cm^3/min. Monitoring of the reaction course and the purity of materials was carried out on Silufol UV-254 plates. The chromatographic separation was effected on a neutral alumina column with benzene:acetone (1:1) as elutent.

3-Aminoacrolein (II). A solution of propargyl aldehyde (10.8 g, 0.2 mole) in benzene (120 ml) was added over 1 h at 25-30°C with stirring to a solution of N-methylpiperidine (0.6 g, 0.005 mole) in a mixture of absolute ethanol (35 ml) and benzene (60 ml). The mixture was stirred for 1 h and gaseous ammonia passed through until the increase in temperature (to 35°C) ceased. The solution was treated with carbon and the solvent evaporated to give the product (7.9 g, 60%) with mp 104-105°C (methanol). PMR spectrum (D_2O): 11.0 (1H, s, CHO), 7.6-7.2 and 6.4-6.0 (2H, dd, CH=CH), 4.4-3.8 ppm (2H, m, NH_2). From the literature: mp [3], 103-104°C.

Polymethylenepyridines (IV). A mixture of II (0.01 mole), the cycloalkanone (0.012 mole), triethylamine (0.5 ml), and piperidine acetate (0.05 g) were sealed in an ampul at 120°C for 24 h. The reaction mixture was poured into water which had been acidified to pH 2-3, extracted several times with ether, the aqueous layer separated and basified to pH 9-10, and then extracted again with ether. The ether extracts were separately dried ($MgSO_4$). Evaporation of the ether extract from the acid solution gave unreacted ketone. After evaporation of the ether extract from the basified solution, the residue was chromatographed on an aluminum oxide column using benzene:acetone (1:1) eluent and monitored by TLC. The yields and mass and PMR spectroscopic data for IV are given in Table 2.

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N-GLYCOSIDES.

7.* SYNTHESIS OF 4,5'-ANHYDRO-3-(2',2'-O-ISOPROPYLIDENE-β-D-RIBOFURANOSYL)-4-HYDROXYHEXAHYDROPYRIMIDINE-2-THIONES

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UDC 547.455.522'854:543.422

Reaction of 2,3-O-isopropylideneribofuranosylamine p-toluene-sulfonate with β-isothiocyantoaldehydes in the presence of bases leads to the formation of 4,5'-anhydro-3-(2',3'-O-isopropylidene-β-D-ribofuranosyl)-4-hydroxyhexahydropyrimidine-2-thiones, whose steric structure was established by PMR spectroscopy.

The reaction of β-isothiocyantocarbonyl compounds with ammonia or primary amines is a convenient method for the synthesis of substituted 4-hydroxyhexahydropyrimidine-2-thiones [2, 3]. In order to enlarge the scope of this reaction and the synthesis of N-glycosides of hydrogenated pyrimidines, we studied the reaction of 2,3-O-isopropylideneribofuranosylamine p-toluenesulfonate (I) with β-isothiocyantocarbonyl compounds in the presence of bases We have already shown [4] that the reaction of compound I with 4-isothiocyanato-4-methyl-2-pentanone in pyridine leads to a mixture of isomeric 3-(2',3'-O-isopropylidene-β-D-ribofuran

*For Communication 6, see [1].

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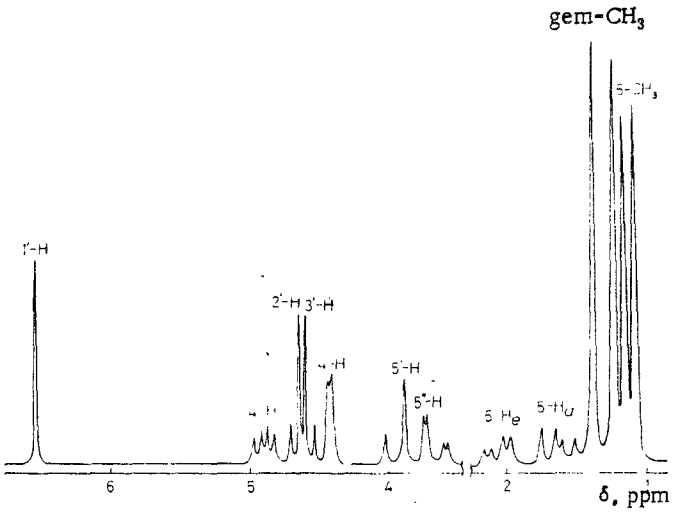
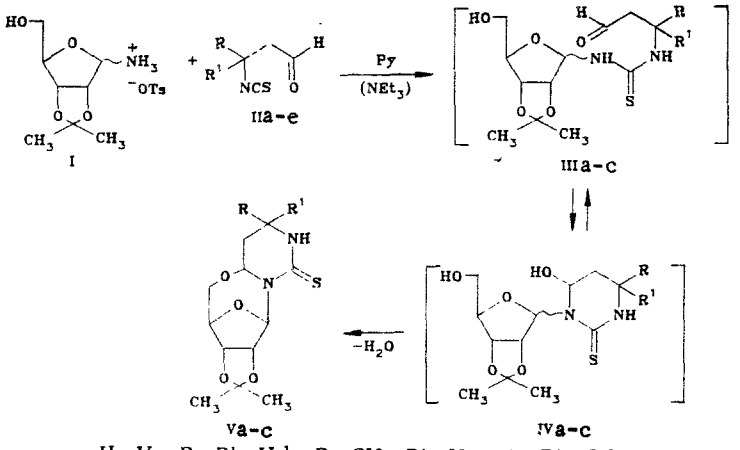


Fig. 1. PMR spectrum of 4,5'-anhydro-3-(2',3'-O-isopropylidene-β-D-ribofuranosyl)-6,6-dimethyl-4-hydrohexahydropyrimidine-2-thione (Vc) (90 MHz).

osyl)-4,6,6-trimethyl-1,2,3,6-tetrahydropyrimidine-2-thione and 3-(2',3'-O-isopropylidene-β-D-ribofuranosyl)-4-methylene-6,6-dimethylhexahydropyrimidine-2-thione in a 10% yield.

In the present work, we studied the reaction of compound I with β-isothiocyantoaldehydes (IIa-c) in pyridine or in chloroform in the presence of triethylamine. Thus, instead of the expected 3-(2',3'-O-isopropylidene-D-ribofuranosyl)-4-hydroxyhexahydropyrimidine-2-thione (IVa-c), products of their intramolecular dehydration, the corresponding 4,5'-anhydro-3-(2',3'-O-isopropylidene-β-D-ribofuranosyl)-4-hydroxyhexahydropyrimidine-2-thiones (Va-c) are obtained in 34-79% yield. Compound Vb is formed as a mixture of two diastereomers (1:1) (see below), which were isolated by column chromatography.



II—V R=R'=H; b R=CH3, R'=H; c R=R'=CH3

The reaction between compounds I and IIa-c probably proceeds with the formation of N-(2,3-O-isopropylidene-D-ribofuranosyl)-N'-(3-oxopropyl)thioureas (IIIa-c), which cyclize into the corresponding glycosides IVa-c. The intramolecular O-alkylation of the β-forms of the molecules of compounds IVa-c is favored by the steric proximity of the 5'-OH and 4-OH hydroxyl groups, and proceeds with splitting off of a water molecule, leading to the formation of the end products of the reaction, cyclonucleosides Va-c. We have already shown [5] that 4-hydroxyhexahydropyrimidine-2-thiones readily undergo O-alkylation by the action of aliphatic alcohols.

The properties and yields of compounds synthesized are given in Table 1.

In the UV spectra of compounds Va-c, as in the spectra of 4-hydroxyhexahydropyrimidine-2-thiones [5], two intense absorption bands are observed in the 200-400 nm region: one in the 210-nm region, and the other corresponding to the $\pi-\pi^*$-transition of the thioureido chromophore [6], in the 250-nm region ($\log \varepsilon$ 4.15).

TABLE 1. Characteristics of Compounds Va-c

Compound	mp, °C (from methanol)	$[\alpha]_D^{20}$ (c, solvent)	R_f*	IR spectrum,† cm^{-1}	UV spectrum,‡ λ_{max}, nm ($\log \varepsilon$)	Found, %				Empirical formula	Calculated, %				Yield, %	
						C	H	N	S		C	H	N	S	A	Б
V	233,5—234	−144° (1,4; DMSO)	0,37	3412, 1526 (3458)	250 (4,14)	50,5	6,5	9,6	11,6	$C_{12}H_{18}N_2O_4S$	50,3	6,3	9,8	11,2	79	63
cis-Vb (4*e*6*e*)	243,5—244	−217° (0,25; DMSO)	0,49	3250, 1540 (3439)	251 (4,17)	51,6	6,8	—	10,8	$C_{13}H_{20}N_2O_4S$	52,0	6,7	—	10,7	66	74
trans-Vb (4*a*6*e*)	199,5—200,5	−83° (0,3; DMSO)		3365, 1508 (3439)												
V	221,5—222,5	−156° (0,2; DMSO	0,57	3212, 1533 (3437)	249 (4,19)	—	—	8,9	10,2	$C_{14}H_{22}N_2O_4S$	—	—	8,9	10,2	68	34

*In a chloroform—methanol (19:1) system.
†In mineral oil; the values of νN-H for the solutions in CCl_4 at a concentration of ~10^{-3} M are given in parentheses.
‡π → π*-Transition band.

TABLE 2. Parameters of PMR Spectra of N-Ribosides Va-c for Solutions in DMSO-D_6

Compound	Chemical shifts, δ, ppm (SSCC, Hz)												
	proton signals of sugar residue							proton signals of aglycone					
	1′-H ($J_{1'2'}$)	2′-H ($J_{2'3'}$)	3′-H ($J_{3'4'}$)	4′-H ($J_{4'5'}$)	5′-H ($J_{4'5''}$)	5″-H ($J_{5'5''}$)	gem-CH_3	4-H ($J_{4,5a}$; $J_{4,5e}$)	5-H_e ($J_{5e,5a}$)	5-H_a ($J_{5e,6a}$)	6-H ($J_{5a,6a}$)	6-CH_3 ($J_{CH_3,H}$)	N H
Va	6,45 s (0)	4,69 d (6,0)	4,62 d (0)	4,47 d (0)	3,95 d (2,3)	3,68 d.d (12,6)	1,23 s, 1,38 s	4,94 d.d (7,0; 5,0)	1,98—2,12 m	1,70—1,86 m	2,94—3,14	—	8,57 s
cis-Vb	6,61s (0)	4,73 d (6,0)	4,62 d (0)	4,49 d (0)	4,03 d (2,2)	3,68 d (12,7)	1,30 s, 1,45 s	5,01 d.d (9,7; 5,1)	2,21 d.q (13,0)	1,49 d.q (3,1)	3,43 m (11,5)	1,12 d (6,5)	8,42s
trans-Vb	6,41 s (0)	4,68d (6,0)	4,67 d (0)	4,51 d (0)	3,94 d (2,4)	3,75d.d (12,6)	1,27 s; 1,42 s	4,95 t (4,8; 4,6)	1,95 d.t (13,5)	1,78 d.q (4,3)	3,33 m (8,2)	1,10 d (6,5)	8,68s
Vв	6,55 s (0)	4,68d (6,1)	4,59 d (0)	4,44 d (0)	3,96 d (2,3)	3,70 d.d (12,6)	1,25 s; 1,40 s	4,91 d.d (8,9; 5,1)	2,07 d.d (13,2)	1,65 d.d	—	1,10 s 1,17 s	8,42 s

In the IR spectra of the ribosides Va-c in the 1500-1600 cm^{-1} region, there are strong absorption bands of thioamide II, characteristic of substituted thioureas [7]. In the 3000-3600 cm^{-1} interval of the IR spectra of compounds Va-c, there are broad absorption bands corresponding to the stretching vibrations of the associated N–H groups. In the spectra of the solutions of ribosides Va-c in $CHCl_3$ or CCl_4 at a concentration of 10^{-3} M, excluding the possibility of intermolecular hydrogen bonds, only one narrow band at 3440-3450 cm^{-1} is observed in this interval (Table 1), which is due to the stretching vibrations of nonassociated N–H groups. In concentrated solutions of Va-c in $CHCl_3$ there are absorption bands of both associated and free N–H groups.

The steric structure of compounds Va-c was found from the data of PMR spectroscopy. Figure 1 shows as an example the PMR spectrum of a solution of compound Vc in DMSO-D_6. The characteristic feature of the spectrum, and also of the PMR spectra of compounds Va, b (Table 2) is the value of three SSCC, $J_{1',2'}$, $J_{3',4'}$, $J_{4',5'}$, equal to zero. As a result, the 1'-H protons of ribosides Va-c appear in the PMR spectra in the form of narrow singlets, while the 2'-H and 3'-H protons appear in the form of a quartet of an AB spin system. The 4'-H, 5'-H, and 5"-H protons form in the spectra an ABX spin system (the X part is a doublet, the AB part is a sextet).

Protons of the heterocyclic bases are observed in the PMR spectra of compounds Va-c in the form of several groups of signals. The signals of the 4-H protons appear in the form of quartets in the 4.91-5.01 ppm region, while the signals of the 5-H_e and 5-H_a protons appear in the form of multiplets at 1.95-2.21 and 1.49-1.86 intervals, respectively. In the PMR spectra of solutions of ribosides Va-c in DMSO-D_6, there are signals of only one mobile proton of the N–H group in the 8.4-8.7 ppm region, which disappear after the addition of D_2O, and signals of protons of the 5'-OH and 4-OH hydroxyl groups are absent.

The formation of 4,5'-anhydroribosides Va-c is possible only with a β-orientation of the glycoside bond. In fact, it has already been noted that the SSCC $J_{1',2'} = 0$ Hz. In accordance with the known criterion for the determination of the configuration of an anomeric center of the ribosides [8], this SSCC value confirms the nature of β-glycoside bonds in the molecules of compounds Va-c.

During the formation of 4,5'-anhydroribosides Va, c, a new chiral center is formed at the $C_{(4)}$ atom as the result of which these compounds can be obtained in two diastereomeric forms. The analysis of the PMR spectra of compounds Va, c (Table 2, Fig. 1) shows that each of these compounds forms as one single diastereomer. Comparison of the chemical shifts of similar protons in the PMR spectra of ribosides Va, c (Table 2) and 4-alkoxyhexahydropyrimidine-2-thiones [5] shows that the most substantial differences are observed for the 4-H protons; in particular, in the spectra of compounds Va, c, they resonate in fields weaker by 0.3-0.6 ppm. From this it can be assumed that in the molecules of ribosides Va, c the 4-H protons approach the oxygen atom of the tetrahydrofuran ring, which is possible at the (S)-configuration of the chiral $C_{(4)}$ atom. This agrees with the data in [9], in which it was shown by PMR spectroscopy and x-ray diffraction analysis that in a reversible isomerization of 1-(2',3'-O-isopropylidene-β-D-ribofuranosyl)-1,2-dihydropyrimidin-2-one, (4S)-4,5'-anhydro-3-(2',3'-O-isopropylidene-β-D-ribofuranosyl)-2-hydroxy-1,2,3,4-tetrahydropyrimidin-2-one is stereospecifically formed.

In the reaction of compound I with (R, S)-3-isothiocyanatobutanal (IIb), four diastereomers of compound Vb can be formed. According to the data of PMR spectra of the reaction product obtained, in which two sets of signals of the corresponding protons are observed, we concluded that compound Vb is obtained in the form of a mixture of two diastereomers only. As has already been shown, these isomers were separated by column chromatography. From the analysis of the values of the chemical shifts of the heterocyclic base protons in the PMR spectra of the diastereomers of compound Vb, it can be assumed that, as in the case of ribosides Va, c, the two diastereomers of compound Vb have an (S)-configuration of the chiral $C_{(4)}$ atom. Thus, the two diastereomers of compound Vb differ probably in the configuration of the chiral $C_{(6)}$ atom only.

To find the orientation of the substituents in the hexahydropyrimidine ring of the molecules of ribosides Va-c, we used as the starting point the data in [10], where by x-ray diffraction analysis it was shown that, in the crystalline state, the six-membered ring of the hexahydropyrimidine-2-thione molecule has the configuration of somewhat compressed chair. From the SSCC values $J_{4,5e}$ (5.0-5.1 Hz) and $J_{4,5a}$ (7.0-8.9 Hz) in the PMR spectra

TABLE 3. Mass Spectra of Ribosides Va-c

Compound	Mass spectrum, m/z (peak intensity in % of maximal)*
Va	286 (78), 271 (20), 228 (57), 171 (10), 132 (13), 117 (11), 116 (22), 115 (100), 113 (11), 103 (12), 72 (16), 69 (14), 68 (16), 59 (13), 58 (92), 57 (22), 56 (28), 43 (34), 41 (17)
Vb†	300 (54), 285 (16), 242 (36), 146 (12), 129 (100), 103 (10), 86 (34), 71 (14), 70 (10), 69 (11), 68 (13), 57 (10), 56 (10), 44 (22), 43 (40), 42 (11)
Vc	314 (49), 299 (15), 256 (40), 160 (15), 159 (16), 144 (22), 143 (100), 100 (62), 85 (12), 84 (15), 83 (11), 69 (16), 68 (15), 59 (11), 58 (26), 57 (21), 56 (19), 55 (14), 44 (10), 43 (40), 42 (17), 41 (32)

*Peaks with intensity of ≥10% are shown.
†Mixture of diastereomers, 1:1.

of N-ribosides Va, c, we concluded that the hexahydropyrimidine ring in the molecule of compounds Va, c exists in a conformation with an equatorial orientation of the 4-OCH_2 group. According to the PMR spectroscopy data, the chromatographically less mobile diastereomer of compound Vb has a cis-disposition of the substituents in the hexahydropyrimidine ring with an equatorial orientation of the 4-OCH_2 and 6-CH_3 groups ($J_{4a,5a}$ = 9.7, $J_{5a,6a}$ = 11.5 Hz); the chromatographically more mobile diastereomer of compound Vb has a trans-disposition of the substituents in the hexahydropyrimidine ring with an axial orientation of the 4-OCH_2 group and an equatorial orientation of the 6-CH_3 group ($J_{4a,5a}$ = 4.8, $J_{5a,6a}$ = 8.2 Hz). Thus the cis-diastereomer of compound Vb has a (4S, 6R) configuration, and the trans-diastereomer the (4S, 6S) configuration.

It should be noted that we have already shown [5] that the most stable conformers in the series of 4-hydroxy(alkoxy)hexahydropyrimidine-2-thiones are those with an axial orientation of the $C_{(4)}$–O bond. However, heating the solution of compound Va for many hours in a water bath at 97°C does not lead to a change in the orientation of the $C_{(4)}$–O bond from an equatorial to an axial one as the result of an inversion of the hexahydropyrimidine ring. It is possible that this is due to the great rigidity of the molecules of 4,5'-anhydroribosides V.

Examination of Dreiding models of compounds Va-c shows that the seven-membered ring, including the $O_{(1')}$ and $O_{(5')}$ atoms can exist in two conformations – with screening or gauche disposition of the $C_{(4')}$–$O_{(1')}$ and $C_{(5')}$–$O_{(5')}$ bonds. From the SSCC values $J_{4',5'} \approx 0$ and $J_{4',5'}$ = 2.2-2.4 Hz in the PMR spectra of compounds Va-c (Table 2), the gauche-disposition of these bonds, and hence a twist–chairlike conformation of the seven-membered ring, can be concluded, which agrees with the data in [9].

We studied the mass spectra and clarified the character of the fragmentation of compounds Va-c by the action of electron impact. In the mass spectra of N-ribosides Va-c (Table 3), there are peaks of molecular ions, intense peaks of rearranged ions $[(B-18) + 1]^+$ (B is the corresponding 4-hydroxyhexahydropyrimidine-2-thione), and also peaks of $[RR^1C{=}N{=}C{=}S]^+$ and $[RR^1{=}CHCH\ O]^{+\cdot}$ ions, formed during the dissociation of the heterocyclic base. Moreover, the mass spectra of ribosides Va-c are characterized by the presence of intense peaks of the $[M - CH_3]$ and $[M - C_3H_6O]^{+\cdot}$ ions.

EXPERIMENTAL

The specific rotations were determined on a Perkin–Elmer 241 MC polarimeter. The IR spectra were recorded on a UR-10 spectrophotometer for suspensions in mineral oil and solutions in $CHCl_3$ and CCl_4. The UV spectra were recorded on a Specord UV-vis spectrophotometer in methanol. The PMR spectra were run on Bruker WM-250 (250 MHz) and Bruker HX-90E (90 MHz) spectrometers in DMSO-D_6, using HMDS as internal standard. The mass spectra were recorded on a Varian MAT-112 apparatus, with energy of ionizing electrons of 70 eV, direct introduction of samples, and temperature of the ionization chamber of 180°C. The thin-layer chromatography was carried out on Silufol UV-254 plates in chloroform–methanol (19:1) and ether systems. The column chromatography was carried out on an L 40/100μ silica gel (CSSR).

3-Isothiocyanato-3-methylbutanol (IIc) is obtained by known method [2] consisting in the addition of thiocyanic acid to the multiple bonds of 3-methyl-2-butenal. BP 56-62°C (0.1 mm Hg); n_D^{20} 1.5078. IR spectrum (thin layer): 1722 (C=O), 2038 cm^{-1} (N=C=S).

4,5'-Anhydro-3-(2',3'-O-isopropylidene-β-D-ribofuranosyl)-4-hydroxyhexahydropyrimidine-2-thione (Va). A. A 5-ml portion of a solution of 251 mg (2.51 mmoles) of triethylamine in chloroform is added to a suspension of 865 mg (2.39 mmoles) of compound I [11] in 7 ml of dry chloroform, cooled to 0°C. A solution of 345 mg (2.99 mmoles) of 3-isothiocyanatopropanal (IIa) [2] ion 15 ml of chloroform, cooled to 0°C, is added at 0°C to the solution obtained. The reaction mixture is allowed to stand for another 24 h at 0°C, the solvent is evaporated in vacuo, and 3 ml of ice water and 2 ml of ether are added to the residue. The precipitate that separates is filtered, and washed on the filter by cold water and ether. Yield, 545 mg (79.4%). An analytically pure sample is obtained by recrystallization from methanol.

B. A solution of 1.0 g (2.77 mmoles) of compound I and 1.0 g (8.70 mmoles) of compound IIa in 15 ml of dry pyridine is allowed to stand at 20°C for 24 h. The solvent is distilled in vacuo at 36°C. The oily residue is dissolved in a minimal amount of chloroform and chromatographed on a 1.8 × 12 cm column with silica gel, and eluted by chloroform. The solvent is distilled off, the residue is treated by cold CCl_4, and the crystalline precipitate is filtered. Yield 0.5 g (63.3%).

4,5'-Anhydro-3-(2',3'-O-isopropylidene-β-D-ribofuranosyl)-6-methyl-4-hydroxyhexahydropyrimidine-2-thione (Vb) is obtained in a similar way as compound Va by methods A and B in the form of a mixture of two diastereomers (1:1) from compound I and (R, S)-3-isothiocyanatobutanal (IIb) [2]. The mixture of the diastereomers (537 mg) is separated on a column with silica gel (50 g) in an ether–hexane system (7:3 → 8:3). The course of the separation is controlled by TLC (eluent–ether). Yield, 198 mg of trans-diastereometer(4a6e), which is the first to be eluted from the column, and 201 mg of the cis-diastereomer (4e6e).

4,5'-Anhydro-3-(2',3'-O-isopropylidene-β-D-ribofuranosyl)-6,6-dimethyl-4-hydroxyhexahydropyrimidine-2-thione (Vc) is obtained in a similar way as compound Va by methods A and B from compound I and 3-isocyanato-3-methylbutanal (IIc).

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