Application of Diffusion-Ordered Spectroscopy (DOSY) as a Solvent Signal Filter for NMR in Neat Ionic Liquids

Ralf Giernoth*[a] and Dennis Bankmann[a]

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The use of common, that is nondeuterated, ionic liquids for NMR spectroscopic purposes as the only solvent causes large signals arising from solvent resonances. Ionic liquids (ILs) with long side chains possess signals throughout the spectral range of protons, thus rendering simple solvent signal suppression techniques ineffective. Here we present solvent signal suppression based on diffusion-ordered NMR spectroscopy (DOSY). In contrast to the well established usage of DOSY to filter water resonances from biological systems, here we filter out the slower moving molecules. This method allows in many cases for the complete removal of the solvent signals from ^{1}H spectra of solutes and may become a useful tool for in situ studies of reactions performed in ILs.

Introduction

Although room temperature ionic liquids[1–4] (ILs) have already found their place in chemical research and industry as novel and "green" solvents for some time now, analytical methods for use in pure ILs or IL reaction mixtures, that is, without additional solvent, are still rather scarce. Attempts have been made using mass spectrometry,[5–8] infrared spectroscopy[9,10] and NMR spectroscopy. The latter has been applied to investigate self-diffusion coefficients and viscosities,[11–13] ion-pair formation,[14] proton and ion conductance,[15,16] the structral consequences of water traces[17] or dissolved substances[18] and in high-pressure systems.[19,20] Recently, we presented the use of NMR spectroscopy as an in situ technique suitable for investigations on ionic liquid reactivity and purity as well as on solutes in pure ILs.[21] We demonstrated that resolution and sensitivity are comparable to that in conventional solvents.

NMR spectroscopy can be used right away for the study of the solvent *itself* with no need for special preparation or deuteration. Recently and in a different context, the use of fully protonated samples of organic substances has been demonstrated in several papers concerning "no-D" NMR[22] and focussing on NMR titrations. The authors claim that solvent signals do not interfere with the measurement. This statement remains true as long as concentrations are sufficiently high and signal overlap is not present.

Investigations on solutes in concentrations typical for reactions in ILs, however, *do* face the complications of dominant solvent signals due to the absent deuteration in common ionic liquids. While deuteration of the ring protons of imidazolium-based ILs can readily be achieved,[23] the side chains mark a substantial barrier towards perdeuterated ILs. A recent publication[24] proposed the use of deuterated substrates and ^{2}D-spectroscopy. This method, however, requires selectively or fully deuterated substrates, which may be unavailable, tedious to synthesize, or unreasonably expensive. In summary, solvent signal suppression techniques suitable for neat ionic liquid solvents can greatly enhance the applicability of NMR investigations in these media.

Results

As we already noted in our earlier publication,[21] solvent signal filtering based on the T_1 values is not feasible due to the similarity between solvent and solute relaxation times. The fact that all ILs exhibit a multitude of signals throughout the whole spectral range of protons precludes the use of selective pulses for complete suppression of the solvent signals. The straightforward use of difference spectroscopy remains possible, but this method suffers from the generally high discrepancy between solvent and solute signal intensities, often leaving artifacts of the solvent signals comparable in size to the solute signals. Therefore, one has to turn to more advanced techniques of solvent suppression.

The introduction of diffusion spectroscopy,[25] and more recently, diffusion-ordered spectroscopy (DOSY)[26,29,30] allows for determination of diffusion coefficients in a noninvasive manner and for discrimination between multiple species in the sample based on their physical, that is diffusion, properties. Thus the separation does not occur along the resonance frequency axis or through the resonance process itself, allowing for solvent/solute signal overlap and removal of all solvent signals (no selective pulses needed) respec-

[a] Institute of Organic Chemistry, University of Cologne, Greinstr. 4, 50939 Köln, Germany
Fax: +49-221-4705102
E-mail: Ralf.Giernoth@uni-koeln.de

tively. The comparatively high viscosities of ILs can be used to the experimentators advantage by separating solvent and solute signals along the diffusion coefficient axis. In contrast to established techniques,[27,28] the signals to be filtered belong to the *slower* moving species. In the former cases, the stronger attenuation of the signals of fast moving molecules allows for simpler onedimensional experiments. We demonstrate here the use of pseudo-twodimensional experiments, from which the filtered 1D spectra of the solutes or the solvent may be extracted. The method that we apply to typical ionic liquids (Figure 1) is based on pseudo-twodimensional DOSY techniques,[29] employing bipolar LED[31,32] and STE[33] pulse sequences.

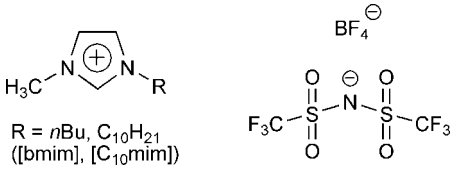

Figure 1. Ionic liquids used as NMR solvents in this work. These liquids are examples for short- as well as long-chain imidazolium ionic liquids and contain two of the most used anions: tetrafluoroborate and bis(trifluoromethylsulfonyl)amide (Tf_2N).

After optimization of gradient strength, delays and high power pulse lengths, a DOSY experiment is run with high resolution in the direct dimension (16 k points) and a comparatively low number of gradient increments (32 to 64), leading to acquisition times of ca. 2 min per experiment – a timescale suitable for studies of organic reactions in ILs. The data are then processed with the instrument vendor-supplied software. In the resulting pseudo-2D spectrum, solvent and solute(s) are separated along the diffusion axis (indirect axis).

The extraction of the solute spectrum is accomplished by summation of the rows (along the diffusion dimension) containing the solute but not the solvent signals. In cases of complete separation due to suitable differences in diffusion coefficients, solvent signals are completely absent from the solute spectrum. The whole process is illustrated in Figure 2. Since the suppression of the solvent signals does not rely on absolute values for the diffusion coefficients, no calibration of the gradient pulses needs to be done. The figures are therefore presented with arbitrary units on the logarithmic diffusion axis.

The power of this method becomes apparent in Figure 2 by the vanishing of solvent signals and the fact that the solute signals are almost free of distortions. As discussed above, the method is readily applicable, since the diffusion axis needs not be calibrated and no special sample preparation is needed.

The suppression and therefore the applicability of this method critically depends on suitable differences in diffusion coefficients between the solvent and the solute species. As the molecular size (or in cases of strong solvation interactions the solvodynamic radius) of the solute approaches that of the solvent, total suppression may not be attainable in this fashion. Solutes of the same geometric size or larger than the solvent tend to have diffusion coefficients very similar to the solvent and hence are not suitable for the application of this method. The detrimental effect of size similarities between solvent and solute can be clearly seen in Figure 3, which shows the pseudo-2D spectra of *N*-methylimidazole in [bmim]Tf_2N and [C_{10}mim]Tf_2N, respectively. While for the larger one total separation is attained, the signal separation is low in the IL with the short side chain. Furthermore, ionic solutes can be expected to have low diffusion coefficients due to their strong interactions with the IL anion.

Complications may also arise in cases with solvent/solute signal overlap, especially when concentrations and separation along the diffusion axis are low. The signals become blurred along the diffusion axis resulting in distortions or residual signals in the extracted solute spectra. In more severe cases, signals may be missing from the solute spectrum altogether.

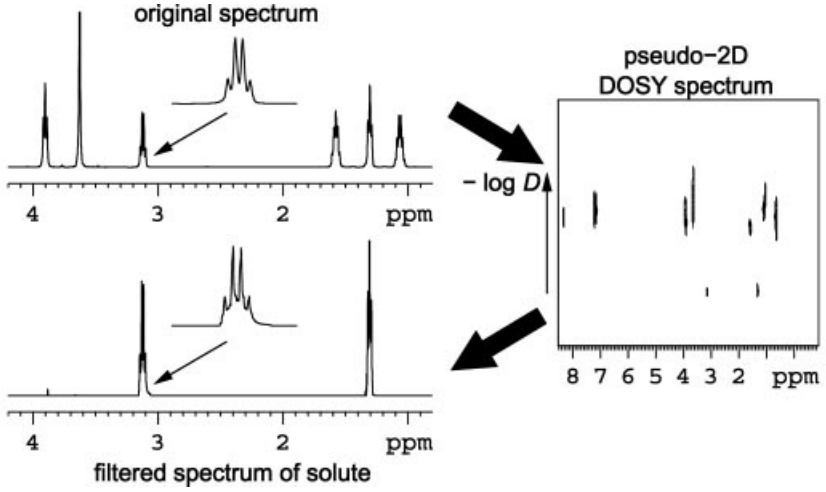

Figure 2. The process of solvent suppression using DOSY techniques demonstrated with ethyl bromide in [bmim]Tf_2N (ca. 0.2 M) employing the STE pulse sequence.

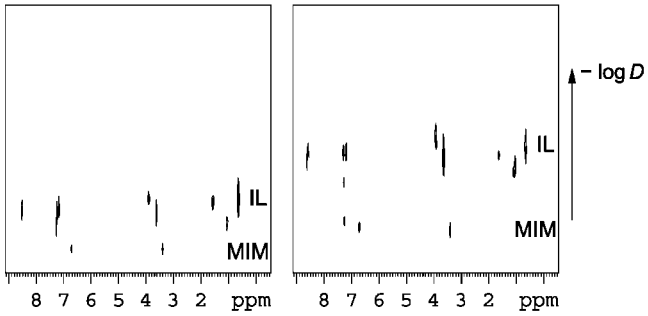

Figure 3. DOSY spectra of *N*-methylimidazole in the ionic liquids [bmim]Tf_2N (left) and [C_{10}mim]Tf_2N (right) (ca. 0.2 M) acquired with the BPLED pulse sequence.

Reaction Monitoring with DOSY Solvent Suppression

The features of the DOSY solvent suppression technique described above, especially the fast acquisition, suggest that it is viable to employ it in monitoring reactions in ionic liquids. To prove this point, we chose a reaction that was already monitored with deuterated substrates by Abu-Omar et al.,[24,34] the ternerisation of dimethylsulfide with methyl iodide.[35]

Figure 4 shows the progression of the reaction from 5 to 132 min, when almost no unreacted dimethyl sulfide is left. The three singlet signals of the reaction components, that is the two reagents (MeI, Me_2S) and the product (Me_3S^+), can be discerned, but of course are quite small compared to the solvent signals.[36]

When applying DOSY solvent suppression, the relative signal intensities almost reverse, that is hardly any solvent signals are left in the spectrum which is now clearly dominated by the two reagents (Figure 5). The method presented here may therefore be considered very suitable for the detection of small amounts of solutes in ILs. The possibility of doing these measurements during reactions makes this method a valuable one for the detection of reactive intermediates in ILs.

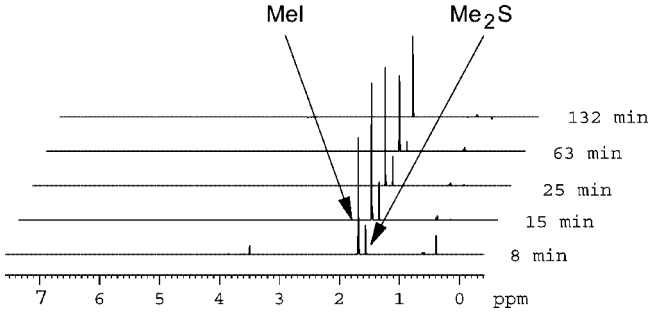

Figure 5. ^{1}H spectra of the ternerisation of Me_2S with MeI in [bmim]BF_4 with DOSY filtering using the BPLED pulse sequence.

It is interesting to note that the product cation, though geometrically quite small, exhibits a diffusion coefficient similar to that of the solvent, which may be attributed to solvation effects or contact ion pair formation. Therefore, the product does not show up in the filtered spectra.

Conclusions

Diffusion-ordered spectroscopy in many cases allows for the complete removal of IL solvent signals from proton spectra of solutes. Thereby, the need for expensive and tedious deuteration of the ionic liquid solvent is circumvented. The method may readily be expanded to include ^{2}D

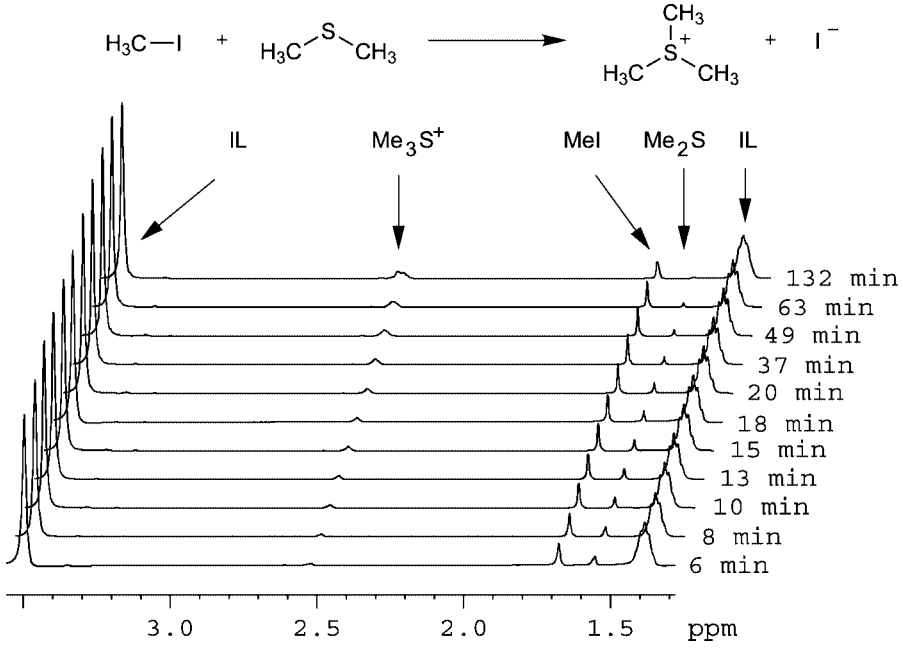

Figure 4. Time-dependent ^{1}H-NMR spectra of the ternerisation of Me_2S with MeI in the ionic liquid [bmim]BF_4.

and ^{19}F and may even be used for carbon NMR using DOSY-INEPT techniques.[37]

The prime limiting factor that remains is the solvodynamic radius of the solute. While the spectra of neutral molecules appreciably smaller than the solvent can be completely cleansed of solvent signals, the suppression becomes less complete for substances that approach the dimensions and therefore the diffusion coefficient of the IL solvent. In the case of molecules larger than the solvent, no suppression has been achieved so far.

The applicability of DOSY solvent suppression to reaction monitoring in ionic liquids has been demonstrated on an example from the literature, demonstrating it not be necessary to use deuterated solvents or reactands. The increasing availability of NMR spectrometers with high power gradient units and purpose-built diffusion probes will certainly widen the applicability and improve the quality of diffusion based solvent signal filtering. The technique demonstrated here has the potential to become a valuable tool in the course of in situ studies of solutes and reactions in ionic liquids.

Experimental Section

All experiments were carried out on a Bruker DRX500 spectrometer (^1H base frequency 500.13 MHz) using a 5-mm BBI 1H-BB-D Z-GRD probe. The experiments were performed at 298 K by using 5-mm NMR tubes (Norell 508-UP). The locking additive and shift standard were placed in 5-mm coaxial inserts.

The ionic liquids were synthesised according to literature procedures[38] and dried for 2 h at 70 °C under high vacuum.

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[34] The other reactions presented in that article have either not been carried out in pure ionic liquids (that is, without additional solvent) or with urea hydrogen peroxide, which in our experiments set free large amounts of gas, causing bubbles in the NMR tube and disrupting the acquisition.
[35] The reaction system consists of 24 μL (385 mmol, 4 equiv.) of methyl iodide, 7.2 μL of dimethyl sulfide (96 mmol, 1 equiv.) and 0.5 mL of the solvent, 1-butyl-3-methylimidazolium tetrafluoroborate ([bmim]BF_4). The fourfold excess was chosen so that the reaction would proceed cleanly towards completion. Concentrations were kept comparable to the original paper.
[36] It has to be noted that throughout the experiments, the solute signals are overpronounced compared with the solvent signals, that is, their integral ratio is larger than expected from stochiometry.
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