# N-GLYCOSIDES.

# 2.* STRUCTURE OF THE PRODUCTS OF THE REACTION OF GLYCOSYL ISOTHIOCYANATES WITH 4-AMINO-4-METHYL-2-PENTANONE

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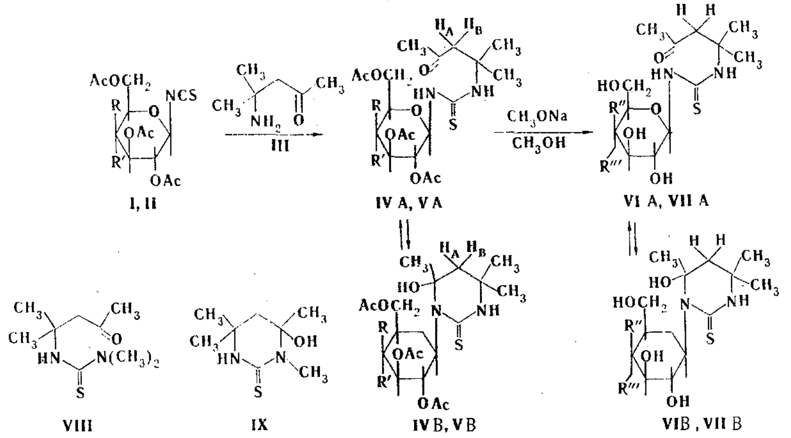
The structures of N-glycosides obtained by the reaction of 2,3,4,6-tetra-O-acetyl-β-D-gluco(galacto)pyranosyl isothiocyanates with 4-amino-4-methyl-2-pentanone and the structures of their deacetylation products were established by means of IR, UV, and PMR spectroscopy. The glycosides have primarily the $N_1$-glycosyl-$N_3$-(4-methyl-2-oxo-4-pentyl)-thiourea structure, which exists in a state of prototropic ring-chain tautomerism with cyclic tautomers, viz., 3-glycosyl-4,4,6-trimethyl-4-hydroxyhexahydropyrimidine-2-thiones.

We have previously described the synthesis of N-glycoside IV, which was obtained by the reaction of 2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl isothiocyanate (I) with 4-amino-4-methyl-2-pentanone (III) [2], and its deacetylation product VI. In the present research we carried out the reaction of 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl isothiocyanate (II) [3] with β-amino ketone III and obtained N-glycoside V. Compound V was converted to N-glycoside VII by Zemplen deacetylation.

As a consequence of ring-chain tautomerism, the aglycone in N-glycosides IV-VII may exist in two tautomeric forms, viz., in the acyclic oxoalkylthiourea form (IVA-VIIA) and in the cyclic 4-hydroxyhexahydropyrimidine-2-thione form (IVB-VIIB). The existence of a tautomeric equilibrium between these two forms was previously demonstrated in the 3-alkyl-4-hydroxyhexahydropyrimidine-2-thione series [4].



I, II

IV A, V A

VI A, VII A

VIII

IX

IV B, V B

VIB, VII B

I, IV R=OAc, R'=H; II, V R=H, R'=OAc; VI R''=OH, R'''=H; VII R''=H, R'''=OH

To establish the structures of the synthesized N-glycosides IV-VII and to study their prototropic ring-chain tautomerism we investigated their UV, IR, and PMR spectra (Tables 1 and 2).

The presence in N-glycosides IV-VII of a thioureide fragment is characterized by the presence in their UV spectra of absorption bands at 215 and 252 nm [5, 6]. The IR spectra of all of the compounds contain a strong band at 1550 cm$^{-1}$, which reflects the $\nu$CN + $\delta$NH Raman vibration that is characteristic for a secondary thioamide group in thioureas [7].

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*See [1] for Communication 1.

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TABLE 1. Characteristics of IV-VII

| Compound | mp, °C | $[\alpha]_D^{20}$ (c, solvent)[a] | IR spectrum,[b] cm$^{-1}$ | UV spectrum,[c] $\lambda_{max}$, nm (log ε) | Found, % |  |  |  | Empirical formula | Calculated, % |  |  |  | Yield, % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|  |  |  |  |  | C | H | N | S |  | C | H | N | S |  |
| IV | 89,5—91 | 0,0<br>(1,1; $CHCl_3$) | 3395 s (NH);<br>3320 s (NH),<br>1750 s ($CH_3CO$),<br>1713 s (C=O),<br>1550 s (NH—CS) | 216 (4,11),<br>253 (4,04) | 50,1 | 6,4 | 5,6 | 6,2 | $C_{21}H_{32}N_2O_{10}S$ | 50,0 | 6,4 | 5,6 | 6,4 | 80 |
| V | 54—55,5 | −7,8<br>(1,3; $CHCl_3$) | 3380 s br (NH),<br>1750 s ($CH_3CO$),<br>1715 s (C=O),<br>1550 s (NH—CS) | 216 (4,10),<br>253 (4,05) | — | — | 5,6 | 6,3 | $C_{21}H_{32}N_2O_{10}S$ | — | — | 5,6 | 6,4 | 67 |
| VI | 92—93,5 | 0,0<br>(0,9; $H_2O$) | 3340 s (OH),<br>1707 s (C=O),<br>1550 s (NH—CS) | 213 (4,12),<br>252 (4,07) | 46,3 | 7,3 | 8,6 | 9,5 | $C_{13}H_{24}N_2O_6S$ | 46,4 | 7,2 | 8,3 | 9,5 | 60 |
| VII | 71,5—73 | −22,9<br>(0,7; $H_2O$) | 3340 s (OH),<br>1710 s (C=O),<br>1550 s (NH—CS) | 213 (4,05),<br>252 (4,00) | 46,2 | 7,5 | 8,2 | 9,3 | $C_{13}H_{24}N_2O_6S$ | 46,4 | 7,2 | 8,3 | 9,5 | 77 |

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[a] $[\alpha]^{20}_{366}$ + 159.2 (c 1.1, $CHCl_3$) for IV, and $[\alpha]^{20}_{366}$ + 4.6 (c 0.9, $H_2O$) for VI. [b] In mineral oil. [c] In methanol.

TABLE 2. Parameters of the PMR Spectra of N-Glycosides IV-VII[a]

| Compound | Chemical shifts, δ, ppm (SSCC, Hz) |  |  |  |  |  |  |  |
|---|---|---|---|---|---|---|---|---|
|  | 1'-H ($J_{1',2'}$) | 2'-, 3'-, 4'-H | 5'-, 6'-, 6''-H | $CH_3COO$ | $CH_2$ ($J_{AB}$) |  | $CH_3$—CO | gem-$CH_3$ |
|  |  |  |  |  | $H_A$ | $H_B$ |  |  |
| IVA<br>↑↓ | 6,47 d<br>(7,5) | 5,00—5,50 m | 4,00—4,23 m | 2,10; 2,06; 2,00; 1,95 | 3,28 d | 3,04 d<br>(17) | 2,10 | 1,53; 1,50 |
| IVB |  |  |  |  | 2,39 d | 2,32 d<br>(6) | 1,74 | 1,21; 1,13 |
| VA<br>↑↓ | 6,45 d<br>(7,5) | 4,80—5,50 m | 3,70—4,45 m | 2,05; 2,05; 1,99; 1,99 | 3,26 d | 3,00 d<br>(17) | 2,12 | 1,53; 1,49 |
| VB |  |  |  |  | 2,39 d | 2,31 d<br>(6) | 1,68 | 1,22; 1,12 |
| VI | 5,00 d<br>(9,0) | 3,50—4,00 m |  | — | 3,46 d | 3,34 d<br>(17) | 2,12 | 1,52<br>s br |
| VII | 5,20 d<br>(8,0) | 3,50—4,00 m |  | — | 3,23—3,50[b] |  | 2,16 | 1,56; 1,54 |

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[a] In $CDCl_3$ for IV and V and in $CD_3OD$ for VI and VII. [b] Overlapped with the signals from the solvent.

The IR spectra of N-glycosides IV-VII in the form of suspensions in mineral oil and solutions in $CHCl_3$ contain an intense absorption band at 1710 $cm^{-1}$ of stretching vibrations of the C = O group of the acyclic form of the aglycone. It follows from these data that IV-VII exist primarily in the acyclic $N_1$-glycosyl-$N_3$-(4-methyl-2-oxo-4-pentyl)thiourea form (IV-VIIA) in both the crystalline state and in solutions in $CHCl_3$.

To establish the structure of N-glycosides IV-VII by means of the PMR spectra and to correctly assign the signals of the protons we examined the spectra of model compounds, viz., $N_1$,$N_1$-dimethyl-$N_3$-(4-methyl-2-oxo-4-pentyl)thiourea (VIII), which has a genuine acyclic structure, and 3,4,6,6-tetramethyl-4-hydroxyhexahydropyrimidine-2-thione (IX), which has a cyclic structure in solutions. The PMR spectrum of VIII in $CDCl_3$ contains the following signals: 6.03 (1H, s, NH), 3.30 (2H, s, $CH_2CO$), 3.25 (6H, s, $[CH_3]_2N$); 2.17 (3H, s, $CH_3CO$), and 1.62 ppm (6H, s, $[CH_3]_2C$). Signals at 7.99 (1H, s, NH), 5.87 (1H, s, OH), 3.23 (3H, s, $NCH_3$), 1.91 (2H, s, $CH_2CO$), 1.46 (3H, s, $CH_3CO$), and 1.28 and 1.12 ppm (6H, d, $[CH_3]_2C$) are present in the PMR spectrum of IX in $d_6$-DMSO. A comparison of the parameters of the PMR spectra of model compounds VIII and IX with the spectra of N-glycosides IV and V shows that in $CDCl_3$ solutions tautomeric equilibrium $A \rightleftarrows B$ is shifted markedly to favor tautomer A with an acyclic aglycone structure. Thus signals of the protons of tautomers B with a cyclic aglycone form and the 3-(2',3'4',6'-tetra-O-acetyl-β-D-glycopyranosyl)-4,6,6-trimethyl-4-hydroxyhexahydropyrimidine-2-thione structure (IVB, VB) are present in the PMR spectra of glycosides IV and V along with signals of the protons of tautomers A with an acyclic aglycone structure. Judging from the relative intensities of the signals of the protons of the methyl and methylene groups in the PMR spectra of tautomers A and B, the ratio of the A and B tautomers in V is 8 : 2, as compared with 9 : 1 in IV.

Signals of protons corresponding only to the acyclic tautomeric form are present in the PMR spectra of solutions of deacetylated N-glycosides VI and VII in $CD_3OD$ (Table 2), while signals of the protons of tautomers with a cyclic aglycone structure do not appear in the spectra.

In contrast to VIII and IX, the geminal protons of the $CH_2CO$ groups of the A and B forms of N-glycosides IV and V are nonequivalent and in the PMR spectra give signals in the form of quartets that are characteristic for an AB system with $J_{AB}=17$ Hz for IVA and VA and $J_{AB}=6$ Hz for IVB and VB. The signals of the protons of the $CH_2CO$ group in the PMR spectra of VI also form a quartet with $J_{AB}=17$ Hz for the A form. The protons of the geminal methyl groups of both tautomers of N-glycosides IV and V and the acyclic A tautomers of N-glycosides VI and VII are also nonequivalent. The reason for the nonequivalence of the protons of the geminal methyl and methylene groups of aglycones IV-VII may be the hindered conformation of the tautomers with the acyclic aglycone structure (IV-VIIA) and the conformational stability of the tautomers with a cyclic aglycone structure (IVB and VB) [8] because of the presence of a sugar residue in their molecules.

On the basis of the spin–spin coupling constant (SSCC) $J_{1',2'}=8$ Hz it was concluded that β-glycoside bonds are present in the molecules of all of the investigated N-glycosides.

As an alternative method for the synthesis of N-glycosides VI and VII we studied the condensation of β-D-glucopyranosylamine [9] with 4-isothiocyanato-4-methyl-2-pentanone (X). We found that deamination of the glucosylamine occurs when hydroxy-containing solvents (water and aqueous alcohol solutions) are used; isothiocyanato ketone X acts as a catalyst and an acceptor of the liberated ammonia. D-Glucose and 4,6,6-trimethyl-4-hydroxyhexahydropyrimidine-2-thione (XI) [10] are formed as a result of the reaction. Brief heating of the glucosylamine with β-isothiocyanato ketone X in aprotic solvents (dimethylformamide, dimethyl sulfoxide, and pyridine) leads to the formation of diglucosylamine [11] and pyrimidinethione XI instead of the expected N-glycoside VI.

## EXPERIMENTAL

The specific rotations were determined with a Perkin-Elmer 241 MC polarimeter. The IR spectra of suspensions of the compounds in mineral oil and solutions in $CHCl_3$ 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 a Bruker HX-90E spectrometer with hexamethyldisiloxane as the internal standard. Thin-layer chromatography (TLC) was carried out on Silufol UV-254 plates in the following systems: 1) $CHCl_3$–ethanol (14 : 1); 2) $CHCl_3$–ethanol (2 : 3). Column chromatography was carried out on L40/100μ silica gel (Czechoslovakia) in the following systems: 3) benzene–ethyl acetate (2 : 1); 4) $CHCl_3$–ethanol (3 : 1). The properties and yields of the synthesized compounds are presented in Table 1.

$N_1$-(2',3',4',6'-Tetra-O-acetyl-β-D-glucopyranosyl)-$N_3$-(4-methyl-2-oxo-4-pentyl)thiourea (V). A 2-ml sample of a solution of 0.16 g (1.4 mmole) of III in benzene was added with stirring to a cooled (to 10°C) solution of 0.54 g (1.4 mmole) of II in 3 ml of dry benzene, and the solution was allowed to stand at 20°C for 1 h, after which it was chromatographed with a 2.6 by 12 cm column in system 3. After removal of the solvent, V was reprecipitated twice from methanol by the addition of anhydrous pentane to give 0.47 g of V with $R_f$ 0.34 (1).

$N_1$-(2',3',4',6'-Tetra-O-acetyl-β-D-galactopyranosyl)-$N_3$-(4-methyl-2-oxo-4-pentyl)thiourea (IV). A solution of 0.09 g (0.78 mmole) of III in benzene was added with stirring and cooling to a solution of 0.30 g (0.77 mmole) of I in 2 ml of dry benzene. After 30 min, the precipitate was removed by filtration, recrystallized from benzene, and reprecipitated twice from methanol by the addition of pentane to give 0.31 g of IV with $R_f$ 0.33 (1).

$N_1$-(β-D-Glucopyranosyl)-$N_3$-(4-methyl-2-oxo-4-pentyl)thiourea (VII). A mixture obtained by the reaction of benzene solutions of 3.7 g (9.5 mmole) of II and 1.24 g (9.52 mmole) of III was evaporated to dryness, the residue was dissolved in 20 ml of anhydrous methanol, and the solution was again evaporated to dryness. The residue was dissolved in 20 ml of anhydrous methanol, 4 ml of a solution of sodium methoxide obtained by dissolving 50 mg of sodium in 10 ml of alcohol was added, and the mixture was maintained at 20°C for 1 h. The solvent was removed, and the residue was chromatographed with a 2.8 by 28 cm column in system 4. The solvent was removed, and the reaction product was reprecipitated twice from dry acetone by the addition of ether to give 2.47 g of VII with $R_f$ 0.52 (2).

Compound VI with $R_f$ 0.41 (2) was similarly obtained.

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