I.R. Evidence for a Strong Hydrogen Bond in the Fluoride-uracil System

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Summary A new 1:1 adduct of KF and uracil has been prepared and its i.r. spectrum reveals the presence of strong asymmetrical N–H . . F^- hydrogen bonds.

THE dramatic influence of high salt concentrations on the physicochemical properties of nucleic acids in aqueous solution has recently been attributed, at least in part, to the formation of specific complexes between the anions and the nucleotide bases.[1,2] Associations of chloride with the NH groups of nucleotide bases have been studied by observing the effects on n.m.r. chemical shifts[3] and ^{35}Cl magnetic relaxation times.[1]

The fluoride anion is a powerful hydrogen bond electron donor and a number of strong or very strong H-bonds of the type AH . . F$^-$ (A = F, O, or N) have been reported.[4] *Ab initio* calculations have been performed on some simple amide–fluoride complexes revealing the presence of remarkably strong NH . . F$^-$ H-bonds[5] and prompting the authors to discuss possible biochemical implications of this H-bond in the light of the prevalence of H-bonding involving NH in biological systems, including nucleic acids.

We now report a novel 1 : 1 complex of KF and the nucleotide base uracil which has an i.r. spectrum characteristic of the existence of strong H-bonding. The complex grows as a white crystalline solid from an 80% dimethyl sulphoxide (DMSO) or *NN*-dimethylformamide–20% H_2O solution of equimolar concentrations of KF and uracil.

The i.r. spectrum of the solid complex shows marked differences from that of pure uracil. In particular, the NH stretching bond ν_s(NH), which occurs as a strong broad band at *ca.* 3050 cm^{-1} in pure uracil is shifted and split by transmission windows into three pseudo-maxima at *ca.* 2950, *ca.* 2600, and *ca.* 1930 cm^{-1} which correspond to A, B, and C bands in Hadzis' classification of the i.r. spectra of H-bonded substances.[6] The relative intensities of the bands are B > C > A suggesting a strong, asymmetrical NH . . F$^-$ H-bond. The KF-[*NN*-$^2H_2$]uracil complex (prepared from a DMSO–D_2O solution of KF and [*NN*-$^2H_2$]uracil) also appears to show an ABC pattern (see Table) although our assignments can only be tentative as the C band is largely obscured by overlap with the ν_s(C=O)/ν_s(C=C) broad band.

Both in-plane and out-of-plane deformations of H-bond electron acceptor groups are known to move to higher frequencies as the H-bond strength increases.[7] The out-of-plane deformations of the NH groups in uracil, ν_t(NH), are clearly recognisable as medium intensity, broad bands which are reduced by deuteriation and move to higher frequencies on association with KF (see the Table). In-plane deformations, ν_b(NH), also appear to move to higher frequencies on association with KF although the exact location of one of these vibrations is prevented by overlap with other bands (Table). Similar shifts in the positions of the ND deformations occur on going from [*NN*-$^2H_2$]uracil to its KF complex (Table). The vibrations of distant bonds and the ring are relatively insensitive to the changes in H-bonding although it is interesting to note that the coupled ν_s(C=O)/ν_s(C=C) band moves by *ca.* 20 cm^{-1} to higher frequency on association with KF whereas the higher energy unconjugated carbonyl group vibration is shifted by no more than 5 cm^{-1}.

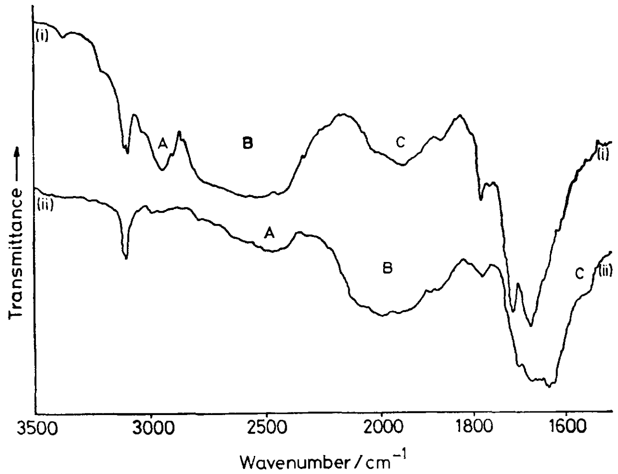

FIGURE. A, B, and C bands in the i.r. spectrum of (i) KF-uracil and (ii) KF-*NN*-D_2-uracil.

There has been a great deal of discussion on the origins of ν_s(AH) multiple bands.[7] The most attractive postulate is that they are due to Fermi resonance interactions with overtones of AH deformation[6] where the expected positions of the overtones may coincide with the band maxima but may also occur at the minima positions.[8] We believe that the complicated ν_s(NH) structure in the i.r. spectrum of KF-uracil is largely due to Fermi resonances between ν_s(NH) and $2\nu_t$(NH) and between ν_s(NH) and $2\nu_b$(NH). The latter, relatively weak resonance, produces a narrow transmission window at *ca.* 2880 cm^{-1} which corresponds nicely to the predicted position of the first overtone of one of the ν_b(NH) vibrations ($\nu_{b(0\rightarrow2)} \simeq 2\nu_b = 2870\,\text{cm}^{-1}$). The former, much stronger resonance, produces a broad transmission window centred at *ca.* 2150 cm^{-1}, the origins of which may be deduced by analysing our spectrum in terms of an A, B ... C Fermi diad[8] whose overall intensity is borrowed from the ν_s(NH) fundamental exclusively. Odinokov's equation[9] (1) gives the expected frequency of

$$\nu_t = \tfrac{1}{2}[R\bar{\nu}_s(AB) + \nu_s(C)]/R + 1 \qquad (1)$$

$$R = \text{C band area/A,B band area}$$

TABLE Hydrogen bond vibrations.[a]

	ν_s[NH(D)]/ cm^{-1}	ν_b[NH(D)]/ cm^{-1}	ν_t[NH(D)]/ cm^{-1}	$\bar{\nu}_s$(NH)/$\bar{\nu}_s$(ND)	ν_b(NH)/ν_b(ND)	ν_t(NH)/ν_t(ND)
Uracil	3050 (s, br)	1510 (w)	850 (m, br)		1·33	1·38
		1417 (m)	805 (sh)	1·34	1·44	1·38
KF-Uracil	2950 (m, br)	—[b]	1038 (m, br)		—	1·35
	2600 (s, br)	1435 (m)	945 (m, br)	1·2	1·39	1·37
	1930 (s, br)					
[*NN*-$^2H_2$]Uracil	2320 (sh)	1140 (m)	618 (m, br)			
	2265 (s)	980 (m)	582 (m, br)			
KF-[*NN*-$^2H_2$]-Uracil	2500 (w, br)	1135? (m)	770 (m, br)			
	2000 (s, br)	1035 (m)	690 (m, br)			
	1560? (sh)					

[a] s = strong, m = medium, w = weak, sh = shoulder, br = broad. [b] Under the ν_s(C=O)/ν_s(C=C) band.

the ν_t vibration for such a situation. This provides a value of 1050 cm^{-1} for ν_t(NH) of KF-uracil which is in satisfactory agreement with the observed value of 1038 cm^{-1}. A further, very narrow, transmission window within the C band is observed at *ca.* 1880 cm^{-1} which corresponds to the predicted position of the first overtone of the second, weaker ν_t(NH) band [$\nu_{t(0\rightarrow 2)} \simeq 2\nu_t = 1890$ cm^{-1}].

We have estimated the positions of the centres of gravity of the ν_s(NH) trios in the fluoride complexes to be *ca.* 2300 cm^{-1} for KF-uracil and *ca.* 1900 cm^{-1} for KF-[*NN*-$^2H_2$]-uracil. The $\bar{\nu}_s$(NH)/$\bar{\nu}_s$(ND) ratio is, therefore, *ca.* 1·2 which is below the expected 1·35 of non-hydrogen bonded modes and again suggests a strong, asymmetrical H-bond,[10] as does the $\Delta\nu_s$ value [ν_s(uracil monomer) − ν_s(KF-uracil)] for NH, of 1100 cm^{-1}.[11]

The observed ability of fluoride to disrupt the self-association in uracil and to produce strong NH . . F$^-$ interactions is obviously of considerable importance to a consideration of the possible biologically disruptive action of the fluoride anion. More detailed studies in this area, including a consideration of medium effects, are, however, required before we can come to any meaningful conclusions.

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