247. *The Vibration Spectra and Structures of the Hydroxypyridines and Hydroxypyrimidines in Aqueous Solution.*

By Adrien Albert and E. Spinner.

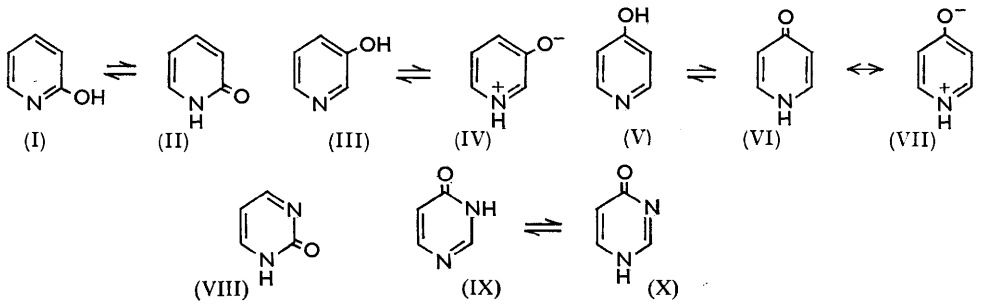
The Raman and infrared absorption spectra of aqueous 2-, 3-, and 4-hydroxypyridine, and 2- and 4-hydroxypyrimidine have been determined. The structures previously assigned have been confirmed and, for the 2- and 4-hydroxy-compounds, further clarified.

Hydroxypyridines and hydroxypyrimidines are capable of tautomerism because the labile hydrogen atom may be attached to either a nitrogen or an oxygen atom [see (I)—(X)]. Previous studies of the ultraviolet spectra [1,2,3] and ionization constants [4] had shown that, in aqueous solution, α- and γ-hydroxyaza-aromatic compounds are present predominantly in the amide forms,* *e.g.*, (II) or (VI), either as such or as resonance hybrids with the corresponding zwitterions, *e.g.*, (VII). On the other hand, 3-hydroxypyridine

* For convenience these substances will nevertheless be referred to by their usual names, hydroxypyridines and hydroxypyrimidines.

[1] Specker and Gawrosch, *Ber.*, 1942, **75**, 1338.
[2] Mason, *J.*, 1957, 5010.
[3] (*a*) Brown and Short, *J.*, 1953, **331**; (*b*) Brown, Hoerger, and Mason, *J.*, 1955, 211.
[4] Albert and Phillips, *J.*, 1956, 1294.

in aqueous solution is divided roughly equally [4,5] between the uncharged form (III) and the zwitterion (IV). Infrared spectral work [6,3a] has shown that a large number of α- and γ-hydroxyaza-derivatives are amides both in chloroform solution and in the solid state (and in several instances [7] *X*-ray crystallographic studies have led to the same conclusion). The previous conclusions have now been confirmed and extended.



Criteria used for Structure Diagnosis.—Since the Raman band due to the carbony stretching vibration is frequently rather weak, Raman spectra cannot be relied upon to detect carbonyl groups. Still less can they be relied upon to detect OH or NH groups in aqueous solution. The six-membered aromatic ring system (unless disubstituted, with at least one polyatomic group) is, however, readily identified by the presence of a strong " ring-breathing " Raman band near 1000 cm.$^{-1}$, which is normally unsurpassed in intensity [8] by any other Raman band below 2000 cm.$^{-1}$. The frequency of this band (960—1060 cm.$^{-1}$ in benzodiazines and picolines [8]) is rather insensitive to polar effects.[8] Thus, if a hydroxypyridine or hydroxypyrimidine is a truly aromatic compound * the strongest band in the Raman spectrum (or, if the two strongest bands are equally intense, at least one of them) must be located in the range 1020 ± 70 cm.$^{-1}$. (The presence of a six-membered aromatic skeleton is, of course, not *proved* thereby.)

In the infrared spectra of these compounds a very strong band in the range 1620—1750 cm.$^{-1}$ shows the presence of a C=O group; neither OH nor NH groups in solutes are detectable in aqueous media. Complete infrared spectra for the solids (agreeing with those previously reported [6,3]), taken for comparison with the aqueous-solution spectra, showed that the tautomer present in the crystalline state is identical with the main species present in water (except for 3-hydroxypyridine). No information about tautomers present only in small proportions is obtainable from the data for aqueous solutions.

Experimental

Materials.—The hydroxypyridines were purified by standard methods. Pure 2- [9] and 4-hydroxypyrimidine were kindly supplied by Dr. D. J. Brown of this Department.

Raman Spectra (*see Table*).—These were determined with a Hilger Raman spectrograph operated at effective slit widths of 2·5—6 cm.$^{-1}$. Spectra were recorded photographically, the

* A six-membered ring is referred to as " truly aromatic " if the main canonical forms that can be written for it are Kekulé structures, as " non-aromatic " if in the main form(s) one of the three double bonds is exocyclic, and as " modified aromatic " if both kinds of form are equally important.

[5] Metzler and Snell, *J. Amer. Chem. Soc.*, 1955, **77**, 2431.

[6] Mason, *J.*, 1957, 4874; Sensi and Gallo, *Ann. Chim. Appl.* (*Italy*), 1954, **44**, 232; Short and Thompson, *J.*, 1952, 168; Gibson, Kynaston, and Lindsey, *J.*, 1955, 4340.

[7] Penfold, *Acta Cryst.*, 1953, **6**, 591; Parry, *ibid.*, 1954, **7**, 313; Newman and Badger, *J. Amer. Chem. Soc.*, 1952, **74**, 3545.

[8] Lord, Marston, and Miller, *Spectrochim. Acta*, 1957, **9**, 113; Long, Murfin, Hales, and Kynaston, *Trans. Faraday Soc.*, 1957, **53**, 1171; Kohlrausch, " Ramanspektren," Akad. Verlagsges. Becker & Erler, Leipzig, 1943, pp. 380—382; Stojiljkovic and Whiffen, *Spectrochim. Acta*, 1958, **12**, 47, 57.

[9] Brown, *Nature*, 1950, **165**, 1010.

*Band peaks * in the vibration spectra (range 1800—680 cm.$^{-1}$).*

2-Hydroxypyridine		3-Hydroxypyridine		4-Hydroxypyridine		1,4-Dihydro-1-methyl-4-oxopyridine	
I.R. Aq. soln.	Raman Aq. soln.	I.R. Soln. in $CHCl_3$ [a]	Raman Aq. soln.[b]	I.R. Aq. soln.	Raman Aq. soln.	I.R. Solid	I.R. Soln. in $CHCl_3$
1652 s	1640 vw	1595 mw	1570 wb	1637 s	1634 w		1750 w
1601 s	1599 w	1585 m			1584 vw		1662 w
1541 m	1542 m	1453 m	1469 w			1641 vs	1641 vs ($\varepsilon \gtrsim 500$)
	1463 m	1387w		**1521** vs	1516 mw	**1548** vs	**1573** vs ($\varepsilon \gtrsim 560$)
1419 m		1375 w		1389 m			1487 mw
	1371 m	~1357 w		1189 m		1396 s	1398 m
	1260 s	**1280** ms		1082 w	1085 vw	1361 m	1359 m
1230 w			1180 vw?		1056?		1231 m
1224 mw		1123 w		1031 vw	**1035** ms	1200 ms	1215 ms
1158 mw		1101 mw	1107?	996 m	999 vw		1190 s
1093 w	1063 ?		**1045** m		872?	1150 w	1144 w
	1010 vw?		966 vw	849 ms	**848** ms		1086 w
993 m			846 mwb	*829* w	824 w	1021 m	1016 mw
	945?		798 vw			998 w	992 w
922 w			757 vw			854 ms	
864 wvb			703 vw?			*825* w	
	850 ms					761 w	
	812 w						
780 m	778 w						
	742 w						
	702 w						

2-Hydroxypyrimidine				4-Hydroxypyrimidine			
I.R. Aq. soln.	Raman Aq. soln.	I.R. Aq. soln.	Raman Aq. soln.	I.R. Aq. soln.	Raman Aq. soln.	I.R. Aq. soln.	Raman Aq. soln.
1644 vs	1653 vw	1106 w	1109 mw	**~1687** s	1675 vw?		1125 w
	1619 w	1052 mw	1061 w		1607 vw	1029 w	1043 w
1557 s	1553 m	997 m		1554 ms	1546 vw	994 m	
	1500?	868 w	**869** ms		1494 vw?		937?
1466 ms		802 m		1424 m	1424 vw?		882 vw
1433 mw				1369 m	1361 vw	849 m	**858** ms
	1399?				1329 vw		801 vw
1347 s	1347 w			1250 mw	1255 w		747 vw?
1216 m	1214 w				1226 mw		
1163 w	1164 m						

Peaks of Raman bands, range 200—680 cm.$^{-1}$ (aqueous solution):
2-Hydroxypyridine: 660?, 607 vw, 562 vw, 514 vw, 473?
3-Hydroxypyridine: 301 vw?
4-Hydroxypyridine: 638 w, 607 vw?, 566 vw, 533 vw, 474 vw
2 Hydroxypyrimidine: 589 m, 536 w, 448 vw
4-Hydroxypyrimidine: 338 vw?

* Wave numbers are given in cm.$^{-1}$. Estimated band intensities are given as very strong (vs), strong (s), medium (m), weak (w), doubtful (?), or intermediate; these represent the actual intensities of the bands in question over and above any background absorption or scatter due to vicinal bands. In the Raman spectra the relative intensities of the bands within each spectrum are given, but no absolute significance attaches to these intensity ratings. Inflexions are in italics; b = broad; the strongest bands are in bold type.

[a] There is solvent obscuration over much of the spectrum (a cell thickness of 1 mm. had to be used for solubility reasons). [b] Solution too dilute to show any but the main bands clearly. [c] In solution in CS_2.

plates being examined visually with a travelling microscope. The spectra were measured over the range 200—2600 cm.$^{-1}$; outside these limits mercury-source emission lines were troublesome (the exciting radiation was of λ 4358 Å). Solutions were treated with activated charcoal, filtered, centrifuged, and left in the specimen tubes for some time before examination. No trouble due to photochemical reaction was encountered, except with 2-hydroxypyridine, which, on irradiation, rapidly develops a pale blue colour that stops all Raman scattering. Concentrations of solutions used (weight of solute to weight of water): 2-hydroxypyridine, 1 : 3; 3-hydroxypyridine, 1 : 16 (solution supersaturated); 4-hydroxypyridine, 1 : 4, 2-hydroxypyrimidine, 1 : 7·5; 4-hydroxypyrimidine, 1 : 3·5.

Infrared Spectra (*see Table*).—These were taken with a Perkin–Elmer Model 12-C single-beam

single-pass spectrometer, fitted with a lithium fluoride prism for the range 3800—2400 cm.$^{-1}$ and a sodium chloride prism for the range 2400—700 cm.$^{-1}$. Aqueous solutions, in thin films pressed between (uncoated) sodium chloride plates, were examined in the sodium chloride range only; the background spectrum was taken with a saturated aqueous solution of sodium chloride. Only absorption bands of appreciable intensity could be observed, especially near the H_2O absorption peak at 1648 cm.$^{-1}$, and the accuracy of the wave-number measurements is lower than that obtainable with the usual infrared solvents. Concentrations used (in weight of solute to weight of water): 2- and 4-hydroxypyridine, 1 : 1, 2- and 4-hydroxypyrimidine, 1 : 2; the solubility of 3-hydroxypyridine in water is far too low to permit a study of its infrared spectrum in aqueous solution (a 1% solution in chloroform was examined). The infrared spectra of the solids were determined with potassium bromide discs (1 mg. of substance in 200 mg. of potassium bromide).

Results and Discussion

The spectral results are collected in the Table.

Raman Spectra.—The strongest band in the Raman spectrum of 3-hydroxypyridine is at 1045 cm.$^{-1}$, as would be expected for a genuine derivative of pyridine. As both the uncharged structure (III) and the zwitterion structure (IV) are truly pyridinoid the Raman spectrum is not well suited to the study of the equilibrium between them. Because of the low solubility of 3-hydroxypyridine in water, the Raman spectrum obtained is weak and shows no evidence of the presence of two tautomers.

On the other hand, in the Raman spectra of 2-hydroxypyridine, and 2- and 4-hydroxypyrimidine, which bear a fair resemblance to one another, only weak bands appear near 1000 cm.$^{-1}$, the strongest bands being in the vicinities of 860 and 1200 cm.$^{-1}$. The major species present in aqueous solution can therefore not be pyridinoid, as in (I), in any of these substances. In the Raman spectrum of 4-hydroxypyridine the two strongest bands, at 1035 and 848 cm.$^{-1}$, are about equally intense. This spectrum is inconclusive, being compatible with structure (V) as a major species, without proving this to be the case.

Infrared Spectra.—These provide more positive evidence. The spectrum of 3-hydroxypyridine is typical of a (3-substituted [10]) pyridine; the others are not. The strongest band below 1800 cm.$^{-1}$ in the infrared spectrum of 3-hydroxypyridine (in non-aqueous media) is at 1280 cm.$^{-1}$; the strong pyridine band near 1580 cm.$^{-1}$ is hardly changed in frequency. By contrast, in the infrared spectra of aqueous 2-hydroxypyridine, 2-hydroxypyrimidine, and 4-hydroxypyrimidine the bands at 1652, ~1644, and ~1687 cm.$^{-1}$ appear clearly above the strong water band as the most intense bands in their respective spectra. They are undoubtedly carbonyl stretching bands; the 2-hydroxyaza-derivatives must therefore be lactams [such as (II) and (VIII)]. These spectra differ markedly from the infrared spectra of normal 2-substituted pyridines, a large number of which have now been determined.[11]

The case of 4-hydroxypyridine is more complicated. The strongest band in the infrared spectrum is located at 1521 cm.$^{-1}$, and there is another strong band at 1637 cm.$^{-1}$. This spectrum resembles that of 1,4-dihydro-1-methyl-4-oxopyridine (VI; NMe in place of NH), where a band at 1548 cm.$^{-1}$ (in the solid state) is stronger * than that at 1641 cm.$^{-1}$. If 4-hydroxypyridine had structure (V), the strong band in this region would be located very close to 1600 cm.$^{-1}$, not at 1637 cm.$^{-1}$, and two more bands would be seen in the range 1400—1600 cm.$^{-1}$ (for a comprehensive collection of data for 4-substituted pyridines, see Katritzky and Gardner [12]).

Possible Structures.—The vibration spectra show that these 2- and 4-hydroxyaza-compounds are not truly aromatic hydroxy-compounds. However, as it is known that

* It is possible that both these bands are due to composite vibrations each of which entails some carbonyl bond stretching.

[10] Katritzky, Jones, and Hands, *J.*, 1958, 3168.
[11] Cook and Church, *J. Phys. Chem.*, 1957, **61**, 458; Katritzky and Hands, *J.*, 1958, 2202.
[12] Katritzky and Gardner, *J.*, 1958, 2198.

aqueous 3-hydroxypyridine contains about 50% of the zwitterion form (IV), one would, on purely chemical grounds, expect that the α- and γ-hydroxy-derivatives of aza-aromatic substances in aqueous solution would be predominantly zwitterions, *e.g.*, (VII), rather than uncharged molecules, *e.g.*, (V); the electron-withdrawing effect of the nitrogen atom would be transmitted more strongly to the α- and γ- than to the β-positions, making the α- and γ-hydroxy-groups more acidic; similarly, the electron-donating effect of O^- would be transmitted more strongly to the α- and γ-positions, making the nitrogen atoms there more basic than that in the 3-hydroxypyridine anion. Thus 2- and 4-hydroxypyridine and 2- and 4-hydroxypyrimidine could exist as zwitterions, which would be truly aromatic provided that the amide forms do not contribute greatly ($\gtrsim$20%) towards the resonance hybrids.

For the α-hydroxyaza-derivatives the presence of appreciable amounts of these truly aromatic structures is ruled out by the absence of strong Raman bands near 1000 cm.$^{-1}$, but for 4-hydroxypyridine this possibility has to be considered. The strong infrared band of 4-hydroxypyridine at 1637 cm.$^{-1}$ could be the equivalent of the fairly strong band at 1630 cm.$^{-1}$ in the spectrum of the pyridine cation,[13] *i.e.*, it could be due to a skeletal stretching vibration. However, the infrared spectrum of 4-hydroxypyridine does not show as many bands as one would expect for a substituted pyridinium ion. In particular, for a zwitterion (VII) the strongly Raman-active ring-breathing vibration would be accompanied by a large change in dipole moment and should give rise to a strong infrared band, whereas actually the infrared band at 1031 cm.$^{-1}$, which would have to be assigned to this vibration, is weak. Finally, on this basis, solid 4-hydroxypyridine and 1,4-dihydro-1-methyl-4-oxopyridine, all of which have infrared spectra similar to that of aqueous 4-hydroxypyridine, would all have to be zwitterionic like (VII); however, the dipole moments of both compounds[4] are far too low to be compatible with predominantly zwitterionic structures.

These low dipole moments and the absence of a strong infrared band due to ring-breathing also represent evidence against a " modified aromatic structure " for 4-hydroxypyridine. As will appear from a discussion of the vibration spectra to be expected for such structures,[13] the observed band frequencies do, in any case, not fit such structures, for any of the substances examined. It is therefore concluded that all these compounds are essentially carbonyl compounds, represented wholly, or, if resonance hybrids, largely, by structures (II), (VI), VIII), and (IX) or (X), respectively. If one accepts that bond stretching frequencies are related to bond orders, and takes the CO bond order in formaldehyde to be 2·00, one will conclude that the CO bonds in 2-hydroxypyrimidine and 2- and 4-hydroxypyridine have 15—20% single-bond character; the dipole moment of the last-named substance is also compatible with a contribution of about 15% from structure (VII).

4-Hydroxypyrimidine is both an α- and a γ-hydroxyaza-compound, and two tautomers containing a carbonyl group, (IX) and (X), are possible. Since the Raman spectrum of this substance is similar to those of the 2-hydroxy-compounds, which are certainly lactams (II) and (VIII), but quite different from that of 4-hydroxypyridine, whose structure (VI) is very like (X), it must be concluded that the main species present in aqueous solution (>80%) is the lactam tautomer (IX), in agreement with earlier conclusions [3b] [and in disagreement with some recent calculations[14] that suggest the presence of 30—40% of (X)].

Band Assignments.—Most of these are quite uncertain. The strong bands in the Raman spectra of the α- and γ-hydroxyaza-compounds at ~850 and ~1200 cm.$^{-1}$ could be due to out-of-plane and in-plane C–H bending deformations, respectively (or, conceivably, to skeletal motions); the position of the former band is remarkably constant. The strong Raman band of 4-hydroxypyridine at 1035 cm.$^{-1}$ is tentatively assigned to

[13] See following paper.
[14] Mason, *J.*, 1958, 674.

the simultaneous stretching of the four skeletal single bonds in (VI), a " pseudo-ring-breathing " vibration. The bands at 1610 $\pm$ 10 cm.$^{-1}$ in the α-lactams are due to in-plane N–H bending, which is probably mixed somewhat with C=O stretching here. The N–H stretching bands (in the solids) occur at 3200 $\pm$ 60 cm.$^{-1}$, the C–H stretching bands from 2700 to 3130 cm.$^{-1}$.

The authors are greatly indebted to Dr. D. J. Brown for samples of 2- and 4-hydroxypyrimidine. Mr. D. T. Light is thanked for technical assistance.

Department of Medical Chemistry, The Australian National University,
Canberra, Australia. [*Received, June 15th*, 1959.]