STRUCTURE OF 3-PHENYL-4-HYDROXYISOQUINOLINE

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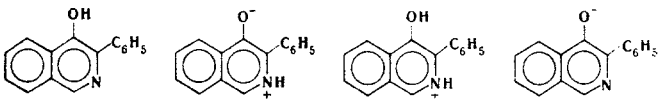
UDC 547.833.6.9:541.67:543.422.6

It was shown by UV spectroscopy that 3-phenyl-4-hydroxy-isoquinoline exists in neutral, dipolar, cationic, and anionic forms, depending on the medium. The angle of rotation between the planes of the phenyl ring and the hetero-ring, the length of the "single" C–C bond connecting these rings, and its degree of double bond character in neutral, acidic, and alkaline media were calculated by means of perturbation theory within the framework of the Hückel MO method. On the basis of a study of the π-electron structure of 3-phenyl-4-hydroxyisoquinoline, it was concluded that its various forms have aromatic character. The energy of conjugation of the phenyl group with the π system of 4-hydroxyisoquinoline was calculated. A method for the calculation of the coulombic and resonance parameters for the heteroatoms from experimental UV spectroscopic data and the ionization potentials of the molecules by means of perturbation theory is presented.

It was previously shown by electronic absorption spectroscopy that 3-hydroxypyridine [1] and 4-hydroxyisoquinoline [3] (I) exist in four different structural forms depending on the medium and the solvent. In the present research we have examined the possibility of the existence of the 3-phenyl-4-hydroxyisoquinoline (II) molecule in the same four forms as a function of the medium and the solvent: in neutral (N) and dipolar (D) forms in neutral media as a function of the polarity of the solvents, in cationic form (C) in acidic media, and in anionic form (A) in alkaline media:



N B C A

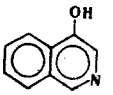
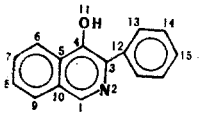
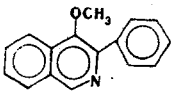
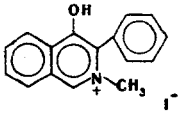
To prove the existence of these forms we used model structures. Thus 4-methoxy-3-phenylisoquinoline (III) is a model of the neutral nonpolar form (N) in neutral media and of the fixed cationic form (C) in acidic media; N-methyl-4-hydroxy-3-phenylisoquinolinium iodide (IV) models the dipolar form (D) (II) in alkaline media and its cationic form in neutral media.

The UV spectrum of II in 25% aqueous ethanol provides evidence in favor of the N and D forms in neutral polar media: of the two longwave absorption maxima of the $\pi-\pi^*$ transitions (340 and 385 nm), the former (λ_{max} 340 nm) is affiliated with neutral form N, inasmuch as it is equal to the longwave absorption maximum of II in ethanol (in which form N primarily exists) and is similar to the maximum (337 nm) of the model structure in alcohol; the other longwave maximum (385 nm), which characterizes dipolar form D, is close to the maximum (373 nm) of the absorption band of IV in alkaline media (see Table 1).

The identical character of the UV spectra in acidic media of II and III and also of IV in ethanol (the fixed cationic forms of II) indicates the presence of form C of II in acidic media (Table 1).

M. V. Lomonosov Moscow State University. Scientific-Research Institute of Organic Intermediate and Dyes, Moscow. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 9, pp. 1244-1249, September, 1975. Original article submitted October 4, 1974.

TABLE 1. UV Spectra of I-IV

	Compound	Medium	λ_{max}, nm (log ε)
I		Ethanol	209 (4,66), 230 (4,22), 295 (3,54), 319 (3,62), 331 (3,65)
		25% Ethanol	209 (4,53), 232* (4,05), 261* (3,62), 330 (3,59), 355 (3,71)
		1 *N* HCl	222* (4,49), 229 (4,53), 284 (3,45), 295 (3,43), 331* (3,86), 342 (3,93)
		1 *N* KOH	223 (4,09), 248 (4,09), 323* (3,75), 345 (3,83)
II		Ethanol	209 (4,61), 251 (4,42), 303 (3,90), 340 (3,81), 398 (3,24)
		25% Ethanol	208 (4.56), 218* (4,49), 246* (4,25), 275 (3,82), 306 (3,65), 340 (3,81), 385 (3,89)
		1 *N* HCl	211* (4,44), 217 (4,46), 246 (4,45), 302 (3,68), 350 (3,98)
		1 *N* KOH	221 (4,39), 263 (4,02), 355 (3.97)
III		Ethanol	209 (4,51), 247 (4,60), 295 (3,91), 337 (3,48), 385 (2,53)
		25% Ethanol	210 (4,56), 246 (4,48), 293 (3,88), 334 (3,50)
		1 *N* HCl	208* (4,29), 216* (4,30), 248 (4,45), 300 (3,80), 348 (3,05)
		1 *N* KOH	220* (3,97), 245 (4,33), 293 (3,78), 333 (3,51)
IV		Ethanol	213* (4,63), 215 (4,63), 252 (4,21), 310* (3,79), 340 (3,84), 392 (3,87)
		1 *N* KOH	209* (3,76), 225 (4,20), 264* (3,62), 340* (3,44), 373 (3,64)

*Shoulder.

TABLE 2. Coulombic (h_r) and Resonance (k_{rs}) Parameters and θ and r_{CC} P% Values for the Various Forms of 3-Phenyl-4-hydroxyisoquinoline

Compound form	Coulombic		Resonance			θ°	r_{CC}, Å	P%
	h_N	h_O	$k_{CC}=k_{CN}$	k_{C-O}	k_{C-C}			
N	0.70	2,00	1.00	0,85	0,50	60°	1,477	13.3
D	1.10	1,20	1,00	0.65	0,95	18°	1,447	22.4
C	1.10	2,00	1,00	0.85	0,40	66°	1,483	11.7
A	0.70	1,20	1,00	0,65	0,70	46°	1,463	17.3

The ionization of the phenolic group of 4-hydroxyisoquinoline (I) is accompanied by a bathochromic shift of the longwave $\pi-\pi^*$ band of 15 nm on passing from N to form A. A bathochromic shift of 15 nm is also observed in the UV spectrum of II on passing from ethanol to alkaline media. Consequently, II exists in anionic form A in alkaline media.

Thus, depending on the medium, II exists in forms N, D, C, and A. In addition, the spectra of ethanol solutions of II, III and IV contain λ_{max} bands at 398, 385, and 392 nm, respectively, which can apparently be assigned to $n-\pi$ bands due to transfer of electrons of the oxygen atom of the hydroxyl group from the nonbonding p atomic orbital to the free π^* molecular orbital. In fact, these maxima satisfy the fundamental features of $n-\pi^*$ transitions: they correspond to longer waves than the other longwave maxima, have the lowest intensities, and vanish in polar – acidic (1 N HCl) and alkaline (1 N KOH) – solutions (Table 1).

The UV spectral data make it possible to also evaluate the angle of rotation (θ) between the planes of the phenyl ring and the heteroring and the lengths (r_{CC}) and degree of double-bond character (P%) of the C–C bond connecting the phenyl ring and the heteroring in neutral, acidic, and alkaline media, as we also did for the analogous models [3]. It is seen from Table 2 that the phenyl ring in 3-phenyl-4-hydroxyisoquinoline is turned at an angle of 46-66° relative to the isoquinoline ring, the C–C bond length lies in the range 1.463-1.483 Å, and the double-bond character of this bond is lower by a factor of three to four than in benzene ($P_{benzene}=50\%$).

For comparison we point out that, according to the experimental data, the diphenyl molecule is planar ($\theta=0°$) in the crystalline phase [4, 5], whereas in the gas phase [6, 7] $\theta=40-45°$ ($r_{CC}=1.48-1.49$ Å). On the basis of the UV spectra and the MO LCAO method, it was found that $\theta=20°$ and $r_{CC}=1.484$ Å [8] for diphenyl. The optimal values $\theta=40°$ and $r_{CC}=1.50$ Å were found by means of a semiempirical calculation of the energy of diphenyl in the gas phase [9].

TABLE 3. Distribution of the π-Electron Density (q_r) and Orders (p_{rs}) and Lengths (r_{rs}) of the Bonds for the Various Forms of 3-Phenyl-4-hydroxyisoquinoline (II)

Form of II	No. of atom r	q_r	Bond r-s	p_{rs}	r_{rs}(Å)	Form of II	No. of atom r	q_r	Bond r-s	p_{rs}	r_{rs}(Å)
N	1	0,901	1—2	0,698	1,324	D	1	0,821	2—1	0,664	1,330
	2	1,272	2—3	0,571	1,345		2	1,419	2—3	0,512	1,356
	3	0,990	3—4	0,685	1,393		3	0,957	3—4	0,656	1,398
	4	0,945	3—12	0,203	1,477		4	0,961	3—12	0,373	1,447
	5	0,992	4—5	0,533	1,419		5	0,974	4—5	0,535	1,419
	6	0,996	4—11	0,275	1,350		6	0,997	4—11	0,286	1,348
	7	0,988	5—6	0,561	1,414		7	0,976	5—6	0,563	1,414
	8	0,998	5—10	0,518	1,421		8	0,998	5—10	0,512	1,423
	9	0,986	6—7	0,721	1,387		9	0,972	6—7	0,718	1,387
	10	1,004	7—8	0,604	1,407		10	1,008	7—8	0,605	1,407
	11	1,926	8—9	0,723	1,387		11	1,916	8—9	0,722	1,387
	12	1,001	9—10	0,554	1,415		12	1,005	9—10	0,554	1,415
	13	1,000	10—1	0,556	1,415		13	0,997	10—1	0,560	1,415
	14	1,000	12—13	0,652	1,399		14	1,000	12—13	0,617	1,404
	15	1,001	13—14	0,670	1,395		15	0,999	13—14	0,677	1,394
			14—15	0,664	1,396				14—15	0,659	1,397
C	1	0,830	2—1	0,663	1,330	A	1	0,895	2—1	0,699	1,324
	2	1,405	2—3	0,544	1,351		2	1,276	2—3	0,561	1,348
	3	0,957	3—4	0,697	1,390		3	0,983	3—4	0,672	1,395
	4	0,951	3—12	0,167	1,483		4	0,963	3—12	0,279	1,463
	5	0,975	4—5	0,529	1,420		5	0,988	4—5	0,535	1,419
	6	0,998	4—11	0,272	1,350		6	0,997	4—11	0,282	1,348
	7	0,977	5—6	0,564	1,414		7	0,987	5—6	0,561	1,414
	8	0,998	5—10	0,515	1,422		8	0,998	5—10	0,517	1,421
	9	0,974	6—7	0,720	1,387		9	0,985	6—7	0,720	1,387
	10	1,006	7—8	0,604	1,407		10	1,005	7—8	0,605	1,407
	11	1,927	8—9	0,724	1,387		11	1,918	8—9	0,722	1,387
	12	1,001	9—10	0,552	1,416		12	1,002	9—10	0,555	1,415
	13	1,000	10—1	0,564	1,414		13	1,000	10—1	0,555	1,415
	14	1,000	12—13	0,657	1,397		14	1,000	12—13	0,639	1,401
	15	1,000	13—14	0,669	1,395		15	1,001	13—14	0,672	1,395
			14—15	0,665	1,396				14—15	0,663	1,396

*See Table 1 for the numbering of the atoms.

TABLE 4. Delocalization Energies (DE) and Delocalization Energies per π Electron (DE/n) for 4-Hydroxy-Isoquinoline (I) and 3-Phenyl-4-hydroxyisoquinoline (II)

Compound and its form	$\varepsilon_\pi^{tot}\cdot\beta$	$E_{loc}^{tot}\cdot\beta$	$DE\times\beta$	$DE/n\times\beta$	$\Delta E^{RS}\times\beta$	$E_{HOMO}\cdot\beta$	$-E_{LFMO}\cdot\beta$	I (eV)
IN	18,708	14,86	3,848	0,320	—	0,558	0,593	8,07
ID	17,594	13,78	3,814	0.317	—	0,544	0,537	8,02
IC	19,240	15,38	3,860	0,322	—	0,570	0,542	8,11
IA	17,032	13,26	3,772	0,315	—	0,533	0,589	7,98
IIN	26,810	20,936	5,847	0,325	0,103	0,533	0,595	7,98
IID	25,942	20,134	5.808	0,322	0,354	0,466	0,533	7.77
IIC	27,310	21,447	5,863	0,326	0,067	0,550	0,541	8,04
IIA	25,256	19,455	5,801	0,322	0,195	0,491	0,589	7,85

The r_{CC} values that we obtained for II are close to the r_{CC} value for diphenyl; however, the angle of rotation for our compound is considerably larger than in the case of diphenyl. The fact is that the exocyclic oxygen atom of the 4-hydroxy group participates in π conjugation with its p pair of electrons, as confirmed by the presence in the UV spectrum of n-π* transitions (see above). In addition, the inductive effect of the nitrogen atom is manifested substantially. All of this leads to nonuniform distribution of the π-electron density (g_r) on the atoms in the various forms of II (Table 3). It follows from a comparison of the g_r value (1.000) and bond order p_{rs} (0.667) in benzene with the corresponding g_r and p_{rs} values in the phenyl ring of II that the interaction of the phenyl ring and the heteroring is weak. Ionization of the hydroxyl group and protonation of the ring nitrogen atom have practically no effect on the g_r and p_{rs} values in the phenyl ring of II.

The interatomic distances calculated from formula [10] from the bond orders (Table 3) are in good agreement with the experimental data on the interatomic C.... N (1.34 Å) and C.... C (1.39 Å) distances in

pyridine and the C–O distance (1.35-1.37 Å) in phenols and also with the interatomic distances in 8-hydroxyquinoline [11].

The energies (ΔE^{RS}) of conjugation or interaction of the phenyl group with the π system of I can be calculated by means of perturbation theory from the formula $\Delta E^{RS} = -p_{r-r} \cdot k_{C-C} \cdot \beta(1)$; the ΔE^{RS} values for the N, D, C and A forms of II are 0.103, 0.354, 0.067, and 0.195 β, respectively.

The delocalization energies per π electron (0.322-0.326 β) for the four forms of II are close to the $DE/n = 0.333\beta$ value in benzene. This constitutes evidence for the high degree of aromatic character of the various forms of II. The existence of the N and D forms in I and II is associated with the closeness of their DE/n values (Table 4).

EXPERIMENTAL

The electronic absorption spectra of I-IV (Table 1) were recorded with a Perkin-Elmer-402 spectrophotometer at concentrations of 10^{-4} to $2.5 \cdot 10^{-5}$ mole/liter.

The N, D, C, and A forms of I and II were calculated by means of perturbation theory within the framework of the Huckel MO (HMO) method. The linear correlation with the HMO method [12] of the absorption maximum (λ_1) of the longwave $\pi-\pi^*$ band with the difference (ΔE_1) in the energies of the lower free MO (LFMO-E_{m+1}) and the higher occupied MO (HOMO-E_m) and the ionization potential (I) with energies E_m was used in the determination of the numerical values of the coulombic (h) and resonance (k) parameters (Table 2):

$$\Delta E_1 = (E_{m+1} - E_m) \cdot \beta = \frac{1241}{\lambda_1 (нм)} \text{ (eV)}; \quad (2)$$

$$I = \alpha + E_m \cdot \beta. \quad (3)$$

The magnitudes of the coulombic ($\alpha = 6.27$ eV) and resonance ($\beta = -3.22$ eV) integrals for the carbon atom were calculated from Eqs. (2) and (3) applied to naphthalene for $\lambda_1 = 311$ nm [13], I = 8.15 eV [14], $E_m = 0.618$, and $E_{m+1} = -0.618$.

Quantitative estimates of the effect of substituents (S) on the $E_m{}^R$ and $E_{m+1}{}^R$ values and, consequently, on the $\Delta E_1{}^R$ and I^R values of the starting π system of R were obtained by means of perturbation theory [15, 16].

Let us initially examine the case of replacement in the aromatic ring of naphthalene (R) of the ≥CH group by a nitrogen atom (r), as a result of which isoquinoline (RS) is formed. In this case, within a first approximation of perturbation theory and the framework of the HMO method we will have

$$\Delta E_1{}^{RS} = \Delta E_1{}^R + (a^2_{m+1,r} - a^2_{m,r}) \cdot h_r \cdot \beta + 2[a_{m+1,r}(a_{m+1,c_1} + a_{m+1,c_2}) - a_{m,r}(a_{m,c_1} + a_{m,c_2})] k_{rc} \cdot \beta; \quad (4)$$

$$I^{RS} = I^R + [a^2_{m,r} \cdot h_r + a_{m,r}(a_{m,c_1} + a_{m,c_2})] k_{rc} \cdot \beta, \quad (5)$$

where $a_{m,r}$, $a_{m+1,r}$, a_{m,c_1}, a_{m,c_2}, a_{m+1,c_1}, and a_{m+1,c_2} are the coefficients of the AO of the r atom and of the adjacent (to r) C_1 and C_2 atoms in the m-th and m+1-th MO of the π system of R.

Substituting the experimental [13, 14] $\Delta E_1{}^R = 3.99$ eV, $\Delta E_1{}^{RS} = 3.92$ eV, $I^R = 8.15$, and $I^{RS} = 8.5$ eV [14] values into Eqs. (4) and (5), we calculate the values of the h_r and k_{rc} parameters for the nitrogen atom (Table 2).

If the unsubstituted compounds (R = I) and the substituent (S = the phenyl group) represent a π system with wave functions $\Phi_k{}^R = \sum_r a_{k,r} \cdot \chi_r$ and $\Psi_n{}^S = \sum_s b_{n,s} \cdot \chi_s$ and MO energies E_k and E_n, respectively, within a second approximation of perturbation theory we will have

$$\Delta E_1{}^{RS} = \Delta E_1{}^R + \left[\sum_n \frac{a^2_{m+1,r} \cdot b^2_{n,s}}{E_{m+1}{}^R - E_n{}^S} - \sum_u \frac{a^2_{m,r} \cdot b^2_{n,s}}{E_m{}^R - E_n{}^S} \right] k^2_{r,s} \cdot \beta, \quad (6)$$

from which we find the desired resonance parameter (k_{rs}) of the r-s bond between the terminal χ_r and χ_s AO, which is considered to be a perturbation.

If substituent S is a single atom or a group of atoms (for example, the hydroxyl group) and it is connected to the R system only by means of a σ bond that has a certain degree of double bond character due

to π conjugation of the unshared pair of electrons of the system with the π system of R, within a second approximation of perturbation theory we have the equation

$$\Delta E_1^{RS} = \Delta E_1^{R} + \left[\frac{a_{m+1,r}^2}{E_{m+1}^{R} - h_s} - \frac{a_{m,r}^2}{E_m^{R} - h_s} \right] k_{rs}^2 \cdot \beta; \quad (7)$$

$$I^{RS} = I^{R} + \frac{a_{m,r}^2}{E_m^{R} - h_s} k_{rs}^2 \cdot \beta \quad (8)$$

for the calculation of the coulombic (h_S) and resonance (k_{rs}) parameters of substituent S.

The I^{RS} value is unknown for I, and we therefore used $h_{OH} = 2$ and $h_O = 1.2$ and Eq. (7) in the calculation of the k_{rs} parameter for the oxygen of the hydroxyl group (Table 2).

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