SYNTHESIS AND PECULIARITIES OF THE STRUCTURES OF BETAINE ALDEHYDES WITH POLYNUCLEAR HETEROAROMATIC CATIONS

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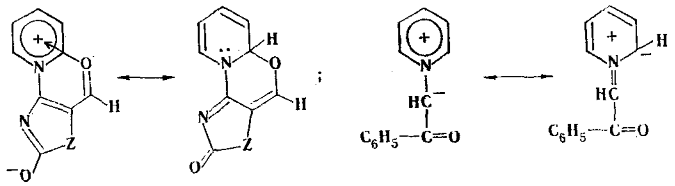
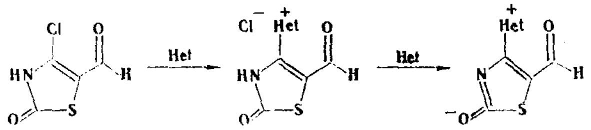
New quinolinium, isoquinolinium, and acridinium betaines were synthesized on the basis of chloroformyl-substituted azolinones and uracil. The peculiarities of their structures were examined by means of the UV and PMR spectroscopic data. It was established that the isoquinolinium betaine exists in the cyclic form.

We have previously reported [1, 2] that the pyridinium betaines of azole aldehydes exist in the acyclic form and that an equilibrium of the Ia$\rightleftarrows$Ib type is virtually imperceptible. This peculiarity is characteristic not only for the indicated betaines but also for pyridinium phenacylids (IIa, b). Replacement of the cation in the phenacylids by the isoquinolinium ion leads to the formation of dimeric products [3].



Ia Ib IIa IIb

In order to compare the properties of the ylids and betaines with heteroaromatic cations we obtained a number of previously unknown betaines on the basis of azoles and uracil with quinolinium, isoquinolinium, and acridinium cations. Compounds IV were synthesized by the reaction of 4-chloro-5-formyl-2-thiazolinone (III) with an excess of the corresponding base. The reaction can be carried out in dimethylformamide (DMF), acetone, and alcohol:



III IV a-f V a-c

Het: a = pyridine; b = 4,4'-dipyridyl; c = 4,4'-dipyridyl·$2H_2O$; d = quinoline; e = isoquinoline; f = acridine.

If special difficulties are not encountered in the formation of salts IV, the structure of the heteroring rather than its basicity has a great effect on the dehydrochlorination step and the yield of betaines V. Thus under the conditions of this reaction 4,4-dipyridyl (pK_a 4.82) forms a betaine in good yield, a smaller yield is observed in the case of quinoline (pK_a 4.87), and only salt IVf was isolated with acridine. The reactions with heterocycles that contain free α positions proceed most smoothly. A betaine cannot be obtained

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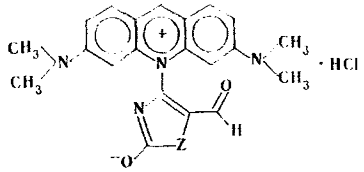
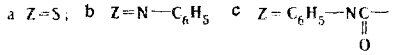
from unsubstituted acridine even when a large excess of the base is used.

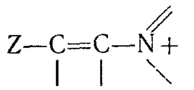
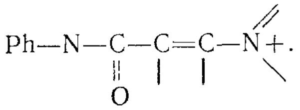
The synthesis of acridinium betaines was realized only when the acridine ring contained electron-donor dialkylamino groups. The possibility that the betaine is formed in this case due to intramolecular dehydrochlorination is not excluded. In contrast to salts IVd,f, a strong-field shift of the signal of the hydrogen atom of the formyl group is observed in its PMR spectrum, in analogy with betaines V. The resonance of the protons of the acridine ring is in good agreement with the data indicated in [4]. Quaternization takes place at the ring nitrogen atom; this was previously proved for other salts obtained on the basis of acridine orange. Thus the structure shown below can be assigned to VI:



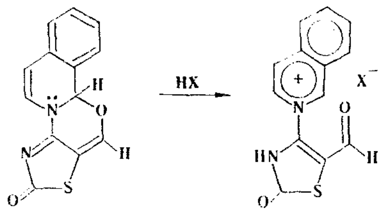
VI a-c



a $Z=S$; b $Z=N-C_6H_5$ c $Z=C_6H_5-N\overset{}{\underset{\underset{O}{\|}}{C}}-$

The UV spectra of the pyridinium betaines are characterized by three principal absorption maxima: A) 263 (log ε 3.93), B) 323 (log ε 4.03), and C) 400 nm (log ε 3.44). The latter peak is of low intensity and develops only in the spectra of betaines (it is absent in the spectra of III and IVd, f); this indicates that it belongs to p—π complexes. The B band is associated with absorption of the  $Z-\underset{|}{C}=\underset{|}{C}-N^+$ chromophore in the betaines and their salts and is not observed in the uracil betaines because of separation of its carbonyl group  $Ph-N-\underset{\underset{O}{\|}}{C}-\underset{|}{C}=\underset{|}{C}-N^+$.

The electronic spectrum of Ve differs from the spectra of the pyridinium and quinolinium betaines with respect to the absence of a C band, and this compound is only slightly soluble in water and organic solvents and does not give the reaction for an aldehyde group with hydroxylamine that is characteristic for pyridinium betaines. The presence of a new intense peak at 373 nm (log ε 4.48) is associated with the development of a chromophore due to dearomatization of the isoquinolinium ion. The resulting cyclic form is unstable and upon protonation is converted to acyclic isoquinolinium salt VII:



Ve VII

The definite molecular mass of Ve indicates its monomeric character, in contrast to the isoquinolinium phenacylid dimer. In our opinion, this is not due to structural factors but rather with localization of the negative charge in the cationoid part in ylid IIb (in contrast to the betaines), which hinders intramolecular ring formation.

The characteristics of the compounds obtained are presented in Table 1.

EXPERIMENTAL

The UV spectra of solutions of the compounds in methanol were recorded with a Specord UV-vis spectrophotometer. The PMR spectra of solutions in DMSO (2.5 ppm) were recorded with a Brucker HX-90 spectrometer with hexamethyldisiloxane as the internal standard.

TABLE 1. Characteristics of the Betaines and Their Salts

Compound	mp, °C (dec.)	PMR spectrum, δ, ppm	Found, %					Empirical formula	Calc., %					Yield, %
			C	H	Cl	N	S		C	H	Cl	N	S	
IV^d	128—130	9,46	53,1	3,3	12,1	9,7	11,0	$C_{13}H_9ClN_2O_2S$	53,3	3,1	12,1	9,6	10,9	46
IV^f	147—149	9,43	59,8	3,4	10,3	8,1	9,3	$C_{17}H_{11}ClN_2O_2S$	59,6	3,2	10,3	8,2	9,3	95
V^a	214—216	9,21	52,2	3,1	—	13,6	15,4	$C_9H_6N_2O_2S$	52,4	2,9	—	13,6	15,5	70
V^b	258—259	9,16	59,2	3,3	—	14,9	11,1	$C_{14}H_9N_3O_2S$	59,4	3,2	—	14,8	11,3	94
V^c	104—106	—	52,6	4,1	—	13,3	9,8	$C_{14}H_{13}N_3O_4S$	52,6	4,1	—	13,2	10,0	94
V^d	226—228	9,13	60,9	3,3	—	10,9	12,3	$C_{13}H_8N_2O_2S$	60,9	3,1	—	10,9	12,5	5
V^{e*}	230—231	9,13	61,0	3,3	—	10,8	12,7	$C_{13}H_8N_2O_2S$	60,9	3,1	—	10,9	12,5	92
VI^a	167—169	9,26	59,0	4,8	8,4	13,1	7,3	$C_{21}H_{21}ClN_4O_2S$	58,8	4,9	8,3	13,1	7,5	94
VI^b	207—209	9,03	64,1	5,6	6,8	13,7	—	$C_{27}H_{28}ClN_5O_3$	64,1	5,5	7,0	13,9	—	93
VI^c	194—196	9,63	63,2	5,5	6,7	13,2	—	$C_{28}H_{28}ClN_5O_4$	63,0	5,4	6,6	13,1	—	95

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*The PMR spectrum was recorded in CF_3COOH, while the PMR spectra of the remaining compounds were recorded in DMSO; only the signal of the formyl proton is presented.

Betaines V and Their Salts IVd,f. A mixture of 5 mmole of 4-chloro-5-formyl-2-thiazolinone and 15 mmole of the heterocyclic base (pyridine, 4,4-dipyridyl, quinoline, isoquinoline, and acridine) in 10 ml of acetone was heated at 60°C until a precipitate formed. The latter was separated, washed with acetone, alcohol, and ether, and crystallized from an appropriate solvent [dimethylformamide (DMF) for Va,c-e, water for Vb and IVf, and propanol (with evaporation) for IVd].

5-Formyl-4-(1-quinolinia)thiazole 2-Oxide Hydrochloride (IVd) and Its Betaine (Vd). A 1.63-g (10 mmole) sample of 4-chloro-5-formyl-2-thiazolinone was dissolved in 5 ml of DMF, 3.5 ml (30 mmole) of freshly distilled quinoline was added, and the reaction mixture was maintained at room temperature for 5 min. The precipitate was separated and washed successively with absolute DMF and two portions of anhydrous ether to give 1.35 g of white plates of IVd. Betaine Vd was isolated from the filtrate of the reaction mixture after heating at 70°C for 18 h; the orange-yellow crystals were washed with DMF and alcohol to give 0.15 g of product (from DMF).

Betaines VIa-c. A mixture of 2 mmole of 3,6-bis(dimethylamino)acridine and 2 mmole of 4-chloro-5-formyl-2-thiazolinone, 3-phenyl-5-formyl-6-chlorouracil, or 1-phenyl-4-chloro-5-formyl-2-imidazolinone in DMF was heated at 60°C, after which the precipitate was separated, washed, and crystallized from DMF.

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