All of the dyes were purified by crystallization from ethanol.

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PYRIMIDINE–PYRIMIDYLIDENE TAUTOMERISM OF SOME 4-PYRIMIDYLMALONIC ACID DERIVATIVES*

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2,6-Diphenyl-4-pyrimidylmalonic esters (I, II) 2,6-diphenyl-4-cyanoacetic ester (III), and 2,6-diphenyl-4-pyrimidylmalononitrile (IV) were obtained for the study of pyrimidine-pyrimidylidene tautomerism by condensation of 4-chloro-2,6-diphenylpyrimidine with the appropriate malonic acid derivatives. The structures of the tautomeric forms and the positions of the equilibria were studied by PMR, IR, and UV spectroscopic methods.

During a study of the structures of some 2-pyrimidylmalonic acid derivatives [1] it was established that in solution the latter exist either in the pyrimidine form or in the pyrimidylidene form. One should probably also expect instances of equilibria between two forms among compounds of this sort, i.e., tautomerism of the type

which is well known for sym-triazine derivatives [2] and some other nitrogen-containing heterocycles [3]. To obtain a pyrimidine–pyrimidylidene system with comparable amounts of both forms and to study the factors that affect their equilibrium, we synthesized 2,6-diphenyl-4-pyrimidylmalonic esters (I, II), 2,6-diphenyl-4-pyrimidylcyanoacetic esters (III), and 2,6-diphenyl-4-pyrimidylmalononitrile (IV).

The structures of the products were studied by means of PMR, IR, UV spectroscopy. The UV spectra of I-IV contain absorption maxima at λ > 300 nm, which cannot belong to tautomer A (see Fig. 1 and the scheme below) and indicate the presence of pyrimidylidene forms (B, C,

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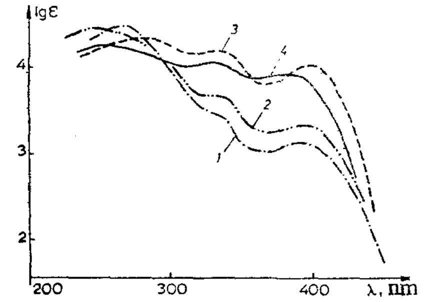
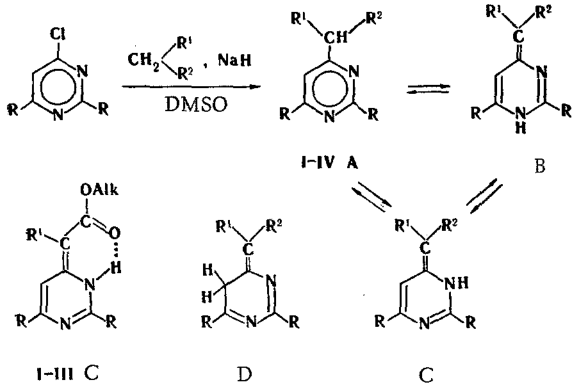


Fig. 1. UV spectra of I-IV in $CHCl_3$: 1) I; 2) II; 3) III; 4) IV.

TABLE 1. Characteristics of the Compounds Obtained

Compound	Amount of $CH_2R_1R_2$ and NaH mmole	Heating temp., °C	Heating time, h	mp, °C	Recrystallization solvent	Empirical formula	Found, %			Calc., %			Yield, %
							C	H	N	C	H	N	
I	6	100	12	86—88	Hexane	$C_{23}H_{22}N_2O_4$	70,4	5,72	7,31	70,7	5,68	7,18	75
II	6	100	7	135—136	Petroleum ether	$C_{21}H_{18}N_2O_4$	69,4	4,92	8,00	69.6	5,00	7,73	90
III	5	80	4	215—218	Ethanol	$C_{21}H_{17}N_3O_2$	73,7	5,07	12,5	73,5	4,99	12,2	90
IV	4	80	3	300—310	Ethanol—dimethylformamide	$C_{19}H_{12}N_4$	77,3	4,40	19,0	77,0	4,08	18,9	67

and D). The presence in the PMR spectra of I and II of signals of a methylidyne proton (4.84 and 4.94 ppm, respectively, on the δ scale) indicates that pyrimidine form A is also realized in solutions of these compounds, whereas the absence of this signal for III and IV constitutes evidence for the pyrimidylidene structure of the latter and the absence of tautomer A.



I $R^1=R^2=COOC_2H_5$; II $R^1=R^2=COOCH_3$; III $R^1=CN$, $R^2=COOC_2H_5$; IV $R^1=R^2=CN$, $R=C_6H_5$

Evaluation of the total energies of the three possible pyrimidylidene structures (B, C, and D), carried out for models with R = H and R_1 = R_2 = $COOCH_3$ by the CNDO-2 method [4, 5], gives the following sequence (the energy of the most favorable form was assumed to be zero): C (0), B (5 kcal/mole), and D (20 kcal/mole).* This relationship provides a basis to assume the possibility of equilibrium B $\rightleftharpoons$ C in the absence of tautomer D. In fact, no appreciable deterium exchange for the 5 position in the pyrimidine ring (PMR data) occurs when I-IV are refluxed in deuteroacetic acid or in CH_3OD—dimethyl sulfoxide (DMSO). With allowance for the fact that intramolecular migration of a proton during the tautomeric transformation A $\rightleftharpoons$ D is unlikely (this sort of 1,3 shift is forbidden from symmetry considerations [8]), the absence of deuterium exchange indicates that form D is not realized even in trace amounts. The position of the band of carbonyl absorption in the IR spectrum of III ($\nu_{C=O}$ < 1650 cm^{-1}) and the δ_{NH} value in the PMR spectrum (14.4 ppm) indicate the presence of a chelate ring with a

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*It should be noted that the CNDO-2 method quite accurately reflects the stabilizing effect of an intramolecular hydrogen bond (IMBH [6, 7].

strong intramolecular hydrogen bond (IMHB) (form IIIC'). The pyrimidinylidene tautomer for I and II has the same structure, as follows from the δ_{NH} value of 15.4 ppm and the practically complete coincidence of the longwave portion of the UV spectra of I, II, and III. The other possible pyrimidylidene form (B) is excluded in the case of III in view of the absence in its IR spectrum of absorption corresponding to a carbonyl group that is not tied up in an IMHB; it is excluded in the case of I and II from the integral intensity of the NH signal in the PMR spectrum.* The IMHB stabilizes form C is absent in the IV molecule. One should expect rapid proton exchange for IVC and IVB, and the problem of the position of the IVC ⇌ IVB equilibrium requires further study.

The position of the A ⇌ C equilibrium in $CDCl_3$ was determined by PMR spectroscopy from the integral intensity of the signals of the OCH_3 groups (32% tautomer C). Proceeding from this, we calculated the molar extinction coefficient of the pyrimidylidene tautomer at λ 400 nm, which was subsequently used for the evaluation of the position of the tautomeric equilibrium of I (16% C). Direct measurement by PMR spectroscopy was difficult because of the almost complete coincidence of the OCH_2CH_3 signals of the different forms, and calculations from the intensity of the signal of the methylidyne proton would be too inaccurate. Another method for the evaluation of the equilibrium from the UV spectra with the aid of III as the model compound gives close results (the percentages of the pyrimidylidene forms in $CDCl_3$ for I and II are 16 and 30%, respectively). One's attention is directed to the high sensitivity of the pyrimidine–pyrimidiylidene A ⇌ B equilibrium to the character of the subsequent attached to the CH fragment. Even the extremely small increase in the acceptor character of R_1 and R_2 on passing from I to II is accompanied by an increase in the percentage of tautomer C from 16 to 30%, and whereas the solid state of I contains both tautomeric forms, II contains only tautomer C (the band at 1740 cm^{-1} in the IR spectrum of a KBr pellet vanishes).

Thus, the data on the tautomerism of 2,6-diphenyl-4-pyrimidylmalonic acid derivatives show that the 4-substituted derivatives of pyrimidine display a higher tendency to undergo conversion to the pyrimidylidene form than the analogous 2-substituted derivatives [1]. We propose to ascertain the common character of this conclusion in the future.

EXPERIMENTAL

The IR spectra of the compounds were recorded with a UR-20 spectrometer. The PMR spectra were recorded with A-56/60a and HA-100 spectrometers with hexamethyldisiloxane as the internal standard. The UV spectra were recorded with a Specord spectrophotometer. The calculations by the CNDO-2 method were made in conformity with the program in [10] with a BESM-6 computer in the computer center of the Siberian Branch of the Academy of Sciences of the USSR.

General Method for Heteroarylation. The appropriate amount of NaH (see Table 1) was added to a solution of 0.53 g (2 mmole) of 4-chloro-2,6-diphenylpyrimidine [11] in 12 ml of dry DMSO in a dry argon atmosphere, after which a solution of the CH_2-active component in 2-5 ml of DMSO was added with vigorous stirring. When hydrogen evolution ceased, the mixture was heated in an oil bath. The heating time and temperature are indicated in Table 1. For isolation of I-III, the cooled reaction mixture was poured into 50 ml of CH_2Cl_2, 100 ml of water was added, and the mixture was acidified with stirring to pH ∿ 2 with concentrated HCl. The aqueous layer was extracted with two 20-ml portions of CH_2Cl_2, and the extracts were combined with the principal organic portion and washed with three 15-ml portions of water and dried with $MgSO_4$. Removal of the solvent gave a slowly (up to 2 days) crystallizing substance, which was purified by recrystallization. For the isolation of IV, the mixture was acidified with 1 ml of concentrated HCl and poured into 30 ml of water, and the precipitate was removed by filtration, dried over KOH, and purified by recrystallization.

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*Since proton exchange between forms B and C involves cleavage of the IMHB for I and II, this sort of exchange would be slow on the PMR time scale, and the signals of the NH protons are separated.

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DERIVATIVES OF CONDENSED PYRIMIDINE, PYRAZINE, AND PYRIDINE SYSTEMS.

XXXIV.* STRUCTURE AND PROPERTIES OF 5-AMINO-6-THIO-1,6-DIHYDROPYRIMIDINES

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543.422.25.4.6

It is shown by means of IR, UV, and PMR spectroscopy that 5-amino-6-thio-1,6-dihydropyrimidines exist primarily in the thione form both in the crystalline state and in solution.

Methods for the preparation of 5-amino-6-thio-1,6-dihydropyrimidines (I-IV) — starting materials in the synthesis of pyrimido[4,5-b]-1,4-thiazine derivatives — have been reported [1-3]. In the present research we investigated the structure of I-IV and their tendency to undergo thione–thiol tautomerism. Model 5-amino-6-methylthiopyrimidines (V-VIII) with a fixed thiol form were obtained by reaction of I-IV with diazomethane, dimethyl sulfate, and methyl iodide in the presence of alkaline agents. 6-Benzylthiopyrimidine IX was similarly obtained from pyrimidine I and benzyl chloride (Table 1). Reaction of thione I with dimethyl sulfate in the absence of potassium carbonate gave X, the structure of which was confirmed by the presence in its IR spectrum of absorption bands of CO (1640 cm^{-1}) and NH (3150, 3195, and 3310 cm^{-1}) groups and in its PMR spectrum of signals of SCH_3 (2.36 ppm), $N(CH_3)_2$ (2.82 ppm), and 2-H (8.20 ppm) groups. Alkylation of X with dimethyl sulfate or methyl iodide in alkaline media gave XI, the IR spectrum of which contains the absorption band of a CO group (1635 cm^{-1}); the stretching vibrations of an NH group are absent in the spectrum.

The PMR spectra of S-methyl derivatives V-VIII with a fixed thiol form contain a three-position signal at 2.5-2.6 ppm, which is characteristic for an SCH_3 group bonded to an aromatic ring (Table 2). In the alternative structure of compounds with a methyl group attached to the ring nitrogen atom the signal of the CH_3 group attached to the nitrogen atom of the thiolactam form (for example, in the case of 1-N-methyl-2-thiodihydropyridine) is found at 3.6-3.9 ppm.

An examination of the IR spectra of 5-amino-6-thiodihydropyrimidines I-IV shows that these compounds exist in the thione form in the crystalline state (from the absence of the

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*See [1] for communication XXXIII.

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