STRUCTURES OF STERICALLY HINDERED p-HYDROXYSTYRYLPYRIDINES AND ACID-BASE TRANSFORMATIONS OF THEIR QUATERNARY SALTS

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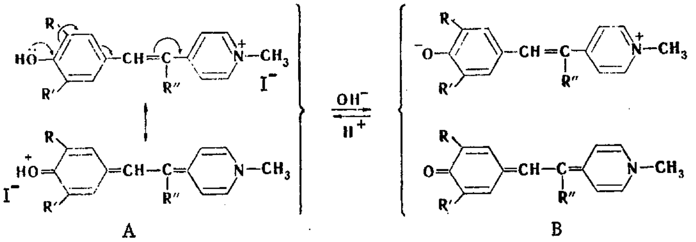
UDC 547.829:543.422.6

The structures of p-hydroxystyrylpyridines and a number of their new quaternary salts were studied by means of electronic absorption spectra. The reverse transformation of the salts to the corresponding quinonoid compounds was examined as a function of the pH of the medium, and the equilibrium constants were determined.

We have previously noted during a study of the properties of sterically hindered hydroxystyrylpyridines that this class of compounds is an extremely interesting subject for diverse physicochemical investigations [1]. In particular, our attention was drawn to the possibility of equilibrium phenol–quinonoid transformations of p-hydroxystyrylpyridines as the pH of the medium changes; these transformations have been previously studied in the case of sterically hindered phenols [2]. The transition of the aromatic system of bonds to a quinonoid system, which is often accompanied by prototropic shifts with the formation of tautomeric oxo forms [3], is in turn characteristic for various derivatives of 2- and 4-hydroxypyridine. In this connection, it seemed of interest to study the effect of bulky substituents in the phenol ring and the ethylene bridge (as factors that determine the spatial orientation of the individual groups in the molecule) on these sorts of acid-base transformations of quaternary salts of p-hydroxystyrylpyridines.

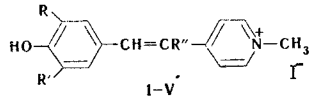
For this, we synthesized a series of sterically hindered p-hydroxystyrylpyridines [1], their methiodides, and, from them, the corresponding quinones (Table 1).

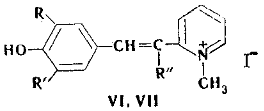
In studying the absorption spectra of p-hydroxystyrylpyridines and their quaternary salts we found that a considerable bathochromic shift of the major absorption band is characteristic for the quaternary salts, and substituents in the phenol ring and in the ethylene bridge have different effects on the conversion of the aromatic system to a quinonoid system. Bulky alkyl substituents in the o-position of the phenol ring induce a small bathochromic shift of the major band of the π,π^* transitions, while the introduction of an alkyl substituent into the ethylene bridge leads to a hypsochromic shift and a decrease in intensity, which indicates disruption of the planarity of the molecule [4] and a decrease in the resonance interaction of the phenol and pyridine rings. The absorption spectra of p-hydroxystyrylpyridines and their quaternary salts in alkaline media have a number of peculiarities. In this case, one particularly notes the substantial effect of bulky alkyl substituents in the o-position of the phenol ring on the position of the absorption band and also

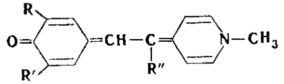


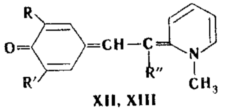
Donetsk Branch, Institute of Chemical Physics, Academy of Sciences of the USSR. Donetsk State University. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 8, pp. 1087-1091, August, 1972. Original article submitted July 12, 1971.

TABLE 1


I–V


VI, VII


VIII–XI


XII, XIII

Compound	R	R′	R″	mp, °C	Empirical formula	Found, %				Calculated, %				Yield, %	pK_a	Electronic absorption spectra*			
																in neutral medium		in alkaline medium	
						C	H	N	I	C	H	N	I			λ_{max}, nm	lg ε	λ_{max}, nm	lg ε
I	t-C_4H_9	t-C_4H_9	H	280—281	$C_{22}H_{30}INO$	58,2 58,3	6,7 6,6	3,2 3,1	27,8 27,7	58,5	6,7	3,1	28,0	85	9,7	385	4,31	550	4,56
II	t-C_4H_9	t-C_4H_9	CH_3	231—233	$C_{23}H_{32}INO$	59,3 59,1	7,0 6,8	2,8 3,0	26,8 26,9	59,4	6,9	3,0	27,0	90	10,0	370	4,22	525	4,18
III	t-C_4H_9	t-C_4H_9	C_6H_5	203—205	$C_{28}H_{34}INO$	63,8 63,6	6,6 6,4	2,7 2,5	24,0 24,2	63,7	6,5	2,7	24,1	80	10,0	390	4,10	550	4,30
IV	H	H	H	233—235	$C_{14}H_{14}INO$	49,6 49,5	4,4 4,1	4,3 4,1	37,1 37,2	49,6	4,2	4,1	37,2	90	8,7	380	4,46	455	4,53
V	H	H	CH_3	222—224	$C_{15}H_{16}INO$	50,8 51,1	4,7 4,8	4,1 4,2	35,8 36,0	51,0	4,6	4,0	35,9	42	9,1	365	4,37	435	4,39
VI	t-C_4H_9	t-C_4H_9	H	227—228	$C_{22}H_{30}INO$	58,4 58,3	6,6 6,7	3,0 3,1	27,9 28,0	58,5	6,7	3,1	28,0	85	9,55	375	4,30	525	4,62
VII	H	H	H	269—270	$C_{14}H_{14}INO$	49,4 49,5	4,2 4,1	4,0 4,2	37,2 37,1	49,6	4,2	4,1	37,2	80	8,95	365	3,99	435	4,19
VIII	H	H	H	228—230	$C_{14}H_{13}NO$	79,3 79,5	6,0 6,1	6,4 6,5		79,6	6,2	6,6		63	—	395	4,48		
IX	H	H	CH_3	164—166	$C_{15}H_{15}NO$	80,0 80,2	6,5 6,6	6,0 6,1		80,0	6,7	6,2		40	—	373	4,26		
X	t-C_4H_9	t-C_4H_9	H	253—255	$C_{22}H_{29}NO$	81,5 81,4	8,9 9,1	4,3 4,0		81,7	9,0	4,3		60	—	400	4,54		
XI	t-C_4H_9	t-C_4H_9	CH_3	245—247	$C_{23}H_{31}NO$	81,5 81,6	4,3 4,4	4,0 4,3		81,8	4,5	4,2		76	—	387	4,33		
XII	H	H	H	150—152	$C_{14}H_{13}NO$	79,4 79,5	6,0 6,1	6,5 6,4		79,6	6,2	6,6		64	—	387	4,34		
XIII	t-C_4H_9	t-C_4H_9	H	238—239	$C_{22}H_{29}NO$	81,5 81,6	8,9 9,1	4,0 4,2		81,7	9,0	4,3		60	—	390	4,44		

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*The electronic absorption spectra of I-VII were obtained with aqueous solutions, while those of VIII-XIII were obtained with methanol solutions.

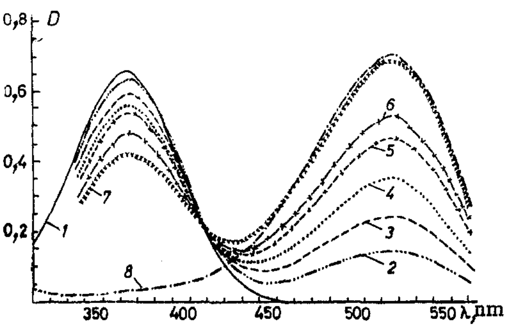

Fig. 1. Absorption spectra of 2-(3,5-di-tert-butyl-4-hydroxystyryl)pyridine and its quinonoid compound as a function of the pH of the medium: 1) pH = 7; 2) pH = 8.48; 3) pH = 8.85; 4) pH = 9.05; 5) pH = 9.25; 6) pH = 9.3; 7) pH = 9.56; 8) pH = 12.5.

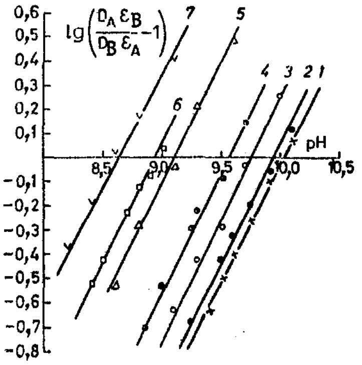

Fig. 2. Dependence of the constants of the phenol–quinonoid transformations on the structure of the hydroxystyrylpyridine methiodides: 1) 4-(3,5-di-tert-butyl-4-hydroxy-β-phenylstyryl)-pyridine methiodide; 2) 4-(3,5-di-tert-butyl-4-hydroxy-β-methylstyryl)pyridine methiodide; 3) 4-(3,5-di-tert-butyl-4-hydroxystyryl)pyridine methiodide; 4) 2-(3,5-di-tert-butyl-4-hydroxystyryl)pyridine methiodide; 5) 4-(4-hydroxy-β-methylstyryl)-pyridine methiodide; 6) 2-(4-hydroxystyryl)pyridine methiodide; 7) 4-(4-hydroxystyryl)pyridine methiodide.

the absence of a solvent polarity effect on the position of the bands and the magnitude of their intensities. These peculiarities are apparently due to the presence of phenol–quinonoid transformations, which was confirmed by the spectral characteristics of fixed quinonoid structures B, which were obtained by treatment of the corresponding quaternary salts with ammonia.

For a quantitative evaluation of the effect of steric factors on this process, we used a spectrophotometric method, by means of which we examined the equilibrium between the quinonoid and aromatic systems of bonds in the case of the reverse transformation of various methiodides of hydroxystyrylpyridines to the corresponding quinonoid compounds as a function of the pH of the medium.

The absorption spectra of 2-(3,5-di-tert-butyl-4-hydroxystyryl)pyridine at various pH values are presented in Fig. 1. As seen from Fig. 1, the presence of one absorption band (of the π,π^* transitions), the intensity of which falls as the pH of the medium rises, is characteristic for neutral solutions of the quaternary salts. The intensity of the absorption band of the quinones increases simultaneously with an increase in the alkalinity, and the solution gradually becomes intensely red. In this case, the absorption spectra are characterized by the presence of a distinctly expressed isosbestic point, which indicates the binary character of the system and makes it possible to determine the equilibrium constants of the phenol–quinonoid transformation.

In accordance with the equation of the dependence of the concentration of the salt form on the pH of the medium in coordinates of pH and $-\log(D_A\varepsilon_B/\varepsilon_A D_B - 1)$, we obtained straight lines with a slope of one for all of the investigated quaternary salts of the hydroxystyrylpyridines (Fig. 2), while the segments cut out by the line on the axis of abscissas correspond to the pK_a values and are presented in Table 1. As seen from Table 1, the equilibrium constants that characterize the conversion of the hydroxy form of p-hydroxystyrylpyridines to the oxo form are an order of magnitude higher for sterically hindered styrylpyridines with bulky alkyl substituents in the o-position, and the introduction of R" substituents does not decrease this difference. A similar effect of a sharp increase in the tendency of the transition of sterically hindered 4-hydroxy-3,5-dialkylbenzaldehydes from the phenol form to the quinonoid form as compared with unsubstituted 4-hydroxybenzaldehyde is known [5].

In our case, this is apparently associated with a change in the direction of protonation. It is well-known that in amides, pyridones, and similar compounds, in which there is conjugation of the carbonyl and amino groups, the stronger nucleophilic center is the carbonyl oxygen atom, at which protonation or addition of different electrophilic agents occurs. Protonation occurs similarly at the oxygen atom in quinones that do not have bulky substituents in the o-position. However, the ring nitrogen atom of the pyridine ring is protonated in shielded quinones B, which also is responsible for the substantial increase in basicity that we observed.

The pK_a values found may serve as the characteristic of the basicity of the quaternary salts of p-hydroxystyrylpyridines: sterically hindered quinones B are the most basic, while unsubstituted p-hydroxypyridinium salts A have the maximum acidity.

EXPERIMENTAL

Quaternary Salts of p-Hydroxystyrylpyridines. The quaternary salts of pyridine derivatives (obtained from freshly distilled α- and γ-picoline, 4-ethylpyridine, 4-benzylpyridine, and methyl iodide) were condensed with an equivalent amount of 3,5-di-tert-butyl-4-hydroxybenzaldehyde in absolute butanol with a catalytic amount of piperidine via the method in [6]. The characteristics of the salts are presented in Table 1. The corresponding quinones were obtained by heating an alcohol solution of the quaternary salt of the p-hydroxystyrylpyridine (0.3 g) in 50 ml of alcohol with 30 ml of ammonium hydroxide in a stream of NH_3 for 30 min. The precipitate was removed by filtration, washed with water, dried, and crystallized from isopropyl alcohol. Data on the fixed structures are presented in Table 1.

Equilibrium Constants. The concentrations of the quinonoid and salt forms of the reverse transformation as a function of the pH of the media were determined from the optical density of these forms with an SF-4a spectrophotometer in standard 0.99-cm-thick cuvettes at 22 ± 0.5°. Aqueous solutions of the quaternary salts of the p-hydroxystyrylpyridines were prepared and diluted with a borate buffer with a fixed pH to a working concentration of $5 \cdot 10^{-5}$ M. A weighed sample of the quaternary salt was taken prior to each experiment and diluted to the necessary concentration before the measurements. The equilibrium constants of the reaction $A \rightleftharpoons B$ were found on the basis of measurements of the absorption densities of the salt and quinonoid forms at various pH values of the media by a graphical method in coordinates of pH and $-\log(D_A\varepsilon_B/\varepsilon_A D_B - 1)$ (Fig. 2).

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