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Additions to Pyridinium Rings. I. 1-Methylpyridinium Iodide

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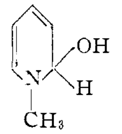
The ultraviolet spectra of aqueous solutions of methylpyridinium iodide have been examined, and Hantzsch's statement that these do not obey Beer's law has been confirmed. Quantitative optical measurements indicate that a new species is present, which is formulated as the product of addition of iodide ion to the pyridinium ring at the 2-position.

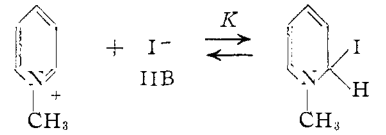
A precise and intimate knowledge of the pyridinium ion would be of considerable value for the interpretation of certain reactions, including those in the biochemical field involving diphosphopyridine nucleotide (DPN). For example, the oxidation of 1-methylpyridinium iodide to 1-methyl-2-(1H)-pyridone with alkaline potassium ferricyanide[3] is presumed to proceed by way of an intermediate "pseudo-base" I.[4]



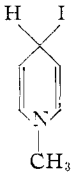
I

While analogous addition products are known for other quaternary heterocyclic nuclei, *e.g.*, 9-phenyl-10-methylacridinium hydroxide,[5] direct evidence is lacking in the pyridine series. This article presents such evidence and, in particular, demonstrates the presence of an equilibrium between the dissociated ions of 1-methylpyridinium iodide (IIA, IIB) and another species, for which the structure III seems most probable, but which may conceivably be IV or V.

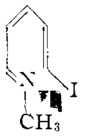
IIA



IIB III

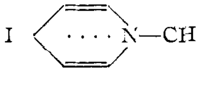


IV



V

In 1911, Hantzsch[6] investigated the spectra of 1-methylpyridinium salts and other heterocyclic salts. He found that many of them did not obey Beer's law for ultraviolet absorption in solution; the various color changes associated with certain salts were considered to be due to "chromoisomerism." This behavior on the part of 1-methylpyridinium iodide[7] led Hantzsch to propose that two "chromoisomers" of the salt existed, one, the normal benzenoid form, the other, a "quinoid" form for which he favored the structure VI,[10] and which he described as a salt.



VI

Experimental

1-Methylpyridinium iodide was prepared from reagent grade pyridine and methyl iodide in absolute ethanol. The yellowish product was recrystallized from absolute ethanol to yield white crystals, m.p. 116–117° (reported 116°,[11] 117°[12]). Weighing and transferring operations were facilitated if the crystals were fairly large since the solid is hygroscopic. Crystals of convenient size were obtained by slowly cooling an absolute ethanol solution *after seeding;* when filtering the salt, it is important to avoid excessive air flow through the solvent-wet solid or a brown tinge indicative of iodine or tri-iodide will appear.

Freshly prepared concentrated aqueous solutions of 1-methylpyridinium iodide are light yellow in color, but on standing in contact with air this color deepens and thin films actually become brown. Almost all the color is removed by addition of a small quantity of sodium thiosulfate. Consistent and reproducible ultraviolet spectra were not obtained until dilute aqueous sodium thiosulfate solution was used as solvent for the iodide. A control using a much lower concentration of thiosulfate than that in most of the solutions showed only a slightly lower absorption, indicating that thiosulfate ion was not responsible for any important amount of the observed absorption.[13]

Aqueous solutions of 1-methylpyridinium iodide were prepared in the concentrations listed underneath (the letters correspond to the curves) Fig. 1. The solvent was aqueous sodium thiosulfate solution, 9.36×10^{-3} *N*, prepared from Mallinckrodt A.R. grade crystals. The ultraviolet absorptions were measured with a Cary Recording Spectrophotometer, Model 11 M.

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[3] H. Decker, *Ber.*, **25**, 444 (1892).

[4] See discussion by H. S. Mosher, "Heterocyclic Compounds," Vol. I, R. C. Elderfield, editor, John Wiley and Sons, Inc., New York, N. Y., 1950, Chapter 8, pp. 415–417.

[5] A. Hantzsch and M. Kalb, *Ber.*, **32**, 3109 (1899).

[6] A. Hantzsch, *ibid.*, **44**, 1783 (1911).

[7] Hantzsch relied to a great extent upon the spectrum of a chloroform solution which showed two bands not present in aqueous or alcoholic solution. Triiodide ions[8] have been shown to possess very strong absorptions at wave lengths very close to those of the "new" bands, and the experiments described in the present work indicate that it would be extremely difficult to prepare and keep 1-methylpyridinium iodide solutions which were completely free of triiodide. In a later article,[9] Hantzsch reports some additional data on iodides, none of which excludes the trivial explanation that triiodide ion is present.

Thus, although the low dielectric constant of chloroform might be expected to favor non-ionic species at the expense of ionic ones, the evidence that the new bands do represent a "chromoisomer" is far from convincing. It also appears unlikely that strong absorption at 3600–3700 Å. would be expected for any molecule closely related to the 1-methylpyridinium ion. Chloroform solutions have not been examined at the present time because ionic association would make the method used in this paper difficult to apply, even were it possible to prepare such non-aqueous solutions of the necessary purity.

[8] F. L. Gilbert, R. R. Goldstein and T. M. Lowry, *J. Chem. Soc.*, 1092 (1931).

[9] A. Hantzsch, *Ber.*, **52**, 1544 (1919).

[10] In the second article[9] on this subject, Hantzsch rejected VI and favored a non-ionic structure with five bonds to nitrogen, R_4N–I. This may be excluded on the basis of the known inability of nitrogen to expand its valence shell.

[11] A. Hantzsch, *Ber.*, **42**, 81 (1909).

[12] A. B. Prescott, THIS JOURNAL, **18**, 91 (1896).

[13] The weak ultraviolet absorption of the thiosulfate ion has been measured by H. Ley and E. König, *Z. physik. Chem.*, **B41**, 365 (1938). The optical density, *D*, for the concentration used in this work would be less than 0.16 at 2700 Å. and absorption falls off rapidly toward longer wave lengths.

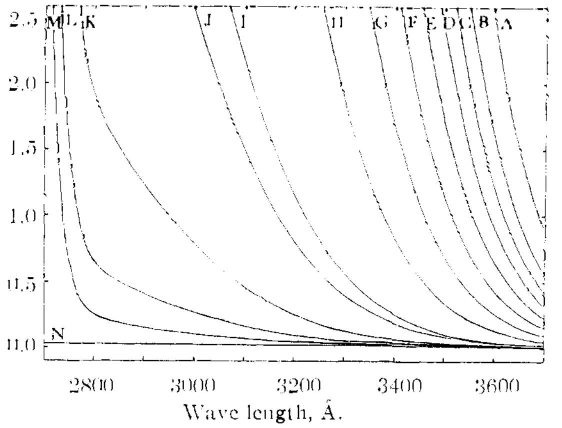

Fig. 1.—Optical density (*D*) *versus* wave length—aqueous 1-methylpyridinium iodide. The concentrations in moles/liter are as follows: A, 0.637; B, 0.510; C, 0.446; D, 0.382; E, 0.319; F, 0.255; G, 0.191; H, 0.128; I, 0.0637; J, 0.0510; K, 0.0255; L, 0.0128; M, 0.00637.

Results

By assuming that Beer's law is followed for each component of the equilibrium IIA + IIB ⇄ III, the relations may be derived

$$D = \epsilon_{IIA}C_{IIA} + \epsilon_{IIB}C_{IIB} + \epsilon_{III}C_{III} \qquad (1)$$

$$K = \frac{C_{III}}{C_{IIA}C_{IIB}};\ C_{IIA} = C_{IIB} = C_{II} \qquad (2)$$

$$C_{III} = KC_{II}^2;\ \epsilon_{IIA} + \epsilon_{IIB} = \epsilon_{II} \qquad (3)$$

$$D = \epsilon_{II}C_{II} + K\epsilon_{III}C_{II}^2 \qquad (4)$$

$$D/C_{II} = \epsilon_{II} + K\epsilon_{III}\,C_{II} \qquad (5)$$

If the effect of any other anion, X^-, is included, as one might desire to do in the case of $S_2O_3^=$, eq. 4 becomes

$$D/C_{II} = \epsilon_{II} + \epsilon_X\frac{C_X}{C_{II}} + K\epsilon_{III}C_{II} \qquad (4')$$

Such a relation implies no addition of X^- to the pyridinium ring. Were there a small amount of such interaction, eq. 6 would be required. (K_X is the equilibrium constant for X^- analogous to K for

$$D/C_{II} = \epsilon_{II} + \epsilon_X\frac{C_X}{C_{II}} + K_X\epsilon_{IIX}C_X + K\epsilon_{III}C_{II} \qquad (6)$$

IIB; ϵ_{IIX} is the absorption coefficient for the species formed from IIA and X^-.)

For low ϵ_X, where C_X is $\leqslant C_{II}$, the second term in (4′) and (6) would be negligible, and eq. 7 may be written to express the situation for the present work.

$$D/C_{II} = \epsilon_{II} + K_X\epsilon_{IIX}C_X + K\epsilon_{III}C_{II} \qquad (7)$$

The second term in (7) would be constant at a given wave length and at constant C_X, which is the case for various dilutions of II with solutions containing identical C_X. Thus, eq. 7 is linear and a test of the validity of the equilibrium hypothesis would be the strictness with which this relation is kept. Equation 7 is also equivalent to a *linear dependence* of the optical density on the *square* of the concentration of 1-methylpyridinium iodide, provided K is sufficiently small.

Values of D/C_{II} (optical density/concentration of 1-methylpyridinium iodide) have been plotted against C_{II} in Figs. 3 and 4. The wave lengths to which the numbered lines correspond are listed below the figures.

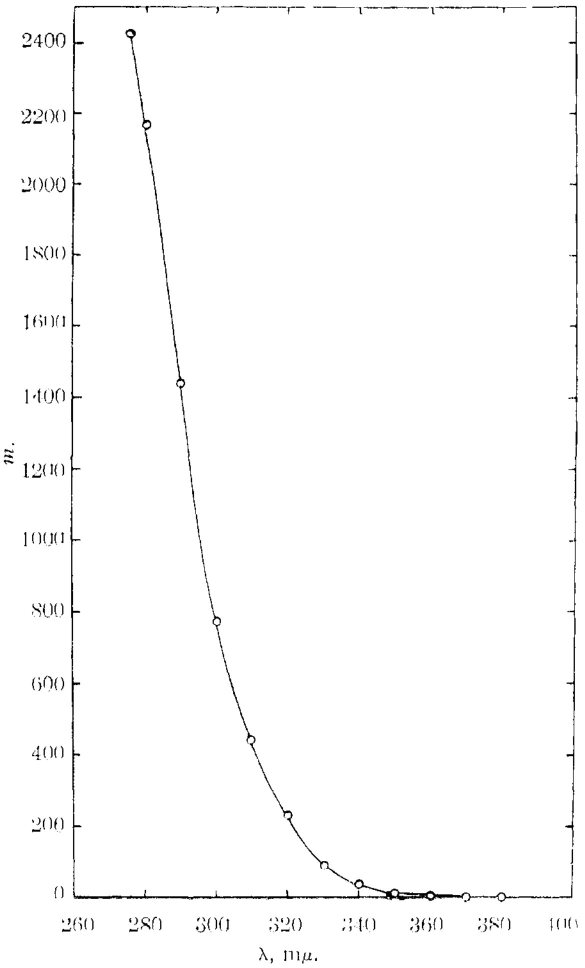

Fig. 2.—$K\epsilon_{III}$ *versus* wave length.

The slopes appear to be remarkably constant; in other words, the concentration of the new absorbing species *is* very closely dependent upon the *square* of the concentration of 1-methylpyridinium iodide. One must conclude that a species like III, IV or V is actually present in aqueous solution.

A still different alternative, that the new species is actually an ion pair in which a shift of ultraviolet absorption occurs due to the polarization of the 1-methylpyridinium ion by the field of the iodide ion, may be excluded on two grounds. First, association of ions into pairs would not be expected in a medium of high dielectric constant.[14] In addition, activity coefficients for 1-1 electrolytes are not linear with respect to concentration over the range from 0.1 to 0.7 molar.[15] The absorption of the new species is linearly dependent on a function of concentration and its formulation as an ion-pair is thus inconsistent with the observations.

The slopes in Figs. 3 and 4 are equal to $K\epsilon_{III}$ and

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(14) R. M. Fuoss and C. A. Kraus, This Journal, **55**, 1019 (1933).

(15) It may be argued that the fall in activity coefficient is really the result of association, but the non-linearity is nevertheless an experimentally observed phenomenon. See the discussion given by H. S. Frank and M. S. Tsao, in "Solutions of Electrolytes, Annual Review of Physical Chemistry," Vol. 5, Annual Reviews, Inc., Stanford, California, 1954, pp. 43-50.

a plot of these numbers against wave length should represent the absorption curve for the new species, III. Figure 2 is such a plot, but the absorption maximum for the new species is "buried" in the much larger absorption of the 1-methylpyridinium ion, making it impossible to complete the curve in Fig. 2. An accurate determination of K is therefore not possible in aqueous solutions.

However, K may be estimated as follows. It seems reasonable that ϵ_{III} will be between 3500 and 35000. By extrapolating the curve in Fig. 3, a value of *ca.* 3500 is obtained arbitrarily at 2600 Å. The equilibrium constant, K, then, must be between 1 and 0.1. Some confirmation of this range is derived from a preliminary examination of the ultraviolet spectrum of a 0.0402 M 1-methylpyridinium iodide solution in 85% alcohol. This solution had D of 1.96 at 3500 Å. while the same concentration in water had a D of only 0.06. Since a decrease in intensity might actually be expected in going to a solvent of lower polarity, one may conclude that the concentration of the new absorbing species has increased by a large factor. It follows that the concentration of III in the aqueous solutions could not have been too high and that, consequently, K must be small for aqueous solutions.

Very dilute solutions of 1-methylpyridinium iodide obey Beer's law; two maxima, 2588 Å. (ϵ 4830) and 2266 Å. (ϵ 13,500) and two shoulders, 2653 Å. (ϵ 3490) and 2527 Å. (ϵ 4240) were exhibited. The maximum at 2266 Å. is that of the iodide ion for which Lederle[16] found 2262 Å. (ϵ 13,500).

Discussion

It was stated earlier that the 2-position (formula III) was favored for the new species. This assignment has its basis in the observation that alkaline oxidation leads to substitution in the 2-position.[3] Oxidation of an asymmetrically substituted pyridinium ring, 3-carbamido-1-methylpyridinium iodide, yields approximately equal quantities of 2- and 6-pyridones.[17] Although the assumption that an intermediate like I is involved may be erroneous,[18] the 2-position will be assigned as the site of addition until more specific information is available.

Theoretically, it is possible to calculate an equilibrium constant for the addition of iodide ion to the ring. Actually, little of the required information is available with the precision required to estimate a free energy change not much different from zero. Several points, however, emerge from preliminary calculations. Loss of the resonance energy of the pyridine ring is not as important as the loss of solvation energy of the ions. The largest single energy factor favoring the reaction is that gained by the neutralization of the positive charge by the negative charge. Since these considerations are not generally used in predicting the course and equilibrium position of an organic reaction, it seems worthwhile to mention them here.

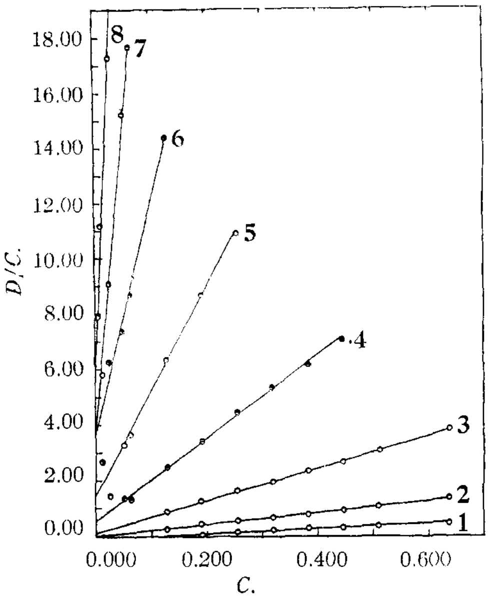

Fig. 3.—Optical density (D) divided by concentration of 1-methylpyridinium iodide (C) plotted against C for the following wave lengths: 1, 3800; 2, 3700, 3, 3600; 4, 3500; 5, 3400; 6, 3300; 7, 3200; 8, 3100. (The data for 1 are not included in Fig. 1.)

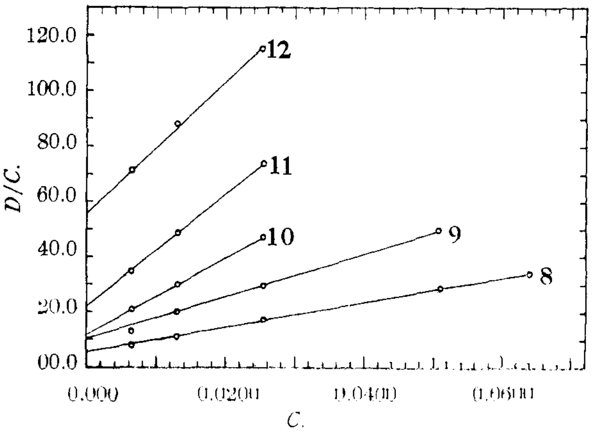

Fig. 4.—Optical density (D) divided by concentration of 1-methylpyridinium iodide (C) plotted against C for the following wave lengths: 8, 3100; 9, 3000; 10, 2900; 11, 2800; 12, 2760.

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(16) E. Lederle, *Z. physik. Chem.*, **B10**, 121 (1930).

(17) M. E. Pullman and S. P. Colowick, *J. Biol. Chem.*, **206**, 121 (1954).

(18) In additional experiments involving the reaction of hydroxide with a pyridinium ring, the reaction was found to be complex, that is, involving more than one step. The results with iodide ion cannot, therefore, be applied directly to the hydroxide ion case, and the results of oxidation may be misleading with regard to the position of addition. Doering and McEwen,[19] in fact, have shown that some addition of the anion (or the enol) of acetophenone to 1-benzoylpyridinium chloride takes place in the 4-position. Reaction at *both* 2- and 4-positions is also not excluded for the present case.

(19) W. E. Doering and W. E. McEwen, This Journal, **73**, 2104 (1951).

(20) Department of Chemistry, University of Chicago.