

Symmetry of Hydrogen Bonds, Infrared Continuous Absorption and Proton Transfer

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In liquid systems in which $\text{BH}^+ \cdots \text{B}$ hydrogen bonds with a symmetrical double minimum potential well are present, i.r. continuous absorption is observed. This shows that the protons have a continuous energy level distribution, caused by various interactions resulting from the extremely high polarizability of such hydrogen bonds. Mixtures of carboxylic acids and nitrogen bases were investigated to see how the occurrence of this continuum depends on the symmetry when the two acceptors B are not identical. The $\text{AH} \cdots \text{B}$ hydrogen bond between acid and base always produces i.r. bands and not continuous absorption. The occurrence of continuous energy level distribution of the protons thus depends to a large extent on the symmetry in the systems investigated in this work. As well as these bands, however, the continuum is observed with some of the above systems, since $\text{BH}^+ \cdots \text{B}$ bonds form between the base molecules. In the $\text{AH} \cdots \text{B}$ bonds proton transfer to the base is observed in anhydrous systems when the acid is more acidic than the base by $\Delta\text{pK}_a \approx 4$. This proton transfer is favoured by excess acid and by the presence of water molecules. In aqueous solutions of mixtures of carboxylic acids and N bases, proton transfer occurs in the $\text{AH} \cdots \text{B}$ bond at $\Delta\text{pK}_a \approx 2$. According to these results the hydrogen bonds between the acidic and basic amino-acid residues could well be largely symmetrical. The possible significance of this result for biological systems is discussed.

Hydrogen bonds with a symmetrical double minimum potential well in which the H nucleus tunnels are extremely polarizable.^{1, 2} Such hydrogen bonds are involved in the case of $\text{BH}^+ \cdots \text{B}$ bonds, e.g. in H_5O_2^+ ^{3, 4} in semi-protonated aqueous imidazole solutions⁵, in anhydrous systems^{5, 6} or with the $(\text{BH} \cdots \text{B})^-$ bonds, for instance in H_3O_2^- [ref. (4), p. 188]. In the presence of such hydrogen bonds, a continuous absorption is observed in liquid systems extending from *ca.* 3000 cm^{-1} to small wave numbers.

The extremely large polarizability of these hydrogen bonds causes three interaction effects. First, the electrical fields of anions and the dipole fields of the solvent molecules adjacent to these hydrogen bonds polarize them to a large extent; this is an induced dipole interaction.^{2, 7} Secondly, these bonds exert a mutual influence on each other. Proton dispersion forces act between the tunnelling protons.⁸ Thirdly, the transitions of the proton in these hydrogen bonds couple with low wave number transitions, especially with the intermolecular vibrations.²

The interactions disturb the symmetry of these hydrogen bonds² and lead to a considerable shift of the energy levels of the protons. Since in liquids the distances and orientations between the hydrogen bonds and between the anions or solvent molecules respectively, and the hydrogen bonds pass through a statistical variety of values, the strength of these interactions and thus the shift of the energy levels also pass through a variety of values. Thus a continuous absorption occurs in the infrared spectrum of such solutions.^{3, 4} In addition to these interactions, the extremely large polarizability of these hydrogen bonds causes the field-sensitive mechanism in the case of the anomalous proton conductivity.¹ More detailed information is given elsewhere.¹⁻⁷

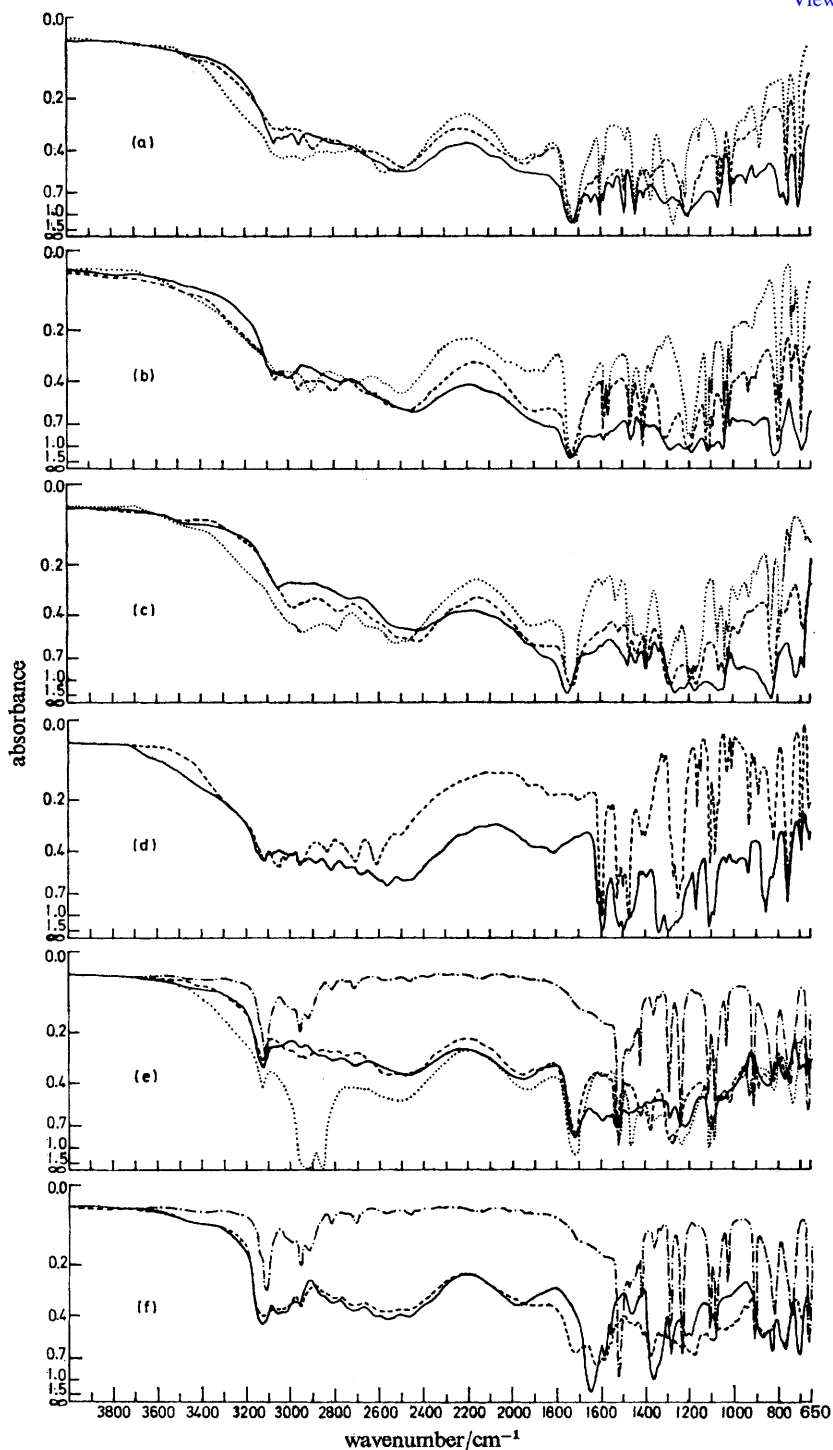


FIG. 1.—Anhydrous mixtures of pyridine, 3-chloropyridine, 2-methylpyrazine and *N*-methylimidazole with different acids, mol ratio 1 : 1. The spectra in fig. (a)–(c) and the spectra in fig. (d) are comparable with regard to sample thickness (see experimental section). (a) — pyridine + monochloroacetic acid (density $\rho = 1.24$; sample thickness $9.4\ \mu\text{m}$), --- pyridine + formic acid ($\rho = 1.09$; $7.75\ \mu\text{m}$), ... pyridine + acetic acid ($\rho = 1.025$; $9.05\ \mu\text{m}$); (b) — 3-chloropyridine + dichloroacetic acid ($\rho = 1.43$; $11.3\ \mu\text{m}$), --- 3-chloropyridine + monochloroacetic acid ($\rho = 1.33$; $10.5\ \mu\text{m}$), ... 3-chloropyridine + formic acid ($\rho = 1.20$; $8.9\ \mu\text{m}$); (c) — 2-methylpyrazine + trichloroacetic acid ($\rho = 1.42$; $12.0\ \mu\text{m}$), --- 2-methylpyrazine + dichloroacetic acid ($\rho = 1.32$; $11.3\ \mu\text{m}$), ... 2-methylpyrazine + monochloroacetic acid ($\rho = 1.23$; $10.4\ \mu\text{m}$); (d) — methylimidazole + 4-nitrophenol ($\rho = 1.19$; $9.5\ \mu\text{m}$), --- methylimidazole + phenol ($\rho = 1.07$; $8.5\ \mu\text{m}$); (e) — methylimidazole + formic acid ($\rho = 1.14$; $5.75\ \mu\text{m}$), --- methylimidazole + acetic acid ($\rho = 1.08$; $6.75\ \mu\text{m}$), ... methylimidazole + stearic acid ($\rho = 0.885$; $21.5\ \mu\text{m}$), - · - · methylimidazole for comparison ($9.8\ \mu\text{m}$); (f) — methylimidazole + dichloroacetic acid ($\rho = 1.145$; $7.75\ \mu\text{m}$), --- methylimidazole + monochloroacetic acid ($\rho = 1.295$; $7.25\ \mu\text{m}$), - · - · methylimidazole for comparison ($9.8\ \mu\text{m}$).

This work investigates the conditions under which proton transfer occurs in hydrogen bonds of the $AH \cdots B$ type, that is, when acceptor and donor are not identical. Various authors^{9, 10} have pointed out remarkable dielectric properties connected with the proton transfer in hydrogen bonds. We plotted the i.r. spectra of homogeneous liquid mixtures for carboxylic acids or phenols with cyclic amines as models for such hydrogen bonds. These systems made it possible to vary the pK_a value of acid and base over a wide range and observe the influence of this variation on the nature of the hydrogen bonds. Whilst we observed mixtures of the acids and bases without solvent, Barrow *et al.*¹³⁻¹⁵ and De Tar and Novak¹⁶ studied similar systems in solution. Also Gusakowa, Denisow *et al.*,¹⁷ subjected pyridine with carboxylic acid and amines with isobutyric acid to spectroscopic investigation in $CHCl_3$ solution.

CONTINUOUS ABSORPTION

The question arises as to how sensitively the occurrence of the continuum depends on the symmetry when acceptor and donor are not of like size. On comparing similar substances, for instance the carboxylic acids or the N bases, the pK_a value serves as a relative measure of donor or acceptor strengths, respectively, which are decisive factors for the nature of the potential well in the hydrogen bond. In order to clarify whether this hydrogen bond can become symmetrical enough to cause continuous absorption, we plotted spectra of anhydrous 1 : 1 mixtures: fig. 1 shows four such series. In the case of the series with *N*-methylimidazole the measurements on carboxylic acids of high pK_a values were supplemented by two on phenols. Table 1 summarizes the results obtained.

In the spectra in fig. 1*a, b* and *c*, three extremely broad bands are found, one at about 2900, one at about 2500 and one at about 1900 cm^{-1} . Many weaker bands caused by CH and CH_3 stretching vibrations and by harmonic ring vibrations are superimposed on the 2900 cm^{-1} band. As the pK_a value of the acid decreases, the band at 2900 cm^{-1} decreases in intensity (fig. 1*a-c*). These bands also show a tendency to shift somewhat towards lower wave numbers with smaller pK_a . The OH stretching vibration which is observed with the pure carboxylic acids is, if observed at all, extremely weak. Thus 1 : 1 adducts of acid and base are formed. A comparison of the spectra of the mixtures with the deuterated acetic acid (fig. 2) shows that the band trio are due to vibrations in hydrogen bonds between the acid and base groups. Hadži^{26a} assigns both bands around 2900 and 2500 cm^{-1} in similar systems

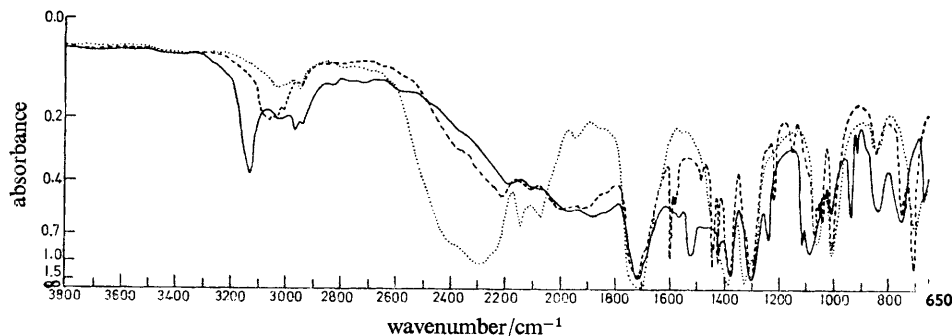


FIG. 2.—Monodeuteroacetic acid and mixtures with *N*-methylimidazole and pyridine; mol ratio 1 : 1; — monodeuteroacetic acid + *N*-methylimidazole (sample thickness 11 μm), --- monodeuteroacetic acid + pyridine (11 μm), ... monodeuteroacetic acid (10.5 μm).

TABLE 1.—BANDS OF THE ANHYDROUS MIXTURES OF THE CARBOXYLIC ACIDS WITH N-BASES.

ΔpK_a	P + HCl in H ₂ O	P + A +0.50	P + F +1.50	P + MCA +2.39	assignment
—	—	2900 s, b *	2850 m, b	2800 m, b	see text $\nu C=O$ $\nu C-O$ and δOH ring vibrations
—	—	2530 s, b	2500 s, b	2480 s, b	
—	—	1950 s, b	1950 s, b	1900 s, b	
—	—	1714 vs	1716 vs	1728 vs	
—	—	1271 s	1206 s	1205 m	
1634 vw	masked †	sh at about 1635 vw	1635 vw	1637 w	see text $\nu C=O$ $\nu C-O$ and δOH ring vibrations
—	1530 s	—	1530 vw	1530 w	
1483 m	1485 s	1487 w	1489 m	1485 s	
1440 s	—	1440 s	1440 s-m	1440 m	
CP	CP + HCl + 2H ₂ O	CP + F -0.91	CP + MCA -0.02	CP + DCA +1.36	
ΔpK_a	—	2850 m, b	2850 m, b	1930 m, b	see text $\nu C=O$ $\nu C-O$ and δOH ring vibrations
—	—	2530 s, b	2480 s, b	1900 s, b	
—	—	1930 s, b	2450 s, b	1850 s, b	
—	—	1720 s	1735 s	1737 m	
—	—	—	—	1624 w	
—	—	—	—	1374 w	see text $\nu C=O$ $\nu C-O$ and δOH ring vibrations
1573 s	—	1588 m	1588 m	1589 w	
1565 m	—	1568 m	1567 m	1569 w	
MP	MP + HCl + 2H ₂ O	MP + DCA -1.41	MP + DCA -0.03	MP + TCA +0.75	
ΔpK_a	—	2800 m, b	2800 m, b	2800 m, b	
—	—	2480 s, b	2480 s, b	2450 s, b	see text $\nu C=O$ $\nu C-O$ and δOH ring vibrations
—	—	1920 s, b	1900 s, b	1850 s, b	
—	—	1732 s	1734 s	1753 m	
—	—	—	—	1640 w	
—	—	—	—	1340 w	
1527 m	—	1527 m	1529 w	1527 sh, w	see text $\nu C=O$ $\nu C-O$ and δOH ring vibrations
—	1500 m	—	—	1500 sh, w	

MI	MI+HCl	MI+PhOH	MI+NPhOH	MI+St	MI+A	MI+F	MI+MCA	MI+DCA	assignment
ΔpK_a									
—	—	2830 vs, vb	2900 s, b	2900 m, b	2900 m, b	2800 w, b	2900-2300 vs, vb	2900-2300 vs, vb	see text
—	—	1850 vw, b	2500 vs, b	2500 s, b	2500 s, b	2450 m, b	1950 m, b	1970 m, b	
—	—	—	1850 w, b	1950 m, b	1950 m, b	1711 vs	1722 s	—	$\nu C=O$
—	—	—	—	1714 vs	1713 vs	1610 w	1622 m	1648 s	$CO_2^{+} \nu_{as}$
—	—	—	—	—	—	1373 w	1370 m	1368 s	$CO_2^{+} \nu_s$
—	—	1395 m	1452 m	1363 w	1366 w	n.i.	n.i.	—	$\nu C-O$ and δOH
—	—	1249 m	1291 m	1240 s, b	1271 s	1212 s	1205 m	—	
—	1583 s	—	—	—	1587 vw	1587 w	1582 w-m	1585 m	ring vibrations
—	1551 s	—	—	—	1553 vw	1554 w	1554 w-m	1554 m	
1519 vs	—	1515 m	1514 m	1516 m	1518 m	1520 m	1521 w	1518 vw	
1234 vs	—	masked	masked	1534 m	1235 sh, m	1234 m	1239 w	—	δNH
—	1178 m	—	—	—	—	1179 sh, w	1179 w	1183 w	
745 s	765 s	masked	masked	745 sh, m	747 sh, m	761 m	768 m	767 m	γCH

pK_a values are taken from ref. (18). For assignment of the bands see ref. (19)-(29).
P, pyridine, CP, 3-chloropyridine, MP, 2-methylpyrazine, MI, N-methylimidazole, A, acetic acid, F, formic acid, MCA, monochloroacetic acid, DCA, dichloroacetic acid, TCA, trichloroacetic acid, ST stearic acid, NPhOH, nitrophenol, PhOH, phenol.
* w = weak, m = medium, s = strong, v = very, b = broad, sh = shoulder, n.i. = not identified.
† in $CHCl_3$ a strong band at 1634 cm^{-1} is found.

to the OH stretching vibration and the δ OH harmonic vibration whereby the 2δ OH vibration receives its intensity through strong Fermi resonance of the stretching vibration. Hadži assigns the band at 1900 cm^{-1} to the 2γ OH vibration, which likewise receives its intensity through Fermi resonance of the OH stretching vibration. Here it is a case of the band trio which Hadži ^{26b} designates ABC or type (i) on investigating similar systems. Hadži and Kobilarov ^{26a} assume that in these hydrogen bonds more or less unsymmetrical double minimum potential wells are present. The Fermi resonance between the vibrations of this band trio ABC have been discussed in detail by Claydon and Sheppard. ^{26c}

With methylimidazole (MI)+phenol (fig. 1d) the OH stretching vibration in the $\text{OH} \cdots \text{N}$ bond is observed as an extremely broad band at about 2850 cm^{-1} : the CH and the CH_3 stretching vibrations and the harmonic ring vibrations are again superimposed on this band. A broad weak band occurs at about 1800 cm^{-1} , probably the overtone of the bending vibration. Since this band is relatively far from the stretching vibration, it only receives a small degree of intensity through Fermi resonance with the latter. With MI+nitrophenol the OH stretching vibration is shifted to lower wave number and the overtone of the bending vibration a little to higher wave number.

In the case of mixtures of MI with stearic and acetic acid, two broad bands are found, one at 2500 and one at 1850 cm^{-1} , whereby the latter shifts with decreasing pK_a value of the acid towards 1950 cm^{-1} . These bands are again the bands of the trio discussed above, whereby the third band, that at 2900 cm^{-1} , is either already extremely weak or is masked by the CH_2 stretching vibrations, as with stearic acid.

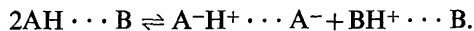
The MI+formic acid mixture forms the transition to a new band structure: a broad absorption in the range $2900\text{--}2300\text{ cm}^{-1}$ overlies the upper two bands at about 2800 and 2500 cm^{-1} ; the lower band maintains the same form and is at about 1950 cm^{-1} . In the MI+monochloroacetic acid and MI+dichloroacetic acid systems, the spectrum is dominated by a broad band in the $2900\text{--}2300\text{ cm}^{-1}$ range. The lower band shifts to larger wave numbers, up to 1970 cm^{-1} in the MI+dichloroacetic acid system. In the MI+dichloroacetic acid system nearly all the acidic protons have been transferred to the N atom of the base, that is, that $\text{O}^- \cdots \text{H}^+\text{N}$ bonds are present. Hence in these systems, the NH stretching vibration causes the broad band in the $2900\text{--}2300\text{ cm}^{-1}$ range and the harmonic vibrations of the NH bending vibration causes the band at about 1970 cm^{-1} , which due to strong Fermi resonance with the stretching vibration has gained in intensity. In the MI+formic acid system, these two bands are superposed by the band trio of the $\text{OH} \cdots \text{N}$ bond.

In summary we can state that bands due to vibrations in the hydrogen bond between the acid and the base are observed. The hydrogen bonds which cause these bands cannot make a contribution to the continuous absorption, i.e. the protons in these hydrogen bonds have no continuous energy level distribution. This is confirmed by the bands of the CO stretching vibrations, for if the proton tunnels frequently to and fro in the hydrogen bridge between acid and base, these bands would be considerably broadened or have disappeared which is not the case.

Fig. 1 also shows that the continuous absorption appears on increasing ΔpK_a between acid and base. With the *N*-methylimidazole series the continuum appears between phenol and 4-nitrophenol. The intensity of the continuum remains constant from 4-nitrophenol (pK_a 7.16) to monochloroacetic acid (pK_a 2.86), a very large ΔpK_a range. It then decreases again with the dichloroacetic acid system. This continuum extends, like the continua investigated, ³⁻⁷ from ca. 3000 cm^{-1} to lower wave numbers. Hence it is distinguished from the extremely broad band at about 1700 cm^{-1} observed by Hadži ^{26b} in some systems and designated D by him. Hadži assigns this band to

extremely strong hydrogen bonds with a symmetrical or almost symmetrical single minimum. In contrast, a continuum which extends over the total range can only be explained by a double minimum potential well, since only such hydrogen bonds are so strongly polarizable that the interaction effects become large enough to cause such a continuity of energy level differences.^{1, 2}

Since we know that the vibrations in the hydrogen bridges between acid and base cause bands and not a continuous absorption, this continuous absorption must be due to the occurrence of other bonds. Groupings $A-H^+ \cdots A^-$ and $BH^+ \cdots B$, which form according to the following equation :



This equilibrium is discussed by Szafran and Dega-Szafran.^{29b} From the results in refs. (3)-(6) and (30) with similar systems, it is known that the $BH^+ \cdots B$ bonds in these cases contribute to the continuum. In liquid systems, $Cl-H^+ \cdots Cl^-$ bonds also produce continuous absorption.⁵ They are $A-H^+ \cdots A^-$ bonds, hence it may be expected that the protons form corresponding bonds between $-CO_2^-$ ions.* The continuum thus indicates that adducts, in accordance with the above equation, are also formed, and hence symmetrical hydrogen bonds with a double minimum potential well are also observed in these systems. Hence, in the systems we investigated, $AH \cdots B$ hydrogen bonds as discussed by Hadži^{26b} may occur as well as $BH^+ \cdots B$ hydrogen bonds, as discussed by Szafran and Dega-Szafran.^{29b}

We will see, however, in the following that the potential well in the hydrogen bond is strongly influenced by its environment. Thus it is probable that at least in the almost symmetrical systems some of the hydrogen bonds between acid and base are symmetric enough to contribute to the continuous absorption. However, most bonds between acid and base cause the discrete absorption bands.

PROTON TRANSFER

The question now arises as to whether proton transfer occurs in the series of carboxylic acids investigated, i.e. that the potential in the hydrogen bridge changes so as to transfer from a minimum at the acid to a minimum at the base. We want to know whether the symmetrical case is passed through in the series investigated.

The following bands give information with regard to this.

(a) The bands of the stretching vibration of the carboxylic acid groups. As with the anions discussed in ref. (4) and (31a), on removal of the proton, the CO bond with single and that with double bond character become equivalent. In the spectrum the $C=O$ stretching vibration in the range $1750-1720\text{ cm}^{-1}$ disappears.† Instead, the vibrations of the $-CO_2^-$ ions arise, ν_{as} in the range $1650-1550\text{ cm}^{-1}$ and ν_s in the range $1400-1330\text{ cm}^{-1}$ (assignment see ref. (21)).

(b) In the range above 1750 cm^{-1} , the three broad strong bands at 2900, 2500 and

* With carboxylic acid dimers, no continuum is observed but, instead, broad bands. Symmetric potential wells would be expected on considering simultaneous transfer of both protons in the hydrogen bonds. Such a cooperative transfer is evidently very rare, since the protons reject each other strongly. In the case of a method such as i.r. spectroscopy whereby the "period of observation" is only very short, the proton will always be found at one of the acid groups. This infrequent transfer does not affect observation. Under these conditions, however, one can say in accordance with the results in ref. (2), that the proton in the one hydrogen bridge, polarizes the other hydrogen bridge, and vice-versa. Hence an unsymmetric potential well occurs in both hydrogen bridges.

† The behaviour of the band with single bond character is complicated, since this vibration couples with the OH bending vibration. Thus instead of only one band, two bands are found, one in the range $1400-1300\text{ cm}^{-1}$ and one in the range $1300-1200\text{ cm}^{-1}$.²⁰ With the phenols, coupling of the δOH with the ring vibrations takes place.²⁷

1900 cm^{-1} disappear and instead only two bands occur, one extremely broad band in the 2900-2300 cm^{-1} range and one at about 1970 cm^{-1} .

(c) When the proton transfer occurs, the band due to the NH bending vibration at about 1200 cm^{-1} appears.

(d) The vibrations of the base change to those of the protonated form.

Consideration of the spectra shown in fig. 1 and the bands compiled in table 1 give the following results. With the systems under investigation no proton transfer takes place when pyridine is used. With the systems with chloropyridine and methylpyrazine some of the protons in the hydrogen bond in systems chloropyridine + dichloroacetic acid (DCA) and methylpyrazine + trichloroacetic acid have been transferred to the base. In the systems with *N*-methylimidazole a considerable number of the protons are found in system MI + formic acid on the base. In the MI + DCA system complete proton transfer to the base has occurred. In these anhydrous systems, 50 % proton transfer accordingly takes place when the pK_a of the acid is smaller than that of the base by $\Delta\text{pK}_a \approx 4$.

This agrees well with previous results.^{12, 17, 32} Gusakowa, Denisow *et al.*¹⁷ found on i.r. investigation of pyridine with carboxylic acids in CHCl_3 solution that partial proton transfer occurs with dichloroacetic acid and to a much greater extent with trichloroacetic acid. These authors also found that in these systems increasing concentration and decreasing temperature favour proton transfer. Johnson and Rumon,³² found a ΔpK_a value of 3.7 for 50 % proton transfer between 1 : 1 adducts of substituted pyridines and benzoic acid. Finally, Ratajczak and Sobczyk,¹² from dielectric investigations of complexes between phenols and triethylamine, found that proton transfer occurs in the hydrogen bonds between phenol and triethylamine when the phenol is more acidic by $\Delta\text{pK}_a \approx 5$ than the amine. The above only applies, however, to the bonds between phenols, carboxylic acids and N bases. These results cannot be transferred directly to other acid base pairs.³³

In summary we can state: even when the potential in the hydrogen bond is changed in relatively small steps so that the minimum shifts from the acid to the base group, the bonds between acid and base cause discrete bands, that is, the occurrence of the continuum depends sensitively on the symmetry. In other systems, however, continua are sometimes observed when hydrogen bonds with an unsymmetrical double minimum potential well occur. These only extend over the range from *ca.* 3000-1700 cm^{-1} .^{30, 34}

DEPENDENCE OF THE POTENTIAL IN THE HYDROGEN BOND ON ITS ENVIRONMENT

(1) VARIOUS MIXTURE RATIOS

The spectra of mixtures of 2-methylpyrazine + trichloroacetic acid and 3-chloropyridine + dichloroacetic acid in mol ratio 1 : 2, 1 : 1 and 2 : 1 are shown in fig. 3. The same amount of acid is always present in the spectrometer light path.

Fig. 3 shows: the intensity of the stretching vibrations of the $-\text{CO}_2^-$ ions increases with increasing acid content (with system chloropyridine + DCA at 1624 cm^{-1} and at 1374 cm^{-1} , with system methylpyrazine + TCA at 1640 cm^{-1} and at 1340 cm^{-1}). Excess acid accordingly favours proton transfer to the base. The bands of the base confirm this result. This can be clearly seen in system chloropyridine (CP) + DCA, for instance, with the band at 1530 cm^{-1} .

When the acid is in excess in the mixtures, considerably more proton transfer to the base occurs than with 1 : 1 mixtures. At the same time, an OH stretching vibration in an $\text{OH} \cdots \text{O}$ bond, with a decreasing base amount in the mixtures, is still

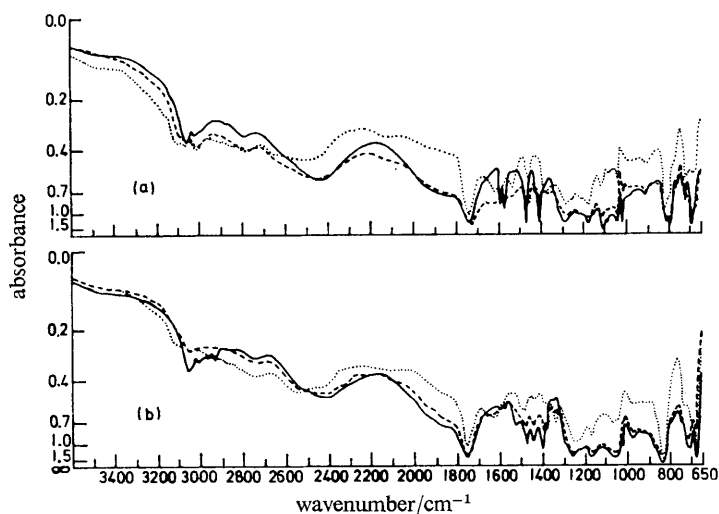
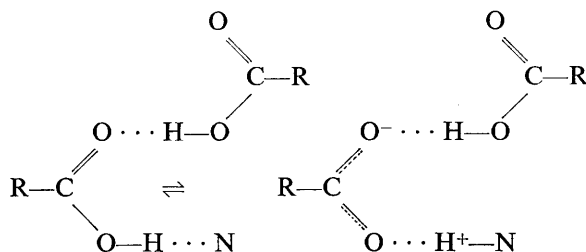


FIG. 3.—Mixtures with different mole ratios: (a) — 2 mol 3-chloropyridine+1 mol dichloroacetic acid (sample thickness $17.7\text{ }\mu\text{m}$), --- 1 mol 3-chloropyridine+1 mol dichloroacetic acid ($11.3\text{ }\mu\text{m}$), ... 1 mol 3-chloropyridine+2 mol dichloroacetic acid ($8.05\text{ }\mu\text{m}$); (b) — 2 mol 2-methylpyrazine+1 mol trichloroacetic acid ($18.4\text{ }\mu\text{m}$), --- 1 mol 2-methylpyrazine+1 mol trichloroacetic acid ($12.0\text{ }\mu\text{m}$), ... 1 mol 2-methylpyrazine+2 mol trichloroacetic acid ($9.25\text{ }\mu\text{m}$).

found at about 3100 cm^{-1} . These results are comprehensible if one assumes the occurrence of 2 : 1 adducts having the following structure :



The symmetry of the carboxylic acid group is increased by the linkage of the second hydrogen bond to the acid molecule, in comparison with the 1 : 1 adduct. This increases the mesomeric bond resonance energy and favours proton transfer to the base. The assumption of 2 : 1 adducts is in good agreement with the results reported in similar systems.^{17, 36}

(2) AQUEOUS SOLUTIONS OF IMIDAZOLE WITH CARBOXYLIC ACIDS

Fig. 4 shows spectra of aqueous solutions containing imidazole and a carboxylic acid (mol ratio 1 : 1) and 4 mol H_2O . Fig. 4 and table 2 show that only the bands of the $-\text{CO}_2^-$ ion are observed in the ranges $1640\text{--}1590\text{ cm}^{-1}$ and $1400\text{--}1350\text{ cm}^{-1}$ in all systems except I+acetic acid(A)+4 H_2O instead of the $\text{C}=\text{O}$ stretching vibration. In I+A+4 H_2O , the $\text{C}=\text{O}$ stretching vibration is found at 1705 cm^{-1} , however, the band of the antisymmetric stretching vibration of the $-\text{CO}_2^-$ ion at 1562 cm^{-1} is readily apparent.

In all systems, apart from I+DCA+4 H_2O , where it is masked, the δNH vibration is observed between 1200 and 1190 cm^{-1} . As expected, in I+A+4 H_2O this band is somewhat weaker. The weak band at about 980 cm^{-1} may be the γNH vibration.

SYMMETRY OF HYDROGEN BONDS

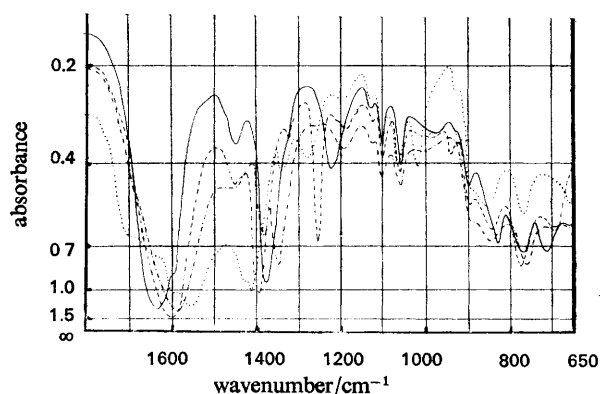


FIG. 4.—Aqueous solutions of imidazole with different acids: — imidazole + dichloroacetic acid + 4H₂O, --- imidazole + monochloroacetic acid + 4H₂O, ... imidazole + formic acid + 4H₂O, . . . imidazole + acetic acid + 4H₂O.

The changes to the bands which occur on protonation show that in contrast to the finding with anhydrous solutions where 50 % proton transfer to the base occurs if ΔpK_a acid–base is about 4 in the aqueous solution, about 50 % proton transfer takes place if ΔpK_a is only about 2. This difference between aqueous and anhydrous solutions is confirmed by an investigation of an anhydrous solution of imidazole in acetic acid. In this system no proton transfer is found, in contrast to the result in aqueous solution.

TABLE 2.—AQUEOUS SOLUTIONS OF IMIDAZOLE WITH DIFFERENT ACIDS

I+A+4H ₂ O	I+F+4H ₂ O	I+MCA+4H ₂ O	I+DCA+4H ₂ O	assignment
2900-2300	2900-2300	2900-2300	2900-2300	see text
s, vb	s, vb	s, vb	s, vb	
1980 m, b	1980 m, b	1980 m, b	1980 m, b	vC=O
1705 m	—	—	—	
1562 m	1595 s	1600 s	1635 s	—CO ₂ ⁻ v _{as}
1410 m	—	—	—	vCO and δ OH
1277 m	—	—	—	
masked	1384 s	1395 s	1376 s	—CO ₂ ⁻ v _s
1190 w	1196 w	1190 w	masked	δ NH
—	1000 w	980 w	970 w	γ NH (?)

According to the above, water favours the proton transfer in the hydrogen bond.^{31b} This is comprehensible, since a water molecule is bound to one oxygen atom of the carboxylic acid group. This water molecule increases the symmetry and hence the mesomeric bond resonance in the carboxylic acid group. This mechanism is analogous to the one already discussed in connection with the formation of the 2 : 1 adducts.

In summary we can state: the value 4 for the ΔpK_a of proton transfer applies only to anhydrous 1 : 1 mixtures. When additional acid is added, the proton transfer to the base is made easier by the formation of 2 : 1 adducts. The same is true in the presence of water. This is in both cases due to an increase in the mesomeric bond resonance in the carboxylic acid group. Hence the value of the ΔpK_a for proton transfer to the base is very sensitive to the environment and especially on the degree of hydration.

ASPECTS WITH RESPECT TO BIOLOGICAL SYSTEMS

In proteins, the pK_a values of glutamic acid and aspartic acid residues are smaller by several units than those of the basic lysine and arginine residues. In an anhydrous medium, therefore, the hydrogen bonds formed between the acid and basic residues could well be largely symmetrical.

The symmetry of these bonds and thus the proton transfer in these bonds can be controlled by changing the environment, especially by the degree of hydration. This symmetry can also be altered by external electrical fields.^{1, 2}

Hydration within the protein molecules is extremely slight. In the case of conformation transitions, the degree of hydration of individual groups can change considerably, however. According to the above results, proton transfer can then be induced. It appears possible that this is of substantial importance in the regulating mechanisms of proteins.

N.m.r. studies have shown that in the enzyme RNase T₁ a hydrogen bond exists between a carboxylic acid group and the imidazole residue of a histidine.^{37, 38} The probability of the proton in these hydrogen bonds being at the carboxylic acid group was found extremely large. In contrast, it is observed on investigating corresponding model substances, such as imidazole+propanoic acid, in aqueous media, that the residence time of the proton is very much greater at the N atom of the imidazole residue. This difference is easily comprehensible, for in enzymes the water, in contrast to the model substance, is unable to approach the carboxylic group for steric reasons and hence proton transfer is not favoured.³⁹

EXPERIMENTAL

The liquids were dried for a period of several days over a 3 Å molecular sieve. After such treatment, the H₂O bands in their spectra disappeared. Acid and base were mixed using a magnetic stirrer. The individual spectra were plotted immediately afterwards, since with some mixtures transition to solid state or decomposition occurred after some days.

All equipment was carefully dried before use. The sample space of the cells, especially the windows, was briefly dried with hot air. In order to plot the spectra at 70°C, the mixtures were heated in an oil bath, with stirring, and put into the previously heated cell. With the exception of the spectra of the nitrophenol+MI and stearic acid+MI, which are plotted at 70°C, all spectra were recorded at 25°C.

The spectroscopic sample thickness was adjusted so that the same number of molecules was present with all substances in the beam. In order to effect this, the sample thickness was varied according to the formula

$$\delta = \delta' \frac{M}{\gamma} \frac{\gamma'}{M'} \quad (M = \text{molecular weight}, \gamma = \text{density})$$

on transfer from one substance to the other. With mixtures M corresponds to the sum of the molecular weights. The densities of the pure substances were literature values¹⁸ or were measured with a pycnometer. This was especially necessary with the mixtures.

Where the mol ratios changed, the amount of acid in the beam remained constant and x mol of base added to 1 mol of acid, respectively ($x = \frac{1}{2}$ or 2). Here

$$M = M_A + xM_B$$

$$M' = M_A + M_B$$

were substituted in the formula given above. M_A = molecular weight of the acid, M_B = molecular weight of the base.

The cell was as described in ref. (5), but the acid resistance of the cell was improved by a Teflon lining at the interface of the platinum-steel-germanium windows, which also acted as a seal.

Measurements were carried out with a Perkin-Elmer i.-r. double-beam spectrophotometer, model 221. On account of the high loss of reflection of the germanium, slit programme 980 was used. The recording speed was one wave number per second. The sensitivity was checked during plotting of the spectra. In order to eliminate loss of energy by absorption of atmospheric water vapour, the spectrophotometer was flushed with dry air. The spectra are corrected by a calibration curve plotted with the help of the values given in the literature.⁴⁰

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