to DNA. Studies currently underway with defined sequences of oligonucleotides should provide a more detailed picture of the peptide conformation in the bound drug. Other drugs should also be amenable to ^{15}N NMR, provided that isotopic enrichment is possible.

Acknowledgment. This work was supported by PHS Grant CA 27343 awarded by the National Cancer Institute, DHHS. P.A.M. was supported by Training Grant GM 07175 from the National Institute of Health. We thank Dr. W. Croasman and Professor S. I. Chan for assistance in obtaining the 50-MHz spectrum at the Southern California Regional High Field NMR Facility, supported by NSF Grant CHE79-16324 at the California Institute of Technology.

Registry No. Actinomycin D, 50-76-0; actinomycin D d(pGpC) complex, 52497-84-4.

Direct Evidence of Microscopic Homogeneity in Disordered Solids

P. Caravatti, J. A. Deli, G. Bodenhausen, and R. R. Ernst*

Laboratorium für Physikalische Chemie
Eidgenössische Technische Hochschule
8092 Zürich, Switzerland

Received June 15, 1982

In this communication, we describe an NMR technique that provides a direct measure for the homogeneity of solids on a molecular level. Most solid systems are to some degree disordered. Disorder may range from rare stacking faults in single crystals to heterogeneous mixtures of amorphous substances. For example, in a solid consisting of two or more molecular species, isomers, conformers, or ions, it is possible that phase separation has occurred on a microscopic scale.

Diffraction methods, which are most suitable for the study of periodic structures, also provide information on disorder.[1-5] Further insight can be obtained from thermal analysis[6] and from electron microscopy.[7] However, strongly disordered solids remain difficult to characterize.

The method proposed in the present communication is based on the phenomenon of nuclear spin diffusion that may occur between pairs of adjacent spins. Pairs of nuclear spins i and k in the solid are coupled by magnetic dipole–dipole interaction which can induce mutual spin flips with a rate proportional to $1/r_{ik}^3$ in the case of a rigid lattice and proportional to $1/r_{ik}^6$ in the presence of motional processes.[8-15] Due to the strong dependence on nuclear separation r_{ik}, spin diffusion is almost exclusively confined to neighboring molecules. If spin diffusion can be measured between two different species, then these species must be intimately mixed on a microscopic level.

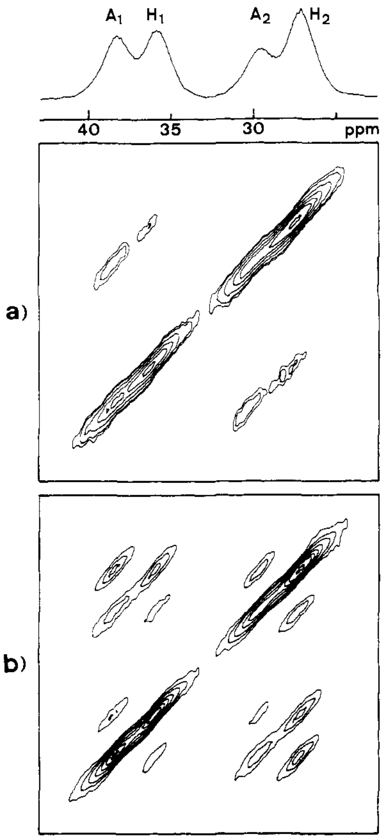

Figure 1. Two-dimensional carbon-13 spin diffusion spectra of mixtures of adamantane and 2,2,3,3-tetramethylbutane: (a) mixture of powders; (b) mixture by melt. Note the absence of cross-peaks between signals belonging to different species in the heterogeneous sample in Figure 1a. The spectra were recorded with static samples at room temperature with a Bruker CXP 300 spectrometer according to the procedure described in the text (τ_m = 5 s) and are presented in phase-sensitive mode. The phases of the last two 90° pulses were cycled together through $x,y,-x,-y$ phases while the signals were alternately added and subtracted.

A prerequisite for the measurement of spin diffusion rates is the ability to resolve NMR signals characteristic of the species under investigation. Carbon-13 solid-state NMR is particularly suitable because the dispersion of the chemical shifts is large compared to the line widths. The low natural abundance of carbon-13 reduces the spin diffusion rate due to large average nuclear separation. However, experiments have shown that in most solids with and without motional processes carbon-13 spin diffusion can be detected.[16,17]

Spin diffusion between individual sites in solids is formally analogous to cross relaxation and chemical exchange in liquids and can most conveniently be traced out by two-dimensional (2-D) exchange NMR spectroscopy, a method that has been used in liquids[18-21] and has recently been applied to solids by Szeverenyi et al.[16] and by Suter and Ernst.[22] After initial cross polarization,

---

(1) A. Guinier, "X-ray Diffraction in Crystals, Imperfect Crystals and Amorphous Bodies", Freeman, San Francisco, 1963.

(2) L. E. Alexander, "X-ray Diffraction Methods in Polymer Science", Wiley, New York, 1969.

(3) H. P. Klug and L. E. Alexander, "X-ray Diffraction Procedures of Polycrystalline and Amorphous Materials", Wiley, New York, 1974.

(4) J. E. Spruiell and E. S. Clark, in "Methods of Experimental Physics", R. A. Fava, Ed., Vol. 16, "Polymers", Part B, Academic Press, New York, 1980, p 1.

(5) Jing-I Wang and I. R. Harrison, in "Methods of Experimental Physics", R. A. Fava, Ed., Vol. 16, "Polymers", Part B, Academic Press, New York, 1980, p 128.

(6) A. Blazek, "Thermal Analysis", Van Nostrand-Reinhold, Princeton, NJ, 1973.

(7) R. G. Vadimsky, in "Methods of Experimental Physics", R. A. Fava, Ed., Vol. 16, "Polymers", Part B, Academic Press, New York, 1980, p 185.

(8) A. Abragam, "The Principles of Nuclear Magnetism", Oxford University Press, 1961.

(9) N. Bloembergen, S. Shapiro, P. S. Pershan, and J. O. Artman, *Phys. Rev.*, **114**, 445 (1959).

(10) I. J. Lowe and S. Gade, *Phys. Rev.*, **156**, 817 (1967).

(11) A. G. Redfield and W. N. Yu, *Phys. Rev.*, **169**, 443 (1968).

(12) A. C. Lind, *J. Chem. Phys.*, **66**, 3482 (1977).

(13) D. L. VanderHart and A. N. Garroway, *J. Chem. Phys.*, **71**, 2773 (1979).

(14) J. Virlet and D. Ghesquieres, *Chem. Phys. Lett.*, **73**, 323 (1980).

(15) J.-P. Korb and J. Maruani, *J. Chem. Phys.*, **74**, 1504 (1981).

(16) N. M. Szeverenyi, M. J. Sullivan, and G. E. Maciel, *J. Magn. Reson.*, **47**, 462 (1982).

(17) P. Caravatti and G. Bodenhausen, unpublished measurements.

(18) J. Jeener, B. H. Meier, P. Bachmann, and R. R. Ernst, *J. Chem. Phys.*, **71**, 4546 (1979).

(19) B. H. Meier and R. R. Ernst, *J. Am. Chem. Soc.*, **101**, 6441 (1979).

(20) S. Macura and R. R. Ernst, *Mol. Phys.*, **41**, 95 (1980).

(21) Anil Kumar, R. R. Ernst, and K. Wüthrich, *Biochem. Biophys. Res. Commun.*, **95**, 1 (1980).

(22) D. Suter and R. R. Ernst, *Phys. Rev. B*, **25**, 6038 (1982).

(23) N. M. Szeverenyi, private communication.

(24) M. Bee, J. P. Amoureux, and R. E. Lechner, *Mol. Phys.*, **40**, 617 (1980); J. P. Amoureux, M. Bee, and J. Virlet, *ibid.*, **41**, 313 (1980).

(25) A. R. Britcher and J. H. Strange, *Mol. Phys.* **37**, 181 (1979); A. R. Britcher and J. H. Strange, *J. Chem. Phys.*, **75**, 2029 (1981).

0002-7863/82/1504-5506$01.25/0

the carbon-13 magnetization precesses during the evolution period t_1 in the presence of proton decoupling. A 90° pulse converts transverse coherence into longitudinal magnetization, which is allowed to migrate by spin diffusion for a time τ_m (typically $1-10^2$ s). In this interval, no decoupling is applied. Finally, a 90° pulse reconverts longitudinal polarization into observable transverse coherence, which is detected in the presence of proton decoupling.

An illustration of 2-D spin diffusion spectroscopy is shown in Figure 1, where heterogeneous and homogeneous disordered mixtures of adamantane and 2,2,3,3-tetramethylbutane are compared. The one-dimensional spectra of the two samples cannot be distinguished and show four resonances: A_1 and A_2 correspond to the CH and CH_2 carbons of adamantane, H_1 and H_2 to the quarternary and methyl carbons of 2,2,3,3-tetramethylbutane, respectively.

Figure 1a for a heterogeneous mixture of finely powdered material exhibits besides the four diagonal peaks four cross peaks connecting pairs of signals belonging to the *same* species, suggesting that spin diffusion proceeds exclusively within domains containing either one of the pure species.

Figure 1b shows a similar spectrum of a sample prepared by melting and cooling equal amounts of adamantane and of 2,2,3,3-tetramethylbutane. The spectrum exhibits all 12 possible cross peaks, indicating that spin diffusion proceeds with similar rates between all four carbon sites. This is unambiguous evidence that the two molecules form a mixed crystal.

The elongated shape of the signal peaks, shown in phase-sensitive representation, indicates the absence of spin diffusion between microcrystallites whose resonances are shifted in frequency by susceptibility effects.

Although the presence of cross peaks, as in Figure 1b, is sufficient evidence for the existence of mixed crystals, care must be taken in interpreting the absence of cross peaks as in Figure 1a. In unfavorable systems, spin diffusion rates may be low and indeed undetectable if spin diffusion is much slower than spin lattice relaxation. However, the ratio of the amplitude of cross peaks connecting different species to the amplitude of cross peaks relating signals of the same species provides a quantitative measure of the homogeneity.

The combination of 2-D spin-diffusion spectroscopy with magic angle spinning may greatly enhance resolution. This is particularly useful for rigid solids where the shielding anisotropy is not averaged by molecular motion. Experiments by Szeverenyi[16] and ourselves[17] have indicated that such combined 2-D MAS experiments are straightforward, although spin diffusion rates may be reduced by sample rotation due to averaging of dipolar interactions.[17,23] For the nonspinning samples presented in Figure 1, the efficiency of spin diffusion is enhanced by rotational and translational molecular diffusion,[24,25] which increases the likelihood that pairs of carbon-13 spins interact.

The spin diffusion experiment described here is by no means restricted to carbon-13 NMR. Diffusion between protons is particularly efficient and sensitive to heterogeneity. To achieve better separation of the signals, the proton magnetization may be transferred to the carbon-13 nuclei by selective cross polarization or pulsed coherence transfer.[26]

In conclusion, spin diffusion provides a useful technique for the study of microscopic heterogeneity in a wide variety of materials. The most promising applications appear to be in the field of synthetic and of biological polymers. Applications in mineralogy and in solid state physics are also conceivable.

Acknowledgment. This research has been supported in part by the Swiss National Science Foundation. We acknowledge stimulating discussions with Dr. N. M. Szeverenyi, Dr. P. M. Henrichs, and Dr. N. Zumbulyadis, who are working on related subjects.

Registry No. Adamantane, 281-23-2; 2,2,3,3-tetramethylbutane, 594-82-1.

---

(26) P. Caravatti, G. Bodenhausen, and R. R. Ernst, *Chem. Phys. Lett.*, **89**, 363 (1982).

Characterization of Novel Rhodium(II) Dimers with *N*-Phenylacetamido Bridging Ligands

J. Duncan, T. Malinski, T. P. Zhu, Z. S. Hu, K. M. Kadish,* and J. L. Bear*

Department of Chemistry, University of Houston
Houston, Texas 77004

Received July 2, 1982

Recently we reported the structure and electrochemical properties of a new dirhodium(II) complex that had trifluoroacetamido in place of carboxylato bridging ligands.[1] This compound, $Rh_2(HNOCCF_3)_4$, undergoes reversible oxidation to yield $[Rh_2(HNOCCF_3)_4]^+$, similar to the rhodium(II) carboxylates[2] but at a much lower potential than $Rh_2(OOCCF_3)_4$. This suggested to us that the synthesis of other rhodium(II) dimers with RNOCR′ ligands could result in a system for which the electronic structure could be "tuned" for redox processes by varying R and R′. This indeed is the case as we report in this communication. Tetrakis(μ-acetato)dirhodium(II) reacts with *N*-phenylacetamide to produce a complex mixture of partially and totally amide-substituted dinuclear rhodium(II) complexes and their isomers. The reaction was carried out by heating a mixture of 1 g of $Rh_2(OOCCH_3)_4$ and 30 g of *N*-phenylacetamide at 150 °C for 48 h. After excess *N*-phenylacetamide was removed by sublimation, the product was a mixture of organic impurities and several different rhodium complexes. The organic impurities were separated from the rhodium complexes by HPLC using a CN-bonded phase column with methanol eluent. As shown in Figure 1 there are four possible isomers of the totally amide-substituted product. Two of the four isomers were isolated and studied. Elemental analysis of one blue isomer complex corresponds to $Rh_2(C_6H_5NOCCH_3)_4(H_2O)$, I (Found: C, 50.61; H, 4.56; N, 7.80; Rh, 26.96. Calcd: C, 50.50; H, 4.58; N, 7.40; Rh, 27.1). Elemental analysis of a second green isomer corresponds to $Rh(C_6H_5NOCCH_3)_4$, II (Found: C, 51.69; H, 4.50; N, 7.45; Rh, 27.73. Calcd: C, 51.75; H, 4.31; N, 7.54; Rh, 27.76). The molecular weight of complexes I and II were determined by liquid chromatography/mass spectrometry, operating in the negative ion mode and showed a parent mass of 742. This is the calculated molecular weight of the dinuclear rhodium(II) complex with four bridging *N*-phenylacetamado ions.

The ^1H NMR spectrum of II gives three CH_3 proton resonances at 1.72, 1.77, and 1.92 ppm with an area ratio of 1:2:1 and strongly suggests that II is isomer C in Figure 1. In addition the ^{13}C NMR spectrum shows that the amide group carbon as well as the *o*-, *m*-, and *p*-benzene carbons are split into three bands, also suggesting isomer C. Compound I shows only one ^1H NMR resonance for the CH_3 groups, at 1.75 ppm, and none of the ^{13}C resonances are split. This is the NMR spectra that would be characteristic for either A, B, or D. Cotton and Felthouse[3] have also reported isomers for dinuclear rhodium(II) complexes with 2-oxy-6-methyl-pyridine and 2-oxy-6-chloropyridine bridging anions. The N,O bonding combination of isomers B and C were found for these ligand systems.

As shown in Figure 2, the electrochemical oxidations of I and II proceeds in two steps without destroying the dimeric cage structure. The currents observed by differential pulse polarography and cyclic voltammetry were of equal height, indicating an identical number of electrons transferred in each step. In addition, the $E_{pa} - E_{pc} = 60 \pm 5$ mV from the cyclic voltammograms, indicating that one electron is transferred in each step. Potentials and coulometric data for each process are given in Table I. It is interesting to note that the initial potential for oxidation of $Rh_2(C_6H_5NOCCH_3)_4$ in CH_2Cl_2 is over 400 mV more negative than for any other rhodium(II) dimer of the form $Rh_2(O_2CCR)_4$. More important, however, the second oxidation has never been

---

(1) Dennis, A. M.; Howard, R. A.; Lancon, D.; Kadish, K. M.; Bear, J. L. *J. Chem. Soc., Chem. Commun.* **1982**, 339.

(2) Das, K.; Kadish, K. M.; Bear, J. L. *Inorg. Chem.* **1978**, *17*, 930.

(3) Cotton, F. A.; Felthouse, T. R. *Inorg. Chem.* **1981**, *20*, 584.

0002-7863/82/1504-5507$01.25/0