ture of 250°C. The temperature of admission of the compounds into the ion source was 50-70°C.

Compounds I [7], II [8], III [9], IV [10], V [13], VI [11], and VII [12] were synthesized by previously described methods.

All of the compounds were purified prior to mass-spectral analysis by recrystallization and were identified from the melting points and the results of elementary analysis.

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METHYLATION OF PYRIMIDINE DERIVATIVES

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A mixture of isomers that differ with respect to the position of the methyl group is formed in the methylation of 5,5-diethyl-6-imino-5,6-dihydro[1H,3H]pyrimidine-2,4-dione with excess methyl iodide in the presence of ethoxide. Isomerization of the Dimroth-rearrangement type was observed. The mass spectra of the isomers are examined, and the IR spectra of the tautomeric forms are discussed.

Iminobarbituric acids are widely used as starting compounds in the synthesis of biologically active barbituric [1] and 4-thiobarbituric acids [2] and their N-alkyl derivatives. The alkylation of barbituric acids, which can lead to both N- and O-derivatives [3, 4], depending on the reagents used, serves as an important method for the synthesis of the latter. In the present research in the case of 5,5-diethyl-6-imino-5,6-dihydro[1H,3H]pyrimidine-2,4-dione and its N-substituted analogs we studied methylation with methyl iodide in the presence of ethoxide as the base. Under the selected conditions and at a reagent molar ratio of 1:1:1 the 3 position of I is methylated to give monomethyl derivative III (see the scheme below); this is in agreement with the high NH acidity of this position and the data in [1].

The action of two or more moles of methyl iodide and sodium ethoxide on 1 mole of pyrimidinedione I leads to the formation of a mixture of isomers IV and V in a ratio of 3:2. A similar result was obtained in the methylation of III under the same conditions, whereas II gives only 1,3-dimethyl derivative IV. This result provides evidence that the dialkylation of I includes the initial formation of monomethyl derivative III, which subsequently undergoes further alkylation. The formation of a mixture of isomers IV and V is associated with

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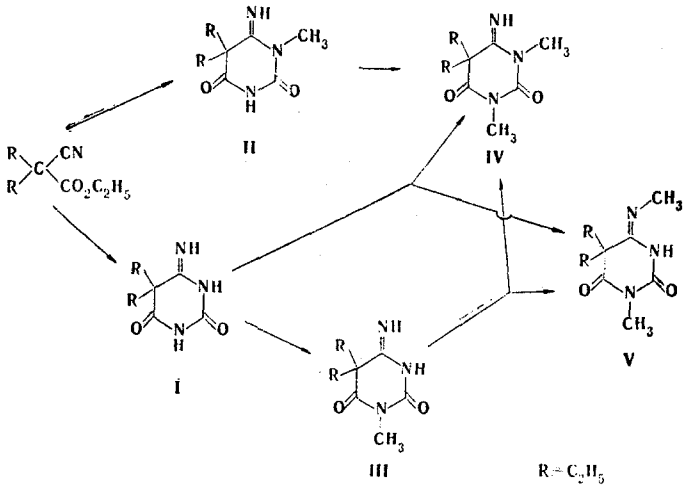
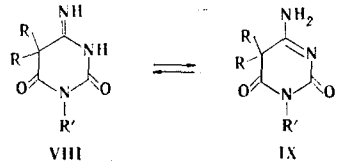


the tautomeric character of the amidine fragment of 6-iminopyrimidinedione. The action of a sufficiently strong base on III leads to the formation of mesomeric amidinium anion VI, which in view of the absence of steric hindrance reacts with the alkyl halide at any of the nucleophilic centers with equal probability.

However, during a study of the individual isomers IV and V under the conditions of the alkylation reaction we observed that IV undergoes irreversible isomerization to V on prolonged heating. The reverse transformation does not occur even under more severe reaction conditions. The isomerization mechanism apparently includes rearrangement steps similar to the Dimroth rearrangement [5, 6]: initial cleavage of the C_2—N_1 bond, rotation about the C_5—C_6 bond, and recyclization to the thermodynamically more stable V isomer, in which conjugation of the ring C=N bond with the C_2=O bond is possible. Compound II also undergoes a similar conversion at a lower rate and is isomerized to 5,5-diethyl-6-methylimino-5,6-dihydro[1H,3H]pyrimidine-2,4-dione (X). We assume that the Dimroth rearrangement in the case of methylation of III has only a slight effect on the ratio of isomers IV and V; however, this factor may be decisive when bulkier alkyl halides are used.

The tautomeric character of 6-iminopyrimidine-2,4-diones, for which equilibrium between the imino (VIII) and amino (IX) forms is possible in solution, is confirmed by the IR spectra of I-V and X in chloroform solutions (Table 1).



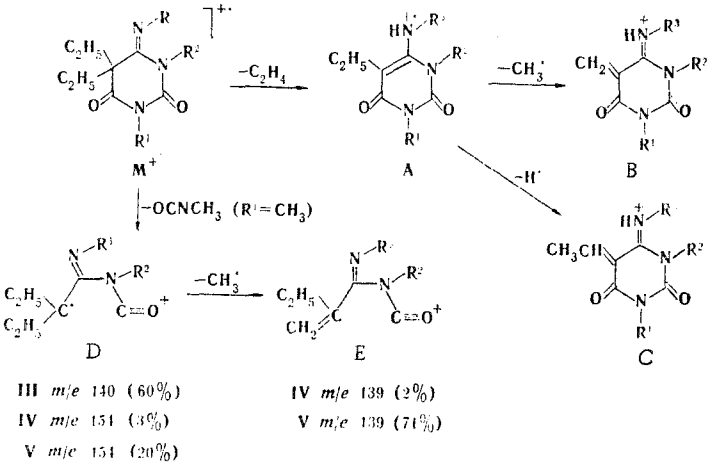
Analysis of the absorption bands in the region of the stretching vibrations of the C=O and C=N groups gives the most valuable information. The spectra of I-V and X contain bands of different intensity at 1660-1730 cm^{-1}, which we assigned to the stretching vibrations of the C_2=O and C_4=O bonds. The absorption bands at 1605-1620 cm^{-1} are due to the vibrations of the exocyclic C=N bond, whereas the absorption at 1550-1590 cm^{-1} in the spectra of I, III, V, and X is associated with the stretching vibrations of the ring C=N bond [7, 8]. By comparing the data obtained one can note that I, III, and X have absorption bands in both of the regions cited above and consequently exist in two tautomeric forms. Compound V, which does not have absorption in the 1620 cm^{-1} region, evidently exists in the amino form. Compounds II and IV can exist only in the imino form, and this shows up in the absence of an absorption band at 1550 cm^{-1}. As expected, the conjugation of the ring C=N bond with the C_2=O group leads to a 10-15-cm^{-1} decrease in the frequency of the C_2=O absorption as compared with the compounds that exist in the imino form. Thus according to the data from the IR

TABLE 1. IR Spectra of I-V and X (10^{-2} M solutions in $CHCl_3$)

Compound	IR spectra, cm^{-1}		
	C=O	C=N (exo)	C=N (ring)
I	1705 br	1617	1590
II	1712 br	1620	—
III	1712, 1665	1620	1563
IV	1728, 1675	1620	—
V	1715, 1684	—	1580
X	1703 br	1605	1575

spectra of solutions in chloroform, I-V and X exist in the imino or amino form or as a mixture of these forms, depending on the substituent attached to the N_1 atom.

We studied the possibility of identification of the structural isomers II-V and X from their mass spectra. Both general and specific regularities are displayed by these compounds during fragmentation under the influence of electron impact.



The fragments of the A, B, and C types common to all of these compounds are characterized by peaks that have approximately identical relative intensities in the spectra obtained at ionizing-electron energies of 70 and 14 eV, regardless of the number and position of the methyl groups. The intensities of the molecular-ion peaks (M^+) of isomers II and III are very low (less than 1%). In contrast to II, cleavage of the C_4—C_5 and N_3—C_2 bonds with splitting out of an $OCNCH_3$ fragment and the formation of ion D is observed for III, IV, and V. This sort of splitting out of an OCNH fragment from the M^+ ion of II is probably less favorable, and the corresponding process is not observed in the mass spectra. The mass spectra of IV, V, and X differ primarily with respect to the relative intensities of the molecular-ion peaks. The M^+ intensities for V and X are, respectively, 16% (22% at 14 eV) and 4% (6% at 14 eV), whereas the intensity of the M^+ peak of IV is 0.7% at both ionizing-electron energies. In addition to this, the $M^+ \rightarrow D \rightarrow E$ processes are clearly expressed in the fragmentation of V, and the analogous fragment peaks are less intense in the spectrum of IV.

Thus mass spectrometry may serve as a reliable method for the determination of the position of the methyl groups in compounds of the investigated type.

The structures of the compounds were confirmed by comparison with authentic samples and the literature data.

EXPERIMENTAL

The mass spectra were obtained with an LKB-9000 spectrometer with direct introduction of the substances into the ion source (the temperature of the source was 250°C, and the temperature of the admission system was 30-50°C) at ionizing voltages of 70 and 14 eV. The IR spectra of 0.01 M solutions of the compounds in chloroform (n = 1 mm) were recorded with a Perkin—Elmer 577 spectrometer. The reaction was monitored by chromatography on Silufol UV-254 in a chloroform—methanol system (10:1) with development in UV light.

5,5-Diethyl-6-imino-5,6-dihydro[1H,3H]pyrimidine-2,4-dione (I). This compound, with mp 294-295°C (aqueous ethanol) (mp 295°C [1]) and R_f 0.15, was obtained in 91% yield by the method in [1].

1-Methyl-5,5-diethyl-6-imino-5,6-dihydro[1H,3H]pyrimidine-2,4-dione (II). This compound, with mp 144-146°C (aqueous ethanol) (mp 145°C [1]) and R_f 0.6, was obtained in 76% yield by the method in [1].

3-Methyl-5,5-diethyl-6-imino-5,6-dihydro[1H,3H]pyrimidine-2,4-dione (III). A 9.2-g (0.05 mole) sample of II was added to a solution of sodium ethoxide obtained from 1.15 g (0.05 mole) of sodium and 200 ml of absolute ethanol, and the mixture was stirred for 30 min. A 7.1-g (0.05 mole) sample of methyl iodide was then added dropwise, and the mixture was heated with stirring on a water bath for 3 h until it was neutral with respect to phenolphthalein. The alcohol was removed by distillation, and the residue was washed with water to give 5.3 g (54%) of III with mp 260-261°C (aqueous ethanol) (mp 258°C [1]) and R_f 0.28.

Methylation of 3-Methyl-5,5-diethyl-6-imino-5,6-dihydro[1H,3H]pyrimidine-2,4-dione. A 3.94-g (0.02 mole) sample of III was added to a solution of sodium ethoxide, obtained from 0.46 g (0.02 mole) of sodium and 100 ml of absolute ethanol, and the mixture was stirred for 30 min. A 2.84-g (0.02 mole) sample of methyl iodide was then dropwise added, and the mixture was heated with stirring on a water bath for 6 h until it was neutral with respect to phenolphthalein. The alcohol was removed by distillation, and the residue was washed with pentane. The filtrate was evaporated to give 2.25 g (64%) of IV. The pentane-insoluble solid was washed with water to give 1.5 g (36%) of 3-methyl-5,5-diethyl-6-methylimino-5,6-dihydro[1H,3H]pyrimidine-2,4-dione (V) with mp 213-214°C (aqueous ethanol) (mp 212°C [1]) and R_f 0.35.

1,3-Dimethyl-5,5-diethyl-6-imino-5,6-dihydro[1H,5H]pyrimidine-2,4-dione (IV). A 5.9-g (0.03 mole) sample of II was added to a solution of sodium ethoxide, obtained from 0.69 g (0.03 mole) of sodium and 70 ml of absolute ethanol, and the mixture was stirred for 30 min. A 4.3-g (0.03 mole) sample of methyl iodide was added dropwise, and the mixture was heated with stirring on a water bath for 5 h until it was neutral with respect to phenolphthalein. The alcohol was removed by distillation, and the residue was washed repeatedly with pentane. The filtrate was evaporated to give 5.4 g (85%) of IV with mp 41-42°C (mp 40°C [1]) and R_f 0.85.

Isomerization of IV. A 2.11-g (0.01 mole) sample of IV was added to a solution of sodium ethoxide, obtained from 0.23 g (0.01 mole) of sodium and 50 ml of absolute ethanol, and the mixture was refluxed for 50 h. The alcohol was removed by distillation, and the residue was neutralized with an ether solution of HCl. The ether was evaporated, and the residue was washed with five 20-ml portions of hot hexane. The hexane was removed by distillation to give 0.62 g (29%) of IV. The hexane-insoluble residue was dissolved in 5 ml of hydrochloric acid (1:1), and the solution was made alkaline with 10% ammonium hydroxide. The resulting precipitate was removed by filtration to give 0.58 g (27.5%) of V.

Isomerization of II. A 1.97-g (0.01 mole) sample of II was added to a solution of sodium ethoxide, obtained from 0.23 g (0.01 mole) of sodium and 50 ml of absolute ethanol, and the mixture was refluxed for 50 h. It was then neutralized with an ether solution of HCl (1:1), and the solvent was removed by evaporation. The residue was separated preparatively by chromatography on UV-254 silical gel in a chloroform–acetone system (5:1) to give 0.87 g (44%) of starting II and 0.12 g (6%) of 5,5-diethyl-6-methylimino-5,6-dihydro[1H,3H]-pyrimidine-2,4-dione (X) with mp 304-305°C (alcohol–hexane) and R_f 0.22.

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