Solvation and Hydrogen Bonding of Pyridinium Ions

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Abstract: Relative solvation enthalpies, $\delta\Delta H_s^{g\rightarrow H_2O}(BH^+)$, for transfer of a series of pyridinium ions from the gas phase to water have been determined by combining relative heats of ionization in the gas phase (by ICR) and in water with relative heats of solvation of the corresponding neutral pyridines, $\delta\Delta H_s^{g\rightarrow H_2O}(B)$. The data are considered from the viewpoint of Krishnan and Friedman. It is shown that the principal factor which determines the difference between gas-phase basicities and those in water, for this series of bases, is the effect of substituents (X) on the strength of hydrogen bonds from the pyridinium ion to bulk water, $XpyH^+\cdots(OH_2)_n$. A small contribution (about one-fourth as large in magnitude and of opposite sign) is also made by substituent effects on hydrogen bonding of the neutral pyridines acting as H-bond acceptors, $Xpy\cdots(H_2O)_n$. Ab initio molecular orbital calculations at the STO-3G level have been employed to provide additional analysis. These results suggest that bulk water has about twice as large an H-bond acceptor effect as does monomeric water toward the pyridinium ions and twice as strong an H-bond donor effect toward the pyridines. There is close agreement between experimental data and theoretical calculations for both bulk and monomeric water, showing that the magnitude of the substituent effects on hydrogen bonding from the pyridinium ions is about four times greater in magnitude than that for hydrogen bonding to the corresponding pyridines.

During the past five years a revolution has occurred in our approach to understanding the thermodynamics of organic ion solvation. This has been occasioned by the simultaneous development of several experimental methods for studying organic ion-molecule equilibria in the gas phase with precision (±0.2 kcal) and range of effects equivalent to (or better than) that normally expected for solution processes,[1-3] and by molecular orbital theory energy calculations for isodesmic processes.[4] Direct comparison of rates and equilibria in the presence and absence of condensed media reveals facts about ion solvation which previously were inaccessible.

Amines are a large and important class of Brønsted bases whose protonation is studied easily in dilute aqueous acid. Accordingly, a large literature of reliable protolysis data is available for comparison with gas-phase values. Extensive analysis by ourselves[1-7] and by Aue and Bowers[8,9] demonstrates clearly the powerful role that solvation can play in modifying or cancelling substituent effects in the protonation of aliphatic amines.

Undoubtedly, an important contribution to the 40–90 kcal/mol of heat which is released by transfer of an organic ion from the gas phase to water is that attributed by classical electrostatics to creating a cavity in the medium and then charging it. Beyond this lies the question of more specific ion–solvent interactions such as hydrogen bonding. Evidence that hydrogen bonding from ammonium ions to solvent is an important factor in determining their solvation energies may be adduced from a variety of sources. First is the tendency for solvation energies of ammonium ions to group themselves according to class as primary, secondary, or tertiary in terms of the number of acidic hydrogens on the nitrogen atom (i.e., $NH_4^+ > RNH_3^+ > R_2NH_2^+ > R_3NH^+$), while the shape and size of the ion is of less importance.[3,6,10,11] Second is the fact that ions which are poor hydrogen bond donors or acceptors, such as carbonium,[11,12] phosphonium, or sulfonium[13,14] ions show remarkably small solvation effects on their relative heats of ionization from neutral precursors. Finally, we have shown[15,16] that oxonium ions are even more exothermically solvated than are ammonium ions and are also differentiated according to the number of acidic hydrogens on the oxygen atoms. Thus, the number and type of hydrogen bond which an onium ion can donate to a basic solvent is a rough first-order guide to its solvation behavior.

We are now concerned to examine, at a somewhat higher resolution, the factors which influence the solvation of ammonium ions. In order to do this we must maintain other factors, such as ionic size and the number of acidic hydrogen, as nearly constant as possible. The substituted pyridinium ions with groups in the 2, and especially the 3 and 4 positions cover a considerable range of electron-releasing and attracting ability while retaining electrostatic energies of the ions, which should be nearly similar in terms of their sizes and shapes. We will see that their solvation energies cover a range of ~8 kcal/mol and that the trend is explicable, using both experimental and theoretical analysis, primarily in terms of varying strength of the hydrogen bond $XpyH^+\cdots(OH_2)_n$. Furthermore, the attenuation factor[15] of the aqueous solvent on the relative basicities of the pyridines in the gas and solution phases can be ascribed largely to these variable hydrogen bond strengths.

Experimental Section

Most of the compounds in this study were available commercially. Their identities and purities were established by melting point, boiling point, refractive index, and gas chromatography.

A pure sample of 4-trifluoromethylpyridine was graciously contributed by Dr. W. A. Sheppard of the DuPont Experimental Station.

Calorimetry. Heats of solution, ionization, and vaporization were determined at 25 °C in a standard solution calorimeter which we have described in detail,[17] including calibration and sources of error. Baseline drift was corrected by use of twinned calorimeters whose contents were returned to 25.0 °C after each addition of solution.[18] Heats of vaporization employed the same calorimeter with a steady-state flow system, which has also been reported.[19] Error limits for these heats are estimated to be ±0.2 kcal/mol. Heats of ionization in water were determined in conjunction with measurements of heats of solution. The heat of solution of the pure pyridine was first determined in several concentrations of dilute aqueous sodium hydroxide of high enough pH to preclude significant ionization of the organic base. Corresponding measurements were then made in several aqueous hydrochloric acid solutions whose pHs were sufficiently low to ensure complete ionization, $\Delta H°_S$, vs. acid or base concentration were extrapolated to infinite dilution to correct for small ionic strength effects. The heat of ionization in water was obtained directly as the difference between the heat of solution of the pyridine in aqueous acid minus its heat of solution in aqueous base.

Ion Cyclotron Resonance Measurements. The pulsed ion cyclotron resonance spectroscopic method[2] for determination of gas-phase proton-transfer equilibrium constants utilized in this study has been described in detail.[20,21] The multiple overlapping sequences of bases used to establish $\delta\Delta G°_i(g) \cong \delta\Delta H°_i(g)$ (cf. ref 21) for the substituted pyridines are shown in Figure 1 of ref 2. The figures given therein have been slightly revised, based upon a final accounting of these results.[22]

Table I. Heats of Ionization of Pyridines[p] in Water and Their Heats of Solution and Vaporization (in kcal/mol)

Pyridine substituent	$\Delta H_i(H_2O)$	$\Delta H_s(MeOH)$	$\Delta H_s(H_2O)$	ΔH_{vap}	$\Delta H_s^{g\rightarrow H_2O}(B)$
4-N$(CH_3)_2$	11.73[n]				
2,6-$(CH_3)_2$	7.24[a]		−3.80[e]	11.01[f]	−14.81
2,4-$(CH_3)_2$	7.17[a]		−3.09[e]	11.42[f]	−14.51
4-OCH_3	6.85,[b] 7.85[c]	−0.91[c]	−1.52	12.61[g]	−14.13
2,5-$(CH_3)_2$	6.82[a]		−3.11[e]	11.43[f]	−14.54
3,5-$(CH_3)_2$	6.37[a]	−1.05[c]	−2.42[e]	12.04[f]	−14.46
4-CH_3	6.10,[d] 6.13,[b] 6.02[a]	−1.14[c]	−2.44[e]	10.83[h]	−13.27
2-CH_3	6.22,[d] 5.99[a]		−3.02[e]	10.15[i]	−13.17
3-CH_3	5.71,[d] 5.87[b] 5.64[a]		−2.43[e]	10.62[j]	−13.05
H	4.80[a,b,c]	−0.98[c]	−2.32[c]	9.61[k]	−11.93
4-Cl	3.58[b]				
3-Cl	2.60,[b] 2.11[d]	0.01[c]	−1.17[c]	11.86[o]	−13.0
3-CF_3	2.0[m]				
4-CF_3	2.22[c]		−1.68[c]	9.98[c,g]	−11.66
4-CN	0.85,[c] 1.26[b]	4.74[c]	3.57[c]	13.60[c,l]	−10.03
3-CN	0.88[b]				

[a] Reference 29. [b] Reference 28. [c] This work. [d] Reference 27. [e] Reference 29. [f] J. D. Cox, *Trans. Faraday Soc.*, **56,** 959 (1960). [g] E. M. Arnett et al., *J. Chem. Educ.*, **52,** 269 (1975). [h] R. J. L. Andon et al., *Trans. Faraday Soc.*, **53,** 1074 (1957). [i] D. W. Scott et al., *J. Phys. Chem.*, **67,** 680 (1963). [j] D. W. Scott et al., *ibid.*, **67,** 685 (1963). [k] J. P. McCullough et al., *J. Am. Chem. Soc.*, **79,** 4289 (1957). [l] This is the heat of sublimation of this compound. [m] Value estimated based upon our value for *p*-CF_3. [n] Reference 23. [o] Ts. B. Konunova and M. F. Franze, *Russ. J. Inorg. Chem.*, **18** (7), 95 (1973). This value is a calculated rather than a measured value. [p] For the reaction: $XpyH^+_{(aq)} + H_2O_{(aq)} \rightleftarrows XPy_{(aq)} + H_3O^+_{(aq)}$. Individual heats of ionization, $\Delta H_i(H_2O)$, as well as the heats of solution and vaporization of this table have estimated uncertainties of ±0.2 kcal/mol.

Not shown is the subsequently obtained result for the 4-NMe_2py. This base was found to be 0.3 kcal more basic than $(Me_2NCH_2)_2$ and 1.3 kcal more basic than *i*-Pr_2EtN, which establishes[22] that it is 31.2 kcal more basic than NH_3 or 14.6 kcal more basic than pyridine. The estimated uncertainities in $\delta\Delta H_i(g)$ values of Table III are ±0.2 kcal/mol.

Infrared Spectroscopy. Pyridinium chlorides were prepared by passing anhydrous HCl gas through an ethereal solution of pyridine. The resulting precipitates were recrystallized from acetone–methanol mixture. Composition of the salts was established by quantitative microanalysis (Galbraith Laboratories, Inc.).

The IR spectra for the salts were recorded on a Perkin-Elmer Model 247 spectrometer with sodium chloride cells. The 0.1 M solutions in Me_2SO were prepared in an argon-filled drybox.

Results

The aim of this paper is to calculate the hydration enthalpies at 25 °C for a series of substituted pyridinium ions in water and to then examine the substituent effects in terms of hydrogen bonding and other possible contributing solvation terms. This involves the assembly and measurement of a variety of types of data as shown by the following thermodynamic cycle I (Scheme I). Following our previous conventions[1-3,5,6] $\delta\Delta H_i(g)$ will be the gas-phase enthalpy change for the isodesmic proton transfer from the substituted pyridinium ion ($XpyH^+$) to pyridine (py). The corresponding value in aqueous solution is $\delta\Delta H_i(H_2O)$. The heat of solution of pyridine or substituted pyridine (Xpy) into water from the gas phase is $\Delta H_s(py)$ or $\Delta H_s(B)$—accordingly, the relative value is defined (as for the other properties) by $\delta\Delta H_s(B) = \Delta H_s(Xpy) - \Delta H_s(py)$. Finally, the hydration enthalpy for $XpyH^+$ relative to pyridine is defined as $\delta\Delta H_s(BH^+) = \Delta H_s(XpyH^+) - \Delta H_s(pyH^+)$. Since neither of these ionic terms is directly measureable, $\delta\Delta H_s(BH^+)$ is determined by addition of the other terms in the cycle:

Scheme I

$$\begin{tikzcd}
XpyH^+ \arrow[d, "\Delta H_s(BH^+)"'] & + & py \arrow[r, "\delta\Delta H_i\ (g)"] \arrow[d, "\Delta H_s(py)"] & Xpy \arrow[d, "\Delta H_s(B)"] & + & pyH^+\ (gas) \arrow[d, "\Delta H_s(pyH^+)"] \\
XpyH^+ & + & py \arrow[r, "\delta\Delta H_i\ (H_2O)"] & Xpy & + & pyH^+\ (H_2O)
\end{tikzcd}$$

$$\delta\Delta H_s(BH^+) = \delta\Delta H_i(g) + \delta\Delta H_s(B) - \delta\Delta H_i(H_2O)$$

Obviously, the calculation of each such ionic solvation enthalpy requires three reliable enthalpy values for the pyridine base (Xpy) in question and of course the three corresponding values for pyridine itself (py), which are used as the standard for deriving all the other relative values. Although many of these properties have been reported for various pyridines, there are only a few members of the series for which all of the necessary data are available. Wherever possible we have used what we think are the most reliable published values. In some cases we have made the necessary measurements ourselves to complete the calculation for a given base. In the following sections we will describe the source of each type of data, either as we have measured it or as extracted from the literature. In cases where several conflicting values have been given, we will explain the reason for our choice of the primary data presented in Table I.

Gas-Phase Enthalpies of Ionization. These were obtained at UCI using pulsed ion cyclotron resonance spectroscopic equilibrium constant determinations.[2,21,22] Wherever direct equilibration of Xpy with py was impractical because of extreme displacement of the proton-transfer equilibrium to right or left, a series of stairstep comparisons was made by equilibrating a series of compounds whose basicity was close enough to allow direct equilibration. The intervals between different base pairs were then matched to ensure self consistency.[2] The standard error in such measurements is estimated to be ±0.2 kcal/mol. Since all compounds reported here are tertiary bases, there is no formal entropy term due to molecular rotational symmetry number[2,21] for the gas-phase proton exchange and therefore $\delta\Delta H^\circ_i(g) \cong \delta\Delta G^\circ_i(g)$. In all cases where comparison is possible, our $\delta\Delta H_i(g)$ values are in generally good agreement with those of Aue et al.,[23] except for 4-NMe_2py. The value given in ref 23 for this compound has been subsequently found to be in serious error.[24] The $\delta\Delta H_i(g)$ values may be placed on the scale of absolute proton affinities by taking pyridine as 218.1 kcal/mol.[25]

Heats of Ionization in Water $\Delta H_i(H_2O)$. Numerous thermodynamic studies of amine protonation in water have focused entirely or in part on very limited series of pyridines. Although many pK_a values have been reported,[26-35] relatively few determinations of enthalpies of ionization are reported which

Table II. Infrared Shifts of Pyridinium Protons in DMSO Solution

Substituted pyridines	$NH^+ \cdots OSMe_2$, cm^{-1}
2,6-$(CH_3)_2$	2300
3,5-$(CH_3)_2$	2300
4-OCH_3	2300
4-CH_3	2285
3-CH_3	2280
2-CH_3	2290
H	2275
3-Cl	2200
3-CF_3	
4-CN	2210

include a significant number of the compounds under consideration here. No study that we know of has included all of them. We have chosen the work of Christensen et al.[27] as a primary source of $\Delta H_i(H_2O)$ values because it includes a large number of the bases for which the other data necessary to close cycle I (Scheme I) are available. Equally important is the fact that their results are part of an extensive thermochemical study, so that any errors are apt to be systematic and not so likely to affect the relative values [i.e., $\delta\Delta H_i(H_2O)$] which are essential to our analysis.

The choice of data for heats of ionization in water raised some problems because of discrepancies between some of the published data from various sources. However, on examining the literature we found that there were relatively few of the substituted pyridines which have so far been studied in the gas phase for which heats of ionization in water and also heats of vaporization are available to allow completion of cycle I for the solvation energy of the corresponding pyridinium ion. Upon considering these, we found five reported systematic studies[27-29,34,35] of $\Delta H_i(H_2O)$ of which only two[27,28] were considered for extensive comparison (Table I), since they met the criteria of being recent and careful calorimetric studies at high dilution. They also included a significant number of compounds for which we wish to make calculations, and, for the most part, the results are in agreement within their experimental errors.

Heats of Solution of Gaseous Pyridines in Water $\Delta H_s(B)$. These values would be available directly from the temperature coefficient of Henry's law constants.[36-38] However, the considerable range of volatility and of solubility in water has discouraged this as a general approach for the pyridines. We have determined these values calorimetrically by subtracting the heat of vaporization (or sublimation) of the pure pyridine base at 25 °C from its corresponding heat of solution at a standard state of infinite dilution in the solvent in question. Thus,

$$\Delta H_s^{g\rightarrow solvent}(B) = \Delta H_s^{pure\rightarrow solvent}(B) - \Delta H_{vap}^{pure\rightarrow gas}(B)$$

For 4-methoxy-, 4-trifluoromethyl-, and 4-cyanopyridines we have measured the heats of vaporization (see Experimental Section). Other values in Table I are taken from the cited literature sources. Heats of solution in water and methanol are reported for 3,5-dimethyl-, 4-methoxy-, 3-chloro-, 4-trifluoromethyl-, and 4-cyanopyridines and for pyridine itself also. The rest of the values are derived from the references cited.

IR Spectral Results. Infrared stretching frequencies for the N^+-H bond of the pyridinium chlorides were determined in Me_2SO, a medium of fairly high dielectric constant ($\epsilon = 47$) and a strong hydrogen bond acceptor. The results are given in Table II. The estimated uncertainty is ±5 cm^{-1}.

Discussion

In order to evaluate the relationship between substituent effects on the solvation and hydrogen bonding of pyridines and pyridinium ions we have assembled the necessary values, relative to pyridine, in Table III. These data [except $\delta\Delta G_i(H_2O)$ and $\delta\Delta H_i(g)$] are derived from those in Table I by using selected or averaged values.

As cycle I demonstrates, the entire difference between $\delta\Delta H_i(g)$ and $\delta\Delta H_i$(water) for a given pyridine base must ipso facto be due to the difference between the relative solvation enthalpies of the neutral base and its pyridinium ion. Each of these solvation factors can in turn be considered in terms of a contribution due to hydrogen bonding (i.e., $Xpy \cdots (HOH)_n$ for the neutral base, and $XpyH^+ \cdots (OH_2)_n$ for its ion) and all other contributions such as those attributable to dispersion forces, hydrophobic bonding, electrostriction, etc. We shall discuss our results first by considering the aqueous solvation enthalpies of the gaseous pyridines and, in turn, their conjugate acids.

Heats of Hydration of Substituted Pyridines. The study of protolysis equilibria in solution has absorbed the efforts of many researchers mainly in physical, analytical, and biochemistry over the past century. Most of them have realized that their results can only be subjected to rational analysis through the separation of intrinsic effects from solvation factors. The latter further requires separation between solvation effects for the neutral acids or bases under study and the conjugate base or acid ions. Obviously, this requires an under-

Table III. Substituent Effects in Pyridines on Gas-Phase and Aqueous Solution Basicities and Ionization Heats, and on Heats of Transfer from the Gas Phase to Aqueous Solution for Pyridines and Pyridinium Ions (in kcal/mol)

Pyridine substituent	$\delta\Delta G_i(H_2O)$[a]	$\delta\Delta H_i(H_2O)$[a]	$\delta\Delta G_i(g) \cong \delta\Delta H_i(g)$[b]	$\delta\Delta H_s^{g\rightarrow H_2O}(B)$	$\delta\Delta H_s^{g\rightarrow H_2O}(BH^+)$
4-$N(CH_3)_2$	5.94	6.93	14.6[c]		
2,6-$(CH_3)_2$	2.18	2.44	8[d]	−2.88	2.7
2,4-$(CH_3)_2$	2.01	2.37	6.9[d]	−2.58	1.9
4-OCH_3	1.87	2.55	6.7[c]	−2.20	2.0
2,5-$(CH_3)_2$	1.43	2.02	6.1[d]	−2.61	1.5
3,5-$(CH_3)_2$	1.13	1.59	5.5[d]	−2.53	1.4
4-CH_3	1.12	1.30	4.0[c]	−1.34	1.4
2-CH_3	1.09	1.40	3.5[c]	−1.24	0.9
3-CH_3	0.63	0.91	2.7[c]	−1.12	0.7
H	(0.00)	(0.00)	(0.0)	(0.00)	(0.00)
4-Cl	−1.88	−1.22	−3.1[c]		
3-Cl	−3.28	−2.44	−5.8[c]	−1.1	−4.5
3-CF_3	−3.75	−2.8 (est)	−8.1[c]		
4-CF_3	−3.52	−2.58	−7.8[c]	0.27	−4.9
4-CN	−4.57	−3.75	−10.5[c]	1.90	−4.8
3-CN	−5.27	−3.92	−11.3[c]		

[a] Selected values, cf. Table I. [b] Cf. ref 21. [c] This work, ±0.2 kcal/mol. [d] Reference 23.

Table IV. Relative Heats of Transfer for Substituted Pyridines (in kcal/mol)

Substituent	$\delta\Delta H_s^{g\to H_2O}(B)$	$\delta\Delta H_{vap}^{g\to l}(B)$	$\delta\Delta H_s^{CCl_4\to H_2O}(B)$	$\delta\Delta H_s^{CCl_4\to MeOH}(B)$
2,6-$(CH_3)_2$	−2.88	−1.40	−1.39	
3,5-$(CH_3)_2$	−2.53	−2.43		
4-CH_3O	−2.20	−3.00	1.05	0.32
4-CH_3	−1.34	−1.22	0.27	
H	(0.00)	(0.00)	(0.00)	(0.00)
3-Cl	−1.1	−2.2	1.28	1.12
4-CF_3	0.27	−0.37	0.52	
4-CN	1.90		1.72	1.55

Table V. Estimation of Substituent Effects on the Energies of Hydrogen Bonding between Methanol and Pyridines. Comparison with Values Measured in CCl_4 (all values in kcal/mol at 25 °C)

Pyridine substituent	$\delta\Delta H_s^{g\to MeOH}(B)$	Corresponding benzene	$\delta\Delta H_s^{g\to MeOH}$	HB(Xpy; MeOH) = difference	$\delta\Delta H_{MeOH}$ in CCl_4[55]
3,5-$(CH_3)_2$	−2.50	*p*-Xylene	−1.81	−0.69	−1.1
4-CH_3	−1.38	Toluene	−0.90	−0.48	−0.4
H	(0.00)	Benzene	(0.00)	(0.0)	(0.0)
3-Cl	−1.2	Chlorobenzene	−2.27	1.1	0.8

standing of the solution chemistry of both nonelectrolytes and of electrolytes. Unfortunately, the traditional separation between "electrolyte chemists" and "nonelectrolyte chemists" has prevented the systematic development of data and theories which would foster a solid understanding of even such a simple reaction as proton-transfer equilibrium in solution. Equally unfortunate has been the failure of solution chemists, until recently, to recognize the necessity of systematically comparing phenomena in water with those in other solvents. Friedman[39-46] has developed simultaneously the necessary theoretical and experimental aspect of the behavior of both organic molecules and related ions in water and nonaqueous media in terms which will be useful to us here.[47]

There are very few precedents for considering the thermodynamics of solution of a series of substituted pyridines in water. Following Krishnan and Friedman[39] we will consider that the enthalpy of solution of a pyridine base from the gas phase to water is the sum of terms due to formation of a cavity [CAV(Xpy; H_2O)], hydrogen bonding from the water to the base [HB(Xpy; H_2O)], van der Waals dispersion force interaction between water and the pyridine molecule [VDW(Xpy; H_2O],[48] and finally a structure modifying term [STR(Xpy; H_2O)], which seems to be almost uniquely associated with the effects of nonpolar groups on the structure of cool, liquid water (cf. ref 49 for a discussion of the origin of these terms).

Isolation of the Hydrogen-Bonding Term in $\delta\Delta H_s^{g\to H_2O}(B)$ for the Pyridines. In spite of similar sizes and shapes for the substituted pyridines, the $\Delta H_s^{g\to H_2O}(B)$ values of Table I appear to involve a complex mixture of the above terms. This conclusion is based upon examination, both qualitatively and quantitatively, of substituent effects, i.e., $\delta\Delta H_s^{g\to H_2O}(B)$ values (Table III), and by comparison with heats of transfer for the substituted pyridines to other media. Hydrogen bonding studies with model compounds, e.g., CH_3OH or *p*-FC_6H_4OH in CCl_4 solution[55,56] indicate that 4-OCH_3, 3- and 4-CH_3 substituents are expected to increase the exothermicity of the HB(Xpy; H_2O) term, whereas 3-Cl, 4-CF_3, and 4-CN substituents should decrease this term. While less exothermic $\Delta H_s^{g\to H_2O}(B)$ values are found (i.e., positive values of $\delta\Delta H_s^{g\to H_2O}(B)$, cf. Table III) for the latter two substituents, the value of $\Delta H_s^{g\to H_2O}(B)$ is more exothermic (not less) for the 3-chloropyridine than pyridine (i.e., $\delta\Delta H_s^{g\to H_2O}(B)$ is negative for 3-Cl). The latter result therefore strongly suggests that other terms than HB(Xpy; H_2O) contribute significantly to the relative heats of solution, $\delta\Delta H_s^{g\to H_2O}(B)$. Further, for example, the negative value of $\delta\Delta H_s^{g\to H_2O}(B)$ of 1.34 kcal/mol for the 4-CH_3 substituent appears quantitatively to be too large (cf. following discussions) to be due solely to a HB(Xpy; H_2O) term.

In view of the appreciable variation in heats of vaporization of the substituted pyridines (Tables I and IV) it seems reasonable to expect some VDW(Xpy; H_2O) terms to contribute to $\delta\Delta H_s^{g\to H_2O}(B)$ values. In the unlikely event that a constant deviation from ideal solution behavior might prevail, the relative heat of transfer of substituted pyridines between dilute solutions in CCl_4 and in water, $\delta\Delta H_s^{CCl_4\to H_2O}(B)$ would involve no contributions from VDW(Xpy; H_2O) terms, and might provide a means of evaluating HB(Xpy; H_2O) terms. However, examination of the limited available data for $\delta\Delta H_s^{CCl_4\to H_2O}(B)$ (given in Table IV) does not show the trends expected in HB(Xpy; H_2O) terms (4-OCH_3 and 4-CH_3 have positive rather than the expected negative values), nor do these values correlate with corresponding $\delta\Delta H_s^{g\to H_2O}(B)$ values. Similar problems appear also in the limited data for the relative heat of transfer of substituted pyridines between dilute solutions in CCl_4 and in methanol, $\delta\Delta H_s^{g\to MeOH}(B)$ (cf. Table IV). Small contributions from any one or all of the VDW, STR, and CAV terms for the substituted pyridines to values of $\delta\Delta H_s^{g\to H_2O}(B)$ are suggested by the results (as summarized in Table IV). Consequently, we have turned to other means to obtain quantitative estimates of the HB(Xpy; H_2O) terms.

The size, shape, and polarizability of unsubstituted benzene and pyridine are quite close—closer than those for benzene and benzonitrile or chlorobenzene, for example.[50] Thus, we may estimate that the entire difference of 4.3 kcal/mol between $\Delta H_s^{g\to H_2O}(B)$ for pyridine (−11.93) and for benzene (−7.6) is attributable only to the formation of the py···$(HOH)_n$ hydrogen bond in the former compound. This estimate (4.3 kcal/mol) agrees well with the recent direct measurement of 4.1 kcal/mol in CCl_4[51] and with a calculation by Hoffmann's group.[52]

Proceeding in a similar manner, the difference of 4.7 kcal/mol between $\Delta H_s^{g\to H_2O}(B)$ for 4-CH_3py (−13.27) and toluene (−8.6) is taken as the expected somewhat greater heat of formation of the CH_3py···$(HOH)_n$ hydrogen bond in the former. Extension of this approach to more compounds is limited by two considerations. There are few enthalpies of solution available for substituted benzenes in water. Further, if the substituent itself hydrogen bonds weakly to water (as for example OCH_3 or CN), such an interaction will be measurably

Table VI. Structure–Energy Relationships and Estimated HB(Xpy; H_2O) Terms (in kcal/mol)

Pyridine substituent	$\delta\Delta H_i$-(g)[a]	$\delta\Delta G°_{HB}$[b]	$\frac{\delta\Delta G_{HB}}{\delta\Delta H_i(g)}$[c]	HB(Xpy; H_2O)
4-NMe_2	14.6	1.27	0.09	−1.5,[e] −1.9[d]
4-OCH_3	6.7	0.31	0.05	−0.7,[e] −0.9[d]
3,5-$(CH_3)_2$	5.5			−0.6,[e] −0.7,[d] −0.7,[g] −1.1[f]
4-CH_3	4.0	0.20	0.05	−0.4,[e] −0.5,[d] −0.4,[f] −0.5[g]
2-CH_3	3.5			−0.4,[e] 0.5[d]
3-CH_3	2.7			−0.3,[e] −0.4[d]
H	0.0	0.00	0.00	0.0
3-Cl	−5.8	−0.79 (Br)	0.14	0.9,[e] 0.8,[d] 0.8,[f] 1.1[g]
4-CF_3	−7.8	−1.04	0.13	1.2,[e] 1.0[d]
4-CN	−10.5	−1.13	0.11	1.7,[e] 1.4[d]

[a] Relative proton affinity, ±0.2 kcal/mol. [b] Relative free energy of formation of hydrogen-bonded complex with p-FC_6H_4OH in CCl_4 at 25 °C.[56] [c] Ratio of (b)/(a), average value for all substituents is 0.10 ± 0.03. For electron-donating substituent the average value is 0.06 ± 0.02. For electron-withdrawing substituent the average value is 0.13 ± 0.01. [d] Estimated value obtained as HB(Xpy; H_2O) = $0.13\delta_R\Delta H_i(g)$. [e] Estimated value obtained as HB(Xpy; H_2O) = $0.16\delta_R\Delta H_i(g)$ for electron-withdrawing substituents, or $0.10\delta_R\Delta H_i(g)$ for electron donating substituents. [f] Value obtained from hydrogen bonding with CH_3OH in CCl_4—cf. Table V. [g] Value obtained from heats of solution in CH_3OH—cf. Table V.

greater in the monosubstituted benzene than for the corresponding substituted pyridine. We overcome the former limitation using Fuchs'[53] data for heats of solution of substituted benzenes in methanol and our heat of solution measurements for the corresponding substituted pyridines in methanol (Table V). To avoid the second limitation, the method is applied only for substituents which have been established[54] to be "chemically inert".

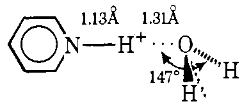
In view of the small probable difference in the ability of water and methanol to act as H-bond donors, the substituent effect on the Xpy···$(H_2O)_n$ and on the Xpy···$(HOMe)_n$ hydrogen bond strengths are expected to be similar. Support for this notion is found by comparing the directly measured heats of formation of the hydrogen-bonded complex between methanol and the series of substituted pyridines in carbon tetrachloride,[55] our estimate based on the difference in $\delta\Delta H_s^{g\rightarrow MeOH}(B)$ of the substituted pyridine and that of the corresponding substituted benzene in methanol (see Table V), and the above figures.

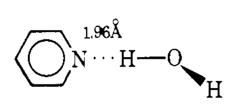
A broader estimation of HB(Xpy; H_2O) terms is made possible by structure-energy relationships. For 3- and 4-substituted pyridines (*only*—cf. ref 2) the relative free energy of hydrogen bonding to p-FC_6H_4OH in CCl_4 solution,[56] $\delta\Delta G_{HB}$, parallels approximately the gas phase $\delta\Delta H_i$ values for relative proton affinities, the H-bonding acting as a partial proton transfer. Values of the ratio $\delta\Delta G_{HB}/\delta\Delta H_i$ are given in Table VI for a number of 3- and 4-substituted pyridines. All values of this ratio are positive and approximately constant (av value is 0.10 ± 0.03). Some minor distinctions may be noted, namely, that the ratio is 0.06 ± 0.02 for electron-releasing substituents, whereas it is 0.13 ± 0.01 for electron-withdrawing substituents. Two lines of experimental evidence suggest that the use of hydrogen bonding of the pyridines to p-fluorophenol to estimate HB(Xpy; H_2O) terms is approximately correct. First, the linear free energy relationship,[56]

$$\log K_{f(H_2O)} = m(\log K_f \equiv pK_{HB})_{p\text{-}FC_6H_4OH} + c$$

is obeyed in CCl_4 solution[51] with $m = 0.65$, a value reasonably close to unity. Secondly, the difference in the heat of hydrogen bonding of p-fluorophenol in CCl_4 to pyridine and to benzene is 6.0 kcal,[57] compared with the 4.3 kcal figure estimated (above) from heats of solution of pyridine and benzene for the hydrogen bonding of water to pyridine.

We have also investigated the energetics of substituent effect on hydrogen bonding of water to pyridine (in the gas phase) by theoretical means. Ab initio molecular orbital calculations have been carried out at the STO-3G level[4,58] of the relative energies of attachment to a series of 3- and 4-substituted pyridines of a H-bond donor water molecule. Geometries for the hydrogen-bonded complexes are based on the (partially) optimized structures. For pyridinium ion–water systems, a linear arrangement of the hydrogen bond has been assumed (∠N–H···O = 180 °), and only the N–H and H···O bond lengths have been optimized as well as a single angle. Other geometrical parameters are those of the individually optimized protonated pyridine[59a] and water[59b] molecules. For pyridine–water systems, a linear hydrogen bond arrangement has again been assumed, and only a single N···H bond length optimized. Optimized geometries for pyridine[59a] and water[59b] have again been employed. For both of these systems substituents on the aromatic rings in pyridine and protonated pyridine have been attached using standard model bond lengths.[60]



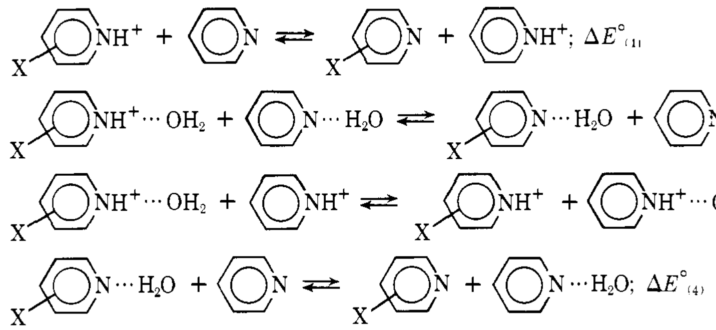


The results are given in Table VII, as $\Delta E°_{(4)}$ values, cf. reaction 4, together with a comparison of the experimental gas-phase $\delta\Delta H_i$ values and corresponding values of the theoretically calculated relative proton affinities (given as $\Delta E°_{(1)}$ values). Since agreement is generally quite satisfactory between corresponding calculated $\Delta E_{(1)}$ and experimental $\delta\Delta H_i$ values, we believe the calculated values of $\Delta E°_{(4)}$ are probably correspondingly accurate (i.e., that about the same percentage errors may be involved). The theoretical calculations of $\Delta E_{(4)}$ faithfully reproduce the above features of the empirical structure-energy relationship, namely, that $\Delta E_{(4)}/\Delta E_{(1)} = 0.06 \pm 0.01$. Furthermore, the same minor distinctions are noted, i.e., $\Delta E_{(4)}/\Delta E_{(1)} = 0.04$ for electron-donor substituents, but a somewhat larger value of $\Delta E_{(4)}/\Delta E_{(1)} = 0.08 \pm 0.01$, is obtained for the electron-acceptor substituents.

As the result of this excellent structure-energy relationship agreement, we believe that the HB(Xpy; H_2O) terms can be estimated quantitatively using the gas-phase $\delta\Delta H_i(g)$ values. Thus, for example, for the 4-CH_3 substituent the HB(Xpy; H_2O) term of 0.4 kcal/mol obtained above from heats of solution data and the corresponding $\delta\Delta H_i(g) = 4.0$ kcal/mol, gives a proportionality constant of 0.10 = 0.4/4.0. Similarly, the HB(Xpy; H_2O) term for 3-Cl from Table VI (taking the average estimated value of 0.95 kcal), together with $\delta\Delta H_i(g) = -5.8$ kcal, gives a proportionality constant of 0.16. Thus, the average of these two values, 0.13 ± 0.03, can be used to estimate the other HB(Xpy; H_2O) from the available $\delta\Delta H_i(g)$ values. The results so obtained are summarized with the other estimated values in the last column of Table VI. Alternate estimates based upon using the proportionality "constant" of 0.10 for electron-donating substituents and the "constant" of 0.16 for electron-accepting substituents are also shown.

It is noteworthy that estimated values of HB(Xpy; H_2O) are almost exactly twice the corresponding theoretical values of $\Delta E°_{(4)}$ (Table VII) for the attachment of a single H-bonding water molecule to the pyridine. This factor of 2 may be interpreted as the factor by which bulk water acts as a better H-bond donor than does a single water molecule.

Table VII. STO-3G Calculations (in kcal/mol) for the Following Reactions



(1)

(2)

(3)

(4)

X	$\delta\Delta H°_i$ (g)	$\Delta E°_{(1)}$	$\Delta E°_{(2)}$	$\Delta E°_{(3)}$	$\Delta E°_{(4)}$	$\frac{\Delta E°_{(1)}}{\Delta E°_{(2)}}$	$\frac{\Delta E°_{(4)}}{\Delta E°_{(1)}}$	$\frac{\Delta E°_{(3)}}{\Delta E°_{(1)}}$	$\frac{\Delta E°_{(4)}}{\Delta E°_{(3)}}$
4-OCH_3	6.7	8.5	6.0	−2.2	0.3	1.4	0.04	−0.26	−0.14
4-CH_3	4.0	5.0	3.3	−1.5	0.2	1.5	0.04	−0.30	−0.13
3-CH_3	2.7	2.5							
3-F	−6.6	−6.3	−4.4	1.5	−0.4	1.4	0.06	−0.24	−0.27
4-CF_3	−7.8	−6.8	−5.1	1.1	−0.6	1.3	0.09	−0.16	−0.55
4-CN	−10.5	−11.4	−8.6	1.9	−0.9	1.3	0.08	−0.17	−0.47
3-CN	−11.3	−12.4	−9.1	2.5	−0.8	1.4	0.06	−0.20	−0.33

Table VIII. Net Contributions from CAV, STR, and VDW Terms to the Substituent Effects on the Heats of Solution of Pyridines

Pyridine substituent	$\delta\Delta H_s^{g\rightarrow H_2O}$(B)	HB(Xpy; H_2O)	Difference	$-\delta\Delta H_V^{g\rightarrow l}$(B)
3,5-$(CH_3)_2$	−2.53	−0.7	−1.8	−2.4
4-CH_3O	−2.20	−0.7	−1.5	−3.0
4-CH_3	−1.34	−0.4	−0.9	−1.2
2-CH_3	−1.24	−0.4	−0.8	−0.5
3-CH_3	−1.12	−0.3	−0.8	−1.0
3-Cl	−1.10	0.9	−2.0	−2.3
4-CF_3	0.27	1.1	−0.8	−0.4
4-CN	1.90	1.6	0.3	

Finally, we may examine the differences in the corresponding values of $\delta\Delta H_s^{g\rightarrow H_2O}(B)$ of Table IV and selected values of HB(Xpy; H_2O) terms of Table VI to obtain estimates of the net contributions of CAV, STR, and VDW terms to the substituent effects upon the heats of transfer of the pyridines from the gas to aqueous phases. These results are given in column 3 of Table VIII, together with values of $-\delta\Delta H_V^{g\rightarrow l}(B)$ (column 4) the substituent effects on the condensation heats of the pyridines.

It is apparent from the results in Table VIII that the net contributions from the estimated CAV, STR, and VDW terms show a very substantial degree of correlation with the heat of condensation terms. Thus, VDW terms[48] are clearly implicated as the second main (but probably not the only) contribution beside the HB terms to $\delta\Delta H_s^{g\rightarrow H_2O}(B)$ values.

Hydration and Hydrogen Bonding of the Pyridinium Ions. The values of $\delta\Delta H_s^{g\rightarrow H_2O}(BH^+)$ for the pyridinium ions in Table III correct and bring up to date some results reported previously by us for some of the members of this series.[3] Comparison of the hydration enthalpies of these ions with those for the corresponding neutral pyridines shows a range of nearly 8 kcal/mol for the ions compared to about 4.5 kcal/mol for the bases. Furthermore, the results for the ions generally trend in the reverse order to those observed for the neutral bases. Note, however, the results for 3-Cl are exceptional.

Since the sizes and shapes of the ions and their conjugate bases must be quite similar, or at least follow similar trends, the inverse trends for solvation enthalpies in the two series are surely not due to cavity effects. Available published data on volumes of ionization (ΔV_i) of amines in water[61-63] or of partial molar volumes $\bar{V}_2$ of ammonium ions[63,64] shed only limited light on the series of pyridines considered here, since they do not include the effects of any groups other than alkyls attached to nitrogen. For variously alkylated amines and ammonium ions, $\bar{V}_2$ is a remarkably additive property.[3,65] Electrostriction of solvent by the intense electrical field of an ion always leads to a reduction in volume when a neutral acid or base is ionized in water. Thus volume of ionization seems to be independent of the size or shape of the few organic amines for which this property has been studied. From this we infer that the STR terms for each pyridine in this study and its ion probably differ by a considerable, but nearly constant amount. Furthermore, the fact that volumes of ionization for a variety of alkylated amines are nearly identical implies that water-structural changes due to 3- or 4-substituents have little or no effect on volumes of ionization.

Terms of the VDW (Xpy; H_2O) type probably make some significant contributions to the values of $\delta\Delta H_s^{g\rightarrow H_2O}(BH^+)$ however. Fuchs and Rodewald[53] have found $\Delta H_s^{g\rightarrow solvent}(B)$ values to depend importantly upon the substituents present in benzenes, a result applicable to both polar and nonpolar solvents. While there is no information of this kind available for ions, the remarkably consistent additive contributions of substituent effects to $\delta\Delta H_s^{g\rightarrow solvent}(B)$ values found by Fuchs and Rodewald is very suggestive of the importance of VDW terms in the $\delta\Delta H_s^{g\rightarrow H_2O}(BH^+)$ values as well. Further, if $\delta\Delta H_s^{g\rightarrow solvent}(BH^+)$ values were nearly entirely due to HB(XpyH$^+$; H_2O) terms, a relatively precise inverse relationship probably should exist between the gas-phase relative proton affinities and the $\delta\Delta H_s^{g\rightarrow H_2O}(BH^+)$ values. This conclusion follows from the notion that bulk water should partially "deprotonate" the pyridinium ions by acting as an H-bond acceptor. While values of $\delta\Delta H_s^{g\rightarrow H_2O}(BH^+)$ of Table III do show such a trend, the relationship is a relatively crude one. This suggests contributions of other terms in addition to a dominant HB(XpyH$^+$; H_2O) term.

If additivity of the VDW (Xpy; H_2O) terms, as well as any STR and CAV terms, were nearly independent of the charging of the pyridines to pyridinium ions (as might be supposed if the polarizability of substituents were not strongly influenced), then the difference $\delta\Delta H_s^{g\rightarrow H_2O}(BH^+) - \delta\Delta H_s^{g\rightarrow H_2O}(B)$ should be essentially free of these kinds of terms. This difference would then give, on a quantitative basis, the difference in hydrogen-bonding terms between the pyridinium ion, as

Table IX. Estimated Substituent Effects on Hydrogen Bonding Energies for Hydration of Pyridinium Ions, HB(XpyH$^+$; H_2O) Terms

	HB(XpyH$^+$; H_2O)[a]	$0.5\delta\Delta H_i$(g)	$\delta\Delta G_i$(aq)	$\delta\Delta H_i$(aq)	Ratio $\frac{\text{HB(Xpy; H}_2\text{O)}}{\text{HB(XpyH}^+\text{; H}_2\text{O)}}$
4-NMe_2	6.5	7.3	5.9	6.9	−0.23
4-OMe	3.9	3.4	1.9	2.6	−0.26
3,5-diMe	3.3	2.9	1.1	1.6	−0.21
4-Me	2.3	2.0	1.1	1.3	−0.17
2-Me	1.7	1.8	1.1	1.4	−0.24
3-Me	1.5	1.4	0.6	0.9	−0.20
H	0.0	0.0	0.0	0.0	
3-Cl	−2.2	−2.9	−3.3	−2.2	−0.41
4-CF_3	−4.0	−4.1	−3.5	−2.6	−0.30
4-CN	−5.0	−5.3	−4.6	−3.8	−0.32

[a] Obtain from eq 5′: HB(XpyH$^+$; H_2O) = $\delta\Delta H_s^{g\rightarrow H_2O}(BH^+) - \delta\Delta H_s^{g\rightarrow H_2O}(B)$ + HB(Xpy; H_2O) = $\delta\Delta H_i(g) - \delta\Delta H_i(aq)$ + HB(Xpy; H_2O). Values used are given in Tables III and VI.

donor, and the corresponding pyridine, as acceptor. That is, the simplified equality would prevail (at least approximately):

$$\delta\Delta H_s^{g\rightarrow H_2O}(BH^+) - \delta\Delta H_s^{g\rightarrow H_2O}(B) \cong \text{HB}(\text{XpyH}^+; H_2O) - \text{HB}(\text{Xpy}; H_2O) \quad (5)$$

Since both HB terms are expected to parallel $\delta\Delta H_i$(g), so also should the difference HB(XpyH$^+$; H_2O) − HB(Xpy; H_2O). Thus, the above equality may be tested for and confirmed by finding a correlation between the quantities $\delta\Delta H_s^{g\rightarrow H_2O}(BH^+) - \delta\Delta H_s^{g\rightarrow H_2O}(B)$ and corresponding $\delta\Delta H_i$(g) values. Indeed, as Figure 1 shows, there is a remarkably linear relationship found for such a plot, at least for a wide variety of 3- and 4-substituents, and for 2-methyl substituents.

Having obtained confirmatory evidence for eq 5 by Figure 1, we have proceeded to utilize this equation with the data from Tables III and VI to make quantitative estimates of the HB(XpyH·; H_2O) terms:

$$\text{i.e., HB}(\text{XpyH}^+; H_2O) \cong \delta\Delta H_s^{g\rightarrow H_2O}(BH^+) - \delta\Delta H_s^{g\rightarrow H_2O}(B) + \text{HB}(\text{Xpy}; H_2O) = \delta\Delta H_i(g) - \delta\Delta H_i(aq) + \text{HB}(\text{Xpy}; H_2O) \quad (5')$$

The results are summarized in Table IX. As expected, the HB(XpyH$^+$; H_2O) terms are precisely reverse to the corresponding HB(Xpy; H_2O) terms (as shown by the ratio HB(Xpy; H_2O)/HB(XpyH$^+$; H_2O), given in the final column of Table IX) and are precisely linear with $\delta\Delta H_i$(g) values (as shown in Table IX by the agreement with 0.5 $\delta\Delta H_i$(g) values listed in the second column).

The average value of the ratio HB(Xpy; H_2O)/HB(XpyH$^+$; H_2O) given in Table IX is −0.3 ± 0.1. That is, the substituent effect on hydrogen bonding attachments of bulk water to pyridinium ions is about four times greater in magnitude, and opposite in sign, than that for the neutral pyridines. A factor of four indeed seems to be in the correct order of magnitude for such an effect of charge as judged by the following unpublished results of Wolf and Taft[66] for the gas-phase attachment exchange equilibria:

$$\text{py}_2\text{H}^+_{(g)} + \text{B}_{(g)} \overset{K_e}{\rightleftharpoons} \text{pyH}^+\cdots\text{B} + \text{py}_{(g)} \quad (6)$$

Values of log K_e for reaction 6 have been found for a series of hydrogen bond acceptors (B) to follow pK_{HB} values for "attachment" to the neutral H-bond donor, p-FC_6H_4OH in CCl_4. The slope, $\delta \log K_e/\delta pK_{HB} = 3.2$, indicates the order of magnitude of the greater H-bond donating ability of pyH$^+$ compared to the neutral proton donor, p-FC_6H_4OH.

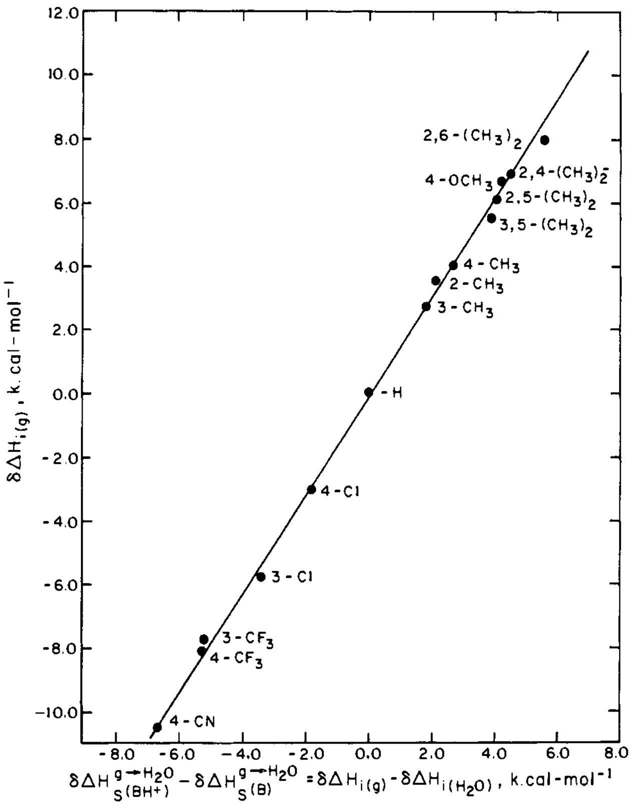


Figure 1. Correlation of substituent effects on gas-phase proton affinities of pyridines with the corresponding aqueous solvation effects on pyridinium ions and pyridines (slope of regressive line is 1.55): ordinate—$\delta\Delta H_i$(g), kcal mol^{-1}; abscissa—$\delta\Delta H_s^{g\rightarrow H_2O}(BH^+) - \delta\Delta H_s^{g\rightarrow H_2O}(B) = \delta\Delta H_i(g) - \delta\Delta H_i(H_2O)$, kcal mol^{-1}.

Other evidence relating hydrogen-bonding ability of the pyridinium ions is found in our own infrared data (Table II) and in the proton transfer study by Delpeuch and Serratrice.[67,68] These workers determined the rates of proton transfer between water and pyridines and pyridinium ions—many of them the same as those in our study. For proton transfer from a pyridinium ion to water through formation of a XpyH$^+\cdots(OH_2)_n$ hydrogen bond, they found a sharp dependence on substitution of the pyridine ring and on the water concentration of the acidic solvent. This rate primarily determines the equilibrium constant for ionization. In contrast, the rates of water exchange for the neutral pyridines through a Xpy$\cdots(HOH)_n$ hydrogen bond are close to the diffusion-controled limit and are much less sensitive to substitution. Comparison of the HB(XpyH$^+$; H_2O) values with the standard free energies of ionization $\delta\Delta G^\circ_i$ (which we have just seen[65,66] are determined by the rate of proton transfer from the pyridinium ion to water) is made in Table IX. The close agreement be-

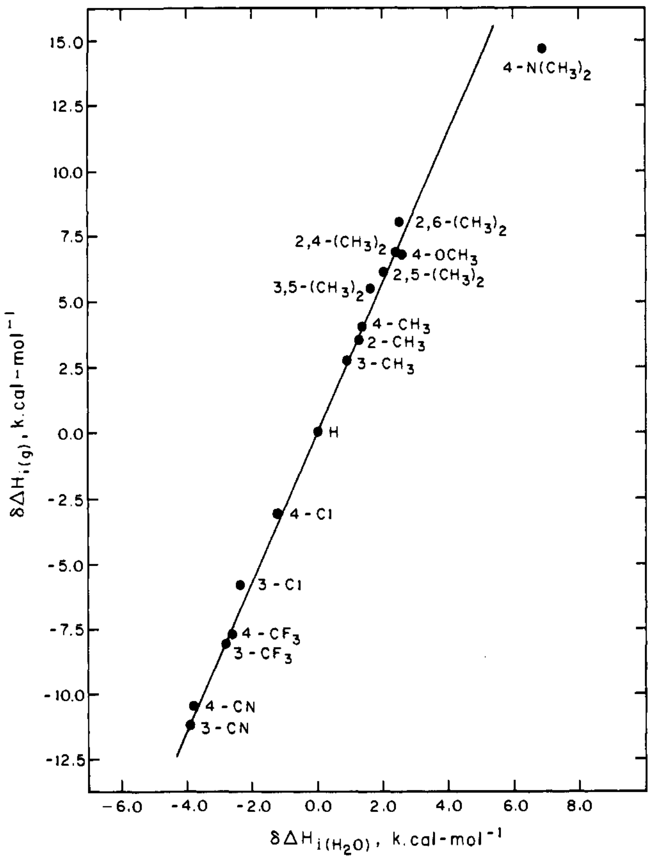


Figure 2. Correlation of substituent effects on gas-phase proton affinities of pyridines with the corresponding effects on aqueous heats of ionization: ordinate—$\delta\Delta H_i(g)$, kcal mol^{-1}; abscissa—$\delta\Delta H_i(H_2O)$, kcal mol^{-1}.

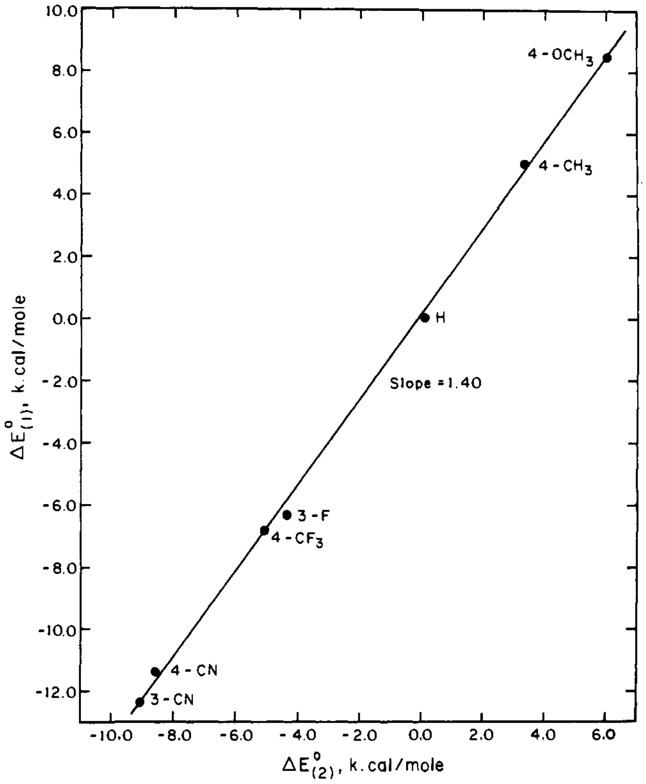
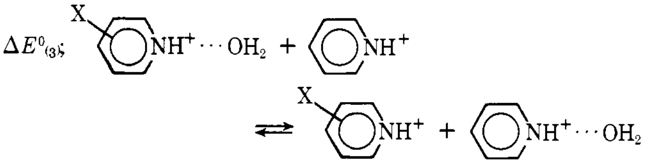


Figure 3. Theoretical linear structure-energy relationship for STO-3G calculated substituent effects on proton affinity with corresponding effects from monohydrated pyridinium ions and pyridines: ordinate—$\Delta E°_{(1)}$, kcal mol^{-1}, cf. Table VII for reaction; abscissa—$\Delta E°_{(2)}$, kcal mol^{-1}, cf. Table VII for reaction.

tween these properties confirms their common source in the strength of the hydrogen bond from pyridinium ion to bulk water.

Finally, we again turn to ab initio molecular orbital calculations at the STO-3G level to provide independent confirmation of this treatment of the hydration of pyridinium ions. Calculations have been carried out for the relative energy change of attaching a water molecule to the pyridinium ion as an H-bond acceptor.



These results are given in Table VII, which also gives values of the ratio, $\Delta E_{(3)}/\Delta E_{(1)}$ ($\Delta E_{(1)}$ is the theoretically calculated value of $\delta\Delta H_i(g)$). The values of this ratio are approximately constant, i.e., $\Delta E_{(3)}/\Delta E_{(1)} \simeq -0.22$, a result having the same functional dependence as observed above for the empiricially estimated HB(XpyH$^+$; H$_2$O) terms. Indeed, the theoretical structure-energy relationship for single water attachments differs from the empirical structure-energy relationship only by indicating that a single water molecule has about one-half as strong a hydrogen bond acceptor effect as does bulk water $(H_2O)_n$. Gordon[69] has earlier demonstrated that this order of H-bond acceptor ability does apply. It is also suggested by attachment energetics (which are not truly equivalent in terms of equivalent numbers of protonic hydration sites) obtained by Kebarle[70] in the gas phase, e.g.,

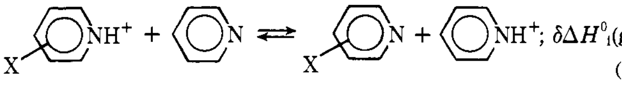
$$H_9O_4{}^+{}_{(g)} + H_2O_{(g)} \rightleftarrows H_9O_4{}^+ \cdots OH_{2(g)}; \quad \Delta E = 15 \text{ kcal/mol}$$

$$H_9O_4{}^+{}_{(g)} + 4H_2O_{(g)} \rightleftarrows H_9O_4{}^+ \cdots (OH_2)_{4(g)}; \quad \Delta E = 44 \text{ kcal/mol}$$

The theoretical calculations of the ratio $\Delta E_{(4)}/\Delta E_{(3)}$ (cf. Table VII), which corresponds to the empirically evaluated ratio HB(Xpy; H$_2$O)/HB(XpyH$^+$; H$_2$O), also confirm the reasonableness of the value of -0.3 ± 0.1, i.e., the approximately four times greater magnitude (but opposite sign) of the substituent effect for hydrogen bonding of water (either monomeric or bulk) to pyridinium ions compared to that for the neutral pyridines.

Summary

In Figure 2 are plotted the relative proton affinities of 3- and 4-substituted pyridines ($\delta\Delta H_i(g)$) vs. the corresponding relative enthalpies of ionization in aqueous solution ($\delta\Delta H_i(aq)$). A linear relationship[71] of good precision is obtained (as, of course, is required by Figure 1) for which the solvent attenuation factor (slope) is 2.5. The proton transfer equilibria involved are given in eq 7 and 8.



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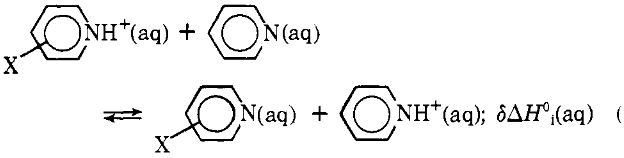
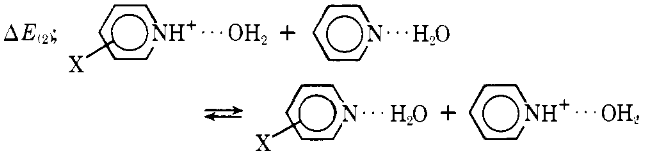


(8)

Earlier ideas[72] on the interpretation of solvent effects such as this have centered largely on the physical picture of an increased (but somewhat artificial) effective dielectric constant acting in the water medium to reduce electrostatic ion-dipole interactions. In this paper we have carried out an analysis of the hydration (solution) equilibria for substituted pyridines and pyridinium ions transferred from the gas phase to dilute aqueous solution. The analysis indicates that these equilibria may be understood on a quantitative basis, as can the aqueous solvent attenuation factor of 2.5, in terms of chemical hydrogen-bonding interactions of bulk water with the pyridinium ions and the pyridines.

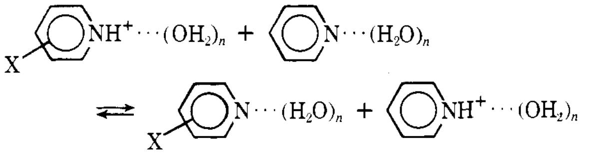
For insight in this analysis, ab initio molecular orbital calculations at the STO-3G level have been carried out for reaction 1 of Table VII, giving $\delta\Delta E°_i$ values which are in generally good accord with the experimental $\delta\Delta H_i(g)$ values. The calculations have been extended to give energy changes for the proton transfer reaction for which a single water molecule is attached as an H-bond acceptor to the pyridinium ions and a single H-bond donor water molecule is attached to the pyridines (Table VII).

$\Delta E_{(2)}$;



In Figure 3 are shown the theoretical values of $\delta\Delta E°_i$ plotted vs. corresponding $\Delta E_{(2)}$ values. As observed in Figure 2 an excellent linear relationship is obtained. The single water molecule attenuation factor (slope of Figure 3) is 1.4.

The aqueous solvent attenuation factor of 2.5 by comparison can be attributed to the notion that bulk liquid water has about twice as strong an H-bond acceptor effect as monomeric water toward the pyridinium ions and twice as strong an H-bond donor effect toward the pyridines. There is close agreement between both experimental data and the theoretical calculations, that the magnitude of the substituent effects on hydrogen bonding to the pyridinium ions is about four times greater in magnitude (but opposite in sign) than that for hydrogen bonding to the pyridines. In these simple terms, the nonspecific reaction 8 may be replaced by the following reaction 9.



(9)

Heats of transfer of the pyridinium ions and pyridines from the gas phase to dilute aqueous solution are found to be somewhat complicated composites of H-bonding, cavity, van der Waals interactions, and water structure modification terms. However, substituent effects on contributions of the latter three terms are nearly additive and thus cancel in the difference between the corresponding heat of transfer of the ion and the neutral pyridine. Thus: $\delta\Delta H_s^{g\rightarrow H_2O}(BH^+) - \delta\Delta H_s^{g\rightarrow H_2O}(B) \cong HB(XpyH^+;\ H_2O) - HB(Xpy;\ H_2O)$. Further, by thermodynamic requirements,

$$\delta\Delta H_s^{g\rightarrow H_2O}(BH^+) - \delta\Delta H_s^{g\rightarrow H_2O}(B) = \delta\Delta H_i(g) - \delta\Delta H_i(aq) \cong HB(XpyH^+;\ H_2O) - HB(Xpy;\ H_2O)$$

Structure-energy relationships for the HB terms are found to be:

$$HB(XpyH^+;\ H_2O) \cong 0.5\delta\Delta H_i(g)$$

and

$$HB(Xpy;\ H_2O) \cong -0.1\delta\Delta H°_i(g)$$

Combining these relationships then gives

$$\delta\Delta H_i(g)/\delta\Delta H_i(aq) = 1/0.4 = 2.5$$

In terms of linear free energy relationships (e.g., $\sigma\rho$) the present treatment provides a specific hydrogen-bonding model for the understanding of solvent effects on ρ values. While the success of this model in the present application offers strong encouragement for further such applications, we believe a word of caution is in order. The proton transfer equilibria for 3- and 4-substituted pyridines (with "chemically inert substituents") were chosen as an optimal reaction series for application of the H-bond solvation model. Such a series offers ions and molecules of very similar sizes and shapes with substituents distant enough to maintain nearly constant cavity formation and structure modifying terms, as well as allowing for the cancellation between pyridinium ion and corresponding pyridine of van der Waal dispersion force terms. In accord with this conclusion, the substituent effects on entropies of ionization in water[73] for this series are relatively small (~±3 eu—cf. Table III). Application of the H-bond model for solvent effects on the ρ values for other proton-transfer equilibria for meta- and para-substituted side-chain derivatives of benzene (especially those having large entropy effects in water) will provide interesting and critical tests of the model. Tests in nonaqueous solvents of varying H-bond donor and acceptor ability are also clearly of great interest.[74]

As Taft has emphasized earlier,[2] there is no *general* relationship between effects of structure upon gas-phase proton-transfer equilibria and corresponding aqueous solution equilibria. Indeed, free energy plots of such data are *exceedingly* scattered. The approximately linear relationship observed for the present series is indeed a special case of the very limited structural variation permitted. Deviations from this relationship for many 2-substituents (other than 2-CH_3) have been noted.[23] We believe that all four hydration terms of Friedman and Krishnan do generally contribute in complex ways to the solvation effects on aqueous proton-transfer equilibria involving wide variations of molecular structure (especially at or near the protonation site). The challenge of analysis of such solvent effects is clearly a very substantial one, but we believe the present findings do offer encouragement toward meeting this task.

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