Solid State NMR Studies of Paramagnetic Coordination Complexes: A Comparison of Protons and Deuterons in Detection and Decoupling

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Received December 8, 1994[®]

Abstract: The solid state nuclear magnetic resonance (SSNMR) spectra of protons, deuterons, and carbons in the ligands of paramagnetic coordination complexes including acetylacetonate complexes, amino acid complexes, hydrates of the first row transition metals, and lanthanide acetates have been obtained. It has been known for some time that, for small paramagnetic species in solution, deuterium NMR can give better resolved spectra than proton NMR. In SSNMR of diamagnetic species in the solid state, it has also been observed that deuterium magic angle spinning (MAS) spectra are often better resolved than proton spectra. This paper reports that many paramagnetic species in the solid state can also have well-resolved deuterium MAS spectra which can be useful in chemical characterizations. In rare examples, such as certain V^{III} and Cu^{II} complexes, the proton MAS spectra are also well resolved at high spinning speeds. In these cases, well-resolved carbon MAS spectra can be measured without need for simultaneous high-power proton irradiation. The MAS line widths we observed for pure microcrystalline coordination complexes are essentially unrelated to the corresponding line widths measured in solution for similar complexes. Compounds with slow electron spin–lattice relaxation times can sometimes exhibit very narrow SSNMR signals due to spin diffusion among the electrons. On the other hand, many paramagnetic compounds, including those that give narrow signals in solution, for example iron complexes and high-valent manganese complexes, can be difficult to detect with solid state carbon or proton NMR experiments. The relatively broad SSNMR signals are presumably due to large anisotropic interactions that are not averaged by MAS alone (e.g., the dipolar hyperfine interaction in the presence of a substantial **g** anisotropy). However, even for these complexes deuterium MAS spectra are generally very easily detected including deuterons that are within 3 Å of the metal. Because of its relatively high resolution and sensitivity, deuterium MAS NMR of paramagnetic solids lends itself for characterization of the local structure of solid paramagnetic systems. For example, well-resolved splittings are often observed and are indicative of subtle Jahn–Teller or other local distortions. Furthermore, we have demonstrated that the sensitivity is sufficient for characterization of paramagnetic biomacromolecules.

Introduction

NMR of paramagnetic species in solution such as metalloproteins and coordination and organometallic complexes has proven to be a useful technique in characterizing ligands and elucidating the electron spin states of the metal ions. General rules concerning the detectability and line widths of paramagnetic signals have been established for solution NMR. For example, the broad classification of paramagnetic complexes as shift reagents or broadening reagents has been based on the electron spin–lattice relaxation times and is very useful in solution NMR.[1,2] In contrast, solid state NMR of paramagnetic compounds is still largely unexplored and predictions about the detection of signals are not very clear. Large bulk susceptibility anisotropy,[3,4] electron spin diffusion, and unaveraged nuclear–nuclear and nuclear–electron dipolar couplings[5,6] present major differences from solution NMR and possible difficulties in

detection and resolution.[7] Despite these issues, solid state NMR of paramagnetic materials remains an interesting technique, since the signals could provide valuable structural and dynamic information at the vicinity of the unpaired electrons. The large dispersion of chemical shifts and fast nuclear spin–lattice relaxation times could also help in assignment and signal averaging, as they do in some cases for solution NMR of paramagnetic samples.

Previous studies demonstrated that high-resolution solid state NMR of paramagnetic materials could be feasible and, in particular, suggested that deuteration of the ligands could be useful. For example Dobson, Grey, and co-workers[8] observed very large chemical shifts in rare earth and tin compounds, and these spectra were detected with rather good sensitivity, presumably because those compounds lack protons. On the basis of this observation, Groombridge and Perkins studied the SSNMR of an organic radical and showed that deuteration resulted in much narrower line widths for carbon and residual proton signals.[5] Furthermore, they presented an interesting case in which the deuterium MAS signals were more easily detected than the corresponding proton signals. Another interesting study by Nayeem and Yesinowski demonstrated that the residual

[®] Abstract published in *Advance ACS Abstracts,* June 1, 1995.

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proton spectrum of $CuCl_2 \cdot 2D_2O$[9] is well resolved, and their simulation of the spectrum yielded information about the electron spin delocalization. Wittebort[10] and Vold[11] and their co-workers have also used static deuterium SSNMR to probe the motion of ligands and spin state equilibria in a variety of paramagnetic coordination complexes, both as powders and as single crystals. These previous studies suggest that deuterium NMR of paramagnetic complexes might be more easily measured than other nuclei and also that the spectra of carbon and nitrogen would often be sharper upon deuteration because it obviates the need for decoupling paramagnetically shifted protons. Previous solution NMR studies also motivate the idea of measuring deuterated ligands: Johnson and Everett showed that deuterium line width is significantly narrower than that of proton in solution for paramagnetic transition metal complexes,[12] and in several examples, far shifted but resolved deuterium signals may be detected while protons at the same positions are too broad to detect.[13] It is also worth mentioning that the potential of deuterium MAS NMR for characterizing hydrogens in diamagnetic solids has been demonstrated by previous studies.[14,15]

We present here ^2H, ^1H, and ^{13}C SSNMR spectra of several paramagnetic coordination complexes. The compounds studied include numerous transition metal acetylacetonate (acac) derivatives, some lanthanide acetates, and amino acid complexes of metals. Many of the compounds are considered as shift reagents, but others are relaxants in solution NMR, such as the copper(II) amino acid complex, which was previously studied as a single crystal at low temperature (<20 K).[16] Although resonances from ligands of copper(II) in solution are difficult to detect, in the solid state, the ligand signals were readily detectable in both our and others' experiments.[17]

We compared the line widths of deuterium with analogous proton signals for several compounds, and the deuterons were always easier to detect with much narrower signals. The sensitivity was only slightly lower than that of protons for most compounds. It must be noted, however, in this comparison that our measure of sensitivity is the integrated intensity, for example measuring the value of the first point of the FID. But the proton spectra are sometimes completely unresolved or unstructured, so even a high-sensitivity experiment can be useless; this is the usual problem of proton NMR of solid state compounds. Many compounds that are difficult or impossible to study by proton or carbon NMR are often easily studied by deuterium NMR because the deuterium spectra are so much better resolved. The large collection of high-resolution deuterium SSNMR spectra of solids presented here gives encouragement for further applications. For a few compounds, which are emphasized in this report, the lines in the proton spectra were resolved from each other and formed spinning sidebands with very fast MAS (ca. 15 kHz). For those cases, the carbon signals could be decoupled from the protons simply by MAS without proton

irradiation. The facts that proton irradiation is unneccessary and the short spin−lattice relaxation times of the carbons both allow rapid collection of the carbon NMR spectra.

Experimental Section

The transition metal acetylacetonate derivatives and lanthanide acetates were purchased from Aldrich Chemical Co. and used without further purification. The 99% deuterated DL-alanine and D_2O used in the preparation of deuterated $Cu^{II}(DL\text{-}alanine)_2 \cdot H_2O$ were purchased from Cambridge Isotope Laboratory. Tetrahydrofuran (THF) was distilled under argon from sodium benzophenone ketyl prior to use. All manipulations of $V^{III}(acac)_3$ and $Co^{II}(acac)_2$ were performed under prepurified argon or nitrogen atmosphere (glovebox).

Preparation of Deuterated Compounds. $V^{III}(acac\text{-}3\text{-}d)_3$ and $Co^{II}\text{-}(acac\text{-}3\text{-}d)_2$. The deuterium exchange procedure is described elsewhere.[18]

$Al^{III}(acac\text{-}3\text{-}d)_3$. The same deuterium exchange procedure as for $V(acac\text{-}3\text{-}d)_3$ was used, starting with 5 g of $Al(acac)_3$ in THF (75 mL) and D_2O (30 mL). The product was 100% $V(acac\text{-}3\text{-}d)_3$ according to integration of the major MS peaks (for 32 scans): MS (CI, NH_3) m/z (relative intensity) 345 (M + 18 100.0). The position of deuterium incorporation was determined by NMR analysis of the product (compared to the original $Al(acac)_3$): ^1H NMR ($CDCl_3$) δ 2.00 (s, CH_3), (no methine peak at δ 5.49 was observed).

$Cu^{II}(DL\text{-}alanine\text{-}d)_2 \cdot H_2O$. $Ba(OH)_2 \cdot 8H_2O$ (1 mol) was added to 1 mol of $CuSO_4 \cdot 5H_2O$ and 1 mol of DL-alanine aqueous solution, in about 40 mL total volume. The reaction mixture was stirred for 20 min, quickly heated to boiling temperature, and then stirred at room temperature for 1 h. The solids were removed by filtration, and the dark blue clear solution was left in a desiccator for 1 week to form the deep blue crystals.[19] This procedure was performed for all the deuterated compounds. For the preparation of the compound with deuterons on the methyl and methine positions, we used commercially available deuterated DL-alanine (Cambridge Isotope Laboratory). D_2O was used as the solvent to make the copper(II) complex with both amine and water deuterated. Anal. Calcd for $Cu(C_6H_{14}N_2O_5)$: C, 27.96; H, 5.47; N, 10.87. Found: C, 27.81; H, 5.34; N, 10.67. Calcd for $Cu(C_6H_8D_6N_2O_5)$: C, 27.33; H, 5.35; N, 10.62. Found for Cu(DL-alanine-$3,3,3$-d_3)$_2 \cdot H_2O$: C, 27.13; H, 5.18; N, 10.32. Found: for Cu(DL-alanine-N-d_2)$_2 \cdot D_2O$: C, 27.13; H, 5.27; N, 10.46. Calcd for Cu($C_6H_6D_8N_2O_5$): C, 27.12; H, 5.31; N, 10.54. Found: C, 27.11; H, 5.13; N, 10.36.

NMR Experiments. All solid state NMR spectra were recorded on a Chemagnetics CMX 400 MHz spectrometer equipped with a 7 or 5 mm CPMAS multinuclear probe.

For proton experiments the Larmor frequency was 396.475 MHz. Proton spectra were recorded using either a Bloch decay or a chemical shift echo pulse sequence with the 180° pulse synchronized with the first rotor echo. T_1 experiments were carried out by applying a standard inversion−recovery pulse program. The receiver spectral sweep width was typically 500 kHz. The proton 90° pulse was 5 μs, yielding a transmitter width of ~50 kHz. Tetramethylsilane was used as an external chemical shift reference. DL-alanine, $Al^{III}(acac)_3$, and tetramethylsilane were used as diamagnetic standards to check the proton signal integrals of the paramagnetic solids; the intensities were measured using the magnitude of the first point of the FID.

For deuterium experiments, alanine-3-d_3 was used as an external chemical shift reference for the deuterium chemical shifts as well as for an integration standard. The magic angle spinning spectra were taken with a chemical shift echo pulse program (generally with a spinning speed of 4 kHz), and the spacing between the two pulses was synchronized with the first rotor echo. The 90° pulse length was 6 μs, and the data sampling rate was 1 MHz. T_1 experiments were measured using an inversion−recovery pulse program with chemical shift echo detection. Due to the relatively long excitation pulse lengths used in these experiments and the rapid relaxation processes for the paramagnetic samples, the inverted spectra were significantly distorted.

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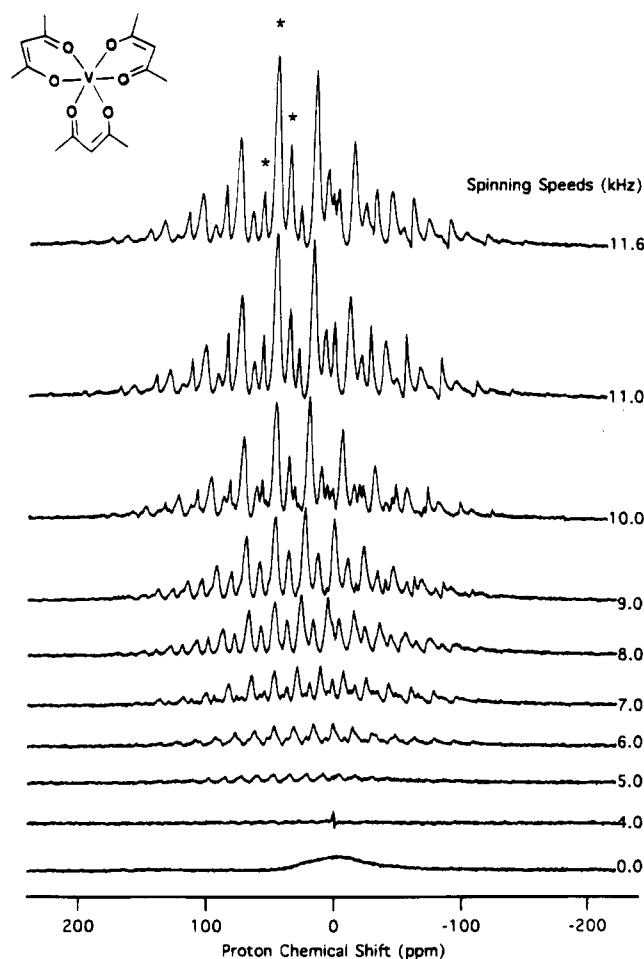
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Figure 1. 400 MHz proton MAS spectra of V(acac)₃ collected using an echo sequence, in which the refocusing pulse was synchronized with the rotor echo. The full signal intensity (based upon comparison with intensity standards) is not achieved until the MAS spinning rate was above 11 kHz. A total of 256 transients were collected with a pulse delay of 1 s. Centerbands at 56.1, 46.3, and 35.7 ppm are marked with asterisks. Although the proton spectrum remains difficult to assign with confidence, please see the assignments on the corresponding deuterium spectra (Figure 3).

Carbon spectra were taken using either a chemical shift echo or a Bloch decay with background suppression.[20] The 90° pulse for carbon was 3 μs. Adamantane was used as an external reference for the chemical shift with the more deshielded peak set to 38.6 ppm.

Results

Proton Experiments. The MAS SSNMR spectra of natural abundance V^{III}(acac)₃ and Cu^{II}(DL-alanine)₂·H₂O showed that in favorable cases proton spectra can be resolved into separate lines at their respective isotropic chemical shifts and families of spinning sidebands, simply by spinning at speeds of 7−15 kHz. The proton signals detected using a chemical shift echo pulse sequence were weak when the spinning speeds were below 5 kHz. If collected with a Bloch decay at low spinning speeds, these compounds showed a featureless broad line that was difficult to distinguish from the background signal. Between 5 and 11 kHz, the proton lines progressively became better resolved from each other (see Figures 1 and 2). Nevertheless, the magnitude of the first point of the FID (which is proportional to the total integral of the peaks) did not change noticeably as the signal became more structured. In contrast, if an echo sequence is used, the intensity depends markedly on spinning
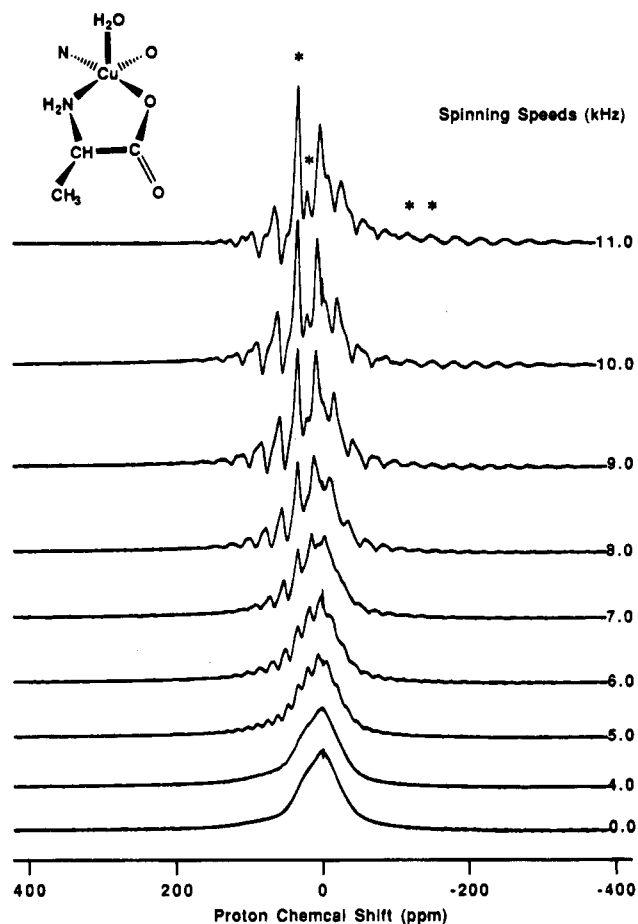
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Figure 2. 400 MHz proton MAS spectra of Cu(alanine)₂·H₂O collected using a Bloch decay. A total of 256 transients were collected with a pulse delay of 1 s. Centerbands at 31.8, 19.6, −116, and −150 ppm are marked with asterisks. For peak assignments refer to corresponding deuterium spectra (Figures 4, 6, and 7).

speed since the experiment "filters" for narrow signals. At 11 kHz spinning speed, the integrals of the signals from V^{III}(acac)₃ and Cu^{II}(DL-alanine)₂·H₂O were respectively equal to 90% and 75% of the expected values on the basis of comparisons with the diamagnetic standards. For the resolved spectra, the protons displayed large chemical shifts between +50 and −150 ppm and were in close agreement with the chemical shifts measured for deuterons at the same hydrogen positions (*vide infra*) or the corresponding proton spectra measured in solution.[21]

Unfortunately, resolved proton spectra at high spinning speeds were not observed in most cases. For Mn^{III} and Ni^{II} acac derivatives, spectra collected at a spinning speed of 11 kHz had very unresolved features (resembling that of V^{III}(acac)₃ at 5 kHz) and assignments were impossible. For Cr^{III}, Co^{II}, Fe^{III}, and Mn^{II} acac complexes, the line shapes at 11 kHz were completely unresolved so that even identification of the peaks was not possible.

Spin−lattice relaxation times of the proton spectra were below 5 ms for V^{III}(acac)₃ and Cu(DL-alanine)₂·H₂O but approximately 100 ms for Sm^{III}(CH₃CO₂)₃·nH₂O. The short relaxation times are a great advantage for the accumulation of transients.

The proton line widths of each sideband often were not as narrow as those of corresponding diamagnetic complexes: these line widths were between 5 and 6 ppm in favorable paramagnetic cases and between 3 and 4 ppm for diamagnetic samples. The spectra from paramagnetic samples were nevertheless better

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resolved than those of the diamagnetic ones simply by virtue of their broad chemical shift range. We noticed that the $V^{III}(acac)_3$ proton signal formed spinning side bands at a lower spinning speeds than the diamagnetic analog $Al^{III}(acac)_3$, but a definite pattern between the chemical shift dispersion and the detectability is not clear. All of the proton spectra from paramagnetic substances displayed a large collection of spinning sidebands, representing an anisotropic or inhomogeneous paramagnetic shift range of almost 200 ppm (considerably broader than that observed from the bulk susceptibility alone). It is noteworthy that the these solids are immobile in the crystalline state, and so the resolved proton spectra are not related to molecular motion (as evidenced by the deuterium NMR experiments discussed below).

We sometimes observed a proton NMR signal that we assign as free ligand adsorbed onto the microcrystals. The line widths of the proton centerbands from these adsorbed organic molecules were very sharp (limited by shimming in general), and the assignment as free ligand was based upon two observations: (i) despite the very narrow homogeneous line widths, the integral was below 20% of the value expected for the mass of the complex, and (ii) the isotropic shifts matched the free ligand and not the paramagnetically shifted values for the metal complex. These narrow, artifactual signals also exhibited a large collection of spinning sidebands (covering at least 100 ppm in the case of $V^{III}(acac)_3$) which apparently result entirely from the bulk magnetic anisotropy of the sample; the sideband pattern was responsive to the grain size and dramatically responsive to dilution by cocrystallization with $Al^{III}(acac)_3$.

Deuterium MAS SSNMR Experiments. We have synthesized several specifically deuterated compounds to test whether deuterium detection has a sensitivity or resolution advantage over proton detection for MAS NMR. We considered different cases in which the proton signals were detected and nearly resolved, such as some Cu^{II}, V^{III} complexes, and cases in which proton signals were poorly resolved or completely unresolved, such as Co^{II} complexes (Figures 3, 4, and 5). We also varied the positions of deuterons in the ligands to study the effect of nuclear—electron distances on line width and relaxation (Figure 4).

The deuterium MAS spectra of these complexes have two noteworthy features: (i) the centerband position gives the isotropic chemical shift, comparable to the shift measured in solution; (ii) a large number of spinning sidebands are present for deuterium MAS, even for diamagnetic complexes, and the envelope formed by the intensity pattern of the spinning sidebands (related to the line shape of the static powder) can be analyzed to obtain information about the motion of the deuterons. For example, the sideband pattern for the methyl groups is characteristically narrower than for methine groups at all accessible temperatures due to the rapid rotation of a CD_3 group (i.e., the apparent spinning sidebands extend over only 40 kHz for CD_3 but over 150 kHz for a static deuteron such as the methine deuteron, see Figure 3). Amine and water sideband patterns often show a dramatic temperature-dependent behavior as the motional correlation times vary from the sub-kilohertz to megahertz range, while symmetric aromatic rings often also show such behavior at higher temperatures. These sideband patterns and their temperature dependencies are therefore very useful in confirming the assignments of functional groups in many cases. Because of the combined effects of paramagnetic shift anisotropy, bulk susceptibility, and the quadrupolar interaction, paramagnetic static line shapes can become noticeably asymmetric compared to the symmetric patterns usually observed for diamagnetic analogs.[11]
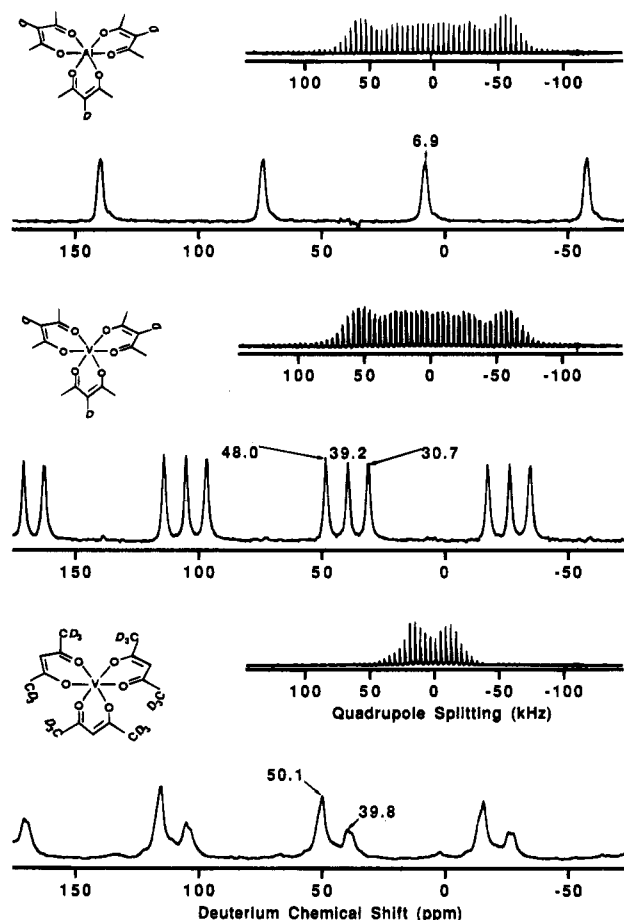

Figure 3. Deuterium MAS NMR of $Al(acac)_3$ and $V(acac)_3$ with selectively deuterated ligands. The triplet structure for the methine of the V compound is presumably due to a Jahn—Teller-type distortion of the d^2 pseudo-octahedral complex. A total of 256 and 2048 transients were collected with pulse delays of 250 and 0.5 s for $Al(acac)_3$ and $Cu(acac)_3$, respectively. Centerbands are marked with the corresponding isotropic chemical shift. The broad pattern of spinning sidebands is primarily due to the quadrupolar anisotropy; the spinning sideband intensities indicate that the methine protons are fairly static in the crystal structure while the methyl deuterons are rapidly rotating.

Motion in the mid-kilohertz to megahertz range can also cause the signal to disappear.[22] For example, for $Cu(DL\text{-}alanine\text{-}N\text{-}d_2)_2 \cdot D_2O$, we expected to observe the amine and the water deuterons, both of which could in principle be represented by two lines. Near room temperature we observed two peaks whose intensities did not have an appreciable temperature dependence (from −40 to 50 °C), and the total intensity of the two signals was only equal to two-thirds of that of the methyl group (Figure 4). We assign these two peaks to the motionally rigid amine group. On the other hand, their chemical shifts showed very strong temperature dependence (about 0.5 ppm/ °C, obeying Curie's law). When the temperature was lowered to −40 °C, a third peak appeared which we assign to the coordinated water. Water can undergo a 180° hop, causing the signal to be invisible at room temperature. Presumably at −40 °C the two deuterons in the water both contribute to this line although they are not crystallographically equivalent.

All of the deuterium center bands were much narrower than those of the corresponding protons (Table 1), making the detection of deuterons by MAS SSNMR in paramagnetic solids a very useful experiment. In several cases we attempted a "hole burning" experiment on the spinning sidebands of narrow

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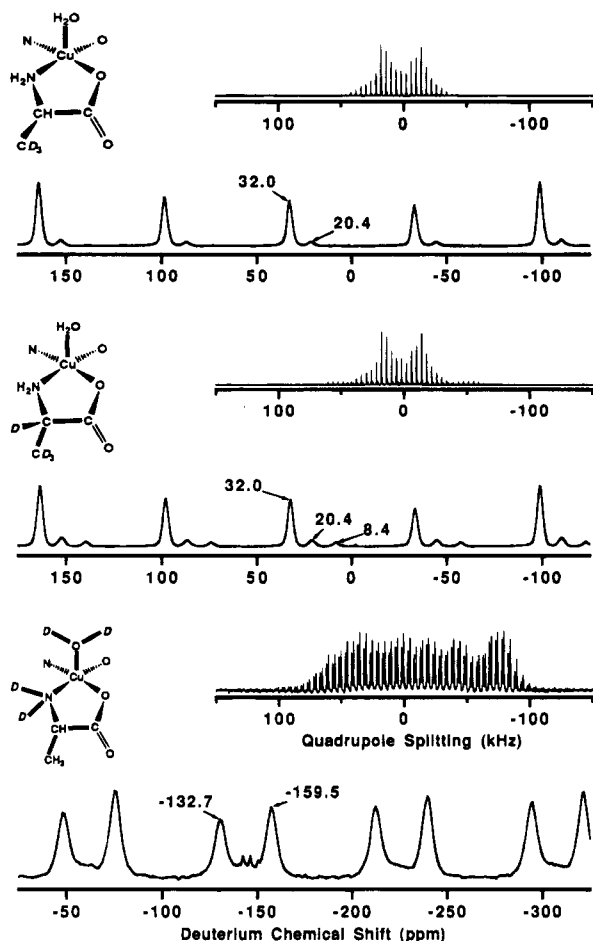
Figure 5. Deuterium MAS NMR of [Co(acac)₂]₄ with the ligand selectively deuterated at the methine position. Centerbands are marked with * and labeled with their isotropic chemical shift. The spectra are a summation of 10 240 transients collected with a pulse delay of 1 s. The sample spinning speed was 11 kHz. The broad pattern of spinning sidebands is primarily due to the quadrupolar anisotropy; the spinning sideband intensities indicate that the methine proton is fairly static in the crystal structure, since the overall width is ~100 kHz. A severe distortion of the powder patten is evident relative to a diamagnetic case (Figure 3). This distortion is not seen for example in V(acac-d)₃ (Figure 3) but is seen to a lesser extent in the water deuteron and amine deuteron of copper alanine (Figure 6).

the chemical shifts change monotonically in magnitude as the distances decreased.

The case of [Co^{II}(acac-3-d)₂]₄ (Figure 5) is somewhat more complicated. The deuterium centerpeak is more than 60 ppm wide, apparently including both homogenous and imhomogenous contributions. (Large electron g anisotropy and the low molecular symmetry could be the dominant inhomogenous contributions.) The quadrupolar line shape is greatly distorted, while the proton signal is not detectable at all using high-speed MAS. In the solution state, this compound has rather narrow line widths for protons due to the rapid electron relaxation times. This compound illustrates the fact that line widths for concentrated paramagnetic complexes in the solid state are dominated by contributions other than the electron T_1 relaxation mechanism. The analogous Mn(III) and Fe(III) complexes also gave detectible deuterium signals at the methine position, which will be discussed further elsewhere.

The high resolution in the deuterium MAS spectrum led to two important observations in experiments with V^{III}(acac-3-d)₃ in the Al^{III}(acac-3-d)₃ matrix: the detection of very small distortions of site symmetry (Figure 3) and facile detection of a minor percentage of paramagnetic material in the presence of a large concentration of Al^{III}(acac-3-d)₃ (Figure 8). The vanadium(III) complex showed three deuterium MAS peaks with equal intensities but unequal spacing in frequency. The reported X-ray crystallographic data indicates a very subtle distortion of octahedral symmetry[23] of approximately 0.03 Å difference in V−O bond lengths. These differences are probably small compared with typical Debye−Waller factors, but the ion is expected to be axially distorted since it is a typical Jahn−Teller state, i.e. O$_h$ d². The deuterium MAS spectrum of this compound cocrystallized and diluted with Al^{III}(acac-3-d)₃

Figure 4. Deuterium MAS NMR of Cu(alanine)₂·H₂O with selectively deuterated ligands. Centerbands are marked with * and labeled with their isotropic chemical shifts. The spectra are a summation of 1024 transients collected with a pulse delay of 1 s. The broad pattern of spinning sidebands is primarily due to the deuterium quadrupolar coupling, and it is modulated by the molecular motion the spinning sideband intensities, indicating that the methine proton is fairly static in the crystal structure while the methyl deuterons are rapidly rotating. In the compound prepared by crystallization from D₂O, the water deutetrons are invisible at room temperature because of their dyanmic properties, but the ND₂ deuterons are visible and resolved.

deuterium spectra and failed to selectively invert a portion of the sidebands. Instead, the pulse sequence inverted the whole peak, which suggests (although does not prove) that the line widths are mainly caused by homogeneous effects. These line widths were often comparable to the deuterium MAS line widths for diamagnetic complexes, ranging between 1.5 ppm (90 Hz) and 3 ppm (180 Hz) for deuterons more than two bonds away from the metals. It is remarkable that coordinated waters were detectable. Broad-line deuterium NMR studies of coordinated waters in a variety of lanthanide complexes have been recently reported,[11] suggesting that the MAS experiment would also be possible for many metal hydrates. In addition to the water in copper alanine, we also detected the water signal from CuCl₂·D₂O (Figures 6 and 7), which has been previously studied by proton NMR.[9] For these hydrogens, which are only two bonds away from the paramagnetic center, the line widths were around 6 ppm (360 Hz). Given the range of chemical shifts (−159.0, −130.6, and 26.0 ppm) these peaks were easily resolved from other deuterium MAS signals. In the copper alanine compound, the nuclear spin−lattice relaxation time did not decrease monotonically as the metal−nuclear distance decreased, as shown by the methyl and the methine group (Table 1) nor did
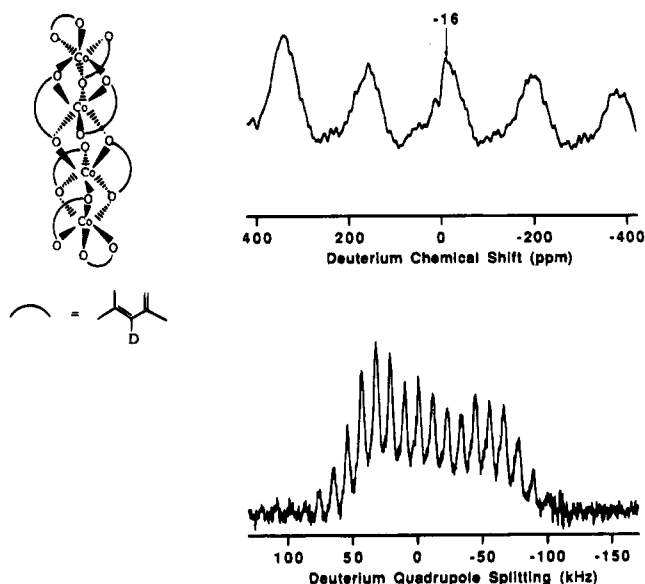
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Table 1. Solid State NMR of Paramagnetic Complexes by ^2H Magic Angle Spinning

	chemical shift, ppm	half-height (line width), ppm (Hz)	spin—lattice relaxation times $(T_1)^a$
$Al^{III}(acac-3-d)_3$	6.9	2.5 (150)	~50 s
$V^{III}(acac-3-d)_3{}^b$	48.7, 39.6, 31.7	1.5 (93), 1.5 (93), 1.7 (100)	~140 ms
$V^{III}(acac-1,5-d_6)_3{}^b$	50.6, 40.5	3.5 (213), 4.1(250)	~180 ms
$[Co^{II}(acac-3-d)_2]_4{}^c$	~−16	~56 (3.4 k)	~140 ms
$Cu^{II}(DL-alanine-2,3,3,3-d_4)_2{}^{\cdot}H_2O^b$	CD$_3$: 31.8, 20.5	3.4 (210), 3.7 (230)	~14 ms
	CD: 7.9	3.5 (216)	~36 ms
$Cu^{II}(DL-alanine-N-d_2)_2{}^{\cdot}D_2O$	ND$_2$: −130.6, −159.0	6.3 (387), 5.7 (349)	~1 ms
	D$_2$O: 26.9^d	6.8 (419)	
$Mn^{III}(acac-1,3,5-d_7)_3{}^{b,e}$	CD$_3$: 36.4, 33.3, 22.1, 17.0		~50 ms
	CD: 30.2, 28.2, 23.8, 19.2, 13.6, 9.4	~2−4 (120−240)	~17 ms
$Fe^{III}(acac-1,3,5-d_7)_3{}^c$	CD$_3$: ~18	30 (1.8 k)	~300 μs
	CD: ~−19	~70 (4.2 k)	~150 μs

^{a} Estimated from the zero crossing time using inversion—recovery pulse program, also taken into account the inevitable spectrum distortion caused by the finite excitation band width of the 180° pulse, the T_1 values are approximate. ^{b} The position gave several lines as discussed in text. ^{c} The line width of some peak is so broad that accurate measurement of the chemical shift is difficult. ^{d} Measured at −40 °C. ^{e} There is serious overlap among the peaks, so accurate measurement of the line width is difficult.
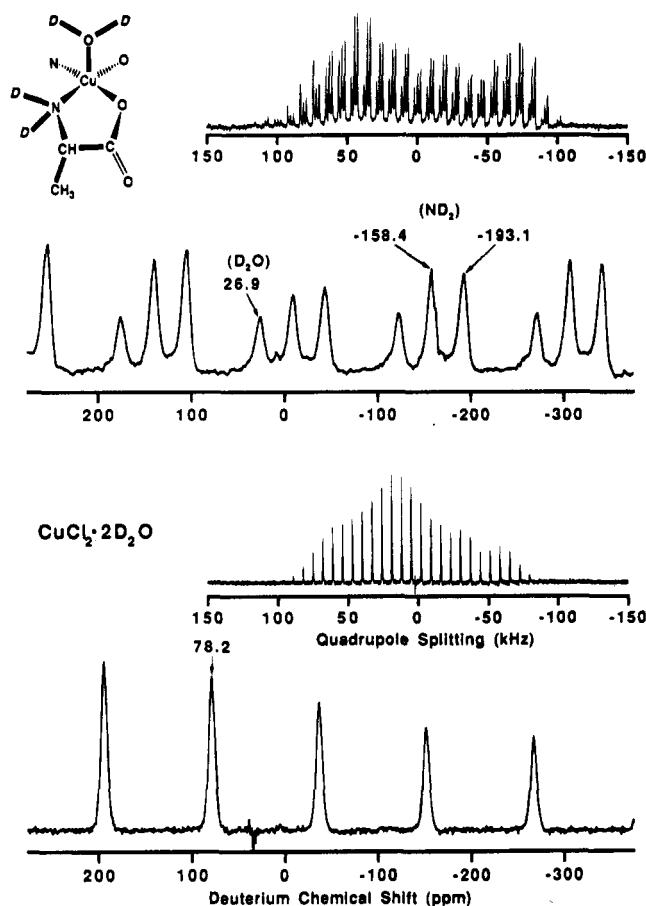

Figure 6. (upper panel) Deuterium MAS NMR of Cu(D,L-alanine-N-d$_2$)$_2{}^{\cdot}$D$_2$O prepared by recrystallization from D$_2$O; the amine and water hydrogens are therefore deuterated. Centerbands are marked with the corresponding isotropic chemical shift. A total of 2048 transients were collected with a pulse delay of 0.2 s and a sample spinning speed of 9 kHz. The broad pattern of spinning sidebands is primarily due to the quadrupolar anisotropy. The sample temperature of −40 °C allows the water deuterons to slow down their molecular motion and become detectable (see Figures 4 and 7 for contrast with the room temperature spectrum). (lower panel) Deuterium MAS NMR of CuCl$_2{}^{\cdot}$2H$_2$O recrystallized from deuterated water. A total of 256 transients were collected using a pulse delay of 0.5 s and a sample spining speed of 7 kHz.

(Figure 8) also exhibited three equal-intensity methine group resonances for the paramagnetic signal in the presence of the much larger deuterium signal from the diamagnetic dilutant. The three paramagnetic peaks in the cocrystalized sample were
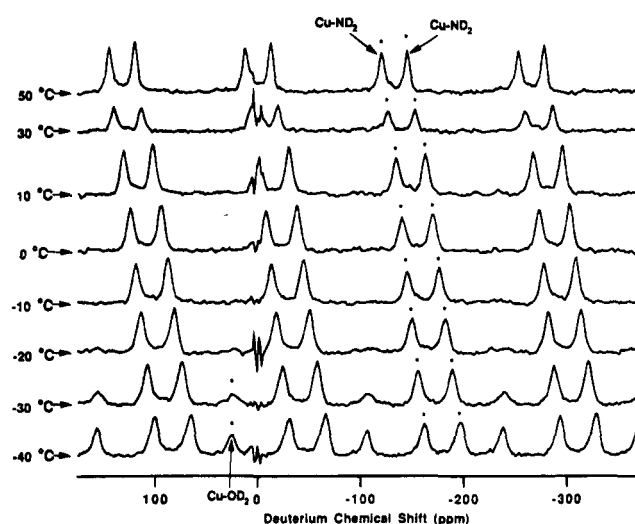

Figure 7. Deuterium MAS NMR of Cu(D,L-alanine-N-d$_2$)$_2{}^{\cdot}$D$_2$O recrystallized from D$_2$O was measured at temperatures ranging from −40 to 50 °C. The Curie-type dependence of the isotropic shift on the temperature is apparent in the ND$_2$ peaks. The water peaks are invisible at room temperature, presumably due to a local motion that interferes with digitization of the signal. At lower temperatures their signal is detected.

also quite sharp but were found at slightly different chemical shifts as compared with the pure sample. Since the splittings of the three peaks are too large to be caused by environmental differences and the presence of three equal-intensity peaks does not vanish after cocrystallization with a diamagnetic analog, we conclude that the splitting of the methine deuterons constitutes reliable proof of the distortion of octahedral symmetry. For an axially distorted state, the expected spectrum would consist of two peaks with a 2:1 ratio. The three equal-intensity peaks in our result clearly indicate a lower symmetry of the molecule. Both the evidence of the Jahn—Teller effects and the effects of the aluminum acetylacetate matrix illustrate that deuterium SSNMR of paramagnetic species is very sensitive to the environment.

Carbon-13 NMR Experiments. We measured the carbon spectra of the Cu(DL-alanine)$_2{}^{\cdot}$H$_2$O both as the natural abundance and as the methyl and methine deuterated forms (Figure 9). The peak assignments for the carbon NMR were made using selectively deuterated and selectively ^{13}C-enriched alanine. The peak at around 100 ppm which appears in all the carbon spectra has been proven to be a "background" signal from the probe. At 4.0 kHz spinning speed, the proton spectrum was completely unresolved, the carbon spectrum was also broad with poor
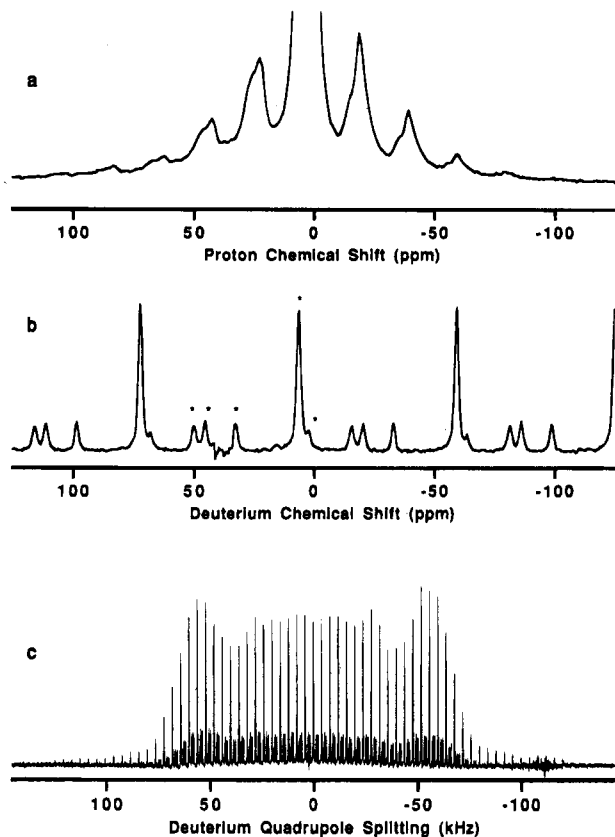
Figure 8. Proton MAS NMR of V(acac)₃ diluted into Al(acac)₃ with a molar ratio of 1:10 and deuterium MAS NMR of V(acac-*3-d*)₃ with Al(acac-*3-d*)₃ at the same ratio. For proton and deuterium spectra, the sample spinning rates were 8 and 4 kHz and the number of transients were 10 240 and 20 480. The 90° pulse lengths were approximately 6 μs, and the relaxation delays were 0.2 s for both. The paramagnetically shifted lines are quite clear in the well-resolved deuterium NMR even in the excess of a diamagnetic diluant; the proton NMR signal is much more poorly resolved, however, and the lines due to the paramagnetic signal cannot be measured. In the deuterium spectrum, the shoulder on the Al(acac-*d*)₃ matrix line is assigned as Al(acac-*d*)₃ with V(acac-*d*)₃ next nearest neighbors.

sensitivity, and the use of proton decoupling improved the ability to detect the methyl group but not the other signals. When the spinning speed was increased to 7 kHz and the proton spectrum became somewhat resolved, the carbon spectrum was also much better resolved and showed better sensitivity. In this case the use of proton irradiation further increased the signal from both the methyl and carbonyl carbons. Finally, when the proton spectrum became completely resolved at 11 kHz spinning speed, the carbon spectra were effectively decoupled by MAS and, as a result, the spectra of the deuterated and natural abundance compounds were similar while the proton decoupling irradiation had nearly no effect on the line width except that it increased the intensity of the methine carbon. The decoupling in the absence of proton irradiation can be understood in terms of the fact that the proton is effectively described by an inhomogeneous Hamiltonian: i.e. dipolar couplings with the protons can be removed by MAS because the couplings can be averaged over the rotor cycle (see further discussion in next section). *The observation that proton irradiation is unnecessary for carbon detection in some paramagnetic solids is remarkable since proton decoupling is generally a significant practical challenge for carbon SSNMR.* Furthermore high-speed spinning resulted in a narrower line width than that achieved with high-power proton decoupling and low spinning speeds. In Figure 9 we show on the top panel some spectra of partially deuterated compounds. Indeed, the quality of high-resolution carbon

spectra of paramagnetic solids have been achieved recently by perdeuteration and moderate spinning speeds.[5] The quality of the spectra is superior to that of the spectra of natural abundance compounds measured during proton decoupling (compare f with g or compare a with b). However, it is clear that the sensitivity improved dramatically with increased spinning speed even for the partially deuterated compounds (compare a with f). Presumably if we had measured the carbon spectra of the totally deuterated complex its line widths would have been narrower yet.

We also observed resolved carbon spectra from $V^{III}(acac)_3$ and $Sm^{III}(CH_3CO_2)_3\cdot(H_2O)_n$ at high spinning speeds which also gave resolved proton spectra. For the samarium complex, the spectrum was so well resolved that a quartet feature was observed for one set of the peaks (Figure 10).

For the compounds with low proton resolution such as Mn(III) complexes, the carbon signal was undetected even with proton decoupling at 11 kHz spinning although the proton signal was partly resolved. Detailed studies of carbon detection will be attempted on ^{13}C-enriched and deuterated compounds.

Discussion

Proton NMR. We have observed that individual lines in proton NMR of paramagnetic solid complexes can be resolved at high spinning speeds in rare cases. Two such cases are the signals associated with ligands in coordination complexes with Cu(II) and V(III). Others that are not shown include some lanthanide complexes. Although the proton homogeneous line widths were generally not as narrow as those of analogous diamagnetic complexes, the proton spectra of some paramagnetic complexes became resolved and developed spinning sidebands, while the diamagnetic complexes rarely do so. Presumably the reason for formation of sidebands in the case of paramagnetic complexes is that the large paramagnetic shift dispersion, chemical shift anisotropy, and the bulk susceptibility anisotropy separate the peaks. If the chemical shift difference is larger than natural line widths determined by the dipolar coupling and paramagnetic relaxation mechanisms, then the proton homonuclear dipolar coupling might be effectively truncated during MAS, thus resulting in a largely inhomogenous Hamiltonian and very little spin diffusion. Resolved proton spectra in diamagnetic solids are also seen in rare cases. The usual considerations for explanation of these well-resolved signals include the geometry and spectral characteristics of the coupled proton spin system and the presence of local molecular motions. Here we propose that, in the special case of paramagnetic solids, the large chemical shift dispersion must also be taken into consideration.

Whether or not the proton spectrum of a particular compound can be resolved at high spinning speeds apparently depends on the identity of the metal ions and the electronic state. Our survey of coordination complexes indicates that, except for V^{III}, Cu^{II}, and some of the lanthanides which are "favorable" cases, most of the first row transition metals fall into "unfavorable" cases and resolved proton spectra are not observed. Our classification of the metals into favorable and unfavorable compounds is obviously different from the useful separation of different metals into relaxants and shift reagents often discussed in relation to solution NMR of paramagnetic complexes. The distinction between a shift reagent and a relaxant in solution is based on the electron relaxation properties. Paramagnetic complexes that have relatively long electron relaxation times ($> 10^{-10}$ s) can cause severe lifetime broadening for the nuclei at the vicinity of the electrons (the usual explanation being that the nuclear resonances are in the intermediate exchange situation
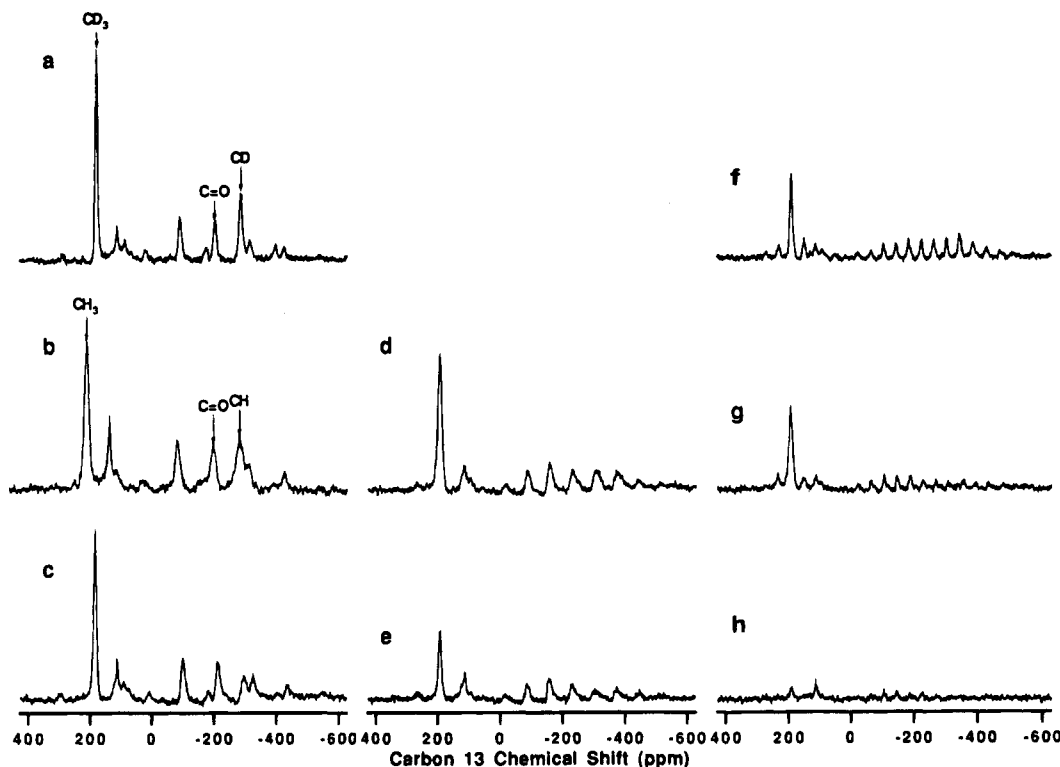
Figure 9. Carbon MAS Bloch decay spectra of natural abundance carbon in Cu (alanine)$_2$·H$_2$O illustrating the effects of proton couplings upon carbon line width and detection of signals. The spinning speed has a dramatic effect upon the sensitivity. Spectra were taken at 11 kHz spinning speed (left panel), 7 kHz spinning speed (middle panel), and 4 kHz spinning speed (right panel). The upper panel (a, f) shows spectra of the partly deuterated compound Cu(alanine-2-d-3-d_3)$_2$·H$_2$O, in which the effects of coupled protons are reduced, the middle panel (b, d, g) shows spectra of the natural abundance compound, measured with proton irradiation (decoupling) during detection, and the lower panel (c, e, h) shows spectra of the natural abundance materials detected without proton irradiation. It is apparent that deuteration is more effective than proton irradiation in narrowing the carbon line width, as had been indicated previously.[5] It is also apparent that high-speed spinning is extremely helpful in narrowing the spectra and improving the sensitivity, which is further discussed in the text. All spectra were sums of 51 200 transients taken with pulse delays of 1 s.
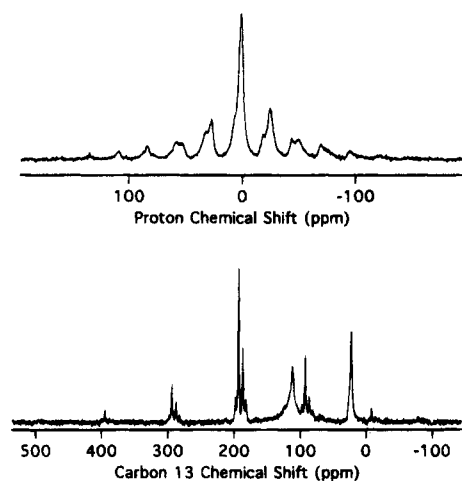

Figure 10. Proton and carbon MAS NMR of samarium acetate using MAS at 10 kHz. Spectra were sums of 128 and 49 152 transients for proton and carbon, respectively, and were added with a pulse delay of 1 s in both cases. Both spectra were taken with a simple Bloch decay (without decoupling).

between two hyperfine states associated with two electron spin states and that the induced relaxation and line shape effects make detection impossible). In the case of pure coordination compounds, we assume that the electron T_1 value for the crystalline Cu(II) complex is not too far from that of the solution state (i.e., roughly 10^{-9} s^{-1}) although we have no direct measurements of the electron relaxation times. Since there is no bridging ligand between paramagnetic centers of different molecules, large isotropic through-bond J couplings among the electrons are unlikely. But, in the solid state, the concentration of the

electron spins is dramatically higher than in solution and consequently the typical distances among the paramagnetic centers are much shorter. Consequently, electron T_2^* spin diffusion driven by electron–electron dipolar couplings can approach 10^9 s^{-1}.[24] The fast electron spin "flip-flop" process between the dipole coupled states makes the electrons appear as averaged magnetic moments to the nuclei during the time scale of an NMR experiment. Therefore the high concentration of paramagnetic centers probably narrows signals from nuclei close to metals with slow electron T_1 processes. Consequently, relaxants in solution can exhibit resolved resonances in the solid state. We are ultimately interested in observing the nuclei in the active site residues of membrane-bound paramagnetic metalloproteins. In such systems, the typical metal–metal separation will probably be over 20 Å, unless other metals are deliberately engineered into the system, and spin diffusion will presumably be less efficient than in the pure complexes that we have studied here but more efficient than for simple complexes in solution. Therefore some of the interesting cases reported here, such as the detection of deuterons in a water coordinated to a Cu(II) center, might be more challenging in a macromolecule. An interesting study which offers a solution to this problem is the nice work of Bertini and co-workers.[1] They increased the slow electron T_1 rate deliberately through J coupling with fast relaxing electrons by substitution of a relaxant metal (Co) into the diamagnetic Zn binding site near the Cu in CuZn SOD; the substitution led to the observation of NMR signals associated with amino acids that serve as ligands to copper in solution NMR.[25]

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We failed to detect the proton signals from ligands surrounding many other metal ions which are often favorable cases for solution studies (e.g., Fe(II/III) and Mn(III)). The cause of this broadening may be related to the anisotropic interactions that are not well averaged by MAS, such as the electron−nuclear dipolar term combined with the effect of a highly anisotropic **g** matrix for the electron. In this case, the expression for the nuclear−electron dipolar coupling should be

$$H_{\text{dipolar}} = SA_{\text{en}}I = B_{\text{o}}\mathbf{g}^2 A_{\text{en}}I$$

where A_{en} is the hyperfine interaction tensor, **g** is the electron **g** matrix, B_{o} is the external magnetic field, and I is the nuclear spin operator, all expressed in the laboratory frame. In this expression, S represents the time-averaged electron spin experienced by the nucleus on an appropriate NMR time scale. Since the observation of nuclear magnetism is performed on a microsecond and millisecond time scale, while electron relaxation occurs on a nanosecond and sub-nanosecond time scale at room temperature, a Boltzmann average of the two quantized electron spin states must be utilized. For this reason the **g** matrix enters as a squared quantity. If the more convenient principle axis system (PAS) or nearly diagonal expressions $\mathbf{g}'$ and A'_{en} and are used in place of the laboratory frame expressions **g** and A_{en}, then these tensors should be rotated into a common reference frame. The full expression with these rotations can be written as

$$H_{\text{dipolar}} = B_{\text{o}}(R^{-1\prime}((R^{-1}(\mathbf{g}')R)^2 A'_{\text{en}})R')I$$

where R and R^{-1} convert $\mathbf{g}'$ from its PAS to the frame of the dipolar interaction and $R^{-1\prime}$ and R' convert the product of the $\mathbf{g}'$ tensor and dipolar coupling tensor A'_{en} from the dipolar PAS into the laboratory frame with B_{o} as the z axis. This expression involves the product of two second rank tensors, **g** and A_{en}; thus not only will the resultant be expanded in terms of the second Legendre polynomial $P_2(\cos\theta)$ but also higher ranked spherical harmonics are needed to describe the anisotropy in the hyperfine shift, and therefore, the hyperfine anisotropy will not generally be removed by magic angle spinning alone. By analogy with the situation for quadrupolar nuclei, narrower lines might result from double axes spinning or dynamic angle hopping experiments.[26−29] Thus electronic spin state properties such as the magnitude of the magnetic moments and the large spin−orbit coupling which result in electron **g** anisotropy could introduce inhomogeneous line width and play important roles in the detectability of the proton signals in the solid state when ordinary MAS experiments are used.

Deuterium NMR. Among the compounds that we studied, the deuterium signals are uniformly easier to detect and better resolved at low spinning speeds than the corresponding proton signals. Nuclei two bonds away from the paramagnetic center were detected in two cases with reasonable resolution. With the higher resolution of the deuterium experiment, small bond length differences in crystalline compounds of distorted symmetry are apparent as well-resolved spectral splittings. The narrower line width from deuterium is in agreement with the Solomon and Bloembergen equation[30,31] which states that the

contribution of a paramagnetic metal ion to the nuclear transverse relaxation rate is proportional to the *square* of the nuclear magnetic moment (or equivalently, the intrinsic line width is proportional to the *square* of γ when nuclear relaxation is dominated by the electron−nuclear hyperfine coupling) and, on the other hand, the chemical shifts (in hertz) are *linearly* proportional to the nuclear magnetic moment. Therefore, low-γ nuclei in paramagnetic complexes will be better resolved, i.e. have a ratio of chemical shift difference to line width that is much larger. In addition, the lower γ will also result in smaller homonuclear dipolar coupling. The signals from a V(III) complex were also easily detected in the presence of a large amount of a diamagnetic dilutant. The reason for this larger dynamic range for deuterium as compared to proton (Figure 8) is simply that the line widths of spinning sidebands for deuterium were generally below 3 ppm with favorable line shapes, (i.e., going to the baseline) while 4 kHz spinning allows a 60 ppm spectral window between spinning sidebands. For the proton spectrum, even at 10 kHz MAS, the spinning sideband spacing only corresponds to a 25 ppm spectral window. The line widths of the centerbands were usually much more than 3 ppm, with significant "tails" in the line shape so that small signals from the paramagnetic complex were unavoidably buried under the large spinning sidebands from the diamagnetic host. These favorable features of the deuterium experiment might also be observed in other low-γ nuclei such as ^{15}N.

Although the deuterium quadrupole line shape contains unique information, the drawback is that the total intensity of the signal is distributed among a large number of spinning sidebands that greatly reduced the sensitivity. One way to overcome this problem is to fold the sidebands into the centerbands by Fourier transforming only the rotor echo points of the FID.[32] This process will be very important for detection of deuterium MAS signals in proteins when sensitivity is much lower due to the large molecular weight.

We observed fast nuclear spin−lattice relaxation times for all of the paramagnetic compounds, indicating that the unpaired electrons played a dominant role in the relaxation mechanisms (as expected). But caution has to be taken if we try to obtain information about the electron−nuclear distances based on the nuclear T_1, since our data indicates that deuterium T_1 does not decrease monotonically as the nuclear−electron distances is changed.

Carbon NMR. Since carbon has typically been a very important nucleus in biological SSNMR, we also studied the carbon detection and the effect of the proton decoupling in the same compounds. Extensive studies on proton decoupling of carbon signals have been done with lanthanide complexes. Raleigh and co-workers[33] found that proton decoupling fails for detection of carbon in paramagnetic systems due to the large inhomogenous proton line widths, and these authors reported that multiple-frequency proton decoupling can improve the resolution of the carbon spectra. We observed that, when the proton spectra became resolved at high spinning speeds, proton decoupling can become unnecessary, which is experimentally convenient. When the proton resonances are resolved, it may be reasonable to think of the coupled carbons and nearby protons as isolated specific spin systems, rather than as a continuous proton bath (e.g., the methine CH pair could be an IS system, or the methyl CH_3 group would be an IS_3 system, etc.). If the carbon is coupled in an IS spin system, the dipolar coupling

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could be averaged by MAS when the spinning speed becomes comparable to the C−H couplings.[34] In contrast, diamagnetic compounds with chemical shifts crowded within a 10 ppm range typically have rapid spin diffusion even at high spinning speeds and this partly homogeneous proton "bath" cannot be decoupled from carbon by MAS unless the speed exceeds typical H−H couplings which are often much larger than C−H coupling.

Conclusions

These studies open possibilities for structural and dynamic studies of paramagnetic solids by deuterium SSNMR. It is our hope that SSNMR of paramagnetic systems will be useful for characterizing catalytic solids and metalloenzymes in the future. It is apparent from our data that subtle structural distortions such as Jahn−Teller distortions can be detecting, which would be useful in the study of spin state equilibria and the electronic states of the metals. It is also clear that the spinning sideband pattern, combined with the isotropic chemical shift, is a powerful spectroscopic probe of slow molecular conformational dynamics at the vicinity of the paramagnetic centers.

This report focuses mainly on the detection of the resonances, and upcoming studies will focus more closely on assignments for complex systems. There are various approaches to assigning the paramagnetically shifted resonances, involving shifts, line shapes, and selective labeling. Magnetization exchange experiments could also be used to confirm the assignments of the signals. Although we do not demonstrate such experiments in this paper, there are many recent examples of homo- and heteronuclear magnetization transfer experiments in solid state NMR.[35,36]

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