Communication

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Chemical Shift Correlation NMR Spectroscopy with Indirect Detection in Fast Rotating Solids: Studies of Organically Functionalized Mesoporous Silicas

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The development of solid-state NMR probes capable of MAS[1] at 40−70 kHz offers the possibility to effectively suppress homonuclear dipolar interactions between high-γ nuclei (^{1}H and ^{19}F).[2] The line narrowing effect, which in homogeneously broadened spectra is roughly proportional to ν_R, can be further enhanced by using a stronger magnetic field, due to the linear increase of separation between the resonance lines. At high magnetic fields, the use of fast MAS is a viable alternative to homonuclear dipolar decoupling via multipulse sequences.[2−4]

We have recently demonstrated numerous advantages of using fast MAS in ^{1}H−^{13}C and ^{1}H−^{29}Si HETCOR NMR of molecules covalently bound to mesoporous silicas.[5] The static ^{1}H line widths in these materials are between 10 and 20 kHz (fwhm), which implies that some molecular mobility is present. MAS at 40 kHz provided sufficient ^{1}H−^{1}H decoupling to allow identification of proton chemical functionalities. The residual line width was mostly inhomogeneous, due to the distribution of chemical shifts, and thus could not be further reduced by the use of multipulse sequences. The loss of sensitivity due to small rotor volume (∼8 μL) was easily offset by the more relaxed requirements for RF magnetic field homogeneity within the sample and the ability to optimally filter the signal compared to more stringent requirements of multipulse decoupling in a larger rotor.[5] Several additional advantages of the use of fast MAS became apparent, including simple experimental setup, lack of scaling factors, ease of acquisition of sideband-free spectra, and the convenience of using low-power decoupling schemes. Highly resolved 2D HETCOR NMR spectra, therefore, became accessible in natural abundance samples containing just a few hundred micrograms of surface-bound species.

The next rational step is to seek sensitivity gain through the detection of high-γ rather than low-γ nuclei. Indirect detection of heteronuclei is commonly used to produce H−X shift correlations in solutions (H and X denote the high- and low-γ nuclei, respectively).[6,7] Here, the sensitivity ratio between the indirect (X{H}-t_1-H{X}-t_2) and direct (H-t_1-X{H}-t_2) detection is roughly $(\gamma_H/\gamma_X)^{3/2}$, which for H = ^{1}H and X = ^{13}C equals 8. Since the sensitivity gain also depends on the square root of the ratio between the line widths of both nuclei,[8] the applicability of indirect detection to solids has been hitherto limited by the lack of adequate decoupling schemes. For example, CRAMPS-type[9] line narrowing via multipulse decoupling implies the use of stroboscopic sampling, which eliminates the potential sensitivity advantage of indirect detection. Although the availability of fast direct digital receivers and advances in probe design (such as the scroll coil[10]) may circumvent this sensitivity loss, the utility of CRAMPS will remain problematic at magnetic fields exceeding 11.7 T due to its inability to remove the CSA effects under slow MAS. However, indirect detection method can become advantageous in solids as soon as sufficient resolution is provided by very fast MAS. Indeed, sensitivity enhancement factors ranging from 1.5 to 3.3 have been reported in ^{1}H detected solid-state NMR of ^{15}N-labeled peptides and in naturally ^{13}C abundant polymers under MAS at ∼30 kHz.[8,11] More recently, 5- to 7-fold signal-to-noise (S/N) advantage was obtained in 2D (^{15}N−^{1}H)[12] and 3D (^{15}N−^{15}N−^{1}H)[13] shift correlation spectra of peptides and proteins. In both studies, MAS was combined with appropriate deuteration strategies to maximize the resolution under MAS rates that are appropriate for most biological applications (20 and 13 kHz, respectively), without compromising sensitivity.

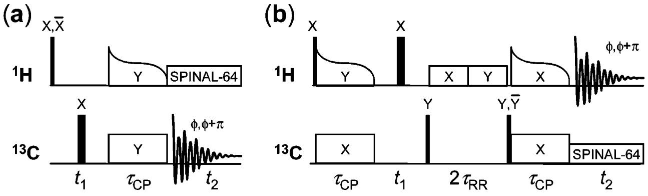

Figure 1. Pulse sequences for ^{13}C (a) and ^{1}H (b) detected HETCOR experiments under fast MAS. Solid rectangles represent $\pi/2$ and π pulses. In addition to phases shown, States-TPPI detection[15] was used through appropriate phase cycling of the first $\pi/2$ pulses in the ^{1}H channel (sequence (a)) and in the ^{13}C channel (sequence (b)). The pulse sequence can be found in the Supporting Information.[16]

Herein we report on the first indirectly detected 2D correlation spectrum of species bound to a surface. The experiment is demonstrated on a sample of mesoporous MCM-41 type silica (allyl-MCM), which contained ∼300 μg of covalently bound allyl groups ($-CH_2-CH{=}CH_2$) in the absence of templating molecules.[14] The sensitivity gain enabled the observation of a well-resolved spectrum without isotope enrichment in 15 min, a result that earlier would have been considered unrealistic.

The experiments were performed at 14.1 T on a Varian NMR System 600 spectrometer, equipped with triple resonance FastMAS probe. The ^{13}C detected HETCOR spectrum was obtained using the pulse sequence from our earlier study (Figure 1a),[5] with tangentially ramped CP.[17] The pulse sequence used for indirect detection (Figure 1b) was derived from that proposed by Ishii and Tycko,[8] except that instead of CW ^{1}H decoupling a single π pulse has been used in the middle of the evolution period. As in the case of scheme (a),[5] this pulse fully refocused the dephasing of non-observed magnetization due to heteronuclear scalar and residual dipolar couplings in the allyl-MCM material. As an added advantage, it helped to thermally stabilize operation of the RF amplifiers and the probe by keeping ^{1}H RF power at a steady duty cycle for every value of t_1, similarly to the previously reported constant time RF scheme.[4] We note that under 40 kHz MAS this simple approach is not useful in strongly coupled ^{1}H systems, such as glycine, where the customary heteronuclear decoupling schemes, such as cw, TPPM,[18] or SPINAL-64,[19] must be used during t_1 to maximize the resolution. Any residual ^{1}H magnetization remaining after the evolution period was eliminated using rotary resonance recoupling by a pair of long pulses with orthogonal phases[11,20] whose amplitudes satisfied the HORROR condition $\nu_{RF}^{H} = n\nu_R$ (with n = 1/2 or 1, see below). These measures helped eliminate t_1 noise. In addition, a great deal of attention has been focused on

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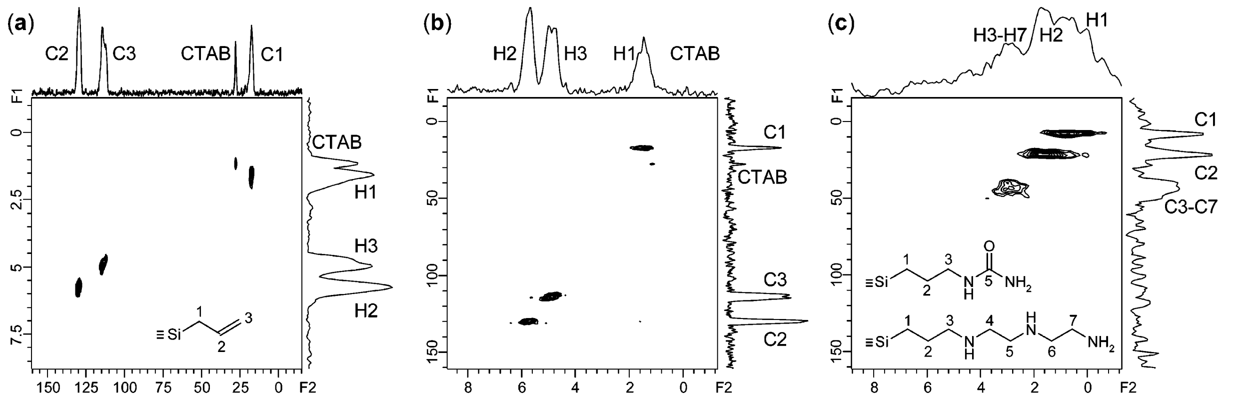

Figure 2. Two-dimensional $^1H-^{13}C$ (a) and $^{13}C-^1H$ (b) spectra of allyl-MCM silica taken using ^{13}C and ^1H detected HETCOR schemes shown in Figure 1a and 1b. Spectrum (c) was performed using indirect detection on bifunctional MCM-41 type silica functionalized with UDP and AEP groups. All experiments were carried out using $\nu_R = 40$ kHz, $\nu_{RF}^{H} = 62.5$ kHz during $\pi/2$ and π pulses, $\nu_{RF}^{H} = (3/2)\nu_R$ (± 3 kHz tangent ramp) during CP, $\nu_{RF}^{C} = 100$ kHz during $\pi/2$ and π pulses, $\nu_{RF}^{C} = (5/2)\nu_R$ during CP, $\tau_{CP} = 2$ ms (except for (c), where $\tau_{CP} = 0.5$ ms), $\nu_{RF}^{H} = \nu_{RF}^{C} = 12$ kHz during SPINAL-64 decoupling, and a delay between scans of 0.8 s. Spectrum (a) was acquired in 100 rows, with 320 scans per row and t_1 increments of 25 μs. Spectra (b) and (c) were acquired in 120 rows, with 4 and 256 scans per row, respectively, and t_1 increments of 25 μs. The 1D projections are shown in skyline mode. F1 and F2 denote indirect and direct dimensions. The total acquisition times in experiments (a), (b), and (c) were about 15 h, 15 min, and 15 h, respectively.

enhancing the overall stability of the experiment by proper management of amplifier blanking, eliminating phase transients, stabilization of the MAS rate and rotor temperature,[16] and maintaining constant ambient conditions.

Directly and indirectly detected HETCOR spectra of the allyl-MCM sample are compared in Figure 2a and 2b. Line assignments follow our earlier report.[5] Both spectra were acquired using similar experimental conditions (see the figure caption). In particular, all $^1H-^{13}C$ and $^{13}C-^1H$ CP transfers used the same pulse shapes and RF amplitudes. The experimental parameters were thoroughly optimized using freely available simplex routines.[21] It was found that the complete suppression of uncorrelated ^1H magnetization under RR required a relatively long period $2\tau_{RR} = 30$ ms and that it was most effective under the condition $\nu_{RF}^{H} = \nu_R$. As expected, the $^1H-^{13}C$ and $^{13}C-^1H$ spectra exhibit similar resolution. The gain in sensitivity per scan, calculated for resonances C1−C3, is approximately 3.8. It is higher than that previously reported[11] due to a more favorable ratio between ^1H and ^{13}C line widths. An interesting, and previously unobservable,[5] splitting of H3 and C3 resonances can be attributed to the coexistence of functional groups in prone and upright positions on the surface. Indeed, the $^1H-^{29}Si$ spectrum of the same sample (not shown) exhibits only the downfield ^1H peak at the H3 position, which suggests that it represents the prone functionality. We note that the intensity due to residual CTAB molecules is severely diminished in spectrum (b). A reasonable but untested explanation of this signal loss is less favorable CP dynamics, the effect of which was compounded following two CP transfers. Also shown (Figure 2c) is the $^{13}C-^1H$ spectrum of a bifunctional MCM-41 type silica, which was functionalized with general acid (ureidopropyl, UDP) and base (3-[2-(2-aminoethylamino)ethylaminopropyl, AEP] groups in a 1:1 ratio as described earlier.[22] Increased line width in both dimensions and less favorable spin dynamics (short $T_{1\rho}$) have contributed to lower intensity of spectrum (c). Acquisition of the $^1H-^{13}C$ spectrum of this sample would require a week of instrument time at 600 MHz.

We have demonstrated that highly resolved 2D $^{13}C-^1H$ correlation spectra of natural abundance surface species on silica can be acquired more than 10 times faster using indirect detection under MAS at 40 kHz. Although advances in probe technology and methodology will continue, 3D ^{13}C NMR of surface-bound molecules is already becoming feasible.

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Supporting Information Available: Additional experimental details. This material is available free of charge via the Internet at http://pubs.acs.org.

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(1) MAS, magic angle spinning; ν_R, the sample rotation rate; HETCOR, heteronuclear correlation spectroscopy; fwhm, full width at half-maximum; 2D, two-dimensional; CRAMPS, combined rotation and multipulse spectroscopy; CP, cross polarization; RF, radio frequency; CSA, chemical shift anisotropy; ν_{RF}^{X}, the magnitude of RF field at the X spin frequency; τ_{CP}, the CP time; and τ_{RR}, the rotary resonance recoupling time.
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