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Spectral Editing in Solid-State MAS NMR Using Chemical-Shift-Anisotropy-Dephasing Techniques

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By combining the signal enhancement of cross polarization (*1*) with the averaging effects of high-power proton decoupling and of magic-angle spinning (*2, 3*), the CPMAS technique extends the widespread applicability of high-resolution liquid-state ^{13}C and ^{15}N NMR into the realm of solids (*4*). The complex nature of spin–spin couplings in rigid solids, however, precludes the straightforward incorporation into CPMAS experiments of heteronuclear coherence-transfer schemes, tools which during recent years have transformed the ways in which solution NMR spectra need to be acquired and interpreted (*5*). Among the most common approaches used in the assignment of solid-state NMR peaks are the dipolar-dephasing and the short-contact-time sequences (*6, 7*). The first experiment relies on a brief period of interrupted decoupling during which magnetizations from strongly proton-coupled $\rangle CH-$ and $-CH_2-$ moieties are allowed to decay, thus leaving simpler ^{13}C NMR spectra in which only resonances from weakly coupled methyl or quaternary carbons appear. Conversely, the second experiment relies on a cross-polarization period short enough to produce a significant ^{13}C magnetization enhancement only for strongly coupled $\rangle CH-$ and $-CH_2-$ carbons, leading to spectra which are essentially free from methyl or quaternary signals.

In spite of their usefulness and simplicity, the incomplete separation provided by these techniques has prompted extensive research toward the development of more complete forms of CPMAS NMR editing (*8–15*). Most of these efforts have focused on how to discriminate between methine and methylene signals, by relying on the slightly stronger ^1H–^{13}C dipolar couplings that characterize the latter groups. Early research demonstrated that this kind of selectivity can be achieved by replacing the decoupler-free decay period of the original dipolar-dephasing sequence by rotor-synchronized multiple-pulse trains (*8, 9, 11–13*). More recently, techniques have been developed which, by elaborating on the operational principles of the short-contact-time experiment, can differentiate methylene from methine groups according to their different rates of ^{13}C cross polarization/cross depolarization (*10, 14, 15*). All these solid-state NMR editing techniques share with their solution counterparts an effort to discriminate signals according to some chemical factor which is otherwise "invisible" in the final spectrum. Solution-phase techniques carry out this discrimination via indirect couplings, separating carbon NMR signals according to their multiplicity or their proximity to a certain heteronucleus. The solid-state NMR editing methods that have been developed so far are also based on differentiating spectral peaks according to heteronuclear couplings, although their performance is complicated by the many-body character of dipole–dipole interactions. In contrast to what happens in solution NMR, however, where J couplings usually constitute the only "invisible" interaction affecting ^{13}C spins, high-resolution solid-state NMR techniques average out *two* broadening mechanisms in order to provide isotropic shift spectra: the dipolar couplings and the chemical-shift anisotropies (CSAs). The first of these interactions constitutes the basis of all solid-state editing methods hitherto proposed; we discuss here the potential applications of the latter as a contrast mechanism for the routine simplification of NMR spectra.

Due to their entirely local nature, shift anisotropies provide a way of distinguishing among carbon signals on the basis of chemical rather than of multiplicity considerations. In some cases, however, these two criteria might overlap, for instance when trying to distinguish quaternary from methyl carbon resonances. Indeed, although the dipolar couplings of these two sites are similar, their shift anisotropies are usually considerably different, thus opening a simple route for their spectral differentiation. One of the most straightforward forms of CSA editing that can be conceived is the elimination of signals arising from carbons with large shift anisotropies via an interrupted averaging procedure, analogous to the one involved in the dipolar-dephasing technique. This would require removing the averaging effects of MAS after the cross-polarization mixing time and reintroducing them after a CSA-dephasing delay and throughout the signal acquisition, a strategy which could be implemented using recently proposed stop-and-go or $0° \rightarrow 54.7°$ dynamic-angle spinning

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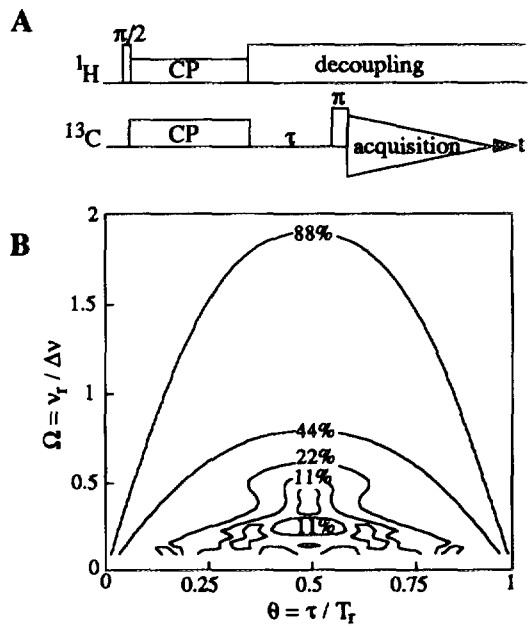

FIG. 1. (A) Basic pulse sequence capable of editing ^{13}C CPMAS NMR spectra according to the chemical-shift anisotropies of individual sites. (B) Calculated percentage of a site's time-domain signal $R(\Omega, \theta)$ remaining upon application of the pulse sequence shown in part (A), as a function of the dimensionless parameters $\theta = \tau/T_R$ and $\Omega = \nu_R/\Delta\nu$. Contour levels without labels correspond to 5% regions of intensity.

experiments (*16, 17*), albeit at the expense of considerable mechanical complications. Alternatively, CSA dephasing can be introduced under constant MAS conditions by applying rotor-synchronized radiofrequency pulses, an approach initially discussed by Lippma *et al.* (*18*) and subsequently developed in detail throughout different theoretical and experimental studies (*19–23*).

One of the simplest RF sequences capable of interfering with the averaging effects of MAS is illustrated in Fig. 1A. It consists of a single π pulse that, by precluding the coherent MAS refocusing of individual spin packets, destroys the macroscopic magnetizations of sites having large anisotropies, while merely introducing linear phase distortions for resonances arising from carbons with no CSA. NMR theories discussed elsewhere in detail can be used to calculate numerically the attenuation that the resulting "anisotropy filter" will have on a given signal (*20–22, 24*). In the absence of spin relaxation and for a given asymmetry of the shift tensor η, these models predict that signal intensities will only depend on the two parameters

$$\Omega = \nu_R/\Delta\nu \qquad [1a]$$

and

$$\theta = \tau/T_R = \tau\nu_R, \qquad [1b]$$

where Ω is the ratio between the spinning rate of the sample (ν_R) and the shift anisotropy ($\Delta\nu$) of a particular site, and θ describes the relative position of the RF pulse within the rotor period. Due to the periodic behavior of the MAS spin Hamiltonian, it is convenient to describe the CSA editing performance of this single-π-pulse sequence by the ratio

$$R(\Omega, \theta) = \left(\frac{S(\Omega, \theta)}{S_0}\right)_{t=T_R}, \qquad [2]$$

which compares the relative intensity of the time-domain powder signal of a site in the presence and absence of a pulse at the end of the first rotor period following cross polarization. Figure 1B illustrates the theoretical contour description of $R(\Omega, \theta)$ for the $\eta = 0$ case, as calculated for a powdered sample containing 400 independent orientations. This plot reveals that the dephasing effects of a basic π-pulse sequence become smaller as the relative rates of spinning increase, are symmetrically distributed with respect to the center of a rotor period, and become less pronounced as the π pulse is moved toward the beginning and end of the rotor cycle.

The CSA editing possibilities of this approach can be further examined by Fourier transforming the powdered time-domain signal of the spins with respect to the acquisition

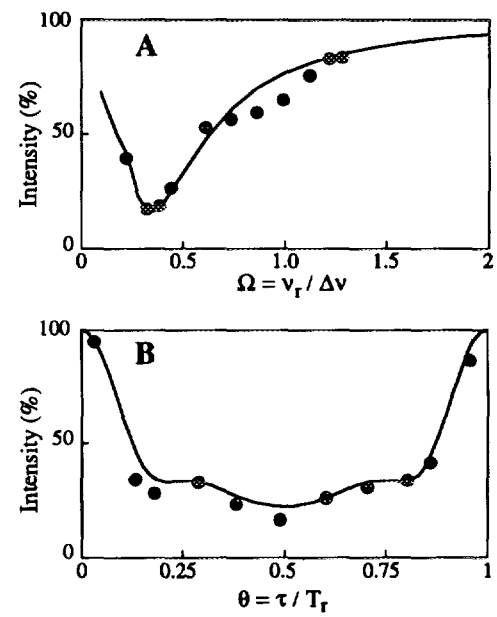

FIG. 2. Comparison between calculated (continuous curve) and experimental (●) variations in the relative intensity of MAS spectral centerbands in the presence of a π pulse, for different values of Ω (A) and of θ (B). Calculated curves were obtained using the literature parameters reported for the shift anisotropies of dimethylsulfone and hexamethylbenzene (*25, 26*). The 100% level would correspond to the centerband intensities in the absence of RF pulses. Experimental data were recorded on a homebuilt spectrometer and probe at a ^{13}C resonance frequency of 75.8 MHz, using standard cross polarization at 60 kHz and a mixing time of 3 ms.

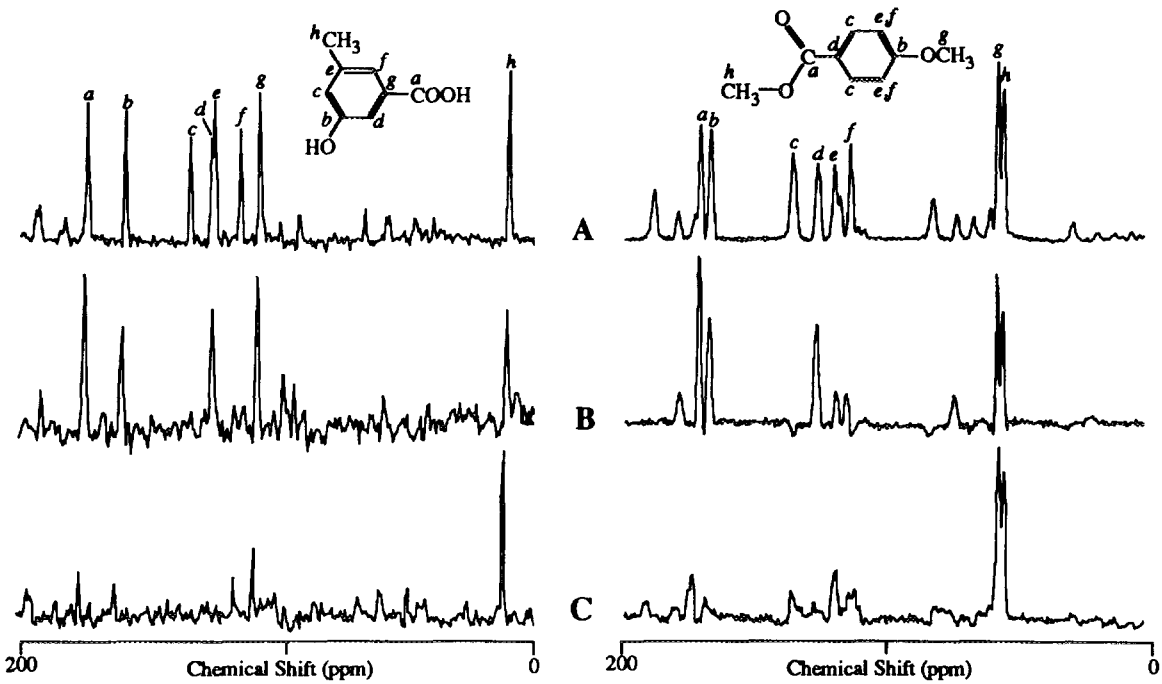

FIG. 3. ^{13}C CPMAS NMR spectra of 3-methylsalicylic acid (left) and methyl *p*-methoxybenzoate (right). All spectra were obtained as described in Fig. 2, externally referenced to $\delta_{TMS} = 0$ ppm, and normalized to equal maximum intensities. (A) Conventional CPMAS NMR spectra, 200 scans. (B) Dipolar-dephased spectra (delay = 50 μs), 1000 scans. (C) CSA-dephased spectra ($\theta = 0.5$), 200 scans.

time t, and monitoring the dependence of the resulting centerbands as a function of the experimental variables Ω and θ. This analysis is shown in Fig. 2, which compares calculated curves of peak attenuation with experimental data obtained on model compounds dimethylsulfone (Fig. 2A) and hexamethylbenzene (aromatic resonance, Fig. 2B). Ω was varied in the first set of experiments by changing the spinning rate while applying a π pulse at a time one-half a rotor period after concluding cross polarization. Thus, if relaxation effects are disregarded, this curve reflects the behavior that can be expected for a fixed spinning rate when there are sites possessing different magnitudes of shift anisotropy. The notch-like filter performance of this curve is far from ideal, but both its flatness and Ω dependence can most likely be improved by resorting to more sophisticated multiple-pulse approaches. Data in Fig. 2B were obtained at a constant rate of spinning (3326 Hz) while moving the π pulse in constant steps within the first rotor period following excitation. It shows a region of maximum attenuation which is relatively broad, and thus insensitive to timing errors.

Figure 3 illustrates practical applications of this form of CSA-dephasing spectral editing to powdered samples of 3-methylsalicylic acid and of methyl *p*-methoxybenzoate. As is evident from these spectra, the most immediate effect of anisotropy-based editing is the separation of methyl group resonances (possessing small anisotropies) from all other kind of signals, a procedure that can be implemented with little detriment to the overall signal-to-noise ratio of a spectrum. It is likely that at the spinning rates normally used in CPMAS NMR, cancellation of all signals arising from *sp*- or sp^2-type quaternary carbons can be achieved as carried out in these examples, i.e., by placing a single π pulse at the center of the first rotor period following cross polarization. Due to their generally smaller shift anisotropies, dephasing of nonprotonated sp^3 carbons might require more sophisticated manipulations, most likely involving multiple-pulse RF irradiation. In view of its simplicity, however, we are confident that even the simple editing approach employed in these experiments could find immediate applications within current methods of total CPMAS NMR spectral analysis.

The main goal of the present work was to illustrate the potential capabilities of hitherto unexplored CSA-dephasing editing approaches. These methods could undoubtedly be used for more subtle differentiations than the one described above, most likely involving complex pulse sequences built on the basis of multiple-pulse trains or of other forms of forced RF precession. Shift anisotropy evolution is actually well suited for this kind of RF-driven manipulations, as its local nature makes it amenable to detailed computer-assisted analyses. Then, in analogy to what happens in solution NMR with J couplings, one can think of developing spectral techniques which use certain values of CSAs as parameters for defining high-, low-, or even band-pass editing filters. Only the second of these possibilities (a low-pass CSA filter) was explored in the present study; further investigations of the remaining editing options are currently under way.

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