

NMR Parameters and Geometries of OHN and ODN Hydrogen Bonds of Pyridine–Acid Complexes

Hans-Heinrich Limbach,^{*,[a]} Mariusz Pietrzak,^[a] Shasad Sharif,^[a] Peter M. Tolstoy,^[a, b] Ilya G. Shenderovich,^[a, b] Sergei N. Smirnov,^[b] Nikolai S. Golubev,^[b] and Gleb S. Denisov^[b]

Abstract: In this paper, equations are proposed which relate various NMR parameters of OHN hydrogen-bonded pyridine–acid complexes to their bond valences which are in turn correlated with their hydrogen-bond geometries. As the valence bond model is strictly valid only for weak hydrogen bonds appropriate empirical correction factors are proposed which take into account anharmonic zero-point energy vibrations. The correction factors are different for OHN and ODN hydrogen

bonds and depend on whether a double or a single well potential is realized in the strong hydrogen-bond regime. One correction factor was determined from the known experimental structure of a very strong OHN hydrogen bond between pentachlorophenol and 4-methylpyridine, determined by

Keywords: acid–base complexes · hydrogen bonds · isotope effects · NMR parameters

the neutron diffraction method. The remaining correction factors which allow one also to describe H/D isotope effects on the NMR parameters and geometries of OHN hydrogen bond were determined by analysing the NMR parameters of the series of protonated and deuterated pyridine- and collidine–acid complexes. The method may be used in the future to establish hydrogen-bond geometries in biologically relevant functional OHN hydrogen bonds.

Introduction

The knowledge about the geometry of hydrogen bonds in the active sites of enzymes can provide important clues to understand the enzyme function.^[1,2] As X-ray and neutron diffraction can only be applied to the study of crystalline solids, it is, therefore, a general strategy to correlate crystal data of hydrogen bonds with appropriate spectroscopic parameters, and to determine in turn the latter for non-crystalline, in particular liquid environments of interest. In the past, mainly IR techniques have been used in this way to classify hydrogen-bonded systems in non-crystalline environment.^[3,4] On the other hand, NMR has become a major tool for the study of hydrogen bonds in enzymes^[1] due to the high selectivity of this method. Unfortunately, in the past, it

has been difficult to establish NMR hydrogen-bond correlations by using small model systems because of the problems of fast intermolecular hydrogen-bond exchange in liquids which makes it difficult to measure intrinsic NMR parameters of individual hydrogen bonds. These difficulties have been recently partially overcome by choosing model solid compounds which can be studied by dipolar high-resolution solid state NMR^[5–9] and by developing liquid state NMR down to 100 K, by using liquefied deuterated gases as NMR solvents.^[10–12] At these low temperatures it is often possible to reach the slow hydrogen-bond exchange regime. Thus, information about the relations between NMR parameters and hydrogen-bond geometries has been obtained.

During this research it was shown that the correlation of NMR parameters with the geometries of hydrogen-bonded systems A–H···B can be substantially simplified by the use of Pauling's^[13] valence bond orders or bond valences using Equation (1).

$$p_1 = \exp\{-(r_1 - r_1^0)/b_1\}$$

and

$$p_2 = \exp\{-(r_2 - r_2^0)/b_2\} \quad (1)$$

$r_1 = r_{\text{AH}}$ represents the A···H distance, $r_2 = r_{\text{HB}}$ the H···B distance, p_1 and p_2 the corresponding valence bond orders of

[a] Prof. H.-H. Limbach, M. Pietrzak, S. Sharif, Dr. P. M. Tolstoy, Dr. I. G. Shenderovich
Institut für Chemie, Freie Universität Berlin
Takustrasse 3, Berlin (Germany)
Fax: (+49)30-838-5310
E-mail: limbach@chemie.fu-berlin.de

[b] Dr. P. M. Tolstoy, Dr. I. G. Shenderovich, S. N. Smirnov, Dr. N. S. Golubev, Prof. G. S. Denisov
V. A. Fock Institute of Physics
St.-Petersburg University, Ulyanovskaja 1
Peterhof (Russia)

the diatomic units. According to Brown^[14] the total valence of hydrogen is unity, that is Equation (2):

$$p_1 + p_2 = 1 \quad (2)$$

Therefore, it follows that r_1 and r_2 depend on each other. This correlation is most conveniently expressed by the natural hydrogen-bond coordinates $q_1 = \frac{1}{2}(r_1 - r_2)$ and $q_2 = r_1 + r_2$. For a linear hydrogen bond, q_1 represents the distance of H from the hydrogen-bond center and q_2 the distance between the heavy atoms A and B. Note that the correlation does not depend on the hydrogen-bond angle.

A typical geometric hydrogen-bond correlation according to Equations (1) and (2) is depicted by the solid curve in Figure 1a. The corresponding behaviour of the bond valences is depicted by the solid lines in Figure 1b. When H is transferred from one heavy atom to the other, q_1 increases from negative values to positive values, q_2 goes through a minimum which is located at $q_1 = 0$ for AHA and near zero for unsymmetrical systems of the type AHB. The bond orders are unity in one and zero in the other limit. The sum of both bond orders is unity as indicated by the upper solid line in Figure 1b.

Steiner et al.^[15] and Grabowski^[16] have collected the available low-temperature neutron diffraction structures in the Cambridge Structural Database (CSD) and have demonstrated that Equation (2) is valid for series of OHO, NHN,

and OHN hydrogen bonds. The parameters in Equation (1) were determined by fitting distance sets r_1 and r_2 obtained by neutron diffraction to Equations (1) and (2). Recently, it has been proposed to correlate NMR parameters of hydrogen bonds not with distances but with the corresponding bond valences which reduce the number of adjustable parameters as the values of r_1^0 and b_1 are already known from the crystallographic data.^[5,6,11,12]

A so far not recognized problem with this approach is that in the Cambridge Database only few reliable data are available for very strong and short hydrogen bonds where the two bond orders are close to each other, that is, $q_1 \approx 0$. Thus, the parameters r_1^0 and b_1 published are based on compounds exhibiting medium and weak hydrogen bonds. Recently, some of us noted deviations of experimental geometries from the valence bond order correlation for some very strong NHN and NDN hydrogen bonds^[17] whose geometries had been elucidated previously^[5] by dipolar solid state NMR. It was found that in the symmetric configuration the values of q_2 were larger than the minimum value predicted from the hydrogen-bond correlation as indicated by the dotted line in Figure 1a. The effect was slightly larger for the symmetric NHN as compared to the symmetric NDN bond. Additional neutron crystallographic data of NHN hydrogen bonds confirmed these deviations. They could be described by assuming that for a hydrogen bond ALB, L=H, D, the sum of the real averaged bond orders in the strong hydrogen-bond regime is smaller than the sum of the equilibrium bond orders, see Equation (3):

$$p_1^L + p_2^L < p_1 + p_2 = 1 \quad (3)$$

Thus, the upper dotted line in Figure 1b leads to the dotted correlation curve in Figure 1a which is flattened in the strong hydrogen-bond regime but which coincides with the equilibrium curve for the weak hydrogen bonds.

As our previous work^[17] was restricted to NHN hydrogen bonds we felt that this first case should be corroborated further. Therefore, we had a closer look at OHN hydrogen bonds which are important in amino acid side chain and co-factor interactions of proteins. We were especially interested in OHN correlations in order to associate NMR parameters with hydrogen-bond geometries. Particularly interesting is a model system representing the so far shortest known OHN hydrogen bond, the crystalline 1:1 complex between 4-methylpyridine and pentachlorophenol; the low-temperature neutron diffraction structure has recently been reported by Steiner et al.^[18] As in the NHN case mentioned above, a deviation of the data points from the correlation established previously^[15d] for weak and medium hydrogen bonds was observed, but the deviation was not discussed further as it represented a first single case.

The scope of this paper is, therefore, twofold. Firstly, we want to describe quantitatively the deviations of the geometries for the strongest OHN hydrogen bonds from those expected from the simple valence bond analysis. The second scope is to use this description in order to derive hydrogen bond–NMR parameter correlations for the related pyridine–carboxylic acid complexes studied previously^[10,11] by low-

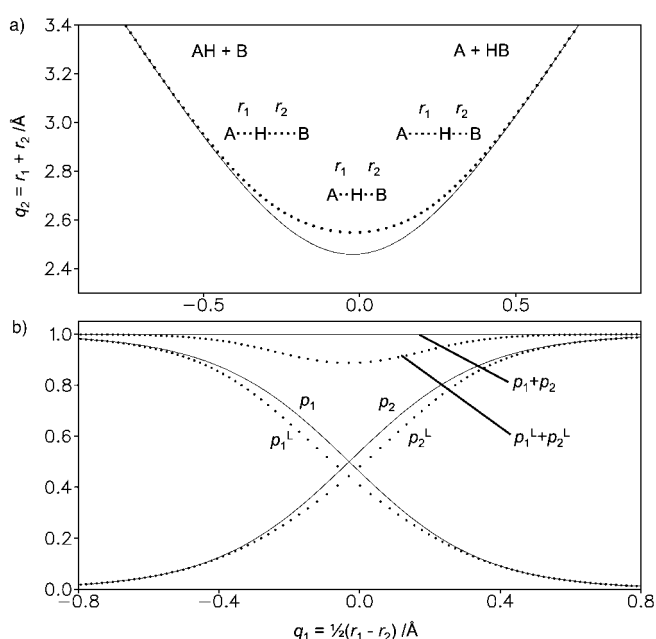


Figure 1. a) q_2 versus q_1 correlation of OHN hydrogen bonds calculated by combination of Equations (1) to (4) using the parameters of Table 1. Solid line: classical or equilibrium correlation. Dotted line: calculated using the empirical anharmonic correction of Equation (4) and the parameters d^H and d^D listed for pyridine- and collidine–acid complexes for freon solution and the solid state in Table 1. The parameters c^H and c^D do not influence the shape of the correlation curves but only provide the “correlation” between the correlation curves for protonated and deuterated hydrogen bonds. b) Evolution of the corresponding valence bond orders and of their sums.

temperature liquid state NMR, as well as for the 2,4,6-trimethylpyridine–carboxylic acids complexes for which liquid and solid state NMR data had been determined.^[6,19] The main goal was to include a description of H/D isotope effects on NMR parameters and hydrogen-bond geometries, and to fill in this way the gap between quantum-mechanical theories which have been developed for isolated molecules and hydrogen-bonded systems in condensed matter.

Theoretical Section

Hydrogen-bond correlations corrected for anharmonic zero-point vibrations: In order to describe anharmonic effects in terms of the valence bond order method we have proposed^[17] the following empirical relations in Equation (4a) and (4b):

$$p_1^L = p_1 - c^L(p_1 p_2)^f (p_1 - p_2) - d^L(p_1 p_2)^g = \exp\{-(r_1^L - r_1^o)/b_1\} \quad (4a)$$

$$p_2^L = p_2 + c^L(p_1 p_2)^f (p_1 - p_2) - d^L(p_1 p_2)^g = \exp\{-(r_2^L - r_2^o)/b_2\}, L = H, D \quad (4b)$$

which allow one to calculate the corrected bond orders p_1^L and p_2^L and hence the distances of AHB and ADB systems from the classical bond orders p_1 and p_2 , and hence the corresponding hydrogen-bond distances using Equations (1) and (2). The first correction term does not change the total bond order sum of unity. This term shifts, therefore, the data points of H and D along the classical correlation curve q_1 versus q_2 , but does not change the form of this curve. The latter is only changed by the second term as was depicted in Figure 1a. Thus, Equation (4) allows one to calculate the *primary* geometric hydrogen-bond isotope effect,^[5] as in Equation (5):

$$\Delta q_1 \equiv q_1^D - q_1^H \quad (5)$$

as well as the *secondary* geometric hydrogen-bond isotope effect [Eq. (6)]:

$$\Delta q_2 \equiv q_2^D - q_2^H \quad (6)$$

The values of the powers f and g as well as the isotope sensitive parameters c^L and d^L are empirical and have to be obtained by fit of experimental data to Equation (4).

In order to demonstrate the physical meaning of the correction terms we have depicted in Figure 2 schematically the one-dimensional potential curves and squared ground state wave functions of some typical strong hydrogen bonds ALB, $L=H, D$. The curves for AHB and ADB are slightly different which does, however, not mean a breakdown of the Born–Oppenheimer approximation. This effect is a result of the reduction of a more-dimensional vibrational problem into a one-dimensional one.^[5,10a] The average values of q_1^H and q_1^D are indicated by vertical bars and are controlled by the parameters c^H and c^D which determine then the *primary*

geometric isotope effect Δq_1 . Generally, c^H will be larger than c^D in agreement with a somewhat larger distance of D from the hydrogen-bond center as compared to H. c^H and c^D have no influence on the geometry of a symmetric hydrogen bond where $p_1^L = p_2^L$. Therefore, the physical meaning of d^L is best demonstrated for this case in Figure 2b exhibiting a single well potential with $q_1^H = q_1^D = 0$. d^L reduces the bond order sum to a value of less than 1, which means that the smallest equilibrium value $q_{2\min}$ is not reached. If d^D is assumed to be smaller than d^H it follows that $q_{2\min} < q_2^D < q_2^H$, that is, the *secondary* geometric isotope effect Δq_2 will be negative for this configuration. This situation has been demonstrated for the FHF⁻ anion,^[20] and has been called as “anomalous Ubbelohde effect”.^[21] By contrast, in the case of a symmetric double well as depicted in Figure 2a, q_2^D is larger than q_2^H and hence d^D larger than d^H . For an intermediate situation it is then conceivable that $d^D \approx d^H$. In this case, the correlation curves of AHB and ADB coincide with the classical correlation curve.

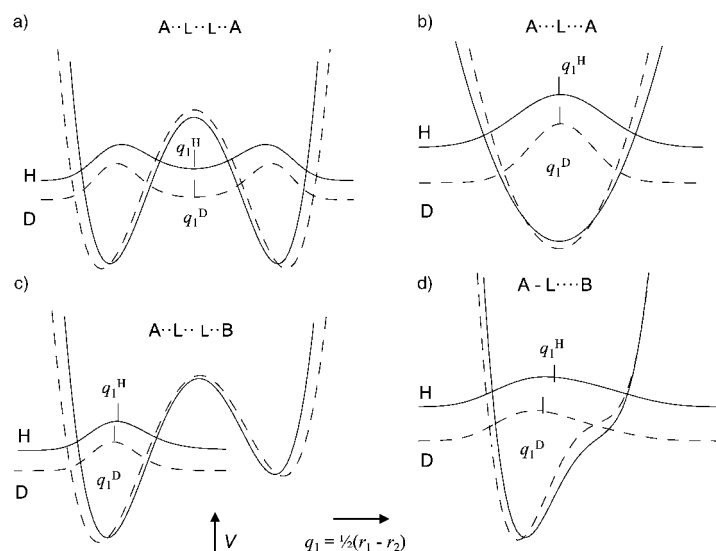


Figure 2. Various one-dimensional hydrogen ($L=H, D$) potentials and squared groundstate wave function (schematically) of a hydrogen bond ALB. a) Symmetric double well case with “half” hydrons close to A and to B. b) Symmetric single well case. c) Asymmetric double well case and d) asymmetric single well case. The vertical bars indicate the averaged hydrogen position.

NMR parameters and hydrogen-bond geometries: The question now arises how to correlate hydrogen-bond geometries with NMR parameters. Desirable is to have isotope insensitive correlation functions which can be applied to both the protonated and the deuterated system. Isotope effects on chemical shifts arise in this approximation only from isotope effects on the hydrogen-bond geometries. Such correlations can be found for the case where the NMR parameters in good approximation depend linearly on q_1 .

This condition is normally met, except the case of the strongest hydrogen bond in a given series exhibiting a single well potential as depicted in Figure 3. Around $q_1^H = q_1^D = 0$ the chemical shift $\delta(\text{ALB})$ of a heavy atom such as ¹⁵N is an

almost linear function of q_1 . This means that the values of $\delta(\text{AHB})$ and of $\delta(\text{ADB})$, averaged over the ground state wave functions, are the same and in good approximation equal to the value at $q_1=0$. Thus, one can associate to each value of q_1 also a unique value $\delta(\text{ALB})$. By contrast, $\delta(\text{ALB})$ is a non-linear function of q_1 . As D is more confined to the hydrogen-bond center compared with H, and as $\delta(\text{ALB})$ exhibits a maximum at $q_1=0$, the average value $\delta(\text{ADB})$ will be larger than the average value $\delta(\text{AHB})$ because the mean square values $\langle q_1^2 \rangle^{\text{H}}$ and $\langle q_1^2 \rangle^{\text{D}}$ are different, whereas the mean values $q_1^{\text{L}}=0$ are the same for both H and D. In other words, a correlation of $\delta(\text{ALB})$ with the mean values q_1^{L} represents an approximation, called in the remainder of this paper “the point approximation” which might lead to a systematic deviation in the case of a symmetric single well hydrogen bond.

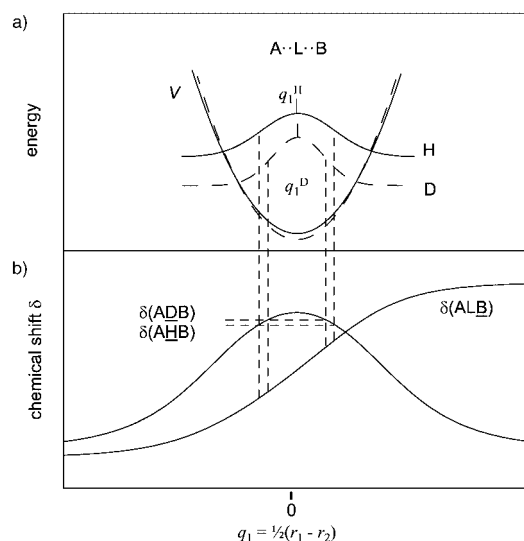


Figure 3. a) One-dimensional potential curve and squared groundstate wave function (schematically) of a symmetric single-well hydrogen bond ALB, L=H, D. b) Chemical shifts $\delta(\text{ALB})$ (schematically) of B and L as a function of q_1 . The average chemical shift of D is larger than for H because of the maximum of $\delta(\text{ALB})$ and the narrower wave function of D compared with H. By contrast, as $\delta(\text{ALB})$ is a linear function q_1 , $\delta(\text{AHB})=\delta(\text{ADB})$.

It is clear that a correct description can be found if the nuclear wave functions and the chemical shielding surface are known. An example is the FHF^- anion, where H/D isotope effects on chemical shielding have been studied theoretically by Golubev et al.^[22] A theoretical analysis showed that averaging over all hydrogen-bond vibrations including the bending vibrations needs to be taken into account. Under normal experimental conditions, the nuclear wave functions and the chemical shielding surfaces are, however, not known. Therefore, we will ignore in the following the breakdown of the correlation between $\delta(\text{AHB})$ and q_1 for the symmetric single-well case.

For a quantitative correlation of NMR parameters and geometries of hydrogen bonds of the type AHB, we therefore, assume the validity of the following equations. For the chemical shifts of the base B it was assumed that:^[12]

$$\delta(\text{ALB}) = \delta(\text{B})^{\circ} p_{\text{AL}}^{\text{L}} + \delta(\text{LB})^{\circ} p_{\text{LB}}^{\text{L}} + 4\delta^{*}(\text{ALB}) p_{\text{AL}}^{\text{L}} p_{\text{LB}}^{\text{L}}, \text{ L} = \text{H, D} \quad (7)$$

for the ^1H chemical shifts that:^[11]

$$\delta(\text{AHB}) = \delta(\text{AH})^{\circ} p_{\text{AH}}^{\text{H}} + \delta(\text{HB})^{\circ} p_{\text{HB}}^{\text{H}} + 4\delta^{*}(\text{AHB}) p_{\text{AH}}^{\text{H}} p_{\text{HB}}^{\text{H}} \quad (8)$$

and for scalar $^1\text{H,B}$ couplings^[12] that:

$$^1J(\text{AHB}) = ^1J(\text{HB})^{\circ} p_{\text{HB}}^{\text{H}} - 8J^{*}(\text{AHB})(p_{\text{AH}}^{\text{H}})^2 p_{\text{HB}}^{\text{H}} \quad (9)$$

$\delta(\text{LB})^{\circ}$, $\delta(\text{HB})^{\circ}$ and $^1J(\text{HB})^{\circ}$ represent the limiting B and ^1H chemical shifts and $^1\text{H,B}$ coupling constants of the fictive free HB, $\delta(\text{B})^{\circ}$ the chemical shift of the free base B, and $\delta(\text{AH})^{\circ}$ the ^1H chemical shift of the free acid. $\delta^{*}(\text{ALB})$, $\delta^{*}(\text{AHB})$ and $J^{*}(\text{AHB})$ are excess terms describing the deviation of the parameters of the strongest AHB hydrogen bond from the average of the limiting values of the free forms. Without the excess term, Equation (7) had been proposed previously.^[11] We note that all the NMR correlation curves exhibit a principal difference to the q_1 versus q_2 curves: the values of the latter can increase to infinity as AH moves away from B or A from HB, but the NMR parameters of the separated molecular units do not change any more when they are separated.

Finally, the quantum correction of Equation (4) influences substantially the correlation analysis of isotopic H/D fractionation between the pyridine–acid complexes AHB and reference complexes XHY, characterized by Equation (10):



The equilibrium constant of this reaction is given by Equation (11):

$$K = \frac{1}{\Phi} = \frac{x_{\text{ADB}} x_{\text{XHY}}}{x_{\text{AHB}} x_{\text{XDY}}} \approx \exp(-\Delta\text{ZPE}/RT) \quad (11)$$

where the inverse equilibrium constant Φ is also called the fractionation factor. x_i are mol fractions or concentrations of the various isotopic species, R the gas constant, T the temperature and ΔZPE the zero-point energy difference of the H and D forms of the hydrogen-bonded complexes. This quantity is given by Equation (12):

$$\Delta\text{ZPE} = \text{ZPE}(\text{XHY}) - \text{ZPE}(\text{XDY}) - (\text{ZPE}(\text{AHB}) - \text{ZPE}(\text{ADB})) \quad (12)$$

In principle, it would be desirable to express the values of $\text{ZPE}(\text{ALB})$, L=H, D, as a function of the corrected bond valences p_1^{L} and p_2^{L} from which ΔZPE could be calculated as a function of the hydrogen-bond geometries. Unfortunately, general correlations for all isotopic sensitive vibrations and, therefore, of their ZPE values are not available at present. Therefore, we use the following approximation in which ΔZPE is expressed as a function of the classical bond valen-

ces p_1 and p_2 as has been proposed previously,^[11] Equation (13):

$$\Delta ZPE = \Delta ZPE^\circ(4p_{\text{OH}}p_{\text{HN}})^2 + \Delta ZPE(\text{OH})^\circ p_{\text{OH}} + \Delta ZPE(\text{HN})^\circ p_{\text{HN}} \quad (13)$$

$\Delta ZPE(\text{OH})^\circ$ and $\Delta ZPE(\text{HN})^\circ$ represent the zero-point energy differences of the hypothetical free diatomic states OH and HN compared with the reference complex XHY of pyridine with triphenylmethanol. ΔZPE° represents the absolute drop of zero-point energy between the non-hydrogen-bonded limiting states and the strongest hydrogen-bonded quasi-symmetric state. Equation (13) provides a link between the world of geometries, NMR parameters and vibrations of hydrogen bonds.

Results

OHN hydrogen-bond correlation: As an example, we discuss in this section the case of hydrogen-bonded acid–base complexes formed by pyridine derivatives and carboxylic acids containing OHN hydrogen bonds. For the use of the equations of the preceding section we set $A \equiv O$ and $B \equiv N$.

Using the parameters published by Steiner for OHN hydrogen bonds^[15d] listed in the first row of Table 1 we obtain the lower solid line in Figure 4a, which is in fact the same as the solid line in Figure 1a. The data points of the weak and medium hydrogen bonds from which these parameters were derived are represented by circles in Figure 4a. This curve constitutes a good approximation to the correlation of the equilibrium distances. The squares originate data obtained by Lorente et al. for 1:1 hydrogen-bonded complexes of 2,4,6-trimethylpyridine (collidine) with various acids by using a combination of dipolar solid state NMR^[6a] and X-ray crystallography.^[6b]

The triangles in Figure 4a result from the low-temperature neutron diffraction data of the very strong OHN hydrogen bonds between pyridine and phenols.^[18] At first sight, one is tempted to neglect the deviation of these data points from the calculated solid correlation curve, but in fact the deviations are systematic. They are similar to those observed for the NHN hydrogen bonds.^[17] The dotted curve was calculated for OHN hydrogen bonds using the correction parameters listed in Table 1. The experimental data are reproduced in a satisfactory way, although the agreement is not perfect because of the point approximation used. As no neutron diffraction data are available to our knowledge for very strong ODN hydrogen bonds, the corresponding ODN correlation curve could not yet be calculated at this stage. Some information about this curve will be obtained in the next section by NMR.

For the data analysis an appropriate computer program based on Equations (1) to (9) was written which allowed us to calculate all the correlation curves in a single run as a function of the adaptable parameters listed in Tables 1 and 2. In other words, these parameters were determined by

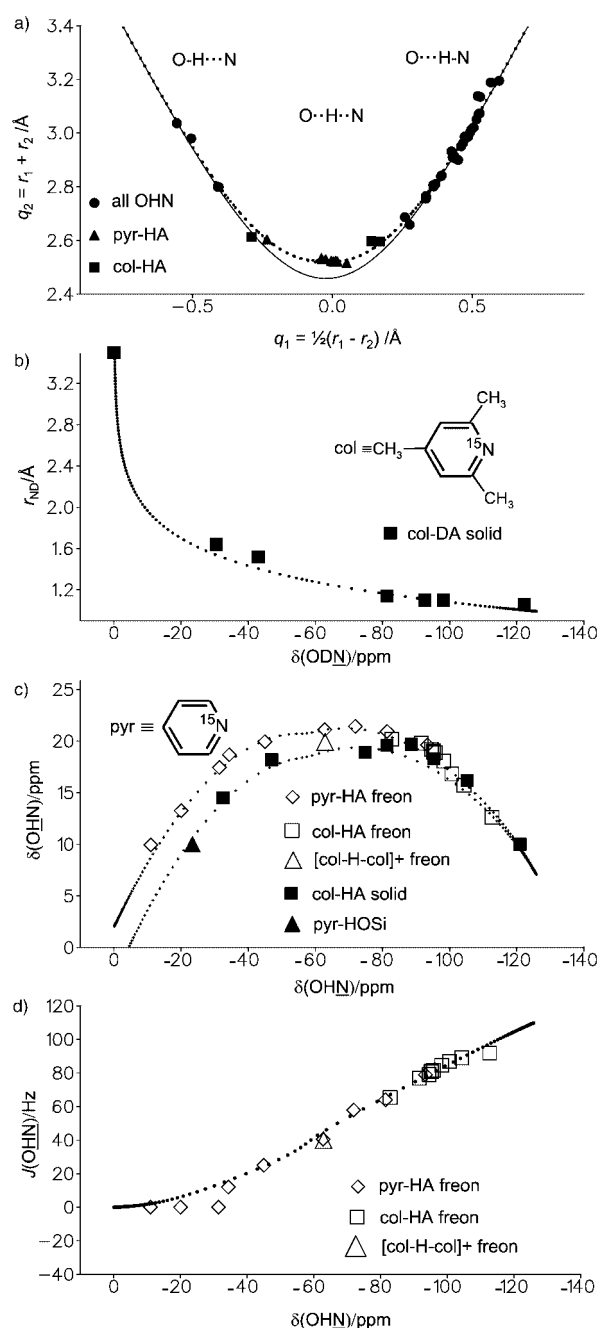


Figure 4. OHN hydrogen-bond correlations. The parameters of the calculated curves are listed in Tables 1 and 2. a) Geometric OHN hydrogen-bond correlations. The circles refer to neutron diffraction data in the Cambridge Structural Database as published by Steiner.^[15d] The triangles represent the recently published new neutron diffraction data.^[18] The squares correspond to crystalline collidine–acid complexes.^[6b] b) ND distance versus ^{15}N chemical shift correlation for polycrystalline collidine–acid complexes obtained by dipolar solid state NMR.^[6a] c) ^1H versus ^{15}N chemical shift correlation of pyridine–acid and collidine–acid complexes. d) Correlation between the H, ^{15}N scalar couplings $J(\text{OHN})$ and the ^{15}N chemical shifts of pyridine–acid and collidine–acid complexes in $\text{CDF}_3/\text{CDF}_2\text{Cl}$ at low temperatures. For further explanations see text.

adapting the calculated dotted curves to the whole body of experimental data.

NMR parameters of OHN hydrogen bonds: All available experimental NMR data of the OHN and ODN hydrogen

Table 1. Parameters of the geometric hydrogen-bond correlations of pyridine- and collidine–acid complexes.

Systems	b_{OH} [Å] ^[a]	r_{OH}° [Å] ^[a]	b_{HN} [Å] ^[a]	r_{NH}° [Å] ^[a]	f	g	c^{H}	d^{H}	c^{D}	d^{D}
weak and medium strong OHN bonds	0.371	0.942	0.385	0.992	0	0	0	0	0	0
pyridine–HA and collidine–HA in CDF ₃ /CDF ₂ Cl	0.371	0.942	0.385	0.992	5	2	360	0.7	50	0.6
pyridine–HA and collidine–HA solid	0.371	0.942	0.385	0.992	5	2	360	0.7	110	0.6

[a] Taken from ref. [15d].

Table 2. Parameters of the NMR hydrogen-bond correlations of pyridine- and collidine–acid complexes.

Systems	$\delta(\text{N})^{\circ}$ [ppm] ^[a]	$\delta(\text{HN})^{\circ}$ [ppm]	$\Delta\delta(\text{N})^{\circ}$ [ppm] ^[b]	$\delta(\text{OH})^{\circ}$ [ppm]	$\delta(\text{HN})^{\circ}$ [ppm]	$\delta^{*}(\text{OHN})$ [ppm]	${}^1J(\text{HN})^{\circ}$ [Hz]	$J^{*}(\text{OHN})$ [Hz]
pyridine–HA in CDF ₃ /CDF ₂ Cl	0	126	–4	2	7	20	110	12.5
collidine–HA in CDF ₃ /CDF ₂ Cl	0	126	–8	2	7	20	110	12.5
solid collidine–HA	0	126	0	–3	7	20	–	–

[a] With respect to neat frozen pyridine and collidine, resonating at 275 ppm and 268 ppm with respect to solid NH₄Cl.^[6a] [b] $\Delta\delta(\text{N})^{\circ}$: ¹⁵N chemical shift difference between the free bases in the freon solution and in the frozen solid state around 130 K.

bonds of pyridine- and collidine–acid complexes with their hydrogen-bond geometries are depicted in Figure 4b to 4d and in Figure 5.

The N–D distances r_{ND} of deuterated polycrystalline collidine–acid complexes are plotted in Figure 4b as a function of their ¹⁵N chemical shifts $\delta(\text{ODN})$. The distances had been obtained previously from the dipolar ¹⁵N,D couplings, and the ¹⁵N chemical shifts by high resolution solid state NMR.^[6] The values of $\delta(\text{ODN})$ are referenced to the ¹⁵N chemical shift of neat frozen collidine, set to $\delta(\text{N})^{\circ}=0$ in Equation (7), resonating at 268 ppm^[6a] with respect to solid ¹⁵NH₄Cl.^[23] The excess term $\delta^{*}(\text{OLN})$ was also set to zero in agreement with our previous analyses.^[11,19] A problem is the ¹⁵N chemical shift of the fictive “free” collidinium which limits the right end of the correlation curve. An exact value can not be determined experimentally. Previously,^[6] we had proposed a value of $\delta(\text{HN})^{\circ}=-130$ ppm. For pyridine–acid complexes in freon we had used a slightly smaller value of -126 ppm.^[11] The difference between the two values is too small to be interpreted in terms of the different chemical structures of “free” pyridinium and collidinium. Therefore, we adopt here the latter value for both data sets.

In Figure 4c are depicted the ¹H chemical shifts $\delta(\text{OHN})$ of the pyridine- and collidine–acid complexes obtained under various conditions as a function of the ¹⁵N chemical shifts $\delta(\text{OHN})$. The filled symbols refer to the solid collidine–acid complexes with OHN hydrogen bonds, whereas in Figure 4b the corresponding complexes with ODN hydrogen bonds were depicted; in addition, a data point is included as solid triangle on the left side, characterizing the complex of pyridine with surface Si–OH groups of mesoporous silica of the MCM-41 and SBA-15 type.^[24] For this complex an ¹H chemical shift of 10 ppm and a ¹⁵N chemical shift of -23 ppm with respect to frozen neat pyridine had been obtained. The open symbols refer to various pyridine–acid complexes^[10a] and of collidine–acid^[19] complexes dissolved in CDF₃/CDF₂Cl mixtures (freon), as well as one data point

referring to the homoconjugate cation of [collidine–H–collidine]⁺ reported in ref. [25].

In this graph, all collidine–acid complexes are referenced to neat frozen collidine, and all pyridine–acid complexes to neat frozen pyridine. The latter absorbs at 275 ppm with respect to solid ¹⁵NH₄Cl.^[6a] As the ¹⁵N chemical shifts for the complexes dissolved in freon had been referenced internally to the free bases we had to take the $\Delta\delta(\text{N})^{\circ}=\delta(\text{N})^{\circ}$ (freon) $-\delta(\text{N})^{\circ}$ (solid) into account, as the formation of weak hydrogen bonds with freon causes small upfield shifts. Unfortunately, it is difficult to measure the values of $\Delta\delta(\text{N})^{\circ}$ directly as they depend slightly on temper-

ature and concentration. Moreover, they also depend on the magnetic susceptibilities and the angle of the spinning samples with respect to the magnetic field, which is 54.4° for MAS experiments and 0° in liquid state NMR. Via the intermediate of a liquid nitromethane sample, we obtained a pyridine reference shift of $\Delta\delta(\text{N})^{\circ}=-3 \pm 3$ ppm. We found that a value of $\Delta\delta(\text{N})^{\circ}=-4$ ppm which was added to the ¹⁵N chemical shift data of the pyridine–acid complexes^[10a] fitted the data well as illustrated in Figure 4c. As collidine in freon resonates at -10.3 ppm upfield from pyridine, the corresponding solvent shift of collidine was then fixed to -8 ppm (Table 2).

The data indicate that the ¹H chemical shifts are larger for freon solution compared with the solid state as long as H is closer to oxygen or in the hydrogen-bond center. In particular, the maximum ¹H chemical shift is about 21.5 ppm for freon solution, but only about 19 ppm for the solid state. We found that we were able to reproduce these findings by using the same values of $\delta(\text{HN})^{\circ}=7$ ppm for “free” collidinium and pyridinium, the same excess term $\delta^{*}(\text{OHN})=20$ ppm, but different values of $\delta(\text{OH})^{\circ}$. For freon solution we had used previously a value of $+2$ ppm^[11] which we kept here, and for “free” oxygen acids in the solid state values between -2 ppm^[9] and -4 ppm had been reported.^[26] We found that a slightly modified value of -3 ppm fitted better the solid state data of Figure 4c. The calculated dotted lines reproduce now the experimental data in a very satisfactory way.

Finally, Figure 4d illustrates how the scalar couplings ${}^1J(\text{OHN})$ between ¹H and ¹⁵N correlate with $\delta(\text{OHN})$. The parameters of Equation (9) leading to the dotted line are included in Table 2.

So far we have only considered the OHN hydrogen bonds. In the following, we include also the data of the ODN hydrogen bonds. In Figure 5a and b are depicted the secondary H/D isotope effects on the ¹⁵N chemical shifts [Eq. (14)].

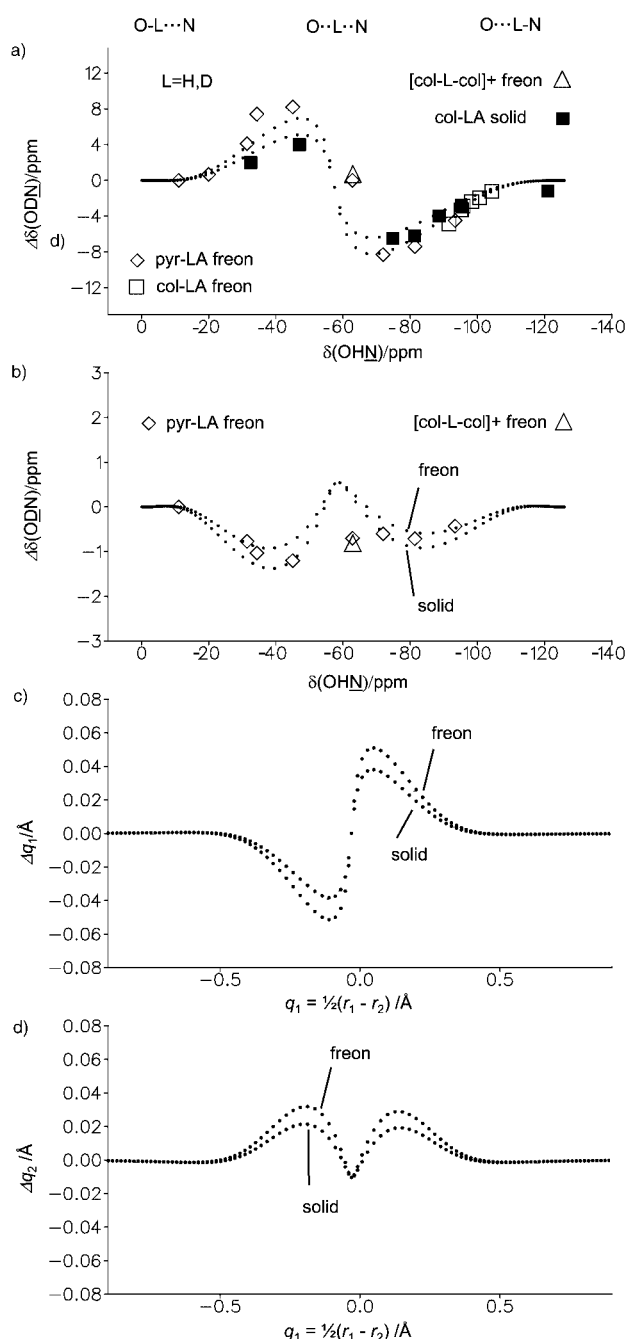


Figure 5. a) Secondary [Eq. (14)] and b) primary isotope effects [Eq. (15)] on NMR chemical shifts of pyridine- and collidine-acid complexes around 130 K, dissolved in $\text{CDF}_3/\text{CDF}_2\text{Cl}$ and solid collidine-acid complexes; data from refs. [6a, 11, 19, 25]. c) Primary geometric isotope effects Δq_1 [Eq. (5)] and d) secondary geometric isotope effects Δq_2 [Eq. (6)] of pyridine-acid and collidine-acid complexes. The curves were obtained as described in the text with the parameters listed in Tables 1 and 2. For further explanation see text.

$$\Delta\delta(\text{ODN}) \equiv \delta(\text{ODN}) - \delta(\text{OHN}) \quad (14)$$

and the primary isotope effects on the hydron chemical shifts [Eq. (15)]:

$$\Delta\delta(\text{ODN}) \equiv \delta(\text{ODN}) - \delta(\text{OHN}) \quad (15)$$

Whereas the secondary effects have been measured for pyridine-acid complexes in freon,^[10a] and for the collidine-acid complexes in the solid state^[6] and in freon,^[19] the primary effects could not be obtained for the solid state and were measured only for the pyridine-acid complexes.^[10a] As described in the Theoretical Section, we make here in the point approximation the assumption that the isotope effects on the NMR parameters are given entirely by the isotope effects on the hydrogen-bond geometries defined in Equations (5) and (6). Therefore, in order to calculate the dotted lines in Figure 5, we only adapted the values of the correction parameters c^D and d^D in Equation (4) listed in Table 1 as the NMR parameters were already determined in Figure 4. Again, two data sets were obtained, one for the complexes in freon and the other for the solid state. Then, we calculated the corresponding ODN correlation curve q_2 versus q_1 . As these curves almost coincided with the dotted ODN curve of Figure 4a, it was not included in this graph. Instead, we calculated the isotope effects on the hydrogen-bond geometries for the freon and solid state data which are included as dotted lines in Figure 5c and d.

Isotopic H/D hydrogen-bond fractionation and NMR parameters: For pyridine-acid complexes the isotopic exchange reaction according to Equation (10) is illustrated in Figure 6a. Using $\text{CDF}_3/\text{CDF}_2\text{Cl}$ mixtures as solvent, and the triphenylmethanol-pyridine complex as a reference, the values of K had been determined around 130 K by NMR.^[11] The K values measured, and the values of ΔZPE calculated according Equation (13) are depicted in Figure 6b as a function of the nitrogen chemical shift, serving again as a measure of the proton coordinate q_1 . The values of K are also plotted in Figure 6c as a function of the ^1H NMR chemical shifts. A systematic correlation with both NMR parameters and hence the hydrogen-bond geometries is observed.

The dotted lines in Figure 6b and c were calculated using all equations discussed so far, by adjusting the parameters of Equation (13), that is Equation (16):

$$\Delta\text{ZPE}^\circ = -3.13 \text{ kJ mol}^{-1}, \Delta\text{ZPE}(\text{OH})^\circ = \Delta\text{ZPE}(\text{HN})^\circ = +0.4 \text{ kJ mol}^{-1} \quad (16)$$

and naturally the other parameters of Tables 1 and 2, including the correction terms of Equation (4).

Discussion

In this section, we will discuss the results obtained in the previous section, depicted in Figures 4 and 5 and assembled in Tables 1 and 2 in more detail.

Empirical corrections of OHN hydrogen-bond geometry correlations arising from anharmonic hydron zero-point vibrations: Empirical corrections to the valence bond order analysis of hydrogen-bond geometries have been proposed which take into account anharmonic zero-point motions of hydrogen isotopes in hydrogen bonds. Thus, it became possi-

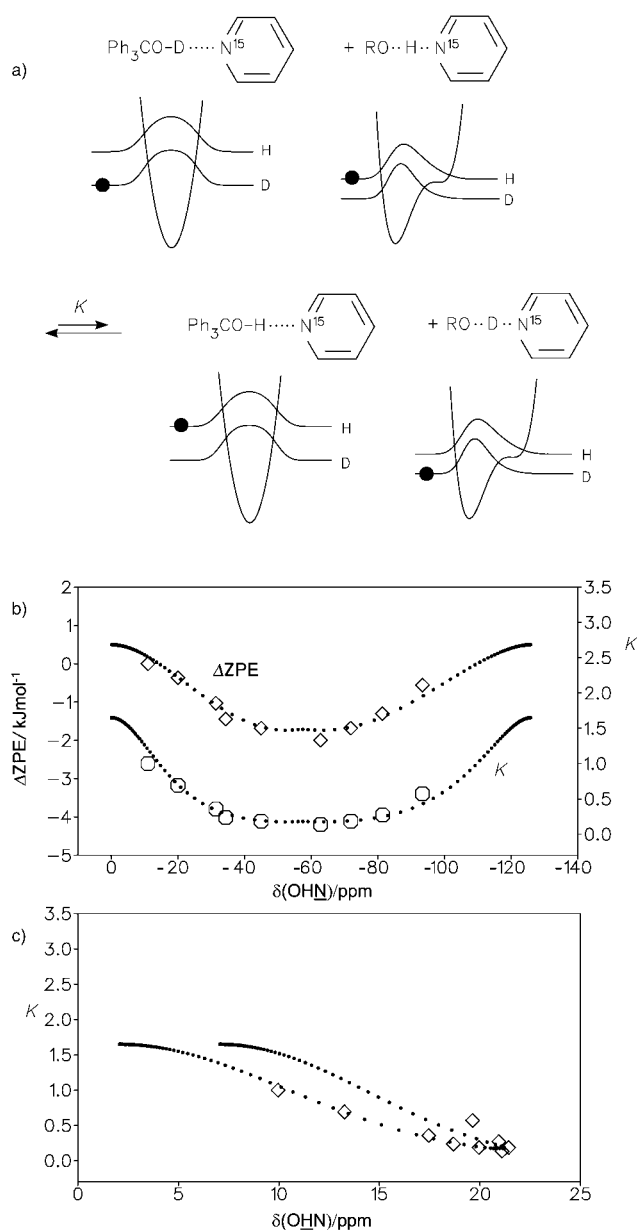


Figure 6. a) Isotopic fractionation between pyridine–acid complexes and the reference triphenylmethanol–pyridine complex studied in ref. [11] around 130 K using $\text{CDF}_3/\text{CDF}_2\text{Cl}$ as solvent. b) Values of K (circles) and zero-point energy differences ΔZPE (squares) as a function of the ^{15}N chemical shifts of hydrogen-bonded acid–pyridine complexes. c) Fractionation factors K as a function of the proton chemical shifts. The dotted lines were calculated as described in the text.

ble to find hydrogen-bond correlations for protonated and deuterated systems. For OHN hydrogen bonds the correction terms c^{H} and d^{H} in Equation (4) were adjusted using the neutron diffraction data of Steiner et al.^[18] obtained for the shortest OHN hydrogen bond known up to date. These data are depicted in the minimum of the dotted correlation curve in Figure 4a which correlates sum of the two hydrogen-bond lengths $\text{O}\cdots\text{H}$ and $\text{H}\cdots\text{N}$ with their half difference. For linear hydrogen bonds these two coordinates represent the $\text{O}\cdots\text{N}$ distances and the deviation of the hydron from the hydrogen-bond center. These correction terms were nec-

essary in order to account for the slightly larger $\text{O}\cdots\text{N}$ distances found experimentally compared with the distances obtained by data fit of weak and medium OHN hydrogen bonds using the classical valence bond model,^[14,15] leading to the solid correlation curve in Figure 4a. This curve is valid only for equilibrium geometries and does not take anharmonic hydron motions into account. The corresponding correction parameters for ODN hydrogen bonds were estimated by NMR as discussed later.

NMR Parameters and OHN and ODN hydrogen-bond geometries:

It was assumed that H/D isotope effects affect the hydrogen-bond geometries, but that the relations which link the geometries with the NMR parameters are isotope independent. These parameters refer to the fictive non-hydrogen-bonded diatomic units that is, limiting structures used in the valence bond order analysis, and to excess terms describing the difference between the average limiting structures and the strongest hydrogen bonds. The parameters were obtained by fitting the calculated correlation curves to the experimental data available. Using a proper referencing, the data of pyridine- and collidine–acid complexes could be described in terms of common parameters.

In a previous study,^[6a] a correlation of the ^{15}ND dipolar interactions and hence the ^{15}N –D distances of solid collidine–acid complexes with the isotropic ^{15}N chemical shifts (Figure 4b) had been observed, which helped us to link the worlds of hydrogen-bond geometries and NMR parameters. Referencing of all pyridine–acid and collidine–acid ^{15}N chemical shift data to the corresponding neat frozen bases allowed us to construct the NMR correlation curves of Figure 4c. Roughly, the ^1H NMR chemical shifts are measures for the $\text{O}\cdots\text{N}$ distances and the ^{15}N chemical shifts measures of the proton positions. Thus, the ^1H NMR versus ^{15}N chemical shifts correlations of Figure 4c represent the NMR analogues of the geometric correlation curves of Figure 4a.

The dotted correlation lines represent very well the experimental data. For this agreement, the above-mentioned empirical valence bond correction terms were essential. Whereas the NMR parameters describing the dotted lines (Tables 1 and 2) are representative for both pyridine- and collidine–acid complexes, a substantial difference is observed for these complexes in the solid state and in freon solution. For the configurations where the proton is closer to oxygen than to nitrogen, as well as for the shortest OHN hydrogen bond, substantially larger ^1H chemical shifts are observed for freon solution compared with the solid state leading to the two different dotted ^1H versus ^{15}N chemical shift correlation curves. Thus, for the shortest OHN hydrogen bonds the ^1H chemical shift is around 21.5 ppm for freon solution as compared to about 19 ppm for the organic solid state. By contrast, the chemical shifts in the zwitterionic region coincide. The origin of this effect which had puzzled us for a long time could not be elucidated in our study, and will surely be subject of future theoretical studies. Nevertheless, the effect has to be taken into account when converting NMR data to hydrogen-bond geometries.

Another solvent effect had been described already previously:^[19] by going from the organic solid state to polar freon

solution, the hydrogen-bond geometries of collidine–acid complexes are strongly shifted along the hydrogen-bond correlation curves towards the zwitterionic structures. The closer H is to oxygen in the solid state, the stronger is the shift towards N in the polar liquid state. Clearly, solvent electric field effects are responsible for these findings as has been discussed previously.^[27,28] It could be that these solvent electric field effects also influence the low-field ¹H NMR chemical shifts.

We come now to the determination of the empirical correction terms c^D and d^D for the ODN hydrogen bonds by NMR. They were derived by adjusting the calculated secondary H/D isotope effects $\Delta\delta(\text{ODN})$ and primary isotope effects $\Delta\delta(\text{ODN})$ as a function of the ¹⁵N chemical shifts as illustrated in Figure 5a and b. The values of $\Delta\delta(\text{ODN})$ change sign when H is moved across the hydrogen-bond center; the absolute maximum and minimum values of $\Delta\delta(\text{ODN})$ are the same. By contrast, the absolute values of $\Delta\delta(\text{ODN})$ in two minima are unequal. This effect arises mainly from the smaller variation of the hydron chemical shifts with the distance from the hydrogen-bond center when the proton is closer to nitrogen compared with oxygen, that is, because of the different slopes of the ¹H versus ¹⁵N curves depicted in Figure 4c. The graphs of Figure 5a and b represent the NMR analogues of the corresponding graphs of the geometric isotope effects depicted in Figure 5c and d which exhibit only slight asymmetries because of the different parameters of OH and HN bonds in Table 1. The “primary” geometric isotope effect describes the different distance of D and H from the hydrogen-bond center. The “secondary” geometric isotope effect describes the change of the hydrogen-bond length upon deuteration. The latter effect is also called the Ubbelohde effect.^[29]

The values of $\Delta\delta(\text{ODN})$ had been obtained previously for collidine–acid complexes in the solid state,^[6a] for freon solution^[19] and for pyridine–acid complexes in freon solution.^[10a] The values observed for pyridine- and collidine–acid complexes in freon coincide within the margin of error. Moreover, in the zwitterionic regime, the values for the complexes in the liquid and the solid state are also very similar. By contrast, in the “molecular complex” regime where H is closer to oxygen absolute smaller isotope effects are observed for the solids. Unfortunately, the origin of the different isotope effects in the liquid and the solid state could not be elucidated in this study.

For the calculation of the dotted lines in Figure 5 we only varied the parameters c^D and d^D as all other parameters were already fixed. c^D mainly influences the curves in Figure 5a and c, and both parameters influence the curves of Figure 5b and d. The liquid state and solid state data are described by two different dotted curves of which the parameters are listed in Table 1. Besides the values of $\Delta\delta(\text{ODN})$ for the quasi-symmetric pyridine–formic acid complex and the [collidine-H-collidine]⁺ cation, the agreement of the calculated curves with the experimental values is quite good.

We note that the correction parameters c^H , d^H , c^D and d^D are very close to those found previously for NHN hydrogen bonds,^[17] where geometric data could directly be analyzed. The agreement gives confidence, that the corresponding

graphs in Figure 5c and d of the geometric H/D isotope effects on the hydrogen bond are close to the reality.

The homoconjugate [collidine-H-collidine]⁺ cation: So far, we have not yet discussed the data points^[25] of the homoconjugate [collidine-H-collidine]⁺ cation represented by open triangles in Figures 4 and 5. Firstly, we would like to note that the ¹H chemical shift of this complex is smaller than expected from the upper dotted correlation line in Figure 4c. Partially, this effect may arise from the fact that we have a NHN rather than an OHN hydrogen bond, but this interpretation seems unlikely. More likely is the interpretation in terms of a larger hydrogen-bond length which implies a barrier for the proton motion. This could be either an intrinsic barrier between two degenerate potential wells of the kind depicted in Figure 2a, or a solvent barrier, where an asymmetric structure of the type depicted in Figure 2d exchanges rapidly with a structure exhibiting a potential corresponding to the mirror image of the one in Figure 2d. As discussed previously,^[17] this interpretation is supported by the observation of a negative primary H/D isotope effect $\Delta\delta(\text{ODN})$ (Figure 5b); this indicates that deuteration increases the hydrogen-bond length, a sign that H is not located in the hydrogen-bond center.

This finding is not in agreement with our treatment which did not take into account two interconverting forms separated by a barrier. Thus, the correction parameters leading to the dotted lines in Figure 5 predict a sign change of $\Delta\delta(\text{ODN})$ for the quasi-symmetric complexes, as expected for systems with single-well potentials in the strongest hydrogen bonds. Such a sign change had been observed for solid complexes exhibiting strong NHN hydrogen bonds,^[17] as well as for systems such as FHF⁻.^[25] Therefore, the calculated values of $\Delta\delta(\text{ODN})$ in Figure 5b deviate from the experimental ones found for freon solution. We did not attempt here to introduce a correction for this effect, in view of the fact discussed in the Theoretical Section that the point approximation breaks down anyway in the case of the values of $\Delta\delta(\text{ODN})$ of very strong hydrogen bonds. However, outside the region of the symmetric hydrogen bonds, the calculated lines in Figure 5b coincide very well with the experimental data, where double wells will not be realized because of the large asymmetries of these complexes.

In order to make further progress in this field, it will be necessary to measure the values of $\Delta\delta(\text{ODN})$ for the symmetric or quasi-symmetric complexes not only for freon solution but also for the solid state. This task is, however, not easy in view of the large quadrupole coupling constant of D, and in view of the smaller gyromagnetic ratio of D compared with H.

H/D Isotopic fractionation in OHN hydrogen bonds: The introduction of the empirical correction terms for anharmonic zero-point vibrations in Equation (4) modifies our previous analysis^[11] of H/D isotopic fractionation according to Figure 6 between pyridine–acid complexes in freon. The dotted lines in Figure 6b were calculated neglecting differences of the zero-point energies in the free OH- and HN-acids and assuming a zero-point energy drop of about 3.5 kJ mol⁻¹

between the free reference states and the strongest OHN hydrogen-bond configuration. Without the correction, only a value of about 2.8 kJ mol^{-1} is obtained.^[11] If the strongest OHN configuration were a classical transition state of a single H transfer reaction, one would expect a kinetic H/D isotope effect at 298 K of $k^{\text{H}}/k^{\text{D}} \approx 4.1$ for the new and of 3.1 for the old value. Generally, even larger values of about 4 kJ mol^{-1} leading to kinetic isotope effects of 5 and more are assumed for this kind of reactions.^[30] From the present analysis it follows that larger kinetic isotope effects than $k^{\text{H}}/k^{\text{D}} \approx 4$ at 298 K will arise from tunneling contributions rather than from the loss of zero-point energy in the transition state.

Conclusion

As in the case of strong NHN hydrogen bonds^[17] we have identified in this paper deviations of the geometries of strong OHN hydrogen bonds from those predicted by the classical valence bond order model. These deviations are associated with anharmonic zero-point vibrations which lead to different geometries of the protonated and deuterated systems. Thus, the classical valence bond order model is strictly valid only for the case of harmonic zero-point vibrations or the equilibrium geometries, that is, for the case of weak hydrogen bonds. The usual parameters of the valence bond order model should be determined for this case. Empirical correction terms are proposed which take into account vibrational anharmonicities and allow one to calculate hydrogen-bond correlations also for strong hydrogen bonds. The correction terms can be taken from the geometries of strong hydrogen bonds. In principle, the correction is different for OHN and ODN systems and can be obtained if appropriate data are available. The corrections also depend on whether a double or a single well potential is realized for strong hydrogen bonds. By establishing correlations between NMR parameters and bond valences it was possible to use NMR chemical shift data to determine H/D isotope effects on the hydrogen-bond geometries in solution. The method may be used in the future to establish hydrogen-bond geometries in biologically relevant functional OHN hydrogen bonds.

Acknowledgement

This research has been supported by the Deutsche Forschungsgemeinschaft, Bonn, the Fonds der Chemischen Industrie (Frankfurt) and the Russian Foundation of Basic Research, grants 03-03-04009 and 03-03-32272. P.M.T. thanks the Fonds for a Kékulé scholarship.

- [1] A. S. Mildvan, M. A. Massiah, T. K. Harris, G. T. Marks, D. H. T. Harrison, C. Viragh, P. M. Reddy, I. Kovach, *J. Mol. Struct.* **2002**, *615*, 163.
 [2] T. K. Harris, A. S. Mildvan, *Proteins Struct. Funct. Genet.* **1999**, *35*, 275.
 [3] A. Novak, *Struct. Bonding (Berlin)* **1974**, *18*, 177.

- [4] a) H. D. Lutz, *Struct. Bonding (Berlin)* **1995**, *82*, 85; b) H. D. Lutz, *J. Mol. Struct.* **2003**, *646*, 227; c) H. D. Lutz, B. Engelen, *Trends Appl. Spectrosc.* **2002**, *4*, 355.
 [5] H. Benedict, H. H. Limbach, M. Wehlan, W. P. Fehlhammer, N. S. Golubev, R. Janoschek, *J. Am. Chem. Soc.* **1998**, *120*, 2939.
 [6] a) P. Lorente, I. G. Shenderovich, N. S. Golubev, G. S. Denisov, G. Buntkowsky, H. H. Limbach, *Magn. Reson. Chem.* **2001**, *39*, S18; b) C. Foces-Foces, A. L. Llamas-Saiz, P. Lorente, N. S. Golubev, H. H. Limbach, *Acta Crystallogr. Sect. C* **1999**, *55*, 377.
 [7] A. McDermott, C. F. Ridenour, *Encyclopedia of NMR* (Eds.: D. M. Grant, R. K. Harris), Wiley, Sussex (UK), **1996**, p. 3820.
 [8] a) U. Sternberg, E. Brunner, *J. Magn. Reson. Ser. A* **1994**, *108*, 142; b) E. Brunner, U. Sternberg, *Progr. Nucl. Magn. Reson. Spectrosc.* **1998**, *32*, 21.
 [9] T. Emmler, S. Gieschler, H. H. Limbach, G. Buntkowsky, *J. Mol. Struct.* **2004**, *700*, 29.
 [10] a) S. N. Smirnov, N. S. Golubev, G. S. Denisov, H. Benedict, P. Schah-Mohammed, H. H. Limbach, *J. Am. Chem. Soc.* **1996**, *118*, 4094; b) N. S. Golubev, S. N. Smirnov, V. A. Gindin, G. S. Denisov, H. Benedict, H. H. Limbach, *J. Am. Chem. Soc.* **1994**, *116*, 12055.
 [11] S. N. Smirnov, H. Benedict, N. S. Golubev, G. S. Denisov, M. M. Kreevoy, R. L. Schowen, H. H. Limbach, *Can. J. Chem.* **1999**, *77*, 943.
 [12] I. G. Shenderovich, P. M. Tolstoy, N. S. Golubev, S. N. Smirnov, G. S. Denisov, H. H. Limbach, *J. Am. Chem. Soc.* **2003**, *125*, 11710.
 [13] L. Pauling, *J. Am. Chem. Soc.* **1947**, *69*, 542.
 [14] I. D. Brown, *Acta Crystallogr. Sect. B* **1992**, *48*, 553.
 [15] a) T. Steiner, W. Saenger, *J. Am. Chem. Soc.* **1992**, *114*, 7123; b) T. Steiner, W. Saenger, *Acta Crystallogr. Sect. B* **1994**, *50*, 348; c) T. Steiner, *J. Chem. Soc. Chem. Commun.* **1995**, 1331; d) T. Steiner, *J. Phys. Chem. A* **1998**, *102*, 7041; e) T. Steiner, *Angew. Chem.* **2002**, *114*, 50; *Angew. Chem. Int. Ed.* **2002**, *41*, 48.
 [16] S. J. Grabowski, *J. Mol. Struct.* **2000**, *552*, 153.
 [17] H. H. Limbach, M. Pietrzak, H. Benedict, P. M. Tolstoy, N. S. Golubev, G. S. Denisov, *J. Mol. Struct.* **2004**, in press.
 [18] a) T. Steiner, I. Majerz, C. C. Wilson, *Angew. Chem.* **2001**, *113*, 2728; *Angew. Chem. Int. Ed.* **2001**, *40*, 2651; b) T. Steiner, C. C. Wilson, I. Majerz, *Chem. Commun.* **2000**, 1231.
 [19] P. M. Tolstoy, S. N. Smirnov, I. G. Shenderovich, N. S. Golubev, G. S. Denisov, H. H. Limbach, *J. Mol. Struct.* **2004**, *700*, 19.
 [20] a) J. Almlöf, *Chem. Phys. Lett.* **1972**, *17*, 49; b) I. G. Shenderovich, H. H. Limbach, S. N. Smirnov, P. M. Tolstoy, G. S. Denisov, N. S. Golubev, *Phys. Chem. Chem. Phys.* **2002**, *4*, 5488.
 [21] a) K. Kawaguchi, E. Hirota, *J. Chem. Phys.* **1987**, *87*, 6838; b) K. Kawaguchi, E. Hirota, *J. Mol. Struct.* **1995**, *352*, 389.
 [22] N. S. Golubev, S. M. Melikova, D. N. Shchepkin, I. G. Shenderovich, P. M. Tolstoy, G. S. Denisov, *Z. Phys. Chem. (Muenchen Ger.)* **2003**, *217*, 1549.
 [23] Solid NH_4Cl has been shown to resonate at -341.168 ppm with respect to external liquid nitromethane by S. Hayashi, K. Hayamizu, *Bull. Chem. Soc. Jpn.* **1991**, *64*, 688.
 [24] I. G. Shenderovich, G. Buntkowsky, A. Schreiber, E. Gedat, S. Sharif, J. Albrecht, N. S. Golubev, G. H. Findenegg, H. H. Limbach, *J. Phys. Chem. B* **2003**, *107*, 11924.
 [25] P. Schah-Mohammed, I. G. Shenderovich, C. Detering, H. H. Limbach, P. M. Tolstoy, S. N. Smirnov, G. S. Denisov, N. S. Golubev, *J. Am. Chem. Soc.* **2000**, *122*, 12878, and references therein.
 [26] P. M. Tolstoy, P. Schah-Mohammed, S. N. Smirnov, N. S. Golubev, G. S. Denisov, H. H. Limbach, *J. Am. Chem. Soc.* **2004**, *126*, 5621.
 [27] M. Ramos, I. Alkorta, J. Elguero, N. S. Golubev, G. S. Denisov, H. Benedict, H. H. Limbach, *J. Phys. Chem. A* **1997**, *101*, 9791.
 [28] J. E. Del Bene, M. J. T. Jordan, *J. Phys. Chem. A* **2002**, *106*, 5385.
 [29] a) A. R. Ubbelohde, K. G. Gallagher, *Acta Crystallogr.* **1955**, *8*, 71; b) A. C. Legon, D. J. Millen, *Chem. Phys. Lett.* **1988**, *147*, 484; c) N. D. Sokolov, V. A. Savel'ev, *Chem. Phys.* **1977**, *22*, 383; d) N. D. Sokolov, V. A. Savel'ev, *Chem. Phys.* **1994**, *181*, 305.
 [30] L. Melander, W. H. Saunders, *Reaction Rates of Isotopic Molecules*, New York, Toronto, Wiley, **1980**.

Received: March 4, 2004

Published online: September 9, 2004