CHAPTER XI

NMR Studies of Elementary Steps of Multiple Proton and Deuteron Transfers in Liquids, Crystals, and Organic Glasses

H.-H. Limbach

Dynamic high-resolution NMR spectroscopy of liquids and solids constitutes a convenient way to study kinetic hydrogen/deuterium isotope and solid-state effects on multiple proton transfer reactions in different environments. In the case of intramolecular double proton transfer reactions, evidence for stepwise reaction pathways is obtained; in each step only one proton jumps, whereas the other remains bound. By contrast, intermolecular double proton transfer reactions behave in a different way. Here, both protons are in flight in the rate-determining reaction step. The origin of the different behavior of both types of reactions is discussed.

It is also found that intermolecular interactions have an influence on the reaction energy surfaces even in cases where kinetic solvent effects are absent. This influence can be monitored when studying the proton dynamics in a timescale of slow molecular motion. It is well known that this timescale is easily reached by IR spectroscopy in the liquid state; it is, however, also reached by NMR spectroscopy when studying fast proton transfers in ordered crystalline or disordered amorphous solids. Recent progress in this field is reported.

1 Introduction

In the past years there has been a special interest for neutral multiple proton transfer reactions including their kinetic hydrogen/deuterium isotope effects

Intermolecular Forces

[1, 2]. The simplest double proton transfer reaction of this kind is shown in Eq. (1):

$$AH^* + BH \rightleftharpoons A\overset{H^*}{\underset{H}{\cdots}}B \rightleftharpoons A\overset{H^*}{\underset{H}{\cdots}}B \rightleftharpoons AH + BH^*. \qquad (1)$$

These reactions can serve as models for the study of the elementary steps of bond breaking and bond formation in different liquid and solid environments, i.e., of the role of intermolecular interactions on the dynamics of bond breaking and bond formation in condensed matter. Proton exchange reactions according to Eq. (1) are most conveniently studied by dynamic NMR spectroscopy. Using this method, rate constants of multiple inter- and intramolecular double proton transfers have been determined not only in liquid solutions [1–14] but also in the solid state [15–26]. A particular feature of neutral multiple proton transfers is that they can also be induced at cryogenic temperatures by visible light [27, 28]. Recently, also an IR-induced proton transfer has been found [29]. In organic and biochemical systems these processes are related to bifunctional catalysis and biological activity [30, 31]. On the other hand, these reactions are an old topic of theoretical chemistry [32–39] and of the theory of primary kinetic hydrogen/deuterium isotope effects [2–6, 11, 14, 40, 41].

In this paper we present an overview of the problems which are currently studied in our laboratory using liquid and solid-state NMR and IR techniques. Our interest has focused on NH...N proton transfer systems for two reasons: (i) proton transfers between nitrogen atoms are, generally, not as fast as proton transfers between oxygen atoms. They are, therefore, easier followed by NMR spectroscopy; (ii) in contrast to oxygen, nitrogen has a stable isotope ^{15}N with a spin 1/2. Thus, it is possible to obtain information on hydrogen bonding and proton transfer dynamics by studying ^{15}N-labeled compounds in the absence of undesired complications arising from interactions with nuclei having a quadrupole moment.

2 Kinetic HH/HD/DD Isotope Effects Studied by Liquid-State NMR

In order to measure kinetic hydrogen/deuterium isotope effects using conventional kinetic methods, it is necessary to perform "proton inventories" where reaction rates are measured as a function of the deuterium fraction D in the mobile proton sites [30]. In principle, the number of protons m transferred in the rate-limiting step can also be obtained from such isotopic dilution studies. However, in order to extract m from a proton inventory the validity of the "rule of the geometric mean" has, generally, been assumed. This rule states for a double proton transfer that:

$$k^{HD} = (k^{HH}k^{DD})^{1/2} \quad \text{i.e.} \quad k^{HH}/k^{HD} = k^{HD}/k^{DD}. \qquad (2)$$

In order to test Eq. (2) experimentally, NMR proton inventory techniques [2–6] have been designed for the direct determination of k^{HH}, k^{HD}, and k^{DD} of inter- and intramolecular reactions. For example, by a combination of ^1H- and ^2H-NMR measurements it was possible to measure complete sets of kinetic isotope effects for the 1:1 and the 2:1 proton exchange between acetic acid and methanol in tetrahydrofuran (Fig. 1a, b) [3, 4]. Substantial deviations from Eq. (2) were observed for the 1:1 exchange in the sense that replacement of the first H atom by D resulted in a stronger decrease of the rate constants than replacement of the second H atom by D, i.e., $k^{HH}/k^{HD} = 5.1$ and $k^{HD}/k^{DD} = 3$ at 298 K. Even larger deviations, i.e.:

$$k^{HH}/k^{DD} \gg 1 \quad \text{and} \quad k^{HD}/k^{DD} \simeq 1 \text{ to } 2 \tag{3}$$

were found for the tautomerism of meso-tetraphenylporphyrin (TPP) [3] which reacts according to Fig. 2. These deviations from the RGM were originally interpreted in terms of a concerted proton transfer pathway involving tunneling [3, 4, 32].

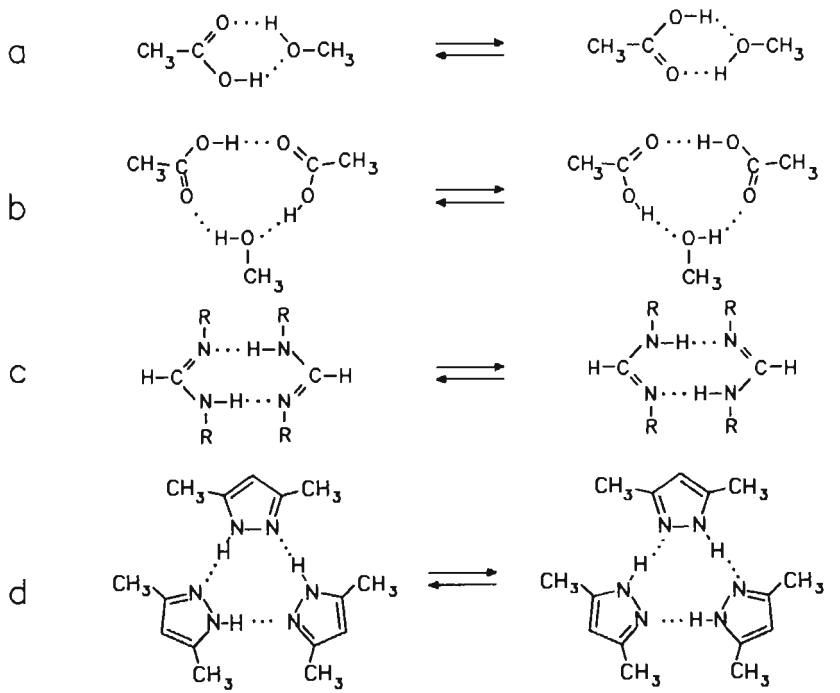

Fig. 1. Intermolecular multiple proton transfer reactions for which kinetic hydrogen/deuterium isotope effects have been studied by dynamic liquid-state NMR spectroscopy. **a** and **b** Double and triple proton transfer between acetic acid and methanol according to Refs. [3] and [4]; **c** double proton transfer in formamidine dimers according to Refs. [5] and [6]; d: triple proton transfer in cyclic trimers of 3,5-dimethylpyrazole according to Refs. [25] and [26]

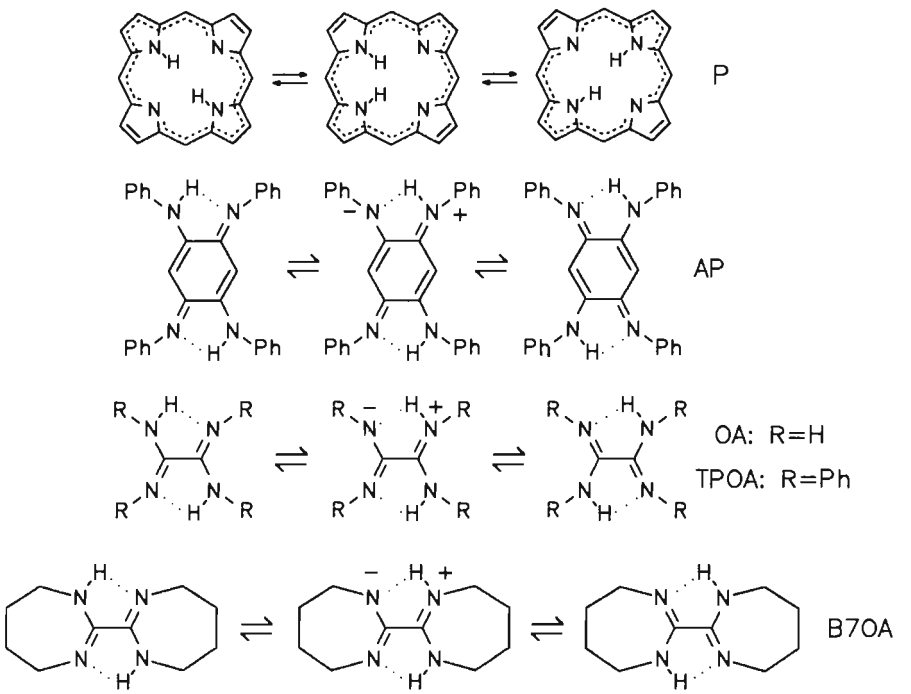

Fig. 2. Intramolecular proton transfer reactions for which kinetic hydrogen/deuterium isotope effects have been studied by dynamic liquid-state NMR spectroscopy. P: porphyrin and derivatives [3]; AP: azophenine [3, 11, 12]; OA: oxalamidine and derivatives [13], B7OA: bicyclic oxalamidine [14]. The dynamics of the tautomerism of P and AP have also be studied by NMR in the solid state (Refs. [15–17] and Ref. [12])

After these initial studies were carried out, it seemed desirable to know whether these deviations are limited to the above systems or whether they are of a general nature. Therefore, the dynamics of different inter- and intramolecular proton and deuteron transfer reactions listed in Figs. 1 and 2 were studied. The results of these studies will be reviewed in the following.

Let us first consider some intramolecular double proton transfer reactions for which full kinetic HH/HD/DD isotope effects have been measured. Actually, let us begin with the example of azophenine (AP), which is subject in liquid solution to a fast intramolecular double proton transfer involving two degenerate tautomers as shown in Fig. 2 [3]. Theoretical calculations [36] gave evidence for a stepwise proton transfer pathway involving a zwitterion as intermediate. The question arose whether this mechanism could be supported experimentally. Therefore, rate constants of this reaction were measured as a function of temperature by applying different methods of dynamic NMR spectroscopy to various isotopically labeled AP species dissolved in different organic solvents [12]. The rate constants did not depend on the dielectric

constant of the solvent, which was varied between 2 (toluene) and 25 (benzonitrile). For $C_2D_2Cl_4$ as solvent, the full kinetic HH/HD/DD isotope effects were obtained at different temperatures. The observed kinetic isotope effects of $k^{HH}/k^{HD} = 4.1$ and $k^{HD}/k^{DD} = 1.4$ at 298 K indicate that Eq. (3) is fulfilled as in the case of tetraphenylporphyrin. A theory of kinetic HH/HD/DD isotope effects for degenerate stepwise double proton transfers was presented and showed that these isotope effects were consistent with the stepwise reaction mechanism. A problem with this interpretation was that during this pathway a highly polar zwitterion should be formed, which in turn should give rise to strong kinetic solvent effects on the reaction, by contrast to the experiment.

Attempts were made to resolve this problem by studying the tautomerism of the related oxalamidine (OA) system (Fig. 2). This process was first monitored in a study of the easily soluble derivative TPOA [13]. Unfortunately, TPOA is also subject in the liquid state to isomerism around the CN double bonds and to intermolecular proton exchange [13]. Therefore, the ^{15}N- and ^{2}H-labeled bicyclic derivative B7OA (Fig. 2) was synthesized for which rate constants including the kinetic HH/HD/DD isotope effects could be measured at 362 K by ^{1}H-NMR lineshape analysis [14]. Experiments were performed using methylcyclohexane-d_{14} (MCY) and acetonitrile-d_3 (AN) as solvents. The kinetic isotope effects were very similar in both solvents. Actually, $k^{HH}_{MCY}/k^{HD}_{MCY} = 2.4$, $k^{HD}_{MCY}/k^{DD}_{MCY} = 1.2$, $k^{HH}_{MCY}/k^{DD}_{MCY} = 3$, $k^{HH}_{AN}/k^{HD}_{AN} = 2.6$, $k^{HD}_{AN}/k^{DD}_{AN} = 1.3$, $k^{HH}_{AN}/k^{DD}_{AN} = 3.5$ at 362 K. Similar values had been obtained for AP at the same temperature [12]. They are again consistent with a stepwise double proton transfer mechanism as shown in Fig. 2. In the case of B7OA this interpretation could, however, be supported by the observation of a substantial kinetic solvent effect of $k^{HH}_{AN}/k^{HH}_{MCY} = 4.5$ at 362 K, indicating a polar transition state as expected. Thus, both the observed kinetic HH/HD/DD isotope and solvent effects point in the same direction. Or, stated in a another way, the observation that Eq. (3) is fulfilled in a degenerate double proton transfer reaction can be taken as a criterion for a stepwise reaction mechanism. This result is important in cases like porphyrins or azophenine where kinetic solvent effects are absent. In these cases the study of the kinetic HH/HD/DD isotope effects represents the only way to establish experimentally a stepwise double proton transfer mechanism.

The absence of kinetic solvent effects on the azophenine tautomerism could be explained in two ways: either the phenyl groups effectively shield the reaction center from the solvent in contrast to B7OA, or the intermediate is an apolar singlet biradical as discussed in Ref. [12].

These results shed also new light on the mechanism of the proton tautomerism in porphyrins, where recent theoretical studies gave evidence for a stepwise proton transfer as shown in Fig. 2 [33, 35, 37]. The previous finding [3] that Eq. (3) is well fulfilled experimentally can now be taken as evidence for the stepwise reaction mechanism. Recent measurements of the low-temperature rate constants of the porphyrin tautomerism as well as of hydroporphyrins [10] corroborates this interpretation and supports the idea of proton tunneling in this reaction [29].

Let us discuss now the intermolecular double proton transfer between diphenylformamidine (DPFA) molecules in tetrahydrofuran (Fig. 1c). DPFA forms in THF an *s-trans* and an *s-cis* conformer which interconvert slowly on the NMR timescale. According to recent liquid-state ^{1}H-NMR results, only the *s-trans* conformer is able to form cyclic dimers in which a double proton transfer takes place according to Fig. 1c [5]. The energy of activation of this reaction is of the order of 17 kJ mol^{-1}. For the related ^{15}N,^{15}N′-di-*p*-fluorophenylformamidine molecule (DFFA) it was possible to measure the full kinetic HH/HD/DD isotope effects at 189.2 K [6]. First, using ^{1}H-NMR spectroscopy, a linear dependence of the inverse proton lifetimes on the deuterium fraction D in the mobile proton site was observed. From this dependence the number of protons transported in the rate-limiting step of the proton exchange was determined to be m = 2, as expected for a double proton transfer in an *s-trans* dimer with a cyclic structure. The full kinetic HH/HD/DD isotope effects on 233:11:1 at 189 K were determined through ^{19}F-NMR experiments on the same samples. This result represents a deviation from the rule of geometric means which is of the same order as in the case of acetic acid/methanol/tetrahydrofuran [4].

It is clear that the kinetic HH/HD/DD isotope effects obtained for the intermolecular double proton transfer between formamidine molecules and in the system acetic acid/methanol are not consistent with a stepwise double proton transfer because Eq. (3) is not fulfilled. In other words, both transferred protons contribute substantially to the observed kinetic isotope effects by contrast to the intramolecular case. This is in agreement with the observation that the overall kinetic HH/DD isotope effects are larger in intermolecular than in intramolecular double proton transfer reactions. How can one then explain the small deviations from the RGM in the case of intermolecular exchange reactions? In the case of the system acetic acid/methanol/THF these deviations could be interpreted in terms of thermally activated tunneling [3, 4]. The deviations arise because tunneling enhances the reaction rates especially of the light hydrogen isotopes. Further temperature-dependent kinetic studies on the formamidine tautomerism are currently in progress in order to confirm this interpretation also for this system.

A qualitative explanation for the different reaction pathways of intra- and intermolecular double proton transfer systems has been given recently [6]. This explanation is based on the observation that intramolecular proton transfer systems such as porphyrin and azophenine lack the usual flexibility of hydrogen-bonded systems, i.e., the usual low-frequency hydrogen-bond stretching vibration [39] which modulates the hydrogen bond distance. Thus, the molecular frame of heavy atoms in these compounds is relatively rigid and a high energy would be required to reduce the hydrogen bond distance in such systems. This feature is expressed in Fig. 3a by an outer square which schematically represents the molecular frame. It is understandable that it costs too much energy to break the bonds of both protons to their neighboring heavy atoms at the same time, and the proton transfer will be asynchronous. Note that

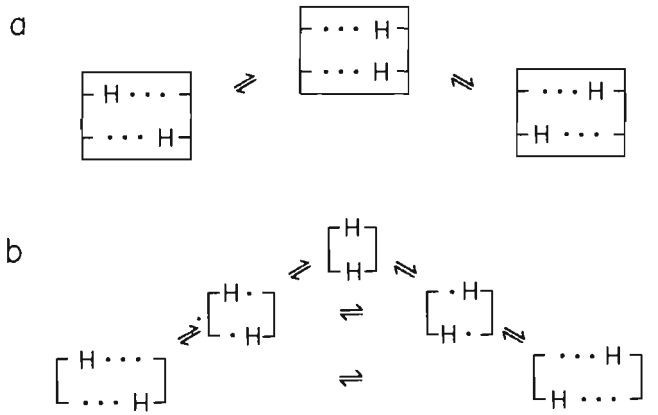

Fig. 3. **a** Stepwise double proton transfer in the case of a fixed molecular frame of heavy atoms; **b** double proton transfer in the case of variable hydrogen bond lengths according to a model proposed in Ref. [4]. Reproduced with permission from Ref. [6]

proton tunneling in this case will always require a minimum energy of activation corresponding to the energy difference between the intermediate and the initial state.

By contrast, the presence of low-frequency hydrogen-bond stretching vibrations in the flexible intermolecular proton transfer systems allows a comparatively easy compression of the hydrogen bond as schematically shown in the model of Fig. 3b. This model has been used for the calculation of the Arrhenius curves of the proton transfer between acetic acid and methanol [3, 4]. In this case the hydrogen bond lengths are variable, i.e., the energy of activation of the proton transfer is pooled into the hydrogen bond stretching vibration which shortens the hydrogen bond length. As a consequence, the barrier for the proton transfer is reduced. At extreme short hydrogen bond lengths the barrier for proton transfer vanishes and, therefore, the difference between a stepwise and a concerted proton transfer mechanism. The imaginary frequency required for a transition state corresponds then to the hydrogen bond stretching rather than to the AH-stretching vibrations. Now, it is well known that the latter are shifted to lower frequencies when the hydrogen bond distance is shortened [42]. Therefore, there will be a considerable loss of zero point energy of both vibrations in the highly compressed transition state. As a consequence, the RGM will be fulfilled at high temperatures. At lower temperatures the transfer may occur by tunneling leading to the above-mentioned deviations from the RGM. Thus, we propose for the intermolecular proton transfer systems a reaction mechanism according to Fig. 3b. Note that one might find intermolecular proton transfer systems with rigid hydrogen bond distances and intramolecular proton transfer systems with flexible hydrogen bonds which could lead to an inverse behavior of kinetic isotope effects.

3 ^{15}N CPMAS NMR Spectroscopy of Proton Transfer Systems in the Crystalline State

One major problem which arises in the theoretical interpretation of kinetic isotope effects of reactions in condensed matter, especially, if tunneling is involved as mentioned above, is the question of how the reaction mechanism is affected by intermolecular interactions in liquid, crystalline, or amorphous glassy environments. In order to obtain information on this problem, one can make use of variable temperature high-resolution solid-state NMR spectroscopy [43]. This method is applicable for spin 1/2 nuclei and exploits line-narrowing techniques such as proton decoupling and magic angle spinning (MAS) in order to remove the effects of dipolar coupling to protons and of the chemical shift anisotropy on the NMR spectra [44]. Cross-polarization (CP) from protons to the nucleus studied enhances the signal-to-noise ratio [44]. Thus, several solid-state hydrogen transfer systems have been studied by natural abundance ^{13}C CPMAS NMR [20, 25, 45, 46]. However, with the exception of hydride transfers in carbonium ions [46], carbon atoms are not directly involved in proton transfers and their NMR lines may not always be sensitive to these processes. Therefore, for NH ... N or NH ... X proton transfer systems ^{15}N CPMAS NMR is a more suitable method. Unfortunately, as stated above, because of the quadrupole moment of the ^{14}N nucleus, it is necessary at present to enrich the

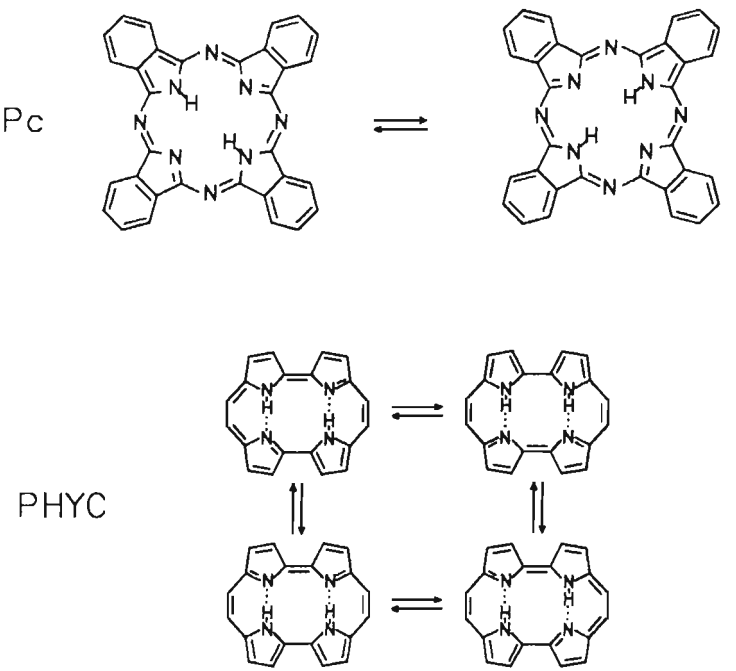

Fig. 4. Solid-state tautomerism of phthalocyanine (Pc) [18–20] and of porphycene (PHYC) [16]

molecules studied with the less abundant spin 1/2 isotope ^{15}N. Using this method, fast proton transfer processes have been monitored in solid porphyrins (Fig. 2) [15–17], phthalocyanine (Fig. 4) [18, 19], porphycene (Fig. 4) [16], azophenine (Fig. 2) [12], tetraazaannulenes (Fig. 5) [21–24] as a function of temperature.

The ^{15}N CPMAS spectra contain a wealth of information about solid-state effects on the proton tautomerism. Let us review only some general results. For this purpose, consider a reaction which is degenerate in the absence of intermolecular interactions. The reaction profile is then symmetric as indicated schematically in Fig. 6a, where possible intermediates have been omitted for simplicity. However, in the ordered crystalline state this symmetry is, generally, removed by intermolecular interactions and an energy difference ΔE between the two minima of the potential curve for the proton motion arises (Fig. 6b). In the first approximation the potential of the proton motion in a particular molecule does not depend on the tautomeric state of the neighboring molecules. Using ^{15}N CPMAS NMR spectroscopy it was possible to measure ΔE for

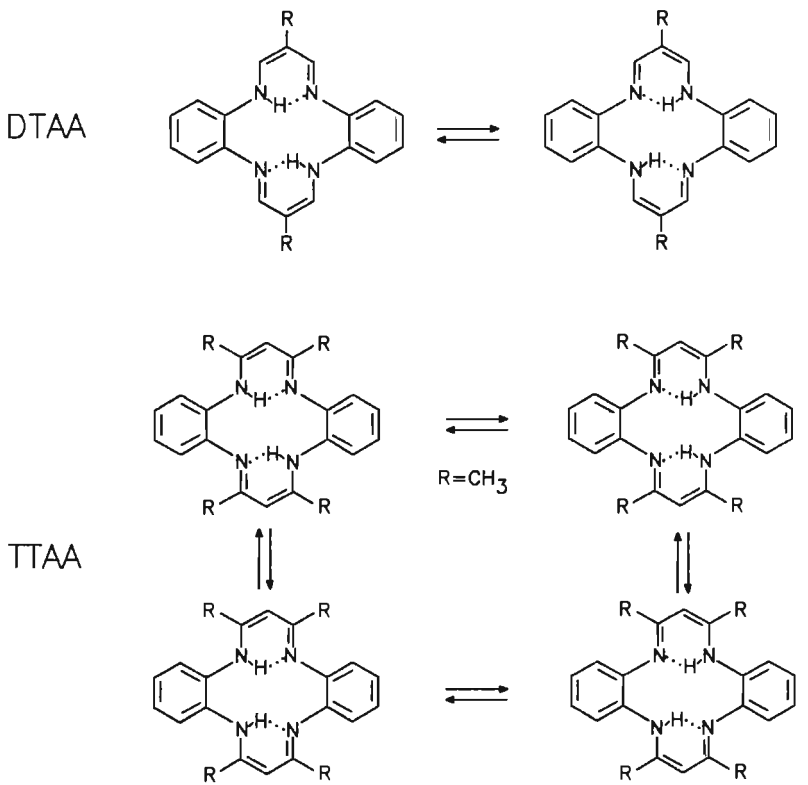

Fig. 5. Solid-state tautomerism of dimethyltetraaza[14]annulene (DTAA) [22] and of tetramethyltetraaza[14]annulene (TTAA) [21, 23, 24]

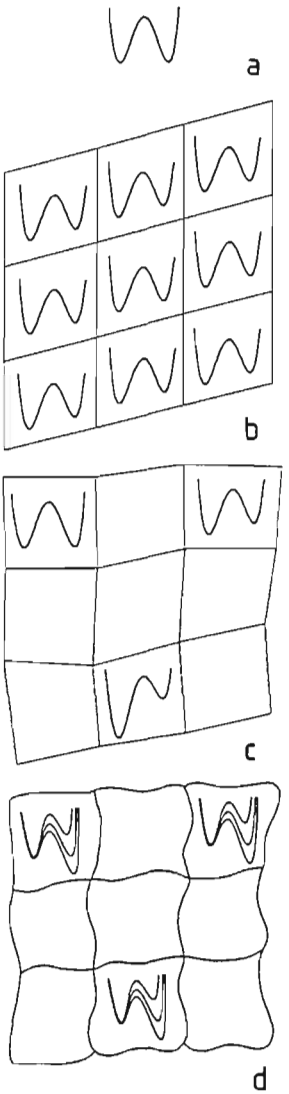

Fig. 6. Perturbation of a symmetric double minimum potential of a bistable molecule by intermolecular interactions. **a** symmetric double minimum potential in the gas phase. **b** Perturbation of the potential in the ordered crystalline state by intermolecular interactions which are the same for all molecules. **c** Perturbation of the potential in the disordered solid state by intermolecular interactions which are the different for all molecules **d** Motional averaged symmetric potentials. (Adapted from Ref. [24])

different porphyrins, azophenine, as well as for the reaction systems shown in Figs. 4 and 5. These values depend on the chemical and the crystal structure; values ranging from 0 to 12 kJ mol^{-1} were found so far. Note that the cases $\Delta E \simeq 0$ were realized within the margin of error for the parent compound porphyrin [16], meso-tetratolylporphyrin [15], and the triple proton transfer in 3,5-dimethylpyrazole (Fig. 1) [25, 26]. In the case of phthalocyanine, different solid-state perturbations were observed depending on the crystal modification [19]. By contrast, no substantial entropy difference between the different tautomeric states could be observed.

From solid-state NMR experiments, not only thermodynamic but also kinetic information on the reaction rates in the solid state can be obtained, as shown for porphyrins, phthalocyanine, and dimethyltetraazaannulene, and pyrazoles [15–26]. It is interesting to note that the rate constants of the tautomerism in solid porphyrin samples coincide with the corresponding solution rate constants [15–17]. Thus, solid-state effects on the thermodynamics of proton tautomerism seem to be more important than kinetic solution solid-state effects provided that the hydrogen bond network is not changed. For strongly hydrogen-bonded proton transfer systems, such as porphycen [16] (Fig. 4) or TTAA [21] (Fig. 5), the rates of proton transfer were found to be too fast in order to be measured by ^{15}N CPMAS NMR. From the observation of temperature-dependent mole fractions of different tautomeric states it was, nevertheless, possible to establish in both cases that the protons move along slightly asymmetric double minimum potentials and not in single minimum potentials. It was also found in both cases that the two NH...N hydrogen bonds of each molecule are perturbed in a different way, which establishes the independent proton motion and the presence of four different tautomeric states shown in Fig. 4 and 5. Note that these NMR results can help to answer the problem of proton localization which arises in the x-ray crystallographic analysis of compounds with labile protons [47–49].

4 ^{15}N CPMAS NMR Spectroscopy of Proton Transfer Systems in the Disordered Solid State

For the crystalline state discussed so far, all molecules of a sample experience the same solid-state perturbation ΔE as expressed by Fig. 6b. This finding is not surprising because of the periodicity of crystals. However, how are the reaction energy surfaces of the proton transfer systems under consideration modulated by an aperiodic amorphous matrix such as an organic glass? Information about this problem is desirable in order to achieve a better understanding of the structure and of rate processes in glasses.

Such information can be obtained by lineshape analysis of suitable high-resolution solid-state spectra. In order to extract thermodynamic and kinetic data from the spectra, first, an appropriate line-shape theory had to be developed [19, 24]. The model on which this theory is based is shown in Fig. 6c. It assumes a continuous distribution of sites characterized by different rate and equilibrium constants of proton tautomerism. The possibility of exchange between the different sites was also taken into account [19, 24]. Actually, bigaussian distributions of the reaction enthalpies and of the enthalpies of activation of proton exchange were employed. Different possibilities, including Marcus theory, of reducing this two-dimensional site distribution function to a one-dimensional distribution were discussed [19].

The theory was then applied to simulate the ^{15}N CPMAS NMR spectra of ^{15}N-labeled amorphous phthalocyanine (Pc) [19]. The spectra show dynamic line-broadening due to proton transfer. Site exchange was found to be absent. The amorphous modification was found to be characterized by a broad distribution of differently perturbed asymmetric double minimum potentials, as expected for a disordered environment. In other words, in a disordered environment not only a distribution of equilibrium constants but also of rate constants were observed [19]. Unfortunately, both distributions are independent from each other and make it difficult to extract a unique set of lineshape parameters by the simulation of the spectra.

Therefore, the effects of a disordered environment on a very fast proton transfer was studied where dynamic line-broadening due to proton transfer is absent. For this purpose, ^{15}N CPMAS NMR measurements were performed on solid solutions of TTAA (Fig. 5) in polystyrene [24]. Since the matrix does not contain nitrogen atoms, the signals of TTAA did not interfere with solvent signals, a problem which arises in ^{13}C studies. We find that the TTAA tautomerism in polystyrene is indeed very fast with respect to the NMR timescale, i.e., much faster than the reorientation of the solvent molecules; therefore, no line-broadening due to slow proton transfer complicates the spectra. However, a distribution of TTAA molecules with different equilibrium constants of tautomerism was found, according to Fig. 6c. Since the latter depend on temperature, this distribution leads to temperature-dependent inhomogeneously broadened lines. Exchange between the different types of TTAA molecules via rotational and translational diffusion is very slow below the glass transition. From the simulation of the NMR spectra, the parameters of a gaussian distribution of free reaction energies of the tautomerism, i.e., the maximum and the width of the distribution, were obtained as a function of temperature [24]. The inhomogeneous line-broadening was confirmed by two-dimensional NMR experiments. Thus, proton transfer dyes such as TTAA are sensitive molecular probes for microscopic order in glasses. In addition, the motional averaging process of the differently perturbed double minimum potential into one effective symmetric double minimum potential within the NMR timescale was observed by performing experiments in the glass transition region [24]. This process indicates that above the glass point the different sites interconvert rapidly within the NMR timesale. This process renders the effective potential of the proton motion apparently symmetric as shown in Fig. 6d.

5 IR Studies of Azophenine in the Liquid and the Crystalline State

The motional averaging of the double minimum potentials described above takes place in a timescale spanned by the correlation time of the molecular motion, which is on the order of nano- to picoseconds for liquids. Since this

averaging process is slow with respect to the IR timescale, the model expressed by Fig. 6c should then be valid also for a symmetric bistable molecule in the liquid state, in a timescale characteristic for IR spectroscopy. Consequently, the IR frequencies of vibrations coupled to the reaction coordinate of the proton motion, e.g., NH stretching bands, are expected to be different in the different sites in Fig. 6c, whereas they are similar in the ordered crystalline state modeled in Fig. 6b. Thus, the corresponding IR bands should be inhomogeneously broadened in liquid solution as compared to the crystalline state.

In order to obtain evidence for this model, it was necessary to study a molecule where other IR line-broadening mechanisms are absent and where the proton transfer was established by NMR for the solution and the solid state. It was found that azophenine was an ideal candidate for such studies. Besides the liquid-state NMR measurements described above which established the tautomerism in Fig. 2, solid-state NMR experiments [12] showed that the protons move in crystalline AP in highly asymmetric double minimum potentials according to Fig. 6b, with $\Delta E = 12\,\mathrm{kJ\,mol^{-1}}$. IR measurements were performed on azophenine dissolved in liquid CCl_4 and on polycrystalline azophenine [11]. The latter is characterized by surprisingly sharp NH stretching bands without a substructure or line-broadening as observed in other systems with intramolecular hydrogen bonds [39]. However, a broad NH stretching band was obtained for the liquid solution. Note that this broadening is only observed for the NH/ND stretching vibration; the other vibrations, e.g., the CH stretching vibrations, are not affected or only to a very minor extent. From NMR measurements the rotational correlation time of the NH vector were known to be of the order of nanoseconds; thus, rotational or translation diffusion cannot be responsible for the observed differential liquid–solid IR line-broadening. In the overtone region, the overall line widths of the NH stretching bands are much larger as compared to the fundamental region, and a possible differential broadening of solid-state and liquid-state overtone NH stretching bands could, therefore, not be observed within the margin of error. This overtone broadening is most easily interpreted in terms of short lifetimes of the higher excited NH stretching states. Thus, a plausible explanation for the differential NH stretching line widths in crystalline AP and AP dissolved in CCl_4 is provided by the assumption of a distribution of different solvation sites in which the force constants of the stretching vibration are different, according to the models expressed by Fig. 6b and 6c. In fact, the observation of the differential line-broadening effect provides evidence for a coupling of the NH stretching vibration to the reaction coordinate of tautomerism.

6 Conclusions

It has been shown that neutral double and triple proton transfer reactions as well as their multiple kinetic isotope effects and the effects of intermolecular interactions on the reaction dynamics can conveniently be studied by dynamic

liquid and solid-state NMR spectroscopy. Intramolecular and intermolecular proton transfer reaction systems behave in different ways. In the intramolecular cases only one proton contributes significantly to the kinetic isotope effect indicating a stepwise reaction mechanism. Highly polar intermediates lead to kinetic solvent effects if the reaction center is not shielded from the solvent. By contrast, in the intermolecular cases both protons contribute substantially to the kinetic isotope effects, thus increasing their size. The origins of the different behavior is discussed. Tunneling is found to play an essential role in these reactions.

Using novel solid-state NMR techniques, the dynamics of this class of reactions can be studied in a timescale of slow molecular motion, in the crystalline ordered as well as in the disordered—amorphous and glassy—solid state. It was found that the proton transfer systems studied are subject to static perturbations of the reaction energy profiles of the proton motion, even in cases where kinetic solvent effects are absent. Molecular motions lead to motionally averaged effective reaction surfaces in the liquid state. For one case the findings could be supported by additional liquid/solid-state IR experiments.

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