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CHEMICAL TRANSFORMATIONS OF TRISUBSTITUTED PYRAZOLO[3,4-d]PYRIMIDINES AND THEIR 1-RIBOSIDES

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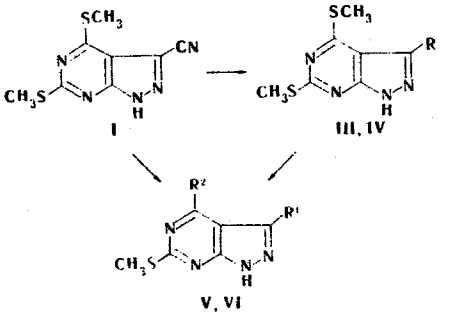
A number of 3,4,6-trisubstituted pyrazolo[3,4-d]pyrimidines and their 1-ribosides were synthesized from 3-cyano-4,6-dimethylmercaptopyrazolo[3,4-d]pyrimidine. The cyano group was converted to thiocarbamoyl, imido ester, carboxamidoximno, carboxamidrazono, carboxy, and amidino groups. The 4-methylmercapto group was replaced by mercapto, methoxy, amino, and hydrazino groups. The reactivities of methylmercapto and 3-cyano groups in substituted pyrazolo[3,4-d]pyrimidines and the corresponding nucleosides with respect to nucleophilic agents were compared. The introduction of a ribose residue in the 1 position facilitates nucleophilic addition to the 3-cyano group and replacement of the 4-methylmercapto group. High resistance of the 6-methylmercapto group to the action of nucleophilic agents and higher reactivity of the cyano groups as compared with methylmercapto groups were observed.

In connection with the fact that compounds that have high antitumorigenic activity are found among 3,4-disubstituted pyrazolo[3,4-d]pyrimidines and their 1-ribosides [1], the preparation of various 3,4,6-trisubstituted pyrazolo[3,4-d]pyrimidines and their 1-ribosides seems of interest. We used 3-cyano-4,6-dimethylmercaptopyrazolo[3,4-d]pyrimidine (I) and 1-(2',3',5'-tri-O-acetyl-β-D-ribofuranosyl)3-cyano-4,6-dimethylmercaptopyrazolo[3,4-d] pyrimidine (II), the synthesis of which was developed in [2], as the key compounds in these synthesis.

The chemical conversions of 3-cyano-4,6-dimethylmercaptopyrazolo[3,4-d]pyrimidine (I) were accomplished via the scheme:



III $R=CSNH_2$; IV $R=C(=NOH)NH_2$; V $R^1=CSNH_2$, $R^2=NH_2$ (from III); VI $R^1=C(=NH)NHNH_2$, $R^2=NHNH_2$ (from I)

3-Thiocarbamoyl-4,6-dimethylmercaptopyrazolo[3,4-d]pyrimidine (III) is formed when hydrogen sulfide is passed through a solution of heterocycle I in ethanol in the presence of triethylamine. 4,6-Dimethylmercaptopyrazolo[3,4-d]pyrimidine-3-carboxylic acid amidoxime (IV) was synthesized by refluxing I with hydroxylamine hydrochloride in ethanol in the presence of triethylamine. Replacement of the 4-methylmercapto group to give 4-hydrazino-6-

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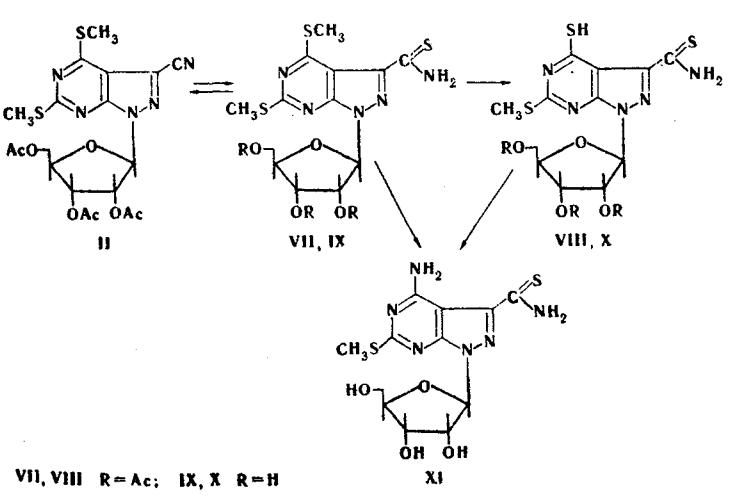
TABLE 1. Data from the PMR Spectra of 3,4,6-Trisubstituted Pyrazolo[3,4-d]pyrimidine 1-Ribosides

Compound	Chemical shift, δ, ppm (SSCC, Hz)							
	$C_H{}^{1'}$ ($J_{1,2'}$)	$C_H{}^{2'}$ ($J_{2,3'}$)	$C_H{}^{3'}$ ($J_{3,4'}$)	$C_H{}^{4'}$—$C_H{}^{5'}$	SCH_3	$COCH_3$	other signals	solvent
VII	6,59 (4,0)	5.97 (5,2)	5,75 (4,8)	4,55—4,24	2,64; 2.59	2,13; 2,10; 2.05	8,31; 7.84 ($CSNH_2$)	$CDCl_3$
IX	6,36 (4,2)	4,77 (5,0)	4,47 (5,2)	4,11—3,75	2,61; 2,57	—	—	CD_3OD
VIII	6.46 (2,4)	6,06 (5.6)	5,87 (6,4)	4,56—4,40	2.62	2,17; 2,13; 2,08	11,42; 8,67 ($CSNH_2$)	$CDCl_3$
X	6,08 (4,2)	4,57 (4,8)	4.25 (4,8)	3,95 -3,56	2,59	—	—	d_6-DMSO
XI	6,26 (4,4)	4,77 (5,2)	4,54 (5,2)	4,08—3.70	2,50	—	—	CD_3OD
XII	6,23 (4,8)	4,72 (4,8)	4,26 (5,0)	3.94—3.54	2,63; 2,58	—	3,94 (OCH_3)	d_6-DMSO
XIII	6,24 (4,8)	4,68 (4,8)	4.27 (5,2)	3,70 - 3,27	2.62	—	4,09; 3.92 (2 OCH_3)	d_6-DMSO
XIV	6,40	4,76	4,50	4,10—3,78	2,61; 2.53;	—	—	CD_3OD
XV	6,04 (4,4)	4,68 (4.8)	4,25 (5,2)	3.87—3,49	2,50	—	—	CD_3OD
XVI	6,55 (2,8)	6,02 (5,2)	5,84 (5,6)	5,22—4,38	2,63; 2,53	2,11; 2,11; 2,01	—	d_6-DMSO
XVII	6,30 (4,2)	4,75 (5,4)	4,46 (5,0)	4,05 -3,69	2,53; 2.46	—	—	CD_3OD
XVIII	6,03 (4,4)	4,86 (4,6)	4,60 (5,4)	4,25 -3,89	2,50	—	11,17 (NH)	d_6-DMSO

methylmercaptopyrazolo[3,4-d]pyrimidine-3-imido carboxylic acid hydrazide (VI) occurs along with addition to the cyano group under the influence of excess hydrazine hydrate. The ammonolysis of I leads to a complex mixture of products, and we therefore subsequently used compounds that do not contain a cyano group for the reaction with ammonia. 3-Thiocarbamoyl-4-amino-6-methylmercaptopyrazolo[3,4-d]pyrimidine (V) was obtained by ammonolysis of III at 80°C with a saturated solution of ammonia in methanol. Compound I does not react with sodium methoxide in methanol at 20°C.

1-(2',3',5'-Tri-O-acetyl-β-D-ribofuranosyl)-3-thiocarbamoyl-4,6-dimethylmercaptopyrazolo[3,4-d]pyrimidine (VII) was obtained when hydrogen sulfide was passed through a solution of II in ethanol in the presence of triethylamine under conditions similar to those in the synthesis of III. 1-(2',3',5'-Tri-O-acetyl-β-D-ribofuranosyl)3-thiocarbamoyl-4-mercapto-6-methylmercaptopyrazolo[3,4-d]pyrimidine (VIII) was isolated as the principal reaction product after the reaction mixture was maintained at 20°C for 3-4 days. Compounds VII and VIII were obtained in 60-65% yields. Two singlets of protons of methylmercapto groups at 2.64 and 2.59 ppm and two signals at 8.31 and 7.84 ppm, which correspond to the signals of the protons of a thiocarbamoyl group and vanish when CD_3OD is added, are observed in the PMR spectrum of



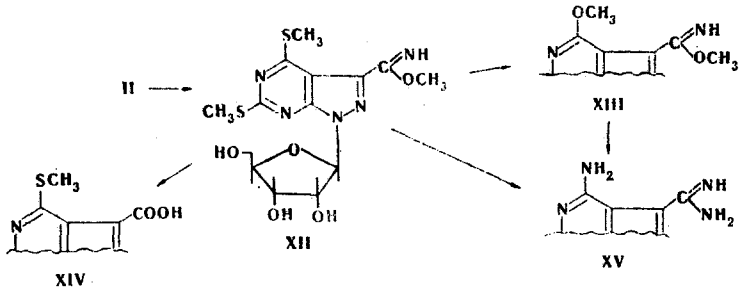
VII (Table 1). The PMR spectrum of VIII contains the signal of the protons of only one methylmercapto group and the corresponding signals of the protons of a thiocarbamoyl group

at 8.67 and 11.42 ppm. The IR spectrum of VII and VIII does not contain the absorption band of a cyano group that was present in the spectrum of starting riboside II (2245 cm^{-1}). The deacetylation of VII and VIII with sodium methoxide in methanol led to the corresponding ribosides (IX and X).

The ammonolysis of II, like the ammonolysis of I, leads to a multicomponent difficult-to-separate mixture of products. Replacement of the 4-methylmercapto group by an amino group and deacetylation to give 1-(β-D-ribofuranosyl)-3-thiocarbamoyl-4-amino-6-methylmercaptopyrazolo[3,4-d]pyrimidine (XI) occur when VII is treated with a saturated solution of ammonia in methanol (in an ampul at 80°C for 8 h). The same compound was obtained as a result of treatment of riboside VIII with liquid ammonia in an autoclave at 20°C.

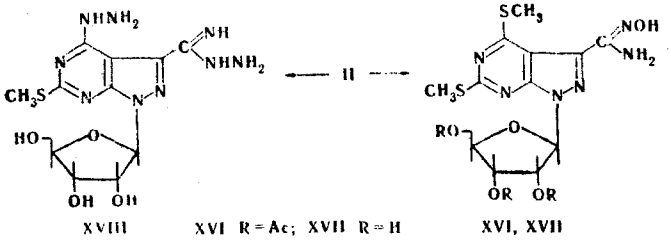
We have found a convenient method for the conversion of the 3-thiocarbamoyl group to a cyano group; this method consists in splitting out of a molecule of hydrogen sulfide under the influence of manganese dioxide in chloroform at room temperature for 4 h. Compound II was obtained in high yield from VII by this method.

Methyl 1-(β-D-ribofuranosyl)-4,6-dimethylmercaptopyrazolo[3,4-d]pyrimidine-3-imidocarboxylate (XII) is formed by the action of a twofold excess of sodium methoxide in methanol on riboside II, while methyl 1-(β-D-ribofuranosyl)4-methoxy-6-methylmercaptopyrazolo[3,4-d]-pyrimidine-3-imidocarboxylate (XIII) was obtained when a fivefold to eightfold excess of sodium methoxide was used in this reaction.



We have previously shown that the corresponding 3-carbamoyl derivative is formed by the action of a catalytic amount of alkali on methyl 1-(β-D-ribofuranosyl)-4-aminopyrazolo[3,4-d]-pyrimidine-3-imidocarboxylate at 20°C [3]. Conversion of the imido ester group to a carboxy group and the formation of 1-(β-D-ribofuranosyl)-3-carboxy-4,6-dimethylmercaptopyrazolo[3,4-d]-pyrimidine (XIV) occur when riboside XII is treated with dilute aqueous alkali solution under similar conditions. An absorption band at 1710 cm^{-1} (COOH group), which is shifted to 1620 cm^{-1} (COO^- group) when the carboxy group is ionized, appears in the IR spectrum of XIV. The absorption band at 1730 cm^{-1} (–C=N–) that is observed in the IR spectrum of XII simultaneously vanishes.

Conversion of the imido ester group to an amidino group and replacement of the 4-methylmercapto group by animo group occur in the ammonolysis of XII with a saturated solution of ammonia in absolute methanol (in an ampul at 80°C for 8 h), and 1-(β-D-ribofuranosyl)-4-amino-6-methylmercaptopyrazolo[3,4-d]pyrimidine-3-carboxamidine (XV) is formed. The same compound was also similarly obtained from riboside XIII.



When nucleoside II is refluxed in ethanol with hydroxylamine hydrochloride in the presence of triethylamine, it is converted to 1-(2',3',5'-tri-O-acetyl-β-D-ribofuranosyl)-4,6-dimethylmercaptopyrazolo[3,4-d]pyrimidine-3-carboxylic acid amidoxime (XVI), the deacetylation of which by the action of a saturated (at 0°C) solution of ammonia in absolute methanol led to the corresponding riboside (XVII). When riboside II was refluxed with a multiple excess of hydrazine hydrate in ethanol, the 3-cyano group was converted to a carboxamidrazono group

with simultaneous replacement of the methylmercapto group in the 4 position by a hydrazino group and O-deacetylation to give 1-(β-D-ribofuranosyl)-4-hydrazino-6-methylmercaptopyrazolo-[3,4-d]pyrimidine-3-imido carboxylic acid hydrazide (XVIII). Only partial or complete O-deacetylation of starting riboside II occurs when this reaction is carried out with a smaller amount of hydrazine hydrate.

It was previously shown in the case of 4,6-dichloropyrazolo[3,4-d]pyrimidine that the substituents in the 4 position have considerably higher reactivities in nucleophilic substitution reactions as compared with the substituents in the 6 position [4]. Similar principles are observed in the purine and pyrrolo[2,3-d]pyrimidine series [5-7]. This provides us with a basis for the assumption that the methylmercapto group in the 4 position participates in all of the described transformations that involve nucleophilic substitution of one of the two methylmercapto groups. The stability of the 6-methylmercapto group is so high in the trisubstituted pyrazolo[3,4-d]pyrimidines and their 1-ribosides that we investigated that we were unable to replace it.

A comparison of the reactivities of the cyano group in the 3 position and the methylmercapto group in the 4 position with respect to nucleophilic agents such as hydrogen sulfide, sodium methoxide in methanol, and hydroxylamine shows that the cyano group, which reacts under milder conditions, is more reactive both in the heterocyclic bases and in the corresponding 1-ribosides. Nucleophilic replacement of the methylmercapto groups by the action of the reagents indicated above without involvement of the cyano group cannot be realized, whereas in some cases we were able to selectively add these reagents to the cyano group.

The reactivities of the 3-cyano groups in the bases and corresponding 1-ribosides with respect to the nucleophilic agents used are not equivalent. The nucleophilic addition of hydrazine, hydroxylamine, and hydrogen sulfide to the cyano group in the nucleosides and corresponding bases takes place under identical conditions. At the same time, heterocycle I does not undergo changes under the influence of sodium methoxide in methanol under conditions for which the 4-methylmercapto group in corresponding nucleoside II is replaced by a methoxy group and the 3-cyano group is converted to an imido ester group. It may be assumed that the lower reactivities of the cyano and 4-methylmercapto groups with respect to sodium methoxide in the heterocyclic base as compared with the corresponding 1-riboside are associated with the formation of the anion of the heterocycle (as a result of deprotonation in alkaline media), which hinders its subsequent nucleophilic attack. The presence of a ribose residue in the 1 position excludes the possibility of the formation of an anion. Deprotonation under the influence of the other nucleophilic reagents indicated above is unlikely, and this makes it possible to explain the identical ease with which they react with both the 1-ribosides and the corresponding heterocycles.

EXPERIMENTAL

The PMR spectra of the compounds were recorded with a JNM-MH-100 spectrometer with tetramethylsilane and hexamethyldisiloxane as the internal standards. The UV spectra were recorded with a Unicam SP-800 recording spectrophotometer. The IR spectra of KBr pellets of the compounds were recorded with a UR-10 spectrometer. The specific rotation was determined by means of a Perkin–Elmer 241 polarimeter. Analytical thin-layer chromatography (TLC) was carried out on Silufol UV-254 in chloroform–methanol [99:1 (A), 95:5 (B), and 9:1 (C)], benzene–acetone [1:1 (D)], and chloroform–methanol [4:1 (E) and 1:1 (F)]. Preparative TLC was carried out in a loose layer of LSL 5/40 silica gel (Czechoslovakian SSR) and on plates with a fixed layer of Merck 60 F-254 silica gel in the same solvent systems. The properties and yields of the synthesized compounds are presented in Table 2.

3-Thiocarbamoyl-4,6-dimethylmercaptopyrazolo[3,4-d]pyrimidine (III). Hydrogen sulfide was passed with stirring at 20°C for 3 h into a solution of 1.2 g (5.05 mmole) of pyrimidine I in 20 ml of ethanol containing 1.2 g (12 mmole) of triethylamine, after which the mixture was allowed to stand at 20°C for 10 h, and the precipitated yellow crystals were removed by filtration, washed with ethanol, and dried in vacuo over P_2O_5 at 60°C to give 0.93 of III with R_f 0.40 (in system C). An analytically pure product was obtained by reprecipitation from dimethylformamide (DMF) by the addition of water. PMR spectrum (d_7-DMF): δ: 2.63 (SCH_3); 9.69 and 9.99 ppm ($CSNH_2$).

4,6-Dimethylmercaptopyrazolo[3,4-d]pyrimidine-3-carboxylic Acid Amidoxime (IV). A solution of 390 mg (1.65 mmole) of pyrimidine I, 140 mg (2 mmole) of hydroxylamine hydrochloride,

TABLE 2. Properties of 3,4,6-Trisubstituted Pyrazolo[3,4-d]pyrimidines and Their Ribosides (II-XVIII)

Compound	mp, °C	$[\alpha]_D^{20°}$ (C)	UV spectra in ethanol, λ_{max} (log ε)	Found, %				Empirical formula	Calc., %				Yield, %
				C	H	N	S		C	H	N	S	
III	232—233	—	—	35,4	3,4	25,7	36,2	$C_8H_9N_5S_3$	35,4	3,4	25,8	35,4	66
IV	185—190	—	198 (4,18), 216 (4,12), 246 (4,26), 258 (4,20), 285 (4,03), 302 (3,99)	34,8	4,2	31,3	—	$C_8H_{10}N_6OS_2$	35,5	3,7	31,1	—	65
V	210	—	197 (4,31), 250 (4,36), 203 (4,25), 248 (4,34), 285 (4,19)	34,7	3,8	34,3	—	$C_7H_8N_6S_2$	35,0	3,4	35,0	—	60
VI	>400	—	203 (4,25), 248 (4,34), 285 (4,19)	33,7	5,2	—	11,2	$C_7H_{11}N_9S \cdot CH_3OH$	33,7	5,3	—	11,2	69
VII	Oil	−130,0 (0,6)[a]	198 (4,34), 254 (4,37), 298 (4,15)	42,7	4,3	14,0	18,2	$C_{19}H_{23}N_5O_7S_3$	43,1	4,4	13,2	18,2	66
VIII	"	−75,6 (0,1)[a]	199 (4,39), 256 (4,47), 334 (4,16)	41,2	4,4	—	18,3	$C_{18}H_{21}N_5O_7S_3 \cdot H_2O$	40,6	4,4	—	18,1	60
IX	"	−138,5 (0,2)[a]	—	37,3	4,6	16,6	22,3	$C_{13}H_{17}N_5O_4S_3 \cdot H_2O$	37,0	4,6	16,6	22,8	90
X	236—237	−68,2 (0,1)[b]	205 (4,34), 252 (4,41), 334 (4,03)	36,9	4,3	—	23,9	$C_{12}H_{15}N_5O_4S_3$	37,0	3,9	—	24,7	88
II	Oil	−42,4 (0,3)[a]	205 (4,28), 2,54 (4,4), 296 (4,19), 322 (4,04)	44,1	4,3	13,2	11,9	$C_{19}H_{21}N_5O_7S_2 \cdot H_2O$	44,4	4,5	13,8	12,5	69
XI	196—199	−71,2 (0,2)[c]	202 (4,18), 253 (4,32), 347 (3,60)	37,1	4,8	21,6	—	$C_{12}H_{16}N_6O_4S_2 \cdot H_2O$	36,9	4,6	21,5	—	76
XII	204—206	−63,1 (0,3)[b]	206 (4,05), 251 (4,20), 292 (4,03)	39,9	5,1	16,4	—	$C_{14}H_{19}N_5O_5S_2 \cdot H_2O$[d]	40,1	5,1	16,7	—	53
XIII	181—182	−65,9 (0,2)b	200 (4,09), 246 (4,39), 281 (3,94)	43,2	4,8	—	8,3	$C_{14}H_{19}N_5O_6S$	43,6	5,0	—	8,3	65
XIV	193—195	−65,1 (0,2)b	202 (4,00), 252 (4,12), 291 (3,89)	—	—	14,2	—	$C_{13}H_{16}N_4O_6S_2$	—	—	14,4	—	93
XV	241—243	−98,8 (0,2)c	201 (4,28), 250 (4,41), 290 (3,94)	40,7	4,6	26,9	8,6	$C_{12}H_{17}N_7O_4S$	40,6	4,8	27,6	9,0	70
XVI	Oil	−15,4 (0,3)[b]	212 (4,13), 247 (4,21), 264 (4,20), 292 (4,05), 306 (4,06)	43,4	4,9	—	12,0	$C_{19}H_{23}N_6O_8S_2$	43,2	4,4	—	12,2	49
XVII	Oil	−10,2 (0,3)[c]	202 (4,21), 249 (4,30), 262 (4,24), 289 (4,08), 308 (4,11)	37,0	4,3	19,9	—	$C_{13}H_{18}N_6O_5S_2 \cdot H_2O$	37,1	4,8	20,0	—	65
XVIII	196—198	−91,8 (0,2)[c]	205 (4,23), 227 (4,25), 251 (4,30), 288 (4,15)	35,9	5,3	—	7,8	$C_{12}H_{16}N_6O_4S_2 \cdot H_2O$[e]	35,7	5,2	—	7,9	46

[a] In $CHCl_3$. [b] In Ch_3OH. [c] In DMSO. [d] Found, %: H_2O 4.59. Calculated, %: H_2O 4.29. [e] Found, %: H_2O 4.59. Calculated, %: H_2O 4.47.

and 202 mg (2 mmole) of triethylamine in 50 ml of ethanol was refluxed for 1.5 h, after which it was evaporated, and the residue was recrystallized from 50% aqueous ethanol to give 270 mg of IV with R_f 0.22 (in system C). PMR spectrum (d_6-DMSO), δ: 2.52 and 2.62 ppm (2-SCH_3).

3-Thiocarbamoyl-4-amino-6-methylmercaptopyrazolo[3,4-d]pyrimidine (V). A suspension of 160 mg (0.7 mmole) of pyrimidine III in 15 ml of liquid ammonia was maintained at 20°C for 3 days in a sealed ampul, after which the cooled ampul was opened, the ammonia was evaporated, and the residue was recrystallized from 50% aqueous ethanol to give 80 mg of V with R_f 0.40 (in system E). PMR spectrum (d_6-DMSO), δ: 2.45 ppm (SCH_3).

4-Hydrazino-6-methylmercaptopyrazolo[3,4-d]pyrimidine-3-imidocarboxylic Acid Hydrazide (VI). A solution of 410 mg (1.73 mmole) of I in 65 ml of ethanol containing 1 ml (10 mmole) of hydrazine hydrate was refluxed for 4 h, after which it was cooled, and the precipitated crystals were removed by filtration, washed with ethanol, and dried in vacuo at 60°C to give 340 mg of VI with R_f 0.13 (in system C). PMR spectrum in d_6-DMSO, δ: 2.45 ppm (SCH_3). The analytically pure product was obtained by recrystallization from 50% aqueous ethanol.

1-(2',3',5'-Tri-O-acetyl-β-D-ribofuranosyl)-3-thiocarbamoyl-4,6-dimethylmercaptopyrazolo-[3,4-d]pyrimidine (VII). This compound was obtained by the method used to obtain III by passing hydrogen sulfide through a solution of 320 mg (0.63 mmole) of riboside II and 0.1 ml (1 mmole) of triethylamine in 25 ml of ethanol for 2.5 h, after which the mixture was evaporated, and the residue was dissolved in 2 ml of chloroform. Preparative chromatography on silica gel in system B yielded 245 mg of VII in the form of a yellow oil with R_f 0.25 (in system A).

1-(β-D-Ribofuranosyl)-3-thiocarbamoyl-4,6-dimethylmercaptopyrazolo[3,4-d]pyrimidine (IX). A 0.5-ml sample of a 5% solution of sodium methoxide in absolute methanol was added to a solution of 140 mg (0.27 mmole) of riboside VII in 10 ml of absolute methanol, and the mixture was stirred at 20°C for 2 h, after which it was neutralized with Dowex 50X2 ion-exchange resin (in the H^+ form). The resin was removed by filtration, and the filtrate was concentrated in vacuo. Preparative chromatography on silica gel in system D yielded 96 mg of IX in the form of a yellow oil with R_f 0.30 (in system D).

1-(2',3',5'-Tri-O-acetyl-β-D-ribofuranosyl)-3-thiocarbamoyl-4-mercapto-6-methylmercapto-pyrazolo[3,4-d]pyrimidine (VIII). Hydrogen sulfide was passed into a solution of 0.79 g (1.54 mmole) of II in 40 ml of ethanol containing 0.2 g (2 mmole) of triethylamine at 20°C for 3 h, after which the mixture was allowed to stand at 20°C for 4 days. It was then evaporated to dryness, and the residue was subjected to preparative chromatography on silica gel in system C to give 0.47 g of riboside VIII with R_f 0.70 (in system C).

1-(β-D-Ribofuranosyl)-3-thiocarbamoyl-4-mercapto-6-methylmercaptopyrazolo[3,4-d]pyrimidine (X). This compound was obtained by the method used to prepare IX by deacetylation of 150 mg (0.385 mmole) of riboside VIII. The yield of product with R_f 0.39 (in system C) was 100 mg.

1-(2',3',5'-Tri-O-acetyl-β-D-ribofuranosyl)-3-cyano-4,6-dimethylmercaptopyrazolo[3,4-d]pyrimidine (II). Manganese dioxide (400 mg) was added to a solution of 110 mg (0.21 mmole) of VII in 15 ml of chloroform, and the resulting suspension was stirred at 20°C for 4 h. It was then filtered, and the filtrate was washed with water. The filtrate and the wash waters were concentrated in vacuo to a volume of 2 ml, and the concentrate was subjected to preparative chromatography on silica gel in system B to give 75 mg of riboside II with R_f 0.37 (in system A). IR spectrum: 2245 cm^{-1} (CN group).

1-(β-D-Ribofuranosyl)-3-thiocarbamoyl-4-amino-6-methylmercaptopyrazolo[3,4-d]pyrimidine (XI). A) Absolute methanol (25 ml) saturated with ammonia at 0°C was added to 240 mg (0.465 mmole) of VII, and the mixture was maintained in a sealed ampul at 70°C for 7 h and at 20°C for 12 h. It was then evaporated, and the residue was recrystallized from methanol to give 120 mg of riboside XI with R_f 0.26 (in system F).

B) As in the synthesis of V, a sealed ampul containing 80 mg (0.15 mmole) of riboside VIII in 10 ml of liquid ammonia was maintained at 20°C for 96 h, after which the ammonia was evaporated, and the residue was recrystallized from methanol to give 42 mg of XI, which was identical to the product obtained by method A.

Methyl 1-(β-D-Ribofuranosyl)-4,6-dimethylmercaptopyrazolo[3,4-d]pyrimidine-3-imidocarboxy-

late (XII). A 2.7-ml sample of a 5% solution of sodium methoxide in absolute methanol (2.5 mmole) was added to a solution of 0.65 g (1.27 mmole) of II in 15 ml of absolute methanol, and the mixture was stirred at 20°C for 4 h. It was then neutralized with Dowex 50X2 ion-exchange resin (in the H^+ form), after which the resin was removed by filtration. The filtrate was evaporated, and the residue was recrystallized from ethanol to give 280 mg of XII with R_f 0.38 (in system D).

Methyl 1-(β-D-Ribofuranosyl)-4-methoxy-6-methylmercaptopyrazolo[3,4-d]pyrimidine-3-imidocarboxylate (XIII). This compound was obtained by the method used to prepare XII by treatment of 308 mg (0.60 mmole) of II with 3 ml of a 6% solution of sodium methoxide (3.3 mmole) in 10 ml of methanol. The reaction product was isolated by preparative chromatography on silica gel in system C to give 150 mg of XIII with R_f 0.38 (in system C). An analytically pure product was obtained by recrystallization from ethanol.

1-(β-D-Ribofuranosyl)-3-carboxy-4,6-dimethylmercaptopyrazolo[3,4-d]pyrimidine (XIV). A suspension of 150 mg (0.386 mmole) of riboside XII in 22 ml of water and 0.2 ml of 1.25 N NaOH was stirred at 20°C for 6 h, after which Dowex 50X2 ion-exchange resin (in the H^+ form) was added up to pH 6. The resin was removed by filtration, the filtrate was evaporated, and the residue was subjected to preparative chromatography on silica gel in system F to give 135 mg of XIV in the form of a colorless oil that crystallized on standing to give a product with R_f 0.40 (in system F).

1-(β-D-Ribofuranosyl)-4-amino-6-methylmercaptopyrazolo[3,4-d]pyrimidine-3-carboxamidine (XV). A solution of 200 mg (0.563 mmole) of riboside XII in 30 ml of absolute methanol saturated (at 0°C) with ammonia was maintained in a sealed ampul at 80°C for 8 h and at 20°C for 12 h, after which the methanol was evaporated, and the residue (190 mg) was recrystallized from ethanol–water (2:1) to give 120 mg of XV with R_f 0.08 (in system E). Compound XV was similarly obtained from riboside XIII in 65% yield.

1-(2',3',5'-Tri-O-acetyl-β-D-ribofuranosyl)-4,6-dimethylmercaptopyrazolo[3,4-d]pyrimidine-3-carboxylic Acid Amidoxime (XVI). This compound was obtained by the method used to prepare IV by refluxing a solution of 480 mg (0.93 mmole) of II, 70 mg (1 mmole) of hydroxylamine hydrochloride, and 100 mg (1 mmole) of triethylamine in 50 ml of ethanol. The reaction product was isolated by preparative chromatography on silica gel in system B to give 240 mg of a product with R_f 0.48 (in system C) and 0.70 (in system D).

1-(β-D-Ribofuranosyl)-4,6-dimethylmercaptopyrazolo[3,4-d]pyrimidine-3-carboxylic Acid Amidoxime (XVII). A solution of 123 mg (0.23 mmole) of XVI in 15 ml of absolute methanol saturated (at 0°C) with ammonia was maintained at 20°C for 25 h in a tightly sealed flask, after which it was evaporated, and the residue was subjected to preparative chromatography twice in system E to give 85 mg of riboside XVII, twice in the form of a colorless oil with R_f 0.20 (in system D) and 0.30 (in system E).

1-(β-D-Ribofuranosyl)-4-hydrazino-6-methylmercaptopyrazolo[3,4-d]pyrimidine-3-imidocarboxylic Acid Hydrazide (XVIII). This compound was obtained by the method used to prepare VI from 250 mg (0.49 mmole) of II and 0.5 ml (5 mmole) of hydrazine hydrate in 15 ml of ethanol. The reaction product was recrystallized from water to give 90 mg of a product with R_f 0.40 (in system E).

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