REACTION OF 6-AMINOPYRIMIDINOANTHRONES WITH MINERAL ACIDS

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How 6-amino derivatives of pyrimidinoanthrone react with mineral acids has been established by IR and electronic spectroscopy and quantum mechanical calculations. Monoprotonation occurs at the cyclic nitrogen in position 3 and the second protonation occurs at the oxygen atom of the carbonyl group.

It has been shown previously that pyrimidinoanthrones are protonated by concentrated acid at the nitrogen atom of the pyrimidine ring and at the oxygen atom of the carbonyl group [1]. The possibility of protonation of pyrimidinoanthrones at the carbonyl group follows from their similarity to benzanthrones which interact with mineral acids and with transition metal salts at the carbonyl group [2].

This paper is concerned with the interaction of 6-amino derivatives of the pyrimidinoanthrones I-VI with mineral acids studied by IR and electronic spectroscopy and also by quantum mechanical calculations. Along with the amino derivatives, unsubstituted pyrimidinoanthrone (VII) and its 6-chloro- (VIII) and 6-hydroxy derivatives (IX) were also examined.



I R = morpholino , II R = NHC₂H₄OH, III R = NHC₆H₅, IV R = NHCOC₆H₅, V R = NHC₄H₉, VI R = NH-C₆H₂(CH₃)₃-2,4,6, VII R = H, VIII R = CI, IX R = OH

Compared with compounds VII and VIII, there is an additional coordination center in the 6-amino derivatives, nitrogen atom of the amino group which is, firstly, capable of protonation and, secondly, may change the basicity of other atoms, particularly the oxygen atom of the carbonyl group. In addition the possibility of the transformation of compounds II-VI from the ketoamine tautomer (A) to the hydroxyimine tautomer (I) must be considered. Since compound I is fixed in the form of tautomer A, its interactions with acids should be characteristic of such a tautomer.



It can be seen from Table 1 that frequency of the carbonyl stretching frequency is decreased by 35-39 cm⁻¹ in comparison with the unsubstituted pyrimidinoanthrone VII and its 6-chloro derivative VIII when the morpholine group is introduced at position 6. Such a decrease in $\nu(C=O)$ may be connected with the inclusion of the unshared pair of electrons of the exocyclic nitrogen atom in the conjugated system of the ring via the ionic canonical form: the greater the polarity of the C=O bond, the lower its bond order, and $\nu(C=O)$ is decreased.

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1	II	111	١V	v	VI	VII	VIII	IX
			1600 vs	1660 VS	1667 5	1667 VS	1668 VS	
1632 s	1630 s	1629 vs	1631 \$	1629 m	1002 3	1007.13	1000 (3	1634 vs
1609 w	1602 W	1615 m	1609 m	1612 m	1625 m	1611 m	1595 \$	1610 15
1592 w	1595 m	1602 s	1595 W	1592 s	1589 m	1590 s	1588 s	1586 w
1582 m	1572 vs	1572 m	1579 s	1569 m	1572 w	1562 m	1558 m	1573 m
1545 m	1548 w	1551 W	1548 S	1545 m	1535 w	1540 5	1534 m	

TABLE 1. IR Spectra of Compounds I-IX (KBr) (ν , cm⁻¹) in the 1700 to 1500 cm⁻¹ Range



The IR spectrum of compound in CCl₄ contains two bands at 1640 and 1675 cm⁻¹ in the ν (C=O) region, the first of which is about twice as intense as the second. The presence of two ν (C=O) bands is most likely due to the presence of two rotamers in solution: in the first (with ν (C=O) 1640) the unshared pair of electrons of the nitrogen atom is included in π -conjugation with the pyrimidinoanthrone system, while in the second (with ν (C=O) 1675 cm⁻¹) the unshared pair is not involved in conjugation. The low value of ν (C=O) for crystalline I shows that the first isomer is present.

The values of $\nu(C=O)$ in the IR spectra of compounds II-IV fall in the range 1631-1629 cm⁻¹, which is practically the same for compounds I and IX. The low values for $\nu(C=O)$ may be caused by intramolecular hydrogen bonding as observed for compound IX [3] and with a conjugative effect similar to that for compound I. The broad diffuse N-H stretching bands observed in the IR spectra of compounds in CCl₄ solution also indicates the presence of strong hydrogen bonds.

In the IR spectra of compounds V and VI, $\nu(C=O)$ is at 1669 and 1662 cm⁻¹ respectively, which is close to that in the unsubstituted pyrimidinoanthrone VII. Retention of the C=O bond order in this case may be linked to a considerably smaller conjugation of the nitrogen lone pair with the pyrimidinoanthrone system in comparison with compounds I-IV, possibly because of steric strain resulting from bulky substituents on the amino group: butyl in V (in comparison with hydroxyethyl in II) and trimethylphenyl in VI (compared with phenyl in III).

The high value of $\nu(C=O)$ (1699 cm⁻¹) for the acetyl group in the spectrum of compound IV indicates that the unshared pair of the nitrogen atom interacts predominantly with the pyrimidinoanthrone system.

There are important differences between the electronic spectra of compounds I-IV on the one hand and compounds V-VIII on the other (Table 2). In the spectra of compounds I-IV the bands in the 300-380 nm region are diffuse and of medium intensity, whereas in the spectra of compounds V-VIII the high intensity band in this region shows vibrational fine structure , i.e., the difference between compounds I-IV and compounds V and VI shows up both in the values of $\nu(C=O)$ in the IR spectra and in the form and number of bands in the electronic spectra of these compounds.

The long wavelength band in the electronic spectrum corresponds to a large extent to the π - π^* transition from the HOMO, which contains a large contribution from the π -AO of the nitrogen atom of the amino group, to the LUMO, which has considerable contributions from the π -AO of the atoms of the C=O and C=N groups. This band lies in the region 490-498 for the alkylamines II and V, in the 475-479 region for the phenylamines III and VI, and at 442 cm⁻¹ for compound IV.

In acidic media (dilute H_2SO_4), compounds I-VI are monoprotonated, as indicated by the presence of an isobestic point, and there is a bathochromic shift by 13-38 nm (Fig. 1) of the long wavelength band. In strongly acid media (concentrated H_2SO_4), diprotonation occurs accompanied by a bathochromic shift of the long wavelength band by 19-71 nm for compounds II-VI and a hypsochromic shift of this band for compound I to 422 nm (Table 2) [4].

Quantum mechanical calculations were carried out for 6-aminopyrimidinoanthrone (X), its tautomers and ionic forms, and unsubstituted pyrimidinoanthrone (VII) (Table 3). It follows from the results that tautomer A ($\Delta H = 149.797 \text{ eV}$) is more stable than tautomer I ($\Delta H = 149.081 \text{ eV}$) for compound X. This result is in agreement with the experimental results which show retention of $\nu(C=O)$ in the spectra of compounds I-VI and their existence as tautomer A.

It follows from the calculations that monoprotonation of compound X occurs predominantly at atom $N_{(3)}$, although the difference between the energies of atomization for the systems $X_A \cdot H^+ N_{(3)}$ and $X_A \cdot H^+ N_{(1)}$ is not large. Protonation at each

Com pound	Medium	λ_{max} , nm ($\epsilon \cdot 10^{-3}$)				
1	Propanol-2	396 (3,34), 417 (3,45), 496 (4,03)				
	$Propanol-2 + H_2SO_4 (dil)$	532 (4.01)				
	$Propanol-2 + H_2SO_4$ (conc)	348 sh, 422 (3,64)				
11	Propanol-2	455 (3,87), 490 (4,04)				
	$Propanol-2 + H_2SO_4 (dil)$	494 (3,72), 518 (3,81)				
	$Propanol-2 + H_2SO_4$ (conc)	346 (3,32), 518 (3,55), 551 (3,74)				
111	Propanol-2	455 (3,79), 479 (4,06)				
	$Propanol-2 + H_2SO_4 (dil)$	514 (3,93)				
	Propanol-2 + H_2SO_4 (conc)	348 sh, 458 (3,65), 581 (3,92)				
IV	Propanol-2	421 (3,33), 442 (3,37)				
	$Propanol-2 + H_2SO_4$ (dil)	436 (3,62), 455 (3,63)				
	$Propanol-2 + H_2SO_4$ (conc)	465 sh, 490 (3.65)				
v	Propanol-2	345 (3,62), 364 (3,72), 385 (3,70), 458 (3,51), 490 (3,67)				
	Propanol-2 + H_2SO_4 (dil)	364 (3,79), 385 (3,78), 399 sh, 495 (3,39), 527 (3,49)				
	$Propanol-2 + H_2SO_4$ (conc)	349 sh, 448 sh, 518 (3,43), 546 (3,56)				
VI	Propanol-2	369 (3,99), 385 (4,02), 451 (3,43), 475 (3,60)				
	Propanol-2 + H_2SO_4 (dil)	369 (4.02), 385 (4.05), 402 sh, 479 (3.33), 510 (3.45)				
	$Propanol-2 + H_2SO_1$ (conc)	335 (3,85), 397 sh, 413 (4,05), 581 (3,40)				
VII	Ethanol	348 (3,93), 361 (4,05), 379 (4,03)				
VIII	Ethanol	309 (3,77), 369 (3,89), 387 (3,92)				
IX	Ethanol	401 (4.02), 415 (3.99), 424 (4.07)				

TABLE 2. Electronic Absorption Spectra for Compounds I-IX in Various Media.



Fig. 1. Electronic absorption spectra of compounds I (a), III (b), and VI (c) in propanol-2 (1), dilute (2,3) and concentrated (4) H₂SO₄.

of the cyclic nitrogen atoms leads to a bathochromic shift of 20 nm, which is in qualitative agreement with the experimental shift of 13-38 nm. Protonation at the exocyclic nitrogen atom is energetically unfavorable and should lead to a considerable (up to 60 nm) hypsochromic shift of the long wavelength band to 379 nm, which is close to the value of 362 nm for the unsubstituted pyrimidinoanthrone. It follows from the calculation that the LUMO has considerable contributions from the π -AO

Compound	Δu_{e} eV	$E(\pi), eV$	λ . nm ທ
VfI	140,465	28,802	362 (0,41)
XI	149,081	29,783	432 (0,51)
XA	149,797	30,262	439 (0,46)
$X_{\mathbf{A}} \cdot \mathbf{H}^{+}(\mathbf{N}_{(1)})$	154,497	30,793	459 (0,46)
$X_{A} \cdot H^{+}(N_{(3)})$	154,544	31,409	459 (0,44)
XA+H (N(6))	152,530	29,363	379 (0,49)

TABLE 3. Atomization Energy ΔH , π -Binding Energy $E(\pi)$, Wavelength λ , and Oscillator Strength f for Long Wavelength Band of Compound VII and Tautomer and Ionic Forms of Compound X

of the atoms of the C=O, C=N₍₁₎ and C=N₍₃₎ (42%), whereas the HOMO has a 30% contribution from the π -AO of the amino group. Introduction of the amino group into the pyrimidinoanthrone molecule, i.e., into compound X (in contrast to compound VII), causes the bond order of the C=O bond to decrease from 0.846 to 0.790 and its calculated length to increase from 0.1255 to 0.1265 nm, which confirms the prediction that inclusion of the π -AO of the amino group in the conjugated system might lead to a decrease in the C=O bond order and a decrease in ν (C=O).

Hence it can be assumed that monoprotonation of compounds I-VI occurs at atom $N_{(3)}$ of the ring. When compound I is diprotonated the second proton adds to the unshared pair of the amino group, removing it from conjugation, and leading to the observed hypsochromic shift from 532 to 422 nm (Table 2). The latter wave length should be close to the value of λ_{max} of the long wavelength band for the monoprotonated form of compound VII. It is known [5] that benzanthrone is protonated at the carbonyl oxygen in concentrated sulfuric acid and its long wavelength band is shifted bathochromically by 112 nm to 506 nm, whereas 3-azabenzanthrone is initially protonated at the ring nitrogen atom and secondly at the carbonyl oxygen atom. The corresponding bathochromic shifts of the long wavelength band were 15-20 and 70-80 nm [6]. Consequently it may be assumed that diprotonation of compounds II-VI, which is accompanied by bathochromic shifts of 19-71 nm, occurs at the carbonyl oxygen.

EXPERIMENTAL

IR spectra were recorded for the 4000-400 cm⁻¹ region with a Specord IR-75 spectrometer in the crystalline state in KBr disks and in CCl₄ solution. Electronic absorption spectra were recorded with a Specord UV-Vis spectrophotometer in the 300-700 nm region with propanol-2 solutions with concentrations of $1 \cdot 10^{-4}$ to $1 \cdot 10^{-5}$ mol dm⁻³. Quantum mechanical calculations for the tautomeric and ionic forms of a molecule were carried out using the Pariser – Parr – Pople method with optimization of interatomic distances to give minimum heat of atomization [7].

General Synthetic Method. Compounds I-VI were obtained by stirring 6-chloropyrimidinoanthrone (VIII) (1 g) with the corresponding amine (50 cm³) and copper ethanoate (0.1 g) at 50°C for 1 h until the starting compound disappeared. The reaction mixture was cooled to room temperature, diluted with 5% hydrochloric acid (50 cm³), the precipitate was filtered off, washed with water until neutral, dried, and recrystallized.

6-Morpholino-7H-benzol[*e*]**perimidin-7-one** (**I**). Yield 0.9 g (87%). M.p. 170-172°C (from petroleum ether). Found, %: C 71.83, H 4.90, N. Calc. for C₁₉H₁₅N₃O₂, %: C 71.91, H 4.76, N 13.24.

6-Ethanolamino-7H-benzol[e]perimidin-7-one (II). Yield 1.0 g (92%). M.p. 134-136°C (from petroleum ether). Found, %: C 69.85, H 4.31, N 14.17. Calc. for $C_{17}H_{13}N_3O_2$, %: C 70.09, H 4.50, N 14.43.

6-Anilino-7H-benzol[*e*]**perimidin-7-one (III).** Yield 0.84 g (76%). M.p. 212-213°C (from aqueous dioxane). Found, %: C 76.25, H 4.15, N 11.70. Calc. for $C_{21}H_{13}N_3O$, %: C 78.00, H 4.05, N 13.00.

6-Benzoylamino-7H-benzol[*e*]perimidin-7-one (IV). Yield 0.87 g (85%). M.p. 295-297°C (from petroleum ether). Found, %: C 72.92, H 3.34, N 12.71. Calc. for $C_{22}H_{13}N_3O_2$, %: C 73.96, H 3.64, N 11.56.

6-Butylamino-7H-benzol[*e***]perimidin-7-one (V).** Yield 0.92 g (91%). M.p. 112-113°C (from propanol-2). Found, %: C 75.01, H 5.72, N 12.34. Calc. for C₁₉H₁₇N₃O, %: C 75.22, H 5.65, N 13.85.

6-Mezidino-7H-benzol[*e***]perimidin-7-one (VI).** Yield 0.84 g (78%). M.p. 123-125°C (from petroleum ether). Found, %: C 76.10, H 5.13, N 10.94. Calc. for C₂₄H₁₉N₃O, %: C 78.92, H 5.20, N 11.50.

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