New Angles in Nuclear Magnetic Resonance Sample Spinning

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Received October 26, 1991 (Revised Manuscript Received December 5, 1991)

Introduction

The resolving power and site specificity inherent in nuclear magnetic resonance (NMR) spectroscopy have helped make this technique one of the most versatile probes available to chemists. With NMR one hopes to assign clearly identifiable transitions, or resonances, to individual nuclei within a molecule and, from these resonances, to acquire a detailed understanding of local chemical and physical perturbations. Many different types of systems can be studied in this way, solid as well as liquid, but for each a key consideration is resolution. How closely and how specifically any material can be studied by NMR depends largely on the possibility of obtaining well-separated peaks corresponding to distinct atomic sites.

High-resolution NMR of the liquid state has become widespread partly because intrinsic line widths are very narrow, and also because commercial spectrometers able to realize this natural potential have been available for many years. The chief reason why NMR lines are so narrow for liquids is motional averaging, as brought about by rapid molecular reorientation. The principal spin interactions, among which are the chemical shift, spin–spin scalar (or J) coupling, electric quadrupole coupling, and magnetic dipole–dipole coupling, all transform as tensors under rotations, and thus their

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magnitudes depend on molecular orientation.[1] Consider, for example, the familiar chemical shift interaction. This interaction, by which the nucleus is partially shielded from the external magnetic field owing to the response of the surrounding electrons, gives rise to the frequency dispersion seen in an NMR spectrum and can often be correlated with molecular topology and structure.[2] The value of the chemical shift is determined by the position of each molecule or crystallite in the sample with respect to the external magnetic field. These positions would be fixed in a rigid lattice, but in a liquid, where molecules are tumbling rapidly compared with the Larmor frequency, each molecule is able to sample all possible orientations on a short time scale. The spectral line that results is a single peak reflecting the average of the chemical shift tensor over a sphere. This average quantity is independent of orientation, in much the same way as an s orbital has no angular dependence, and is called, accordingly, the isotropic chemical shift.

Although most nuclei in solids typically are affected by chemical shift anisotropy (CSA), in some cases molecular tumbling is still sufficiently fast that narrow NMR lines are also obtained. It was this characteristic of adamantane that made it so desirable for the early high-resolution solid-state ^{13}C cross-polarization experiments.[3] Molecules of the newly discovered C_{60}

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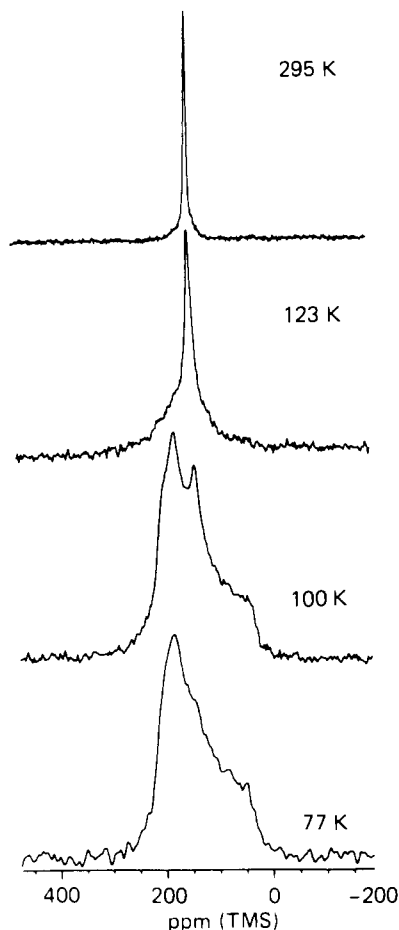(3) Pines, A.; Gibby, M. G.; Waugh, J. S. J. Chem. Phys. 1972, 56, 1776–1777.

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Figure 1. ^{13}C NMR spectra of solid C_{60} (buckminsterfullerene). At low temperatures the spectra are broad, reflecting the chemical shift anisotropy of the carbon-13 sites in the rigid molecules. At higher temperatures the molecules reorient rapidly, averaging the anisotropy and leaving a sharp resonance line at the isotropic chemical shift. Reprinted with permission from ref 4. Copyright 1991 American Chemical Society.

buckminsterfullerene, with the shape of a truncated icosahedron, also tumble rapidly at room temperature and thus produce narrow resonances even in the solid state[4,5] (Figure 1). In most solids, however, molecular reorientation is not sufficiently fast to average the spin interactions, and broad lines result. One can envision the broad solid-state line as being composed of a series of narrow lines, each coming from a different crystallite orientation. Indeed, as shown in Figure 1, such is the case for C_{60} at lower temperatures.

The regime between fast tumbling and slow tumbling can be exploited to distinguish different types of molecular dynamics. For example, Wittebort et al.[6] used line-shape simulations of proton and deuterium spectra taken over a range of temperatures to show that reorientation of the hydrogen bonds in polycrystalline hexagonal ice occurs via tetrahedral jumps rather than continuous rotational diffusion. For $I > {}^1/_2$ nuclei, such as deuterium ($I = 1$), an electric quadrupole interaction arises from the coupling of a nonspherical nuclear charge distribution with the electric field gradient of the electrons surrounding it. The resulting orientation-dependent splitting of the spectral line provides information about bond order and site symmetry.[7] Figure 2 shows how this interaction is averaged under tetrahedral jumps, which give rise to a tetrahedral pseudorotation of individual water molecules.

Since most solids at room temperature exhibit broad spectral lines, much effort over the last 30 years has gone into developing ways to average the anisotropic broadening artificially, either by manipulating the spins or by manipulating the sample. One important class of the latter approach involves imposing macroscopic motion on the solid sample in an attempt to mimic the microscopic motion of the molecules in liquids. Appropriate motion of the sample container can yield narrowing comparable to that found in solution. In what follows, we discuss some recent developments in sample reorientation techniques which enable high-resolution spectra to be obtained from a wide range of nuclei in the solid state.

Averaging First-Order Interactions: Magic-Angle Spinning

Approximately 100 of the various atomic nuclei possess a nonzero spin angular momentum, characterized by a spin quantum number I. Of these, over half are quadrupolar, i.e., they have $I > {}^1/_2$. When a spin I is placed in an external magnetic field, the spin states are dispersed over $2I + 1$ energy levels (each characterized by a quantum number m) due to the Zeeman interaction. In addition, the spins are subject to a wide range of interactions among themselves and with their environment, such as chemical shift, J coupling, dipole–dipole coupling, and quadrupole coupling.

Consider now the case of a sample contained in a rotor spinning rapidly about an axis inclined at an angle with respect to the external magnetic field. A calculation of the average resonance frequencies of the nuclei from first-order static perturbation theory or from coherent averaging theory[8,9] gives the following results for the first-order chemical-shift (CS), scalar-coupling (J), dipolar-coupling (DD), and quadrupolar-coupling (Q) interactions:

$$\omega_\lambda^{(1)} = \omega_{\lambda,iso}^{(1)} + \omega_{\lambda,2}^{(1)} P_2(\cos \theta) \qquad (1)$$

where $\lambda = CS, J, DD,$ or Q. θ is the angle between the sample-spinner axis and the external magnetic field. The chemical-shift and scalar-coupling interactions consist of an isotropic (orientation-independent) part and an anisotropic (orientation-dependent) part, while the dipolar and first-order quadrupole interactions contain only an anisotropic part ($\omega_{DD,iso}^{(1)} = 0$, $\omega_{Q,iso}^{(1)} = 0$). In all four cases the anisotropic contribution is scaled by $P_2(\cos \theta)$, the second-order Legendre polynomial of $\cos \theta$. A useful way to picture the spatial distribution of these interactions is to think of the isotropic parts as s orbitals whose radii determine the strength of the interaction, and to envision the anisotropic parts as d_{z^2} orbitals (Figure 3). While there is, of course, no spatial

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Experimental (a)   Simulation (b)
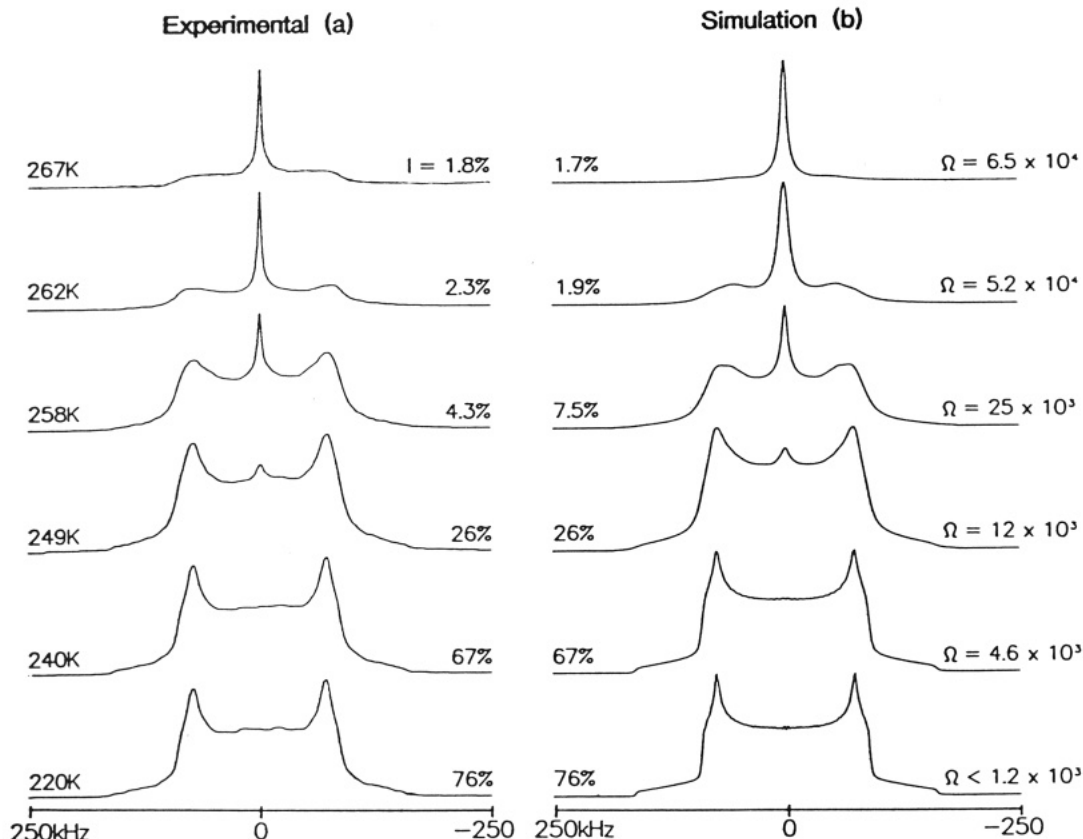

Figure 2. (a) Experimental deuterium spectra of hexagonal ice as a function of temperature. (b) Simulated deuterium spectra of hexagonal ice using a tetrahedral jump model. The appearance of a sharp central peak at low jump rates (Ω) is characteristic of tetrahedral symmetry. Reprinted with permission from ref 6. Copyright 1988 American Chemical Society.
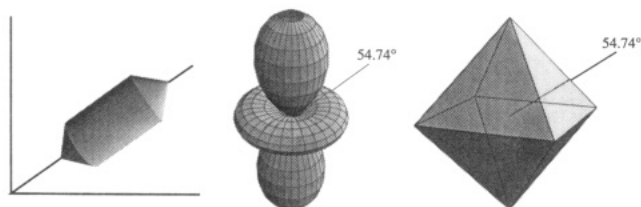
Magic-Angle Spinning (MAS)

Figure 3. Magic-angle spinning (MAS) averages first-order (second-rank) interactions. These interactions have an orientation dependence that transforms like d orbitals. MAS can be thought of as a dynamical implementation of cubic (octahedral) symmetry.

angle at which the s orbital goes to zero, the d orbital has a null when $P_2(\cos\theta) = 0$ at 54.74°. This angle is called the magic angle, $\theta_m^{(2)}$, and spinning a sample about an axis at an angle of 54.74° with respect to the external magnetic field is called magic-angle spinning or MAS. Magic-angle spinning was first suggested independently by Andrew et al.[10] and Lowe[11] as a way to narrow lines in dipolar-broadened spectra. Magic-angle spinning was combined with cross-polarization and spin decoupling by Schaefer and co-workers to produce high-resolution spectra for ^{13}C in solid polymers.[12]

The dipole–dipole coupling is a direct through-space interaction which depends upon the distance between nuclei as $1/r^3$. Because of the homogeneous nature of
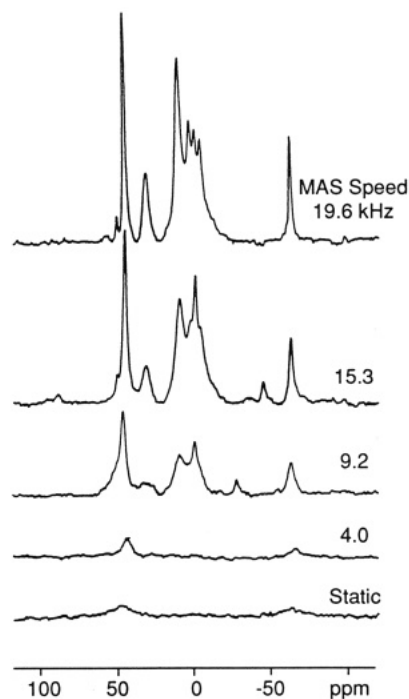

Figure 4. ^{19}F MAS spectra as a function of spinning speed for a fluorocarbon polymer with monomers CH_2CF_2, CF_2CF_2, and CF_3CFCF_2. Only at high spinning speeds are the lines appreciably resolved. Courtesy of S. F. Dec, R. A. Wind, and G. E. Maciel, Colorado State University.

this interaction in a many-spin system, the sample-spinning rate must be on the order of the spread of spectral frequencies in order to produce substantial narrowing.[9] Large dipolar couplings are typically on the

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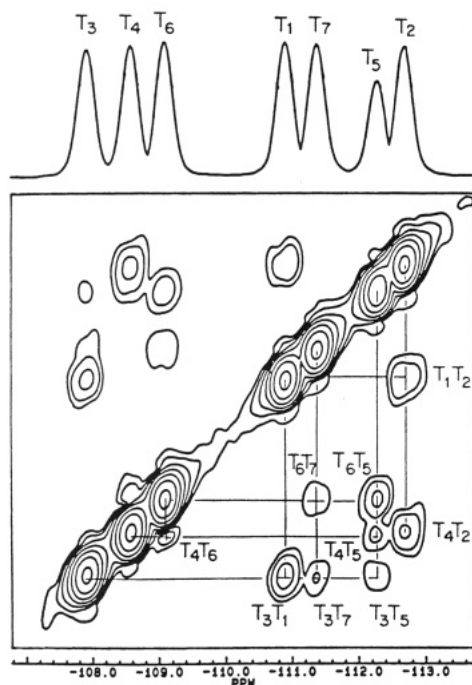(12) Schaefer, J.; Stejskal, E. O.; Buchdahl, R. *Macromolecules* **1977**, *10*, 384–405.

Figure 5. Contour plot of a ^{29}Si–^{29}Si COSY experiment of the zeolite ZSM-12. The one-dimensional spectrum from the F_2 dimension projection showing the seven crystallographically distinct silicon sites is at the top. Reprinted with permission from ref 16. Copyright 1989 Nature.

order of tens of kilohertz and hence require such speeds to average them. Although efficient multipulse radiofrequency excitation sequences have been available for some time to decouple the dipolar interaction,[13] fast rotors such as those recently developed by Maciel and co-workers[14] now allow moderately large dipolar couplings to be averaged to give motionally narrowed lines without the scaling of chemical shifts incurred by decoupling sequences (Figure 4).

With MAS, experiments previously possible only for liquids are now being performed also on solids. In particular, two-dimensional experiments such as COSY,[15] which have been so powerful for the elucidation of organic and biomolecular structure and conformation in solution, have recently been performed by Fyfe and co-workers on polycrystalline inorganic materials.[16] The COSY experiment produces correlations (visible as cross peaks) between scalar-coupled nuclei, thus elucidating the bonding network since this coupling is a through-bond interaction. Figure 5 shows a ^{29}Si–^{29}Si COSY spectrum for the zeolite ZSM-12. The correlations allow the Si–O–Si connectivities to be traced throughout the structure, allowing assignment of the individual silicon resonances to specific sites.

Another way in which the power of 2D NMR has been exploited in the solid state is to correlate isotropic spectra with their anisotropic counterparts.[17-19] While

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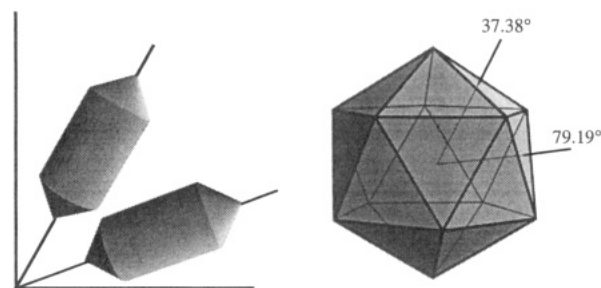(15) Aue, W. P.; Bartholdi, E.; Ernst, R. R. *J. Chem. Phys.* **1976**, *64*, 2229–2246.
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Dynamic-Angle Spinning (DAS)
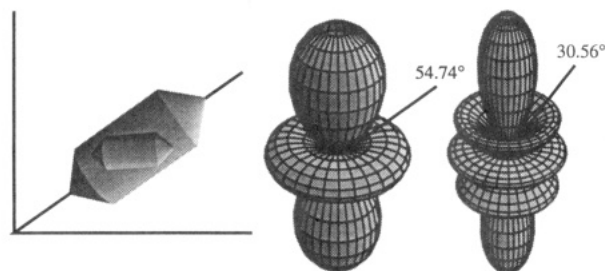

Double Rotation (DOR)

Figure 6. Dynamic-angle spinning (DAS) and double rotation (DOR) average both first-order (second-rank) and second-order (fourth-rank) broadening to zero. Spatially, the interactions look like a linear combination of a d and a g orbital. DAS can be thought of as a dynamical implementation of icosahedral symmetry.

orientational anisotropies give rise to broad lines, it is important to recognize that these same anisotropies also contain useful information which is lost upon averaging. By correlating a magic-angle spectrum in one frequency dimension with a second spectrum obtained with the spinner away from the magic angle, for example, we can resolve individual powder patterns for individual sites. Line-shape simulations of slices through the 2D plot may then provide information about each site.

An interesting way to view MAS is as an expression of dynamics under cubic symmetry. Motion over three orthogonal orientations is the minimum required to average an anisotropic interaction that transforms as a rank $l = 2$ spherical harmonic. Indeed, the magic angle is the angle formed between the vertical and a line drawn from the center of an octahedron to the center of any face, as shown in Figure 3. Maciel and co-workers have brought about such discrete, three-orientation motion in their "magic-angle hopping" experiments.[20] Cubic symmetry can be thought of as an approximation to the essentially spherical symmetry characteristic of molecular tumbling in liquids.

Averaging Second-Order Interactions: Dynamic-Angle Spinning and Double Rotation

In contrast to the previously considered chemical-shift, scalar-coupling, and dipolar-coupling interactions, which are typically only considered to first-order, the quadrupolar interaction often has an important sec-

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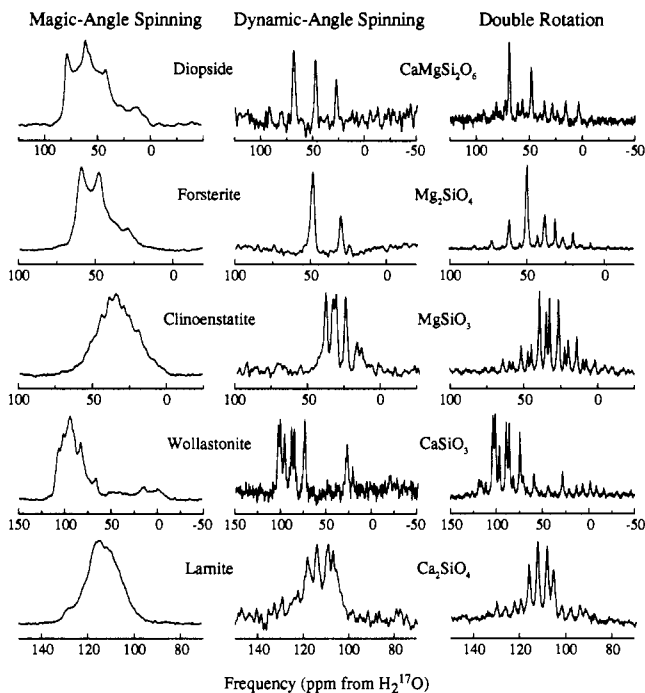(20) Szeverenyi, N. M.; Bax, A.; Maciel, G. E. *J. Magn. Reson.* **1985**, *61*, 440–447.

Figure 7. Magic-angle spinning (MAS), dynamic-angle spinning (DAS), and double rotation (DOR) NMR spectra for oxygen-17 nuclei in five minerals. In DAS and DOR, isotropic resonances are resolved for the crystallographically distinct oxygen sites in these silicates. The samples used were enriched to between 20 and 40% in oxygen-17, and spectra were recorded at a spectrometer frequency of 54.25 MHz (corresponding to a magnetic field strength of 9.4 T). In the MAS and DAS experiments the rotor frequency is approximately 5.4 kHz, and for the DOR experiments the inner rotor spins at 5 kHz while the outer rotates at approximately 800 Hz.

ond-order contribution. For an integral spin such as that of deuterium ($I = 1$), the first-order broadening is the dominant contribution; however, for the central $(-^1/_2 \leftrightarrow +^1/_2)$ transition of half-odd-integer spins such as that of ^{17}O ($I = {}^5/_2$), there is no first-order contribution since the first-order shift of a spin energy level depends on the value of m^2. The broadening is dominated by the second-order effect. A perturbation treatment to second-order of the quadrupolar (Q) interaction for a spinning sample yields the following result for the central transition:

$$\omega_Q^{(2)} = \omega_{Q,iso}^{(2)} + \omega_{Q,2}^{(2)}P_2(\cos\ \theta) + \omega_{Q,4}^{(2)}P_4(\cos\ \theta) \quad (2)$$

where a and b contain the orientation dependence of the interaction tensor with respect to the sample spinner. There are both an isotropic and an anisotropic second-order quadrupolar shift, and unlike the first-order case, which only depends upon $P_2(\cos\ \theta)$, the quadrupolar interaction depends upon both $P_2(\cos\ \theta)$ and $P_4(\cos\ \theta)$. Thus the spatial form of these interactions resembles a linear combination of a d orbital and a g orbital. Consideration of Figure 6 shows that there is no single angle at which the sample can be spun to average both $P_2(\cos\ \theta)$ and $P_4(\cos\ \theta)$, and therefore MAS (or spinning at any one angle) will not fully narrow the second-order anisotropic broadening.

Although this problem with MAS was known for many years, the solution to the problem of spectral broadening for quadrupolar nuclei was realized only recently.[21-24] Two experiments have, in fact, been im-

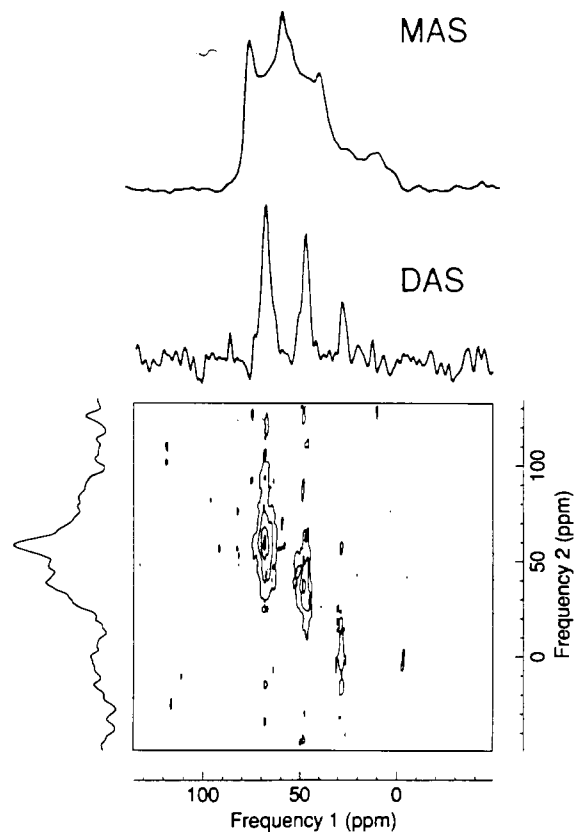(21) Llor, A.; Virlet, J. *Chem. Phys. Lett.* **1988**, *152*, 248–253.

Figure 8. DAS spectrum of ^{17}O-labeled diopside. Resonances corresponding to the three crystallographically distinct oxygen sites are resolved along the high-resolution dimension. Slices in the second dimension reveal the anisotropic line shapes for each site with the sample spinning at the second DAS angle ($\theta_2 = 79.19°$). The MAS spectrum is shown at the top for comparison.

plemented at Berkeley: dynamic-angle spinning (DAS), in which a sample spins sequentially about two different angles,[23] and double rotation (DOR), in which a sample is spun simultaneously about two angles.[24] A comparison between the two techniques has been presented in application to high-resolution ^{17}O NMR of solid silicates,[25] and representative results are shown in Figure 7.

In DAS, the rotor hops between two angles, θ_1 and θ_2, such that

$$P_2(\cos\ \theta_1) = -kP_2(\cos\ \theta_2) \quad (3)$$

$$P_4(\cos\ \theta_1) = -kP_4(\cos\ \theta_2) \quad (4)$$

The convenient choice of $k = 1$ gives the DAS complementary angles $\theta_1 = 37.38°$ and $\theta_2 = 79.19°$, generating frequencies

$$\omega(\theta_1) = \omega_{iso} + \omega_{aniso} \quad (5)$$

$$\omega(\theta_2) = \omega_{iso} - \omega_{aniso} \quad (6)$$

for the spin evolution at the first and second angles, respectively. The result is that the anisotropic frequencies at one angle cancel those at the other. The experiment is therefore naturally two-dimensional, with

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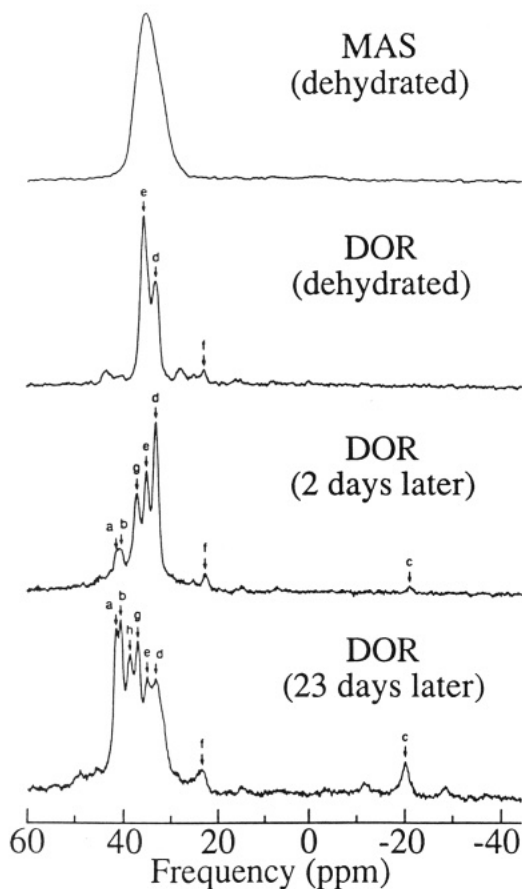
Figure 9. ^{27}Al NMR spectra of dehydrated and partially re-hydrated VPI-5. In the dehydrated sample, two peaks are resolved under DOR in a 2:1 intensity ratio, corresponding to two distinct tetrahedrally coordinated aluminum sites. As water is introduced into the structure, subtle changes occur leading to a number of distinct new tetrahedral sites as well as a peak c from octahedrally coordinated aluminum sites.

the first frequency dimension containing only isotropic lines occurring at the sum of the isotropic chemical shift and the isotropic second-order quadrupolar shift.[23] The second dimension contains anisotropic lines governed by eq 2. As seen in Figure 8, the power of this technique lies not only in its ability to resolve individual lines through motional narrowing but also in the separation of the powder patterns corresponding to those sites. These powder patterns in the second dimension can then be used to extract interaction parameters.

In DOR there are two rotors spinning simultaneously: an outer one inclined to the magnetic field at the magic angle of 54.74°, and an inner rotor containing the sample, inclined at an angle of 30.56° with respect to the first rotor axis (Figure 6). The central transition second-order quadrupolar frequency under DOR is given by[22]

$$\omega_Q^{(2)} = \omega_{Q,iso}^{(2)} + \omega_{Q,2}^{(2)} P_2(\cos\theta_1) P_2(\cos\theta_2) + \\ \omega_{Q,4}^{(2)} P_4(\cos\theta_1) P_4(\cos\theta_2) \quad (7)$$

The "magic angles" in the DOR experiment of 54.74° and 30.56° are zeros of $P_2(\cos\theta)$ and $P_4(\cos\theta)$, respectively. The anisotropies are always zero, since motional averaging is performed in parallel for the $P_2(\cos\theta)$ and $P_4(\cos\theta)$ terms. DOR, unlike DAS, is a convenient one-dimensional NMR experiment, albeit technically demanding. Figure 9 shows an example of the application of DOR to the traditionally difficult case of ^{27}Al

Chart I.
Averaging of Spherical Harmonics Y_{lm} under Subgroups of the Rotation Group SO(3)^a

^{a}The shaded numbers indicate those ranks (l) for which the average of Y_{lm} is 0. For example, rank $l = 2$ is averaged to 0 under cubic (or octahedral) symmetry (O) while $l = 2$ and $l = 4$ are averaged under icosahedral symmetry (I). All ranks $l \neq 0$ are averaged under the full symmetry of SO(3) characteristic of the isotropic reorientation of molecules in solution.

NMR in a solid aluminophosphate, VPI-5.[26] The spectra reveal resolved lines corresponding to different types of tetrahedrally coordinated Al sites, which change as a function of hydration. In addition, some of the tetrahedrally coordinated sites are converted into octahedral sites upon introduction of water.

In analogy to the cubic symmetry of MAS, DAS can be thought of as an expression of the higher icosahedral symmetry required to average both $l = 2$ and $l = 4$ rank spherical harmonics. The minimum number of discrete orientations that accomplish this are six of the orientations in an icosahedron. Indeed, the DAS angles for $k = 1$ are the angles of inclination between the vertical and the line joining the center with the faces of the structure as shown in Figure 6. A summary of how spherical harmonics of different ranks are averaged under point subgroups of the full rotation group SO(3) is given in Chart I.[27]

Conclusion

We have discussed how new developments in techniques of sample reorientation can yield narrow lines in solid-state NMR spectra, in some cases comparable

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to those for liquids. Since high-resolution solid-state spectra are now routinely obtained, even in the difficult case of quadrupolar nuclei, many of the versatile techniques pioneered in liquids can now be applied to solids. This should pave the way for many new applications of NMR to problems in chemistry and materials science.

While the DAS and DOR techniques have found early applications to inorganic materials such as minerals and zeolites, the techniques are equally applicable to organic and biological molecules in the solid state, and perhaps to some disordered systems such as glasses. Just as methods like cross-polarization were combined with MAS, the same may be done with DAS and DOR to increase the sensitivity obtained from nuclei such as ^{17}O. It is also important to note that while we have emphasized narrowing of the central transition of

half-odd-integer quadrupolar nuclei, broadening due to other second-order effects such as dipole–quadrupole interactions should be eliminated by DAS and DOR as well. In particular, we see some further possibilities for the dynamical consequences of icosahedral symmetry in a number of recent NMR experiments and applications.[28,29]

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Determinations of Transition-State Geometries by the Endocyclic Restriction Test: Mechanisms of Substitution at Nonstereogenic Atoms

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Received August 26, 1991

The description of a transition state on the basis of experimental evidence is the central, if sometimes elusive, goal of most studies of reaction mechanisms. The value of transition-state structures for understanding reactions is well established, and the concept is widely used.[1] Selection of a preferred transition state from reasonable alternatives is the classic approach to determining the mechanism of a reaction. Recognition of analogous structural features of transition structures for nominally different reactions provides a fundamental basis for establishing general reaction pathways. As the structures at the highest energy point over which a reactant must pass to become a product, transition states provide probes of the limits of chemical bonding and can serve as a test of theories. In synthetic chemistry, hypotheses about transition structures are useful for using and inventing reactions.

Studies of kinetics and stereochemistry are the most common experimental approaches to determinations of transition-state structures for reactions in solution. Reaction order and rate comparisons provide data which can be used to define the composition and electronic distribution in the transition state. The stereochemical consequences of a reaction provide information from which inferences are drawn about the arrangement of atoms in the transition-state structure. Classically, stereochemical analyses of reactions have been carried out by determinations of the course of a

reaction at a stereodefined center. A reaction which has been thoroughly studied by the stereochemical approach is nucleophilic substitution at carbon. Over 50 years ago it was suggested that substitution at the stereogenic carbon of an optically active substrate to give a racemic product involves a planar symmetrical carbocation as an intermediate in an S_N1 reaction, while substitution with inversion at carbon involves a trigonal bipyramidal transition state which has the entering and leaving groups disposed at 180° in an S_N2 process.[2]

The geometries of substitution reactions at nonstereogenic atoms have not been widely investigated experimentally although this information could be of considerable value for understanding the mechanisms of a wide variety of reactions. For most reactions of this formal type in which an arrangement of atoms in a transition state has been suggested, the paradigm has been S_N1 and S_N2 substitutions at carbon. In a recent approach, due to Burgi and Dunitz, trigonal bipyramids have been inferred as transition-state structures for concerted substitutions at nonstereogenic atoms on the basis of correlations of interactions in the solid-state structures.[3]

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