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The Ionic Hydrogen Bond. 1. Sterically Hindered Bonds. Solvation and Clustering of Protonated Amines and Pyridines

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Abstract: The hydrogen-bonded dimer ions $BH^+{\cdot}B$ and monohydrates $BH^+{\cdot}H_2O$ of 2-alkylpyridines, 2,6-dialkylpyridines, and tertiary amines were investigated in the gas phase in the absence of solvent effects. The dissociation energies $\Delta H_D°$ of the dimers and hydrates are not affected by steric crowding. Thus, $\Delta H_D°$ of the dimers $BH^+{\cdot}B$ remains constant at 23 ± 1 kcal mol^{-1} even as the substitution varies from (2-methylpyridine)$_2$H$^+$ to (2,6-di-*tert*-butylpyridine)$_2$H$^+$ and from $(Me_3N)_2H^+$ to (n-Bu$_3$N)$_2$H$^+$. Similarly, $\Delta H_D°$ of the hydrates $BH^+{\cdot}H_2O$ show only small variations that can be entirely ascribed to proton affinity differences. However, steric hindrance causes major entropy effects unfavorable to dimerization or hydration. Entropies of dissociation (cal mol^{-1} K^{-1}) vary from $\Delta S_D° = 27.8$ for (2-methylpyridine)$_2$H$^+$ to 48.4 for (2,6-disopropylpyridine)$_2$H$^+$, from 32.0 for $(Me_3N)_2H^+$ to 56.5 for (n-Bu$_3$N)$_2$H$^+$, from 26.6 for (2-methylpyridine)H$^+{\cdot}$H$_2$O to 41 for (2,6-di-*tert*-butylpyridine)H$^+{\cdot}$H$_2$O. The entropy contribution, i.e., $\Delta S°_{\text{steric}}$, ranges up to 12, 17, and 14 cal mol^{-1} K^{-1} in (2,6-diisopropylpyridine)$_2$H$^+$, (n-Bu$_3$N)$_2$H$^+$, and (2,6-di-*tert*-butylpyridine)H$^+{\cdot}$H$_2$O, respectively. The large steric entropy factor in the latter hydrate may be due to the simultaneous freezing of the rotations of the two *tert*-butyl groups and of H_2O upon monohydration. The gas-phase proton affinities of hindered pyridines were also measured and compared with aqueous basicities to evaluate steric effects in aqueous solution. It appears that steric hindrance to ion solvation in bulk water is comparable in magnitude to steric hindrance of solvation by only one H_2O molecule. Our observations may be summarized as follows: as long as there exists a single confirmation in which the hydrogen bond in $BH^+{\cdot}B$ or $BH^+{\cdot}H_2O$ can obtain optimal geometry, the bond strength is not weakened by steric crowding. However, steric crowding may result in major entropy effects due to the hindrance of internal rotors in the dimers and monohydrates.

Intermolecular interactions of structurally complex species can be affected by unique factors that are absent in simple molecules. For example, in previous publications we observed that multiple hydroen-bonding sites can substantially increase the stabilities of dimer ions,[1] that in polyfunctional ions intramolecular hydrogen bonding can affect the interaction with external solvent molecules,[2] and that in ions with large π systems intramolecular charge delocalization can weaken the resonance interactions with external electon donors.[3] In the present work we investigate the effect of another type of structural complexity, the steric crowding of hydrogen-bonding sites, on the thermochemistry of ion solvation and clustering.

2- and 2,6-substituted pyridines are model compounds that reflect the effects of steric crowding on hydrogen bonding, basicity, and reactivity. For example, the hydrogen-bonded complexes of 2- and 2,6-substituted pyridines with phenol are less stable by 0.2–0.3 kcal mol^{-1} than comparable complexes of 3- and 4-substituted pyridines.[4] Also, 2-6-di-*tert*-butylpyridine 2,6-(t-Bu)$_2$PyrH$^{+\,5}$ is less basic in aqueous solution by 3–4 kcal mol^{-1} than may be expected on the basis of its gas-phase proton affinity (PA), and the diminished basicity has been assigned to steric hindrance. Further, steric hindrance can also decrease the rate constants of proton-transfer reactions of alkylpyridines.[7]

The physical basis of steric effects in 2- and 2,6-substituted pyridines was discussed by several authors. Brown and Kanner,[8] who discovered the reduced basicity of 2,6-(t-Bu)$_2$Py, attributed the effect to crowding of the proton in the protonated ion, or the interference of the *tert*-butyl groups with the $N{-}H^+{\cdots}OH_2$ ion–solvent hydrogen bond, or the interference of the substituents with the overall solvation of the ionic charge. The high gas-phase PA of 2,6-(t-Bu)$_2$Pyr subsequently showed that the diminished basicity is not an intrinsic molecular property, and thus the first factor is ruled out. Furthermore, measurements of volumes of ionizaton do not support interference with bulk charge solvation.[9] Solvent effects on the pK's indicate that the significant factor is the interference of the bulky substituents with the ion–solvent hydrogen bond.[10-12] Our observations will support and quantify this conclusion and extend it to the other 2- and 2,6-alkylpyridines.

The nature of steric interference of bulky substituents with the hydrogen bond to the solvent has not been clarified. In discussing the steric effect on basicity[8,9] hydrogen bonding,[4] and reactivity,[7] the investigators invoked two possibilities. One suggestion is that the substituents interfere with approach of the solvent to the hydrogen-bonding site in the ion. This would result in a less than optimal hydrogen bond and thereby decrease the disociation energy of the hydrogen bond. Alternatively, the substitutents may hinder the rotation of the bonding partners about the hdyrogen bond. This factor would result in an unfavorable entropy term. Hopkins and Ali[13] have, in fact, concluded from solution data that the rotational motions of the *tert*-butyl groups in 2,6(t-Bu)$_2$Pyr are more hindered in the cation than in the neutral ion, indicating an entropy loss.

Equilibrium studies by pulsed, variable-temperature high-pressure mass spectrometry yield enthalpies and entropies of the reactions leading to hydrogen-bonded dimer ions. We have therefore used this technique to identify the factors that contribute to steric interference with the hdyrogen bond.

Experimental Section

The measurements were taken with the NBS pulsed high-pressure mass spectrometer. The basic configuration is similar to that reported previously for the photoionization mode,[14] except that a 0.3-mm electron entrance hole replaced the window on the ion source. An electron gun was used as the electron source. Pulsing was obtained by deflecting the electron beam away from the entrance hole, except when a pulse was applied to the focusing plates. Usually 500–1000-V electrons were used. The pulse widths were 100–500 μs, and ions were observed to reaction times of 2–10 ms, in channels of 10 or 20 μs widths. The ion signal was fed from the ion multiplier through an amplifier to a signal averager.

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(5) We will use the abbreviations Me, Et, Pr, Bu, and Pyr to denote methyl, ethyl, propyl, butyl, and pyridine, respectively, throughout the text.

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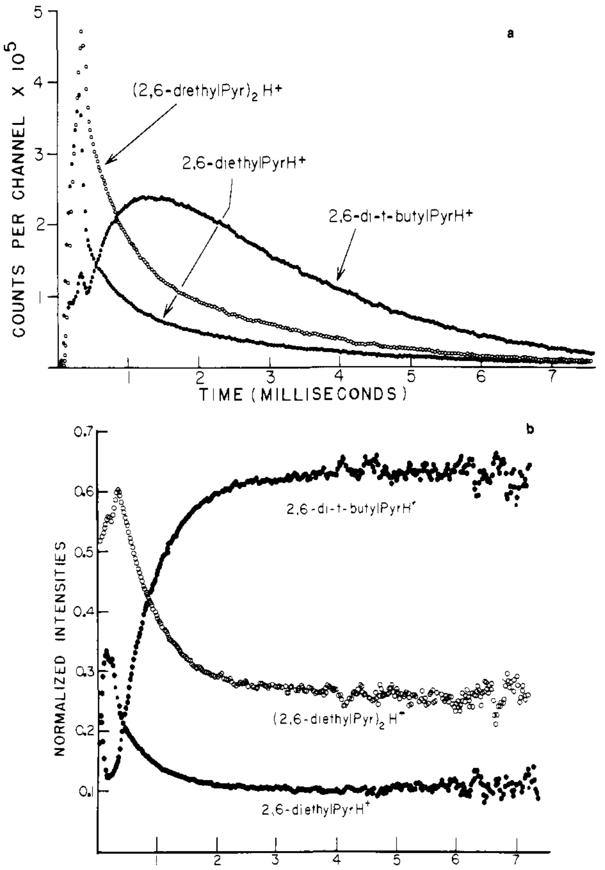


Figure 1. Ion intensities in an equilibrium system: 2,6-Et_2Pyr (2.0%) and 2,6-(t-Bu)$_2$Pyr (0.125%) in cyclohexane, P_{total} = 0.800 torr; T = 378 K: (a) absolute ion signal intensities; (b) normalized ion intensities. Equilibrium in dimerization is reached "instaneously", and in the proton-transfer reaction after about 3 ms.

Collected data were fed to a microcomputer, which was used to normalize ion intensities at each reaction time and to calculate equilibrium constants in the usual manner. Typical plots of ion intensities vs. reaction time in an equilibrium system are shown in Figure 1.

In clustering and proton-transfer experiments, liquid mixtures of 0.1–3.0% of the base of interest in cyclohexane or 2,2,4-trimethylpentane were injected into a heated bulb. The mixture was allowed to flow to the ion source, and the solvent served as both the carrier and protonating gas. In solvation experiments similar mixtures were used, but water was also injected into the sample reservoir; usually 90% of the overall carrier gas was H_2O. Pressures in the ion source ranged from 0.2 to 1.0 torr.

Reagents and bases were obtained from commercial sources, were of 98% purity or higher, and were used as purchased. A highly purified sample of 2,6-(t-Bu)$_2$Pyr was donated by Dr. J. Day of Hunter College, NY.

Results

Hydrated ions are formed by association reactions (1) or ligand-transfer reactions (2), followed by equilibrium.

$$BH^+ + H_2O \rightleftarrows BH^+{\cdot}H_2O \qquad (1)$$

$$H_3O^+{\cdot}(H_2O)_n + B \rightarrow BH^+{\cdot}H_2O + nH_2O \qquad (2)$$

In all of our hydration reactions equilibrium was achieved during the ~200–500-μs ionizing pulse. Similtaneously with process 1, the dimer-forming reaction is also observed:

$$BH^+ + B \rightleftarrows BH^+{\cdot}B \qquad (3)$$

In some systems K_3 is quite large, especially at lower temperatures. The interference of reaction 3 with equilibrium 1 was then minimized by using only trace concentrations of B, usually below 0.1% of the total gas in the ion source. In other systems, as (n-Bu)$_3NH^+$ + H_2O, equilibria 1 and 3 were obtained simultaneously. Generally, dimerization equilibria 3 were measured with only B and the reagent gas in the ion source. In cases where (3) was measured in both the absence and presence of water, the value of K_3 was not affected by the simultaneous presence of equilibrium 1.

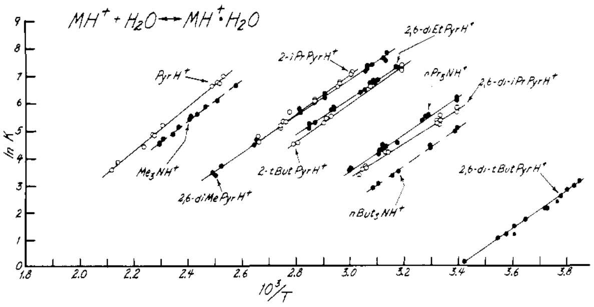


Figure 2. van't Hoff plots for the hydration of pyridinium and ammonium dimer ions, $BH^+ + H_2O \rightleftarrows BH^+{\cdot}H_2O$.

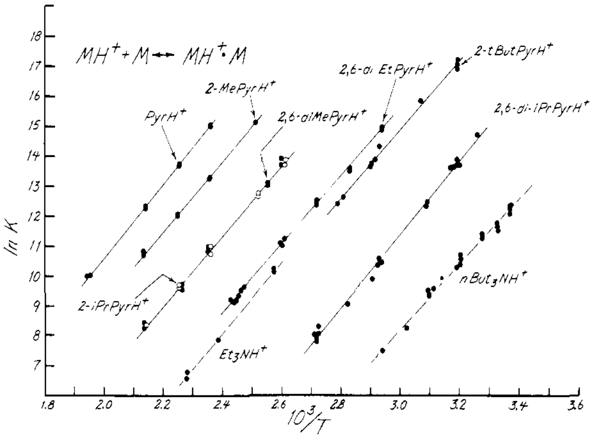


Figure 3. van't Hoff plots for the formation of pyridinium and ammonium dimer ions, $BH^+ + B \rightleftarrows BH^+{\cdot}B$.

In reaction systems containing n-Pr_3H or (n-Bu)$_3$N we observed the slow formation of a B_2H^+–C_2H_4 or B_2H^+–C_3H_8 ion:

$$(n\text{-}C_3H_7)_3NH^+ + (n\text{-}C_3H_7)_3N \rightarrow (n\text{-}C_3H_7)_3NH^+{\cdot}N(n\text{-}C_3H_7)_2CH_3 + C_2H_4 \qquad (4)$$

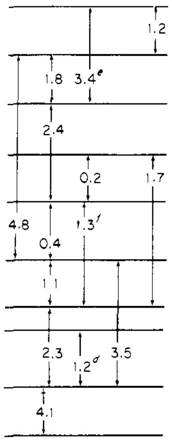
The formation of these ions from BH^+ + B was an irreversable second-order process with a rate constant of (8 ± 2) × 10^{-12} cm^3 s^{-1}; the rate constant was not significantly dependent on the temperature between 20 and 60 °C. The overall production of these ions can be written as (4) and the analogous reaction in (n-Bu)$_3$N. The measurement of equilibria 1 and 3 at various amine concentrations from 0.1% to 1% showed that reaction 4 was too slow to affect the measured values of K.

In addition to the clustering reactions, we also measured proton-transfer equilibria at a single temperature. A few temperature studies were also carried out to establish the gas-phase basicities and proton affinities of some of the 2- and 2,6-alkylpyridines. The results are given in Table I.

All of the equilibrium constants used to construct the van's Hoff plots (Figures 2 and 3) were measured in the range 0.5–1 torr. van't Hoff plots for the hydration of protonated alkylpyridines and alkylamines are given in Figure 2 and for the formation of B_2H^+ dimers in Figure 3. The thermochemical data derived from the van't Hoff plots are presented in Tables I–III. The average of standard deviations from the slopes and intercepts of the van't Hoff plots yields an error estimate of ±0.5 kcal mol^{-1} for $\Delta H°$ and ± 1.5 cal mol^{-1} K^{-1} for $\Delta S°$. In the worst cases, clustering of (n-Bu)$_3NH^+$ and hydration of 2,6-(t-Bu)$_2$PyrH, the standard deviations of the slopes were 0.6 kcal mol^{-1} in $\Delta H°$ and 2.0 cal mol^{-1} K^{-1} for $\Delta S°$.

Some of systems were studied previously in other laboratories. Our values for $\Delta H_D°$ and $\Delta S_D°$ of pyridineH$^+$·pyridine agree well with the values published by Meot-Ner,[1] and our values for (pyridine)H$^+$·H_2O agree well with those obtained by Davidson et al.[15] Although we did not investigate the $Me_3NH^+{\cdot}Me_3N$

Table I. Relative Gas-Phase Basicities (or Proton Affinities), pK_a's and Relative Aqueous Free Energies of Protonation of Alkylpyridines[a, b]



	$\delta\Delta G_{\mathrm{prot,gas}} \cong \delta \mathrm{PA}$			
	MS[c]	AB[d]	p*K*a, H_2O	$\delta\Delta G_{\mathrm{prot,H_2O}}$
2,6-(*t*-Bu)$_2$	13.6	10.6	4.91[g]	−0.42
2,6 (*i*-Pr)$_2$	12.0		6.44[h]	1.68
2,6-Et$_2$	10.2		6.75[j]	2.11
2-Hex	8.0			
2,6-Me$_2$	7.8	6.7	6.72[i]	2.07
2-*t*-Bu	7.4	6.0	5.80[i]	0.80
2-*i*-Pr	6.3		5.83[i]	0.84
2-Et	5.3		5.92[i]	0.97
2-Me	4.1	3.3	5.97[i]	1.04
Pyr	(0)	(0)	5.22[i]	(0.0)

[a] All values in kcal mol^{-1} (except p*K*'s). [b] Ladder shows measured $\Delta G°$ values, at 425 K, for proton-transfer equilibria. [c] This work. [d] Aue and Bowers.[17] [e] From van't Hoff plot, $\Delta H° = 3.1 \pm 0.3$ kcal mol^{-1}, $\Delta S° = -0.7 \pm 0.6$ cal mol^{-1} K^{-1}. [f] From van't Hoff plot, $\Delta H° = 1.8 \pm 0.4$ kcal mol^{-1}, $\Delta S° = 0.9 \pm 0.6$ cal mol^{-1} K^{-1}. [g] Reference 11. Considering the observed variation of p*K*'s with ethanol concentration in ethanol-water mixed solvent, we equate these values, given in 2% ethanol, with p*K*'s in neat water. [h] To estimate pK_{H_2O} of 2,6-(*i*-Pr)$_2$Pyr from the $pK_{50\%\ \mathrm{ethanol}}$,[11] note that ($pK_{H_2O} - pK_{50\%\ \mathrm{ethanol}}$) is 0.45 for 2,6-dimethylpyridine and 1.26 for 2,6-di-*tert*-butylpyridine. The differences for 2-ethyl-, 2-isopropyl-, and 2-*tert*-butylpyridine also fall in this range. We therefore estimate a difference of 1.1 p*K* units for 2,6-diisopropylpyridine. A similar value is obtained on the basis of $pKa_{\mathrm{methanol}} = 6.6$, and the fact that $pKa_{\mathrm{methanol}} - pKa_{H_2O} \approx 0.15$ for pyridine and 2,6-Me$_2$Pyr.[7] [i] Perrin, J. J. "Dissociation Constants of Organic Bases in Aqueous Solution"; Butterworths: London, 1965. [j] Estimated on the basis of $pKa_{\mathrm{methanol}} = 6.9$, and that $pKa_{\mathrm{methanol}} - pKa_{H_2O} \approx 0.15$ for pyridine and 2,6-Me$_2$Pyr.

system, the $\Delta H_D°$ obtained by us for several $R_3NH^+ \cdot R_3N$ pairs agrees well with the value obtained by Yamdagni and Kebarle[16] for $Me_3NH^+ \cdot Me_3N$.

Discussion

Proton Affinities and Aqueous Basicities of Hindered Bases. Before examining the interactions of protonated hindered bases with a solvent molecule, we shall review and extend the data pertaining the steric effects on basicity in bulk solution.

Some time ago Aue et al.[6] and Arnett et al.[12] observed that aqueous free energies and heats of protonation ($\Delta G°_{\mathrm{prot,H_2O}}$ and $\Delta H°_{\mathrm{prot,H_2O}}$) of unhindered 3- and 4-substituted pyridines correlated with the gas-phase PAs of these compounds. 2-Me and 2,6-Me$_2$Pyr fit on the correlation line, indicating that steric effects are not significant when the 2- and 2,6-substituents are methyl groups. However, $\Delta G°_{\mathrm{prot,H_2O}}$ of 2,6-(*t*-Bu)$_2$Pyr deviated by 3–4 kcal mol^{-1} from the correlation line, and this deviation was used to quantify the effect of steric hindrance on the aqueous basicity of this compound.

In order to define the correlation between gas-phase PA's or basicities and $\Delta G°_{\mathrm{prot,H_2O}}$, a consistent ladder of the gas-phase values, including those of the hindered compounds, is required. Since the PAs of some of the hindered compounds have been published and since there are some small differences betwen the two published scales[12,17] for unhindered pyridines, we determined experimentally a PA ladder for these compounds (Table I). In general, our ladder agrees well with the published values, the only significant difference being the PA of 2,6-(*t*-Bu)$_2$Pyr.

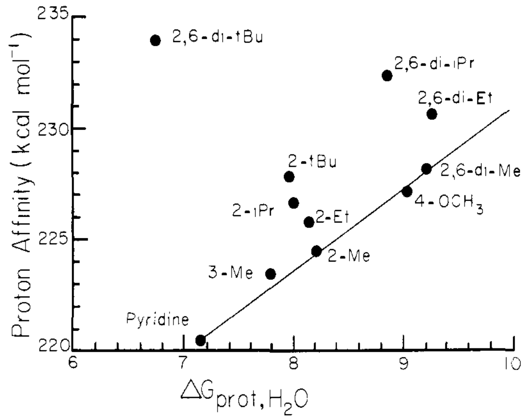


Figure 4. Relation between relative gas-phase basicities (or relative proton affinities) and aqueous basicities for alkylpyridines. The points of pyridine, 3-MePyr, 4-OCH$_3$Pyr, 2-MePyr, and 2,6-Me$_2$Pyr define the correlation line for sterically unhindered bases (see text).

We note that in equating differential PAs to differential gas-phase basicities, the assumption is made that $\Delta S°$ for the proton-transfer reactions is negligible. We confirmed this via temperature studies for the 2-*i*-PrPyr + 2,6-Me$_2$Pyr, 2-*t*-BuPyr + 2,6-Me$_2$Pyr and 2,6-Et$_2$Pyr + 2,6-(*t*-Bu)$_2$Pyr systems, all of which show entropy changes within ±1 cal mol^{-1} K^{-1} of zero.

The values of relative PAs or gas-phase basicities obtained from the ladder of table I are used to construct Figure 4.

We can now examine in Figure 4 the relation between $\Delta G°_{\mathrm{prot,H_2O}}$ vs. PA for the present compounds. In accordance with the method of Aue et al.[6] and Arnett et al.[12] we shall use 2-methyl- and 2,6-dimethylpyridine to construct the correlation line for unhindered compounds. The unhindered compounds 3-MePyr and 4-MePyr also fit on this line. However, the points for 2-isopropyl-, 2-*tert*-butyl-, 2,6-diisopropyl-, and 2,6-*di-tert*-butylpyridine clearly deviate from the relationship. The magnitudes of the deviations ($\Delta\Delta G_{\mathrm{steric,bulk\ H_2O}}$, table II) give a measure of the reduction of aqueous basicities by steric hindrance.

We note that the effects of adding one and two isopropyl groups to pyridine are roughly additive, but the effect of adding two *tert*-butyl groups is much larger (4.6 kcal mol^{-1}) than twice the addition of a 2-*tert*-butyl substituent. The extraordinarily large effect in 2,6-di-*tert*-butylpyridine was also noted by Brown and Kanner,[8] although in the absence of gas-phase data, the magnitude of steric effects on the k*K*'s of the other compounds could not be evaluated. Indeed, the existence of steric effects on the p*K*'s of alkylpyridines except 2,6-di-*tert*-butylpyridine have not been established previously.

In the next section we shall compare quantitatively the steric effect on the basicities of 2- and 2,6-dialkylpyridines in bulk water with the steric effect of solvation by one water molecule.

Solvation of Alkylpyridinium Ions by One Water Molecule. Table II gives the enthalpy and entropy changes for the addition of one water molecule to protonated alkylamines and alkylpyridines. The major trend that we observe is that $\Delta H_D°$ does not change substantially throughout the series, while $\Delta S_D°$ becomes significantly more positive with increasingly bulky substitution (see footnote *b* in Table II for signs of ΔH and ΔS terms).

We observe a slight decrease in $\Delta H_D°$ in going from pyridine to the more highly substituted compounds, which also have increasingly higher proton affinities. This trend is consistent with the observations of Davidson et al.,[15] who studied the association of pyridinium ions with H_2O. The trend results from the fact that

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Table II. Thermochemistry[a] of the Hydration Reactions $BH^+ + H_2O \rightleftarrows BH^+ \cdot H_2O$

	$\Delta H°_D$[b]	$\Delta S°_D$[b]	$-\Delta S°_{tr,rot}$[f]	$\Delta S°_{internal}$	$-\Delta S°_{steric}$[g]	$T\Delta S°_{steric}$	$\Delta\Delta G°_{steric,bulk\ H_2O}$
pyridine H^+	16.1[c]	27.0[c]	43.9	16.9	≈0		
4-Me	14.7[d]	26.6[d]	44.5	17.9	≈0		
2,6-Me_2	13.2	25.9	44.7	18.8	≈0		
2,6-Et_2	(13.0)	28.6[e]	45.3	16.7	1.2	0.4	0.7
2-*i*-Pr	14.2	28.8	45.0	16.2	1.7	0.5	0.8
2-*t*-Bu	14.2	30.8	45.2	14.4	3.5	1.1	1.2
2,6-$(i\text{-Pr})_2$	12.8	32.1	45.6	13.5	4.4	1.3	1.5
2,6-$(t\text{-Bu})_2$	12.5 ± 1.5	41 ± 4	45.7	4.4	13.5	4.1	4.6
Me_3NH^+	14.5	24.1	42.3	18.2	(0)		
Et_3NH^+	13.2	27.3	43.0	15.7	2.5		
n-Pr_3NH^+	12.5	30.2	43.7	13.5	4.7		
n-But_3NH^+	13.6	36.4	44.3	7.9	10.3		

[a] $\Delta H°$ and $\Delta G°$ in kcal mol^{-1}, $\Delta S°$ in cal mol^{-1} K^{-1}. Error estimate, based on scatter in van't Hoff plots, is better than ±0.5 kcal mol^{-1} for $\Delta H°$, 1.5 cal mol^{-1} K^{-1} for $\Delta S°$. [b] $\Delta H°_D$ and $\Delta S°_D$ refer to dissociation of the monohydrate, i.e., the reverse of the equilibrium indicated above. [c] Compare with $-\Delta H° = 15.0$ kcal mol^{-1}, $-\Delta S° = 25.5$ cal mol^{-1} K^{-1}.[15] [d] Reference 15. [e] Estimated from $\Delta G°_{394} = -2.3$, and assuming the value for $\Delta H°$ from the $\Delta H°$ values for the other compounds. [f] Calculated (see text). [g] Calculated as $\Delta S°_{steric} = \Delta S°_{internal} =$ 17.9 kcal mol^{-1}, where 17.9 cal mol^{-1} represents $\Delta S°_{internal}$ for unhindered compounds (see text).

Table III. Thermochemistry[a] of the Clustering Reactions $BH^+ + B \rightleftarrows BH^+ \cdot B$

B	$\Delta H°_D$[b]	$\Delta S°_D$[b]	$-\Delta S°_{tr,rot}$[c]	$\Delta S°_{internal}$	$-\Delta S°_{steric}$
pyridine	24.6[d]	28.2[d]	56.8	28.6	(0)
2-Me	23.0	27.8			
2,6-Me_2	23.3	33.2	60.7	27.5	1.1
2,6-Et_2	22.8	37.4	63.6	26.2	2.4
2-*i*-Pr	23.0	32.7	63.0	30.3	≈0
2-*t*-Bu	23.0	39.4	64.3	24.9	3.7
2,6-$(i\text{-Pr})_2$	23.6	48.4	65.3	16.9	11.7
2,6-$(t\text{-Bu})_2$	(23)[e]	>60[e]			
Me_3N	22.5[f]	32.0[d]	63	31	(0)
Et_3N	23.8	41.0	66	25	6
n-Pr_3N	23.5[g]	54.9[g]	69	14	17
n-Bu_3N	24.4	56.5	71	14	17

[a] $\Delta H°$ (±0.5) and $\Delta G°$ in kcal mol^{-1}, $\Delta S°$ (±1.5) in cal mol^{-1} K^{-1}. [b] $\Delta H°_D$ and $\Delta S°_D$ refer to dissociation of the proton-bound dimer $BH^+ \cdot B$. [c] Calculated by using the Moments of Inertia Program of Schachtschneider (obtained by private communication from Dr. S. Stein, NBS). [d] Compare with $\Delta H°_D = 23.7 \pm 1$ kcal mol^{-1}, $\Delta S°_D = 28 \pm 2$.[1] [e] Reference 16. [f] Estimated from $-\Delta G°_{assoc,313K} <$ 4.5 kcal mol^{-1}. [g] $\Delta H°$ estimated, $\Delta S°$ obtained from $\Delta G°$ (experimental, 293 K) = −7.4 kcal mol^{-1}.

as the PA of the base increases, the residual charge on the proton becomes smaller and thus hydrogen bonding to the solvent molecule becomes weaker. For the present set of molecules this effect is small, and for the higher pyridines the variation in $\Delta H_D°$ is comparable to the experimental error.

The conclusion from the experimental results is that hydrogen bonding between BH^+ and one water molecule is not weakened by steric effects.

The variation in $\Delta S_D°$ (Table II) may be assigned to two factors. First, with increasing molecular weight aand size the overall molecular translational and rotational terms $\Delta S°_{trans,rot}$ become somewhat more negative. A second factor reflects the changes in internal rotors and vibrations upon the formation of the complex. This factor results from the creation of an internal rotation and/or low-frequency vibrations about the hydrogen bond (a positive entropy term) and the hindrance of internal rotors upon the formation of the complex (a negative entropy term). The combined effect of these positive and negative terms will be denoted $\Delta S°_{internal}$. The variation in this term reflects the effects of steric hindrance. $\Delta S°_{internal}$ is calculated directly from

$$-\Delta S_S° = \Delta S°_{internal} + \Delta S°_{trans,rot} \tag{5}$$

$-\Delta S_D°$ is given by the experimental values. To find $\Delta S°_{internal}$ we calculated $\Delta S°_{trans,rot}$, using standard equations and a molecular geometry computer program.[18] The results are listed in Table II.

We observe that $\Delta S°_{internal}$ contributed 16.9 cal mol^{-1} to the entropy of the (pyridine)$H^+ \cdot H_2O$ complex. $\Delta S°_{internal}$ increases somewhat with molecular size in the unhindered compounds, which may be due to increasing moments of inertia and increasing reduced masses of the internal rotation and bending modes about the H bond. We take the average of $\Delta S°_{internal}$ for the three compounds pyridine, 4-MePyr and 2,6-Me_2Pyr, $\langle \Delta S°_{internal} \rangle_{av}$ = 17.9 cal mol^{-1} K^{-1} to represent the value of $\Delta S°_{internal}$ in the absence of hindrance. The interference of the H_2O molecule with the rotation of the 2- and 6-isopropyl and *tert*-butyl groups and the interference of these gorups with the rotation and bending modes of H_2O lower $\Delta S°_{internal}$ from this value. The magnitude of the interference is calculated from

$$\Delta S°_{steric} = \Delta S°_{internal} - 17.9 \text{ cal mol}^{-1} \text{ K}^{-1} \tag{6}$$

The values of $\Delta S°_{steric}$ are shown on table II.

The value of $T\Delta S°_{steric}$ (at 300 K) is compared with the steric effect on aqueous basicities, i.e., $\Delta\Delta G°_{steric,bulk\ H_2O}$, in the last two columns of Table II. The general observation is that the entropy effects of hindrance of one water molecule duplicate in trend and even in absolute magnitude the overall steric effect in bulk water.

Before discussing further the agreement between $T\Delta S°_{steric}$ and $\Delta\Delta G°_{steric,bulk\ H_2O}$, we must express some reservations about the numbers. Both numbers reflect relatively small deviations in the hindered compounds from values assumed to apply in the absence of hindrance. The uncertainty in $\Delta S°_{steric}$ reflects the uncertainty in the reference number, i.e., 17.9 cal mol^{-1} K^{-1}, which is an average of three values with a spread of ±1 cal mol^{-1} K^{-1}, plus the uncertainty in the actual experimental values of $-\Delta S_D°$, also about ±1 cal mol^{-1} K^{-1}. $\Delta\Delta G°_{steric}$ also reflects uncertainties associated with the selection of the reference line in Figure 4 plus the errors in ΔPA and $\Delta G°_{prot,H_2O}$. Bearing these error limits in mind, the good agreement between $T\Delta S°_{steric}$ and $\Delta\Delta G°_{steric,bulk\ H_2O}$ may be somewhat fortuitous. However, given the uncertainties, it is encouraging that the derived values of $-T\Delta S°_{steric}$ increase with increasingly bulky substitution, as may be expected.

We note that, in the gas phase as well as in bulk H_2O, the steric effects of two isopropyl groups are roughly additive. We can compare the value of $\Delta S°_{steric}$ for 2-*i*-PrPyr, 1.7 cal mol^{-1} K^{-1}, with the entropy of an isopropyl group plus water (as internal rotors), which is[19] 8.6 ± ~5 = 13.6 cal mol K^{-1}.

The steric hindrance amounts to the loss of about 10% of this entropy due to steric interference between H_2O and the 2-isopropyl group and a comparably small further fractional loss upon the addition of the further 6-isopropyl group. Inspection of the structure shows that, with the tertiary hydrogen of the isopropyl groups oriented toward the H_2O molecule, much librational freedom of the isopropyl groups and H_2O can be preserved in the hydrated complex (Figure 5).

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[18] Schachtschneider, 1963, obtained by private communication from Dr. S. E. Stein, NBS.

[19] Benson, S. E. "Thermochemical Kinecits"; Wiley: New York, 1976.

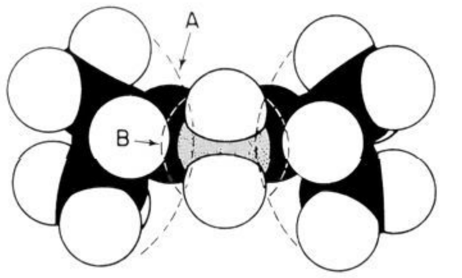

Figure 5. Steric hindrance in hydrated ions: the 2, 6-(i-Pr)$_2$PyrH$^+$·H$_2$O ion. A indicates the edge of the volume of rotation of the isopropyl groups with the methyl groups frozen to provide minimum hindrance to H$_2$O, and B indicates the edge of the volume of rotation of H$_2$O.

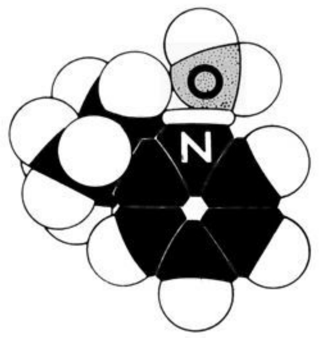

Figure 6. Steric hindrance in hydrated ions: the 2-*t*-BuPyrH$^+$·H$_2$O ion, with the NH$^+$···O bond distorted from 180 to 200°.

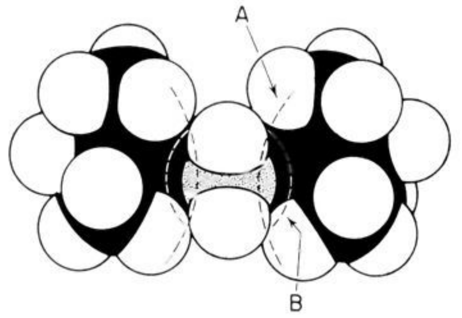

Figure 7. Steric hindrance in hydrated ions: the 2,6-(*t*-Bu)$_2$PryH$^+$·H$_2$O ion. Plotted volumes of rotation show that both *tert*-butyl groups and H$_2$O rotations are frozen (A indicates *tert*-butyl, B indicates H$_2$O).

The most interesting observation in Table II is that the hydration of 2,6-(*t*-Bu)$_2$PyrH$^+$ even by only one H$_2$O molecule exhibits an anomalously high steric effect. Unlike the isopropyl substituents, the effect of the second *tert*-butyl group is much more than additive, indicating a cooperative phenomenon between the substituents upon association with H$_2$O.

The large difference between $\Delta S°_{\text{steric}}$ of 2-*tert*-butyl and 2.6-di-*tert*-butylpyridine may be explained by assuming that the geometry of the hydrogen bond can be distorted with ease in the former, but due to steric interference, not in the latter case. Thus, in 2-*t*-BuPyr, $\Delta S°_{\text{steric}}$ is 4.4 cal mol^{-1} K^{-1}, compared with $S°_{\text{internal}}$ = 9.2 cal mol^{-1}K^{-1} for the *tert*-butyl group plus ca. 5 cal mol^{-1} K^{-1} for H$_2$O. Here $\Delta S°_{\text{steric}}$ amounts to the loss of only 30% of $S°_{\text{internal}}$ associated with the *tert*-butyl function and H$_2$O, indicating that vibrational modes of the *tert*-butyl and H$_2$O groups largely compensate for the loss of internal rotations. This occurs even though the *tert*-butyl group and H$_2$O strongly interfere with each other if the NH$^+$···OH$_2$ hydrogen bond assumed the optimal geometry of 180°. A large fraction of the rotational entropies can be preserved only if the H$_2$O group is easily pushed aside by the *tert*-butyl group, i.e., the energy required for distorting the NH$^+$···OH$_2$ hydrogen bond angle is small. Such a distortion of geometry will allow the H$_2$O group and *tert*-butyl group to become only slightly hindered rotors (Figure 6)

In comparison, in 2.6-(*t*-Bu)$_2$PyrH$^+$·H$_2$O such displacement of the water molecule is not possible (Figure 7). In this case the addition of an H$_2$O molecule simultaneously freezes the two *tert*-butyl group as well as H$_2$O itself, resulting in the loss of 70% of the rotational entropy associated with the *tert*-butyl and H$_2$O groups.

Hydration of Tertiary Alkylammonium Ions by One Water Molecule. As in the alkylpyridines, $\Delta H_D°$ changes only slightly throughout the R$_3$N series, decreasing with increasing PA as may be expected. The fact that $\Delta H_D°$ for (n-Bu)$_3$N does not follow this trend may be ascribed to experimental error. We therefore conclude that steric hindrance does not weaken the hydrogen bond, even though some conformations of the alkyl groups, expecially in (n-Pr)$_3$NH$^+$ and (n-Bu)$_3$NH$^+$, can completely obstruct the access of H$_2$O to the proton.

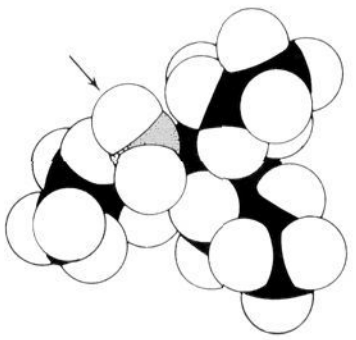

Figure 8. Steric hindrance in hydrated ions. The (n-Bu)$_3$NH$^+$·H$_2$O ion.

Similarly to the pyridines, $\Delta S_D°$ also increases with increasing steric hindrance. $\Delta S°_{\text{tr,rot}}$ varies only slightly through the series, and the variation is due to $\Delta S°_{\text{internal}}$ (Table II).

Molecular models show that the solvent H$_2$O molecule can exclude about 10% of the free volume accessible to each propyl group in (n-Pr)$_3$NH$^+$ and about 20% of the volume accessible to each butyl group in (n-Bu)$_3$NH$^+$ (Figure 8). At the same time, there is a high probability that at least one of the three alkyl groups will interfere with the rotation of H$_2$O at any time. Combined steric effects decrease $S°_{\text{internal}}$ of (n-Pr)$_3$NH$^+$·H$_2$O by 4.7 cal mol^{-1} K^{-1} and of (n-Bu)$_3$NH$^+$ by about 10.3 cal mol^{-1} K^{-1}, compared with Me$_3$NH$^+$·H$_2$O.

Unlike the pyridines, there is not set of tertiary amines where steric hindrance is absent or constant while the PA varies. Therefore, a relation like Figure 4 cannot be constructed, and we cannot evaluate the steric effect in bulk water. However, we note that the regular increase of gas-phase basicities from $Me_3N < Et_3N < Pr_3N < Bu_3N$ is attenuated and even reversed in water. Our results suggest that, of the solvent attenuation of $\Delta G°_{\text{prot,H}_2\text{O}}$ of Et$_3$N, (n-Pr)$_3$N and (n-Bu)$_3$N, compared with Me$_3$N, at least 0.9, 1.8, and 3.6 kcal mol^{-1}, respectively could be due to steric entropy effects. This would be in variance with the analysis of Taft et al.[20] which indicates that the differential attenuation in tertiary amines is entirely an enthalpy effect.

Higher Solvation. While the first solvent molecule interacts with the 2- and 6-substituents in the pyridinium ions, models show the second H$_2$O molecule to be entirely beyond the rotational volume of the alkyl substituents. Correspondingly, the second and higher clustering steps should show no hindrance effects.

We made some observations that support this suggestion. Thus, we found that for 2,6-(i-Pr)$_2$PyrH$^+$·H$_2$O + H$_2$O, $\Delta G°_{300} = -4.0$ kcal mol^{-1}, and for the analogous reaction in 2,6-(t-Bu)$_2$Pyr, $\Delta G°_{300} = -2.7$ kcal mol^{-1}. From the results of Davidson et al.,[15] we can estimate $\Delta H°$ for both cases as −9 kcal mol^{-1}. Then we obtain $\Delta S_D° = 17$ and 23 cal mol^{-1} K^{-1}, respectively. These values are similar to the $\Delta S_D°$ values of 20 ± 1 cal mol^{-1} K^{-1} in unhindered bases.

Thus, if steric hindrance plays a role beyond the first solvation shell, it would probably not effect the intermediate solvation near the proton-bonded H$_2$O molecule.

Clustering of Hindered Pyridinium and Ammonium Ions. The thermochemistry of clustering reactions leading to the symmetric dimers BH$^+$·B is given in Table III. The trends in $\Delta S_D°$ and $\Delta S_D°$ are qualitatively similar to the trends observed in the hydration reactions. $\Delta H_D°$ is constant throughout the entire series of bases, even though the PAs vary widely. This results from the compensating effects on the hydrogen bond of the decreasing acidity of BH$^+$ along with the increasing basicity of B. The present set extends the data of Kebarle[16] to show that in symmetric dimers of protonated nitrogen bases $\Delta S_D°$ remains constant within ±2 kcal mol^{-1} over more than 30 kcal mol^{-1} variation in the PAs, i.e., from ammonia to (n-Bu)$_3$N.

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[20] Taft, R. W.; Wolf, J. F.; Beauchamp, J. L.; Scorrano, G.; Arnett, E. M. *J. Am. Chem. Soc.* **1978**, *100*, 1240.

With respect to steric hindrance the important point is that the hydrogen bond is not weakened even in the highly crowded dimers such as $(2,6\text{-}(i\text{-Pr})_2\text{Pyr})_2\text{H}^+$ or $((n\text{-Bu})_3\text{N})_2\text{H}^+$. Again, molecular models show that with the alkyl functions properly oriented, the hydrogen bond can assume its optimal geometry even though other conformations could keep the reactants more widely separated (in the pyridines) or block the hydrogen bond completely (in the amines).

The effects of steric hindrance are manifested in $\Delta S_D°$, which becomes substantially more positive as the rotation of B and BH^+ about the hydrogen bond and the rotations of the substituents become increasingly hindered. The entropy effects are analyzed in terms of $\Delta S°_{\text{tr,rot}}$ and $\Delta S°_{\text{internal}}$ as above. The overall $\Delta S_D°$ in the most hindered compound reaches more than 50 cal mol^{-1} K^{-1}, the largest entropy change observed so far in any gas-phase ion clustering reaction. As may be expected, $\Delta S°_{\text{internal}}$ is greater in the dimers than is $BH^+{\cdot}H_2O$ complexes. Interestingly, despite the great difference between H_2O and the alkylpyridines as neutral ligands, $\Delta S°_{\text{steric}}$ displays a similar trend in the $BH^+{\cdot}H_2O$ and $BH^+{\cdot}B$ sets. In both sets, pyridine, 2-Me, and 2,6-Me_2 show no significant hindrance effects, and for the other compounds $\Delta S°_{\text{steric}}$ varies in the order 2,6-Et_2 ≈ 2-*i*-Pr < 2-*t*-Bu < 2,6-$(i\text{-Pr})_2$ < 2,6-$(t\text{-Bu})_2$Pyr.

The evaluation of $\Delta S°_{\text{tr,rot}}$ and therefore also of $\Delta S°_{\text{internal}}$ in the amine dimers is more difficult than in the pyridines since $\Delta S°_{\text{tr,rot}}$ depends somewhat on the alkyl conformations, which are not fixed. Table III shows $\Delta S°_{\text{tr,rot}}$ calculated with the alkyl groups in the most extended, all-trans conformations. These conformations maximize the variation of $-\Delta S°_{\text{tr,rot}}$ and thus minimize the variation of $\Delta S°_{\text{internal}}$ and $\Delta S°_{\text{steric}}$. Even so, the amines show substantial steric hindrance, which increases with the alkyl chain length (the leveling off between $(n\text{-Pr})_3\text{N}$ and $(n\text{-Bu})_3\text{N}$ may be experimental error). Molecular models show that up to about 30% or 50% of the volume available for the rotations of the alkyl groups may be lost in the dimers $((n\text{-Pr})_3\text{N})_2\text{H}^+$ and $((n\text{-Bu})_3\text{N})_2\text{H}^+$, respectively.

Blocking of Clustering in 2,6-(*t*-Bu)$_2$. While we measured the dimer equilibria in all the other alkylpyridines including $(2,6\text{-}(i\text{-Pr})_2\text{Pyr})_2\text{H}^+$, the $(2,6\text{-}(t\text{-Bu})_2\text{Pyr})_2\text{H}^+$ dimer could not be detected even at the lowest accessible temperature (300 K). Molecular models show that even this highly hindered dimer could reach the optimal hydrogen bond distance of 2.6 Å, and thus, in line with the above observations, we can estimate $\Delta H_D° \approx 23$ kcal mol^{-1}. However, the models also show that ths optimal geometry can be reached only with the *tert*-butyl groups locked in a specific conformation, with complete loss of the rotation about the hydrogen bond and also complete loss of the rotations of all the *tert*-butyl groups. Experimentally, we observe that $-\Delta G°_{\text{assoc,313K}} < 4.5$ kcal mol^{-1}, and using $\Delta H_D° = 23$ kcal mol^{-1}, we obtain that $\Delta S_D° > 60$ kcal mol^{-1} K^{-1}. Since here $-\Delta S°_{\text{tr,rot}} \approx 45$ cal mol^{-1} K^{-1}, we obtain that $\Delta S°_{\text{internal}} \lesssim -15$ cal mol^{-1} K^{-1}. Indeed the complete freezing of four *tert*-butyl internal rotors would yield $\Delta S°_{\text{internal}} = -(4 \times 9.2) = -36.8$ cal mol^{-1} K^{-1}, and thus $\Delta S°_{\text{assoc}}$ for this reaction could be as negative as $-45 + (-36.8) \approx -82$ cal mol^{-1} K^{-1}.

Conclusions

In protonated pyridines and tertiary amines, the first solvent molecule associated with the ion constitutes the first solvent shell. We observe that 2- and 2,6-substituents affect the interactions of the ion with this monomolecular first solvent shell only through entropy effects, as long as the substituent can assume conformations that allow optimal geometry for the hydrogen bond, even if other possible conformations can completely block the hydrogen bond. These observations disprove previous suggestions[4,6] that steric crowding in the protonated pyridine dimers may reduce the stability of the hydrogen bond. These conclusions apply to the interactions of the pyridinium and ammonium ions with neutral molecules as small as H_2O or as large as alkylamines or alkylpyridines.

Our results suggest that the steric effects that reduce the aqueous basicities of 2- and 2,6-alkyl- (except methyl) pyridines should be primarily entropy effects and not due to the weakening of the hydrogen bonding beteen the ion and its first solvent shell. However, aqueous data on 2,6-$(t\text{-Bu})_2$Pyr[10,11] indicates that enthalpy effects are also important in bulk solvation. If enthalpy effects are indeed involved in bulk solution, these should result from the interactions of the ion with outer solvation shells. Accurate data on heats and free energies of solvation of pyridinium ions are now required to clarify the relation between the gas-phase observations and steric effects in bulk solvent.

Acknowledgment. We thank Dr. J. Day for a sample of purified 2,6-$(t\text{-Bu})_2$Pyr, Dr. S. E. Stein for a computer program, and E. P. Hunter for part of the computer programming work. This study was supported by the Office of Basic Energy Sciences, the United States Department of Energy.

Registry No. Oxonium, 13968-08-6; 2,6-di-*tert*-butylpyridine, 585-48-8; 2,6-di(isopropyl)pyridine, 6832-21-9; 2,6-diethylpyridine, 935-28-4; 2-hexylpyridine, 1129-69-7; 2,6-dimethylpyridine, 108-48-5; 2-*tert*-butylpyridine, 5944-41-2; 2-isopropylpyridine, 644-98-4; 2-ethylpyridine, 100-71-0; 2-methylpyridine, 109-06-8; pyridine, 110-86-1; pyridine·H^+, 16969-45-2; 4-methylpyridine·H^+, 16950-21-3; 2,6-dimethylpyridine·H^+, 17033-11-3; 2,6-diethylpyridine·H^+, 85048-76-6; 2-isopropylpyridine·H^+, 76065-75-3; 2-*tert*-butylpyridine·H^+, 62907-59-9; 2,6-di(isopropyl)pyridine·H^+, 74570-68-6; 2,6-di-*tert*-butylpyridine·H^+, 62907-61-3; trimethylammonium, 16962-53-1; triethylammonium, 17440-81-2; tripropylammonium, 50985-90-5; tributylammonium, 19497-26-8; 2-methylpyridine·H^+, 16969-46-3; trimethylamine, 75-50-3; triethylamine, 121-44-8; tripropylamine, 102-69-2; tributylamine, 102-82-9; 4-methoxypyridine, 620-08-6.