Matrix-Assisted Diffusion-Ordered Spectroscopy: Application of surfactant solutions to the resolution of isomer spectra

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Abstract

The component spectra of a mixture of isomers with nearly identical diffusion coefficients cannot normally be distinguished in a standard diffusion-ordered spectroscopy (DOSY) experiment, but can often be easily resolved using matrix-assisted DOSY (MAD), in which diffusion behaviour is manipulated by the addition of a co-solute such as a surfactant. Relatively little is currently known about the conditions required for such a separation, for example how the choice between normal and reverse micelles affects separation, or how the isomer structures themselves affect the resolution. The aim of this study was to explore the application of sodium dodecyl sulphate (SDS) normal micelles in aqueous solution and sodium 1,4-bis(2-

ethylhexyl)sulfosuccinate (AOT) aggregates in chloroform, at a range of concentrations, to the diffusion resolution of some simple model sets of isomers such as monomethoxyphenols and short chain alcohols. It is shown that SDS micelles offer better resolution where these isomers differ in the position of a hydroxyl group, while AOT aggregates are more effective for isomers differing in the position of a methyl group. For both normal SDS micelles and the less well-defined AOT aggregates, differences in the resolution of the isomers can in part be rationalised in terms of differing degrees of hydrophobicity, amphiphilicity and steric effects.

Introduction

NMR spectroscopy is the first choice technique for structure elucidation of pure materials in solution,[1] but for mixtures it is often difficult or even impossible to assign resonances to an individual species. Techniques such as HPLC, HPLC-NMR and HPLC-NMR-MS, which physically separate the components present in a mixture, are generally used for this purpose. These chromatography-based methods require specialist equipment, and they are not applicable to intact mixtures, which is of particular importance e.g. when studying interactions between species or when volatile compounds are present.[2-6]

Volatile compounds are common in mixtures from fermentation processes, where alcohols are the most important components.[7-11] Alcohols containing four, five and six carbon atoms are the most abundant odour and flavour components of fermentation beverages.[7] In addition to such volatile compounds, some phenolic derivatives can also be found as products of fermentation processes.[12]

Analytical methodologies such as Diffusion-Ordered Spectroscopy[13,14] (DOSY), that involve only a virtual separation (i.e. the signals from different compounds are disentangled without the need for physical separation), can be applied to volatile samples as an alternative to traditional techniques. The advantages of such virtual separation techniques include simplicity, ease of sample preparation, and economy; they also avoid the need to combine expertise in two distinct areas.

DOSY[15-17] allows NMR signals of different species to be distinguished by virtue of their different diffusion behaviour. DOSY techniques are typically applied to mixtures containing species of different sizes (hydrodynamic radii) and hence different diffusion coefficients. The analysis of mixtures of species of similar size (e.g. isomers) by conventional DOSY is difficult and often impossible.[18] However, it has been shown[19-33] that diffusion behaviour in DOSY experiments can be manipulated by adding a co-solute or co-solvent. In principle, the use of surfactants (and/or other co-solvents) in DOSY could afford the NMR spectroscopist the same degree of freedom to separate *signals* as is enjoyed in the use of liquid chromatography to separate *species*. Thus, for example, surfactants can be used as co-solutes for the systematic manipulation of diffusion resolution, changing the criteria by which molecules are differentiated in a DOSY experiment, but such methods have to date attracted surprisingly little attention.[19,27-29]

It was shown recently[30] that SDS micelles can be used as separation agents to distinguish between the isomers of methoxyphenol in DOSY experiments. Successful resolution of isomer spectra is seen over a very wide range of concentrations of solutes and of surfactant. Resolution is even seen in some cases at surfactant concentrations below the normal critical micelle concentration (*cmc*) and in solutions where the

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surfactant concentration is significantly less than that of the solutes, the presence of solute decreasing the concentration of surfactant needed for micelles to form.

While micellar surfactant systems as aids to signal resolution in diffusion-ordered NMR spectroscopy are only just beginning to be exploited, their use in other fields such as capillary electrophoresis is well-established (see e.g. reference 34). There is an extensive literature on the interactions between solutes and micelles; slightly confusingly, the topic is often referred to as "solubilization". While a strict definition restricts the use of this term to the dissolution by a surfactant system of a material that is otherwise insoluble or only sparingly soluble (see e.g. references 35-37 and references therein) – i.e. to the case where solutes are in saturated solution in the solvent phase – it is now often used in the much looser sense of the study of solute – micelle interactions irrespective of the solubility of the solute in the solvent.[38] NMR has played a major part in building the understanding of solute-micelle interactions.[35,36,39]

In the present study two types of system, methoxyphenols and medium chain length alcohols, were investigated. The behaviour of methoxyphenol isomers in $CDCl_3$ solutions containing AOT aggregates is reported, and the results are compared with those for aqueous SDS micelles. SDS in water forms well-characterised, large, relatively monodisperse micelles. AOT in chloroform, in contrast, forms much smaller aggregates for which the term "reverse micelles", while commonly used, probably exaggerates the degree of order. For the alcohols a systematic investigation of the range of concentrations over which diffusion resolution is obtained using normal SDS and AOT aggregates is reported for isomeric mixtures containing respectively 1- and 2-butanol, 2-methyl-1-butanol, 3-methyl-1-butanol and 3-methyl-2-butanol, 1-, 2- and 3-pentanol, and 2-methyl-1-pentanol and 4-methyl-1-pentanol. The binding of short chain

alcohols, including many of those studied here, to aqueous SDS micelles at high surfactant concentration (229 mM) has previously been investigated by Stilbs.[40] SDS micellisation can be disrupted by short chain alcohols at high concentration,[41,42] but here the total alcohol concentrations remained too low for such effects to be seen.

Experimental

All measurements were carried out non-spinning on a 400 MHz Varian INOVA spectrometer, using a 5 mm indirect detection probe equipped with a *z*-gradient coil producing a nominal maximum gradient of 30 G cm^{-1}. DOSY data were acquired using the Oneshot pulse sequence[43] with a total diffusion-encoding pulse duration δ of 5 ms, a diffusion delay Δ of 60 ms and 10 nominal gradient amplitudes ranging from 3.0 to 27.3 G cm^{-1}, chosen to give equal steps in gradient squared; each FID was acquired using 32k data points. The experiments were carried out at a nominal probe temperature of 25 °C for SDS samples, with standard VT regulation. For AOT samples experiments were carried out without active temperature regulation, at the nominal probe quiescent temperature of 19 ± 1 °C, to avoid convection in the $CDCl_3$ solutions.

DOSY spectra were constructed in the DOSY Toolbox[44] by standard methods,[15,16] using fitting to a modified Stejskal-Tanner equation parameterized to take into account the effects of pulsed field gradient non-uniformity.[16,45] Reference deconvolution[46] was used to correct for instrument inconsistencies,[47,48] with Gaussian target lineshapes chosen to optimize the resolution of signals. For the methoxyphenols, diffusion coefficients were obtained using the proton signals of the methoxy groups or, where the latter are overlapped, signals of aromatic protons. For the alcohols the protons

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alpha to the hydroxyl group were used, in each case because the signals concerned were well-resolved with no overlap.

All chemicals used in this study are commercially available and were used without further purification. Stock solutions for all compounds, SDS and AOT were prepared in D_2O and in $CDCl_3$, and were diluted as necessary to obtain the concentrations used in this study; the concentration ratio [AOT]:[H_2O] was maintained at approximately 1:1 throughout to keep the AOT aggregate composition consistent. TMS and TSP [sodium 3-(trimethylsilyl)-1-propanesulfonate] were used as chemical shift reference for $CDCl_3$ and D_2O samples respectively.

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Results

Simple spectra with sharp lines for all species were seen for all the samples studied, confirming that solutes (methoxyphenols and short chain alcohols), AOT and SDS all remain throughout in fast exchange on the chemical shift timescale between free and micellar/aggregate solution. The DOSY spectra for the *ortho*-, *meta*- and *para*-methoxyphenol isomers in normal $CDCl_3$ solution show similar diffusion coefficients for all three isomers, as is the case in D_2O solution.[30] As with D_2O, however, when DOSY spectra were obtained for a solution containing methoxyphenol isomers and AOT aggregates in $CDCl_3$, significant differentiation in diffusion coefficient was observed between isomers (Fig. 1). (At this composition the methoxy signals for the *meta* and *para* isomers are partially overlapped, and, as noted above, the diffusion coefficients were determined using the aromatic signals.)

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Results were fitted to a simple, if limited, model in which it is assumed that surfactant molecules S assemble to form aggregates S_n of uniform size, and that these in

turn associate with solute molecules A without the aggregation equilibrium being affected and with an association constant independent of the number of solute molecules bound.

$$nS \rightleftarrows S_n$$

$$A + S_n \rightleftarrows AS_n$$

$$A + AS_n \rightleftarrows A_2S_n$$

In such a model the bound $[A]_b/[A]_0$ and free $[A]_f/[A]_0$ solute fractions may be expressed in terms of a critical aggregate concentration or critical micelle concentration (*cmc*) for the surfactant, the total surfactant concentration $[S]_0$, and an association constant K defined in terms of the concentration $[S]_m = [S]_0 - cmc$ of surfactant monomer in aggregate form:

$$\frac{[A]_b}{[A]_0} = \frac{K([S]_0 - cmc)}{1 + K([S]_0 - cmc)}$$
$$\frac{[A]_f}{[A]_0} = \frac{1}{1 + K([S]_0 - cmc)} \qquad [1a,b]$$

Here the association constant K in terms of aggregate surfactant monomer concentration is equal to the K_S defined in chapter 1 of reference.[3] If, finally, the diffusion coefficient D_m of the aggregates is assumed to be unaffected by bound solute, the average surfactant and solute diffusion coefficients D_S and D_A may be expressed in terms of the corresponding free diffusion coefficients D_S^0 and D_A^0:

$$D_S = \frac{D_S^0 \, cmc + D_m([S]_0 - cmc)}{[S]_0}$$
$$D_A = \frac{D_A^0 + D_m K([S]_0 - cmc)}{1 + K([S]_0 - cmc)} \qquad [2a,b]$$

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This model is quite a reasonable, if limited, approximation for aqueous solutions containing SDS, for which well-defined micelles are formed and the assumption of constant aggregate size is appropriate over the concentration range of interest here, but a much less good approximation for AOT, which forms small aggregates of variable size and does not show a simple *cmc*. It also does not take into account obstruction effects, which can be significant at high surfactant concentrations. For the purposes of comparing solute binding affinities for analytical purposes, however, the model performs adequately for both systems and provides a useful framework for the quantitative description of the effects of the micellar matrix on solute diffusion. If experimental data on surfactant solutions in the absence of other solutes are used to find the quantities D_S^0, D_m and *cmc*, the only free parameters for fitting experimental solute diffusion data are the free diffusion coefficient D_A^0 and the apparent association constant K.

The effect of AOT concentration on the diffusion of the methoxyphenol isomers was investigated using six samples containing 20 mM of each of the three isomers, varying the concentration of AOT from 52 to 310 mM. All six samples were well above the two *cmc*s reported previously for AOT in chloroform (0.8 mM obtained by both UV and NMR,[49] and 6.5 mM by NMR[50]). The diffusion coefficients for the methoxyphenol isomers are plotted as a function of AOT concentration in Fig. 2a. Increasing the AOT concentration leads to a significant decrease in diffusion coefficient for *meta*- and *para*-methoxyphenol isomers, while a lesser decrease is observed for the *ortho* isomer. The decrease in diffusion coefficient for TMS is less than that for the methoxyphenols, confirming that the decrease in diffusion coefficient for the latter solutes is at least in part due to association with AOT aggregates rather than to viscosity

or obstruction effects. The strongest association (i.e. the lowest diffusion coefficient) is seen for *m*- and *p*-methoxyphenols, while the weakest is observed for *o*-methoxyphenol; this behaviour is opposite to that seen for the methoxyphenol isomers in aqueous SDS, where the degree of separation between isomers is greater than in AOT.[30]

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The dotted line for D_{AOT} in Figure 2a shows the behaviour predicted assuming an effective *cmc* of 6.5 mM, and free and aggregate diffusion coefficients of 3.65×10^{-10} m^2 s^{-1} and 1.5×10^{-10} m^2 s^{-1}. Measurements of the effect of AOT concentration on diffusion coefficient in $CDCl_3$ carried out for this work showed a limiting diffusion coefficient of $3.65 \pm 0.1 \times 10^{-10}$ m^2 s^{-1} below 0.8 mM, but no clear *cmc* and aggregation behaviour that was very dependent on water concentration. The estimated aggregate diffusion coefficient of 1.5×10^{-10} m^2 s^{-1} was therefore obtained by optimising the fit of the experimental data for AOT in the mixtures studied here, with approximately equal AOT and water concentrations, rather than in dry chloroform. As noted above, the associative model is a poor description of the aggregation behaviour of AOT in chloroform, as reflected in literature values for the *cmc* that vary over almost an order of magnitude. The *cmc* used here is the higher of the two values previously reported by NMR,[48] but the experimental data show that a sharp *cmc* is a poor representation of the aggregation behaviour. As expected, the variable aggregate sizes for AOT lead to significant differences between the calculated and experimental values for the average surfactant diffusion coefficient, but the differences are sufficiently small not to perturb the fitting of the solute diffusion coefficients D_A, and hence the quantitative estimation of binding affinity, too greatly.

When the concentration of AOT was increased from 51 mM to 206 mM, deshielding was observed for the OH groups, the chemical shift changing from 5.30 to

6.54 ppm ($\Delta\delta$ = 1.24 ppm) for *m*-methoxyphenol and from 5.67 to 6.93 ppm ($\Delta\delta$ = 1.26 ppm) for *para*-methoxyphenol. The chemical shift change for *ortho*-methoxyphenol was much smaller than that observed for the *meta* and *para* isomers, from 5.74 to 6.08 ppm ($\Delta\delta$ = 0.34 ppm), providing further evidence that the *meta* and *para* isomers associate more strongly with AOT, and suggesting that this association involves some degree of penetration of the OH group into the aggregate.

The effect of varying the solute:cosolute concentration ratio at constant AOT concentration was investigated by measuring diffusion coefficients in a further six samples (Fig. 2b) in which the concentrations of the three methoxyphenol isomers were increased from 19 to 114 mM, while keeping the concentration of AOT fixed well above the *cmc* at 52 mM. Again the separation ratio between the isomers was almost constant over the concentration range studied (Fig. 2b). Interestingly, Figure 2b shows that the simple model described above, which predicts average solvent diffusion coefficients independent of solute concentration, performs well even when the total solute concentration (i.e. 3× the concentration of the individual solutes) approaches that of the surfactant.

In an attempt to improve the separation between *meta*- and *para*-methoxyphenol isomers, the solvent used to obtain the AOT aggregates was changed. Normally, the "core" solvent is water; however recently[51] it has been demonstrated that aggregates or reverse micelles can also be obtained using non-aqueous polar solvents such as formamide, dimethylformamide, ethylene glycol and glycerol. Various different concentrations of water, ethylene glycol and glycerol were used to obtain AOT aggregates in the present study, and almost the same degree of separation (around 3%) between *meta*- and *para*-methoxyphenol isomers was found throughout. This suggests

that, under the present conditions, the hydrophilic core of the aggregate is not a dominant influence on association, with the rider that the solutes may rather be associating with the outer layer.

As noted earlier, volatile compounds are common in mixtures from fermentation processes, where alcohols are the most important components. Short chain alcohols are responsible for the odour and flavour of fermentation beverages, so their identification during the fermentation process is a key step in assessing the quality of final product. Matrix-Assisted DOSY can be applied to volatile samples as an alternative to traditional techniques. As a test, a set of short chain alcohols was chosen and a systematic investigation of the range of concentrations over which diffusion resolution is obtained using normal SDS micelles and AOT aggregates is reported.

The effect of SDS concentration on the diffusion of the 1-butanol and 2-butanol isomers was investigated using eight samples containing 20 mM and 24 mM of each isomer, respectively, varying the concentration of SDS from 6.3 to 194 mM. The first two samples were around the critical micelle concentration (*cmc*) of SDS in D_2O of ca. 7 mM[52] while the others were well above the *cmc*.

The apparent diffusion coefficients for butanol isomers are plotted as a function of SDS concentration in Fig. 3a. Increasing the SDS concentration leads to a significant decrease in diffusion coefficient for both butanol isomers. The decrease in diffusion coefficient for TSP is less than that for the butanols, confirming again that at least part of the decrease in diffusion coefficient for the alcohols is due to association with SDS micelles rather than to viscosity or obstruction effects. It is clear looking at the samples with high SDS concentration that stronger association (i.e. lower diffusion coefficient) is seen for 1-butanol than for 2-butanol. In the absence of SDS the opposite behaviour is

observed, 1-butanol diffusing slightly faster than the 2-butanol isomer. Thus the two diffusion coefficients approach each other for SDS concentrations between 12 and 25 mM and then separate again, in the opposite order, at higher SDS concentration. As expected for SDS, which shows a sharp *cmc* and for which the associative model works well, the values seen for SDS are in good agreement with those calculated from the literature *cmc* of 7 mM. The close agreement down to low [S] shows that the solutes neither perturb micellisation significantly nor advance its onset.

A clear differentiation between 1-butanol and 2-butanol isomers was also found using AOT aggregates in $CDCl_3$ for six samples containing 47 mM of each isomer, varying the concentration of AOT from 24 to 428 mM. All six samples were well above the *cmc* values reported for AOT in chloroform.[49,50] The diffusion coefficients for butanol isomers are plotted as a function of AOT concentration in Fig. 3b. As before, increasing the AOT concentration leads to a significant decrease in diffusion coefficient for both isomers, and the smaller decrease in diffusion coefficient for TMS confirms that the changes in butanol diffusion are due in part to association with AOT aggregates. Association is stronger for 1-butanol, as in aqueous SDS solution, although the reasons for this are likely to be different in the two different surfactant systems. The maximum difference in diffusin coefficient seen was 9%, compared to 13% for SDS solution. Once again, the poor adherence to the associative model leads to experimental AOT diffusion coefficients rather higher than those predicted by the model, but as previously this does not significantly perturb the fitting of the solute *D* values. As Figure 3 shows, the spectra of these isomers can quite easily be differentiated using either aqueous SDS micelles or AOT aggregates in $CDCl_3$. Of the two systems, aqueous SDS solution is generally preferable to AOT in chloroform for matrix-assisted DOSY experiments,

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primarily because water convects much less readily than chloroform, but also for cost reasons and because aqueous stock solutions of surfactant evaporate much more slowly than those in chloroform.

The same methodology was applied to a sample containing 1-pentanol, 2-pentanol and 3-pentanol isomers. However, in this case the differentiation in aqueous SDS solution between pentanol isomers is more marked than for the butanol isomers, as shown by the results in Figure 4. The fit to the associative model follows the same path as previously, except that the solutes in this case cause a clear reduction in the SDS *cmc*. The effect of this on the fitting of the solute diffusion coefficients is very small, as only a very small proportion of the solute molecules are involved at such low micelle concentrations. The *cmc* in the presence of the pentanols is straightforward to determine; fitting the experimental surfactant diffusion coefficients to Equation 2a with D^0_m and *cmc* allowed to vary gives a *cmc* of 4.6 mM. The solute binding seen in chloroform/AOT solution was, as for the butanols, qualitatively similar to that in water/SDS but slightly weaker.

Similar behaviour was found when MAD experiments were applied to differentiate between 2-methyl-1-butanol, 3-methyl-1-butanol and 3-methyl-2-butanol isomers, using aqueous SDS micelles and $CDCl_3$ AOT aggregates (Fig. 5). For aqueous SDS solution (Fig. 5a) the strongest association between micelles and methyl-butanol isomers occurs for species where the OH group is located at the end of the carbon chain (2-methyl-1-butanol and 3-methyl-1-butanol), while the weakest is observed for 3-methyl-2-butanol.

Only very slight differentiation between 2-methyl-1-butanol and 3-methyl-1-butanol is seen here when using SDS micelles (Fig. 5a), though the secondary alcohol is

well resolved; once again, the solutes significantly advance the onset of micellisation for SDS. All three isomers (2-methyl-1-butanol, 3-methyl-1-butanol and 3-methyl-2-butanol) can be differentiated using $CDCl_3$ AOT aggregates (Fig. 5b), although the differences are small. The somewhat greater ability of AOT aggregates to differentiate between the 2-methyl-1-butanol and 3-methyl-1-butanol isomers may be attributable to the bulky structure of the AOT polar head group, which contains two carbonyl ester groups and a sulphate group bonded to an asymmetric carbon, posing greater steric demands than the head group of SDS. Experiments were also performed with 2-methyl-1-pentanol and 4-methyl-1-pentanol, using aqueous SDS micelles and $CDCl_3$ AOT aggregates. For both types of solution, 2-methyl-1-pentanol and 4-methyl-1-pentanol showed similar discrimination to that observed (Fig. 5) for 2-methyl-1-butanol and 3-methyl-1-butanol.

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The apparent association constants K and solute diffusion coefficients D found by fitting of the experimental data are listed in Tables 1 and 2, along with logP data[53] on the octanol:water partition coefficients of the solutes investigated.

Discussion

Comparison between the data presented here for methoxyphenol mixtures in AOT/$CDCl_3$ solutions and those presented earlier[30] for SDS/D_2O solutions shows both that the factors determining the strength of association between solute and micelles/aggregates are different in the two media, and that both media show useful diffusion resolution between isomers (albeit only partial in the case of AOT) over a wide range of solute and surfactant concentrations.

The range of chemical space covered in the study of alcohol mixtures allows some of the factors determining association to be explored in greater detail. The relative affinities of the different solutes investigated for SDS micelles and for AOT aggregates are correlated in Fig. 6 with experimental and calculated logP values. The latter provide a useful quantitative index of relative hydrophilicity/phobicity. If the association between solutes and micelles were entirely determined by the thermodynamic drive to partition between environments of different hydrophobicity, all points for a given aggregate type would be expected to lie along a straight line of unit slope.

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It can be seen immediately that there is indeed an approximately linear general correlation between logP and logK for alcohols in SDS solution, but that there is essentially no correlation for AOT solutions. Taken together with the observation noted above that the association of these solutes with AOT aggregates is relatively insensitive to the polar medium providing the core of the aggregates, this suggests that medium effects *per se* are not the primary determinant of solute binding in such systems, but that more specific interactions with the AOT head group are involved. This suggestion is reinforced by the sensitivity to alkyl chain branching and to the position of the hydroxyl group, which have the effect of reducing binding as the steric demands they impose increase.

Steric effects also play a clear role in modulating medium effects in the association between alcohols and SDS micelles, causing branched chain and secondary alcohols to show lower association constants than those for the straight chain primary alcohols. The effects of increasing chain length and of chain branching on binding of alcohols to SDS micelles have previously been rationalised by Stilbs[38] in terms of an increment in binding free energy of 2.6 kJ mol^{-1} per CH_2 unit, and of packing

constraints in the micellar environment. The changes in binding between 1-butanol and 1-pentanol and between 2-methyl-1-butanol and 2-methyl-1-pentanol are in almost exact agreement with the previous observations. In the case of SDS micelles, a third factor comes into play at low surfactant concentrations. While the SDS diffusion data in Fig. 3 show good agreement with diffusion coefficients calculated using the known *cmc* and diffusion coefficients for free SDS and for SDS micelles, the data of Figs. 4 and 5 show clearly that the presence of the longer chain alcohols leads to an earlier onset of micellisation. Thus in addition to logP and stereochemistry, the degree of amphiphilia of solutes also plays a part in determining the extent to which the diffusion coefficients of different species are modulated by the presence of surfactant.

The main practical consequences of the observations reported here for analytical applications are twofold. First, differences in diffusion behaviour caused by the presence of surface-active agents in solutions of mixtures are seen over a very wide range of relative and absolute surfactant concentrations. Thus matrix-assisted DOSY using surfactant solutions (sometimes termed micelle-assisted DOSY) is likely to be relatively robust with respect to experimental conditions (as indeed are other analytical methods that exploit association between solutes and surfactant aggregates). Second, the multifactorial relationship between solute structure and association strength bodes well both for the use of matrix-assisted DOSY for distinguishing the NMR spectra of isomeric species, and more generally for its versatility and specificity as an analytical tool.

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Table 1. Experimental values for apparent association constants K and diffusion coefficients D for alcohols in aqueous SDS solution, obtained by fitting experimental data using the simple model described in the text, with literature or calculated values of logP.

Solute	K	$D/(10^{-10}\ m^2\ s^{-1})$	logP
1-butanol	4.9 ± 0.3	7.4 ± 0.4	0.84[a]
2-butanol	3.4 ± 0.2	7.2 ± 0.4	0.65[a]
1-pentanol	14.6 ± 0.6	6.2 ± 0.3	1.51[a]
2-pentanol	9.0 ± 1.3	6.1 ± 0.3	1.25[a]
3-pentanol	7.4 ± 1	6.1 ± 0.3	1.21[a]
2-methyl-1-butanol	11 ± 1	6.7 ± 0.3	1.37[b]
3-methyl-1-butanol	12 ± 1	6.7 ± 0.3	1.28[a]
3-methyl-2-butanol	6.9 ± 0.7	6.7 ± 0.3	1.28[a]
2-methyl-1-pentanol	31 ± 5	6.0 ± 0.3	1.78[b]
4-methyl-1-pentanol	36 ± 4	6.0 ± 0.6	1.75[a]

[a] Experimental value of logP from reference 53; [b] value estimated using ChemDraw 7.0 (CambridgeSoft, Cambridge, MA, USA)

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Table 2. Experimental values for association constants K and diffusion coefficients D for methoxyphenols and alcohols in chloroform solution containing AOT, obtained by fitting experimental data using the simple model describe in the text.

Solute	K	$D/(10^{-10}\ m^2\ s^{-1})$
o-methoxyphenol	2.3 ± 0.3	17 ± 1
m-methoxyphenol	8.4 ± 1.7	16 ± 1
p-methoxyphenol	7.9 ± 1.4	16 ± 1
1-butanol	2.4 ± 0.3	19 ± 1
2-butanol	1.9 ± 0.2	20 ± 1
1-pentanol	3.0 ± 0.4	17 ± 1
2-pentanol	2.6 ± 0.5	17 ± 1
3-pentanol	2.2 ± 0.4	18 ± 1
2-methyl-1-butanol	1.7 ± 0.1	17 ± 1
3-methyl-1-butanol	2.0 ± 0.2	17 ± 1
3-methyl-2-butanol	1.3 ± 0.2	17 ± 1

Figure Captions

Figure 1. 400 MHz ^{1}H Oneshot[40] DOSY spectrum, with the least attenuated 1D spectrum shown at the top, for a sample containing 20 mM of each of the methoxyphenol isomers and 52 mM AOT in $CDCl_3$, with TMS as reference. The signals for the 1,2-, 1,3- and 1,4-methoxyphenol isomers are labelled *ortho*, *meta* and *para* respectively.

Figure 2. a) diffusion coefficient as a function of AOT:D_2O (1:1.2) concentration for a $CDCl_3$ solution containing 5 mM TMS and 20 mM of each of the methoxyphenol isomers; **b)** diffusion coefficient as a function of the concentration of each of the methoxyphenol isomers for a $CDCl_3$ solution containing 5 mM TMS and 52 mM AOT. Error bars show ±2× the standard error estimated from the fit of the experimental peak heights to the modified Stejskal-Tanner equation. Solid lines for solute diffusion coefficient represent fits to Equation 2b, dotted lines the calculated surfactant diffusion coefficient from Equation 2a, for the simple model described in the text. Experimental D values for the solutes were fitted to Equation 2b, varying D^0_A and K but keeping D^0_S, D^0_m and *cmc* fixed at the values given in the text.

Figure 3. **a)** diffusion coefficients as a function of SDS concentration for a D_2O solution containing 4.5 mM TSP, 18 mM 1-butanol and 20 mM 2-butanol; **b)** diffusion coefficients as a function of AOT concentration for a $CDCl_3$ solution containing 5 mM TMS and 47 mM 1-butanol and 2-butanol. Error bars show ±2× the standard error estimated from the fit. Solid lines for solute diffusion coefficient represent fits, dotted

lines the calculated surfactant diffusion coefficient, for the simple model described in the text.

Figure 4. **a)** diffusion coefficients as a function of SDS concentration for a D_2O solution containing 5 mM TSP, 16 mM 1-pentanol, 16 mM 2-pentanol and 17 mM 3-pentanol isomers; **b)** diffusion coefficients as a function of AOT concentration for a $CDCl_3$ solution containing 5 mM TMS and 38 mM each of 1-pentanol, 2-pentanol and 3-pentanol. Error bars show ±2× the standard error estimated from the fit. Solid lines for solute diffusion coefficient represent fits, dotted lines the calculated surfactant diffusion coefficient, for the simple model described in the text.

Figure 5. **a)** diffusion coefficients as a function of SDS concentration for a D_2O solution containing 5 mM TSP, 16.8 mM 3-methyl-2-butanol, 14.8 mM 2-methyl-1-butanol and 16.8 mM 3-methyl-1-butanol isomers; **b)** diffusion coefficients as a function of AOT concentration for a $CDCl_3$ solution containing 5 mM TMS and 53 mM of each 3-methyl-1-butanol, 3-methyl-2-butanol and 2-methyl-1-butanol isomers. Error bars show ±2× the standard error estimated from the fit. Solid lines for solute diffusion coefficient represent fits, dotted lines the calculated surfactant diffusion coefficient, for the simple model described in the text.

Figure 6. Scatter plot showing the decadic logarithm of association constant *K* versus logP for the alcohol solutes listed in Tables 1 and 2. Open symbols denote data for SDS solutions, filled for AOT; triangles, squares, pentagons and circles denote straight chain primary, 2-hydroxy straight chain, 3-hydroxy straight chain, and branched alcohols

respectively. The dotted line is of unit slope; the solid line, showing the result of linear regression of the data for water/SDS solutions, has a slope of 1.1 and a correlation coefficient of 95%.