in 68% yield and had mp 181-182°C (from benzene–petroleum ether). Found: N 18.1; S 13.9%; M (ebullioscopic) 228. $C_{12}H_{13}N_3S$. Calculated: N 18.2; S 13.8%; M 231.

1-Phenyl-3-methyl-4-formyl-5-imidazolium Dehydrooxide (Va). A 0.9-g (4.5 mole) sample of I was heated with 0.42 ml (4.5 mmole) of dimethyl sulfate at 140-150°C for 2 h, after which the mixture was cooled, and the solid material was pulverized and dissolved at room temperature in an aqueous solution of sodium hydroxide (9 mole). The resulting precipitate was removed by filtration, washed with water, and precipitated twice from ethyl acetate by the addition of petroleum ether. The yield of product with mp 178-180°C was 0.14 g (15%). Found: N 13.8%. $C_{11}H_{10}N_2O_2$. Calculated: N 13.9%.

1-Phenyl-3-methyl-4-formyl-5-imidazolium Dehydrothiooxide (Vb). This compound was similarly obtained by treatment of methylated I with an aqueous solution of potassium hydrosulfide. Two reprecipitations from ethyl acetate by the addition of petroleum ether gave a product with mp 237-239°C. The yield was 0.66 g (67%). Found: N 13.1; S 14.9%. $C_{11}H_{10}N_2OS$. Calculated: N 12.9; S 14.7%.

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NEW REACTION FOR THE DIRECT INCORPORATION OF PURINES IN NUCLEOPHILIC ORGANIC COMPOUNDS

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UDC 547.857.07

The direct incorporation of purine and theophylline residues in indole, oxindole, and pyrazolone rings was accomplished in the presence of acylating agents.

Very little is known regarding reactions involving the replacement of a hydrogen atom of the purine ring, and those that have been reported pertain mainly to electrophilic substitution [1]. Almost no study whatsoever has been devoted to the quaternary salts of purine and their reactions with nucleophiles. It is known that purine itself is a weak base and that the most nucleophilic center of the molecule is the N_1 atom of the pyrimidine ring. Protonation [2] and the formation of N-oxides [3] take place at this atom. It might have been assumed that purine in acylating agents would be capable of forming N-acyl salts, which in situ, in analogy with other N-acyl heteroaromatic cations [4], would serve as electrophilic agents for the incorporation of purine in nucleophilic organic compounds.

In fact, in the case of the reaction of purine with 1-methylindole, oxindole, and 1-phenyl-3-methyl-5-pyrazolone in acetic anhydride we obtained the corresponding N_1-acetyl heterocyclic derivatives of 1,6-dihydropurine (I-III):

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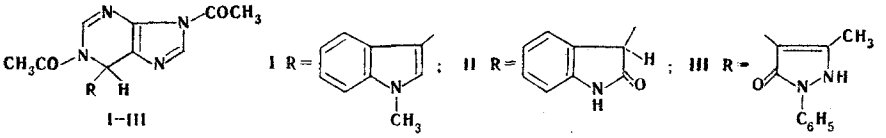
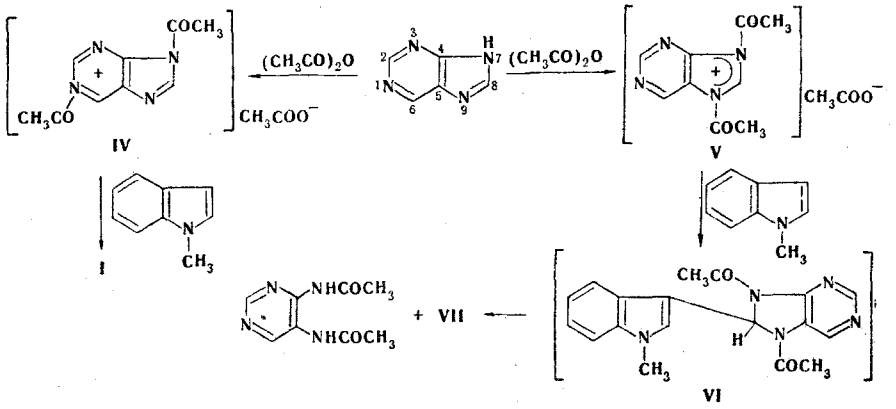


I-III

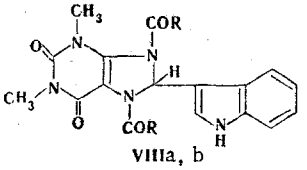
The production of these compounds is easy to explain if one assumes the intermediate formation of the N_1-acetyl salt of purine (IV). However, in some cases such as, for example, in the reaction of purine with 1-methylindole in acetic anhydride or in the presence of benzoyl chloride, we isolated tris(1-methyl-3-indolyl)methane (VII) along with I; this constitutes evidence for the acylation of purine not only with the formation of N_1-acetyl salt IV but also with the formation of $N_{7,9}$-diacyl salt V. In the reaction of this salt with methyl-



IV V VI VII

indole the opening of the imidazole ring that is characteristic for 7,9-disubstituted purines [5-7] occurs along with the formation of VII, which has also been previously observed in the reactions of indoles with N-acyl salts of benzooxazolium [8] and other N-acyl heteroaromatic cations [9].

We were also able to extend this reaction to theophylline, but acetic anhydride proved to be unsuitable as an acylating agent in this case. We were able to carry out the reaction in the presence of acyl halides in an inert solvent, in which case the indole added to the C_8 atom of the purine ring to give VIII:



VIIIa, b

VIII a $R=CH_3$; b $R=C_6H_5$

The individuality of the compounds obtained was established by means of thin-layer chromatography (TLC).

The IR spectra of I-III and VIII contain bands at 1650-1700 (C=O and C=N), while the spectra of II, III, and VIII also contains bands at 3400-3490 (indole ring NH) or 3300-3400 cm^{-1} (oxindole and pyrazolone NH). Signals of five aromatic protons of the indole fragment (m, 6.98-7.47 ppm), of the methyl group of the indole ring (s, 3H, 3.73 ppm), and two methyl groups of the acetyl residues — one attached to the N_1 atom of the pyrimidine ring (s, 3H, 2.02 ppm) and one attached to the N_7 atom of the imidazole ring (s, 3H, 2.50 ppm) — are observed in the PMR spectrum of I. In addition, the spectrum contains single signals of purine 2-H (8.62 ppm), 8-H (8.97 ppm), and 6-H (7.63 ppm) protons. Thus the nonequivalence of the signals of the two acetyl groups and the position of the signals of the protons of the purine ring confirm the correctness of structure I as opposed to alternative structure VI.

The mass spectrum of this compound also corresponds to structure I: In the first stage of the fragmentation of M^+ an acetyl group or ketene is eliminated, as is usually the case for such structures [10]. In our case the spectrum contains two $[M - CH_2CO]^+$ (293) and $[M - 2CH_2CO]^+$ (251) ion peaks. As in the case of I, in the mass spectrum of II one observes, in addition to M^+ peaks, $[M - CH_2CO]^+$, $[M - 2CH_2CO]^+$, and $[(M - CH_2CO) - CH_3]^+$ ion

TABLE 1. Heterocyclic Derivatives of Dihydropurines

Compound	mp, °C*	R_f	IR spectrum, † cm^{-1}		Found, %			Empirical formula	Calc., %			Yield,
			C=O	N=H	C	H	N		C	H	N	
II	322—323	0,65‡	1650 1702		59,8	4,3	20,6	$C_{17}H_{15}N_5O_3$	60,5	4,5	20,7	40
III	284—285	0,81‡	1650 1700		60,0	4,9	22,3	$C_{19}H_{18}N_6O_3$	60,3	4,8	22,2	34
VIIIa	183	0,25**	1645 1692	3390	60,3	5,3	18,1	$C_{18}H_{13}N_5O_4$	60,0	5,0	18,3	28
VIIIb	220—221	0,45**	1650 1700	3400	68,7	4,3	13,5	$C_{29}H_{23}N_5O_4$	68,9	4,5	13,8	20

*From n-butanol. †In mineral oil. ‡In System A. ** In system B.

peaks, an oxindole fragment (133), a purine residue (120), and other ion peaks that confirm the structure of II.

Evidence for the correctness of the structure of VIIIa is provided by the very close location of the signals of the protons of the CH_3CO groups in the PMR spectrum (2.50 ppm), which indicates that they are almost completely equivalent. The presence in the mass spectrum of VIII of M^+, $[M - COCH_3]^+$, and $[M - 2COCH_3]^+$ ion peaks and indole and theophylline fragments, as well as ions formed in the fragmentation of the theophylline ring [11], is also indicative of this.

EXPERIMENTAL

The IR spectra of mineral oil suspensions of the compounds were recorded with a UR-20 spectrometer. The mass spectra were recorded with a Varian MAT-311 spectrometer at an accelerating voltage of 3 kV, a cathode-emission current of 300 mA, an ionizing voltage of 75 eV, and an ion-source temperature of 250-300°C. The PMR spectra of solutions of the compounds in d_6-DMSO were recorded with a Varian XL-100 spectrometer at room temperature with tetramethylsilane as the internal standard. Chromatography was carried out in a loose thin layer of Al_2O_3 (activity II on the Brockmann scale) in chloroform—benzene—hexane [30:6:1) (system A) and chloroform—benzene—hexane—methanol (30:6:1:1) (system B). The chromatograms were developed with iodine vapors.

1,7-Diacetyl-6-(1-methyl-3-indolyl)-1,6-dihydropurine (I). A mixture of 1.2 g (0.01 mole) of purine, 1.3 g (0.01 mole) of 1-methylindole, and 20 ml of acetic anhydride was refluxed for 4 h, and the precipitated tris(1-methyl-3-indolyl)methane was removed by filtration and washed with acetic anhydride to give 0.55 g (32%) of a product with mp 292°C [from dimethylformamide (DMF)] (mp 292°C [12]). The acetic anhydride mother liquors were combined and poured with stirring into 100 ml of water, and the initially formed oil that subsequently began to crystallize was separated, washed three times with methanol, and recrystallized from n-butanol. The yield of I, with mp 219-220°C and R_f 0.4 (system A), was 0.85 g. IR spectrum: 1650 cm^{-1} (C=O). PMR spectrum: 2.02 s, 2.50 s, 3.73 s, 6.98-7.47 m, 7.63 s, 8.63 s, and 8.97 s ppm. Found: C 64.3; H 5.3; N 21.6%. $C_{18}H_{17}N_5O_2$. Calculated: C 64.5; N 5.1; N 20.9%.

Compounds II and III, the characteristics of which are presented in Table 1, were similarly obtained.

1,7-Dibenzoyl-6-(1-methyl-3-indolyl)-1,6-dihydropurine. A mixture of 1.2 g (0.01 mole) of purine, 1.3 g (0.01 mole) of 1-methylindole, and 1.4 g (0.01 mole) of benzoyl chloride in 15 ml of dry DMF was heated at 100°C for 3 h, after which it was cooled, and the precipitated tris(1-methyl-3-indolyl)methane was removed by filtration, dried, and recrystallized from DMF to give 0.55 g (63%) of a product with mp 292°C. The mother liquor was diluted with water, and the solid compound that separated out was recrystallized from n-butanol. The yield of 1,7-dibenzoyl-6-(1-methyl-3-indolyl)-1,6-dihydropurine, with mp 225°C and R_f 0.3 (system A), was 0.15 g (18%). IR spectrum: 1650 cm^{-1} (C=O). Found: C 73.4; H 4.9; N 15.2%. $C_{28}H_{21}N_5O_2$. Calculated: C 73.2; H 4.6; N 15.3%.

Compounds VIIIa, b (Table 1) were similarly obtained.

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PYRIMIDINES. 69.* SYNTHESES BASED ON ACETYLPYRIMIDINES. DIPYRIMIDINYLS AND PYRIMIDINE ANALOGS OF CHALCONE

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Substituted pyrimidinyl styryl ketones were obtained by condensation of 4-methyl-2-phenyl-5-acetylpyrimidine with aromatic aldehydes, and their conformations in KBr and in solution in $CHCl_3$ were examined. 4',5-Dipyrimidinyl derivatives were obtained by cyclization of the pyrimidinyl styryl ketones with benzamine. The isomeric trioxo-4',5- and -4,6'-dipyrimidinyls were obtained by reaction of 5- and 6-acetyluracils with benzalbisurea.

Interest in 4,4'- and 4,5'-dipyrimidinyl derivatives has arisen in connection with their formation as the principal products in the photolysis of frozen aqueous solutions of uracil, cytosine, etc. [2, 3]. The methods that have been developed for the synthesis of dipyrimidinyls pertain for the most part to symmetrical derivatives — 2,2'- or 5,5'-dipyrimidinyls [4]. A number of methods for the synthesis of 4,5'-dipyrimidinyls from 4-methylpyrimidine [5, 6], by photolysis of uracil and cytosine [7, 8], through pyrimidinyllithium compounds [9] and by condensation of aminomethylene derivatives of acetylpyrimidines [2, 10] have been recently published.

Continuing our study of the synthesis of pyrimidine derivatives from substituted acetophenones [11], we attempted to use acetylpyrimidines for the synthesis of dipyrimidinyl derivatives.

Using the readily accessible 4-methyl-2-phenyl-5-acetylpyrimidine (I) as the starting compound, we tried to subject it to condensation with benzalbisurea in CH_3COOH or n-butanol—HCl [11]; however, the expected 4,5'-dipyrimidinyl (II) was not detected among the reaction products. Protonation of pyrimidine I probably occurs in acidic media, and electrophilic substitution by the ureidobenzyl cation at the acetyl group does not take place.

Another possible method for the synthesis of 4,5'-dipyrimidinyls from ketones is through the corresponding chalcone analogs [12, 13]. The pyrimidine analogs of chalcone

*See [1] for Communication 68.

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