Geometrical Features of Hydrogen Bonded Complexes Involving Sterically Hindered Pyridines

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The ability of strongly sterically hindered pyridines to form hydrogen bonded complexes was inspected using low-temperature ^{1}H and ^{15}N NMR spectroscopy in a liquefied Freon mixture. The proton acceptors were 2,6-di(tert-butyl)-4-methyl- and 2,6-di(tert-butyl)-4-diethylaminopyridine; the proton donors were hydrogen tetrafluoroborate, hydrogen chloride, and hydrogen fluoride. The presence of the tert-butyl groups in the ortho positions dramatically perturbed the geometry of the forming hydrogen bonds. As revealed by experiment, the studied crowded pyridines could form hydrogen bonded complexes with proton donors exclusively through their protonation. Even the strongest small proton acceptor, anion F^-, could not be received by the protonated base. Instead, the simplest hydrogen bonded complex involved the $[FHF]^-$ anion. This complex was characterized by the shortest possible N···F distance of about 2.8 Å. Because the ortho tert-butyl groups did not prevent the hydrogen bond interaction between the protonated center and the anion completely, an increase of the pyridine basicity caused a further shortening of the N−H distance and a weakening of the hydrogen bond to the counterion.

Introduction

Sterically hindered bases provide a specific selectivity toward proton transfer from different acidic species based on the steric interference of their bulky substitutes and the proton donor molecules. Due to this selectivity, 2,6-substituted pyridines are effectively used as proton scavengers in organic synthesis, for example in living or controlled polymerization, to suppress the concentration of protic impurities.[1,2] However, the ability of these molecules to form hydrogen bonds of the molecular type is still under discussion as is the role of bulky ortho-substituents in proton-transfer processes.

The proton acceptor ability of the ortho-substituted pyridines causes much attention due to huge variety in the values measured at different conditions. The anomalously low basicity of 2,6-di(tert-butyl)-substituted pyridines (DTBP) was first noted by Brown and Kanner.[3] Namely, for DTBP itself, they observed $pK_a = 3.58$, whereas the value expected from its gas-phase proton affinity was 4.98. The reduced basicity, attributed to the incapability of tert-butyl groups to minimize steric strains, resulted both in preventing the base protonation and crowding of the proton in the protonated ion. This suggestion was argued later by several authors. Arnett and Chawla[4] showed that although DTBP was protonated by HCl and trifluoroacetic acid, the base and its conjugated acid, the $[DTBP-H]^+$ cation, were precluded from hydrogen bond interaction with water. Indeed, DTBP differs markedly from the other pyridines in all ionization and hydration properties in water. Additional studies on the basicities of these pyridines in a variety of alcohol−water mixtures also proved that the basicity of DTBP was lower than expected, probably due to steric inhibition of solvation of the $[DTBP-H]^+$ cation.[5] Furthermore, Hopkins et al.[6] studied the thermodynamics of 2,6-substituted pyridines protonation and concluded that a hydrogen-bonded complex between water and DTBP could exist in the gas and the aqueous phase, but the barriers to internal rotation of the water molecule and the tert-butyl groups in the complex were substantial. The enthalpy of solvation of the $[DTBP-H]^+$ cation is not affected appreciably in magnitude by steric requirements, but the entropy of the cation in the aqueous environments is markedly reduced by steric interactions. Several studies were carried out on kinetic aspects of DTBP protonation.[7] Jasinski and Brauman[8] showed that the rates of proton transfer between acids and DTBP were much lower than the same rates for the other substituted pyridines.

In this study, we concentrated on developing an understanding of how the sterical hindrance and the proton acceptor ability of crowded pyridines affect geometry of hydrogen bonded complexes formed between these bases and acids in an aprotic polar solvent. The main question to be addressed by this research is whether crowded pyridines can form hydrogen bond of the molecular type. The question also arises about the inner size of the cavity formed by bulky ortho tert-butyls. It is not a priori clear whether small anions can enter inside the cavity to form a short hydrogen bond with the protonated nitrogen. Another question is whether the bulky substitutes can slow proton exchange with the environment. Hydrofluoric acid was chosen as the most suitable proton donor. Previously, the hydrogen bonded complexes between 2,4,6-trimethylpyridine (collidine) and HF formed in a highly polar aprotic mixture of liquefied Freons were characterized by some of us.[9,10] The influence of

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the proton transfer from F to N on the NMR parameters was described in details. These studies indicated that HF can hardly protonate DTBP in their 1:1 complex.

Here, we have applied the same method to study hydrogen bonded complexes involving the bulky ortho-substituted pyridines. For this purpose ^{15}N enriched 2,6-di(tert-butyl)-4-methylpyridine (MDTBP) and 2,6-di(tert-butyl)-4-diethylaminopyridine (NDTBP) were synthesized. These pyridines are potentially very basic. SciFinder reports for these pyridines the predicted pK_a values of 6.9 and 11.1, respectively.[11] At the same time, the bulky ortho-substituents restrict strongly the accessibility of the nitrogen for proton donors that might considerably change the hydrogen bonds geometry.

The scope of this paper is, therefore, to describe the effect of the ortho groups on the distance between the base and acid molecules and their ability to protect the protonated base from close contact with proton acceptors.

Experimental Section

Synthesis of 2,6-Di(tert-butyl)-4-methylpyridine: ^{15}N-enriched 2,6-di(tert-butyl)-4-methylpyridine (MDTBP) was synthesized from 95% ^{15}N-enriched NH_4Cl (Deutero) and corresponding pyrylium salt. 2,6-Di(tert-butyl)-4-methylpyrylium triflate was obtained according to ref 12. Then pyrylium salt (11.5 g, 0.033 mol) was dissolved in water (200 mL) in an Erlenmeyer flask. The mixture was heated at 30 °C for 40 min. Ammonium chloride (1.7 g, 0.031 mol) and sodium hydroxide (2.5 g, 0.062 mol) aqueous solutions were added into the hot mixture consecutively. The reaction mixture was heated further for 1 h at 60 °C. The resulting yellow solution was extracted with 6 portions of pentane (50 mL) and dried over magnesium sulfate. Pentane was removed on a rotary evaporator. The residual light yellow oil was chromatographed on an activated alumina column using pentane as an eluent. Removal of pentane yielded 62% of a colorless oil (4 g, 0.02 mol), which formed thin long needles on cooling. All ingredients were supplied by Aldrich, if not stated otherwise.

Synthesis of 2,6-Di(tert-butyl)-4-diethylaminopyridine: ^{15}N-enriched 2,6-di(tert-butyl)-4-diethylaminopyridine (NDTBP) was prepared by a seven step synthesis[13] including formation of α-oxoketene dithioactal, 2,2,8,8-tetramethyl-5-methylthio-4-nonan-1,5-dion, 2,6-di(tert-butyl)-4(methylthio)pyrylium tetrafluoroborate, and 2,6-di(tert-butyl)-4-diethylaminopyrylium tetrafluoroborate. The pyrylium salt was treated with aqueous ^{15}N ammonia (25%) in ethanol yielding 60% of corresponding pyridine. Aqueous ^{15}N enriched ammonia solution was prepared from^{15}N labeled ammonium chloride (Deutero) in a Clasius retrograding modified gas-development apparatus. Pinacolone was supplied by Aldrich, iodomethane by Merck, all other ingredients for synthesis by Acros.

NMR Samples Preparation. To prepare the NMR samples, an excess of HF (40% aqueous solution, Aldrich) was added to the bases dissolved in dichloromethane, using a Teflon flask. Water and dichloromethane were removed by repeated azeotropic distillation leaving a solid product. Due to high volatility of MDTBP, the base−HF ratio was varied by addition of the graduated amounts of the base to the former solid product. To prepare the complex with excess of NDTBP 40% aqueous solution HF was added to the excess of base in dichloromethane. All solvents were removed as described above. Then the solid product was placed in an NMR sample tube equipped with a Teflon valve (Wilmad) and cooled to 77 K to prevent reaction with the glass. The tube was connected to a high vacuum line, and Freon was added by vacuum transfer.

MDTBP/HCl samples were prepared by mixing of MDTBP solution in dichloromethane (2 mg/mL) and 0.1 M aqueous solution of HCl in 1:1 molar ratios. Water and dichloromethane were removed by repeated azeotropic distillation as described above for HF complexes. The same procedure was used for preparing the samples with HBF_4.

The solvent mixture $CDF_3/CDClF_2$ for low-temperature NMR experiments whose composition varied between 1:2 and 1:3 was prepared by a modified recipe proposed by Siegel et al.[14] According to the latter method, the chlorines of chloroform-*d* can be exchanged for fluorine at atmospheric pressure using antimony(III) fluoride as fluorinating agent and antimony(V) chloride as a catalyst.

NMR Measurement. NMR spectra were recorded on a Bruker AMX-500 spectrometer supplied with low-temperature probeheads. The ^{1}H chemical shifts were measured using the CHF_3 peaks as internal references and then converted into the conventional TMS scale. The ^{15}N chemical shifts were referenced to the free base.

Results

The identification of the structure of hydrogen bonded complexes formed between bases and acids in solution using NMR spectroscopy becomes much easier when a fast hydrogen bond and proton exchange between different species is suppressed. Experimentally, this can be achieved by lowering the temperature. Substantial progress has been achieved in recent years by using liquefied deuterated $CDF_3/CDClF_2$ gas mixtures as NMR solvents which are fluid enough to allow high-resolution NMR measurements down to 100 K when the regime of a slow hydrogen bond exchange can be reached for certain hydrogen bonded systems. The NMR spectral parameters are then characteristic for the individual hydrogen bonded sites although they still present averages over fast exchanging solvent configurations. Usually, the fast hydrogen bond and proton exchange is promoted by water traces which freeze out below 170 K. For the studied ortho-substituted pyridines, the slow exchange regime was achieved in $CDF_3/CDClF_2$ Freon mixture already at 200 K because of an extremely weak interaction of the employed pyridines with the residual water presented in the solution. In fact, these substances were not soluble in water.

At the same time, NMR spectra of MDTBP and NDTBP solution in dichloromethane are sensitive to the presence of water due to weak interactions between the base and water. However, water precipitated from the solution upon cooling. Thus, the crowded pyridines were able to interact with water but unable to trap a proton or water molecule from water clusters.

MDTBP−HBF$_4$ Complexes. Bulky fluoroboric acid is one of the most suitable proton donors to analyze properties of practically unperturbed protonated bases. One does not expect that $[BF_4]^-$ may specifically interact with the corresponding cation, especially in the case of ortho-substituted pyridines. At room temperature, a ^{1}H NMR spectrum of a MDTBP/HBF_4 solution prepared with an excess of the base displayed a fast proton exchange between free and protonated pyridine. This exchange became slow in the NMR time scale at 200 K. At this temperature, there were two sets of peaks that corresponded to free and protonated pyridine molecules. The peaks of the nonexchangeable protons of protonated pyridine were shifted low-field as compared to free pyridine (Figure 1a). The mobile proton in $[MDTBP-H]^+$ resonated at 11.27 ppm and was split into a doublet with $J = 91$ Hz. Upon cooling, free pyridine precipitated from solution. Thus, at 130 K, the mixture contained

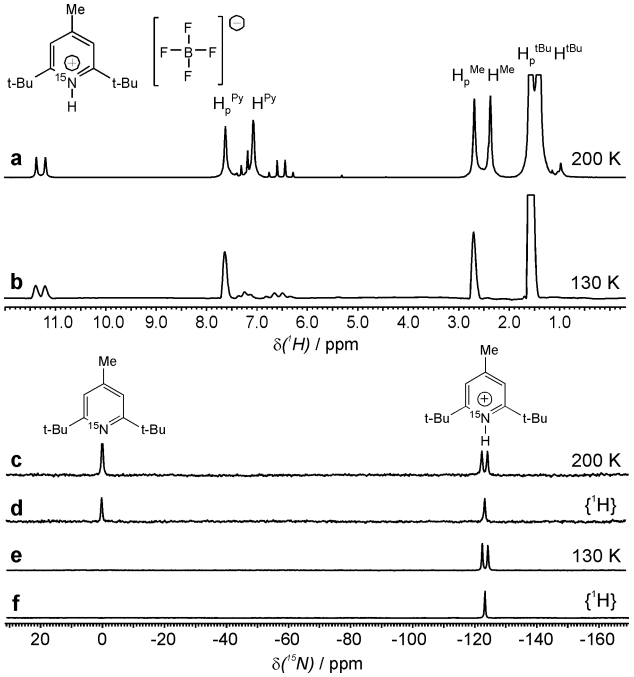

Figure 1. ^{1}H and ^{15}N NMR spectra of MDTBP/HBF_4 mixture in CDF_3/$CDClF_2$ solution at excess of MDTBP. (a) and (b) ^{1}H NMR spectra at 200 and 130 K, respectively; (c) and (d) ^{15}N NMR spectra at 200 K with and without proton decoupling, respectively; (e) and (f) the same spectra at 130 K. ^{1}H peaks belonging to the protonated form of MDTBP are labeled as H_p. ^{15}N spectra are referenced to free MDTBP.

exclusively $[MDTBP-H]^+$ species (Figure 1b). The position and splitting of the $[N-H]^+$ proton peak did not vary with temperature within the experimental errors.

A ^{15}N NMR spectrum of the same MDTBP/HBF_4 mixture obtained at 200 K contained a singlet of free MDTBP referenced to 0 ppm and a doublet of $[MDTBP-H]^+$ with $J = 91$ Hz shifted to -124 ppm (Figure 1c). Proton decoupling converted the latter doublet to a singlet (Figure 1d). At 130 K, the singlet of free MDTBP was absent whereas the splitting and chemical shift of the doublet of $[MDTBP-H]^+$, or the corresponding singlet when proton decoupling was used, stayed constant within the margin of experimental errors (Figure 1e,f).

MDTBP−HCl Complexes. Hydrogen chloride is a strong acid and one expects protonation of pyridine upon the hydrogen bond formation. ^{1}H and ^{15}N NMR spectra of MDTBP/HCl mixture in Freon at low temperatures are displayed in Figure 2. In the low-field part of the proton spectra we observed a doublet around 12.9 ppm with $J = 91$ Hz. The chemical shift of the doublet slightly depended on temperature. At 140 K, it was shifted to 12.5 ppm. In contrast, the chemical shift of a singlet at -117 ppm in the corresponding ^{15}N NMR spectra obtained with proton decoupling did not vary with temperature within the experimental errors (Figure 2d,e).

MDTBP−HF Complexes. Figure 3 gives an overview of the temperature-dependent ^{1}H NMR spectra of MDTBP/HF mixture in Freon at different base/acid ratios. When the mixture contained an excess of MDTBP, a combination of a triplet and doublet dominated in the whole temperature interval between 200 and 140 K. At 200 K, these signals were especially well resolved (Figure 3a). The triplet was at 16.26 ppm with $J = 142$ Hz and the doublet was at 15.44 ppm with $J = 88$ Hz. Upon cooling, the signals became broader. The doublet was monotonically shifting to high field and the triplet was shifting to low field. The coupling constant of the triplet was slightly decreasing upon cooling.

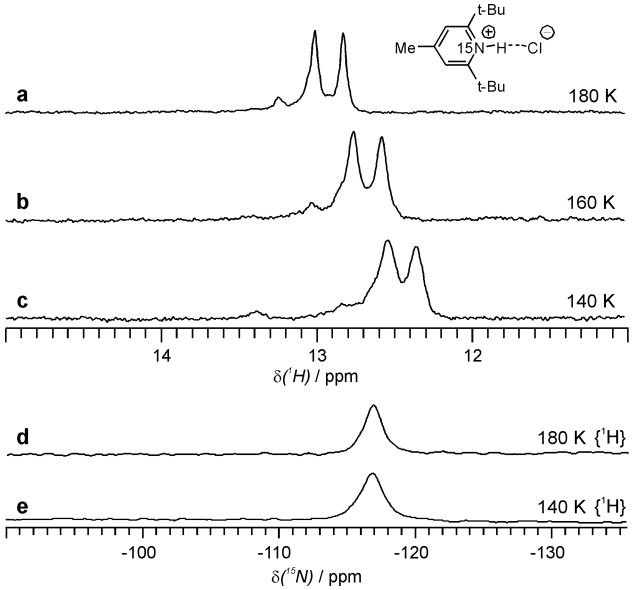

Figure 2. ^{1}H and ^{15}N NMR spectra of MDTBP/HCl mixture in CDF_3/$CDClF_2$ solution. (a), (b), and (c) ^{1}H NMR spectra at 180, 160, and 140 K, respectively; (d) and (e) ^{15}N NMR spectra with proton decoupling at 180 and 140 K, respectively. ^{15}N spectra are referenced to free MDTBP.

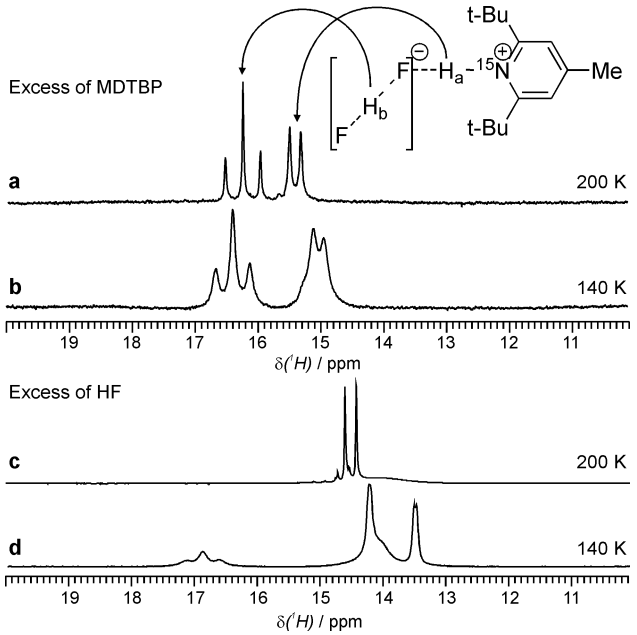

Figure 3. Low-field ^{1}H NMR signals of the hydrogen bond proton of various complexes between MDTBP and HF in CDF_3/$CDClF_2$ solution. (a) and (b) Spectra of a sample containing MDTBP in excess at 200 and 140 K, respectively; (c) and (d) spectra of a sample containing HF in excess at 200 and 140 K, respectively.

When the mixture contained an excess of HF, at 200 K a doublet at 14.48 ppm with a coupling constant J of 91 Hz dominated in the spectrum (Figure 3c). Upon cooling (Figure 3d) this doublet disappeared. Instead, at 140 K, the low field part of the spectrum contained badly resolved signals that were broadened by some moderately slow exchange.

NDTBP−HBF_4 Complexes. ^{1}H and ^{15}N NMR spectra obtained for a NDTBP/HBF_4 mixture prepared with an excess of the base strongly resembled the corresponding spectra of the MDTBP/HBF_4 mixture. A fast proton exchange between free and protonated pyridine molecules became slow in the NMR time scale at 200 K. The mobile proton in $[NDTBP-H]^+$

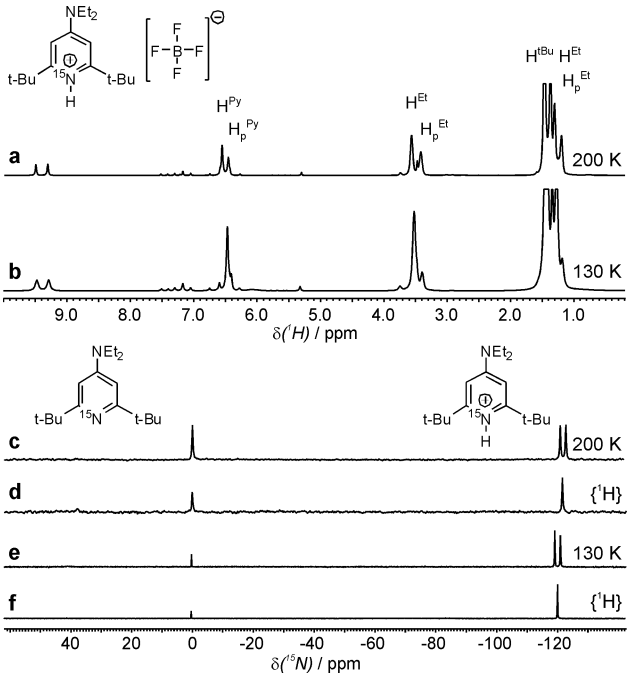

Figure 4. ^{1}H and ^{15}N NMR spectra of NDTBP/HBF_4 mixture in CDF_3/$CDClF_2$ solution at excess of NDTBP. (a) and (b) ^{1}H NMR spectra at 200 and 130 K, respectively; (c) and (d) ^{15}N NMR spectra at 200 K without and with proton decoupling, respectively; (e) and (f) the same spectra at 130 K. ^{1}H peaks belonging to the protonated form of NDTBP are labeled as H_p. ^{15}N spectra are referenced to free NDTBP.

resonated at 9.40 ppm and was split into a doublet with $J = 94$ Hz (Figure 4a). The position and splitting of this peak did not depend on temperature (Figure 4b).

Free NDTBP did not precipitate completely at low temperatures. Thus, the temperature dependence of the ^{15}N chemical shifts of the $[NDTBP-H]^+$ doublet relative to the ^{15}N chemical shift of free base could be measured precisely in this case. At 200 K, the ^{15}N spectrum displayed a singlet of free NDTBP referenced to 0 ppm and a doublet of $[NDTBP-H]^+$ with $J =$ 94 Hz shifted to -122.7 ppm (Figure 4c). At 130 K, the doublet of $[NDTBP-H]^+$ was shifted to -120 ppm as compared to the position of free NDTBP at the same temperature (Figure 4e). In contrast, the coupling constant of the doublet did not vary with temperature within the experimental errors. Proton decoupling converted the doublets to singlets at both temperatures (Figure 4d,f).

NDTBP−HF Complexes. Figures 5a−d display the low field parts of the ^{1}H NMR spectra of two samples of NDTBP/HF mixtures. The spectra were grouped into two series. Figures 5a−b present the ^{1}H NMR of a sample prepared with an excess of pyridine and Figures 5c−d of that prepared with an excess of HF. In all spectra, a doublet−triplet pair dominated. As well as for MDTBP/HF mixtures, the spectra of the mixture contained an excess of NDTBP were the simplest. At 200 K, the triplet with $J = 132$ Hz was observed at 16.54 ppm. The chemical shift and the coupling constant of the triplet depended only slightly on temperature and acid/base ratio. The doublet which was at 13.17 ppm at 200 K was shifted to 12.50 ppm at 140 K. Its coupling constant was about 94 Hz.

At 200 K, the ^{1}H spectra of the mixture contained HF in excess exhibited a triplet at 16.66 ppm with $J = 132$ Hz and a doublet with $J = 94$ Hz at 12.62 ppm (Figure 5c). Upon cooling, the doublet was shifted to high field to 11.64 ppm at 140 K. Besides the triplet−doublet pair at 140 K, the doublet of doublets was stabilized at 14.11 ppm with $J = 358$ and 21 Hz.

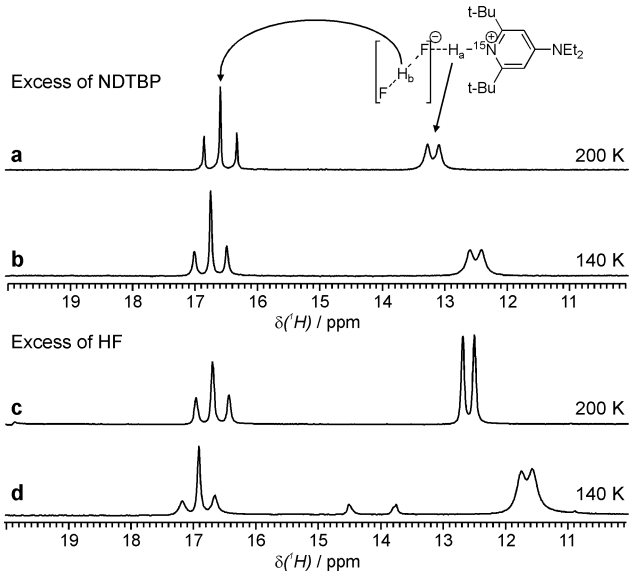

Figure 5. Low-field ^{1}H NMR signals of the hydrogen bond protons of $[NDTBP-H]^+[FHF]^-$ complex in CDF_3/$CDClF_2$ solution. (a) and (b) Spectra of a sample containing NDTBP in excess at 200 and 140 K, respectively; (c) and (d) spectra of a sample containing HF in excess at 200 and 140 K, respectively.

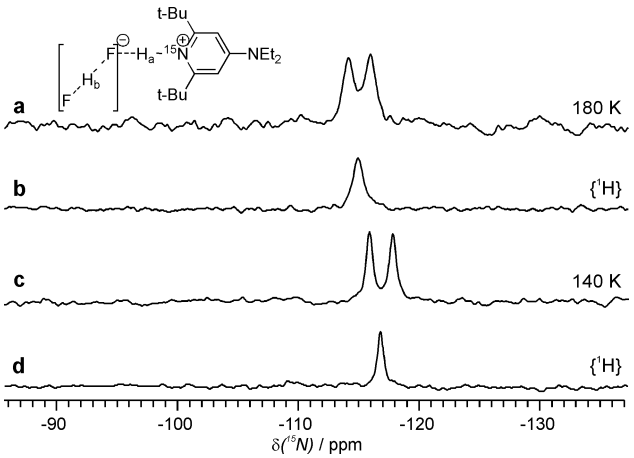

Figure 6. ^{15}N NMR signals of $[NDTBP-H]^+[FHF]^-$ complex in CDF_3/$CDClF_2$ solution. The sample contains an excess of HF. (a) At 180 K without proton decoupling; (b) at 180 K with proton decoupling; (c) at 140 K without proton decoupling; (d) at 140 K with proton decoupling. ^{15}N spectra are referenced to free NDTBP.

^{15}N NMR spectra for the sample with an excess of HF are shown in Figure 6. The doublet at -115 ppm with J of 94 Hz was changed to a singlet when the proton decoupling was applied. The signals were shifted slightly to the high field upon cooling.

Discussion

First we need to discuss why NMR parameters of hydrogen bonded complexes depend on temperature. Recently, this problem was investigated in details by some of us.[15] The electric dipoles of the individual solvent molecules create a temperature-dependent effective electric field at the solute site. This field is larger at low temperatures, when the dipoles are ordered, and smaller at high temperatures, when they are more disordered. As a consequence, the temperature-dependent electric field induces in the solute a dipole moment which increases as the temperature is lowered. In other words, the increasing electric field of the solvent polarizes the hydrogen bridge. In a molecular

complex A−H···B exhibiting a relatively small permanent electric dipole moment the latter can only be enhanced by charge transfer. The energy for the charge separation is provided by the electric field; this energy is minimized by a contraction of the hydrogen bond. In other words, a molecular complex A−H···B contracts in the presence of an electric field. This contraction is accompanied by a displacement of the proton toward B. Once the proton has crossed the point at which it interacts equally with A and B, an increase of the dipole moment is achieved by a further displacement of the proton toward B, accompanied by an increase of the A···B distance.[16,17] Thus, temperature dependence of NMR parameters of hydrogen bonded complexes directly reflects changes in their geometry.

For the studied complexes, we have used three NMR parameters sensitive to hydrogen bond geometry, namely, the ^{1}H and ^{15}N chemical shifts and $^1J(^{15}\text{N-H})$ scalar coupling constant. The dependence of the ^{1}H chemical shift on the hydrogen bond length was inspected experimentally and theoretically for individual hydrogen bonded complexes whose geometries were changed due to a variation of external electric field.[9,15,18] Upon an increase of the solvent dielectric constant, NMR spectra indicated a gradual transformation of an asymmetric molecular complex A−H···B to a quasi-symmetric complex $A^{\delta-}\cdot\cdot H\cdot\cdot B^{\delta+}$ and eventually to an ionic species $A^-\cdot\cdot\cdot H-B^+$. As a result, while the dielectric constant was increased the proton signal first shifted to low field, went through a maximum and then shifted back to high field. Correlation between the isotropic ^{15}N chemical shift of pyridines and the N···H bond length was established experimentally on a series of hydrogen-bonded solid 1:1 acid−base complexes of ^{15}N-labeled collidine with carboxylic acids.[19] Upon contraction of the N···H bond the ^{15}N chemical shift of the base monotonically shifted to the high field by 120−130 ppm as compared to the free base. This correlation was successfully used later to evaluate hydrogen bond geometries in more complicated systems. In liquid solutions a contraction of the N···H bond resulted as well in an increase of the $^1J(^{15}\text{N}-^1\text{H})$ scalar coupling constant value up to ca. 100 Hz for protonated pyridines.[20]

Now we are ready to summarize the most obvious conclusions following from the experimental results. Bulky $[BF_4]^-$ anion did not perturb the $[N-H]^+$ bonds of protonated ortho tert-butyl substituted pyridines. As a result the corresponding ^{1}H and ^{15}N chemical shifts did not depend practically on temperature. Thus, the proton of "free" $[MDTBP-H]^+$ resonated at 11.27 ppm and was split into a doublet with $^1J(^{15}\text{N}-^1\text{H}) = 91$ Hz. The ^{15}N nucleus resonated at −124 ppm as compared to free base. The proton chemical shift of unperturbed $[NDTBP-H]^+$ was smaller and the ^{1}H-^{15}N coupling constant was bigger as compared to $[MDTBP-H]^+$, 9.4 ppm and 94 Hz, respectively. The ^{15}N chemical shift of free NDTBP depended slightly on temperature. The difference between the chemical shifts of free and protonated forms was reduced from 122.7 ppm at 200 K to 120 ppm at 130 K. We assume that these features were connected to electrostatic interactions of the nitrogen of the diethylamino-group in the para position with solvent molecules.

When HCl was used instead of HBF_4, the $[N-H]^+$ bond became perturbed. The ^{1}H chemical shift of $[MDTBP-H]^+$ increased and became temperature dependent indicating that Cl^- was hydrogen bonded to pyridinium. The ^{1}H chemical shift value slightly decreased upon cooling. This trend indicated a weakening of the $[N-H]^+\cdot\cdot\cdot Cl^-$ interaction due to an increase of the solvent polarity and proved that the hydrogen bond was of the ionic type. We did not observe the presence of $[ClHCl]^-$ that was described earlier by Brown and Kanner.[3] If this complex would be stable on the NMR time scale, an additional singlet should be seen in the proton spectra. It is worth to remind that the 1:1 hydrogen bonded complex formed between ^{15}N-labeled pyridine and HCl in the aprotic Freon mixture was described in details earlier (Figure 7).[21] The chemical shift of the bonding proton in this complex showed the same trend upon cooling. However, the values of the chemical shifts were much higher. The corresponding signal was at 18.3 ppm at 251 K and moved to 17.1 ppm at 107 K. Pyridine is a weaker base as compared to MDTBP. As a result, the hydrogen bond formed by pyridinium cation with Cl^- anion was relatively strong. One was even able to observe the temperature dependence of the $^1J(^{15}\text{N}-^1\text{H})$ coupling constant. In contrast, the interaction between $[MDTBP-H]^+$ and Cl^- was much weaker. The binding proton resonated below 13 ppm and the $^1J(^{15}\text{N}-^1\text{H})$ coupling constant did not depend on temperature any more.

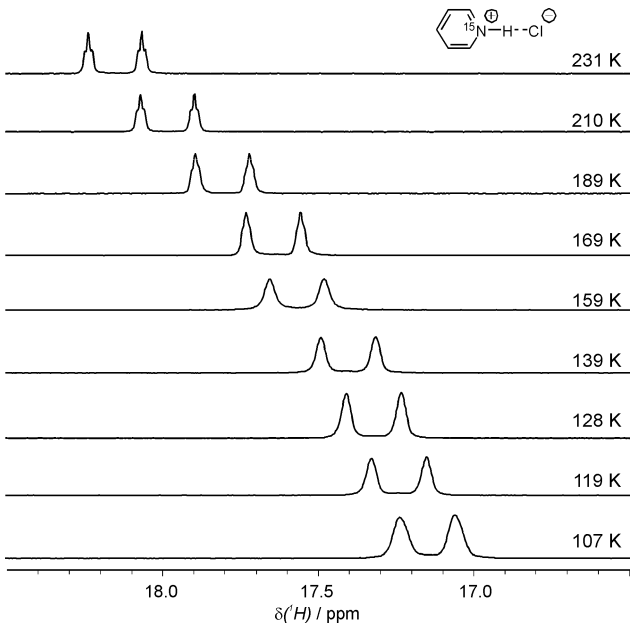

Figure 7. Temperature-dependent NMR signals of the hydrogen bond proton in 1:1 complex of pyridine−^{15}N with hydrochloric acid (0.2 M) in $CDF_3/CDClF_2$ solution. The sample contained a 10% excess of pyridine−^{15}N.[21]

Hydrogen fluoride was one of the smallest proton donors available. One can expect that the steric hindrance of the nitrogen of DTBP due to the ortho tert-butyl groups might be insufficient to prevent the formation of different $DTBP\cdot\cdot\cdot(HF)_n$ complexes depending on the acid/base ratio. However in most cases a combination of a triplet and doublet dominated in the whole temperature interval in ^{1}H NMR spectra of MDTBP and NDTBP mixtures with HF regardless of the acid/base ratio. Therefore, in the analysis described below we focused especially on this topic. The most important information extracted from the experimental data is collected in Table 1.

HF Complexes with a Sterically Unprotected Active Site. To interpret the new findings, we first consider in Figure 8 hydrogen bonded complexes which HF forms with a much less crowded pyridine derivative, namely 2,4,6-trimethylpyridine (collidine, Col), described in detail recently.[9,10,22−26] The multinuclear low-temperature NMR experiments and analysis of the scalar ^{19}F−^{1}H, ^{1}H−^{15}N, and ^{19}F−^{15}N couplings revealed the chemical structure of several stable collidine(^{15}N)−HF hydrogen bonded complexes which were formed in aprotic solvent. The spectral patterns of the following complexes: ColHF, $ColH^+$-$[FHF]^-$, $[ColHFHCol]^+[FHF]^-$, and $[ColH]^+[F(HF)_2]^-$ as well as $[FHF]^-$, $[F(HF)_2]^-$, and $[F(HF)_3]^-$ were observed and

TABLE 1: Selected Parameters of the FHF, NHF, and NHCl Hydrogen Bonds of $[F(HF)_n]^-$, $Col(HF)_n$, $MDTBP(HF)_n$, MDTBP−HCl, $MDTBP-HBF_4$, $NDTBP(HF)_n$, and $NDTBP-HBF_4$ Clusters in $CDF_3/CDClF_2$

species	BHA	T/K[b]	$\lvert^1J_{BH}\rvert$/Hz	$\lvert^1J_{HA}\rvert$/Hz	δ_H/ppm[c]	δ_N/ppm[c]	r_{BH}/Å	r_{HA}/Å
$[FHF]^-$[a]	FHF	130	124	124	16.60	−	1.148	1.148
$F^-(HF)_2$[a]	FHF	130	24.5	354	14.015	−	1.349	1.012
$F^-(HF)_3$[a]	FHF	130	45	430	11.79	−	1.451	0.979
ColHFHF[a]	FHF	130	145	145	15.55	−	−	−
$ColHF(HF)_2$[a]	FHF	130	38	400	12.9	−	1.46	0.98
ColHF[a]	NHF	180	39	88	19.4		1.24	1.17
ColHF[a]	NHF	130	51	15	20.10	−67	1.18	1.24
ColHF[a]	NHF	112	55	−	20.12	−	1.15	1.29
$[ColHFHCol]^+$[a]	NHF	120	75	71	18.40	−88	1.08	1.46
$Col(HF)_2$[a]	NHF	120	86	75	16.69	−94	1.05	1.61
$Col(HF)_3$[a]	NHF	130	90	45	15.09	−99	1.02	1.85
$ColHBF_4$[d]	NH^+[e]	130	92	−	13.01	−	<1.02	
$MDTBP(HF)_2$	FHF	200	142	142	16.26	−		
$MDTBP(HF)_2$	NHF	200	88	−	15.44	−	∼1.03	∼1.77
MDTBP(HCl)	NHCl	200	91	−	12.90	−117	<1.02	
$MDTBP(HBF_4)$	NH^+[e]	200	91	−	11.27	−124	<1.02	
$NDTBP(HF)_2$	FHF	200	132	132	16.54	−		
$NDTBP(HF)_2$	NHF	200	94	−	13.17	−114	<1.02	>1.85
$NDTBP(HBF_4)$	NH^+[e]	200	94	−	9.40	−123	<1.02	

[a] Data adapted from ref 10; theoretical analysis of NMR and geometrical parameters for the same complexes can be found in refs 23−26. [b] Dielectric constant of the $CDF_3/CDClF_2$ mixture is a function of temperature and solvent composition. [c] Chemical shifts are measured with respect to TMS (^{1}H) and free bases (^{15}N) as internal standards. [d] Lesnichin, S.; Shenderovich, I. G.; Limbach, H. H. − unpublished data. [e] These complexes are typical ion pairs.

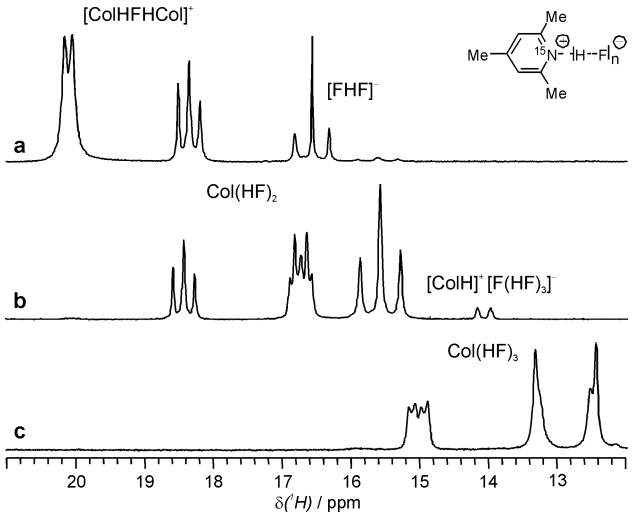

Figure 8. Low-field ^{1}H NMR signals of the hydrogen bond protons of various complexes between collidine and HF in $CDF_3/CDClF_2$ at 120−130 K. The relative concentration of HF increases from (a) to (c). Adapted from ref 10.

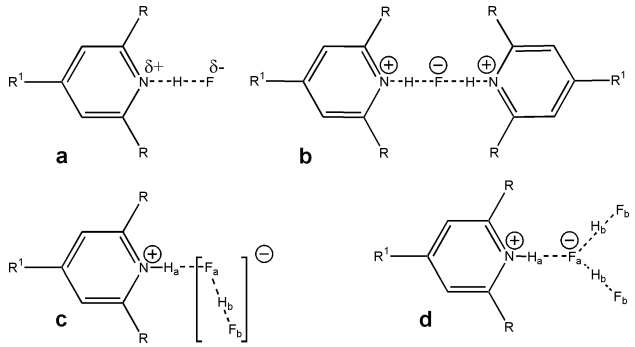

Figure 9. Possible structure of hydrogen bonded complexes between a pyridine derivative and HF. The prediction based on the low-temperature NMR study of complexes between collidine and HF and ab initio studies.[10,23−26] R = Me or ^{t}Bu and R^1 = Me or NEt_2.

assigned.[10,22] The structures of these complexes are drawn in Figure 9 where R = R^1 = Me. ColHF complex (Figure 8a,9a) was characterized by a signal whose ^{1}H chemical shift and splitting are extremely temperature dependent. Upon cooling, the proton was shifted toward the base due to increase of the dielectric constant of Freon.[15] As a result, this signal, which was a doublet with the dominating coupling to fluorine, turned into a quartet at 170 K, into a triplet at 150 K, and finally became a doublet with the dominating coupling to the nitrogen at 120 K. Only the latter spectrum is shown in Figure 8a. The structure of $[ColHFHCol]^+$ gave rise to a doublet of doublets at 18.4 ppm which resembled a triplet since $^1J_{NH} \approx {}^1J_{FH}$ (Figure 8a). Its counterion, free $[FHF]^-$, appeared as a triplet at 16.6 ppm. With excess of the acid, the $ColH^+[FHF]^-$ and $[ColH]^+$-$[F(HF)_2]^-$ species appeared. The former was characterized by a doublet of triplets because of the couplings of H_a with the nitrogen and both fluorine nuclei due to a fast $[FH_bF]^-$ counterion reorientation (Figure 8b,9c). The signal of H_b, which was a triplet due to the averaging of its coupling to the fluorines, was shifted to high field as compared to free $[FHF]^-$ due to the effective asymmetry induced by the counterion. $[ColH]^+[F(HF)_2]^-$ exhibited a doublet of doublets with $^1J_{NH}$ = 90 Hz and $^1J_{HF}$ = 45 Hz (Figure 8c,9d). Its counterion $[F(HF)_2]^-$ was seen on the spectra as a doublet of doublets with $^1J_{FaHb} \ll {}^1J_{FbHb}$. To make the further discussion easier we added in Table 1 the most important information about the $Col(HF)_n$ complexes adapted from literature.[10]

HF Complexes with a Sterically Protected Active Site. Based on the above-described species, we were able to assign the experimental results obtained from the pyridine derivatives with the hindered basic center. It is easier to start our discussion with the sample having an excess of NDTBP (Figure 5a−b). When an excess of NDTBP was added to HF solution in Freon, the ^{1}H NMR spectrum displayed at 200 K the triplet and the doublet whose integral intensities were equal (Figure 5a). This spectrum corresponded to the $[NDTBP-H_a]^+[FH_bF]^-$ species where the proton H_a was much strongly transferred to the nitrogen as compared to the same complex of collidine. As a result, the N−H_a scalar coupling was increased to 94 Hz, in contrast to 86 Hz in $ColH^+[FHF]^-$, while the H_a−F coupling became unresolved. This reduced the multiplicity of the peak from the doublet of triplets in $ColH^+[FHF]^-$ to the doublet in

$[NDTBP-H_a]^+[FH_bF]^-$. It is worth emphasizing that the values of the $^1J(^{15}N-^1H)$ scalar couplings in $[NDTBP-H_a]^+[FH_bF]^-$ and "free" $[NDTBP-H]^+$ were equal. The proton-transfer had reduced the hydrogen bond strength, so the signal of the H_a proton was strongly high-field shifted as compared to $ColH^+$-$[FHF]^-$. In contrast, the signal of the H_b proton was low-field shifted closer to the position of the corresponding signal in free $[FHF]^-$. We remind that in $ColH^+[FHF]^-$ the $[FHF]^-$ counterion was strongly perturbed due to the hydrogen bonding with the protonated collidine. This perturbation resulted in about 1 ppm high-field shift of the proton signal and an increase of the averaged splitting of the corresponding triplet by 16 Hz as compared to free $[FHF]^-$.[10] In contrast, in $[NDTBP-H]^+[FHF]^-$ this perturbation was reduced. The splitting was only 8 Hz stronger and the proton chemical shift was practically the same as in free $[FHF]^-$. However, the ion pair $[NDTBP-H]^+\cdots[FHF]^-$ was still hydrogen bonded that resulted in a measurable temperature dependence of the ^1H chemical shifts which indicated that the N−H···F hydrogen bond became weaker upon cooling. The spectrum did not change significantly when acid was in excess (Figure 5c). Under these conditions, $[F(HF)_2]^-$ species were stabilized in the NMR time scale as the doublet of doublets at 14.1 ppm[22] at 140 K. It seems that the presence of the more complex anions decreased the perturbation of the pyridinium cation, so at 140 K its proton signal shifted further to high field. However, at this temperature, the cations became involved in some exchange processes and the spectral lines became broader. The N−H distance in the $[NDTBP-H]^+$-$[FHF]^-$ complex was much shorter as compared to $ColH^+[FHF]^-$. Indeed, recently some of us showed that ^{15}N chemical shift of symmetrically substituted pyridines could be correlated with the N···H distance.[10] In $ColH^+[FHF]^-$, the ^{15}N chemical shift was −94 ppm as compared to free base. This value was ascribed to the N···H distance of about 1.05 Å.[10] In $[ColH]^+[F(HF)_2]^-$ the difference increased to −99 ppm which corresponded 1.02 Å (Table 1). In $[NDTBP-H]^+[FHF]^-$ the ^{15}N signal was at −124 ppm that meant that the N−H distance should be less than 1.02 Å and the corresponding N···F distance longer than 2.87 Å.

When an excess of MDTBP was added to HF solution in Freon, the ^1H NMR spectrum displayed at 200 K also the triplet and doublet whose integral intensities were equal (Figure 3a). The spectrum corresponded to the $[MDTBP-H_a]^+[FH_bF]^-$ species where the proton H_a was closer to the nitrogen than in $ColH^+[FHF]^-$, but farther than in the $[NDTBP-H]^+[FHF]^-$ complex. As a result the $^1J(^{15}N-^1H_a)$ scalar coupling in $[MDTBP-H_a]^+[FH_bF]^-$ was about 88 Hz, in contrast to 86 Hz in the case of $ColH^+[FHF]^-$, and 94 Hz in the case of $[NDTBP-H]^+[FHF]^-$. Remarkably, this scalar coupling in $[MDTBP-H_a]^+[FH_bF]^-$ was slightly smaller than the corresponding value in "free" $[MDTBP-H]^+$ cation, 91 Hz, whereas the corresponding couplings in the case of NDTBP were the same. That is a direct indication that the $[N-H]^+\cdots[F]^-$ hydrogen bond in the case of MDTBP was stronger as compared to NDTBP. The positions of the signals of the H_a and H_b protons in $[MDTBP-H_a]^+[FH_bF]^-$ were between the corresponding values in $ColH^+[FHF]^-$ and $[NDTBP-H]^+[FHF]^-$. A qualitative analysis of the ^1H_a chemical shift values in $[MDTBP-H_a]^+[FH_bF]^-$ and $[ColH]^+[F(HF)_n]^-$ complexes predicted that geometry of the $[N-H_a]^+\cdots[F]^-$ bridge in $[MDTBP-H_a]^+$-$[FH_bF]^-$ was slightly closer to geometry of the same bridge in $[ColH]^+[F(HF)_2]^-$ than to that in $ColH^+[FHF]^-$. Thus, the $N-H_a$ distance in $[MDTBP-H_a]^+[F_aH_bF]^-$ should be about 1.03 Å whereas the $N\cdots F_a$ distance is expected to be about 2.80 Å.

When an excess of HF was added, an exchange between different counterions prevented their identification at 200 K. At these conditions, the nitrogen of MDTBP was protonated and involved in a fast hydrogen bond exchange with different counterions. In contrast, the proton exchange was slow because the $^1J(^{15}N-^1H)$ value was the same as in "free" $[MDTBP-H]^+$ cation. Thus, at high temperatures, counterions could not be stabilized in the NMR time scale near the $[N-H]^+$ center, which was strongly protected from the environment. At lower temperatures these different hydrogen bonded species became less mobile in the solution but the hydrogen bond exchange processes still prevented the identification of their structures.

Conclusion

The first goal of this work was to investigate the effect of the ortho tert-butyl groups on the geometry of hydrogen bonded complexes formed between ortho-substituted pyridines and different acids, in particular, whether crowded pyridines can form hydrogen bond of the molecular type. The second goal was to inspect the ability of these groups to protect the protonated base from proton exchange with proton acceptors.

As a reference molecule for this study, a pyridine derivative with relatively small ortho substitutions, 2,4,6-trimethylpyridine (collidine), was used. It was shown previously that the shortest known N···H···F hydrogen bridge formed in the ColHF cluster is about 2.41 Å.[10] Although the basicities of MDTBP and collidine were approximately the same, the presence of tert-butyl groups in the ortho positions perturbed dramatically the geometry of the hydrogen bonds. The shortest N···F distance achievable for MDTBP was about 2.80 Å. As a result, the only stable structure in the NMR time scale formed in solution at low temperature was the $[MDTBP-H]^+[FHF]^-$ cluster, whose geometry was strongly perturbed by the presence of the ortho substituents. The $[N-H]^+$ proton of $[MDTBP-H]^+$ was strongly protected from the environment. Thus, this cation was practically excluded from any proton exchange when the temperature of the solvent was below 200 K. However, the N···H distance was still long enough so that the $[N-H]^+$ could be weakly hydrogen bonded to a relatively bulky anion, for example, Cl^-. When the basicity of DTBP increased, the proton of the $[N-H]^+$ group was moved closer to the nitrogen. As a result, hydrogen bonds formed by $[NDTBP-H]^+$ became even weaker.

Thus, the main conclusion of this study is that sterical hindrance caused by the ortho tert-butyl groups in pyridine derivatives strongly protect the protonated base from hydrogen bonding and proton exchange with the environment. Even the strongest and one of the smallest proton acceptors, anion F^-, could not be received by the $[N-H]^+$ center. As a result, an increase in the basicity of DTBP may help to protonate pyridine but would not lead to longer living hydrogen bonded complexes. The bulky ortho substitutes provide the specific protection of the captured proton from exchange processes and solvent interferences. One may expect that recent progress in accurate calculation of pK_a values and multidimensional potential surfaces in the condensed phase will provide further details of the discussed phenomena.[27,28]

As a side effect, we obtained information about the sensitivity of different experimental NMR parameters to hydrogen bond geometry for weakly bonded complexes. The most sensitive parameter was the ^1H NMR chemical shift. Even small changes in the structure caused by temperature dependent solvent polarity varied the proton chemical shift. Indeed, the difference in the proton chemical shifts between "free" $[NDTBP-H]^+$ and the hydrogen-bonded $[NDTBP-H]^+[FHF]^-$ was about 4 ppm,

whereas the whole range of the changes could not exceed 10−11 ppm. In contrast, the difference in the ^{15}N NMR chemical shifts between "free" $[NDTBP-H]^+$ and the hydrogen bonded $[NDTBP-H]^+[FHF]^-$ was 11 ppm whereas the whole scale between "free" $[NDTBP-H]^+$ and NDTBP was 124 ppm. The least sensitive parameter was the $^1J(^1H-^{15}N)$ scalar coupling whose value did not change detectably in the discussed species. However, the trend was different for a strong, low-barrier hydrogen bond formed in the $Col^{\delta+}\cdots H\cdots F^{\delta-}$ complex.[9] In the latter complex, the $^1J(^1H-^{15}N)$ coupling constant was strongly changed from 39 to 54 Hz due to a gradual proton shift toward the nitrogen upon an increase of the solvent polarity. The corresponding changes of the ^1H chemical shift were only about 1 ppm.

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