UV SPECTRA AND BASICITY CONSTANTS OF 2-SUBSTITUTED QUINOXALINES

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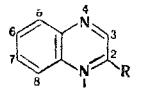
The UV spectra of the bases and cations of a number of 2-substituted quinoxaline derivatives were investigated, and their basicity constants were determined. The investigated compounds were divided into two series, characterized, respectively, by ortho and meta orientations of the substituent and cationoid center, on the basis of correlations of the pK_a values with the Hammett–Taft σ constants. The effect of the position of the protonation center relative to the substituent on the energy of the $\pi \rightarrow \pi^*$ transitions was examined within the framework of the simple MO LCAO method. The results of the calculations are compared with the experimentally observed shift in the ^1L_b band in the UV spectra of some 2-substituted quinoxalines on passing from the bases to the monocations.

The presence of two nonequivalent protonation centers (the ring nitrogen atoms in the 1 and 4 positions) in 2-substituted quinoxaline molecules corresponds to two possible structures of the monocations. The realization of one of these structures is apparently determined primarily by the electronic effects of the substituents.

The UV spectra of neutral and protonated forms of unsubstituted and 2-substituted quinoxalines I-IX were recorded to study the effect of substituents on the position of the protonation center during formation of the monocations, and the basicity constants in water of III-VII and IX were determined. The experimental results, supplemented by the data of others [1-3], are presented in Table 1.



I-XI

I R=H; II R=COOH; III R=$COOC_2H_5$; IV R=$CONH_2$; V R=Cl; VI R=OCH_3; VII R=CH_3; VIII R=NH_2; IX R=$NHCOCH_3$; X R=$NHCH_3$; XI R=$N(CH_3)_2$.

An examination of the pK_a values shows that the effect of substituents in the 2 position on the basicity corresponds to the scale of σ constants. An increase in the basicity constants as compared with the unsubstituted I molecule is observed in compounds containing substituents with high +C [NH_2,$NHCH_3$, and $N(CH_3)_2$] and +I and +C (CH_3) effects. Moreover, the electron-donor effect of amino and methylamino groups in the 2 position of quinoxaline (ΔpK_a 3.2-3.5) increases considerably as compared with 2-aminopyridine [3] (ΔpK_a 1.63) and 2-aminoquinoline [3] (ΔpK_a 2.40). This is apparently due to the substantial increase in the contribution of the effect of direct polar conjugation of the amino group with the cationoid center in the quinoxaline derivatives.

The introduction of substituents with −I, −C, and also −I and +C effects (II-VI, IX) into the 2 position of quinoxaline leads to an increase in the basicity. The trend in the decrease in the basicity constants in the order VI > IV > III > V is similar to the trend in the increase in the inductive constants of the substituents. In addition, the effect of substituents of this type on the basicity of quinoxaline proved to be considerably

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TABLE 1. UV Spectra of Bases and Cations and Basicity Constants of 2-Substituted Quinoxalines

Compound	R	Compound form*	Medium	λ_{max}, nm (lg ε)			pK_a	ΔpK_a
				^1B_b	^1L_a	^1L_b		
I	H	B	pH 6,2	234,5 (4,36)		315(3,76)	0,56[1]	—
		C	7,10 *N* H_2SO_4	242 (4,40)		332(3,88)		
II	COOH	B	0,1 *N* H_2SO_4	244,5 (4,55)		318—324(3,87)	—	—
		C	15,3 *N* H_2SO_4	254,5 (4,53)		338—346(4,01)		
III	$COOC_2H_5$	B	0,01 *N* H_2SO_4	245 (4,65)		322(3,95)	−0,70	−1,26
		C	14,1 *N* H_2SO_4	255 (4,62)		345(4,05)		
IV	$CONH_2$	B	0,01 *N* H_2SO_4	243 (4,56)		318—324(3,89)	−0,66	−1,22
		C	14,1 *N* H_2SO_4	253,5 (4,53)		335—345(3,98)		
V	Cl	B	0,01 *N* H_2SO_4	240,5—243,5 (4,45)		322—332(3,84)	−1,32	−1,88
		C	15,3 *N* H_2SO_4	250,5 (4,50)		343(3,98)		
VI	OCH_3	B	0,001 *N* H_2SO_4	223 (4,17), 242—246 (4,25)	290(3,50)	325—334(3,73)	0,08	−0,48
		C	11,4 *N* H_2SO_4	221 (4,07), 249—252 (4,25)		333—358(3,75)		
VII	CH_3	B	pH 4,50	236 (4,34)		317—325(3,76)	1,42	0,86
		C	5,22 *N* H_2SO_4	244—246 (4,39)		336(3,96)		
VIII	NH_2	B	pH 7,05	241,5—251,5 (4,26)	290—310(3,38)	354(3,80)	3,96[3]	3,40
		C	0,1 *N* H_3SO_4	232 (4,23) 253—258 (4,05)	310—325(3,70)	350(3,83)		
IX	$NHCOCH_3$	B	pH 4,02	227 (4,01) 255 (4,51)		336—344(3,93)	0,39	−0,17
		C	8,58 *N* H_2SO_4	236 (4,09) 262 (4,41)		353(4,04)		
X	$NHCH_3$[2]	B	pH 7,2	248 (4,43)	286—296(3,25)	363(3,79)	4,10	3,54
		C	pH 1,0	237 (4,29) 253—259 (4,06)	304—312(3,74)	352(3,85)		
XI	$N(CH_3)_2$[2]	B	pH 7,2	254 (4,40)	296—304(3,17)	382(3,84)	3,72	3,16
		C	pH 1,0	241—253 (4,22)	314—320(3,72)	368(3,93)		

* B is base, and C is monocation.

TABLE 2

Reaction series	σ	Q	ρ	r*
1	σ_{meta}	0,55	−4,25	0,954
1	σ_{para}	−0,15	−1,56	0,647
2	σ_{meta}	0,84	−12,88	0,919
2	σ_{para}	0,59	−4,26	0,982

* Symbol r is the correlation coefficient for the dependence $pK_a = \rho\sigma + Q$.

TABLE 3

Structure of the monocation	R	Cationoid center	E_D (β)	$\Delta E_{\pi\to\pi^*}$ (β)		^1L_b (λ_{max}, nm)		Δλ, nm
				m→m+1	m−1→m+1	base†	cation	
Ia(Ib)	H	$N_1(N_4)$	3,60	−0,172	−0,265	316	332	16
Va	Cl	N_1	3,70	−0,173	−0,269	328	343	15
Vb		N_4	3,64	−0,173	−0,262			
VIa	OCH_3	N_1	4,03	−0,095	−0,222	336	358	22
VIb		N_4	3,93	−0,213	−0,253			
VIIIb		N_4	4,02	−0,293	−0,207			
VIIIa	NH_2	N_1	4,18	−0,014	−0,151	354	350	−4
VIIIc		N_1	4,32	+0,084	−0,119			
VIIId		N_1	4,51	+0,092	−0,016			

†The experimental data for bases I, V, and VI pertain to solutions in n-heptane [11].

less than that observed in the corresponding 2-substituted pyridines and quinolines. Thus the ΔpK_a value (−1.88) of 2-chloroquinoxaline is lower by a factor of ~2.5 than the value for 2-chloropyridine [4] (−4.45). The ΔpK_a values in a number of 2-methoxy derivatives of pyridine [5], quinoline [5], and quinoxaline are −1.95, −1.77, and −0.48, respectively. Since the inductive effect also predominates in the effect of substituents of this type on the basicity constants of pyridine and quinoline [6], the noted differences in the ΔpK_a values may indicate a change in the position of the protonation center relative to the substituent in quinoxaline derivatives III-VI.

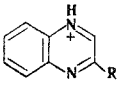
Correlation of the ΔpK_a values of 2-substituted quinoxalines with the inductive constants (σ_i) and conjugation constants (σ_c^0) [7] showed that the investigated compounds are divided into two series. Except for the $NHCOCH_3$ group, the substituents that lower the basicity of quinoxaline lie on a single line on the graph of the dependence of the $\Delta pK_a/\sigma_c^0$ values on σ_i/σ_c^0 (Fig. 1):

$$\Delta pK_a = -4.378\sigma_i - 1.066\sigma_c^0 + 0.085. \quad (1)$$

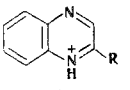
The points that correspond to electron-donor substituents (VII, VIII, X, and XI), which raise the basicity of quinoxaline, and to the $NHCOCH_3$ group lie below line (1) and form another series:

$$\Delta pK_a = -7.066\sigma_i - 8.010\sigma_c^0 - 0.127. \quad (2)$$

The separation of 2-substituted quinoxalines into two series apparently corresponds to two different protonation centers during the formation of the monocations. It is known that 2-aminoquinoxaline is protonated at N_1 [2]; it is natural to assume that protonation of all of the rest of the compounds of this series also occurs at this center to form monocations VIIa-XIa. The structures of the cations of compounds that lie on line (1) correspond to the addition of a proton to N_4 (IIIb-VIb).*



IIb-VIb



VIIa-XIa

The correlation of the ionization constants (pK_a) with the Hammett σ_{meta} and σ_{para} constants [8] is examined for each of the series obtained (Table 2). Satisfactory correlation for series (1) is obtained only

*2-Carboxyquinoxaline (II), the pK_a of which could not be determined by spectrophotometry, can also be assigned to this series.

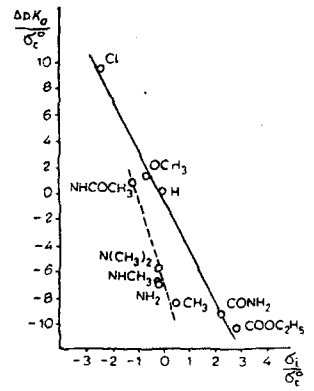


Fig. 1. Correlation of the ΔpK_a values in 2-substituted quinoxalines with the σ_i and σ_c^0 substituent constants.

when σ_{meta} constants are used (r = 0.954), while satisfactory correlation (r = 0.982) is obtained for series (2) only with σ_{para} constants. This result and the relative values of the coefficients of σ_i and σ_c^0 in Eqs. (1) and (2) are in agreement, respectively, with meta and ortho orientations of the substituent and the cationoid center in these series.

The effect of the relative orientation of the substituent and the cationoid center on the changes in the UV spectra on passing from the base to the corresponding monocations was examined in addition to the correlation analysis of the ionization constants. Three absorption bands, previously classified (Platt) in order of increasing energy as ^1L_b, ^1L_a, and ^1B_b types [9, 10], are observed in the spectra of the neutral molecules of the investigated compounds at 210-400 nm. Perkampus [10] has shown that the observed vibrational structure of the long-wave absorption pertains mainly to the ^1L_b band. The ^1L_a band does not appear in the spectra of most of the 2-substituted quinoxalines because of overlap with the vibrational quantum of the ^1L_b band.

An examination of the data in Table 1 demonstrates that the transition from the bases to the monocations of most of the investigated compounds is accompanied by a long-wave shift of the observed absorption bands. The most noticeable bathochromic shift and distinct increase in intensity is experienced by the low-energy ^1L_b band ($\Delta\lambda$ = 9-24 nm). An exception to this is observed in the case of 2-amino- and 2-methylamino derivatives of quinoxaline (VIII, X, and XI), the protonation of which leads to a short-wave shift in the ^1L_b band of 4-14 nm.

Our previous calculation of the electronic spectra of quinoxaline (I) and its 2-chloro (V), 2-methoxy (VI), and 2-amino (VIII) derivatives by the Pariser–Parr–Pople method with allowance for interaction of 12 singly excited configurations [11] demonstrated that the long-wave ^1L_b band is due to the interaction of predominantly (by 94-98%) two configurations corresponding to the one-electron $\psi_m \rightarrow \psi_{m+1}$ and $\psi_{m-1} \rightarrow \psi_{m+1}$ transitions (m is the upper occupied MO here). This makes it possible to qualitatively examine the effect of the position of the protonation centers of molecules of I, V, VI, and VIII on the relative changes in the energies of the indicated transitions within the framework of the simple MO LCAO method.

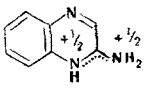
To carry out this examination, we calculated the energy indexes of the neutral and protonated forms of I, V, VI, and VIII molecules by the simple MO LCAO method with the Pullman parameters [12]. The calculated changes in the energies of the examined $\pi \rightarrow \pi^*$ transitions, which are due to protonation of the molecules at both the N_1 atom and the N_4 atom, are compared in Table 3 with the experimentally observed shift in the ^1L_b band. In the case of the calculation of the two protonated forms of 2-chloroquinoxaline (Va and Vb), it can be seen that protonation at both N_1 and N_4 leads to correspondingly close changes in the energies of both of the transitions under consideration in the presence of a substituent with a high −I effect (to the degree to which this is taken into account by the relative changes in the parameters used). In this case, both ΔE in V are close to the corresponding values found for the unsubstituted I molecule. This result is in agreement with the close values of the bathochromic shift of the ^1L_b band ($\Delta\lambda$) observed during protonation of these compounds. In addition, it follows from these data that for substituents of this type comparison of the calculated and experimental changes in the energy of the ^1L_b band does not enable one to draw any conclusions regarding the position of the protonation center of the molecule.†

A decrease in the −I effect and a simultaneous increase in the +C effect of the substituent in VI and, particularly, in VIII leads to a more selective effect of protonation on the relative changes in the energies of both transitions. It follows from the results of the calculation that protonation of 2-methoxyquinoxaline at the N_1 atom should lead to a lesser decrease in the energy of the ^1L_b transition as compared with the unsubstituted I molecule, while protonation at the N_4 atom should lead to a greater decrease in this energy. A comparison of the $\Delta\lambda$ values observed in I and VI shows that the experimental data are in better agreement with the structure of monocation VIb.

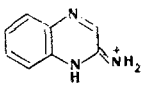
A comparison of the calculated and experimental data for 2-aminoquinoxaline also confirms the conclusion that this molecule is protonated at N_1, and the energy indexes calculated for monocation structures

†This conclusion is undoubtedly limited by a consideration of the energy indexes within the framework of the simple MO LCAO method. Calculation of the energies of the transitions in the monocations by more rigorous methods will possibly lead to a different result.

that correspond to delocalization of the positive charge on the exocyclic amino group (VIIIc and VIIId) are in best agreement with the experimental data. It is interesting to note that structure VIIId also corresponds to the greatest energetic favorability of the monocation; this is quite distinctly manifested in the relative delocalization energies (E_D).



VIIIc



VIIId

EXPERIMENTAL

The UV spectra of the compounds were recorded with a Hitachi EPS-3 spectrophotometer. The basicity constants were determined spectrophotometrically at 25° in aqueous solutions of sulfuric acid with a known acidity function (H_0) [13, 14]. The concentrations of the sulfuric acid solutions were determined by potentiometric titration with an LP-58 potentiometer with an electrode pair (glass electrode–saturated calomel electrode). The optical densities at the analytical wavelengths were measured with an SF-4 spectrophotometer.

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