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^{2}H Natural-Abundance MAS NMR Spectroscopy: An Alternative Approach to Obtain ^{1}H Chemical Shifts in Solids

Takashi Mizuno,[*,†] Takahiro Nemoto,[†] Masataka Tansho,[‡] Tadashi Shimizu,[‡]
Hiroki Ishii,[§] and K. Takegoshi[§]

Contribution from JEOL Ltd., 3-1-2 Musashino Akishima Tokyo 196-8558, Japan, National Institute for Material Science, 3-13 Sakura Tshukuba Ibaraki 305-0003, Japan, and Department of Chemistry, Graduate School of Science, Kyoto University, Sakyo Kyoto 606-8502, Japan

Received April 4, 2006; E-mail: mizuno@kuchem.kyoto-u.ac.jp

Abstract: ^{2}H NMR was examined as an approach to determine ^{1}H chemical shifts in solids. For high-resolution observation, the line width due to ^{2}H quadrupole interaction and chemical-shift anisotropy was removed by magic-angle spinning and that due to ^{1}H−^{2}H dipolar interactions by ^{1}H decoupling. Further, we showed that the sensitivity can be enhanced by applying ^{1}H to ^{2}H cross polarization and by adding spinning-sideband spectra. These make it possible to obtain ^{2}H natural-abundance MAS spectra revealing highly resolved ^{2}H signals. The second-order quadrupole effects of ^{2}H are also examined.

Introduction

Despite the popularity of ^{1}H NMR in solution, ^{1}H NMR in solids has not been widely used. One reason for such unpopularity should be attributed to its low resolution due to large ^{1}H−^{1}H dipolar interactions and chemical-shift anisotropies in solids. For removal of the dipolar broadening and the chemical-shift anisotropy, a ^{1}H combined rotation and multiple pulse spectroscopy method (CRAMPS) can be used.[1,2] However, chemical-shift values obtained by a ^{1}H CRAMPS experiment should be carefully calibrated by taking account of the chemical-shift scaling factor, which varies with experimental settings, such as pulse width and timing. Here, we propose to measure NMR of ^{2}H, a stable isotope of ^{1}H. Since the isotope effect for the chemical shift is negligibly small (the difference between ^{1}H and ^{2}H chemical shift is −0.2 to +0.6 ppm in solution),[3] ^{2}H NMR would give chemical-shift information equivalent to that from ^{1}H NMR. However, such application of ^{2}H NMR in solids is rare because it is difficult to obtain chemical shift information under large quadrupole interaction ($e^2qQ/h\sim$ 200 kHz). Further, the sensitivity is low due to its low gyromagnetic ratio being 1/6.5 times of that of ^{1}H and the low natural-abundance ratio of ^{2}H (0.016%). It is worth noting that the former line width is due to the inhomogeneous first-order quadrupole interaction and thus can be removed by magic-angle spinning (MAS), leading to high resolution ^{2}H MAS NMR in solids.

So far, ^{2}H natural-abundance MAS NMR has been reported with motionally averaged quadrupolar broadening (approximately a few 10^1 kHz), such as methyl groups,[4−6] rotator phase solids,[7] rubbers,[8] and liquid-crystallines.[9−12] ^{2}H natural-abundance MAS NMR for rigid molecules, however, has not yet been examined, because its signal would be distributed over many spinning sidebands, so the signal-to-noise ratio is extensively lower compared to that of mobile ^{2}H. In this work, we overcome the low sensitivity by three methods; (i) ^{1}H to ^{2}H cross-polarization (CP),[13−15] (ii) sideband addition, and (iii) application of a strong magnetic field of 21.8 T. Further, effects of the second-order quadrupole interaction and ^{1}H decoupling on resolution were examined.

Experimental Section

As for a rigid organic system, we adopted dimedone (5,5-dimethyl-1,3-cyclohexanedione: the inset in Figure 1b) purchased from Nakarai Tesque, Ltd., and used without further purification. Dimedone forms a rigid crystalline structure due to the intermolecular hydrogen bonding[16,17] and is suitable for the present work because it includes a variety of proton species of methine, hydroxyl, methylene, and methyl. We also examine partially deuterated dimedone (dimedone-[2-^{2}H 100%,

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[†] JEOL Ltd.

[‡] National Institute for Material Science.

[§] Kyoto University.

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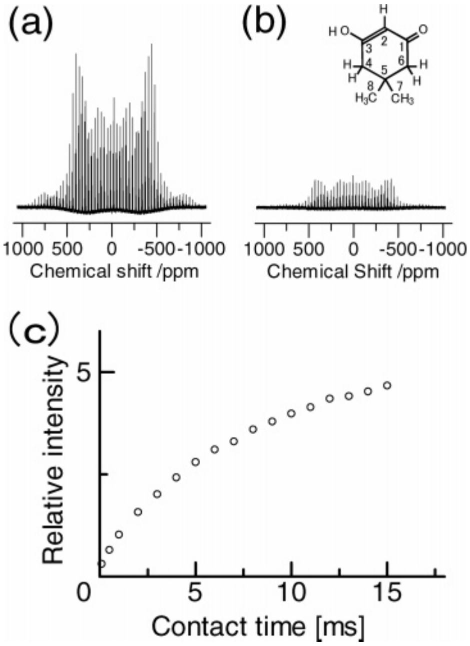

Figure 1. (a) 2H CPMAS spectrum of dimedone-[2-^{2}H 100%, 3-^{2}H 40%]. Experimental conditions are as follows. The spinning speed was 5.18 kHz and the rf strength of ^{1}H TPPM decoupling was 83 kHz. The CP contact time of 15 ms was used and 32 FIDs were accumulated with the repetition time of 5 s ($T_1(^1H)$=0.94s). The ^{1}H spin-locking field strength was 56.8 kHz and that of ^{2}H was 60 kHz. (b) ^{2}H spectrum taken by using a single $\pi/2$ pulse with the duration of 2.7 μs. 32 FIDs were accumulated with the repetition of 21.5s ($T_1(^2H) = 4.32$ s). These spectra a and b are plotted on the same amplitude scale and can be directly compared. (c) Contact time dependence of the total ^{2}H intensity. The vertical scale was expressed by taking the observed total ^{2}H intensity in Figure 1b as unity.

3-^{2}H 40%]) prepared by repeated recrystallization from D_2O. NMR experiments have been done using the 21.8 T magnet at the National Institute of Material Science operated by a JEOL ECA-930 spectrometer with a JEOL ^{1}H−^{2}H double-resonance MAS probe for a 4 mm rotor. ^{1}H Larmor frequency was 930.03 MHz, and that for ^{2}H was 142.76 MHz. All experiments were demonstrated under the spinning frequency of 5.18 kHz. The weight of the sample was ca. 50 mg for all experiments. The ^{2}H chemical shifts were calibrated in ppm relative to ^{2}H in 99.99% D_2O appearing at 4.72 ppm.

Results and Discussion

First, we examined ^{1}H to ^{2}H CP using the partially deuterated dimedone (p-^{2}H-dimedone). Figure 1a shows the CPMAS spectrum of p-^{2}H-dimedone, and Figure 1b is the ^{2}H spectrum taken by a single $\pi/2$ pulse excitation. Since the MAS spinning speed in Hz is much smaller than the quadrupole line width, these spectra show many spinning sidebands. Figure 1, panels a and b, shows that applicable signal enhancement per scan was realized by applying ^{1}H to ^{2}H CP. The difference in the envelopes of sidebands in the CP and the single pulse spectra (Figure 1, panels a and b) should be ascribed to orientational dependences of the ^{2}H spin−lattice relaxation time and the CP enhancement factor. Note here that for a static sample $^1H \rightarrow {}^2H$ CP enhances only parts of the ^{2}H spectrum due to off-resonance effects.[18,19] Under MAS, however, the enhanced part spreads to the whole ^{2}H spectrum by sample rotation, leading to the observed nonselective CP enhancement.[20] The maximum enhancement factor for ^{1}H to ^{2}H CP is given by[21]

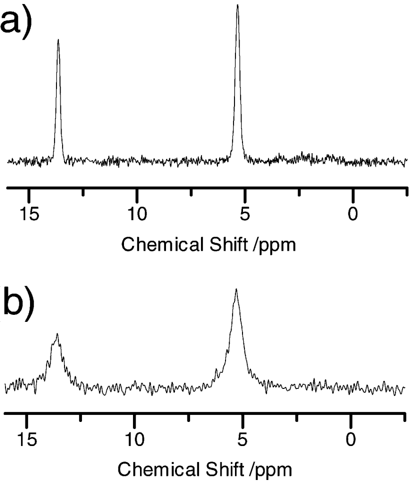

Figure 2. Centerband spectrum of the ^{2}H CPMAS spectrum shown in Figure 1a, (a) with and (b) without ^{1}H decoupling.

$$\frac{S_{CP}}{S_0} = \frac{\gamma_I}{\gamma_S}(1+\epsilon)^{-1} = 6.514\left(1+\frac{8N_S}{3N_I}\right)^{-1} \qquad (1)$$

where S_{CP} is the equilibrium polarization of ^{2}H under CP, S_0 is the thermal equilibrium polarization of ^{2}H, γ_I and γ_S is the gyromagnetic ratio of ^{1}H and ^{2}H, respectively, N_I and N_S is the number of ^{1}H and ^{2}H spin in a molecule, respectively, and ϵ is given by $[S(S+1)/I(I+1)]N_S/N_I$. The CP contact-time dependence of the total ^{2}H intensity (the sum of all sidebands and centerband intensities) was observed (Figure 1c). The ^{2}H intensity increased with increasing the contact time and finally attained S_{CP}/S_0 of 4.7 which is in good agreement with the theoretical enhancement factor of 4.8 derived from eq 1 with the given ratio of ^{2}H enrichment ($N_S/N_I = 1.4/10.6$). Note that sensitivity gain in natural abundance ^{2}H ($N_S/N_I = 0.00016$) becomes larger ~6.5. Since the repetition time of the ^{1}H−^{2}H CPMAS experiment was ca. 1/4 of that of the single $\pi/2$ pulse experiment, the gain in a total sensitivity enhancement factor becomes ~20 times per unit time by using CP. We would like to point out that, at spinning frequencies ≥10 kHz, the experimental enhancement factor decreases significantly. Effects of MAS on CP dynamics and ^{2}H line width are currently being examined and will be published elsewhere.

These spectra in Figure 1 were taken under ^{1}H decoupling. The line narrowing effects of decoupling is shown in Figure 2. In Figure 2a, only the centerband of the MAS spectrum (Figure 1a) is shown. Note that the spinning speed was that enough to push the first spinning sideband out of the centerband spectrum. The full-width at half-maximum of the hydroxyl peak at ~13 ppm is 84 Hz for the spectrum taken without decoupling (Figure 2b), and decreases to 30 Hz by decoupling (Figure 2a). For the methine peak at ~5 ppm, we observed narrowing of 91 Hz to 33 Hz. The observed line width is therefore ca. 0.2 ppm at 142.8 MHz, which is comparable to or better than the typical line width of ^{1}H obtained by CRAMPS: ~0.2 ppm in adipic acid[22] and ~1.2 ppm in some amino acids.[23] Hence, ^{1}H decoupling is

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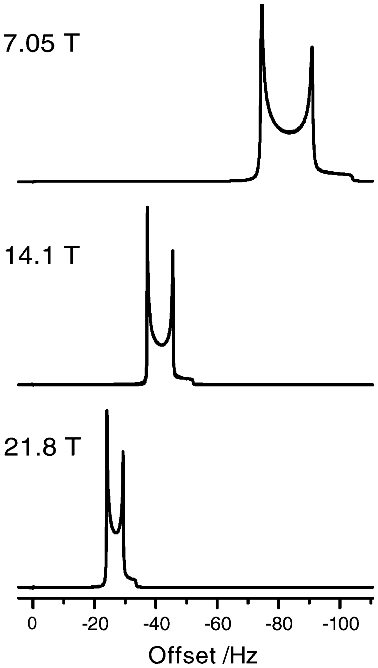

Figure 3. Calculated ^{2}H MAS NMR spectra. Infinitely fast MAS is assumed. The intensity of an external magnetic field is shown on the left side of each spectrum. Offset = 0 Hz corresponds to the isotropic chemical shift. A quadrupole coupling constant of 160 kHz and an asymmetric parameter of 0.0 were used for this calculation.

indispensable for high-resolution observation. It should be pointed out here that faster MAS can be used alternatively for ^{1}H decoupling.

Another possible cause of the line broadening would be the second-order quadrupole interaction.[24,25] To examine the second-order effect, we calculated ^{2}H MAS line shape (Figure 3) at three different magnetic fields by using theoretical equations in Kundla et al.[26] describing the second-order quadrupole interaction. The calculated line shapes show powder patterns with two-peaks with a small "bank", reflecting orientation dependence of the quadrupole interaction. Further, the apparent shift of the whole pattern due to the so-called isotropic second-order shift is appreciable. Even at a lower field of 7.05 T, the calculated peak splitting is small (ca. 16 Hz $\sim$ 0.36 ppm) and decreases with increasing the external field intensity to 5.3 Hz $\sim$ 0.037 ppm at 21.8 T. Hence, the line broadening effect is negligible for magnets $\geq$7 T. However, with respect to the spectral shift, a larger magnetic field is desirable; Figure 3 shows that the overall shift at 7.05 T is 74.6 Hz ~ -1.6 ppm, whereas that at 21.8 T is 25 Hz ~ -0.2 ppm. A magnetic field larger than 20 T is required for accurate measurement of the chemical shifts.

In practice, the deviation of the sample rotation axis from magic angle is the most probable cause for broadening of the ^{2}H MAS line shape. Here, we assume that the line width is approximately given by the first-order quadrupole interaction written as

$$|\Delta\nu(\theta)| = \left|\frac{3}{4}\frac{e^2qQ}{h}\frac{1}{2}(3\cos^2\theta - 1)\right| \tag{2}$$

where θ [rad] is the angle between the rotation axis and the external field. Equation 2 is expanded about a small deviation from magic angle, θ_{m}, as

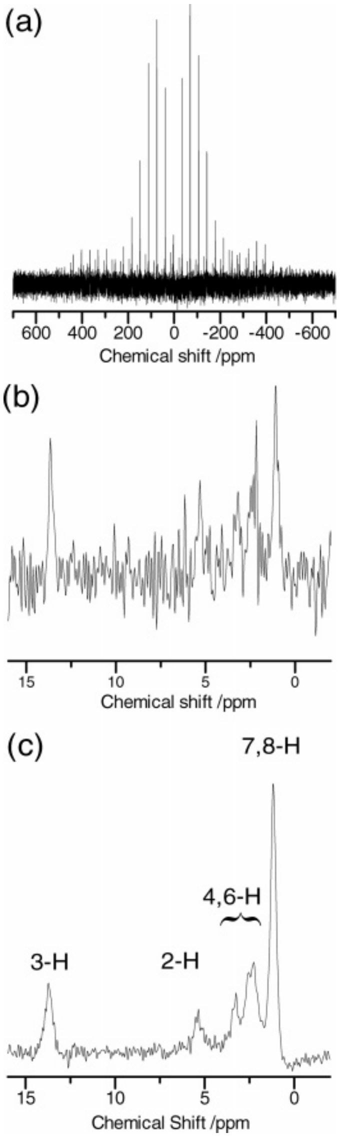

Figure 4. (a) ^{2}H natural-abundance CPMAS spectrum of dimedone. Experimental conditions are as follows; the spinning speed was 5.18 kHz, the rf strength of ^{1}H spin-lock field was 56.8 kHz, ^{2}H field was 61 kHz, and the rf strength for ^{1}H TPPM decoupling field was 61 kHz. The contact time of 15 ms was used. Total 12000 FIDs were accumulated with the repetition time of 4.0 s. (b) The centerband spectrum of (a). (c) The spectrum after adding −14th to +14th rotational sidebands.

$$|\Delta\nu(\theta)| \simeq \frac{3}{4}\frac{e^2qQ}{h}\sqrt{2}|\delta\theta| \tag{3}$$

where $\delta\theta = \theta - \theta_{\mathrm{m}}$. With $e^2qQ/h = 160$ kHz, this gives us the residual line width of the order of 10^2 Hz for $\delta\theta \sim 5.2 \times 10^{-4}$[rad] $\sim 0.03°$. For $\sim$30 Hz resolution, θ should be adjusted to θ_{m} within the error of 0.01°. In this work, we adjusted the angle by monitoring the ^{2}H spectrum of the sample itself.

Figure 4a shows the ^{1}H-decoupled ^{2}H CPMAS spectrum of the natural-abundance dimedone. Figure 4b is the centerband spectrum of Figure 4a and may exhibit all peaks corresponding

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to the chemical structure; however, it suffers from insufficient signal-to-noise ratio. To increase the signal-to-noise ratio, we numerically reconstructed the isotropic chemical-shift spectrum by shifting each member of a sideband array to centerband and adding them all together.[24] Here, we added the −14th to +14th rotational sidebands, and the sensitivity of the isotropic spectrum is effectively enhanced (Figure 4c). The reconstructed spectrum (Figure 4c) exhibits all ^{2}H signals expected for dimedone. Due to the different CP enhancement factors for each ^{2}H site, the observed intensities do not correspond to the expected abundance. Further, the differences in the quadrupolar coupling constants would affect the apparent intensities through the addition procedure of spinning sidebands. Note that slight broadening occurs by the sideband addition. This is attributed to missetting of the spinning angle and also to instability of the spinning speed. The present procedure has the advantage of compensating spinning-speed instabilities manually by choosing the order of the sidebands to be added. Instead of numerical sideband addition applied in this work, one can also reconstruct the isotropic spectrum by the rotor-synchronized FID sampling method.[24]

The observed chemical-shift values were collected in Table 1 and compared with the solution data.[27] The chemical-shift value of the hydroxyl group significantly differs from that in solution, indicating the strong hydrogen bonding in solids. The narrow line shape of the hydroxyl ^{2}H as compared to those commonly observed in ^{1}H CRAMPS spectra exhibits the apparent merit of ^{2}H NMR; a hydroxyl proton signal in ^{1}H CRAMPS usually broadens due to the off-resonance effects.[23] Although the chemical shifts of 4,6-H are equivalent in solution due to fast keto−enol tautomeric exchange, the different shifts indicate the exchange does not occur in solids. These results typically indicate the usefulness of ^{2}H high-resolution NMR in solids. Similar to ^{13}C CPMAS signals,[15] the intensities of each ^{2}H peak do not directly correspond to the abundance, owing to nonuniform CP enhancement.

Table 1. ^{2}H Chemical Shifts in Solids and ^{1}H Chemical Shifts in Solution[27] for Dimedone

δ [ppm]	2-H	3-H	4-H	6-H	7-H	8-H
^{2}H (this work)	5.4	13.8	(2.3)[a]	(3.3)[a]	1.2	1.2
^{1}H (in $CDCl_3$)	5.47	6.42	2.27	2.27	1.09	1.09

[a] The assignments of these sites are tentative.

In summary, we showed that highly resolved ^{2}H natural-abundance NMR for a rigid organic compound can be obtained with sufficient sensitivity by using (i) MAS, (ii) CP, (iii) ^{1}H decoupling, (iv) sideband addition, and (v) a high magnetic field of 21.8 T. The ^{2}H chemical-shift information should be very useful in solid-state chemistry as well as biochemistry, where hydrogen bonding plays an important role.

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