SYNTHESIS OF SCHIFF BASES OF 2-SUBSTITUTED 5-AMINOPYRIMIDINES AND THEIR MESOMORPHIC PROPERTIES

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Schiff bases of 2-substituted 5-aminopyrimidines were synthesized, and their liquid-crystal and dielectric properties were investigated. It is shown that narrow ranges of the existence of meso phases and a greater (as compared with benzylideneanilines) tendency for the development of a smectic state are characteristic for 2-alkoxy-, 2-alkyl-, and 2-cyano-5-arylideneaminopyrimides. The introduction of an aryl substituent into the 2 position of the pyrimidine ring gives rise to a pronounced increase in the thermostability of the meso phase and significantly increases the range of its existence. The use of groups with higher dipole moments as terminal groups leads to the production of compounds with high positive dielectric anisotropies.

Many compounds of the heterocyclic series that have liquid-crystal properties are known [1]. Among these compounds, 2,5-disubstituted pyrimidines, primarily aryl and diaryl derivatives, have shown a number of interesting properties, viz., high positive dielectric anisotropy [2], polymorphism [3], the formation of a low-temperature smectic [4], etc. At the same time, one of the most widely investigated types of liquid crystals in the aromatic series are azomethines — represented primarily by individual derivatives of the pyridine series for the heterocyclic compounds [5-7].

The literature contains very little information regarding the synthesis of Schiff bases of aminopyrimidines [8], and one usually deals with 5-aminopyrimidine derivatives; the synthesis of the p-nitrobenzylidene derivative of 2-aminopyrimidine was described only very recently [9].

In order to search for new liquid-crystal compounds we synthesized Schiff bases of 2-substituted 5-aminopyrimidines and investigated their liquid-crystal and dielectric properties.

The 2-substituted 5-aminopyrimidines (Ia-e) were obtained from 2-dimethylaminomethyleneamino-3-dimethylaminopropenylidenedimethylamine (II) through aminomethylene derivatives III by the method in [10, 11], which was found to be a more convenient method for the preparation of 5-amino-2-methylpyrimidine than previously described methods [12, 13]. However, we were unable to realize the synthesis of 5-amino-2-alkylpyrimidines with an alkyl chain longer than a methyl chain via this scheme: butyl- and amylamidines did not react with salt II.

It was shown that this method is also unsuitable for the preparation of 5-amino-2-arylpyrimidines. In contrast to derivatives IIIa-e 2-arylmethyleneaminopyrimidines IIIf, g did not undergo hydrolytic cleavage. Only traces of the corresponding amines (If, g) were formed even after refluxing for many hours with 2 N NaOH, and when pyrimidine IIIf was refluxed with H_2SO_4 (0.2 mole/liter), it was converted only to 5-formylamino-2-phenylpyrimidine. 5-Amino-2-arylpyrimidines (If-j) were obtained in good yields by reduction of the corresponding 5-nitro derivatives IV, which were synthesized by the method in [14], with iron in acetic acid and alcohol [15], in contrast to the unsuccessful attempts to reduce the same compounds by other methods [14]. In the case of reduction with hydrazine hydrate and Pd/C the reaction proceeded without complications only for the described reduction of nitropyrimidine IVf [16]. In the case of nitro-bromo derivatives IVg under these conditions the bromine atom in the aromatic ring underwent simultaneous replacement by hydrogen along with reduction of the nitro

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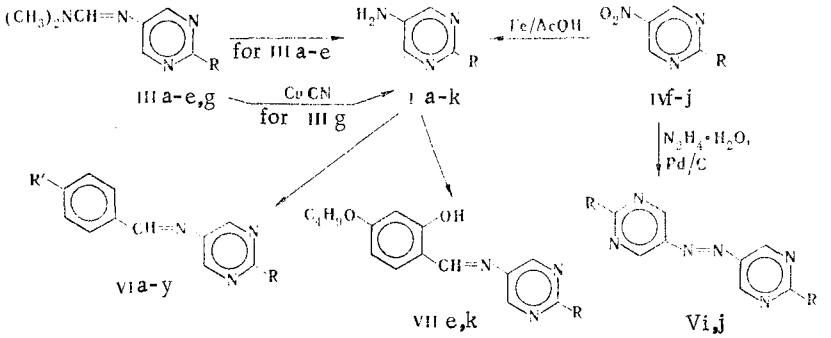
TABLE 1. 2-Substituted 5-Arylideneaminopyrimidines VI

Compound	R	R′	Transition temp., °C (from alcohol)			Found, %			Empirical formula	Calc., %			Yield, %
			S	N	I	C	H	N		C	H	N	
VIa	CH_3O	CH_3O	—	—	116,7	64,2	5,3	17,5	$C_{13}H_{13}N_3O_2$	64,2	5,3	17,3	38
VIb	CH_3O	C_2H_5O	—	(93,3)	110,4	65,5	5,7	16,6	$C_{14}H_{15}N_3O_2$	65,4	5,4	16,3	68
VIc	CH_3O	C_4H_9O	—	(86,6)	91	66,9	6,6	14,9	$C_{16}H_{19}N_3O_2$	67,3	6,7	14,7	83
VId	CH_3O	$C_6H_{13}O$	71,7	72,7	92,3	313,1798[a]			$C_{18}H_{23}N_3O_2$	313,1790[a]			80
VIe	CH_3O	$C_9H_{19}O$	77,3	—	96,4	71,5	8,2	11,9	$C_{21}H_{29}N_3O_2$	71,1	8,2	11,8	97
VIf	C_4H_9O	C_4H_9O	89,0	—	112,0	70,2	7,6	12,7	$C_{19}H_{25}N_3O_2$	69,7	7,6	12,8	41
VIg	C_4H_9O	$C_6H_{13}O$	90,6	—	115,5	71,4	8,2	12,1	$C_{21}H_{29}N_3O_2$	71,1	8,2	11,8	40
VIh	C_4H_9O	$C_8H_{17}O$	85,0	—	115,5	72,5	8,7	11,0	$C_{23}H_{33}N_3O_2$	72,1	8,6	10,9	47
VIi	C_4H_9O	NO_2	—	—	116,6	59,7	5,2	18,6	$C_{15}H_{16}N_4O_3$	60,0	5,3	18.6	64
VIj	CH_3	$C_6H_{13}O$	—	—	105	72,7	7,7	14,1	$C_{18}H_{23}N_3O$	72,7	7,7	14,1	60
VIk	CH_3	$C_8H_{17}O$	—	—	108	73,6	8,1	12,9	$C_{20}H_{27}N_3O$	73,8	8,3	12,9	81
VIl	CH_3	$C_9H_{19}O$	—	—	107,7	74,3	8,3	12,6	$C_{21}H_{29}N_3O$	74,3	8,5	12,4	66
VIm	Cl	C_4H_9O	—	—	119	62,1	5,6	14,5	$C_{15}H_{16}ClN_3O$	62,2	5,5	14,5	83
VIn	Cl	$C_9H_{19}O$	—	—	106,3	67,1	7,3	11,8	$C_{20}H_{26}ClN_3O$	66,8	7,2	11,7	83
VIo	CN	C_4H_9O	—	98,7	109,5[b]	68,8	5,9	20,1	$C_{16}H_{16}N_4O$	68,6	5,7	20,0	73
VIp	CN	$C_6H_{13}O$	102	110	115[b]	70,4	6,4	18,2	$C_{18}H_{20}N_4O$	70,1	6,5	18,2	67
VIq	CN	$C_9H_{19}O$	89	—	126[b]	72,3	7,5	16,2	$C_{21}H_{26}N_4O$	72,0	7,6	16,0	77
VIr	*p*-$CH_3OC_6H_4$	CH_3O	169	296	298	71,5	5,4	13,1	$C_{19}H_{17}N_3O_2$	71,5	5,3	13,1	90
VIs	*p*-$CH_3OC_6H_4$	C_4H_9O	105	149	250	73,1	6,6	11,6	$C_{22}H_{23}N_3O_2$	73,1	6,4	11,6	53
VIt	*p*-$CH_3OC_6H_4$	$C_6H_{13}O$	90	180	245	74,4	7,0	10,8	$C_{24}H_{27}N_3O_2$	74,0	6,9	10,8	76
VIu	*p*-$C_4H_9OC_6H_4$	C_4H_9O	123	190	254	74,5	7,2	10,4	$C_{25}H_{29}N_3O_2$	74,4	7,2	10,4	86
VIv	*p*-$C_4H_9OC_6H_4$	$C_6H_{13}O$	109,6	211,3	238,5	75,1	7,3	9,9	$C_{27}H_{33}N_3O_2$	75,2	7,7	9,7	56
VIw	*p*-$C_6H_{13}OC_6H_4$	$C_6H_{13}O$	98,1	214,1	228,5	76,0	7,8	9,1	$C_{29}H_{37}N_3O_2$	75,8	8,0	9,1	32
VIx	C_6H_5	$C_6H_{13}O$	80	—	155	76,7	6,9	11,8	$C_{23}H_{25}N_3O$	76,9	6,9	11,7	69
VIy	*p*-BrC_6H_4	$C_6H_{13}O$	95	—	258	63,1	5,5	9,4	$C_{23}H_{24}BrN_3O$	63,0	5,5	9,6	100

[a]Molecular mass. [b]From hexane.

group to give only aminopyrimidine If. In the case of nitropyrimidines IVi, j with kaloxyphenyl groups the only products isolated were azo compounds V, of which Vi displayed liquid-crystal properties (see the experimental section).

5-Amino-2-(p-cyanophenyl)pyrimidine (Ik) was obtained in one step from aminomethylene-bromo derivative IIIg by the reaction with CuCN in N-methylpyrrolidone, since, in addition to replacement of bromine by the CN group, the aminomethylene substituent in the 5 position is converted to an amino group.

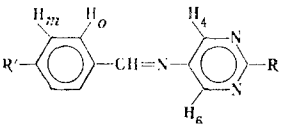


I, III—V, VII a R=Cl; b R=OCH_3; c R=OC_4H_9; d R=CH_3; e R=CN; f R=C_6H_5; g R=C_6H_4Br-*p*; h R=$C_6H_4OCH_3$-*p*; i R=$C_6H_4OC_4H_9$-*p*; j R=$C_6H_4OC_6H_{13}$-*p*; k R=C_6H_4CN-*p*; VI R, R′ see Table 1

Schiff bases VIa-n, r-x were synthesized by refluxing aminopyridines I and the corresponding aldehydes in alcohol, while derivatives VIo-q with a cyano group in the 2 position were obtained by carrying out the reaction in toluene (Table 1). The latter were found to be rather stable compounds, although it was noted that they undergo complete decomposition upon prolonged contact with air. On the other hand, the Schiff base from 5-amino-2-(p-cyanophenyl)pyrimidine (Ik) and p-butoxybenzaldehyde was found to be so unstable that we were unable to isolate it in pure form without admixed starting amine.

It is known that the introduction of an o-OH group in a Schiff base molecule stabilizes the latter due to the formation of an intramolecular hydrogen bond [17]. In this connection, we obtained 5-(4-butoxy-2-hydroxybenzylideneamino)-substituted 2-cyano- (VIIe) and 2-(4-cyanophenyl)pyrimidines (VIIk). However, both of the compounds obtained were extremely un-

TABLE 2. PMR Spectra of the Arylideneaminopyrimidines



Compound	Chemical shifts, δ, ppm				
	R, R′	H_o[a]	H_m[a]	$H_{4,6}$	CH=N
VId	0,9—1,17 (m, 11H); 3,98 (s, 5H)	7,82[b]	6,95	8,37 (s, 2H)	8,35 (d, 1H, J=0,5Hz)
VIe	0,83—1,23 (m); 3,97 (s, 5H)	7,80	6,90	8,40 (s, 3H)[c]	
VIj	0,69—2,10 (m, 11H); 2,59 (s, 3H); 3,91 (t, 2H)	7,74	6,87	8,33 (s, 3H)[c]	
VIm[d]	0,75—1,80 (m); 4,00 (t, 2H)	7,80	6,87	8,34 (s, 3H)[c]	
VIn	0,63—1,50 (m); 3,93 (t, 2H)	7,88	6,90	8,35 (s, 2H)	8,27 (s, 1H)
VIp	0,64—1,96 (m, 11H); 3,99 (t, 2H)	7,79	6,89	8,51 (s, 2H)	8,29 (s, 1H)
VIq	0,56—1,96 (m); 3,96 (t, 2H)	7,81	6,95	8,52 (s, 2H)	8,32 (s, 1H)

[a]Doublet, 2H, J = 9 Hz. [b]The signal is broadened. [c]The signals are overlapped. [d]In a mixture of $CDCl_3$ and d_6-acetone.

stable (they decomposed in a few days upon standing) and were even less stable than their analog, which does not contain an o-OH group, IVo, which is stable for several months. It is possible that for weakly basic amines such as aminocyanopyrimidines Ie, k, a hydrogen bond is not realized in Schiff bases VII. An increase in the frequency of the stretching vibration of the C=N group to 1640 cm^{-1} as compared with 1620 cm^{-1} in VId, p, x is observed in the IR spectrum of anil VIIk (see [18]).

In the literature it is noted that, as compared with the "aldehyde" substituent in the "amide" part of the molecule, the Schiff bases have a weaker effect on its spectral characteristics and, in particular, on the signal of the proton of the CH=N group [19, 20], although an appreciable (up to 0.6 ppm) weak-field shift of the signal of the methylidyne proton as compared with benzylideneanilines [9], has been observed for Schiff bases from α-amino-substituted nitrogen heterocycles. In fact, for VI (Table 2) the effect of the substituent in the 2 position of the pyrimidine ring is small: the CH=N signal is found in the same region as in the case of aromatic compounds [20] even when a CN group is introduced (VIp, q). The influence of the CH=N group as an acceptor is exerted to the greatest extent on the position of the signal of the ortho aromatic protons (a 0.5 ppm shift to weak field), whereas it has a weak effect on the pyrimidine ring due to the nonplanar orientation of the "amine" aromatic ring [20, 21]. Nevertheless, shielding of the protons (a shift of up to 0.3 ppm) in the 4 and 6 positions as compared with pyrimidine [22], which becomes even more pronounced when an acceptor is introduced into the 2 position (VIp, q), is observed, although to a smaller extent than the usual shielding for aminopyrimidines.

It is apparent from Table 1 that the first members of the 5-arylideneamino-2-alkoxypyrimidine series either do not have a liquid-crystal state (VIa) or are monotropic liquid crystals (VIb, c). An increase in the length of the alkyl chain in the 4 position of the benzylidene fragment (VId, e) or in the pyrimidine ring (VIf-h) gives rise to the development of a smectic A phase. Replacement of the alkoxy group in the aldehyde part of the molecule by a nitro group leads to disappearance of the liquid-crystal properties (VIi). A comparison of the 5-arylideneamino-2-alkoxypyrimidines with the corresponding benzylideneanilines [23] shows that vis-á-vis a slight decrease in the thermostability of the meso phase the 2-alkoxy derivatives of pyrimidine have a wider range of the existence of the smectic meso phase due to lower temperatures of transition to the smectic state. The meso phases that are characteristic for the analogous Schiff bases of the benzene ring are absent in the case of 5-aryldieneamino-2-alkylpyrimidines VIj-l. The introduction of a chlorine atom, which polarizes the molecule much more strongly (VIm, n), into the pyrimidine ring in place of a methyl group also led to the development of liquid-crystal properties. A narrow range of the exis-

tence of a nematic phase (5-11°C) and the development of a smectic meso phase (VIp, q) are characteristic for 2-cyano derivatives VIo-q.

The introduction of an aryl substituent into the 2 position of the pyrimidine ring (VIr-y) gives rise to a sharp increase in the thermostability of the meso phase (see Table 1), in addition to a substantial increase in the range of its existence; whereas lengthening of the alkyl chain in the "aldehyde" fragment (VIr-t) leads to the development of a smectic state in the case of lower temperatures and to a broad range of the existence of the nematic meso phase (60-100°C), a substantial decrease in the range of the nematic state with retention of the smectogenic properties of the molecule is characteristic for VIu, v.

Measurement of the dielectric characteristics of VI was made in order to reveal in the most general form the relationship with the structures of the molecules. Inasmuch as the Schiff bases of the pyrimidine series are either monotropic liquid crystals or the range of their nematic meso phase lies in the high-temperature range (above 100°C) or is narrow, we made measurements for 10-20% solutions of the investigated substance in the liquid-crystal matrix. As an experimental model we used a mixture of azoxy compounds (mixture A [24]), which has a wide-ranging nematic meso phase (−5 to +73°C), the parameters of which are also well known. Although the molecules of the substances that constitute mixture A also have a dipole moment, it is small (correspondingly, the dielectric anisotropy for the mixture $\Delta\varepsilon = -0.4$ at 25°C*), one might therefore expect a slight interaction between the molecules of the investigated substance and the molecules of the matrix (i.e., the matrix is physically "neutral"). The $\Delta\varepsilon$ value presented in Table 3 was calculated from data obtained for a mixture of the investigated substance and mixture A via the additivity rule [25]. The $\Delta\varepsilon$ value obtained in this way is not equal to the $\Delta\varepsilon$ value of the examined substance itself because of the dipole correlation [26], which is expressed appreciably for molecules with high dipole moments (it decreases the $\Delta\varepsilon$ value). However, inasmuch as in solution the interaction of the molecules of the investigated substance among one another is weakened, the calculated $\Delta\varepsilon$ value nevertheless should correlate satisfactorily with the structures of the molecules and the magnitude of their dipole moments.

In the case of pyrimidine derivatives VI and VII (Table 3) the effect of the dipole moment of the pyrimidine ring directed along the long axis of the molecule on the dielectric properties is appreciable. This dipole moment is responsible for the positive dielectric anisotropy of the indicated compounds, in contrast to the Schiff bases of the benzene series such as N-p-ethoxybenzylidene)-p-butylaniline (VIII, Table 3). The increase in $\Delta\varepsilon$ in VIw, h, d is associated with the decrease in the size of the molecules, which leads to an increase in the effective dipole moment per unit of volume [27]. In the series of compounds VId, n, o the increase in $\Delta\varepsilon$ correlates with the increase in the dipole moment of the molecule, the direction of which along the long axis of the molecules leads to a large ε value. In the case of VIIe (as compared with VIo) the introduction of an OH group, which has a dipole mo-

TABLE 3. Anisotropy of the Dielectric Permeability and Dipole Moments of the Schiff Bases of Aminopyrimidines and Their Analogs

Compound	Percentage of A in the mixture, %	$\Delta\varepsilon$ (25°)	μ, D
VId	20	+7,0	4,04
VIh	20	+5,3	—
VIn	20	+19,2	5,70
VIo	10	+66,17[a]	8,15
VIw	10	+2,95	—
VIIe	10	+39,07[a]	—
VIII	—	−0,15 [17]	—
IX	—	+12,8 [1]	—

[a] At 30°C.

*The formula $\Delta\varepsilon = \varepsilon_{\parallel} - \varepsilon_{\perp}$, where $\varepsilon_{\parallel}$ and $\varepsilon_{\perp}$ are the dielectric permeabilities of the substances measured in directions parallel and perpendicular to the director of the liquid crystal.

ment, in the ortho position of the phenyl ring should give rise to a decrease in $\Delta\varepsilon$, and this is actually observed experimentally.

Compound VIIo, which has a unique positive dielectric anisotropy ($\Delta\varepsilon$ = +66) and a relatively low temperature of transition to the nematic meso phase, is of greatest interest. The sharp increase in $\Delta\varepsilon$ in this case [compare with N-(p-amyloxybenzylidene)-p-cyanoaniline (IX),* Table 3] is due to the overall contribution of the dipole moments of the CN group and the pyrimidine ring, which are directed to the same side. Compounds with high positive dielectric anisotropies are of interest for the efficient regulation of the $\Delta\varepsilon$ values of various liquid-crystal materials.

EXPERIMENTAL

The IR spectra of KBr pellets of the compounds were recorded with a UR-20 spectrometer. The UV spectra of solutions in alcohol were obtained with a Specord UV-vis spectrophotometer. The PMR spectra of solutions in $CDCl_3$ were recorded with a Varian A56/60A spectrometer with hexamethyldisiloxane as the internal standard. The molecular masses were determined by mass spectrometry with a high resolution MS 902 spectrometer. The experimental dipole moments were calculated by the Guggenheim–Smith method [28]. The dielectric permeabilities of the solutions in dioxane were determined at 25°C by the heterodyne method with a Tangens apparatus, and the refractive indexes were determined with an Abbe refractometer. The temperatures of the phase transitions were measured with a Mettler FP-5 apparatus with a Mettler FP-52 heating stage with a Polam-211 polarization microscope and with a small-scale heating stage of the Boetius type with an RNMK-0.5 visual device. The dielectric constants were measured by the method in [24].

The characteristics of the compounds obtained are presented in Tables 1-4. The symbols in the tables are as follows: S pertains to the smectic, N pertains to the nematic, and I pertains to the isotropic mesophase (the monotropic transformations are indicated in parentheses).

5-Amino-2-butoxypyrimidine (Ic). A mixture of 3.76 g (16.9 mmole) of pyrimidine IIIc and 45 ml of a 5% aqueous solution of K_2CO_3 was heated at 110°C for 8 h, after which it was cooled and filtered to give 1.6 g (55%) of aminopyrimidine Ic in the form of shiny plates with mp 71-73°C (mp 72-72.5°C [15]).

5-Amino-2-methylpyrimidine (Id). A mixture of 2.43 g (15 mmole) of pyrimidine IIId and 30 ml of a 5% solution of K_2CO_3 was refluxed for 2 h, after which the water was removed by distillation, and the residue was distilled in vacuo (2 mm) at 140°C to give 1.3 g (81%) of a product with mp 158-161°C (mp 158-159°C [11]). PMR spectrum ($CDCl_3$): 2.57 (s, 3H, CH_3), 3.91 (broad, 2H, NH_2), and 8.14 ppm (s, 2H, 4,6-H, pyrimidine ring).

5-Amino-2-phenylpyrimidine (If). A mixture of 0.4 g (1.43 mmole) of bromophenylpyrimidine IVg [14], 0.5 ml of hydrazine hydrate, and 0.4 g of 10% Pd/C in 10 ml of benzene was refluxed for 2 h, another 0.5 ml of hydrazine hydrate was added, and the mixture was refluxed for another 2 h.

5-amino-2-arylpyrimidines (Ig-j). A 0.02-mole sample of nitropyrimidine IV, 4 g (0.07 mole) of powdered iron, and 8 ml (0.14 mole) of glacial acetic acid were added to 50 ml of absolute alcohol, and the mixture was heated at 100°C with vigorous stirring for 6 h. It was then poured into 2 liters of water containing ice, and the aqueous mixture was allowed to stand for 2 h. The precipitate was removed by filtration, washed with water, and dried. Pyrimidine Ih was sublimed at 190°C (4 mm), Ig was recrystallized from alcohol, and Ii, j were recrystallized from heptane with the addition of activated charcoal.

5-Amino-2-(p-cyanophenyl)pyrimidine (Ik). A 1.67-g (18.6 mmole) sample of CuCN was added with stirring to a suspension of 3.6 g (11.8 mmole) of pyrimidine IIIg in 15 ml of N-methylpyrrolidone, and the mixture was refluxed for 3 h. It was then cooled and diluted to three times its original volume with water, treated with 20 ml of a 10% solution of ethylenediamine, and extracted with 10 30-ml portions of methylene chloride. The extract was washed with a 10% solution of ethylenediamine and water until the wash waters were neutral, dried with $MgSO_4$, and evaporated. The residue was allowed to stand in air until it solidified, after which it was titurated with ether. The mixture was filtered to give 0.67 g of pyrimidine Ik. The product was sublimed at 200-220°C (1 mm).

*In the case of a more rigorous comparison one should take into account the effect of the dipole–dipole correlation and the degree of orderliness of the liquid crystal.

TABLE 4. 2,5-Disubstituted Pyrimidines

Compound	mp, °C	IR spectrum, ν, cm^{-1}	Found, %			Empirical formula	Calc., %			Yield, %
			C	H	N		C	H	N	
Ig	249—251	3190, 3320 (N—H)	48,2	3,2	16,4	$C_{10}H_8BrN_3$	48,0	3,2	16,7	58
Ih	200—205	3200, 3310, 3420, 3540 (N—H)	66,0	5,5	21,0	$C_{11}H_{11}N_3O$	65,7	5,5	20,8	44
Ii	133—135	3380, 3450, (N—H)[a]	243,1367[b]			$C_{14}H_{17}N_3O$	243,1371[b]			82
Ij	129—132	3400, 3500 (N—H)[a]	70,4	7,9	15,3	$C_{16}H_{21}N_3O$	70,9	7,8	15,5	69
Ik	260(dec.)	2230 (CN), 3230, 3350, 3420 (N—H)	196,0749[b]			$C_{11}H_8N_4$	196,0748[b]			25
IIIc	69,5—70,5	1640 (CH=N)[a]	59,7	8,3	25,3	$C_{11}H_{18}N_4O$	59,4	8,1	25,2	68
IIId	68—70	1640 (CH=N)[a]	58,6	7,2	34,1	$C_8H_{12}N_4$	58,5	7,3	34,1	70
IIIf	103—104	1640 (CH=N)	68,8	6,2	25,0	$C_{13}H_{14}N_4$	69,0	6,2	24,8	75
IIIg	207—208	1625 (CH=N)	51,1	4,3	18,1	$C_{13}H_{13}BrN_4$	51,1	4,3	18,4	55
IVi	165—167	1350, 1580 (NO_2)	—	—	15,5	$C_{14}H_{15}N_3O_3$[c]	—	—	15,4	77
IVj	d	1350, 1580 (NO_2)	63,7	6,7	14,0	$C_{16}H_{19}N_3O_3$	63,7	6,9	13,9	84

[a]In $CHCl_3$. [b]Molecular mass. [c]M 273. [d]157°C S → 162°C I.

5-Formylamino-2-phenylpyrimidine. A 0.5-g sample of pyrimidine IIIf was refluxed in 4 ml of H_2SO_4 (0.2 mole/liter) for 5 h, after which the precipitate was removed by filtration, washed with water, and dried to give 0.41 g (93%) of a product with mp 170-171°C (30% aqeous alcohol). IR spectrum ($CHCl_3$): 1715 (C=O) and 3410 cm^{-1} (N—H). Found: C 66.7; H 4.5; N 21.1%. $C_{11}H_9N_3O$. Calculated: C 66.4; H 4.5; N 21.1%.

5-Dimethylaminomethyleneamino-2-butoxypyrimidine (IIIc). A mixture of 3 g (0.016 mole) of chloropyrimidine IIIa [29] and 80 ml of a 1-N solution of sodium butoxide in absolute butanol was heated at 50-60°C for 3.5 h, after which it was evaporated to dryness, and the residue was dissolved in butanol. The butanol solution was washed with water, dried with $MgSO_4$, and evaporated. The residue was triturated with petroleum ether, and the mixture was filtered to give 2.47 g (68%) of pyrimidine IIIc.

5-Dimethylaminomethyleneamino-2-methylpyrimidine (IIId). A solution of 5.4 g (0.1 mole) of sodium methoxide in 50 ml of absolute methanol was added dropwise with stirring to a refluxing suspension of 11.84 g (0.04 mole) of salt II [30] and 4.67 g (0.05 mole) of acetamidine hydrochloride in 30 ml of absolute methanol, and the mixture was refluxed for 2 h and filtered in the hot state. The filtrate was evaporated, the residue was extracted with methylene chloride, and the solvent was evaporated. The resulting solid brown residue (4.5 g) was recrystallized from hexane.

A similar procedure was used to obtain the 2-phenyl and 2-(p-bromophenyl) derivatives. The reaction mixture was evaporated after heating was completed, and the residue was washed with water and recrystallized (IIIf from petroleum ether and pyrimidine IIIg from alcohol).

5-Nitro-2-(p-butoxyphenyl)pyrimidine (IVi) and 5-Nitro-2-(p-hexyloxyphenyl)pyrimidine (IVj). Aqueous solutions of 0.015 mole of the sodium salt of nitromalonic dialdehyde and 0.015 mole of the corresponding amidine hydrochloride were mixed, 1 ml of piperidine was added, and the mixture was stirred for 1-2 h. The precipitated nitropyrimidine was removed by filtration, washed with water, dried, and recrystallized from benzene. Nitropyrimidines IVg, h were obtained by the method in [14].

2-Hydroxy-4-butoxybenzaldehyde. A 20-g (0.143 mole) sample of 2,4-dihydroxybenzaldehyde and 29.8 g (0.218 mole) of butyl bromide were added to a solution of 8 g (0.143 mole) of KOH in 60 ml of alcohol, and the mixture was steam distilled for 30 h. It was then extracted with methylene chloride, and the extract was dried with $MgSO_4$ and distilled to give 4.87 g (17%) of a product with bp 120-130°C (3 mm) and mp 28-29°C. Found: C 68.4; H 6.9%. $C_{11}H_{14}O_3$. Calculated: C 68.0; H 7.2%.

5-[2-(p-Hexyloxyphenyl)]azopyrimidine (Vj). A 1.5-g (5 mmole) sample of pyrimidine IVj was dissolved in 30 ml of benzene, 0.75 g of 10% Pd/C and 2 ml of hydrazine hydrate were added, and the mixture was refluxed for 2 h. Another 2 ml of hydrazine hydrate were added, and the mixture was again refluxed for 2 h. The catalyst was removed by filtration, washed with benzene, and cooled to precipitate 0.2 g of bright-orange Vj with mp 340-345°C. Found: M 538.2973. $C_{32}H_{38}H_6O_2$. Calculated: M 538.3056.

5-[2-(p-Butyloxyphenyl)]azopyrimidine (Vi). A similar procedure was used to obtain bright-orange needles (from benzene). The product has the following liquid-crystal prop-

erties: 204°C S_1, 225°C S_2, 290°C S_3, and 310°C I. Found: C 69.7; H 6.4; N 17.5%. $C_{28}H_{30}N_6O_2$. Calculated: C 69.7; H 6.2; N 17.4%.

5-Arylideneaminopyrimidines VIa-n, r-y. A 2.5-mmole sample of the 2-substituted 5-aminopyrimidine and 2.5 mmole of the corresponding aldehyde were refluxed in 5 ml of absolute alcohol for 2-4 h, after which the mixture was cooled, and the precipitate was removed by filtration and recrystallized (Table 1). UV spectra, λ_{max} (log ε): IVd 204 (4.18), 228 (4.12), and 308 nm (4.43); VIo 202 (4.25), 236 (4.19), 288 shoulder (4.15), and 334 nm (4.44).

5-Arylideneaminipyrimidines VIo-q and VIIe, k. Equimolar amounts of the corresponding pyrimidines I and the aldehyde (2.5 mmole) were refluxed in 10 ml of dry toluene in the presence of three drops of piperidine for 5-6 h, after which the mixture was filtered to remove the unchanged starting amine. The filtrate was evaporated to dryness, and the residue was washed with ether to give VIo-q and VIIe. Schiff base VIIk was precipitated by cooling the reaction mixture, and it was removed by filtration, washed with ether, and recrystallized from toluene.

5-(2-Hydroxy-4-butoxybenzylideneamino)-2-cyanopyrimidine (VIIe). This compound was obtained in 45% yield as yellowish-green needles with mp 157-160°C. UV spectrum, λ_{max} (log ε): 205 (4.37), 238 shoulder (4.13), 303 shoulder (4.20), and 368 nm (4.39). Found: N 19.0%. $C_{16}H_{16}N_4O_2$. Calculated: N 18.9%.

5-(2-hydroxy-4-butoxybenzylideneamino)-2-(4-cyanophenyl)pyrimidine (VIIk). This compound was obtained in 56% yield in the form of bright-yellow crystals. The product has the following liquid-crystal properties: 216°C N and 286°C I. IR spectrum ($CHCl_3$): 1615, 1640 (C=N); 2230 cm^{-1} (C≡N). UV spectrum, λ_{max} (log ε): 206 (4.44), 261 (4.22), 314 (4.33), 363 nm (4.53). Found: C 70.5; H 5.2; N 15.2%. $C_{22}H_{20}N_4O_2$. Calculated: C 71.0; H 5.4; N 15.1%.

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ACETALS OF LACTAMS AND ACID AMIDES.

37.* REACTIONS OF AMIDE AND LACTAM ACETALS WITH DERIVATIVES OF UREA AND URETHANE AND SYNTHESIS OF CONDENSED PYRIMIDINES

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The reactions of diethylacetals of dimethylacetamide and N-methylbutyro-, -valero-, and -caprolactams with urea, thiourea, and urethane lead to the corresponding N-carbamide- and N-ethoxycarbonylamides, on the basis of which derivatives of pyrimidine and pyrrolo- and pyrido[2,3-d]pyrimidine and pyrimido[4,5-b]azepine, as well as triazole derivatives, were synthesized.

A large amount of literature has been devoted to the chemistry of acetals and amides and lactams [2, 3]; however, their reactions with urea and urethane have remained virtually uninvestigated. Only the synthesis of N-carbamido(thiocarbamido)formamidines by the reaction of dimethylformamide diethylacetal (I) with urea and thiourea has been realized [4], and the reaction of acetal I with urethane has been mentioned [5].

The aim of the present research was to study the possibility of the preparation of N-carbamido(or N-ethoxycarbonyl)amidines on the basis of acetals of amides and lactams and the development of the synthesis of azaheterocycles (primarily condensed pyrimidines) from these amidines.

The reactions of dimethylacetamide diethylacetal (II) and lactam acetals IIIa-c with urea proceed smoothly, and the corresponding N-carbamidoamidines (IV, Va-c) are formed in high yields. A peculiarity of the amidines obtained is the fact that they crystallize with urea molecules; repeated crystallization from various solvents does not change the ratio of the amidines and the urea in the reaction product.

Signals of NCH_3 groups (2.91-3.14 ppm), ring NCH_2 groups (3.49-3.62 ppm), 3-CH_2 groups (2.58-2.91 ppm), and the remaining CH_2 groups (1.50-2.00 ppm) are observed in the PMR spectra of Va-c in D_2O and d_6-DMSO. Signals of the carbon atom of the CO group of urea at 160.19 ppm and signals of amidine Vc [170.29 and 169.42 (C=O, C=N), 53.50 and 54.47 (3CH_2 and 7-CH_2), 36.18 (NCH_3), and 28.49, 25.63, and 23.36 ppm (4,5,6-CH_2)] were present in the ^{13}C NMR spectrum of Vc.†

Peaks of molecular ions, the most favorable pathways from the fragmentation of which involve splitting out of NH_2 and $CONH_2$ fragments, are present in the mass spectra of IV and V. In addition, intense peaks with m/z 60, which are related to the urea molecule, are observed in the spectra. When amidine Va is heated in vacuo at ∿100°C (2-3 mm), one can sublime the urea and obtain a urea-free compound, in the mass spectrum of which the peak with m/z 60 is

*See [1] for Communication 36.

†Signals of an impurity (possibly a second geometrical isomer) are observed in the PMR and ^{13}C NMR spectra of Vc in d_6-DMSO.

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