Infrared and ^{1}H Nuclear Magnetic Resonance Studies of Hydrogen Bonds in Some Pyridine *N*-Oxide Trifluoroacetates and Trichloroacetates in Chloroform. Correlation of OH Stretching Frequencies and Proton Chemical Shifts with Pyridine *N*-Oxide p*K*a Values

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The i.r. and ^{1}H n.m.r. spectra are reported for the trifluoro- and trichloro-acetates of 12 substituted pyridine *N*-oxides in dry chloroform. If the centre of gravity of the OH stretching absorption ($\tilde{\nu}_H$) and the chemical shift of hydrogen-bonded protons (δ) are plotted against the pK_a values of the *N*-oxides, the points fall on two intersecting straight lines. The correlations reflect changes in the hydrogen-bond strength. Plots of $\tilde{\nu}_H$ and δ of trifluoroacetates against the corresponding values for the trichloroacetates are used to show that the proton-donor properties of the acids are comparable. A direct plot of δ *versus* $\tilde{\nu}_H$ gives a straight line consistent with data for the monomeric acids. This correlation is discussed with respect to the difference between hydrogen bonds in molecular and ion-pair complexes.

In hydrogen-bond-complex formation between Brønsted acids (AH) and bases (B), the proton is magnetically deshielded and the A–H (or B^+–H) stretching frequency decreases. Both the change in the AH (or B^+H) stretching frequency ($\Delta\nu$) and the change in proton shielding constant (Δ) upon hydrogen-bond-complex formation have been correlated with pK_a, proton affinities, bond lengths, i.r. intensities, polarity of hydrogen bonds ($\Delta\mu$), heats of hydrogen bonding (ΔH_f), heats of ionization (ΔH_i), *etc.*[1-3] There is now almost unanimous agreement that no general linear correlation exists. However, for closely related compounds (such as those of a single functional group) interacting with the same AH or a single base B with a series of similar AH, good linear correlations are found. These correlations tell us that such systems must involve a bewildering array of hydrogen-bonded complexes between the neutral species [equation (1)] and the ion pairs produced by protolysis [equation (2)]. Arnett *et al.*[2] have expressed the opinion that the structural and energy differences between products and reactants in equation (1) must be vastly different from those represented in equation (2).

$$(AH)_s + (B)_s \rightleftharpoons (A{-}H \cdots B)_s \qquad (1)$$

$$(AH)_s + (B)_s \rightleftharpoons (A^- \cdots H{-}B^+)_s \qquad (2)$$

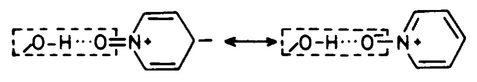
These observations are made on complexes mainly with various nitrogen or weak oxygen bases, and *N*-oxides were used only occasionally.

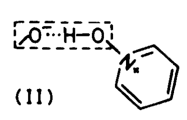
Molecular orbital calculations, dipole moments, and other physical and chemical properties [4-6] demonstrate that the ring system in aromatic *N*-oxide compounds in general has a greater π-electron density than that of the corresponding parent *N*-compounds. This can be attributed to the power of the N^+–O^- group to donate electrons to the ring when required.[7] In this respect, pyridine *N*-oxide is isoelectronic with a phenoxide anion.[8] The negative charge in an *N*-oxide is in the oxygen, and hence there is a deficit of electrons in the nitrogen. Both hydrogen bonds and protonation increase the deficit of electrons on nitrogen [9] [(I) and (II)]. In the parent aromatic *N*-compounds the negative charge is in the nitrogen, and hence protonation changes this negative charge to positive [(III) and (IV)]. Thus the structural and hence energetic difference between molecular complexes and hydrogen-bonded ion pairs in aromatic *N*-oxides (I) and (II) should be much smaller than those in their parent *N*-heterocycles, (III) and (IV). To test this prediction i.r. and ^{1}H n.m.r. spectra of 24 complexes of substituted pyridine *N*-oxides with trifluoroacetic (TFA) and trichloroacetic (TCA) acids have been measured in dry chloroform.

The second aim of this paper is to test whether these complexes with TFA and TCA should be treated as the same family or as two different families. Different pK_a(H_2O) values for these acids are available in the literature: TFA, pK_a = 0.23 [10] and 0.52; [11] TCA, pK_a = 0.63 [10] and 0.512.[11]

Experimental

Most of the complexes with TCA were obtained in a crystalline form by dissolving the anhydrous *N*-oxide in a small volume of $CHCl_3$–CCl_4 (1 : 3) and adding the acid. The resulting precipitates were recrystallized from $CHCl_3$–CCl_4 (1 : 3) and correct analyses obtained. The melting points were: 4-Cl, m.p. 72 °C; H, m.p. 64 °C; 4-Me, m.p. 96—97 °C; 3-Me, m.p. 81 °C; 4-OMe, m.p. 71—72 °C; 4-OEt, m.p. 65—66 °C; 4-OPh, m.p. 86—87 °C; 4-OBz, m.p. 65 °C; 4-NMe_2, m.p. 82—83 °C. Two complexes (4-NO_2 and 4-CN derivatives) were prepared by dissolving the *N*-oxide in a chloroform solution of TCA. Complexes with TFA were prepared as described previously.[12] Chloroform, used as the i.r. and ^{1}H n.m.r.


(I)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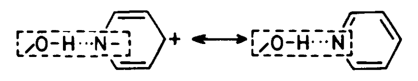
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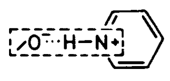
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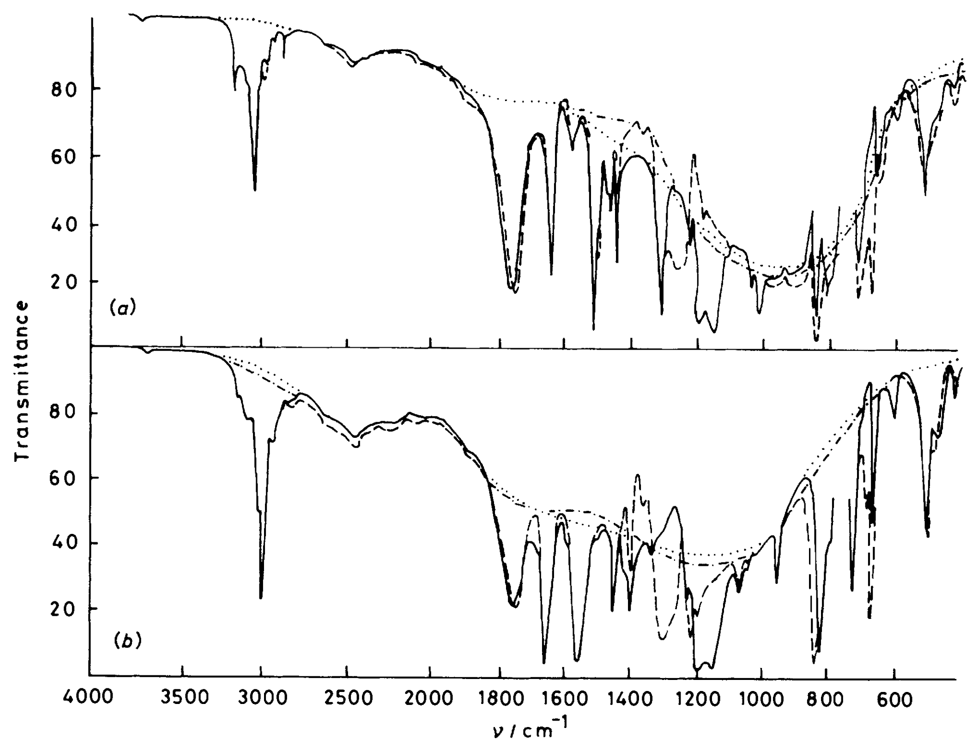

Figure 1. I.r. spectra of complexes of substituted pyridine *N*-oxides with trifluoroacetic (——) and trichloroacetic (— — —) acids in chloroform and [^{2}H]chloroform; (*a*) 4-MeO and (*b*) $4\text{-}Me_2N$ (· · · · and — · — · — broad absorptions in complexes of trifluoroacetic and trichloroacetic acids, respectively)

Table. Characteristic i.r. bands and ^{1}H n.m.r. chemical shifts of hydrogen-bonded protons of complexes of substituted pyridine *N*-oxides with trifluoroacetic and trichloroacetic acids in chloroform

No.	Substituent	pK_a [a] of *N*-oxide	CF_3CO_2H			CCl_3CO_2H		
			ν(C=O)/cm^{-1}	$\tilde{\nu}_H$/cm^{-1}	δ/p.p.m.	$\tilde{\nu}$(C=O)/cm^{-1}	$\tilde{\nu}_H$/cm^{-1}	δ/p.p.m.
1	$4\text{-}NO_2$	− 1.70	1 777	2 050	14.60 [b]	1 750	2 073	14.40 [b]
2	4-CN	− 1.17	1 776	2 015	14.97 [b]	1 750	2 038	14.75 [b]
3	4-Cl	0.36	1 771	1 506	17.12	1 752	1 512	16.85
4	H	0.79	1 763	1 346	17.98	1 750	1 366	17.72
5	3-Me	1.08	1 762	1 275	18.37	1 750	1 294	18.15
6	4-Me	1.29	1 762	1 225	18.57	1 747	1 233	18.38
7	4-OEt	1.97	1 757	1 187	18.81	1 740	1 176	18.68
8	4-OMe	2.05	1 755	1 199	18.78	1 740	1 178	18.71
9	4-OBz	1.99	1 754	1 193	18.82	1 739	1 187	18.68
10	4-OMe-2-Me	2.41	1 751	1 235	18.48	1 738	1 225	18.42
11	4-OPh	2.67	1 757	1 192	18.57	1 742	1 185	18.39
12	$4\text{-}NMe_2$	3 88	1 747	1 527	17.22	1 732	1 509	17.12

[a] Values are taken from refs. 6 and 14. [b] With excess of base (C_B/C_{AH} = 2 : 1).

solvent, was passed through alumina immediately prior to use. All solutions were prepared and all transfers of non-aqueous solutions were made in a dry box.

The i.r. spectra were recorded on Perkin-Elmer, models 180 and 580, spectrophotometers using cells with KBr windows (0.12 mm and 0.2M). ^{1}H N.m.r. spectra (0.2M) were measured at 60 MHz on a Tesla BS 467 spectrometer at 24 ± 2 °C. All chemical shifts were taken downfield relative to the resonance of the solvent and then converted into the δ values.

The broad OH stretching absorption was graphically separated from the skeletal absorptions (see Figure 1). Centres of gravity of the reconstructed bands were obtained as $\tilde{\nu}_H = \int A(\nu)\nu d\nu / \int A(\nu) d\nu$ by numerical integration.

Results and Discussion

The i.r. spectra of complexes of pyridine *N*-oxides with TFA and TCA show, as for other compounds with strong hydrogen bonds,[13] an extremely broad absorption that extends from *ca.* 3 000 down to 400 cm^{-1} and is topped by some badly defined maxima (A > 2 800, B *ca.* 2 500, C *ca.* 1 900, D *ca.* 1 100, and E *ca.* 850 cm^{-1}). This absorption is assigned to the strongly hydrogen-bonded OH stretching vibration in the investigated complexes (Figure 1). The Table lists the centres of gravity ($\tilde{\nu}_H$) of the very broad stretching vibration. The $\tilde{\nu}_H$ values are accurate to ±30 cm^{-1}. As shown in the Table the difference in the $\tilde{\nu}_H$ values between complexes of TFA and TCA is smaller than the experimental error and could be a fiction. The i.r.

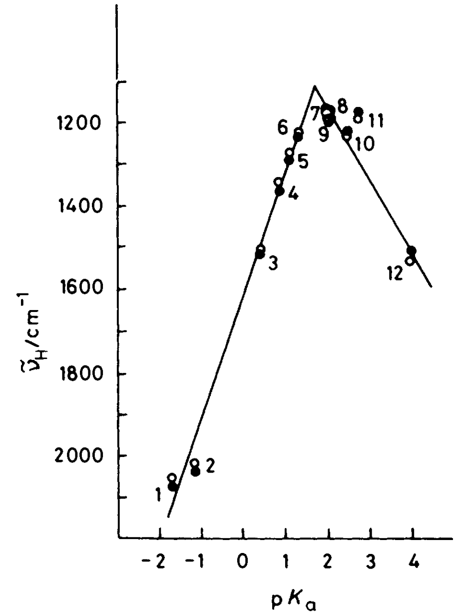

Figure 2. Correlation of the centre of gravity ($\tilde{\nu}_H$) of the broad absorption with the pK_a values of pyridine *N*-oxides in water (○, TFA; and ●, TCA) (numbers refer to the Table)

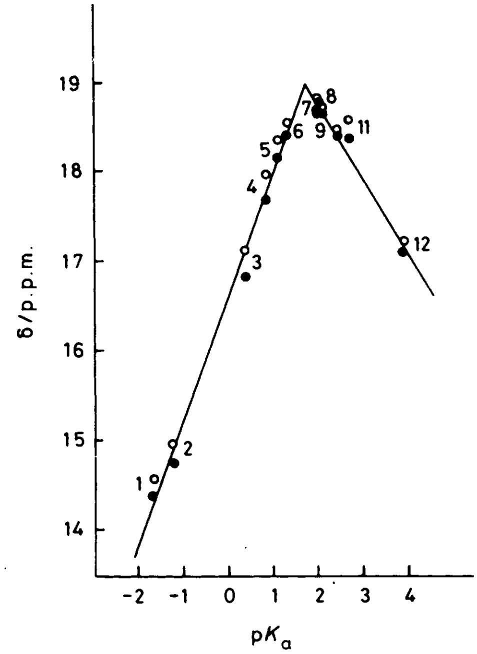

Figure 3. Correlation of the chemical shift of hydrogen-bonded protons (δ) with the pK_a values of pyridine *N*-oxides in water (○, TFA; and ●, TCA) (numbers refer to the Table)

spectra of the same *N*-oxide with TFA and TCA look very much the same (Figure 1). There is, however, a slight difference in intensity between the two series of complexes. In the spectra of complexes of the weakest bases (*e.g.*, 4-nitro-, 4-cyano-, and 4-chloro-derivative) and the strongest bases (*e.g.*, the 4-dimethylamino-derivative) the absorption in TFA complexes in the 2 500 cm^{-1} region is smaller than in TCA complexes. In the case of the medium-strong *N*-oxides (*e.g.*, 4-methyl-, 4-ethoxy-, and 4-methoxy-derivative) the differences appear in the 900 cm^{-1} region and again in the TFA series absorption is less intense. The main difference between the two series of complexes is shown, however, in the 1 250—1 450 cm^{-1} region (Figure 1). These differences between complexes of TFA and TCA are consistent with the differences in the $\tilde{\nu}_H$ values listed in the Table.

Since small amounts of water affect the chemical shifts of the hydrogen-bonded protons,[15] the measured chemical shifts are accurate to ±0.15 p.p.m. The difference in the chemical shifts in the Table for the same *N*-oxide with TFA and TCA is within the limits of error. Replicate experiments in the same sample of solvent were performed for the complexes of the 4-methoxy- and 4-dimethylamino-derivative with TFA and TCA. Similar differences in chemical shifts to those in the Table were observed. It is worth noting that the observed differences in the proton shifts between TFA and TCA complexes are slightly larger than those of the protons in the corresponding CH_3CH_2X,[16] and have a similar sign. This may suggest that the differences in chemical shifts of TFA and TCA complexes can be caused by the long-range shielding of halogens.[17] This problem requires further investigation.

Plots of both the frequencies and the chemical shifts of TFA complexes against the corresponding values for the TCA complexes show that the data distribute themselves very nicely about a straight line, given by equations (3) and (4). A *t*-test confirmed that the lines go through the origin

$$\tilde{\nu}_H^{TFA}\ (\pm 14\ \mathrm{cm}^{-1}) = 41.688 + 0.969\ \tilde{\nu}_H^{TCA};\ r = 0.999 \quad (3)$$

$$\delta^{TFA}\ (\pm 0.07\ \mathrm{p.p.m.}) = 0.535 + 0.979\ \delta^{TCA};\ r = 0.999 \quad (4)$$

[$t_{calc.}$ = 1.49 (i.r.); $t_{calc.}$ = 2.16 (n.m.r.); $t_{99.9}$ = 3.25]. The slopes do not differ significantly from unity. This suggests that the proton-donor properties of TFA and TCA are quite similar and the investigated complexes can be treated as one series.

Figures 2 and 3 show a reasonably good correlation between the centre of gravity ($\tilde{\nu}_H$), the chemical shift of the hydrogen-bonded protons (δ), and the pK_a values of the pyridine *N*-oxides, respectively. A deviation from the correlation lines is seen for 4-phenoxypyridine *N*-oxide complexes. A similar deviation for one of these complexes was observed in our previous investigations on dichloromethane.[14] These data have been deleted from further correlations. Data at the intersection points * are: i.r., pK_a = 1.65 and $\tilde{\nu}_H$ = 1 119 cm^{-1}; ^{1}H n.m.r., pK_a = 1.69 and δ = 19.02 p.p.m. Similar correlations have been obtained previously for complexes with TFA in dichloromethane.[14] The characteristic alterations of both the centre of complex absorption and the chemical shift reflect the variations of the hydrogen-bond strength. The strongest hydrogen bond appears in the complexes that are close to the intersection point.

The Table lists the frequencies of the ν(C=O) band. Most bands are smooth and have nearly constant width. Both the band width and the observed decreases of the ν(C=O) frequency with increasing proton-acceptor properties of the *N*-oxide (Table) are strong evidence in favour of a continuous shift of the proton from carboxy to the *N*-oxide group with increasing pK_a value of the *N*-oxide. This problem was previously discussed in more detail.[14] The observed difference in frequency of the ν(C=O) bands between complexes of TFA and TCA can be explained by the inductive effect.[18]

A direct plot of the chemical shift of the hydrogen-bonded protons *versus* the centre of complex absorption gives a straight line (Figure 4), which has the least-squares equation given in (5). The slopes, intercepts, and standard deviations

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* Points of intersection are given in ΔpK_a values: ΔpK_a = pK_a(AH) − pK_a(B$^+$H) and pK_a(AH) = 0.23, hence pK_a = 1.55 ± 0.08.

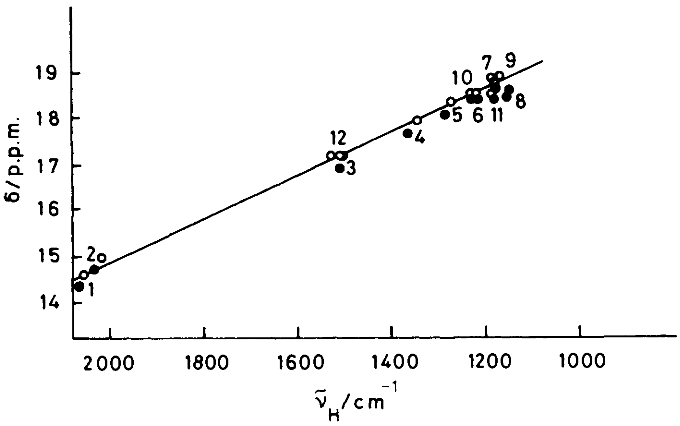

Figure 4. Correlation of the chemical shift of hydrogen-bonded protons (δ) with the gravity centre ($\tilde{\nu}_H$) of the broad absorption (○, TFA; and ●, TCA), (numbers refer to the Table)

of the separate δ *versus* $\tilde{\nu}_H$ equations for the molecular complexes (1—6 in the Table) and hydrogen-bonded ion pairs the (7—12 in the Table) are very similar to those in equation (5), and therefore statistically are indistinguishable.

$$\delta(\pm 0.12 \text{ p.p.m.}) = 24.298 - 4.722 \times 10^{-3}\,\tilde{\nu}_H;\ r = 0.997 \quad (5)$$

Protonated pyridine *N*-oxides interact with unprotonated pyridine *N*-oxides to form homoconjugated cations, $(BHB)^+$ (see, for example, ref. 19). Carboxylic acids form homoconjugated anions, $(AHA)^-$.[20] Both the chemical shift and the centre of gravity of homoconjugated cations and anions are comparable with the data of complexes of the medium-strong *N*-oxides (complexes which are close to the intersection points in Figures 2 and 3). Thus an equilibrium $2(AHB) \rightleftharpoons (BHB)^+(AHA)^-$ proposed previously [21,22] cannot be rejected. Vapour pressure osmometry data demonstrate, however, that the concentration of dimers $[(AHB)_2]$ is low and strongly decreases with increasing electric permittivity of the solvent.[23]

The monomeric TFA and TCA show a single band, due to 'free' ν(OH) at 3 483 and 3 485 cm^{-1}, respectively. Substituting these values into equation (5) the following values for the chemical shift for monomeric acids can be obtained: $\delta^{TFA} = 7.85 \pm 0.12$ p.p.m. and $\delta^{TCA} = 7.84 \pm 0.12$ p.p.m. These values are very close to the published data for monomeric acids: CCl_3CO_2H in CCl_4, δ = 7.71 p.p.m.;[24] RCH_2CO_2H in cyclohexane, δ = 5.2 ± 0.8 p.p.m.;[25] CH_3CO_2H in CCl_4, δ = 8.66 p.p.m.;[26] and $C_6H_5CO_2H$ in benzene, δ = 6.27 ± 0.4 p.p.m.[27] Although the extrapolation is about 1 400 cm^{-1} to a higher frequency, the predicted values for monomeric acids seems to be realistic. The fact that both molecular complexes and ion-pair complexes fit the same relationship (Figure 4) seems to indicate that the suggestion given in the introduction is reasonable; the difference between molecular complexes and ion pairs is seen to be quite small when indexed by $\tilde{\nu}_H$ and δ.

A number of authors have attempted to correlate acid-base behaviour through the change of frequency (Δν) and the change in chemical shift (Δ).[1,28] A plot of Δ values *versus* Δν values gives a good linear correlation between these two parameters over a range of 11 p.p.m. for the chemical shifts and 2 300 cm^{-1} for the frequency. The least-squares equation for the data is given in equation (6), where $\Delta = \delta_{AHB} - 7.85$ p.p.m. and $\Delta\nu = \tilde{\nu}_{AH}^{free} - \tilde{\nu}_{AHB}$ cm^{-1}. The results presented here for 22 complexes are the most extensive set of such data yet available for very strong hydrogen bonds.

$$\Delta(\pm 0.12 \text{ p.p.m.}) = -2.103 \times 10^{-2} + 4.731 \times 10^{-3}\,\Delta\nu;\ r = 0.997 \quad (6)$$

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