Aromaticity and Tautomerism. Part I. The Aromatic Resonance Energy† of 2-Pyridone and the Related Thione, Methide, and Imine[1]

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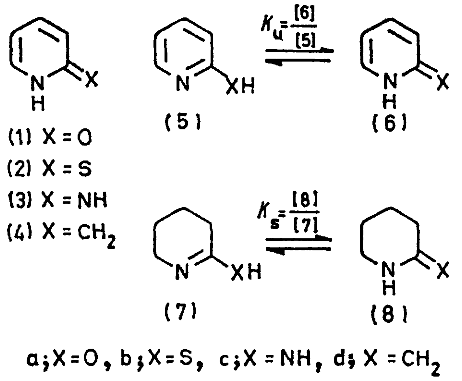
Tautomeric equilibria in the heteroaromatic and the analogous saturated series are compared. Available methods of conversion of free energy $\Delta G°$ into enthalpy $\Delta H°$ terms are applied and discussed. The $\Delta H°$ values obtained are used to demonstrate that 2-pyridone and 2-pyridinethione retain most of the aromatic resonance energy of pyridine, that 2-pyridone imine is also strongly aromatic, but that 2-pyridone methide is far less so. The work is compared with other estimates of the aromaticity of these compounds.

THE concept of aromaticity is of vital importance in the teaching and practice of organic chemistry, despite difficulties in its precise definition and quantitative measurement. Such difficulties have been particularly acute in dealing with heterocyclic compounds, to an extent that a compound such as 2-pyridone (1) is often referred to implicitly, and occasionally explicitly,[2] as 'non-aromatic.' In the present paper, we attempt to quantify the aromaticity of 2-pyridone (1) and its analogues (2)—(4) with the help of considerations of tautomeric equilibria.



$$\Delta H_s° = \text{Interact (NH/CX)} - \text{Interact (N/XH)} \quad (1)$$

$$\Delta H_u° = [A_x + \text{Interact (NH/CX)}] - [A_{py} + \text{Interact (N/XH)}] \quad (2)$$

The method now proposed involves a comparison of the tautomeric equilibrium (5) $\rightleftharpoons$ (6) with that for the corresponding saturated compounds (7) $\rightleftharpoons$ (8). For equilibria of the latter type, the difference in heat content of (7) and (8) ($\Delta H_s°$) [equation (1)] will be due to differences in electronic interactions, principally those between the N and the XH group in (7) [which we denote: Interact (N/XH)] and those between the NH and C=X in (8) [denoted: Interact (NH/CX)]. Such terms will also contribute to the difference in heat content between (5) and (6) ($\Delta H_u°$) but here the difference between the aromaticity of (5) and (6) will also be of major importance [equation (2)]. We now assume that ' Interact (N/XH) ' is the same for (5) as for (7) and that ' Interact (NH/CX) ' is the same for (6) as for (8): support for these assumptions comes from the very similar dipole moments[3] of 1-methyl-2-pyridone (9) (4·00 D) and 1-methyl-2-piperidone (10) (4·04 D); the moderate difference between the moments of (11) and (12) (1·08 and 1·49 D, respectively) may be due to varying conformational equilibria about the C(2)–O bonds in these compounds. Estimates of the contribution of charge-separated forms in amides (from dipole moments,[4,5] bond lengths,[6] and ^{13}C-coupling constants[7]) and in pyridones (from dipole moments[8a] and bond lengths[9]) are of similar magnitudes. Again, the larger dipole moment of pyridinethione compared to pyridones[8a] and the greater rotation barrier in

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† The term ' Aromatic Resonance Energy ' is defined by the Scheme (*cf.* Empirical Resonance Energy determinations of benzene using the ' cyclohexatriene ' model) and does not include amide (or iminol) type resonance terms.

[1] For preliminary communication of part of this work see M. J. Cook, A. R. Katritzky, P. Linda, and R. D. Tack, *Chem. Comm.*, 1971, 510.

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[7] P. Haake, W. B. Miller, and D. A. Tyssee, *J. Amer. Chem. Soc.*, 1964, **86**, 3577.

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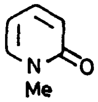
thioamides compared to amides[10] indicates greater charge separation for the sulphur compounds; a conclusion in agreement with n.m.r. studies of pyridinethiones[11] (see also Appendix).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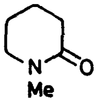
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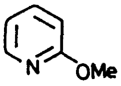
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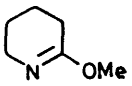
(12)

$$A_{\mathrm{py}} - A_{\mathrm{x}} = \Delta H_{\mathrm{s}}^\circ - \Delta H_{\mathrm{u}}^\circ \qquad (3)$$

$$\Delta G_{\mathrm{s}}^\circ - \Delta G_{\mathrm{u}}^\circ = -\mathrm{RT}\ln K_{\mathrm{s}} + \mathrm{RT}\ln K_{\mathrm{u}} = \mathrm{RT}\ln(K_{\mathrm{u}}/K_{\mathrm{s}}) \qquad (4)$$

$$\Delta G_{\mathrm{s}}^\circ - \Delta G_{\mathrm{u}}^\circ = 1{\cdot}37\,[\mathrm{p}K(N\text{-Me})_{\mathrm{u}} - \mathrm{p}K(X\text{-Me})_{\mathrm{u}} - \mathrm{p}K(N\text{-Me})_{\mathrm{s}} + \mathrm{p}K(X\text{-Me})_{\mathrm{s}}] \qquad (5)$$

It follows that the difference in the aromaticities of (5) and (6) is given by equation (3). If we now consider the free-energy difference corresponding to the difference between the ΔH_s° and ΔH_u° values, this is given by equation (4), or, expressed in terms of the pK_a value of the individual tautomers (which are approximated by the corresponding *N*- and *X*-methylated compounds[12]), by equation (5) because $\ln K_s = \mathrm{p}K(N\text{-Me})_s - \mathrm{p}K(X\text{-Me})_s$ and $\ln K_u = \mathrm{p}K(N\text{-Me})_u - \mathrm{p}K(X\text{-Me})_u$. To convert the experimentally available ΔG° quantities of equation (5) into the ΔH° required for equation (3) several procedures are available.

(i) Larson and Hepler[13] have reviewed the subdivision of ΔH° and ΔS° terms into *internal* effects, *viz.* those intrinsic to a species, and environmental (*external*) effects, and have discussed the relationship between ΔG° and ΔH_{int} for symmetrical reactions of the type: $\mathrm{HA\ (aq)} + \mathrm{R^-\ (aq)} = \mathrm{A^-\ (aq)} + \mathrm{HR\ (aq)}$. Statistical thermodynamic calculations (for refs. see ref. 13) show that for this type of reaction $\Delta S_{\mathrm{int}} \cong 0$; thus $\Delta S^\circ \cong \Delta S_{\mathrm{ext}}$ (a similar conclusion was reached by Beak[14] regarding the entropy difference between 4-methoxypyridine and 1-methyl-4-pyridone). Models for ion-solute interactions lead to the conclusion that $\Delta H_{\mathrm{ext}} \propto \Delta S_{\mathrm{ext}}$ whence $\Delta H^\circ = \Delta H_{\mathrm{int}} + \beta\Delta S^\circ$ where β is a proportionality constant, found to be approximately equal to T. It follows that $\Delta G^\circ \cong \Delta H_{\mathrm{int}}$. A refinement, to accommodate incomplete compensation of ΔH_{ext} by $T\Delta S_{\mathrm{ext}}$, introduces a solvent dependent parameter γ which gives the modified relationship, $\Delta G^\circ = \Delta H_{\mathrm{int}}(1 + \gamma)$. Extrapolation to the present work suggests that ΔG° should provide at least a good approximation for ΔH_{int}, a term appropriate to a discussion of aromatic character of a molecule, although the uncertainties in this approach must be emphasised.

(ii) The ΔH° values for the ionisation of many bases have been obtained from variable temperature measurements of pK_a values. If it is possible to discern a linear free-energy relationship between ΔG° and ΔH° from such work, then the ΔG° obtained from pK_a can be converted into ΔH°. Some of the available data is summarised in Figure 1: it is of variable reliability, but it seems probable that if linear $\Delta G^\circ/\Delta H^\circ$ relations exist, they vary for different base types. This conconclusion is emphasised by work on 1,3,5-triaminobenzene which shows that the ΔS° for protonation at carbon and nitrogen are quite different.[15] Two lines do seem to be well defined: for substituted anilines in the pH region, Bolton and Hall[16] found the equivalent of equation (6), and this relation was extended far into the H_0 region by Bolton, Johnson, Katritzky, and Shapiro[17] where the same equation was found to hold within the experimental error [in equations (6) and (7) ΔH° is expressed in kcal mol^{-1}].

$$\Delta H^\circ_{25^\circ} = 1{\cdot}13\ \mathrm{p}K_a + 2{\cdot}03 \qquad (6)$$

$$\Delta H^\circ = 1{\cdot}49\ \mathrm{p}K_a - 2{\cdot}85 \qquad (7)$$

The second line is that for substituted pyridines, defined by equation (7), which incorporates the results of Sacconi *et al.*[18] Results of Mortimer and Laidler[19] were later shown to be in doubt.[20] Equation (7) has been tested for pK_a values extending only over a short range (1·6 units). The different slopes for the lines for anilines and pyridines could be due to the different hybridisations of the nitrogen atoms in the two systems and to differences in the entropy of the two types of cations. The different lines for anilines and pyridines in $\Delta\nu$ (OH-phenol) $-$ pK_a correlations[21] could be due to the same causes; the sources of different lines for $\Delta\nu/\mathrm{p}K(\Delta\nu_{(x)}/\Delta\nu_{(y)})$ in different H-bonding systems have been reviewed by Bellamy[22] and Schleyer.[23]

(iii) Arnett *et al.*[24,25] have reported a linear relation [equation (8)] between the enthalpies of protonation of nitrogen and oxygen bases in fluorosulphuric acid

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[10] R. C. Neuman, jun., D. N. Roark, and V. Jonas, *J. Amer. Chem. Soc.*, 1967, **89**, 3412, and references therein.

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and the corresponding pK_a values determined in water or aqueous sulphuric acid. This equation clearly represents a method of obtaining ΔH° from pK_a; the line defined by this equation is also shown in Figure 1.

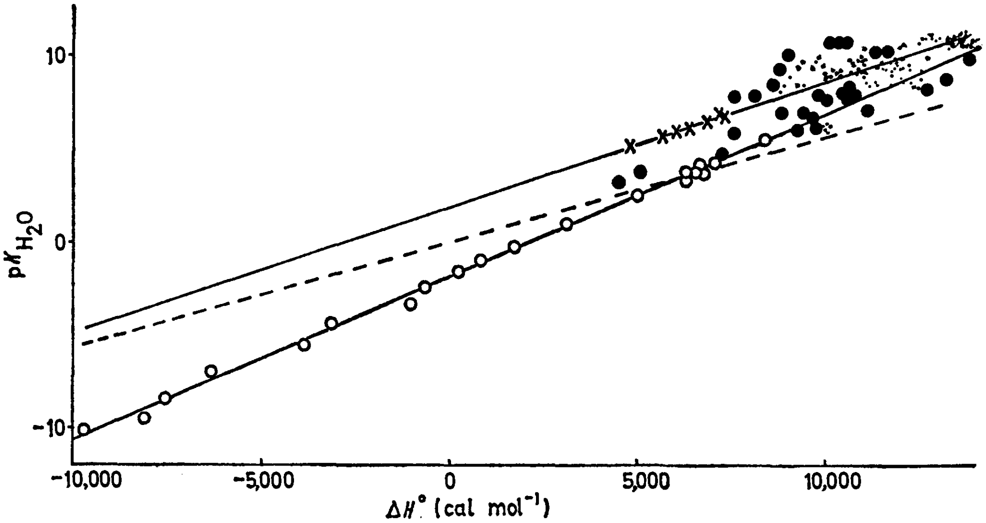

FIGURE 1 Relation between ΔH° and pK_a for the protonation of bases: ○ primary aromatic amines; × pyridines; ● other bases. The lines shown —— are least squares for primary aromatic amines [equation (6)] and for substituted pyridines [equation (7)] and the line – – – – is defined by Arnett's equation [equation (8)]

The method is subject to two assumptions: (*a*) that the heat of solvation of the free base is the same in fluorosulphuric acid as in the reference state (CCl_4 or $CHCl_2$-$CHCl_2$) and (*b*) that the heat of solvation of the conjugate acid in fluorosulphuric acid is independent of structure. For fluorosulphuric acid all bases are stated to follow the same equation; however, the ΔH° for aniline and pyridine were slightly different for solution in sulphuric acid [24] [equations (9) and (10)].

$$-\Delta H^\circ = (1{\cdot}78\,\mathrm{p}K_a + 28{\cdot}1)\ \mathrm{kcal\ mol^{-1}} \tag{8}$$

$$-\Delta H^\circ\ (\text{anilines}) = (1{\cdot}62\,\mathrm{p}K_a + 17{\cdot}9)\ \mathrm{kcal\ mol^{-1}} \tag{9}$$

$$-\Delta H^\circ\ (\text{pyridines}) = (1{\cdot}65\,\mathrm{p}K_a + 20{\cdot}3)\ \mathrm{kcal\ mol^{-1}} \tag{10}$$

(iv) Instead of correcting the ΔG° values for the individual protonation equilibria, we can also attempt to correct the ΔG° for the tautomeric equilibria of type (5) $\rightleftharpoons$ (6) and (7) $\rightleftharpoons$ (8). The temperature dependence of tautomeric equilibria has been studied for a variety of types (for a summary see ref. 26). Available data are plotted in Figure 2, it is evident that in the pyridine series a line is defined [equation (11)]

$$\Delta H^\circ = 1{\cdot}32\Delta G^\circ - 0{\cdot}85 \tag{11}$$

(correlation coefficient 0·985): the data included are 2-trichloroacetamido-, 2-dichloroacetamido-, and 2-methane sulphonamido-pyridine [27] and 6-bromo- and 6-chloro-2-pyridone.[26]

Other data on the temperature dependence of K_T are not included in Figure 2 because they refer to non-aqueous media, and also because the Arrhenius plots

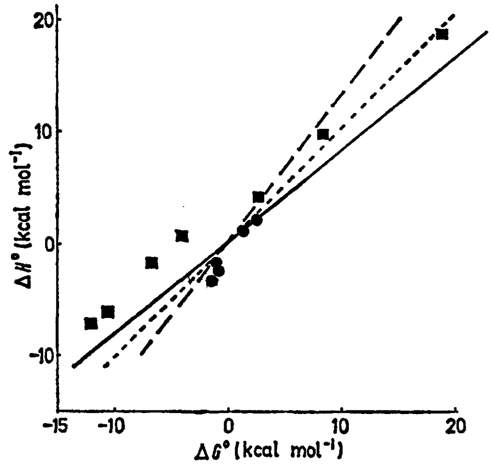

FIGURE 2 Relation between ΔH° and ΔG° for tautomeric equilibria. Experimental points for tautomerism of pyridines (see text): ● Lines defined by: equation (6) for primary aromatic amine ionisation behaviour ——; Arnett's equation (8) – – – –; assumption of $\Delta H_{\mathrm{int}} = \Delta G^\circ$ · · · ·. Theoretical points using treatment of equation (12): ■

were curved: such data includes work on β-keto-esters,[28,29] acetylacetone,[28,30] *NN*-diethylacetoacetamide,[31] and hydroxybenzazines.[32]

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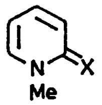
Figure 2 also includes for comparison the lines for the treatment by methods (i), (ii), and (iii) above and also points plotted on the assumption that the ionisation of (6) and (8) follow primary amine behaviour and (5) and (7) follow pyridine behaviour, *i.e.* using equation (12).

$$\Delta H^\circ = 1{\cdot}13\ [\mathrm{p}K\ (6\ \text{or}\ 8)] - 1{\cdot}48\ [\mathrm{p}K\ (5\ \text{or}\ 7)] \qquad (12)$$



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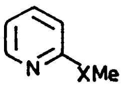

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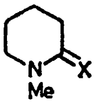

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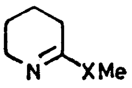

(16)

RESULTS

The results are collected in Table 1. The pK_a values quoted for the *N*- and *X*-methyl derivatives of the tautomeric pyridines are taken from the literature except for 1-methyl-2-pyridone imine and 1-methyl-2-pyridone methide which were redetermined (see Experimental section). The previous value (12·20) for 1-methyl-2-pyridone imine, determined by potentiometric titration[42] seemed likely to be too low in view of the redetermined value for the 4-analogue;[43] we find 13·03 ± 0·04. The only value for 2-pyridone methide previously reported[44] is >16·7: we measured the pK_a as 20·0 ± 0·2 using the method of Bowden and Cockerill.[45]

The pK_a values for many of the saturated compounds (10) and (12), *etc.* are not available; however, pK_a values from models are satisfactory as there is ample evidence that changing an alkyl group for another (in the absence of steric effect) has only a minor influence on pK_a values: *cf. e.g.*, $MeCONH_2$ and $EtCONH_2$, ΔpK_a 0·07;[46] Me-CO·NHMe and MeCO·NHEt, ΔpK_a 0·01.[47] In the oxygen series we have utilised literature pK_a values for *NN*-dimethylacetamide[36] and ethyl iminoacetate[39] (recently, a series of 3,3-dialkyl-2-ethoxy-3,4,5,6-tetrahydropyridines were shown to have pK_a 6·6 ± 0·05[48]), in the sulphur series thioacetamide[37] and ethyl iminothiolacetate,[40] and in the carbon series 1,2-dimethyl-3,4,5,6-tetrahydropyridine[38] and cyclohexanone methylimine.[41] As regards the nitrogen series, to a first approximation the pK_a values of the two compounds in the saturated series will be equal, as they are both simple alkylated amidines.

From the measured pK_a values, estimates of the aromatic resonance-energy differences, $A_{\mathrm{py}} - A_{\mathrm{x}}$, are obtained by the five equations (13)—(17) which [other than (13)] are derived from the appropriate equations discussed above. We define $\Sigma\mathrm{p}K_a = \mathrm{p}K\ (6) - \mathrm{p}K\ (5) - \mathrm{p}K\ (8) + \mathrm{p}K\ (7)$.

It is encouraging that the results for methods (i) and (ii)b, are closely similar, probably within experimental error. However, method (ii)a gives results which are significantly lower, and methods (iii) and (iv) results which are consistently higher. The use of method (ii)b rather than the method (ii)a can be justified as the nitrogen atom hybridisation both in (5) and in (7) will resemble that of the nitrogen atom in pyridine rather than that in aniline. Excluding method (ii)a gives the following estimated $(A_{\mathrm{py}} - A_{\mathrm{x}})$ values: 2-pyridone, 7·5 ± 1 kcal mol⁻¹; 2-pyridinethione, 6 ± 1 kcal mol⁻¹; 2-pyridone imine, 10 ± 2 kcal mol⁻¹; 2-pyridone methide, 18·5 ± 3·5 kcal mol.⁻¹ The ranges quoted are the probable errors in obtaining ΔH° from ΔG°: other uncertainties, in the choice of model and solvent interactions could raise the total error to say ±5 kcal mol⁻¹.

$$(A_{\mathrm{py}} - A_{\mathrm{x}})_{(\mathrm{i})} = 1{\cdot}37\Sigma\mathrm{p}K_a \qquad (13)$$

$$(A_{\mathrm{py}} - A_{\mathrm{x}})_{(\mathrm{ii})\mathrm{a}} = 1{\cdot}13\Sigma\mathrm{p}K_a \qquad (14)$$

$$(A_{\mathrm{py}} - A_{\mathrm{x}})_{(\mathrm{ii})\mathrm{b}} = 1{\cdot}13\ [\mathrm{p}K\ (6) - \mathrm{p}K\ (8)] - 1{\cdot}48\ [\mathrm{p}K\ (5) - \mathrm{p}K\ (7)] \qquad (15)$$

$$(A_{\mathrm{py}} - A_{\mathrm{x}})_{(\mathrm{iii})} = 1{\cdot}78\Sigma\mathrm{p}K_a \qquad (16)$$

$$(A_{\mathrm{py}} - A_{\mathrm{x}})_{(\mathrm{iv})} = 1{\cdot}81\Sigma\mathrm{p}K_a \qquad (17)$$

TABLE 1 [a]

Results for 2-pyridone and related compounds

X	(13) pK_a	(14) pK_a	ΔG°_u (kcal mol⁻¹)	(15) pK_a	(16) pK_a	ΔG°_s (kcal mol⁻¹)	$(A_{\mathrm{py}} - A_{\mathrm{x}})$ (kcal mol⁻¹) (i)	(ii)a	(iib)	(iii)	(iv)
O	0·32 [b]	3·28 [b]	−4·1	−0·19 [f]	7·5 [j]	−10·6	6·5	5·3	6·8	8·4	8·6
S	−1·22 [c]	3·62 [c]	−6·7	−1·76 [g]	6·9 [k]	−12·0	5·3	4·3	5·5	6·8	6·9
NH	13·02 [d]	6·86 [b]	8·5	*h*	*h*	0	8·5	7·0		11·0	11·1
CH_2	20·0 [d]	5·97 [e]	19·2	11·4 [i]	9·43 [l]	2·7	16·4	13·6	14·9	21·4	21·7

(ii)a From aniline line. (ii)b From two lines (see text).

[a] All values refer to aqueous solutions. [b] *Cf.* ref. 33. [c] *Cf.* ref. 34. [d] Present investigation. [e] *Cf.* ref. 35. [f] Value for *NN*-dimethylacetamide, *cf.* ref. 36. [g] Value for thioacetamide, *cf.* ref. 37; for thiopiperidone, pK_a −1·4 has been reported by J. T. Edward and H. Stollar, *Canad. J. Chem.*, 1963, **41**, 721. [h] Assumed equal by inspection. [i] 1,2-Dimethyl-1,4,5,6-tetrahydropyridine, *cf.* ref. 38. [j] Value for ethyl iminoacetate [MeC(:NH)·OEt], *cf.* ref. 39. [k] Value for ethyl iminothiolacetate [MeC(:NH)·SEt)], *cf.* ref. 40. [l] *N*-Methylcyclohexanone imine, *cf.* ref. 41.

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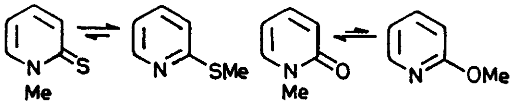
Comparison with Beak's Work.—The approach used in the present work has, in some respects, been considered by Beak *et al.*[14] who have rejected the use of protomeric tautomerism for the calculation of resonance energies. They believe that prototropic equilibria could be dominated by intermolecular association effects, referring to the strong self-association of 2-pyridone and 2-pyridinethione [8] in non-polar solvents, and that specific H-bonding may contribute significantly to differences in solvation energies between 2-pyridone and 2-hydroxypyridine. A difference in K_T for the 2-pyridone/2-hydroxypyridine equilibrium in solution and the vapour phase [49] is also cited; [14] however, as is discussed later, this work [49] has been revised. Whereas intermolecular association effects can dominate tautomeric equilibria in the solid or melt and even in concentrated solutions in non-polar solvents, this does not apply to dilute solution in water. Support for this conclusion derives from the good qualitative agreement between K_T from pK_a measurements on methyl derivatives (for which association is not possible at least by H-bonding) and by u.v. and other spectroscopic techniques for those cases where both can be applied.[12]


(17) (18) (19) (20)

Recently, Beak and Lee [50] found that the equilibrium between 1-methyl-2-pyridinethione (17) and 2-methylthiopyridine (18) favours the methylthio-compound (18) whereas that between 1-methyl-2-pyridone (19) and 2-methoxypyridine (20) favours (19). They imply that the contrast between these results and those for the corresponding tautomeric equilibria, in which the equilibrium favours 2-pyridinethione even more than 2-pyridone, supports their contention that protomeric equilibria are less satisfactory than the equilibria in the methylated analogues for studies of aromatic resonance energies. However, these differences would seem to be a necessary consequence of σ-bond energy differences. Comparison of the 2-pyridone/2-hydroxypyridine equilibrium with the 1-methyl-2-pyridone/2-methoxypyridine equilibrium needs account to be taken of (N–H less O–H) *vs.* (N–C less O–C) bond energies: from the (not strictly applicable) values of Pauling [51] we find that the equilibrium for the methyl derivative of the oxygen compounds should lie 2·9 kcal mol^{-1} further in favour of the 2-pyridone form than the protomeric equilibrium, whereas that for the methyl derivatives in the sulphur series should lie 4·6 kcal mol^{-1} *less* towards the 2-pyridinethione form than the analogous protomeric equilibrium.

The Dependence of (A_{py} — A_x) *on Solvent and Phase.*—The results so far discussed have all referred to aqueous solution. It is known [52] that solvent can have a considerable effect on tautomeric equilibria, and the influence of such changes on the calculation just described needs consideration. A considerable quantity of results for the temperature variation of tautomeric equilibria in different solvents has been reported by Russian workers: [26,27] in Figure 3 we have plotted $\Delta H°$ *vs.* $\Delta G°$ for water, ethanol, and dioxan, and carried out least-square fits to equations of type $\Delta H° = x\Delta G° + y$. We find the results given in Table 2.

As the solvent becomes less polar, we should find that solute–solvent interactions weaken, and $\Delta H°$ should approach ΔH_{int}, *i.e.* become more similar to $\Delta G°$. At first sight, this appears to be happening, from water to ethanol to dioxan, the coefficient x decreases from 1·28 to 1·02 to 0·98. However, great caution is needed before any firm conclusion can be drawn because of the curious behaviour found in mixed solvents (Table 2), and also because of the considerable scatter shown in Figure 3. (Anomalous behaviour of $\Delta H°$ of ionisation with compensation by $\Delta S°$ for mixtures of methanol : water has been reported.[53])

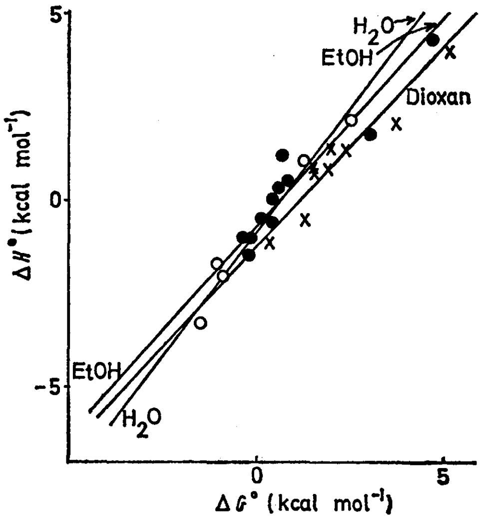


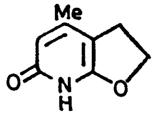
FIGURE 3 Relation between $\Delta H°$ and $\Delta G°$ for tautomeric equilibria in various solvents: water ○; ethanol ●; dioxan ×. Lines shown were obtained by least-squares method

TABLE 2

$\Delta H° = x\Delta G° + y$ correlations for tautomeric equilibria of pyridines: variation with solvent [a]

Solvent	x	y	Correlation coeff.	No. of points
H_2O	1·28	−0·85	0·985	5
EtOH	1·02	−0·59	0·950	11
Dioxan	0·98	−1·06	0·957	9
EtOH : H_2O (75 : 25)	1·53	−0·99	0·896	4
EtOH : H_2O (50 : 50)	2·16	−0·08	0·827	6
Dioxan : EtOH (50 : 50)	2·53	−2·47	0·946	4

[a] Calculated from data in refs. 26 and 27.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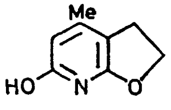
(22)

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In the vapour phase, initial work[49] appeared to suggest that 2-pyridone existed in comparable amounts of the OH- and oxo-forms because both the ν(OH) and ν(NH) could be detected. However, Levin and Rodionova[54] have recently shown that the apparent K_T values which they had previously reported were not necessarily for systems at equilibrium: thus for the 2-pyridone derivative (21) $\rightleftharpoons$ (22), the lactim form (22) predominated greatly initially in the vapour, but the band intensity ratio changed gradually in favour of the lactam form (21) at a rate which increased with temperature above 620 K, but which below 620 K was so low that equilibrium was not reached. At 370 °C, *ca.* 20% of the OH-form existed at equilibrium. In aqueous solution, for (21) $\rightleftharpoons$ (22), 15·7% of the OH-form exists at equilibrium.[55] It is clear that there is no evidence for a large difference between the tautomerism in the solution and vapour phases. Because it is expected that K_s and K_u will vary in the same direction with solvent polarity, the preceding results indicate that the differential effect of solvent on $\Delta H°$ will be smaller than the enthalpy of solvation variations between the individual forms of a tautomeric pair.

Previous Estimates of the Aromaticity of 2-*Pyridone*, etc.—Beak, Bonham, and Lee[14] studied the equilibrium of 2-methoxypyridine and 1-methyl-2-pyridone; they conclude that the aromaticity of 1-methyl-2-pyridone is 6 ± 7 kcal mol^{-1} less than 2-methoxypyridine. Unfortunately their method could not be extended to the 2-pyridinethione and 2-pyridone imine system.[50]

Elvidge and Jackman[56] from proton chemical shifts estimated 2-pyridones to possess *ca.* 35% of the aromaticity of benzene, *i.e.* 12—15 kcal mol^{-1} stabilisation. The use of ring current considerations of this type has been criticised,[57,58] defended,[59] and used further[60] but it remains highly controversial as a *quantitative* criterion.[61] Batts and Spinner[62] in a discussion of chemical shifts state that 'the fractional aromaticity is probably not appreciable for either (4-pyridone or 4-pyridone imine),' and Japanese authors[63] have also assigned to 1-methyl-2-pyridone a low aromaticity on chemical shift considerations.

Bell, Egan, and Bauer[64] have suggested the use of CH_3-*ortho*-hydrogen proton coupling constants as a criterion of aromaticity of pyridones and pyridinethiones, and conclude that both these classes provide substantial aromaticity. Meislich has estimated[65] that 2-pyridone is '50% aromatic' based on a valence-bond treatment of *X*-ray crystallographic bond lengths:[66] a similar conclusion might be reached for the bond lengths of 2-pyridinethione.[67]

On the basis of MO calculations, Dewar[68] discussed the partial loss of aromaticity by 2-pyridone as compared with 2-hydroxypyridine, and pointed out that the loss is greater for 2-pyridone imine: his general qualitative conclusions on this point are in line with ours. Other calculations[69] while less specific are also not in disagreement.

General Conclusions.—We conclude that 2-pyridone and 2-pyridinethione are only some 6—7 kcal mol^{-1} less aromatic than pyridine whereas the difference for 2-pyridone imine at *ca.* 10 kcal mol^{-1} is rather more than this. The difference is some 20 kcal mol^{-1} for 2-pyridone methide.

The use of tautomeric equilibria comparisons as criteria for aromaticity seems to be of general applicability and to offer a useful quantitative method for investigating the phenomenon.

EXPERIMENTAL

pK_a data were obtained using an Unicam SP 500 series 2 spectrophotometer.

1-Methyl-2-picolinium iodide, m.p. 228—230° (lit.,[70] 224—224·5°), and 2-amino-1-methylpyridinium iodide, m.p. 149—151° (lit.,[71] 149°), were prepared by the reaction of methyl iodide on the corresponding bases.

pK_a *of* 1-*Methyl*-2-*pyridone Methide.*—The ionisation constant was obtained using the procedure of Bowden and Cockerill.[45] Solutions of 1-methyl-2-picolinium iodide in $(Me)_2SO$ and of tetramethylammonium hydroxide in a known water–$(Me)_2SO$ mixture were prepared (under nitrogen) such that when mixed, after degassing, the mixed solution was 0·0471M in tetramethylammonium hydroxide. H_- For this solution was obtained from a graph of H_- against mol % $(Me)_2SO$ in water, plotted from values in refs. 45 and 72. The u.v. absorbance at 380 nm was recorded at intervals and ε was extrapolated to the time of mixing ($t = 0$). From the variation of $\varepsilon(t = 0)$ with H_- the pK_a of 1-methyl-2-pyridone methide was calculated to be 20·0 ± 0·2.

APPENDIX

The approximations made in taking the saturated system (7) $\rightleftharpoons$ (8) as a model for the interactions which occur between the nitrogen and the oxygen atoms in the unsaturated system (5) $\rightleftharpoons$ (6) can be visualised by consideration of the energy diagram. In effect, the energy difference between the pyridone with the localised double bonds and the 2-hydroxypyridine with localised double bonds is equated to the energy difference between piperidone and 2-hydroxytetrahydropyridine. The error introduced by such an approximation can be estimated by the following consideration. The ΔΔ pK for replacing

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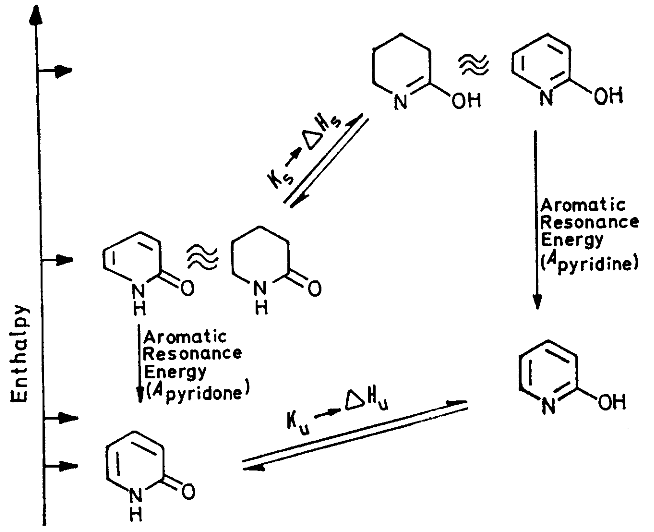

Scheme

R = methyl by R = phenyl in the system $RCONH_2 \rightleftharpoons RC(OH){:}NH$ is 1·8 p*K* units [*N*-benzoylaniline pK_a −2·6,[73] methyl-*N*-phenylbenzimidate pK_a 3·3; * *NN*-dimethylacetamide pK_a −0·19 [36] and ethyl *N*-methyliminoacetate pK_a 7·5 [39]]. The difference on replacing a saturated carbon atom by a ‘ non-conjugated ’ double bond should be considerably less, and the error introduced by the approximation is therefore probably less than one p*K* unit.

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* Estimated from ethyl-*N*-methyliminoacetate pK_a 7·5 (ref. 39), methyl benzimidate pK_a 5·7 (ref. 74) and 2-phenyliminotetrahydrofuran pK_a 5·1 (ref. 75).

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