Anal. Chem. **2008,** *80,* 4295–4300

Solid-State NMR Spectroscopy

Cecil Dybowski* and Shi Bai

Department of Chemistry and Biochemistry, University of Delaware, Newark, Delaware 19716

Review Contents

Solid-state NMR is a mature field with many applications. This review covers the period from early 2005 to March, 2008. A search of the literature showed that there were at least 3100 articles published that contain some emphasis on solid-state NMR. We do not pretend to make a complete or exhaustive review of all of these; rather we have attempted to highlight some reports that seem to indicate the broad sweep of solid-state NMR at this time. In this review, therefore, you should expect the choice of examples to be incomplete, and it is quite possible that another reviewer could have chosen other equally appropriate examples. With a field as wide as this one has become, there are multiple special reviews. One may find published reviews on subjects as diverse as applications of solid-state NMR to material science, polymer chemistry, biomolecular solids, and inorganic solids (*1*–*4*). In addition, there are always reviews in such series as *Specialist Periodical Reports* and *Progress in Nuclear Magnetic Resonance Spectroscopy* that may cover the solid-state techniques.

METHODOLOGY AND TECHNICAL DEVELOPMENTS

One of the major concerns in solid-state NMR is quantification of spectra, both relative quantification and absolute quantification. Factors such as efficacy of cross-polarization in experiments using that procedure or uniform excitation across very broad line shapes affect quantification, but other factors also determine the ability to quantify solid-state NMR with precision. Some of these factors have been addressed recently, including sample location in the coil, rotor packing design, as well as the ERETIC method for absolute quantification using an external signal (*5*, *6*). A quantitative cross-polarization (QUCP) scheme has been proposed for quantitative analysis in cross-polarization magic angle spinning (CPMAS) spectroscopy (*7*). The problems with obtaining relative quantitation of broad ^{207}Pb NMR resonances of lead-containing materials in a mixture have been discussed and a proposed scheme for obtaining relative quantification has been demonstrated on model mixtures (*8*).

A consideration in working with biological samples has been the heating of the sample when subject to the radio frequency fields associated with NMR spectroscopy. Heating of biological solid samples in a high magnet field (and therefore at high frequencies) has been discussed (*9*). Attempts at reducing, eliminating, or ameliorating heating caused by the electric fields impinging on a biological solid sample have been reported (*10*, *11*). Such problems will no doubt continue to be the subject of further investigations.

One problem with biological samples is often caused by the lack of large amounts of the material. The design of a microvolume coil to allow detection of a biological solid available in limited quantities was described (*12*, *13*). In other cases, the problem is not limited amounts of material but some special requirement of the biological system for a specific geometry or size. For example, a large-volume flat coil has been described that is useful for detection of ^{15}N in oriented membrane proteins (*14*). To improve efficiency in such high-throughput applications in the pharmaceutical industry, a CPMAS probe that handles seven samples simultaneously has been developed and demonstrated (*15*). To improve magnetic field stability, and therefore resolution, an attempt to introduce a transmission-line lock probe using D_2O as the lock solvent in a high-resolution solid-state NMR experiment (*16*) has been reported.

A significant line of development in solid-state NMR is the ever-increasing rate at which the sample can be spun. These very fast spinning experiments often "undo" some effects that are important to the execution of the experiment, such as reduction of dipolar coupling between carbons and protons. In addition, the faster speeds often come at the price of reduced volume and therefore reduced sample size. To utilize the increased spinning rates accessible in some modern MAS probes and retain the essence of signal enhancement by cross-polarization, dipolar recoupling schemes have been developed and heteronuclear decoupling schemes have been modified. As one example, a recent report indicates that one can still achieve relatively good sensitivity with recoupling experiments under very fast MAS in paramagnetic systems (*17*, *18*). Indirect-detection 2D heteronuclear correlation spectra obtained under conditions of very high rotation frequency have been reported (*19*). Other recently reported schemes include dipolar recoupling enhanced by amplitude modulation (DREAM) (*20*), radio frequency-driven recoupling (RFDR) at high MAS frequency (*21*), and triple oscillating field technique (TOFT) (*22*). The advantage of the use of reduced-volume samples is that one may often use lower radio frequency power in the smaller coils, which avoids some complications engendered by application of high radio frequency power.

Frequently, one finds in the literature of solid-state NMR reports of modifications of existing experimental protocols or conditions that enhance the analysis or isolate factors contributing to the spectrum. For example, a recent report indicates that fast adiabatic pulses are useful for very fast MAS experiments (*23*). These types of pulses are also reputed to have potential applica-

10.1021/ac800573y CCC: $40.75 © 2008 American Chemical Society
Published on Web 05/15/2008

tions for paramagnetic systems having very large shift anisotropies (*23*). The application of selective pulses such as a general 180° pulse has been employed in some cases to improve performance, as was noted in the multidimensional spectra of a protein (*24*). Radio frequency pulse schemes that work with fast MAS to obtain high-resolution ^{1}H spectra have been described (*25*). A sequence has been demonstrated to selective three-spin coherences in solid-state ^{13}C spectra, which allows one to select out methylene resonances (*26*). A new double quantum solid-state NMR pulse sequence for measuring $^{13}C-^{13}C$ spin−spin coupling constants was reported (*27*). An analogue of the bilinear rotation decoupling (BIRD) sequence in liquid-state NMR was reported to select satellite signals due to scalar coupling to spin-$^{1}/_{2}$ isotope in experiments on solids (*28*). Two-dimensional homonuclear correlation and separated-local-field experiments have been demonstrated for the case in which strong homonuclear dipolar couplings are present (*29*). Dipole−dipole interactions between ^{1}H and low-γ nuclei have been studied with a newly proposed 2D sequence that suppresses $^{1}H-^{1}H$ dipolar interactions (*30*). The polar inversion spin exchange at magic angle (PISEMA) method for determining the structure of an oriented membrane protein has been reviewed (*31*). The measurement of multiple carbon−nitrogen distances in solids containing these nuclei at natural abundance has been demonstrated with a rotary resonance echo saturation pulse double resonance (R-RESPDOR) experiment (*32*). A new pulse sequence for constant-time homonuclear dipolar recoupling has been introduced (*33*). The influence of heteronuclear decoupling on symmetry-based homonuclear recoupling has been examined (*34*). A theoretical bimodal-Floquet approach to the description of amplitude-modulated decoupling and recoupling in solids has been reported (*35*, *36*). A spin-state-selective coherence-transfer experiment has been demonstrated that improves resolution of ^{13}C spectra of solids (*37*). A potentially important technological demonstration of a method to enhance a solid-state NMR signal has been the development of polarization transfer from unpaired electrons in the neighborhood of the nucleus (*38*). The technology and some examples are reported. A means of monitoring the spinning axis in experiments in which the sample is spun, involving attachment of a Hall effect magnetic flux sensor to the spinning housing, has been demonstrated to be sensitive to the orientation of the stator in the magnetic field (*39*).

MATERIALS AND NANOTECHNOLOGY

Solid-state NMR spectroscopy is ideal for studies of materials that are of the order of atomic distances or slightly larger, making it a tool that can characterize materials at nanoscale dimensions. For example, multinuclear (^{19}F, ^{139}La, ^{45}Sc, and ^{31}P) NMR studies of lanthanum fluoride capped particles (*40*) were used to demonstrate the uniformity of capping of these particles with organic species. Similarly, detailed solid-state ^{13}C and ^{15}N NMR spectra showed structural differences between granules and nanofibers (*41*). ^{13}C CPMAS NMR was combined with Raman spectroscopy to study fluorinated single-walled carbon nanotubes, and the unusual chemical shift was confirmed by calculation and the data were shown to be in agreement with Raman, IR, XPS, and other spectroscopic analyses (*42*). In studies of nanodiscs, discoidal nanoscale self-assembled lipid/protein particles, NMR analysis supported a belt model structure for these materials (*43*). The mobile and reactive hydride ligands coordinated to ruthenium nanoparticles have been observed using solid-state and gas-phase NMR (*44*). The structure of surface-immobilized peptides on gold nanoparticles has been described by the NMR determination of their Ramachandran angles (*45*). Analysis of proton conductivity in titanate nanotubes with a variety of techniques has been aided by solid-state NMR studies of the protons that indicated the nature of proton mobility as a function of treatment of the material (*46*).

The use of spin-$^{1}/_{2}$ nuclei other than ^{1}H and ^{13}C can be found in many of the recent uses of NMR spectroscopy in the solid state. For example solid-state ^{111}Cd NMR has been used to characterize some insoluble Cd-containing complexes (*47*). In another study, combined ^{77}Se, ^{113}Cd, and ^{15}N analyses were used to investigate Zn(II), Cd(II), and Hg(II) complexes of thiourea and selenourea (*48*). Similarly ^{31}P, ^{77}Se, ^{113}Cd, and ^{199}Hg solid-state NMR studies have examined dichalcogenoimidodiphosphonato complexes of the form $M[N((iPr)_2PSe)_2]_2$ where M = {Zn, Cd, Ng} (*49*). Calculations with density functional theory of the shifts in MAS spectra of organometallic complexes and metalloporphyrins show that these calculations can give good agreement with experimental results (*50*). Such calculations have shown great promise in predicting the properties of systems with heavy metals in them.

A recent suggestion is that a kind of crystallography can be performed by measuring NMR parameters that specify structural constraints. To carry out this protocol, one would require a large number and variety of measurements, as well as theoretical support for the predictions of crystallographic parameters from calculations to predict the NMR parameters as a function of these structural features. In a recent report, the three-dimensional structure of β-L-aspartyl-L-alanine was determined, using a back-calculation technique to predict proton spin diffusion data (*51*). The analysis was done on a powder, rather than a single crystal. The resulting averaged structure compared favorably with the known crystal structure. In a study combining solid-state NMR, X-ray diffraction, and quantum chemical calculations, hydrogen bonding in histidine dipeptides has been studied (*52*). The results suggest that the ^{13}C resonance parameters of some sites may be particularly sensitive to the local environment, allowing these to be used as indicators of changes, for example when a drug molecule interacts with these kinds of structures.

PHARMACEUTICAL CHEMISTRY

Characterization of solid pharmaceutical preparations is a major area of study, since many drugs rely on slightly different forms of a chemical to achieve efficacy. Treatments of the material may cause changes, both wanted and unwanted, that affect these materials. Solid-state NMR spectroscopy is beginning to be used in addressing some of these questions, as recent general-interest articles (*53*, *54*) and a review of solid-state NMR analysis in drug design and discovery for membrane-embedded targets (*55*) have demonstrated. One area in which NMR demonstrates a strength is the identification of conformational polymorphism, as demonstrated by studies of the forms of 5-methyl-2-[(2-nitrophenyl)-amino]-3-thiophenecarbonitrile (*56*). The relationship between molecular structure features and crystal polymorphism has been studied by solid-state NMR for 24 local anesthetics (*57*). Polymorphism of the low-dose solid formulation of the steroidal drug, Org OD 14, was studied with ^{13}C NMR by specific labeling to enhance the sensitivity (*58*). Quantification of the forms of the sweetener, neotame, with various carbon NMR techniques was

demonstrated on mixtures (*59*). Amorphous and crystalline materials could be distinguished, and standard materials were found to be mixtures of the forms. A discussion of the effects of various NMR parameters on quantification accompanies the measurements. Variable temperature ^{13}C CPMAS was used to examine the polymorphic forms of two drug molecules, indomethacin and nifedipine (*60*). ^{13}C NMR studies of Nystatin in a cast film of an ethylene vinyl acetate copolymer complemented other studies of the time release of the drug from this matrix (*61*). The structure and dynamics of the drug trifluoroperazine in dimyristoylphosphatidylcholine has been studied by classical solid-state NMR measurements of $^{13}C-^{1}H$ dipolar couplings at natural abundance (*62*). The results provide insight into absorption, distribution, and metabolism of the drug molecule in this material. Of particular interest was the ability to suggest the positioning of the drug due to coupling to paramagnetic Mn(II) ions that selectively broadened the ^{13}C peaks (*62*).

CATALYSIS AND SURFACES

Molecules at surfaces, such as one finds in a heterogeneous catalytic sample or an intercalated material, often have very different electronic environments, a fact reflected in the NMR spectra obtained for materials in such environments. Applications of MAS NMR to in situ studies of heterogeneous catalysis have been discussed recently in two general papers (*63*, *64*). Surface ethoxy intermediates were captured by the in situ CPMAS approach (*65*). Arrangement, conformation, and mobility of surfactant molecules intercalated in montmorillonite have been examined by solid-state NMR methods (*66*). The dynamics along the chain, as examined by relaxation times, is seen to depend on concentration, indicating a relation between structure and mobility. The structure of the solid substrate, such as an aluminophosphate, can be studied with solid-state NMR, as a recent report indicates (*67*). In these experiments, both rotational echo double resonance (REDOR) and transfer of populations double resonance (TRAPDOR) techniques were applied to anionic aluminophosphates to determine the Al/P ratio. The authors conclude that the TRAPDOR experiment provides more detailed structural information on this system than other techniques. In a similar kind of experiment REDOR was used to determine the location and acid strength of protons on a Keggin structure from its effects on the NMR spectroscopy of adsorbed acetone (*68*).

QUADRUPOLAR NUCLEI

The NMR of quadrupolar nuclei in the solid state continues to grow, as techniques to excite and analyze the spectra have been developed. Since a large portion of the nuclei in the periodic table have isotopes that are NMR-active quadrupolar nuclei ($I > {}^{1}/_{2}$), the development of techniques to address the spectroscopy of these elements adds to the capabilities of studying a wider range of chemical problems than one could study with spin-$^{1}/_{2}$ nuclei. Two recent reviews (*69*, *70*) provide information on obtaining structural information from the spectra of these quadrupolar nuclei, including examples from applications to minerals, ceramics, and microporous solids. A review that deals exclusively with the quadrupolar halogen nuclei, Cl, Br, and I, has also appeared (*71*), including a large amount of data gleaned from the literature.

A wide variety of applications can be envisioned for quadrupolar NMR. For example, the calcium sites of hyroxyapatite have been studied by solid-state ^{43}Ca NMR triple quantum magic angle spinning (3QMAS) and $^{1}H-^{43}Ca$ REDOR methods (*72*). ^{51}V NMR, together with density functional theory (DFT) calculations, allowed a description of the vanadium environment in $V(V)O_2-$dipicolinate complexes (*73*) and crystalline vanadium oxides (*74*). Pressure-induced structural changes in a B_2O_3 glass have been investigated using ^{11}B NMR (*75*). The first solid-state ^{131}Xe spectrum of a xenon-containing material, for the perxenate anion, has been reported (*76*). The combination of the two NMR-active isotopes of xenon ^{129}Xe ($I = {}^{1}/_{2}$) and ^{131}Xe ($I = {}^{3}/_{2}$) was exploited to characterize the xenon magnetic shielding and quadrupolar interactions for two sodium perxenate salts. Quadrupolar multiple-quantum magic angle spinning (MQMAS) spectra of ^{27}Al spectra at an ultrahigh magnetic filed strength of 21.8 T demonstrate that the sensitivity and resolution are enhanced at the higher field (*77*). Enhanced S/N for the quadrupolar-spin-$^{1}/_{2}$ heteronuclear chemical shift correlation (HETCOR) experiment has been demonstrated when a soft pulse added mixing (SPAM) is incorporated in the traditional experiment (*78*). A three-dimensional homonuclear/heteronuclear correlation experiment between a quadrupolar nucleus (^{27}Al) and a spin $-{}^{1}/_{2}$ nucleus (^{31}P) in solid ALPO-14 that makes use of the sole scalar *J*-coupling has been reported (*79*, *80*). From the results of ^{17}O NMR spectroscopy of an ion-binding model peptide taken at 19.6 T, ion binding was found to be almost 1 order of magnitude greater than hydrogen bonding (*81*).

Quadrupolar constants tend to be very sensitive to the local electronic environment. This accounts for the recent trend to use the NMR spectroscopy of these nuclei to probe electronic structure. Examples in the recent literature include a study of diamagnetic octacyanomolydate ions using ^{95}Mo NMR (*82*), a study of local symmetry in polycrystalline copper dialkyldithiophosphate clusters using ^{65}Cu NMR (*83*), a study of alkali−DNA interactions using ^{23}Na NMR (*84*, *85*), a study that distinguishes the two possible calcium sites in hydroxyapatite using ^{43}Ca NMR with dipolar dephasing (*86*), and a study of the metal ion site in vanadium-chloroperoxidase using ^{51}V NMR (*87*). A wide-ranging ^{93}Nb solid-state NMR study of inorganic niobates with different oxygen coordination demonstrates the variation of quadrupolar constants and chemical shielding constants with local environment in these systems (*88*). ^{87}Rb NMR spectroscopy was used to characterize the rubidium ion environment when they are in a complex formed by self-association of guanosine 5′-monophosphate with 5-*tert*-butyl-dimethylsilyl-2′,3′-*O*-isopropylidene guanosine in a G-quadraplex (*89*), where the NMR spectroscopy shows that there are two different binding sites for the rubidium ion. ^{39}K chemical shift and quadrupolar parameters of several crown-ether-based complexes, determined at fields as high as 21.1 T, have been reported (*90*). The advantage of higher field is clearly shown in this type of study of quadrupolar nuclei.

Sensitivity enhancement of noninteger quadrupolar nuclei in powders being spun at the magic angle has been demonstrated through single-sweep irradiation at a satellite transition spinning sideband, use of hyperbolic secant pulses, and multiple pulse excitation (*91–93*). Several methods based on MQMAS and satellite transition magic angle spinning (STMAS) for half-integer quadrupolar nuclei have been compared theoretically and experimentally, and suggestions for the proper use of each for particular situations have been made (*94*).

BIOMOLECULES

Several reviews and general-interest articles on the kinds of information one can obtain about protein dynamics from solid-state NMR (*95–99*) have appeared, including one on sensitivity enhancement methods in solid-state NMR of biological materials (*97*) and one on studies of enzyme function (*99*). Another review focuses on the use of ^{19}F as a probe of the structure of biomembranes (*100*). Another focuses on the combination of dynamics and static features of NMR spectra to determine features of protein structure (*101*). Another reviews solid-state NMR studies of bone, bone mineral, and collagen (*102*). The use of numerical tools from simulating the chemical shift tensor for design of solid-state NMR experiments in bimolecular systems has also been reviewed (*103*). The prevalence of reviews shows that solid-state NMR is being widely used to probe biological systems. There has been a trend toward treating solid-state and liquid-state NMR spectroscopies of supramolecular and bimolecular systems in common when working on these systems (*104*).

A wide variety of NMR investigations have dealt with NMR assignments in a variety of systems. The ^{13}C and ^{15}N chemical shifts assignments of several proteins and enzymes have been reported (*105–112*). Solid-state NMR spectroscopy has been applied to the characterization of recent and archeological wood materials (*113*), Australian spider silks (*114*), cellulose materials (*115*), flagelliform silks (*116*), and plant materials (*117*).

While the NMR spectroscopy of solid materials is difficult, the procedures for creating biologically significant samples are also an important consideration in developing an appropriate experiment. Protocols of preparation of stable bicelle samples containing transmembrane peptides appropriate to MAS spectroscopy have been described (*118–120*). Obtaining and examining uniformly ^{13}C- and ^{15}N-labeled ubiquitin (*121*, *122*) and polypeptide phospholamban (*123*) are examples that demonstrate various solid-state NMR methods in three-dimensional structural determinations, including a discussion of the solid-phase protein preparation on the quality of the spectra (*121*). Methods for structural investigations of G protein-coupled receptors have also been presented (*124*).

A major impact of solid-state NMR, particularly of spin-$^1/_2$ nuclei, has been in specifying structural features of a biological system. In one report (*125*), the use of anisotropic chemical shift parameters of carbon, along with calculations to predict these parameters, was suggested as a means to determine geometry and structure in proteins and peptides. A similar proposal to use the parameters of uniformly enriched proteins and peptides for structural specification provides chemical shift assignment strategies and structure determinations of enriched proteins (*126*). In the case of bicelles containing the antimicrobial peptide $(KIGAKI)_3$ and cholesterol, $^{13}C-^{1}H$ heteronuclear dipolar interactions were used to specify topology and structure in this membrane-mimetic system (*127*). A classical example of the study of structure is the use of solid-state NMR to probe the structure of amyloid fibrils associated with Alzheimer's disease (*128–135*).

In biological systems, a problem that often limits the spectroscopy is the concentration of "rare" spins at natural abundance. It has been demonstrated by measurements on tyrosine·HCl, histidine·HCl, and all-C-retinal that chemical-shift tensors at each carbon site in samples at natural abundance and in uniformly ^{13}C-labeled material are identical in both kinds of material, even though the spectra show differences due to different dipolar couplings (*136*). Thus, one can use uniformly labeled biomaterials to enhance signals and be assured that the chemical-shift tensors are unchanged from their values in materials containing ^{13}C at natural abundance. Of course, one has to deal with the effect of homonuclear dipolar interactions. In cases where the $^{13}C-^{13}C$ homonuclear dipolar interactions are present, the homonuclear decoupling and magic-angle spinning can produce resolution equivalent to that of materials with ^{13}C at natural abundance, allowing one to gain the signal enhancement of additional spins without losing resolution (*137*). Such techniques are especially valuable for biomolecular applications. Paramagnetic metal ions were used to shorten proton T_1 and hence enhance the sensitivity for detection of ^{13}C for ubiquitin and lysozyme (*138*) and in the SH3 domain of chicken α-spectrin (*139*).

Dipolar interactions contain information on structure. For systems undergoing nonrandom dynamics, the order parameters describing the motion can be derived from dipolar tensor measurements. For example order parameters were obtained for a globular protein from dipolar parameters of a uniformly labeled ubiquitin sample (*140*). The order parameters were compared to those obtained by solution NMR and X-ray crystallography. Another form of information available from dipolar couplings is contained in the dynamics of spin-diffusion. Recently, the center-band-only detection of exchange (CODEX), which is based on dipolar-driven spin diffusion, has been demonstrated to allow the measurement of oligomeric number and intermolecular distance up to the 10 Å range in the transmembrane peptide of the M2 protein of the influenza A virus bound to 1,2-dimyristoyl-*sn*-glycero-3-phophotidylcholine bilayers (*141*) and in protegrin-1 integrated into materials such as palmitoyloleylphosphatidyl ethanolamine bilayers (*142*). Dipolar interactions of ^{13}C were also used to probe the binding of D-glucose to the *Escherichia coli* sugar transport protein, GalP (*143*), as well as in the determination of protein structure refinement of the β1-immunoglobulin binding domain of protein G (*144*). Nuclear Overhauser effect (NOE) between a small organic molecule and phospholipid membranes has been observed under solid-state MAS conditions (*145*). A solid-state delay alternating with nutation for tailored excitation (DANTE)-REDOR sequence is reported for determining the global secondary structure of uniformly labeled protein (*146*).

The use of multidimensional NMR has provided new ways to address structural questions, particularly in peptides and proteins. A 3D and 4D semiconstant-time transferred echo double resonance (SCT-TEDOR) MAS NMR experiment to measure multiple long-range dipolar couplings is demonstrated on a uniformly ^{13}C- and ^{15}N-labeled peptide *N*-acetylvaline and the B1 immunoglobulin-binding domain of protein G (GB1) (*147*). The experiment offers gains in sensitivity over other ways of carrying out the analysis, allowing measurement of weaker long-range dipolar couplings, and the experiment is inherently sensitive to methyl resonances. In another study, 3D *J*-based MAS experiments carried out on uniformly labeled GB1 are shown to give connectivity information complementary to the dipolar results (*148*). The conformational and dynamics changes of transmembrane domain of the protein M2TMP in the apo- and amantadine-bound states in lipid bilayers were characterized by MAS ssNMR methods (*149*). Double-quantum dipolar recoupling with a

windowless sequence (DQ-DRAWS) has been used to measure torsion angles in a number of tripeptides (*150*). The pentameric structure of the pinwheel topology of phospholamban is verified using ^{15}N chemical shift measurements and $^{1}H-^{15}N$ dipolar couplings (*151*).

CONCLUSION

Reports of solid-state NMR spectroscopy carried out between 2005 and early 2008 show that the technique is widely used. The array of questions to which it might provide answers is constantly expanding. The traditional emphasis on development of technology and modification of older methods is still present in many reports on NMR applied to solid materials. A particular theme has been the application of solid-state NMR techniques to an ever-widening array of chemical and biological problems.

ACKNOWLEDGMENT

C.D. acknowledges the support of the National Science Foundation under Grant CHE-04-11790.

Cecil Dybowski *is a professor of chemistry at the University of Delaware. He received B.S. and Ph.D. degrees from the University of Texas at Austin and was a research fellow in chemical engineering at the California Institute of Technology before coming to Delaware. He has over 170 publications on various aspects of spectroscopy, including two books on NMR spectroscopy. His work is supported by the National Science Foundation under Grant CHE-04-11790.*

Shi Bai *is manager of the NMR facility at the University of Delaware. He received a B.S. degree from Lanzhou University in the People's Republic of China and a Ph.D. degree from Brigham Young University. He has over 30 publications on NMR spectroscopy. His research interests include structure elucidation of small organic and biomolecules and chemical-shift-tensor measurements.*

LITERATURE CITED

(1) Edgar, M. *Annu. Rep. NMR Spectrosc.* **2007**, *103B*, 331–351.
(2) Aliev, A. In *Specialist Periodical Reports*; Webb G. A., Ed.; Royal Society of Chemistry: London, U.K., 2007; Vol. 36, pp 196−243.
(3) Aliev, A. E.; Law, R. V. In *Specialist Periodical Reports*; Webb G. A., Ed.; Royal Society of Chemistry: London, U. K., 2006; Vol. 35, pp 2346−312.
(4) Baldus, M. *Angew. Chem., Int. Ed.* **2006**, *45*, 1186–1188.
(5) Ziarelli, F.; Viel, S.; Sanchez, S.; Cross, D.; Caldarelli, S. *J. Magn. Reson.* **2007**, *188*, 260–266.
(6) Ziarelli, F.; Caldarelli, S. *Solid State Nucl. Magn. Reson.* **2006**, *29*, 214–218.
(7) Hou, G.; Deng, F.; Ding, S.; Fu, R.; Yang, J.; Ye, C. *Chem. Phys. Lett.* **2006**, *421*, 356–360.
(8) Glatfelter, A.; Stephenson, N.; Bai, S.; Dybowski, C.; Perry, D. L. *Analyst* **2006**, *131*, 1207–1209.
(9) d'Espinose de Lacaillerie, J.-B.; Jarry, B.; Pascui, O.; Reichert, D. *Solid State Nucl. Magn. Reson.* **2005**, *28*, 225–232.
(10) Krahn, A.; Priller, U.; Emsley, L.; Engelke, F. *J. Magn. Reson.* **2008**, *191*, 78–92.
(11) Gor'kov, P. L.; Witter, R.; Chekmenev, E. Y.; Nozirov, F.; Fu, R.; Brey, W. W. *J. Magn. Reson.* **2007**, *189*, 182–189.
(12) Janssen, H.; Brinkmann, A.; Van Eck, E. R. H.; Van Bentum, P. J. M.; Kentgens, A. P. M. *J. Am. Chem. Soc.* **2006**, *128*, 8722–8723.
(13) Kentgens, A. P. M.; Bart, J.; van Bentum, P. J. M.; Brinkmann, A.; van Eck, E. R. H.; Gardeniers, J. G. E.; Janssen, J. W. G.; Knijn, P.; Vasa, S.; Verkuijlen, M. H. W. *J. Chem. Phys.* **2008**, *128*, 052202.
(14) Gor'kov, P. L.; Chekmenev, E. Y.; Fu, R.; Hu, J.; Cross, T. A.; Cotten, M.; Brey, W. W. *J. Magn. Reson.* **2006**, *181*, 9–20.
(15) Nelson, B. N.; Schieber, L. J.; Barich, D. H.; Lubach, J. W.; Offerdahl, T. J.; Lewis, D. H.; Heinrich, J. P.; Munson, E. J. *Solid State Nucl. Magn. Reson.* **2006**, *29*, 204–213.
(16) Paulson, E. K.; Zilm, K. W. *Rev. Sci. Instrum.* **2005**, *76*, 026104.
(17) Wickramasinghe, N. P.; Ishii, Y. *J. Magn. Reson.* **2006**, *181*, 233–243.
(18) Wickramasinghe, N. P.; Shaibat, M.; Ishii, Y. *J. Am. Chem. Soc.* **2005**, *127*, 5796–5797.
(19) Wiench, J. W.; Bronnimann, C. E.; Lin, V. S.-Y.; Pruski, M. *J. Am. Chem. Soc.* **2007**, *129*, 12076–12077.
(20) Verel, R.; Ernst, M.; Meier, B. H. *J. Magn. Reson.* **2001**, *150*, 81–99.
(21) Bayro, M. J.; Ramachandran, R.; Caporini, M. A.; Eddy, M. T.; Griffin, R. G. *J. Chem. Phys.* **2008**, *128*, 052321.
(22) Khaneja, N.; Nielsen, N. C. *J. Chem. Phys.* **2008**, *128*, 015103.
(23) Kervern, G.; Pintacuda, G.; Emsley, L. *Chem. Phys. Lett.* **2007**, *435*, 157–162.
(24) Li, Y.; Wylie, B. J.; Rienstra, C. M. *J. Magn. Reson.* **2006**, *179*, 206–216.
(25) Vinogradov, E.; Madhu, P. K.; Vega, S. *Top. Curr. Chem.* **2005**, *246*, 33–90.
(26) Mao, D.-J.; Schmidt-Rohr, K. *J. Magn. Reson.* **2005**, *176*, 1–6.
(27) Lai, W. C.; McLean, N.; Gansmueller, A.; Verhoeven, M. A.; Antonioli, G. C.; Carravetta, M.; Duma, L.; Bovee-Geurts, P. H. M.; Johannessen, O. G.; De Groot, H. J. M.; Lugtenburg, J.; Emsley, L.; Brown, S. P.; Brown, R. C. D.; DeGrip, W. J.; Levitt, M. H. *J. Am. Chem. Soc.* **2006**, *128*, 3878–3879.
(28) Iuga, A.; Iuga, D.; Cross, A. R.; Gerken, M.; Hazendonk, P. *J. Chem. Phys.* **2007**, *126*, 054305.
(29) Cho, H. *Solid State Nucl. Magn. Reson.* **2006**, *29*, 219–226.
(30) Yamamoto, K.; Ermakov, V. L.; Lee, D. K.; Ramamoorthy, A. *Chem. Phys. Lett.* **2005**, *408*, 118–122.
(31) Quine, J. R.; Achuthan, S.; Asbury, T.; Bertram, R.; Chapman, M. S.; Hu, J.; Cross, T. A. *J. Magn. Reson.* **2006**, *179*, 190–198.
(32) Gan, Z. *Chem. Commun.* **2006**, *45*, 4712–4714.
(33) Tycko, R. *J. Chem. Phys.* **2007**, *126*, 064506.
(34) Marin-Montesinos, I.; Brouwer, D. H.; Antonioli, G.; Lai, W. C.; Brinkmann, A.; Levitt, M. H. *J. Magn. Reson.* **2005**, *177*, 307–317.
(35) Ernst, M.; Geen, H.; Meier, B. H. *Solid State Nucl. Magn. Reson.* **2006**, *29*, 2–21.
(36) Ernst, M.; Samoson, A.; Meier, B. H. *J. Chem. Phys.* **2005**, *123*, 064102.
(37) Verel, R.; Manolikas, T.; Siemer, A. B.; Meier, B. H. *J. Magn. Reson.* **2007**, *184*, 322–329.
(38) Weis, V.; Griffin, R. G. *Solid State Nucl. Magn. Reson.* **2006**, *29*, 66–78.
(39) Mamone, S.; Dorsch, A.; Johannessen, O. G.; Naik, M. V.; Madhu, P. K.; Levitt, M. H. *J. Magn. Reson.* **2008**, *190*, 135–141.
(40) Lo, A. Y. H.; Sudarsan, V.; Sivakumar, S.; van Veggel, F.; Schurko, R. W. *J. Am. Chem. Soc.* **2007**, *129*, 4687–4700.
(41) Hopkins, A. R.; Hwang, S. *Polym. Prep.* **2007**, *48* (1), 63–64.
(42) Alemany, L. B.; Zhang, L.; Zeng, L.; Edwards, C. L.; Barron, A. R. *Chem. Mater.* **2007**, *19*, 735–744.
(43) Li, Y.; Kijac, A. Z.; Sligar, S. G.; Rienstra, C. M. *Biophys. J.* **2006**, *91*, 3819–3828.
(44) Pery, T.; Pelzer, K.; Buntkowsky, G.; Philippot, K.; Limbach, H.-H.; Chaudret, B. *ChemPhysChem* **2005**, *6*, 605–607.
(45) Bower, P. V.; Louie, E. A.; Long, J. R.; Stayton, P. S.; Drobny, G. P. *Langmuir* **2005**, *21*, 3002–3007.
(46) Thorne, A.; Kruth, A.; Tunstall, D.; Irvine, J. T. S.; Zhou, W. *J. Phys. Chem. B* **2005**, *109*, 5439–5444.
(47) Mendoza-Diaz, G.; Rigotti, G.; Piro, O. E.; Sileo, E. E. *Polyhedron* **2005**, *24*, 777–783.
(48) Isab, A. A.; Wazeer, M. I. M. *J. Coord. Chem.* **2005**, *58*, 529–537.
(49) Demko, B. A.; Wasylishen, R. E. *Dalton Trans.* **2008**, *4*, 481–90.
(50) Zhang, Y.; Sun, H.; Oldfield, E. *J. Am. Chem. Soc.* **2005**, *127*, 3652–3653.
(51) Elena, B.; Pintacuda, G.; Mifsud, N.; Emsley, L. *J. Am. Chem. Soc.* **2006**, *128*, 9555–9560.
(52) Cheng, F.; Sun, H.; Zhang, Y.; Mukkamala, D.; Oldfield, E. *J. Am. Chem. Soc.* **2005**, *127*, 12544–12554.
(53) Berendt, R. T.; Sperger, D. M.; Munson, E. J.; Isbester, P. K. *Trends Anal. Chem.* **2006**, *25*, 977–984.
(54) Offerdahl, T. *J. Pharm. Technol.* **2006**, S24–S42.
(55) Watts, A. *Nat. Rev. Drug Discovery* **2005**, *4*, 555–568.
(56) Smith, J. R.; Xu, W.; Raftery, D. *J. Phys. Chem. B* **2006**, *110*, 7766–7776.
(57) Schmidt, A. C. *Pharm. Res.* **2005**, *22*, 2121–2133.
(58) Booy, K.-J.; Wiegerinck, P.; Vader, J.; Kaspersen, F.; Lambregts, D.; Vromans, H.; Kellenbach, E. *J. Pharm. Sci.* **2005**, *94*, 458–463.
(59) Offerdahl, T. J.; Salsbury, J. S.; Dong, Z.; Grant, D. J. W.; Schroeder, S. A.; Prakash, I.; Gorman, E. M.; Barich, D. H.; Munson, E. J. *J. Pharm. Sci.* **2005**, *94*, 2591–2605.
(60) Apperley, D. C.; Forster, A. H.; Fournier, R.; Harris, R. K.; Hodgkinson, P.; Lancaster, R. W.; Rades, T. *Magn. Reson. Chem.* **2005**, *43*, 881–892.
(61) Kalachandra, S.; Lin, D. M.; Stejskal, E. O.; Prakki, A.; Offenbacher, S. *J. Mater. Sci.: Mater. Med.* **2005**, *16*, 597–605.
(62) Boland, M. P.; Middleton, D. A. *PCCP Phys. Chem. Chem. Phys.* **2008**, *10*, 178–185.
(63) Hunger, M. *Chem. Ing. Tech.* **2007**, *79*, 781–793.
(64) Wang, W.; Jiang, Y.; Hunger, M. *Catal. Today* **2006**, *113*, 102–114.
(65) Wang, W.; Jiao, J.; Jiang, Y.; Ray, S. S.; Hunger, M. *ChemPhysChem* **2005**, *6*, 1467–1469.

(66) Wen, X.; He, H.; Zhu, J.; Yang, J.; Ye, C.; Deng, F. *J. Colloid Interface Sci.* **2006**, *299*, 754–760.
(67) Zhou, D.; Xu, J.; Yu, J.; Chen, L.; Deng, F.; Xu, R. *J. Phys. Chem. B* **2006**, *110*, 2131–2137.
(68) Yang, J.; Janik, M. J.; Ma, D.; Zheng, A.; Zhang, M.; Neurock, M.; Davis, R. J.; Ye, C.; Deng, F. *J. Am. Chem. Soc.* **2005**, *127*, 18274–18280.
(69) Ashbrook, S. E.; Duer, M. J. *Concepts Magn. Reson.* **2006**, *28A*, 183–248.
(70) Rocha, J.; Morais, C. M.; Fernandez, C. *Top. Curr. Chem.* **2005**, *246*, 141–194.
(71) Bryce, D. L.; Sward, G. D. *Magn. Reson. Chem.* **2006**, *44*, 409–450.
(72) Laurencin, D.; Wong, A.; Hanna, J. V.; Dupree, R.; Smith, M. E. *J. Am. Chem. Soc.* **2008**, *130*, 2412–2413.
(73) Bolte, S. E.; Ooms, K. J.; Polenova, T.; Baruah, B.; Crans, D. C.; Smee, J. J. *J. Chem. Phys.* **2008**, *128*, 052317.
(74) Gee, B. A. *Solid State Nucl. Magn. Reson.* **2006**, *30*, 171–181.
(75) Lee, S. K.; Mibe, K.; Fei, Y.; Cody, G. D.; Mysen, B. O. *Phys. Rev. Lett.* **2005**, *94*, 165507.
(76) Forgeron, M. A. M.; Wasylishen, R. E.; Gerken, M.; Schrobilgen, G. J. *Inorg. Chem.* **2007**, *46*, 3585–3592.
(77) Shimoda, K.; Kanehashi, K.; Hatakeyama, M.; Tobu, Y.; Shimizu, T.; Saito, K. *Chem. Lett.* **2007**, *36*, 834–835.
(78) Wiench, J. W.; Tricot, G.; Delevoye, L.; Trebosc, J.; Frye, J.; Montagne, L.; Amoureux, J.-P.; Pruski, M. *Phys. Chem. Chem. Phys.* **2006**, *8*, 144–150.
(79) Deschamps, M.; Massiot, D. *J. Magn. Reson.* **2007**, *184*, 15–19.
(80) Deschamps, M.; Fayon, F.; Montouillout, V.; Massiot, D. *Chem. Commun.* **2006**, *18*, 1924–1925.
(81) Chekmenev, E. Y.; Waddell, K. W.; Hu, J.; Gan, Z.; Wittebort, R. J.; Cross, T. A. *J. Am. Chem. Soc.* **2006**, *128*, 9849–9855.
(82) Forgeron, M. A. M.; Wasylishen, R. E. *J. Am. Chem. Soc.* **2006**, *128*, 7817–7827.
(83) Rusanova, D.; Forsling, W.; Antzutkin, O. N.; Pike, K. J.; Dupree, R. *J. Magn. Reson.* **2006**, *179*, 140–145.
(84) Wu, G.; Wong, A. In *NMR Spectroscopy of Biological Solids*; Ramamoorthy, A., Ed.; CRC Press: Boca Raton, FL, 2006; pp 317−344.
(85) Ida, R.; Wu, G. *J. Am. Chem. Soc.* **2008**, *130*, 3590–3602.
(86) Laurencin, D.; Wong, A.; Hanna, J. V.; Dupree, R.; Smith, M. E. *J. Am. Chem. Soc.* **2008**, *130*, 2412–2413.
(87) Pooransingh-Margolis, N.; Renirie, R.; Hasan, Z.; Wever, R.; Vega, A. J.; Polenova, T. *J. Am. Chem. Soc.* **2006**, *128*, 5190–5208.
(88) Lapina, O. B.; Khabibulin, D. F.; Romanenko, K. V.; Gan, Z.; Zuev, M. G.; Krasil'nikov, V. N.; Fedorov, V. E. *Solid State Nucl. Magn. Reson.* **2005**, *28*, 204–224.
(89) Ida, R.; Wu, G. *Chem. Commun.* **2005**, *34*, 4294–4296.
(90) Lee, P. K.; Chapman, R. P.; Zhang, L.; Hu, J.; Barbour, L. J.; Elliott, E. K.; Gokel, G. W.; Bryce, D. L. *J. Phys. Chem. A* **2007**, *111*, 12859–12863.
(91) Nakashima, T. T.; Wasylishen, R. E.; Siegel, R.; Ooms, K. J. *Chem. Phys. Lett.* **2007**, *450*, 417–421.
(92) Siegel, R.; Nakashima, T. T.; Wasylishen, R. E. *Chem. Phys. Lett.* **2006**, *421*, 529–533.
(93) Siegel, R.; Nakashima, T. T.; Wasylishen, R. E. *Concepts Magn. Reson.* **2005**, *26A*, 47–61.
(94) Trebosc, J.; Amoureux, J.-P.; Gan, Z. *Solid State Nucl. Magn. Reson.* **2007**, *31*, 1–9.
(95) Krushelnitsky, A.; Reichert, D. *Prog. Nucl. Magn. Reson. Spectrosc.* **2005**, *47*, 1–25.
(96) Hong, M. *Acc. Chem. Res.* **2006**, *39*, 176–183.
(97) Fujiwara, T.; Ramamoorthy, A. *Annu. Rep. NMR Spectrosc.* **2006**, *58*, 155–175.
(98) Baldus, M. *Curr. Opin. Struct. Biol.* **2006**, *16*, 618–623.
(99) McDermott, A.; Polenova, T. *Curr. Opin. Struct. Biol.* **2007**, *17*, 617–622.
(100) Ulrich, A. S. *Prog. Nucl. Magn. Reson. Spectrosc.* **2005**, *46*, 1–21.
(101) Hong, M. *J. Phys. Chem. B* **2007**, *111*, 10340–10351.
(102) Kolodziejski, W. *Top. Curr. Chem.* **2005**, *246*, 235–270.
(103) Sivertsen, A. C.; Bjerring, M.; Kehlet, C. T.; Vosegaard, T.; Nielsen, N. C. *Annu. Rep. NMR Spectrosc.* **2005**, *5*, 243–293.
(104) Schnell, I. *Curr. Anal. Chem.* **2005**, *1*, 3–27.
(105) Li, Y.; Berthold, D. A.; Frericks, H. L.; Gennis, R. B.; Rienstra, C. M. *ChemBioChem* **2007**, *8*, 434–442.
(106) Balayssac, S.; Bertini, I.; Lelli, M.; Luchinat, C.; Maletta, M. *J. Am. Chem. Soc.* **2007**, *129*, 2218–2219.
(107) Palmas, P.; Girard, E.; Pasquinet, E.; Caron, T.; Poullain, D. *Magn. Reson. Chem.* **2007**, *45*, 65–71.
(108) De Angelis, A. A.; Howell, S. C.; Opella, S. J. *J. Magn. Reson.* **2006**, *183*, 329–332.
(109) De Angelis, A. A.; Howell, S. C.; Nevzorov, A. A.; Opella, S. J. *J. Am. Chem. Soc.* **2006**, *128*, 12256–12267.
(110) Frericks, H. L.; Zhou, D. H.; Yap, L. L.; Gennis, R. B.; Rienstra, C. M. *J. Biomol. NMR* **2006**, *36*, 55–71.
(111) Franks, W. T.; Zhou, D. H.; Wylie, B. J.; Money, B. G.; Graesser, D. T.; Frericks, H. L.; Sahota, G.; Rienstra, C. M. *J. Am. Chem. Soc.* **2005**, *127*, 12291–12305.
(112) Marulanda, D.; Tasayco, M. L.; Cataldi, M.; Arriaran, V.; Polenova, T. *J. Phys. Chem. B* **2005**, *109*, 18135–18145.
(113) Alesiani, M.; Proietti, F.; Capuani, S.; Paci, M.; Fioravanti, M.; Maraviglia, B. *Appl. Magn. Reson.* **2005**, *29*, 177–184.
(114) Bonev, B.; Grieve, S.; Herberstein, M. E.; Kishore, A. I.; Watts, A.; Separovic, F. *Biopolymers* **2006**, *82*, 134–143.
(115) Erata, T.; Kohno, H. *Cellulose Commun.* **2006**, *13*, 26–30.
(116) Ohgo, K.; Kawase, T.; Ashida, J.; Asakura, T. *Biomacromolecules* **2006**, *7*, 1210–1214.
(117) Smernik, R. J.; Baldock, J. A. *Plant Soil* **2005**, *275*, 271–283.
(118) De Angelis, A. A.; Opella, S. J. *Nat. Protoc.* **2007**, *2*, 2332–2338.
(119) Hu, J.; Qin, H.; Li, C.; Sharma, M.; Cross, T. A.; Gao, F. P. *Protein Sci.* **2007**, *16*, 2153–2165.
(120) Lorch, M.; Fahem, S.; Kaiser, C.; Weber, I.; Mason, A. J.; Bowie, J. U.; Glaubitz, C. *ChemBioChem* **2005**, *6*, 1693–1700.
(121) Seidel, K.; Etzkorn, M.; Heise, H.; Becker, S.; Baldus, M. *ChemBioChem* **2005**, *6*, 1638–1647.
(122) Zech, S. G.; Wand, A. J.; McDermott, A. E. *J. Am. Chem. Soc.* **2005**, *127*, 8618–8626.
(123) Andronesi, O. C.; Becker, S.; Seidel, K.; Heise, H.; Young, H. S.; Baldus, M. *J. Am. Chem. Soc.* **2005**, *127*, 12965–12974.
(124) Lange, A.; Baldus, M. In *Drug Discovery Series*; CRC Press: Boca Raton, FL, 2006; Vol. 4, pp 297−314.
(125) Wylie, B. J.; Rienstra, C. M. *J. Chem. Phys.* **2008**, *128*, 052207.
(126) Polenova, T. In *NMR Spectroscopy of Biological Solids*; Ramamoorthy, A., Ed.; CRC Press: Boca Raton, FL, 2006; pp 57−85.
(127) Lu, J.-X.; Damodaran, K.; Lorigan, G. A. *J. Magn. Reson.* **2006**, *178*, 283–287.
(128) Petkova, A. T.; Leapman, R. D.; Guo, Z. H.; Yau, W. M.; Mattson, M. P.; Tycko, R. *Science* **2005**, *307*, 262–265.
(129) Petkova, A. T.; Yau, W.-M.; Tycko, R. *Biochemistry* **2006**, *45*, 498–512.
(130) Tycko, R. *Q. Rev. Biophys.* **2006**, *31*, 1–55.
(131) Shewmaker, F.; Wickner, R. B.; Tycko, R. *Proc. Natl. Acad. Sci. U.S.A.* **2006**, *103*, 19754–19759.
(132) Bu, Z.; Shi, Y.; Callaway, D. J. E.; Tycko, R. *Biophys. J.* **2007**, *92*, 594–602.
(133) Iwata, K.; Fujiwara, T.; Matsuki, Y.; Akutsu, H.; Takahashi, S.; Naiki, H.; Goto, Y. *Proc. Natl. Acad. Sci. U.S.A.* **2006**, *103*, 18119–18124.
(134) Makin, O.; Sumner, S.; Louise, C. *FEBS J.* **2005**, *272*, 5950–5961.
(135) Chimon, S.; Ishii, Y. *J. Am. Chem. Soc.* **2005**, *127*, 13472–13473.
(136) Kiihne, S. R.; Creemers, A. F. L.; Lugtenburg, J.; de Groot, H. J. M. *J. Magn. Reson.* **2005**, *172*, 1–8.
(137) Chevelkov, V.; Chen, Z.; Bermel, W.; Reif, B. *J. Magn. Reson.* **2005**, *172*, 56–62.
(138) Wickramasinghe, N. P.; Kotecha, M.; Samoson, A.; Past, J.; Ishii, Y. *J. Magn. Reson.* **2007**, *184*, 350–356.
(139) Linser, R.; Chevelkov, V.; Diehl, A.; Reif, B. *J. Magn. Reson.* **2007**, *189*, 209–216.
(140) Lorieau, J. L.; McDermott, A. E. *J. Am. Chem. Soc.* **2006**, *128*, 11505–11512.
(141) Luo, W.; Hong, M. *J. Am. Chem. Soc.* **2006**, *128*, 7242–7251.
(142) Mani, R.; Cady, S. D.; Tang, M.; Waring, A. J.; Lehrer, R. I.; Hong, M. *Proc. Natl. Acad. Sci. U.S.A.* **2006**, *103*, 16242–16247.
(143) Patching, S. G.; Henderson, P. J. F.; Herbert, R. B.; Middleton, D. A. *J. Am. Chem. Soc.* **2008**, *130*, 1236–1244.
(144) Peng, X.; Libich, D.; Janik, R.; Harauz, G.; Ladizhansky, V. *J. Am. Chem. Soc.* **2008**, *130*, 359–69.
(145) Scheidt, H. A.; Huster, D. *Acta Pharmacol. Sin.* **2008**, *29*, 35–49.
(146) Andreas, L. B.; Mehta, A. K.; Mehta, M. A. *J. Am. Chem. Soc.* **2007**, *129*, 15233–15239.
(147) Helmus, J. J.; Nadaud, P. S.; Höfer, N.; Jaroniec, C. P. *J. Chem. Phys.* **2008**, *128*, 052314.
(148) Chen, L.; Kaiser, J. M.; Polenova, T.; Yang, J.; Rienstra, C. M.; Mueller, L. J. *J. Am. Chem. Soc.* **2007**, *129*, 10650–10651.
(149) Cady, S. D.; Hong, M. *Proc. Natl. Acad. Sci. U.S.A.* **2008**, *105*, 1483–1488.
(150) Mehta, M. A.; Eddy, M. T.; McNeill, S. A.; Mills, F. D.; Long, J. R. *J. Am. Chem. Soc.* **2008**, *130*, 2202–2212.
(151) Traaseth, N. J.; Verardi, R.; Torgersen, K. D.; Karim, C. B.; Thomas, D. D.; Veglia, G. G. *Proc. Natl. Acad. Sci. U.S.A.* **2007**, *104*, 14676–14681.

AC800573Y