Investigation of an N· · · H hydrogen bond in a solid benzoxazine dimer by $^1$H–$^{15}$N NMR correlation techniques under fast magic-angle spinning

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Received 3 May 2001; Revised 18 May 2001; Accepted 1 June 2001

The N· · · H distance within the unusual hydrogen-bonding arrangement adopted by a pair of methyl-substituted benzoxazine dimers ($\text{C}_6\text{H}_3(\text{OH})_2\text{CH}_2\text{N(CH}_3\text{)}$) has been determined by solid-state NMR to be 194 ± 5 pm. This indicates that the proton is shared between the nitrogen and oxygen atoms, with a preference for an O–H rather than an N–H bond character. It is to be noted that a previous X-ray single crystal study was unable to localize the position of this hydrogen-bonded proton. The advanced solid-state NMR methods employed utilize REDOR-type recoupling under fast magic-angle spinning to recouple the heteronuclear $^1$H–$^{15}$N dipole–dipole interaction, such that rotor-encoded spinning-sideband patterns are obtained, the analysis of which yields the $^1$H–$^{15}$N dipole–dipole coupling and hence the N· · · H distance. Different designs of recoupling pulse sequences are discussed, which allow the experiment to be adapted to the system under investigation in terms of the required $^{15}$N or $^1$H chemical shift resolution, conventional ($^{15}$N) or inverse ($^1$H) detection as well as the importance of the perturbing influences of further spins. The chosen recoupling scheme employs inverse, i.e. $^1$H, detection, because it provides a dramatic increase in signal sensitivity, resulting in savings in measurement time by a factor of at least 20, as well as $^1$H chemical-shift resolution in the directly detected spectral dimension. This is the method of choice for cases such as this, where chemical shift resolution is not required in the $^{15}$N dimension. In addition, the perturbing effect of further protons on the N· · · H coupling of interest is minimized, such that a relatively long N· · · H distance can be determined despite the presence of several other couplings of comparable strength. Copyright © 2001 John Wiley & Sons, Ltd.

INTRODUCTION

Investigations into hydrogen-bonded structures, including self-organized and biologically relevant molecules, are being pursued in many disciplines of science.1,2 The motivating factor behind these studies is the structure stabilizing, or even structure-directing role played by hydrogen bonds, which is as yet not fully understood, and represents one of the current frontiers of scientific endeavour. The question addressed in this paper concerns the characterization of an unusual N· · · H–O hydrogen bond, through assessment of the $^{15}$N· · · H bond length, using advanced solid-state NMR methods. Whereas other studies focus on the measurement of short N· · · H bonding interactions in the region of 110 pm, our study demonstrates the ability of magic-angle spinning (MAS) and heteronuclear dipolar recoupling techniques to determine the length of a comparatively long hydrogen bond uniquely.

$^1$H solid-state NMR has developed into a versatile tool for the investigation of hydrogen-bonding structures in organic solids, and also in peptides.3–5 Compared with alternative methods used to study hydrogen bonds, $^1$H NMR has the unique advantage of directly detecting the nuclei forming the hydrogen bonds via the $^1$H chemical shift. The degree to which a $^1$H resonance is shifted to higher frequency has been correlated to the strength of the hydrogen bonding in which it is involved. This correlation has been established for a range of O· · · H· · · O hydrogen bonds, e.g. in carboxylic acids, through comparison of the $^1$H chemical shift to the O· · · O distances,6 or O· · · H distances,7 determined by X-ray and neutron diffraction respectively. Another study of the hydrogen bonding protons in carboxylic acids using the combined rotation and multiple pulse sequence (CRAMPS) to achieve better $^1$H chemical shift resolution was presented by Harris et al.8 Consistently, the $^1$H resonance frequency increased as the distance between the heteroatoms decreased. Recently, a study of amide protons in hydrogen-bonded structures of glycine-containing peptides and poly-peptides in the solid

DOI: 10.1002/mrc.931 Copyright © 2001 John Wiley & Sons, Ltd.
state correlated the N···(H)···O distances with \(^1\)H chemical shifts obtained at a high magnetic field and under fast MAS.\(^9\) A trend towards high-frequency shifts for shorter N···(H)···O distances was observed and confirmed by ab initio calculations, although there was significant scatter in the experimental data. However, this latter study did not attempt to place the proton between the two heteroatoms, and thus the hydrogen-bonding structures were not fully determined.

Another approach to investigate hydrogen bonds involves studies of dynamics in \(^{15}\)N···(L)···\(^{15}\)N low-barrier hydrogen bonds, where L represents either hydrogen or deuterium, which have examined the two \(^{15}\)N···H interdependent distances using solid-state \(^{15}\)N NMR and quantum chemical calculations.\(^{10}\)

In solid-state NMR the \(^1\)H chemical shift information is usually obscured by substantial line broadening effects caused by strong homonuclear \(^1\)H–\(^1\)H dipole–dipole couplings. Various approaches to the problem of gaining sufficient \(^1\)H spectral resolution have been presented,\(^{1}\) e.g., the application of multiple-pulse sequences, such as WAHUHA,\(^{11}\) to single-crystal samples, as well as the combination of such multiple-pulse sequences with MAS in the CRAMPS approach.\(^{12}\) Recently, significant technological and methodological progress in \(^1\)H NMR has been afforded by extending MAS to spinning frequencies in excess of 30 kHz. The improvement in the \(^1\)H resolution of hydrogen-bonded protons afforded by MAS at such frequencies is illustrated by Yamauchi et al.\(^9\), Schnell et al.,\(^13\) and Brown et al.\(^{14}\). It is to be noted that significantly narrower \(^1\)H linewidths can be obtained in experiments involving the application of ‘windowless’ homonuclear decoupling sequences, such as the Lee–Goldburg (LG) technique\(^{15}\) and refinements, namely the frequency-switched and phase-modulated LG (FSLG\(^{16,17}\) and PMLG\(^{18}\)) sequences, as well as the computer-optimized sequence DUMBO-1.\(^{19}\) Recently, Lesage et al. have shown that a linewidth as low as 60 Hz can be obtained for the aliphatic resonances in \(L\)-alanine using a constant-time (CT) CRAMPS experiment.\(^{20}\)

In addition to achieving high resolution, and hence \(^1\)H chemical shift information, it is desirable to access the structural and dynamic information inherent to the \(^1\)H–\(^1\)H dipole–dipole coupling. One approach by which this can be achieved is the combination of MAS with \(^1\)H–\(^1\)H double-quantum (DQ) spectroscopy.\(^{3,4,21,22}\) Using the \(^1\)H DQ MAS method, it has been shown that valuable insight into the hydrogen-bonded structures adopted by different alkyl-substituted benzoxazine dimers,\(^{15}\) as well as the change in the quadrupole hydrogen-bonding arrangement formed by dimers of 2-ureido-4-pyrimidone units upon a ketenol tautomerism,\(^{25}\) could be obtained. In addition, it has recently been demonstrated that an analysis of \(^1\)H DQ MAS sideband patterns allows the quantitative determination of proton–proton distances for the complex hydrogen-bonded arrangement adopted by the biologically important molecule bilirubin.\(^{14}\) Furthermore, the kinetics of the making and breaking of hydrogen bonds could be followed by analysing the loss of signal in a DQ-filtered experiment.\(^{24}\)

As noted above, in a previous study, hydrogen-bonded benzoxazine dimers have been investigated by \(^1\)H NMR using fast MAS and \(^1\)H–\(^1\)H DQ spectroscopy.\(^{13}\) Benzoxazine dimers serve as model compounds for the polybenzoxazines, a new class of phenolic resins, which have been investigated extensively in the past 10 years.\(^{23,27}\) Studies have focused both on the synthesis of new members of this family of compounds and on the characterization of the unique properties of these materials. This substantial research effort has been motivated by the observation that the polybenzoxazines exhibit a number of unusual properties, such as low volumetric shrinkage or expansion upon curing,\(^{28}\) lack of water absorption and excellent resistance to chemicals and UV light,\(^{29,30}\) as well as surprisingly high \(T_g\) values given the low crosslinking density,\(^{31}\) all of which make them attractive candidates for many commercial applications. The key structural feature that is presumed to be responsible for the remarkable behaviour of these polymers is the formation of N···H···O and O···H···O hydrogen bonds.\(^{32}\) A better understanding of these hydrogen-bonding structures is therefore of much importance.

The \(^1\)H–\(^1\)H DQ studies of the benzoxazine dimers resulted in a proposal of two unique intermolecular hydrogen-bonding arrangements: one in which the dimers arrange pairwise, and a second in which a twist of half of the dimer unit about the central nitrogen atom allows for a ladder-like extended structure.\(^{13}\) Whereas the former structure was first determined by X-ray crystallography,\(^{33}\) the latter was originally proposed exclusively on the basis of the \(^1\)H–\(^1\)H DQ NMR spectra, and has subsequently been verified, in the case of the propyl dimer by a single-crystal X-ray diffraction study.\(^{34}\) This illustrates the power of the NMR methods to provide accurate structural information in the absence of crystallographic data. Beyond the determination of structural elements that can also be accessed through diffraction methods, NMR offers the ability to locate protons accurately. In general, proton positions are difficult to determine via diffraction methods, where this can only be accomplished successfully through Fourier difference mapping in X-ray scattering studies of small organic molecules, or with the assistance of a nuclear reactor and deuterium labelling in neutron scattering.\(^{35,36}\) By comparison, solid-state NMR is routinely available, offers superior sensitivity, and specific isotope enrichment is required only in special cases.

Here, we present such a special case, in which we make use of \(^{15}\)N isotopic enrichment, and extend our previous study of hydrogen-bonded benzoxazine dimers. Heteronuclear \(^1\)H–\(^{15}\)N approaches, based on REDOR-type dipolar recoupling methods, were used to determine the N–H distance in the dimers. Relying on fast MAS (\(V_g\) typically 30 kHz) for dipolar decoupling and \(^1\)H resolution enhancement, dipolar recoupling is used to generate heteronuclear single-quantum correlation (HSQC) and to observe rotor-encoded MAS sideband patterns, which serve as a sensitive measure for the underlying N–H dipole–dipole coupling.\(^{39–41}\) In addition, different variants of the pulse sequence are discussed, which employ conventional (\(^{15}\)N) or inverse (\(^1\)H) detection and suppress perturbing influences of further N–H couplings to varying degrees. The sensitivity enhancement
and optimization of experimental time achievable by an appropriate design of the pulse sequence are demonstrated.

Besides the heteronuclear correlation techniques presented here, CRAMPS can also be used to measure X-·-H distances in the solid state through the analysis of dipolar sideband patterns obtained at low spinning speeds. In a recent example, the N·-H distance in 15N labelled poly(phenylenediamine) was measured using 1H CRAMPS NMR.42 Differing bond lengths were determined for the a-helical morphology (112 pm) compared with b-sheet (105 pm), and attributed to a stronger hydrogen bond in the latter case. These results show that dipolar 1H–15N methods are capable of resolving very fine differences in close N·-H distances, and in the following we show that longer N·-H distances can also be investigated, even in the presence of further protons, by taking advantage of the 1H resolution enhancement achievable using very fast MAS.

PRIMARY SAMPLE CHARACTERIZATION

Crystal structure

Figure 1 shows a schematic drawing of the chemical structure of a benzoxazine dimer pair, together with a portion of the crystal structure of the methyl benzoxazine dimer, with the N·-H-O interaction of interest indicated with arrows.30 Owing to different averaging effects of vibrational motions, scattering methods tend to yield shorter bond lengths than NMR methods based on dipole–dipole couplings.13 In Fig. 1b, the respective hydrogen atoms are placed on the trajectory between the oxygen and nitrogen, but without a defined position. The position of these N·-H·-O and O·-H·-O protons is expected to depend significantly on the character and the strength of the hydrogen bonds. It is relevant to mention that the N·-H-O bond is not expected to be linear, but likely is part of a distorted six-membered ring. This intramolecular hydrogen-bonded ring has been shown to be stable both in the solid at elevated temperatures, and in solution using FT-IR studies.32,43 While investigating the hydrogen-bond N·-H distance in the following, potentially perturbing influences of further 1H–15N dipole–dipole couplings involving the labelled 15N site need to be considered. Apart from the proton in the hydrogen bond, there are four CH2 protons and the three protons of the methyl group, whose N·-H distances can be reliably estimated from the crystal structure to be ~200 pm (CH2) and ~190 pm (CH3), the N·-H dipole–dipole couplings are partially averaged, though, due to fast methyl rotation). Hence, it is to be expected that the perturbing N·-H dipole–dipole couplings of N·-CH2 and N·-CH3, as well as the N·-H coupling of interest, are of comparable strength. Therefore, the distinction of the proton species (CH2, CH3 and hydrogen bond) interacting with the nitrogen is vital, and perturbing effects of N·-CH2 and N·-CH3 couplings on the N·-H coupling need to be minimized.

1H fast MAS and 1H–1H DQ spectra

First we consider 1H spectra of the dimer obtained under fast MAS. Whereas the 1H MAS spectrum provides chemical shift information and, in this way, primary evidence for the presence of hydrogen bonds, the 1H–1H DQ spectrum is well suited for obtaining insight into the proximities between proton species and for identifying the structure of multiple hydrogen bonds.3,4 In 1H–1H DQ NMR spectroscopy, the generation of DQ coherence (DQC) requires the existence of a dipolar coupling between two protons. Thus, the observation of particular DQ peaks implies the existence of a sufficient dipolar coupling between the respective nuclei. However, detailed information about internuclear proximities can be readily obtained from the signals in two-dimensional (2D) DQ spectra, which correlate a DQ spectral dimension (t1) with a single-quantum (SQ) dimension, with the latter being used for signal detection. In the DQ dimension, each observed resonance frequency ωAB corresponds to the sum frequency of the two nuclei, A and B, involved in the coherence: ωAB = ωA + ωB. Hence, 2D DQ spectra show signals at the positions (ωA, ωAB) and (ωB, ωAB), and such signal patterns straightforwardly allow the identification of internuclear proximities.3,13

The 1H MAS spectrum and the 2D 1H–1H DQ MAS spectrum of the dimer are shown in Fig. 2a and b, respectively.

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Figure 1. (a) The molecular structure and (b) the crystal structure of a pair of methyl benzoxazine dimers. The N·-H·-O hydrogen-bonding interaction is highlighted.
an AC cross peak, which was weakly evident in the previous spectrum, and arose from a $^1$H–$^1$H contact between (N···H·O) and (O···H·O), attributed to the presence of a second conformation. The absence of the AC cross peak is, therefore, taken as evidence of the high purity achieved in the synthesis of the labelled compound, and indicates a lower degree of structural dispersion present in this sample. Based on the previous study of the series of benzoxazine dimers, including methyl-, ethyl- and propyl-substituted materials, both the ethyl and propyl variants were found to exhibit a ladder-like structure, achieved by twisting the dimer about the central nitrogen atom and thus creating an extended hydrogen bonding arrangement. The primary evidence for this arrangement was the presence of a strong AC peak in the 2D DQ spectra of these compounds.

$^1$H–$^{13}$C recoupled-dipolar HSQC spectrum

$^1$H–$^1$H DQ spectra provide much information concerning inter- and intra-molecular proximities, and the experiment is also facile to implement and inexpensive in terms of experimental time. However, important structural details are only available through the heteronuclear correlation methods, as described above; thus we extended our study to include a $^1$H–$^{13}$C correlation spectrum. In Fig. 3, the $^1$H–$^{13}$C correlation spectrum of the methyl benzoxazine dimer is shown, which was obtained in a rotor-synchronized fashion using recoupled polarization transfer (REPT) under MAS.$^{39,40}$ The pulse sequence is described below (see the chemical shift resolution in heteronuclear dipolar correlations section and Fig. 6a). The $^1$H and $^{13}$C chemical shifts are observed in the indirect ($F_1$) and direct ($F_2$) dimensions respectively. Of interest is the observation that all the $^{13}$C resonances are split except for that of the methyl group at 40.8 ppm, which is bound to the nitrogen. The expanded aliphatic and aromatic regions, depicted in Fig. 3b and c, clearly show the splitting of the peaks in the $^{13}$C dimension, whereas the frequencies of the $^1$H resonances essentially remain single peaks. A comparison of the $^{13}$C resonances obtained by solution- and solid-state NMR is given in Table 2.

The splitting of the $^{13}$C resonances in the solid state indicates a degree of asymmetry in the dimer, pivotal about the central nitrogen, since the resonance of the attached methyl group is not split. Increasing the temperature incrementally in steps of 10 K, to a maximum of 380 K, did not cause the lines in the corresponding one-dimensional $^{13}$C REPT spectra to coalesce (data not shown). The observed splitting is consistent with the crystal structure,$^{33}$ in which a $C_2$ symmetry element in the centre of the dimer pair dictates that the two dimers of the pair are equivalent, but the two halves of the dimer, i.e. the phenol units, are crystallographically distinct.

A splitting of $^1$H resonances in the solid state has recently been observed in several cases, for example L-tyrosine,$^{40,41}$ hexabenzocoronenes,$^{42}$ and molecular-tweezer host–guest complexes.$^{43}$ These splittings emerge due to intermolecular interactions in the solid state, namely aromatic π-electron effects on nearby protons. The electronic environment of the proton is strongly influenced by its orientation with respect to proximal aromatic units and their ring currents, which

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**Table 1. Assignment of proton chemical shift resonances in single quantum and double quantum dimensions of the 2D DQ spectrum (Fig. 2a), acquired with 1/2$T$ excitation time**

<table>
<thead>
<tr>
<th>Proton</th>
<th>Single quantum chemical shift/ppm</th>
<th>Double quantum coherences</th>
<th>Double quantum chemical shifts/ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>N··H (A)</td>
<td>11.2</td>
<td>AB</td>
<td>18.3</td>
</tr>
<tr>
<td>O··H (B)</td>
<td>7.2</td>
<td>AD</td>
<td>13.2</td>
</tr>
<tr>
<td>Aromatic H (C)</td>
<td>6.0</td>
<td>CC</td>
<td>12.0</td>
</tr>
<tr>
<td>CH$_2$ (D)</td>
<td>2.0</td>
<td>CE</td>
<td>7.3</td>
</tr>
<tr>
<td>CH$_3$ (E)</td>
<td>1.3</td>
<td>EE</td>
<td>2.6</td>
</tr>
</tbody>
</table>

The $^1$H SQ and DQ chemical shifts observed in the spectra are listed in Table 1. Three SQ resonances and a shoulder are evident, and are assigned to N··H··O (A), O··H··O (B), aromatic protons (C), and CH$_2$ protons (E). Based on the resolution achieved in the DQ spectrum, a fifth resonance is differentiated, and is attributed to CH$_3$ protons (D). Both the presence and absence of DQ peaks provide valuable information for structure determination. A comparison between this spectrum and that originally documented by Schnell et al.$^{39}$ confirms that the intermolecular hydrogen-bonded structure described previously is also present in the labelled sample. In fact, in this spectrum there is no evidence for

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Figure 2. (a) $^1$H MAS spectrum and (b) 2D rotor-synchronized $^1$H–$^1$H DQ MAS spectrum of the $^{15}$N-labelled methyl benzoxazine dimer acquired with 1/2$T$ excitation time ($T_R = 30$ kHz and 700 MHz $^1$H Larmor frequency).

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give rise to the shifts of the $^1$H resonance frequencies. These effects have been quantitatively investigated by means of quantum chemical calculations.$^{47-49}$ In the case of the methyl benzoxazine dimer, no clear splitting of the $^1$H resonances is observed, although the $CH_2$ resonances are very broad, spanning 4 ppm. The latter is most likely due to ring current effects. For the $CH_3$ and aromatic protons, the experimental absence of a splitting of the $^1$H resonances is consistent with the X-ray crystal structure, where significantly different exposure of protons to $\pi$-electrons, or even $\pi$-stacking, is not present.$^{33}$

**METHODS FOR N···H DIPOLAR DISTANCE DETERMINATION**

In this study, the heteronuclear dipole–dipole coupling is exploited for N–H distance determination by means of recoupling techniques, which generate heteronuclear dipolar correlations under fast MAS. As revealed by the crystal structure and the $^1$H–$^1$H DQ spectrum, the N···H distance of interest is embedded among a multitude of other N–H proximities. Though the $^{15}$N nucleus can easily and selectively be accessed using isotopic enrichment, $^1$H chemical shift resolution is required to distinguish the different proton species and to select the hydrogen-bonded one. In addition, the N···H coupling of interest needs to be independently measured in the presence of several further N–H dipolar interactions of comparable strength. Thus, an approach is required that combines N–H coupling measurement with $^1$H spectral resolution and which is as insensitive as possible to perturbing N–H interactions.

**Rotor-encoded MAS sideband patterns**

Whereas MAS at 30 kHz provides homonuclear dipolar decoupling and resolution enhancement among the protons, heteronuclear dipolar recoupling is used for generating the $^1$H–$^{15}$N correlations. Recoupling is accomplished by trains of radio frequency (RF) $\pi$-pulses in a REDOR fashion$^{37,38}$ applied during two periods of the pulse sequence (see Figs 4 and 6). It is preferable to apply the $\pi$-pulses on the channel, where there is no evolution of transverse magnetization, although the application of a central $\pi$-pulse on the other channel is necessary in order to compensate for chemical shift or off-resonance effects. The recoupling approach is a dedicated fast MAS technique with a well-defined average Hamiltonian,$^{44}$ which ensures coherent polarization transfer. Cross polarization (CP) approaches, in contrast, need to be adapted to fast MAS conditions$^{50}$ and tend to non-coherent transfer processes, an exception being the recently proposed FSLG-CP approach.$^{51}$ In this sense, heteronuclear dipolar recoupling bears a direct analogy...
to the INEPT technique\textsuperscript{52} used in solution-state NMR, with dipole–dipole and $J$-couplings serving as mediating interactions respectively.

The heteronuclear correlations generated are based on the dipole–dipole coupling between two spins, denoted $I$ and $S$. The average Hamiltonian describing the evolution during the interval ($t; t + N\tau_R$) of dipolar recoupling is given by\textsuperscript{40}

$$\hat{H}_I(t; t + N\tau_R) = \frac{N\Phi_I}{\tau_R} \hat{J}_z$$

(1)

where $\Phi_I$ is the dipolar phase factor, which is given by

$$\Phi_I = -\frac{D_{IS}}{\omega_R} 2\sqrt{2} \sin 2\beta \sin(\omega_R t + \gamma)$$

(2)

The angles $\beta$ and $\gamma$ relate the principal axes system of the dipole–dipole coupling tensor to the rotor-fixed frame, and $\omega_R$ is the rotor frequency. $D_{IS}$ is the dipolar coupling constant in units of angular frequency, and depends on the internuclear distance $r_{IS}$ and the respective magnetogyric ratios of the nuclei:

$$D_{IS} = \frac{\mu_n}{4\pi} \cdot \frac{\gamma_I \gamma_S h}{r_{IS}}$$

(3)

The recoupled heteronuclear dipolar Hamiltonian given in Eqn (1) implicitly depends on the rotor phase $\Phi_I$ via $\omega_R t$. Hence, by combining two such recoupling periods with different phases, corresponding to different initial rotor orientations, the signal becomes rotor encoded.\textsuperscript{\textdagger} The difference in phases can easily be created by introducing a ‘waiting time’ $t_1$ between the two recoupling periods. This leads to a 2D experiment consisting of four periods, which will henceforth be referred to as the excitation, $t_1$, reconversion, and detection periods. A schematic representation of the experiment and its variants is depicted in Fig. 4. The particular placement of the $\pi/2$-pulses allows the pathway of the polarization to be selected such that either the $I$-spins or the $S$-spins are the evolving species during each of the four periods. In order to subject the spins to a dipolar evolution under the Hamiltonian given in Eqn (1), transverse $I$ or $S$ spin states need to be created by applying an RF $\pi/2$-pulse before the $\pi$-pulse train accordingly. After two such periods of dipolar evolution, a signal can be detected (in a final detection period $t_2$), the amplitude of which is modulated in the form

$$S \propto (\sin(N_{exc}\Phi_0) \sin(N_{rec}\Phi_{t1}))$$

(4)

where $N_{exc}$ and $N_{rec}$ denote the number of rotor periods used for excitation and reconversion respectively, and the brackets $\langle \cdot \cdot \cdot \rangle$ indicate that an average is taken over all orientations for powdered samples. Fourier transformation of this signal yields characteristic sideband patterns that, for the ideal case of an isolated spin pair, consist of odd-order sidebands only and can serve as a sensitive measure for $D_{IS}$, because the appearance of the pattern depends strongly on the parameter $N_{exc/\text{rec}}D_{IS}/\omega_R$. It is to be noted that such sideband patterns are observed for both homonuclear and heteronuclear spin pairs.\textsuperscript{\textdagger} The larger the value of the parameter, the broader the span of the pattern, and the more accurate the determination of the coupling from the pattern. With longer recoupling times (i.e. with increasing $N_{exc/\text{rec}}$), however, perturbing effects of additional interactions and relaxation come increasingly into play. Consequently, the duration of the recoupling periods must be optimized.

Figure 4 shows the generalized build-up curve for a dipolar IS two-spin correlation calculated as a function of $D_{IS}T_{\text{rcpl}}/2\pi$ (where $T_{\text{rcpl}} = N_{\text{rcpl}}\tau_R$ and $N_{\text{rcpl}} = N_{\text{exc}} = N_{\text{rec}}$), together with the rotor-encoded sideband patterns observed for three choices of $D_{IS}T_{\text{rcpl}}/2\pi$. Since a short excitation time favours the first-order sidebands, it does not produce a sideband pattern from which a valid dipolar-coupling constant can be determined. To generate higher-order sidebands, data must be acquired beyond $D_{IS}T_{\text{rcpl}}/2\pi = 0.8$ in the build-up curve, but excessively long excitation times eventually obliterate signal intensity due to relaxation effects. Empirically, the relaxation typically observed for dipolar two-spin correlation build-up curves can be described by an exponential decay, as is also displayed in Fig. 5. Such build-up curves and rotor-encoded sideband patterns have been extensively studied and used for the determinations of homonuclear and heteronuclear dipolar interactions.\textsuperscript{\textdagger} The larger the value of the parameter, the broader the span of the pattern, and the more accurate the determination of the coupling from the pattern. With longer recoupling times (i.e. with increasing $N_{exc/\text{rec}}$), however, perturbing effects of additional interactions and relaxation come increasingly into play. Consequently, the duration of the recoupling periods must be optimized.

Chemical shift resolution in heteronuclear dipolar correlations

In the previous section, a sensitive and efficient way of measuring dipole–dipole couplings under MAS conditions has been described. In general, and in particular for the benzoxazine sample investigated here, the distinction of different couplings with respect to the spins involved is of major importance. For this purpose, spectral dimensions

Figure 4. Schematic representation of the possible structure of heteronuclear dipolar recoupling pulse sequences, where different options for the pathways followed by the transverse coherences are indicated with arrows.
Figure 5. The build-up of intensity in a heteronuclear experiment of the type illustrated in Fig. 4 as a function of the unitless parameter, $D_{IS} \tau_{repl}/2\pi$, for the ideal case of an isolated I/S spin pair. Exponential damping, which mimics relaxation effects, is included for decay time constants of 2 ms (dashed line) and 0.5 ms (dotted line). Simulated frequency-domain sideband patterns for the indicated $D_{IS} \tau_{repl}/2\pi$ values (i)–(iii) are shown to the right.

Figure 6. A comparison of REPT and DIP pulse sequences: (a) directly detected REPT-HSQC, (b) inversely detected REPT-HSQC, (c) inversely detected DIP-HSQC, and (d) directly detected DIP-HSQC.

providing chemical shift resolution of the I and S spins can straightforwardly be introduced into the $t_1$ and $t_2$ periods of the basic scheme for generating rotor-encoded sideband patterns (see the pulse sequences depicted in Fig. 6). The product operator formalism will be used to describe the relevant spin states during their time-dependent evolution. Starting the excitation period with a transverse I state (generated by an initial $\pi/2$-pulse on I with phase $x$), the system evolves under the recoupled dipolar interaction

$$-I_y N_{ex} \Phi_0,1,2,1,2 \rightarrow -I_y \cos N_{ex} \Phi_0 + I_x S_z \cos N_{ex} \Phi_0$$

In this way, an antiphase correlation, $I_x S_z$, is created. When no $\pi/2$-pulse is applied at the end of the excitation (as in Fig. 6a), the transverse I component evolves under the I-spin chemical shift during the subsequent $t_1$ period as follows (the residual $I_y$ magnetization is removed by phase cycling, and...
Following the $t_1$ evolution period, simultaneous \( \pi/2 \)-pulses are applied to the $I$ and $S$ spins, interchanging transverse and longitudinal $I$ and $S$ components and, in this way, preparing the polarization transfer from $I$ to $S$. By alternating the phase of the $\pi/2$-pulse on the $I$-spins in subsequent experiments, both cosine and sine components of the $I$-spin $t_1$ signal are acquired, allowing for sign discrimination in the indirect dimension. Considering only the cosine component in Eqn (6), the $I_S$ antiphase state evolves to $S_I$ during the reconversion period, which is finally detected, following a $\chi$-filter:

\[
2I_S \sin N_{exc} \Phi_0 \cos \theta_{CS} t_1 \rightarrow 2I_S \sin N_{exc} \Phi_0 \cos \theta_{CS} t_1 + 2I_S \sin N_{exc} \Phi_0 \sin \theta_{CS} t_1 \tag{6}
\]

In the course of the reconversion, the signal acquires one more dipolar phase factor $\Phi_{11}$, which differs from $\Phi_0$ unless $t_1$ is incremented in full rotor periods, i.e. $\Delta t_1 = nT_R$. In this particular case, the resulting 2D spectrum corresponds to a heteronuclear correlation spectrum, where $t_1$ is modulated only by the $I$-spin chemical shift.

The experiment described above yields an HSQC spectrum, familiar from solution-state studies,\(^\text{52b}\) where the $I$- and $S$-spin chemical shifts occur in the indirect and direct dimensions, respectively, and was performed in order to obtain the $^1H$-$^13C$ HSQC spectrum discussed above (see the $^1H$-$^13C$ recoupled dipolar HSQC spectrum section and Fig. 3). Effectively, $I$-spin polarization is transferred to the $S$-spins via dipolar recoupling, with an $I$-spin spectral dimension dividing the $\pi$-pulse train into two periods. Such an experiment has been termed REPT.\(^\text{39,40}\) Its one-dimensional version ($t_1 = 0$ in Fig. 6a) is identical to the TEDOR (transferred-echo, double resonance) sequence, which has been shown to be useful for extracting heteronuclear dipolar couplings for the case of selectively pairwise labelled systems.\(^\text{58}\) However, the focus of this paper is on the determination of dipolar coupling constants from rotor-encoded spinning sideband patterns, which are observed in the indirect ($t_1$) dimension of two-dimensional experiments. The differences between REPT and TEDOR experiments have also been discussed in Ref. 39. Although it appears natural for $^1H$-$X$ experiments to start with the excitation period on the abundant $I$ ($^1H$) spins, the experiment can of course be performed inversely, as depicted in Fig. 6b. The initial $S$-spin polarization can, for example, be created by a preceding CP step, while the detection takes place on the $I$-spins. In the case of $^1H$, a significant advantage is obtained for the inverse variant on account of detecting the nuclei with the higher magnetogyric ratio and, hence, the higher sensitivity. In combination with fast MAS, inverse detection has not been widely applied in solid-state NMR, and has only recently attracted renewed attention,\(^\text{55,61}\) whereas it is routinely used in solution-state NMR.\(^\text{52}\)

Regarding the $^{15}N$-labelled benzoxazine sample investigated here, it is important to note that spectral resolution of resonances in the $^1H$ dimension is vital in order to distinguish the different proton species present in the sample and to identify the N–H coupling of interest. In the $^{15}N$ dimension, in contrast, only a single line will be observed due to the selective isotopic enrichment and the presence of a single nitrogen site in the crystal structure.\(^\text{33}\) Generally, to optimize the use of measuring time for 2D data sets, it is advisable to record data \(\nu_p\) the nucleus making higher demands on resolution and spectral width in the direct dimension.\(^\text{50}\) Here, the NH correlation experiment should therefore be designed in the inverse fashion, such that the single $^{15}N$ signal is recorded in the indirect ($t_1$) dimension, whereas the $^1H$ chemical shifts are resolved in the direct ($t_2$) dimension. Furthermore, under on-resonance conditions for $^{15}N$, procedures ensuring phase-sensitive detection can be omitted. Thus, major advantages in terms of signal sensitivity, as well as minimum experiment times, are expected for inverse, i.e. $^1H$, detection.

**Multi-spin effects**

Another important point besides the distinction of resonances in the spectra is the perturbing effect that other dipolar interactions have on the measurement of the coupling of interest. So far, heteronuclear dipolar correlations were derived for the simple case of a single $IS$ spin pair. In many cases, particularly when protons are involved, further couplings need to be taken into account, for example by considering an $I_2S$ multi-spin system with abundant $I$-spins and rare $S$-spins. Whereas, in the $IS$ spin-pair case it is irrelevant which of the two spins occupies a transverse state and evolves under the heteronuclear dipolar interaction to the other, the situation is critically different for $I_2S$ systems.

The heteronuclear couplings in an $I_2S$ system behave ‘inhomogeneously’, following the terminology introduced by Maricq and Waugh.\(^\text{64}\) In other words, the Hamiltonians for the $n$ different $IS$ couplings commute, such that the overall propagation of the spin system under the combined action of all $n$ couplings can be simplified to the sequential action of the individual couplings. Thus, when a transverse state of the $I$ spins, i.e. $I_{x,y}$, is subject to the heteronuclear couplings to the $S$ spin, the situation can simply be viewed as a projection of the $I$-spin density at the $S$-spin site, converted into the total effective Hamiltonian for the $I_2S$ system.

\[
\begin{align*}
\text{a)} \quad \text{I} & \quad \text{I} \\
\text{b)} \quad \text{S} & \quad \text{I} & \quad \text{I} \\
\end{align*}
\]

**Figure 7.** The local dipolar fields experienced by the $^{15}N$ (S) and $^1H$ (I) nuclei.
as each I-spin experiencing only one coupling, because the
spin 1_0 is unaffected by couplings H_{I_S} \propto I_0^2 S_j; for j \neq i. This
scenario is depicted schematically in Fig. 7a. Consequently,
in the I_S spin system the evolution of the transverse state of
each I-spin is identical to the IS spin-pair case described by
Eqn (5). However, when the single S-spin occupies a
transverse state, S_{x,y}, it evolves in the local dipolar fields
of all I-spins, because the S-spin is part of all heteronuclear
dipolar Hamiltonians. During the excitation period, an S_j
state evolves into heteronuclear antiphase states in which
successively more and more I-spins are incorporated:\(^{41}\)

\[
S_y \rightarrow S_y \prod_i \cos N_{exc} \Phi_0^{(i)}
- 2 \sum_i I_0^2 S_i \sin(N_{exc} \Phi_0^{(i)}) \prod_{j \neq i} \cos N_{exc} \Phi_0^{(j)}
+ 4 \sum_{i,j} I_0^2 [S_i \sin(N_{exc} \Phi_0^{(i)}) \sin(N_{exc} \Phi_0^{(j)})]
\sum_{k \neq i,j} \prod_k \cos N_{exc} \Phi_0^{(k)} \pm \cdots \quad (8)
\]

As demonstrated by Saalwächter and Spiess,\(^{41}\) this growth
process can be followed by spin-counting experiments, or IS
multi-spin states can be selected with respect to the number
of I-spins involved by the use of appropriate phase cycles.
For simplicity, we will restrict our considerations here to
the leading terms, i.e. two-spin I_S antiphase states, which
acquire the dipolar phases of all heteronuclear couplings in
the following way:

\[
S_y \rightarrow -2 \sum_i I_0^2 S_i \sin(N_{exc} \Phi_0^{(i)}) \prod_{j \neq i} \cos N_{exc} \Phi_0^{(j)} \quad (9)
\]

Equivalently, during reconversion the I_S antiphase state
picks up the same dipolar phases when evolving back to a
transverse S_y state:

\[
2 \sum_i I_0^2 S_i \rightarrow -2 \prod_i \sin(N_{exc} \Phi_0^{(i)}) \prod_{j \neq i} \cos N_{exc} \Phi_0^{(j)} \quad (10)
\]

Hence, considering heteronuclear two-spin states, the
important difference between the evolution of an IS and
an I_S spin system is the presence of the product term\(^{41}\)
\[\prod_{j \neq i} \cos N_{exc} \Phi_0^{(j)}\] in the IS case in addition to the
\[\sin N_{exc} \Phi_0^{(j)}\] term, which is similar from the two-spin case.
Hence, for an I_S spin system the rotor-encoded sideband
patterns of IS two-spin correlations arise from one of the
following four expressions:

\[
S \propto \left\langle \sum_i \sin(N_{exc} \Phi_0^{(i)}) \prod_{j \neq i} \cos N_{exc} \Phi_0^{(j)} \right\rangle \quad (11)
\]

\[
S \propto \left\langle \sum_i \sin(N_{exc} \Phi_0^{(i)}) \prod_{j \neq i} \cos N_{exc} \Phi_0^{(j)} \sin(N_{exc} \Phi_0^{(j)}) \right\rangle \quad (12)
\]

\[
S \propto \left\langle \sum_i \sin(N_{exc} \Phi_0^{(i)}) \sin(N_{exc} \Phi_0^{(j)}) \right\rangle \quad (13)
\]

\[
S \propto \left\langle \sum_i \prod_{j \neq i} \cos N_{exc} \Phi_0^{(j)} \sin(N_{exc} \Phi_0^{(j)}) \right\rangle \quad (14)
\]

depending on the particular choice of transverse I- or S-states
during excitation and reconversion. In the experiments,
the ‘pathway’ of transverse states can be selected by
placing the \(\pi/2\)-pulses at the start and/or at the end of
the recoupling periods accordingly (see also Fig. 4). The
pulse sequences giving rise to the signals described by
Eqns (11)–(14) are shown in Fig. 6a–d. Note that the pulse
sequences depicted in Fig. 6a and b, which have been
discussed above, include a polarization transfer from I to
S or vice versa respectively. The propagation of the spin
states in the two recoupling blocks occurs asymmetrically,
in that the transverse and longitudinal components are
interchanged between the two blocks. The variants shown
in Fig. 6 c and d, in contrast, are symmetrically designed,
and the polarisation in not transferred from one spin
to the other, i.e. the same spin species occupies
a state of transverse polarisation during both excitation
and reconversion. This type of sequence (Fig. 6 c and d)
is termed DIP, taken from dipolar.\(^{40}\) DIP sequences can also
be considered 2D REDOR experiments, where the central
\(\pi\)-pulse is split into two \(\pi/2\)-pulses and the \(t_1\)-dimension
is inserted in between. A previous example of such a type
of REDOR experiment (termed 3D REDOR) was proposed
by Michal and Jelinski, from which multiple distances could
be extracted based on the REDOR curves.\(^{65}\) In that case,
chemical shift information in two dimensions provided the
necessary resolution for measuring several \(^{13}\)C-\(^{15}\)N
distances. The important difference between the REDOR
and the REPT/DIP approaches is how the information about
the heteronuclear dipolar coupling is accessed. While in
REDOR experiments the spectral intensity is recorded as a
function of the recoupling time (yielding REDOR curves), in
REPT/DIP experiments a rotor-encoded sideband pattern is
observed in the indirect (\(t_1\)) dimension. From this pattern,
the dipolar coupling strength can be determined in a single
two-dimensional REPT/DIP experiment (which can in addition
be performed for various recoupling times, \textit{vide infra}),
while the REDOR approach is based on a dephasing behaviour
which is observed for a series of experiments with different
recoupling times.

Additional complications in the I_S spin system could
obviously arise from homonuclear dipolar interactions
among the I spins. Such interactions cause the system to
come ‘homogeneous’, and the overall propagation of the
spin system under the combined action of all couplings
can no longer be fully separated, but approximate approaches
through series expansions become necessary. Under the
fast MAS conditions used here, however, the homonuclear
couplings have only minor effects because they are not
recoupled, but are sufficiently suppressed by spinning
frequencies exceeding 25 kHz.\(^{41,65}\)

Recalling the spin system encountered in the benzoxazine
sample, there are eight protons proximate to the nitrogen,
only one of which is involved in the hydrogen bond, but

\[\sum N_{exc} \Phi_0^{(i)} 2I_0^2 S_i \rightarrow S_y \prod_i \cos N_{exc} \Phi_0^{(i)}
- 2 \sum_i I_0^2 S_i \sin(N_{exc} \Phi_0^{(i)}) \prod_{j \neq i} \cos N_{exc} \Phi_0^{(j)}
+ 4 \sum_{i,j} I_0^2 [S_i \sin(N_{exc} \Phi_0^{(i)}) \sin(N_{exc} \Phi_0^{(j)})]
\sum_{k \neq i,j} \prod_k \cos N_{exc} \Phi_0^{(k)} \pm \cdots \quad (8)
\]
which can be identified from its chemical shift. Hence, in order to measure the N···H pair coupling of interest by means of rotor-encoded sideband patterns, influences of further N-H couplings need to be avoided as much as possible. This can be accomplished by performing the \(^1\)H–\(^{15}\)N dipolar recoupling experiment given in Fig. 6c, which gives rise to a spin-pair sideband pattern in the \(F_1(t_1)\) dimension [corresponding to Eq. (13)], and which provides resolution of the \(^1\)H chemical shift in the \(F_2(t_2)\) dimension.

From the consideration of different possible \(^1\)H–\(^{15}\)N dipolar recoupling experiments, it is, thus, concluded that an experiment consisting of two recoupling periods with \(^1\)H transverse states and detecting the \(^1\)H signal during \(t_2\) is the optimum choice for the complex spin system under investigation.

RESULTS AND DISCUSSION

The primary objective of this work is to determine the dipolar coupling constant of the N···H interaction and, thereby, the distance between these two atoms. Based on the phenolic character of the benzoxazines, and on the anticipated six-membered ring geometry, a relatively weak hydrogen bond, corresponding to a long N···H distance, was anticipated.\(^{14}\) A standard \(^1\)H–\(^{15}\)N CP MAS spectrum acquired at a slow spinning frequency of 4 kHz (not shown) shows a single \(^{15}\)N resonance at \(-342.5\) ppm with only first-order sidebands of approximately 1\% intensity with respect to the isotropic resonance. \(^{15}\)N shift is comparable to the NH\(_4\)··· shift of the reference compound, NH\(_4\)NO\(_3\), at \(-358.4\) ppm, and the small chemical shielding anisotropy is also characteristic for a tetrahedral symmetry at the nitrogen atom.\(^{66}\) Hence, both the chemical shift and its anisotropy are indicative of a tetrahedrally coordinated nitrogen in the methyl benzoxazine dimer, requisite for the hydrogen-bonded N···H···O arrangement to be present.

As has been outlined above, REPT and DIP approaches can be carried out such that a sideband pattern is observed, in which the dipolar coupling information is encoded. Figure 8 shows an example of a rotor-encoded \(^1\)H-detected DIP-HSQC spectrum (using the pulse sequence given in Fig. 6c). The displayed \(F_2\) and \(F_1\) projections correspond to the (DIP-HSQC-filtered) \(^1\)H spectrum and the rotor-encoded spinning-sideband patterns, respectively. Note that the pulses were applied on-resonance on the \(^{15}\)N channel, and the \(t_1\) signal was detected as phase-insensitive cosine data. Since a pure dipolar rotor-encoding of the \(t_1\) signal, as observed in our case, gives rise to a periodic amplitude modulation, the acquisition can be restricted to a single rotor period, i.e. \(0 < t_1 \leq t_2\). However, to prevent correlated noise from being superimposed with the sideband pattern, signal acquisition for \(0 < t_1 \leq 2t_2\) is preferable. In the course of data processing, the \(t_1\) signal is catenated before Fourier transformation in \(t_1\).

The N···H proton chemical shift of \(11.2\) ppm corresponds to values expected for hydrogen-bonded structures, for example in bilirubin\(^1\) as well as in ureido-pyrimidinone complexes studied using high-resolution \(^1\)H MAS\(^2\), where

\[ \text{N–H} \quad \begin{array}{c} \text{OH} \quad \text{CH} \quad \text{CH} \quad \text{CH}_3 \end{array} \]

Figure 8. The 2D \(^1\)H–\(^{15}\)N spectrum of the \(^{15}\)N-labelled methyl benzoxazine dimer obtained using the inversely (\(^1\)H) detected DIP-HSQC sequence (Fig. 6c), with \(\tau_{\text{rcpl}} = 18\,\tau_\text{R}.\,\, F_1\) and \(F_2\) skyline projections, corresponding to the (DIP-HSQC-filtered) \(^1\)H spectrum and the rotor-encoded spinning-sideband patterns, respectively, are shown. The \(^1\)H resonances in the \(F_2\) dimension are assigned according to the \(^1\)H MAS spectrum.

\(^1\)H resonances in the range of 10–15 ppm were assigned to protons involved in N···H···O or N···H···N hydrogen bonds. Similar chemical shifts are also observed among imidazole-containing enzymes, in which the N···H···O interaction has been extensively studied using solid-state NMR.\(^3\) These observations give qualitative assurance of the hydrogen-bonding nature of the N···H interaction in the methyl benzoxazine dimer. The N···O distance, determined crystallographically,\(^3\) is 265.4 pm, corresponding to a comparatively close interaction. For such N···O (or O···O) distances, typical \(^1\)H chemical shifts range from 12 to 17 ppm.\(^3\) These examples, however, examined an N-H bonding interaction, with a hydrogen ‘bridge’ to oxygen. Thus, the relatively low chemical-shift value observed in the benzoxazine dimer points toward a preferred O–H bonding and, therefore, a relatively long N···H hydrogen bonding distance. This is consistent with the expected phenolic character of the benzoxazine, in which the proton is involved in a continuous, bent O···H···N bond in a distorted six-membered ring.

Of vital importance is the observation that the \(^1\)H resonance of interest is well resolved from the other \(^1\)H resonances in Fig. 8. Moreover, this resonance experiences the strongest coupling to the \(^{15}\)N nucleus, since only this resonance exhibits third-order sidebands in the \(^{15}\)N dimension. For longer recoupling times, third-order sidebands for the CH\(_3\) and CH\(_2\) groups become evident, too, but these are not analysed here.

The build-up of rotor encoded N···H sideband patterns observed at the 11.2 ppm \(^1\)H shift are presented in Fig. 9 for a range of recoupling times \(\tau_\text{rcpl}\), together with the corresponding fits, generated by numerically evaluating the
expression given in Eqn 13. The expected trend is observed, as the relative intensity of the third-order sidebands increases with increasing recoupling time. The relative intensities, together with the dipolar coupling constants, and corresponding N-H hydrogen-bond lengths are given in Table 3.

For sideband patterns recorded with longer recoupling times, i.e. \( \tau_{\text{rcpl}} = 26 \tau_R \) and \( \tau_{\text{rcpl}} = 30 \tau_R \), as illustrated in Fig. 9e and f, the fitting procedure yields N-H distances that are accurately determined.

<table>
<thead>
<tr>
<th>Table 3. Dipolar coupling constants and internuclear N-H distances determined from the inversely detected DIP-HSQC rotor-encoded sideband patterns in Fig. 9</th>
</tr>
</thead>
<tbody>
<tr>
<td>3rd/1st sidebands (%)</td>
</tr>
<tr>
<td>( N_{ac} / \tau_R )</td>
</tr>
<tr>
<td>10</td>
</tr>
<tr>
<td>14</td>
</tr>
<tr>
<td>18</td>
</tr>
<tr>
<td>22</td>
</tr>
<tr>
<td>26</td>
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<td>30</td>
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The goal of this investigation was to measure the N-H distance in an N-H-O hydrogen bond of methyl-substituted benzoxazine dimers, which are presumed to contain the hydrogen bond as a part of a distorted six-membered ring. To determine relatively weak dipole-dipole couplings, special care had to be taken to select the most informative experiments. In particular, in the methyl benzoxazine dimer the single \( ^{15}\text{N} \) nucleus is subject to several N-H couplings of comparable strength. Therefore, the chemical shift resolution in the \( ^1\text{H} \) dimension is essential to the study in order to identify and access the N-H coupling relevant to the hydrogen bonding. Moreover, the perturbing influence of further couplings to other spins must be minimized. To this end, \( ^1\text{H}-^{15}\text{N} \) dipolar recoupling methods under fast MAS have been considered with respect to \( ^1\text{H} \) or \( ^{15}\text{N} \) signal detection and the pathway of transverse \( ^1\text{H} \) or \( ^{15}\text{N} \) spin states. Of the methods described, the inversely detected symmetric DIP-HSQC sequence was chosen, on the basis of its ability, firstly, to provide \( ^1\text{H} \) chemical shift resolution, and, secondly, to avoid possible heteronuclear multi-spin effects in the case of the methyl benzoxazine dimer, such that a relatively long N-H hydrogen bonding distance could be determined despite the presence of several other NH couplings of comparable strength. Using this experiment, a long N-H distance of 194 ± 5 pm was determined, which indicates that, in the hydrogen bond, the proton is proximal to the oxygen, while being shared to some extent with the nitrogen. Thus, the dimer exhibits a predominant phenolic character. Furthermore, with regards to the experimental time necessary to achieve comparable spectral quality, the \( ^1\text{H} \)-detected variants are known to provide significant sensitivity enhancement.23,61

**SUMMARY AND OUTLOOK**

For sideband patterns extracted from \( ^1\text{H}-^{15}\text{N} \) REPT inversely (\( ^1\text{H} \)) detected DIP-HSQC spectra with \( \tau_{\text{rcpl}} = 10 \tau_R \), (b) \( \tau_{\text{rcpl}} = 14 \tau_R \), (c) \( \tau_{\text{rcpl}} = 18 \tau_R \), (d) \( \tau_{\text{rcpl}} = 22 \tau_R \), (e) \( \tau_{\text{rcpl}} = 26 \tau_R \), (f) \( \tau_{\text{rcpl}} = 30 \tau_R \). Experimental data are shown on the left, together with the corresponding best-fit simulated spectra.

\[ \text{N-H distance} = 194 \pm 5 \text{ pm} \]

In Fig. 9a, only first-order sidebands are evident; therefore, no dipolar coupling constant can be obtained. In Fig. 9b–d, the relative intensity of the third-order sidebands increases uniformly, from which dipolar coupling constants and N-H distances are accurately determined.

Fig. 9. Spinning-sideband patterns extracted from \( ^1\text{H}-^{15}\text{N} \) REPT inversely \( ^1\text{H} \) detected DIP-HSQC spectra with (a) \( \tau_{\text{rcpl}} = 10 \tau_R \), (b) \( \tau_{\text{rcpl}} = 14 \tau_R \), (c) \( \tau_{\text{rcpl}} = 18 \tau_R \), (d) \( \tau_{\text{rcpl}} = 22 \tau_R \), (e) \( \tau_{\text{rcpl}} = 26 \tau_R \), (f) \( \tau_{\text{rcpl}} = 30 \tau_R \). Experimental data are shown on the left, together with the corresponding best-fit simulated spectra.

\[ \text{N-H distance} = 194 \pm 5 \text{ pm} \]
In conclusion, the inversely detected DIP-HSQC experiment has achieved three major goals. Firstly, the resolution in the $^1H$ dimension allows us unambiguously to identify the $^1H$–$^{15}N$ coupling of interest. Secondly, the effect of dipolar interactions between the $^{15}N$ and other protons, though of comparable strength, could be suppressed by using fast MAS and selecting a coherence transfer pathway with $^1H$ transverse states during both recoupling periods. In this way, the $^1H$–$^{15}N$ coupling of interest could be measured selectively. Thirdly, by employing $^1H$ detection signal, sensitivity is enhanced and experiment times are minimized by more than an order of magnitude.

It should be noted that the $^1H$–$^{15}N$ dipolar NMR methods described here focus on elucidating average structural features, and maximizing the spectral intensity. The dynamics of proton transfer within N···H···O and N···H···N hydrogen bonds is also a topic of intense investigation, particularly for low-barrier hydrogen bonds. However, in our investigation of benzoxazine dimers, we have assumed a rigid structure, which does not include possible proton-transfer effects. Examination of the influence of dynamics on dipolar recoupling NMR experiments and the development of methods to access dynamical information on different time scales in the millisecond range is in progress (see also Ref. 70).

Moreover, further methodological developments will exploit the different ways by which the variants of the HSQC recoupling experiment discussed here are sensitive to multi-spin interactions. The combination of different $^{15}N$- and $^1H$-detected variants of REPT and DIP-HSQC approaches offers promising potential for studying both a spin-pair interaction of interest as well as for exploring, e.g., the geometry of the multi-spin environment.

**EXPERIMENTAL**

**Synthesis**

The synthesis of a $^{15}N$-labelled methylamine-based benzoxazine dimer, $N,N$-bis(3,5-dimethyl-2-hydroxybenzyl)methylamine-$^{15}N$, was carried out according to a previous study with the exception that methylamine-$^{15}N$ hydrochloride was substituted for methylamine. To produce the methylamine-$^{15}N$-based benzoxazine monomer, the mixture of (methylamine-$^{15}N$ hydrochloride (99%): NaOH (98%): water = 1 : 1 : 10) was stirred at 10°C for 1 h in order to obtain methylamine-$^{15}N$ solution. Subsequently, a 2 : 1 ratio of $p$-formaldehyde:2,4-dimethylphenol was added to the methylamine-$^{15}N$ solution with chloroform as a reaction solvent, following which the reaction was refluxed heterogeneously for 2 h. The reaction product in the chloroform layer was washed by 2 m NaOH solution several times, and finally washed using distilled water. 1 m of methylamine-$^{15}N$-based benzoxazine monomer was reacted with 1 m of 2,4-dimethylphenol at 105°C for 30 min without solvent, and the final product was recrystallized three times using n-hexane, with an overall yield of 81%. White, irregular crystals were obtained. $^1H$ NMR (200 MHz, CDCl$_3$, 298 K) δ: 2.21, 2.22 (15H, CH3), 3.64 (4H, Ar–CH2–N), and 6.73, 6.87 (4H, Ar–H). $^{13}C$–NMR (50.1 MHz, CDCl$_3$, 298 K) δ: 121.80, 124.24, 128.24, 130.84, 152.00 (12C, Ar). 20.41 (4C, Ar–C), 41.06 (1C, N–C), 59.25 (2C, Ar–C–N), and 121.80, 124.24, 128.24, 130.84, 152.00 (12C, Ar).

**Solid-state NMR**

Data were collected on a 16.4 T magnet with a Bruker DRX spectrometer, using a double-resonance MAS probe supporting rotors of 2.5 mm outer diameter. The resonance frequencies of $^1H$, $^{13}C$ and $^{15}N$ are 700 MHz, 176 MHz, and 71 MHz respectively. The sample was spun at 30 kHz. The $\pi/2$ pulse lengths were set to 2 µs for $^1H$ and $^1H$–$^{15}N$ experiments, and to 2.5 µs for $^1H$–$^{15}N$ experiments. A recycle delay of 3 s was used. The spectra are referenced to $^{15}NH_4NO_3$ ($-358.4$ ppm, $^{15}N$), adamantanate (1.63 ppm, $^1H$) and alanine (52 ppm, $^{13}CH$). The rotor-synchronized $^1H$–$^1H$ DQ spectrum was recorded using a five-pulse sequence with $\tau_{exc} = 1/2t_R$. States-TPPI was applied for phase-sensitive detection in $t_1$, and 64 slices were detected in the indirect dimension, with 16 transients averaged per slice. The experimental time was about 1 h.

All heteronuclear dipolar recoupling experiments were carried out with equal excitation and reconversion times. For the rotor-synchronized $^1H$–$^{13}C$ spectrum, an excitation time of $t_{exc} = t_R$ was used, and the number of slices in the indirect dimension was 24, with 512 transients averaged per slice. Phase-sensitive detection in $t_1$ was achieved through States-TPPI, and the experiment time was ~8 h. The time signal for the $^1H$–$^{15}N$ HSQC spinning sideband patterns was recorded at excitation times of $t_{exc} = 2, 6, 10, 14, 16, 18, 20, 22, 26$ and 30 $\tau_R$, with $t_1$ being incremented in steps of 1.67 µs. 20 slices were collected in the indirect dimension, with 128 transients averaged per slice The experimental time was approximately 90 min. The $^1H$ transmitter frequency was set to ~6 ppm, and the on-resonance transmitter frequency for the $^{15}N$ signal was selected.

For heteronuclear experiments employing $^1H$ detection in the solid state, an adequate phase cycle is of particular importance to ensure pure signal. The basic phase cycling scheme starts with a sign alternation through a phase inversion of one of the two 90° pulses applied to $^{15}N$ in every other transient. In this way, the signal of $^1H$ involved in NH correlations is selected after two steps. A further sign alternation is performed on the initial $^1H$ polarization by changing the phase of the first $^1H$ pulse accordingly, as familiar from CP experiments (two more steps in the cycle). In addition to these fundamental selection procedures, the suppression of contributions from possible $^1H$ higher-order coherences to the signal is important. This was achieved by implementing two nested four-step phase cycles of the excitation and reconversion blocks on the $^1H$ channel. In the case of $^{15}N$ detection, simple two-step cycles usually suffice, because dilute $^{15}N$ spins do not usually form homonuclear double or triple quantum coherences. Heteronuclear pulse sequences employing $^1H$ detection, in contrast, need to eliminate spurious signal of homonuclear $^1H$ double, and potentially higher, quantum coherences to ensure undistorted patterns of purely heteronuclear origin. Consequently, in our experiments the overall phase cycle consisted of $2 \times 2 \times 4 \times 4 = 64$ steps.

**Acknowledgements**

Financial support from the DFG is acknowledged. HI and GRG thank the Alexander von Humboldt Stiftung and NSERC (Canada).
for a senior scientist award and a post-doctoral fellowship respectively. Stimulating discussions with Kay Saalwächter are gratefully acknowledged.

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