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Maximum Value of the Chemical Shift in the ^{1}H NMR Spectrum of a Hydrogen-Bonded Complex

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Abstract—The values of chemical shifts in the ^{1}H NMR spectra of complexes with the strongest quasi-symmetrical hydrogen bond $A^{\delta-}\cdots H\cdots B^{\delta+}$ with a minimal A···B distance were analyzed theoretically. According to the calculations, the maximum of the chemical shift is somewhat displaced from the shift of this structure toward that of limiting structure (free acid or protonated base) in which the proton is less shielded, but the value of this displacement is insignificant and does not correlate directly with the difference between the chemical shifts of the limiting structures.

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The geometry of a hydrogen bond is largely determined by its surrounding. It is supposed that it can play a key role in biochemical processes [1, 2]. In spite of still remaining doubts in the correctness of this statement [3–7], it initiated a wide discussion about the possibility for experimental determination of the geometry of hydrogen bonds in complex systems. In an overwhelming number of cases this problem cannot be solved by traditional methods, as they require rather large crystalline samples. Other methods are needed, that allow geometric parameters to be determined indirectly. At present one of most dynamically developing spectral methods is ^{1}H NMR spectroscopy, which feature high selectivity and is undemanding in terms of sample quality. ^{1}H NMR spectroscopy has been widely used in studying hydrogen bonds in water [8], organic solvents [9], condensed phases [10], and proteins [7]. There have been numerous attempts to correlate the strength (energy) of a hydrogen bond with the chemical shift of the corresponding ^{1}H NMR spectral signal or with the scalar spin-spin coupling constant [11–14]. Special attention has been given to the chemical shift, as its variations are easier to observe experimentally. Theoretical analysis suggests linear correlation between bond energies and chemical shifts for structurally related hydrogen-bonded complexes [12]. At the same time, the correlation is disturbed when principally different structures are compared. For example, the energy of the strongest known hydrogen bonds in the $[FHF]^-$ anion is 190–160 kJ mol^{-1} [15, 16], whereas their proton resonance is observed fairly upfield (16 ppm [17, 18]). The dissociation energy of the similar anion $[ClHCl]^-$ is ~2 times lower (96 kJ mol^{-1} [15, 19]), and the proton signal is slightly shifted upfield (to 14 ppm [17]). Vice versa, the proton signal of a much weaker complex in conjugated biscollidinium is observed at 20 ppm [20]. Displacement of ^{1}H NMR signals as a function of hydrogen bond strength was studied experimentally for separate complexes by varying external electric field acting on the complex in polar solvents [21–24]. As shown, as solvent polarity increases the asymmetry of the molecular complex with an A–H···B hydrogen bond gradually decreases, and a quasisymmetrical $A^{\delta-}\cdots H\cdots B^{\delta+}$ complex is formed, in which proton is equally strongly bound to both heavy atoms. If the dielectric constant of the solvent increases further, the quasi-symmetrical structure converts to an ionic hydrogen-bonded complex $A^-\cdots H\text{–}B^+$ in which proton is transferred to the base molecule. The change in the geometry of the hydrogen bridge is accompanied by a change in the position of the corresponding signal in the ^{1}H NMR spectrum. When solvent polarity increases, the signal gradually shifts downfield, reaches the maximum value, and then gradually shifts back upfield. What is the geometry that corresponds to the maximum chemical shift? Obviously, the maximum precisely corresponds to the strongest $A^{\delta-}\cdots H\cdots B^{\delta+}$ bond in the symmetrical hydrogen bridge taking place in homoconjugated ions with A = B [25]. However, the behavior of the chemical shift in the vicinity of an unsymmetrical complex $A^{\delta-}\cdots H\cdots B^{\delta+}$ with $A \neq B$ is difficult to predict [13]. It is logical to assume that when the proton chemical shifts in limiting structures, i.e. in free acid and free protonated base, strongly differ from each other, the chemical shift maximum will be

Table 1. Geometric parameters and ^{1}H NMR chemical shifts calculated for equilibrium geometries of HF and HF complexes with amines and protonated amines

Compound	$\delta(^1H)$, ppm	F···H, Å	H···N, Å	F···N, Å
HF	2.27	0.9213	[a]	[a]
$(CH_3)_2HN\cdots HF$	9.08	0.9536	1.6818	2.6354
$[(CH_3)_2HN\cdots H]^+$	4.38	[a]	1.0234	[a]
$(CH_3)_3N\cdots HF$	9.24	0.9559	1.6637	2.6196
$[(CH_3)_3N\cdots H]^+$	4.27	[a]	1.0239	[a]

[a] Experimental geometries of these complexes are unavailable.

displaced from the $A^{\delta-}\cdots H\cdots B^{\delta+}$ structure to the limiting structure with the largest chemical shift.

The main goal of the present work was to study theoretically the behavior of the chemical shift of a binding proton in the vicinity of a quasi-symmetrical $A^{\delta-}\cdots H\cdots B^{\delta+}$ complex. Taking into consideration the experience of previous studies, we chose hydrogen fluoride and hydrogen chloride as model acids and dimethylamine, trimethylamine, and pyridine as model bases. The study was carried out as follows: (1) optimal gas-phase structure of a hydrogen-bonded complex was determined; (2) proton shielding for the given geometry of the complex was calculated; (3) A···H bond length was increased and fixed; and (4) geometry of the perturbed complex was optimized, and variation in the proton shielding was determined. This approach was used earlier to describe the geometry of a complex on proton transfer and change of the type of the hydrogen bond [26].

Table 2. Geometric parameters and ^{1}H NMR chemical shifts calculated for equilibrium geometries of HF, HCl, and HF and HCl complexes with pyridine and pyridinium cation

Complex	$\delta(^1H)$, ppm	A···H, Å	H···N, Å	A···N, Å	Experiment, Å
*H*F	2.27	0.9213	–	–	H–F 0.9239 [28] 0.925595 [29]
Py···*H*F	9.08	0.9449	1.7383	2.6831	N–F 2.609(5) [30]
HCl	0.55	1.2694	–	–	H–Cl 2.28387 [29]
Py···*H*Cl	10.56	1.3185	1.7469	3.0654	N–Cl 2.999(2) [31]
[Py···*H*]$^+$	10.50	–	1.0166	–	–

Calculation technique. Geometry optimization was performed with inclusion of electron correlation by the second-order Moeller–Plesset (MP2) perturbation theory method with the 6-31G(d,p) basis set, and its correspondence to equilibrium state was checked by vibrational analysis. The proton chemical shift was calculated by the GIAO (Gauge-Invariant Atomic Orbital) method at the MP2/6-311++G(d,p) level. All calculations were carried out using the GAUSSIAN-98 package [27].

To explain the procedure for simulating the influence of the reactive field of a solvent on a hydrogen-bonded complex, we should consider general properties of such complexes discussed earlier [21–23]. Enhancing external field causes polarization of the hydrogen bridge. The neutral molecular complex A–H···B is characterized by a fairly low constant dipole moment, and it can only be increased via charge transfer. The energy required for charge transfer and obtained from the external electric field is the lower the shorter is the hydrogen bridge. Therefore, in the presence of external electric field the molecular-type hydrogen bond becomes stronger and the hydrogen bridge becomes shorter, which is accompanied by a shift of proton to its center. Once the proton has crossed the center of the bridge, further increase of induced dipole moment is reached by proton displacement to base B, which is accompanied by simultaneous increase in the A···B distance. For simplicity let us consider a linear A–H···B bridge. The distances r_{AH} and r_{HB} depend on each other. Therefore, at least in the first approximation, the effect of external solvent reactive field can be simulated by forced increase of r_{AH}. The r_{HB} distance, as well as the geometry of the complex are optimized now for each fixed r_{AH} distance. The linearity of the hydrogen bridge is forcibly maintained when necessary. The geometric parameters of A–H and H–B bonds in free acids and protonated bases, hydrogen bridges in equilibrium complexes, and corresponding proton chemical shifts are given in Tables 1 and 2. The experimental geometries of pyridine complexes with HF and HCl in the gas phase [28–31] are given in Table 2 for comparison. We failed to find analogous data for complexes of amines with HF. The results of simulation of the effect of external electric field on the geometry of complexes are shown in Figs. 1 and 2. Instead of shielding constants [$\sigma(^1H)$] obtained in theoretical calculations, in the tables and figures we give proton chemical shifts [$\delta(^1H)$] on the commonly accepted TMS scale.

$$\delta(^1H) \equiv \sigma_{TMS}(^1H) - \sigma(^1H)[\sigma_{TMS}(^1H)\ 32.05\ \text{ppm}].$$

The equilibrium geometry and proton shielding in

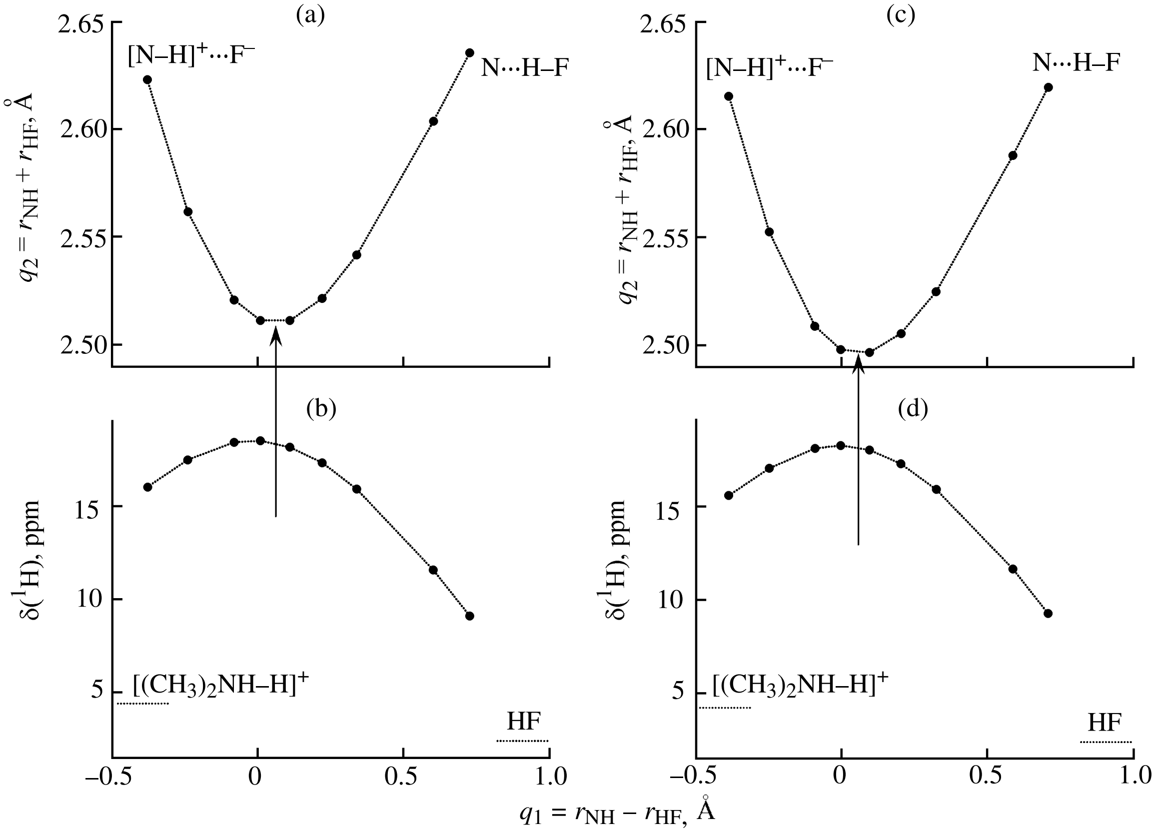

Fig. 1. Distances between heavy atoms of hydrogen bridge (q_2) and chemical shift of binding proton [δ(^{1}H)] in the ^{1}H NMR spectra as functions of proton displacement relative to the geometric center of the hydrogen bond (q_1), calculated for the (a, b) $Me_2HN\cdots HF$ and (c, d) $Me_3N\cdots HF$ complexes.

TMS [$\sigma_{TMS}(^1H)$] were calculated at the same level as for the complexes under study. For the sake of convenience we used, instead of r_{AH} and r_{HB}, the variables q_1 and q_2 defined as $q_1 = r_{HB} - r_{AH}$ and $q_2 = r_{HB} + r_{AH}$.

The q_2 value for a linear hydrogen bridge corresponds to the distance between heavy atoms forming the bridge. The q_1 value is equal to proton displacement relative to the geometric center of the bridge. It is positive, if the proton is closer to the acid molecule and becomes negative when the proton is transferred on the base. In spite of the fact that the geometrical center of an asymmetric hydrogen bridge has no physical sense, the change to this coordinate system makes the resulting data easier to compare with available published data [32].

The equilibrium geometries of the complexes formed by hydrogen fluoride with dimethylamine and trimethylamine are very close to each other. In the second case, the hydrogen bridge is slightly shorter (Table 1). When proton is gradually displaced to the nitrogen atom, the hydrogen bond first becomes stronger, i.e. the hydrogen bridge becomes shorter, reaches a maximum strength, and then becomes weaker again (Figs. 1a and 1c). Like with the equilibrium geometries, the length of the shortest hydrogen bridge is minimal for the complex with trimethylamine. In both complexes, the protons involved in the strongest, short bond are slightly displaced toward the fluorine atom relative to the geometric center. The dependence of the proton chemical shift on q_1 represents a convex asymmetric parabola with the center slightly displaced to the nitrogen atom relative to the minimum q_2, as a result of which the center of the parabola coincides with the geometric center of the bridge (Figs. 1b and 1d). The maximum chemical shifts for dimethylamine and trimethylamine are 18.5 and 18.3 ppm, respectively.

The main distinction between the equilibrium geometries of the complexes formed by pyridine with hydrogen fluoride and hydrogen chloride (Table 2) consists in that the H···Cl distance is much longer than H···F. In the complex with HF, again, proton is slightly displaced relative to the minimum q_2 toward

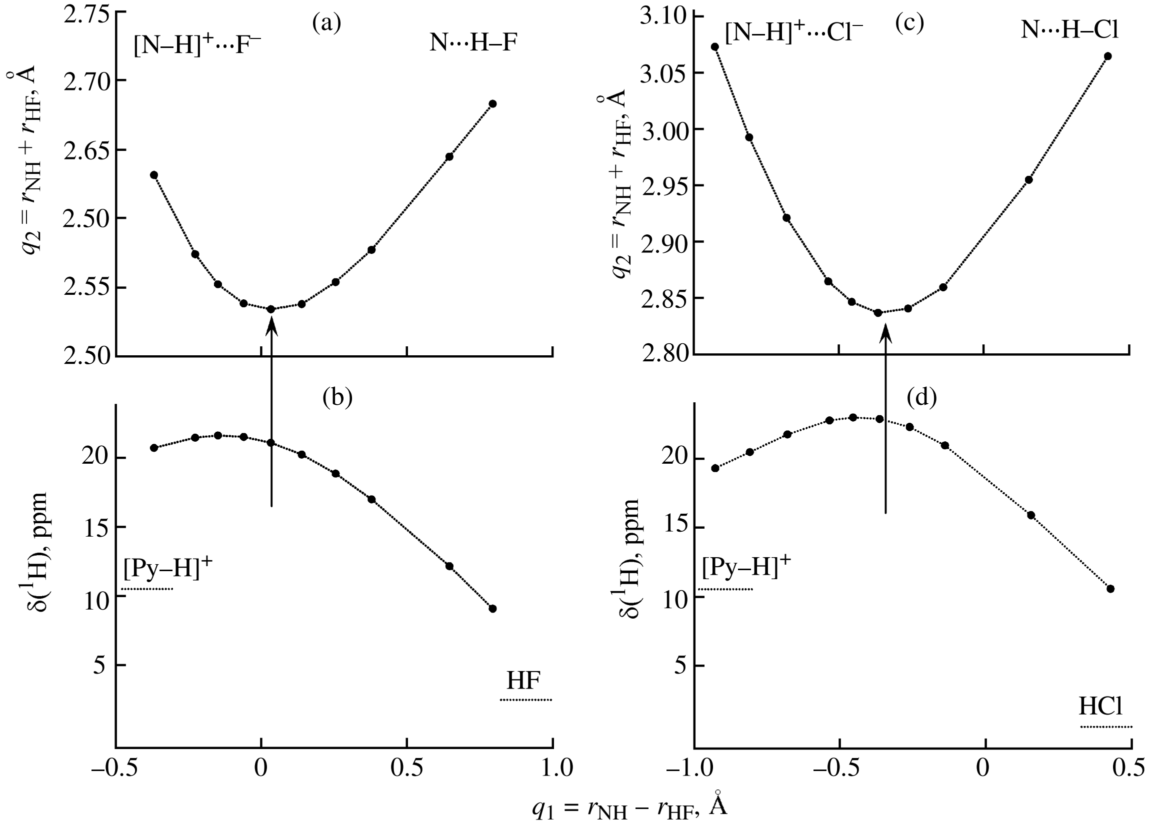

Fig. 2. Dependences of q_2 and $\delta(^1H)$ on q_1 calculated for the complexes (a, b) Py···HF and (c, d) Py···HCl.

the fluorine atom (Fig. 2a). In the complex with HCl, the hydrogen bridge, vice versa, is strongly asymmetric, and proton is much closer to the nitrogen atom than to the chlorine atom (Fig. 2c). Generally, dependence of the chemical shift of binding proton on the symmetry of the hydrogen bridge in the pyridine complexes qualitatively coincides with the analogous dependence for the HF complexes with amines, discussed above. The maximum chemical shifts, again, are displaced relative to the minimum toward the nitrogen atom. Now, however, their positions no longer coincide with the geometric center of the hydrogen bridge. For the HF complex, the maximum value of the chemical shift reaches 21.1 ppm (Fig. 2b), and for the HCl complex, 22.9 ppm (Fig. 2c). Note that our data for the pyridine complex with hydrogen chloride completely agree with the results obtained earlier for this system in the research into the dependences of its geometry and the chemical shift of the binding proton on the strength of external electrostatic field [33].

The results of the theoretical calculations point to the fact that the structures of the hydrogen-bonded complexes of hydrogen fluoride with dimethyl- and trimethylamine are close both in the case of equilibrium geometries and in the case of the shortest bridges. Moreover, the proton chemical shifts of the corresponding protonated cations practically coincide (Table 1). It is not surprising that the behavior of the chemical shift at varied geometry of the complexes is generally the same. It will be remembered that even though the largest chemical shifts do not correspond to the strongest structures in which the variable q_2 reaches its minimum, the deviations in both cases are small. It would be expected, as the chemical shifts of protonated cations and free acid differ by only 2 ppm. At the same time, both the chemical shift and the N···F distance in the vicinity of the minimum q_2 are slightly smaller in the complex $(CH_3)_3N$···F than in the complex $(CH_3)_2HN$···F, that should not take place. The available experimental data allow us to state that trimethylamine in the gas phase is a stronger base, so in fact the N···F distance in this complex may be shorter. However, the fact that a smaller chemical shift corresponds to a shorter distance suggests that the linear correlation between bond energy and chemical shift can be disturbed, when structurally similar hydrogen-bonded complexes are compared. The coincidence of the maximum chemical shifts in these complexes with the geometric center of the hydrogen bridge is most likely incidental.

When pyridine is substituted for amines, the geometry of the hydrogen bridge changes only slightly. By contrast, the value of the maximally attainable chemical shift sharply increases and shifts to negative q_2 values. These changes seem to be connected with the larger chemical shift of the protonated pyridine cation compared to protonated amines. Furthermore, reduced shielding may be caused by enlarged N···F distance near the minimum q_2 in the pyridine complex.

The shortest hydrogen bridge in the Py···HCl complex is strongly asymmetric and longer than in all the other complexes studied (~2.84 Å). As a result, the maximum chemical shift of this complex is also the largest. Note that this maximum is again very close to the minimum q_2, even though this complex has the largest difference between the proton chemical shifts of free acid and protonated base (10 ppm). Therefore, we were wrong, though partly, when assumed that the displacement of the chemical shift maximum from the strongest quasi-symmetrical structure $A^{\delta-}\cdots H\cdots B^{\delta+}$ toward the least shielded structure, i.e. A–H or $H–B^+$, is proportional to the difference between the chemical shifts of these structures. The chemical shift maximum is actually displaced toward the least shielded limiting structure, but the value of this displacement does not correlate directly with the difference between the chemical shifts of the limiting structures. In spite of the fact that the method used in this work for simulation of the influence of solvent reactive field on the geometry of hydrogen-bonded complexes is oversimplified, it allows us to predict qualitatively the behavior of the chemical shift of the binding proton in an asymmetric complex on the formation of the strongest quasi-symmetrical structure $A^{\delta-}\cdots H\cdots B^{\delta+}$.

The aforesaid shows that the maximum chemical shift in such a complex generally does not correspond to the quasi-symmetrical structure $A^{\delta-}\cdots H\cdots B^{\delta+}$ structure with the shortest A···B distance. However, contrary to intuitive expectations, the displacement of the chemical shift maximum is insignificant and not proportional to the difference between the proton chemical shifts of free acid and protonated base. Therefore, it is appropriate to state that on gradual transfer from the asymmetrical molecular complex A–H···B to quasi-symmetrical $A^{\delta-}\cdots H\cdots B^{\delta+}$ and further to ionic $A^-\cdots H–B^+$, the chemical shift of the binding proton first increases, passes through a maximum when the strongest complex is formed, and the decreases again. At the same time, it is necessary to note that the maximum of the chemical shift does not coincide with the maximum of the primary isotope effect, $\delta(^2H) - \delta(^1H)$, observed experimentally in the 2,4,6-trimethylpyridine···H(D)F complex [22]. This convergence may result from the displacement of the chemical shift maximum relative to the minimum q_2 toward the limiting complex with the least shielded proton, here to the pyridinium cation here. On the other hand, the dependence of the primary isotope effect on q_1 in the vicinity of the quasi-symmetrical $A^{\delta-}\cdots H\cdots B^{\delta+}$ bond is not known in detail. Studying this dependence can help in approaching the problem of exact experimental identification of the strongest and shortest quasi-symmetrical hydrogen bond.

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