REACTION OF HETEROCYCLIC BETAINES.
SYNTHESIS OF A NEW HETEROCYCLIC SYSTEM

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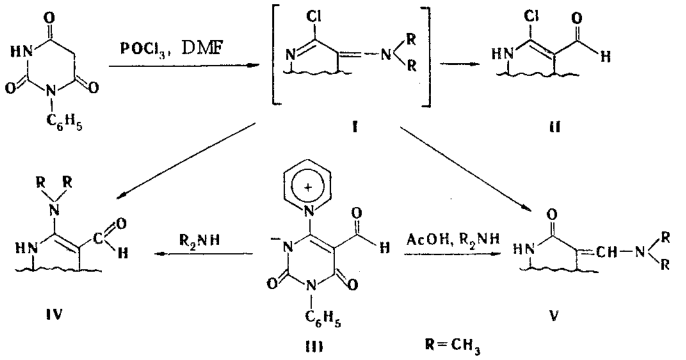
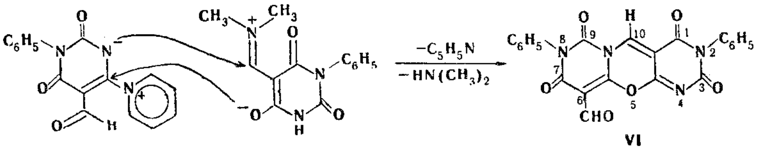
A new condensed heterocyclic system, viz., 1,3,7,9-tetra- oxo-2,8-diphenyl-6-formylpyrimido [3',4'-a]pyrimido[4'',5''-d]oxazine, was synthesized, and its electronic and PMR spectra were recorded. Factors that affect the orientation of nucleophilic substitution in betaines of the pyrimidine series with aliphatic amines are discussed.

In a previous study [1] of the synthesis of pyridinium betaines of uracil (III) we directed our attention to the formation of very small amounts of a diamagnetic substance that displays powerful red fluorescence on a blue background and thermochromism when the reaction mixture is allowed to stand. We attempted to isolate this substance and establish its structure. We found that the dye is not produced when betaine III is heated or when it is condensed with 6-chloro-5-formyluracil (II). This provided a basis for the assumption that Vilsmeier—Haack intermediates or side products [2] of the 5-dimethylaminomethylenebarbituric acid (V) type or of the "isomeric" 6-dimethylamino-5-formyluracil (IV) type, which could be formed via the Decker—Forster reaction from I, participate in the synthesis.



The condensation of IV or V with betaine III leads to the formation of the dye. The process is realized with the participation of catalytic additions of mineral or carboxylic acids. The reaction proceeds most smoothly and gives the products in highest yields in the case of V.

The PMR spectra of the dye are characterized by a singlet at δ 9.67 ppm, the form and position of which are similar to the signal of the proton of the aldehyde group in 3-phenyl-6-(1-pyridinia)-5-formyluracil-2-olate (III), and a multiplet of protons of two phenyl rings centered at δ 7.34ppm and of the C—H proton at δ 9.27 ppm, which is capable of undergoing a shift to weak field in acidic media ($\Delta\delta$ 0.46 ppm). This constitutes evidence for the development, in the case of protonation, of a positive charge on the methylidyne carbon atom or for its α orientation with the heteronium group. On the basis of the material presented above and a determination of the molecular weight (by the Rast method) we proposed the 1,3,7,9-tetraoxo-2,8-diphenyl-6-formylpyrimido[3',4'-a]pyrimido[4'',5''-d]oxazine (VI) structure and the following scheme of formation:



The proposed structure is also confirmed by the electronic spectra. Compound VI displays a negative

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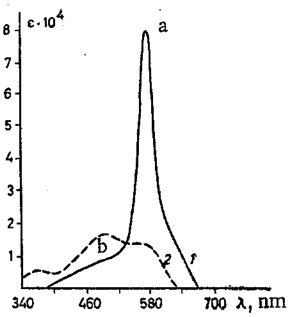

Fig. 1. Absorption spectrum in methanol of 1,3,7,9-tetraoxo-2,8-diphenyl-6-formylpyrimido[3',4'-a]pyrimido[4'',5''-d]oxazine (VI): 1) base; 2) protonated form.

solvatochromic effect in solutions. Its electronic absorption spectra in the visible region are characterized by high-intensity absorption at 575 nm (log ε 4.90) and 495 nm (log ε 3.90) (Fig. 1). The high intensity of the a band (curve 1) indicates that it belongs to permitted $\pi-\pi^*$ transitions. However, its disappearance upon acidification, which is accompanied by an increase in the intensity of the band with λ_{max} 495 nm, and the development of a new band with λ_{max} 363 nm (curve 2) make it possible to conclude that the free electron pair of the nitrogen or oxygen atom, protonation of which leads to cleavage of the chromophore and the formation of smaller chromophore groups, participates in the formation of the conjugated chain of the dye. This recalls the situation that is observed in monomethylidynebis(pyrylocyanines), in which the high sensitivity and the disappearance of the long-wave maximum corresponding to $\pi-\pi^*$ transitions in the presence of acids are associated with cleavage of the chromophore when the central methylidyne bridge is protonated [3].

The synthesis of IV and V was realized by the reaction of betaine III with dimethylamine. The indicated process in acetic acid leads primarily to V, whereas in alcohol and other organic solvents it leads primarily to "isomer" IV. Their structures were confirmed by data from the PMR, IR, and mass spectra. They are chromatographically distinguishable. This made it possible to establish the presence of "isomer" V in the reaction mixture in the condensation of 6-chloro-5-formyluracil (II) with pyridine by ascending linear chromatography on paper and its responsibility for the formation of dye VI.

EXPERIMENTAL

The PMR spectra of solutions of the compounds in dimethyl sulfoxide (DMSO) were recorded with a BS-467 spectrometer with hexamethyldisiloxane as the internal standard. The mass spectra were recorded with a Varian MAT-311 spectrometer at an ionizing-electron energy of 70 eV. The electronic spectra of solutions of the compounds in methanol were recorded with a Specord UV-vis spectrophotometer.

1,3,7,9-Tetraoxo-2,8-diphenyl-6-formylpyrimido[3',4'-a]pyrimido[4'',5''-d]oxazine (VI). Pyridine (4 ml), 2.5 ml of acetic acid, and 0.8 ml of hydrochloric acid were added to a mixture of 1 g (3.4 mmole) of III and 0.88 g (3.4 mmole) of V in 30 ml of acetonitrile, and the mixture was refluxed for 8-9 h. It was then cooled, and the resulting precipitate was crystallized from acetic acid to give 1.3 g (90%) of a product with mp 218-220°C and R_f 0.39 [on paper, elution with isopropyl alcohol–acetic acid–water (8 : 2 : 2)]. Found: C 61.8; H 4.2; N 13.0%. $C_{22}H_{12}N_4O_6$. Calculated: C 61.6; H 2.8; N 13.0%. M 411 (by the Rast method, in phenol).

1-Phenyl-5-dimethylaminomethylenebarbituric Acid (V). A mixture of 1.47 g (5 mmole) of III, 0.41 g (5 mmole) of dimethylamine hydrochloride, 0.41 g (5 mmole) of sodium acetate, and 30 ml of acetic acid was refluxed for 20-30 min, after which it was cooled and treated with ether to give 1.1 g (88%) of a yellow product with mp 247-250°C (from ethanol) and R_f 0.85 (on paper, in water). PMR spectrum: 3.32 [6H, d, 5-$N(CH_3)_2$], 7.19-7.58 (5H, m, 1-C_6H_5), 8.08 (1H, s, 5-CH), and 10.79 ppm (1H, broad s, 1-NH). Mass spectrum: m/e 259 (100), 243 (9.2), 215 (9.1), 167 (5.2), 166 (5.2), 124.9 (5.7), 124 (12.4), 122 (16.6), 119 (21.5), 112 (12.8), 97 (19.4), 93 (12.7), 91 (10.0), 84 (5.5), 82 (6.2), 77 (6.0), 73 (21.4), 69 (23.3), 68 (18.2), 53 (7.6), 43 (26.4), 42 (40.4), 41 (46.3), 40 (17.7), 27 (9.0). Found: C 58.0; H 4.9; N 14.8%. $C_{13}H_{13}N_3O_3$. Calculated: C 60.2; H 5.0; N 16.2%.

3-Phenyl-6-dimethylamino-5-formyluracil (IV). A mixture of 1.47 g (5 mmole) of III, 0.41 g (5 mmole) of dimethylamine hydrochloride and 0.28 g (5 mmole) of potassium hydroxide was refluxed in methanol for

20-30 min, and the resulting precipitate was crystallized from ethanol to give a product with mp 225-227°C and R_f 0.65 (on paper, in water). PMR spectrum: 3.03 [6H, s, 6-$N(CH_3)_2$], 7.00-7.33 (5H, m, 3-C_6H_5), and 9.56 ppm (1H, s, 5-CHO). Found: C 60.6; H 5.8; N 18.5%. $C_{13}H_{13}N_3O_3$. Calculated: C 60.2; H 5.0; N 16.2%.

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