4-AZAINDANE-1,3-DIONE DERIVATIVES

I. STUDY OF THE TAUTOMERIC AND PROTOTROPIC EQUILIBRIA OF SOME ANALOGS OF 4-AZAINDANE-1,3-DIONES

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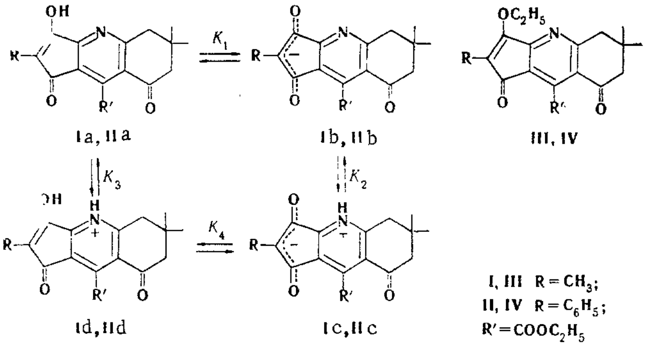
The acidity constants of 2,6,6-trimethyl- and 6,6-dimethyl-2-phenyl-9-ethoxycarbonyl-5,6,7,8-tetrahydro-4-azabenz[*f*]indane-1,3,8-triones were determined by a spectrophotometric method, and the position of the tautomeric equilibria was established for various pH values.

The electronic spectra of 2,6,6-trimethyl- and 6,6-dimethyl-2-phenyl-9-ethoxycarbonyl-5,6,7,8-tetrahydro-4-azabenz[*f*]indane-1,3,8-triones [1], analogs of 4-azaindane-1,3-diones, in aqueous and aqueous ethanol solutions at various pH values were recorded to study the tautomeric and prototropic equilibria of these compounds. In conformity with the data for 4-azaindane-1,3-diones (see, for example, [2, 3]) in solutions one might expect equilibria between enol a, anion b, betaine c, and N-protonated enol d.



I, III $R=CH_3$;
II, IV $R=C_6H_5$;
$R'=COOC_2H_5$

The ratios of the corresponding forms in various solvents at various pH values are due to the relative magnitudes of the K_1, K_2, K_3, and K_4 acidity constants (the diketo structures in these equilibria are not considered, and their presence could not be detected).

Both alkaline and neutral solutions of I and II have identical absorption spectra (Fig. 1) and are characterized only by the presence of forms Ib and IIb. The characteristic long-wave band of indane-1,3-dione anions [4], which is responsible for the red color of the solutions, is observed in the spectra. The absorption pattern changes in solutions with suppressed ionization of I and II (0.1 N HCl), and hypsochromic shifts with a reduction in the absorption intensity are observed; this is characteristic for enols rather than the anionic forms of indane-1,3-dione [4, 5].

One's attention should be directed to the inflections of low intensity at 560-590 nm for I and 620-650 nm for II, which are absent in the spectra of the fixed enol forms – enol esters III and IV (Fig. 1) – and attest to the presence of small amounts of betaine forms Ic and IIc (the betaine structures of 4-azaindane-1,3-diones are characterized by a markedly bathochromically shifted long-wave absorption, as compared with the absorption of the anion [2, 3]). In the case of I in aqueous solutions, more of form Ic is present in aqueous solutions than in 50% aqueous ethanol solutions. An electronic spectrum could not be obtained for II in aqueous solutions because of its low solubility ($<10^{-5}$ M).

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TABLE 1. Electronic Spectra of Some 4-Azaindane-1,3-diones

Compound	λ_{max}, nm (ε)					
	anion b		betaine c		enol a	
	H_2O	50% ethanol	H_2O	50% ethanol	H_2O	50% ethanol
I	358 (9600) 474 (1800)	362 (9100) 478 (1850)	540—580	560—590	334 (6300) 400—410 (1600)	330 (8000) 400 (1600)
2-Phenyl-4-azaindane-1,3-dione [2, 3]	340 (14900) 460 (2100)	340 (15800) 460 (2000)	393 (12100) 500 (2700)	410 (6300) 490—530 (2500)		
II	382 (15100) 485—490 (2800)	390 (16200) 506 (3100)	Insoluble	620—650	Insoluble	352 (13800) 442 (4500)

TABLE 2. OH Acidity Constants of I and II and Some Indane-1,3-diones

Compound	pK_{OH}		ΔpK_{OH}
	H_2O	50% ethanol	
I	2,84	3,32	0,48
2-Methylindane-1,3-dione [4, 5]	4,29	4,80	0,51
	$\Delta pK = 1,45$	$\Delta pK = 1,48$	
II	(0,57)	2,39	(1,82)
2-Phenylindane-1,3-dione [4, 5]	2,00	3,82	1,82
	$\Delta pK = 1,43$	$\Delta pK = 1,43$	

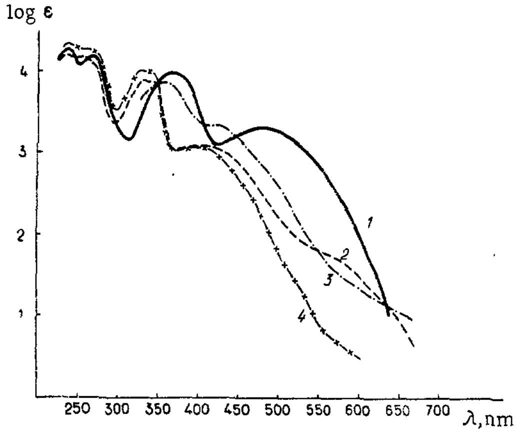

Fig. 1. Electronic spectra: 1) I in 50% ethanol; 2) I in 50% ethanol (0.1 N HCl); 3) I in water (4 N HCl); 4) III in 50% ethanol.

The electronic spectra of anions Ib and IIb very much recall the spectrum of the anion of 2-phenyl-4-azaindane-1,3-dione but with a considerable bathochromic shift of the two long-wave absorption maxima (Table 1).

The acidity constants of I and II were calculated. In contrast to 2-phenyl-4-azaindane-1,3-dione, these constants characterize the OH acidity of enols Ia and IIa (Table 2).

It is seen from Table 2 that the OH acidities increase on passing from a 50% aqueous alcohol solution to an aqueous solution. Moreover, the changes are identical for 2-methylindane-1,3-dione and its analogs (I). This provided a basis for calculating the OH acidity in aqueous solutions for II using the difference $\Delta pK_{OH} = 1.82$ obtained for 2-phenylindane-1,3-dione. It is interesting that almost identical changes in the acidities are retained for both aqueous and 50% aqueous ethanol solutions on passing from indane-1,3-diones to their aza analogs, I and II (the OH acidity increases on the average by 1.45 orders of magnitude).

The reason for the difference in I and II from 2-phenyl-4-azaindane-1,3-dione, for which anion, betaine, and protonated enol forms were detected [2, 3], should be sought in the reduced basicity of the nitrogen atom of the pyridine ring as a result of the electron-acceptor effect of the ketone and ethoxycarbonyl groups. The $\overset{\oplus}{N}H$ acidity increases and becomes greater than the OH acidity of the enol, and the less acidic form – the enol – in this case begins to dominate in the equilibrium. For 2-phenyl-4-azaindane-1,3-dione in aqueous solutions, $pK_{NH}^{\oplus} = -3.94$ [3]. The basicity of pyridine under the influence of two electron-acceptor groups may change by even three to four orders of magnitude (this estimate can be made on the basis of correlation analysis), such that $pK_{NH}^{\oplus}$ for system II in aqueous solutions may be ~0-1. This value is comparable to $pK_{OH} = 0.57$, and there may be 20-70% of the betaine form IIc in an equilibrium mixture in aqueous medium, as demonstrated by the calculations.

EXPERIMENTAL

The spectrophotometric measurements of $5 \cdot 10^{-5}$ and 10^{-4} M aqueous solutions and 50 and 60% (by volume) ethanol–water solutions of compounds I and II were measured with an SFD-2 spectrophotometer. Hydrochloric acid (0.1-6 N) was used to create a definite acidity of the medium. The pH values of buffer solutions were measured with an LPM-60M pH meter. The buffer solutions were prepared in accordance with the data in [6]. The acidity constants were determined at 20 ± 1°C by a spectrophotometric method [7] with correction for the salt effect. The accuracy in the determinations was ±0.05 pH units.

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