Z. Phys. Chem. **220** (2006) 641–653 / **DOI** 10.1524/zpch.2006.220.5.641

Determination of Reaction Rate Constants and T_2 Relaxation Times Using Integrated NMR Power Spectra

By D. Lennartz and H. Strehlow*

Max-Planck-Institut für Biophysikalische Chemie, Am Fassberg 11, D-37077 Göttingen, Germany

(Received October 14, 2005; accepted in revised form February 10, 2006)

NMR Power Spectra / Reaction Kinetics / T_2 Relaxation

An alternative method of evaluating chemical rate constants from NMR measurements is proposed. The integral over the NMR power spectrum depends on the life times of reacting species in contrast to the integral over the conventional phase sensitive NMR spectrum. Using this effect the range of measurable rates can be increased by about two orders of magnitude as compared to those obtained with the line shape method.

From integrated power spectra also the ratio of T_2 to a precisely known reference T_2^{ref} can be determined. Inhomogeneous magnets do not deteriorate T_2, thus obtained.

1. Introduction

The influence of chemical exchange on the line shape of spectra is not restricted to NMR and EPR spectroscopy. It has also been used to determine chemical rates of very fast reactions from line broadening with Raman- or infrared spectra. The evaluation of these spectra was performed in analogy to the equations developed for NMR spectroscopy. The increase of the line width in vibration spectroscopy is thus correctly obtained. However, a difference between NMR (or EPR) and vibration spectroscopy remains: While in magnetic spectroscopies the integrals over the resonance lines depend neither on the relaxation times T_2 nor on fast chemical exchange, the corresponding integrals in vibrational spectroscopies decrease with fast chemical exchange [1]. The physical reason is that in NMR spectroscopy the signal is proportional to the real component of the complex magnetization G, whereas in vibration spectroscopy the signal is proportional to EE^*, the norm of the complex electric field E. The

---

* Corresponding author

power spectrum in NMR spectroscopy is proportional to GG^*, therefore the integral over the NMR power spectrum depends on fast chemical exchange in analogy to vibrational spectra.

2. Theory

Powerful methods for the evaluation of chemical rate constants using NMR techniques have been developed and optimised even for complicated chemical systems [2]. The present method will be of particular advantage with weakly kinetically broadened NMR spectra when established techniques are most sensitive towards experimental error.

For the most simple reaction of the type

$$\mathrm{A} \rightleftharpoons \mathrm{B} \tag{1}$$

the complex magnetization is proportional to G [3] with:

$$G = -\mathrm{i}\frac{\tau_\mathrm{A} + \tau_\mathrm{B} + \tau_\mathrm{A}\tau_\mathrm{B}(\alpha_\mathrm{A} p_\mathrm{B} + \alpha_\mathrm{B} p_\mathrm{A})}{(1+\alpha_\mathrm{A}\tau_\mathrm{A})(1+\alpha_\mathrm{B}\tau_\mathrm{B}) - 1} \tag{2}$$

where

$$\alpha_\mathrm{A} = 1/T_{2\mathrm{A}} - 2\pi\mathrm{i}(\nu_\mathrm{A} - \nu) \quad \text{and} \quad \alpha_\mathrm{B} = 1/T_{2\mathrm{B}} - 2\pi\mathrm{i}(\nu_\mathrm{B} - \nu)\,. \tag{3}$$

p_A and p_B are the proton fractions, τ_A and τ_B the life times, and $T_{2\mathrm{A}}$ and $T_{2\mathrm{B}}$ the relaxation times of A and B. ν is the frequency and ν_k the resonance frequency of species k (k = A or B). From Eq. (2) the normal phase sensitive NMR spectrum (index n) $S_\mathrm{n}(\nu)$ of system (1) is given by:

$$S_\mathrm{n}(\nu) = K_\mathrm{n} c G_\mathrm{real}\,. \tag{4}$$

K_n is a constant independent of the kinetics and $c = c_\mathrm{A} + c_\mathrm{B}$ is the total concentration. The corresponding power spectrum (index p) $S_\mathrm{p}(\nu)$ for reaction (1) with G^*, the conjugate complex of G, is:

$$S_\mathrm{p}(\nu) = K_\mathrm{p} c G G^*\,. \tag{5}$$

I_n the measured integral of $S_\mathrm{n}(\nu)$ over ν is

$$I_\mathrm{n} \equiv \int_{-\infty}^{\infty} S_\mathrm{n}(\nu)\mathrm{d}\nu = \pi K_\mathrm{n} c\,. \tag{6}$$

I_n is independent of reaction times τ_k, relaxation times T_{2k} and the chemical shift. However, the corresponding integral I_p over $S_\mathrm{p}(\nu)$ does depend on these parameters:

$$I_\mathrm{p} \equiv \int_{-\infty}^{\infty} S_\mathrm{p}(\nu)\mathrm{d}\nu = \pi K_\mathrm{p} c \cdot f[\tau, T_{2k}, (\nu_\mathrm{A} - \nu_\mathrm{B})] \,. \tag{7}$$

The evaluation of rate constants using the integral method is superior to the line width technique for rather fast or rather slow reactions where changes in line width due to chemical reactions are comparable to or even smaller than changes of line widths, which are due to inhomogeneous magnets. An experimental example will be discussed in Sect. 4.2.

For kinetically decoupled slow exchange ($\tau \to \infty$) $I_{\mathrm{p}k}$ is given by:

$$I_{\mathrm{p}k}^{\tau\to\infty} = \pi K_\mathrm{p} c p_k T_{2k} \,. \tag{8}$$

The integration is extended either over the resonance of A ($k = \mathrm{A}$) or over B ($k = \mathrm{B}$). For extreme fast exchange ($\tau \to 0$) I_p is given by:

$$I_\mathrm{p}^{\tau\to 0} = \pi K_\mathrm{p} c T_{2\mathrm{AB}} \tag{9}$$

where

$$T_{2\mathrm{AB}} = \frac{T_{2\mathrm{A}} T_{2\mathrm{B}}}{p_\mathrm{A} T_{2\mathrm{B}} + p_\mathrm{B} T_{2\mathrm{A}}} \,. \tag{10}$$

To evaluate the kinetics of reaction (1) the integral I_p and $I_{\mathrm{p}k}^{\tau\to\infty}$ or, for fast exchange, $I_\mathrm{p}^{\tau\to 0}$ are measured. This is achieved by adding to the probe a reference substance with a single NMR resonance line not subject to chemical exchange. (Also a non-exchanging line of the molecule under investigation or a capillary filled with the reference substance inserted into the sample as an external reference may serve this purpose). Then one obtains for slow exchange (with index $k = \mathrm{A}$ or B):

$$I_{\mathrm{p}k}^{\tau\to\infty} = \left(\frac{I_\mathrm{n}^k}{I_\mathrm{n}^\mathrm{ref}}\right) \frac{T_{2k} I_\mathrm{p}^\mathrm{ref}}{T_2^\mathrm{ref}} \tag{11}$$

and for fast exchange:

$$I_\mathrm{p}^{\tau\to 0} = \left(\frac{I_\mathrm{n}}{I_\mathrm{n}^\mathrm{ref}}\right) \frac{T_{2\mathrm{AB}} I_\mathrm{p}^\mathrm{ref}}{T_2^\mathrm{ref}} \,. \tag{12}$$

The terms in brackets take care of different concentrations of the exchanging protons and of not exchanging protons of the reference. The relaxation times T_2 and the proton fractions p_k are available from independent measurements.

Let the kinetic damping factor F be defined as the ratio of the measured kinetically decreased integral I_p of the power spectrum and that obtained for the kinetically decoupled integrals (8) or (9). F is then for slow reactions:

$$F_k \equiv \frac{I_\mathrm{p}}{I_{\mathrm{p}k}^{\tau\to\infty}} = \left(\frac{I_\mathrm{p}}{I_\mathrm{p}^\mathrm{ref}}\right)\left(\frac{I_\mathrm{n}^\mathrm{ref}}{I_\mathrm{n}}\right)\frac{T_2^\mathrm{ref}}{T_{2k}} \,. \tag{13}$$

For fast reactions F is given by:

$$F \equiv \frac{I_\mathrm{p}}{I_\mathrm{p}^{\tau\to 0}} = \left(\frac{I_\mathrm{p}}{I_\mathrm{p}^\mathrm{ref}}\right)\left(\frac{I_\mathrm{n}^\mathrm{ref}}{I_\mathrm{n}}\right)\frac{T_2^\mathrm{ref}}{T_\mathrm{2AB}} \,. \tag{14}$$

In Table 1 calculated data for F as a function of τ and the corresponding increase of the line widths due to chemical exchange $\Delta\nu_{1/2}^\mathrm{exch}$ are listed. $\Delta\nu_{1/2}^0$ is the line width due to T_2 relaxation and $\Delta\nu_{1/2}^\mathrm{exch}$ is the increase of $\Delta\nu_{1/2}$ due to chemical exchange.

Table 1. Calculated values of line width and damping factor F as function of life time τ. $T_\mathrm{2A} = T_\mathrm{2B} = 1\,\mathrm{s}$, $\tau_\mathrm{A} = \tau_\mathrm{B} = \tau$, $\Delta\nu_{1/2}^0 = 0.318\,\mathrm{Hz}$.

slow exchange			fast exch. $\lvert\nu_\mathrm{A}-\nu_\mathrm{B}\rvert = 100\,\mathrm{Hz}$			$\lvert\nu_\mathrm{A}-\nu_\mathrm{B}\rvert = 1000\,\mathrm{Hz}$	
τ	F_slow	$\Delta\nu_{1/2}^\mathrm{exch}$	τ	F_fast	$\Delta\nu_{1/2}^\mathrm{exch}$	F_fast	$\Delta\nu_{1/2}^\mathrm{exch}$
s		Hz	s		Hz		Hz
10^4	1.000	0.000	10^{-3}	0.020	15.7	*	*
100	0.990	0.003	3×10^{-4}	0.063	4.71	*	*
30	0.967	0.011	10^{-4}	0.169	1.57	*	*
10	0.909	0.032	3×10^{-5}	0.403	0.471	0.007	47
3	0.750	0.106	10^{-5}	0.670	0.157	0.020	15.7
1	0.500	0.318	3×10^{-6}	0.871	0.047	0.065	4.71
0.3	0.230	1.061	10^{-6}	0.953	0.016	0.169	1.57
0.1	0.091	3.183	3×10^{-7}	0.985	0.005	0.403	0.471
0.03	*	*	10^{-8}	0.999	0.0002	0.953	0.016

* Intermediate exchange rates

2.1 The line shape method

For slow reactions two Lorentzian curves separated by the chemical shift are observed whose line widths $\Delta\nu_{1/2}$ are given by ($k = \mathrm{A}$ or B) [3]:

$$\Delta\nu_{1/2} = \frac{1}{\pi T_{2k}} + \Delta\nu_{1/2}^\mathrm{inh} + \frac{1}{\pi\tau_k} \,. \tag{15}$$

$\Delta\nu_{1/2}^{\text{inh}}$ is the increase of the line width due to inhomogeneous magnets [see appendix A, Eq. (A3)]. It may be reduced considerably by deconvolution using an internal reference signal [4]. With less than ±1% error equation (15) is valid if

$$\tau|\nu_A - \nu_B| \geq 5\,. \tag{15a}$$

With short life times only one Lorentzian line is observed and the half line width $\Delta\nu_{1/2}$ is:

$$\Delta\nu_{1/2} = \frac{1}{\pi T_{2AB}} + \Delta\nu_{1/2}^{\text{inh}} + \Delta_{1/2}^{\text{exch}} \tag{16}$$

with

$$\Delta_{1/2}^{\text{exch}} = 4\pi p_A^2 p_B^2 (\nu_A - \nu_B)^2 (\tau_A + \tau_B)\,. \tag{16a}$$

Equation (16a) may be used with less than 1% error if

$$p_A p_B |\nu_A - \nu_B| (\tau_A + \tau_B) < 0.03\,. \tag{16b}$$

Equations (15)–(16b) are valid for the normal and for the power NMR spectrum.

2.2 The integral method

The half line width of power spectra with chemical exchange is calculated to be (see Appendix A):

$$\Delta\nu_{1/2}^{\text{exch}} = \frac{1-F}{\pi T_2 F}\,. \tag{17}$$

Equation (17) is valid for fast and for slow exchange. Restrictions (15a) and (16b) apply also to Eq. (17).

For slow reactions τ_k is conveniently evaluated by (see also [5]):

$$\tau_k = \frac{T_{2k} F}{1-F}\,. \tag{18}$$

For the evaluation of fast reactions τ_A is obtained by:

$$\tau_A = \frac{1-F}{4\pi^2 p_A p_B^2 (\nu_A - \nu_B)^2 T_{2AB} F}\,. \tag{19}$$

The correct use of Eq. (19) presupposes the applicability of Eqs. (16)–(16b).

3. The determination of T_2 from integrated spectra

An additional application of integrated NMR spectra is the measurement of the true relaxation time T_2 using inhomogeneous magnets in systems without chemical exchange.

If a substance with a single line spectrum and a precisely known T_2 is available it may be added to the probe and serve as a reference.

From Eqs. (11) and (12) the true relaxation time T_2 is obtained:

$$T_2 = \left(\frac{I_\mathrm{n}^\mathrm{ref}}{I_\mathrm{n}}\right) \frac{I_\mathrm{p}}{I_\mathrm{p}^\mathrm{ref}} T_2^\mathrm{ref} . \tag{20}$$

The evaluation of T_2 with the integral method [Eq. (20)] may be advantageous compared with the competing spin echo methods [6], (especially with low concentration samples and with multiline spectra).

4. Experimental

All measurements were performed using a 600 MHz Bruker NMR spectrometer. The solutions were free of oxygen.

Two examples using the proposed integration method will be presented. The first one is the exchange of water molecules with the gem OH groups in chloral hydrate. This reaction displays a strong kinetic damping coefficient: ($F = 0.0141$).

As a second example the interaction of acetate ions in D_2O as solvent with the two Lewis acids D_3O^+ and CH_3COOD was investigated at three temperatures. This system with a kinetic damping coefficient F near unity ($F \approx 0.95$) demonstrates the advantage of the integral method as compared with the line shape technique.

4.1 The hydration kinetics of chloral hydrate

$$\mathrm{Cl_3CCH(O\mathbf{H})_2 + H_2O \rightleftharpoons Cl_3CCH(OH)_2 + \mathbf{H}_2O} \tag{21}$$

The measurements were performed with two solutions, one using a 5 mol%, the other a 10 mol% solution of chloral hydrate in H_2O containing (5 or 10 mol%) D_2O for lock in, both at 25 °C and pH = 3.0. The aldehyde proton of chloral hydrate served as an intramolecular reference. Figure 1 displays a spectrum in a 10 mol% chloral hydrate solution.

The results are listed in Table 2.

Earlier measurements in a 60 MHz spectrometer [7] with 5 mol% $Cl_3CCH(OH)_2$ using the Luz Meiboom method [8] lead to $\tau(\mathrm{Cl_3CCH(OH)_2}) = 140\ \mu\mathrm{s}$. With 60 MHz, reaction (21) runs with fast exchange rate and Eq. (16) is valid.

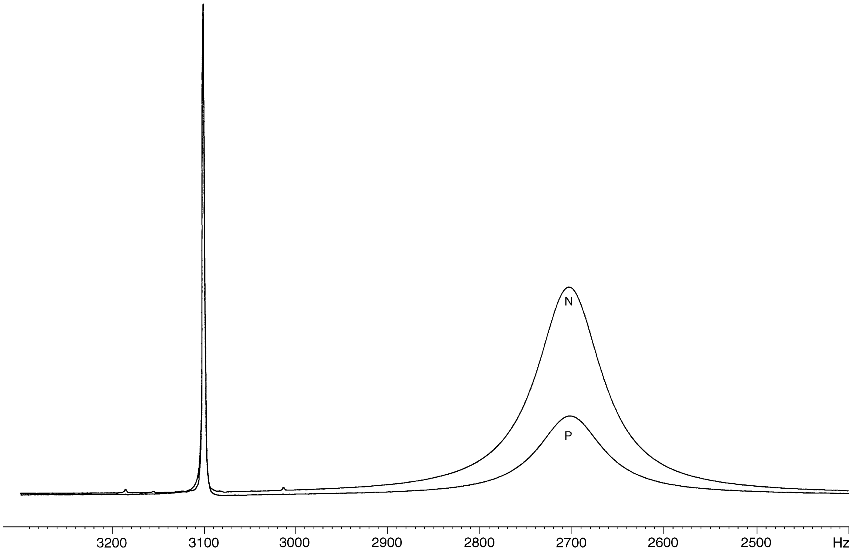

Fig. 1. The normal and the NMR power spectrum of 10 mol% chloral hydrate in water. Temp. 25 °C, pH = 3.0, $T_2(H_2O) = 3.8$ s, $T_2 = 1.44$ s for the aldehyde and the gem-diol protons of chloralhydrate, $F = 0.119$. $N = S_n$ (normal NMR spectrum), $P = S_p$ (power NMR spectrum). The two spectra have been calibrated such that $S_p^{ref} = S_n^{ref}$. Then: $S_p = T_{2AB} F S_n$.

Table 2. Proton exchange between chloral hydrate and water. pH = 3.0, Temp. = 25 °C, $T_2^{ref} = 1.44$ s, $T_2(H_2O) = 3.8$ s, $T_2(Cl_3CCH(OH)_2) = 1.44$ s, $\tau = \tau(Cl_3CCH(OH)_2)$. Equation (16): τ from line width. Equation (19): τ and $\Delta\nu_{1/2}^{exch}$ from integrals.

chem. shift Hz*	p_A	I_n/I_n^{ref}	I_p/I_p^{ref}	F	$\Delta\nu_{1/2}^{exch}$(exp) Hz**	τ µs Eq. (16)	τ µs Eq. (19)	$\Delta\nu_{1/2}^{exch}$ Hz Eq. (19)
1950	0.05	36.9	1.27	0.0142	36.0	17	2.94	6.34
1730	0.10	16.2	4.38	0.119	84.4	28	0.24	0.73

* Taken from [7]. ** Corrected for inhomogeneous magnet: $\Delta\nu_{1/2}^{inh} = 1.0$ Hz.

The reason for the large difference of τ obtained by either the integral or by the line width method is the larger chemical shift in a 600 MHz spectrometer. Then reaction (21) is too slow and Eqs. (16) and (19) can not be applied.

Although the present measurements do not provide new kinetic results they show that the amplitude of the power spectrum is strongly reduced by the proton exchange reaction in reaction (21).

4.2 The kinetics of reactions (22) in D_2O

$$D_3O^+ + CH_3COO^- \rightleftharpoons CH_3COOD + D_2O \tag{22a}$$

and

$$CH_3COO\mathbf{D} + CH_3COO^- \rightleftharpoons CH_3COO^- + CH_3COO\mathbf{D} \tag{22b}$$

Only the integral method is suitable for the kinetic investigation of reactions (22), since the increase of the line width due to chemical exchange is smaller than 0.02 Hz whereas the kinetic damping factor F is near 0.95. Dioxane was chosen as reference.

4.2.1 The proton relaxation times T_2 of CH_3COOD and CH_3COO^-

Reactions (22) are too fast for kinetic NMR measurements at pH < 2 using either the line width or the integral method since the proton fraction of CH_3COO^- is nearly zero. The corresponding is true at high pH with negligible concentration of CH_3COOD. The concentrations of CH_3COO^- and of CH_3COOD in both probes were 20 mM. The concentration of dioxane protons was similar to those of CH_3COO^- or of CH_3COOD.

The measurements with the spin echo method were performed according to Hahn [6] using ten echoes. T_2^{ref} was determined in a third probe with 20 mM dioxane in D_2O. The results for acetate and those for acetic acid are listed in Tables 3 and 4.

Table 3. Relaxation time $T_2(CH_3COO^-)$. 0.02 M CH_3COOK in D_2O. Reference: dioxane.

temp. °C	T_2^{ref} s spin echo	I_n/I_n^{ref}	I_p/I_p^{ref}	$T_2(Ac^-)$ s spin echo	$T_2(Ac^-)$ s integral
25	3.0_8	1.19_2	1.46_4	3.9_4	3.7_9
20	2.7_9	1.20_5	1.47_6	3.6_7	3.4_2
10	2.5_7	1.19_8	1.48_5	3.8_2	3.1_2
Average		$1.20_0 \pm 0.6\%$			

Table 4. Relaxation time $T_2(CH_3COOD)$. 0.02 M CH_3COOD in D_2O. Reference: dioxane.

temp. °C	T_2^{ref} s spin echo	I_n/I_n^{ref}	I_p/I_p^{ref}	$T_2(AcD)$ s spin echo	$T_2(AcD)$ s integral
25	3.0_8	1.24_5	1.48_4	2.9_5	3.6_7
20	2.7_9	1.22_6	1.50_1	3.1_5	3.4_0
10	2.5_7	1.22_4	1.50_2	3.2_9	3.1_1
Average		$1.23_2 \pm 0.7\%$			

The precision of the spin echo data for T_2 is worse than that obtained with the integral method. T_2 increases monotonously with temperature. This is observed for T_2(dioxane) but not for $T_2(CH_3COO^-)$ and $T_2(CH_3COOD)$. For CH_3COO^- in H_2O at 20 °C $T_2 = 3.4$ s has been reported [9]. Therefore the T_2 data obtained from Eq. (20) were used in calculating the kinetics of reactions (22). The ratios I_n/I_n^{ref} depend only on the concentration ratio and should be independent of temperature for a given solution. Therefore the average values of I_n/I_n^{ref} were used for calculating T_2.

4.2.2 Deuteron transfer in an acetate buffer in D_2O

In a D_2O solution containing CH_3COOD and CH_3COOK in equal concentrations (20 mM) the normal and the power spectrum of the methyl groups were measured. The chemical shift between the methyl protons of acetate and acetic acid was determined using dioxane as internal reference.

Table 5. Determination of F and τ for reaction (22) with acetate and acetic acid (each 20 mM) in D_2O. Reference: dioxane. T_2: Tables 3 and 4.

temp. °C	T_2^{ref} s	I_n/I_n^{ref}	I_p/I_p^{ref}	chem. shift	F	τ µs
25	3.0_8	1.28_6	1.48_7	108.2	0.95_5	0.2_2
20	2.7_9	$1,27_5$	1.48_4	106.7	0.95_0	0.2_7
10	2.5_7	1.27_1	1.49_9	103.8	0.95_1	0.3_1
Average		$1.27_7 \pm 0.5\%$				

The damping factor F is about 0.95; that is we are near the limit of the proposed integral method for the determination of rate constants. If $F = 0.95$ is in error by 1% then the factor $(1-F)/F$ in Eq. (17) and with it the life time τ is wrong by 20%. However, the increase of line width $\Delta\nu_{1/2}^{exch}$ for reactions (22) is less than 0.02 Hz and the line shape method is certainly not applicable.

4.2.3 Discussion

Reaction (22a) is a diffusion controlled reaction. Its rate constant has been determined by Eigen and Schön [10] to be $k_r = 4.5 \times 10^{10}\ M^{-1}\ s^{-1}$ in H_2O. In the acetate buffer solution with $[H^+] = 1.8 \times 10^{-5}$ M the lifetime τ of the acetate ion in reaction (22a) is then 1.2 µs in H_2O (and longer in D_2O due to the kinetic isotope effect). Therefore reaction (22a) contributes only to a minor extent to the lifetime of acetate and reaction (22b) is mainly responsible for the observed lifetime τ of about 0.25 µs.

$$\begin{array}{lcl}
\overset{(1)}{\mathbf{CH_3COO^-} + \mathrm{CH_3COOD}} & \rightleftharpoons & \overset{(2)}{\mathbf{CH_3COO^-} \cdots \mathrm{CH_3COOD}} \\
 & & \qquad \upharpoonleft\!\downharpoonright k_{23} \\
\underset{(4)}{\mathbf{CH_3COOD} + \mathrm{CH_3COO^-}} & \rightleftharpoons & \underset{(3)}{\mathbf{CH_3COOD} \cdots \mathrm{CH_3COO^-}}
\end{array} \tag{22c}$$

In a first step acetate and acetic acid molecules approach each other with a rate constant k_{12} to form an association complex. This complex may either dissociate with a rate constant k_{21} or the acetate ion (bold print) is deuterated by acetic acid (normal print) with a rate constant k_{23}. It is the lifetime $\tau_{23} = 1/k_{23}$, which is determined in NMR experiments.

The diffusion controlled rate constants k_{12} and k_{21} are estimated approximately using Smoluchowskis equations [11]. With reasonable parameters one obtains

$$k_{12} = 2.3 \times 10^9\,\mathrm{M^{-1}\,s^{-1}} \quad \text{and} \quad k_{21} = 6.9 \times 10^9\,\mathrm{s^{-1}}\,.$$

Therefore with $k_{23} = 1/\tau_{23} = 4.5 \times 10^6\,\mathrm{s^{-1}}$ at 25 °C (Table 5) only the small ratio q

$$q = \frac{k_{23}}{k_{23} + k_{21}} = 6.5 \times 10^{-4} \tag{23}$$

of the association complexes experience a deuteron exchange during the lifetime of the complex. The large majority of the association complexes dissociates without change of the NMR state of the methyl protons.

5. Conclusion

The determination of kinetic rate constants using the proposed integral technique is much more precise than the NMR line shape method with weakly broadened lines. The time range of applicability with the integral method compared with the line shape technique is increased by about one order of magnitude with slow and even more, depending on the chemical shift, with fast exchange.

The determination of T_2 relaxation times using the integral technique will be useful especially with multiline spectra and with low concentrated samples.

Acknowledgement

Useful discussions with Prof. C. Griesinger are gratefully acknowledged.

Appendix A

T_2 in Eq. (17)

For the correct use of Eqs. (17), (18), and (19) in the evaluation of experiments it must be established that the integral I_p of NMR power spectra in systems without chemical exchange is independent of the inhomogeneity of the magnetic field. Only then is T_2 in Eqs. (17)–(19) the true relaxation time T_2 and not the effective relaxation time $T_2^\mathrm{eff} = T_2/(1+\pi T_2 \Delta\nu_{1/2}^\mathrm{inh})$, [see Eqs. (15) and (16)].

In a sufficiently small volume $\delta V_i = \delta x \delta y \delta z$ of the probe the magnetic field may be assumed to be constant with a field strength $B_i(x, y, z)$ and an absorption frequency $\nu_i(x, y, z) = \gamma B_i(x, y, z)/2\pi$. (In a reasonably homogeneous magnet the field gradient is very small and diffusion as a second order effect may safely be neglected.)

With V, the total volume of the probe, the contribution $\delta S_{\mathrm{n}i}$ to the total signal S_n is then in a probe without chemical exchange:

$$\delta S_{\mathrm{n}i} = K_\mathrm{n} c \frac{T_2 \delta V_i}{V\left\{1+4\pi^2 T_2^2[\nu_i(x, y, z)-\nu]^2\right\}} \,. \tag{A1}$$

This is a Lorentzian curve with a half line width $\Delta\nu_{1/2} = 1/\pi T_2$, where T_2 is the true relaxation time not deteriorated by the inhomogeneity of the magnet in volume V. The integral of $\delta S_{\mathrm{n}i}$ over ν is:

$$\delta I_{\mathrm{n}i} = \int \delta S_{\mathrm{n}i}(\nu)\mathrm{d}\nu = K_\mathrm{n} c \pi \delta V_i / V \,. \tag{A2}$$

The sum over all δV_i of the total volume V of the probe is the observed signal:

$$S_\mathrm{n}(\nu) = K_\mathrm{n} c \sum_i \frac{T_2}{1+4\pi^2 T_2^2[\nu_i(x, y, z)-\nu]^2} \,. \tag{A3}$$

$\Delta\nu_{1/2}$, the half line width of $S_\mathrm{n}(\nu)$ is larger than $1/\pi T_2$ due to the local dependence of the frequency $\nu_i(x, y, z)$. However, I_n, the sum of all $\delta I_{\mathrm{n}i}$ [Eq. (18)], is independent of the inhomogeneity of the magnet:

$$I_\mathrm{n} = \sum_i \delta I_{\mathrm{n}i} = K_\mathrm{n} c \pi \,. \tag{A4}$$

Without chemical exchange the power spectrum $\delta S_{\mathrm{p}i}$ in δV_i is:

$$\delta S_{\mathrm{p}i} = K_\mathrm{p} c \frac{T_2^2 \delta V_i}{V\left\{1+4\pi^2 T_2^2[\nu_i(x, y, z)-\nu]^2\right\}} \tag{A5}$$

and

$$S_\mathrm{p}(\nu) = K_\mathrm{p} c \sum_i \frac{T_2^2}{1+4\pi^2 T_2^2[\nu_i(x, y, z)-\nu]^2} \,. \tag{A6}$$

The sum over the integrals $\delta I_{\mathrm{p}i}$ is

$$I_{\mathrm{p}} = \sum_i \delta I_{\mathrm{p}i} = \sum_i \int \delta S_{\mathrm{p}i} = K_{\mathrm{p}} c \pi T_2 \,. \tag{A7}$$

Therefore not only I_{n} but also I_{p} are independent of the inhomogeneity of the magnet. While Eq. (A4) is valid also for systems with chemical exchange, I_{p} is then given by

$$I_{\mathrm{p}} = K_{\mathrm{p}} c \pi T_2 F \,. \tag{A8}$$

T_2 in Eqs. (A7) and (A8) is the true relaxation time T_2.

The errors produced by finite integration ranges cancel in the quotients of Eqs. (13) and (14).

Derivation of Eq. (17)

The integral over the normal spectrum with chemical exchange is proportional to the product of the line width and the amplitude $\mathrm{A}^{\mathrm{exch}}$.

$$I_{\mathrm{n}}^{\mathrm{exch}} = k_{\mathrm{n}} \left(\frac{1}{\pi T_2} + \Delta\nu_{1/2}^{\mathrm{exch}} \right) A^{\mathrm{exch}} \tag{A9}$$

Without chemical exchange ($\Delta\nu_{1/2}^{\mathrm{exch}} = 0$ and $F = 1$) we have:

$$I_{\mathrm{n}} = k_{\mathrm{n}} \frac{A}{\pi T_2} \,. \tag{A10}$$

The ratio of the integrals (A9) and (A10)

$$I_{\mathrm{n}}^{\mathrm{exch}} / I_{\mathrm{n}} = 1 \,. \tag{A11}$$

The half line widths $\Delta\nu_{1/2}^{\mathrm{exch}}$ of normal and power spectra are equal (even in the intermediate state near to either fast or slow exchange). Then the corresponding integrals over the power spectrum are [see Eq. (A8)].

$$I_{\mathrm{p}}^{\mathrm{exch}} = k_{\mathrm{p}} \left(\frac{1}{\pi T_2} + \Delta\nu_{1/2}^{\mathrm{exch}} \right) A^{\mathrm{exch}} T_2 F \tag{A12}$$

and

$$I_{\mathrm{p}} = k_{\mathrm{p}} \frac{A}{\pi T_2} T_2 \tag{A13}$$

The ratio of (A12) and (A13) is:

$$I_{\mathrm{p}}^{\mathrm{exch}} / I_{\mathrm{p}} = \left(\frac{1}{\pi T_2} + \Delta\nu_{1/2}^{\mathrm{exch}} \right) \frac{A^{\mathrm{exch}} F}{A \pi T_2} \,. \tag{A14}$$

Eliminating A^{exch}/A in Eq. (A14) using (A9)–(A11) leads to:

$$\Delta\nu_{1/2}^{\mathrm{exch}} = \frac{1-F}{\pi T_2 F} \,. \tag{17}$$

Equation (17) is valid only for Lorentzian curves. These, however, are also observed in systems reacting with exchange rates in the near intermediate range.

References

1. H. Strehlow, I. Wagner, and P. Hildebrandt, Ber. Bunsenges. **87** (1983) 516; H. Strehlow, Ber. Bunsenges. **93** (1989) 617.
2. G. Binsch and H. Kessler, Z. Angew. Chem. Int. Ed. **19** (1975) 411; G. Fraenkel, *Investigation of Rates and Mechanisms of Reactions*, C. F. Bernasconi (Ed.). Wiley, New York (1986) Chap. 10; J. Sandström, *Dynamic NMR Spectroscopy*. Academic Press, New York (1982); C. L. Perrin and T. J. Dwyer, Chem. Rev. **90** (1990) 935.
3. H. M. McConnell, J. Chem. Phys. **28** (1958) 430.
4. G. A. Morris, J. Magn. Reson. **80** (1988) 547.
5. H. Strehlow, Ber. Bunsenges. **92** (1988) 467.
6. E. L. Hahn, Phys. Rev. **80** (1950) 580.
7. R. Lachmann, M.-L. Ahrens, and H. Strehlow, Adv. Mol. Relax. Proc. **6** (1974) 29.
8. Z. Luz and S. Meiboom, J. Chem. Phys. **39** (1963) 366.
9. T. Michaelis, Diploma Thesis Göttingen (1989).
10. M. Eigen and J. Schön, Z. Elektrochem. **59** (1955) 483.
11. M. v. Smoluchowski, Phys. Z. **15** (1916) 515, 585.