

[CONTRIBUTION FROM THE CHEMISTRY LABORATORY OF THE UNIVERSITY OF MICHIGAN]

The Absorption Spectra of the Aminopyridines

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A study has been made of the ultraviolet absorption of the three aminopyridines and of some of their derivatives in order to obtain data which might be used to indicate their structure. Curves for the quantitative absorption of ether solutions of 2-aminopyridine, 3-aminopyridine, 2-(methylamino)-pyridine, 2-(dimethylamino)-pyridine and 1-methyl-2-pyridoneimine are presented in Fig. 1.

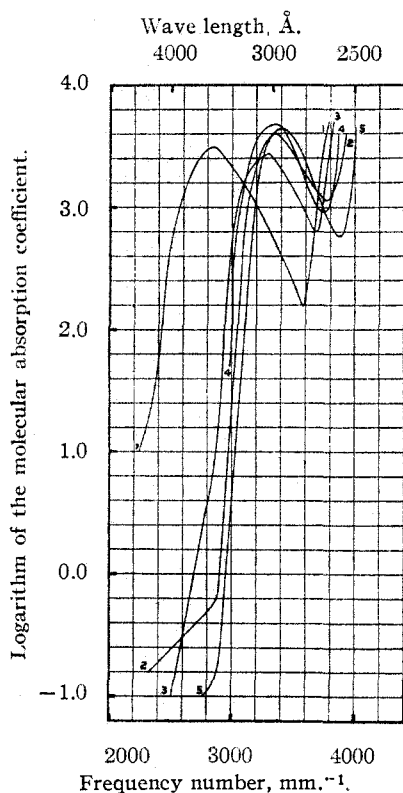
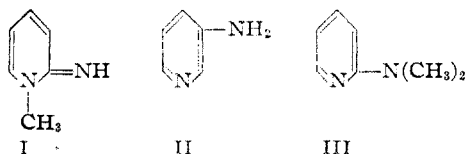


Fig. 1.—Absorption in ether solution of: 1, 1-methyl-2-pyridone-imine; 2, 3-aminopyridine; 3, 2-(dimethylamino)-pyridine; 4, 2-(methylamino)-pyridine; 5, 2-aminopyridine.

1-Methyl-2-pyridoneimine has a pyridone structure (I) and its ether solution is yellow in color with one broad absorption band at 2850 mm.^{-1} . 3-Aminopyridine and 2-dimethylaminopyridine can possess only a pyridine structure (II, III) and their ether solutions are colorless and have the peaks of the absorption bands at approximately the same position, 3350 mm.^{-1} .



The absorption curve of 2-aminopyridine has only the one broad band at 3350 mm.^{-1} which is characteristic of the pyridine ring structure. If 2-aminopyridine existed in two tautomeric forms, two bands might be expected, one for the pyridone imine structure at approximately 2850 mm.^{-1} and one for the pyridine structure at approximately 3350 mm.^{-1} . The absorption curves were determined for solutions having concentrations of nearly 40 g. per liter, yet only one band in the pyridine absorption region appeared. The conclusion drawn from these observations is that 2-aminopyridine possesses the pyridine structure exclusively and does not tautomerize in ether at room temperature.

The effect on the absorption curve of substituting a methyl group for an amino hydrogen is only minor. This is illustrated by the absorption curves of 2-(methylamino)-pyridine and 2-(dimethylamino)-pyridine. There is only a slight change in position of the peak and height of the band of 2-(methylamino)-pyridine when compared with 2-aminopyridine.

The possibility of tautomerization of 2-aminopyridine in a water type solvent was studied by determining the curve of the absorption spectrum of this compound in a dioxane-water solution as given in Fig. 2. In this case, 1-methyl-2-pyridoneimine in pure dioxane and 3-aminopyridine in a dioxane-water solution (72%:28% by volume) were used as reference compounds. The curves of 2- and 3-aminopyridines are very similar, both possessing the single broad band as was found in ether solution, indicating that only the pyridine structure is present.

In order to explain the fact that the dipole moment of 2-aminopyridine decreased with increasing temperature, Goethals¹ suggested that the equilibrium between tautomeric pyridine and pyridone forms was altered by changes in temperature. To study the supposed effect of temperature, absorption curves of 2-aminopyridine in dioxane-water solution were obtained at 65 and 80° by placing the absorption cells in an electrically-heated aluminum block. However, the absorption curves at these temperatures were found to be identical with the curves determined at room temperature.

2-Aminopyridine does not diazotize readily in dilute acid solutions. Since there appeared to be a possibility that tautomerization of 2-aminopyridine to the pyridoneimine structure would render the amine difficult to diazotize, the absorption curves of 2-aminopyridine in dilute sulfuric acid solutions were determined in order to attempt to establish the structure of 2-aminopyridine under

(1) Goethals, *Rec. trav. chim.*, **54**, 304 (1935).

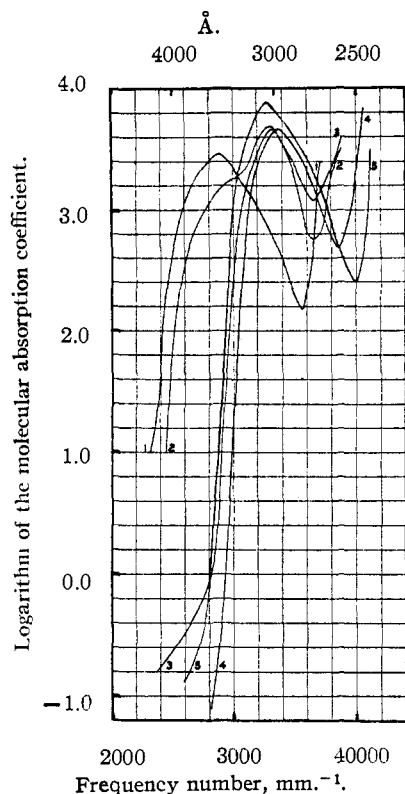
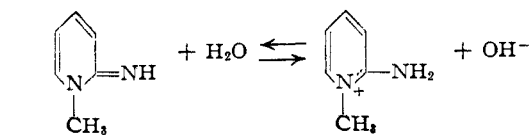


Fig. 2.—1, 1-Methyl-2-pyridoneimine in dioxane; 2, 1-methyl-2-pyridoneimine in 72%:28% dioxane-water; 3, 3-aminopyridine in 72%:28% dioxane-water; 4, 2-aminopyridine in 72%:28% dioxane-water at 25°, 65° and 80°; 5, 2-aminopyridine sulfate in 72%:28% dioxane-water.

conditions of diazotization. In Fig. 2, the absorption curve of 2-aminopyridine sulfate in dioxane-water solution (72%:28%) is given. It was found that the acid solutions have identical absorption curves over a wide range of acid concentration. No evidence of tautomerization can be observed from these curves since they contain only one absorption band characteristic of 2-aminopyridine. The curves of 2-aminopyridine in neutral and acid solutions are similar, although the curve in acid solution is slightly higher and broader. This fact has also been pointed out by Ley and Engelhardt.²

1-Methyl-2-pyridoneimine which is yellow, dissolves in water to form 1-methyl-2-aminopyridinium hydroxide which is colorless and strongly basic. The absorption curve of 1-methyl-2-pyridoneimine in 72%:28% dioxane-water shows clearly that in this solution an equilibrium is established as indicated by the following equation:



(2) Ley and Engelhardt, *Z. physik. Chem.*, **74**, 59 (1910).

This equilibrium is shifted to the right on the addition of more water to the solution in which case the color gradually disappears and the solution becomes more basic. The absorption band in the region of 2850 mm^{-1} appears to be a measure of the amount of 1-methyl-2-pyridoneimine present in the solution while the band at 3300 mm^{-1} appears to be a measure of the amount of pyridinium hydroxide. It will be noted that the latter band corresponds to the bands of 2- and 3-aminopyridines.

The absorption curve of 1-methyl-4-pyridoneimine (Fig. 3) was determined in 90%:10% dioxane-water solution because the compound was quite insoluble in pure dioxane. In the dioxane-water mixture the absorption curve of this compound shows the existence of an equilibrium similar to that found for the corresponding 1-methyl-2-pyridoneimine.

The absorption curves of the 2- and 4-compounds are very similar in shape but occur at different positions. The band for 1-methyl-2-pyri-

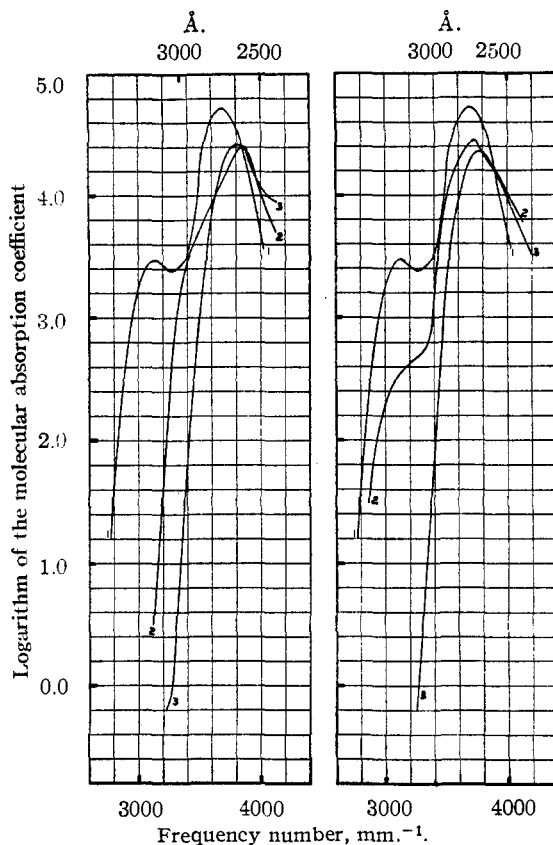


Fig. 3.—1, 1-Methyl-4-pyridoneimine in 90%:10% dioxane-water; 2, 4-(dimethylamino)-pyridine in 72%:28% dioxane-water; 3, 4-aminopyridine in 72%:28% dioxane-water.

Fig. 4.—1, 1-methyl-4-pyridoneimine in 90%:10% dioxane-water; 2, 1-methyl-4-pyridoneimine in 72%:28% dioxane-water; 3, 4-aminopyridine sulfate in 72%:28% dioxane-water.

doneimine lies at 2850 mm.^{-1} , whereas that for 1-methyl-4-pyridoneimine lies at 3150 mm.^{-1} , while the bands at 3300 mm.^{-1} and 3700 mm.^{-1} correspond, respectively, to the 2- and 4-aminopyridine structure.

Evidence for the structure of 4-aminopyridine has been determined in a manner similar to that used in the case of 2-aminopyridine. The curves for 4-aminopyridine and 4-(dimethylamino)-pyridine given in Fig. 3 were determined in 72%:28% dioxane-water solution due to the insolubility of 4-aminopyridine in ether. The curve for 4-aminopyridine has only a single band corresponding to the band for 4-(dimethylamino)-pyridine which is unable to tautomerize. From this evidence, it may be concluded that only the pyridine ring structure can be assigned to 4-aminopyridine, no evidence for tautomerization being shown.

The curve for the absorption spectrum of 4-aminopyridine sulfate in dioxane-water (72%:28%) (Fig. 4) indicates that sulfuric acid does not induce tautomerization of the 4-aminopyridine. Only the one band for the 4-substituted pyridine derivatives is observed, there being no bands corresponding to the 4-pyridoneimine structures. From these data it would appear that the difficulty in diazotizing 4-aminopyridine in acid solution is not due to a migration of an amine hydrogen to the ring nitrogen.

Experimental

The absorption spectral data were obtained by methods which have been described.³ The dioxane was fractionated by successive crystallizations and was finally distilled. All solvents were optically clear in the spectral region investigated.

2-Aminopyridine.—This amine was obtained by the action of ammonia on 2-bromopyridine.⁴ After several recrystallizations from benzene-petroleum ether, it melted at 57–58°.

1-Methyl-2-pyridoneimine.—This compound resulted from the action of a concentrated solution of sodium hydroxide on the methiodide of 2-aminopyridine.⁵ The

product was extracted with ether and purified by distillation under reduced pressure; b. p. 108° (16 mm.).

2-(Methylamino)-pyridine.—This substance was prepared by the action of a concentrated aqueous methylamine solution on 2-bromopyridine in a sealed Pyrex tube heated to 150° for ten hours. After addition of alkali, the amine was extracted with ether and distilled; b. p. 200–201°. The picrate melted at 190°.

2-(Dimethylamino)-pyridine.—This compound, obtained by the action of dimethylamine on 2-bromopyridine⁶ was purified by distillation; b. p. 196° (740 mm.). The picrate, recrystallized from absolute alcohol, melted at 182°.

3-Aminopyridine.—This amine was prepared by the action of ammonia on 3-bromopyridine using $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ as a catalyst.⁷ The product was extracted with ether and recrystallized from a benzene-petroleum ether solution; m. p. 64°.

4-Aminopyridine.—This substance was obtained by heating crude 4-pyridylpyridinium dichloride with concentrated aqueous ammonia.⁸ After recrystallizing several times from water and treatment with norite, the product melted at 150°.

1-Methyl-4-pyridoneimine.—This imine was prepared by the action of concentrated sodium hydroxide on the methiodide of 4-aminopyridine. The product was extracted with hot benzene and the solvent evaporated; m. p. 150–151°. It liquefies in the air since it is very hygroscopic and soon becomes red in color.

4-(Dimethylamino)-pyridine.—This compound was obtained by heating crude 4-pyridylpyridinium dichloride with a concentrated aqueous solution of dimethylamine and was recrystallized from benzene; m. p. 114°.⁹ The picrate melted at 204°.

Summary

1. Curves for the absorption of visible and ultraviolet light by solutions of the aminopyridines and some of their derivatives in ether, dioxane, water and acid are presented.

2. No evidence was found for the presence of a pyridone structure for the 2- and 4-aminopyridines in the solutions studied.

3. The absorption spectra indicate the presence of tautomeric equilibria between pyridine and pyridone forms of 1-methyl-2- and 1-methyl-4-pyridoneimines in dioxane-water solutions.

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(3) Anderson and Gomberg, *THIS JOURNAL*, **50**, 203 (1928).

(4) Hertog and Wibaut, *Rec. trav. chim.*, **55**, 125 (1936).

(5) Tschitschibabin, Konowalowa and Konowalowa, *Ber.*, **54B**, 818 (1921).

(6) I. G. Farbind A.-G., French Patent 802,105 (1936).

(7) Maier-Bode, German Patent 586,879 (1933).

(8) Koenigs and Greiner, *Ber.*, **64B**, 1054 (1931).

(9) Koenigs, Friedrich and Jurany, *ibid.*, **58B**, 2571 (1925).