4-Methyl-5-n-amylketovinyl-2-imidazolinone (XV). With cooling (−10°) and stirring, to a solution of 0.4 g of (II) and 1.5 g of a mixture of chlorovinyl ketones (XIII) and (XVIII) in 10 ml of nitrobenzene was gradually added 1.63 g of $AlCl_3$, after which the mixture was stirred for another hour at 20° and for 16 h at 42-46°. After the above described workup we obtained 0.77 g (89%) of (XV), mp 190-192° (decompn.) (from 10:1 EA—alcohol), R_f 0.60 (0.5:4.5 alcohol—EA). Ultraviolet spectrum: 357 nm. PMR spectrum (CF_3COOH, δ, ppm): 0.80 t (CH_3CH_2, J = 5 Hz), 1.37 m, ($CH_2CH_2CH_2$), 2.32 s (CH_3), 2.72 t (CH_2CO, J = 8 Hz), 6.40 d (trans-CH=CHCO, J = 16 Hz), 7.10 d (trans-CH=CHCO, J = 16 Hz). Found: C 60.18; H 8.72; N 11.47%. $C_{12}H_{18}N_2O_2 \cdot H_2O$. Calculated: C 59.98; H 8.39; N 11.65%.

CONCLUSIONS

1. The reaction of 4(5)-methyl-2-imidazolinone with crotonyl chloride, chlorovinyl phenyl ketone or chlorovinyl n-amyl ketone in the presence of $AlCl_3$, respectively, gives 4-methyl-5-crotonyl-, 4-methyl-5-phenylketovinyl- or 4-methyl-5-n-amylketovinyl-2-imidazolinone.

2. The regioselective bromination of 1,3-diacetyl-4-methyl-5-ethyl-2-imidazolinone with N-bromosuccinimide leads to 1,3-diacetyl-4-bromomethyl-5-ethyl-2-imidazolinone, which with sodioacetoacetic ester gives 1,3-diacetyl-4-ethyl-5-(2'-carbethoxy-3'-ketobutyl)-2-imidazolinone.

3. The reaction of methyl n-amyl ketone with ethyl formate and sodium in the presence of Me_3SiCl and subsequent treatment of the formylation products with $SOCl_2$ gives a mixture of chlorovinyl n-amyl ketone and 1-chloro-2-n-butyl-1-buten-3-one in a 7.5:1 ratio.

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ACYLATION OF 4,6-DIAMINO-2-MERCAPTOPYRIMIDINE AND ITS SALTS WITH CARBOXYLIC ACID CHLORIDES

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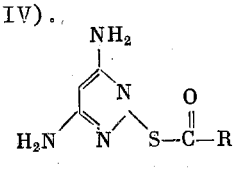
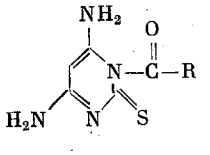
The data on the acylation of aminomercaptopyrimidines are contradictory [1-7]. We studied the acylation of 4,6-diamino-2-mercaptopyrimidine (I) and its salts with carboxylic acid chlorides (CAC) under various conditions. The formation of three types of monoacylated derivatives of (I) is theoretically possible: 2-acylthio-4,6-diaminopyrimidines (II), 1-acyl-4,6-diamino-1,2-dihydro-2-pyrimidinethiones (III), and 6-amino-4-acylamido-1H(3H)-dihydro-2-pyrimidinethiones (IV).



(II)



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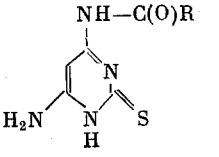

(IV)

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TABLE 1. 2-Acylthio-4,6-diaminopyrimidines (II)

R	Yield, %	mp, °C (decompn.) (from MeCN)	Found, %			Empirical formula	Calculated, %		
			C	H	N		C	H	N
C_6H_5	80	260 *	53,75	4,00	22,43	$C_{11}H_{10}N_4OS$	53,64	4,09	22,75
p-$CH_3C_6H_4$	88	320	55,43	4,32	21,46	$C_{12}H_{12}N_4OS$	55,36	4,64	21,51
p-$NO_2C_6H_4$	88	215	45,98	3,62	26,40	$C_{11}H_9N_5O_3S$	45,61	3,44	26,60
m-$NO_2C_6H_4$	92	190	45,84	3,25	26,12	$C_{11}H_9N_5O_3S$	45,61	3,44	26,60
p-$CH_3OC_6H_4$	89	277	51,90	4,46	21,24	$C_{12}H_{12}N_4O_2S$	52,16	4,37	21,36
m-$CH_3OC_6H_4$	95	300	51,98	4,21	21,60	$C_{12}H_{12}N_4O_2S$	52,16	4,37	21,36
p-BrC_6H_4	81	236	40,84	2,50	16,89	$C_{11}H_9BrN_4OS$	40,62	2,79	17,23
β-C_5H_4N	85	300	48,43	3,80	28,36	$C_{10}H_9N_5OS$	48,56	3,66	28,32

*Without decomposition.

TABLE 2. 2-Acylthio-4,6-dimethylpyrimidines (VI)

R	Yield, %	mp, °C (from ether)	Found, %			Empirical formula	Calculated, %		
			C	H	N		C	H	N
C_6H_5	74	72,5–73,5	64,00	5,32	11,30	$C_{13}H_{12}N_2OS$	63,90	4,95	11,46
p-$NO_2C_6H_4$	70	126–127	53,74	3,61	14,57	$C_{13}H_{11}N_3O_3S$	53,96	3,83	14,52
p-$CH_3OC_6H_4$	85	97–98	61,19	4,98	10,01	$C_{14}H_{14}N_2O_2S$	61,29	5,14	10,21
m-$CH_3OC_6H_4$	87	99–100	61,39	5,33	10,31	$C_{14}H_{14}N_2O_2S$	61,29	5,14	10,21

TABLE 3. 1-Acyl-4,6-diamino-1,2-dihydro-2-pyrimidinethiones (III)

R	Yield, %	mp, °C (decompn.) (from DMF)	Found, %			Empirical formula	Calculated, %		
			C	H	N		C	H	N
C_6H_5	93	254–256	53,48	4,13	22,78	$C_{11}H_{10}N_4OS$	53,64	4,09	22,75
p-$CH_3C_6H_4$	88	280	55,51	4,46	21,74	$C_{12}H_{12}N_4OS$	55,36	4,64	21,51

TABLE 4. 6-Amino-4-acylamido-1H(3H)-dihydro-2-pyrimidinethiones (IV)

R	Yield, %	mp, °C (decompn.) (from MeOH)	Found, %			Empirical formula	Calculated, %		
			C	H	N		C	H	N
$(CH_3)_2CH$	87	266	45,16	5,42	26,31	$C_8H_{12}N_4OS$	45,26	5,70	26,40
$C_6H_5CH_2$	51	250	55,55	4,30	21,69	$C_{12}H_{12}N_4OS$	55,36	4,64	21,52
C_6H_5	61	220	53,18	4,55	22,98	$C_{11}H_{10}N_4OS$	53,64	4,09	22,76
β-C_5H_4N	47	300	48,52	3,66	28,27	$C_{10}H_9N_5OS$	48,56	3,66	28,32
m-$CH_3OC_6H_4$	84	300	51,84	4,44	21,38	$C_{12}H_{12}N_4O_2S$	52,16	4,37	21,36
p-$NO_2C_6H_4$	88	300	45,65	3,65	26,72	$C_{11}H_9N_5O_3S$	45,61	3,44	26,60
m-$NO_2C_6H_4$	85	320	45,36	3,76	26,72	$C_{11}H_9N_5O_3S$	45,61	3,44	26,60

The addition of the CAC to an equimolar mixture of (I) and Et_3N in either MeCN or DMF at ∿20°C gives the corresponding (II) compounds in 75-95% yields (Table 1). Variation in the order of adding the reactants has no effect on the acylation result. Under analogous conditions, the 2-acylthio-4,6-dimethylpyrimidines (VI) were obtained in 70-80% yields (Table 2) from 4,6-dimethyl-2-mercaptopyrimidine (V) and the CAC. The IR spectra of (II) and (VI) have intense absorption bands at 1660-1670 cm^{-1} (νC=O) [8], and absorption is absent at 1100 (νC=S) and 3000-3100 cm^{-1} (νNH of thiolactams) [9]. In addition, the spectra of the (II) compounds have intense bands at 1630-1640 (δNH_2) [10] and 3100-3500 cm^{-1} (νNH_2) [11].

Varying the order of adding the reactants at elevated temperature changes the direction of the acylation. The addition of Et_3N to a mixture of (I) and either benzoyl or p-toluyl chloride in either MeCN or DMF at 80° gives the (III) derivatives in 85-95% yields (Table 3). Under analogous conditions, the m- and p-nitrobenzoyl, m- and p-methoxybenzoyl, p-bromobenzoyl, and nicotinoyl chlorides form only the (II) compounds, while the (VI) compounds are obtained

TABLE 5. Acylation Products of (I) Salts with Benzoyl Chloride in DMF

Cation	T, °C	Composition of mixture, %	
		(III)	(II)
Li	20	100	–
Na	20	31	69
K	20	70	30
Li	80	87	13
K	80	34	66

from (V). The (III) compounds are the first 1-acyl-2-pyrimidinethiones with a fixed thiono structure to be isolated in the pure state. The IR spectra of the (III) compounds have intense bands at 1670 (νC=O) [8], 1100 (νC=S) [8, 9], 1640 (δNH_2) [10], and 3100-3500 cm^{-1} (νNH_2) [11]. Absorption is absent in the 3000-3100 cm^{-1} region (νNH of thiolactams) [9].

The acylation of (I) in DMF at 110-120° and an equimolar ratio of the reactants gives the (IV) compounds in 45-80% yields (Table 4), in which connection varying the order of adding the reactants has no effect on the reaction course. The IR spectra of the (IV) compounds have intense bands in the regions: 1680-1710 (νC=O) [12], 1640 (δNH_2) [10], 3000-3100 (νNH of thiolactams) [9], 3100-3300 (νNH_2) [11], and 3420-3450 cm^{-1} (νNH) [12].

In contrast to the acylation of (I) in the presence of Et_3N, the acylation of the (I) salts is less clear-cut. Based on the TLC data, the acylation of the Li, Na, and K salts of (I) with PhCOCl in DMF at ∿20° gives a mixture of the (II) and (III) compounds (Table 5), which could not be separated due to their close solubility. It should be mentioned that increasing the acylation temperature leads to an increase in the yield of the (II) compounds.

EXPERIMENTAL

The IR spectra were measured on a UR-10 spectrophotometer as a Nujol mull. Compounds (I) and (V) were obtained as described in [13, 14]. The (I) salts were obtained from (I) and the corresponding metal alcoholates. The purity of all three types of monoacylated derivatives of 4,6-diamino-2-mercaptopyrimidine was confirmed by the TLC data on Silufol UV-254 plates in the systems: DMFA–CH_3CN–CH_2Cl_2 = 1:1.5:1.5 or DMF–CH_2Cl_2 = 1:1.

2-Acylthio-4,6-diaminopyrimidines (II). To 0.035 mole of (I) and 0.05 mole of Et_3N in 20 ml of DMF was added in drops, at 20°, 0.035 mole of the CAC. The mixture was stirred for 1 h at ∿20°, and the precipitate was filtered and washed with 200 ml of $CHCl_3$ to remove the $Et_3N \cdot HCl$. The residue was recrystallized from MeCN. The (II) compounds are white crystalline compounds that in most cases have ill-defined melting points, are difficultly soluble in pyridine, DMF or MeCN, and are insoluble in C_6H_6, $CHCl_3$ or ether. The yield and characteristics of the (II) compounds are given in Table 1.

2-Acylthio-4,6-dimethylpyrimidines (VI). To 0.1 mole of (V) and 0.14 mole of Et_3N in 50 ml of MeCN at 20-25° was added in drops 0.1 mole of the CAC. The mixture was stirred for 1 h at ∿20°, the precipitate was filtered, the solvent was removed in vacuo, and the residue was recrystallized from ether. The (VI) compounds are white crystalline compounds with a sharp melting point, and they are soluble in most organic aprotic solvents. The yield and constants of the obtained (VI) compounds are given in Table 2.

1-Acyl-4,6-diamino-1,2-dihydro-2-pyrimidinethiones (III). To a mixture of 0.017 mole of (I) and 0.017 mole of the CAC in 40 ml of MeCN at 80° was added in drops 0.02 mole of Et_3N. The mixture was immediately cooled to ∿20°, the precipitate was filtered and washed with 200 ml of $CHCl_3$, and the residue was recrystallized from DMF. The (III) compounds are white crystalline compounds that lack a sharp melting point and decompose when heated. They are difficultly soluble in DMF and are insoluble in most organic aprotic solvents. The yields and constants of the (III) compounds are given in Table 3.

6-Amino-4-acylamido-1H(3H)-dihydro-2-pyrimidinethiones (IV). To a suspension of 0.017 mole of (I) and 0.017 mole of the CAC in 30 ml of DMF, heated to 120°, was added in drops 0.017 mole of Et_3N. The mixture was stirred for 5 min at 120°, cooled, the precipitate was filtered, and the DMF was evaporated in vacuo. The residual oil was dissolved in boiling methanol and filtered. The filtrate on cooling deposited pale yellow crystals, which are

insoluble in most organic solvents except DMF. The crystals were dissolved in the minimum amount of DMF, the solution was filtered, and the DMF was removed in vacuo. The residual oil was dissolved in boiling methanol. The (IV) compounds deposited from the solution on cooling (see Table 4).

Acylation of (I) Salts. To a suspension of 0.017 mole of the (I) salt in 20 ml of DMF at ~20° was added 0.017 mole of PhCOCl in drops. The mixture was stirred for 30 min, and the precipitate was filtered and analyzed via the intensity of the band at 1100 cm^{-1} ($\nu C{=}S$) using a calibration graph (see Table 5). The yields of the (II)-(III) mixtures were 84-97%.

CONCLUSIONS

1. The acylation of 4,6-diamino-2-mercaptopyrimidine with carboxylic acid chlorides in the presence of an organic base proceeds at all of the nucleophilic centers: the S atom, the ring N atom, or the amino group. The direction of the acylation depends on the temperature, the nature of the reactants, and the order of their addition.

2. Members of all three types of monoacylated derivatives were obtained, and specifically the 2-acylthio-4,6-diaminopyridines, the 1-acyl-4,6-diamino-1,2-dihydro-2-pyrimidinethiones, and the 6-amino-4-acylamide-1H(3H)-dihydro-2-pyrimidinethiones.

3. The acylation of the 4,6-diamino-2-mercaptopyrimidine salts gives a mixture of the S- and N_1-acylated derivatives, whose composition is affected by the nature of the cation.

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