ACID DISSOCIATION CONSTANTS OF SOME NITROGEN-CONTAINING MULTINUCLEAR SYSTEMS

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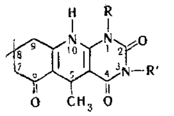
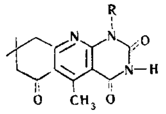
The pK$_a$ values have been determined spectrometrically of the 5,8,8-trimethyl-2,4,6-trioxo-1,2,3,4,5,6,7,8,9,10-decahydropyrimido[4,5-b]quinolines Ia–Ic, the 5,8,8-trimethyl-2,4,6-trioxo-1,2,3,4,6,7,8 9-octahydropyrimido[4,5-b]quinolines IIa and IIb, the 2,4,6-trioxo-5-phenyl-1,2,3,4,5,11-hexahydro-11-azapyrimido[4,5-b]fluorenes IIIa–IIIc, and the 4-amino uracils IVa–IVc. The following sequences of the dissociation of the protons attached to the nitrogen atoms have been established: for I, $N_{(1)} > N_{(10)} > N_{(3)}$; for II, $N_{(1)} > N_{(3)}$; for III, $N_{(11)} > N_{(1)} > N_{(3)}$; and for IV, $N_{(3)} > N_{(1)}$.

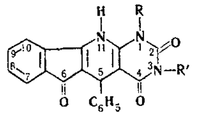
The present work was devoted to a determination of the dissociation constants of nitrogen-containing multinuclear compounds that we have synthesized previously: the 5,8,8-trimethyl-2,4,6-trioxo-1,2,3,4,5,6,7,8,9,10-decahydropyrimido[4,5-b]quinolines Ia–Ic, the products of their oxidation IIa and IIb [1], and the 2,4,6-trioxo-5-phenyl-1,2,3,4,5,11-hexahydro-11-azapyrimido[4,5-b]fluorenes IIIa–IIIc [2]. The pKa values of the corresponding tetrahydropyrimidoazafluorenes could not be determined because of their extremely low solubility in aqueous solutions. The IR spectra of some 4-amino uracils (IVa–IVc) have been recorded and their dissociation constants have been calculated.



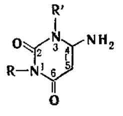
I



II



III



IV

I, III а R=R'=H б R=CH$_3$, R'=H, в R=R'=CH$_3$; II а R=H, б R=CH$_3$; IV а R=R'=H, б R'=CH$_3$, R=H; в R'=H, R=CH$_3$

All the compounds mentioned are polybasic acids. We were interested in the sequence of dissociation and also in the influence of the residual nitrogen-free conjugate part of the molecule on the mobility of the protons

Dissociation Constants of the Compounds Studied

Compound	pK_{a_1}	pK_{a_2}
Ia	6.64±0.04	>12
Ib	9.68±0.06	>12
Ic	9.85±0.06	—
IIa	8.64±0.04	>12
IIb	9.70±0.02	—
IIIa	5.99±0.03	11.49±0.02
IIIb	6.27±0.03	>13
IIIc	6.20±0.05	—
IVa	8.39±0.05	>13
IVb	11.00±0.05	—
IVc	8.63±0.02	—

The results that we obtained are given in the table and in Figs. 1–3. In a comparison of the pKa values of compounds of the series Ia–Ic we may note the low pKa value of Ia, having no substituents on the nitrogen atoms. When the hydrogen on $N_{(1)}$ is replaced by a methyl group (Ib), the pKa value increases markedly and the UV spectrum of the anion of compound Ib is different from that of the anion of compound Ia (Fig. 1,2) which shows a change in the structure of the anions. Consequently, in compound Ia the hydrogen on $N_{(1)}$ dissociates first. The UV spectrum of the anion of compound Ic is similar to that of the anion of compound Ib; the pKa values of these compounds are also extremely close. This makes it possible to assume that the same proton, i.e., that at $N_{(10)}$, dissociates in both cases. The nature of the UV spectra and the bathochromic shift of the maxima in an alkaline medium of compounds Ib and Ic correspond to the di(oxovinyl)amine system that we have studied previously [3]. It follows from this that the sequence of dissociation of the protons in I is: $N_{(1)} > N_{(10)} > N_{(3)}$. It was impossible to determine the dissociation constants of the anions of compounds Ia and Ib.

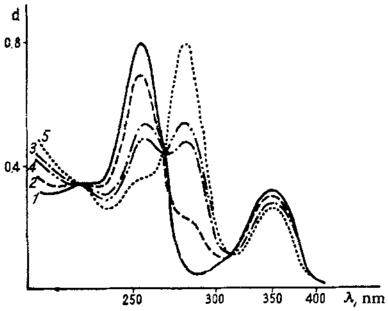


Fig. 1. UV spectrum of 5,8,8-trimethyl-2,4,6-trioxo-1,2,3,4,5,6,7,8,9,10-decahydropyrimido[4,5-b]quinoline (Ia): 1) pH 3.97; 2) pH 6.18; 3) pH 6.79; 4) pH 7.00; 5) pH 9.00

In the case of the pyrimidoazofluorenes IIIa–IIIc, the structure of which contains a benzoylene grouping, the nature and sequence of the dissociation of the protons are different. As a result of the strong influence of the benzoylene grouping the proton at $N_{(11)}$ dissociates first. To demonstrate the sequence of the dissociation of the protons it is sufficient to compare the absorption spectra of IIIa–IIIc, which proved to be almost identical (Fig. 3). Consequently, in all cases similar anions are formed in an alkaline medium. This is possible only if the proton at $N_{(11)}$ dissociates first. For the anion of IIIa we obtained $pKa_2 = 11.49$, and in the case of IIIb it was impossible to determine pKa_2, since $pKa_2 > 13$. It follows from this that the sequence of dissociation is: $N_{(11)} > N_{(1)} > N_{(3)}$.

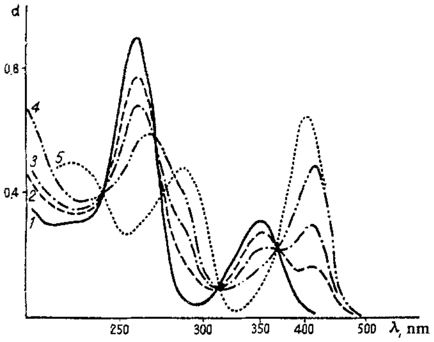


Fig. 2. UV spectrum of 1,5,8,8-tetramethyl-2,4,6-trioxo-1,2,3,4,5,6,7,8,9,10-decahydropyrimido[4,5-b]quinoline (Ib): 1) pH 6.65; 2) pH 9.23; 3) pH 9.61; 4) pH 10.42; 5) pH 13.80.

Compounds IIa–IIc, which have a pyridine ring, unlike Ia–Ic have only two protons capable of dissociation under the given conditions (sequence of dissociation: $N_{(1)} > N_{(3)}$).

It is interesting to compare these results with the dissociation constants of the 4-amino uracils (IVa–IVc). The mobilities of the protons at $N_{(1)}$ and $N_{(3)}$ differ markedly: for IVa, $pK_a = 8.39$ and for IVc $pK_a = 8.68$; in contrast to this, for IVb $pK_a = 11.00$. It follows from this that the protons of these compounds dissociate in the following sequence: $N_{(3)} > N_{(1)}$. The same sequence of dissociation of the protons of 4-amino uracil is preserved if the perimidine ring is included in the structure of a multinuclear compound.

The results that we have obtained show that the mobility of the proton of the dihydropyridine ring can be increased on conjugation with a benzoylene grouping. In the 4-amino uracil ring, regardless of whether it forms part of a multinuclear system or not, the proton attached to the nitrogen adjacent to the amino group is always the first dissociate.

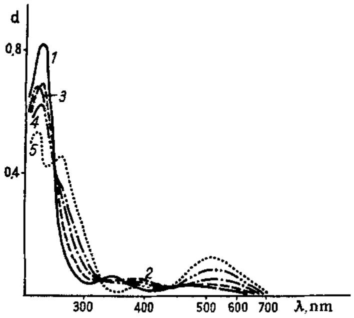


Fig. 3. UV spectrum of 1,3-dimethyl-2,4,6-trioxo-5-phenyl-1,2,3,4,5,11-hexahydro-11-azapyrimido[4,5-b]fluorene (IIIc): 1) pH 1.00; 2) pH 5.36; 3) pH 5.80; 4) pH 6.60; 5) pH 12.55.

EXPERIMENTAL

The dissociation constants were determined by the spectrophotometric method. The working solutions were prepared by dissolving the substances under investigations in ethanol or dimethylformamide (concentrations 2×10^{-3}–5×10^{-3}M) with subsequent 100-fold dilution with aqueous buffer solutions [4] to the required pH.

The analytical wavelength λ_{anal} was found from spectra taken on a UV-2 automatic spectrophotometer and the points of the pK_a values were determined on an SF-4 instrument in buffer solutions with pH values of pK_a, $pK_a \pm 0.2$, and $pK_a \pm 0.4$. The error of the method does not exceed 0.06 pK_a units. In the case of IIIc, the substance decomposed in an alkaline medium and the true value of the optical density of the anion was found by extrapolating the curve of the absorption as a function of the time to "zero time." The pH values of the working solutions were read with an accuracy of ±0.4 units on a LPU-01 laboratory pH-meter. The influence of the ionic strength was not taken into account.

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