refluxing for 7 h, the product was diluted with water (10 ml), acidified with acetic acid, the precipitated solid filtered off, and crystallized from DMF.

2-Methylquinoline-3,4-dicarboxylic Acid N-Phenylimides (IIa-d). A solution of Ia-d (3 mmole) in isopropanol (50 ml) was refluxed for 4 h, cooled, and the precipitate filtered off to give the desired product.

2-Methylquinoline-3,4-dicarboxylic Acid N-Phenylimide (IIa). A solution of Ia (1 g, 3 mmole) in acetic anhydride (5 ml) was refluxed for 2 h, poured into water (50 ml), and the precipitated solid filtered off and crystallized from ethanol to give IIa (0.5 g, 53%) with mp 161-163°C. A mixed melting point with a sample of IIa prepared as described before was not depressed.

2-Styrylquinoline-3,4-dicarboxylic Acid N-Phenylimides (IIIa-e). A mixture of anilide Ia-e (7 mmole), benzaldehyde (1.06 g, 10 mmole), p-xylene (2 ml), and piperidine (3-4 drops) was heated at 175°C in a metal bath for 5 h. The product was crystallized from ethyl acetate.

Under the same conditions, compound Ic (4 g, 11 mmole) and furfural (1.63 g, 17 mmole) gave 2-[2-(α-furyl)vinyl]-6-chloroquinoline-3,4-dicarboxylic acid N-phenylimide (4 g, 80%) with mp 263-265°C (ethyl acetate). Found: Cl 8.6; N 7.2%. $C_{23}H_{13}ClN_2O_3$. Calculated: Cl 8.8; N 7.0%.

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ACYLATION OF 2- AND 4-HYDROXYAMINOPYRIMIDINES

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Monoacylation of alkyl (aryl)-containing 2- and 4-hydroxyaminopyrimidines with acid anhydrides and acid chlorides leads preferentially to the acyloxyaminopyrimidines; the corresponding reaction with isocyanates leads to the (N-carbamoyl)hydroxyaminopyrimidines.

The exhaustive acylation of N-aryl (hetaryl)hydroxylamines leads to N,O-diacylhydroxylamines [1], the stability of which depends on the structure of the acyl group [2]. The monoacylation of N-aryl (hetaryl)hydroxylamines proceeds preferentially at the nitrogen atom with the formation of the N-aryl (hetaryl)-N-acylhydroxylamines [1], and the acylation at the oxygen atom is only observed in the case of acceptor or sterically hindered aryl substituents [2]. The O-acylhydroxylamines are unstable compounds [2-5], which undergo a series of conversions via the intermediate nitrenium ions [4].

We investigated the acylation of 2- and 4-hydroxyaminopyrimidines with acid anhydrides and acid chlorides, and isocyanates, to explain the influence of the pyrimidinyl substituent on the properties of the hydroxyamino group. It is known that the corresponding O-acyl derivatives are formed by the acylation of 2-hydroxy-4-hydroxyamino-5-fluoropyrimidine with acetic anhydride, and of 6-hydroxyamino-1,3-dimethyluracil with ethyl isocyanate [7, 8].

We obtained the 4-(N-acetyl-N-acetoxy)amino-6-methyl-2-phenyl- and 4-(N-acetyl-N-acetoxy)amino-2,6-diphenylpyrimidines (IIa, b) by the action of an excess of acetic anhydride

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TABLE 1. Characteristics of the Compounds Obtained

Compound	mp, °C*	IR spectrum, ν_{CO}, cm^{-1}	Found, %				Empirical formula**	Calculated, %				Yield, %
			C	H	Cl	N		C	H	Cl	N	
IIa	128—129	1720, 1815	63,4	5,3	—	15,1	$C_{15}H_{15}N_3O_3$	63,1	5,3	—	14,7	98
IIb	168—170	1715, 1800	68,5	5,2	—	11,8	$C_{20}H_{17}N_3O_3$	69,1	4,9	—	12,0	98
IIc	180—182	1700, 1760	73,7	4,7	—	10,5	$C_{25}H_{19}N_3O_3$	73,3	4,7	—	10,3	71
IId	150—152***	1710, 1815	—	—	16,9	—	$C_{20}H_{15}Cl_2N_3O_3$	—	—	17,0	—	95
IIIa	65—68	1770	64,3	5,4	—	17,4	$C_{13}H_{13}N_3O_2$	64,2	5,4	—	17,3	36
IIIb	89—92	1770	70,7	5,1	—	13,9	$C_{18}H_{15}N_3O_2$	70,8	4,9	—	13,8	78
IIIc	134—135	1750	70,1	4,9	—	14,1	$C_{18}H_{15}N_3O_2$	70,8	4,9	—	13,8	60
IIId	176—177***	1750	—	—	—	11,3	$C_{23}H_{17}N_3O_2$	—	—	—	11,4	93
IIIe	147—149	1760	58,6	3,3	—	11,3	$C_{18}H_{13}Cl_2N_3O_2$	57,8	3,5	—	11,2	95
IVf	137—141	1675	—	—	11,3	12,2	$C_{18}H_{14}ClN_3O_2$	—	—	10,5	12,4	38
Va	142—143	1750, 1775	66,1	4,8	—	11,3	$C_{20}H_{17}N_3O_4$	66,1	4,7	—	11,6	81
Vb	162—163	1730, 1770	62,4	4,3	9,2	11,0	$C_{20}H_{16}ClN_3O_3$	62,9	4,2	9,3	11,0	98
VIIc	166—168	1770	64,8	5,3	—	17,4	$C_{13}H_{13}N_3O_2$	64,2	5,4	—	17,3	64
VIId	156—158	1780	50,0	3,3	23,3	13,5	$C_{13}H_{11}Cl_2N_3O_2$	50,0	3,5	22,7	13,5	60
VIIIa	101—103	1760, 1780	60,6	5,2	—	14,4	$C_{15}H_{15}N_3O_4$	59,8	5,2	—	13,9	100
VIIIb	123—127	1720, 1790	56,4	4,4	11,8	13,3	$C_{15}H_{14}ClN_3O_3$	56,3	4,4	11,1	13,1	100
VIIIc	110—112	1720, 1790	46,5	3,0	27,8	10,8	$C_{15}H_{12}Cl_3N_3O_3$	46,4	3,1	27,4	10,8	80
VIIId	171—173	1700, 1800	—	—	—	12,0	$C_{20}H_{12}N_3O_3$	—	—	—	12,1	65
VIIIe	158—161	1725, 1815	—	—	16,8	—	$C_{20}H_{15}Cl_2N_3O_3$	—	—	17,0	—	90
IXc	148—150	1700	65,7	5,3	—	17,2	$C_{16}H_{16}N_4O_2 \cdot 0{,}5H_2O$	65,6	5,2	—	17,0	88
IXd	189—192***	1700	72,3	4,8	—	14,5	$C_{23}H_{18}N_4O_2$	72,2	4,7	—	14,7	90
IXg	145—147	1675	69,5	6,1	—	15,3	$C_{21}H_{22}N_4O_2$	69,6	6,1	—	15,5	85
IXh	205—208***	1700	61,4	4,1	—	12,4	$C_{23}H_{16}Cl_2N_4O_2$	61,2	3,6	—	12,4	58
X	142—145	1720, 1790	69,5	5,0	—	12,1	$C_{26}H_{22}N_4O_4$	68,7	4,9	—	12,3	90

*Compounds were recrystallized from the following solvents: alcohol for (IIa-c), (IIId), (IVf), (VIIId), (IXc, d, g), and (X); dioxane for (IXh); benzene for (Va, b) and (VIIIa); petroleum ether for (IIIa, b, c) and (VIIIc); the mixture of benzene with petroleum ether for (IIIe), (VIIc, e), and (VIIIb).

**The M by mass spectrometry was as follows: 258 for (IIa), 367 for (IIId), 339 for (IVf), (^{35}Cl), and 320 for (IXc).

***The compound decomposes on recrystallization; an analytical sample was not obtained. A discrete compound is indicated by TLC.

[4]**With decomposition.

on the substituted 4-hydroxyaminopyrimidines (Ia, b). The IR spectrum of (IIa, b) has two absorption bands of the CO groups at 1720, 1815, and 1715, 1800 cm^{-1} correspondingly (Table 1); these are characteristic of the N- and O-acyl groups in diacylhydroxylamines [2, 9]. The 4-(N-acyl-N-acyloxy)aminopyrimidines (IIa-c, f) are also obtained by the acylation of the compounds (Ia, b) with benzoyl chloride, acetyl chloride, or chloroacetyl chloride (the 1:2 ratio).

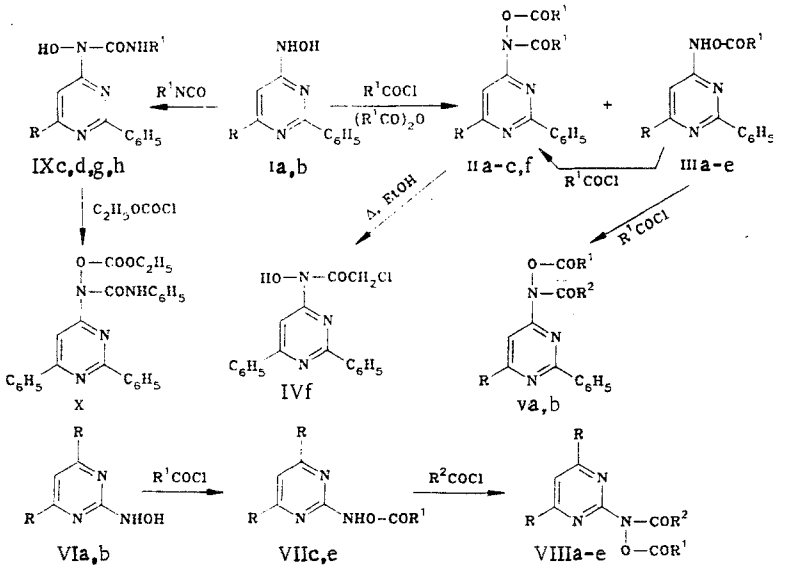
When the amount of the acid chloride decreases to 1 mole, either the mixture of the diacyl and monoacyl derivative or only the monoacyl derivative is formed. The absorption band of the CO group thereby lies in the region of 1750-1770 cm^{-1} in the IR spectra of the latter, and these compounds do not give a coloration with ferric chloride solution; this corresponds with the formation of the 4-(N-acyloxyamino)pyrimidines (III). Thus, the mixture of the compounds (IIa) and (IIIa) is obtained by the acylation of compound (Ia) with acetyl chloride; the compounds (IIIc) and (IIIe) are obtained in the corresponding reactions with benzoyl chloride or 2,4-dichlorobenzoyl chloride.

In contrast to the previously mentioned acid chlorides, the reaction of chloroacetyl chloride with compound (Ib) (the 1:1 ratio of the reagents; the change in the reaction temperature from 20 to −30°C) led to a mixture of unstable compounds, from which it was not possible to isolate individual compounds.

Of the obtained O-acylhydroxylamines (II) and (III), only the pyrimidine (IIf) (R = C_6H_5, $R^1 = CH_2Cl$) proved to be unstable on heating and storage at room temperature. On recrystallization, compound (IIf) is converted to the monoacyl derivative having the ν_{CO} 1675 cm^{-1} in the IR spectrum; this permits the assignment of the structure 4-(N-chloroacetyl-N-hydroxy)amino-2,6-diphenylpyrimidine (IVf) to it. The latter compound is unchanged in the course of several days on the storage of the solid. It is, however, converted to a complex mixture of compounds with low stability in the course of 2 h as the alcoholic solution at 20°C, or on heating it for several minutes.

The behavior of the 2-hydroxyamino-4,6-disubstituted pyrimidines (VIa, b) on acylation is identical to the behavior of the compounds (I). The action of an excess of acetic anhydride or 2 moles of chloroacetyl chloride on the hydroxyaminopyrimidine (VIb) gives the 2-(N-acyl-N-acyloxy)amino-4,6-diphenylpyrimidines (VIIId, e); the action of an equimolar amount of benzoyl chloride or 2,4-dichlorobenzoyl chloride on the compound (VIa) leads to the preferential formation of the 2-acyloxyamino-4,6-dimethylpyrimidines (VIIc, e).

The acylation of the hydroxyaminopyrimidines (Ia, b) by isocyanates (the 1:1 ratio of the reagents) leads to the isolation of the N-monocarbamoyl derivatives (IXc, d, g, h) having the ν_{CO} at 1680-1700 cm^{-1} and the ν_{OH} in the region of 2600-3300 cm^{-1} in the IR spectrum.



I, VI a R=CH_3, b R=C_6H_5; II, III, VII, IXa,c,e R=CH_3, b,d,f-h R=C_6H_5; a,b $R^1=CH_3$, c,d $R^1=C_6H_5$, e $R^1=C_6H_3Cl_2$-2,4, f $R^1=CH_2Cl$, g $R^1=C_4H_9$-p, h $R^1=C_6H_3Cl_2$-3,4; V, VIIIa—c R=CH_3, d,e R=C_6H_5, a,b $R^1=C_6H_5$, c $R^1=C_6H_3Cl_2$-2,4, d $R^1=CH_3$, e $R^1=CH_2Cl$; a $R^2=OCH_3$, b,c,e $R^2=CH_2Cl$, d $R^2=CH_3$

TABLE 2. PMR Spectral Data of the Compounds (II)-(IV) and (VIII)-(X) (δ, ppm)*

Compound	5-H**	CH_3	CH_{arom}	Other groups
IIa		2,36; 2,43; 2,50	7,37—7,67; 8,17—8,47 (4 : 2)	—
IIb	8,27	2,37; 2,43	7,37—7,63; 8,10—8,60 (6 : 4)	—
IIf	8,05	—	7,38—7,72; 8,17—8,55 (6 : 4)	4,95 (s, $COCH_2Cl$), 5,03 (s, $COCH_2Cl$)
IIIa	6,50	2,13; 2,43	7,30—7,63; 8,17—8,63 (3 : 2)	—
IIIb	7,07	2,23	7,37—7,63; 8,05—8,63 (6 : 4)	—
IIIc	6,63	2,40	7,37—7,70; 7,90—8,40 (6 : 4)	—
IVf	8,13	—	7,70—7,73; 8,03—8,67 (6 : 4)	4,97 (s, $COCH_2Cl$)
VIIId	7,90	2,13 ($2CH_3$)	7,00—7,47; 7,51—7,83 (6 : 4)	—
VIIIe		—	7,47—7,77; 8,20—8,50 (7 : 4)	4,83 (s, $COCH_2Cl$), 5,23 (s, $COCH_2Cl$)
IXc	7,35	2,48	7,45—7,65; 8,28—8,52 (8 : 2)	—
IXg	7,66	0,87 (t, J=7Hz)	7,27—7,53; 7,95—8,37 (6 : 4)	1,17—1,73 (m, $2CH_2$), 3,10—3,53 (m, CH_2), 8,97 broad (NH)
X		1,37 (t, J=7Hz)	7,03—7,63; 7,93—8,43 (12 : 4)	4,35 (q, CH_2, J=7Hz)

*The solvents are as follows: $CDCl_3$ for (IIa, b), (IIIb), (IXg), and (X), DMSO-d_6 (dry) for (IIf), (IIIa, c), (IVf), (VIIIe), and (IXc), and CF_3COOH for (VIIId).
**The signal of 5-H in the compounds (IIa), (VIIIe), and (X) coincides with the signals of the aromatic protons.

In contrast to the acyloxyaminopyrimidines (III), these compounds gave a characteristic coloration with a solution of ferric chloride.

The further acylation of the hydroxyaminopyrimidine derivatives (III), (IX), and (VII) permitted the isolation of the stable diacyl derivatives (Va, b), (VIIIa-c), and (X) both with the same and with different acyl groups (for the instability of the analogous compounds in the series of arylhydroxylamines, cf. [2]).

The obtained acylated derivatives of the 2- and 4-hydroxyaminopyrimidines show fungicidal activity (in vivo and in vitro) and growth regulating activity; they are, however, less active than the standards (tetramethylthiuram disulfide, karathane, zineb, and zuparen).

EXPERIMENTAL

The IR spectra were recorded on a UR-20 instrument using tablets with KBr (c 0.25%). The PMR spectra were recorded on a Varian A 56-60 instrument using HMDS as the internal standard. The mass spectra were recorded on an MS-902 spectrometer at 14 and 70 eV.

The characteristics of the compounds synthesized are presented in the Tables 1 and 2. The synthesis of the compounds (Ia, b) and (VIa, b) was described in [6].

Acylation of the Hydroxyaminopyrimidines by Acid Chlorides. A. To the solution of 0.5 g (5 mmole) of triethylamine in 20 ml of dry ether are added 1.3 g (5 mmole) of compound (Ib); a solution of 0.4 g (5 mmole) of acetyl chloride in 10 ml of dry ether is then added with stirring. The reaction mixture is stirred for 0.5 h. The solvent is evaporated. The residue is washed with ether and water, and is recrystallized. Compound (IIIb) is obtained.

The compounds (IIIc-e), (Va, b), (VIIc, e), (VIIIa-c), and (X) are obtained analogously by the acylation with acid chlorides in dry ether, dioxane, or chloroform.

During the isolation of compound (IIIa), the residue of the reaction mixture dissolves when it is washed with water. The substance is extracted from the aqueous solution with chloroform, dried, and concentrated; the residue is chromatographed on a column with silica gel using the 4:1 mixture of chloroform—acetone as the eluent. Compound (IIIa) (0.25 g) and 0.1 g of the mixture of (IIa) and (IIIa) (in the 7:3 ratio according to the data of the PMR spectrum) are obtained.

B. To the solution of 1.0 g (10 mmole) of triethylamine in 20 ml of dry ether are added 1.3 g (5 mmole) of compound (Ib); a solution of 0.8 g (10 mmole) of acetyl chloride in 10 ml of dry ether is then added with stirring. The mixture is stirred for 1 h. Further treatment proceeds by analogy with the method A; the pyrimidine (IIb) is obtained.

C. To the suspension of 1.3 g (5 mmole) of compound (Ib) in 20 ml of dry ether, cooled to −10°C, is added 1.0 g (10 mmole) of triethylamine; a solution of 0.8 g (10 mmole) of chloroacetyl chloride in 10 ml of dry ether is then added with stirring. The reaction mixture is stirred with cooling for 0.5 h. The residue is filtered off prior to the washing with ether and ice water. Compound (IIf) is obtained; it is unstable at room temperature, and should be stored in a refrigerator. The recrystallization of compound (IIf) from alcohol gives the compound (IVf).

The diacylated derivative (VIIIe) is obtained analogously from the compound (VIb).

Acetylation of the Hydroxyaminopyrimidines with Acetic Anhydride. A. The solution of 5 mmole of the hydroxyaminopyrimidine (Ia, b) or (VIb) and 3 ml of acetic anhydride in 30 ml of acetic acid or dioxane is left for 18 h at 20°C. Water is added to the solution. The residue is filtered off and washed with sodium bicarbonate solution and water; the compounds (IIa, b) or (VIIId) are obtained correspondingly.

B. To the solution of 1.0 g (5 mmole) of compound (Ia) and 0.5 g (5 mmole) of acetic anhydride in 30 ml of chloroform is added 0.7 g (5 mmole) of potassium carbonate, and the reaction mixture is stirred at 20°C for 0.5 h. The residue is filtered off. The filtrate is concentrated, and the residue is chromatographed on a column with silica gel (40-100 μ) using the 4:1 mixture of chloroform–acetone as the eluent. The monoacetyl derivative (IIIa) is obtained.

Acylation with Isocyanates. To the suspension of 1.0 g (5 mmole) of compound (Ia) in 20 ml of dry ether is added the solution of 0.6 g (5 mmole) of phenyl isocyanate in 10 ml of dry ether dropwise with stirring and cooling with ice. The reaction mixture is stirred for 0.5 h; the residue is filtered off and washed with ether and water. Compound (IXc) is obtained. An additional amount of the substance is isolated from the mother liquor.

The compounds (IXd, g, h) are obtained analogously from the substances (Ia, b) by the treatment with the corresponding isocyanates.

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