Proton Double Minimum Potentials in Asymmetric Hydrogen Bonds

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Summary A wide series of hydrogen bonded cations $(B^1HB^2)^+$, where B^1 and B^2 are different heterocyclic bases, have been characterised spectroscopically, and the proton potential appears to depend on the difference of the pK values of the bases.

IN the preceding communication we presented spectroscopic evidence relating to the symmetric cations $(BHB)^+$, which is most readily interpreted in terms of a double minimum potential for the proton motion, with a low barrier. Two questions naturally follow: does the spectroscopic behaviour carry over into asymmetric complexes $(B^1HB^2)^+$, which may be of far-ranging biological significance and to what extent does information from asymmetric systems support the inferences made for the symmetric systems?

We are not aware of any previous reports of asymmetric cations of the type $(B^1HB^2)^+$, where B^1 and B^2 are different heterocyclic bases. The following observations indicate the occurrence of these complexes.

(1) The appearance of the ν_s band doublet for the $(B^1HB^1)^+$ and $(B^2HB^2)^+$ cations is frequently closely similar. In solutions containing both bases, *e.g.* HBF_4^+ in $(B^1 + B^2)$ the profile is often markedly changed, the higher frequency component being relatively intensified (Figure 1). This cannot arise from any mixture of the symmetric species.

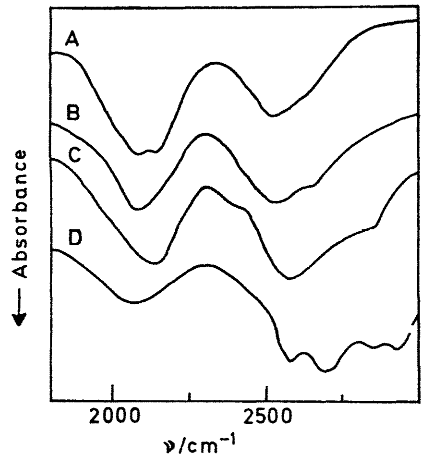

FIGURE 1. ν_s *Band of* A, $(4MepyHpy)^+$; B, $(2,6\text{-di-Me-pyHpy})^+$; C, $(4\text{-Me-pyH3-Cl-py})^+$; D, $(2,4,6\text{-triMe-PyH3-Cl-py})^+$. ΔpK_a *increases from* A *to* D.

(2) 2,4,6-Trimethylpyridine does not form a symmetric complex. However, 'inert' salts, such as 2,4,6-trimethylpyridine–$\overset{+}{H}\ \overset{-}{ClO_4}$ dissolve in pyridine. The ν_s band is quite dissimilar to that of $(pyHpy)^+$. All the acid protons are hydrogen bonded (no 3300 cm^{-1} band). Internal mode frequencies show 2,4,6-trimethylpyridine is protonated, not free. This strongly supports the presence of $(B^1HB^2)^+$ ions.

(3) In the far i.r. spectra, 2,4,6-trimethylpyridine salts in pyridine have a band at *ca.* 118 cm^{-1}. As 2,4,6-trimethylpyridine does not form a complex $(B^1HB^1)^+$, and the only band of $(pyHpy)^+$ in this range lies at *ca.* 137·5 cm^{-1}, a new species is present and the frequency is compatible with $(B^1HB^2)^+$.

(4) The spectra are independent of the nature both of the counter-ion, and of the solvent if they are inert towards hydrogen bonding.

We assume that the mixed complexes have the formula (B^1HB^2) since (*a*) if *e.g.* $(pyHpy)^+$ and $(4\text{-Me-pyH4-Me-py})^+$ have this formula, it is reasonable on chemical grounds to interpolate the same molecularity to $(pyH4\text{-Me-py})^+$, (*b*) the spectra smoothly relate to those of the symmetric complexes.

The spectra exhibit a high degree of consistency from system to system and show the following characteristics.

(1) The ν_s band is a doublet in the H bridged complexes, and when the difference in the pK_a values of the bases is small, is very similar in appearance to the band in symmetric systems. As the difference in pK_a values of the bases increases, the intensity of the lower member of the doublet falls relative to the higher one. The intensity ratio is remarkably independent of the structures of the individual bases involved, the frequency of ν_σ, or of their individual pK_a values, but is almost linearly dependent on ΔpK_a (Figure 2). All the symmetric systems discussed in the

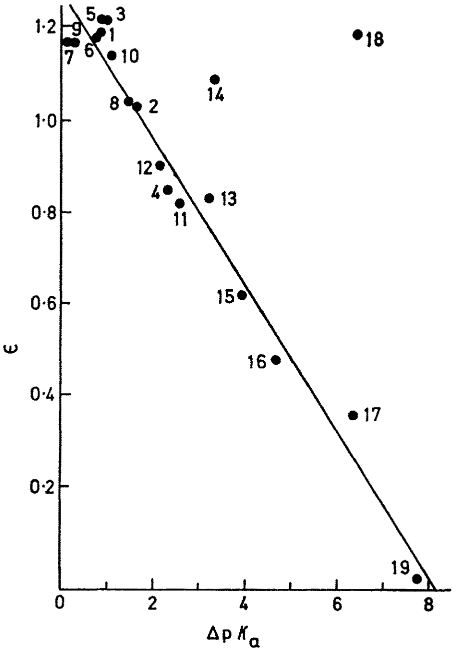

FIGURE 2. *Ratio of the intensity of the lower/upper bands of the* ν_s *doublet* (ϵ) *vs. difference in base strength* ΔpK_a. *The abnormal ratios for* 14 *and* 18 *are due to a* 3,5-*dimethylpyridine combination band underlying the lower member of the doublet.*

previous communication fit this correlation. In the limit of very large ΔpK_a (*ca.* 6 or more) the lower band disappears, while the upper band moves towards higher frequency (Tables 1 and 2).

(2) The ν_s band in the corresponding $(\mathrm{B^1\overset{+}{D}B^2})$ ions when examined is always found to be a singlet (Table 1).

(4) Sensitive internal modes of the bases shift on complexing. In a particular system each internal mode of B^1 gives rise to only a singlet shifted band, and likewise for B^2.

(5) The shift of an internal mode of a base B is very close to that in a symmetric complex, (unless ΔpK_a is very large), whether it forms the stronger or the weaker partner in the asymmetric complex.

TABLE 1

ν_s and ν_σ Frequencies for $(B^1HB^2)^+$ systems

System	$(B^1HB^2)^+$	ν_s (H)/cm^{-1}		ν_s (D)/cm^{-1}		ν_σ(H)/cm^{-1}	ν_σ(D)/cm^{-1}	ΔpK_a	ϵ_{ratio}
$(\gamma\text{-picHpy})^+$	(1)	2530s		1905s		137	133 cm^{-1}	0·85	1·19
			2150sh		1800sh				
		2080s			1675m				
$(2,6\text{-lutHpy})^+$	(2)		2660sh		2200sh			1·60	1·03
		2530s			2120sh				
			2105sh	2000s					
		2070s							
$(3,5\text{-lutHpy})^+$	(3)		2735sh	1915s		130		0·95	1·22
			2545sh						
		2490s							
		2145s							
$(2,4,6\text{-collHpy})^+$	(4)		2700sh		2200w	118		2·30	0·85
			2650sh		2100w				
		2570s		2005s					
		2075s							

pK_a = stability constants

TABLE 2

ν_s Frequencies for $(B^1HB^2)^+$ systems

System	$(B^1HB^2)^+$	ν_s/cm^{-1}		ΔpK_a	ϵ_{ratio}
$(4\text{-Et-pyHpy})^+$	(5)	2525s		0·85	1·22
			2160sh		
		2090s			
$(2,6\text{-lutH}\gamma\text{-pic})^+$	(6)	2520s		0·75	1·18
			2125sh		
		2070s			
$(3,5\text{-lut-H}\gamma\text{-pic})^+$	(7)	2490s		0·10	1·17
		2140s			
$(2,4,6\text{-collH}\gamma\text{-pic})^+$	(8)	2525s		1·45	1·04
		2080s			
$(\text{pyHquin})^+$	(9)	2520s		0·25	1·17
			2150sh		
		2075s			
$(\gamma\text{-picHquin})^+$	(10)	2530s		1·05	1·14
			2160sh		
		2070s			
$(2,4,6\text{-collHquin})^+$	(11)	2640s		2·55	0·82
			2580sh		
			2150sh		
		2075s			

System	$(B^1HB^2)^+$	ν_s/cm^{-1}		ΔpK_a	ϵ_{ratio}
$(\text{quinH3-Cl-py})^+$	(12)	2550s		2·10	0·90
		2140s			
$(\gamma\text{-picH3-Cl-py})^+$	(13)		2850sh	3·20	0·83
		2575s			
			2375sh		
		2150s			
$(3,5\text{-lutH3-Cl-py})^+$	(14)	2640s		3·30	1·09
		2140s			
$(2,6\text{-lutH3-Cl-py})^+$	(15)		2895sh	3·90	0·62
			2850sh		
		2730s			
		2600s			
		2070s			
$(2,4,6\text{-collH3-Cl-py})^+$	(16)		2930sh	4·65	0·48
			2845sh		
		2710s			
			2575sh		
		2070s			
$(\gamma\text{-picH2-F-py})^+$	(17)	~2840vs		6·30	0·36
			2720sh		
			2640sh		
$(3,5\text{-lutH2-F-py})^+$	(18)	2140s		6·40	1·19
		2560s			
		2135s			
$(2,4,6\text{-collH2-F-py})^+$	(19)	~2850vs	2930sh	7·70	0
			2740sh		
			2590sh		

(3) In the far i.r. spectra an 'intermolecular' band occurs. The insensitivity to deuteriation shows that this is not a transition between proton levels in the asymmetric proton potential. The frequency is comparable with those of symmetric systems, after allowance for the masses of the bases, and assignment to ν_σ is confident. The band has a single maximum in both H and D complex ions.

(6) We have not so far been able to follow the behaviour of δ_{NH} on complexing, since the many fundamentals from the several species necessarily present complicate this range of the spectrum.

We infer that the proton potential function evolves smoothly from that present in the symmetric ions, since the spectra, in particular the ν_s band, are continuously related.

Thus, in the nearly symmetric systems a shallow double minimum with slight asymmetry provides the most plausible model. Several observations argue against the occurrence of a high barrier, *i.e.* of a pair of tautomers.

$$(B^1H -- B^2)^+ \rightleftharpoons (B^1 -- HB^2)^+$$

(a) This would lead to two sensitive internal modes of each base in the complex, whereas never more than one is observed. (b) The ν_s doublet would be preserved in the D bridged systems. (c) Each tautomer might be expected to give a ν_σ band, wherease ν_σ is found to have a single maximum.

Thus a high barrier can be strongly discounted. When the pK_a values of the bases differ by several units, the ν_s band changes to a 'normal' singlet, with a decreasing $\Delta\nu_s$ shift, indicative of weakening hydrogen bonding. There can be little doubt that in this limit the proton potential changes to an asymmetric single minimum, represented by the structure $(B^1H -- B^2)^+$. The continuity of the spectra suggests that as the pK_a difference increases, the proton potential evolves smoothly from that in symmetric systems to the asymmetric single minimum in highly asymmetric systems.

Since it appears that considerable differences in the basicity of the bases can be introduced before the characteristic features of symmetric systems are lost completely, we are examining further complexes, particularly those of biological significance, as well as making a quantitative treatment of the model.

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