Journal of Magnetic Resonance 211 (2011) 25–29

Contents lists available at ScienceDirect

Journal of Magnetic Resonance

journal homepage: www.elsevier.com/locate/jmr

High resolution ^{13}C DOSY: The DEPTSE experiment

Adolfo Botana [a], Peter W.A. Howe [b], Valérie Caër [b,c], Gareth A. Morris [a], Mathias Nilsson [a,*]

[a] School of Chemistry, University of Manchester, Oxford Road, Manchester M13 9PL, UK
[b] Analytical Sciences, Syngenta Limited, Jealott's Hill Research Centre, Bracknell, Berkshire RG42 6EY, UK
[c] Syngenta Crop Protection AG, Swarzwaldallee 215, Basel CH-4058, Switzerland

ARTICLE INFO

Article history:
Received 10 February 2011
Revised 11 March 2011
Available online 22 March 2011

Keywords:
DOSY
Polarization transfer
Diffusion
Carbon
Mixture analysis
Spin echo
DEPT
DEPTSE

ABSTRACT

High Resolution Diffusion-ordered Spectroscopy (HR-DOSY) is a valuable tool for mixture analysis by NMR. It separates the signals from different components according to their diffusion behavior, and can provide exquisite diffusion resolution when there is no signal overlap. In HR-DOSY experiments on ^{1}H (by far the most common nucleus used for DOSY) there is frequent signal overlap that confuses interpretation. In contrast, a ^{13}C spectrum usually has little overlap, and is in this respect a much better option for a DOSY experiment. The low signal-to-noise ratio is a critical limiting factor, but with recent technical advances such as cryogenic probes this problem is now less acute. The most widely-used pulse sequences for ^{13}C DOSY perform diffusion encoding with ^{1}H, using a stimulated echo in which half of the signal is lost. This signal loss can be avoided by encoding diffusion with ^{13}C in a spin echo experiment such as the DEPTSE pulse sequence described here.

1. Introduction

Diffusion-ordered spectroscopy (DOSY [1,2]) is a powerful tool for the analysis of intact mixtures by NMR. In DOSY we distinguish between signals from different components by their diffusion behavior, which is typically governed not only by the hydrodynamic radius but also by the interactions between mixture components [3,4]. DOSY is usually carried out by measuring a set of NMR spectra with increasing pulse field gradient strength, using a pulse sequence derived from the gradient spin echo or stimulated echo. This results in signals being attenuated as described by the Stejskal–Tanner equation [5]:

$$S = S_0 \mathrm{e}^{-D\gamma^2\delta^2G^2\Delta'} \tag{1}$$

where S is the signal amplitude, S_0 is the amplitude in the absence of diffusion, D is the diffusion coefficient, δ is the gradient pulse width, γ is the magnetogyric ratio, G is the gradient strength, and Δ' is the diffusion time corrected for the effects of finite gradient pulse width.

In High Resolution DOSY [6,7] (HR-DOSY) each peak height (or area) attenuation curve from the arrayed experiment is fitted to an appropriate form of Eq. (1) to obtain the diffusion coefficient [8]. A 2D plot is calculated with the NMR spectrum in one dimension and with diffusion in the other. This second dimension is constructed by centering the peak at the fitted diffusion coefficient and giving it a Gaussian peak shape determined by the fit statistics. The signal shape in the diffusion dimension can be defined as:

$$S_j(D) = \frac{1}{\sqrt{2\pi\sigma_j^2}} e^{\frac{(D-D_j)^2}{2\sigma_j^2}} \tag{2}$$

where σ_j is the standard error of the fit for the signal j and D_j is the diffusion coefficient obtained in the fit.

The underlying assumption in HR-DOSY is that only one signal contributes to each peak, i.e. that there is no signal overlap. When this is true the resolution in the diffusion dimension can be as good as 0.5% [9]. When signals do overlap, however, as is commonly the case for at least a small proportion of signals in typical ^{1}H HR-DOSY experiments, the result is normally a diffusion coefficient intermediate between those of the components contributing to the overlapped signal (J-modulation can complicate matters further [10]). Signal overlap thus makes a HR-DOSY spectrum difficult to interpret. Alternative processing methods include fitting each peak to a sum or distribution of exponentials [9,11,12], or using the covariance between different peaks from the same compound to decompose a DOSY dataset into its component spectra in so-called multivariate methods [13–20]. These can be very efficient, but require high quality data and typically a minimum difference in diffusion coefficient of 30%. The best diffusion resolution is clearly achieved when component spectra do not overlap, and therefore many different DOSY experiments have been devised in an attempt

* Corresponding author.
E-mail address: mathias.nilsson@manchester.ac.uk (M. Nilsson).

1090-7807/$ - see front matter © 2011 Elsevier Inc. All rights reserved.
doi:10.1016/j.jmr.2011.03.016

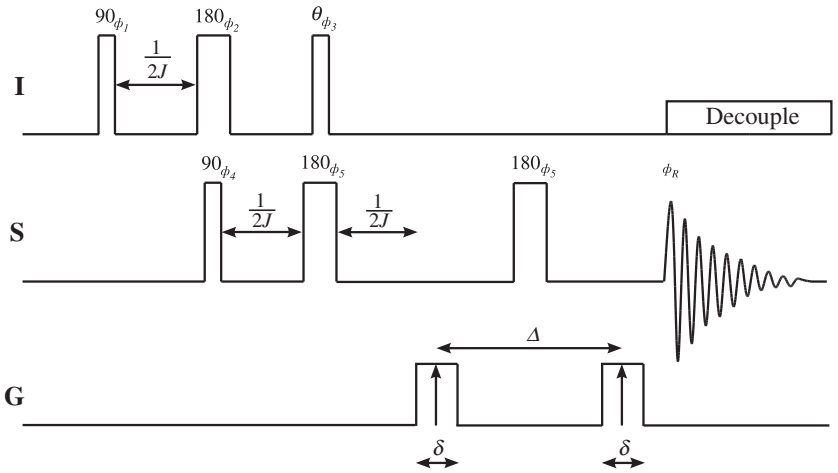

Fig. 1. DEPTSE pulse sequence. *I* and *S* are normally ^{1}H and ^{13}C respectively. Phases (in multiples of 90°) are cycled as follows: $\Phi_1 = 02$; $\Phi_2 = 1$; $\Phi_3 = 1$; $\Phi_4 = 0_8 1_8 2_8 3_8$; $\Phi_5 = 1_2 2_2 3_2 0_2$; and $\Phi_R = (02)_4(13)_4(20)_4(31)_4$.

to minimize overlap. This can mean spreading the signals out in more dimensions, as in 3D DOSY experiments [21–28] (e.g. COSY–DOSY [21–23]), or using a less crowded parent spectrum (e.g. pure shift DOSY [29,30]).

Most DOSY experiments use ^{1}H because of its high NMR sensitivity and because of the efficient diffusion encoding afforded by its high magnetogyric ratio. However, ^{1}H spectra often contain overlap, so the use of other nuclei such as ^{13}C [25,31–37], ^{31}P [32,38], ^{6}Li [39], ^{29}Si [26,40] or ^{19}F [41–43] can be beneficial. ^{13}C is generally a good choice for organic compounds as typical spectra are very informative and seldom suffer from overlap. Indeed the first published mixture analysis by diffusion NMR was performed using ^{13}C, [44] but due to the low signal-to-noise ratio it was not a viable experiment for many mixtures. Recent improvements in sensitivity using cryoprobes and microcoils [45–48], and other methods [49,50] now allow the acquisition of ^{13}C DOSY data in reasonable times. It is common practice to use polarization transfer to improve sensitivity (albeit sacrificing signals from quaternary carbons), as in modern ^{13}C DOSY experiments such as INEPT-DOSY and DEPT-DOSY [25,33]. In these experiments, diffusion encoding is typically carried out on the ^{1}H magnetization in a stimulated echo (STE) of some form, followed by polarization transfer to ^{13}C. The main advantages of using the STE for diffusion encoding are reduced relaxation losses during the diffusion time, and much less severe *J*-modulation effects.

For diffusion encoding using ^{13}C, there is no significant problem with *J*-modulation (unless a ^{13}C enriched sample is studied [34]), and in small molecules T_2 is often similar to T_1. Thus for mixtures of small molecules it can make sense to use a spin echo (SE) for diffusion encoding of the ^{13}C magnetization, avoiding throwing away 50% of the signal in a STE. The fourfold lower gyromagnetic ratio of ^{13}C necessitates using four times the gradient pulse area required for ^{1}H experiments with the same diffusion time, but using a spin echo allows much longer gradient pulses to be accommodated. Polarization transfer not only allows increasing the signal using the magnetization from ^{1}H, but it also allows increasing the repetition rate of the experiments. The population difference used for the polarization transfer is that of the ^{1}H, so the repetition rate depends on the longitudinal relaxation time T_1 of the ^{1}H, which is typically shorter than that of the ^{13}C. The combination of DEPT with SE (the DEPTSE pulse sequence of Fig. 1) is illustrated here using a mixture of medium chain alcohols.

Introducing adiabatic inversion pulses into these SE based sequences can be helpful: they provide high inversion bandwidths,

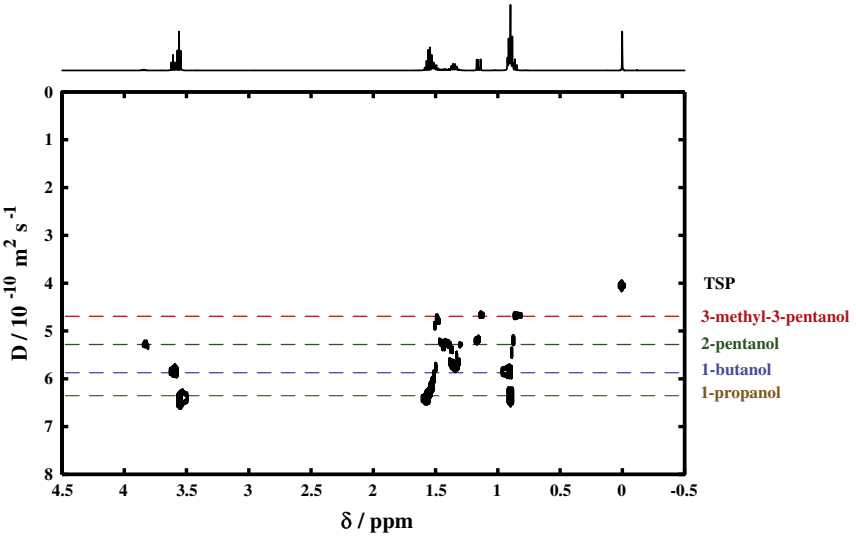

Fig. 2. ^{1}H Oneshot [56] DOSY spectrum of a mixture of 1-propanol, 1-butanol, 2-pentanol and 3-methyl-3-pentanol.

are insensitive to RF field inhomogeneity, and in appropriate implementations can partially compensate for $^1J_{CH}$ variations by exploiting the correlation between chemical shift and coupling constant [51]. Such pulses need to be used in pairs to avoid severe offset-dependence of signal phase [52]. Therefore, they can readily be implemented in this sequence simply by replacing the two 180° ^{13}C pulses with adiabatic pulses. Further improvement in compensation of $^1J_{CH}$ variations can be achieved by introducing a *J*-compensated excitation element [53]. It should be noted that it is important not to attempt to decouple during the diffusion-encoding echo. This is for two reasons: first, the field gradients used create large position-dependent resonance offsets that defeat broadband decoupling, causing rapid signal loss, and second, decoupling between but not during the gradient pulses can introduce strong signal modulations as a function of the duration of the gaps in decoupling necessitated by the gradient pulses [54]. In experiments where decoupling is important, as in the analysis of liquid crystals, other approaches may be needed [55].

2. Experimental

Data were acquired for a mixture of 1-propanol, 1-butanol, 2-pentanol and 3-methyl-3-pentanol with a concentration of around 14 mg mL^{-1} each in deuterated water, with 4 mg mL^{-1} TSP (sodium 3-(trimethylsilyl)-propionate-2,2,3,3-d$_4$) as a reference. Measurements were carried out non-spinning on a Varian VNMRS 500 spectrometer in an air-conditioned room at approximately 18 °C, with spectrometer temperature regulation set at 23 °C and with an active air preconditioning system used to minimize temperature variations. A ^{1}H DOSY spectrum was measured in 30 min using the Oneshot sequence [56] with 12 gradient amplitudes ranging from 12 to 54 G cm^{-1} in equal steps of gradient squared, using 16 transients, 16384 complex data points, a total diffusion-encoding gradient pulse duration of 1.4 ms and a diffusion time of 0.1 s. The time averaging was used to improve the signal-to-noise ratio, but also serves to attenuate signals from unwanted coherence transfer pathways. ^{13}C DEPTSE measurements were carried out using 10 gradient amplitudes ranging from 6 to 54 G cm^{-1} in equal steps of gradient squared, 1024 transients, 65,536 complex data points, a pulse flip angle θ of 45°, a diffusion-encoding gradient pulse duration of 6.0 ms, and a diffusion time of 0.05 s, in a total time of 43 h. Oneshot-INEPT [25,56] measurements were carried out using 10 gradient amplitudes ranging from 6 to 54 G cm^{-1} in equal steps of gradient squared, 1024 transients, 65,536 complex data points, a refocusing delay of $1/(4^1J_{CH})$ (equivalent to a pulse flip angle θ of 45° in DEPT), a diffusion-encoding gradient pulse duration of 1.4 ms, and a diffusion time of 0.05 s, in a total time of 43 h. All spectra were manually phase corrected, and either Fourier transformed with 1 Hz Lorentzian line broadening to minimize the effect of any variation in lineshape between spectra while avoiding excessive loss of resolution, or in the case of ^{1}H DOSY, reference deconvoluted [57] to a line width of 1 Hz. All data processing was carried out using the DOSY Toolbox [58].

3. Results and discussion

The ^{1}H DOSY spectrum of the mixture of 1-propanol, 1-butanol, 2-pentanol and 3-methyl-3-pentanol (Fig. 2) is not straightforward to interpret. Severe overlap in the region between 0.8 ppm and 1.6 ppm, and the similar diffusion coefficients of the mixture components, make it difficult to disentangle the spectra of the individual components. The diffusion coefficients are also too similar for more advanced processing methods such as biexponential fitting [9] or SCORE [20] to be successful. The resolution increase in ^{13}C experiments means that they show no significant signal overlap for this sample, allowing simple monoexponential fitting to be used; results for the Oneshot-INEPT experiment are shown in Fig. 3. The signal-to-noise ratio for the first increment of the latter experiment was about 200:1, while that in the corresponding ^{1}H Oneshot data was about 50,000:1. In the former it is the *S*/*N* ratio of the data that limits the accuracy of the diffusion coefficients obtained, whereas in the latter it is signal overlap. The effect of the twofold improvement in *S*/*N* ratio afforded by the DEPTSE experiment can be seen in Fig. 4, where the diffusion resolution is significantly better than in Fig. 3. In both Figs. 3 and 4, peaks belonging to the different alcohols all appear at the correct diffusion coefficient, allowing the identification of all the species present, in contrast to the situation in Fig. 2, where signal overlap results in ambiguity.

Similar results to those of Figs. 3 and 4 can be achieved by combining the INEPT sequence with a ^{13}C spin echo. The applicability of both DEPTSE and INEPTSE sequences is limited by the transverse

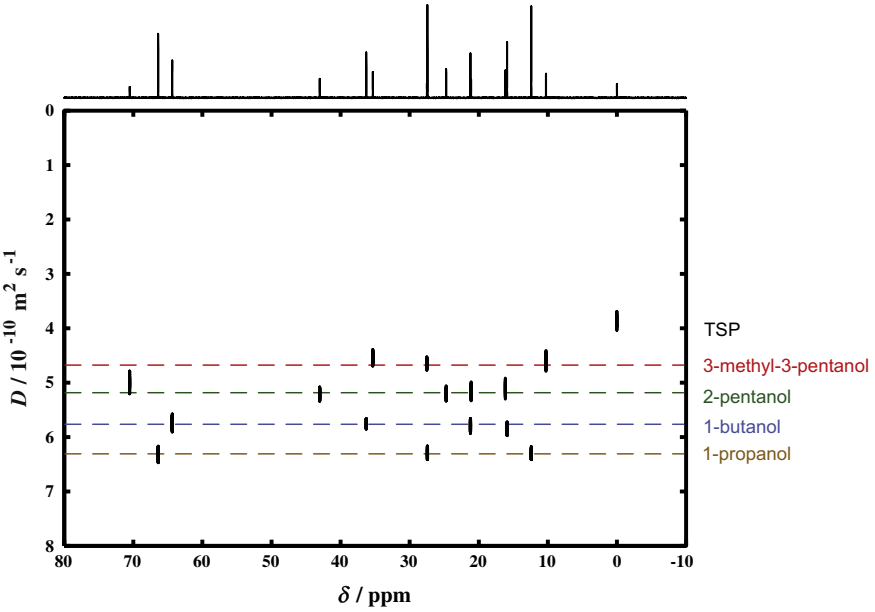

Fig. 3. ^{13}C Oneshot-INEPT DOSY spectrum of a mixture of 1-propanol, 1-butanol, 2-pentanol and 3-methyl-3-pentanol.

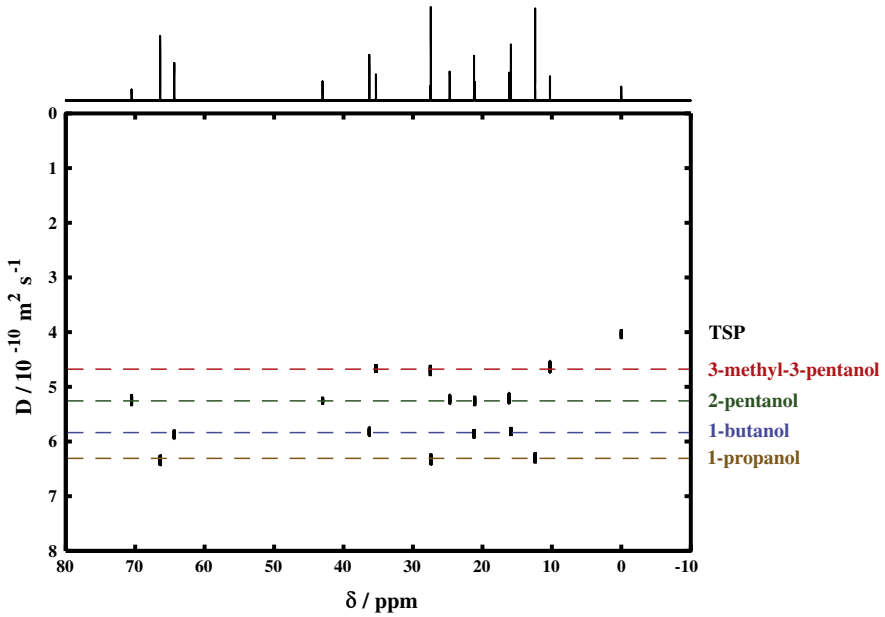

Fig. 4. ^{13}C DEPTSE DOSY spectrum of a mixture of 1-propanol, 1-butanol, 2-pentanol and 3-methyl-3-pentanol.

^{13}C relaxation of the molecules in the mixture; this is not a problem inside the extreme narrowing condition, where the T_2s are close to the T_1s, as is the case for small molecules. Sequences performing diffusion encoding on ^{13}C require a diffusion-encoding gradient area four times larger than that for ^{1}H-encoded experiments such as the previous INEPT-DOSY and DEPT-DOSY sequences, so it is necessary to choose experimental parameters that do not exceed the gradient duty cycle or pulse width that the gradient coil can sustain. Most modern gradient systems can however provide significantly longer pulses and higher duty cycles than those used here.

4. Conclusion

The use of heteronuclei such as ^{13}C for DOSY analysis is very beneficial when the corresponding ^{1}H spectrum is too highly overlapped for successful interpretation of the HR-DOSY spectrum, but suffers from low sensitivity. When diffusion encoding is performed using a spin echo instead of a stimulated echo there is a sensitivity improvement of a factor of two for small molecules. This technique is potentially useful in the analysis of mixtures of small molecules, for example liquid foods [59], where overlap is a problem in the ^{1}H spectrum.

Acknowledgment

This work was supported by the Engineering and Physical Sciences Research Council [Grant Numbers EP/E05899X/1 and EP/E057888/1].

References

[1] G.A. Morris, Diffusion-ordered spectroscopy, in: D.M. Grant, R.K. Harris (Eds.), Encyclopedia of Magnetic Resonance, vol. 9, John Wiley and Sons, Ltd., 2002, pp. 35–44;
G.A. Morris, Diffusion-ordered spectroscopy, in: R.K. Harris, R.E. Wasylishen (Eds.), Encyclopedia of Magnetic Resonance, John Wiley and Sons, Chichester, 2009 (doi: 10.1002/9780470034590.emrstm0119.pub2).
[2] C.S. Johnson, Diffusion ordered nuclear magnetic resonance spectroscopy: principles and applications, Prog. Nucl. Magn. Reson. Spectrosc. 34 (1999) 203–256.
[3] R. Evans, S. Haiber, M. Nilsson, G.A. Morris, Isomer resolution by micelle-assisted diffusion-ordered spectroscopy, Anal. Chem. 81 (2009) 4548–4550.
[4] C.F. Tormena, R. Evans, S. Haiber, M. Nilsson, G.A. Morris, Matrix-assisted diffusion-ordered spectroscopy: mixture resolution by NMR using SDS micelles, Magn. Reson. Chem. 48 (2010) 550–553.
[5] E.O. Stejskal, J.E. Tanner, Spin diffusion measurements: spin echoes in the presence of a time-dependent field gradient, J. Chem. Phys. 42 (1965) 288–292.
[6] H. Barjat, G.A. Morris, S. Smart, A.G. Swanson, S.C.R. Williams, High-resolution diffusion-ordered 2D spectroscopy (HR-DOSY) – a new tool for the analysis of complex mixtures, J. Magn. Reson., Ser. B 108 (1995) 170–172.
[7] M.D. Pelta, H. Barjat, G.A. Morris, A.L. Davis, S.J. Hammond, Pulse sequences for high-resolution diffusion-ordered spectroscopy (HR-DOSY), Magn. Reson. Chem. 36 (1998) 706–714.
[8] M.A. Connell, P.J. Bowyer, P. Adam Bone, A.L. Davis, A.G. Swanson, M. Nilsson, G.A. Morris, Improving the accuracy of pulsed field gradient NMR diffusion experiments: correction for gradient non-uniformity, J. Magn. Reson. 198 (2009) 121–131.
[9] M. Nilsson, M.A. Connell, A.L. Davis, G.A. Morris, Biexponential fitting of diffusion-ordered NMR data: practicalities and limitations, Anal. Chem. 78 (2006) 3040–3045.
[10] A. Botana, J.A. Aguilar, M. Nilsson, G.A. Morris, J-modulation effects in DOSY experiments and their suppression: the Oneshot45 experiment, J. Magn. Reson. 208 (2011) 211–220.
[11] S.W. Provencher, CONTIN: a general purpose constrained regularization program for inverting noisy linear algebraic and integral equations, Comput. Phys. Commun. 27 (1982) 229–242.
[12] K.F. Morris, C.S. Johnson, Resolution of discrete and continuous molecular size distributions by means of diffusion-ordered 2D NMR spectroscopy, J. Am. Chem. Soc. 115 (1993) 4291–4299.
[13] L.C.M. Van Gorkom, T.M. Hancewicz, Analysis of DOSY and GPC-NMR experiments on polymers by multivariate curve resolution, J. Magn. Reson. 130 (1998) 125–130.
[14] W. Windig, B. Antalek, Direct exponential curve resolution algorithm (DECRA): a novel application of the generalized rank annihilation method for a single spectral mixture data set with exponentially decaying contribution profiles, Chemom. Intell. Lab. Syst. 37 (1997) 241–254.
[15] M. Nilsson, G.A. Morris, Improved DECRA processing of DOSY data: correcting for non-uniform field gradients, Magn. Reson. Chem. 45 (2007) 656–660.
[16] B. Antalek, J.M. Hewitt, W. Windig, P.D. Yacobucci, T. Mourey, K. Le, The use of PGSE NMR and DECRA for determining polymer composition, Magn. Reson. Chem. 40 (2002) S60–S71.
[17] P. Stilbs, K. Paulsen, Global least-squares analysis of large, correlated spectral data sets and application to chemical kinetics and time-resolved fluorescence, Rev. Sci. Instrum. 67 (1996) 4380–4386.
[18] P. Stilbs, K. Paulsen, P.C. Griffiths, Global least-squares analysis of large, correlated spectral data sets; application to component-resolved FT-PGSE NMR spectroscopy, J. Phys. Chem. 100 (1996) 8180–8189.
[19] M. Nilsson, G.A. Morris, Correction of systematic errors in CORE processing of DOSY data, Magn. Reson. Chem. 44 (2006) 655–660.
[20] M. Nilsson, G.A. Morris, Speedy component resolution: an improved tool for processing diffusion-ordered spectroscopy data, Anal. Chem. 80 (2008) 3777–3782.

[21] M. Nilsson, A.M. Gil, I. Delgadillo, G.A. Morris, Improving pulse sequences for 3D DOSY: COSY–IDOSY, Chem. Commun. (2005) 1737–1739.
[22] D. Wu, A. Chen, J.C.S. Johnson, Three-dimensional diffusion-ordered NMR spectroscopy: the homonuclear COSY-DOSY experiment, J. Magn. Reson., Ser. A 121 (1996) 88–91.
[23] J.M. Newman, A. Jerschow, Improvements in complex mixture analysis by NMR: DQF-COSY iDOSY, Anal. Chem. 79 (2007) 2957–2960.
[24] H. Barjat, G.A. Morris, A.G. Swanson, A three-dimensional DOSY-HMQC experiment for the high-resolution analysis of complex mixtures, J. Magn. Reson. 131 (1998) 131–138.
[25] D. Wu, A. Chen, J.C.S. Johnson, Heteronuclear-detected diffusion-ordered NMR spectroscopy through coherence transfer, J. Magn. Reson., Ser. A 123 (1996) 215–218.
[26] M.J. Stchedroff, A.M. Kenwright, G.A. Morris, M. Nilsson, R.K. Harris, 2D and 3D DOSY methods for studying mixtures of oligomeric dimethylsiloxanes, Phys. Chem. Chem. Phys. 6 (2004) 3221–3227.
[27] M. Nilsson, A.M. Gil, I. Delgadillo, G.A. Morris, Improving pulse sequences for 3D diffusion-ordered NMR spectroscopy: 2DJ-IDOSY, Anal. Chem. 76 (2004) 5418–5422.
[28] L.H. Lucas, W.H. Otto, C.K. Larive, The 2D-J-DOSY experiment: resolving diffusion coefficients in mixtures, J. Magn. Reson. 156 (2002) 138–145.
[29] M. Nilsson, G.A. Morris, Pure shift proton DOSY: diffusion-ordered ^{1}H spectra without multiplet structure, Chem. Commun. (2007) 933–935.
[30] J.A. Aguilar, S. Faulkner, M. Nilsson, G.A. Morris, Pure shift ^{1}H NMR: a resolution of the resolution problem?, Angew Chem. Int. Ed. 49 (2010) 3901–3903.
[31] G.S. Kapur, M. Findeisen, S. Berger, Analysis of hydrocarbon mixtures by diffusion-ordered NMR spectroscopy, Fuel 79 (2000) 1347–1351.
[32] G.S. Kapur, S. Berger, Pulsed field gradient (PFG) NMR spectroscopy: an effective tool for the analysis of mixtures of lubricating oil components, Tribotest 6 (2000) 323–336.
[33] D. Li, R. Hopson, W. Li, J. Liu, P.G. Williard, ^{13}C INEPT diffusion-ordered NMR spectroscopy (DOSY) with internal references, Org. Lett. 10 (2008) 909–911.
[34] K. Vermillion, N.P.J. Price, Stable isotope-enhanced two- and three-dimensional diffusion ordered ^{13}C NMR spectroscopy (SIE-DOSY^{13}C NMR), J. Magn. Reson. 198 (2009) 209–214.
[35] Y. Oda, S. Matsuda, T. Yamanoi, A. Murota, K. Katsuraya, Identification of the inclusion complexation between phenyl β-d-($^{13}C_6$)glucopyranoside and α-cyclodextrin using 2D ^{1}H or ^{13}C DOSY spectrum, Supramol. Chem. 21 (2009) 638–642.
[36] B.S. Akpa, D.J. Holland, A.J. Sederman, M.L. Johns, L.F. Gladden, Enhanced ^{13}C PFG NMR for the study of hydrodynamic dispersion in porous media, J. Magn. Reson. 186 (2007) 160–165.
[37] D. Li, I. Keresztes, R. Hopson, P.G. Williard, Characterization of reactive intermediates by multinuclear diffusion-ordered NMR spectroscopy (DOSY), Acc. Chem. Res. 42 (2008) 270–280.
[38] G. Kagan, W. Li, R. Hopson, P.G. Williard, Internally referenced diffusion coefficient – formula weight (D-FW) analysis of ^{31}P diffusion-ordered NMR spectroscopy (DOSY), Org. Lett. 11 (2009) 4818–4821.
[39] G. Kagan, W. Li, R. Hopson, P.G. Williard, ^{6}Li diffusion-ordered NMR spectroscopy (DOSY) and applications to organometallic complexes, Org. Lett. 12 (2009) 520–523.
[40] V. Blechta, M. Kurfürst, J. Sýkora, J. Schraml, High-performance liquid chromatography with nuclear magnetic resonance detection applied to organosilicon polymers: part 2: comparison with other methods, J. Chromatogr. A 1145 (2007) 175–182.
[41] A. Lledó, P. Restorp, J. Rebek, Pseudo-capsule assemblies characterized by 19F NMR techniques, J. Am. Chem. Soc. 131 (2009) 2440–2441.
[42] S. Sato, J. Iida, K. Suzuki, M. Kawano, T. Ozeki, M. Fujita, Fluorous nanodroplets structurally confined in an organopalladium sphere, Science 313 (2006) 1273–1276.
[43] A.A. Marchione, E.F. McCord, Spectral separation of gaseous fluorocarbon mixtures and measurement of diffusion constants by ^{19}F gas phase DOSY NMR, J. Magn. Reson. 201 (2009) 34–38.
[44] P. Stilbs, Molecular self-diffusion coefficients in Fourier transform nuclear magnetic resonance spectrometric analysis of complex mixtures, Anal. Chem. 53 (1981) 2135–2137.
[45] R. Subramanian, A.G. Webb, Design of solenoidal microcoils for high-resolution ^{13}C NMR spectroscopy, Anal. Chem. 70 (1998) 2454–2458.
[46] G. Schlotterbeck, A. Ross, R. Hochstrasser, H. Senn, T. Kuhn, D. Marek, O. Schett, High-resolution capillary tube NMR. A miniaturized 5-μL high-sensitivity TXI probe for mass-limited samples, off-line LC NMR, and HT NMR, Anal. Chem. 74 (2002) 4464–4471.
[47] R. Subramanian, M.M. Lam, A.G. Webb, RF microcoil design for practical NMR of mass-limited samples, J. Magn. Reson. 133 (1998) 227–231.
[48] M.E. Lacey, R. Subramanian, D.L. Olson, A.G. Webb, J.V. Sweedler, High-resolution nmr spectroscopy of sample volumes from 1 nL to 10 μL, Chem. Rev. 99 (1999) 3133–3152.
[49] Hans W. Spiess, NMR spectroscopy: pushing the limits of sensitivity, Angew. Chem. Int. Ed. 47 (2008) 639–642.
[50] D. Sakellariou, G.L. Goff, J.F. Jacquinot, High-resolution, high-sensitivity NMR of nanolitre anisotropic samples by coil spinning, Nature 447 (2007) 694–697.
[51] E. Kupče, R. Freeman, Optimized adiabatic pulses for wideband spin inversion, J. Magn. Reson., Ser. A 118 (1996) 299–303.
[52] E. Kupče, R. Freeman, Compensated adiabatic inversion pulses: broadband INEPT and HSQC, J. Magn. Reson. 187 (2007) 258–265.
[53] A.M. Torres, R.E.D. McClung, J-compensated DEPT sequences, J. Magn. Reson. (1969) 92 (1991) 45–63.
[54] M.H. Levitt, G. Bodenhausen, R.R. Ernst, The illusions of spin decoupling, J. Magn. Reson. (1969) 53 (1983) 443–461.
[55] S.V. Dvinskikh, R. Sitnikov, I. Furó, ^{13}C PGSE NMR experiment with heteronuclear dipolar decoupling to measure diffusion in liquid crystals and solids, J. Magn. Reson. 142 (2000) 102–110.
[56] M.D. Pelta, G.A. Morris, M.J. Stchedroff, S.J. Hammond, A one-shot sequence for high-resolution diffusion-ordered spectroscopy, Magn. Reson. Chem. (2002) S147–S152.
[57] G.A. Morris, Reference deconvolution, in: D.M. Grant, R.K. Harris (Eds.), Encyclopedia of Nuclear Magnetic Resonance, vol. 9, John Wiley and Sons, Ltd., 2002, pp. 125–131.
[58] M. Nilsson, The DOSY Toolbox: a new tool for processing PFG NMR diffusion data, J. Magn. Reson. 200 (2009) 296–302.
[59] A.M. Gil, I. Duarte, E. Cabrita, B.J. Goodfellow, M. Spraul, R. Kerssebaum, Exploratory applications of diffusion ordered spectroscopy to liquid foods: an aid towards spectral assignment, Anal. Chim. Acta 506 (2004) 215–223.