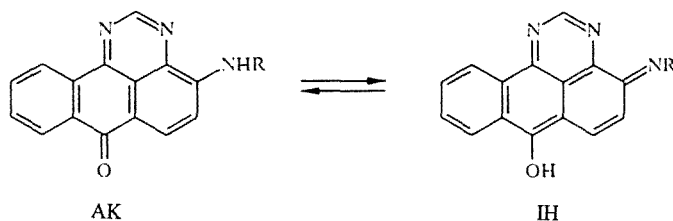


## SPECTROSCOPIC AND QUANTUM CHEMICAL STUDY OF THE STRUCTURE OF 4-AMINOPYRIMIDINOANTHRONES

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*4-Amino derivatives of pyrimidinoanthrone exist in the form of an aminoketone isomer in the crystalline state in neutral organic solutions, but in acid and alkaline media the tautomeric equilibrium is shifted toward formation of ionic forms of the iminohydroxyl tautomer. We present the characteristics of the IR and electronic absorption spectra and quantum chemical calculations for the neutral and ionic forms of the tautomers indicated above.*

Earlier [1-3] it was shown that pyrimidinoanthrones and pyrimidinoanthrone structures have properties characteristic of benzanthrones. These properties include enhanced basicity of the oxygen of the ketone group. Upon introduction of an amino group into these molecules, we may expect competition for addition of a proton between the amine and ketone groups. The presence of primary or secondary amino groups in the 4 position creates the prerequisites for the existence of amino derivatives of pyrimidinoanthrone in the form of aminoketone (AK) and iminohydroxyl (IH) tautomers:



I R - Ph; II R - H; III R - Bu

This paper is devoted to the spectroscopic and quantum chemical study of the structure of 4-anilinopyrimidinoanthrone (I), 4-aminopyrimidinoanthrone (II), and 4-butylaminopyrimidinoanthrone (III) in different media. Furthermore, we investigated 4-morpholinopyrimidinoanthrone (IV), which is a fixed form of the AK tautomer of 4-aminopyrimidinoanthrone.

In the region of vibrations of the C=O groups in the IR spectrum of compound I in KBr pellets, we observe a triplet band (1663/1653, 1643  $\text{cm}^{-1}$ ), and in  $\text{CCl}_4$  solution we observe a doublet at 1667/1653  $\text{cm}^{-1}$  (Table 1). The observed splitting is most likely due to Fermi resonance. In the spectrum of compound IV we observe a single band at 1645  $\text{cm}^{-1}$ ; in the spectrum of the unsubstituted pyrimidinoanthrone in KBr, we observe a band at 1670  $\text{cm}^{-1}$  [4]. The decrease in  $\nu\text{C}=\text{O}$  in the spectrum of compound IV compared with  $\nu\text{C}=\text{O}$  in the spectra of compound I and the unsubstituted pyrimidinoanthrone can be explained by the effect of the morpholine group.

In the region of stretching vibrations of the NH bond in the spectrum of compound I, we observe a narrow band at 3360  $\text{cm}^{-1}$  in dilute  $\text{CCl}_4$  solution ( $10^{-2}$ - $10^{-3}$  M), while in the crystalline state we observe a band at 3300  $\text{cm}^{-1}$ ; i.e., we can say that the NH group is connected by an intramolecular hydrogen bond with a ring nitrogen atom [5]. Thus the presence of bands for the stretching vibrations of the NH and C=O bonds in the IR spectra of compounds I-IV suggest the existence of these compounds in the AK form.

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TABLE 1. IR Spectra of Compounds I-IV (KBr),  $\nu$ ,  $\text{cm}^{-1}$

I	I'	III	III'	IV	IV'	Assignment
3300 m <sup>*2</sup>	3360 m	3367 w	3387 m			$\nu_{\text{NH}}$
1663 vs	1667 vs	1663 s	1670 s		1680 s	$\nu_{\text{CO}}$
1653 shldr	1653 shldr	1653 shldr		1645 vs	1656 m	
1643 m		1633 m	1642 m			

\*In  $\text{CCl}_4$  solution. <sup>2</sup>Qualitative estimates of intensity: m) medium; w) weak; s) strong; vs) very strong; shldr) shoulder.

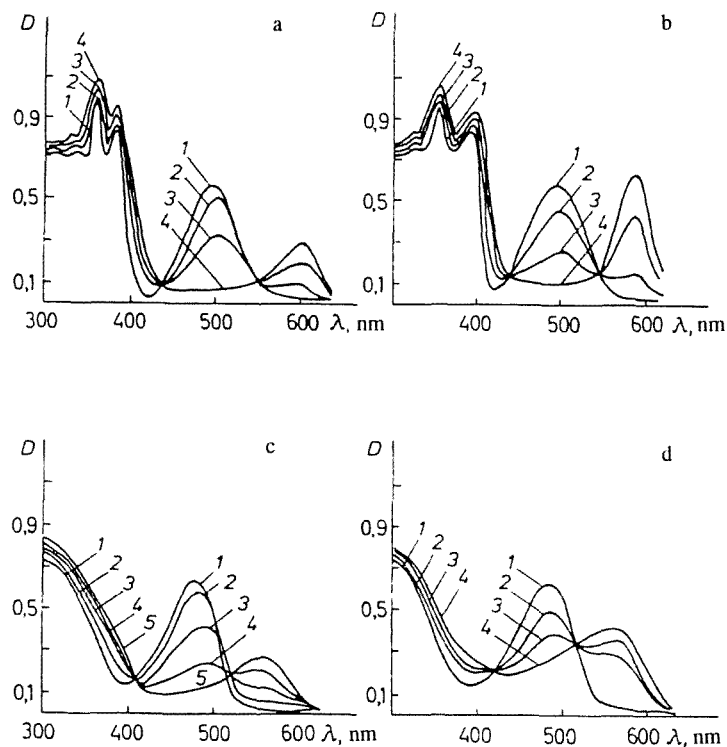


Fig. 1. Electronic absorption spectra of compounds I and II in the system 2-propanol- $\text{H}_2\text{SO}_4$  (a and c) and in system 2-propanol-KOH (b and d): 1) compound I or II in 2-propanol; 2-4(5) compound I or II in propanol with successive increase in the  $\text{H}_2\text{SO}_4$  or KOH concentration.

The electronic absorption spectra of compounds I-IV in solutions are presented in Table 2 and in Fig. 1. They are characterized by a long-wavelength band with  $\lambda_{\text{max}} = 476-495$  nm. Since the maximum of the long-wavelength band of the fixed AK tautomer (compound IV) is close to that for the rest of the compounds I-III, we can say that the values of  $\lambda_{\text{max}}$  found for compounds I-II are characteristic of the AK tautomers of these compounds.

As we see from Fig. 1, with a decrease in the pH of the solutions of compounds I-III in isopropyl alcohol, with addition of  $\text{H}_2\text{SO}_4$ , the long-wavelength band in the spectrum undergoes a bathochromic shift by 76-104 nm. The isobestic points in the spectra suggest the presence in solution of a neutral and protonated forms in equilibrium. The molecules I-III have several proton-acceptor centers: amino-, keto groups and ring nitrogen atoms. Based on the basicity of these groups in the

TABLE 2. Electronic Absorption Spectra of Compounds I-IV in Different Media

Compound	Solvent	$\lambda_{\max}$ , nm ( $\epsilon \cdot 10^{-3}$ )
I	2-Proponal	220 (21,1), 240 (33,2), 311 (7,0), 368 (8,5), 386 (7,6), 495 (4,1)
	2-Proponal + H <sub>2</sub> SO <sub>4</sub>	220 (45,2), 270 (44,4), 311 shldr 373 (8,5), 392 (7,6), 599 (2,3)
	2-Proponal + KOH	222 (41,8), 240 (40,3), 311 (6,3), 368 (8,5), 388 (7,6), 588 (4,7)
	DMF	338 (13,6), 368 (13,0), 389 (10,4), 495 (9,8)
	DMF + H <sub>2</sub> SO <sub>4</sub>	368 (15,8), 389 (13,8), 592 (1,8)
	DMF + NaOH	338 (21,2), 421 shldr 562 (13,4), 617 (10,6)
II	2-Proponal	219 (6,9), 263 (15,9), 314 (3,2), 483 (7,9)
	2-Proponal + H <sub>2</sub> SO <sub>4</sub>	221 (17,0), 268 (21,6), 280 shldr 314 (7,8), 562 (3,0)
	2-Proponal + KOH	221 (20,2), 254 (11,4), 263 (12,6), 328 (3,7), 483 (5,5), 568 (4,4)
	DMF	368 (1,3), 472 (7,4)
	DMF + H <sub>2</sub> SO <sub>4</sub>	388 shldr 549 (2,2)
	DMF + NaOH	400 shldr 581 (6,8), 617 (6,5)
III	2-Proponal	210 (21,9), 236 (30,7), 254 (19,7), 264 (20,8), 309 (7,9), 338 (7,9), 362 (8,8), 380 (7,8), 492 (7,1)
	2-Proponal + H <sub>2</sub> SO <sub>4</sub>	221 (46,2), 270 (51,5), 313 (15,9), 358 (11,2), 382 (11,6), 397 shldr 521 (2,1), 581 (2,7)
	2-Proponal + KOH	223 (23,4), 236 (23,4), 254 (18,2), 264 (17,5), 309 (7,5), 340 (10,8), 364 (11,1), 382 (11,6), 493 (6,7), 609 shldr
	DMF	338 (8,9), 362 (9,6), 380 (8,1), 492 (5,2)
	DMF + H <sub>2</sub> SO <sub>4</sub>	353 (11,6), 377 (10,7), 391 shldr 581 (1,9)
	DMF + NaOH	346 (9,6), 362 (10,7), 380 (10,4), 568 (10,0), 606 (10,7)
IV	2-Proponal	222 (10,4), 265 (13,2), 324 (2,3), 478 (5,0)
	2-Proponal + H <sub>2</sub> SO <sub>4</sub>	220 (18,4), 263 (23,4), 362 (10,0), 387 shldr
	2-Proponal + KOH	222 (14,8), 262 (13,5), 324 (2,5), 487 (5,3)
	DMF	372 shldr 476 (9,1)
	DMF + H <sub>2</sub> SO <sub>4</sub>	386 shldr 478 (4,1)
	DMF + NaOH	372 shldr 488 (7,3), 602 (0,9)

molecules, analogs of which are moieties of the tautomers of 4-aminopyrimidinoanthrone, they can be arranged in the following series according to decreasing proton-acceptor ability: NH<sub>2</sub> > NHPH > N=C > C=O. In fact, in aminopyrimidines, the pK<sub>a</sub> (NH<sub>2</sub>) is 2.6-5.7; in pyrimidine, the pK<sub>a</sub> (N=C) is 1.3 [6]; in benzanthrone, the pK<sub>a</sub> (C=O) is equal to -0.5 [2]. Consequently, taking into account the basicity of the proton-acceptor centers in molecules I-III, we should expect centers in molecules I-III, we should expect protonation first at the amino group of the AK tautomer, and then at the nitrogen atoms of the pyrimidine moiety and the ketone group.

We know [7] that upon protonation of the amino group, the unshared p electron pair of the nitrogen atom is blocked by protons, which leads to its exclusion from conjugation with the aromatic  $\pi$ -system. The result of this exclusion should be the disappearance of the long-wavelength ( $\sim 480$  nm) band of the  $\pi l - \pi^*$  transition in the spectrum. Such disappearance of the band due to protonation at the amino group is observed in the spectrum of compound IV in acidic media (Table 2). The observed shift (by 76-104 nm) in the spectra can be explained by three types of monoprotonation: a) the nitrogen atom of the pyrimidine moiety of the AK tautomer is protonated; b) the nitrogen atom of the imino group of the IH tautomer is protonated, with formation of an intramolecular hydrogen bond with the cyclic nitrogen atoms; c) the oxygen atom of the keto group is protonated, analogously to benzanthrone.

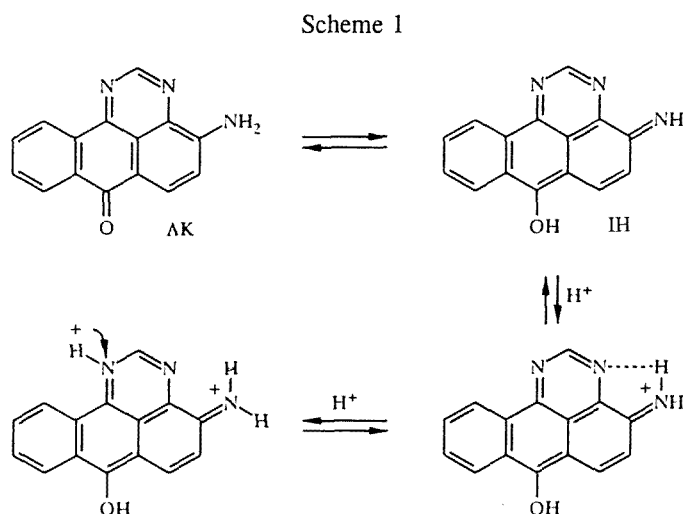
The first type of protonation should lead to a bathochromic shift of the long-wavelength band of the  $\pi l - \pi^*$  transition and a significant increase (by a factor of 1.5-2) in its intensity [7, 8]. Thus in spectra of protonated aminopyrimidines and aminoquinolines, the bathochromic shift of the band compared with the neutral form is equal to 17-60 nm, and the increase in intensity  $\epsilon_{\max}$  in this case is 1.2-1.5 times [6]. We should note that the increase in the intensity of the long-wavelength band is due to the increase in sp<sup>2</sup> hybridization of the amino group. The second type of protonation at the nitrogen atom of the imino group of the IH tautomer is more consistent with the observed spectrum of compounds I-III, since the proposed protonation of the IH tautomer also should lead to a bathochromic shift of  $\lambda_{\max}$  of the band. Furthermore, under these conditions

TABLE 3. Calculated Characteristics\* of Tautomeric and Ionic Forms of 4- Aminopyrimidinoanthrone

Molecule	$E\sigma$ , eV	$E\pi$ , eV	$\Delta H$ , eV	M, eV	$\mu$ , D	Homo eV	Lumo eV
AK	79,53	30,65	149,65	2,39	5,6	-8,22	-2,87
IH	79,41	29,54	148,82	1,32	6,9	-8,27	-2,98
AK · H <sup>+</sup> (N <sub>am</sub> )	79,53	29,62	152,21	1,54	2,6	-9,06	-3,12
IH · H <sup>+</sup> (N <sub>pm</sub> )	79,50	30,11	153,32	2,44	9,9	-8,61	-3,35

\* $E\sigma$  and  $E\pi$ ) energies of the  $\sigma$  and  $\pi$  bonds;  $\Delta H$ ) energy of atomization; M) solvation coefficient;  $\mu$ ) dipole moment;  $E_{\text{HOMO}}$  and  $E_{\text{LUMO}}$ ) energies of the highest occupied and the lowest unoccupied molecular orbitals.

diprotonation is possible: at the imine atom and at a ring nitrogen atom. This is consistent with the fact that the pyrimidine adds a single proton [6]. Based on the above, diprotonated pyrimidinoanthrone may be represented in the form of Scheme 1.



We can also propose a third type of protonation, involving protonation of the oxygen atom of the ketone group of the AK tautomer. But this hypothesis is not consistent with the nature of the protonation of the fixed AK tautomer IV, which is protonated with formation of the ammonium form.

Evidence in favor of the tautomeric equilibrium considered above ( $\text{AK} \rightleftharpoons \text{IH}$ ) for compounds I-III is the nature of the change in the spectra of these compounds upon going from a neutral medium to a basic medium. As we see from Fig. 1, with an increase in the pH of the medium, the long-wavelength band for compounds I-III undergoes a bathochromic shift by 85-134 nm. The process is reversible, i.e., upon addition of acid to a basic solution of compounds I-III, the spectrum returns to its original form. The spectrum of the fixed form of the AK tautomer (compound IV) in basic medium is practically unchanged. In order to explain the observed shift, we can propose the following: a) dissociation of the OH group of the IH tautomer occurs; b) the NH bond of the amino group of the AK tautomer dissociates. In both cases, we should observe a bathochromic shift and a single anion (common to both tautomers) should be formed. Based on the acidity constants of the phenol OH ( $\text{pK}_a = 7.0-10.0$ ) and the aromatic NH groups ( $\text{pK}_a = 19$  for nitroaniline [6]), we should expect that dissociation of the IH form is most likely. The AK form under these conditions practically does not dissociate. The invariance of the spectrum of the fixed AK tautomer (compound IV) in basic medium contraindicates the possibility of dissociation of the aromatic CH bonds.

Thus examination of the IR and UV absorption spectral data as a function of the pH of the medium allows us to conclude that primary and secondary 4-aminopyrimidinoanthrones exist in two equilibrium tautomeric forms (AK and IH), and the equilibrium is strongly shifted toward the AK tautomer in neutral media while in acidic and basic media it is shifted toward the ionic forms of the IH tautomer.

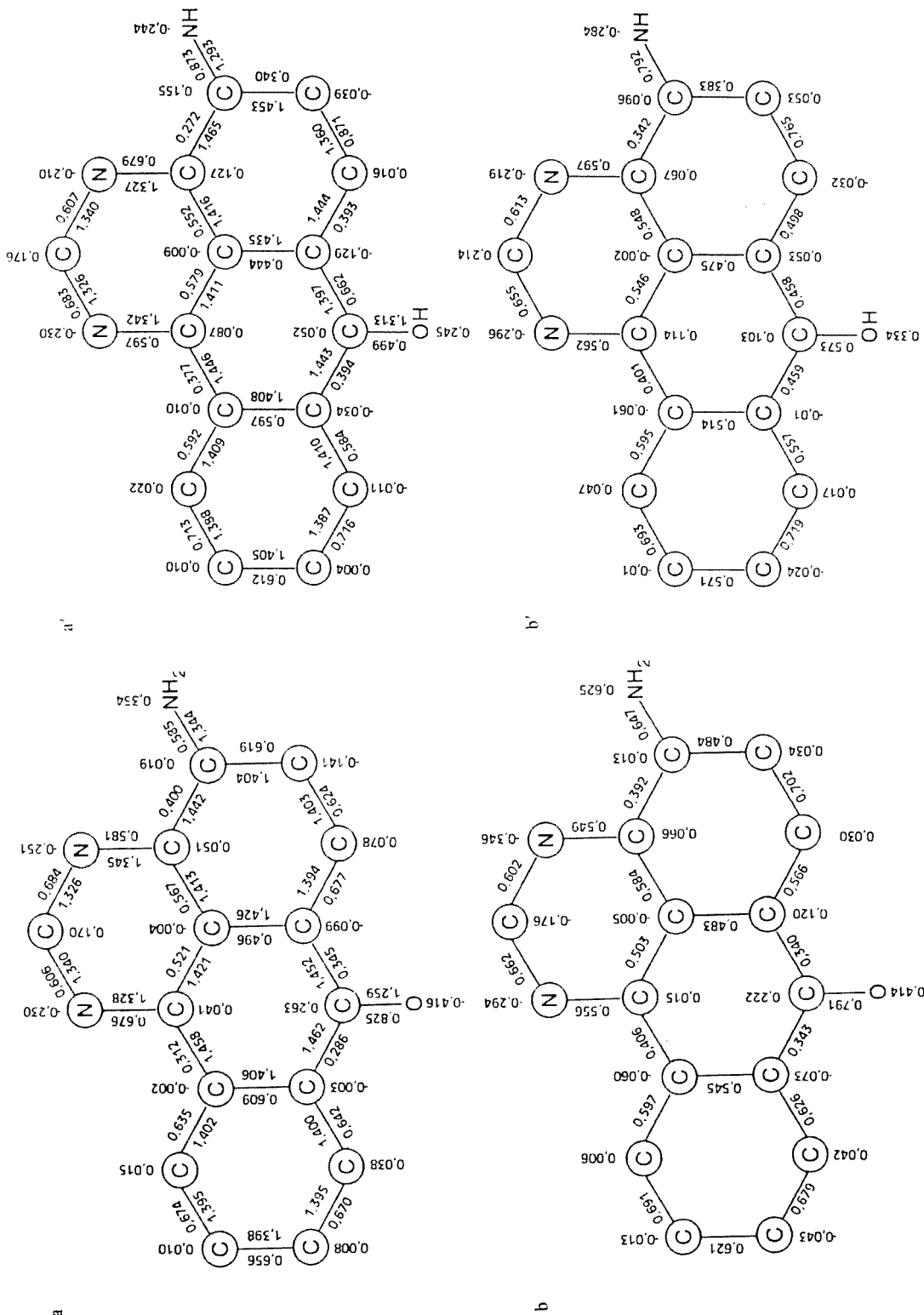


Fig. 2. Molecular diagram of ground states of AKL (a) and IH (a') tautomers and the first excited states of the AK (b) and IH (b') tautomers of compound II. The  $\pi$ -charges are indicated on the atoms of the molecules; the bond orders are indicated on the bonds; and for the molecules in the ground state, the bond lengths are given in Å.

In order to estimate the stability of the tautomers and to interpret the UV spectra, we performed a quantum chemical calculation by the PPP method for the neutral AK and IH tautomeric forms of molecule I, and also the AK tautomer protonated at the amine nitrogen atom ( $\text{AK}\cdot\text{H}^+$  ( $\text{N}_{\text{am}}$ )) and the IH tautomer protonated at the imine nitrogen atom ( $\text{IH}\cdot\text{H}^+$  ( $\text{N}_{\text{im}}$ )). From Table 3 we see that the heat of atomization  $\Delta H$  and the solvation coefficient  $M$  for the AK tautomer are respectively 0.83 eV and 1.07 eV higher than for the IH tautomer. This result, indicating higher stability for the AK tautomer, is consistent with experimental data on the presence of the AK tautomer in neutral solutions and the crystalline state. At the same time, the atomization energy and the solvation coefficient of the IH tautomer monoprotonated at the imine nitrogen atom of the IH tautomer is 1.11 eV and 0.90 eV higher than for the AK tautomer monoprotonated at the amine nitrogen atom. This calculation result indicates higher stability for the protonated form of the IH tautomer and is consistent with the conclusion drawn on the basis of experimental data that in acidic solutions compounds I-III exist as the protonated forms of the IH tautomer. From Table 3 we see that the energy of the  $\sigma$  bonds vary little with a change in the tautomeric or ionic form of compound II, while the stability of a specific form is due to changes in the energy of the  $\pi$ -bonds of the molecule.

Analysis of the molecular orbital composition of the AK tautomer showed that the HOMO contains a large contribution (25%) from the  $\pi$ -AO of the amine nitrogen atom (the unshared electron pair). At the same time, the contribution from this AO to the LUMO (the lowest unoccupied MO) is considerably less (6%). Protonation at this atom lowers the energy of both MO's, but the energy of the HOMO is lowered to a greater extent (Table 3), which predetermines the significant hypsochromic shift observed, as already noted, in the case of protonation of compound IV. The contribution of the  $\pi$ -AO of the imine nitrogen atom of the IH tautomer to the LUMO is somewhat greater than its contribution to the HOMO (14% and 12% respectively). Therefore upon protonation of the IH tautomer at the imine nitrogen atom, the energy of the LUMO is lowered to a greater extent than the energy of the HOMO (Table 3), which is responsible for the bathochromic shift. Moreover, the differences in the MO populations are not great and cannot explain the significant bathochromic shift observed in the experiment. The latter obviously is connected with the fact that the proton also interacts simultaneously with the ring nitrogen atom forming the intramolecular hydrogen bond. Since the  $\pi$ -AO of the ring nitrogen atom makes a contribution only to the LUMO (5%), protonation of this atom also leads to a bathochromic shift.

The calculated bond lengths and  $\pi$  charges at the atoms of the AK and IH tautomers in the gas phase for flat molecules with bond angles of  $120^\circ$  are presented in Fig. 2. The significantly shortened C-N bond length of the amino group and the positive charge  $0.5\bar{e}$  at the nitrogen atom suggest strong conjugation of the amino group with the  $\pi$  system of the benzene ring. In the pyrimidine ring, the C-N bonds are shortened; there is excess negative charge ( $0.259\bar{e}$ ) at the nitrogen atoms, i.e., they are strong electron acceptors. The bond length of the ketone group is increased compared with the length of this group. For example, in quinones [9], the negative charge on the oxygen atom ( $0.426\bar{e}$ ) suggest electron-acceptor character of the C=O group. In the IH molecule, the length of the imino bond corresponds to almost a C=N double bond. The length of the CO bond of the hydroxyl group is shortened compared with the bond length in phenols and naphthols [9]. This suggests strong interaction between the OH group and the  $\pi$ -aromatic system. The positive  $\pi$  charge on the oxygen atom is due to the donor properties of the OH group. The imino group and the pyrimidine ring are acceptors.

## EXPERIMENTAL

The IR spectra were recorded in the  $4000\text{-}400\text{ cm}^{-1}$  region of a Specord IR-75 spectrophotometer in the crystalline state in KBr pellets and in  $\text{CCl}_4$  solutions. The electronic absorption spectra were recorded in the 200-700 nm region on a Specord UV-vis spectrophotometer in 2-propanol and DMF solutions with concentrations  $1\cdot 10^{-4}$ - $1\cdot 10^{-5}$  M. The quantum chemical calculations for the tautomeric and ionic forms of molecule I were performed by the Pariser-Parr-Pople method with optimization of the interatomic distances with respect to the minimum in the heat of atomization [11].

The elemental analysis data with respect to C, H, and N for compounds I, IV correspond to the calculated values.

Compound I-IV were synthesized according to the techniques in [10].

**4-Aminopyrimidinoanthrone ( $\text{C}_{15}\text{H}_9\text{N}_3\text{O}$ ).** 1 g of 4-chloropyrimidinoanthrone, 20 ml of the corresponding amine, and 0.1 g copper acetate were stirred with heating for 1 h until disappearance of the starting material. The reaction was monitored by TLC on Silufol UV-254 plates. The reaction mass was cooled down to room temperature, 50 ml of a 2% HCl solution was added, and the residue was filtered. This was dried and recrystallized.

**4-Anilinopyrimidinoanthrone (I, C<sub>21</sub>H<sub>13</sub>N<sub>3</sub>O).** The reaction was done at 150-160°C by treatment of the 4-chloro derivative with aniline. Obtained: 1.32 g (95% yield) 4-chloroderivative with aniline. Obtained: 1.32 g (95% yield) 4-aminopyrimidinoanthrone II. mp 212-213°C (from toluene).

**4-Morpholinopyrimidinoanthrone (IV, C<sub>19</sub>H<sub>15</sub>N<sub>3</sub>O<sub>2</sub>).** The reaction was done at 70°C. Obtained: 1.26 g (97% yield) 4-morpholinopyrimidinoanthrone. mp 254-255°C (from petroleum ether, 80-100°C).

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