N-GLYCOSIDES.

3.* REACTION OF 2,3-O-ISOPROPYLIDENERIBOFURANOSYLAMINE TOSYLATE WITH 4-METHYL-4-ISOTHIOCYANATO-2-PENTANONE

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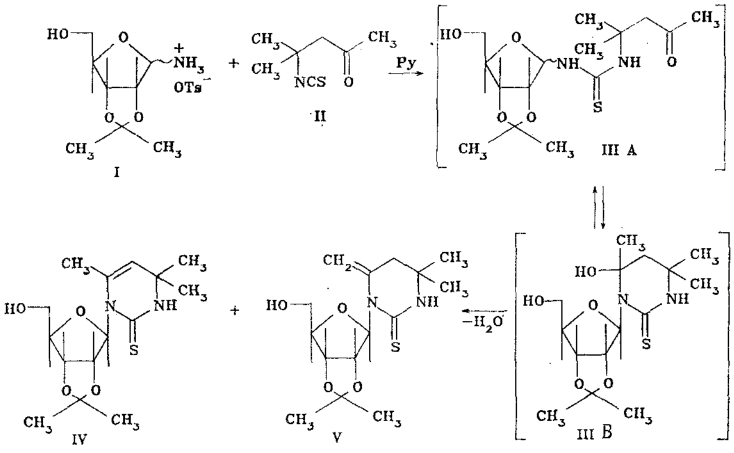
UDC 547.522'854.1.07:543.422

The condensation of 2,3-O-isopropylideneribofuranosylamine tosylate with 4-methyl-4-isothiocyanato-2-pentanone in the presence of bases was studied. In pyridine the reaction gives a mixture of 3-(2',3'-O-ispropylidene-β-D-ribofuranosyl)-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 order to develop methods for the synthesis of N-ribosides of hydrogenated pyrimidine-2-thiones we studied the reaction of 2,3-O-isopropylideneribofuranosylamine tosylate (I) [2] with 4-methyl-4-isothiocyanato-2-pentanone (II) [3].

The expected N-glycosides are not formed when I is heated with isothiocyanato ketone II in various solvents (dioxane, ethyl acetate, aqueous alcohol, and methanol) in the presence of bases (triethylamine, pyridine, sodium bicarbonate, and sodium methoxide). In individual cases the ribosylamine is deaminated to give a product of reaction of ammonia with isothiocyanato ketone II, viz., 4-hydroxy-4,6,6-trimethylhexahydropyrimidine-2-thione.

A mixture of compounds, which, according to the results of elementary analysis and data from the IR, UV, and PMR spectra, consists of 3-(2',3'-O-isopropylidene-β-D-ribofuranosyl)-4,6,6-trimethyl-1,2,3,6-tetrahydropyrimidine-2-thione (IV) and 3-(2',3'-O-isopropylidene-β-D-ribofuranosyl)-4-methylene-6,6-dimethylhexahydropyrimidine-2-thione (V), is formed in up to 10% yield in the reaction of I and II in anhydrous pyridine (at 20-50°C for 3-30 h). According to data from the PMR and IR spectra, the ratio of isomers IV and V depends on the reaction conditions (time and temperature). In addition to IV and V, we isolated 4,6,6-trimethyl-1,2,3,6-tetrahydropyrimidine-2-thione (VI) from the reation mixture in ∿20% yield.



Absorption bands corresponding to the stretching vibrations of OH and NH groups at 3200-3400 cm^{-1}, the position of which depends on the ratio of the isomers in the mixture, are observed in the IR spectra of the mixture of ribosides IV and V. A "thioamide II" ab-

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*See [1] for communication 2.

M. V. Lomonosov Moscow Institute of Fine Chemical Technology, Moscow 119831. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, pp. 244-246, February, 1984. Original article submitted July 19, 1983.

0009-3122/84/2002-0201$08.50

sorption band is observed in the IR spectra at 1517 cm^{-1}; the bands at ∿1680 and 1640 cm^{-1} correspond to stretching vibrations of C=C bonds in IV (with an endocyclic double bond) and V (with an exocyclic double bond) respectively [4].

The UV spectra of the mixture of IV and V contain an absorption band at 264 nm, which corresponds to the $\pi \rightarrow \pi^*$ transition of the thioamide group [5, 6].

Signals of protons of both isomers are present in the PMR spectra of the mxiture of ribosides IV and V. The protons of the H_2C=C group of V give two singlet signals at 5.15 and 4.43 ppm, whereas the 5-H protons give a quartet of an AB system centered at 2.21 ppm. The protons of the 4-CH_3 group and the 5-H proton of isomer IV show up in the PMR spectrum in the form of singlets at 2.04 and 4.76 ppm, respectively. In addition, ribosides IV and V give separate signals of 1'-H and 4'-H protons and protons of gem-methyl groups of a dioxolane ring for each isomer.

A possible sequence of reactions that leads to the production of ribosides IV and V is presented in the scheme and includes the formation of N_1-ribosyl-N_3-oxoalkylthiourea IIIA, which is capable of undergoing cyclization to 3-β-ribosyl-4-hydroxyhexahydropyrimidine-2-thione IIIB. The latter compound is readily dehydrated to give ribosides IV and V; this is evidently due to steric factors. The possibility of the formation of the proposed intermediates is confirmed by an examination of Dreiding molecular models of I-V. It follows from an analysis of the models that the cyclization of IIIA is possible only for the β anomer, and this enabled us to assign N-glycosides IV and V to the β series.

Rapid cleavage of the glycoside bonds to give tetrahydropyrimidine-2-thione VI occurs when one attempts to remove the isopropylidene protective group (by heating at 95°C in 25% acetic acid).

EXPERIMENTAL

The IR spectra of KBr pellets of the compounds were recorded with a UR-10 spectrometer. The UV spectra of $6 \cdot 10^{-5}$ mole/liter solutions of the compounds in methanol were obtained with a Specord UV-vis spectrophotometer. The PMR spectra were recorded with Brucker WM-250 (250 MHz) and Brucker HX-90E (90 MHz) spectrometers. Thin-layer chromatography (TLC) was carried out on Silufol UV-254 plates in a chloroform—methanol system (19:1).

3-(2',3'-O-Isopropylidene-β-D-ribofuranosyl)-4,6,6-trimethyl-1,2,3,6-tetrahydropyrimidine-2-thione (IV) and 3-(2',3'-O-Isopropylidene-β-D-ribofuranosyl)-4-methylene-6,6-dimethylhexahydropyrimidine-2-thione (V). A mixture of 4.2 g (11.6 mmole) of I and 3.1 g (19.7 mmole) of isothiocyanato ketone II in 20 ml of dry pyridine was heated at 50°C for 3 h, after which the solvent was evaporated in vacuo, and the residue was dissolved in chloroform and chromatographed with a column packed with L 40/100μ silica gel (Czechoslovakian SSR) by elution with chloroform. The solvent was removed from the eluate, and the crystals were washed several times with cold alcohol to give 0.39 g (9.7%) of a mixture of IV and V (in a ratio of 3:7, respectively). An analytically pure product was obtained by recrystallization from methanol. IR spectrum: 3240 broad (NH, OH), 1680 (C=C of isomer IV), 1640 (C=C of isomer V), and 1517 cm^{-1} (NH—CS). UV spectrum, λ_{max} (log ε): 264 nm (4.19). PMR spectrum (d_6-DMSO), signals of the protons of isomer IV: 7.13 (d, $J_{1',2'}$ = 4.6 Hz, 1'-H), 4.76 (s, 5-H), 4.07 (m, 4'-H), 2.04 (s, 4-CH_3), and 1.41 and 1.25 ppm [s, $(CH_3)_2C$—O]. PMR spectrum, signals of the protons of isomer V: 7.07 (d, $J_{1',2'}$ = 4.6 Hz, 1'-H), 5.15 and 4.43 (s, H—C=C), 4.15 (m, 4'-H), 2.21 (center of the quartet of an AB system, J_{AB} = 12.5 Hz, 5-H), and 1.37 and 1.24 ppm [s, $(CH_3)_2C$—O]. PMR spectrum, signals of the protons common to both isomers: 4.85 (dd, $J_{2',3'}$ = 6.5 Hz, 2'-H), 4.74 (dd, $J_{3',4'}$ = 6.5 Hz, 3'-H), 3.30-3.56 (m, 5'- and 5"-H), and 1.13 ppm (s, gem-CH_3). Found: C 55.1; H 7.2; S 9.8%. $C_{15}H_{24}N_2O_4S$. Calculated: C 54.9; H 7.4; S 9.8%.

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