strength of the metal–ligand bond (reflected in the high stability constant of this complex) which must be stretched or broken in the activation process. Furthermore because of the large charge separation involved, the energy required to stretch this bond will increase, and the reactivity correspondingly decrease, with decreasing solvent polarity. Silver forms a much weaker acetate complex and its high reactivity relative to the aqua-ion suggests that the increase, if any, in the metal–ligand bond strength is more than compensated for by the higher ligand basicity. Further, because of the smaller charge separation involved in stretching the metal–ligand bond, the reactivity of silver carboxylates should be much less dependent on solvent polarity. This should be the case also for cuprous salts while cupric salts, in view of the fact that Cu^{++} resembles Hg^{++} in its charge but forms much weaker carboxylate complexes, should exhibit behavior intermediate between that of mercuric and silver salts. As noted earlier, this is the case.

VANCOUVER, B. C., CANADA

[CONTRIBUTION OF THE DEPARTMENT OF CHEMISTRY, CLARK UNIVERSITY]

Pyridoxine and Pyridoxal Analogs. III. Ultraviolet Absorption Studies and Solution Equilibria of 2- and 4-Hydroxymethyl-3-hydroxypyridines and Pyridine-2, 3- and 4-Aldehydes[1]

BY KAZUO NAKAMOTO AND A. E. MARTELL

RECEIVED NOVEMBER 7, 1958

The ultraviolet spectra of compounds related to vitamin B_6, such as 2- and 4-hydroxymethyl-3-hydroxypyridines and pyridine-2, 3- and 4-aldehydes have been measured at various *p*H values in buffer solutions and in dioxane–water mixtures. Assignments of the observed bands are made, and a general rule for the band shifts of the dipolar and the uncharged species has been found from measurements in dioxane–water mixtures. The over-all ionization constants are determined from plots of *p*H *versus* the absorbancy. On the basis of empirical assignments of the absorption bands, and reasonable assumptions of the influence of solvent on absorption intensities, individual ionization constants and the percentage of each species are calculated. The values obtained for each compound are compared and discussed from the viewpoint of electronic structures of the molecules involved.

It has been suggested[2] that the hydroxyl and the aldehyde groups are the ones mainly involved in the biological functions of pyridoxal. For this reason, Heinert and Martell[3] recently have synthesized 3-hydroxypyridine-2- and 4-aldehydes and their methoxy derivatives as simple models of vitamin B_6. The purpose of the present work is to study the reaction mechanism between these compounds and amino acids in the presence of metallic ions by spectroscopic measurements.

In order to apply the spectroscopic method to such a system, it is first necessary to study the spectra of the hydroxypyridinealdehydes as a function of *p*H. It was found, however, that even hydroxypyridinealdehydes and their methoxy compounds are in complicated equilibria in aqueous media. Therefore, in this paper, detailed studies of the spectra of 2- and 4-hydroxymethyl-3-hydroxypyridines and pyridine-2-, 3- and 4-aldehydes are described. Investigation of the ultraviolet spectra and solution equilibria of 3-hydroxypyridine-2 and 4-aldehydes and their methoxy compounds is now in progress and will be described in a subsequent communication.

Similar work already has been reported by Metzler and Snell[4] on 3-hydroxypyridine, pyridoxine, 5-desoxypyridoxal, pyridoxal and related compounds. More extensive measurements of the equilibria between the two neutral species of a number of N-heteroaromatic hydroxy compounds were made recently by Mason[5] with ultraviolet and infrared spectra. However, the present study differs from those of previous workers in the following respects: (1) All the observed bands are empirically classified either as $n-\pi^*$, $\pi-\pi_1^*$, or $\pi-\pi_2^*$ transitions. (2) The *p*H of the dioxane–water mixtures was calibrated with acetate buffer to take into account any solvent effects on the measurement of *p*H. (3) A new general rule was found for the band shifts in dioxane–water mixtures. (4) The over-all ionization constants obtained from a plot of *p*H *versus* absorbancy were broken down into the individual ionization constants for each equilibrium, and these values are discussed in detail from the viewpoint of electronic theory. The percentages of the various species as a function of *p*H are estimated from the spectral data.

Experimental

Measurements.—The ultraviolet spectra were obtained with a Cary model 14 spectrophotometer at 20°. A pair of 1 cm. quartz cells with stoppers was used. In all measurements, the concentration of the solution was 10^{-4} *M*. The *p*H of the solution was measured after the spectral measurement with a Beckman model G *p*H meter fitted with extension glass and calomel electrodes. The *p*H meter was calibrated with Beckman standard buffer solutions.

Materials.—2- and 4-hydroxymethyl-3-hydroxypyridines were prepared by Heinert and Martell.[3] Pyridine-2-, 3- and 4-aldehydes were purchased from Fluka A. G., Switzerland. All the compounds were freshly recrystallized or distilled immediately before the preparation of solutions.

Buffer Solutions.—For each *p*H range, the following buffer solutions were employed: *p*H 0, 1 *N* HCl; $1 \sim 2.2$, $HCl + KCl$; $3.6 \sim 5.4$, $CH_3COOH + CH_3COONa$; $6.0 \sim 8.0$, $NaOH + KH_2PO_4$; $8.9 \sim 11.4$, $NaHCO_3 + Na_2CO_3$; $12.0 \sim 14.0$, NaOH. For most of the solutions, the ionic strength was 0.2.

---

[1] This work was supported by a research grant, H-3246, from the National Heart Institute, Public Health Service.

[2] D. E. Metzler, M. Ikawa and E. E. Snell, THIS JOURNAL, **76**, 648 (1954).

[3] D. Heinert and A. E. Martell, *Tetrahedron*, **3**, 49 (1958).

[4] D. E. Metzler and E. E. Snell, THIS JOURNAL, **77**, 2431 (1955).

[5] S. F. Mason, *J. Chem. Soc.*, 4874, 5010 (1957); 674 (1958).

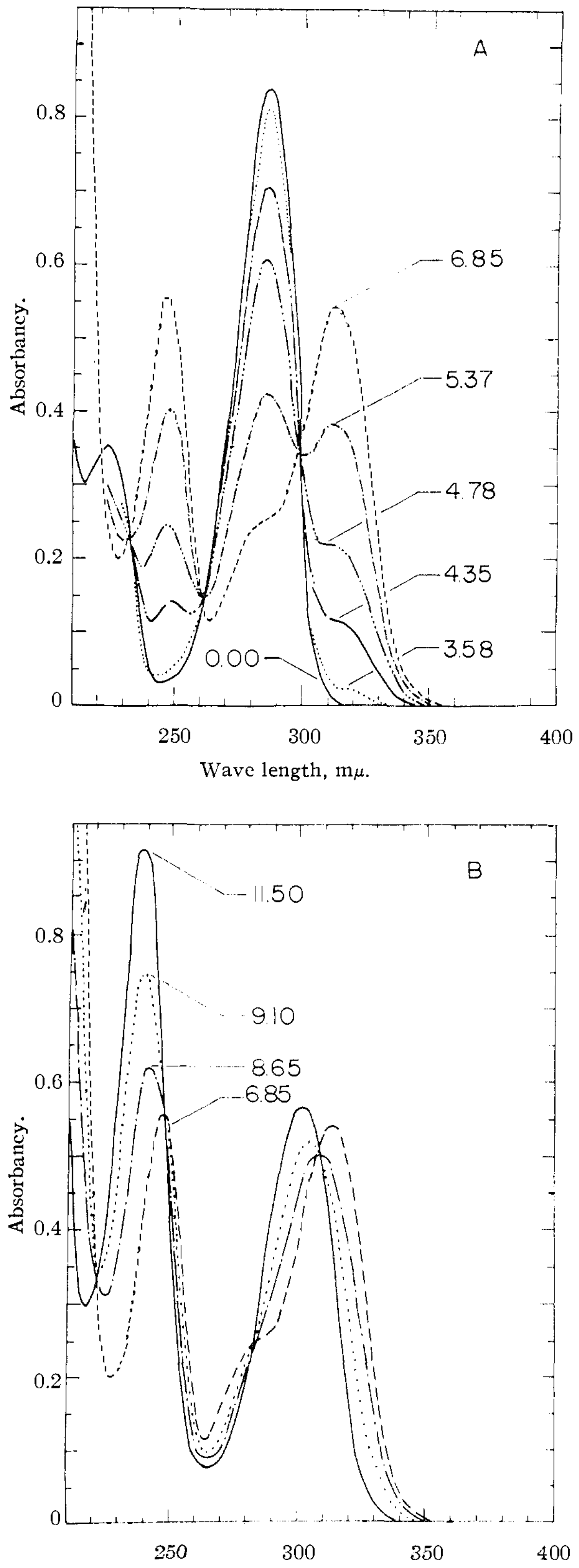


Fig. 1.—Absorption spectra of 2-hydroxymethyl-3-hydroxypyridine: A, in acidic solutions; B, in basic solutions. The numbers beside the curves denote the *p*H of the solutions.

Dioxane-Water Mixtures.—*p*-Dioxane was purchased from Eastman Organic Chemicals and was used without distillation since it was transparent down to 220 mμ.

Results and Discussion

Hydroxymethyl-3-hydroxypyridines.—Figure 1 (A, B) shows the spectra of 2-hydroxymethyl-3-hydroxypyridine at various *p*H values in buffer solutions. The two bands at 286 and 224 mμ in acidic solution are ascribed to the $\pi-\pi_1^*$ and the $\pi-\pi_2^*$ transitions (hereafter, abbreviated as π_1- and π_2-bands, respectively) of the cation Ia, shown in Plate I. These assignments may be compared to those made for pyridine,[6] which exhibits two bands at 256 mμ (π_1-) and 194 mμ (π_2-). The n–π^* transition due to the non-bonding electrons of the pyridine nitrogen is hidden at the longer wave length side of the π_1-band. In the reaction scheme shown, intramolecular hydrogen bonded structures were assumed for all the species, although no direct evidence is given in this paper. However, this assumption is not unreasonable since *o*-hydroxybenzyl alcohol was shown by infrared measurements to have such an intramolecular hydrogen bond.[7]

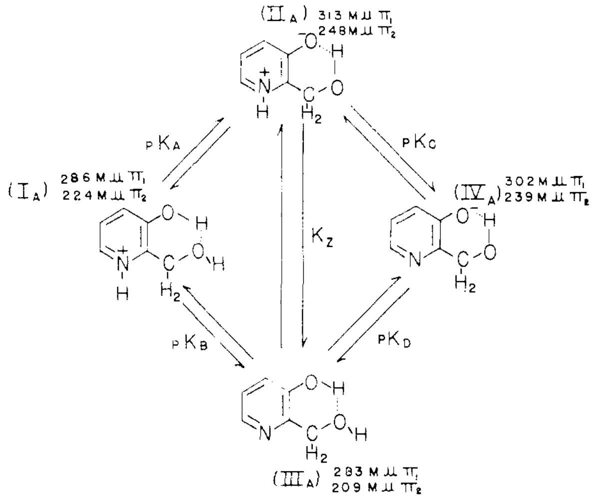


Plate I.—The solution of equilibrium of 2-hydroxymethyl-3-hydroxypyridine.

In neutral solution, the two bands which appear at 313 and 248 mμ are due to the π_1- and π_2-transitions of the dipolar form IIa. The shoulder at *ca.* 285 mμ in the spectrum at *p*H 6.85 can be ascribed to the uncharged form IIIa since the spectrum of this compound in pure dioxane shows the same band at 280 mμ. The strong absorption at 209 mμ is assigned to the π_2-band of IIIa. Although this band is not shown in Fig. 1, it was clearly observed. Thus, the dipolar form and the uncharged form are in equilibrium in neutral solution. In basic solution, the two bands observed at 302 and 239 mμ are assigned to the π_1- and π_2-bands of the anion IVa.

These assignments are in agreement with the general rule for band-shifts (for ionization) given by Metzler and Snell[4]: that ionization of a hydroxyl hydrogen causes a "red-shift." In the present case, ionization of the phenolic hydrogen

---

(6) H. P. Stephenson, *J. Chem. Phys.*, **22**, 1077 (1954).

(7) A. E. Martin, *Nature*, **166**, 474 (1950).

(Ia → IIa) causes the red-shifts of the π_1- (+27 mμ) and the π_2-band (+24 mμ), and a similar ionization from IIIa to IVa causes the red-shifts of the π_1-band (+19 mμ) and the π_2-band (+30 mμ). On the other hand, ionization of the pyridinium hydrogen (Ia → IIIa) causes the blue shifts of the π_1-band (−3 mμ) and the π_2-band (−15 mμ). A similar ionization (IIa → IVa) results in the blue-shifts of the π_1-band (−11 mμ) and of the π_2-band (−9 mμ). As a result, the order of the wave length of the π_1- and π_2-bands of various species is zwitterion > anion > cation > neutral. This series has been verified by independent results recently reported by Mason[8] after this paper had been submitted for publication. The agreement between our work and the theoretical assignments made by Mason on the basis of M.O. calculations, lends further support to our calculations of ionic constants of individual species.

The method of calculating the individual ionization constants already has been described by Metzler and Snell.[4] From a plot of *p*H *versus* the absorbancies of each band such as is shown in Fig. 2, the over-all ionization constants pK_1 and pK_2 were obtained. For example, at *p*H 0, only the cation Ia exists, and the absorbancy of the 286 mμ band is 0.84. At *p*H 6.85, all the species of Ia are converted into either IIa or IIIa, and the absorbancy at 286 mμ is 0.255.

The equilibrium between Ia, IIa and IIIa is expressed by

$$\text{Ia} \rightleftarrows \text{H}^+ + (\text{IIa, IIIa});$$

$$K_1 = \frac{[\text{H}^+][\text{IIa} + \text{IIIa}]}{[\text{Ia}]} = K_a + K_b \quad (1)$$

Then

$$pH = pK_1 + \log \frac{[\text{IIa} + \text{IIIa}]}{[\text{Ia}]} \quad (2)$$

If the initial concentration of Ia is a, and, at some *p*H, $[\text{H}^+] = [\text{IIa}] + [\text{IIIa}] = x$, then, the degree of dissociation α is given by x/a, and

$$pH = pK_1 + \log \frac{\alpha}{1 - \alpha} \quad (3)$$

Thus, *p*H is equal to pK_1 when α is $^1/_2$. Since the absorbancy of the 296 mμ band is proportional to the concentration of Ia, the *p*H at which the intensity becomes an average value of the limiting values at *p*H 0 and 6.85 gives pK_1. The value of pK_1 thus obtained from Fig. 2 is 5.00. The value of pK_2 was similarly estimated as 9.07.

Equilibrium Constant, K_z.—It is impossible to determine K_z rigorously from spectroscopic data alone, since IIa and IIIa are tautomeric forms of the same neutral species. Although the pure dioxane solution would contain only IIIa, the molecular extinction coefficients ϵ of IIIa in aqueous solution may be different from those in pure dioxane solution. Therefore, in this work, the following assumption was made

$$\frac{\epsilon(\text{3-methoxypyridine}^9 \text{ in } 1\ N\ \text{HCl})}{\epsilon(\text{3-methoxypyridine in } pH\ 7.0)} = \frac{\epsilon(\text{Ia})}{\epsilon(\text{IIIa})} \quad (4)$$

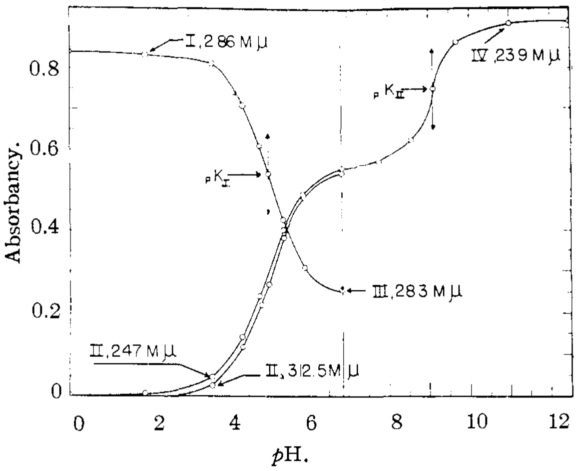


Fig. 2.—Absorbancy of 2-hydroxymethyl-3-hydroxypyridine as a function of *p*H.

This relationship is the best for our purposes since the methoxy group is very similar to the hydroxy group with respect to the effect of substitution on the intensity.[10]

Then, from the measurements of the spectra of 3-methoxypyridine in 1 *N* HCl and in neutral solutions

$$\epsilon(\text{IIIa}) = 8400 \times \frac{4220}{6281} = 5644 \quad (5)$$

If the wing correction[11] is considered assuming symmetrical shape for the 313 mμ band, the optical density of IIIa at 283 mμ is 0.255 − 0.05 = 0.205 at *p*H 6.85. Then, the percentage of IIIa is

$$\%(\text{IIIa}) = \frac{2050}{5644} \times 100 = 36$$

and $K_z = 64/36 = 1.8$ is obtained. With the relations

$$K_1 = K_a + K_b, \qquad 1/K_2 = 1/K_c + 1/K_d \quad (6)$$

$$K_z = \frac{K_a}{K_b} = \frac{K_d}{K_c}$$

the individual ionization constants were calculated as

$$pK_a = 5.2,\ pK_b = 5.4,\ pK_c = 8.9,\ pK_d = 8.7$$

With the same assumption, it is possible to calculate the percentage of each species in the solution at various *p*H values. The result is shown in Fig. 3.

The same procedure was employed for 4-hydroxymethyl-3-hydroxypyridine. The spectra at various *p*H values in buffer solutions are almost the same as those of 2-hydroxymethyl-3-hydroxypyridine, and, therefore, are not shown here. The numerical data obtained from the spectra and the ionization constants calculated from these data are listed in Tables I and II, respectively.

Spectra in Dioxane–Water Mixtures.—Figure 4 indicates the spectral change of 2-hydroxymethyl-3-hydroxypyridine in dioxane–water mixtures at a

---

[8] S. F. Mason, *J. Chem. Soc.*, 1253 (1959).

[9] The absorption maxima of 3-methoxypyridine are: in 1 *N* HCl, 285 mμ (ϵ 6281), and 226 mμ (ϵ 4112); in the buffer solution at *p*H 7.00, 276 mμ (ϵ 4220), 217 mμ (ϵ 6398); in dioxane, 277 mμ (ϵ 3980), and 218 mμ (ϵ 5770).

[10] See F. A. Matsen, "Chemical Applications of Spectroscopy," Interscience Publishers, Inc., New York, N. Y., 1956, p. 676.

[11] Without the wing correction, %(IIIa) = 45 and K_z = 1.2 are obtained. However, the individual ionization constants derived from this K_z value differ at most only by ±0.1 *p*K unit from those shown in Table II.

TABLE I

ULTRAVIOLET SPECTRA[a] OF 3-HYDROXYPYRIDINE DERIVATIVES AND PYRIDINE-ALDEHYDES

	Acidic (1 N HCl)	Neutral (pH 6.85)			Basic (1 N NaOH)
Compound	(I), cation	(II) dipolar	(III) uncharged	(III) in dioxane	(IV) anion
3-Hydroxypyridine[b]	283(0.59)	313(0.30)	277(0.22)	277)0.39)	298(0.45)
	222(0.33)	246(0.47)	....	....	235(1.02)
2-Hydroxymethyl-3-	286(0.84)	313(0.543)	283(0.25)	280(0.54)	302(0.569)
hydroxypyridine	224(0.352)	248(0.555)	209(1.39)	....	239(0.912)
4-Hydroxymethyl-3-	280(0.613)	313(0.471)	280(0.19)	276(0.368)	298(0.485)
hydroxypyridine	225(0.331)	248(0.498)	210(2.01)	....	239(0.881)
Pyridoxine[b]	291(0.86)	324(0.72)	....	286(0.57)[c]	310(0.68)
	232(0.21)	254(0.39)	....	....	245(0.63)
Pyridine-2-aldehyde	....	....	320(0.007)	320(0.02)	....
	259(0.702)	259(0.346)	274(0.338)	269(0.434)	259(0.37)
			235(0.529)	233(0.876)	
Pyridine-3-aldehyde	....	....	320(0.003)	320(0.003)	....
	258(0.54)	258(0.305)	274(0.305)	269(0.365)	260(0.29)
			233(0.865)	230(1.075)	
Pyridine-4-aldehyde	....	....	....	....	....
	256.5(0.511)	256.5(0.183)	285(0.120)	284(0.242)	257(0.26)
			224(0.515)	224(0.923)	

[a] The wave length is given in mμ; numbers in parentheses give the absorbancy for a 1-cm. light path and 10^{-4} mole/l. For (I), (III) (in dioxane) and (IV), the absorbancy $\times 10^{-4}$ gives the molecular extinction coefficient of that species. [b] Data due to Metzler and Snell.[4]

constant pH of 7.0. It is seen that the bands at 313 and 248 mμ (the dipolar form IIa) become progressively weaker, whereas the band at 283 mμ (the uncharged form IIIa) becomes progressively stronger, as the per cent. of dioxane increases. This result is expected since the dipolar form is relatively more stable in water than the uncharged form.

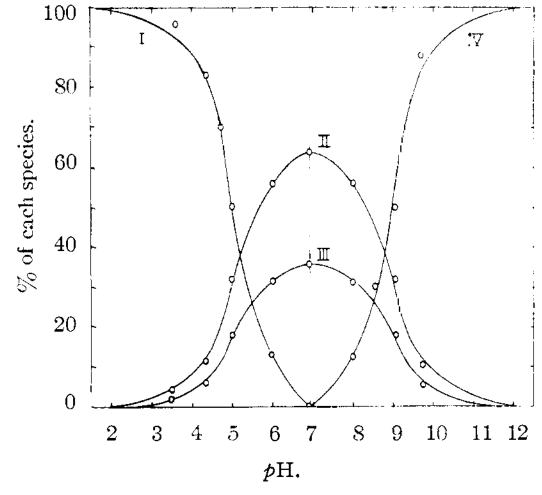


Fig. 3.—The percentage of each species of 2-hydroxymethyl-3-hydroxypyridine at various pH values.

In order to study the equilibrium between IIa and IIIa, it is necessary to keep the pH at some value where only IIa and IIIa exist. For some compounds such as 3-hydroxypyridine-2- and 4-aldehydes, the pH required is 5.5. Therefore, instead of distilled water, an acetic acid–sodium acetate buffer solution of pH 5.5 must be used. Then, in order to keep the same pH values at higher dioxane concentration, it is necessary to add weak acid to the dioxane–water mixtures. However, the reading of the Beckman pH meter does not give true pH values in such mixed solvents. Using the data by Harned and Owen,[12] we made a correction of the reading of the Beckman pH meter at each dioxane concentration. Acetic acid was added to the dioxane–water mixture until the desired true pH value was obtained.

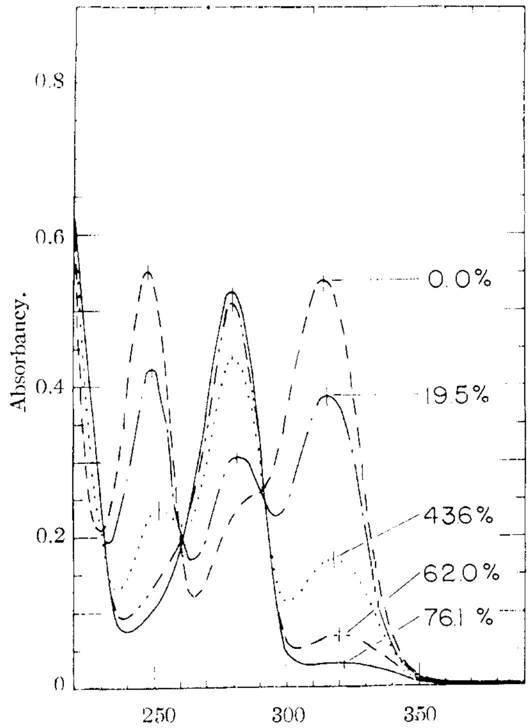


Fig. 4.—Absorption spectra of 2-hydroxymethyl-3-hydroxypyridine in dioxane–water mixture at pH 7.0; numbers beside the curves give the volume percentage of dioxane.

---

(12) H. S. Harned and B. B. Owen, "The Physical Chemistry of Electrolytic Solutions," Reinhold Publ. Corp., New York. N. Y., 1950. p. 581.

TABLE II

EQUILIBRIUM CONSTANTS (20°, μ = 0.2 KNO_3)

Compound	pK_1	pK_2	pK_a	pK_b	pK_c	pK_d	$Kz(pH)$
3-Hydroxypyridine	4.86[a]	8.72[a]					1.27(6.8)[a]
	5.10[b]	8.60[b]	5.37[b]	5.44[b]	8.33[b]	8.26[b]	1.17(6.8)[b]
2-Hydroxymethyl-3-hydroxypyridine	5.00	9.07	5.2	5.4	8.9	8.7	1.8(6.9)[c]
4-Hydroxymethyl-3-hydroxypyridine	5.00	8.95	5.2	5.4	8.8	8.5	1.7(6.9)[c]
Pyridoxine	5.00[b]	8.96[b]	..	..	..	..	7.3(6.8)[b]
Pyridine-2-aldehyde	3.80	12.80	4.2	4.0	12.6	12.6	0.6(7.0)[c]
Pyridine-3-aldehyde	3.80	13.10	4.0	4.2	12.9	12.7	0.8(7.0)[c]
Pyridine-4-aldehyde	4.77	12.20	5.2	5.0	11.8	12.0	0.6(7.0)[d]

[a] Albert and Phillips, *J. Chem. Soc.*, 1294 (1956). [b] The data for 3-hydroxypyridine and pyridoxine were reported by Metzler and Snell.[4] [c] Wing correction was considered. [d] Wing correction was not necessary since the two bands are far apart.

Figure 4 also indicates that the bands at 313 and 248 mμ (the π_1- and π_2-bands of the dipolar form, IIa) show blue-shifts, whereas the band at 283 mμ (the π_1-band of the uncharged form IIIa) shows a red-shift as the volume percentage of dioxane decreases (as the dielectric constant of the solvent increases). It is well known[13] that in neutral uncharged molecules the $\pi-\pi^*$ bands show red-shifts, whereas the n$-\pi^*$ bands show blue-shifts, as the dielectric constant of the solvent increases. McConnell's explanation for the blue-shift of the n$-\pi^*$ bands, seems, however, to be more suitable for the present blue-shift of the bands of the dipolar form, since the ground state of the dipolar form is stabilized relative to the excited state by a solvent medium of high dielectric constant. It can, therefore, be generally stated that the $\pi-\pi^*$ bands of the dipolar forms, such as IIa, show blue-shifts, whereas the $\pi-\pi^*$ bands of the uncharged forms such as IIIa undergo red-shifts, as the dielectric constant of the solvent increases. This general rule was confirmed in all the compounds studied in this series of investigations, and was found useful for the assignment of the bands observed in neutral solutions.

Pyridinealdehydes.—Ultraviolet spectra of the pyridinealdehydes at various *p*H values in buffer solutions, and also in dioxane mixtures, have not been reported previously. In order to interpret the spectra of pyridinehydroxyaldehydes and pyridinemethoxyaldehydes which will be discussed in a later paper, the spectra of pyridine-2-, 3- and 4-aldehydes are reported here in detail.

Many studies have been made on the acetal formation of aliphatic aldehydes. For example, Wolf and Herold[14] determined the degree of acetal formation of aliphatic aldehydes in various media from the intensities of the carbonyl bands in the ultraviolet spectra. Their results indicate that hydration is completed in a few minutes in aqueous media and the degree of hydration is more than 30% for most of the aliphatic aldehydes.

It is obvious, however, that the carbonyl (n$-\pi^*$) band cannot be used as a measure of hydration for aromatic and heterocyclic aldehydes since the π_1-band usually hides the weak carbonyl band. In such a case, the π-bands themselves may be used for this purpose, because the location of the π-bands of the hydrated and unhydrated forms are different. Figure 5 shows the absorption spectra of pyridine-2-aldehyde at various *p*H values in buffer solutions. The acidic (1 *N* HCl) and basic (1 *N* NaOH) solutions exhibit only one band at 259 mμ, whereas the neutral solution has one maximum at 265 mμ plus a shoulder on each side (*ca.* 259 and 274 mμ) and another band at 235 mμ. From the shape of the absorption curves at intermediate *p*H values between 0 and 5.90, it seems that the band maximum at 265 mμ is produced by the superposition of the 259 and 274 mμ bands.

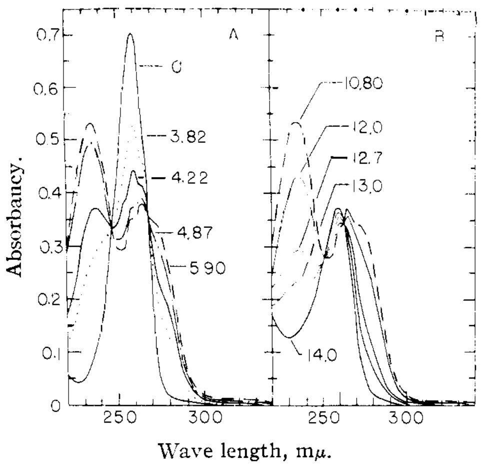


Fig. 5.—Absorption spectra of pyridine-2-aldehyde: A, in acidic solutions; B, in basic solutions; numbers beside the curves denote *p*H.

Thus, the observed band maxima were assigned to the species shown in Plate II.

According to the above assignments, the π_1-transitions of Ib, IIb and IVb absorb at the same wave length, 259 mμ, which is near to that of the π_1-band of pyridine itself (256 mμ). This result is quite reasonable since the $-CH(OH)_2$ group has little or no effect on the π_1-band whether it is ionized or not. Although the change from IIb to IVb involves the ionization of the pyridinium hydrogen, the magnitude of the blue-shift in this case is almost zero. The π_2-band of these hydrated forms will probably lie near 200 mμ.

---

[13] H. McConnell, *J. Chem. Phys.*, **20**, 700 (1952).

[14] K. L. Wolf and W. Herold, *Z. physik. Chem.*, **B5**, 124 (1929); **B12**, 165 (1932); **B18**, 265 (1932).

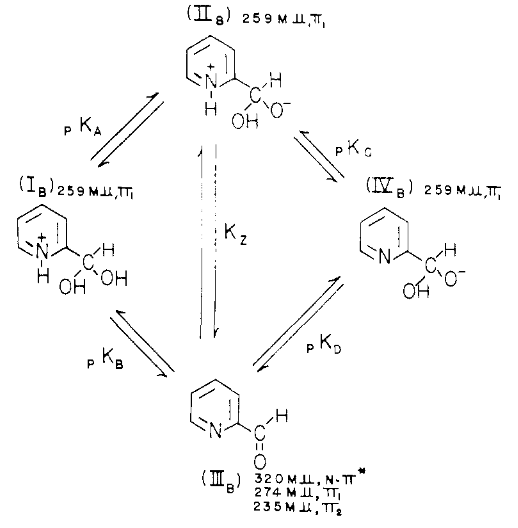


Plate II.—The solution equilibrium of pyridine-2-aldehyde.

The spectrum of pyridine-2-aldehyde in pure dioxane gives three bands at 320 mμ (carbonyl n-π*, weak), 268 mμ (π_1) and 235 mμ (π_2). It is evident that these three bands are due to the uncharged form IIIb. An hydrated and uncharged form fails to account for the appearance of these bands. Thus, it is concluded that the spectrum of the neutral solution consists of the two species IIb and IIIb.

Figure 6 indicates the spectral change of pyridine-2-aldehyde in water–dioxane mixtures. It is seen that, at high concentration of dioxane, only one band appears at 269 mμ. This result may indicate that, as the dioxane percentage *increases*, the band at 274 mμ (IIIb) is shifted to the blue with an increase in intensity, and the band at 259 mμ (IIb) is shifted to the red, with a decrease in intensity. It is also seen that the behavior of the π_2-band of IIIb at 235 mμ is similar to that of the π_1-band of the same species. This result is also in agreement with the general rule for the wave length shift stated above.

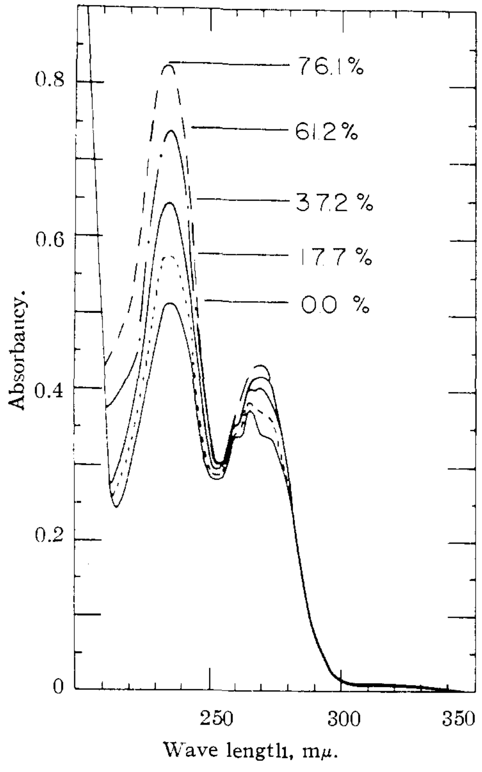


Fig. 6.—Absorption spectra of pyridine-2-aldehyde in dioxane–water mixtures. The numbers beside the curves indicate the volume percentage of dioxane.

Figure 5 clearly indicates that two isosbestic points exist at 268 and 247 mμ in the shift from acidic to neutral solution, and at 263 and 251 mμ in the shift from neutral to basic solution, respectively. Since Ib, IIb and IVb all absorb at 259 mμ, these isosbestic points are produced even though the actual dissociation mechanism involves two separate steps (Ib → IIb and Ib → IIIb). From a plot of *p*H *versus* the absorbency, the over-all ionization constants were determined as pK_1 = 3.80 and pK_2 = 12.80.

With the assumption that the molecular extinction coefficient of Ib is the same as that of IIb and by considering the wing correction[15] resulting from overlapping of the 274 mμ band, K_z was estimated to be 0.6. From an alternate assumption that the optical density of the 235 mμ band in pure dioxane solution is due only to IIIb and that IIIb does not differ appreciably in dioxane and in aqueous solutions, a similar value was obtained. This result may be considered as support for the validity of the assumptions made in the calculations of the individual constants.[16] With this value of K_z, the individual ionization constants shown in Table II were calculated, and the percentage of each species as a function of *p*H, shown in Fig. 7, was then obtained. It is seen that Ib rapidly decreases and IIb and IIIb gradually increase, as the *p*H increases from 0 to 5.8. Between 5.9 and 10.8, only IIb and IIIb exist, and no spectral

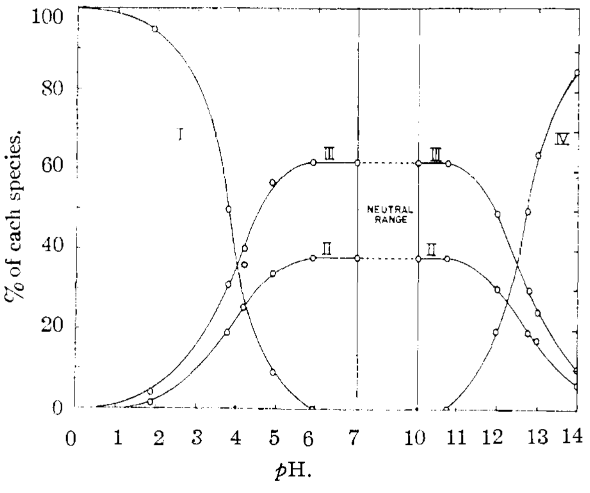


Fig. 7.—The percentage of each species of pyridine-2-aldehyde at various *p*H values.

---

[15] Symmetrical form of the 274 mμ band was assumed.

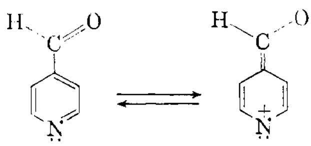
[16] The individual ionization constants differ at most only by ± 0.1 *pK* unit with and without the wing correction mentioned above, although the K_z value differs appreciably.

change occurs. Again, from pH 10.8 to 14, IIb and IIIb decrease, and IVb rapidly increases. A rather wide pH region between 5.9 and 10.8 is the "neutral range" of this compound.

The same treatment was employed for pyridine-3- and 4-aldehydes. The band maxima, absorbancy and ionization constants of these compounds are listed in Table I and II, respectively.

Comparison of the Three Aldehydes.—As is shown in Table I, the band maxima of Ib, IIb and IVb species in the three kinds of pyridinealdehydes are located at almost the same position, which is near to that of the π_1-band of pyridine (256 mμ). This is the expected result, since the $-CH(OH)_2$ group has little effect on the π_1-band of the pyridine ring, regardless of the position of substitution.

The neutral unhydrated form IIIb has a weak carbonyl $n-\pi^*$ band in the case of 2- and 3-aldehydes but not for the 4-aldehyde. This difference may be due to the fact that the π_1-band of the 4-aldehyde is located at much longer wave length than that of the other two aldehydes, and, therefore, hides the weak $n-\pi^*$ band. The longer wave length shift of the π_1-band may be due to the fact that polar resonance forms such as those shown below preferentially stabilize the excited state of the 4-aldehyde



Although similar resonance occurs in the 2-aldehyde, the inductive effect of the ring nitrogen (electron-attracting) which is opposite to the resonance effect is especially strong in the *ortho* position.

It is interesting to note that, in pyridinealdehydes, the ultraviolet spectra and ionization constants of the 2- and 3-aldehydes are similar to each other whereas that of the 4-aldehyde is different from the former two compounds. On the other hand, in hydroxypyridine, the 2- and 4-hydroxy compounds are similar and different from the 3-hydroxy compound.[5]

WORCESTER, MASSACHUSETTS

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF CLARK UNIVERSITY]

Pyridoxine and Pyridoxal Analogs. IV. Ultraviolet Spectra and Solution Equilibria of 3-Methoxypyridine-2(and 4-)-aldehydes and of 3-Hydroxypyridine-2 (and 4-)-aldehydes[1,2]

BY KAZUO NAKAMOTO AND A. E. MARTELL

RECEIVED FEBRUARY 25, 1959

The ultraviolet spectra of four new compounds, 3-methoxypyridine-2- and 4-aldehydes and 3-hydroxypyridine-2- and 4-aldehydes have been measured at various pH values in buffer solutions and in dioxane–water mixtures. Assignments of the absorption bands are made, and the equilibria between the various molecular species in solution are established. The over-all ionization constants are calculated from the variation of absorbancy with pH. From the band assignments, dissociation constants of the individual species and the equilibrium constants for their interconversion are calculated. The values obtained are compared and discussed from the viewpoint of the electronic structures of the molecules involved. The results are compared with the properties of pyridoxal and 5-desoxypyridoxal, which have been reported previously.

The ultraviolet spectra and solution equilibria of 2- and 4-hydroxymethyl-3-hydroxypyridines, and pyridine-2, 3, and 4-aldehydes have been reported in a previous publication.[3] This paper deals with more complex compounds of the same type: 3-methoxypyridine-2- and 4-aldehydes and 3-hydroxypyridine-2- and 4-aldehydes, the synthesis of which has been described recently by Heinert and Martell.[4,10] The hydroxypyridine-aldehydes are models of vitamin B_6 and are of interest in connection with the mechanism of transamination and other vitamin B_6-catalyzed reactions, studied previously by Metzler, Ikawa and Snell.[5]

Experimental

Measurements.—The experimental method is described in the preceding paper.[3]

Materials.—3-Hydroxypyridine-2- and 4-aldehydes and 3-methoxypyridine-2- and 4-aldehydes were supplied in pure form by Heinert and Martell.[4] The preparation and purification of these compounds already have been described by these authors, and therefore are not given here.

Results and Discussion

I. 3-Methoxypyridine-2- and 4-Aldehydes.—The ultraviolet spectra of 3-methoxypyridine-2-aldehyde at various pH values in buffer solutions are illustrated in Fig. 1. In acidic solution, two bands appear at 288 and 225.5 mμ which are assigned to the π_1- and π_2-bands of the hydrated cation, Ia, shown in Plate I.. Moreover, a weak band at 316 mμ may be attributed to the π_1-band of the unhydrated cation, I'a, which is present even in 1 N HCl solution. The neutral solution exhibits three bands at 316, 281 and 236 mμ. Since the spectrum of this compound in pure dioxane shows two bands at 307 and 233.5 mμ, it is reasonable to attribute the bands at 316 and 236 mμ to the π_1- and π_2-bands of the uncharged unhydrated form IIIa. The remaining band at 281 mμ is therefore assigned to the π_1-band of the dipolar hydrated form IIa. The basic solution shows one strong

---

[1] This investigation was supported by a research grant, H-3246, from the National Heart Institute, Public Health Service.

[2] Presented at the 134th Annual Meeting of the American Chemical Society in Chicago, Illinois, September 11, 1958.

[3] K. Nakamoto and A. E. Martell, THIS JOURNAL, **81**, 5857 (1959).

[4] D. Heinert and A. E. Martell, *Tetrahedron*, **3**, 49 (1958).

[5] D. E. Metzler, M. Ikawa and E. D. Snell, THIS JOURNAL, **76**, 648 (1954).