STRUCTURE AND REACTIVITY OF 3-HYDROXYPYRIDINE N-OXIDE

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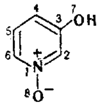
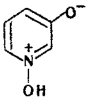
It has been established by UV spectroscopy that 3-hydroxypyridine N-oxide in aqueous and acid solutions exists in the form of the conjugate acid, and in an alkaline medium in the anionic form; no bipolar form has been detected in aqueous solution. Using Huckel's MO LCAO method the indices of the π-electronic structure have been calculated for various forms of 3-hydroxypyridine N-oxide. The values of the localization energies L_r^+ obtained agree with the experimentally observed sequence of electrophilic substitution in 3-hydroxypyridine N-oxide in acid and alkaline media.

It has been established by UV spectroscopy that 3-hydroxypyridine N-oxide (I) exists in ethanol [1] in the form of the free base (Ia) and in an acid medium [2, 3] in the form of the conjugate acid (Ic).

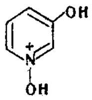
It has been shown by IR spectroscopy [4] that compound (I) in the crystal state exists in the form of the ion pairs (Ia → Ib).



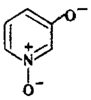
Ia



Ib



Ic



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Electrophilic substitution in compound (I) takes place in position 2 in an acid medium [5] and in positions 2 and 6 in an alkaline medium [6]. It has been established by PMR [7] that in the acid-catalyzed exchange of hydrogen in position 2, compound (I) reacts as the free base, but it is not known whether in form (Ia) or (Ib).

In the present work we have measured the UV spectra of compound (I) and its derivatives in various media (Table 1) and have calculated the indices of the π-electronic structure by Huckel's MO LCAO method [8].

In aqueous solution, 3-hydroxypyridine exists in the neutral and bipolar forms [9], which are characterized by long-wave $\pi\rightarrow\pi^*$ absorption bands at 277 and 313 nm, respectively. The $\pi\rightarrow\pi^*$ band, which characterizes the bipolar form, is at a longer wavelength than the band characteristic for the anionic form (298 nm) in an alkaline medium. The UV spectra of compounds of type (I) (Table 1) in aqueous and acid solutions are similar to one another. This indicates the presence in aqueous solution of only the cationic form (Ic). In ethanolic and alkaline solutions bathochromic shifts of the long-wave $\pi\rightarrow\pi^*$ band are observed, averaging 9 and 16 nm, respectively. This can be explained by the loss of one, and then of another, proton by the conjugate acid (Ic). Thus, compound (I) and its derivatives exist in three forms in ethanolic, aqueous, and alkaline media: (Ia), (Ic), and (Id), respectively. It follows from the calculated values of the delocalization energies for one π electron, equal to 0.228, 0.216, and 0.234 β for forms (Ia), (Ic), and (Id), respectively, that the stabilities of the three forms of compounds (I) are similar. This is in harmony with the case of transition of compound (I) from one form to another. The lowest empty and highest occupied MOs calculated from energy differences, of 1.68, 1.77, and 1.62 β and the values of λ_{max} for the long-wave $\pi\rightarrow\pi^*$ band at $\beta = -2.445$ eV [10] for the forms (Ia), (Ic), and (Id) agree well with the experimental values

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TABLE 1. UV Spectra of 3-Hydroxypyridine N-Oxides

Compound	R	R′	Medium	λ_{max}, nm				ε			
I	H	H	Ethanol	224	244	262	302	3,56	3,75	3,97	2,98
			Water	220		253	295	4,16		3,94	3,29
			1 *N* HCl	220		255	289				
			1 *N* KOH	234			314				
II	CH_3	H	Ethanol	222	262		300	4,22		3,92	3,32
			Water	220	254		295	4,23		3,87	3,40
			1 *N* HCl	220	255		291	3,92		3,42	3,66
			1 *N* KOH	235			316	4,34			3,75
III	H	CH_3	Ethanol	222	257		307	4,19		3,90	3,38
			Water	220	250		301	4,22		3,95	3,59
			1 *N* HCl	220	252		295	4,05		3,57	3,63
			1 *N* KOH	232			320	4,41			3,64
IV	CH_3	CH_3	Ethanol	222	257		305	4,32		3,90	3,38
			Water	220	251		300	4,32		3,92	3,56
			1 *N* HCl	220	251		297	3,93		3,27	3,74
			1 *N* KOH	232			320	4,43			3,75
V	C_6H_5	H	Ethanol	244	265		310	4,22		3,80	3,50
			Water	222	255		302	4,26		3,38	3,56
			1 *N* HCl	220			302	4,20			4,00
			1 *N* KOH	240			324	4,32			4,00
VI	p-$CH_3C_6H_4$	H	Ethanol	230	246		310	4,26		4,31	3,75
			Water	222			305	4,23			3,70
			1 *N* HCl	222			305	4,28			3,83
			1 *N* KOH	236			323	4,35			3,86
VII	p-$CH_3OC_6H_4$	H	Ethanol	230	255		316	3,49		3,48	3,06
			Water	222	248		306	4,29		4,07	3,72
			1 *N* HCl	222			305	4,27			3,83
			1 *N* KOH	235			329	4,25			3,78
IIIA	p-ClC_6H_4	H	Ethanol		245		312			4,34	3,69
			Water	222	238		303	4,28		4,16	3,68
			1 *N* HCl	222	238		302	4,16		4,00	3,68
			1 *N* KOH	237			323	4,36			3,85
IX	p-$(CH_3)_2CHC_6H_4$	H	Ethanol	230	242		312	4,26		4,31	3,74
			Water	222	238		304				
			1 *N* HCl	222	238		305				
			1 *N* KOH	236			323	4,36			3,86
X	p-$NO_2C_6H_4$	H	Ethanol	220	265		305				
			Water	220	258		300				
			1 *N* HCl	220	258		302				
			1 *N* KOH	237	258		315	3,96		3,73	3,41
XI	3-Hydroxy-2-methylpyridine		Ethanol	220			282	3,62			3,66
			Water	220	249	290	316	3,62	3,61	3,47	3,60
			1 *N* HCl	224			288	3.44			3,80
			1 *N* KOH	220	245		306	3,42		3,90	3,72
XII	3-Hydroxy-2-phenylpyridine		Ethanol				300				4,15
			Water		295		345			3,77	3,62
			1 *N* HCl		245		317			4,02	4,36
			1 *N* KOH		252		322			3,91	4,06

of λ_{max}. The values of the ionization potentials found from the energies of the highest occupied MOs of 0.738 and 0.887 β for forms (Ia) and (Ic) are 8.60 and 9.00 eV, respectively, and are close to the ionization potential of phenol (8.50 eV).

The length of the C=C and C=N bonds calculated from the bond orders by means of the formulas of Dewar and Morita and those of the N–O bond from Günter's formula [12] agree with the known experimental results for pyridine, phenol, and the conjugate acid of pyridine N oxide [13].

The calculated values of the localization energies (L_r^+) for compound (I) in the forms (Ia, c, and d) give a sequence of electrophilic substitution of 2 > 6 > 4 > 5, which agrees completely with the known experimental facts for acid and alkaline media (Table 3). At the same time, it can be seen from Table 3 that the calculated π-electronic charges Q_r and the limiting electron densities f_r^+ do not give the experimentally observed sequence of electrophilic substitution of compound (I). This leads to the conclusion that the electrophilic substitution of compound (I) takes place through the formation of an intermediate σ complex, and not a π complex. It must be noted that the values of L_r^+ and Q_r for the forms (Ia), (Ic), and (Id) show

TABLE 2. π-Electronic Charges, Bond Orders and Lengths of the Forms (Ia, c, and d) of 3-Hydroxypyridine N-Oxide

Atom	π-Electronic charge			Bond	Bond order (bond length, Å)		
	Ia	Ic	Id		Ia	Ic	Id
1	+0,123	+0,168	+0,123	1—2	0,636 (1,334)	0,647 (1,332)	0,639 (1,334)
2	−0,011	+0,026	−0,026	2—3	0,659 (1,397)	0,656 (1,397)	0,647 (1,399)
3	+0,029	+0,027	+0,033	3—4	0,649 (1,399)	0,651 (1,398)	0,637 (1,401)
4	−0,022	+0,006	−0,036	4—5	0,665 (1,396)	0,667 (1,396)	0,668 (1,395)
5	−0,001	−0,002	−0,001	5—6	0,671 (1,395)	0,669 (1,395)	0,669 (1,395)
6	−0,003	+0,037	−0,016	1—6	0,633 (1,335)	0,644 (1,333)	0,631 (1,336)
7	+0,039	+0,039	+0,076	1—8	0,282 (1,368)	0,182 (1,406)	0,282 (1,368)
8	+0,093	+0,041	+0,093	3—7	0,197 (1,361)	0,197 (1,361)	0,275 (1,350)

TABLE 3

Form	No. of atoms	Q_r	f_r^+	f_r^-	f_r^0	F_r	L_r^+	L_r^-	L_r^0
Ia	2	−0,011	0,045	0,170	0,107	0,440	2,358	2,486	2,422
	4	−0,022	0,202	0,295	0,248	0,421	2,394	2,522	2,458
	5	−0,001	0,011	0,123	0,062	0,399	2,544	2,544	2,544
	6	−0,003	0,137	0,044	0,090	0,431	2,374	2,504	2,439
Ic	2	−0,026	0,150	0,170	0,110	0,432	2,482	2,544	2,513
	4	+0,006	0,077	0,300	0,188	0,417	2,516	2,580	2,548
	5	−0,002	0,080	0,088	0,084	0,399	2,542	2,542	2,542
	6	+0,033	0,280	0,083	0,182	0,422	2,500	2,562	2,531
Id	2	−0,026	0,010	0,193	0,101	0,449	2,278	2,496	2,387
	4	−0,036	0,194	0,282	0,238	0,430	2,314	2,532	2,424
	5	−0,001	0,022	0,140	0,131	0,398	2,546	2,546	2,546
	6	−0,016	0,220	0,031	0,130	0,435	2,310	2,530	2,420

the greater reactivity of compound (I) in an alkaline medium than in an acid medium, which is also in agreement with experiment. There is no information in the literature on nucleophilic and radical substitution reactions in compound (I). The reactivity indices for nucleophilic substitution (L_r^-, Q_r, and f_r^-) and for radical substitution (L_r^0 and f_r^0) and the free-valence index (F_r) for the reaction centers of forms (Ia), (Ic), and (Id) have been calculated and are given in Table 3.

EXPERIMENTAL

Compounds (V-X) were obtained by oxidizing the corresponding bases [14]. The UV spectra were recorded on a SF-8 spectrophotometer. In the calculation we used the Coulomb and resonance parameters which we found for 3-hydroxy-2-phenylpyridine [10] and an auxiliary inductive parameter for the nitrogen atom of $h_1 = h_8/10$. The resonance parameters $R^+_{N-O} = 0.76$ and $R^+_{N-OH} = 0.68$ were found from the values of λ_{max} for the long-wave $\pi \to \pi^*$ absorption band in the UV spectra of compound (I) in neutral and acid media [10].

LITERATURE CITED

1. E. Shaw, J. Amer. Chem. Soc., 71, 67 (1949).
2. H. H. Jaffe, J. Amer. Chem. Soc., 77, 4451 (1955).
3. J. N. Gardner and E. Snell, J. Chem. Soc., 4375 (1957).
4. K. M. Dyumaev, G. N. Rodionova, and R. E. Lokhov, Khim. Geterotsikl. Soedin. (1974).
5. K. Lewicka and E. Plazek, Rec. Trav. Chim., 78, 644 (1959).
6. K. Lewicka and E. Plazek, Roczn. Chem., 40, 405 (1966).
7. G. P. Bean, P. J. Brignell, C. D. Johnson, A. R. Katritzky, B. I. Ridgewell, H. O. Tarhan, and A. M. White, J. Chem. Soc., B, 1222 (1967).
8. E. Streitwieser, Molecular Orbital Theory for Organic Chemists, Wiley (1961).
9. D. E. Metzler and E. Snell, J. Amer. Chem. Soc., 77, 2431 (1955).
10. V. T. Grachev, V. N. Kostylev, B. E. Zaitsev, V. I. Kuz'min, K. M. Dyumaev, and L. D. Smirnov, Teoret. Éksperim. Khim., 8, 224 (1972).
11. M. J. S. Dewar and T. Morita, J. Amer. Chem. Soc., 97, 796 (1969).
12. H. Günter, Ber., 103, 3370 (1970).

13. L. E. Sutton, Tables of Interatomic Distances and Configuration in Molecules and Ions, The Chemical Society, London (1958).
14. L. D. Smirnov, V. I. Kuz'min, A. E. Zbarskii, V. P. Lezina, and K. M. Dyumaev, Izv. Akad. Nauk SSSR, Ser. Khim. (1974).