(2H, m, 8-H and 11-H), 11.56 ppm (1H, s, NH). Mass spectrum: [M]+ 442.1314; $M_{calc}$ 442. The yield was 0.28 g (51%).

**Photolysis of 3-Phenyl-4-benzylidene-1H-naphtho[2,3-h]quinazoline-2,7,12-trione (VI).** A 0.13-g (0.7 mmole) sample of a 1:1 mixture of Z- and E-isomers VIa, b was applied to 15 Silufol plates (150 × 150 mm), and the plates were maintained in light until the color changed from red brown to yellow. The photolysis products were extracted with chloroform, chromatographed with a column packed with silica gel (elution with chloroform), and recrystallized from dioxane to give 0.07 g (65%) of anthrapyrimidine V with mp 325-328°C. The IR spectrum was identical to the spectrum of a sample obtained from amine IV.

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# SYNTHESIS OF 5-HYDROXY-6-METHYLURACIL 3-β-D-RIBOFURANOSIDE

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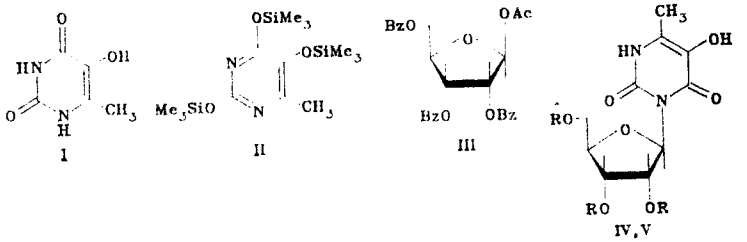
*3-(β-D-Ribofuranosyl)-5-hydroxy-6-methyluracil was synthesized by the silyl method in the presence of $SnCl_4$ using 1-O-acetyl-2,3,5-tri-O-benzoyl-β-D-ribofuranose as the carbohydrate component. The structures of the glycosides were confirmed by spectral methods.*

5-Hydroxy-6-methyluracil (I, hydroxymethacil) is of interest as an immunomodulator and cardiostimulator [1-3]. To obtain the transport form of this compound we began research on the synthesis of nucleosides that are analogs of 6-methylpyrimidine nucleosides [4, 5]. The present communication is devoted to the synthesis of 3-(β-D-ribofuranosyl)-5-hydroxy-6-methyluracil by the silyl method [6].

5-Hydroxy-6-methyluracil (I) was obtained by the method in [7] and was silylated with excess hexamethyldisilazane in the presence of trimethylchlorosilane in dry dioxane as in [8]. The yield of 2,4,5-tris(trimethylsilyloxy)-6-methyluracil (II) was 59%. 1-O-Acetyl-β-D-ribofuranose tribenzoate (III) was obtained by our modification of the method in [9]



IV R=Bz; V R=H; Bz=$C_6H_5CO$

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using KU-2-8 cation-exchange resin ($H^+$ form) in the step involving the synthesis of the methyl-substituted D-ribofuranoside. The reaction of silylated base II with protected ribofuranose III in dry dichloroethane at 20°C proceeds stereospecifically to give $N_3$-β-D-glycoside IV (40-43% yield).

Nucleoside IV was isolated by column chromatography on silica gel. Its deblocking with a 0.1 N solution of NaOMe in MeOH leads to 3-(β-D-ribofuranosyl)-5-hydroxy-6-methyluracil (V). The purity of the compounds obtained was monitored by TLC and HPLC.

The structures of glycosides IV and V were established on the basis of data from the IR, UV, and $^1H$ and $^{13}C$ NMR spectra. An 11.4 ppm diamagnetic shift of the signal of the $C_{(1')}$ atom as compared with 1-O-acetate III is observed in the $^{13}C$ NMR spectrum of nucleoside IV, and the chemical shifts (CS) of the $C_{(2')}$—$C_{(4')}$ atoms in the spectrum of nucleoside IV are virtually the same as those in the spectrum of starting sugar III, which indicates a β configuration of the anomeric center in nucleoside IV.

Signals of protons of a uracil fragment — a singlet of a methyl group (2.14 ppm) and broad signals of NH (10.8 ppm) and OH (3.67 ppm) groups — are observed in the PMR spectrum of nucleoside IV.

In the spectrum of starting acetate III the 1-H proton is observed in the form of a singlet at 6.43 ppm, i.e., a vicinal constant of spin-spin coupling (SSC) of the 1-H and 2-H protons is virtually absent, which indicates a gauche-equatorial-equatorial orientation of the 1-H and 2-H protons or a trans orientation of the substituents attached to the $C_{(1)}$ and $C_{(2)}$ atoms (a β configuration of the anomeric center). In the spectrum of nucleoside IV the signal of the 1-H proton (6.64 ppm) also has the form of a singlet, which indicates retention of the β configuration of the anomeric center. In addition, it is known [10] that the presence of singlet of a 1-H proton in the spectra of substituted 6-methylpyrimidine nucleosides is a confirmation of the β configuration of the anomeric center.

The formation of 1,2-trans isomers is generally preferable for the glycosylation of sugar derivatives with 2-O-acyl groups; this is explained by the formation of a 1,2-acyloxonium ion in the rate-determining step of the reaction [11, 12].

The N-glycoside structure of IV was confirmed by its IR spectrum, in which strong carbonyl absorption ($\nu_{C=O}$) of a uracil ring is observed at 1660-1675 and 1700-1730 $cm^{-1}$, which excludes an O-glycoside structure.

The assignment to an $N_{(3)}$-glycoside structure was made on the basis of the UV spectra of nucleoside V, for which a bathochromic shift of the absorption bands in an alkaline medium of ~30 nm, which is typical for $N_{(3)}$-substituted uracil derivatives [10, 13], is characteristic.

## EXPERIMENTAL

The $^1H$ NMR spectra of solutions of the compounds in $CDCl_3$ were recorded with a Tesla BS-567 spectrometer (100 MHz) with tetramethylsilane (TMS) as the internal standard. The $^{13}C$ NMR spectra of solutions in $CDCl_3$ were obtained with a JEOL FX-90-Q spectrometer (22.5 MHz) with broad-band and extra-resonance suppression of the protons and TMS as the internal standard. The IR spectra were recorded with a UR-20 spectrometer. The electronic absorption spectra were recorded with a Specord M-40 spectrophotometer. The melting points were measured with a Boetius apparatus (East Germany). The specific rotation was determined with a Perkin—Elmer 241-MC polarimeter in a 1-dm long tube. Thin-layer chromatography was carried out on Silufol UV-254-366 plates (Czechoslovakia) using the following solvent systems: A) chloroform—methanol (19:1); B) chloroform—methanol (4:1). The spots of the substances were detected with UV light and iodine vapors. Silica gel L (40/100μ, Chemapol, Czechoslovakia) was used for column chromatography. Analysis by HPLC was carried out with a Du Pont chromatograph with columns packed with Zorbax CN (for IV) or Zorbax ODS (for V): the mobile phase was a mixture of chloroform with hexane (9:1) or distilled water, respectively, and a UV detector was used. Gas-liquid chromatography was carried out with a Chrom-5 chromatograph (Czechoslovakia) with a glass column packed with SE-30 sorbent; the length was 1.2 m, the inner diameter was 3 mm, the temperature was 150°C, the detector temperature was 200°C, the vaporizer temperature was 200°C, the carrier gas was helium, and the flow rate was 40 ml/min.

The dichloroethane was fractionated twice over $P_2O_5$. The dioxane was maintained for 24 h over KOH and was then fractionated over sodium metal.

The results of elementary analysis for C, H, and N were in agreement with the calculated values.

**2,4,5-Tris(trimethylsilyloxy)-6-methylpyrimidine (II, $C_{14}H_{27}N_2O_3Si_3$).** A mixture of 14.2 g (100 ml) of I [7], 40 ml of hexamethyldisilazane, and 2 ml of trimethylchlorosilane in 50 ml of dry dioxane was refluxed without access to moisture until the solid material had dissolved (3 h), after which the solvent and excess silylating agent were removed by vacuum distillation. The residue, which, according to GLC data, contained ~5% admixed silylated 6-methyluracil, was subjected to fractional distillation in vacuo to give 22.9 g (59%) of silylated base II in the form of a colorless oil, which crystallized on standing (to give white crystals) and was homogeneous according to GLC data. IR spectrum (liquid film): 760, 850, 1250 [$Si(CH_3)_3$]; 1040 (C—O—Si); 1460, 1580 $cm^{-1}$ (pyrimidine ring). PMR spectrum ($CDCl_3$,

relative to $CDCl_3$): 0.087, 0.21, 0.26 [27H, s, $3Si(CH_3)_3$]; 2.14 ppm (3H, s, $CH_3$). PMR spectrum relative to tetramethylsilane (TMS): 0.23, 0.35, 0.40 [27H, s, $3Si(CH_3)_3$]; 2.28 ppm (3H, s, $CH_3$).

**1-O-Acetyl-2,3,5-tri-O-benzoyl-β-D-ribofuranose (III, $C_{28}H_{24}O_9$).** A suspension of 5 g (33.3 mmole) of D-ribose in 100 ml of methanol was stirred with 5 g of KU-2-8 cation-exchange resin ($H^+$ form) until the sugar had dissolved (2 h), after which the resin was removed by filtration and washed with methanol (10-15 ml), and the filtrate was evaporated in vacuo to give a syrup (5.3 g). The resulting mixture of methyl-substituted D-ribofuranosides was dried in vacuo at 50°C for 2 h, after which it was dissolved in a mixture of 27 ml of dry methylene chloride and 59 ml of pyridine. The solution was cooled to 0°C, 20 ml of distilled benzoyl chloride was added dropwise with stirring, and the mixture was stirred at 0-5°C for 4 h, maintained at 4-5°C for 12 h, and then poured into 300 ml of ice water. The organic layer was separated, and the aqueous layer was extracted with $CH_2Cl_2$ (3 × 50 ml). The extracts were combined, washed with water (2 × 50 ml), and dried with $MgSO_4$. The solvent was removed by distillation in vacuo at 20°C to give a red oil, which was dissolved in a mixture of $CH_3COOH$ (5 ml) and $Ac_2O$ (12 ml). The solution was cooled to 0°C, 1.6 ml of concentrated $H_2SO_4$ was added slowly, and the mixture was allowed to stand overnight at 4-5°C. It was then poured into 200 ml of ice water, and the liberated viscous oil was washed with water (4 × 50 ml). The resulting product was recrystallized successively from dry isopropyl alcohol and absolute ethanol to give a product with mp 131-133°C (mp 126-128°C [9], mp 131-132°C [10]) and $[\alpha]_D^{20}$ +43° (c 0.5; $CHCl_3$). The product was homogeneous according to GLC data. PMR spectrum ($CDCl_3$): 2.00 (3H, s, $CH_3$); 4.46 (1H, dd, $J_{5,5'} = -14.0$ Hz; $J_{5,4} = 5.6$ Hz, 5-H); 4.78; 4.81 (2H, s, 5′-H—4-H); 5.78 (1H, d, $J_{2,3} = 5.3$ Hz, 2-H); 5.87 (1H, dd, $J_{3,2} = 5.3$ Hz; $J_{3,4} = 6.2$ Hz, 3-H); 6.43 (1H, s, 1-H); 7.27-7.49 (3H, m) and 7.81-8.12 ppm (2H, m, $3C_6H_5CO$). $^{13}C$ NMR spectrum ($CDCl_3$): 20.86 (acetate $CH_3$); 63.72 [$C_{(5)}$]; 71.41 [$C_{(2)}$]; 74.44 [$C_{(3)}$]; 79.97 [$C_{(4)}$]; 98.39 [$C_{(1)}$]; 128.41; 128.52; 128.68; 128.84; 129.76; 133.23; 133.66 ($C_6H_5$); 164.48; 165.36; 165.95 ppm (C=O). The yield was 8.2 g (52%).

**3-N-(2,3,5-Tri-O-benzoyl-β-D-ribofuranosyl)-5-hydroxy-6-methyl-1,2-dihydropyrimidine-2,4-dione (IV, $C_{31}H_{26}N_2O_{10}$).** A solution of 1.1 g (3.1 mmole) of silylated base II in 10 ml of dichloroethane was added to a solution of 1.3 g (2.6 mmole) of ribofuranose III in 50 ml of dry dichloroethane, the mixture was cooled to 0-5°C, 0.5 ml (3.3 mmole) of distilled $SnCl_4$ in 10 ml of dry dichloroethane was added dropwise with vigorous stirring without access to moisture, and the mixture was stirred for 3 h at 0-5°C and for 22 h at 20°C. The course of the reaction was monitored by TLC in system A. The solution was diluted with 150 ml of dichloroethane, and the mixture was treated with 50 ml of a saturated solution of $NaHCO_3$. The organic phase was separated, washed with water, and dried with $MgSO_4$. Evaporation of the solvent in vacuo at 50°C gave 1.2 g of a yellowish syrupy substance, which was chromatographed twice with a column packed with silica gel L by successive elution with benzene, benzene—ethyl acetate (1:1), ethyl acetate, chloroform, and chloroform—ethanol (50:1). The fractions containing nucleoside IV were combined and evaporated in vacuo to give 0.60-0.64 g (40-43%) of IV in the form of an amorphous yellowish substance, which, according to TLC and HPLC, was an individual substance. The product had mp 96-99°C (dec.) and $R_f$ 0.45 (A). IR spectrum (mineral oil): 3200-3500 (OH, NH); 1730 ($OCOC_6H_5$); 1650 (C=O); 1590, 1610 (pyrimidine ring); 730, 775, 820 $cm^{-1}$ ($C_6H_5$). PMR spectrum ($CDCl_3$): 2.14 (3H, s, 6-$CH_3$); 3.67 (1H, broad s, OH); 4.68; 4.70; 4.73 (3H, 5-H, 5′-H, 4-H); 5.87 (1H, 2-H); 6.22 (1H, 3-H); 6.64 (1H, s, 1-H); 7.32-7.51 (3H, m) and 7.92-8.07 (2H, m) ($3C_6H_5CO$); 10.80 ppm (1H, broad s, NH). $^{13}C$ NMR spectrum ($CDCl_3$): 18.31 (6-$CH_3$); 63.45 [$C_{(5')}$]; 70.92 [$C_{(2')}$]; 73.96 [$C_{(3')}$]; 78.94 [$C_{(4')}$]; 87.01 [$C_{(1')}$]; 128.35, 128.79; 128.80; 129.55; 129.76; 133.12; 133.39 ($C_6H_5$); 150.03 [$C_{(6)}$]; 165.20; 165.46; 166.33 ppm (C=O).

**3-(β-D-Ribofuranosyl)-5-hydroxy-6-methyl-1,4-dihydropyrimidine-2,4-dione (V, $C_{10}H_{14}N_2O_7$).** A 0.2-g (0.34 mmole) sample of benzoate III was stirred in 30 ml of a 0.1 N solution of NaOMe in dry methanol for 48 h at 20°C (monitoring by TLC using system B), after which the mixture was neutralized with KU-2×4 cation-exchange resin ($H^+$ form). The resin was removed by filtration, the solution was evaporated in vacuo at 50°C, and the residue was triturated with ether to remove the methyl benzoate to give 0.08 g (88.9%) of V in the form of an amorphous powder, which, according to TCL (system B) and HPLC data, was an individual substance. The product, which could not be crystallized, had $[\alpha]_D^{20}$ +33° (c 0.04; water) and $R_f$ 0.61 (B). UV spectra: $\lambda_{max}^{0.1\ N\ HCl}$ 282 nm (ε 4100), $\lambda_{max}^{H_2O}$ 282 nm (ε 4700), $\lambda_{max}^{0.1\ N\ NaOH}$ 312 nm (ε 9300). IR spectrum (KBr): 1650, 1725 (C=O); 3200-3500 (OH, NH); 1560 $cm^{-1}$ (NH). $^{13}C$ NMR spectrum ($D_2O$): 17.67 (6-$CH_3$); 64.31 [$C_{(5')}$]; 72.33 [$C_{(2')}$]; 74.01 [$C_{(3')}$]; 86.15 [$C_{(4')}$]; 90.86 [$C_{(1')}$]; 130.09; 138.32 [$C_{(5)}$, $C_{(6)}$]; 152.95; 164.16 ppm (C=O).

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# DIAZABICYCLOALKANES WITH NITROGEN ATOMS IN THE NODAL POSITIONS.

## 21.* HETEROATOM-PROMOTED LITHIATION OF BENZO[b]-1,4-DIAZABICYCLO[2.2.2]OCTENE AND INTRODUCTION OF SUBSTITUENTS INTO THE ANNELATED BENZENE RING

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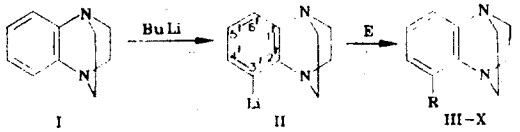
*The action of n-butyllithium on benzo[b]-1,4-diazabicyclo[2.2.2]octene leads to lithiation in the 3' position of the aromatic ring. The reaction of this lithium derivative with electrophilic reagents was used to synthesize 3'- and 3',6'-substituted derivatives of benzo[b]-1,4-diazabicyclo[2.2.2]octene.*

The reaction of benzo[b]-1,4-diazobicyclo[2.2.2]octene (I) with electrophiles under severe conditions leads to primarily 4'-substituted I [2].

It is known that when substituents that are capable of coordinating with the lithium atom are present in the aromatic ring, lithiation proceeds selectively in the ortho position relative to the substituent [3]. According to the data in [4], prolonged heating of the reaction mixtures is required to accomplish the direct lithiation of aromatic tertiary amines. We have established that treatment of benzodiazabicyclooctene I with n-butyllithium in tetrahydrofuran (THF) leads to 3'-lithiobenzo[b]-1,4-diazabicyclo[2.2.2]octene (II). It follows from the PMR spectra that the reaction is complete after a few minutes at room temperature. During the reaction the symmetrical multiplet of aromatic protons of I centered at 6.99 ppm is gradually converted to two 4'-H and 6'-H doublets at 7.63 and 6.65 ppm (J = 7.0 Hz) and a 5'-H triplet at 6.84 ppm (J = 7.0 Hz), which confirms lithiation in the 3' position. The ease of lithiation of




I II III–X

III R=Br, IV R=I, V R=COOH, VI, R=OH, VII R=$SiMe_3$, VIII R=$B(OH)_2$, IX R=$SC_6H_{13}$-*n*, X R=CHO

*See [1] for Communication 20.

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