

CPMAS Polarization Transfer Methods for Superposed Chemical Exchange and Spin Diffusion in Organic Solids*

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The question of how CPMAS polarization-transfer experiments (CP, cross polarization; MAS, magic-angle spinning) should be conducted in order to distinguish between slow chemical exchange and spin diffusion in the solid state has been studied. Both contributions can be separated by performing different types of polarization-transfer experiments in the laboratory and the rotating frame, since dynamics of spin diffusion but not chemical exchange differs from one experiment to the next. Generally, if both processes are present, polarization transfer is expected to be nonexponential and chemical-exchange as well as spin-diffusion rate constants can be obtained in one series of experiments. If the exchange is symmetric, however, polarization transfer is single exponential and a combination of different pulse experiments is required for obtaining rate constants of both processes. The results for ^{15}N CPMAS NMR polarization-transfer experiments on crystalline *meso*-tetra-*tolyl*porphin- $^{15}\text{N}_4$ (TTP) are presented. Experiments in the laboratory frame show that spin diffusion between the ^{15}N atoms of TTP is characterized by a temperature-independent rate constant. The nature of this process was established by ^1H decoupling during the mixing time, which results in quenching of the polarization transfer. Thus, the role of the ^1H spin reservoir for laboratory-frame spin diffusion among chemically inequivalent ^{15}N spins in ^{15}N -enriched material is confirmed. At higher temperatures, polarization transfer in the laboratory and the rotating frame is observed due to a symmetric exchange of the nitrogen atoms arising from a double proton transfer which has been previously established. The double proton transfer rates observed with the different polarization-transfer methods agree well with the values predicted from high-temperature lineshape analysis and are found to be very close to the solution data. © 1988 Academic Press, Inc.

INTRODUCTION

In the past few years, CPMAS NMR studies have become popular for elucidating the dynamics of molecular rearrangements or motions in the solid state (1-6). As in solution, it has been possible to obtain rate constants of different solid-state reactions, such as carbonium ion rearrangements and valence tautomerism (1), or proton transfers (4, 6) by complete lineshape analysis. However, it is well known from solution studies that lineshape analysis does not yield reliable kinetic data in the slow-exchange regime, and polarization-transfer experiments have been designed as a remedy for this situation (7-11). These experiments are based either on the transfer of longitudinal polarization

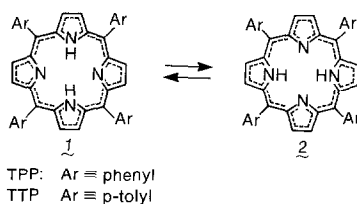
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in the laboratory frame (7, 8) or on transverse polarization in the rotating frame under spin-locking conditions (10). For complex exchange networks it is preferable to perform two-dimensional polarization-transfer experiments (9, 11). In solution, polarization transfer between different sites can be caused not only by chemical exchange but also by cross relaxation between the spins in these sites (7), and it is, therefore, not always easy to separate the two effects. In high-resolution solid-state NMR experiments a similar competition of chemical exchange and spin flips between dipolar coupled spins arises (12–17). So far, chemical-exchange rates have been obtained in only one solid by laboratory-frame ^{13}C CPMAS polarization-transfer experiments at and above room temperature, and a direct transfer of spin energy between the spatially well-separated naturally abundant ^{13}C spins could be neglected (3). However, this neglect is not always justified, especially if abundant spins such as ^1H , ^{19}F , or ^{31}P are studied, or if samples are artificially enriched with spins such as ^2H , ^{13}C , or ^{15}N (12–17).

Spin diffusion in solids in the absence of chemical-exchange processes has been studied under high-resolution conditions for nonspinning samples by Suter and Ernst (13). Stochastic rigid-lattice-induced “spectral” spin diffusion between inequivalent dipolar coupled spins S and X, characterized by different Larmor frequencies ν_S and ν_X occurs even in isolated S/X spin clusters provided that S and X are in contact with an extraneous dipolar reservoir of abundant spins I. The latter will be constituted by protons in most organic compounds (13). Oscillation of spin energy between S and X spins is hindered by the different values of ν_S and ν_X . The necessary energy $\hbar(\nu_S - \nu_X)$ for the spin flips between S and X is provided by fluctuating magnetic fields induced by the motions of the I spins in spin space. These spectral spin-diffusion processes have been studied theoretically and experimentally (13), although not yet under MAS conditions.

In view of the fact that valuable information on structure and dynamics of solids can be obtained from the knowledge of both chemical-exchange and spin-diffusion processes, it seemed desirable to obtain kinetic data for both processes in one series of experiments.

In this paper, we discuss a strategy in order to obtain spin-diffusion and chemical-exchange rates separately. A model case is treated which incorporates both processes and which helps to define the conditions under which spin-diffusion and chemical-exchange rate constants can be obtained from one series of experiments or whether a combination of different experiments is needed. In the latter case, one can exploit the fact that polarization transfer due to spin diffusion depends on the type of experiment performed (e.g., in the laboratory or rotating frame) in contrast to polarization transfer through chemical exchange. As an example, we describe ^{15}N CPMAS polarization-transfer experiments on solid *meso*-tetratolylporphyrin- $^{15}\text{N}_4$ (TTP), which is capable of exchange between the ^{15}N atoms as shown in Scheme I. There has been considerable interest in the mechanism of proton tautomerism in porphyrins and related compounds in solution (18, 19). We have recently shown that the porphyrin tautomerism also takes place in the solid state (4), where, generally, the degeneracy of the rearrangement is lifted. However, for solid TTP, both tautomers were found to be present in amounts which are equal within the margin of error of our NMR experiments. This result has been confirmed by X-ray analysis (20). As shown in Fig. 1, at low temperatures a high-field signal for the NH atoms and a low-field signal for the =N— atoms are



SCHEME I

observed in the ^{15}N CPMAS spectra of TTP, but there is only one sharp signal at high temperatures, due to the fast hydrogen migration shown in Scheme I. While this chemical-exchange process leads to polarization transfer between the two ^{15}N lines at low temperatures, spin diffusion between ^{15}N atoms should also occur in TTP under MAS conditions because of the isotopic enrichment. Different laboratory- and rotating-frame ^{15}N CPMAS experiments from which spin-diffusion and chemical-exchange rates were obtained were performed on TTP at low temperatures. Although the one-dimensional experiments we report here are sufficient for the study case of a two-line system such as TTP, the conclusions apply equally well to two-dimensional experiments; the latter have already proven useful for structural assignments in a more complicated case (6).

EXPERIMENTAL

^{15}N TTP was synthesized according to literature procedures (21). The ^{15}N CPMAS experiments reported here were performed at 6.082 MHz on a homebuilt apparatus described previously (22). The spectra shown in Fig. 1 were measured at 9.12 MHz on a Bruker CXP-100 NMR spectrometer equipped with a Doty probe (23) for an electromagnet with a 2.2 cm gap, using variable-temperature equipment described previously (5). Spinning rates were between 2 and 2.5 kHz in all experiments.

PULSE SEQUENCES FOR CPMAS POLARIZATION-TRANSFER STUDIES

We have tested the three different CPMAS polarization-transfer pulse sequences shown in Fig. 2. S and X represent the polarization of the observed inequivalent spins which are subject to chemical exchange and spin diffusion. I represents the abundant third spin. In the example given below, S and X are ^{15}N nuclei and I are protons. During the CP pulse sequence and the evolution period t_1 , the initial polarizations of S and X are prepared; their exchange during the mixing period t_m is monitored in the acquisition period t_2 . Sequence A is a variation of a sequence proposed previously (3, 9); the polarization transfer takes place in the laboratory frame. Sequence B is essentially the same as sequence A, however, with I-spin decoupling during the mixing period t_m . In sequence C the polarization transfer takes place in the rotating frame under spin-lock conditions; this sequence was adapted from its solution analog (10) by replacing the initial $\pi/2$ pulse on the exchanging spins by the CP sequence. Due to limited RF field strength, I-spin decoupling is applied during the mixing time t_m to maintain an S, X spin lock. The possibility of cross polarization during t_m is minimized

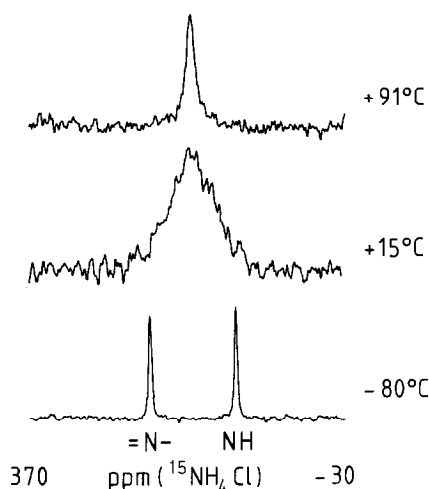


FIG. 1. ^{15}N CPMAS NMR spectra of $^{15}\text{N}_4$ -tetratolylporphin (TTP) at 9.12 MHz at -80 , 15 , and $+91^\circ\text{C}$; 20 ms CP time; 2.2 s repetition time; 5 kHz sweep width; external $^{15}\text{NH}_4$ reference. Note that a small high-field line assigned previously (4) to the presence of some *meso*-tetratolylchlorin (TTC) is now absent in the spectra which otherwise show the same features as reported previously (4). Thus, a small amount of TTC is not responsible for the apparent symmetric exchange situation in TTP, a possibility which has been discussed recently (20).

by deliberately mismatching the spin-lock and decoupling fields. In contrast to chemical exchange, the spin-diffusion rate is expected to be different in the three pulse sequences. Thus, if equal polarization-transfer rates are obtained in the different experiments, spin diffusion as major contribution to these rates can be neglected.

In order to obtain quantitative kinetic data it is necessary to vary the mixing time t_m in increments which makes a quantitative two-dimensional experiment with Fourier transformation along t_1 and t_2 (3, 9) very time consuming. In the case of a small number of well-resolved exchanging lines the desired kinetic information can, however, be obtained by performing one-dimensional experiments by choosing a special set of t_1 values for each value of t_m (3, 10). When only two lines S and X are present two experiments are needed with $t_1 = 0$ in experiment I and $t_1 = (2\Delta\nu)^{-1}$ in experiment II, where $\Delta\nu = \nu_S - \nu_X$ is the frequency difference between S and X, and where the carrier frequency is set on one of the exchanging lines. These conditions ensure that the polarizations S and X are parallel in experiment I, and antiparallel in experiment II during the mixing time. The evolution of S and X during experiment II is illustrated in Fig. 2. Thus, by combination of both experiments the longitudinal relaxation rates ρ_i and the polarization-transfer rates can be obtained as shown in the next section.

EVALUATION OF THE KINETIC DATA

During the mixing period the different polarizations evolve according to a set of coupled differential equations for the polarizations which must be specified for each particular exchange problem. We treat here the case of two superposed asymmetric two-site chemical-exchange systems which are coupled together by spin diffusion. The

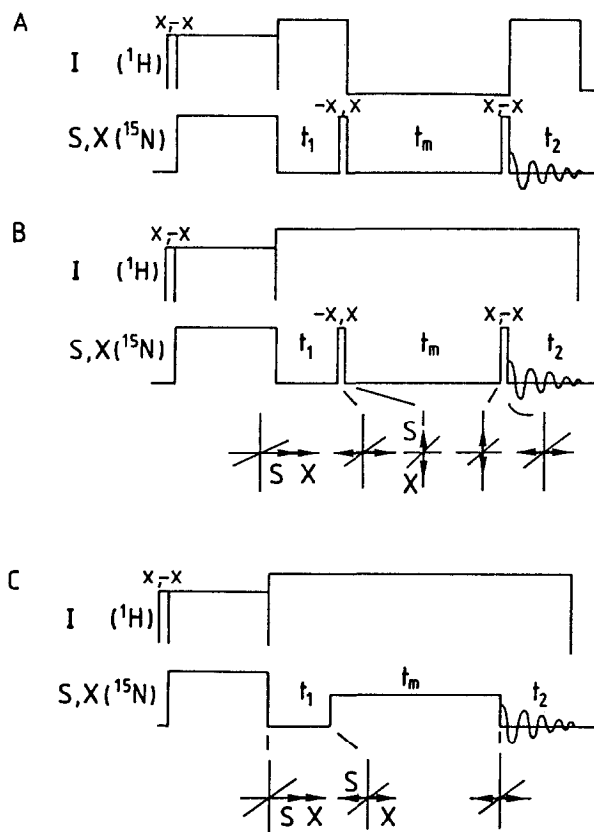


FIG. 2. CPMAS pulse sequences used for the detection of polarization transfer in TTP. (A) Laboratory-frame experiment without and (B) with I spin (^1H) decoupling; (C) rotating-frame experiment with I spin (^1H) decoupling. The arrows labeled S and X show the direction of the polarization for S and X (^{15}N) spins in the rotating frame (vide infra) at various times during experiment II (see text); $-x, x$ ($x, -x$) are $\pi/2$ pulses.

model is illustrated in Fig. 3a. Consider a cluster of two spins S and X, where S and X are located either in the same molecule or in neighbor molecules. Let these molecules be subject to exchange between two different molecular states 1 and 2 with the probabilities, x_1 and x_2 , characterized by the equilibrium constant $K = x_2/x_1 = k_{12}/k_{21}$, where k_{12} and k_{21} are the rate constants of state exchange. We assume absence of resolved scalar or dipolar interactions between S and X. In the slow-exchange regime the spectra should then contain four lines corresponding to the polarizations $S_1, S_2, X_1,$ and X_2 , where the subscript indicates the molecular state. Since we assume a two-spin system, the equilibrium polarizations of $S_{1\infty} = X_{1\infty}$ and $S_{2\infty} = X_{2\infty}$. The ratios $S_{1\infty}/S_{2\infty}$ and $X_{1\infty}/X_{2\infty}$ reflect the probabilities of the states 1 and 2. In the fast-exchange regime only two coalesced lines S and X can be observed. We now allow spin diffusion to take place within each spin system, i.e., between S_1 and X_1 and between S_2 and X_2 , via residual nonresolved dipolar coupling. We assume that (i) these spin-diffusion processes can be characterized by the rate constants $\sigma_{1SX}, \sigma_{2SX}, \sigma_{1XS},$ and σ_{2XS} , as

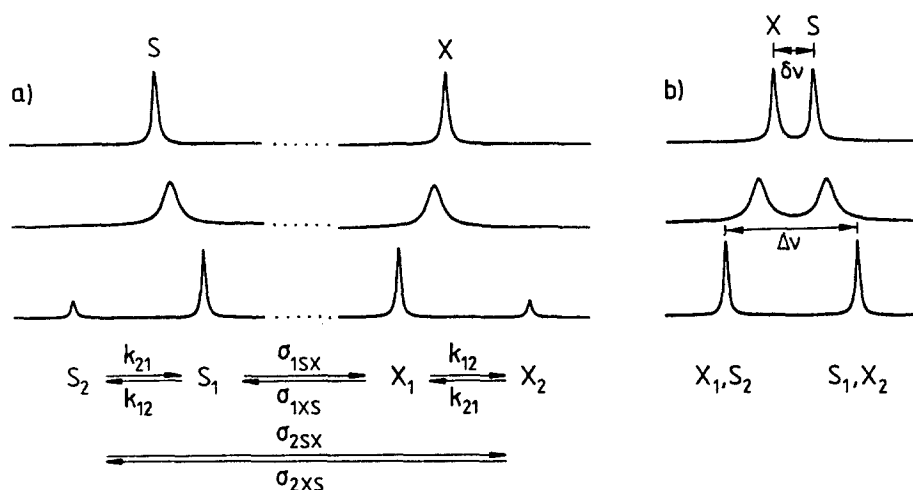


FIG. 3. (a) Calculated spectra for an asymmetrical two-site exchange system for different k_{12} but constant K values. For further explanation see text. (b) Spectra calculated for the case of the validity of Eq. [1].

shown in Fig. 3a. Since the equilibrium polarizations $S_{1\infty}$ and $X_{1\infty}$ (and $S_{2\infty}$ and $X_{2\infty}$) are equal, the relations $\sigma_{1SX} = \sigma_{1XS} = \sigma_1$ and $\sigma_{2SX} = \sigma_{2XS} = \sigma_2$ hold. Additionally, we assume that (ii) spin diffusion between different clusters, i.e., between S_1 and S_2 (and between X_1 and X_2) can be neglected. Figure 3b shows a special case where S_1 and X_2 as well as S_2 and X_1 are characterized by the same chemical shifts, i.e., where

$$\nu_{S_1} = \nu_{X_2} \quad \text{and} \quad \nu_{S_2} = \nu_{X_1}. \quad [1]$$

In this case only the sums $S_1 + X_2$ and $S_2 + X_1$ are observable. The asymmetric character of the exchange problem shown in Fig. 3b is easily seen in the fast-exchange case where a splitting $\delta\nu \neq 0$ results for equilibrium constants $K \neq 1$. The value of $\delta\nu$ is related to the chemical-shift difference $\Delta\nu = \nu_{S_1} - \nu_{S_2}$ and K in the following way (4):

$$\delta\nu/\Delta\nu = (1 - K)/(1 + K). \quad [2]$$

It is now straightforward to set up the differential equations which govern the time evolution of the polarizations during the mixing time t_m :

$$\frac{d}{dt_m} \begin{bmatrix} S_1 \\ X_1 \\ X_2 \\ S_2 \end{bmatrix} = \begin{bmatrix} -k_{12} - \sigma_1 - \rho_{1S} & \sigma_1 & 0 & k_{21} \\ \sigma_1 & -k_{12} - \sigma_1 - \rho_{1X} & k_{21} & 0 \\ 0 & k_{12} & -k_{21} - \sigma_2 - \rho_{2X} & \sigma_2 \\ k_{12} & 0 & \sigma_2 & -k_{21} - \sigma_2 - \rho_{2S} \end{bmatrix} \begin{bmatrix} S_1 - S_{1\infty} \\ X_1 - X_{1\infty} \\ X_2 - X_{2\infty} \\ S_2 - S_{2\infty} \end{bmatrix}. \quad [3]$$

As far as the application of Eq. [3] is concerned, an add/subtract scheme is usually employed in CPMAS experiments using phase alternation for the first $\pi/2$ ^1H pulse, leading to an alternating positive or negative observed signal for compensation of base line and acoustic ringing effects (24). Thus, the apparent values $S_{i\infty}$ and $X_{i\infty}$, $i = 1, 2$ are zero both in the rotating- and in the laboratory-frame experiments. Depending

on the pulse sequence used, ρ_{iS} and ρ_{iX} are the longitudinal relaxation rates in the laboratory or in the rotating frame under spin-locking conditions of spins S and X in the molecular state i , i.e., Eq. [3] applies to all pulse sequences A to C. Whereas k_{12} and k_{21} do not depend on the pulse sequence used, the spin-diffusion rate constants σ_i do. The general solution of Eq. [3] can be written in the form

$$y_i = \sum_{j=1}^4 C_j B_{ij} \exp(\Lambda_j t_m), \quad [4]$$

where Λ_i are the eigenvalues of the exchange matrix, B_{ij} the coefficients of the corresponding eigenvectors, y_i the different polarizations (S_i and X_i). In principle, the measurement of S_i and X_i as a function of t_m permits the determination of all spin-diffusion and chemical-exchange rate constants. The constants C_j are obtained by solving Eq. [3] at $t_m = 0$.

In this study, Eq. [3] was solved numerically and programmed as part of a nonlinear least-squares fitting routine (25). There are, however, some special solutions of Eq. [3] which can be obtained in an analytical form. For the case where

$$\rho = \frac{1}{2}(\rho_{1S} + \rho_{1X}) = \frac{1}{2}(\rho_{2S} + \rho_{2X}) \ll \frac{1}{2}(k_{12} + k_{21}), \quad \text{and} \quad \sigma = \sigma_1 = \sigma_2, \quad [5]$$

Eq. [3] can be reduced to two sets of coupled differential equations of order two, and the solution is given by

$$\begin{aligned} S_1 - X_1 &= A \exp[(-2\sigma - \rho)t_m] + B \exp[(-2\sigma - \rho - k_{12} - k_{21})t_m], \\ A &= (S_{10} - X_{10} + S_{20} - X_{20})/(1 + K), \\ S_2 - X_2 &= KA \exp[(-2\sigma - \rho)t_m] - B \exp[(-2\sigma - \rho - k_{12} - k_{21})t_m], \\ B &= (KS_{10} - KX_{10} - S_{20} + X_{20})/(1 + K), \\ S_1 + X_1 &= C \exp[(-\rho)t_m] - D \exp[(\rho - k_{12} - k_{21})t_m], \\ C &= (S_{10} + X_{10} + S_{20} + X_{20})/(1 + K), \\ S_2 + X_2 &= C \exp[(-\rho)t_m] + D \exp[(-\rho - k_{12} - k_{21})t_m], \\ D &= (-KS_{10} - KX_{10} + S_{20} + X_{20})/(1 + K), \end{aligned} \quad [6]$$

where S_{i0} and X_{i0} are the polarizations at $t_m = 0$. If Eq. [1] is valid as shown in Fig. 3b and if k_{21} is small enough the observables are $S = S_1 + X_2$ and $X = X_1 + S_2$. Note that if k_{21} is large enough to cause line broadening, S_1 and X_1 are the observables instead of S and X . With the condition

$$K = X_2/S_1 = S_2/X_1 \quad [7]$$

we obtain

$$S - X = (S_0 + X_0) \left[\frac{(1 - K)^2}{(1 + K)^2} \exp[-(\rho + 2\sigma)t_m] + \frac{4}{(1 + K)^2} \exp[-(\rho + 2\sigma + 2k)t_m] \right], \quad [8]$$

$$S + X = (S_0 + X_0) \exp(-\rho t_m), \quad k = (k_{12} + k_{21})/2 = k_{21}(1 + K)/2. \quad [9]$$

For values of K between 0.7 and 1 the first term in Eq. [8] can be neglected and we obtain by combination of Eqs. [8] and [9]

$$S = \frac{1}{2}(S_0 + X_0)\exp[-\rho t_m] + \frac{1}{2}(S_0 - X_0)\exp[-(\rho + 2\sigma + 2k)t_m], \quad [10]$$

$$X = \frac{1}{2}(S_0 + X_0)\exp[-\rho t_m] + \frac{1}{2}(-S_0 + X_0)\exp[-(\rho + 2\sigma + 2k)t_m]. \quad [11]$$

Thus, for the K values between 0.7 and 1 (symmetric exchange), S and X are not sensitive to K , which can then be arbitrarily set to unity. From experiment I ($S_0 = X_0$) and experiment II ($S_0 = -X_0$), one obtains ρ and $\rho + 2\sigma + 2k$, respectively, but not k_{12} , k_{21} , and σ separately. Spin diffusion cannot be distinguished from chemical exchange under these conditions. The situation is illustrated in Fig. 4a, where the decays of S and X are single exponentials. As mentioned above, a nonzero value of σ must then be detected by applying a combination of pulse sequences, in which σ is different but k is the same. For asymmetric exchange ($K \ll 1$), and when $k \gg \sigma$ (a condition achievable by changing temperature), both exponentials in Eq. [8] might be observable as shown in Fig. 4b. The value of k is then obtained from the initial decay, σ from the final decay of the polarizations, and K from the relative amplitudes of both exponentials, which are equal when $K = 0.17$. Thus, if both exponentials can be observed, there is no need to perform different pulse sequences in order to detect spin diffusion.

RESULTS

A number of different ^{15}N CPMAS polarization transfer experiments using pulse sequences A, B, and C were performed on TTP and the data obtained are assembled in Table 1.

A comparison of Fig. 1 and Fig. 3b leads to the conclusion that the two tautomers **1** and **2** in Scheme I have equal populations within the margin of error and that Eq. [1] is valid. Therefore, $\sigma_1 = \sigma_2 = \sigma$. Note that TTP contains ^{15}N four-spin clusters; i.e., in principle, the exchange problem of TTP has the dimension 8. The set of differential equations can, however, be reduced to a smaller set of the type given in Eq. [3] because of the fact that the two NH nuclei and the two $=\text{N}-$ nuclei have the same chemical shifts; rate constants of spin diffusion between isochronous nuclei cannot be observed. The value of σ given above is then double the spin-diffusion rate between two individual NH and $=\text{N}-$ nuclei.

Figures 5 and 6 show laboratory-frame experiments using pulse sequences A without proton decoupling performed at -150° and at -88°C . The integrated intensities as function of time could be described in terms of Eqs. [10] and [11] with $\rho_S = \rho_X \approx 0$, i.e., with negligible longitudinal relaxation during the mixing period. According to Eqs. [10] and [11] it follows then that $S = X = (S_0 + X_0)/2$ at longer mixing times. In experiment II this quantity was greater than 0 since $S_0 \neq -X_0$ because of different CP times of S and X . Therefore, in experiment II, X is predicted by Eqs. [10] and [11] to be first negative and then go through zero at longer mixing times in order to reach the positive value $(S_0 + X_0)/2$. This effect of a vanishing X but a nonvanishing S line is nicely seen in Figs. 5 and 6. From the nonlinear least-squares fit we obtained $k + \sigma = 0.7 \text{ s}^{-1}$, independent of temperature, in the range between -75 and -150°C (Table 1). The question was now how to obtain separate values for k and σ . In view

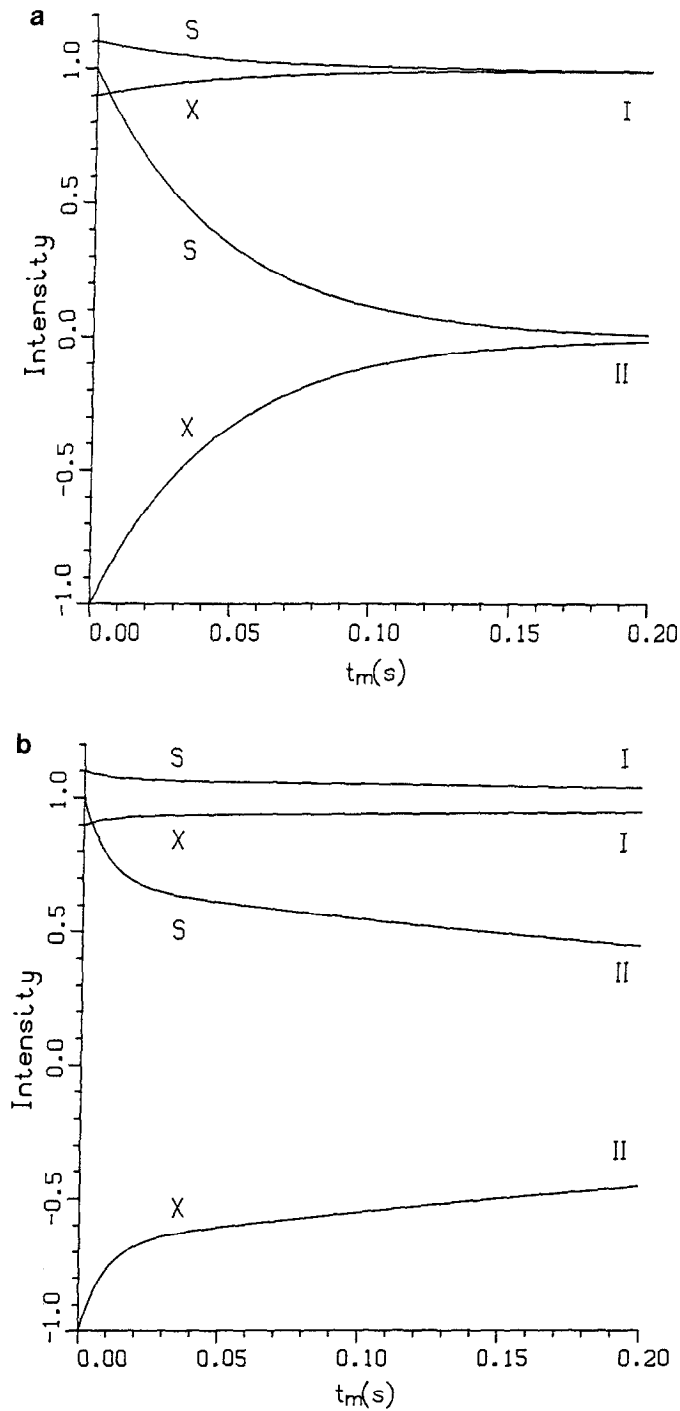


FIG. 4. Illustration of Eqs. [8] and [9] for the symmetrical case (a) $K = 1$ (equivalent to Eqs. [10] and [11]) and the asymmetrical case (b) $K = 0.1$. Other parameters used $k_{12} = 10 \text{ s}^{-1}$, $\sigma = 1$, and $\rho = 0$.

TABLE I
Results of the Polarization-Transfer Experiments on TTP

T (°C)	Pulse sequence	ρ_S (s ⁻¹)	ρ_X (s ⁻¹)	$k + \sigma$ (s ⁻¹)	k (s ⁻¹)	σ (s ⁻¹)	k_{sol}^a (s ⁻¹)
-45	C	17	17	23	23	—	60
-54	A	0.01	0.01	10.5	9.8	0.7 ^b	25
-60	C	6.7	6.7	6	6	—	14
-69	C	1.2	7.2	3.7	3.7	—	5
-88	A	0	0	0.69	≈0	0.69	0.5
-107	A	0	0	0.69	≈0	0.69	0.02
-150	A	0	0	0.66	≈0	0.69	10 ⁻⁷

^a k_{sol} , solution rate constants calculated according to Eq. [13].

^b Extrapolated from low temperature.

of the fact that the rate constants of the tautomerism in solid TTP are strongly dependent on temperature (4), it was highly probable that the above value of $k + \sigma$ was entirely due to spin diffusion. In order to test this idea we have performed laboratory-frame polarization-transfer experiments using pulse sequence B, i.e., with ¹H decoupling during the mixing time. An example is shown in Fig. 7, with $t_m = 250$ ms. There is no difference in the absolute integrated intensities of the lines in experiments I as compared to experiments II within the margin of error. Note that there should be a measurable difference at 250 ms in these experiments if there was a polarization-transfer rate of the order of 0.7 s⁻¹ as was found in the experiments shown in Figs. 5 and 6. Thus, the suppression of the polarization-transfer rates below -75°C in the presence of ¹H decoupling implies the dominance of spin diffusion and not of chemical exchange in the experiments of Figs. 5 and 6.

Since the rate constants k of the exchange increase rapidly with temperature (4) we were able to observe the effect of chemical exchange on the polarization-transfer rates at temperatures above -70°C. Figure 8 shows the effect of chemical exchange on polarization transfer in the rotating frame using pulse sequence C. In order to destroy the Hartmann-Hahn condition during the mixing time, the ¹⁵N spin-locking field was reduced by 6dB. The analysis of the data shows that the residual relaxation rates in the rotating frame are finite and are different for both types of nuclei as shown in Table 1. The effect of polarization transfer is manifest in the different time dependences of the polarizations in experiments I (lower right) and II (upper right). In experiment II the X polarization loses about as much intensity by rotating-frame relaxation ρ_X ($=T_{1\rho X}^{-1}$) as it gets from S by polarization transfer, and thus stays fairly constant. Above -60°C, the polarization-transfer rate constants became so fast that coalescence of the longitudinal relaxation rates in the rotating frame (Eq. [5]) was achieved (Table 1).

An example of applying sequence A at higher temperatures is shown in Fig. 9. Here, we obtained by simulation a value of $k + \sigma = 10.5$ s⁻¹, from which we subtract the temperature-independent value of $\sigma = 0.7$ s⁻¹ and obtain $k \approx 10$ s⁻¹. Note that the value of σ is approximately the margin of error of our measurements, and the correction for spin diffusion is really important only in the region where $\sigma \gtrsim k$, i.e., at low

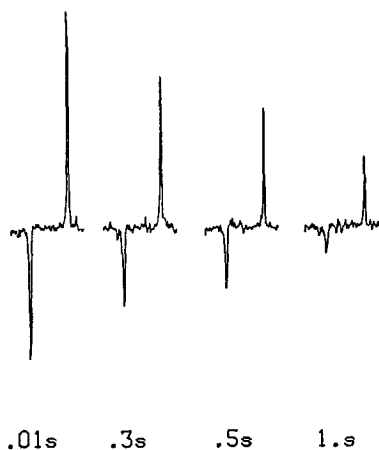
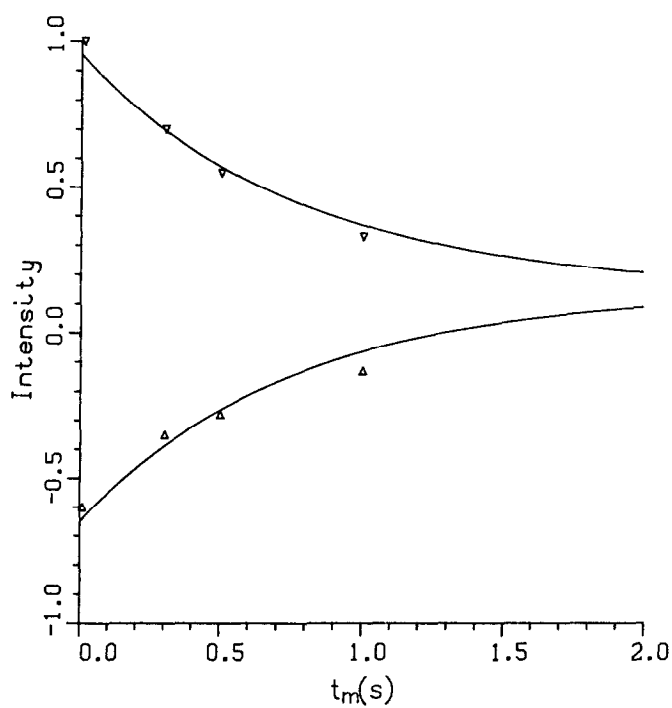


FIG. 5. Laboratory-frame ^{15}N CPMAS polarization-transfer experiment on TTP at 6.082 MHz and -150°C using pulse sequence A. Bottom: experiment II with $t_1 = 761 \mu\text{s}$ corresponding to a line separation of $\Delta\nu = 657 \text{ Hz}$; 1600 scans per spectrum; 35 ms CP time; 1.2 s repetition time; 2.4 kHz sweep width. Top: nonlinear least-squares fit of the data using Eq. [3]. The polarization transfer arises mainly from spin diffusion.

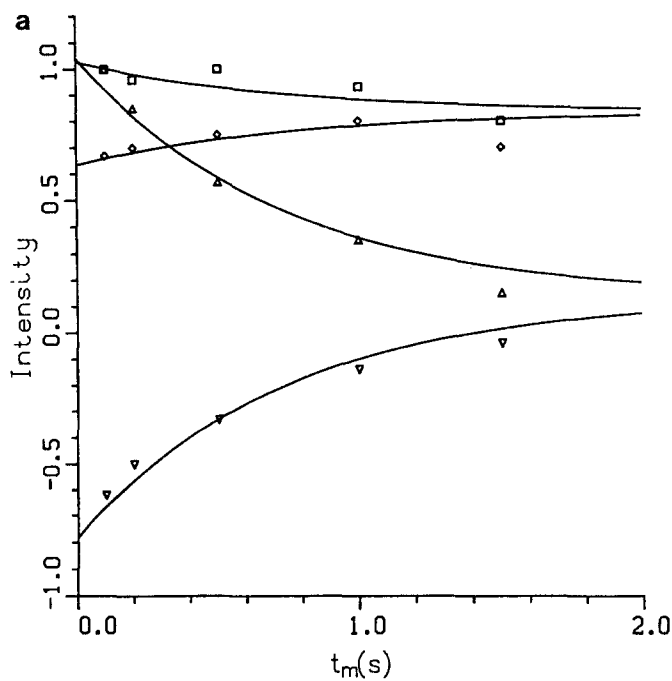


FIG. 6. Laboratory-frame ^{15}N CPMAS polarization-transfer experiment on TTP at 6.082 MHz and -88°C using pulse sequence A. CP time 25 ms, 3000 scans per spectrum, 1.2 s repetition time, 2.4 kHz sweep width. (b) top: experiment II with $t_1 = 761 \mu\text{s}$; (b) bottom: experiment I with $t_1 = 0$; (a): nonlinear least-squares data fit using Eq. [3]. The polarization transfer arises again (see Fig. 5) mainly from spin diffusion.

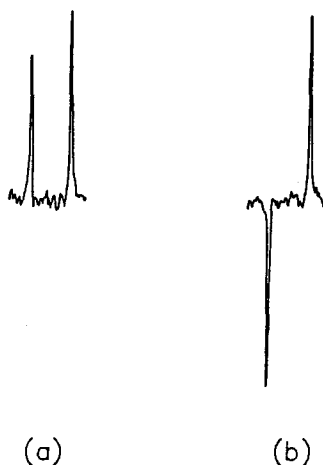


FIG. 7. Laboratory-frame ^{15}N CPMAS polarization-transfer experiment on TTP at 6.082 MHz and -72°C using pulse sequence B, with $t_m = 0.25$ s; conditions otherwise as in Fig. 6. (a) Experiment I, $t_1 = 0$; (b) experiment II, $t_1 = 761 \mu\text{s}$. The polarization transfer is suppressed by ^1H decoupling.

temperatures. The k values (Table 1) obtained here by polarization transfer are consistent with those obtained previously by ^{15}N CPMAS lineshape analysis of solid TTP (4) and can be described by the common Arrhenius equation,

$$k = 10^{11.1} \exp[-5040/T], \quad [12]$$

which is in good agreement with the solution rate constants of TPP (19):

$$k = 10^{10.9} \exp[-4787/T]. \quad [13]$$

DISCUSSION

Our finding that at low temperatures laboratory-frame polarization transfer of the order of 0.7 s^{-1} between the S (NH) and the X ($=\text{N}-$) spins of solid ^{15}N enriched *meso*-tetratolylporphyrin can be almost eliminated by ^1H decoupling during the mixing time t_m demonstrates that this transfer is indeed due to spin diffusion among the S and X spins and not due to chemical exchange which would be impossible to manipulate by ^1H decoupling. Because of the observed temperature independence of the spin-diffusion rates obtained using pulse sequence A we were able to subtract this contribution from the high-temperature values in order to obtain the corrected chemical-exchange rate constants k . As an alternative, chemical-exchange rate constants free from spin-diffusion effects could be measured using pulse sequence B, which is presently restricted to small mixing times due to heating. The use of partial ^1H decoupling during the mixing time in order to reduce the problem of heating is not necessarily a remedy, since this can result in an enhanced spin-diffusion rate (14).

Rotating-frame polarization-transfer experiments involving pulse sequence C are a good alternative to sequences A or B, or, at least a complementary method to measure chemical-exchange rates. A disadvantage of sequence C is $T_{1\rho} < T_1$, a condition that is unfavorable for measuring small polarization-transfer rates. Despite this limitation,

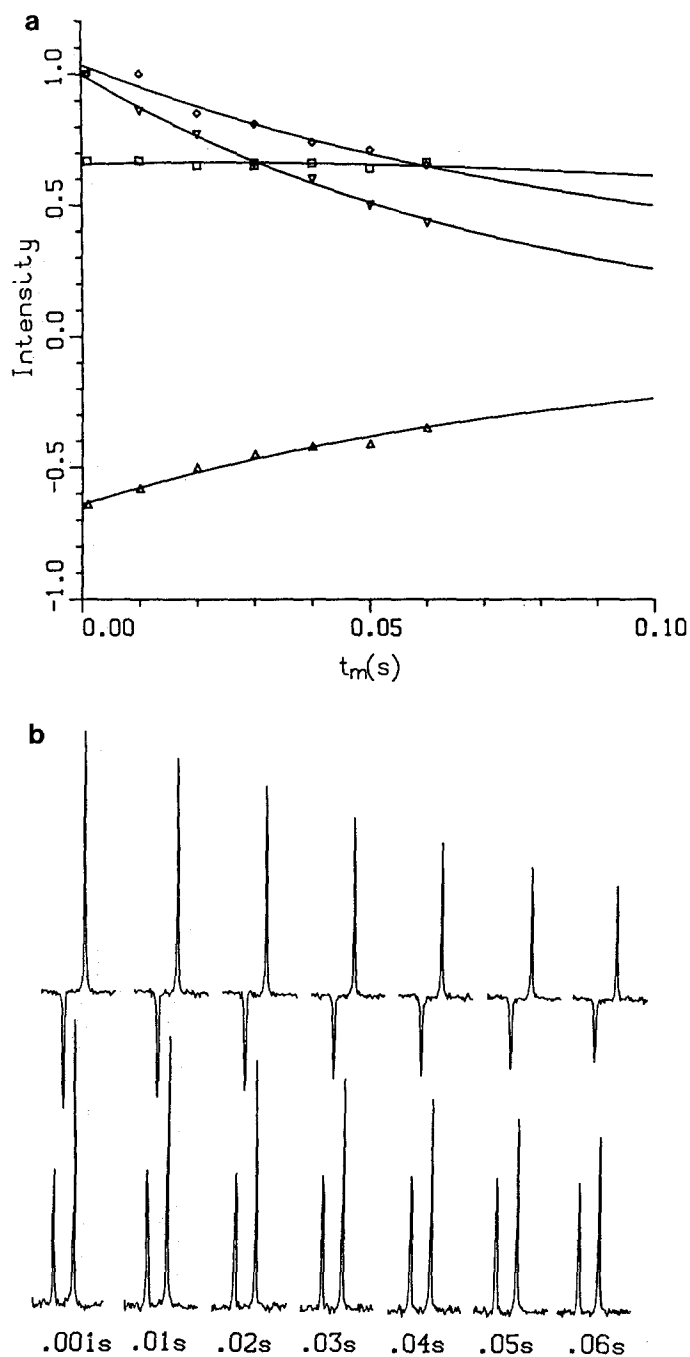


FIG. 8. Rotating-frame ^{15}N CPMAS polarization-transfer experiment on TTP at 6.082 MHz and -69°C using pulse sequence C. CP time 10 ms, 6 dB reduction of the spin-locking pulse strength with respect to the CP pulse; 5000 scans. (b) bottom: experiment I with $t_1 = 0$; (b) top: experiment II with $t_1 = 761 \mu\text{s}$; (a): nonlinear least-squares data fit using Eq. [3]. The polarization transfer arises mainly from chemical exchange.

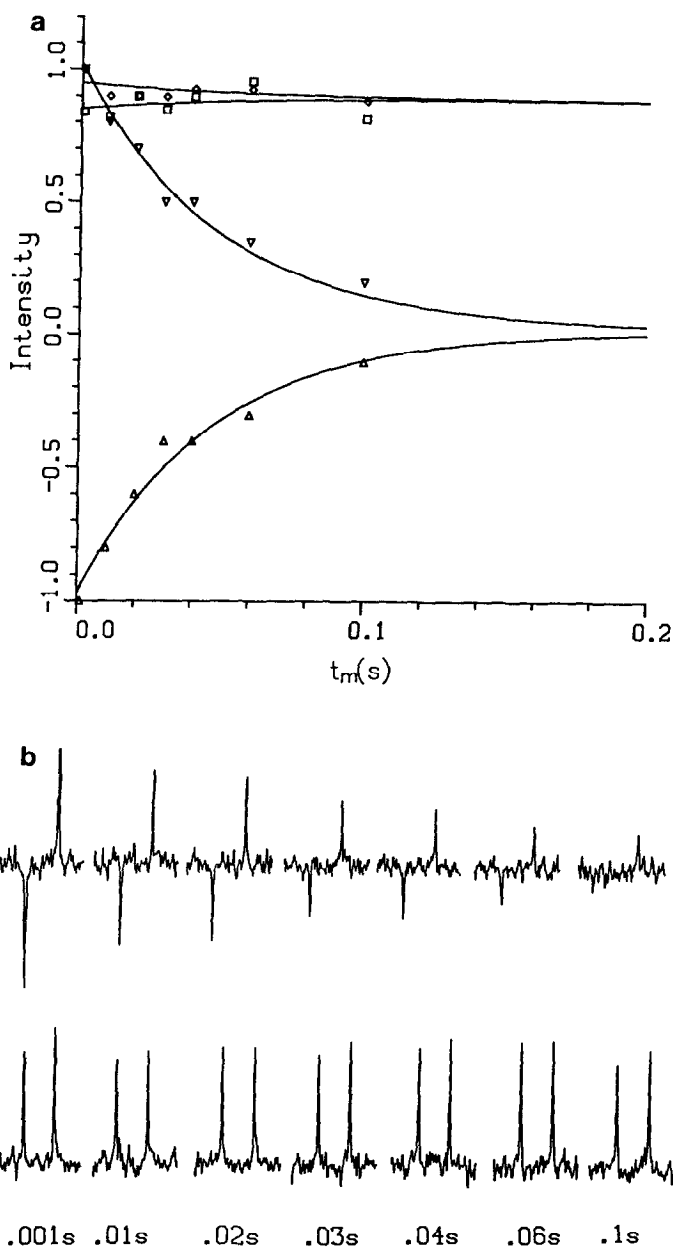


FIG. 9. Laboratory-frame ^{15}N CPMAS polarization-transfer experiment on TTP at 6.082 MHz and -54°C using pulse sequence A. CP time 25 ms, conditions otherwise as in Fig. 6. (b) bottom: experiment I with $t_1 = 0$; (b) top: experiment II with $t_1 = 761 \mu\text{s}$; (a): nonlinear least-squares data fit using Eq. [3]. The polarization transfer arises mainly from chemical exchange.

we have measured a rate constant of 4 s^{-1} at -69°C , where $T_{1\rho}^{-1} \approx 7 \text{ s}^{-1}$ (see Table 1). In fact, as long as heating prevents the use of longer mixing times, sequences B and C are more or less equivalent for obtaining chemical-exchange rates down to t_m^{-1} , where t_m is the mixing time. A direct polarization transfer between the S and the X spins under spin-locking conditions is possible because of the identical nutation frequencies. However, this could not be detected in our experiments presumably because ^{15}N - ^{15}N dipolar coupling is suppressed by magic-angle spinning. The situation might, however, be different in spin systems with more strongly coupled spins. Nevertheless, it is always a good idea to perform sequences B or C whenever there is a possibility that the results obtained by pulse sequence A might be influenced by spin diffusion. Since spin diffusion is suppressed by sequences B and C, but not A, the effect of spin diffusion on the observed polarization-transfer rates can be neglected if one finds similar values of polarization transfer from all three sequences because only chemical-exchange rates are independent of the type of experiment used. Of course, for asymmetric exchange systems, where the polarization transfer is nonexponential, it is sufficient to perform experiments I and II using sequence B or C with only one value of t_m in order to verify the presence of spin diffusion. Rate constants of spin diffusion and of chemical exchange are then obtained from the nonexponential decay by varying t_m in sequence A. Note that in addition to the combination of pulse sequences A to C proposed here, other sequences or experiments may be imagined for the separation of spin diffusion and chemical exchange which all rely on the effect that spin diffusion can be manipulated in contrast to chemical exchange.

We find a very good agreement of the chemical-exchange rates obtained by CPMAS polarization transfer in the rotating frame, spin-diffusion-corrected polarization transfer in the laboratory frame, and the values extrapolated from the complete lineshape analysis performed at higher temperatures. It is clear from Table 1 that we could never have been obtained by lineshape analysis rate constants of the order of 1 to 10 s^{-1} , which correspond to exchange broadenings of only 0.3 to 3 Hz , when the residual linewidths in the CPMAS spectra are in the 50 Hz range. It is interesting to note that the rate constants for tautomerism found here for TTP are very close to those obtained previously (19) for *meso*-tetraphenylporphyrin (TPP) in solution. Thus, the reaction mechanism must be very similar in both phases.

In summary, we have described a strategy for separating the effects of spin diffusion from chemical exchange in solids and have experimentally confirmed the validity of this approach in the molecule TTP in which both effects are present. Although spin diffusion occurred here in well-defined spin clusters because of the high isotopic enrichment which leads to simple kinetics (Eq. [3]), the general strategy will also be valid in cases of low isotopic enrichment where the spin-diffusion dynamics might be more complicated.

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