Journal of Magnetic Resonance 214 (2012) 151–158

Contents lists available at SciVerse ScienceDirect

Journal of Magnetic Resonance

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

Practical choice of ^{1}H–^{1}H decoupling schemes in through-bond ^{1}H–{X} HMQC experiments at ultra-fast MAS

Yusuke Nishiyama [a,*], Xingyu Lu [b], Julien Trébosc [b], Olivier Lafon [b], Zhehong Gan [c], P.K. Madhu [d], Jean-Paul Amoureux [b]

[a] JEOL RESONANCE Inc., 3-1-2 Musashino, Akishima, Tokyo 196-8558, Japan
[b] UCCS (CNRS-8181), Lille North of France University, Villeneuve d'Ascq 59652, France
[c] Center of Interdisciplinary Magnetic Resonance, NHMFL, Tallahassee, FL 32310, USA
[d] Department of Chemical Sciences, TIFR, Colaba, Mumbai 400 005, India

ARTICLE INFO

Article history:
Received 9 June 2011
Revised 5 October 2011
Available online 9 November 2011

Keywords:
Solid-state NMR
^{1}H
Very fast MAS
1 mm MAS
HMQC
CRAMPS

ABSTRACT

Three ^{1}H–^{1}H homonuclear dipolar decoupling schemes for ^{1}H indirect detection measurements at very fast MAS are compared. The sequences require the following conditions: (i) being operable at very fast MAS, (ii) a long T_2' value, (iii) a large scaling factor, (iv) a small number of adjustable parameters, (v) an acquisition window, (vi) a low rf-power requirement, and (vii) a z-rotation feature. To satisfy these conditions a modified sequence named TIlted Magic-Echo Sandwich with *zero* degree sandwich pulse (TIMES$_0$) is introduced. The basic elements of TIMES$_0$ consist of one sampling window and two phase-ramped irradiations, which realize alternating positive and negative 360° rotations of ^{1}H magnetization around an effective field tilted with an angle θ from the B_0 axis. The TIMES$_0$ sequence benefits from very large chemical shift scaling factors at ultra-fast MAS that reach $\kappa_{cs} = 0.90$ for $\theta = 25°$ at $\nu_r = 80$ kHz MAS and only four adjustable parameters, resulting in easy setup. Long $\kappa_{cs}T_2'$ values, where T_2' is a irreversible proton transverse relaxation time, greatly enhance the sensitivity in ^{1}H–{^{13}C} through-bond J-HMQC (Heteronuclear Multiple-Quantum Coherence) measurements with ^{1}H–^{1}H decoupling during magnetization transfer periods. Although similar sensitivity can be obtained with through-space D-HMQC sequences, in which ^{13}C–^{1}H dipolar interactions are recoupled, J-HMQC experiments incorporating ^{1}H–^{1}H decoupling benefit from lower t_1-noise, more uniform excitation of both CH, CH$_2$ and CH$_3$ moieties, and easier identification of through-bond connectivities.

1. Introduction

Sensitivity enhancement by indirect detection of ^{13}C and ^{15}N spectra via ^{1}H nuclei is a well established method in solution nuclear magnetic resonance (NMR) experiments [1–3]. Since the magnetization is transferred via J-coupling, the resulting 2D spectra show through-bond correlations which are useful for resonance assignments. The sensitivity enhancements are due to high natural abundance (≈99.99%) and gyromagnetic ratio of ^{1}H. The narrow line-widths of ^{1}H nuclei and their long T_2' values, which are much longer than the magnetization transfer periods, even for small J couplings, greatly contribute to sensitivity enhancement. However, high natural abundance and gyromagnetic ratio also lead to strong ^{1}H–^{1}H homonuclear dipolar interactions, which are fortunately averaged out by fast isotropic tumbling motions in the solution state. On the other hand, these interactions induce rapid spin diffusion among ^{1}H nuclei in rigid-solid samples, resulting in short T_2' relaxation times, typically less than tens of micro-seconds, and in broad ^{1}H line-widths usually more than 50 kHz under static conditions. These two facts quickly quench ^{1}H magnetization during the magnetization transfer periods and signal acquisition. Thus, indirect detection via ^{1}H nuclei in solid state seems not to be as efficient as in solution state, especially if ^{1}H–^{1}H interactions are not greatly decreased [4–11].

Decoupling of ^{1}H–^{1}H homonuclear dipolar interactions is hence essential to achieve efficient indirect-detection via ^{1}H nuclei in solids. Theoretically, ^{1}H–^{1}H homonuclear decoupling is easily realized by only applying an infinitely fast magic-angle spinning (MAS) sample rotation. Recently, rotation frequencies have largely increased with the advent of small diameter rotors [12]. However, even at $\nu_r = 80$ kHz, which is the fastest spinning frequency commercially available now [13], ^{1}H–^{1}H interactions still show significant effect on ^{1}H line-width and T_2' value (see Figs. 2 and 4). Therefore, rf irradiations, as well as MAS, are needed to decouple efficiently these interactions. Numerous ^{1}H–^{1}H decoupling schemes have been designed from the early stage of NMR [14–49]. Recently, sophisticated methods were developed by considering rf and mechanical averaging

* Corresponding author. Fax: +81 42 546 8068.
E-mail address: yunishiy@jeol.co.jp (Y. Nishiyama).

1090-7807/$ - see front matter © 2011 Elsevier Inc. All rights reserved.
doi:10.1016/j.jmr.2011.10.014

simultaneously [25–32]. Synchronized [29–32] or non-synchronized [33,34,38–41] Combined Rotation And Multiple Pulse Spectroscopy (CRAMPS) methods with ultra-fast MAS above $\nu_r = 60$ kHz have been introduced, including SAM [29–31], RN_n^{ν} [32], wPMLG$_{pp}^{x\bar{x}}$ [33], eDUMBO [38,40], and TIMES [41]. All of these rf-assisted ^{1}H–^{1}H decoupling methods suppress ^{1}H–^{1}H dipolar interactions, but inevitably introduce scaling down of ^{1}H isotropic chemical shifts, as well as of ^{13}C–^{1}H J-couplings, by a factor of κ_{cs}. As CRAMPS direct ^{1}H signal acquisition introduces a large additional noise and artifacts, very fast MAS alone is frequently preferred for line-narrowing in the direct ^{1}H dimension [5,50–52]. To our knowledge, no measurement of T_2' enhancement by ^{1}H–^{1}H dipolar decoupling during magnetization transfer periods has been reported for ^{13}C indirect detection in fast MAS through-bond ^{1}H–{^{13}C} correlation experiments. Although, this T_2' enhancement has been demonstrated in the ^{13}C direct detection scheme at moderate MAS frequencies [53].

In this article, we investigate the ^{1}H–^{1}H decoupling schemes during the magnetization transfer periods in through-bond ^{1}H–{^{13}C} correlation experiments with indirect ^{13}C observation via ^{1}H nuclei. The decoupling scheme should: (i) work well at very fast MAS to narrow the ^{1}H line-widths, (ii) enhance the T_2' relaxation time to reduce signal decay during the magnetization transfer periods, and (iii) show a large scaling factor to shorten the magnetization transfer periods. In addition to these features, it is preferable that the decoupling scheme presents several additional features: (iv) a small number of parameters to be optimized, (v) an acquisition window enabling a direct 1D observation during optimization, (vi) a moderate rf power requirement, and (vii) an effective global precession of the spins around B_0, usually called a z-rotation. Features (iv) and (v) enable a fast optimization of experimental parameters by directly observing 1D spectra. Features (vi) and (vii) are preferable to avoid sample heating and artificial modulations due to zero or symmetrical false ^{1}H peaks, respectively. Usually, feature (vii) presents the disadvantage of reducing the scaling factor; but it has experimentally been found that this is not the case for very fast MAS [49], as shown below.

First, we investigate two ^{1}H–^{1}H decoupling schemes, wPMLG$_{pp}^{x\bar{x}}$ and TIMES, at very fast MAS. We also introduce a new version of TIMES, named TIMES$_0$, in which the sandwich pulses are removed, thus leading to favorable features for ^{1}H–{^{13}C} J-HMQC (Heteronuclear Multiple-Quantum Coherence) experiments at ultra-fast MAS. To conclude, we compare two different ^{1}H–{^{13}C} indirect HMQC observations, either based on through-bond or on through-space correlations.

2. ^{1}H–^{1}H homonuclear decoupling schemes

In the article, we focus on three windowed non rotor-synchronized ^{1}H–^{1}H decoupling schemes: wPMLG$_{pp}^{x\bar{x}}$, TIMES and TIMES$_0$ (Fig. 1a). Indeed, these sequences work well at very fast MAS, enhance the T_2' relaxation time, have an acquisition window, and offer an effective z-rotation for ^{1}H magnetization [33,41]. The gray sandwich pulses are removed in wPMLG$_{pp}^{x\bar{x}}$ and TIMES$_0$, and hence, experimentally their pulse sequences are similar. However, as shown below, the two basic concepts of wPMLG$_{pp}^{x\bar{x}}$ and TIMES$_0$ sequences are very different and their optimizations do not only correspond to a re-parameterization process. In the three sequences the magnetization is rotated during each τ_p period with an angle ψ around the effective field, which is tilted from the B_0 axis by the angle θ. Every cycle period, $\tau_c = 2(\tau_p + \tau_\theta) + \tau_w$, the global rotation is cancelled in each R or $\bar{R}$ unit, since the direction of the rotation in the second τ_p period is reversed. Thus, the interaction frame of the rf-field is coincident with the rotating frame in each sampling window, τ_w, where the NMR signal is sampled. An effective z-rotation for the magnetization is achieved by applying two effective fields symmetrical with respect to B_0 during two consecutive τ_c periods [46–48]. The major difference between these methods is the ψ angle value and the presence or absence of sandwich pulses. These sequences are summarized in Table 1.

Let's first analyze the wPMLG$_{pp}^{x\bar{x}}$ sequence, which is composed with the R $\left(\text{wPMLG}_p^x\right)$ and $\bar{R}$ $\left(\text{wPMLG}_p^{\bar{x}}\right)$ units. Each unit was originally designed by adding an acquisition window to the windowless PMLG sequence, which is essentially the same as the Frequency-Switched Lee–Goldburg (FSLG) sequence [20]. In FSLG, the tilt of the effective field is achieved by an off-resonance irradiation at ν_{off} frequency, whereas PMLG employs an on-resonance irradiation and the tilt of the effective field results from a sweep of the rf phase from 0 to ϕ_{last} [22]:

$$\phi_{last}(^\circ) = 360 \cdot \nu_{off} \cdot \tau_p, \tag{1}$$

where τ_p is the length of the ramped on-resonance irradiation. The rotation angle ψ about the effective field during τ_p is described by:

$$\psi(^\circ) = 360 \cdot \nu_{eff} \cdot \tau_p = 360 \cdot \sqrt{\nu_{1p}^2 + \nu_{off}^2} \cdot \tau_p = \sqrt{(360\nu_{1p}\tau_p)^2 + \phi_{last}^2}, \tag{2}$$

where ν_{1p} is the strength of the on-resonance B_1 field during the phase ramp. ν_{eff} is the strength of the effective field, which is tilted by the angle θ with respect to the B_0 magnetic field:

$$\tan\theta = \frac{\nu_{1p}}{\nu_{off}}. \tag{3}$$

$\theta = \theta_m = 54.74^\circ$ is used in FSLG and PMLG to achieve the Lee–Goldburg condition, and the theoretical length of the phase ramp irradiation is chosen to achieve a full $\psi = 360^\circ$ rotation about the effective field, thus leading to $\tau_p = 1/\nu_{eff} = 1/\left(\nu_{off}^2 + \nu_{1p}^2\right)^{1/2}$ and $\phi_{last} = 208^\circ$. In practice, wPMLG$_{pp}^{x\bar{x}}$ is experimentally optimized by changing τ_p, while keeping the phase ramp final value of $\phi_{last} = 208^\circ$. This optimization leads to a concurrent variation of the offset frequency, ν_{off}, and of the θ and ψ angles. Indeed, after optimization, the experimentally optimized τ_p value tends to become shorter than its theoretical value [54], which corresponds to a θ angle smaller than θ_m (Eqs. (1), (3)), and to a ψ angle smaller than 360° (Eq. (2)).

With TIMES and TIMES$_0$, the effective rotation is always kept equal to $\psi = 360^\circ$ by changing not only the length of the on-resonance irradiation, but also simultaneously the phase sweep value (Eq. (2)) to:

$$\phi_{last}(^\circ) = 360.\left(1 - \tau_p^2\nu_{1p}^2\right)^{1/2}. \tag{4}$$

The length of sandwich pulses in TIMES is experimentally optimized, but the flip angle of these pulses is always found to be close to the θ value described with Eq. (3). These pulses hence align the z axis of the precession axis, tilted with the phase ramp, with the B_0 field. Under fast MAS, these two axes tend to be very close, and therefore the two sandwich pulses can be dropped, thus leading to the TIMES$_0$ sequence.

It is important to reduce experimentally the number of optimized parameters for quick, stable, and reproducible experimental setup. There are six experimentally adjustable parameters in TIMES: the lengths of sandwich pulses, τ_0, of ramp pulses, τ_p, and of window, τ_w, as well as the amplitudes of rf fields during sandwich pulses, ν_{10}, and ramp pulses, ν_{1p}, and the resonance offset frequency $\Delta\nu_0$. On the other hand, only four parameters (τ_p, ν_{1p}, $\Delta\nu_0$, τ_w) have to be optimized for wPMLG$_{pp}^{x\bar{x}}$ and TIMES$_0$ sequences.

As the interaction and rotating frames coincide every τ_c, the isotropic chemical shift scaling factor can be analytically calculated with first-order average Hamiltonian: