Distance measurements between carbon and bromine using a split-pulse PM-RESPDOR solid-state NMR experiment

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Abstract

Solid-state Nuclear Magnetic Resonance have been long used to probe atomic distances between nearby nuclear spins by virtue of the dipolar interaction. New technological advances have recently enabled simultaneous tuning of the radio-frequency resonance circuits to nuclei with close Larmor frequencies, bringing a great promise, among other experiments, also to distance measurements between such nuclei, in particular for nuclei with a spin larger than one-half. However, this new possibility has also required modifications of those experiments since the two nuclei cannot be irradiated simultaneously. When measuring distances between a spin S=1/2 and a quadrupolar spin (S > ½), this drawback can be overcome by splitting the continuous-wave recoupling pulse applied to the quadrupolar nucleus. We show here that a similar adjustment to a highly-efficient phase-modulated (PM) recoupling pulse enables distance measurements between nuclei with close Larmor frequencies, where the coupled spin experiences a very large coupling. Such an experiment, split phase-modulated RESPDOR, is demonstrated on a 13C-81Br system, where the difference in Larmor frequencies is only 11 MHz, and distances are extracted using an unscaled analytical formula. Since bromine usually experiences particularly high quadrupolar couplings, as in the current case, we suggest that the split-PM-RESPDOR experiment can be highly beneficial for the research of bromo-compounds, including many pharmaceuticals, where carbon-bromine bonds are prevalent. We show that for Butyl triphenylphosphonium bromide, solid-state NMR distances are in agreement with a low-hydrated compound rather than a water-caged semi-clathrate form. The split-PM-RESPDOR experiment is suitable for distance measurement between any quadrupolar↔spin-1/2 pair, in particular when the quadrupolar spin experiences a significantly large coupling.

Keywords: Solid-state NMR; dipolar interaction; quadrupolar interaction; phase-modulated RESPDOR; distance measurement; tetra-n-butylammonium bromide hydrates; Br-81

1. Introduction

The introduction of the Rotational Echo Double Resonance (REDOR)¹ experiment in 1989 by Gullion and Schaefer has opened the path to accurate and robust distance measurements by magic-angle spinning solid-state NMR (MAS ssNMR) techniques, and these have been proven extremely useful in numerous works since. In the REDOR experiment, pairs of rotor-synchronized π pulses are applied every rotor period thereby decoupling all but the dipolar interaction (‘S” signal). When the pulses are omitted from the coupled spin, a reference signal is obtained (“S₀” signal). Promotion of time is achieved by incrementing the number of these pairs of π pulses, and therefore the increase of the REDOR fraction 1-S/S₀ is a measure of the dipolar interaction, that is, the inter-nuclear distance. Different versions of the experiment located the pulses either one per rotor period on every channel, or all but a single refocusing
pulse at one of the channels. Recent developments also facilitated efficient applications of the experiment at spinning speeds that exceed the available practical radio-frequency power levels.

Despite the great robustness of the experiment, the requirement for the pairs of $\pi$ pulses to fully invert the spin coherence in order for the interactions to fully be decoupled has prevented these kinds of measurements to be conducted on nuclei possessing large anisotropic couplings, such as the quadrupolar interaction, chemical shift anisotropy, and paramagnetically broadened species. This obstacle has led to further developments of REDOR-based experiments that could be (with varied efficiency) applied to quadrupolar nuclei as well. REAPDOR, LA-REDOR and S- or R-RESPDOR are some of the experiments that were developed and allowed the expansion of distance measurement potential to a larger variety of pairs of nuclei. All these experiments utilize a continuous-wave (cw) single pulse on the coupled quadrupolar nucleus lasting between a third and two rotor periods, and a spin-1/2 recoupling period where either pairs of $\pi$ pulses or symmetry-based recoupling is used. Nevertheless, for nuclei possessing quadrupolar interactions exceeding several megahertz, these widely and successfully used approaches begin to deteriorate in their efficiency and accuracy and hence many spin systems remained challenging.

A few examples for nuclei that tend to experience large quadrupolar interactions (v$_Q$ greater than ~5 MHz) are halogens, and various metals, all appearing in many biological, catalytic, and other important systems. Clearly there was a benefit to be gained from developing an experiment that could recouple distances to quadrupolar nuclei with larger quadrupolar frequencies more efficiently. Such improvement was achieved with the replacement of the cw pulse with a phase-modulated pulse, an experiment termed initially PM LA-REDOR, and later in accordance with the general acronym approach, PM-RESPDOR. Indeed, we have recently shown that the PM-RESPDOR experiment enabled us to retrieve distances in two challenging systems - a $^{13}$C-$^{209}$Bi (spin-9/2, v$_Q$=10.7 MHz) distance was obtained in bismuth-acetate, and a $^{31}$P-$^{79/81}$Br (spin-3/2, v$_Q$= 4.7 MHz for $^{81}$Br and 5.6 MHz for $^{79}$Br) distance in a different compound. Combining the PM pulse with the symmetry-based recoupling for the spin-1/2 nucleus, we have recently demonstrated the advantages of this pulse in the measurements of $^{13}$C-$^{14}$N distances as well, in an experiment acronymed PM-S-RESPDOR.

The main limitation in the distance measurement experiment is the inability of standard probes to tune to two channels simultaneously if the difference between their Larmor frequencies is in the order of 1-25 MHz. A notable innovation of this kind was introduced by Haase, Curro and Slichter in 1998, when they suggested a new probe design that allowed measuring such spin pairs. In 2002, $^{13}$C-$^{27}$Al REAPDOR distance measurements were demonstrated by Wullen and co-workers using a homebuilt double-resonance set-up. Those distances were used to characterize the geometry of methanol in HZSM-5 zeolite in order to explore methanol to gasoline reaction pathways. A different combination of frequencies, $^7$Li-$^{31}$P, was utilized by van Wullen et al. to study lithium-phosphate glasses.

A commercial frequency splitter is now available for splitting a single frequency into a double-resonance circuit, thus allowing a broader usage of distance measurements between nuclei with close Larmor frequencies. However, when using this new device, REDOR-based approaches evolving simultaneous irradiation on both channels still requires an adjustment, as it only enables irradiation of one of the channels at a time. Such an adjustment was proposed for the S-RESPDOR experiment in 2012 where $^{13}$C-$^{27}$Al distances were measured by splitting the saturation pulse applied on $^{27}$Al into two equal parts, and fitting the $\pi$ pulse on $^{13}$C in the gap. This work paved the way for S-RESPDOR distance measurement experiments to be used for systems with close Larmor frequencies, such as the first $^{51}$V-$^{13}$C distance measurement by NMR. Additional studies demonstrated correlation measurements between nuclei with close...
Larmor frequencies such as DNP enhanced $^{27}\text{Al}-^{13}\text{C}$ 2D D-HMQC that was used for probing the structure of a metal-organic framework material\textsuperscript{17}, and $^{27}\text{Al}-^{13}\text{C}$ HETCOR D-HMQC and J-HMQC 2D experiments conducted on two co-catalysts that have importance for the polymerization process of olefins\textsuperscript{18}. Recently we demonstrated how $^7\text{Li}-^{31}\text{P}$ 2D TEDOR and REDOR experiments can be utilized to define the binding environment of the mood stabilizer Li in ATP\textsuperscript{19}.

In all the studies mentioned above the quadrupolar spins had relatively small couplings (~0.4-2 MHz for Al, 0.3 MHz for $^{51}\text{V}$, 25 kHz for $^7\text{Li}$), allowing measurements of inter-nuclear distances, and acquisition of correlation experiments by techniques involving direct inversion pulses or using cw saturation pulses. $^{81}\text{Br}$ is an example of a spin that usually possesses much stronger quadrupolar couplings, and its abundance in pharmaceuticals and other organo-bromine compounds makes the ability to measure $^{13}\text{C}-^{81}\text{Br}$ distances highly desirable. Since $^{13}\text{C}$ and $^{81}\text{Br}$ have only a difference of 11.2 MHz (6.9\%) in their Larmor frequencies (on a 14.1 T magnet - 600 MHz proton frequency), carbon-bromine distances have not been reported up to date by NMR techniques. In this work we show that a split PM-RESPDOR experiment can be used with a frequency splitter to successfully recouple $^{13}\text{C}-^{81}\text{Br}$ distances, opening its usage potential to nuclei with close Larmor frequencies. We show that this approach is sufficiently robust so that the distance can be obtained with a universal analytical formula fitted with a single parameters, the distance.

2. Methods

2.1. Materials:
Butyl triphenylphosphonium bromide (C$_{22}$H$_{24}$BrP, BrBuPPh$_3$) and tetra-n-butylammonium bromide (C$_{16}$H$_{36}$BrN, TBAB) were purchased from Acros Organics and Chem-impex intl respectively, and used without further modifications.

2.2. NMR experiments:
All experiments were performed on a Bruker AvIII spectrometer with a magnetic field of 14.1 T yielding Larmor frequencies of 599.9 MHz for $^1\text{H}$, 242.8 MHz for $^{31}\text{P}$, 162.0 MHz for $^{81}\text{Br}$, and 150.8 MHz for $^{13}\text{C}$. Triple resonance mode was used for all $^{31}\text{P}-^{81}\text{Br}$ distances. $^{13}\text{C}-^{81}\text{Br}$ distances in TBAB were measured using the split PM-RESPDOR experiment with the probe set to a double resonance ($^1\text{H}$-$^1\text{X}$) mode with a frequency splitter obtained from NMR Service, which allowed measuring both $^{13}\text{C}$ and $^{81}\text{Br}$ on the same channel (X). $^{31}\text{P}$-$^{81}\text{Br}$ distances were measured in BrBuPPh$_3$ both with PM-RESPDOR and the split PM-RESPDOR methods omitting the frequency splitter, for comparison. All PM-RESPDOR experiments were performed using only two $\pi$-pulses on the spin-half nucleus during the PM saturation interval\textsuperscript{10}.

Experimental parameters are described in the table below:

| Compound and experiment | BrBuPPh$_3$, $^{31}\text{P}(^{81}\text{Br})$ PM-RESPDOR | BrBuPPh$_3$ $^{31}\text{P}(^{81}\text{Br})$ split PM RESPDOR* | TBAB $^{13}\text{C}(^{81}\text{Br})$ split PM-RESPDOR** |
|-------------------------|-------------------|-------------------|-------------------|
| spinning speed          | 11 kHz            | 11 kHz            | 11 kHz            |
"Overall" PM pulse length | 10 Tr | 10 Tr*** | 10 Tr***
--- | --- | --- | ---
Actual PM pulse length | 10 Tr | 9.5834 Tr, 9.5867 Tr | 9.5526 Tr
recovery time (~5T₁) | 70 s | 70 s | 35 s
number of scans | 8 | 8, 32 | 128
acquisition time | 30 ms | 30 ms | 38 ms
`¹H π/2` pulse power | 100 kHz | 100 kHz | 100 kHz
`¹H CP power` | 61 kHz | 61 kHz, 63 kHz | 53 kHz
Spin 1/2 (³¹C for TBAB, `³¹P for BTPPB`) CP power | 47 kHz | 47 kHz | 37 kHz
CP duration | 3 ms | 3 ms | 2 ms
SWF-TPPM decoupling power | 100 kHz | 100 kHz | 100 kHz
Spin 1/2 (³¹C for TBAB, `³¹P for BTPPB`) π pulses power | 47 kHz | 47 kHz, 48 kHz | 37 kHz
Split length | --- | 26.3 µs | 26.3 µs
PM pulses power (on `⁸¹Br`)**** | 37 kHz | 37 kHz | 41 kHz
Phase Cycling on the spin-half π pulses (φ in fig. 1)** | XY64 | XY64 | XY8

Table 1: Experimental parameters for butyltriphenylphosphonium bromide (BrBuPPh₃) and Tetra-n-butylammonium bromide (TBAB) PM-RESPDOR experiments.

*Some rows have two values, because points of longer dephasing times on the recoupling curve were measured few days later, after a new optimization on the power levels of `³¹P` and `¹H`. The number of scans was also increased from 8 to 32.
**With a frequency splitter
***Including the splitting. In other words, this is the time duration between the red dots in fig. 1.
****Power level for `⁸¹Br` was estimated from KBr (KBr was also used to determine the `⁸¹Br` carrier frequency).

2.3. Simulations:
Numerical simulations of `¹³C{⁸¹B}` and `¹³C{²⁷Al}` PM-RESPDOR and its split version were performed using SIMPSON22 version 4.1.2 on a 16-core Ubuntu-linux system. Ideal π pulses were used on `¹³C`, except the two pulses between the red dots in Figure 1 (the echo pulses). A quadrupolar coupling constant (C_Q) of 9 MHz was used for `⁸¹Br`. The `¹³C-⁸¹B` simulations were performed with a dipolar coupling constant of 132 Hz corresponding to a distance of 3.95 Å, and with a spinning speed (vR=1/T_R) of 11 kHz, using 18 Euler γ-angles and 320 α/β angles employing the `Repulsion` method for powder averaging. A radio-frequency (rf) irradiation power of 40 kHz was used for all the pulses on both `¹³C` and `⁸¹B`, leading to a π pulse length of 12.5 µs. Following the actual experiments, a splitting gap of 0.3Tr-1µs was used, leading to a rescaling the PM pulse segments by 0.95625 and to an actual PM pulse length of 9.5625 T_R.

`¹³C{²⁷Al}` split-PM-RESPDOR simulations, representing a spin-1/2 ↔ spin-5/2 spin pair, were performed with a varying dipolar constant, quadrupolar coupling constant, and splitting gap, as
described in the inset of figure 2. All other parameters were the same as for the $^{13}\text{C}[^{81}\text{B}]$ simulations.

3. Results and discussion

3.1. The split PM-RESPDOR experiment

The split PM-RESPDOR experiment shown in Figure 1 resembles the original PM-RESPDOR experiment\(^9\), with the exception of the phase-modulation period, marked by the red dots. While in the original pulse sequence the phase-modulated saturation pulse lasts for the whole "confined by the red dots" period, here it only starts after the spin-half \(\pi\) pulse has ended and lasts a period of \(\text{PM1} = \frac{1}{2}(n \cdot 10T_R - \tau_\pi - 0.3T_R)\) where \(\tau_\pi\) is the \(\pi\) pulse duration on the spin-half nucleus, 0.3\(T_R\) is the time interval chosen for the splitting (other time periods might have worked as well, see below), and \(n\) is the PM saturation pulse length in units of 10\(T_R\) including the splitting (in other words, \(n \cdot 10T_R\) is the interval between the red dots in fig. 1). In all our experiments here \(n=1\) was sufficient however when \(C_Q\) is larger, \(n>1\) may be required.

After the 0.3\(T_R\) gap another PM1 saturation pulse is applied, and ends exactly where the second red dot is located. Both PM1 blocks are of the same length but are continuous in the order of phases; they consist of two kinds of pulses - one with length of \(\frac{2\text{PM1}}{10T_R} \cdot 0.75T_R\) and a constant phase of 225°, and the other one that lasts \(\frac{2\text{PM1}}{10T_R} \cdot 0.109375T_R\), with phases that vary between 2.2°-348.1°, as described in the PM-RESPDOR original work\(^9\). Here the duration of these two pulses was slightly rescaled by \(\frac{2\text{PM1}}{n \cdot 10T_R}\), in order to make room for the splitting gap. In addition, \(\frac{2\text{PM1}}{n \cdot 10T_R}\) was multiplied by \(n\) in order to extend the time interval between the red dots to last \(n \cdot 10T_R\) instead of 10\(T_R\), similarly to the extension that was used in previous work\(^10\). In our case \(n=1\).

In this version of PM-RESPDOR, only two \(\pi\) pulses are applied on the spin-half nucleus during the quadrupolar saturation pulse, which makes interlacing them in the non-irradiative intervals easier\(^10\). The first \(\pi\) pulse is applied at the beginning of the "overall" saturation period (marked by the first red dot), and the second one starts exactly 5\(n\) rotor-periods afterwards (as in the original sequence).

![Figure 1](image.png)

**Figure 1.** Split PM-RESPDOR pulse sequence. Filled bars on the half-spin are \(\pi\) pulses. The quadrupolar S-spin pulse is color-coded in a gray scale according to phase, which appears in the plot below. The actual phase values can be found elsewhere\(^9\) and their lengths are described above. The length of 10\(T_R\) may be extended to more rotor periods (either \(n \cdot 10T_R\) with integer \(n\), or any multiple of the rotor period with proper adjustment of the PM pulse).
3.2. Simulating split PM-REPSDOR – the effect of the gap

In order to examine the effect of introducing a gap into the pulse, we simulated several cases including variations in the gap length, quadrupolar coupling strength, and the dipolar coupling strength. All cases, summarized in Figure 2, show that the effect of the gap is minimal and that the experiment can still safely be fit with the analytical Bessel function with a single parameter fit (be it the distance or the dipolar interaction).

In Figure 2a, we show the entire RESPDOR curve for a spin-3/2 experiencing a quadrupolar frequency $v_Q=C_Q/2=4.5$ MHz. It is practically impossible to decipher the PM-RESPDOR curve from the split version and from the analytical Bessel function given by equation (1):23

$$\frac{\Delta S}{S_0} = n_a \cdot \frac{1}{4} \left\{ 3 - \frac{\pi \sqrt{2}}{16} \sum_{k=1}^{16} (6 - 2(k - 1)) J_1(k \sqrt{2}(2N + 2)DT_R) - J_1(k \sqrt{2}(2N + 2)DT_R) \right\} $$ (1)

Here ‘$n_a$’ is the natural abundance of the quadrupolar-spin isotope, and $(2N + 2)T_R$ is the total dephasing time and does not include the PM pulse time itself.

In Fig. 2b we varied the quadrupolar coupling strength experienced by a spin-5/2. We now fit the data with the Bessel function adjusted for a spin-5/2 (eq. 2):

$$\frac{\Delta S}{S_0} = n_a \cdot \frac{1}{6} \left\{ 5 - \frac{\pi \sqrt{2}}{24} \sum_{k=1}^{24} (10 - 2(k - 1)) J_1(k \sqrt{2}(2N + 2)DT_R) - J_1(k \sqrt{2}(2N + 2)DT_R) \right\} $$ (2)

The fit values, denote by $D_{fit}$, are compared to the actual dipolar coupling we simulated ($D=130$ Hz), and this fit is repeated for both split and non-split versions. In all cases, the two methods are hardly separable, and all fit well to $D$, never below 93% of the expected value, and inline with results obtained for the non-split PM-RESPDOR technique. As shown before\(^{10}\), when the quadrupolar coupling strength becomes large, the PM pulse needs to be extended in order to obtain an efficient curve that can be fit with Eq. 2. This is demonstrated for the simulations with $v_Q=3C_Q/20=10.2$ MHz where a short PM pulse of 10$T_R$ does not provide a good distance estimate, but with 30$T_R$ the value is again within 10% of the actual dipolar coupling constant (more accurately, 4%), and is accurate also for the split version. A similar fit procedure was repeated for variations of the dipolar coupling value yielding again negligible dependence on the small gap of 26.3$\mu$s. Finally, fig. 2d shows that even if we increase the gap up to three rotor periods, the experiment is still viable and the error in the fit is still smaller than 10%. Up to a single rotor period, the accuracy is even higher, below 4%. This result is important since it allows one to perform a spin-1/2 selective experiment by incorporating a long weak selective pulse on this spin, without compromising the efficiency of the experiment.
Figure 2. Simulations of the split-PM RESPDOR experiment. (a) A recoupling curve obtained for a spin-3/2 with (blue cross) and without (red squares) the gap, and the corresponding Bessel function (Eq. 1, solid black line) with $D=132$ Hz, $v_Q=4.5$ MHz, a spinning speed of $T_R^{-1}=11$ kHz, and a gap of 26.3 μs (0.3$T_R$-1μs). (b) Simulations of the recoupling curve for a spin-1/2 coupled to a quadrupolar spin-5/2, with and without the gap, were fit using the Bessel function in Eq. 2 ($na=1$) and the values of $D_{mm}/D$ are plotted for different quadrupolar coupling constants. The simulations were done with $D=130$ Hz and fitting was performed for simulation points at the entire rise of the curve up to $t=11.3$ ms. The gap is 26.3 μs. For the strongest coupling the PM pulse was also extended to 30$T_R$ since a short 10$T_R$ pulse is insufficient to saturate the entire quadrupolar lineshape and thus does not provide a reasonable fit. (c) Simulations of the system in (b) as a function of the dipolar coupling constant with $v_Q=4.5$ MHz, and a gap of 26.3 μs. (d) Simulations of the system in (b) as a function of the gap with $D=750$ Hz, $v_Q=4.5$ MHz.

3.3. Experimental verification – $^{31}$P-$^{81}$Br distance measurements.

Initially we tested the performance of the split-PM pulse with respect to a known system, which has been measured already before. We used a regular commercial triple-resonance 4 mm probe to measure a $^{31}$P-$^{81}$Br distance in BrBuPPh$_3$. Figure 3 shows the $^{31}$P($^{81}$Br) split-PM- and regular PM-RESPDOR experimental $\Delta S/S_0$ fraction curves and the corresponding distance fits. For a spin-3/2, the experimental data points were fit to the analytical Bessel function given by equation (1). Here we used $na=0.495$ to account for the natural abundance of bromine-81. Both curves yield almost an identical distance (within the error range), 4.57(±0.05) Å for the regular experiment without splitting the pulse, 4.61(±0.02) Å for the split-PM experiment. Both match excellently to the crystallographic distance of 4.54 Å. This comparison validates experimentally the use of the pulse splitting to two parts and we could thus safely proceed to measure $^{13}$C-$^{81}$Br distances.
Figure 3. $^{31}P\{^{81}Br\}$ PM-RESPDOR (red squares) and split-PM-RESPDOR (blue crosses) fraction curves of BrBuFPhs. The experimental points were fitted to equation (1) using ‘cftool’ of MATLAB.

3.4. Close frequencies: $^{13}C\cdot^{81}Br$ distance measurements and identification of the hydrate form of tetra-n-butylammonium bromide

Measuring distances between carbon and bromine is usually hampered by the fact that their Larmor frequencies are either so close $|v_0^{13C} - v_0^{81Br}| = 0.547 \text{ MHz}$ (at 14.1T) that both are pulsed simultaneously, or close enough $|v_0^{13C} - v_0^{81Br}| = 11.247 \text{ MHz}$ to avoid triple-tuning on a conventional probe. Another limitation is on the efficiency of the experiment imposed by the large quadrupolar coupling constant of bromine, usually in the order of several Megahertz. Thus, in order to probe carbon-bromine distances, we combine the frequency splitter with the split-PM-RESPDOR technique.

We applied the experiment on the quaternary ammonium salt tetra-n-butylammonium bromide (TBAB), Figure 4. The positive charge on the nitrogen in this material is compensated for by the negatively charged bromine ion however, the position of this bromine ion depends strongly on the hydration state of this highly hygroscopic semi-clathrate hydrate crystal. Hydrated forms are known that include between $2\frac{1}{3}-38$ water molecules and the bromine ion position varies. Also, those structures show some disorder in the position of the carbon chains, and they can take two alternate conformations in some of the hydrates.

Figure 4. The chemical structure (left, generated by ChemSketch) and a single unit cell (right, generated with Mercury version 3.10.3) of TBAB•38H$_2$O$^{27}$. In one unit cell, two TBAB molecules are caged by the water molecules. Carbon numbering is from the nitrogen outwards making the methyl group C4. The two possible positions of the chains are manifested by the doubling of the carbons in the unit cell. The Br-C distances increase from the C4 methyl group (4.04Å) to C1 (5.01Å) and are shorter for the bromines
on the top left and down-right of the image. In the plot, oxygen in red, carbon in gray, nitrogen in cyan, bromine in orange.

The $^{13}$C spectrum of TBAB shown in Figure 5 contains four main shifts, corresponding to the different carbons on the butyl chain. Some of the signals further split showing some fine structure. The fine structure may be attributed to the disorder of the chain however since those split signals show almost identical recoupling curves ($3.86\pm0.06\text{Å}$, $3.83\pm0.04\text{Å}$ for C2, $3.9\pm0.1\text{Å}$, $4.03\pm0.09\text{Å}$, $3.95\pm0.08\text{Å}$ for C3, $4.21\pm0.06\text{Å}$, $4.34\pm0.07\text{Å}$, $4.16\pm0.06\text{Å}$ for C4), we also slightly broadened the spectra so that those signals merge and analyzed each of the four carbons on the chain.

![Figure 5. CPMAS spectrum of TBAB showing the four carbons on the chain. The spectra were slightly line-broadened with 20Hz. The peaks correspond from left to right to C1 (63.6 ppm), C2 (28.4 ppm), C3 (23.4 ppm), C4 (17.9, 17.4, 16.8 ppm). Chemical shifts are reported with respect to Adamantane methylene line at 40.48 ppm.](image)

Split-PM REPSDOR $^{13}$C{$^{81}$Br) recoupling curves and fits to equation (1) with ‘$n_a$’=0.495 are shown in Figure 6. The data (up to 4.5 ms) fit well to single $^{13}$C-$^{81}$Br spin pairs and the distances are for C1 $3.98(\pm0.04)$Å, for C2 $3.84(\pm0.04)$Å, for C3 $3.95(\pm0.04)$Å and for C4 $4.21(\pm0.03)$Å. Both the order of the distances as well as their absolute values do not fit the semi-clathrate structure shown in Figure 4. They also do not fit the hydrate with 32.5 water molecules where the closest distance for C1 is 6.6 Å, and not the one with 24 water molecules, where very short C-Br distances are encountered (2.8Å, 3.1Å). They fit pretty well to the lowest hydrate containing 2 1/3 water molecules$^{25}$. Interestingly, in this compound the water and bromine ions are caged between several TBAB units, unlike the structure shown above for TBAB$^{38}$H$_2$O. Analysis of C-Br distances below 4.5Å in this compound show that C1 is at distances of 3.9-4.4 Å, C2 at 3.7-4.2 Å, C3 is at 3.9-4.3 Å, and C4 is at distances of 3.9-4.5 Å. Some of these distances are reported to a disordered bromine site (Br2) and thus produce some distance distributions. In other cases a carbon may be in proximity to two bromine ions but such proximity results in an error of no larger than 15% in the distance when the two distances are equal, and even a difference as small as 0.5 Å reduces this error to below 10%. We can find in the crystal structure C1 at a distance of 3.9Å, and then C1 on a different chain having two distances of 4.1Å and 4.3Å. Summing on these contributions, and considering the error, we still remain with a results that fits our curves. C3 also exhibits two close distances at 4.6Å to Br1 and between 3.8-4.3Å to the disordered bromine resulting again in a small potential under-estimation of the NMR distance but still in agreement with our data. Thus, although the curves corresponding to our sample, used ‘as is’, represent a distribution of distances around some values, the results are very close to this hydrate, with C2 indeed showing the shortest distance.
In no case do we observe a distance of >5 Å or <3 Å as in the semiclavatrate materials with 20 water molecules and more, and we can safely state that our sample corresponds to the reverse structure of TBAB•2 1/3H₂O showing the octahedral arrangement of the six organic moieties, as shown in Figure 7. In this structure, one bromine ion is located between two water molecules, and the other is somewhat disordered between three close positions. The outer disordered bromine is the closest to the C3 and C4 carbons, while the interior bromine ion is closer to C1 and C2.

Figure 6. Split-PM RESPDOR $^{13}$C($^{81}$Br) recoupling curves of the compound TBAB, and fits to equation (1) are shown for the four carbons in the chain. Distances and error estimations were obtained by the ‘cftool’ for non-linear fit in MATLAB.

Figure 7. The structure of TBAB • 2 1/3H₂O showing the arrangement of 6 TBAB molecules around the water and bromine ions. Br₂ is slightly disordered. The distances for this form are in good agreement with the solid-state NMR data.

4. Summary and Conclusions

Magic-angle spinning solid-state NMR is an excellent tool to measure highly accurate (down to fractions of an Angstrom) inter-atomic distances. Robust techniques exist to study distances between pairs of nuclei with spin equaling one-half. Recent developments allowed to measure distances also in cases where one of the spins possess a significantly large quadrupolar coupling
constant. This works further extended the NMR distance measurement toolbox. Using split phase-modulated quadrupolar-spin recoupling pulses, combined with a proper hardware modification, we have shown how distances between spins having close Larmor frequencies can be measured, in this particular case between $^{13}\text{C}$ and $^{81}\text{Br}$ having a difference of only 7% in their gyromagnetic ratios. Simulations suggest that the method is robust and allows to increase the gap in the phase-modulated recoupling pulse so as to fit extended spin-1/2 pulses if desired, for example in the case of selective pulses. In addition, the recoupling curve under the split-pulse is not sensitive to the strength of the dipolar or quadrupolar coupling strengths, and in all cases can be fit to an analytical Bessel function.

In the experimental example we provide, we show how the distance determination can provide a means to differentiate between two hydrates of Tetrabutylammonium Bromide by probing distances between the halogen nuclei to all carbons of the butyl chain. Beyond this particular example, the split-PM RESPDOR experiment can be reliably, accurately and easily used to measure distances between many other spin pairs with close Larmor frequencies where one has a spin larger than one-half, for example $^{13}\text{C}-^{51}\text{V}$, $^{13}\text{C}-^{27}\text{Al}$, $^{13}\text{C}-^{45}\text{Sc}$, $^{117}\text{Sn}-^{11}\text{B}$, and other similar spin pairs that cannot be tuned on a commercial probe, or pulsed simultaneously. Moreover, it is also suitable when a multi-spin system exists since the half-spin can be excited selectively and the existence of several quadrupolar spins can be treated either analytically or by numerical simulations to provide the distances.

5. Acknowledgements

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