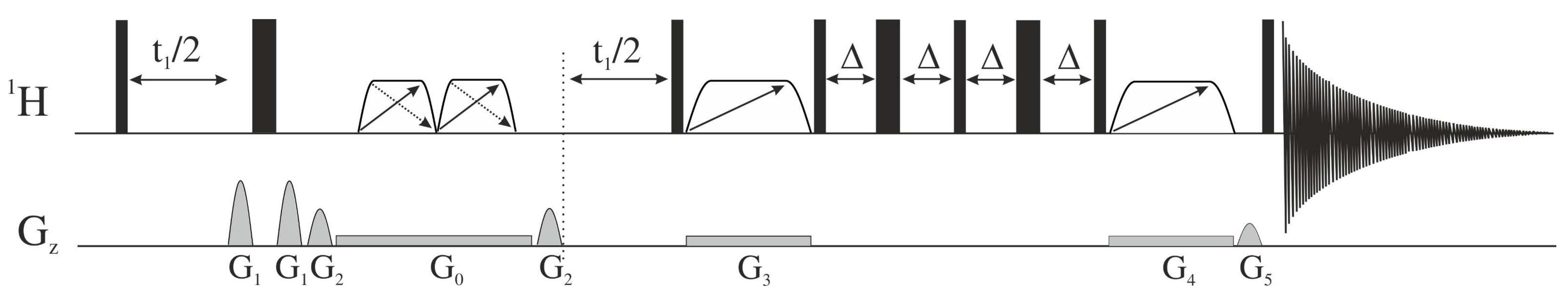

Figure 3. Pulse sequence the for F_1-PSYCHE-CLIP-COSY experiment. The narrow and wide filled rectangles denote hard 90° and 180° RF pulses, respectively. Trapezoids with cross-diagonal arrows are low-power chirp pulses of small flip angle β (β=20°) that sweep frequency simultaneously in opposite directions (saltire elements). Trapezoids on either side of the perfect echo element are low-power 180º chirp pulses used to suppress zero quantum coherences. G_1 and G_2 indicate pulsed field gradients for CTP selection, G_5 is a homospoil gradient pulse, and G_0, G_3, G_4 are weak rectangular gradient pulses applied during the double saltire element and the two single chirp pulses, respectively.

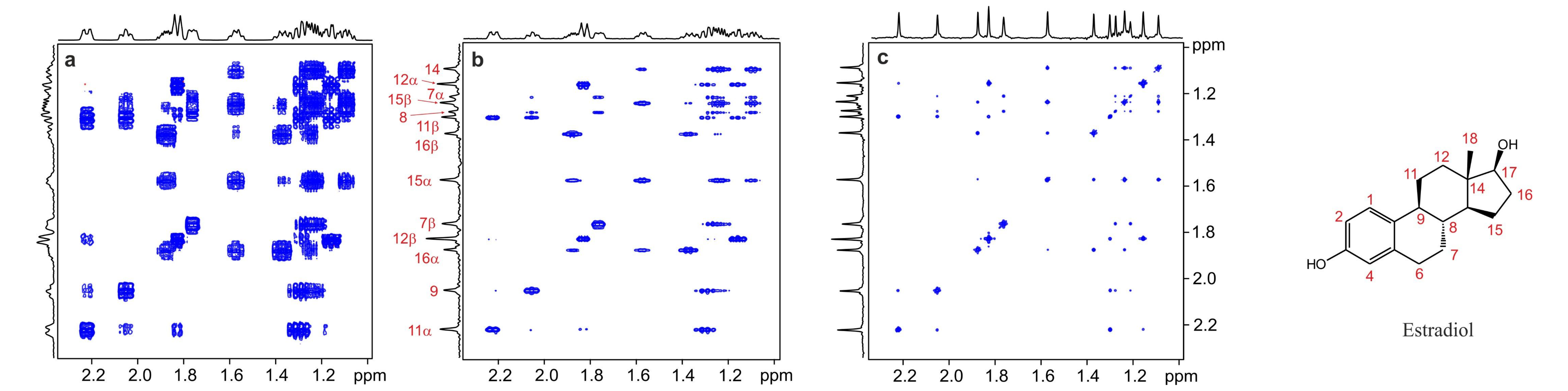

Figure 4. 500 MHz a) CLIP-COSY, b) F_1-PSYCHE-CLIP-COSY, and c) double pure shift COSY spectra after covariance processing in F_2, for an estradiol sample (0.1 M) in DMSO-d_6. All experiments were acquired with Δ=12.5 ms, a spectral window of 2000 Hz, 1024 complex points in the direct and 512 points in the indirect dimension.

High resolution diffusion-ordered spectroscopy: Oneshot-PSYCHE DOSY

The new Oneshot-PSYCHE DOSY experiment (Figure 5) - which combines DOSY with PSYCHE pure shift NMR - facilitates the analysis of complex mixtures. Misleading peaks in the diffusion dimension due to signal overlap are minimized, and accurate high-resolution diffusion measurements are obtained (Figure 6).

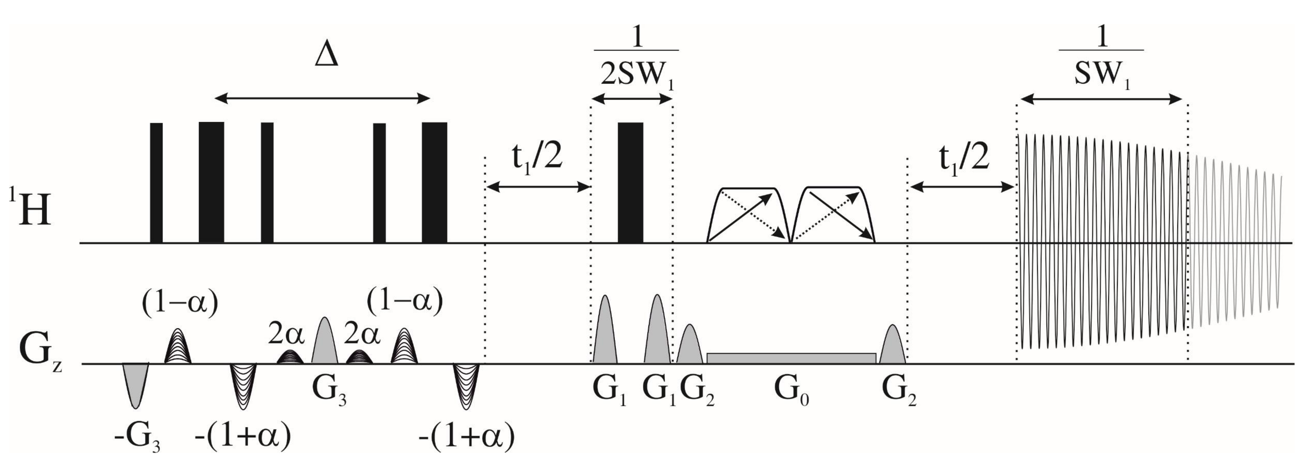

Figure 5. Pulse sequence for the Oneshot-PSYCHE DOSY experiment. The narrow and wide filled rectangles denote hard 90° and 180° RF pulses, respectively. Trapezoids are low-power chirp pulses of small flip angle β (β=20°) that sweep frequency simultaneously in opposite directions (saltire elements). Filled half-sine shapes (G_1 to G_3) indicate pulsed field gradients for CTP selection and G_0 is a weak rectangular gradient applied during the double saltire element. Incremented open half-sine shapes indicate gradient levels which are changed to vary the diffusion weighting of signals.

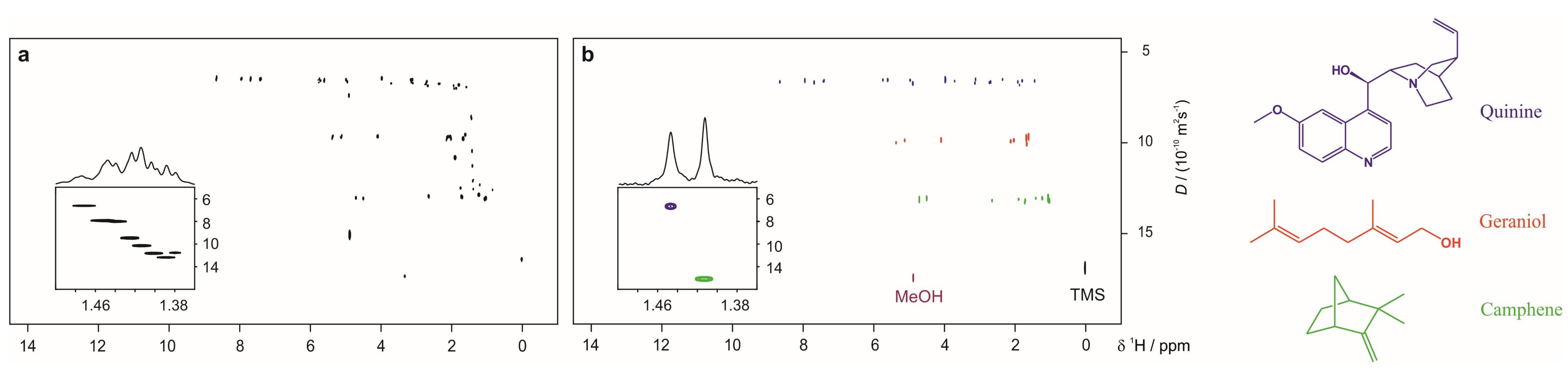

Figure 6. 500 MHz a) Oneshot and b) Oneshot-PSYCHE DOSY spectra for a mixture of quinine (0.1 M), geraniol (0.1 M), camphene (0.2 M) and TMS in methanol-d_4, acquired in 5 min and 1 hr 40 min, respectively. The Oneshot-PSYCHE DOSY spectrum was acquired with 20 t_1 increments (with a chunk duration of 20 ms). In both experiments a diffusion delay Δ of 0.1 s was used, α was set to 0.2, and 12 gradients strengths ranging from 2.65 to 18.55 G/cm were used. DOSY data were processed using the DOSY Toolbox.[6]

References:

[1] R. W. Adams, *eMagRes*, **2014**, 3, 1.

[2] K. Zangger, *Prog. Nucl. Magn. Reson. Spectrosc.*, **2015**, 86-87, 1.

[3] L. Castañar *et al.*, *Magn. Reson. Chem.*, **2015**, 53, 399.

[4] M. Foroozandeh *et al.*, *Angew. Chem. Int. Ed.*, **2014**, 53, 6990.

[5] M.R.M. Koos *et al.*, *Angew. Chem. Int. Ed.*, **2016**, 55, 7655.

[6] M. Nilsson, *J. Magn. Reson.*, **2009**, 200, 296.

Acknowledgements:

This work was supported by the Engineering and Physical Sciences Research (grant number EP/L018500/1 and EP/M013820/1) and by Science Without Borders – Brazil.