SYNTHESIS OF ACID—BASE TRANSFORMATIONS OF 3-AROYL-6-METHYL-2-OXOPYRIDINES

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In hydrolysis of 3-aroyl-6-methyl-2-methoxypyridines, 3-aroyl-6-methyl-2-oxopyridines are formed, which with methyl iodide in an alkaline medium give the corresponding 1-methyl derivatives.

Compounds have been found among 3-aroyl-2-oxopyridines with valuable biological properties [1]. In [2] we have noted the ease of hydrolysis of 3-aroyl-6-methyl-2-methoxypyridine (Ia-e) to the corresponding 2-oxo derivative. In the present work, we describe methods of synthesis of 3-aroyl-6-methyl-2-oxopyridines (IIa-e) based on this reaction and their UV spectra and acid-base transformations are examined.



I-III a R=H, b R=p-CH₃, c R=p-Cl, d R=p-Br, e R=p-CH₃O; IV R¹=H; V R¹=CH₃

When ketones Ia-e are boiled with 10% hydrochloric acid, 3-aroyl-6-methyl-2-oxopyridines (IIa-e) are formed in 77-87% yields. Compounds IIa-e are colorless crystalline substances, in whose IR spectrum absorption bands are present at 3290 (NH) and 1640-1660 cm⁻¹ (CO). In the PMR spectrum of compound IIa, proton signals are observed at 2.15 (3H of the CH₍₃₎ group) 6.08 (H of the pyridine ring at $C_{(5)}$); 7.32 (H of the pyridine ring at $C_{(4)}$); a multiplet with a center at 7.58 (5H of the benzene ring) and 11.88 ppm (NH of pyridone). The PMR spectra of compounds IIb-e also correspond to the structure ascribed to them.

When ketones IIa-d are heated with methyl iodide in an aqueous-alcoholic solution of potassium hydroxide, 3-aroyl-1,6-dimethyl-2-oxopyridines IIIa-d are formed in good yields. Their IR spectra contain an absorption band at 1650-1660 cm⁻¹ (CO), but in contrast to the spectra of the initial compounds IIa-d, they do not have an absorption band of the pyrodine NH group at 3290 cm⁻¹.

To clarify the structure of the ketones, we examined their UV spectra and evaluated them on the example of the spectra of Ia, IIa, and IIIa. In the spectrum of IIa in ethanol, there are bands with maxima at 254 and 335 nm. An intense absorption is also observed in the 220 nm region, but the maximum of this band lies beyond the limits of the resolving power of the apparatus. The UV spectra of compounds IIa and IIIa are similar to one another. The absorption curve of compound Ia differs substantially from those of IIa and IIIa and has a maximum at 260 and 292 nm. From the similarity of the spectra of compounds IIa and IIIa, it can be concluded that compounds IIa-e in alcoholic solution have a pyridone and not a pyridol structure.

In the spectra of compound IIa at a 0.01 H_2SO_4 concentration, a 6 nm bathochromic shift of the maximum at 254 nm is observed, which is probably due to the influence of the medium.

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 $M H_2SO_4$; 4) in 6 $M H_2SO_4$; 5) in 0.1 N NaOH.

TABLE 1. Characteristics of Compounds Synthesized

Com- pound	тр , °С	-pK _{ap.a.} zw	Found, %				Empiric a l	Calculated, %				d, %
			с	н	Hal	N	formula	с	H	Hal	N	Yiel
Ila IIb IIc IId IIe IIIa IIIb IIIc IIIc	$\begin{array}{c} 228 - 230 \\ 230 - 232 \\ 238 - 239 \\ 242 - 243 \\ 233 - 234 \\ 110 - 112 \\ 139 - 140 \\ 125 - 127 \\ 123 - 124 \end{array}$	$\begin{array}{c} 0.78 \pm 0.04 \\ 0.83 \pm 0.05 \\ 1.27 \pm 0.06 \\ 1.22 \pm 0.05 \\ \hline \\ 1.09 \pm 0.06 \\ \hline \\ 1.35 \pm 0.05 \end{array}$	73,1 73,8 69,2 73,8 74,5 	5,3 5,8 5,4 5,4 5,8 6,2	$ \begin{array}{c} - \\ 14.3 \\ 27.4 \\ - \\ 13.6 \\ 26.2 \end{array} $	$\begin{array}{c} 6.6 \\ 6.3 \\ 5.6 \\ 4.9 \\ 5.7 \\ 6.3 \\ 6.0 \\ 5.3 \\ 4.4 \end{array}$	C ₁₃ H ₁₁ NO ₂ C ₁₄ H ₁₅ NO ₂ C ₁₃ H ₁₀ CINO ₂ C ₁₃ H ₁₀ BrNO ₂ C ₁₄ H ₁₃ NO ₃ C ₁₄ H ₁₃ NO ₂ C ₁₅ H ₁₅ NO ₂ C ₁₅ H ₁₅ NO ₂ C ₁₄ H ₁₂ BrNO ₂	73,2 73,9 	5,2 5,8 	$ \begin{array}{c} - \\ 14.3 \\ 27.3 \\ - \\ 13.5 \\ 26.1 \\ \end{array} $	$\begin{array}{c} 6.6 \\ 6.2 \\ 5.6 \\ 4.8 \\ 5.7 \\ 6.2 \\ 5.9 \\ 5.4 \\ 4.6 \end{array}$	87 84 82 87 77 75 76 67 69

When the acidity of the medium is further increased, the intensity of the bands at 260 and 335 nm gradually decreases. Parallel to this, the intensity of the absorption at 306 nm increases and reaches its highest value at a 6 M concentration of the acid, and a maximum appears instead of minimum. The spectrum of compound IIa is similar to the spectrum of derivative Ia [3] in 15% sulfuric acid, where it is present in the form of a singly charged pyridinium ion. This leads us to conclusion that in 6 M sulfuric acid, compound IIa exists in the form of a pyridinium ion of type IV. In the acidity range from 0.1 to 6 M, an equilibrium between forms IIa and IV is observed. In this case, the presence of only two ions is confirmed by an isobestic point at 272 nm. The absorption spectra of compounds IIIa in sulfuric acid solutions are characterized by a similar pattern, and are only inappreciably shifted to the long-wave region, and hence under these conditions they exist in the form of pyridinium ions V.

There is a linear interdependence between the optical densities of the solutions of compounds IIa-d, IIIa-c, and the acidity of the medium expressed in H_o units, with an angular coefficient close to unity.

The equilibrium constants of II \neq IV and III \neq V were determined spectrophotometrically. Since 2-pyridones represent a resonance hybrid of pyridone and zwitterionic structures [4, 5], with a considerable predominance of the latter, the K_a values of compounds II and III should also be considered as ionization constants of the corresponding zwitter ions (K_a^{zw}). The values of pK_{ap.a.}zw* of compounds IIa-d vary from -0.78 to -1.27, and for IIIa they are equal to -1.09 and -1.35 H₀ units. They are little dependent on the substituents in the aryl radical and are one order of magnitude lower than the values of pK_{ap.a.}zw of 2-pyridone and its N-methyl derivative [4], which is explained by the electron-acceptor influence of the aroyl group. In the spectrum of compound IIa in sodium hydroxide solution (Fig. 1), the maximum of the long-wave band is bathochromically shifted compared with the spectrum of IIa in ethanol. It was thus possible to determine the value of pK_{ap.s.}^{zw}, equal to 10.85 ± 0.051 and to find the characteristic IIa \neq VI equilibrium.

*The indexes p.a. and p.s. designate the addition and splitting off of a proton.

EXPERIMENTAL

The IR spectra were recorded on a UR-20 spectrophotometer in chloroform (for compounds IIa-e) and in carbon tetrachloride (for IIIa-d). The PMR spectra were run on a RYa-2310 spectrometer (60 MHz), using HMDS as internal standard. The UV spectra were recorded on a SF-16 spectrophotometer for $1 \cdot 10^{-4}$ mole/liter solutions. The constants of the basic (for compounds IIa-d and IIIa, c) and acidic (for IIa) ionization in a sulfuric acid-water or sodium hydroxide-water system were determined spectrophotometrically on the same apparatus at 20 ± 1°C. The analytical wave-length corresponded to the basic ionization of compounds (IIa-d at 306 nm, compounds IIIa, c at 315 nm, and for acidic ionization at 365 nm. The pKap.a.²W and pKap.s.²W values were calculated from seven points at a given reliability of 0.98 according to formulas given in [6]. The yields, physical constants, and analytical data of the compounds obtained are listed in Table 1.

<u>3-Aroyl-6-methyl-2-oxopyridines (IIa-e)</u>. A 0.05 mole portion of 3-aroyl-6-methyl-2methoxypyridine (Ia-e) in 20 ml of 10% hydrochloric acid is boiled for 4 h. The mixture is cooled, the precipitate is separated and crystallized from ethanol.

<u>3-Aroyl-1,6-dimethyl-2-oxopyridines (IIIa-d)</u>. A solution of 0.014 mole of potassium hydroxide in 8 ml of water and 5 ml of methyl iodide are added to a solution of 0.01 mole of compound II in 30 ml of ethanol. The mixture is boiled for 2 h, the solvent and excess of methyl iodide are distilled, and the residue is crystallized from water.

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SYNTHESIS AND ACID-BASE TRANSFORMATIONS OF (4-STYRYLPYRIDINIO)-

ALKANESULFONATES

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(4-Styrylpyridinio)alkanesulfonates were synthesized by condensation of 2-(4methylpyridinio)- and 2-(4-ethylpyridinio)-l-ethanesulfonates with aromatic aldehydes, and also by quaternization of 4-styrylpyridine by sulfoalkylating agents. For the p- and o-hydroxystyrylpyridinium compounds in aqueous solutions, the pK_{α} values were determined spectrophotometrically. It is believed that the planarity of the o-hydroxypyridinium compounds is disturbed because of the reaction of the hydroxy and the α -sulfonatomethyl groups.

It is known that pyridylsulfobetaines [1] and also unsaturated quaternary pyridine salts [2] are used in galvanotechniques. The possibility was examined of using stilbazoles as antioxidants and antitumorigenic preparations [3], and also as solvent polarity indicators [4]. We synthesized quaternary pyridinium salts containing a sulfo group and a double bond

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